

855. *Concomitant First- and Second-order Nucleophilic Substitution.*

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Isotopic exchange reactions between radioactive lithium chloride and both benzyl and diphenylmethyl chloride in dimethylformamide have been studied over a range of ionic concentrations at three different temperatures. No detectable first-order contribution to the exchange was found with benzyl chloride. With diphenylmethyl chloride, however, the first- and the second-order mechanism were found to contribute equally to the overall exchange at a concentration of $\sim 0.01M$ -lithium chloride. The Arrhenius activation energies for both these reactions are reported.

In a nucleophilic exchange reaction of the type $RX + Y^- \rightleftharpoons RY + X^-$, two well-known mechanisms can occur, namely, the first-order unimolecular S_N1 and the second-order bimolecular S_N2 process. The existence of a more universal "mesomechanism" has been postulated on theoretical grounds,¹ and it is generally recognised that there is "no sharp line of demarcation" between S_N1 and S_N2 reactions.²

¹ Prevost, *Ind. Chim. belge*, 1958, **23**, 1231.

² Hughes, Ingold, and Shapiro, *J.*, 1936, 225.

The experimental evidence for the concomitant occurrence of the two mechanisms is, however, somewhat meagre and relates to systems in which the possible, or actual, occurrence of elimination, solvolysis, the mixed nature of the exchange ($X \neq Y$), or other factors complicates interpretation of the results.²⁻⁴ Thus, although a borderline region is known to exist,⁵ the actual nature of the reaction mechanism in such borderline regions is a matter of some controversy.⁶

There is, nevertheless, no reason why the overall exchange should not be regarded as the sum of unimolecular and bimolecular processes.⁷ In support of this view, we now report a simple unambiguous example of simultaneous S_N1-S_N2 exchange between diphenylmethyl chloride and chloride ions ($X = Y$) in dimethylformamide, where radiochloride ions were used in the form of lithium chloride, a system in which elimination cannot occur. The system benzyl chloride-chloride ions in the same solvent was also studied and found to be overwhelmingly of S_N2 type.

The two reactions studied are both of the homogeneous form, $RX + *X^- \rightleftharpoons R*X + X^-$, where RX represents an organic halide and $*X^-$ radioisotopically labelled halide.

In these circumstances the rate of isotopic exchange R (in mole l^{-1} sec.⁻¹) follows a logarithmic law regardless of mechanism, the relevant equation being⁸

$$R = -\left[\frac{ab}{t(a+b)}\right] \ln \left[1 - \frac{x}{b} \left(\frac{a+b}{a}\right)\right] \quad (1)$$

where a and b are the concentrations of the alkyl halide and halide salt, respectively, x is the net number of gram-ions per litre that have exchanged at time t , and x/b is given by the ratio between the activity of RX and the total radioactivity.

Le Roux and Swart³ have shown that the constant rate of exchange R can be equated to the sum of the unimolecular and bimolecular processes (Gold⁷) by the relationship

$$R = k_1a + k_2\alpha ab, \quad (2)$$

where k_1 and k_2 are the respective rate constants for the first- and the second-order process, and α is the degree of ionisation of the halide salt in the solvent used. The assumption is made, in using this equation, that changes in ionic strength do not affect the rate constant k_1 , at low salt concentrations. The straight-line plot of R/a against ab thus enables both k_1 and k_2 to be evaluated.

The importance of allowing for incomplete ionisation for both S_N2 and mixed S_N1-S_N2 reactions has not always been recognised and its neglect can obviously distort the results considerably. Allowance has sometimes been made for ionisation on a purely empirical basis⁹ and in a few cases the actual values of α have been calculated from conductivity data.^{3,10}

Part of the purpose of this paper is to show that there is no reason why the values of α should not be obtained directly from the kinetic data themselves, without assumptions as to whether a given reaction is of pure S_N2 or mixed S_N1-S_N2 type.

The value of the ionisation constant K is related to the degree of ionisation by the equation

$$K = \alpha^2fb/(1 - \alpha), \quad (3)$$

³ le Roux and Swart, *J.*, 1955, 1475.

⁴ Gold, Hilton, and Jefferson, *J.*, 1954, 2756; Kohnstam, Queen, and Shillaker, *Proc. Chem. Soc.*, 1959, 157.

⁶ Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, pp. 313 *et seq.*

⁶ Grunwald, Jones, and Winstein, *J. Amer. Chem. Soc.*, 1951, **73**, 2700; Kornblum, Smiley, Blackwood, and Iffland, *ibid.*, 1955, **77**, 6299; Crunden and Hudson, *J.*, 1956, 501.

⁷ Gold, *J.*, 1956, 4633.

⁸ Wahl and Bonner, "Radioactivity Applied to Chemistry," John Wiley and Son, New York, 1951, p. 7.

⁹ de la Mare, *J.*, 1955, 3180.

¹⁰ Sugden, *J.*, 1949, 270; Swart and le Roux, *J.*, 1956, 2110.

where f^2 is the product of the activity coefficients for alkali and halide ions.

Combining equations (2) and (3) gives

$$\frac{(R/a - k_1)}{b} = k_2 - \frac{f^2(R/a - k_1)^2}{Kk_2b} \quad (4)$$

A plot $[(R/a) - k_1]/b$ against $f^2(R/a - k_1)^2/b$ is, therefore, a straight line of slope $1/Kk_2$ and intercept k_2 .

The value of the activity coefficient f can be calculated from the standard Debye-Hückel equation

$$\log f = \frac{-1.82 \times 10^6 (\alpha c)^{1/2} / (\epsilon T)^{3/2}}{1 + 50.3 \text{ \AA} (\alpha c)^{1/2} / (\epsilon T)^{3/2}}$$

the value of the mean distance of closest approach of the ions \AA (in Ångströms) being estimated from the theory of Bjerrum or of Fuoss.¹¹

By successive approximation it was thus found possible to obtain the values of K , k_1 , and k_2 as well as the individual values of α purely from kinetic data by using the linearity of equations (2) and (4). Clearly it is much simpler to calculate K and k_2 if k_1 is negligibly small. This in fact proved to be the case for the benzyl chloride exchange. Moreover, once K has been found for a given solvent-salt combination, from any arbitrary reaction, it can be used to obtain values of α for other reactions at other concentrations.

The values of K obtained in this way, by using Bjerrum's equation, are recorded in Table 1, the corresponding value of the mean distance of closest approach of the ions \AA being 1.87 Å.

These values are not significantly altered if the Fuoss equation is used instead of

TABLE 1.
Ionisation constants K for lithium chloride in dimethylformamide from kinetic data.

Temp. (K)	303.2°	313.2°	323.2°
K	0.0171	0.0156	0.0142

TABLE 2.
Rate constants k_2 (l. mole⁻¹ sec.⁻¹) for the benzyl chloride-lithium chloride exchange in dimethylformamide.

Temp. (K)	10 ² a	10 ² b	10 ² R/ab	α	10 ² $k_2 = 10^2 R/axb$	Temp. (K)	10 ² a	10 ² b	10 ² R/ab	α	10 ² $k_2 = 10^2 R/axb$	
303.2°	1.42	1.07	0.204	0.790	0.258	323.2°	1.39	1.05	1.35	0.770	1.75	
303.2	1.42	0.704	0.207	0.831	0.249	323.2	1.39	0.692	1.41	0.811	1.73	
303.2	1.42	0.343	0.225	0.892	0.252	323.2	1.39	0.337	1.50	0.878	1.71	
303.2	1.47	0.106	0.245	0.955	0.257	323.2	1.45	0.104	1.60	0.948	1.72	
			Mean 0.254 ± 0.004								Mean 1.73 ± 0.02	
313.2	1.40	1.06	0.536	0.780	0.687							
313.2	1.40	0.698	0.556	0.821	0.677							
313.2	1.40	0.340	0.606	0.885	0.685							
313.2	1.46	0.105	0.667	0.951	0.701							
			Mean 0.688 ± 0.010									

Bjerrum's. The necessary values for the dielectric constant ϵ of dimethylformamide were obtained from the data of Leader and Gormley¹² by using a plot of $\log \epsilon$ against T .

The corresponding kinetic results for benzyl chloride are recorded in Table 2.

The increase in the apparent second-order rate constant R/ab with decrease in concentration can be wholly accounted for by an increase in the degree of ionisation. The rate constants for the reaction are unexpectedly high, being some 80 times greater than the rate for the same reaction in acetone.¹³

¹¹ Bjerrum, *Kgl. Danske Videnskab. Selskab*, 1926, **7**, No. 9; Fuoss, *J. Amer. Chem. Soc.*, 1958, **80**, 5059.

¹² Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5731.

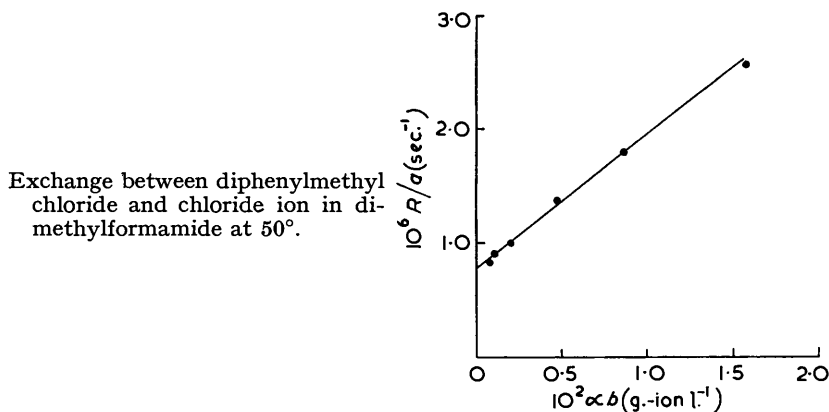
¹³ de la Mare and Hughes, *J.*, 1956, 845.

The results for the diphenylmethyl chloride-chloride ion exchange are recorded in Table 3, the values of α used being obtained from the benzyl chloride exchange.

TABLE 3.
Kinetic data for the diphenylmethyl chloride-lithium chloride exchange in dimethylformamide.

Temp. (K)	10^2a	$10^2\alpha b$	$10^6R/a$	$10^4R/\alpha ab$	Temp. (K)	10^2a	$10^2\alpha b$	$16^6R/a$	$10^4R/\alpha ab$
303.2°	5.42	1.67	0.272	0.163	323.2°	5.34	1.59	2.53	1.59
303.2	5.42	0.916	0.188	0.205	323.2	5.34	0.876	1.77	2.02
303.2	5.42	0.499	0.132	0.265	323.2	5.34	0.478	1.35	2.82
303.2	5.42	0.215	0.085	0.395	323.2	5.34	0.209	1.00	4.79
303.2	5.96	0.092	0.073	0.793	323.2	5.86	0.110	0.923	8.39
313.2	5.38	1.63	0.842	0.517	323.2	5.86	0.091	0.830	9.12
313.2	5.38	0.895	0.606	0.677					
313.2	5.38	0.488	0.431	0.883					
313.2	5.38	0.212	0.292	1.38					
313.2	5.91	0.092	0.261	2.84					

In this case the value of $R/\alpha ab$ increases continuously with decrease in ionic concentration, showing that the reaction is not purely of the second order. Plots of



R/a against αb according to equation (2), however, give good straight lines from which both k_1 and k_2 can be evaluated. An example of such a plot, namely, that at 50° c, is shown in the accompanying Figure. The rate constants thus obtained are shown in Table 4.

TABLE 4.
First- and second-order rate constants for the diphenylmethyl chloride-lithium chloride exchange in dimethylformamide.

Temp. (K)	303.2°	313.2°	323.2°
10^7k_1 (sec. ⁻¹)	0.631 ± 0.016	2.30 ± 0.06	7.76 ± 0.19
10^6k_2 (l. mole ⁻¹ sec. ⁻¹)	1.28 ± 0.03	3.86 ± 0.10	11.2 ± 0.3

These results are a clear-cut example of the simultaneous occurrence of the S_N1 and the S_N2 mechanism both contributing equally to the overall exchange at a concentration of about 0.01M-lithium chloride.

The absence of solvolysis was confirmed for both benzyl chloride and diphenylmethyl chloride by allowing these reactions to proceed to completion (12 times the half-time of exchange). Both reactions gave within <1% the theoretical maximum exchange. Moreover, there was no trend in the measured rates of exchange for the diphenylmethyl chloride reaction with time, the value of R at 50° c (for $a = 5.34 \times 10^{-2}$; $b = 2.31 \times 10^{-2}$ mole l.⁻¹) being 1.34, 1.37, 1.32, and 1.34×10^{-7} mole l.⁻¹ sec.⁻¹ at 1, 6, 21.5, and 45 hr., respectively.

The Arrhenius activation energies and frequency factors were determined for both reactions, with the results recorded in Table 5.

TABLE 5.
Arrhenius activation energies and frequency factors.

	E_1 (kcal. mole ⁻¹)	$\text{Log}_{10} A_1$	E_2 (kcal. mole ⁻¹)	$\text{Log}_{10} A_2$
PhCH ₂ Cl	—	—	18.6	10.8
Ph ₂ CHCl	24.4	10.4	21.1	10.3

The activation energy E_2 for the S_N2 process shows the expected increase in going from benzyl to diphenylmethyl chloride, due to the greater energy necessary to invert the molecule in the Walden inversion.

Ingold and his co-workers have shown¹⁴ that changes in ionic strength can affect the rate constant k_1 for unimolecular nucleophilic substitution, particularly in solvents of low dielectric constant, according to the equation

$$k_1^{(\mu)} = k_1^{(0)} \text{antilog}_{10} (0.912 \times 10^{16} \sigma \mu / \epsilon^2 T^2)$$

where $k_1^{(0)}$ is the rate constant at zero ionic strength, $k_1^{(\mu)}$ is the rate constant at ionic strength μ , and σ is the ionic strength constant.

The presence of this effect would alter equation (2) to the form

$$R/a = k_1^{(0)} \text{antilog} (0.912 \times 10^{16} \sigma \alpha b / \epsilon^2 T^2) + k_2 \alpha b. \quad (5)$$

Under the conditions of dielectric constant and salt concentration chosen by us, the value of $\text{antilog} (0.912 \times 10^{16} \sigma \alpha b / \epsilon^2 T^2)$ is close to unity and it is therefore impossible to evaluate the parameter σ from our results. However, it has been shown,¹⁴ both on theoretical and on experimental grounds, that for diphenylmethyl halides σ is of the order of 2 Å.

Recalculation of our results, according to equation (5) with this value of σ , does not alter the values of $k_1 = k_1^{(0)}$ for the S_N1 mechanism as recorded in Table 4; nor does it alter the values of the activation energies for either the S_N1 or the S_N2 process as recorded in Table 5. The only parameter to be affected is k_2 and the values recorded in Table 4 are lowered by about 2%. This change is of the same order of magnitude as the experimental error.

In view, therefore, of the negligible change involved, we feel that the effect of ionic strength on the rate constant k_1 may legitimately be ignored for the diphenylmethyl chloride-chloride ion exchange in dimethylformamide at salt concentrations less than 0.02M.

In order to check the values of the degree of ionisation obtained from the kinetic measurements, the conductivity of lithium chloride in dimethylformamide was measured at a series of concentrations at 30° c. The results obtained were then used to calculate ionisation constants by Shedlovsky's method.¹⁵ No value for the viscosity of dimethylformamide at 30° could be found in the literature and this was accordingly measured by means of an Ostwald viscometer and found to be 7.49 centipoises.

The value of the ionisation constant obtained in this way was 0.0178, which is in excellent agreement with the value (0.0171) obtained from the kinetic data. For comparison the values of the degrees of ionisation obtained by these two methods are recorded in Table 6.

It is interesting that simple extrapolation of the kinetic data for benzyl chloride gives values of α in fair agreement with those obtained by the more rigid procedure involving equations (2) and (4). The latter procedure is, however, the more reliable, especially if the α values are small and/or the reaction considered is to be of mixed S_N1 - S_N2 type.

¹⁴ Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979; Bateman, Hughes, and Ingold, *ibid.*, p. 1017.

¹⁵ See Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, 3rd edn., p. 288.

TABLE 6.

The degree of ionisation of lithium chloride in dimethylformamide at 30°.

10 ^{2b}	2.099	1.044	0.5222	0.2611	0.1305	0.0653	$\Lambda_0 = 87.20$
Λ	51.08	59.37	66.81	73.04	76.78	81.06	
α (condy.)	0.725	0.801	0.865	0.917	0.940	0.975	
α (kinetic)	0.720	0.795	0.855	0.908	0.945	0.978	

EXPERIMENTAL

Dimethylformamide.—Commercial dimethylformamide was dried (Na₂SO₄) and fractionated three times through a 20'' column packed with Fenske helices. Only the middle fraction was collected for use; it had d_4^{25} 0.9442, n_D^{25} 1.4290 (lit., 1.4294), b. p. 62°/25 mm.

Benzyl Chloride.—Commercial benzyl chloride was dried (K₂CO₃) and twice fractionated through the same 20'' column; it had b. p. 171.5—172°/643 mm.

Diphenylmethyl Chloride.—The commercial chloride was dried (Na₂SO₄) and fractionated three times; it had b. p. 167°/17 mm., n_D^{20} 1.5960 (lit., 1.5959), m. p. 17.0° (lit., 17—18°), Cl (Stepanov's method) 17.3% (theor. 17.5%).

Lithium Radio-chloride.—2N-[³⁶Cl]Hydrochloric acid supplied by the Radiochemical Centre, Amersham, was neutralised with pure lithium carbonate (potentiometric titration). Inactive lithium chloride was then added until the required specific activity was obtained. The solution was evaporated to dryness and the resultant active lithium chloride baked at 200° overnight (argentometric assay, 99%).

Solutions.—Solutions of both the organic halides and the lithium chloride were prepared by weighing of the respective samples and dilution to the required volume.

³⁶Cl-Labelled Organic Chlorides.—These were prepared by keeping mixtures of the chlorides with lithium chloride in dimethylformamide for prolonged periods (in excess of 2 days) at 50° (thermostat). The labelled organic halide was separated by pouring the mixtures into water and then drying the organic chloride (K₂CO₃).

Kinetic Measurements.—The reactions were carried out in H-shaped reaction vessels essentially as done by le Roux and Sugden.¹⁶ After the reaction had proceeded for the required time, 10 ml. of the mixture were shaken with benzene (10 ml.) and water (100 ml.) in order to quench the reaction. The benzene layer was then washed with further portions of water (2 × 25 ml.).

The activities of the benzene solution and of 10 ml. of the reaction mixture in dimethylformamide were then measured consecutively in the same Geiger-Müller counter tube. When corrected, the ratio of the activity of the benzene solution to that of the reaction mixture itself gives the value of the ratio x/b in equation (1).

The correction factor by which x/b had to be multiplied was determined experimentally. Radioactive alkyl chloride, prepared as above, was dissolved in dimethylformamide to give the requisite molarity. It was then extracted with benzene in the way described for the reaction mixtures. The required correction factor F was then given by:

$$F = \frac{\text{Activity of alkyl chloride in dimethylformamide}}{\text{Activity of alkyl chloride in benzene}}$$

The value of this factor depends on the molarity of the alkyl chloride, its partition coefficient between benzene and water-dimethylformamide mixtures, and the relative β -ray absorption of benzene and dimethylformamide. The values obtained were found to be independent of the lithium chloride concentration in the range 0.02—0.2M. For 0.05M-diphenylmethyl chloride $F = 0.908$ and for 0.015M-benzyl chloride $F = 0.940$.

All concentrations were corrected for change in temperature and, where necessary, count rates were corrected for the dead time of the counting apparatus.

One of us (P. C.) is indebted to Lever Brothers (Rhodesia) (Pvt.) Limited for a Research Fellowship and we gratefully acknowledge a gift of apparatus from the Shell Company of Rhodesia Limited. We also acknowledge our debt to Dr. V. Gold (King's College, London) for helpful discussion and advice.

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[Received, December 16th, 1960.]

¹⁶ le Roux and Sugden, *J.*, 1939, 1279; 1945, 586.