

59. *Rate-determining Factors in Certain ortho-Nitrations.*

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The relative velocities of nitration of $p\text{-X}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$ and $p\text{-X}\cdot\text{C}_6\text{H}_4\cdot\text{NMe}_3^+$ (X = Me, Bu^t, Cl, Br, and H) have been measured in sulphuric acid solution. Halogen and alkyl substituents reduce the relative velocity, $k_{\text{NO}_2}/k_{\text{NMe}_3^+}$, compared with the unsubstituted compounds, and this effect is discussed in terms of the differential interaction of the substituent with the remainder of the system. The velocity coefficients for nitration of $p\text{-Hal}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$ are in the order Br > Cl > F, and this may represent the order of electromeric polarisability of the halogen atom in these molecules.

A *p*-METHYL substituent reverses the comparative ease of sulphonation (in fuming sulphuric acid) of the systems $\text{C}_6\text{H}_5\cdot\text{NO}_2$ and $\text{C}_6\text{H}_5\cdot\text{NMe}_3^+$, the order of reactivity being $p\text{-Me}\cdot\text{C}_6\text{H}_4\cdot\text{NMe}_3^+ > p\text{-Me}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2 \gg \text{C}_6\text{H}_5\cdot\text{NO}_2 > \text{C}_6\text{H}_5\cdot\text{NMe}_3^+$. The results, at 25°, are (Brand, *J.*, 1950, 997, 1004):

$$\left. \begin{array}{l} (a) \ p\text{-Me}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2 \\ (b) \ p\text{-Me}\cdot\text{C}_6\text{H}_4\cdot\text{NMe}_3^+ \end{array} \right\} k_{(a)}/k_{(b)} = 0.8 \quad \left. \begin{array}{l} (c) \ \text{C}_6\text{H}_5\cdot\text{NO}_2 \\ (d) \ \text{C}_6\text{H}_5\cdot\text{NMe}_3^+ \end{array} \right\} k_{(c)}/k_{(d)} = 1.5$$

These figures, however, were obtained indirectly. In the media employed, the nitro-compounds were converted almost quantitatively into the conjugate ions, $\text{Ar}\cdot\text{NO}\cdot\text{OH}^+$, and it was necessary to allow for this before comparing the experimental velocities. The accuracy with which this was possible was low. The degree of conversion was, in general, too high to be measured directly and was evaluated from the ionisation constant of the nitro-compound and the acidity function of the medium. Furthermore, the relative velocity coefficients above were calculated on the assumption that the ions were unreactive and that sulphonation occurred entirely through the small, equilibrium concentration of *un-ionised* base. The kinetic evidence for this assumption was discussed in the original paper but, if it is correct, similar velocity ratios would be expected to hold for other substitution reactions. Partly as a test of this, the relative rates of nitration of systems of the same type have now been measured in 90–96% sulphuric acid. In this solvent the degree of ionisation of the nitro-compounds is negligibly small. The results have confirmed the analysis of the sulphonation experiments.

Effect of p-Substituents on the Relative Rate of Nitration of $\text{C}_6\text{H}_5\cdot\text{NO}_2$ and $\text{C}_6\text{H}_5\cdot\text{NMe}_3^+$.—The relative velocities were, for the most part, measured competitively and are collected in Table I. Relative nitration velocities are approximately independent of medium composition (Bonner, James, Lowen, and Williams, *Nature*, 1949, 163, 955) and temperature (for small differences) and the results in the table may be compared with one another directly. *p*-Nitrotoluene and *p*-*tert*-butylnitrobenzene were not completely un-ionised in the media employed, but the concentration immobilised in this way (*ca.* 3–4 moles %) was low enough to be neglected for our purpose. With the exception of nitrobenzene,

nitration occurs quantitatively in position 3, *i.e.*, *ortho* to the substituent X, if one is present.

Nitrobenzene yields about 92% of *m*-dinitrobenzene (Pounder and Masson, *J.*, 1934, 1352) and the relative velocity in Table I refers to nitration in the 3-position only. The fact that nitrobenzene and the phenyltrimethylammonium ion are nitrated at similar speeds is, of course, fortuitous, for the character of the two substituents is entirely different.

TABLE I. *Relative velocities of nitration of p-X·C₆H₄·NO₂ and p-X·C₆H₄·NMe₃⁺ in sulphuric acid.*

Substituent, X	Temp. 25°			Temp. 18°	
	H	Cl		Bu ^t	Me
Medium, % H ₂ SO ₄	90.7	90.7	89.8	95.8	95.3
<i>k</i> _{NO₂} / <i>k</i> _{NMe₃⁺}	1.7	1.1 ₅	—	0.5 ₂	0.3 ₂
	1.9 *	—	1.22 *	—	—

* Ratio of velocity coefficients (Table 2). The value for X = H in this row is from Bonner, James, Lowen, and Williams (*loc. cit.*).

The relative rate of nitration, $k_{\text{NO}_2}/k_{\text{NMe}_3^+}$, is a maximum for the unsubstituted compounds; it is lowered by halogen and alkyl substituents, and the latter produce the inversion already encountered in sulphonation. The important fact for the interpretation of this behaviour is that the halogen and alkyl substituents *both* reduce the relative rate. Because alkyl groups in all circumstances release electrons, this suggests that the explanation must be connected also with the electron-releasing properties of the halogen. The principal effect of the latter is to lower the energy of the transition state, provided the carbon atom at which substitution takes place is conjugated to the halogen. The primary factor determining the relative velocity is probably located, therefore, in the transition state of the nitration. The argument will be illustrated with reference particularly to *p*-chloronitrobenzene and the ion *p*-Cl·C₆H₄·NMe₃⁺. The structure (I; X = Cl) is known, *e.g.*, from the following dipole-moment data (in D)

$$p\text{-Cl}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2; \mu = 2.78, \text{ calc. } 2.52 : \text{ cf. } m\text{-Cl}\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2; \mu = 3.69, \text{ calc. } 3.68$$

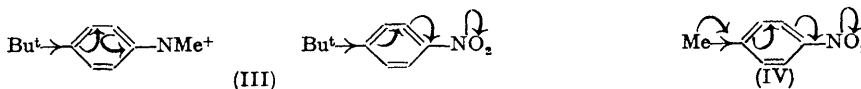
to contribute appreciably to the complete wave function of *p*-chloronitrobenzene in the normal state. The interaction between the substituents must exist also in the collisionally excited state although it may alter in magnitude. In the transition state of nitration (Hughes, Ingold, *et al.*, *J.*, 1937, 1257; 1941, 608; Wheland, *J. Amer. Chem. Soc.*, 1942, 64, 900; Dewar, *J.*, 1949, 463) this conjugation between the substituents will compete with important resonance structures such as (II; X = Cl) and thus reduce the stabilisation afforded by the chlorine atom. The essential assumption is that this conjugation is much



more imperfectly developed in the ion *p*-Cl·C₆H₄·NMe₃⁺, because the NMe₃⁺ group is purely inductive, and interference with the normal function of the halogen in the transition state is correspondingly smaller. The same view is expressed in the statement that the *p*-NO₂ group (compared with NMe₃⁺) more effectively reduces the electromeric polarisability of the chlorine atom, because the halogen surrenders a greater electron density to the nitro-group and is, therefore, less polarisable in the field of the attacking nitronium ion.

The argument for the *p*-Bu^t compounds, although the substituent is inductive, must be similar. For our purpose it is unnecessary to distinguish between transmission along the σ -bonds or through the unsaturation electrons and both are referred to as inductive or inductomeric effects of the Bu^t group. The "inverted" reactivities are thought to arise partly from a greater inductomeric polarisability of the Bu^t substituent in the ion *p*-Bu^t·C₆H₄·NMe₃⁺. This results, much as in the previous case, from the diminution of the polarisability of the alkyl group owing to the loss of electrons by the processes represented

in (III), which proceed further in the nitro-compound than in the quaternary ammonium ion. However, an additional factor operating in the same direction will be discussed below. In the systems with a *p*-methyl substituent (which have also been discussed by Lowen, Murray, and Williams, *J.*, 1950, 3318), hyperconjugation and induction act in co-operation (IV) and the greater differential effect further lowers the relative rate.



The explanation of why the alkyl groups depress the relative rate of nitration more than do the halogens is perhaps as follows. Although only the differential effect of the $\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$ and $\cdot\text{C}_6\text{H}_4\cdot\text{NMe}_3^+$ system on the substituent has been discussed hitherto, the differential effect of the substituent on the rest of the system is also significant. The point in question is the extent to which $\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$ and $\cdot\text{C}_6\text{H}_4\cdot\text{NMe}_3^+$ polarise in the field of different substituents, and we assume that the former, having the greater conjugation path, polarises more, *i.e.*, that NO_2 , compared with NMe_3^+ , will smooth out differences of electron density at the point of substitution caused by substituents elsewhere in the ring. If this is accepted, taken by itself it means that an activating substituent will decrease the relative rate, $k_{\text{NO}_2}/k_{\text{NMe}_3^+}$ (because more of the electrons released by the substituent accumulate in the nucleus linked to the quaternary nitrogen atom) and that a deactivating substituent will increase it. This effect does not involve the nitronium ion explicitly and is not confined to collisionally activated states; neither is it the whole truth because it must operate simultaneously with the effects considered previously. It is the resultant that is significant. With alkyl substituents the two factors co-operate to reduce the relative rate, whereas with the halogens they are in opposition.

Influence of Polarisability on Nitration Velocity.—The influence of halogens on the velocity of nitration in the *p*-nitrophenyl series can be seen from the results in Table 2.

TABLE 2. Nitration of derivatives of $\text{Ph}\cdot\text{NO}_2$ and $\text{Ph}\cdot\text{NMe}_3^+$ in H_2SO_4 (Temp. 25°).

Initial concn. (moles/l.) of :				
ArH		HNO_3	Medium, % H_2SO_4	k_2 (mean) †
<i>p</i> -Cl· $\text{C}_6\text{H}_4\cdot\text{NMe}_3^+$	0.005	0.094	89.8	0.340
<i>p</i> -Br· $\text{C}_6\text{H}_4\cdot\text{NMe}_3^+$	0.004	0.094	89.8	0.71 ₂
<i>p</i> -Cl· $\text{C}_6\text{H}_4\cdot\text{NO}_2$	0.001	0.094	89.8	0.41 ₄
<i>p</i> -Br· $\text{C}_6\text{H}_4\cdot\text{NO}_2$	0.001	0.094	89.8	0.85
<i>p</i> -F· $\text{C}_6\text{H}_4\cdot\text{NO}_2$	0.002	0.084	90.6	0.06 ₉
$\text{C}_6\text{H}_5\cdot\text{NO}_2$ *	{ —	—	90.0	4.6
			95.5	1.8
<i>p</i> -Me· $\text{C}_6\text{H}_4\cdot\text{NO}_2$	{ 0.00024	0.00030	95.5	590
	{ 0.00025	0.001	99.0	240 (300)
<i>p</i> -Bu ^t · $\text{C}_6\text{H}_4\cdot\text{NO}_2$	0.00016	0.001	99.0	33.2 (45)

* Bonner, James, Lowen, and Williams, *loc. cit.*

† k_2 is given in the units $\text{min.}^{-1} \text{mole}^{-1} \text{l.}$

Values of the velocity coefficients given in parentheses (99% H_2SO_4) are calculated on the *molecular* concentration of nitro-compound, to correct for ionisation.

Measurements with *p*-iodonitrobenzene were impracticable because of the insolubility and ease of decomposition; otherwise the order in which the halogens were effective in retarding nitration was $\text{F} > \text{Cl} > \text{Br}$. This differs from the known influence of halogens in the simple halogenobenzenes (Table 3), especially in the case of fluorine, and the new order is presumably the result of the modifying influence of the nitro-group. A plausible explanation is that we are observing the order of electromeric polarisability of the halogens, the mesomeric effect having become subordinate. The conjugation between the halogen and the nitro-group (I) is presumably responsible for this, because electrons are transferred in this way from one substituent to the other without activating the nucleus. The order of electromeric polarisability, $\text{F} < \text{Cl} < \text{Br}$, is the same as that deduced by Bird and Ingold (*loc. cit.*) from reaction (2) (Table 3), in which the electromeric and mesomeric effects are thought to be of comparable importance.

Finally, it is interesting to note the quantitative influence of methyl and halogen substituents on nitration velocity in the nitrophenyl series. Methyl being compared with chloro-, for example, nitration is, respectively, accelerated 330-fold and retarded 11-fold (Table 3). By combining the results in Tables 1 and 2 it can be seen that corresponding substitutions in the quaternary ammonium ion systems increase the disparity. This behaviour is consistent with our view that the nitration velocity of these highly electron-deficient systems is determined by polarisability factors which would enhance the reactivity of the substituted, with respect to the unsubstituted, systems. Unfortunately, to compare the ratios above with those observed for reactions of simple monosubstituted benzenes, it is necessary to assume that the physical effect of the change of solvent can be neglected; this being granted, our nitrations closely resemble the chlorination, but not the nitration, of PhX. The substituent effects in chlorination of the phenyl halides are also thought (de la Mare, *J.*, 1949, 2871) to show that the influence of polarisability is relatively important; however, in this case the electron-demanding character of the reaction is due primarily to the nature of the *reagent*, and the order in which the halogens are effective in retarding chlorination is, therefore, normal.

TABLE 3. *Relative effect of methyl and halogen substituents on the speed of nuclear substitution.*

Reaction	Medium		Substituent, X						Ref.
	Solvent	Temp.	Me	H	F	Cl	Br	I	
(1) <i>o</i> -Nitration of PhX	Ac ₂ O	18°	43	1.0	0.05	0.030	0.034	0.2	1, 2
(2) Overall nitration of PhX ...	Ac ₂ O	18	25	1.0	0.15	0.033	0.030	0.18	1, 3
(3) Overall chlorination of PhX	AcOH	24	350	1.0	1.2	0.11	0.079	—	4
(4) Nitration of <i>p</i> -X·C ₆ H ₄ ·NO ₂	+H ₂ O H ₂ SO ₄ +H ₂ O	25	330	1.0	0.015	0.090	0.185	—	Table 2

1, Bird and Ingold, *J.*, 1938, 918. 2, de la Mare and Robertson, *J.*, 1948, 100. 3, Ingold, Lapworth, Rothstein, and Ward, *J.*, 1931, 1959. 4, de la Mare and Robertson, *J.*, 1943, 276; de la Mare, *loc. cit.*

EXPERIMENTAL

Materials.—*p*-Bromo-, *p*-chloro- and *p*-tert.-butyl-phenyltrimethylammonium methyl sulphate were prepared from the corresponding tertiary amine and methyl sulphate in acetone, and purified by recrystallisation from slightly aqueous acetone. They had, respectively, m. p. 121° (also 138°) (Found : C, 36.9; H, 4.6; N, 4.3. C₁₀H₁₆O₄NBrS requires C, 36.8; H, 4.9; N, 4.3%), m. p. 143° (Found : C, 42.5; H, 5.7; N, 5.2. C₁₀H₁₆O₄NClS requires C, 42.6; H, 5.7; N, 5.0%), and m. p. 214° (Found : C, 56.0; H, 8.2; N, 4.7. C₁₄H₂₅O₄NS requires C, 55.5; H, 8.3; N, 4.6%).

p-tert.-Butylnitrobenzene, m. p. 28.3° after fractional solidification, and 1-tert.-butyl-2 : 4-dinitrobenzene, m. p. 62°, were prepared by nitration of *tert*-butylbenzene (cf. Craig, *J. Amer. Chem. Soc.*, 1935, 57, 195). Other compounds employed were : *p*-bromonitrobenzene, m. p. 126°; *p*-chloronitrobenzene, m. p. 83.5°; *p*-fluoronitrobenzene, m. p. 26.8°; nitrobenzene, m. p. 5.7°; *p*-nitrotoluene, m. p. 52°; phenyltrimethylammonium methyl sulphate, m. p. 126°; *p*-tolyltrimethylammonium methyl sulphate, m. p. 144° (m. p.s are uncorrected).

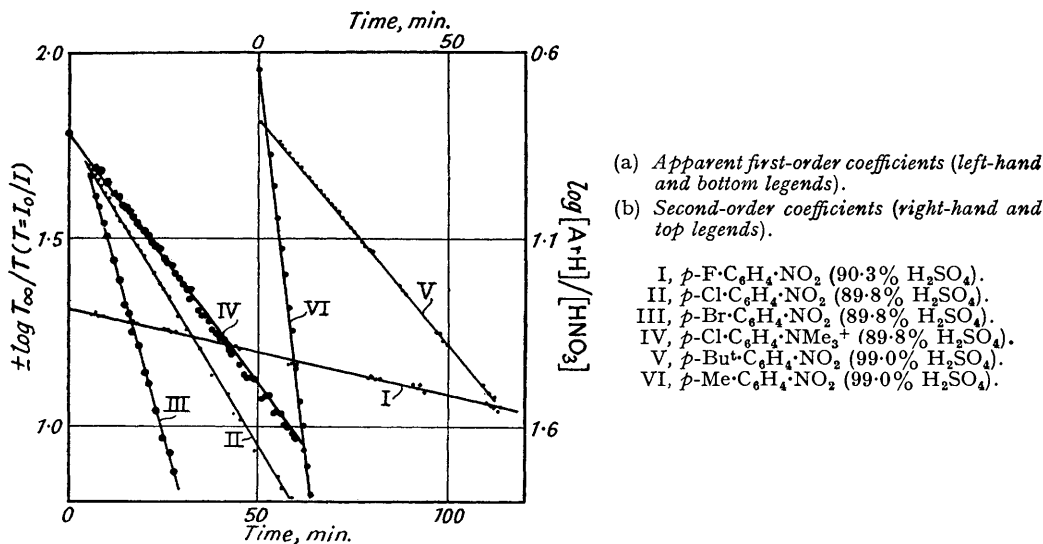
Competitive Nitrations.—In these experiments the product was analysed by measuring the optical density of the solution after nitration, at a wave-length of 3650 Å, a Hilger "Spekker" Absorptiometer being used. The method was to allow a mixture of nitro-compound and quaternary ammonium salt to compete in sulphuric acid solution for nitric acid, all at suitable, known initial concentrations, and subsequently to measure the transmission of diluted samples. This procedure was possible because the nitrations were known to yield one product only, and because the nitration of the nitro-compound brought about a very large change (*ca.* ten-fold in favourable media) of extinction coefficient. Essentially, the optical measurement was an analysis for the mononitro-compound, which was the only strongly absorbing constituent of the solution at the wave-length employed; for this reason, two nitro-compounds or two quaternary ions were not compared directly by the competitive method. The calculation of the relative velocity (Bird and Ingold, *loc. cit.*), from the initial concentrations and the optical density of the nitrated solution, is illustrated by the results in Table 4. The sum of the errors

TABLE 4. *Relative velocity of nitration of p-Bu^t-C₆H₄·NO₂ and p-Bu^t-C₆H₄·NMe₃⁺ in 95.8% H₂SO₄ (Temp. 18°).*

p-tert.-Butylnitrobenzene, ε = 6200; *1-tert.*-butyl-2:4-dinitrobenzene, ε = 610; *1-tert.*-butyl-2-nitrophenyltrimethylammonium ion, ε = 385 (cm. mol./kg.)⁻¹.

	Initial concn. × 10 ³ (molal) (A)	Dilution ratio and optical density (after nitration)	Final concn. × 10 ³ (molal) (B)	log A/B	$\frac{k_{NO_2}}{k_{NMe_3^+}}$
(a) Bu ^t -C ₆ H ₄ ·NO ₂ ...	4.662	30.40 × 0.665	(a) 2.905	(a) 0.206	—
(b) Bu ^t -C ₆ H ₄ ·NMe ₃ ⁺	4.650	—	(b) 1.744	(b) 0.426	0.48
(c) KNO ₃	4.663	—	—	—	—
(a) As above	4.801	30.21 × 0.668	(a) 2.967	(a) 0.209	—
(b) „	4.782	—	(b) 1.852	(b) 0.412	0.51
(c) „	5.764	—	—	—	—
Second analysis:					
(a)	4.801	31.60 × 0.627	(a) 2.905	(a) 0.218	—
(b)	4.782	—	(b) 1.915	(b) 0.397	0.54
(c)	4.764	—	—	—	—
(a)	2.342	14.66 × 0.779	(a) 1.523	(a) 0.187	—
(b)	6.977	—	(b) 3.110	(b) 0.351	0.53
(c)	4.688	—	—	—	—
(a)	6.966	43.24 × 0.621	(a) 3.925	(a) 0.249	—
(b)	2.392	—	(b) 0.758	(b) 0.499	0.50
(c)	4.676	—	—	—	—

(about ±2 parts %) in the optical measurements corresponded to about ±10 parts % in the relative rate, depending on the amount by which the extinction coefficients fell during nitration. In the case of *p*-chloronitrobenzene, the change which occurred in the nitration medium itself (90.7% H₂SO₄) was too small, and the solution was analysed by dilution with 15.7% fuming sulphuric acid (103.5% H₂SO₄) in which the much more strongly absorbing conjugate cation was formed. A similar procedure was adopted with nitrobenzene and *p*-nitrotoluene.



A fully nitrated solution of *p*-chloronitrobenzene (nitration at 25° in 90.7% H₂SO₄) was found to have the same extinction coefficient [ε = 1923 (cm.mol./kg.)⁻¹ in 103.5% H₂SO₄] as a solution of 1-chloro-2:4-dinitrobenzene in the same medium (ε = 1928). This test was also applied satisfactorily to *p-tert.*-butylnitrobenzene and *1-tert.*-butyl-2:4-dinitrobenzene [ε = 610 (nitrated) and 595 (cm.mol./kg.)⁻¹ respectively in 95.8% H₂SO₄].

Velocity Measurements.—Nitration velocities were determined from the rate of change of optical density at 3650 Å. The reaction proceeded in optical cells (depth, 1 cm.) immersed in a water thermostat at 25°. Media were prepared by dissolving potassium nitrate in sulphuric

acid, the low concentration of potassium hydrogen sulphate liberated having no appreciable effect on the nitration velocity (Bennett *et al.*, *J.*, 1947, 474). The initial concentration of nitratable material was 10^{-2} — 10^{-4} molar, depending on the intensity of absorption. *p*-Iodonitrobenzene was too insoluble and too easily decomposed to be investigated in this medium. For nitration of the *p*-halogen derivatives of nitrobenzene and the phenyltrimethylammonium ion, the nitric acid concentration was in invariant excess and the reaction of first order. This condition could not be preserved with the reactive alkylbenzenes, for which second-order velocity coefficients were evaluated directly (see figure, where $\log T_{\infty}/T = \log I/I_{\infty} \propto [\text{ArH}]$). Except for the most rapid reactions, the substances were added as solids to the nitrating mixture, the quaternary ammonium salts being introduced as their methyl sulphates.

Microanalyses were carried out by Miss R. H. Kennaway.

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