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1. *Rearrangement and Substitution in Anionotropic Systems. Part I.
Test for Bimolecular Isomerisation in α -Phenylallyl Esters.*

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In these papers a relationship is traced between the mechanism of aliphatic substitution and the mechanism of isomerisation and of substitution, with and without rearrangement, in anionotropic systems. Isomerisation may generally be regarded as a special case of substitution with rearrangement, and it is shown that it usually depends, like the unimolecular mechanism of aliphatic substitution, on an ionisation process (equation 1 below). In the isomerisation of α - to γ -phenylallyl *p*-nitrobenzoate, in methyl cyanide and acetic anhydride as solvents, the rate is increased by added lithium *p*-nitrobenzoate, but the increase is of a type which can be accounted for as an effect of ionic strength on the rate of ionisation to the mesomeric carbon cation. No evidence of any considerable incursion of a bimolecular isomerisation (see equation 2) could be obtained under conditions known from our experience of bimolecular aliphatic substitution to be favourable. Detailed discussion is deferred to Part III (this vol., p. 8).

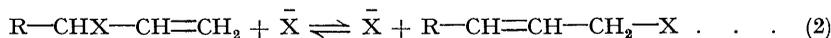
THESE papers are the first of a series in which it is intended to carry further forward an investigation which was commenced by Burton and Ingold in 1928 and continued in fairly direct sequence by Meisenheimer and his collaborators until Professor Meisenheimer's death in 1934. Our main reason for taking up the subject in 1937 was that, since a connection between the mechanism of anionotropy and of substitution at a saturated carbon atom was manifest, it was opportune to apply the knowledge gained in the studies of substitution, which had then been partly completed, to a re-investigation, along somewhat analogous lines, of rearrangement and substitution in anionotropic systems. The full presentation of our initial results has been delayed, although a partial summary was published by one of us in 1941 (*Trans. Faraday Soc.*, 1941, **37**, 627).

Burton and Ingold (*J.*, 1928, 904) adduced reasons for the belief that anionotropic change is initiated by the separation of the mobile group as an anion, the simultaneously produced carbonium ion being necessarily mesomeric, and therefore capable of recombining with an anion in either of two alternative positions. Obviously, if the anion with which the carbonium ion recombines is of the same kind as that originally eliminated, an isomeric rearrangement may result :



However, recombination with another anion derived from some foreign source is equally possible, and this would lead to substitution with or without rearrangement. Therefore, in this mechanism, isomeric rearrangement is to be regarded as a particular case of substitution with rearrangement. Further, the substitution mechanism itself is now seen to be a particular case of the unimolecular substitution mechanism, S_N1 , which since 1935 has become recognised as general among aliphatic compounds.

One result of these successive inclusions of the particular within the more general was that the second type of mechanism which has been found to be common in aliphatic substitution, namely, the bimolecular mechanism, S_N2 , was hypothetically particularised, in corresponding stages, to yield, for anionotropic systems, first, a possible bimolecular mechanism for substitution with rearrangement, and, secondly, a possible mechanism for isomeric rearrangement (Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185). The latter mechanism may be written



This idea contained a possible interpretation of some experiments carried out by Burton. He showed (*J.*, 1928, 1650) that the isomerisation of α - to γ -phenylallyl *p*-nitrobenzoate, in

organic dipolar solvents such as phenyl cyanide and acetic anhydride, could be largely diverted into a non-isomeric substitution with rearrangement by the introduction of acetate ions. The production in this experiment of a high proportion of γ -phenylallyl (cinnamyl) acetate in place of *p*-nitrobenzoate was regarded by Burton as strong evidence in favour of the ionisation mechanism of rearrangement. He adduced further support for this conclusion by means of rate comparisons which excluded the alternative idea of successive internal isomerisation and group replacement (*J.*, 1934, 1268).

The possibility remains, however, that the bimolecular mechanism represented in equation (2) above might account for the isomerisation, and, by a completely natural generalisation, for the substitution with rearrangement which occurs on the introduction of acetate ions. As to the isomerisation, no fundamental difficulty need be felt in assuming the availability of *p*-nitrobenzoate ions in small concentration; for Meisenheimer, Schmidt, and Schäfer have shown (*Annalen*, 1933, 501, 131) that the isomerisation of α -phenylallyl *p*-nitrobenzoate is accompanied by side reactions, which in certain conditions include the formation of *p*-nitrobenzoic acid.

The main verifiable consequence of this hypothesis of the mechanism of anionotropic isomerisation is that the anion corresponding to the mobile group should be a powerful catalyst for the rearrangement. We have sought to apply this test in the example of the isomerisation of α -phenylallyl *p*-nitrobenzoate* by examining the effect of added *p*-nitrobenzoate ions on the rate of the rearrangement. The rate of isomerisation of α -phenylallyl *p*-nitrobenzoate, as well as of α -phenylallyl 3 : 4 : 5-tribromobenzoate, was first investigated by Meisenheimer, Schmidt, and Schäfer (*loc. cit.*) by the method of thermal analysis. Owing to the difficulty of inducing crystallisation in the mixtures obtained, the method is, as they mildly remark, "keineswegs restlos erfreulich"; but they were able, nevertheless, to show that, while autocatalytic phenomena appear when the rearrangements are carried out in the absence of a solvent, the isomerisations of both esters in solution approximately follow the first-order rate law. We used the same method and consider that their description of it would be an understatement if it were applied to our conditions: the difficulties mentioned have, in our hands, precluded anything better than semi-quantitative results, which, however, settled the main point in which we were interested.

We show that, in methyl cyanide and acetic anhydride as solvents, the effect of the addition of lithium *p*-nitrobenzoate, though considerable, is not greater than can be accounted for as an activity effect of an added salt on a reaction whose rate is controlled by an ionic dissociation.

In explanation it may be pointed out that, according to the ionisation mechanism of equation (1), there should be no acceleration by *p*-nitrobenzoate ions under the mass law, the rate being proportional to the concentration of the original ester only. On the other hand, there should be an accelerative activity effect, due essentially to the electrostatic attraction of any pre-existing ions for the ions that can be formed by dissociation of the original ester. This can raise the rate by a small multiple at the concentrations at which it is convenient to work, as was shown, both practically and theoretically, in analogous instances, by Bateman, Church, Hughes, Ingold, and Taher (*J.*, 1940, 979). In an example even more closely related to our present case, namely, the unimolecular solvolysis of α -methylallyl chloride in acetic acid, a considerable ionic strength effect of acetate ions has been clearly demonstrated by Roberts, Young, and Winstein (*J. Amer. Chem. Soc.*, 1942, 64, 2157). The requirements of the bimolecular mechanism of equation (2) are quite different. Here activity effects are expected to be comparatively negligible in such experiments as ours, and, if observable at all, they should produce a quite small retardation (*idem, ibid.*). On the other hand, the mass law requires a very great acceleration; for the rate is now proportional to [Anion] [Ester], and the anion concentrations (0.1 to 1.1M) of which we investigated the effects were overwhelmingly large in comparison with the traces which might be formed from the esters.

The rate of isomerisation is definitely increased by the addition of lithium *p*-nitrobenzoate. For example, in methyl cyanide as solvent ([α -phenylallyl *p*-nitrobenzoate] \sim 0.35M) the presence of 0.1M ions increased the extent of isomerisation under comparable conditions from about 28% to about 50%. In acetic anhydride solution, a considerable accelerative effect was observed with 1M concentrations of salt (see experimental section), but it should be noted that the rate of isomerisation in the complete absence of extraneous ions was, nevertheless, of a

* This compound is a particularly appropriate example for study, because, apart from the general desirability of applying our tests to a system for which the data of the previous workers were available, there is a special convenience established by their work, namely, that the isomerisation to γ -phenylallyl *p*-nitrobenzoate can be carried substantially to completion in suitable solvents.

comparable order of magnitude to that obtaining even with such high concentrations of lithium *p*-nitrobenzoate. In no case were we able to induce a facile reaction in the presence of added salt when little or no isomerisation existed in its absence.

We may conclude that the bimolecular mechanism of isomerisation plays no rôle of any importance in the isomerisation of α -phenylallyl *p*-nitrobenzoate in the absence of added salt in the solvents used and under the conditions of our experiments. Until we have completed a more refined and extensive investigation (the results of which will be reported later) of this and other structures we cannot, of course, assert that the isomerisation reactions of anionotropic systems generally, and particularly those taking place in the presence of considerable concentrations of extraneous ions of the same kind as the mobile anion from the structure undergoing rearrangement, cannot in any circumstances follow the bimolecular route; but we may at this stage express the view that this type of mechanism is at least uncommon, if not non-existent, in anionotropic systems. Further evidence bearing on this point is given immediately below and in the following paper.

Reference may now be made to some similar experiments by Meisenheimer and Beutter (*Annalen*, 1934, 508, 58), who used α -phenylallyl acetate and metallic acetates in place of our *p*-nitrobenzoates, and operated in acetic acid medium. Consistently with our results, they found that added lithium and potassium acetates had only fairly small effects on the rate of isomerisation of the ester. Originally we were doubtful whether these results were significant, for the reason that the acid catalysis of anionotropic change is well established, and we had no knowledge of its quantitative importance in Meisenheimer and Beutter's acidic solvent, or of the extent to which it would be modified by the addition of salts, which would suppress the hydrogen-ion concentration. It seemed to us that these authors might have been observing the difference of two contrary effects. Furthermore, since water had not been excluded from the solvent, the results could have been complicated by hydrolysis and subsequent re-esterification. A detailed analysis of Meisenheimer and Beutter's results indicates that these disturbances were, in fact, not completely eliminated, but the absence of any great increase of rate with added acetate ions, taken in conjunction with our similar results in dry, non-acidic solvents, may be regarded as affording some evidence that the bimolecular mechanism is also unimportant in the isomerisation of α -phenylallyl acetate under these conditions. Meisenheimer and Beutter also showed that lithium chloride caused a considerable increase in the rate of isomerisation, although it took no stoichiometric part in the reaction, and, since this is unlikely to be anything other than an activity effect, its existence affords some confirmation of the adequacy of the activity explanation generally.

The existence of salt effects of the order of magnitude of those which appear in Meisenheimer and Beutter's experiments, and in our own, would be very difficult to reconcile with a purely intramolecular picture of the isomeric changes concerned (cf. also the following papers); and we may remark in conclusion that our investigations point to the existence of ionisation as a mechanism of anionotropic rearrangement, and confirm the work of Burton and Ingold in this field of study.

EXPERIMENTAL.

The esters were prepared as described by Burton and Ingold and by Meisenheimer, Schmidt, and Schäfer (*loc. cit.*). Lithium *p*-nitrobenzoate was obtained from *p*-nitrobenzoic acid by exact neutralisation with lithium hydroxide in methyl alcohol and crystallisation from the same solvent.

The isomerisation experiments were carried out in small sealed bulbs, pairs of tubes each containing fixed quantities of α -phenylallyl *p*-nitrobenzoate and solvent, and one of them an added amount of lithium *p*-nitrobenzoate, being heated at the same temperature for known times, after which they were cooled and opened, and the products examined. Two solvents and a variety of heating periods and temperatures were used. The method of working up the products for examination varied slightly according to the solvent employed, as described later. The m. ps. of the solids obtained were determined in capillary tubes with adequate stirring both of the material and of the bath, and with special attention given to the clearing temperatures. The m. ps. observed, together with m. ps. of mixtures with α - or γ -phenylallyl *p*-nitrobenzoate in so far as these were required in order to identify the isolated mixture with the correct branch of the curve, were used in conjunction with the m. p.-composition curve for known mixtures of the two esters (Meisenheimer, Schmidt, and Schäfer, *loc. cit.*) to estimate the rough composition in each case. We record below the details of some typical experiments in the solvents employed.

Methyl Cyanide.—Pairs of tubes each containing α -phenylallyl *p*-nitrobenzoate (0.5 g.) and methyl cyanide (5 ml.), with addition of lithium *p*-nitrobenzoate (0.1 g.) to one, were heated at 112° for 12 hours. The tubes were then cooled and opened, and the solvent was removed under reduced pressure so that no further isomerisation took place. The mixed esters were then extracted completely with light petroleum. The petroleum solution was filtered and the solvent again removed under reduced pressure; the product solidified on cooling. The solid thus obtained from the isomerisation without the addition of lithium *p*-nitrobenzoate had m. p. 35° (corresponding to about 28% of γ -phenylallyl *p*-nitrobenzoate) and that

obtained from the reaction in the presence of the salt had m. p. 48—54° (corresponding to about 50% of γ -phenylallyl *p*-nitrobenzoate). Results obtained after heating tubes, with contents the same as the above, for 2 hours at 120° indicated that the presence of the salt had increased the isomerisation approximately from 10% to 20%.

Acetic Anhydride.—Preliminary experiments showed that a small amount of impurity was present in the products resulting from the use of this solvent, and the procedure used in the isolation of the esters was modified as follows. The tubes, after being heated, were broken into ice-cold water and the mixture was made just alkaline with dilute sodium hydroxide solution. After much stirring, the oily product then partly solidified. It was dissolved in light petroleum, and the solution was filtered from traces of residue, concentrated to a small volume, and cooled. The bulk of the product crystallised after this treatment and was separated, dried, and examined as previously described. A second (small) fraction was obtained after complete removal of the petroleum solvent, and this solidified with great difficulty after being cooled and agitated. When α -phenylallyl *p*-nitrobenzoate (5 g.) was heated for 20 hours in acetic anhydride (25 ml.) at 100°, the two fractions obtained as described had the following m. ps.: (1) 58—64°, (2) 54° (corresponding to about 60% of γ -phenylallyl *p*-nitrobenzoate). The addition of 5 g. of lithium *p*-nitrobenzoate to a similar solution containing 5 g. of the ester in 25 ml. of solvent gave, after 5 hours' heating at 100° and subsequent treatment as before, two fractions as follows: (1) m. p. 74°, (2) m. p. 62—64°, these results indicating about 85% conversion into γ -phenylallyl *p*-nitrobenzoate in the presence of the salt.

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