Inductive and Field Effects in Aromatic Substitution. Part VIII.[1] Kinetics of Nitration and Bromination of the 'Onium Salts of Dithia- and Diazacyclophanes

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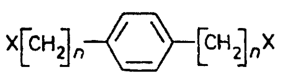
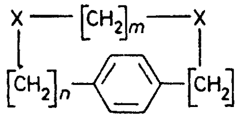
The reactivities, with respect to benzene, of certain open-chain ions (I; X = $\overset{+}{N}Me_3$ or $\overset{+}{S}Me_2$) and bridged ions (II; X = $\overset{+}{N}Me_2$ or $\overset{+}{S}Me$) have been compared in nitration and bromination with special reference to the rate retardation caused by bridging [(I) $\longrightarrow$ (II)]. This retardation decreases with an increase in the degree of methylation of the poles and in the length (*m*) of the methylene chain. For the compounds studied here, the retardation is greater when $n = 2$ than when $n = 1$ provided that the length of the bridge and the extent of alkylation of the poles are held constant. The retardation is attributed mainly to the change in the form of the molecular cavity with a further contribution, when $n > 1$ from the change in the distance of the poles from the aromatic ring.

PREVIOUS studies [2,3] on electrophilic substitution in the 'onium salts of diazacyclophanes have been concerned with the relative reactivity in nitration and hydrogen isotope exchange of the open-chain ions (I; X = $\overset{+}{N}H_3$ or $\overset{+}{N}Me_3$) and the bridged ions (II; X = $\overset{+}{N}H_2$ or $\overset{+}{N}Me_2$). The latter are much less reactive, and this was attributed in part to the effect of the bridge in reducing the distances of the nitrogen poles from the aromatic ring and in part to the change in the form of the molecular cavity. It is implicit in the first part of this argument that the open-chain ions react mainly in extended conformations, *e.g.* (III), rather than in conformations with the nitrogen poles near the aromatic ring, *e.g.* (IV).



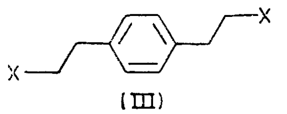
(I)

X = $\overset{+}{N}H_3, \overset{+}{N}Me_3, \overset{+}{S}Me_2$

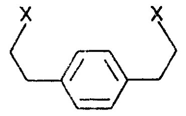


(II)

X = $\overset{+}{N}H_2, \overset{+}{N}Me_2, \overset{+}{S}Me$



(III)



(IV)

The results in the preceding paper have since raised doubts over whether the substituent effect of a $[CH_2]_2\overset{+}{N}H_3$ group does in fact depend on the conformation of the carbon chain. The work now reported was carried out to reinvestigate this matter with particular reference to the open-chain and bridged ions with $n = 1$ and 2. The comparison of these classes of compound is of value because, when $n = 1$, the distance of the positive poles from the ring in the transition state is independent of whether or not the bridging group is present. When $n = 2$, this is not so, providing that the open-chain ion reacts essentially through the extended structure (III).

RESULTS

The new work concerns how the rate of nitration of the ions (I) and (II) varies with the following structural changes: (a) the complete methylation of the nitrogen pole for $n = 1$; (b) the replacement of a nitrogen pole by a sulphur pole; and (c) the variation in the length of the bridging group in

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[1] Part VII, J. H. Rees and J. H. Ridd, preceding paper.

[2] A. Ricci, R. Danieli, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1547.

[3] R. Danieli, A. Ricci, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 2107.

structure (II). In addition, some of the above rate comparisons are repeated for bromination by hypobromous acid.

The nitration of these ions has been followed as described previously[2] and the rate coefficients are given in the Experimental section. For the ions with $n = 1$, the rate profiles are given in Figure 1b. As usual, these rate profiles are effectively parallel and so the relative rates with respect to the rate of nitration of benzene in 68% sulphuric acid have been calculated by a set of stepwise comparisons at the acidities used previously[2] and the results * are given in Table 1. The column headed Δ lists the reactivities of the bridged ions relative to the corresponding open-chain ions.

TABLE 1

Rates of nitration at 25° of the cyclophane derivatives (II) and the related open-chain ions (I) relative to that of benzene as unity

	Compound	log (rel. rate)	Δ[a]	Ref.
	$n = 1$			
A	(I; $X = \overset{+}{N}H_2Me$)	-6.43		b
B	(II; $X = \overset{+}{N}H_2$, $m = 8$)	-8.73	-2.30	b
C	(I; $X = \overset{+}{N}Me_3$)	-10.33		c
D	(II; $X = \overset{+}{N}Me_2$, $m = 8$)	-10.53	-0.20	d
E	(I; $X = \overset{+}{S}Me_2$)	-8.73		c
F	(II; $X = \overset{+}{S}Me$, $m = 6$)	-9.93	-1.20	d
G	(II; $X = \overset{+}{S}Me$, $m = 8$)	-9.57	-0.84	d
H	(II; $X = \overset{+}{S}Me$, $m = 10$,	-9.17	-0.44	d
	$n = 2$)			
I	(I; $X = \overset{+}{S}Me_2$)	-2.01		c
J	(II; $X = \overset{+}{S}Me$, $m = 4$)	-4.93	-2.92	d
K	(II; $X = \overset{+}{S}Me$, $m = 6$)	-3.72	-1.71	d
L	(II; $X = \overset{+}{S}Me$, $m = 8$)	-3.55	-1.54	d

[a] log (rel. rate) of the bridged ion minus log (rel. rate) of the corresponding open-chain ion. [b] Taken from ref. 2. [c] Based on the rate coefficients in ref. 4. [d] This work.

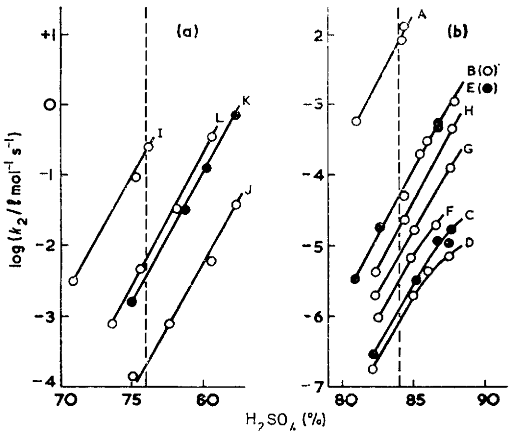


FIGURE 1 Plot of log k_2 for the nitration of ions of structures (I) and (II) in aqueous sulphuric acid at 25°: (a) ions with $n = 2$; (b) ions with $n = 1$. The dashed lines indicate the acidities used in the calculation of relative rates. For lettering, see Table 1.

Rate profiles for the related ions with $n = 2$ are shown in Figure 1a and the Δ values, calculated as described above, are included in Table 1.

TABLE 2

Rates of bromination at 25° by hypobromous acid of the cyclophane derivatives (II) and the related unbridged ions (I) relative to that of benzene as unity. For lettering, see Table 1

Compound	log (rel. rate)	Δ	Ref.
$n = 1$			
C	-6.38		4
D	-7.06	-0.68	
E	-5.30		4
F	-6.59	-1.29	
$n = 2$			
I	-0.56		4
K	-2.00	-1.44	

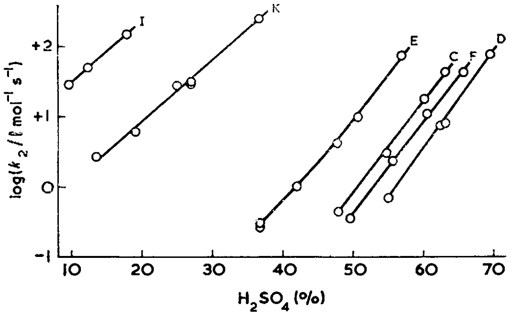
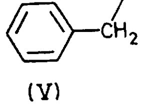


FIGURE 2 Plot of log k_2 for the bromination by hypobromous acid of ions of structures (I) and (II) in aqueous sulphuric acid at 25°. For lettering, see Table 1

The results for bromination have been followed as described previously[5] and the rate coefficients are given in the Experimental section. The rate profiles are not entirely linear (Figure 2) but the slopes are similar at a given acidity leading to the relative rates and Δ values given in Table 2.

DISCUSSION

Since the results and following discussion involve both nitrogen and sulphur poles, we start by noting the effect of this difference on the reactivity of the aromatic ring. The plots in Figure 3 shows that (i) the reactivity of the monosubstituted ion (V; $X = \overset{+}{S}Me_2$) is very similar to that of the ion (V; $X = \overset{+}{N}HMe_2$), (ii) the reactivity of the disubstituted ion (I; $X = \overset{+}{S}Me_2$, $n = 1$) is what would be expected for the reactivity of the corresponding ion with $X = \overset{+}{N}Me_2H$, and (iii) the reactivity of the bridged ion (II; $X = \overset{+}{S}Me$, $n = 1$, $m = 8$) is what



(V)

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* The relative rates of nitration of the open-chain ions in this Table have been reported recently in a paper on the Additivity Principle.[4] For that purpose, the reactivity of benzene, the monosubstituted benzene, and the disubstituted benzene were compared directly at the same acidity (68% H_2SO_4). Since the rate profile for benzene is not parallel to those of the positive ions, this method yields slightly different rates (by a factor of *ca.* 2) from those listed in Table 1.

[4] R. Danieli, A. Ricci, H. M. Gilow, and J. H. Ridd, *J.C.S. Perkin II*, 1974, 1477.

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

would be expected for the corresponding ion with X = $\overset{+}{N}MeH$. We have therefore taken the substituent effect of the sulphur poles as equivalent to that of the nitrogen poles with the same number of methyl groups.

In considering the change in reactivity resulting from bridging [(I) $\longrightarrow$ (II)], it is convenient to take first those systems with $n = 1$ and in which a methyl group on each pole is replaced by the methylene chain $[CH_2]_m$. The previous work [2] provided one example of this type, for the ion (II; $n = 1$, $m = 8$, X = $\overset{+}{N}H_3$) is less reactive than the ion (I; $n = 1$, X = $\overset{+}{N}H_2Me$) by a factor of 200; the reason for this change in reactivity of the ring was not clearly established.[2] The present work extends this type of comparison to the pairs of ions lettered (C and D) and (E and G) in Table 1. The methylene bridges in these ions have eight methylene groups as previously.

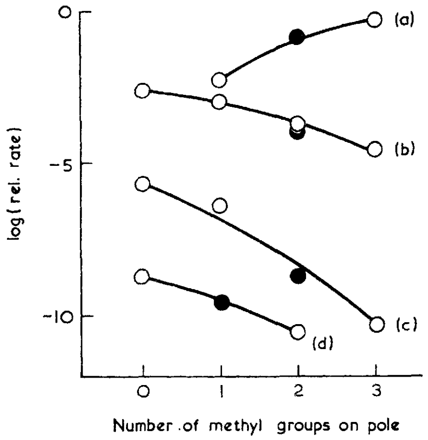

FIGURE 3 The effect of methylation at the positive pole on various relative reaction rates for nitration in aqueous sulphuric acid at 25°. (a) The change in rate (Δ value) when an ion (I; $n = 1$) with the indicated number of methyl groups is converted to the corresponding bridged ion with one fewer methyl group on each pole. (b) The relative reactivity of the ions (V) with respect to benzene. (c) The relative reactivity of the ions (I; $n = 1$) with respect to benzene. (d) The relative reactivity of the ions (II; $n = 1$) with respect to benzene. ○ nitrogen poles; ● sulphur poles

One explanation considered for the retardation observed previously [2] is that the substituent effect of a $CH_2\overset{+}{N}H_3$ group depends on its conformation with respect to the ring; the deactivation being greatest when the C–N bond is perpendicular to the plane of the ring, as is necessarily found in the bridged ion. This explanation accords with the very small retardation found in bridging the fully methylated ion C to give D (Table 1), for models suggest that the $CH_2\overset{+}{N}Me_3$ groups in the open-chain ion are constrained to adopt this conformation by steric interaction between the protons of the methyl groups and the *ortho*-protons of the ring.

Nevertheless, for several reasons, we doubt whether this conformational effect is large enough to account for the observed results. Studies with atomic models suggest that the steric constraints on conformation in the open-chain ions (I; $n = 1$) are present only when X = $\overset{+}{N}Me_3$ and yet the plots on Figure 3 indicate that the Δ values (Table 1) and the reactivities of the monosubstituted ions (V) and open-chain ions (I; $n = 1$) vary smoothly with the extent of methylation of the pole. In addition, the semiquantitative treatment developed in the following paper suggests that the conformational factor, although probably present, contributes little to the reactivity changes produced by bridging.

If bridging in the fully methylated systems C $\longrightarrow$ D (Table 1) is taken as standard, then the plots in Figure 3 show that the large reactivity changes observed in such systems as A $\longrightarrow$ B arise because the replacement of a methyl group on the pole by a lone pair or a proton increases the reactivity of the open-chain systems much more than that of the bridged systems. This supports the view [2] that the changes in reactivity produced by bridging come from the modifications in the form of the molecular cavity: [6] the changes are greatest when the charges in the open-chain ion are most exposed to the solvent. On this interpretation, both bridging and methylation increase the electrostatic interaction between the poles and the charge on the ring in the transition state.

The characteristics of the molecular cavity should also influence the reaction rate through steric hindrance to the solvation of the transition state, irrespective of the change in the intramolecular electrostatic interactions. Some preliminary experiments on hydrogen isotope exchange in [10]paracyclophane [7] suggest that this molecule is much less reactive than *para*-xylene probably from this cause. However, for our present purposes it is unnecessary to distinguish between this type of cavity effect and that described above.

The important point is that, if the retardation produced by bridging derives from the change in the form of the molecular cavity, then this factor will also operate when $n > 1$ although not necessarily to the same extent. In addition, when $n > 1$, there may be a further retardation arising from a change in the distance of the poles from the aromatic ring. Thus, if, in the open-chain ion with $n = 2$, the conformation (III) is much more reactive than the conformation (IV), then the effect of bridging should reflect this difference in reactivity as well as the change in the form of the molecular cavity.

The results in Table 1 permit the comparison of the Δ values for three pairs of ions in which n is changed from 1 to 2 while the length of the total saturated chain ($= 2n + m + 2$) and the degree of alkylation is held constant. These pairs are F and J, G and K, and H and L. Within each pair the retardation produced by bridging is greater with $n = 2$, than with $n = 1$. If there were no difference in the reactivity of the different conformations of the ions with $n = 2$, then the reverse

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[6] A. J. Layton, J. H. Rees, and J. H. Ridd, *J.C.S. Chem. Comm.*, 1974, 518.

[7] J. H. Rees, Ph.D. Thesis, London, 1973.

should be true, for more of the space near the ring is occupied in the open-chain ion with $n = 2$ [*cf.* structure (IV)] than in the open-chain with $n = 1$. We conclude therefore that the ions with $n = 2$ react mainly in an extended conformation, *e.g.* (III), as originally expected. This is not wholely consistent with the results obtained in Part VII and the reason for this is considered in the following paper.

One unexpected feature of the results in Table 1 is that the reactivities of the bridged systems with both $n = 1$ and 2 increase with the length of the bridging group. Presumably, the longer and more flexible the bridge, the more the molecular cavity is opened up to incursion by the solvent. In the systems with $n = 2$, the longer bridges are also less effective at holding the positive poles near the aromatic ring.

The key comparisons above have been repeated for aromatic bromination. A plot of the relative rates for nitration against those for bromination gives somewhat more scatter than expected but the slope is consistent with that obtained previously and the deviations are not sufficient to cast doubt on the above conclusions.

EXPERIMENTAL

Materials.—The preparation of the open-chain ammonium and sulphonium perchlorates has been described previously.[4] The perchlorate of the bridged ion (II; $X = \overset{+}{\mathrm{N}}\mathrm{Me}_2$, $n = 1$, $m = 8$) was prepared by the methylation of the corresponding unmethylated ion [2] with methyl iodide in dry ether followed by treatment of the resulting iodide with 30% aqueous perchloric acid. The product was recrystallised several times from acetonitrile–ether. The bridged sulphonium perchlorates were prepared from the corresponding dithiacyclophanes [8] by methylating with a slight excess of methyl fluorosulphonate in methylene dichloride. The reagents were mixed at $-60°$ and the reaction mixture was then brought to room temperature and stirred for 2 h. The precipitated fluorosulphonate salts were treated with several samples of 40% perchloric acid and the resulting perchlorates were recrystallised from water or acetonitrile–ether. Analytical data for these compounds are given in Table 3.

The inorganic reagents were as described previously.[5]

TABLE 3

Analytical results for new 'onium ions (II) as perchlorates. For lettering, see Table 1

Compound	M.p. (°C)	Found (%)			Calc. (%)		
		C	H	N	C	H	N
D	221	47.3	7.3	5.5	47.4	7.2	5.6
				S			S
F	174	39.8	5.6	13.2	39.9	5.4	13.3
G	185	42.4	6.1	12.3	42.4	5.9	12.6
H	214	44.9	6.2	11.8	44.7	6.4	11.9
J	120	39.9	5.6	13.0	39.9	5.4	13.3
K	223	42.4	5.7	12.7	42.4	5.9	12.6
L	199	44.7	6.4	11.7	44.7	6.4	11.9

Kinetics.—The kinetic results for the open-chain ions (I) in Tables 1 and 2 have already been published. The results for the bridged ions (II) were obtained using the same spectrophotometric techniques and are listed in terms of the usual second-order rate coefficients (first-order with respect to the aromatic substrate and first-order with respect to stoicheiometric nitric acid or stoicheiometric hypobromous acid) in Tables 4 and 5. The plots in Figure 3 required the measurement of rates of nitration of the monosubstituted ions (V; $X = \overset{+}{\mathrm{N}}\mathrm{H}_2\mathrm{Me}$ or $\overset{+}{\mathrm{N}}\mathrm{HMe}_2$) and these are included in Table 4. The relative rates (with respect to benzene) for the ions (V) have been calculated by comparison with that [4] of (V; $X = \overset{+}{\mathrm{N}}\mathrm{Me}_3$) and are as follows: (V; $X = \overset{+}{\mathrm{N}}\mathrm{H}_2\mathrm{Me}$), -3.00; (V; $X = \overset{+}{\mathrm{N}}\mathrm{HMe}_2$), -3.73. Some of the kinetic runs on bromination in Table 5 were sufficiently fast to require direct recording of the optical density on chart paper at chart speeds of up to 500 mm min^{-1}.

TABLE 4

Second-order rate coefficients (l mol^{-1} s^{-1}) for nitration at 25° of the 'onium salts from substituted cyclophanes (II) and related ions. For lettering, see Table 1

Substrate					
D	H_2SO_4 (%)	82.18	84.95	86.05	87.51
	log k_2	-6.740	-5.700	-5.381	-5.142
H	H_2SO_4 (%)	82.30	84.37	87.58	
	log k_2	-5.374	-4.634	-3.325	
G	H_2SO_4 (%)	82.30	85.06	87.58	
	log k_2	-5.700	-4.773	-3.903	
F	H_2SO_4 (%)	82.54	84.80	86.52	
	log k_2	-6.017	-5.167	-4.693	
L	H_2SO_4 (%)	73.92	76.14	76.93	82.41
	log k_2	-2.950	-2.063	-2.039	0.112
K	H_2SO_4 (%)	75.00	78.70	80.25	82.33
	log k_2	-2.794	-1.497	-0.893	-0.144
J	H_2SO_4 (%)	75.11	77.66	80.58	82.30
	log k_2	-3.843	-3.094	-2.207	-1.413
$\mathrm{PhCH_2\overset{+}{N}H_2Me}$	H_2SO_4 (%)	74.84	77.69	79.54	
	log k_2	-1.563	-0.500	0.239	
$\mathrm{PhCH_2\overset{+}{N}HMe_2}$	H_2SO_4 (%)	74.84	77.69	79.54	
	log k_2	-2.020	-1.206	-0.401	

TABLE 5

Second-order rate coefficients (l mol^{-1} s^{-1}) for the bromination at 25° by hypobromous acid of the 'onium ions from substituted cyclophanes (II). For lettering, see Table 1

Compd.						
D	H_2SO_4 (%)	54.93	62.40	63.10	69.45	
	log k_2	0.039	0.868	0.899	1.878	
F	H_2SO_4 (%)	49.50	55.56	60.49	65.75	
	log k_2	-0.446	0.375	1.036	1.634	
K	H_2SO_4 (%)	13.58	19.18	25.07	27.10	36.70
	log k_2	0.432	0.783	1.437	1.472 1.487	2.410

[5/1191 *Received, 19th June,* 1975]

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[8] A. Ricci, R. Danieli, R. A. Phillips, and J. H. Ridd, *J. Heterocyclic Chem.*, 1974, **11**, 551.