3. *Rearrangement and Substitution in Anionotropic Systems.   Part III.   Mechanism of, and Equilibrium in, Anionotropic Change.*

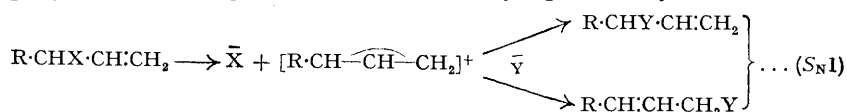By A. G. Catchpole, E. D. Hughes, and C. K. Ingold.

The discussion given by Burton and Ingold in 1928 of the subjects indicated in the title is modernised and extended.   It is shown that the general mechanism both of isomerisation and of substitution with rearrangement in anionotropic systems is dependent on ionisation, although an intramolecular mechanism can make its appearance in certain special cases of isomerisation Bimolecular rearrangement appears to be excluded, and a reason for this is suggested.   The distinctions between the kinetic and thermodynamic control of rearrangement are emphasized.

The theory of conjugation and hyperconjugation energy is used in the discussion of anionotropic equilibria, with results which are qualitatively satisfactory and hold some promise of successful quantitative development.
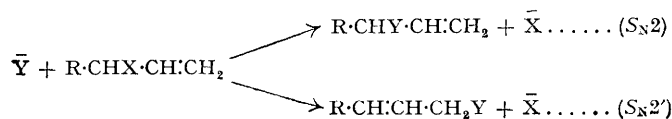
(1) *Mechanism of Rearrangement in Anionotropic Systems.*

SINCE the appearance in 1928 of Burton and Ingold's paper on anionotropy, no revised general discussion of the subject has been published, although in the meantime it has passed through quite a history. This has been partly a written history * of direct investigations by Burton, Meisenheimer, Kenyon, Young, Winstein, and others. To a large extent, however, it has been an unwritten history arising out of the bearing on the subject of our knowledge of nucleophilic substitution, as this has developed in the intervening years. The primary effect of the more recent knowledge was to introduce previously unsuspected ambiguities of interpretation. Therefore, new experimental work was undertaken, the results of which were summarised by Hughes in 1941, and are now recorded in the accompanying papers by Catchpole and Hughes. As this work succeeded in its object of resolving the difficulties referred to, some further discussion seems profitable.

It was assumed by Burton and Ingold (*J.*, 1928, 904) that the rate-controlling step in anionotropic change is the separation of the mobile group (always an electron-attracting group such as halogen or acyl) as a fully dissociated anion. The residual carbonium ion was then necessarily mesomeric, its distributed positive charge being capable of concentration, for the purposes of ionic recombination, on either of two alternative carbon atoms. It made no difference of principle whether the anion, which in the final, rapid stage combined with the carbonium ion, was one of those formed in the original ionic dissociation or was some other anion, possibly of a different kind, specially provided for the purpose : the mechanisms of the strictly isomeric change, and of the substitution of the mobile group by a group derived from a different anion, with a completely analogous rearrangement of the unsaturated system, were regarded as identical in all essentials. This mechanism clearly belongs to the type of substitution mechanism which was subsequently recognised as being of wide occurrence in saturated compounds, was termed unimolecular nucleophilic substitution, and was labelled S_N1. It is formulated for the anionotropic case (using the curved bond-sign to represent a distributed electron pair) in the following scheme, in which $\bar{Y}$ may represent any anion, not excluding $\bar{X}$:

$$R \cdot CHX \cdot CH\mathord:CH_2 \longrightarrow \bar{X} + [R \cdot CH \mathord{\frown} CH \mathord{\frown} CH_2]^+ \quad \bar{Y} \quad \begin{cases} R \cdot CHY \cdot CH\mathord:CH_2 \\ R \cdot CH\mathord:CH \cdot CH_2 Y \end{cases} \dots (S_N1)$$

(*a*) *Non-appearance of Bimolecular Rearrangement.*—It was a natural outcome of the work on saturated compounds that Hughes later considered the application to rearrangement and substitution in anionotropic systems of the other homogeneous mechanism which had been found general for substitution at a saturated carbon atom, namely, bimolecular nucleophilic substitution, S_N2 (*Trans. Faraday Soc.*, 1938, **34**, 194). He pointed out that this type of mechanism might lead not only to substitution of the ordinary type, S_N2, that is, without rearrangement, but also to substitution with rearrangement, S_N2'. The latter possibility provided a simple, and superficially attractive, explanation of an important observation by Meisenheimer which will be discussed presently. In the following scheme $\bar{Y}$, as before, intended to denote any anion, not excluding $\bar{X}$:

$$\bar{Y} + R \cdot CHX \cdot CH\mathord:CH_2 \begin{cases} R \cdot CHY \cdot CH\mathord:CH_2 + \bar{X} \dots\dots (S_N2) \\ R \cdot CH\mathord:CH \cdot CH_2 Y + \bar{X} \dots\dots (S_N2') \end{cases}$$

However, the work of Catchpole and Hughes (*Trans. Faraday Soc.*, 1941, **37**, 629; this vol., pp. 1, 4), confirmed by that of Roberts, Young, and Winstein (*J. Amer. Chem. Soc.*, 1942, **64**, 2157; cf. Young and Andrews, *ibid.*, 1944, **66**, 421), shows that, although the simple substitution mechanism, S_N2, can readily be observed, the substitution with rearrangement, S_N2', apparently cannot be realised.

* A useful review covering a part of the subsequent work has been given by H. B. Watson (*Ann. Reports*, 1938, 233).

It is relevant to enquire to what extent this finding is likely to prove general. The most obvious plan by which one might endeavour to suppress reaction S_N2, in the hope of observing reaction S_N2', would be to build up a condition of steric inhibition to the transition state of the substitution S_N2. The α-substituent, R, which in the experiments mentioned was a methyl group, already does this to some extent. However, our knowledge of aliphatic substitution in general, and Catchpole and Hughes's work on substitution in alkylated allyl compounds in particular, show that the introduction of another hydrocarbon radical in the α-position would render ionisation, which amongst allyl compounds generally can only be suppressed in a limited range of conditions, well-nigh impossible to avoid : the dominant mechanism would then be S_N1. The same is true if the α-alkyl group should be replaced by an α-aryl group. Substitution in the β-position would affect the α- and γ-positions similarly, and substitution in the γ-position would act in the wrong direction. The most hopeful possibility would be to use a *tert.*-butyl group for R, an experiment which we hope to try; but whether this works or not, it is already evident that mechanism S_N2' is not going to apply in the most simple and typical cases of anionotropic systems.

Although this result was not anticipated, it seems, in retrospect, reasonable in relation to the broad picture of substitution which has been built up since 1926. This shows that at a saturated carbon atom nucleophilic substitution is the general rule, whilst at an unsaturated, and, in particular, an aromatic, carbon atom electrophilic substitution is the prevalent mode. In more detail, it appears that a carbon atom which possesses only σ-electrons is fundamentally rather sensitive to nucleophilic, but is much less sensitive to electrophilic, reagents. Since all the valency electrons of such a carbon atom are mainly localised between two nuclei, they are to that extent protected from electrophilic attack; and since their charge density is maximal along the lines of the geometrical bonds, they leave, in between, regions of lower electron density, through which a nucleophilic reagent may make its approach. On the other hand, it appears that a carbon atom possessing π-electrons is less sensitive to nucleophilic, and more so to electrophilic, reagents. Since π-electrons are unprotected laterally to the plane of the adjacent atoms, they may be expected to be vulnerable to electrophilic reagents; furthermore, they have their maximum charge density in just that direction in which, but for their presence, it would be sterically most natural for a nucleophilic reagent to approach the carbon nucleus. These, of course, are general considerations, and are subject to modification in the presence of a strong electrostatic deformation of the π-electrons as in the carbonyl group or a nitro-substituted benzene nucleus. We assume that in the anionotropic case the π-electrons of the double bond to a considerable extent protect the γ-carbon atom from the attack of the nucleophilic reagent $\bar{Y}$, thus inhibiting bimolecular rearrangement by mechanism S_N2', at least in the absence of strong electrostatic deformation or of other special influences. These stereo-electronic considerations clearly have some bearing on the π-bond theory of Dewar (*J.*, 1946, 406).

(b) *Kinetic and Thermodynamic Control of Rearrangement.*—We may now consider the observation of Meisenheimer, the interpretation of which for some time remained equivocal.* It was found by Meisenheimer and Link (*Annalen*, 1930, **479**, 221) that γ-phenylallyl (cinnamyl) chloride, the more thermodynamically stable member of a pair of anionotropic chlorides, on treatment with potassium acetate in acetic acid, gave a mixture of α- and γ-phenylallyl acetate, even though, after a considerably longer period in the same solvent (or a sufficient period in any polar solvent), the α-phenylallyl acetate isomerised completely to γ-phenylallyl acetate, the more thermodynamically stable member of the pair of acetates. Analogously, γ-phenylallyl bromide with alcoholic alkali yielded a mixture of ethyl α-phenylallyl ether and ethyl γ-phenylallyl ether; in this case no direct interconversion of the ethers was realised, but by analogy, as well as for theoretical reasons (see below), we should expect the equilibrium between them to be entirely in favour of the γ-phenylallyl compound. The formation of the two acetates was further investigated by Meisenheimer and Beutter (*ibid.*, 1934, **508**, 58). They found that the solvolytic reaction of γ-phenylallyl chloride in acetic acid, with no salts present, gave a qualitatively similar result, the mixture of acetates, as first formed under these conditions, containing 18% of the α-phenylallyl compound. The addition of those soluble metallic acetates which yielded, after the interaction, soluble metallic chlorides (so that the system remained homogeneous) decreased this proportion; as also did the addition of water to the acetic acid; whilst metallic acetates which gave precipitated metallic chlorides increased the figure. Approximate first-order kinetics were established for the change γ-phenylallyl chloride ⟶

* The difficulty of this matter was first made apparent in a discussion given by Baker ("Tautomerism", Routledge, 1934, p. 232).

total acetate in acetic acid containing lithium acetate (homogeneous system). The reaction was accelerated by added water or lithium chloride.

At first the bimolecular mechanism, S_N2', appeared to provide a simple explanation of these observations, and Roberts, Young, and Winstein (*loc. cit.*) were inclined to consider this as a serious possibility. We hold, however, that, in view of Catchpole and Hughes's conclusions, the theory can no longer be entertained. The exclusion of this possibility enables the alternative view to be advanced with some confidence, namely, that Meisenheimer was dealing with a case in the field of anionotropy of the phenomenon, familiar in prototropy, of the distinction between kinetic and thermodynamic control in ion-recombination. The close analogy between the two cases provides, we think, a definite piece of circumstantial evidence in favour of the ionisation picture of anionotropy.
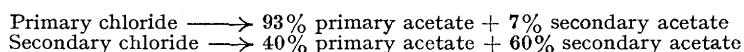
In the field of prototropy the phenomenon is exhibited in an extreme form in pseudo-acids. If a solution of an alkali metal salt of such a compound is acidified, the mesomeric anion reassociates with a proton more quickly to form the true acid, but with a greater diminution of free energy to form the pseudo-acid; and the true acid will yield the common ions much faster than will the pseudo-acid. The accompanying schematic energy diagram shows these relationships : kinetic control of the proportions of the isomerides is regulated by the top two
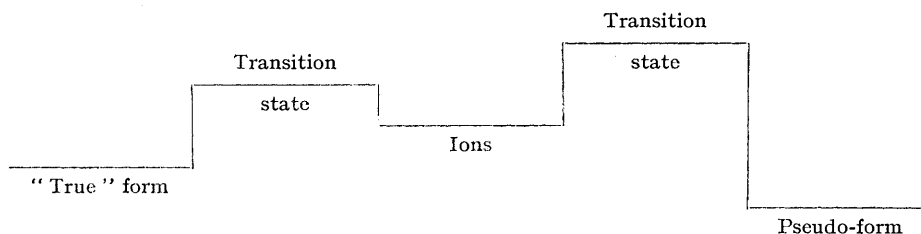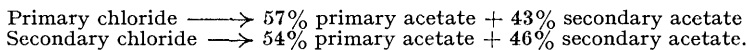

levels, thermodynamic control by the bottom two. Thus, by operating speedily at a low temperature we may isolate *aci*-phenylnitromethane, although this is the thermodynamically less stable form and eventually must re-ionise and isomerise to the pseudo-form. Less extreme examples are known amongst isomeric $\alpha\beta$- and $\beta\gamma$-unsaturated carbonyl compounds. The former are commonly the thermodynamically more stable isomerides, though, by acidification of salts, the latter may be first formed in considerably more than their equilibrium proportions. In view of these analogies, Meisenheimer's phenomenon would seem to require the assumption that the γ-phenylallyl halide first forms a mesomeric carbonium ion, and that this combines with an anion, such as acetate or ethoxide, in the two possible positions at comparable speeds, thus first producing the α-phenylallyl compound in far more than its equilibrium proportion, though the re-ionisation of this substance must eventually yield the γ-phenylallyl isomeride almost exclusively.

The details fit satisfactorily into this picture. Effects due to highly polar molecular solutes and to ionised salts in dilute solution on rates of ionisation are, for electrostatic reasons, qualitatively similar; and so also they must be on rates of ion recombination; such effects are generally greater the smaller the free energy difference between the molecule and its ions (Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979). The direction of the influence on ion recombination is retardation, and this effect is expected to be exerted more strongly on the formation of the more readily ionisable α-phenylallyl compound. This would explain the effect of added water and salts on the proportion in which α-phenylallyl acetate is formed, except for those systems which become heterogeneous, when a surface reaction is possible. The effect of dipoles and ions on ionisation is accelerative. Since the rate of the total reaction is controlled by an ionisation, we may readily understand the approximate first-order kinetics, the acceleration produced by added water, and the considerable positive salt effect of lithium chloride (Bateman *et al.*, *loc. cit.*). For a bimolecular reaction these effects would be much smaller and in the opposite direction.
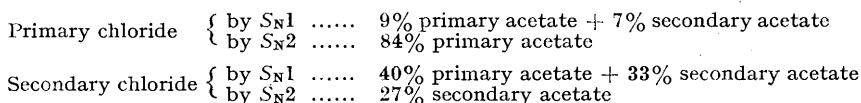
It is also possible to interpret the supplementary investigation which Meisenheimer and Link carried out (*loc. cit.*) on the acetolysis of γ- and α-ethylallyl chlorides, which, although tautomeric, are both stable enough to be studied separately. Under the conditions used, corresponding acetates underwent no measurable interconversion. With acetate ions in acetic acid the following results were obtained :

Primary chloride ——→ 93% primary acetate + 7% secondary acetate
Secondary chloride ——→ 40% primary acetate + 60% secondary acetate

With silver acetate as the reagent the results were as follows :

> Primary chloride $\longrightarrow$ 57% primary acetate + 43% secondary acetate
> Secondary chloride $\longrightarrow$ 54% primary acetate + 46% secondary acetate.
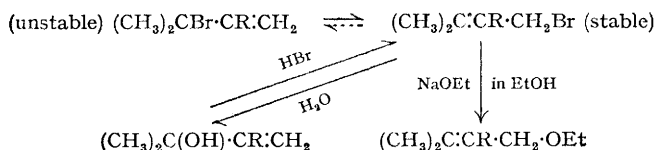
We assume that the smaller tendency to ionisation possessed by these aliphatic chlorides lends considerably greater importance to the bimolecular mechanism of substitution when comparison is made with γ-phenylallyl chloride; this is in agreement with well-established principles. But, according to the findings of Catchpole and Hughes, and of Roberts, Young, and Winstein, bimolecular substitution can produce only that acetate which corresponds in structure to the chloride. That is why, in the acetate ion reaction, the two chlorides give different results. However, substitution with the aid of a silver salt, although heterogeneous, is closely analogous in mechanism to the homogeneous reaction $S_N 1$ (Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252). Thus it is that, in the silver acetate reaction, both chlorides give a nearly common result. If we provisionally accept this result as furnishing the kinetically controlled ratio (55 : 45) in which the two acetates are formed from the mesomeric carbonium ion, a tentative analysis of the acetate ion reaction may be made as follows :

Primary chloride $\begin{cases} \text{by } S_N 1 \quad \ldots\ldots & \text{9\% primary acetate + 7\% secondary acetate} \\ \text{by } S_N 2 \quad \ldots\ldots & \text{84\% primary acetate} \end{cases}$

Secondary chloride $\begin{cases} \text{by } S_N 1 \quad \ldots\ldots & \text{40\% primary acetate + 33\% secondary acetate} \\ \text{by } S_N 2 \quad \ldots\ldots & \text{27\% secondary acetate} \end{cases}$

It is, of course, consistent with the general picture of nucleophilic aliphatic substitution that the proportion of bimolecular substitution $S_N 2$ comes out greater for the primary than for the secondary chloride.

Some older observations similarly receive a satisfactory explanation. The most complete of these is that of Claisen (*J. pr. Chem.*, 1922, **105**, 65), who showed that $\gamma\gamma$-dimethylallyl bromide, which, like γ-phenylallyl bromide, is the thermodynamically stable member of the anionotropic system to which it belongs, on treatment with dry alcoholic sodium ethoxide gave ethyl $\gamma\gamma$-dimethylallyl ether, but with water or dilute aqueous sodium carbonate produced $\alpha\alpha$-dimethylallyl alcohol, from which $\gamma\gamma$-dimethylallyl bromide could be regenerated by treatment with hydrogen bromide (formulæ below, R = H). Similar transformations were carried through with the β-methyl homologues (R = Me) :

$$\text{(unstable) } (CH_3)_2CBr \cdot CR{:}CH_2 \quad \rightleftharpoons \quad (CH_3)_2C{:}CR \cdot CH_2Br \text{ (stable)}$$

$$(CH_3)_2C(OH) \cdot CR{:}CH_2 \qquad (CH_3)_2C{:}CR \cdot CH_2 \cdot OEt$$

Here the $\gamma\gamma$-dimethylallyl structure is the thermodynamically stable one (see below), although only the bromide system, not the alcohol system or ether system, is mobile under the conditions employed. However, in unimolecular substitution, which, as Catchpole and Hughes's investigation proves (this vol., p. 4), will occur when water or dilute aqueous alkali acts upon the bromide, kinetic control of ion-recombination favours the $\alpha\alpha$-dimethylallyl product. The appearance, on the contrary, of a $\gamma\gamma$-dimethylallyl product in the bimolecular substitution, which, as Catchpole and Hughes's work also shows, is to be expected when the reagent is alcoholic sodium ethoxide, is necessitated by the non-existence of bimolecular replacement with rearrangement, $S_N 2'$. Once again a thermodynamically unstable isomeride is formed from the mesomeric carbonium ion in far more than the equilibrium proportion.

(*c*) *Status of Intramolecular Isomerisation.*—The other main ambiguity to be dealt with arises from the circumstance that, besides mechanisms $S_N 1$ and the hypothetical mechanism $S_N 2'$, a third view of anionotropic rearrangements has always been possible (cf. Hughes, *loc. cit.*), namely, that they are intramolecular. This idea has been much discussed by Kenyon and his collaborators. Balfe and Kenyon have drawn a sharp distinction between non-isomeric replacements involving rearrangements and the corresponding isomeric changes (*Trans. Faraday Soc.*, 1941, **37**, 723). For the former they adopt (as Kenyon has done consistently) the ionisation scheme labelled $S_N 1$ on p. 9. But now, desiring to restrict its application to non-isomeric replacements, they introduce a subtle difference into the formulation by (i) replacing the single arrow on the left-hand side of the above-written scheme, $S_N 1$ (p. 9), by the sign for a reversible reaction, and (ii) allowing $\bar{Y}$ to represent, not any anion, but any anion *excepting* $\bar{X}$. To us it does not seem likely that the mesomeric carbonium ion should be able to combine at either end
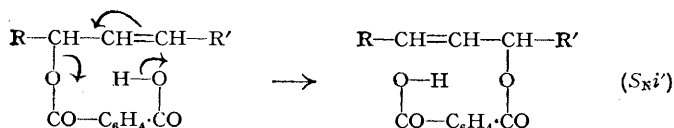
with $\bar{Y}$, but only at one end with $\bar{X}$, when these anions might be, say, an acetate and a benzoate ion, or two even more closely similar ions. Indeed, the suggested discrimination appears untenable when it is remembered that X and Y might be interchanged; for by agreed hypothesis, the same carbonium ion would be an intermediate when (to continue with the same example) acetate ions act upon an allyl benzoate as when benzoate ions act on an allyl acetate.

Kenyon and his collaborators have adduced important evidence for the ionisation mechanism of non-isomeric replacements with rearrangement by their discovery that optical activity dependent on asymmetry which would be destroyed by ionisation is actually lost in the rearrangement process. In an example such as the solvolysis of optically-active $\alpha\gamma$-dimethylallyl hydrogen phthalate with formic acid, acetic acid, methyl alcohol, etc., the symmetry of the anionotropic system renders it impossible to prove directly that rearrangement has occurred; but Balfe, Hills, Kenyon, Phillips, and Platt showed (*J.*, 1942, 556), not only that the solvolytic product was completely, or nearly completely, racemised, but also that the original ester recovered from an incomplete reaction was often largely racemised, just as though most of it had once been ionised. It is significant that with the best ionising solvents, such as formic acid, the activity of the product was vanishing, whilst it was only with poor ionising solvents, such as *n*-butyl alcohol, that racemisation was appreciably incomplete (greatest observed activity, 9%). In the light of Catchpole and Hughes's results, this residual activity may perhaps be interpreted as arising from bimolecular substitution without rearrangement (S_N2). Consistently the sign of the activity was found to represent an inverted configuration (Cowdrey, *et al.*, *loc. cit.*). For some similar solvolyses of γ-methyl-α-*n*-propylallyl chloride, and the corresponding hydrogen phthalate, Arcus and Kenyon ingeniously proved (*J.*, 1938, 1912) that the small residual activity found in some of the solvolysis products (maximum 2%) was really due to substitution without rearrangement; they did this by showing that the activity was lost when the double bond was reduced, a process which must destroy asymmetry in the original, but not in the rearranged, structure.

The position with respect to the isomeric changes is less simple. Balfe and Kenyon follow Arcus and Kenyon in regarding them as intramolecular, essentially on evidence earlier presented by Kenyon, Partridge, and Phillips (*J.*, 1937, 207). Arcus and Kenyon refer to those authors as having proved, in the example of the isomerisation of α-phenyl-γ-methylallyl compounds to the corresponding γ-phenyl-α-methylallyl derivatives, " that the migrating anion is not kinetically free since there is a high retention of asymmetry " on rearrangement. We think that this is an over-simplification of Kenyon, Partridge, and Phillips's findings, which it is necessary to restate in more detail.

These authors studied four α-phenyl-γ-methylallyl derivatives, namely, the alcohol in acid conditions (presumably the active entity is the hydroxonium ion), the *p*-nitrobenzoate, the acetate, and the hydrogen phthalate. Now a necessity for the provision of any proof of an *intramolecular* mechanism is to separate the rearranging molecules from one another by operating in a solution at least so dilute that the specific rate shall be independent of the concentration. The alcohol was examined in dilute aqueous acetic acid, and, though the rate was not studied, we may assume that the dilution was suitable; but the retention of optical activity in the product was only 3%. The *p*-nitrobenzoate gave a substantial retention of activity when isomerised in the fused state; but on isomerisation in moderately dilute solution in chloroform it gave a completely inactive γ-phenyl-α-methylallyl ester. The acetate was studied in more concentrated solution in acetic acid, and the product showed a 14% retention of activity. Only in the case of the hydrogen phthalate was a large degree of optical activity retained after isomerisation, not only in the fused state, but also (up to 58%) in solutions of demonstrably sufficient dilution.

It would thus appear that the hydrogen phthalate is a special case, and Hughes has already suggested that the free carboxyl group is involved in its racemisation (*Trans. Faraday Soc.*, 1941, **37**, 725). We here slightly modify his scheme by making a proton transfer between the carboxyl groups (internal acid catalysis assisting fission of the C–O bond) essential to the change :

$$
\begin{array}{ccc}
\text{R—CH—CH=CH—R'} & & \text{R—CH=CH—CH—R'} \\
\quad | \quad \quad | & \longrightarrow & \quad | \quad \quad | \\
\text{O} \quad \text{H—O} & & \text{O—H} \quad \text{O} \quad \quad (S_N i') \\
\quad | \quad \quad | & & \quad | \quad \quad | \\
\text{CO—C}_6\text{H}_4\text{·CO} & & \text{CO—C}_6\text{H}_4\text{·CO}
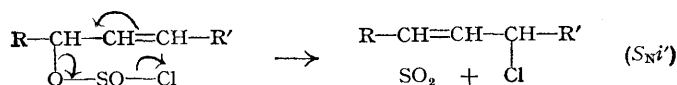\end{array}
$$

We do this in order to accommodate the observation that the salts (*i.e.*, the anions) of the hydrogen phthalates are much less prone to isomerise than are the free acids. This fact is, of

course, consistent with the exclusion of mechanism S_N2' in isomerisation, as indicated by Catchpole and Hughes (this vol., p. 1), since such a rearrangement of the anion would be an internal S_N2' reaction. The type of internal mechanism which the above formulæ illustrate is labelled S_Ni' because it is related to the substitution mechanism S_Ni of Cowdrey *et al.*—internal rearrangement leading to group replacement on a single carbon atom—exactly as the hypothetical mechanism S_N2' is related to mechanism S_N2.

Naturally mechanism S_Ni' is not in principle excluded from participation in the rearrangement of halides or of simpler esters, such as *p*-nitrobenzoates. However, the mechanism does not seem usually to play a major rôle for such reactions in dilute solution. A number of general circumstances concerning anionotropic isomerisation would be difficult to accommodate on a purely intramolecular picture of the reaction, for instance, the solvent and salt effects to which reference is made later. Probably the most notable single point which arises in this connection is Burton's demonstration (*J.*, 1929, 1650) that the isomerisation of α-phenylallyl *p*-nitrobenzoate could be largely diverted in the direction of a non-isomeric substitution with rearrangement by the introduction of acetate ions into the solution in which it was taking place. Balfe and Kenyon's remark on this subject is curious. They say : " The argument, that the rearrangement involves complete ionic dissociation, because in the presence of acetate ions α-phenylallyl *p*-nitrobenzoate yields cinnamyl acetate, . . . is shown to be invalid, because this reaction is a replacement and not a rearrangement ". We have already remarked that, if the formation of the carbonium ion is a step on the way to a replacement involving a structural change of the anionotropic system—and Balfe and Kenyon agree, and have helped to prove, that it is—then it must also be a step towards isomeric rearrangement : there is no difference of principle between the two cases. Of course, one can picture an intramolecular rearrangement which is so rapid that the ionisation has no time to occur; but if this were true, Burton would not have been able to divert the reaction.

Mechanism S_Ni' appears again amongst the replacements with rearrangement which take place on the conversion of a substituted allyl alcohol into mixtures of isomeric halides by means of reagents such as hydrogen halides, phosphorus halides, and thionyl chloride. The reactions of α- and γ-methylallyl alcohols with hydrogen bromide and phosphorus tribromide have been studied by Young and Lane (*J. Amer. Chem. Soc.*, 1937, **59**, 2051; 1938, **60**, 847), and those of α- and γ-ethylallyl alcohols with hydrogen chloride and thionyl chloride by Meisenheimer and Link (*Annalen*, 1930, **479**, 211). The results obtained with the hydrogen and phosphorus halides can be satisfactorily correlated, as Young and Lane have shown, by mechanisms identical with those labelled S_N1 and S_N2 by Cowdrey, Hughes, Ingold, Masterman, and Scott for the corresponding substitution reactions of saturated alcohols (*loc. cit.*). Mechanism S_N1 involves the formation of the carbonium ion; and since in the case of the substituted allyl compounds this ion is mesomeric, the mechanism produces from either of two isomeric alcohols the same mixture of isomeric halides. Mechanism S_N2 involves the attack by halide ion on an oxonium ion or phosphorous ester halide and proceeds without rearrangement of the anionotropic system; no mechanism S_N2' requires to be assumed. As with saturated alcohols, so also with these allyl alcohols, the introduction of pyridine into reactions involving phosphorus halides brings mechanism S_N2 into special prominence, with consequential reduction in the amount of rearrangement accompanying substitution. For these reagents neither mechanism S_Ni nor the analogous S_Ni' clearly appears. However, with thionyl chloride, which, as shown by Cowdrey *et al.*, is the best reagent for bringing mechanism S_Ni into prominence in the reactions of saturated alcohols, Meisenheimer and Link obtained this unusual result, namely, that their primary alcohol gave mainly the secondary chloride and their secondary alcohol mainly the primary chloride. As Roberts, Young, and Winstein have already noted (*loc. cit.*) this seems rather a clear indication of the rearrangement of a first-formed chlorosulphinic ester in accordance with mechanism S_Ni' :

$$\begin{array}{ccc} \text{R—CH—CH=CH—R'} & & \text{R—CH=CH—CH—R'} \\ \quad | & \longrightarrow & \qquad\qquad\quad | \\ \text{O—SO—Cl} & & \text{SO}_2 \;+\; \text{Cl} \end{array} \quad (S_Ni')$$

(*d*) *General Mechanism of Anionotropic Rearrangement.*—Our conclusions are, then, that mechanism S_N2' rarely if ever appears, and mechanism S_Ni' becomes prominent only in rather special circumstances. It follows that the ionisation mechanism, S_N1, though not the only mechanism, is to be regarded as the most general mechanism of both the isomeric and non-isomeric rearrangements of anionotropic systems. It seems desirable to put the arguments in favour of this mechanism more positively. In summary, they are as follows.

(i) Rearrangement, either isomeric or non-isomeric, in R·CHX·CH:CH·R' is strongly

correlated with the general chemistry of the group X, in particular, with its tendency to separate from carbon as the anion $\bar{\text{X}}$ (Burton and Ingold, *loc. cit.*). This becomes intelligible only if X is required to separate as $\bar{\text{X}}$ in the rate-controlling stage of reaction. The relationship indicated is not one which is normal for internal isomeric change (cf., *e.g.*, the known internal changes of allyloxybenzene and its derivatives).

(ii) Rearrangement in R·CHX·CH:CH·R′ is kinetically facilitated very strongly by electron-releasing substituents R and R′ (Burton and Ingold, *loc. cit.*; Hughes, *Trans. Faraday Soc.*, 1941, **37**, 627). Speaking generally, the effect is as important for isomerisation as for non-isomeric rearrangement, and is as prominent for anionotropic systems as a whole as it is for the ordinary unimolecular nucleophilic substitutions of saturated compounds, where it is agreed that the rate-controlling step is the formation of a carbonium ion. No other substitution mechanism is so sensitive to polar constitutional influences (cf. Polanyi, *Chem. and Ind.*, 1943, 166).

(iii) Kenyon and his collaborators have shown that both the isomerisations and non-isomeric rearrangements of optically active systems R·CHX·CH:CH·R′ in dilute solution are normally accompanied by a large degree of racemisation; though they have also discovered an explicable exception in the field of isomerisations (see above). A large degree of racemisation (not necessarily complete racemisation—cf. Cowdrey *et al.*) may be regarded as diagnostic for mechanism $S_N 1$.

(iv) Meisenheimer and his collaborators have shown that both the isomerisation and substitution of α-phenylallyl esters in solution follow the first-order rate law, except for deviations explicable as salt effects. In the substitution, the stoicheiometric reaction was essentially with added anions, so that the reaction may be classed as non-solvolytic. Catchpole and Hughes, and Roberts, Young, and Winstein have established similar kinetics for substitutions of α-methylallyl chloride, and this halide is sufficiently insensitive to alkali to render improbable a bimolecular solvolytic interpretation. For the substitutions with rearrangement these results may be regarded as definitely diagnostic of mechanism $S_N 1$. For the isomerisation they are not diagnostic by themselves, but Catchpole and Hughes have excluded the bimolecular interpretation by showing that the anion derived from the system is not a catalyst. (There is evidence of the incursion of acid catalysis in certain circumstances, but this can be explained as arising from a pre-equilibrium involving the catalysing acid and unshared electrons of the mobile group, the original anionotropic system being thus converted into a more mobile one. Acid catalysis must be mentioned in any general statement of the kinetic findings, but it hardly bears, except as stated, on the question of the mode of rearrangement of the unsaturated system.)

(v) Catchpole and Hughes have shown that the first-order substitutions of two isomerides of form R·CHX·CH:CHR′ and R·CH:CH·CHXR′ produce nearly the same mixture of isomeric substitution products (above). This is diagnostic for the $S_N 1$ mechanism of the substitution with rearrangement, and also for the substitution without rearrangement which occurs under the same conditions. It is not inconsistent that, as Meisenheimer in particular proved, the mixture of isomerides formed in such conditions may not be the equilibrium mixture (above).

(vi) It has been shown in the example of α-phenylallyl esters by Burton and Ingold (*loc. cit.*) and by Meisenheimer, Schmidt, and Schäfer (cf. this vol., p. 1) that the rate of isomerisation in solution is very sensitive to the solvent, and in general increases with the dielectric constant of the solvent. A similar effect has been established for alcohol–water mixtures by Catchpole in the example of the non-isomeric substitutions of various substituted allyl chlorides (Thesis, Univ. London, 1942). The magnitude and direction of these effects would be difficult to reconcile with any but a predominating or exclusive $S_N 1$ mechanism.

(vii) Meisenheimer and Beutter have shown (*loc. cit.*) that the isomerisation of an allyl acetate in acetic acid is accelerated by small additions of salt or of water. They have also proved that the non-isomeric substitution of an allyl chloride by acetate ions is accelerated by the inert salt, lithium chloride, and also by small additions of water (above). These effects, due to added ions or dipoles, are of the order of magnitude to be expected of a reaction dependent on primary ionisation, and they would be very difficult to reconcile with any other mechanism.

(viii) Burton has linked the mechanism of isomerisation to the $S_N 1$ mechanism of substitution with rearrangement by showing that the former process may be partly diverted in the direction of the latter by adding foreign anions. He has further shown that the diverted reaction is not a step-wise rearrangement and substitution, and that it must therefore be simultaneous with the undiverted isomerisation (above). There is abundant evidence that the diverted reaction is

unimolecular, and therefore that the carbonium ion is formed fast enough to provide a route for the isomerisation.

The general shape of the evidence, as it stands at present, is shown in the following tabular conspectus of these arguments and inferences :

|		Inference.	
Method of experiment.		Isomerisation.	Substitution.
(i) Facilitation according to the stability of X^-		S_N1 or S_N2	S_N1 or S_N2
(ii) Strong acceleration by electron release from R		S_N1	S_N1
(iii) Optical activity (usually lost)		S_N1 usually	S_N1
(iv) Rate law (first-order, etc.)		S_N1 or S_Ni'	S_N1
(v) Common product-mixture in substitution		—	S_N1
(vi) Solvent effect (direction and sensitivity)		S_N1	S_N1
(vii) Effect of added ions and dipoles		S_N1	S_N1
(viii) Burton's diversion experiments		Same for both	

The tabulated inferences are those which might be drawn from the different lines of attack if each were the only source of evidence available.   But if we take all the points together, it is clear that the fundamental inference is what is common to, or consistent with, them all : obviously we must conclude that there is only one general mechanism, *viz.*, the ionisation mechanism, S_N1, whatever may happen in special circumstances.   It should again be emphasised that we are discussing reactions in solution, and not those undergone by materials in the fused, crystalline, or gaseous state.

(2) *Equilibrium in Anionotropic Systems.*

When Burton and Ingold originally discussed this subject, the resonance energy associated with conjugation had not yet been recognised, and hyperconjugation had still to be discovered. Consequently the only picture which could be given was in qualitative kinetic terms, which are incapable of quantitative development in the foreseeable future owing to the unavailability of sufficiently precise information concerning the transition states of reactions.   The situations then dealt with can now, however, be more simply redescribed in terms of the energies of normal molecules, in terms that is to say, which, though still essentially qualitative, show the first vestiges of quantitative development, and are at any rate in the right form for quantitative treatment as soon as the factors of energy in normal molecules are understood in greater detail.

The simplest examples arise when an aryl, vinyl, or substituted vinyl radical is attached to the anionotropic system in such a way that it becomes conjugated with the anionotropic double bond in one of its possible positions.   The energy effect of this conjugation will then count as a direct contribution to the free energy of one of the isomerides.   No doubt other influences, constitutional and environmental, will affect the free energies of both isomerides, but the order of magnitude of the over-all differential effect will be correctly given if we neglect these other factors in comparison with the conjugation energy.   It is probable also that the conjugation energy itself can only in first approximation be treated as a constant characteristic of the unsaturated system; and that it will in different cases be subject to modification from influences arising both from within the molecule and from the solvent : it is just this kind of influence about which we need more information, from the further study of heats of reaction and solution, before a quantitative theory can become possible.   Nevertheless an assumed constant value will still serve to assess the order of magnitude of the effect.

For example, we know from experiment that in the γ-phenylallyl–α-phenylallyl system the equilibrium proportion of the α-phenylallyl isomeride is too small for experimental detection (Burton and Ingold; Meisenheimer;   X = Hal or O·Acyl) :

$$C_6H_5 \cdot CH{:}CH \cdot CH_2X \;\rightleftharpoons\; C_6H_5 \cdot CHX \cdot CH{:}CH_2$$
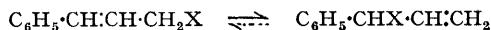
The energy of conjugation of a phenyl group with a vinyl group is usually taken as 7 kilocals. (Pauling, " Nature of the Chemical Bond ", Cornell Press, 1940, p. 137).   Neglecting other factors, we can calculate from this figure that at 300° K. the equilibrium proportion of the α-phenylallyl isomeride should be of the order of 0·001%.   Alkyl-γ-phenylallyl systems are, of course, in substantially the same case.

Baker and Nathan produced the first evidence of the hyperconjugation existing between alkyl groups and double bonds (*J.*, 1935, 1844).   The influence of this factor on the free energies of transition states was more rigorously proved by Hughes, Ingold, and Taher (*J.*, 1940, 949), and its effect on the free energies of normal molecules was finally established by Baker and

Hemming (*J.*, 1942, 191).* Although the effect was correctly associated by Baker specifically with the presence of CH-bonds, H—C—C=C, Hughes, Ingold, Masterman, and MacNulty pointed out (*J.*, 1940, 909) that a comparable energy effect arises even when quaternary carbon is attached to an ethenoid system; this is because of the reduction of electronic zero-point energy, which can result from the concentration of *CC*-electrons in the direction of the unsaturated centre. For our purposes it is convenient to include this effect in the hyperconjugation energy associated with the attachment of alkyl groups to ethenoid carbon. Looking back we can identify this hyperconjugation energy, at least roughly, with some of the differences observed by Kistiakowsky, Ruhoff, Smith, and Vaughan in the heats of hydrogenation of simple olefins (*J. Amer. Chem. Soc.*, 1935, **57**, 876). Even for one particular alkyl group, such as methyl, the effect on hydrogenation heat was found to be largely constitutive, but the range 1·5 ± 1 kilocal. for the methyl group covers the data.

In the system (R = H or CH$_3$)

$$(CH_3)_2C:CR·CH_2Br \quad \rightleftharpoons \quad (CH_3)_2CBr·CR:CH_2$$
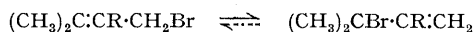
the equilibrium proportion of the αα-dimethylallyl isomeride is too small for experimental detection (Claisen, *loc. cit.*). Taking 3 kilocals. as the order of the contribution made by the hyperconjugation of the *gem*-methyl groups to the free energy difference, and disregarding other influences, we find the equilibrium proportion of the αα-dimethylallyl compound at 300° K. should be of the order of 1%. The system

$$CH_3·CH:CH·CH_2Br \quad \rightleftharpoons \quad CH_3·CHBr·CH:CH_2$$
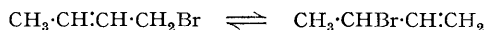
provides a better check on the assumed energy effects, inasmuch as the equilibrium ratio is measurable and known (Winstein and Young, *J. Amer. Chem. Soc.*, 1936, **58**, 104). Taking 1·5 kilocals. as the free energy difference contributed by the hyperconjugated methyl group, and neglecting other factors, we calculate that at 293° K. the equilibrium ratio, γ- to α-methylallyl, should be 93% : 7%, and at 373° K. it should be 88% : 12%. The figures are accidentally in better agreement with the observational values, 87% : 13% at 293° K., and 85% : 15% at 373° K., than would have been expected in view of the uncertainty in the energy difference. The general principles here illustrated may, of course, be quite extensively applied.

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