

SUBSTITUENT EFFECTS OF POSITIVE POLES IN AROMATIC NITRATION¹

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This paper is concerned with a re-examination of the effect of such positive poles as the $-NMe_3^+$ group on the rate and orientation of nitration. The work has been carried out at University College, London, the initial experiments by Miss Sheena Johnson and the bulk of the material by Dr. Madeline Brickman and Dr. J. H. P. Utley. It is convenient to consider first the $-NH_3^+$ group as in the anilinium ion.

The nitration of aniline under preparative conditions in concentrated sulphuric acid has long been known to give a mixture of *meta*-nitroaniline and *para*-nitroaniline in almost equal amounts [4].² This product composition could be considered to arise from the concurrent nitration of the protonated amine (giving the *meta*-compound) and the free amine (giving the *para*-compound). However, if this were so, the *meta*-*para* ratio should be a marked function of acidity, for the extent of the protonation equilibrium is determined by the h_0 function [5] and this varies greatly with the composition of the medium.

Dr. Brickman estimated this product composition spectrophotometrically and found it to be surprisingly insensitive to the acidity of the medium (Table 1): the

Table 1

The nitration of aniline in concentrated sulphuric acid at 25°.

% H ₂ SO ₄	89.4	92.4	94.8	96.8	98.0	100
<i>ortho</i> %	3	—	—	—	—	—
<i>meta</i> %	45	53	57	58	62	64
<i>para</i> %	52	47	43	42	38	36

Where the percentage of *ortho* substitution is not given, it is considered to be below 2%.

meta/para ratio changes by less than a factor of 2 over the range 92.4-100%. Her results were obtained by using very low reactant concentrations (10⁻²M) so that these concentrations do not themselves modify the acidity. Since the h_0 function changes by more than a factor of 100 over the above range of acidity [5, 6], it is clear that the *meta/para* ratio is not simply proportional to the ratio of protonated amine to free amine.

The results on the product analysis can be understood if either the protonated amine gives rise to a significant amount of *para*-substitution or the free amine gives rise to a significant amount of *meta*-substitution. The relevant interpretation can be determined by kinetic studies.

At a given acidity, the nitration of aniline obeys second order kinetics: first order with respect to the stoichiometric concentration of the amine and first-

order with respect to that of the nitric acid. Almost the whole of the aniline is protonated at the acidities listed in Table 1 and hence, if the reaction is limited to the protonated amine, the variation of these second-order rate coefficients with acidity should be similar to that for a corresponding quaternary ion, e.g., the trimethylanilinium ion. The rate coefficients for such nitrations have a maximum value in about 90% sulphuric acid and then decrease by a factor of about four over the range 90-100% sulphuric acid [7]. In Fig. 1, the rate profiles for *meta*- and *para*-nitration of the anilinium ion are compared with those obtained by Gillespie and Norton [7] for *meta*-substitution in the trimethylanilinium ion.³ The reactions differ considerably in speed and so the logarithmic scales are displaced but the medium effects for the two *meta*-substitutions are very similar. The substitution at the *para*-position in the anilinium ion has a slightly greater medium effect than that at the *meta*-position: this may reflect the incursion of some reaction through the free amine in 90% sulphuric acid or may arise from the different charge distribution in the transition state for substitution at the *para*-position. Medium effects on the rate of nitration over the range 90-100% sulphuric acid are sometimes about twice that for the trimethylanilinium ion [7, 8]. Both rate profiles therefore are consistent with a reaction of the conjugate acid and both differ greatly from those expected for the reaction of the neutral aniline molecule. Even if the neutral molecule contributes in part to the observed reaction rate in 90% sulphuric acid, this contribution would become negligible in 98% sulphuric acid. The isomer proportions observed in 98% sulphuric acid therefore can be attributed to a reaction of the anilinium ion and the results in Table 1 show that the *para*-position is then slightly more reactive than one *meta*-position.

There is a further, independent, kinetic argument that leads to the same conclusion. From the pK_a of the anilinium ion (4.6) and the value [6] of H_0 in 98% sulphuric acid (-10.4), the fraction of the stoichiometric aniline present as the free amine in 98% sulphuric acid should be about 1/10¹⁵. The rate of reaction of the aniline molecules with nitronium ions cannot be any faster than their rate of diffusion together and in 98% sulphuric acid the second-order rate coefficient for a diffusion controlled reaction [9] should be about 2.5 x 10⁸ mole⁻¹ sec.⁻¹. When this value is

¹ Some of these results have already been published [1, 2] and others will become available shortly [3]; the present discussion however is more detailed than that given previously.

² Numbers in brackets refer to Literature Cited.

³ The figures in ref. 7 have been corrected to allow for the small amount of *para*-substitution now known to be present. This amount of *para*-substitution in the trimethylanilinium ion has been assumed to be independent of the acidity of the medium.

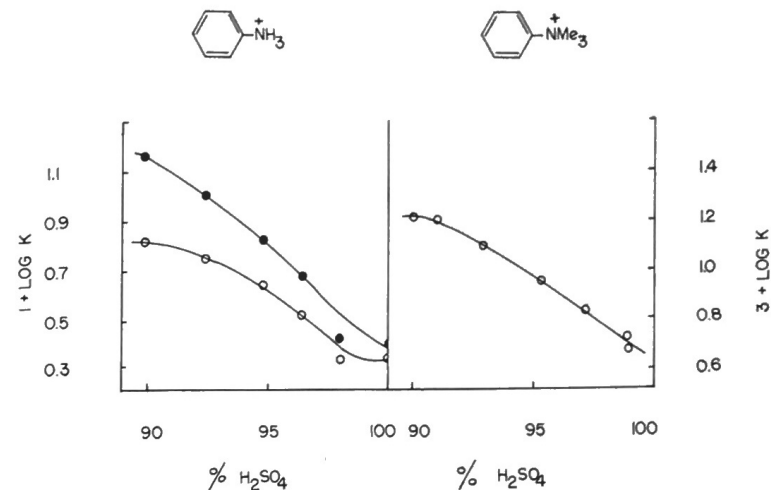


Fig. 1. Rate profiles for nitration at the *para*-position and at one *meta*-position in the anilinium ion compared with that for one *meta* position in the trimethylanilinium ion.

multiplied by the fraction of the stoichiometric amine present as the free molecule, the resultant second-order rate coefficient⁴ becomes 2.5 x 10⁻⁷ mole⁻¹ sec.⁻¹. This is about a million times less than the observed rate coefficient for the *para*-substitution in 98% sulphuric acid. This supports the view that the *para*-substitution involves a reaction of the anilinium ion.

Dr. Brickman then studied the *N*-methyl and *N,N*-dimethylanilinium ions obtaining very similar rate profiles but with lower percentages of *para*-substitution in 98% sulphuric acid ($-NH_2Me^+ \rightarrow 30\%$ *para*; $NHMe_2^+ \rightarrow 22\%$ *para*). Extrapolation from these figures suggested that the trimethylanilinium ion should give about 14% of substitution in the *para*-position. The most frequently quoted result for this ion is that of Vorländer and Siebert [11], who claimed that only *meta* substitution occurs; however, more recently, Nesmeyanov and his co-workers [12] have isolated 4% of *para*-nitrodimeylaniline after heating the iodide of the nitrated product. In our preliminary communication on this work [1], we reported a study of the infra-red spectrum of the reaction product together with an examination of the ultraviolet spectrum of the mixture of *para*- and *meta*-nitrodimeylanilines obtained by Nesmeyanov's method from the nitrated product; both approaches suggested that about 11% *para*-substitution occurred in the nitration. More recently, Dr. Utley has

developed the use of ion-exchange chromatography for the separation of the *meta* and *para*-nitrotrimethylanilinium ions. His results are illustrated in Fig. 2 and

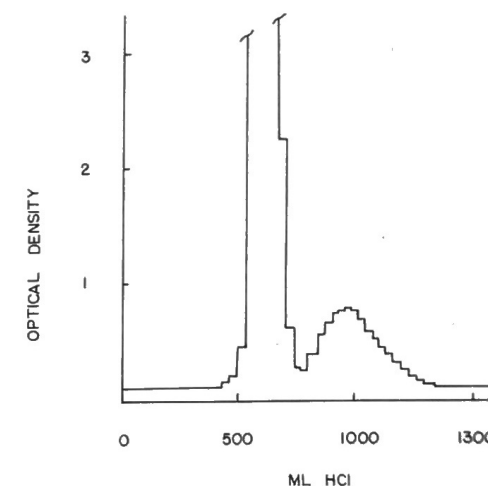


Fig. 2. Ion exchange separation of products from a nitration of the trimethylanilinium ion.

show that the percentage of *para*-substitution is 11.1 ± 0.6. This result, and those obtained by Dr. Brickman for the protonated ions are collected in Table 2, together with the corresponding rate coefficients.

These rate coefficients show that the replacement of

⁴ This treatment of the free amine as a separate species assumes that the ionisation $ArNH_2 = ArNH_3^+ + H^+$ is slow in comparison with the time of a molecular encounter between a nitronium ion and an anilinium ion. This assumption is supported by the n.m.r. spectrum, for, in concentrations of sulphuric acid above 60%, the exchange of the *N*-H protons is slow enough to contribute a separate peak to the spectrum [10]. The possible effect of the nitronium ion on the rate of ionisation is considered later in the form of an S_E2' substitution.

N-H by N-Me leads to a steady decrease in the reactivity at both the *meta*-position and the *para*-position. To see this decrease in perspective it is useful to relate these reaction rates to that of the nitration of benzene. These substrates are too deactivated to be compared

Table 2

Rate coefficients (mole⁻¹ sec.⁻¹) and the percentage of *para*-substitution for nitration in 98% sulphuric acid at 25°.

	PhNH ₃ ⁺	PhNMeH ₂ ⁺	PhNMe ₂ H ⁺	PhNMe ₃ ⁺
k _p	0.26	0.064	0.0095	0.0014*
k _m ^x	0.21	0.074	0.0163	0.0055**
% <i>para</i> 38	30	22	11	

*Calculated for one *meta* position.

**Calculated from the orientational studies of Dr. Utley and the kinetic results in ref. 6.

directly with benzene but an indirect comparison is possible by the use of compounds of intermediate reactivity. The necessary information is available in the literature [9] and the results in terms of partial rate factors are collected in Table 3. The relative values in Table 3 are known with greater accuracy than are the

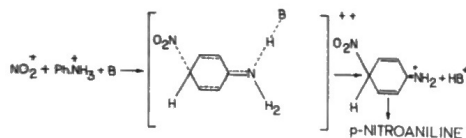
Table 3

Partial rate factors for nitration in 98% sulphuric acid.

	PhNH ₂ ⁺	PhNMeH ₂ ⁺	PhNMe ₂ H ⁺	PhNMe ₃ ⁺
10 ⁴ k _{meta}	179	62.9	13.9	4.67
10 ⁴ k _{para}	220	54.4	8.07	1.15

absolute magnitudes for some error is necessarily introduced in estimating the exact deactivation of such unreactive substrates. These partial rate factors show that the differences in the reactivity of these ions are small in comparison with the strong deactivating effect of the positive poles.

Before considering the reactivity of these ions in detail it is necessary to decide whether the higher reaction rates observed with the protonated poles come from different substituent effects on the same reaction path or from the incursion of some new reaction path depending on the mobility of the -N-H protons. Such a path might involve a type of S_E2' reaction as illustrated below.



Two pieces of evidence suggest that the first interpretation is correct. First, the successive replacement of the N-methyl groups by hydrogen atoms leads to a steady increase in the rate of substitution at both the *meta*- and the *para*-position. If the nitration of the systems with protonated poles involved a new mechanism of substitution, the main increase in reactivity should be associated with the replacement of the first methyl group by hydrogen. Secondly, the results in Table 4 show that the replacement of sulphuric acid

Table 4

Relative rates of nitration of the anilinium ion (A) and the trimethylanilinium ion (B) in sulphuric acid and deuteriosulphuric acid at 25°. Each solvent contained 11.4 moles % of water (H₂O or D₂O respectively).

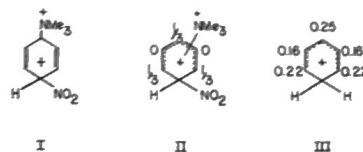
	H ₂ SO ₄ [*]	D ₂ SO ₄ ^{**}
k _A /k _B	63.8	66.0

*Taken in part from the data in ref. 6.

**Atom fraction of deuterium = 0.92.

by deuteriosulphuric acid does not change the relative rates of nitration of the anilinium ion and the trimethylanilinium ion. These results were carried out on a smaller scale than the other kinetic experiments and were designed to detect large isotope effects; they are being repeated with greater accuracy and at lower acidities.

The most surprising feature of the results in Tables 2 and 3 concerns the similarity of the rates of substitution at the *meta*- and *para*-positions. In recent years the supposedly powerful *meta*-directing effect of positive poles frequently has been rationalized in terms of the electrostatic repulsion between the positive charges in structure (I). A related semi-quantitative approach has involved the difference in the electrostatic interaction of the transition state charge distribution (II)



with a positive pole in the *meta* and *para* positions; this calculation has suggested that the transition states for *meta* and *para* substitution can differ by as much as 10 kcal [13]. For several reasons, it is now possible to see that this calculation could considerably overestimate the difference involved. Thus, the charge distribution in such ions as (II) is now considered to be more evenly distributed, as illustrated by the n.m.r. results on the charge distribution in protonated hydrocarbons (e.g. III) [14]. Also, the overall deactivation of such ions as

the trimethylanilinium ion is much less than would be suggested by the electrostatic calculations carried out on structure (II); a result consistent with the modern belief that only a part of the charge on the electrophile is transferred to the benzene ring in the transition state. It seemed of interest to repeat the earlier calculations using the charge distribution shown in structure (III) and then scaling down the result until the overall deactivation (as calculated from the partial rate factors in Table 3) was correct for *meta*-substitution. The results are given in Table 5; the final difference between

Table 5

The energy of interaction of the positive pole with the charge on the benzene ring in the transition state.

	obs. ΔΔF‡ calc. ΔΔF‡ (k. cal. per mole)*			
	Structure II	Structure III	Structure III (scaled down)	
<i>meta</i> -NMe ₃ ⁺	9.94	57.0	65.3	(9.94)
<i>para</i> -NMe ₃ ⁺	10.8	66.5	69.0	10.5

† Values for standard states.

* As in previous calculations [13], a uniform dielectric constant of 2 is assumed between the positive pole and the ring.

the free energies for *meta* and *para* substitution is less than a kilocalorie. Such calculations contain too many approximations to be a useful guide to the isomer proportions, but they are of interest in showing that the electrostatic interaction associated with structure (I) does not provide an a priori reason for believing in the strong *meta*-directing effect of a positive pole.

Consider now the relative deactivating effect of the nitrogen poles in Table 3. Comparison of these phenyl derivatives with the benzyl derivatives in Table 6 shows that the greater reactivity of the anilinium ion over the

Table 6

Second-order rate coefficients (mole⁻¹ sec.⁻¹) for the nitration of benzylammonium ion and the benzyl trimethylammonium ion in aqueous sulphuric acid at 25°.

% H ₂ SO ₄	PhCH ₂ NH ₃ ⁺	PhCH ₂ NMe ₃ ⁺	k _A /k _B
78.70	1.58	0.0252	63
80.05	3.72	0.0600	62

trimethyl derivatives is maintained when a -CH₂ group is introduced between the pole and the aromatic ring. The greater reactivity of the protonated ions is therefore unlikely to come mainly from N-H hyperconjugation, for it does not depend on the overlap of the N-H σ-electrons with the π-electrons of the ring.

The correct explanation almost certainly involves the

difference in the solvation of the protonated and methylated poles. The weaker electron withdrawing effect of the -NH₃⁺ pole compared to the NMe₃⁺ pole has been commented on before by Ingold and his co-workers [15] and ascribed to this cause. The most recent evidence comes from Will's [16] demonstration that the effect of an -NH₃⁺ pole on the free energy of ionisation of an anilinium ion is about 10% less than that of an -NMe₃⁺ pole. The relative effects in nitration differ by somewhat more than this but not by enough to justify a different interpretation. Presumably the close association of the -NH₃⁺ pole with the medium is effective in spreading the charge or, on the Kirkwood-Westheimer model [17], in increasing the effective dielectric constant between the pole and the ring.

The above argument accounts qualitatively for the relative rate of substitution *meta* to these positive poles but the relative rates of *para*-substitution still present some problems. One of these problems is illustrated by the comparison of the different substituents in Table 7:

Table 7

Comparison of the overall rate of nitration with the percentage of *para*-substitution.

	PhNMe ₃ ⁺	PhNH ₃ ⁺	PhCH ₂ NMe ₃ ⁺
Relative rate	1	55	2,400
% <i>para</i>	11	38	15*

The percentages of *para* substitution for PhNMe₃⁺ and PhNH₃⁺ refer to nitration in 98% sulphuric acid; that for PhCH₂NMe₃⁺ refers to 80% sulphuric acid but this should not affect the comparison for the product composition from methylated poles is believed to be relatively insensitive to changes in the medium.[†]

*Not yet studied by ion exchange chromatography.

in reactivity the anilinium ion is intermediate between the two methylated ions but this is not true for the extent of *para* substitution. This tendency of protonated poles to give more *para*-substitution can still be attributed to the charge-spreading associated with the solvation of the protonated poles for this should do something to equalize the effect of the pole on the 1- and 2-carbon atoms and hence at the respective *para*-positions. Another possibility would be the incursion of some hyperconjugative electron donation from the -NH₃⁺ group in the transition state [18]. Nesmeyanov and his co-workers [12] have recently stated that the nitration of the triphenyloxonium ion gives almost complete *para*-substitution: this surprising result appears to require conjugative electron donation from a positive oxygen atom in the transition state. If this can occur, then hyperconjugative electron donation from the -NH₃⁺ group has to be considered as a possibility.

Dr. Utley has extended the study of positive substituents to the phenyltrimethylonium ions of other Group V elements. This part of the work is still incomplete and is somewhat more difficult because the ease of separating the corresponding *meta* and *para*-nitro derivatives appears to decrease with an increase in the

Table 8

Comparison of the overall rates of nitration with the percentage of *para*-substitution.

Relative Rate	$-\text{NMe}_3^+$	$-\text{PMe}_3^+$	$-\text{AsMe}_3^+$	$-\text{SbMe}_3^+$
	1	4.8	38.5	5,580
% <i>para</i>	11	3	4	14*
% <i>para</i>	$-\text{CH}_2\text{NMe}_3^+$	$-\text{CH}_2\text{PMe}_3^+$	$-\text{CH}_2\text{AsMe}_3^+$	$-\text{CH}_2\text{SbMe}_3^+$
	15 ^x	>70 ^x	>64 ^x	—

*Not yet studied by ion exchange chromatography. For references, see text.

atomic weight of the positive atom. The kinetic results and the percentages of *para*-substitution are collected in Table 8, together with some results from the literature [19] concerning the related benzyl 'onium ions.

The kinetic results show that the rate of nitration increases steadily with the atomic weight of the positive atom. The direction of this effect is as expected [20], for although each positive pole carries the same formal charge, the heavier atoms should be the more polarisable and hence the more able to provide an electronic screen between the charges in the transition state. The fact that the $-\text{SbMe}_3^+$ group has little more than half the deactivating effect of the $-\text{NMe}_3^+$ group illustrates the importance of this screening effect.

The orientational results are more surprising, for the percentage of *para*-substitution appears to pass through a minimum in the series N, P, As, Sb; the earlier orientational studies [19] on the phosphorus and arsenic substituents are therefore more nearly correct. Since the stronger *meta*-directing effect of phosphorus over nitrogen is not observed in the corresponding benzyl series (Table 8), we have suggested that it stems from electron acceptance by the vacant d-orbitals of phosphorus [20]. Such interaction would give the $-\text{PMe}_3^+$ group some $-\text{M}$ character, analogous to that of the nitro-group. The percentage of *para* substitution in the nitration of nitrobenzene [21] is below 1% and so only slight electron acceptance by the $-\text{PMe}_3^+$ group would be sufficient to produce the observed orientation.

Our main conclusion is therefore that the inductive and field effects of a positive pole lead to rather similar deactivation at the *meta* and *para* positions in electrophilic substitution. This conclusion appears theoretically reasonable and is supported by the limited data available on other substitution reactions.⁵ However a

⁵ Thus the results of Pearson and his co-workers [22] suggest that the bromination of the dimethylanilinium ion gives about 30% of substitution in the *para* position; those of Brand and Rutherford [23] show that the sulphonation of the trimethylanilinium ion gives about 14% of *para*-substitution. Eaborn and Pande have shown that *meta* and *para* $-\text{NMe}_3^+$ groups have rather similar deactivating effects on the rate of protode-triethylgermylation [24].

great deal remains to be done concerning the details of these substituent effects. We are, therefore, extending our nitration studies to include other positive poles and also investigating the solvent effect on the nitration of protonated poles at lower acidities.

LITERATURE CITED

- [1] M. Brickman, S. Johnson and J. H. Ridd, *Proc. Chem. Soc.*, 1962, 228.
- [2] J. H. Ridd and J. H. P. Utley, *Proc. Chem. Soc.*, 1964, 24.
- [3] J. H. Ridd, Proceedings of Warsaw Symposium on Nitro-compounds, to be published as a supplement to *Tetrahedron*, 1964.
- [4] A. F. Holleman, J. C. Hartogs and T. van der Linden, *Ber.*, 1911, 44, 704.
- [5] M. A. Paul and F. A. Long, *Chem. Rev.*, 1957, 57, 1.
- [6] M. J. Jorgensen and D. R. Hartter, *J. Amer. Chem. Soc.*, 1963, 85, 878.
- [7] R. J. Gillespie and D. G. Norton, *J. Chem. Soc.*, 1953, 971.
- [8] P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworths, London, 1959, Chap. 5.
- [9] M. W. Austin and J. H. Ridd, *J. Chem. Soc.*, 1963, 4204.
- [10] B. N. Figgis, Personal Communication.
- [11] D. Vorländer and E. Siebert, *Ber.*, 1919, 52, 283.
- [12] A. N. Nesmeyanov, T. P. Tolstaya, L. S. Isaeva and A. V. Grib, *Doklady Akad. Nauk S.S.S.R.*, 1960, 133, 602.
- [13] J. D. Roberts, R. A. Clement, and J. J. Drysdale, *J. Amer. Chem. Soc.*, 1951, 73, 2181.
- [14] J. P. Colpa, C. Maclean and E. L. Mackor, *Tetrahedron*, 1963, 19 S2, 65.
- [15] C. K. Ingold, E. H. Ingold, and F. R. Shaw, *J. Chem. Soc.*, 1927, 813.
- [16] A. V. Willi, *Z. Phys. Chem. (Frankfurt)*, 1961, 27, 233.
- [17] J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, 1938, 6, 506.
- [18] cf. P. B. D. de la Mare, Hyperconjugation Conference, Bloomington, Pergamon Press, 1959, p. 126.
- [19] C. K. Ingold, F. R. Shaw, and I. S. Wilson, *J. Chem. Soc.*, 1928, 1280; M. R. Brickman, Ph.D. Thesis, London, 1963.
- [20] C. K. Ingold, "Structure and Mechanism in Organic Chemistry", G. Bell, London, 1953, Chap. 6.
- [21] A. F. Holleman, *Chem. Rev.*, 1925, 1, 187.
- [22] B. R. Suthers, P. H. Riggins and D. E. Pearson, *J. Org. Chem.*, 1962, 27, 447.
- [23] J. C. D. Brand and A. Rutherford, *J. Chem. Soc.*, 1952, 3927.
- [24] C. Eaborn and K. C. Pande, *J. Chem. Soc.*, 1961, 5082.