Aromatic Substitution with Rearrangement. Part IV.[1] Catalysis by Halide Ions of the Acid-catalysed Prototropic Rearrangement of 4-Bromo-2,6-di-t-butylcyclohexa-2,5-dienone in Acetic Acid

By **P. B. D. de la Mare** * and **A. Singh**, Chemistry Department, University of Auckland, Private Bag, Auckland, New Zealand

The acid-catalysed prototropic rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone to 4-bromo-2,6-di-t-butylphenol has been studied in acetic acid and in aqueous acetic acid in the presence of some added anions. Whereas lithium perchlorate influences the rate only through an environmental effect, lithium bromide exerts specific catalysis; in part by attack on the 4-proton, thus giving rearrangement, and in part by removing positive bromine. Kinetic evidence indicates that the catalytic power is exerted only within an ion pair of bromide ion and the protonated dienone; from the results, the equilibrium constant between ion pairs involving perchlorate and bromide respectively as counter-ions has been evaluated. Primary ($k_1^{4-H}:k_1^{4-D}$) and solvent ($k_1^{HOAc}:k_1^{DOAc}$) isotope effects have been recorded for the various stages of reaction, and the mechanistic consequences are discussed. Lithium chloride also shows specific catalytic power, though to a lesser extent than lithium bromide.

In Part III[1] we discussed the kinetics of the acid-catalysed prototropic rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone to 4-bromo-2,6-di-t-butylphenol in acetic acid and in aqueous acetic acid. The rates were shown to depend on the acidity function, H_0, of the medium as measured by the extent of protonation of *o*-nitroaniline or of *NN*-dimethyl-*p*-nitroaniline. In solvents ranging in water content from 0 to 2·2M, they are represented by equation (1) with a maximum

$$3 + \log_{10} k_1 + H_0 = 1{\cdot}58 \qquad (1)$$

deviation of 0·14, and a standard deviation of 0·066. The solvent deuterium isotope effect was found to be numerically almost the same as that on the protonation of *o*-nitroaniline, and so can be regarded as characterising a proton pre-equilibrium with a reverse isotope effect of *ca.* 4, as represented by equation (2).

$$3 + \log_{10} k_1 + D_0 = 2{\cdot}22 \pm 0{\cdot}15 \qquad (2)$$

The primary deuterium isotope effect, $k_1^{4-H}:k_1^{4-D}$, was 4·2 in acetic acid, diminishing to 3·8 in aqueous acetic acid (H_2O, 3M), a result which establishes that the removal of the proton is concerned in the rate-determining stage of the reaction and suggests by invocation of the Hammond[2] principle that the stretching of the C–H bond in the transition state lies somewhat to the side of reactants rather than of products.

We have now extended this work by examining the effects of some added anions as catalysts for the reaction. It will be seen that the perchlorate ion has only a minor effect; but chloride and particularly bromide ions have specific influences on the course of the acid-catalysed rearrangement. Base-catalysed rearrangement, and the influence of added sodium acetate, will be discussed in a later paper.

EXPERIMENTAL

Most of the materials and methods have already been described.[1,3] Lithium perchlorate was heated in a weighed container under a current of dry nitrogen until the crystals melted. It was then allowed to cool, and the dry salt was reweighed and dissolved in a known volume of acetic acid. Solutions of lithium bromide, which was first recrystallised twice from acetone, and of lithium chloride were prepared similarly. Rates were always monitored by the determination of the value of H_0 for the solutions used for the reaction.

Influence of Lithium Perchlorate.—Table 1 shows the influence of added lithium perchlorate on the rate of rearrangement. The value of the expression $3 + \log_{10} k_1 + H_0$ has a mean value, 1·55 ± 0·08, nearly the same as that without lithium perchlorate. There seems to be no clear systematic trend in the deviations; so the influence of the perchlorate ion on the acid-catalysed rearrangement is small, like that of added water; though of course it exerts some effect (much smaller than that of water) by altering the protonating power of the medium.

---

[1] Part I, P. B. D. de la Mare, A. Singh, J. G. Tillett, and M. Zeltner, *J. Chem. Soc.* (*B*), 1971, 1122.

[2] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[3] P. B. D. de la Mare, O. H. M. El Dusouqui, J. G. Tillett, and M. Zeltner, *J. Chem. Soc.*, 1964, 5306.

Influence of Added Lithium Chloride.—Table 2 shows the influence of added lithium chloride on the rate of rearrangement of the dienone. It is clear that at constant [LiCl], the reaction is catalysed by $HClO_4$, and at constant [$HClO_4$] it is catalysed by LiCl. The values of $3 + \log_{10} k_1 + H_0$, which correct the rate for the acidity of the medium, all lie rather higher than the values found for the reaction catalysed only by perchloric acid and for the reaction in the presence of lithium perchlorate (1·58 and 1·55 respectively). But the catalysis is sufficiently small that the uncatalysed rate is always a considerable proportion of the catalysed rate, so detailed analysis of the results is probably unjustified. Direct comparison of the rates of reaction in the presence of lithium chloride for the dienone and its 4-deuterio-derivative, however, shows that the value of $k_1^{4\text{-H}} : k_1^{4\text{-D}}$ is 2·6 at high concentrations of chloride. Since the corresponding ratio for the uncatalysed reaction [1] is 4·2 under these conditions, the catalysed path must be subject to a still smaller primary deuterium isotope effect, calculated to be 2·2 subject to some error because of the contribution from the uncatalysed rate.

TABLE 1

Rates of rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone in acetic acid in the presence of lithium perchlorate at 25 °C

[$LiClO_4$]/mM	[$HClO_4$]/mM	H_0	k_1/min^{-1}	$3 + \log_{10}k_1$
7·00	0·310	−0·29	0·0760	1·88
35·0	0·310	−0·28	0·0750	1·88
8·00	0·340	−0·21	0·0750	1·88
37·0	0·340	−0·20	0·0740	1·87
7·00	0·510	−0·53	1·06	2·03
35·0	0·510	−0·51	0·115	2·06
7·00	0·560	−0·44	0·107	2·03
37·0	0·560	−0·46	0·115	2·06
7·00	1·00	−0·84	0·184	2·26
35·0	1·00	−0·83	0·177	2·25
7·00	1·09	−0·79	0·185	2·28
37·0	1·09	−0·75	0·177	2·25

TABLE 2

Rates of rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone and its 4-deuterio-derivative in acetic acid containing lithium chloride at 25 °C

[LiCl]/mM	$4 + \log_{10}$ [LiCl]	[$HClO_4$]/mM	H_0	k_1/min^{-1} (4-H, with LiCl)	k_1/min^{-1} (4-D, with LiCl)	k_1/min^{-1} (4-H, without LiCl) *	$3 + \log_{10} k_1 + H_0$ (4-H, with LiCl) †
0·380	0·58	1·0	−0·63	0·247		0·163	1·76
0·920	0·97	1·00	0·28	0·0400		0·0200	1·88
1·90	1·27	1·00	0·70	0·0160		0·00760	1·91
8·00	1·90	0·630	0·92	0·00950		0·00460	1·90
9·30	1·97	1·00	0·51	0·0310		0·0120	2·01
18·0	2·26	11·0	−0·35	0·168		0·0850	1·88
37·0	2·57	2·00	0·25	0·0500	0·0188	0·0210	1·95
37·0	2·57	7·00	−0·13	0·125	0·0478	0·0510	1·97
40·0	2·60	4·00	0·01	0·106		0·0370	2·04
71·0	2·85	2·10	0·57	0·0360		0·0100	2·13
80·0	2·90	4·00	0·13	0·0880		0·0280	2·07

* From equation (1). † Mean value without LiCl, 1·58.

Influence of Added Lithium Bromide.—*Stoicheiometry*. The addition of lithium bromide gave much more substantial catalysis, and the results could therefore be analysed more satisfactorily. It was noted first that the course of the reaction under these conditions was more complex than that taken in the earlier experiments. The spectrum of the reacting mixture, when scanned at intervals, failed to give good isosbestic points at 285 and at 292 nm. The oxidation, which affected the late stages of the reaction catalysed by perchloric acid, was absent, but in the region 280—320 nm the optical density at first increased to a magnitude much greater than that which could be attributed to 4-bromo-2,6-di-t-butylphenol, and then slowly decreased. This increase could be attributed to the formation of bromine, most of which would be present as tribromide ions under these conditions. If 2,6-dimethylphenol was added to the reaction mixture to remove free bromine as soon as it is formed, the reaction proceeded normally. The results in Table 3 illustrate this.

The molar extinction coefficient of bromine in acetic acid containing 0·061M-LiBr is 6·9 × 10^3 l mol^{-1} at 320 nm; a value of 0·505 after 15 min corresponds with the formation of 0·073mM-Br_2. In further experiments the values of H_0 for the reacting solutions were determined, and hence the amount of dienone expected to have been decomposed was estimated by reference to the kinetic measurements described below. Table 4 shows the results.

Under these conditions the maximum optical density was reached in approximately one-tenth of the half-life for the bromination of 2,6-di-t-butylphenol, so the rate of the latter reaction could be neglected; the optical densities of other components of the reaction mixture were also negligible, as was further confirmed by repeating the measurements by use of the optical densities at 330 nm and at 340 nm.

TABLE 3

Formation of bromine, as measured by the optical density at 320 nm, accompanying the rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone (0·82mM) in acetic acid containing lithium bromide (0·061M) at 25 °C

(*a*) No additive

t/min	0·16	2·0	4·0	8·0	10·0	15·0
Optical density (320 nm)	0·225	0·349	0·410	0·474	0·490	0·505

(*b*) With added 2,6-dimethylphenol (4·3 mM)

t/min	0·33	2·0	4·0	8·0	10·0	15·0
Optical density (320 nm)	0·145	0·100	0·060	0·030	0·010	0·000

Kinetics. It is implied by the above experiments that, in the presence of added lithium bromide, the acid-catalysed reaction of the dienone gives some bromine, which can be removed by the addition of sufficient excess of a rapidly reacting aromatic compound. Cross-bromination of added phenol was confirmed preparatively. To a solution (50 ml) of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone (0·095 g) was added a mixture of phenol (0·71 g) and lithium bromide (0·08M) in acetic acid (350 ml). When reaction was complete (12 h at room temperature), the reaction mixture was poured into water and extracted several times with diethyl ether. The ethereal fraction was washed ($NaHCO_3$, H_2O) and dried (Na_2SO_4). After removal of the solvent, t.l.c. of the residue on silica gel with benzene as solvent showed the presence of phenol, 2,6-di-t-butylphenol, 4-bromo-2,6-di-t-butylphenol, and *p*-bromophenol.

Table 4

Formation or bromine accompanying the rearrangement of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone (0·405mM) and its 4-deuterio-derivative in acetic acid containing 0·2mM-$HClO_4$ at 25 °C

[LiBr]/mM	H_0	Max. optical density at 320 nm (4-H)	Dehalogenation (% of dienone decomposed) (4-H)	Max. optical density at 320 nm (4-D)	Dehalogenation (% of dienone decomposed) (4-D)
15·0	0·04	0·121	9·4	0·258	20·0
30·0	−0·07	0·161	9·4	0·346	20·2
38·0	−0·08	0·176	9·5	0·373	20·1

Preparative t.l.c. gave 0·0068 g of material the i.r. spectrum of which was identical with that of *p*-bromophenol.

Table 5

Rates of decomposition of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone (0·11mM) in acetic acid containing lithium bromide (0·0455M) with added aromatic substrates at 25 °C

Added substrate	Concn./ mM	H_0	k_1/min^{-1}	$3 + \log_{10}k_1 + H_0$
2,6-Dimethylphenol	2·60	0·60	0·0980	2·59
2,6-Dimethylphenol	3·90	0·72	0·0800	2·62
2,6-Di-t-butylphenol	2·60	0·65	0·0950	2·63
2,6-Di-t-butylphenol	3·80	0·72	0·0790	2·62
1,3-Dimethoxybenzene	2·50	0·68	0·0930	2·65
1,3-Dimethoxybenzene	3·80	0·65	0·0920	2·62

Table 6

Rates of decomposition, in the presence of excess of phenol (0·02M), of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone (1·1mM) in acetic acid containing relatively high concentrations of LiBr at 25 °C

[LiBr]/mM	[$HClO_4$]/mM	H_0	k_1/min^{-1}	$3 + \log_{10} k_1 + H_0$
2·25	0·540	−0·28	0·660	2·54
2·50		+0·57	0·0810	2·48
3·40		+1·02	0·0420	2·65
6·80		+0·84	0·0890	2·61
8·30	0·490	−0·29	0·770	2·60
10·0		+0·88	0·0580	2·64
17·0		+0·61	0·0810	2·52
25·0		+0·62	0·0810	2·53
28·0		+0·92	0·0560	2·67
33·0	0·490	−0·20	0·570	2·56
42·0		+0·80	0·0660	2·62
43·0		+0·57	0·102	2·58
43·0	0·290	+0·06	0·340	2·59
48·0	0·540	−0·23	0·655	2·59
50·0		+0·34	0·140	2·49
51·0		+0·41	0·140	2·56
56·0		+0·77	0·0740	2·64
70·0		+0·73	0·0740	2·60
83·0	0·490	−0·34	0·890	2·61
84·0		+0·70	0·0780	2·59
100		+0·25	0·170	2·48
100		+0·23	0·170	2·46
100	0·490	−0·06	0·430	2·57

The kinetics of decomposition of the dienone in the presence of lithium bromide were difficult to measure accurately, since the tribromide ion formed as part of the reaction product absorbs strongly at 260 nm, the wavelength best for following the rate of disappearance of dienone in acetic acid. Reasonable estimates of the initial rates could be obtained by extrapolating the curves of optical density against time, but it was found preferable to include in the reaction mixture a rapidly reacting phenol to remove bromine as it was formed. Under these conditions the measured rate-coefficients showed good first-order behaviour for 90% reaction at relatively low acidities, and for 50% reaction at the highest acidities where the overall rate was very fast. The results in Table 5 illustrate that the measured rate was not affected by change in the amount or concentration of the aromatic compound added. Hence most of the rates recorded in the later Tables were obtained in the presence of added phenol. The results given in Table 6 establish that the rate of the catalysed reaction is still dependent on the acidity.

All the experiments quoted in Tables 5 and 6 refer to concentrations of lithium bromide higher than 0·0023M, and the rates corrected for acidity are all the same, and about ten times faster than the rate of the corresponding non-catalysed rearrangement. At sufficiently low concentrations of bromide, the rate diminishes; and the point at which a fall-off is noted depends on the total concentration of perchlorate ions, as is shown by the results given in Table 7.

Table 7

Rates of decomposition * of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone in acetic acid containing added electrolytes at 25 °C

[LiBr]/ mM	[$LiClO_4$]/ mM	[$HClO_4$]/ mM	H_0	k_1/min^{-1}	$3 + \log_{10} k_1 + H_0$ Found	$3 + \log_{10} k_1 + H_0$ Calc.
0·00130		0·490	−0·50	0·125	1·60	1·60
0·0100		0·380	−0·37	0·200	1·93	1·79
0·0120		0·490	−0·50	0·147	1·67	1·78
0·0120		0·490	−0·50	0·126	1·60	1·78
0·0450		0·540	−0·20	0·155	1·99	2·02
0·0500		0·380	−0·33	0·302	2·15	2·12
0·0900		0·540	−0·25	0·229	2·11	2·17
0·100		0·380	−0·40	0·490	2·29	2·27
0·420		0·490	−0·54	0·77	2·35	2·44
0·505	0·402	0·384	−0·38	0·680	2·45	2·42
0·505	1·00	0·384	−0·39	0·560	2·35	2·33
0·505	1·30	0·384	−0·41	0·520	2·31	2·29
0·505	2·78	0·384	−0·41	0·417	2·21	2·16
1·00			+0·08	0·39	2·67	2·57
1·26		0·380	−0·44	0·910	2·52	2·53
1·26	7·02	0·380	−0·42	0·480	2·26	2·18
1·26	36·72	0·380	−0·37	0·191	1·91	1·84
1·26	73·82	0·380	−0·32	0·118	1·75	1·73
1·26	107	0·380	−0·60	0·204	1·71	1·69

* Rates were obtained in the presence of 0·02M-phenol except for the last five entries; for these, initial rates are recorded.

The calculated values of $3 + \log_{10} k_1 + H_0$ given in the last column of Table 7 are obtained by using expression (3) with the values $K_{ip} = 3{\cdot}0$ and $k_1^{(Br^-)}$, the limiting rate-

$$\log_{10} k_1 = \log_{10} k_1^{(HClO_4)} + \log_{10} \frac{K_{ip}\{k_1^{(Br^-)}/k_1^{(HClO_4)}\}[Br^-] + [ClO_4^-]}{K_{ip}[Br^-] + [ClO_4^-]} \qquad (3)$$

coefficient corrected for acidity in the presence of excess of bromide ion $= 9{\cdot}9\, k_1^{(HClO_4)}$, the constant rate-coefficient corrected for acidity in the presence of perchloric acid. These values were found by trial and error to minimise the standard deviation of the mean difference between observed and calculated values of $(3 + \log_{10} k_1 + H_0)$ for the results in Tables 6 and 7; the combined standard deviation is 0·06. The use of equation (3) is considered further in the Discussion section.

Primary deuterium isotope effect. Table 8 shows that the value of the primary deuterium isotope effect, $k_1^{4\text{-H}} : k_1^{4\text{-D}}$, which in the absence of bromide ion [1] is 4·2, decreases with added bromide ion to a constant value when bromide ion has been added in sufficient amount to give the limiting rate. Since only a small proportion of the catalysed reaction gives bromine, and the remainder involves catalysis of deprotonation, a primary kinetic isotope effect of 2·3 (Table 8) would be exepcted to be reflected in a similar product deuterium isotope effect. Results were included in Table 4, and bear out the above conclusion; detailed interpretation is given in the Discussion section.

TABLE 8

Rates of decomposition of [4-$^2H_1$]4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone in acetic acid containing lithium bromide at 25 °C

[LiBr]/mM	[HClO$_4$]/mM	H_0	k_1/min^{-1}	$k_1^{4\text{-H}} : k_1^{4\text{-D}}$
0·045	0·54	−0·20	0·084	3·3
0·090	0·54	−0·25	0·084	2·7
2·30	0·54	−0·28	0·264	2·5
43·0	0·54	−0·23	0·300	2·2
43·0	0·29	0·06	0·148	2·3
43·0		0·57	0·0437	2·3

TABLE 9

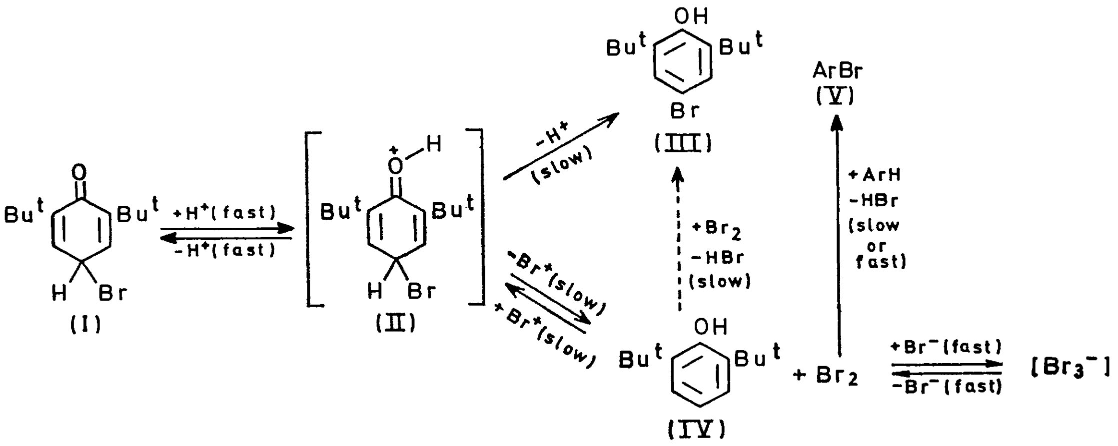
Rates of decomposition of 4-bromo-2,6-di-t-butylcyclohex-2,5-dienone in deuterioacetic acid ($CH_3{\cdot}CO_2D$) at 25 °C

[LiBr]/mM	D_0	k_1/min^{-1}	$3 + \log_{10} k_1 + D_0$
7	1·43	0·062	3·22
28	1·13	0·101	3·13

Solvent deuterium isotope effect. Table 9 gives results for the rate of bromide-catalysed decomposition of the dienone in deuterioacetic acid. Comparisons of results in Tables 6 and 9 indicate that at constant acidity (as measured by D_0 in deuterioacetic acid and H_0 in acetic acid) the rate is faster in deuterioacetic acid than in acetic acid by a factor which averages (antilog$_{10}$ 0·58), *i.e.*, 3·8.

DISCUSSION

The Scheme shows the stoicheiometry of the various reactions considered in Part I [1] and in this paper, together with an indication of the relative speeds of the processes involved. The results in Part I [1] established the existence and rapidity of the proton pre-equilibrium (I) $\rightleftharpoons$ (II), and the conversion of the conjugate acid (II) of the dienone into the bromophenol (III) by a slow process having a significant primary isotope effect, reduced slightly by increase in the proton-accepting power of the medium.



SCHEME

The present work shows that in the presence of extra added perchlorate ion, which has relatively low nucleophilic power, no obvious change occurs in the course of the reaction. In the presence of added chloride or bromide ions, however, new phenomena are observed, and an elaboration of the mechanism is required. Since bromide is more powerful than chloride ion in evoking the change in mechanism, we chose this ion for detailed study.

The stoicheiometry being considered first, it is clear that a new reaction becomes evident, namely debromination. With a reasonable excess of bromide ions, this route comprises 9·5% of the total reaction. The formation of bromine can be established both from its spectrum (which under the conditions of our study is mainly that of the tribromide ion, into which bromine is largely converted by bromide) and, in the presence of sufficiently reactive added substrates, by diversion of the reaction to give products (V) of cross-bromination.

This path, however, accounts for only a small part of the catalysed process. With sufficient excess of bromide ions, the proportion of reaction giving bromine becomes constant within experimental error, and so does the measured overall rate of reaction. Under these conditions the rate of the catalysed reaction has become ten times that expected for the uncatalysed reaction under the same conditions, so that interference by the uncatalysed reaction has become small and can be allowed for without much error. The measured rates recorded in Tables 5—8 as involving decomposition, rather than rearrangement, of the dienone are those of total disappearance of dienone to give both bromophenol (III) and phenol (IV), and some 90·5% of the total catalysed portion leads to the product of rearrangement (III).

Both components of the bromide-catalysed reaction are catalysed also by acids; the results of Table 6, for example, show that at constant concentration of bromide ion the addition of perchloric acid is associated with the expected increase in the protonating power of the medium (as indicated by decrease in the numerical value of H_0), and with a corresponding increase in the overall rate of decomposition; the latter involves rearrangement as the major, and debromination as the minor component. The Scheme provides a sensible interpretation in mechanistic terms if it is assumed that the function of bromide ions is to act as a nucleophile, removing [H^+] to give (III), and Br^+ to give (IV) in a ratio which is independent of the concentration of bromide provided that this is high enough. It provides also a sensible interpretation of the solvent deuterium isotope effect; at constant acidity as measured by D_0 or H_0 respectively the rate is faster in deuterioacetic acid than in acetic acid by a factor of *ca.* 3·8. An alternative way of expressing this, since *o*-nitroaniline is more protonated in deuterioacetic acid than in acetic acid ($\Delta pK_a = 0{\cdot}61$),[1,4] is that at the same indicator ratio for *o*-nitroaniline, the rate in deuterioacetic acid is not very different from that in acetic acid. The results are therefore very similar to those for the reaction catalysed only by perchloric acid, and imply that a proton pre-equilibrium precedes further reaction.

The Scheme provides also an immediate interpretation of the primary deuterium isotope effect. Table 8 shows by direct comparison of the rates of decomposition of 4-bromo-2,6-di-t-butylcyclohexa-2,5-dienone and its 4-deuterio-derivative in acetic acid that the observed primary deuterium isotope effect falls as bromide is introduced, from 4·2 (the value obtained without added bromide) to a limiting value of 2·3. The total reaction when this limiting value is reached includes a component from the reaction involving loss of bromine; the latter process can have only a small secondary isotope effect. We assume as what we shall call the first hypothesis that the total reaction also includes a component from the path catalysed only by acid. The experimental isotope effect needs to be corrected approximately in order to obtain a value of the primary deuterium isotope effect for the bromide-catalysed deprotonation, namely 2·5. In confirmation of this interpretation, the proportion of bromide-catalysed dehalogenation is greater for 4-deuterio-dienone than for its protio-analogue. The results are in Table 4; the experimental value for the proportion of dehalogenation of the deuterio-dienone, expressed as a percentage of the total deuterio-dienone decomposed, is 20·1%; the value calculated from the measured kinetic isotope effects for the various reaction paths open to the protonated dienone and the proportion in which these paths are adopted by the protio-dienone is 21·6%. The results of studies of kinetics and of product-proportions are thus in reasonable agreement. If it is assumed as the second hypothesis that the path catalysed by acid is eliminated by bromide ion, the primary isotope effect on the bromide-catalysed reaction is 2·7, and the calculated percentage of dehalogenation of the deuterio-dienone in the presence of bromide ion is 26·8%, in poorer agreement with experiment. We return later to the mechanistic interpretation of these two hypotheses.

The Scheme is still incomplete, in that it gives no interpretation of the fact that the rate of decomposition of the dienone reaches a limit in the presence of sufficient added bromide ion. In interpreting this result kinetically it should be noted that, as with the acid-catalysed rearrangement, this rate is subject to acid-catalysis, and that its major component is subject both to a substantial inverse solvent deuterium isotope effect and to a normal primary deuterium isotope effect. When one remembers that acetic acid has a very low dielectric constant, and hence that the formation of ion pairs is very important in this solvent, even at low concentrations of electrolytes,[5-7] it seems very likely that the correlation of rate with acidity as measured by the extent of protonation of *o*-nitroaniline should be regarded as a correlation between the extents of protonation of the base and the substrate to give ion pairs, only slightly dissociated at reasonably high concentrations of electrolyte. Homer *et al.*[8] have used an analogous treatment in discussing the kinetics of removal of the *N*-benzyloxycarbonyl group from *N*-benzyloxycarbonylglycine ethyl ester and related compounds in acetic acid containing hydrobromic acid or sulphuric acid. Equations (4) and (5) represent the situation when the formation of ion pairs is dominated by the presence of perchlorate ion as the most important counter-ion.

This interpretation being accepted, in the presence of a mixture of anions the measurements of the indicator-ratio, and hence of the extent of protonation of *o*-nitroaniline, measure in fact the sum of the concentrations

---

[4] E. Högfeldt and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1960, **82**, 15.

[5] I. M. Kolthoff and A. Willman, *J. Amer. Chem. Soc.*, 1934, **56**, 1007.

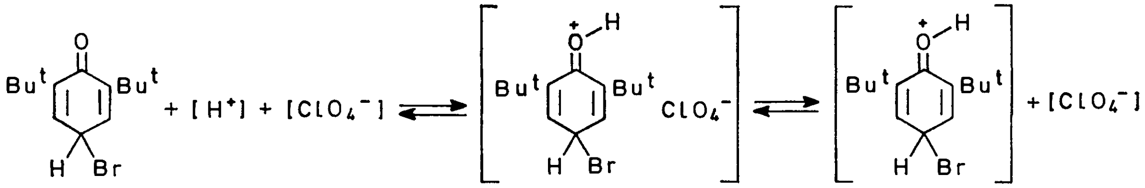
[6] S. Winstein, B. Appel, R. Baker, and A. Diaz, 'Organic Reaction Mechanisms,' Chem. Soc. Special Publ. No. 19, p. 109 (1965).

[7] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' 2nd edn., Bell, New York, 1969, p. 497.

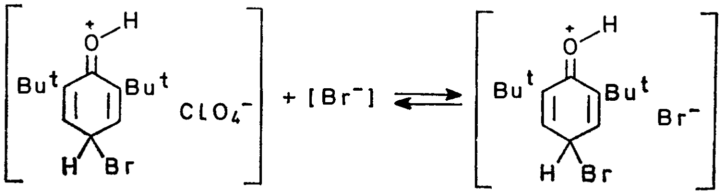
[8] R. B. Homer, R. B. Moodie, and H. N. Rydon, *J. Chem. Soc.*, 1965, 4403.

of all the forms of the protonated species, *i.e.*, of all the ion pairs, together with any dissociated ions which may be present. The fact that the extent of catalysis by bromide reaches a limit, giving a rate which is still related through the acidity function to the extent of protonation of *o*-nitroaniline, then reflects the fact that at sufficiently high concentrations of bromide ion the equilibrium between the ion pairs involving perchlorate and bromide counter-ions respectively is fully to the right of equation (6), so that further addition of bromide ion cannot further increase the rate.

$$\mathrm{ArNH_2} + [\mathrm{H^+}] + [\mathrm{ClO_4^-}] \rightleftharpoons [\mathrm{ArNH_3^+ClO_4^-}] \rightleftharpoons [\mathrm{ArNH_3^+}] + [\mathrm{ClO_4^-}] \qquad (4)$$



(5)



(6)

Equation (6) defines an ion-pair equilibrium, written as in (7), where S is the unprotonated dienone. A test of

$$K_{ip} = [\mathrm{SH^+Br^-}][\mathrm{ClO_4^-}]/[\mathrm{SH^+ClO_4^-}][\mathrm{Br^-}] \qquad (7)$$

the applicability of this treatment to our kinetic system comes through the fact that, at any given concentration of perchlorate ion, increase in concentration of bromide ion will increase the rate until the limiting rate is reached. At that point, if the concentration of bromide ion is kept constant but perchlorate ion is added, the rate will be decreased as the ion-pair equilibrium [equation (6)] is shifted back to the left. That this happens is shown by the results in Table 7, where it appears that addition of 3mM-$\mathrm{LiClO_4}$ considerably reduces the rate of decomposition of the dienone catalysed by 0·384mM-$\mathrm{HClO_4}$ and 0·5mM-LiBr; and that 7mM-$\mathrm{LiClO_4}$ similarly reduces the rate catalysed by 0·38mM-$\mathrm{HClO_4}$ and 1·26mM-LiBr.

A quantitative test of this theory can be made, since the acid-catalysed rate in the absence of bromide ion, $k_1^{(\mathrm{HClO_4})}$, is known experimentally to be given by $3 + \log_{10} k_1^{(\mathrm{HClO_4})} + H_0 = 1{\cdot}58$. Then, if two reactions are concerned, one of *any* protonated species with the solvent (in accordance with the first hypothesis above) and one of the bromide-containing ion pair, the rate-behaviour in the region where both perchlorate- and bromide-containing ion pairs are present in significant proportion can easily be shown to be represented by the relationship of equation (3). From this and the experimental data, values of K_{ip} and of $k_1^{(\mathrm{Br}^-)}/k_1^{(\mathrm{HClO_4})}$ can be found by trial; values of 3·0 and 9·9 respectively give the best fit.* The last two columns of Table 7 show the comparison between observed and calculated rates. We are not aware that this constant has been determined previously, but qualitatively its value seems reasonable by comparison with other ion-pair equilibrium constants which have been established in acetic acid.[9]

Adoption alternatively of the second hypothesis, that the path catalysed only by acids is available only for the perchlorate-containing ion pair and becomes negligible in the presence of bromide ions, can be shown also to allow treatment of the results by equation (3), but we have preferred the former treatment for two reasons. First, the correlation of rate with h_0 over a very wide range of solvent-acidity, including solutions not containing the perchlorate ion and solutions containing water,[1] makes it seem very likely that the pathway involving proton-loss to the solvent, with its primary kinetic isotope effect of *ca.* 4, is available for the protonated dienone no matter what the counter-ion is. Secondly, as we have mentioned, the product deuterium isotope effect is better represented by the first hypothesis.

The sequence of measured primary isotope effects for nucleophiles HOAc, HOAc + $\mathrm{H_2O}$, and $\mathrm{Br^-}$, namely 4·2, 3·8,[1] and 2·5 respectively, is consistent with the view that the transition states in these reactions lie well towards the reactants. The catalytic power of the bromide ion for deprotonation and for debromination is apparently exercised only within the ion pair, and not by free bromide ion, since when all the protonated dienone is present as ion pair neither the rate of reaction nor the proportion of debromination is further increased by added bromide ion.

---

* The results of Table 6 define the latter value with 95% confidence limits 9·9 ± 0·6; those of Table 7 are less sensitive to the value of K_{ip}, which can reasonably be considered to be defined within the limits 3·0 ± 0·8.

[9] M. R. Crampton and E. Grunwald, *J. Amer. Chem. Soc.*, 1971, **93**, 2987, 2990.

In our treatment we have for convenience represented only two of the possible ion pairs which could be considered; further disposable parameters would be provided by including the possible acetate-containing ion pair and the free dissociated ion in our considerations; indeed it may be that some of the small deviations from the relationship between the rate and the acidity function reflect not imperfections in our measurements, but neglect of these complications. We think, however, that the results would not justify the still more elaborate treatment that would be necessary.

We assume that the chloride ion exerts its catalytic power similarly, but we have examined this reaction only by kinetic measurements, which make it clear that chloride ion is less effective than bromide ion as a nucleophile for hydrogen in this solvent. The chloride ion is known to be effective as a catalyst for removing positive iodine from iodo-2,4,6-trimethoxybenzene in water under catalysis by acids,[10] and one of the transition states suggested for this reaction is similar in general character to that involved in the bromo- and chlorodebromination described in the present paper.

[2/700 *Received, 24th March,* 1972]

---

[10] B. D. Batts and V. Gold, *J. Chem. Soc.*, 1965, 5753.