Mechanism of Substitution at a Saturated Carbon Atom. Part XLII. Introductory Remarks, and Kinetics of the Interaction of Chloride Ions with Simple Alkyl Chlorides in Acetone.*

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[Reprint Order No. **6206**.]

The background and scope of a group of closely related papers are indicated. Kinetic experiments on the second-order reactions of chlorine exchange between lithium radio-chloride and three simple alkyl chlorides in acetone are reported. Rate constants and parameters of the Arrhenius equation are evaluated.

Introduction to a Group of Papers.—Our knowledge of the bimolecular mechanism of nucleophilic substitution (S_N2) is now so far developed that further significant advance is likely to come mainly from quantitative approaches; and for study on such lines the

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* Part XLI, *J.*, **1954**, 2939.

simplest systems are the most profitable. Finkelstein's reaction of halide replacement in alkyl halides by attacking halide ion offers a maximum of simplicity, inasmuch as both the substituting agent and the displaced group are monoatomic. Moreover, they can be made identical, and the reaction can still be studied with the aid of isotopic labelling, so that, for a given alkyl group, we can have, not only the substitution involving the fewest possible atoms, but also that involving the fewest kinds of atom, and therefore a theoretical problem already partly simplified by its symmetry.

For these reasons it was decided to build up a body of data on rates and their temperature coefficients for Finkelstein reactions of simple, substituted, and cyclic alkyl halides. The work is still incomplete, but has been followed far enough to justify, it is thought, the report which the present group of papers constitutes.

The bimolecular mechanism of substitution being now the main subject of interest, acetone was the first solvent used in this work, though it has been extended to other solvents since. The merit of acetone is that it dissolves many ionic halides, and yet is not so highly ionising that it fails to retain the Finkelstein substitutions in their bimolecular form. In fact, it preserves the bimolecular mechanism over a wide variety of alkyl structures, thereby permitting most of the kinetic comparisons which it was desired to make. And it cannot solvolytically substitute the alkyl halides. The present papers are restricted to an account of reactions conducted in homogeneous solution in dry acetone.

With four halogens, sixteen types of Finkelstein reaction are possible; but, for homogeneous reactions in acetone, the seven which depend on fluorine have to be excluded as involving inconveniently low solubilities. Of the nine substitutions dependent only on chlorine, bromine, or iodine, seven have so far been examined for simple alkyl groups in solvent acetone. Certain classes of modified alkyl groups, such as aralkyl and alicyclic groups, have been studied also, usually with respect to one type of substitution only.

As to the history of kinetic study of the Finkelstein reaction, the basic exploratory work of Conant, Kirner, and Hussey (*J. Amer. Chem. Soc.*, 1924, **46**, 232; 1925, **47**, 476, 488) showed that, in acetone, the reactions of potassium, sodium, and lithium iodides with alkyl chlorides were kinetically of the second order, *i.e.*, first order in each reactant. Rate comparisons were made for a considerable number of alkyl groups, though many of the actual rates were somewhat inexact, partly because, when potassium and sodium salts were used, the solutions did not remain homogeneous. Of subsequent investigations, the more extensive have employed solvents, such as ethyl alcohol or aqueous acetone (Seelig and Hull, *ibid.*, 1942, **64**, 940; McKay, *ibid.*, 1943, **65**, 702; le Roux, Lu, Sugden, and Thomson, *J.*, 1945, 586), which are not as suitable as is dry acetone for the purpose of maintaining the bimolecular mechanism and avoiding solvolytic side-reactions over a range of alkyl groups, including tertiary groups. In all the above work, moreover, salt effects, which are not negligible, were not standardised. A number of investigations have employed dry acetone as solvent, but have dealt with a single case, or a very few cases, often in order to illustrate some special phenomena, such as the Walden inversion, or anionotropy, or salt effects (Hughes, Juliusberger, Masterman, Topley, and Weiss, *J.*, 1935, 1525; Bartlett and Rosen, *J. Amer. Chem. Soc.*, 1942, **64**, 543; Dostrovsky and Hughes, *J.*, 1946, 161; Evans and Sugden, *J.*, 1949, 270; England and Hughes, *Nature*, 1951, **168**, 1002; McKinley-McKie and Moelwyn-Hughes, *J.*, 1952, 838). Similar restrictions of scope apply to most investigations of Finkelstein substitutions with modified alkyl groups (Juvala, *Ber.*, 1930, **63**, 1539; Hughes, Juliusberger, Scott, Topley, and Weiss, *J.*, 1936, 1173; Cowdrey, Hughes, Nevell, and Wilson, *J.*, 1938, 209; Bither, Sturtevant, and Thomas, *J. Amer. Chem. Soc.*, 1945, **67**, 1562; Solomon and Thomas, *ibid.*, 1950, **72**, 2024; Bordwell and Cooper, *ibid.*, 1951, **73**, 5034; Olson, Frashier, and Spieth, *J. Phys. Colloid Chem.*, 1951, **55**, 860; Hatch *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 6002, and earlier papers of the series; Vernon, *J.*, 1954, 4462), but exception must be made of some systematic studies with *cyclo*alkyl halides (van Stratten, Nickolls, and Winkler, *Canad. J. Chem.*, 1951, **29**, 373; Roberts and Chambers, *J. Amer. Chem. Soc.*, 1951, **73**, 5034; Fierens and Verschelden, *Bull. Soc. chim. Belg.*, 1952, **61**, 427). Further rate data on substitutions of simple alkyl halides are given by le Roux and Swart (*J.*, 1955, 1475).

The new rate measurements for Finkelstein substitutions with simple alkyl groups are given in Parts XLII—XLVIII, and are collectively discussed in Part XLIX. Some preliminary and partial reports of them have appeared already (de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. phys.*, 1948, **45**, 236; Hughes, *J.*, 1949, S **400**; de la Mare, *Ind. chim. Belg.*, 1950, **15**, 189; Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, 1953, p. 408). Some results for certain modified alkyl groups will be presented later.

Reactions of Chloride Ions with Alkyl Chlorides.—As far as the author is aware, chlorine exchange by the Finkelstein reaction in simple aliphatic halides has not been studied before, though the exchange has been observed in *p*-nitrobenzyl chloride (Bither, Sturtevant, and Thomas, *loc. cit.*).

In the present experiments, the exchange, followed in anhydrous acetone, was between methyl, ethyl, and *iso*propyl chlorides and chloride ion, which was supplied as lithium chloride containing the radioactive isotope ^{36}Cl. The results are in Table 1. The counting rates, C, $C - X_1$, and $C - X_2$, measure, respectively, specific activities in the inorganic chloride initially, on separation at a time t_1 soon after the reaction solution had attained thermostat temperature, and on separation at a later time t_2. The spread of the calculated second-order rate constants k_2 for each temperature is typical of such experiments, and arises mainly from random fluctuations in the counts recorded within finite time intervals. Usually, counts of about 10,000 were taken on each sample, and it can be computed that this number should lead to probable errors in individual rate constants of about 3%. Consistently, the standard deviation of the rate constants from their means averages about 5%.*

TABLE 1. *Second-order rate constants (k_2 in sec.$^{-1}$ mole^{-1} l.) of chlorine exchange between lithium radio-chloride and alkyl chlorides in acetone.*

Temp. (c)	a = [AlkCl]	b = [LiCl]	Counting rates			$t_2 - t_1$ (min.)	10^5k_2	10^5k_2 (Mean)
			C	$C-X_1$	$C-X_2$			
				Methyl chloride.				
+44·6°	0·2805	0·0267	154·5	152·1	129·4	35·6	28·5	
					117·1	46·3	35·1	
					109·3	56·6	36·2	
					113·7	66·2	27·3	31·8
+25·0	0·2905	0·0275	154·5	—	66·1	1353	3·78	
					65·0	1366	3·83	
					61·9	1374	4·04	3·88
− 3·2	0·3038	0·0286	154·5	—	99·2	20170	0·121	
					95·0	24450	0·110	
					86·8	30205	0·107	
					89·3	30450	0·100	0·109
				Ethyl chloride.				
+60·5	0·2285	0·0258	131·2	128·4	73·3	1788	2·39	
					75·1	1852	2·20	
					50·9	2824	2·60	2·40
+39·6	0·2356	0·0266	132·4	—	81·3	11470	0·311	
					83·5	11638	0·289	
					67·9	15217	0·326	0·309
+25·1	0·2411	0·0272	111·0	—	85·9	36010	0·050	
					80·2	41850	0·055	
					74·0	47990	0·061	0·055
				iso*Propyl chloride.*				
+60·1	0·2219	0·0283	162·0	—	78·5	131040	0·0442	
					81·3	131040	0·0419	
					75·1	131040	0·0471	
+60·1	0·2219	0·0283	162·6	—	59·8	169920	0·0488	0·0455

The exchanges of methyl chloride and ethyl chloride were studied each at three temperatures. However, the exchange of *iso*propyl chloride was examined only at 60°. At

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* This is consistent, because, when both concepts are significant in relation to the same data, the probable error is 0·67 times the standard deviation. Here each reading has a probable error, but not a standard deviation, whereas the collection has a standard deviation, but not, except formally, a probable error.

this temperature a period of 3 months was required in order to obtain a convenient amount of exchange, and hence no experiments at lower temperatures were tried. Attempted experiments at the higher temperatures, 79° and 100°, failed, for the reason that lithium chloride, which has a negative temperature coefficient of solubility in acetone, crystallised from the solutions. Because of these difficulties with *iso*propyl chloride, no attempt was made to extend the work to *tert.*-butyl chloride, which in bimolecular substitutions is still less reactive.

As will be illustrated in several of the following papers, Finkelstein substitutions in acetone are subject to a negative salt effect, which requires the standardisation of salt concentrations in any comparison of rates. In the present work, the kinetic salt effect was not directly measured, but, in the experiments here quoted, it was standardised by maintaining the concentrations of lithium chloride close to 0·027M.

The main results of this investigation are summarised in Table 2. They show that, in the series MeCl, EtCl, Pr^iCl, the rates of chlorine exchange by the Finkelstein reaction decrease with branching homology in steps of 50- to 80-fold, and that, for MeCl and EtCl, the parameters of the Arrhenius equation $k_2 = B_2 \exp(-E_A/\boldsymbol{R}T)$ indicate that the fall in rate from methyl to ethyl is due in part to a decrease in the probability, and in part to an increase in the energy of the transition state of the reaction of the higher alkyl group.

TABLE 2. *Rate constants* (k_2 *in* sec.$^{-1}$ *mole*$^{-1}$ *l.*), *relative rates at common temperatures, and Arrhenius parameters* (B_2 *in* sec.$^{-1}$ *mole*$^{-1}$ *l., and* E_A *in kcal. mole*$^{-1}$) *of reactions of lithium radio-chloride with alkyl chlorides in acetone.*

	10^5k_2 (25°)	10^5k_2 (60°)	Rel. k_2 (25°)	Rel. k_2 (60°)	$\log_{10} B_2$	E_A
MeCl	3·88	140	71	57	10·3	20·1
EtCl	0·055	2·45	1	1	9·5	21·5
Pr^iCl	—	0·045	—	0·019	—	—

EXPERIMENTAL

Lithium radio-chloride was prepared by a Szilard–Chalmers separation from potassium perchlorate, which had been irradiated for one month in the Harwell pile under a flux of 10^{10} neutrons per cm.^{2} per sec., and kept for a further month in order to allow decay of most of the potassium activity. To a solution of this material in water, a small amount of sodium chloride was added as carrier, and then the chloride was precipitated as silver chloride, and converted by reduction with hydrogen at red heat into hydrogen chloride, and thence into lithium chloride, which was purified with the aid of acetone, and dried.

" AnalaR " acetone was dried with calcium chloride, and distilled with a little quinol through an efficient column at high reflux ratio. Sufficient for each kinetic run was distilled from anhydrous magnesium perchlorate immediately before use.

The dried and redistilled alkyl chloride was introduced by distillation into a solution of lithium radio-chloride, in a closed system designed to permit the subsequent operations without loss of the volatile materials. The original lithium chloride solution having been standardised with respect to chloride ion, the concentration of alkyl chloride was determined by estimation of total chloride after reaction with silver nitrate at 100°. Samples for radiochemical analysis were evaporated at a low temperature, and the residual salt was dissolved in water. The radioactivity was measured with the type of counter usual for liquid samples, and the standard counting equipment.

If a and b are respectively the concentrations of alkyl chloride and lithium chloride, and if C and $C - X$ are respectively the specific radioactivities of the initial solution of lithium chloride and of a solution of the salt recovered from a reaction stopped after a time t, the second-order rate constant is given (le Roux and Sugden, *J.*, 1939, 1279) by the equation,

$$k_2 = \frac{2 \cdot 303}{(a+b)t} \log_{10} \left[1 - \frac{X}{C}\left(1 + \frac{b}{a}\right) \right]^{-1}$$

Although it made little difference to the calculation of the present results, this equation was sometimes used in a form which allowed for the reaction's occurring during the time the reaction mixture took to reach thermostat temperature. This involved measurement of the specific activity X_1 at a time t_1 soon after the solution had attained the proper temperature, and the specific activity X_2 at a later time t_2. The appropriate form of equation is as follows :

$$k_2 = \frac{2 \cdot 303}{(a+b)t} \log_{10} \left\{ [1 - \frac{X_1}{C}(1 + \frac{b}{a})][1 - \frac{X_2}{C}(1 + \frac{b}{a})]^{-1} \right\}$$

In use of these formulæ, the concentrations a and b are computed with due allowance for the change of volume of the solvent between the temperature of standardisation and the temperature of reaction.

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[*Received, March 8th,* 1955.]