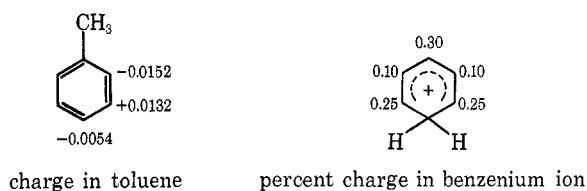


of course, meta. For the most frequently studied reactions of toluene with strongly electrophilic reagents the ortho/para isomer ratio is generally close to or greater than 2:1, in spite of possible steric ortho hindrance. On the other hand, in selective reactions with increasingly weaker electrophiles (or with aromatics of lesser nucleophilicity) which show higher substrate selectivity, the σ transition states are of "late" nature resembling the intermediates and the ortho/para ratio decreases, para substitution becoming predominant. Early transition-state reactions will reflect charge distribution of the aromatics. In alkylbenzenes, such as toluene, charge density is highest around the ortho and para positions (as shown in the case of toluene, based on Pople CNDO/2 calculations). Further as there are two ortho but only one para position, the ortho/para ratio will be high ($\gtrsim 2$).

In reactions indicating late transition states of highest energy, *e.g.*, resembling the Wheland intermediates, the isomer distributions obtained relate to charge density in the cyclohexadienyl cations (Wheland intermediates, σ complexes). Nmr studies of σ complexes^{8p} including the recent study of the $C_6H_7^+$ ion itself³⁰ and semiempirical self-consistent-field calculations, indicate a charge distribution in benzenium ions with 5–10% of the charge present at each meta carbon atom, about 26% at each ortho carbon, and about 30% at the para carbon (relative to the methylene group). It



follows that a substituent will exert a more powerful effect on the benzenium ion (σ complex) when it is para to the entering reagent than when it is ortho, and even more so than when it is meta. With an electron-donating substituent like the methyl group

in toluene, the stability of intermediate ions will decrease in the order para > ortho > meta, resulting in a low ortho/para isomer ratio, as indeed is found experimentally in high-selectivity reactions.

Consideration of the nature of the transition states enables an understanding of substrate selectivities separate from that of positional selectivities. It also brings to light the importance of ortho/para isomer ratios in the context of positional selectivities and further allows their correlation with substrate selectivities. This realization supplements the well-demonstrated importance of meta/para isomeric substitution ratios, on which the Brown-selectivity treatment is based.

It should be pointed out that Norman and Taylor³¹ must be credited with first emphasizing the importance of the ortho/para ratio, discussing contributions from (a) steric hindrance, (b) steric acceleration, (c) interaction between the substituent and the reagent, (d) electronic effects, and (e) solvent effects. They considered that, due to the complexity of factors involved, it is difficult to evaluate individual effects separately. Our work provided, however, clear indication for the dependence of the ortho/para isomer ratios on the nature of the transition states, effected through electrophilicity of the reagents or nucleophilicity of the aromatics.

Some years ago it seemed that electrophilic aromatic substitution was a closed field in which most of the significant work was already done. It is rewarding to see that recent work opened up new aspects and interest, which is expected to continue.

Support of our work by the Petroleum Research Fund, administered by the American Chemical Society, and the U. S. Army Research Office (Durham, N. C.), is gratefully acknowledged. Drs. Masashi Tashiro and Shiro Kobayashi and Mr. H. C. Lin should be credited with our recent work on electrophilic aromatic substitution; their dedicated work and many original contributions can be hardly overestimated. My colleagues Chris Cupas, Gilles Klopman, and Eric Nordlander are thanked for stimulating discussions.

(30) G. A. Olah, R. H. Schlosberg, D. P. Kelly, and Gh. D. Mateescu, *J. Amer. Chem. Soc.*, **92**, 2546 (1970).

(31) R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier, Amsterdam, 1965, pp 301–310; G. Klopman, *J. Amer. Chem. Soc.*, **90**, 223 (1968); G. Klopman, personal communication.

Mechanism of Aromatic Nitration

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Up to 1960, the nitration of aromatic compounds by solutions of nitric acid in sulfuric acid or organic solvents was confidently discussed in terms of the attack by the nitronium ion. In the following 5 years, the

contributions of several groups of workers combined to raise doubts over the importance of this mechanism of nitration and to raise new problems concerning the form of the transition state. Recent work has gone some

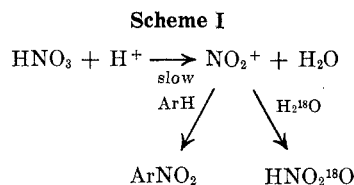
way toward clarifying the reaction mechanism so that a reassessment of the position is now appropriate. This reassessment is concerned only with what may be termed the basic mechanism of nitration: the mechanism applying to the nitration of aromatic compounds of reactivity similar to that of benzene by nitric acid or nitronium salts.

Historical Background

It is helpful to consider first the situation in 1960;¹ this provides a useful starting point for comparison with later work.

Spectroscopic techniques with some help from cryoscopic measurements had shown the presence of a small equilibrium concentration of the nitronium ion (NO_2^+) in anhydrous nitric acid. In the presence of a large excess of sulfuric acid, the nitric acid was known to be completely converted to nitronium bisulfate, so there was no reason to doubt that nitration under these conditions involved the nitronium ion. When water was added to these solutions, the concentration of nitronium ions and the rate of nitration were observed to decrease, but nitration of compounds of reactivity similar to that of benzene was still observed when the concentration of nitronium ions was too small to be detected.

The most convincing evidence that nitration in such aqueous media still involved the nitronium ion came from the comparison between the rate of nitration and the rate of ^{18}O exchange between nitric acid and the medium.² With sufficiently reactive substrates, the rate of nitration in partly aqueous media shows zero-order kinetics; *i.e.*, the rate is independent of the nature and concentration of the aromatic compound. This indicates that the nitrating agent is formed from nitric acid in a slow step prior to attack on the aromatic ring. In the absence of the aromatic compound, oxygen isotope exchange occurs between the water and the nitric acid, and the rate of this reaction is equal to the zero-order rate of nitration. Thus the reverse of the formation of the nitrating agent introduces one oxygen atom from water into the nitric acid. The only convincing interpretation of these observations involves the intermediate formation of the nitronium ion (Scheme I).³



(1) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969; (b) P. B. D. De la Mare and J. H. Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworths, London, 1959.

(2) C. A. Bunton and E. A. Halevi, *J. Chem. Soc.*, 4917 (1952); C. A. Bunton and G. Stedman, *ibid.*, 2420 (1958).

(3) The formation of the nitronium ion is usually regarded¹ as the two-step process: $\text{HNO}_3 + \text{H}^+ \rightleftharpoons \text{H}_2\text{NO}_3^+ \rightarrow \text{H}_2\text{O} + \text{NO}_2^+$. The first step of this process is never rate determining, and so this distinction need not concern us here.

Table I

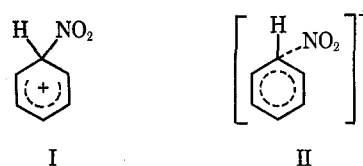
Orientation and Relative Reactivity in the Nitration of Toluene

Conditions	Relative ^a rate	Orientation			Ref
		o	m	p	
HNO_3 in CH_3NO_2 , 30°	21	58.5	4.4	37.1	<i>b</i>
HNO_3 in HOAc , 45°	24	56.5	3.5	40.0	<i>c</i>
NO_2BF_4 in $\text{C}_4\text{H}_8\text{SO}_2$, 25°	1.67	65.4	2.8	31.8	<i>d</i>
NO_2PF_5 in $\text{C}_4\text{H}_8\text{SO}_2$, 25°	1.40	67.6	1.4	31.0	<i>d</i>
NO_2ClO_4 in $\text{C}_4\text{H}_8\text{SO}_2$, 25°	1.60	66.2	3.4	30.4	<i>d</i>

^a With respect to the rate of nitration of benzene as unity. ^b C. K. Ingold, A. Lapworth, E. Rothstein, and D. Ward, *J. Chem. Soc.*, 1959 (1931). ^c H. Cohn, E. D. Hughes, M. H. Jones, and M. G. Peeling, *Nature*, **169**, 291 (1952). ^d G. A. Olah, S. J. Kuhn, and S. H. Flood, *J. Amer. Chem. Soc.*, **83**, 4571 (1961).

A similar zero-order kinetic form had previously been observed for nitration in mixtures of nitric acid with nitromethane or acetic acid and had been interpreted^{4a} as the slow formation of the nitronium ion. The detailed arguments⁴ for this interpretation received strong support from the experiments in aqueous media, for a mechanism which occurs in anhydrous nitric acid and in mixtures of nitric acid and water may be presumed to operate when the nitric acid is diluted with the organic solvents. The generality of the nitronium ion mechanism also received support from the similarity in relative rates of nitration under these conditions; this is illustrated by the first two results in Table I.

By 1960, it was generally recognized that nitration involved the formation of a σ complex (I) or Wheland intermediate and that the subsequent proton loss was not kinetically significant. However, the magnitudes of the substituent effects in nitration were known to be far less than those for molecular halogenation or those for the protonation of aromatic compounds. These differences were rationalized⁵ by assuming that the transition state for nitration lay between the initial state and the σ complex. Such a transition state (*cf.* structure II) still involves attack at an individual carbon atom.



In 1961, several changes in this picture of the reaction path were suggested by Olah and his coworkers⁶ as a result of studies on the competitive nitration of aromatic substrates by preformed nitronium salts in sulfolane or nitromethane. Under these conditions, relative rates of nitration are much closer to unity than the results obtained from nitration by nitric acid, but the differences in the orientation of nitration are much less

(4) (a) E. D. Hughes, C. K. Ingold, and R. I. Reed, *J. Chem. Soc.*, 2400 (1950); (b) J. H. Ridd in "Studies of Chemical Structure and Reactivity," J. H. Ridd, Ed, Methuen, London, 1966, Chapter 7.

(5) M. J. S. Dewar, T. Mole, and E. W. T. Warford, *J. Chem. Soc.*, 3581 (1956); *cf.* ref 1b, Chapter 17.

(6) G. A. Olah, S. J. Kuhn, and S. H. Flood, *J. Amer. Chem. Soc.*, **83**, 4571 (1961); G. A. Olah, S. J. Kuhn, and S. H. Flood, *ibid.*, **83**, 4581 (1961).

marked. These results are illustrated with respect to toluene in Table I. The results imply that the reactivity of the meta position in toluene is much less than the reactivity of one position in benzene.

The relative reaction rates observed in the nitrations by nitronium salts resemble the relative stability of the loose π complexes formed by aromatic compounds with weak electrophiles (Br_2 , I_2).⁶ The rate-determining step of the nitration was therefore suggested to be the formation of a π complex between the nitronium ion and the π -electron shell of the aromatic ring; this was considered to be followed by the formation of a normal σ complex. The extent to which the position of the electrophile in the π complex influenced the final position of the substitution was not exactly defined but, in principle, this concept of a rate-determining π -complex formation followed by a product-determining σ -complex formation is capable of reconciling the "abnormal" relative rates with the "normal" orientation of substitution.

The major difficulty with this interpretation is in explaining why the π -complex formation should be rate determining for nitration by nitronium salts but not for nitration by the nitronium ion under other conditions. This difficulty was met by the suggestion⁷ that the nitration conditions giving values of ~ 20 for the relative reactivity of toluene involve attack by precursors of the nitronium ion, *e.g.*, the nitric acidium ion (H_2ONO_2^+) or protonated acetyl nitrate (AcONO_2H^+). The problem of reconciling this conclusion with the earlier kinetic studies was not discussed in detail.

The possible involvement of protonated acetyl nitrate as the electrophile for nitration in acetic anhydride received support from evidence that, in certain substrates (*e.g.*, *o*-xylene), acetoxylation accompanies nitration and that the two reactions involve the same electrophilic species.⁸ Protonated acetyl nitrate could clearly act as an acetoxyating agent as well as a nitrating agent. However, it now appears clear that this acetoxylation involves an addition-elimination reaction⁹ and as such could be initiated by the attack of a nitronium ion.^{4b} This argument against the nitronium ion mechanism is therefore no longer applicable.

Recent Studies

The main weakness in the π -complex interpretation of the relative rates is that these competitive nitrations may be invalid because of extensive reaction during the mixing of the reactants.¹⁰ Olah and his coworkers were aware of this objection and sought to overcome it by showing that the relative rates were not very sensitive to the relative concentrations of reactants or to the conditions of mixing. In an extension of this approach

using low concentrations of nitronium salts and very efficient means of mixing, Tolgyesi¹¹ claimed to increase the relative reactivity of toluene to the "normal" figure (~ 20). However, the significance of these experiments with low concentrations of nitronium salts appeared doubtful when Olah and Overchuk¹² showed that the amount of impurities in the sulfolane used might have been sufficient to react with all of the nitronium salt with the formation of other nitrating agents.

Indirect evidence on the extent of reaction during mixing has now been obtained from the nitration of dibenzyl. The aromatic rings in this compound should be about as reactive as that of toluene, and the presence of the two methylene groups implies that the transmission of substituent effects between the rings should be slight.

Consider first that substitution in the two rings occurs independently so that the fractions of unsubstituted (x), monosubstituted (y), and disubstituted¹³ (z) products can be calculated from the random pairing of substituted and unsubstituted rings. Then, if a moles of nitronium salt is added to an excess, b moles, of dibenzyl and if mixing is complete before reaction, the product composition is related to the ratio R ($= 2b/a$) of aromatic rings to nitronium ions by

$$x = (1 - 1/R)^2$$

$$y = (2/R)(1 - 1/R)$$

$$z = 1/R^2$$

Thus, with equimolar concentrations ($R = 2$), one would expect 25% unsubstituted dibenzyl, 50% monosubstituted dibenzyl, and 25% disubstituted dibenzyl. Incomplete mixing before reaction should increase the percentages of unsubstituted dibenzyl and disubstituted dibenzyl at the expense of the monosubstituted dibenzyl.

The nitration of dibenzyl with nitronium tetrafluoroborate in sulfolane has now been studied over a range of concentrations and conditions of mixing.^{14a} The experimental work is complicated by the formation of two main mononitro derivatives (the 2 and 4 isomers) and three main dinitro derivatives (the 2,2', 2,4', and 4,4' isomers); however, for the present purpose only the extent of disubstitution as a percentage of total (mono + di) substitution need be considered. The comparisons of the observed and calculated percentages in Table II are for experiments carried out with rather less concentrated solutions than those used for the reactions involving nitronium salts in Table I, but with similar conditions of mixing. The high percentages of disubstitution point clearly to reaction during the mixing of the solutions.

(7) G. A. Olah, S. J. Kuhn, S. H. Flood, and J. C. Evans, *J. Amer. Chem. Soc.*, **84**, 3687 (1962).

(8) A. Fischer, A. J. Read, and J. Vaughan, *J. Chem. Soc.*, 3691 (1964).

(9) D. J. Blackstock, A. Fischer, K. E. Richards, J. Vaughan, and G. J. Wright, *Chem. Commun.*, 641 (1970); D. J. Blackstock, J. R. Cretney, A. Fischer, M. P. Hartshorn, K. E. Richards, J. Vaughan, and G. J. Wright, *Tetrahedron Lett.*, 2793 (1970).

(10) Cf. A. W. Francis, *J. Amer. Chem. Soc.*, **48**, 655 (1926).

(11) W. S. Tolgyesi, *Can. J. Chem.*, **43**, 343 (1965).

(12) G. A. Olah and N. A. Overchuk, *ibid.*, **43**, 3279 (1965).

(13) Disubstituted products containing both nitro groups in the same ring are not considered in this calculation; the amount formed should be very small because of the deactivating effect of the first nitro group.

(14) (a) P. F. Christy, J. H. Ridd, and N. D. Stears, *J. Chem. Soc. B*, 797 (1970); (b) A. Gastaminza and J. H. Ridd, unpublished observations.

Table II
Nitration of Dibenzyl by Nitronium
Tetrafluoroborate in Sulfolane^a

[Dibenzyl], M	[NO ₂ BF ₄], M	Disub product, mole %		R	R'
		Obsd ^b	Calcd ^c		
0.20	0.20	82.7	33	2	1.10
0.125	0.125	80.1	33	2	1.12
0.25	0.125	77.8	14	4	1.14
0.625	0.125	71.0	5	10	1.21

^a P. F. Christy, J. H. Ridd, and N. D. Stears, *J. Chem. Soc. B*, 797 (1970). ^b Disubstitution as a percentage of total (mono + di) substitution. ^c Calculated as $100z/(y+z)$; see text.

It is instructive to reverse the statistical calculations by using the ratio of disubstitution to monosubstitution to calculate the amount of dibenzyl available to the nitronium salt during the reaction. Such an approach assumes that the aromatic substrate present in the solution can be divided into two parts, one part undergoing complete mixing with the nitronium salt and the other part being precluded by its position in the solution from undergoing nitration. This can be only a crude approximation to the true situation, but it provides a guide to the extent of mixing before reaction is complete.

The resulting values of the effective ratio of aromatic rings to nitronium ions (R') are included in Table II. These values indicate that the reactivity of the nitronium salt is sufficient for reaction to be complete in the time required for the nitronium ions to mix with 1.1–1.2 equiv of the aromatic substrate. It is easy to see that such incomplete mixing would be sufficient in itself to explain the low values of the relative reactivity of toluene listed for the reactions with nitronium salts in Table I. Thus if 0.05 mole of nitronium tetrafluoroborate were added to a solution containing 0.25 mole of toluene and 0.25 mole of benzene and if reaction were complete when the nitronium salt had mixed with 1.2 equiv of the aromatic substrate, then the maximum amount of nitrotoluenes formed would be 0.03 mole, leaving 0.02 mole of nitrobenzene. The use of these values in the usual equation for competitive nitrations gives toluene an apparent relative reactivity of 1.6.

The assumption that substitution occurs independently in the two aromatic rings of dibenzyl is an oversimplification. A recent study^{14b} of the product composition in the nitration of dibenzyl by nitric acid in acetic anhydride shows that, where mixing is unimportant, the extent of disubstitution is about 55% of that expected on the above treatment. The calculated percentages of disubstitution in Table II are therefore too high; this strengthens the argument for incomplete mixing in the nitrations by nitronium salts.

Independent evidence on the very rapid reaction between benzene and nitronium ions is provided by the work of Coombes, Moodie, and Schofield¹⁵ on nitration in aqueous sulfuric acid.¹⁶ Their results (Table III)

(15) R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc. B*, 800 (1968).

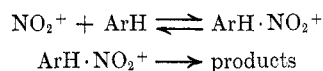
Table III
Nitration of Reactive Aromatic Compounds at 25°:
Evidence for a Limiting Encounter Rate

	Relative reaction rate		
	H ₂ SO ₄ ^a (68.3%)	HClO ₄ ^b (61.05%)	C ₄ H ₈ SO ₂ ^b (7.5% aq)
Benzene	1	1	1
Toluene	17	19	20
Naphthalene	28	26	33
2-Methylnaphthalene	28	56	230
<i>o</i> -Xylene	38		61
<i>p</i> -Xylene	38	84	114
<i>m</i> -Xylene	38		100
Phenol	31	24	700
Mesitylene	36	78	350

^a R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc. B*, 800 (1968). ^b J. C. Hoggett, R. B. Moodie, and K. Schofield, *ibid.*, 1 (1969).

indicate that, in this solvent, the rate of nitration does not increase as expected with additional activating substituents but reaches a limit at about 40 times the reactivity of benzene. From the reactivity of toluene and the additivity principle, *p*-xylene would be expected to be more reactive than benzene by a factor of 50; *m*-xylene, by a factor of 400; and mesitylene, by a factor of 16,000.

The limiting rate of nitration is interpreted by these authors as the rate-determining formation of an encounter pair between the nitronium ion and the aromatic substrate (written here as ArH·NO₂⁺). The nitration reaction of Scheme I is expanded by Coombs, *et al.*,¹⁵ as



The rate coefficient of such an encounter reaction when calculated using the concentrations of the reacting species should be related to the viscosity of the solvent (η) by the equation¹⁷ $k_{\text{en}} = 8RT/3000\eta$; this gives $k_{\text{en}} = 6 \times 10^8 \text{ mole}^{-1} \text{ sec}^{-1} \text{ l.}$ for reactions at 25° in 68.3% sulfuric acid.¹⁵ The value¹⁵ obtained from the rate of nitration of benzene under these conditions based on the estimated concentration of nitronium ions is $4.2 \times 10^6 \text{ mole}^{-1} \text{ sec}^{-1} \text{ l.}$ It is reasonable therefore that the rate of nitration of benzene should differ from the limiting encounter rate by about two orders of magnitude.

Other evidence for this limiting encounter rate in the reaction of aromatic substrates with nitronium ions comes from the nitration of certain amines in concentrated sulfuric acid.¹⁸ Weakly basic amines, such as *p*-nitroaniline, then undergo nitration through the neutral molecule with a rate coefficient (based on the

(16) The concentration of the nitronium ion in these solutions is very low and so the reaction rate is slow enough to be followed by normal kinetic methods. The problem of reaction during the mixing of the reagents does not then arise. The concentration of the aromatic substrate is also low; the formation of the nitronium ion is therefore not rate limiting.

(17) E. A. Moelwyn-Hughes, "The Kinetics of Reactions in Solution," 2nd ed, Oxford University Press, London, 1947, Chapter 8.

(18) S. R. Hartshorn and J. H. Ridd, *J. Chem. Soc. B*, 1068 (1968).

Table IV
Kinetic Equation for Nitration at a Given Acidity^a
Rate = $k_1 k_2 k_3 [\text{ArH}] [\text{HNO}_3] / \{k_{-1}(k_3 + k_{-2}) + k_2 k_3 [\text{ArH}]\}$

Conditions	$k_{-1} \ll k_2 k_3 [\text{ArH}] / (k_3 + k_{-2})$	$k_{-1} \gg k_2 k_3 [\text{ArH}] / (k_3 + k_{-2})$	$k_3 \ll k_{-2}$
Rate	$k_1 [\text{HNO}_3]$	$(k_1 k_2 / k_{-1}) [\text{ArH}] [\text{HNO}_3]$	$(k_1 k_2 k_3 / k_{-1} k_{-2}) [\text{ArH}] [\text{HNO}_3]$
Rate-determining step	Formation of NO_2^+ (step 1)	Encounter of reactants (step 2)	Formation of σ complex (step 3)

^a The conditions necessary to make the individual steps of Scheme II rate determining and the corresponding kinetic forms are also given.

concentrations of the free amine and the nitronium ion equal to that expected for reaction on encounter. In the nitration of *p*-nitroaniline, the observed activation energy (18.2 kcal, 98% H_2SO_4) is also close to that recently¹⁹ calculated for this process (19.1 kcal).²⁰

The evidence of a limiting encounter rate for nitration in other solvents is less clear-cut (Table III), but the spread of rates is sufficiently restricted to require an interpretation of this kind. The solvent dependence of the limiting rate with respect to the rate of nitration of benzene has been discussed by Hoggett, Moodie, and Schofield.²¹

If the second-order rate coefficient for the reaction of benzene with nitronium ions is taken as 4.2×10^6 mole⁻¹ sec⁻¹ l. (see above), then the half-life for the reaction of 0.01 *M* nitronium fluoroborate with 0.01 *M* benzene in a homogeneous solution would be *ca.* 2×10^{-5} sec. The half-life for a similar reaction with toluene would be even less. Such calculations support the view that competitive nitrations involving the addition of nitronium salts to solutions of benzene and toluene must be invalid as measurements of relative reactivity because of reaction during mixing.

Present Situation

There is now no reason to doubt that the normal mechanism of nitration by nitric acid in aqueous media, in nitromethane, and in acetic acid involves attack by the nitronium ion and that the relative reactivity of toluene to that of benzene is ~ 20 when the reaction stage leading to the σ complex is rate determining. The mechanism of nitration by nitric acid in acetic anhydride presents special problems,^{4b} and most recent authors^{8, 22} have stressed the evidence for reaction through protonated acetyl nitrate. However, the evidence for attack by this species is not compelling, and there are certain difficulties over the formation of such a strongly acidic species in a zero-order step.^{4b} Reaction through the nitronium ion is not excluded by the information at present available.

(19) C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, **91**, 6654 (1969).

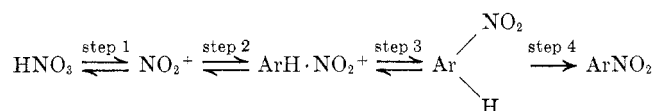
(20) In the original paper,¹⁸ the calculated activation energy was given as 13 kcal, and the discrepancy between this value and that observed experimentally caused the authors to doubt whether a simple encounter process was the best model of the rate-determining step. The temperature variation of H_0 (which enters this calculation) has since been redetermined,¹⁹ and the revised values give the activation energy quoted in the text.

(21) J. G. Hoggett, R. B. Moodie, and K. Schofield, *J. Chem. Soc. B*, **1** (1969).

(22) N. Bodor and M. J. S. Dewar, *Tetrahedron*, **25**, 5777 (1969).

The reaction path for nitration by nitric acid must now be considered to involve four possible rate-determining steps (1–4, Scheme II), of which the last is only rate determining in special structural situations.²³ If the last step is taken to be fast, then the kinetic equation for nitration at a given acidity can be obtained by applying the steady-state approximation to the intermediate nitronium ion and encounter pair ($\text{ArH} \cdot \text{NO}_2^+$). This equation is shown in Table IV together with the various inequalities which lead to the simpler forms appropriate to a single rate-determining step. In Table IV, the rate coefficients (k_1 , k_{-1}) refer to the forward and reverse reactions of the appropriately numbered stage in Scheme II.²⁴

Scheme II



This equation illustrates how the position of the rate-determining stage depends on the rate coefficients of the individual steps and on the concentration of the aromatic substrate. A slight extension of this treatment, using separate rate coefficients for attack ortho, meta, and para to a substituent in stage 3, shows that the product composition is independent of the position of the rate-determining stage, providing that the formation of the encounter pair is considered to involve the aromatic molecule as a whole, not a particular carbon atom within it. This concept of the encounter pair, as implied in the discussion of Coombes, Moodie, and Schofield,¹⁵ is, in some ways, similar to the concept of an intermediate π complex suggested in a different context by Olah, Kuhn, and Flood.⁶ Since the rate coefficient k_2 accords with that expected from diffusion theory, the term "encounter pair" is to be preferred.

The use of rates of nitration by nitric acid in discussing the electronic effects of substituents is of little value unless stage 3 of Scheme II is rate determining. It may be useful therefore to summarize the factors which can complicate such studies by introducing other rate-deter-

(23) (a) P. C. Myhre and M. Beug, *J. Amer. Chem. Soc.*, **88**, 1569 (1966); (b) H. Cerfontain and A. Telder, *Recl. Trav. Chim. Pays-Bas*, **86**, 371 (1967); (c) P. Kreienbühl and H. Zollinger, *Tetrahedron Lett.*, 1739 (1965).

(24) In deriving this kinetic equation, the forward reaction of stage 2 is treated as a second-order reaction and all other reactions as first order. This treatment involves some simplifications but should be appropriate for nitration by small amounts of nitric acid in aqueous sulfuric acid. The acidity of the medium and the activity of water would then be effectively constant throughout the reaction.

mining steps. These factors include: (a) macroscopic diffusion control: when the rate is determined by the rate of mixing the reactant solutions; (b) microscopic diffusion control: when the rate is determined by the formation of encounter pairs in homogeneous solution; (c) limitation of rates of nitration by the rate of formation of nitronium ions; (d) contributions from other mechanisms of nitration, especially from nitration *via* nitrosation.

Factors a, b, and d can complicate competitive nitrations and factors b, c, and d can complicate kinetic

studies. Nitration *via* nitrosation is often very important with highly reactive substrates.^{15,21,25} Another possible complication comes from the incursion of addition-elimination reactions,⁹ for these may deflect some of the initial σ complex to products without nitro groups. Thus, although recent studies have helped to reestablish the importance of nitration through the nitronium ion, they have shown that the interpretation of the relative rates obtained requires considerable care.

(25) J. G. Hoggett, R. B. Moodie, and K. Schofield, *Chem. Commun.*, 605 (1969).

Conformational Analysis of Tris(ethylenediamine) Complexes

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The principles of conformational analysis were first applied to the stereochemistry of coordination complexes in a seminal paper by Corey and Bailar¹ published in 1959. These authors recognized that coordination of a ligand such as ethylenediamine² with a metal ion forms a five-membered chelate ring with many of the stereochemical characteristics of cyclopentane or cyclohexane. The ring is twisted or puckered so that the hydrogen atoms on adjacent atoms are in a staggered or gauche conformation. This confers an approximately axial or equatorial character to each hydrogen atom with respect to the plane of the metal ion and two nitrogen atoms (Figure 1).

When the bidentate ligand is propylenediamine,² in which a methylene hydrogen atom is replaced by a methyl group, the conformer with the methyl group equatorial is preferred, just as in methylcyclohexane. The conformational preference is probably much greater in the metal complex than in cyclohexane since there are steric interactions in the complex with other ligands about the metal ion whereas in cyclohexane there are only 1,3 interactions with hydrogen atoms.

An additional feature of the stereochemistry of metal complexes is absent in cyclohexanes. Steric interactions *between* the ligands in a tris(ethylenediamine) complex lead to preferred conformations for the chelate rings. Octahedral complexes of three bidentate ligands exist as optical isomers differing in the configuration of the three rings about the metal ion, designated Δ or Λ according to the relative helicity of any pair of chelate rings³ (Figure 2). Moreover, each ligand can adopt a δ or λ conformation defined by the helicity

of the carbon-carbon bond relative to the plane of the nitrogen atoms and metal ion (Figure 1).

Examination of interactions between the ligands indicated that the most stable configuration for the Λ configuration occurs with each ethylenediamine ligand in the δ conformation, designated $\Lambda(\delta\delta\delta)$, while in the Δ isomer each ring is in the λ conformation, designated $\Delta(\lambda\lambda\lambda)$. These *enantiomers* were designated as parallel or *lel* configurations since the carbon-carbon bond of each ligand is approximately parallel to the threefold axis of the complex. Since inversion of each ligand from its stable conformation results in an increase in interligand repulsions, estimated⁴ at approximately 0.6 kcal mole⁻¹ ligand⁻¹, the relative enthalpies of the complexes are $\Lambda(\delta\delta\delta) < \Lambda(\delta\delta\lambda) < \Lambda(\delta\lambda\lambda) < \Lambda(\lambda\lambda\lambda)$.⁴ Statistical and other entropy effects were not explicitly considered. It was recognized that solvation effects might differ among the various configurations and lead to a modification of the relative energies estimated from intramolecular interactions alone.

These ideas are consistent with the crystal structure⁵ of tris(ethylenediamine)cobalt(III) chloride, which contains the $\Lambda(\delta\delta\delta)$ isomer predicted to be most stable, and with the contemporary studies of Dwyer and his associates⁶ on the relative abundance of isomers of cobalt-amine complexes in solution. Assuming that the methyl group of a coordinated propylenediamine ligand is almost exclusively equatorial, the λ conformation is formed with (-)-propylenediamine, which

(4) Only the conformations of the ligands in the Λ configuration will be given. Since enantiomers have the same free energy and give identical nmr spectra in the absence of an optically active environment, only one configuration will be specified for $M(en)_3$ complexes, although in the nmr studies both Δ and Λ configurations were present in solution, *i.e.*, $\Lambda(\delta\delta\lambda)$ implies that $\Delta(\lambda\lambda\delta)$ was also present.

(5) K. Nakatsu, M. Shiro, Y. Saito, and H. Kuroya, *Bull. Chem. Soc. Jap.*, **30**, 158 (1957).

(6) F. P. Dwyer, F. L. Garvan, and A. Shulman, *J. Amer. Chem. Soc.*, **81**, 290 (1959); F. P. Dwyer, T. E. MacDermott, and A. M. Sargeson, *ibid.*, **85**, 2913 (1963).

(1) E. J. Corey and J. C. Bailar, Jr., *J. Amer. Chem. Soc.*, **81**, 2620 (1959).

(2) Ethylenediamine = 1,2-diaminoethane = en; propylenediamine = 1,2-diaminopropane = pn.

(3) *Inorg. Chem.*, **9**, 1 (1970).