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Nobel Prize
Winners
in
CHEMISTRY
1901-1950

19 0 1

JACOBUS HENRICUS VAN'T HOFF

(1852-1911)

*"For the discovery of laws of chemical dynamics and
of osmotic pressure."*

BIOGRAPHICAL SKETCH

JACOBUS VAN'T HOFF WAS BORN ON AUGUST 30, 1852, IN Rotterdam. Although he decided to study chemistry, his interests were not limited to it; mathematics, poetry, and medicine attracted him strongly. His studies began in Delft, Holland, and were concluded in Utrecht, in 1874. In between, he spent a few months in Bonn, where the noted chemist Kekule took little notice of him, and in Paris, under Adolphe Wurtz, where his first scientific conception took shape. Upon his return to Utrecht, he published an eleven-page booklet: "Proposal to extend the presently used chemical structural formulae into space, connected with a remark concerning the relationship between optical rotation and chemical constitution of organic compounds." In this "proposal" he started from older attempts to represent atoms by geometric symbols and combined them with Kekule's teaching of a quadrivalent carbon atom. J. Wislicenus (Wiirzburg) gave his enthusiastic endorsement to van't Hoff's theory that substances which show optical rotation do so because of the asymmetric structure of their molecules, and the University of Amsterdam thereupon offered him its professorship in chemistry.

During twenty years (1877-1896) in Amsterdam van't Hoff enriched science by the development of other relationships—those between the physical and chemical concepts of energy, and those between the botanical-physiological concepts of osmosis and the chemical state of substances in solutions. For this work he received the Nobel Prize for 1901, the first year in which the Nobel Prizes were distributed.

Tired by twenty years of teaching, van't Hoff accepted a call to the Prussian Academy of Sciences in 1896, where he concentrated his investigations on the salts found in the mines of Stassfurt, the richest source of potassium salts used as fertilizers.

In his student days, van't Hoff had been more interested in theories than in experiments. Later he learned to combine these two sources of chemical progress.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Now, what physical chemistry in the latest period has done, or has claimed to do, did not consist in the introduction of new apparatus or of a new method of observation. The most recent development of physical chemistry has been characterized rather by the establishment of comprehensive principles which fertilize the whole foundation of the science, and promise to furnish nourishment for a large part of the chemistry of the future.

"There are in the main two foundations on which the recent development of physical chemistry rests: the extension of the law of Avogadro, and thermodynamics.

"The extension of Avogadro's principle consists in this: that for a given substance the osmotic pressure is equal in value to the gaseous pressure, provided the temperatures and concentrations, that is the quantities in unit volume, are the same. From that it follows immediately that two solutions of different bodies containing equal numbers of molecules in equal volumes, provided they are at the same temperature, exercise the same osmotic pressure. Not

* From J. H. van't Hoff, *Physical Chemistry in the Service of the Sciences* (Chicago: University of Chicago Press, 1903). Lectures delivered June 20-24, 1901, at the University of Chicago.

only so, but when the molecular weight is known, this pressure, like the gaseous pressure, can be calculated with ease.

"[This law] claims strict accuracy, both in the original and extended forms, only when the dilution is very great, or, in other words, only under conditions which cannot be realized practically. Nevertheless, at dilutions which correspond to that of atmospheric air, that is to say, in the case of gases at a pressure of one atmosphere and in the case of solutions of an analogous concentration (about one-tenth normal *), the deviations in most cases where the principles find application are insignificant.

"So much for the first principle, which . . . is often named the theory of solutions. The second concerns the application of thermodynamics, and particularly of conservation of work or energy, and of the Carnot-Clausius principle to chemical questions.

"It may be applied by carrying out so-called reversible cycles of operations or by the introduction of abstract physical conceptions and mathematical functions, such as entropy, as is done by physicists like Gibbs, Planck, and Duhem. I am convinced that, for the chemist, the first form, in which reversible cycles are employed, is the most advantageous. Briefly stated, a cycle consists in a series of changes in course of which the original condition is reached. Thus, for example, we permit ice to evaporate, condense the vapor to water, and then freeze the water."

CONSEQUENCES IN THEORY AND PRACTICE

Van't Hoff's work represents the culmination of a century of endeavors to find a scientific meaning of affinity, the "love" and "hatred" between chemical substances. He brings together, in mathematical form, heat of reaction, chemical affinity, and temperature of chemical change. The mathematical form has the alluring qualities of being simple and universal, but both these qualities are obtained by the substitution of an idealized symbol for the realities of chemical substances and behaviors. The completely reversible cycle of chemical change, for which he once gave the

* A solution containing one tenth of an equivalent weight in one liter—e.g., 4.6 grams of ethyl alcohol per liter.

dissecting and cooking of a goose as the opposite example, is one of van't Hoff's idealizations. He was conscious of the fact that the ideal state, which lends itself to such mathematical treatment, does not exist. Nevertheless, he showed its amazing consequences. Relationships are revealed between vapor pressure and concentration of solutions. The influence of the dissolved substances on raising the boiling point and lowering the freezing point of the solvent can be calculated. The way in which chemical reactions change direction by changing temperature or pressure can be foreseen. The word "equilibrium" becomes just another expression for relationships of compounds and their components to controllable conditions. These relationships provide a general knowledge of what to do in order to achieve specific, desired results. The practical value of idealized theory thus becomes apparent, and van't Hoff demonstrated this practical value in his last years through his work on inorganic salts.

19 0 2

EMIL FISCHER

(1852-1919)

"For his syntheses in the groups of sugars and purines."

BIOGRAPHICAL SKETCH

EMIL FISCHER WAS GRADUATED, AT THE HEAD OF HIS CLASS, FROM the Gymnasium of Bonn in 1869. He could have joined his father's thriving and expanding business in real estate and industrial enterprises, but he desired to study physics and mathematics. Sickness (stomach disorders) prevented him from entering the University of Bonn until Easter of 1871. Dissatisfied with the poor conditions of instruction there, he changed to Strasbourg, where his teachers were Adolf von Baeyer in chemistry, Paul Groth in mineralogy, and Adolph Kundt in physics.

Fischer received his doctor's degree in 1874. In the year following, he published his discovery and investigation of a new organic compound which was to form a powerful tool in his later research on sugars. He called it phenyl-hydrazine. Hydrazine was the name he gave to an inorganic compound of two nitrogen atoms linked with each other and each carrying two hydrogen atoms. In the new substance, one of the hydrogens was replaced by the phenyl group, which is benzol minus one hydrogen atom. He found that phenyl-hydrazine combines with simple sugars, such as glucose or fructose, and that these new derivatives of the sugars could be easily purified and identified.

Fischer continued this investigation after he joined Baeyer in Munich in 1875, and pursued it when he went to Erlangen in 1882, to Wurzburg three years later, and finally to Berlin in 1892. The general plan of work was always carefully prepared, but unexpected results were followed through to wherever they might lead. Such strategy was successfully applied to the investigation of uric acid, which in snakes is a normal product of excretion but which in humans causes certain kinds of rheumatism. Uric acid had interested Baeyer; Fischer expanded the latter's research, and in doing so he elucidated the chemical structure of caffeine and theobromine. These substances can be regarded as derived from a basic substance which he called purine, which means the pure basic material of uric acid (*purum uricum*).

This investigation was rounded out in 1899. When Fischer received the Nobel prize for his sugar and purine research in 1902, he had already begun the systematic approach to the chemistry of proteins. Again combining premeditation with alertness to the unexpected, and with the help of numerous students and assistants from many countries, he developed new and improved methods of analysis. When the basic constituents of some proteins had been found and their chemical structure cleared up, synthesis according to plan followed. Thus he built large molecules of proteinlike substances in well-controlled steps. His summary, given in a lecture in 1906, led to exaggerated reports that the riddle of life had been solved; Fischer deplored them.

Fischer's work on tannins was barely concluded when the First World War broke out. Contrary to widespread assumptions, the production of chemicals and food materials had not been organized in Germany when the war started. Emil Fischer, the recognized leader of German chemistry, was charged with creating such organization.

Depressed by the loss of two of his three sons, one of them a war casualty, and by the outcome of the war for Germany, Emil Fischer succumbed in 1919 to his old ailment.

DESCRIPTION OF THE PRIZE-WINNING
WORK *

This following passage from Fischer's Nobel Prize lecture is selected because it shows the connection between his researches on sugar and on proteins. The basic connection was his interest in the chemistry of life. Glucuronic acid, which, in the laboratory, is produced by oxidizing the carbon number six to convert its alcoholic group into an acidic group, occurs as a product of metabolism in animals. Plants and animals have special chemical tools by means of which they produce chemical changes of sugars and their derivatives, such as the glucosides. These tools are the ferments. They are delicate in stability and sensitive to changes of temperature. They are easily destroyed by certain chemical influences which act like poisons, yet they are sufficiently powerful under their own conditions to convert many thousand times their own weight of physiologically specific substances. Emil Fischer had tried to correlate this exceptional activity with the intricate arrangement of the atoms in a molecule of sugar or protein.

The most common sugars consist of chains of six carbon atoms, each connected with an oxygen atom. Five of these oxygen atoms carry hydrogen besides, in the linkage which is characteristic of alcohols. One of the oxygens, however, is in the more reactive form in which it exists in formaldehyde. The carbon atom carrying this aldehydic oxygen is usually numbered as one. Combinations of this atom with alcohols are designated as glucosides. The alcoholic groups connected with the other carbons can be reacted with acids, like all alcohols, and esters are thus formed. Fischer found that certain tanning substances contain gallic acid thus esterified with sugars. Again, he confirmed his analysis by synthesis.

"Now the synthesis in this field has been directed to new problems. Of the simple derivatives of glucose, the physiologist knows glucuronic acid best, since the animal organism makes use of this acid to render harmless such poisonous substances as carbolic acid, chloral, and turpentine. Its configuration, its relationships to glucose, and a likely explanation for its production in the body were easily made clear by the synthetic method. Great difficulties were found with glucosamine, a peculiar nitrogen-containing substance which was first obtained from lobster shells, but which we now

* Translated from *Les Prix Nobel en 1902*.

know is widely distributed in the animal world. Its synthesis, which I succeeded in carrying out only in the last few weeks, shows that glucosamine is an intermediary between glucose and the alpha-amino acids and thus forms one of the long-sought bridges between carbohydrates and proteins.

"Of general interest are the results obtained with the glucosides, which are widely spread over the plant world and which are to be considered as compounds of sugars with other substances of very different natures. Examples are amygdalin, a component of bitter almonds, or salicin, a fever remedy of the older medicine.

"Ferments, called enzymes in more recent times, have so prominent a place among the chemical tools of the living organism that it can be postulated that the chemical conversions in the living cell are predominantly bound to the collaboration of the enzymes. The examination of the artificial glucosides has shown the result that the effect of the enzymes depends to a high degree upon the geometric structure of the subjected molecule, that the two must fit together like lock and key. Consequently, the organism can carry out very special chemical conversions with their help, such as can never be achieved with the common agents."

CONSEQUENCES IN THEORY AND PRACTICE

The chemical tool for sugar research, which Emil Fischer discovered seventy-five years ago, is still being used. Many modifications have been made, and a number of further applications have been found. Glucuronic acid, in which he was so greatly interested, is acquiring new prominence because of remarkable medicinal effects which have recently been observed.

Ribose is one of the carbohydrates which Fischer investigated purely for its systematic role, as an example of a specific configuration of atoms in a sugar molecule. This sugar has since been recognized as an important part of highly active substances in blood and muscle. It is there combined with adenine, one of the purines. This compound is perhaps the only really valuable substance in the famous Liebig's meat extract, a concentrated "soup" for which high nutritional value had been claimed.

Fischer himself drew practical conclusions from his scientific work by synthesizing veronal (1904) and, together with Joseph von Mering, introducing it as a hypnoticum. The patent for which they applied included the whole series of barbiturates.

By the addition of hydrogen to the aldehydic oxygen in simple sugars the oxygen is reduced to an alcoholic group. This reaction was of considerable help in elucidating the fine structure of sugars. It has become an industrial operation for producing sugar alcohols on a large commercial scale. Certain compounds of these alcohols with acids (esters) are widely used as wetting agents and detergents.

Since Fischer's work on sugars and purines is closely related to that on proteins, it may also be mentioned here that the amino acids, which he found to be the building stones of the proteins, are being produced and used for special nutritive purposes.

19 0 3

SVANTE AUGUST ARRHENIUS

(1859-1927)

'For his theory of electrolytic dissociation.'

BIOGRAPHICAL SKETCH

SVANTE ARRHENIUS WAS BORN IN WIK, NEAR LAKE MALAR, Sweden. He learned to read at the age of three and became ardently interested in mathematics and physics in early school years. Although he began his studies at the University of Uppsala, he carried out his actual research work in Stockholm, returning to Uppsala to receive his doctor's degree in 1884.

At that time the physicist, Friedrich Kohlrausch, in Wiirzburg, had developed a convenient method for measuring the electrical conductivity of solutions. The electrical conductivity of a length of metal could be easily determined. When two pieces of the same metal are immersed in pure water, current will not pass from one to the other; in this respect pure water is an insulator. The addition of a salt or an acid to the water imparts conductivity to it. It had been assumed that the electric current was transported through the solution by becoming attached to the molecules of the dissolved substance, which were thereby split into carriers of positive and negative electricity. Faraday had given these carriers the name "ions," and those substances which form ions for the transportation of electric current were called "electrolytes."

When Arrhenius measured the change of conductivity caused by changing the concentration of an electrolyte, he arrived at the con-

elusion that a part of the electrolyte is active and another inactive as a carrier for electricity. As dilution increases, the active parts increase, until at infinitely great dilution all of the electrolyte is split, or dissociated, into the active parts. This dissociated state exists independently of the passage of electricity through the solution. Arrhenius' dissertation of 1884 interested Wilhelm Ostwald (see pp. 37-41) so greatly that the latter went to Uppsala to discuss the meaning and application of these results with Arrhenius. Swedish academic circles thus learned of the importance of this work and facilitated the academic career of their young countryman. Travels brought him to Ostwald in Riga, Kohlrausch in Wiirzburg, Boltzmann in Graz, and van't Hoff in Amsterdam. The electrolytic theory took definite shape in these years. It formed the basis for extended work, but Arrhenius, having become professor in Stockholm, in 1891, was chiefly interested in the widest application of the fundamental theory of chemical reactions. E. A. von Behring and Paul Ehrlich arrived at an explanation for the action of poisons (toxins) in the living organism and its ability to neutralize their effects by elaborating antitoxins. Arrhenius sought the general, or physical-chemical, laws which govern organismic changes. He found that these reactions follow the same laws as all "ordinary" chemical reactions, and that there is no essential difference between those in the test tube and those in the human body. Here again was a theme which could have captured all his energies, but Arrhenius' curiosity reached out further. He developed a theory of cosmic physics, in which the pressure of light-radiation sent particles, even germs of living organisms, through space and thus connected all the world.

In 1905 Arrhenius assumed the directorship of the Nobel Institute for Physical Chemistry, a fitting position for a man of such universal interests.

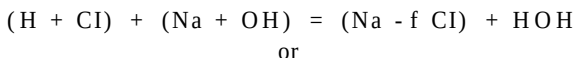
DESCRIPTION OF THE PRIZE-WINNING WORK *

"The conductivity depends upon the velocity with which the ions (Zn and SO_4) of the molecules (ZnSO_4) are carried through the liquid by the electric force, i.e. the potential difference. If this potential difference remains constant, the velocity depends only on the friction that the ions in their passage through the liquid exert on the surrounding molecules. As these, at higher dilutions, are only water molecules, it might be expected that the conductivity would remain constant and independent of the dilution if it be supposed that all the molecules, ZnSO_4 , take part in the electric transportation. As experiment now teaches us that the molar conductivity increases with dilution, even if this is very high (1,000 molecules or more of water to one molecule of ZnSO_4) we are led to the hypothesis that not all, but only part of, the ZnSO_4 molecules take part in the transportation of electricity. This part increases with the dilution in the same proportion as the molecular conductivity k . The limiting value k^{00} is approached at infinite dilution and corresponds to the limit that all molecules conduct electricity. The conducting part of the molecules I called the active part. It may evidently be calculated as the quotient $k : k^{00}$.

"The most far reaching conclusion of the conception of active molecules was the explanation of the heat of neutralization. As this is much more easily understood by means of the theory of electric dissociation I anticipate this for a moment. According to this theory, strong acids and bases, as well as salts, are at great dilution (nearly) completely dissociated into their ions, e.g. HCl in $\overset{+}{\text{H}}$ and $\overset{-}{\text{Cl}}$,
 NaOH into Na and OH , NaCl into Na and Cl . But water is (nearly) not dissociated at all. Therefore the reaction of neutralization at mixing a strong acid, e.g. HCl , with a strong base, e.g.

* From Arrhenius' Nobel Prize acceptance lecture, published in the *Proceedings of the Royal Institution of Great Britain*, Vol. XVII (1904), pp. 553 ff. Given in his own English version. He uses as examples zinc sulfate, ZnSO_4 ; hydrochloric acid, HCl ; and sodium hydroxide, NaOH . The ions are indicated by placing a -J- or — sign on top of the symbol for the substance.

NaOH, both in great dilution, may be represented by the following equation:



"The whole reaction is equivalent to the formation of water out of both the ions, H and OH, and evidently independent of the nature of the strong acid and of the strong base. The heat of any reaction of this kind must, therefore, always be the same for equivalent quantities of any strong acids and bases. In reality, it is found to be 13,600 calories in all cases. This thermal equality was the most prominent feature that thermo-chemistry had discovered.

"It was now asked in what respect the active state of the electrolytes differs from the inactive one. On this question I gave an answer in 1887.

"The active molecules of the salts are divided into their ions. These are wholly free and behave just as other molecules in the solutions.

"An important role is played by the water which may be regarded as a weak acid or base. By its electrolytical dissociation it causes the hydrolysis of salts of weak acids and bases.

"For physiological chemistry this question is of greatest importance, as is confirmed by the experimental results of Sjogvist and others. Also for the explanation of volcanic phenomena, the concurrence between water and silicic acid at different temperatures has found an application."

CONSEQUENCES IN THEORY AND PRACTICE

At first Arrhenius found considerable resistance to his theory. It was argued that sodium is known to decompose water violently, and that chlorine has a penetrating odor. How could these elements be contained in a quiet, odorless solution? The answer was connected with the electrical charge. Not sodium itself but its positively charged atoms, not chlorine itself but its negatively charged atoms

were present in these solutions of sodium chloride. This split of one molecule into two parts explained the fact that the osmotic pressure was found to be much higher than calculated for the combined substance, and the change of osmotic pressure with dilution indicated the relative amount of dissociation. The chemical activity of all strong acids in dilute solutions turned out to be the same in Ostwald's measurements; the new theory accounted for that. The hydrogen ions were the active part in chemical reactions as they were in electrical conductivity. Soon the discovery of the electron as the unit of electrical charge further justified Arrhenius' theory. The positive ion of sodium now became an atom which had lost one of its electrons to the chlorine atom, which thus acquired its negative charge.

Facts of many kinds—heat of reaction, color, osmotic pressure, and chemical affinity—thus found a unifying explanation. In the enthusiasm about the beauty of this idealization the discoverer of the theory and his immediate followers went too far. The influence of the nature of the electrolyte made itself known in refined experiments. The idealization might be acceptable for very highly dilute solutions; for more concentrated ones it oversimplified things. The theory proved to be a first approximation to the real behavior of electrolytes. Its basis, however, the dissociation of acids, bases, and salts into parts of opposite electrical charge, remained fruitful. The exchange of electrons became the fundamental explanation of chemical bonding.

19 0 4

WILLIAM RAMSAY

(1852-1916)

*"For the discovery of gaseous, indifferent elements
in the air and the determination of their place in the
periodic system."*

BIOGRAPHICAL SKETCH

SIR WILLIAM RAMSAY DESCRIBED THE ORIGIN OF HIS INTEREST in chemistry as follows: "My grandfather on my Father's side, William Ramsay, was a chemical manufacturer in Glasgow; he came from a long line of dyers, who carried on their work in Haddington, a small country town in the east of Scotland. He was the first, I believe, to distill wood for the production of pyroligneous acid; and he purified it by 'torrefying' the acetate of lime formed by its neutralization, and distilling with oil of vitriol. He also was the first to manufacture bichrome; and for many years, he and his partners, the Messrs Turnbull, made Turnbull's Blue.'

"My mother's Father was a medical man, practicing in Edinburgh. He was the author of a series of textbooks, one of which was entitled 'Colloquium Chymica.' Hence I inherited the taste for Chemistry from my ancestors on both sides of the family."

Ramsay obtained his doctor's degree in Tübingen in 1872 for work on ortho-toluic acid and its derivatives, carried out under Rudolf Fittig (1835-1910). For more than ten years, after his return to Glasgow and as professor in Bristol (1880), he continued organic chemical research. The new developments in physical chem-

istry found his active interest, particularly after he took over the chair in inorganic chemistry at the University College, London, in 1887. When Lord Rayleigh described the discrepancy in specific gravities between nitrogen from ammonia and nitrogen from air, Ramsay was prepared to suggest an answer. ". . . in my copy of Cavendish's life, published by the Cavendish Society in 1849, opposite his statement that on passing electric sparks through a mixture of nitrogen with excess of oxygen, he had obtained a small residue, amounting to not more than 1/125th of the whole, I find that I had written the words 'look into this/ It must have been the latent memory of this circumstance which led me, in 1894, to suggest to Lord Rayleigh a reason for the high density which he had found for atmospheric nitrogen." The result of his "looking into this" was the discovery of a new element, argon, which he soon followed with the discovery of neon, krypton, and xenon. He identified as helium the gas developed from certain uranium minerals when they were treated with acids.

The great experimental skill developed in this research later permitted Ramsay (with R. Whytlaw-Gray) to separate and weigh tiny quantities of the radioactive gas emitted by radium and to determine its atomic weight. His ideas about radioactive decomposition [*Elements and Electrons*, London, 1912) were not generally accepted at that time.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Helium, like argon, is a gas, sparingly soluble in water, withstanding the action of oxygen in presence of caustic soda, under the influence of the electric discharge, as well as of red-hot magnesium. Like argon, the ratio of its specific heat at constant volume to that at constant pressure shows it to be a monatomic element, the atom and the molecule being the same; and its density was found both by Langlet and myself to be nearly 2; it is therefore the lightest gas known, with the exception of hydrogen. These properties in common made it evident that helium and argon belong to the same

* From *Les Prix Nobel en 1904*.

natural family; and it was also obvious that there must exist at least three other elements of the same class; this is evident on inspection of the periodic table where the following elements are in apposition:

hydrogei> (?)	Fluorine	Chlorine	Bromine	Iodine
1	19	35.5	80	127
helium	?	Argon	?	p
4	20	40	82	132
lithium	Sodium	Potassium	Rubidium	Caesium
7	23	39	85	133

"While 15 litres of argon were being purified, Dr. Hampson had succeeded in perfecting his machine; and he placed at our disposal about a litre of liquid air. After 'playing' with it, so as to familiarize ourselves with its properties, there remained in the vessel about 100 cubic centimetres. I suggested that we should allow this portion to evaporate almost entirely away, and that we should collect the last 10 cubic centimetres by allowing it to boil off into a gas-holder. This was done; and after removal of oxygen and nitrogen, there remained 26 cubic centimetres of a gas which showed, besides the spectrum of argon, a bright yellow and a bright green line, of wavelengths 5571, and 5570.5 respectively. Although the density of the new gas, which we named 'krypton,' or 'hidden,' was found to be only 2.25, we conjectured that, when purified, it would turn out to be forty times as heavy as hydrogen, implying the atomic weight 80, for our earlier experiments established the fact that, like argon, its molecular and atomic weights were identical.

"An account of this discovery was communicated to the Royal Society on June 3rd, 98; and no time was lost in examining the argon by liquefaction and fractional distillation. On June 13th, we were able to announce that the lower boiling portions of the 15 litres of argon contained a gas which we called 'neon,' or 'new.' It showed a spectrum characterized by a brilliant flame coloured light, consisting of many red, orange, and yellow lines.

"In September 98, the discovery of another gas was announced; it was separated from krypton by fractionation, and possessed a still higher boiling point. We named it 'xenon,' or the 'stranger.'

"The amounts of neon and helium in air have once been meas-

ured; the former is contained in air in the proportion of 1 volume in 81,000; the latter, 1 volume in 245,000. The amounts of krypton and xenon are very much smaller, not more than 1 part of krypton by volume can be separated from 20,000,000 of air; and the amount of xenon in air by volume is not more than 1 part in 170,000,000."

CONSEQUENCES IN THEORY AND PRACTICE

Helium, neon, argon, krypton, and xenon are alike in their chemical inertness. The discovery of this group of "noble gases" was in part predicted from the regularities of the periodic system, and it enlarged this system by an entire new group. It is the group of elements with valency 0. These exceptional chemical elements which have no chemical reactivity formed the perfect transitions from the end of one period to the beginning of the next in the periodic system. These new links in the chain of elements permitted the erection of a theory of atomic structure which Niels Bohr began to build in 1913.

The methods developed by Ramsay and his associates became increasingly important as work with minute quantities of substances was required in radioactivity and biochemistry. On the other hand, the principles on which the separation of the gases were based soon found applications in industrial production. Helium, neon, and argon did not remain chemical curiosities of which only one or two scientific laboratories possessed a small supply. Helium, of which rich sources were discovered in mineral deposits, replaced the dangerously inflammable hydrogen as the gas with which balloons were filled. Helium or argon forms the protective gas under which magnesium, aluminum, and stainless steel are welded; because of the inert gas atmosphere, the metals are not oxidized in spite of the high temperature. Neon, argon, and krypton are used in fluorescent lamps and in "neon" signs. The electric discharge through neon, its mixtures with mercury, or traces of krypton produce intense light at low temperature and with high efficiency.

19 0 5

ADOLF VON BAEYER

(1835-1917)

"For his researches on organic dyestuffs and hydro-aromatic compounds"

BIOGRAPHICAL SKETCH

ADOLF BAEYER WAS BORN IN BERLIN. HIS FATHER, AT THAT TIME a captain in the Prussian General Staff, later became a general and after retiring was made president of the Geodetic Institute of Prussia. His mother was the daughter of a famous jurist and literary historian. Baeyer's inclination to chemistry was developed at an early age. In his lecture on indigo synthesis, in 1900, he mentioned that as a boy he was greatly impressed with "the strange behavior and peculiar odor" of the dyestuff from the East Indies. Berlin had no laboratory for instruction in chemistry; Baeyer therefore went to Heidelberg, in 1856, to study under Bunsen. There he met Friedrich August Kekule (1829-1896) and, after being graduated in 1858 with a thesis on organic arsenic compounds, followed him to Ghent, Belgium. Baeyer considered himself a self-taught chemist, although Bunsen introduced him to laboratory practice and Kekule to theory.

In 1860, Baeyer found a modest position at the Trade Academy (Gewerbe Institut) in Berlin. Uric acid became his main theme of research; he derived from it an interesting acid which he called barbituric acid, because his best girl friend's name was Barbara. * Barbituric acid and other products of the oxidation of uric acid

supplied him with analogies by means of which to distinguish between the products obtained from indigo. This king of all dye-stuffs contains oxygen. It was therefore to be considered as the oxidation product of a "mother-substance" which Baeyer stated to be a substance somewhat related to aniline and called indole. It was relatively easy to obtain an oxidized indole, called oxindole, and the next more highly oxidized indole, called isatin, from indigo. Comparing indole with benzene, oxindole could be considered analogous to phenol, although there is an important difference between them. Phenol is derived from benzene by substituting hydroxyl for the hydrogen of one of the six carbon atoms. The adjacent carbon atom, called the ortho-position, is also substituted in indole. Without having to depend on indigo, isatin could be prepared from a benzene molecule in which one carbon had its hydrogen replaced by a nitric acid residue (nitro-group), and the adjacent carbon atom by a residue of acetic acid, or its neighbor in the chemical system, propionic acid.

Baeyer's work on indigo synthesis extended over the years 1865 to 1883. From 1872-1875 he was at the newly organized University of Strasbourg and from 1875 on he was in Munich as the successor to Liebig. He continued to teach and to experiment into his eightieth year. Chemistry to him was experimenting with one of the simplest of tools, the test tube. Richard Willstätter used to tell the story that Baeyer once invited Emil Fischer to inspect a wonderful apparatus he had built—it consisted of a test tube held in a clamp over a small Bunsen burner. With this tool Baeyer disclosed fundamental relationships for products of benzene and terpenes (hydro-aromatic substances), for dyestuffs, and for a new class of compounds in which oxygen displays four instead of the conventional two chemical valences.

Fundamentally, Baeyer was averse to theorizing. However, he developed two very general concepts which remained valid, although with subsequent refinements. One of these concepts referred to the basic chemical reactions by which plants convert carbon dioxide and water into sugars and starch; the other was derived from van't Hoff's theory of the tetrahedron as the model for the carbon atom with its four valences. When carbon atoms combine to form rings, according to Baeyer's theory, the angle of these

valences is more or less deflected, and a "strain" is set up which is decisive for the degree of stability of these structures.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"In order to find the mother-substance of indigo I started from oxindole, which contains only one oxygen atom and behaves like a phenol. The problem of producing indole was thus reduced to that of converting phenol into benzene. This analogy was of little use, since this task, simple as it is in theory, can be solved only in ways which are forbidden for the easily resinifying oxindole. After a half year's fruitless work I talked of my predicament with my colleague Stahlschmidt, who, at that time, lectured on technical chemistry at the Trade Academy. I learned from him that zinc dust, which had formerly been used only as a paint ingredient, now served as an industrial reducing agent. I immediately tried an experiment; but oxindole withstood all efforts, until, in despair, I heated it with zinc dust in a combustion tube to near glowing temperature. Now (1866) I finally had in my hands the mother-substance of indigo, and I rejoiced the way Emil Fischer may have done when he found purine, the mother-substance of uric acid, after fifteen years' work.

"Artificial indigo first saw the light of the world in 1870, when I, together with my student Emmerling, converted isatin into the dyestuff by reaction with phosphorus-containing trichloride of phosphorus. At that time, isatin was obtainable only from indigo, so that the synthesis became a complete one only when I produced isatin artificially from phenyl-acetic acid, on June 6, 1878.

"In 1878 and '79 I developed further the method of indigo synthesis from isatin and found that it is based upon the reduction of isatin chloride, which is formed first. The method also permitted the production of substituted indigoes, such as dibromo, tetrabromo, dinitro, and diamido indigo, and gave particularly high yields for tetrabromo indigo.

* From the lecture "Ueber Die Geschichte der Indigo Synthese" (On the History of Indigo Synthesis), in *Berichte der Deutschen Chemischen Gesellschaft* (1900); reprinted in *Gesammelte Werke* (Braunschweig: Friedr. Vieweg und Sohn. 1905), Vol. II.

"In the course of experiments to obtain ortho-nitro-phenyl-acetaldehyde I boiled the bromide of ortho-nitro-cinnamic acid with alkalis and I observed that some indigo was formed thereby. The further prosecution of this discovery led to the discovery of ortho-nitro-phenyl-propionic acid and to the production of indigo from it. The first patent on this invention was filed on March 19, 1880, and the first scientific publication appeared in December of the same year."

CONSEQUENCES IN THEORY AND PRACTICE

Baeyer's long, systematic work on the constitution and synthesis of indigo began with the accidental finding of a method for getting at the core of certain compounds. This method of heating the compound with finely divided zinc metal proved to be of great importance. At Baeyer's insistence, Carl Graebe applied the method to the famous red dyestuff alizarin and thus discovered its chemical skeleton. An industry for manufacture of alizarin grew out of this laboratory finding in a short time, and the success of this enterprise encouraged chemical manufacturers to persist in the costly efforts toward the technical synthesis of indigo. On the basis of Baeyer's work, but not following his *specific* steps, indigo was finally made from aniline and acetic acid. The impact on industry and agriculture was world-wide. In Bengal, over a half million acres of land had been devoted to the culture of the indigo plant. At the end of the nineteenth century, the chemical factory began to replace the indigo plantation, and the German chemical industry, staffed partly with men who had received their chemical training from Baeyer, came into its dominant position.

In 1883, Baeyer announced that he had determined the place of every atom in the molecule of indigo. A correction was found necessary forty years later. Baeyer's clear picture of the dyestuff molecule, as modified by other chemists, made possible the production of valuable derived coloring substances. Among them was an indigo derivative containing two atoms of bromine, a purple dyestuff which is identical with that secreted by a snail (*Murex brandaris*). This was the purple used in antiquity.

19 0 6

HENRI MOISSAN

(1852-1907)

"For his research on the isolation of the element fluorine and for placing at the service of science the electric furnace which bears his name!"⁹

BIOGRAPHICAL SKETCH

HENRI MOISSAN WAS BORN IN PARIS AND STUDIED CHEMISTRY there while working in a pharmacy. His chemistry professor, Deherain, helped to convince him that his field was pure science. After publishing a thesis on the respiration of leaves in the dark, in 1876, he turned to inorganic chemistry, at that time a somewhat neglected branch. First he investigated a peculiar form of iron, a finely divided powder which ignites readily and is, therefore, called pyrophorous. On June 20, 1888, after four years of work, he announced the isolation of the element fluorine. This was only the beginning of his research on this highly reactive and poisonous element. He investigated organic compounds from methyl-fluoride to carbon tetrafluoride, and showed that the hexafluoride of sulfur is nearly as stable and inert as nitrogen, N

All this was done under rather poor laboratory conditions. No wonder Moissan later declared that fluorine may have shortened his life by ten years. Later, as professor at the Faculty of Sciences of the University of Paris (from 1900 on) he obtained better facilities.

In 1892 Moissan found a particularly practical arrangement for

an electric oven in which he made calcium carbide without any thought of its industrial possibilities. Tungsten metal and a steel in which carbon was replaced by boron were prepared in this oven.

From geological studies Moissan concluded that diamond must have been formed from a liquid or pasty mass. "This carbon must have crystallized under the action of a strong pressure; the iron was in a liquid state and owing to rapid cooling, due to some cause, there was a violent contraction of the mass and the carbon passed from a density of 2 to 3.5, giving the diamond."

In his later years Moissan devoted much time to his book on inorganic chemistry, which comprises five large volumes.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"Our first model of electric furnace, shown to the Academy of Sciences in December 1892, was of quicklime. It was composed of two well-dressed blocks of lime laid one on the other. The lower piece contained a longitudinal groove through which passed the two electrodes, and in the center was a small cavity which served as a crucible. The depth of this cavity can vary and contains a layer several centimeters thick of the substance which is to be heated by the arc. It is also possible to introduce into this cavity a small carbon crucible containing the material to be heated. The upper block is slightly hollowed in the part which lies directly over the arc, and as the intense heat of the current soon melts the surface of the lime and gives to it a high polish there is formed a dome which reflects all the heat on the small cavity which contains the crucible.

"This apparatus is a reverberatory electrical furnace with movable electrodes. This last point is of importance, as the moving of the electrodes gives an easy means of establishing the arc, for lengthening or shortening at will, and in a word, it materially simplifies the conduct of the experiment.

"Many experimenters have hitherto used the electric arc to obtain high temperatures, but those who have preceded me have not

* The first excerpt is from *The Electric Furnace*, translated by Victor Lenher (Easton, Pa.: The Chemical Publishing Co., 1904), pp. 5 and 21; the second is from *Smithsonian Institution Reports for 1897*, pp. 268 ff.

separated the electrolytic action of the current from the thermal.

"The models of furnaces have allowed us to readily attain temperatures bordering on at least 3,500° C.

"Synthetic diamonds: 200 grams of soft Swedish iron cut into cylinders, 1 cm to 2 cm in length and about 1 cm in diameter were placed in a carbon crucible and completely covered with sugar carbon. It was heated from three to six minutes with a current of 35 amperes at 60 volts. The cover of the furnace was raised and, with the hand wrapped with a cloth, the edge of the crucible was grasped with a pair of iron tongs and was plunged into a vessel filled with cold water. The crucible and contents remained at red heat for several minutes, with evolution of bubbles of gas which burst at the surface without taking fire. The temperature fell rapidly, the light faded and the experiment was ended."

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"I prepared at first pure anhydrous hydrofluoric acid, and found, as shown by Faraday and by Gore, that it was a nonconductor.

"In order to make the acid a conductor there is added to it before the experiment a little of the dried and fused fluohydrate of potassium fluoride, about 2 grams to 10 cubic centimeters of the liquid. Under these conditions the decomposition takes place continuously, and we obtain at the negative pole a gas which burns with a colorless flame, and which has all the characteristics of hydrogen. At the positive pole there is a colorless gas of a very disagreeable, penetrating odor, resembling that of hydrochlorous acid, and irritating to the mucous membrane of the throat and the eyes. The new gas is endowed with very energetic properties—for instance, sulfur inflames upon contact with it.

"Crystallized silicon, even when cold, kindles immediately upon contact with the gas, and burns with much brilliancy, sometimes giving off sparks."

CONSEQUENCES IN THEORY AND PRACTICE

The most spectacular of Moissan's successes was the artificial production of diamond. He developed the method which, as he

speculated, nature had used, the rapid cooling of molten iron containing carbon, so that a hard outer shell kept the still liquid iron under high pressure while it was cooling. Interesting as this discovery was, his work on calcium carbide and fluorine had much greater practical consequences. In the year of his death, 1907, the production of calcium carbide already totaled about 165,000 tons. Twenty years later, this figure was about quadrupled, and many more products made in the electric furnace had been added—aluminum, phosphorus, metal alloys, silicon carbide (carborundum).

The development of fluorine as a chemical raw material was much slower. Fluorinated polymers of ethylene came into use in 1939; teflon, a tetra-fluoro-ethylene plastic, followed in this country shortly afterward. Methane, reacted with chlorine and fluorine, found wide application as a refrigerant (freon). Fluorinated acetic acid, a deadly internal poison, is the basis for a rodenticide.

19 0 7

EDUARD BUCHNER

(1860-1917)

*"For his biochemical researches and his discovery of
cell-less fermentation"**

BIOGRAPHICAL SKETCH

EDUARD BUCHNER BEGAN STUDYING CHEMISTRY IN HIS NATIVE Munich, but he had to interrupt his studies for financial reasons. His older brother Hans helped him to return to science in 1884. Chemistry, under Baeyer, and botany, under Carl von Nageli, were his main subjects, and Hans directed his attention to problems involved in fermentation. Buchner's first publication, which appeared in 1885, dealt with the influence of oxygen on fermentations. He received his doctor's degree in 1888 and continued to work as Baeyer's assistant for five years. Fermentation was still his favorite subject, although his superiors told him that nothing new could be expected in the direction which he intended to follow, grinding yeast finely to see what the destruction of the cell structure would do to its activity. Hans Buchner at that time hoped to obtain medically valuable proteins from the digestion of bacteria with alkalies; he was therefore also interested in cell juices pressed out of bacteria or yeast. Eduard Buchner continued experiments with such juices during vacation from his teaching of analytical and pharmaceutical chemistry in Tübingen. In 1896 he made a fundamental observation. He had used concentrated sugar solutions to act as a conserving agent in pressing juice from yeast, and

he discovered that a slow fermentation started; he soon established that no yeast cells were present in this fermentation, and that yeast killed by treatment with alcohol and acetone still functioned to ferment sugars. In January 1897 he reported on alcoholic fermentation without yeast cells. He found much opposition to his views. A professorship at the agricultural college in Berlin, in 1898, gave him the means to extend his biochemical work. Buchner died as a major in the German army in Rumania.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"Yeast cells are to be considered as small bubbles containing a semiliquid mass, called protoplasm, which is enclosed in a relatively tough cell membrane.

"As far as the microscope shows, these membranes are uniform, yet they must be pierced by fine holes through which food materials enter and excretions leave the cell.

"In order to investigate the cell content, it was necessary to remove the membrane and the plasma tube. Chemically active solvents or the use of high temperatures had to be avoided. Finally, it was important to complete the process in the shortest time to exclude changes during the preparation.

"Marie von Manassein, in Wiesner's institute in Vienna, showed perhaps for the first time in 1872 that the difficulties in grinding yeast disappear when quartz powder or sand is added. Then the pestle finds the required points of attack. In this manner micro-organisms were ground by Adolph Mayer, A. Fernbach, and Amthor, before I started my experiments.

"When yeast is mixed with an equal weight of quartz sand and one fifth of its weight of kieselguhr, the initially dust-dry mass can be ground within a few minutes by placing it into a large mortar and using a heavy pestle on a long handle. The mass becomes dark gray and plastic, like dough.

"When this thick dough is wrapped in strong cloth and put into a hydraulic press, a liquid juice seeps out under a pressure which is

* Translated from *Les Prix Nobel en 1907*.

gradually increased to 90 kg./sq. cm. (about 1250 lbs./sq. in.). Within a few hours, 500 cu. cm. of liquid can be obtained from 1000 grams of yeast, so that considerably more than half of the cell content is pressed out.

"Summarizing the results of all our experiments, it can be stated that the fermenting activity has been separated from the living yeast cells.

"The cells of plants and animals appear, with increasing distinctness, as factories where in separate workshops all kinds of products are produced. The foremen in this work are the enzymes."

CONSEQUENCES IN THEORY AND PRACTICE

Fermentation has always held a prominent position in chemistry. The ability of a small amount of "ferment" to convert large quantities of plant materials was considered by the alchemists as the model for the action of the magic philosophers' stone. That the action is exerted by a living organism was a discovery of the nineteenth century. This finding was used as a strong argument in favor of vitalistic theories which attributed fermentation to the action of a force which is the exclusive property of life. In opposition, the mechanistic theories claimed that the molecules of sugars are torn apart by vibrations accompanying the decomposition of organisms. The extreme positions were held to be irreconcilable. They broke down only slowly, as the experimental approach showed that neither vitalism nor mechanism had a definite meaning unless the problem were stated in specific relationships. When Buchner declared that he could ferment sugar without living cells, he felt that he had disproved vitalism. The situation was similar to that which had existed just about sixty years before Buchner's discovery, when the German chemist Wohler stated that he could make urea without a living organism. Vitalists did not give up their position then, and they defended it against Buchner now. Max Rubner, a leading physiologist, offered direct proof that fermentation was a vital, not an enzymatic, process. The proof consisted in the fact that tannin has an inhibiting effect on juice or macerated cell suspensions but does not prevent the fermentation caused by living cells. For

Eduard Buchner, the explanation was obvious: the enzyme which causes fermentation, zymase, does not leave the living cell and cannot, therefore, be damaged by tannin. Zymase goes into solution only after the cell has been killed or its wall disrupted, and then tannin can act upon it.

The new concept of fermentation as an enzyme action stimulated the manufacturing of yeast and alcohol. It was a great advantage to understand that nutritive substances, such as ammonia salts and peptones, and even phosphoric acid salts, contributed to the formation of zymase, and that this beneficial enzyme had to be protected against destruction by a digestive enzyme, peptase. The mystery of yeast action was dissolved into controllable factors. Further investigation disclosed that the number of actions and factors was much greater than had been foreseen.

19 0 8

ERNEST RUTHERFORD

(1871-1937)

"For his investigation into the disintegration of the elements and the chemistry of radioactive substances."

BIOGRAPHICAL SKETCH

ERNEST RUTHERFORD WAS BORN TO ENGLISH PARENTS IN Nelson, New Zealand. His excellence at school won him a scholarship to the University of New Zealand, which at that time had seven professors and about 150 students. For his B.Sc. in 1894 he prepared an investigation of "the magnetization of iron by high-frequency discharges." In this work, which was stimulated by the new discoveries of Hertz, Rutherford showed, among other things, that the magnetization is only skin deep and can be removed from a magnetized iron needle by dissolution of the surface layer in acid. He won fame with his oscillators and detectors at J. J. Thomson's laboratory at Cambridge, where he began work in 1895. Three years later, J. J. Thomson recommended him for the professorship at McGill University, Montreal. Frederick Soddy joined Rutherford there in work on radioactive disintegrations. From 1907 on he was professor at the University of Manchester. The competition with Ramsay in London was sometimes rather keen. During the First World War, Rutherford applied his experiences with oscillators and detectors to problems of submarine detection. In 1919 he discovered the "artificial disintegration" of nitrogen; under the

impact of alpha radiation, nitrogen, although an element, is decomposed and hydrogen is formed.

Rutherford felt very strongly that professors should spend more time thinking than doing, and he urged the professional men "to take an interest in the administration of their own affairs or else the professional civil servant would step in—and then, the Lord help you!"

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The study of the properties of the alpha rays has played a notable part in the development of radioactivity and has become instrumental in bringing to light a number of facts and relationships of the first importance.

"While the evidence as a whole strongly supported the view that the alpha particle was a helium atom, it was found exceedingly difficult to obtain a decisive experimental proof of the relation. If it could be shown experimentally that the alpha particle did in reality carry two unit charges, the proof of the relation would be greatly strengthened. For this purpose an electrical method was devised by Rutherford and Geiger for counting directly the alpha particles expelled from a radioactive substance. The ionization produced in a gas by a single alpha particle is exceedingly small and would be difficult to detect electrically except by a very refined method. Recourse was had to an automatic method of magnifying the ionization produced by an alpha particle. For this purpose it was arranged that the alpha particles should be fired through a small opening into a vessel containing air or other gas at a low pressure, exposed to an electric field near the sparking value. Under these conditions the ions produced by the passage of the alpha particles through the gas generate a large number of fresh ions by collision. In this way it was found possible to magnify the electric effect due to an alpha particle several thousand times.

"This method was developed into an accurate method of counting the number of alpha particles fired in a known time through

* From *Les Prix Nobel en 1908*.

the small aperture of the testing vessel. From this was deduced the total number of alpha particles expelled per second from any thin film of radioactive matter. In this way it was shown that 3.4×10^{14} alpha particles are expelled per second from one gram of radium itself and from each of its alpha ray products in equilibrium with it.

"We have seen that there is every reason to believe that the alpha particles, so freely expelled from the great majority of radioactive substances, are electric in mass and constitution and must consist of atoms of helium. We are consequently driven to the conclusion that the atoms of the primary radioactive elements like uranium and thorium must be built up in part at least of atoms of helium. These atoms are released at definite stages of the transformation at a rate independent of control by laboratory forces.

"It is very remarkable that a chemically inert element like helium should play such a prominent part in the constitution of the atomic system of uranium and thorium and radium. It may well be that this property of helium of forming complex atoms is in some way connected with its inability to enter into ordinary chemical combinations."

CONSEQUENCES IN THEORY AND PRACTICE

At one time the smallest particle of matter, which could not be further divided, was represented as a solid ball. This model, drawn from experiences with visible and weighable materials, was useful in explaining certain chemical reactions. An entirely different model became necessary when optical and electrical properties had to be considered. First of all, the atom had to be divided into positively and negatively charged electric parts. One of the next steps was to account for the negatively charged part as a number of small points compared with the relatively large extent of the positive part of the atom, as J. J. Thomson did. The decay of radioactive elements caused Rutherford to think in terms of more definite structures. The disintegration of these elements is accompanied by the emission of positively charged helium atoms and negatively charged particles of almost no mass, the electrons. The atom, con-

eluded Rutherford, is not a last unit of matter. It is composed of an arrangement of subatomic particles. In radioactive elements this arrangement is unstable. The unstable atom reaches stability by unloading itself of particles which can form the atoms of other elements. These particles come out of a positive nucleus, in which the mass of the atom is concentrated, and out of an atmosphere of electrons which surround the nucleus like a number of shells, in distances which are vast compared with the size of the nucleus.

The apparatus for counting the alpha particles, which Rutherford developed together with H. Geiger, made it possible to derive the mathematical formulation of the decay process. The basic assumption was similar to that used for any chemical reaction, which presupposes that the number of atoms reacting, or decaying, per unit of time (second or minute) is proportional to the number of existing atoms.

The concept of the atom as consisting of a small, very heavy nucleus surrounded by electrons circulating at specific, relatively wide distances from the center, was further developed by Niels Bohr and many others. It is the fundamental concept of nuclear physics. The mathematical formulation of the disintegration of atoms made it possible, in many cases, to identify substances (by correlation with their characteristic radiations) which existed in quantities too small to permit any other identification. The time within which the number of originally present active atoms is reduced to half, the "half-life" of a radioactive element, can readily be derived from the basic mathematical relationship.

19 0 9

WILHELM OSTWALD

(1853-1932)

"For his work on catalysis and on the conditions of chemical equilibrium and velocities of chemical reactions/"

BIOGRAPHICAL SKETCH

WILHELM OSTWALD BECAME INTERESTED IN CHEMICAL EXPERIMENTATION at an early age. As an eleven-year-old he made his own fireworks and contraptions for transparent pictures. At the University of Dorpat he read Julius Thomsen's measurements of the heat connected with chemical reactions. The thought suddenly occurred to him that any other property could serve as well to indicate the actual conditions of the substances in a watery solution. The simplest property, within the means of his instrumentation, appeared to be density. He was so convinced of the general importance of the method that he created the name "volume chemistry" to designate a field of equal rank with thermochemistry.

These investigations, together with measurements of another physical property, optical refraction, served Ostwald as the theme of his doctoral thesis (1878). His driving goal was to learn more about the nature of chemical affinity. As full professor in Riga, from 1882 on, he widened the search for an answer with investigations in chemical dynamics, the measurement of the rate at which chemical change takes place. Calculations based on the velocity with which acids split esters into alcohols and organic acids led to

the same relative values for affinity as did previous results obtained volumetrically.

These special investigations were undertaken from the point of view of their general meaning. They offered a new basis for all of chemistry and required a rewriting of much of its contents. Ostwald had scarcely undertaken the task of writing a new textbook, in 1883, when Svante Arrhenius' work on affinity and electrical conductivity and van't Hoff's views of the analogy between solutions and gases opened still wider horizons. Ostwald welcomed them enthusiastically.

At the University of Leipzig, where he began his work in 1887 with two students, Ostwald soon created a focal point of the new field of physical chemistry. Physical-chemical experiments were instituted as a regular part of the chemistry curriculum. Analytical chemistry was lucidly described by Ostwald from the new standpoint in his book of 1893. About sixty years before this time, Berzelius had introduced the name "catalysis" for the action of substances which influence chemical reactions without taking part in them. Through Ostwald's work this strange action now became accessible to measurement and connection with affinity. The most important practical consequence was his discovery, in 1901, of a method for obtaining nitric acid by burning ammonia in the presence of platinum.

Ostwald's relations with administrators and colleagues at the University of Leipzig deteriorated. His resignation from the professorship in 1906 gave him freedom to devote himself to his many general interests—painting and the measurement of colors, the organization of science and international cooperation, the role of energy ("energy is everything"), and the monistic structure of universal life. For several years he published "monistic Sunday sermons" every Sunday.

Of his many publications Ostwald liked his book on electrochemistry (1895) best; it was the only one of his books which saw only one edition.

In the early years of his career, somebody gave him the advice not to generalize too quickly. He never heeded this advice. As the creator of a new system in chemistry, and in other respects, Ostwald may be called the German Lavoisier.

DESCRIPTION OF THE PRIZE-WINNING
WORK *

"Initially I was exclusively busy with the task of finding a quantitative measure for the concept of chemical affinity, which is so important and was then so indefinite, and I had considered . . . using both static or equilibrium methods and dynamic methods based upon the measurement of velocities of reactions.

"I remembered from the literature of organic chemistry, which I had to follow for my teaching job, several cases where esters had been split by strong acids, like hydrochloric or sulfuric acid, in concentrated form into acid and alcohol. In order to be able to work with aqueous solutions I turned to those esters which are sufficiently soluble in water, and I still remember today the joyful excitement with which I pursued the increase in acidity in a solution of the common acetic ether with hydrochloric acid added (1883).

"This is not the place to describe the development of the problem of affinity and, specifically, the measurement of the 'strength' of acids which at that time were the intended objects of my investigations. Suffice it to say that the connection between static and dynamic methods really came to light and the 'strength' was recognized as a general property of the specific acid, independent of the nature of the particular reaction. Soon afterward the inversion of sugar was investigated from the same point of view, with the immediate result that this classical reaction also was quantitatively determined by the same property of the acids, as had been expected on the basis of previous results.

"Thus, the close connection between the strength of the acids and their catalytic action came undeniably to the fore, and I searched for other acid catalyses so as to study this relationship more broadly. These experiments showed, in contrast to previous ones, that the reacting substances themselves exerted an action of measurable velocity upon each other, even before the foreign substance was added. At present, one would say that the reaction was

accelerated by the presence of hydrogen ions already existing in the reacting substances; at that time such explanation was not yet possible, since the work was carried out in 1887, just before the theory of free ions had been formulated and communicated to the world. Thus, I was irresistibly urged to the conclusion that the essence of catalysis is not to be sought in the origination of a reaction but in its acceleration. In the corresponding publication of 1888 I gave the proper mathematical formulae explicitly; they are perhaps implicitly contained in the methyl acetate paper of 1883."

CONSEQUENCES IN THEORY AND PRACTICE

The inversion of sugar is a change of saccharose (beet or cane sugar) under the influence of small amounts of acids. The optical rotation is reversed in this reaction, and the crystallizable sugar is converted into a noncrystallizable mixture of its components, glucose and fructose. The reaction, dreaded by the manufacturer of crystal sugar, was deliberately carried out for the production of an artificial honey. On the basis of Ostwald's work on catalysis it was found that the inversion could be obtained at high sugar concentrations with a minimum of acid.

Ostwald rediscovered and redefined catalysis. Although his original intention was purely and very broadly scientific, he saw the great importance of its technical applications. He failed in his attempts to produce ammonia by a catalyzed reaction of its elements, nitrogen and hydrogen, but he succeeded in achieving its catalytic oxidation to nitric acid. The catalytic ammonia synthesis became a reality soon afterward. Sufficient raw material for the new nitric acid process thus was available. The extent and fury of the First World War would have been impossible without this method of manufacturing a basic material from which all important explosives are derived.

The revived interest in catalysis was a powerful stimulant for the chemical industry. Mineral oil is converted into improved motor fuel and natural gas into a host of chemicals by catalytic processes. The production of synthetic methanol, developed with the aid of a pupil of Ostwald's by catalytic combination of carbon

monoxide and hydrogen, had profound repercussions in the old wood distillation industry.

The measurement of physical properties to gain insight into rate and extent of chemical reactions has become the basis for the design of industrial plants.

OTTO WALLACH

(1847-1931)

"For his initiative work in the field of alicyclic substances."

BIOGRAPHICAL SKETCH

OTTO WALLACH WAS BORN IN KONIGSBERG, EAST PRUSSIA. HE received his doctor's degree at the University of Gottingen, in 1869. From there, he went to Bonn, where Kekule offered him a "scientific artist's life." One of the advantages of Bonn, for him, was the proximity to the Dutch and Belgian art treasures. After a brief interlude in the chemical industry he returned to Bonn, where he became extraordinary professor in 1876 and was in charge of instruction in pharmacy from 1879 on.

In his courses of instruction Wallach had to give lectures about ethereal oils and became interested in this subject. Kekule told him that these oils are mixtures which no chemist could hope to disentangle. Nevertheless, Wallach began a systematic study of this whole class of pharmaceutically used oils. They were routinely made by distillations of selected plant leaves, petals, bark, and fruits. He separated pure substances from them by careful redistillations, identifying the products by their physical properties and following transitions between some of them. Most of these substances were similar in their basic structure, a ring of six carbon atoms which differed from that present in benzene by a higher hydrogen content. The ring, or cycle, of most of these "terpenes"

is formed of saturated carbon atoms, like those in the "fatty," or aliphatic, substances. They were, therefore, called alicyclic. Wallach continued these studies in Gottingen, from 1889 to 1915, the year in which he retired to devote himself more exclusively to his interests in art.

"Wallach's highest ideal was not theory, not the formula, but carefully and reliably performed experiment." *

DESCRIPTION OF THE PRIZE-WINNING WORK†

"By appropriate conversion of the hydrocarbons into oxygen-containing compounds, and conversely of oxygen-containing compounds into hydrocarbons, we succeeded in connecting by transformations a very great number of the terpene-like substances which occur in ethereal oils and to trace the genetic relationships of the several compounds.

"Pure empiricism reigned in the manufacture of ethereal oils up until about twenty-five years ago. The fragrant components of plants were merely distilled and the distillate brought to market. In this process, the products obtained were not always handled rationally, in the absence of all knowledge of their chemical nature, and the doors were wide open for every kind of falsification. When this was carried out with only some skill, the consumer was helpless against it.

"This has now been changed thoroughly. Thanks to the possibility of distinctly characterizing the single components of the ethereal oils, we now possess a sufficient analytical system to detect falsifications and to guard against them. Besides purely chemical methods we have, for these examinations, the physical properties such as boiling point, density, refraction, and optical rotation, which have been determined during the work on terpene compounds with utmost care.

"Another progress consists in our having learned to evaluate

* Leopold Ruzicka in his biography of Wallach in the *Journal of the Chemical Society* (London), 1932, p. 1596.

† Translated from *Les Prix Nobel en 1910*.

correctly the single parts of the oils on the basis of our new knowledge.

"Among the oils which are particularly preferred as odoriferous materials, the most common are mixtures of substances which cooperate in producing the effect. Unexpectedly it was found that in especially fragrant natural oils there are, in very small quantities, extremely bad-smelling substances which nevertheless are also decisive for the odor. These are products of the decomposition of plant proteins, closely related to those which are formed from animal proteins during digestion and which cause the repugnant odor of the feces. Among these substances is indole. This is found, for example, as Dr. Albrecht Hesse has proved . . . as a characteristic component in oil of jasmine.

"Insight of this and similar kind, which could be attained only through the progress of scientific research, has been utilized particularly in that branch of the industry which is concerned with the artificial composition of perfumes.

"We now are in a position to prepare substances which are analogues of natural odoriferous materials. We are able to predict, within certain limits, that synthetically produced substances of specific molecular structure will have the odor of peppermint, camphor, caraway, or lilac.

"Already the chemical synthesis of camphor is a complete success, whereas up to now we were nearly completely dependent upon the production of the island of Formosa and the good will of the Japanese.

"One would think that plants of the same genus would all produce the same, or at least similar, oils, but this is not at all the case.

"Thus, botanically closely related plants form entirely different products, and conversely, unrelated plants sometimes form the same products."

CONSEQUENCES IN THEORY AND PRACTICE

Wallach solved the task which Kekule had considered hopelessly difficult, by separating pure substances out of the ethereal plant dis-

tillates and showing chemical relationships among them. A common principle of chemical structure was thus discovered which linked substances such as those contained in turpentine with isoprene, the simple hydrocarbon obtained by depolymerizing natural rubber. A unity of chemical building principles in nature became visible. It attracted later investigators, among them Leopold Ruzicka (see pp. 162-165).

Wallach did not base his conclusions on syntheses, as Tiemann and Semmler did, and he was not interested in the industrial applications of his scientific findings. Former students of his brought the scientific foundation to the industry of perfumery.

Wallach's elucidation of the terpenes was of considerable help in the scientific development of an apparently quite unrelated field. The biologically important carotinoids were found to contain a terpenelike structure as a part of their more complicated molecule.

1 9 1 1

MARIE SKLODOWSKA CURIE

(1867-1934)

"For her services to the advancement of chemistry by the discovery of the elements radium and polonium, by the isolation of radium and the study of the nature and compounds of this remarkable element."

BIOGRAPHICAL SKETCH

MARIE SKLODOWSKA WAS BORN IN WARSAW, THE CAPITAL OF that part of Poland which was then under Russian domination. She received most of her education in science from her father. In 1891, an invitation from her elder sister enabled her to go to Paris to continue her studies. She met Pierre Curie, professor at the school of physics of the Sorbonne, in 1894 and married him the following year. From measurements of radiation she concluded, in early 1898, that pitchblende might contain an element which is much more radioactive than uranium. Then began the systematic search for this element in cooperation with her husband and with Andre Debierne; in 1902 radium was prepared as a pure salt. The following year, she received her doctor's degree from the Sorbonne and, together with her husband, one half of the Nobel Prize for Physics.

After Pierre Curie died in a traffic accident, in 1906, Mme. Curie was offered his chair at the Sorbonne. A radium institute was organized for her work in 1914. During the First World War she was active in hospital work and in nurses' training.

When she received the gift of the women of America, one gram

of radium, in 1921, she was already suffering from the effects of exposure to radium rays, which gradually attacked her nerves and blood.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"We gradually developed a new method of search for new elements, a method which is based upon radioactivity considered as an atomic property of matter. Every chemical separation is followed by a measurement of the activity of the products obtained. This gives an account of the way in which the active substance behaves from the chemical point of view. This method has found general application; it is somewhat analogous to spectral analysis. Owing to the great variety of radiations emitted, the method should be refined and extended so that it permits one not only to discover radioactive substances but also to distinguish them from one another with certainty.

"By the use of the indicated method it has been established that it is actually possible to concentrate the activity by chemical operations. We have ascertained that there are in pitchblende at least two new radioactive bodies; one of them, which accompanies bismuth, has received the name polonium, while the other, which accompanies barium, has been called radium.

"We had the conviction that the substances which we had discovered were new chemical elements. This conviction was based solely on the atomic character of radioactivity. From the chemical point of view, however, everything in the beginning looked as if our new substances were pure bismuth or pure barium respectively. It was essential to demonstrate that the radioactivity is bound to traces of elements which are neither bismuth nor barium. These hypothetical new elements, therefore, had to be isolated. This isolation has been completely achieved for radium. It took several years of continued effort to do that. Radium in the form of a pure salt is, today, a product manufactured by an industry; for no other new radioactive substance have such definite results been obtained.

* Translated from *Les Prix Nobel en 1911*.

"The radioactivity of radium in its pure salts is about five million times as great as the radioactivity of an equal weight of uranium. Because of this radioactivity the salts have a spontaneous luminescence. I should also like to mention that radium constantly develops energy which, measured as heat produced, corresponds to an hourly 118 calories per gram of radium.

"We are now used to work with substances which manifest their presence to us only by their radioactive properties, and which we can, nevertheless, measure, dissolve, reprecipitate from their solutions, or deposit by electrolysis. This is a particular kind of chemistry for which the electrometer, not the balance, is used as the common tool and which could well be called the chemistry of the imponderable."

CONSEQUENCES IN THEORY AND PRACTICE

The discovery of radium was perhaps more important than the discovery of any other element since oxygen. The very concept of element had to be changed, and a new "force" of matter had to be recognized. Radium made its presence known by imparting an increased electrical conductivity to the surrounding air. This characteristic property served as the guide for Marie Curie in her efforts to remove all ordinary matter from the uranium ore and so to separate the radioactive substance. The method of determining the presence of radium was similar to that of analysis by optical spectrum in the great sensitivity to smallest amounts of the substances involved. For the optical analysis, however, the substance had to be heated to high temperatures, so that part of the heat was transformed into emitted light. Radium carries its electrical activity with it at all temperatures, undiminished even at the temperature of liquid air. It is a source of energy which manifests itself in strange kinds of a cold glow connected with a lasting development of heat. Radium diminishes slowly, at a rate from which it can be calculated that freshly isolated radium will be almost two-thirds transformed into nonradioactive substances in about 2450 years.

Although one ton of pitchblende gave only about one tenth of a gram of pure radium in the form of its chloride salt, radium is

widely distributed in tiniest quantities. It is accompanied by a still more powerful radiator of energy, the element polonium, which Marie Curie and A. Debierne isolated and named in honor of Poland. The radiation emitted from these elements has a strong influence on living organisms. The water of many springs is radioactive, and much of its medical value was attributed to this fact. More concentrated forms of radioactive materials were applied in medicine soon after the discovery of radium. On the other hand, as in the early work on Rontgen rays, many investigators suffered from the ill effects of uncontrolled doses of radiation.

1912

VICTOR GRIGNARD

(1871-1935)

"For the discovery of the so-called Grignard reagent, which has greatly helped in the development of organic chemistry during these last years"

(The award for 1912 was shared with Paul Sabatier; see below, pp. 52-55)

BIOGRAPHICAL SKETCH

FRANÇOIS AUGUSTE VICTOR GRIGNARD WAS BORN IN CHERBOURG, where his father was a sailmaker, "a simple man with much common sense and a practical mind." He made good grades as a student, but chemistry seemed to him incoherent, just a collection of single facts to be memorized. The beauty of chemical experimentation gradually impressed him, however, during his studies at the University of Lyons. His chemistry professor, Philippe Antoine Barbier (1848-1922), was working on reactions in which the methyl group, CH_3 , is introduced into organic compounds. Such reactions had been carried out with the iodine derivative of methane, methyl iodide, CH_3I . Zinc had earlier been found to form very reactive organic compounds, and this metal had been added to further the methylation reaction. Barbier replaced it by magnesium. The results were satisfactory, and he asked Grignard to continue this research. Grignard found that methyl iodide reacts very well with magnesium metal when ether is added. Every trace of water had to be excluded. Once the compound was formed, it

could be used immediately, without being separated from the solution in ether, for further reactions.

Grignard published the results of this investigation as his doctoral thesis in 1901. The new method aroused great interest. Publications on organo-magnesium compounds soon began to appear from many laboratories; in 1905, there were already over 200 such publications, and the number rose to about 6000 in the year of Grignard's death. He became professor in Lyons in 1906, then in Nancy in 1910, and he remained there with interruptions during the war years. He did war work on the production of toluene from heavy oils by cracking, in spite of a heavy burden of administrative duties.

Grignard was not quite satisfied with the decision of the Nobel Prize Committee; he felt that Sabatier should have shared the prize with Senderens (see p. 53), and that afterward a prize should have been divided between him and his former teacher, Barbier.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"The preparation of the organo-magnesium ethers is, in general, extremely simple. The apparatus is just a round-bottomed flask connected with a good ascending condenser and with a dropping funnel with stopcock, but it is indispensable that everything be absolutely dry.

"One atomic weight of magnesium, in the form of fine filings, is placed into the flask. On the other hand, one molecular weight of the halogenated hydrocarbon to be used—for example, methyl iodide—is dissolved in an almost equal volume of perfectly dry ether which was kept over sodium. Of this mixture, 25-30 c.c. are added to the magnesium. A lively reaction begins after a very short time. Then, 250-300 c.c. of ether are added, and the reaction is kept going by addition of the rest of the reaction mixture drop by drop. The reaction is completed by short heating, if necessary. Under these conditions the magnesium disappears completely. In general, a clear or slightly colored solution is obtained, in which,

* Translated from "Le magnésium en chimie organique," *Bulletin de la Société Chimique de France*, Vol. XIII (1913), p. 1.

however, very fine particles of iron, an impurity in the magnesium, produce a momentary haze of slate color.

"The compound, prepared as just indicated, shows all the characteristics of organo-metallic compounds; it changes rapidly in air, absorbs oxygen and carbon dioxide, is decomposed violently by water, and reacts strongly with almost all functional groups. These operations can usually be carried out without any change in the apparatus. It suffices to add, through the dropping funnel, the antagonistic compound dissolved in a convenient quantity of water-free ether. Thus, either a solution or an oily or crystalline separation is obtained, and the reaction is completed, if necessary, by a more or less prolonged heating. After that, all that remains to be done is to hydrolyze the compound."

PAUL SABATIER

(1854-1941)

"For his method of hydrogenating organic compounds in the presence of finely divided metals/"
(The award for 1912 was shared with Victor Gri guard;
see above, pp. 50-52)

BIOGRAPHICAL SKETCH

PAUL SABATIER WAS BORN IN CARCASSONNE, IN SOUTHERN France. After graduation from the famous Ecole Normale, where he studied physics, he became assistant to Marcelin Berthelot (1827-1907) in Paris. His doctoral thesis dealt with sulfur compounds of metals, and he continued to work on inorganic compounds as professor in Toulouse. At first he lectured there on

physics; the border line of physics and chemistry interested him most. Investigations on the heat connected with chemical reactions show the influence of his old master, Berthelot, which can also be detected in Sabatier's research on reactions with hydrogen. Berthelot had discovered that alcohol vapor, in contact with a red-hot iron surface, forms a permanent gas which he called acetylene. It contains only two hydrogen atoms for two carbons. When carbon is chemically saturated with hydrogen, one carbon atom binds four hydrogens, as in methane, CH_4 . When two carbons are combined, as in ethane, the number of hydrogens is six, C_2H_6 . Acetylene is, therefore, highly unsaturated, as the symbol C_2H_2 shows. By the addition of hydrogen, a process called hydrogenation, ethane can be obtained by way of an intermediately unsaturated compound, ethylene, C_2H_4 . In 1897, Sabatier and his colleague, the Abbe Jean-Baptiste Senderens (1856-1936) found that finely divided metals furthered the reaction of such unsaturated substances with hydrogen. The metal had to be freshly prepared from its oxide or salt, because a peculiar influence was exerted by the surface of the metal. The behavior of benzene in this reaction was of especial interest. Benzene is different from the methane series; it contains six carbon atoms linked with one another into a closed hexagon, and each connected with one hydrogen atom. Hydrogenation in the presence of nickel added six hydrogen atoms to the molecule without opening the carbon-to-carbon bonds.

Sabatier declined offers to go to the Sorbonne as Moissan's successor. He remained in Toulouse and published books on catalysis in organic chemistry and on agricultural chemistry.

DESCRIPTION OF THE PRIZE - WINNING WORK *

Moissan (see pp. 25-28) and Moureu found that freshly reduced nickel, cobalt, iron, or platinum begin to glow when acetylene is present. A decomposition occurs with formation of carbon, of a gas which Moissan thought was hydrogen, and of liquid condensates containing benzene and other aromatic substances.

* Translated from *Les Prix Nobel en 1912*.

"I thought, and I still think . . . that the real cause of the catalytic action of porous platinum is not a simple phenomenon of physical condensation which produces a local rise in temperature, but that it is a real chemical combination on the surface of the metal with the free gas.

"In the experiments of Moissan and Moureu, I attributed the decomposition of the acetylene to an affinity of the metal either for acetylene itself or for its constituents, carbon or hydrogen, which it could easily detach from the endothermic molecule of this hydrocarbon.

"Having ascertained that Moissan did not intend to continue the study of this reaction, I thought of taking it up myself and, first, I tried with Senderens an analogous experiment with ethylene.

"When one directs a stream of ethylene on to nickel, cobalt, or iron which has been freshly reduced and is kept at around 300 ° C, one observes a vivid incandescence of the metal with voluminous deposition of char from the destruction of ethylene. However, the gas which comes out of the apparatus is not hydrogen; it is mostly composed of ethane.

"This latter could originate only in a hydrogenation of undestroyed ethylene, and without a doubt this hydrogenation was provoked by the metal.

"In effect, if one passes a mixture of ethylene and hydrogen over a column of reduced nickel, the ethylene is changed into ethane, and the metal can serve indefinitely to produce the same transformation (June 1897).

"At the end of 1900, success was decisive and, with Senderens, I recognized that, in contact with nickel at about 180⁰ C, benzol can be completely changed into cyclohexane. Since then I have had absolute confidence in the generality of the method of which we announced the principle in early 1901: Pass the vapors of the substance, together with an excess of hydrogen, over freshly reduced nickel kept at a convenient temperature (150-200⁰ C).

"Direct hydrogenation permits one to convert vapors of liquid fatty acids (oleic acid) into solid acids (stearic acid), and it has been found that this reaction, which is easily carried out, can be applied to the oils themselves, with the metal catalyst kept in sus-

pension in the presence of hydroger into solid fats. This is actually being in England and Germany."

CONSEQUENCES IN IWUWIYX AND PRACTICE

Both Grignard's and Sabatier's methods, now about a half-century old, use metals to obtain reactions of carbon compounds. In Grignard's method, magnesium is combined with an organic halogen compound. The metal, which has great affinity for chlorine, bromine, or iodine, accepts the organic radical to which these halogens are attached a little unwillingly. The presence of ether facilitates the reaction, because it offers at least an opportunity for the magnesium to attach oxygen to itself, even if this oxygen is strongly bound to the carbon atoms in the molecule of ether. When a more reactive, freer oxygen is offered, the magnesium compound in Grignard's reagent readily combines with it in releasing the organic radical for further reactions. A great number of combinations are thus opened up for obtaining new bonds between carbon atoms by the intermediary action of the magnesium-organic halogen substances. Carbon dioxide is easily introduced into a hydrocarbon, converting it into the corresponding organic acid. On the other hand, the organic acids in fats, which are there combined with glycerine, can be reduced to alcohols. After the rules for these manifold combinations were established, new substances could be produced with the possibility of predicting the constitution of the expected products. Medicines, perfumes, and detergents were among the new products.

In Sabatier's method, nickel forms a fleeting association with hydrogen and with the unsaturated substance which then receives the hydrogen into more permanent bond. Soon after its discovery, the method was applied to convert low-melting fats into more saturated, higher-melting, and thus "hardened" substitutes for butter.

Magnesium and nickel remained the foremost agents in these two methods, although the question was frequently raised whether other metals could not offer specific advantages in some cases.

Lithium has such effects when substituted for magnesium. Nickel alloys and mixtures in distribution on silicic carriers have acquired technical importance. Both the Grignard and Sabatier reactions are widely used in research and industrial production.

1913

ALFRED WERNER

(1866-1919)

"In recognition of his work on the linkage of atoms in molecules, by which he has thrown fresh light on old problems and opened up new fields of research, particularly in inorganic chemistry."^f

BIOGRAPHICAL SKETCH

ALFRED WERNER, LIKE OSTWALD AND BAEYER, DEVELOPED AN active interest in chemical experiments at an early age. He installed a laboratory in the barn of his parents' property in Muhlhausen (Alsace). His study of chemistry began in Karlsruhe and continued in Zurich. There Arthur Hantzsch had found certain nitrogen-containing organic substances which differ in properties although they have the same analytical composition. The explanation for this particular case of isomerism was developed by Werner in his doctoral thesis, in 1890. He extended van't Hoff's theory of the tetrahedral carbon atom and modified it for nitrogen.

Werner's "contributions to the constitution of inorganic compounds" started in 1893 and were continued through twenty publications. Physical measurements showed optical and electrical differences between complex compounds and gave access to their inner structure. Geometric models were still helpful in visualizing the structures, but they were models of a higher order than the previous ones. Werner did not need the guidance which these models afforded. He lived so intensely with these substances that he understood their relationships and natures by their appearances.

Certain complex compounds of metals such as cobalt (Co), chromium (Cr), or rhodium (Rh) with oxalic acid residues (C₂O₄) should be nonidentical with their mirror images. Characteristic of such compounds is the asymmetry which van't Hoff saw as the cause of their property of turning the plane of polarized light. It was a wonderful confirmation of Werner's theory when he found optically active complexes in which one of these metals formed the center.

Werner became full professor at the Technische Hochschule in Zurich before he was thirty (in 1895). At times he had 25 graduate students working under his direction for the doctor's degree in his relatively small laboratory. A new chemical institute was built for him in Zurich in 1909; he taught and worked there until, in 1915, his fatal sickness began to show itself.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Elementary atoms, even when they are saturated in the sense of the old theory of valence, still have sufficient chemical affinity at their disposal to bind other atoms and atom groups, which themselves seemed to be saturated. New atom compounds of a definite nature are thus formed. This rule is, today, so well founded in experiments on a great number of molecular compounds that we are justified in taking it as a starting point for further developments.

"One of the first questions to be answered is concerned with the number of atoms which can be directly bound to an atom in the center of a complex molecule. It was found that this number, called maximum coordination number, depends upon the nature of the elementary atoms which are combined. Up to now the maximum coordination numbers four, six, and eight have been observed. This corresponds to the theoretically possible symmetrical arrangement of a number of points around a center in such a manner that the distances between neighboring points are equal. However, the composition of the complex chemical compounds does not always

* Translated from *Les Prix Nobel en 1913*.

have to correspond to the maximum coordination numbers, because there are coordinatively unsaturated atoms just as there are valence-unsaturated ones.

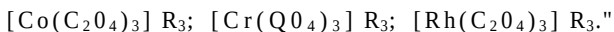
"The most recent investigations have shown that there is no fundamental difference between principal valences (which cause the bond in compounds of the first order) and auxiliary valences (as I called those valences which cause the formation of complex compounds). The two kinds of valences have precisely equal importance for the strength with which the atoms hold together in the molecule.

"So far we have considered only the affinity relationships between the atoms in a coordination compound, and we have disregarded the relative position of these atoms in the molecules. The question now is directed to the manner in which the six groups A, forming the complex radicals MeA_6 with the central atom Me, are arranged in space around this central atom. This question can be answered experimentally by comparing the actually found isomerisms with the several possibilities of spatial arrangements.

"The explanation of isomerisms, which were found first in the platinum series and then in the cobalt series, has required long years of work. Today we know twenty different series of compounds of cobalt with the described isomerism, and for chromium similar isomerisms have been proven by P. Pfeiffer. The differences in the properties of the isomeric compounds are so great that it is frequently possible to distinguish them by their appearance.

"If the six groups which are combined with the central atom are not identically the same, it is possible to construct molecular configurations which are not identical with their mirror image. Compounds with such molecular configurations could, therefore, be expected to exist in optically active mirror-image isomers.

"We have, therefore, tried to separate such compounds into optically active isomers. This has actually been achieved in many cases. . . . Most recently, we have separated into active forms and thereby definitely established the constitution of metal-trioxalic acids of the general formulae



CONSEQUENCES IN THEORY AND PRACTICE

Werner's theories advanced chemistry beyond concepts which had become too rigid. In some respects, as in his distinction between primary and auxiliary valences, he had to reach compromises. Few chemists of his time were ready to follow him when he assumed multiple valences even for the traditional unit of hydrogen. Recent developments have, independently, led back to Werner; in Linus Pauling's words: "It has been recognized in recent years that under certain conditions an atom of hydrogen is attracted by strong forces to two atoms, instead of only one, so that it may be considered to be acting as a bond between them. This is called the 'hydrogen bond.' "

Inorganic chemistry was the model upon which organic chemistry developed. By the end of the nineteenth century, the interest in inorganic chemistry which had been stimulated at the beginning of the century had faded. Werner's work contributed to a vigorous new growth in this field, and soon organic chemistry was in a position to help its sister science. The investigation of the arrangement of the atoms in the space occupied by the molecule, a topic of stereochemistry, developed as a branch of inorganic chemistry.

With the new laboratory experiences, complex compounds were soon found in many minerals. Methods of separating metals from their ores and of preparing gold and platinum metals were improved on the basis of the new concepts in inorganic chemistry.

1914

THEODORE WILLIAM
RICHARDS

(1868-1928)

*"For his exact determinations of the atomic weights
of a great number of chemical elements."*

BIOGRAPHICAL SKETCH

THEODORE W. RICHARDS WAS BORN IN GERMANTOWN, PA. HIS father was a painter, his mother a poet. The son soon proved to be an artist in chemical experimentation. He studied at Harvard, where Professor Josiah Parsons Cooke entrusted him with the delicate task of redetermining the atomic weight of oxygen. He found a value of 15.869 with a possible error of plus or minus 0.0017, compared to hydrogen as the unit. This was the subject of his doctoral thesis in 1888. He completed his studies in Germany and returned to Harvard in 1894 to become assistant professor. A full professorship was offered by Gottingen University in 1901; he declined, and Harvard thereupon gave him a full professorship with reduced teaching duties.

Highest accuracy in determining atomic weights and heat values in neutralization and combustion led to many corrections of previously accepted measurements. When K. Fajans in Munich needed a definite comparison of the atomic weights of lead from ordinary deposits and from radioactive transformation of uranium, he sent the samples to Richards (1913). Richards expanded this investiga-

tion to research on atomic weights of elements from varied sources and of varied geological background. In his words, "the success in a precise chemical or physico-chemical measurement lies in so choosing the particular substance and process and so checking every operation by parallel experiments that both chemical and physical errors may be avoided as effectively as possible; and this choice often involves much study and above all sound common sense. The precautions must be of a consistent order of refinement. Far more depends upon this intelligent choice of conditions than upon a mere mechanical execution of the operations, although that too is important."

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Sodium bromide had been prepared in a state of very great purity for the purpose of determining the transition temperature of its hydrated crystals. Such a transition temperature, especially of a substance with small heat of transition, is very sensitive to impurity. This sodium bromide, which gave a very constant transition point, was analyzed with precision as a matter of routine. To my amazement more bromine was found in it than corresponded to the atomic weights as determined by Stas. The only reasonable explanation seemed to be that Stas' atomic weight of sodium was too high. Such an iconoclastic conclusion, however, needed verification in other ways. Especially Stas' experiments with common salt must be repeated, for sodium chloride was the chief substance upon which his atomic weight of sodium rested. The research was not an easy one, and because it involved the disproving of results among the most carefully obtained in the whole field of chemistry, it demanded unusual precautions and meticulous care. The story is long, and can only briefly be summarized here. We found that not only the atomic weight of sodium, but also that of chlorine, was in error. Indeed the error in the latter was partly responsible for that in the former: for Stas, because of an unsuspected impurity in his silver, had obtained less silver chloride from a specimen of the metal than

***From *Les Prix Nobel en 1914-1918*.**

really should have been produced by it. This led him to an atomic weight of chlorine distinctly too small, and to values for sodium and silver distinctly too large. The excessive value for silver was augmented still further by the fact that his method of precipitating the silver chloride by placing fused common salt in a solution of silver nitrate tended to cause impurity in the precipitate. But these are technical details. . . . The higher atomic weight of chlorine has been amply justified by others in many ways. . . .

"The next important contribution, involving a new method and a somewhat new problem, was that in which lithium and silver were compared directly with oxygen through the analysis of lithium perchlorate and the precipitation of the chlorine in lithium chloride by silver. These two processes together give a new means of comparing oxygen with silver—an eventuality much to be desired, because many atomic weights are determined by reference to silver, and all are stated in relation to oxygen.

"Years ago my present colleague, Gregory P. Baxter, and I had worked upon the atomic weight of terrestrial iron, and found it to have a value distinctly lower than that usually assigned to it. In connection with never-ceasing curiosity as to the constancy of the atomic weights, I wondered later whether or not iron in meteorites, possibly having its birth far beyond the limits of the solar system, might have a different atomic weight from ordinary iron. Baxter kindly consented to investigate this question and, with characteristic ease, using methods similar to those used upon terrestrial iron, he found that the iron from meteorites has precisely the same atomic weight as this metal smelted on the earth. The outcome, although not unexpected, is, nevertheless, of interest, and thrills one who appreciates it with an added realization of the unity of the universe."

CONSEQUENCES IN THEORY AND PRACTICE

Richards' improved methods gave atomic weights which were accurate to the third decimal. It may seem strange that this development came at a time when atomic weight had lost its meaning as an absolute constant. A paradox of great consequence in the history

of science is here illustrated. By the time experimentation reaches a stage such that it can provide a thorough test for a scientific idea, this idea has often changed. Because Richards succeeded in determining atomic weights with such precision and reliability, it could be proved that an element may consist of several species which are identical except in weight. Radioactive transformation of uranium results in a metal of atomic weight 206 which is chemically identical with common lead of atomic weight 207.21. These species of lead are isotopes (see p. 83).

One of the most important of Richards' investigations was the first one, concerning the atomic weights of hydrogen and oxygen. When it was discovered, in 1929, that oxygen contains isotopes, the most accurate methods of measuring the atomic weight of hydrogen had to be interpreted as indicating the existence of a "heavy" hydrogen (see p. 140).

The International Committee on Atomic Weights was the first organization of international scientific cooperation, created for the unified critical survey of atomic weights. This organization, which published annual tables of the accepted figures, later including those of the isotopes, has survived the two world wars.

1915

RICHARD WILLSTATTER.

(1872-1942)

"For research on coloring matter in the vegetable kingdom, principally on chlorophyll."

BIOGRAPHICAL SKETCH

RICHARD WILLSTATTER WAS BORN IN KARLSRUHE, BADEN, GERMANY; he went to school there and in Nuremberg, with equally good results in mathematics, literature, and languages. In his autobiography, he said of himself: "I lacked the intensity of one natural ability, especially of one-sided natural ability; I had to create a partial equivalent for it by a one-sided life occupation during the important decades." Chemistry was his choice for study. His strong inclination toward physiology and medicine found its way into his later work. After completing his courses in Munich, he was drawn into the field of alkaloid chemistry by Alfred Einhorn, the discoverer of novocaine. In many years of research Willstatter elucidated the chemical structure of tropine, the basic part of the molecules of atropine and cocaine. He found methods for separating intermediate substances of delicate stability in the oxidation of benzene and naphthalene derivatives. This enabled him to give a chemical explanation for the black dyestuff which is produced by oxidizing aniline.

In 1905 Willstatter left Munich, where he had become associate professor in 1902, for a professorship in Zurich. There he began his work on chlorophyll. His principal idea was to use gentle

methods of splitting the molecule gradually by acid and then by alkali, and to recover, identify, and combine the products. Chlorophyll was found to contain about 3 percent of magnesium, held by chemical bond to four nitrogen atoms which themselves are parts of a cycle closed by carbon atoms. Later Willstatter discovered that iron is held in a similar position in the molecule of hemoglobin, the red dyestuff of blood.

It was necessary to bring the living plant into the laboratory if the real chemistry of its most important constituents was to be investigated. The methods of investigation had to be refined so as to imitate the means by which the plant carries out chemical changes. Willstatter pronounced this principle and followed it in his work on plant dyestuffs and enzymes.

This work was in part interrupted during the First World War. Willstatter had accepted a call to the Kaiser Wilhelm Institut *m* Berlin-Dahlem in 1911. Actually, he had only about twenty months of productive time there before returning to Munich in 1916. One of his remarkable achievements during this time was the development of an effective gas mask which contained three layers of active absorbents.

The process of assimilation was one of the first themes which Willstatter developed in Munich (from 1917 on). He now approached the chemistry of enzyme action, which had begun to occupy him in Zurich, in a new, systematic way. Saccharase, the sugar-splitting enzyme, was obtained in a form 4000 times purer than its raw material, dried yeast, and the oxygen-splitting enzyme peroxylase was purified to 12,000 times the activity of the dried plant root in which it occurs. This was a triumph of Willstatter's chemical viewpoint over a somewhat nebulous, but widespread, biological explanation.

Willstatter resigned from his professorship at Munich in 1924, as a protest against anti-Semitic forces at the university. However, he remained active in research for the chemical industry, to which he gave medically used substances such as avertin, a narcoticum, and as an adviser to professional organizations. After heartbreaking difficulties caused by the Nazi regime, he left Germany for Switzerland in 1939.

DESCRIPTION OF THE PRIZE-WINNING
WORK *

"The same characteristics which serve for comparing the dyestuffs from any kind of leaves also enable us to decide whether the chlorophyll remains unchanged in the fine details of its molecule during the preparatory work. Thus, this characterization was the basis for preparing chlorophyll itself in a pure and unharmed state and for confirming, by its analysis, the conclusions which had first been reached by investigation of its derivatives. The isolation of chlorophyll relied on colorimetric measurement of the degree of purity of its solutions and depended upon the systematic raising of purity by methods of distribution between several immiscible solvents such as petroleum ether and aqueous alcohol. By this method, colorless admixtures and the yellow pigments of the leaves were removed. The association of these yellow pigments, the carotinoids, with green dyestuffs seemed to indicate a special physiological role of these substances which are conspicuous by their great affinity to oxygen. Therefore, these yellow substances also were prepared in pure form and analyzed. Two easily crystallizing, nitrogen-free pigments occur in every green part of the plant and in many yellow ones. One of them, identical with the long-known carotene of carrots, is an unsaturated hydrocarbon of the formula $C_{40}H_{56}$. Its partner, xanthophyll, was not previously known in substance, although it predominates in leaves; according to composition and properties it is an oxide of carotene, $C_{40}H_{56}O_2$. Only in the phaeophyceae carotene and xanthophyll are accompanied and repressed in quantity by a third oxygen-rich carotinoid, fucoxanthin, which can be isolated in crystal form and which is composed of $C_{40}H_{76}O_6$.

"While chlorophyll in plant extracts is accompanied by 8 to 15 times its weight in other substances, solutions of 70 percent pure chlorophyll can be obtained by operations of partition. From there, a surprising observation helped to solve the problem. When this substance has reached a certain degree of purity it reveals its true solubility relationships, which before were distorted by the admix-

tures. Pure chlorophyll is not soluble in petroleum ether and separates out of the alcoholic solvent when the alcohol is washed away. The procedure permits the isolation of pure chlorophyll in good yields from dried or fresh leaves as easily as that of any other plant substance, such as alkaloids or sugars.

"This pure chlorophyll is, however, not yet a uniform substance. (It consists of about 3 moles of the blue-green chlorophyll a and one mole of the yellow-green component b.)

"Chlorophyll, that is to say, each of the two components, combines in a colloid state with carbon dioxide to form a dissociable addition compound. This observation can form the basis for a theory of assimilation which assumes that the light which is absorbed does its chemical work in the chlorophyll molecule itself, of which carbon dioxide has become a part by attachment to the magnesium complex. This chemical work consists in rearranging the valences of the carbon dioxide into a form suitable for voluntary decomposition, which occurs in such a manner that all the oxygen of the carbon dioxide is liberated.

"The isolation of the anthocyanins in pure form and their analysis are based upon their basic nature and were achieved by preparing well crystallized salts with hydrochloric or picric acid. These acidic compounds are red, the alkali salts are blue, and the violet neutral forms are to be understood as inner salts, as phenol-betaines. Many variations of flower colors are caused solely by the occurrence of these three forms.

"Anthocyanins proved to be glucosides in which the real dye-stuffs, compounds with phenolic hydroxyl groups, are paired with one or two (or even more) sugars, with glucose, galactose, and rhamnose."

CONSEQUENCES IN THEORY AND PRACTICE

The separation of dyestuffs from leaves was accomplished by new methods, and the chemical investigation of the molecular composition showed new principles of chemical constitution. One of the methods was based upon the earlier discovery of Mikhail Tswett. Tswett filtered a solution containing leaf extracts through

a glass tube filled with calcium carbonate powder and observed that only the carotenes came through in the filtrate, while others of the dissolved dyestuffs were withheld on the surface of the powder. This method of separating a mixture of substances by means of the gentle forces of adsorption was varied and refined by Willstatter. New adsorbing materials were prepared, and the solvents were selected which gave the best effect. This method of chromatography has become an indispensable tool in the laboratory and in the manufacturing plant.

The discovery of the specific sensitivities of chlorophyll, of the influence of impurities on its solubilities, of the reaction with ethyl alcohol under the action of a special enzyme present in the leaf, of the ease with which its magnesium is lost and replaced by other metals, served to improve the technical preparation of this substance. Valuable properties, including those responsible for its medical use, could thus be kept unharmed during the industrial manufacturing processes.

Carotinoids were laboratory curiosities until it was found that some of them are closely related to vitamin A. One of the carotenes occurring in carrots is a direct precursor of this growth-promoting vitamin and is used as a growth promoter by the human organism.

Extracts from flower petals had long been used in the laboratory for their property of changing color in relation to the acidic and alkaline reactions of solutions. Willstatter's work explained the chemical basis for such use and, at the same time, disclosed the common pattern of anthocyanins, the flower pigments.

19 16 - 1917

No Award

1 9 1 8

FRITZ HABER

(1868-1934)

*"For the synthesis of ammonia from its elements,
nitrogen and hydrogen*"*

BIOGRAPHICAL SKETCH

AFTER FINISHING HIS STUDIES IN HIS NATIVE Breslau, Fritz Haber made an unsuccessful attempt at working in his father's business. At the recommendation of a friend, he then went to Karlsruhe. He liked the connection between industry and science which he found there at the Technische Hochschule, a university preparing its students for technical positions. He began, in 1893, to investigate the decomposition of organic compounds at high temperatures, called pyrolysis. Marcelin Berthelot, the foremost French chemist of this time, had worked in this field. Haber was soon able to correct Berthelot's arbitrary generalizations by his intimate studies. Pyrolysis reactions could have offered enough work for a busy lifetime. Haber, however, was attracted by the influence of electricity on organic substances. The connecting links between the two fields were gas reactions and chemical energetics. Walther Nernst had just developed the theory that the electrochemical driving force, when gases are involved, is determined by the effective concentration of the gases in or on the electrode, the metal which serves to introduce electrical current into a solution. By regulating this driving force, the voltage, in particular chemical reactions, Haber demonstrated the several steps in which these reactions can

take place. An example of great technical interest was the reduction of nitro-benzol to aniline, in which the two oxygen atoms of the former are exchanged gradually by two hydrogen atoms.

Starting from this success, Haber wrote a book on the entire field of technical electrochemistry and its scientific basis. In a similar way, he brought science and technology together in a book on the energy relationships in gas reactions.

Haber did not have to wait long for recognition of his efforts; his own Hochschule made him full professor in 1906. At this time, he had already begun to investigate the possibility of synthesizing ammonia from its elements. Karl Engler, the great authority in chemical technology, interested the Badische Anilin und Soda Fabrik (the forerunner of the I.G.), in near-by Ludwigs-hafen, in the project, and on July 2, 1909, Carl Bosch (see p. 123) and Alwin Mittasch (b. 1869, director of the BASF) came to Karlsruhe to witness the making of the first 100 grams of synthetic ammonia by Haber and his assistants.

When the Kaiser Wilhelm Institute for Chemistry was founded, Haber was elected its first director. From 1911 to the fatal year 1933, he remained in Berlin-Dahlem, widening the activities of the Institute, and in the early years of the war organizing chemical warfare. He directed the first use of gas—it was chlorine—in 1915. The French army reciprocated with the deadly phosgene the following year.

In 1919 Haber remembered Arrhenius' estimate that there are eight billion tons of gold in the seas. He organized an expedition to try to recover some of this gold, hoping that this would be a way in which chemistry could supply Germany with the means to pay the reparations. The result was completely disappointing. Heart-broken, he did not even carry out Richard Willstätter's friendly advice to convert the failure into an interesting book.

Later on, Haber came back to the work with which he had started, deepening it by experiment and thought concerning chemical chain reactions at high temperatures and under the influence of catalysts.

Haber's outstanding combination of wide knowledge with keen insight and splendid ideas made the Institute a center of varied research. His efforts in the interest of young scientists helped

greatly in the postwar recovery of German chemistry. Nevertheless, the "awakened" Germany of 1933 had no use for him, because he was born a Jew. He died, broken in health and in spirit, in exile in Switzerland.

DESCRIPTION OF THE PRIZE-WINNING WORK*

"The colleagues' interest in the preparation of ammonia from the elements is based on the fact that a simple result is achieved by unusual means. The interest of a wider circle has its source in the recognition that ammonia synthesis on a large scale represents a useful, at present even the most useful, way to satisfy an economic need. This practical usefulness was not the preconceived goal of my experiments. I was not in doubt that my laboratory work could furnish no more than a scientific statement of the foundations and a knowledge of the experimental equipment, and that much had to be added to this result in order to attain economic success on an industrial scale.

"In the course of this research (on the equilibria) I returned in 1908, together with my young friend and collaborator Robert Le Rossignol . . . , to the task of ammonia synthesis, which I had abandoned three years before. Immediately before this time I had become acquainted with the liquefaction of air; at the same time I had received insight into the industry of formate manufacture, where flowing carbon monoxide is reacted with alkali under heat and pressure, and now I no longer deemed it impossible to manufacture ammonia under high pressure and at high temperature. However, the unfavorable opinion of the experts taught me that an impressive progress was necessary in order to awaken technical interest in the subject.

"It was clear in the beginning that it was advantageous to resort to high pressure. This produced a favorable position of the equilibrium, and the same could be expected for the reaction velocity. The compressor at our disposal permitted the densification of the gases to 200 atmospheres and thereby determined the working

* Translated from *Les Prix Nobel en 1914-1918*.

pressure which could not conveniently be exceeded in the large series of experiments. In the neighborhood of these pressures, the metals with which we had become familiar during our measurements of the equilibria, first manganese, then iron, easily gave a rapid combination of nitrogen with hydrogen at above 700 ° C. For an impressive result, it was necessary to find contacts which produced a rapid conversion between 500 and 600° C. We hit upon the idea of searching the sixth, seventh, and eighth groups of the periodic system, in which the top metals chromium, manganese, iron, and nickel are excellent catalysts, for metals which are still more active, and we discovered them in uranium and osmium. With their aid, at 200 atmospheres, the two requirements could be met which we believed had to be asked of a technically convincing execution of the experiment; one of these requirements related to the content [of the gas] in ammonia, the other to the amount of ammonia produced per cubic centimeter of the contact space and per hour. With a content of 5 percent the recycling apparatus of 1905 gave no longer only the demonstration of a mode of combination, but a method of preparation. At a yield of several grams of ammonia per hour and cubic centimeter of heated high-pressure space, the dimensions of this space could remain so small that the objections of industry, in our opinion, had to disappear.

"Finally, it was necessary to build a recycling apparatus which could serve as a model for the technical performance.

"Of the characteristics of our laboratory work, the following are retained in today's large-scale operations: the working pressure of about 200 atmospheres, the working temperature of around 500-600 ° C, the recirculation under continuing high pressure, the feature of heat transfer from exhaust gas to incoming gas."

CONSEQUENCES IN THEORY AND PRACTICE

The synthesis of ammonia has been attempted since the time, toward the end of the eighteenth century, when it was known that ammonia is a compound of nitrogen and hydrogen. The failure of these attempts would have deterred new efforts had not the theory of energy in chemical reactions led not only to the proof that this

synthesis should be possible but, in addition, to the prediction of promising conditions for it. That the prediction was found correct showed the great value of the theory as a practical tool. Since it was necessary to have special vessels, pipes, valves, and so on, engineering for high-pressure reactions became an important field.

Four years after Haber had demonstrated the production of 100 grams of synthetic ammonia, industrial production was 6500 tons (metric) per year. The figure was doubled during each following year; 200,000 tons were produced in 1918.

From the start this development had the twofold purpose of sustaining life and of destroying it. As the basis for plant nutrients, it increased crop yields and gave more abundant food supplies. As the starting material for producing nitric acid, synthetic ammonia made possible the manufacture of larger amounts of highly explosive substances not only for mining and quarrying operations but also for ammunition.

Important modifications of the Haber process were developed in France, Italy, and the United States. With all these methods, about 5.5 million tons of nitrogen were converted into chemical compounds in 1948.

19 19

No Award

1920

WALTHER NERNST

(1864-1941)

"For his thermochemical work."

BIOGRAPHICAL SKETCH

WALTHER NERNST WAS BORN IN BRIESEN, WEST PRUSSIA. HE studied, mainly physics and mathematics, at several universities before he was graduated in Wiirzburg, in 1887, with a thesis on electromotive forces which are produced by magnetism in heated metal plates. His interest in the relationships between electric and caloric energies was extended to include chemical affinity after he met Wilhelm Ostwald (see pp. 37-41) in Graz, in 1887, and later joined him in Leipzig. Ever since Volta had made his discovery, in 1801, how to explain the electric potential, or "voltage," of an electrochemical battery had been a controversial problem. Nernst found a very lucid solution. He considered the metal electrode as a reservoir of electrically charged metal atoms, which Faraday had called ions. These ions stand under a certain pressure in the metal, the "electrolytic pressure of dissolution." In the liquid surrounding the metal, the same ions are present and exert osmotic pressure. When the metal dissolves, the ions expand from the pressure of dissolution to that osmotic pressure which is determined by the concentration of the ions in solution. This causes the voltage, and the electric charge of the dissolving ions carries the current.

In 1891, Nernst wrote a survey of theoretical chemistry as the introduction to O. Dammer's handbook of inorganic chemistry.

Two years later, he enlarged it into a separate book with the characteristic title *Theoretische Chemie vom Standpunkte der Avogadro'schen Regel und der Thermodynamik* (Theoretical Chemistry from the Standpoint of Avogadro's Rule and Thermodynamics). He thought, as he stated in the Foreword, that "a period of quiet but successful elaboration has arrived for the physico-chemical scientist; not only are the ideas available, but they have also matured to a certain conclusiveness." He did not feel that he had been wrong in this thought when he wrote the Foreword to the tenth edition in 1921: "Theoretical physics at the present time produces, besides a wealth of durable material, one-day hypotheses rather plentifully, and thus I have found myself induced either to a waiting attitude or to outright rejection." In the first edition of his great textbook he discussed the Principle of Maximum Work which M. Berthelot had formulated in 1867: "Every chemical change which takes place without the aid of external energy tends to the production of that which is accompanied by the development of the maximum amount of heat." This so-called third principle of thermodynamics can be expressed as an equation between A , the maximum work, and Q , the heat of reaction: $A = Q$. The two older laws of energy show, however, that a distinction must be made between A and the change of the total energy U of a system, and $U - A = Q$. Nernst concluded that Berthelot's principle holds true at the lowest possible temperature, the absolute zero or -273°C . He saw a "sound core" in this principle which some day might be extracted from its shell. Thirteen years later he had fulfilled this prediction; his new heat theorem was developed in 1906 and in his Silliman lectures of 1907.

In his research work on chemistry of solutions, on relations between compressibility and atomic volume, and many other subjects, he was more successful than in his technical inventions. The Nernst Lamp, which used a ceramic body, might have assumed importance had not the new tantalum and tungsten lamps been developed. His electrical piano, which replaced the sounding board with radio amplifiers, did not find favor with musicians.

As professor in Berlin, from 1905 on, and as director of the Institute for Experimental Physics in Berlin, from 1924 to 1933, he had many fruitful contacts with industry. His scientific genius

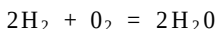
enabled him to understand industrial developments. He felt that Rontgen would have furthered science and industry more if he had patented his discovery.

DESCRIPTION OF THE PRIZE-WINNING WORK*

"In these researches I found, to begin with, distinct relations between the position of the chemical equilibrium and the development of heat of a particular reaction, but this was true only when reactions were compared in which the change of the number of molecules was the same. This change is the same, e.g. for the two reactions



since in both cases the number of molecules remains unchanged in the reaction. Incidentally the two reactions above have about the same development of heat, and thus the position of the equilibrium is at least approximately the same. This relationship disappears when the two reactions are compared with chemical processes which take place with a change of the number of molecules, like



and it reappears when the dissociation of water vapor is compared with the analogous dissociation of carbon dioxide.

"I then pursued these questions in long-winded and wearisome calculations and I believe I clarified them, in principle, by the publication of my *Calculation of Chemical Equilibria from Thermal Measurements* (1906). The simple rule at which I arrived at that time can be expressed in the words that in all cases affinity and heat development become identical at low temperatures. And it is essential that this occur not as an intersection between affinity and heat development at the absolute zero of temperature, but in such a manner that they become equal to each other before reaching the absolute zero point; in other words, the two curves are tangential to each other near the absolute zero point.

* Translated from *Les Prix Nobel en 1920*.

"In generalizing this rule—that is to say, in applying it not only to chemical processes but to all occurrences—we obtain the new heat theorem which leads to a series of quite far-reaching consequences.

" i . The maximum work which is obtainable from a process can be calculated from the evolution of heat in this process, provided the latter is known over a range down to the lowest temperatures.

"2. This can also be expressed by saying that the evolution of heat at any one temperature and the specific heats of the substances involved over a range down to very low temperatures must be *given*.

"3. The specific heats must be rigorously additive at very low temperatures; in other words, the evolution of heat must always be independent of the temperature at low temperatures.

"It is in the nature of things that the foregoing rules, while applicable to all natural processes, are especially useful for chemical events. It is here that Berthelot, as is well known, believed that chemical affinity is equal to the heat developed; however, this assumption, although correct in many cases, could not be sustained. We now recognize clearly in which cases the Berthelot assumption is correct. For very great heat values and with restriction to condensed systems, the influence of specific heat becomes relatively small, and Berthelot's rule is right in usually sufficient approximation when the temperatures are not too high. It often fails completely for processes with little evolution of heat—for example, for the simple process of melting.

"In conclusion I may point out that Eggert, Saha, and others have used my heat theorem successfully for the answers to astrophysical questions."

CONSEQUENCES IN THEORY AND PRACTICE

One's first impression is likely to be that Nernst's heat theorem is concerned with events at a temperature range which is far remote from that of nearly all our scientific and industrial operations. It seems irrelevant to ordinary conditions that at -273°C the

entropy of every substance is zero, or that volume and surface tension become independent of the temperature. However, the relationship between the greatest amount of work which we can obtain from a process and the amount of heat which is developed in its course is of far-reaching practical importance. The recognition that work and heat approach the same value as the temperature is reduced to absolute zero can be extended from this limit-state to more practical conditions. This requires a judicious evaluation which may appear like a trick-conversion of the absolute into its relative counterpart. The use of this evaluation was decisive in the work on ammonia synthesis (see pp. 71-75). A first group of results was in conflict with the predictions of the new theory; this caused a re-examination and led to figures which now held much more promise that a technical process might be developed.

Conflicts between the new theory and measurements were also discovered in electrochemical investigations which were of fundamental importance for technical processes. The maximum of work which the combustion of hydrocarbons—e.g., gasoline—generates can be calculated and evaluated according to the new theory. For properties of the nucleus of the atom the new theory leads to predictions at temperatures of a very high order, where even gravitation and radioactivity should lose their usual independence of temperature.

Nernst's heat theorem removes an indefiniteness which is contained in the second law of energetics and thus broadens the possible extent of general thermodynamics.

19 2 1

FREDERICK SODDY

(1877-)

"For his contributions to the chemistry of radioactive substances and his investigations into the origin and nature of isotopes."

BIOGRAPHICAL SKETCH

FREDERICK SODDY WAS BORN IN EASTBOURNE, SUSSEX. FROM Oxford University he went to Montreal, in 1899, to join Ernest Rutherford (see pp. 33-36) at McGill University. Three years of most fruitful collaboration resulted in the general theory of radioactive disintegration and a new conception of the atom as a structure built from a positive nucleus surrounded by negative electrons. The instability of this structure is the cause of radioactivity.

After Soddy returned to England, in 1902, a certain competition developed between him and Rutherford, particularly with regard to the publication of a book on radioactive chemistry. An amiable solution was reached, and Soddy deferred his publication until after Rutherford's book had appeared.

The position of the new radioactive elements in the system of chemistry was the object of much research at that time. All the known elements had been arranged in the sequence of their atomic weights and grouped according to their chemical analogies and similarities. There seemed to be no place in this system, the periodic table of the elements, for some of the products of radioactive transformation. On the other hand, no means for separating such new

elements from similar, ordinary ones was found. Soddy concluded that there were elements which belonged in the same place as the older ones, and he indicated this property in the name "isotope," meaning something like "the same place."

Soddy was greatly interested in the general conditions for the growth of science. As professor in Aberdeen (1909-1919) he collected some of his addresses in a book under the title *Science and Life* (London, 1920).

Soddy became professor at Oxford University in 1919 and retired from this famous institution in 1936.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Auer von Welsbach also, in 1910, carried out a masterly technical separation of ionium and actinium of the 'hydrate' fraction obtained from 30,000 kg of Joachimsthal pitchblende in the manufacture of radium, and prepared a very concentrated ionium preparation, upon the spectrum and atomic weight of which other investigators subsequently worked. He failed completely to separate the ionium from the thorium although many fresh methods were tried.

"Hershinkel tried numerous methods to concentrate radium D (radiolead) from lead and failed completely. Three years later, Paneth and von Hevesy tried twenty different methods, also completely without result, and upon this failure they based their valuable and elegant method of using the radio elements as indicators. For example, in the present case, the solubility of very insoluble lead compounds was determined by adding radium D to the lead and determining the almost unweighable quantities of lead dissolved by radioactive methods. This use has wide applicability in chemical problems.

"On broader and quite general philosophical grounds, and without in the least postulating a continuation of the genetic series of the radioelements throughout the Periodic System I arrived at the conclusions reached by Stromholm and Svedberg (that the Men-

* From *Les Prix Nobel en 1921*.

delejeff scheme is only an approximate rule as concerns atomic weight, but does not possess the exactness of a natural law; this would not be surprising if the elements of the scheme were mixtures of several homogeneous elements of similar but not completely identical atomic weight).

"It was certain that among the groups of chemically identical radioelements differences of atomic weight of whole units must exist. Thus from the atomic weights of the parent elements and the number of α -particles expelled, the atomic weights of ionium (230) and radio-thorium (228) must differ by 2 and 4 units, respectively, from that of the chemically identical thorium (232). Once one enquired what evidence the chemist had for the real homogeneity of the elements as distinct from their chemical homogeneity, the conclusion followed at once that if all the elements were mixtures in constant proportions of chemical identities differing stepwise by whole units in atomic mass, the chemist with his methods must have remained unaware of it.

"The expulsion of two α -charges as an α -particle and of two electrons as β -particles from the nucleus causes the element to come back to the original place it occupied in the Periodic Table. It follows therefore that the place in the Periodic Table is an expression of the net nuclear charge—that is of the difference between the number of positive and negative charges in the nucleus. Thus the chemically identical elements—or isotopes, as I called them for the first time in this (1913) letter to Nature, because they occupy *the same place* in the Periodic Table—are elements with the same algebraic or net nuclear charge, but with different numbers of α - and β -charges in the nucleus. On the view that the concentrated positive charge is the massive part in the atom structure, since positive electricity has never been observed free possessing less than the mass of an atom, the atomic weight of the isotope is a function of the *total* number of positive charges in the nucleus and the chemical character a function of the *net* number."

CONSEQUENCES IN THEORY AND PRACTICE

The chemical definition of elements, clearly conceived toward the end of the eighteenth century, characterized them as being indestructible and inseparable units of matter. The first of these characteristics had to be abandoned at the end of the nineteenth century, when the chemistry of radioactive disintegration was developed; the second characteristic was modified by the experience of isotopy, at the beginning of our century. The occurrence of isotopes was soon shown not to be limited to radioactively produced elements. Aston (see pp. 86-89) demonstrated that amply.

B. B. Boltwood (1870-1927), of Yale University, one of the first to prove that ionium and thorium cannot be separated by chemical means, developed the idea that the new findings could serve to indicate geological age of rocks. Soddy, in his *Science and Life*, described this very clearly: "To-day we know that radioactive minerals are in reality geological clocks, and they record more accurately than in any other way the age of the stratum in which they occur. In a uranium mineral, for example, each 1 per cent, of lead in terms of the quantity of uranium signifies the lapse of a period of 80,000,000 years. . . . On the other hand, every cubic centimeter of helium per gram of uranium in a uranium mineral signifies 9,000,000 years, and—as here helium, being a gas which forms no compounds, cannot have been initially present, and as, moreover, some will have escaped—the age of the mineral by this method is a minimum, whereas the age by lead content may be too high. The carboniferous rocks tested by this new method appear to have an age of some 350,000,000 and the oldest Archean rocks of over 1,500,000,000 years."

19 2 2

FRANCIS WILLIAM ASTON

(1877-1945)

"For his discovery, by means of his mass spectrograph, of the isotopes of a large number of non-radioactive elements, as well as for his discovery of the whole-number rule"

BIOGRAPHICAL SKETCH

FRANCIS WILLIAM ASTON WAS BORN IN HARBORNE, ENGLAND. When graduated from high school, in 1893, he received highest honors in mathematics and was the first in his class in sciences. He entered Mason College, which later became the University of Birmingham, in the same year. He worked with P. F. Frankland, professor at Birmingham, on optical properties of complex organic substances and published the results in 1901 in his first scientific paper. While employed with a brewing company, he continued experimenting with special equipment which he designed and built with great skill. Electrical discharge in glass tubes, evacuated by an automatic Toepler-type pump of his own construction, proved so interesting that he returned to the University to pursue his investigations. In 1910, he joined J. J. Thomson at Trinity College, Cambridge, for research on the special discharge tube which Thomson had developed. It consisted essentially of an evacuated glass bulb with the anode (positive pole of electricity) on one end and a narrow outlet to the cathode on the other. The positively charged particles passed from there through a magnetic field into

a tube of very low pressure, where they described their paths on a photographic film. Aston changed this arrangement so that the particles which struck the photographic film were cleanly separated according to their relative masses, as light of different wave lengths is separated in an optical spectrum. The apparatus was therefore called a mass spectrograph.

The first apparatus which Aston constructed after returning from his war work as an aircraft engineer was an immediate success. This mass spectrograph of 1919 permitted measurements of relative masses with an accuracy of 1:1000; the third construction, in 1927, gave an accuracy of 1:100,000. The knowledge of exact values of atomic masses enables chemists who study atomic nuclei to synthesize elements, just as other chemists synthesize compounds from elementary substances; this was Aston's prediction in 1936.

Aston found his recreation in travel and sports, and his interest in music was so great that he served as music critic of the *Cambridge Review*. In the obituary notice of the Royal Society (*Proceedings of the Royal Society*, London) it is stated: "Aston's life was a chain of uninterrupted success."

DESCRIPTION OF THE PRIZE - WINNING WORK *

"When neon was introduced into the apparatus, 4 new lines made their appearance at 10, 11, 20, and 22. The first pair are second-order lines and are fainter than the other two. All 4 are well placed for direct comparison with the standard lines, and a series of consistent measurements showed that to within about one part in a thousand the atomic weights of the isotopes composing neon are 20 and 22 respectively. Ten per cent of the latter would bring the mean atomic weight to the accepted value of 20.20, and the relative intensity of the lines agrees well with this proportion. The isotopic constitution of neon was therefore settled beyond all doubt.

"The element chlorine was naturally the next to be analyzed, and the explanation of its fractional atomic weight was obvious from the first plate taken. Its mass spectrum is characterized by 4

* From *Les Prix Nobel en 1922*.

strong first-order lines at 35, 36, 37, 38. There is no sign whatever of any line at 35.46. The simplest explanation of the group is to suppose that the lines 35 and 37 are due to the isotopic chlorines and lines 36 and 38 to their corresponding hydrochloric acids.

"The most important result of these measurements is that, with the exception of hydrogen, the weights of the atoms of all the elements measured, and therefore almost certainly of all elements, are whole numbers to the accuracy of experiments, namely about one part in a thousand.

"This enables the most sweeping simplification to be made in our ideas of mass. The original hypothesis of Prout, put forward in 1815, that all atoms were themselves built of atoms of protyle, a hypothetical element which he tried to identify with hydrogen, is now reestablished, with the modification that the primordial atoms are of two kinds: Protons and electrons, the atoms of positive and negative electricity.

"We know from Einstein's Theory of Relativity that mass and energy are interchangeable, and that in C.G.S. units a mass m at rest may be expressed as a quantity of energy mc^2 where c is the velocity of light. Even in the case of the smallest mass this energy is enormous.

"Take the case of one gramme atom of hydrogen, that is to say the quantity of hydrogen in 9 cu.cm. of water. If this is entirely transformed into helium, the energy liberated will be $0.0077 \times 9 \times 10^{20} = 6.93 \times 10^{18}$ ef g^s. Expressed in terms of heat this is 1.66×10^{11} calories, or in terms of work 200,000 kilowatt-hours. We have here at last a source of energy sufficient to account for the heat of the sun.

"Should the research worker of the future discover some means of releasing this energy in a form which could be employed the human race will have at its command powers beyond the dream of scientific fiction, but the remote possibility must always be considered that the energy once liberated will be completely uncontrollable and by its intense violence detonate all neighbouring substances. In this event the whole of the hydrogen on the earth might be transformed at once and the success of the experiment published at large to the universe as a new star."

CONSEQUENCES IN THEORY AND PRACTICE

A few black spots are found on developing a strip of photographic film, and it is concluded that it may some day be possible to convert our earth into a flaming star! The particular arrangement of that strip of film and the conclusion were results of only a few decades of intensive developments in chemistry, physics, and mathematics. The measurement of atomic weights had begun little more than a hundred years before Aston's method distinguished between atoms of different masses with such accuracy that the values could be used for far-reaching conclusions. They may have appeared entirely too far-reaching to many chemists in 1922 who felt that all this did not change the practical and industrial chemistry with which they were concerned. However, besides preparing the foundations for the later development of atomic energy, research by means of the mass spectrograph gradually became a method for analyzing difficult mixtures of substances.

A. J. Dempster had begun in 1918, in Chicago, to develop a mass spectrograph which used an incandescent platinum plate to convert the investigated salts into vapors and subjected them to electrostatic and electromagnetic fields. Dempster's instrument of 1935, with an electrical spark to produce ions of the elements, made possible the identification of 33 new isotopes in 17 elements. Today one can buy mass spectrographs from instrument dealers, and many laboratories use these instruments as highly refined and efficient tools—for example, in analyzing the complex mixtures of substances present in natural gas or mineral oil fractions.

1923

FRITZ PREGL

(1869-1930)

*"For his invention of the method of microanalysis of
organic substances"*

BIOGRAPHICAL SKETCH

FRITZ PREGL WAS BORN IN LAIBACH, AUSTRIA. AT FIRST HIS INCLINATION was toward medicine, and he became Dr. med. of the University of Graz in 1893. While acting as an assistant in physiology and histology, he also studied chemistry. In 1904 he traveled in Germany, spending a little time in Leipzig in Ostwald's institute and more time in Berlin, attracted by Emil Fischer.

When he returned to Graz the following year, Pregl undertook physiological research, particularly on bile acids. The yields of pure substances were so small that he had to decide whether to work with very large quantities of raw materials or whether to find methods through which he could carry out the necessary analytical investigation with very small quantities of his valuable products. He decided on the latter approach.

Pregl completed the elaboration of a method for determining carbon, hydrogen, and nitrogen by careful combustion of very small quantities during the years 1910-1913, when he was professor in Innsbruck. From 1913 to his death he remained at the University of Graz, which he preferred to the larger University of Vienna. He continued to refine the method in details and later succeeded in making the combustion automatic. He applied the

microanalysis method extensively in his work on enzymes, sera, and bile acids. Besides, he showed the value of his method in forensic analysis, where minimal quantities of poisonous alkaloids could be measured with comparative ease.

DESCRIPTION OF THE PRIZE - WINNING WORK *

In order to determine the proportionate amounts of the elements in the molecule of an organic substance, it is burned under conditions which convert all the carbon into carbon dioxide and all the hydrogen into water, with complete absorption of the carbon dioxide in potassium hydroxide or a mixture of lime and soda, and of the water in calcium chloride. The change in weight of the absorbing materials then gives the quantities of the combustion products, and they can be calculated back to proportions of carbon and hydrogen in the analyzed substance. The combustion is carried out in a tube made of high-melting glass, of a length sufficient to accommodate the sample and copper oxide together with other substances which are necessary to complete the combustion. Nothing but carbon dioxide and water is permitted to reach the absorption system. Nitrogen, sulfur, and phosphorus, when present in the substance, are measured separately. The next step, after the elementary composition has been found, is to measure groups of elements, such as the carboxyl group, which is responsible for the acid character of the substance, or methoxyl, which consists of a methanol residue linked to the rest of the molecule by its oxygen atom, or methyl-imide, in which the oxygen group of methanol is replaced by an ammonia residue of the formula NH .

"When the substance which is to be analyzed contains nitrogen, halogen, or sulfur, its combustion gives rise to gaseous products which would erroneously be weighed and calculated as carbon dioxide, because these products are retained by the soda-lime used to absorb the carbon dioxide. In these cases, these products must at any cost be prevented from reaching the absorption apparatus.

"While macroanalysis recommends different fillings for its combustion tube, in correspondence with the composition of the different substances, I aimed at developing a filling which retains in

* Translated from *Les Prix Nobel en 1923*.

every case everything that is not carbon dioxide or water. I call this a universal filling. It consists of a mixture of copper oxide and lead chromate between two sections of silver and finally a section of lead superoxide with asbestos heated to 180° .

"By watching all conditions it is easy to obtain entirely accurate analyses with an amount of substance of 2-4 mg. The smallest quantity ever used was 1 mg, and the deviation still was within normally permitted limits of error. Thus we have reduced the quantity of substance required for an analysis quite extraordinarily, and when we consider that Liebig used half of one gram, originally even one gram of substance, while at the end of the last century 0.15-0.2 g were generally accepted as necessary, we may say that through the method of microanalysis the quantity required for an analysis has been reduced to a hundredth part of that customary as recently as ten years ago without reducing accuracy in the least. I can even state, and I see it with my own students, that much higher accuracy is asked for in microanalysis than was asked for formerly in macroanalysis, obviously for the reason that the fundamental conditions are much better and more completely fulfilled than is possible in macroanalysis. Besides, there are two other advantages. The first is the great economy in gas and reagents, and the second, perhaps still more valuable, is the economy of time. It is possible to obtain results in a third of the time required for macroanalysis.

"In addition to quantitative measurement of the elements in an organic substance, the quantitative content of certain atom groups is of greatest importance. I have, therefore, elaborated the determination of carboxyl groups acidimetrically with phenolphthalein as indicator, as well as the determination of the methoxyl and the methyl-imide group.

"Besides, the method of determining the molecular weight by boiling points has been made accessible to microanalysis. We are able to obtain reliable values with quantities of 7 mg of substance."

CONSEQUENCES IN THEORY AND PRACTICE

Methods for identifying substances in very small quantities are not new in chemistry. Almost one hundred years ago, Bunsen and

Kirchhoff estimated that they could detect sodium or other metals which color a flame when present in quantities of a hundred-thousandth of a milligram. Certain sugars or proteins could be identified by colored products which they form in solution with special reagents. The exact determination of the composition of an organic substance with milligram quantities, however, was a new achievement. It fitted beautifully into the new development of physiological-chemical research. Substances present in extremely small proportions in plants or animals proved to have important biological functions. Only a few grams could be prepared from tons of the organic material. Research on pigments, vitamins, and hormones required microanalytical methods.

Radioactivity measurements indicated the presence of even smaller quantities. Thus it became necessary to continue on the way from macro- to microanalysis and to develop techniques for ultra-microanalysis.

The balances used to weigh micro-quantities at first were based on conventional principles; an example was the Kuhlmann balance, which made Pregl's work possible. For ultra-micro weighing, other principles had to be used.

19 2 4

No Award

19 2 5

RICHARD ZSIGMONDY

(1865-1929)

*"For his elucidation of the heterogeneous nature of colloid solutions and for the methods he has devised in this connection, which have since become of fundamental importance in modern colloid chemistry!"**

BIOGRAPHICAL SKETCH

RICHARD ZSIGMONDY WAS BORN IN VIENNA, WHERE HIS FATHER was a medical doctor and inventor of surgical instruments. Richard began to be interested in chemistry and physics at an early age. He studied in Vienna and Munich. Of great importance for his future work was the time he spent as an assistant to the physicist A. Kundt (1839-1894), in Berlin. Among the subjects of Kundt's research was the abnormal spectrum exhibited by substances of high specific absorptions of light. He interested Zsigmondy particularly in the luster colors produced when organic solutions of gold mixtures are spread on porcelain. The substances mixed with the gold have a great influence on the colors which develop after the coated porcelain is heated. When Zsigmondy returned to Austria to join the faculty at the University of Graz, he began to pursue the subject of gold colors systematically. It was an old subject—late alchemists had been interested in it. In 1679, Johann Kunckel started out to make gold and invented, instead, a secret method for producing ruby glass. Another alchemist, Andreas Cas-sius, discovered a wonderful purple pigment when he precipitated

a gold solution by solutions of stannic chloride. In 1857 the English chemist Michael Faraday explained the color of ruby glass as caused by finely dispersed gold. He also experimented with solutions of gold salts which he transformed into deeply colored fine dispersions of the metal by the addition of a little phosphorus dissolved in ether. Such fine dispersions were called colloidal, an expression which had originally been used (by Graham) to indicate that solutions of animal glue or gelatin are in a class by themselves.

Zsigmondy continued these investigations when he joined the glass works of Schott in Jena, in 1897, and from 1900 to 1903 in his private laboratory. John Tyndall's method (1881) of making ultra-microscopically small particles visible by illumination at right angles to the line of observation formed the basis on which Zsigmondy, in 1903, together with the physicist Siedentopf, developed the ultra-microscope, a universal tool for detailed observation of colloids.

From 1907 on Zsigmondy was director of the Institute for Inorganic Chemistry at the University of Gottingen.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"I investigated gold-ruby glass and certain ceramic colors which are based upon the finest dispersion of gold. It struck me particularly that closely related chemical compounds displayed fundamentally different effects on the production and appearance of these colors. This observation was the more astonishing since compounds of entirely opposite properties frequently have the same kind of effect on colors of gold in finest dispersions, or colloidal gold.

"These findings were not in accord with previous experiences in chemistry. Therefore, I sought to explore the cause of these observations in a way which was not purely chemical. Cassius' Purple served as the first special object of this research. At that time, the safest method for preparing deep-red colloidal gold was

* Translated from *Les Prix Nobel en 1924-1925*.

the use of formaldehyde. With this method I prepared a sufficient amount of pure, deep-red colloidal gold. With this gold I attempted the synthesis of Cassius' Purple, and when this experiment succeeded, the conception of Cassius' Purple as a mixture of finely divided gold with colloidal stannic acid was proved. Since, on the other hand, this purple behaves completely like a chemical substance, as Berzelius already had observed, I arrived at an important experience as to the understanding of colloidal precipitates. In order to avoid errors it is necessary to consider this experience in explaining colloidal systems. In summary it can be said that a colloidal mixture can behave like a chemical compound under certain circumstances and sometimes can be mistaken for it.

"Liquids of the same gold content can appear different to the ordinary observation; on the other hand, the intensity of the Faraday-Tyndall cone of light can vary in solutions which appear clear on mere direct inspection.

"For certain problems the simple observation of the cone of light under the microscope was insufficient. I endeavored, therefore, to develop microscopic observation for the light-cone to greatest efficiency.

"The method was, therefore, refined in collaboration with H. Siedentopf in Jena. An instrument of great efficiency was constructed, the slit-ultra-microscope, with which gold particles down to a diameter of a 10-millionth of a millimeter could be made visible in sunlight.

"The particles of gold in colloidal solutions have a negative electric charge, like the particles of many other irreversible colloids. The electrical charge on these colloids has great importance as the essential cause for their stability. If the charge is removed from the particles—e.g., by adding salts—the particles immediately combine and the system coagulates. This is visible for colloidal gold by the color change from red to blue. The ultra-microscope shows not only the color change of the single particles but also a considerable change of the number of particles.

"Coagulation can be interrupted at any time by the addition of protective colloids. Thus it is possible to determine the number of ultra-microns after each definite time interval, following the addi-

tion of the coagulant, and thus to measure the velocity of coagulation."

CONSEQUENCES IN THEORY AND PRACTICE

Three states of matter have long been recognized: gas, solid, and liquid. A fourth state began to draw attention to itself about a hundred years ago, the state of fine dispersion; matter in this state may be in any one of the three fundamental states. A great many materials are found in this colloid state. Metals, salts, organic materials occur in finely dispersed forms, as fog or foam, as liquid or solid solution. They are found in the atmosphere, in natural waters, in rocks, in organisms. They are applied in medicine as salves or ointments, and in technical operations—e.g., as absorbent silica gel. Their large surfaces are seats of electrical charges and specific chemical actions. However, the colloid state is a delicate one, easily destroyed when not stabilized by protective colloids. Very small admixtures of certain foreign colloidal substances can protect a colloidal system; others can have the opposite effect.

The technically important cases in which colloidal dispersions are desired are almost as numerous as those in which they are harmful. For example, although oil emulsions of many kinds are produced by special efforts, the separation of oils from their emulsions is often required. In making or breaking colloid dispersions, the basic knowledge of their behavior is of great value. The ultra-microscope has, therefore, been improved in several ways. Siedentopf added the cardioid condenser, through which light is concentrated within the object at such an angle that only the light reflected from the colloidal particles reaches the eyepiece.

19 2 6

THEODOR SVEDBERG

(1884-)

"For his work on disperse systems"

BIOGRAPHICAL SKETCH

THEODOR SVEDBERG WAS BORN IN VALBO, SWEDEN. HE STUDIED at the University of Uppsala. His doctoral thesis described a new method for preparing colloidal solutions of metals by dispersing them under the influence of electric currents of high frequency. When such currents were caused to flow between gold or nickel electrodes, the metal dispersed in the water. Observation under the ultra-microscope showed the fine particles of the metals. In 1909, a year after his graduation, he described these methods in a book of some 500 pages. Finely dispersed particles are in a constant state of motion or vibration. The Scottish botanist R. Brown had observed them, in 1827, on suspensions of pollen. Svedberg studied this "Brownian Movement" and saw in it the result of the movement of the molecules themselves which are impinging on the relatively coarser colloidal particles. These experimental studies were published in 1912 under the title *The Existence of the Molecules*.

In the same year, Svedberg became professor in Uppsala. He turned his attention to methods for increasing the pull of gravity on colloidal particles. This can be achieved by rotation at high speed in a centrifuge. Svedberg developed an ultra-centrifuge, partly as a result of work carried out while he was a guest researcher

and lecturer in Madison, Wis., in 1922-1923. The main objects of research by means of the ultra-centrifuge were solutions of organic substances such as proteins and others characterized by the large size of their molecules. He is continuing this work as director of the Institute of Physical Chemistry at the University of Uppsala.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"The procedure was based on the fact . . . that it should be possible to determine the mass of heavy molecules by measuring the sedimentation equilibrium in the ultra-centrifuge.

"When a solution is centrifuged in a closed cell for a sufficiently long time a state of equilibrium is finally reached when sedimentation and diffusion balance each other. To determine the molecular weight it is therefore necessary only to measure the relation between the concentration of the solution at two points situated x_1 and x_2 cm from the center of rotation and to know the temperature, the speed of the centrifuge, the partial specific volume of the solute and the density of the solvent.

"The formula holds only for dilute solutions. In the case of concentrated solutions the formula for the molecular weight will include the expression for the partial specific free energy of the solute.

"A small quantity of the solution to be studied, from 0.01 to 0.25 cc, is enclosed in a glass or quartz cell possessing plane parallel walls and rotated at constant temperature in a special centrifuge which permits photographing the solution when exposed to a centrifugal force up to 5,000 times the force of gravity. After equilibrium has been reached and the cell photographed, a series of solutions of different concentrations is photographed in the same cell shortly after starting the centrifuge, that is, before any marked sedimentation has set in. The plate carrying the photograph of the solution on its way to sedimentation equilibrium and after reaching it, as well as the scale of different concentrated solutions is then

* From "A Method for the Determination of the Molecular Weight of the Proteins," *Journal of the American Chemical Society*, Vol. XLVIII (1926), p. 430.

recorded by means of a self-registering micro-photometer. From the record thus obtained the curve giving the relation between concentration of the solution and distance from the center of rotation can easily be constructed.

"The eminent physiological importance of hemoglobin has made the determination of its molecular weight, which enters as a factor in the formula for the respiratory power of the blood, an urgent task. . . . The ordinary methods based upon freezing-point and vapor pressure determinations of course fail for a substance of such high molecular weight, and the previous attempts to measure the molecular weight of hemoglobin all deal with the measurement of osmotic pressure against a semi-permeable membrane.

"Our first experiments were made with dialyzed oxy-hemoglobin in pure aqueous solution and in 1% potassium chloride solution. They gave for the molecular weight of hemoglobin values which were between three and four times the minimum value of 16,700."

CONSEQUENCES IN THEORY AND PRACTICE

The separation of molecules from their solutions by the action of gravity seems to be the simplest and directest way to the determination of molecule weights. There are, however, many influences which have to be considered and evaluated in the light of a great amount of comparative data. The mass of the molecule is only one of the factors which enter into a calculation of the effect of gravity; shape and specific gravity of the substance have to be considered, and bonds with the solvent which in turn are influenced by the degree of acidity or alkalinity and by the presence of other substances—for example, salts. The equipment for obtaining high speeds of rotation was modified in many ways. The material from which the rotor was built had to be selected for its strength and weight, and the driving method was changed from electrical to turbines. The optical system for observing and photographing the sedimentation required much attention." Very small centrifuges, with rotors of only about 1 centimeter in diameter, could be run up to speeds of over a million rotations per minute. On the other hand, rotors of larger diameters, up to 20 centimeters, gave centrif-

ugal forces up to 34,800 times gravity when driven at only 18,000 rotations per minute.

Molecular weights of proteins, viruses, and synthetic resins were measured by means of the ultra-centrifuge. Hemoglobin thus shows a molecule of 68,000 in higher vertebrates, 34,000 in certain bacteria, and 17,000 in the lowest class of vertebrates. Another blood pigment, hemocyanin, gave about 9 million. Cellulose appears to contain up to 2000 glucose units, according to some methods of measurement; *in* the ultra-centrifuge, much smaller molecular units can be observed, consisting of groups of 100 glucose residues. In the processes for manufacturing highly polymeric synthetic resins, the investigation of the sedimentation under great centrifugal force can serve as a guide to building the size and form of molecules which have the best technical value.

19 2 7

HEINRICH WIELAND

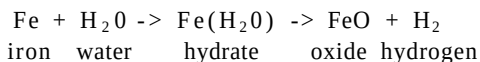
(1877-)

"For his research on bile acids and analogous substances."

BIOGRAPHICAL SKETCH

HEINRICH WIELAND WAS BORN IN PFORZHEIM, BADEN. HIS father was a chemist. Heinrich studied chemistry at several universities in Germany and received his doctor's degree from the University of Munich in 1901. He became professor of organic chemistry there in 1913. After war work at the Kaiser Wilhelm Institute for Chemistry in 1917-1918 with Haber, he returned to academic research and teaching at Freiburg, in 1921. From 1926 on he has served as successor to Willstätter at Munich.

The new biochemistry which began to be shaped in the early part of this century attracted Wieland strongly. In his first Munich period he devoted much original work to the central process of oxidation in life. We breathe to supply oxygen to the blood, from which oxygen emerges loaded with carbon, as carbon dioxide, and with hydrogen, as water. The simplest chemical explanation of oxidation seemed to be an addition of oxygen. Wieland emphasized the role of hydrogen and showed that what is commonly conceived as oxidation may, in many important cases, be a dehydrogenation. Even when a metal is oxidized—when iron rusts, for example—the decisive process is a loss of hydrogen, because an intermediary compound is formed between metal and water.



In the "oxidation" of intermediate compounds in the organism, a transfer of hydrogen from the compound to an acceptor of hydrogen takes place.

Many years of work on alkaloids, bile acids, and highly toxic biological substances followed. While his friend Windaus (see pp. 107-110) studied digitalis glucosides, Wieland elucidated the chemical structure of heart-poisons of animal origin, particularly a toxin produced by certain toads. Together with C. Schopf, he developed the chemical picture of pigments in the wings of butterflies and found analogous substances in fish skins. This apparently remote subject proved of great importance in the research on anti-anemic substances in liver.

DESCRIPTION OF THE PRIZE-WINNING WORK *

In his Nobel Prize lecture, Wieland described the way in which he located the atoms in the molecule of the most important of the acids obtained from bile, cholic acid. This way had many stations, marked by derived products for which the names were also derived from that of the parent substance, bile. A general plan had to be drawn; numbers were assigned to the 24 carbon atoms as they are supposed to follow one another, distributed over four rings of carbons and side chains of carbons attached to definite places of the rings. The molecule then had to be simplified by partial, well-controlled destruction, but sometimes it had to be made more complicated first—for example, by a Grignard reaction (see p. 51) to protect the hydroxyl groups. A few uncertainties remained at that time, but many of the artificially produced changes were "transparent" in giving a picture of the "inside" of the large molecules.

"The formula of cholic acid shows a structure built from four condensed carbon rings containing three branching side chains.

"The carboxyl group, which is responsible for the acidic character of the substance, is situated in one side chain. The three other oxygen atoms of cholic acid are distributed in the molecule as

* Translated from *Les Prix Nobel en 1927*.

alcoholic hydroxyl groups; in cholic acid they are placed at carbon atoms number 3, 7, 12. Desoxycholic acid, $C_{24}H_{40}O_4$, lacks the hydroxyl group at C-atom 12, and one of the OH-groups of lithocholic acid is bound to C 3. A cholic acid, $C_{24}H_{40}O_4$, which is isomeric with desoxycholic acid has been isolated by Windaus and myself from gall of several organisms, particularly goose, cattle, and man. This cholic acid is designated by the names cheno-desoxycholic acid and anthro-po-desoxycholic acid. Although the two discoverers are otherwise on excellent terms with each other, no agreement has been reached with regard to uniform nomenclature. In this acid the two hydroxyl groups are situated at C 7 and C 12. As can be seen, the four most important cholic acids are closely related to one another, not only regarding the fundamental skeleton, but also with regard to the distribution of their hydroxyl groups.

"The first breach of the molecule has been made starting from desoxycholic acid, which is split, by way of the diketo-acid, in ring I. The two isomeric desoxybilianic acids are thus obtained.

"The cyclic ketone obtained from desoxybilianic acid was split open, after several intermediate products, into a hexacarboxylic acid, $C_{23}H_{34}O_{12}$, in which only one ring was conserved and which was, therefore, designated as solanelllic acid. By decomposition of this solanelllic acid through heating, a new pentanone ring was obtained . . . and its further splitting led to an acid, $C_{22}H_{32}O_{12}$, called biloidanic acid.

"All attempts to penetrate into the last ring of the molecule, starting from biloidanic acid, remained without success.

"It will be seen that in the experiments described so far only two carbon atoms had been removed from the large molecule in a controlled transparent manner. The rule followed so far, to proceed step by step, had to be abandoned, if the goal was to be approached within a reasonable time.

"We started from the ester of cholanic acid, $C_{24}H_{40}O_2$, the parent of the whole group, converted this into the diphenylated carbinol by a Grignard reaction, and oxidized this product with chromic acid. In this manner one C-atom after the other was split off. Together with the third C-atom, the fourth split off, a proof of its being connected with a CH_3 -group. Beginning with the acid

COH₃2O₂, the monotony of this process showed a welcome change. . . . The opening of the fourth ring was achieved. . . . This fourth ring was recognized as a five-carbon ring. . . . The relationship of the side chain to ring II (lactonization with the OH-group of C 7, condensation with the CO-group of the dehydro-acids) defines the place of the side chain at C 18.

"The present state of our knowledge of the formula for cholic acid is hypothetical insofar as the situation of the last two carbon atoms has not been determined accurately."

CONSEQUENCES IN THEORY AND PRACTICE

Shortly after presenting this picture of cholic acid Wieland had to change some of its details. New chemical analogies and the calculation of the relative distances of the carbon atoms from X-ray diagrams showed that carbon atoms 1 to 14 were connected in three benzene rings connected with one another by two carbons, and that only one five-carbon ring was attached to one of them, again by two carbon atoms. Various side chains on this skeleton account for differences among the main bile substances from different animals. The same skeleton was found in sterols from plants. Bufo-toxin from the toad *Bufo vulgaris* proved to be chemically related to scillaren, a toxin from squill, a plant from the class of lilies.

Bile acids have an important function in the digestion of food substances. With a little variation in their chemical structures, these beneficial substances become powerful poisons. Similar relationships were discovered for chemicals which, in very small quantities, are of decisive influence in the growth and sexual development of man and animals. The availability of the new knowledge of bile substances made it possible to determine the chemistry of sex hormones within a relatively short time (see p. 166).

19 2 8

ADOLF WINDAUS

(1876-)

"For his studies on the constitution of the sterols and their connection with the vitamins."

BIOGRAPHICAL SKETCH

ADOLF WINDAUS WAS BORN IN BERLIN AND RECEIVED HIS EARLY schooling there. He studied medicine at Freiburg and Berlin. Emil Fischer's personality and work turned his interest, like that of so many others, toward chemistry. After receiving his doctor's degree at Freiburg, with chemistry as major and physics and zoology as minors, he returned to Berlin for a year at Fischer's laboratory, then went back to Freiburg in 1901. His work on cholesterol and on digitalis started soon thereafter.

Cholesterol received its name from the Greek words for bile {chole} and solid {stereos}. M. Chevreul had shown its presence in fats, as that part of them which could not be converted into soap by reaction with soda or potash. Similar unsaponifiable residues were found in many plant seeds and fruits, but they were not identical with cholesterol. The work which Windaus performed in defining these substances as members of a whole group of sterols can be compared with that of Wallach (see pp. 42-45) in the field of terpenes. Cholesterol itself, which can be easily prepared in crystallized form from gallstones, has 27 carbon atoms in one molecule. Eight of these carbon atoms are split off by a mild oxidation; they represent a side chain attached to the larger part of the molecule, which contains four rings of carbon atoms.

A connection between research on sterols and on digitalis was found in the ability of one of the substances from the digitalis leaves, digitonin, to form insoluble precipitates with certain sterols. Windaus used this reaction to distinguish between the products obtained by irradiating ergosterol. At that time, he was professor at the University of Gottingen, a post which he had held since 1915, after having occupied the chair of applied medical chemistry at Innsbruck for two years.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"What is the biological role of cholesterol itself? Many experiments have been designed to answer this question. Several investigators emphasize the physical, especially the colloid-chemical, properties of cholesterol. They point to the ability of cholesterol to emulsify fats and to the importance for the permeability of the cell. These relationships are very much in need of further clarification.

"One fact in particular has aroused the interest of chemists and physiologists during recent years, the connection between sterols and the anti-rachitic vitamin. This vitamin is relatively abundant in the unsaponifiable part of cod-liver oil, which is a good remedy for rachitis. The German doctor Huldshinski was the first, to my knowledge, who found that, besides cod-liver oil, irradiation by ultra-violet light is a remedy for rachitis. Two American scientists, Hess and Steenbock, later found independently of each other that it is not at all necessary to irradiate the sick organism, but that it is sufficient to irradiate the food which he gets. The same scientists and, at about the same time, the Englishmen Rosenheim and Webster, in London, found later on that the reactive substance is present in the unsaponifiable part of the foodstuffs and that it is identical with the sterols.

"It was at first believed that all sterols, from animals, plants, and fungi, could be activated by ultra-violet light. Physical measurements and biological experiments showed later that cholesterol and sitosterol contain an admixture in trace quantities which is respon-

* Translated from *Les Prix Nobel en 1928*.

sible for the formation of the active compound. Cholesterol can be freed of this impurity quite easily. This admixture has been proved to be identical with the ergosterol of fungi, or, to express it more cautiously, it has exactly the same absorption spectrum and exactly the same physiological behavior as ergosterol.

"The conversion of ergosterol into the anti-rachitic vitamin takes place in ultra-violet light of wave length between 253 and 302 *m/μ*; light of longer wave length than 313 *m* or shorter than 248 *m/μ* does not have a reliable effect.

"The activation succeeds even at -183° C. About 700 to 1000 ergs are required to produce a quantity which is just biologically active (about 1/50,000 mg). By irradiation for too long a period, vitamin D is destroyed.

"In order to obtain reproducible results of irradiation, it is necessary not only to exclude oxygen completely—which is very difficult—but also to irradiate all parts of the solution as uniformly as possible. We tried the activation at first by pumping a 0.25 percent alcoholic solution of ergosterol under nitrogen pressure through a quartz spiral wound around a mercury lamp.

"Later on we heated the ethereal solution of ergosterol, through which purified nitrogen was percolating in a double-walled quartz vessel, while inside the quartz vessel electric sparks were produced between magnesium poles."

CONSEQUENCES IN THEORY AND PRACTICE

Although Windaus's work on cholesterol helped to provide the foundation for the chemistry of sex hormones (see p. 166), and although his research on digitalis similarly influenced the technical preparation of cardiac tonics and sedatives, his investigation of methods for producing vitamin D had the widest applications. In these investigations, Windaus combined physical and biological procedures with those of organic chemistry. Absorption spectra and feeding tests were correlated with purely chemical reactions. The advantages which can be obtained from group work were spectacularly demonstrated. This meticulous research showed that irradiations can be beneficial, but that they have to be closely con-

trolled, because overdoses may be detrimental. The energy required for the conversion of ergosterol into the vitamin is small; the combustion of one gram of petroleum furnishes the energy-equivalent necessary for the conversion of 10 grams of ergosterol. The specific form in which this amount of energy is applied is decisive for the effect. Bourdillon called this vitamin calciferol; Windaus later designated it as vitamin D₂, to distinguish it from the mixture originally called vitamin D. One ounce of the pure vitamin would be sufficient to provide the vitamin D requirements of three thousand children for one year! In continued research, safe and efficient methods for enhancing the vitamin D content of foods, particularly milk, have been developed, using the principles which Windaus stated. Milk in continuous, regulated flow streams through stainless steel tubes which have a rod-shaped ultra-violet lamp in the center, and air is carefully excluded.

Who could calculate in precise figures the value of the work from which this development grew, and to which a great number of scientific and technical studies contributed?

19 2 9

ARTHUR HARDEN

(1865-1940)

HANS VON EULER-CHELPIN

(1873-)

*"For their investigations on the fermentation of
sugar and of fermentative enzymes."*

BIOGRAPHICAL SKETCH

HARDEN

ARTHUR HARDEN WAS BORN IN MANCHESTER, ENGLAND. HE received his doctor's degree in chemistry from the University of Erlangen, Germany, in 1888. As lecturer and demonstrator in chemistry at Owens College, Manchester (1888-1897) he was mostly interested in teaching. He collaborated with Henry Roscoe (1833-1915) on his great textbook and wrote a *Practical Organic Chemistry* together with F. C. Garrett. After joining the Jenner Institute of Preventive Medicine (later Lister Institute) in 1897, he began to study fermentations as a means for differentiating among varieties of bacteria. He included work with yeast juices. When yeast is kept in a warm place, its enzymes liquefy the cell substance. The self-digested, or autolyzed, yeast juice still contains the fermentation enzyme-complex called zymase. Heating autolyzed yeast juice to boiling should destroy all enzyme activity. Yet, as Harden

found, the addition of boiled autolyzed yeast increases the rate of fermentation considerably. The active agent, which Harden called co-zymase, contains phosphoric acid or its salts. Are they responsible for the activity? He added potassium phosphate to a mixture of sugar and Buchner-juice (see p. 30) and observed a great increase in carbon dioxide. More detailed measurements showed relationships between CO_2 and phosphate (PO_4). Later on, a compound of sugar (hexose) and phosphate was discovered. Obviously, it had to be assumed that a special enzyme was here involved. Since it appeared to act upon phosphates, its name was to be phosphatase. Further research led to the finding that several compounds are formed in which sugar acts like an alcohol, so that these sugar-phosphates are comparable to other compounds of an alcohol with an acid, which are usually called esters.

Harden retired as head of the biochemical division of the Lister Institute in 1930.

In personal contact, he was uncommonly reserved, but to the scientific public he gave much of his efforts, as an author of books and as editor of the *Biochemical Journal*.

EULER-CHELPIN

HANS VON EULER-CHELPIN WAS BORN IN AUGSBURG, BAVARIA. At first he intended to become an artist and studied painting in particular; then his interest in colors made him change to physics and chemistry. After graduation from the University of Berlin, in 1895, he continued physico-chemical work in Nernst's laboratory, became physics assistant to Arrhenius in 1897, and spent two summers (1899 and 1900) with van't Hoff. By 1900 he was already docent for physical chemistry at Stockholm, where he became professor of general and organic chemistry in 1906.

With physical chemistry as a foundation he turned to biochemistry, as Arrhenius had done. New prospects were seen to open up when the general laws of the course of chemical change, and the physical concepts and equipment used to measure characteristic single properties, were applied to the complexities and mysteries of chemical change occurring in organisms and caused by them. Fermentation and enzyme chemistry in general could thus be brought

into systematic connection with the rest of chemistry. Euler presented such a system in his book *Chemie der Enzyme* (The Chemistry of Enzymes), which was published in 1910 and saw several later editions.

The familiar chemical relationships illuminated the darkness of enzyme reactions when Euler and his collaborators showed that a chemical bond between an enzyme and the substance upon which it acts, its substrate, is in effect a bond between an acidic (carboxyl) group and an alkaline (amido) group. His particular interest was directed toward the subsidiary agents which co-act with the enzymes, the co-enzymes. Harden had found a heat-stable, or at least boil-proof, co-enzyme of zymase. Euler purified it and dissected it chemically. The result was that this co-enzyme has the nature of a special ester of sugar and phosphoric acid which is chemically combined with a purine and is related to compounds found in muscle. He characterized the purity of co-zymase (abbr. Co) by its activity A per unit weight of "Co."

This co-action, the fact that a bio-active substance needs a helper, had its analogies in immunology. Euler also found its counterpart in certain "poisoning" effects on enzyme actions, where the inhibiting force of one substance is disproportionately increased by the addition of a second inhibitor. On the other hand, substances of high biological effect usually have counteracting substances. Vitamins have anti-vitamins, and, in general, if the active agents are designated as ergones, we may discover their specific anti-ergones.

With such thoughts, always substantiated by extensive experiments, Euler came from enzymology to questions of medicine and of heredity. In the foreword to the first edition of his book on the chemistry of enzymes, he had expressed the thought that in this field, as in others, theory will be of practical value to the physician and the technician. His assistance in showing the practical value of theory found a particular recognition in 1929, when a new institute, the biochemical institute of the University of Stockholm, was dedicated to his work. It has been directed by Euler since then.

DESCRIPTION OF THE PRIZE - WINNING
WORK

HARDEN *

"A striking feature of fermentation by yeast preparations is that it proceeds much less rapidly than fermentation by a corresponding amount of living yeast. Thus Buchner's yeast-juice ferments at only about 1/20-1/40 of the rate of the yeast from which it is derived.

"The fact that the rate of fermentation of such a juice can be raised under favourable circumstances some 10-20 times simply by increasing the supply of phosphate seems to me to indicate clearly that a large fraction, at least half, of the fermenting complex of the yeast has escaped injury in the preparation and has passed into the juice, but that the mechanism for the supply of inorganic phosphate has been to a large extent destroyed. Neither arsenate nor phosphate has an accelerating action on the rate of fermentation by living yeast. This may be due to the fact that the supply of inorganic phosphate in the interior of the yeast-cell is already optimal, but some doubt exists as to whether or not these salts freely penetrate the cell. If, however, as seems to me probable, it is true that in the preparation of yeast-juice etc. it is the phosphate-supplying mechanism that is thrown out of gear, it becomes an object of enquiry in what way this is brought about.

"The process least likely to inactivate an accelerating substance is probably that used by Buchner, but the possibility also exists that such a substance, if present, might be absorbed and thus be removed from the juice by the large quantity of kieselguhr employed.

"Experiments (not yet published) have recently been made in my laboratory by Miss Macfarlane to find out at what stage in the process the change occurs and whether a juice richer in phosphatase could be obtained by modifying the process of grinding and pressing out. It appears, however, that simple grinding with sand pro-

* From *Les Prix Nobel en 1929*.

duces a change of the same order as that observed in Buchner's yeast-juice.

"Minor differences were observed when different substances were substituted for the kieselguhr used by Buchner, the most active juice for example being obtained by the use of CaCO_3 whereas BaCO_3 yielded totally inactive material.

"When fermentation of sugar by yeast preparations is carried out under suitable conditions in the presence of added inorganic phosphate, a rapid production of CO_2 and alcohol occurs and a phosphoric ester of a sugar accumulates, the amount of phosphate found in this form being approximately proportional in the ratio (CO_2/PO_4) to the increased production of CO_2 and alcohol caused by the addition of the phosphate (Kluyver and Struyk, it is true, have found lower ratios than this, but there is no doubt that high ratios 0.8-1 are often observed).

"The phosphoric ester produced, however, may consist mainly of the hexosediphosphate originally described by Young and myself or of the hexosemonophosphate described by Robinson and myself and subsequently studied by Robinson or it may be a mixture of these in any proportions. In the case of fermentation by dried yeast (and possibly by other preparations) a further complication is afforded by the fact that a disaccharide-phosphoric ester (trehalosemonophosphate) may also be present."

EULER-CHELPIN *

"An enzyme acts by combining with its substrate according to a definite affinity. For example, when *egg* white is digested, it becomes a long chain of amino acids from which *egg* white more or less is composed, and by-products which contain two such amino acids, so-called dipeptides.

"Dipeptides have their special enzymes, dipeptidases. The question arises with which group contained in the dipeptide the combination with the enzyme occurs. It is a general fact that the split-product which results from an enzyme reaction has an impeding action; here, amino acids do it. Now we wanted to find experi-

* Translated from *Les Prix Nobel en 1929*.

mentally what kind of group a split-product had to contain to exert this impeding action, and from the work of Josephson with a special dipeptidase we found that it had to be an amino group.

"Studies of the circumstances under which the impeding effect takes place and those under which enzymes combine with dipeptides showed that it is a carboxyl group attached to the enzyme which combines with the substrate, and thereby the bond between enzyme and substrate was for the first time explained by definite atom groups.

"The reason for our devoting much time and work to the purification and chemical investigation of co-enzyme is that co-enzyme is one of the most widely spread and most important of activators in plants and animals. The difficulties of isolating co-zymase begin with the great dilution in which it occurs. Yeast is considered the most convenient raw material, although one kilogram of yeast gives only 20 milligrams at best.

"After a long sequence of purification procedures we obtained a substance with the maximum activity, expressed in rational units, of $A_{Co} = 85,000$, while the starting material is characterized by $A_{Co} : 200$. This substance could be converted into salts from which the co-zymase was regenerated in unchanged activity. The composition of the purest product corresponds to that of a nucleotide; it contains a sugar residue, a purine residue, and phosphoric acid and is thus closely related to adenylic acid."

CONSEQUENCES IN THEORY AND PRACTICE

Phosphates are important in the life processes of organisms. Plants need them and they have become an essential part of fertilizers. Proteins such as casein contain phosphates, and they occur in bones and in urine. It was known that they are present in yeast, so that it was quite natural to look for them in the boiled yeast juice which had such an unexpected influence on fermentations. Harden's discovery that sugar combined with phosphate as a first step in fermentation indicated something of the biochemistry of phosphate. It was clear, from the standpoint of enzymology, that the intermediate compound needed a splitting enzyme, phosphatase,

but first another enzyme had to exert a combining, or phosphorylating, action. Phosphorylase was found in animal tissues, yeast, plants, and bacteria, although it was not of the same kind in all these cases. Adenylic acid was sometimes involved in its structure. Although it may appear strange that sugar had to be built up into the phosphoric acid ester in order to be degraded into the simpler products of fermentation, the paths of sugars in nutritional change to utilize its energy are still more complicated. Transfers of phosphoric acid between substrate and enzymes of several kinds take place before the muscle obtains the calories from sugars.

Sugar phosphates found a practical application for special nutritional needs. Calcium salts of hexosephosphate are very soluble in water and offer the possibility of supplying both calcium and phosphorus in easily assimilated form.

That enzyme reactions proceed through the intermediary of a bond between enzyme and substrate is widely accepted. The nature of this bond, which Euler and Josephson were able to interpret so simply for their dipeptide, is far from clear in most other cases. Much more work will be required to explain the high specificity of enzyme response to chemical constitution.

19 3 0

HANS FISCHER

(1881-1945)

*"For his researches into the constitution of hentin
and chlorophyll, especially for his synthesis of
hemin."*

BIOGRAPHICAL SKETCH

HANS FISCHER, BORN IN HOCHST, NEAR FRANKFORT ON THE Main, was equally interested in chemistry and in medicine. He received his doctor's degree in chemistry from Marburg University in 1904, and in medicine from Munich University in 1908. Medical work in Munich was followed by chemical research in Berlin at Emil Fischer's institute. Fischer succeeded Windaus at Innsbruck, in 1916, as professor of medical chemistry, and returned to Munich as professor of organic chemistry in 1921. He filled this office as a teacher, researcher, and editor of scientific journals to the end of his life.

When Fischer began his extensive study of the blood dyestuff, the chemical nature of the corresponding green pigment of plants had become much clearer. The red hemin and the green chlorophyll had a peculiar structure in common: magnesium in the center of a large molecule in chlorophyll, iron in a corresponding place in the molecule of hemin. In both cases, this center atom can be removed without hurting the rest of the structure. Hemin, thus gently deprived of its iron, proved to be identical with substances previously found as products of a mild degree of putrefaction of hemin and called porphyrin. There was, however, great uncertainty concern-



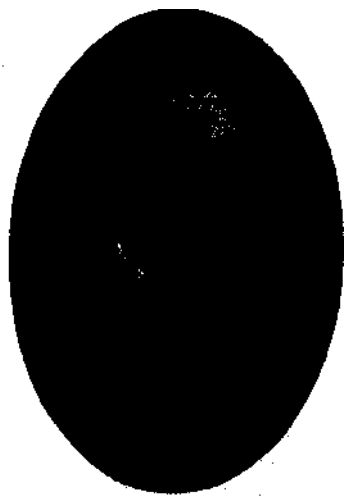
JACOBUS HENRICUS
VAN'T HOFF



EMIL FISCHER



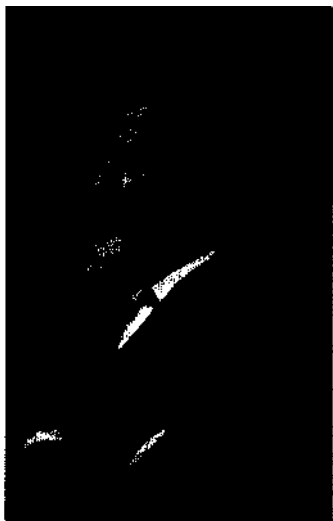
SVANTE AUGUST ARRHENIUS



WILLIAM RAMSAY



ADOLF VON BAEYER



HENRI MOISSAN



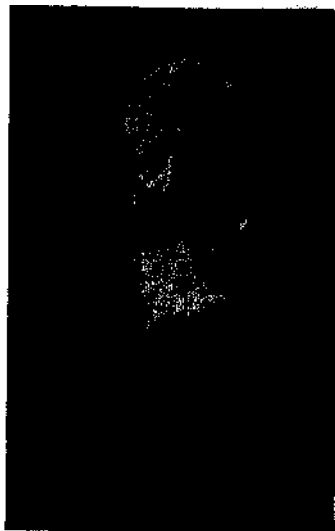
EDUARD BUCHNER



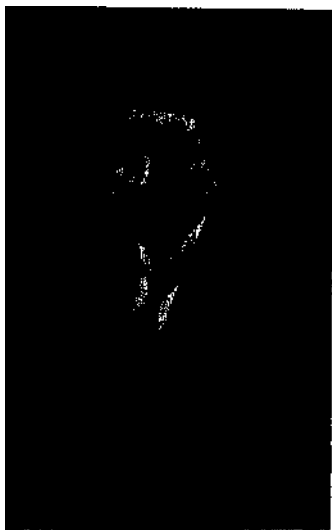
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WILHELM OSTWALD



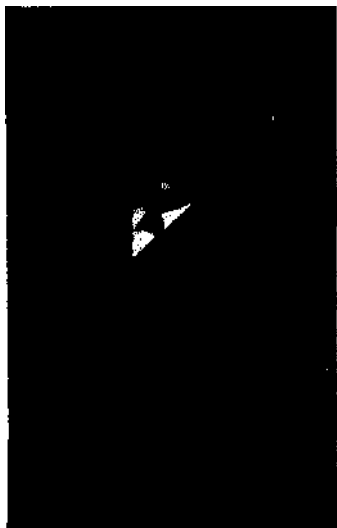
OTTO WALLACH



VICTOR GRIGNARD



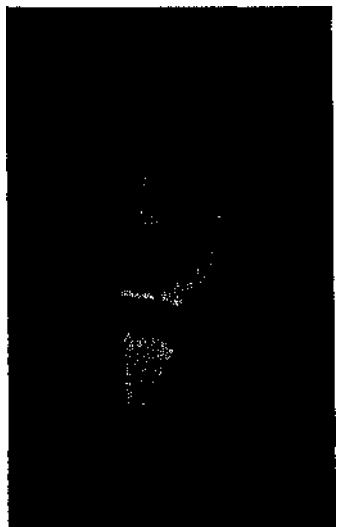
PAUL SABATIER



ALFRED **WERNER**



THEODORE WILLIAM RICHARDS



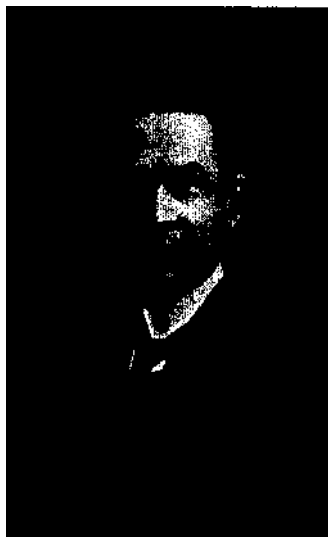
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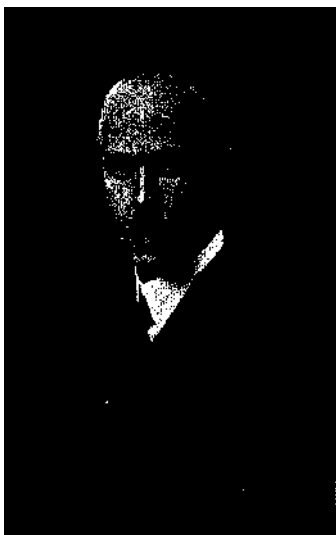
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WALTHER NERNST



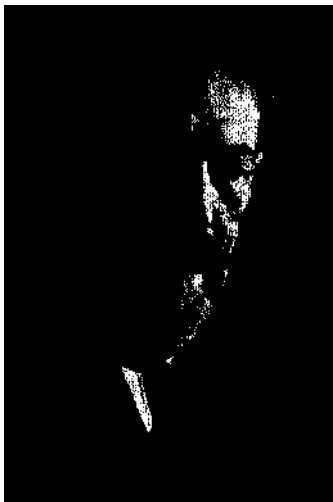
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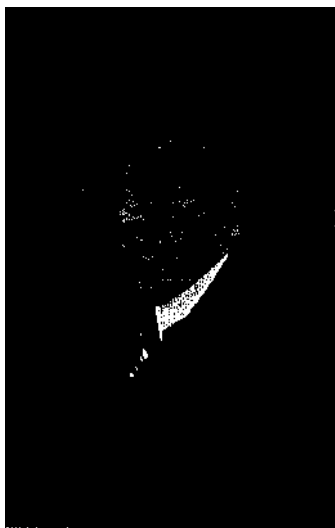
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RICHARD ZSIGMONDY



THEODOR SVEDBERG



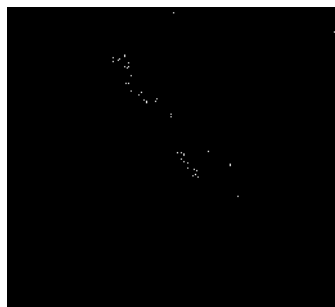
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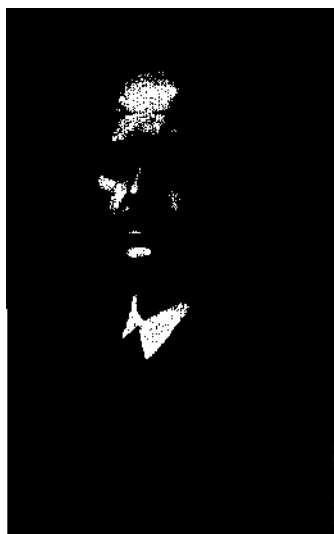
ADOLF WINDAUS



ARTHUR HARDEN



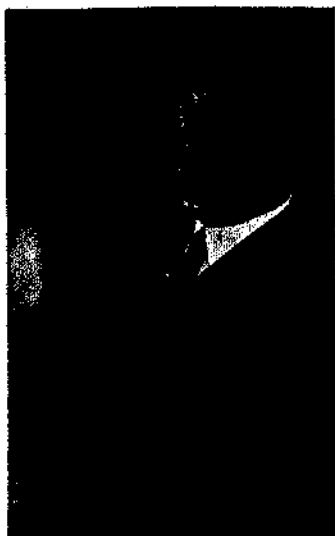
HANS VON EULER-CHELPIN



HANS FISCHER



CARL BOSCH



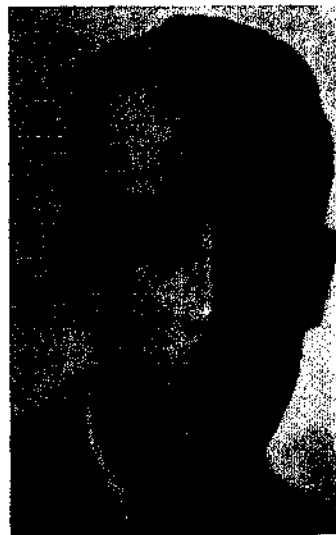
FRIEDRICH BERGIUS



IRVING LANGMUIR



HAROLD C. UREY



FRÉDÉRIC JOLIOT



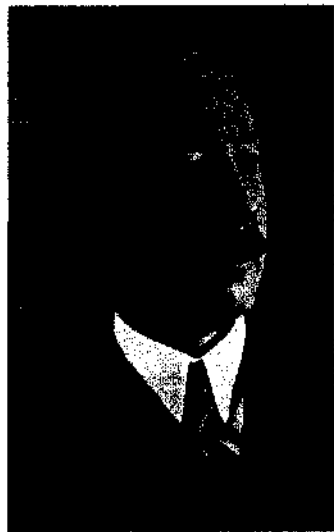
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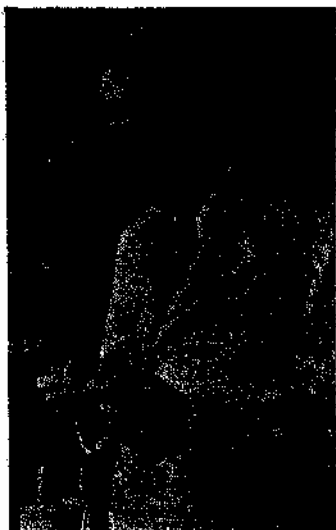
PETER J. W. DEBYE



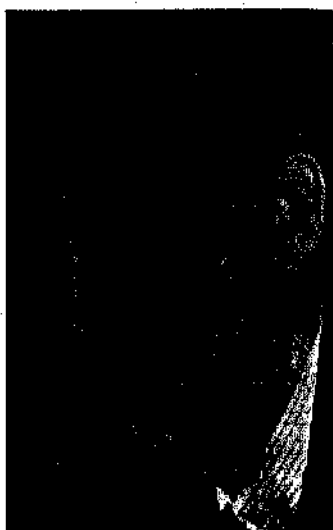
WALTER NORMAN HAWORTH



PAUL KARRER



LEOPOLD RUZICKA



GEORGE DE HEVESY



OTTO HAHN



ARTTURI ILMARI VIRTANEN



JOHN HOWARD NORTHROP



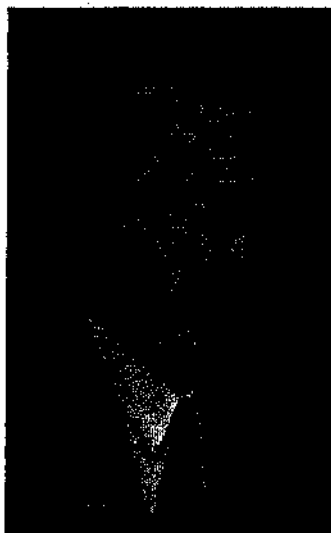
WENDELL MEREDITH STANLEY



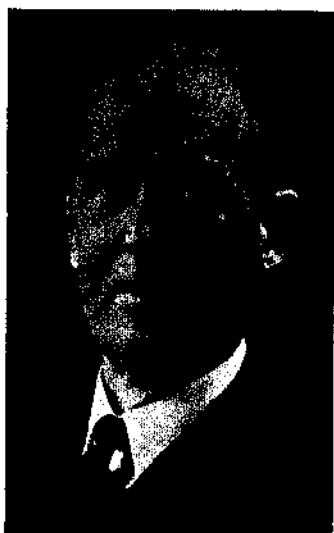
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ROBERT ROBINSON



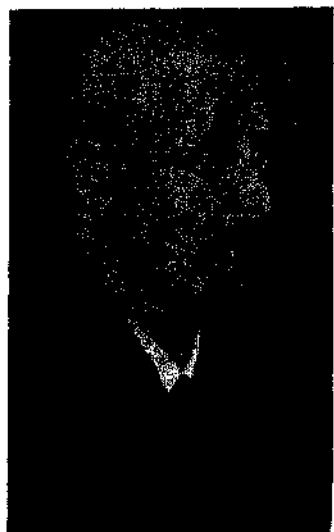
ARNE TISELIUS



WILLIAM FRANCIS GIAUQUE



KURT ALDER



OTTO DIELS

ing the relationships and identities of substances obtained by chemical change of hemin. A first important step toward deeper insight into the chemistry of hemin was made with Fischer's investigation of a natural degradation product of hemin from gall (bile). Among the gall pigments, one is bilirubin. As the name indicates—fortunately, among the great number of artificial names in this field, there are a few which have at least a partial relation to some general properties—bilirubin, although a degraded hemin, is still red. By splitting of the molecule in half on heating with acetic and hydro-iodic acid, a new acid was obtained in which a section of the hemin molecule was still intact. It was relatively easy to identify its structure and to relate it to pyrrole, the oily and smelly product which earlier chemists had obtained by heating animal substances to high temperature and condensing the oil out of the vapors.

From this basis, which was secured by W. Kiister in 1912, Fischer began the approach to the chemistry of hemin itself. Bilirubin and its close relatives could be made by synthesis. A fundamental structure of four pyrrole molecules was recognized. The pyrrole, a simple ring of four carbon atoms closed by one nitrogen atom, is modified by methyl, ethyl, and propionic acid groups and an unsaturated ethyl group which has the name vinyl, now so familiar to users of plastics. The number of possible variations of these groups combined with the pyrrole ring, and the sequence in which the four modified pyrroles are arranged to form hemin, were gradually tested. The vinyl group caused particular difficulties, until it was saturated with hydrogen and thus reduced to ethyl. A porphyrin so altered was designated as mesoporphyrin.

After elimination of unlikely arrangements, the final test for the proposed structure of hemin was made by its synthesis from simpler organic materials of which the structure was known.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The blood pigment hemoglobin is a complex compound which can be split up into its components, dyestuff and protein, by several

* Translated from *Les Prix Nobel en 1930*.

methods. Teichmann observed this cleavage first in a microscopic preparation in which a mixture of glacial acetic acid and sodium chloride acted on blood. Schälfeff, Nencki, Piloty, Willstätter, and others developed this method on a larger scale, so that the Teichmann crystals are now available by the kilograms. The Swedish scientist Morner had also worked out a method of disaggregation by means of alcoholic sulfuric acid. By this method esters of hemin are formed.

"Hemin has the formula $\text{Q4H}_{32}\text{O}_4\text{N4FeCl}$. Innumerable variations of this atomic combination are possible. The pyrrole-nature of hemin was proved by the methods of analytical degradation developed by Nencki, Kiister, Piloty, Willstätter, H. Fischer, and their students. By these methods it was also possible to obtain a far-reaching insight into the constitution of hemin. When hemin is deprived of its iron, porphyrins are formed. These substances have [photochemical] sensibilizing effects, as Hausmann has shown.

"These porphyrins are widely distributed in nature. It was possible to start with the assumption of a relationship with the porphyrins of the blood pigment as a working hypothesis, and it was to be expected that the determination of the constitution of the natural porphyrins would also offer some clues for the constitution of hemin itself; just as the disaggregation products of bilirubin, which had been formed from blood pigment in a biological way, had given evidences for the determination of the constitution of the blood pigment itself. This was the reason why I attacked the investigation of the natural porphyrins in a systematic way, and similarly also the biological degradation of the blood pigment itself.

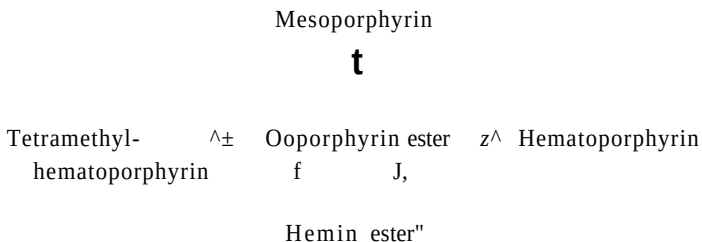
"In porphyrinuria, a light-disease, man secretes large quantities of porphyrins. It was formerly assumed that only hemato-porphyrin was involved, but this assumption could be refuted. At least two porphyrins are secreted, uroporphyrin and coproporphyrin, which both occur in the urine, although coproporphyrin occurs in greater amounts in the excrements. One of them, probably coproporphyrin, had been observed already by Hammersten. It is not always the same coproporphyrin which is present in the urine. Hijmans van den Bergh observed an isomeric coproporphyrin, but up to now

only in one case of porphyrinuria. It may be of interest to note that uroporphyrin occurs also in the flight-feathers of African birds of the Turacus family, in which it is present as a complex copper salt.

"Closely related to uroporphyrin is conchoporphyrin, which is present in mussel shells, probably as a calcium salt. Natural coproporphyrin is very widely distributed. Traces of it are contained in normal urine and also in yeast. It is possible to force yeast to produce considerable quantities of coproporphyrin by inadequate culture conditions. Yeast is thus brought into a state which is comparable to human porphyrinuria.

"A porphyrin (ooporphyrin) is also contained in the eggshells of birds breeding in the open. By putrefaction of the blood pigment a porphyrin is produced which is identical with this ooporphyrin and was called Kammerer's porphyrin. By protracted putrefaction deuteroporphyrin is formed.

"Ooporphyrin is identical with protoporphyrin or Kammerer's porphyrin. When iron is introduced into ooporphyrin by a complex bond, hemin is obtained. When ooporphyrin ester is reduced with hydrogen iodide, mesoporphyrin is formed. In a similar manner it is possible to transform the ooporphyrin ester into tetramethyl-hematoporphyrin and hematoporphyrin. The following diagram may illustrate these transformations, some of which are reversible:



CONSEQUENCES IN THEORY AND PRACTICE

There is a close relationship between hemin and chlorophyll. Fischer, who showed details of this relationship, proceeded from the synthesis of hemin to that of chlorophyll; the latter work was

nearly completed at the time of his death. The way in which the organism synthesizes these substances is still obscure, although Fischer himself obtained pyrroles from acetic acid and ammonia. The degradation of hemin into bile pigments, into urobilin and coproporphyrin is better understood in its chemical results since the structure of hemin is known. A recent survey of this research comes to the conclusion that "we have undoubtedly made only a beginning in these studies."

Even the synthesis of the dyestuff in blood, the crowning event of long research, is only a beginning of more intimate studies of the natural compound formed by hemin and the protein-substance globin, itself containing about 136 amino acid residues. In the red blood cell, hemoglobin is again associated with other substances—sugars, fats, cholesterol. The chemical unit hemin is only a small part of the biological unit, hemoglobin.

19 3 1

CARL BOSCH

(1874-1940)

FRIEDRICH BERGIUS

(1884-1949)

"In recognition of their contributions to the invention and development of chemical high-pressure methods."*

BIOGRAPHICAL SKETCH

BOSCH

FROM EARLY YOUTH, CARL BOSCH, A NATIVE OF COLOGNE, GERMANY, was interested in things one can do, in materials one can shape by hand. At school he was in advance of his class in mathematics, physics, and chemistry, but he disliked language studies. In preparation for a planned chemical career he spent a year in machine shops and took up mechanical engineering at the Technische Hochschule in Charlottenburg. He was graduated from Leipzig in 1898 under Johannes Wislicenus with a thesis in pure organic chemistry. In 1899^{ne} started on the synthesis of ammonia at the Badische Anilin und Soda Fabrik. Experienced as a carpenter, mechanic, engineer, and laboratory chemist, he was well equipped to attack the problem of manufacturing an inorganic chemical substance. Studies in the behavior of metals and alloys as materials of

construction, in equipment for automatic indication and control of temperatures and pressures, and in the development of safety devices made it possible for Bosch to take Fritz Haber's invention (see p. 73) out of the laboratory into production.

A solid scientific foundation was to Bosch the first requirement for industrial success. He criticized the conditions under which engineering was taught at Charlottenburg and most technological institutes where rule of thumb prevailed and science was neglected. For him the way from pure science to practice did not include speculation or philosophy but steady, systematic search for fundamental facts. His systematic investigation of catalysts included practically all available chemical elements and combinations of them. For this and for research on raw materials, purifications, and utilizations, he organized the Ammonia Laboratory in Oppau, which at times employed 180 academically trained people and more than one thousand helpers. For research on the cooperation of soil, fertilizer, and plant he created a large experiment station (Versuchsanstalt), in 1915, and in addition a "biolaboratory" to explore the function of nitrogen in life.

Germany's advantage, "the only advantage we still have," Bosch stated in 1925, was that its scientists had a broad foundation and that they did not specialize immediately, at the beginning of their education. He took a prominent part in the efforts to help students and to provide fellowships for scientists. When he succeeded Max Planck as director of the Kaiser Wilhelm Gesellschaft his efforts led to the organization of an Institute for Biophysics.

One of Bosch's hobbies was the collection of butterflies. As a leading figure in the German I. G. Farben concern, he was one of the most prominent men in industry; yet he stated (in an interview in 1936) that in the scientific occupation with nature man "feels the great heart-beat of the world, and only here man moves to his own modest place as a minimal part of the cosmos."

BERGIUS

FRIEDRICH BERGIUS WAS BORN IN GOLDSCHMIEDEN (NEAR BRES-lau), Germany, where his father had a chemical factory. He received the doctor's degree in 1907 for an investigation of con-

centrated sulfuric acid as a solvent, carried out at the University of Leipzig. In order to continue work in the field which connects physics and chemistry, he went to Nernst in Berlin. Here and during his short period in Haber's laboratory at Karlsruhe he was impressed with the growing importance of high pressure in chemical reactions. He decided to enter this relatively new field. In Hanover he began, in 1909, to work on the production of calcium superoxide by reacting lime with oxygen under high pressure; at first he worked at the Technische Hochschule, then in his private laboratory. Technical problems of constructing vessels and valves had to be solved. High pressure became for Bergius the method by which to produce commercial chemicals. His interest was not so much in new compounds as in known substances with a potential future. It was the visionary part of his endeavors to foresee this future and to help in bringing it into industrial being.

A method for obtaining hydrogen by reacting water with coal seemed promising. When Bergius' attention was drawn to the future importance of converting heavy oils into motor fuel, he conceived the idea that this should be accomplished by adding hydrogen under pressure. The old method of cracking, in which heavy oils were split into smaller molecules by heat, had the serious disadvantage that methane gas on the one hand and solid coke on the other were formed, with the desired light oil as only a small part in between. The addition of hydrogen remedied this. In 1913 Bergius was ready for a first basic patent application. When the war started, in 1914, he joined the Goldschmidt organization in Essen for the purpose of developing hydrogenation on an industrial scale. Soon the problem of converting wood into sugar to relieve the food situation was added to the program, and in 1916 Willstätter's method of treating cellulose with highly concentrated hydrochloric acid became the basis for a new development.

Work on both processes was far from being completed when the war ended. It was continued in laboratory and pilot plant. The hydrogenation patents were sold to the I. G. Farben interests in 1927. The production of sugar from wood and its further conversions into alcohol, yeast, and dextrose remained Bergius' main

project. This work furnished a sizable amount of carbohydrate and food materials in Germany during the last war.

The production of ethylene glycol from ethylene gas and phenol from chlorinated benzene, for which he invented methods, later developed into large-scale operations with which Bergius was no longer directly connected.

Although he remained deeply interested in the chemical and industrial progress of his work, Bergius' foremost activity gradually became the financing of these developments. Motor fuel, alcohol, and foodstuffs have wide economic implications. Bergius saw his great task in securing the right place for the new industrial products against much shortsightedness and selfishness.

At the end of the Second World War Bergius moved to Austria; later, upon invitation by the governments, he went to Spain and then to Argentina. He died in Buenos Aires.

DESCRIPTION OF THE PRIZE-WINNING WORK

BOSCH *

"We started from the apparatus which Haber had used for his experiments. . . . Since this apparatus had several disadvantages, it was completely remodeled; in its new form it has been in use in 24 units uninterruptedly, days and nights, for years. Thus we could carry out the numerous investigations necessary to find the catalysts and to develop highest efficiency. The number of experiments has gradually reached the figure 20,000.

"We constructed an apparatus which comprised circulation pump, ammonia separator, and, the most important and interesting part, a contact tube (of about 30 mm wall thickness).

"The two contact tubes, made by Mannesmann, had an operating life of 80 hours; then they burst. If we had filled them with osmium instead of the new catalyst, the entire world store of this precious metal, which we had by now bought, would have disappeared.

"Chemical investigation showed no trace of nitrogen in the embrittled metal. The explanation came through metal logographic research, a method of approach which was, at that time, almost unknown in chemical engineering, but with which I happened to be familiar because I had started my career as a metallurgist.

"Our starting point was that the diffusion of hydrogen into the iron, the decarbonization of the perlite, and the formation of brittle iron-hydrogen were unavoidable. They had to be rendered harmless by a change of construction. The contact-tube wall has two tasks: to withstand the pressure of the highly compressed gas and to form a gas-tight enclosure. How would it be if the two functions were separated and assigned to different elements of construction? This could soon be carried out. The first experimental oven built upon this principle showed that the idea was correct.

"The long sought solution consisted in providing a pressure-bearing steel mantle with a thinner inner lining made from soft iron, so that hydrogen, which alone diffuses through the thinner lining, finds an opportunity to escape without pressure, before it can attack the outer steel mantle at the prevailing high temperature.

"In the beginning we had great trouble with the high-pressure compressors. Up to that time, larger compressors were known only for the compression of air. These high-pressure compressors had been built in only moderate size. Little attention had been paid to the stuffing boxes. With air, leakages were not critical, and short periods of idle time were accepted as unavoidable. The situation was quite different with hydrogen and the delicate contact process. . . . In long years of work we succeeded, starting with experiences with small compressors which ran no more than half a day without disturbances, to build the mighty 3000-horsepower aggregates which run reliably for six months without interruption.

"It is not exaggerated when I say that profitable technical operation depends entirely upon even and undisturbed procedure. A great help in achieving this were the control instruments. We paid great attention to them from the beginning, since the processes in the ovens could be followed only by continuous registration. To-day all this has become commonplace, and most of this equipment

is commercially available. We had to construct and test it ourselves."

BERGIUS *

"As early as 1910 Ludwig Landsberg had suggested to me that I take over the problem of splitting heavy oils and oil residues into gasoline. Experts could conjecture that the progress of automobilism would lead to a substantial increase in the consumption of gasoline, although nobody at that time had as yet developed a real concept of the extent of this development. The then known cracking processes were extremely unaccomplished.

"We tried to incorporate the highly compressed hydrogen in the molecular structure of the high-boiling petroleum fractions loosened by high temperature. Experiments carried out at first in vertical autoclaves showed distinctly an increase in hydrogen in the cracked oils, with no coke formation and a less unsaturated character of the newly formed lighter oils.

"It soon became evident that the range of temperatures within which hydrogen reacted favorably was quite narrow.

"Conditions of temperature and pressure for the hydrogenation of heavy oils are practically the same as for coal, and since in both reactions good contact of the hydrogen with the liquid or suspension to be hydrogenated was necessary, it could well be assumed that an apparatus which was suitable for oil hydrogenation would, with some additional equipment, also be applicable to coal liquefaction. In both processes it was required that solid materials be introduced into the reaction chambers—in oil hydrogenation a relatively small quantity of iron oxide for desulfuring, in coal hydrogenation the entire raw material. It was clear from the beginning that this introduction of solids into a high-pressure vessel and the removal of solid residues would cause special difficulties. The work of several years was necessary before a satisfactory solution for this technical task was found.

"Heating was carried out inside the pressure vessel by installing in the pressure-carrying tube a second, relatively thin-walled tube.

* Translated from *Les Prix Nobel en 1931*.

The heating medium under the pressure of the reaction zone was pumped through the narrow space between the two tubes.

"The splitting reaction is the better the more rapidly the newly formed products are removed from the system. Hydrogen was therefore used in excess. It had to be kept in circulation. Hydrogen left the reaction vessel with the gaseous and liquid products. It separated upon cooling from the condensed oils and from the greater part of the oil-soluble methane and was then returned to the reaction by a circulating pump.

"Hydrogen consumption was, on an average, 5 percent of the weight of coal. There was no difficulty in bringing much more hydrogen to react with the primary products and thus increasing the yield of low-boiling products at the expense of the high-boiling oils. Economic considerations will decide about how far to increase the hydrogen consumption in hydrogenating coal and its liquefied products.

"From the gaseous products, methane and ethane, hydrogen and carbon dioxide can be produced in a high-temperature reaction with water vapor. We have carried out this reaction successfully for some time. . . . It is sufficient to convert a part of the methane-ethane mixture in this manner in order to obtain the amount of hydrogen required for the process. The carbon dioxide admixed with the hydrogen can be separated easily by water under pressure after compressing the gases. This principle of hydrogen production is now, as far as I know, used in America for oil hydrogenation.

"The separation of the heavy oils from inorganic substances has presented considerable difficulties. . . . The separation was the less difficult the more completely the product had been subjected to hydrogenation.

"From the heavy fractions of the coal oil it was possible to obtain oils of good lubricating qualities."

CONSEQUENCES IN THEORY AND PRACTICE

The technical development described in the excerpts from Dr. Bosch's Nobel Prize lecture started from the production of am-

monia and soon extended to several other chemicals produced in high-pressure reactions. The continued effort resulted in special metal alloys and a new principle of reactor construction, catalysts of specific activities, improvements in gas compressors, a new science of instrumentation for indicators and regulators of important process factors. The progress achieved through continuous research can be characterized by comparative figures for the weight of steel required for a given production of synthetic ammonia. In 1913, this figure was 27; in the two following years it dropped to 11, then 6; in 1924 it was only 3.6, and in 1927 just about half of this value.

On this foundation grew the production of methanol by synthesis from carbon monoxide and hydrogen. Until 1923, wood distillation had been the only source of this alcohol. When the I. G. Farben concern began to manufacture the synthetic alcohol and to export it to the United States, it seemed as though the wood distillation industry were doomed. It survived, but its production in 1946 was just about 3 percent of the synthetic product of the United States. In 1931, Bosch proudly pointed to a German annual production of 40,000 tons; in 1946, the United States produced about 250,000 tons of synthetic methanol by this process.

Of still greater importance is the synthesis of urea from ammonia and carbon dioxide under high pressure. Urea is a convenient form of fertilizer with high nitrogen value, and it is a basic raw material for a synthetic resin which has found extensive application for molding and as a glue.

The work on hydrogenation of oil and coal was carried out in the Bergius organization in the years 1910 to 1925. When the I. G. Farben concern took it over, it expanded particularly the investigation of catalytic effects. A great store of experience from the methanol-synthesis developments was available. The hydrogenation of heavy oils could be speeded up and directed toward special products by the use of selected catalysts. The problem of avoiding the poisoning influence of sulfur, which is always present in mineral oils, was solved. Catalytic hydrogenation became an important method for increasing the efficiency of motor fuels up to the highest "octane numbers."

In a first approximation, Bergius had declared that the dividing

line between coals which are easily hydrogenated and those which do not respond readily was characterized by a carbon content of 85 percent in the coal. It has been found since then that carbon content is not a sufficient means for distinguishing between coals; the proportions of hydrogen to oxygen and the age, rank, and type of coal influence its chemical behavior toward hydrogen very greatly.

Hydrogenation methods furnished a considerable part of the motor fuels produced in England and in Germany during the last war. Recently, large-scale experiments have begun in which the pressure and temperature conditions for coal hydrogenation are sought in a considerably higher range than before.

19 3 2

IRVING LANGMUIR

(1881-)

"For his discoveries and investigations in surface chemistry/"

BIOGRAPHICAL SKETCH*

"IRVING LANGMUIR WAS BORN IN BROOKLYN, NEW YORK, January 31, 1881. His early education was obtained in the public schools of Brooklyn which he attended until 1892 when he went with his parents to Paris. There he studied in French schools for three years. Returning to the United States in the fall of 1895, he entered Chestnut Hill Academy at Philadelphia. The following year he returned to Brooklyn for study at Pratt Institute High School. Upon completion of his course at this institute, he entered the School of Mines at Columbia University from which he was graduated in 1903 with the degree of metallurgical engineer. He took up post graduate work at the university of Gottingen under Professor Nernst, being awarded the degree of M.A. and Ph.D. in 1906, his major subject having been physical chemistry.

"Returning to America, Dr. Langmuir became instructor in chemistry at Stevens Institute of Technology, Hoboken, New Jersey, where he taught until July 1909, when he entered the Research Laboratory of the General Electric Company at Schenectady where he is at present associate director.

"Dr. Langmuir's researches have been conducted in the fields of chemistry, physics and engineering, and have largely been the out-

* From Autobiography in *Les Prix Nobel en 1932*.

growth of studies of vacuum phenomena. In attempting to derive the atomic and molecular mechanisms of these chemical and physical phenomena, he has been led to make fundamental investigations of the properties of adsorbed films and surfaces and of the nature of electric discharges in high vacuum and in gases at low pressures.

"Dr. Langmuir has published about 150 papers in scientific journals. A list of his contributions in the field of low pressure, chemical reactions and adsorption phenomena is given at the end of his Nobel lecture. Some of his publications in other fields concern: Heat Flow, Tungsten Filaments and Lamps, Rates of Evaporation and Vapor Pressures of Metals, Electric Discharges in High Vacuum, Electric Discharges in Gases, High Vacuum Pumps, Atomic Structure and Valence and some General Matters."

DESCRIPTION OF THE PRIZE-WINNING WORK *

"Thorium on Tungsten. When a tungsten filament which is made from tungstic oxide containing about 1 percent of ThO_2 is heated to temperatures of $2,800^\circ$ or more, a minute fraction of the thoria is reduced to metallic thorium. The thoria exists in the filament in the form of minute spherical particles distributed throughout the tungsten crystals and not at the boundaries of the crystals. If the filament is then heated for a period of a few minutes at $1,900$ to $2,000^\circ \text{K}$, the metallic thorium which has been produced at the higher temperatures diffuses slowly through the crystal grains to the crystal boundaries, then diffuses rapidly along these boundaries to the surface of the filament and then spreads over the surface of the filament by surface migration and forms a monatomic film of adsorbed thorium atoms on the surface of the filament. At $2,000^\circ$ the rate of evaporation of thorium from the filament is so small that sufficient thorium soon accumulates on the filament to form a nearly complete monatomic film. If the temperature is raised to $2,200$ or $2,400^\circ$, the rate of evaporation of the thorium from the surface increases so much more rapidly than the rate of arrival

* From *Les Prix Nobel en 1932*.

from the interior by diffusion, that the actual surface concentration decreases greatly.

"These changes in the thorium content of the adsorbed film can be studied by measurements of the electron emission from the filament at a standard low temperature, called the testing temperature, which is chosen so low that neither diffusion to the surface, nor evaporation from the surface, causes appreciable changes in the adsorbed film. A convenient testing temperature is $1,500^{\circ}$. At this temperature the presence of adsorbed thorium on the surface may increase the electron emission as much as 10^5 fold over that from a pure tungsten surface.

"0/7 Films on Water. When a pure saturated liquid hydrocarbon is placed upon the water, it remains on the surface as a drop or lens which has no effect on the surface tension of the surrounding water. If, however, an insoluble fatty or oily substance, such as the common vegetable and animal oils, is placed upon clean water, it spreads out almost instantly as a thin film over the surface. If the motions of the surface are made visible by dusting the surface with powdered talc, it may be seen that, with a limited amount of oil, the film only spreads out sufficiently to cover a definite area, or at least if the area exceeds a rather definite value, the oil has no effect on the surface tension of the water. A comparison of various insoluble organic substances has proved that the spreading tendency depends upon the presence of certain active groups or radicals in the organic molecule, these being the groups which tend to increase the solubility of organic substances in water. For example, pentane, QH_{12} , is practically insoluble in water but amyl alcohol, $\text{C}_5\text{RH}_{10}\text{OH}$, is relatively soluble. Thus the OH groups in organic molecules exert strong attractive forces on the OH groups in the water molecules and these manifest themselves by an increase in solubility. Similarly the carboxyl group COOH tends to make the lower fatty acids much more soluble in water than the corresponding hydrocarbons.

"Hydrocarbons with high molecular weight such as QsH_{38} are extremely insoluble in water. If the carboxyl group replaces the CH_3 group at the end of the chain Ci_8H_{38} , one end of the molecule only tends to dissolve in water, whereas the rest of the molecule still retains the insolubility of the hydrocarbons. By spreading over

the surface of the water, molecules of this kind can bring their carboxyl group in contact with the water without separating from one another.

"An oil film formed in this way must consist of a single layer of molecules packed closely on the surface layer of the water. If there is a surplus of the fatty acid, as compared with the limited area over which it can spread, the endeavor of the carboxyl groups to come in contact with water causes the molecules to become so crowded at the surface that they stand nearly erect, side by side on the surface. The area occupied by each molecule is thus determined by the cross section of the hydrocarbon chain or by that of the head in contact with water, if this happens to be larger than the cross section of the chain. The thickness of the film is then determined by the length of the hydrocarbon chain.

"Catalytic Action of Surfaces. A monatomic film of oxygen on tungsten at $1,500^{\circ}$ acts as a catalytic poison for nearly all the reactions which would otherwise occur in contact with the tungsten surface. Thus the dissociation of hydrogen into atoms at $1,500^{\circ}$ K is stopped by a trace of oxygen, as is also the decomposition of ammonia, methane or cyanogen. The effect of the oxygen is to cover the surface so that the other gas cannot make contact with the tungsten surface.

"Similarly hydrogen and carbon monoxide act as catalytic poisons on platinum surfaces. The rate at which carbon monoxide and oxygen combine in contact with platinum is proportional to the pressure of oxygen and inversely proportional to the pressure of the monoxide. The reaction velocity depends on that fraction of the platinum surface which is not covered by adsorbed molecules of carbon monoxide. The oxygen molecules that can become adsorbed in these vacant spots and so be adsorbed on the platinum surface can thus react with adjacent adsorbed molecules of carbon monoxide."

CONSEQUENCES IN THEORY AND PRACTICE

The surfaces of water, glass, and metals are the seats of peculiar forces. It is as though a substance could not end abruptly and com-

pletely with its surface, but had to communicate with the surroundings. Although the forces residing in surfaces are delicate, they are very important. Interactions through surfaces govern our physiological life processes. Actions on surfaces are the bases of great industrial operations. Most of the motor fuels we use are made by chemical conversions which are governed by apparently inert substances with specific surface actions.

Langmuir's research on such actions started with metal wires in electrical lamps. As a result of his work, incandescent lamps last longer and convert more of the electrical energy into light.

Langmuir's investigation of the spreading of water-insoluble substances on water has led to applications for reducing the amount of light reflected from glass surfaces and thus reducing glare.

Recently Langmuir has applied surface research to the formation of water droplets from clouds. By "seeding" clouds with centers of aggregation—dry ice or finely dispersed silver iodide—he has sought artificial induction of rain. The method has been widely, and in part adversely, discussed. Whatever its real possibilities of causing rainfall, we may share with Langmuir the hope that it may develop into a means for modifying and diverting hurricanes.

19 3 3

No Award

19 3 4

HAROLD CLAYTON UREY

(1893-)

"For his discovery of heavy hydrogen"

BIOGRAPHICAL SKETCH

HAROLD C. UREY WAS BORN IN WALKERTON, IND. AFTER graduation from the high school in Waterloo, Ind., he taught three terms in country schools, then entered the University of Montana and received the Bachelor of Science degree in zoology there in 1917. His experience during the war years is best described in his own words from the autobiographical note submitted to the Nobel Prize Committee: "When the United States entered the World War he went to Philadelphia to help in the manufacture of war materials. He regards this experience as most fortunate, for it convinced him that industrial chemistry was not to be his major interest, and definitely directed him toward academic work." He returned to the University of Montana as instructor in chemistry, and then went to the University of California. His interests in physical and mathematical chemistry developed there under the stimulating influence of Gilbert N. Lewis. He found further inspiration for them during the year 1923-1924 with Niels Bohr at the Institute for Theoretical Physics in Copenhagen. Then followed a few years as associate in chemistry at Johns Hopkins, and his appointment as associate professor of chemistry at Columbia University in 1929. He became a full professor at Columbia in 1934.

From Aston's research on isotopes, combined with quantum

theory and thermodynamics, Urey calculated that it should be possible to separate the hydrogen isotope of atomic weight 2 by physical operations. This isotope, which he named deuterium, had twice the weight of the ordinary element, while all the other isotopes differed from their common element only by fractions of their atomic weights. Experiments verified the theoretical predictions. Later Urey extended this work to the separation of a nitrogen isotope of atomic weight 15; common nitrogen has an atomic weight of 14.

Urey had a prominent part in the development of the scientific work underlying the production of the atom bomb during the Second World War. He has since then made fundamental contributions to the use of isotope research in problems of geology and paleontology.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The determination of the exact atomic weight of H^1 relative to O^{16} , taken as the standard of atomic weights equal to 16 units, and the determination of the chemical atomic weight of the natural mixture of the oxygen isotopes showed, as was first pointed out by Birge and Menzel, that a hydrogen isotope of mass 2 might be present to the extent of 1 part in 4,500 of the light variety. This was the maximum abundance that could be expected, since the presence of any heavier isotope of hydrogen would have meant that all additional isotopes must be less abundant than one part in 4,500. This estimate is based upon a difference of 2 in the fourth decimal place in atomic weights when reduced to the same standard; this is only slightly greater than a reasonable estimate of the probable error of the chemical determinations. More recent determinations of the abundance of O^{18} necessitate a revision of this estimate to 1 : 3,700 instead of 1 : 4,500.

"In order to demonstrate the existence of such a rare isotope, it seemed to be necessary to concentrate it in some way, for no isotope so rare as this had been found by any of the methods known at that

* From *Les Prix Nobel en 1934*.

time. This was subsequently shown not to be true because of the adoption of a very sensitive method for the detection of this isotope, namely the use of atomic spectra, which can be used in this case because of the relatively large atomic isotope effect to be expected from the theory of Bohr. However, the isotope of hydrogen of atomic weight 2, or deuterium, was concentrated by the distillation of hydrogen in order to facilitate its detection.

"The use of this simple theory gives for the ratios of vapor pressures of hydrogen to hydrogen deuteride and of hydrogen to hydrogen tritide, the values 2.23 and 3.35 respectively. Using these values for the ratios of vapor pressures, simple calculations showed that very effective concentration of deuterium should be secured by the simple distillation of solid hydrogen at the triple point. Of course, it was impossible to be certain that these differences would apply to the liquid state, but it was a reasonable postulate that at least some of the effect would persist into the liquid state.

"Dr. F. G. Brickwedde, of the United States Bureau of Standards, very kindly prepared samples of hydrogen evaporated in accordance with the conditions indicated by the theory outlined above. The best sample was obtained from 4,000 cc. of liquid hydrogen which was evaporated near the triple point until a residue of approximately 1 cc. remained. My research assistant, Dr. G. M. Murphy, and I, in the fall of 1931, investigated the atomic spectrum of this sample and other samples of fractionated hydrogen as well as natural hydrogen, using a 21-ft. concave grating having 15,000 lines to the inch. We found three members of the Balmer series of deuterium even when commercial electrolytic hydrogen was used. The light of these wave-lengths was increased by a factor of four or five times in the samples prepared by Dr. Brickwedde.

"Though the deuterium line is easily detectable in the natural hydrogen, it would have been very difficult to have definitely established its existence if the more concentrated samples prepared by distillation had not been used, for irregular "ghosts" of a ruled grating might conceivably have accounted for the observed additional lines. Thus, the method of concentration devised for and used in these original researches, was important in proving the existence of this isotope.

"Rittenberg and I have used this theory to show that easily detectable differences in the equilibrium constants of reactions involving hydrogen and deuterium should exist, and subsequent experimental work confirmed these calculations in the case of hydrogen and deuterium with iodine to give hydrogen iodide and deuterium iodide. This confirmation was confidently to be expected, but this seems to have been the first time that an equilibrium constant of a chemical reaction had been calculated before one of the elements involved had been prepared in sufficient quantities to confirm the theory.

"The extensive researches which have been carried out with the use of deuterium in the last two years were made possible in a large part by the discovery by Washburn of the electrolytic method for the separation of hydrogen and deuterium. Other methods could be used at the present time for the separation of these isotopes. The exchange reaction between water and hydrogen could probably be adapted to counter-current scrubbing methods, and could be used effectively for the separation of the hydrogen isotopes as suggested by Farkas."

CONSEQUENCES IN THEORY AND PRACTICE

Urey announced the discovery of hydrogen having the atomic weight 2 in December 1931. Almost immediately after this confirmation of a theoretical prediction, the industrial production of heavy hydrogen was contemplated. The method to be used was not the fractional distillation near the triple point where hydrogen exists in all three states, solid, liquid, and gas, but followed the late E. W. Washburn's way, electrolysis. When hydrogen gas is made from water by electrolytic decomposition, the gas is rich in the light isotope and the residual water contains a higher proportion of deuterium. The Norwegian hydroelectric plant at Rjukan started to manufacture deuterium and its oxide, "heavy water." The use of heavy water as a means for slowing down neutrons in atomic piles was so important that a daring, and successful, raid was made on the occupied Norwegian plant during the Second

World War to remove the store of heavy water from German hands.

Interest is now concentrated on the next higher isotope, tritium, and its possible use for atomic fission in a "hydrogen bomb."

19 3 5

IRENE JOLIOT- CURIE

(1897-)

FREDERIC JOLIOT

(1900-)

Tor their synthesis of new radioactive elements''

BIOGRAPHICALSKETCH

THE DAUGHTER OF PIERRE AND MARIE CURIE INTERRUPTED HER studies of mathematics and physics during the First World War to help in radiologic hospital work. She assisted her mother and was graduated in 1925 from the Curie Laboratory of the Radium Institute in Paris with a doctor's thesis on alpha rays of polonium.

At that time, Frederic Joliot, after receiving his engineer's diploma from the School of Physics and Chemistry of Paris in 1923, joined the staff of the Radium Institute.

They married in 1926. In their collaboration, Irene Joliot-Curie was more concerned with the physical aspects, while Frederic Joliot was particularly interested in the chemical identification of the radioactive substances. They extended the investigation of artificially radioactive substances to the products of atomic fission and were greatly concerned with the use of atomic forces for peace. Frederic Joliot combined radiological with biochemical research in the synthesis of hormones and thyroid substances containing radioactively labeled elements.

Together with R. Gregoire, the Joliot's published a book on nuclear physics in 1948.

DESCRIPTION OF THE PRIZE - WINNING WORK

IRENE JOLIOT-CURIE *

In addition to the electro-negative electron which constitutes β -radiation, and the positively charged helium-particles of α -radiation, Rutherford's hypothesis contained a positive hydrogen-particle called proton. James Chadwick discovered a neutral particle of the mass of the hydrogen atom, the neutron. A proton can lose its positive charge by giving off a positive electron and thereby changing into a neutron. (See: Nobel Prize Winners in Physics, year 1935.)

"In studying the transmutations occurring with the emission of neutrons from light elements upon irradiation by alpha particles, we encountered certain difficulties in interpreting the emission of neutrons by fluor, sodium, and aluminum. Aluminum can be transformed into a stable atom of silicon by capture of an alpha particle and emission of a proton. If, however, a neutron is emitted, the product of the reaction is not a known atom.

"We then observed that when aluminum or boron is irradiated by alpha rays, not only protons and neutrons but also positive electrons are emitted. We thereupon assumed that the neutron and the positive electron were simultaneously emitted instead of a proton; the resulting atom should be the same in both cases.

"It was in the beginning of 1934 that we noticed a fundamental difference between this transformation and all those which had been produced up to that time; all reactions of artificial nuclear chemistry were instantaneous, even explosive. On the contrary, the positive electrons produced by aluminum under the action of a source of alpha rays continue to be emitted for some time after the source is removed. The number of emitted electrons decreases by one half in three minutes.

* Translated from *Les Prix Nobel en 1933*.

"This is, therefore, a real radioactivity, indicated by the emission of positive electrons.

"We have shown that a radioactivity can also be communicated to boron or magnesium through bombardment with alpha rays and with emission of positive or negative electrons. These artificial radio-elements behave entirely like natural radio-elements."

FREDERIC JOLIOT *

"A thin film of aluminum which has been irradiated with alpha rays is attacked and dissolved in a solution of hydrochloric acid. The chemical reaction produces hydrogen which entrains the radioactive element into a thin-walled tube which is inverted over water. This separation shows that a chemical element, different from aluminum, was formed during the irradiation. It furnished an indisputable proof of the achieved transformation; traces of phosphorus would have separated from the aluminum under the same conditions.

"The activated aluminum can also be dissolved in an acidic oxidizing solution. A small quantity of a sodium phosphate and of a zirconium salt is added to this solution; the phosphate of zirconium which precipitates carries the radioactive element with it. In the case of aluminum, these experiments are delicate, since they have to be carried out in about 6 minutes, because the half-life of the newly formed radioactive atoms is less than 5 minutes. Chemical tests of this kind have shown that the radio-element formed in boron under the influence of alpha rays is an isotope of nitrogen.

"We have proposed to name these new radio-elements (isotopes of known elements, but not found naturally) radio-nitrogen, radio-phosphorus, radio-aluminum (in the case of alpha-irradiated magnesium), and to designate them by the symbols RN^{13} , RP^{30} , $RA1^{28}$.

"Soon after these first findings we suggested that the same phenomenon could occur for kinds of transformations which are produced by the impact of particles other than those of alpha rays, for example, protons, deuterons, neutrons."

* Translated from *Les Prix Nobel en 1935*.

CONSEQUENCES IN THEORY
AND PRACTICE

All the usual means we have for influencing the properties of substances—heat, pressure, chemical reaction—do not change radioactivity, which thus seemed to be as immutable as the elements themselves. Now a method was found by which radioactivity could be imparted to an ordinary element. This element becomes radioactive and is converted into the isotope of its neighbor in the system of elements. Since this discovery, over four hundred new isotopes have been described. The method which the Joliot's discovered for imparting artificial radioactivity did not remain the only one; cyclotron and nuclear reactor pile furnished radioactive materials in great variety and increased quantities. Originally, the new elements were known only as radiations. Then, sizable quantities of the pure radioactive elements were produced. Since they follow their normal isotope in all its chemical reactions, they could be used as indicators which reveal their presence, even in smallest quantities, by the specific radiation. Radioactive carbon of atomic weight 14, a long-lived radiating substance, oxidized to carbon dioxide, thus served to show the ways in which green leaves convert carbon compounds in assimilation. Radioactive iodine is quickly absorbed in the thyroid. This absorption can be used for medical purposes or for studies of comparative anatomy. Radioactive phosphorus fed to animals in the form of sodium phosphate permits one to follow the chemical metabolism of this substance and its conversion into body substance, or even serves as a means for identifying individual animals by a radioactive mark. Radioactive elements were built into synthetic medicaments and much information about their fate and action in the organism were thus obtained.

These artificially radioactive elements are isotopes of previously known elements. Most recently, such artificial production has been extended to a complete synthesis of elements with higher atomic weights than any known before.

1936

PETER J. W. DEBYE

(1884-)

"For his contributions to the study of molecular structure through his investigations on dipole moments and on the diffraction of X rays and -electrons in gases."

BIOGRAPHICAL SKETCH

PETER DEBYE WAS BORN IN MAASTRICHT, HOLLAND. HE ATTENDED the high school in his home town and then went across the border, to Aachen, to become an electrical engineer. From there, he traveled to centers of research in theoretical physics, particularly Munich, where he received his doctor's degree in 1910. After one year as professor of theoretical physics in Zurich (1911-1912) he returned to Holland (Utrecht) for two years. Gottingen, with its prominent school of mathematics and theoretical physics, held him for five years. Then followed Zurich (1919-1927), Leipzig, and Berlin, where he was director of the Kaiser Wilhelm Institute for Theoretical Physics from 1935 to 1940. Since 1940 he has been at Cornell University.

In his many important contributions to physics and chemistry Debye seeks to probe the state of atoms and molecules by their response to vibrations. These vibrations may be the large waves of heat or the very short waves of light. An example from the early part of his work is his theory of specific heat. The number of calories needed to raise the unit weight of a substance by one degree

in temperature changes with the temperature. Since heat waves are large in comparison with the distance of atoms from each other, he assumes that for this particular property a solid substance can be considered as continuous instead of molecular. This permits him to develop a relationship of specific heat to temperature which becomes particularly simple at very low temperatures, where heat waves are longest.

At the same time, 1912, Debye also investigated substances by electromagnetic waves. These waves reveal molecular structures, and particularly the degree to which positive and negative electrical charges coincide. Where the resultant centers of gravity of these charges are at a distance from each other, the molecule is polar. This is shown by their alignment when they are subjected to a magnetic field. Such a structure can be found in gases, and even in solutions. The atoms in such molecules are restricted in their rotatory movements around each other.

For the state of molecules in solution Arrhenius had given a theory (see p. 14) which was limited to high dilutions. Debye extended the concept of ionization to the solid, crystallized state of matter. For concentrated solutions, the influence of the solvent could now be measured and defined. The closest that ions can approach each other, the mean ionic diameter, is much greater than the distance found in crystallographic measurements. The diameter of ions appears to be enlarged by the association with molecules of the solvent (Debye-Hückel theory, 1923).

The type of information obtainable through irradiation of matter depends upon the size of structural detail in relation to the wave length. Gamma, or Röntgen, rays show the atomic structure of crystals. In Göttingen, Debye and P. Scherrer discovered that it is not necessary to use well-developed crystals to obtain the interferences of gamma rays which indicate the spatial arrangement of the molecules, but that a fine powder can serve as well. In most recent years, Debye derived a method for investigating solutions containing large molecules by means of optical waves. The light is scattered by the molecules, particularly those of high polymers or soap. The degree of light scattering is easily measured and correlated with size, shape, and concentration of the dissolved substances. With the aid of mathematical developments which make

use of earlier (1910) theories of Einstein, optical methods can thus serve to measure osmotic pressures or molecular weights.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"The atoms of the noble gases are non-polar, in correspondence with the central-symmetrical structure of their electron cloud. Diatomic molecules which consist of equal atoms (N_2 , O_2) have, in the same way, been proved to be non-polar. However, as soon as the two atoms are different, a polarity of the molecule appears at once. This polarity is small if the two atoms are close to each other in the periodic table (CO), and becomes great only in molecules such as HCl. The magnitude of the dipole moment, however, does not come near the value which would be proper to a structure consisting of an H-ion and a Cl-ion in the given nuclear distance. In fact the moment is only about 1/6 of that value, since μ was found to be $1.04 \cdot 10^{-18}$. Considering the HCl molecule as formed from two ions which are brought close together, the hydrogen nucleus penetrates the electron sphere of the Cl-ion, whereby 5/6 of the originally existing moment becomes compensated. A real quantum-theoretical calculation of moments seems rather difficult. In any case up to now the calculation of Kirkwood for the molecules HF, HCl, HBr, and HI is the only one which has led to a result.

"Molecules which consist of three atoms can be divided into two groups: CO_2 and CS_2 are non-polar, but the molecules H_2O , H_2S , SO_2 have a permanent moment. The explanation is that in the first case the arrangement of the atoms in the molecule is linear, whereas in the second case the atoms are situated at the corners of a triangle. The moments of inertia, which follow from the analysis of the band spectra, furnish an independent proof of those structures. In a similar manner the observed polarity of the molecules NH_3 , PH_3 , AsH_3 leads to a structure in which N, P, or As is placed at the point of a three-sided pyramid and the three H-atoms at the corners of its basis.

* Translated from *Les Prix Nobel en 1936*.

+ JU is the symbol for the relationship between electric charge, mass and length called "magnetic moment."

"The conviction of the chemists that the structural formula is in fact a representation of the spatial arrangement of the atoms in the molecule which corresponds to nature is apparently completely confirmed by the previous enumeration. Sometimes only one thing is missing, that the representation be according to a scale. We shall, therefore, look for a method to perform measurements of the distances within the molecule. We know since Laue's discovery of crystal-interferences that the wave lengths of X rays are small enough to be adapted to this purpose. If, however, we want to examine free molecules, the difficulty arises that we have to operate with particles which cannot be fixed in a definite orientation in space, like a crystal. Fortunately, however, I was able to demonstrate that every atomic structure that is irradiated with X rays must produce recognizable interferences in its dispersed radiation, even when it changes its orientation in space permanently and uncontrollably. I was led by this consideration when, together with Scherrer, the interferences of crystalline powders and of liquids were discovered. These experiments were the preliminary steps for the first attempt, carried out in 1928, together with Bewilogua and Ehrhardt, to produce interferences by dispersion on CCU—vapor.

"It can be proved for the benzene molecule, and most beautifully for hexa-chloro-benzene, that the six-membered ring is planar and that it corresponds to the carbon-ring of graphite and not to that of diamond. This is indicated also by the C-C distance itself, which has the value 1.54 Å in aliphatic compounds, but 1.41 Å in aromatic substances. This distance becomes still smaller in double or even triple bonds."

CONSEQUENCES IN THEORY AND PRACTICE

The concept of electrical polarity in molecules and the measurement of its magnitude gave added accuracy to the pictures which chemists had drawn. Now the actual distances between the atoms in a molecule could be determined. Where doubts existed concerning the relative positions of the atoms, as in cases of complicated isomerisms, the new method often made it possible to reach deci-

sions. Polarity was of practical importance when materials of construction had to have certain electrical properties, particularly when they had to be good insulators. The knowledge of polar moments in synthetic resins and their plasticizers serves to direct selection of existing materials and construction of new materials for use in sonar or radar equipment.

Debye's pioneering work in this field was recognized by the designation of the unit of polar moment (which is of the order of 10^{-18}) as "one Debye."

19 3 7

WALTER NORMAN HAWORTH

(1883-1949)

"For his researches into the constitution of carbohydrates and vitamin C."

(The award for 1937 was shared with Paul Karrer; see below, pp. 156-159)

BIOGRAPHICAL SKETCH

WALTER HAWORTH WAS BORN IN CHORLEY, LANCASHIRE, ENGLAND. He studied at the universities of Manchester and Gottingen, where Otto Wallach and W. H. Perkin were his teachers. Since both were prominent in research on essential oils, it is not surprising that Haworth, with a doctor's degree from Gottingen (1910) and a D.Sc. from Manchester (1911), worked on the chemical substances found in fir needle oil and pine root oils as a professor at the University of St. Andrews, Scotland, from 1912 on. He undertook research in sugar chemistry a few years later and continued it at Armstrong College, Newcastle, in 1920, and at the University of Birmingham from 1925 on.

The two fields of research were, at least in part, connected by the common starting material, wood. Organic solvents extract essential oils, aqueous alkaline solutions extract a complex sugar which had been given the name xylan (from the Greek word for wood) at the time when this was the only sugarlike substance obtained from wood. When boiled with slightly acidified water, xylan is split (hydrolyzed) into xylose, a sugar with five carbons in

its molecule, and a small proportion of an isomer, arabinose. Emil Fischer's method of reacting sugars with methanol to attach the methyl group to the aldehyde group or to replace hydrogen by methyl groups was extended by Haworth and his co-workers. Methylated sugar derivatives can be used to characterize the constitution of sugars. One of the results was to demonstrate that the carbon atoms in sugars are linked by oxygen into the form of rings. They contain either five carbons and one oxygen, in which case they are called pyranose, or four carbons and one oxygen, which is a furanose structure, because it underlies the structure of furfural. A perspective representation of these structures, proposed by Haworth, found general acceptance.

The fundamental molecule of xylan contains *five* carbon atoms; that of starch and cellulose contains six. A relative of these plant-carbohydrates is glycogen, a polymeric carbohydrate occurring in liver. Glucose is the building unit in glycogen, as it is in starch and cellulose. With the experience gained in work on the constitution of these carbohydrates, Haworth and his collaborators approached the problem of vitamin C, or ascorbic acid. This vitamin had been shown by F. Micheel to be related to carbohydrates as a special product of oxidation. It can be derived from a sugar which is similar to fructose, sorbitose. The acids obtained upon its oxidation split off water within their molecule, in a manner first observed with lactic acid and therefore called lactone-formation. In 1934, Haworth and his colleagues found a way to synthesize ascorbic acid. This gave the final proof of its chemical constitution and indicated directions in which technical methods for artificial production of this important vitamin could be found.

During the Second World War, Sir Norman took an active part in chemical problems related to the application of atomic energy.

DESCRIPTION OF THE PRIZE-WINNING WORK*

"The Structure of Carbohydrates and of Vitamin C. A question of particular moment is concerned with the length of the chain

* From *Les Prix Nobel en 1937*.

of repeating units in starch, cellulose and glycogen. For it may now be said that glycogen has the same internal constitution as starch. On the other hand xylan or wood gum is constituted on a similar plan to cellulose except that it is built up of xylose units, largely, in place of glucose. Wisdom dictates that in a problem of this complexity all the available polysaccharides should be studied together as a group. Information which may not be readily available from the study of one polysaccharide may be revealed by the study of another, and it is probable that a conclusion will be reached which is common to all of them. It is a reasonable supposition that Nature in building up polysaccharides follows a common plan. For this reason I have developed what is now known as the end-group assay of methylated polysaccharides as a preliminary to the study of the chain length. Unless these chains are constituted as continuous loops then there must be a terminal group which carries one more non-reducing hydroxyl than any of the intermediate units in the chain, or than the remaining end-group which will terminate with a reducing unit. Our study of xylan has been important from this point of view. In xylan some 17 or 18 β -xylopyranose units are assembled in a chain which is terminated by one unit of arabinofuranose. This latter can be easily removed by hydrolysis and there remains only a chain of xylose residues. In 1934 I pointed out that this picture of xylan was probably typical of other polysaccharides in that these chains of limited length aggregated to form a larger entity and the nature of the bonds effecting the union of adjacent chains was discussed. It was suggested that these might be either united by principal valency links or by some other type of bond such as that which is responsible for co-ordination. Whatever this kind of agency or link may be, I prefer to describe it as the polymeric bond and as such it may differ from ordinary valency bonds and may find currency in the whole field of polymeric substances.

"In starch, for example, the individual chains terminate after 26 or 30 α -glucopyranose units and the chains are assembled by the same aggregative force as that just mentioned. It has been found possible to effect the reverse change of disaggregation in the case of starch. This was effected by mild acid treatment of the starch grains followed by acetylation and methylation. Very recently this observation has been confirmed by my former colleague E. L. Hirst

who has isolated the methylated form of a single chain of 26 a-glucopyranose units. In the case of glycogen the chains differ from starch in being shorter in length and we have examined specimens of glycogen which contain continuous chains of both 12 and 18 a-glucose units. These chains again are interlinked by the polymeric bond to form a very large molecular complex showing a molecular weight of 1,000,000 or more.

"The same experimental methods have been applied in order to gain an insight into the molecular size of cellulose.

"Constitution of Ascorbic Acid. Ascorbic acid is a monobasic acid, giving well denned salts of the type QH7O0M. It is a powerful reducing agent and its oxidation can be effected in stages, the first of which requires the equivalent of one atomic proportion of oxygen for each molecule of ascorbic acid. When oxidation is arrested at this stage the product can be reduced quantitatively to ascorbic acid by reducing agents such as hydriodic acid or hydrogen sulfide. Ascorbic acid is specially sensitive to oxidation by gaseous oxygen in the presence of minute traces of copper as catalyst, but in these circumstances the reaction proceeds beyond the reversible stage and involves destruction of the molecule.

"An important observation was that, when newly formed, the primary reversible oxidation product from ascorbic acid does not possess acidic properties but behaves in all respects as a lactone, which develops acidity when kept in aqueous solution. It followed that the acidic character of ascorbic acid is due to an enolic hydroxy 1 group and not to a free carboxyl group and, in order to determine the structure of ascorbic acid, it remained only to discover the nature of the lactone ring in the primary oxidation product. The main features of the constitution of ascorbic acid were now established and its formulation as a lactone of 2-keto-l-gulonic acid, capable of reacting in various tautomeric modifications, was first announced from the University of Birmingham early in 1933.

"A still simpler method for the synthesis of 1-ascorbic acid consists, as I have shown by my experiments, in the direct oxidation of 1-sorbose, which like d-fructose, is specially sensitive to oxidation at the primary alcoholic group at Q."

19 3 8

PAUL KARRER

(1889-)

"For his researches into the constitution of carotinoidSf flavins, and vitamins A and B."

BIOGRAPHICAL SKETCH

PAUL KARRER WAS BORN IN MOSCOW. HIS PARENTS WERE SWISS and in 1892 moved to Switzerland, where he went to school and received his doctor's degree in 1911 from the University of Zurich. He remained there as lecture-assistant to Alfred Werner and began work on organic arsenic compounds. Paul Ehrlich became interested in this work and invited Karrer to join him at the Georg Speyer-Haus in Frankfort. Combining his experience with complex metal salts as Werner's student with the new research on therapeutic arsenicals, Karrer developed a silver-salvarsan complex. After six years in Frankfort, he returned to Zurich and succeeded Werner in 1919. Medicinal chemistry was now replaced by biochemical research on high-molecular carbohydrates, including starch, cellulose, and lichenin from lichen. Soon tannin, lecithin, and amino acids from proteins were added to the program.

In 1926, Karrer began to investigate plant pigments, particularly the yellow ones which are related to the pigment in carrots and are, therefore, called carotinoids. Carotene itself was separated into several components of the same chemical composition, but with different arrangement of the double bonds between carbon atoms at the end of the long molecules. In the central chain of carbon

atoms of the carotenes, single bonds alternate with double bonds. Since the presence of double bonds between carbon atoms in a molecule is indicated by adding the syllable -ene to the name, carotenes are called polyenes. They are converted into vitamin A in the human body, through a process which Karrer found to consist in a chemical hydration *in* the middle of the symmetrical molecule. The yellow substance present in milk or yeast, lactoflavin, is chemically different from carotenes and related to vitamin B and to important enzymes.

In 1927, Karrer published his textbook on organic chemistry, which has gone through many editions in several languages.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"The blue and red pigments of blossoms and berries, the anthocyanins, were formerly thought to be uniform and characteristic for the several plants. Newer investigations have shown these anthocyanins to be mixtures of many closely related substances. There is perhaps not one flower, not one berry, which owes its coloration to one single anthocyan. Similar conditions prevail in another group of natural pigments, the carotenoids. In the well known book of L. S. Palmer on carotenoids which had been published in 1922, only six carotenoids are described which had been crystallized and analyzed (carotene, lycopene, xanthophyll, lutein, fucoxanthin, and rhodoxanthin). In addition also bixin was known at that time. Until four years ago the number of these pigments which can be found in nature had risen to 15; today we know already 40 natural pigments of this group. Their purification was made possible only by the new methods of separation.

"The carotenoids have found attention in recent work not only for their unique structure, but also for their close relation to the vitamins. Some carotenoids are provitamins of vitamin A and are transformed into vitamin A by the animal organism. The investigation of the structural constitution of the vitamins started from carotene. When it was possible, in 1930, to establish the correct

* From *Les Prix Nobel en 1937*.

constitutional formula for β -carotene, the structural formula for no other vitamin or provitamin was known as yet. Shortly after that (1931), however, it was also possible to clear up the constitution of vitamin A itself. Thus, insight into the structure of a vitamin was obtained for the first time. We may perhaps remember, that not ten years have passed since the time when some scientists questioned the material specificity of the vitamins, and thought that a special state of matter, a special colloidal nature was the cause for the peculiar vitamin effects which had been observed.

"The vitamin A action is, therefore, extraordinarily specific, it depends upon a very definite structure. Today it is possible to show the atomic arrangements in a poly-ene which are characteristic of vitamin A much more reliably by biological assay with animals, than by any chemical reaction of degradation or measurements by spectral analysis. This high specificity is the more surprising as it is hardly possible to speak of a specificity of constitution with regard to most hormones, e.g. the female sexual hormones and the plant-growth hormones. In the animal organism similar physiological effects are caused by not only closely related chemical substances, but it often occurs that compounds of entirely different constitutions have the same effects as the natural products.

"This strongly pronounced specificity of the constitution of vitamins may be connected with the results of some recent investigations, which revealed that many vitamins are functional groups of ferments; the highly specific properties of ferments have been known for a long time. It was possible to prove this close relationship between ferments and vitamins first for vitamin B₂ or lactoflavin. According to investigations of Warburg and Theorell the phosphoric acid ester of vitamin B₂ is the functional group of the yellow oxidation ferment. Today lactoflavin and any number of other flavins can be synthesized, and thus it was possible for us to investigate to what extent the vitamin-effect is connected with a certain constitution."

CONSEQUENCES IN THEORY AND PRACTICE

Haworth and Karrer came to vitamin research with a background of work on polymeric carbohydrates. The new information concerning the structure of starch and cellulose was of great help in the technical preparation of modifications and derivatives for use as plastics, fibers, and glues.

It had long been known that citrus fruits and green vegetables prevent and cure scurvy. The factor in these natural products which is anti-scorbutic, an "ascorbic" acid, was now shown to be a definite chemical compound. It could be made in the laboratory, and soon also in the manufacturing plant. When the chemical constitution of indigo had been disclosed, the chemical synthesis of this dyestuff was quickly followed by the production and application of a host of chemically modified indigoes; for vitamins, the biological action is so specific that no changes or modifications of the molecular structure are permitted. This is true of vitamin C, and particularly of vitamin A. The importance of vitamin C in fruits and vegetables caused a great amount of investigation into the stability of this valuable constituent during storage and cooking. Milk and butter won increased attention as sources of vitamin A; its extraction from fish-liver oils developed into a carefully controlled chemical industry.

The sensitivity of vitamin C to oxidation suggested its role in processes of food assimilation. The influence of vitamin A on the functioning of the eye was further elucidated when its relationships to pigments in the retina were found (by G. Wald).

RICHARD KUHN

(1900-)

"For his work on carotinoids and vitamins,"

BIOGRAPHICAL SKETCH

WHEN RICHARD KUHN WAS AWARDED THE NOBEL PRIZE, ITS acceptance was forbidden by the German government. After the war he received the gold medal and diploma of the Prize.

Kuhn was born in Vienna and was one of the youngest graduates of Willstätter's laboratory in Munich. His doctor's thesis (1922) continued Willstätter's work on enzymes. In 1926 he became professor at the Swiss technical high school in Zurich. Three years later he moved to Heidelberg as professor at the University and director of the chemical division of the Kaiser Wilhelm Institute for Medical Research.

Kuhn's textbook on the chemistry, physico-chemistry, and biology of enzymes (1927) was distinguished by the combination of skill in experimental detail with systematic coordination of the new experiences. He followed Willstätter's example in combining studies of enzymes with investigations of plant pigments. A deep connection between color and enzymic activity had been discovered by Otto Warburg (see "Nobel Prize Winners in Physiology and Medicine," 1931), and Kuhn tried to penetrate into its chemical and biological meaning. The way began with systematic organic chemistry. For a long time, chemists were fascinated by the six-carbon ring structure of benzene. Willstätter diverted this fascination by showing that a derivative of the alkaloid peltierine (from pomegranates) had as its basis a ring formed from eight carbon atoms. The bond between these carbon atoms was alternately single and double, a sequence of conjugated bonds.

Kuhn constructed substances with an open chain of such conjugated carbon atoms, called polyenes. They were interesting for the system of organic chemistry, and much more so because long chains of conjugated carbons occur in many plant pigments—in carotenes from carrots, in lycopene from tomatoes, in crocetins from crocus. Kuhn and Karrer (see pp. 156-158) were lively competitors in elucidating the intimate chemical structure of these pigments which have pronounced biological activity and, in part, are related to vitamins. For crocetin in particular, Kuhn showed highly specific influences on the sexual ripening of spores (gametes) of certain lower plants. With fine technique and clear reasoning, complex chemical structures were determined on milligrams of substance. Nature uses many different kinds of chemical structures for specific biological actions. Sea urchins, for example, secrete a sex hormone which is a naphthalene derivative (hydroxylated naphthoquinone). Yeast contains enzymes and vitamins. One of the vitamins, ascribed to the vitamin B group, acts against a skin disease; it was therefore called *adermin*. It has other names too: vitamin B₆ and pyridoxin. This latter name indicates its chemical composition; it is an oxygen-containing derivative of pyridine. In the year of the Nobel Prize award, Kuhn gave the complete chemical formula of this vitamin, of which one-hundredth of a milligram in the daily diet of a rat is able to heal its dermatitis.

In their natural habitat, enzymes, pigments, and vitamins are combined with sugars, fats, and particularly with proteins. Willstätter called such loose chemical combinations symplexes, because they are comparable to symbioses of several different kinds of organisms living together. Kuhn found a practical method for dissolving symplexes from plants in the use of invert-soaps, so called because the role of organic acid with inorganic base of ordinary soap is inverted to inorganic acid with organic base. Some of these invert-soaps are old, but they have only recently found applications in the medical field.

After the recent reorganization of the I. G. Farben concern Richard Kuhn accepted an important position in its technical administration.

19 3 9

LEOPOLD RUZICKA

(1887-)

*"For his work on poly methylenes and higher
terpenes,"
(The award for 1939 was shared with Adolf Butenandt;
see below, pp. 166-168)*

BIOGRAPHICAL SKETCH

LEOPOLD RUZICKA WAS BORN IN VUKOVAR, YUGOSLAVIA. HE started his academic career in Zurich, in 1918. In 1926 he became professor at the University of Utrecht, Holland, and three years later returned to the Technische Hochschule in Zurich. His research on essential oils led him to recognize the presence of a group of "higher" terpenes. Otto Wallach (see pp. 42-45) had found that terpenes are related to a substance which was obtained on distilling natural rubber. Its chemical formula is C_rH_s ; its molecule is formed from four carbon atoms connected by alternating (conjugated) double bonds, with a methyl group attached to the second of these carbon atoms. Terpenes have the general formula $C_{10}H_{16}$, and Wallach considered the C_5H_8 substance, called isoprene, as a half- or hemi-terpene. More than two isoprene units combine to form the higher terpenes. Ruzicka detected the isoprene unit in many non-terpene natural substances, and he derived therefrom his isoprene rule. This is a great help in understanding the molecular structure of carotinoids.

Nature does not use isoprenes to build fatty acids, which have a long chain of carbon atoms without any side chains. The structure of some natural oils of strongly pronounced scent appeared as a ring-closing of fatty acid chains, in which the acidic carboxyl group COOH of the fatty acid was converted into a $\text{C} = \text{O}$ group, the ketone group.

Civet is an important material in perfumery. Ruzicka found an exceptionally large ring of 17 carbon atoms in one of the basic substances of this material. Later on he investigated ambergris, a pathological product from the digestive tract of the sperm whale, and established its relationship with the substance which gives violets their delicate odor.

The 6-carbon rings in terpenes contain more hydrogen than the comparable ring in benzene. One of the methods which Ruzicka used in his research on terpenes consisted in eliminating sufficient hydrogen, by dehydrogenation, to convert the hydro-aromatic substances into benzenelike, aromatic products which were then more readily connected with known substances.

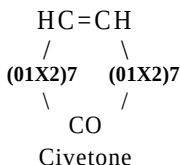
Ruzicka is continuing this work in several directions at the Technische Hochschule in Zurich.

DESCRIPTION OF THE PRIZE - WINNING WORK *

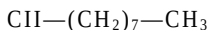
"The fundamental experiments were carried out with civetone. I had to struggle less with the intricacies of this substance than with the general and personally shared prejudice against the possible existence of a 17-membered ring.

"After it had been found that the hydrogenation product dihydro-civetone, as well as the hydrocarbon obtained from civetone in the Wolff-Kirschner reaction, form the same dicarboxylic acid $\text{C}_{17}\text{H}_{32}\text{O}_4$, the completely symmetric formula for civetone had to be considered. The formulation of the dicarboxylic acid $\text{G}_{7}\text{H}_{32}\text{O}_4$ as hepta-decane-di-acid could be definitely proved by a comparison with the synthetic acid.

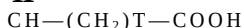
* Translated from *Les Prix Nobel en 1939*.



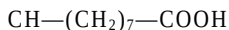
"Civetone and muscone seemed to contradict, as compounds of nature and in the system of organic chemistry, the old experience 'nature does not jump' ('Natura non fecit saltus'). Deliberations about the probable mechanism of the biochemical origin of the two ketones lead to a plausible explanation of their peculiar structure. Civetone might be formed by an co-oxidation of oleinic acid and subsequent cyclization of the unsaturated dicarboxylic acid in the organism of the civet cat. Muscone might similarly be a product of fat metabolism.



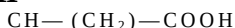
II



Oleic acid



II



Unsaturated dicarboxylic acid

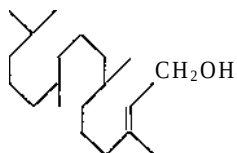
"The ring-homologous series of the cyclic ketones is a characteristic example of the relationship between physiological properties and details of molecular structure. While 5- to 8-membered ring ketones have the well-known odor of mixed bitter almond, caraway, and peppermint, the 10- to 12-membered ring ketones show typical camphor odor. The ketones with 14- to 18-membered rings represent musk odor.

"Since 1920 we have investigated, on a broad basis, sesquiterpenes, diterpenes, and later on also triterpenes, compounds which can be grouped together as "higher terpenes" or "polyterpenes." The persistent application of a simple working hypothesis and of an expedient working method revealed aspects of the structure of the carbon skeleton which soon led to a system of the higher terpene compounds. The working hypothesis of that time, which is now known as the isoprene rule, was founded on the assumption that the carbon skeleton of the higher terpenes is erected out of isoprene parts.

"The great number of higher terpene compounds in nature and their usually very complicated structure indicated that the usual

methods of systematic structural analysis would not afford a general evaluation of the isoprene rule in a desirably short period of time. It appeared to us that the method of dehydrogenation should give results more rapidly.

"In summary, it may be emphasized that the selected method proved to be fruitful and that the results obtained by it corresponded to expectations.



Phytol

**V**

Vitamin A

"These are the formulae for two important natural compounds: phytol, which is the alcoholic constituent of chlorophyll, and vitamin A. It would have been extremely difficult to explain the constitution of these compounds, of which only small quantities were available, if the way had not been shown by the isoprene rule. In both cases, it was necessary only to control and confirm the formula derived according to the isoprene rule by synthesis either of the natural product itself (for phytol) or of its perhydro-derivative (for vitamin A).

"The over-all formula of androsterone had not been established definitely by analysis, but if our assumption concerning the connection of the sex hormones with cholesterol were correct, androsterone should have the formula $C_{19}H_{30}O_2$. There were four different stereometrically isomeric saturated sterines which might be used for the artificial production of androsterone. On oxidizing the acetates of the four isomers, we were able, in 1933/4, actually to obtain the acetates of the expected four isomeric oxy-ketones $C_{19}H_{32}O_2$, of which the one obtained from epi-dihydrocholesterol was identical with androsterone.

"This was not only the first artificial production but also the first complete proof of the constitution of a sex hormone, and it also was the first stringent demonstration of the connection of a sex hormone with a sterol which includes the finest steric details."

ADOLF BUTENANDT

(1903-)

*"For his work on sex hormones,"
(The award for 1939 was shared with Leopold Ruzicka;
see above, pp. 162-165)*

BIOGRAPHICAL SKETCH

ADOLF BUTENANDT WAS BORN IN WESERMUNDE, GERMANY. HE studied chemistry in Gottingen, under Windaus, and was graduated in 1927; he became director of the organic and biochemical laboratory three years later. His meteoric career resembles that of Richard Kuhn, with whom he shared the fate of not being permitted to accept the Nobel Prize.

The year 1929 is remarkable in the history of biochemistry, because the hormone which determines the sexual development of females was obtained in pure and crystallized form by Doisy in this country and, independently, by Butenandt in Germany. This substance, first called folliculin to indicate its source, the follicle, or estrone, the substance preparing the organism for the pregnancy cycles, can be distilled at high vacuum. It has a definite melting point of 256° C, and 0.025 millionth of a gram is sufficient to produce uterus developments in the castrated mouse.

This hormone was found in the urine of pregnant women. It was logical to search for male sex hormones in the urine of males. C. Funk in London showed the presence of such a hormone and initiated methods for its isolation. When this material is fed to capons, the comb begins to grow. A unit of hormonal activity can be defined by the rate of growth per weight of substance used. In a purified, neutral oil from male urine, the hormone is enriched to the extent that about 20 milligrams provide one hormonal unit.

Butenandt removed more of the accompanying material by extractions with acids and alkalis, by transferring it from one selective solvent to the other. The activity of 20 mg was thus obtained in only 0.3 mg. This product must still be quite impure, compared with the activity found for the pure female hormone. Methods of adsorption or extraction failed to remove any of the suspected impurities; but when hydroxyl-amine was added, this common reagent which combines with ketone ($C=O$) groups, a small fraction of the material crystallized out. The carefully separated crystals gave a threefold increase in activity. When the amine group was split off again and the residue subjected to sublimation in a vacuum, a crystallized substance was obtained, of which one millionth of a gram, applied in ten portions over five days, had a definite hormone effect. In 1931, Butenandt reported that 15 milligrams of this substance had been prepared; they represented the active substance contained in about 7000 gallons of urine.

Butenandt continued this work in Danzig, in 1933, and as director of the Kaiser Wilhelm Institut for Biochemistry in Berlin-Dahlem, from 1936 on. He found the relationship to the basic carbon skeleton of cholic acid and cholesterol simultaneously with Merrian (London, 1930), and discovered a number of different derivatives having specific activities in animals and plant seeds. In one of these hormones, a ketone group is situated at carbon number 3, and a hydroxyl group at carbon number 17. If in this compound carbons 4 and 5 are connected by a double bond, it acts as a strong male hormone; if the double bond is translocated to extend between carbons 1 and 2, the hormone has strong estrogenic effects. This was one of the most surprising and important results of this work.

This interesting discovery contains the implicit warning that great care must be exercised in the medical use of hormone concentrates. At the same time, the relationships in chemical structure of sex hormones and cancer-producing substances is not only of scientific interest. In an extended test in which about 3000 mice were used, Butenandt searched for possible carcinogenic properties of hormones obtained from follicles; for these particular hormones at least, he found no indications of such effects.

Since 1945, Butenandt has combined the direction of the insti-

tute (now the Max Planck Institut) in Tübingen with a professorship of physiological chemistry at the University there.

CONSEQUENCES IN THEORY AND PRACTICE

When we draw general conclusions from experimental results we have to be alert for exceptions and limitations; they lead, often enough, to new and surprising general rules. The chemistry of the higher terpenes offers many such examples. Older generalizations concerning the way in which carbon atoms form ring structures had to yield to new rules when Ruzicka found that as many as 17 carbon atoms could be involved. On the other hand, we have to use our generalizations to their largest extent so as to make them more definite by finding their limitations. The "isoprene rule" will remain a valuable guide even when its field is restricted by other rules.

Generalizations are particularly difficult in the field of biologically and medically active chemicals. An apparently slight change in the composition or in the relative position of the atoms in the molecule of such a substance may cause a decided change in its actions on organisms. Such relatively small changes in the molecular structure cause cholesterol to influence the development of organs which are connected with sexual ripening of the organism. With knowledge of the intimate chemical structure of sex hormones it has become possible to manufacture synthetic products of great therapeutic value. A close relative of these hormones proved to cure arthritis. The synthetic production of this substance, cortisone, reduced its price from \$200 to about \$35 per gram and proved necessary in order to supply the increased demands.

1 9 4 0 - 1 9 4 1 - 1 9 4 2

No Award

19 4 3

GEORGE DE HEVESY

(1885-)

"For his work on the use of isotopes as tracer elements in researches on chemical processes!."

BIOGRAPHICAL SKETCH

HEVESY WENT TO SCHOOL IN HIS NATIVE BUDAPEST AND CONTINUED his studies in Germany and England. From Freiburg im Breisgau, where he received his doctor's degree in 1908, he went to Haber in Karlsruhe and then to Rutherford in Manchester. Rutherford gave him the problem of separating radioactive radium D from the inactive radium G and lead. The attempt to solve this problem became decisive for Hevesy's life work. After he had shown that the separation by all available chemical means was impossible, he turned the failure into success by using just this property of radium D as a means for indicating the presence of lead and measuring its amount through the radioactivity imparted to the ordinary lead by the radioactive isotope. He developed the method in cooperation with F. Paneth at the Vienna Institute of Radium Research, in 1913.

Hevesy returned to Budapest and became professor there in 1918, but he did not stay long. Upon invitation by Niels Bohr, he spent a few years at the Institute of Theoretical Physics in Copenhagen. The investigation of zirconium minerals by Rontgen rays led Hevesy and Coster to the discovery of a new element, called hafnium, in 1922. At this time, he also attempted to separate

isotopes by a physical method. It was based on the premise that the vapor phase over a mixed element should contain more of the lighter isotope, provided it is rapidly removed from the equilibrium with the mixed element. In delicate experiments with mercury and chlorine (in the form of hydrochloric acid) the more volatile fraction really showed an atomic weight which was smaller by less than 0.1 percent than the atomic weight of the residue.

Once more in Freiburg, in 1926, Hevesy studied the relative abundance of the chemical elements on the earth and in the cosmos. The calculations were based on chemical analysis by means of X-ray fluorescent radiation.

In 1934, the production of a radio-phosphorus of atomic weight 32, instead of the normal 31, gave Hevesy a powerful tool for unlocking the secrets of chemical reactions which have importance for life processes. From inorganic chemistry, through physics, Hevesy thus turned to organic chemistry.

Since 1943, Hevesy has been professor at the Institute of Organic Chemistry at the University of Stockholm.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"Suppose that we dissolve 1 g. of lead in the form of nitrate in water, add radium D of negligible weight showing a radioactivity of one million relative units (an electroscope being used to measure the activity) and proceed to carry out the most intricate operations with this 'labelled' lead. If we then ascertain the presence of one radioactive unit in a fraction obtained in the course of these operations, we must conclude that 1/10000th mg. of the lead atoms present in the lead nitrate we started from are now present in the fraction.

"The first application of labelled lead was the determination of the solubility of some very slightly soluble lead compounds such as lead chromate. In these experiments, not radium D but another isotope of lead, thorium B, was applied as an indicator. Labelled lead chromate was obtained by adding a solution of 100,000 rela-

* From *Les Prix Nobel en 1940-1944*.

tive units of thorium B to lead nitrate containing 10 mg. of lead and converting the nitrate thus labelled into chromate. After the saturated solution of this compound had been held at the desired temperature in a thermostat for a sufficient time, its composition was ascertained by evaporating a few cubic centimeters to dryness and measuring the activity of the almost invisible residue in the electroscope. From the number of units of thorium B found, the amount of lead was calculated, one unit corresponding to 10^{-6} grams of lead; finally, the solubility of the lead chromate in moles per liter ($2 \cdot 10^{-7}$) was computed.

"We prepared the radioactive phosphorus isotope by neutron bombardment of carbon disulphide and used this isotope in collaboration with Chiewitz in the study of phosphorus metabolism. In these experiments, 10 liters of carbon disulphide were used to absorb most of the neutrons emitted by a mixture of radium and beryllium kindly put at our disposal by professor Niels Bohr. The ^{32}P formed was extracted by treatment with dilute nitric acid or with water, the carbon disulphide being immediately available after the extraction for further neutron bombardment.

"The most remarkable result obtained in the study of the application of isotopic indicators is perhaps the discovery of the dynamic state of the body constituents. The molecules building up the plant or animal organism are incessantly renewed. In the course of this renewal, not only the atoms and molecules taken up with the food participate, but atoms and molecules located in one organ or in one type of molecule will soon be found in another organ or in another type of molecule present in the same or in another organ. A phosphate radical taken up with the food may first participate in the phosphorylation of glucose in the intestinal mucosa, soon afterwards pass into the circulation as free phosphate, enter a red corpuscle, become incorporated with an adenosine triphosphoric acid molecule, participate in a glycolytic process going on in the corpuscle, return to circulation, penetrate into the liver cells, participate in the formation of a phosphatide molecule, after a short interval enter the circulation in this form, penetrate into the spleen, and leave this organ after some time as a constituent of a lymphocyte. We may meet the phosphate radical again as a constituent of the plasma, from which it may find its way into the skeleton. Being

incorporated in the uppermost molecular layer of the skeleton, it will have a good chance of being replaced by other phosphate radicals of the plasma or the lymph, but it may also have the good fortune to find a more or less lasting abode in the skeleton. This will be the case when it becomes embedded in a newly formed apatite-like bone crystallite."

CONSEQUENCES IN THEORY AND PRACTICE

By attaching a radioactive label to an element, we actually fasten onto that element a new physical property and one which can easily be measured. This makes it possible to determine quantities of the order of a millionth of a gram without preparing them in pure, isolated form. That the determination of such small quantities may have practical meaning can be realized when we consider that one billionth (10^{-9}) of a gram represents 600,000 billion atoms of an element such as chlorine. It has been found that some elements exert important biological actions on plant growth and ripening, or on the health of animals, when they are present in small traces.

Hevesy's method has served to give a direct proof of the theory which Arrhenius developed for the ionic state of substances in solution (cf. p. 14). It has advanced our knowledge of the assimilation of carbon dioxide and water by green plants. The fixation of iodine by the thyroid has been accurately measured by using radioactive iodine. The fate of foods, medicines, and poisons has become clearer through radioactive tracer techniques. When thin sections of tissue from glands, muscle, or bone are placed on photographic film, the development of two million β -particles per square centimeter of film can be detected.

Since isotopes of carbon, phosphorus, iodine, and other elements are now available in convenient quantities produced by cyclotrons or uranium piles, the medical use of these substances grows in importance. "Cobalt 60" is the most recent addition to these isotopes of high medical activity and radiation.

19 4 4

OTTO HAHN

(1879-)

"For his discovery of the fission of heavy nuclei."

BIOGRAPHICAL SKETCH

OTTO HAHN WAS BORN IN FRANKFORT ON THE MAIN, Germany. He studied chemistry in Munich and Marburg and in 1901 received the doctor's degree for a thesis in organic chemistry. After a few years of assistantship at Marburg, he spent a year in Sir William Ramsay's laboratory in London. His investigation of the radioactive decomposition of thorium resulted in the discovery of radio-thorium as one of the new elements of the thorium series, to which he later (1907) added a meso-thorium as a predecessor. The year before, he discovered radio-actinium during work in Rutherford's laboratory in Montreal. The mysteries of actinium, this radioactive element which is chemically similar to one of the rare-earth elements, lanthanum, attracted him again after he returned to scientific research from the war in 1918. Together with Lise Meitner, he found in a new element, prot-actinium, the mother-substance of the complex actinium series.

This research was carried out at the Kaiser Wilhelm Institut for Chemistry in Berlin-Dahlem, of which Hahn became a director in 1928. In all radioactive transformations, even in those which were artificially induced by bombardment with neutrons, the products were either isotopes or close neighbors of the originating elements. On January 6, 1939, there appeared Hahn's first publication

of "experiments which contradict all previous results of nuclear physics." The nucleus of uranium was split into two parts, into two elements which were far removed, in the system of elements, from uranium. He soon found that this was not a clean break and that a host of debris in the form of other elements arose from the fission of the heavy nucleus.

Hahn was able to continue scientific work during the war years in Germany. In April 1946 he became president of the Kaiser Wilhelm Gesellschaft of the Western zones—the highest position in German science.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"As the result of several years of work we (Hahn, Meitner and Strassmann) produced in 1935-1938 a considerable number of artificially radioactive kinds of atoms which seemed to originate directly or indirectly from the supposed short-lived artificial uranium isotopes by β -radiation and which would thus have to represent trans-uraniums—elements beyond uranium. . . .

"Curie and Savitch (1937 and 1938), independently from these trans-uranium investigations by Hahn, Meitner, and Strassmann, described a so-called 3.5-hour substance which they also had obtained by irradiating uranium with neutrons and of which the chemical properties were not easy to determine.

"Since this 3.5-hour substance was considered a trans-uranium I tried to reproduce it, in collaboration with Strassmann. Upon closer examination we arrived at remarkable results which we formulated about as follows: 'In addition to the trans-uraniums described by Hahn, Meitner, and Strassmann, there are produced, by two successive α -radiations, three artificially active β -radiating radium-isotopes of different half-lives which then go over into artificially active β -radiating actinium-isotopes.'

"However, the production of radium under the described irradiation conditions was very strange. Never had transformations with α -radiation been observed when neutrons of low energy had been

* Translated from *Les Prix Nobel en 1940-1944*.

used, whereas here again, as with the 'trans-uraniums,' several isotopes appeared at the same time!

"Experiments were carried out in different directions. Since the products radiated only weakly and the β -rays of the most stable of the new isotopes were strongly absorbed . . . , we tried to separate the artificial 'radium' as much as possible from the barium which had been added as a carrier.

"The attempts to separate our new artificial 'radium-isotopes' from barium failed completely.

"We mixed pure natural radium-isotopes with our artificial 'radium-isotopes' from which transformation products had been removed, and fractionated by the same method as before. The result was that the natural radium-isotopes could be separated from barium, but not the artificial ones.

"We checked these results in other directions. . . . Thus we again found that the alkaline-earth-isotope which we had mistaken for radium actually was an artificially active barium.

"The process, therefore, consists in a fission of the nucleus of uranium which has the nuclear charge 92, into two medium-heavy nuclei. If one of them is barium, which has the atomic number 56, then krypton, of the atomic number 36, must be generated at the same time. The two atomic numbers add up to 92. Both nuclei, as becomes obvious on comparing the mass of uranium with those of the natural stable isotopes of barium and krypton, have too great a mass—in other words, an excess of neutrons; they will therefore emit β -rays and form stable elements of higher atomic numbers.

"Mr. Strassmann and I also considered (in our communication of February 10, 1939) the possibility that neutrons might also be liberated in the fission process. F. Joliot was the first to find that this actually occurs.

"During the war we continued, at the Kaiser Wilhelm Institut für Chemie, the systematic search for chemical disentanglement of the rather complicated fission reactions, and new reactions were discovered. Japanese workers found that with rapid neutrons uranium splits more symmetrically than with neutrons which had been slowed down. And in early 1945 the Kaiser Wilhelm Institut für Chemie was able to tabulate 25 different chemical elements with atomic numbers 35 (bromine) to 59 (praseodymium) in the form

of about 100 different active kinds of atoms as the immediate or indirect fractions of uranium fission. The active kinds of atoms which we had considered as trans-uraniums until 1939 were all active fission products and their active derivatives, but they were not elements beyond uranium!"

CONSEQUENCES IN THEORY AND PRACTICE

Natural radioactivity is a spontaneous reduction of the size of the atomic nucleus, a disintegration in which small particles are expelled at high speed. A reversed process could be produced artificially, with a slight increase of the atomic weight (see Joliot-Curie, p. 144). Hahn discovered that the disintegration can take place in such a manner that the heavy nucleus breaks apart approximately in the middle. Artificially radioactive elements emit β -particles, and Hahn's attention at first was concentrated on this kind of radiation, while the liberation of neutrons from the overloaded breakdown products appeared as a side reaction. Lise Meitner found, by calculating the new results on the basis of Bohr's theory of atom structure, that extremely high energies should be developed in this reaction. The great recoil-energy of the nuclear fission was measured experimentally by Frisch and somewhat later confirmed by Joliot.

A long development of theoretical considerations concerning the relationships of the elements to one another and of matter to energy had led to the conclusion that extremely high amounts of energy are stored in the heavier atoms. Aston had thought of what the consequences might be if we should learn to liberate this energy (see p. 88). Now the way was opened to the conversion of matter into energy, a way which may lead to destruction or to a wonderful future for mankind.

19 4 5

ARTTURI ILMARI VIRTANEN

(1895-)

"For his researches and inventions in agricultural and nutritive chemistry, especially for his method of fodder preservation."

BIOGRAPHICAL SKETCH

ARTTURI I. VIRTANEN WAS BORN IN HELSINKI, FINLAND. HE studied chemistry at the university there. His doctor's thesis, carried out under the guidance of professor O. Aschan, contributed to the elucidation of the constitution of abietic acid, the main part of pine rosin. He did not consider his chemical education as completed with his graduation in 1919, but studied physical and biochemical methods during travels in Switzerland, Germany, and Sweden. He became docent at the University of Helsinki in 1924, professor of biochemistry at the Tekn. Hogskolan (technical high school) of Finland in 1931 and at the University in 1939.

From about 1920 on, Virtanen investigated the processes which occur during storage of green fodder. Fermentations produce lactic acid, butyric acid, and breakdown products of the proteins which spoil the fodder, besides reducing its content in nutritive substances. By acidifying the pressed green fodder to a hydrogen-ion concentration below that corresponding to 10^{-4} (also expressed as $\text{pH} = 4$) the detrimental biological processes were arrested. How good was such an acidified fodder? Did it adversely influence health and milk? Extensive tests in 1928-1929 showed that the

fodder was excellent, even when hydrochloric acid (with some sulfuric acid) was used for the conserving acidification. Not only calories and taste were satisfactory, but vitamins A and C remained undiminished.

Bacterial and enzymatic processes in the utilization of nitrogen, particularly by the nitrifying bacteria present in the root nodules of the leguminous plants, were the subject of extensive work spread over many years. Virtanen's hypothesis concerning the enzymatic reactions and affinities which are responsible for the utilization of nutritive materials has not yet found full recognition.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"In 1925, when I, in connection with the investigations on legumes and legume bacteria, came to deal with the problem of preservation of fresh fodder, the situation was such that the rational exploitation of leguminous crops necessitated a complete reinvestigation of the silage problem in theory and practice.

"I had earlier studied the ability of different bacteria to decompose proteins and to form ammonia from amino acids. On the basis of these important observations it was held probable that harmful processes in silage could be prevented by an artificial acidification of the fresh forage to a pH below 4.

"Practical silage trials were needed to show whether the deteriorating processes: respiration, protein breakdown (and particularly ammonia formation) and harmful fermentations could actually be prevented by an acidification of the fresh crop to below pH 4. In this respect, the results of practical trials were in perfect accord with the theoretical postulations, in that the said harmful processes were indeed most effectively arrested.

"Another important practical question was the maintenance of the given pH value of 3-4 in the silage throughout the period of storing. If fresh grass is packed in a water tight container and acidified with mineral acids to, say, pH 3.5, the acidity of the mass will gradually decrease so that, after a few months, the pH value will

* The first selection is from *Cattle Fodder and Human Nutrition* (Cambridge, 1938); the second is from *Nature*, Vol. CLVIII (1946), p. 515-

have risen over the critical limit of pH 4. Once this occurs the detrimental breakdown process immediately sets in and the material gets spoilt. Even if this is not very serious, cattle generally dislike, and often refuse to eat, silage which has been soaking in the liquid. It appears, however, that the once-attained pH value of the fodder mass remained unchanged if the effluent was drained off.

"Nine years extensive practical use of the A.I.V. process in Finland has definitely proven the entire wholesomeness of the A.I.V. silage. It has been used up to 45 kg per cow per day without any harmful effects."

* * #

"In the light of our new experiments, especially the ones regarding the favourable competition of some amino-acids with nitrate and ammonia-nitrogen, it seems probable to us that in natural conditions plants use also organic nitrogen compounds for their nitrogen nutrition, at least in certain soils. As a rule, however, the uptake of organic nitrogen by cultivated plants is not great, since ammonium salts and nitrates are rapidly formed from organic nitrogen compounds in soil. Since however the uptake of organic nitrogen compounds even in small amounts may affect the plant markedly, the significance of these nitrogen compounds can be great. In the foregoing, alanine has been noted to cause pronounced changes in the shape of peas, and phenyl-ethylamine, the decarboxylation product of phenyl-alanine, which has been added to nitrate-containing nutrient solutions, has produced a branching of different type in pea. Effects of this kind can be expected to occur under certain conditions also in Nature."

CONSEQUENCES IN THEORY AND PRACTICE

Virtanen developed his method particularly for conditions in Finland, with its long winters. The acidification of green crops by addition of acids in a controlled measure makes a constant supply of palatable and nutritious fodder available at all times. The farmer has become independent of weather at harvest time. Extensive

experiments showed that milk and butter of best grades are obtainable when cows are fed acid-preserved silage. The method has found wide application.

In his research on the nitrogen nutrition of higher plants, Virtanen found that the root nodules of legumes contain hemoglobin and methemoglobin. The equilibrium between the red and the brown pigment depends on the intensity of light and the development of the plant. Vigorously growing plants have red root nodules on days of sunshine, indicating high hemoglobin content. Brown color of the cut root nodules indicates lower activity. When neither hemoglobin nor methemoglobin is present, the color is green and nitrogen fixation has ceased.

Legumes are the only plants which can "fix" and use nitrogen from the air. Some of this nitrogen is secreted from the roots into the soil. The importance of organic nitrogen compounds, such as those amino acids which Virtanen found, still needs much further study before a clear picture can be obtained.

19 4 6

JAMES B. SUMNER

(1887-)

"For his discovery that enzymes can be crystallized"
{The award for 1946 was shared with John Howard Northrop and Wendell Meredith Stanley; see below, pp. 184-188.)

BIOGRAPHICAL SKETCH

JAMES BATCHELLER SUMNER WAS BORN IN CANTON, MASS. At school he was interested in physics and chemistry, but not in any of the other subjects. He studied chemistry at Harvard College, from 1906 to 1910. After a brief interlude of work in the cotton-knitting factory which belonged to the family, and some chemistry teaching, he returned to Harvard, this time to the Medical School under Otto Folin, and became doctor of biochemistry in 1914. Shortly afterward he accepted a position at the Cornell Medical School, where he has been professor of biochemistry since 1929, the year he went to Stockholm to investigate his crystallized enzyme with Hans von Euler-Chelpin (see pp. 112-117) and The Svedberg (see pp. 99-102).

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The jack bean appeared to me to be extraordinarily rich in urease and I could see no reason why this enzyme could not be

* From *Les Prix Nobel en 1946*.

isolated in pure form and characterized chemically. Claude Bernard has said that success or failure may depend upon the lucky choice of some reagent or raw material. Willstatter was unfortunate in his choice of saccharase as an enzyme to isolate. I was fortunate in choosing urease.

"I started trying to isolate urease in the fall of 1917, having been occupied previously with analytical methods.

"At first we used to extract urease from jack bean meal with water. These aqueous extracts were viscous and therefore very difficult to filter. Glycerol extracts were even more bothersome. I learned that Folin used 30 per cent alcoholic extracts of jack bean meal as a source of urease for analytical purposes. It was found that extraction with 30 per cent alcohol was of distinct advantage, inasmuch as this solvent dissolved most of the urease but failed to dissolve a rather large quantity of the other proteins. Hence a considerable purification was achieved through the use of this solvent. The alcoholic extracts filtered very rapidly, leaving the undissolved material behind on the filter paper. The only disadvantage of 30 per cent alcohol lay in the slow inactivating action of this solvent upon the urease. However, if kept at low temperatures there was no inactivation of the enzyme.

"When kept at low temperatures 30 per cent alcoholic extracts of jack bean meal formed precipitates. These precipitates contained practically all of the urease, together with concanavalin A, concanavalin B and other proteins. At this time we had no ice chest in our laboratory and we used to place cylinders of 30 per cent alcohol extracts on our window ledges and pray for cold weather.

"It seemed to me of interest to employ dilute acetone instead of 30 per cent alcohol and to see whether this substitution would result in any improvement in the method of purification. Accordingly I diluted 316 cc. of pure acetone to 1000 cc. and used this as the means of extracting the urease. I routinely employed this dilution of acetone, since I had been preparing 30 per cent alcohol through diluting 95 per cent alcohol in this manner. The acetone extract was chilled in our newly acquired ice chest overnight. The next morning I examined the filtrate. It contained practically no precipitate, thus differing from alcoholic filtrates. However, upon observing a drop of the liquid under the microscope it was seen to

contain many tiny crystals. These were of a shape that I had never observed previously. I centrifugated off some of the crystals and observed that they dissolved readily in water. I then tested this water solution. It gave tests for protein and possessed a very high urease activity. I then telephoned my wife, 'I have crystallized the first enzyme.' "

JOHN HOWARD NORTHROP

(1891-)

WENDELL MEREDITH

STANLEY

(1904-)

*"For their preparation of enzymes and virus proteins
in a pure form."*

*(The award for 1946 was shared with James B. Sumner, see
above, p. 182)*

BIOGRAPHICAL SKETCH

NORTHROP

JOHN HOWARD NORTHROP WAS BORN IN YONKERS, N. Y., IN 1891. His father was a zoologist, his mother a botanist. He received his Ph.D. from Columbia University in 1915. During his connection with the Chemical Warfare Service, from 1917 to 1919, he "discovered and worked on a fermentation process for manufacturing acetone." He has been a member of the Rockefeller Institute at Princeton since 1924.

STANLEY

WENDELL MEREDITH STANLEY WAS BORN IN RIDGEVILLE, IND., in 1904. He was graduated from the University of Illinois in 1929 and worked for a year under Heinrich Wieland, in Munich, on sterols. Since 1931 he has been connected with the Rockefeller Institute for Medical Research. During the Second World War, he undertook extensive work on the separation of influenza virus and the preparation of a vaccine from it.

DESCRIPTION OF THE PRIZE - WINNING
WORK

NORTHROP *

"THE early workers were of the opinion that enzymes were probably proteins and in 1896 Pekelharig isolated a protein from gastric juice which he considered to be the enzyme pepsin. He was not able to crystallize the protein and his conclusion as to the identity of the enzyme and the protein was never accepted. I repeated these experiments about 1920 but was unable to carry them further at that time.

"Sumner's results encouraged me to take up the pepsin problem again and in 1930 I isolated a crystalline protein from a commercial pepsin preparation which appeared to be the enzyme pepsin. Since then five more enzymes, as well as some of their precursors, have been isolated in my laboratory. Trypsin, and its precursor trypsinogen, a polypeptide which inhibits trypsin, and a compound of this substance with trypsin, chymotrypsinogen, and three forms of chymotrypsin were isolated and crystallized by Kunitz and myself. Kunitz and McDonald isolated and crystallized ribonuclease and hexokinase. Anson crystallized carboxypeptidase, and Herriott isolated and crystallized pepsinogen. These experiments required a great deal of the most painstaking and difficult work and could not have been successfully carried out without my collaborators, Herriott, Anson, Desreux, McDonald, Holter, Krueger, Butler, and especially, Dr. Kunitz, who possesses a real genius for handling these unstable and elusive substances.

"As a result of these experiments, it appears probable that all enzymes and at least some viruses are proteins. The mere fact that

* From *Les Prix Nobel en 1946*.

the preparations are crystalline proteins is not, of course, sufficient to warrant this conclusion and we have spent a great deal of time in establishing the purity of our preparations and in testing by every method available the relation between the activity and the protein.

"Before discussing these results, I will describe briefly the experimental methods we have used in the isolation and crystallization of these active proteins. No one general method has been found which will lead to the isolation and crystallization of an enzyme, but certain general principles have been found to be of great assistance. In the first place large quantities of material are used, so that actual solid material is handled and not merely dilute solutions. The failure of so many early attempts to isolate enzymes was due, I believe, largely to the fact that nearly all of the work was carried out with dilute solutions. In the second place filtration by suction was used wherever possible since this method results in far better separation of the precipitate from the mother liquor than does the use of the centrifuge. Had Pekelharing filtered his pepsin preparation and then dissolved it in a very small amount of water, instead of centrifuging the precipitate and dissolving it in a large amount of water, I am quite sure he would have crystallized the enzyme nearly fifty years ago.

"In the third place fractionation was carried out largely by the use of concentrated neutral salts in the presence of which proteins are much more stable than in dilute salt solutions.

"Pepsin, for instance, decomposes at a rate of about 3 per cent a day in hydrochloric acid solution at pH 2.7 and 0° C. Even in nearly saturated magnesium sulfate solution at 0° C, the most stable condition known, the rate is 1 per cent a day.

"Trypsin at pH 8.0 and 30° C loses 90 per cent or more of its activity in a day. This reaction is exceptional since it is bimolecular so that in this case dilute solutions are more stable than concentrated ones."

STANLEY *

"ATTEMPTS to learn something about the nature of viruses through studies on their general properties began with Beijerinck's work in

* From *Les Prix Nobel en 1946*.

1898 and were continued in different laboratories for over thirty years without too much success. Although Beijerinck and Allard made important contributions, perhaps the most significant work was that of Vinson and Petre during the years from 1927 to 1931 when they showed that tobacco mosaic virus could be subjected to several kinds of chemical manipulations without loss of virus activity. Nevertheless, when the work on viruses, which is recognized by the 1946 Nobel Prize for Chemistry, was started in 1932, the true nature of viruses was a complete mystery. It was not known whether they were inorganic, carbohydrate, hydrocarbon, lipid, protein or organismal in nature. It became necessary, therefore, to conduct experiments which would yield information of a definite nature. Tobacco mosaic virus was selected for these initial experiments because it appeared to provide several unusual advantages. Large amounts of highly infectious material were readily available and the virus was known to be unusually stable. Furthermore, it was possible to titrate or measure the amount of this virus in a preparation with ease and rapidity and with great accuracy.

"As a result of studies on the effects of over one hundred different chemicals on tobacco mosaic virus, it was found that the only chemicals which had a direct inactivating action could be classified as oxidizing agents, protein-precipitating agents and agents causing a hydrogen ion concentration known to inactivate the virus. It was concluded that, as a whole, the results are in harmony with the conception that the virus is a protein. As a result of these studies efforts were directed more definitely towards the development of procedures useful in the concentration and purification of proteins. The optimum hydrogen-ion concentration for carrying out the three principal steps in the lead acetate process for the purification of tobacco mosaic virus proposed by Vinson and Petre were determined. . . . Utilization of this process yielded colorless, partially purified solutions having a virus content equal to or somewhat greater than that of the starting material. Subsequently it was found that concentration and purification of the virus could be effected readily by means of a combination of isoelectric precipitation and salting out with ammonium sulfate.

"The protein in the filtrate is crystallized by adding slowly, with sufficient stirring, sufficient of a saturated solution of ammonium

sulfate to cause a slight cloudiness, followed by a solution of 10 per cent glacial acetic acid in one half saturated ammonium sulfate sufficient to increase the hydrogen-ion concentration to about pH 5.

"Needless to say, for a time there was great scepticism that the crystalline material could be tobacco mosaic, due chiefly to the old idea that viruses were living organisms. A wide variety of experimental approaches has been used to test the proposal that the crystalline material represented tobacco mosaic virus. It was found that essentially all of the virus activity present in infectious juice could be isolated in the form of the crystalline material. The virus activity of this material was about 500 times that of the starting material. One ml of a solution containing but 10^{-9} grams of the material has usually proven infectious.

"Early determinations of viscosity and sedimentation yielded data which permitted the conclusion that the particles of tobacco mosaic virus consisted of rods, about 12 m in diameter and about 400 m/* in length, with a molecular weight of about 40 millions.

"An interesting and potentially very important property of the rods of tobacco mosaic virus is their ability to aggregate end-to-end. . . . The entire rod appears necessary for virus activity, for breakage of the rod into two halves is accompanied by loss of virus activity."

CONSEQUENCES IN THEORY AND PRACTICE

The word "enzyme," taken literally, means "in yeast." From yeast or malt sprouts, extracts were obtained which acted upon large quantities of organic substances, as in the conversion of starch to sugar and of sugar to alcohol. Willstatter (see pp. 65-69), who did much to introduce quantitative measurements into enzymology, had much opposition to his view that enzymes are chemicals. Real proof for this view was demonstrated when enzymes were purified to pure substances. It meant a triumph of the chemical technique and the chemical theory. The previously mysterious cause of activity was here shown to be enclosed within the unit which is the molecule of a pure substance. The activity is a molecular property, like the color of a dyestuff.

Crystallization was successfully carried out, for example, with potato-X-virus; with tomato bushy stunt virus, which forms rods, like tobacco mosaic virus; and also with strains of influenza virus, of which the pure particles have spherical form. The building stones of these viruses are amino acids, as in other proteins. Certain chemical changes can be carried out with the pure viruses so that the derivatives are still active and infectious. Structural changes produced by reaction with formaldehyde were accompanied with changes of activity; when the original chemical structure was restored, the activity also was restored.

These results closed a chapter of uncertainties in a biologically and medically very important investigation. And yet Dr. Stanley ended his Nobel lecture with the words: "The new field of virus research is really in its infancy and much remains to be accomplished." The same could be said of the new enzyme research. For dyestuffs, certain relationships between color and chemical constitution have been found. Corresponding relationships for enzymes and viruses are not yet in sight, but the problem can now perhaps be formulated with more confidence than ever before.

19 4 7

ROBERT ROBINSON

(1886-)

"For research on certain vegetable products of great biological importance, particularly alkaloids."

BIOGRAPHICAL SKETCH

ROBERT ROBINSON WAS BORN IN BUFFORD, NEAR CHESTERFIELD, Derbyshire, England, where his father manufactured cardboard boxes and surgical materials on machines of his own invention. He became Doctor of Science in Manchester, in 1910, and was professor of organic chemistry at the University of Sidney, Australia, from 1912 to 1915. After his return to England he was professor at several universities; since 1929 he has been at Magdalen College of Oxford University.

Robinson's interest in the chemical constitution of plant dyestuffs soon extended to alkaloids. The red, blue, and violet pigments in flowers or roots, wood and bark, are highly complex substances which are called anthocyanins. They can be split into a sugar component and the basic colored compound, the anthocyanidin. Robinson was at first particularly interested in the dyestuff contained in certain kinds of wood which had long been used for dyeing. The dyestuffs which can be extracted from them are brazilin and hematoxylin. Robinson always attempted to supplement analysis by synthesis. He found a method for synthesizing tropinone, a relative of a substance which forms the characteristic part of the molecule of atropine, an alkaloid which is used in

medicine, for example, to enlarge the pupil before eye examinations. He contributed greatly to the art of defining the arrangement of the atoms in the molecule structures of morphine and other alkaloids found in the sap of the seeds of poppies, which include papaverine and narcotine. Open chains of carbon atoms are closed into rings, and the orientation of attached atom groups in space relative to each other is determined.

Robinson said of himself: "Such contributions as I have been able to make are to the science itself and do not derive their interest from the economic or biological importance of the substances studied."

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The study of brazilin and haematoxylin is by no means finished and in this connexion I would like to make a general observation. The synthesis of brazilin would have no industrial value; its biological importance is problematical, but it is worth while to attempt it for the sufficient reason that we have no idea how to accomplish the task. There is a close analogy between organic chemistry in its relation to biochemistry and pure mathematics in its relation to physics. In both disciplines it is in the course of attack of the most difficult problems, without consideration of eventual applications, that new fundamental knowledge is most certainly garnered.

"From the incidents of the brazilin investigation two fresh topics developed. In the first place the pyrylium salt synthesis led to the much later extension to the synthesis of anthocyanidins and still later to that of the anthocyanins (see below). Secondly the facile ring closure of β -3:4~dimethoxyphenylpropionic acid to the ketone (II) suggested an application to the synthesis of papaverine.

"The structural or biogenetic relations of plant products as deduced from the recognisable architectural components of the molecules have been consistent guides in my investigations. An early instance was the change proposed in the constitution of berberine (1910). It seemed highly improbable that hydrastine and berber-

* From *Les Prix Nobel en 1947*.

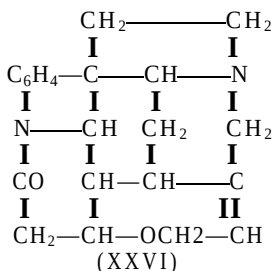
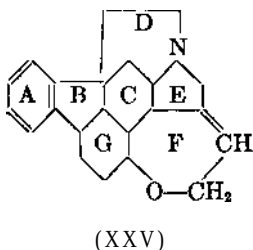
ine, congeners in *Hydrastis canadensis*, could have totally differently oriented methoxyl groups. The change suggested was justified by the first synthesis of berberine by way of oxyberberine (with Perkin and Ray, 1925). Similar considerations underlay the revision of the structures of morphine and its relatives, made with J. M. Gulland in 1923-24.

"The interlocking developments of the chemistry of strychnine and brucine cannot be usefully summarised and demands separate treatment. This is a most fascinating molecule and with its seven fused rings it is a kind of organic chemist's playground. For many years to come it will provide material for degradative studies. Nevertheless I believe that the problem of its constitution is finally solved in every detail. For a long time the formula (XXV) seemed satisfactory, but in 1945 Prelog and Szpilfogel gave good reasons for supposing that ring E is six-membered. Other evidence in the same direction has since accumulated. The chemistry of neostrychnine, an isomeride depending on a change in position of a double bond, created some temporary difficulties. These have been over-

come by the recognition that neostrychnine contains $\begin{array}{c} \backslash \quad \epsilon t \quad p / \\ N-CH=C \end{array}$

which can be oxidized by perbenzoic acid to $N-CHO \quad CO$, and changed by bromine to a bromo-hydrobromide which in warm

water becomes $\begin{array}{c} \backslash \quad 0 \quad I \quad a \\ N-C-CHO, \quad HBr \end{array}$ (with R. N. Chakravarti, 1945-46). After careful and prolonged consideration I am satisfied that strychnine is (XXVI) (Experientia, 1946) and that no alternative can now be entertained."



CONSEQUENCES IN THEORY AND PRACTICE

The synthesis of complicated organic substances such as alkaloids starts with the preparation of simpler compounds in a manner which is chemically transparent. It continues with the combination of such compounds into higher structures which we can then understand because we built them. The knowledge so gained is not limited to the particular alkaloid constructed; the substance is linked with others by similarities and analogies. Thus, the methods of synthesis and the insight into the structure of certain alkaloids had great consequences for the task of producing anti-malarial drugs. Sir Robert Robinson took a prominent part in this task during the last war.

The knowledge of natural alkaloids made it possible to set up specific objectives for the new effort and to formulate expected structures for which medical value could be reasonably predicted. The previously developed methods helped to pave the way to the new substances.

19 4 8

ARNE TISELIUS

(1902-)

*"For his researches on electrophoresis and **adsorption analysis**, especially for his **discoveries concerning the complex nature of the serum proteins**"*

BIOGRAPHICAL SKETCH

ARNE WILHELM KAURIN TISELIUS WAS BORN IN STOCKHOLM. He went to school in Gothenburg and studied chemistry at Uppsala, where his grandfather had been professor of mathematics. From 1925 on, he was assistant to The Svedberg. His doctoral thesis, published in 1930, dealt with "The moving boundary method of studying the electrophoresis of proteins." The displacement of dissolved molecules under the influence of an electrical charge which is called electrophoresis is the result of many factors, such as concentration of the solution, size and form of the molecules, the medium in which they are dissolved, and the magnitude of the electrical charge. Many efforts had been made to use this displacement for the study of the sensitive, large molecules of proteins. It was necessary to select suitable conditions and optical systems with which the movement of the molecules could be followed. The front of this movement represents the "moving boundary."

Shortly after receiving his doctor's degree, Tiselius began the investigation of the second subject mentioned in the citation for the Nobel Prize, adsorption. He continued this work at Princeton,

¹934"¹935- Having returned to Uppsala, in 1937, he applied electrophoretic methods to the separation of proteins in the blood serum. A new professorship for the study of the chemistry and physics of life was created for him, and a new institute was built for this purpose.

Tiselius is greatly interested in general problems of scientific research. He has been president of Sweden's State Council for Research in Natural Sciences since its foundation, in 1946.

DESCRIPTION OF THE PRIZE-WINNING WORK *

"The advantages of the electrophoretic method are above all its gentleness and its marked specificity. During the entire course of a separation the substance remains in solution of approximately constant composition, thereby eliminating the risk of denaturation and other irreversible changes which so easily influence processes dependent on precipitation. This advantage is also characteristic of separation by ultracentrifugation. Frequently proteins, enzymes, and other substances which have been purified by precipitation or by repeated recrystallization are nevertheless found by electrophoretic analysis to be inhomogeneous. This is probably due to the fact that substances of such a nature show a great tendency to carry foreign substances with them on precipitation. The components are more likely to be free from one another in solution, and as the electrophoretic separation depends only on difference in mobilities it is of little importance if the impurities are present only in very small quantities. The separation proceeds just about as readily—in contrast to what is usually the case in most other separation methods.

"The method's great convenience has, however, certain limitations which should be indicated. In electrophoretic migration only those molecules or particles which are free from one another in the solution are separated. If complex groups or associations of some type exist, a separation can only be expected to the extent in which these complexes are dissociated. A component which under

* From *Les Prix Nobel en 1948*.

certain conditions in electrophoresis is observed to be homogeneous can also very well, under different conditions (with less gentle treatment or merely by a change of pH) show itself to be of complex nature. However, electrophoretic (as ultracentrifugal) observations are of considerable interest also in such a case from an entirely different point of view. The gentleness of the method should often make it possible to draw the conclusion that such demonstrated complexes may even be present in the original material, that is to say, when we deal with proteins, in the living organism itself. It is not necessary to be a vitalist in order to express the opinion, that what from a chemist's viewpoint may be taken as a strongly retained impurity (for example the lipid in a lipo-protein complex), from a biological viewpoint perhaps may possess a vital function. Throughout the course of biochemistry—quite naturally—principal interest has been directed to the chemical entities that have been isolated from biological materials, but there is little doubt that in the future much closer attention must be paid also to the existence of specific complexes in the living organism. It is the chain of events with linked reactions which is the key note of life's processes and its interrelationship or linkage can perhaps best be conceived as the result of an association of substances with different specific functions.

"In 1940 I began some experiments in order to make use of the chromatographic analysis in the separation of proteins and of their breakdown products. This was considered worth a trial on account of the remarkable specificity which this separation method shows for different organic substances, which had become evident in the course of numerous investigations during the years following the original work of Tswett in 1906. The particular difficulties which had been encountered (such as boundary anomalies) in the electrophoresis of peptides and similar breakdown products of proteins made it also desirable to find a method especially adaptable for the separation of these substances.

"Just as chromatographic methods in general, these methods are useful for the analysis of substances of the most varied sort. We have performed a very large number of model experiments on amino acids, peptides, sugars, fatty acids and fats, etc.

"For a quantitative estimation of these diagrams it is of utmost importance that as low a concentration as possible can be used. It is accordingly of great interest that Claesson has recently been successful in constructing a new adsorption analysis interferometer with approximately five times the sensitivity of the previous model. The large separation of high polymers of the polymetacrylate and nitro-cellulose types which Claesson has succeeded in accomplishing indicates that adsorption analysis in this field will come to assume great importance."

CONSEQUENCES IN THEORY AND PRACTICE

The methods developed by Tiselius and in his institute offer very gentle means for separating substances which differ only slightly in their chemical constitution. This is of especial importance, for such substances may differ widely in their effect on living organisms. In order to develop these methods, the chemist had to be a good physicist and instrument designer.

Separations thus obtained are indicated by marked changes in the refraction of light. Electrophoretic diagrams show several peaks when the dissolved substance is not uniform. Thus, it is possible to use the method as a fine analytical tool, as was done during the work at Harvard on producing pure proteins by fractionating blood plasma. The medical value of these fractions is highly specific and greatly increased by the removal of biologically interfering substances. In some cases, the fractionating can even be carried out in the electrophoresis apparatus.

The separation of related substances by adsorption is versatile, because several influential factors can be selected and combined. Such factors are the materials on which the substances are to be held by adsorption and the solvents used first in anchoring the substance on the materials and then in removing it from them. This method has furnished valuable information about the presence of polymeric substances in synthetic resins. Although the method is usually described as the chromatographic method, it can now be applied not only to the colored substances for which it was first developed but also to colorless ones.

A particularly impressive use of the chromatographic method was the recent separation of rare-earth element compounds which have very similar chemical properties and play a role in research on atom fission.

19 4 9

WILLIAM FRANCIS GIAUQUE

(1895-)

"For his work in the field of chemical thermodynamics, particularly concerning the behavior of substances at extremely low temperatures/"

BIOGRAPHICAL SKETCH

WILLIAM GIAUQUE WAS BORN IN NIAGARA FALLS, ONTARIO. After graduation from high school and an interval of two years at an industrial laboratory, he studied chemistry at the University of California. There Gilbert N. Lewis directed his interests to the beauties and problems of thermodynamics. A few years after obtaining the doctor's degree (1922), his study of the capacity which substances have to hold internal energy at a specified temperature led him to calculations of the influence of magnetism on this capacity, usually called entropy. Several years elapsed before the calculations were put to experimental test. In 1933, Giauque in California and de Haas in Holland attained a temperature which was only 0.5 degrees above the absolute zero of temperature.

From the viewpoints of entropy and thermodynamics all the properties of matter are interrelated, and one of them can be used to influence another or in interpreting another. Just as he combined magnetism with heat, Giauque concluded from spectroscopic measurements on oxygen that not all its atoms could have the same weight. He predicted that, in addition to the well-known species of oxygen atoms which have a weight of 16.00, atoms of

weight 17 and 18 should be present. This prediction of 1928 was soon proved correct.

As professor of chemistry at the University of California since 1934, Giauque has continued the development of low-temperature research with a great body of equipment. During the Second World War, his theoretical work found urgently needed applications in the construction of mobile units for the production of liquid oxygen.

DESCRIPTION OF THE PRIZE - WINNING WORK *

"The careful determination of entropy has often been accompanied by the discovery of unexpected physical properties. The discovery of the oxygen isotopes of atomic weights 17 and 18 was a case of this kind.

"An accurate measurement of the low temperature heat capacity of oxygen was undertaken with Dr. H. L. Johnston. . . . In this case, as had long been known, there are three crystal forms and the liquid before the gas state is reached and thus it was also necessary to measure the increase in entropy during each change of state.

"One of the principal lines of research which we had pursued in connection with the determination of entropy is the calculation of this, and other thermodynamic quantities, by means of quantum statistics and the entropy levels of gas molecules. These entropies can be obtained from band spectra. . . .

"This spectrum permits the determination of the energy levels of the oxygen molecule. When the entropy of oxygen gas was calculated from these strong lines [in the oxygen spectrum] it agreed exactly with the value obtained from our low temperature measurements.

"The spectrum also contains many weak lines, which were believed to be due to oxygen, but which were not understood. . . . It is rather interesting that these weak lines are themselves an unexpected by-product of a solar investigation by Babcock. When

sunlight passes through the molecules in the earth's atmosphere, some of the light is absorbed selectively by them. The effect may be enhanced by photographing the sun when it is low on the horizon because the light then passes through a greater amount of air.

"An entropy calculation based on band spectra is not considered to be satisfactory unless the spectrum is completely explained. One way to explain weak lines is to assume that they are due to some higher energy state of the molecules, and are weak because not many molecules are in the higher energy state. Many of the weak lines in the oxygen spectrum are actually due to this effect, but they could not all be explained in this way.

"Months of thinking about this problem led to memorization of the essentials of the data and I literally awoke one morning with the realization that the lines must originate from an isotopic species. Detailed calculations by Dr. Johnston and myself confirmed this accurately and it was determined that isotopes of atomic weights 17 and 18 exist in the earth's atmosphere.

"The commonest question asked in the early days of this work [on very low temperatures] was 'How do you know it gets cold?' This was a fair question. Obviously, no one had ever made thermometers which were calibrated at temperatures that had never been produced. Since even helium gas has negligible pressure, at the low temperatures obtained, a gas thermometer is useless.

"Temperature can only be measured by some property of a substance which varies with temperature. In this case the magnetic susceptibility increases as temperature decreases.

"When an alternating electric current is passed through a measuring coil it becomes increasingly difficult for the current to pass as the magnetic susceptibility of the substance increases. This effect permits the quantitative determination of magnetic susceptibility.

"The resistance of the wire in measuring coils drops to such low values at the temperature of liquid helium that very large numbers of turns can be used. The sensitivity which is obtained with coils at these low temperatures is such that it is necessary to compensate for the small fluctuations in the Earth's magnetic field."

CONSEQUENCES IN THEORY AND PRACTICE

The relationships of all chemical and physical changes to temperature are the central theme of thermodynamics, and its central concept is entropy. Temperature is the result of the movements of the molecules, and it is measured on a scale derived from the expansion of gases upon heating. According to this scale and the concepts upon which it is erected, there is an absolute zero point of temperature. At this point, 273 degrees below the zero of the centigrade scale of Celsius, all molecular movement should come to a standstill. This absolute zero of temperature is a highly interesting state; Nernst derived some very practical applications from theories concerning the approach to this state. He could do this because we postulated this state from our experiences at normally accessible temperatures. The liquefaction of air and the production of liquid oxygen and nitrogen are very tangible results of thermodynamic calculation. When air is compressed, a part of the energy of molecular movement is converted into heat. This energy can be removed from the system by absorption in a cooling medium. When subsequently the cooled compressed gas is allowed to expand, internal energy is converted into greater movement of the molecules in the enlarged space at their disposal, so that the temperature drops. By repetition of the cycle of compressing, cooling, expanding, air is liquefied, and by the use of liquid air as the cooling medium, even helium could be converted into a liquid.

The effect of a magnetic field on a para-magnetic substance consists in bringing a higher degree of order into the movement of its electrons. This effect increases inversely with the temperature; it is 300 times as great at 1° as at room temperature (300° on the absolute scale). Imposing such a higher degree of order of internal movement upon a substance is equivalent to a compression; it results in a development of heat. This heat can be removed by a cooling medium which itself is at a lower temperature, such as helium at 1° . After such cooling, the removal of the magnetic field causes a further drop of temperature, because this corresponds to an

expansion of the gas. Temperatures of only 0.003 above absolute zero were thus obtained.

The measuring of such extremely low temperatures is exceedingly difficult. The gas thermometer can be used only down to the boiling point of helium; from there on it has to be replaced by thermometers based on the electrical resistance of a pure metal. This method is complicated by the fact that there is a temperature that is characteristic for the specific metals, at which they suddenly become super-conductors of electricity with zero resistance. It is one of the objects of infra-low temperature research to obtain more information about this particular state of metals. Another aspect, of practical interest, is the relationship of para-magnetism with energy levels of electron movements around their own axis ("spin"). This kind of movement, associated with absorptions in the micro-wave range of the spectrum, must be better understood for the construction of improved radar equipment.

1950

OTTO DIELS

(1876-)

KURT ALDER

(1902-)

"For the development of the diene synthesis"

BIOGRAPHICAL SKETCH

DIELS

OTTO DIELS WAS BORN IN HAMBURG, GERMANY. HE STUDIED chemistry in Berlin and received his doctor's degree in 1899 for work carried out under Emil Fischer's inspiring direction. In the widely diversified field of organic chemistry the importance of many results of research remains confined to small areas. It was different in Diels's case. He made three main discoveries which aroused general interest.

The first of these discoveries was a substance, a gas which made its presence uncomfortably known by a penetrating odor and an irritating action on the eyes. He proved it to be a carbon oxide with the proportions of three carbon atoms for two of oxygen; the proportions in carbon monoxide are one to one and, in the most common of the carbon oxides, one to two. This discovery (1906) was remarkable not only for the properties of the highly reactive compound, but also because it concerned such widely known elements.

Discovery number two was a method of removing part of the hydrogen from the molecule of organic substances in a gentle and controllable way. The reagent used in this method is selenium, a metal which is a relative of sulfur, according to the periodic system of the elements. The selectivity of the action of this metal on hydrogen-rich compounds was of great help in recognizing the structure of such complex substances as sterols.

The third discovery again gave a generally useful method to organic chemistry. It is a method of synthesis which proceeds under mildest conditions and which, therefore, easily reveals the structure of the product. This synthesis is based on a peculiar property of compounds which contain two double-bonded groups of carbon atoms separated by a single bond. Since chemical nomenclature characterizes double bonds by the syllable *-ene*, these compounds are dienes. Butadiene $\text{CH}_2 = \text{CH} - \text{CH} = \text{CH}_2$ is a simple ex-



ample. Isoprene, the building block of natural rubber, is a butadiene with a methyl group (CH_3) attached to carbon number 2. An important diene with five carbons in a closed ring (cycle) is cyclopentadiene.

Diels, since 1916 professor at the University of Kiel, discovered and explored organic synthesis by means of dienes together with Kurt Alder.

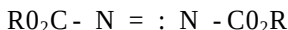
ALDER

ALDER STUDIED CHEMISTRY IN BERLIN, THEN IN KIEL, AND received his doctor's degree at Kiel in 1926. The great variability of diene synthesis remained one of the primary subjects of research at the Kiel laboratory and spread from there to many places of research. Alder became professor at Kiel University in 1934. He applied results of his scientific work to technical problems of building large molecules for use in plastics and their ramifications while acting as a director of research for one of the plants of the I. G. Farben Industries. In 1940 he accepted the directorship of the chemical institute at the University of Cologne.

DESCRIPTION OF THE PRIZE-WINNING WORK*

"We have been successful in establishing that dienes, of which isoprene is a typical representative, are capable of an astonishingly great number of synthetic reactions which proceed under the mildest conditions. On the strength of our observations we do not doubt that they have an important role as a valuable principle of construction in all real organic syntheses, that is to say, in the organisms.

"The most essential step in developing diene synthesis, the transfer of experiments made with the azo-ester



to a suitable nitrogen-free system, was initiated by the study of an older publication by Albrecht, a pupil of Thiele's. He had observed that cyclo-pentadiene can combine with one or two moles of quinone, and he had suggested formulae for the two products of this reaction which we . . . proved to be wrong. The addition of cyclo-pentadiene to quinone occurs in the 1 — 4-position.

"According to this principle we succeeded in adding simple dienes such as butadiene itself or its alkylated derivatives, or even cyclic dienes, to alpha-naphtho-quinone and thus building many homologues of anthra-quinone. There is no visible limit to the number of syntheses possible according to this method. Since these reactions take place spontaneously, at any rate without involving other reagents, it seems generally logical to me that nature also uses this method in many cases to build up complicated derivatives of anthracene and other hydrocarbons.

"The incomparable fecundity of diene synthesis is the result of the fact that the two components of the reaction can be varied at will without changing their tendency to unite, and thus to form hydro-aromatic compounds."

*Translated from *Zeitschrift für Angewandte Chemie*, Vol. XLII (1929), pp. 911 ff.

CONSEQUENCES IN THEORY
AND PRACTICE

Diene synthesis shows a gentle way in which formidably complicated molecules are built by a reaction in which the parts are simply put together. The reaction does not require or produce temperatures outside of those at which organisms live. The formation of anthracene-structured dyestuffs or of cholesterol is thus brought closer to biochemical understanding. To a certain extent, we can imitate the production of these organismic substances. We establish the rules of these syntheses with the aid of simplified models. In the course of such work we can give proof by synthesis of the atomic arrangement in the molecules of, for example, higher terpenes. Phellandrene, a terpene obtainable from water fennel or eucalyptus plants, gave diene reactions which easily revealed its molecular structure. The diene synthesis of furane with maleic acid anhydride, two simple and readily available chemicals, furnished cantharidin, an old, medically used venom produced by the so-called Spanish fly and certain beetles.

Naphtho-quinone, one of the substances mentioned above (naphthalene containing two oxygen atoms at opposite ends of one of the rings in its molecule) forms derivatives which have vitamin K activity. They have been synthesized by adding butadiene to an appropriate partner. Similar reactions are being used and sought for the artificial production of other vitamins and of hormones.

Diene compounds can combine with one another to form polymers. The polymerization of butadiene, alone or in conjunction with styrene, leads to synthetic rubber. The experience with diene synthesis offers theoretical explanations for such polymerizations. With their guidance, the methods for manufacturing plastic and rubberlike materials have been improved.

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