182. *Mechanism of Substitution at a Saturated Carbon Atom. Part LI.** ortho-*Effects in Solvolysis of Arylalkyl Halides, illustrating Steric Retardation in a Unimolecular Substitution.*

By J. C. Charlton and E. D. Hughes.

This paper records rates of solvolysis of (i) benzyl chloride and methyl-substituted benzyl chlorides in 50% aqueous ethyl alcohol at 35° and (ii) 1-phenylethyl chloride and its methyl-substituted derivatives in ethyl alcohol at several temperatures. For the chlorides of the benzyl series, *o*- and *p*-methyl substituents cause comparable acceleration and it is concluded that practically pure polar influences are operative. In 1-phenylethyl chlorides, while the introduction of *p*-methyl and of one *o*-methyl substituent exerts similar facilitating effects, a second *o*-methyl group has much less influence. It is concluded that with two *o*-methyl groups present we have, superimposed on a general accelerating influence of a polar nature, a retarding steric effect. This is attributed to the development of a steric pressure (resulting in an increase of activation energy of *ca.* 1·0—1·5 kcal./mole) between α- and *o*-methyl substituents in the transition state of ionisation.

The existence of a pattern in the incidence of steric hindrance among reactions was first indicated in 1941, when it was noted that unimolecular mechanisms should be generally insensitive, and bimolecular mechanisms generally sensitive, to steric hindrance.[1]

This difference between unimolecular and bimolecular mechanisms represents a broad distinction. It does not mean either that steric conditions have no effect at all on the rate of any unimolecular reaction, or that all bimolecular reactions are similarly sensitive to steric hindrance. In each of the main parts of the pattern there is a light and shade of steric effects. The present papers are concerned with the closer description of some of this detail, within the limited field of nucleophilic substitution, and this particular paper deals with one of the details relating to the unimolecular mechanism of substitution.

We can think of two general reasons why steric conditions might have somewhat mild kinetic effects of either sign on unimolecular nucleophilic substitutions. First, in the formation of the unimolecular transition state, a bond has to be stretched. Now, although normal molecules do not sustain internal pressures nearly as large as those which can be built up in bimolecular transition states, many normal molecules probably do sustain appreciable internal pressures, which might to some extent be relieved by the stretching of a bond.[2] Thus an activation energy would be reduced, and a steric acceleration of the reaction would be observed. The second possibility is that the whole geometry of the atomic system around the reaction centre might be so changed, on the formation of the transition state, that some completely new pressures would be developed. If such new pressures should more than outweigh any relief of pressure due to the bond-stretching, we should observe a (probably mild) steric retardation of a unimolecular substitution.

Several possible examples of steric acceleration in unimolecular nucleophilic substitution have been suggested. This type of explanation was tentatively applied to the solvolysis of highly branched *tert.*-alkyl halides, RCl ⟶ ROH, ROEt, etc., in order to account for the considerable acceleration which follows upon the complete γ-methylation of *tert.*-butyl chloride $(H_3C)_3CCl$, to give tri-*tert.*-butylmethyl chloride $(Me_3C)_3CCl$.[3] It was similarly applied to the solvolysis of diazonium ions, ArN_2^+ ⟶ ArOH, etc., in order to interpret the acceleration which follows the introduction of methyl and phenyl substituents into an *ortho*-position in the aryldiazonium ion, though polar factors so operate that the introduction of the same groups into the *para*-position retards this reaction.[4]

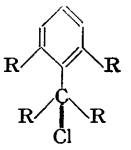
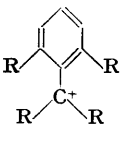
* Part L, preceding paper.

[1] Hughes, *Trans. Faraday Soc.*, 1941, **37**, 603; Day and Ingold, *ibid.*, p. 686.
[2] H. C. Brown, *Science*, 1946, **103**, 385, and later papers.
[3] F. Brown, Davies, Dostrovsky, Evans, and Hughes, *Nature*, 1951, **167**, 987; Hughes, *Bull. Soc. chim. France*, 1951, **18**, C47; Bartlett, *ibid.*, p. C108; *J. Amer. Chem. Soc.*, 1955, **77**, 2801.
[4] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell, London, 1953, p. 801.

We now record an attempt to realise steric retardation in a unimolecular nucleophilic substitution by arranging for a suitable geometrical change in the transition state.

For this purpose, we go over to the series of simple and substituted benzyl halides, most of which undergo unimolecular solvolysis in easily realised conditions; and we examine the kinetic effect of any interaction there may be between α-substituents and *ortho*-substituents, using also *para*-substituents as a control on such polar effects as may be exerted by the *ortho*-substituents employed.

The geometrical situation is as follows. In a benzyl-type halide, the bonding in the side chain is tetrahedral; and so neither of the two α-groups need be, and in general neither will be, in the plane of the ring and its *ortho*-substituents (see I). In the carbonium ion, however, the side-chain bonding is trigonal, and, on account of conjugation, is coplanar with the aromatic ring, so that both α-groups and both *ortho*-groups necessarily come into the same plane (see II). It follows that, if, in the original molecule, α-groups are not much further off from *ortho*-groups than the distances at which steric compression would begin, then, in the carbonium ion, appreciable steric pressures might be developed; and that if steric pressure between α-groups and *ortho*-groups is incipient in the original molecule, then it will certainly become considerable in the carbonium ion.

(I)   (II)

The transition state of the rate-controlling ionisation is in an intermediate stereochemical situation: the side-chain will not be fully co-planar with the ring; but the bonds holding the α-groups will have moved in that direction; and therefore, if steric compression was incipient in the original molecule, it could become appreciable in the transition state. This would lead to an increased energy of activation, and thus to a steric retardation of the reaction.

This investigation is restricted to the effect of methyl substituents. We may describe, first, the results obtained in the series that provides our standard of reference, a series in which steric effects are absent, so that we isolate kinetic behaviour under the polar effects of the methyl substituents. This is the series of benzyl halides having two α-hydrogen atoms (*i.e.*, no methyl group) in the side chain, and up to three methyl groups in *ortho*- and *para*-positions in the ring. Measurement of models shows that steric compression between α-hydrogen and *ortho*-groups is inappreciable or scarcely appreciable, not only in the original molecule, but also in the fully formed carbonium ion, and therefore also in the transition state of ionisation. In this series, no substantial steric effects can influence unimolecular substitution.

The reaction studied was the solvolysis of the benzyl chlorides in 50% aqueous ethyl alcohol, one of the more favourable solvents for unimolecular reactions. The reactions were followed by measuring the production of either chloride ion or hydrogen ion. Some first-order rate constants at 35°, and corresponding relative rates are collected in Table 1.

TABLE 1. *First-order rate-constants (k_1 in sec.$^{-1}$) of solvolysis of benzyl chloride and of methyl-substituted benzyl chlorides in 50% aqueous ethyl alcohol at 35·0°.*

	10^5k_1			
Benzyl chloride	By Cl^-	By H^+	Relative rates	
Parent	0·243, 0·236	—	1	—
2-Me	1·26, 1·25	—	5·2	—
2 : 6-Me_2	6·87	6·82	29 = 5·2 × 5·6	—
4-Me	2·32, 2·31	—	9·6	**1**
2 : 4-Me_2	20·7, 20·5	20·0	85	8·8
2 : 4 : 6-Me_3	—	313, 312	1300	135 = 8·8 × 15·3

It will be seen that *o*- and *p*-methyl substitutents exert comparable accelerating effects, and that, in particular, the second *ortho*-group introduces a factor of acceleration which

is of the same order of magnitude as that given by the first. This must be a practically pure polar effect. Steric hindrance is characterised by the suddenness of its build-up after the first onset; and, if the first *ortho*-group were introducing an appreciable steric retarding factor, then the second would introduce a much larger one, and the rates would not show the relations they do. Equally, the accelerations are too nearly uniform to be regarded as steric accelerations. All this is consistent with the models of the molecules and transition state, which tell us to expect no steric effect of any kind.

The general consistency of the data supports the view that the unimolecular mechanism is the main reaction route. It will undoubtedly be the sole mechanism in most cases, and particularly in those in which we are concerned to show the absence of steric effects by pairs of *o*-methyl groups. In the example of 2 : 4 : 6-trimethylbenzyl chloride, Brown and Hudson [5] showed that solvolysis followed the unimolecular mechanism exclusively in a less ionising solvent than ours.

Against this background, we describe a study of the series of similarly methyl-substituted 1-phenylethyl chlorides. Here we have always one α-methyl group. Models show that steric compression between α-methyl and *o*-hydrogen is insignificant, not only in the original molecule, but also in the fully formed carbonium ion, and therefore also in the intermediate transition state. However, models also show that significant compressions can arise between α-methyl and *o*-methyl, though only when two *o*-methyl groups are present, since, with one alone, compression can be relieved by a rotation of the side chain. Such compression between α-methyl and one of two *o*-methyl groups is incipient, but relatively small, in the original molecule; but it is large enough to raise the energy by some kcal./mole in the carbonium ion; and therefore, although the compression will be smaller than this in the transition state, it may well be large enough to raise the energy appreciably, and hence to lead to a significant steric retardation. Of course, such a steric effect will appear in superposition upon the nearly uniform, polar, accelerative effect of *o*- and *p*-methyl groups, already illustrated in the benzyl series. But still the steric effect may be detectable, because it should not be uniform, but should be distinguished by its sudden appearance on the introduction of a second *o*-methyl group.

The process examined was the solvolysis of the 1-phenylethyl chlorides in dry ethyl alcohol, a solvent which, for this series of halides is ionising enough fully to establish the unimolecular mechanism. Actually, the rates of these reactions have been measured over ranges of temperature, but we shall first compare them at a common temperature, in the same simple way as for the benzyl series. The reactions were followed by determination of the chloride ion produced. The rates at 34·8°, and corresponding relative rates, are given in Table 2.

TABLE 2. *First-order rate-constants (k_1 in sec.$^{-1}$) of solvolysis of 1-phenylethyl chloride and of methyl-substituted 1-phenylethyl chlorides in dry ethyl alcohol at* 34·8°.

1-Phenylethyl chloride	10^5k_1	Relative rates	
Parent	0·0782	1	—
2-Me	1·26	16	—
2 : 6-Me_2	2·35	30 = 16 × 1·9	—
4-Me	3·10	40	1
2 : 4-Me_2	43·5	560	14
2 : 4 : 6-Me_3	112	1440	38 = 14 × 2·7

We notice that, in this series, the polar effects of the nuclear methyl groups are slightly larger than in the benzyl series, each methyl group (apart from a second *o*-methyl group) raising the rate by a factor of 15—40. However, second *o*-methyl groups, instead of increasing the rate by factors of at least as much, raise it by factors of 2—3 only. Evidently a retarding effect has entered here; and the manner of its entry is as expected for the steric retardation due to the flattened structure of the unimolecular transition state.

There can be no doubt that these effects do indeed apply to the unimolecular mechanism. For 1-phenylethyl chloride itself this is clear from previous work; and for representative

[5] D. A. Brown and Hudson, *J.*, 1953, 3360.

derivatives, *viz.*, the 2-methyl, 2 : 4-dimethyl, and 2 : 4 : 6-trimethyl compounds, we have verified that the rate of alcoholysis is scarcely, if at all, sensitive to added lithium ethoxide up to concentrations about 0·05M.

We should expect the polar effect of the methyl substituent to be exerted mainly on the energy factor of reaction rate, and the steric effect considered above is again an effect on energy. We have therefore measured the solvolysis rates over a temperature range with the results contained in Table 3.

TABLE 3. *First-order rate-constants* (10^5k_1 *with* k_1 *in sec.*$^{-1}$) *of solvolysis of* 1-*phenylethyl chloride and its methyl derivatives in dry ethyl alcohol at various temperatures.*

Temp.	Parent	2-Me	2 : 6-Me_2	4-Me	2 : 4-Me_2	2 : 4 : 6-Me_3
−10·0°	—	—	—	—	—	0·311
0·0	—	—	—	—	0·583	1·47
+11·6	—	—	—	—	2·83	—
14·3	—	—	—	—	—	10·8
24·9	—	0·403	0·747	0·913	14·8	36·5
34·8	0·0782	1·26	2·35	3·10	43·5	112
45·1	0·278	3·86	7·48	10·1	—	—
55·1	0·844	—	21·7	30·1	—	—
63·6	2·09	25·5	51·1	72·2	—	—
75·7	6·75	—	—	—	—	—
76·7	7·35	—	—	—	—	—
84·1	13·9	—	—	—	—	—

The Arrhenius parameters which follow from these figures are in Table 4. We see that, whereas the first *o*-methyl substituent substantially reduces the activation energy, the second does not. We assume that the similar reduction, which its polar effect would produce, is approximately cancelled by the appearance at this point of steric energy. The amount of steric energy seems to be about 1·0—1·5 kcal./mole; and, although we have not enough data to permit a theoretical treatment of the problem, such a value may be taken to imply that, in the transition state of ionisation, the system of bonds which the carbonium ion is going to retain is very considerably flattened (cf. the following paper).

TABLE 4. *Arrhenius energies of activation* (*E in kcal./mole*) *and frequency factors* (*B in sec.*$^{-1}$) *for the solvolysis of* 1-*phenylethyl chloride and its methyl derivatives in dry ethyl alcohol.*

	E	$\log_{10} B$		E	$\log_{10} B$
Parent	22·8	10·2	4-Me	22·2	11·3
2-Me	21·5	10·4	2 : 4-Me_2	20·7	11·4
2 : 6-Me_2	21·6	10·8	2 : 4 : 6-Me_3	20·6	11·7

EXPERIMENTAL

Preparations.—The benzyl chloride, twice distilled, had b. p. 66°/13·5 mm., n_D^{25} 1·5360. *p*-Toluic acid was reduced with lithium aluminium hydride in ether to 4-methylbenzyl alcohol, m. p. 59°, which was converted, by treatment with thionyl chloride in benzene, into 4-methylbenzyl chloride: the latter after non-ebullient distillation at a low pressure, and fractional freezing, had m. p. 5·2°, n_D^{25} 1·5320, and the theoretical content of hydrolysable chlorine. *o*-Toluic acid was similarly converted into 2-methylbenzyl alcohol, m. p. 35·5—36°, and thence into 2-methylbenzyl chloride, m. p. 4·8°, n_D^{25} 1·5400.

2 : 4-Dimethylbenzyl chloride, prepared directly from *m*-xylene, formaldehyde, and hydrogen chloride as described by Nauta and Dienska,[6] had b. p. 108—109°/20 mm., n_D^{25} 1·5372, and the correct chloride content. Its identity was checked by hydrolysis in aqueous acetone to the alcohol, m. p. 28—29° (Found: C, 79·3; H, 8·4. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·9%) (Hinrichsen [7] gives m. p. 22°), and oxidation of the latter with permanganate to 2 : 4-dimethylbenzoic acid, m. p. 124° (Found: C, 71·8; H, 6·8. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%) (Stephen, Short, and Gladding [8] give m. p. 125°). 2 : 6-Dimethylbenzoic acid, m. p. 116°, prepared from 2-bromo-*m*-xylene (from *m*-2-xylidine) by the Grignard method with carbon dioxide, was reduced with lithium aluminium hydride to 2 : 6-*dimethylbenzyl alcohol* (48%

[6] Nauta and Dienska, *Rec. Trav. chim.*, 1936, **55**, 1000.
[7] Hinrichsen, *Ber.*, 1888, **21**, 3085.
[8] Stephen, Short, and Gladding, *J.*, 1920, **117**, 522.

yield), which, when crystallised from light petroleum, had m. p. 83·5° (Found : C, 79·8; H, 9·0. $C_9H_{12}O$ requires C, 79·4; H, 8·9%), and, on treatment with thionyl chloride in benzene, gave 2 : 6-*dimethylbenzyl chloride*, m. p. 34° (Found : C, 69·7; H, 7·3; Cl, 23·0. $C_9H_{11}Cl$ requires C, 69·9; H, 7·2; Cl, 22·9%). 2 : 4 : 6-Trimethylbenzyl chloride, prepared from mesitylene by Nauta and Dienska's method,[6] had m. p. 45—46°. Its identity was checked by hydrolysis with aqueous acetone to 2 : 4 : 6-trimethylbenzyl alcohol, m. p. 88° (Found : C, 80·4; H, 9·7. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·4%) (Carré [9] gives m. p. 88—89°).

1-Phenylethyl alcohol, purified by way of its hydrogen phthalate,[10] had b. p. 106—107°/22—23 mm., n_D^{25} 1·5254, and on treatment with thionyl chloride in benzene, gave 1-phenylethyl chloride having b. p. 80—81°/19 mm., n_D^{25} 1·5252, and the theoretical content of hydrolysable chlorine. 1-*p*-Tolylethyl alcohol, prepared from *p*-bromotoluene and acetaldehyde by the Grignard method, had b. p. 108—110°/12 mm., n_D^{25} 1·5221, and with thionyl chloride in benzene gave 1-*p*-tolylethyl chloride, which was purified by non-ebullient distillation. 1-*o*-Tolylethyl alcohol, similarly prepared, had b. p. 119°/21 mm., n_D^{25} 1·5292, and gave 1-*o*-tolylethyl chloride, b. p. 99·5°/19 mm., n_D^{25} 1·5318.

2 : 4-Dimethylacetophenone [11] had b. p. 109°/14 mm., n_D^{25} 1·5319, and gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 170° (Found : C, 58·0; H, 4·8; N, 16·5. $C_{16}H_{16}O_4N_4$ requires C, 58·5; H, 4·9; N, 17·1%). The ketone was reduced with lithium aluminium hydride in quantitative yield to 1-(2 : 4-dimethylphenyl)ethyl alcohol, b. p. 125—126°/16—17 mm., n_D^{25} 1·5245. This was converted with thionyl chloride into 1-(2 : 4-dimethylphenyl)ethyl chloride, which was purified by non-ebullient distillation, had a correct chlorine content, and was characterised by conversion into 1-[1-(2 : 4-dimethylphenyl)ethyl]pyridinium chloride, m. p. 153° (Klarges and Keil [12] give m. p. 153°). 1-(2 : 6-*Dimethylphenyl)ethyl alcohol* prepared by the Grignard method from 2-bromo-*m*-xylene and acetaldehyde, had m. p. 69° after crystallisation from light petroleum (Found : C, 80·6; H, 9·5. $C_{10}H_{14}O$ requires C, 80·0; H, 9·4%), and, on treatment with thionyl chloride as usual, gave 1-(2 : 6-*dimethylphenyl)ethyl chloride*, which was purified by non-ebullient distillation (Found : Cl, 20·8. $C_{10}H_{13}Cl$ requires Cl, 21·1%). 2 : 4 : 6-Trimethylacetophenone was prepared from mesitylene, and converted into 1-mesitylethyl alcohol, and 1-mesitylethyl chloride, as described by Charlton and Hughes.[13]

Kinetics.—For the chlorides of the 1-phenylethyl series the sealed-tube method was used. The tubes were charged with the aid of an automatic pipette, jacketed at 0° when necessary. With chlorides of the benzyl series, the halide was contained in a flask in a thermostat and, from a pipette jacketed at the same temperature, a volume of dry ethyl alcohol was first added and then, with efficient stirring throughout, an equal volume of water. In this way homogeneity and temperature control were quickly attained and aliquot portions of the reaction mixture were withdrawn at suitable intervals and analysed. The progress of reaction was determined by measurement of either acid or chloride ion in work with benzyl chlorides, and by the latter method only in work with 1-phenylethyl chlorides. For acid determination the samples were added to cooled acetone, and the resulting solutions were titrated with 0·1N-sodium hydroxide, with lacmoid as indicator. For the chloride-ion measurements, the tube contents or aliquots were partitioned between carbon tetrachloride and water, and the aqueous solution was titrated electrometrically with 0·01N-silver nitrate.

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[9] Carré, *Compt. rend.*, 1910, **151**, 150.
[10] Houssa and Kenyon, *J.*, 1930, 2260.
[11] Perkin and Stone, *J.*, 1925, **127**, 2283.
[12] Klarges and Keil, *Ber.*, 1903, **36**, 1637.
[13] Charlton and Hughes, *J.*, 1954, 2939.