The Order and Mechanism of the Isotopic Exchange Reactions of Secondary and Tertiary Alkyl Bromides in Anhydrous Acetone.

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Isotopic-exchange reactions between radioactive lithium bromide and *iso*propyl bromide and *tert.*-butyl bromide were studied in anhydrous acetone over a range of ionic concentrations. An equation was found according to which the first- and second-order rate constants for these reactions were determined.

The first-order contribution to the exchange reaction of *iso*propyl bromide is too small to be accurately determined. For the reaction of *tert.*-butyl bromide at 40° and a lithium bromide concentration of 0·01N, the first- and the second-order reaction contribute about equally to the exchange rate.

The frequency factors and Arrhenius energies of activation for these reactions were determined.

MANY data have been published on exchange reactions between halogen ions and alkyl halides in different solvents (for summaries, see Wahl and Bonner, " Radioactivity Applied to Chemistry," Chapman and Hall, London, 1952, p. 31; National Bureau of Standards, Circular 510, U.S. Dept. of Commerce, Tables of Chemical Kinetics, 1951, p. 279). Hughes and his co-workers used these reactions to demonstrate the mechanism of the Walden inversion (*J.*, 1935, 1525; 1936, 1173; 1938, 209). More recently this type of reaction has been used in investigating the mechanism of nucleophilic substitution reactions and making a semi-quantitative study of the effect of steric retardation (Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173; 1949, S 400; de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. phys.*, 1948, **45**, 246).

Ingold (" Structure and Mechanism in Organic Chemistry," Bell and Sons, London, 1935, p. 310) makes the fundamental postulate that a nucleophilic substitution S_N, as a heterolytic reaction in solution, normally has available two reaction mechanisms. In the case where a radioactive halogen ion undergoes exchange with the halogen atom in an alkyl halide, these mechanisms may be represented as follows:

$$\text{(i)} \qquad RX + {}^*X^- \rightleftharpoons {}^*X \cdots\cdots R \cdots\cdots X \rightleftharpoons {}^*XR + X^-$$

a bimolecular mechanism giving rise to a second-order reaction and

$$\text{(ii)} \qquad RX \rightleftharpoons R^+ + X^+$$

followed by

$$R^+ + {}^*X \rightleftharpoons R{}^*X$$

The slow step in this exchange, which determines the rate of the reaction, is the ionization of the organic halide which can be followed by a rapid combination of the alkyl ion with a radioactive bromine ion. This ionization mechanism results in a first-order reaction, the rate constant being dependent on the concentration of the organic molecule alone.

It is realized that in a homologous series of reactions, there is no abrupt change from the one mechanism to the other. In a weak ionizing solvent such as acetone the ionization mechanism is imperceptible in reactions of primary halides; hence a second-order rate law is followed, as was shown by le Roux and Sugden (*J.*, 1939, 1279; 1945, 586). On the other hand, tertiary halides react according to an ionization mechanism in a strongly ionizing solvent such as anhydrous formic acid, as was shown by Kokoski, Thomas, and Fowler (*J. Amer. Chem. Soc.*, 1941, **63**, 2451). It is conceivable that between these two extremes there will be exchange reactions where the two mechanisms contribute in varying proportions to the overall exchange rate. The relative contributions will depend on the extent of branching in the organic molecule near the reactive carbon atom, and on the solvent used. The problem is then to determine the relative contribution of each of these mechanisms to the overall reaction in a particular solvent. This can conveniently be done by using radioactive tracers.

In the reaction $RX + M^{*}X \rightleftharpoons R^{*}X + MX$ the constant rate of exchange is given by

$$R = -[ab/t(a + b)] \ln [1 - x/c(1 + b/a)] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where a and b are the total concentrations of the alkyl and alkali halides, RX and MX, respectively. The concentrations of $R^{*}X$ and $M^{*}X$ are negligibly small in comparison with those of RX and MX; x/c is the ratio of the radioactivity in RX to the total radioactivity after time t.

If the exchange follows a purely second-order rate law, the constant rate of exchange is given by

$$R = k_2ab \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and when a purely first-order rate law is followed, this value is given by

$$R = k_1a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

If, however, the exchange takes place by both the bimolecular and the ionization mechanism simultaneously, giving rise to a mixed first- and second-order reaction, the rate of exchange is given by

$$R = k_1a + k_2ab$$

whence

$$R/a = k_1 + k_2b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Equation (4) is that of a straight line for the plot of R/a against b. The values of k_1 and k_2 are obtained from the intercept and gradient of this line, respectively.

When MX is a strong electrolyte in the solvent used, as is potassium iodide in acetone, the ionic concentration equals that of MX at fairly low concentrations. When MX, however, is a weak electrolyte in the solvent concerned, as is lithium bromide in acetone, the degree of dissociation of the salt in the solvent must be taken into account. Evans and Sugden (*J. Chim. phys.*, 1948, **45**, 147; *J.*, 1949, 270) showed that in the last-mentioned circumstances the reaction follows Acree's hypotheses (*J. Amer. Chem. Soc.*, 1915, **37**, 902), in which case $k_2 = k_i\alpha + k_m(1 - \alpha)$. It was found by Evans and Sugden, and confirmed by the authors, that the value of k_m is of the same order as the probable error. The actual specific rate of exchange between halide ions and alkyl halide molecules is therefore given by $k_i = k_2/\alpha$, and the rate equation for the second-order reaction becomes

$$R = k_ia\alpha b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

On use of this second-order constant, equation (4) becomes

$$R/a = k_1 + k_i\alpha b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

which is a straight line for the plot of R/a against αb (cf. Fig.).

Application of equation (6) to the experimental results of the reaction between bromide ions and *n*-butyl bromide in dry acetone gives a straight line passing through the origin. It shows that the first-order component of this reaction is imperceptibly small.

The order of the exchange reaction between bromine ions and *tert.*-butyl bromide in dry acetone at 40° was tested by using concentrations of lithium bromide from *ca.* 0·1N to 0·005N. The results of these experiments are summarized in Table 1. The values of α in the second column were calculated as described in the Experimental section. The last column contains values of k_i calculated according to equation (5), and the penultimate column contains the values of k_1 which is equal to R/a. It is seen that neither a first- nor a second-order rate law is followed. The plot of R/a against αb, however, gives a straight line within the limits of the experimental accuracy. The values of k_1 and k_i calculated from these results according to equation (6) by the method of least squares are $k_1 = 32 \times 10^{-8}$ sec.$^{-1}$ and $k_i = 6{\cdot}05 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$. These values when substituted in equation (6) give $R/a = 32 \times 10^{-8} + 6{\cdot}05 \times 10^{-5}\alpha b$. It is seen that for values of b of the order of 0·01N, the two mechanisms contribute about equally to the exchange rate.

TABLE 1. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 40°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i
96·43	0·175	16·88	129	7·6	10·05	0·280	2·824	52	18·4
,,	,,	,,	139	8·2	,,	,,	,,	53	18·8
48·36	0·194	9·380	81	8·6	9·91	0·281	2·785	47	16·9
,,	,,	,,	91	9·7	,,	,,	,,	49	17·6
24·67	0·237	5·846	65	11·1	5·03	0·348	1·750	40	22·9
,,	,,	,,	71	12·1	,,	,,	,,	40	22·9

Experiments similar to the above were carried out with *iso*propyl bromide in acetone at 40°. The experimental results, summarized in Table 2, show from the values of k_i in the last column that there is only a 20% increase in this constant for a 10-fold change in concentration. This variation is nevertheless substantial and indicates that the exchange does not take place solely according to a second-order rate law. The rate constants calculated according to equation (6) are $k_1 = 22{\cdot}6 \times 10^{-8}$ and $k_i = 44{\cdot}3 \times 10^{-5}$. Substituted in equation (6) these values give $R/a = 22{\cdot}6 \times 10^{-8} + 44{\cdot}3 \times 10^{-5}\alpha b$. For values of b of the order of 0·01N the first-order component contributes about 5% to the rate of exchange. This value is of the same order of magnitude as the experimental error in determining the exchange rate. It is therefore probable that k_1 is even much smaller and it is clear that this method of analysing the experimental results does not give reliable values of k_1 where this is so small. This analysis nevertheless shows that there is a perceptible first-order contribution to the exchange rate and it gives more reliable values for k_2 than would have been obtained by neglecting the first-order contribution. In the case of *tert.*-butyl bromide, where the first-order contribution is much larger, reliable values of k_1 are obtained.

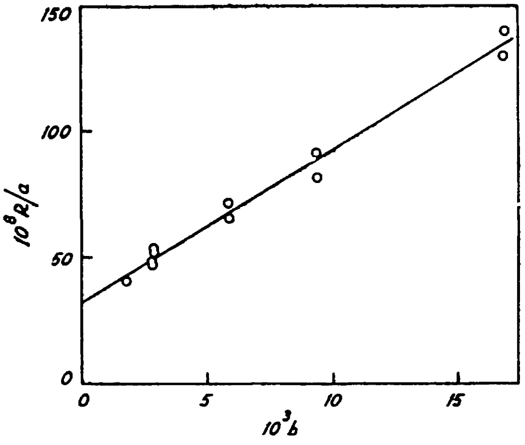
tert.-*Butyl bromide at* 40°.

TABLE 2. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 40°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i
48·36	0·194	9·380	432	46·0	10·05	0·280	2·824	147	52·0
,,	,,	,,	444	47·3	,,	,,	,,	151	53·0
24·67	0·237	5·846	278	47·6	9·81	0·282	2·767	146	52·8
,,	,,	,,	283	48·4	5·03	0·348	1·750	97	55·4
					,,	,,	,,	101	57·7

To determine the activation energies and frequency factors of these reactions, experiments were carried out at two more temperatures, the concentrations of lithium bromide ranging from 0·05 to 0·005N. The experimental results for *tert.*-butyl bromide are summarized in Tables 3 and 4 and those for *iso*propyl bromide in Tables 5 and 6.

TABLE 3. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 20°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$
49·80	0·220	10·95	9·34, 9·58	19·70	0·265	5·220	6·12, 6·42	5·18	0·379	1·963	4·38, 4·60
25·40	0·253	6·425	6·63, 7·06	10·34	0·316	3·268	4·92, 5·35				

TABLE 4. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 60°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$
46·96	0·165	7·741	560, 590	99·72	0·248	2·416	316, 325	4·88	0·307	1·500	248, 253
23·92	0·196	4·689	415, 431	9·61	0·249	2·393	340, 341				

TABLE 5. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 20°.

10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$
49·8	0·220	10·95	53·7, 55·1	10·34	0·316	3·268	17·3, 17·5	9·335	0·325	3·034	14·8
25·4	0·253	6·425	31·8, 32·5	10·05	0·319	3·206	15·6, 16·3	5·18	0·379	1·963	11·0, 11·5

TABLE 6. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 60°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8/Ra$
46·91	0·165	7·741	2447, 2466, 2512	9·70	0·248	2·410	854, 913
23·92	0·196	4·689	1586, 1624	9·46	0·250	2·367	868, 886
9·74	0·248	2·416	937, 944	9·48	0·307	1·500	640, 648

The first- and second-order rate constants were calculated for the *tert.*-butyl bromide reaction according to equation (6). Only the second-order constants of the *iso*propyl bromide reaction were calculated. The values of these constants are summarized in Table 7, and from these data the frequency factors and Arrhenius activation energies of the first- and second-order reactions of the two bromides were calculated by the method of least squares. The results are given in Table 8, the subscripts 1 and 2 referring to the first- and second-order reactions.

TABLE 7. *First- and second-order rate constants at* 20°, 40°, *and* 60°.

	10^8k_1			10^5k_i		
	20°	40°	60°	20°	40°	60°
Bu^tBr	3·6	32	200	0·55	6·05	48·7
PrⁱBr	—	—	—	4·86	44·3	295

TABLE 8. *Arrhenius energies of activation and frequency factors.*

	E_1 (kcal./mole)	$\log_{10} A_1$	E_2 (kcal./mole)	$\log_{10} A_2$
Bu^tBr	19·7	7·2	21·8	11·0
PrⁱBr	—	—	20·0	10·6

The Arrhenius energy of activation for the *iso*propyl bromide reaction was also calculated from the experimental results by ignoring the first-order contribution and using only those values for which the ionic concentration is about 0·01N. The values so obtained are $E_a = 20{\cdot}9$ kcal. and $\log_{10} A = 11{\cdot}3$. These values differ appreciably from those obtained by the more laborious method which must, however, be considered the more accurate way of determining these quantities.

The value of 20·0 kcal. for the activation energy of the *iso*propyl bromide reaction is only 0·2 kcal. higher than the value used by Ingold (*op. cit.*, p. 408). The above value of the activation energy for the second-order reaction of *tert.*-butyl bromide is in exact agreement with the value quoted by Ingold. This is, however, only incidental, because it is not clear how the latter value was obtained (cf. de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. phys.*, 1948, **45**, 236). Moreover, other activation energies for these bromide-exchange reactions as determined by us are about 0·8 kcal. higher than the values used by de la Mare *et al.*

TABLE 9. *Calculated values of* $K_{\text{therm.}}$.

Temp.	0°	10°	20°	25°	30°	40°	50°	60°
D	21·46	20·48	19·56	19·10	18·67	17·80	16·98	16·26
$10^4K_{\text{therm.}}$	7·07	6·52	5·52	5·02	4·83	4·23	3·48	3·18

EXPERIMENTAL

Acetone.—To pure acetone was added anhydrous magnesium perchlorate and it was left for 2 days with occasional shaking. It was then distilled from the perchlorate through a 20″

fractionating column packed with glass helices and surrounded by a vacuum-jacket, at a take-off ratio of 1 : 10. Only the middle fraction was collected for use.

Radioactive Lithium Bromide.—Radioactive bromine was obtained from Harwell in batches of 2 g. of ammonium bromide, with an activity of *ca.* 30 mc at delivery. This was dissolved in 50 ml. of water, an excess of lithium hydroxide added, and the mixture heated to convert all the bromide into lithium bromide. The impure lithium bromide was then recrystallized several times from pure, dry acetone to remove excess of lithium hydroxide and other impurities. It was finally dissolved in 100 ml. of the acetone and this was kept as the stock " active solution."

Pure lithium bromide was prepared by neutralizing the purest obtainable lithium hydroxide with hydrobromic acid solution. The product was recrystallized several times from pure acetone and finally heated to above 200° to expel all water of crystallization.

Alkyl Bromides.—The purest Eastman Kodak products were fractionated through the column described above. Only the middle portions, distilling within 0·1°, were retained. The *tert.*-butyl bromide was fractionated twice, the second time just before use. *tert.*-Butyl bromide had n_D^{20} 1·4282, and *iso*propyl bromide 1·4251.

Standard Solutions and Methods of Analysis.—All solutions were made up at 20°, and concentrations at the reaction temperatures were corrected for by using the following expression for the volume expansion of acetone :

$$V_t = V_0\,(1 + 1{\cdot}324 \times 10^{-3} + 3{\cdot}809 \times 10^{-6} - 0{\cdot}8798 \times 10^{-8})$$

The concentrations of the lithium bromide solutions were determined by titration against standard silver nitrate solution with eosin as indicator. The concentrations of the alkyl bromides were determined gravimetrically by precipitation as silver bromide.

Kinetic Procedure.—The reactions were carried out essentially as done by le Roux and Sugden (*loc. cit.*). After completion of reaction the alkyl halide was extracted with benzene. The activities of the benzene solution and of the acetone solution were then determined consecutively in the same liquid-type Geiger–Müller counter tube. When corrected, the ratio of the activity of the benzene solution and the activity of the acetone solution gave the value of x/c in equation (1).

The correction factor by which x/c had to be multiplied was determined experimentally as follows. Radioactive alkyl bromide was dissolved in acetone to give the requisite molarity. It was extracted by benzene in exactly the same way as was done with the reaction mixtures. The required correction factor was then given by

$$f = \frac{\text{activity of the alkyl bromide in acetone}}{\text{activity of alkyl bromide in benzene}}$$

The value of this factor is dependent upon the molarity of the bromide, its molecular weight, density, and solubility in water, and upon the extent to which it is hydrolysed during the extraction process. These values vary from 1·027 for 0·1M-*n*-butyl bromide to 1·255 for 0·4M-*tert.*-butyl bromide.

Calculation of Degree of Dissociation.—Sugden and Evans (*loc. cit.*) calculated the degree of dissociation of lithium bromide in acetone at 25° and 65·5°, and by a slightly different method we have obtained the value $K_{\text{therm.}} = 5{\cdot}02 \times 10^{-4}$ at 25° in good agreement with their value. The degree of dissociation at any other temperature can then be calculated from Bjerrum's theory (*Kgl. Danske Videnskab. Selsk.*, 1926, **7**, No. 9) and use of standard values for the necessary coefficients (Åkerlöf, *J. Amer. Chem. Soc.*, 1932, **54**, 4125; Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, p. 123). The values of $K_{\text{therm.}}$ so obtained, and used for the values of α shown in the Tables, are given in Table 9. It must be emphasized that the values of α obtained by the above method are only approximate and await confirmation from accurate conductivity measurements at the various temperatures.

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