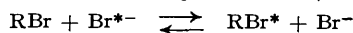


303. *The Kinetics of Exchange Reactions. Part IV. Substituted Phenyl and Benzyl Bromides.*

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The exchange of radioactive bromide ion with a number of substituted phenyl and benzyl bromides in ethylene diacetate has been studied. In all cases the non-exponential term in the Arrhenius equation was found to increase with the withdrawal of electrons from the benzene ring, which suggests that the approach of the attacking anions is facilitated by the "thinning" of the π -electron screen round the ring. With increasing electron withdrawal from the ring the activation energy falls in the phenyl series and rises in the benzyl series : it seems that in the former the influence of electron displacement is chiefly on the formation of the new C-Br bond, whereas in the latter it mainly affects the breaking of the initial bond.

As a continuation of earlier work on isotopic exchange reactions of organic bromo-compounds with radioactive bromide ion (Le Roux and Sugden, *J.*, 1939, 1279; Elliott and Sugden, *ibid.*, p. 1836; Le Roux, Lu, Sugden, and Thomson, *J.*, 1945, 586), the reaction



has been investigated for a series of phenyl and benzyl bromides with lithium bromide in ethylene diacetate.

Improvements in technique, together with the availability of radio-bromine of much higher activity, have enabled more accurate results to be obtained than was possible in the earlier work.

The concentration of organic bromide in the reaction mixture was 0.050M. in all cases, and that of lithium bromide 0.030M. Any effect caused by incomplete dissociation of the lithium bromide (cf. Evans and Sugden, *J.*, 1949, 270) is therefore eliminated. No conductivity measurements in ethylene diacetate are at present available, but since there was found to be no measurable variation of rate constant with lithium bromide concentration over the range 0.01—0.1M. it is probable that the degree of dissociation of lithium bromide does not vary over this range.

EXPERIMENTAL.

Materials.—*cycloHexylmethyl bromide.* *cycloHexylmethylcarbinol* was prepared by the action of paraformaldehyde on the Grignard reagent from *cyclohexyl bromide* (Adams and Noller, *Org. Synth.*, 1926, 6, 22). This was converted into the bromide by phosphorus tribromide at 0° (Hiers and Adams, *J. Amer. Chem. Soc.*, 1926, 48, 2385). The product, dried over freshly ignited potassium carbonate and distilled in *vacuo*, had b. p. 60—62°/10 mm., n_D^{25} 1.4891.

Picryl bromide. The best method of preparation was found to be the nitration of bromobenzene by a modification of the methods of Frankland and Garner (*J. Soc. Chem. Ind.*, 1920, 39, 257) and of Jackson and Earle (*Amer. Chem. J.*, 1903, 29, 212). Bromobenzene (25 ml.) was heated at 140° for 17 hours with concentrated sulphuric acid (300 ml.) and fuming nitric acid (d 1.51; 100 ml.). The crystals which separated were heated at 140° for a further 12 hours with half of the above quantities of acids, and the mixture then cooled and poured into ice-water. The product, recrystallised twice from alcohol, had m. p. 122—123.5°.

Benzyl bromide. Material of laboratory reagent grade (B.D.H.) was dried (K_2CO_3) and distilled : the fraction of b. p. 196—197° was kept over potassium carbonate and then distilled in *vacuo*. The colourless product had b. p. 55°/2 mm., n_D^{25} 1.5728.

p-Nitrobenzyl bromide. A commercial specimen, crystallised twice from 90% aqueous alcohol, had m. p. 99—99.5°.

2 : 4-Dinitrobenzyl bromide. *p*-Nitrobenzyl chloride (35 g.) was suspended in concentrated sulphuric acid (155 ml.), and nitric acid (21 ml.) added at <25°. After 30 minutes the mixture was poured on crushed ice, and the 2 : 4-dinitrobenzyl chloride filtered off. This was heated with sodium bromide (35 g.) in 90% aqueous acetone (250 ml.) for 3 hours. The acetone was distilled off, and the residue extracted with water, recrystallised three times from alcohol, and dried in *vacuo*; it had m. p. 46—46.5°.

p-Cyanobenzyl bromide. *p*-Tolunitrile was brominated at 200°, the product extracted with hot benzene, and the solvent allowed to evaporate at room temperature. The residue was purified by sublimation in *vacuo* at 110°, recrystallisation from alcohol, and resublimation. The white product had m. p. 114.5°.

p-Methoxybenzyl bromide. *p*-Anisaldehyde was reduced to the alcohol by Carothers and Adams's method (*J. Amer. Chem. Soc.*, 1924, 46, 1675) and treated in benzene with dry hydrogen bromide. The bromide, purified by two distillations in an all-glass apparatus at 0.3—0.4 mm. of nitrogen, was a pale amber-coloured liquid, b. p. 91°/0.3 mm., n_D^{25} 1.5790. Considerable resinification occurred even when a

relatively pure product was distilled. Bromine was determined by silver nitrate (a very rapid reaction) (Found: Br, 39.2. Calc. for C_8H_9OBr : Br, 39.8%). The compound is very unstable (cf. Späth, *Monatsh.*, 1913, **34**, 2000; Baker, *J.*, 1932, 2631). For the present work a stock solution was made in ethylene diacetate through which nitrogen had been bubbled, and the kinetic runs were carried out as soon as possible. No irregularities were noted in the experimental results to indicate decomposition of such solutions.

Ethylene diacetate. Commercial "ethylene glycol diacetate" was distilled in an all-glass apparatus, and the first 20% rejected to eliminate water. This treatment proved adequate, as was shown by tests of the rate of reaction of *p*-cyanobenzyl bromide and lithium bromide at -7.40° in samples of ethylene diacetate treated as shown in Table I. The effect of small amounts of water is in agreement with the view expressed by Hughes and Ingold (*J.*, 1935, 244) that increased solvation should retard the rate of a S_N2 reaction.

TABLE I.

Reaction of *p*-cyanobenzyl bromide with lithium bromide at -7.40° .

Treatment of solvent.	10^4k (l. mole ⁻¹ sec. ⁻¹).
Simple distillation	2.28
Redistilled after being dried over anhyd. $CuSO_4$	2.31
Redistilled in <i>vacuo</i> after being dried over $Mg(ClO_4)_2$	2.29
0.5% of water added	1.59
0.75% of water added	1.40

The coefficient of expansion by heat of ethylene diacetate, determined by measurements of the density, was 0.00112 per degree over the range 15–100°.

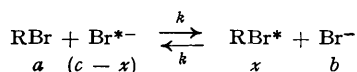
Thermostats.—Ordinary water-filled thermostat baths served for temperatures between 15° and 50°. Temperatures down to -30° were obtained by the use of a wide-mouthed Dewar flask containing alcohol. Cooling was provided by a jacketed tube, filled with solid carbon dioxide and acetone, dipping into the alcohol. A small electric heater controlled in the ordinary way served to keep the temperature constant to within $\pm 0.02^\circ$. For temperatures up to 150° a thermostat bath filled with heavy oil was used and was accurate to $\pm 0.05^\circ$.

Radio-bromine.—The earlier runs were carried out with lithium bromide prepared by neutron irradiation of ethylene dibromide (Lu and Sugden, *J.*, 1939, 1273). Later, extremely active specimens were produced by the neutron bombardment of sodium bromate or ammonium bromide in the pile at Harwell, and were converted into lithium bromide in this Laboratory.

Counting Equipment.—All-glass β -ray counters of the annular type containing *ca.* 10 ml. of liquid were used. They were constructed in these Laboratories, and supplemented in the later work by several counters purchased from Alltools Ltd. The impulses were amplified and fed to a scaling unit, either a Wynne-Williams scale-of-eight or a Morley-Duke scale-of-thirty-two.

Kinetic Technique.—The technique of Le Roux and Sugden (*loc. cit.*) had to be greatly modified, as it was found to be unsuitable for work using ethylene diacetate as solvent. Radioactive lithium bromide was thoroughly dried by heating it just below its point of fusion, and dissolved in ethylene diacetate to give a solution of twice the concentration required in the reaction mixture; the strength of this solution was determined by a Volhard titration. Equal quantities of the lithium bromide solution and of a 0.100M-stock solution of the aryl bromide in ethylene diacetate were pipetted one into each arm of a Y-shaped reaction vessel, and the arms sealed off. The vessel was placed in the thermostat bath and allowed to warm to thermostat temperature before mixing of the contents. The reaction was terminated by removing the vessel from the thermostat, breaking off the end of one arm, and rapidly pouring the contents into a water-benzene mixture in a separating funnel. For 20 ml. of reaction mixture, 10 ml. of water and 40 ml. of benzene were used. The aqueous layer, containing the lithium bromide, was shaken with a further 40 ml. of benzene. Two further quantities (*ca.* 8 ml. and 5 ml.) of water were shaken successively with the two benzene layers to wash out any residual lithium bromide, and the combined aqueous extracts evaporated to *ca.* 10 ml. A small volume of the original solution of lithium bromide was extracted and made up in the same way for counting. With this technique there is no necessity either for complete washing out of the reaction mixture, or for complete recovery of the lithium bromide, though it was found that the above procedure does give practically 100% recovery. The extracted aqueous solutions were kept for $1\frac{1}{2}$ hours before counting, to allow the attainment of radioactive equilibrium (Le Roux and Sugden, *loc. cit.*). Each solution was counted at least twice, and the rate of decay at some standard time found, so that after titration for bromide ion by the usual Volhard method the activity per unit concentration of bromide could be calculated.

In the reaction



it may readily be shown that, since $x \ll a$ and $c \ll b$,

$$k = -\frac{2.303}{t(a+b)} \log_{10} \left[1 - \frac{x}{c} \left(1 + \frac{a}{b} \right) \right]$$

The quantity $(c-x)/c$, which is the fraction of the original radio-bromide remaining after time t , is the ratio of the activities per unit concentration of bromide ion in the exchanged and the original solution.

The reactants were measured out in pipettes which had been calibrated to deliver ethylene diacetate, and the concentrations of the solutions at the temperature of reaction were corrected for expansion of the solvent. The main source of error in experiments such as these is in the counting of the radioactive solutions. The probable error in counting of n particles from a radioactive source is $0.67n^{\frac{1}{2}}$, so that the probable error in counting 10,000 particles, which was about the number counted for any one solution, is less than 0.7%.

Tests for Hydrolysis of Organic Bromides.—Known volumes of the stock solutions of the aryl bromides were extracted with benzene-water as in an actual run, and the aqueous extracts titrated for bromide. Only *p*-methoxybenzyl bromide showed any detectable hydrolysis, and as this amounted at the most to 0.5% no correction was applied to the experimental figures.

Test of the Order of the Reaction.—It is well established that halide exchange reactions are bimolecular in media of low ionising power, and Le Roux and Sugden (*loc. cit.*) showed that the exchanges of several aliphatic bromides with bromide ion have second-order kinetics in acetone, 90% aqueous acetone, and ethylene diacetate. For this reason it was considered sufficient to test the order of reaction for one of the compounds used. For this purpose *p*-nitrobenzyl bromide was studied, at -6.60° . The concentration of organic bromide was varied from 0.02 to 0.10M., and the lithium bromide from 0.01 to 0.10M., but the rate constant, calculated for a second-order reaction, remained constant within experimental error.

RESULTS.

Table II summarises the average rate constants for each substance. The concentration of aryl bromide in every case was 0.050M. and that of lithium bromide was 0.030M.

TABLE II.

Compound.	Temp.	No. of results.	10^4k (l. mole ⁻¹ sec. ⁻¹).	Compound.	Temp.	No. of results.	10^4k (l. mole ⁻¹ sec. ⁻¹).
<i>cyclo</i> Hexylmethyl bromide	89.73°	8	1.23	<i>p</i> -Nitrobenzyl bromide	— 5.10°	6	4.57
	99.61	9	2.67		0.00	8	7.56
	111.40	8	6.13		5.58	8	13.7
	122.20	12	11.9		11.39	5	24.5
			15.18		7	33.7	
					20.00	9	54.1
Picryl bromide	— 5.30	9	1.99	2 : 4-Dinitrobenzyl bromide	—27.29	5	3.10
	0.00	12	3.92		—19.94	3	8.16
	10.19	9	13.1		— 6.60	6	42.0
	21.62	9	45.3				
Benzyl bromide	5.58	8	1.21	<i>p</i> -Cyanobenzyl bromide	— 7.40	9	2.29
	16.86	6	3.38		4.78	9	9.47
	24.91	13	7.89		15.14	11	27.1
	34.90	9	16.8		25.01	9	75.9
	44.88	11	36.4				
<i>p</i> -Methoxybenzyl bromide	— 5.30	6	3.14				
	4.88	8	8.33				
	14.80	8	20.0				
	25.00	9	45.2				

TABLE III.

Bromide.	10^4k_{25} (l. mole ⁻¹ sec. ⁻¹).	A .	E' (kcal.).	σ (A.).
<i>cyclo</i> Hexylmethyl	0.00284	6.81 ± 0.08	19.88 ± 0.14	0.18
2 : 4-Dinitrophenyl *	0.00287	6.42 ± 0.13	19.34 ± 0.23	0.09
Picryl	64.8	9.73 ± 0.09	17.93 ± 0.12	3.93
Benzyl	7.40	6.62 ± 0.07	14.97 ± 0.10	0.11
<i>p</i> -Nitrobenzyl	83.2	7.77 ± 0.06	15.11 ± 0.08	0.40
2 : 4-Dinitrobenzyl	1130	9.66 ± 0.07	16.14 ± 0.08	3.61
<i>p</i> -Cyanobenzyl	73.8	8.79 ± 0.04	16.57 ± 0.05	1.77
<i>p</i> -Methoxybenzyl	45.6	6.45 ± 0.06	13.66 ± 0.08	0.09

* Le Roux, Lu, Sugden, and Thomson, *loc. cit.*

All the reactions followed the Arrhenius law, and Table III gives the parameters of the modified Arrhenius equation

$$\log_{10}(k/T^{\frac{1}{2}}) = A - 1000E'/4.57T \quad (E' \text{ is in kcal.})$$

The Arrhenius activation energy is approximately 0.3 kcal./mole greater than E' . Table III also gives the rate constant calculated for an arbitrary temperature (25°), and the effective collision diameter σ , calculated as described by Le Roux and Sugden (*loc. cit.*). The probable

errors were obtained during the calculation of A and E' by a "least-squares" treatment of all the velocity constants for the compound. Too much significance should not be attached to these probable errors, as the statistical method fails to allow for any systematic errors.

DISCUSSION.

*cyclo*Hexylmethyl bromide is non-aromatic and gives almost the same values as were found earlier for *isopropyl* bromide in ethylene diacetate ($A = 6.71 \pm 0.09$; $E' = 19.75 \pm 0.15$ kcal.; Le Roux, Lu, Sugden, and Thomson, *loc. cit.*). When the ring becomes aromatic in benzyl bromide there is a fall in E' of nearly 5 kcal., while A remains almost unchanged.

Bromobenzene and *p*-bromonitrobenzene were found (*loc. cit.*) not to undergo exchange at an appreciable rate at temperatures up to 200°, but 1-bromo-2:4-dinitrobenzene gave a measurable rate. We have now added picryl bromide to this series. The most striking effect of the accumulation of nitro-groups is the large increase of A , but there is also a small drop in the activation energy.

In the benzyl series, too, the introduction of electron-withdrawing groups (*p*-nitro, 2:4-dinitro, *p*-cyano) produces a large increase in A . Conversely, the *p*-methoxy-group, which by its $+T$ effect tends to release electrons into the ring, decreases A . In this series, however, the accumulation of electron-withdrawing groups raises the activation energy.

The change of A on the introduction of substituents may be caused by electrostatic shielding of the carbon atoms of the benzene ring by the distribution of π -electrons in layers above and below the ring (cf. Catchpole, Hughes, and Ingold, *J.*, 1948, 4). These will hinder the approach of anions attaching the ring carbon atoms or those on short side-chains, as in benzyl compounds. Substituents such as nitro- or cyano-groups, which withdraw electrons from the ring, will diminish this effect and increase A , whilst electron-repelling groups will have the reverse effect.

The effect of substituents on the distribution of electrons in the ring may be considered in relation to two processes. The first is associated with the stretching of the original C-Br bond, and in the case of benzyl bromide can be formulated as in (a). This change will clearly be facilitated by substituents in the ring with a $+T$ effect and opposed by those with a $-T$ effect. The second process is the development of a positive charge on the carbon atom at which substitution occurs, which will attract the attacking anion. This charge cannot conjugate with the ring in benzyl compounds because of the single bond in the side-chain, but in the phenyl series such conjugation is possible as in (b). An incipient positive charge is produced at the carbon atom being attacked, and attracts the attacking anion. The effect of substituents will be the reverse of that expected for (a).



In the benzyl series the significant process appears to be (a), since (b) is prevented by the single bond between the ring and the carbon atom of the side-chain. In agreement with this view *p*-nitro- and *p*-cyano-groups raise the activation energy, whilst a *p*-methoxy-group lowers it. Saturation of the ring, as in *cyclo*hexylmethyl bromide, prevents conjugation and raises the activation energy.

The alternative process (b) appears to be the more important for the phenyl derivatives. This would be expected to be so, since conjugation of the ring electrons will hinder the transfer of one of them to the bromine atom to expel it as an anion. In this series it is found experimentally that the nitro-group, which withdraws electrons from the ring and would facilitate process (b), lowers the activation energy.

We are very grateful to Professor C. K. Ingold for valuable discussion. The work was carried out in 1946—1948 during the tenure by one of us (J. B. W.) of a Senior Studentship awarded by the Council for Scientific and Industrial Research, Australia. Professor Sugden wrote a rough draft of the paper early in 1949, and after his death in October 1950 it was revised and completed by the junior author (present address: C.S.I.R.O., Division of Industrial Chemistry, Melbourne, Australia).