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INTRODUCTION

TO

ORGANIC RESEARCH

BY

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PREFACE

CHEMISTRY, as a science, is very young but the study of chemical reactions and the accumulation of chemical facts have occupied many of the best minds from the earliest times. Tubal-Cain was a metallurgist of note; he was also a research chemist in so far as he sought to improve his methods of producing iron. In his day progress was painfully slow on account of the lack of guiding theories and the absence of systematic coöperative endeavor, but the sum total of the knowledge of chemical processes thus gained was enormous.

With a growing understanding of natural laws and with the introduction of scientific methods, discovery has gone forward with ever-increasing speed so that more progress has been made in the last century than in preceding ages. The world is beginning to realize that its material progress depends on research. The population of the earth is increasing and the wants of the individual are multiplying. With but small additions to the farming area possible and with the dwindling of coal, oil and mineral reserves, the demand on research is becoming more insistent. Research as a vocation, or even as an avocation, offers alluring joys to the individual as well as benefits to the race. This book is put forth with the hope of assisting those beginning research and of aiding some not now engaged in it to take it up. In its preparation free use has been made of the publications of many and not a few distinguished chemists have honored it with specially prepared contributions. Its incompleteness and inadequacy are realized by the Author who will welcome suggestions, additions or corrections.

Blessed are the researchers for they shall see Truth.

E. E. R.

JOHNS HOPKINS UNIVERSITY,
BALTIMORE, MD.
August, 1924.

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INTRODUCTION TO ORGANIC RESEARCH

CHAPTER I

INTRODUCTION

Research and the Research Spirit. In these days of scientific and industrial progress, "research" is a word to conjure with. The word has an impressive sound, and rightly too, since by research great discoveries have been made, by research great inventions have been perfected, by research new processes have been devised, and by research great chemical plants have come into being. We think of indigo, of alizarine, of the aniline dyes, of the extraction of aluminum, of tungsten lamps, of the synthesis of sugars, of salvarsan and of dozens of other epoch-making discoveries. If "one who causes two blades of grass to grow where one grew before" is a benefactor of mankind, surely he who enables two chemical plants to flourish where formerly there was only one deserves well the gratitude of the race. We can not honor too highly those who lead out into new lines of thought and investigation. The real dates of history are those of scientific discoveries, not the accession of kings or the outbreak of revolutions. The discovery of the extraction of iron from the ore meant more for the human race than the founding of Rome and the invention of Bessemer steel was a greater advance than the American Revolution. The advent of railroads, steamships, steel buildings, none of which would be possible without cheap and uniform steel, has altered the everyday life of our people more than a change of government could possibly do. The fruits of research are greater than the fruits of war. Pasteur was right when he said: "In our century, science is the soul of the prosperity of nations and the living source of all progress. Undoubtedly, the tiring daily discussions of politics seem to be our guide. Empty appearances! — What really lead us forward are a few scientific discoveries and their applications."

But what is research? the achievement of the super-man? the sport of kings? the privilege of the exalted few? It is all of these and more:

super-men may exhaust themselves in its pursuit, a king might pawn his crown to taste its joys, and the highest of earth may be made rich by its rewards, but it is like faith and love, which can not be exhausted by the greatest yet may be partaken of by the humblest, provided they are pure in heart. There are no limitations as to age, wealth or social position, yet the restrictions are severe enough to keep out the unworthy.

What then is research? It is not something portentous, something to be spoken of with bated breath as if pertaining to a higher sphere, but as Professor Remsen says:[1]

" There is nothing mysterious about research. Every human being, in fact every animal, is by nature engaged in research, that is to say, trying to find out something about its environment. Perhaps the word research is a rather large one to connote these elementary activities, but it is nevertheless true that they are in principle of the same kind as those which are commonly understood when the word is used. There have always been researchers, and the knowledge we have of the universe is due to them. Notwithstanding all that has been learned in the ages past, the problems that have been solved are almost insignificant compared with those that remain to be solved. Every important discovery, or perhaps it is safe to say every discovery, suggests new problems."

Closer examination shows that " research " is simply re-search, the ordinary word " search " with " re " prefixed, which means that if we search and do not find we must re-search, — go back and search till we do find. There is no limit to the " re " as to time or trouble, the requirement being that the object of the search be located. This " re " means not simply again but again and again, not " until seven times: but until seventy times seven." Looking for a needle in a haystack has long been the popular idea of futility and it is unlikely that a superficial search would reveal the hiding place of the elusive needle but *research* would examine every several straw, splitting it open if need be, and would inevitably locate the needle.

The quest may be the discovery of the chemistry of life or the determination of the sixth decimal place in the density of alcohol and elaborate or simple resources may be required but there must be thoroughness in either case and nothing must be left undone that might contribute to the certainty and accuracy of the result.

Research is an elastic term and may be applied to the greatest efforts of the mightiest intellects and also to the slow painful motions

[1] Written for this book by President Emeritus Ira Remsen.

of small minds. Research may be comprehensive and colossal or it may be minute and even inconsequential.

Research is finding out something, adding something to the known. It is the reality and not the size of the addition that matters: a small advance in knowledge may be just as real as a large one and a number of small gains make up progress. Columbus discovered the western continents but it has required the labors of thousands of explorers, on a lesser scale, to chart the inlets and coves along their shores, and to explore the mountains and plains of their vast inland territory. It is all the same work and the one explorer is as real a discoverer as the other. No one realizes as well as the chemist that a properly chosen sample, however small, may truly represent the composition of an entire ship load of thousands of tons. The composition of the water of the seven seas has been determined by the analysis and synthesis of a few grams of water. A gram, or even a milligram, of gold is as truly gold as all the gold in the crown jewels of the kingdoms of the world. Gold, if it be gold at all, is real gold: it is so with research. The smallest fact ascertained, provided it is new and is positively proved, is a real advance in knowledge, just as real as the greatest discovery. We do not speak of some gold as valuable and other gold as not. All gold is valuable. One nugget may be larger than another and hence bring more at the mint but gold is gold, and whether it be nuggets panned in the Klondike or microscopic particles extracted by the cyanide mills of Africa, every grain of the shining dust adds that much to the wealth of the world. The determination of the melting point of a single new substance adds to the sum of human knowledge. This is research and is valuable. A number of such facts would be of greater, though not more real value. The door is open and whosoever will may enter the sacred company of discoverers and stand with Columbus, Newton, Lavoisier, Berzelius, Liebig, Perkin and their like, as those who advance into the unknown and enlarge human knowledge, the benefactors of mankind.

In thus admitting to the exalted caste of discoverers those who offer small contributions as freely as those who come laden with rich treasures, we dare not make any discount on the quality. Brass and pyrites, however they may glitter, can not pass the assayer; only twenty-four karat gold can be accepted. To be an advance in human knowledge the alleged discovery must be new and it must be true. To be a discovery it must be an actual advance on what was previously known by any mortal on that subject and to be of any worth it must be proved beyond any peradventure of a doubt. A piece of work to be of value must be so done and so recorded that it will never

have to be done over. An accurate observation is true till the end of time. The interpretation of a fact may change, as theories come and go, but the fact itself, once established, is true for all time. There is nothing as unsatisfactory as climbing a mountain through loose cinders or over rolling stones where one slips back at every step. One would fain mount on solid rock where one's tread is sure and each step upward is a permanent advance. A vast amount of chemical work goes for naught because it is not quite good enough for publication and permanent record and has to be done over every time any one needs the information.

One purpose of this book is to encourage those who can not do great things to do small ones but to do them with a spirit and in a manner that will make them great. We must insist on the same high standard for small contributions to science as for large. The same criterions of newness, of truth, and of accuracy must be applied to the one as to the other. Good technique, keen analysis and sound reasoning may be shown in a small task as well as in a large one. He who is limited in opportunities has this encouragement, that although he can not undertake as large a problem as some one else, he can do what he does do just as well.

There are comparatively few so situated as to be able to carry out extensive investigations continuously over long periods of time, but there are many who can find some time and get together sufficient apparatus for the study of some small point or the preparation of some compound. There are many who stand back for years waiting for the opportunity and facilities to undertake some big problem. One should be ambitious to attack the biggest possible problem but meantime many small ones may be solved. Even a large problem may be handled on the installment plan. An ex-president may make a trip to Africa with a whole regiment of hunters, guides, naturalists, photographers, writers, etc., and bring back enough big game to stock a museum while an humbler man may add one butterfly or one snail at a time and at the end of his life have a world-famous collection. Small problems well solved are the best preparation for larger ones. "He that is faithful in little is faithful also in much." The Scotch say "many mickles make a muckle" which is certainly true in finance and in science also, provided the "mickles" are properly related. A house is builded by adding one small brick at a time but the bricks must be accurately laid and placed according to a well drawn plan if the result is to be a worthy structure.

Of course there is no desire to discourage the study of great problems but climbing small hills is good practice for those who would

scale the Matterhorn and in ascending the great mountain the best way is to make sure of one step at a time. The better equipment, mental and material, one has, the better work one can do and the larger problem one can undertake. Without training one can accomplish little of value but many problems can be handled with meagre material equipment.

It is doubtful if any man ever had a keener eye for research ability in others or did more to develop it than Daniel Coit Gilman. Of the research spirit he wrote:[2]

" It is perpetually active. It is the search for the truth — questioning, doubting, verifying, sifting, testing, proving, that which has been handed down; observing, weighing, measuring, comparing the phenomena of Nature, open and recondite. In such researches, a degree of accuracy is nowadays reached which was impossible before the lens, the balance, and the metre, those marvelous instruments of precision, had attained their modern perfection.

" With the growth of the scientific spirit grows the love of truth, and with the love of truth in the abstract comes the love of accuracy in the concrete."

According to Dr. Nichols there must be the will to research.[3]

" True research must be intentional and intensive. We must really seek if we would find. We must really knock at the doors of the secret chambers of knowledge, if they are to be opened to us. We must have imagination, it is true, but we must have more than that. There must be the foundation of sound education, and the ability to extend it to embrace new and unexpected knowledge, and apply this in turn as we progress upwards.

" Scientific discovery is really not a haphazard matter. The art of making it can be cultivated and definite rules of research can be laid down."

According to Dr. Whitney the limitations are internal rather than external.[4]

" It is important to realize that the need, facilities and *possibilities* of research are all about us, retarded only by the inertia that is in us."

Qualities of Research

Newness. According to the accepted use of the word, research is the process of discovering something new. In science the line is drawn

[2] D. C. Gilman, Launching a University, 1906, pp. 147–150.
[3] W. H. Nichols, *Jour. Ind. Chem.*, 11, 918 and 919 (1919).
[4] W. R. Whitney, *Jour. Ind. Eng. Chem.*, 8, 533 (1916).

sharply and the object discovered must not have been known before. A mine may be found by a number of people but it belongs to the one who locates it first, so in chemistry. Ethyl benzoate has been prepared by hundreds of chemists but it was discovered by only one, the first one who made and described it. The proper description of it is as essential as the staking out and recording of the mining claim. A mining claim is invalidated if a prior discovery can be shown and it is considered one of the worst things that can happen to a chemist to find that his discoveries had been anticipated by others. One who publishes as new something which is already in the literature has made a scientific *faux pas* and incurs the ridicule of his colleagues.

While newness is an absolute quality in the sense that a thing is either new or not new, yet the newness may be limited in the extent of its application. A hatchet may have a new handle in which case the newness applies only to the handle and even then the new handle may have been fashioned from a piece of wood centuries old — the newness being restricted to its form and present relation to the hatchet. The nine hundred and thirtieth person who prepares ethyl benzoate may find out something new about it, may determine its boiling point, or some other property more accurately than had been done before. or may devise some easier or more economical way of making it, in either case adding to the sum of human knowledge and making a discovery.

There is no substance known about which something new may not yet be found out. New investigations are constantly appearing on the best known substances such as water and alcohol. In the index of Chemical Abstracts for 1920 there are 148 references to articles containing something new about ethyl alcohol. Many of these are on commercial sources and applications, and ten are on the determination of alcohol in various mixtures but there are others that add to our information as to its properties, such as density corrections, dielectric constant, oxidation of, physiological effect of, vapor tension, etc. If so much can yet be done on ethyl alcohol which has been studied, at least since the time of Noah, there is little difficulty in finding out something new about thousands of other substances which have been only superficially examined.

When planning a research the first thing to be ascertained is just what has been done so as to make sure that what is to be undertaken is really new and a definite advance on what is already known. The density of ethyl alcohol has been determined with great accuracy and with most carefully prepared materials. It would not be worth while to redetermine the density of ethyl alcohol unless one had discovered

some new means for purifying it or some more accurate method of finding the density.

Accuracy, reliability and truth. These qualities may be grouped together, as they are closely related; in fact one need not try to differentiate between them as no one of them is of any value without the other two.

Accuracy involves close observation and minute attention to all essential details. In the determination of physical constants, accuracy is required not only in making the observations themselves but also in the instruments and apparatus employed. One might determine the density of a liquid to the fifth decimal place but if the weights used are faulty, or the regulation of the thermostat unreliable, or the purity of the liquid questionable, the result would be worthless. In a building, strength must extend from the foundation up and the foundation must rest on bed rock: so accuracy must extend from the ground up. False ideas of accuracy are often conveyed by calculating to four or five places of decimals, results which are doubtful in the third or even in the second. It is much easier to read a thermometer to 0.01° than it is to be sure that it is correct to 0.1° and it is obviously silly to record the hundredths unless one is certain of the tenths.

The standard of accuracy should be determined by the circumstances and the class of the investigation. Good judgment and common sense must decide the degree of accuracy that is needed in each part of an experiment. The only excuse for doing an atomic weight determination is the possibility of excelling previous work in accuracy. In redetermining the physical constants of organic compounds the same statement holds. In determining the constants of a new compound the standards accepted by the best investigators in that field should be regarded. Thus densities should be determined to four decimals. It is usually sufficient to state melting and boiling points to the nearest degree.

Accuracy may be secured by practice in the manipulations and by testing all instruments employed. Before making a determination on a new compound, one should test out the apparatus and methods, and also one's skill on a compound of assured purity whose constants are accurately known. By calibrating one's instruments in this way, accurate results may be obtained with imperfect instruments. Thus a thermometer may read 98.4° when it should read 100°, yet accurate temperatures may be found with it by adding the proper corrections to the readings. It is a nuisance to have to use corrections all the time, but accuracy may be attained, provided the corrections are known and applied. One should repeat the determinations on known

compounds till reproducibility is attained and the results agree with the best figures in the literature. Only then may results with new compounds be trusted.

It is common to speak of theories as evanescent and to regard facts as eternal, but how long the facts will endure depends on their accuracy, since, as Prins[5] has pointed out, future refinements in apparatus or methods may wipe out the facts as we now know them. A more accurate determination supersedes a less, just as we throw away old shoes when we buy new ones. If we wish long life for our data we must take the utmost care that they are so accurate that it will be difficult to improve upon them.

Reliability may be regarded as an addition compound of accuracy and truth for if either of these is lacking the result is untrustworthy, but it goes somewhat further and includes some other qualities. Measurements may be accurately and conscientiously made, and yet lead to unreliable results if some source of error has been overlooked. An unsuspected impurity, perhaps an unknown isomer, may be present and lead to erroneous results.

There are so many organic compounds to be made that we can seldom afford the time to prepare any one compound in more than one way, and for that reason many of the determinations of properties are in error. A compound nearly always retains more or less impurities derived from the materials from which it is produced, or from by-products in the reactions involved. If it is a solid and is recrystallized to constant melting point, we assume that it is pure but we may still have a mixture. If the same substance is prepared in an entirely different way from other materials and by different reactions, it will also carry impurities, but they will probably be different. Now if the two lots are purified separately till their properties are identical, we will be far more sure of them.

A good example of this is thio-carbanilide,[6] one of the stand-bys in our courses in organic preparations. When it came to be necessary to manufacture this substance on the large scale, a process avoiding the use of alcohol had to be devised. The crude product from the new process had a higher melting point than the most carefully purified made by the classical method. When produced in alcohol solution, it contained phenylurethane which resulted from a side reaction and which could not be eliminated.

It is valuable to read atomic weight determinations to see how one source of error after another has been discovered and eliminated. A

[5] *Chem. Weekbl.* 15, 1381 (1918).

[6] Information from the laboratory of Arthur D. Little, Inc.

vast number of painstaking and accurate measurements were made of esterification velocities in absolute alcohol by men of unquestioned honesty before it was realized that a trace of water, even as little as several hundredths of one percent, influences the results so profoundly that all measurements made with so called "absolute" alcohol were worthless unless the utmost precautions had been taken to eliminate traces of water.

Reliability is impaired by omission as well as by commission. We must do our utmost to make sure that we have not been deceived or tricked by appearances.

A student found a considerable difference in the velocities of the same reaction between the same chemicals in two similar flasks, the one in an electric field and the other not. He was just about to make an important discovery on the effect of an electric field on the velocity of chemical reactions when he found that the metal in the coil was influencing the temperature of the reaction mixture and that this was responsible for the change in reaction velocity on which the current itself had no influence.

Reliability requires not only that experiments be accurately carried out and truthfully reported but that they be properly designed for the purpose in hand. All conclusions must be carefully tested and checked up.

The last of these three, and the greatest, is truth. In the World War camouflage, which has figured in every war since the beginning, even in fights between animals and insects, was developed to a science as well as an art; in horse trading it is not customary to be brutally frank in telling all of the horse's failings, but in science the most absolute and unsparing honesty is a prime requisite.

At first sight it would seem an easy matter to be truthful and frank about matters which do not involve money or personal advantage, but intellectual honesty and scientific fairness are difficult to attain. Sometimes the deviation from them is apparently unconscious and due to lack of ability to make the fine distinctions required. Material property is objective and one can usually ascertain when he has taken another's overcoat, but not so with ideas. It is easy for one to take part in a conversation and come away with the firm belief that one had been the first to suggest a certain idea and had a right to its exploitation. Two men frequently have the same idea in somewhat different forms or stages of development. It is frequently difficult to say whether the fundamental idea is the chief thing and the rest only a natural development or whether the special way of carrying out an obvious reaction is the discovery. We encounter in patents

and also in pure science many difficult distinctions between "mine and thine."

In the presentation of one's work it is easy to depreciate the progress made by others on the problem before one took hold of it and it is as difficult for an enthusiastic investigator not to paint his own results in bright colors as it is for young parents not to feel the superiority of their first son over all previous accessions to the human race.

Of course the moral distinction between an enthusiastic over-statement and an intentional misrepresentation is obvious and important, but in science we must be on our guard against both.

Temptations. There are many insidious temptations in scientific work. In making a series of observations, particularly before experience has been acquired, there will be some low and some high and perhaps a few that are a good way off. It is frequently hard for the young chemist to see why he cannot leave out the "bad" results and report only the "good" ones. We usually have more or less well defined notions of what the results "ought" to be and naturally trust the observations which fall in line with our ideas. It hurts to report "bad" results. The only square thing to do is to consider all observations impartially and report them frankly. It is allowable to repeat the whole series and to keep on doing this till, by improved technique, concordant results predominate. It is not only allowable but is right to throw out any result, in the obtaining of which we know of an error, but the temptation is to line up the figures and then beat around for excuses for throwing out the "bad" ones, even when we can recall more serious mistakes in the history of some of the "good" ones.

It sometimes happens that subsequent experiments prove that the out-of-line results, which we at first consider errors, are the correct ones after all, in which case we should be quick to give up our pet theories and make new ones to accord with the facts. It is far better for us to be the first to detect flaws in our theories and to abandon or modify them voluntarily than to be driven from our position by the bombardment of an enemy.

Louis Agassiz said "The temptation to impose one's own ideas upon Nature, to explain her mysteries by brilliant theories rather than by patient study of the facts as we find them, still leads us astray."

When we have a theory we are prone to choose experiments which are designed to prove our theory and omit those which might turn out the other way. Rigid honesty demands that we be just as keen to devise experiments which will put our pet theory on the rack. If it

is sound it will survive the severest ordeal and come out all the stronger, if it is damaged, well and good.

It is morally and scientifically dangerous to become a partizan of a theory. When a scientist becomes a partizan he is in danger of losing his standing as a scientist. When the judge takes sides in a case he is no longer fit to be judge. The judge must see that every credible witness has a fair show in court. All readers of recent chemical literature can recall certain chemists who having accepted the ion theory, have become ionic champions and have undertaken to prove that all reactions of whatever kind are ionic and others, who, in their opposition to ions, have become as rabid as the anti-vivisectionists. Both sides are wrong in taking sides. It is far better to go out to ascertain the facts without prejudice.

It has happened more than once, and almost any chemist of experience can supply names and dates, that a professor has outlined experiments to a student and has indicated how he expected the results to come out and the student has brought in reports exactly as expected, which were subsequently found to have been obtained by the " paper and pencil method," sometimes even without going through the tedious operations of preparing substances and setting up apparatus. In fortunate cases some slip or some over-exact analysis has aroused suspicion in time and the results have been checked up and the crookedness located before the results were printed, while in other cases a humiliating retraction has to be made of published work. The possibility of such a misfortune is a nightmare to those who direct research.

In rare cases the director of the investigation has been to blame by being so set in his ideas as to refuse to accept any results at variance with them. In some such cases the student, finding that only such and such results will be accepted, has turned in only such and gotten along famously.

It is deep in human nature to want to make the best appearance possible. There is indeed little hope for one who does not wish to appear well before his fellows, but this desire may lead to concealment or pretense. The chemist is tempted to make his preparation of materials appear to be more thorough than it actually was, to mention precautions in the experiments which were not actually taken or which were not always adhered to, or to describe a more perfect form of apparatus than was in reality employed, thus making his work appear better than it actually was. Suppressing results that vary from the mean is another way of doing the same thing. Suppose the following ratios are obtained in titrating an acid against a base:

1.021, 1.022, 1.020, 1.025, 1.021, 1.022, 1.017. Omitting the 4th and last will not change the average but will give the impression of much greater accuracy to the series, as 2 parts in a thousand is considered good in many cases while from 1.017 to 1.025 is 0.008, nearly 1%, and is bad.

Research Ethics. The paramount importance of truth and honesty in obtaining and reporting one's results has been emphasized above, but we are all parts of a complex social system and consideration must be given to squaring our relationships with others, particularly with a brother chemist. To truth in one's self must be added fairness and consideration in dealing with others. The young scientist must start out with the determination to play the game fair, whether he wins or loses.

" Very often ethical conduct is nothing more or less than ordinary good sportsmanship — but at other times complications arise which make it more difficult to follow the ethical path.[7]

" Some of the principles and ideals that should be adhered to by the research chemist *in his daily routine* may be summarized as follows:

(*a*) He must strive at all times to seek the truth and his honesty must never be open to question. Attempts to defraud are not part of any research program.

(*b*) He must give due credit to his co-workers, his colleagues and his friends for courtesies extended to him, and for suggestions that he has received at their hands. He should be punctilious also in giving proper acknowledgment to previous investigators, who have blazed the trail that he is seeking to follow. This is more than courtesy; it is justice.

(*c*) He must free himself from pettiness. If other chemists have overlooked his work and have given him scant recognition, he should recall that they are human and not infallible, that their acts are probably due to ignorance rather than to malice. As a result of such lack of recognition, he should never permit himself to become embittered or cynical, nor should he leave his own constructive work to plunge into useless and unprofitable wranglings and polemics. He must also be able to take in good part just and constructive criticism, without manifesting hypersensitiveness or bitterness.

(*d*) He must always stand ready to help other workers in his field. Since the research chemist's true objective is to further not his own progress, but the progress of his science, he should prove a stimulus and an aid to other investigators. Coöperation, suggestions regarding

[7] Written for this book by Professor Louis E. Wise, N. Y. School of Forestry.

chemical literature, and constructive criticism are all included in such a program. Help should be given unstintingly, frankly, and without reservation. Human relationship is an important factor in modern scientific research. Very few of us today can play the rôle of a Henry Cavendish, whose chief aim in life (besides his monumental researches) was to avoid the rest of the world. Men who live in such a rarefied intellectual atmosphere that they are kept apart from their fellows are seldom contributing their maximum to scientific progress.

" Many of the principles set forth above are self-evident; none are original and yet some of them are overlooked by many scientists whose output and influence would be remarkably increased, if they recognized them and put them into practice. Fortunately in the truly *great* man of science, ethical conduct is second nature.

" Two actual instances may be cited to illustrate some of the points mentioned above. The first is very obviously an example of unethical behavior. The second shows a very different picture.

(1) An investigator, *A*, submitted a manuscript to a colleague, *B*, interested in the same field of organic chemistry. *A* asked for a frank detailed criticism of his work, which *B* gave to the best of his ability and without reservation. In the letter, conveying these criticisms to *A*, *B* stated that there was still an important branch of the work which required reinvestigation and extension and which he, *B*, hoped to undertake at the earliest opportunity (presumably the following summer). *B* went on to show how the results of such a study would have a very real bearing on the conclusions in *A*'s article. *A* acknowledged *B*'s criticism but remained silent on *B*'s proposed work. A few months later, however, at a scientific meeting *B* was surprised by a preliminary report by *A* on the very problem previously outlined in *B*'s letter.

" The most charitable interpretation of the episode is that *A* thought of the same general problem and had *begun* the work before receiving *B*'s letter. Under the circumstances it behooved *A* to notify *B* without delay that the work was already in progress in *A*'s laboratory. Less charitable interpretation, however, puts *A* in a far uglier position. *B*'s letter may have actually *suggested* to *A* the importance of the reinvestigation, in which case *A* deliberately appropriated *B*'s idea. Under any circumstances *A*'s methods were entirely unethical and deserve the fullest condemnation.

" The other instance presents a striking contrast to the foregoing one. Two investigators *C* and *D* were engaged in a piece of research in a government laboratory. Quite by accident they learned that *E* and *F*, two university investigators, while working on a broader problem had covered a part of their own field. This accidental informa-

tion led to a friendly correspondence which indicated that the work of *E* and *F* was somewhat more advanced than that of *C* and *D*. The latter investigators, therefore, deliberately withheld publication of their results until *E* and *F* could publish a progress report of their own work which gave them priority in this field. Subsequently *C* and *D* published an article confirming *E* and *F*'s results and extending them.

"The conduct of *C* and *D* in the matter requires little comment. They allowed the results of their colleagues to be published before their own, since they recognized not only a just claim to priority, but because they felt that *E* and *F* had a better grasp of this part of the subject than they had themselves. They also knew that the chemical literature would gain by a presentation of the results at the hands of *E* and *F*, rather than at their own.

"In case of doubt, when an ethical question arises, the investigator must remember that he must resort to *right, not expedient acts.* He need only take a *detached* view of the situation and ask himself — "What course of action will be the *right* one, *irrespective of its effect on me, personally?*" If he is able to put his answer into practice, he can face the world with a mind at rest."

Hard Work. The reason that get-rich-quick schemes catch so many is that so many of us are looking for easy money. If the vendors of gold mine and oil stock — the writer has bought both — did not come after us we would go after them, as their wares appeal to the human race. It is an almost universal belief, except in those who have tried it — that somewhere there is a machine in which we can drop pennies and dollars will fall out, that sometime in our lives we can invest a few dollars in a sure thing proposition and draw thousands or millions in dividends.

In young chemists there is the lurking hope that a few offhand experiments will bring fame and fortune, but the sooner that idea is dissipated the better for all concerned. The only sure road to success in chemistry is the long road and there are many rough and sandy stretches in it and all the grades are upgrades. Sometimes there seems to be no bottom to the sand and no end to the hills. The chemist must count on hard work and then more work. Investigation is slow and often tedious but results come in the end and success that is won is a thousand times sweeter than that which just happens.

Much quantitative work is involved in investigation and quantitative work is essentially slow. So many are tempted to slight or abridge the quantitative part: it takes so long to calibrate weights, pipettes, burettes and pycnometers. It requires so much trouble and time to make sure, while it is so easy and quick to take things for

granted. A vast deal of moral courage is necessary to hold one's self to the road, to plod right straight through.

In upper South Carolina, there is a stream called Hard Labor Creek because, on one of its sudden rises, it swept away the rails which had cost the hard labor of two brothers for months to split. As a boy the writer often crossed that creek, as a man he has many times felt that he was standing on its brink as he has seen the fruits of his hard labor lost, not indeed in its turbid waters but by the breaking of a flask or the explosion of a sealed tube. It is no rare experience to the chemist to see materials, which it has cost months of labor to prepare, lost or ruined in a moment by an accident to his apparatus, and to the injury of the loss is frequently added the insult of having to spend the rest of the day cleaning up the resulting mess. No matter what precautions are taken, disheartening accidents come to all chemists.

Those who love hard work and love it all the better because it is hard, those who try and fail, and keep on trying, those who can suffer the loss of months of hard labor and start all over again, those who can not be discouraged no matter what happens, are invited to undertake research.

Originality. This is the *sine qua non* of research; unless we do something different from what has been done, it is not research, and the more original the better. This deters many who doubt their originality from undertaking investigation but that is unfortunate. It is not that they overestimate the originality required but that they underestimate the amount they have. Those who study finger prints tell us that no two of us human beings have identical markings on our fingers. The convolutions of our brains are far more complicated than the whorls on our dactyl epidermis. Our varied experience, training and environment serve still further to differentiate us. If our fingers are individual and original, our minds certainly must be.

Being different from others is originality and we are all different, so all have originality. The real difficulty is that we do not recognize our originality, capitalize it, and use it. When we encase our fingers in the same style gloves they all look alike and leave no identifying clues behind, as the crooks well know; they lose their individuality and the originality of their whorl patterns. In society we cloak our individuality in conventional phrases till most of us forget that we have any. The gloves and the conventions are good in their way and serve well in society but neither are to be adhered to in research. There it is proper to turn oneself loose, to look at things in one's own way, to work as one works best on what one can do best, to

trust oneself, to draw upon oneself to the utmost. It is not that we have not enough originality. It is more often that we do not trust ourselves and use what we have. When we imitate, we are lost; when we strike out for ourselves and originate, we win.

Imagination. Some place poets and scientists far apart, crediting the poet with a wonderful imagination and the scientist with none at all. Of the two, the poet can get along with less imagination, or at least with a less definite one. The architect builds his cathedral first in his imagination and must see the bridge spanning the river before the blue prints are made. Chemists must see things that are doubly invisible, for cathedrals and bridges are constructed of stone and girders that we can see and the structures are visible to anyone after they materialize while the molecules with which the chemist conjures are invisible structures built of invisible materials and are just as invisible after they are realized as before. The chemist requires a super-imagination. Dalton owed his atomic theory to a vivid and materialistic imagination that insisted in seeing atoms singly and in pairs, trios and quartets, combining with each other and changing places. While Kekulé "nodded, nearly napping" he visioned the carbon atoms linked in chains till one of these turned serpent, swallowed his tail and rolled off as a ring. This dream did more for the science of chemistry than the labor of scores of men.

The imagination can be used to great advantage in materializing the properties of substances so that we may see the relationships between them to the end that our mathematical calculations represent realities and are not simply juggling with symbols.

CHAPTER II

RESEARCHERS

Classes, Opportunities and Limitations

Researchers may be classified in several ways; we may divide them horizontally according to rank, originality and leadership or vertically according to the environment in which they work, whether in universities, research institutions, or in industries.

Dr. Alsberg divides them into three groups:[1]

" The first are the scouts of science who wander out into the field of the unknown and discover new territory to conquer. They are usually very original workers and often solitary. They are to be found, as a rule, in the universities and to some extent in research foundations, and occasionally they have no official connections. Now and then they are amateurs, and of this last group, Charles Darwin is of course the greatest example. However, they are likely to appear anywhere. They cannot be manufactured or produced. The country that wishes to develop them can only do so by developing a large body of general research workers on the chance that, according to the law of averages, a large body of research workers is more liable to contain a few of these scouts than a small body.

" The second group consists of the vanguard that follows in the steps of the scouts and conquers and consolidates the territory discovered by them. This group consists of the able, reliable workers to be found wherever scientific work is done, except that they are scarcer in industries than in universities, government research bureaus, or research foundations. They should not be solitary workers but men who are capable of team play, capable of conquering rapidly the new territory discovered by the scout, because they are capable of directing a large group of routine workers.

" The third group consists of the average and routine workers who are either directed by the second group or who, if they are working more or less independently, must be content with developing the minutia of science. It is exceedingly important that research workers

[1] Written for this book by Dr. C. L. Alsberg, Food Research Institute, Stanford University.

should know themselves so that they may fit themselves into that group of workers for which their native ability and training is adequate. It is often a sad spectacle to see men of average or routine ability wasting their life in attacking fundamental problems when they might perform useful services if they realized their limitations and were more modest in the problems that they undertook."

The qualifications of investigators are well presented by Dr. Bacon [2]

"It is particularly adverse to progress to regard able investigators as abnormal men; for successful research demands neither any peculiar conformity nor any peculiar deformity of mind, but it requires, rather, peculiar normality and unusual industry and patience. It is little less inimical to expect productive work from those who are absorbingly preoccupied with other affairs than research; for fruitful scientific inquiry entails, in general, prolonged and arduous, if not exhausting, labor, for which all of the researcher's time is none too much. This is the experience of the Carnegie Institution and all other research organizations. It is only to be expected, therefore, that those most likely to produce important results in research are those who have qualified for the responsibilities thereof by the completion and publication of several worthy investigations, and who are at the same time able to devote the bulk of their energies thereto. The productive researchers in our universities are those who are devoting their whole time, or practically their whole time, to investigatory work.

"On account of the extraordinary importance of new ideas, particular emphasis should always be laid upon finding and supporting brilliant researchers. Such individuals can best be found in the universities. The function of the university is to work with the beneficent idea of increasing the sum of human knowledge. and among its most valuable products are those who will work for the exercise of the investigative instinct and the pleasure of overcoming difficulties.

"Research men frequently possess adequate training and scientific acumen, but fail in their ability to use it. There is no question that the element most noticeably lacking in the modern graduate is resourcefulness. A qualified research chemist who possesses initiative is usually a creator; but owing to the neglect of existing difficulties in chemical pedagogy, the present-day graduates of our schools of chemistry are too often deficient in inspiration, ingenuity and insight." What is so uncommon as "common sense" and what can compare with it for general utility?

[2] Chairman of subcommittee on research A. A. A. S. *Science*, **45**, 35 and 36 (1917).

"The[3] general mental qualification necessary for scientific advancement is that which is usually denominated 'common sense,' though, added to this, imagination, induction, and trained logic, either of common language or mathematics, are important adjuncts. Nor are the objects of scientific culture difficult of attainment. It has been truly said that the 'seeds of great discoveries are constantly floating around us, but they only take root in minds well prepared to receive them.'"

University Laboratories. We turn now to consider the special opportunities and limitations of the various classes to which we must look for recruits for our research army and call first at the university laboratory.

It is hard to say much that is general and also true about university professors as a class since they do not belong to any one class, some of them have laboratory facilities but little library, some have laboratory and library, but most are in the condition described by Professor Stieglitz.

"Contrasting[4] the conditions in German universities with ours, we find the American professor, as a rule, overburdened with an excessive amount of routine work, consisting of lecturing, laboratory instruction and administrative duties. Some teaching must be considered as essential for the welfare of the investigator since, in presenting his subject before a critical student body, he is held to an iron logic, he must ever go to the very foundations of our science and, detecting a weak point here, a missing link, a circle proof, a traditional rut there, his mind continually receives ideas for critical work on the very essence of chemistry. But every profound investigation requires a degree of abstraction and absorption as great as that demanded for creative art. And for such work the best powers of the brain are obviously needed, but after lecturing two hours or giving laboratory instruction for half a day and attending to innumerable petty administrative details, that best power is gone for the day, and each year is made up of just such days or worse in most American universities: the mental alertness, the critical and creative faculties, are wasted on routine work, which to a large extent could be done as well or better by a different type of man."

In the past the universities have been looked to for leadership and the bulk of the chemistry that fills our journals has come from their laboratories. This is all the more true since results obtained in

[3] Joseph Henry, Address Nov. 24, 1877, Philos. Society of Washington. Quoted by Bauer, *Chem. News*, 100, 59 (1909).

[4] Julius Stieglitz, *Science*, 26, 701 (1907).

commercial laboratories, either those of consulting chemists or those maintained by plants, are seldomed published.

"I am convinced,[5] however, that the university is the proper place for research in pure chemistry. The conditions at the university which should make for quiet, undisturbed study, and rich and abundant association with minds alert in chemical and allied sciences, offer the very best opportunities for the development of the true chemist. The young man develops thus in the broadest manner and his outlook is characteristically broad. His subjects for investigation should be purely scientific and not necessarily commercial. The industrial chemical problems ought not to be overly emphasized in the earlier years. The closer the young man keeps to the pure science itself the better for him, the better for the universities, and the better for the industries. When, later, he may choose to enter industrial work he will find his training none amiss and his breadth of view most highly serviceable."

"Research[6] and teaching are inseparable from, and indispensable to, each other in a real university. An institution which does radically separate or oppose them is not a university, however good and useful some other thing it may be.

"Anything, therefore, which lessens the interest and activities of the universities in research and hence reduces their actual output of research and research workers, is a menace to our national strength and well-being."

"In secondary school and in college, human knowledge is bent to the development of the student:[7] he is being given information; he is being disciplined and trained as an end in itself; he is being formed to go higher, to go out into practical life, or perhaps to become a research student. In the university, on the other hand, the emphasis is laid on the extension of knowledge and on public service through its application."

"But there is something holding us back at school.[8] This something is lack of contact with interesting work and inspiring workers.

"Every technical school is now overcrowded with anxious students. Every technical teacher is so swamped by his need of imparting, in wholesale quantities, accumulated knowledge that he has no time to realize the tremendous strides which science is making, much less to take any active part in bringing them about. As for mature and material inquisitiveness, it is almost absent.

[5] W. J. Hale, *Jour. Ind. Eng.*, **12**, 694 (1920).
[6] Vernon Kellogg, *Science*, **54**, 19 and 23 (1921).
[7] N. M. Butler, *Jour. Ind. Eng. Chem.*, **7**, 1070 (1915).
[8] W. R. Whitney, *Elec. World*, **75**, 152–3 (1920).

"The heart of this note is the hope that we may realize that we must raise and support as teachers inquisitive searchers of nature."

"Other countries have provided for the education, support, and encouragement of men who practically devoted their lives to pure or scientific research.[9] Their investigations seem more or less academic. There were careful physical analyses of natural phenomena which at the time, had no visible utilitarian value. As we look into the lives of these pioneers, we find that they were usually much like keenly interested but highly intelligent boys in their appreciation of Nature. They were always learning, and spreading their information broadcast. By some public plan they were immune from the interruptions of conflicting cares, and could pursue their studies uninterrupted. It is not surprising to find that most of the foundations of engineering, whether they be antitoxines or ether vibrations, have come to us through professors of science in European universities or institutions. . . . The point I wish to make is that apparently most of our advances may be traced back to one of these professors, who, trained to be an observer, matured in a laboratory supported by the state, has had time and facilities to follow the lead of some natural observation.

"As we review the history of scores of such cases, it is evident that most foreign universities have held teaching to be secondary to research and have, for several decades, at least, employed and given great facilities to men who made experiments their life work and taught science for the purpose of preparing similar investigators."

The great advantage in the university laboratory is freedom; problems of all sorts can be taken up solely on account of their scientific interest and without regard to practical application. Almost all of the so-called "pure" chemistry has come from the university and this is likely to continue. Along with freedom in work there is freedom in publishing, which is equally important.

Research Assistants. In the great universities where there are many graduate students there are usually some at least of the professors who give their energies chiefly to research. These have usually been chosen for such positions on account of research ability and it is to them that we look for both quantity and quality in research. But even they have their difficulties and limitations; much of their time is taken up with administrative work and more of it goes in planning, supervising and writing up the work of others so that

[9] W. R. Whitney, *Elec. World*, 69, 13 (1917).

they are frequently debarred from experimenting with their own hands.

"A second important factor in the productiveness of our American chemists as compared with those abroad is found in the problem of research assistants;[10] the creative imagination of the investigator in chemistry must always be held in check, as Richards has said, by the experimental realization of the logical outcome of his flights of fancy; but chemical experimentation is one of great minuteness, infinite attention to details and endless preparation. Where the German investigator can have, when he needs them, several assistants, ranking from a newly fledged doctor of philosophy to an associate professor, when necessary, a single research assistant in chemistry has until recent years been a rare specimen in America and even now the species is not flourishing — it is being starved to death by low salaries."

The Professor. Except where paid assistants are capable and plentiful, which is rare, the professor has to depend on graduate students to carry out the investigations that he plans and is limited by their number and capabilities. The experiments must be so planned as to be within the manipulative skill of the students, which is more or less limited, particularly in the earlier part of their course.

Then too, the graduate student has to be considered, he must have the prospect, at least, of a dissertation, hence a problem must be chosen big enough but not too big for a dissertation, important enough to be worthy of that use and not so complicated that it can not be handled by the student in the time available. Problems have, so to speak, to be screened to a certain size, and big ones have to be rejected or broken up into pieces. Different students of equal ability have different tastes and capabilities and it sometimes happens that a particular problem has to wait quite a while until a student comes along with the peculiar combination of taste and training that fits the problem. The student does his best work only when the problem appeals to him.

The greatest prizes are won where the odds are greatest and brilliant discoveries are made where the risk of finding nothing at all is great. In a worth-while problem the difficulties are large and the probability of success may be small. The student is usually limited as to time and leans toward a commonplace problem which promises a dissertation rather than to a recondite one which, if solved would bring a great discovery, but which is more apt to yield nothing, at least in the time available.

[10] Julius Stieglitz *Science*, 26, 701 (1907).

It is very desirable that the professor have some time for experimenting or that he be provided with capable assistants who can do the pioneer work, blazing trails through new territory which is to be more thoroughly worked by the students who come after. Sometimes a tunnel has to be driven through solid rock for a mile before pay dirt is encountered; and an important problem may require the labor of a number of men for years in preparing materials and apparatus and working out methods for obtaining significant results. Where assistants are not available, such problems are difficult to handle, as it is hard to find a succession of students who will be content to merge their efforts into one long drawn out communistic endeavor, the real fruits of which are to be reaped years later, The student is not free to follow his own bent and can not develop much originality when he is forced to keep step with others, or when his results must fill in a certain blank space in the professor's program.

For the benefit of science, and incidentally for enlarging the reputation of the director of the research, it is best for all available forces to be concentrated on one line of investigation, and fortunate is the professor who can plan the parts so that they will fit into an important whole and yet leave place for originality and freedom in the fabrication of the parts.

There is another consideration; the student who has done his dissertation on a small problem, which he can comprehend and make his own and solve in his own way, is more likely to attack a problem of the same kind later on and thus go on with research after receiving his degree. It is in the interest of science to start a man so that he will keep going and will continue to produce after he has gotten away from the university.

The failures of some teachers are pointed out to Dr. Alsberg.[11]

"And this brings me to what I regard as one of the severest true indictments of American university professors although I do not know that any one has made it. It is the custom of a great many American university professors to give their students for their Doctor's dissertation, problems of so large and fundamental a character that it is exceedingly doubtful whether the beginner can get anything out of them or, if he can, can do so within the limits of time set for the obtaining of his degree. To this rather wide-spread custom I attribute, in no small measure, the fact that so many of our Ph.D.'s do not remain in research even when they are placed after graduation in positions in which this is possible.

[11] Written for this book by Dr. C. L. Alsberg.

"It is in this respect that many of the German university professors have acted, at least in my day, differently. It is their custom to keep on hand a lot of partially finished researches which they themselves, either with or without the aid of their assistants, have carried to the point at which it is possible to determine whether or not the problem is worth while, and by what method it can best be attacked. This is a form of enlightened unselfishness. The student is sure to get something worth while within a reasonable time. This makes him eager to undertake further work, and the professor can then give him a second somewhat more difficult problem. In this manner a love of research is developed which in this country is often lost in the case of men who slave away for a couple of years after graduation without getting anywhere, for the reason that the professor has set them a problem beyond the powers of a beginner. In Germany such men are more likely to go on.

"Another way in which our university professors very frequently sin against graduate students is that they use them as a pair of extra hands, as a sort of personal assistant, giving them all sorts of hack work to do on their own researches, without enough consideration as to whether or not the students are obtaining something worth publishing or will be particularly well-trained."

Graduate Students. For graduate students, research is an apprenticeship, an initiation into the bright company of discoverers, an opportunity to try out their own powers. For many who are destined to disappear in the industries where interesting problems are thick and where great discoveries are indeed made but where the only way the results are published is by the announcement of promotions or by the size of automobile one drives, the dissertation is the one bright opportunity to pass across the stage and to leave behind something akin to the famous "footprints on the sands of time." For these it is the golden opportunity of a lifetime and no effort is too great to put into it, but those who are over anxious — or anxious at all — to dazzle by their discoveries, are apt to make none, unless it be to discover their own failures. Students are prone to think too much of the degree and to be nervous as the months pass and results do not pour in. Those work best who hasten not and worry not, but strive day by day to unravel the mysteries of nature, who think, and work and think and read and then think and work some more.

Research is the best part of the training of a graduate student for his development is most rapid while he is engaged on it, and it is desirable that he should enter upon it as early in his course as may

be, but his research is not apt to be of much value if it is undertaken before he is prepared for it. Sufficient routine courses must be taken and skill must be acquired in handling the known before launching out into the unknown. In these routine courses breadth of training and skill in a variety of lines are acquired without which one who devotes too much time to research in a single line is unprepared to handle the variety of problems that are sure to come later on.

Breadth of Training. According to Professor Smith the researcher must be much broader than his special line, much more than a chemist. He should be:

"Broadly trained; not running off into some narrow field without a comprehensive knowledge of chemistry as a whole. I'd have him know his mathematics and physics, his botany, mineralogy, and geology — and literature, for he will need them all. I would have him be a chemist — sometime later he may subscribe himself an organic chemist, physical chemist." [12]

According to Rose the training of a research chemist should begin with the five senses:

"Logic is judgment and judgment is a matter of sense; [13] the facts which are used in forming judgments will be gaged accurately only if properly observed. The underlying requirement, then, of all research in which data are gathered first-hand, is that of accurate observation, the exercise of well-trained senses; upon this must be built a sound interpretation of the facts observed.

"Our education, elementary as well as advanced, makes scarcely an effort to train the senses; instead, emphasis is placed on the development of the memory and of reasoning, though both are really capable of useful development only when there are first-hand observations to remember and conditions which call for the exercise of judgment. Efforts to develop the power of reasoning are essential, because facts in themselves lead nowhere, but it is none the less true that accurate observation is the first requirement.

"For the chemist it is of the very first importance to be able to discriminate between slight variations of hue or shade, to recognize minute differences in the macroscopic and microscopic structure of precipitates, to recognize trifling changes in bodies, and to recall them; he should have a delicate sense of touch and of smell. Not only should he be able to recognize these differences absolutely, but he should have sufficient accuracy of observation to judge of

[12] Edgar F. Smith, *Jour. Ind. Eng. Chem.*, 13, 255 (1921).
[13] R. E. Rose, *Jour. Ind. Eng. Chem.*, 12, 948 (1920).

them relatively, even when both are not before him at once. He should have a very keen memory for sense impressions. To have such keen senses he must have developed them during the period extending from infancy through the first years of childhood. That the chemist fails so often to observe rightly is thus an outcome of the fact that there is nothing like a concentrated effort made by the community to develop the senses through the period of childhood and thus to train the faculty of observation. The evolution of the physical organs of sense is left to chance and in the majority of human beings remains in a very slightly developed condition."

Acquaintance with many things outside of chemistry is essential. "A good research man must have a broad training;[14] he must be familiar with subjects other than chemistry, other than the sciences. He must be able to write his own language clearly and state his conclusions with proper emphasis. But the highest attribute of the human mind is constructive imagination; it is this which, in its greatest perfection, leads to the creation of works of art which add to the beauty of the world, and gives us our men of science, those whose vision makes possible the formulation of new theories, new interpretations of the universe. In a lesser degree it is essential to all good research, and our educational institutions should strive to develop it. The best food for the growing imagination are the products of man's mind; more effort should then be made to interest the student in becoming familiar with the beauties of music, poetry, and the graphic arts; in his chosen field he should be led to see the grandeur of the achievements of the human mind by a study of the history of the growth of the great theories of science. He should be encouraged to learn more of the other sciences than is usually the case, more especially the biological group, and he should be given an interest in the development of human society."

Professor and Student. The relationship between professor and student on research should be close and friendly. Selfishness and distrust eliminate the possibility of effective coöperation. The professor is dependent on the student for getting that piece of work done and the professor's fine ideas are valueless and his plans go for naught if the student's work is inaccurate and inconclusive. Usually the student needs the advice and guidance of the more mature and experienced professor. The two should be genuine partners in the adventure as they fare forth into the unknown. It is desirable, if possible, that the professor should have done some work

[14] R. E. Rose, *Jour. Ind. Eng. Chem.*, 12, 949 (1920).

on the problem previously, preferably with his own hands, so that he can understand better the difficulties met by the student. Otherwise the embarrassing situation may arise of the professor directing the work of the student who, by his intimate contact with it, knows the problem better than the professor.

In rare cases the professor is intolerant of any ideas but his own and wishes to restrict the student to doing only what he is told to do, and resents or ignores suggestions and ideas coming from the student. It is proper that the student be taught to walk on his own feet and to do his own thinking and to contribute his own ideas to the solution of the problem but it is well for the student to discuss with the professor any ideas he may have before trying them out, as otherwise valuable time may be wasted on experiments that can be shown to be futile before they are tried.

The student should avail himself to the fullest extent of the experience and knowledge of the professor without becoming too dependent. It is well for the student to start out along the path suggested by the professor and to rely more and more on his own judgment as his comprehension of the problem and his maturity increase.

Graduate students, like other people, vary greatly in independence of thought and action, some are able and willing to walk alone and others want to lean on some one all the time. A self-reliant student may meet his own difficulties and never ask assistance, while another will run to the professor every time an experiment goes wrong. One of the chief ends in graduate work is to develop independence of thought and the ability to conquer difficulties without calling for help. Research offers the best opportunity of doing this, and it should be the aim of the professor to develop the student as well as the problem. When it is found that the student is incapable of development in this respect, it is better for science and for the world in general, that the student be shifted to some calling in life in which independence of thought and action is not essential.

The reception of a higher degree is supposed to stamp a man as a trained and self-reliant worker who is prepared to go out on his own. Unless the degree stands for this it had better not be conferred, as a degree without the corresponding ability can not carry a man far. It is possible to give a degree to an incompetent man and to boost him into a good position but he soon finds the back door, and wrong has been done to all concerned, to the employer who has wasted his money on him, to the institution since the worth of its instruction and of its degrees has been called in question, to others

who have received the same degree as their worth may de discounted, and most of all to the man himself since he has been exalted only to be abased and may lose confidence in his ability to do the things that he can do.

A professor may accomplish a really good piece of research through an incompetent student who will obey instructions implicitly, provided he have reasonable manipulative skill, by working with him, supplying all the ideas and helping him over all the hard places. Such a student is only an extra pair of hands for the professor, like a plumber's helper who holds the pipe while the workman screws something on to it. The student, of course, gets little out of the research in which only his hands take part, as he has only a vague idea as what it is all about.

In some cases the professor is forced to make use of such a student because he must have help and has no better, as some build houses of sun-dried bricks since they can not afford fuel to burn them. Having used the student and having no money with which to recompense him for his time, the professor may have to pay him with a degree which apparently costs the institution and the professor nothing but which in reality tends to bankrupt both.

Research Institutions are comparatively recent creations. The university laboratories have been too limited in resources to advance science as rapidly as the needs of civilization require and the professors, in following their own tastes and ideas as to research problems, have left many fields uncultivated. Hence the call for institutions, either endowed by individuals or supported by the State, to devote themselves to research along broad lines with large resources and continuity of purpose. Since in the university both professors and students must occupy their time and attention with many other things besides research, much more can be expected of a staff of workers whose sole interest and occupation is research. In the university continuity is difficult to maintain since the students who do much of the work are constantly changing, while an institution can keep the same corps of workers on a problem till it is finished. Besides, the students choose the university and select the professor under whom they are to work and have to be consulted as to the problems, but the institution employs whom it wishes and assigns the problems as it sees fit.

There are, however, limitations on the research institutions and on those who work in them, there is much less liberty in the selection of problems. If the institution is supported by the State all of its activities must be directed towards ends that are of value to the

State. Almost any knowledge may be of value to the State and this restriction may be liberally construed but, however broad the interpretation, the limitation is still there. When an individual endows an institution he usually has in mind certain problems which he wants investigated, such as the combating of some disease, and if he sets aside a sum of money for attempting communication with the planet Mars, those who accept the money are legally bound to make an effort to carry out his wishes. While different endowments vary in the breadth of their purposes, every one is limited and be the limits broad or narrow they must be regarded.

The institution must direct its efforts in certain directions and the individuals who compose the research staff must coöperate loyally to further the common aims. As the organization is more or less rigid and moves as a whole its several members are further restricted. Each worker must confine himself not only to the chosen field of investigation but to the particular part which has been allotted to him.

It would seem that some fraction of one's time might be given to individual research or one might cultivate his own little field after hours or on holidays, as in bye-gone years a slave would work his own little patch of cotton after his required task was done. However it is difficult to do research in scraps of time, and ambitious investigators work overtime on their regular problems.

Plant Laboratories. Research laboratories are maintained by many large industrial concerns for the solution of problems relating to their own lines. What has been said above about research institutions applies to such laboratories except that there is usually much greater restriction in the matter of publication of results and the lines of investigation taken up are commonly more or less closely related to present or proposed factory processes. There is wide variation in different companies in the relation of the research to the plant. Some executives are short-sighted and will not appropriate money for experiments which have not a direct bearing on plant processes and which do not promise immediate financial returns, while others are broad-minded and grant large liberty to their scientific staff to undertake problems which have no immediate practical bearing. In the one case the research laboratory is little more than a trouble wagon to be called out every time a pot boils over or a batch turns out bad; of real research there is none: while investigators who are given a free hand are scouts into strange territory and discover paths which may not be trodden for years.

The best results are gotten when there is the largest liberty and where the clamor for immediate results is not heard. Of course

industrial corporations are organized to make money and their directors must aim at dividends but, as long time investments bring greater returns than get-rich-quick schemes, so a broad policy toward research is the most productive in the end. The supremacy that Germany so long enjoyed in the manufacture of dyes and pharmaceuticals was due to the far-sighted policy of its great companies in securing the best chemists available, providing them with all possible facilites and leaving them the widest possible liberty in investigation, without demanding or expecting immediate returns.

Every chemist is, or should be, enthusiastic about his problems and as he goes along sees all sorts of ways in which investigation might be extended and the young investigator frequently feels that he is being sorely restricted and that his ideas are not appreciated if he is not allowed to follow these lines out to the great discoveries which seem to him imminent. If every one in a plant laboratory were given free rein to follow his own fancy, untold money would be spent and little would be accomplished on the central problems for which the laboratory is organized. There must be limitations, of course, and much wisdom is required in those who direct to determine where to draw the line.

The largest ultimate returns may be expected where research is laid out on the broadest lines and where those responsible for its direction are given the widest possible liberty. The directors will get the best service from those under them if they encourage them to think and initiate, that is, if they employ the heads as well as the hands of their chemists.

Grades of Research. In the research organization of a large establishment where a considerable number of chemists are employed there are many grades of research. There are many problems directly connected with plant processes which demand and must have immediate attention, although such work is but a step removed from routine plant control. It is frequently said that charity begins at home and research must begin with the processes which are going on in the plant and endeavor to control and better them. The chemical investigation has to be paid for out of the profits arising from the operation of the plant and it is fair that the chemists should help make the plant run smoothly. There is not much use to exhort the chemists to help keep the plant running as the directors will always see to that.

Next comes investigation of possible improvements of present processes or working out new processes which it is proposed to in-

troduce. This gives more opportunity for the use of the imagination as something different from what now exists is to be created. The differences may be small or great and it is best to start with a thorough study of present processes, attempting to see what is now lacking and what can be done to improve methods. Success in small things will show the way to larger.

In large laboratories there should be some, the most experienced and most original, to whom it is given to penetrate far into the unknown, untrammeled by the limitations of immediate utility. It is to such that the industry must look for its future prosperity and those executives are wise who secure and encourage research men of the highest ability.

According to Dr. Hill the laboratories should not be expected to revolutionize processes immediately but should be given time and liberty.

"Some managements expect a laboratory to be an immediate source of profit to the company.[16] They sometimes expect wonderful and profitable results within a very short time and with a relatively small expenditure. As a rule this can not be. It should be a sad commentary on the factory and technical men who have been in the business many years if a research laboratory could uncover startling discoveries regarding an old process in a short period of investigation. If money-making discoveries are possible with a small expenditure of time and money every research man in the country would be experimenting on his own account in his cellar or attic if he could not afford a better place. Barring virgin fields, industrial research does not, as a rule, bring immediate results commensurate with the cost. It is therefore necessary for ultimate success that the general management foster research generously and wait a reasonable time for returns. One may possibly secure some profitable returns within two or three years after a well equipped laboratory is in full swing.

"A certain proportion of men should be engaged with problems of a fundamental nature which carry the investigator into new fields. Such work is the most profitable source of new processes or products which can be protected by patents and which protect the company against future competition in its field. Where necessary for the complete understanding of a practical problem, it is profitable to carry a certain amount of theoretical experimentation."

When times are hard industries must curtail. Near-sighted

[16] C. W. Hill, *Met. and Chem.*, **18**, 182–3 (1918).

boards of managers frequently begin to economize by cutting down research appropriations. Dr. Baekeland is right in maintaining that research efforts should then be redoubled.

"To the wide-awake manufacturer,[17] the present industrial depression should be an incentive to engage more chemists, to do more chemical research work, instead of laying off the men of their chemical staff, as has happened in too many instances since we got out of that fool's paradise of so-called 'prosperity.'

"Most of our industries badly need 'fertilizing' and fertilizing is better done while the land lies fallow than during planting or harvesting time.

"Whenever I see such shortsightedness which is bound to stunt our industrial efficiency for the future, then I wonder whether some of the financial or business men at the head of large industrial enterprises are not occupying their positions on an assumed and unearned reputation.

"Let those who at present lay off their research chemists, their physicists, their research engineers, remember that the tremendous gap between that toy electric machine of Franklin and the present electrical industry, would never have been bridged but for research, invention and good engineering."

Consulting Chemists. Consulting chemists do not have their time taken up with such matters as engross the university professor and they are not confined to one particular line as are many plant chemists. They do not have to seek problems, since problems are thrust upon them. In the course of a few years almost every sort of question is asked them and they acquire an enormous amount of varied information much of which can not be found in books. If they could but follow up all the leads and solve all the problems which they encounter, they would soon be famous and the journals would be filled with interesting information which they had garnered.

Financial considerations come in to prevent such happy fruition; they are in chemistry for profit to themselves as well as to their clients. Unless they make some money for themselves they can not stay in the game and unless their efforts are profitable to their clients they are soon out of business. The situation is well stated by Dr. Little:

"Consulting chemists are in a somewhat anomalous position as regards research.[18] Their contacts with industry are generally so varied that they have exceptional opportunities to recognize im-

[17] L. H. Baekeland, *Science*, 54, 421 and 424 (1921).
[18] Written for this book by Dr. A. D. Little.

portant research problems, but it is commonly difficult to prevail upon clients to authorize research except upon the 'no-cure—no-pay' basis and this basis is objectionable from the professional viewpoint and frequently involves more risk than the consulting chemist is financially able to assume. Where the work is done for clients and at their expense it is commonly restricted within rather narrow limits, and the chemist is not at liberty to wander off into those by-paths which not infrequently lead to results of greater potential value than the original objective. Moreover, the arrangement under which such industrial research is generally carried on is seldom wholly fair to the chemist who succeeds in solving the designated problem. The results are turned over to the client for a fee which usually is based upon the time expended rather than the actual potential value of the results obtained. If consulting chemists are to place themselves in a position to prosecute research advantageously they should, wherever possible, insist in their preliminary negotiations for such work that they shall have secured to them a continuing interest in the research results. Better still, they should so arrange their budgets as to permit the allotment of a substantial portion of their effort to research on their own account and in their own interest directed toward the solution of problems in fields where the market is assured."

It is a pity that the consulting chemist does not form the habit of following up problems in pure science which he is led into in the course of work on industrial problems for clients. There are certainly many of these which could be worked up and published without sacrificing any financial interests. The trouble is that the chemist is too busy getting out the report for his client and must hurry from this to the next case that comes in.

The observations he makes are interesting and suggestive but usually require some following up and working out to put them in shape for publication and the chemist has not the time for this extra work. Sometimes, perhaps, he has the time but lacks the energy.

One of the first things that a chemist learns when he goes into commercial work is not to talk and frequently this lesson is learned too well, so that he does not tell things that could be told without damaging any one's interests.

Amateur Research. The amateur is usually thought of as a half-baked, would-be professional but in research the amateur is the one that counts. Of course the majority of the leading investigators are in universities, research institutions and industrial laboratories but those who achieve results of the highest grade are amateurs at

heart and investigate for the love of the results without regard to financial reward. Those whose minds are on the money have the "form of godliness but deny the power thereof."

A review of the great names in chemical history reveals a large percentage who were amateurs in the narrowest sense, never receiving money for their research as Priestley and Griess who have been already mentioned.

Scheele, the co-discoverer of oxygen, compounded drugs for a living and mixed chemicals for the love of it. When after many years of struggle he had the prospect of an income he wrote: "Oh, how happy I am, with never a care about eating or drinking or dwelling. . . . There is no delight like that which springs from a discovery; it is a joy that gladdens the heart."

Lord Cavendish inherited a title and a fortune and was utterly indifferent to both. Research was not only simply his chief love but was his only concern throughout the years of his long life. He shunned human companionship and devoted his time to experimenting, turning his large residence into a series of laboratories.

Lavoisier was busy in politics and philanthropy and devoted to science the fortune that he made as tax collector and business administrator.

Carey Lea, who laid the foundation for the science of photography and discovered colloidal silver in its multifarious forms, was an amateur and spent his long life experimenting in a laboratory in his own home from which he published some four hundred scientific communications.

Dr. Whitney has directed the spending of millions for research but is intensely interested in the amateur.[19]

"The part of research I am most interested in promoting is what we may call the *unpaid* kind, not because it is cheapest, but because it is the most valuable. It is most neglected, most poorly understood, most in need of appreciative support in America. The separate industries do not need encouragement in research nearly so much as the nation needs it. The industries can be depended on to estimate its value to them, for they take annual inventories. But a country which keeps no books, seems to have to depend on accident for its most valuable research work."

We take a look at the past: [20]

"The great bulk of all our scientific discovery and research in the past has been due to individual labour and initiative; much of

[19] W. R. Whitney, *Jour. Ind. Eng. Chem.*, **8**, 537 (1916).
[20] J. A. Fleming, *Electrician*, **76**, 711 (1916).

it a labour of love, unrecognized at the time. Men of great genius have opened up new lines of thought or pursued private researches often with very inadequate appliances. In fact the greater part of past British research may be said to have been amateur work, not in the sense that it was lacking in the highest qualities, but only in the sense that it was pursued for the sheer pleasure and interest of it by private individuals."

We strain our eyes to see the utopia of the future: [21]

"There is no reason to suppose that the number of amateur investigators may not greatly increase under a more favorable form of society. In the ideal commonwealth of the future it may not be in the least surprising to find that the communal furnace-man, after his four-hour day, is conducting elaborate investigations in paleobotany, and that the communal laundress is an acknowledged authority on colloid chemistry."

Then we listen to the words of a chemist, who is also a most practical man, as to the insistent present: [22]

"I cannot forbear in this connection to refer to the opportunity which research offers to the sons of rich men. Their independent financial postion enables them to attack problems, the study of which in any comprehensive way is denied to most chemists by reason of the expense involved. It is, therefore, relatively easy for the financially independent chemist to achieve distinction by intensive work in a wisely selected field. He will reap the satisfactions which come through the fellowship of science and through public recognition. There will open to him a new world of mystery and wonder and opportunity. There are many rich men's sons to whom a career in science offers far more worthy objects than the making of money which they do not need or the devotion of their lives to sport."

Charles Darwin was just such an amateur.

[21] W. M. Wheeler, *Science*, 53, 60 (1921).
[22] Written for this book by Dr. A. D. Little.

CHAPTER III

INCENTIVES

The Urge from Within and the Reward from Without. These are many and frequently get so intertwined that it is hard to distinguish them. In almost every thing a man does, his motives are more or less mixed. Why does one go into business? To make money that he may eat and have clothes. Yes, but many go into business who have these things and to spare and many more stay in business, toiling early and late, long after a competence has been obtained. Men love business because it is a game, a man's game in which one may find scope and exercise for one's wits and most strenuous efforts. Why do men go to war? For pure patriotism, to fight for the defense of their homes and the honor of their country's flag. Yes, but just a little bit because others are going and it does not look nice to be a coward. Why do men build hospitals and give to charity? On account of a disinterested desire to help those who are suffering and in need and because they love their fellow man — may their tribe increase. Yes, but it is nice to be considered a benefactor of mankind, or of one's city, and it is sweet to enjoy the sensation of beneficence.

The relative importance of the various motives varies with the individual and even with his mood or necessities.

It is the same with research. There are many and varied motives, curiosity, starting early in life with a desire to know what is inside the doll, reaching to the wish to know why the planets go round the sun; the fun of playing a game, of beating the other fellow to a piece of knowledge, of snatching from nature herself something which she has concealed from mankind for thousands of years, — a wonderful game it is too; pleasure of overcoming difficulties, many make the exhausting ascent of the Matterhorn for the rare exhilaration of triumphing over glaciers and craggy steeps, scientific achievement has its difficulties just as trying and its ecstatic moments of triumph when victory is won; the desire to increase human knowledge and to "think the thoughts of God after him"; and for others the lure of money, the pot of gold at the end of the rainbow of the experiments. Mixed motives these, sometimes high and sometimes sordid, but men are urged on to achievement and the results are for the good of the race.

Professor Remsen applies chemical terms to our motives: [1]

"It is not surprising that those who enjoy mental exercise should have a desire to spend their lives in research. Those who have engaged in this kind of work know that it is very satisfying. Ask anyone who has thus spent his life what his principal motive has been, and it is certain that he will say that it has been the satisfaction he has derived from it. There are other motives, of course, for motives are always mixed. Speaking in chemical terms motives are mixtures not elements. It is, however, not necessary to subject these motives to a complete analysis. It is sufficient to say that the chief constituent of those motives that lead us to undertake research is the mental satisfaction derived from it. If that were the only constituent, however, only comparatively few would be engaged in it, for fortunately it is necessary for most of us to make a living. Now, it is possible by practicing research to make a living, and this is coming more and more to be the case. The universities, the research institutes, and the more enlightened industrial establishments are calling for the services of researchers.

"If one who is giving his life to research asks himself whether his work is of benefit to his fellow man there can be but one answer. Every result of research must be of value ultimately. These results differ very widely among themselves. Some have the glory of the sun, some of the stars, but all help to illuminate the wonderful universe in which we live."

Curiosity, or the desire to know, a characteristic of mankind and apparently of some of the lower animals, is a great driving force in investigation. It leads men to pry into the secrets of nature and the more securely hidden they are the greater is the incentive to persist in the search. The philosophers of Athens spent much of their time wondering and arguing about the make-up of matter but were lacking in the experimental method which was brought to the front by Bacon in more modern times. Acquiring knowledge is like drinking sea water, each draught intensifies the thirst. If one is haunted by the desire to know what will happen when certain chemicals are mixed, one is likely to take the first opportunity to mix them and observe the result. One experiment awakens curiosity still further and others follow.

Professor Richards says of himself:[2]

"In my case the incentive to the pursuit of science was primarily that intense curiosity concerning the nature of things which echoes

[1] Written for this book by President Emeritus Ira Remsen, Johns Hopkins University.

[2] T. W. Richards, *Science*, **44**, 39 (1916).

down the ages from the time of the ancient philosophers. To the feeling of curiosity, as time went on, was added the perception that only through a knowledge of the fundamental laws of chemistry can men use the resources of the world to the best advantage. Any further gain in this knowledge must, sooner or later, directly or indirectly, give mankind more power. Even an abstract chemical generalization must ultimately be of priceless service to humanity, because of the extraordinarily intimate relation between theory and practice."

Dr. Whitney describes some of the joys and benefits of increasing knowledge.[3]

"To the devotee scientific research may well become a religion, but whether he sees in the infinite possibilities of matter only the necessary results of permutations among seventy-odd decaying elements or the hand of an all-wise Creator ever uncovering new principles to hopeful investigators, he cannot be blind to the blessings of new truth. This is not produced to order. . . . It comes only from following with interest Nature's devious and unexpected ways, studying apparently irrelevant phenomena, learning by experiment regardless of aim. And since it is important to us that pioneer effort be individualistic, wanton, clean, but vagabond, it is this type of teacher whom we must support."

Research as a Game. Of all aspects of research perhaps the view of it as a game is the most alluring to the great number who follow it. It has all of the characteristics of a game, and of a good one too. The fascination of baseball is in the infinite variety of situations and the utter impossibility of predicting from one moment to the next what will happen. Chemistry offers an even greater variety of combinations among its seventy odd player-elements, some of which can play any position on the whole diamond, and there is always enough uncertainty as to the results to keep us in suspense.

Games of chance appeal to many. In a sense there is no chance in chemistry as the atoms act according to laws. Dice obey the laws of physics with mathematical exactness. In both cases there are so many factors that we can not know or control, that we can not predict the results. In chemistry there are many long shots, but in some of them the stakes are so high that one chemist after another puts time and money on them.

Others are fond of games of skill, billiards or golf; chemical investigations give scope for the exercise of the utmost dexterity in manipulation as well as the highest skill in construction of apparatus combined with keen discernment in planning.

[3] W. R. Whitney, *Elec. World*, **75**, 152 (1920).

Much of the zest of a game is in rivalry, and the desire to excel our opponents in the contest. This element is present also in research, as we are ever in competition with other investigators, sometimes in close rivalry, in fact we are always playing a world's series, since our work must stand in comparison with that of the whole civilized world. We must go ahead of what anyone else in the wide, wide world has done in our particular line, or our results are not worth publishing, and when we do publish we present our results to an audience made up of thousands of chemists of all nations and tongues under heaven.

Competition is particularly keen in the industrial field; the chemists of one rubber company may be regarded as a team playing a series of games with teams from all the other rubber companies. To be sure the scores are not posted at the end of each inning but those interested know who is winning. It is just as thrilling to distance another chemist by manufacturing something at 78 cents per pound which he can not make for less than 80, as it is to go around in 78 to the other fellow's 80. The fact that the company's dividends and the chemist's prospects of promotion depend on the score does not make the game less interesting.

All in all, chemistry is a splendid game, a man's game, into which we can put the best that is in us of strength and of cunning and not seldom of daring. If played properly it is a clean game which trains and elevates, and develops the highest qualities.

What Dr. Whitney says of engineering, he might have said with equal force of chemistry.[4]

"No college sport could be put over if it did not contain some of the same elements which make engineering attractive. No one would play the game if it were always a copy or a repetition. If there were no feared defeat nor hoped for victory, no new stresses applied, no new materials discovered and no return but gate receipts, there would be no real amateurs and no sport. When this is applied to engineering proper it meets a perfect analogue. Few good engineers play for the gate receipts; they are led on by a will to accomplish. They seldom reproduce a move or repeat a major operation. They are usually trying some new stunt and are elated or depressed with emphasis because effects are relatively permanent. But the mental tools and processes are just like those of clean-cut sport."

Professor Metcalf believes in research for the fun of it and the love of it.[5]

[4] W. R. Whitney, *Elec. World*, **75**, 153 (1920).
[5] Maynard M. Metcalf, *Science*, **59**, 27 (1924).

"The motives to research may be as varied as are the characters and interests of the men engaged in the pursuit, but the urge which seems the most productive of the highest grade work is that of the fun of the game, the pleasure in the research itself, the love of truth and its pursuit. Ulterior motives of personal profit or even the desire to promote the progress of civilization and the well-being of society, all have an element of danger. They are likely to persuade the student, perhaps unconsciously, to control the direction of his search, turning it into so-called profitable channels. But no man can know where lie the great undiscovered truths. Truth itself is a safer guide into the unknown than is any man's guess as to the probable best line of approach to worth-while knowledge. The student who humbly follows where the subject itself seems to lead him, eager to follow whatever turn the investigation naturally takes, is the one most likely to find the richest deposits for his mining. Truth is too manifold, too unexpected, too great, oftentimes too profoundly simple, for any man's successful anticipating. From the most unexpected sources come discoveries that open great vistas far beyond the previous imagining of any man. The humble following of the subject itself and the suggestions that develop in the research is the method that usually brings the largest results. Interest in the subject itself, the desire to know the truth, the pleasure, the uplift of soul, that comes with the gaining of some new vision into a hitherto unexplored field of reality, these are the safest guides, leading one to results in value far beyond fame or financial profit or some invention that shall increase the perhaps already too great complexity of human life. The instinct for truth, the love of understanding for its own sake is ingrained in the human soul. And to it may safely be made the strongest appeal in inducing students to enter upon the life of research. The fun of the game, the worth of the game for its own sake, makes a keener appeal to men of the finest type than does the thought of possible dollars to accrue or possible fame to be attained."

Those whose minds are on the gate receipts make poor players in any game. Those who regard research as a means of self advancement are warned by Professor Williams.[6]

"If achievement comes by means of spiritual forces then the animus of research must be spiritualized. . . . Too much have we been stimulated by personal ambition in our 'search for truth.' Promotion, because of the amount of research we do is not the spiritualization sought for in this plea. The fundamental virtue

[6] S. R. Williams, *Science*, **54**, 538–9 (1921).

of the investigator is a passion for truth whatever it be and through whatever channels it may come.

"There is a grave danger for the spirit of research when the chief criterion for the advancement of an individual in his position is his ability to turn out voluminous material describing his experiments. This motive prompting the researcher tends more and more to satisfy personal ambition. There will gradually appear a greater amount of polemical writing and controversies over priority of discovery. Nor is this all or the worst of the results attained by such a stimulus to research. Inaccuracies and carelessness in obtaining results are inevitable, it is the logical outcome of a system where bulk and not quality weighs so heavily in seeking promotion.

"On the other hand, that land whose cricket and other sports have imbued its citizens with a sense of the 'sport for the game's sake' has contributed a succession of epoch-makers in the field of science that makes one wonder whence the inspiration of it all. One can not imagine the immortal Newton worrying very much about the status of his position because the first computation concerning the force of gravity due to the earth at the moon did not yield results as he had anticipated. To him and a great host of his fellow countrymen succeeding him it was sufficient to seek first the kingdom of truth, leaving it to others to judge whether the honors of earth, if they had any value, would be added as a natural result of ability."

Desire to Increase Human Knowledge. This is socialized curiosity. We pass by stages from individual selfishness to world-wide philanthropy: as the higher nature develops one tires of piling up goods for exclusive use and comes to think of the good of the community, of the state and finally of the world. So we pass from the gratification of personal curiosity to the desire to unite with others in dissipating the dense darkness of ignorance which surrounds us.

Science as it stands today represents the toil of thousands, each of whom has added an observation, a deduction or a generalization. It is a pious act to add to this accomplishment, according to our ability, our little or our much. We lean heavily on the labor of others when we use an analytical method or make an organic preparation and it is but our duty to make some return to the general store for that by which we benefit. This is lost sight of by the industrial establishments which draw so much from the literature of chemistry and lock up in secrecy the results of their own experiments. The dye companies of this country have spent some millions of dollars on research in the last few years but even then probably 99% of what they know was drawn from the free accumulated stores of knowledge. They

should return in kind to the common fund at least a tithe of the knowledge they get from their own experiments. Perhaps the income tax schedules might be made to apply to knowledge as well as to the wealth gained by its use.

There are some who do not care to contribute to charity unless the subscription list is published, or to erect a building for a college unless it bears their names. The published list is forgotten and the building which bears one's name crumbles in time and the donor's name is lost. Not so with our contributions to chemistry. Each new compound or observation when described by the author in a standard journal becomes an integral part of the fabric of chemistry. These journals are distributed to the libraries of institutions and of private individuals all over the known world. The torch of the fanatic fired the library at Alexandria and blotted out much of the accumulated knowledge of that time but a hundred such catastrophes would only make sets of journals harder to obtain. Published work, small or great, good or bad, goes into the record to stay. Wherever a research is started in any field, all that has gone before is reviewed. The surest way to have one's name preserved is to attach it to some discovery in science: one's name thus becomes known not only as long as a certain building stands and to those who pass along a certain street but for all time to all the world. Lest we be unduly puffed up, be it said that our names go in with many thousands of others and there is little likelihood of getting a ton of credit for an ounce of effort.

Keeping Company with the Great. Who would not like to have been a friend and companion of Washington, or Lincoln, or Lee, or Roosevelt? Coming into close contact with great persons is one of the exalted privileges of life. If it is denied us to walk the streets with these men we can come into even more real fellowship with them by sharing their views and engaging in the activities that they loved. So we may become companions of discoverers by being discoverers ourselves, not great perhaps, but actual contributors to science.

"Though sundered far in time and space" we may be fellow workers and thought companions of Priestley, Scheele, Lavoisier, Dalton, Berzelius and Liebig, if we too become investigators.

It is not simply high sounding phrase but literal fact that the only way to understand and appreciate the investigations of others is to engage in similar work ourselves. This is an important reason for including research in university courses.

Reflex Influence of Research. Those who have had to do with the instruction of graduate students have noted the accelerated rate

of their development as soon as research is taken up. A student may be quick at grasping what is given in the lectures and retentive of what he hears or reads but he is merely a schoolboy of larger growth till he is seasoned by research. The average student is quite bewildered when he first essays the unknown and has no laboratory manual or journal article on which to rely: he is apt to clutch at his instructor as a pupil in a swimming lesson; for a time he wants some one to O. K. his results and assure him that he is on the way, but soon he finds his feet on the ground and learns to walk with firmer tread, as he begins to realize that all the *terra firma* of accepted chemical knowledge was once only hazy hypothesis.

With the vanishing of the supports on which he previously leaned the student develops self reliance and begins to think for himself, to draw his own conclusions, and to formulate his own hypotheses; from being a follower he becomes a leader; from memorizing results obtained by others, he produces something for others.

"Small pieces of routine research can be carried out by any intelligent graduate, and the results obtained are often of some direct objective value, although not by any means always. The chief value of such research is to the man who conducts it. The worker has learned to look on a problem, however small, with a clear, unprejudiced eye, to come into contact at first hand with facts, to distrust text-books and references generally; in fine to rely upon himself." [7]

Life in the great world outside the laboratory is in verity research, new situations and unsolved problems await one every morning and follow one home at dusk, so of all parts of one's training, research is that which best fits one for the life into which one is to plunge on graduation. It has often been noted that many who win all honors in examinations during their college course sink into oblivion soon after, while their less brilliant classmates forge steadily ahead and ultimately reach high positions. High examination grades may frequently be made by a retentive memory and judicious cramming, with little actual grasp of the subject. Independence of thought and self reliance in the face of unforeseen difficulties, resourcefulness in surmounting obstacles, and perseverance when things look most hopeless are qualities that make for success alike in research and in one's subsequent work.

It does not follow that one who does well in research will make money in business: it is frequently quite the reverse, since one who concentrates his whole attention on the scientific side of a problem may fail to see the practical side. The mistake is, however, not in

[7] James Walker, *Jour. Soc. Chem. Ind.*, 34, 1122 (1915).

the research method but in the failure to apply research to the practical as well as to the scientific part of the problems.

Keeping Young by Research. There are but two ages of man, two divisions of life, ascending and descending, crescendo and diminuendo, growth and decay, youth and old age. It has been suggested that old men be chloroformed and sixty has been tentatively set as the age when men become old, but senescence is in attitude and in life processes, not in years. Many are old at thirty, while others are in vigorous and expanding youth at seventy. One starts to grow old when one passes the peak in one's life. It has often happened that a chemist who had toiled and produced and grown thereby, till he had attained fame and position, has ceased these activities, on being appointed to some high professorship, and has never been worth much afterward. That appointment was the climax of the career and old age set in with the relaxation of efforts. Some young men work splendidly in their undergraduate years and continue to develop through their period of graduate study, accomplishing something worth while in research, under guidance, but when they attain the doctor's degree and start out on their own, they seem to hesitate and falter. For them graduation day is the apex and senescence sets in immediately thereafter. Such were lacking all along but did well while they were in the university atmosphere and were continually stimulated.

If old age begins when the crest is passed, when the mind ceases to expand and produce, then it is within the power of every man to postpone old age, perhaps not indefinitely since the tissues of our bodies and our brain cells do get old in time and cease to function, but at least till he is well stricken in years.

Teaching is wonderfully stimulating to the young instructor; every lecture, every quiz period reacts on the teacher and as he leads others, he climbs to new heights and sees vistas of truth; fogs that covered the landscape are lifted and the relations of fact to fact and of law to law become plain. There is exhilaration in working out new courses and putting them across, but after a time the novelty wears off. Though to themselves, the members of each college class appear immensely superior to all who have gone before, to the bored professor they are apt to blend into a monotonous line. A teacher is prone to settle down into a rut and start to grow old long before the age set for his retirement. To one so circumstanced the means of staving off old age, of keeping alive, is the finding of some interest, some endeavor, into which energy and effort can be put, to the quickening of the intellectual pulse.

Research supplies this need better than almost anything else and keeps one thinking, working and growing, thus maintaining the upward slope of the curve; the publication of the results of the research is tangible evidence to the world that life is not extinct. Would that all teachers were like Nef and Emil Fischer from whose laboratories papers appeared regularly right to the end — some being published after the obituaries!

Universities grow, science grows and the professor must grow too: shall he only grow old? Rather let him keep active in research and expand as rapidly as his institution: rather let him occupy his mind with problems in chemistry than worry over the Carnegie Foundation's postponement of the date for retiring on pension.

There are few things that enchance the respect of students for a professsor as much as the knowledge that he is in the vanguard of his science.

Material Results. Living as we do in a highly developed civilization, it is impossible for us to realize what we owe to chemical research in the past. We use stones for building that have have been shaped by mechanical processes only but even then we call on chemistry to supply the mortar. We eat fruits and a few vegetables as they come to hand, but most of our food materials have to be transformed by some chemical process, at least that of cooking, before they are suitable for our use. We are not content to wear unbleached cotton or suits of wool as it comes from the sheep. Almost every article of commerce has involved chemistry in its manufacture.

A humorist has given us a circumstantial story of how the Chinese discovered the art of roasting pork by the accidental burning of a building and how prevalent fires became, endangering all the buildings of the empire till some one by research discovered that a pig could be roasted even more effectually and at far less cost by a small fire of sticks. How other races discovered cooking or how long it took them has never been told us.

A large proportion of our chemical knowledge was amassed long before chemistry had a name and a standing as a science. The prehistoric blacksmith who smelted a few ounces of iron in his rude forge was carrying out a chemical process and was truly a research chemist, in so far as he strove to improve the yield and quality of his iron. By such research as this vast numbers of facts were accumulated and enormous progress made in all of the arts, but the rate of progress was painfully slow on account of the lack of co-operation between individual workers, lack of system in recording results, the crudity of experimental methods, and the barrenness of early theories relating

to matter. As with modern transportation facilities we cover, in a few hours, distances which required of our forefathers many days of toil, so by modern research methods we compress into decades achievements equal to those that formerly required thousands of years.

Chemical research, though only recently known by that name, has been one of the greatest factors in the development of civilization as we know it today, and " it doth not yet appear what we shall be " but we know that whatever progress is made by the race, chemical research will be responsible for a large part of it.

" The world has always been improving, and the real growth and development has come to those nations which have been responsible for the original research work and not for the mere storage of conservation of knowledge." [8]

The Wall Street Journal, always keen to discern values, gives the following estimate of the services of chemistry:

" It has been well said that if we were to take away what the chemists have contributed, the whole structure of modern society would break down at once. . . . Faith may remove mountains, but modern society relies on dynamite. Without explosives our great engineering works must cease and the Panama Canal, no less than modern warfare, become impossible! Chemistry has made possible the transportation systems which span the leading countries of the world. It has made it possible to turn to man's service the wealth of the mineral world. By analysis of plants and soils, the waste materials of the world have been brought to the growing crops. Indeed, every great industry, whether it be farming, manufacturing, transportation or mining, would almost immediately relapse into barbarism if the secrets of the chemist and physicist, the geologist and mineralogist, could be gathered up and cast into the sea." [9]

Professor Noyes agrees with this estimate: [10]

" I think that few who have not paid especial attention to the subject realize how completely the world, as a place to live in, has been transformed during the past century. This transformation rests for its basis almost entirely on our fund of science knowledge, and especially upon the knowledge of physics and chemistry and biology which has been accumulated by scientific workers during the last seventy-five years."

Professor Wheeler bears similar testimony: [11]

[8] W. R. Whitney, *Jour. Ind. Eng. Chem.*, **8**, 535 (1916).

[9] Editorial in *Wall Street Journal*, quoted by Wm. McMurtrie, *Science*, **26**, 398 (1907).

[10] W. A. Noyes, *Science*, **26**, 706 (1907).

[11] W. M. Wheeler, *Science*, **53**, 65 (1921).

"Science is of the most overwhelming social value in the sense that the welfare of every individual, physically, mentally, and morally, absolutely depends on its developments, or in other words, on scientific research."

Dr. Nichols emphasizes the importance of systematic endeavor: [12]

"At the foundation of all this advance research is firmly imbedded. Without it, the structure could not have risen or the glowing anticipations of the future be even imagined. No one can deny that there have been accidental discoveries, some of great moment; but this has not been and will not be a safe dependence. Accidental discoveries are not to be relied on, of course, although they are not to be scorned. In chemistry the accidental good fortunes have usually come to those who were really seeking, although possibly for something far different, but, note this, they were usually made by men qualified to recognize an important discovery when it flashed across their vision."

The following words are from Dr. Little who is a leader in industrial research: [13]

"It is difficult to speak of the commercial possibilities of research without conveying to those who are unfamiliar with them an impression of exaggeration. They are as great as those of industry itself. In fact, many of our greatest and most profitable industries are based directly upon research results and as such are familiar to every chemist. To make the demonstration one has only to recall the aluminum industry, artificial indigo, carbide and acetylene and cyanamide, artificial alizarine, artificial silk, the whole coal-tar color industry with its by-products of synthetic drugs, the hydrogenation of vegetable oils, the manufacture of explosives, the fixation of nitrogen, and so on through an almost interminable series of the triumphs of applied science. These, to be sure, are things of the past, but since both industry and science touch to-day upon innumerably more points of the unknown, the industrial opportunities of research are to-day innumerably greater than ever before. Practically the whole field of petroleum chemistry awaits development; we are facing a revolution in our use of fuels; physical chemistry and especially colloid chemistry and our growing knowledge of catalysts open up endless vistas of opportunity, while industry and finance are to-day so organized that industrial developments of the successes of the laboratory follow with a speed incomparably greater than that possible even twenty years ago."

[12] W. H. Nichols, *Chem. Engineer*, 27, 285 (1919).
[13] Written for this book by Dr. A. D. Little.

If Dr. Juritz is correct, and there is reason to believe that he is, then chemists should assume the responsibility and exert themselves to accomplish their mission.[14]

"So we may rightly claim that the present age is the age of the chemist. The chemist has never before had such opportunity for the application of his knowledge to the betterment of material conditions upon earth, and never has he more effectively applied it to the attainment of this aim."

What will put America in the lead among the nations? Because other nations owe us great sums of money can we assume that we are in the first place and will hold that place? Dr. Whitney has very definite ideas as to the rate and means of progress: [15]

"I want you to realize that in America we are going ahead in the future at a rate dependent *entirely* upon our preparation. . . . I want you to see that we must be foremost in systematic, organized research, or we shall be distanced by other countries which already well recognize the value of *new* knowledge. . . . Research is preparation. It is preparing in one decade for the problems and the necessary work of the next."

The importance of research is well stated by Dr. Dushman [16] who has seen many investigations undertaken to satisfy scientific curiosity yield unexpected results which subsequently became the basis of undreamed of industrial applications.

"The last class of research problems, and that which I consider the most important, may be called pioneering. By this I mean research work of a purely scientific nature — investigations which aim at the discovery of new facts, new principles, or new points of view. The results of such investigations may be altogether unexpected; they are as it were, gambles on the future; nevertheless such investigations are absolutely vital to the existence of any industry. For no individual, no industry, any more than a nation, can stand still. It must either progress or go backwards, and what makes towards lack of progress is *lack of ideas*. An industry may fail just as badly because of lack of new ideas as on account of lack of capital, and of the two failures, the former is the more hopeless.

"The day is past when progress in industry could be made to depend upon accidental discoveries. We are realizing more and more with the increasing complexity in our daily lives that 'each advance in industrial science must be studied, organized and fought like a

[14] C. F. Juritz, *Nature*, 102, 58 (1918).

[15] W. R. Whitney, *Jour. Ind. Eng. Chem.*, 8, 534 and 535 (1916).

[16] Saul Dushman of the General Electric Co. Research Laboratory. *Canadian Chem. Jour.*, 3, 118 and 121 (1919).

military campaign.' The ammunition for this kind of campaign is the discovery of new facts. A knowledge of facts is the only sure foundation for any progress in science. And it is furthermore not at all necessary that the search for these facts should be made with the definite view of their possible application. Our past experience teaches us that there is no fact of natural knowledge that does not at some time or other find an application in the course of industrial progress, and we may therefore afford to take this risk with all the assurance that the time and labor spent in so-called purely scientific investigations will be well repaid. As a matter of fact, the whole of our industrial fabric is a voluminous commentary on the practical applications of investigations in pure science.

"That industrial research pays, both for the company and the men engaged, is a self-evident conclusion from the very fact that the Research Laboratory has grown and is still growing. But I would not wish you to get the impression that the Research Laboratory of the General Electric Company, is unique in this respect. If I had time and more facts at my command I could convince you that the same broad policy pursued in other laboratories has also been found to yield equally good results. The Research Laboratory of the General Electric Company has merely had the advantage in this respect of being one of the first in the field of industrial research and its success has prompted dozens of other large industrial concerns to follow the same example. Wherever industrial research has been attempted along broad lines and with intelligent appreciation of the difficulties to be overcome — the results obtained have more than repaid the the capital invested and have furnished the strongest guarantee for the future success of the manufacturers."

Exclusive information obtained by research is an important part of the capital of manufacturers.

"In fact the final triumph of the big firm is to have at its disposal, more clearly set out than in a scientific text-book, a mass of purely scientific information which the professors will not chance upon for many years to come. This is the secret of strength of the great German chemical firms." [17]

It is impossible to estimate the value of great discoveries and of the results from research in general but Dr. Reese, who is in a position to know, gives us partial figures for certain investigations carried out under his direction.

"It might be interesting to state that the total expenditure of the du Pont Research Organization for the years 1912 to 1918 inclusive

[17] Anon., *Electrician*, 83, 15 (1919).

was $6,051,000, and the calculable saving, disregarding those benefits which cannot be figured in dollars and cents, though extremely important, amounts to $82,401,000. This large figure, of course, is increased very much by the enormous production during the war, and as a large part of this saving was in connection with the manufacture of smokeless powder, it enabled the company to reduce the price of powder materially during the war, in spite of the increased cost of raw materials and labor."[18]

[18] Charles L. Reese, Reprint and Circular Series, National Research Council, No. 18, p. 11.

CHAPTER IV

PROBLEMS

Finding and Attacking. Finding a problem is a serious difficulty to many, and all the more troublesome because it is imaginary. It is a difficulty until one gets started and then the trouble is how to dodge problems, they come from the east and from the west, from within and from without, they come in droves like the locusts came to afflict Pharaoh, they disturb one's reveries in church, pop into one's head during one's bath, they start from every page one reads and even break into one's dreams. The thing is to get started on some piece of research — then every experiment performed suggests two more, and each of these, two more and so on: they multiply like flies, but the multiplication process does not start till one begins to work. One who begins to work and think will never lack for something on which to work and think, the only difficulty is in getting the first "think." The process is auto-catalytic, the products of the reaction accelerating it.

By reading and pondering the published investigations of others, we frequently see something that the author has not considered properly or think of some experiment which would verify or disprove his hypothesis. Some of the greatest advances in chemistry have been made by men opposing each other in an experimental debate as in the case of Stas who upheld the idea of the definiteness of chemical combination and Bertholet who opposed it, or the great discussion between Hantzsch, Bamberger and Bloomstrand as to the constitution of diazo compounds. In each of these cases the leaders on the two sides marshalled many supporters and an enormous amount of careful experimenting was done from which emerged important conclusions, which were accepted by both sides and have stood the test of subsequent investigation. This sort of discussion is far removed from polemical articles the aim of which is not to advance science but to exalt the writer by depreciating someone else and from the acrimonious personalities in which some indulge.

If one compares two articles on the same subject discrepancies are apt to be found which may not be cleared up by the later author. Further investigation to find where the truth lies is in order. The

literature abounds in articles describing work taken up for just such reason. In working out ideas suggested by the work of others, great care must be taken not to infringe on their rights.

A good way to obtain problems is to look through *Beilstein* and note compounds or reactions that have not been studied for twenty or thirty years. A large number of such can be found and in almost every case something of value can be accomplished by repeating and extending the old experiments. New light may make old problems look very different. Sometimes by applying modern interpretations to the experimental data of a past generation new relations can be seen and important deductions made, even without new experimental work. A field that has lain fallow for a score of years is apt to yield a harvest to one who tills it, particularly if improved methods of agriculture are used, just as the tailings from old mining operations sometimes yield more gold to the cyanide process than was originally obtained from the ore.

Problems that resisted old methods with old apparatus are frequently solved by the new. When no work has been done on a scientific claim for ten or twenty years it is considered to have lapsed and to have become public property, so it is safe and proper to take up such.

One of the great historical researches is that of Liebig and Wöhler on the benzoyl radical and it appears that their reason for undertaking that subject was that one of them happened to process a bottle of oil of bitter almonds. According to the famous receipe for making hare soup, catching the hare is the first step, so with an investigation, obtaining the research material is an important consideration and it is well not to pass by any substances that may be at hand without making sure that they have been thoroughly studied.

Opportunity is said to knock at least once at every man's door and happy is he who recognizes and answers the summons. Such fortune comes to a chemist in the way of some special material which is not generally available: it may be the product from some unusual local industry or something obtained through friendly relations with an industrial plant, of the by-product from some other investigation. A large number of papers have appeared recently on "mustard gas" derivatives. This substance became available to a number of chemists: it had been very little studied. Here was an opportunity and various chemists have taken advantage of it and added greatly to our knowledge of sulphur chemistry. The war led many chemists into paths infrequently trodden and many have

turned these new experiences to scientific advantage. The possession of a quantity of some unusual material is a special opportunity which should not be overlooked. The reporter who happens to be passing when something sensational occurs burns the wires to make a "scoop" for his paper.

Many opportunities come to consulting and industrial chemists in the way of contact with new materials and processes. Of course commercial considerations and the restriction of confidential relations are great hinderances but there are certainly occasions when science can be greatly benefited without betraying clients or wrecking enterprises.

It is most helpful to keep a record of one's ideas as they occur by having library cards convenient, at home and in the laboratory, and noting down any suggestion of an experiment that may come from one's reading, or thinking or work. The date should be noted and the thought stated fully enough to insure its reproducibility. These cards are to be filed in a special place and are looked over and considered from time to time. On second sight, some of one's ideas will look trivial and some impossible but some will still appear worth working out. In case something of commercial value should eventuate, the dated card, showing the genesis of the invention, may be of great value in connection with a patent application.

"Now it is an extremely interesting and suggestive fact that the greatest experimental discoveries to-day are not made in the older, well recognized sciences but on their borderlands — in the 'twilight zone' of more or less related sciences. I have but to mention the words 'physical chemistry,' 'physical geology,' 'astrophysics,' 'biochemistry,' etc. and you will readily grant the assertion made. In the overlapping regions there seem to be the greatest opportunities afforded for solid, thorough, and at the same time remarkably rapid, experimental achievements."[1]

Choosing a Problem. Out of the multitude that present themselves a suitable one is to be selected. It is better to take a small one that is within one's mental and material resources than one that can not be handled, but a portion of a large problem may be undertaken and when this is completed, a second portion. The mistake is frequently made, particularly by young experimenters, of undertaking too large a problem. In the battle against nature it is better to actually kill a little problem than to bruise a much larger one. It would be easy to name a number of large problems that have been

[1] L. A. Bauer, Address of retiring president Philosophical Soc. of Washington. Bull. XV, 103. Quoted in *Chem. News*, 100, 56 (1909).

more or less mauled by a long succession of light weight experimenters and are still in good condition to withstand many more such attacks. It is the thoroughness and conclusiveness of the work that count and even a small piece of work well done can not fail of its reward. It can not fail of its reward because good work is its own sufficient reward, and any recognition it may receive is a bonus.

The same advice is given by Dr. Alsberg: [2]

"In my judgment, a very important point to emphasize is to counsel modesty on the part of the research worker in the selection of his problem. This is particularly important for the beginner. He should be impressed that every new fact, however small or circumscribed is worth while and that, in the beginning of his career, he should be satisfied with problems dealing with some definite, specific and concrete point, even if it is a small one. If he has ability to do better than this, he will find that each small point he settles opens up vistas of other small points, and if he settles these one by one, very soon he has built up a mass of new data that often represents an important and far-reaching result, not anticipated in the beginning. Many important generalizations are arrived at piece-meal this way. Evolution is as important in research as in anything else."

It is desirable to select something in which one can become intensely interested, which will absorb one's entire force of creative energy, something which will saturate one's dreams, something which one really wants to accomplish. It is remarkable how fascinating an apparently uninteresting problem can become when we get really acquainted with it. Selecting a problem is not like choosing a partner for life, take one that comes to hand and dispose of it and then go after another.

Attacking a Problem. Devising methods of attack is the occupation of the chemist as well as of the general, and methods must vary according to the peculiarities of the situation and special means that are at hand. The methods of attack will vary with the problem and with the individual chemist, but several typical plans will be considered.

In the ancient Greek courts, the orator stated his case in complete and logical form and later called in witnesses to substantiate his statements, while in present day practice, the witnesses are examined first and the lawyers make what they can out of the recorded testimony.

Both methods are used in chemistry. A hypothetical structure may be built up on certain assumptions, predictions made as to what

[2] Written for this book by Dr. C. L. Alsberg.

happen if so and so is tried and then the required experiments are made to verify the assumptions. This is frequently the method of physical chemists. The other extreme is to go ahead with the experiments and later on construct theories to fit them; though theories are seldom evolved without some experimental basis and experiments are not apt to lead anywhere unless guided by some hypothesis.

A long series of experiments may be arranged in advance, or planning may go along with experimenting. The plans for a bridge must be complete in every detail before the foundations are put in but the explorer starts off into a new country without any fixed program of discovery. He pushes ahead and observes what he can. When one is laying out work for assistants more definite plans are needed than when one is investigating alone. It is frequently advisable to cover variations of several factors, as in a study of the sulphonation of anthraquinone a long series of runs were made at 10° intervals to see the influence of temperature, at 1, 2, 3 and 4 hour periods of time, and with different strengths of oleum. In this case about sixty experiments were planned in advance and all the operator had to do was to see that the manipulation was exactly the same in each case and that the temperatures, etc. were strictly maintained.

Sometimes the explorer has a definite objective, scaling a certain mountain or reaching the north pole: a chemist may set out to prepare a certain compound the structural formula of which he writes down and nails to his masthead or he may desire a substance having certain chemical or physical properties. In such cases the path is pretty well marked out. Another time a chemist may start out to investigate the properties of a little known class of compounds without any ideas as to what is coming out, believing that there must be something of interest. He tries one experiment after another and finds out as much as he can. The bag of game may be large or small but if he is a good hunter he brings home whatever game there is.

It is desirable to be helped by a plan but not to be hampered by it. Nature is more intricate and has vaster possibilities than we can imagine. If in a cut and dried commonplace lot of experiments something extraordinary unexpectedly falls out, a good investigator is quick to see and appreciate it. The discovery of saccharine by Remsen and Fahlberg was entirely unexpected though by no means accidental. For some years Remsen had been investigating sulphonic acids systematically preparing one after another and studying their reactions and properties: one of these acids acted queerly, yielding benzoic sulphinide, or saccharine, some hundreds of times as sweet as sugar and of considerable commercial importance.

Perkin, the elder, was attempting to obtain quinine by the oxidation of aniline, an impossibility by the way, and got no quinine but did get a colored substance which he investigated further till he produced mauve, the first of the aniline dyes and a much more important discovery than he had planned. His greatness was manifested by the way he followed up and turned to account an unexpected observation. An ordinary chemist would have called the experiment a failure and poured the mess into the sink.

The greatest discoveries, those that open up totally new lines of thought and study, that usher in new eras in science, are naturally unexpected. Phenomena that are entirely new can not be predicted. Burbank did not improve the potato: he noticed an abnormally productive plant and he knew what to do with it. This potato was fortunate in growing in Burbank's garden. This is no plea or excuse for haphazard experimenting. Let us go out well prepared for the game we expect and if a bird of brighter plumage or a beast of richer pelt crosses our path let us add it to our bag. It may take extra keen observation or unusual marksmanship.

The wonderful property of silica gel of absorbing impurities from petroleum distillates was discovered by Patrick by investigating an experiment on absorption which went exactly opposite to his calculations and predictions.

"Readers of *Popular Mechanics* some time ago selected by vote the seven wonders of the modern world. The highest votes were received by wireless, the telephone, the aeroplane, radium, antiseptics, antitoxins, spectrum analysis, and X-rays. How were these originated? All of them were produced by the identical formula. In the first place, they were not the result of a direct attempt to accomplish what was really attained. The end was not visible when the foundations were laid. The real work was done by thoroughly well-trained observers — not by laymen. They were professors in every case. They followed up a lead opened by an observation which was too insignificant to attract the attention of less trained men." [3]

"Necessity is not the mother of invention; knowledge and experiment are its parents. This is clearly seen in the case of many industrial discoveries; high-speed cutting tools were not a necessity which preceded, but an application which followed, the discovery of the properties of tungsten-chromium-iron alloys; so, too, the uses of titanium in arc lamps and of vanadium in steel were sequels to the industrial preparation of these metals, and not discoveries by sheer force of necessity." [4]

[3] W. R. Whitney, *Elec. World*, 69, 14 (1917).
[4] W. R. Whitney, *Min. & Met.* Dec. 1921, p. 11.

In attacking a big problem we should not be discouraged if we are not able to see the complete solution from the beginning, if we see a way to attack one part of it, even a small part, that justifies making an assault upon it. We scale the highest peaks by ascending one step at a time. By climbing one of the foothills we can see a little further up the mountain and when this additional height is reached, then on till the summit is attained. As we work on a problem the way opens before us. It is well to study the old masters and see how they met and surmounted similar difficulties.

This much has been said about methods of attacking a problem to show that there is more than one way, one must find that way which suits him best. "But the centurion . . . commanded that they which could swim should cast themselves first into the sea and get to land: and the rest, some on boards, and some on broken pieces of the ship. And so it came to pass, that they escaped all safe to land."

Time for Research. "So teach us to number our days that we may apply our hearts unto wisdom." This prayer is attributed to Moses whose "eye was not dimmed nor his natural force abated" at the end of his hundred and twenty strenuous years. The days of the years of our sojourn are few and are crowded with duties and diversions. We must needs number them with care lest all of them be swallowed up in routine duties or casual enjoyment and none are left for higher things. We are sure that we could carry out some wonderful investigation if we only had the time but we are "cumbered with much serving" — of ourselves as well as of others — and never find time to choose the better part.

Our money will not buy as much as formerly and many other things have changed but there are the same number of hours in the day and the same number of days in the year as in ancient times. According to astronomical observations the year has not changed by the minutest fraction of a second since history began. If we do not accomplish as much in a day or in a year as did Berzelius or Liebig we can not lay the blame to Father Time. In addition to having the same time that they had we are blessed with incomparably better facilities, well equipped laboratories, electric motors and hot plates, resistance glass and standardized reagents.

As a matter of history many of the famous investigators of the olden time devoted only their spare time to chemistry as an avocation. Priestley was a minister and engaged in enough religious controversies to keep several ordinary men busy. He turned aside to chemicals for reaction and to satisfy his curiosity. Peter Griess was chemist for a brewery and had to see that good ale was plentiful

in merry old England — not a trifling task, we may be sure. No one knows how he found time for his monumental investigation of the diazo compounds. Doubtless he made a place for research and did not wait for a convenient season.

It is wonderful how we can find time for something which we really want to do, as when fishing time comes around and they are biting good, or our favorite baseball team is going to play, or golf calls. We can make way for research if there is the will for it.

By cutting and fitting our various tasks an astonishing amount can be packed into a day. Efficiency experts advise us to set aside a quiet period in the early morning for thinking over the day's duties, making out a schedule, allotting so much time to each, taking care to arrange the sequence so that mind and body will be refreshed by the change from one sort of occupation to another rather than wearied by unduly prolonged effort of one kind. By compressing our routine tasks into smaller space, room may be left for research.

We get mired down in absurdities when we attempt to apply the canons of efficiency to research itself. It is easy enough to tell when half of a cord of wood has been sawed and at any moment it takes only a glance to see how fast the sawing is going forward, but it is utterly impossible to estimate progress on a research problem. Months may go by filled with feverish activity and no progress be made towards a solution and then in the twinkling of an eye an idea may come and the whole be clear; a chance observation may give the clue while long series of carefully executed experiments may avail nothing. The Star Spangled Banner was dashed off in a tense moment under the spell of a great emotion, few know what Francis Scott Key did the rest of his life. Kekulé spent a long life in careful experimenting and clear thinking but his one great achievement, the benzene theory, was the product of an hour of dreaming. As the clock ticked the time away and Kekulé sat in his reverie who could have known that a new world of chemistry was being born and that the celebration of that hour, a quarter of a century later, would draw together chemists from all lands.

We can not say: go to now let us discover a third law of thermodynamics between 3 and 5 this afternoon but if we are able to arrange our schedule so as to set aside time for thinking and experimenting we put ourselves in the way of discovering something.

Working out a new idea usually involves a considerable amount of laboratory drudgery such as the preparation and purification of the necessary research materials, the isolation or estimation of reaction products, and analyses of new compounds. To this part of

an investigation efficiency methods may be applied without damage. Thus if many analyses have to be made, as in velocity studies, quicker methods may be sought or the samples may be grouped and run in sets so as to require a minimum of the operator's time and attention. At the start of a certain investigation of reaction velocities, it required nearly a day to analyze one sample but, by setting up a battery of stills, eight determinations were made simultaneously. Two sets of receivers were provided and one eight were titrated while the next eight were distilling. Thus twenty-four samples a day were handled instead of one.

Strength for Research. Our strength, mental and physical, as well as our time, is doled out to us, so much each day, to some in more bountiful measure but to none in unlimited amount. We can no more afford to squander strength than we can time. It is not a question of becoming so weary that we fall in our tracks and have to be carried home on a stretcher. It is rather a question of maintaining physical and mental freshness and alertness throughout the day till the last task is done. When the fine edge is worn off of the axe the wood cutting slows up; we do not have to wear out the whole axe. The problems we face demand the very best that is in us, the keenest perception, the steadiest hand, the surest thinking and the most active imagination.

By continuous standing for hours in the laboratory, by overtaxing our eyes, by keeping at one kind of work too long and in many other ways we bring on incipient weariness thereby dulling ous faculties so that the best work can not be done, but by alternating sitting and standing and interspersing some library work with experimenting, much can be done to keep mind and body fresh till the end of a perfect day. Chemical research offers many possibilities of variety of occupation on account of the diversity of the operations to be carried out.

CHAPTER V

CHEMICAL LITERATURE

Books and Journals and Their Uses

The use of Books. In the use of each of his five senses man is excelled by many of the beasts of the field; his powers of observation and ability to profit by experience are shared to a considerable extent by the higher animals; but man is able to transmit information so that one begins where the last left off. Every monkey has to start his investigations just where his father did, and there is little, if any, advance of knowledge in monkeydom. The total that a monkey can know is what one monkey can discover, but a man may know all that others have found out and written down, plus what he adds.

The science of chemistry is the orderly arrangement of the facts accumulated by the toil of thousands of chemists. If one were to live more years than Methuselah and work more hours a day than Edison, he could discover for himself only a small fraction of what has been found out by the hosts of those who have labored in chemistry for generations.

In the decennial author index of Chemical Abstracts (1907–1916) there are about 80,000 names, but as many articles bordering on chemistry are included we can figure that some 40,000 chemists contributed to the progress of chemistry in these 10 years, and that on the average, each one is to be credited with 0.0025% of the advance made; so that if a chemist knows only so much as he has learned through his own experimenting he is acquainted with only a minute fraction of one percent of current chemistry not to mention the vast accumulation of knowledge left by past generations of chemists.

The man who does not avail himself of books puts himself on a plane with the monkey who has to learn by his own experiments how to crack a coconut. If we are to add to human knowledge we must know exactly how far that knowledge has gone, at least at the point where we are to do the adding: we must find the end of a rope before we can splice a piece onto it.

Hardly anything more humiliating can happen to a chemist than to publish his research and then to have some one step forward and

point out that the work had been done previously and had been published in some journal that the chemist should have consulted. In the industries thousands of dollars are frequently spent on experiments to find out facts which have long ago been discovered, stored and cataloged in the library and which might have been learned by an intelligent search.

"There is nothing more pitiable than the spectacle of an enthusiast, fancying himself a pioneer, laboriously digging in ground already explored, exhausted and abandoned by others. My friend Clarence King told me once how he set his heart upon the ascent of a certain high peak in the Sierra. With infinite exertion, and no little peril, he scaled the precipitous mountainside, and reached at last the summit, only to find there an empty tomato can and a copy of a newspaper, relics left there by a picnic party, which had ascended by an easy trail on the other side of the mountain. A little preliminary research would have saved him from this scientific fiasco." [1]

"Your isolated and concentrated scientist must know what has gone before, or he will waste his life in doing what has already been done, or in repeating past failures. He must know something about what his contemporaries are trying to do, or he will waste his life in duplicating effort. The history of science is so vast and contemporary effort is so active that if he undertakes to acquire this knowledge by himself alone his life is largely wasted in doing that; his initiative and creative power are gone before he is ready to use them. Occasionally a man appears who has the instinct to reject the negligible. A very great mind goes directly to the decisive fact, the determining symptom, and can afford not to burden itself with a great mass of unimportant facts; but there are few such minds even among those capable of real scientific work. All other minds need to be guided away from the useless and towards the useful." [2]

"The research chemist can reduce his work in the laboratory by increasing his work in the library — and in the latter case he is at no expense for reagents." [3]

Need of Library Training. Liebig is credited with the introduction of the laboratory method of teaching chemistry which has spread all over the world and given a tremendous impetus to our science. Good laboratory instruction is everywhere to be had but library training for chemists is strangely rare: scores of books tell us in detail how

[1] R. W. Raymond, *Jour. Ind. Eng. Chem.*, **7**, 331 (1915).

[2] Elihu Root, Bulletin National Research Council, Vol. I, Pt. I, p. 8 (1919). Quoted by Hale, *Science*, **51**, 150 (1920).

[3] McClelland, *Jour. Ind. Eng. Chem.*, **11**, 578 (1919).

to operate burettes and balances but frequently the student must find out for himself how to use *Beilstein* and *Richter*. A few only of our universities give systematic training in the use of the chemical library. Hence the average chemist is much more capable in the laboratory than in the library. The student needs to be trained in both, for it is no more to be expected that a student will acquire good library technique without instruction than that he will become a skilful analyst without guidance. We are born neither with laboratory dexterity nor with library facility: both have to be acquired. It is true that an individual may attain to either untaught and unaided by others, but schools exist for the purpose of shortening the toilsome road of self instruction.

To be a chemist one must be capable of doing accurate and reliable work in the laboratory and must also be adept in searching the literature so as to be sure just what has been done. No one wishes to employ a pseudo-chemist who bungles along in the laboratory and takes several times as long to complete a determination as he should and is then not certain of the result; nor is one wanted who wastes time in inconclusive literature searches.

In legal cases, particularly in patent causes, it is of the utmost importance to be able to find what is in the literature pertaining to the matter in hand, and equally important to make sure that other things have not been previously published. The validity of a patent depends on the newness of the facts disclosed and if a part or all of these facts can be found in publications antedating the patent, its force and validity are lost. The statements in a patent are construed in the light of what was known at the time the patent was conceived, and to interpret them we must establish just what was the state of the art at that time.

The importance of library training is emphasized in the report of the committee on industrial research.[4]

"The failure to provide adequate and systematic instruction in chemical literature is illustrative of this contention.

"Before commencing laboratory work upon any problem, it is obviously necessary to digest intelligently the important contributions which have been made upon the subject and to take advantage of what other workers have done in the same field. The average graduate is usually almost helpless when attempting to do this and consequently requires close supervision. The main difficulties are:

(*a*) He does not know how to go about it; he does not know

[4] R. F. Bacon, C. E. K. Mees, M. C. Whitaker, W. R. Whitney and W. H. Walker. *Science*, **45**, 36 (1917).

where to look as the most probable source; and he is not familiar with the standard treatises and important journals.

(*b*) He fails to analyze the subject into its factors and hence generally looks for topics which are too general. Because he does not find any references to the problem as a whole as he has it in mind, he assumes that nothing has been done upon it and that there is nothing in the literature which will be of aid to him in the investigation. Were he to separate his subject into its essential parts and then to consult the literature on each factor, he would find considerable information which he otherwise would miss.

(*c*) He does not critically digest articles under examination, but often he makes only a few disconnected quotations and fails to interpret the work done.

"The solution is to be found in the provision in the chemical curriculum, preferably in the senior year, of a course of lectures on the literature of chemistry, with particular reference to the character of the writings and the status of the authors. The purpose of these lectures should be to present a general survey of the voluminous literature and to impart an accurate, systematic working knowledge of chemical bibliography. A concurrent seminar should be devoted to indexing and tracing chemical literature, to the cultivation of an acquaintanceship with authorities, and to the solution of bibliographic problems."

The necessity of training in the use of books and the value of wide reading are well stated by Professor Bishop [5]

"May I as a layman, venture a suggestion to you who are experts? I feel that most of you tend to ignore in the organization of your work of instruction any presentation of two things which help to mark a scientist of real distinction. The first of these is a knowledge of how to use to the full the various bibliographic tools provided. It seems to me that such instruction in their use is real necessity — perhaps not for elementary classes, but certainly for any study of an advanced character. The loss which comes from an ignorance of what has been done on any given problem is pathetic — loss of time, unnecessary labor, discouragement. It is a loss which can be avoided by very simple means. The gain which comes with full knowledge of previously published results is uncounted. It marks the successful from the halting start on any task. The complexity of the bibliographic indexing in most fields is so great that there is real need for formal instruction in handling bibliographic tools. No one of you ignores instruction in laboratory method. Should he overlook the

[5] W. W. Bishop, *Science*, **56**, 214 (1922).

need of instruction in bibliographic method? The second of my two marks of distinction is a broad, general view of the history, methods and scope of his subject, what in my youth the Germans used to call, 'Encyclopædie.' Few men are willing to take the time from their own particular researches to lecture on a general introduction to their subjects. But I venture to point out that precisely such a broad, sweeping view of the whole topic is what the younger men need most. It can be given only by one whose reading has been wide, whose grasp of the whole subject is firm, whose judgment is matured, and whose experience entitles him to speak with authority. What in a master makes disciples? What qualities in some men enable them to found a real school? Is it not precisely that grasp of method, that sense of relations of parts to the whole, that historic view and that prophetic insight which comes from a deliberate attempt to survey the whole of one's subject, to weigh its importance, to contemplate not alone its past but its present and future? My suggestion is that students should not be left to pick up either bibliographic method or a general view of their subject from incidental allusion or chance comment. The need of both is too great and too serious to warrant the indifference or neglect which they now seem to encounter."

It is important to know all that is in the literature, but judicious discrimination is required.

"There is one point in particular in connection with the study of the literature which I think should always be kept in mind. That is, the temptation to consider everything true that is found in print. One will find in the literature a great number of physical constants of compounds which are inaccurate. Also there is a large number of methods of analysis, preparation and purification which have been published, but which cannot be made to work. Frequently these methods are copied from book to book, each author in turn believing them to be accurate, but not having the time to check them up. The fact that the same statement occurs in a large number of books should never be considered as proof of its accuracy, unless it can be proved that the different authors obtained the results independently and did not simply copy them from each other." [6]

To undertake research we must know how to manipulate apparatus in the laboratory and we must be equally skilful in handling books in the library. If we are lacking in either, we must get rid of this handicap.

The Need of Foreign Languages. Chemical investigation is carried on all over the world and is therefore published in many

[6] Written for this book by W. J. Murray of A. D. Little, Inc.

anguages but in the early days of science England, France and Germany took the lead in investigation and particularly in the founding of journals for the publication of research. In addition to this the wide dissemination of these languages aided them in coming to be recognized as the languages of science. If anything is published in one of these languages it is regarded as published to the world and every one is held responsible for knowing it. This distinction is partly shared by Italian and Russian. The recognized and widely circulated journals published in these languages have attracted contributors who spoke other tongues. Journals are printed in these languages even in countries where they are not spoken; thus some Japanese chemical journals appear in English, and some Dutch in French. There are several Italian journals which contain important contributions but these form only a small percentage of those which appear in the three major languages. Italian is so like Latin and French that one who is trained in these can take a dictionary and get what is necessary out of an occasional Italian article and can thus get on with little formal study of Italian, though a knowledge of this language is a considerable asset. Until recently the Russian Physical Chemical Society published an important journal but it has been the custom of the chemists of that country to republish almost all their researches in German journals, which has made it possible for chemists to get on fairly well without Russian, though at times special translations have to be obtained involving trouble and delay. In addition to the journals there are handbooks, indexes, compendiums and monographs which are seldom translated.

To succeed as a chemist one needs English, German and French at least and to make any speed in searching chemical literature, one must handle these three languages with facility. An extremely small proportion of what is published in one of these three languages is ever translated into the others. One can not afford to wait a year or two for a translation. If one wants the information, one must go and get it in the original publication.

Speaking of the German students' deficiency in foreign languages, Grossman says: [7]

"In many cases the candidates do not realize this unfortunate condition since for their purposes the references in the Chemisches Zentralblatt in German are sufficient. Under such circumstances not only does the individual suffer in his own general development but the science as well. On this account this condition must be terminated once for all as soon as possible, if we wish to give the future

[7] Z. *angw. Chem.*, 32, I, 328 (1919).

chemists sufficient development to enable them to take up the struggle for existence at home and abroad, which is certain to be more severe in the future. To this end the active aid of the *whole German teaching system* is needed. First of all we must call the attention of beginners in chemistry repeatedly to the importance of more thorough language study. But besides the academic study, which should be continued, practical instruction specially designed to meet the needs of the young chemist is to be recommended."

Learning Foreign Languages. The young chemist is sometimes appalled when he is told that he will have to acquire facility in German and French. It simply must be done. It can be done and it is not as serious a task as it appears at first sight, since one must needs only read these languages which is quite a different thing from having to speak or write them. Futhermore scientific articles are usually written in simple, direct style and they are comparatively easy to translate. The fact that many scientific terms appear in various languages with little change in form is of great assistance to the beginner.

To acquire the desired reading knowledge of one of these languages it is best to start with a short course in the rudiments of grammar but one can get on with a comparatively limited amount of this as the subjunctive mood, future perfect tense and other complexities are rare in scientific writing. Irregular verbs give little trouble as one rarely meets any of their parts except third person singular and plural, present and past tenses. Of course a thorough knowledge of French and German grammar and an acquaintance with the masterpieces of poetry, drama and fiction are desirable attainments, but these are not necessary for the chemist whose present task is to extract a number of facts from a straightforward scientific article.

Given a modicum of grammar, facility in reading is to be acquired by extensive reading and the more extensive the better. It is sometimes best to lay aside the dictionary and read rapidly without translating. At first one gets only a glimmer of an idea now and then and may read a page without finding what it is all about but as one reads and reads one gets more and more of the meaning; strange words look less strange and their meaning is guessed from the context. Words learned in this way stick better than those gotten from the dictionary, though it is always safe to verify guessed at meanings by reference to the dictionary. As Professor Noyes [8] says:

"There must be an intensive study of grammar and of a few articles or books till these are thoroughly mastered and then there must

[8] *J. Amer. Chem. Soc.*, **42**, 2102 (1920).

be a large amount of more superficial reading, best in elementary chemistries dealing with subjects with which they are familiar. In studying a foreign language we sometimes forget that we have not looked up in a dictionary one word in a thousand of those we understand in our mother tongue. We have acquired a knowledge of the meaning of these words by meeting them over and over again in a great variety of connections and each time we see the word we add something to our knowledge of its meaning. It is for this reason that the words of our mother tongue have for us a wealth of meaning that the words of a foreign language can never acquire until we have lived with them intimately for many years. But a knowledge of the meaning of words in a foreign language may be acquired by extensive reading and use without a dictionary, exactly as we acquire our own language. There may even be some question whether our teachers of language do not overdo the study of grammar. Young children do not study grammar."

Early in the process, one must quit translating into English and must go directly from the foreign word to the object or action which it represents. As the eyes read the French or German the mind should be filled with the images suggested and not be cluttered up with English words. To translate, one must change the order of French nouns and adjectives and must go to the end of a long German sentence to pick up the verb; must get the meaning of the sentence and then search for English words to express that meaning. Supposing that the reader knows all of the words, it takes about three times as long to translate as it does to get the meaning directly. The chemist has thousands of pages to search through and can not afford the extra time required by translating. Much assistance may be obtained from several books that have been written to aid the student in acquiring the necessary knowledge of French and German.[9]

One must learn to skim in foreign languages as well as in English. It frequently happens that only a few paragraphs, or perhaps only a sentence or two, in a long article are pertinent to the particular ob-

[9] First German Course for Science Students by H. G. Fiedler and F. E. Sandbach, London, 1920. Oxford Univ. Press.

Chemical French, M. L. Dolt, 2nd. ed. 413 pp., Easton: The Chemical Publishing Co. — for review see *J. Phys. Chem.* 24, 754, 1920.

A French-English Dictionary for Chemists by Austin M. Patterson, 1921, New York. John Wiley & Sons, Inc.

French technical words and phrases, John Topham, London: Marlborough & Co., 5s net.

Chemical German, by Francis C. Phillips, 252 pages, Easton: The Chemical Publishing Co.

A German-English Dictionary for Chemists by Austin M. Patterson, 1st ed. 1917, New York. John Wiley & Sons, Inc.

ject of the search. Two things are required: rapidity in skimming through what does not concern the matter in hand and certainty in spotting the things that may be of service. Much time is wasted if we read every word of a fifty page article to find a single fact but it is disastrous if there are two facts in the article that are of great importance to us and we miss one of them.

Chemical Journals. Chemical literature is published in periodicals and in books. At the present time practically all the results of investigations appear as articles in the journals, some journals containing nothing else while others have editorials, reports of meetings and other material. It is possible to get all that has been found out about any subject from the journals ignoring books completely but books may be of great assistance as summaries and particularly as guides to the journals. The student should learn to make the best possible use of both.

By reading the journals the student sees science in the making and observes how one fact is added to another as bricks are laid in a wall, though in science the structure is never finished nor does it grow according to blue prints previously prepared.

The current journals keep us abreast of the chemical thought of the time, of the latest discoveries in the laboratories and of the newest developments in plant processes. The chemist who does not read them is like a blind man at the movies. The student should cultivate the habit of reading them. Of course he can not read all of the journals that are published even if he has access to them, but he can browse through several at least reading the articles which appeal to him most. It is advantageous for the student to join the chemical society of his own country as early as possible in his career, for then its journals come to his own study table where they are constantly in his sight so that he can pick them up a few minutes at a time each day. To be sure the research chemist spends a large part of his time searching the literature for things that bear directly on his own problem and necessarily so, but he can not afford so to narrow himself as to see one small segment of chemistry. The man of one idea has not a whole idea for his one idea is incomplete without its relations to other ideas: the zenith is related to the whole horizon. One must read broadly of many things in order to think deeply on one thing. The research chemist must read everything about his own field but can not afford to neglect the rest of chemical literature. It is remarkable how much light is thrown upon a problem from distant sources: one can hardly read a piece of investigation of any sort without finding something that suggests an idea about his own problem.

By reading the old journals we come in contact with the masters of experimentation and of reasoning who have gone before: their results may have been superseded by more modern observations but they laid the foundations of the science of today and they have much to teach us as to methods of thinking and working. The young artist spends much of his time copying the productions of the painters of centuries ago or of sculptors of ancient Greece so the young chemist must study the masterpieces of investigation for inspiration and guidance. In the old journals we have the works of these ancient worthies told in their own words and in the reading of them there is great reward.

Kinds of Journals. Of chemical journals there are many kinds, some containing only records of investigations in pure science others filled chiefly with trade news and touching upon investigations only in so far as they have a practical bearing. There are journals that devote themselves exclusively to chemistry and there are others which include several sciences. Journals of physics, geology and other sciences frequently publish articles containing more or less of interest to chemists. *Chemical Abstracts* publishes from time to time a list of those which are abstracted by this publication. The last published, October 1922, contains the names of 1010 such journals. This list is an impressive one and is valuable for reference and worthy of study too. Only a small minority of these are devoted entirely to chemistry.

The young chemist should get acquainted with the chief journals in pure and applied chemistry: he should know how they are arranged and indexed. Some of the chief journals are named below with a few facts about them.

Publications of Societies. At present the most important journals are those published by the chemical societies of the various countries. A large membership enables a society to publish a bulky journal at moderate cost to the individual member. Many independent journals have been merged into the society organs or their publication taken over by the societies.

In most cases the journals published by a chemical society are distributed without extra cost to its members, it being understood that the dues go chiefly to defray the expense of printing. The publication of journals is usually the chief function of societies though the organization and growth of the great national societies have aided greatly in the diffusion of scientific knowledge and the general betterment of the position of the chemical profession. Self interest and loyalty to the science should impel every chemist to join at least one

chemical society. Patriotism and the possibility of attending meetings make it natural to begin with the national society of one's own country. Societies representing some application of chemistry make a strong appeal to those engaged in that particular line, as the meetings afford contact with others having kindred interests and the publications contain information bearing directly on their daily problems. The general society with its broader outlook and more varied contacts should come first and the specialized society should follow closely. Membership in one or more foreign societies also is valuable.

The United States boasts the largest chemical society in the world and, what is more surprising, claims the first two devoted to chemistry exclusively, the Chemical Society of Philadelphia founded by James Woodhouse in 1792 and continuing 17 years, and the Columbian Chemical Society started in the same city in 1811 under the patronage of Thomas Jefferson. These societies left no foot prints on the sands of chemical time, since they published no journals.

The importance of the societies in bringing in the era of modern science as well as many interesting facts about society journals and about other chemical publications may be gathered from a presidential address by Professor Noyes[10] from which the following is quoted:

"Through the middle ages and at their close the alchemists and iatrochemists had no journals or organized methods of publication. Their researches, if we can dignify their random experiments by such a name, were published in books, usually in the Latin language. Many of the alchemists used mystical symbols and expressions and some of their writings were designed rather to conceal than to reveal their knowledge — an art which has not been altogether lost in the writing of German and sometimes of other patents.

"It is very significant and interesting for us as a Society to recall that the beginning of a different and better form of publication had its origin in the organization of national societies, about the middle of the seventeenth century. Between 1650 and 1670 such societies were begun in London, Vienna, Florence and Paris. The Royal Society, which grew from the union of small scientific societies in Oxford and London has been, perhaps, the most effective of the group, in its influence upon the growth of science. The meeting of small groups of kindred spirits in these societies gave an opportunity for the announcement of new results and for the exchange of ideas upon scientific topics which was most useful, not only in the dissemination of new knowledge, but perhaps still more in that growth of ideas which comes

[10] W. A. Noyes, *J. Amer. Chem. Soc.*, 42, 2099 (1920).

from the action of keen minds upon each other. We miss something of this very valuable side of society life in the large meetings of the present time. It is better represented, now, by the discussions among small groups in our laboratories.

" The publication of the *Philosophical Transactions of the Royal Society,* begun in 1665, represents a new function of the Society which became of vastly greater importance than the scientific meetings. It would be difficult to overestimate the value of those Transactions in their effect on the growth of science. In their pages are to be found the first notice of the microscopic organisms which we now call bacteria. There, too, we find an account of the epoch-making discoveries of Davy and of Faraday and of others who did some of the fundamental work of the nineteenth century.

" The publication of the *Comptes rendus* in France was begun in 1776, the year of our American Independence. Like *Transactions of the Royal Society* it publishes articles in many different lines of science. In other respects the policies of the two journals are very radically different. The Royal Society aims to publish papers which are the finished product, frequently of years of work, and publication has often been long delayed. Publication in the *Comptes rendus* is prompt but the papers are very brief and frequently lack details which are essential to make them useful. Both kinds of publication are desirable but for the permanent growth of our science and for the future, publication of the form used in the *Transactions* is much more valuable.

" As far as I can learn, the first journal devoted to chemistry apart from other sciences was Crell's *Chemische Annalen,* which began as the *Chemisches Journal* in 1778. The oldest chemical journal which has had a continuous existence is the *Annales de chimie,* which was begun in 1789, the year of the French Revolution, by de Morveau, Lavoisier, Berthollet, de Fourcroy and four others, less well known. The subtitle of the journal was ' Recueil de mémoires concernant de chimie et les arts qui en dependent.' In the introduction the value of chemistry for the arts is emphasized, also the purpose of making new work in chemistry, wherever undertaken, available to all. Another object was, undoubtedly, to give untrammelled expression to the new ideas advocated by Lavoisier at a time when the *Journal de physique* was still controlled by adherents of the ' phlogiston ' theory. This journal must have been one of the factors which made Paris a chief center for the development of chemistry for fifty years following. Four volumes were published the first year, at 12 francs each. Volume 18 was published in July, 1793, and we find in it some signa-

tures on blue paper, a reflection, doubtless, of the troublous times when it was printed, for that was the beginning, of The Terror. After that there is a hiatus for four years and Volume 19 appeared in 1797 " Par les Citoyens Guyton, Monge, Berthollet, etc." We miss the name of Lavoisier, who was executed in 1794. In resuming publication the editors explain the interruption by saying that it was because of the necessity of busying themselves with the defense of the Republic, the events of the Revolution and the public occupations and functions of the authors. In 1816 the second series of the journal was commenced under the name *Annales de chimie et de physique.* The ninth series began in 1914, once more under the original name *Annales de chimie.* The other part of the ninth series is published as *Annales de physique.*

" A second journal of very great importance was founded in 1832 under the name *Annalen der Pharmacie.* The editors were Brandes, Lorenz, Geiger and Liebig. Volume 25, published in 1838, bears the names of Dumas of Paris, Graham of London and Liebig, evidently an attempt to make the journal international. Apparently this did not prove successful, for with Volume 41, four years later, we find only the names of Wöhler and Liebig. In 1840 the name was changed from *Annalen der Pharmacie* to *Annalen der Chemie und Pharmacie* and this name continued till the death of Liebig in 1873. In 1874 we find the name which is still retained, Justus Liebig's *Annalen der Chemie.* Through the middle of the nineteenth century the *Annalen* was doubtless more valuable than any other journal for the development of chemistry. It remains one of our most valuable journals but its relative value has decreased for three reasons — the growth of the journals of national societies, the establishment of special journals for various fields and the fact that it has become exclusively a journal of organic chemistry.

" *Silliman's Journal,* which later became the *American Journal of Science,* was organized in 1818. This has published some chemical articles throughout its history but when Professor Remsen and others began the intensive study of organic chemistry in the seventies they did not find that journal a very suitable medium of publication. This led to the establishment of the *American Chemical Journal* in 1879. For the following thirty years that journal contributed much toward the development of chemistry in America and to the recognition of the work of American chemists abroad. During that period it was more often quoted than any other American journal. In 1913 we had the good fortune to incorporate it in our own *Journal.*

" Just as it was in England that the first scientific journal, the

Philosophical Transactions, appeared, so it was in England, again, that the first representative of the group of journals which has become the most important of all, was published. The *Quarterly Journal* of the Chemical Society of London began in 1847. (The Chemical Society had published previously, however, the '*Memoirs and Proceedings,*' Vols. I to III, 1841–43, 1843–5, 1845–47, containing original papers and some abstracts.) It was followed by the *Bulletin de la Société chimique de Paris* in 1864, the *Berichte der deutschen chemischen Gesellschaft* in 1868, the *Gazzetta chimica italiana* in 1871, and our own *Journal of the American Chemical Society* in 1876. These journals fulfill, more nearly than any others the function of the older volumes of the *Annalen* in furnishing their readers with an account of researches from all fields of chemistry. I believe we are justified in thinking our own *Journal* performs this function more fully than any other journal published at the present time. In these days of intense specialization it is very important for us to retain some knowledge of fields remote from our own. President Remsen once told me that in his student days he read the older volumes of the *Annalen* till he was familiar, in a general way, with all of the important researches recorded in them. Even as late as the eighties we heard of chemists who read the *Berichte* from cover to cover and I am sure that some of those who did so gained a breadth of view that is too rare today. I should consider it a very great misfortune, especially for our younger men, if there were any important branch of chemistry which was not occasionally represented by papers in our *Journal.*"

Chemical Societies and Their Publications. The following list was furnished in the main by the Research Information Service of the National Research Council. The list of American societies is that published in *Industrial and Engineering Chemistry* **14, 1141** (1922) with further details obtained directly from the secretaries.

ARGENTINE REPUBLIC

Asociación química Argentina, Buenos Aires (Prior to 1921 called Sociedad química Argentina).
Anales.

AUSTRALIA

Society of Chemical Industry of Victoria, Melbourne (1900)
Bulletin, 1887–. (In progress?)

BELGIUM

Société chimique de Belgique (Est. 1887 as Association belge des chemistes; present name since 1904), membership 425, dues F. 15 a year.
Bulletin, 1887–.

Federation des industries chimiques de Belgique.
Bulletin. 1921–.

(Chemical Abstracts list states: "Bound with Bulletin de la société chimique de Belgique.")

CANADA

Canadian Institute of Chemistry (1916), membership 257 (1921), initiation fee $10, annual dues $10.

Canadian Chemistry and Metallurgy 1916–. (v. 1–4 have title *Canadian Chemical Journal.*)

CZECHOSLOVAK REPUBLIC

Společnost pro průmysl chemický v kralovství českem Prague.

FRANCE

Société chimique de France. (Est. 1857 as Société chimique de Paris; present name since 1906), membership 1000, initiation fee F. 50, annual dues F. 60.

Bulletin, 1858– (From 1892, i.e. 3. ser. t. 7, the numbers comprise two parts, "Mémoires" and "Travaux étrangers" or abstracts, paged to form two volumes annually; the Memoires are the old numbered volumes, the Travaux étrangers the even numbers).

Société de chimie industrielle.

Chimie et industrie, 1918–.

Bulletin, No. 1– Oct. 1921–.

Société de chimie biologique.

Bulletin, 1919–.

Association des chimistes de sucrerie et de distillerie de France et des colonies (1882).

Bulletin, 1883–.

GERMANY

Deutsche chemische Gesellschaft zu Berlin (1867), membership 3000, dues $2, publications at reduced prices to members, *Berichte* $10, *Zentralblatt* $15.

Berichte, 1867–.

Chemisches Zentralblatt, since 1897 (founded 1830).

Bibliographia chimica, 1922–.

A number of handbooks are published by the society.

Verein deutscher Chemiker. (1887; absorbed Verein analytischer Chemiker, founded 1878; was Deutsche Gesellschaft für angewandte Chemie, 1887–1895).

Zeitschrift für angewandte Chemie, 1887– ("und *Zentralblatt für technische chemie*" added to title 1908 to date). Absorbed *Chemische Industrie* 1920 and *Chemische Zeitschrift* about 1921.

Verein zur Wahrung der Interessen der chemischen Industrie Deutschlands.

Die chemische Industrie. 1877–. (This is now printed as Wirtschaftlicher Teil of the *Zeitschrift für angewandte Chemie*).

GREAT BRITAIN

Chemical Society, London (1841), membership 3900, entrance fee £3, dues £3.

Memoirs and *Proceedings* 1841–47.

Journal, v. 1– (1847–) (v. 1–14, 1847–62, have title *Quarterly Journal;* from v. 33– (1878–) the Journal is divided into two sections, viz.: *Transactions* and *Abstracts,* forming separate volumes).

Proceedings, 1885–1914 (discontinued as a separate issue; v. 1–5 have title "Abstract of the proceedings").

Annual reports on the Progress of Chemistry, 1904–.

Jubilee volume (history of Society, 1841–91).

Memorial Addresses 1893–1913, two volumes.

Society of Chemical Industry (1881), membership 5000, initiation fee, £1 1s., dues £2 10s.

Journal, 1882– (monthly, until 1902, then twice a month until 1923 when it became a weekly. The *Review* was published as part of the *Journal* from 1916–1923.) Beginning Jan. 1, 1923, a weekly called *Chemistry and Industry* takes the place of the *Review* and is published as the official organ of the Federal Council for pure and applied chemistry. This is bound with the Journal for members, but paged separately.

Reports of the progress of Applied Chemistry, 1916–.

Society of Public Analysts and other analytical chemists. (Est. 1874 as "Society of Public Analysts"; present name since 1907.)

The Analyst, 1877–.

Faraday Society of London (1903).

Transactions v. 1–. 1905–.

Oil and Colour Chemists' Association.

Journal.

Society of Dyers and Colourists.

Journal.

Society of Leather Trades' Chemists.

Journal.

HOLLAND

Nederlandsche Chemische Vereeniging (1903).

Chemisch Weekblad, 1903–.

Recueil des travaux chimiques des Pays-Bas, 1882–. (Taken over by the society in 1920.)

Vereiniging van de Nederlandsche chemische Industrie, joined the other society, 1920, in publication of *Chemisch Weekblad.*

ITALY

Associazione Italiana di chimica generale ed applicata.

Gazzetta chimica italiana, 1871–.

In this journal were published from 1903 the "*Rendiconti*" of the Società chimica di Roma which merged with the corresponding society at Milan to form Società chimica italiana.

Società di chimica industriale di Milana (1895), membership 450, entrance fee 10 lire, dues 60 lire.

Annuario, 1896–.

Giornale di chimica industriale ed applicata, 1919–.

Published by the two Italian societies and also the official organ of the Federazione Nazionale delle Associazione fra industriali chimici.

JAPAN

Nippon Kwagaku Kwai (Chemical Society of Japan; organized 1878 as Tokyo Kwagaku Kwai, i.e. Chemical Society of Tokyo; present name since 1921).

Nippon Kwagaku Kwai Shi (*Journal. . .*), 1880–.

Kogyo Kwagaku Kwai (Society of Chemical Industry, 1898).

Kogyo Kwagaku Zasshi (*Journal of chemical industry*) 1898–.

POLAND

Polskie Towarzystivo Chemiczne (Polish Chemical Society)

Roczniki Chemji, 1921–.

PORTUGAL

Sociedade chimica portuguesa (1912).

Revista de chimica pura e applicada, 1916–19 (possibly discontinued).

RUMANIA

Societăte de chimie din România.
Buletinul.

RUSSIA

Russkoie fizikochimitcheskoie obschestvo (Russian physical and chemical society).
Zhurnal (Journal) 1869–.

SOUTH AFRICA

Chemical, Metallurgical & Mining Society.
Journal.

South African Chemical Institute (prior to 1921 named South African association of analytical chemists).
Journal.
Proceedings.

SPAIN

Sociedad española de física y química, Madrid.
Anales.

SWEDEN

Kemistsamfundet i Stockholm
Svensk Kemisk Tidskrift, 1899– (1887–88) has title *Kemiska Notiser*). This is also the official organ of the sections at Lund and Upsala, as well as for the industrial society.

K. Svenska Vetenskapsakademien
Arkiv för kemi, mineralogi och geologi 1903; this had previously appeared as the chemical section of the publication of the Swedish Academy of Sciences; articles may be either in Swedish or German, and chemistry has had the most space so far.

SWITZERLAND

Société suisse de chimie (Schweizerische chemische gesellschaft)
Helvetica chimica acta, 1918–.
Articles are published in French, German or Italian.

UNITED STATES

American Chemical Society (1876), sec. Charles L. Parsons, 1709 G St., N. W., Washington, D. C., membership 14,400, dues $15 (students $10), meets April and September.
Proceedings, 1876–78.
Continued in the following:
Journal, v. 1.– , 1879– , 3011 pages in 1922. In July, 1893, the *Journal of Analytical and Applied Chemistry* and in January, 1914, the *American Chemical Journal* were incorporated with this publication.
Review of American Chemical Research (v. 1–7, April 1895–Dec. 1901, appeared in Technology Quarterly, v. 8–14), v. 3–12, 1897–1906, was issued with v. 19–28 of the Journal and continued as the following publication:
Chemical Abstracts, 1907– , 4719 pages in 1922.
Journal of Industrial and Engineering Chemistry, 1909– , 1198 pages in 1922, not counting advertisements. Since 1922 — *Industrial and Engineering Chemistry.*
Chemical Reviews, 1924.

American Associations of Textile Chemists and Colorists, sec. W. E. Hadley, Clark Thread Co., Newark, N. J. Organized 1921, membership 475, dues $5.

The American Dyestuff Reporter is the official organ and contains the proceedings.

American Ceramic Society, sec. Ross C. Purdy, Ohio State University, membership 1100, dues, personal $7.50, corporation $25, organized 1899 and publication of *Journal* began same year. In 1922 this contained pages of 940 original papers, 350 of abstracts and 350 of discussions, making 1640 pages. Society meets in February and August.

American Electrochemical Society, sec. Colin C. Fink, Columbia University, New York, organized 1908, membership 2100, initiation fee $5 dues $8, meets in April and September.

The *Transactions,* begun 1902, is issued twice a year and contains 400 to 500 pages per year.

American Institute of Chemical Engineers, sec. J. C. Olsen, Polytechnic Institute of Brooklyn, N. Y., organized 1908, membership 575, initiation fee $15 dues, active $18, junior $12, meets June and December.

The Transactions, issued annually since 1908, contains 500–700 pages.

American Institute of Fertilizer Chemists, sec. W. J. Gascoyne, Jr. 27 S. Gay St., Baltimore, Md., organized 1919, membership 26, initiation fee $10, dues $10 meets usually in July.

American Leather Chemists Association, sec. H. C. Reed, 22 E. 16th St., New York, organized 1903, membership 500, dues $10, meets in May or June.

The *Journal,* begun 1906, is issued monthly and contains about 700 pages per year.

American Oil Chemists Society, sec. Thomas B. Caldwell, Law & Co., Wilmington, N. C., organized 1910, membership 300, dues, individual $6, corporation $10, meets in May.

The "Chemists' Section" of the *Cotton Oil Press* is the official monthly publication, about 150 pages per year.

American Pharmaceutical Association, sec. H. V. Arny, 115 W. 68th St., New York, organized 1852, membership 3000, dues $5, meets annually. The first publication was *Proceedings* in 1852.

The *Journal* contains about 1000 pages per year and the *Year Book* about 500.

American Society of Biological Chemists, sec Victor C. Myers, 308 E. 20th St., New York, organized 1907, membership 250, dues $2, meets last week in December. The proceedings of its meetings have always been published in the *Journal of Biological Chemistry,* which was founded in 1905 as an independent publication but became the property of the Society in 1919. This is monthly, about 4 volumes per year aggregating 3116 pages in 1922, subscription independent of society dues.

American Waterworks Association, sec John M. Divers, 153 W. 71st St., New York, organized 1881, membership 1777, initiation fee $5–$10, dues $7–$15, meets annually.

Journal, founded in 1881, contains 800 to 1000 pages per year.

Association of Official Agricultural Chemists, sec. R. W. Balcom, Box 290, Penn Ave. Station, Washington, organized 1884, dues, institutions $5, meets usually in November.

Prior to 1913 the proceedings were published by the U. S. Department of Agriculture as *Bulletins* of the Bureau of Chemistry.

Journal, begun 1915, about 600 pages per year.

Official and Tentative Method of Analysis — republished from time to time.

Technical Association of the Pulp and Paper Industry, sec. W. G. MacNaughton, 18 E. 41st St., New York, organized 1915, membership 500, initiation fee $5, dues $15, meets spring and fall. The proceedings of the conventions were published 1917–1921.

List of Chief Chemical Journals

This list is taken from the longer list of 1010 journals which are regularly abstracted by *Chemical Abstracts*, as published in Oct. 20 number of vol. 16 (1922) of *Chemical Abstracts*. The longer list includes hundreds of journals which are only part chemistry but which are regularly searched for the chemical articles they contain, while in the shorter list below only those are given which are distinctly chemical.

The information given is taken bodily from *Chemical Abstracts*.

The list as published in *Chemical Abstracts* contains numbers after each journal which designate libraries in the United States which receive it regularly. Information is given as to which libraries are willing to lend journals and which have facilities for photostating and translating. This makes it possible for the chemist to get in minimum time any information he needs. This list can be purchased from Editor of *Chemical Abstracts* for 25 cts.

Title and order. In the full titles, given just as they appear on the periodicals, the letters which constitute the official abbreviations used in the abstracts are printed in **black-face** type.

The names of the periodicals are arranged in the alphabetical order of *their abbreviations*.

Frequency of appearance. The following symbols are used: *a* annual, *sa* semi-annual, *q* quarterly, *bm* bimonthly, *m* monthly, *sm* semimonthly, *bw* biweekly, *w* weekly, *sw* semiweekly, *irr* irregular.

Volume. If the number of volumes per year is other than one, the number is next given. The volume number of the first issue in 1922 (or if another year the year is given) is printed in bold-face type. If the first issue is not number 1 of the volume its number is given in parentheses after the volume number. In some cases the "whole number" is given in this way. If the volume number belongs to a new series, this is indicated in brackets placed before the volume; [3] 29 (4) states that the first issue in 1922 is number 4 of volume 29 of series 3.

Price. The letter *d* following a price means "domestic" (that is, in the country of publication); *f* means "foreign" (Postal Union). Prices in parentheses are for single numbers; prices not so enclosed, unless otherwise stated, are for a year's subscription. In some instances an asterisk is used to indicate that the members of some organization enjoy a lower rate than that given. It is to be noted that prices of German journals are far from constant at the present time. F = franc, f = florin, L = lira, K = krone (Austria) or krona (Sweden), R = ruble, Re, Rs = rupee, rupees, s = shilling, d = penny, Y = yen, M = mark, pfg. = pfennig.

Publisher. The name and address of the publisher or person to whom orders are to be sent are given in italics.

Anales de la **sociedad española** de fisica y quimica. *m.* except Aug and Sept. 20 (189). 15 pestas *d. Manuel Tomás Gil, Corredera Baja de San Pablo*, núm. *59, Madrid, Spain.*

Analyst, The. *m.* 47 (550). 30s* (3s). *Simpkin, Marshall, Hamilton Kent & Co. Ltd., 2 4, 6, 8 Orange St., Leicester Sq., London, W. C. 2, England.*

Annalen der Chemie, Justus Liebig's. *irr* 2 to 4 vols. of 3 nos. each. **426.** M150. *C. F. Winter'sche Verlagshandlung, Rosstr. 6, Leipzig, Germany.*

Annales de **chimie.** *bm* 2 vols. 17 F32*d*, F40*f* (or F60*d*, F70*f* for both Annales de chimie and Annales de physique). *Masson et Cie, 120 Boulevard St.-Germain, Paris (VIe) France.*

Annales de **chimie analytique** et revue de chimie analytique. Name changed to Annales de chimie analytique et de chimie appliquée et revue de chimie analytique reunies, which see.

Annales de chimie analytique et de chimie appliquée et revue de chimie analytique reunies. *m* [2] 4. F20 (F2)*d*, F24*f*. *M. Crinon, 20 Boulevard Richard-Lenoir, Paris. (11e), France.*

Annali di chimica applicata. Name changed to Giornale di chimica industriale to form Giornale di chimica industriale ed applicata, which see.

Annales de chimie et de physique. Now two separate journals, **Annales de chimie** and **Annales de physique**, which see.

Annales des falsifications et des fraudes, Les. *m* 15(159). F25(F4)*d*, F30*f*. *M. Filaudeau 42 bis rue de Bourgogne, Paris (7e), France.*

Berichte der deutschen chemischen Gesellschaft. *irr* about *m* 55. M110**d*, $10.00 U. S. *Deutsche chemischen Gesellschaft, Jordanstr. 1. Berlin, S. O. 36, Germany.*

Bibliographia chimica (Internationaler Literatur-Anzeiger für Chemie, Chemische Technologie und alle Grenzgebiete). *m* 1. M50*d* M100*f*. Issued free with Berichte der deutschen chemischen Gesellschaft or with Zeitschrift für angewandte Chemie. *Verlag Chemie, G. m. b. H., Nurnbergerstr. 48 I, Germany.*

Biochemical Journal, The. *bm* 16. 35s*d*, $13.25 U. S. *Cambridge University Press, Fetter Lane, London, E. C. 4, England; University of Chicago Press, Chicago, Ill.*

Biochemische Zeitschrift. *irr* 8 to 10 vols. 126(5&6). M168 per vol. *Julius Springer, Link-Str. 23–24, Berlin, W. 9 Germany.*

Brennstoff-Chemie. *sm* 3. M120(M4. 50)*d*. *Verlag von W. Giradet, Essen, Germany.*

Bulletin of the National Research Council. *irr* 3.Pt.II(17). $5 per vol. Sold separately at varying prices. *National Research Council, 1701 Massachusetts Ave., Washington, D. C.*

Bulletin de la société chimique de Belgique, *m* 31. *A. J. J. Vandevelde, Houtbriel 22 Grand, Belgium.*

Bulletin de la société de chimie biologique. *m* 4. F25(F3)*d*, F30*f*. *Masson et Cie, 120 Boulevard St.-Germain. Paris (6e), France.*

Bureau of Mines, Bulletins, Circulars, Reports of Investigations and Technical Papers. Limited edition, free. *Superintendent of Documents, Government Printing Office, Washington, D. C.*

Bureau of Standards, Bulletins, Circulars, Scientific and Technical Papers, etc. Price varies. *Superintendent of Documents, Government Printing Office, Washington, D. C.*

Canadian Chemical Journal. Name changed Jan. 1921, to Canadian Chemistry and Metallurgy, which see.

Canadian Chemistry and Metallurgy. *m.* 6. $3.($.40)*d* and *f*. *72 Queen St., West, Toronto, Canada.*

Chemical Age, The **(London).** *w* 2 vols. 6(134). 21s(6d)*d*,26s*f*. *Benn Brothers, Ltd., 8 Bouverie Street, London, E. C. 4, England.*

Chemical Age, (New York). *m* 30. $3($.50)*d*, U. S. Possessions, Cuba and Mex., $4*f*, $3.50 Can. *McCready Publishing Co., 381 4th Ave., New York City.*

Chemische Apparatur. *sm* 9. M48*d*. *Otto Spamer, Heinrichstr. 9, Leipzig-R, Germany.*

Chemische Industrie, Die. Combined in Jan., 1921, with Zeitschrift für angewandte Chemie, which see.

Chemical and Metallurgical Engineering. *w.* 2 vols. 26. $4($.25)*d*, U. S. Possessions, Argentina, Bolivia, Canada, Canal Zone, Colombia, Cuba, Dominican

Republic, Ecuador, Honduras, Mex., Nicaragua, Peru, Salvador, Shanghai, China and Spain, $8*f*. *McGraw-Hill Co., Inc., 10th Ave. at 36th St., New York City.*

Chemical News and Journal of Industrial Science, The. *w* 2 vols. 124(3221). 1/12s (6d, post free 7d) *d* and *f*. *The Chemical News, 97 Shoe Lane, London, E. C. 4, England.*

Chemical Reviews *q*. $5**d*. $5.50*f*. *Williams & Wilkins Co., Baltimore, Md.*

Chemical Technology, The, (Japan). (Kwagaku-Kogei.) *m* 6. Y4.40(40 sents plus 1 sent 5 rin postage)*d*, Y5.76(YO.48)*f*. *Kwagaku-Kogei-sha, 122 Takehayaschi-cho, Koishi Kawaku, Tokyo, Japan.*

Chemische-technische Wochenschrift. *w* 6. *Verlagsgellschaft m. b. H., Bülowstr. 66, Berlin, W. 57, Germany.*

Chemiker-und Techniker-Zeitung, Allgemeinen österreichische. *sm* 40. *Hans Urban, Gerthoferstr. 70, Wien, XVIII/2, Austria.*

Chemical Trade Journal and Chemical Engineer, The. *w* 2 vols. 70(1807). 19s6*d*(6d plus postage)*d*, 24s British Possessions and *f*. *Davis Bros., 265 Strand, London, W. C. 2, England.*

Chemische Umschau auf dem Gebiete der **Fette, Oele, Wachse** und **Harze.** *w* 29. M240(M5)*d*. *Verlag der Wissenschaftlichen Verlagsgesellschaft m. b. H. Postfach 40, Stuttgart, Germany.*

Chemisch Weekblad. *w* 19. f10.50(f0.25)*d* f15*f*. *D. B. Centen, O. Z. Voorburgwal 115, Amsterdam, Holland.*

Chemical World. Continued as Chemical Age (London).

Chemisches Zentralblatt. *w* 4 Bands. 93 (I&II). M1000*d*, $15 U. S. *Deutschen chemischen Gesellschaft, Jordanstr. 1, Berlin, S. O. 36, Germany.*

Chemiker Zeitung. 3 times a week. 46. M680*d*. *Walter Roth, Cöthen, Germany.*

Chimie & industrie. *m* 2 vols. 7. F100– (F10)*d*, F110*f*. *Société de chimie industrielle 49 rue de Mathurins, Paris, France.*

Comptes rendus hebdomadaires des seances de l'academie des sciences. *w* 2 vols. 174. F120*d*, F140*f*. *Gauthier-Villars et Cie, 35 Quai des Grands Augustins, Paris 6e, France.*

Dinglers polytechnisches Journal. 26 nos a year. 337. M40*d*. *Richard Dietz, Verlagsbuchhandlung, Buchhändlerhaus 2, Berlin, W. 66, Germany.*

Elektrochemische Zeitschrift. *m* 28(7). M12– (M4)*d*, M30*f*. *A. Neuburger, Neue Winterfeldstr. 24, Berlin, W. 30, Germany.*

Fortschritte der **Chemie**, Physik und physikalischen Chemie. *irr* 17(3) *Gebr. Borntraeger, Schöneberger Ufer 12a, Berlin, W. 35, Germany.*

Gazzetta chimica italiana. *m* 1 vol. (2 parts). 52, I. L90*(L15)*d*, L130*f*. *Via Tre Novembre 154, Rome, Italy.*

Gesammelte Abhandlungen zur Kenntnis der Kohle. Price varies. *Gebr. Borntraeger, Schöneberger Ufer, 12a, Berlin, W. 35. Germany.*

Giornale di chimica applicata. Combined in Mar., 1920, with Giornale di chimica applicata to form Giornale di chimica industriale ed applicata, which see.

Giornale di chimica industriale. Combined in Mar. 1920, with Giornale di chimica applicata to form Giornale di chimica industriale ed applicata, which see.

Giornale di chimica industriale ed applicata. *m* 4. L75(L7.50)**d*, L100*f*. *Via S. Paolo, 10, Milan (3), Italy.*

Giornale di farmacia, di chimica e di scienze affini. *m* 71, L12(L1.50)*d*, L14*f*. *Cav. Paolo Fiora, Direttore della "Mutua farmaceutica italiana" Filiale di Torino, Via Garibaldi 31, Torino, Italy.*

Helvetica chimica acta. 6 to 8 numbers a year. 5. F25*(F10)*d*, F25 plus F3.60 postage *f. Georg & Co., Basel, Switzerland.*

Industrial and **Engineering Chemistry**, The. *m* 14, $7.50*($.75*)*d*, $7.50 plus $1 postage *f. Charles L. Parsons, Sec'y, 1709 G St., N. W., Washington, D. C.*

Industrie chimique, L'. *m* 9(96). F40*d*, F45*f. H. Mounier, 8 rue de Miromesnil, Paris, France.*

Journal of the **American Chemical Society.** *m* 44. $7.50*($.75*)*d*, $7.50 plus postage *f. Charles L. Parsons. Sec'y, 1709 G St., N. W., Washington, D. C.*

Japanese Journal of **Chemistry.** 10 nos. a year. *National Research Council of Japan, Tokyo, Japan.*

Journal of the **Association** of **Official Agricultural Chemists.** *q* 5. $5d, $5.50 or 27*sf.* per vol. *Association of Official Agricultural Chemists, Box 290, Pennsylvania Ave. Sta., Washington, D. C.*

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Recueil des memoires les plus intéressants de chimie et d'histoire naturelle, contenus dans les actes de l'académie d'Upsal et dans ceux de l'académie royale des sciences de Stockholm, Paris, 2 vols. 1764.

Répertoire de chimie, pharmacie, matière pharmaceutique et de chimie industrielle, Louvain, 2 vols. 1828–30.

Nouvelle répertoire (etc.), Louvain, 1 vol. 1831.

Répertoire de chimie, de physique, et d'applications aux arts. Paris, 1 vol. 1837.

Répertoire de chimie scientifique et industrielle, Paris, 4 vols. 1837–38,
Continued under the title:
Répertoire de chimie, Paris, 1 vol. 1839.

Répertoire de pharmacie, de chimie, de physique, d'hygiene publique, de la médecine légale et de thérapeutique, Bruxelles, 1 vol. 1842.

Repertorio italiano di chimica e di farmacia, Firenze. 1865.

Repertorium der analytischen Chemie für Handel, Gewerbe und offentliche Gesundheitspflege, Hannover (later), Hamburg, 7 vols. 1881–87,
Incorporated with Zeitschrift fur die Chemische Industrie, *and continued under the title:* Zeitschrift für angewandte Chemie.

Repertorium der Chemie und Pharmacie, St. Petersburg. 1837.

Repertorium der organischen Chemie, Leipzig, 2 vols. in 5 parts. 1826–28,
Continued under the title:
Repertorium der neuen Entdeckungen in der organischen Chemie, Leipzig, 2 vols. 1829–33.

Repertorium der neuen Entdeckungen in der unorganischen Chemie, Leipzig, 2 vols. 1826–27.

Repertorium für organische Chemie, Zurich, 3 vols. 1841–43.

Repertorium für Pharmacie und praktische Chemie in Russland, St. Petersburg. 1842.

Reports of the Royal College of Chemistry, London. 1849.

Revista quimico-farmecéutica de Madrid, Madrid. 1851.

Revue de chimie analytique, Paris. 1893–.

Revue de physique et de chimie et de leurs applications industrielles, Paris. 1896–.

Revue des industries chimiques et agricoles, Paris, 14 vols. 1878–91.

Revue des industries et des sciences chimiques et agricoles, Paris, 6 vols. 1873–82.

Revue hebdomadaire de chimie scientifique et industrielle, Paris, 7 vols. 1869–75.

Revue scientifique et industrielle des faits les plus utiles et les plus curieux observes dans la medecine, l'hygiene, la physique, la chimie, la pharmacie, l'economie rurale et domestique, l'industrie nationale et étrangère, Paris, 41 vols. 1840–52,

Followed by:

Moniteur (Le) scientifique du chimiste et du manufacturier, Paris, 5 vols. 1857–63,

Continued under the title:

Moniteur (Le) scientifique. Journal des sciences pures et appliquées, Paris, 7 vols. 1864–70,

Continued under the title:

Moniteur scientifique — Quesneville, Paris, 21 vols. 1871–91.

Riforma (La) chimica, Napoli. 1897–.

Rivista di chimica medica e farmaceutica, tossicologia, farmacologia e terapia, Totino, 3 vols. 1883–85.

Rundschau für die Interessen der Pharmacie, Chemie, und der verwandten Fächer, Leitmeritz, 11 vols. 1875–85. (New series) Prag, 3 vols. 1886–92.

Russisches Jahrbuch der Pharmacie, Riga, 6 vols. 1803–08,

Continued under the title:

Russiches Jahrbuch für die Chemie und Pharmacie, Riga, 2 vols. 1809–10.

Savonnerie (La), Zurich, 5 vols. 1887–92.

Schweizerische Wochenschrift für Chemie und Pharmacie, Zürich. 1848–.

Skandinaviens kemisk-tekniske Centralblad for Danmark, Sverige, Norge og Finland, Kjobenhavn, 10 vols. 1882–91.

Technisch-chemisches Jahrbuch, Berlin, 12 vols. 1880–91.

Technisches Centralblatt, Halle. 1884.

Tidsskrift (Nyt) for Fysik og Kemi, Kjøbenhavn. 1896.

Ueber die neueren Gegenstände in der Chemie, Breslau, Hirschberg und Lisa, 11 parts. 1791–1802.

Vermischte Abhandlungen der physisch-chemischen Warschauer Gesellschaft, Warschau und Dresden, 1 vol. 1768.

Vierteljahresschrift für technische Chemie, Quedlinburg, 10 vols. 1859–69.

Zeitschrift für das chemische Grossgewerbe, Berlin, 7 vols. 1876–82.

Zeitschrift für die chemische Industrie, Berlin, 2 vols. 1887.

Continued under the title:

Zeitschrift für angewandte Chemie, Berlin. 1887–.

Zeitschrift für Elektrotechnik und Elektrochemie, Halle. 1894.

Continued under the title:

Zeitschrift für Elektrochemie.

A national union list of serials is in preparation by the H. W. Wilson Co. This will show in what libraries each serial may be found.

CHAPTER VI

SECONDARY PUBLICATIONS

Abstracts, Reviews Bibliographies and Compendiums

The primary publications are the journals which contain the facts of chemistry as they are dug out by their discoverers. Raw materials from field or mine must be more or less manufactured before they enter into commerce. The facts of chemistry must be gathered, sorted, stored and worked over before they are used. Abstract journals and bibliographies locate and index them while reviews and compendiums assemble and arrange them. On these ordered facts are built our systems and theories and certain of them are selected to be put into text-books for the instruction of chemists to be.

These publications which are concerned with the presentation of material that has already been published may be called secondary publications. This does not mean that they are of secondary importance for they are indispensable to the student and to the research chemist.

Abstract Journals.

With the growth of chemistry, its division and subdivision into numerous fields, and the rapid expansion of these, with the increase in number and variety of contributions published by the ever growing host of investigators, the task of searching all the journals has become too great for the individual. What is impossible for one soldier is easy for a disciplined army. The task of reading, digesting, and abstracting chemical literature has been taken up by the great national societies. *Chemical Abstracts* published by the American Chemical Society is the syndicated work of one editor, 2 associates and 45 assistant editors, supported by approximately 250 abstractors. These regularly and systematically examine over a thousand scientific journals (1922) of all sorts and make abstracts of all articles therein of interest to chemists. About 100 of these journals are strictly chemical, the rest being in contiguous fields. In 1923, 24,256 articles were abstracted, 3924 pages being required for printing the abstracts and 332 more for author index, and 687 for subject index and formula index.

This illustration gives an idea of the intensity of chemical activity at the present time and also shows the power and usefulness of a great chemical organization. The cost of the preparation and publication of *Chemical Abstracts* is enormous (approximately $100,000 per year) but being distributed over such a large membership the tax on the individual is small. Without abstract journals the chemist would be well nigh hopeless but by their aid the enormous mass of information which is so rapidly accumulating is made available to the humblest student. Probably no realm of human knowledge is so well digested and cataloged as is chemistry; in no other subject can a fact be located as readily and as certainly.

However wonderful the abstract journals are, they are of little benefit unless one learns how use them. One must know their scope and their limitations, how they are arranged and how they are indexed. The thorough acquaintance that is desirable can come only by long association but an attempt is made below to introduce them to the student in the hope that they may become his intimate friends.

It is only in comparatively recent years that abstracts have been completely segregated into special journals. In the earlier times nearly all chemical journals carried some sort of digest or review of articles published outside of their own pages, particularly those from other countries, each aiming to keep its readers informed as to the progress of chemistry as a whole. There was no uniformity; sometimes an important article would be translated and published almost entire while only a few extracts would be made from others, the majority going unnoticed. There was no attempt to make the service comprehensive; each editor presented such a selection as he thought would interest his readers.

The investigator of the earlier literature must search through all the journals of the period and get what he can. A list is given below taken from Miss Sparks' useful book [1] of the chief journals which contain abstracts or reviews and the periods over which such abstracts were published. In most cases the abstracts have been given up or have been segregated or made into a separate journal.

Some of the Principal Index, Abstract and Review Serials, in the Order of Time Covered.

General Chemistry

1789–1870 Annales de chimie et de physique; a few abstracts to 1873
1822–1849 Jahresbericht über die Fortschritte der Chemie und Mineralogie (Berzelius)

[1] Chemical literature and its use -- Marion E. Sparks. 2nd ed. Urbana, 1921 p. 34–37.

1830–date Chemisches Zentralblatt; name varies
1832–1860 Annalen der Chemie; abstracts were never numerous and gradually decreased
1834–1873 Journal für praktische Chemie; abstracts practically ceased in 1873.
1840–1858 The Chemist; ceased publication
1841–date Journal of the Chemical Society, London; the volumes for 1841 to 1846 had title Memoirs, but index for them is in first collective one
1842–1859 The Chemical Gazette; continued by the Chemical News
1858–date Bulletin de la société chimique de France
1859–date Chemical News; abstracts few but often long, even to reprints
1867–1896 Berichte der deutschen chemischen Gesellschaft; after this date the abstracts are in the Chemisches Zentralblatt
1877–date Chemiker-Zeitung: Repertorium; sometimes bound separately
1879–1905 Journal of the American Chemical Society
1891–date Jahrbuch der Chemie (Meyer); selected abstracts only
1899–1918 Revue générale de chimie pure et appliquée; abstracts section called Répertoire, and sometimes bound separately
1901–date International Catalogue of Scientific Literature; Chemistry; this is an index serial, no abstract of contents of papers
1904–date Chemical Society, London: Annual Reports; this reviews the progress made, noting important articles only
1907–date Chemical Abstracts; has collective index for 10 year period to 1916

Analytical

1862–date Zeitschrift für analytische Chemie
1877–date The Analyst
1896–date Annales de chimie analytique et de chimie appliquée
1908–date Annales des falsifications (now, et des fraudes)

Physical

1899–1904 Zeitschrift für physikalische Chemie
1894–1907 Jahrbuch der Elektrochemie und angewandten physikalischen Chemie
1896–1906 Journal of Physical Chemistry
1903–1912 Journal de chimie physique
1904–date Fortschritte der Chemie, Physik und physikalische Chemie, this was an abstract serial, 1904–09 with title Physikalisch-chemisches Centralblatt and was called "international"; with the new name it became a review serial

Technological

1855–date Jahresbericht über die Leistungen der chemischen Technologie (Wagner)
1877–date Chemiker-Zeitung: Repertorium
1880–1905 Technisch-chemisches Jahrbuch
1882–date Journal of the Society of Chemical Industry
1887–1918 Zeitschrift für angewandte Chemie; abstracts 1919 on are technological section of Chemisches Zentralblatt; the Zeitschrift was preceded by Repertorium der analytischen Chemie, 1881–87
1898–date La revue des produits chimiques; organ of Le Cercle de la Chimie
1909–date Journal of Industrial and Engineering Chemistry; the abstracts in this began in 1914, and are for U. S. and State publications

1914–1917 Journal of Chemical Technology; for chemists of the British empire; seems to have been stopped by war
1914–date L'industrie chimique
1916–date Reports of the Progress of Applied Chemistry, by the Society of Chemical Industry; review serial, similar to the Annual Reports of the Chemical Society
1918–date Chimie et industrie
1919–date Giornale di chimica industriale ed applicata.

At the present time comprehensive abstracts are published by the American, English, German, and French chemical societies. While the ground covered is largely the same yet each society has its own aims and methods so that the resulting abstracts differ considerably, apart from the matter of language. Each abstract journal excels the rest in some respects and falls behind in others. Each society is limited as to the amount that can be spent on preparing and publishing abstracts, hence if more abstracts are printed they must be shorter; if one workman spreads a gallon of paint over twice as large a surface as another, he can not put it on so thick. If he puts all the paint on the house he will have none left for the fence, so if the abstractors devote an extra amount of attention to one sort of chemistry they may have to skimp somewhere else.

Chemical Abstracts. In 1907 the American Chemical Society began the publication of *Chemical Abstracts*. This is the most extensive and inclusive abstract journal ever published. In addition to covering the strictly chemical journals it goes into those of the bordering sciences and even into trade journals in search of any and every sort of new chemical information. After the combing process is completed, the editors check up the articles they have gathered with those noticed in the other abstract journals and if they find that they have missed an article, it is promptly abstracted either directly or through the foreign abstract. This is done, of course, with the approval of the editors of the other journals. Hence if an article of chemical interest is abstracted in any journal it will be noticed in *Chemical Abstracts* — and hundreds are found here which are not in the other abstract journals. *Chemical Abstracts* excels all others as an index and guide to chemical information, whether it is found in the regular chemical journals or tucked away in some place where no one would ever think of looking for it. A vast deal of information is brought together which is not strictly chemical but which is apt to be of service to chemists. Patents of all countries are abstracted in so far as they relate to chemistry, no partiality being shown to American patents. By being more extensive, *Chemical Abstracts* is necessarily somewhat less intensive. It locates more articles for

the searcher for information but frequently supplies less of the substance of a particular article than may be found in some other abstract journals. If the reader has access to the journal containing the original article, he has little use for the abstract anyway, except as it guides him to the original; he cares little whether the abstract be full or meagre but if he has to depend on the abstract to supply him with a complete working knowledge of the article, he is greatly interested in the fullness of the abstract. It may be said that the research chemist can seldom afford to rely on any abstract, however long, for the substance of an article which has an important bearing on his problem. He needs more than the bare facts, such as formulae, melting points and boiling points; he must get the atmosphere of the article and the point of view of its author. All the branches of pure and applied chemistry are looked after by *Chemical Abstracts,* the abstracts being divided into 29 heads, each cared for by assistant editors and abstractors particularly interested in that line. It is the policy of *Chemical Abstracts* to make use of a large number of abstractors because of the desire to get papers into the hands of specialists in the subjects involved. To make a good abstract one needs to be trained in abstracting as well as thoroughly familiar with the paper and the subject which it covers. The abstract journal which utilizes only a limited number of abstractors has the advantage that its abstractors are likely to be more experienced as abstractors but has the disadvantage that many abstracts are bound to be made by individuals who are not in a position to appreciate fully all of the points brought out in the paper nor properly to evaluate them. Special efforts in training abstractors have been made so as to minimize the disadvantage of having a larger number of abstractors. The other abstract journals depend upon a comparatively small number of abstractors.

A record, such as an abstract journal constitutes, is of little value if the information is not made readily and certainly available by thorough indexing. More attention has been given to the subject index of *Chemical Abstracts* than to any other feature. The formula index is of particular service to the organic chemist. In 1917 a comprehensive index was issued for the ten years period, 1907–1916. This contains many entries which are not in the annual indexes.

American chemists of all varieties have kept together in one great society which has aimed to further the interests of chemistry both pure and applied: *Chemical Abstracts* has endeavored to keep its balance between academic and industrial chemistry and to cover both.

British Abstracts. In Great Britain the situation is different from what it is in America; there are two great societies, the Chemi-

cal Society and the Society of Chemical Industry. Both of these have strong journals and both publish abstracts. They have amicably divided the field, the one taking pure chemistry and the other its industrial applications, including chemical patents, but beginning with 1924 they will publish abstracts jointly. The *Journal of the Chemical Society* has published abstracts since 1871. From 1871 to 1877 the first part of each monthly issue was devoted to original papers and the latter to abstracts. These were paged consecutively and bound together. The annual index made no distinction between original articles and abstracts. Starting with 1878 the two sections, though issued together, have been paged independently and are segregated in binding, the odd numbered volume being designated "transactions" and the even "abstracts." The two volumes are indexed independently. Starting with 1916 the abstracts have been further divided into part 1, "organic," and part 2, "inorganic," the two being paged independently and usually bound separately but having a common index. There are cumulative indexes for 1841–1872, 1873–1882, 1883–1892, 1893–1902, 1903–1912, and 1913–1922.

In the *Journal of the Society of Chemical Industry* until recently, the abstracts have not been segregated. They have occupied a large part of the publication since its beginning in 1882 and have been extremely important to any one looking up a technical subject. For this period one may well begin his investigations with this journal. In addition to purely technical articles, those on pure chemistry which contain data on compounds of commercial importance are noticed. Chemical patents of all countries are well and impartially covered. When the same thing is patented in a number of countries, the first patent is abstracted and the patents in other countries are all noted as they appear with number date and patentee, reference being made to the abstract of the original patent.

Starting with volume 37 (1918) the material presented has been segregated into "review," "transactions," and "abstracts" which are paged independently. One index covers all three parts the letters R, T, and A being added to the page numbers. Starting with volume 42 (1923) the "review" is replaced by a new section called "chemistry and industry," published weekly.

Beginning with volume 20 (1901) there is appended to the index a numerical list of English patents abstracted with page references and from volume 35 (1916) there are similar lists for United States, German and French patents.

French Abstracts. *The French Chemical Society* has always published abstracts in its *Bulletin.* Since 1892 these have been segregated

in a similar manner to the British and fill even numbered volumes of the *Bulletin.*

German Abstracts. The *Berichte* of the German Chemical Society carried abstracts till 1897 when the Society acquired the *Chemisches Centralblatt.* The abstracts in the *Berichte* are called *Referate* and are paged separately and usually bound separately but with the same volume number as the original articles. A reference to *Ber.* **25,** 897(1892) would be to an original article but *Ber.,* **25,** 429R(1892) designates an abstract and is to be found in the *Referate section.*

The *Chemisches Zentralblatt,* until 1897 spelled *Centralblatt* and commonly designated by *C.,* has been a great factor in the development of chemistry. It was begun in 1830 as the *Pharmaceutisches Centralblatt,* and became *Chemisch-Pharmaceutsches Centralblatt* in 1850 and assumed its present name in 1856. Till 1892 it was issued as one volume a year but since then it has been divided into two: I January-June, and II July-December, each with its own indexes. It has a volume number but is always referred to by the year thus: *C.* 1910, I, 254, or *C.* 1912, II, 459. Indexing at half year intervals is convenient if we are interested in obtaining the most recent information but is troublesome when it comes to going through back years. There are collective indexes for four year periods since 1897 which reduce the labor of a search which is to cover a long period of time.

The *Zentralblatt* has always covered German chemical patents thoroughly but until recently few from other countries have been noticed but now all are included. In 1922, 2535 German patents were abstracted and 5360 foreign. For many years there have been numerical indexes for German patents and now there are like indexes for United States, English, French, Dutch, Austrian and Swiss. In looking for a patent in the numerical index it must be remembered that German patents are not issued in the same order in which they are numbered, so D.R.P. 369,127 may be abstracted in the first half of a given year and 369,111 in the second half, while 369,145 may have been granted earlier and gotten into the abstracts for the preceding year. Hence a German patent of a given number must be searched for not only in the volume which contains the bulk of the numbers near it but in one or two volumes earlier and later.

Starting with 1919 the Zentralblatt for a year is divided into four parts instead of two. These are designated I, II, III, IV. I and III contain abstracts of " scientific " and II and IV of technical. Parts I and II are issued together, though paged separately and cover the period January to June as I did formerly. These are

to be separated in binding but are indexed together. Parts III and IV cover the latter half of the year in the same way. A reference on atomic energy *C.* 1920, III, 464 is to the scientific section, last half of year 1920.

For 1922, we have the following statistics for the Zentralblatt

Part I	1416	pages	4275	abstracts
II	1250	"	7461	"
III	1388	"	4359	"
IV	1208	"	7026	"
Total	5262	"	23,121	"

It will be seen from these figures that the average scientific abstract occupies 0.33 page and the technical 0.17 page.

Borderland abstracts. The abstract journals mentioned above are devoted solely to chemistry. There are abstract journals in contiguous fields which are often of interest to the chemist, as *Physiological Abstracts, Botanical Abstracts, Abstracts of Bacteriology, Experiment Station Record,* etc., as well as journals devoted to rather restricted fields of chemical interest which carry abstracts, as, for example, *Journal of the American Ceramic Society, Journal of the American Leather Chemists' Association, Zeitschrift für Untersuchung der Nahrungs- und Genussmittel sowie der Gebrauchsgegenstande, Journal of the American Water Works Association, American Gas Association Bulletin of Abstracts, Pulp and Paper Magazine of Canada, International Sugar Journal, India Rubber World,* etc.

Reviews

These differ from the abstract journals in that the advances of a period, usually a year, are summed up more or less critically with regard to relative importance and perspective. In the annual reviews of the present day only the outstanding articles are mentioned while the *Jahresberichte* of the past covered their fields quite completely. The growth of chemistry has rendered completeness harder to attain and the development of the abstract journals has made it unnecessary.

Annual reports. Since 1904 the Chemical Society (London) has issued *Annual reports on the progress of chemistry,* one in each major division. These are very readable and are important to those who wish a general view. Similar reports are published by the Society of Chemical Industry covering technical subjects. The American

Chemical Society has just begun (1924) the publication of *Chemical Reviews.*

Jahresberichte. In 1822 Berzelius began his great *Jahresbericht* which continued till 1849 and was in its day of immense service to investigators. It is still an important source of information on topics of that period, particularly since the originals which are quoted are frequently not accessible. It was published in Swedish and also in German.

"The *Jahresbericht* (Liebig and Kopp) 1847–, started as a review serial and kept this form in part until 1893, when it began to give titles of articles. It has good annual and collective indexes, with, for the later years, formula indexes of organic compounds . . . Meyer's *Jahrbuch* 1891–, gives abstracts of the selected articles that seem to the editors of the greatest importance; it has annual indexes and one collective one." [3]

The *Fortschritte der Chemie* 1904–, was called *Physikalisch-chemisches Centralblatt* till 1909.

Ahren's Sammlung, full name *Sammlung chemischer und chemisch-technischer Vorträge.* This publication is a series of comprehensive articles on special topics in chemistry. Each of these is a brief monograph written by an expert in the particular line, frequently by the man who has done the most important part of the work that is described. There are abundant references to the original literature. These articles are valuable for the topics they cover which are, of course, relatively few.

Addresses. These are for the general reader and the student rather than for one making an exhaustive search on a given topic but they frequently give broad views of fields of research or technology which are to be had in no other way. In an address a general picture of a forest is presented leaving out the exact height and diameter of the several trees, while in publishing research the individual trees require so much attention that little is said about the forest and sometimes it is forgotten. At meetings of chemical societies, eminent chemists are frequently asked to deliver prepared addresses on important subjects, usually those that they know best. An address of that sort giving a bird's eye view of the work of years is always helpful. Technical problems are discussed from many angles in meetings of the technical organizations such as the *American Institute of Chemical Engineers* or the *American Electrochemical Society.* These addresses are usually published in their year books. The various divisions of the *American Chemical Society* frequently

[3] Miss Sparks — Chemical Literature and its uses — 1921, p. 22.

hold symposiums on selected subjects at which time many papers are presented. These give valuable composite views of the fields which they cover.

Monographs. The American Chemical Society has for some years sponsored a series of monographs in pure chemistry and another series on technical topics. Each is prepared by a specialist in the particular line and sums up, in a comprehensive way, all that is known on that subject. Each contains an exhaustive bibliography. The Carnegie Institution of Washington has published monographs for many years, but these are usually restricted to investigations carried on by the Institution.

Bibliographies. Allied to the abstract journals are bibliographies and catalogs of scientific publications. Descriptions of some of these are taken from Barrows.[4]

Select Bibliography of Chemistry. An important work of a bibliographical character is the "Select Bibliography of Chemistry," by Henry C. Bolton, published by the Smithsonian Institution (Smithsonian Miscellaneous Collection Nos. 850, 1170 and 1253).

"The first volume of this bibliography was published in 1893 and covers the periods from 1492 to 1892. The first supplement, published in 1899, covers the period from 1492 to 1897. The character of this bibliography will be apparent from the following quotations from the preface of the first volume:

"An attempt has been made in the following pages to collect the titles of the principal books on chemistry published in Europe and America from the rise of the literature to the close of the year 1892. The term chemistry is taken in its fullest significance, and the Biblography will be found to contain books in every department of chemical literature, pure and applied; . . .

"The Bibliography is confined, however, to independent works and their translations, and does not, as a rule, include Academic Dissertations (which are so numerous as to require a special catalogue), nor so-called "reprints" or "separates" (Separate-Abdrücke); of the latter only a few score are ordinarily printed and they must be regarded as belonging to periodicals. No attempt has been made to index the voluminous literature of periodicals except in the section of Biography as noted below. . . .

"To facilitate reference the work is divided into seven sections: I, Bibliography; II, Dictionaries; III, History; IV, Biography; V, Chemistry, pure and applied; VI, Alchemy; VII, Periodicals.

[4] Frank E. Barrows, Investigations of the Chemical Literature, pp. 14–19. Reprinted from *Chem. and Met.*, 24, 10, 11, and 12, March 9, 16, and 23 (1921). Used by permission.

"Altogether the first volume contains about twelve thousand titles, while the first supplement has fifty-five hundred more, making more than 17,500 in all. Of these titles 273 of the first volume and 95 of the supplement relate to bibliographies, while 327 of the first volume and 84 of the supplement relate to dictionaries and tables.

"A second supplement was published by the Smithsonian Institution in 1904. This contains 3,500 additional titles and brings the bibliography down to end of 1902.

"The third volume of this 'Select Bibliography of Chemistry,' by Bolton, relates to 'Academic Dissertations.' The dissertations are indexed under the authors' names, but the book is also provided with a subject-matter index. The nature of the work will be apparent from the following extracts from page 3:

"This bibliography is not an index to the chemical dissertations that have appeared in periodicals, but a list of those that have been printed independently. When compiling the list of titles I was fortunate in securing permission to make copies of the card catalogues of two large collections of dissertations on chemistry, those in the University Library, Strassburg, and those in the library of the United States Geological Survey, Washington City. I had also the opportunity of catologuing several thousand dissertations deposited by the Smithsonian Institution in the Library of Congress; the latter were chiefly of German origin. . . .

"For the convenience of residents of the United States the dissertations found in the libraries of the Geological Survey and of the Smithsonian Institution are indicated by the letters 'G.S.' and 'S.I.' respectively.

Catalog of Scientific Papers. "This work, which is still incomplete, has been compiled and published by the Royal Society of London. It has properly been referred to as the most comprehensive index to general science ever attempted. The first six volumes, published 1867–1872, cover the period from 1800 to 1863. In the preface of vol. 1, it is said:

"The catalog is intended to serve as an index to the titles and dates of scientific papers contained in the transactions of societies, journals and other periodical works which have been published from the beginning of the present century to the end of the year 1863."

"In the introduction of this same volume the subject-matter of the catalog is discussed in part as follows:

"The following catalog is intended to contain the title of every scientific memoir which appears in the various transactions and pro-

ceedings of scientific societies, and in the scientific journals published within the time which it comprehends; with the reference, the date, the author's name and the numbers of pages in the memoir. . . .

"A list of the works indexed, nearly fourteen hundred in number, arranged alphabetically according to the contraction employed in the catalog, will be found at the end of the introduction.

"The titles are arranged alphabetically according to the authors' names, the arrangement under the head of any one author being chronological.

"The second series of the catalog, vols. 7 and 8, published 1877–1879, covers the period from 1864 to 1873. The third series, in three volumes (9–11) published 1891–1896, covers the period from 1874 to 1893. A supplementary volume, vol. 12, was published between 1800 and 1883.

"The papers of this supplementary volume were taken from more than 350 added periodicals, so that, with the nearly 1,400 periodicals indexed in the first volume, and with the 130 more added in vol. 6, the total numbers of periodicals indexed in the "Catalog of Scientific Papers" up to 1883 is between eighteen and nineteen hundred.

"The fourth series of the catalog covers the period from 1884 to 1900. Vols. 13 to 16, for about half of the papers of the series, have so far been published, although their publication is of comparatively recent date (1914–1918). The remaining volumes are yet to appear.

"When the catalog is completed, it will consist of an author catalog and a subject index covering the entire period from 1800 to 1910. That is, the volumes of the author catalog are to be supplemented by index volumes of subject-matter covering the entire period from 1800 to 1900. The subject indexes are to be issued separately for each of the seventeen sciences dealt with in the 'International Catalog of Scientific Literature,' and will be arranged in accordance with the schedules of the International Catalog. The index volumes of 'Pure Mathematics, Mechanics and Physics' have thus far been published. Unfortunately the index volume for chemistry is not yet available. Until this volume is available, the 'Catalog of Scientific Papers' cannot be readily searched, except as an author index. However, for investigating the various papers of any given author between the dates 1800 and 1900, the catalog undoubtedly furnishes the most complete and comprehensive single index available. When the subject-matter index volumes are likewise available, it will then be the most complete and one of the most valuable indexes of the chemical literature of the nineteenth century."

"The International Catalog of Scientific Literature,[5] published yearly before the war (beginning with 1901 so as to continue the *Catalog of Scientific Papers*), by Harrisons and Sons, 45 St. Martin's Lane, London (prices of volumes vary), contains a practically complete list of all scientific books, papers, pamphlets and articles in scientific journals which have been published during the year in all countries of importance. The word "journal" is intended to include the proceedings, transactions, reports of learned societies. The catalog is published in 17 sections, of which those for Mechanics, Physics, Mathematics, Chemistry are of direct interest to engineers. . . . The yearly volume of any section contains (1) the name or author index; (2) subject index. The subject index is very complete; under any particular subject will be found the author's name and title of the article. On turning to the name index, one finds where the article appeared, or when the book was published, if it was a book, and its price and publisher. The various subjects dealt with in the book or article are indicated by numerical reference numbers; if an article has reference to various subjects it will be found indexed under each subject.

"In the list of the journals, published as a separate volume in 1903, the surprising number of 4,673 journals is listed from twenty-five different countries. Germany leads with 1,308, France is second with 919, the United States third with 539, and the United Kingdom fourth with 455, while Russia is fifth with 397."

Repertorium der technischen Journal-Literatur.[6] "This work goes back to 1823, was edited by Schubarth for the volume covering the period 1823 to 1853, and by Kerl for the two volumes covering the periods 1854 to 1868 and 1869 to 1873. Beginning 1874 it appeared annually, and since 1877 it has been published by the German Patent Office. Prior to 1879 it was known as the '*Repertorium der technischen Literatur*'; since 1879 it has been known as the *Repertorium der technischen Journal Literatur.*"

"It has had an author index since 1879, in addition to the subject index which it has always contained. The last volume of the "Repertorium" was published in 1908.

"The general arrangement of the *Repertorium* is alphabetical, by subjects, and it contains reference to a large number of the leading articles appearing both in the German and in other periodicals for the current year. The field covered includes much that has no relation to chemistry and metallurgy, but it is nevertheless a valuable index for use in searches of the chemical and metallurgical

[5] A. B. Eason, Electrician, **82**, 326 (1919).

[6] From Barrows, p. 17.

literature. It is of course equally valuable in other fields than chemistry.

The Industrial Arts Index. "This index is published by the H. W. Wilson Co., 958–964 University Ave., New York. The plan of the index is set forth by the publishers in the following language:

"The Industrial Arts Index is an indexing service to eighty-one [7] technical journals which have been selected by our subscribers as the leaders in their respective fields. It reaches you in magazine form (instead of loose cards) ten times a year. The entries are arranged alphabetically by subject and repeated under place names when necessary. Every article of importance in these eighty-one magazines is indexed under as many subject headings as will bring out all points of interest and cross-references direct the searcher to allied subjects in other parts of the alphabet.

"The rate for this service is based on the number of periodicals indexed for which you subscribe.

"Annual volumes of the index have been published since 1912.

"This index is not comparable with *Chemical Abstracts,* either in the scope of the field covered or in the detailed information which it gives, but it is nevertheless a useful index for many purposes, and one with which the searcher should be familiar. It includes much that is of general interest which is outside the field of chemical literature. Its two great drawbacks are the poor arrangement of material, all sentences being printed 'run in,' instead of in tabular form and the small, difficult type used.

Engineering Index. "The *Engineering Index* is an index which is likewise of more particular interest in connection with technical and engineering subjects, but it will, nevertheless, in some cases be found useful in those branches of applied chemistry which are included within its scope. Four volumes of the index cover the period from 1884 to 1905, and annual indexes have since been published. In 1906 the index covered about 250 technical and engineering journals in six different laguages, about one-fourth of the periodicals indexed being in languages other than English."

Current bibliography. We now have a journal devoted to listing chemical books as they appear, *Bibliographia chimica,* 1922–, published by the German Chemical Society.

Lists of new books with reviews of some of them are regularly published in *Industrial and Engineering Chemistry* and other chemical journals. In *Chemical Abstracts* books are noted as well as articles.

[7] Now (1924) increased to two hundred.

Books of reference

Everything that is discovered, with few exceptions, is published in the journals and these are condensed into the abstract journals. If we have the journals we have everything there is, so why should we want more? The compendiums and handbooks do not add to the facts of chemistry; they contain only a portion of the facts that have been published elsewhere, but these facts are selected and arranged so as to be readily available. In addition to the facts presented there are references to the journals where related facts can be found. In reading up a subject one can not stop with the handbooks but one saves much time by beginning with them.

Dictionaries and Encyclopedias. Books of this sort give a general view of a subject which serves as a good starting point for a more minute study. The articles, particularly on technical subjects, are usually contributed by specialists and give much valuable information in small compass. The serious drawback to such works is that they can not be kept up to date and the information in many of the articles is older than the date on the title page indicates. They are frequently of great value in patent litigation as showing the state of the art at a particular period. The best known are noted below.

Watts' *Dictionary of Chemistry* in 4 volumes was published in 1892–94.

Thorpe's *Dictionary of Applied Chemistry* was published in 1890–93 in 3 volumes and revised in 1912–13, 5 volumes. A new impression was made in 1918–19 and the second revision and enlargement is now appearing. Five volumes are already available and there will be two more.

Wurtz's *Dictionnaire de chimie pure et appliquée* was published in 1874 in 3 volumes, followed by a two volume supplement and a second supplement in 7 volumes in 1892–1908.

Fremy's *Encyclopédie Chimique* in 93 volumes with an index was published in 1882–1890.

Ullmann's *Enzyklopaedie der technischen Chemie* has just been completed in 12 volumes.

Beilstein and Richter. Attention has already been called to the fact that chemistry is one of the most thoroughly indexed branches of human knowledge. Of all the divisions of chemistry organic is the most splendidly systematized and catalogued. This is largely due to the efforts of two men who have left massive monuments to

their painstaking labors in chemical literature. These men are Beilstein and Richter, a Russian and a German. Both of them were overwhelmed by the multitudes of organic compounds turned out in later years and both had to resign their tasks in favor of the German Chemical Society with its larger resources. Both of them covered the whole field of organic chemistry and arranged its myriads of compounds in orderly fashion so that each may be located, but their systems are entirely different. Each work is valuable and each supplements the other.

F. K. Beilstein[8] was born in Petrograd in 1838, studied with Wöhler and also in France. He returned to Russia and was Professor of Chemistry in the University of Petrograd for 40 years, from 1866 to his death. He began to index organic compounds for his own use and printed his *Handbuch der Organischen Chemie,* known to chemists as '*Beilstein,*' in 1881–3 in two volumes. The second edition was issued in 3 volumes in 1886–1890, and the third, aggregating 6635 pages, appeared in 1893–1899. Supplements to these four volumes adding 4047 pages and an index volume of 441 pages came out in 1901–1906.

Beilstein prepared the first two editions unaided and had one assistant on the third. The enterprise has been taken over by the German Chemical Society and the fourth edition is now being prepared by Bernard Prager and Paul Jacobson. It is expected to contain about 16,000 pages divided according to a slightly modified plan into some 15 or 16 volumes. Up to 1924 six of these have been published. This fourth edition will cover organic chemistry to Dec. 31, 1909 and be coextensive with Richter.

The contents and arrangement of the third edition will be described in some detail as this edition will have to be used, in part at least, for some years to come and because one understanding the use of the third edition will have little trouble with the fourth. The student should devote much time to the study of this wonderful compendium. The organic chemist who can not handle *Beilstein* with facility is simply mistaken about being an organic chemist. We would become suspicious if we would see a preacher fumbling through the Old Testament looking for the Gospel of John and doubts arise when we notice an organic chemist pick up the wrong volume of *Beilstein.*

The subject matter of *Beilstein* is arranged systematically as follows:

Vol. 1 (1893) Aliphatic compounds.

[8] See article by Paul Jacobson in *Zeit. angew. Chem.,* 33, I, 178 (1920).

Vol. 2 (1896) Aromatic hydrocarbons, their halogen derivatives, phenols, alcohols and acids.

Vol. 3 (1897) Aromatic aldehydes, ketones, quinones, terpenes, etc.

Vol. 4 (1899) Aromatic series, bases, azoxy-, azo-, hydrazo-, diazo, etc., with miscellaneous ring compounds and organic compounds of metals and near metals.

The supplements, one to each volume, follow exactly the same arrangement, each page bringing the subject matter of a certain page, or pages, of the main volume down to a later date. The main volumes have separate indexes while the supplements have none, but if a compound is located in the main volume it is easy to find it in the supplement by following the numbers in the center at the top of the pages of the supplement. The fifth volume is a comprehensive index to all the volumes and their supplements.

The student should become so familiar with the system that he can locate most compounds without the index. In volume 1 the aliphatic hydrocarbons are first considered starting with the C_nH_{2n+2} series in ascending order from methane to the highest known. Then follow in like manner hydrocarbons of the C_nH_{2n} series, then C_nH_{2n-2} and so on till the most unsaturated are reached. The halogen derivatives are next treated in the same order beginning with mono-chlor-methane. Then come alcohols, acids, etc. These likewise follow the order of the hydrocarbons from which they are derived.

Beilstein gives a brief account of the modes of formation, best method of preparation and the properties of the compounds with references to the original literature. The space devoted to any one compound varies from a line to several pages according to its importance. It is possible to prepare and characterize a great many compounds with no more information than it contains, though, of course, it would be very wrong to be satisfied with such abridged descriptions if the journals to which references are given are accessible. *Beilstein* is a complete condensed library of organic chemistry. It describes 96,000 compounds. At the top of each page is the date to which the information is complete so that one knows just where to begin in searching the abstract journals for later data.

Richter's "*Lexikon der Kohlenstoff-Verbindungen*" was first published as "*Tabellen der Kohlenstoff-Verbindungen*" in 1884. The second edition of 3937 pages consisted of 2 volumes and 3 supplements. Volume 1 was published in 1899, vol. 2 in 1900, supplement 1 in 1901, suppl. 2 in 1903 and suppl. 3 in 1905. The third edition of

4751 pages appeared in 4 volumes in 1910–12. This contains 144,150 compounds and is complete to Dec. 31, 1909. The compounds are arranged according to their empirical formulae so that substances from all four volumes of *Beilstein* may appear side by side on a single page of *Richter*. There is no index any more than there is one to a dictionary: if the empirical formula is known the compound can be located with absolute certainty. A given substance commonly has more than one name and the index-maker may list it under one or more of these while the reader looks for it under some other alias and is sure that it has been left out. *Richter* is really a formulae index with references and little other information. It averages 30 compounds to a page while *Beilstein* contains only 9. References to articles subsequent to *Beilstein* are given together with volume and page references to *Beilstein* so that *Richter* indexes *Beilstein* and brings it down to its own date. Where the literature is meager all the references are given in *Richter* but for more important compounds only the late ones are inserted with the statement that the literature is considerable so that an important substance like alcohol or acetic acid occupies little more space than the most insignificant compound. *Richter* has been of great service as a means of locating the nearly 54,000 compounds which it contains which are not in the third edition of *Beilstein*.

The student should make a close study of the arrangement of *Richter* both for the purpose of being able to locate substances in *Richter* and because the same arrangement with slight modifications is used in the formulae indexes of chemical abstracts and in other publications.

Stelzner. The cost of preparing and reprinting ever enlarged editions of *Beilstein* and *Richter* is too great and so the expedient has been adopted by the German Chemical Society of issuing biennial volumes covering the literature for two or three year periods starting where the third edition of *Richter* and the fourth of *Beilstein* leave off, Jan. 1, 1910. Up to 1924, four of these have been issued, 1910–11, 1912–13, 1914–15 and 1916–18, under the title "*Literatur-register der organischen Chemie.*" These are under the editorship of Robert Stelzner. They combine *Beilstein* and *Richter* and are more complete than either. The arrangement is according to the formula index of *Richter* but the effort is made to include every reference bearing on a given substance which has appeared in the two year period. These are arranged according to the phase of the subject of which they treat.

Handbooks of Inorganic Chemistry. Inorganic chemistry is not

so well taken care of as organic but the following handbooks are of great assistance to the research chemist. The descriptions are taken from Barrows.[9]

"Gmelin's '*Hand-book of Chemistry*' was translated by Watts, and published by the Cavendish Society, in eighteen volumes, the first six of which relate to inorganic chemistry and the last twelve to organic chemistry. The first volume was published in 1848, the eighteenth in 1871. A separate index volume was published in 1872. Seventy-seven periodicals are listed in the beginning of the first volume. The original German work of Gmelin was published in seven volumes, three relating to inorganic chemistry and four to organic chemistry.

"This publication is one of the best and most valuable of the early reference works, and it contains, in digest or abstract form, reference to most of the important chemical literature prior to the middle of the Nineteenth Century.

"There is a tendency among students and among some chemists to consider that the main strides in the advance of chemical knowledge have been within the last few years, but reference to Gmelin's hand-book shows that far more information was available half a century ago, both in inorganic and organic chemistry than is commonly appreciated.

"Perhaps the most elaborate and exhaustive digest of inorganic chemistry is Gmelin-Kraut's '*Handbuch der anorganischen Chemie.*' This hand-book follows the same general plan as the earlier handbooks by Gmelin, giving a bibliography at the beginning of each subject and a discussion of the properties, methods of preparation and commercial methods of manufacture of the various metals and of their various compounds. About 170 periodicals are listed in the introductory portion of the first volume. The work is incomplete, but the volumes which have been published and the fields which they cover, are indicated by the following table:

"Vol. 1, Pt. 1, published 1907, 888 pages. Oxygen, Hydrogen, Helium, Argon, Neon, Krypton, Xenon, Nitrogen, Sulphur, Selenium.

"Vol. 1, Pt. 2, published 1909, 441 pages. Fluorine, Chlorine, Bromine, Iodine.

"Vol. 1, Pt. 3, published 1911, 907 pages. Phosphorus, Boron, Carbon.

"Vol. 2, Pt. 1, published 1906, 512 pages. Potassium, Rubidium, Calcium, Lithium, Sodium.

"Vol. 2, Pt. 2. published 1909, 726 pages. Barium, Strontium, Calcium, Magnesium, Glucinum, Aluminum.

"Vol. 3, Pt. 1, published 1912, 1568 pages. Titanium, Silicon, Chromium, Tungsten, Molybdenum, Uranium.

[9] Barrows, Investigations of the Chemical Literature, pp. 11–12.

" Vol. 3, Pt. 2, published 1908, 1135 pages. Radioactive material (Uranium, Thorium, Radium, Polonium, Radio-Tellurium, Radioactive Lead, Actinium and Emanium, etc). Vanadium, Manganese, Arsenic, Antimony, Tellurium, Bismuth.

" Vol. 4, Pt. 1, published 1911, 1056 pages. Zinc, Cadmium, Indium, Gallium, Germanium, Tin, Thallium.

" Vol. 4, Pt. 2, Lead, Iron.

" Vol. 5, Pt. 1, published 1909, 1595 pages. Nickel, Cobalt, Copper.

" Vol. 5, Pt. 2, published 1914, 1752 pages. Silver, Gold, Mercury.

" Vol 5, Pt. 3, published 1915, 992 pages. Platinum. The unpublished volumes of this Hand-book are as follows:

" Vol. 5, Pt. 4, Palladium, Rhodium, Iridium, Ruthenium, Osmium.

" Vol. 6, Zirconium, Thorium, Tantalum, Niobium, Cerium, Lanthanum, Didymium, Neodymium, Praseodymium, Yttrium, Ytternium, Scandium, Erbium, Terbium.

" Abegg's *Handbuch der anorganischen Chemie,* published 1905–1920, is another standard reference work on inorganic chemistry, and is perhaps better known than Gmelin-Kraut, although it also is incomplete. It is arranged according to the groups in the periodic table.

" Dammer's *Handbuch der anorganischen Chemie* is of similar character, though of earlier date.

" Dammer's *Handbuch der chemischen Technologie,* 5 volumes, published 1895–1898, supplemented by " Chemische Technologie der Neuzeit," 3 volumes, 1910–1911, is a valuable survey of applied chemistry.

" Roscoe and Schorlemmer's *Treatise of Chemistry,* in English, and Moissan's *Traité de chimie minérale,* in French, are useful reference works."

CHAPTER VII

LIBRARIES

Methods of Arrangement and of Use

When will some Homer or Vergil arise to sing of the library, of the labors, seventy times greater than those of Hercules, that have brought together information from every age and clime, tidings from stars whose light started on its headlong flight to the earth before Tut-ankh-Amen was born, measurements of suns in comparison with which our earth is but a speck, pictures of monsters that trod the earth in antediluvian ages, tracings of ferns of the carboniferous era, wisdom of the sages of all times, songs of poets, whisperings of lovers, secrets of antiquity? Here we find also the greatness of small things, the revelations by the microscope of empires whose contending armies do battle in a drop of blood, glimpses through the ultra-microscope of the dancing of the trillions of particles in colloidal solutions, and explorations by the scientific imagination of the interior of atoms with their solar systems of electrons. The riches in the vault of the Bank of England are paltry as compared with the treasures stored in a great library. Measured in human labor a library represents more toil in the gathering of information than the pyramids in the cutting and piling up of stone. The bank vault is protected with bolts and locks and armed guards lest some one purloin a single gold piece; the library doors open wide and over its portal is inscribed: "Whosoever will let him come and take of the wisdom of life freely." We travel miles and stand in thoughtful reverence before the tombs where lie buried the mortal remains of Napoleon, of Shakespeare or of the "Unknown Soldier," but here in the library the immortal thoughts of the world's great are preserved, not in sealed urns or mouldy vaults, but spread open before us. He who enters here leaves not hope but ignorance behind.

Let us pause a moment to give a tribute to the librarian, the high priest in this temple of knowledge. His is an altruistic calling, his highest ambition is to serve, his greatest reward, the opportunity for greater service. Even a physician accepts money from those whose sufferings he relieves but the librarian is quick to serve all

who come and never receives more than a thankful smile from those who profit by his helpful attention. Few even of those who use public libraries realize how much the librarian does to aid his customers and how willing he is to do it.

The importance of library service to chemists was well brought out in the Symposium at the Buffalo meeting of the American Chemical Society in May 1919. The papers there given are well worth reading.[1]

Using a library. In order to use a library to the best advantage the reader should acquire familiarity with the system of arrangement of books, with subject and author catalogs and other aids in finding books. In some libraries the reader must order books from the card catalog and have them brought to the reading room. The success of this plan depends on the thoroughness with which the cataloging has been done and on an intelligent use of the catalog with a thorough understanding of its construction, what it contains and what it does not. In other libraries, particularly those that specialize in technical subjects, the reader is allowed access to the shelves. In this case he is not so dependent on the catalog as he may scan the rows of books in search of those that are likely to bear on the topic in hand, but even in this case the use of the catalog can save much time. If the name of the author or the title of the book is known, reference to the catalog will tell whether or not it is in the library and its exact location on the shelf if it is there. The searcher will more frequently be interested in a topic than in a particular book. In that case he will find under this topic all the books which the library contains which bear on it. He will make a list of these and proceed to obtain them. It is advisable to look under a number of headings which may suggest themselves as related and under which books may be found bearing on the main topic. The cataloging in various libraries differs much in the thoroughness of cross indexing. There is a minimum of two cards to a book, an author and a title, or subject card. There may be a large number of subject cards bringing out the various topics and sub-topics treated. In some cases even journal articles are indexed. The more headings under which a book is cataloged the more likely it is to be found but if there is only one card for it this is more likely to be located if one looks for it under all possible headings. The process is much the same as looking for an article in an abstract journal and what is quoted from Dr. Crane in Chapter VIII (p. 124) applies also to the use of a library catalog.

[1] *J. Ind. Eng. Chem.*, 11, pp. 578–89 (1919).

The main card catalog usually contains author, title and subject cards arranged as in a dictionary. There is usually also a shelf list in which the cards are arranged exactly as they are on the shelves of the library. As the books are grouped on the shelves according to subject matter, the cards are similarly grouped in the shelf list and if one book on distillation is located, others on the same topic will be found on adjacent cards. Fingering the cards on the shelf list is like looking along the shelf of books. This list is not always available to the reader. Some libraries have a separate author catalog.

Call numbers. In all cases the location of the book is indicated by certain markings in the corner of the card. These look enigmatical at first but become clear by a little study. They are known as the "call numbers" since they are used in asking for a book and are all that is needed to show its exact location on the shelf. To understand these important call numbers one must understand the classification of books in modern libraries. It is equally useful to have this knowledge if one has access to the books on the shelves, since by knowing the system one can locate the class of books one wishes by following along the call numbers which are commonly more conspicuous than the titles. It is a common mistake to associate books with particular locations on the shelves. It must be remembered that the numbers show relative locations, *i.e.* relative to other books, not to library furniture. New books take their proper places in the line and do not go to the end like late arrivals at the ticket seller's window.

The two systems of classification used in American libraries are given in detail at the end of this chapter.

Supplementing Library Facilities

All libraries are limited, the difference being that in some cases the limits are so narrow that few of the books or journals one wants are within them and, in others, they are so wide that it is only now and then that one need go outside, but there is nowhere on earth a library which contains all journals or all books on chemistry. Hence one must know how to obtain the desired information from a distance. Three methods are available, (1) loan of desired volume, (2) photostating of pages containing the information, (3) abstracting and translating.

Loans from Libraries. With the growth of library service many courtesies are being extended to readers at a distance. Loans are

made from one library to another rather than to individuals. One goes to a nearby library and asks the librarian to borrow the desired book from another library. The librarian of the borrowing library sees that the volume is properly used and returns it to the other library, the reader paying mailing charges. The immense resources of the Library of Congress and of other large libraries thus become available for the isolated investigator who gains access to almost any book or journal published. This service is a great concession on the part of the lending library, since at best the volume is absent from its shelves for some days and there is danger of loss or damage in transportation. For this reason the privilege should not be abused and books should be used and returned with the greatest possible promptness.

Photostat Service. This has recently been greatly extended and now many libraries are prepared to furnish in brief time and at small cost, photostat copies of any desired portions of publications which they contain.

Abstracting and Translating service. Some of the larger libraries can arrange for translating or abstracting articles, this service being paid for by the hour or by the number of words translated. At first sight, it may be asked why should one require an abstract of an article of which an abstract has already been published in *Chemical Abstracts* or in the *Zentralblatt*. The printed abstract is designed for the general reader and to show what is covered by the article: perhaps twenty new compounds are mentioned as having been prepared by some general method and their melting or boiling points are given. Only one of these may be of interest to a certain investigator but that one may be of great importance and he may want some one to go through the article and jot down everything bearing on this particular compound. Or information may be desired as to some special point that may or may not be covered in the article. Sometimes one only wants to know whether or not it has been taken up. Abstracting may be combined with translating and photostating. Thus one has a reference to an article which may cover a hundred pages and contains a mass of information on many compounds in only a few of which one is interested at the present time. To photostat the whole article would be cumbrous: what one wishes is for a competent abstractor to go through the article noting brief references to the required subjects, photostating the pages which deal chiefly with them, and answering any specific questions as to whether or not the article contains so and so. This demands chemical training on the part of the abstractor as well as some judgment, while

requests for photostats can be handled by library employees who need not know the contents of the journals they handle.

The list of journals published in *Chemical Abstracts,* Oct. 20, 1922, has notations showing which of the prominent libraries contain each of the journals listed. Information is also given of the loan, photostat and abstract service available at these libraries. With this information at hand one is in a position to obtain almost anything that appears in a journal. One reads the abstract in *Chemical Abstracts,* turns to this list to see what libraries receive the journal in which the article was published, then notes the nearest of these libraries that will lend, or photostat the article.

The National Research Council. This exists for the furtherance of research. One of the ways in which it does this is by aiding individual investigators to obtain information not otherwise accessible. The Council is prepared to give the investigator advice as well as information and also to put him in touch with others interested in the same line. Much is to be expected of this powerful agency in strengthening and correlating the research activities of the country.

The Chemists' Club Library. This is one of the most complete chemical libraries in the United States. It offers an efficient service to the members of the Club in loaning books and journals, photostating, abstracting and translating articles. This is a great advantage to the isolated chemist and is worth many times the comparatively small dues charged out-of-town members.

Cooperative Work. The teacher in a small college at a distance from the great library centers is more hampered by the lack of books than by anything else: in fact this lack is the one and the only one which really stands in the way of effective research. A few dollars will usually buy chemicals which may serve as starting points for whole series of new compounds and flasks, condensers, thermometers, beakers, etc., are found in every laboratory in sufficient variety for most of the operations of organic research. Problems in physical chemistry usually require more expensive apparatus, potentiometers, conductivity cells and the like, but even here several hundred dollars worth of special apparatus added to that in stock will enable one to undertake the investigation of an important problem. But when it comes to journals, the individual or a small institution is helpless: to purchase an adequate library would entail an outlay of tens of thousands of dollars and to gather the journals and books requires years of effort.

Somewhere in a small college there is an ambitious young teacher with some time and abundance of energy, having chemicals and ap-

paratus but no journals: somewhere else at the big university there is a wonderful library and a professor who has ten times as many ideas as he and his students will ever have time to work out and there may be also some graduate students who need practice in library searches. Cooperation may be a blessing to both: the young chemist may find his way into productive research and the professor may have the pleasure of seeing some of his ideas worked out and the satisfaction of helping a younger man to start his career.

Chemical literature contains many excellent researches carried out by cooperation. The most impressive example is the long series on diazo-compounds carried out by Peter Griess in his little laboratory somewhere in the big brewery at Burton-on-Trent in England and Schmidt and his students at the University of Dresden. Chemistry boasts few more important researches. Cooperation has its limitation and its dangers: it fails utterly when either party fails to cooperate. The enthusiastic young teacher is going to do wonderful things if he can just get his hands on a live problem not more than twice his size; he writes to the university and the professor sends him one of his pet problems and spends several days looking up the literature and writing out abstracts and directions. The young man starts out with enthusiasm but the problem does not respond to treatment and results come slowly, meanwhile teaching duties or other diversions come in and the research is crowded out: the professor's time has been wasted and he is less thrilled the next time he is called on for a similar service. It is a saying among chemists that one positive result proves a case in spite of hundreds of negative ones: cooperation has worked more than once which proves that it can work, though it has failed many times. This means that we should make sure of the basis of cooperation and not enter into it lightly, but when conditions are right let us cooperate heartily and industriously. It is well for each to play the game with all his skill and power, but it is still better for each to have regard for his fellow players and to support them. Science offers many opportunities for team work.

Systems of Library Classification

There are two commonly used systems of classification, or rather of designating the classification. In the Dewey, or decimal system, the classes are given numbers, while in the Library of Congress, or the Cutter system, combinations of letters and figures are used. With both we may have more or less minute subdivisions according to the size and purposes of the library and the ideas of the librarian. A subject on which a particular library specializes and on which it

contains a large number of books may be minutely subdivided, while books in some other line may be bunched under some broad division. The arrangement of books within the classes or subclasses is much the same. One must locate the class and then find the individual book, which is much like finding the desired street and then a given number on that street. A sketch of parts of the two systems which are of special use to the chemist is given below.

The more elaborate Library of Congress system is used by the more important special libraries but the Decimal system will be considered first since its description is simpler and serves well as an introduction to the other.

The Decimal System. All books are first divided into 10 great classes each of which is subdivided into 10 lesser classes and so on. Using 3 digits we have 999 subclasses. After these we place a decimal point and proceed with still finer divisions. Thus 5 is natural science, 540 chemistry, 543 chemical analysis, which is further divided into 543.1 analysis of food, 543.2 of milk, 543.3 of water, 543.4 of drugs, 543.5 of poisons, 543.6 of rocks, 543.7 of gases, 543.8 of oils and fats, 543.9 of animal body.

General classes	*Secondary classes*	*Sub-classes*
0 General		
1 Philosophy		
2 Religion		
3 Sociology		540 General 541 Theory, physical 542 Lab. methods 543 Analysis 544 Qual. anal. 545 Quant. anal. 546 Inorganic 547 Organic 548 Crystallography 549 Mineralogy
4 Philosophy	510 Mathematics 530 Physics 540 Chemistry..... 550 Geology 580 Botany 590 Zoölogy	
5 Natural Science		
6 Useful Arts	610 Medicine 620 Engineering 630 Agriculture 640 Household science 660 Chem. technology 670 Manufactures	660 General processes 661 Chemicals 662 Explosives 663 Beverages 664 Foods 665 Fuel, gas, oil 666 Ceramics, glass 667 Dyes, paint, &c. 668 Soap, glue, glycerine 669 Metallurgy, assaying
7 Fine Arts		
8 Literature		
9 History		

We find some chemical topics scattered among the other divisions thus: under 3, sociology, we have 389 weights and measures and 389.05 publications of Bureau of Standards; under 580, botany, 581.6 plant chemistry; under 610, medicine, 612 physiology, 612.01 physiological chemistry; under 620, engineering, 628 sanitary engineering, 628.1 water supply and 628.16 water purification; under 630, agriculture, 630.16 agricultural chemistry, 631 soils and fertilizers, 635.4 feeding stuffs.

In the Cutter System we have Q science and QD chemistry; T is technology and TP chemical technology. Agricultural Chemistry is found in Class S, agriculture, pharmaceutical chemistry in Class R, medicine, physiological chemistry in QP and mineral industries, including metallurgy, &c., in TN.

Whether the class be TP 541 or 628.16, all the books in that class are arranged according to the first letters of the authors' names. If the author's name begins with a consonant only the one letter is used but if the initial is a vowel a second letter is added. The numbers following the initial usually show the order in which the books bearing the same initial were acquired by the library. Thus a book on agricultural chemistry might be 630.16 S 1 if it were written by Smith; if another book on this subject by Saunders is acquired it will be 630.16 S 2 and so on.

Library of Congress System. In this the general classes of knowledge are designated by letters, Q denoting science — is it because scientists are always asking questions? — the several sciences being differentiated by the addition of a second letter. Thus QA is mathematics, QB astronomy, QC physics, QD chemistry, QE geology, QH natural history, QK botany, QL zoology, QM human anatomy, QP physiology, QR bacteriology. Each of these may be divided into 999 classes by the addition of figures, thus QD 111 is volumetric analysis and QD 321 comprises carbohydrates. Volumetric analysis may concern many different substances and if we have many publications we may classify them still more minutely by adding a letter qualified by another number to designate the element chiefly concerned. (See list below.) Thus a book relating to the volumetric analysis of chromium compounds would be classed QD 111.C 7. It must be noted that the second number is treated as a decimal, that is .C 7 follows .C 65 as if it were 0.70 which comes after 0.65. The numbers following the QD are whole numbers and QD 101, quantitative analysis, follows QD 87, blow pipe analysis. The individual books on volumetric analysis of chromium compounds, QD 11 C 7, will carry the initials of authors as described above for the decimal

system. Thus if one of them is by Jones and another by Joyce they will bear the call numbers QD 111.C 7.J 1 and QD 111.C.J 2.

The chief classes under QD are given below as taken from the Library of Congress Classifications (1912).[2]

CLASS QD

CHEMISTRY

Physiological chemistry, see QP501–801
Chemical technology, see TP.
Medical and Pharmaceutical chemistry, see RS403–431.
Agricultural chemistry, see S583–588.

1 Periodicals, Societies, etc.
3 Collections (non-serial).
4 Encyclopedias.
5 Dictionaries.
See also QD66, Dictionaries of solubilities.
7 Nomenclature.

History

11 General.
13 History of alchemy.
14 Period before Lavoisier.
15 Modern.
18 Local (by countries alphabetically).

Biography of Chemists

21 Collective.
22 Individual.
23 *Directories.*

Early Works

25 Alchemy and iatro-chemistry.
See also R126–128, Early medical works.
27 Boyle to Lavoisier.
28 Lavoisier to 1860.
30 Manuals and text-books to 1860.
31 *Recent Treatises and Advanced Text-books.*
33 Elementary text-books.
35 Rudiments and juvenile works.
37 Popular works.
39 *Essays, Lectures, Addresses,* etc.
40 *Study and Teaching.*
41 Outlines, syllabi, etc.
42 Problems and exercises.
43 Lecture experiments.
45 Laboratory experiments (School labaratory manuals).
Elementary qualitative analysis in QD83
51 *Laboratories.*
53 Apparatus.
61 Laboratory technique (general).
63 Special operations, A–Z.
e.g. .D5 Dissolution; .D6, Distillation.
Cf. QD258, Organic operations.
QD526–536, Thermochemistry.
QD157 and 277, Electric furnace operations.
65 Pocket-books, Tables, etc.
66 Dictionaries of solubilities.

ANALYTICAL CHEMISTRY

71 *Periodicals, Societies,* etc.
72 *History.*
73 General Principles, Theory of Reactions, Calculations, etc.
75 *General Works.*
77 Reagents, indicators, test papers, etc.

[2] Washington, Government Printing Office.

Qualitative analysis

81 Treatises.
83 Elements.
85 Tables, outlines, etc.
87 Blowpipe analysis.
See also QE367, Determinative mineralogy.
95 Spectrum analysis (chemical only).

101 *Quantitative analysis*
Special elements classed QD181 with added entry QD111–139
111 Volumetric.
115 Electrolytic.
For Organic analysis, see QD271
121 *Gas Analysis*
See also TP754, Illuminating gas — Analysis, tests, etc.

Technical Analysis

See also S587, Agricultural chemical analysis; TX545, Food Analysis
131 General
133 Metals.
Assaying, see TN550–580.
135 Alloys

137 Special metals, A–Z.
N.B. Iron and steel in QD133.
139 Other technical (alphabetically).
See also TD735, Sewage Analysis; TP511, 609, Testing of wines and spirits; TP671, Oil analysis; TP811, Clay analysis.
142 Water analysis.

INORGANIC CHEMISTRY

151 Treatises.
N.B. See QD33 for school-textbooks
155 Inorganic preparations.

157 Electric furnace operations (inorganic).
Cf. QD277
161 *Non-metals*
163 Chemistry of the air.

Metals

171 General.
172 By groups (alphabetically).

181 Special topics.
(Alphabetically by chemical symbol of principal element according to the following table of abbreviations):

A3. = Ag Silver (argentum).
A4. = Al Aluminum
A6. = Ar Argon
A7. = As Arsenic
A9. = Au Gold (aurum).
B1. = B Boron
B2. = Ba Barium
B4. = Beryllium
B5. = Bi Bismuth
B7. = Br. Bromine
C1. = C Carbon
C15 = CN Cyanogen
C2. = Ca Calcium
C3. = Cd Cadmium
C4. = Ce Cerium
C5. = Cl Chlorine
C6. = Co Cobalt
C7. = Cr Chromium
C8. = Cs Caesium
Columbium, see N3.
C9. = Cu Copper
E6. = Er Erbium
F1. = F Fluorine
F4. = Fe Iron (ferrum)
G2. = Ga Gallium
G4. = Gd Gadolinium
G5. = Ge Germanium
H1. = H Hydrogen
H4. = He Helium
H6. = Hg Mercury (hydragyrum)
H65. = Amalgams
I1. = Iodine
I5. = In Indium
I7. = Ir Iridium
K1. = K Potassium (kalium)
K6. = Kr Krypton.

L2. = La Lanthanum
L5. = Li Lithium
M4. = Mg Magnesium
M6. = Mn Manganese
M7. = Mo Molybdenum
N1. = N Nitrogen
N15. = Nitrogen hydrides (ammonia, hydrazine, hydroxylamine, etc.)
N2. = Na Sodium (natrium).
N3. = Nb Niobium or Columbium
N4. = Nd Neodymium or Didymium.
N5. = Ne Neon
N6. = Ni Nickel
O1. = O Oxygen
O7. = Os Osmium
P1. = P Phosphorus
P3. = Pb Lead (plumbum).
P4. = Pd Palladium
P7. = Pr Praseodymium
P8. = Pt Platinum
R1. = Radium
See also QC721
R3. = Rb Rubidium
R5. = Rh Rhodium
R9. = Ru Ruthenium
S1. = S Sulphur
S2. = Sa Samarium
S3. = Sb Antimony (stibium)
S4. = Sc Scandium
S5. = Se Selenium
S6. = Si Silicon
S7. = Sn Tin (stannum)
S8. = Sr Strontium
T2. = Ta Tantalum
T3. = Tb Terbium
T4. = Tc Tellurium
T5. = Th Thorium
T6. = Ti Titanium
T7. = Tl Thallium
T9. = Tu Thulium
U7. = Ur Uranium
V2. = Va Vanadium
W1. = W Tungsten (Wolfram)
X1. = X Xenon
Y7. = Yr Yttrium
Y8. = Yt Ytterbium
Z6. = Zn Zinc
Z7. = Zr Zirconium

N.B. — Here are classified all special works on the origin, properties, preparation, reactions, and analytical chemistry of inidividual elements and their inorganic compounds, excluding determinations of atomic weight (see QD464). The subdivision C5 (= Chlorine) includes also the halogens collectively.

191 Double salts
199 Miscellaneous.

ORGANIC CHEMISTRY

251 Treatises.
253 Elements.
255 Essays, lectures, etc. (theory, fundamental notions, etc.).
258 General organic reactions (condensation, oxidation, etc.)
261 Laboratory manuals (organic preparations).
263 Electrosynthesis of organic compounds.
271 Organic analysis.
277 Electric furnace operations. cf. QD157.
291 Indexes. Nomenclatures.

Fatty compounds (Aliphatic).

301 General.
305 Special groups (alphabetically).
e.g. .A2 Acids and esters.
.A4 Alcohols.
.A6 Aldehydes and ketones.
.A7 Amides, amino acids and hydrazides.
.A8 Amino compounds.
.A9 Azo, hydrazo and diazo compounds.
.E7 Ethers and oxides.
.F2 Fats and fatty oils. Hydrocarbons.
.H5 General.
.H6 C_nH_{2n+2}.
315 Urea and related compounds
319 Miscellaneous pamphlets
321 *Carbohydrates* (sugars, starch, etc.).
See also TP375–416, Sugar manufacture.
325 Glucosides. 327 Tannins.

Aromatic compounds (Carbocylic and heterocyclic).

331 General.
335 Synthesis from fatty compounds. Orientation. Other theoretical topics.
341 Special groups (alphabetically).
e.g. .A2 Acids and esters.
.A4 etc. same as under 305.
369 Miscellaneous pamphlets.

Condensed Benzene-rings

391 Naphthalene.
393 Anthracene.
395 Phenanthrene.
399 Miscellaneous.

Mixed Cycloids

400 General works.
401 Cycloids containing N.
403 Cycloids containing S.
405 Cycloids containing O.
409 Miscellaneous.

Organometallic and Allied Compounds

411 General.
412 Special (alphabetically by symbol of element according to scheme under QD181).
415 *Chemistry of vital products.*
See also QH345, Chemical properties of living matter.
416 *Terpene and Camphors. Essential Oils.*
See also TP958, Essences (chemical technology).
419 Resins.
421 *Alkaloids.*
See also QK865–866, Chemical analysis of plants; QP801.P7, Ptomaines and leucomaines.
431 Proteids.
See also QP551, Physiological chemistry.
441 *Colored Compounds.*
See also TP910–929, Dyes.
449 Miscellaneous.

PHYSICAL AND THEORETICAL CHEMISTRY

(Periodicals, Societies, etc. in QD1)

453 General works.
457 Laboratory manuals.
461 *Atomic theory and laws of chemical combination.*

Atomic Weights.

463 General.
464 Of individual elements (alphabetically by chemical symbol).

Chemical Elements

466 Nature and properties
467 Classification. Periodic Law, etc.
469 Valency.
471 Chemical compounds — Structure and formulae.
475 Inorganic compounds.
Alloys, see TN690, TS650, TA490.
481 *Stereochemistry.*
499 Miscellaneous speculations.
501 *Conditions and laws of chemical change.*
Chemical equilibrium.
Chemical affinity.
Velocity of reaction.
511 *Thermochemistry.*
515 Chemistry of high and low temperatures (general).
516 Combustion, flame, explosion.
517 Dissociation.
518 Melting and boiling points.
Electric furnace operations, see QD157, 277.
536 Fractional distillation.
See also TP589–607, Distilling.
531 Manipulation of gases and vapors.
533 Vapor densities.
535 Liquefaction of gases.
536 Research at low temperatures.

Theory of solution.

Dictionaries of solubilities in QD66.
541 General.
Special topics.
543 Solubility, osmotic pressure, diffusion, etc.
See also QC183–189.
545 Freezing points and vapor pressures. Determination of molecular weight.
548 Supersaturated solutions. Crystallization, etc.
549 Colloidal state.

Electrochemistry. Electrolysis.

See also QD115, Electrolytic analysis; QD263, Electrosynthesis of organic compounds; TP250–261, Electrochemical industries.
553 General works.
557 Laboratory manuals.
559 Apparatus, etc.
Special topics.
561 Electrolytic dissociation. Migration and velocity of ions. Transport rates.
565 Conductivity of electrolytes.
568 Concentration of cells.
571 Electrode phenomena. Polarization, etc.
581 Chemical constitution determined electrically.
585 Other special.
591 *Magnetochemistry.*
601 *Photochemistry.*
See also TR200, Photographic chemistry.
651 Optical properties of chemical substances.

CRYSTALLOGRAPHY

See also QE372, Descriptive mineralogy.

901 *Periodicals, Societies,* etc.
902 Dictionaries and Nomenclature.
903 History.
905 General works.
911 *Geometrical and Mathematical Crystallography.*
913 Diagrams, etc.
Outlines, syllabi, etc.
915 Gonimetric measurements.
921 Crystal structure and growth.
Liquid crystals.
931 *Physical Properties of Crystals.*
933 Cohesion, elasticity, cleavage, hardness.
935 Etching.
937 Thermal properties.
939 Electric properties.
See also QC595, Pyro- and Piezo-electricity.
941 Optical properties.
See also QC445, Polarization.
951 *Chemical Crystallography.*
999 Miscellany and curiosa.

CHAPTER VIII

LITERATURE SEARCHES

Finding and Preserving Information

Much space has been given to the description of abstract journals, etc. but the searcher must know how to get into them: the index is the door, so to speak, by which we enter these storehouses of information. It is easy to say to one: "Look in the index" but it is quite another matter to teach one how to use an index effectually. Few realize how difficult it is to be sure that all possible information on a given subject has been found and yet the completeness of a search is frequently of the utmost importance. Finding out a great deal about any topic is easy: finding everything that has been published about it is quite another matter. A hole in a literature survey may be as disastrous as a puncture in a tire.

The following helpful information on indexes and their use has been given by one who speaks from long study of the subject.[1]

"The main problem, of course, in using the journal literature is in finding references, all that are pertinent to the subject at hand, in order that one may learn what the literature contains and all that it contains relating to this subject. This is often difficult. It is doubtful if there is a more important problem for students, in college or out, to learn how to solve. Its solution involves to some extent a familiarity with the more important journals, particularly the abstract journals, but above all it involves a knowledge of indexes and how to use them. References to the journal literature are often obtained from books or from one paper to others, but mostly they are obtained from indexes, usually of abstract journals. It is frequently assumed that the use of indexes in making literature searches is a simple matter requiring no special experience or ability. This is a mistake. The making of indexes is an art in itself, involving more than a comprehensive knowledge of the general subject being covered, and the use of indexes is no less an art. This deserves emphasis. It is true partly because existing indexes vary greatly in

[1] E. J. Crane in *Jour. Ind. Eng. Chem.*, **14**, 901 (1922), used by permission of author.

kind, thoroughness, and quality. Even in the use of the best subject indexes the user must meet the indexer part way for really good results. Conscious effort to become a good index user will repay any scientist. Many a day has been spent in the laboratory seeking information by experiment which might have been obtained in a few minutes, or hours at the most, in the library, had the literature search been efficient. Because of the belief that index searching is a neglected art and yet one of much importance, the remainder of my limited time will be devoted to subject indexes — the most useful kind.

"What constitutes a good index? The test is to determine whether or not an index will serve as a reliable means for the location, with a minimum of effort, of every bit of information in the source covered which, according to the indexing basis, that source contains. To meet this test an index must be accurate, complete, sufficiently precise in the information supplied, and so planned and arranged as to be convenient to use. Existing indexes fall far short of this ideal in many cases, and of course somewhat short of it in all cases.

"The main purpose in indexing is sometimes partially lost sight of through an effort to bring some sort of classification into it. Classification in connection with indexing frequently detracts from, rather than enhances, the efficiency and usefulness of an index, and is beside the main purpose.

How to Use an Index

"The first step in learning how to use subject indexes with maximum effectiveness is to become familiar with the characteristics and peculiarites of important existing chemical indexes. The most significant point to note is whether or not a so-called subject index is really an index of subjects or an index of words. The tendency to index words instead of thoroughly to enter subjects constitutes the greatest weakness in the literature of chemistry. There is a vast difference. Words are of course necessary in the make-up of a subject index, but it is important for an indexer to remember that the words used in the text of a publication are not necessarily the words suitable for index headings or even modifying phrases. Word indexing leads to omissions, scattering, and unnecessary entries. After the most suitable word or group of words from the indexing point of view has been chosen for a heading, it should of course be used consistently no matter what the wording of the text may be. To illustrate a kind of scattering of entries which may result from

word indexing, let us consider such a series of article titles as follows: follows:

"'An Apparatus for the Determination of Carbon Dioxide,' 'A New Absorption Apparatus,' 'Apparatus for Use in the Analysis of Baking Powder,' 'An Improved Potash Bulb' and 'Flue Gas Analysis.' Word indexes would no doubt contain an entry under the heading 'Carbon dioxide' for the first title, one under 'Absorption apparatus' for the second, under 'Baking powder' for the third, under 'Potash bulb' for the fourth, and one under 'Flue gas' for the fifth, and probably no others. These entries seem reasonable enough if the titles are considered separately without thought of the others. And yet the articles may all be descriptive of the same sort of apparatus. As a matter of fact, all these titles might conceivably be used for the same article; if the author happened to be working on baking powder or on flue gas analysis when he conceived the idea for his novel piece of apparatus, or had it in mind particularly for one purpose or the other, he might choose one of the more specific titles for his article rather than one of the more general ones.

"In an index entirely based on subjects rather than words, it would be the task of the indexer to see that all these articles get indexed under one heading, or under each of more than one heading, best with cross references pointing from the other possible headings to the one or more headings used. Or, if there seems to be some justification for scattering owing to differences in point of view (word indexing cannot be gotten away from entirely), he would make sure that the necessary cross references are supplied to lead the index user about from heading to heading so that all entries can be readily located. It is not hard to determine whether or not an index is a word index; when this is suspected or noted, one should look around pretty thoroughly in its use instead of being satisfied that the entries found under the obvious heading are all that the index contains on a subject.

"It is important to note the approximate degree of completeness of an index in use. There is perhaps no definite point at which a subject index may be said to be complete. The indexing basis is too indefinite. A great many subject indexes are not as full as they ought to be. Aside from word indexing the indexing merely of titles is the most common reason for incompleteness. Titles cannot be depended upon to furnish the information necessary for adequate subject indexing. An index may be reasonably complete from one point of view and not from others. For

example, a publication devoted to bacteriology may not reasonably be expected to be indexed fully from the chemical viewpoint. Completeness in the information supplied in modifying phrases, as well as completeness in index headings, needs to be taken into consideration. It is necessary, of course, to call forth one's resourcefulness to a special degree if a relatively incomplete index is to be used.

"Cross references play an important rôle in subject indexing and in the use of subject indexes. Word indexing is really hard to avoid and cross references are the great preventive. It is a good sign if a subject index has a plentiful supply of cross references, both of the 'see' kind and the 'see also' kind. They make for uniformity and proper correlation. 'See also' cross references are of just as much importance as the 'see' kind though not as much used. The service which they render in directing the index user to related headings or to headings which, though dissimilar for the most part, have entries under them likely to be of interest to the investigator who refers to the original heading, is often the chief means of making a search complete. It is not reasonable to expect an index user, or an indexer, as a matter of fact, to think of all the headings representing related or significant subjects under which headings he may find valuable references that might otherwise be missed. Nevertheless, in the careful indexing year after year of a periodical devoted to a more or less definite field, as an abstract journal for example, subjects are come upon in such a variety of connections and from so many angles that it is possible for a truly comprehensive list of cross references to be built up. The suitability of a given 'see also' cross reference may not be clear, much less suggest itself, until a specific case in which it is helpful is observed. It often pays to follow up such a cross reference even when it does not look as if it applies in a given case. The indexer, in surveying the whole field year after year, is in a position to make valuable suggestions in the form of cross references calculated to lead the index user from place to place in the index, so that the chances that his search will be really exhaustive as far as that particular index is concerned are much increased.

"Persistence is a good qualification for index searching. It is desirable to avoid being too soon satisfied. There is no task in which thoroughness is more important. It involves first a knowledge of the indexing system and of the characteristics of the index. Then one needs to be resourceful, exhausting all possibilities, if he

is to avoid some futile searches or incomplete findings. One's fund of general knowledge can usually be brought into service to good advantage.

"On account of the necessity of drawing on one's general knowledge in making a literature search in any field, it is in many instances important that one should make his own searches. It is not always safe to let some one less well informed in a certain field make an index search when a complete survey is desired, even though his familiarity with indexes and the literature in general may be better than one's own. Just as some tasks in the laboratory can be turned over to another to advantage but not the more important determinations and experiments, so some tasks in the library can be delegated to an assistant, but not all such tasks. Knowledge, skill, and power of observation, are factors fruitful of important results in the library as well as in the laboratory. Literature searching is a dignified pursuit, and it cannot with impunity be assigned to a lower level than that of the laboratory side of problems, as far as the attention it receives is concerned.

"With a given problem at hand the first step, of course, is to think out the most likely places to look in the indexes to be used. This may be a simple matter or it may be a very difficult one, depending on the nature of the problem. Difficulty increases with indefiniteness. Experience is necessary. In fact, the beginner is often completely at a loss to know what to do at this very stage of his search. This point is stressed in the Report of the Subcommittee on Research in Chemical Laboratories, presented to the Committee of One Hundred on Scientific Research, New York, December 26, 1916. In this report, which commends and recommends courses in chemical literature searching in universities, it is pointed out that the average graduate 'fails to analyze the subject' in which he is interested 'into its factors, and hence generally looks for topics which are too general. Because he does not find any references to the problem as a whole as he has it in mind, he assumes that nothing has been done upon it and that there is nothing in the literature which will be of aid to him in the investigation. Were he to separate his subject into its essential parts and then to consult the literature on each factor, he would find considerable information which he otherwise would miss.' Even though some index headings to which to turn, perhaps the more important ones, may be brought to mind without ingenuity, the completeness of a search may be marred by a failure properly to analyze the problem. Indexes with cross references, particularly 'see also' ones, help.

"Too much dependence on cross references is not advisable. They may not be available at all and they are never complete. With a given heading in mind it is well to cudgel one's brain for synonymous words or phrases to try, as well as for variously related subjects, and it is advisable to try these even though entries as expected are found in the first place to which one has turned. Words or phrases with an opposite meaning to the one in mind may serve as subject headings under which desired entries may be found. For example, the searcher interested in viscosity may find significant entries under the heading 'Fluidity' in additon to those under 'Viscosity.' Incidentally, it may be noted that the word 'consistency' may serve as a heading for still other entries. Or, some entries under 'Electric resistance' may interest the searcher whose thought on turning to an index was of 'Electric conductivity.' If such related subjects are not suggested by cross references and have not been thought of in advance, they may be suggested by the nature of some entry under the heading first turned to if one is on the look-out for them.

"The resourcefulness required in making a thorough search through subject indexes can best be discussed by treating of an example:

"Suppose one were interested in looking up all possible references on vitamins. The first place to which to turn naturally would be the heading 'Vitamins' in the indexes to the various reference sources to be used. This would rarely, if ever, be far enough to go. If only one of the indexes contained 'see also' cross references, these might be helpful in the use of the other indexes. This playing of one index against another, so to speak, is always a possible means of helping out. Cross references should be looked for. Since it is not always possible to find such cross references and it is not safe to depend too much on them, to be complete one might follow out a line of thought as follows: Vitamins are constituents of foods. It may be worth while to look under 'Foods.' Entries may be found there with some such a modifying phrase as 'accessory constituents of.' Vitamins are a factor in health and the effect of foods on health involves the idea of diet or ration. These headings, or this heading if they are combined under 'Diet,' for example, as would seem best in a true subject index, would no doubt prove fruitful of significant references. Studies of proper diet or of adequate ration for an army would beyond doubt involve the vitamin theory. Experiments to determine the nutritional value of foods are frequently called feeding experiments, so a heading 'Feeding Experiments' may be looked for to advantage. Food is taken for the purpose of nutrition and the

vitamin problem is a nutrition problem. Therefore, the general subject 'Nutrition' needs to be examined in the indexes. There is, of course, such a thing as plant nutrition as well as animal nutrition. One might seek to determine, if he did not know, whether or not there is a theory of plant nutrition analogous to the vitamin theory in animal nutrition, so the heading 'Plant nutrition' or the heading 'Plants' would be suggested. If he did not know it, he would likely learn that there are substances supposed to be factors in plant life called *auximones* by Bottomley, which are analogous to the vitamins in animal nutrition. The heading 'Auximones' would, of course, then be suggested for reference. The lack of vitamins in the diet is considered by some to be the cause of certain diseases (beriberi, pellagra, polyneuritis, scurvy, xerophthalmia). These ought, therefore, to be referred to as index headings. The general heading 'Diseases' should be tried also, such a modifying word as 'deficiency' being looked for. Perhaps the next thing for the index user to do would be to ask himself, or someone else, whether or not there is a definite name for this general type of disease; he would find that there is and that the name is avitaminosis, which should then be turned to as a heading. Certain specific foods have been used and studied, particularly with reference to the vitamin theory — as, for example, polished rice, milk, butter, orange juice, yeast, tomatoes, etc. It seems unreasonable to be expected to think of these, or at least all of them, and yet an article entitled, say, 'The Effect on Pigeons of Eating Polished Rice,' may be word-indexed only in some index, and therefore only get under the headings 'Rice' and 'Pigeons.' Vitamins have been differentiated as 'fat-soluble A,' 'water-soluble B,' etc. and are sometimes spoken of merely in these ways. It is conceivable that some indexes may have these names as headings. In the earlier literature studies resembling the modern vitamin studies are to be found in which other names for the accessory food constituents are used, as nutramines (Abderhalden), bios (Wildiers) and oryzanin (Suzuki). The text referred to from any one of the above mentioned headings may suggest still other headings, as the names of specific foods supposed to be rich in vitamins.

"The principle of referring to the general as well as to the specific subject, as exemplified in the preceding paragraph by the subject 'avitaminosis' for the general and by the individual deficiency diseases (beriberi, etc.) for the specific, is a good one to keep constantly in mind in using subject indexes. This principle applies aptly in searches for information regarding compounds. Group names for compounds may serve as index headings under which entries of in-

terest to the searcher interested in an individual compound may be found. An example will serve to illustrate:

"Supposing one were interested in finding all the information he could with reference to the electrolysis of sodium chloride. In addition to looking up references under 'Sodium chloride' in the indexes to be used, it would be desirable to look also for entries of interest under such headings as the following: 'Alkali metal halides,' 'Chlorides,' and 'Halides.' A process described for the electrolysis of alkali metal halides in general may be of just as much interest and value to the search in hand as one specified to be particularly for sodium chloride, and yet the indexes are not likely to carry entries for each of the members of a group of compounds if a definite group is under discussion. Cross references may be supplied in some cases but it is hardly reasonable to expect an index to go further. A process for electrolyzing chlorides, for instance, could not within reason be entered under headings representing each of the numerous known chlorides. The index user must expect to think of such possibilities and make his search complete accordingly. Another different kind of lead to follow to insure a complete search, particularly when the indexes to be used are word indexes, is to think of products of the process being studied, in this case chlorine, sodium hydroxide, and possibly sodium hypochlorite. And in addition to looking up the headings represented by the names of these compounds, completeness is insured only by trying the headings 'Halogens,' 'Alkalies,' or 'Alkali metal hydroxides,' and again possibly 'Alkali metal hypohalites' and 'Hypohalites.' The product of some simple electrolytic process which does not involve the recovery of chlorine of alkali may be merely called 'bleaching solution' or be given some like name. And still further it may be worth while to look up such a heading as 'Potassium chloride' as a representative of a closely related compound which might be subjected to a similar process, or at least might be studied as to the possibilities. Still other headings worthy to be tried are 'Electrolytic cells' and possibly 'Electrolysis'; this last heading, however, is too general to be used as an index heading for every process involving electrolysis, and is not likely to be used for studies or discussions of specific substances. This whole example serves to show again that resourcefulness and the use of one's general knowledge of chemistry must come prominently into play in the making of index searches.

"The resourcefulness necessary in the location of information by means of the great variety of subject indexes in existence may seem to be little more than clever guessing at times. A paper on glass, so

called and indexed only under ' Glass,' may reveal a principle governing the action of metals or other under-cooled melts. Authors often fail to see the full significance of their experimental results, and it is not often that the indexer will go further than the author in bringing out this significance for attention. The kind of flexible ingenuity necessary for the location of information in this way is perhaps only to be acquired by experience. It is really more than guessing that results in the location of information in this way, and yet it seems as if a little more than reasoning power, something like intuition, is sometimes necessary.

" Chemical publications present a special problem, both to the subject indexer and to the index user, in that many headings must consist of the names of chemical compounds. The difficulties encountered are to be attributed (1) to the fact that many compounds have, or may have, more than one name, (2) the names, or at least the best names, of the more complex compounds may be difficult to ascertain, and (3) new compounds are constantly being prepared, which, if named at all, may receive more than one name which is justified from one point of view or another, and the possibilities of incorrect names are great.

" It is not feasible to enter into a detailed discussion of the best procedure in building or using indexes of chemical compounds. Some indexes are based on systematic nomenclature, irrespective of names used by authors; others are not. Cross references within an index and introductions thereto, and the use by index searchers of dictionaries, chemical encyclopedias, hand-books, and other sources of information leading to a knowledge of the names, sometimes numerous, of compounds, are helps to be utilized. As mentioned above, a knowledge of what constitutes good nomenclature is a great aid in the location of compounds in name indexes. This is particularly important for the organic chemist. It is on account of the almost insurmountable difficulties due to the complexities of chemical nomenclature and because of language differences, that a basis other than their names — namely, their empirical formulas —has been sought and, to a limited extent, used, in the indexing of compounds. A formula index provides a certain means for the location of individual compounds; it is very doubtful if the average chemist can locate compounds in all cases in name indexes even though systematic nomenclature may have been consistently followed in the indexing. In name indexes it is possible, by appropriate devices, to group related compounds to good advantage. This is well brought out in a discussion written in 1919 by Dr. Austin M. Patterson.

"The subject index searcher is confronted with nomenclature problems relating to fields other than that of chemical compounds. For example, the chemist interested in plants must contend with the fact that some indexes use the scientific names (genus and species) of plants as headings and others use common names, of which there are frequently several for the same plant.

"The use of indexes in foreign languages presents obvious difficulties. It is one thing to be able to read a foreign language and another to translate one's thoughts into that language. The use of an English-French, English-German, or other like dictionary, depending on the language involved, is about the only help available. The introduction to Patterson's German-English Dictionary for Chemists and that to his French-English Dictionary contain some helpful suggestions useful for determining German and French names of chemical compounds.

"May I conclude by asking a question? Of the limited amount of information which we as individuals can store in our heads, is it not preëminently desirable that a part of that information consist of a thorough knowledge of where and how to locate additional information when needed?"

Author index. It may not appear that one searching for information on a particular subject would have any use for the author index but an individual who writes an article or takes out a patent in some field is apt to repeat the offence and may well be watched for several years thereafter. After finding a considerable number of articles or patents on the subject in hand, it is well to make a list of the authors concerned and look them up in the name indexes for some years covering the period of their probable activity. This can be done rapidly if the names are arranged in alphabetical order, as then one can follow the index right through. The references found are scanned for possible bearing on the problem in hand. This method is particularly useful as an aid in patent searches, since patents are made as broad as possible and their titles frequently do not suggest many of the processes which they are intended to cover or which they may be later stretched so as to cover.

Chain letter system. If Smith writes to five friends advising them to buy his cough drops and asking each of them to write to five and each of these to five and so on for eleven times, 61,035,155 people or about as many of the people of the United States who may be supposed to have coughs at one time will receive letters, provided every one writes. If one reads an article on a topic, one usually finds more than five references to the work of others along the same line.

These are looked up and new references obtained from each and so on back. A surprisingly full literature review of a subject may be made in this way and this method should never be neglected in making a search, though it is to be regarded as supplemental. There are two weaknesses to this plan; the references multiply as one goes backward in the years while as a matter of fact the number of articles appearing is increasing from year to year; thus one locates only a small proportion of recent articles. Sometimes an author omits a reference to an important article, usually by failing to make the proper search, sometimes because it was published in a foreign language which he did not read easily or in a journal to which he did not have access, and even in some rare cases, because he wished to slight the other chemist. The next man to treat this topic may assume that his predecessor's search was thorough and so it sometimes transpires that such an omission persists through decades.

When the index method is employed, it is best to begin with the last index and work backward from year to year and add to the references thus found all those in the articles as they are looked up. As each article is abstracted references to other articles may be added to the abstract to be checked off as they are looked up. All the references, primary, secondary, tertiary, and so on, may be written down on sheets of paper. As they are looked up they are checked off, the important ones being abstracted in the notebook or on cards. Some time may be saved by placing all references to one journal on one sheet of paper and those to another journal on another and then looking up all those in a given journal in succession rather than running from one part of the library to the other.

Recording Information

There is little use in obtaining information if it is not preserved, and preserving it is of no great value unless it is so arranged as to be readily accessible. Information is rarely accumulated for the sake of having it, we must assemble what we have gathered here and there into some connected whole, the history of an art, a paper study of a proposed manufacturing process, a literature report to serve as a basis for research, the introduction to an article so as to show the setting of the new results, a survey of the state of the art to aid in interpreting or in overthrowing a patent claim, a monograph, a book or a compendium.

The system of recording facts as found must be chosen with a view to the intended use. If there is a possibility of the records

oming into court extra care must be taken to make exact quotations r better photographic reproductions of important parts. Flexibility ; also important, we usually need to arrange and re-arrange many imes before putting the material in final form.

Library cards are extremely useful and may be used alone where ıe reference and information are placed on the card or as an index ɔ a notebook of filing system which contains the material. The ystem adopted depends on the purposes and tastes of the investiator. Some prefer large cards on which extensive abstracts may e written while others use small cards and add a second or third in ase much information needs to be recorded. In case the reference , in a book or journal which is always accessible, the abstract may mply indicate the contents of the article which may be turned to for ıller information but if one journeys far to locate an article in a ıre book, one will want to copy or photograph everything that may e of possible use.

One great advantage in having the abstracts on cards is that ıey may be arranged in different sequences for different purposes. ı looking up a large number of references it frequently saves time ɔ write them on cards first. The cards are sorted according to the ɔurnal, those to the *American Chemical Journal* in one pile, those ɔ the *Berichte* in another and so on. Those in each pile may be ɔrted according to year so as to minimize the handling of volumes. /hen the library search is complete the cards are all brought to-ɛther and arranged to bring out the desired facts. It may be desirɔle to make out extra cards in some cases to serve as cross references. hey may be sorted according to authors and an author index copied ɔm them, then chronologically so as to bring out the historical ɛvelopment, then according to subject, and so on till everything value has been brought out. A loose leaf note book may be used much the same way as library cards but if there is to be frequent ɛference to the material the cards are to be preferred as they are ısier to finger.

Card sizes. It is desirable to start in with a size and style of ırd that is always readily obtainable. Unless cards are well cut ıd of exactly the same size, much time is lost in handling them. ɔme standard make should be selected and adhered to. It is not ɛcessary to buy the heavy, highest grade cards which are used in ɔraries where they are to go into permanent indexes which are to be ındled thousands of times. Unless one is careful there is apt to be ɔnfusion on account of the fact that some cards are cut according the metric system and others in inches. It is a nuisance that the

75 x 125 mm. and the 3 x 5 inch sizes are so near alike. Since the 3 in. = 76.2 mm. and 5 in. = 127 mm. there is only 1.2 mm. difference in height and 2 mm. in length. The two sizes are indistinguishable to the eye unless the cards are placed side by side but the difference is great enough to make it impossible to finger with any speed an index in which the two sizes are mingled. Differences in texture or thickness of cards are not so serious. In some cases cards of several colors may be employed to advantage, each color being reserved for some special sort of references. For filing the cards, boxes to hold several hundred are to be had at a small price. As the collection grows more space can be provided in a card cabinet.

Writing the cards. It is much easier to find the desired information if the various items are always arranged in the same fashion on the cards. Just what things are to be featured and the order of prominence will depend on the purpose in hand. There are several things: general subjects, particular subject, author, and reference to journal which should be prominent on every card and which should always be in the same relative positions so that the eye falls on the desired item without loss of time as the cards are handled. Below is given a specimen arrangement which is useful:

Catalysis *Dec. of Acids.*

C.A. 8, 3438. C.r. 159, 217–20. P. Sabatier and A. Mailhe.
Cat. dec. BzOH at 450–500° over various oxides.
CdO, TiO_2 and ZnO and Cu dec. BzOH rapidly.
ThO_2, Cr_2O_3 & Al_2O_3, slightly active.
Ce, Zr, Mo & W oxides, inactive.

The fact that the *C.A.* reference is placed first indicates that the article was first noted in *Chemical Abstracts*. When the article is looked up in the *Comptes rendus* a check mark may be put over the "*C.r.*" to show this fact If much additional information is to be taken from the original article it is usually desirable to write a new card on which the *C.A.* reference will be put last. This is only one form of arrangement: other forms may be devised to suit particular purposes or individual tastes.

Remembering instead of writing. A somewhat different view is presented by Dr. Alsberg. Each reader should employ the method best suited to his own mind and to the problem in hand.

"With reference to abstracting and preserving information obtained, I would suggest that many men waste an awful lot of time in the preparation of their own abstracts and of card catalogs of

literature. None of these devices, in my judgment, can compare with a trained retentive memory. I have myself in my youth wasted much time in filling notebooks with abstracts of papers that I studied. I have hardly ever had occasion again to refer to these notebooks. The only useful purpose served has been that the act of taking notes served to fix the contents of the papers in my memory. With the modern facilities in the line of abstract journals, etc., in my judgment, a man should confine his note taking to the thoughts and ideas that come to him as he reads the literature. I have, following this plan for a number of years, kept a series of notebooks which I call my problem books. Whenever I get an idea from reading or otherwise, or whenever I think, in reading over a paper, of a different interpretation of the facts recorded therein from that given by the author, I put the thoughts into my problem book together with the citation to the article that aroused the thoughts in my mind. In this way I have accumulated a vast amount of material for work — far more than I shall ever be able to attempt myself." [2]

[2] Written for this book by Dr. C. L. Alsberg.

CHAPTER IX

PATENT SEARCHES

Facilities for Searches and Methods of Making Them

A chemist working on a technical problem must, of course, take into account all patents in the field. It is obviously poor business to spend time and money elaborating a process which has been covered by patents belonging to other people. An exact knowledge of the patents in a particular field is necessary to avoid infringing them and is good insurance against the possibility of unfair prosecution. The investigator in pure chemistry is not in fear of legal penalties in case he trespasses on a field covered by a patent but is bound by the scientific code to give due credit for ideas and data wherever published, so must be able to search patents as well as articles.

The modern abstract journals treat patents as any other publication, abstracting, classifying and indexing them so that the chemist frequently does not need to go further, but when a thorough search is to be made it must be based on the patents themselves. An abstract of a patent is not the patent either in science or in law. A fortune may hang on the wording of a sentence: a patent supposed to be worth millions may be invalidated by the unearthing of a statement or claim in a prior patent. There are special facilities provided for making patent searches that the searcher should know about and there are efficient ways of making these searches. The ways and the facilities are described in the following section by W. W. Ammen of the Philadelphia Patent Bar.

PATENT SEARCHES

By W. W. Ammen

The nature of patents. A patent is essentially a grant by a government of the right to exclude others from practicing or otherwise exploiting the patented invention. In modern patent systems, the grant is limited to a definite term of years, which varies in different

countries, seventeen years in the United States. The aim of patent systems is to promote the progress of useful arts in two ways:

(1) By inducing inventors to make their inventions known rather than to practice them secretly;

(2) By encouraging people to expend time, money, and effort in devising and perfecting inventions.

The prototype of modern patent systems is the British, whose inception is traced to the "Statute of Monopolies," enacted in the reign of James I (in 1623), as a curb on the ancient and oppressive royal prerogative of granting monopolies of particular industries or manufactures: *e.g.*, salt, iron, powder, vinegar, bottles, saltpetre, oil, starch, etc. After prohibiting such monopolies in general, the statute declared an exception of:

"Any letters-patent and grants of privilege, for the term of one and twenty years or under, heretofore made of the sole working or making of any manner of new manufacture, within this realm, to the first and true inventor or inventors of such manufactures, which others, at the time of the making of such letters-patent and grant did not use," etc.

In accordance with the peculiar genius of English institutions, the patent system as we know it gradually developed from this seemingly insignificant exception in a statute of general prohibition. The granting of patents in England did not, however, assume large proportions till about the seventies.

In this country, patents were granted by various colonies prior to the Revolution, and were provided for in the Constitution as originally signed in 1787:

"The Congress shall have power . . . to promote the progress of Science and Useful Arts, by securing for limited times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." (Art. I, sec. 8.)

The first patent statute was enacted by Congress in 1790. In substantially its present form, our patent system dates from 1836, when the examination of inventions for novelty was instituted, and the present series of patent numbers begun. The rate of issue remained rather low until the late sixties, however: through 1867 the total output had only amounted to about seventy thousand, — less than twice the number granted in the year *1922* alone.

The Peculiar Position of Patents in Technical Literature

As possible sources of information, patents present two characteristics which together differentiate them rather sharply from the rest of the technical literature.

(1) Patents are avowedly and primarily *practical,* and are concerned with scientific observation or theory only as it bears on practice. It is not necessary to know the scientific explanation of a process or of an alloy, for example, in order to secure a valid patent on it: indeed the underlying scientific principles of an invention are not as such patentable. And although a correct understanding of underlying principles is of great assistance toward patenting an invention most effectively, yet a great many inventions are continually being patented without any such fundamental understanding of their real nature. They are based on mere empirical observations, not yet advanced to the stage of scientific explanation or generalization.

(2) Contradictory to what has just been said, as it may at first blush appear, patents are not necessarily to be relied on as stating what has been tested by actual practical experience. Many represent inventors' speculations or "pipe dreams," so to speak: what someone had *thought* of doing, and wished to preëmpt without the delay or expense of practical test. Here the proof of the pudding is altogether in the eating: such patents are valid only if what they propose actually does work.

In the technical literature generally, on the other hand, statements and descriptions are at least *supposed* to be based on actual test or experience.

Determining the scope and field of search. It is well to realize at the outset that at present no search of scientific and technical literature is ever "*complete.*" The practical question, then, is merely as to how far one can or ought to go in a particular case? According to the nature of the subject and the object with which the search is undertaken, a point will always be reached, eventually, where all competent judges must agree that the probability of finding "a reference" and its possible value if or when found do not warrant the time, trouble or expense involved in continuing.

Surprising as it may seem, this broad proposition holds good even in so special a field as that of patents. Up to the present time, in round numbers, there have been granted a million and a half of United States patents; something like as many or more British patents; about two hundred thousand Canadian patents; some four

hundred thousand German patents; and over a half a million French — not to mention patents in most of the other European and American countries, in many colonies of various countries, in Japan and other Asiatic countries, etc. The specifications and drawings of U. S. patents alone form a library half a block long in one of the corridors of the Patent Office. And while the patents of many or most countries have been digested or classified to aid and shorten searching, no digest or classification puts in its proper place *every* item of information in *every* patent. Even though the patent be digested or cross-referenced a dozen times, the particular point that the *searcher* is interested in may have been overlooked or slighted.

Generally, therefore, it is necessary to make some preliminary study of the point under investigation, as well as of the possible field of search. Often it may be worth while to do a little preliminary reading in text-books, encyclopedias, or other works, — or to consult someone with practical and historical as well as "book" knowledge of the general subject, to enable one to lay out a program more intelligently. The initial program may require repeated revision as the search progresses; but it should usually, nevertheless, enable the searcher to cover the ground in the order of the likelihood of making a find.

This is of some practical consequence in cases where a good reference at the start would not justify dropping the search; because when good references are found early, the searcher's notebook will not at the end be overloaded with a lot of inferior material to be ordered, paid for, and then tediously weeded out.

It is here impracticable, of course, to do more than notice briefly some of the points that ought generally to be considered in determining what ground to cover.

When should patents be examined? The answer to this question must depend especially on the nature of the matter under investigation.

(1) Is it purely scientific and academic, without practical phases or possibilities to bring it into the vision of inventors?

(2) Has the industry involved resorted much to patents?

In many industries, every slightest variation of practice is marked by a patent; while text-books and the technical literature as a whole, deal rather with generalities, or with shop practice, etc. In other industries the case is just the reverse, — as it has been considered feasible to keep important processes and improvements secret. In such industries, relatively little is ever patented, and only meager outlines of actual practice find their way into print at all.

Countries and Periods. Here a background of general and his torical knowledge regarding the broad subject involved in the searc often affords valuable guidance. No chemist is likely to overloo Germany where dyestuffs are involved; but he also needs to kno something of dates at which certain classes of dyes came into us Likewise, one interested in vacuum tubes or in some classes of elec trolytic apparatus may overlook an important field or waste muc time if not adequately informed as to the use of vacuum tube c electrolytic detectors in wireless telegraphy.

But besides such special points arising out of the particular sul ject matter under investigation, certain more general consideratior are helpful.

On inventions that are patented at all, applications are generall filed earliest in the country of the inventor's residence. A ver large majority of all inventions are made in the progressive industri countries: Austria, England, France, Germany, and the Unite States: to a less extent, Switzerland, the Scandinavian countrie Italy, Canada, and Japan; also Belgium, Holland, and Australi However, most inventions of any practical value that are patente in *any* country are usually eventually patented in one or more of th five more important ones first mentioned.

Of the nationalities above mentioned, those for which good searc ing facilities are available in this country are the American, Britis German, French, Austrian, Swiss, Swedish, Danish, and Norwegia After these have been examined with reasonable thoroughness, th labor of covering other countries becomes so much greater in propor tion to the diminished chance of finding a reference as to be well nig prohibitive, — unless, of course, peculiar circumstances point to som particular country's patents as especially promising.

More or less frequently, the searcher will find a relevant pater in some country other than that of the patentee. It is then ofte desirable to examine the indexes of patentees issued by that inven tor's own country, to see whether he has not patented the inventio at home. The reason for this is two-fold: the home patent ma sometimes contain descriptive matter that is omitted from the patent taken out in other countries; and its date may be earlier.

It is frequently useful also, to know something about the practic of issuing patents in various countries. In England, for exampl all applications on which patents are not granted within a certai time are thrown open to public inspection. In most of the importan countries, patents are granted only after an examination for novelty which necessarily consumes more or less time, and may result in mor

or less change of the specifications. In France, however, the specification regularly issues just as filed with the application; and in Belgium, the specification so issues with extreme and invariable promptitude, — in fact only about one month after the application there.

Hence some concerns have agencies in these countries to watch and send them copies of all patents along certain lines as soon as made public, in order to know at the earliest moment what patents they must ultimately expect to see granted in the countries where they have important interests.

In this connection, it is desirable to refer briefly to the *International Convention for the Protection of Industrial Property*, — an agreement to which most of the countries mentioned above are parties. Under this agreement, a patent application filed in any of the countries adhering to it, by a citizen of *any* adhering country has the same effect as if filed on the date of the *first* application filed by the same applicant (or his assignor) in any *other* adhering country: *i.e.*, in case of several applications for the same invention, preference is given to the one with earliest filing date in *any* " convention country."

This right of priority, however, is subject to one important limitation: It exists only in favor of applications filed *within one year* after the first in a convention country. Hence we rarely find a patentee with patents for which the applications spread over more than a year; for otherwise the later patents would generally be void. This limitation greatly reduces the period to be covered in running down all patents issued under the right of one inventor to a particular invention. It does *not*, however, of course, preclude the existence of *other* patents on a like invention under the right of some *other* inventor. However, by a series of minor modifications, one patent may be strung out into a series covering a number of years.

Facilities for Patent Searching. A great many libraries in this country have substantially complete sets of United States patents, and a smaller number have sets of the patents of various foreign countries, — British, French, German, etc. German patents are rare in this country. In most or all cases, however, such sets are simply bound in numerical order for convenient reference, so that it is really impracticable to use them for searching. In the U. S. Patent Office at Washington, however, sets of American, British, German, Austrian, Swiss, Swedish, Danish, Norwegian, and French are available, classified nearly according to the official classifications of the several countries. Generally speaking, it is on the whole rather preferable to search them about in the order of their enumeration here: the

French last for the reason that the classification is unsatisfactory and a search in them often proves excessively tedious.

In detail, the resources of the U. S. Patent Office available to the searcher of patents include:

Publications of the U. S. Patent office: Its own *Manual of Classification,* enumerating in detail the official classes and subclasses that form the basis of its own work, and containing an extensive subject-index. The current edition is that of 1920; it is supplemented by semi-annual *Classification Bulletins.* It should be mentioned that the classification has for some years been in process of sweeping revision by the "Classification Division" instituted about the beginning of the present century, and that this revision is still far from completion.

The much bulkier volume of *Definitions of Revised Classes and Subclasses,* likewise supplemented in the *Classification Bulletins.*

Its own published translations of the official classification of the German Patent Office, and of its index.

These are inexpensive, and can be bought in the U. S. Patent Office or obtained by mail from the Government Printing Office, Washington, D. C.

The *Official Gazette,* published weekly, giving particulars of each week's issue of U. S. patents, including the official classification, one or more claims, and one figure of the drawing of each, as well as an index. This can be subscribed for through the Government Printing Office.

The *Annual Report of the Commissioner of Patents,* contains particulars of all patents granted each year including indexes and names of inventors and patentees and is also obtainable from the Government Printing Office. In recent years the indexes have been published separately from the annual report, under the title *Index of Patents.*

Copies of all of these are available for reference in the "Search Room" or the "Attorneys' Room":

Location of facilities. In the "Classification Division."

A numerical list giving the official classification of all U. S. patents in the "Revised Classes," and of a considerable number of those of other countries.

In the "Search Room":

(Open during regular business hours of the Patent Office; may also be used from 5 P.M. to 10 P.M. and on holidays by securing special permission and paying a small fee for attendance).

A complete set of U. S. patents, arranged according to the official classification, and extensively cross-referenced

A complete set of the *Official Gazette.*

In the " Attorneys' Room " :

The application for any U. S. patent may be ordered down from the files and examined. This is not only useful in determining the proper scope of the " claims " of such patent, but as showing what references the Patent Office cited as bearing on its subject-matter. Often these references extend to features not involved in the claims as issued.

In the corridor adjacent to the Search Room:

A complete set of U. S. patents in numerical order.

In the various " Examining Divisions " :

Duplicate classified sets of the U. S. patents in the classes over which each has jurisdiction in reference to applications for U. S. patents; also foreign patents relating to the subjects handled in the division, *classified more or less according to the U. S. official classification.*

In addition, various examiners (especially in the chemical divisions) have " unofficial " cross-references, digests of particular subjects along lines different from those of the official classification, or have further subdivided the official subclasses for their own convenience. Permission to examine such material can generally be secured, and may result in shortening the search or putting one on the track of references he might not otherwise find, and of classes one otherwise might not think of investigating.

In the " Scientific Library," adjacent to the " Search Room." (With the same hours and privileges for evening work:)

Besides the official classification of the German Patent Office and its index, mentioned above, the official *Classification of the British Patent Office,* and a small booklet published by the British Patent Office containing (in English) the official classification of the remaining six of the nine countries mentioned above, and one or two others.

As to all of these, it may be said generally that the British, French, German and Swiss classifications differ greatly from the U. S. and from one another; the Swedish, Danish and Norwegian are arranged according to the German scheme, but with less subdivision; and the Austrian is likewise much like the German, with some minor modifications.

Periodical publications of most of the patent offices of the world corresponding more or less to the *Official Gazette* of the U. S. Patent Office and to the indexes in the *Annual Report of the Commissioner of Patents* mentioned above, etc. These are sometimes useful in ascertaining the exact dates of issue, publication or " sealing," etc., of foreign patents, or in running down patents in various

other countries corresponding to one found, or in determining whether or not a particular patent is still in force; also in ascertaining the native classification of a particular patent.

Besides the classified sets of British, German, Austrian, Swiss, Swedish, Danish, Norwegian, and French patents, *numerically* arranged sets of these and of the patents of a considerable number of other countries. These are useful not only for general reference, but also in ascertaining the native official classification of such patents known to relate to the subject under investigation, — for the patents of most foreign countries bear the official classification as part of the title at the head of the specification.

Of all patents the British are, perhaps, the easiest and most satisfactory to search, especially as so many inventions made elsewhere are patented in England. Not only is the classification exceedingly good, but the search is carried out in a very excellent system of abridgments, so that it proceeds more rapidly than if the patents themselves had to be examined. Instead of being subdivided, each class is provided with periodic sets of "*index headings,*" which bring together cognate patents of the period on almost every conceivable basis of similarity: indeed, this feature is equivalent to a number of independent classifications rolled together, with thorough cross-referencing thrown in. The system appears to have been applied to all the patents regardless of the division into main classes, as well as within each class. Its only drawback is that in recent years the number of patents to be looked up under any heading tends to be tediously large, — so that where the feature sought for can be picked out in a drawing, at least, it is often quicker to go through a class page by page.

As the searcher will quickly find, the numbering of the older British patents starts afresh each year, — the numbers, indeed, being those of the applications as originally filed. In 1916, however, the continuous system of numbers used in most other countries was adopted, starting at 100,000.

The present system of British abridgments begins with the year 1855. There are abridgments prior to that, but differently classified, and intrinsically much inferior. In many cases, of course, it is not necessary to look at them; but occasionally it may be found well worth while.

After the British, the German patents are the most satisfactory to search. The classification is good; and the subdivision has been carried to the point where the number of patents in a final subclass is generally small, so that a number of subclasses can often be

searched in a very short time. The German set in the U. S. Patent Office begins with 1892, just about coinciding with the period of our more modern industrial development.

The Austrian, Swiss, and the Scandinavian countries' patents are very much on a par: the ultimate divisions to be searched are larger than in the German: and the likelihood of a reference not duplicated or paralleled elsewhere is generally small.

The French patents are exceedingly unsatisfactory to search. The classification is cumbersome and unscientific. They begin with the year 1791, but at 1900, there is a break of two years in the set in the U. S. Patent Office. In the earlier years, especially, the set is avowedly incomplete, owing to the fact that many patents were never published. Only in exceptional cases is a search in the French classified set likely to be worth while, as a last chance.

Procedure in a Patent Search. While everyone will naturally develop his own procedure with experience and vary it according to peculiar circumstances of particular cases, for the beginner, who feels at a loss where to start, the following suggestions may not come amiss.

(1) If one knows of any patents closely relevant to his subject, it is well to ascertain their classification in their native patent systems. This will serve as a starting point in examining the classifications. If the closeness of such pre-known references to the points on which the search is being made seems to show that the closest existing references should probably be found there, it may be well to search such subclasses at once. In this way one gains a certain perspective, as well as a standard of comparison for references to be later examined. Both of these lines of orientation are useful in determining what further portions of the classified patent sets it is advisable to examine.

(2) Examine the U. S. *Manual of Classification.* Besides looking in its subject index under such terms as may naturally suggest themselves, it is always advisable to go over the list of main classes and to examine the subclass-lists of all main classes that seem liable to contain relevant matter.

It is also to be noted that in the front of the 1916 edition of the *Manual* there is a comprehensive analytical arrangement of the main classes which may be found of great value, if one takes the trouble to master it. (Needless to say, it will not do to rely entirely on this rather out of date edition, since much of the classification has been profoundly revised since 1916.)

Approaching the matter from these angles, it is only a question of interpreting the class and subclass titles and understanding the

general scheme of classification (explained in the front of the *Manual*) to make sure, at least, of not overlooking any possibly relevant subclasses. At the risk of repeating what is stated in the *Manual,* it may not be amiss to advise here that the searcher note for first examination the subclasses with the most specific titles that might embrace relevant material, marking those with broader and more inclusive titles to be looked at later.

In determining what subclasses to examine, it is necessary, of of course, to consider such possibilities as the following in reference to to the essentials of the ideas sought:

Their application to other uses than that particularly sought, or under more or less different conditions.

Their use in various combinations with other instrumentalities, or outside of any combination.

Their possibilities in reference to the several components of the idea sought, especially in cases where the idea sought is in the nature of an improvement in one component of some old combination.

If after exhausting the apparent possibilities of the *Manual,* no promising subclasses are found, or the number to be examined seems extravagantly large, it may be worth while to ascertain from the *Manual* which of the Examining Divisions of the Patent Office has the classes that seem most relevant, and consult some of the Examiners. Otherwise, it is usually advisable to postpone such consultation to a later stage of the search. It may be added that the classification of chemical subjects is exceedingly unsatisfactory and difficult to understand; it has recently been receiving considerable attention from the Classification Division.

(3) Having arrived at an apparently complete program of subclasses, proceed with the actual examination of the United States patents in the "Search Room," as taking the various subclasses in the order of promise.

The reasons for starting with U. S. patents are, first, the advantage of "breaking in" on a subject in a familiar language with the possibility of expert assistance and, second, the saving in cost, since U. S. Patents are sold at 10 cents each as compared with 15 cents or more *a sheet* for photostats of foreign patents. It is wasteful to order extensive foreign references if equally good are to be found amongst U. S. patents. When there is plenty of time, foreign patents can be obtained more cheaply from the governments that issue them.

In examining the U. S. patents, one is usually justified in relying on a rather rigorously enforced rule of the Patent Office: that everything described in a specification which admits of illustration in

drawings *must* be so illustrated. Whenever the thing sought falls within this rule, much time is saved by looking primarily at the patent drawings, — only referring to the reading matter when one is at a loss to understand the drawings. (In this connection, it is not amiss to remark that the published *Rules of Practice* of the U. S. Patent Office contain charts of symbols for the use of draftsmen in making patent drawings, and that these rules can be had gratis.) In chemical cases, unfortunately, illustration by drawings is often impossible, and the searcher must read the printed text, which makes the work much slower. Even so, however, it is rarely necessary to read it through from beginning to end in order to determine whether the patent is of interest. Usually reading the first and last claims is sufficient.

When the text or "specification" must be referred to, it is worth while to realize the usual arrangement of such documents, — foreign as well as domestic:

First, the heading, including the title of the invention patented.

Second, an explanation of the general nature or objects of the invention.

Third, a brief explanation of the several figures of the drawings, if there are drawings.

Fourth, a specific, detailed description of one or more ways of embodying and carrying out the invention practically. In the case of a machine or other apparatus of any complexity, this often concludes with an explanation of its operation.

Fifth, one or more "claims" defining concisely the invention that the patent is granted to cover, in its various aspects and phases of breadth and of subject-matter.

Where the patent lacks drawings, or the point sought for is such as does not admit of illustration, the title of the invention is first noted. If this does not seem to definitely preclude relevance, one naturally looks to the general explanation of the invention or to a few of the claims. If these neither indicate nor seem absolutely to preclude relevance, one skims over the detailed description. If, on the other hand, the claims show some connection with the general subject of the search, it will not do to rely on the fact that they do not involve the particular points sought; for many matters of which no trace appears in the claims may be dealt with in the description.

In each subclass that has been revised by the Classification Division should be found a "search card," bearing the definition of that subclass and references to such other classes and subclasses as

may contain relevant material. Where applicable to the problem in hand, these references should, of course, be incorporated in the searcher's program.

In working in the "Search Room," it is well to bear in mind that the material is handled many times over by a great number of people in the course of a year, so that copies of patents become misplaced or even lost and may remain so for some time before the mischance is discovered and rectified by those in charge. It will not do to rely overmuch upon the dates marked on the bundles composing a subclass, — and still less on the supposedly chronological arrangement of the patents in each bundle. In cases where great thoroughness is desired, it is even advisable to review in the "Examining Division" such subclasses as have proved potentially relevant. This review will proceed much faster than the initial search, and besides affording a check on both searcher's vigilance and "Search Room" files, it gives the now better oriented searcher a clearer perspective of the subject, — with a chance to pick up references whose full bearing may not have been apparent before.

(4) The examination of U. S. patents in the "Search Room" completed (including any extensions of the original program suggested by the actual search), consultation with the Examiners or Assistant Examiners in charge of the various classes covered is fairly in order. By postponing such consultation to this stage of the search, the searcher gains the advantage of being able to weigh the general value of the advice received and to judge of its applicability to his case. Also, he knows better what to ask about: he can tell where he has searched, and show his best finds, and ask whether the Examiner knows of better references, or can suggest other subclasses. Time in travel about the office can be saved, of course, by making this consultation the occasion for looking at the Examiners' sets of domestic patents (if it is desired to make such a review as above suggested), cross-references, foreign patents, etc.

Almost universally, the Examiners and the other employees of the Patent Office will be found courteous and obliging in their attention to inquiries to a degree quite surprising in view of their own onerous work of examining some 80,000 fresh patent applications filed each year. It is also a source of satisfaction to the searcher to know that he can communicate to them freely the specific subject of his quest without apprehension of its going further.

(5) Before considering the examination of U. S. patents complete, one should, of course, make a point of ascertaining definitely that no new classes or subclasses of interest to him have been created

by the Classification Division since its latest bulletin. For this purpose, the head of the " Search Room " may be consulted, and also the Classification Division. Occasionally, it may seem desirable to consult the Examiner of Classification himself to ascertain whether any possible field of search has been overlooked.

(6) The next step is naturally to examine foreign patents in the " Scientific Library."

It may naturally be asked why this should be thought worth while, seeing that the Examining Divisions have the like material classified according to the *Manual?* Or else why look at the Examiners' sets at all?

In the first place, there is a great advantage in covering the patented " art " from the different points of view of several different classifications, since each classification may take cognizance of some feature of a patent that may have been overlooked or disregarded in another. Moreover, it is naturally to be expected that the patents of each country will be dealt with most carefully by the patent office that granted them.

In the second place, it is a fact that the files of foreign patents in the Examining Divisions of the U. S. Patent Office are by no means so reliable as the files of U. S. patents. Instead of being attended to by the Classification Division, the foreign patents are classified by the assistant examiners in charge of the various classes and subclasses, who are seldom familiar with all the languages involved, and have not the time to read the patents through carefully anyhow. When, moreover, the U. S. classification is changed, and classes or subclasses are transferred from one Examining Division to another, the foreign patents are liable to receive very imperfect attention. As a consequence the files of some very recently revised classes contain scarcely any foreign patents at all.

On the other hand, the Examiners' foreign files afford at least *some* chance at the patents of certain countries not classified for searching in the Scientific Library.

Experience shows that in the long run each way of searching the foreign patents will reveal material not discovered in the other way. Where only *one* way can be afforded, the search in the Scientific Library is to be favored as on the whole likely to be the more complete: it has also the advantage that one always has the drawings and text of each patent together before him. However, the search in the Examiner's files (where the text is often filed away separately) can usually be carried through more rapidly.

(7) The final step is naturally to run down any leads or " loose

ends" of the previous work, — such as examining the application files of the nearest U. S. patents found and the records of any interferences in which they may have been involved. On occasion, copies of the application files of foreign patents may also be ordered from the patent offices of the various countries.

It is usually worth while to examine the technical literature at large for published articles by patentees of closely allied processes.

(8) As a check, — or in case of necessity, as a substitute, — reference should be made to books of the sort listed below which sum up chemical patents.

"A valuable digest [1] of the older United States patents relating to chemical industry has been published in Census Bulletin 210 (pub. 1902), but this list includes only patents granted prior to 1902, and hence only expired patents. Although the bulletin is now out of print, this list was also published as an appendix to Census Reports, Vol. X, Twelfth Census of the United States, Manufactures, Part IV, Special Reports on Selected Industries.

"One of the few partial lists of United States patents that have been published appears in a German publication — viz., in vol. 3 of Winther's 'Patente der organischen Chemie' (pub. 1910). This list includes patents relating to organic chemistry granted between 1895 and 1908, with the number, date, patentee and title of the patent, and the number of the corresponding German patent, if any.

"Another of the partial lists of United States patents published is that of patents granted to Germans and Austrians, compiled by the Federal Trade Commission as *prima facie* enemy-owned patents. This list, or the part of it of more particular relation to chemistry, has been published by the *Oil, Paint and Drug Reporter* during the past year, and also appears in the *1918 Year Book* of that periodical.

"A similar list of formerly enemy-owned patents, which have been taken over by the Alien Property Custodian and transferred to the Chemical Foundation is contained in a 'Temporary List' issued by the Chemical Foundation. This list includes about four thousand patents now in force.

"All of these lists are at best but partial and incomplete, and unsatisfactory from the standpoint of making any comprehensive search."

What *Beilstein* and *Richter* are to organic chemistry in general, *Friedlaender* is to German organic patents. The title "Fortschritte

[1] Barrows, Investigations of chemical literature p. 31. Reprinted from *Chem. & Met.*, March 9, 16 & 23, 1921.

der Teerfarbenfabrikation" (Published by Julius Springer — Berlin) sounds rather restricted, but, as a matter of fact, all branches of organic chemistry are included. Each volume covers a certain period and takes up the patents according to classes. Patents from 1877 to 1916 are covered in the 12 large volumes so far issued. The patents are given nearly in full. The number indexes are cumulative from one volume to another. There are also subject and patentee indexes.

"A similar work[2] is the three-volume compilation by Winther, 'Patente der Organischen Chemie.' This work is not so well known as Friedlaender's, but it is in some respects more accessible for search purposes. The first volume contains abstracts or digests of the German patents and applications between 1877 and 1905, relating to organic compounds other than dyestuffs. These are classified according to subject matter — for example, hydrocarbons, alcohols, ketones, alkaloids, photographic developers, etc.

"Vol. 2 contains abstracts or digests of German patents relating to organic dyestuffs within the same period, 1877 to 1905, and these patents are classified according to classes — for example, sulphur dyes, indigo dyes, azo dyes, etc.

"The third volume, published in 1910, is the index volume, and contains several different indexes, including a numerical list of German patents relating to organic chemistry, with the corresponding United States, English, French, Austrian and Russian patents, if any; also a list of United States patents (organic chemistry) between 1895 and 1908 with the number, date, patentee and title of the invention and the corresponding German patents, if any. Similar lists are given of the British, French, Austrian and Russian patents, with the corresponding German patents, if any. The volume also contains a list of patentees, with the patents of each patentee and of each company classified by subjects. The volume includes finally a subject-matter index of the various organic compounds, intermediates, etc., with reference to the volume and page of the first two volumes of the work where they will be described.

"A useful list of trade names of chemical compositions and products of various kinds is also included in this same volume (Winther, vol. 3), with indication of the chemical composition, manufacturer, and the patent or literature citation where a description of the substance will be found."

[2] Barrows, Investigations of chemical literature p. 33.

German Patent Publications

German patent publications and their use are well described by Dr. Jessop.

"In most cases,[3] it is a difficult and tedious task to find the specification data of a German Patent unless one is familiar with the method of procedure.

"The German Patent system differs from the United States Patent system, in that the German Patents are not published in the 'Auszuge aus den Patentschriften' ('Abstracts of Patent specifications,' corresponding to the *U. S. Patent Office Gazette*) in chronological order, but are distributed, according to their subjects, among various classes and subclasses. At present there are approximately 380 classes and subclasses which include many and varied subjects; such as *Sprengstoffe* (Explosives), *Photographie* (Photography), *Tabak, Zigarren, Zigaretten* (Tobacco, Cigars, Cigarettes), etc. with appropriate subclasses. The class especially interesting to chemists is Class 12, *Chemisches Apparate und Processe* (Chemical Apparatus and Processes). There are numerous subclasses (denoted by letters) to Class 12; *e.g.*, Class 12d, *Klaren, Scheiden, Filtrieren* (Clarification, Separation, Filtration), Class 12h, *Allgemeine elektrochemische Verfahren und Apparate* (General Electrochemical Processes and Apparatus), etc.

"Thus the patents are placed in the particular class to which they belong, regardless of a chronological arrangement of numbers, and present rather a confused appearance; *e.g.* in 1913, Patent No. 266,863, is followed by Patent No. 267,138.

"Corresponding to the Index to the *U. S. Patent Office Gazette* is the *Verzeichnis erteilten Patente* (Index of Patents granted), which is the proper starting point in a search for a patent.

"There are five sections to the *Verzeichnis* (Index), as follows:

(1) *Chronologische Uebersicht der Patente* (Chronological List of Patents), a chronological list of the patent numbers, followed by the number and letter, showing in which class the patent has been placed.

(2) *Systematische Uebersicht der Patente* (Systematic List of Patents), a chronological list of classes and subclasses, with the patents as they have been distributed, including the patent number, title of patent, date, and a page reference to the *Auszuge* (Abstracts).

(3) *Alphabetisches Namenverzeichnis der Patentinhaber* (Alphabetical Name-Index of Patentees) gives the names of patentee, number of patent, class, and a page reference to the above class from which can be obtained the data desired.

[3] Earl N. Jessop, *J. Ind. Eng. Chem.*, **8**, 1053 (1916). Quoted by permission.

(4) *Alphabetisches Sachverzeichnis* (Alphabetical Subject-Index) indexes the patents according to subjects and gives the patent number, class, and a page reference to Section 2 above. This list gives no names.

(5) *Verzeichnis der Patente* (Index of Patents):

(*a*) *Nach Patentklassen geordnet* (Arranged according to classes).

(*b*) *Nach Patentnummern geordnet* (Arranged according to numbers).

This list gives all patents which are in effect at that date, but gives only the patent numbers. In (*b*) the patent numbers are given, and after them are the class numbers and letters given in parentheses.

"The only index given in the *Auszuge* (Abstracts) is the chronological list of classes and subclasses, with the patents included in them.

"With this preliminary information, the method of procedure, which is comparatively simple, is as follows: There are three possible starting points, *viz:*

"I. Patent Number. II. Name of Patentee. III. Subject of Patent.

"I. If the number of the patent is known, look first in the following table to find in which year of the *Verzeichnis* (Index) the patent was published.

YEAR	PAT. NO.	YEAR	PAT. NO.	YEAR	PAT. NO.
1877–8	1—4390	1890	50781—55460	1902	128483—139092
1879	4391—8800	1891	55461—61010	1903	139093—149056
1880	8801—12766	1892	61011—66910	1904	149057—158245
1881	12767—17105	1893	66911—73340	1905	158246—167845
1882	17106—21236	1894	73341—79620	1906	167846—181275
1883	21237—26084	1895	79621—85340	1907	181276—194525
1884	26085—30543	1896	85341—90750	1908	194526—206135
1885	30544—34561	1897	90751—96190	1909	206136—218130
1886	34562—38569	1898	96191—101760	1910	218131—230230
1887	38570—42451	1899	101761—109190	1911	230231—242870
1888	42452—46374	1900	109191—117974	1912	242871—255950
1889	46375—50780	1901	117975—128482	1913	255951—269470

"Then look in either the first or last table in the *Verzeichnis* (Index) for that year — where the patent numbers are arranged alphabetically — and a class number will be found following the patent number. Then look under that class in the *Systematische Uebersicht* (Systematic List) and here will be found the patent number, name of patentee, title of patentee, date, and a page reference to the

Auszuge (Abstracts) for the same year. On this page in the *Auszuge* (Abstracts) will be found a short abstract of the patent (such as appears in the *U. S. Patent Office Gazette*).

"II. If only the name of the patentee is known, look in *Alphabetisches Namenverzeichnis der Patentinhaber* (Alphabetical Name-Index of Patentees) and there will be found the patent number, class number, and a page reference to *Systematische Uebersicht* (Systematic List). From this point the procedure is the same as in I.

"III. If only the subject of the patent is known, look in *Alphabetisches Sachverzeichnis* (Alphabetical Subject-Index) and there will be found the patent number, class number, and a page reference to *Systematische Uebersicht* (Systematic List), but no names are given in this section. From this point the method is the same as before.

"An example would probably be helpful. Suppose one wishes to find Pat. No. 266,863. First look in above list and there it will be seen that No. 266,863 is in the *Verzeichnis* (Index) for 1913. Upon looking in the first table in the 1913 *Verzeichnis* (Index), Pat. No. 266,863 will be found in Class 12i. Then by looking under Class 12i in the following section of the *Verzeichnis* (Index) there will be found the following:

Pat. No. 266,863. A. Messerschmidt.

'Process for Generation of Hydrogen by Alternate Oxidation and Reduction of Iron, etc.' 9/7 11 2534.

"(Note that the Germans, as other Europeans, in writing the date in this manner always reverse the month and day. Where we write 9/7 for Sept. 7, the Germans use 7/9; where we use 7/9 for July 9 the Germany use 9/7.)

"'An abstract of the patent will be found on page 2534 of the *Auszuge* (Abstracts) for 1913.

"If only the name 'Messerschmidt' were known, there would be found by looking in the *Alphabetische Namenverzeichnis der Patentinhaber* (Alphabetical Name-Index of Patentees) under 'Messerschmidt' the No. 266,863, Class 12i. Knowing the patent number or class, the above method can be used.

"If neither the number of the patent nor the name of the patentee were known, but only the subject, the patent could be located by looking under *Wasserstoff* (Hydrogen) in the *Alphabetische Sachverzeichnis* (Alphabetical Subject-Index), where there would be given the patent number, class, etc. and from this the patent could be traced as explained above."

CHAPTER X

STUDY OF KNOWN COMPOUNDS

Perfecting and Consolidating Our Knowledge of Compounds Already Made

Some two hundred thousand organic compounds are known, but how well known are they? With a few we are well acquainted but of the great majority our information is meager indeed. The properties of a substance are simply the things we know about it. If we consider ethyl alcohol, which has been thoroughly studied in recent times, a bulky monograph would be required to sum up all we know about it. For the three years, 1916–18, the work on ethyl alcohol as summarized by Stelzner requires twelve large pages containing 991 references to articles. The information contained in these is only the three year increment to the ever growing mass of facts already gathered about this one substance.

Of course alcohol is exceptional in its importance and its study is facilitated by its accessibility but it has scarcely any more properties than any one of other thousands of organic compounds on which a like amount of study would produce a corresponding mass of information. Every substance has a large number of properties which may be ascertained and the more of these we know the better position we are in to prepare the substance, to separate it from others, to identify it, and to apply it to some useful purpose. Of the tens of thousands of organic compounds that have been made there may be scores or perhaps hundreds or even thousands which have valuable properties as pharmaceuticals, perfumes, plastics, reagents, or dye intermediates but which blush unseen in *Richter* and spread their fragrance on the desert air of *Beilstein* because no one has gone to the trouble to ascertain their properties further than to take a melting point, or perchance a density or refractive index. It is putting the case mildly to say that ten times the investigation that has been done up to date might be put upon the compounds already known, and that the resulting advance in our knowledge of chemistry would be incalculable.

A thorough knowledge of the properties of individual substances is important but the interest grows as we study a number of sub-

stances so as to compare one with another throughout the list of properties in order to trace the intricate connections between properties and finally relate properties to constitution. A table of logarithms with one leaf torn out is of little value: a table containing inconsistent and inaccurate values for the logarithms of a minority of the numbers scattered here and there over the list would be scorned as utterly worthless for purposes of comparison and calculation, but such a table would compare most favorably with the tables we are now able to construct of the properties of organic compounds.

When we obtain accurate data for a large number of properties of all the members of a great number of series of organic compounds we will have the data required for attacking the great problem of the relation of properties to constitution. When we arrive at this knowledge, chemistry will become a deductive science.

Constitution and properties. No one doubts that the properties of a compound are dependent on its constitution. If a given number of atoms of given kinds are linked together in a certain way the molecule has certain properties. The properties of butyric acid, for example, its density, boiling point, refractive index, solubility, odor, taste, degree of ionization heats of formation, of solution, of neutralization and all other imaginable properties are dependent on the atoms that go to make up the molecule and their grouping: if the molecule is altered in any way, all of these properties change. We know the properties of the series of saturated fatty acids from acetic to stearic well enough so that if some member of the series, say the C_{15} acid, had not been made, we could approximate its properties quite closely from the regular progression of these properties shown by the other members of the series. In the far-off consummation of organic chemistry we may expect to be able to calculate exact values for all the properties of a compound when we know its constiution and, conversely, to write the structural formula of any substance presented to us from exact measurements on a number of its properties. We are constantly endeavoring to do both of these things and frequently meet with considerable success, but our present data are not complete or accurate enough to insure the correctness of our deductions except in relatively few cases. Whoever measures accurately any property of an organic compound of established purity and known constitution supplies that much of the needed data. Even now certain questions as to constitution, such as whether a triple bond or two double bonds are present in a molecule, are best decided by determination of molecular refraction and dispersion.

The crying need of extensive and persistent research on the prop-

erties of long known substances is realized when we look up substances in *Beilstein*. It is a common thing to find four or five divergent figures given for the melting or boiling point of a common substance the highest and lowest being frequently five or even ten degrees apart. An investigation was recently held up for some time because the melting point of piperidine hydrochloride was given as 237° when it really is 244°. The hydrochloride of a base obtained in a certain reaction melted at 244° and the base was supposed to be something else till piperidine hydrochloride was prepared and found to melt at 244°.

Incompleteness of present data. A statistical view of the state of completeness of our data on organic compounds may be obtained by a study of any table of physical constants of organic comopunds. That in Van Nostrand's Chemical Annual is here taken as an example. Great labor has been put on the collection of data for this table and every effort has been made to fill in blank spaces. This list includes 2746, a little over 1% of the organic compounds known, and it is to be remembered that these have been selected as the commonest and most likely to be of interest to the users of the manual. Hence our information on these selected few is far more nearly complete than on the average of the other 99%. The solubilities of compounds are not difficult to determine and are of great service no matter whether we are preparing, purifying or using the compounds. Numerical statements of solubilities are of real use while such statements as "very soluble," "slightly soluble" and "insoluble" have little meaning. Taking the first thousand compounds given in the table (pp. 314 to 348 of 1922 edition) and considering their solubility in water we have the following:

Mix in all proportions	19	or	1.9%
Very, very soluble	6		0.6
Very soluble	64		6.4
Soluble	66		6.6
Slightly soluble	116		11.6
Very slightly soluble	106		10.6
Insoluble	331		33.1
Decompose with water	26		2.6
Numerical solubilities	136		13.6
No information	130		13.0

For the whole table we find numerical data for the solubilities in water of 429 compounds or 15.6%, in alcohol of 181 or 6.6% and in ether of 83 or 3%. That is, of these selected, most used, best known, organic compounds we know the solubility in water of one in 6, in alcohol of one in seventeen, and in ether of one in thirty. Of course

a large number of organic liquids, such as the lower esters, aldehydes, ketones, acids and hydrocarbons, mix with alcohol or ether in all proportions at ordinary temperatures so that their solubilities are not to be measured.

Of the solubilities given some are for 95% alcohol and some for absolute while some are for ordinary ether and others for anhydrous. In the data for all three media there is no uniformity as to temperature and frequently uncertainty. Many of the date given need confirmation not to say correction. The situation is well illustrated in a recent article by Hill,[1] on the mutual solubility of water and ether. Of all organic liquids few are better known than ether, yet, as shown in this article, our data on it are conflicting: the solubilities of water in ether according to various observers varying as much as 300%. This article shows the need of overhauling and extending our knowledge of the mutual solubilities of pairs of liquids. The methods are worked out by Hill so as to bring these measurements within the range of many who lack the long periods of time or the elaborate apparatus demanded by many other problems. There are hundreds of important and readily obtainable liquids which can be studied. The data so obtained would be of great service to science and to industry.

Melting and boiling points. The state of our information as to the other properties of these compounds is not so readily shown by statistics but it may be said that the agreement of melting point and boiling point data is practically limited to those compounds which have been prepared only once. The temperatures given in the table are selected from among many divergent figures given in the literature. The compiler's best judgment was used in the selection, preference being given to recent determinations and to those which appear to have been made with the most care and the best instruments. Many chemists use any thermometer which is at hand without regard to its idiosyncrasies and there is usually uncertainty as to whether stem corrections have been applied. Most of the data are from a time when modern thermometers and methods were unknown. It would take a good sport to bet on the correctness of a melting point taken at random from the literature.

The inaccuracy of our data as to melting and boiling points has been pointed out. The incompleteness of our information must be emphasized. Of the first thousand compounds in our table we have melting points given for 636, or 63.6%, and boiling points for 575, of 57.5%, while for 284 substances, or 28.4%, we have both melting and boiling points. For a compound to be properly characterized

[1] A. E. Hill, *J. Amer. Chem. Soc.*, **45**, 1143 (1923).

both should be known. Of course some substances like cellulose decompose long before they melt or volatilize but there are many others which must have measurable vapor pressures below their decomposition temperatures. If something decomposes when we try to boil it at atmospheric pressure, it should be tried at 20 mm. or 5 mm. or 1 mm. or even at 0.001 mm. before we leave it. In fact it is most desirable that the boiling points of all available substances be known at several pressures, say 760, 20, 10, 5 and 1 mm. The complete vapor pressure curves should be determined for a large number of selected organic compounds and one or two points at least on the curves for as many as possible of the rest. This would enable us to approximate the vapor pressure curves of all since the curves for similar compounds are of nearly the same shape. In times past when the reliance in the chemical laboratory was on injector water pumps, a vacuum of around 20 mm. was considered good and boiling points of many substances were determined at this pressure, those that would not go over in this region being neglected, but now since low cost, motor driven oil pumps giving vacuum of 1 mm. or better are available many additional substances can be handled. By adding a mercury vapor pump, still more compounds can be distilled. Distillation and sublimation at extremely low pressures offer valuable methods of purification which have been too long neglected by organic chemists. It is certainly possible to determine boiling points, at some pressure or other, for a large proportion, possibly half, of the 425 which are missing in our first thousand.

It has become important to know, at least approximately, the vapor tensions of organic compounds at temperatures far removed from their boiling points and even at far lower temperatures than those at which we would ever expect to distil them even in vacuum. Lacquers, varnishes, coatings for artificial leather etc. are used in thin films on the outside of objects, that is under the most favorable conditions for evaporation. It is, of course, desirable that such coatings should remain permanent for years even under trying conditions. Substances which are difficult to distil in the laboratory, disappear in a short time from films of this sort. The choice of constituents for such mixtures cannot be put on a scientific basis till we know the vapor pressure curves of a large number of high boiling substances, particularly in the region of low pressures.

Turning to melting points, we find them given for 63.6% of the first thousand compounds in our table. Of the remaining 364 a few are solids which decompose before their melting points are reached but the great majority are liquids which must solidify at some tem-

perature or other. Helium does not solidify at —271° but it is not likely that there are many liquids in its class. It is probable that nearly all organic compounds solidify at temperatures above that of liquid air, and many of them above —80° which is readily attained by the use of carbon dioxide snow. There have been a number of investigations of low melting points but a comparatively few compounds have been studied. We have a plethora of data for a few and none at all for the many. We need many more determinations before we will be in a position to generalize about melting points.

As solid carbon dioxide is everywhere available and liquid air is accessible to many and reliable low temperature measurements are not so difficult with modern methods, the investigation of low melting points should be a fruitful field.

Densities. An inspection of our table of properties of organic compounds shows that we are by no means well off in the matter of densities. It is true that we find them for the majority of the liquids but they are by no means comparable: some are taken at 20° and referred to water at 4°, which is the proper standard, but others are compared with water at the same temperature. Others are taken at 0°, 15° or 25° which are not so bad as odd temperatures such as 14°, 17°, 22°, 18.5° or 19.5°. We frequently wish to make comparisons between members of a series such as toluene, ethyl-benzene, propyl benzene, etc., or methyl, ethyl, propyl, and butyl acetates or benzoates. When we look them up we usually find that some of the densities have been taken at one temperature and others at another so that it is impossible to get the information. Of course it is not difficult to change a density referred to water at 20° to water at 4°, and we may approximate the density of a hydrocarbon at 20° from weighings made at 18° by assuming its coefficient of expansion to be the same as that of a similar hydrocarbon but much trouble and uncertainty can be saved by adopting a standard temperature. In the old days in Europe "specific gravities" were usually taken at 60° F., which is equal to 15.5° C. as this was supposed to be the highest temperature likely to be reached in the laboratory but in our luxury-loving age we want our laboratories warmer than that and have come to use higher temperatures. It is much easier to maintain a bath above the temperature of its surroundings than below hence a temperature safely above that of the laboratory is to be chosen. With the spread of physical chemistry with its multitude of conductivity measurements which have to be made under standard conditions, constant temperature baths have become common and are available for density determinations. The physical chemists first worked at 20° but soon

adopted 25°, as that is more convenient to maintain, so now densities are commonly taken at 25°. It is desirable to determine them at 0° and at 25°, since thereby two things are accomplished, the coefficient of expansion is measured and it is made easy to calculate with accuracy the density at 15° or 20° so as to make comparisons with densities taken at these temperatures. Taking the density at the two temperatures involves little extra trouble and no additional material. The pycnometer, which must have a bulb to take care of expansion, is filled, placed in a slush of ice and water to set for 0°, after which it is hung in the balance case for a time and weighed. It is then immersed in the 25° bath and set again and reweighed.

There are a number of liquids in our table for which no density determinations can be found. When we turn to the solids given in the table we find that those whose densities are known are hopelessly in the minority: out of the first 144 we have densities for only 20 and many of these are given to only two or three places and frequently no mention is made of the temperature. The densities of solids are not so easy to measure as are those of liquids and are not frequently used for identification but are theoretically just as important or perhaps more so as they are connected with crystalline form. In fact polymorphous substances have a corresponding number of different densities which may be used for identifying the various forms and in following their transformations. Much of value has come from a study of the molecular volumes calculated from the densities of liquids. With solids the relationships are certainly much more complicated and are not to be unravelled without great labor but when sufficient data are available generalizations may be expected. The study of the densities of solids is a vast field. The methods are somewhat troublesome but are not overly difficult and many solids are at hand which can be obtained in great purity.

Crystalline form. Of the first 200 solids in our table the crystalline form is given for 72 or 36%. Many of the others are described as " needles " or " plates " but such terms mean little. For a thorough comparison of compounds we need to know their crystalline forms and habits. Obviously there is here an opportunity for a vast deal of work, the results of which should prove interesting both to the chemist and to the crystallographer. Unfortunately few chemists have the required technique but coöperation might be effected with someone who would handle the measurements, the chemist supplying the purified substances and interpreting the findings from the chemical point of view. The study of crystals has revealed many things recently as to the structure of matter.

An example of what may be accomplished by the study of one physical property is the monumental work of Brühl on the refractive indices of organic compounds. The reader is referred to the following articles:

Annalen, **200,** 139 (1880);
203, 1, 255, 363 (1880);
211, 121, 371 (1882);
235, 1 (1886);
236, 233 (1886);
Z. phys. Chem. **7,** 1, 140 (1891;
16, 193, 226, 497, 512 (1895);
22, 373 (1897);
25, 577 (1898).

CHAPTER XI

PREPARATION OF KNOWN SUBSTANCES

Improving Processes and Products

This is an attractive and profitable field for the beginner in research who has patience, a desire to do good work and who is not nervously anxious to do something startlingly new. Almost any one can accomplish something here, since there are problems of all sizes down to the very smallest. In its simplest form, this amounts to little more than making organic preparations of about the same grade as those in the usual laboratory course and then varying the conditions somewhat and noting whether there is improvement or not in the amount and quality of the product. The worker need not stop with mere modifications of a cook-book recipe, but may go on and on in the study until he finds out not only what are the best conditions for the preparation but why these conditions are the best. The study may develop into a thorough study of the reaction with a discovery of all the by-products and why these are formed and their amounts under different conditions, or into a study of the velocity of the reaction and of the factors that modify this velocity. The study may then be carried to analogous substances and may widen until light is thrown on a whole field in chemistry. There is a considerable advantage in this sort of work in that the product is already known and time does not have to be spent on its analysis and identification, so that the whole effort may be directed to the study of its formation. The amount of work of this kind to be done is very large, since of the tens of thousands of compounds that have been made only a comparatively small number have been thoroughly studied with a view of finding out what is the best method of preparation and why such method is best.

A study of the literature on almost any compound will reveal the present state of the case. The chemist who first makes a compound publishes the method he used for making it. He took so many grams of this and so many of that and heated them together for so long at such a temperature and then isolated the product in such and such a way. The rules of the game require him to tell how he actually

made it rather than to idealize his methods and describe method which he may be sure would give better results. Usually it is nec essary to obtain only enough of a new substance to characterize i and the chemist is usually satisfied to set down the first set of con ditions that he came across that gave the product and seldom make experiments to ascertain whether these are the best conditions o not. The next one who finds himself in need of this particular com pound, repeats the preparation exactly as described and commonly gets the desired substance, though the yield is usually lower or th quality poorer than was to be expected from the description. Thi is natural, as it is impossible, working from written directions, t duplicate exactly the original work. Sometimes the second chemis pauses and spends some time improving the method of preparatio and publishes a modified or improved method. Other chemists may from time to time, publish more or less additional information s that the process may be gradually improved. Any one desiring t make this compound must read the original method and then con sider all the modifications and improvements that have been sug gested. The final process may be quite satisfactory or it may not b A service, large or small according to circumstances, but a real ser vice in any case, may be rendered the chemical world by taking u the study of the present methods of preparation of almost any know organic compound. All of the proposed methods should be carefull worked over and the reasons for the improvements considered. The conclusions may be drawn as to further possible improvements. Thes should be tried to see whether they really are improvements or nc and the reasons found out as to why they are or are not. The ex periments are then followed up until conclusions are reached. B and by a really good process is evolved.

The major portion of the effort of plant chemists is directe along these lines since the commercial success of a process depenc not on simply obtaining the desired material but in making it in goo quality at a cost low enough to yield a profit. It is quite possibl to obtain gold from sea water but present methods will have to b improved before it can be done at a profit. As yields go up cos come down. When several concerns are competing in the manufa ture of a given product the one that can produce it for less, even the margin be small, has the inside track and can control the marke A horse race can be decided by a nose as well as by a neck or length and many an industrial race has been won by a fraction a cent per pound.

Separating the steps in a process. It is hard to name any man

facturing process that involves only one operation. The preparation of a dye usually requires a long succession of reactions each of which demands a number of operations such as mixing, heating, cooling, crystallizing, filtering, drying or evaporating. The over-all yield depends on the yields in the several reactions and the perfection with which the various attendant operations are carried out.

In many cases the product from one step may not need to be purified in order to be used as the starting material for the next; it may even not be necessary to isolate it. Thus if benzene is nitrated, the crude nitrobenzene without even being dried may be reduced to aniline which is finally purified. If we start with 78 parts of benzene and nitrate and reduce and get 80 instead of 93 of aniline we have no means of knowing where the loss took place. To keep on repeating the whole process from benzene to aniline, making changes in one place or another, takes much time and does not get us anywhere. The proper way is to take the process to pieces and test each step, so that we know exactly where the losses are. When a tire leaks we do not put patches all over it, but first locate the leak: the puncture is nearly mended when we know where it is. In the above case mechanical losses may occur, 1), in the handling of benzene, 2), by leaving nitrobenzene dissolved or suspended in spent acid, 3), by aniline remaining with the iron or in the water solution. The nitration may not be complete or dinitro-benzene be formed and the reduction may also be faulty. The only way is to study all the steps separately till we know just how we stand on each of them. Then we know what part needs further study. Thus we mix a known amount of pure aniline with the volume of water that is used in the process and go through the recovery to see how much we can isolate. If the deficit is considerable we see what can be done to cut it down. Then we try to separate a known amount of aniline from the sludge from a reduction experiment. When we know just how to do this effectively, we are in a position to study the reduction of nitrobenzene but this must be done with known amounts of pure dry nitrobenzene. The process is thus followed step by step from one end to the other as we would examine each link in a chain and effort is concentrated on each weak spot.

In a process involving a large number of steps it takes much time and trouble to isolate, purify, dry and weigh each intermediate product and the young chemist is tempted to take short cuts but the long way around frequently turns out to be the shortest way through.

There is another reason why each step of the process should be studied by carrying it out with highly purified materials. Each chem-

ical reaction in the series gives more or less of by-products and these, if not removed, may influence the course of the subsequent reactions or may appear in the final product as impurities. When a reaction has been thoroughly studied starting with pure materials and the yield and quality of the product ascertained one can repeat it using crude intermediates and find how the product is affected. Means may be found of counteracting the effects of the impurities.

Generalizing a particular method. Any method of preparation is worked out in terms of one particular compound. For instance, on account of the accessibility of ethyl alcohol, the ethyl compounds in a series are almost always prepared first and then methyl, isoamyl, isobutyl, propyl and other derivatives are studied. There will be found, in the literature, many cases in which only the ethyl, or possibly the ethyl and methyl, derivatives have been made by some process. In such cases it is in order to try the preparation of the derivatives from such other alcohols as may be available. This may be considered as generalizing a process. More or less of such work is usually done by any one who puts out a new process. He almost always wishes to show that it is applicable to other substances of the same class, but a study of the literature will reveal many cases in which this has not been carried far enough. In case a process has been published for five to ten years and nothing further published on it, such extension work may be properly taken up by any one, though even then it is courteous to write the author and tell him of the proposed work and make arrangements with him.

To extend the application of a method to other substances, no matter how similar they may be, frequently involves considerable thinking and experimenting. As an example, take the preparation of aldehydes from the simple aliphatic alcohols. Nothing could be easier than this seems to be as it is simply a case of oxidation and any one can write the reaction. It is perfectly obvious that chromate mixture will do the work. This mixture works well for acetaldehyde, but as we go up the series, it is harder and harder to get satisfactory yields. One difficulty is that the aldehydes are less and less volatile and for that reason more and more difficult to remove from the sphere of action of the oxidising mixture before further action takes place and they are converted into the acids. Another difficulty is that there is less and less difference between the boiling point of the alcohol and of the corresponding aldehyde as we ascend the series and this makes it harder to effect the separation of the aldehyde from the alcohol. Hence to generalize a method involves modifying it more or less at each step so as to take into account the changed physical properties

of the substance with which one has to deal. Analogies are not identities and no matter how closely analogous the compounds of one series may be to those of another there are some differences. If a process has been satisfactorily worked out for methyl compounds, it may be assumed that it will work for the corresponding ethyl derivatives, but it is also safe to predict that some modifications will have to be made in order to secure the best results. Such study, when well carried out, may be seen to involve a thorough comprehension of chemical analogies and differences and may show much skill in adapting a process so as to take these into account. A large proportion of the mass of chemical research that fills our journals is a study of the generalization of a known process and its extension to less obviously analogous substances. The point is not simply to extend the application so that one or two other substances may be made, but to find the modifications that are necessary to adapt the process to the changed conditions, etc.

Analogous reactions. The above may be spoken of as generalization of a method to homologs; there is another sort which may be called generalization to analogs. This is by no means so obvious or easy, but has been the plan of many researches. Ammonia, hydrogen sulphide, hydrogen peroxide, etc., are in some senses analogs of water, hence, with proper modifications, reactions in which water is split off or taken up may be carried over to analogous substances and reactions worked out in which ammonia, hydrogen sulphide, or hydrogen peroxide are taken up or split off, or compounds may be built up in which $-NH_2$, $-SH$, or $-O.OH$ occupy positions commonly held by the $-OH$ group. Thus amines take the places of alcohols and amides of acids and the reactions of amines and of amides may be studied with this in view. Thus a reaction which is well known in one group may be generalized into an analogous group. This idea has led Franklin to build up an ammonia chemistry analogous to the well known water chemistry. The same reasoning has led Sabatier, Senderens and others to extend recent catalytic methods to a number of classes of compounds. They found that the mixed vapors of alcohols and acids passed over certain catalysts, thoria, titania, etc., at high temperature caused the splitting off of water and the formation of esters. They tried the same method on mixtures of alcohol vapors and ammonia and got amines and on alcohol vapors and hydrogen sulphide to form mercaptans, water being split off in each case but from quite different compounds. Methods of this sort frequently lead to the formation of new compounds and this subject will be taken up again under that head.

Particularizing a general method. The converse of generalizing a process is particularizing one and it is just as important and may be made the subject of fruitful study. The method of approach has been indicated in the foregoing, and we may use the preparation of aldehydes as an illustration. Suppose that it is desired to prepare a quantity of isovaleric aldehyde from isoamyl alcohol, and it is desired to use oxidation by chromate mixture. A study of the volatility of the aldehyde and of mixtures of the aldehyde with the unchanged alcohol must be made to determine the temperature at which the reaction is to be carried on and the temperature at which a possible reflux condenser must be kept so as to return a maximum of the unchanged alcohol and a minimum of the aldehyde. Experiments may be made on the proportions and concentration of the oxidising mixture in order to effect the maximum oxidation to the aldehyde and the minimum oxidation of the aldehyde to the acid. In this particular case a number of experiments are already on record, but there is need for considerable more work as the yields are still poor and uncertain. When this and a number of other similar preparations are worked out thoroughly, we will be in a better position to generalize and figure out what changes must be made in a process to fit certain conditions. It is well known that alkyl halides may be made from the corresponding alcohols by the action of phosphorous trichloride, etc. This reaction takes place with all alcohols doubtless, but in some cases large amounts of phosphorous acid esters are formed and the yields of the halides are small. Alkyl halides can be made by the action of red phosphorous and bromine or iodine, but here again, the yields vary considerably. It would be a great convenience to the working chemist to have some one work out thoroughly just what conditions are best for each particular case and what yield can be expected. The preparation of alkyl halides from the alcohols and the halogen acids is also about as well known as any process in organic chemistry, but the directions given are various. One chemist will saturate the alcohol with the gas and heat in a sealed tube at a high temperature, while in another case longer time and lower temperatures are called for. No one knows just what is the best for, say, isobutyl alcohol and hydrobromic acid. It would be of great service if some one would work out this and other particular cases. One method may be expected to work for all, but to get the best results the method must be particularized for each of the compounds that it is desired to make. That is, a particular temperature and time of heating may be best for isobutyl alcohol and a somewhat different time and temperature best for isoamyl alcohol and so on

for the higher alcohols of the primary series. Entirely different conditions may prove best for the secondary alcohols and yet others for the tertiary. Our books on organic methods give us a large variety of methods for making these halides and the usual way is to try one and then another till enough of the desired compound is prepared for the work in hand. The object of this discussion is to call attention to such studies as these as worth-while pieces of research. The two lines of work, the preparation of aldehydes and the preparation of alkyl halides, are, at the present moment, lines of work which would be profitable, since the exploitation of the Barbier-Grignard reaction has made it desirable to obtain various aldehydes and various alkyl halides in quantity and in known purity.

Similar study is needed of the particular applications of almost every general method in organic chemistry. Mention may, however, be made specially of the Barbier-Grignard reaction. There is hardly any reaction known to chemists that has been as fruitful in providing for the preparation of such a vast number and variety of compounds. By it we can make hydrocarbons, primary, secondary and tertiary alcohols without number, and a vast number have already been so prepared. The general methods of applying the reaction are well known and there is usually little variation in the methods used. The yields are excellent in some cases and poor in others, and little is known as to the reason for this difference. There is need that each one of a large number of these preparations be studied intensively to find out just what are the conditions of a good yield in each case and particularly what the by-products and impurities are. It is known that in many cases the products are contaminated by by-products that it is difficult to eliminate. It would be of great service if more should be found out about particular cases and finally these particulars would be combined into a more general knowledge. If any one of a large number of compounds be looked up it will be found that it has been made by this reaction, but when one comes to make a quantity of the desired compound one finds many uncertainties. For showing that the reaction works in any particular case, the exact quantities used are of minor importance, but when it is necessary to make a large quantity of one of these compounds, the matter is different. For instance, on the large scale, it makes much difference whether a certain proportion of ether is used or twice that proportion. In case the substance is volatile with ether vapor, the amount of the ether used comes in again. Before this method is of great service in preparative chemistry each one of the individual preparations must be worked over with care.

We have an example of particularization whenever any substance becomes of commercial importance. A good example of this is shown in the study that has been put on isoprene [1] since it has been found out that rubber may be made from it. All the processes by which this interesting compound can be obtained have been subjected to the most intense scrutiny by the chemists of three nations and the exact conditions of maximum yield and best quality of product have been determined. A similar story may be told of every compound which has attained commercial importance.

In general, a method has to be particularized for each substance for the preparation of which it is applicable, since each product has somewhat different physical properties from all the rest. A greater volatility calls for better condensation to avoid loss, in some cases even requiring the use of freezing mixture or even more extreme means. As different products have different solubilities in water, more or less thorough methods of washing must be used. For instance, in preparing a high alcohol by the Barbier-Grignard method, the ether solution may be washed many times with relatively large volumes of water, but in making a lower alcohol as trimethyl carbinol which is quite soluble in water, the volume of the wash water must be kept down and even then the water layer as well as the ether layer must be worked up for the alcohol. The relative cost of materials is also a matter which must be considered. In working with methyl and ethyl alcohols, which are relatively very cheap, it is not required to convert all of the alcohols into the halides or other derivatives, but if we are working with some rare synthetic alcohol of which only a small amount is available, much more pains need be taken to obtain complete transformation.

There are many cases in which some peculiar property of some substance renders the application of a general method difficult or impossible. In such cases some modification of the general method must be sought that will be free from the objections. An interesting case is the preparation of linalyl acetate from linalool. In this case the common method of making an ester by warming the alcohol with acetic acid and hydrochloric or sulphuric acid is out of the question since the addition of the mineral acid causes the isomerization and destruction of the linalool and none of the desired acetate is obtained. Boiling the linalool with acetanhydride gives the desired acetate, but contaminated with more or less terpenyl acetate and other products. This problem is a very important one since linalool is comparatively

[1] Harries, *Annalen*, **383**, 157 (1911). Perkin, *J. Soc. Chem. Ind.*, **31**, 616 (1912). Duisberg, *Eighth Int. Cong.*, **28**, 81 (1912).

cheap and the linalyl acetate brings a much higher price on account of its value in perfumery. A number of modified methods of acetylation have been proposed for the solution of this problem, but no entirely satisfactory process has yet been devised.

Comparison of various methods of preparation. Almost every organic compound can be prepared in a number of different ways. Frequently widely different materials may be used as starting points for making the same substance or even if the same original substances are used different courses may be taken in building up the desired compound. In the simplest cases, in which only one step may be involved, a number of reagents may sometimes be used in taking this step. For instance, the transformation of an acid into its chloride is a simple process, but the change may be accomplished in several different ways. Phosphorous pentachloride is commonly used, but this may frequently be replaced, with advantage, by phosphorous trichloride and sometimes it is better to use thionyl chloride. The same acid chloride may be made by all three methods and the yields and purity of the products compared. This may seem an uninteresting thing to do, but in commercial chemistry such studies as these come to be of the utmost importance. A number of factors have to be considered in the final choice of method. The cost of materials suggests itself first, but the time of operation and purity of the product are of no less importance. Sometimes the size of the plant required is a determining factor. Where land is cheap and unlimited space is available, one process is to be preferred, while in some other cases the necessity of carrying on a process in small space influences the choice in the other direction. The need of special apparatus is frequently a determining factor. If a product is to be made on the small scale and in limited amount, a process that does not require much special apparatus is to be chosen instead of a cheaper process which would require such apparatus. While such problems as these preëminently concern the commercial chemist, yet this sort of study may be made profitably on the small scale in the laboratory. The amount of attention required in carrying out a process is to be considered. The student does not commonly take this into account as he has to put in the time anyway, but this becomes a matter of prime importance in the factory. The degree of skill required in the operator is also important, since there is much difference in the cost of skilled and of unskilled labor.

It would be of great service to chemists in general if a large number of studies were made in the preparation of common organic compounds by a number of different processes with an accurate

comparison of yields, cost of material and time required for the preparation of, say, 100 g. Such work as this would be excellent preparation for some of the problems that are likely to be met with in the factory.

Obtaining compounds of high purity. This is a different point of view still, and one which is important in several ways. There are certain uses of substances that demand extraordinarily high purity. Chloroform and ether may be made at low cost and in what would ordinarily be considered high purity, but the products would be totally unfitted for use in anaesthesia. Interesting studies of this sort have been made by Baskerville and Hamor.[2] The same is true of many pharmaceutical preparations. Such studies as those by Baskerville are likely to be of much service and are within the reach of many. The work may be divided into two parts, finding out what impurities are present in the products made by different processes and then devising means for either preventing the formation of such impurities or of eliminating them. It may turn out that one or more of the possible processes of preparing the substance will have to be abandoned on account of difficulty in coping with the impurities thus introduced. In studying an organic compound, it should always be prepared in as many different ways as possible and all the products carefully compared. When all of the products are brought to be identical in every way, there is a presumption that purity has been attained. It will be recalled that argon was discovered by a comparison of the properties of nitrogen prepared from various sources.

In perfumery as well as in pharmacy, mere traces of some impurities are extremely objectionable. The particular impurities may be quite different in the two cases and may be different in kind and amount from those that would be objectionable for some other use. A given substance may be highly impure from one point of view and of excellent quality from another. Traces of chlorine compounds render benzaldehyde worthless for use in perfumery but would be unobjectionable for some other uses. Hence the problem for the perfumer is to prepare benzaldehyde by some process by which no chlorine compounds can possibly be formed. Perfume materials are always distilled with great care and at as low a temperature as possible, vacuum distillation being almost always used, since traces of acrid products are apt to be formed in the distillation at higher temperatures and render the product unfit for use. Organic chemists,

[2] Baskerville and Hamor, *J. Ind. Eng. Chem.*, 3, 301 and 378 (1911); 4, 212, 278, 362, 422, 499, 571 (1912); 5, 828 (1913).

as a rule, work with too small amounts of substances for satisfactory purification. It is only by preparing a comparatively large amount of a compound that the necessary number of recrystallizations or distillations can be made and the compound obtained in high purity. It is advisable for every organic chemist to read, at frequent intervals, atomic weight work and articles of that character so as to be impressed with the desirability of working with compounds, the purity of which is beyond question.

Study of yields. In what has been said already, the matter of the size of the yield has been frequently mentioned. When a process has been decided upon and the question of impurities satisfactorily settled, the question of yield may be studied by itself. It divides itself into two parts, first a study of the process so as to obtain the maximum amount of the substance in the crude product and then of devising ways and means for isolating the maximum amount of the pure substance from the crude product. One method of work may produce a large amount of the desired product, but so much water or other solvent may be added in the process that its isolation becomes difficult and such heavy losses may occur that the process may have to be given up in favor of one which produces really less of the product but yields it in a condition that renders the isolation less difficult. For the first study, some analytical process is required which will determine the amount of the substance formed in each experiment, without its isolation. In this way the different available processes may be compared as to the amount of product formed. Then the isolation problem may be considered, working with each of the crude products. A systematic method of working up and purifying mother liquors, tailings, etc., is a large part of the study. For liquids, systematic fractionation of heads and tails, so as to increase the main fraction, is of importance.

This topic may be thought to be entirely utilitarian and only suited for the factory chemist, but when it is considered that in many of our organic preparation methods, only 5, 10, or 20% of the desired product is obtained, it will appear that we really do not know the reactions very well till we can guide them better than we do. A thorough knowledge of a reaction should enable us so to carry it out that almost the entire amount of substance put in should undergo the same change and produce a quantitative yield of the desired products. Organic reactions should be quantiative as well as inorganic. Every molecule that is put in either reacts or does not. The process should be so conducted that every molecule should be caused to react. In case a molecule does react, it produces the desired sub-

stance or some other. It should be possible, in many cases if not in all, to determine so accurately the conditions under which each of the possible reactions takes place, that when the process is held within proper conditions, the desired reaction should take place to the exclusion of the other. In cases, such as the nitration of toluene, in which two isomers are formed, it may never be possible so to conduct the reaction that only one shall be formed, but even in cases of this kind considerable progress has already been made with a number of processes.

Quick methods for small quantities. It frequently happens in the laboratory that a small quantity, a gram or two it may be, of some compound is needed and is needed at once. On a gram of substance, it does not make much difference whether the cost in quantity be one dollar a hundred grams or five dollars. The compound is needed and must be obtained. For such purposes, it is very desirable to have methods at hand that have been well worked out and can be relied upon to give the desired substance as quickly as possible even if expensive materials have to be used in the making. Under this head we may class compounds that are commonly used as reagents in qualitative tests or in quantitative analyses or substances suitable for standardization of volumetric solutions, etc. It would be of real service to chemists if such methods could be worked out and put in convenient form for immediate use. When one wants a method of this kind, one does not want to have to hunt up a number of methods and compare them to select the one that will give the desired result. The method must also be worked out and directions given for making the small quantity that is commonly required for the purposes for which the compound is used. The starting materials for the preparation should be such as are commonly at hand in an organic laboratory, as much time is apt to be wasted adapting a method so as to avoid the use of some rare chemicals that may not be at hand.

Such work as this looks small and is not calculated to bring fame, but a certain amount of it could be made useful to chemists at large. It should be published in condensed, succinct form.

Diminution of costs. In the factory, one of the chief subjects of study is the diminution of manufacturing cost. The same problem may be studied on the small scale in the laboratory and with reference to almost any organic preparation. The costs consist in the materials required for the preparation, the apparatus used or, at least, the deterioration of the apparatus during one or more operations, the water, fuel, etc., that are required to carry on the process, and the time of the operator. A study of possible increases in the yield is equiva-

lent to a study in the diminution of cost or, at least, constitutes an important element in such study. The substitution of cheaper for more costly starting materials is an important matter. It may be found that a crude product may take the place of one partially or completely purified as the starting material. It may be found possible to substitute a cheaper reagent for a more expensive one in the process of preparation. In some cases it has been found that less concentrated and less pure grades of mineral acids can replace the more expensive concentrated chemically pure acids. These matters may be made the objects of systematic and minute study, the more important the substance, the more minute the study. An interesting case, and one which has engaged a large number of chemists, particularly young chemists, has been the vanilline problem. A large number of methods have been devised for making vanilline, one important aim being the use of cheaper and cheaper materials as the starting point. The most of the processes have narrowed down to eugenol, or isoeugenol which is readily made from eugenol by heating with alkali. The later patents have been on means of oxidation of the isoeugenol, the difficulty being that in most processes, much of the eugenol is either not attacked by the oxidising agent or the oxidation is carried too far resulting in the formation of considerable amounts of the worthless vanillic acid.

One item in the diminution of cost is to find means for working on a larger scale. In many cases the preparation can be carried on with double quantities in the same time and with the same amount of attention as with the single quantities. In such a case the labor cost per unit of the product would appear to be just half. This may be the case, but the yield may be somewhat less than the double yield expected and the saving in time might not compensate for the loss in chemicals. Each preparation has to be tried on varying scales to find out which is the most economical, all things considered. When the scale of operations is increased, the capacity of the apparatus at hand may be exceeded and some other form may have to be devised. As the scale is changed, more or less alterations have to be made in the procedure. Of course the alteration of a small scale laboratory process to a large scale factory process is a serious problem, but some experiments may be made on a comparatively small scale in the laboratory.

Another item is the shortening of the time required for the preparation. In factory work this is an important consideration. Suppose a certain product is being manufactured in a plant costing, say $100,000, and that such plant is running at full capacity. Suppose

now it is discovered that, by some modification of the process, each batch of material can be run through in just half the time. Such a discovery is worth to the concern just as much as an additional plant costing $100,000 would be since the one plant now turns out just as much as the two could using the old method. In fact the discovery might be worth far more than this since by shortening the time the cost of labor per unit of product might be decreased. Taxes and insurance would have to be paid on the additional factory, but do not have to be paid on the discovery. A vast deal of work has been done on quick processes. We are familiar with the quick vinegar processes and with various rapid processes for making white lead instead of the famous old Dutch process. Many organic preparations involve the use of heterogeneous mixtures as in the case of oxidation or reduction processes such as the oxidation of a substituted toluene to the corresponding substituted benzoic acid by heating with chromate mixture or the reduction of cinnamic acid by hydrogen amalgam. In cases of this kind the velocity of the reaction depends mainly on extent of contact surface and such reactions may be hastened greatly by improved stirring methods. As an example 200 g. of *p.*-nitrotoluene had to be boiled five days with the chromate mixture to obtain nearly complete oxidation to *p.*-nitrobenzoic acid. Even then a part of the *p.*-nitrotoluene was recovered unchanged. With the same amounts of chemicals in the same sized flask standing on the water bath, that is, at a lower temperature than the boiling point of the concentrated solution, the operation was found to be practically complete in eight hours, when the mixture was stirred with a Witt stirrer running at high speed. As much was accomplished in one day as previously in five by substituting stirring for boiling since the stirring broke up the globules of oil and increased the contact with the oxidising mixture. Similar improvements can be made in a large number of methods of preparing organic compounds. The advent of the small high speed electric motor to the laboratory gives opportunity for improving many old processes. Mechanical shaking is a great improvement on hand shaking and can be relied upon to shorten many operations.

Improvements in processes. This is discussed by Dr. O. B. Helfrich from the point of view of a chemical manufacturer.[3]

"In industrial research the importance of working out improvements in existing processes is widely recognized. Indeed it is perhaps the only form of research for which it can truly be said that there is any general appreciation by business men concerned with industry.

[3] Written for this book by O. B. Helfrich of Kessler & Co.

In proceeding with a discussion of this subject it will be essential to keep in mind the practical side of the problem. To begin with, the two general factors of paramount importance concerning the industrial chemical produced by any process are cost and quality. In the organic chemical industries the item of cost can usually be resolved into three components: (1) material cost, (2) production cost, and (3) development overhead. These will be considered later in their relation to subject in hand. The quality can usually be at least partially defined in terms of chemical purity, where the product is a chemical or mixture of chemicals sold as such. In case the product is not sold as a chemical, *e.g.* perfumery, paint, rubber, celluloid, etc., it is impossible to define the quality in chemical terms, at least in the present state of the science.

"Now let us consider briefly those improvements which might lower the cost of a chemical. The fundamental factor, the material cost, or total cost of materials consumed per pound of product, at once comes up for consideration and it is right here that the chemist's great opportunity lies. It will be impossible in this discussion to do more than generalize and leave it to the reader to make his own specific application. In the first place it is essential to obtain accurate yield figures for variations in the proportions of the reacting raw materials, in the temperature, the time, and the method of admixture. In case the reacting system is heterogeneous the fineness of the suspended particles, whether liquid or solid, is very important. In any case the agitation of the reactant mixture is worthy of study. The effect of the various industrial metals upon the reaction and of the reactants upon these metals must be known in order to avoid dangerous mistakes in choice of equipment and to take advantage of any favorable influence.

"In many organic reactions equilibrium is reached before completely using up the reactants. It has become, in consequence, a usual thing in such processes to use an excess of the cheaper reactant in order to increase the yield based on the more expensive reactant. The extent to which this is feasible in a special case is of course dependent upon the relative cost of the raw materials and upon the extent to which the excess of cheap raw material may be recovered economically. In some processes even when using an excess of the cheaper reactant the equilibrium is reached so far short of completion that it is necessary to recover the unreacted expensive raw material in order to put the process on a paying basis. A few examples will not be amiss on these points. In the oxidation of naphthalene by air to phthalic anhydride, the cost of air is so negligible that it may be

used in very large excess to improve the yield and shorten the time. On the other hand in the manufacture of ethyl acetate from weak acetic acid and excess of 95% ethyl alcohol, it is only possible to use a large excess of alcohol by efficient recovery of the same. Finally in the sulfonation of anthraquinone to give β-anthraquinone sulfonic acid it is essential that the 25% unchanged anthraquinone be recovered.

" In addition to these fundamental but more or less routine points of attack the research chemist must keep abreast of the times in the chemical world, in order that he may apply to his problems the results that have been obtained in related fields. New organic compounds are being made available to the industries by the score. The costs of well known chemicals are often halved by improvements or changes in process which in turn may make that chemical available for hitherto undreamed of uses. The possibilities of catalysis in solving the problems of organic chemical industry are frequently manifested.

" To return to a little more material consideration, it will be possible to choose from the data which have been assembled on all the relevant points discussed, the conditions which enable the chemical to be produced at the lowest material cost. The reliability and comprehensiveness of the data from which this choice is made are dependent upon the ability of the chemist on the job and upon the time at his disposal.

" With the production cost the chemist is not so fundamentally concerned although he has certain definite responsibilities. It would be wrong to expect to put through a change in process that would only slightly improve the yield and at the same time double the risk to life and limb and plant property. Primarily a low production cost is obtained by a large output of the chemical relative to the outlay for plant and labor. Therefore the chemist must remember that he is seeking not merely the highest yield but the best yield compatible with a reasonably simple plant and short cycle of operation.

" The development overhead is widely different on different chemicals and even on the same chemical with different companies. It is largely determined by the difficulties, both chemical and engineering, attending the successful production, and by the efficiency of the chemical and engineering talent handling the problem. In the case of a process operated under a royalty or license the actual development overhead might be quite low but the royalty per pound would have to be added in order to arrive at the cost.

" Improvement in quality offers a large opportunity for the re-

search chemist to exercise his abilities but this applies more particularly to the rubber, celluloid, lacquer and similar industries than to the synthetic organic chemical industry. But even here let it be called to mind that only within the last year there has been put on the market aniline that is *water white and stays so.* It must be said for most of the organic chemicals on the market that their purity is rather high. In a product like celluloid there is still considerable room for improvement in reducing the combustibility and increasing the stability. These properties may not appear chemical but chemical facts are certainly at the bottom of them. Every chemical product has its own specific imperfections which it will be impossible to treat more fully here. It is not intended to discuss the question of uniformity of quality because this is essentially a question of plant control and efficiency of industrial equipment.

"In conclusion let it be remembered that the industries which consume chemicals may be conservative but usually when they are shown something worth while they go right after it. A new rubber accelerator like diphenyl-guanidine rapidly grows in favor and demand after its superiority is once shown. Butyl acetate has cut a terrible gap in the amyl acetate demand as a pyroxylin solvent. May we not indeed assume that nothing is yet perfect in this world of ours — so there is plenty left to improve."

From laboratory to plant. This is a large problem with the commercial chemist. Nearly all processes are worked out on a laboratory scale and then have to be adapted to factory conditions. It is a long step from beakers and laboratory dishes to soap kettles 50 ft. deep and 20 ft. in diameter holding a million pounds and from diazotising in a beaker to vats as large as railroad tanks. The need of such work has recently given rise to a new profession, or at least to a new designation for a profession, that of chemical engineers. A chemical engineer is one who is able to translate grams into tons, beakers int- tanks, and flasks into autoclaves.

The first part, and in many respects the most troublesome pai of the problem is having to give up glass vessels. One never realizes the wonderful utility of glass apparatus till one has to find a substitute for it. There is a limit to the size of glass vessels, beyond which they are difficult to construct and dangerous to use on account of breakage from weight of liquids or still more from changes of temperature. The determining factor in constructing tanks to take the place of laboratory glass ware is to find material that will resist corrosion. There is nothing, except fused quartz, that resists corrosion by as large a variety of chemicals as glass. As no material can

be found to resist every kind of chemical the problem is to find some material that will stand up with the particular chemicals that are used in the process. Lead lined tanks are used in many processes, while, if only low temperatures are required, coatings of tar or paraffine may protect the walls. Great progress has been made in recent years in devising iron alloys which are remarkably resistant to the action of strong acids and other corrosive chemicals. Each case demands special study as unexpected weaknesses may develop and cause serious loss. A number of protective coatings are now on the market each one of which has special adaptabilities and special weaknesses, being very resistant to certain reagents and easily attacked by others. Much useful information may be gained from laboratory studies of proposed coatings or other materials under the action of the chemicals that are to be used in the process.

When working in the laboratory, it is sufficient to shake a flask to mix its contents, but not so in the factory. An important part of nearly all large scale operations is the mixing of the ingredients or reagents. Tanks and other containers must be provided with some form of agitator which will bring the various reagents into intimate contact and do so as quickly as possible. Even with substances that mix or dissolve to homogeneous solutions, the mixing is a much more serious matter than it appears to be to the beginner. When it comes to reactions that involve heterogeneous systems such as washing an oil with a water solution or acting upon a suspended solid by something in solution, or in the extreme case, acting on a solid suspended in a liquid by a gas which is pumped into the liquid, the question of agitation becomes much more important, in fact it frequently becomes the matter of supreme importance and the success or failure of the process may depend on the one question of the efficiency of the agitator. A sharp distinction is to be made between agitators which cause a liquid mixture to circulate as a whole and those that cause intimate internal mixing. In the case of an oil and water in a circular tank, a stirrer that causes rapid rotation of the whole mass may even aid in the separation of the oil and water, centrifugal action sending the heavier water to the outside of the tank and segregating the lighter oil in the centre. Such an agitator might even unmix instead of mixing the oil and water. In case a mass of homogeneous liquid is to be circulated over heating or cooling coils, such action would be satisfactory, but in case intimate contact is to be maintained between the portions of a non-homogeneous mixture, an entirely different sort of agitator is demanded. It is possible, by properly designed apparatus to maintain

a mass of liquid in the most intense internal mixing while the liquid, as a whole, appears almost quiescent and circulates to a minimum amount. Catalytic hydrogenation processes, which have recently occupied so much attention, have largely come down to a question of proper agitation. In this reaction, an oil, a finely divided solid, and a gas have to be brought into the reaction. All three must be present at the same place at the same time for the reaction to take place. The result is that the process depends almost entirely on the intensity of the mixing. In this case it is the internal mixing and not the motion of the mass as a whole.

The question of designing agitators is, of course, a matter of machinery and engineering and not at all of chemistry, but the chemist is the one who must see the need of it and must see that it is provided when needed. The chemist is the one to decide whether the process is one that demands such mixing and to decide how much and what kind of mixing is demanded. After all, the chemist is likely to be the one to be blamed if the process does not work and he is the one to make it work. Chemical action takes place only at infinitesimal distances and if it is desired to make chemicals react they must be brought within such distances of each other and must be kept in such relation till the action is complete.

Another important difference between the laboratory and the factory is in the matter of heating. In the laboratory we have Bunsen burners and gas while, in the factory, heating must be done directly or indirectly by coal, except in special cases. The organic chemist is not called upon to use the high temperatures that are required in metallurgy and seldom has to consider direct furnace heating. He is almost always concerned with some form of steam heating, either by steam coils or by blowing live steam into the liquid in a tank. Steam at 140 lbs. pressure has a temperature of 180° which is near the limit for the temperature that can be obtained by steam heat under ordinary conditions. This temperature is high enough for the vast majority of organic chemical operations. In the matter of heating, the passage from laboratory conditions to factory steam heat is rather in the direction of going from the harder to the easier method, since steam heat offers so many advantages. There is far less danger of burning or local overheating with steam jackets or coils than with the Bunsen burner flame. The danger of fire in working with inflammable materials is almost eliminated. Here again, the designing of the steam coils etc., is a matter for the engineer, but the chemist is the one to decide, by experiment, what the proper temperature is for the most advantageous operation of the process and from this to

find what pressure steam must be used to maintain the desired temperature. From the amount of heat absorbed in the process the chemist can calculate the amount of steam that will be required to furnish the required thermal units. By proper operation, the heat evolved in one chemical reaction in a process may sometimes be used to furnish the required heat to some other part of the process and the heating costs nearly eliminated.

In the matter of heating liquids etc., under pressure, the factory chemist has great advantages over the laboratory chemist. Work with sealed tubes of glass at high temperatures is tedious and dangerous and an autoclave with its safety valve and tested steel walls and bolts is a welcome substitute. This gives more latitude to the industrial chemist and allows him to carry on many processes that are well nigh impossible in the ordinary laboratory. Such autoclaves are readily supplied with stirring apparatus which greatly increases the efficiency. As autoclaves are not transparent, the chemist is at a disadvantage in not being able to follow the course of the reaction by changes that are visible to the eye and means must be devised for finding out when the process is terminated. In some cases the reaction may be followed by the changes of pressure read on the gauge and, in others, the necessary temperature and time must be determined by experiment.

In nearly all processes that have been carried from the laboratory to the factory, a large amount of experimental work has had to be done before the process could be made a commercial success. In many cases the cost of such work and the delays and expenses before the factory could get on a paying basis have jeopardized the enterprise and even ruined the company. Of course, in many cases, the new process has suffered from over-promotion and too much has been expected in the way of immediate returns. In some cases, established interests have cut prices and seen to it that a new process, which threatened their profits, was not suffered to have a fair trial. An instance is reported (*Chem. Ind.* **33,** 106) in which a company paid $772,000 for patents and spent $1,351,000 in the first year and turned out $1,930 worth of camphor. Their downfall was partly due to a decline in the price of camphor and there is no doubt that the price of natural camphor has been manipulated to the detriment of concerns trying to produce it artificially.

In the most favorable case, it requires much experimental work and work of a high order, to transplant a process from the laboratory to the factory and it is much to the advantage of the company that is putting up the money if a large part of this work can be done before the money is put into the factory and operating expenses begin.

There are many processes, notably several for the manufacture of alcohol from various waste materials, that have so far not been successful on the factory scale even after they had been well proved on the laboratory scale.

Encouragement can be gained from thinking of the number of processes that have originated in the laboratory and have been successfully introduced into the factory and have been great producers. The list is too long to mention all, but we may think of saccharine, of the copper process for taking sulphur from petroleum, of the manufacture of indigo, and of all the aniline dyes, of the hydrogenation of oils, of making ionone, vanilline and many other artificial perfume and flavoring materials, of Kolbe's process for salicylic acid, of bakelite, of artificial silk, of wood alcohol and acetic acid, and of many other important manufacturing processes which, at one time, were worked out in the chemical laboratory and have since grown to be large industries.

These industries and others that are established employ many chemists to investigate and improve the already successful processes. Of course it is the duty of these chemists to investigate and they will do it, but there are scores of processes yet to be transferred from the laboratory to the factory and to be made commercial successes. There are processes which chemists must prove to be commercial before companies can be organized to work them. It is the privilege and the duty of every chemist to think from the little to the large. We think from molecules to gram molecules and we must learn to think ton molecules. The vast majority of organic compounds that have been made and that will be made will never have any commercial application, but many of them that now simply occupy a line in *Beilstein* or *Richter,* doubtless, have properties that will make them of value when these properties are discovered. Then it will be a question of making them on the large scale.

The problem of adapting a laboratory preparation to the scale and apparatus of the factory is here presented as a scientific problem and a good problem it is too, whether it be taken up simply for mental exercise or for commercial gain.

Bringing plant processes into the laboratory. This is the converse of the problem that has just been considered. The need of it does not seem so apparent, but it is just as real. Many of the industries, such as tanning, dyeing, dairying, brewing, wine making, and distilling spirits were well developed industries long before there were any chemical laboratories. These processes were to be studied in the laboratory, but the processes as carried on in the factories could not

be transplanted to the laboratory. Small models, so to speak, had to be constructed so that they would accurately represent the process as carried out in the factory and yet of such size that they would be of laboratory dimensions. This is a real problem and one which frequently requires much ingenuity. The surveyor must work from the field to the map and, later on, from the map back to the field.

When a process is to be studied experimentally, it must be reduced to a small scale, since the cost of making numerous experiments on the factory scale would be prohibitive. Unless the laboratory process is an accurate copy of the factory process, conclusions drawn from modifications of it will not apply to the factory process and the information gained is not pertinent to the problem. In many processes it is easy to make the laboratory imitation but in others it is difficult. The attempt is frequently made to construct apparatus which is on the same plan as the factory apparatus, but with the size reduced to scale, say, 1 to 10 or some other such ratio. This is seldom satisfactory for it is difficult to give the small amount of material in the small apparatus exactly the same treatment that is given in the factory and any variation vitiates the conclusions. We saw, in the last section, some of the advantages of autoclaves over sealed tubes and can see that it would be difficult to imitate in sealed tubes, processes that are successful in the autoclave. Of course small autoclaves can be made and are made for just such experiments.

Distillations on the large scale, with the large still heads and other appliances that are used in factories effect far better separations than the distilling bulbs, even the improved forms, that are available in the laboratory. It has proved very difficult to study distillation processes to advantage in the laboratory. A number of forms of stills for experimental purposes have been proposed. In these the factory stills are more or less perfectly represented on a scale which is usually in between the sizes of the usual laboratory apparatus and factory apparatus, that is they hold a few gallons instead of a few cubic centimeters or some hundreds or thousands of gallons.

The problem is too varied to be treated in a paragraph, but attention is called to it as an interesting and essential part of research. There would be much possible teaching value in adaptations of factory processes that could be carried out in the laboratory with the usual laboratory apparatus.

Trying out patented processes. In plant laboratories this occupies much of the attention of the chemists but is seldom touched in universities. There are thousands upon thousands of chemical patents which cover the preparation of chemical compounds, per-

fumes, dyes, pharmaceuticals, etc., and the requisite intermediates. Thousands of these substances are not described outside of the patent literature and our knowledge of them rests on this insecure basis. Many statements in patents are " interesting if true."

In a scientific article the preparation of a new substance is described so that it can be prepared by others and the author does his utmost to make it easy for those who repeat his experiments to obtain good results. The object of taking out a patent is to *prevent* others from making the product. The information given is only there to make the patent valid; not to assist anyone. There are several ways to prevent a man from making a given product. One way is to cover it with a patent and threaten him with legal action in case he makes it. However, you have to catch him making it and have to prove it to the satisfaction of the court and when damages are awarded there may be trouble in getting the money. A much neater plan is to give him the information in such a way that he will waste money and time on a nearly good process. Every chemist knows that the details of a process are the most important part, when it comes to getting good results: these insignificant but all-important details are often lacking in patents. The net result is that frequently poor results are obtained when one has only the directions given in a patent. If good results are desired, one must get down and dig out the process. In some cases it is better to forget the contents of the patents entirely and set to work as if nothing had ever been done on the problem. It may be that American chemists would have built up the dye industry quicker than they did if they had not had the German patents to guide them.

Suppose Smith and Co. patent a new process for making vanilline. How are they to know that the vanilline sold by Jones and Co. was made by the new process or by one of a dozen old ones? The vanilline is discreetly silent as to its antecedents. If Smith and Co. disclose their process in such a manner that Jones and Co. miss some little point and get five per cent less yield, that is sufficient to cut their profit so that they cannot compete with Smith and Co. The inventor may know more about the process than he is obliged to disclose in his patent to make it valid. That margin of knowledge may be sufficient to give him the edge on one who follows the published patent.

Patents vary greatly in the sufficiency of the information given, some countries being lax and others strict in regard to accuracy as well as novelty. Germany is strict in requiring the inventor to describe the process so that it is workable, but it is commonly a long

distance to go from a process that is merely workable to one that is suitable for putting into the plant. When someone discovers a new process he usually applies for a patent before he has finished working out all the fine points, framing the patent so that it will cover a number of possible variations. A patent is naturally drawn to be inclusive rather than definite, specifying ranges of temperatures, concentrations, and the like, thus leaving, perhaps, hundreds of possible combinations to be tried out by one having only the patent as guide.

It is possible for a man to write up a patent right out of his head without so much as trying a single experiment. He thinks of a reaction or a process that might work, writes it up and sends it in to the Patent Office. Should he wait to experiment, someone else might be thinking along the same line and get there first. He may think up a dozen possible ways of accomplishing the same end and patent all of them. Somebody will want to make the material and will work out a process which is apt to infringe one of these paper patents. Several of them may be shown not to work as specified and be voided, but it is always troublesome to prove a negative. The one who has a patent has more or less advantage and many are tempted to patent their intuitions, their suspicions or their hopes as well as their proved discoveries.

Any statement that is published whether in a patent or in a journal is accepted as true unless refuted, and finds its way into text-books, compendiums, and encyclopedias. Baron Munchausen was a wonderful narrator and his travels have entertained many readers but they are never quoted in serious histories. Some patentees are no less imaginative but their wildest flights of fancy are indexed and abstracted right along with Morley's determination of the atomic weight of hydrogen. It is as much a service to science to weed out the bad as it is to add to the good.

Calling attention to some abuses of the patent system is not meant as a reflection on the system from which untold good has come. It has its faults but no one has yet been able to devise a patent system which will function perfectly. With all its faults the patent system has been a wonderful help in stimulating invention and research on which the progress of the world so largely depends.

As mentioned above, plant laboratories devote a large proportion of their energies to working over patented processes, sorting out the good from the bad and improving the good. Plant chemists do not need to be exhorted to study patents: it is their business to study them and they do not neglect it. The trouble is that what they find

out about them is usually buried in confidential files and the nex one who comes along wanting to know the facts has to do all th work over and so it continues. The Trojans were told to beware o the Greeks bearing gifts and trusting young plant chemists may b warned to beware of the Germans bringing gifts of information i patents. Do not follow *Friedländer* slavishly. Take the informatio that is there, try to find out what it is worth and see what is bac of it. Think it through to the fundamentals and trust yourself t improve it. Above all things do not permit yourself to be led awa from the right path and get mired up. Make the patent help you if you can, but do not let it stand in the way of your finding ou something.

The chief object of this section is to call the attention of inde pendent researchers in university laboratories and elsewhere to th wide field for investigation that is offered by patents. When th information given in patents is entirely correct, the experiments ar carried only far enough to serve commercial ends; new substance prepared are not always fully characterized and considerations o theory are left out altogether. Chemical patents do contain a immense number of fruitful ideas. Patents contain fact, fancy, ca mouflage, and bluff in various proportions but in the aggregate ther are enough facts to serve as bases for thousands of investigation and some of the fancies might work, if sympathetically and skillfull handled.

It would be a great service to pure as well as to applied chemistr for independent investigators to go through *Friedländer*, section b section, repeating the processes there described and reporting th results without fear or favor. Time enough should be given to eac important process to go into its theoretical basis so as to see ho it might be perfected and related to others. Some of this wor might be done by students who are candidates for the master's de gree and have very limited time for research, and some even b undergraduates who specialize in chemistry. Multitudes of topic can be found suitable for doctor's dissertations.

All of the processes mentioned in this chapter may be employe in working over patents. The examples given in the patent are par ticular cases: the reactions involved may be generalized and thei limits of application determined by studying homologs and analog On the other hand a patent usually aims to be as broad as possibl in order to cover classes rather than particular compounds. T get good results for any individual compound the process must b

particularized and suitable details worked out. Various patents covering the same substance may be compared as to yields, cost of materials, amount of equipment and labor required or the alternative processes mentioned in a single patent studied so as to decide on the most advantageous. Working to increase the yield and to diminish costs is ever in mind when repeating patented processes.

CHAPTER XII

PREPARATION OF NEW COMPOUNDS

Scientific and Technical Importance of Making New Compounds

Nature furnishes us with thousands of substances and the hand of man has been busy with the synthesis of other thousands. In 1910 *Richter* listed 144,150 which have probably increased by now to 250,000, but when we come to look at a page of *Beilstein* we see that only a few representatives of each class have been described and how many undiscovered classes there are no man knows. Certain it is that we have barely scratched the surface and that millions more are waiting to be made and that the present fourth edition of *Beilstein*, 1910, will look like a pamphlet beside its 2010 A.D. successor.

Making new compounds has always occupied much of the attention of organic chemists. When the constitution of a natural substance is unraveled the way is usually opened for the synthesis not only of the original compound but also of scores of homologs and analogs. We are driven on by the thirst for knowledge and also by the urge of the industries.

Organic chemists have frequently been called " compound makers " and the designation is not always spoken in as complimentary a way as it should be. True it is that it is easy to make a host of new compounds and that little service is rendered by simply turning out a large number. Bricks are of no value unless they are well made and unless they are built into a worth-while structure. A new compound may be made in an hour, to purify it may take days, to determine its physical and chemical properties may require weeks, and to test its physiological effects or industrial application may consume months or even years. Mustard gas, or $\beta\beta'$-dichlor-ethyl sulphide was doubtless prepared from the glycole in an hour but its manufacture, use, and effects have occupied for years the chemists, technicians, strategists and physiologists of two continents. Inconsequential substances frequently acquire importance when they are thoroughly studied.

Characterizing new compounds. The first one who makes a compound goes down in chemical history as its discoverer and is con-

sidered as having a certain proprietary right to it. Parents who desert their children in infancy and leave them to be fed, clothed and educated at public expense are very remiss and do not deserve to be honored as the parents of the children. The same rule should hold for the chemist who makes a new compound and describes the method of preparation so imperfectly that it is difficult for anyone else to get the compound and characterizes it so inaccurately or so inadequately that it is difficult to identify it when it is made. The physical constants of a new compound should be given with such accuracy and certainty that they may be used in making tables of such properties in which this compound is compared with other compounds. As the case now stands, any one desiring to make a comparative study of any physical property of a number of compounds, whether it be melting points, boiling points, densities, etc., must go to work and prepare many of the compounds and obtain more accurate data than are at present available in the literature, before the comparison of such constants can be made. When a new compound is made it should be so accurately and so fully studied that it will be unnecessary for others to work over the same ground.

In order that a new compound may be included in *Beilstein* an analysis is required. This is necessary to show that the substance is what it is supposed to be and must be made, but an analysis agreeing fairly well with the assumed formula may be obtained on a preparation that is not of a high degree of purity. In fact, large amounts of impurities of somewhat similar composition may be present and not show in the analysis, though they would greatly alter the physical constants. This is particularly true when, as is often the case, the impurity is an isomer.

Standards needed. It would be desirable, were there some proper authority to do it, for a set of standard specifications to be drawn up as to the properties that must be determined and the methods to be used with limits of accuracy required for such determinations. The following tentative suggestions are made. In case the substance is a solid, it should be recrystallized till the melting point is constant to 0.1 or 0.2°, and this temperature stated to the nearest 0.1°. Such corrections should be applied as are required to make the readings accurate to 0.1°. The thermometer should be standardized and also checked by taking melting points of substances of known purity melting at nearly the temperature in question. Its ice point should be taken from time to time to detect changes. In case such accuracy is not attainable, the m.p. should certainly be determined to the nearest 1° and corrections made accordingly. It is to be remem-

bered that it is not only unnecessary but is positively dishonest to state the melting point to tenths of 1° unless the known accuracy of the thermometer and of the work justify this degree of accuracy. The same degree of accuracy should be aimed at in obtaining the boiling point, though it is harder, in this case, to obtain the same accuracy. It should be given to the nearest degree and all corrections applied to make this accurate. With substances that can be obtained in large quantity and in high purity accuracy of 0.1° should be aimed at.

Even when substances are solids and their melting points have been determined, it is of value to determine the boiling points as well. In case decomposition takes place before the substance melts, the temperature of decomposition should be given, and then the attempt made to distil the substance under diminished pressure and the boiling point thus determined. A pressure of 15 or 20 mm. is readily obtained by a water pump and the boiling point should be given at one of these pressures or even at a lower pressure of 5 or 10 mm. in case a mechanical pump is available. A boiling point at 20 mm. is the most useful as that pressure is most readily obtained in laboratories in general. For common organic liquids the boiling point at 760 mm. is very nearly 100° above that at 20 mm. In the case of solids which are to be characterized by their melting points, the boiling point is of subsidiary importance but, even then, it is essential to a satisfying knowledge of the substance. On the other hand, where the boiling point is the main constant and fractional distillation is to be relied upon for the purification of the substance, a knowledge of the melting point would be very desirable in order to complete our knowledge of its properties, and chemists should make all reasonable efforts to obtain melting points of even low melting substances.

Accurate temperatures. In Chapter X attention is called to the unsatisfactory state of our knowledge of melting and boiling points. These important temperatures have frequently been taken without proper precautions. Some chemists are frank enough to state that the temperatures are "uncorrected." Even when this is not stated it is usually to be assumed. When we remember that the ordinary laboratory thermometer of unknown origin may be from 1 to 5° off when new and may change its reading every time it is carried to a high temperature and cooled and when it is considered that the correction for the stem being out of the vapor or bath may be 1° or more at 100°, 3 or 4° at 200° and 5 to 10° at 300°, there is little cause for surprise in the lack of agreement between the results given by different observers. It is also seen that the figures given may be of little value. This is not intended as a reflection upon all organic

chemists, but is intended as a caution and as a plea that when melting and boiling points are given, that these figures should be as dependable as it is possible to make them.

Densities. The densities of liquids should be determined to 0.0001 and should be so stated. Of course if the substance is not known to be pure enough for its density to be reliable to this limit, such accuracy is not required and is misleading when given. In such case the liquid should be purified till the density is reliable. It is very desirable that densities should be taken at several standard temperatures rather than at any temperature that may be convenient to the operator at the moment. If the density is taken at 0°, 15°, or 25° it is a great convenience to other chemists who may wish to compare their preparations with data in the literature. As physical chemists have chosen 25° as the temperature for conductivity measurements, etc. it would seem wise to adopt the same for densities. It is strongly urged that densities should be taken at 0° and also at 25°. The two determinations may be made with one filling of the pycnometer. The pycnometer is set in the ice bath, taken out and weighed. It is then placed in the 25° bath and set again and weighed and the densities calculated for the two temperatures. There are two advantages. From the two values, the coefficient of expansion between 0° and 25° may be calculated. This is of value as a characteristic of the liquid in question. Having densities at these two temperatures it is easy to interpolate for such temperatures as 20° or 17.3° for making comparisons with data in the literature. It is common to compare densities of members of a series etc., in tables of properties; densities taken at the same temperature are most desirable. Densities taken, as here suggested, would supply the data needed for such tables. It is desirable that the densities should be expressed at 25° referred to water at 25° and also at 4°, *i.e.*, stated as specific gravities and also as densities. The determination at 0° can be calculated also according to both systems. Here again, it is highly desirable that some uniform practice be adopted by chemists in general. Logically all densities should be referred to water at 4° and it is suggested that all determinations be given this way if not in both ways.

As was pointed out in Chapter X, the density of a solid, though not required for identification as is the density of a liquid, is yet of scientific importance and should be determined. In case of substances melting at comparatively low temperatures, it is desirable to determine the density of both the solid and liquid forms.

From the density at 25° compared with water at 4°, the molecular volume should be calculated and the value thus found compared with

that calculated for a substance of the supposed formula and constitution from the known atomic volumes and the corrections for these for double bonds, differences of linking up of atoms, etc.

Index of refraction. This is an important property and should be determined where practicable. If this is determined for two different colors, the dispersion may be calculated. From these the molecular refraction and dispersion are to be calculated and compared with the values calculated for the supposed structural formula of the compound.

Viscosity and fluidity. These are also important properties and should be determined whenever possible. When we find out more about the connection of these properties with constitution, they will become more important. If accurate data for the viscosity and fluidity of a large number and variety of compounds are on record, they will be available when they are needed.

Solubilties. Far too little attention has been given to the solubility of compounds and the statements regarding solubility commonly made are far too vague to be used. To say that a substance is "slightly soluble" or "very soluble" does not convey any definite idea, since these terms have different meanings with different chemists. It is most desirable that, at least, approximate determinations be made of the solubility of any new compound in water, alcohol and ether. Such determinations may be made without much labor if only approximate values are desired. To say that a substance is soluble in 10 parts of water at 20° really tells something that will be of use to any one who ever wants to work with it. In case the substance studied is likely to be of importance or of any utility, it is desirable to make really accurate determinations on its solubility in these three solvents and in any others which may prove convenient to use in working with it.

Crystalline form. The crystalline form of organic substances is of great importance and should be determined whenever possible. This may frequently be done by coöperation with someone who has the technical skill required.

Unexpected properties. The chemist who makes a new compound should be desirous of so describing it as to give the sense of completeness to the work and facilitate the work of others who may need it in their studies. He should also be on the lookout for new properties or for special and interesting manifestations of old properties. A new compound may be made simply to fill in a gap or to extend a well known series and yet it may show some unexpected property that may make it of great interest or value. Saccharine is the imide

of *o.*-sulphamine-benzoic acid. The making of this acid was a step in the systematic investigations of sulphonic acids. The ready formation of the imide and the property of intense sweetness which was possessed by that imide were entirely unexpected. This illustration is not brought up to encourage chemists to expect to find commercially valuable substances at every turn in a scientific investigation. It is better not to work with ideas of dazzling wealth in one's mind, but one should look carefully and discerningly at every substance that passes through one's hands for possible unexpected properties of interest or of value. Doubtless there are among the 144,000 compounds in Richter's lexicon a large number that have most valuable properties which were not observed by those who made them. An important industry has recently been built up on "bakelite" which is a condensation product of phenol and formaldehyde. Such condensation products have been known a long time without any one considering that they were of any value. The difficulty is that no one chemist is familiar with all the industries, and one not familiar with a particular line may miss seeing the possibilities of a given compound for use in that line. Thus a chemist not interested in pharmacy might work with such substances as acetanilide and salicylic acid without discovering their valuable medicinal properties. It is for everyone to see as much as he can possibly see in every compound with which he has to deal and fortunate is he who sees the important where others see only the commonplace.

Building chemistry. The preparation and description of a new compound is a brick, or perhaps it is better to say a stone, as the sizes differ, in the structure of organic chemistry. It is dumping rather than building simply to add a stone to a pile. In order that the process may be building, the stone must fit somewhere and must be added at some place in an orderly way so as to aid in carrying out the design of the structure. If we contemplate organic chemistry as a structure, we see that the building has been largely haphazard, some parts being remarkably advanced while others have been almost neglected with only a random stone here and there in place. The structure will grow more symmetrically if those who bring the stones will look first to see what is needed.

Completing a series. The first need of preparing new compounds is to complete and extend series of compounds now known. Take esters of acids as an example. If we look up almost any organic acid in *Beilstein,* we find that the ethyl and methyl esters have been made, sometimes only the ethyl, and in some cases we find the propyl, iso-

butyl and isoamyl esters. There the series usually ends. In order to complete the series, the normal butyl and normal amyl esters are needed as well as hexyl and higher esters.

Let us take the mercaptans as an example. According to *Beilstein,* the following normal primary aliphatic mercaptans have been made. Methyl, CH_3SH, ethyl C_2H_5SH, propyl C_3H_7SH, butyl C_4H_9SH, hexyl $C_6H_{13}SH$, heptyl $C_7H_{15}SH$, cetyl $C_{16}H_{33}SH$ and myricyl $C_{30}H_{61}SH$. To fill in the series, n.amyl mercaptan must be made and all of those from octyl up to noneikosyl, $C_{29}H_{59}SH$, with the exception of cetyl, must be prepared and studied. In the butyl group all four of the possible isomers have been made. From unsaturated alcohols only one, allyl mercaptan, has been prepared. We cannot feel that we know much about any series till a large number of its members have been prepared and the blanks filled in. Filling in blanks in an existing series of compounds has long been an accepted object in the preparation of new compounds. We find that Kekule[1] was led to prepare monomolecular formaldehyde because he hated to say in his lectures that that space was blank. In this particular case, owing to peculiar properties of the compound in question, there was special difficulty in obtaining this member of the series, while the higher members are easily made. In the case of the mercaptans there is no more difficulty to be anticipated in making a number of those that are now unknown than has been found with those that are known. Some of them have not been prepared on account of the high cost of some of the alcohols.

The preparation of missing members of a well known series is recommended to those who have had comparatively little experience in research, as a convenient place to begin. The methods of preparation can usually be gotten by slight adaptations of the methods that have been used for making the members already known. This will serve as a good example of the adaptation of a general method to special cases. The methods of purification to be used will be nearly the same as those that have been used for the others, adaptation being made again for higher boiling points and decreasing solubility in water if we are going up the series, or the reverse, if we are going down. When the compound is made and purified and its physical constants have been obtained, we can compare them with the constants of the known members of the series and see whether they fall in line. In this way we can tell pretty well whether the work is going straight and locate errors. Such problems are well suited for those who have only a comparatively small amount of time to

[1] *Berichte,* **25**, 2435–6 (1893).

devote to such work. Yet the work is important and if enough pieces, though each one is small, were done the science would be solidly built up as a result. Such work is largely neglected in the university laboratories as not offering suitable material for dissertations.

The Completion of a Group of Compounds

The term "group" is here used to designate a number of compounds of different kinds which can be prepared from, or are related to, a given substance. The definition is not to be taken strictly. Thus if we regard some particular alcohol as a starting point, a number of esters such as acetate, propionate, formate, benzoate, nitrobenzoates, salicylate, phenylurethane, α- and β -naphthylurethanes may readily be prepared from this alcohol, so may the corresponding chloride, bromide, and iodide and from these the amines, primary, secondary and tertiary, the mercaptans, the nitriles, ethers, etc. These may be regarded as a family which surround the parent alcohol, and the preparation of any one of which is a routine matter when once a supply of the alcohol is at hand. The classes of compounds included in the group may be largely extended to include esters of any number of acids as well as other classes of derivatives. A study of *Beilstein* and *Richter* will reveal any number of vacancies in such groups. Thus from dipropyl carbinol, $(CH_3CH_2CH_2)_2CH(OH)$, the corresponding iodide and amine have been made but the chloride and bromide have not. Di-isopropyl carbinol, $[(CH_3)_2CH_2]_2CHOH$, has been prepared but the corresponding chloride, bromide, iodide, and amines have not been. Or we may change the idea of a group and consider the esters that may be derived from any acid as forming a group around that acid. In whatever way the group may be made up, there is an interest in preparing a number of its members and studying their mutual relations and also their relations with corresponding members of other similar groups. Any or all of the properties of the compounds may be made the basis for such study. When we know all of the properties accurately enough, it will, doubtless, be possible to work out exact relationships which may in some cases be reduced to mathematical statements or formulae. In the following table the boiling points of the normal alcohols, and the corresponding primary amines, chlorides, bromides and iodides are given from the methyl to the octyl series. In each series there is a regular rise of the boiling point as we go from C_1 to C_8, the increments decreasing somewhat as we pass to the higher members, the decrease being different for each

series. When we study any one group we find interesting relations between the members. Some of the irregularities may be due to inaccuracy in the data.

TABLE I.

Boiling Points of the normal Alcohols and of the corresponding Amines, Chlorides, Bromides, and Iodides:

R	ALCOHOL		AMINE		CHLORIDE		BROMIDE		IODIDE
	-OH	dif.	$-NH_2$	dif.	-Cl	dif.	-Br	dif.	-I
CH_3....	65°	− 71	− 6°	− 18	− 24°	29	5°	37	42°
dif ..	13		23		36		33		30
C_2H_5...	78°	− 61	17°	− 5	12°	26	38°	34	72°
dif. ..	19		32		34		33		30
C_3H_7...	97°	− 48	49°	− 3	46°	25	71°	31	102°
dif. ..	21		26		32		30		28
C_4H_9...	118°	− 40	78°	0	78°	23	101°	29	130°
dif. ..	20		27		29		28		26
C_5H_{11}..	138°	− 34	104°	+ 4	107°	22	129°	27	156°
dif. ..	17		25		27		27		25
C_6H_{13}..	155°	− 27	128°	6	134°	22	156°	25	181°
dif. ..	23		25		25		23		23
C_7H_{15}..	178°	− 25	153°	6	159°	20	179°	25	204°
dif. ..	17		28		25		24		21
C_8H_{17}..	195°	− 14	181°	3	184°	19	203°	22	225°

Groups of isomers. The most characteristic thing about organic chemistry is the study of isomers. The whole fabric of structural formulae is built on the study of isomers. Some one compound is found in nature or is prepared in the laboratory and later another of the same percentage composition is discovered and then begins the study of the two to devise formulae for them and to fit each formula to the proper compound. The theory which is worked out from this study predicts other compounds and the chemist sets out to make the possible isomers and confirms the theory. So the science of chemistry has grown. Fischer's work on sugars was of this sort. Several sugars were known, the structures of these were determined and the existence of others foreseen which led to the preparation of the important group of synthetic sugars. It is only by completing the group that a satisfactory study may be made of the whole group. A collector of coins or stamps will pay an enormous price for a rare coin or stamp to complete a section of the collection, so chemists should be willing to undertake even difficult preparations to complete some of these groups of isomers. The preparation of isomers to complete a group is fre-

quently difficult as it may involve a different starting point for each isomer.

Much of the study of the relation of properties to constitution depends on the comparison of isomers.

Octanes. The preparation and study of the isomeric octanes has been carried out by Clarke and his co-workers.[2] They have prepared a number of new octanes and compared these with others that had been made and have deduced a number of interesting conclusions from this study. The same sort of study might profitably be made of the octyl alcohols, etc. This work shows how almost any alcohol may be synthesized and how water may be split off from it to leave an unsaturated hydrocarbon which may then be hydrogenated to give the parent hydrocarbon. There are 89 possible octyl alcohols and it would require a long time for one chemist to make all of them, but a sub-group having a common skeleton might be taken. The octyl alcohols are rather too volatile for use in perfumery, but doubtless many of them have pleasant odors and some might prove valuable either as such or in the form of esters. There are too many possible nonyl and decyl alcohols to suggest that any one undertake to make all of them, but when the octyl alcohols are finished, it would be most desirable, from the scientific point of view, to prepare a selection of the nonyl and decyl alcohols to extend certain series. Some of the decyl alcohols have very pleasant odors and their volatility is just about right to make them usable in perfumery. There may be some valuable ones to be discovered. They would offer one of the best fields for the study of the relation of odor to constitution.

Properties and structure. When a group of isomers has been completed, the next thing is to compare the properties in every imaginable way and to see what relations can be found between the various properties and the structures of the individual compounds. Many relations have already been observed; thus we see in the alcohol derived from any particular hydrocarbon that the nearer the –OH is to the centre of the molecule, the lower the boiling point. When enough such observations have been made and enough accurate data have been accumulated, general statements of this kind may give place to mathematical formulae. Ferguson had devised a formula[3] which gives the boiling points of the normal hydrocarbons from C_4 to C_{17} with considerable accuracy:

$$\log \delta = 1.929(\log M)^{0.4131}$$

[2] *Jour. Am. Chem. Soc.*, 33, 520 (1911); 34, 170 and 674 (1912); *Am. Chem. Jour.*, 39, 574 (1908).

[3] *Phil. Mag.*, 29, 599–608 (1915); *C. A.*, 9, 1575.

in which δ is the absolute boiling point and M the molecular weight. He gives similar formulae for the normal primary alcohols and bromides as well as one for critical temperatures. These formulae hold over a comparatively small range and apply only to normal hydrocarbons and to their primary hydroxyl and bromine derivatives, but they are a step in the right direction and when we have more extensive and more accurate data we can expect to be able to find formulae with a wider application.

Hexane and heptane derivatives. The following tables, II and III, give the alcohols, amines, chlorides, bromides and iodides derived from the various hexanes and heptanes. In each case the derivatives from the same hydrocarbon are grouped together. These bulky tables are not inserted to weary the reader or to pad the book, but as a sort of appeal to chemists to fill up some of the many vacant spaces. We may consider each as a whole or may break it up into small sections according to the hydrocarbon skeletons. Of the 17 possible hexyl alcohols, $C_6H_{13}OH$, all 17 have been made. There are the same number of possible amines, chlorides, etc., and of these 11 amines, 10 chlorides, 8 bromides, and 12 iodides have been made. It may be said that we know the hexyl group about half way. When we examine the heptyl derivatives, we find that a smaller proportion of the possible compounds has been studied, and when we come to the octyl derivatives, we find that the known are a very small fraction of the possible number, only 26 alcohols, 5 amines, 6 chlorides, and 3 bromides having yet been studied, while the theory calls for 89 of each. Right here is a vast deal of work for those who wish to make and study a number of new compounds. This work would go to complete our present knowledge and to verify or modify our present theories. Each compound that is made may be regarded as extending a series, helping to complete a group. If all of these blanks were filled in and not only the boiling points but the other properties of these hexane and heptane derivatives were accurately and completely known, we would be in a good position to make a satisfactory study of the relation of properties to structure. It is not likely that one man will ever make all of these, but if one chemist should make one or two and another add others the table would eventually be filled in and the complete study could then be made. Everyone who prepares and studies even one compound will supply a part of the material for that study. Some of the compounds would be difficult to prepare, but there are many others that would offer no serious difficulty. The chemist with limited experience and resources might select a few of the easy ones, at least, for a beginning. At the

TABLE II

Hexane Derivatives

This table shows what hexyl derivatives of these classes have been made and which remain to be made. In case a compound has been prepared its boiling point is put down in the proper place. A "known" designates that the compound has been made but its b.p. not determined. $72°^{32}$ means b.p. 72° at 32 mm. Only the skeletons of the compounds are given and the place of the substituent is denoted by a dot.

	ALCOHOL	AMINE	CHLORIDE	BROMIDE	IODIDE
CCCCCC..	156°	128°	133°	153°	180°
CCCCCC..	139°	117°	123°	——	167°
CCCCCC..	135°	130°	known	——	165°
.C CCCCC..	147°	——	——	144°	$72°^{32}$
C CCCCC	123°	known	100°	138°	142°
C. CCCCC...	126°	——	116°	——	147°
C . CCCCC.. . .	130°	101°	——	——	160°
C . CCCCC.. .	153°	124°	125°	147°	172°
. C CCCCC.. ..	153°	——	——	146°	——
.C CCCCC. .	134°	——	——	——	$83°^{65}$
C CCCCC...	122°	109°	116°	——	144°
C· CCCCC.....	143°	125°	——	——	——
.C CCCC...	135°	113°	——	——	——
C C. CCCC...	121°	103°	113°	132°	142° (?)
C C . CCCC.....	143°	——	——	130°	——
C . CC CCCC.....	141°	——	124°	——	——
CC CCCC.....					
Known.....	120° 17	105° 11	112° 10	133° 8	141° 12

TABLE III

HEPTANE DERIVATIVES

	ALCOHOL	AMINE	CHLORIDE	BROMIDE	IODIDE
CCCCCCC	175°	153°	159°	179°	204°
CCCCCCC	159°	145°	——	166°	98° [50]
CCCCCCC	157°	——	——	——	64° [8]
CCCCCCC	154°	140°	——	——	185°
C CCCCCC	164°	——	——	——	78° [19]
C CCCCCC	142°	——	135°	——	——
C CCCCCC	144°	——	——	——	——
C CCCCCC	148°	——	——	——	——
C CCCCCC	149°	——	136°	——	170°
C CCCCCC	171°	146°	——	——	——
C CCCCCC	——	——	——	——	——
C CCCCCC	80° [52]	58° [36]	——	known	——
C CCCCCC	140°	39° [15]	——	——	——
C CCCCCC	——	——	——	——	——
C CCCCCC	150°	——	——	——	——
C CCCCCC	——	——	——	——	——
C CCCCCC	——	——	——	——	——
C C CCCCC	——	——	——	——	——
C C CCCCC	150°	——	——	——	——
C C CCCCC	143°	known	known	——	——
C CCCCC C	——	——	——	——	——

TABLE III. —*Continued*

	Alcohol	Amine	Chloride	Bromide	Iodide
C CCCCC C	133°	known	—	—	—
C CCCCC C	—	—	—	—	—
C CCCCC C	—	—	—	—	—
CC CCCCC	—	—	—	—	—
CC CCCCC	—	—	—	—	—
CC CCCCC	140°	—	136°	—	146°
CC CCCCC	—	—	—	—	—
CC CCCCC	—	—	—	—	—
CC CCCCC	—	—	—	—	—
C CCCCC C	—	—	—	—	—
C CCCCC C	—	—	—	—	—
C CCCCC C	—	—	—	—	—
C C CCCCC	—	—	—	—	—
C C CCCCC	133°	122°	126°	85° [150]	142°
C C CCCCC	132°	125°	—	160°	55° [30]
CC CCCC C	—	—	—	—	—
CC CCCC C	—	—	—	—	—
CC CCCC C	131°	—	130°	143°	141°

present time means are at hand for making all, or nearly all, of the compounds lacking in the tables above. The Barbier-Grignard reaction has rendered the preparation of primary, secondary, and tertiary alcohols of all possible structures comparatively easy. A large number of the missing heptyl and octyl alcohols could be made by this reaction by using aldehydes, ketones, and alkyl halides that are available or might readily be prepared.

Application of a New Method to Old Substances

A new reaction or a novel method of work is a new tool with which one may accomplish things hitherto impossible. When a man has gotten all the apples off of a tree that he can reach from the ground he gets a stepladder or a pole and brings down more apples. The tailings from old gold mines are being worked over by the cyanide process and additional values recovered. Modern industry teems with new processes and new machines.

Epochs dependent on methods. The history of chemistry is largely made up of epochs each of which has been ushered in by the discovery of a new method which was taken up by a large number of chemists and applied to existing materials. This is particularly true of physical chemistry, which is not a division of chemistry, co-ordinate with organic and inorganic, but a series of new methods of treating facts and solving problems. The application of its methods and conceptions to inorganic chemistry has brought brilliant results. Organic chemists as a class have failed to avail themselves of the aid of physical chemistry as much as they should. There are many problems that have resisted regulation organic methods which might yield if attacked with the new weapons which physical chemistry supplies.

If we wish to apply new methods to old materials we may bring to bear the methods of physical chemistry on organic reactions.

Grignard reaction. As an example of a straight organic reaction applied to old materials, no better example can be given than the Barbier-Grignard reaction. This was discovered in 1901 and was quickly taken up by the chemists of the world. To prepare the reagent one needs an alkyl or aryl halide. The reagent reacts with practically any aldehyde, ketone or ester, and with a number of other classes of compounds, hence the number of possible products is the number of halides available multiplied by the number of aldehydes, ketones and esters, not to mention the other reactants. The number of substances that can be prepared by this reaction is ex-

tremely large. In a recent biblography, 1900–1921, of the Grignard reaction there cataloged 1552 papers by about 1100 authors.[4] The index contains about 3500 entries of substances to which this reaction has been applied or which have been produced by its aid. For all that, the possibilities of this reaction are far from exhausted and hundreds of chemists may yet busy themselves applying it to yet other substances.

Hydrogenation. We may mention also catalytic hydrogenation a recently discovered reaction of great commercial as well as scientific interest. This is applicable to nearly all compounds containing unsaturated carbon chains. Nitro and nitroso groups may be reduced to amine groups and aldehydes and ketones to alcohols or hydrocarbons.

Since this reaction was discovered by Sabatier about twenty years ago it has become common property and has been applied by perhaps a thousand chemists to a host of substances, but we are only beginning to learn its possibilities and there are yet hundreds of substances to which it may be applied, and furthermore most of the processes in which it has been used can be improved by further study.

New apparatus. A new analytical method may enable us to follow the progress of reactions that have baffled chemists in the past. When we can follow a reaction we are in a position to study it and perhaps to control it. Along with new methods we may put new or improved forms of apparatus. For a long time chemists had to content themselves with the water-jet pump which gives a vacuum of 15 to 20 mm. when it is working well. It was possible to fractionate many substances in that vacuum which could not be distilled under atmospheric pressure but recently several types of rotary pumps have become available which evacuate to 1 or 2 mm. or even less, and by adding a mercury vapor pump we can easily go down to hundreths or thousandths of 1 mm. This makes hundreds of additional substances amenable to distillation, so that mixtures which would otherwise boil too high may be separated by fractionation. Many substances which defy purification by ordinary means may be obtained water-white and very pure by distillation in high vacuum.

The improvement of almost any sort of apparatus enables us to work over and perfect some process which has been unprofitable heretofore.

The chemist should be ever on the lookout for new reactions, new syntheses, new methods or new apparatus, and when he finds one of

[4] C. J. West, Reprint and Circular Series of the National Research Council· Organomagnesium compounds in synthetic chemistry, Washington, 1922.

these, cast about to find some substance or process which may be improved by its use.

The Application of Old Methods to New Compounds

This is one of the most obvious methods of making new compounds, and is used more or less by every one who makes them. Some chemist prepares a new alcohol. It is not enough to describe the properties of the alcohol and give its analysis, some derivatives, as they are called, must be made from it. The most common of these is the acetate, and we find almost always the description of the preparation and properties of the acetate of a new alcohol right after the description of the alcohol itself. In some cases the author goes further and makes the propionate and other esters.[5] The benzoate is very commonly made by the Schotten-Baumann reaction since the benzoates of many of the higher alcohols are solids and have melting points suitable for use in the identification of the alcohol. It has of late become an almost universal custom to prepare the phenylurethane from a new alcohol and to consider its melting point as one of the characteristics of the alcohol. It is obvious that this process of making derivatives may be carried much further than is necessary simply for the identification of the alcohols. The new alcohol may be transformed into the corresponding chloride, bromide, and iodide, and from these the amines, the mercaptan, the nitrile, etc., may be prepared. A large group of compounds may be built up from this one new alcohol and the mutual relations of the members of this group studied. All of this can be done by the application of well known reactions and almost as a matter of routine when once the new alcohol is obtained in sufficient quantity to form a basis for the work. A new acid, in like manner, may form the starting point for the preparation of a large number of compounds by well known methods of work. Its salts may be prepared and studied and then its esters, amide, substituted amides, anhydride, mixed anhydrides, etc. Going a step further we may make the ketones containing the radical of the acid either in connection with itself or with methyl or some other radical. From such ketones we can go on to the preparation of other compounds. When a new acid is made available the way is opened for the preparation of scores and even hundreds of new compounds.

In a similar way, a new aldehyde or a new ketone may become the starting point in the preparation of a large number of new com-

[5] *Berichte*, 9, 3218 (1886); 21, 2744 (1888); 23, 2962 (1890); 27, 2545 (1894).

pounds. Having one of these in sufficient quantity, by the use of the Barbier-Grignard reaction, a host of secondary and tertiary alcohols may be made and from these other compounds. In fact almost any compound that can be obtained in sufficient quantity for work, can become the starting point for the preparation of a number and variety of new compounds.

When rare materials become common. The cheapening of an old compound may serve the same purpose as the discovery of a new one. Many acids, alcohols, etc., have been discovered and a few of their derivatives made, but, in some cases, the difficulty of obtaining the starting material has cut short the work of preparing other derivatives. Now when, by some new method of preparation or the discovery of some new source, one of these compounds becomes readily accessible in large quantities, it can be used as the starting point in other syntheses. When some rare organic compound is found to have some technical or medicinal application, it comes to be manufactured on the large scale and is consequently obtainable as a starting point for further work. The technical chemist is always on the lookout for cheapened products that may possibly serve as raw materials or intermediates. In the industries a slight change of price of some substance may make it available for the manufacture of something. The scientific chemist is not limited in quite the same way, but as long as a given substance costs five or ten cents a gram, there are few that are so situated as to use it by the kilo. Hence the chemist may also look out for cheapened materials as opportunities for research. The recent catalytic methods of Sabatier and Mailhe [6] for the preparation of ketones and aldehydes have rendered these compounds far more accessible than they once were and made possible the use of many of them as research materials.

Normal butyl alcohol is a good example of a substance formerly inaccessible and hence little studied which has recently come upon the market in large quantities at a low price. For our purposes it may be considered a new substance. A search of the literature reveals that comparatively few normal butyl derivatives are on record while there are a host of isobutyl. This situation is an opportunity to chemists to do a deal of useful preparative work with little cost for materials. Industry and care rather than originality are required for such study. This practically new alcohol may be put through all the processes that have been worked out for isobutyl and other alcohols and a long list of normal butyl compounds may be prepared. Many gaps in our scientific knowledge will be filled and some tech-

[6] *Compt. rend.*, **158**, 830–5, 958–91. *C.A.*, **8**, 2673, 2674.

nically important substance will be found. In fact several normal butyl compounds are already being used in several industries.

From this alcohol we can prepare the corresponding halides which by the Grignard reaction may serve as materials for many syntheses. Normal butyric aldehyde becomes readily accessible and may be coupled with a host of Grignard reagents besides having possibilities as a starting point for resins and plastics.

Isopropyl alcohol, sec. butyl, $CH_3CH_2CH(OH)CH_3$, and sec. amyl, $CH_3CH_2CH_2CH(OH)CH_3$, are now available in quantity and make possible many interesting syntheses. Cyclohexane, cyclohexanol, tetrahydro-naphthalene (tetralin) and decahydro-naphthalene (dekalin) have recently escaped from chemical museums and are jostling common substances in the race for industrial applications. They are now on the market and are attracting much attention from chemists. The article by Schroeter [7] on tetralin is a good example of a systematic study of the derivations from a new substance, but his work, extensive as it is, covers but a small portion of the ground.

Fumaric and maleic acids, long famous in chemical treatises for their Dr. Jekyll and Mr. Hyde relationship, but seldom seen outside of books, have recently become common substances. Along with them may be put mucic acid and furfural which has recently tumbled in price from $16.50 per pound to 25 cents. It is coming from one plant at the rate of 800 lbs. per day with prospects of lower price and greater supply as soon as research shall lead the way to new and larger applications.

Each of these substances is a starting point for scores of syntheses which were out the question at the old prices. The substances cited above are some whose prices have dropped spectacularly but frequently a drop of 25% or even 10% in the price of a chemical will set commercial research chemists to work. A horizontal cross section of a mountain increases in area as we come from higher levels to lower, and likewise the extent of the commercial applications of a substance increases as the price comes down. Thus a substance costing $50 a pound might be used for preparing perfumes or pharmaceuticals, but these will have to be very desirable to stand the cost. One at $5 per pound may enter into many more preparations, and on a more liberal scale. Materials whose prices are quoted in cents are the ones which are used for the largest number of purposes. Commercial chemists are keen to find new applications for substances which are appearing on the market at lower prices.

[7] *Annalen*, 426, 1 (1922).

The Preparation and Study of Optically Active Compounds

A great many optically active compounds have been discovered in natural products and a great many more have been prepared artificially, but in most cases, the compounds that have been made do not form groups or series, so that an extensive comparison that would throw light on the various theories of optical activity, is possible in but few cases. In a recent study of the causes of optical activity Wessen [8] was fortunate enough to be able to compare 100 closely related compounds for which numerical data were available and was able to draw interesting conclusions. Before final conclusions can be reached, it will be necessary to have a number of such groups of optically active compounds of widely varying kind. Anyone who prepares an active compound and studies it carefully enough to put on record reliable data concerning it, does just so much towards furnishing a broad basis for theories of optical activity. To be of value, each compound must be studied carefully so that the data obtained will be reliable and comparable with data obtained by others on other compounds. The great advantage found in the above mentioned study of this group of 100 optically active compounds was that the measurements on them had been made by the same observers and were strictly comparable, while comparisons in which are included data from various sources have commonly proved unsatisfactory on account of inaccuracies in the various determinations. With modern accurate instruments and good working methods data obtained by different observers should be comparable.

An examination of the literature will reveal scores of accessible compounds containing asymmetric carbon atoms which have not as yet been separated into their antipodes. The investigator may select the most available and set to work using the methods which have been successful in similar cases. To complete any series it may be necessary to synthesize new compounds.

The Preparation of Derivatives for Identification

This is a very large and important field in which much has been done but in which there is still much to do. There are scores of known compounds from which derivatives are to be made by well known methods. Much of this work can be done by those who have limited resources, as only small amounts of chemicals are required,

[8] *J. Am. Soc.*, 36, 2522–32 (1914).

and patience, rather than originality, is needed. There are, however, cases in abundance which will require all the ingenuity that is available and much pioneer work is needed in devising new methods and in discovering new classes of derivatives suitable for identification. There are important classes of compounds of which there are no characteristic derivatives known that can be obtained by simple means. Even where one of two derivatives of a compound are known it is desirable to have others, since the more witnesses the better, when anything is to be proved.

When picric acid is added to boiling benzene and the solution is cooled, bright yellow rhombic crystals separate. The melting point is 84.3° and the composition is $C_6H_6\,C_6H_2(NO_2)_3OH$. This double compound serves to identify benzene far better than any color reaction could possibly do. The melting point is a number which can be put down in figures, while the color can only be described. In case one is working with an unknown oil and treats it with picric acid and obtains yellow crystals melting at 84.3° the evidence is strong that benzene is present. It is made almost conclusive by making a mixed melting point test with some of this preparation and some of the picrate prepared from known benzene. If both preparations melt at the same temperature and a mixture of the two melts at the same, the presence of benzene in the unknown oil is practically proved. In an important case it would be very desirable to be able to make some other derivative, with a definite melting point, from both the unknown and the known oils and take their melting points and a mixed melting point of the two. If all of these proved to be identical, we would have two independent witnesses and the case would be established. Identification by two crystalline derivatives is sufficient in any ordinary case, but there is a possibility that some admixture in the unknown, or some other untoward circumstance, might interfere with the application of one of these tests, hence it is desirable to have a number of crystalline derivatives that can be made from each important compound that may have to be identified. The more such derivatives that can be made, the better and the more certain we are to be able to identify that substance under all conditions. Hence no matter how many crystalline derivatives of any compound are already known, it is a service to chemistry to prepare others.

To be of use such derivatives should have sharp melting points which are neither too high nor too low. In case they melt below 50°, it is difficult to recrystallize them as they are deposited from hot solvents as oils and the process of purification by recrystallization is

tedious. For the sake of completeness, it is desirable to make such derivatives and put their properties on record, but it is well to continue the work till higher melting ones are obtained.

It is highly desirable to have derivatives which can be prepared as readily as possible and with reagents that are accessible. Those that can be prepared from small quantities of materials are desirable. In many cases it is necessary to work with as small a quantity as 0.1 g. or less while 1 g. may be considered the upper limit. A survey of the field shows the desirability of much further work.

Paraffines. Systematic organic chemistry begins with the paraffines, yet for these we have no readily prepared crystalline derivatives. The same is true of the naphthenes which occur so abundantly along with the paraffines in some petroleums. The investigation of petroleum would be immensely aided by the discovery of suitable crystalline derivatives for the identification of its constituents. It is agreed that this problem is hopeless with our present methods. Fractionation is adequate up to the hexanes but fails utterly to separate the numerous higher hydrocarbons.

When we find means for identifying the paraffines we will be in a position to study their transformations. A great deal of study has been put on the "cracking" of oils. We know that heat effects marked changes in the hydrocarbons but as we do not know what we put into the stills and do not know what comes out, it is difficult to find out much about the reactions.

The paraffines have little or no residual affinities and can hardly be expected to form crystalline addition products as do the aromatic hydrocarbons. They are amenable to substitution by chlorine or bromine though the reactions are difficult to control. The resulting halides may be turned into Grignard reagents which can be made to react with ketones containing groups with great power of crystallization so as to form crystalline tertiary alcohols. Or the halogenated hydrocarbons may be treated with alkali so as to split off halogen acids leaving unsaturated hydrocarbons which may be identified in various ways.

Fluorine attacks paraffines more promptly than the other halogens but little is known as to the abstraction of hydrogen fluoride.

There is a possibility that paraffins might be identified by nitration, the nitro-paraffines being reduced to amines which can be converted into crystalline derivatives in many ways.[9] Konowalow and Worstall[10] have shown how the paraffines can be nitrated. It re-

[9] *J. Russ. Phys. Chem. Soc.*, 1893, 1, 389–425, 472–500; *Berichte*, 26 *Ref.* 878–81; *Berichte*, 28, 1852–65 (1895); 29, 2199–2205 (1896).

[10] *Amer. Chem. J.*, 20, 202 (1898); 21, 210 and 218 (1899).

mains for some one to work out the proper conditions for the complete nitration of small quantities and for the reduction of the resulting compounds.

Unsaturated hydrobarbons. We are well provided with means for converting these into crystalline compounds since the halogens, halogen acids, nitrosyl chloride,[11] nitrosyl bromide and nitrous acid[12] are taken up readily and many of the addition products are well crystallized solids with suitable melting points. The nitroso-chlorides and bromides of the hydrocarbons react readily with amines to form nitrol-amines. Since a variety of amines may be used a corresponding variety of nitrolamines may be obtained. Aniline, piperidine and benzylamine are the ones most commonly used and the products are called nitrol-anilides, nitrol-piperidides and nitrol-benzylamides. These usually have satisfactory melting points and are suitable for the identification of the hydrocarbons.

The intricate relationships of the terpenes have been explored by means of the addition products enumerated above. A sufficient number and variety of these derivatives should be made from all known unsaturated hydrocarbons so that we can identify them wherever found. Many cracking processes yield large proportions of unsaturated hydrocarbons which might be studied.

Aromatic hydrocarbons. These frequently form crystalline addition compounds with picric acid. It is possible that they might combine also with *s.*-trinitro-benzene[13] which gives good compounds with aryl-amines. Aromatic hydrocarbons are most commonly identified through their nitration products. Either the nitration is carried far enough to obtain crystalline dinitro-derivatives or the mono-nitro compounds are reduced to the amines which are converted to crystalline derivatives. Thus we have benzene → nitrobenzene → aniline → benzanilide m. 160° and acetanilide, m. 114.2° or directly into *m.*-dinitro benzene, m. 90°.

Aromatic hydrocarbons are frequently sulphonated and identified by the melting points of the sulphone chlorides or amides which usually have satisfactory melting points.

Alcohols. Since alcohols are important constituents of many valuable ethereal oils and are prominent in the terpene class they have been more satisfactorily studied than any other class, unless it be the aldehydes.

[11] Wallach, *Annalen,* **252,** 109 (1889). Schmidt, *Berichte,* **35,** 2323 and 3727 (1902).

[12] Tönnies, *Berichte,* **11,** 1511 (1878). Wallach, *Annalen,* **245,** 243 and 270 (1888); **248,** 162 (1888); Wallach and Gildemeister, *Annalen,* **246,** 282 (1888).

[13] Sudborough and Beard, *J. Chem. Soc.,* **97,** 773 (1910).

The phenylurethanes[14] are the most satisfactory derivatives and it has come to be the custom that when a new alcohol is described the melting point of its phenylmethane is given along with its density and boiling point. Along with these go diphenylurethanes[15] and α- and β-naphthylurethanes.[16] The *p.*-nitrobenzoic[17] and *p.*-brombenzoic[18] esters have been used to some extent. The *p.*-nitrobenzoates melt higher than the corresponding *p.*-brombenzoates, but the latter have the advantage that a bromine determination gives the molecular weight of the alcohol.

An alcohol may be combined with phthalic anhydride to form the acid ester and the sodium salt of this heated with *p.*-nitro-benzyl bromide[19] or other halide which gives characteristic esters with acids. This is cumbersome when the pure alcohol is available but may prove convenient in case the alcohol is isolated from a mixture by heating with phthalic anhydride, since it is unnecessary to isolate the alcohol.

It is desirable that a number of these derivatives be made from all available alcohols. A good selection would be phenylurethanes, α- and β-naphthylurethanes, *p.*-nitrobenzoates, and *p.*-brombenzoates. It is also desirable that the search for suitable derivatives be extended. *m.*-Dinitrobenzoic acid might yield some good derivatives. Although the derivatives above mentioned are frequently solid, in fact generally so, yet in many cases they are oils that cannot be induced to solidify. For instance, all the urethanes and *p.*-nitro- and *p.*-brombenzoates of citronellol are oils and can not be made to solidify even in a freezing mixture. In fact no crystalline ester has been made from this alcohol, which is one of the most important with which the perfumery chemist has to deal.

In the case of citronellol, extreme measures have to be taken and a satisfactory result has been obtained by making its pyroracemate, which is an oil, but which, being a ketone, forms a semicarbazone. Fortunately, this turns out to be a solid with a good melting point and can be used for the identification of citronellol.

[14] Hofmann, *Annalen,* **74,** 17 (1850); Hofmann and Snape, *Berichte,* **18,** 2428 (1885); Hentschel, *ibid.,* **17,** 1284 (1884); Tessmer, *ibid.,* **18,** 968 (1885); Bloch, *Bull.* [3], **31,** 49 (1904); Goldschmidt and Zanoli, *Berichte,* **25,** 2573 (1892) Blumann and Zeitschel, *ibid.,* **47,** 2626 (1914).

[15] Erdmann and Huth, *J. prakt. Chem.* [2], **56,** 6 (1879).

[16] Willstätter and Hocheder, *Annalen,* **354,** 253 (1907); Neuberg and Kansky, *Biochem. Zeitsch.,* **20,** 445 (1909).

[17] Pope and Wood, *J. Chem. Soc.,* **101,** 1825 (1912). Claisen, *Berichte,* **45,** 3162 (1912); Henderson and Heilbron, *Proc. Chem. Soc.* **29,** 381 (1913), *C.A.,* **9,** 611.

[18] Jackson and Rolfe, *Amer. Chem J.,* **9,** 82 (1887).

[19] Reid, *J. Amer. Chem. Soc.,* **39,** 1249 (1917).

Aldehydes and ketones. These have been comparatively well studied. The oximes,[20] phenylhydrazones[21] and semicarbazones[22] have been the most used. In special cases recourse is had to *p.*-bromphenyl-hydrazones,[23] *p*-nitrophenylhydrazones,[24] benzyl-phenyl-hydrazones, diphenylhydrazones, β-naphthylhydrazones, and diphenylmethane-dimethyl-dihydrazones (from $CH_2(C_6H_4N(CH_3).NH_2)_2$).[25]

Acids. We have not been well provided with characteristic crystalline derivatives of acids, particularly of the aliphatic. The amides, anilides and *p.*toluides have been commonly relied upon but the melting points of these are not as widely scattered as might be desired and they are somewhat troublesome to make since one must use the acid chloride.

Recently it has been found that the *p.*-nitro-benzyl,[26] phenacyl[27] and *p.*-brom-phenacyl[28] esters of many acids have characteristic melting points. It is a great convenience that these esters are readily prepared from a water solution of the sodium salts of an acid. It is likely that further study would reveal still more desirable derivatives. There remain many acids of which these derivatives have not yet been prepared.

When the individual acids have been thoroughly studied we will be in a position to undertake the unscrambling of scores of mixtures which occur in fruits and other natural products.

The classes of compounds mentioned above have received the most attention from chemists but even these are far from covered. There are many others which need better means for characterization.

The identification of an unknown substance is like detective work, one follows all possible clues, circumstantial as well as direct. Every effort should be made to obtain crystalline derivatives. When these are obtained and their properties point to a certain substance as being present, a known sample of this substance should be procured

[20] V. Meyer and Janny, *Berichte,* **15,** 1324 and 1525 (1882). Wohl, *ibid.,* **24,** 994 note (1891); Schmidt and Söll, *ibid.,* **40,** 2455 and 4258 (1907).

[21] E. Fischer, *Berichte,* **16,** 661 (1883); **17,** 572 (1884); **22,** 90 (1889); **30,** 1240 (1897); Baeyer, *ibid.,* **27,** 813 (1894); Boeseken, *Chem. Wekbl.,* **7,** 934 (1910),. *C.* 1910, I, 1836; Neubrew, *Berichte,* **32,** 3384 (1889); Bertrand, *Compt. rend.,* **130,** 1332 (1900).

[22] Thiele and Stange, *Berichte,* **27,** 31 (1894); Baeyer, *ibid.,* **27,** 1918 (1894); Zelinsky, *ibid.,* **30,** 1541 (1897).

[23] Fischer, *Berichte* **24,** 4221 note (1891).

[24] Bamberger, *Berichte,* **32,** 1806 (1899); **34,** 546 (1901); Hyde, *ibid.,* **32,** 1810 (1899).

[25] v. Braun, *Berichte,* **41,** 2169 and 2604 (1908).

[26] Reid, *J. Am. Chem. Soc.,* **39,** 124 (1917); Lyman and Reid, *ibid.,* **39,** 701 (1917); Lyons and Reid, *ibid.,* **39,** 1727 (1917).

[27] Rather and Reid, *J. Am. Chem. Soc.,* **41,** 75 (1919); **43,** 629 (1921).

[28] Judefind and Reid, *J. Amer. Chem. Soc.,* **42,** 1043 (1920).

and the same derivatives prepared from it so that mixed melting points may be taken to verify the conclusions.

In the above discussion melting points are spoken of as if they were the only properties of the derivatives. They are most commonly used since they can be expressed in figures and are readily determined with the usual equipment of the organic chemist, but any other property that can be numerically expressed may likewise be employed. Attention should be called to crystalline form and index of refraction and other optical properties. Under the microscope identifications may be made and even the proportions estimated in mixtures. For correct melting points we must recrystallize until a complete separation is effected but, provided mixed crystals are not formed, the several constituents of a mixture may be directly recognized under the microscope, since it shows up each individual particle and enables us to measure the properties of each independently.

Preparation of Compounds for Specific Purposes

A long time ago some of our ancestors found a tree which had fallen across a stream a convenient way to get on the other side. Soon they were imitating nature and were placing trees across other streams. Later on they constructed more elaborate bridges.

The most common method of designing a compound for a particular use is to start with a known substance which has been found to serve the purpose and work out from it. The one that is in use has proved to be good but has some drawback, perhaps it is somewhat too volatile, perhaps it causes discoloration or gets rancid, or a change in the market may raise its price too high. We set about finding something with all its desirable qualities, trying to avoid the undesirable. We usually start with things of similar structure and progressively modify the molecule changing one group after another. Each time we must test out our product to see whether it is better or worse than our standard substance so as to know whether we are going in the right or wrong direction.

In gas warfare we started with the knowledge that certain things are toxic and tried to imitate them by preparing homologs and analogs. Thus a homolog of mustard gas was made by using propylene instead of ethylene and an analog by substituting selenium for sulphur.

Chemical architecture. Building up compounds that will have predetermined qualities may be called chemical architecture. The architect, aided by the engineer, designs structures for specific pur-

poses. If a bridge is required, the width of the river, the character of the banks, and the sort of load to be carried are ascertained in advance and the structure designed accordingly. Engineering formulae are so exact and the strength of standard materials so well known that the figure and precise dimensions of each piece entering into the structure may be worked out. Drawings and blue prints are prepared and put into the hands of the contractor who realizes in steel or stone the visions of the designer. The specified beams, girders, rods, bolts and nuts are fabricated and delivered to the site. When these are assembled each piece goes into its proper place and rarely does the completed structure fail to fulfill the expectations of the architect.

Bridges have been built by man for some thousands of years and vast and varied is the experience that has been accumulated. Organic chemists have been designing molecular structures for only a few decades and the specifications which have to be met are not so easily ascertained and are not capable of such exact statement, hence the greater difficulties and uncertainties. We have gone only a little way toward our goal but we have made definite progress. To find a suitable material for a given purpose we must as yet cut and try; a number of things must be prepared and tested before we find one best suited. We do know enough to decide in advance against many proposals and so limit the labor.

Designing a "softener." To make it concrete, suppose we wish to design a "softener" to be added to some coating to increase its flexibility. If we know the chemical nature of the coating material we know pretty well what groups must be present in a compound for it to be a good solvent for such material. If the coating is to retain its flexibility for months or years, the "softener" must not evaporate from the film, hence it must have an extremely low vapor pressure at service temperatures, *i.e.* its boiling point must be very high. This gives us something tangible, as in any series the boiling point rises pretty regularly with the molecular weight and we can, by putting in larger or smaller groups, prepare a compound of any type boiling close to any point we wish.

On the other hand the film must remain flexible at low temperatures so we will avoid groups that raise the melting point of our molecule, as a nitro group in the para position. Too many phenyls in a molecule are apt to give a solid, and ethyl derivatives usually melt lower than methyl. We must avoid acid groups which might start decomposition or corrosion, also a multiplicity of hydroxyl or amino groups or double bonds which would increase oxidisability.

Aldehydes are apt to oxidise and may cause polymerization and hence are not desirable.

The great difficulty is usually in the testing. Our hypothetical softener is mixed with a number of other things to produce a complex finished product and it is usually hard to relate the properties of this product with changes in the one constituent. Progress in engineering has come about by making exact measurements. It is necessary to give numerical expression to the desirable properties of our finished product before we are in a position to plot curves showing the effects of our variables.

The " feel " of a fabric is all important, but is difficult to state in figures. The same may be said of other properties. Until we can devise tests which are reproducible and which can be set down in numbers we are not in a position to make much progress. In building our bridge we do not get anywhere by saying that a certain girder is too short; we must measure and find just how many inches it lacks so we can fabricate another to fit exactly. Frequently the hardest and also the most important part of the task of the chemical architect is devising suitable quantitative tests by which his products may be tested.

In building a particular bridge there is usually set a cost figure which must not be exceeded. This limits the architect to certain materials: if a large bridge must be constructed for a moderate sum, he can not use carved marble but must content himself with reinforced concrete. In a similar way the chemist is limited by cost of materials. The use for which a substance is designed limits its cost and in its synthesis we must use intermediates which are suitably priced. Considering the selling price of the product in which our " softener " is to be used, its cost may be limited to, say, 75 cents per pound. Taking this as a limit the chemist must look around for materials which are obtainable at an average cost of, say, 40 cents per pound of the product or less, so as to leave a margin for manufacturing costs.

Perfumes. Suppose the chemist sets out to synthesize a new perfume material. The most practical way is to look over the structural formulae of substances that have found favor for this purpose. There are many such, belonging to a variety of classes, alcohols, esters, aldehydes, ketones and lactones. We find few hydrocarbons and few halogenated hydrocarbons. Almost any compound belonging to one of the above classes may have a pleasant odor, but as yet we have great difficulty in predicting odors. For perfume materials we are not hampered by low price limits as in many other lines: products

that bring $50, $100 or even $500 per pound are not uncommon. This gives the chemist greater latitude in the choice of his starting materials and permits more complicated manufacturing processes. However, to bring high prices materials must have some particularly desirable qualities as many sweet-smelling materials are sold at $5 per pound or less.

Certain rather well defined limits may be set as to the boiling points of proposed perfume materials. Substances boiling below 200° C. are of little use as they evaporate too quickly. Hence we must have a m.wt. of about 150 and about 10 carbon atoms. Geraniol $C_{10}H_{18}O$, m.w. 154 b. 230°, linalool $C_{10}H_{18}O$ m.w. 154 b. 199°, citronellol $C_{10}H_{20}O$ m.w. 156 b. 222° may serve as examples. Phenylethyl alcohol, $C_8H_{10}O$ m.w. 122, b. 220°, and benzyl alcohol, C_7H_8O m.w. 108, b. 206°, have lower molecular weights than these but their boiling points are not correspondingly low. On the other hand boiling points of perfume substances must not be excessively high, in general not much above 300°, else not enough of them will evaporate at room temperature to be effective. Benzophenone boiling at 306° is useful. The volatility of natural musk and of the artificial is infinitesimal but these have such powerful intrinsic odors that their odors are strong.

A great deal has been accomplished in the field of synthetic perfumes but progress has been seriously hampered by the impossibility of objective standards of odors. Science is based on accurate measurements and it is extremely difficult to make progress when measurements are impossible.

Dyes. The color chemist has an enormous advantage over his fellow in perfumery since colors are so easily defined and recorded. This enables us to work out the relation of color to constitution in a thoroughly scientific way. The strategic importance as well as the profits in the synthetic dye industry have been so great that an enormous amount of endeavor has been put into that field with the result that designing dyes to order is a common thing. For some classes the color, fastness and other properties of a dye can be predicted with certainty and exactness before it is synthesized.

A wide field. The organic chemist is called upon to design chemical structures for all sorts of uses. One man wants a dye of a certain hue that will be fast to light and washing and which may be applied in a particular way; another wishes a gas that will kill boll-weevil but will not hurt the cotton plants or the laborers, and will not cost more than a fraction of the price of the crop. The medical folk are always looking for remedies which are more effective

in curing the disease and are less harmful to the patient. Manufacturers of all sorts of goods are out for materials which will improve the quality or lower the cost of their products.

In the next chapter the structures of a number of typical drugs are given so that the chemical designer may use these as models for his creations.

CHAPTER XIII

SYNTHESIS OF MEDICINALS

By A. D. HIRSCHFELDER, M.D.[1]

Constitution and Pharmacological Action, Types of Drugs

The structural formula and the physical properties of a substance reveal much about its actions as a drug; and particularly they point toward the type of drug to which it belongs. The body acts like a vast test-tube in which foreign substances react much as they do in the test-tube, but many new factors play their rôles in determining the reactions, which are therefore infinitely more complicated. In order for a new drug to be of any value it is necessary that it have certain desired actions within the body, that it shall perform the desired function better than substances already in use for the purpose; and that it shall do so in doses which are less poisonous than the older drugs.

It is often possible to foretell that a new substance will belong to a group which has certain desirable actions as a drug; and even that it will have a more potent effect than those in use; but it is difficult to predict whether the active dose will be less poisonous than the others; and it is often almost impossible to know whether it is too pungent or irritating for use as a medicine.

Solubility in lipoids. The first point to ascertain is whether the substance is relatively more soluble in lipoids than in water or vice versa. Most of the active drugs are more soluble in organic solvents, fats and oils than they are in water; and most substances which are more soluble in water than in the organic solvents are readily excreted through the kidneys and exert less action on the tissues of the body.

In order to explain this fact Overton and Meyer have assumed that the cells of the body and particularly those of the nervous system are all surrounded by a surface layer of fats or lipoids. A substance which is soluble in the lipoids would thus be readily extracted out of the blood, or lymph, in which the tissues are bathed and would readily enter the cell, just as it would be removed by

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ether in a separatory funnel; and if it is not lipoid soluble, it would pass around in the blood vessels and be filtered out of the blood through the filtering or secreting cells in the kidneys. Overton and Meyer have shown for example that chemically inactive substances which are very soluble in organic substances all induce sleep or anaesthesia (*i.e.* are soporifics or anaesthetics). Among members of homologous series the therapeutic activity seems to vary in accordance with variations in the distribution coefficient,

$$\frac{\text{solubility in fats, oils and lipoids}}{\text{solubility in water and blood serum}}$$

Homologous series. In groups of substances which differ from one another only by the elongation of an aliphatic chain, the larger the chain the more intense the therapeutic action of the drug and the greater the toxicity. Among the simpler aliphatic alcohols, each successive member is three times as active and three times as toxic as the next lower member of the series (Richardson, Traube, Kamm). Kamm claims that in all these substances, the therapeutic activity and the toxicity are more dependent upon the molecular volume than upon any other factor, except the $\frac{\text{lipoid}}{\text{serum}}$ distribution coefficient.

Changes in the body. However, the action of a substance is also influenced by the changes which it undergoes in the body and by the ease and rapidity with which it is changed. For example, benzene, which is lipoid soluble and difficultly oxidized in the body, is a general anaesthetic though too poisonous for use; but it has the peculiar action of destroying the white cells (leucocytes) of the blood and the blood-forming tissues in the red marrow of the bones. Toluene, however, with the same physical properties does not have this blood- and marrow-destroying action because it is rapidly oxidized to benzoic acid in the body and is then excreted as the harmless hippuric acid. The oxidation product may also be more toxic than the parent substance (arsphenamine to arsinoxide).

The principal changes which drugs undergo in the body are:

(1) Oxidation — especially rapid in the case of aldehydes and alcohols;

(2) Reductions — especially of aldehydes to alcohols;

(3) Hydrolysis — as in the case of the esters and of acetylated amines (acetanilid, etc.).

These reactions are often reversible (Scherwin).

(4) Combinations especially with glycocoll (benzoic acid, C_6H_5COOH + glycocoll, H_2NCH_2COOH = hippuric acid, $C_6H_5CONHCH_2$-

COOH), and glycuronic acid, CHO.CH(OH).CH(OH).CH(OH).-COOH. In these cases the synthesized substance is usually less toxic than the parent substance and is the form in which the drug is excreted in the urine.

One cannot be certain that exact analogies will hold even between very similar substances. Thus benzoic acid is combined in the body with glycocoll to form hippuric acid, but salicylic acid does not form the homologous compound — and is excreted unchanged (Hanzlik).

Alkaloids and glucosides. Most of the active drugs in use, especially those which have been in use for many decades, are either alkaloids or glucosides, derived from plants.

The alkaloids constitute an indefinite group of substances derived from plants and are all either primary, secondary or tertiary substituted ammonia derivatives, most of them the last. Hence, the alkaloidal bases themselves are almost insoluble in water, but they form water soluble salts; and they are usually administered in this form.

There are very few alkaloids which are formed in the animal body, the most notable being epinephirin or adrenalin,

$$3,4(HO)_2C_6H_3CH(OH)\ CH_2NHCH_3$$

Some animal and plant tissues, and bacteria, especially those of the colon group, are capable of decarboxylating amino acids to form amines; *e.g.* tyrosine → tyramine:

$$p.HO.C_6H_4.CH_2CH(NH_2)COOH \rightarrow p.HO.C_6H_4.CH_2CH_2NH_2 + CO_2,$$

and these amines have an intense action on the nerves and smooth muscles of the blood vessels and the hollow organs. Some of the proteogenic amines stimulate the heart, like tyramine: some depress it, like histamine.

The ordinary medicinal alkaloids such as morphine, strychnine, and quinine are of much more complicated structure; with several simple rings condensed together.

Pictet has suggested that in the plant they are formed in several stages, which may be typified as follows:

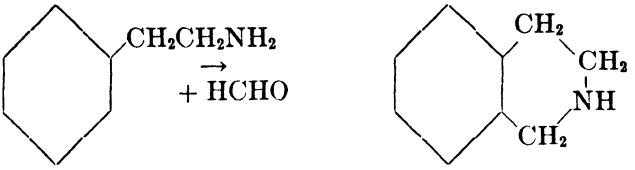
1. Splitting off of CO_2 from an amino-acid:

e.g. phenylalanine → phenyl-ethylamine

$$C_6H_5CH_2CH(NH_2)COOH \rightarrow C_6H_5CH_2CH_2NH_2 + CO_2$$

2. Condensation of this amine with the formaldehyde which is formed in the leaf from carbon dioxide and water;

phenyl-ethylamine → tetrahydro-isoquinoline:



Thus, morphine has a very complicated formula containing a pyridin and a phenanthrene ring, and a secondary alcohol group; while strychnine has a carbazol group; and quinine an oxyquinolin united by a secondary alcohol bridge with a so-called loipon fraction which is a nitrogen containing complex ring somewhat suggesting the terpene type.

Most of the alkaloids are, moreover, either secondary alcohols or the esters of secondary alcohols.

The glucosides represent another group of drugs, some of which like digitalis or strophanthus are very active and important; while others like some of the saponins, though possessed of toxic actions when injected into the blood stream, have little effect when taken by mouth and are of importance chiefly for their power of lowering surface tension and thus giving rise to the foaming properties of beverages.

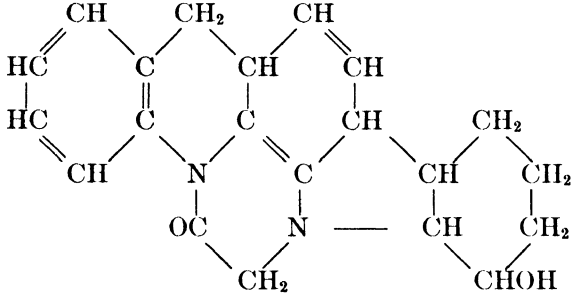
In the glucosides, the nucleus of the active substance is in combination with a glucose or other sugar molecule, usually in accordance with the following formula:

$$\mathrm{ROCH.CH(OH).CH(OH).CH.CH(OH).CH_2OH}$$
$$\mathrm{\quad\quad\quad

(analgesics); or they may diminish sensitiveness to pain without inducing sleep; and in this case they usually also lower the body temperature, especially in fevers (antipyretics).

Local anaesthetics, like cocaine, act on the endings or on the trunks of the nerves in such a way that they lose their power to conduct sensations toward the brain across the area which has come in contact with the drug, even though the motor fibers in the same nerve trunk may still retain the power of conducting nerve impulses outwards toward the muscles and of causing the latter to contract.

Strychnine



is about the only drug which is a stimulant for the nerves, *i.e.* the nerves to those muscles which are under the control of the will. It acts by increasing the irritability of the nerve cells in the spinal cord. Many other compounds such as nicotin and most of the phenol derivatives stimulate the spinal cord somewhat, but only when they are given in doses which are very poisonous.

Camphor and cocaine in poisonous doses produce convulsions by stimulating the brain cells (cerebral cortex). None of these substances, however, except strychnine, is of use for stimulating the nerves.

Some substances paralyze the motor nerve endings in the voluntary muscles (these are not used in medicines). All quaternary ammonium bases and their halides, *e.g.* tetra-ethyl-ammonium iodide, $(C_2H_5)_4NI$, do this, especially curare, an Indian arrow poison, which is a quaternary ammonium base. Strychnine, when treated with ethyl or methyl iodide, becomes a quaternary ammonium compound and then paralyzes the nerves instead of producing convulsions.

Actions on the vegetative nervous system. Drugs may also act upon the purely vegetative nervous system and either stimulate or depress the secretions of the glands which produce sweat, saliva, pancreatic secretion (influencing the oxidation of sugar, etc.). Usually all of these glands are influenced in the same way by the

same drug. These same drugs usually also stimulate or paralyze the contractions of all the hollow organs. The drugs which stimulate the secretions usually also cause these organs to contract (inducing bronchial asthma, painful stomach contractions, diarrhoea, contractions of the bladder, and painful menstruation); while the drugs which depress the secretions of the glands usually relieve these conditions of the hollow organs by causing them to relax.

Purgative or cathartic drugs act either by stimulating the nerves that supply the intestines (also stimulating the glandular secretions and the walls of the other hollow organs); or by irritating the nerve endings in the lining of the intestines; or, on the other hand, as in the case of the saline purgatives, by increasing the bulk of the intestinal contents through endosmosis, after which peristalsis (contractions) results from stretching of the intestinal walls.

Emetic drugs, which cause vomiting, may act in either of the two ways somewhat like those in which purgatives act — either by stimulating the nervous system in the "vomiting center" in the medulla oblongata and thus bringing on vomiting movements (as is the case when apomorphin is administered), or by directly irritating the lining of the stomach (mustard, copper sulphate, etc.).

Diuretics, or drugs which increase the secretion of urine, act either by widening the small blood vessels within the kidneys, and thus allowing blood to pass more rapidly through the kidney and the urine to filter out more rapidly through the little filters or glomerular tufts; or they may keep the bulk of the urine large by preventing the filtrate from being reabsorbed in the tubules of the kidneys after it has been filtered out in the glomeruler tufts. The saline cathartics which have a similar action in the intestine, are therefore diuretics.

Actions on the heart and blood vessels. Drugs which act on the circulation may either slow down or accelerate the contractions of the heart (pulse rate); or these may increase or decrease the force of the heart beat; or they may cause the arteries to contract or to relax. The head of pressure in the arteries (blood pressure) is increased, or raised, either when the heart beats more forcibly or when the arteries and especially the smallest branches of the arteries (arterioles) contract. The largest rises of blood pressure are usually brought about when the arteries are strongly contracted.

Correspondingly, the blood pressure falls either when the contractions of the heart weaken or when the arteries widen because their walls relax. Recently a great deal of attention has been drawn to fall of blood pressure brought about by a great widening of the

very smallest tubes in the whole circulation, the capillaries. These are so small that they barely let the red blood corpuscles pass through one at a time: and at any given time many of them are contracted to such small diameter that no corpuscles are passing through at all.

Antisepsis, chemotherapy, etc.* Besides these actions, drugs may have germicidal, bactericidal, antiseptic, or disinfectant actions, either by killing germs and bacteria or merely preventing them from growing. Such substances may act either outside the body — as in the case with the general antiseptics — or by direct action upon germs or bacteria which have infected the tissues of the living body. Since the tissues are all of protein nature, the problem of antisepsis resolves itself largely into two phases — of disinfection in the presence of or in the absence of protein. Most antiseptics act by precipitating the proteins of the bacteria, and therefore are much more active in the absence of protein than they are in liquids which are rich in protein, or than they are in tissues which are infected with bacteria. The disinfection of infected tissues is rendered still more difficult by the fact that the bacteria or other germs do not lie on the surface but invade the depths of the tissues for several millimeters or more. Moreover, all the substances which kill germs also kill the cells of the tissues and dead tissues are more susceptible to new infections than are healthy tissues. So that even though the application of an antiseptic may kill the germs that lie on the surface, it may actually do more harm than good by leaving the untouched germs in the depths to feed upon the tissues which have been injured by its own poisonous action. The chief problem in the development of new antiseptics lies in discovering substances which will be much more poisonous to the germs than to the tissues, and so kill the former while leaving the tissues uninjured. In this regard, there is great variation in the sensitiveness of different germs, some being sensitive to one substance, some to another. In other words antiseptics are relatively specific in their actions, and each antiseptic should be tested not merely upon certain typical bacteria, but upon the particular bacteria which it is desired to kill.

Germs may be killed not merely by local application but when the drug is administered by mouth, under the skin (subcutaneous or hypodermic), or into the vein (intravenous). Thus, germs infecting the bladder may be killed by such drugs (like hexamethylen-tetramin) when they are excreted in the urine. Or, on the other hand, they may be killed in the blood or in the tissues, as is the case when quinine is administered to persons infected with malaria, or when

* The chemical warfare on germs and parasites.

arsphenamin (salvarsan) is injected into the veins of a person whose tissues are infected with the spirochaete of syphilis. In such cases, the best drug may be one which in the test tube has a relatively weak action upon the parasite. Its curative action may be due either to the fact that large doses can be administered to the patient, or because within the body it reacts with substances produced in the liver or other tissues and forms a combination more poisonous to the germ than is the original substance administered. Much work is being done at present along these lines. New substances are being synthesized step by step. Ehrlich has termed the synthesis of substances to accomplish a definite therapeutic purpose, *Chemotherapy;* and this term is applied particularly to the development of new drugs to cure specific infectious diseases after the drug has been administered either by mouth, subcutaneously or intravenously.

Drugs which are used in the treatment of intestinal worms (anthelmintic, vermifuges) act in either of two ways — either by killing the worm outright, or by anaesthetizing it, so that it loses its hold on the intestinal wall and is then excreted like any other undigested material when a purgative is given a few hours afterwards.

Testing a new substance. In order to determine whether the substance has any of these medicinal actions it must always be tested out first on animals and then on patients.[2] On animals, the lethal (*i.e.* just fatal) dose must be determined, then the exact mode of action on different organs and parts of the nervous system; and finally the therapeutic index; *i.e.*, the ratio:

$$\frac{\text{lethal dose}}{\text{dose sufficient to produce desired effect}}$$

. In synthesizing the drugs for the treatment of syphilis, Ehrlich used none which had a therapeutic index lower than 10; and since a certain number of patients are unusually sensitive to various drugs, drugs should as a rule possess a therapeutic index at least as high as this.

Chemical structure and drug action. Both the nucleus and the side chains must be taken into consideration; and, as in ordinary chemical reactions, the most reactive group is always the one which determines the type of action of the drug.

A good bird's-eye view of side chain influences may be obtained from the actions of a series of simple benzene derivatives.

[2] The methods and technique for the study of drugs upon laboratory animals, as well as the doses of the common drugs for various animals are to be found in Sollmann's and in Jackson's Laboratory manuals.



Benzene

Slowly oxidized in body to phenol. Volatile general anaesthetic too toxic for use. Causes convulsions. In very small doses, repeated, destroys white blood cells and bone marrow.



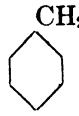
Toluene

Oxidized readily to benzoic acid. Does not destroy white blood cells or bone marrow.



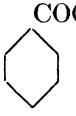
Benzyl alcohol

Oxidized readily to benzoic acid. Local anaesthetic (cocaine like action). Relaxes hollow organs, lowers blood pressure.



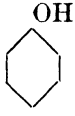
Benzyl esters

Hydrolyzed to benzyl alcohol. Have no local anaesthetic action. Relax hollow organs relieving asthma, diarrhœa, and painful menstruation. Lower blood pressure.



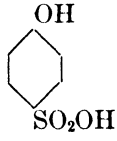
Benzoic Acid

Combines with glycocoll to form hippuric acid. Very weak antiseptic.



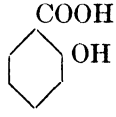
Phenol

Partly oxidizes to quinon; partly combined as phenol sulphonic acid. Poisonous. Moderately powerful antiseptic. Causes convulsions. Local anaesthetic but cauterises tissues.



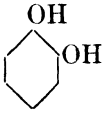
Phenol Sulphonic Acid

Excreted readily in urine. Not antiseptic or anaesthetic. Less than one fifth as toxic as phenol.



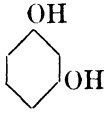
Salicylic Acid

More active than meta or para compounds. Excreted unchanged. Fairly active antiseptic. Relieves pains, especially in acute rheumatism; also lowers temperature in fevers. Large doses cause convulsions.



Catechol

Oxidized further in the body. All catechol derivatives raise blood pressure (as in epinephrin or adrenalin), relax contracted hollow organs; and diminish secretions.



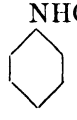
Resorcinol

Oxidized further in the body. Antiseptic, used rather extensively in skin diseases. Effects on nerves like those of phenol.



Aniline

Oxidized to p. aminophenol.* Lowers body temperature, injures blood cells. Converts haemoglobin to methaemoglobin. Injures heart. Lessens pain sensations.



Acetanilid

Hydrolyzed to anilin, acts like anilin but much less toxic.

* Scherwin has shown that some of the aniline is also acetylated in the body to acetanilide. (The reaction is reversible.)

CHEMICAL STRUCTURE OF VARIOUS TYPES OF DRUGS

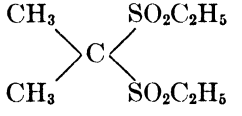
If due allowances are made for the above-mentioned conditions and the sequence of chemical changes which take place in the body, the action of any substance may be surmised by comparing it with that of the most closely related substances. The chemical constitution of substances having the most important types of drug action are given below:

I. **General anaesthetics.** — Volatile chemically inactive substances of the aliphatic series, soluble in lipoids and organic solvents. Ethyl ether, chloroform, ethylene, nitrous oxide.

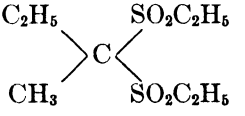
II. **Soporifics or hypnotics.** — Lipoid soluble, non volatile substances of low chemical activity.

1. Aldehydes; — especially paraldehyde.
2. Chloral hydrate $CCl_3CHO + H_2O$ (reduced in the body to trichlorethylalcohol CCl_3CH_2OH)
   And similar derivatives;
   Chlorbutanol (chloretone) $CCl_3C(CH_3)_2OH$.
3. Sulphone esters:

sulphonal



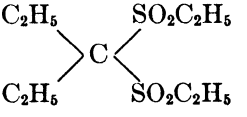
trional



more potent

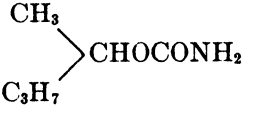
(greatest $\frac{\text{oil}}{H_2O}$ distribution coefficient)

tetronal



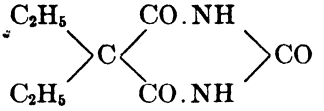
(less active, distribution coefficient less).

4. Ketones — *e.g.* acetophenone (soporific but too toxic for use).
5. Urea derivatives — esters of carbamic acid (urethanes)
   Ethyl urethane $C_2H_5OCONH_2$ (ethyl carbamate)
   Hedonal (methylpropyl-carbinol urethane)

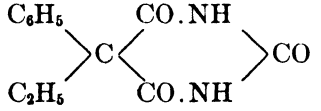


6. Barbituric acid derivatives

Barbital (diethyl-barbituric acid, veronal)

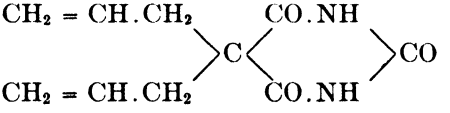


Phenobarbital (phenyl-ethyl-barbituric acid, luminal)



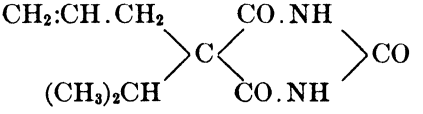
More potent than barbital

Di-allyl-barbituric Acid (Dial)



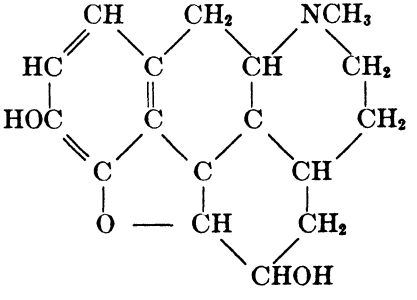
Very potent soporific

Allylisopropyl barbituric Acid



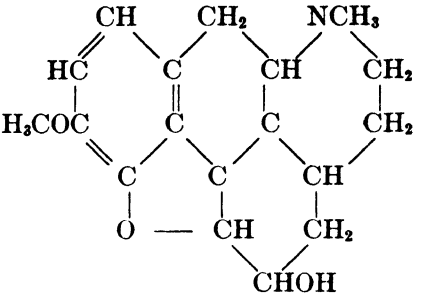
Very potent soporific. Low toxicity.

III. **Narcotics,** especially drugs of the morphine group, phenanthren-pyridin derivatives and hyoscine (Scopolamine).



Morphine

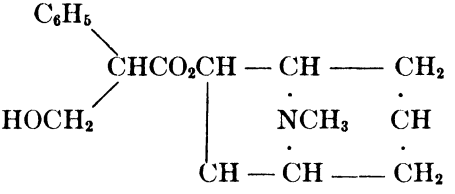
Narcotic, diminishes cough, habit forming.



Codeïne

Methyl-ether of morphine — diminishes cough — only slightly narcotic (not habit forming).

Heroin — diacetyl ester of morphine diminishes cough — slightly narcotic — habit-forming.



Hyoscine (scopolamine)

Inorganic bromides and organic bromine-containing substances

KBr, $NaBr$, NH_4Br, $CaBr_2$.

Bromipin

IV. Analgesic and antipyretic drugs.

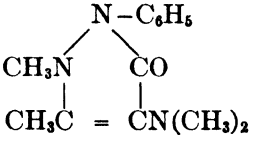
1. Derivatives of aniline

$C_6H_5NHCOCH_3$

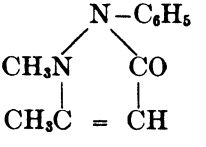
Acetanilid

$p.C_2H_5OC_6H_7NHCOCH_3$

Acetphenitidin (phenacetin)

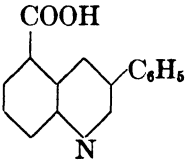


Pyramidon



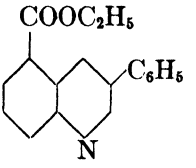
Antpyrine

Derivatives of phenyl quinolin carboxylic acid, relieve pains especially in gout and other joint diseases



Cinchophen (*atophan*)

Very slightly soluble in water; — low toxicity.

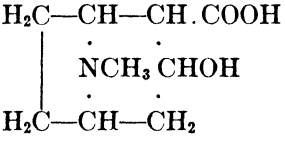


Neo-cinchophen (*novatophan*)

Ethyl ester of cinchophen. Very non-toxic on account of its slow absorption from intestine.

V. Local anaesthetics

1. Cocaine group, esters of ecgonin.

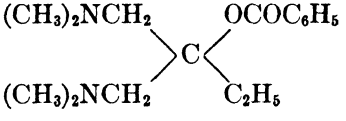


Ecgonin

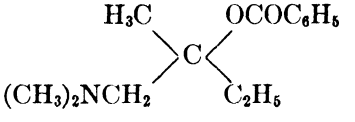
Cocaine = (1) methyl ester of (2) benzoyl ecognin.

Tropacocaine = (1) methyl ester of (2) mandelyl ecognin.

2. Nitrogenous benzoyl compounds.

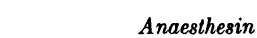


Alypin



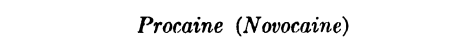
Stovain

3. Derivatives of *p*.-aminobenzoic acid.



Anaesthesin

Insoluble, dusting powder. Anaesthetic for ulcerated surfaces.



Procaine (*Novocaine*)

Very useful local anaesthetic in general surgery but does not anaesthetize the mouth, tongue or many mucous membranes.



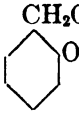
Butyn. — Much more powerful than procaine, anaesthetizes tongue and all mucous membranes as well as cocaine, but about as poisonous as cocaine.

4. Benzyl alcohol series.



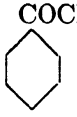
Benzyl alcohol

Local anaesthetic action less than that of procaine; toxicity much less. Often irritating to tissues.



Saligenin

Local anaesthetic action somewhat greater than benzyl alcohol: toxicity about the same. More soluble in water.



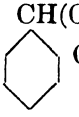
Phenacyl alcohol

Local anaesthetic action, etc., about the same as sal igenin.



Phenyl-ethyl alcohol

Local anaesthetic, action less than saligenin, more irritant to tissues.



Phenyl glycol

Local anaesthetic action too slight for practical use.



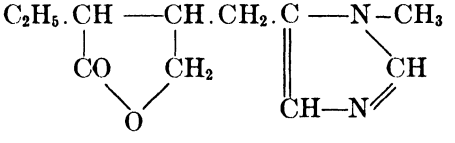
Hydroxy-ethyl anilin

Local anaesthetic action less than seliganin. Toxicity greater.

The primary alcohols are more potent than the secondary alcohols, the tertiary alcohols (except the phenols) have entirely lost the local anaesthetic action (Quigley and Hirschfelder).

VI. **Drugs** which **stimulate** the **parasympathetic nerves** (secretion of glands and contraction of hollow organs).

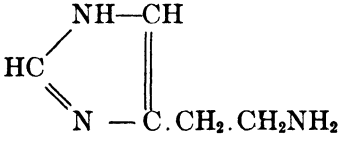
1. Vegetable alkaloids, pilocarpin and physostegmin.



Pilocarpin

Also pituitoin (amine of unknown composition).

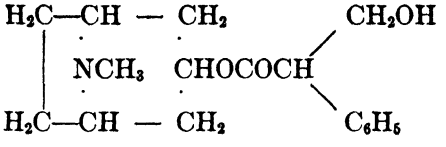
2. Some amines derived from protein, especially histamine.



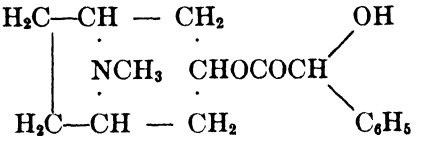
Histamine

VII. **Drugs** which **paralyze** the **parasympathetic nerves,** and decrease the secretion of glands and the contraction of hollow organs.

1. Alkaloids such as atropin-hyescin and homatropin.



Atropine

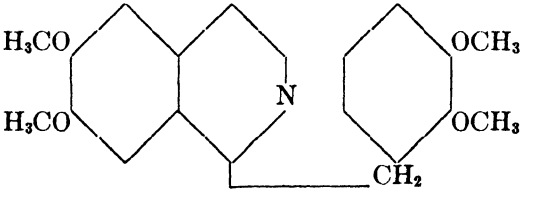


Homatropin

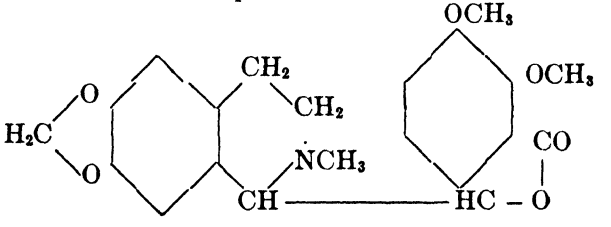
Action much less prolonged than that of atropin; otherwise similar.

VIII. **Substances** which **diminish contraction** of the **smooth muscles** to hollow organs.

1. All drugs of the nitrite series.
2. Benzyl alcohol and its esters, saligenin, and all soluble substances of the benzyl alcohol or ester series.
3. Mandelic acid $C_6H_5CH(OH)COOH$, and its esters.
4. The plant alkaloids papaverin and narcotin of the benzyl isoquinolin group.



Papaverin



Narcotin

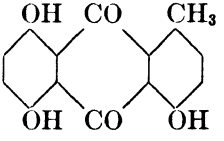
Substances which stimulate the sympathetic nerves and thus diminish secretions and relax the hollow organs (see circulatory stimulants, adrenalin type of drug).

IX. **Purgative or Cathartic Drugs.**

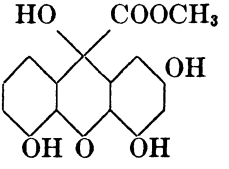
1. All drugs which stimulate the parasympathetic nerves, see above — and pituitin.

2. Irritating true fats and vegetable oils — especially castor oil (glycerine ester of ricinoleic acid) and croton oil (glycerine ester of tiglic acid), also containing an irritant resin.

3. Vegetable purgatives — cascara, jalap, aloin, colocynth, podophyllin, rhubarb, etc., which contain anthraquinone and emodin derivatives.

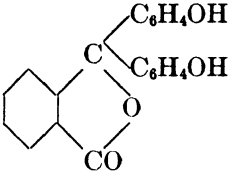


Emodin of rhubarb



Aloin (Violent purgative)

4. Phenolphthalein.



X. **Saline purgatives.** Ions of the so-called Hofmeister series in the order of their purgative action, power of preventing swelling and of causing shrinking of proteins. (Many of them are also precipitants of calcium.)

Cations	*Anions*	
K	NO_3	not purgative
	Cl	
	Br	
Na	I	
	CNS	
Mg	Acetate	
	Citrate	
	Tartrate	
	Phosphate	

XI. **Circulatory Stimulants**

Drugs which increase force of heart beat.

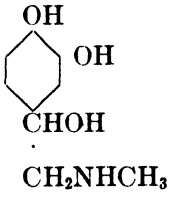
Digitalis and its active glucosides — digitoxin and digitalin, not digitonin.

Strophanthus and its glucosides, strophanthin and ouabain (strophanthin is methyl ouabain).

Spartein.

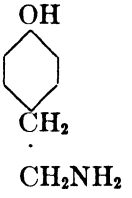
Caffeine (see diuretics).

Epinephrin or adrenalin, and other less potent catechol derivatives and amines.



Epinephrin or Adrenalin

(Laevorotatory is twice as active as racemic; thirty times as active as the dextro-rotatory.)

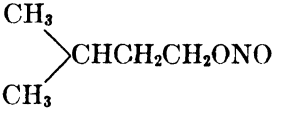


Tyramine

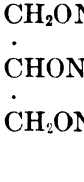


Iso-amylamine

XII. **Drugs** which **dilate blood vessels** and lower blood pressure — also relieve pains arising in heart (angina pectoris).

Iso-amyl nitrite 

By inhalation; very rapid intense action lasts 2–5 minutes — accelerates pulse also relaxes smooth muscles.



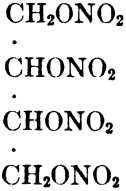
Nitroglycerine

Active 15–30 minutes less intense

$NaNO_2$

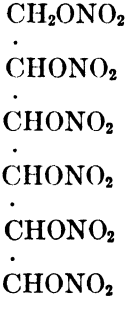
Sodium nitrite

Action less intense, lasts 2 hours



Erythol Tetranitrate

Less intense action 2–4 hours.



Mannitol hexanitrate

Action larger than erythrol tetranitrate

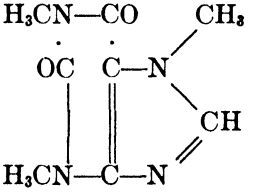
$C_6H_5CH_2ONO$

Benzylnitrite

Action more prolonged than nitroglycerine.

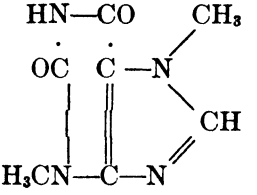
XIII. **Diuretic drugs**

Purin group.



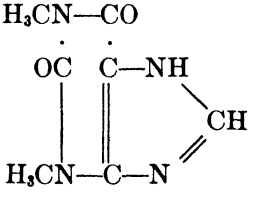
Caffeïne

Increases strength of heart beat; stimulates brain activity; causes sleeplessness. Administered with sodium citrate.



Theobromine

Very much less action on heart and brain than caffeïne; more action on kidneys. Administered with sodium salicylate.



Theophyline (Theocin)

More action on kidneys than theobromine. Administered with sodium acetate.

XIV. **Antiseptics.**

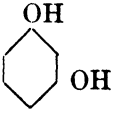
1. Soluble salts of all the heavy metals, which act as protein precipitants, and also as caustics to the tissues; and as poisons to the kidneys and heart.

Salts of Ag, Zn and bivalent Hg are very strong antiseptics. Cu salts act in very great dilution on algae and fungi.

2. Soluble phenol derivatives.



Phenol



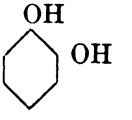
Resorcin

Stronger than phenol — more toxic.



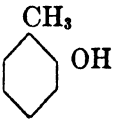
Hydroquinon

Still more toxic.



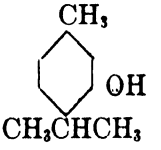
Catechol

Most toxic — not used as antiseptic.



o.Cresol

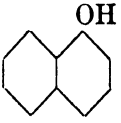
Strong antiseptic. Tricresol (*o.-m.*- and *p.*-cresols mixed, much used as antiseptic and 0.1% as preservative for sera, etc.



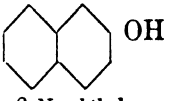
Thymol

Useful as a preservative, anthelmintic.

Naphthols



α-Naphthol



β-Naphthol

Somewhat stronger antiseptics than phenol. Irritant to the kidneys and sometimes cause cataract in eyes.

Oxidizing antiseptics.

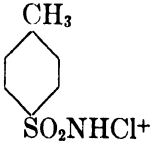
Peroxides. H_2O_2, $NaBO_4$ (perborate), MgO_2 all act by liberating nascent oxygen in presence of bacteria and pus.

Organic peroxides, like dibenzoyl peroxide $C_6H_5CO.OO.OCC_6H_5$, are active, the most active being benzoyl acetyl peroxide (C_6H_5CO–OO–$OCCH_3$).

Halogen antiseptics. Cl^+, Br^+, I_2^+ are very active. Cl^+ (in very high dilution) is used to disinfect city drinking water.

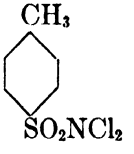
During the World War a nearly neutral NaClO solution having pH+8.8; and Cl^+ 0.45–0.48% (Dakin's solution) was used to irrigate infected wounds. It is very bland and non-irritating.

Organic Cl+ substances, highly antiseptic.



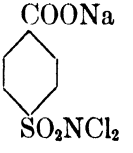
Chloramin T

Water soluble.



Dichloramin T

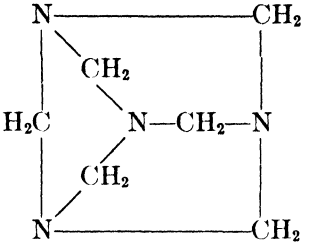
Insoluble in water, applied dissolved in chlorinated paraffin oil.



Halozone

Used to disinfect small amounts of drinking water.

Formaldehyde and formaldehyde derivatives.



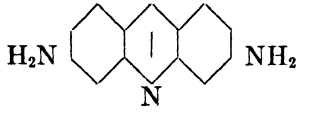
Hexamethylen tetramine

Splits off formaldehyde in acid solutions. Useful as antiseptic in acid urine, not in alkaline urine.

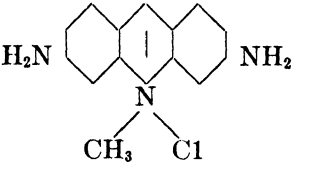
Substances which split off formaldehyde in alkaline solutions are not useful, for in an alkaline urine or in body fluids the formaldehyde at once combines with NH_3 to form hexamethylen tetramine.

Dyes. Triphenyl-methane dyes. Basic dyes of this series are especially active on Gram positive bacteria; but they are very poisonous. Acid dyes are much less toxic and are especially active on Gram negative bacteria (Churchman). Much less active in presence of proteins.

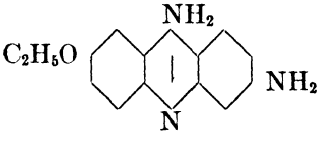
Flavine dyes are very active antiseptics. They do not lose their activity in presence of proteins.



Sulphate, used as Proflavin



Acriflavin

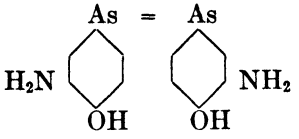


Rivanol

Most active antiseptic against streptococcus in infected tissues. Still active in tissues in concentration of 1:40000.

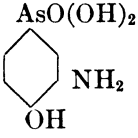
XV. **Chemotherapy.** Drugs useful in the treatment of infectious diseases when given.

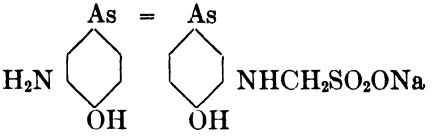
1. Antisyphilitic drugs.



Arsphenamin

Salvarsan) (Ehrlich 606)
Given intravenously oxidized in the body to

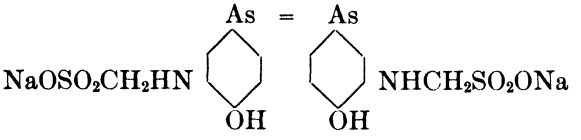




Neoarsphenamin

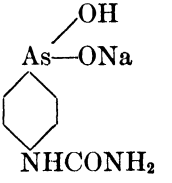
(Neosalvarsan)

Water soluble, less toxic but less active than arsphenamin. Given intravenously.



Sulpharsphenamin

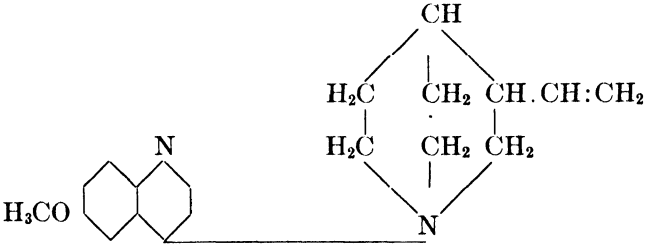
Water soluble — much less irritant than arsphenamin or neoarsphenamin. May be given hypodermically.



Tryparsamid

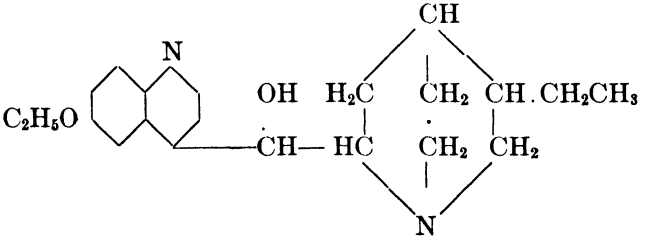
Less toxic than arsphenamin compounds. Enters cerebrospinal fluid bathing the brain, and is useful in African sleeping sickness and in brain syphilis.

Quinine derivatives, useful in treatment of malaria, etc.



Quinine

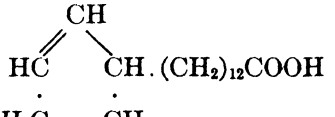
Specific against parasite of malaria. Lowers body temperature; diminishes oxidations. Sometimes useful in the treatment of rapid and irregular heart (auricular flutter and auricular fibrillation).



Ethylhydrocuprein (Optichin, Morgenroth).

Specific antiseptic against coccus of pneumonia in tissues, also curative against experimental infection with this germ in mice. Too toxic for use in lobar pneumonia in man. Causes blindness, etc.

Derivatives of chaulmoogra oil. The esters and Na salts of chaulmoogric acid are specific in the treatment of leprosy — of doubtful use in the treatment of experimental and clinical tuberculosis. Given hypodermically.



Chaulmoogric Acid

XVI. **Anthelmintics** or **vermifuges,** remedies for intestinal worms. Oleoresin of aspidium (male fern; chenopodium oil (American wormseed oil; santonin; thymol; carbon tetrachloride).

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Quarterly Cumulative Index, — Published by Am. Med. Assoc.

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CHAPTER XIV

STUDY OF STRUCTURE

Methods for the Determination of Structure

Organic chemistry, as we know it, is an edifice reared of structural formulae. They have become so commonplace that we seldom stop to wonder at them, to marvel at the boldness of chemists who presumed to enter into the infinitely minute and to imagine that such infinitesimals have structure, or to admire the infinite patience and consummate skill that have been displayed in working out the system and applying it to tens of thousands of organic compounds. Few structures built by the human mind can rival organic chemistry. Of a truth physics has lately gone further and essayed to take the atoms apart, an even bolder thought.

During the siege of Paris the news of a great city, the business letters of its merchants and the private messages of its citizens were concentrated by photography on to tiny films to be tied to the leg of a carrier pigeon and at the destination were reproduced in full. Into the structural formula of an organic compound are compressed the results of the work of perhaps scores of chemists and if we could but read it aright, it would recall to us this mass of information. Sometimes the structural formula has seemed to be an object in itself, but it should be only a means to an end, a wonderfully compact way of setting down in minute space a large amount of information. There can hardly be a more wanton waste of mental energy than memorizing structural formulae without a full understanding of their meaning.

In times past the determination of structural formulae was the chief occupation of the organic chemist: it must ever remain an important part of his task. Though so much labor has been put upon problems of this sort and though a vast deal has been accomplished, there remain tasks in abundance, as difficult and as imposing as those that have taxed the strength of the chemical giants of the past.

It is not the purpose of this book to go into specific methods of determining structure as there are excellent books devoted to this

subject,[1] but rather to discuss the subject in general mentioning some of the chief lines of attack. In this, as in other things, the beginner makes the best progress by studying the methods of the masters. So many of the great chemists have published articles on the constitution of organic substances that it is easy to find an abundance of examples all the way from the time that chemists were struggling with type formulae and organic radicals down to recent times when all the latest and most refined methods are employed. Or we can take some of the triumphs of organic chemistry, the unravelling of the constitution of such things as indigo, alizarine, camphor, uric acid or the sugars. A practical way is to look up a number of substances resembling the one in hand and see how they came by their accepted formulae. Of course methods must not be followed blindly but must be adapted to suit the present case as it is the habit of the research chemist to do.

The ambitious chemist can find every sort and size of problem in the determination of structure both of synthetic and natural compounds. The structure of many of the alkaloids, of most of the sulphur dyes, in spite of their enormous importance, of starch, of cellulose and of thousands of other substances remain unknown and like Goliath challenge the chemical Davids.

Determining the skeleton or parent hydrocarbon. We think of all organic compounds as derived from hydrocarbons by the substitution of atoms or groups for one or more hydrogen atoms. We know the constitution of any compound when we know the hydrocarbon from which it is derived and also the kind and location of the substituents. We have made much progress when we determine the parent hydrocarbon. There are various ways of doing this. One way is the old zinc dust method which has done great service in certain cases. The compound is heated with zinc dust which in some way removes all the oxygen leaving the hydrocarbon to pass on. A famous example of the use of this was the determination of the constitution of alizarine. On heating this with zinc dust, anthracene was obtained.[2] Analysis showed the presence of four oxygen atoms, two of which were accounted for by considering it to be an anthraquinone derivative. Comparing the formula of alizarine, $C_{14}H_8O_4$ with that of anthraquinone, $C_{14}H_8O_2$, and remembering that alizarine

[1] The following may be mentioned: Analyse und Konstitutionsermittlung organischer Verbindungen. Hans Meyer, Berlin. Julius Springer. 4th ed. 1922. Determination of radicles in organic compounds. H. Meyer, tr. by J. B. Tingle. John Wiley and Sons. N. Y., 1903.

[2] Gräbe and Liebermann, *Berichte*, 1, 49 (1868); 2, 14 and 332 (1869); 3, 359 and 636 (1870); *Annalen, Sup.*, 7, 257–322 (1870); 160, 133 (1871).

is soluble in alkali it was easy to conclude that the two extra oxygen atoms are present in phenol groups. It then remained to locate these two groups.

By exhaustive hydrogenation, geraniol and linalool, both of which have the formula $C_{10}H_{18}O$, are converted into 2,6-dimethyl-octane. As both of these form esters and give other reactions of alcohols they must contain hydroxyl groups which must be located. Linalool is difficult to esterify, which indicates that it is a tertiary alcohol. For it to be a tertiary alcohol, the hydroxyl would have to be at 2 or 6 but the fact that it is optically active shows that the hydroxyl must be in the 6-position. It then remains to locate the double bonds which is done by careful oxidation.

Baeyer's [3] justly famous investigation on mellitic acid was all founded on the observation that benzene is produced by heating this acid with soda-lime. The elimination of carbon dioxide from benzoic acid to leave benzene was well known, so that this experiment proved to Baeyer that mellitic acid is also a carboxy derivative of benzene like benzoic acid but having six carboxyl groups instead of one since its composition is $C_{12}O_{12}H_6$ which he considered to be $C_6(COOH)_6$. This was the basis for the solution of the problem though much tedious work had to be done to clear it all up.

Determining the presence of groups or radicals. Since an organic compound consists of a carbon skeleton decorated with various groups, hydrogen satisfying the remaining valences, a large part of the game of constitution determining consists in identifying the groups present. Inorganic analysis rests on the assumption that copper or tungsten may be found and estimated in any of their compounds, though copper is not so easy to find in a silicate as it is in copper sulphate. In a sense groups, or radicals, are the elements of which organic compounds are constructed. We can now speak of hydroxyl, carboxyl, ethyl or phenyl as elements without apology since detectives have pried into the private life of the orthodox elements and dug up their buried past with the result that we now know that they too are complex, even more so than our organic radicals. Phenyl, ethyl, and allyl are made up of carbon and hydrogen just as chlorine and iron are constructed of positive nuclei and electrons, the properties of the radicals as well as of the elements depending on the number and arrangement of the constituent parts.

The presence of a certain group in an organic molecule causes it to have certain properties though the influence of the other constituents of the molecule modify their manifestation. Thus any

[3] Baeyer, *Annalen, Sup.*, 7, 1–55 (1870).

compound containing a carboxyl group, –COOH, is an acid and will give the typical reactions of an acid. It may be a strong, volatile, water soluble acid as formic, H.COOH, or a weak, non-volatile, practically insoluble acid as *o*.-benzoyl-benzoic, $C_6H_5COC_6H_4COOH$. The hydroxyl group is present in ethyl alcohol and in cellulose, which are dissimilar in most respects but both of which give nitrates and acetates, reactions characteristic of alcoholic hydroxyl.

The groups that are commonly found in natural products are comparatively few, carboxyl, –COOH, alcoholic and phenolic hydroxyl, –OH, methoxyl, $-OCH_3$, aldehyde –CHO, and acetyl, $-COCH_3$, being the most common. Synthetic products contain many others such as the nitro, $-NO_2$, amino, $-NH_2$, mercapto, –SH, sulphonic, $-SO_3H$, and the halogens. In the more complicated compounds two or more groups of the same or of different kinds may occur. Thus mucic acid contains two carboxyl and four hydroxyl and vanilline, an aldehyde, a hydroxyl and a methoxyl. A remarkable thing about organic compounds is the independent way in which the groups react. Thus vanilline shows typical aldehyde reactions as well as typical phenol reactions in one case as if it were only aldehyde and in the other as if it were solely phenol, though the aldehyde group renders the phenol group more acidic so that it can be titrated using phenol-phthalein. The methoxyl group can be determined as if the others were not present.

While a simpler organic substance such as vanilline, may be a derivative of a simple hydrocarbon, benzene in this case, in which certain comparatively small groups, –CHO, –OH and $-OCH_3$, have been substituted, more complicated substances may be derived from the union of several comparatively complex molecules. Many such unions take place by the elimination of water and may be dissolved by the addition of water, so called hydrolysis. Thus cetyl palmitate, a natural product, is resolved by hydrolysis into palmitic acid and cetyl alcohol:

$$C_{15}H_{31}COOC_{16}H_{33} + H_2O \rightarrow C_{15}H_{31}COOH + HOC_{16}H_{33}$$

We determine the constitution of this substance when we hydrolyze it, identify the palmitic acid and cetyl alcohol, and show that the amounts obtained account for all the material taken. This presupposes that the constitutions of the palmitic acid and the cetyl alcohols were already known. In this case since an alcohol and an acid are known to unite in a certain way we are sure as to the manner in which the two parts of the molecule are joined together. We have long known that cane sugar is produced by the union of a

molecule of glucose with one of fructose but the manner of the union is still a mystery, and we are fairly sure that the extremely complex cellulose molecule is built up of a large number of glucose units but how the structure is put together is unknown. The brilliant work of Fischer [4] on tannin and on polypeptides may be cited as a study of the constitution of highly complex substances which are built up of a large number of relatively simple units.

Locating groups on a skeleton. Supposing that we have determined the hydrocarbon skeleton in a substance, and determined the nature of the substituents it remains to locate them. In synthetic chemistry we sometimes start with a known hydrocarbon and introduce a known group as in the nitration of meta xylene, then the only thing that has to be found out is the position of the entering group.

The enunciation of Kekulé's famous theory of the construction of benzene [5] gave the greatest single impulse in the history of chemistry to the determination of structure, particularly of aromatic compounds of which hundreds were known but had not been properly related to each other for lack of a guiding theory. Many investigations were required to line up the numerous substitution products of benzene into the ortho, meta, and para ranks.

A study of *Beilstein* will reveal many synthetic substances the constitutions of which are still in doubt. When a new compound is prepared, its maker is under obligation to determine the location of all the groups he introduces.

Locating double bonds. This is frequently a delicate task since in many compounds the double bonds may be shifted from one position to another by the very means used to locate them. Chemical literature contains many erroneous constitutional formulae for the reason that fusion with alkali and treatment with concentrated sulphuric acid have been used for this purpose. It is now known that these reagents frequently move the ethylene linkage some distance and what we find out is its new position and not where it was originally. This oleïc acid was long considered to be $CH_3(CH_2)_{16}CH{:}CHCOOH$ since [6] by fusing it with caustic potash, palmitic and acetic acids were obtained. By shaking oleic acid with cold dilute potassium permanganate a dihydroxy stearic acid is obtained which on further oxidation [7] yields pelargonic and azelaic acids,

[4] *Berichte*, 39, 530–610 (1906).

[5] *Bull.*, [3], 3, 98 (1865); *Annalen*, 137, 129 (1866). To get the importance of this theory one must read the addresses at the celebration in 1890, *Berichte* 23, 1265 ff (1890).

[6] Varrentrapp, *Annalen*, 35, 209 (1840).

[7] Edmed, *J. Chem. Soc.* 73, 627–34 (1898).

$CH_3(CH_2)_7COOH$ and $HOOC(CH_2)_7COOH$.

This shows that dihydroxy stearic acid is:

$$CH_3(CH_2)_7CH(OH).CH(OH).(CH_2)_7COOH$$

and oleïc acid must be:

$$CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH.$$

In recent years many double bonds have been located by ozonizing at low temperatures and treatment of the ozonides with water by which the compound is broken in two at the double bond, RCH:CHR′ becoming RCHO + OHCR′. With oleïc acid[8] this method gives $CH_3(CH_2)_7CHO$ and $OHC(CH_2)_7COOH$ in complete agreement with the above.

The terpenes form one of the most interesting and important groups of organic compounds. It has required decades and a large number of skilful workers to unravel their complicated relationships. As there are groups of sugars the members of which differ only in configuration, so we have groups of terpenes where the individuals differ only in the location of double bonds. The difficulty is made much greater by the ease with which many of these are shifted. In some of the most important terpene derivatives, geraniol, citral, citronellol, citronellal and linalool the position of one ethylene linkage is still uncertain.

Building down or "Abbau." The German language has the word "*abbauen*," to build down, as "*aufbauen*" is to build up. When we have a building to get rid of we call in a wrecking concern and the roof is off and the walls are pulled over in short order. Little can be learned from the debris that is hauled off as to how the house looked. If we take the pains to remove one brick or one timber at a time as we tear down a structure we can find out just how it was put up.

One of the important methods of determining the structure of complex organic compounds is by abbau; we take off a carboxyl, a methoxyl or some other group, analyze the remainder, remove another group and so on until we get to something we can recognize. If we know just what we have taken off we can form an idea of what the structure was. If we start with a hydrocarbon which analysis and molecular weight determination show to be $C_{10}H_{14}$ and oxidise it to $C_8H_6O_4$ which we identify as $p.$-$C_6H_4(COOH)_2$, we see that two carbon atoms have been lost and assign the formula $p.$-$C_6H_{11}(C_2H_5)_2$

[8] Harries and Thieme, *Annalen*, **343**, 333–354 (1905).

to the substance. Careful oxidation is one of the most used processes in abbau.

Determination of structure by physical methods. When we know the relation of physical properties to constitution as we should we will be able to look at a structural formula and tabulate the physical properties of the substance it represents and, conversely, write the structural formula after measuring a sufficient number of the physical properties. One versed in anatomy can look at an animal and draw an accurate picture of one of its bones: the paleontologist digs up a bone and presents us with a picture of the prehistoric animal and makes a guess as to how it walked and what it ate. While organic chemists have not arrived at that goal, we have made substantial progress in that direction and constantly use physical properties to corroborate conclusions arrived at by chemical methods or to decide between two or more formulae which agree equally well with our chemical findings.

We can start with some simple illustrations: suppose for a moment that the butyl alcohols were unknown to us but that we came into possession of three liquids boiling at 99.5°, 107.9° and 117.7°, which gave analytical figures corresponding to $C_4H_{10}O$. Molecular weight determinations might be used to confirm this formula but would not be required since a substance, $C_8H_{20}O_2$, could not possibly boil at so low a temperature. Comparing these boiling points with those of propyl and isopropyl alcohols, 97.2° and 82.3° we find 117.7 $-$ 97.2 $=$ 20.5 and 99.5 $-$ 82.3 $=$ 17.2 while 107.9 $-$ 97.2 $=$ 10.7 and 107.9 $-$ 82.3 $=$ 25.6 It is more reasonable to consider the liquid boiling at 117.7° to be normal butyl alcohol and the one boiling at 99.5° as secondary butyl alcohol, the true homolog of isopropyl alcohol. Diethyl ether and methyl propyl ethers, which likewise have the composition $C_4H_{10}O$, are excluded from consideration since the boiling points given are far too high for ethers of this molecular weight.

The above conclusions, based as they are on the boiling points alone, would not be sufficiently supported but should be confirmed by comparisons of densities, refractive indices, etc., and finally verified by chemical reactions.

The famous discussion on the structure of diazo compounds was finally decided on the basis of physical properties since the chemical reactions in their formation and decomposition could be explained by either formula. The diazonium formula $C_6H_5N(N)Cl$ representing a salt containing pentavalent nitrogen agrees well with the known

facts that diazo compounds are colorless, and very soluble in water, giving good conducting solutions in which the positive ion acts similarly to a tetra-alkyl-ammonium ion while a substance having the constitution represented by the Kekulé formula, $C_6H_5N{:}N.Cl$ would probably be colored, insoluble in water and non-ionizable.

The classical investigation of Brühl [9] on refractive indices shows what can be done by a study of one property. His work has furnished the means for deciding the structure of many of the terpenes and of keto-enol tautomers. One well known formula for benzene was based on Thompson's determination of [10] the heat of combustion of benzene.

As we accumulate more extensive and more accurate data on a larger number of the properties of organic compounds, physical data will play an increasingly important part in the determination of constitution. These few paragraphs are intended to call attention to this subject on which whole books have been written.[11]

Verification of structure by synthesis. We are never satisfied with our conclusions as to the constitution of a compound till we build up the structure represented by our formula and prove that the synthetic compound is identical with the original. When this is done the whole line of reasoning is vindicated and all the experiments checked. To prove that we know the structure of a watch we must not only take it apart but put it together again. This verification by synthesis is always desirable but is not always possible though persistent and ingenious thinking and working are apt to find a way. From the commercial point of view the very object in determining the constitution of a substance is to lay a foundation for a study of its synthesis.

In two triumphs of organic chemistry, which are often mentioned, the synthesis of indigo and of alizarine, syntheses followed the determination of constitution and plant processes were devised and perfected, so that the cultivation of madder has become only a memory and natural indigo is a rarity. In the case of rosaniline and para rosaniline it is possible to build up the dye by reversing the process by which it was taken to pieces but this is too expensive for the

[9] See end of Chapter X, p. 164.

[10] *Berichte,* 19, 2944 (1886).

[11] Ueber die wichtigsten Beziehungen zwischen der chemische Zusammensetzung von Verbindungen und ihrem physikalischen Verhalten. W. Herz. Stuttgart, F. Enke, 1898.

Beziehungen zwischen physikalischen Eigenschaften und chemischen Konstitution. Hugo Kauffmann. Stuttgart, F. Enke, 1920.

plant. The dye is manufactured by oxidation of mixtures of aniline and toluidine, in the same general way as it was before its constitution was known, but a haphazard and inefficient process has been so improved that the dye is obtained in better yield and standard quality. The knowledge of its constitution has made it possible to perfect the plant process.

CHAPTER XV

STUDY OF REACTIONS

By F. O. RICE[1]

Reaction Velocities, Equilibria, Heterogeneous Systems

A study of reaction rates is of particular interest to the organic chemist because the great proportion of organic reactions when carried out at ordinary temperatures proceed with measurable speed. It is unusual to find in the inorganic field such a reaction as that between hydrogen peroxide and the iodine ion[2] which proceeds with measurable speed, and it is just as rare to find a reaction in the organic field which proceeds "instantaneously" at ordinary temperatures. We may therefore consider reactions to be divided into two classes, the first class consisting of reactions like that between iodine and sodium thiosulfate which proceed practically instantaneously and the second class consisting of reactions which proceed with measurable speed and which constitute the bulk of the reactions occurring in organic chemistry. An important characteristic of these "slow" reactions is that in most cases they are catalytic; ever since Ostwald introduced his criterion of a catalyst as something which increases the rate of a chemical reaction without modifying the energy factors, it has been customary to regard organic reactions as taking place at an extremely slow rate in absence of a catalyst, the only function of which is to increase the rate of a change which is already taking place: various popular illustrations of this have been given, such as the comparison of a catalyst to a lubricant which diminishes friction in a machine or to a whip which makes a horse go faster. There is, however, another point of view, namely that the catalyst is essential and without the catalyst the reaction would not take place. On the Ostwald view we are tempted to regard a catalyst as comparable to the crowd which cheers on the players in a game, whereas on the second view we must regard the catalyst as an essential player, perhaps the captain of the team who directs the plays and without whom the

[1] Associate in Chemistry, Johns Hopkins University.

[2] Harned, *Jour. Amer. Chem. Soc.*, **40**, 1461 (1918).

game could not take place. It is not possible at present to distinguish between these two postulates because of the difficulty of establishing the complete absence of a catalyst; however, the second postulate will be adopted in this section because it has some advantages from the point of view of the classification of reactions.

This field of research is important for two reasons; firstly from a theoretical standpoint, further study of rates of reactions is necessary to throw light on the very puzzling fact that the rate of reaction changes very rapidly with the temperature. It seems probable that when we find the explanation of this phenomenon, we shall also have an explanation of some of the factors that underlie all chemical changes. Secondly, the study of the rate of any particular reaction often gives us an insight into its mechanism. Frequently two or more reactions occur at the same time and a study of the velocities enables us to control conditions so as to obtain the maximum yield of the desired product. Frequently also a study of velocities determines the conditions of maximum stability of a particular compound. This field of research is in a very chaotic state at present. Some reactions have had literally hundreds of investigations made on them; in other cases only one investigation has been made and the results obtained were only for one temperature. Sometimes the results obtained by different workers are contradictory, and there are also many types of reaction for which no reliable data are available.

The study of reaction velocity provides us with an important weapon to attack the many problems arising in the study of homogeneous solutions.

Measuring Reaction Velocities

The various types of methods used will be mentioned and references given from which the experimental details may be obtained; the type of method best suited to the reaction under investigation may then be selected. Before doing this, it is well to refer briefly to the different classes of reactions, the method of stating the velocity constant and certain precautions to be taken when measuring reaction velocities.

Orders of reactions. Reactions are divided into different classes or orders according to the number of molecules taking part in the reaction. Thus we have reactions of the first order, or unimolecular reactions, reactions of the second order, or bimolecular reactions, and so on. Reactions as high as the eighth order are known, but the great majority of chemical reactions belong to the second and third

orders. There is a lack of clearness in this subject due to the practice of writing stoichiometric equations which do not represent what takes place in the solution and classifying the reaction accordingly. For example, the reaction between methyl acetate and sodium hydroxide in dilute aqueous solution is ordinarily written $CH_3COOCH_3 + NaOH = CH_3COONa + HOCH_3$. Now, whatever the mechanism of the reaction may be, we can be quite sure that it is not that represented by the above equation. It would be more nearly correct if we wrote:

(1) $CH_3COOCH_3 + nH_2O \rightleftarrows CH_3COOCH_3 . nH_2O$.

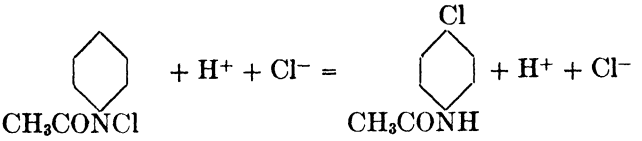
(2) $CH_3COOCH_3 . nH_2O + OH^- = CH_3COO^- + H^+ + CH_3OH + nH_2O$.

where reaction (1) is a very fast reaction and reaction (2) is the slow reaction whose velocity we are measuring. Probably in all hydrolytic reactions we are not dealing with a single isolated reaction as is commonly represented, but two or more successive reactions as represented above. When studying reactions we should write down equations which represent, so far as we know, what actually occurs in the solution and classify the reaction accordingly.

Another source of confusion in the study of reactions arises from the fact that if the concentration of one of the reactants remains constant, the reaction will appear to belong to a lower order than represented by the chemical equation of the change. Consequently the custom has grown up of referring to reactions in which one or more of the reactants are commonly present in constant concentration as being unimolecular when they are in reality bimolecular or trimolecular. Examples of this are the conversion of the enolic form of aceto-acetic ester to the ketonic form [3] and the conversion of acetylchloro-amino-benzene to *p.*-chloro-acetanilide,[4] both of which are commonly referred to as unimolecular reactions. The recent work of Kurt Meyer has shown that the enolic form of aceto-acetic ester may be kept unchanged and even distilled, if quartz vessels are used so that no trace of alkaline catalyst is present. The equation for the isomeric change of aceto-acetic ester should therefore be written $CH_3COH{:}CHCOOC_2H_5 + OH^- \rightleftarrows CH_3COCH_2COOC_2H_5 + OH^-$ and the reaction is properly classed as bimolecular. The formation of *p.*-chloro-acetanilide from acetylchloro-amino-benzene is catalysed by the simultaneous presence of hydrogen and chlorine ions so that the reaction is probably trimolecular as shown by the following equation:

[3] Meyer and Schoeller, *Berichte*, **53**, 1410 (1920).

[4] Harned and Seltz, *Jour. Amer. Chem. Soc.*, **44**, 1475 (1922).



The fact that one or more of the reactants happens to be present in constant concentration is a mere accidental circumstance and in no way affects the true order of the reaction. The classification of reactions should be based on the actual chemical equations which represent the change, so that attention is directed to essential similarities or differences rather than to non-essentials.

The study of rate of reaction is complicated by the fact that it is only very rarely that we have an isolated reaction taking place without the complication of secondary reactions at the same time. Simultaneous reactions may be divided up into three classes: 1. The products of the reaction recombine to give a back reaction. 2. The products of the reaction react to produce new substances giving successive reactions. 3. The reactants may combine in more than one way to give side reactions. Owing to our lack of knowledge of homogeneous solution it is not usually possible to study rate of reaction when more than two simultaneous reactions are occurring; in the more complicated cases the necessity of making a number of questionable assumptions seriously diminishes the value of the results.

Velocity constant. The method of stating the velocity constant is very important because this is a measure of the rate of the reaction when the reactants are present in unit concentrations. Suppose we have a reaction:

$$B + C + A = D + E + \ldots$$

where A is an acid catalyst and B and C are two substances which interact under the influence of the acid catalyst. Ordinarily this equation will not represent what takes place in the solution, because the acid dissociates and the substances B and C usually form double compounds with the water or with each other. It would be most desirable to write down the equation for the reaction actually occurring in the solution and then calculate the velocity constant per unit concentrations of the actual reactants. Here we meet the difficulty that the acid in the solution is present as undissociated molecule, hydrated hydrogen ion, and unhydrated ion, and there is no general agreement as to whether one of these entities is catalytically active or whether all of them are active; even if we knew which are active there is no reliable method of measuring the concentrations, if A is

a strong acid. Further if the reaction involves the hydrated forms of B or C, we have no method of measuring the concentrations of the hydrated forms. In these circumstances it is best to give the velocity constant per unit concentration of the materials added to the solution. Thus the value of k for the above reaction should be the (calculated) number of moles of B or C disappearing per minute from 1 liter of a solution containing 1 mole of B, 1 mole of C and 1 g. equivalent of A. The complete statement of the velocity constant should give the value of k calculated in the above manner and also the actual concentrations of A, B and C used in the experiment. With these data available it will be an easy matter to recalculate k at any time when our knowledge of solution problems is more advanced. It is also of the greatest importance to measure the velocity constant at two temperatures preferably 25° and 35°; the reasons for this will be discussed later.

Degree of precision. When measuring velocity of reaction the degree of precision of the result should always be stated because, although the velocity of a given reaction may be varied widely by altering the conditions, the temperature coefficient is usually only slightly affected, and from theoretical considerations a knowledge of the temperature coefficient and its variation is even more important than a knowledge of the velocity. For example, von Halban[5] has measured the rate of decomposition of triethylsulfonium bromide in a large number of different solvents. Using his results, and calculating the value of Q from the Arrhenius formula,

$$Q = R \frac{I_1 \times I_2}{I_1 - I_2} \log \frac{k_1}{k_2}$$

we find that the reaction has the highest temperature coefficient in benzyl alcohol where $Q = 34{,}080$ and the lowest in acetic acid where $Q = 27{,}840$; the mean value of all his results is 30,930 so that the maximum deviation from the mean value is only about $\pm$ 10%. In order to distinguish between the different values of Q the error in measuring the velocity of the reaction should not be greater than $\pm$ 1%, whereas the error in von Halban's work is probably about $\pm$ 5%. A study of the errors occurring in measuring velocity of reaction[6] has been made recently in which it was shown that they may be diminished so that the precision measure of a single experiment is $\pm$ 0.20%. While this degree of precision is somewhat greater than is ordinarily necessary, it is desirable that velocity measure-

[5] von Halban, *Zeit. physik. Chem.*, **67**, 129 (1909).
[6] Rice and Kilpatrick, *Jour. Amer. Chem. Soc.*, **45**, 1401 (1923).

ments should not be in error by more than $\pm 1\%$; the error in many of the measurements of rate of reaction is probably not less than $\pm 3\%$.

Perhaps the two greatest sources of error lie in measuring the temperature and in loss of the reactants by volatilization. A change in temperature of only 0.1° changes the velocity about 1%. Before constructing thermostats the following papers [7] should be read in conjunction with the directions given in text-books. Since most organic compounds have an appreciable vapor pressure the error due to loss of one of the reactants may be quite large. This is particularly the case if the compound is only slightly soluble in water since in a saturated solution it has almost the same partial pressure as the pure substance. As the flask containing the reacting solution is opened to withdraw samples there is a loss of any volatile reactant into the air space above the solution. Perhaps the best way of avoiding this loss is to fit the flask containing the solution with a quick-running siphon and fill a number of smaller vessels with the solution as described in the above paper.

Methods of measurement. There are a number of different methods of measuring reaction velocity but in the most important, the change of concentration with time of one of the reactants or resultants is measured. We may therefore classify according to the analytical methods employed. In many organic reactions there is no convenient method for estimating any of the reactants or resultants. In such cases if one of the reacting substances is highly colored we have a method for estimating the speed of the reaction which avoids all the difficulties of analytical measurements. Lapworth [8] in a study of the rate of addition of hydrocyanic acid to camphorquinone states: "It was decided to resort to a method of investigation in which the speed of reaction could be roughly gauged by means of a color change, and for this purpose, advantage was taken of the fact that camphorquinone has a bright yellow color, which is perceptible even in very dilute solutions, whilst its cyanohydrin is almost, if not quite, colorless." A similar method was used by Harcourt [9] in a study of the reduction of ferric chloride by stannous chloride in presence of potassium sulfocyanide. When an optically active substance changes in concentration during the course of a reaction the polarimeter provides a convenient method of measuring the rate of the reaction. This

[7] Notes on Thermostats. Marshall. *Trans. Far. Soc.*, 7, 249 (1911); Cumming, *ibid.*, 7, 253 (1911). Control of Thermostats, Beaver, *Jour. Ind. Eng. Chem.*, 15, 359 (1923).

[8] Lapworth, *J. Chem. Soc.*, 83, 995 (1903).

[9] Harcourt and Esson. *Trans. Roy. Soc.*, A 212, 187 (1913)

method [10] has been applied more especially in the study of sugar hydrolysis.

When an acid or alkali is produced or used up, conductivity measurements provide a convenient method of following the course of the reaction. This method has been applied to the measurement of the rate of hydration of acid anhydrides.[11] It is not possible to measure the rate of these reactions by titrating with alkali the acid produced because the reactions are extraordinarily sensitive to traces of alkali. Recently Skrabal [12] has devised an ingenious method for measuring the velocity of hydration of acetic anhydride by conducting the reaction in presence of sodium iodide and iodate, the acetic acid liberating an equivalent quantity of iodine which can be estimated in the usual way. By having thiosulfate and starch present, the change of color when all the thiosulfate had reacted could be used for measuring the velocity. The measurement of velocity of reaction by measuring the rate of gas evolution has been carefully studied by Harned.[13] Among other such measurements are those of Francis and Geake [14] on the decomposition of nitrosotriacetonamine by alkalis into phorone and nitrogen, and those of Fraenkal [15] on the decomposition of diazoacetic ester. A list of papers is given below [16] illustrating the application of acidimetry, alkalimetry and iodimetry to measuring rate of reaction.

Theoretical

Since a knowledge of the theoretical side of this study is necessary in order that laboratory work may be directed in fruitful channels, this section contains an outline of the theories which have been advanced to explain the experimental results. The outstanding difficulty in this connection is the rapid change of velocity with temperature; the ratio of the velocities at 35° and 25°, k_{35}/k_{25}, varies between 2 and 4 depending on the reaction studied, and is only very rarely outside these limits. The increased velocity of the molecules

[10] Rosanoff, Clark and Sibley, *Jour. Amer. Chem. Soc.*, **33**, 1911 (1911).

[11] Rivett and Sidgwick, *J. Chem. Soc.*, **97**, 732, 1677 (1910). Wilsdon and Sidgwick, *ibid.*, **103**, 1959 (1913).

[12] Skrabal, *Monatsh*, **43**, 493 (1923).

[13] Harned, *Jour. Amer. Chem. Soc.*, **40**, 1461 (1918).

[14] Francis and Geake, *J. Chem. Soc.*, **103**, 1722 (1913).

[15] Fraenkal, *Z. phys. Chem.*, **60**, 202 (1907).

[16] Lamble and Lewis, *J. Chem. Soc.*, **105**, 2330 (1914); Dean, *Am. J. Sc.*, **35**, 605 (1913); Reicher, *Annalen*, **232**, 103 (1886); Lapworth, *J Chem. Soc.*, **86**, 30 (1904); Harned and Seltz, *Jour. Amer. Chem. Soc.*, **44**, 1475 (1922); Rice, Kilpatrick and Lemkin, *ibid.*, **45**, 1361 (1923).

due to the increase in temperature and the decrease in the viscosity of the solvent, will account for a 2 or 3% increase in the velocity instead of the 200 to 400% rise obtained per 10° rise in temperature. The explanations for the high temperature coefficients of chemical reactions usually centre round the empirical equation of Arrhenius connecting velocity of reaction and temperature. This equation may be written:

$$\frac{d}{dt}\ln\ k = \frac{Q}{RT^2}$$

where Q is a constant; in the integrated form it becomes:

$$2.3\ \log\frac{k_1}{k_2} = \frac{Q}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

Writing out the equation for the hydrolysis of cane sugar by hydrochloric acid we have:

$$C_{12}H_{22}O_{11} + H_2O + H^+ = C_6H_{12}O_6 + C_6H_{12}O_6 + H^+.$$

Arrhenius [17] suggested that the cane sugar is present in two forms, active and inactive, in mass action equilibrium; also that the active form is present in very minute concentration at equilibrium, which is supposed to be attained practically instantaneously. A little consideration will show that in such a case as this, the concentration of the active form will vary rapidly with the temperature, for it will be proportional to the equilibrium constant of the reaction, active to inactive molecules, and the quantity Q in the Arrhenius equation will be the heat of the reaction, active to inactive molecules. The radiation theory offers a somewhat similar explanation in that only a small fraction of the sugar is supposed to be chemically active. A sugar molecule is supposed to become chemically active by absorption of infra-red radiation; when its internal energy exceeds a certain amount it will react chemically, so that on this theory there is no mass action equilibrium between the two forms of sugar. The empirical equation of Arrhenius may be deduced on the basis of either theory but it must be confessed that further development of either of these theories leads to results not in accord with facts.

Radiation theory. A recent discussion of the radiation theory of chemical action showed that there is considerable divergence of views amongst chemists. Perrin [18] in support of the radiation theory pointed out that in unimolecular chemical reactions the velocity is independent of the number of collisions per second, and can there-

[17] Arrhenius, *Z. physik. Chem.*, **4**, 226 (1889).
[18] *Trans. Far. Soc.*, **17**, 546 (1922).

fore be due only to some outside agency presumably radiation. This view was criticised by Lowry who showed that all the examples quoted by Perrin are really pseudo-unimolecular, in which a catalyst or traces of water vapor are required for the reaction to proceed. It would be the strongest possible argument in favor of the radiation theory if we had even a single case of a chemical reaction which proceeds with measurable speed and which we are reasonably certain is a true unimolecular reaction. It appears, however, that no such reaction is known. It may be pointed out here that the decomposition of nitrogen pentoxide which appeared to be an example of a unimolecular change has now been shown to be at least bimolecular,[19] small traces of the decomposition products being necessary to secure a constant specific rate of decomposition. From a knowledge of the value of Q calculated from the Arrhenius formula Lewis [20] has shown that the frequency of the radiation may be calculated and that it corresponds to short wave infra-red radiation. Perrin's comment on this is as follows: " The result appears very satisfactory and remarkable even, because we might have obtained altogether unreasonable values of any order of magnitude, if the theory were arbitrary." The most severe criticisms of the radiation theory were made by Langmuir during the discussion. The following are some excerpts from his remarks. " When we think over the matter we find that we have no direct evidence in confirmation of the radiation hypothesis. It is all surmise. There has not been a single argument today that can be definitely considered as concrete evidence in favor of the radiation hypothesis. In the first place, it has been our desire to trace a similarity between two relations that are of the same form. We try to get a common explanation of them. . . . We have a large number of natural phenomena which are characterized by this; that if we plot the logarithm of some quantity, we will say Y, you get a straight line. . . . We like to get one explanation for all these phenomena. But why adopt radiation as the explanation? . . . If we look back over the history of the radiation hypothesis during the last few years we see that it has all the characteristics of the typical unsuccessful hypothesis. It has not contributed anything of value to our knowledge of chemical reactions. The obvious relations which should follow from the radiation hypothesis in its original form are found not to be in accord with the facts. . . . As far as I have been able to find the radiation hypothesis has not led

[19] Daniels and Johnston, *Jour. Amer. Chem. Soc.*, **43**, 53 (1921). Daniels, Wulf and Karrer, *ibid.*, **44**, 2402 (1922).

[20] Lamble and Lewis, *J. Chem. Soc.*, **105**, 2330 (1914).

to a single prediction which has subsequently been verified by experiment. . . . The methods that have been evolved for evading the objections to the radiation theory involve assumptions unsupported by experiment." It is obvious that there is far from being any general agreement regarding the theoretical side of reaction velocity.

It must be admitted, however, that both these theories explain another difficulty connected with velocity of reaction which is quite as puzzling as the high temperature coefficient. If we consider such reactions as that between the thiosulfate ion and iodine, or between silver nitrate and sodium chloride we find that even if the reacting species are present in concentrations as low as N/100,000 the reaction proceeds practically instantaneously, and a great many other cases may be mentioned in which there is practically instantaneous reaction although the concentrations of the reactants may be very low. It follows therefore that even at concentrations as low as N/100,000 the number of molecular collisions is sufficient to permit a reaction to be practically instantaneous. If, however, we consider reactions which proceed with measurable velocity, the stoichiometric concentrations of the reactants may all be N/10 or even higher, yet it may take over an hour for one tenth of the reactants to disappear. Evidently our stoichiometric equations do not represent what occurs in the case of reactions which proceed with measurable speed. The explanation of the radiation theory is that only a small fraction of the collisions are effective. W. C. McLewis [21] commenting on this says: "The fact that many reactions occur with a finite and measurable velocity, shows us that all the molecules are not in the same chemical state. If they were, the speed of the reaction would either be zero or infinite." Taylor [22] has shown that the phenomena of negative catalysis may be explained on the basis of these considerations. "The theory emphasizes anew the fact that the concentration of a substance is not the active mass of the substance, but a very much greater quantity."

Acid catalysis. The nature of the catalytically active particle in an aqueous acid solution is still under discussion. The early workers attributed the catalytic activity to the hydrogen ions but it soon became apparent that the simple theory would have to be altered to explain the increased catalytic activity of acids in strong solution and more especially the abnormal effects of neutral salts. Consequently the dual theory of acid catalysis was developed in which the undissociated acid is supposed to be catalytically active

[21] W. C. McC. Lewis, *Scientia*, **25**, 450 (1919).
[22] Taylor, *J. Phys. Chem.*, **27**, 322 (1923).

as well as the hydrogen ion. The present tendency seems to be to increase the number of catalytically active particles still more. For example in the hydrolysis of ethyl acetate by aqueous hydrochloric acid, the catalytically active particles would be considered to be the unhydrated hydrogen ion H_+, the hydrated hydrogen ion $(H.nH_2O)^+$, the undissociated molecule HCl, and a compound of the hydrogen ion and the ethyl acetate $[H(CH_3COOC_2H_5)]^+$. All these are supposed to have a different catalytic activity so that we would have four simultaneous reactions proceeding in the solution and, since the hydrolysis is probably a case of a successive reaction, we have according to this theory eight simultaneous reactions. When we consider that there is not a single reliable method for determining the concentration of any one of the reactants, the prospect of solving the problem is sufficiently discouraging. It seems unfortunate that more attention has not been paid to some earlier work which tended to show that the only active particle present in aqueous solution is the unhydrated hydrogen ion. Lapworth [23] and his co-workers first put forward the view that the unhydrated hydrogen ion is the catalytically active particle and that the hydrated hydrogen ion has little or no catalytic activity. They examined a number of widely different cases of hydrogen ion catalysis in alcohol and showed that they all occur enormously faster in alcohol than in water, and further that the addition of minute quantities of water causes a marked retardation of the velocity. He states: "The proposition that free hydrogen ions are responsible for the catalytic activity of acids leads to the conclusion that they must be relatively few in number in aqueous solution. On the other hand the original conception of hydrogen ions was applied to explain the conductivity of acids in aqueous solution, so that the terms are not synonymous. In the latter case, they must be complex ions, probably of the form $(H_2O.H))^+$." Dawson [24] from experiments on the reaction $CH_3COCH_3 + I_2$ in water and water-alcohol mixtures also supported this view. He showed that in alcohol solutions containing small quantities of water, the reaction velocity is proportional to the concentration of the acetone, but is not proportional to the concentration of the acid catalyst. In such solutions the velocity increases much more rapidly than the concentration of acid catalyst. He concludes: "By comparison of the observations in aqueous with those in alcohol solution we are led to the conclusion that the ionic

[23] Fitzgerald and Lapworth, *J. Chem. Soc.*, **93**, 2163 (1908). Lapworth, *Ibid.*, **93**, 2187 (1908).

[24] Dawson, *J. Chem. Soc.*, **99**, 1 (1911); Dawson and Powis, *ibid.*, **105**, 1093 (1914).

component responsible for the catalytic effect is the free hydrogen ion, and that the effect of the hydrated ion is relatively unimportant. The concentration of the free hydrogen ions is very small in comparison with the total ion concentration, and in order to produce the observed effects it must be assumed that their specific catalytic activity is very great. Since the ratio of the free hydrogen ion to the total hydrogen ion concentration is so small the electrical conductivity of the solution is mainly determined by the complex ions, and the catalytically active ions are of little consequence in so far as the conductivity of the acid solution is concerned." The whole problem will be considerably simplified should this theory prove to be correct, and it seems probable that its development would clear up many of the puzzling features of homogeneous solution.

If the unsolvated hydrogen ion is the only catalytically active particle we may expect surprising results from a study of the catalytic activity of acids in a range of solvents. A comprehensive study of this nature has not been undertaken, but Dawson and Powis [25] have investigated the catalytic activity of five acids on the reaction between acetone and iodine, in water and in alcoholic solution. The nature of the results may be judged from the following examples: in an alcoholic solution of hydrochloric acid the velocity constant is approximately one thousand times as great as in an aqueous solution of hydrochloric acid. In water the reaction proceeds at about the same rate when catalysed by equal concentrations of hydrochloric acid and trichloracetic acid; in alcohol, hydrochloric acid is 200 times as active catalytically as trichloracetic acid. Monochloracetic acid and dichloracetic acid which are moderately strong acids in water have practically no catalytic activity in alcohol. Following the method of Kendall [26] and his co-workers we may write the equilibria involved in these solutions:

$$HA + 2S \rightleftarrows [HA.2S] \quad (1)$$
$$[HA.2S] \rightleftarrows [H.S]^+ + [A.S]^- \quad (2)$$
$$[H.S]^+ \rightleftarrows H^+ + S \quad (3)$$
$$[A.S]^- \rightleftarrows A^- + S \quad (4)$$

where HA is the acid and S is the solvent. In order to simplify the equations we may assume that two molecules of solvent combine with one molecule of the acid HA, and that one molecule of solvent combines with the hydrogen ion and one molecule with the anion of the acid. In an aqueous solution of hydrochloric acid

[25] Dawson and Powis, *J. Chem. Soc.*, **103**, 2135 (1913); *ibid.*, **105**, 1093 (1914).

[26] See Kendall and Gross, *Jour. Amer. Chem. Soc.*, **43**, 1416 (1921).

reactions (1) and (2) go practically to completion, and in equation (3) the equilibrium concentration of the unhydrated hydrogen ion must be extremely small since the affinity of hydrogen ion for water[27] is so great.

On the other hand, in an alcoholic solution of hydrochloric acid reactions 1 and 2 do not go to completion; however the equilibrium concentration of the unsolvated hydrogen ion will be much greater than in water if, as is probable, the affinity of hydrogen ion for water is much greater than for ethyl alcohol.

It would appear therefore that the conditions for maximum catalytic activity in an acid solution are that the anion of the acid should have a maximum affinity for the solvent and the hydrogen ion a minimum affinity for the solvent. Since no such affinity measurements are available we would have to use the empirical method of search for solutions of high catalytic activity; it is probable that such a search would yield cases of such astonishing catalytic activity as that found by Lowry[28] when studying the isomeric change of nitrocamphor. When making such studies reactions such as esterification or hydrolysis should be avoided. A number of studies have been made using such reactions: because these are probably successive reactions, and in addition the water or alcohol formed during the reaction affects greatly the catalytic activity of the hydrogen ion.

Recently attempts have been made to replace volume concentrations of the reactants by their activities or thermodynamic concentrations; G. N. Lewis and Randall[29] have shown that these may be calculated in a consistent manner from vapor pressure measurements, distribution ratios and electromotive force measurements. Jones and W. C. McC. Lewis[30] have studied the inversion of cane sugar and conclude that the activity of the hydrogen ion is the determining factor[31] for the rate of the reaction; they conclude also that the most probable mechanism of the reaction is expressed by the equation $RH^+ + H_2O =$ dextrose + laevulose, so that the reaction measured is a bimolecular one, between a molecule of water and a complex ion, formed by the addition of hydrogen ion to the

[27] Born, *Ber. deut. physik. Ges.*, 21, 679 (1919); Fajans, *ibid.*, 21, 549 (1919). A résumé of this work is given by Taylor, Newer Aspects of Ionization Problems, *Trans. Amer. Electrochem. Soc.*, 43, 31 (1923).

[28] Goldschmidt, *Z. phys. Chem.*, 70, 627 (1910); *Z. Elektrochem.*, 17, 684 (1911); Goldschmidt and Thuesen, *Z. phys. Chem.*, 81, 30 (1912). Bredig, Millar and Braune, *Z. Elektrochem.*, 18, 535 (1912); Snethlage, *ibid.*, p. 539.

[29] G. N. Lewis and Randall, *Jour Amer. Chem. Soc.*, 43, 1150 (1921).

[30] Jones and W. C. McC. Lewis, *Jour. Chem. Soc.*, 117, 1120 (1920).

[31] See also Harned, *Jour. Amer. Chem. Soc.*, 40, 1461 (1918).

sucrose molecule; this latter process is supposed to be practically instantaneous. On these foundations and allowing a stoichiometric correction for the water present they show that the alteration in the velocity constant in various mixtures can be accounted for completely. Harned and Seltz [32] studied the conversion of acetyl-chloro-amino-benzene to *p*-chloro-acetanilide: this is particularly adapted to study from the activity standpoint, because both the hydrogen and chlorine ions enter into the catalysis; the product of the activities of these ions should therefore determine the velocity at any temperature and this may be calculated by electromotive force measurements without any errors caused by liquid-junction potential difficulties. Excellent constants were obtained in presence of hydrochloric acid, but when neutral salts were present the velocity constant varied considerably. Many other similar studies have been made but the results of different workers on the same reaction do not always lead to the same conclusion.[33]

Dawson,[34] commenting on the paper of Moran and W. C. McC. Lewis, states: "... observations on the velocity of inversion, in which the concentration of the sucrose was varied from 100 to 700 grams per litre, have been found to yield a constant velocity coefficient when the participation of the sucrose, water, and hydrogen-ion is supposed to be proportional to the activities. The derivation of this coefficient involves, however, a number of other assumptions, namely, that the sucrose is mainly present in the solution in the form of a tetrahydrate, that the rate of inversion is determined by the rate of combination of a hypothetical sucrose dihydrate with the hydrogen-ion, and that the activity of the latter is very largely influenced by the viscosity of the medium. In these circumstances, it is very difficult to say whether the measurements in question are to be regarded as favorable or otherwise to the view that the active masses of the reactants are to be expressed in terms of the thermodynamic concentrations."

Experimental

Isomeric change. A solution of nitrocamphor contains the normal form and a pseudo form in equilibrium. The velocity of change, which can be conveniently followed by the polariscope was studied in

[32] Harned and Seltz, *Jour. Amer. Chem. Soc.*, **44**, 1475 (1922).

[33] See Clark, *Jour. Amer. Chem. Soc.*, **43**, 1759 (1921); Scatchard, *ibid.*, **43**, 2387, 2406 (1921); **45**, 1580, 1716 (1923); Fales and Morrell, *ibid.*, **44**, 2071 (1922); Moran and W. C. McC. Lewis, *J. Chem. Soc.*, **121**, 1613 (1922). Akerlöf, *Z. physik. Chem.*, **98**, 260 (1921).

[34] Dawson, *Chem. Soc., Ann. Report*, 1922, p. 19.

a number of solvents by Lowry and by Lowry and Magson.[35] They found that the reaction is sensitive to minute traces of impurities; hence the experiments were unusually tedious in character, owing to the extraordinary difficulty of attaining and keeping the necessary degree of purification; the difficulty may be gauged from one experiment, in which they show that an amount of piperidine in benzene equivalent to 0.1 g. per ton of benzene doubles the rate of reaction. After completing the work and measuring the velocity in a number of carefully purified solvents, a chance observation led them to the conclusion that all their measurements of the velocity were not characteristic of the particular solvent but simply depended on minute traces of alkaline impurities, which were still present even after the most rigorous purification. They found that when all traces of aminic impurities are removed, and when the solution is kept in a silica flask to prevent contamination by alkali from the glass, the velocity of isomeric change is practically zero. They were led to this observation by a study of the velocity in chloroform solution, which gave erratic results; these they showed were due to oxidation of the chloroform and production of carbonyl chloride which is a most efficient agent for removing aminic impurities by converting them into neutral carbamides. The use of this reagent and the preservation of the solutions in silica flasks enabled them to show that isomeric change is a catalytic phenomenon and that in the absence of hydroxyl ion it does not occur.

Effect of solvent. After reading this paper one may well suspect that the effect of solvent on velocity of reaction, which has been variously ascribed to the dielectric constant of the solvent, thermodynamic environment, and density of infra-red radiation, may be due in many cases, if not in all, to the presence of traces of catalytic impurities in the solvents used. The erratic results which Lowry and Magson obtained when using chloroform solutions have been noted by other authors; von Halban[36] in his study of the decomposition of triethylsulfonium bromide obtained erratic results for different specimens of chloroform but he attributed the results to polymerisation of the solute. Lowry and Magson examined the effect on the velocity, of adding small quantities of water to solvents. They found that 1% of water in alcohol, acetic acid or ether causes a considerable increase in the velocity. From a consideration of acid catalysis we would expect the opposite behavior; possibly the water

[35] Lowry, *J. Chem. Soc.*, **75**, 211 (1899); Lowry and Magson, *ibid.*, **93**, 107, 119 (1908).

[36] von Halban, *Z. physik. Chem.*, **67**, 129 (1909).

dissolved traces of alkali from the glass vessels containing the reacting mixture; it seems desirable to repeat these experiments using silica vessels to find out whether or not small quantities of water have the same effect in acid and alkaline catalysis. The velocity of the reaction varied enormously with different alkaline substances when dissolved in inert solvents and further work is necessary to clear up this behavior.

The experiments of Meyer [37] and his co-workers on acetoacetic ester also show that isomeric change is a catalytic phenomenon which does not occur in the absence of the hydroxyl ion. Thus in the vapor state the two forms are stable and do not undergo isomeric change; it is only when one of the isomers is in contact with glass or when there is some other source of hydroxyl ions present that the isomer changes to the equilibrium mixture; similar results were obtained for other keto-enol isomers. The importance of this subject would justify further study of the velocity and temperature coefficient, especially as there is the added advantage that the only complication in these changes is the back reaction. Other examples of isomeric change which have been studied are the conversion of acetyl-chloro-amino-benzene into *p*-chloracetanilide,[38] and the halogenation of ketones.[39]

Alkyl halides. Although the reactions of the alkyl halides may almost be said to comprise synthetic organic chemistry, the literature on the kinetics of such reactions, especially when compared with that on ester hydrolysis or sugar inversion, is not very extensive. The following is a summary of the studies that have been made; the equations are intended to represent the actual reactions which take place in the solutions so far as they have been determined, and in all cases of ethyl iodide is used as typical of the reactions which occur with other alkyl halides.

Acid hydrolysis: [40]

$$C_2H_5I + H_2O \rightleftarrows C_2H_5I \cdot H_2O$$
$$C_2H_5I \cdot H_2O + H^+ \rightleftarrows C_2H_5OH + I^- + 2H^+$$

Alkaline hydrolysis: [41]

[37] Meyer and Schoeller, *Berichte*, **53**, 1410 (1920); Meyer and Hopff, *ibid.*, **54**, 579 (1921).

[38] Armstrong, *J. Chem. Soc.*, **77**, 1047 (1900); Acree and Johnson, *Am. Chem. J.*, **38**, 265 (1907); Harned and Seltz, *Jour. Amer. Chem. Soc.*, **44**, 1475.

[39] Lapworth, *J. Chem. Soc.*, **85**, 30 (1904); Dawson and co-workers, *ibid.*, **95**, 1860 (1909); **97**, 2048 (1910); **99**, 1740 (1911).

[40] Lengfeld, *Am. Chem. J.*, **11**, 40 (1889); Olivier and Berger, *Rec. trav. chim.*, **41**, 637 (1922).

[41] Lengfeld, *Loc. cit.*, Brusoff, *Z. phys. Chem.*, **34**, 129 (1900).

$$C_2H_5I + H_2O \rightleftarrows C_2H_5I \cdot H_2O$$
$$C_2H_5I \cdot H_2O + OH^- \rightleftarrows C_2H_5OH + I^- + H_2O$$

With sodium thiosulfate: [42]

$$C_2H_5I + S_2O^-{}_3^- = C_2H_5 \cdot S_2O_3^- + I^-$$

Catalytic decomposition: [43]

$$C_2H_4I_2 + I^- = C_2H_4 + I_2 + I^-$$

With organic bases: [44]

$$C_2H_5I + (C_2H_5)_3N = (C_2H_5)_4NI$$

With silver salts: [45]

$$C_2H_5I + AgNO_3 = C_2H_5NO_3 + AgI$$

With sodium naphthoxide: [46]

$$C_2H_5I + NaOC_{10}H_7 = C_2H_5OC_{10}H_7 + Na^+ + I^-$$

The hydrolysis of these compounds will be included in a later section when treating the hydrolysis of esters. Slator has made a very complete study of the reaction between alkyl halides and sodium thiosulfate. The reaction is complete in the direction indicated and is substantially free from secondary reactions; it is bimolecular, the velocity being proportional to the concentration of the halide and to the concentration of the thiosulfate ion. A puzzling exception to this is shown by certain ethylene derivatives, with some of which ($C_2H_4I_2$, C_2H_4IBr, $C_2H_4Br_2$) the change proceeds as a bimolecular reaction whilst with others (C_2H_4BrCl, C_2H_4ICl) as a unimolecular reaction, the velocity in this case being independent of the thiosulfate concentration. He also showed that neutral salts containing a common ion diminish the velocity, an opposite effect to that obtained in acid catalysis; the action of potassium iodide is not clear because it reduced the velocity even more than potassium chloride yet Slator

[42] Slator, *J. Chem. Soc.*, **85**, 1286 (1904); *ibid.*, **87**, 481 (1905); Slator and Twiss. *ibid.*, **95**, 93 (1909).

[43] Slator, *J. Chem. Soc.*, **85**, 1697 (1904).

[44] Menchutkin, *Z. phys. Chem.*, **5**, 589 (1890); Menchutkin and Vasileff, *J. Russ. phys. Chem. Soc.*, **22**, 346 (1890); Clarke, *J. Chem. Soc.*, **97**, 416 (1910); Long, *ibid.*, **99**, 2164 (1911); Preston and Jones, *ibid.*, **101**, 1930 (1912); Hawkins, *ibid.*, **121**, 1170 (1922).

[45] Lengfeld, *Loc. cit.;* Burke and Donnan, *J. Chem. Soc.*, **85**, 555 (1904); *Z. phys. Chem.*, **69**, 148 (1909); Donnan and Potts, *J. Chem. Soc.*, **97**, 1882 (1910); Senter, *ibid.*, **97**, 346 (1910).

[46] Cox, *J. Chem. Soc.*, **113**, 666, 821 (1918); *ibid.*, **117**, 493 (1920); *ibid.*, **119**, 142 (1921).

shows that the iodide ion catalyses the decomposition of alkyl halides. It is significant that in all the cases investigated the temperature coefficient of the reaction between alkyl halides and sodium thiosulfate was 3 within experimental error.

The iodide ion catalyses the decomposition of alkyl halides, especially the dihalide derivatives; in the case of ethylene iodide the velocity is proportional to the concentration of the halide and to that of the iodide ion; the temperature coefficient $k_{35} / k_{25} = 2.5$. That this reaction is quite distinct from that between ethylene iodide and sodium thiosulfate is shown by carrying out the two reactions in the same solution when the rate of disappearance of the thiosulfate is approximately equal to that calculated from the velocity of the two single reactions.

The mechanism of these reactions between alkyl halides and thiosulfate is not yet completely understood; this can be seen by considering that the concentrations of the two entities reputed to be reacting is about 0.05 M, so that the reaction should be practically instantaneous: on the bases of the radiation theory we can account for the slow velocity by saying that one of the reactants is present in two forms the active form being present in minute concentration; possibly the reaction is similar to the inversion of nitrocamphor (p. 267) investigated by Lowry, and is conditioned by the presence of a trace of some catalyst as yet undiscovered. The identity of the temperature coefficients in all the measurements supports the latter view.

These remarks apply also to the reactions of alkyl halides with organic bases which have been studied from time to time since Menchutkin's work. The temperature coefficient has been measured in very few of the studies, but appears to have the same value in all cases, namely $k_{35} / k_{25} = 2.2$ (approximately); this is distinctly lower than the value 3 obtained for the reaction between alkyl halides and thiosulfate. Hawkins measured the velocity and temperature coefficients of the reaction between allyl bromide and pyridine in seven solvents; the mean value of $k_{38.3} / k_{28.3}$ was 2.06 and the maximum deviation from this value was $\pm$ 9% . Owing to the analytical difficulties, the error of a single experiment was probably about $\pm$ 5 %, so that the maximum deviation of the temperature coefficient is probably not much greater than the errors of experiment. From the value $k_{38.3} / k_{283} = 2.06$ we obtain $Q = 13{,}500$ by applying the Arrhenius formula, and hence $k_{35} / k_{25} = 2.10$. Preston and Jones who studied the reaction of allyl bromide with dimethyl aniline and tri-isoamylamine obtained a mean value for $k_{35} / k_{25} = 2.28$. While

this identity of the temperature coefficients is merely an empirical observation it can hardly be without theoretical significance; it suggests that each of these classes of reactions has some factor in common, which would not be expected from the equations reputed to represent the change. This identity of the temperature coefficients is strikingly brought out in a paper by Cox [47] in which he measured the temperature coefficient of the reaction between sodium naphthoxide and ethyl iodide in nine solvents; the mean value for $k_{47\cdot8}/k_{37\cdot8}$ was 2.80 and the maximum deviation 4.7%; the combined errors of two experiments which are necessary to measure the temperature coefficient can hardly be less than $\pm 4.7\%$.

The reaction between silver nitrate and alkyl iodides is still very puzzling in spite of several comprehensive investigations; this is partly because the reaction is not the simple one represented, but is complicated by simultaneous reactions. Thus in a solution containing both alcohol and water we may have:

$$AgNO_3 + EtI = AgI + EtNO_3$$
$$AgNO_3 + EtI + EtOH = AgI + Et_2O + HNO_3$$
$$AgNO_3 + EtI + H_2O = AgI + EtOH + HNO_3$$

Burke and Donnan showed that the reaction is bimolecular, but that the bimolecular velocity constant increases with increased concentration of the silver nitrate; the presence of alkali nitrates also increases the velocity and these two observations led to the conclusion that the non-ionised silver nitrate reacts with the ethyl iodide: they showed that the products of the reaction, nitric acid, ethyl nitrate and ether, had no effect on the velocity. Senter studied the reaction between α-brom fatty acids and silver nitrate, the following equation representing the reaction when α-brom-propionic acid is used:

$$CH_3CHBrCOOH + AgNO_3 + H_2O = CH_3CH(OH)COOH + AgBr + HNO_3$$

Senter made the remarkable observation that reactions of this type are markedly accelerated by the silver halide. He appears to assume that the whole of the precipitated silver halide is active catalytically stating that: "Unfortunately, an accurate investigation of this effect is rendered very difficult by the fact already mentioned, that the precipitate soon coagulates and is withdrawn from the sphere of action by rising to the top or sinking to the bottom of the solution." It is possible, however, that only the dissolved silver halide is active and that we have a case of catalytic decomposition of the ethyl

[47] Cox, *J. Chem. Soc.*, 119, 142 (1921).

iodide by the minute quantity of dissolved iodide ion followed by reaction with the silver nitrate; it would be very desirable to know whether those influences which affect the velocity affect also the solubility of the silver halide. Lengfeld (p. 268) has measured the temperature coefficients of the reactions of silver nitrate with ethyl, propyl and isopropyl bromides; his values for k_{30}/k_0 are erratic, being 32.4, 26.8 and 38.6 respectively. Taking the value 32.4 for ethyl bromide and applying the Arrhenius formula we obtain $Q = 19{,}000$ and $k_{35}/k_{25} = 2.8$.

Hydrolysis and esterification. Owing to our lack of knowledge of solution problems it is not possible to state with any degree of certainty the mechanism of these changes; probably they consist of two reactions, first the formation of a hydrate by the substance being hydrolysed followed by the decomposition of the hydrate by the catalyst present. For ethyl acetate the following equations would represent the change:

$$CH_3COOC_2H_5 + H_2O \rightleftarrows CH_3COOC_2H_5.H_2O$$

$$CH_3COOC_2H_5.H_2O + H^+ \rightleftarrows CH_3COOH + C_2H_5OH + H^+.$$

The equilibrium concentration of the ethyl acetate hydrate is probably small and is attained practically instantaneously, so that we are measuring the velocity of the second reaction; in dilute solution the velocity of this reaction would be proportional to the concentration of the hydrogen ion and to the concentration of total ethyl acetate since the total ethyl acetate concentration will be proportional to the concentration of the ethyl acetate hydrate. If we assume that the active catalyst is the unhydrated hydrogen ion, the concentration of the unhydrated ion will be proportional to the concentration of total acid in dilute solution; for stronger solutions of acid and ester these proportionalities will no longer hold and consequently we would expect the velocity constant to vary; Ostwald [48] found that using 1.6 N hydrochloric acid as catalyst the velocity constant for methyl acetate increased from 19.91 in dilute solution to 24.19 when the concentration of methyl acetate was about 1.5.M. Lewis and his co-workers [49] have made several extensive studies of hydrolytic reactions.

Recently Olivier and Berger [50] showed that certain esters such as esters of phosforic acid, esters of sulfonic acids, disubstituted

[48] Ostwa'd, *J. prakt. Chem.* [2], **28**, 449 (1883).

[49] Lamble and Lewis, *J. Chem. Soc.*, **105**, 2330 (1914); Griffith and Lewis, *ibid.*, **109**, 67 (1916); Griffith, Lamble and Lewis, *ibid.*, **111**, 389 (1917).

[50] Olivier and Berger, *Rec. Trav. Chim.*, **41**, 637 (1922).

esters of sulfuric acid, lactones and benzyl chloride are not hydrolysed by hydrogen ions; in addition they showed experimentally that hydrogen ions have no effect on the rate of hydrolysis of benzyl chloride, monochlorhydrin, butyl chloride, isobutyl chloride or ethyl nitrate: this behavior therefore appears to be common to all esters derived from strong mineral acids. Further experiments showed that this was true for esters of strong organic acids because hydrochloric acid only feebly accelerated the rate of hydrolysis of methyl trichloracetate. Senter [51] has examined the reaction $CH_2ClCOOH + H_2O \rightleftarrows CH_2(OH)COOH + HCl$ and found that it is not affected by a strong acid. Sudborough's results show that the esters of strong acids are fairly easily hydrolysed by water [52] alone. Olivier and Berger conclude that the results are best explained by the theory of Stieglitz according to which esters form oxonium salts with the water before undergoing hydrolysis.[53] Stieglitz studied the hydrolysis of imido-esters, in which the imido group (:NH) replaces the oxygen atom of the ordinary esters. The following equations represent the action for methyl imido-benzoate:

$$C_6H_5C(:NH)OCH_3 + HCl \rightleftarrows [C_6H_5C(:NH)OCH_3.HCl]$$
$$[C_6H_5C(:NH)OCH_3.HCl] \rightleftarrows [C_6H_5C(:NH)OCH_3.H]^+ + Cl^-$$
$$[C_6H_5C(:NH)OCH_3.H]^+ + H_2O \rightleftarrows C_6H_5COOCH_3 + NH_4^+$$

Stieglitz claims that the positive ion of the salt is the reacting substance and that the acid catalyses by forming larger amounts of the active ion, since the salt would ionize more extensively than the weak base. Olivier and Berger suppose that since esters of strong acids cannot form these oxonium salts the rate of hydrolysis should not be accelerated by hydrogen ions.

The esterification of strong acids shows similar abnormalities; Sirks has found [54] that weak organic acids esterify more quickly than stronger organic acids in presence of hydrochloric acid, but the opposite occurs when there is no added catalyst.

The hydrolysis of methyl acetate and ethyl acetate by buffer solutions has been investigated by Karlsson [55] who found that the velocity of hydrolysis was a minimum at pH values between 4.7 and 5.1; this has been shown to hold for other reactions [56] and to follow

[51] Senter, *J. Chem. Soc.*, **91**, 460 (1907).
[52] Sudborough, *J. Chem. Soc.*, **101**, 1236 (1912).
[53] Stieglitz, *Am. Chem. J.*, **39**, 29, 402 (1908); *Jour. Amer. Chem. Soc.*, **35**, 1774 (1913).
[54] Sirks, *Rec. trav. chim.*, **27**, 248 (1908).
[55] Karlsson, *Z. anorg. Chem.*, **119**, 69 (1921).
[56] Rice, *Jour. Amer. Chem. Soc.*, **45**, 2808 (1923).

from the theory that only the unhydrated hydrogen ion is catalytically active.

The hydrolysis of substituted fatty esters has been very completely studied; the hydrolysis of chlor derivatives [57] in the case of ethyl chlor-acetate may be represented by the following equation:

$$CH_2ClCOOC_2H_5 + H_2O \rightleftarrows CH_2ClCOOH + C_2H_5OH.$$

Preliminary experiments showed that there was no splitting out of halogen either from the ester or the acid during the course of the experiment. The introduction of the halogen atom in all cases diminished the velocity, the diminution being greater in the β substituted compounds; the temperature coefficients k_{35} / k_{25} of the α substituted ester is 2.0 and of the β substituted ester or unsubstituted ester is 2.4. The hydrolysis of ethyl cyanacetate and its homologues [58] in acid solution gave results similar to the halogens but the reduction in velocity was greater; unlike the halogens, the α cyanogen group retards the velocity more than the β cyanogen group; the temperature coefficients are all about 2.4. The action in acid solution is represented by the following equation:

$$CH_2CNCOOC_2H_5 + H_2O \rightleftarrows CH_2CNCOOH + C_2H_5OH.$$

Hydrolysis by barium hydroxide gave

$$CH_2CNCOOC_2H_5 + OH^- = CH_2CNCOO^- + C_2H_5OH$$

which occurred with great rapidity followed by a slow reaction:

$$CH_2CNCOO^- + H_2O + OH^- = CH_2{:}(COO)_1^{--} + NH_3.$$

The acid hydrolysis of hydroxy-acid esters and alkyloxy acetic acid esters [59] showed that in practically all cases the effect of the substitution was to diminish the velocity; substitution in the β position produces greater retardation than in the α position; the temperature coefficients were about 2.4 in all cases. Similar experiments but in alkaline solution [60] showed that the effect of substitution in most cases was to cause a great increase in the rate of hydrolysis; the velocity increase caused by α substitution is much greater than that caused by β substitution. The temperature coefficients in alkaline solution were about the same in all cases, the value of

[57] Drushel and Hill, *Am. J. Sc.*, **30**, 72 (1910); Drushel, *ibid.*, **34**, 69 (1912).

[58] Drushel, *Am. Jour. Sc.*, **33**, 27 (1912), **37**, 514 (1914).

[59] Drushel and Dean, *Am. J. Sc.*, **34**, 293 (1912); **35**, 486 (1913); Drushel, *ibid.*, **39**, 113 (1915).

[60] Dean, *Am. J. Sc.*, **35**, 605 (1913); **37**, 331 (1914).

k_{25}/k_0 being 5.3; this corresponds to a value of $Q = 10{,}800$ which compares favorably with the value of 10,950 obtained by Reicher:[61] from Reicher's value we may calculate that $k_{35}/k_{25} = 1.82$ for ester hydrolysis in alkaline solution; the corresponding value for acid hydrolysis is 2.4, an increase of 33%.

Hydrolysis of amides. A number of investigations on the hydrolysis of amides have been made but the results are not in good agreement; Crocker[62] studied the hydrolysis of acetamide in acid and in alkaline solution over the temperature range 40° to 60°; the corresponding values of k_{35}/k_{25} obtained are 3.14 and 1.5 respectively. Sulo Kilpi[63] confirmed Crocker's result for acid solution. Peskoff and Meyer[64] investigated a number of aliphatic amides; their results are somewhat erratic for the different amides; the mean value of k_{35}/k_{25} for the acid hydrolysis is 2.86 and for alkaline hydrolysis is 2.65. Euler and Rudberg[65] measured the rate of hydrolysis of acetamide by hydrochloric acid at 64.3° and 49.3° and obtained a value of $Q = 15{,}400$ whence k_{35}/k_{25} is 2.4. Reid[66] measured the rate of hydrolysis of benzamide by alkali at 100° and 25°; from his results the value of Q is 14,800 whence $k_{35}/k_{25} = 2.25$; he also found that with substituted benzamides substitution diminishes the rate of hydrolysis in acid solution, ortho substitution having the greatest effect; in alkaline solution substitution produced a much wider range of velocities, ortho substitution usually diminishing the velocity. Acree and Nirdlinger[67] discussing the hydrolysis of amides by acids conclude that all these catalytic reactions involve the primary union of the acid with the weak base (which may be an amide, ester, organic acid or cane sugar) and the subsequent saponification of this intermediate salt by water or alcohol; they quote[68] Kastle, Stieglitz, and Acree and Johnson in support of this.

Reid[69] found that in absolute alcohol amides are esterified according to the following equation: $C_6H_5CONH_2 + C_2H_5OH \rightleftarrows C_6H_5COOC_2H_5 + NH_3$; in common with other reactions small amounts of water greatly retarded the reaction, and a discussion of this is given in connection with the theories of Goldschmidt and

[61] Reicher, *Ann.*, **228**, 257 (1885); **232**, 103 (1886).
[62] Crocker, *J. Chem. Soc.*, **91**, 593, 955 (1907).
[63] Sulo Kilpi, *Z. phys. Chem.*, **80**, 165 (1912).
[64] Peskoff and Meyer, *Z. phys. Chem.*, **82**, 129 (1913).
[65] Euler and Rudberg, *Z. anorg. Chem.*, **127**, 244 (1923).
[66] Reid, *Am. Chem. J.*, **21**, 284 (1899); **24**, 397 (1900).
[67] Acree and Nirdlinger, *Am. Chem. J.*, **38**, 489 (1907).
[68] Kastle, *Am. Chem. J.*, **27**, 481 (1902); Stieglitz, *loc. cit;* Acree and Johnson, *Am. Chem. J.*, **27**, 481 (1902); **38**, 258 (1907).
[69] Reid, *Am. Chem. J.*, **41**, 483 (1909).

Lapworth. Goldschmidt [70] who first observed this phenomenon supposed that the active catalyst is $[C_2H_5OH.H]$ and when water is introduced the hydrogen ion goes to the water to form $[H_2O.H]^+$; the amount of this change depends on the amount of water added.[71] Lapworth showed that many different cases of hydrogen ion catalysis in alcohol were affected by water in a similar manner; this suggested to him that there was a common explanation of them all, namely that the uncombined hydrogen ion was catalytically active but when the ion was combined either with alcohol or with water the resulting compound had no catalytic activity or a negligibly small catalytic activity.

The foregoing discussion comprises only a very small fraction of the number of studies on velocity of reaction; only a few of the most important classes of reactions were selected to show the development of the field. A list of reactions which are referred to in the text and which require further investigation is given below.[72]

Equilibrium

Menchutkin [73] and Lichtz [74] showed that when an organic acid and an alcohol are heated they reach the same equilibrium point as a mixture of the corresponding ester and water; for acetic acid and ethyl alcohol this corresponds to about 66.6% conversion to ester and water. Reid [75] regards this as a partitioning of the CH_3CO- group between the $-OH$ and the $-OC_2H_5$ groups; he studied the partition of an acid between two alcohols by the reciprocal transformation of the ethyl and methyl esters of benzoic acid. His own work as well as that of others [76] shows that under the influence of either hydrogen

[70] Goldschmidt, *Z. Elektrochem.*, **15**, 4 (1909).

[71] Lapworth, *J. Chem. Soc.*, **93**, 2187 (1908).

[72] Catalytic activity of acids in different solvents (p. 264) with measurements of the temperature coefficients. Effect of small amounts of water on the isomeric change of nitrocamphor when catalysed by alkali (p. 267). The temperature coefficient of simple isomeric changes (p. 668). The reaction between sodium thiosulfate and ethylene derivatives (p. 269). Neutral salt effect in the reaction between sodium thiosulfate and alkyl iodides (p. 269). Temperature coefficients of the reactions between alkyl halides and organic bases (p. 270). The rôle of the silver halide in reactions between organic halogen compounds and silver nitrate (p. 271). Temperature coefficients of the hydrolysis of esters of strong acids (p. 273). Study of the alkaline hydrolysis of esters of strong acids (p. 273). Hydrolysis of amides in acid and in alkaline solutions (p. 275).

[73] Menchutkin, *Berichte*, **10**, 1728 (1877).

[74] Lichty, *Am. Chem. J.*, **17**, 27 (1895); **18**, 590 (1896).

[75] Reid, *Am. Chem. J.*, **45**, 479 (1911).

[76] Pfannl, *Monatsh.*, **31**, 301 (1910); Kremann, *ibid.*, **29**, 23 (1909).

ion or hydroxyl ion such transformations take place readily at ordinary temperatures and all are readily reversible; this applies also to the partition of an alcohol between two acids and to the double decomposition of two esters. The equilibrium point in such reactions as these [77] must be independent of the kind of catalyst employed but sometimes changing the catalyst causes a new reaction to take place and a new equilibrium is formed; for example, in aqueous solution acetone and iodine react to form iodo-acetone and hydriodic acid under the influence of an acid catalyst; if, however, an alkaline buffer solution is used the iodine reacts with the iodo-acetone and finally iodoform is produced quantitatively, a reaction which does not take place in an acid solution.[78]

Jones and Lapworth studied the reaction $CH_3COOC_2H_5 + H_2O \rightleftarrows CH_3COOH + C_2H_5OH$ when catalysed by hydrochloric acid; the value of K in

$$K = \frac{[C_2H_5OH] \times [CH_3COOH]}{[CH_3COOC_2H_5] \times [H_2O]}$$

is approximately 0.25 for the homogeneous system over a wide range of temperature and the value is only slightly affected by small quantities of catalysts or alterations in the relative amounts of constituents or by the use of indifferent solvents. That the simple equation is not sufficient to represent the equilibrium was shown by the fact that the equilibrium constant decreases from 0.25 to 0.125 as the concentration of the hydrochloric acid increases; they suggest that this is due to the removal of water by the hydrochloric acid.[79]

Such variations of an equilibrium constant with change in concentration of the reactants may perhaps be explained on the basis of a theory of chemical reactivity [80] recently published, in which it is assumed that the law of mass action first enunciated by Guldberg and Waage is correct in its classical form, namely, that the concentration of a substance is a sufficiently exact and complete mode of representing its chemical reactivity. Such statements as "One and the same substance exhibits a different degree of reactivity according to the nature of its surroundings," *i.e.* according to the nature of the medium in which it is dissolved, are explicitly denied. It is not the mass action law but our system of stoichiometric equations that has

[77] See Koelichen, *Z. phys. Chem.*, **33**, 129 (1900).
[78] Jones and Lapworth, *J. Chem. Soc.*, **99**, 1427 (1911).
[79] See, however, Euler and Rudberg, *Z. Physik.*, **16**, 54 (1923).
[80] Rice, *Jour. Amer. Chem. Soc.*, **45**, 2808 (1923).

broken down. For example, it is very probable that only the unhydrated hydrogen ion is catalytically active yet in our stoichiometric equations and in our methods of determining hydrogen ion concentrations it is implicitly assumed that the total hydrogen ion is catalytically active. It is not surprising therefore that the mass action law fails to hold. In the equilibrium between ethyl acetate and water in presence of hydrochloric acid, the simple equation:

$$CH_3COOC_2H_5 + H_2O \rightleftarrows CH_3COOH + C_2H_5OH$$

does not represent even approximately the equilibrium in the solution which is really much more complex and comprises the anhydrous forms and the hydrates of all the substances taking part in the equilibrium: that any equilibrium constant is obtained at all is probably because certain of the hydrates largely determine the value of the constant and in dilute solution the concentrations of these hydrates are proportional to quantities in the stoichiometric equation representing the change.

Lowry and his co-workers [81] have developed an interesting method for studying the equilibrium between isomeric compounds. Normal nitro-camphor can be obtained pure and stable in the solid state; it is stable in solution provided there is no trace of alkaline catalyst present; in presence of such a catalyst an equilibrium mixture of the normal form and a pseudo form appears. The first step is to measure the solubility of the pure normal form in a solution free from catalyst; a minute quantity of catalyst is then added and the dissolved material is allowed to reach equilibrium in presence of an excess of the solid form; more of the normal form will now dissolve and a new solubility determination is made. If the solubility of the substance is not very great we can assume that the solubility of the normal form remains constant throughout the experiment and is not affected by the product of the isomeric change, so that we have the necessary data for calculating the equilibrium concentrations of both forms. This is a valuable method because often the less stable isomeride is unknown or cannot be prepared in the pure state. These equilibria have been investigated for various camphor derivatives and the β and α forms of glucose and galactose.

Meyer [82] has determined the equilibrium constant K = enol/keto of ethyl aceto-acetate and many similar keto-enol isomers in different

[81] Lowry and Robertson, *J. Chem. Soc.*, **85**, 1541 (1904); Lowry, *ibid.*, **85**, 1551 (1904); **89**, 1033 (1906); Lowry and Magson, *ibid.*, **89**, 1042 (1906).

[82] Meyer, *Berichte*, **47**, 826 (1914); Meyer and Willson, *ibid.*, **47**, 832 (1914).

solvents; although K for any one substance varied greatly with the solvent he found that the ratio of K for aceto-acetic ester to K for any other of the compounds was a constant independent of the solvent. The equilibrium constants in the same solvent are very different from each other even when the compounds are closely related; the acetyl group favors enolisation more than the benzoyl group except in camphor derivatives. Rise in temperature favors the production of the keto form. In any one solvent the temperature coefficient is the same for different isomeric compounds but it varies considerably with the solvent, so that the temperature coefficient is characteristic of the keto-enol group.

Heterogeneous Reactions

If chloroform and water be shaken together and the two saturated solutions be cooled to $-0.1°$ a compound separates $CHCl_3.18H_2O$.[83] The compound is formed at the interface between chloroform and water and cannot be obtained from either of the saturated liquids alone. A great many examples of such reactions which do not occur in the interior but only at the boundary between two phases have been observed; Faraday [84] found that a perfect crystal of sodium carbonate or sodium sulfate does not effloresce until the surface is scratched or broken, and that the efflorescence spreads from the injured place; crystalline organic compounds show a similar behavior when decomposition sets in; for example [85] the acetyl derivative of hydroxy-methyl dimethyl sulfonium iodide which is a crystalline solid develops brown spots from which the decomposition spreads throughout the mass.[86] If copper oxide is reduced by passing hydrogen over it the reduction is preceded by an "incubation" period [87] during which there is no perceptible reaction; the length of the incubation period is longer the lower the temperature. The authors' description of the process is instructive: "The reduction commenced visibly by the formation of a red speck amongst the little mass of copper oxide at the lowest part of the bulb; this quickly became a reddish metallic powder, the progress of the reaction reminding one of the slow deflagration of a quantity of touch paper, the reducing action being apparently propagated from particle to particle through the mass."

[83] Hill, *Science*, **58**, 314 (1923).
[84] Faraday, Experimental Researches, Everyman's Library Edition, p. 109.
[85] Private communication from R. R. Renshaw.
[86] See also Hinshelwood and Bowen, *Phil. Mag.*, **40**, 569 (1920); Hinshelwood, *J. Chem. Soc.*, **119**, 721 (1921).
[87] Wright, Luff and Rennie, *J. Chem. Soc.*, **33**, 1 (1878); **35**, 475 (1879).

Pease and Taylor [88] confirmed and extended these observations and showed that the incubation period could be practically eliminated by adding copper granules to the copper oxide.

The importance of chemical action at an interface has been illustrated in a recent paper [89] by the dissociation of calcium carbonate; at the equilibrium point between calcium carbonate, calcium oxide and carbon dioxide, two opposing reactions are taking place at equal rates; we may assume that the rate at which carbon dioxide is converted into carbonate is proportional to the pressure p of carbon dioxide and to the fraction θ_1 of the surface which is covered by CaO, and the rate of dissociation of the carbonate would be proportional to the fraction θ_2 of the surface covered by $CaCO_3$; if we equate these two rates we obtain at equilibrium $p\theta_1 = K\theta_2$ where K is the equilibrium constant. This equation indicates that the pressure of the CO_2 should depend on the ratio between θ_1 and θ_2; in other words it should depend on the relative proportions of the CaO and the $CaCO_3$, and as this is contrary to fact we must have made a wrong assumption regarding the mechanism of the reaction. By stating that the rate of dissociation of $CaCO_3$ was proportional to the fraction of the surface covered by $CaCO_3$ we have implicitly assumed that a solid solution phase was present because the surface would soon consist of CaO and $CaCO_3$ molecules distributed haphazard over the surface; this is exactly the kind of surface we should expect a solid solution to have. The Phase Rule indicates that in the dissociation of calcium carbonate two solid phases, CaO and $CaCO_3$, are present together; in order that $CaCO_3$ may dissociate and form a phase of CaO instead of a solid solution it is necessary that the reaction shall occur only at the boundary between two phases; we are forced to conclude that the CO_2 in passing through the CaO does not react until it reaches the boundary of the $CaCO_3$ phase; in a sense therefore calcium carbonate must be looked upon as a catalyst for the reaction between calcium oxide and carbon dioxide. This behavior is characteristic of all reactions between phases.

Films. Since it is now generally recognized that in heterogeneous catalytic reactions the surface action occurs only in the film that is absorbed, it is necessary to consider the structure of surfaces and the nature of absorbed films. The older ideas due to Nernst and to Bodenstein [90] are that solid surfaces are covered with absorbed films of considerable thickness, and that the reacting substances must

[88] Pease and Taylor, *Jour. Amer. Chem. Soc.*, **43**, 2179 (1921).
[89] Langmuir, *Jour. Amer. Chem. Soc.*, **38**, 2263 (1916).
[90] See Bodenstein and Fink, *Z. physik. Chem.*, **60**, 46 (1907).

diffuse through these films before coming in contact with the underlying metal or other substance constituting the solid. In general the rate of the reaction is supposed to be limited by this diffusion for in the absence of this absorbed film the reaction should be practically instantaneous: the thickness of the film is supposed to vary with the partial pressure of the gases in contact with the solid. The more recent view [91] is that absorbed films are one molecule thick and that the molecules are orientated on the surface; this view is based on the conclusion that the force of attraction between molecules is inversely proportional to a very high power (perhaps the ninth or tenth) of the distance between them, so that we can conclude that the attractive force becomes practically negligible when the distance between the centers of the atoms becomes about twice as great as the distance at which the atoms are in equilibrium. In cases where atoms are not joined firmly to one another by the sharing of pairs of electrons, we should never expect the transmission of electric force to extend through more than about one atom and on this basis the existence of thick stable absorbed films of gas molecules is denied; if for example a surface is covered with a layer of oxygen molecules, there will be very little tendency for a second layer to form because the molecules of such a layer would be out of range of the forces at the surface of the solid. On this theory thick films are not regarded as examples of true adsorption but result only from condensation in capillary spaces in presence of nearly saturated vapors or are due to sorption or solution; glass can sorb large quantities of water vapor, but this is a real penetration of the water molecules into the solid material and is not a strictly surface action. Rideal [92] has suggested that in some cases in which an easy liquefiable gas is adsorbed it is possible to get layers banking up on the surface owing to residual affinity. For films which are one molecule thick Langmuir supposes that the forces holding them on the surface are of the same chemical nature as those in the interior of the solid; sometimes these forces are of great magnitude; the adsorbed film of oxygen on tungsten is held so strongly that the force necessary to pull it off results in the top tungsten atom also being pulled off with it. Platinum will adsorb sulfur or iodine but either can be removed by heat, the sulfur evaporating more easily than the iodine; here we have a looser type of chemical combination but the mechanism is supposed to be the same. The second point of interest in connection with these unimolecular

[91] Langmuir, *Jour. Amer. Chem. Soc.*, **38**, 2222 (1916); **39**, 1848 (1917); **40**, 1361 (1918); *Trans. Far. Soc.*, **17**, 607 (1922).

[92] Rideal, *Trans. Far. Soc.*, **17**, 657 (1922).

films is that the molecules are orientated on the surface and are sometimes capable of orientation in more than one position; the spreading of oils on water surfaces confirm these views for only those oils containing an active group, such as the –COOH, –OH, etc., spread on the water: the active groups which have an affinity for the water are drawn into the water and the hydrocarbon chains all remain in contact with each other above the water; the actual surface therefore consists of the hydrocarbon part of the molecule, while the active groups are all turned downward towards the surface of the water. Oils which contain no active group do not spread on water but roll on the surface as small globules. A benzene molecule appears to lie flat on the surface of liquids so that it might be expected to take up this position when adsorbed on the surface of a catalyst; since the benzene molecule lies flat on the catalyst surface and cannot get off until it is completely hydrogenated, only hexa-hydrobenzene should be formed and none of the di- or tetra-hydro product at all; the experimental evidence available [93] confirms this view. When gas molecules condense on a solid surface in such a way that they are held on the surface by primary valence forces, involving a rearrangement of their electrons, their chemical properties become completely modified. It is not surprising, therefore, that in some cases such adsorbed films should be extremely reactive, while in other cases they may be very inert to outside influences. Thus oxygen adsorbed on platinum reacts readily with hydrogen or carbon monoxide, while oxygen on tungsten or carbon monoxide on platinum show very little tendency to react with gases brought into contact with their surfaces. The reaction which takes place at the surface of a catalyst may occur by interaction between molecules or atoms adsorbed in adjacent spaces on the surface, or it may occur between an adsorbed film and the atoms of the underlying solid, or again, it may take place directly as a result of a collision between a gas molecule and an adsorbed molecule or atom on the surface. The development and application of these ideas is treated in the series of papers by Langmuir.

Adsorption and catalysis. Recent work has confirmed these views [94] by showing that adsorption and catalytic activity are intimately connected, that adsorption by metallic catalysis is a highly specific property, and that catalytic reactions at surfaces have a high

[93] Rideal, *loc. cit.*

[94] Taylor and Burns, *Jour. Amer. Chem. Soc.*, **43**, 1273 (1921); Pease, *ibid.*, **45**, 1196 (1923); **45**, 2236 (1923); Dougherty and Taylor, *J. Phys. Chem.*, **27**, 533 (1923); Benton, *Jour. Amer. Chem. Soc.*, **45**, 887, 900 (1923); Gauger and Taylor, *ibid.*, **45**, 920 (1923).

temperature coefficient characteristic of a chemical reaction as opposed to a diffusion process.

The exploitation of these ideas in organic chemistry has been so great that a mere list of titles of catalytic studies made in the last twenty-five years would perhaps double the size of this section; consequently a brief list of publications is given, selected because they contain general discussions of the subject of lists of references.[95]

[95] Catalysis in Theory and Practice. Rideal and Taylor, Macmillan Co. Catalytic action. Falk. Chemical Catalog Co. Catalysis in Organic Chemistry. Sabatier, translated by Reid. Van Nostrand Co., Report of the Committee on Contact Catalysis, Division of Chemistry and Chemical Technology of the National Research Council. Reprinted from *Jour. Ind. Eng. Chem.*, **14**, 326, 545, 642 (1922). Catalysis. Taylor. *ibid.*, **15**, 902 (1923). Catalytic action at solid surfaces. Armstrong and Hilditch. *Proc. Roy. Soc.*, **98**, A, 37 (1920). Contact Catalysis, Bancroft, *Jour. Phys. Chem.*, **21**, 573, 644, 734 (1917); **22**, 22, 433 (1918). Promoter action catalysis. Pease and Taylor, *ibid.*, **24**, 241 (1920).

CHAPTER XVI

ORGANIC ANALYSIS

The Identification and Estimation of Organic Compounds

This is hardly a field of research; it is more like a continent. Whenever we study organic compounds we are more or less concerned with their identification and estimation. Our progress in the past has depended largely on being able to recognize substances, either those produced in reactions or those found in natural products and to estimate their amounts. Our hopes for the future extension of chemical knowledge are to a great extent contingent on discovering and perfecting methods of detection and estimation of organic substances.

We have hundreds of books written on "qualitative analysis" meaning the detection of a dozen and a half metals and of about the same number of anions. All of us spent some months of our chemical adolescence trying to sort out tin, antimony and arsenic or that equally exasperating trio, iron, aluminum and chromium. The organic chemist has to deal not with dozens but with tens of thousands of known substances and with as many or more unknown. The situation looks hopeless and in fact many mixtures defy separation but patient endeavor has already accomplished wonders and may be expected to add to its triumphs in the future.

Need of special methods. The successful attack on any class of natural compounds has always waited on the discovery of methods of separation and identification suited to that particular class. Fischer's famous work on sugars was made possible by his discovery of the reactions of phenyl-hydrazine on the sugars to give the phenyl hydrazones and the osazones, slightly soluble crystalline compounds with distinctive melting points. So it must ever be. The intricacies of terpene chemistry have been unraveled by crystalline nitrosites, dibromides, and the like.

Each class of substances demands a special set of reactions for identification and estimation. In the pharmacopoeia directions are given under nearly every drug for its assay. Each drug has been a research problem for some one, to devise tests for its purity and means for estimating its strength.

There are important classes of substances waiting for analytical methods. We have heard much of vitamines of late: with the study of them has come a new science of nutrition. We now know that animals can starve while gorging themselves on the fat of the land if they fail to get their ration of vitamines, "Water-soluble A" and "fat-soluble B." The progress that has been made in this field has been startling, yet it has been hindered by the lack of some chemical test for vitamines or means of estimating them. Their presence and potency are shown by feeding experiments but these are tedious and laborious to carry out. The discovery of some chemical test for vitamines, some crystalline derivatives that could be isolated, or some titration method that would give even a fair idea of their amount would be of incalculable service to the science of nutrition. The vitamines must be substances with definite properties and reactions: these must be different from the properties and reactions of other substances. The trouble is that the vitamines are present in such small proportions in such complicated mixtures that so far we have not been able to learn their chemistry.

We may say much the same about the secretions of the ductless glands in our bodies and of toxins and antitoxins. These substances which affect us so greatly for weal or for woe are all, doubtless, chemical substances as definite as benzoic acid or cane sugar. They are formed by chemical processes, they react chemically with other chemical substances in the blood or in the tissue. At present we know nothing of their chemistry because it has not been found possible to isolate them and to study them apart from other things. We are dependent on physiological reactions to show their presence or absence. The chemical study of substances of this class looks hopeless on account of the extreme complexity of the mixtures in which they are present and the relatively small amounts in which they occur. It would be rash to predict their early isolation but we can not afford to give the problem up as impossible. The discovery of suitable methods for isolating and estimating substances of this sort would be of the greatest conceivable service to physiological science. The limit for the commercial recovery of gold is said to be about ten cents per ton of sand, or 1 part in 7,000,000. Definite color reactions have been found for some organic compounds in comparable concentrations. Vitamines, toxins, etc., may be present in higher ratios than this.

Proximate Analysis. Ultimate analysis comes in when we know that we have a pure compound and want to determine its composition as a step towards its synthesis but an estimation of carbon

and hydrogen does not get us far in organic analysis. There are tens of thousands of substances made up of carbon, hydrogen and oxygen, and to know the percentages of these elements frequently does not help us much. What we want is to be able to separate and estimate organic compounds when mixed with other organic compounds. Citronellal and geraniol both have the empirical formula $C_{10}H_{18}O$; a combustion will not tell us the proportions of the two in a mixture. In this case one is an aldehyde and the other is an alcohol and we can separate them by means of sodium bisulphite: it is even possible to titrate the aldehyde in presence of the alcohol.

Few methods of determining organic substances approach in accuracy the typical quantitative methods of inorganic chemistry such as the estimation of chlorine or of silver chloride. We must commonly content ourselves with approximate methods; those that give results correct within one per cent are frequently the best available and sometimes we have to employ methods of considerably less accuracy. It is commonly a question of finding a method that will give us useful information, the more accurate, the better, of course.

The hopeful side is that organic compounds are of so many kinds and differ from each other in so many ways. Any difference may be made the basis of an analytical method. Thus oleic acid mixed with stearic may be determined readily by titrating the double bond with iodine chloride as in the Wijs method for iodine numbers. Acetic acid is volatile with steam and stearic is not, so they may be readily separated by steam distillation, the distillate being titrated for acetic acid and the residue for stearic. Combining these we may analyze a mixture of oleic, stearic and acetic acids. We have several methods for differentiating primary, secondary and tertiary amines from each other and from ammonia. We can titrate mercaptans and thio-acids with iodine. Quantitative saponification of esters, including fats and waxes, has been carried to a high degree of accuracy.

Identifying and testing products that are mixtures. In addition to methods for the detection and estimation of pure compounds, means are needed for examining a host of organic substances which are always mixtures. The commercial organic chemist is frequently required to pass upon the genuineness or quality of such things as butter, olive oil, linseed oil, pepper, attar of rose, bergamot, peppermint, etc. Nearly every substance that appears in commerce is liable to adulteration or contamination. Most countries have pure food and drug laws and regulations relative to fuels and many other commodities. The enforcement of these requires elaborate methods of organic analysis. The " official " methods adopted by the Asso-

ciation of Official Agricultural Chemists pertain largely to organic products. A vast amount has been accomplished in this direction but many methods still leave much to be desired. This is a line of research that is important for the physical well-being as well as for the financial profit of the human race.

Such substances as fats and waxes are identified by the determination of a number of physical and chemical constants, such as density, solidifying point, refractive index, saponification value, iodine number and ratio of volatile to non-volatile acids. Two fats may agree in density, refractive index or iodine number but hardly in all their properties. The values for different samples of pure olive oil, for instance, vary somewhat but usually only within certain limits. Values outside of these limits excite suspicion. Chemically olive oil is a mixture of a large number of substances, commercially it is an individual product, the oil expressed from olives and free from admixture. So with butter, lard, linseed oil and scores of other important articles of commerce.

It is even harder to define a manufactured product since what it is depends much on variations in the process. Some years ago the question was asked: "What is whiskey?" It remains unanswered though genuine whiskey, whatever it was, has disappeared from United States commerce to be replaced by liquids still harder to characterize.

The variety and extent of this sort of analysis may be realized by a study of Allen's Commercial Organic Analysis, a book of nine volumes aggregating 5,722 pages.[1]

The identification of pure organic compounds has been worked out in a masterly and elaborate way by Mulliken[2] and has been put into convenient laboratory manuals by Clarke and by Kamm.[3]

Organic compounds as analytical standards. Among the tens of thousands of organic compounds available there are many that can be prepared in a state of high purity. It should be possible to select from these some that are suitable for standards in various sorts of analytical procedure. Those should be chosen that are readily obtainable in pure state and at reasonable cost, and particularly those whose purity can be tested by melting points or other constants. Non-hydroscopic substances that can be dried at 100° are desirable.

[1] Published by P. Blakiston's Son & Co.

[2] S. P. Mulliken, A method for the identification of pure organic compounds, 4 vol. so far pub. John Wiley & Sons, N. Y.

[3] Oliver Kamm, Qualitative organic analysis, 260 pp. John Wiley and Sons, N. Y., 1923.

Oxalic acid has long been used as an acidimetric standard but it is not desirable for several reasons, though it can be obtained in quantity in pure condition. It contains water of crystallization and can be dried to constant composition only under certain specific conditions.[4] Its equivalent weight is only 63 so that care must be taken with the weighings. Anhydrous oxalic acid has a definite melting point but the hydrated form that is used has not. For a standard *p.*-nitrobenzoic acid is much better than oxalic. It has a molecular weight of 167, does not contain crystal water, and is non-hydroscopic. It is readily obtainable in extreme purity. It melts at 238°, so may be dried in a steam oven. It has the disadvantage that it is only slightly soluble in cold water, 0.021 g. per 100 cc. at 15°. Its melting point is inconveniently high. It should be possible to find an organic acid with a higher equivalent weight, melting at about 150° and soluble in about 100 parts of water.

For the standardization of titanium trichloride, *p.*-nitrobenzoic acid can be used but here its equivalent weight is only 27.85 and its low solubility is troublesome. For this purpose a nitro-compound of very high molecular weight is desirable.

Certain dyes, particularly of the triphenyl-methane series, are readily titrated by reducing solutions, the dye serving as its own indicator.

The beauty of organic chemistry is that there is such a host of compounds from which to choose that almost any requirements can be met. If one can not be found that suits exactly, one may be synthesized to order.

IDENTIFICATION OF ORGANIC COMPOUNDS

By LOUIS E. WISE[5]

(1) Ideal Conditions.

When ample material is at hand, the classical procedure for the identification of a single chemical individual which predominates in a natural or artificial mixture, involves preliminary isolation, followed by purification. If the substance is solid, a suitable solvent is found from which the substance may be crystallized. Preferably the substance should be readily soluble in that solvent, at a temperature approaching the boiling point of the solution, and difficultly soluble

[4] Arthur E. Hill and Thomas M. Smith, *J. Amer. Chem. Soc.*, **44**, 546 (1922).

[5] Written for this book by Prof. Louis E. Wise of New York School of Forestry.

when the mixture is cooled. The accompanying impurities should have a high solubility in the cold solvent, and the conditions of crystallization should be such that the minimum amount of impurity is adsorbed by the depositing crystals. If necessary boneblack or other purifying agent may be resorted to to remove tarry or coloring matter prior to the crystallization.

The main component should then be recrystallized from the same or from different solvents, until some definite physical property remains unchanged after successive crystallizations. We thus gauge the purity of the substance. In the case of a solid substance an unaltered melting point (or freezing point) or unchanged solubility after successive recrystallizations gives an index of its purity. There are times however, especially in the case of isomers that form mixed crystals, when these criteria fail.[6] Less frequently a solid substance may be purified by sublimation or steam distillation than by fractional crystallization. In the case of liquids, fractional distillation with the use of suitable stillheads, distillation with steam, or vacuum distillation may be used in the purification. The criterion of purity of a liquid that has been isolated is usually the boiling point at a definite pressure — and this boiling point should remain constant after repeated distillation. Not infrequently the refractive index and the specific gravity of the liquid may also be used in gauging its purity. It often becomes necessary to isolate a solid or a liquid in the form of a readily purified crystalline derivative.

The purified compound may then be subjected to qualitative and to quantitative ultimate analysis. Its molecular weight is subsequently determined by the use of one or more of the classical procedures so fully described in the literature. The molecular weight coupled with the physical constants of the substance may be sufficient to give a clue to its identity.

Mulliken's[7] work gives a highly useful systematic procedure for the identification of the more common organic compounds, and his methods involve many short-cuts that may be invaluable. Qualitative and quantitative methods for determining organic groups (like the alcoholic and phenolic hydroxyls, carboxyl, carbonyl, amines, nitriles, etc.) are admirably outlined in Meyer's excellent monograph, and these methods are very useful as aids in identification.[8]

It is not our purpose to prolong the discussion of the ideal pro-

[6] Hans Meyer, Analyse und Konstitutionsermittlung organischer Verbindungen, p. 43. Julius Springer, Berlin, 1922.

[7] S. P. Mulliken, A method for the identification of pure organic compounds. 4 volumes so far published. John Wiley & Sons. New York.

[8] Analyse und Konstitutionsermittlung organischer Verbindungen.

cedure, where the usual methods of identification can be used. There are many cases that are far from ideal, when identification of one or more substances in a mixture is required.

(2) Identification when the amounts that can be isolated and purified are very small.

This condition is frequently met with in biochemical work. In the investigations on the organic constituents of soils, the amount of a definite compound that can be isolated is often less than *100 mgs. per 20 kilograms of air-dried soil.* A somewhat similar, though less exaggerated condition is met with in the isolation of certain organic compounds from plant and animal tissues. Friedländer's isolation of *1.5 grams of 6,6'-dibromindigo (the famous "Tyrian Purple") from twelve thousand snails (Murex purpura)* will serve as an example.[9] Needless to say, when substances occur in such very small amounts, special methods must be devised to effect their isolation and purification. Often accompanying substances which occur in the colloidal state must be removed before isolation becomes possible. Here only general methods of attack can be referred to. The thought that must be kept uppermost is that we have a dearth of material. Hence the amounts used in various tests must be *minimal* amounts, and micromethods must be resorted to. Our quantitative analytical procedure takes the form of a microanalysis,[10] and the molecular weight determination must be carried out with and adapted to small amounts of material.[11]

The microscope becomes an exceedingly useful instrument, and frequently the optical properties of a microscopic amount of crystalline material will give a valuable indication of its identity in the hands of an experienced crystallographer.

If the substance happens to be a dyestuff, very small amounts in solution may be used in determining its spectral absorption curves by means of the spectrophotometer. These curves may then be compared with those of known dyestuffs, and at times the identity of the dye may be clearly established. During the War, the Bureau of Chemistry, using the spectrophotometer as a control instrument, was able to reproduce the expensive German photosensitizing dye "dicyanin"[12] the chemical constitution of which is still unknown.

[9] Meyer-Jacobsen, Lehrbuch der organischen Chemie, Vol. II, part 3, page 312.

[10] Pregl, in Abderhalden's Handbuch d. biochem. Arbeitsmethoden [11], 5, 1307.

[11] Barger and Ewins, *J. Chem. Soc.*, 85, 286 (1904); 87, 1756 (1905).

[12] U. S. Patent No. 1,338,349 (April 1920).

The method of " mixed melting points " will frequently aid in the identification of small amounts of material. If preliminary tests indicate that the substance resembles a certain class of organic compounds, it may be expedient to actually synthesize one or more of these compounds and to determine the melting point of each alone and in admixture with the isolated unknown compound. A mixed melting point determination, which shows no depression, furnishes strong evidence that the substances are identical.

At times the formation of a miniature amount of a characteristic derivative will serve to identify a compound. As an example: small amounts of cyanuric acid may be identified by the formation of its very characteristic salt $[Cu(C_3H_2N_3O_3)_2.2NH_3]$ which forms rhombic crystals of a magnificent amethyst color.[13] A simple microanalysis serves to determine the per cent of copper in as little as 16 mgs of material.

In the case of liquids, or low melting solids, it is often expedient to convert them into some crystalline derivative which can be more readily purified than the original compound. On occasion however, the Abbé refractometer which requires only a few drops of liquid may be used to advantage.

Needless to say there are times when the amount of substance that can be isolated becomes so small that definite identification becomes impossible. It is at such times that group reactions (color reactions, reducing reactions etc.) may serve a useful purpose. The results of such qualitative tests must always be taken with a grain of salt, since their interpretation is not always a simple matter. Not infrequently traces of accompanying material may be responsible for color reactions that appear at first blush to characterize the principal component. In this connection it is well to recall the classic example of the blue indophenine reaction given by benzene derived from coal-tar, when treated with isatine and sulphuric acid. This reaction was believed to be characteristic for benzene, until Victor Meyer found to his surprise that the reaction was not given by benzene prepared from calcium benzoate. The color was in fact due to small amounts of thiophene which accompanied the main coal-tar product.[14]

(3) Identification where Isolation is Impracticable

This condition also obtains in the case of natural products, plant and animal tissues, and in animal fluids and secretions. Problems involving the identification of substances in mixtures often lead to

[13] *J. Agric. Research.*, 10, 85 (1917).
[14] Thorpe, *J. Chem. Soc.*, 77, 189 (1900).

difficulties, although the intelligent use of the microscope and of special analytical micromethods have proved of immense help, especially when the presence of a definite compound is strongly suspected. Several cases may be cited. In certain plant tissues, calcium oxalate crystals can be definitely identified in the mounted section of the tissue by the use of the microscope. In acid urinary sediments the experienced microscopist can definitely recognize uric acid crystals although these may occur in a variety of forms (" whetstone," " quadrate " etc.) and may be greatly discolored. Similarly the presence of sodium acid urate and ammonium urate may be definitely recognized in admixture with other urinary deposits.

The presence of glucose in small amounts of blood may be tested for qualitatively (and quantitatively) by the coloration with picric acid [15] in the presence of sodium carbonate (probably due to the formation of picramic acid). Here again precautions must be taken to avoid, or insure the removal of, other substances that will cause a similar reaction.

Micromethods to be used in testing for specific compounds (not normally present in certain plant or animal tissues or fluids) frequently must be devised before a biochemical research requiring routine tests for such substances can be undertaken. Thus in the case of a protracted series of experiments on the action of sodium citrate in the animal body it was necessary to find a method that would permit the detection of very small amounts of citrates in blood, urine, etc. This could only be accomplished after a large number of control experiments had been undertaken, in which it was clearly shown that the blood, urine, etc., of experimental animals that had received no citrates gave negative tests.[16]

Sometimes it becomes possible to convert the substance that defies isolation into a derivative that may be removed by some suitable means like steam distillation, and tested for by appropriate methods in the distillate. This principle is applied in testing for the pentoses (or pentosans) in the presence of other carbohydrates.

There is little need of giving a multiplicity of examples. Each case requires individual treatment. Several important facts must be considered in the development of any problem in identification. (*a*) Physical instruments like the polarizing microscope, the goniometer, the refractometer, the polariscope and the spectrophotometer may be of tremendous service in the detection of small amounts of substances. (*b*) General reactions like those involving the reduction

[15] Lewis and Benedict, *J. Biol. Chem.*, 20, 61 (1915).
[16] Salant and Wise, *J. Biol. Chem.*, 28, 27 (1916).

of Fehling's solution or colorimetric tests for organic groups must be used with extreme caution. (*c*) The ease of identification of a compound depends in large measure on the ease with which reasonably large quantities of the substance can be isolated and purified. (*d*) Microanalytical methods are serviceable especially in orientating experiments.

QUANTITATIVE ANALYSIS OF MIXTURES OF ORGANIC COMPOUNDS

By LOUIS E. WISE [17]

A branch of organic chemistry which in the past twenty years has been stimulated by the rapid advances in industrial chemistry and in the various phases of biochemistry may be termed organic analytical research.

The manufacturing chemist interested in the production of complex organic substances like the dyes and dye intermediates, synthetic drugs, explosives and perfumes has demanded analytical methods that would aid him in the proper control and standardization of such production. The pharmaceutical chemist has required methods that would serve in the analysis of natural drugs. Food chemists have had similar requirements with regard to food stuffs. The physiological chemist, the pharmacologist, and the physician have called for the development of methods that could be used for the estimation of organic compounds in animal secretions and excretions, and in the various tissues and fluids of the human body.

It may be fairly said that organic analytical research is a means to an end — rather than an end in itself. It must prove serviceable to other branches of pure and applied science, and hence its development requires careful consideration of a number of factors. These include: (*a*) the accuracy demanded of the method; (*b*) the rapidity with which the determination can be made; (*c*) the simplicity of the method; (*d*) the cost of an individual determination.

The first factor requires a little discussion. In certain determinations in biochemical and industrial control, the analysis serves as little more than a rough approximation. In other cases — and these would be of special interest to the investigator — a high degree of accuracy is required. Needless to say the organic research chemist should know at the outset of his research just what will be demanded of his method with regard to accuracy.

[17] Written for this book by Professor Wise.

The time factor in the analysis is often a very important one. In control, or routine analysis, whether in the plant or in the hospital, results are usually demanded within a comparatively short time after samples have been taken, hence the time consumed in actual analysis must not be too great. Protracted analytical procedures are seldom popular, and are often valueless. This fact has given impetus to volumetric and colorimetric methods in perference to the longer and more accurate gravimetric methods.

The simplicity of the method also deserves close consideration. Difficulties in acquiring the technique of an analytical procedure will often serve to vitiate a control method. Not infrequently the plant chemist is harassed enough by problems of production without being further hampered by the demands of refined or unusual technique.

The cost of the method is also of some importance, although this may be exaggerated. In general, expensive and readily breakable apparatus and expensive or unstable reagents are not desirable. However the research chemist's rather than the control chemist's judgment must determine whether or not the expense of a method should be curtailed.

In approaching analytical research various modes of attack are possible. The following procedure is suggestive rather than all-inclusive. Some of the steps may be omitted in special cases, and they are not necessarily chronologically arranged.

Let us assume a natural or artificial mixture containing a number of organic components, several of which are to be determined. The research chemist synthesises and carefully purifies those components that he wishes to determine analytically. It is often important that he prepare these compounds in a high state of purity, so that when he makes up his mixtures for analysis, he may know with what he is dealing. He then makes a study and preferably prepares a summary of the analytical methods in the chemical literature that may be of use to him in his procedure. Quite often such a review will save a great amount of time and many false moves during the course of the research. If he finds a well described analytical procedure that appears to satisfy his requirements, this should be tried with known mixtures of the pure components.

If such a method does not appear to be satisfactory, the chemist carefully searches further in the chemical literature with a view towards differentiating between the various components by the use of certain *outstanding* physical or chemical properties that will be of use in his procedure. At times the chemist himself will be called upon to make a study of such properties during the course of his investigation.

On the basis of these properties, the investigator develops an analytical procedure. This will involve repeated analyses of mixtures containing varying amounts of the *pure components*. If the procedure has developed satisfactorily, *i.e.* if the components can be determined with a satisfactory degree of accuracy within a reasonable time period, artificial mixtures are made containing not only known amounts of the components to be determined, but also varying amounts of those impurities that are known to be present, or suspected of being present, in the reaction mixtures. If the procedure still holds for the main components of such mixtures, actual "plant samples" or (in the case of biological work) natural mixtures are subjected to similar analysis.[18] Known amounts of the principal components and impurities are subsequently added to these same plant samples, and the analyses are repeated. If the analytical results remain satisfactory, and the amounts of the added components can be satisfactorily estimated, the analytical research is presumably complete.

Since discretion is the better part of valor, it is best at this point for the investigator to describe his procedure in detail to some one who has had nothing whatsoever to do with the investigation, so as to assure himself that the analysis is satisfactory in hands other than his own, and that he has fully described his technique.

In individual cases there will of course be wide variations in the mode of approach to an analytical problem. Quite frequently it is necessary not so much to determine a single substance as a group of substances or a definite radical or substituent group. Under these conditions the analytical research may be decidedly modified.

Difficulties are often met with in analytical research, when the components of a mixture are chemically related. It is no easy matter for example to determine with a high degree of accuracy acetic acid and its higher homologs in admixture.[19] Nor is it a simple problem to analyze mixtures obtained in the chlorination of some simple compound like acetic acid, in which the final products may include acetic acid, hydrochloric acid and the chlorides, monochloracetic acid, dichloracetic acid, etc. It is obvious here that a determination, let us say of total chlorine, or total acidity, will not necessarily tell us

[18] In the case of solid non-homogeneous material, suspensions, etc., the question of proper sampling becomes a very important one. The organic analytical research chemist is often called upon to devise the proper method for obtaining representative samples. In biochemical work the proper preservation of samples containing substances that may ferment or putrefy also demands consideration.

[19] Gillespie and Walters. "The possibilities and the limitations of the Duclaux method for the estimation of volatile acids." *J. Am. Chem. Soc.*, **39**, 2027 (1917).

very much about the components or the degree of chlorination, and special methods must be devised for the accurate estimation of these components, even though they cannot be separated from each other.

Even greater difficulties are sometimes met with in the estimation of one isomer in the presence of large amounts of another. Often the production of an organic substance involves the formation of a compound isomeric with the main component. Frequently also, the process demands that the amounts of such an isomer must be kept at a minimum, so as to insure success in the next step of the process. It then becomes necessary for the analyst to have a method enabling him to estimate the contaminating isomer. Often chemical reactions of the isomers are very similar and differentiation is extremely difficult. If crystalline derivatives of the mixed isomers can be obtained it may be possible at times to use to good advantage the services of an expert crystallographer, who may be in a better position to effect an estimation of the contaminating isomer than is the chemist himself.

It is quite obvious that the chemist must never limit himself to one line of thought or one mode of attack. It is well for him not to rely merely on classical or text-book procedures. Keen observation, good judgment and an open mind are required of him. Common-sense and initiative are accessories. The investigator must always be on the *qui vive*. If the differences between the components of a natural mixture suggest physical-chemical methods, these should be tried. Similarly if the chemist can resort to a biochemical method, *e.g.* the use of an enzyme which will have a specific action on one component and not on the others — such a method should be investigated. If the physical properties of one component are outstanding properties, if the component is optically active, if it has an abnormally high refractive index, or if it is colored, the use of suitable optical instruments is suggested.

CHAPTER XVII

PLANT PROCESSES FROM LABORATORY EXPERIMENTS

By C. M. STINE[1]

Research work which is undertaken with a view to developing a process applicable to manufacturing practice should have certain very definite characteristics. All research work should be characterized, of course, by breadth of conception, accuracy of execution and completeness. There are certain additional qualities which have a vital bearing upon the applicability of the laboratory process to plant practice, in addition to those which ordinarily characterize the successful prosecution of a piece of research work. The possibility of translating the laboratory process into successful manufacturing practice is by no means wholly bound up either with chemical research ability or familiarity with chemical engineering.

A Broad Consideration of the Problem Indispensable.

Referring to the three characteristics of research work which have just been enumerated, and particularly to the first one, namely, "breadth of conception," the ability to translate a chemical process into a successful manufacturing process goes back to that stage in the development of a process when the research chemist is covering the literature of his problem with a view to selecting that line of attack which holds out the best prospects of a successful solution. It is in this initial stage of the work that the research chemist should begin to think of his embryonic process in terms of plant equipment, as well as in terms of a chemical reaction. A nice co-ordination of the two is involved. We have assumed that the manufacturing problem is susceptible of solution in more than one way, that is, by the utilization of at least two different processes or variations of the same process. In those cases where there is an alternative to choose from, the selection of the process to be worked upon should receive a good deal of careful thought from different viewpoints. There are two important points which should be uppermost in the mind of the investigator. The first is that the ultimate success of a process will be measured in terms of net cost per unit of product. The second is

[1] Chemical Director E. I. du Pont de Nemours and Co.

this, namely, that *simplicity* in equipment and method of operation is nearly always the keynote to the success of a process.

The problem of selecting a process, can, therefore, not be definitely solved until sufficient data are at hand to enable the research chemist to compare each process or variation in a process from the net cost standpoint. The potential process should be viewed from this angle even though the research chemist's preliminary cost estimates can be only approximately correct. Of course, a chemist will make his selection of a process which offers the best promise of producing the product in question in good yields and of the requisite degree of purity, but the process should produce the product with *maximum* yields and with minimum consumption of raw materials. These two things are not synonymous.

In determining which of two or more alternate processes to work upon, consideration must be given to such questions of vital importance as:

Factors in Devising a Chemical Process.

1. Are the raw materials and intermediate products involved the cheapest which may be used? This involves the question: 1-A. Are the by-products valuable?

2. Which process requires the smallest amount of equipment as well as the least expensive type?

3. Is the equipment required highly specialized and is it, therefore, likely to prove expensive to construct and replace?

4. What are the factors of chemical corrosion or mechanical erosion which are likely to affect the success of the process?

5. Which process will consume the least power in the form of heating or cooling facilities, mechanical agitation, comminution, etc.?

6. Which process will best fit in with existing methods of manufacture from the standpoint of utilization of buildings and equipment which may be available?

7. Which process will be the most economical in its labor requirements?

Before proceeding to the more particular discussion of these factors, let us look at the problem in a somewhat general fashion. Ex-

The Research Chemist Assists the Design Engineer in Selection of Equipment.

perience has taught us that many excellently trained chemists, who repeatedly have demonstrated their ability in the research laboratory, have been unable to select the best equipment and decide upon the most efficient method of assembling the complete plant. It is true that when the question of plant design arises the inexperience or lack of training of the research chemist is supplemented by expert engineering advice and assistance, but the chemical engineer, or the

design engineer, is largely guided in his recommendations as to type of equipment and method of assembling same by the ideas of the research chemist who has developed the process. It follows, therefore, that the research chemist who attempts to develop a process in the laboratory which shall be applicable to plant practice should have at least some knowledge of the types of chemical equipment and their specialized adaptabilities. Complete unfamiliarity with chemical equipment is a tremendous handicap in the successful development of a process which shall be well adapted to plant practice. It is not only indispensable that the research chemist familiarize himself, at least in some degree, with chemical equipment, but he should also obtain at least a rudimentary knowledge of the sort of data and the kind of mathematics upon which are based the type of apparatus, the selection of the materials from which the apparatus is to be constructed, and the detailed design of the finished piece of equipment.

Some Knowledge of Chemical Equipment Indispensable for the Technical Chemist.

The research chemist should appreciate that the successful operation of a process is based upon a nice co-ordination of various dissimilar equipment, and especially upon the proper selection of the types of equipment. I wish especially to emphasize that this should by no means be left entirely to the design engineer. While the process is still in the mind of the originator and while it is growing in test tube, beaker and flask, the research chemist must think of the reactions which he is employing in terms of the manufacturing equipment which would be required for the successful fabrication of the product by the process in question. The research chemist should, therefore, select his reactions with a special view to their feasibility — their plant workability. If the research chemist will keep in mind the general types of elementary processes which enter into all chemical processes he will be considerably assisted in his efforts to select a type of reactions with a view to the limitations under which his reactions must be carried out.

Familiarity with Elementary Processes.

Perhaps the foregoing may be somewhat clarified and certainly the significance of the statements may be emphasized by some illustrations. It is frequently necessary to resort to crystallization as a means of separation. But to obtain effective separation the size of the crystals, the extent of crystallization, the separation of crystals and mother liquor must all receive consideration. It is frequently necessary to transfer liquids from one level to another in manufacturing practice. If the design engineer is told that for the liquid in

Optimum Conditions as Regards Temperature and Concentration of Liquor.

question the angle of flow must be 60° at least, or that only gravity flow is permissible, that the material cannot be successfully handled by any type of pump or elevator, either because of the physical or chemical nature of the liquid, he designs his equipment accordingly. It is very important, therefore, that he be given *correct* information by the research chemist.

If a filtration is necessary there are available as filters in the laboratory, paper, glass-wool, asbestos fibre, gooches, etc., and the filtering materials are ordinarily placed in glass funnels or porcelain gooches. But these are, for the most part, not applicable upon a manufacturing scale. And the process devised with a complete disregard of the necessity for filtering in such types of equipment as are available or mechanically feasible, often requires complete revision before it can be blocked out upon the drawing board. Furthermore, an increased cost of a cent a pound for constant replacements of filter cloths or repair and up-keep of filtration equipment may be, sometimes actually is, the exact margin between success and failure for a promising chemical process.

If the research chemist wishes to heat material in the laboratory he lights a gas burner, turns on a steam valve, or closes an electric circuit. He practically never gives a thought to the number of heat units he consumes in a given time; but this becomes a question of vital importance when these heat units are drawn from plant power house boilers instead of chemical laboratory gas burners. More than one promising process has been abandoned because of its intolerable power or heat requirements. Such questions as length of time of heating and temperature at which a reaction must be carried out can, therefore, by no means be disregarded in connection with the determination of a suitable process for the commercial fabrication of a product.

Power Requirements often Ignored by the Young Chemist.

The design engineer is often dependent upon the research chemist for the indispensable data, such as physical constants, required in drawing plans and specifications for apparatus for a given process. If the necessary data are not available in the literature they must be accumulated by the research chemist in connection with his laboratory investigation while selecting and developing his process. The design engineer requires information as to specific gravity, viscosity, specific heat, melting point, boiling point, chemical stability in the presence of various metals and other materials of apparatus construction, stability in terms of temperature limits or time and temperature, vapor pressure curves, solubilities,

Physical Data are Essential.

and, very often, type of crystals produced and method of controlling same from the standpoint of ease of filtration and tendency to retain mother liquor, and many other data of similar character. Unfortunately, the research chemist too often overlooks the necessity for the accumulation of these data. He is too apt to think of these questions as dependent upon the size of the equipment or the nature of the equipment rather than upon the nature of the process and its inherent requirements.

Let us turn now to the seven factors mentioned as important in the selection of a chemical process adapted to manufacturing practice.

1. Are the raw materials and intermediate products involved the cheapest which may be used? In his consideration of the questions involved under this heading the chemist should know whether the raw materials involved are readily obtainable and what fluctuation in prices they have undergone in the last decade. If some attention is paid to this question of price variations the chemist will be enabled to avoid the error of assuming that a current quotation, which may happen to be a minimum quotation over a period of years, represents a *fair average* cost of the product required as a raw material for his process. This question of raw material requirements may call for very extended consideration in connection with the selection of a chemical process. It is not merely a question of the principal raw materials selected as the starting points in the fabrication of the finished product, but involves a consideration of all the inorganic or organic materials required by the process (whether these materials are actually consumed in the process or obtained as by-products from the process) with reference to any transformation of these constituent materials into some other form of chemical combination brought about by the reactions incidental to the process.

Raw Material Requirements.

Essential Raw Materials.

Principal Intermediates.

A few examples will serve to illustrate. If caustic fusion is one of the steps of the synthesis, may caustic *soda* be employed or is caustic *potash* essential? If caustic soda may be employed, what degree of *purity* and *dehydration* of the caustic must be prescribed? In what *form* will the caustic be recovered, *i.e.*, will it appear as dilute caustic, as an alkali carbonate or in the form of some other alkali metal salt? Will the material be salable as such or must it be reworked to render it salable, or should an attempt be made to recausticize in order that it may be re-employed in the process? Possibly a mixture of caustic potash and caustic soda might be more desirable for carrying out the caustic fusion either from the standpoint of the temperature limits dictated

Caustic Fusions. Type. Reactions.

by the stability of the principal materials under the conditions of the reaction, or from the standpoint of the initial cost of the raw caustic. If a *mixture* of caustic potash and caustic soda is employed for the fusion, the question of the final disposition of the by-product alkali calls for still more careful consideration.

Solvent Media.

If a reaction is to be carried out in a solvent medium, what is the cheapest solvent which may be employed, both from the standpoint of initial cost as well as from the standpoint of ease of recovery? There may be involved here such questions as the inflammability of a solvent as affecting the safety of the operation; its volatility at ordinary temperatures and pressure, and the consequent solvent losses; the behavior of the solvent when distilled, such as tendency to form constant boiling mixtures; the vapor pressure of the solvent under reasonably high vacuum from the standpoint of ease of condensation with ordinary water cooling rather than brine cooling; the chemical stability of the solvent in the apparatus and under the conditions necessitated by the reaction; and other questions incidental to the handling and recovery of the solvent.

Nitrations.

If nitration is required in one of the steps of the process, the question of the cheapest ingredients for the nitrating mixture, not merely from the standpoint of initial cost but from the standpoint of yield and quality of product, the solubility of the product in the spent acid, as affecting both the yield of the principal product, and the recoverability of the spent acid, these all constitute important factors in making a decision as to the method to be employed.

General Questions in Connection with Commercial Consideration of Type Reactions.

In the same way it is possible to take such processes as reduction, oxidation, and the like, and make a critical study of the process from the standpoint of the materials involved, their availability, their recoverability, the commercial value of the form in which they are recovered, both from the standpoint of further usefulness in the process either as such, or by regeneration, or their usefulness in other processes carried on in the same plant, and from the standpoint of marketability, etc. This brings us to the consideration of the next question:

By-Products.

1-A. Are the by-products valuable? A very important factor is the nature and amount of by-products other than those referred to in the foregoing paragraph. The problems involved in this connection merit the most careful consideration — the most painstaking analysis of the bearing of such factors upon the selection of the process. A portion of the principal initial ingredients

may be obtained in the form of products other than the desired finished product, either because of the formation of chemical isomers or because of the unavoidable occurrence of side reactions. The value of the by-products depends not only upon the initial form in which these by-products occur in the process, but involves the question of the amount of further treatment required in order to put them in shape for disposal in the open market, provided they cannot be re-used somewhere within the plant.

The technical chemist should thoroughly appreciate that this consideration of the initial materials really involves not only the selection of materials which shall produce the principal desired end product, but involves also the determination of the nature and amount of the by-products emanating from the process, and the uses to which these by-products lend themselves, either in the form in which they are obtained or in some form into which they may be readily converted.

2. Which process requires the smallest amount of equipment as well as the least expensive type? The general questions of the nature and the extent of the equipment required and the type of construction must be considered in connection with the selection of the process. That is, they cannot be properly considered after the process has been selected and worked out in the laboratory. New processes are very often worked out which produce a given product from cheaper raw materials or in larger yields than existing processes. Sometimes a process is cheaper than existing processes because of the comparatively greater value of by-products which it yields, but when the question of the cost of installation of the necessary equipment for carrying out the process is considered along with the cost of replacements and up-keep of the equipment, it often happens that the existing process will produce the desired product for the smaller manufacturing cost. Conversely, then, a new process frequently interests the manufacturer not because it gives greater yield or a purer product, or involves cheaper raw materials, but because it enables him to make very considerable savings either in the original cost of installation of the equipment or in its up-keep. The necessity for selecting equipment of the least expensive type leads, logically, to " 3."

Equipment Requirements of the Chemical Process.

3. Is the equipment required highly specialized and is it, therefore, likely to prove expensive to construct and replace? It is to be expected that the research chemist trained in pure science will not attach the importance to this phase of his problem which it merits. It would be absurd to say that the research chemist engaged upon

the development of the process must be capable of deciding all questions involved in a proper selection of equipment and apparatus. It is just as absurd to devise a process calling for complicated and expensive equipment when the process might, by slight modification, be carried out perfectly well in similar and less expensive equipment. It is recognized that the mere working of a process in laboratory apparatus is frequently not sufficient to provide the necessary data for a proper selection of the best apparatus. A great deal of emphasis must, therefore, be placed upon the importance of carrying out a process on an adequate semi-works scale. By semi-works is meant, of course, that size of installation intermediate between the test tube, beaker and flask and the full works scale. In some cases an adequate semi-works scale may be apparatus such as is afforded by the ordinary laboratory supply room. It is true that the decision as to what constitutes an adequate semi-works scale is, itself, an important one and may at times call for a very thorough understanding of the manufacturing requirements; but there are many cases where if some attention is given to this phase of the problem, the chemist can carry out his program on a semi-works scale to insure a proper basis of results for his opinion as to the kind of equipment which his process will demand. If there is available at the laboratory where the work of process development is carried out something like an adequate variety of size and kind of pump, blowcase, filter press, nutsch, wooden tank, still, nitrator, reducer, crystallizer, autoclave, and comminuting machinery, it is often possible for the research chemist to assemble quickly and easily the necessary equipment to enable him to put his process to a test approaching actual manufacturing operations. Sometimes, the purchase or construction of some more specialized piece of equipment is necessary. Further, in connection with this kind of a test of a process, much useful information is accumulated which is indispensable in the subsequent design of a suitable plant, and the possibility of many economies frequently becomes evident in connection with such a semi-works operation of a process. In other words, the research chemist frequently discovers his own shortcomings and the weakness of his process or incompleteness of his laboratory data, when he attempts the operation of his process on something like a small manufacturing scale.

Necessity for Semi-Manufacturing Scale Operation of a Process.

The question of cost of construction is a factor in the cost of replacement, *i.e.*, the cost of plant up-keep. The other factor is the *life* of the equipment. This leads, logically, to "4."

4. What are the factors of chemical corrosion or mechanical ero-

sions which are likely to affect the success of the process? These are important factors in connection with the selection of equipment from the standpoint of equipment design and the materials from which the equipment is to be fabricated. They must not be lost sight of by the research chemist. They may be very easily completely overlooked when working in ordinary laboratory apparatus which consist for the most part of glass and porcelain equipment. It should be recognized that glass or enamel-lined equipment is expensive, fragile, and very often does not properly endure the hard usage incidental to manufacturing practice. Therefore, the research chemist must select his process with a view to avoiding in so far as possible reactions likely to prove highly corrosive in ordinary metal equipment. It is often the case that while the liquids or solids employed in a reaction do not themselves react with the metals used in the construction of the apparatus, the vapors or gases which are given off during the course of the reaction are highly corrosive. This is a possibility which should by no means be overlooked.

Chemical Corrosion Easily Overlooked When Working in Laboratory Scale Equipment.

Enamel to be Avoided When Possible.

It is often of the greatest assistance to the design engineer to have data available as to the chemical corrosion which may be expected in connection with one or another step in a process. The accumulation of this data is a legitimate part of the study of the process by the research chemist responsible for the selection and evolution of that process. He should study the effect of his reagents upon such materials as cast iron, cast steel, wrought iron, and the like. In many cases there are available in the literature corrosion data which may answer the questions involved. In other cases the research chemist must accumulate these data for himself because of the fact that his process calls for new combinations of reagents. He should, therefore, have some knowledge of the types of equipment ordinarily available for carrying out the reactions which he has in mind, in order that he may be familiar with the nature of the metals or *alloys* from which this equipment is ordinarily fabricated.

Chemical Corrosion Data Essential To the Design Engineer.

Mechanical erosion becomes a very important factor in the life of equipment which is designed to carry out reactions involving the stirring together of liquids and solids, or pastes consisting either of crystals or mixtures of hard solids, and the like; for example, in the reduction of nitrobenzenes to aniline, where iron is employed as the reducing agent, mechanical erosion of the ploughs and of the sides and bottom of the reducer by the continual stirring of the iron is an

important factor in the life of the equipment. Special consideration must, therefore, be given to reactions of such a type as this with a view to the installation of equipment adapted to the exacting requirements of the process.

5. Which process will consume the least power in the form of heating or cooling facilities, mechanical agitation, comminution, and various other power requirements? The power requirements of the chemical process must unavoidably form a part of the original cost consideration which the research chemist must give to the processes. We have already on page 298 referred to the necessity for the research chemist considering his proposed process from the angle of cost and making at least an approximate estimate of the same. This question of the power requirements of a process is one of the principal factors involved in such a cost consideration. It, therefore, calls for early consideration. The questions comprised in the power requirements of a process are too frequently entirely ignored by the research chemist engaged in the development of new processes or products. He is too apt to think of these questions as dependent upon the size of the equipment rather than upon the nature of the process and its inherent power requirements. The young research chemist carries out his laboratory work with flasks, evaporating dishes, electric hot plates, electric ovens, etc. For example, it is very often true that his experience in drying material consists in spreading his product in a thin layer on a watch crystal and leaving it in a thermostatically controlled electric oven until the moisture is gone, or perhaps his laboratory is equipped with a small vacuum oven so that his tendency may be to specify vacuum dryers for his process. If this happens to be the case, he usually specifies unnecessarily low temperatures for the operation of the vacuum dryer and it may often be true that drying at atmospheric pressure or under partial vacuum with the proper degree of humidity for incoming gases, might work very much better than a high vacuum dryer through which is circulated air containing varying amounts of water vapor determined by the varying humidity happening to exist from day to day.

Power Requirements of the Chemical Process.

The question of the power requirements for mechanical agitation is sometimes a very important one. A familiar example is afforded by the process for the manufacture of aniline by the reduction of nitrobenzene. A number of methods have been proposed for removing the aniline from the water and hydrated iron oxide in the reducer at the end of the reduction. Filtration of the whole mass for the removal of the iron oxide, with subsequent gravity separation of the

aniline from the water has been tried on a works scale. Coupled with this method is the necessity for subsequent recovery of the aniline dissolved in the water. This must be removed by some method such as solvent extraction or distillation with live steam or distillation with closed steam. Another method for separating the aniline from the reducer charge is to distill it out with live steam while the mass is continually stirred to prevent settling of the heavy iron oxide at the bottom of the reducer. Still another method is the removal of the aniline by distillation of the whole charge in a suitably heated still provided with mechanical agitation. The attempt to apply any of the foregoing methods brings out various difficulties inherent in each of them. Since it is indispensable that aniline be manufactured as cheaply as possible, because it is the essential ingredient in very many products, savings in power assume great importance in connection with the decision as to the proper method for use on a manufacturing scale. The research chemist cannot properly leave such questions as the foregoing entirely to the design engineer charged with the selection and assemblage of equipment into a finished plant.

I believe that a consideration of the cost items involved in various methods of manufacturing aniline will serve very well indeed to illustrate some of the points which we have been endeavoring to emphasize in the foregoing discussion. Let us look at some of the items of cost actually involved in the production of aniline on a manufacturing scale.

If nitrobenzene is reduced to aniline in an agitated reducer by means of a mixture of iron and water the power consumption for the reduction under good manufacturing conditions approaching the ideal might be somewhat as follows:

Reduction:

To heat 1500# Nitrobenzene	from 60°–212° F.	113,300 B.t.u.
To heat 1660# Water	from 60°–212° F.	253,300 B.t.u.
To heat 1660# Iron	from 60°–212° F.	33,300 B.t.u.
To heat Reducer		33,300 B.t.u.
Radiation loss (estimated) for 18 hrs.		500,000 B.t.u.
Refluxing 35 gals. per hr. for 3 hrs. (estd.)		750,000 B.t.u.
Total		1,683,200 B.t.u.

Assume steam will furnish 900 B.t.u. per lb.

$$\frac{1,683,200}{900} = 1870 \text{ lbs. of steam required for reduction.}$$

It will be noted that about half the steam used in the reduction is for refluxing, *i.e.*, it is estimated that the amount of steam required to keep the contents of the reducer boiling up into a reflux condenser

amounts to nearly half the total requirements for the process. It is obvious then that the chemist should attempt to so regulate this strongly exothermic reaction as to utilize the heat of the reaction for bringing about the reflux ordinarily employed as a control of the reaction, rather than to introduce steam from the power house boilers to bring about this refluxing.

It might be interesting to compare the estimated power requirements for two different methods of recovering the aniline from the sludge in the reducer:

1. Distillation of the aniline from the reducer by means of live steam with subsequent recovery of the aniline from the distillate by means of secondary distillation.

2. Extraction of aniline from aniline water by means of a suitable solvent, such as nitrobenzol, for example.

1. In each of two typical works runs of aniline there was distilled off from the reducer:

3,000 lbs. of water layer and
430 lbs. of aniline layer

3,000 lbs. of water layer will contain 120 lbs. of aniline and 2,880 lbs. water.
430 lbs. of aniline layer will contain 410 lbs. of aniline and 20 lbs. water.

Heat to distill	530 lbs. aniline	@ 180 B.t.u. per lb. =	95,500	B.t.u.
Heat to distill	2,900 lbs. water	@ 970 B.t.u. per lb. =	2,815,000	B.t.u.
Total for distillation			2,910,500	B.t.u.
Radiation estimated			375,000	B.t.u.
Total heat required			3,285,500	B.t.u.

$$\frac{3,285,500}{900} = 3,650 \text{ lbs. steam}$$

If we assume the yield of aniline to be about 75.5 lbs. per 100 lbs. of nitrobenzol the *steam* consumption per 1,000 lbs. of aniline should not then exceed:

For reduction	1,650 lbs.
For distillation	6,890 lbs.
Total	8,540 lbs.

If steam costs 50c per M, the power cost for the raw, wet aniline would amount to $4.25, or about 0.42c per lb. of raw aniline so far as steam is concerned. Of course, to this must be added the consumption of compressed air, and of water for operating the necessary condensers, and of electricity for the motors, etc. The cost of the air, water and electricity consumed may far exceed the cost of the steam consumed. For every 1,000 lbs. of steam consumed as such,

about 3,700 lbs. of steam may be consumed in the form of power for compressed air, water and electricity. The cost of rectifying this aniline and the cost for operating the various pumps, steam syphons, etc., incidental to the manufacture of the aniline would probably make the power charge for refined aniline very close to 0.85c per lb. for *steam alone* under good operating conditions; if we add the cost of air, water and electricity we obtain a figure very close to 3½ times this figure, or 3.16c per lb.

2. If we compare with the live steam distillation method of removing aniline from the reduction mass, a method based on the use of a suitable solvent such as nitrobenzol, for example, we find that while the losses of nitrobenzol, due to solubility, about off set any saving in additional recovery of aniline, so far as materials are concerned, there *is* a tangible saving in power consumed because of the large amount of live steam required to distill the aniline out of the reducers. This figure we have just seen amounts to close to 0.3c per lb. of aniline. Furthermore, if we compare the consumption of air, water and electricity by the two processes we find that the actual saving realizable through the substitution of nitrobenzol extraction for steam distillation, amounting to a few tenths of a cent per lb., still persists. Even such a small saving becomes significant when a large poundage is involved. Of course, there are other important considerations involved in a comparison of processes. For example, increase in yield which one process may show may entirely offset small differences in labor or power charges. This simply emphasizes the importance of taking into consideration all the phases of the problem when endeavoring to decide upon the value of a process. The significance of small differences in yield may be worth a little further discussion.

A yield of 68 lbs. of aniline per 100 lbs. of nitrobenzol is equivalent to saying that 147 lbs. of nitrobenzol would be required for 100 lbs. of aniline; a yield of 73 lbs. of aniline per 100 lbs. of nitrobenzol means that 137 lbs. of nitrobenzol would be required for every 100 lbs. of aniline. If nitrobenzol cost 15c per lb. the cost of 147 lbs. of nitrobenzol is $22.00, and the cost of 137 lbs. of nitrobenzol is $20.50, or a saving of $1.50 per 100 lbs. of aniline, or 1.5c per lb. At first glance this might be regarded as the improvement to be expected from increased yield provided the consumption of power and iron per charge of nitrobenzol remains the same. A little thought, however, makes clear that practically all costs including such items as operating labor, plant depreciation, interest and taxes, will be reduced by the amount of 5/68 or 7.35% of the cost with the lower yield.

This then becomes a first-class illustration of the way the research chemist should endeavor to analyze a process in order that the significance of the various factors involved may be properly appreciated and the proper weight assigned to each factor in arriving at a decision as to which may be the more economical process to employ in a given case. It may appear upon cursory consideration that entirely too much space has been devoted to a very unnecessarily detailed enumeration of the various factors which we have just considered, but it seemed wise to insert at least one rather detailed illustration of the method which the technical chemist employs in reaching his conclusions.

6. Which process will best fit in with existing methods of manufacture from the standpoint of utilization of buildings and equipment which may be available? At first thought the research chemist will be inclined to leave the foregoing question until the time when he may be called upon to do work of this kind for a manufacturer. It is true that specific questions of this nature depend upon the industrial connections of the chemist. I have in mind a somewhat broader use of the term " existing methods of manufacture." By raising this question here, it is desired to emphasize the fact that a knowledge of the existing methods of manufacture employed for the fabrication of some of the typical articles of commerce is an exceedingly valuable asset. In the light of such a knowledge, the research chemist devises his processes with a more or less conscious effort to employ equipment with the exact functions of which he is familiar in one or more existing manufacturing processes. His laboratory work in connection with devising new processes is, therefore, carried out with a view to avoiding, when possible, working out his processes along such lines as would call for the scrapping of all the equipment used in the existing methods of manufacture of a given product. He attempts, wherever possible, to improve upon existing processes by displacing or eliminating steps in a process, at the same time utilizing existing equipment or simplifying such equipment. The complete substitution of an existing process by a new process should be regarded as an extreme case. I do not, by any means, wish to discount the value of new inventions or the ability to devise entirely new processes. What I wish to bring out is that the young research chemist too often limits his consideration of a problem to the effort to devise an entirely new process. After all, the entirely new processes which have been devised, and which have effected marked economies, are far less in number than the modifications and improvements of existing processes which have resulted in very desirable economies.

Value of General Knowledge of Methods of Manufacture and Equipment Employed for Typical Chemical Products.

7. Which process will be the most economical in its labor requirements? The labor requirements of a process is another prime consideration in a cost estimate. It, therefore, like power, must early receive the attention of the technical chemist in connection with the cost estimate or cost approximation which he must make in order to properly decide which process he shall elaborate in detail in the laboratory. The inexperienced technical research chemist unfortunately, as a rule, completely ignores labor requirements. For example, the poking and stirring of a pasty mass in a porcelain dish with a stout porcelain spatula or heavy glass stirring rod, until it crystallizes or has assumed the form in which it is desired for the next step in the process, may be a matter of very little concern to the research chemist in his laboratory work. When he has observed perspiring operators attempting to similarly manipulate 400 to 500 pound batches of material in the form of an unwieldy, sticky mass, he realizes that some attention on his part to this particular phase of his reaction is indispensable. But such consideration of his process the successful research chemist must bestow upon the various steps involved while he is assembling his reactions into a finished process, and before his recommendations crystallize into finished form upon the drawing board of the design engineer.

There are other problems of labor requirements much less obvious than the one just cited. The research chemist must by no means lose sight of the human element in the operation of his process. He should devise his process with a view to minimum requirements both as to chemical supervision and as to skilled and unskilled labor. He should, further, realize the necessity for safeguarding the personal safety of such operators as may be required. This is by no means solely a problem for the design engineer. The proper control of the reactions employed, in order that they may go forward normally at a predetermined rate to the desired point, calls for the most painstaking attention from the research chemist. It goes back to the initial stages in the evolution of a process in the chemical laboratory, because it is here that the research chemist is confronted with the necessity for selecting his reactions with the proper understanding of all the factors properly involved in such a selection.

In the evolution of his process the mind of the research chemist should also concern itself with the various steps in his process from the standpoint of the relation of these steps to one another. For example, it is unfortunate if it is unavoidable that one important step in a process should require ten minutes to complete the reaction in a given portion of the equipment, while some other step requires ten hours. The time factor has another

Effect of Time Factor.

bearing upon the workability of the finished process in that it may not only call for the multiplication of a given type of equipment to an intolerable degree from the standpoint of the expenditures involved in the installation, but this time factor is important as constituting the limiting factor in output. There is always some step in a process which constitutes the limiting factor or "neck of the bottle." It is important that the output limitations imposed upon a process by the amount of equipment provided for a given step in the process, occur at a logical point in the process. This point will be determined either by the length of time consumed in carrying out a given step, with its requirements for multiplication of apparatus in order to speed up fabrication at this point, or by the complexity of the apparatus required for a given step with the consequent limitations which it imposes from the standpoint of investment cost. It is obvious that the initial investment may be largely increased because of the necessity for considerably increased size or number of expensive pieces of equipment in a given step. Such factors as the foregoing become the limiting factors in selecting the size of unit most logical to install for the production of a given amount of a desired material.

From the contents of this chapter it will be evident that the research chemist who is concerned with the evolution of manufacturing processes must concern himself with his reactions from standpoints other than the mere chemical nature of these reactions if he is to insure his success in the development of really workable manufacturing processes.

CHAPTER XVIII

WRITING UP RESULTS

The Preparation of Journal Articles and Technical Reports

At the Baltimore meeting of the American Chemical Society ir 1908 a speaker told a story of how a crusty old manufacturer wh(did not believe in technical education was shown his error. A youn(graduate applied for a position. As a sort of a dare and also to shov the young fellow how his time had been wasted in school, the ol(chap told him to go into the plant for the afternoon and steal th(process if he could. He did so and later spent the evening in writin(up a description of the process, handing it the next morning to th(manufacturer who was horrified that his treasured secret process ha(been found out and so astonished at the insight of the young graduat(that he hired him on the spot "and they lived happily ever after." A second speaker said that the part of the story about unravellin(the process seemed reasonable enough but that a technical graduat(could write it up so that it could be understood was to him unbeliev able. He slandered chemists, as there are some of them that ca write, but the proportion who can express themselves clearly an(forcefully is sadly small. There are men who have excellent idea and can do splendid work but will always hold subordinate position because they lack the ability to present their results.

Marketing knowledge. Every business has two ends: producin(and selling. It may be true that "if you can make something bette than anyone else, the world will make a path to your door" but i may take the world a long time to find out about the product and stil longer to locate your door. Modern business has decided to haste the wearing of the path by judicious advertising of the product an(erecting signboards along the way to the proper door. Million upon millions of dollars are spent in advertising and, if it is wel done, the more that is spent this way the greater the profit to th manufacturer and the less the cost of the product to the public. Som go to the extreme of trying to market a mediocre product by super lative advertising and fail because no one buys a second time. Suc cess comes when a strictly first class product is properly introduce(to those who need it.

It is well recognized that the chemical profession does not occupy the position it should because chemistry has not been "sold" to the public. If we are convinced that we have something that the world needs, it is for us to apprise the world of that fact; we can hardly expect the lawyers, doctors and preachers to do it for us. If they do eventually discover us and sing our praises many of us by that time may be too old to enjoy the music.

The success of the great fruit raising industry of California has been due to coöperative marketing associations. Oranges on the trees are pretty to look at but those that are delivered in sound condition and in attractive form to the consumer in the East are the ones that pay for the orchards. Perhaps sometime a great organizer like unto those that have gathered together the fruit growers and the tobacco raisers and made them wealthy will take hold of us chemists and market our product for us but until then we must do it ourselves.

Chemists of every sort are called upon to present their results either orally or in writing and should see that their findings do not fail of their purpose through faulty presentation. If the results may be published they must be put into such form that they shall meet the requirements of the editors of the journals and shall produce the desired effect on the reader. The plant chemist must write his monthly reports or must sum up his investigations so that they are properly put on record and reach the desired persons. If he has an idea which he wishes to investigate, he usually has to write it up and present it in order to get an appropriation for the experimental work. The consulting chemist accepts money for solving some problem: he must present his findings so that they will be of the utmost service to his client. The form of presentation may be different in these different cases but the necessity of making clear and forceful statement is common to all.

The university man writes for fellow chemists and has the great advantage of having readers who understand technical language and who can appreciate his results. The plant chemist is under the double necessity of recording his results so fully and clearly that his successors in the laboratory can repeat his experiments, and of translating his conclusions into such language as will be understood by the executive or directors of the company who may be non-technical business men. The consulting chemist must direct the technical men that are to carry out his recommendations and must give the proper impression to the business men or bankers who have to decide whether or not to go forward with the enterprise.

The researcher who publishes his results but fails to present them

adequately discounts his own labors. The plant operative who spills half of the product on the floor or lets it go out dirty or in soiled packages will soon be replaced. He is not as bad as the plant chemist who fails to report his experiments or who writes them up so poorly that the proper conclusions can not be drawn. A restaurant advertises: "the value is on the platter," and so it is; for the diner does not ransack the kitchen. The consulting chemist must realize that the value must be in the report for it is the report that is handed the client in exchange for his check.

To put the process in chemical terms: suppose a process employs expensive chemicals and troublesome processes, yet is so worked out that each step is under perfect control and the successive operations give maximum yields right up to the end but in the final isolation of the product a faulty still or leaky filterpress wastes half of the product. The plant would soon suspend operations. Reporting a chemical investigation corresponds to separating and boxing up the factory product.

According to Tingle [1] one should treat his own results with respect:

"Authors should remember that the simple act of publication constitutes, in itself, an invitation to the world to give due credit and honor for the work which is described in their papers. A chemist is, presumably, not likely to underrate the value of his own work; if *he* does not consider it worthy of clear and accurate description, he has no right to expect that busy people will take the time and trouble to acquaint themselves with his results, no matter how important they may be."

Raymond [2] thinks that an article should be as clear as a patent. Perhaps it would be better to say as clear as a patent should be.

"What our patent law requires of an inventor, that his invention shall be so stated as to enable any one skilled in the existing art to practice it, is equally required of every discoverer, whether he seeks the reward of a patent or the recognition of his fellow men in other ways. He must be able to describe and define as well as discover."

Bauer has several things to say about publication: [3]

"I think it may be taken as almost axiomatic that whatever is worthy of investigation should be made known in some effective manner, so as to reach without question those concerned.

"The publication of any research work should, in general, be of such form and size as to permit the widest distribution possible, not

[1] J. B. Tingle, *Science*, 26, 627 (1907).
[2] R. W. Raymond, *J. Ind. Eng Chem.*, 7, 331 (1915).
[3] Bauer, *Chem. News*, 100, 62 (1909).

only among libraries and the principal seats of learning, but also among the workers and institutions immediately interested."

"It should be noted that it as important to make research work known as it is to do it. To get our friends to read the contributions we may make to science requires now-a-days no little skill and diplomacy and an attractiveness of literary style on the part of the author, not so essential in the days of less frequent printed works.

"Reduction in the pretentiousness, size and cost of scientific publications appears to me to be one of the greatest needs of research today."

In an elaborate and most useful book on graphic methods of presentation, which every chemist should study, Brinton makes some strong statements about presenting ideas and conclusions. Any one who has had much experience must agree that he is not far wrong.[4]

"After a person has collected data and studied a proposition with great care so that his own mind is made up as to the best solution for the problem, he is apt to feel that his work is about completed. Usually, however, when his own mind is made up, his task is only half done. The larger and more difficult part of the work is to convince the minds of others that the proposed solution is the best one — that all the recommendations are really necessary. Time after time it happens that some ignorant or presumptuous member of a committee or a board of directors will upset the carefully-thought-out plan of a man who knows the facts, simply because the man with the facts cannot present his facts readily enough to overcome the opposition. It is often with impotent exasperation that a person having the knowledge sees some fallacious conclusion accepted, or some wrong policy adopted, just because known facts cannot be marshalled and presented in such a manner as to be effective.

"Millions of dollars yearly are spent in the collection of data, with the fond expectation that the data will automatically cause the correction of the conditions studied. Though accurate data and real facts are valuable, when it comes to getting results the manner of presentation is ordinarily more important than the facts themselves. The foundation of an edifice is of vast importance. Still, it is not the foundation but the structure built upon the foundation which gives the result for which the whole work was planned. As the cathedral is to its foundation so is an effective presentation of facts to the data.

"We daily see facts presented in the hope of creating interest and

[4] Willard C. Brinton, Graphic Methods for Presenting Facts. The Engineering Magazine Co., N. Y., 1919, pp. 1 and 2.

action for some really worthy piece of work to benefit the people as a whole. In many of these cases the attitude of the person presenting the matter seems to be that the facts will speak for themselves and that they need little or no assistance. Ordinarily, facts do not speak for themselves. When they do speak for themselves, the wrong conclusions are often drawn from them. Unless the facts are presented in a clear and interesting manner, they are about as effective as a phonograph record with the phonograph missing.

"For matters affecting public welfare, it is hard to estimate the benefits which may accrue if a little care be used in presenting data so that they will be convincing to the reader. . . . Archimedes wanted only a fulcrum for his lever and he would move the world. If the world is ever moved it will probably be by facts properly presented. The method of presentation is the fulcrum without which facts, as a lever, are useless."

Looking at things as they are, we do not always find elegant English and lucid logic in our articles, as the following, which appeared in a prominent chemical journal, will illustrate:

"By varying the time factor at constant temperature and pressure, the recovered oil differed in constitution from the starting oil and from each other widely. . . . Due to the time factor at constant temperature of 700° C. and 150 lbs. pressure, the initial oil had changed from a paraffine oil to a mixture of . . ."

This blames a great deal on the innocent time factor.

That technical chemists are alive to the need of better English is shown by one of the recommendations adopted at a recent conference on chemical engineering education held May 16, 1922.[5]

"The committee considers a thorough grounding in English, a reading knowledge of some foreign language and a reasonable familiarity with English literature essential to the adequate training of the chemical engineer, and regards English as one of his most effective working tools. It recommends a special course in report writing and the oral presentation of projects."

The source of the difficulty. The present day tendency toward specialization has gone too far and many students are allowed to spend their time in college and even in high-school on the subjects that they like best without due regard to a well rounded development. Those who are fond of science frequently neglect languages. Happy are those who are not dwarfed by so doing.

Of course it can not be expected that a student who is brilliant in science will be equally good in a number of other lines but a certain

[5] *Chem. and Met.*, 26, 995 (1922).

amount — and not a small amount either — of training in English is necessary to success as a chemist. If we are fortunate enough to have it, well and good, otherwise we must set about obtaining it.

Improving our English. Numerous aids are offered us by correspondence schools and by intensively advertised courses in forceful English. These may help but the only things that can be relied upon are determination and hard work.

Benjamin Franklin tells us in his autobiography how he found himself at a disadvantage in an argument with a friend because his friend had a better command of words and could present the weaker arguments so forcefully that they appeared to be the stronger. He determined then and there to rid himself of that handicap. A volume of the *Spectator* came into his hands. He says:

"I bought it, read it over and over, and was much delighted with it. I thought the writing excellent, and wished if possible to imitate it. With this view I took some of the papers, and making short hints of the sentiments in each sentence, laid them by for a few days, and then without looking at the book, tried to complete the papers again, by expressing each hinted sentiment at length, and as fully as it had been expressed before, in any suitable words that should come to hand. Then I compared my *Spectator* with the original, discovered some of my faults and corrected them."

He turned some of the articles into verse and then back into prose which he compared with the originals. Later on he would note down all the ideas in an article, jumble them up, then arrange them and put them into form.

Franklin's method should appeal to the chemist: it was much like mixing a pound of pure benzoic acid with sand and then trying to recover and purify it. He could test his product almost as one would weigh the recovered benzoic acid and take its melting point. Expressing Franklin's experience in an equation we have:

$$W_p + Q_i = W_e$$

in which W_p is any poor writer and W_e an excellent one. Q_i stands for intelligent work. It is the work term that balks the most of us. Franklin's method may be used on chemical articles.

Translating has been recommended as a useful exercise in improving our English. For the chemist who must study French and German for other purposes there is a double advantage. We have in the German article certain definite ideas which must be put into English. We can keep going over our translation till we are sure that every idea has been fully expressed. The benefit will be lost if we

stop with a sloppy so-called translation which but for being couched in English words sounds like the German. Only ideas must be brought over into the translation and they must be so expressed in idiomatic English that no trace of the original is left and the reader can not tell whether it came from French or from German.

It is useful to take a poem and turn it into prose or to rewrite a piece of prose in a different style.

Reports and chemicals. If we are selling benzoic acid in pound packages, we inspect our acid before shipping. We may find the weight short, or we may find trash mixed with the product or its melting point may be low. There is no use paying freight two ways and losing a customer. We should inspect our writings. They may be short weight; we have not said all we wanted to say. In filling an order, the items are checked over and over to see that nothing is left out. It is a good thing before starting to write an article, or even a letter, to list the things that must go in it and then check over the list when we have finished writing.

Slang expressions and irrelevant statements mar a report in very much the same way as trash or shavings do our benzoic acid. We must adjust our packing operations so as to keep such things out.

If we find the quality of our benzoic acid is low we repurify it till it is fully up to standard. We must be as rigid with our writings and not let them leave our hands till they are up to specifications. We may experiment with our writings and test them as objectively as we do the benzoic acid. It is advisable to get some one not familiar with the work described to read the report and study his reactions. If he does not get the idea, there is no use to call him stupid. Here is an experimentally ascertained fact: a man has read that report and failed to get the idea. It must be rewritten so that that can not happen. Suppose he has to turn back and reread something in the first part to see its connection with something later on. The ideas should be put in such sequence that this would be unnecessary; the report should be rearranged.

Suppose that the reader has to stop and think a minute at one or two places before seeing the meaning. This is an experimental fact and shows that the writing is not clear. The writer is prone to say that since the reader did get the idea that the report will pass. It is possible to drive a car on a muddy dirt road, but we do not usually find such roads thronged with motorists. A report must be so clearly written that it will be like a concrete road and not waste the time of those who have to go over it.

There are many little things, such as questionable expressions

and doubtful constructions, which jar the reader as he goes along even though they do not hinder his progress materially. A hole in a concrete road will not prevent speedy driving but it is hard on tires and machinery and must be eliminated. We must see that our writings are free from little imperfections.

Qualities of style required. Simplicity, sincerity and directness may be put first. A florid or pompous style is out of place, and high-sounding circumlocutions are to be shunned. Lincoln's Gettysburg speech is regarded as a literary classic. It is as simple, as sincere, and as direct as anything that was ever penned and may well be taken as a model for scientific writing.

Accuracy is essential in our observations but goes for naught unless it is sustained by accuracy in our statements. No pains must be spared to insure a logical sequence in the presentation of our facts. When facts are logically arranged and accurately stated with simplicity, sincerity and directness we must have clearness and force, provided there *is* any force in the facts. If our facts have no force in them we had better postpone our writing till we get some facts that have.

Fairness and moderation are virtues of the mind rather than of style but they must watch over us and see that we do not write our historical introductions so as to minimize the achievements of our predecessors and that we are fair and moderate in drawing conclusions.

Brevity. In recent times, with the high cost of printing and of paper and with a multitude of articles coming in, our journals have been in a difficult position. The editors have been forced to insist on brevity, and to exalt it to the position of the cardinal virtue. We may cut down an article so far that we destroy its vitals, thereby killing it, but dispensing with excess baggage is as beneficial to articles as it is to persons. It requires skill and much hard labor to condense twenty pages into ten without leaving out anything, but frequently the article is the better for it. There are many articles in the old journals that are so long and rambling that one forgets the first part before one finishes. Some of these would have made a deeper impression on chemists if their authors had been compelled to condense them. Succinctness is not an enemy to clearness, it is rather its ally.

Hard writing, easy reading. Some writers have great facility and can turn off pages while others are toiling over a paragraph. Even the same author may write rapidly at one time and slowly at another according to mood. In writing, as in most things that are worth while, painstaking labor and patient plodding mingled with midnight

oil bring the results. Under the inspiration of a moment, something excellent may be dashed off but perspiration is more dependable than inspiration. Some writers maintain that they must write rapidly if they would give swing and style to their product. It is probably best to write as rapidly as one can but nothing should be allowed to go out from the shop till it is as good as we can make it. An article may be written in an hour or two but many gallons of midnight oil may be used in rewriting and polishing it.

Woodrow Wilson could pound out immortal documents on his typewriter but for the most of us a pencil and scratch pad are the best tools. With these we can write and rewrite, scratch out and interline. We can look back over the pages and see whether we have repeated the same expression. We can cut off the top part of a page and paste it at the bottom and move our sentences around till we get them in the proper order. When one is dictating one often wonders whether a thing has been said explicitly enough and goes ahead and says it again without striking out the first. With pencil and paper one can go back and strengthen a doubtful statement. Of course it takes time to write and rewrite but it is better to spend ten hours and produce a page that will be effective than to turn off ten pages that will fail.

The road which costs the most labor to build is the one on which it is easiest to ride.

Writing a Journal Article

The first thing to do is to lay out the article, *i.e.* to decide on its divisions and their order. Write one division at a time. Two plans are in use, corresponding to the two plans for introducing evidence and argument in legal cases. In our courts the witnesses are all heard and then the lawyers make their speeches using the testimony that has been introduced, while the Greeks started out with the arguments calling the witnesses from time to time to back up statements made in the speeches.

According to one plan the headings commonly used have been 1) introduction, 2) historical, 3) theoretical, 4) materials, 5) apparatus, 6) methods of experimenting, 7) results, 8) discussion of results, 9) conclusions, 10) summary. Of course some of these sections, particularly if they are short, may be combined. Thus " introduction " and " historical " or " materials " and " apparatus " or " discussion " and " conclusions " may be run together. In this arrangement everything in the first part leads up to the " results " which are made to tell their full story and are then discussed and worked up into " conclu-

sions," the " summary " being tacked on for the benefit of abstractors. This arrangement is the logical one and is the most satisfactory for those who are interested enough to read the whole article.

There are many who would like to know the new facts but who have not the time to go into all of the details as to how they were established, or to put it another way, suppose a chemist has the time to peruse ten complete articles but would rather read the high lights of fifty. To save the trouble of looking at the end of the story to see how it all turned out, as we frequently do when we read novels, the conclusions are put at the beginning.

We then have an order like this: 1) introduction, 2) historical, 3) theoretical, 4) conclusions, 5) experimental, 6) summary. The " historical " and " theoretical " are made brief and lead directly to the " conclusions " under which heading all of the facts that have been ascertained are fully set forth. Thus the reader learns why the work was undertaken, gets its historical and theoretical background and learns all of the facts in three or four pages of print. If he is especially interested in the topic and wishes to repeat some of the experiments or doubts some of the conclusions, he delves into the " experimental."

In the " experimental " section, which is frequently printed in small type to save space in the journal, are put all of the other headings given above, " materials," " apparatus," " methods " and " results." Even historical details may be put here along with the experimental data. The usual summary is appended.

There is a strong tendency now to adopt the second arrangement as being the most suited to the busy reader. Even if this form is to be used in the journal it is usually better for the chemist to write up his material in the order first given and then transpose the section containing the " conclusions."

A practical way to write is to select from the many well written articles in the journals one on a similar line of investigation and adopt it as a model.

The arrangement and style of an article should be appropriate to the journal in which it is intended to publish it. Normally one publishes in the journal one reads most. Most journals furnish " style sheets " which give the forms of abbreviation, arrangement of references, etc., preferred by that journal. Trouble will be saved if these are followed.

Drawings. Sketches of apparatus, diagrams and curves are required for many articles. These must be made on proper paper with India ink. When these get into the journal they may be only two or

three inches square, but it is customary to draw them on any convenient large scale. The plates are made photographically and are reduced at the same time to the desired size. It is much easier to draw the originals on a large scale and minor imperfections tend to vanish on reduction.

The beginner usually forgets that if the height of his figure is reduced 4:1 the width of his lines will be correspondingly reduced. All lines must be drawn very heavy or they will nearly vanish. Lettering also must be large and heavy.

Curves. Coördinate paper printed with a light blue or violet ink can be used for drawing curves. The ruling on this paper does not take in the photographic process so only the curves are reproduced. The axes of reference and any other coördinate lines that are to appear in the print are traced with ink.

Another way is to draw the curves on ordinary coördinate paper then fasten this at one edge to the drawing paper and transfer the points of the curve by sticking holes with a fine point. The curves are then sketched in with pencil, inked, and the pencil marks erased.

Writing Reports

About half of the chemists in this country are employed in the industries, a large number of them are on research. Some of the larger companies are spending millions each year for research while many smaller corporations are spending proportionate sums. Possibly ten million dollars a year is spent for industrial research in the United States and what is gotten in return is reports. All of the information garnered by the keen-eyed toilers in the laboratory must be condensed into these reports. It is from these reports that the executives draw their information as to what is possible and on them they base their decisions as to what it is best to undertake. These reports must supply the information needed by the engineers in planning new equipment and must guide the purchasing department as to what and how much to buy. These reports accumulated from year to year constitute the most real assets of our industries, their most active working capital. Reports constitute one of the most serious problems in any industrial organization.

A report differs from a journal article in that it is directed partly, at least, to business men who do not understand chemistry and also that the conclusions usually relate more or less to recommendations for spending money on plants or processes. There is not the demand for condensation that oppresses us in writing a journal article since

the cost of typewriting a few extra pages is negligible. There is rather a desire for completeness and insistence that no experimental details be left out.

What follows is quoted from a paper by Dr. Tanberg.[6]

The report is divided into the following sections:

(1) Introduction
(2) Summary and conclusions
(3) Experimental
(4) Literature.

" This particular arrangement is preferred because it makes easier the consideration of the report by those men who are not interested in reading, or who do not have time to read, the sections concerned with the details of the work and the literature. The first two sections should always therefore be written with the understanding that they should cover the essential features and results of the investigation without making necessary any reference to the other sections of the report. Attention is called to the reason for the above arrangement because chemists too often follow this same order in *preparing* their reports, whereas it is undoubtedly easier and more conducive to a well-rounded, concise report to write the ' Experimental ' and ' Literature ' sections first and the ' Introduction ' and ' Summary and Conclusions ' sections last, and then rearrange the four sections in their proper order.

The most important requirements of the first and second sections are clearness and brevity; but care should be taken that neither section is made brief by the omission of essential facts. The important requirement of the third section is that it shall cover all details of the experimental work in such a way that any well trained chemist will find it possible by following the report to repeat the work and to duplicate the results.

" Before submitting a report, a chemist should try to place himself in the position of a reader to whom the subject is entirely new in order to make sure that he has not made use of such expressions, abbreviations, or symbols as are intelligible only to those especially familiar with the subject. Examples of such practices, such as the use of the word ' soda ' where caustic soda is meant, or the use of ' D. M. A.' for dimethylaniline, will readily occur to any one who has written or read chemical reports.

" It is best to use ruled paper, and a good margin should be left

[6] Suggestions relative to the preparation of formal reports by A. P. Tanberg, Director of Experimental Station, E. I. du Pont de Nemours and Co., written for guidance of the du Pont Company's chemists. Used by permission.

so that inserts may be made if necessary. If any one of the sections or subdivisions of a section ends in the middle of a page, start the next section on a new sheet so that additional matter may be added if necessary. Suggestions of this kind, many of which are made below, if followed will result in a great decrease in the time at present required to get out reports.

"**Introduction.** The introduction should include statements as to the object of the work and the reason for it, with a brief explanation of the nature of the compound or process under investigation, its origin, etc.; and the statements should be made clear by chemical formulas or equations. Reference should be made in the introduction to previous reports on the same subject or to any report which has been found of assistance in the work. In many cases a description should be included of the 'prior art': that is, any previously published process which has been used as a basis for experiments described in the report.

"**Summary and Conclusions.** This section should include a brief description of the process or processes investigated, a description of the conditions which are recommended as best, a brief statement as to why these conditions are selected and the general effect of a departure from these conditions, a statement of the results which may be expected by following the recommended conditions (including yields in percent of the theoretical, quality of product, etc.), and the total cost of the materials required per pound of product based on a detailed estimate of this total cost which is included in the 'Experimental' section. It may occasionally be necessary to include in this section some discussion of apparatus, especially when this phase of the subject has an influence on the selection of the method recommended.

"**Experimental.** It is usually best to subdivide the 'Experimental' section under the following headings, especially in reports of investigations along the lines of organic chemistry:

"*Apparatus:* If the investigation is carried through the stage of semi-works scale experiments, or if the report described works operations, this subdivision is especially important. The apparatus should be described in detail so that it may be duplicated and operated at some future time, if it becomes necessary, by some one previously unfamiliar with the work. If the apparatus has been purchased, the name and address of the manufacturer should be given; if built at the Experimental Station, all details as to materials of construction, sizes, etc., should be included. Wherever possible, descriptions of apparatus should be accompanied by blue-prints. If the investigation

has been confined to laboratory work and the apparatus has been ordinary laboratory apparatus, a simple statement to this effect will ordinarily be sufficient, although such details as the type of column used in distillations, etc., should be included. If, as is often the case, the experiments have shown certain apparatus to be not altogether suitable, this point should be brought out and recommendations made for improving it.

"The sucess or failure of experiments often depends upon such details as the kind of gasket used in an autoclave, and in general no detail should be considered too insignificant to be included. It is easier to cut matter out of a report than to put it in.

"*Materials:* Very often our investigations require certain materials which vary widely in quality or which are difficult to obtain. The subdivision on 'Materials' should therefore include a description of all materials used as to purity, sources of supply, cost, etc. If it has been necessary to synthesize raw materials, the process used and the results obtained should be described. If the materials are ordinary, easily obtainable supplies, it is sufficient to state whether they were c.p., commercial, etc., or to give the melting points, boiling ranges, etc. If materials were purified before use, the process of purification should be described. If the investigation included experiments with different grades of the same material, the different grades should be described, and assigned brief names which may be sed in the tables of numerical data included in the subdivision headed 'Experimental Details.'

"*Analyses and Tests:* All tests and methods of analysis used in connection with the work should be carefully described, or if a standard method has been used, reference should be made to the book or journal in which a description of it may be easily found. The description of each method should be accompanied by some statement as to its merits or shortcomings.

"*Experimental Details:* The numerical data recorded in connection with each experiment should be assembled as far as possible in tabular form. The tabulated data should include all conditions of the experiments such as quality of materials (unless the quality of materials was the same in all the runs), the duration of runs, the temperatures used, the pressures (if the pressures varied), the yields in percent of the theoretical, the conversions in percent (unless the main raw material is completely utilized), the quality of the product (expressed, if possible, in some simple manner, such as the melting point, boiling range, etc.), etc. It is usually advisable to include a

column headed 'Remarks,' to be used in recording any unusual features of the experiments. It is just as important to include data with regard to experiments in which poor or negative results are obtained as it is to record successful experiments. If the laboratory notebooks have been properly kept the same experiment numbers can be used in the final report so that reference can be made if necessary to the original record. It might be well to call attention here to the importance of carefully kept notebooks, not only from the standpoint of report writing, but from other standpoints of equal or even greater importance. Original records are often required in interference suits in patent cases, and granting of priority may depend entirely on whether the chemist has kept a clear, properly dated record of his experiments at the time they were carried out. A carelessly kept notebook is inexcusable, not only because it may mean an actual loss of valuable rights, but because it represents an actual waste of time in digging out the data for the purpose of preparing a report.

"In making up tables of numerical data, use paper large enough so that the headings may be written without crowding and without using unusual abbreviations. If the tables cover more than one page, see that the headings on the several pages are identical and the columns placed in the same order. Especial care should be taken to make figures clear so that the tables may be copied by the stenographer without errors. Use decimals wherever possible instead of fractions, and under no circumstance use a decimal in one place and a fraction in another. If a certain figure consists of a fraction of a unit, as for example seventy-five hundredths of a percent, write it 0.75% and not .75%, in order to avoid mistakes in copying. Remember that ditto marks should not be used for repeating figures. Put the units, such as per cent, grams, hours, etc., at the head of the columns, instead of repeating them after each figure. The proper abbreviation for 'grams' is 'g.'; for 'cubic centimeters,' 'cc.' Some of these points may not seem worthy of mention, but most of them are a constant source of trouble and annoyance in revising and approving final reports.

"It is often necessary to precede a table of numerical data with an explanation of the headings of the columns. This should be done whenever there seems to be a chance that the headings will not be clear.

"It is also advisable to put at the beginning of the subdivision on 'Experimental Details' a description of the general procedure

followed, such as the method and order of mixing the ingredients used, the method of working up or purifying the crude product, the method of heating, etc.

"**Discussion of Results.** The tables of numerical data should be followed by as full a discussion of the results as is considered necessary, covering such points as the reasons for the selection of a certain procedure, the proper grade of materials to be used, recommendations for plant equipment, causes of poor results in unsuccessful experiments, etc. This section should, in general, include any discussion, explanation or statement of theory necessary to connect the 'Summary and Conclusions' and 'Experimental' sections.

"**Estimate of Materials Costs.** This subdivision should include, in detail, figures upon which the estimated materials costs given in the 'Summary and Conclusions' section are based. These estimates should, of course, be made as accurate as possible, and it may be necessary in some cases to obtain figures from the main office. In any case, the source and data of the figures used should be given.

"For the sake of uniformity, the estimates of cost should be arranged in a table under the following headings:

MATERIALS REQUIRED	WEIGHT REQUIRED PER LB. OF PRODUCT	MATERIALS COST	
		per lb.	Total
	lbs.		
Aniline	0.987	$0.11	$0.109
H_2SO_4, 94%	2.350	0.008	0.019
etc.			

"The totals of the fourth column will then give the total costs of materials required for the preparation of one pound of product. If the process involves the recovery of valuable materials, a second set of columns should be given under the following headings:

MATERIALS RECOVERED	WEIGHT RECOVERED PER LB. OF PRODUCT	RECOVERED MATERIAL	
		Value per lb.	Total Value
.....	.....	.....	.....

"By subtracting the totals of the fourth column of this second set from the totals of the corresponding column of the first set, the net materials costs per pound will be clearly shown.

"It is believed that an estimate presented in this way is the most easily accessible for any recalculations made necessary by changes in the market.

"**Literature.** The section on 'Literature' is probably the most elastic part of a formal report. In some cases literature may be wholly lacking. In other cases the investigation may have been preceded by a careful review of the literature which has been submitted to the Chemical Director as a separate report or memorandum. In the latter case it is often necessary only to refer to this review and to give the date and file of the letter of transmittal. In most cases this should, however, be followed by a list of the references, or at least of the most important references. In cases where the experiments have been based on special information received in the form of a letter or report, a statement should be made as to where this information may be found. If information has been obtained from an article or patent not easily available in our libraries or files, a brief abstract of the reference should be given. In general, this section should contain all information necessary for a complete review of the subject under investigation, or if a complete review of the literature has not been made, such information as will serve as a starting point for a complete review."

Preparation of the Manuscript

Whether it be an article for publication or a report for private circulation and filing, it must be typewritten. Fortunate is the author who has a typist to transform his scrawl into fair copy. The typist can do much more work and produce far better results if she receives full coöperation from the author. Miss Wareheim, who copied this book from long-hand, advises us as follows:

"Your article for the journal must be typewritten.[7] Perhaps you will type it yourself. If so, some of the suggestions given here will be helpful, but they are of more value if you ask a typist to do the work for you. Before putting your manuscript into final form read the requirements of the particular journal in which you expect to publish the article with regard to margin, spacing, number of copies, abbreviation for references, with manner of writing and inserting.

[7] Written for this book by Miss Esta Wareheim, Librarian and Stenographer of the Chemistry Department, Johns Hopkins University.

When you have noted these requirements write *your manuscript* in harmony with them.

"It is hardly necessary to remind you to write on one side of the paper only. Whenever possible write with ink on *ruled* paper. This is especially important if your writing is hard to read, and if you are inclined to crowding. *Yellow glazed* paper and a very hard or very soft pencil should never be used. It is next to impossible for a typist to produce a perfect copy from a poorly written manuscript. Since it is your desire to have your typewritten copy neat and accurate, it is to your interest to see that your manuscript is written legibly and in such form that it is easily understood and read. Corrections require much time and make a mussy manuscript.

"In this connection it is well to remember that the typist is compelled to read from copy at a distance of 18 or 20 inches from the eye instead of the normal reading distance of 12 or 14 inches. Writing which is quite legible at the ordinary distance often takes on a different aspect at the greater. Consider too that since typewriting is a mechanical operation and one of the 'desiderata' is speed, the typist reads individual letters without reference to their connection. The fingers are directed by reflex stimuli not by conscious thought and so if the eye signals 'e' instead of 'i' because the writer omitted the dot, the 'e' will be written before the brain flashes 'it is a mistake,' a slightly longer time being required to place it in its context.

"Write your headings, formulae, equations, tables and diagrams in such a way that there can be no doubt as to just how you wish them to appear. Make clear distinctions between capitals and small letters, especially in equations, formulae and descriptions of diagrams. On preparing tables remember that the number of letters or spaces to a line is limited to about 70 for ordinary type and typewriter carriage, a few more for 'élite' type on some machines. If the number of figures or letters plus the allowance for spaces between columns is greater than 70, the table will have to be typed in two parts.

"Especial care should be used to write clearly proper names and unfamiliar words as well as figures and symbols. Never take it for granted that the typist will know what you mean. Make your meaning so clear that she cannot misinterpret, then you will not be disappointed with the results."

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