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SUBSTITUTION AT ELEMENTS  
OTHER THAN CARBON

**WEIZMANN MEMORIAL LECTURES**

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December 1953

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Weizmann Science Press (1959)

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SUBSTITUTION  
AT ELEMENTS  
OTHER THAN CARBON

*Being the  
Fifth Weizmann Memorial Lecture Series  
May 1958*

BY

C. K. INGOLD

*University College, London*

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## PREFACE

Earlier this year, I had the great privilege of contributing to a highly distinguished lecture-series. This little book is a record of the set of four lectures which, accordingly, as Chaim Weizmann Lecturer for 1958, I gave during the latter part of May in the Weizmann Institute of Science at Rehovot, Israel.

My original invitation to fulfil this honourable task came through Dr. Israel Dostrovsky, then Chairman of the Scientific Committee of the Weizmann Institute. The Administrative and Scientific Chairmen under whom this commission was eventually fulfilled were respectively Mr. Meyer Weisgal and Professor C. L. Pekeris. No one could have been treated with greater kindness than I was by them and by all my hosts, and no duty could thus have been converted more completely into a pleasure. I cannot in this place make a list of all of those who have my deep gratitude on this account, for it would include that considerable proportion of the delightful and stimulating members of the Institute with whom it was my privilege to become acquainted at that time.

After the lectures had been delivered, and their manuscript handed in, the Editor—in—Chief of the Weizmann Science Press was kind enough to meet me in Jerusalem, in order to facilitate the solution of problems of the kind which always do arise during the preparation of a scientific book. I am most grateful to the Editor and Staff of the Press for their good work on the production of this book.

Concerning the book itself, all that need be said by way of introduction to its subject matter is this. It has been characteristic of the progress of organic chemistry during the last quarter-century that, to the already established study of structure, has been added a study of mechanism. This newer dynamic side of organic chemistry has today attained a state of incorporation as well-shaped and viable as that which the older static side of the subject has long enjoyed. The object of the lectures recorded in this book was to point out that the first attempts are contemporaneously being

made to start the development of a corresponding extension of scope in the very much more diversified field of inorganic chemistry, which hitherto has been essentially restricted, as organic chemistry used to be, to the study of structure; and to point out, furthermore, that in these current attempts to set on its feet the subject of mechanism in inorganic chemistry, the model and methods of the corresponding study of organic chemistry are available, and that to have such a guide is of some advantage in attacking the generally more formidable problems of mechanism that inorganic chemistry presents. There is no well-rounded story here, for the subject is at its beginnings. But even these seem worth indicating, for the prospects are very extensive and devotees are needed.

University College, London, W. C. 1.  
November 1958.

C. K. INGOLD

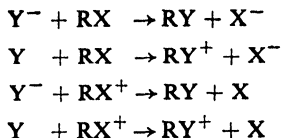
## CHAPTER 1

### NUCLEOPHILIC SUBSTITUTION AT OCTAHEDRAL METAL ATOMS, IN PARTICULAR COBALT

Substitution mechanism was first comprehensively studied in the field of organic chemistry. Substitutions were classified as nucleophilic or electrophilic according as the substituting agent attacked a nucleus or electrons. A third class of substitutions is now known, homolytic substitutions, but it is still true that most of our more exact knowledge of substitutions refers to the longer studied nucleophilic and electrophilic substitutions. Nucleophilic substitution was found to prevail at saturated carbon, wherein all the valency electrons are of the  $\sigma$ -type and lie well-protected between the nuclei. Electrophilic substitution appeared most typically at unsaturated carbon, where the externally lying  $\pi$ -electrons are relatively easy to attack. The mechanism of nucleophilic substitution was studied in its basic features in the 1930's, and of electrophilic substitution largely in the 1940's, with overlap into this decade.

But in this decade another development is arising: substitution mechanisms are beginning to be regarded more comprehensively than the conventional boundaries of organic chemistry would allow. It is being asked whether the mechanism of substitution at carbon should not be regarded as a pattern for the study of the mechanism of substitution at other elements. Might not such an extension of the study of substitution disclose mechanisms best appreciated in terms of their analogies with and differences from the known mechanisms of substitution at carbon?

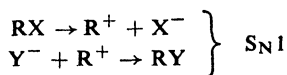
I propose to illustrate this expansion of the field, commencing with nucleophilic substitution. So let us, in preparation, recall the results of our prototype study, that of nucleophilic substitution at saturated carbon. This is known in four types of charge distribution, as shown below, the differences between which, however, are trivial in comparison with the fundamental similarities in the mechanisms utilised:



*Charge types in nucleophilic substitution at carbon*

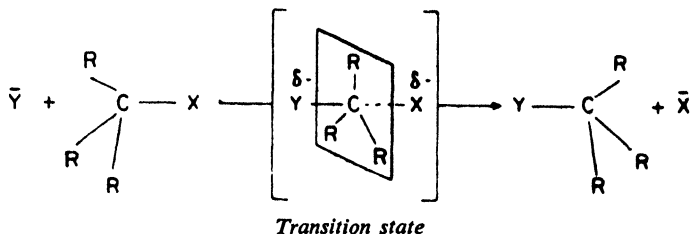
It has been found that two mechanisms of substitution are utilised, which we name "unimolecular" and "bimolecular", and sometimes, for greater brevity, label  $\text{S}_{\text{N}}1$  and  $\text{S}_{\text{N}}2$ . Which mechanism will in fact be used depends jointly on the substituting agent, the compound substituted, and the solvent; but we can often change the mechanism by changing only one of those variables. There are some marginal or dubious cases, but the great majority of studied cases can be sharply classified.

Unimolecular nucleophilic substitution at carbon ( $\text{S}_{\text{N}}1$ ) involves two steps: a preliminary heterolysis is succeeded by a normally faster reaction of the formed carbonium ion with the substituting agent, as formulated below for the one charge type:



The kinetics have a limiting first-order form, subject to modification when a retarding reversal of the first step competes effectively with the forward second step. This mechanism can give all stereochemical results between the three limits of retained configuration, inversion, and racemisation, the actual result depending mainly on the constitution of the compound substituted, but also to some extent on the substituting agent and the solvent.

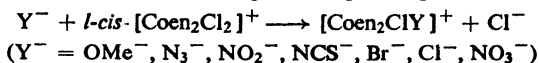
Bimolecular nucleophilic substitution at carbon ( $\text{S}_{\text{N}}2$ ) proceeds in one step, with limiting second-order kinetics. Its most striking characteristic is that it always produces inversion, independently of all constitutional details, even of charge-type. Its transition state is therefore a trigonal bipyramid with a three-centre split-bond along the main axis:



Outside carbon substitutions, a vast class of nucleophilic substitutions presents itself in the ligand replacements at transition metals. They offer co-ordination numbers higher than four, and space-figures higher than the tetrahedron. One is attracted to the prevalent co-ordination number 6, and to its regular figure the octahedron, which, like the tetrahedron, admits of and was indeed established through the criterion of optical activity.

Cobalt-III with a co-ordination number of 6 is diamagnetic and has fully closed sub-shells, a circumstance which, one felt, might exclude some unwanted complications. Werner<sup>1</sup> characterised the factors and products of ligand replacements in the cobalt-III series so extensively that, when Nyholm, Brown and I took up the subject of mechanism some years ago<sup>2</sup>, our obvious course was to set out from the base-camp which he had established. It was necessary to pursue a kinetic study of the substitutions, and thereafter explore quantitatively the products formed with defined kinetics.

The first compound investigated was the optically active *cis*-form of dichloro-*bis*-ethylenediaminecobalt-III. It was substituted, with replacement of one chlorine atom, as shown in the equation below, by seven anionic substituting agents, here arranged in approximate order of decreasing nucleophilic power:



Water as solvent was avoided, because its high complexing power would have caused it to usurp the substituting function from all the more weakly nucleophilic anions. Methyl alcohol, which has no appreciable complexing power, and dissolves the reactants sufficiently, was the solvent employed. Kinetics were followed by

four methods, polarimetric, spectrophotometric, titrimetric, and radiochemical, each substitution being studied by all the methods conveniently applicable to it.

The results are schematically and qualitatively summarised in Figure 1, in which the substituting agents are arranged in the already given order of decreasing nucleophilic power. The first three reagents produced a second-order reaction, the absolute rate of which decreased strongly with the nucleophilic power of the reagent. A further argument, mentioned and developed below, to the effect that the attack of the reagent was on cobalt, allowed the conclusion to be drawn that bimolecular nucleophilic substitutions,  $S_N2$ , were here under observation:



For the last four reagents a first-order reaction was observed, the rates being independent of the concentration and nature of

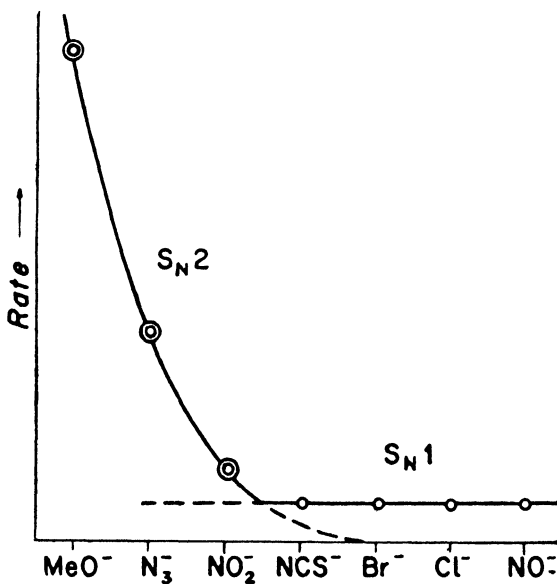
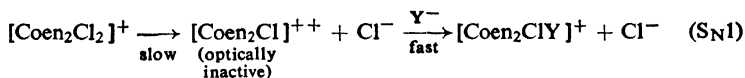


Figure 1

Rate of reaction of substitution of one chlorine atom of *cis*-form of dichloro-*bis*-ethylenediaminecobalt-III by various anionic substituting agents

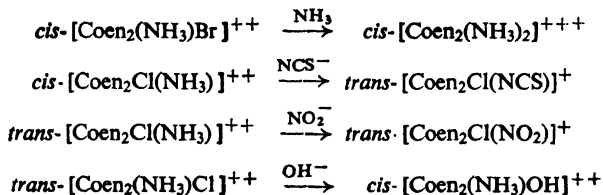
the substituting agent. In these substitutions, optical activity was lost completely, and at a rate which was identical with the common rate of the chemical changes. These reactions were therefore identified as unimolecular nucleophilic substitutions,  $S_N1$ , involving a non-asymmetric intermediate ion, formed by a preliminary rate-controlling heterolysis.



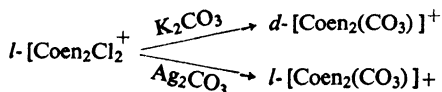
These reactions showed an accelerating inert-salt effect and a specific retardation by chloride ion, kinetic phenomena characteristic of the unimolecular mechanism<sup>3</sup>.

The schematic diagram in Figure 1 is closely similar to one given by Gleave, Hughes and myself<sup>4</sup> in 1935 in support of the case which was then being presented for a corresponding duplexity of mechanism in nucleophilic carbon substitution.

The existence of a problem in the stereochemical course of ligand replacements has long been appreciated. What Walden discovered for carbon substitutions in 1895, Werner disclosed for cobalt substitutions about 1910, namely, that stereo-change often, but not always, accompanies substitution<sup>1,3</sup>. Werner dealt largely with substitutions by Y in complexes of the type  $\text{CoR}_4\text{AX}$ , containing one replaceable ligand X and five non-replaced ligands, of which one, A, acted as a stereochemical reference point, with respect to which X, and after substitution Y, could be described as *cis* or *trans*; and in an examination of about 40 such substitutions, he obtained every possible type of stereochemical result: in different cases, *cis* gave *cis*, *cis* gave *trans*, *trans* gave *trans*, and *trans* gave *cis*, as in the following examples:



In 1934, the incidence in some conditions of stereo-change in cobalt substitutions was observed in another form. Before that time Werner and McCutcheon had converted the *l*-dichloro-*bis*-ethylenediaminecobalt-III ion with potassium carbonate into a *d*-carbonato-*bis*-ethylenediaminecobalt-III ion; and now, from the same *l*-dichloro-ion, Bailar and Auten, by changing the reagent to silver carbonate, obtained a *l*-carbonato-ion<sup>5</sup>:



This case was claimed as the first "Walden inversion" of inorganic chemistry, but such a description could be misleading, for firstly, it suggests a geometrical inversion of octahedral valencies, which is a very difficult concept, and secondly it diverts attention from the circumstance that *cis-trans* and D-L changes in octahedral substitutions are not as different as are some similarly described changes in carbon chemistry. For either type of change in the octahedral system can be reduced to what has been called an "edge displacement," as depicted in Figure 2.\* How we describe the change there shown depends, not on the groups Y, R, and X directly involved, but on the position of some unaffected group A

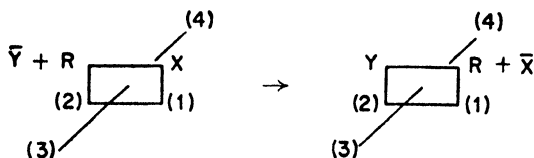


Figure 2.

\* "Displacement" means "shift", and refers to the change of place of R. Some authors use "displacement" as a synonym for "substitution", though a more accurate synonym (if one were needed) would be "replacement".

arbitrarily selected from among the unaffected groups as the stereochemical reference mark. If A is at (1), we shall call the change *cis* → *trans*, if at (2), *trans* → *cis*, and if at (3) or (4), either D → L or L → D. Yet the process of substitution is the same in all cases.

This is an illustration of the point that in octahedral substitution, the correlation between microchemical process and macrochemical observation is not as close as it is in tetrahedral substitution. In an organic substitution, an inversion is an inversion, whether we refer to the molecular process or to experimental samples of factor and product. In octahedral stereochemistry, however, the relations are more involved. Without going into the general geometrical theory, we may note three points. First, as mentioned already, any kind of observed stereo-change, *cis-trans* or *d-l*, can be referred to a molecular edge-displacement. Secondly, an edge-displacement, even with optically active compounds, does not necessarily produce observable stereo-change. For example, if in Figure 2 the groups (1) and (2), and likewise the groups (3) and (4), are superposable, either on the other, by a common rotation, then the product of an edge-displacement will show no sign at all of having passed through one, not even by its sign of rotation if it is optically active. Thirdly, areas of good correlation between microchemical process and macrochemical product exist, as illustrated for the form  $\text{CoR}_4\text{AX}$  in Table I. Thus a conversion *trans*-to-*cis* must have involved edge-displacement, but a conversion *cis*-to-*cis* might have done so. The basic reason is, of course, that there are four *cis* positions with respect to any reference position.

TABLE I.

*Stereochemical possibilities of the reaction  $Y + \text{CoR}_4\text{AX} \longrightarrow \text{CoR}_4\text{AY} + X$*

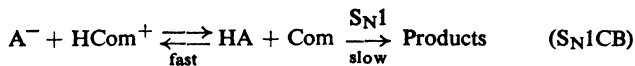
<i>Observation</i>	<i>Molecular Inference</i>
<i>cis</i> ⇌ <i>trans</i> D ⇌ L	} Edge-displacement
<i>cis</i> ⇌ <i>cis</i> D(L) ⇌ D(L)	
<i>trans</i> ⇌ <i>trans</i>	} Ambiguous
	} No edge-displacement

The first experiments<sup>2</sup> on the proportions in which stereoisomers are formed in kinetically defined conditions of substitution were made with two reactions of *l-cis*-dichloro-*bis*-ethylenediamine-cobalt-III having the kinetic characteristics of the unimolecular mechanism,  $S_N1$ . They were the reactions with chloride ion and with thiocyanate ion in methyl alcohol.

Analogy with  $S_N1$  carbon substitutions would not lead us to expect of this mechanism any particular stereochemical uniformity. The theory of the  $S_N1$  mechanism in this octahedral application, and the results of these experiments, are set out together in Figure 3. A primary rate-controlling heterolysis gives a short-lived, optically inactive, 5-covalent, intermediate ion. Whether this has trigonal-bipyramidal or square-pyramidal geometry is not yet settled, though there are reasons which incline one towards the former alternative. Whichever form it has, it takes up the substituting anion at comparable speeds in all the distinguishable positions among its five ligands, to give stereoisomeric substitution products in the proportions noted, which evidently depend on the constitutional details of the substituted complex.

Before coming to the stereochemistry of the second order substitutions with strongly nucleophilic reagents, we have to consider a possible mechanistic ambiguity. Second order kinetics are consistent with two mechanisms. The first is direct ligand replacement,  $S_N2$ . The second involves preliminary extraction of a ligand proton, one of the nitrogen-bound protons, to give a conjugate base of the original complex, the conjugate base then undergoing unimolecular loss, and eventual replacement of a ligand; this mechanism is commonly called unimolecular substitution in the conjugate base, and is labelled  $S_{N1CB}$ . It is a known mechanism: Brønsted established it long ago for substitution in aquo-complexes<sup>8</sup>, which, as acids of medium strength, can give their conjugate bases in large concentration. The present question is whether this mechanism is the effective one of the very much less acidic amino-complexes. Writing  $A^-$  for the attacking anion and  $HCom^+$  for the original complex, the mechanism may be formulated as follows:





Hydrogen exchange experiments show that, wherever the equilibrium may lie, the transference of nitrogen-bound protons in basic conditions is fast, and therefore, in mechanism  $S_N1CB$ , we have to think of the conjugate base "Com" as formed in pre-equilibrium, and the loss of a ligand from it as rate-controlling.

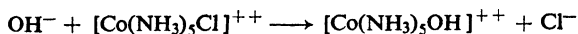
There has been quite an extensive discussion as to whether the second-order reactions of, for example, *cis*-dichloro-*bis*-ethylenediaminecobalt-III with strongly nucleophilic anions do indeed go by mechanism  $S_N2$ , as Brown, Nyholm and I originally suggested, or by mechanism  $S_N1CB$ , as Adamson, Basolo and Pearson prefer to think.

Before summarising the main points of evidence, let me clear away the irrelevancies which have been introduced by remarking that no conclusion can be reached by altering the constitution of the complex by changing the ligands or the metal and discussing the consequent changes in absolute rate. There are so many factors affecting rate, most of which cannot be relatively weighted, that it is always possible plausibly to rationalise observations of this character. I know of no such significant observations that cannot quite reasonably be discussed on the basis of mechanism  $S_N2$ . (For detailed support of this statement, see Appendix, p. 50)

However, real criteria emerge when we notice that mechanism  $S_N1CB$  starts with a pre-equilibrium, and that therefore rate must be proportional to the stationary concentration of the conjugate base written "Com" above. It follows, in the first place, that for different anions,  $A^-$ , rate should be strictly proportional to the basic strength of the anion. Now, Brown, Nyholm and I noticed that, for the second order substitution of *cis*-dichloro-*bis*-ethylenediaminecobalt-III, no such proportionality holds, not even within orders of magnitude. It is true that, as Basolo and Pearson subsequently pointed out, a neglected solvolytic disturbance affected some of the rate-constants on which this conclusion was originally based; but it did not change their orders of magnitude, and therefore the conclusion holds.

A second distinction arises inasmuch as rate by mechanism  $S_N1CB$  with a given anion  $A^-$  should be inversely proportional, quite accurately so in dilute solution, to the concentration of added acid  $HA$ . For the reactions of *cis*-dichloro-*bis*-ethylenediaminecobalt-III with azide ion and with acetate ion in methyl alcohol, Pearson, Henry and Basolo showed<sup>12</sup> that this was not true: once enough of the acid  $HA$  had been added to cut out the solvolytic disturbance, further added  $HA$  did not depress the rate of reaction of  $A^-$ , which remained accurately constant and of second order at suitably low ion concentrations. I must point out, because they did not, that these observations completely exclude a mechanism based on a pre-equilibrium proton transfer for these second order reactions.

We have a third criterion of mechanism in the kinetic hydrogen isotope effect. Adamson and Basolo examined this in the example of the second order reaction of hydroxide ion with chloropentamminecobalt-III in water<sup>14</sup>:



They showed that the rate drops to 0.6 of its value when the reagent and solvent are changed from  $OH^-$  in  $H_2O$  to  $OD^-$  in  $D_2O$ . Again I must point out, because the observers themselves did not, that if the mechanism really did depend on the pre-equilibrium proton transfer of mechanism  $S_N1CB$ , they should have observed an increased rate in the deuterated system,\* as in the classical example of the hydrolysis of diacetone-alcohol. The observed rate depression is consistent with a rate-controlling attack by hydroxide ion, as required by mechanism  $S_N2$ .\*\*

\* It is improbable that the reduction of rate could be due to an over-riding secondary isotope effect of deuteration of the amino-hydrogen atoms<sup>15</sup>.

\*\* In spite of their consistent objections to the  $S_N2$  mechanism in second-order octahedral substitutions by powerful nucleophiles, and the invariable absence of suitable comment whenever they themselves obtain results supporting that mechanism, Basolo and Pearson have actually suggested it<sup>9</sup> in what would seem to be the most unlikely case of all, by proposing that a preliminary  $S_N2$  substitution by an attacking methyl alcohol molecule may underlie the already described first-order substitution in *l-cis*-dichloro-*bis*-ethylenediaminecobalt-III by weakly nucleophilic anions in solvent methyl alcohol. It is sometimes said that one should at least be either consistent or inconsistent, and not switch about from one to the other.

The stereochemical course of several second order reactions of hydroxide ions with *bis*-ethylenediaminecobalt-III complexes in water has been examined by Asperger, Nyholm, Tobe and myself<sup>8,16,17</sup>. The examples, all of the form



involve a unique preserved ligand A, which was NCS, NH<sub>3</sub> or NO<sub>2</sub>, and a replaced ligand X, which was Cl or Br. The rates and product ratios are given in Table II. When translating observed stereo-changes into molecular terms, we have to remember that, whilst an observed *trans*-to-*cis* conversion accurately measures the amount of edge-displacement, an observed *cis*-to-*trans* conversion measures only a lower limit to the edge-displacement which must have occurred on the molecular scale. The reason is, as we have seen, that a *cis*-to-*cis* conversion could result from substitution either without or with an edge-displacement of one of the ligands.

The most obvious conclusion to be drawn from Table II is that S<sub>N</sub>2 substitutions at octahedral cobalt do not involve quanti-

TABLE II  
Rates ( $k_2$  in  $s^{-1} M^{-1}$ ) and product ratios of reaction  
 $\text{OH}^- + [\text{Coen}_2\text{AX}]^+ \longrightarrow [\text{Coen}_2\text{AOH}]^+ + \text{X}^-$  in water at 0°

A	X	$k_2$	Products	
			<i>Cis</i> -factors	
			% <i>Trans</i>	
NCS	Cl	1.40	19*	} Lower limits to edge-displ.
NH <sub>3</sub>	Cl	0.50	16	
NH <sub>3</sub>	Br	0.32	15	
NO <sub>2</sub>	Cl	0.032	34	
			<i>Trans</i> -factors	
			% <i>Cis</i>	
NCS	Cl	0.34	76	} Actual % edge-displ.
NCS	Br	1.95	81	
NH <sub>3</sub>	Cl	1.25	76	
NO <sub>2</sub>	Cl	0.080	6	

\* Since confirmed by Dr. Margaret Baldwin, who, using optically active *l-cis*-[Coen<sub>2</sub>NCsCl], has shown further that the 81% of *cis*-aquo-product contains 24% of the *d-cis*- and 57% of the *l-cis*-isomers<sup>18</sup>. Thus there is at least 43% of edge-displacement in this substitution. For all four *cis*-factors, the proportions of demonstrable stereo-change lie between 40% and 54%.

tative stereochemical change, as do  $S_N2$  substitutions at tetrahedral carbon. The  $S_N2$  cobalt substitutions do, however, involve considerable and often preponderating amounts of edge-displacement, how much depending on an orienting effect of groups already present. The nitro-group orients very differently from the other groups, and the rates show that it acts as it does mainly by selective inhibition. Now the nitro-group is unique among the orienting groups in its constitutional ability conjugatively to absorb unshared electrons from the cobalt  $3d$  shell; and it is a plausible idea that displacement of this shell towards the nitro-group selectively exposes the other side of the cobalt atom to attack by the anionic reagent. The same polarisation of the cobalt atom will oppose separation of the out-going chloride ion; and since, in our  $S_N2$  mechanism, this is an essential part of the rate-controlling process, we can understand the reduced rates shown by the nitro-complexes.

This implies that, just as with  $S_N2$  substitutions at tetrahedral carbon, so with these  $S_N2$  substitutions by anions at octahedral cobalt, bond fission and bond formation are truly synchronous. To put it another way, just as for the  $S_N2$  carbon substitutions, the valency, that is, the number of carbon orbitals used, is not raised much above four, even when five groups are being bound in the transition state, so in these  $S_N2$  substitutions by anions at cobalt, the number of cobalt orbitals used is not raised much above six, even when seven groups are being bound in the transition state. This conclusion, which means that the outer,  $4d$ , orbitals of cobalt do not to any marked extent provide a site for the attachment of the substituting agent, may well apply only to substitution by more or less electropositive ligands, such as most anions. It may not, as we shall see later, apply to aquation, in which the strongly electronegative water ligand is being bound.

The fact that orientation can be changed so easily by pre-existing ligands in bimolecular substitutions must mean that the transition states, shown in Figure 4, for substitution without and with edge-displacement have energies which are the same to within a very few kilocalories, although the transition state (II) leading to edge-

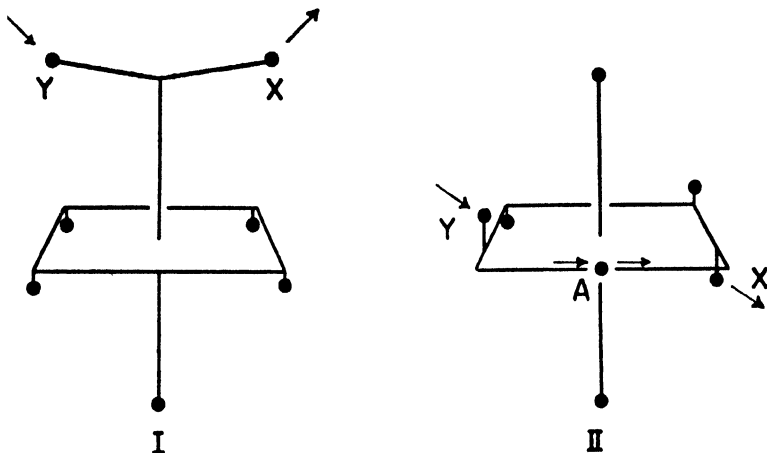


Figure 4

Transition states for substitution without (I) and with (II) edge-displacement

displacement seems to be the more stable, except in the presence of a strong conjugative disturbance, such as that attributed to the nitro-ligand.

I now wish to discuss aquation. This problem in the chemistry of octahedral complexes is analogous to that of solvolysis in organic chemistry, and, like the latter problem, involves the difficulty that, as approximate first order kinetics are inevitable, kinetic order (except in a refined study of deviations), gives no guide to mechanism. If organic chemical experience may be taken as a guide, the most hopeful way of reaching definitive conclusions about mechanism in aquation would be to study rates and products when aquation runs in competition with anion substitutions; but this has not yet been done. In the meantime the known facts concerning rates and products of aquations running alone lead to tentative suggestions regarding mechanism.

The longest comparable series of available rates relate to the replacement of chlorine by water in the aquation of *cis*- and *trans*-complexes of the form  $[\text{Coen}_2\text{ACl}]^+$ , wherein the variable group A covers the series OH, Cl, NCS,  $\text{NH}_3^+$ ,  $\text{OH}_2^+$ ,  $\text{NO}_2$ . Consistent, but much more fragmentary, data are available for series

in which bromine replaces chlorine in the complex, and in which tetra-ammine replaces *bis*-ethylenediamine. If we assume that, as in organic nucleophilic substitutions, conjugative polar effects are kinetically the most important, we should place OH, followed by Cl, at one end of the ligand series, and NO<sub>2</sub> at the other end, filling in the inductively-acting ligands in order of electronegativity, as has been done above. We then find that, along the series, the aquation rate at first falls and then rises, as shown in Table III. The incomplete figures given there for product-composition will be referred to later.

When the theory of duality of mechanism in nucleophilic carbon substitutions was advanced in 1935, the main evidence then supporting the idea was expressed in two schematic diagrams. One showed the variation of substitution rate with progressive changes in the nucleophilic power of the reagent as two crossing curves whose intersection represented a change of mechanism. An exactly similar diagram for cobalt substitutions has already been shown in Figure 1. The other diagram of 1935 for carbon substitutions

TABLE III  
*Aquation rates and product-proportions at 25° for*  
 $H_2O + [Coen_2ACl]^+ \longrightarrow [Coen_2AOH_2]^{++} + Cl^-$

A				
<i>Cis</i> -chloro	$10^7 k_1$ (sec <sup>-1</sup> )	% <i>Trans</i> -aquo		Ref.
OH	130,000	—	} Lower limits to edge displ.	19
Cl	1,250*	—		19
NCS	1.14	0		18
NH <sub>3</sub> <sup>+</sup>	4.5	—		17
OH <sub>2</sub> <sup>+</sup>	150	0		20
NO <sub>2</sub>	1,120	0		8
<i>Trans</i> -chloro		% <i>Cis</i> -aquo		
OH	14,000	—	} Actual % edge displ.	19
Cl	160*	—		19
NCS	0.42	43**		16
NH <sub>3</sub> <sup>+</sup>	3.3	—		17
NO <sub>2</sub>	8,900	0		8

\* Half the rate measured for the dichloro-complex.

\*\* Figure for the corresponding *trans*-bromo-complex.

expressed rate changes with progressive polar changes in the influencing substituents, again as two curves crossing at a change of mechanism. Although it has not the status of a proof, it does seem significant that the variations of rate with the influencing groups in the cobalt aquations, can, for either of the series tabulated, be represented schematically in an identical form, carrying the same suggestion of a change of mechanism where the two curves cross, as shown in Figure 5.

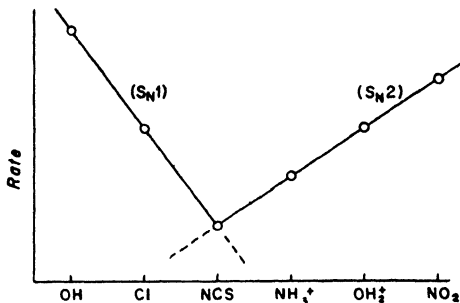


Figure 5

Variations of rate with influencing groups in cobalt aquations

The fall in rate by the presumed  $S_N1$  mechanism as electron supply by the variable ligand diminishes is easy to understand; for the expelled halogen carries away electrons, and no compensating importation of electrons by entering water occurs in the rate-controlling stage of this mechanism.

However, the rise in rate by the presumed  $S_N2$  mechanism with increasing electron-withdrawal by the variable ligand requires discussion. We do not find a rule of this nature applying to  $S_N2$  substitutions by reagent anions. That we do find it in the  $S_N2$  aquations must mean that, when the transition state of bimolecular aquation is reached, the binding of water has made more progress than has the liberation of the halide ion. Put another way, our conclusion is that the valency of cobalt, that is, the number of its orbitals in use, rises to well above six in the transition states of  $S_N2$  aquations. This is in contrast to our previous conclu-

sion that, in  $S_N2$  substitutions by reagent anions, the valency of cobalt at no time rises much above six. The seventh orbital which the entering water molecule appears to have the power considerably to implicate must be a  $4d$  orbital.

The inference that water may enter by the use of a  $4d$  cobalt orbital, whilst anions cannot do so, can readily be understood on the basis of Craig's theory of the contraction induced in outer  $d$ -orbitals by electronegative ligands<sup>21</sup>. Anions are initially electro-positive, becoming less so as they are bound. Outer  $d$ -orbitals are not useful for binding such ligands, because of the great spread and low amplitude of the orbitals: they provide plenty of overlap, but scarcely any overlap integral over the limited effective volume of the ligand orbital. However, the water molecule is a strongly electronegative ligand. Such a ligand has the power to draw back the naturally diffuse  $d$ -orbital, and to concentrate it on the ligand, thus providing an adequate amplitude in the right region to produce an adequate binding energy.

The difference of binding mechanism which should result from this difference in the binding energy of an anion and of a water molecule by the use of a  $4d$  orbital is made the more certain when we consider the difference in the expenditure of energy necessary to accomplish the solvation changes that require to be negotiated in order to secure such  $4d$ -binding by these two types of reagent. To secure the binding of an anion by the cobalt cation, it is necessary to supply a large ion-desolvation energy, because of the net neutralisation of charge which accompanies binding. But to secure the binding of water, it is necessary to supply essentially only the much smaller heat of evaporation of a water molecule. Thus, where outer  $d$ -orbital binding liberates hardly any energy, as in binding anions, much more than it liberates is required to overcome solvation forces; and where it liberates energy plentifully, as in the binding of water, solvation forces make no great energy demand.\*

\* A more quantitative discussion would take account of the difference of coulombic energy of binding of an anion and of water. This will compensate for a part of the solvation energy difference, but, in such a polar solvent as water, only a part.

Thus, for this double reason, it seems a very plausible assumption that ligand binding initially runs ahead of ligand loss, or, in other words, that the cobalt valency temporarily rises during binding, much more in  $S_N2$  substitution by reagent water than in  $S_N2$  substitution by reagent anions. This is the conclusion we require in order to understand the rate relations.

The few reliable data which are available for the proportions in which isomeric aquation products are formed are entered in Table III. They indicate (a little uncertainly because there are so few figures) that very appreciable amounts of edge-displacement arise in examples belonging to that part of the ligand series in which the  $S_N1$  mechanism is, or might be, in operation; but that no evidence of edge-displacement appears in examples belonging to that part of the series for which an exclusive  $S_N2$  mechanism is suggested.

This gives some slight further support to the idea of two mechanisms. The  $S_N1$  mechanism is unlikely to be stereochemically specific, although we cannot assume that the 5-coordinated ion, first formed in this mechanism by ligand loss, would always last long enough in so reactive a medium as water to attain its equilibrium configuration. Indeed, there is evidence to the contrary. Mathieu<sup>22</sup> found that the aquation of optically active *cis*-dichloro-*bis*-ethylenediaminecobalt-III, a reaction for which we are tempted to assume an  $S_N1$  mechanism, proceeds with a fairly high retention of optical activity, in the sense probably indicating predominantly retained configuration. Here, if ligand dissociation is in the lead, the water uptake must follow it almost immediately—a type of situation with which we are also familiar in organic chemistry. It contrasts with the already described situation found for substitution of the same optically active *cis*-dichloro-complex with low concentrations of weak substituting agents in the much less reactive solvent methyl alcohol. Here, the rate of loss of optical activity during substitution was equal to the common first-order rate of all the substitutions, and the products, as first formed, were optically inactive. In these conditions, the intermediate ion, formed by dissociation in the  $S_N1$  mechanism, has plenty of time

to lose optical activity, and settle down into its symmetrical configuration, before it enters into combination with the substituting agent.

Mathieu also found that optically active *cis*-chloroisothiocyanato-*bis*-ethylenediaminecobalt-III is aquated with an apparently complete retention of optical activity and configuration. However, it is difficult to know how to classify this aquation on the evidence of rate, and it is possible that we should classify it with those aquations to which we tentatively assign the  $S_N2$  mechanism.

To all observation, these latter aquations retain configuration completely, and in the theoretically diagnostic example of the *trans*-chloronitro-complex we can be sure that no edge-displacement at all occurs. If this is a definite stereochemical rule, namely, that aquations at least, and perhaps other substitutions by molecular reagents, when proceeding by the  $S_N2$  mechanism, do so with complete microchemical retention of configuration, then it is the first uncompromising stereochemical rule that we have encountered in the field of octahedral substitutions; and so it may be worth while to consider the lines on which it might be rationalised.

Although we should not assume that an  $S_N2$  ligand replacement goes in steps, it shortens the description of a picture of the process to neglect its essential continuity, and to describe the main changes as if they occurred in successive steps without overlap. In order to account for the rate relations we want to assume that binding of the strongly electronegative ligand, water, is initiated largely in the  $4d$  shell. In this initial "step" of binding there can be no strong directional specificity, since, apart from perturbing effects of the relatively compact group of interior ligands, any normalised linear combination of these wholly available  $4d$  orbitals is as good as any other. The water ligand can therefore be pictured as moving over the  $4d$  shell until it finds a position in which the binding process can conveniently be continued. We can now take as the next "step" of binding, a progressive exchange of cobalt orbitals between the entering water and the leaving anion. This exchange can occur most easily when the involved ligands

are adjacent. The effect of it is to bring the water ligand into the usual bonding shell of the cobalt atom, and to drive the departing anion into the outer shell. Here, in the third so-called "step" of the substitution, the anion is captured by the solvent, solvated eventually all round, and so is carried away. We see in the need to have the exchanging ligands adjacent in this form of substitution a reason why it should lead to retention of configuration.

In the study of mechanism in nucleophilic substitution, outside the well-explored field of substitution at carbon, more attention has so far been paid to substitution at cobalt than at any other element, though investigations on mechanism in substitutions at several other elements, silicon and platinum, for example, have been begun. Yet it must be confessed that the first five years of published work consciously directed to the disclosure of mechanism in substitution at octahedral cobalt by the correlated study of kinetics and products has yielded little in the way of fully proved conclusions. It has yielded suggestions which together form the outlines, even if rather shadowy outlines, of a mechanistic pattern. In fact, the present position seems very like that which had been reached in the study of mechanism in substitution at tetrahedral carbon in 1935, when also a mechanistic pattern could be adumbrated, which hardly anyone then accepted, because the contemporary evidence was suggestive rather than compelling; however in the next five years the evidence in that case was greatly strengthened. Perhaps this problem of mechanism in octahedral cobalt substitutions, now that it has reached a stage at which a tentative mechanistic pattern can be delineated, will also enter on a period of more consolidated and critical demonstration. But it is an almost essential condition for doing such work that one must believe in the pattern, sufficiently at least to accept its guidance in designing really critical experiments. I do not dare to hope that the interpretations I have suggested are correct in their entirety. But I do believe them sufficiently to think that they are more likely to be modified than scrapped.

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## CHAPTER 2

### ELECTROPHILIC SUBSTITUTION AT NITROGEN AND OXYGEN

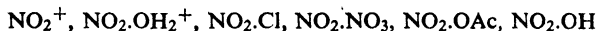
Electrophilic substitution has hitherto been studied mainly in the form of substitution at aromatic carbon by such electron-seeking reagents as nitrating, nitrosating, halogenating, sulphonating, and diazo-coupling reagents. These reagents attack the  $\pi$ -electrons, which are carbon  $2p$  electrons acting cooperatively because they share a common nodal plane through the atomic nuclei. We know that the unshared  $2p$  electrons of trivalent nitrogen or of bivalent oxygen can join in with such a cooperative, or "conjugated", system. Therefore we should expect that the non-bonding  $2p$  electrons of nitrogen and oxygen would share with the  $2p$  electrons of unsaturated carbon the property of vulnerability to electrophilic substituting agents.

Nitration has occupied such a leading part in the study of electrophilic aromatic substitution that it is natural to take it as a first example of electrophilic substitution at nitrogen and oxygen. Let us in preparation recall what is known of the mechanism of nitration at carbon.

In general, electrophilic substituting agents occur in families: a given group  $X$  is introduced to the electrons of the substrate either by an entity which is the group itself less one electron,  $X^+$ , or by some ion or molecule  $X-Y$  so constituted that  $Y$  tends to split off with its bonding electrons, thereby leaving  $X$  to be held by the electrons of the substrate. Of this family of "carriers" of  $X$ , the specifically most active will be the  $Y$ -free entity  $X^+$ , whilst the specific activity of carriers  $X-Y$  will depend on how easily  $Y^-$  splits off. Of course, the practical importance of a carrier depends jointly on its specific activity and how much of it is present; and, as these two factors are countervailing when, as often, the more active carriers are formed only in low concentration, one can ob-

serve a considerable distribution of practical effectiveness among the carriers of a family.

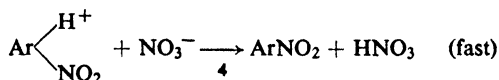
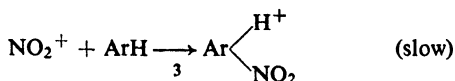
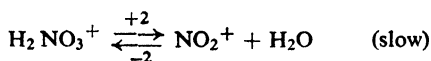
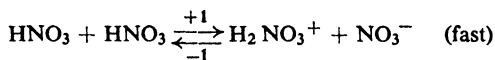
Now, nitration has proved to be atypical in this respect. We can consider a series of conceivable nitrating agents, such as



here arranged in an approximate order of expected diminishing specific activity. But experiment shows the mechanism of nitration to be dominated by the formation and reactions of one carrier, the nitronium ion.

Even the nitric acid acidium ion,  $\text{H}_2\text{NO}_3^+$ , which is certainly produced freely, has never been shown to nitrate as such: it appears to act simply as a reservoir of nitronium ions. As far as we know, that is true of all the other theoretical carriers, with the exception that  $\text{N}_2\text{O}_5$  has been shown partly to act as such in a very limited range of conditions, though it too acts mainly as a source of nitronium ions.

From nitric acid, the nitronium ion is formed by way of the nitric acidium ion, and therefore in two steps, of which the first, the proton transfer, is always fast. The nitronium ion acts as the aromatic molecule by adding first, and so the substitution proceeds in two steps, of which the second, the final proton loss, is always fast:

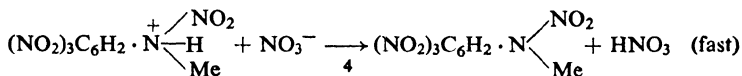
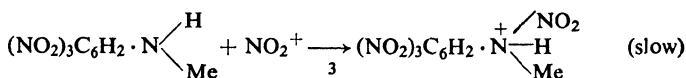
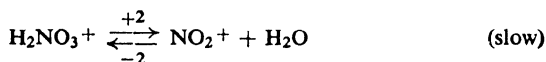
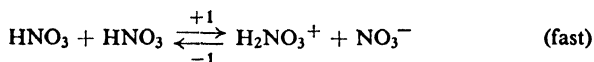


The kinetic form of nitration depends on whether step 2 or step 3 is rate-controlling. With a sufficiently reactive aromatic compound in a not too aqueous medium, for example, when benzene is nitrated by nitric acid in nitromethane as solvent, step (3) prevails over step (-2), as a means of consumption of formed nitronium ion, and so the measured rate of nitration is that of the production of nitronium ion in step (+2). This, in turn, is proportional to the stationary concentration of nitric acidium ion. And so, if we add a very strong acid, such as sulphuric acid, to take the place of the proton-donating nitric acid molecule in step (1), the rate will increase in direct proportion to the concentration of the added strong acid; and likewise, if we add nitrate ions, the rate will become diminished, showing inverse proportionality to the concentration of nitrate ions. But, provided the aromatic compound is of sufficient reactivity, and is in sufficient concentration, to pick up all the formed nitronium ion, the nitration rate will depend neither on the nature nor on the concentration of the aromatic compound. We describe this situation by saying that nitration is of zero-th order in the substrate.

The other limiting case arises when the aromatic compound is so unreactive, or the medium so aqueous, that step (-2) prevails over step (3) in the consumption of formed nitronium ion. The nitronium ion is then built up to a stationary concentration, from which the aromatic compound draws its supply relatively slowly, and so without seriously depleting the reservoir of that material. The rate of nitration will still increase proportionally to the concentration of an added strong acid, and decrease with inverse proportionality to added nitrate ions. But now it will be proportional to the concentration of aromatic compound, and the rate constant will differ from one compound to another, according to their reactivities. This form of nitration is described as being of first order in the substrate.

Hughes, Blackall and Pearson have studied the kinetics of N-nitration<sup>23</sup> in the example, among others, of the conversion of methyl picramide to "tetryl". They have used the conditions in which some of the most critical of the kinetic experiments

on aromatic nitration were done, namely, nitration by a 2-4 M excess of nitric acid in solvent nitromethane. The N-nitration of methyl picramide is quantitative in these conditions. Also, the nitrogen atom is not appreciably protonated at this level of acidity, and so what might have been a tiresome complication in a kinetic study does not arise. The results are quite sharp, and point to the conclusion that the mechanism of this N-nitration is exactly the same as the nitronium-ion mechanism of aromatic nitration:

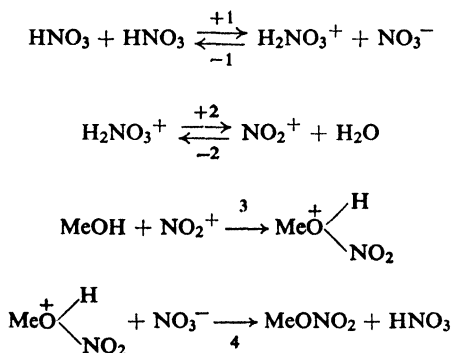


The rates were increased proportionally to the concentration of an added strong acid, actually sulphuric acid, and decreased by nitrate ions with an inverse proportionality to their concentration. The rate was, however, independent of the concentration of methyl picramide, and was absolutely identical with what it would have been if the compound nitrated had been benzene or toluene, or any aromatic compound reactive enough to nitrate with kinetics of zero-th order form. This shows that methyl picramide traps almost the whole of the formed nitronium ion, which is not allowed appreciably to recombine with water, and that therefore the measured rate is just the rate of formation of nitronium ion in the step labelled (+2).

By adding a somewhat large amount of water initially, e.g. 1 M, it can be arranged that most of the formed nitronium ion does

recombine with water. The nitronium ion is then produced in a stationary concentration, from which the methyl picramide taps off its requirements, without sensibly depleting the reservoir. The rate now becomes proportional to the concentration of methyl picramide, and the rate-constant a reflexion of the reactivity of its unshared nitrogen electrons. Working in this way, one can discover that the nitrogen electrons of methyl picramide are about  $3/2$  times more reactive towards nitronium ion than are the unsaturation electrons of benzene, and about 17 times less reactive than are the aromatic electrons of toluene.

The same workers have examined the kinetics in similar conditions of the reaction usually described as the esterification of alcohols by nitric acid to give alkyl nitrates. The reaction is found to be an O-nitration by nitronium ion, following the same mechanism as applies to C-nitration and N-nitration. It is formulated for methyl alcohol below:



Most simple alcohols, including methyl alcohol, are sufficiently reactive to trap practically all the formed nitronium ion provided that we work in a more or less anhydrous solvent, such as nitromethane. The reaction is accelerated proportionally to the concentration of an added strong acid, and retarded by added nitrate ions with inverse proportionality of rate to their concentration. But the rate is of zero-th order in the substrate, that is, it is quite independent of the concentration of the alcohol, and is the same

for different alcohols, and also the same for the alcohols as for an aromatic hydrocarbon, or for methyl picramide. The figures in Table IV will illustrate this.

The figures are zero-th order rate constants for *mono*-nitration. This is a significant point for the polyhydric alcohols. The two hydroxyl groups of ethylene glycol and of trimethylene glycol, and the two  $\alpha$ -hydroxyl groups (but only these two) of glycerol, are all reactive enough to be nitrated in zero-th order form. They are therefore nitrated independently of one another. It follows that if we measure the rate constant for the formation of ethylene dinitrate from ethylene glycol, it will be one-half of the figure listed, because one has to wait for the formation of two nitronium ions in order to secure the complete conversion of one ethylene glycol molecule. Similarly the zero-th order rate of nitration of glycerol is one-half of the figure listed, but that again is because this is a rate of dinitration.

TABLE IV  
Zero-th order rate-constants for mononitration in nitromethane at 25°  
( $10^5 k_0$  with  $k_0$  in  $M s^{-1}$ )

	[HNO <sub>3</sub> ]		
	2.0	2.25	2.5
<i>C-nitration</i>			
Benzene	—	—	1.66
Toluene	0.688	—	1.72
Ethylbenzene	—	—	1.70
<i>N-nitration</i>			
Methyl picramide	0.675	—	—
<i>O-nitration</i>			
Methyl alcohol	0.680	1.08	1.69
<i>p</i> -Nitrobenzyl alcohol	—	1.00	—
Ethane-1:2-diol	—	—	1.66
Propane-1:3-diol	—	—	1.68
Glycerol ( $\alpha$ and $\alpha'$ only)	—	—	1.76

It is interesting to compare the reactivity towards nitronium ion of the oxygen electrons of, say, methyl alcohol, with that of the nitrogen electrons of methyl picramide. That can be done by the technique of adding so much water — about 1 M is necessary —

to the medium that nearly all the formed nitronium ions are trapped by water, and only an occasional one is caught by the substance undergoing nitration. Then the rate becomes proportional to the concentration of the substance, and also dependent on its intrinsic reactivity: in other words, the kinetics pass over from zero-th order to first order form. It is found that methyl alcohol reacts with nitronium ion about 5/4 times faster than toluene does. We can set up a scale of kinetic reactivity of the compounds as follows:

Benzene	Methyl picramide	Toluene	Methyl alcohol
1	1.5	25	31

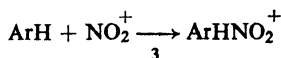
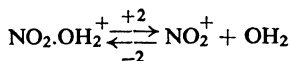
Not all alcohols are reactive enough to show zero-th order kinetics on nitration by nitric acid in an initially dry solvent, such as nitromethane. Neopentyl alcohol, which shows marked steric retardation in many of its reactions, is nitrated relatively slowly and with approximate first order kinetics, in these conditions. This alcohol captures only a small fraction of the formed nitronium ions, most of which recombine with the water along with which they are produced. Exactly the same is true for nitration of the  $\beta$ -hydroxyl group in glycerol *aa'*-dinitrate. When glycerol is trinitrated, the first two nitro-groups enter the  $\alpha$ -positions with zero-th order kinetics, just as fast as nitronium ions can be supplied; and then, when that is over, the third nitro-group enters the  $\beta$ -position much more slowly, and with first order kinetics.

The most fundamental case of O-nitration is nitration of water. The product is nitric acid, and so an isotopic label, originally distinguishing the oxygen of water, appears in the formed nitric acid. This reaction has been studied by Bunton, Halevi and Llewellyn by the use of  $O^{18}$ -water<sup>24</sup>. They showed that water and nitric acid, in aqueous nitric acid, undergo oxygen exchange at a rate which increases, just as rate of aromatic nitration does, as a very steep function of the concentration of nitric acid. The oxygen-exchange rate passed through the range of conveniently measurable values in the neighbourhood of a composition of 40 mols. % nitric acid to 60 mols. % water. These workers solved the problem of the mechanism of the oxygen exchange by com-

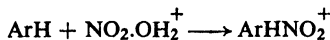
parison of its absolute rate with that of aromatic nitration under the same conditions; but in order to obtain a conclusion from such a comparison, they had first to solve the problem of the mechanism of aromatic nitration in aqueous solution; for that had not previously been accomplished successfully.

In order to appreciate the problem, let us look again at the nitronium ion mechanism for aromatic nitration. In restating this, as is done below, we can omit the now familiar initial and final fast proton transfers and reproduce only the two central steps, which embody the distinctive characteristics of the mechanism. Now, we can look at these two steps in the following alternative way. Instead of regarding them as describing an electrophilic nitration of the aromatic molecule, we can consider them as delineating a nucleophilic substitution by the aromatic molecule, acting as substituting agent, in the nitric acidium ion, regarded as substrate. Looked at in this way, the mechanism is that of an  $S_N1$  substitution, because the nitric acidium ion has first to undergo a heterolytic dissociation, which can be rate-controlling. There is, however, the obviously possible alternative of an  $S_N2$  substitution by the aromatic molecule in the nitric acidium ion. If we think of this in the more conventional way, it amounts to an aromatic nitration by the nitric acidium ion directly, without preliminary heterolytic dissociation. The crux of the mechanistic problem is to distinguish between these two possibilities:

(a) Nitration of ArH by  $\text{NO}_2^+ \equiv S_N1$  by ArH in  $\text{H}_2\text{NO}_3^+$



(b) Nitration of ArH by  $\text{H}_2\text{NO}_3^+ \equiv S_N2$  by ArH in  $\text{H}_2\text{NO}_3^+$



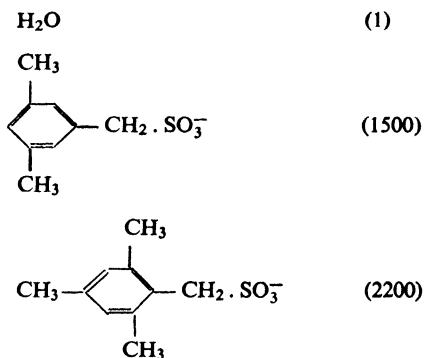
The first of these mechanisms will be proved to the exclusion of the second, if we can trap the intermediate, the nitronium ion which the first alone provides; and in particular if we can trap it so completely by the aromatic compound that the rate of sub-

stitution becomes independent of the aromatic compound, being given, as in  $S_N1$  mechanisms generally, by the rate of the dissociative process, the step here labelled (+2). This type of demonstration was frequently given in the early days of the study of the mechanism of aromatic nitration, but always for nitration in more or less dry solvents, such as nitromethane or acetic acid. When nitration is actually going on in such solvents, the concentration of water present is of the same order of magnitude as the concentration of the compound undergoing nitration. Therefore in order to secure that the aromatic compound captures nearly all the formed nitronium ion, we merely have to pick a compound—benzene is itself just adequate—say, 10 to 20 times faster-reacting than is water towards the nitronium ion. The problem of providing such a demonstration when water is the solvent, or main component, of a nitration solution is much more difficult; for then, one is restricted not only to water-soluble aromatic compounds, but also to those which are thousands of times more reactive than water towards nitronium ion, in order to secure that they, in kinetic concentrations, can snatch the nitronium ions away from so much water.

Bunton and Halevi solved this problem for nitration by mixtures of about 40 mols. % of nitric acid and 60 mols. % of water with the aid of certain sodium arylalkanesulphonates. In sufficiently low concentration these sulphonates underwent nitration in first order form, a result which in itself does not distinguish one mechanism from the other. But on increasing the concentrations of the sulphonates, the nitrations of the more reactive of them went over, not quite completely, but nearly completely, to zero-th order form; rate had become almost independent of the nature and concentration of the aromatic compound. This proves that aromatic nitration, even in excess of water, takes place by way of the nitronium ion. That in itself was a new and significant, and indeed rather unexpected, demonstration.

Bunton and Halevi now had a figure for the rate of formation of nitronium ion, in the dissociative process labelled (+2) above, for these aqueous conditions. For they had measured the rate at

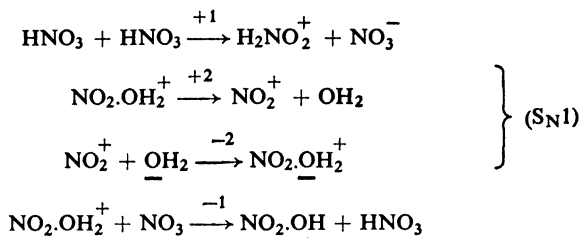
which they could trap nitronium ion by the most reactive of their sulphonates: this gave a moderately close lower limit. But furthermore, they could estimate a correction for incompleteness of trapping by employing the first order rates obtained at low concentrations, and noting the concentrations at which changes of kinetic order occurred, so assessing the competing powers of their sulphonates, against water, for nitronium ion. Their most reactive sulphonates were the mesitylene- $\alpha$ -sulphonate and the isodurene-2 $\alpha$ -sulphonate, and it was estimated that these compounds react 1500 and 2200 times, respectively, faster than water with the nitronium ion:



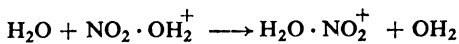
It was with these two sulphonates that they were able to trap some 80–90% of the formed nitronium ion, and so to reach, after correction as explained, quite a good estimate of the rate of formation of nitronium ion in these aqueous solutions.

The use that they made of this information can be understood as follows. For the nitration of water, we have, at the outset, the same fundamental mechanistic ambiguity. If we rewrite the nitronium ion mechanism for nitration, leaving out the steps involving the compound nitrated, but otherwise separating retrograde steps from forward steps, we find that the retrograde step labelled (–2) takes the exact place of the nitration step previously labelled (3), and that the retrograde step (–1) similarly takes the place of the previous nitration step (4). The mechanism is thus the same as before, except that now the compound being nitrated

is water. It is nitrated by the nitronium ion. Alternatively expressed, the nitric acidium ion undergoes an  $S_N1$  substitution with water as the substituting agent:



This is one possibility. The other is that water is being nitrated by the nitric acidium ion. We can re-express this by stating that the nitric acidium ion is undergoing an  $S_N2$  substitution with water as the substituting agent. We then have to replace the two middle steps of the previous scheme by a single step, as follows:



Now whatever the mechanism might be, Bunton and Halevi knew the rate of the complete sequence of changes, because that was the rate at which an oxygen-isotopic label, originally in the water (as indicated by the underlines) appeared in the nitric acid. If the mechanism were the nitronium ion, or  $S_N1$ , mechanism, then, since the nitronium ion is trapped wholly by water, the rate of the overall sequence of changes is the rate of formation of nitronium ion by the dissociation process (+2). Bunton and Halevi knew that rate because it was given by the rate of nitration of their reactive sulphonates. On the other hand, if the mechanism of water nitration were the nitric acidium ion, or  $S_N2$ , mechanism, then there should be no relation between its rate, as measured by oxygen exchange, and the rate of the aromatic nitrations.

Bunton, Halevi and Llewellyn's results are set out comparatively in Table V. The third column of figures are zero-th order nitration rates of mesitylene- and isodurene-sulphonates, as observed. In the next column, these rates are corrected for incompleteness

of trapping of the nitronium ion by the concentrations of the sulphonates actually used. These corrected nitration rates are to be compared with the isotopic exchange rates of oxygen between water and nitric acid, in the aqueous nitric acid solutions used, as given in the last column. The rates are the same to within the observational error. This established the nitronium ion mechanism for the nitration of water.

TABLE V

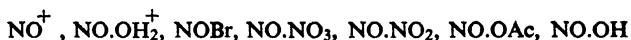
*Zero-th order rates of aromatic nitration and rates of oxygen exchange between nitric acid and water in aqueous nitric acid at 0°*  
( $10^4k_0$ , with  $k_0$  in mols %/sec)

ArH	[HNO <sub>3</sub> ] mols %	[ArH] mols %	Nitration		Exchange
			Obs.	Corr.	
M	39.02	0.23	1.81	2.12	2.16
M	38.89	0.32	1.47	1.66	1.66
D	39.37	0.27	1.60	1.76	1.93
D	37.39	0.29	1.09	1.19	1.26

(M = mesitylene- $\alpha$ -sulphonate; D = isodurene-2 $\alpha$ -sulphonate)

It is a striking general feature of nitration, whatever the substrate, that the conjugate acid of nitric acid always acts by dissociation, or, as we may say, undergoes itself an S<sub>N</sub>1 substitution. The result is that the actual carrier of the nitro-group is practically always the nitronium ion, whilst the other members of the theoretical family of nitro-carriers scarcely ever appear on the scene.

We find a strongly contrasting situation in the subject of nitrosation, to which I now turn. Again we have to contemplate a theoretical family of carriers of the substituent. The most active specifically will be the nitroso-group itself, less one electron, the so-called nitrosonium ion. From this we can in theory construct other, progressively less active, carriers, by combining it with molecular anionic nucleophiles of progressively increasing strength, that is, decreasing tendency to break away and exist separately. The following list of nitrosating agents is in an expected approximate order of decreasing specific activity:



Now, of course, the first of the more active carriers to be produced

in nitrosating conditions is always the one that can be formed from supplied nitrous acid by the instantaneous process of proton-transfer: it is its conjugate acid, the nitrous acidium ion. What has been found is that this conjugate acid, unlike the nitric acidium ion, has no great tendency to dissociate in an  $S_N1$ -like manner. The result is that the nitrosonium ion, although it can be produced, and, if formed, will nitrosate, does not dominate the whole chemistry of nitrosation, as the nitronium ion dominates that of nitration. The nitrous acidium ion rather tends to react with whatever is available to be nitrosated in an  $S_N2$ -like manner, that is, without prior dissociation; and this type of substitution mechanism also serves for the fairly free interconversion of many of the carriers. The result is that one observes a wide distribution of effectiveness in nitrosation among the different carriers. Nitrosation does not put all its eggs into one basket, as nitration does.

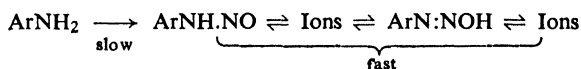
Our programme requires us to survey what is known of nitrosation at nitrogen and at oxygen, and I shall start with nitrogen. Nitrosation at nitrogen covers not only simple nitrosation, as of secondary amines to form nitrosamines, but also the diazotisation of primary aromatic amines, and the deamination of primary aliphatic amines and amides, and corresponding reactions of simple inorganic amines and imines, such as hydroxylamine, hydrazoic acid and ammonia itself. All the more complex reactions are chains of successive processes; but they all start with a nitrosation, which is always rate-controlling; and they then continue with a series of rapid ionisations or other heterolyses, which contribute nothing at all to the kinetics. It is suspected, though we have as yet no firm proof, that the oxidations that some amines undergo with nitrous acid, are nitrosations followed by homolysis, the nitrosation again being rate-controlling.\* So far, it has

\* There is firm proof for just such an oxidation mechanism, starting with rate-controlling nitrosation and followed by rapid homolytic loss of nitric oxide, in the oxidation by nitrous acid of some reducing alcohols, such as ascorbic acid. This conclusion rests on some very recent work, not yet published, by H. Dahn, as interpreted by Bunton and Dahn, and kindly communicated to me by these investigators.

been the universal finding that when one examines the kinetics of any of these reactions between nitrous acid and an amine, one is following the kinetics of a nitrosation.

The particular manifestation in which N-nitrosation has been best studied kinetically up to now is that of diazotisation. However, a sufficient proportion of the findings has been paralleled with respect to the formation of secondary nitrosamines and the deamination of primary aliphatic amines and inorganic amines to make one feel that the pattern is the same all through. I shall describe the work of Hughes and Ridd on the diazotisation of primary aromatic amines<sup>20</sup>, referring, as occasion arises, to the parallel results of others obtained with other types of amine.

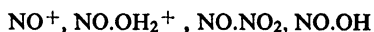
The general course of diazotisation may be represented by the following outline-scheme, from which much detail is omitted, both as regards the nitrosation stage with which we shall deal further and with respect to the subsequent prototropic change and its associated ionisation:



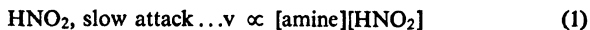
The two main groups of processes must come in this order for obvious reasons. The work of Hantzsch showed that the nitrosamine-diazotate prototropic system is very mobile; and in any case, analogy with other prototropic systems in which hydrogen separates only from electronegative oxygen or nitrogen, as in amides or amidines, would convince us that the nitrosamine-diazotate system must come practically instantaneously into isomeric and ionic equilibrium. The slow step, which diazotisation undoubtedly contains, must therefore belong to the nitrosation stage of the process. The questions which this conclusion raises are just those which a kinetic study is particularly well adapted to answer: What precisely is the slow step? What nitrosating carriers does it involve? Is rate controlled by the formation of this carrier, or by its attack on the amine?

The simplest series of experimental results that can provide

answers to these questions relate to the diazotisation, for example of aniline, in dilute aqueous solutions made weakly acid with perchloric acid. In these simplified conditions, no nitrate or halide ions, and no buffer anion, are present, and therefore a number of the carriers included in our previous list, nitrosyl bromide and dinitrogen tetroxide, for example, cannot be formed. The only conceivable carriers are the nitrosonium ion and its adducts with the nucleophiles which we cannot exclude, water, nitrite ion, and hydroxide ion. Our list of possible carriers is thus reduced to the following four:



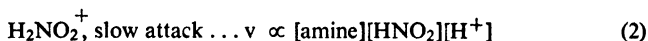
Before noting any experimental results, it will be convenient to set down the forms of kinetics that would be expected to follow from nitrosation by each of these four carriers. In the general case, we have to take account of the two possibilities that the carrier in question is freely available, its attack on the amine being rate-controlling, and that the carrier is formed from supplied materials in a slow and rate-controlling manner, to be snapped up as fast as it is formed by the amine. However, not all cases allow both possibilities. To deal with the simplest first, that of nitrosation by the nitrous acid molecule, we know that this is freely available, so that the only possible cause of slowness, if this were the reagent, would be slow attack by the nitrous acid on the amine. Therefore, the rate must be proportional both to the concentration of what is attacked, the amine, and to that of what attacks it, the nitrous acid: thus the rate equation is (1):



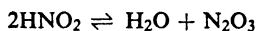
Here it may be worth pointing out that, in this and all our kinetic equations, the concentration factors are to be interpreted literally. In equation (1), "amine" means uncharged, free-basic amine, not including such ammonium cation as will be present in the acidic solution; and "HNO<sub>2</sub>" means undissociated molecules of nitrous acid, not including its conjugate base or conjugate acid or any

other species that would register in an analytical determination of what is often called "nitrous acid". All our other kinetic equations will similarly mean exactly what they look like. The only feature of the various species involved that is not expressed is their solvation, and consistently hydrogen ion will be written simply as  $H^+$ .

Nearly as simple a situation arises if the nitrous acidium ion is the reagent. It is formed by an instantaneous proton transfer, and hence its formation cannot be rate-controlling. Its attack could be, and then the rate would be proportional to the concentration of the amine attacked, and to that of the nitrous acidium ion, which, on account of the acid-base equilibrium in which the ion is involved, will itself be proportional to the concentration of nitrous acid molecules, and to that of hydrogen ions. Therefore, the kinetic equation is (2):

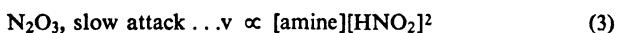


With dinitrogen trioxide as the reagent, account has to be taken of the two possibilities of slow attack and slow supply. In case of slow attack, the rate will be proportional to the concentration of attacked amine and to the stationary concentration of dinitrogen trioxide, now taken to be maintained through the equilibrium

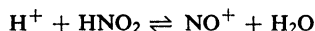


Water being in constant active mass, the rate equation for slow attack will be equation (3). This assumes that very nearly every formed dinitrogen trioxide molecule is trapped by the water, and only an occasional molecule is caught by the amine: that is why rate is increased with increasing concentration of amine. In the other extreme case, that of slow supply, nearly every dinitrogen trioxide molecule formed is at once captured by the amine, and the rate cannot therefore be increased by raising the concentration of amine. The reaction now becomes of zero-th order in amine, and its rate is simply that of the production of dinitrogen trioxide

molecules in the forward process of the reversible reaction written above, as expressed in equation (4):



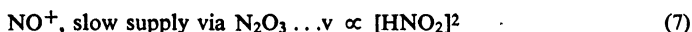
Finally, with the nitrosonium ion as reagent, we have the possibility of slow attack, the ion being maintained in stationary concentration by the equilibrium,



and the possibilities of slow supply by either of two routes, one involving the separation of water from nitrous acidium ion and the other the separation of nitrite ion from dinitrogen trioxide:



The kinetic equation (5), for slow attack, contains the concentration of the amine and also the concentrations to which the assumed stationary concentration of nitrosonium ion must be proportional. Equation (6), for slow supply by way of the nitrous acidium ion, contains the concentrations of the factors of the equilibrium maintaining the stationary concentration of nitrous acidium ion, the assumed precursors of slowly formed nitrosonium ion; but it does not contain the concentration of the amine, because that is now supposed to take up the nitrosonium ion as fast as the latter is formed. Equation (7), for slow supply by way of dinitrogen trioxide, similarly allows for the stationary concentration of that assumed precursor of nitrosonium ion, but once again does not involve the amine, which is assumed immediately to take up the dinitrogen trioxide:



We notice here that, in this set of theoretical rate-equations (1)–(7), several equations occur twice: (2) and (5) are duplicates; so are (4) and (7).

Let us now turn from theory to observation: the latter has an interesting history. The kinetics of diazotisation were first investigated in 1899 by Hantzsch<sup>26</sup>. He used reagents in equivalence and quite dilute acid, about 0.002 M. These were early days for reaction kinetics: such work had previously been done mainly on reactions of carboxylic esters, but one knew from these the law under which rate falls off with time in what we now call second order reactions. Hantzsch observed the same rate-time law for his diazotisations, and concluded that they were second order reactions, subject to the only type of kinetic equation then known to apply to such reactions, the type applying, for example, to ester saponifications, which assigns unit order to each reactant. Hantzsch also drew from his measurements the remarkable conclusion that all aromatic amines diazotise at the same rate. In 1913–1920 Tassilly<sup>27</sup>, and in 1920 a group under Boeseken<sup>28</sup>, reinvestigated the matter, and again concluded in favour of second order kinetics, with the same rate equations. But Boeseken, who used slightly stronger acid than Hantzsch, about 0.01 M, observed differences in the diazotisation rates of different amines, and was very critical of Hantzsch's contrary suggestion. However, in 1935 Reilly<sup>29</sup> diazotised three aromatic amines of very different basic strengths in very dilute acid, about 0.002 M, and recorded that they diazotised at the same second order rate, a result which stimulated Boeseken<sup>30</sup> to write an immediate paper to say that he did not believe it.

A new type of result now emerged. In 1936 Schmid<sup>31</sup> reinvestigated the diazotisation of aniline in considerably stronger acid, about 0.2 M, and found third order kinetics; and he proved the overall order to be made up of an order of unity in amine and an order of two in nitrous acid. Now this kinetic equation, though new for diazotisation, was not new in principle; for it had been obtained in 1928 by Taylor<sup>32, 33</sup> for the deamination of primary aliphatic amines, again in 1929 by Taylor<sup>33</sup> for the simple nitrosation of secondary amines, and yet again in 1931 by Abel<sup>34</sup> for what we may call the deamination of ammonia, that is, the decomposition of ammonium nitrite. Schmid seems to have been unaware in 1936 of the long history, running from 1899 to 1935, of observed

second order kinetics in diazotisation, for he makes no reference to these apparently discrepant findings. All writers, and there were several, who from 1936 onward until 1950 discussed possible meanings of the third order law similarly ignored the second order findings. The following is a tabular summary of this equivocal history:

1899 Hantzsch (ArNH <sub>2</sub> )	} Found second order and assumed $v \propto [\text{amine}][\text{HNO}_2]$
1913 Tassilly (ArNH <sub>2</sub> )	
1920 Boeseken (ArNH <sub>2</sub> )	
1935 Reilly (ArNH <sub>2</sub> )	
1928 Taylor (AlkNH <sub>2</sub> )	} Found third order with $v \propto [\text{amine}][\text{HNO}_2]^2$
1929 Taylor (Alk <sub>2</sub> NH)	
1931 Abel (NH <sub>3</sub> )	
1936 Schmid (ArNH <sub>2</sub> )	

The discrepancy was resolved in 1950, when it was shown that the overall kinetic order of diazotisation does indeed drop from three to two as the acidity is reduced from the decimolar to millimolar region or below; and further, that whilst the third order law had been correctly formulated,

$$v \propto [\text{amine}][\text{HNO}_2]^2 \quad (3)$$

the second order law was constituted not, as had been assumed without proof, from an order of unity in each reagent, but from an order of zero in amine and an order of two in nitrous acid:

$$v \propto [\text{HNO}_2]^2 \quad (4)$$

This observation of a transition from first order to zero-th in amine, with maintenance of second order in nitrous acid, proves conclusively that dinitrogen trioxide is the carrier. At high acidities, too little free amine is present to capture the dinitrogen trioxide as the latter is formed, and so it is formed in a stationary concentration, the slow step being that of its withdrawal by the amine in accordance with equation (3). At low acidities, there is plenty of free amine to trap the dinitrogen trioxide as the latter is produced, and hence the observed rate is simply that of its

production, as expressed in equation (4). All amines diazotising with these kinetics will diazotise at the same rate — as Hantzsch observed, though he, like Reilly, was criticised for observing it.

By extending their investigation, Hughes and Ridd were able to identify other nitrosating agents. In the experiments just described, a certain "extra" rate, not accounted for in equations (3) and (4), was noticed at low concentrations of nitrous acid. This indicated the presence of some other rate term, one of lower order than second in nitrous acid. By reducing the concentration of nitrous acid to  $10^{-4}$  M, which is low enough to suppress rates depending on its square, the new rate term could for certain amines, such as *o*-chloroaniline, be isolated, and provided rates large enough for measurement. The new rate equation proved to be of the form

$$v \propto [\text{amine}][\text{HNO}_2][\text{H}^+] \quad (2)$$

From our list of theoretical equations (1–7), we see that this observed equation might have either of two interpretations: it could mean rate-controlling attack by nitrous acidium ion (equation 2); or it could mean rate-controlling attack by nitrosonium ion (equation 5). Actually, we can show that the former alternative is the correct one, because diazotisation according to this equation can proceed more rapidly than an upper limit which can be set, by a method that I shall next describe, to the possible rate of production of nitrosonium ion in the solution under the conditions of the measurements.

This conclusion emerges from another set of Hughes and Ridd's experiments. These dealt with the catalysis of diazotisation by bromide ions and by iodide ions. By providing, for example, bromide ions during diazotisation, a catalysis is produced which is so strong that the catalytic rate term can be isolated sufficiently for the working out of its detailed form. This is the form expressed by equation (8). By using a fairly weakly basic aromatic amine, such as *o*-chloroaniline, so that the concentration of free amine at the acidities employed is substantial, it becomes possible, at

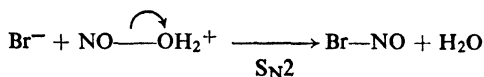
convenient stoichiometric concentrations of amine, to observe that with sufficient amine, the rate becomes independent of the concentration of amine. The kinetic equation is now (9):

$$v \propto [\text{amine}][\text{Br}^-][\text{HNO}_2][\text{H}^+] \quad (8)$$

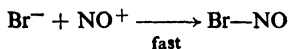
$$v \propto [\text{Br}^-][\text{HNO}_2][\text{H}^+] \quad (9)$$

Exactly as the former kinetic transition proved nitrosation by dinitrogen trioxide, so this one proves nitrosation by nitrosyl bromide. When nitrosyl bromide is built up in a stationary concentration, from which the amine draws material only slowly, the kinetic equation is (8). When the amine takes up the nitrosyl bromide as fast as this is formed, then the rate of diazotisation is just the rate of formation of nitrosyl bromide, in accordance with equation (9).

The chemical translation of equation (9) is that it represents a bimolecular attack of bromide ion on nitrous acidium ion:



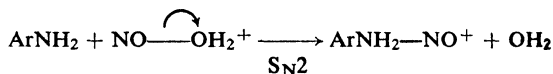
This is an  $\text{S}_{\text{N}}2$  substitution in the nitrous acidium ion, and the reaction is measurably slow, because a bond has to be broken, as well as one having to be formed. Now we can imagine an instantaneous process for the formation of nitrosyl bromide, if both the required materials were present, namely, by direct union of bromide ion with nitrosonium ion:



The bromide ion certainly is present. Therefore, the measured rate of diazotisation according to equation (9), which is the rate of production of nitrosyl bromide, sets an upper limit to the rate of any possible appearance of nitrosonium ions in the solution.

Now it is found that rate of diazotisation according to equation (2) is not in any way limited by rate according to equation (9), and can, indeed, easily be made the faster when the two reactions

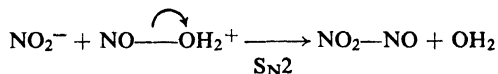
are running concurrently. This shows that equation (2) represents nitrosation by the nitrous acidium ion, not by the nitrosonium ion. The chemical translation of kinetic equation (2) is that it represents a bimolecular attack by the aromatic base on the nitrous acidium ion, another  $S_N2$  substitution, quite analogous to that by bromide ions:



Going back to equation (4), which represents the rate of formation of dinitrogen trioxide, we can now see that it has a similar chemical meaning. For first, we can rewrite it in the kinetically equivalent form:

$$v \propto [\text{NO}_2^-][\text{HNO}_2][\text{H}^+] \quad (4a)$$

The chemical translation of this equation is that nitrite ion is the substituting agent in another bimolecular nucleophilic substitution of nitrous acidium ion:



One suspects that this mechanism for the self-dehydration of nitrous acid, namely, by substitution of the conjugate base of the acid in the conjugate acid of the acid, is a fairly general mechanism for the self-dehydration of acids.

Anions of weak acids, such as acetic acid or phthalic acid, also catalyse diazotisation, and it is possible to observe such catalysis in a kinetic form which does not involve amine concentration, and therefore represents the rate of some inorganic chemical process. This rate equation for catalysis by acetate ions is (10), which can be rewritten in two equivalent forms (10a) and (10b):

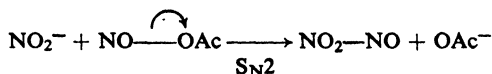
$$v \propto [\text{AcO}^-][\text{HNO}_2]^2 \quad (10)$$

$$v \propto [\text{AcO}^-][\text{N}_2\text{O}_3] \quad (10a)$$

$$v \propto [\text{NO}_2^-][\text{NO.OAc}] \quad (10b)$$

Of these alternative forms, only (10b) is chemically realistic, because rates in this catalysed reaction are greater than the rate of

formation of dinitrogen trioxide by the self-dehydration of nitrous acid. The catalysed reaction therefore depends on a new route to dinitrogen trioxide, which is still the nitrosating agent for the amine; and the new route consists in a bimolecular nucleophilic substitution by nitrite ion in nitrosyl acetate, presumably first formed relatively rapidly in stationary concentration, analogously to nitrosyl bromide:



This shows that conversions by bimolecular nucleophilic substitutions are not confined to the one nitrosyl substrate, the conjugate acid of nitrous acid, but are a general property of nitrosyl compounds. Indeed, we can summarise all the observed mechanisms of diazotisation as is done in Figure 6, which shows a network of bimolecular nucleophilic substitutions,  $\text{S}_{\text{N}}2$ , among nitrosyl compounds. Each link in the network has separately been made rate-controlling, and the numbers entered against the links are the numbers we have used for the corresponding kinetic equations. The first step of all is, of course, the instantaneous proton uptake by nitrous acid to form its conjugate acid. In this, a water molecule occupies the place that has to become occupied by an amine molecule in order to secure diazotisation. The replacement of water by amine may be direct. But a faster route may be provided by first replacing the water by nitrite ion, and then replacing the nitrite ion by amine. Again some "foreign" anion,  $\text{X}^-$ , if present, which might, for example, be bromide or acetate, might displace the water faster than the nitrite ions can; and so, it will itself have subsequently to be displaced either by the amine, or by the nitrite ion, which then must become still later displaced by amine. Hughes and Ridd observed all these variations.

The only compound in which nitrosation on oxygen has been studied in any detail (apart from certain oxidations which depend on nitrosation; cf. footnote p. 34) is water. The nitrosation of water can be studied by following the transfer of an oxygen iso-

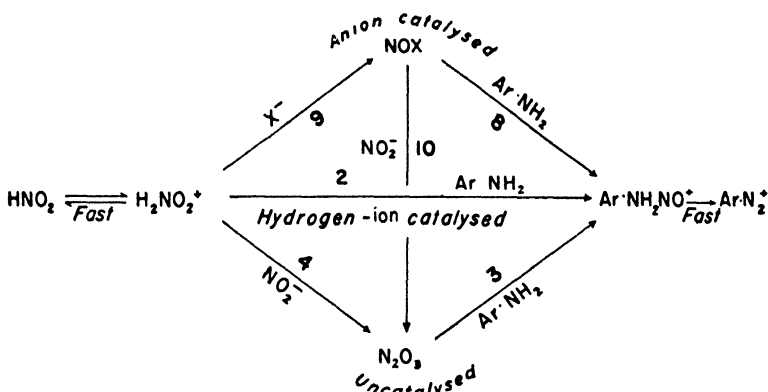


Figure 6  
Mechanisms of aqueous diazotisation

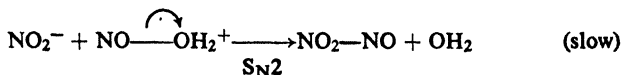
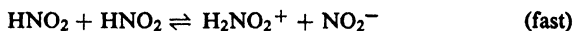
topic label from water to nitrous acid or *vice versa*; and this was the method used by Bunton, Llewellyn and Stedman<sup>30</sup>.

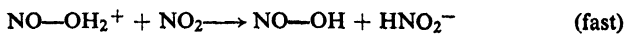
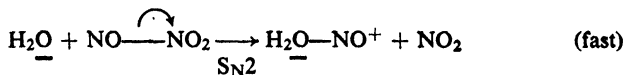
In their basic series of experiments, the only substances introduced were sodium nitrite, perchloric acid, and water; no reactive "foreign" anions were admitted. The rate equation proved to be our previous equation (4), rewritten below as (4'), and in the alternative form (4a') which expresses better the chemistry of the reaction:

$$v_{\text{exchange}} \propto [\text{HNO}_2]^2 \quad (4')$$

$$v_{\text{exchange}} \propto [\text{NO}_2^-][\text{HNO}_2][\text{H}^+] \quad (4a')$$

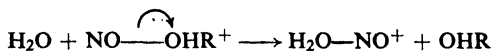
The process of which the rate is measured is the self-dehydration of nitrous acid by the mechanism we already know, namely, attack by the conjugate base of the acid on the conjugate acid of the acid; and the formed dinitrogen trioxide is rehydrated as fast as it is formed. This latter process is the one which transfers the isotopic label, as indicated by the underlines in the scheme written below:





The rate of the transfer is the rate of the slow step, the formation of dinitrogen trioxide, and the observed rate of label transfer is in fact the same as the rate of the self-dehydration of nitrous acid as deduced from studies of diazotisation, to within the allowance which has to be made for the negative salt effect expected in a reaction between oppositely charged ions at the considerable ionic strengths of the exchange experiments.

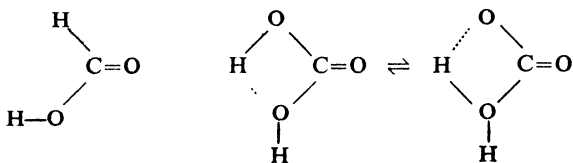
Other mechanisms have been established for the nitrosation of water. The simplest chemically is that which corresponds to the diazotisation process of our previous equation (2), the process represented by the horizontal link in the network of Figure 6, and in which the compound being nitrosated, water in the present case, substitutes directly in the conjugate acid, without previous intervention by nitrite or other anions. Allen<sup>36</sup> established this mechanism in a particularly favourable case for it, namely, the acid hydrolysis of alkyl nitrites; for with an alkyl nitrite taking the place of hydrogen nitrite, no nitrite ion is present initially. Allen showed by a method similar to the one already illustrated in the reaction of diazotisation that the nitrous esterium ion in which the substitution by water occurs, does not undergo an S<sub>N</sub>1 substitution, involving dissociation to the nitrosonium ion; on the contrary, it undergoes a simple, one-step, S<sub>N</sub>2 substitution:



Several investigators<sup>35,36,37</sup> have studied the catalysis by anions of weak acids, such as acetate, phthalate, and phosphate, of oxygen exchange between nitrous acid and water, and the catalysis by bromide ion of this reaction and of the acid hydrolysis of alkyl nitrites. The results, though less complete than those applying to the anion catalysis of diazotisation, disclose parts of the same pattern—a pattern of S<sub>N</sub>2 substitutions among nitrosyl compounds.

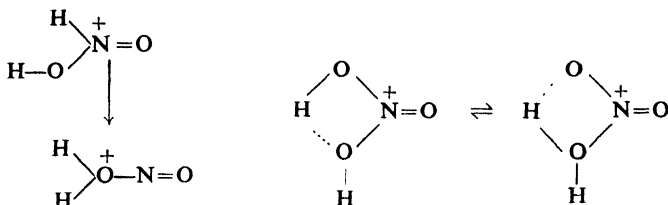
This leads to the last question we shall have time to consider, which is as follows. Why is it that nitrosation, whatever the substrate, is dominated by  $S_N2$  substitutions in the nitrous species, especially in the nitrous acidium ion, whereas nitration, whatever the substrate, is dominated by  $S_N1$  substitutions in the nitric species, especially the nitric acidium ion? A possible answer to this, suggested by Lidstone<sup>38</sup>, is that it is a simple matter of structure.

The familiar analogy is that of formic and carbonic acids. Carbonic acid is much more easily dehydrated to carbon dioxide than formic acid is to carbon monoxide, if, indeed, formic acid can be dehydrated at all without first being further protonated. A plausible reason for the difference appears in the formulae of the substances. In carbonic acid, hydrogen-bonding between the two hydroxyl groups puts into the structure a water molecule, which is ready made after the facile interchange of bond type which occurs between the two sides of the hydrogen bond. In formic acid, if extra protonation is excluded, a 1:2-proton-shift would have to occur in order to produce a water structure that could dissociate by simple heterolysis:



Lidstone suggests that the nitrous and nitric acidium ions, in their thermodynamically most stable forms, may be constituted similarly to formic and carbonic acids. The stable form of the nitric acidium ion will also be the reactive form for  $S_N1$  reactions, because it contains the water structure in a condition ready to separate. In the nitrous acidium ion, on the other hand, a proton must first undergo a 1:2-shift in order to produce a form of the ion that could dissociate by simple heterolysis. This proton shift is sure to be endothermic, since it transfers a positive charge to a

more electronegative atom; and the endothermicity, added to the activation energy of the heterolysis, may well make  $S_N1$  reactions of the nitrous acidium ion very difficult:



Of course the situation is different in a solvent so strongly acidic that extra protonation of the nitrous acidium ion becomes possible. We know from other work that the nitronium ion is formed, and is stable in, for example, solvent sulphuric acid.

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## APPENDIX

Perhaps the statement on the  $S_N2$  mechanism on p. 10 ought to be supported. The first argument<sup>7</sup> of the kind described was to the effect that the replacement in cations such as *trans*-dichloro-*bis*-ethylenediamine-cobalt-III of *bis*-ethylenediamine by either tetrapyridine or *bis*- $\alpha'$ -dipyridyl ligands, which have no nitrogen-bound hydrogen, leads to a fast aquation, which is not appreciably accelerated by alkali up to  $pH$  9.18. It has been pointed out<sup>8</sup>, however, that this alkalinity was too low by several  $pH$  units to make the second order reaction with hydroxide ion competitive with aquation. What requires to be explained is the particularly high rate of aquation in the presence of the aromatic ligands, and a plausible explanation is that aromatic  $\pi$ -electrons conjugate with the electrons of the breaking bond. In the matter of formal conjugation the replacement of an ethylenediamine ligand by two pyridine ligands is like passing from a *cyclo*-pentyl halide to a benzhydryl halide, a change which, as is well known, produces a great increase in the rate of halogen solvolysis. Since this reply was given, the original argument has been repeated<sup>9</sup> without reference to the reply.

The next argument of the same class<sup>10</sup> was that the replacement in chloropentaminecobalt-III of four ammonia groups by two ethylenediamine ligands, and thereafter by one triethylenetetramine ligand, causes alkaline hydrolysis rates successively to rise, and aquation rates to fall. But we know that the carbonium ion, produced in water, reacts bimolecularly with anions with an activation energy, presumably because the attacking anion has to get through the solvation layer, but reacts multimolecularly with water without appreciable activation energy, presumably by collapse of the solvation shell itself, the delay in this case being essentially entropic<sup>11</sup>. Therefore a plausible explanation of the rate relations is simply that, as more hydrocarbon ties stretch across the surface

of the complex ion, the solvation shell becomes less compact and less intimate with the ion, and so is more easily penetrated by an attacking anion, but is less disposed itself to enter into reaction with the central ion. This reply also has been given before<sup>8</sup>, but once again the original argument has been repeated<sup>12</sup> without reference to the reply.

The most recent<sup>13</sup> of these inconclusive arguments is to the effect that, whilst complexes of chromium-III are more rapidly aquated than are corresponding complexes of cobalt-III, "as expected on the basis of crystal field theory" (so it is said), inasmuch as the cobalt ions contain three more unshared *3d* electrons to resist disturbance to the metal valency shell, it is the cobalt complexes which more rapidly undergo second order reaction with hydroxide ion, which therefore (so it is argued), cannot be attacking the valency shell of the metal, and so cannot be using the  $S_N2$  mechanism. The figures offered in support of these conclusions are interesting. Expressed as rate-ratios, at the experimental temperature, 25°C, they are as follows for the *trans*-complexes:

	<i>Trans</i> -Cren <sub>2</sub> Cl <sub>2</sub> <sup>+</sup>	<i>Trans</i> -Coen <sub>2</sub> Cl <sub>2</sub> <sup>+</sup>
H <sub>2</sub> O (first order)	1	0.8
OH <sup>-</sup> (second order)	1	80,000

Quite similar figures apply to the corresponding *cis*-complexes. The first comment that one is bound to make on these figures is that the contrast in the first order rates is much too trivial to be discussed in terms of electron configuration; and to cite this energetically negligible rate difference as an "expected" effect of three electrons should be considered as fantastic. However, the contrast in second order rates is energetically worth discussing. It is declared "not compatible with an  $S_N2$  mechanism"; but there is no need to be so uncompromising; for it can very plausibly be discussed on the basis of the  $S_N2$  mechanism, no doubt inadequately, but at least in very simple electrostatic terms. What the authors of this controversy have forgotten is that cobalt, as compared with chromium, has not only three more electrons, but also three more

units of nuclear charge. The combined electrostatic effect of these two charge differences is likely to be felt much more in reaction with an ion, the charge on which has to be carried along a potential gradient into the transition state, than in reaction with a neutral molecule. This combined electrostatic effect on the potential energy of an approaching anion will sum to zero only well outside the cobalt atom. But at the distance critical for the determination of binding, the electrostatic effect of the extra nuclear charge of cobalt will predominate, because the point in question will be within the spread of the cobalt electron shell, the outer parts of which will, in spherical first approximation, exert no force there. In any approximation, nuclear screening is lost as the anion approaches the transition-state distance.





