1265. *Substituent Effects of Positive Poles in Aromatic Substitution. Part I. The Nitration of the Anilinium Ion in 90—100% Sulphuric Acid*

By Madeline Brickman and J. H. Ridd

The rate profile for the nitration of aniline in concentrated sulphuric acid shows that the main reaction is between the nitronium ion and the anilinium ion: in 98% sulphuric acid, the contribution of reaction through the free amine is negligible. This conclusion is supported by the consideration of encounter rates, by a study of the reaction in deuterosulphuric acid, and by the effect of a *para*-chloro-substituent. The products of nitration in 98% sulphuric acid show that the reactivity of the *para*-position in the anilinium ion then slightly exceeds that of one *meta*-position.

The substituent effects of positive poles in aromatic nitration were last investigated in detail about thirty-five years ago [1] as part of the development of the electronic theory of organic chemistry. This early investigation was limited to the products obtained and, although some details of the reaction rates have since become available,[2,3] there has been no attempt at a comprehensive survey. The present study is intended to provide quantitative information concerning a number of these substituent effects by combining kinetic studies with an examination of the isomer ratios obtained.

These first two Papers are concerned with the positive poles obtained by successively replacing the hydrogen atoms of the $-N^+H_3$ group by methyl groups. Any study of the substituent effects of protonated poles in aromatic nitration must necessarily be preceded by an examination of the reaction mechanism, for the speed of proton-transfer reactions implies that substitution can, in principle, occur through the neutral substrate as well as its conjugate acid. This first Paper is therefore concerned with the mechanistic problem: the second Paper deals with the relative substituent effects obtained. Subsequent Papers will deal with the substituent effects of other positively charged elements.*

(1) *Products.*—The nitration of aniline in concentrated sulphuric acid was first studied in detail by Holleman and his co-workers; [7] they found the reaction to be almost quantitative and to give about equal amounts of the *meta*- and *para*-substituted products together with a trace of *ortho*-substitution. The product composition was not very sensitive to the conditions of nitration. Rather similar results, but with more *ortho*–*para* substitution were obtained at slightly lower acidities by Hughes and Jones.[8]

This product composition has occasioned little comment, probably because it has been attributed to the concurrent reaction of the conjugate acid (giving the *meta*-compound) and the free amine (giving the *para*-compound). If this were the correct explanation, the *m*/*p* ratio should be a marked function of acidity, although the variation of this ratio might be partly masked under preparative conditions by the buffering action of the high concentration of reactants. To simplify the interpretation, the product composition has been re-investigated using very low concentrations of the reactants (*ca.* 10^{-2}M). The analysis of the reaction product has been based on the different ultraviolet spectra of the three

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* The material of these two Papers and some of the material to be published later has formed the subject of two preliminary Notes [4,5] and of a lecture given at the Warsaw Symposium on Nitro-compounds [6] (September 1963).

[1] C. K. Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell, London, 1953, ch. 6.

[2] T. G. Bonner, F. Bowyer, and Gwyn Williams, *J.*, 1952, 3274.

[3] R. J. Gillespie and D. G. Norton, *J.*, 1953, 971.

[4] M. Brickman, S. Johnson, and J. H. Ridd, *Proc. Chem. Soc.*, 1962, 228.

[5] J. H. Ridd and J. H. P. Utley, *Proc. Chem. Soc.*, 1964, 24.

[6] Proceedings of the International Symposium on Nitro-compounds. Published as a Supplement to *Tetrahedron*, 1964, p. 43.

[7] A. F. Holleman, J. C. Hartogs, and T. van der Linden, *Ber.*, 1911, **44**, 704.

[8] E. D. Hughes and G. T. Jones, *J.*, 1950, 2678.

nitro-compounds in feebly alkaline media. Over the range 90—100% sulphuric acid, the concentration of the *ortho*-nitro-compound appeared too small to be estimated in this way and its concentration is probably below 2%. The spectrophotometric results are given in Table 1 together with those obtained by Hughes and Jones.[8]

The results show that there is some dependence of the product composition on the acidity of the medium but that this is far less than would be expected if the *meta*- and *para*-substituted products derived only from substitution in the conjugate acid and free amine respectively. The further analysis of these results requires a knowledge of the corresponding variation in the overall reaction rate and is therefore deferred to section (3).

TABLE 1

Products of nitration of aniline in concentrated sulphuric acid at 25°

H_2SO_4 (%)	85 *	89·4	92·4	94·8	96·4	98·0	100
ortho (%)	6	3	—	—	—	—	—
meta (%)	34	45	53	57	58	62	64
para (%)	59	52	47	43	42	38	36

* Taken from experiments under preparative conditions at 10° (ref. 8).

(2) *Kinetics*.—The rate of nitration of aniline has been followed by the spectrometric examination of neutralised samples of the reaction mixture. At a given acidity, the reaction is of the first order with respect to the stoicheiometric concentrations of both reactants and follows equation (1).

$$\text{Rate} = k_2\,[\text{amine}]\,[\text{nitric acid}] \qquad (1)$$

The variation in the values of k_2 at a given acidity is somewhat greater than expected but the results (Table 2) show a scatter of about $\pm 5\%$ rather than a definite trend; it is clear that equation (1) is essentially obeyed. The variation of k_2 with the concentration of sulphuric acid is illustrated in Table 3 together with the variation of the corresponding rate coefficients calculated for substitution at the *para*-position (k_p) and at one *meta*-position (k_m). The values of k_p and k_m are calculated by the use of the product compositions in Table 1. The results in Table 3 are mean values based on the rate coefficients for a number of kinetic runs at each acidity.

TABLE 2

Dependence of the rate of nitration (k_2, mole^{-1} sec.$^{-1}$ l.) on the concentrations of the reactants

Sulphuric acid = 96·4% 10^4[Aniline]	Temperature = 25·05° 10^4[Nitric acid]	k_2 (eqn. 1)	Sulphuric acid = 96·4% 10^4[Aniline]	Temperature = 25·05° 10^4[Nitric acid]	k_2 (eqn. 1)
4·95	4·31	1·13	6·60	7·18	1·09
4·95	2·87	1·05	8·25	7·18	1·04
3·30	2·87	1·08	6·60	5·75	1·14
6·60	2·87	1·02	6·60	4·31	1·10
3·30	4·31	1·10	8·25	5·75	1·06
				Mean k_2 =	1·08

TABLE 3

Dependence of the rate of nitration at 25·05° on the concentration of sulphuric acid

% H_2SO_4	89·4	92·4	94·8	96·4	98·0	100
k_2 (eqn. 1)	2·61	2·01	1·47	1·08	0·668	0·655
k_m	0·587	0·533	0·419	0·313	0·207	0·210
k_p	1·36	0·945	0·632	0·454	0·254	0·236

All rate coefficients in mole^{-1} sec.$^{-1}$ l.

The effect of a change in the solvent from sulphuric acid to deuterosulphuric acid is illustrated in Table 4. This solvent change replaces the $-N^+H_3$ group by the $-N^+D_3$ group. The comparison with the results for the $-N^+Me_3$ substituent was designed to separate any substituent effect deriving from this isotope exchange from the concomitant medium effect. The agreement between the values of $k_2{}^A/k_2{}^B$ in the two media shows that, at this acidity, the replacement of the N–H protons by deuterons has no significant effects on the reaction rate; this replacement also appears to have no marked effect on the orientation of the substitution.

These experiments were carried out on a smaller scale than the other kinetic runs and were designed to show the presence of any large isotope effects of the magnitude associated with acid–base equilibria and the heterolysis of N–H bonds; the accuracy is not sufficient for the discussion of small secondary isotope effects.

TABLE 4

Comparison of the rate and product composition for nitration in sulphuric acid and deuterosulphuric acid at 25·05° (both containing 11·4 moles % of H_2O or D_2O)

	PhN^+H_3			PhN^+Me_3	
	$k_2{}^A$ (eqn. 1)	*meta* (%)	*para* (%)	$k_2{}^B$ (eqn. 1)	$k_2{}^A/k_2{}^B$
H_2SO_4 *	0·83	61	39	0·013	64
D_2SO_4 †	0·99	58	42	0·015	66

* The rate coefficient and product composition for the nitration of aniline in sulphuric acid are interpolated from the data in Tables 1 and 3. The corresponding rate coefficient for the nitration of the phenyltrimethylammonium ion is taken from ref. 3. † Atom fraction deuterium = 0·92.

TABLE 5

Comparison of the rate of nitration at 25° of the *p*-chloroanilinium ion and the *p*-chlorophenyltrimethylammonium ion

H_2SO_4 (%)	*p*-$Cl{\cdot}C_6H_4N^+H_3$ ($k_2{}^C$)	*p*-$Cl{\cdot}C_6H_4N^+Me_3$ ($k_2{}^D$) (ref. 3)	$k_2{}^C/k_2{}^D$
91·0	0·231	0·0058	40
99·5	0·056	0·0015	37

Rate coefficients in mole^{-1} sec.$^{-1}$ l.

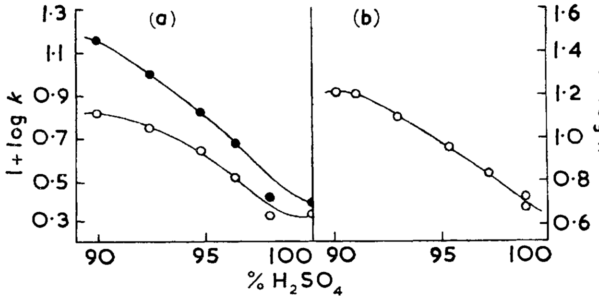
The rate of nitration of the *p*-chloroanilinium ion is compared with that of the *p*-chlorophenyltrimethylammonium ion in Table 5. The relative reaction rate is not a significant function of acidity.

(3) *Mechanism.*—The following discussion is restricted to a single question: to what extent can the kinetic results be attributed to the direct nitration of the anilinium ion? It is convenient to consider the question as involving first a simple distinction between reaction through the anilinium ion and reaction through the small equilibrium concentration of the free amine. There are then four distinct mechanistic criteria that lead to the same conclusion. The first two criteria involve the reasonable assumption that aniline behaves as a Hammett base even in highly acidic media.

First, consider the evidence from the rate profile. Under the reaction conditions, the aniline is almost entirely present as the anilinium ion; hence, if the anilinium ion were the effective reactant, the rate profile should be similar to that of the phenyltrimethylammonium ion. The values of k_m and k_p from Table 3 are compared in the Figure with those of Gillespie and Norton[3] for the *meta*-nitration of the phenyltrimethylammonium ion (after correction for the amount of *para*-substitution now known to be present). The substrates differ considerably in reactivity (cf. Part II, following Paper) and so the two logarithmic scales are displaced but the medium effects on all three reactions are very similar. The similarity is most marked for the two *meta*-substitutions and there is therefore no reason to believe that the formation of *m*-nitroaniline occurs other than through the anilinium ion.

The slope for substitution at the *para*-position is slightly greater than that for substitution at the *meta*-position; this necessarily follows from the change in the isomeric proportions listed in Table 1. However, the difference is far too slight to indicate that substitution at the *para*-position comes simply from a reaction of the free amine. Thus, in changing the acidity from 90 to 98% sulphuric acid, the value of h_0 and hence also that of $[ArNH_2]/[ArN^+H_3]$ changes by a factor [9] of 31; over the same range the *p*/*m* ratio changes by a factor of less than 2. The *p*/*m* ratio clearly fails to reflect the relative amounts of free amine and protonated amine in the medium. Much, if not all of the *para*-substitution appears therefore to come from a reaction of the protonated amine.

From this mechanistic criterion, it is still possible to attribute the greater slope of the plot for *para*-substitution to the incursion of some reaction through the free amine as the acidity is decreased. The above arguments concerning acidity functions then imply that the reaction through the free amine must be responsible for less than half of the *para*-substitution in 90% sulphuric acid and less than 2% of that in 98% sulphuric acid. The rate profile therefore suggests that the results in 98% sulphuric acid can be taken as characteristic of reaction through the anilinium ion.



The rate profiles for the *meta*-nitration (open circles) and *para*-nitration (dots) of the anilinium ion (a) compared with that for the *meta*-nitration of the phenyltrimethylammonium ion (b)

Consider next the evidence from the magnitude of the rate coefficient for substitution in 98% sulphuric acid. From the pK_a of aniline (4·6) and from the value [9] of H_0 in 98% sulphuric acid (—10·4), it follows that only one part in 10^{15} of the stoicheiometric aniline is present as the free molecule.

The rate of reaction through this small equilibrium concentration of the free amine cannot exceed the rate of encounter of aniline molecules with nitronium ions, and the rate coefficient for such an encounter reaction at this acidity is given [10] by diffusion theory as $\sim 2{\cdot}5 \times 10^8$ mole^{-1} sec.$^{-1}$ l. The corresponding stoicheiometric rate coefficient is obtained by dividing this encounter rate coefficient by 10^{15} and is therefore about $2{\cdot}5 \times 10^{-7}$ mole^{-1} sec.$^{-1}$ l. This value is about a million times less than the oberved rate coefficient for *para*-substitution recorded in Table 3; it follows therefore that the observed *para*-substitution cannot come from reaction through the small equilibrium concentration of free aniline.

The third piece of evidence comes from the effect of changing the reaction medium from sulphuric acid to deuterosulphuric acid. This change should reduce the concentration of the free amine [11] by a factor of about four and therefore should reduce also the extent of any *para*-substitution involving the free amine. No such change is observed (Table 4); indeed the trend is in the other direction. The absence of any change in the relative rate of nitration of aniline and the phenyltrimethylammonium ion in these two media (Table 4) also points against any significant contribution of reaction through the free amine. Expressed in the usual form of wt.-% sulphuric acid, the results in Table 4 refer to 97·3% H_2SO_4 and hence to the more acidic end of the range of acidities listed in Tables 1 and 3; the investigation of solvent isotope effects in nitration is currently being extended to lower acidities.

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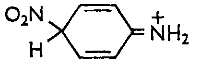
[9] M. J. Jørgensen and D. R. Hartter, *J. Amer. Chem. Soc.*, 1963, **85**, 878.

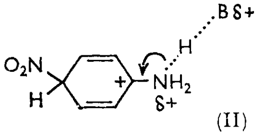
[10] M. W. Austin and J. H. Ridd, *J.*, 1963, 4204.

[11] E. Hogfeldt and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1960, **82**, 15.

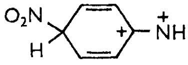
The final piece of evidence concerns the effect of a *para*-chloro-substituent. The introduction of an electron-withdrawing substituent into aniline should favour reaction through the free amine by increasing the amount of free amine in the solution. It is unlikely that this effect would be outweighed by the corresponding reduction in the reactivity of the aromatic system for the nitronium ion would not be expected to discriminate markedly between differently substituted amine molecules (cf. the studies of R. P. Bell and his co-workers[12] on the bromination of amines). However, the results in Table 5 do not suggest that *p*-chloroaniline undergoes significant reaction through the free amine in 98% sulphuric acid for the relative reactivity of *p*-chloroaniline and the *p*-chlorophenyltrimethylammonium ion is not greatly changed when the acidity is reduced from 99·5 to 91% sulphuric acid. The ultraviolet spectrum of the product shows that reaction occurs *meta* to the amino-group; this is also consistent with reaction through the conjugate acid. Reaction through the free amine should occur *ortho* to the amino-group (cf. iodination[13]).



(I)



(II)



(III)

The above arguments all suggest that nitration through the small equilibrium concentration of molecular aniline contributes very little to the reaction rate in 98% sulphuric acid; by implication, therefore, the reactant appears to be the anilinium ion. However, this treatment of the problem as a clear distinction between two possible mechanisms is an oversimplification. The transition states corresponding to reaction through the free amine (structure I)* and the anilinium ion (structure III) can be considered as the two limiting forms of a continuous range, the intermediate states (*e.g.*, II) corresponding to partial proton transfer to a base.

The mechanistic criteria discussed above are not equivalent in the information they give on the transition state. On this matter, the encounter argument is irrelevant; it shows only that the aniline must be protonated at the time of encounter with the nitronium ion, but the proton could still be lost before or during the rate-determining stage. The evidence from the rate profile does not suggest that a base is necessary for *meta*-substitution, but the somewhat greater slope of the rate profiles for *para*-substitution could be interpreted as a consequence of partial proton loss in the transition state. Probably the most significant evidence comes from the replacement of $-\mathrm{N}^+\mathrm{H}_3$ by $-\mathrm{N}^+\mathrm{D}_3$ [section (2)]; this change has no marked effect on the orientation or on the reaction rate. For this reason, and for a further reason discussed in Part II, we regard the transition state of the nitration in 98% sulphuric acid as involving no significant heterolysis of the N–H bonds of the anilinium ion.

From this conclusion, and from the orientational results in Table 1, it appears that the substituent effect of the $-\mathrm{N}^+\mathrm{H}_3$ group in 98% sulphuric acid leads to almost equal deactivation at the *meta*- and *para*-positions.

EXPERIMENTAL

Materials.—AnalaR aniline was dried over magnesium sulphate and distilled from powdered zinc. Laboratory grade *p*-chloroaniline was recrystallised from alcohol and distilled under reduced pressure. 4-Chloro-2-nitroaniline (m. p. 115—116°) was obtained as a Hammett indicator from Aldrich Chemical Co., and was not further purified. 4-Chloro-3-nitroaniline was prepared by the method of Morgan and Porter[14] and, recrystallised from water, had m. p. 102°. The other aniline derivatives were of Laboratory Reagent grade and were recrystallised.

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* For simplicity we represent these transition states by the conventional Wheland structures although the charge transfer from the nitronium ion to the aromatic ring is unlikely to be complete.

[12] R. P. Bell and E. N. Ramsden, *J.*, 1958, 161.

[13] E. Berliner, *J. Amer. Chem. Soc.*, 1956, **78**, 3632.

[14] G. T. Morgan and J. W. Porter, *J.*, 1915, 645.

Sulphuric acid (AnalaR, *d* 1·84) was standardised by titrating a known weight with aqueous sodium hydroxide. The diluted solutions required as reaction media were also standardised in this way. The deuterosulphuric acid was prepared by distilling sulphur trioxide into deuterium oxide (Norske-Hydro, 99·81% D_2O) following the method of Solomons.[15] The product, standardised as above, contained 97·3% D_2SO_4. Nitric acid (AnalaR, *d* 1·42) was standardised by diluting and titrating a known volume with standard sodium hydroxide.

Reactions.—Preliminary experiments,[16] based on the infrared spectrum of the reaction product, indicated that a mixture of *m*- and *p*-nitroaniline was formed over the range 90—100% sulphuric acid; in concentrations of sulphuric acid below 90%, some *o*-nitroaniline appeared also to be present.

In the main experiments, solutions of aniline and nitric acid were prepared separately in sulphuric acid of the required composition and were brought to the required temperature (usually 25·05°). After mixing, aliquot portions (2 or 5 ml.) were withdrawn at suitable times and added to a sufficient volume of aqueous sodium hydroxide (2N) to make the final medium slightly alkaline. After further dilution, where necessary, such solutions were examined in a Unicam S.P. 500 spectrophotometer. The spectra of such solutions are fortunately insensitive to small changes in the pH of the slightly alkaline media. These solutions were then used for both the product analyses and the kinetic studies. Ancillary experiments established that the rate of dinitration was too slow to be significant and that the mixture of *m*- and *p*-nitroanilines was stable under the reaction conditions.

For the product analyses, the spectrum of the sample corresponding to complete reaction was plotted over the range 2700—4000 Å. The products from sulphuric acid concentrations above 90% were treated as mixtures of *m*- and *p*-nitroaniline. The optical density of the reaction product at 3025 Å, where the *meta*- and *para*-isomers have equal extinction coefficients, was as expected for 100% reaction. The relative amounts of *meta*- and *para*-substitution were accordingly calculated on the assumption of complete reaction using the optical density at 3800 Å where the extinction coefficients of the two isomers are very different. As a check, the expected spectrum for this isomer ratio was calculated over the range 2700—4000 Å and compared with that observed, allowance being made for the absorption by unchanged aniline. The agreement was very satisfactory for the products from the more acidic media but, as the concentration of sulphuric acid approached 90%, the observed optical density at about 2800 Å rose by a few per cent above the expected values. This may result from the formation of some *o*-nitroaniline. The deviation was more marked in the product from 89·4% sulphuric acid and the fit of the theoretical and experimental curves was then improved by assuming the presence of 3% of *o*-nitroaniline.

These calculations require a knowledge of the absorption spectrum of pure *o*-, *m*-, and *p*-nitroaniline under the above conditions. Standard solutions of these substances in concentrated sulphuric acid were therefore neutralised and diluted in the same way as used for the reaction mixtures.

The kinetics were followed from the increase in the optical density at the absorption maximum (*ca.* 3800 Å). Since the reactants do not absorb at this wavelength, the combined concentration of the nitroanilines was taken as proportional to the optical density and, from the above arguments, the concentration of nitroanilines in the " infinity " samples was equated to the lower of the two initial concentrations of the reactants. The resulting calculation is illustrated by the kinetic run in Table 6.

TABLE 6

Nitration of aniline in 92·4% sulphuric acid at 25°

	10^4[Amine] = 4·025M				10^4[Nitric acid] = 1·45M		
Time (sec.)	O.D.*	10^4x †	k_2 ‡	Time (sec.)	O.D.*	x †	k_2 ‡
300	0·048	0·326	2·27	1800	0·153	1·04	2·09
600	0·080	0·543	2·08	2400	0·163	1·105	1·81
900	0·108	0·733	2·06	3600	0·208		
1200	0·129	0·877	2·24	∞	0·214	Mean	2·09

* At 3800 Å after diluting by a factor of 18·5. † Combined concentrations of *meta*- and *para*-nitroanilines (M). ‡ k_2 in mole^{-1} sec.$^{-1}$ l.

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[15] C. Solomons, Ph.D. Thesis, London, 1955.

[16] Cf. M. R. Brickman, Ph.D. Thesis, London, 1963.

The kinetic runs in the deuterated medium were carried out by using a calibrated microsyringe to add small volumes of each reactant solution (*ca.* 0·25 ml.) in protiosulphuric acid to 10 ml. of deuterosulphuric acid. The solution of aniline was added first, to give time for the equilibration of the *N*–H protons with the deuterons of the medium. After the addition of the solution of nitric acid, samples (1 ml.) were extracted and neutralised as described above.

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