Mechanism of Substitution at a Saturated Carbon Atom. Part XLI.*
Unimolecular Racemisation of 1-Mesitylethyl Chloride in Acetone.

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Optically active 1-mesitylethyl chloride undergoes racemisation in anhydrous acetone at a rate which has the kinetic characteristics associated with unimolecular reactions. This is the first evidence that such reactions can be realised in that solvent.

WHEN searching for evidence of the occurrence of unimolecular non-solvolytic reactions in polar aprotic solvents, we were not confident that we could encounter it in a solvent so far down the polar series as acetone. However, we have observed that optically active 1-mesitylethyl chloride racemises spontaneously in anhydrous acetone at a rate which has the kinetic characteristics of a unimolecular reaction. By introducing a mesityl group close to the site of reaction, we favour unimolecular substitution; but, as will be illustrated in a later paper, certain bimolecular substitutions, although somewhat slow, can be realised in this system. Again, by the use of a chloride, rather than a bromide or iodide, we offer bimolecular competition only by the least nucleophilic reagent-anion among the three halogens. The observations to be described depend on the assistance given to the unimolecular process by both the factors indicated.

Certain kinetic complications have to be dealt with. In the absence of any added substance, the spontaneous racemisation of 1-mesitylethyl chloride approximately follows a first-order law for nearly one-quarter of its course, and then becomes markedly autocatalytic. We ascribe the autocatalysis to a concomitant elimination of hydrogen chloride, the evidence being that it can be detected, and that added hydrogen chloride strongly accelerates the racemisation, almost completely cutting out the autocatalysis.

* Part XL, preceding paper.

Added neutral salts, such as lithium perchlorate, have a much smaller, but still considerable, accelerating influence on the first-order racemisation. They seem to have less influence on the autocatalytic process, with the result that they reduce the extent of this disturbance, and enable good rate coefficients to be obtained from a larger proportion, often one-half or more, of the total reaction. A large salt effect would be expected if the racemisation depends on a rate-controlling ionisation in anhydrous acetone. And though, for the convenience of the delay of autocatalysis, we used larger salt concentrations (up to 0·4M) than would justify an electrostatic calculation of the resulting kinetic effects (Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979), it does appear that, up to about 0·2M-salt, the observed accelerations are of the order of those which could be calculated on the reasonable assumption that the ionic-strength constant σ for mesitylethyl chloride in acetone (which measures the polarity of the transition state of the ionisation) is not very different from that of the nearest analogous case for which we know it, *viz.*, for *pp'*-dimethylbenzylhydryl chloride in aqueous acetone (*loc. cit.*).

The crucial test of mechanism is, then, to keep the salt concentration constant, but to replace the inert salt, lithium perchlorate, by the conceivably active salt, lithium chloride. If the racemisation were bimolecular, depending, therefore, on adventitious chloride ion

Racemisation of 1-mesitylethyl chloride in acetone at 35° in the presence of salts.

● *With* 0·2M-LiClO$_4$.
○ *With* 0·2M-LiCl.
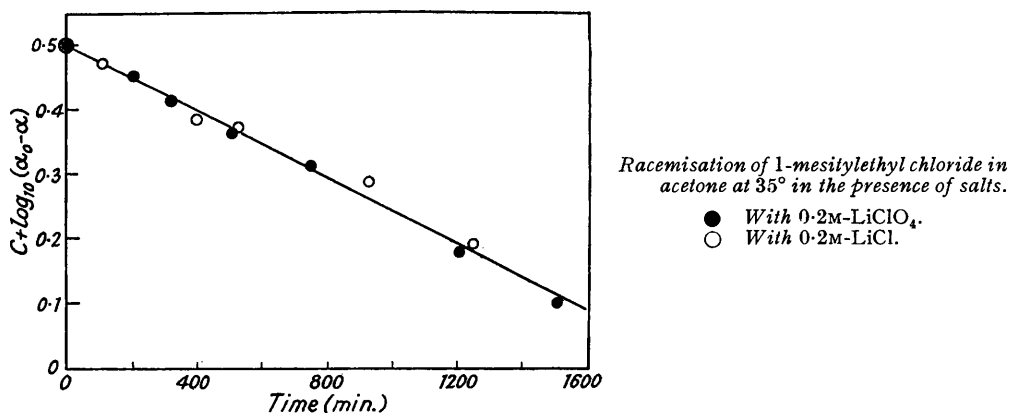
when none is added, then the introduction of lithium chloride should produce a great acceleration. In fact, as illustrated in the Figure for the concentration 0·2M of either salt, the first-order rates with added lithium perchlorate and with lithium chloride are almost the same. We conclude that the racemisation is essentially unimolecular, its velocity being dependent on a rate-determining fission of the carbon–halogen bond.

A selection of first-order rate coefficients, taken, where necessary, from the initial parts of the racemisations, are given in the Table, which illustrates, *inter alia*, the large

First-order rate coefficients (k_1 in sec.$^{-1}$) of racemisation of 1-mesitylethyl chloride (RCl) in acetone.

Run no.	[RCl]	[LiClO$_4$]	[LiCl]	[HCl]	10^5k_1	Run no.	[RCl]	[LiClO$_4$]	[LiCl]	[HCl]	10^5k_1
		At 35·0°						*At* 44·0°			
35	0·26	None	None	None	~0·05	167	0·23	None	None	None	0·11
37	0·27	0·20	,,	,,	1·03	164	0·16	0·20	,,	,,	1·9
38	0·26	None	0·20	,,	0·96	165	0·18	0·40	,,	,,	4·5
						168	0·054	0·20	,,	0·13	13

specific effect of hydrogen chloride. This cannot be due to its chloride ion, and must therefore be ascribed either to the molecule itself, or to its hydrogen ion. We interpret the effect as an electrophilic catalysis, dependent on hydrogen-bonding, of the ionisation of the alkyl halide, as illustrated for other reactions in the first of these three papers.

Comparison with the kinetics and rates of other reactions suggests that the margin of

rate, on which depends our ability to find unimolecular racemisation in the presence of, say, 0·2M-chloride ion, is narrow. It will appear from results to be published later that substitution by iodide ion in 1-mesitylethyl chloride is predominantly bimolecular, and that at 0·2M-salt concentration, its rate is of order 10^1 times greater than the rate of racemisation. From this, and the known rates of substitution by chloride and iodide ions in simple alkyl halides, we may infer that the rate of bimolecular racemisation in the presence of 0·2M-chloride ion is unlikely to be much smaller than 10^1 times less than the observed unimolecular rate. Another such comparison can be based, first, on results, later to be reported, which show that the effect of removing the three aromatic methyl substituents from 1-mesitylethyl chloride is to reduce the rates of both bimolecular and unimolecular substitutions, *viz.*, the iodide-ion substitution, and ethyl alcoholysis, but the latter by a factor of order 10^1 times larger; and secondly, on the evidence, from known substitution rates in simple alkyl halides, that, on going from an alkyl chloride to the corresponding bromide, both bimolecular and unimolecular racemisation rates should increase, the former by a factor not more than 10^1 times larger than the latter. Therefore the known result (Hughes, Juliusburger, Scott, Topley, and Weiss, *J.*, 1936, 1173), that the racemisation of 1-phenylethyl bromide in the presence of 0·2M-bromide ion in acetone is bimolecular, would be difficult to understand unless the rate of bimolecular racemisation of 1-mesitylethyl chloride in the presence of 0·2M-chloride ion is at least as large as 10^2 times smaller than the observed unimolecular rate.

The Experimental section describes a ketonic derivative of mesityl methyl ketone (of interest, because previous failures to prepare such derivatives have been ascribed to steric hindrance; Kadesch, *J. Amer. Chem. Soc.*, 1944, **66**, 1207), a new preparation of 1-mesitylethyl alcohol, an optical resolution (probably not complete) of this alcohol, and a preparation of optically active (not optically pure) 1-mesitylethyl chloride.

EXPERIMENTAL

Mesityl Methyl Ketone.—Mesitylene (200 g.), acetyl chloride (160 c.c.), and aluminium chloride (200 g.) in carbon disulphide (400 c.c.) yielded the ketone (210 g.), b. p. 128—130°/20 mm. (Dittrich and Meyer, *Annalen*, 1891, **264**, 138). A combined solution of the ketone (0·3 g.) in ethyl alcohol (10 c.c.) and of 2 : 4-dinitrophenylhydrazine (0·5 g.) in sulphuric acid (1 c.c.), after being boiled for 1·5 hr., deposited, on cooling, the 2 : 4-*dinitrophenylhydrazone*, which, after purification gave light yellow crystals (from aqueous ethyl alcohol), m. p. 141° (Found : C, 59·3; H, 5·6; N, 16·5. $C_{17}H_{18}O_4N_4$ requires C, 59·7; H, 5·3; N, 16·4%).

1-Mesitylethyl Alcohol.—The ketone (350 g.) was added gradually to lithium aluminium hydride (28 g.) in ether (1500 c.c.). After addition of dilute sulphuric acid, the ether solution was separated and evaporated, and the residue was poured into water; the alcohol solidified (338 g.). Crystallised from ether at −80°, it had m. p. 71—72° (in agreement with Klages and Allendorf, *Ber.*, 1898, **31**, 998). Its phenylurethane had m. p. 125°. The alcohol (82 g.), phthalic anhydride (74 g.), and pyridine (40 c.c.) were together heated on the steam-bath for 5 hr., cooled, mixed with acetone (100 c.c.), and poured on a mixture of ice (500 g.), concentrated hydrochloric acid (55 c.c.), and ligroin (200 c.c.) ; and the solidified *hydrogen phthalate* (127 g.) was collected and crystallised quickly from benzene–ligroin; its m. p. was then at first 90°, but during several days rose to 131—132°; slow crystallisation yielded large prisms, m. p. 134—135° (Found : C, 73·5; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·0; H, 6·5%). From this acid-ester (127 g.) and brucine (160 g.), the brucine salt was formed in boiling ethyl alcohol (1200 c.c.), collected from the hot suspension (86 g.), extracted with fresh hot solvent (360 c.c.), and then crystallised 5 times from ethyl alcohol, to yield a sample (25 g.) having $[\alpha]_D^{23}$ −8·7° (*c* 5 in CHCl$_3$). The free acid-ester, liberated from this salt, did not solidify, but had $[\alpha]_D^{23}$ −67° (*c* 5 in EtOH), and, on saponification for a few minutes with boiling 2N-sodium hydroxide (400 c.c.), gave a mesitylethyl alcohol, which separated as an oil and then rapidly solidified (3·4 g.). Crystallised from ligroin at −80°, it had $[\alpha]_D^{23}$ +45·8° (*c* 5 in EtOH). In a subsequent preparation the final rotation, measured in the same conditions, was raised to $[\alpha]_D^{17}$ +49·7°.

1-Mesitylethyl Chloride.—The optically active alcohol (1·0 g.) and thionyl chloride (0·6 c.c.) were allowed to react in boiling benzene (10 c.c.) for 10 min., and the solvent and excess of thionyl chloride were pumped off at room temperature. The 1-*mesitylethyl chloride* was then collected by short-path high-vacuum distillation, without application of heat, on a cold-finger

at $-80°$, and was subsequently run into an ampoule, which was sealed and kept at $-80°$ until required. The chloride content was determined by electrometric titration in aqueous ethyl alcohol (Found : Cl, 19·5. $C_{11}H_{15}Cl$ requires Cl, 19·5%). The above-mentioned sample of 1-mesitylethyl alcohol, having $[\alpha]_D^{23}$ $+45·8°$ in ethyl alcohol, gave a chloride which had $[\alpha]_D^{23}$ $+60·4°$, as measured on the pure liquid.

Kinetic Measurements.—The acetone was purified with the aid of potassium permanganate and dried finally with magnesium perchlorate. The purified and dried lithium salts were precipitated by filtering their acetone solutions into benzene, and were then again dried at 100° in a vacuum. The faster reactions were followed in a 10-cm. jacketed polarimeter tube, using sodium-D light. For the slower runs, the sealed tube technique was used in conjunction with polarimetric measurements. Concentrations were as given by weighing, except that of hydrogen chloride, which was passed in as gas, and determined by analysis. The details are here given of Run 168 : [mesitylethyl chloride] $= 0·054$M, $[LiClO_4] = 0·0201$M, $[HCl] = 0·128$M, k_1 in sec.$^{-1}$ (mean $10^5 k_1 = 13·2$) :

t (min.)	α	Racn. (%)	$10^5 k_1$	t (min.)	α	Racn. (%)	$10^5 k_1$
0	0·90°	0·0	—	52	0·60°	33·8	13·7
12	0·83	9·2	13·4	62	0·55	38·9	13·5
17	0·79	12·2	12·5	72	0·51	43·3	13·1
22	0·75	16·7	13·8	82	0·47	47·8	13·2
32	0·70	22·2	13·1	92	0·43	51·7	13·2
42	0·66	26·7	12·4	207	0·18	80·0	13·0