Deviations from the Additivity Principle in Rates of Aromatic Nitration and Aromatic Bromination (by ' Positive Bromine ')

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Kinetic studies have been carried out on the bromination by hypobromous acid of a series of disubstituted benzenes with substituents Me, OMe, and $[CH_2]_nX$ where n = 0—3 and X = $\overset{+}{N}Me_3$, $\overset{+}{N}H_3$, or $\overset{+}{S}Me_2$. Deviations from the additivity principle are small but appear to be systematic. With two strongly deactivating substituents, the substrate is less reactive than expected (negative deviation). With one activating and one deactivating substituent the deviation is usually negligible or positive. Unexpectedly, two weakly deactivating substituents of type $[CH_2]_2X$ also give a positive deviation.

For deactivating substituents, the results in nitration parallel those in bromination. However, for the combination of a methyl substituent and a deactivating substituent the deviations in nitration are much greater than in bromination. This difference is attributed in part to the effect of diffusion control in distorting the relative reactivity of toluene in nitration. From the comparison with bromination, the relative reactivity of toluene to benzene in reaction with the nitronium ion in the absence of diffusion control is estimated to be about 79. This value is unexpectedly high in relation to direct measurements on the nitration of toluene.

RECENT work has produced evidence on the partial rate factors for the nitration [1-3] and bromination [4,5] of benzene derivatives carrying a substituent of type $[CH_2]_nX$ where X is a positive pole, usually $\overset{+}{N}Me_3$ or $\overset{+}{N}H_3$. This work, together with some related studies on disubstituted compounds,[6] is here extended to provide a comparison of the

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[1] T. A. Modro and J. H. Ridd, *J. Chem. Soc.* (*B*), 1968, 528.

[2] A. Ricci and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1544.

[3] H. M. Gilow, M. De Shazo, and W. C. Van Cleave, *J. Org. Chem.*, 1971, **36**, 1745.

[4] A. Gastaminza, J. H. Ridd, and F. Roy, *J. Chem. Soc.* (*B*), 1969, 684.

[5] H. M. Gilow and J. H. Ridd, *J.C.S. Perkin II*, 1973, 1321.

[6] (*a*) A. Ricci, R. Danieli, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1547; (*b*) R. S. Cook, R. Phillips, and J. H. Ridd, *ibid.*, 1974, 1166.

deviations from the additivity principle in these two reactions. The interest in comparing deviations from the additivity principle in nitration and in bromination by positive bromine stems from the fact that these reactions involve electrophiles of similar selectivity so that the same aromatic compounds can be used for both. However, the reactions differ in other ways. Bromination by hypobromous acid in aqueous mineral acids is well suited to provide a test of the additivity principle: the reaction is not subject to a limiting encounter rate,[3] steric interactions are less than those in nitration or bromination by molecular bromine,[7] and the reactivity of the reagent enables a wide range of aromatic systems to be studied. Nitration is kinetically a more complex reaction, mainly because it reaches a limiting encounter rate for compounds somewhat more reactive than benzene.[8] Thus the comparison should provide evidence on the general applicability of the additivity principle and on one type of deviation from it.

Bromination Results.—The partial rate factors needed for the present comparisons are collected in Table 1 together with the corresponding relative reactivities and product compositions. The new relative reactivities have been calculated by using the rate coefficients listed in the Experimental section. Where the rate of bromination is too high or too low to permit direct comparison with the rate of bromination of benzene, the method of stepwise comparison has been used.[4,5] This method involves the assumption that relative rates are independent of acidity. The rate profiles illustrated in previous papers [4,5] show that this assumption appears reasonably correct for the ionic substrates used in much of the present work. However, the fact that the relative reactivity of the phenyltrimethylammonium ion (the most unreactive compound studied) appears to be $2{\cdot}6 \times 10^{-6}$ for reaction in aqueous sulphuric acid [4] and $1{\cdot}6 \times 10^{-5}$ for reaction in aqueous perchloric acid [9] shows that the use of such stepwise comparisons can introduce considerable errors, since both of these values cannot correspond to reaction in an infinitely dilute solution of a mineral acid. In this example, the discrepancy probably arises because the high concentrations of mineral acid needed for reaction (*ca.* 45% $HClO_4$) also give rise to medium effects on relative reactivities. Such effects should be much less in the feebly acidic media used in the bromination of many of the other substrates.

Considerable difficulty was experienced in obtaining reproducible results for the bromination of anisole: both the reaction rate and the product composition varied with different batches of hypobromous acid and in addition the amount of *ortho*-substitution appeared to increase with the acidity of the medium. This variation is probably derived from bromination by traces of bromine present in the hypobromous acid. As anisole is the most reactive substrate examined and the one studied at the lowest acidity, the bromination of anisole should be particularly liable to contributions from reaction *via* molecular bromine. The results for anisole in Table 1 have been obtained from a series of experiments using carefully purified hypobromous acid and have been checked by determining the effect of added silver nitrate (see Experimental). It is believed that, in this way, the complication of reaction through molecular bromine has been avoided. This complication did not arise with the other compounds studied.

TABLE 1

Relative rates (PhH ≡ 1), product compositions, and partial rate factors (p.r.f.) for the bromination of monosubstituted benzenes by hypobromous acid at 25°; medium aqueous sulphuric acid except where indicated; values taken from the literature in parentheses

Substituent	Relative rate	Product composition (%) *o*	*m*	*p*	log (p.r.f.) *o*	*m*	*p*
Me	29 [a]	(70·3	2·3	27·4) [b]	1·78	0·23	1·69
OMe	$1{\cdot}2 \times 10^{5}$ [a]	22		78	4·90		5·75
$[CH_2]_2{\cdot}\overset{+}{N}Me_3$	(0·51) [c]	44·3	5·7	50·0	−0·17	−1·06	0·185
$CH_2{\cdot}\overset{+}{N}Me_3$	($1{\cdot}4 \times 10^{-3}$) [c]	30	50	20	−2·89	−2·68	−2·77
$\overset{+}{N}Me_3$	($2{\cdot}6 \times 10^{-6}$		66	33		−5·28	−5·28) [c]
	($1{\cdot}6 \times 10^{-5}$) [a,d]	(	66	33) [c]		−4·49	−4·49
$[CH_2]_2{\cdot}\overset{+}{S}Me_2$	0·72	57·8	5·0	37·2	0·10	−0·96	0·21
$CH_2{\cdot}\overset{+}{S}Me_2$	$3{\cdot}8 \times 10^{-3}$	38·3	32·8	28·9	−2·36	−2·43	−2·18

[a] In aqueous perchloric acid. [b] In 50% aqueous dioxan (P. B. D. de la Mare and J. T. Harvey, *J. Chem. Soc.*, 1956, 36). [c] Taken from ref. 4. [d] P. B. D. de la Mare and I. C. Hilton, *J. Chem. Soc.*, 1962, 997.

The partial rate factors in Table 1 have been used in the usual way to calculate the relative reactivities (R) of a number of di- and poly-substituted benzene derivatives. This involves expressing the partial rate factor (f_i) for each unsubstituted position (i) in the di- or poly-substituted benzene in terms of the partial rate factors for the appropriate positions in the monosubstituted benzenes (f_s) using equation (1). The reactivity relative to

$$\log f_i = \sum_s \log f_s \qquad (1)$$

benzene (R) is then calculated using equation (2). The

$$R = \sum_i f_i/6 \qquad (2)$$

calculated reactivities are compared with the observed

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[7] P. B. D. de la Mare and J. H. Ridd, 'Aromatic Substitution, Nitration and Halogenation,' Butterworths, 1959, ch. 10.

[8] J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, 'Nitration and Aromatic Reactivity,' Cambridge, 1971, ch. 2.

[9] P. B. D. de la Mare and I. C. Hilton, *J. Chem. Soc.*, 1962, 997.

results in Table 2. The compounds in this Table are divided into three groups depending on whether the substituents are both activating, one activating and one deactivating, or both deactivating.

Table 2

Comparison of the observed relative rates of bromination with those calculated from the additivity principle; values taken from the literature in parentheses

Substituents	log (relative rate) obs.	calc.	Δ [a]
1-Me, 3-Me	3·04 [b]	3·21	0·17
1-Me, 2-Me	2·20 [b]	1·79	0·41
1-$[CH_2]_2\cdot\overset{+}{N}Me_3$, 3-Me, 5-Me	(3·18) [b,c]	3·21	−0·03
1-$[CH_2]_2\cdot\overset{+}{N}Me$, 3-Me	(1·38) [b,c]	1·44	−0·06
1-$CH_2\cdot\overset{+}{N}Me_3$, 4-Me	−0·40 [d]	−1·37	0·97
1-$\overset{+}{N}Me_3$, 4-OMe	(−0·38) [b,c]	−0·07	−0·31
1-$\overset{+}{N}Me_3$, 4-Me	(−2·54) [b,c]	−3·19	0·65
1-$[CH_2]_2\cdot\overset{+}{N}Me_3$, 3-$[CH_2]_2\cdot\overset{+}{N}Me_3$	0·24 [d]	−0·38	0·62
1-$[CH_2]_2\cdot\overset{+}{N}Me_3$, 4-$[CH_2]_2\overset{+}{N}Me_3$	−0·44 [d]	−1·40	0·96
1-$[CH_2]_2\cdot\overset{+}{S}Me_2$, 4-$[CH_2]_2\cdot\overset{+}{S}Me_2$	−0·56 [d]	−1·04	0·48
1-$CH_2\cdot\overset{+}{S}Me_2$, 4-$CH_2\cdot\overset{+}{S}Me_2$	−5·30 [d]	−4·97	−0·33
1-$CH_2\cdot\overset{+}{N}Me_3$, 4-$CH\cdot\overset{+}{N}Me_3$	−6·38 [d]	−5·74	−0·64

[a] log (obs. rel. rate) − log (calc. rel. rate). [b] In $HClO_4$. [c] Ref. 5. [d] In H_2SO_4.

Nitration Results.—For nitration in aqueous sulphuric acid, the work of Coombes, Moodie, and Schofield [10] has shown that reactivities relative to benzene can depend significantly on the acidity of the medium. This arises because, for concentrations of sulphuric acid >70%, the slope of the rate profile for benzene is markedly greater than those of most other substrates. In the present work we have sought to avoid this complication by comparing the reactivity of benzene, the monosubstituted benzene, and the disubstituted benzene at the same acidity (usually 73% H_2SO_4) using when necessary an extrapolation of the rate profile. This has not been possible for the compounds with an NMe_3^+ substituent in the ring, and so for the phenyltrimethylammonium ion the previous relative reactivity obtained by stepwise comparison has been quoted.

Table 3

Relative rates, product compositions, and partial rate factors (p.r.f.) for the nitration of a series of monosubstituted benzenes in aqueous sulphuric acid at 25°; values taken from the literature in parentheses

Substituent	$[H_2SO_4]$ (%)	Relative rate	Product comp. (%) o	m	p	log (p.r.f.) o	m	p
$[CH_2]_3\cdot\overset{+}{N}H_3$	73	1·38	18	4·5	77·5	−0·23	−0·67	0·81
$[CH_2]_2\cdot NH_3$	73	(0·129	22	14	64) [a]	−1·07	−1·27	−0·31
$CH_2\cdot\overset{+}{N}H_3$	73	(2·3 × 10^{-3}	21	45	34) [a]	−2·84	−2·51	−2·33
$[CH_2]_3\cdot\overset{+}{N}Me_3$	73	(1·41) [b]	14	5	81	−0·23	−0·67	0·84
$[CH_2]_2\cdot\overset{+}{N}Me_3$	73	(0·129	6	16	78) [a]	−1·63	−1·20	−0·22
$CH_2\cdot\overset{+}{N}Me_3$	80	2·63 × 10^{-5}	(2	88	10) [c]	−5·80	−4·16	−4·80
$\overset{+}{N}Me_3$		(3·4 × 10^{-8}		89	11) [d]		−7·04	−7·65
$[CH_2]_2\cdot\overset{+}{S}Me_2$	69	(0·20) [d]	10	11	79	−1·22	−1·18	−0·03
$CH_2\cdot\overset{+}{S}Me_2$	80	(9·3 × 10^{-5}	16·6	38·8	44·6) [e]	−4·33	−3·97	−3·60

[a] Ref. 2. [b] Extrapolated to this acidity by using the rate coefficients given in ref. 1. [c] F. R. Goss, W. Hanhart, and C. K. Ingold, *J. Chem. Soc.*, 1927, 250. [d] Ref. 4. [e] See text and ref. 3.

The relative rates, product compositions, and partial rate factors for the monosubstituted compounds are listed in Table 3. Most of these data are taken from the literature but the complete set of results has required some further measurements of reaction rates and product compositions. The relative reactivities of the sulphur compounds have been calculated by combining the published rate coefficients [3] with the most recent results on the reactivity of benzene.[10] Since the rate profile for the nitration of the $Ph[CH_2]_2\cdot\overset{+}{S}Me_2$ appears to have an abnormal slope,[3] the partial rate factors have been calculated for the region of acidity used (69% H_2SO_4) to avoid a possibly misleading extrapolation.

The corresponding results for the disubstituted compounds are given in Table 4. In the two examples where the acidity is unspecified, the observed relative reactivity has been obtained by combining the relative reactivity for the monosubstituted compound in Table 3 with the activating effect of the methyl group as reported in the literature. The calculated relative reactivities have been obtained as before by using equations (1) and (2). No calculated relative reactivities have been given for compounds with a methyl substituent: these results are analysed in a different way (see later) because of the uncertainty over the appropriate partial rate factors to use for this substituent.[10]

DISCUSSION

The bromination results are discussed first since these are the easiest to understand. The main feature of these results is the extent of agreement with the additivity principle: thus, the r.m.s. deviation corresponds to an error by a factor of 3·6 in a range of reactivities of almost 10^{10}. The extent of agreement in compounds containing one activating and one deactivating

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

substituent is particularly surprising in view of the marked deviations found in nitration.[11,12]

Deviations from the additivity principle can arise in a large number of ways [13] of which the most important are probably (*a*) conjugation between the substituents,[11] (*b*) steric interactions between the substituents,[14] (*c*) limitation of reaction rates by diffusion,[8] and (*d*) *ipso*-attack followed by rearrangement.[15] In addition there is now increasing interest [14,16] in systematic deviations from the additivity principle but no general agreement on the form that a possible 'second approximation' to the additivity principle might take. The nature and position of the substituents in the present reactions eliminate deviations arising from causes (*a*) and (*b*) and the reaction is apparently not subject to cause (*c*).[5] It is reasonable therefore to examine the results as evidence for systematic deviations and *ipso*-attack.

TABLE 4

Comparison of the observed relative rate of nitration with that calculated from the additivity principle

Substituents		$[H_2SO_4]$ (%)	log (relative rate)		
			obs.	calc.	Δ
$1\text{-}[CH_2]_3\cdot\overset{+}{N}H_3$	4-Me	73	0·12		
$1\text{-}[C$ [illegible] $\cdot\overset{+}{N}H_3$	4-Me	73	−0·12		
$1\text{-}CH_2\cdot NH_3$	4-Me	73	−0·76		
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$	4-Me		(−1·81) [a]		
$1\text{-}\overset{+}{N}Me_3$	4-Me		(−4·10) [b]		
$1\text{-}[CH_2]_3\cdot\overset{+}{N}Me_3$	$4\text{-}[CH_2]_3\cdot\overset{+}{N}Me_3$	73	0·00 [c]	−1·08	1·08
$1\text{-}[CH_2]_3\cdot\overset{+}{N}H_3$	$4\text{-}[CH_2]_3\cdot\overset{+}{N}H_3$	73	0·03 [c]	−1·08	1·11
$1\text{-}[CH_2]_2\cdot\overset{+}{N}H_3$	$4\text{-}[CH_2]_2\cdot\overset{+}{N}H_3$	73	−1·66 [c]	−2·51	0·85
$1\text{-}CH_2\cdot\overset{+}{N}H_3$	$4\text{-}CH_2\cdot\overset{+}{N}H_3$	73	−6·02 [c]	−5·53	−0·49
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$	$4\text{-}CH_2\cdot\overset{+}{N}Me_3$	80	−10·62	−10·14	−0·48
$1\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	$4\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	73	−2·27	−2·58	0·31
$1\text{-}CH_2\cdot\overset{+}{S}Me_2$	$4\text{-}CH_2\cdot\overset{+}{S}Me_2$	80	−9·05	−8·47	−0·58

[a] See text and ref. 1. [b] Calculated from the relative reactivity of $Ph\overset{+}{N}Me_3$ and *p*-$MeC_6H_4\cdot\overset{+}{N}Me_3$ in 82% H_2SO_4 [J. H. P. Utley and T. A. Vaughan, *J. Chem. Soc.* (*B*), 1968, 196]. [c] Recalculated for this acidity from the rate coefficients in ref. 6.

The results in Table 2 for substrates with one activating and one deactivating substituent show that (with one exception) the deviations are negligible when the deactivating substituent is weak and positive when the deactivating substituent is strong. This is as expected for systematic deviations [11,14,16] and can be understood as resulting from a slight change in the position of the transition state on the reaction co-ordinate. The transition state for the disubstituted compound should be later than that for the activated compound and hence more sensitive to the substituent effect of the activating group. The exception is the ion *p*-$MeO\cdot C_6H_4\cdot\overset{+}{N}Me_3$ but the calculated relative rate for this ion is more subject to error since it is based on the partial rate factors for the most activating and most deactivating groups. The listed value of Δ is based on the results for bromination of $Ph\overset{+}{N}Me_3$ in perchloric acid, but had the results for sulphuric acid been used (Table 1) the value of Δ would have been +0·48. The bromination of *p*-$MeO\cdot C_6H_4\cdot\overset{+}{N}Me_3$ was in fact carried out in perchloric acid but the acidity was so low ($[H^+] = 0\cdot08$—$0\cdot8$ mol l^{-1}) that the nature of the acid is probably unimportant.*

The results in Table 2 for substrates with two strongly deactivating substituents ($CH_2\cdot\overset{+}{N}Me_3$ or $CH_2\cdot\overset{+}{S}Me_2$) show negative deviations from the additivity principle. This type of deviation does not appear to have been reported before but it is consistent with the expected change towards a later transition state in the disubstituted compound. In contrast, the marked positive deviations observed with two weakly deactivating substituents ($[CH_2]_2\cdot\overset{+}{N}Me_3$, $[CH_2]_2\cdot\overset{+}{S}Me_2$) were most unexpected. These deviations are also found in nitration and hydrogen-isotope exchange.[17] The deviations are unlikely to be derived only from *ipso*-attack followed by rearrangement because they occur in both 1,4- and 1,3-disubstituted derivatives (Table 2). The $[CH_2]_2\cdot\overset{+}{N}Me_3$ group is *ortho,para*-directing (Table 1) and so the extent of *ipso*-attack in the 1,3-disubstituted derivative should be negligible. The reason for these deviations is not yet clear but they may be derived from conformational equilibria involving these substituents. In the disubstituted compounds, the electrostatic interaction between the substituents should reduce the population of conformations with the charges near the aromatic ring and this should increase the rate of substitution above that predicted by the additivity principle.

In nitration, the results for the compounds with two $[CH_2]_nX$ substituents ($X = \overset{+}{N}H_3$, $\overset{+}{N}Me_3$, or $\overset{+}{S}Me_2$) parallel those for bromination: when $n = 2$ or 3 the deviations from the additivity principle are positive and when $n = 1$ the deviations are negative. These results can be understood as outlined above.

However, the results with the methyl substituents point to an interesting difference between these reactions. These results are compared in Table 5 in terms of the relative reactivity of toluene needed to bring the calculated reactivity of the disubstituted compound into agreement with the observed value. For the purpose of these calculations the isomer proportions in the nitration of toluene have been taken to be: *ortho*, 62%; *meta*, 3%;

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* We thank a referee for pointing out that the activating effect of a methoxy-group in protodetritiation is also variable, depending particularly on the acidity of the medium (R. Baker, R. W. Bott, C. Eaborn, and P. M. Greasley, *J. Chem. Soc.*, 1964, 627). Some variation in this substituent effect is also observed in nitration.[6b]

[11] Ref. 7, ch. 6.

[12] J. H. P. Utley and T. A. Vaughan, *J. Chem. Soc.* (*B*), 1968, 196.

[13] For a general discussion see L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35 (especially pp. 135 *et seq.*).

[14] J. E. Dubois, J. J. Aaron, P. Alcais, J. P. Doucet, F. Rothenberg, and R. Uzan, *J. Amer. Chem. Soc.*, 1972, **94**, 6823; J. J. Aaron, J. E. Dubois, F. Krausz, and R. Martin, *J. Org. Chem.*, 1973, **38**, 300.

[15] R. C. Hahn and M. B. Groen, *J. Amer. Chem. Soc.*, 1973, **95**, 6128 and references quoted therein.

[16] K. E. Richards, A. L. Wilkinson, and G. J. Wright, *Austral. J. Chem.*, 1972, **25**, 2369.

[17] R. Danieli and A. Ricci, unpublished results.

para, 35%.[18] If the additivity principle were obeyed, the values for each reaction would be constant. For both reactions, the values generally increase with a decrease in the reactivity of the aromatic system but the increase is far greater for nitration than for bromination.

TABLE 5

Relative rate of substitution in toluene (on scale PhH $\equiv$ 1) as calculated from the reactivities of the compounds C_6H_5X and MeC_6H_4X assuming the additivity principle to hold

Nitration		Bromination	
X	Rel. rate	X	Rel. rate
H	*ca.* 10 [a,b]	H	29
$4\text{-}[CH_2]_3\cdot\overset{+}{N}H_3$	9·6 [a]	$3\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	25
$4\text{-}[CH_2]_2\cdot\overset{+}{N}H_3$	20·8 [a]	$4\text{-}CH_2\cdot\overset{+}{N}Me_3$	288
$4\text{-}CH_2\cdot\overset{+}{N}H_3$	89 [a]	$4\text{-}\overset{+}{N}Me_3$	130
$4\text{-}CH_2\cdot\overset{+}{N}Me_3$	360 [c]		
$4\text{-}\overset{+}{N}Me_3$	1420 [d]		

[a] In 73% H_2SO_4. [b] Calculated from the rate profiles in ref. 10. [c] In 69·7% H_2SO_4. [d] In 82% H_2SO_4; see ref. 12.

One factor leading to this difference appears to be the much greater concentrations of mineral acid required for the study of deactivated substrates in nitration, for this increases medium effects on relative rates. Thus Utley and Vaughan [12] have shown that the rate of nitration of $p\text{-}MeC_6H_4\cdot\overset{+}{N}Me_3$ relative to $C_6H_5\cdot\overset{+}{N}Me_3$ increases with acidity. If their results are extrapolated back to 30% H_2SO_4 (the acidity appropriate for the bromination studies) the corresponding figure in Table 5 becomes 726 instead of 1420.

TABLE 6

Analytical results for benzene derivatives with two positive poles (anion ClO_4^-)

Substituents	M.p. (°C)	Found (%)				Calc. (%)			
		C	H	N	S	C	H	N	S
$1\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$, $3\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	284	43·1	7·0	6·3		42·8	6·7	6·2	
$1\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$, $4\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	320	43·1	6·7	6·3		42·8	6·7	6·2	
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$, $4\text{-}CH_2\cdot\overset{+}{N}Me_3$	314	39·7	6·2	6·5		39·9	6·2	6·7	
$1\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$, $4\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	298	36·7	5·2		14·1	36·9	5·3		14·1
$1\text{-}CH_2\cdot\overset{+}{S}Me_2$, $4\text{-}CH_2\cdot\overset{+}{S}Me_2$	236—237	33·7	4·8		14·9	33·7	4·7		15·0

Another factor, first suggested by Coombes, Moodie, and Schofield,[10] is that the rate of nitration of toluene in these solutions is reduced by the nearness of the encounter limit. If this is accepted, the comparison with bromination can be used as a guide to the ' true relative reactivity ' of toluene. Experiments with deactivated substrates [4] in aqueous sulphuric acid have shown that a logarithmic plot of relative rates for nitration against those for bromination has a slope of 1·3. From this slope and the relative rate of bromination of toluene (Table 1), the relative rate of nitration of toluene by the nitronium ion comes to be 79. In terms of this relative rate, the reactivity of $p\text{-}MeC_6H_4\cdot\overset{+}{N}Me_3$ (extrapolated to 30% H_2SO_4) is about 9 times more than expected from the additivity principle ($\Delta = 0{\cdot}96$); a result similar to the corresponding result in bromination ($\Delta = 0{\cdot}65$).

Thus, this comparison of nitration with bromination suggests that the large deviations from the additivity principle in the nitration of methyl-substituted compounds [11,12,19] arise in part from the use of inappropriate partial rate factors for the nitration of toluene. However, the foregoing relative rate of 79 obtained for toluene is unexpectedly high since, in aqueous acids, this relative reactivity reaches a limiting value of *ca.* 20 as the acidity is decreased.[10] It is important to know which of these values represents the relative reactivity of toluene in the absence of diffusion control and we hope to provide further evidence on this later. If the higher value is correct, then variations in the relative rate of nitration of toluene (up to a value of *ca.* 80) in different nitrating media need not reflect changes in the nature or discrimination of the electrophile but instead changes in the partitioning of the encounter pair (ArH,NO_2^+) between dissociation and substitution, for it is this factor which determines the influence of diffusion rates on the rate of reaction.[10,20]

We have not attempted a detailed analysis of the other deviations from the additivity principle because these deviations are not large and because of the difficulty of eliminating medium effects and the consequences of *ipso*-attack followed by rearrangement.[15] However, the consistency of the pattern of results observed with deactivating substituents in nitration and bromination suggests that such effects do not invalidate the interpretation given above.

EXPERIMENTAL

Materials.—The majority of the compounds studied were as described in previous papers.[1-6] Analysis results for the new compounds are shown in Table 6. The ammonium salts were prepared from the corresponding *NN*-dimethylamides by the procedures described previously.[6a] The sulphonium salts were prepared by heating the corresponding dibromides with sodium methanethiolate in ethanol for 8—10 h under reflux followed by methylation of the resulting thioether with the stoicheiometric amount of methyl fluorosulphonate. The solid obtained after evaporation of the solvent was crystallised several times from 30% perchloric acid to give the sulphonium perchlorate. The amines $p\text{-}MeC_6H_4[CH_2]_n\cdot NH_2$ (n = 1, 2, or 3) were obtained

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from Fluka or Aldrich and were purified by fractional distillation before use.

TABLE 7

Second-order rate coefficients (k_2/l mol^{-1} s^{-1}) for bromination of substituted benzenes in aqueous acids at 25°

Substituents									
$1\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	$4\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	$[H_2SO_4]$ (%)	3·86	6·29	11·01				
		log k_2	0·786	1·120	1·650				
$1\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	$3\text{-}[CH_2]_2\cdot\overset{+}{N}Me_3$	$[H_2SO_4]$ (%)	3·40	5·71	7·90				
		log k_2	1·381	1·730	2·024				
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$	$4\text{-}CH_2\cdot\overset{+}{N}Me_3$	$[H_2SO_4]$ (%)	39·40	47·97	54·93	60·20	63·10		
		log k_2	−1·477	−0·351	0·478	1·255	1·635		
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$	4-Me	$[H_2SO_4]$ (%)	1·03	5·53	11·84				
		log k_2	0·164	1·174	1·846				
$1\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$		$[H_2SO_4]$ (%)	0·87	1·74	2·80	5·59			
		log k_2	0·423	0·765	1·101	1·483			
$1\text{-}CH_2\cdot\overset{+}{S}Me_2$		$[H_2SO_4]$ (%)	13·28	19·72	25·20				
		log k_2	−0·008	0·481	1·185				
$1\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	$4\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	$[H_2SO_4]$ (%)	6·25	9·75	12·40	18·00			
		log k_2	0·981	1·455	1·699	2·178			
$1\text{-}CH_2\cdot\overset{+}{S}Me_2$	$4\text{-}CH_2\cdot\overset{+}{S}Me_2$	$[H_2SO_4]$ (%)	36·80	42·00	47·84	50·75	57·02	59·21	
		log k_2	−0·521 −0·563	0·006	0·612	0·988	1·856	2·142	
1-Me		$10^2[HClO_4]$/M	0·378	0·756	1·13	1·51	1·89	3·77	5·65
		log k_2	0·18	0·57	0·76	0·95	1·04	1·33	1·52
1-Me	2-Me	$10^2[HClO_4]$/M	0·246	0·356	0·492	0·732	0·944		
		log k_2	0·79	1·02	1·18	1·23	1·42		
1-Me	3-Me	$10^2[HClO_4]$/M	0·0283	0·0567	0·113	0·170	0·227	0·283	
		log k_2	0·83	1·06	1·30	1·48	1·60	1·71	

TABLE 8

Second-order rate coefficients (k_2/l mol^{-1} s^{-1}) for the nitration of substituted benzenes in aqueous sulphuric acid at 25°

Substituents								
$1\text{-}CH_2\cdot\overset{+}{N}H_3$	4-Me	$[H_2SO_4]$ (%)	63·58	67·35	70·00	71·37		
		log k_2	−3·308	−2·029	−1·118	−0·726		
$1\text{-}[CH_2]_2\cdot\overset{+}{N}H_3$	4-Me	$[H_2SO_4]$ (%)	64·50	67·67	70·16			
		log k_2	−1·799	−1·137	−0·452			
$1\text{-}[CH_2]_3\cdot\overset{+}{N}H_3$	4-Me	$[H_2SO_4]$ (%)	67·50	68·23	70·99			
		log k_2	−0·864	−0·661	0·100			
$1\text{-}CH_2\cdot\overset{+}{N}Me_3$	$4\text{-}CH_2\cdot\overset{+}{N}Me_3$	$[H_2SO_4]$ (%)	82·18	85·20	86·70	87·47	87·66	97·00
		log k_2	−6·540	−5·486	−4·927	−4·960	−4·762	−4·671
$1\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	$4\text{-}[CH_2]_2\cdot\overset{+}{S}Me_2$	$[H_2SO_4]$ (%)	70·93	75·25	76·15	76·65		
		log k_2	−2·508	−1·021	−0·604	−0·399		
$1\text{-}CH_2\cdot\overset{+}{S}Me_2$	$4\text{-}CH_2\cdot\overset{+}{S}Me_2$	$[H_2SO_4]$ (%)	80·83	82·54	86·70	90·60	93·07	
		log k_2	−5·473	−4·743	−3·294 −3·269	−2·664 −2·631	−2·775	

Products.—The product analyses for the bromination of the 'onium' salts in Table 1 were carried out by g.l.c. on the methyl esters of the bromobenzoic acids obtained by oxidation. A solution of the 'onium' salt (0·8 mmol) was treated with hypobromous acid (0·5 mmol) in aqueous sulphuric acid (45 ml) of an appropriate acidity. After reaction was complete, the solution was neutralised (Na_2CO_3) and the aromatic compounds were oxidised by gradual addition of a slight excess of potassium permanganate at 90 °C. The solution was finally heated under reflux for 9 h and filtered. The oxides of manganese were washed and the combined filtrates were concentrated, acidified, and extracted several times with ethyl acetate and ether. The organic layer was dried (Na_2SO_4) and evaporated to give a mixture of bromobenzoic acids. This mixture was suspended in dry ether and methylated with an excess of diazomethane. The resulting methyl bromobenzoates were dissolved in ethyl acetate and analysed on a Varian 1440 g.l.c. instrument [150 cm column; 5% Bentone on Chromosorb W (80—100 mesh) at 180°]. The results in Table 1 are mean values of those obtained from several experiments.

Unfortunately, the analysis of the bromination products of the salt $PhCH_2\cdot NMe_3^+$ ClO_4^- did not give reproducible results by the foregoing procedure probably because of incomplete oxidation. The analysis for this compound was therefore based on the n.m.r. spectrum of the fully brominated product. The neutralised reaction mixture (see above) was evaporated and all the organic material in the residue extracted with acetone. The extract was evaporated and the residue was dissolved in 1 : 1 (v/v) nitrobenzene–pyridine. Under these conditions, the methylene signals of the three bromo-products are sufficiently resolved to permit the product composition to be determined. The peaks were identified by comparison with spectra of model compounds. The result in Table 1 is the mean from six independent experiments.

The products of bromination of anisole were also determined by g.l.c. (3 ft column; 10% diethylene glycol succinate on 60—80 mesh Chromosorb P). A number of experiments were carried out at acidities varying from pH 3 to 4·9 and with samples of hypobromous acid purified in different ways. The amount of *ortho*-substitution varied markedly over the range 5—20%, the higher values being given by hypobromous acid which had been twice distilled, extracted three times with carbon tetrachloride, and used within 3 h of distillation. As outlined above, this variation is attributed to reaction *via* molecular bromine. The figure of 20—22% *ortho*-substitution is reproducible given highly purified hypobromous acid and is not exceeded in the presence of added silver nitrate ($1{\cdot}4 \times 10^{-5}$ mol l^{-1}); this value was therefore taken as corresponding to the pure 'positive bromine' reaction path.

The new analyses of nitration products (Table 3) were performed by g.l.c. following oxidation and methylation as described for the bromobenzoate esters above. The same g.l.c. column was used but at 200°. The procedure was checked by using known mixtures of the *ortho-*, *meta-*, and *para*-nitro-derivatives of $Ph[CH_2]_2{\cdot}\overset{+}{N}Me_3\ ClO_4^-$ and shown to give a mean error of ±1·5%. The results for the nitration of $PhCH_2{\cdot}\overset{+}{N}Me_3\ ClO_4^-$ were taken from the literature but were shown to agree with an analysis of the methylene chemical shifts in the n.m.r. spectrum of the reaction product by using the procedure outlined above for the corresponding bromo-compounds.

Kinetics.—The kinetics of bromination were followed by the spectrophotometric method described previously.[5] The new second-order rate coefficients [k_2; equation (3)] are listed in Table 7. The slopes of the rate profiles given by these compounds agree with those published previously.

$$\text{Rate} = k_2[\text{ArH}][\text{HOBr}] \qquad (3)$$

The kinetics of bromination of anisole were found to present special problems. The value of k_2 [equation (3)] for reaction in 0·000142M-perchloric acid has been given previously [5] as 910 l mol^{-1} s^{-1} but it was recognised then that this value was less reproducible than those obtained for less reactive substrates. It now appears from the product composition (see above) that much of this reaction occurs through molecular bromine presumably present as an impurity in the hypobromous acid. Both the product composition and the reaction rate are very sensitive to the purity of the hypobromous acid. The hypobromous acid solutions giving the limiting product composition (22% *ortho*) give a value of k_2 of 300 l mol^{-1} s^{-1} and this has been taken as characteristic of the 'positive bromine' mechanism. In the presence of silver nitrate ($1{\cdot}42 \times 10^{-5}$ mol l^{-1}) the value of k_2 is reduced to 220 l mol^{-1} s^{-1}, but a similar reduction is found in the rate of bromination of less reactive compounds where the kinetic form and reproducibility of the results suggest that the contribution of reaction through molecular bromine is negligible.

The present work has required a few further kinetic studies on nitration. These reactions were followed as described previously and the relevant rate coefficients are given in Table 8.

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