Inductive and Field Effects in Aromatic Substitution. Part VI.[1] The Kinetics of Hydrogen Isotope Exchange in Quaternary Salts of Diazacyclophanes and in the Related Unbridged Ions

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The kinetics of hydrogen isotope exchange between deuteriosulphuric acid and the aromatic protons of diquaternary ions belonging to the series (I; n = 1—3) and (II; n = 2 or 3) have been studied by n.m.r. spectroscopy. A logarithmic plot of the rates of hydrogen isotope exchange against the rates of the corresponding nitration reactions is linear with a slope of 1·5. This relationship supports the view that steric hindrance is not a major factor in determining the deactivation of the bridged ions (II) relative to the open-chain ions (I) for a given value of n. This deactivation is attributed to the greater field effect of the nitrogen poles in the bridged ions.

THE reactivities for aromatic nitration of the two series of diquaternary ions (I) and (II) have recently been compared. For a given value of n, the reactivity of the bridged system (II) was much less than that of the open-chain system (I). For $n > 1$, the relative deactivation of the bridged systems was attributed mainly to the greater field effect of the nitrogen poles since these poles are then constrained to lie near the aromatic ring. However, the results for nitration[1] also provided evidence that the distance of the nitrogen poles from the aromatic ring was not the only factor in determining the greater deactivation of the bridged systems. Thus, the bridged system with $n = 1$ was also less reactive than the corresponding open-chain systems and in this comparison, the distance of the nitrogen poles from the centre of the aromatic ring should (assuming no distortion of bond angles) be independent of the presence of the bridge.

Because of these results and some related problems,[1] it appeared desirable to determine whether the pattern of reactivities observed in nitration could be reproduced in another electrophilic substitution. We now report the corresponding results for hydrogen isotope exchange in deuteriosulphuric acid. This is a particularly suitable reaction for comparison with nitration since the lower steric requirements of hydrogen isotope exchange should reduce any contribution of steric interaction to the rate ratios.[2]

Hydrogen isotope exchange in these systems is easy to follow by n.m.r. spectroscopy because, in all the compounds considered, the four aromatic hydrogen atoms are equivalent. The rate of exchange has been determined

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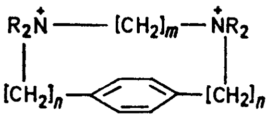
[1] Part V, A. Ricci, R. Danieli, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1547.

[2] R. O. C. Norman and R. Taylor, ' Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965, p. 212.

from the change in the integrated absorption of these aromatic protons. Since the compounds considered cover a very wide range of reactivity (a factor of *ca.* 10^9), we have not thought it worth while to extrapolate the rate coefficients to zero concentration of the aromatic substrate and have instead used a similar concentration for all the compounds studied (*ca.* 0·1M). The corresponding first-order rate coefficients are listed in Table 1. The n.m.r. spectra show that the exchange reactions are not complicated by concurrent sulphonation.

(I)



(II)

Table 1

First-order rate coefficients for aromatic hydrogen isotope exchange in the diquaternary ions of structures (I) and (II) in deuteriosulphuric acid at 50°

Substrate	D_2SO_4 (%)	10^5k_1/s^{-1}
(A) (I; $n = 3$, R = H)	65·5	1·05
	69·2	4·2
	77·3	138
	(96·0	$1{\cdot}82 \times 10^5$) *
(B) (I; $n = 3$, R = Me)	72·7	19·6
	77·6	120
	(96·0	$1{\cdot}35 \times 10^5$) *
(C) (I; $n = 2$, R = H)	77·2	0·85
	85·4	13·2
	86·0	20·0
	89·6	63·3
	(96·0	725) *
(D) (I; $n = 1$, R = H)	94·4	$8{\cdot}3 \times 10^{-5}$
	(96·0	$1{\cdot}5 \times 10^{-4}$) *
(E) (II; $n = 3$, $m = 2$, R = Me)	96·0	2·10
(F) (II; $n = 2$, $m = 4$, R = Me)	96·0	$1{\cdot}32 \times 10^{-1}$

* Extrapolated value, see text.

Rates of exchange in 96% deuteriosulphuric acid were used to calculate relative reactivities. The open-chain ion (I; $n = 2$, R = H) was somewhat too reactive to study accurately under these conditions and so the rate coefficient was estimated by the extrapolation shown in Figure 1. Some rather approximate runs carried out in 96% acid agreed with the extrapolated value within a factor of 2. The rate coefficients for the exchange reactions of the ions (I; $n = 3$, R = H) and (I; $n = 3$, R = Me) in 96% acid were estimated by a step-wise comparison with the reactivity of the ion (I; $n = 2$, R = H) at lower acidities (see Figure 1). The slight extrapolation required to obtain the rate coefficient for exchange in the ion (I; $n = 1$, R = H) in 96% acid was obtained by assuming that this rate profile was parallel to that for the corresponding ion with $n = 2$.

In principle, the substrates with protonated poles could undergo aromatic hydrogen isotope exchange by preliminary loss of an N–H proton to form the mono-conjugate base. No evidence for such reaction paths was found in the kinetic studies of nitration[1] and the very similar reactivity of the ions (I; $n = 3$, R = H) and (I; $n = 3$, R = Me) in hydrogen isotope exchange (see Figure 1) suggests that such reaction paths are unimportant under the conditions reported here. The rate coefficients for the substrates with R = H will therefore be discussed on the basis of reaction through the dications.

Unfortunately, the most deactivated substrate studied in the nitration work, the ion (II; $n = 1, m = 8$, R = H) proved too unreactive for kinetic studies of hydrogen isotope exchange under these conditions. The relationship between the rates of exchange of the other ions in 96% deuteriosulphuric acid and the relative reactivity of the same ions in nitration is shown in Figure 2. These relative rates of nitration are taken from Table 2 of ref. 1 and refer to the reactivity of benzene as unity.

To a good approximation, the plot in Figure 2 is linear; thus much of the general discussion of the nitration results[1] can be carried over to hydrogen isotope exchange and will not be repeated here. Two additional points deserve comment.

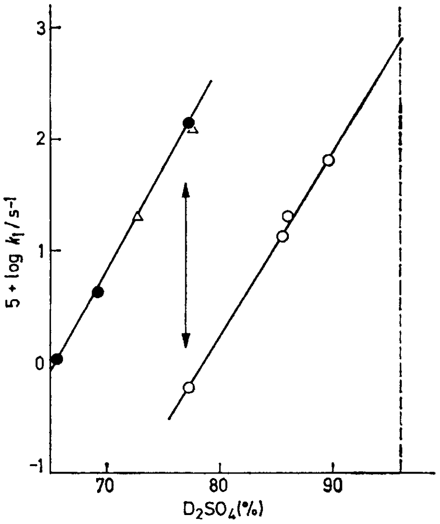


Figure 1 Rate profiles for hydrogen isotope exchange in the ions (I; $n = 2$, R = H) (open circles) and (I; $n = 3$, R = H) (filled circles). The points for exchange in the methylated ion (I; $n = 3$, R = Me) are represented by triangles

One derives from the magnitude of the slope (1·55) in Figure 2. This implies that substituent effects on hydrogen isotope exchange provides the clearest evidence that the deactivating effect of a $[CH_2]_n\overset{+}{N}R_3$ group depends on the conformation of the carbon chain. Thus, if the rate of exchange in the bridged ion (II; $n = 3$, $m = 4$, R = Me) is taken as unity, that in the corresponding open-chain ion (I; $n = 3$, R = Me) is $6{\cdot}4 \times 10^4$. The corresponding rate ratio in nitration is $1{\cdot}8 \times 10^3$. Presumably the transition state for hydrogen isotope exchange has more charge on the aromatic ring and so the field effect of the nitrogen poles is correspondingly increased.

The greater sensitivity of hydrogen isotope exchange to structural changes accords with studies on benzene and toluene. The partial rate factor for the *para*-nitration of toluene[3] in 68% sulphuric acid at 25° is 38; the corresponding value for hydrogen isotope exchange has been given[4] as 83 and also as 250.[5]

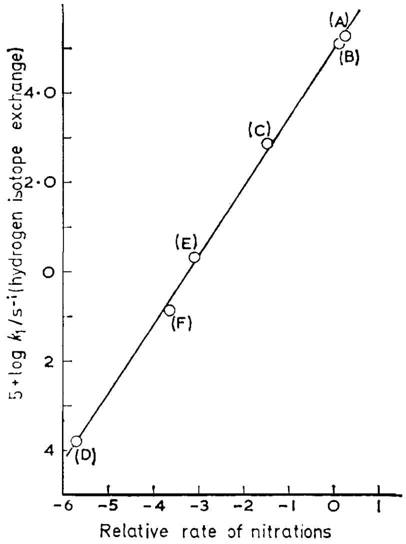


FIGURE 2 The relationship between the rate of hydrogen isotope exchange in 96% deuteriosulphuric acid at 50° and the relative rate of nitration in aqueous sulphuric acid at 25°. The lettering of the points corresponds to that in Table 1

The other point comes from the small deviations from linearity in Figure 2. The results in Table 2 compare the rate ratios for increasing the number of methylene groups (n) from 2 to 3 in the open-chain and bridged series. On taking the logarithms of these ratios, the result for the open-chain series is *ca.* 3 times that for the bridged series in nitration and twice that for the bridged series in hydrogen-isotope exchange. In terms of the analysis given previously,[1] this implies a greater contribution from the inductive effect of the poles in hydrogen isotope exchange. However, we do not wish to stress this difference, because the errors inherent in this method of following the kinetics of hydrogen isotope exchange are considerably magnified in calculating the ratio of the logarithms of rate ratios.

TABLE 2

Rate ratios corresponding to a change from 2 to 3 in the number of methylene groups (n) in structures (I) and (II)

		Open-chain structures (I; R = H)	Bridged structures * (II; R = Me)
$\frac{k(n = 3)}{k(n = 2)}$	Nitration	52	3·4
	Hydrogen isotope exchange	251	15·9

* The total number of atoms in the bridge ($2n + m + 2$) is kept at 10.

With the exception of the above point, the results for hydrogen isotope exchange show the expected relationship with those for nitration (*cf.* Figure 2). In particular, the bridged ions (E) and (F) show no abnormally high reactivity in hydrogen isotope exchange. Since hydrogen isotope exchange is believed to be less sensitive than nitration to steric interactions,[2] the above relationship implies that steric hindrance is not an important factor in determining the relative reactivities in nitration.

EXPERIMENTAL

Materials.—The amines and quaternary salts were prepared as described previously.[1] Merck, analytical grade, deuteriosulphuric acid was diluted as required with deuterium oxide (99·7% deuterium). The composition of the diluted solutions was determined by the titration of weighed portions with sodium hydroxide.

Kinetic Runs.—These were followed by the integration of the aromatic peaks using a PS100, 100 MHz JEOL n.m.r. spectrometer. The reaction was started by adding a weighed quantity of the aromatic compound to the deuteriosulphuric acid (0·5 ml) in an n.m.r. tube at 50° to give a concentration of *ca.* 0·1M. The methylated ions [R = Me in structures (I) and (II)] were added as perchlorates; the protonated ions (I; n = 1 or 2, R = H) were added as the corresponding amines. To facilitate rapid solution, one of the protonated substrates (I; n = 3, R = H) was added as the chloride. The concentrations of deuteriosulphuric acid

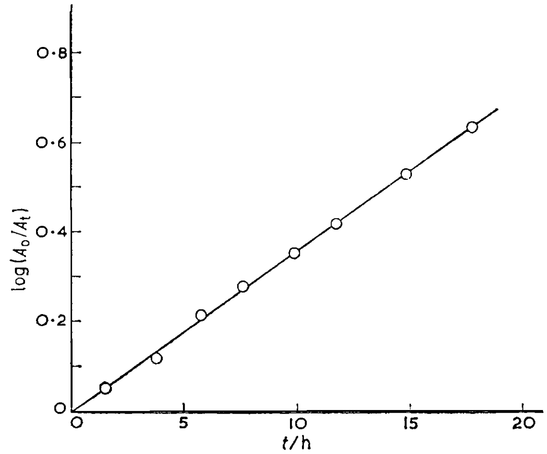


FIGURE 3 Hydrogen isotope exchange in the bridged ion (II; n = 3, m = 2, R = Me) in 96% deuteriosulphuric acid at 50°. The variation of the integrated absorption of the aromatic protons at time t (A_t) divided by that at the start of the measurements (A_0)

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[3] Calculated from the kinetic data and product analysis given by R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc.* (*B*), 1968, 800.

[4] V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 1956, 2743.

[5] C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1960, 3301; 1961, 247.

in Table 1 are corrected to take account of the acid removed by protonation of the amines and chloride ions.

The decrease in the integrated absorption (A) of the aromatic peaks was found to follow a first-order law. A typical plot of $\log(A_0/A_t)$ against time is shown in Figure 3. At the concentrations of aromatic compounds used, the amount of hydrogen in the solution at complete reaction (2—3%) is too small to give significant deviations from a first-order plot. Many of the kinetic runs were done in duplicate: the rate coefficients normally differed by <5%.

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