50. *Mechanism of Substitution at a Saturated Carbon Atom. Part XXXII. The Rôle of Steric Hindrance. (Section G) Magnitude of Steric Effects, Range of Occurrence of Steric and Polar Effects, and Place of the Wagner Rearrangement in Nucleophilic Substitution and Elimination.*

By I. Dostrovsky, E. D. Hughes, and C. K. Ingold.

This abstract is intended to render intelligible any of the three main divisions, (*A*), (*B*), and (*C*), of the paper without the need of reading the others.

Discussion starts from the following facts and conclusions derived from the preceding six papers. Whitmore had shown qualitatively that the *neo*pentyl halides are singularly unreactive to certain substituting agents. It has now been established that this behaviour is special to bimolecular nucleophilic substitution (S_N2); and that a measure of it is that for *neo*pentyl bromide rates are reduced, as compared with lower primary bromides, by factors of about 10^5, and activation energies are increased by about 6 kg.-cals. It is also proved that in unimolecular nucleophilic substitution (S_N1) the reactivity of *neo*pentyl halides is comparable with that of the other primary alkyl halides. Finally it is shown that, whilst in bimolecular substitutions the form of the *neo*pentyl group is preserved, in unimolecular substitution the group becomes converted into a *tert.*-amyl group, and, in the accompanying unimolecular elimination, into *iso*amylene.

(*A*, p. 175). A semi-quantitative theoretical treatment of steric hindrance in bimolecular nucleophilic substitution is given as a development of the transition state theory of reaction rate. It is possible to calculate the steric increment of activation energy in certain cases, and an upper limit to this increment in other cases. The calculations show clearly how the apparently peculiar position of *neo*pentyl compounds arises, puts their behaviour in perspective with that of other alkyl compounds, and leaves no doubt that the observed rate and energy effects are of steric origin. It is shown, *e.g.*, that steric effects in bimolecular nucleophilic substitution of *tert.*-butyl halides are relatively small; and it is explained why the effect of an inserted methylene group, as revealed by comparison of *tert.*-butyl with the homologous *neo*pentyl halides, is qualitatively opposite to the effect shown by comparison of ortho-substituted benzoic acids with the homologous phenylacetic acids in relation to Victor Meyer's classical experiments on steric hindrance in esterification.

(*B*, p. 186). Our general picture of bimolecular and unimolecular substitutions and eliminations is broadened by these conclusions. It is perceived that much of the evidence formerly held to support the Thorpe–Ingold valency deflexion hypothesis can be consistently explained as an effect of steric hindrance. Surveying, in other fields, the evidence of reaction rates in the light of our more sharply defined views on steric hindrance, we find confirmation of those mechanisms for the conversion of alcohols into halides, which had earlier been inferred only from evidence on the Walden inversion; we find confirmation also of various other previously assumed mechanisms, including the mechanisms of carboxyl esterification and hydrolysis. Polar and steric effects are in general superposed in bimolecular substitutions. The two effects jointly determine the bimolecular nucleophilic rate sequence Me > Et > Pr^β. There is no discernible steric effect in unimolecular substitution. Consequently, for structures which are sterically hindered in bimolecular substitution, more success may sometimes be achieved in effecting reaction by the addition of an ionising solvent (*e.g.*, water) than by the introduction of powerfully nucleophilic reagents (*e.g.*, hydroxide ion). Polar effects are responsible for the increasing rate of ionisation in the series primary, secondary, tertiary, alkyl halides, a measure of which is the rate factor of about 10^8 between primary and tertiary bromides, and an activation energy difference of about 7 kg.-cals. Our view with regard to the proportions in which bimolecular and unimolecular mechanisms are superposed in the aqueous or alcoholic solvolysis of secondary alkyl halides is adjusted in the sense implying that the racemisation accompanying their unimolecular solvolysis is more nearly complete than we used to believe.

(*C*, p. 192). The Wagner and related rearrangements in the major field of heterolytic substitutions used to be classified with 1 : 3-eliminations, but it is now clear that they belong to unimolecular nucleophilic processes, either of substitution or elimination (S_N1 or *E*1). This type of mechanism is a necessary condition for rearrangement, but not a sufficient condition. Rearrangement depends otherwise, in an intelligible way, on resonance energy due to conjugation and hyperconjugation in the carbonium ion. Shoppee's rule for relative migratory aptitudes can be understood. In one case it can be proved that rearrangement follows, and does not accompany, the ionisation which is necessary for it. The Wagner rearrangement may also occur in unimolecular homolytic reactions, which involve the formation of an intermediate free radical, instead of a carbonium ion.

THIS group of papers, Parts XXVI—XXXII, marks a new departure in the research to which it contributes, the general plan of which was set out in Part V (J., 1935, 244). Our concern has been (*a*) to classify substitutions, particularly nucleophilic substitutions, at a saturated carbon atom according to their polar type, (*b*) to establish the mechanisms, in particular the bimolecular and unimolecular mechanisms, of such substitutions, and (*c*), for each class of substitution, to examine constitutional and solvent effects on the mechanism, velocity, and spatial orientation of reaction. Objects (*a*) and (*b*) have been largely accomplished, whilst (*c*) is being actively pursued. However, in the discussions of constitutional effects published hitherto,* we have given attention almost entirely to polar influences, and hardly at all to steric effects. Indeed, the suggestion has been made that we have neglected steric effects, though it should have been clear from our reference to them in Part V that we have simply been putting first things first. Our view was, and is, that polar effects determine all the broad phenomena, while steric hindrance makes only quantitative differences in general, though it can create qualitatively special situations in particular cases.† However, a more detailed description of the effects of steric hindrance is obviously necessary to a general statement of the theory, and we now take the first steps in this direction, even though our work on the polar effect is still far from finished. The main conclusions set out in this paper, as well as the more important of the experimental data given in the accompanying papers, were reported in summary by one of us in 1941 (Hughes, *Trans. Faraday Soc.*, **37**, 620).

The idea of steric hindrance, as a factor reducing reaction rate, originated in the last century, and is the subject of an extensive literature, which we shall not here summarise, since other reviews are available. But inasmuch as the steric concept has usually been applied simply to the molecular models of reactants, it has not hitherto been employed in a form capable in principle of quantitative development. For the transition state theory teaches that, in the discussion of effects on reaction rate, the transition state and the initial state must be treated differentially; and it is obvious that, in relation to steric hindrance, the most important part of any such differential treatment may well be the discussion, not of the initial state of the reactants, but of the transition state, in which a larger number of atoms may have to be brought into a particular stereochemical relation with one another than in the initial state. It is inherent in this point of view that steric hindrance should not be associated, as it so often is by implication if not explicitly, with a particular reactant, or a particular over-all chemical reaction: rather it is a property of a particular reaction mechanism. It follows also that the steric hindrance associated with a particular mechanism cannot usefully be discussed unless the mechanism itself has been studied at least to a point such that the composition and approximate configuration of the transition state is known. However, our work on nucleophilic substitution at saturated carbon atoms seems to have reached a stage at which this preliminary condition is fulfilled.

The problem of steric hindrance being essentially quantitative, its complete treatment in relation to any particular mechanism of reaction requires, in principle, a quantitative knowledge of (*a*) the configuration of the transition state, and (*b*) its internal force system. Even in the most favourable cases our existing knowledge of these geometrical and dynamical particulars is not very accurate or complete. This is especially true of the force system. Therefore we thought it advisable to commence the study of steric hindrance in nucleophilic substitution, not with an average or typical case of this nearly universal phenomenon, but with an extreme case, in which the steric effect produces such a qualitatively striking situation that quantitative precision in the theoretical treatment is not necessary to a demonstration. Though relieved in this way of the need to face the difficulties of an exact calculation, we do include a semi-quantitative treatment in the present discussion.

Our attention was directed to the *neo*pentyl halides, as possibly providing an extreme example of steric hindrance, by Whitmore's statements about these substances: he discovered (see Part XXVI) their remarkable inactivity towards powerfully nucleophilic substituting agents, such as hydroxide or ethoxide ions. In the accompanying papers (Parts XXVI—XXXI) these observations are placed in perspective by quantitative comparisons of the rate of nucleophilic substitution of *neo*pentyl and of other simple, primary alkyl halides. It is a notable outcome of this work that the striking lack of reactivity of *neo*pentyl halides is particularly characteristic of the bimolecular mechanism of nucleophilic substitution (S_N2). However, even in reactions by this mechanism, these halides are not absolutely inactive, the rates of bimolecular substitution of *neo*pentyl bromide, for example, with ethoxide or iodide ions being merely some 10^4—10^6 times smaller than for the other primary alkyl bromides which have been studied under similar physical conditions. The general character of the evidence is indicated by the data in Table I, taken from Parts XXVI and XXVII, for relative rates of substitution of the various alkyl halides, and for the corresponding Arrhenius activation energies. It has been pointed out how the successive replacement by methyl groups of the three β-hydrogen atoms of the ethyl group causes a fall of rate which steepens rapidly as the third methyl is introduced. It has also been noted that the changes of rate are largely accounted for by changes in the apparent energy of activation.

---

* Since 1933; but some of the relevant papers appear under serial titles other than that here used, *e.g.*, "Reaction Kinetics and the Walden Inversion," and "Criterion for the Mechanism of the Reactions of Alkyl Halides with Hydroxylic Solvents."

† "We envisage the operation of steric hindrance, *i.e.*, repulsions due to the interpenetration of atomic electron clouds at very small distances: such effects are quantitatively important, though they seldom seem to alter the direction of the broader distinctions. . . ." (Part V, *ibid.*, p. 246).

TABLE I.

Relative Rates and Arrhenius Activation Energies of Bimolecular Substitutions of Primary Alkyl Bromides.

	Methyl.	Ethyl.	*n*-Propyl.	*iso*Butyl.	*neo*Pentyl.
Substitution by OEt^- *in* EtOH					
Relative rates at 55°	17·6	1	0·28	0·030	0·0000042
E (kg.-cals.)	20·0	21·0	—	22·8	26·2
Substitution by I^- *in* $COMe_2$					
Relative rates at 64°	—	1	—	—	0·000053
E (kg.-cals.)	—	19	—	—	25

We shall now endeavour to show that the interpretation, as an effect of steric hindrance, of the low rates and high activation energies obtained for the reactions of *neo*pentyl bromide, indeed, that the whole set of phenomena illustrated in Table I, is consistent with what is known concerning the geometrical and dynamical factors which affect the bimolecular mechanism of substitution (S_N2).

(A) *Discussion of Steric Effects in Bimolecular Nucleophilic Substitutions of Alkyl Compounds, particularly of Alkyl Halides.*

(a) *Geometrical Factors.*—In principle the initial and transition states of reaction have to be treated differentially, though the more important part of the present considerations relates to the transition state. As to the geometry of the " model " of the alkyl compound in its initial state, we assume bond lengths corresponding to summed covalent radii, and carbon bond angles equal to the tetrahedral angle. All single bonds are assumed to be without any internal resistance to torsional movement. The data employed are collected in Table II, and are substantially as recorded by Pauling (" Nature of the Chemical Bond," Cornell Press, 1940), though the lower lines of figures require some further explanation, to be given later (p. 177).

TABLE II.

Atomic Dimensions (A.) *used in Evaluation of Steric Effects in Bimolecular Substitutions of Alkyl Halides.*

	H.	C.	Cl.	Br.	I.
Covalent radius (ρ_{co})	0·32	0·77	0·99	1·14	1·33
Univalent ionic (crystal) radius (ρ_{ion})	—	—	1·81	1·95	2·16
Maximal van der Waals radius ($\rho_{max.}$)	1·2	1·6	1·8	1·95	2·15

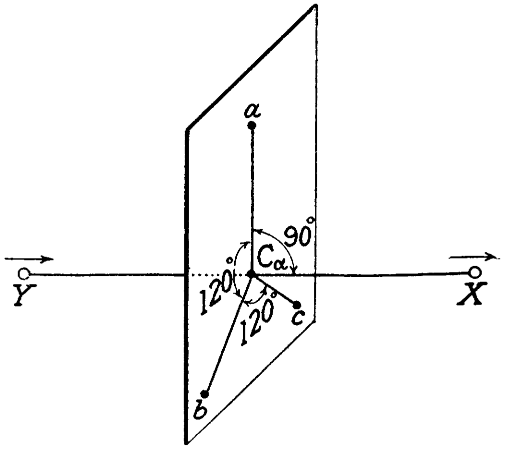
It is generally agreed that, in the transition state of a bimolecular nucleophilic substitution, the nuclei of the substituting atom Y, of the carbon atom C_α at which the substitution takes place, and of the displaced atom X, are collinearly arranged, whilst the nuclei of the other atoms, *a*, *b*, and *c*, to which C_α is covalently bound lie in directions from C_α inclined at angles of 120° to one another, and in a plane which passes through C_α, and is perpendicular to the line of Y and X (Fig. 1). This statement refers to the " model " of the transition state, *i.e.*, to its equilibrium configuration with respect to all those normal co-ordinates which are associated with minima of potential energy. The statement is to be regarded as exact only for certain special cases, *e.g.*, for a " symmetrical " substitution,* such as

$$Br^- + CH_3\text{–}Br \longrightarrow Br\text{–}CH_3 + Br^-.$$

It is only an approximate description of the model of the transition state in more general cases, because it neglects such deviations as may arise from steric hindrance itself. However, such deviations will almost always be relatively small: the nuclei of Y, C_α, and X will at least lie near a straight line, and the nuclei of *a*, *b*, *c*, and C_α near a plane perpendicular to the line. The theoretical argument in favour of this type of model is that it minimises repulsive energy in the transition state; and experimentally the model has been well established by kinetic investigations relating to the Walden inversion (for a summary, see Cowdrey, Hughes, Ingold, Masterman, and Scott., J., 1937, 1252; and Hughes, *Trans. Faraday Soc.*, 1938, **34**, 186).

FIG. 1.

Fundamental model of the transition state in bimolecular nucleophilic substitution.



Since our purpose is to examine steric effects, we shall be justified in using the idealised model of the transition state, and in regarding the determination of any allowances necessary for deviations of steric origin from this model as part of the problem to be solved. With the idealised model as basis, we can calculate the distances between the nuclei of the attacking and displaced atoms and those of all the other atoms of the structure.

---

* The term is applied by Polanyi to substitutions in which the introduced and expelled groups are identical. We use it in this way without implications respecting mechanism.

A consideration of these distances provides an estimate of the relative importance of the steric factor in different structures. In a second stage of the argument the steric effects associated with the different distances have to be evaluated in terms of energy, and it is at this stage that any deviations from the idealised model which would reduce the total energy should be taken into account.

The model of the transition state, as described up to this point, fixes the directions of the bonds of C_α. The bonds of all other carbon atoms are assumed to make angles equal to the tetrahedral angle. All single bonds are assumed to have a normal length, corresponding to summed covalent radii (Table II), and to be devoid of internal resistance to torsional movement. The lengths of the partial, and partially ionic, bonds, YC_α and $C_\alpha X$, require to be specially estimated. Because of the difficulty of at once making a precise estimate, we shall start with an arbitrary approximation, being prepared later to correct it if necessary, after calculation of a closer approximation. For the present, we estimate YC_α and $C_\alpha X$ by adding the covalent radius of carbon to the mean of the covalent and negative ionic radii of Y or X (Table II).* This procedure differs, it should be remarked, from that of Baughan and Polanyi (*Trans. Faraday Soc.*, 1941, **37**, 648), who take the full negative ionic radii of Y and X, though only one unit of charge is shared between them. Furthermore, they employ gaseous ionic radii, whilst we prefer the well-established crystal radii, believing that the condition of an ion in a crystal is a better approximation than that in a gas to its condition in a dipolar solvent, since the heats of solution of ionic crystals in polar solvents are so very much less than their heats of sublimation (a few kg.-cals. at most, as against about 50 kg.-cals. for univalent crystals). Our distances, YC_α and $C_\alpha X$, for the transition state are accordingly considerably shorter than theirs: in the example BrC_α, the smaller value for the distance is supported by the closer approximation calculated later (p. 184).

The particulars given fix the stable positions of those atoms, the α-hydrogen and β-carbon atoms, which are directly bonded to C_α: their positions are in fact completely determined by the bonding forces. By contrast, the stable positions of those atoms which are linked through one intermediate carbon atom to C_α, *viz.*, the β-hydrogen and γ-carbon atoms, are left indeterminate in one degree of freedom by the bonding forces, because these forces provide no resistance to rotation round the C_α–C_β bond. The disposition of the atoms with respect to rotation about this bond must therefore be determined by the non-bonding forces. Between any pair of atoms which are not bonded to each other, these forces consist of van der Waals attractive, and steric repulsive, forces; which balance, with minimisation of the non-bonding energy, when the internuclear distance has a value called the van der Waals distance. In general, the bonding forces make it impossible to secure an orientation about the C_α–C_β bond which will simultaneously equate to the van der Waals distances all the non-bonded internuclear distances in which the β-hydrogen and γ-carbon atoms are concerned. However, the condition determining the actual orientation is evidently that the total non-bonding energy shall be a minimum. This condition might appear difficult to use for purposes of calculation, but in fact it is not in the cases in which we are interested; for when there is any appreciable steric hindrance involving a β-hydrogen or γ-carbon atom, *i.e.*, if the bonding forces restrict any non-bonded internuclear distance involving any of these atoms to values substantially less than the van der Waals distance, then the general condition almost always reduces to the following, namely, that the orientation of the group will be so determined that the non-bonded internuclear distance which falls furthest below the corresponding van der Waals distance will be a maximum. This follows because, whilst van der Waals attractive energy varies relatively slowly with distance, steric repulsive energy increases with diminishing distance according to a curve which steepens exceedingly rapidly at distances substantially smaller than the van der Waals distance. Obviously it will be the particular internuclear distance which falls on the steepest part of the energy curve which will determine the direction of the forces tending to adjust orientation when the group of atoms affected by rotation about the C_α–C_β bond is out of equilibrium with respect to non-bonding energy. When no non-bonded distance is restricted to such small values, the simplified condition for minimal energy will not necessarily apply; but we shall not worry, because in this case the atoms concerned will not contribute appreciably to the steric effect.

The position of a γ-carbon atom being determined according to these principles, a similar series of statements will apply to the γ-hydrogen and δ-carbon atoms, whose disposition with respect to rotation about the C_β–C_γ bond is left indefinite by the bonding forces, and must again be determined so as to minimise the non-bonding energy. Similar principles apply to the still more remote atoms.

We now enter into some detail with respect to the relatively simple case of a symmetrical substitution, taking as example the displacement of bromine as bromide ion from an alkyl bromide by means of an attacking bromide ion. This type of displacement has been experimentally studied by Hughes, Juliusberger, Scott, Topley, and Weiss by the use of radio-active bromine, as well as by methods dependent on optical activity (J., 1936, 1173); and also by Sugden and his collaborators using radio-bromine (J., 1939, 1279, 1836; 1945, 586).

The alkyl groups to be compared with respect to the steric effects exerted in this and similar substitutions are selected in order to show the influence of successive α- and β-methyl substitution:

methyl	ethyl	*iso*propyl	*tert.*-butyl	(α-methylated series)
ethyl	*n*-propyl	*iso*butyl	*neo*pentyl	(β-methylated series)

The arrangement of most of these groups in the transition state of substitution can be followed with the

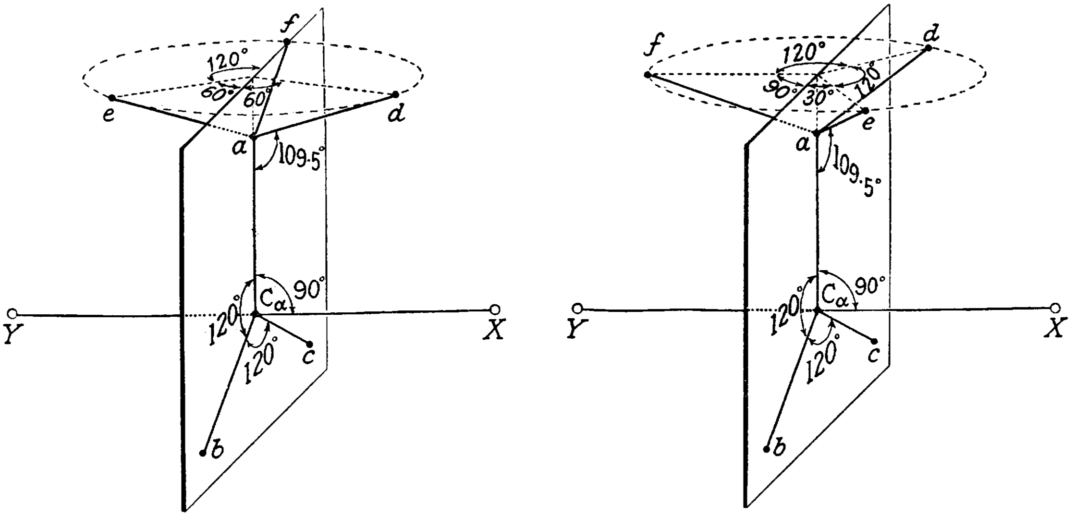
---

* The approximation formula, three-quarters of the $C_\alpha X$ bond length plus one-quarter of the C_α-to-X van der Waals distance (which is suggested by known relations between bond length and bond order), gives the same results.

aid of Fig. 2*a*. For the methyl group, *a*, *b*, and *c* represent three hydrogen atoms. In the ethyl group *a* becomes the β-carbon atom, whilst *d*, *e*, and *f* are the three β-hydrogen atoms; they are so oriented with respect to rotation about the C_α–C_β bond that the planes daC_α and eaC_α are each inclined at 60° to the plane $bcC_\alpha af$. In *iso*propyl, *b* also becomes a β-carbon atom, and the three β-hydrogen atoms it carries are similarly oriented with respect to rotation about their C_α–C_β bond. In *tert.*-butyl, *c* becomes yet another β-carbon atom, carrying three β-hydrogen atoms analogously oriented.

FIG. 2*a*. FIG. 2*b*.

Configurations of alkyl groups in transition states of bimolecular substitution.



In the case of the *n*-propyl group, *b* and *c* are α-hydrogen atoms, *a* is the β-carbon atom, *d* and *e* are the β-hydrogen atoms, and *f* is the γ-carbon atom. The γ-hydrogen atoms are not indicated in the diagram, and, as none of them produces any steric effect, it is not necessary to consider their precise positions. However, as a step towards showing that they in fact yield no steric effect, we imagine them to be arranged as they would be if they did produce one: denoting them by *g*, *h*, and *i*, we find that the planes *gfa* and *hfa* will make angles of 60° with the plane $bcC_\alpha afi$.

The case of the *iso*butyl group requires reference to Fig. 2*b*. Here *b* and *c* are the α-hydrogen atoms, *a* is the β-carbon atom, *f* is the β-hydrogen atom, and *d* and *e* are the γ-carbon atoms. The planes daC_α and eaC_α are each inclined at 30° to the plane $bcC_\alpha a$; whilst the plane faC_α is perpendicular to the plane $bcC_\alpha a$, and contains the atoms Y and X. The γ-hydrogen atoms are not shown. The three γ-hydrogen atoms, *g*, *h*, and *i*, attached to the γ-carbon atom *d*, are so oriented with respect to rotation about the *a*–*d* bond that atom *i* is the most remote of the three from X, whilst *g* and *h* are equidistant from X. Similarly the γ-hydrogen atoms, *j*, *k*, and *l*, attached to *e* are oriented about the *a*–*e* bond so that *l* is the most remote from X, whilst *j* and *k* are equidistant from X.

The arrangement of the *neo*pentyl group can be illustrated by Fig. 2*a*. In this case *b* and *c* are the α-hydrogen atoms, *a* is the β-carbon atom, and *d*, *e*, and *f* are the three γ-carbon atoms. The three γ-hydrogen atoms, *g*, *h*, and *i*, attached to *d* are so oriented by rotation round the *a*–*d* bond that atom *i* is the most remote from X, whilst *g* and *h* are equidistant from X. The γ-hydrogen atoms, *j*, *k*, and *l*, attached to *e* are oriented about the *a*–*e* bond so that *l* is the most remote from Y, whilst *j* and *k* are equidistant from Y. The three γ-hydrogen atoms attached to *f* may be imagined to be arranged like the three γ-hydrogen atoms of the *n*-propyl group: they do not contribute to the steric effect.

Table III contains the distances calculated for the models described, between the nuclei of the bromine atoms and those of the carbon and hydrogen atoms of the alkyl groups, first for the initial states, and then for the transition states, of the bromine exchange reactions under discussion. The table also contains a note of the numbers of carbon or hydrogen atoms situated at these distances from the bromine atoms, as well as of the numbers of identical distances (which may be greater, where, in the transition state, carbon or hydrogen atoms are situated on a plane of symmetry between the two bromine atoms). When several different distances exist in an alkyl group between atoms of the same kind and classification, we give only the smallest such distance, because in no case does any omitted longer distance give rise to a notable steric effect. The numbers of these omitted distances can readily be deduced from the numbers of stated distances, since the total number of distances, stated plus omitted, is obviously equal to the number of like carbon or hydrogen atoms in the initial state, and equal to twice that number in the transition state.

It is necessary to compare these distances (" model distances ") with the distances below which compression would occur (" touching distances "). The latter, the van der Waals distances between the different pairs of

TABLE III.

Model Distances between the Nuclei of the Bromine Atoms and those of the Carbon and Hydrogen Atoms in the Initial and Transition States of the Substitution $Br^- + RBr \longrightarrow BrR + Br^-$.

Key.—r = Distance (in A.), n = number of C or H atoms at the stated distance from Br atoms, N = number of occurrences of the stated distance.

Group R.		CH_3.	$MeCH_2$.	Me_2CH.	Me_3C.	$MeCH_2{\cdot}CH_2$.	$Me_2CH{\cdot}CH_2$.	$Me_3C{\cdot}CH_2$.
				Initial state.				
$H_\alpha \ldots Br$	r	2·50	2·50	2·50	—	2·50	2·50	2·50
	$n = N$	3	2	1	—	2	2	2
$C_\beta \ldots Br$	r	—	2·81	2·81	2·81	2·81	2·81	2·81
	$n = N$	—	1	2	3	1	1	1
$H_\beta \ldots Br$	r	—	2·98	2·98	2·98	2·98	2·98	—
	$n = N$	—	2	4	6	2	1	—
$C_\gamma \ldots Br$	r	—	—	—	—	4·22	3·16	3·16
	$n = N$	—	—	—	—	1	1	2
$H_\gamma \ldots Br$	r	—	—	—	—	4·53	3·05	3·05
	$n = N$	—	—	—	—	2	2	4
				Transition state.				
$H_\alpha \ldots Br$	r	2·55	2·55	2·55	—	2·55	2·55	2·55
	n	3	2	1	—	2	2	2
	N	6	4	2	—	4	4	4
$C_\beta \ldots Br$	r	—	2·78	2·78	2·78	2·78	2·78	2·78
	n	—	1	2	3	1	1	1
	N	—	2	4	6	2	2	2
$H_\beta \ldots Br$	r	—	2·43	2·43	2·43	2·43	2·30	—
	n	—	2	4	6	2	1	—
	N	—	2	4	6	2	1	—
$C_\gamma \ldots Br$	r	—	—	—	—	3·41	2·88	2·42
	n	—	—	—	—	1	2	2
	N	—	—	—	—	2	2	2
$H_\gamma \ldots Br$	r	—	—	—	—	2·99	2·71	2·15
	n	—	—	—	—	2	4	4
	N	—	—	—	—	2	4	4

atoms, are obtained by the summation of appropriately determined van der Waals radii. Table II contains a list of what we call *maximal* van der Waals radii, the figures, except for carbon, being those given by Pauling as van der Waals radii (*op. cit.*). The value for carbon is estimated by adding 0·8 A. to the covalent radius, since the maximal van der Waals radii for all atoms for which directly determined values exist are about this amount greater than the corresponding covalent radii. Reference to the significance of the value for carbon is made below.

These radii are here called " maximal " because, as Pauling has noted, smaller radii are effective for directions making moderate or small angles with the direction of a covalency (*loc. cit.*). This is shown by the properties and dimensions of molecules such as carbon tetrachloride and methylene chloride, in which the chlorine–chlorine distance is considerably less than twice the maximal van der Waals radius of chlorine. Our knowledge of the variation of the effective van der Waals radius with angular separation from a covalency direction is at present very meagre : support can be adduced for the assumption of a shortening (from the maximum radius) of about 0·8 A. for angular separations approaching zero, and a shortening of zero for angular separations of about 90° or greater; whilst Pauling estimates that for an angular separation of 35° the shortening is about 0·5 A. These figures seem to be largely independent of the nature of the atom. If we suppose that, as the angular separation rises from 0° to 90° the shortening of the radius drops from 0·8 A. to zero as a cosine curve drops from its maximum to its minimum, the shortening for an angle of 35° would be 0·53 A., in satisfactory agreement with Pauling's estimate. Arbitrarily, we assume a relation of this form :

$$\rho_{\max.} - \rho_\theta = 0{\cdot}4(1 + \cos 2\theta) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $\rho_{\max.}$ is the maximal, and ρ_θ the effective, van der Waals radius (in A.), and θ ($<90°$) is the angular separation from a covalency. In a polycovalent atom a given direction may lie within 90° of more than one covalency, and when this is so, the smallest angular separation is considered to determine the shortening of the radius. In the case of carbon the maximal van der Waals radius, estimated as 1·6 A. in Table II, will be greater than the effective radius in any actual direction, since in this atom all directions lie within 70° of at least one covalency.

The above applies to covalently bound atoms. We have still to deal with the partially ionic halogen atoms of the transition state. If they were fully ionic the appropriate radius would be the ionic radius, and it would be the same for all directions. We shall assume that, in the partially ionic halogens of transition states, the radius, at a given angular separation from the partially ionic bond, will be reduced below the ionic radius (which is practically the same as the maximal van der Waals radius) by half as much as, in a neutral atom, the effective van der Waals radius, at the same angular separation from a full covalency, would be reduced below the maximal van der Waals radius :

$$\rho_{\text{ion}} - \rho_{\theta} = 0{\cdot}2(1 + \cos 2\theta) \qquad (2)$$

with $\theta < 90°$. This formula is obviously consistent with our method of estimating the lengths of the carbon–halogen partial bonds in the transition states.

Table IV contains the angles which, in the models of the initial and transition states, the various " model distances " of Table III make with the directions of the covalencies or partial covalencies of the atom concerned. From these angles, and the values of $\rho_{\text{max.}}$ and ρ_{ion} in Table II, it is possible to calculate, using equations (1) and (2), the effective van der Waals distances, or " touching distances," corresponding to each of the tabulated model distances. By subtraction we can then find the " compression," experienced by the model of the initial or transition state as the case may be, in respect of each model distance which is shorter than the touching distance.

TABLE IV.

Angular Separations (θ) *in Degrees of Model Distances* (*Table III*) *from Covalency and Partial Covalency Directions.*

Key.
(*a*) All alkyl groups with H_α atoms.
(*b*) All alkyl groups with C_β atoms.
(*c*) Ethyl, *iso*propyl, and *tert.*-butyl groups.
(*d*) *n*-Propyl group.
(*e*) *iso*Butyl group.
(*f*) *neo*Pentyl group.

Bond or partial bond.	C_α–Br.	C_α–H_α.	C_α–C_β.	C_β–H_β.	C_β–C_γ.
Model dist.		*Initial state.*			
$H_\alpha \ldots$ Br	24 (*a*)	46 (*a*)	—	—	—
$C_\beta \ldots$ Br	31 (*b*)	—	40 (*b*)	88 (*cde*)	149 (*d*), 88 (*ef*)
$H_\beta \ldots$ Br	46 (*cde*)	—	—	70 (*cde*)	—
$C_\gamma \ldots$ Br	20 (*d*), 53 (*ef*)	—	—	—	19 (*d*), 63 (*ef*)
$H_\gamma \ldots$ Br	17 (*d*), 65 (*ef*)	—	—	—	66 (*d*), 56 (*ef*)
		Transition state.			
$H_\alpha \ldots$ Br	25 (*a*)	65 (*a*)	—	—	—
$C_\beta \ldots$ Br	34 (*b*)	—	56 (*b*)	60 (*cd*), 53 (*e*)	100 (*d*), 78 (*e*), 60 (*f*)
$H_\beta \ldots$ Br	54 (*cd*), 56 (*e*)	—	—	97 (*cd*), 105 (*e*)	—
$C_\gamma \ldots$ Br	48 (*d*), 57 (*e*), 64 (*f*)	—	—	—	54 (*d*), 71 (*e*), 86 (*f*)
$H_\gamma \ldots$ Br	67 (*d*), 73 (*e*), 81 (*f*)	—	—	—	67 (*d*), 77 (*e*), 90 (*f*)

The model distances, touching distances and compressions (in A.) for the various alkyl groups, in the initial and transition states of the bromine exchange reaction, are assembled in Table V, which also contains statements about the numbers of compressed distances affecting the energies of the states. We see at once that there is no compression worth mentioning in any initial state. Hence, although in principle the energy of steric hindrance must be calculated as a difference of compression energy in the initial and transition states, in practice

TABLE V.

Compressions in the Initial and Transition States of the Bromine Exchange Reaction.

	Model dists. (A.).	Touching dists. (A.).	Compressions (A.).	Number of compressed distances.						
				Me.	Et.	Pr^β.	Bu^γ.	Pr^α.	Bu^{iso}.	*neo*Pentyl.
				Initial state.						
$H_\alpha \ldots$ Br	2·50	2·44	None	[3	2	1	—	2	2	2]
$C_\beta \ldots$ Br	2·81	2·78	None	[—	1	2	3	1	1	1]
$H_\beta \ldots$ Br	2·98	2·86	None	[—	2	4	6	2	2	—]
$C_\gamma \ldots$ Br	4·22	2·49	None	[—	—	—	—	1	—	—]
	3·16	3·23	0·07	—	—	—	—	—	1	2
$H_\gamma \ldots$ Br	4·53	3·67	None	[—	—	—	—	2	—	—]
	3·05	3·07	0·02	—	—	—	—	—	2	4
				Transition state.						
$H_\alpha \ldots$ Br	2·55	2·68	0·13	6	4	2	—	4	4	4
$C_\beta \ldots$ Br	2·78	3·01	0·23	—	2	4	6	2	—	2
	2·78	2·98	0·20	—	—	—	—	—	2	—
$H_\beta \ldots$ Br	2·43	3·01	0·58	—	2	4	6	2	—	—
	2·30	3·02	0·72	—	—	—	—	—	1	—
$C_\gamma \ldots$ Br	3·41	3·09	None	[—	—	—	—	2	—	—]
	2·88	3·34	0·48	—	—	—	—	—	2	—
	2·42	3·47	1·05	—	—	—	—	—	—	2
$H_\gamma \ldots$ Br	2·99	2·95	None	[—	—	—	—	2	—	—]
	2·71	3·05	0·34	—	—	—	—	—	4	—
	2·15	3·13	0·98	—	—	—	—	—	—	4

we may hereafter restrict attention to the transition state. We note the special position of the *neo*pentyl group, which alone involves compressions of the order of 1·0 A., whilst the other alkyl groups, except methyl, have compressions of the order of 0·6 A., and methyl scarcely any compression. It will be obvious from these figures alone that there is hope of providing a satisfactory explanation, on the basis of steric hindrance, of the peculiar facts about the *neo*pentyl halides to which Whitmore first called attention, and which are reduced to quantitative terms by the work of the preceding papers. The more does this seem likely when we remember the sudden way in which resistance to atomic compression mounts as the compression becomes greater.

We shall attempt to evaluate the significance of these compressions in terms of energy, but, before proceeding to further discussion of the bromine exchange reaction, we should point out that a qualitative similarity with reference to steric effects is to be expected of many of the commoner nucleophilic substitutions. This is because opposite, and therefore partly compensating, effects arise from changes in the size of the attacking and displaced groups. When the two bromine atoms of the above problem are replaced by two iodine atoms, the latter set themselves farther from C_α, and therefore farther from all the atoms of the alkyl group, in the transition state, so that all the model distances are increased; but, because of the larger ionic radius of iodine, so also are all the touching distances. The result is that the compressions are not greatly changed, as is shown in Table VI: even compressions of about 1·0 A. are only changed by 0·08 A. One can be sure without calculation that, if one of the two halogen atoms in the transition state were bromine and the other iodine, the compressions would lie between those appropriate to the symmetrical substitutions. Similar statements would be true if both or one of the bromine atoms of the original problem were chlorine, or if the bromide ion were a hydroxide ion.

TABLE VI.

Compressions in the Transition States of Halogen Exchange Reactions.

	Transition state compressions (A.).			Number of compressions.						
	Cl + RCl.	Br + RBr.	I + RI.	Me.	Et.	Pr$^\beta$.	Bu$^\gamma$.	Pr$^\alpha$.	Bu^{iso}.	*neo*Pentyl.
H_α . . . Br	0·10	0·13	0·16	6	4	2	—	4	4	4
C_β . . . Br	0·18	0·22	0·27	—	2	4	6	2	2	2
H_β . . . Br	0·52	0·58	0·64	—	2	4	6	2	—	—
	0·66	0·72	0·78	—	—	—	—	—	1	—
C_γ . . . Br	0·39	0·48	0·55	—	—	—	—	—	2	—
	0·97	1·05	1·13	—	—	—	—	—	—	2
H_γ . . . Br	0·25	0·34	0·44	—	—	—	—	—	4	—
	0·90	0·98	1·06	—	—	—	—	—	—	4

(b) *Dynamical Factors : Non-bonding Forces.*—We now continue the discussion of the bromine exchange reaction by calculating the energy values of the various compressions listed in Table V. We take account only of the compressions of transition states.

The energy ${}^pW$ of interaction of either of the bromine atoms of a transition state with any carbon or hydrogen atom, excepting C_α, is the sum of three contributions, of which the first two, ${}^pW_E$ and ${}^pW_D$, are negative, and the third, ${}^pW_I$, positive; the superscript p refers throughout to a particular pair of atoms :

$${}^pW = {}^pW_E + {}^pW_D + {}^pW_I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Here ${}^pW_E$ is the electrostatic energy, which we identify with its principal term, the induced dipole energy :

$${}^pW_E = -\tfrac{1}{2}\alpha_1(e/2)^2/{}^pr^4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

This formula assumes that each bromine semi-ion of the transition state bears a charge $e/2$, where e is the electronic charge, $4{\cdot}80 \times 10^{-10}$ e.s.u. The charge creates a dipole of moment $\alpha_1(e/2)/{}^pr^2$ in the carbon or hydrogen atom; and the work of creating this dipole is ${}^pW_E$. Since ${}^pr$ is taken as the internuclear distance, the assumption is implicit that both the charge and the dipole can be considered to be located at the centres of the respective atoms. The polarisability α_1 of the carbon or hydrogen atom is given by $3[R_1]/4\pi N$, where $[R_1]$ is the atomic refraction constant and N is Avogadro's number, $6{\cdot}024 \times 10^{23}$. We take $[R_1]$ for carbon as 2·41 c.c., and for hydrogen as 1·09 c.c. (Eisenlohr, " Spektrochemie," Enke, Stuttgart, 1912, p. 48). The accuracy of the calculation is not such as would justify a correction for dispersion. A reason is given later for the neglect of electrostatic energy terms dependent on more than two atoms.

The quantity ${}^pW_D$ is the so-called dispersion energy. We calculate it with the aid of London's formula,

$${}^pW_D = -3\alpha_1\alpha_2 I_1 I_2/2(I_1 + I_2)\,{}^pr^6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where the subscripts 1 and 2 designate the atoms of the pair p, α_1, and α_2 are their polarisabilities, and I_1 and I_2 their ionisation potentials. Several of these quantities can be estimated only roughly. To obtain the polarisability α_2 of semi-ionic bromine, we estimate its refraction constant $[R_2]$ as 10·5 c.c., the mean between the constant, 8·8 c.c., of covalent bromine (Eisenlohr, *op. cit.*), and the constant, 12·2 c.c., of the dissociated bromide ion (Smyth, " Dielectric Constant and Molecular Structure," Chemical Catalog Co., 1931, p. 148). For the ionisation potentials of carbon and hydrogen atoms in alkyl groups we take 12·0 and 14·5 electron-volts respectively, these being Mulliken's estimates of the respective ionisation energies of a CC- and CH-electron in ethane (*J. Chem. Physics*, 1935, **3**, 517). For the bromine ionisation potential we take the lower of Price's two values 10·5 and 10·8 electron-volts for methyl bromide, as deduced from the limits of Rydberg series in the vacuum ultra-violet (*ibid.*, 1936, **4**, 539). It is difficult to say how appropriate to our case this value may be; but a trial of various rough methods of allowing for the semi-ionic charge, and its solvation, suggests an uncertainty of the order of 10%, the effect of which is no greater than that of the other uncertainties of equation (5), and would make no important difference to our final results.

The term ^pW_I of equation (3) is much the most important, and represents the atomic interpenetration energy. Quantal calculations by Slater (*Physical Rev.*, 1928, **32**, 349) and others have indicated that the variation of ^pW_I with distance ^pr should be represented by an exponential law, $^pW_I \propto e^{^pr/a}$, rather than by any of the previously employed power laws. Born and Mayer have shown (*Z. Physik*, 1932, **75**, 1) that the exponential law gives a more satisfactory account, than do the power functions, of the properties of the alkali halide crystals. These authors empirically evaluated the length constant *a*, and found it to be substantially the same, 0·345 A., for all alkali halides. On this evidence we use the equation

$$^pW_I = {}^pb e^{^pr/0\cdot345} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

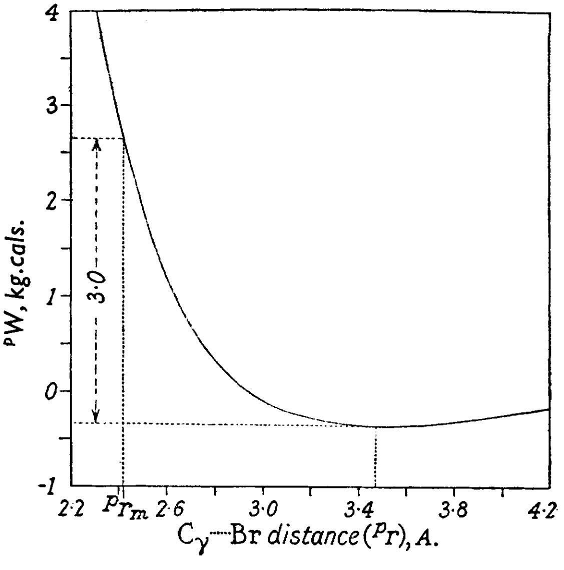
in which ^pr is, of course, to be expressed in Ångström units. The important constant ^pb is evaluated from the consideration that the attractive and repulsive forces between the atoms balance at the touching distance :

$$\mathrm{d}^pW/\mathrm{d}^pr = 0 \text{ when } {}^pr = {}^pr_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

It can now be explained why we neglect those terms of ^pW_E which depend in part on atoms outside the pair *p*, although the main such term, that dependent jointly on the two bromine atoms and the alkyl carbon atom, could easily have been taken into account. The reason is that the effect of this term on the touching distance is not allowed for, and therefore, since ^pb is estimated from the attractive forces which determine a particular touching distance, we should not include it amongst the forces used to determine ^pb. No such point arises with respect to ^pW_D, which is strictly additive in pairs of atoms.

FIG. 3.

neo*Pentyl* Cγ . . . Br *compression energy in the transition state of bimolecular bromine exchange.*



As an illustration of the employment of equations (3)—(7) for the calculation of ^pW as a function of ^pr, Fig. 3 is given, which shows the results for the C_γ . . . Br distance in the transition state model for the bromine exchange reaction of *neo*pentyl bromide. It is observed that compression from the touching distance $^pr_t = 3\cdot47$ A. to the model distance $^pr_m = 2\cdot42$ A. involves an energy increase of 3·0 kg.-cals. per g.-mol. And, as Table V shows, there are two such compressed distances in the transition state. Similar calculations have been carried out, and curves drawn, for all the transition state compressions listed in Table V.

It is necessary to consider the choice of the zero of non-bonding energy. As can be seen from Table V, all non-bonded distances in the initial state, corresponding to those which become compressed in the transition state, are quite close to the touching distances. This means that although the non-bonding forces are negligible in the initial state, the non-bonding energies of the various pairs of atoms are negative with respect to the conventional zero of energy corresponding to infinite atomic separation. These negative energies, " cohesion energies " as we may call them, are never more than 0·2 to 0·4 kg.-cal. for any particular pair of atoms, but the effect summed over all pairs is quite appreciable. Strictly, we should take account of the difference between this total cohesion energy of the initial and transition state, but, because, at this stage of our study of steric hindrance, we are adopting the simplification of omitting all calculations of non-bonding energy in the initial state, it is necessary to choose as appropriately as is possible in the circumstances our energy zero for calculations relative to the transition state. Our method is to regard compressions in the transition state as starting from the touching distances, rather than from infinite atomic separations. This amounts to supposing that the cohesion energies of the initial and transition states balance. The cancelling of the cohesion energies is, of course, an approximation, but it must be a considerably better approximation than taking account of cohesion energy in one state only. Therefore we transfer the energy zero as suggested, correcting the ^pW of equation (3) to $^pW'$, where

$$^pW' = {}^pW - {}^pW({}^pr_t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and $^pW(^pr_t)$ denotes the value of ^pW when $^pr = {}^pr_t$.

The energy $^pW'$ is a function of ^pr and can therefore be written $^pW'(^pr)$. Its value when ^pr is equal to the model distance ${}^{p}r_m$ is denoted by ${}^{p}W'({}^{p}r_m)$. (This is the quantity which amounts to 3·0 kg.-cals. in the illustration of Fig. 3.) For each reacting system, we sum this quantity over all the transition state atom-pairs whose model distances are given in Table V.

$$W'_m = \sum_p {}^{p}W'({}^{p}r_m) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The total, W'_m, represents a first upper limit to the increment of activation energy caused by steric hindrance : subject to the approximations made in the calculation, it is what the increment of activation energy would amount to if the bonding forces alone determined the geometry of the transition state, *i.e.*, if steric hindrance itself had no effect on the configuration of the state. The results of the summation are given in Table VII. The special position of the *neo*pentyl group is clearly in evidence. It will be noted that the methyl group can exert no steric effect on the bromine exchange reactions, and is therefore a possible reference group, by comparison with which the steric effects of other groups might be assessed from experimentally determined activation energies. It is also seen that the calculated upper limit to the increment of activation energy caused by the steric effect of the *neo*pentyl group in the bromine exchange reaction is about twice as great as the amount by which Table I indicates the activation energy of the substitution of *neo*pentyl bromide by ethoxide or iodide ions to exceed that of the corresponding substitution of methyl bromide.

TABLE VII.

First Upper Limits to Contributions of Steric Hindrance to the Activation Energies of Bromine Exchange, as Calculated by assuming Rigid Bonding Forces.

	Me.	Et.	Pr^{β}.	Bu^{γ}.	Pr^{α}.	Bu^{iso}.	*neo*Pentyl.
$H_{\alpha} \ldots Br$	0·0	0·0	0·0	—	0·0	0·0	0·0
$C_{\beta} \ldots Br$	—	0·2	0·4	0·5	0·2	0·2	0·2
$H_{\beta} \ldots Br$	—	0·7	1·5	2·2	0·7	0·6	—
$C_{\gamma} \ldots Br$	—	—	—	—	0·0	1·3	6·0
$H_{\gamma} \ldots Br$	—	—	—	—	0·0	0·2	6·4
W'_m (kg.-cals.)	0·0	0·9	1·9	2·7	0·9	2·3	12·6

(c) *Dynamical Factors : Bonding Forces.*—So far, our procedure has been to use the bonding forces in order to determine the geometry of the transition state, and then, assuming this geometry to persist in the presence of non-bonding forces, to calculate the non-bonding energy. This leads to an upper limit to the steric energy, as already described. The complete problem, however, needs a simultaneous evaluation of the geometry of the transition state and of its energy, the geometry being such as to minimise the total, bonding *plus* non-bonding, potential energy. Although we have not yet been able fully to solve this problem in a general form, the following considerations do lead to a solution when the model of the transition state possesses an axis of three-fold symmetry, and to closer upper limits to the steric energy in other cases.

As a simplification we concentrate attention on the weakest bonds in the transition state, the partly broken or partly formed covalencies by which the bromine atoms are bound, and assume that substantially the whole of the relief from non-bonding strain which the non-rigidity of the bonding forces can provide is furnished by the stretching and bending of these partial bonds. In other words, we assume that, in the presence of a steric effect, the only atoms which are seriously displaced from the positions we have hitherto assumed them to occupy are the bromine atoms. The number of possibly adjustable atomic co-ordinates is thus at once reduced to six. If we assume a plane of symmetry normal to the Br . . . Br line, the number of independent, possibly adjustable, parameters is then only three. Such a plane is present in all the transition states hitherto considered, except the one involving the *iso*butyl group. One parameter will measure the symmetrical stretching of the Br . . . C_{α} . . . Br system, and two others are available to define its bending. But the bending will take place in a plane, determined by the direction of the resultant pressure from the alkyl group, and if we choose one bending co-ordinate to be in this plane there will be no displacement in the other. Thus a large class of cases can be covered, in this approximation, if the total, bonding *plus* non-bonding, potential energy can be evaluated as a function of the two independent variables, x and y. We take the model positions of the two bromine atoms, 2·31 A. on each side of the α-carbon atom, as the origins of normal co-ordinates, and measure the outward displacements x of the bromine atoms along the axis containing the origins, and the lateral displacements y, parallel to each other and perpendicular to x, in the plane of the resultant displacements (Fig. 4). In those special cases in which the Br . . . Br line is a three-fold axis of symmetry there can be no displacement in the y direction, and hence the potential energy can be treated as a function of one variable only, namely x. Transition states involving the methyl and *tert.*-butyl groups belong to this specially simple class.

It is a simple matter to re-express the non-bonding energy as a function of x and y. Each ${}^{p}W'$ in equation (8) is a function of the appropriate ${}^{p}r$, the internuclear distance between the atoms concerned, one of which is always one of the bromine atoms. Once the plane of y is determined, by considerations either of symmetry or of dynamics, it is a purely geometrical problem to express ${}^{p}r$ in terms of x and y. By substitution, each term of the sum

$$W' = \sum_p {}^{p}W'(x, y) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

becomes a function of the same two variables, and W' can be plotted as an energy surface. For a reason which will appear, we have had, for the purposes of this discussion, only to plot curves, of which Fig. 5 is a sample, showing W' as a function of x when $y = 0$—a section, that is to say, of the aforesaid surface. Such a curve has been plotted for each alkyl halide. The minimum value of W' is taken as the zero of energy.

The problem of expressing the bonding energy W'' of the Br . . . C_α . . . Br system as a function of its extension co-ordinate x and bending co-ordinate y has not yet been fully solved. By using partly empirical methods, an approach can be made towards the problem of estimating the dependence of W'' on x when $y = 0$. We carry the matter this far in the present paper, obtaining a definite estimate of the contribution of steric hindrance to the activation energy in those cases in which the symmetry of the system precludes bending of the Br . . . C_α . . . Br bond, and a second and closer upper limit to the steric contribution to the activation energy in other cases. The problem of calculating the bending potential energy function does not seem to be susceptible to a similarly simplified treatment, and we have as yet made no headway with the quantal calculations which appear to be the only alternative.

Let r_{00} be the equilibrium length of the C_α–Br bond in the initial state of the alkyl bromide, and r_0 the C_α–Br distance in the model of the transition state, assuming no deformation by non-bonding forces ($r_{00} = 1{\cdot}91$ A. and $r_0 = 2{\cdot}31$ A.). The general C_α–Br distance we shall take as $r = r_0 + x$, the system Br . . . C_α . . . Br being supposed linear. Following Ogg and Polanyi (*Trans. Faraday Soc.*, 1935, **31**, 604), we assume the activation energy of substitution to be the sum of five independent parts, r being so chosen that the sum shall be a minimum. The five contributions are : (*a*) the energy required to press the Br^- ion to a distance r from C_α ; (*b*) the energy required to stretch the C–Br bond to a length r ; (*c*) the work of replacing a solvent molecule by an alkyl halide molecule in the solvent shell of the bromide ion ; (*d*) the work needed to bring into a plane three of the bonds of C_α ; and (*e*) the electronic resonance energy. Ogg and Polanyi regard the resonance energy as small and neglect it. We doubt its smallness and have no need to neglect it ; but we do neglect its variation with x over the small range of distances with which we are concerned.[*] We also treat the solvation and bond-bending contributions, (*c*) and (*d*), as independent of x. This leaves only the atom-pressing and bond-stretching contributions, (*a*) and (*b*), to be calculated as functions of x.

FIG. 4.

Transition state deformation co-ordinates in bromine exchange.

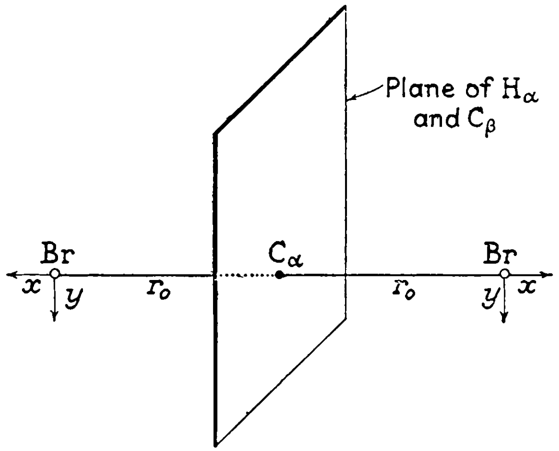
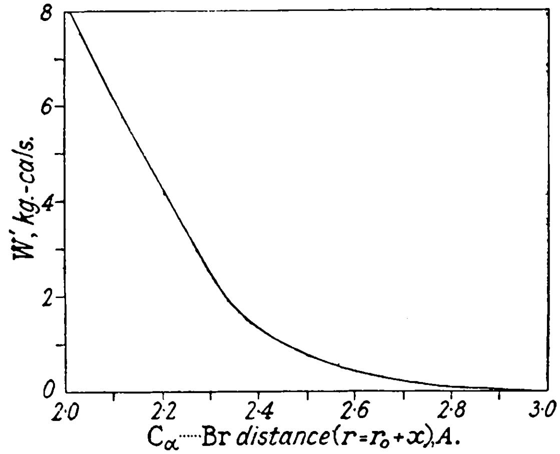


FIG. 5.

Total non-bonding energy as a function of C_α–Br *separation in the tert.*-Bu *transition state of bimolecular bromine exchange.*



The calculation of the atom-pressing contribution (*a*) is treated as a two-atom problem, involving only the bromide ion and the α-carbon atom. All interactions involving the second bromine atom are neglected in this part of the calculation, since otherwise the energy could not be treated as independent of that of bond-extension, which is to be separately evaluated. Electrostatic interactions involving the two bromine atoms seem to be best classified along with the resonance energy, since the latter represents the electronic zero-point energy released when the anionic charge of the first bromine atom spills over into the second, and, if we were calculating it, we should have to assume an appropriate initial state of charge for the nominally neutral bromine atom. Any positive charge on the carbon atom is disregarded because the assumed van der Waals radius is that of the neutral atom, and the main point of calculating the attractive forces is to estimate resistance to compression from the fact that the attractive and compression forces balance at the van der Waals distance. We consider then, the action of a bromide ion on a neutral but polarisable carbon atom of van der Waals radius 1·6 A. (Table II), the valencies of which are supposed to have been displaced sufficiently not to affect approach of the bromide ion.

There will be three terms in this energy contribution. The first is the induced dipole energy which is to be calculated by means of an equation similar to (4), except that the factor $(e/2)^2$ must now be replaced by e^2.

---

[*] This may be justified because the resonance energy passes through its maximum in this region.

The second is the dispersion energy which is given by an equation similar to (5), in which α_2 and I_2 now refer to the polarisability and ionisation potential of a bromide ion. Its refraction constant $[R_2]$ we take as 12·2 c.c. (Smyth, *op. cit.*). The energy required to remove to infinity an electron from a solvated bromide ion is not known. The corresponding quantity is known for a gaseous bromide ion, and it has been calculated by Mott and Gurney for a bromide ion in a potassium bromide crystal ("Electronic Processes in Ionic Crystals," Oxford, 1940, p. 80). We take their figure, 9·0 electron-volts, as the better approximation, but realise that it may not be very accurate; fortunately it is not vitally important to have an accurate value. The third, and most important, part of the atom-pressing energy is the interpenetration energy, which is given by an equation similar to (6), in which the compression constant b has to be evaluated from the condition that the total of the three terms must pass through a minimum when $r = 1{\cdot}6 + 1{\cdot}95 = 3{\cdot}55$ A. Its value is $18{\cdot}5 \times 10^3$ kg.-cals., the complete equation for the energy of compression being

$$W_a'' = -\,158/r^4 - 810/r^6 + 18500\ \text{antilog}_{10}(-\,1{\cdot}259r) \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Here W_a'' is in kg.-cals. if r is in Ångström units; and the zero of energy corresponds to infinite atomic separation.

The estimation of bond-stretching contribution (*b*) is likewise treated as a two-atom problem, to which, therefore, we can apply Morse's formula :

$$\left.\begin{aligned} W_b'' &= D\{e^{-2\alpha(r - r_{00})} - 2e^{-\alpha(r - r_{00})}\} \\ \alpha &= 0{\cdot}1227\omega\sqrt{\mu/D} \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Here W_b'' is given, relative to an energy zero at infinite atomic separation, in the same units as D, the dissociation of the C–Br bond reckoned from its potential energy minimum at $r = r_{00}$. The lengths r and r_{00} are in Ångström units, provided that the constant α is in reciprocal Ångströms; as in fact it is, if, in computing it by the formula given, both the vibration frequency ω and the dissociation energy D are expressed in terms of wave-numbers, and the reduced mass μ is expressed in ordinary atomic weight units.

Methyl bromide is a sufficiently good approximation to a diatomic molecule to be treated as a source of the parameters which are needed in order to apply the Morse equation to the C–Br bond of alkyl bromides. Owing to the lightness of the hydrogen atoms, and the slight coupling of their vibrations with those of the C–Br bond, the methyl group acts almost like a single atom of mass 15 with respect to the latter vibrations, of which the frequency ω is 594 cm.$^{-1}$ (Kohlrausch, " Smekal–Raman Effekt," Springer, 1931, p. 307), and the mass factor μ is 12·6 atomic weight units. We take the dissociation energy D as 70·6 kg.-cals. $= 70{\cdot}6 \times 351{\cdot}6$ cm.$^{-1}$, this being Baughan and Polanyi's value (*Nature*, 1940, **146**, 685), corrected for the zero-point energy of the C–Br vibrations. These data give $\alpha = 1{\cdot}64$ A.$^{-1}$.

By adding W_a'' and W_b'' we obtain W''_{a+b}, a function of r which passes through a minimum value, $-\,43{\cdot}2$ kg.-cals., when $r = 2{\cdot}25$ A. This minimum lies above the energy minimum of the Morse curve of methyl bromide by 27·4 kg.-cals. The defect of this energy below the activation energy of the bromine exchange reaction of methyl bromide, probably 18—19 kg.-cals., may be taken to represent the total (negative) value of the solvation, bond-bending and resonance contributions, (*c*), (*d*), and (*e*), to the activation energy; for there is no non-bonding contribution to the activation energy of this reaction (p. 182). The fact that the mimimum occurs at $r = 2{\cdot}25$ A., and not, as exact consistency would demand, at $r = r_0 = 2{\cdot}31$ A., may be a result of the approximations we have made, particularly, perhaps, the assumption that the three contributions (*c*), (*d*), and (*e*) to the activation energy can be treated as independent of r; alternatively, our original estimate of 2·31 A. may be slightly too high, though a closer agreement could hardly have been expected.* In order to bring our calculation of the dependence upon $r = r_0 + x$ of the bonding energy of the transition state into a form in which, by combination with our previous estimates of the non-bonding energy, we can find out how much of the latter is released, and how much becomes converted into bonding energy, through the stretching of the Br . . . C_α . . . Br system, we draw new axes to the curve of W''_{a+b} so that its minimum rests upon an energy origin at $x = 0$:

$$W''(x) = W_a''(r - 0{\cdot}06) + W_b''(r - 0{\cdot}06) + 43{\cdot}2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where $x = r - 2{\cdot}31$ A. In short, we treat the small discrepancy of 0·06 A. as affecting the position of the curve, but not its shape.

The lowest curve of Fig. 6 is the curve of this equation. It represents a section, cut at 45° through the origin, of the conventional energy surface, in rectangular co-ordinates, for the linear three-particle reaction, and viewed as a projection on one of the co-ordinate planes, *i.e.*, reduced in one direction by the factor $1/\sqrt{2}$. It is assumed to apply to all the alkyl bromides. In order to take account of the non-bonding energy we utilise the curves of equation (10) with $y = 0$, curves of the type of which Fig. 5 is an example : there is one such curve for each alkyl halide. By adding the ordinates of each of these W' curves to those of the common W'' curve, we obtain $W = W' + W''$ curves, one for each alkyl halide, which all show minima variously shifted towards positive values of x, and variously raised with respect to energy. Sample W curves are shown in Fig. 6, including one for the bromine exchange reaction of *tert.*-butyl bromide and one for that of *neo*pentyl bromide.

The energies at the minima represent the various steric effects, as far as we have calculated them, on the activ-

---

* It is doubtful whether any of the distances given in this paper (except covalent radii) are reliable to within 0·05 A.

ation energy of the substitution. They should be equal to the steric contribution to the activation energy in the cases of methyl and *tert.*-butyl bromides, but only an upper limit in other cases in which bending of the Br . . . C_α . . . Br system, which we have had to neglect, can release part, as well as storing part, of the calculated potential energy. The values obtained are in Table VIII. Fig. 6 again emphasises the special position of the *neo*pentyl group as a source of steric hindrance, since the curves for all the other alkyl groups treated fall between the curves shown for the methyl and the *tert.*-butyl group.

TABLE VIII.

Calculated Values of, or Limits to, the Steric Activation Energy of Bromine Exchange (Linear Transition State).

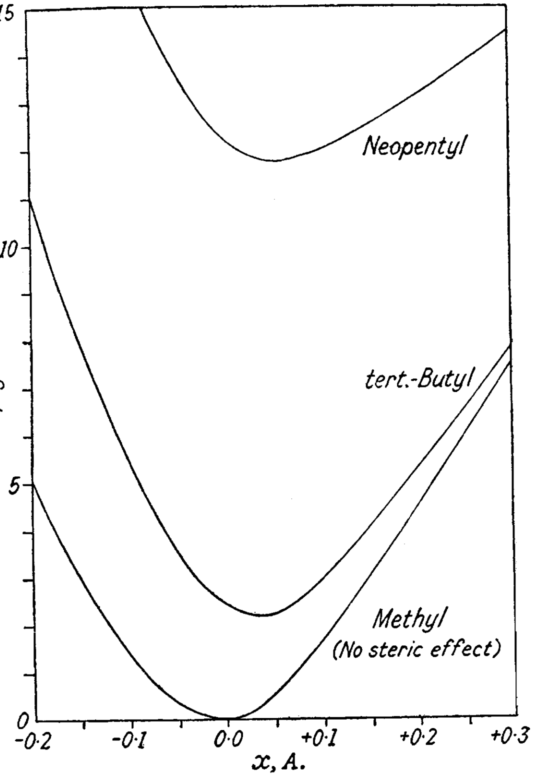
	Me.	Et.	Pr^β.	Bu^γ.
W_m (rigid model—Table VII)	0·0 kg.-cals.	0·9 kg.-cals.	1·9 kg.-cals.	2·7 kg.-cals.
$W_{min.}$ (with $BrC_\alpha Br$-stretching)	0·0 kg.-cals.	0·7 kg.-cals.*	1·4 kg.-cals.*	2·2 kg.-cals.
$2x_{min.}$ (amount of stretching)	0·00 A.	0·02 A.	0·04 A.	0·07 A.
	Pr^α.	Bu^{iso}.	*neo*Pentyl.	
W_m (rigid model—Table VII)	0·9 kg.-cals.	2·3 kg.-cals.	12·6 kg.-cals.	
$W_{min.}$ (with $BrC_\alpha Br$-stretching)	0·7 kg.-cals.*	—	11·7 kg.-cals.*	
$2x_{min.}$ (amount of stretching)	0·02 A.	—	0·11 A.	

* Upper limits.

(d) *Comparison with Experiment.*—For the representation of experimental data we use the Arrhenius equation, $k_2 = Be^{-E/RT}$ and not any of the modified forms which have been proposed, since it is generally recognised that no simple and universal temperature function is adequate to express the temperature dependence of the Arrhenius parameters. It will therefore be understood that the Arrhenius activation energy should never be exactly equal to the theoretically calculated activation energy, though we have no easy way of estimating the difference, which is presumed to be small.

FIG. 6.

Total potential energy as function of C_α–Br *separation in linear transition states of* Br *exchange with and without steric hindrance.*



The simplest comparisons are with the β-methylated alkyl groups, since β-branches in the alkyl group are unlikely to contribute any notable polar effect to the energy of activation (because of the loss which polar effects suffer on transmission through saturated carbon chains). As we have concluded before, and shall confirm in the course of the present discussion, α-branches in alkyl groups give rise to a very appreciable polar effect in bimolecular reactions.

Using radio-bromine as an indicator of exchange, le Roux and Sugden (J., **1939**, 1279) and Elliot and Sugden (J., **1939**, 1836) have measured the rates of the bromine exchange reaction of three primary alkyl bromides in "90%" acetone at several temperatures.* From the graphs of their values for $\log_{10} k_2$ against $1/T$, we obtain the following Arrhenius activation energies (in kg.-cals.) : † *n*-Propyl, ∼19; *n*-Butyl, 19·3; *iso*Butyl, 20·6.

So far as the steric effect is concerned the exchange reactions of ethyl, *n*-propyl, and *n*-butyl bromides should have the same activation energy, whilst the reaction of *iso*butyl bromide should have an activation energy about 1·4 kg.-cals. greater (certainly less than 2·3 kg.-cals. greater). The observed difference of 1·3 kg.-cals. between the values for *n*- and *iso*-butyl bromides agrees satisfactorily with these theoretical estimates.

A comparison between ethyl and *iso*butyl bromides with respect to substitution by ethoxide ions in ethyl alcohol is available in Table I (p. 175) : the Arrhenius activation energy for the ethoxylation of *iso*butyl bromide is 1·8 kg.-cals. greater than for the corresponding reaction of ethyl bromide. It is true that we have not carried out a calculation for the ethoxylation process; but it has been pointed out (p. 180) that theory indicates the steric effect on activation energy to be not very

---

* They calculated activation energies from a modified Arrhenius equation (containing a $\sqrt{T}$ factor), and their values are therefore slightly different from those now quoted.

† The slope of the graph for *n*-propyl bromide is not very exactly defined by the experimental points, and hence the Arrhenius energy is given only in an approximate form.

sensitive to the size of the ionic reagent; and, on the experimental side, Table I itself shows, particularly in relation to the reactions of *neo*pentyl bromide, that quite similar steric effects on activation energy arise in ethoxylation and in halogen exchange. Thus the observed difference of activation energy for the ethoxylation of ethyl and *iso*butyl bromide is roughly of the expected magnitude.

The outstanding steric effect revealed in Table I is that shown by *neo*pentyl bromide in both halogen exchange and ethoxylation, and represented in either case by about 6 kg.-cals. of activation energy. Our calculated upper limit of 12 kg.-cals. to the steric increment of activation energy is expected to be considerably above the true increment, because so great a strain in the transition state will undoubtedly be largely relieved by the bending of the $BrC_{\alpha}Br$ system, the effect of which we have not calculated. As Table VII shows, the stretching of the $BrC_{\alpha}Br$ system releases about 1 kg.-cal. from the potential energy of the transition state. Since, with full covalencies, the forces which resist bending are always several times weaker than those which oppose stretching, it is a reasonable expectation that the bending of the $BrC_{\alpha}Br$ system will release several more kg.-cals. Thus our calculated upper limit of 11·7 kg.-cals. is not irreconcilable with the observed value of 6 kg.-cals. in the substitutions studied.

We now turn to the α-methylated alkyl groups: here, if anywhere, a polar effect, as well as a steric effect, is to be expected. Using radio-iodine as an isotopic indicator, McKay has measured the rate of exchange between iodide ions and various primary and secondary alkyl iodides in alcohol at various temperatures (*J. Amer. Chem. Soc.*, 1943, **65**, 702). He reports definite differences in the Arrhenius activation energies for the primary and secondary iodides: for ethyl iodide and its primary homologues the values were grouped around 19·0 kg.-cals., whilst *iso*propyl and *sec.*-butyl iodides gave about 20·5 kg.-cals. Professor Sugden has kindly shown us the manuscript of a forthcoming paper by le Roux, Lu, Sugden, and Thomson.* Using radio-active bromine as an indicator for exchange, these authors have measured the rates of the bromine exchange reaction of a primary, a secondary, and a tertiary alkyl bromide, at a number of temperatures in ethylene diacetate as solvent. By plotting their values of $\log_{10} k_2$ against $1/T$, we obtain the following Arrhenius activation energies (kg.-cals.): † *n*-Butyl, 18·2; *iso*Propyl, 20·0; *tert.*-Butyl, ~23.

The activation energy of the reaction of methyl bromide is unknown, but we may assume that the observed value for *n*-butyl bromide would approximately apply to ethyl bromide. Taking this as the starting point, the increase of activation energy is found to be 1·8 kg.-cals. in the reaction of *iso*propyl bromide, and about 5 kg.-cals. in that of *tert.*-butyl bromide. As Table VII shows, theory indicates that the steric increase of activation energy should be about 0·7 kg.-cal. (certainly not more than 1·4 kg.-cals.) for *iso*propyl bromide, and about 2 kg.-cals. (not more than 2·2 kg.-cals.) for *tert.*-butyl bromide. The observed increases are considerably larger, and we attribute the amounts by which they exceed the calculated values to the expected polar effects of the additional α-methyl substituents in the secondary and tertiary alkyl groups (Hughes and Ingold, J., 1935, 244; cf. this paper, p. 174).

The relatively small steric effect calculated for bimolecular halogen exchange in *tert.*-butyl compounds, contrasted with the large steric effect calculated for, and found in, *neo*pentyl compounds, illustrates the difference between the classical picture of steric hindrance and the new treatment of this phenomenon. We think that no one acquainted with Victor Meyer's experiments, showing how steric hindrance in the esterification of *o*-disubstituted benzoic acids largely disappeared when an interposed methylene group removed the carboxyl group one atom further away from the branched structure, as in correspondingly substituted phenylacetic acids, would have predicted, before the immediate foundations of the present work were laid, that steric effects which were relatively weak in the bimolecular substitutions of *tert.*-butyl halides would be strongly *enhanced* when an interposed methylene group removes the displaced halogen one atom further from the branched structure, as in *neo*pentyl halides.

It remains to be pointed out that steric hindrance must affect not only the energy, but also the entropy, of activation, *i.e.*, the probability factor of reaction rate. It is easily seen how a development of the considerations which have been outlined could lead to an evaluation of the steric effect on the entropy of activation. It is essentially a question of calculating the partition function of the transition state, or at least those factors of the partition function which do not approximately cancel similar factors in the partition function of the initial state in the complete statistical mechanical expression for reaction rate. As data we require the dimensions and vibration frequencies of the transition state. Part of such a calculation could be carried through now, using the positions and curvatures (leading to frequencies) of W–x curves, such as are illustrated in Fig. 6; but even for trigonally symmetrical transition states, such as the *tert.*-butyl group would yield, the calculation could not now be completed, because we do not yet know the $BrC_{\alpha}Br$ bending potential energy function, and therefore cannot estimate the bending frequency, which, because of its lowness, is likely to be an important determinant of the entropy. We are trying suitably to extend and improve the calculations, concurrently with the development of more accurate and crucial experimental tests.

(B) *Further Review of Bimolecular and Unimolecular Nucleophilic Substitutions in Relation to Steric Effects.*

(a) *Steric Hindrance in Bimolecular Nucleophilic Substitution.*—1. *Reactions of halogen compounds.* Many years ago one of us made attempts to open a route to the preparation of *spiro*-compounds by condensation of

---

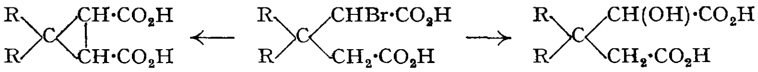
* This paper has since appeared (J., 1945, 586).

† The slope of the graph for *tert.*-butyl bromide is not very exactly defined by the experimental points, and therefore the Arrhenius activation energy is given only in an approximate form.

pentaerythrityl tetrabromide, $C(CH_2Br)_4$, with such compounds as potassium cyanide, ethyl sodiomalonate, ethyl sodiocyanoacetate and ethyl disodioethanetetracarboxylate. These attempts, which have remained unrecorded, were frustrated by the marked lack of reactivity of the bromide. It was only afterwards learnt by private discussion that the late W. H. Perkin, junr., at a still earlier period, had made some similar experiments, with a like result. According to the organic chemical ideas of those days, the concept of steric hindrance could not be very plausibly associated with the halogen reactions of a compound the bromine atoms of which all project outwards from the corners of a regular tetrahedron. We now realise, however, that pentaerythrityl tetrabromide is a substituted *neo*pentyl bromide, and that accordingly its bimolecular substitutions are of necessity sterically hindered. The example illustrates very well the difference in point of view which results from the association of the older notions of steric hindrance with our modern ideas on reaction mechanism.

A similar example exists, which has before received some public notice: trimethylene dibromide, $BrCH_2{\cdot}CH_2{\cdot}CH_2Br$, has a normal reactivity towards nucleophilic reagents, but ββ-dimethyltrimethylene dibromide, $BrCH_2{\cdot}CMe_2{\cdot}CH_2Br$, is said to be extremely inert (Hickinbottom, "Reactions of Organic Compounds," Longmans, 1936, p. 365). The explanation is clearly the same.

With this case as a connecting link, we may reconsider some of the experimental evidence which has been interpreted by means of the valency deflexion hypothesis of Thorpe and Ingold; for it seems certain now that at least some of the observations which this hypothesis was employed to correlate are susceptible of explanation on more general lines. A typical example is provided by the alkaline hydrolysis of various α-bromoglutaric acids, including the acid not otherwise substituted, β-alkylated acids, ββ-dialkylated acids, and acids with the β-carbon atom forming part of an alicyclic ring. These acids (I) when hydrolysed with alkalis yield two main products, *viz.*, the α-hydroxyglutaric acid (II) (which is always isolated as its γ-lactonic acid), and the *cyclo*propane-1 : 2-dicarboxylic acid (III). The special point, which the valency deflexion hypothesis was brought in to explain, was that, as the β-hydrogen atoms of the parent compound were successively replaced by alkyl groups, the proportions in which these two products were formed under fixed conditions progressively shifted in the direction favouring the ring-compound (Ingold, J., 1921, **119**, 305; 1922, **121**, 2676; cf. Beesley, Ingold, and Thorpe, J., 1915, **107**, 1080; and Baker and Ingold, J., 1923, **123**, 122) :


(III.) (I.) (II.)

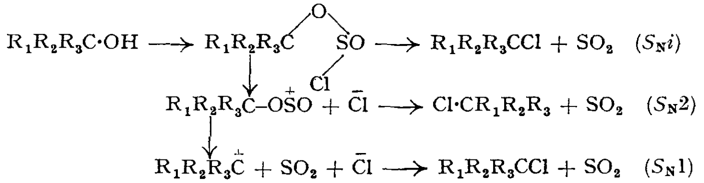
When dilute aqueous sodium carbonate was the reagent, the hydroxy-acid (II) was the main product in all cases; but when concentrated potassium hydroxide was employed, more and more of the hydroxy-acid, the quantity depending on the number, and to some extent the size, of the β-alkyl groups, became replaced in the product by the ring compound (III).

Our present interpretation of these facts would be on the following lines. In all cases, and under all conditions, the compound hydrolysed is not the bromo-acid, but is its anion, $\bar{C}O_2{\cdot}CH_2{\cdot}CR_2{\cdot}CHBr{\cdot}\bar{C}O_2$, or possibly, in some circumstances, the acid anion $CO_2H{\cdot}CH_2{\cdot}CR_2{\cdot}CHBr{\cdot}\bar{C}O_2$. The electron repulsion of a $\bar{C}O_2$ group adjacent to a bromine-bearing carbon atom produces, as we already know, a definite tendency to unimolecular substitution, S_N1, a reaction mechanism which, as will be emphasized later, is not subject to steric hindrance. In particular we can be sure, by reference to existing experimental data, that, with aqueous sodium carbonate as the reagent, the principal hydrolytic mechanism would be the unimolecular one (Cowdrey, Hughes, and Ingold, J., 1937, 1217; *idem* and Masterman and Scott, J. 1937, 1254). When this reagent is replaced by concentrated potassium hydroxide, the unimolecular mechanism must become replaced by the bimolecular mechanism of substitution, S_N2; or, in a case in which a bimolecular elimination, $E2$, is also possible, the unimolecular solvolysis, S_N1, will become replaced by a total bimolecular reaction, substitution plus elimination, $S_N2 + E2$, which will grow in importance with the increasing concentration of hydroxide ions. In the anion of the parent α-bromoglutaric acid, the substitution part of this total bimolecular reaction, S_N2, is not sterically hindered to any serious extent. However, the anion of α-bromo-β-methylglutaric acid is a substituted *iso*butyl bromide; and the anion of α-bromo-ββ-dimethylglutaric acid is a substituted *neo*pentyl bromide. Thus the bimolecular substitution, which can take place freely in the unalkylated substance, is more or less markedly impeded in the β-methyl derivative, and practically stopped altogether in the ββ-dimethyl compound. In the meantime there is nothing to prevent the concomitant bimolecular 1 : 3-elimination process, $E2$, which will not be sterically hindered to anything like the same extent, because it depends on attack by the hydroxide ions on the potentially ionisable α′-hydrogen atom (rather than on the less accessible α-carbon atom), from making the best of the situation created by the difficulties which face its competitor. Of course, a kinetic investigation is necessary to prove this theory, but its internal consistency seems to be a strong point in its favour.

Since the essence of the valency deflexion hypothesis is that the angular parameters of a molecular structure, as it would have been determined by the bonding forces, become modified by the non-bonding repulsive forces, the old theory (like the classical theory of steric hindrance) may be regarded as absorbed in the new. However, the differences should not be minimised : the concentration of attention in the new theory on the transition state seems particularly important for the development of spatial explanations having such quantitative objectives as would have been considered inappropriate to organic chemists in an earlier epoch.

McDonald, Rothstein, and Robison recently reported (*J. Amer. Chem. Soc.*, 1944, **66**, 1984) that *iso*butyl chloride is much less reactive than *iso*amyl chloride towards potassium iodide in acetone. They expressed surprise at the observation, which, since the reaction in this solvent is always bimolecular, is fully consistent with our observations and calculations (pp. 175 and 180).

2. *Reactions of alcohols.* The sharper definition of our views on steric hindrance permits further consideration of the group of reactions by which alcohols may be converted into alkyl halides by means of thionyl chloride, phosphorus halides and hydrogen halides. These reactions were discussed by Cowdrey, Hughes, Ingold, Masterman, and Scott (*loc. cit.*), but almost entirely on the basis of data relating to optical activity, no kinetic evidence being then available. It was supposed that the first stage was always the formation of a complex, such as Alk·O·SOCl or Alk·OH·H·Br; which might then rearrange with retention of configuration in the alkyl group, (S_Ni), provided there was a sufficient electron supply in the alkyl group to permit the breaking of the C–O bond; alternatively, the complex could ionise one halogen atom. If, in the latter case, on account of the positive charge produced in the residual cation, the electron supply in the alkyl group became sufficient, the C–O bond might break at this stage, producing a carbonium ion, and a largely racemised substitution product (S_N1). If, on the other hand, the electron supply remained insufficient, a bimolecular attack by the halide ion on the α-carbon atom of the alkyl group would supervene, and the produced alkyl halide would have an inverted configuration (S_N2). These ideas may be illustrated thus:



The tendency to mechanism S_Ni was most marked with thionyl chloride, though, even with this reagent, it was suppressed in conditions conducive to the ionisation of the halogen atom. With hydrogen halides, to go to the other extreme, mechanism S_Ni was very difficultly available, since the ionisation of the halogen atom could scarcely be stopped. So far as the evidence of optical activity disclosed the situation, mechanisms S_Ni and S_N1 required the presence of an electron-releasing α-aryl group in the alkyl group: secondary alcohols used mechanism S_N2, except when such an unsaturated group was attached to the α-carbon atom. Presumably, therefore, aliphatic primary alcohols would be entirely restricted to the use of mechanism S_N2. There was no direct evidence from optical activity relating to tertiary alcohols, but, by analogy with the behaviour of halides and ammonium and sulphonium ions, we should expect that, when an α-arylated secondary alkyl compound can split up to give a carbonium ion, an analogous tertiary alphyl compound should also be able to do so.*

We now have a supplementary criterion of mechanism, since the bimolecular process, S_N2, must be subject to drastic steric hindrance in structures of the *neo*pentyl type, whilst the alternative mechanisms, S_Ni and S_N1, will not be sterically hindered to any comparable extent. However, as noted, mechanisms S_Ni and S_N1 should be unavailable, or at most difficultly available, to saturated, primary aliphatic alcohols, though either might become readily available in secondary alcohols with an α-aryl substituent, or in tertiary alcohols. It is consistent that *neo*pentyl halides cannot be prepared by the action of thionyl chloride, or the halides of phosphorus or of hydrogen, on *neo*pentyl alcohol (Whitmore and Rothrock, *J. Amer. Chem. Soc.*, 1932, **54**, 3431). Contrary to statements by Tissier (*Ann. Chim. Phys.*, 1893, **29**, 34) and Richard (*ibid.*, 1910, **29**, 344), no *neo*pentyl chloride could be obtained by Whitmore by the use of hydrogen chloride, whilst prolonged treatment of *neo*pentyl alcohol with hydrogen bromide gave a mixture of bromides formed largely through rearrangement of the carbon structure. The general result confirms the conclusion that a bimolecular mechanism, S_N2, is normally the only one available to saturated primary alcohols; whilst it will be clear from Part XXIX (this vol., p. 166; cf. also p. 192) that the observation of rearrangement on prolonged treatment with hydrogen bromide means that the mechanism next in order of availability, when the bimolecular mechanism is ruled out by steric hindrance, is, as we should have expected for hydrogen halide reactions, the unimolecular mechanism S_N1, dependent on the intermediate formation of a carbonium ion. Consistent again is the observation of Bartlett and Knox (*J. Amer. Chem. Soc.*, 1939, **61**, 3184) that αα-diethyl*neo*pentyl alcohol is converted into the chloride "instantly" by dry hydrogen chloride. In this alcohol the steric inhibition of the bimolecular mechanism must be even stronger than in *neo*pentyl alcohol. But diethyl*neo*pentyl alcohol is a tertiary alcohol, and therefore readily yields the carbonium ion, which is the essential intermediate in the unimolecular mechanism. Thus the new criterion provides good confirmation of two of the mechanisms postulated in 1937 for this group of reactions. A survey, from our present point of view, of the work of Bennett and Reynolds (J., 1935, 131) on the rate of reaction of hydrogen bromide with alcohols in phenol as solvent, concerning which no certain conclusion could be reached in 1937 (Cowdrey *et al.*, *loc. cit.*, p. 1269), strongly suggests that the bimolecular mechanism was under observation, as is indicated particularly by the low reaction rates observed for *iso*butyl alcohol.

3. *Reactions of carboxyl compounds.* Probably no subject has been more discussed in relation to steric

---

* The reactions of α-phenylethyl and *tert.*-butyl halides, etc., are very similar with regard to mechanism.

hindrance than carboxyl esterification and hydrolysis. We know now that the subject is more complicated than used to be thought, inasmuch as seven mechanisms have been recognised (Datta, Day, and Ingold, J., 1939, 838; Hughes, Ingold, and Masterman, *ibid.*, p. 840), four of which are bimolecular and should therefore be subject to steric hindrance (Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686). Two of them, the commonly observed acid- and base-catalysed reactions involving acyl–oxygen fission, R–CO¦OR′, are well known to be. One of the three unimolecular mechanisms, the acid reaction with acyl–oxygen fission, is known not to be (see below). The evidence is summarised by Day and Ingold (*loc. cit.*). The other mechanisms await the completion of kinetic investigations now in progress.

Concerning bimolecular reactions with acyl–oxygen fission, the reason why *neo*pentyl alcohol esterifies at a normal rate with carboxylic acids, in contrast to its behaviour towards halogen acids (Quayle and Norton, *J. Amer. Chem. Soc.*, 1940, **62**, 1170), is that the mode of fission *is* acyl–oxygen : as compared to the reaction with halogen acids, there is one more atom between the seat of attack of the nucleophilic reagent and the groups which, in the formation and hydrolysis of halides, are mainly responsible for the steric hindrance. The nearest analogies, amongst carboxyl reactions with acyl–oxygen fission, to the conditions of steric hindrance present in the bimolecular nucleophilic substitutions which might form or destroy *neo*pentyl halides, would arise in the hydrolysis of *tert.*-butyl esters, or, alternatively, esters of trimethylacetic acid, or, of course, in the formation of such esters by direct esterification. In fact, these reactions are known to be slow * (cf. data by Skrabal, Sudborough, and others, summarised by Hammett, " Physical Organic Chemistry," McGraw-Hill, 1940, pp. 211—213; also Evans, Gordon, and Watson, J., 1938, 1439). They are not extremely slow like the substitution of *neo*pentyl halides, but then the steric hindrance is not expected to be so marked, since the unsaturation of the carboxyl group allows a transition state with only four groups attached to the seat of substitution. In some experiments which are not yet complete enough for publication it has been found that the rates of bimolecular substitution of tritylmethyl chloride, $Ph_3C{\cdot}CH_2Cl$, are extremely low, an effect obviously attributable to steric hindrance. Consistently, triphenylacetic acid, $Ph_3C{\cdot}CO{\cdot}OH$, has recently been shown to be notably inert in esterification (Smith and Burn, *J. Amer. Chem. Soc.*, 1944, **66**, 1494). We are using this method of stopping nucleophilic attack on the carboxyl carbon atom (and therefore stopping acyl–oxygen fission) in a concurrent investigation of the kinetics and stereochemical course of carboxyl esterification and hydrolysis with alkyl–oxygen fission, R·CO·O¦R′.

(b) *Superposed Polar and Steric Effects in Bimolecular Nucleophilic Substitution.*—The problems of evaluating these effects in superposition could, of course, be more advantageously discussed if we had more strictly quantitative information about the steric effect; but it seems desirable, even at this stage, to review the position with respect to the series of α-methylated alkyl groups, the study of which played a large part in the original recognition of the bimolecular and unimolecular mechanisms of substitution. It was noted then (1933; 1935) that rates of bimolecular substitutions, particularly of the hydrolytic and alcoholytic substitutions of halides, descended in the series CH_3, $MeCH_2$, Me_2CH (not much was known about bimolecular substitutions with the group Me_3C). It was suggested that the polar effects of the alkyl groups might account for the observed trend, the conclusion being subject to possible quantitative modification on account of steric effects (Hughes and Ingold, J., 1935, 244).

We can assume as a first approximation that, compared to the polar effects of the successively introduced methyl groups in the α-methylated series, CH_3, $MeCH_2$, Me_2CH, Me_3C, the polar effects of the methyl groups of the β-methylated series, $CH_3{\cdot}CH_2$, $MeCH_2{\cdot}CH_2$, $Me_2CH{\cdot}CH_2$, $Me_3C{\cdot}CH_2$, are negligible. This is because of the large loss by relay through a saturated carbon atom which is a recognised characteristic of the inductive effect. Accordingly, our observations of the rate changes in the β-methylated series will represent a practically pure steric effect. And the trends have been accounted for by calculation, not very precisely, but consistently enough to suggest that limited conclusions could be drawn by application of the same methods of calculation to the α-methylated series, where a real problem of the superposition of effects arises. Such calculations make it seem unlikely that the factor of 18, by which at 55° the rate of alkaline alcoholysis decreases from methyl bromide to ethyl bromide (Table I, p. 175), is wholly to be explained as a steric effect. The calculated upper limit to the steric increment of activation energy for bromine exchange is 0·7 kg.-cal. (Table VIII, p 185), an energy difference corresponding to a rate-ratio of about 3. Much the same can be said of the factor of 34, which represents the observed further decrease of rate on passing from ethyl bromide to *iso*propyl bromide (Bateman, Cooper, Hughes, and Ingold, J., 1940, 925). The calculated steric effect would be of the same order of magnitude as in the previous comparison. Thus the question which we had to leave open in 1935 as to how much, if any, of the rate decrease in the α-methylated series was to be attributed to the steric factor seems now to be tentatively answerable in the statement that a substantial part, though not the whole, of the observed effect is of steric origin (cf. Evans and Polanyi, *Nature*, 1942, **149**, 608).†

Confirmation of this conclusion follows from the already mentioned measurements, recently made by

---

* The record for one of three reactions, the acid-catalysed hydrolysis of *tert.*-butyl acetate (Hammett, *op. cit.*) does not indicate a slow reaction : but this may well be due to the incursion of alkyl–oxygen fission, R·CO·O· ¦ R′, in view of Cohen and Schneider's demonstration that this type of reaction does in fact occur in the analogous case of *tert.*-butyl benzoate (*J. Amer. Chem. Soc.*, 1941, **63**, 3382).

† It must be remembered that near the mechanistic transition point a reaction may pursue a marginal mechanism, which, though kinetically of the second order, may exhibit in an incipient form some of the characteristics of the unimolecular process, notably in relation to the dependence of rate on structure (Hughes, Ingold, and Shapiro, J., 1936, 225).

Sugden and his collaborators with the aid of radio-bromine, of the activation energies of the bromine exchange reactions of typical primary, secondary and tertiary alkyl bromides (cf. p. 186). The observed primary–tertiary difference of activation energy is 5 kg.-cals., considerably greater therefore than 2 kg.-cals., the estimated difference due to steric causes only. The balance may be interpreted as a polar effect of the additional α-methyl substituents in the tertiary alkyl group; and it appears that the polar and steric effects of the α-methyl substituents of alkyl groups may be of comparable importance in bimolecular nucleophilic substitutions. A similar conclusion follows if we consider the primary–secondary, or secondary–tertiary difference of activation energy.

When we compare the observed increments of activation energy in the β-methylated alkyl series with the estimated steric contributions, no similarly obvious margin of energy appears which could be attributed to polar effects (cf. p. 185). In this series polar effects seem to be of an altogether smaller order of magnitude, as we should have expected from the elementary theory of the general inductive effect.

(*c*) *Steric Hindrance and the Unimolecular Mechanism of Nucleophilic Substitution.*—1. *Reactions of halogen compounds.* We now take a comparative view of the rate data contained in four of the preceding papers (Parts XXVI, XXVIII, XXX, and XXXI). Some of the more significant figures are collected in the form of relative rates in Table IX ($CH_3{\cdot}CH_2{\cdot} = 1$ or $CH_3{\cdot}CMe_2 = 1$). Those cases in which the mechanism of substitution is undoubtedly or very probably bimolecular are marked with a superscript (2). Those for which the evidence is very strong that the mechanism is wholly or substantially the unimolecular one (including its silver-ion-catalysed modification) are indicated by a superscript (1). The other figures relate to reactions for which the evidence on the whole indicates a mixture of mechanisms, or at least would permit this interpretation.

TABLE IX.

Relative Rates in Bimolecular and Unimolecular Hydrolysis or Alcoholysis.

Bromides.	CH_3.	$CH_3{\cdot}CH_2$.	$MeCH_2{\cdot}CH_2$.	$Me_2CH{\cdot}CH_2$.	$Me_3C{\cdot}CH_2$.
OEt^- in EtOH, 55°	17·6$^{(2)}$	1$^{(2)}$	0·28$^{(2)}$	0·030$^{(2)}$	0·0000042$^{(2)}$
H_2O–EtOH, " 50%," 95°	2·03$^{(2)}$	1$^{(2)}$	0·58$^{(2)}$	0·080	0·0064$^{(1)}$
$Ag^{\cdot}$ + H_2O–EtOH, " 70%," 64°	0·81	1	0·55	0·084	0·013$^{(1)}$
H_2O–$H{\cdot}CO_2H$, 95°	0·64	1$^{(1)}$	0·69$^{(1)}$	—	0·57$^{(1)}$
Chlorides.	—	$CH_3{\cdot}CMe_2$.	$MeCH_2{\cdot}CMe_2$.	—	$Me_3C{\cdot}CEt_2$.
H_2O–EtOH, " 80%," 25°	—	1$^{(1)}$	1·76$^{(1)}$	—	13·7$^{(1)}$

(For the meaning of " 50% " and " 70% " see pp. 165 and 170.)

The already discussed relationships in the first line are characteristic of the bimolecular mechanism : the steric effect is dominant. It appears that in the *dry* alcoholic solvent the rate of ionisation of primary halides is insufficient to allow the ionisation mechanism to show itself even in the case of *neo*pentyl bromide.* This follows, *inter alia*, because the rate is proportional to the ethoxide concentration, and because the substitution product has a normal *neo*pentyl structure (Parts XXVI and XXIX). In aqueous alcohol the ionisation rate is much greater, sufficiently so to dominate the reaction of *neo*pentyl bromide, the bimolecular substitution of which must be sterically hindered as before. This is deduced because, *inter alia*, added alkali does not increase the rate, and the substitution product has a rearranged carbon structure (Part XXIX). The incursion of an ionisation type of mechanism seems to be carried a little further in the silver reactions, and much further still in the best ionising solvent which it has yet been possible to find for the hydrolysis of alkyl halides, *viz.*, moist formic acid (cf. Bateman and Hughes, J., **1937**, 1187; **1940**, 935, 940, 945). Here all the rates are of the same order of magnitude, and we assume in consequence that the unimolecular mechanism is important throughout the series. It is likely, however, that the unimolecular rates for methyl, ethyl, and *n*-propyl bromide are smaller than the observed rates, which probably contain a substantial bimolecular contribution (cf. Bateman and Hughes, J., **1940**, 940, 945). The theoretical sequence for the polar effect in unimolecular substitution is Me < Et < Pr^a < *iso*Bu < *neo*pentyl, but all the differences, except the first, should be small. One might expect the initial difference Me < Et to be reproduced in the observed rates, as indeed it is in the formic acid solvent. The smaller differences might not be so reproduced, for the reason that we do not measure rates near the absolute zero of temperature, but make observations with vibrating and rotating molecules, rather than the static molecules which implicitly are under consideration when a polar sequence such as the above is written. We do, in fact, observe the correct polar sequence, as can be seen in the last line of the table, in the rates for the tertiary halides, for which the mechanism is indubitably unimolecular, and the theoretical polar effect is enhanced in the last member of the series by the use of α-Et_2 groups. Clearly, the polar effect dominates rate in the unimolecular mechanism; indeed, it is impossible to survey these kinetic relationships comprehensively without reaching the conclusion that steric hindrance plays no appreciable part in the unimolecular substitutions of alkyl halides.

It is an evident consequence of these relations that, for structures which are sterically hindered in bimolecular substitution, more success may sometimes be gained in effecting reaction by the addition of an ionising solvent than by the introduction of a powerfully nucleophilic reagent. For instance, Whitmore took drastic measures with limited success in his attempts to hydrolyse *neo*pentyl halides with reagents such as concentrated alcoholic alkali, although hydrolysis could easily have been effected, without any alkali, by simply adding water

---

* Experiments which will be published later make it probable that the ionisation rate is between 10 and 100 times too small to make itself felt in these experiments.

to the alcohol. It is true that, in the particular case of *neo*pentyl compounds, substitution by the unimolecular mechanism is accompanied by a rearrangement which, if the object in view were preparative, it might be desired to avoid; but there are many other structures which can be predicted to be subject to marked steric hindrance in bimolecular substitution, and not subject to rearrangement in unimolecular substitution. One example is now being studied, and there will be a later opportunity to discuss it.

2. *Reaction of alcohols.* Reference has already been made (p. 188) to Bartlett and Knox's observation that αα-diethyl*neo*pentyl alcohol is instantaneously converted into the corresponding chloride by dry hydrogen chloride. Setting this fact besides others (this vol., p. 188) relating to the conversion of alcohols into halides, we have already concluded that Bartlett and Knox must have had the unimolecular mechanism, S_N1, under observation. The further conclusion can be drawn that this mechanism also is unaffected by steric hindrance.

3. *Reactions of carboxyl compounds.* Day and Ingold discussed three unimolecular mechanisms of carboxyl esterification and hydrolysis, of which one, involving acid catalysis and acyl–oxygen fission, had been kinetically investigated (by Graham), in the example of benzoic acid and its esters and their nuclear substitution products, in sulphuric acid solvents (*loc. cit.*). The rates of these reactions depend on the slow heterolysis of a rapidly formed oxonium ion $\mathrm{R{\cdot}CO{\cdot}\overset{+}{O}HR'}$, to give the carbonylium ion $\mathrm{R{\cdot}\overset{+}{CO}}$, which is thereafter rapidly attacked by water or alcohol. Treffers and Hammett first discovered by qualitative observation (*J. Amer. Chem. Soc.*, 1937, **39**, 1708) what has since been confirmed kinetically, *viz.*, that *o*-methyl substitution, which would sterically inhibit any reaction dependent on a bimolecular transition state centred at the carbonyl carbon atom, actually accelerates esterification and hydrolysis in sulphuric acid solvents. Day and Ingold (*loc. cit.*) attributed these results to the polar effect, *i.e.*, to the electron supply, which is needed to assist the formation of the carbonylium ion, and which the *o*- and *p*-methyl groups can furnish; and it was pointed out that there was not, and should not be, any appreciable steric effect.

Summarising, we conclude that, according to the evidence now available, there is no steric effect in *any* unimolecular substitution; and no doubt the reason is that given by Day and Ingold for the case which they were discussing, *viz.*, that, in contrast to the inevitable congestion of the bonds in bimolecular transition states, no new covalencies are being formed in the transition state of an ionisation, the attack on the separating particles being more or less external, and the forces largely of the longer range, electrostatic type.

(d) *Superposed Bimolecular and Unimolecular Mechanisms in Nucleophilic Substitution.*—Although our discussion of the hydrolytic and allied reactions of alkyl halides has referred almost exclusively to various primary and tertiary alkyl halides, the conclusions reached inevitably affect our view of the corresponding reactions of secondary halides. In illustration, we may consider the following comparison of the parameters B and E of the Arrhenius equation, $k_1 = Be^{-E/RT}$, as applied to the solvolytic reactions of a primary and a tertiary alkyl halide in aqueous alcohol. We choose the reactions so that they shall be mechanistically simple and comparable, and therefore take *neo*pentyl bromide as the primary halide, since we can prove that its solvolysis is unimolecular and thus comparable with the demonstrably unimolecular solvolysis of *tert.*-butyl bromide. The following data concerning *neo*pentyl bromide are given in Part XXIX (this vol., p. 166); the figures for *tert.*-butyl bromide are taken from an earlier paper (Bateman, Cooper, Hughes, and Ingold, J., 1940, 925):

Bromide.	Solvent.*	$k_{25°}$ (sec.$^{-1}$).	B (sec.$^{-1}$).	E (kg.-cals.).
*neo*Pentyl	" 50% " EtOH	$8{\cdot}3 \times 10^{-11}$	$1{\cdot}5 \times 10^{11}$	29·0
tert.-Butyl	" 60% " EtOH	$3{\cdot}8 \times 10^{-3}$	$3{\cdot}1 \times 10^{13}$	21·7

* The expression " x% " EtOH means the solvent obtained by mixing at room temperature x vols. of anhydrous ethyl alcohol with $100 - x$ vols. of water.

It will be noticed that the compositions of the aqueous-alcoholic solvents are not the same; but the difference of solvent composition is not important in relation to the large rate differences now under consideration. Judging from data on *neo*pentyl bromide in " 50% " and " 70% " ethyl alcohol, a factor of about 0·4 applied to the rate for *neo*pentyl bromide would make it correspond to the solvent used for *tert.*-butyl bromide. The broad conclusion is that the rate of ionisation of the tertiary bromide is about 10^8 times greater than that of the primary bromide, and that, of this ratio, a factor of about 10^2 is represented by an increase in the Arrhenius parameter B, whilst the complementary factor arises from a decrease of activation energy, amounting to about 7 kg.-cals.

It seems a reasonable assumption in the light of these data that if we could obtain a pure unimolecular solvolysis, S_N1, of a secondary alkyl bromide in aqueous alcohol, the rate should be about 10^4 times smaller than for the *tert.*-butyl bromide, and the Arrhenius activation energy should be about 25—26 kg.-cals. Now Cooper, Hughes, and Shapiro showed (J., 1937, 1177, 1183) that the rates of solvolysis of the *iso*propyl halides in aqueous alcohol are in fact about 10^4 times smaller than for the corresponding *tert.*-butyl halides. The puzzling feature was, however, that the differences from the *tert.*-butyl halides were mainly represented by reduced B-factors, and not to any large extent by increased E-values. At that time (1937) the solvolysis of secondary halides was regarded as mechanistically marginal, but as following mainly the unimolecular process (S_N1). The marginal nature of these reactions has been consistently evident, but in 1940 Bateman, Cooper, Hughes, and Ingold (*loc. cit.*), as a result of considering the sensitivity of the rate of substitution to solvent composition, and to dissolved nucleophilic anions, concluded that a large part of the observed solvolytic rate was probably that of the bimolecular process (S_N2). Our new work shows that Cooper, Hughes, and Shapiro's results can be fitted into this revised picture of the reaction. The observed rates could be 10^4 times smaller than for *tert.*-butyl halides if a unimolecular rate of this order were overlaid by a bimolecular rate which could be smaller, or up to two or three times larger, but should not be of a larger order of magnitude. But if the bimolecular contribution to the total reaction were the larger, then the Arrhenius activation energy would approximate more closely to the activation energy of a bimolecular solvolytic substitution S_N2, than to that of a unimolecular substitution S_N1. It is true that we do not exactly know the activation energies of S_N2 solvolyses; but the reaction consists in the attack of a neutral molecule, H_2O or ROH, on an alkyl halide; and analogy with the Menschutkin reaction (involving attack by neutral R_3N, etc., on an alkyl halide), which belongs to the same sub-class of nucleophilic substitutions and has been the subject of many kinetic investigations, suggests low values, probably not much above 20 kg.-cals. The apparent activation energy for the solvolysis of *iso*propyl bromide should fall between this not accurately known lower limit for an S_N2 reaction, and an upper limit of about 25—26 kg.-cals. corresponding to the S_N1 reaction; indeed, according to Bateman, Cooper, Hughes, and Ingold's revised view of the mechanistic constitution of the reaction, its activation energy should lie nearer the lower limit. The observed value, 22·7 kg.-cals., tends to confirm this revised view against the opinion which had earlier prevailed.

Data are on record which show that the same type of view applies to the solvolysis of *iso*propyl chloride and iodide (Cooper, Hughes, and Shapiro, *loc. cit.*), and also to the solvolysis of other simple secondary alkyl halides, such as β-*n*-octyl chloride, bromide and iodide (Hughes and Shapiro, J., **1937**, 1192). In all these cases a fairly large part of the reaction in aqueous alcohol is bimolecular. The exact proportions we do not yet know, but it will be evident that the foregoing discussion provides the principles of a method, which we are even now proceeding to apply, for the quantitative mechanistic analysis of solvolytic reactions of mixed molecularity. We require, as reference data, the activation energies of solvolysis of pure S_N1 and S_N2 mechanisms. For the S_N1 reaction we can use, *e.g.*, α-methyl*neo*pentyl bromide, since the *neo*pentyl group will ensure the absence of the bimolecular process; and the result will apply to secondary alphyl bromides generally, because there is no steric effect in unimolecular substitutions (sub-division *c* of division *B*) and the polar effect of β-methyl groups is in first approximation negligible (sub-division *b*). For S_N2 solvolysis in aqueous alcohol, methyl bromide is a safe choice. For this case small corrections for both polar and steric factors are necessary in order to obtain a value appropriate to secondary alphyl bromides; but we have already illustrated (division *A* of this paper) how, by a combination of experiment and calculation, such corrections might be estimated.

It is a consequence of the revised picture of the mechanistic constitution of the solvolytic reactions of secondary alphyl halides that the degree of racemisation accompanying *a strictly unimolecular* solvolysis of optically active secondary halides must be more extensive than was at first inferred from the experimental data on the assumption that most of the observed reaction was unimolecular (Hughes, Ingold, and Masterman, J., **1937**, 1196). We hope to make a quantitative assessment of the degree of racemisation by associating mechanistic analyses on the lines indicated above with studies of the changes of optical rotatory power.

It will be appreciated that, in contrast to the differences of activation energy in S_N2 substitutions, an important part of which is due to steric hindrance, the drop of 7 kg.-cals. in the activation energy of S_N1 substitutions, on passing from primary, through secondary, to tertiary alkyl groups, is to be regarded as a pure polar effect. Part of it will be inductometric and part electromeric. The inductomeric part is of an electrostatic nature, and can be shown by calculation to be of magnitude sufficient to account for a substantial part of the observed energy difference. The electromeric part depends on the energy of hyperconjugation between the alkyl branches and the breaking C–Br bond, $\mathrm{H_3\overset{\curvearrowright}{C{-}C}\ldots\overset{\curvearrowright}{Br}}$; and it might also be considerable, since we know that in systems such as $\mathrm{H_3\overset{\curvearrowright}{C{-}C_6H_4}{-}\overset{\curvearrowright}{C}\ldots Cl}$ hyperconjugation energies may amount to several kg.-cals. (Hughes, Ingold, and Taher, J., **1940**, 949). Further discussion of this matter is deferred, since the quantitative calculation of polar effects requires a separate paper for its development.

(C) *The Wagner Rearrangement in Relation to Unimolecular Mechanisms of Substitution and Elimination* (S_N1 and $E1$).

(a) *Ionisation a Preliminary to Rearrangement.*—The work of Whitmore and his associates, extended, as it has been, in one direction by Kharasch and in others by ourselves, on the reactions of *neo*pentyl halides and analogous compounds, forms a basis for assessing the position of that class of rearrangements of which the Wagner change is typical, in relation to the mechanisms of substitution and elimination which we have been studying for several years.

The following four statements concerning the Wagner change in this group of examples can be made on the basis of the evidence mentioned. Statements (1) and (2) follow from Whitmore's work and ours, taken together, on certain reactions of *neo*pentyl compounds (Whitmore and Rothrock, *J. Amer. Chem. Soc.*, 1932, **54**, 3431; Whitmore and Fleming, *ibid.*, 1933, **55**, 4161; Whitmore, Wittle, and Popkin, *ibid.*, 1939, **61**, 1586; the preceding six papers by Dostrovsky and Hughes; division *B* of this paper). Statement (3) has been established by Whitmore (Whitmore and Fleming, *loc. cit.*; Whitmore, Wittle, and Harriman, *ibid.*, 1939, **61**, 1585; cf. Whitmore and Zook, *ibid.*, 1942, **64**, 1783). Statement (4) has been denied by Whitmore (cf. Whitmore, Popkin, Bernstein, and Wilkins, *ibid.*, 1941, **63**, 124; Whitmore and Zook, *loc. cit.*), even though, in his work on "neophyl" compounds (having the group $CPhMe_2{\cdot}CH_2{\cdot}$), he has provided some of the evidence in favour of it (Whitmore, Weisgerber, and Shabiea, *ibid.*, 1943, **45**, 1469); its truth has been well established by Urry and Kharasch (*ibid.*, 1944, **66**, 1436).

(1) No rearrangement of the carbon skeleton occurs in those reactions of *neo*pentyl compounds in which the *neo*pentyl group remains covalently bound continuously throughout the process. (The bimolecular ethoxylation of *neo*pentyl bromide by sodium ethoxide is an example.)

(2) Rearrangement to the *tert.*-amyl structure always takes place in reactions in the course of which the *neo*pentyl group is liberated as a cation. (The main examples are the unimolecular nucleophilic substitutions and eliminations, with rearrangement, and the allied heterogeneous reactions, of *neo*pentyl halides to give, *e.g.*, *tert.*-amyl alcohol or ethyl *tert.*-amyl ether, and trimethylethylene.)

(3) No rearrangement takes place in those reactions of *neo*pentyl compounds in the course of which the *neo*pentyl group becomes converted into an anion. (Electrophilic substitutions, proceeding by an ionic mechanism, have been illustrated by the conversion of *neo*pentyl-metal compounds into halides, *e.g.*, the conversion of *neo*pentylmercuric chloride into *neo*pentyl iodide by the action of iodine.)

(4) Rearrangement occurs in those reactions of neophyl compounds in the course of which the neophyl group is liberated as a neutral radical. (This is the case in homolytic * substitutions and eliminations, as exemplified by the conversion of neophyl chloride, with migration of the phenyl group, into *iso*butylbenzene and ββ-dimethylstyrene, under the conditions of the Würtz reaction, or through the use of phenylmagnesium bromide together with cobaltous chloride.)

These four statements can obviously be generalised and condensed into a single statement: It is a necessary condition for the Wagner rearrangement that substitution or elimination should proceed through a *carbon cation or radical*—in either case, through an entity with an incomplete carbon octet.

Ingold and Shoppee originally classified the pinacol–pinacolin and Wagner rearrangements with elimination reactions (J., 1928, 365; cf. Shoppee, *Proc. Leeds Phil. Soc.*, 1928, **1**, 301), though Ingold stressed the formation of a carbonium ion (*Ann. Reports*, 1928, **25**, 133).† It now appears that, so far as the class of heterolytic reactions is concerned, these rearrangements should be associated with the *unimolecular nucleophilic substitutions and eliminations*, S_N1 *and* E1, which have only since that time been recognised. Isomeric changes are automatically included as "symmetrical" unimolecular substitutions (cf. p. 175, footnote).

The condition for rearrangement, stated above as necessary, is not sufficient; for the formed cation or radical might be more stable than any isomeride it could produce by rearrangement. The important factor here is the resonance energy between the groups present and the carbonium ionic or radical centre in its various possible positions. Thus $CMe_3{\cdot}\overset{+}{C}H_2$ rearranges, $CMe_3{\cdot}\overset{+}{C}HPh$ does not, and $CPh_3{\cdot}\overset{+}{C}HPh$ does (Skell and Hauser, *J. Amer. Chem. Soc.*, 1942, **64**, 2633). These facts illustrate the importance of hyperconjugation, $H_3\overset{\curvearrowright}{C{-}}\overset{+}{C}$, and the greater importance of conjugation, $Ph\overset{\curvearrowright}{-}\overset{+}{C}$, as factors of stability.

The migrating group moves *with* its shared electrons, *e.g.*, $Me_2C(-Me){\cdot}\overset{+}{C}H_2 \longrightarrow Me_2\overset{+}{C}{\cdot}CH_2(-Me)$: these electrons must be vitally concerned in establishing the link with the original position of the carbonium or radical centre. Accordingly, Shoppee's rule (see Baker, "Tautomerism," Chapter XIV, Routledge, 1934) seems quite reasonable—that, when alternative groups might migrate from a given carbon atom to its neighbour, that group will preferentially migrate which can develop the greatest electron density at the point of its attachment (*e.g.*, anisyl > phenyl > methyl).

Whether or not rearrangement occurs in a formed carbonium ion, two sequelæ are normal: the carbonium ion either adds an anion or loses a proton: the result is either unimolecular nucleophilic substitution, S_N1, or unimolecular elimination, *E*1, or the modified forms of these processes involving rearrangement.

When the place, which in the preceding discussion is accorded to a carbon cation, is taken by a nitrogen cation with an open sextet, we obtain a picture of the Hofmann, Lossen, Curtius, and Beckmann rearrangements,‡ as Whitmore has already recognised (*J. Amer. Chem. Soc.*, 1932, **54**, 3274). Although Whitmore has objected to being associated with "ionic" mechanisms of rearrangement (Whitmore and Fleming, J., 1934, 1269), it seems to us that no one has done more than he to establish such mechanisms.§

---

* "Homolytic" reactions are those in which the bonds break according to the scheme A.¦.B. The reactions of classes (1), (2), and (3) are "heterolytic"; *i.e.*, the bonds break thus, A .B (the dots represent electrons).

† Though we do not summarise the earlier history, it is impossible not to mention that Meerwein's work first suggested the importance of ionisation in the Wagner change.

‡ These four rearrangements are often described as "intramolecular" on the evidence of preserved configurations in suitable optically active compounds. But they are just as truly "extramolecular": it all depends on which of the two interchanging groups one is thinking about. In the Wagner change, $R{-}C_\alpha{-}C_\beta{-}X \longrightarrow X{-}C_\alpha{-}C_\beta{-}R$, group X separates as X^-, then R migrates internally, and then X returns externally, unless it is eliminated; so that the original configuration about C_β becomes lost, whilst configurations in R are preserved. Similarly, in the Hofmann, Lossen, Curtius, and Beckmann rearrangements, X in $R{-}C_\alpha{-}N{-}X$ or $R{-}C_\alpha{=}N{-}X$ separates as $\bar{X}$, R migrates internally and X returns if it is not eliminated. Only configurations within R have yet been tested with respect to their optical stability.

§ In the substitutions with rearrangement of *neo*pentyl halides studied by Whitmore, the halogen was generally removed by an added reagent such as a silver salt, whilst we have achieved the same chemical result in suitable solvents without any such addition. Probably it was the particular range of his experience that led Whitmore to reject the ionic interpretation. In our picture the silver ion is an electrophilic catalyst for ionisation (Cowdrey, Hughes, Ingold, Masterman, and Scott, J., 1937, 1252; Bateman, Cooper, Hughes, and Ingold, J., 1940, 930).

(b) *Rearrangement as a Sequel to Ionisation.*—Rearrangement is not essential to the formation of a carbonium ion, for many well-established carbon ionisations do not involve rearrangement. Nevertheless, the question has been raised as to whether, when rearrangement does occur, it accompanies or succeeds the ionisation (Skell and Hauser, *loc. cit.*). The life of a *neo*pentyl cation, before its rearrangement to the *tert.*-amyl cation, must be very short, because it yields no detected substitution products with an unrearranged *neo*pentyl structure. The question is whether the lives of such unrearranged cations are in general and in principle too brief to be significant for reactions. It is not an answer to point out that some other carbonium ions yield unrearranged and rearranged substitution products side by side : mesomeric ions do that, and their canonical forms are universally believed not to exist as separate chemical entities. General evidence of a really unequivocal kind seems, indeed, very difficult to obtain; but we know of one case in which a special stereochemical situation discloses the answer.

This is the conversion, already cited by Bateman, Cooper, Hughes, and Ingold (*loc. cit.*), of camphene hydrochloride into *iso*bornyl chloride, a reaction which has been intensively studied by means of several tools, including kinetics, optical activity, and hydrogen and chlorine isotopic indicators. There is plenty of evidence that the initial stage is a rate-controlling ionisation of the chlorine atom. A possible route would therefore be : camphene hydrochloride ⟶ " camphene hydro- " cation ⟶ bornyl cation ⟶ *iso*bornyl chloride. The original question, as applied to this case, is whether the " camphene hydro- " cation has a separate existence, or whether, on the other hand, the camphene hydrochloride ionises and rearranges " all at once " to give the bornyl cation directly. The answer is known, and is unequivocal : it is the bornyl cation which has no separate existence in this chain of reactions. This follows because the stereochemical difference between bornyl and *iso*bornyl chloride disappears in the bornyl cation; which, when it *is* formed, and subsequently associated with a chloride ion, produces bornyl, not *iso*bornyl, chloride. Here then, it is clear that, although the reaction proceeds to give rearranged products almost completely, the unrearranged cation is the only one which exists long enough to enter into reaction. It has been shown that this cation needs the presence of a chloride ion in order to undergo the rearrangement of structure (*idem, ibid.*).

We are much indebted to the Department of Scientific and Industrial Research for their financial support of the work described in this group of papers, and to the Chemical Society and Imperial Chemical Industries Ltd. for providing some of the materials required. Part of the work was carried out at Aberystwyth in the laboratories of Professor T. Campbell James, whom we wish to thank for his hospitality.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR.
SIR WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, August 28th,* 1945.]