ASYMMETRIC SYNTHESIS
IN ANIONOTROPIC CHANGES.

A Study of Mobile Anion Tautomerism in the Esters of
α-Phenyl-γ-Methylallylalcohol and γ-Phenyl-α-Methylallylalcohol.

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In investigations of \((\pm)\-\text{Y-dimethylallyl alcohol}\) (Hills, Kenyon, and Phillips, J., 1936, 576.) led to the belief that an optically active product would be obtained when \((-)\-\text{phenyl-\text{\(\alpha\)}}\-methylallyl alcohol (and its derivatives) was converted into \(\text{\(\gamma\)}}\-\text{phenyl-\(\alpha\)}}\-methylallyl alcohol (and its derivatives). This expectation has been fully realized; the hydrogen phthalic ester of \(\,\text{\(\epsilon\)}}\-\text{phenyl-\(\epsilon\)}}\-methylallyl alcohol changes into the isomeric ester containing \(87\%\) of one optical enantiomorph.

The transformation

\[
\text{CHPhX.CH:CHMe} \rightarrow \text{CHPh:CH.CHXMe}
\]

also proves to be an exceptionally convenient anionotropic system for investigation since the more reactive esters of \(\,\text{\(\epsilon\)}}\-\text{phenyl-\(\epsilon\)}}\-methylallyl alcohol change into their isomerides at ordinary temperatures either in solution or (in the case of the hydrogen phthalic ester) in the crystalline state. By using optically active compounds this change can readily be followed polarimetrically, and thus a convenient and accurate method of studying the reaction is available. Like the hydrogen phthalic ester of \(\,\text{\(\epsilon\)}}\-\text{dimethylallyl alcohol}, esters of \(\,\text{\(\epsilon\)}}\-\text{phenyl-\(\epsilon\)}}\-methylallyl alcohol undergo conversion in methylalcoholic and acetic acid solution and yield respectively the methyl ether and the
acetic ester of γ-phenyl-α-methylallyl alcohol. Esters of γ-phenyl-α-methylallyl alcohol undergo similar replacement reactions but much more slowly.

On addition of bromine, (+)γ-phenyl-α-methylallyl alcohol yields two methyl-αβ-dibromo-β-phenylethyl carbinols which may be separated by fractional crystallization. One of these, on oxidation, yields (+)methyl-αβ-dibromo-β-phenylethyl ketone, while the other gives the (-)-enantiomorph possessing numerically the same rotatory power. When bromine is added to (+)γ-phenyl-α-methylallyl and the mixture oxidised without any form of previous separation the resulting ketone is optically active. As the original centre of asymmetry in the compound has been destroyed by oxidation this reaction represents a new type of asymmetric synthesis.
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INTRODUCTION.

A study of the optical behaviour of \( \alpha\gamma \)-dimethylallylalcohol undertaken by Hills, Kenyon and Phillips, has led to some unexpected results, and it was in an effort to throw some light upon these, that the present work was undertaken. The similarly constituted alcohol, \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol, as had already shown by Burton, readily undergoes a tautomeric change into its isomer \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol; and an investigation of this change in the optically active alcohols has not only helped in elucidating the difficult problems raised by the original investigation, but has proved of considerable interest in itself.
Until 1828 when urea was first synthesised from purely inorganic sources by Wöhler, it was maintained by many that carbon compounds of the type still known as "Organic" were solely the product of vital forces, and could not be produced in the laboratory except from material itself, a product of metabolism.

During the first half of the nineteenth century the science of organic chemistry as we know it today was in process of development, and an enormous number of carbon compounds were synthesised both from organic and inorganic sources. However one great point of dissimilarity between compounds synthesised in the laboratory and naturally occurring material still remained apparent. When a substance whose molecule is asymmetric is produced by vital synthesis in a living cell it is nearly always found in an optically active state, while the same material synthesised in the laboratory is invariably inactive.

In 1898 F.R. Japp held that "The production of single asymmetric molecules, or their isolation from the mixture of their enantiomorphs is, as Pasteur firmly held, the prerogative of life" and this opinion was held by many of his contemporaries. In opposition
to this view, Van't Hoff was of the opinion that an unsymmetrical physical force could be used by human operators to effect the unsymmetrical synthesis of optically active compounds.

Numerous attempts to effect such a synthesis are described in the literature, but for many years all efforts met with complete failure. Only in recent years has any real advance been made, whereby the asymmetrical photochemical decomposition of several externally compensated compounds has at last been conclusively demonstrated. This result was obtained by Kuhn and Brawn\(^2\) by the photochemical decomposition of optically inactive ethyl \(\alpha\)-bromopropionate with circularly polarised light. This success was largely due to the recognition that circularly polarised light would constitute an unsymmetrical physical agency, and a realisation that the asymmetric group to be destroyed must possess an optically active absorption band near the optimum wavelength for its photochemical decomposition to ensue.

Another method of attack upon the problem of preparing an asymmetric molecule unaccompanied by its enantiomorph has produced a great variety of interesting results. In 1908 Rosenthaler\(^3\) carried out the unsymmetrical addition of hydrocyanic acid to many different
aldehydes in the presence of an enzyme "Oxynitrolase" occurring in almond emulsin. In each case the cyanhydrin was produced in a highly optically active state, but the reaction amounts to little more than carrying out a natural process under laboratory conditions.

Many other cases where an asymmetric carbon atom has been synthesised by the catalytic action of an enzyme appear in the literature, and in nearly every instance one enantiomorph is produced in excess of the other. Perhaps the most striking reaction of this type is that investigated by Neuberg who used the enzyme "Ketonaldehydemutase" to transform methylglyoxal into lactic acid by addition of the elements of water. The reaction yields almost theoretical amounts of optically pure lactic acid.

Emil Fischer was one of the first to attempt to synthesise an optically active compound without the use of enzymes as directing agents. In 1901 he attempted to prepare optically active salicylaldehyde-cyanhydrin from helicin in the following way:

\[
\text{CHO(CHOH)}_4\text{CH}_2\text{OC}_{6}\text{H}_4\text{CHO} \rightarrow \text{CHO(CHOH)}_4\text{CH}_2\text{OC}_{6}\text{H}_4\text{CH}^*\text{CN} \\
\text{helicin} \rightarrow \text{helicin cyanhydrin}
\]

\[
\text{CHO(CHOH)}_4\text{CH}_2\text{OH} + \text{OHC}_{6}\text{H}_4\text{CH}^*\text{CN} \]

\text{glucose}
hoping that the optically active helicin would take the place of enzymes or circularly polarised light in providing the source of an asymmetrical bias upon the reaction. The desired product could not however be isolated, and there followed many other attempts, by Fischer himself, and by other investigators, to carry out similarly conceived experiments.

About the same time Marckwald gave his classical definition of asymmetric synthesis which is essentially the same as that now generally accepted. In order to produce a "Partial Asymmetric Synthesis" as they are now known, it is necessary to generate a new asymmetric carbon atom in association with the molecule of a substance already optically active. The intermediate product so produced must not be subjected to any form of analytical separation, and the original optically active material must be removed leaving the new asymmetric compound in an optically active state.

Marckwald then claimed to have produced the first positive result, but his work was severely criticised by Cohen and Patterson. Soon afterwards however, McKenzie reported a series of undoubted asymmetric syntheses. It was found that the pyruvic esters of (-)menthol, (-)borneol, and (-)amylalcohol all yielded optically active lactic acid on reduction and
subsequent saponification.

\[
\text{CH}_3\text{COOCOR} \rightarrow \text{CH}_3\text{CH(OH)COOR} \rightarrow \text{CH}_3\text{CH(OH)COOH}
\]
active.

In the same publication Mc Kenzie reported the asymmetric synthesis of atrolactinic acid from benzoylformic acid by the directing agency of \((-\))menthol.

The action of methyl magnesium iodide on \((-\))menthy1 benzoyl formate gives the two compounds

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C} & \text{O}_{\text{OMgI}} \quad \text{(A)} \\
\text{CH}_3\text{COOC}_{10}\text{H}_{19} & \text{(-)} \\
\text{C}_6\text{H}_5\text{C} & \text{O}_{\text{OMgI}} \quad \text{(B)} \\
\text{CH}_3\text{COOC}_{10}\text{H}_{19} & \text{(-)} \quad \text{(+)} \\
\end{align*}
\]
with an excess of \((A)\) over \((B)\). When the mixture was decomposed with ice and mineral acid the menthyl atrolactinates formed yielded on hydrolysis \((-\))atrolactinic acid (\([\alpha]_b = -9.5^\circ\) in ethyl alcoholic solution).

Optically pure \((-\))atrolactinic acid has \([\alpha]_b = -37.7^\circ\) in the same solvent.

It is to be noticed that the first stage in all asymmetric syntheses of this type is the production in unequal amounts of two diastereoisomerides. In order to produce an asymmetric synthesis in the sense of the term originally defined by Fischer and by Marckwald and Mc Kenzie, it is necessary to remove the original asymmetric centre, leaving the new asymmetric centre in an optically active state. Thus the action of methyl
magnesium iodide on \((-\)benzoin apparently proceeds entirely unsymmetrically, one only of the two possible diastereoisomerides (A) and (B) being isolated.

\[
\begin{align*}
C_6H_5 & \quad C_6H_5 \\
H-C-OH & \rightarrow \quad H-C-OH \\
CO & \quad CH_3-C-OH \\
C_6H_5 & \quad C_6H_5
\end{align*}
\]

But this is not regarded as an asymmetric synthesis as the original asymmetric carbon atom has not been removed.

Other investigators have since performed similar experiments with equal success, but it should be noticed that in all cases hitherto recorded the optical activity of the product is small, a fact which has led some authors to doubt whether vital syntheses are of the same type. However, in the present work asymmetric syntheses are described which result in products containing a much higher proportion of one enantiomorph.
The fact that asymmetric syntheses are possible was taken to indicate some connection between the spatial configuration of the optically active directing agent used in the synthesis and that of the new dissymmetric molecule formed. The action of the force which was assumed to arise in all asymmetric systems, and to be capable of influencing an adjacent system in such a way as to make it optically active was called "Asymmetric Induction" for the first time by Erlenmeyer in 1911.

In 1892 it was tentatively suggested by Le Bel that an unsaturated ethylenic double bond might act as a centre of optical activity; and Erlenmeyer later claimed to have isolated cinnamic acid and benzaldehyde in optically active forms. The rotatory powers of his products however were very small and may have been due to traces of foreign matter; but his later claim to have prepared (-)-αβ-dibromo-β-phenylpropionic acid by bromination of cinnamic acid in the presence of glucose or fructose appears to rest on a more secure foundation.

In 1924 Lowry and Walker postulated that unsaturated chromophoric groups in optically active
molecules exhibit "Induced Asymmetry" if coupled sufficiently closely to the centre of fixed asymmetry. The Drude equation expressing the complex rotatory dispersion of certain optically active ketones was found to contain one term whose dispersion parameter corresponds closely to the ketonic absorption band, and it was suggested that this term represents the contribution of the keto group towards the total rotatory power of the molecule.

McKenzie and Mitchell\textsuperscript{10} sought to show the presence of induced asymmetry in the carbonyl group, in an ingenious series of experiments of the following type:

\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{CO COOC}_1\text{0H}_{19}^{(-)} + \text{C}_6\text{H}_5\text{CO COOC}_1\text{0H}_{19}^{(+)} \\
\downarrow
\end{array}
\]

in equal quantities.

\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{CO COOC}_1\text{0H}_{19}^{(-)} + \text{C}_6\text{H}_5\text{CO COOC}_1\text{0H}_{19}^{(+)} \\
\end{array}
\]

in unequal quantities.

The starting materials in each case were esters of \(\alpha\) ketonic acids and optically active alcohols such as \((-\text{)}\) menthol or \((+\text{)}\) \& \((-\text{})\) borneol. All these esters displayed definite mutarotation in ethyl alcoholic solution, and some of them in higher alcohols. Mutarotation was not displayed in non alcoholic solvents such as benzene nor in methyl alcoholic solution but it was found that the esters after recovery from
an ethyl alcoholic solution, on redissolving in the solvent, showed the same initial rotatory power followed by the same mutarotation phenomenon as before. The mechanism of the mutarotation process suggested by the investigators was that, under the influence of the fixed asymmetric centre, the centre of labile asymmetry in the carbonyl group passed into an unequal mixture of the (d) and (l) forms; but it is unfortunate that the mutarotation may be ascribed more simply to coordination with solvent molecules, particularly as it has been observed only in highly coordinating solvents.

These experiments led McKenzie to suggest that the ethereal solution of (−)-menthyl benzoyl formate used in the synthesis of atrolactic acid described in the previous section already contained a mixture of

$$\text{C}_6\text{H}_5\text{CO.COCO}_\text{H}_2$$

and

$$\text{C}_6\text{H}_5\text{CO.COCO}_\text{H}_2$$

in unequal amounts which, on addition of the Grignard reagent gave rise to a correspondingly unequal mixture of the diastereoisomeric Grignard complexes. Optically active benzoyl formic acid is not regarded as existing except in close contact with another optically active molecule, as attempts made to resolve the acid by crystallisation of its alkaloidal salts proved entirely negative.

McKenzie has actually used this theory to predict
the sign of rotation of the product resulting from an asymmetric synthesis. When the numerical value of the rotatory power of an α-ketonic ester increases during mutarotation in alcoholic solution, the substituted glycollic acid formed by interaction with a suitable Grignard reagent should rotate the plane of polarised light in the same sense as the initial ester. In the large majority of cases this prediction has been realised. It is demonstrated in a particularly striking way by the synthesis of anisylmethyl glycollic acid. ¹¹ (-)Menthyl anisylformate shows an increase in laevorotation in isobutyl alcohol, and it was consequently predicted that the acid obtained from it by the action of methyl magnesium iodide would be laevo-rotatory. On the other hand, (-)menthyl pyruvate decreases in laevorotation in alcoholic solvents and should therefore give rise to the same acid in its dextrorotatory form by the interaction of anisyl magnesium bromide. This proved to be the case, and as the enantiomorphous forms of anisylmethylglycollic acid are less soluble than the racemic mixture, each hand separated from benzene in an optically pure state.
Phillips and Kenyon\textsuperscript{12} clearly demonstrated the possibility of optical activity due to the presence of an atom to which only three groups are attached, by the resolution of sulphinic esters (I) and unsymmetrical sulphoxides (II).

\[
\text{I} \quad \begin{array}{c}
\overset{-}{\overset{+}{S}} \overset{\text{OR}}{\text{C}_7\text{H}_7} \\
\end{array} \\
\text{II} \quad \begin{array}{c}
\overset{-}{\overset{+}{S}} \overset{\text{CH}_3}{\text{C}_6\text{H}_4\text{COOH}} \\
\end{array}
\]

There is strong theoretical and experimental support for the existence of semipolar double bonds in these compounds, which may thus be formulated

\[
R : O : S : O : \\
R'
\]

and the tentative suggestion put forward by Phillips and Kenyon was that the lone pair of electrons on the sulphur atom acts as a fourth radical, and the asymmetry
in the compound is of the same type as that shown by a compound containing a tetravalent carbon atom.

This view does not readily lend itself to the idea that the carbonyl group or ethylenic double bond can retain anything more than a transient asymmetry; for on theoretical grounds Sugden, Reed and Wilkins\textsuperscript{13} state that semipolar double bonds are not found when their existence would necessitate the presence of a sextet around one or other of the carbon atoms concerned; that is to say, the arrangements:

\[
\begin{align*}
R & \quad \text{and} \quad R \\
\cdot & \quad \cdot & \quad \cdot \\
\text{C} & \quad \text{C} & \quad \text{C} \\
\cdot & \quad \cdot & \quad \cdot \\
\text{X} & \quad \text{X} & \quad \text{X}
\end{align*}
\]

\[
\begin{align*}
R & \quad \text{and} \quad R \\
\cdot & \quad \cdot & \quad \cdot \\
\text{C} & \quad \text{C} & \quad \text{C} \\
\cdot & \quad \cdot & \quad \cdot \\
\text{H} & \quad \text{H} & \quad \text{H}
\end{align*}
\]

could not in any case be considered stable ones.

It is also to be noticed that only in the case of an assumed polar ethylenic compound where two types of tricovalent carbon atoms would exist, could the postulated asymmetric carbon atom possess a lone pair of electrons; and a stable optically active carbonyl group is consequently not to be expected, even, if under some conditions, the double bond could be semipolar.

Bergmann and Tschudnowsky\textsuperscript{14} state that the existence of a semipolar double bond need not be postulated in order to explain the asymmetry of the sulphoxides. They have shown from measurements of the dipole moments
that the oxygen atom in a sulphoxide does not lie in the same plane as the sulphur atom, and its two attached radicals. They suggest that the enantiomorphic forms of the sulphoxide could be represented as follows:

A similar view could also be applied to the carbonyl and ethylenic groups and would be free from the necessity of assuming polarity of the bonds, but as this distortion would involve a strain on the valency bonds, it could only be assumed to arise under the direct influence of an associated asymmetric carbon atom.

Wallis and Adams differentiate clearly between the two types of tricovalent carbon radicals:

\[
\begin{align*}
\text{I} & \quad \left[ \begin{array}{c}
R_1 \\
\vdots \\
R_2: C \\
\vdots \\
R_3
\end{array} \right]^- \quad \text{"Carbanion"} \\
\text{II} & \quad \left[ \begin{array}{c}
R_1 \\
\vdots \\
R_2: C \\
\vdots \\
R_3
\end{array} \right]^+ \quad \text{"Carbonium ion"}
\end{align*}
\]

On treating \((-\)12-phenyl-12-\(\beta\)-benzoxyanthrenethioglycollic acid (1) with sodium in liquid ammonia
they show that the resulting product is optically active. The intermediate product (ii) is a true carbanion and must have been able to retain asymmetry while existing in the free state. This seems to show that in the case of a carbanion the three carbon valency bonds are not coplanar.

On the other hand, when the same radical is produced as a cation by addition of silver nitrate to (i) the resulting product is totally inactive, showing that a carbonium ion intermediate is incapable of maintaining asymmetry and is therefore probably coplanar.

Walden inversion reactions have yielded further information on this point. It has been shown that where the asymmetric carbon atom is left as a carbonium cation by the removal of an attached radical the incoming group
attaches itself in such a way as to produce inversion of configuration often accompanied by a high degree of racemisation. If, however, the displaced group is removed as a cation, leaving the asymmetric carbon atom as a 'carbanion', optical activity is largely maintained and no inversion of configuration results.

Since the work of Brlenmeyer, the idea of asymmetric induction has been used extensively in theoretical discussion but, in spite of attempts by many investigators, unless the recent publication of Hills, Kenyon and Phillips may be regarded as such, no single piece of experimental evidence has been forthcoming, which definitely proves its existence without the possibility of alternative explanations.

In this paper, Hills, Kenyon and Phillips show that (+) α,γ-dimethylallyl chloride prepared from (-) α,γ-dimethylallyl alcohol is hydrolysed by cold water to form a (-)-alcohol possessing optical properties quite different from those displayed by the original alcohol. It was shown that on reducing the new alcohol with hydrogen over a platinum catalyst, optical activity disappears completely with removal of the double bond, while the original (-)-alcohol on reduction by the same method readily gave the corresponding saturated alcohol in an almost optically pure
The only explanation of this phenomenon appears to be that during the process of hydrolysis, the original centre of asymmetry is completely racemised, leaving a compound which owes its optical activity to induced dissymmetry in the double bond. If this is the case, the new product is surprisingly stable, as it retains its optical activity for many days after preparation. The optical behaviour of \((-\)\(\alpha\gamma\)-dimethylallylalcohol itself, however, is quite different from that of other members of the same series, \(\alpha\gamma\)-dimethylallylalcohol displays complex rotatory dispersion, while its esters, and the related alcohols \(\alpha\)-phenyl-\(\gamma\)-methylallylalcohol and \(\gamma\)-phenyl-\(\alpha\)-methylallylalcohol and their esters, all display simple dispersion.
III. TAUTOMERISM.

Since Laar first drew attention to it in 1885, the structural isomerism displayed by acetoacetic ester has become the classical case of tautomerism. The structure to be ascribed to this compound was one of the long debated problems of organic chemistry: one school of thought believing with Geuther that the molecule was best represented by

\[ \text{CH}_3\text{C(OH)}:\text{C} = \text{O}:\text{C} = \text{O}\text{C}_2\text{H}_5 \]

while Frankland and others held that the compound was a ketone

\[ \text{CH}_3\text{CO.CHi } : \text{C} = \text{O.C}_2\text{H}_5 \]

The substance displays the properties both of a ketone and of an alcohol: on hydrolysis with dilute alkalies it yields acetone, and with nitrous acid isonitroso acetone is formed, while on the other hand acetoacetic ester readily forms a sodium salt and a crystalline copper salt.

The question was finally set at rest by the separation of two isomeric compounds by Knorr who succeeded in freezing out the pure ketonic form by cooling concentrated solutions to -78°C. This form separates in crystals m.p. -39°C and gives no immediate colouration with ferric chloride. The enol form, which
gives an intense colouration with ferric chloride, is separated by treating the sodio derivative with dry hydrogen chloride at -78°C.

Since 1885 many other cases of tautomerism have come to light, a very important section of which have been those of the keto-enol type of which acetoacetic acid itself is a good example. The types of tautomerism vary a great deal in lability and in the equilibrium position of the isomers. In some cases the velocity of interconversion of the isomers is so great that the individuals cannot be isolated, or is so small that the change is unnoticed except in the presence of catalysts or under the influence of higher temperatures. In others the position of equilibrium may be so one-sided that the reversibility may readily escape detection.

In view of the extreme mobility of many of the dynamic isomers it is evident that chemical methods for determining the position of equilibrium are of limited application, as the reagents used are likely to upset the equilibrium by removal of one isomer. In these cases physical methods present the only means of attack.

It has been found that in keto-enol transformations, solvents effect the position of equilibrium; while a rise in temperature usually favours production
of the keto form, showing that this form has the greater energy content.

Density and volume changes have been applied to this type of change, Schaum\textsuperscript{18} observing that freshly distilled acetoacetic ester acquires a different density on standing. Refractivity and dispersion changes have also been applied, while a study of changes in optical rotatory power has been used with great success by Lowry\textsuperscript{19} in the investigation of nitro camphor and bromonitrocammor.

Many views as to the nature of tautomeric changes have been put forward; Laar, referring especially to keto-enol transformations, held that the mobile hydrogen atom was in a state of constant oscillation, so that both forms might be regarded as present in the substance in a labile state: on the other extreme Lowry holds that "dynamic isomerism" is merely a special case of ordinary isomeric change, where the reaction conditions are such that the change is reversible. Lowry points out that in many cases the presence of a catalyst is essential, and shows that the enolic form of benzoyl camphor in chloroform solution will remain unchanged for a long period, but that the dust of the laboratory or the soft glass of a polarimeter tube is sufficient to start the transformation.
In 1892 Wislicenus clearly expressed for the first time the ionic theory of tautomerism. In his article "Uber Tautomerie" he points out that the mobility of a tautomeric change is greatly affected by the dissociating power of the medium, and comes to the conclusion that the interconversion of the forms is preceded by liberation of mobile hydrogen as a cation. Movement of the bonds in the anion then occurs followed by recombination of the hydrogen in a new position. J.W. Bruhl found that the velocity of conversion of ethyl mesityloxide oxalate from the enolic to the ketonic form is closely related to the dielectric constant of the medium. The importance of the nature of the attached groups upon the ease of dissociation of the mobile hydrogen was pointed out by Claisen who formulated the rule that "the enol is the more easily formed the more negative is the character of the acid radical united to the methylene group".

Between 1920 and 1926 many papers bearing upon the subject of mobile hydrogen tautomerism were published by Ingold, Kon, and others, which had a special bearing upon the influence of structural conditions upon the mobility and equilibrium of the reversible changes. Under the name of mobile cation tautomerism or cationotropy the whole matter was reviewed, attention
being especially directed towards "two carbon systems" of the general type

\[ x - y = z \rightarrow x - y = z \rightarrow x = y - z \rightarrow x = y - z \]

and "three carbon systems" where the hydrion, on removal from the system leaves an anion, \( \text{C} = \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} \)

which, as a result of tautomeric electronic displacement, results in either of two modifications;

\( \text{C} = \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} \) or \( \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} \); the returning cation having the choice of two positions of re-entry.

A convenient system of representing the displacement of electrons was adopted: \( \text{C} = \text{C} \cdot \text{O} \) representing the displacements:

\[
\begin{align*}
R_1 \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} \cdot H & \rightarrow R_2 \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} \cdot H \\
R_3 \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O} & \rightarrow R_4 \text{C} \cdot \text{C} \cdot \text{C} \cdot \text{O}
\end{align*}
\]

Below is an example of the type of system investigated as a member of the three carbon system.

\[
\begin{align*}
\text{CH}_2 \text{CH}_2 \text{C}=\text{CH} \cdot \text{C}=\text{CH}_2 & \xrightarrow{\text{slow}} \text{CH}_2 \text{CH}_2 \text{C}=\text{CH} \cdot \text{CO} \cdot \text{CH}_3 \\
\text{CH}_2 \text{C}=\text{CH} \cdot \text{C}=\text{CH}_2 \text{OH} & \xrightarrow{\text{rapid}} \text{CH}_2 \text{C}=\text{CH} \cdot \text{C}=\text{CH}_2 \text{CO} \cdot \text{CH}_3
\end{align*}
\]

It was found that the activating efficiency of groups
terminating the three carbon system may be represented by the sequence

$$\text{CO.CHi} \succ \text{COCl} \succ \text{COOR} \succ \text{COOH}$$

which is also the sequence arranged in order of meta-directing power in organic substitution. This connection is justified from theoretical considerations, as in both cases the activating effect may be traced to the ability of the oxygen atom in the terminal group to act as the seat of a negative charge.

The successful elucidation of many difficulties with regard to cationotropy naturally led investigators to study the conditions under which tautomerism of the opposite type, "mobile anion tautomerism" takes place. Here the mobile group separates as an anion, leaving an electromeric cation in which the positive charge tends to redistribution.

In 1927 Ingold began an investigation of the $\alpha$- and $\beta$-methylallyl alcohols as a case of mobile anion tautomerism affording an interesting parallel with the mobile cation tautomerism under investigation at that time.

His work led him to postulate that the facility with which $X$ separates as an anion in the following system

$$\begin{align*}
\text{R} - \text{CH} - \text{CH} = \text{CH} \_ & \rightleftharpoons \text{R} - \text{CH} - \text{CH} = \text{CH}_2 \\
\end{align*}$$
depends:

1. on the intrinsic stability of X as indicated for example by the strength of the acid HX.
2. on the presence of external cations, or in their absence, on the polar field of the neutral solvent as indicated by its dielectric constant.
3. the ability of R to supply electrons to the depleted carbon atom as shown by its o-p-orienting power in aromatic substitution.

In 1928 a paper by Ingold and Burton appeared, in which mobile anion tautomerism in substituted allylalcohols was investigated with reference to the effects of the groups R and R' on the mobility and equilibrium of the system.

\[
\text{R-CH=CH-CH}_2^+ \quad \text{R'-CH-CH=CH}_2^- \quad \text{R-CH-CH=CH}_2^- \quad \text{R'-CH=CH-CH}_2^+ \\
\]

where \( X \) is the migrating anion (OH, Cl, OAc etc.).

It was found that in the system

\[
\text{I} \quad \text{Ph-CH=CH-CH}_2^+ \quad \text{Ph-C-CH=CH}_2^- \quad \text{II} \quad \text{Ph-CH=CH-CH}_2^+ \quad \text{Ph-C-CH=CH}_2^- \\
\]

the degree of mobility is not very great. The alcohols can be obtained as separate individuals and each gives a crystalline p-nitrobenzoate derivative. Burton and Ingold were unable to transform (I) into (II) by means of dilute sulphuric acid. The alcohol (I) however, is smoothly converted into the acetate of (II) by boiling
with acetic anhydride, while the two alcohols give the same crystalline bromide, cinnamyl bromide.

The p-tolyl analogues of (I) and (II) also exist separately, but the former is converted by acetic anhydride into the acetate of the latter more readily than in the phenyl series. Smooth conversion into substituted cinnamyl bromide occurs when the p-tolyl analogue of (I) is treated with cold hydrogen bromide in acetic acid solution. The tautomerism is therefore rather more labile in the case of the p-tolyl substituted analogues than with the alcohols (I) and (II) themselves.

In the case where R is methyl and R' is hydrogen the facility of the tautomerism proves to be perceptibly less than in the phenyl series. In the system

\[
\text{Me} \rightarrow \text{C} - \text{CH} = \text{CH}_2 \rightleftharpoons \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_2
\]

each alcohol yields its own acetyl derivative on boiling with acetic anhydride. Furthermore both alcohols yield an equilibrium mixture of isomeric chlorides in which the chloride of (IV) is the main constituent.

It was suggested that the greater facilitation of the isomeric change by the phenyl group, than by the methyl group, was due to the more complete neutralisation of the positive charge left on the \(\alpha\)-carbon atom
by the separation of the anion in the former case, the phenyl group possessing the looser electronic system. If this hypothesis be correct the $C_6H_5Cl(p)$ group should show a strong activating effect in comparison with the $p-\text{CH}_3C_6H_4\rightarrow$ group, for only in the former case is a lone pair of electrons available to supply the deficit of electrons on the $\alpha$-carbon atom left by removal of the anion $X$.

It was found that in the $p$-chlooro series

$$\begin{align*}
\text{Cl} & \quad \text{CH} = \text{CH} = \text{CH} - C_6H_5 \\
\text{VII} & \quad \longleftrightarrow \quad \text{Cl} \quad \text{CH} = \text{CH} = \text{CH} - C_6H_5 \\
\text{VIII} & \quad \text{Cl} \quad \text{CH} = \text{CH} = \text{CH} - C_6H_5 \\
\end{align*}$$

not only the acetates, but the alcohols themselves passed into the equilibrium mixture, (VIII) being the major component.

This establishes the order of facilitation of three carbon anionotropy by $\alpha$-substituents as

$$\text{pClC}_6\text{H}_4 \gg \text{pMeC}_6\text{H}_4 > C_6\text{H}_5 \gg \text{CH}_3 > H$$

which agrees, as it theoretically should, with the $\alpha$-$p$-orienting sequence $\text{Cl} > \text{Me} > H$ inferred in the ordinary way from the proportion of isomers formed in benzene substitution. In each case the activity of a radical depends upon its capability of acting as an electron donor, or increasing the tolerance of the
a-carbon atom for a shared sextet.

In 1928 Burton investigated this type of tautomerism with special reference to the fate of the anion and examined the following hypothesis.

1. "Concomitantly with the elimination of X, its equivalent, derived from an assumed catalyst, such as HX, may be introduced in the new position by an internal cyclic process.

\[ R.CHX.CH:CHR' \overset{\text{X}}{\rightleftharpoons} R.CH.CHiCHR' \]

2. X leaves the molecule as X in combination with a catalyst (e.g. solvent molecule) to be returned subsequently to the electromeric cation derived from another molecule.

\[
\begin{align*}
R.CHX.CH:CHR' & \rightleftharpoons \overset{\oplus}{RCH.CH:CHR'} \\
& \overset{\leftarrow}{\mathcal{V}X} (\text{catalyst}) \\
R.CH:CH.CHXR' & \rightleftharpoons \overset{\oplus}{RCH:CH.CH:CHR'}
\end{align*}
\]

Hypothesis (2) raises the question as to whether the departing anion combines with the solvent by formation of a coordinate link or whether the formation of residual electrovalencies arising from attraction due to external molecular fields ("molecular combination", "dipole association" etc.) would suffice. Furthermore the volatile non-salt-like character of the anionotropic
substances indicates that ionization of X might not be followed by dissociation of the ions; so that X might, throughout the isomeric change, remain in electrovalent association with the cation of the molecule which gave rise to it.

Thus the possible modifications of mechanism (2) are:

(2a) Covalent interaction with catalyst, and ionic dissociation.

(2b) Molecular association with the catalyst and ionic dissociation.

(2c) Covalent interaction with catalyst; ionization but no dissociation.

(2d) Molecular association with catalyst; ionization but no dissociation.

In the system:

```
  O.CO.C₆H₄NO₂
  Ph.CH.CH₂CH₂

I  I
  Ph.CH:CH.CH₂
  O.CO.C₆H₄NO₂
```

(1) α-Phenylallyl-p-nitrobenzoate may be left some months in acetic acid without change, or in acetic acid containing a few drops of 30% hydrobromic acid or alcoholic hydrochloric acid. These observations tell against mechanisms (1), (2a), and (2c) for which either a weak or strong acid ought to furnish the best catalyst.
(ii) With boiling acetic anhydride (I) passes smoothly into its isomeride — this tells against mechanism (1) as it would lead to the production of the isomeric acetate.

(iii) Carboxyl groups are well known for the facility with which they form covalent addition compounds with anions, and the catalytic activity of acetic anhydride may be due to this cause (2a), (2c). The dielectric constant of acetic anhydride is high, 20.5, and its external electric field as measured by the molecular dipole moment must be high. This might also be the cause of its activity. (2b), (2d).

(iv) Benzonitrile has a high dielectric constant but does not coordinate readily, and in this solvent conversion occurs just as readily. (2b), (2d).

(v) In chlorobenzene (dielectric constant 6) which is structurally incapable of forming a covalent union with an anion, the isomeric change occurs smoothly but more slowly (2b), (2d).

From this evidence it now appears that the decision rests between (2b) and (2d).

\(\alpha\)-Phenylallyl-\(p\)-nitrobenzoate was therefore heated in acetic anhydride containing acetate ions supplied by the addition of tetramethylammonium acetate. A mixture of the \(p\)-nitrobenzoate and the acetate was produced, a result which favours (2b).
It was therefore suggested that the anion combines electrostatically with the catalyst, according to mechanism (2b).
IV. ASYMMETRIC SYNTHESIS IN ANIONOTROPIC CHANGES.

The resolution of the isomeric \(\alpha\)-phenyl-\(\gamma\)-methylallyl and \(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohols, and the study of their tautomerism, was undertaken with the object of investigating the nature of the dissymmetry induced in the double bond by the centre of fixed asymmetry contained in the molecule. Results obtained in the investigation of \(\alpha\),\(\gamma\)-dimethylallyl alcohol by Hills, Kenyon and Phillips, led to the belief that an optically active product would result from the isomeric change. This expectation was fully realised, and it was found that the hydrogen phthalic ester of \(\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol changed into the isomeric ester containing 87.3\% of one optical enantiomorph.

The tautomeric change

\[
\begin{align*}
H \\
\text{I} & \quad \text{Ph} \xrightleftharpoons{\text{OH}} \xrightarrow{\text{Me}} \text{OH} \\
\text{II} & \quad \text{Ph} \, CH \, CH \, Me \, CH \, CH \, OH \\
\end{align*}
\]

also proves to be an exceptionally convenient system for investigation as an example of anionotropy, for the reason that the more reactive esters of \(\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol change into their isomers at ordinary temperatures either in solution, or (in the case of the hydrogen phthalic ester) in the crystalline
state. By using optically active compounds this change can readily be followed polarimetrically, thus giving an accurate and convenient method of studying the reaction.

This finer method of investigation has confirmed the general principles elucidated by earlier investigators, but, as is often the case, has disclosed contradictions and anomalies, showing that the earlier and simple rules are insufficient to determine all the behaviour of the tautomeric system.
Preparation and Resolution of the Isomeric Alcohols.

\( \gamma \)-Phenyl-\( \alpha \)-methylallylalcohol was prepared by the interaction of cinnamaldehyde with a Grignard complex formed by the addition of methylbromide to magnesium, and had b.p. 129-131\(^\circ\)/11 mm., m.p. 33\(^\circ\). Its resolution was effected by means of the fractional crystallization of the cinchonidin and brucine salts of the hydrogen phthalic ester. The optically active carbinol is a beautifully crystalline compound, and showed no tendency to undergo mutarotation either in solution or in the fused state. From it the acetate, p-nitrobenzoate, hydrogenphthalate and p-xenylurethane were readily prepared in an optically active condition. In order to prove its constitution and to show that the resolution had been complete, \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol was reduced to the corresponding saturated carbinol. The product was shown to be optically pure \( \gamma \)-phenyl-\( \alpha \)-methylbutylalcohol which had been resolved previously by Pickard and Kenyon\(^{27}\).

\( \alpha \)-Phenyl-\( \gamma \)-methylallylalcohol was prepared by the interaction of crotonaldehyde with the Grignard complex formed by the addition of bromobenzene to magnesium. In attempting the resolution of \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol, it was found that the usual method of preparing the acid phthalic ester (i.e. heating with phthalic
anhydride and pyridine on a steam bath) resulted in the production of the pure γ-phenyl-α-methylallyl ester. The isomeric ester was also produced when the reaction mixture was allowed to stand 14 days at room temperature. If however the reaction mixture is kept at 40-45° for 2.5 hours the product is a hydrogen phthalic ester m.p. 94°. Mixed with γ-phenyl-α-methylallylhydrogen phthalate (m.p. 93°) the melting point is also 93°. But the former product appeared to be less soluble in organic solvents than that prepared from the isomeric alcohol. It was found that the new hydrogen phthalic ester would not give a crystalline cinchonidinic acid salt, but readily gave a crystalline quinidinic salt, while if it was heated with pyridine at 95° for two hours, or if it was simply brought to its melting point, the product no longer gave a quinidinic salt, but readily formed a crystalline salt with cinchonidinic which proved to be that of γ-phenyl-α-methylallylhydrogenphthalate. It was therefore assumed that this new ester was the hydrogen phthalic ester of α-phenyl-γ-methylallyl-alcohol, and that it instantaneously changed into γ-phenyl-α-methylallylhydrogenphthalate at the melting point of the latter. From its sparing solubility it would appear that its real melting point would be considerably higher than 94°.
Three crystallizations of the quinidine salt resulted in the pure d-quinidine-1-phthalate salt, and the active hydrogen phthalic ester, a crystalline body m.p. 82° was prepared by decomposition of the salt with acid, care being taken to keep the solutions ice-cold, and excess of acid carefully avoided.

The resolution of α-phenyl-γ-methylallyl alcohol was shown to be complete, and its constitution proved by reducing the (−)-alcohol to the corresponding saturated alcohol. Phenyl-α-propylcarbinol was produced having $[\alpha]_{587}^\circ +40.9^\circ$, $l=2$, c,2.0 in benzene, and proved to be a beautifully crystalline compound m.p. 46°.

Levene and Marker obtained 1-phenyl-α-propylcarbinol by fractional crystallization of the strychnine salt of its hydrogen phthalic ester with $[\alpha]_{587}^\circ -35.8^\circ$ in benzene solution, but made no mention of its property of solidifying. An attempt was therefore made to effect a more complete resolution. dl-Phenyl-α-propylcarbinol was readily prepared by the ordinary Grignard method, and resolved by fractional crystallization of the quinidine salt of the hydrogen phthalic ester, when it showed $[\alpha]_{587}^\circ +43.6^\circ$, $l=2$, c,4.79 and readily solidified to a mass of long needles m.p. 46°.
Hydrolysis of the Hydrogen Phthalic Esters.

In the case of the \( \alpha - \gamma \)-phenyl-\( \alpha \)-methylallyl hydrogen phthalic ester it was found that when hydrolysis was attempted with aqueous caustic soda or sodium carbonate, the resulting carbinol was always of low activity. The more dilute the alkali the lower the rotatory power of the resulting alcohol. When however, the hydrolysis was effected in hot alcoholic caustic soda, the carbinol was produced in good yield and in an almost optically pure condition.

In the case of \( \alpha \)-phenyl-\( \gamma \)-methylallyl hydrogen phthalate, hydrolysis with aqueous alkalies always gave rise to a mixture of the almost completely racemised isomeric alcohols. Hydrolysis with alcoholic solutions of sodium hydroxide containing some water, resulted in some isomerisation, but hydrolysis in a solution in absolute alcohol resulted in optically pure \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol in good yield.

The modern view of alkaline saponification of carboxylic esters has been defined by E.H. Ingold and C.K. Ingold\(^{29}\) as follows:

\[
\begin{align*}
-\text{C}^{\cap} \text{OR} + \text{OH}^- & \rightarrow -\text{C}^{\cap} \text{OH} \\
& \rightarrow -\text{C}^{\cap} \text{OH} + \text{OR}^- \\
\text{OR}^- + \text{H}_2\text{O} & \rightarrow \text{HOR} + \text{OH}^-
\end{align*}
\]
and is consistent with the fact that a Walden inversion is not observed during the saponification of carboxylic esters of optically active alcohols.

However, the fact that in the case of \( \gamma \)-phenyl-\( \alpha \)-methylallyl hydrogen phthalate, hydrolysis with dilute aqueous alkali results in considerable racemisation; and in the case of \( \alpha \)-phenyl-\( \gamma \)-methylallyl hydrogen phthalate results in a racemic mixture of the two isomeric alcohols, seems to indicate that in these cases an additional mechanism is acting, which leads to the actual removal of the radical \( R \) as a cation. The explanation of this phenomenon probably lies in the extreme mobility of the negative hydrogen phthalic ion in the case of these compounds which is probably greatly enhanced by the presence of a solvent of high dielectric constant such as water. The tendency of \( RO \) to become an anion is a process analogous to prototropic change rather than to anionotropy, as the latter would lead to the separation of the radical \( R \) as a cation. It is for that reason that a powerful catalyst for the prototropic change such as strong aqueous alkali or preferably alcoholic soda, favours the normal mechanism of saponification, while dilute aqueous solutions of alkalis are inefficient inhibitors of the anionotropc change, and lead to a type of reaction
analogous to the replacement of the hydrogen phthalic ion by that of acetic acid in solution of the anhydrous acid.

In the same paper Ingold and Ingold show that in the less mobile anionotropic system

\[
\begin{align*}
\text{CH}_2\text{MeCH}_2\text{CH}_2 & \rightleftharpoons \text{CH}_2\text{MeCHCH}_2 \\
\text{O} & \text{C} & \text{O} & \text{O} & \text{C} & \text{O}
\end{align*}
\]

both acid and alkaline hydrolysis of the carboxylic esters yield the corresponding alcohol unmixed with its isomer; a result which leads them to postulate as a mechanism for acid hydrolysis of carboxylic esters as a whole:

\[
\begin{align*}
\text{-COOR} + \text{H}^+ & \rightarrow \text{CO.O} & \rightarrow & \text{-CO} + \text{HOR} \\
\text{-CO} + \text{H}_2\text{O} & \rightarrow & \text{-COOH} + \text{H}^+
\end{align*}
\]

This reaction serves to indicate the marked increase in reactivity of \(\alpha\)-phenyl-\(\gamma\)-methylallyl esters over those of \(\alpha\)-methylallylalcohol, as in the former case the smallest trace of acid initiates a rapid anionotropic change.
Derivatives of α-Phenyl-γ-methylallylalcohol:

It was found that if care in the avoidance of high temperature and acid catalysts was taken, the acetic, hydrogen phthalic, p-nitrobenzoic esters and the p-xenyl urethane of α-phenyl-γ-methylallylalcohol could be prepared unmixed with the corresponding isomeric body, the isomerisation process being much slower at these moderate temperatures than the esterification reaction. It was however, found impossible to prepare the methyl ether of α-phenyl-γ-methylallylalcohol, while its dibromide rapidly decomposed in chloroform solution, hydrobromic acid being evolved.

Attempts to prepare the α-phenyl-γ-methylallyl and γ-phenyl-α-methylallyl chlorides from the corresponding alcohols by the action of phosphorus trichloride or thionyl chloride in the presence of pyridine all failed, the product being in both cases an isomer of phenylbutadiene, which readily formed an insoluble silver salt on shaking with aqueous silver nitrate. On warming with alcoholic caustic soda, this product yielded its isomer, phenylbutadiene. From this and other evidence it appears likely that the new compound possesses the double tautomeric structure

\[
\text{Ph.C} = \text{C.C}_3\text{H}_5 \quad \text{Ph.CH} = \text{C} = \text{CH.CH}_3\text{H}
\]

and is formed by removal of the elements of hydrogen.
chloride from the unstable esters. This experiment is of particular interest as it demonstrates the extreme instability of the chloride as compared with that of the other esters.

In the attempted preparation of the methyl ether, metallic potassium was dissolved in the carbinol in benzene solution, and methyl iodide added. The reaction product distilled over a wide range and appeared to contain unsaturated hydrocarbons and a small quantity of the methyl ether of the isomeric alcohol.
The Isomeric Change:

Various methods were used in following the tautomeric changes undergone by α-phenyl-γ-methylallyl esters. In the case of the hydrogen phthalic ester, where the reaction proceeded readily at ordinary temperatures in solvents, the method used was to dissolve the ester and follow the mutarotation in a polarimeter tube, the reaction being taken as complete when the rotatory power reached a constant value. It was sometimes found more convenient to use the α-c-phenyl-γ-methylallyl hydrogen phthalate, in which case, the isomers could not be distinguished by the ordinary melting point method, as transition is almost instantaneous at the melting point of the more stable isomer. However, the hydrogen phthalic esters may be distinguished by making use of the fact that α-phenyl-γ-methylallyl hydrogen phthalate readily forms a crystalline quinidine salt, but the cinchonidined salt will not solidify, while the reverse applies to the isomeric hydrogen phthalic ester. The polarimetric method also found a more limited application in the study of the tautomerism of the p-nitrobenzoic and acetic esters. As an alternative method, the mixture of the isomers could be separated, in the former case by fractional crystallization or in the case of the acetic esters by means of distillation under reduced pressure.
<table>
<thead>
<tr>
<th>Ester</th>
<th>Temp.</th>
<th>Time</th>
<th>Conditions of Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen</td>
<td>20</td>
<td>19 days</td>
<td>In crystalline state in closed tube.</td>
</tr>
<tr>
<td>Phthalic</td>
<td>20</td>
<td>24</td>
<td>Crystals sealed in high vacuum.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>15</td>
<td>Carbon disulphide solution.</td>
</tr>
<tr>
<td></td>
<td>95</td>
<td>0</td>
<td>Solid → liquid.</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>0</td>
<td>Benzene solution.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>67 hrs.</td>
<td>Methyl alcohol gave the methyl ether.</td>
</tr>
<tr>
<td>p-Nitrobenzoic</td>
<td>20</td>
<td>-</td>
<td>Homogeneous state (partial after 1yr.)</td>
</tr>
<tr>
<td></td>
<td>95</td>
<td>3 hrs.</td>
<td>Homogeneous state.</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>3</td>
<td>Benzene solution.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>6 days</td>
<td>Methyl alcohol gave the methyl ether.</td>
</tr>
<tr>
<td>Acetic</td>
<td>170</td>
<td>-</td>
<td>Can be distilled unchanged.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>17 hrs.</td>
<td>In acetic acid solution.</td>
</tr>
<tr>
<td></td>
<td>95</td>
<td>5</td>
<td>In acetic anhydride.</td>
</tr>
<tr>
<td>Alcohol</td>
<td>20</td>
<td>42 hrs.</td>
<td>1% aqueous acetic acid.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>4 days</td>
<td>Glacial HAc. gives isomeric acetate.</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>-</td>
<td>Unaffected by boiling aqueous caustic soda</td>
</tr>
<tr>
<td></td>
<td>170</td>
<td>-</td>
<td>Can be distilled unchanged.</td>
</tr>
<tr>
<td>p-Xenyl urethane</td>
<td>80</td>
<td>-</td>
<td>Unchanged after 4hrs. in boiling benzene.</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>-</td>
<td>Unchanged at its melting point 3mins.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>-</td>
<td>Unchanged in benzonitrile 14 days.</td>
</tr>
</tbody>
</table>
The Ionic Stability of the Anion:

The speed of isomerisation of the various esters of α-phenyl-γ-methylallylalcohol as set out in Table I show that, in agreement with the hypothesis due to C.K. Ingold, the rate of reaction varies with the intrinsic ionic stability of X as indicated by the strength of the acid HX; and the esters may be arranged in the order of increasing ionic mobility:—Hydrogen phthalic > p-nitrobenzoic > acetic > alcohol. The great reactivity of the hydrogen phthalic ester may in some part be due to the constant presence of catalytic hydrogen ions, though the secondary dissociation constant of phthalic acid in organic solvents must be excessively small.
Solvents and Catalysts:

In connection with the effect of solvents and catalysts upon the lability of anionotropic change in solution, Ingold suggests that the mobility of the tautomerism should be increased by the presence of hydrogen ions, and should be greater in solvents of greater dielectric constant. As will be seen from Table II, the tautomerism is rapid in ether containing a little aqueous hydrochloric acid, but is very slow in neutral ether. The tautomerism is depressed in basic solvents. Tautomerisation is certainly more rapid in solvents of high dielectric constant such as benzonitrile and chlorobenzene, but the reaction velocities in different solvents are too diverse to be accounted for by the effect of solvent polarity alone. It is noticed, for instance, that the dielectric constants for carbon disulphide, chloroform and ether are 2.64, 5.05, 4.34, respectively, while the corresponding times of transformation are 15 days, 22 hours, 134 days.

All solvents were dried and distilled before use, but no elaborate precautions were taken to free them from small traces of impurity which might have catalytic activity. The greater speed of reaction in the case of chloroform might in some part be accounted for by the
presence in it of hydrochloric acid as a decomposition product, a view which is substantiated by the fact that there is greater separation of phthalic acid from chloroform solutions than when the mutarotation takes place in other solvents; but the excellent agreement obtained in measurements of the rate of transformation in different concentrations in the same solvent performed for the purpose of energy of activation measurements, lead to the belief that incidental impurities do not have any marked effect on the character of a solvent as a catalyst in the anionotropic change. It is also possible that certain solvents have the property of supplying electrons to the $\alpha$-carbon atom by formation of loose coordination complexes, thus aiding the removal of the hydrogen phthalic anion.

It is at any rate clear that the effect of neutral solvents in catalysing the removal of the anion is a complicated one, and does not depend on any single property of the solvent. The solvent is conceivably capable of affecting the rate of tautomerism in any of the following ways.

(i) By formation of loose coordination complexes with either the anion or cation.

This effect would be expected to occur most readily in solvents such as ethyl and methyl alcohols,
which are well known to be highly coordinating. But in these cases the product is an ether, showing that the anion has been removed in combination with a hydrogen cation, the ethoxy and methoxy anion replacing the phthalic radical in the electromeric molecule.

(ii) Dipole association.

\[
\begin{array}{ccc}
(+) & (-) & (\delta-) \\
R & Y & \delta+
\end{array}
\begin{array}{ccc}
(+) & (-) & (\delta+) \\
X & Y & Z
\end{array}
\]

It is well known that the electrostatic attraction between the radical \( R \) and the potential anion \( X \) may be weakened by the presence of a foreign dipole \( YZ \), which might orient itself in the way shown. The effect would occur more readily in solvents of high dipole moment such as benzonitrile, chlorobenzene, ethyl and methyl alcohol.

(iii) Solubility Effect.

While in cases of relatively feeble anionotropic systems such as \( \alpha \)-methylallyl esters the catalytic effect of a solvent is largely governed by its dipole moment, non-polar solvents such as benzene having no activity, in the case of more labile systems, it is probable that the weak Van der Waal forces which surround the solvent molecules are also able to initiate the separation of an anion. These forces are related to such phenomena as latent heat and surface tension.
and their interplay between the molecule of a solvent and that of a solute may be correlated with the molar-solubility of the latter. Table II shows that there is a marked connection between the solubility of an ester and its rate of transformation in a solvent. It is also remarkable that while in benzene or in the molten state, the isomerisation is almost instantaneous at 80° or 94° respectively, α-phenyl-γ-methylallyl hydrogen phthalate can be crystallised from boiling hexahydrobenzene (b.p. 82°); the hydrogen phthalic ester being almost insoluble in cold hexahydrobenzene while it is very soluble in benzene.
### TABLE III.

**Anionic Mobility of Esters of Saturated and Unsaturated Alcohols.**

<table>
<thead>
<tr>
<th>SOLVENT</th>
<th>TIME</th>
<th>TEMP.</th>
<th>PRODUCT.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>α-Phenyl-γ-methylallyl hydrogen phthalate.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetic acid</td>
<td>2.5 hrs.</td>
<td>15°C</td>
<td>Acetic Ester</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>5 days.</td>
<td>15</td>
<td>Ethyl Ether</td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>67 hrs.</td>
<td>15</td>
<td>Methyl Ether</td>
</tr>
<tr>
<td>Acetic anhydride</td>
<td>4 hrs.</td>
<td>95</td>
<td>Acetic Ester</td>
</tr>
<tr>
<td><strong>γ-Phenyl-α-methylallyl hydrogen phthalate.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>114 days.</td>
<td>15</td>
<td>Methyl Ether</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>10 months.</td>
<td>25</td>
<td>Ethyl Ether</td>
</tr>
<tr>
<td><strong>αγ-Dimethylallyl hydrogen phthalate.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>7 hrs.</td>
<td>65</td>
<td>Methyl Ether</td>
</tr>
<tr>
<td><strong>Hexanoyl hydrogen phthalate.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>-</td>
<td></td>
<td>No action.</td>
</tr>
<tr>
<td><strong>Octanoyl hydrogen phthalate.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td>-</td>
<td></td>
<td>No action.</td>
</tr>
</tbody>
</table>
Replacement Reactions:

Table III shows tautomeric transformations in which the departing anion is replaced by an anion derived from the solvent. It is to be noted (Table II) that where a solvent catalyses simple isomerisation of the ester, the optical activity of the product is high (about 50%), but when the solvent itself supplies a new ion, the activity of the product is low, (about 5%). The reactions in which a new anion enters the molecule are generally faster than the simple tautomerism, a fact which lends itself to the view that in the former cases the departing anion is removed in combination with a positive ion from the solvent.

\[ RX + H + Y \rightarrow R + HX + Y \rightarrow R^+ + HX + Y \rightarrow R^+ Y + HX \]

The slower speed of the simple tautemeric reactions also shows that reactions of the above type do not occur by a replacement reaction, followed by an anionotropic change.

\[ HX + HY \rightarrow RY \rightarrow R^+ Y \]

The more stable molecule \( R^+ X \) (in this case, \( \gamma \)-phenyl-\( \alpha \)-methylallyl hydrogen phthalate) is also capable of losing the anion \( X \) under the influence of a solvent, though the reaction is much slower than with \( \alpha \)-phenyl-\( \gamma \)-methylallyl hydrogen phthalate in the same solvent. This fact is of interest as it throws light upon the
conduct of the simple isomeric change. The speeds of the replacement reactions undergone by the esters of \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol and \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol are an approximate indication of the relative tendency of these esters to ionise. If the isomeric change under examination is regarded as a reversible reaction, then at equilibrium there will be a preponderance of the isomer which is more stable in its un-ionised form. This conception of the tautomeric change is further discussed in the following section.
\( \alpha \)- and \( \gamma \)-Substitutions:

As may be seen from Table III hydrogen phthalic esters of saturated secondary alcohols show no tendency to react with methyl or ethyl alcohol, and it seems reasonable to assume that as the tendency of the radical \( X \) to leave the molecule as an anion is enhanced in unsaturated bodies, the mobility of the tautomeric system is due to a mechanism which acts specifically through the double bond. It therefore seems probable that the initiating process is the electromeric change, the \( \alpha \)-carbon atom losing an anion only because of a compensating movement in the loose ethylene system attached to it. As has already been stated the view held by Burton and Ingold as to the nature of the anionotropic system is as follows:

\[
\begin{align*}
\text{RX} & \xrightarrow{(i)} R + X \xrightarrow{(ii)} R^+ + X \xrightarrow{(iii)} R'X
\end{align*}
\]

The rate of reaction measured in these experiments will obviously be that of stage (i) or (ii) in the above scheme, whichever is the slower. Stage (i) according to accepted theory, will be accelerated by hydrogen ions or highly polar solvents, while the velocity of stage (ii) will depend upon the difference in energy levels of the electromeric cations, and will be a function of the final position of equilibrium of the isomers at the
temperature of the reaction.

It is therefore apparent that in cases where Stage (i) is the slower, the velocity of isomeric change will be greatly affected by the electron donating ability of the substituent attached to the \( \alpha \)-carbon atom, and by external conditions in the solvent; while the final position of equilibrium, which is determined after the anion has left the system, will depend upon the inductive effects of the end groups. The experimental results indicate that the tautomerism of \( \alpha \)-phenyl-\( \gamma \)-methylallyl-alcohol is of this type.

\[
\text{Ph} \xleftrightarrow{X} \text{CH.CH} \xrightleftharpoons{X} \text{CHCH} \xrightarrow{X} \text{Me} \xrightarrow{X} \text{Ph.CH} \xrightarrow{X} \text{CH.CH} \xrightarrow{X} \text{Me}
\]

In the cases where the anion is split off and a new anion, derived from the solvent, enters the system, the mechanism may be described in detail as follows.

\[
\text{Ph} \xleftrightarrow{X} \text{CH.CH} \xrightleftharpoons{X} \text{CH} \xrightarrow{X} \text{Me} + \text{H} + \text{Y} \xrightarrow{X} \text{Ph.CH} \xrightarrow{X} \text{CH.CH} \xrightarrow{X} \text{Me} + \text{HX}
\]

(a) The group \( X \) borrows an electron from its attached carbon atom and remains in electrovalent combination with it.

(b) The \( \alpha \)-carbon atom is compensated by a shift in the loose electronic systems on either side of it - the
phenyl group and the ethylenic double bond.

(c) Splitting off of \( X \) follows, and under the action of the inductive effect of the terminal radicals, the cation undergoes an electromeric change, the \( \alpha \)-carbon atom becoming the new centre of positive charge.

(d) Association with the ion \( Y \) now completes the process.

The proportion of \( X \) and \( Y \) in the final product depends upon

1. The relative strengths of the acids \( HX \) and \( HY \).
2. The excess of \( HY \) over the ester in solution.

It follows that if this view of the mechanism is true,

1. The initial mobility of the anion \( X^- \) is dependent upon the power of the adjacent radical (in this case \( Ph_\text{c}^- \)) and the ethylenic double bond to compensate the \( \alpha \)-carbon atom. That is to say, the rate of reaction is determined by the strength of the "tautomeric effect" of the group adjacent to the migrating ion, and the "inductive effect" of the group terminating the ethylenic system.

2. The decision as to which of the isomers is the more stable, rests upon the + or - I effect of the terminal groups. That is to say, the position of equilibrium will be such that the isomer in which the \( X \) radical lies nearest the strongest +I group, predominates.
The position of equilibrium will however also be effect-
ed by the general mobility of the system.

\[ \text{fast} \quad \begin{array}{c}
\text{R-CH.CH=CH}_2 \\
\text{OH}
\end{array} \rightleftharpoons \begin{array}{c}
\text{RCH.CH=CH}_2 \\
\text{OH}
\end{array} \]

\[ \text{slow} \quad \begin{array}{c}
\text{R-CH=CH-CH}_2 \\
\text{OH}
\end{array} \rightleftharpoons \begin{array}{c}
\text{RCH=CH-CH}_2 \\
\text{OH}
\end{array} \]

If, owing to the electron donating property of the radical
R, (I) readily ionises, while (II) is more stable, the
equilibrium \( A \rightleftharpoons B \) will be upset in favour of \( B \), independ-
ently of the directing influence of the + or - I effects
of the radical R. It is this effect which probably
accounts for the variation of position of equilibrium of
with experimental conditions noticed in many anionotropic
changes. Thus, whereas the action of hydrogen halides on
either cinnamyl or \( \alpha \)-phenylallyl alcohol gives only
cinnamyl halides, treatment of cinnamyl chloride with
70% aqueous alcoholic potash gives 20-25%, and with silver
oxide in absolute alcohol 35-45% \( \alpha \)-phenylallylether^{30}.

The far greater mobility and completeness of the reaction

\[ \text{Ph CHX.CH : CH.CH}_3 \rightarrow \text{PhCH : CH.CHX.CH}_3 \]

than either

\[ \text{Ph CHX.CH : CH}_3 \rightarrow \text{PhCH : CH.CH}_X \]
clearly shows that the end groups cannot logically be arranged in any sequence such as Ph > Me > H; for if they could, the first system ought to be less mobile than the second, as in the first system, the groups Me- and Ph- would be acting in opposition.

It appears therefore, that in classifying the behaviour of the related alcohols and their esters the additional tautomeric effect of the aryl end groups ought to be kept distinct from inductive effects. Thus as a general rule, the radical X will tend to migrate away from an aryl group, but towards an alphyl group, which is more specific in its effect of influencing the polarity of the double bond in the tautomeric cation. An alphyl group might also have an effect which is more analogous to the effect of the phenyl group, that of aiding the removal of the anion by increasing the toleration of the α-carbon atom for a shared sextet. Thus α-phenylallylalcohol gives cinnamyl acetate upon heating with acetic anhydride because the acetate of the former is much more readily ionised than that of the latter, owing to the presence of the phenyl group in the α-position. In the case of methylvinyl carbinol, the mobility is less because the methyl radical is less able to
increase the toleration of the \( \alpha \)-carbon atom for a shared sextet than is the phenyl group. However an equilibrium mixture is obtained when the alcohol is warmed with trichloracetic acid. Here methylvinylcarbinyltrichloracetate is the favoured isomer, being formed in a proportion of 55%, although other experiments point to crotylalcohol as the major isomeride.

If the ionisation of each isomer were complete, the position of equilibrium would be entirely governed by the inductive effect of the end groups, since the tautomeric effect aids ionisation only. It is therefore probable that where the intrinsic stability of the anion is great, as in the case of trichloracetic esters, the most pronounced effect of the end groups is the inductive effect, while tautomeric effects play the more decisive part in the isomerism of less mobile esters.

As a general rule, therefore, it may be stated that the position of equilibrium in an anionotropic reaction will be such that the potential anion will occupy a position adjacent to the end radical exhibiting the strongest +I effect and farthest away from the end radical most capable of increasing the toleration of its attached carbon atom for a shared sextet.
Retention of Asymmetry during Anionotropic Change.

In 1933 Ingold and Wilson began a series of investigations to ascertain whether asymmetry is retained during prototropic (I) and anionotropic changes (II) in which the proton or anion moves from one asymmetric centre to a new asymmetric centre arising as a result of the isomeric change.

\[
\begin{align*}
[H] & \rightarrow ^*A - B = C \quad \Rightarrow \quad A - B - C - [H] & (I) \\
[X] & \rightarrow ^*A - B = C \quad \Rightarrow \quad A - B - C - [X] & (II)
\end{align*}
\]

In a detailed discussion these Authors suggest that asymmetric induction is an effect associated with restriction of rotation about the A—B link (I and II) due to interaction of the electric field about the asymmetric carbon atom A, on that about B and C. This effect is described as the "Asymmetric Synthesis Effect". It is pointed out by the Authors that the propagation of asymmetry by this mechanism is normally very small; the measurable optical activity of the product of transformation of linalyl acetate being explained by the operation of a ring mechanism, which has the effect of completely stopping intramolecular rotation at the moment of reaction.

After exploratory experiments with both prototropic and anionotropic systems the mutually interconvertible
azomethines (III) and (IV), were selected for study, and from the equilibrium mixture obtained after the isomerisation of the optically active isomeride (III), the isomeride (IV) was isolated in an optically inactive condition. Later kinetic studies of the rates of racemisation and of tautomeric change led Hsu, Ingold and Wilson\textsuperscript{33} to conclude that the racemisation observed during the prototropic change of the azomethines did not occur during the ionisation which precedes the tautomeric change, and therefore that the mesomeric anions were capable of retaining their optical activity.

\[
\begin{align*}
\text{Me} & \quad \text{CH[H]} \quad \text{H:C} & \quad \text{Ph} \\
\text{Ph} & \quad \text{C}_6\text{H}_4\text{Cl(p)} & \quad \text{C}_6\text{H}_4\text{Cl(p)}
\end{align*}
\]

(III) (IV)

Additional evidence in support of this conclusion was drawn from the influence of constitutional factors on the rates of racemisation of prototropic compounds\textsuperscript{34}, and from comparisons of the rates of racemisation and bromination of optically active ketones\textsuperscript{35}.

In the case of the anionotropic change between esters of $\alpha$-phenyl-$\gamma$-methylallylalcohol and those of $\gamma$-phenyl-$\alpha$-methylallylalcohol asymmetry is actually retained during the process, and the product isolated in an optically active state.
Two views of the nature of the reaction have been examined:

(a) the original ion may be removed leaving a tautomeric cation which is itself responsible for retaining asymmetry for a period long enough to allow the new ion to be attached.

(b) the ion may be in loose combination with the positively polarised carbon atom before the tautomeric change takes place.

The experiment of Hills, Kenyon, and Phillips (loc. cit.) shows that the asymmetry induced in the double bond of the related α,β-dimethylallylalcohol is stable for some time after the original asymmetric carbon atom has been racemised and the induced asymmetry takes a correspondingly long time to be generated, a fact which tends to show that mechanism (a) is a possible one.

However strong evidence in favour of mechanism (b) comes from another source.
The Mechanism of Asymmetric Synthesis with reference to a New Type:

The more stable (+) \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol on addition of bromine in chloroform solution yields a solid derivative which may be separated by fractional crystallization into two forms of different melting point and crystalline form. The less soluble dibromo-alcohol (hairy needles m.p. 112°C) on oxidation with chromic acid in acetic acid yields optically pure (+) \( \alpha \)-methyl-\( \alpha \beta \)-dibromo-\( \beta \)-phenylethyl ketone, while the more soluble form (glassy prisms from light petroleum m.p. 88°C) yields the corresponding (-)ketone in a state of optical purity. If the bromination and oxidation is carried out without crystallization or other form of separation of the intermediate dibromo-alcohols, the resulting dibromo-ketone is separated in an optically active state, its rotatory power depending upon the temperature at which the initial bromination was performed, and reaching a maximum value of 41.1% optical purity.

In this experiment two new centres of asymmetry are produced while the original centre is yet undisturbed, the latter being afterwards destroyed by oxidation.

\[
\begin{align*}
\text{CH}_3\text{CH(OH)CH}_{2}\text{CHPh} & \rightarrow \text{CH}_3\text{CH(OH)CHBr}\cdot\text{CHBrPh} \rightarrow \text{CH}_3\text{CO}\cdot\text{CHBr}\cdot\text{CHBrPh}
\end{align*}
\]
The anionotropic changes of the esters of \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol clearly show that when a substituent enters the \( \gamma \)-carbon atom an asymmetric synthesis results, but it is not clear whether the \( \beta \)-carbon atom is also capable of unsymmetrical substitution.

In order to test this hypothesis, a similar experiment was undertaken with (\( d \))-ethylvinylcarbinol.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}_2 \quad \text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CHBr-CH}_2\text{Br} \\
(\text{d}) \quad (\text{d}) \\
\text{C}_2\text{H}_5\text{CO.CHBr-CH}_2\text{Br}
\end{align*}
\]

Here, bromination of the carbinol results in the production of one new asymmetric carbon atom; that in the \( \beta \)-position with respect to the carbinyl group. In this case the product is an oil and is consequently not readily purified, but the fact that the resulting ketone has a rotatory power of opposite sign from, and of greater numerical value than, the dibromcarbinol shows that an asymmetric synthesis has taken place.

Most recorded cases of asymmetric synthesis where a compound of known constitution is used to impart a disymmetric bias to the reaction depend for their success upon the production of a mixture of two diastereoisomerides in unequal amounts which yield an optically active product when the original centre of asymmetry has been removed. In order to account for a similar inequality
in the diastereoisomerides:

\[
\begin{align*}
  &\text{I} & &\text{II} \\
  &\text{C}_6\text{H}_5\text{C} & \text{OMgI} & \text{CH}_3\text{C} & \text{OMgI} \\
  &\text{CH}_3\text{COOC}_{10}\text{H}_{19} & &\text{C}_6\text{H}_5\text{COOC}_{10}\text{H}_{19} \\
  &(-) & (-) & (+) & (-)
\end{align*}
\]

prepared as intermediate products in the asymmetric synthesis of \((-\text{-})\) atrolactinic acid from benzoyl formic acid McKenzie\textsuperscript{37} suggests that the ethereal solution of \((-\text{-})\) menthyl benzoyl formate used in the Grignard reaction contained a mixture of:

\[
\begin{align*}
  &\text{A} & &\text{B} \\
  &\text{C}_6\text{H}_5\text{COOC}_{10}\text{H}_{19} & \text{and} & \text{C}_6\text{H}_5\text{COOC}_{10}\text{H}_{19} \\
  &(-) & (-) & (+) & (-)
\end{align*}
\]
in unequal amounts. It is assumed that the ketonic double bond under the influence of "Asymmetric Induction" is capable of contributing to the optical rotatory power of the molecule, and further that on addition of methyl magnesium iodide, A leads to (I) and B leads to (II) so that (I) and (II) are also formed in unequal amounts.

Clearly, in order to account for the production of the diastereoisomerides (I) and (II) in unequal amounts it is necessary to assume:

(c) A constitutional difference in A and B and an excess of one over the other.
or (d) that methylbenzoylformic acid is homogeneous; but that collisions with the addendum likely to give rise to (I) are more favoured than those giving rise to (II) owing to the obvious constitutional difference in (I) and (II), and as a result, the side reactions

\[ C_6H_5CO.COC\text{H}_{10} \overset{\text{I}}{\longrightarrow} \]

progress at different speeds, leaving the isomeride (I) in excess at the end of the reaction. The following experiment was designed to test which of the mechanisms (c) or (d) is the more probable.

It was found by Hills, Kenyon and Phillips that \((-\alpha\beta\text{-dimethylallylalcohol}) \text{(III)} \) yields with phosphorus trichloride \((+\alpha\beta\text{-dimethylallyl chloride}) \), which on hydrolysis with a cold aqueous suspension of calcium carbonate gives a dextrorotatory form of \(\alpha\beta\text{-dimethylallylalcohol} \text{(V)} \).

\[
\begin{align*}
\text{CHMe(OH).CH:CHMe} & \rightarrow \text{ClMe.CH:CHMe} \rightarrow \text{CHMe(OH).CH:CHMe} \\
(-) & \rightarrow (+)
\end{align*}
\]

Compound (III) on catalytic reduction yields optically pure \((-\text{methyl-\(n\)-propylcarbinol}) \), whereas (V) yields the dl-carbinol. A possible explanation of these reactions is that during the hydrolysis of (IV) the optical activity due to the fixed centre is lost, whilst that due to induced dissymmetry in the double bond remains.
Thus a compound owing its optical activity solely to a centre of induced dissymmetry is available for a comparative study. The (-) alcohol (III) readily combines with bromine to give (+)methyl-αβ-dibromo-n-propylcarbinol (VI). This on oxidation with chromic anhydride in acetic acid solution yields (+)methyl-αβ-dibromo-n-propyl ketone (VII).

\[
\text{CHMe(OH)·CH:CMe} \rightarrow \text{CHMe(OH)·CHBr.CHBr.Me} \rightarrow \text{COMe.CHBr.CHBrMe}
\]

(III) (VI) (VII)

On the other hand, the dextrorotatory alcohol (V), by similar treatment, yields a dl-dibromoalcohol and subsequently dl-methyl-αβ-dibromo-n-propyl ketone.

\[
\text{CHMe(OH)·CH:CMe} \rightarrow \text{CHMe(OH)·CHBr.CHBrMe}
\]

(+) (inactive)

(V) (VIII)

It appears to follow therefore, that induced dissymmetry of a double bond as indicated by its contribution to the optical rotatory power of a compound is incapable of effecting an asymmetric synthesis, and that, as in mechanism (d) it is a difference in energy associated with the diastereoisomeric intermediate products which is responsible for the one-sided addition.

If the retention of asymmetry during the anionotropic change between α-phenyl-γ-methylallyl esters and
those of \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol may fairly be considered analogous, then as in mechanism (b) the mobile ion must be in contact with the positive polarised \( \gamma \)-carbon atom before the mesomeric change takes place. This view would imply a pseudo-cyclic intermediate during simple anionotropic change, involving the temporary formation of a four membered ring (X) or a six membered ring (IX) according as to which oxygen atom of the carboxylic ester finally becomes attached to the \( \gamma \)-carbon atom.

\[
\text{H} \quad \text{H} \quad \text{C} = \text{C} \quad \text{Me} \\
\text{Ph} \quad \text{C} \quad \text{O} - \text{C} \\
\text{H} \quad \text{H} \quad \text{O}(\text{IX})
\]

In cases where a new anion derived from the solvent is successful in competition with the original, it appears likely that this will be obliged to take the unoccupied position on the opposite side of the \( \gamma \)-carbon atom; reaction products of opposite configuration resulting from the two different kinds of combination. An attempt has therefore been made to correlate the configurations of the starting materials and reaction products of the experiments already described.
Stereochemical Aspects of the Anionotropic Changes and Replacement Reactions undergone by (-) α-phenyl-γ-methylallylalcohol and its Derivatives:

A summary of the anionotropic changes is given in the following scheme (Diagram I) which includes also reactions in which the anionic groups of the p-nitrobenzoic and hydrogen phthalic esters of (-) α-phenyl-γ-methylallylalcohol were replaced by the anions -OAc and -OMe, by interaction with acetic acid and methyl alcohol respectively. From this scheme it will be seen that if the relative configurations of (+) phenyl-n-propyl and (-) methyl-β-phenylethyl carbinols were known, it would be possible to deduce which of these changes were accompanied by inversion and which took place without configurative change.

The relative configurations of these two alcohols can be decided from published data when use is made of the generalisations which have emerged from studies with optically active compounds. These include the experimental results of Pickard and Kenyon on the determination of the rotatory powers of homologous series of alcohols and their esters, the work of Clough, showing that the rotatory powers of compounds of similar configuration are, in general, influenced similarly by changes in external conditions, and the investigations
of Rule 40, on the influence of the polarity of the substituent, X, on the magnitude of the rotatory powers of the series RX. From these investigations it can be concluded that the rotatory powers of the series of alcohols, Ph.CHOH.R, in which R is a lengthening alkyl chain, and also of the series, Me.CHOH.R, in which R contains a phenyl group becoming separated from the asymmetric carbon atom by an increasing number of methylene groups, should alter in a regular manner. The experimentally determined rotatory powers of some of the alcohols belonging to these two series both in the homogeneous state and also in benzene solution for light of three different wavelengths are given in Table IV.

It will be seen that the rotatory powers of the (+) alcohols of the second series (3, 4 and 5) steadily decrease in magnitude both in the homogeneous state and in benzene solution. The decrease in the rotatory powers of the first series (1, 2 and 3) is not so regular: (+) phenylethyl carbinol, the middle member of the series, having slightly lower rotatory powers than either phenylmethyl or phenyl-n-propyl carbinol. This small irregularity is not serious however, since the lack of simplicity in the rotatory dispersive powers of these alcohols makes a comparison under strictly
comparable conditions difficult. (+) Phenylmethyl carbinol thus appears to be configuratively related to the alcohols of both series, and hence all five alcohols probably have the same configuration. Confirmation of this conclusion is afforded by a comparison of the temperature-rotation curves of these alcohols. All five alcohols give temperature-rotation curves which tend to be concave to the temperature axis. From these considerations it follows that (+) phenyl-\(n\)-propyl carbinol and (+) methyl-\(\beta\)-phenylethyl carbinol, if they are regarded as members of the series

\[ \text{Ph.}(\text{CH}_2)_n \text{CH(\text{OH}).(CH}_2)_m \text{CH}_3 \], have the same configuration.

As the two unsaturated alcohols were reduced by the same method, it can be concluded that (-) \(\alpha\)-phenyl-\(\gamma\)-methylallylalcohol has a configuration opposite to that of (+) \(\gamma\)-phenyl-\(\alpha\)-methylallylalcohol. Hence the new asymmetric centre produced by the isomeric change of (-) \(\alpha\)-phenyl-\(\gamma\)-methylallylalcohol has the opposite configuration to the asymmetric centre which is destroyed.

Furthermore, since the hydrogen phthalic, acetic and p-nitrobenzoic esters are produced from the unsaturated alcohols by methods unlikely to lead to a configurative change, the isomeric change of these esters of the \(\alpha\)-phenyl alcohol to the corresponding esters of \(\gamma\)-phenyl alcohol, is accompanied by inversion of
configuration.

Other conclusions can be drawn concerning the stereochemical changes which occur during the reactions given in the scheme. For example, it can be concluded that (+) $\gamma$-phenyl-$\alpha$-methylallyl methyl ether, produced from the potassium derivative of the (+) alcohol by the action of methyl iodide, possesses the same configuration as the parent (+) alcohol and also its (+) hydrogen phthalic ester. The (-) $\gamma$-phenyl-$\alpha$-methylallyl methyl ether slowly produced when the (+) hydrogen phthalic ester was warmed with methyl alcohol arose, therefore, with inversion of configuration. On the other hand, if as suggested, (-) $\alpha$-phenyl-$\gamma$-methylallyl hydrogen phthalate and (-) $\alpha$-phenyl-$\gamma$-methylallyl p-nitrobenzoate have a configuration opposite to that of (+) $\gamma$-phenyl-$\alpha$-methylallyl hydrogen phthalate and (-) $\gamma$-phenyl-$\alpha$-methylallyl p-nitrobenzoate, then they must have the same configuration as (-) $\gamma$-phenyl-$\alpha$-methylallyl methyl ether. Hence both these esters undergo anionic replacement with the occurrence of inversion of configuration. It is also noteworthy that both these esters react rapidly with methyl alcohol: the anionic replacements are unlikely therefore to have been preceded by isomeric change, since the corresponding $\gamma$-phenyl esters react slowly with methyl alcohol.
The proposed configurational relationships as indicated in Diagram I fit in with a relatively simple picture of the reaction mechanism. This is provided by assuming that the (-)\(\alpha\)-phenyl-\(\gamma\)-methylallyl esters adopt a pseudo-cyclic configuration (Diagram II) in which the cis-form predominates. The arrangement of the groups around the \(\gamma\)-carbon atom will then be favourable to the adoption of an \(\alpha\)-configuration, opposite to that of the \(\alpha\)-asymmetric carbon atom, when the anion migrates.

Isomerisation involves therefore the establishment of a link between the carboxylic oxygen atom and the \(\gamma\)-carbon atom, as indicated by the broken line; complete migration of the anion involves inversion of configuration. Anionotropic migration may be forestalled, however, by union of the \(\gamma\)-carbon atom with an external anion. When this occurs, as indicated by the dotted line, the new asymmetric centre acquires the same configuration as that previously possessed by the \(\alpha\)-carbon atom. On the other hand when the internal anion is attached to the \(\gamma\)-carbon atom and shows no tendency to migrate, but can nevertheless undergo displacement by an external anion, then a Walden inversion occurs as in most other simple anionic replacement reactions.

In view of the fact that this picture of the space-mechanism of the isomerism and of the replacement
TABLE IV.
The Specific Rotatory Powers of Related Semi-Aromatic Alcohols.

<table>
<thead>
<tr>
<th></th>
<th>Homogeneous state. In Benzene, c,5.00,</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\alpha$</td>
<td>$\beta$</td>
<td>$\gamma$</td>
<td>$\delta$</td>
</tr>
<tr>
<td>1. PhCHOHMe</td>
<td>+41.51° 49.46 85.92</td>
<td>+48.88° 57.93 99.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. PhCHOHCH Me</td>
<td>+30.24° 36.02 60.49</td>
<td>+40.05° 47.78 79.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. PhCHOHCH₂CH₂Me</td>
<td>- 36.58 63.00</td>
<td>+43.60° 52.20 87.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. PhCH₂CHOHMe</td>
<td>+27.58° 33.43 61.22</td>
<td>+41.82° 50.82 93.58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. PhCH₂CH₂CH₂CHOHMe</td>
<td>+14.74° 17.46 29.28</td>
<td>+19.41° 25.45 42.79</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. From data already given.

DIAGRAM II.
Suggested Mechanism of the Anionotropic Change of Esters of
$\alpha$-Phenyl-$\gamma$-methylallylalcohol.

\[ \text{X} = \text{C}_6\text{H}_4\text{CO}_2\text{H}(o-) \text{ or } \text{C}_6\text{H}_4\text{NO}_2(p-) \]

\[ \text{l- and d- denote configurations.} \]
reaction assumes the proximity of the ester-oxygen atom and the \( \gamma \)-carbon atom, it is of interest that \( \alpha \)-phenyl-\( \gamma \)-methylallylalcohol has a low parachor (360.6), whilst the parachor of \( \gamma \)-phenyl-\( \alpha \)-methylallylalcohol (367.4) is nearer the calculated value which is 372.1 using the constants of Sugden, or 368.2 when the constants of Mumford and (J.W.C.) Phillips, are used.

If such a pseudo-cyclic configuration is adopted by anionotropic systems prior to ionic migration, then a mechanism is provided which does not postulate the occurrence of complete ionic dissociation prior to isomeric change. This is a modification of the views of Burton (loc. cit.), who assumed that the formation of cinnamyl acetate resulting from the action of tetramethylammonium acetate on \( \alpha \)-phenylallyl \( p \)-nitrobenzoate in acetic anhydride indicated that ionic dissociation proceeded sufficiently far to permit of direct competition between the internal and external anions for the electromeric cation. This interpretation would however appear to be more in accord with the conclusions reached by Hsu, Ingold and Wilson, from their studies of prototropic systems, namely, that the ionisation products of the system do not become kinetically free to such a degree as to allow of asymmetry being destroyed.
CONCLUSION.

In the earlier conceptions of asymmetric induction it was assumed that an unsaturated group adjacent to an asymmetric carbon atom in the molecule of an optically active compound is distorted in such a way that it is itself capable of contributing to the optical rotatory power of the molecule. Evidence in support of this view has been outlined in Chapter II., and although it must be admitted that its existence has not been conclusively proved, the presence of induced dissymmetry of this type is supported by a large bulk of circumstantial evidence, culminating in the experiment of Hills, Kenyon and Phillips, whereby the centre of fixed asymmetry in \( \gamma \)-dimethylallylalcohol is removed, leaving a compound which apparently owes its optical activity entirely to induced dissymmetry in the double bond.

These views of asymmetric induction have been modified somewhat by McKenzie and his co-workers, in their attempt to explain asymmetric synthesis on the basis of asymmetric induction. In order to explain the asymmetric synthesis of substituted lactic acids by hydrogenation of ketonic esters of optically active alcohols, these investigators are led to suggest that the dissymmetry of the group \( >C:O \) is to a certain
extent permanent, an optically active ketonic ester containing molecules both of the type (+)(+) and those of the type (+)(−). The generation of induced dissymmetry, it is assumed, arises as the types reach an equilibrium condition in which one of them predominates.

Certain difficulties arise if these ideas are applied to cases where an ethylenic double bond takes the place of the ketonic group. The semi-permanent distortion of the double bond, as it would lead to an unnatural strain in the valency bonds, could only be accounted for by some type of polarisation. But measurements by Dr. A.R. Martin of the dipole moments of the three alcohols, pentanol, α-phenyl-γ-methylallyl-alcohol and its isomer, show that these unsaturated alcohols do not differ in polarity from saturated alcohols to any great extent. The fact that both carbon atoms terminating the ethylenic double bonds are capable of assuming optical activity on addition of the ions of an addendum is significant, as the atoms at each end of the double bond would be oppositely polarised, and experiments on the Walden inversion indicate that only negatively charged carbon is capable of retaining asymmetry.

Experiment has shown (p. 63) that the induced dissymmetry in the double bond of pentanol is incapable of
effecting an asymmetric synthesis. It is not, however, necessary to assign any importance to asymmetric induction in the mechanism of asymmetric synthesis. The diastereoisomerides formed during all asymmetric syntheses of this type are separate chemical individuals, having different melting points, and different physical properties; and their formation in unequal amounts during the side reactions

\[ A \rightarrow B \text{ and } A \rightarrow C \]

would be expected, as in any other case of similar side reactions.

In the isomeric changes studied in this work, it has been shown that a probable mechanism involves the preliminary junction of the migrating anion with the \( \gamma \)-carbon atom to form a ring. Here the cis- and trans-ring take the place of the diastereoisomerides more usually formed, and a study of the configurational changes has shown that in this case the more favoured intermediate is the cis-ring. Where an external ion, is successful in competition with the internal ion, the former is probably forced to take up the vacant position on the opposite side of the \( \gamma \)-carbon atom.

From these considerations the reactions may be regarded as falling into two main types; a division which is supported by evidence from the polarimetric...
measurements of the velocity of the anionotropic changes. The first type, simple isomerisation reactions, are generally slower than those of the second type, in which a very reactive anion such as $\text{-Ac}$ or $\text{-OMe}$ displaces the original ion of the ester, but yield products of higher optical rotatory power and of opposite configuration.

While this work was primarily undertaken with the intention of investigating the dissymmetry induced in the double bond, it was realised that in order to overcome the experimental difficulties encountered, a knowledge of the conditions determining the anionotropic change between the isomeric alcohols and their esters was essential. The use of optically active material proved to be a valuable weapon in the attack upon the problem, and the data collected are more precise and more far reaching than those hitherto available. This section of the work has confirmed the general principles enunciated by Burton and Ingold, but has shown that in certain connections, their simple rules are insufficient to account satisfactorily for all the phenomena.

The discovery that the esters of the more stable alcohol were themselves capable of exchanging an anion for one obtained from the solvent brings out quite clearly the part played by the relative ease of ionisation of the esters in determining the equilibrium position as
a whole, and an attempt has been made, on this basis, to form a constructive theory to account for the system's great mobility. Unfortunately, the comparative study of the anionotropy of members of the allyl alcohol series has so far been pursued with reference to $\alpha$-substituents only, but the way is now open for a thoroughgoing investigation of the effects of $\gamma$-substitution alone, and of substituents in both the $\alpha$- and $\gamma$-positions.
EXPERIMENTAL.
The (+) and (−) \(\gamma\)-Phenyl-\(\alpha\)-methylallyl Alcohols.

Recrystallisation of the cinchonidine salt of \(\text{dl-}\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate yields the optically pure (+) hydrogen phthalic ester: the (−) hydrogen phthalic ester can be obtained by recrystallisation of the corresponding brucine salt. The rotatory powers \((±44.6°)\) of the two hydrogen phthalic esters thus obtained are unchanged when the esters are recrystallised, although \(\text{d+dl}\)-hydrogen phthalic esters obtained from incompletely resolved alkaloidal salts can be separated by crystallisation from solvents, notably carbon disulphide, into pure \(\text{dl}\)- and (+)-acid esters. The specific rotatory powers of the (+)-acid ester in various solvents are given in Table V. When saponified with sodium carbonate solution, these esters gave unexpectedly the \(\text{dl}\)-alcohol. The optically active alcohols can be obtained, however, by saponifying the hydrogen phthalic esters with sodium hydroxide solutions; the more concentrated the solution employed, the higher the rotatory powers of the resulting alcohols. Even under the most favourable experimental conditions some racemisation occurs, since the rotatory power and melting point of the optically active alcohols obtained
can be raised by recrystallisation, being finally obtained from a mixture of methylene chloride and petroleum ether with m.p. 61° and \([\alpha]_{554} +28.3°\) in carbon disulphide solution. The recrystallised alcohol when reconverted into its hydrogen phthalic ester gave a product of rotatory power identical with that of the hydrogen phthalic ester from which it had been obtained. The (+) alcohol thus obtained can be reduced to (-)methyl \(\beta\)-phenethyl carbinol possessing a rotatory power in close agreement with that of the \(1\)-methyl-\(\beta\)-phenethyl carbinol obtained by direct resolution. This affords fairly conclusive evidence that the (+) and (-) \(\gamma\)-phenyl-\(\alpha\) -methylallyl alcohols have been isolated in an optically pure state. In Table VI, the rotatory powers of the (+) alcohol are compared with those of (-) methyl-\(\beta\)-phenethyl carbinol.
FIGURE III.
The Specific Rotatory Power of \( \gamma \)-Phenyl-\( \alpha \)-methylallyl Hydrogen Phthalic Ester in Various Solvents. (See Table V.).
**TABLE V.**

Specific Rotatory Powers of (+)-1-Phenyl-α-methylallyl Hydrogen Phthalate in Various Solvents.

(1,2; α,5.00) at room temperature. (See Fig. III).

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$[\alpha]_{546}^0$</th>
<th>$[\alpha]_{576}^0$</th>
<th>$[\alpha]_{546}^0$</th>
<th>$[\alpha]_{546}^0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon Disulphide</td>
<td>+37.38°</td>
<td>+39.00°</td>
<td>+44.71°</td>
<td>+87.4°</td>
</tr>
<tr>
<td>Pyridine</td>
<td>+19.8°</td>
<td>+21.2°</td>
<td>+24.2°</td>
<td>+43.0°</td>
</tr>
<tr>
<td>Acetic Acid.</td>
<td>+19.1°</td>
<td>-</td>
<td>+23.8°</td>
<td>+47.6°</td>
</tr>
<tr>
<td>Benzene</td>
<td>+4.0°</td>
<td>+4.7°</td>
<td>+5.1°</td>
<td>+7.8°</td>
</tr>
<tr>
<td>Carbon Tetrachloride</td>
<td>+3.3°</td>
<td>+4.7°</td>
<td>+4.9°</td>
<td>+7.2°</td>
</tr>
<tr>
<td>Chloroform.</td>
<td>+1.8°</td>
<td>+2.0°</td>
<td>+2.2°</td>
<td>+5.3°</td>
</tr>
<tr>
<td>Methyl Alcohol (c,14.6)</td>
<td>-7.2°</td>
<td>-7.4°</td>
<td>-8.4°</td>
<td>-15.3°</td>
</tr>
<tr>
<td>Ethyl Alcohol.</td>
<td>-13.5°</td>
<td>-14.1°</td>
<td>-15.4°</td>
<td>-28.0°</td>
</tr>
<tr>
<td>Acetone.</td>
<td>-10.3°</td>
<td>-11.8°</td>
<td>-12.6°</td>
<td>-22.3°</td>
</tr>
<tr>
<td>Ether.</td>
<td>-13.9°</td>
<td>-14.5°</td>
<td>-16.3°</td>
<td>-32.2°</td>
</tr>
<tr>
<td>Ethylene Dibromide.</td>
<td>-8.9°</td>
<td>-</td>
<td>-11.1°</td>
<td>-19.6°</td>
</tr>
<tr>
<td>Ethyl Acetate.</td>
<td>-19.0°</td>
<td>-</td>
<td>-23.7°</td>
<td>-41.5°</td>
</tr>
<tr>
<td>Dioxan.</td>
<td>-7.2°</td>
<td>-8.2°</td>
<td>-9.2°</td>
<td>-17.7°</td>
</tr>
</tbody>
</table>

(-)-1-Phenyl-α-methylallyl Hydrogen Phthalate.

| Carbon Disulphide.       | -36.23             | -57.39             | -44.53             | -88.74             |
### TABLE VI.

Comparative Rotatory Powers of Saturated and Unsaturated Alcohols.

<table>
<thead>
<tr>
<th>Compound</th>
<th>$[\alpha]^{20}_D$</th>
<th>$\frac{\alpha_{365}}{\alpha_{546}}$</th>
<th>$[\eta]^{20}_D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{(-)} \text{ Ph.CH}_2\text{.CH}_2\text{.CHOH.Me}$</td>
<td>$-16.75^\circ$</td>
<td>$1.670$</td>
<td>$-25.12^\circ$</td>
</tr>
<tr>
<td>$\text{(-)} \text{ CH}_3\text{.CH}_2\text{.CHOH.Me}$</td>
<td>$-16.10$</td>
<td>$1.662$</td>
<td>$-11.91$</td>
</tr>
<tr>
<td>$\text{(+)} \text{ Ph.CH=CH.CHOH.Me}$</td>
<td>$+39.48$</td>
<td>$2.06$</td>
<td>$+58.43$</td>
</tr>
<tr>
<td>$\text{(+)} \text{ CH}_2\text{=CH.CHOH.Me}$</td>
<td>$+40.38$</td>
<td>$1.802$</td>
<td>$+29.07$</td>
</tr>
</tbody>
</table>
The rotatory powers of (+)-butan-2-ol and (+)-methyl-vinyl carbinol are also included in this table because they show (a) that when the hydrogen atom in the $\beta$-position in both the saturated and unsaturated aliphatic alcohols is replaced by a phenyl group, the molecular rotatory powers are approximately doubled, (b) that the introduction of an $\Delta\alpha$-bond into both the aliphatic and semi-aromatic alcohols not only more than doubles the rotatory power but also reverses its sign. In compiling this table it has been assumed that (-)methyl-vinyl carbinol has the same configuration as (+)-butan-2-ol, since (-)n-butyIvinyl carbinol has been proved to have the same configuration as (+)-ethyl-n-butyl carbinol.

In Table VII, the properties of (+)-$\gamma$-phenyl-$\alpha$-methylallyl alcohol and its derivatives are compared with those of the corresponding saturated alcohol, (+) methyl-$\beta$-phenethyl carbinol.
TABLE VII

The Properties of (+)Methyl-β-phenethyl carbinol and
(+) γ-Phenyl-α-methylallyl alcohol.

<table>
<thead>
<tr>
<th>Component</th>
<th>(+) Alcohol</th>
<th>(+) Methyl β-phenethyl carbinol</th>
<th>(+) γ-Phenyl-α-methylallyl alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol (1,3.0)</td>
<td>α₂₄₀° (1,1.0)</td>
<td>+16.94°</td>
<td>+42.0°</td>
</tr>
<tr>
<td></td>
<td>dispersion</td>
<td>α₂₄₀°/α₅₄₀°</td>
<td>1.680</td>
</tr>
<tr>
<td>Acetate of (+) alcohol</td>
<td>α₂₄₀° (1,1.0)</td>
<td>1.72</td>
<td>166.0°</td>
</tr>
<tr>
<td></td>
<td>dispersion</td>
<td>α₂₄₀°/α₅₄₀°</td>
<td>0.2</td>
</tr>
<tr>
<td>Hydrogen Phthalate of (+) alcohol</td>
<td>[α]₅₄₀° c,5 in ethyl alcohol</td>
<td>+54.4</td>
<td>-15.4</td>
</tr>
<tr>
<td></td>
<td>m.p.</td>
<td>oil</td>
<td>92-93.5°</td>
</tr>
<tr>
<td>Hydrogen Phthalate of dl-alcohol</td>
<td>m.p.</td>
<td>oil</td>
<td>68.5°</td>
</tr>
</tbody>
</table>
FIGURE IV.

Variation of Specific Gravity of dl-\(\alpha\)-Phenyl-\(\alpha\)-methyl
allylalcohol with Temperature.
### TABLE VIII

**Variation of Rotatory Power of (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Alcohol with Temperature. (1,0.5).**

<table>
<thead>
<tr>
<th>(\theta^\circ)</th>
<th>(\alpha_{5780})</th>
<th>(\alpha_{5461})</th>
<th>(\alpha_{4350})</th>
</tr>
</thead>
<tbody>
<tr>
<td>51°</td>
<td>+17.96°</td>
<td>+21.00°</td>
<td>+43.25°</td>
</tr>
<tr>
<td>59.5°</td>
<td>17.66</td>
<td>20.68</td>
<td>41.56</td>
</tr>
<tr>
<td>74.5°</td>
<td>16.54</td>
<td>19.26</td>
<td>39.65</td>
</tr>
<tr>
<td>95.0°</td>
<td>15.28</td>
<td>17.82</td>
<td>35.63</td>
</tr>
</tbody>
</table>

### TABLE IX

**Specific Rotatory Powers of (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Alcohol in Various Solvents. (1,2.0). at room temperature.**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Gms. per 1000 c. soln.</th>
<th>([\alpha]_{5513})</th>
<th>([\alpha]_{5780})</th>
<th>([\alpha]_{4350})</th>
<th>([\alpha]_{435v})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridine.</td>
<td>5.000</td>
<td>+28.8°</td>
<td>+32.3°</td>
<td>+36.5°</td>
<td>+73.3°</td>
</tr>
<tr>
<td>Carbon Disulphide.</td>
<td>5.000</td>
<td>23.65</td>
<td>25.0</td>
<td>28.3</td>
<td>59.3</td>
</tr>
<tr>
<td>Chloroform.</td>
<td>5.000</td>
<td>24.7</td>
<td>26.5</td>
<td>30.9</td>
<td>60.7</td>
</tr>
<tr>
<td>Ether.</td>
<td>5.000</td>
<td>22.2</td>
<td>24.8</td>
<td>28.5</td>
<td>54.5</td>
</tr>
<tr>
<td>Ethyl Alcohol.</td>
<td>5.000</td>
<td>18.5</td>
<td>20.8</td>
<td>23.7</td>
<td>49.0</td>
</tr>
<tr>
<td>Benzene.</td>
<td>4.070</td>
<td>18.2</td>
<td>19.4</td>
<td>22.2</td>
<td>43.0</td>
</tr>
<tr>
<td>Acetone.</td>
<td>5.000</td>
<td>16.8</td>
<td>19.1</td>
<td>21.8</td>
<td>45.0</td>
</tr>
</tbody>
</table>

\((-\gamma\)-Phenyl-\(\alpha\)-methylallyl Alcohol.\)

| Carbon Disulphide.   | 4.498                  | -23.55°              | -24.1°               | -28.0°               | -56.0°               |
FIGURE V.
Variation of Rotatory Power of (+)-γ-Phenyl-α-methyl-allylalcohol with Temperature (1,0,5). (See Table VIII).
FIGURE VI

Specific Rotatory Powers of (+)-β-Phenyl-α-methylallyl Alcohol in Various Solvents at Room Temperature. (See Table VIII)
In Figure (III) and Figure (VI) the specific rotatory powers in various solvents of (+)-γ-phenyl-α-methylallyl hydrogen phthalate and (+)γ-phenyl-α-methylallylalcohol, respectively, are plotted. The method of plotting used was to place the values of \([\alpha]_5461\) in different solvents, on any arbitrarily chosen straight line passing through the origin. The values of \([\alpha]_4358\) and \([\alpha]_5993\) were then plotted for each solution, taking as abscissa, that of the corresponding value of \([\alpha]_5461\).

In each case the values of \([\alpha]_4358\) and \([\alpha]_5993\) were found to lie upon straight lines, all three lines intersecting at the origin. (+)-γ-Phenyl-α-methylallylalcohol and its hydrogen phthalic ester, therefore, display the same dispersion in all solvents; that is to say - in the visible region of the spectrum - both compounds have "Normal Dispersion".
**EXPERIMENTAL DETAILS.**

dl-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl alcohol (119g.), prepared by the addition of cinnamaldehyde (126g.) to the Grignard reagent prepared from magnesium (24g.) and methyl bromide (98g.), has b.p. 129-131°/11mm. It sets to a solid mass of small, irregular, prismatic needles, m.p. 30-31.5°. Its phenyl urethane separates from ether and petrol in fine hairy needles, m.p. 93-94° (Klages gives m.p. 94-95°) and its \(p\)-xenylurethane from benzene in rosettes of small needles, m.p. 162-163° (Found, N, 4.26; \(C_{23}H_{21}O_2N\) requires N, 4.1%).

Attempts were made to separate dl-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol into cis- and trans-forms by (a) fractional distillation, (b) partial fusing of the solidified alcohol and draining off the liquefied portion and (c) crystallisation from methylene chloride and petroleum ether. The various fractions of the alcohol from (a) and (b) all had m.p. 30-31.5°; the alcohol after crystallisation from methylene chloride and petroleum ether, from which it separates in spherical clusters of fine needles, has m.p. 33°.

dl-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl-\(p\)-nitrobenzoate.

\(p\)-Nitrobenzoyl chloride (18.8g.) was added in portions to a stirred mixture of dl-\(\gamma\)-phenyl-\(\alpha\)-methylallylalcohol (14.8g.) and pyridine (10g.) and the solid reaction
product taken up in ether and sodium carbonate solution
The dried ethereal solution was evaporated to small
bulk, mixed with petroleum ether and allowed to crystal-
lise. The p-nitrobenzoate (22g., m.p. 56-58°) separates
from ether and petroleum ether in almost colourless,
short, fine needles, m.p. 58-59°. (Found, N,4.7;
C_{14}H_{15}O_{4}N requires N,4.7%).

*dl-Y-Phenyl-α-methylallyl hydrogen phthalate.*

(i). A mixture of the alcohol (148g.), phthalic anhydride
(148g.) and pyridine (100g.) was heated for 1.5 hours
on the steam bath when it became a homogeneous viscous
liquid. Next day the product was dissolved in acetone
(500c.c.) and mixed with ice-cold dilute hydrochloric
acid; the liberated oil after stirring with a large
volume of water soon set to a crystalline mass (218g.
= 73%, m.p. 85-90°). The hydrogen phthalic ester
separates from carbon disulphide or from a mixture of
erther and petroleum ether in irregular glassy rhombs,
m.p. 92-93.5°.

(ii). Phthalic anhydride (3.5g.) was added to the
Grignard complex obtained by the interaction in ethereal
solution of magnesium (0.3g.) methyl iodide (3.6g.) and
subsequently of cinnamaldehyde (3.2g.) and the resultant
paste triturated for a few minutes until it changed to
a yellowish brown powder easily removable by filtration.
It was taken up in ether and dilute sodium carbonate solution: the sodium carbonate extracts on addition of hydrochloric acid gave an oil which rapidly crystallised. The hydrogen phthalic ester (2.5g., m.p. 90-91°) separated from carbon disulphide in glassy rhombs, m.p. and mixed m.p. 92-93°. Found, by titration with NaOH, M.W. 295. C\textsubscript{18}H\textsubscript{16}O\textsubscript{4} requires M.W. 296. Repeated crystallisation of dl-Y-phenyl-\(\alpha\)-methylallyl hydrogen phthalate did not alter its m.p. and the dl-Y-phenyl-\(\alpha\)-methylallyl alcohol obtained from it by saponification had b.p. 123°/10mm., and m.p. 50-51.5°; \(d\textsubscript{27}^\circ\) 1.072, \(d\textsubscript{29}^\circ\) 1.046, \(d\textsubscript{35}^\circ\) 1.012, \(d\textsubscript{43}^\circ\) 0.999, \(n\textsubscript{D}^\circ\) 1.5741, \(n\textsubscript{D}^{19}\) 1.5692, \(n\textsubscript{D}^{62}\) 1.5521, [\(\Box\)] 367.4 (Mean Value between 17-45°C) Calc. 372.1.

(+)-Y-Phenyl-\(\alpha\)-methylallyl hydrogen phthalate.

Cinchonidine (30g.) was dissolved in a hot solution of the dl-hydrogen phthalic ester (30g.) in ethyl acetate (90c.c.). The cinchonidine salt of (+)-Y-phenyl-\(\alpha\)-methylallyl hydrogen phthalate (25g.) separated on cooling; it was obtained optically pure, tufts of fibrous needles, m.p. 179° (decomp.) 7.5g., with \([\alpha]\)\textsubscript{590} -28.9°, \([\alpha]\)\textsubscript{5790} -30.1°, \([\alpha]\)\textsubscript{5461} -36.4°, \([\alpha]\)\textsubscript{4358} -59.2°, (\(c\), 5.050; 1,2) in chloroform solution. The cinchonidine salt on decomposition with dilute hydrochloric acid yielded (+)-Y-phenyl-\(\alpha\)-methylallyl hydrogen phthalate which crystallises from carbon disulphide and petroleum
ether in felted masses of fine, hairy needles, m.p. 68.5° (this value was unchanged after 18 months.). The rotatory powers are given in Table V

(+)-1-Phenyl-α-methylallyl Alcohol.

The alcohol of highest rotatory power was obtained when the following procedures were followed (a) (+)-hydrogen phthalic ester (30g.) was heated 1 hour on the steam bath with sodium hydroxide (45c.c. 5N.) and the mixture distilled in a current of steam. Extraction of the steam distillate yielded the (+)-alcohol (13g.) b.p. 128°/10mm., m.p. 49°-50° with \( \alpha_{58°}^{N} = +6.4°, \alpha_{54°}^{N} = +7.5°, \alpha_{43°}^{N} = +14.4° \) \((1,0.25)\). After keeping the alcohol in a closed vessel for nearly 2 years it had \( \alpha_{58°}^{N} = +11.86° \) \((1,0.5)\).

(b) (-)-hydrogen phthalic ester (12g.) in hot ethyl alcohol (40c.c.) was mixed with aqueous sodium hydroxide (30c.c. 5N.) and after heating under reflux 15 minutes distilled in a current of steam. The alcohol, which solidified in the distillate, had, after desiccation, m.p. 55° and \([\alpha]_{546}^{N} = -21.2°\) in carbon disulphide solution (c,5.00; \( \frac{1}{2},2 \)). Even under these conditions some racemisation had occurred since both the rotatory power and the m.p. of the alcohol thus obtained were raised by crystallisation. That from experiment (b) after one crystallisation from a mixture of methylene chloride
and petroleum ether had m.p. 61°, \( \eta^2_D = 1.5486 \) and 
\([\alpha]_{546}^\infty = -28.0° \) (c, 5.00; 1/2) in carbon disulphide solution.

The maximum values obtained are recorded in Tables VIII and IX.

\((-\)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl hydrogen phthalate.

The first filtrate from the crystallisation of the cinchonidine salt yielded a hydrogen phthalic ester (18g.) with 
\([\alpha]_{546} = -24° \) (c, 5 in carbon disulphide). This was 
dissolved in acetone (30c.c.) and brucine (34g.) dissolved 
in the solution. On cooling, the brucine salt of \((-\)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate separated in 
small needles, and was obtained optically pure after two 

further crystallisations from acetone, (decomp. about 110)
\([\alpha]_{589} = -31.0°\), \([\alpha]_{578} = -36.9°\), \([\alpha]_{546} = -48.7°\), \([\alpha]_{439} = -102.0°\)
(c, 5.325; 1/2) in chloroform solution. On decomposition 
of the brucine salt with hydrochloric acid \((-\)-\(\gamma\)-phenyl-
\(\alpha\)-methylallyl hydrogen phthalate was obtained. It 
separates from carbon disulphide and petroleum ether in 
masses of felted needles, m.p. 68.5°.

The optically active forms of \(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate are much more soluble than the 
inactive variety: when carbon disulphide solutions 
containing equal amounts of the (+)- and of the (-)- 
forms were mixed the crystals which separated were glassy 
rhombs of the \(\text{dl}\)-hydrogen phthalic ester m.p. 92-93°.
(-)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl alcohol, obtained from the
(-)-hydrogen phthalic ester crystallised from methylene
chloride and petroleum ether in large hexagonal plates
or long four-sided prisms, m.p. 61°. Equal amounts of
(+)- and of (-)- \(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohols of m.p.
61° were fused together; after solidification the dl-
product had m.p. 33.5°.

(+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl alcohol, \([\alpha]_{D}^2 +28.3^\circ (c, 5.0;\)
1,2 in carbon disulphide solution) was reconverted into
its hydrogen phthalic ester; this had m.p. 68° and
\([\alpha]_{D}^2 +44.7^\circ (c, 2.908; 1,2)\) in carbon disulphide solution.
The \(p\)-xenyl urethane of (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol,
needles, m.p. 179-180°, from methylene chloride and
petroleum ether, has \([\alpha]_{5893}^2 +163.3^\circ, [\alpha]_{5780}^2 +176.6^\circ,\)
\([\alpha]_{5441}^2 +200.1^\circ, [\alpha]_{4358}^2 +408^\circ (c, 0.6385; 1,2)\) in chloroform
solution. Found, N, 4.2; \(C_{23}H_{21}O_2N\) requires N, 4.1%.

(+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl acetate, prepared by gently
heating a mixture of the (+)-alcohol (5g.), pyridine (4g.,
and acetic anhydride (5g.), has b.p. 132-133/9mm.,
\(n_D^2 1.5369; \alpha_{5993}^1 +34.16^\circ; \alpha_{5780}^1 +35.78^\circ; \alpha_{5441}^1 +41.51^\circ;\)
\(\alpha_{4358}^1 +80.0^\circ (1, 0.25); \) in chloroform solution (c, 5.020;
1,2) it had \([\alpha]_{5893}^2 +132.8^\circ; [\alpha]_{5780}^2 +86.2^\circ; [\alpha]_{5441}^2 +108.7^\circ;\)
\([\alpha]_{4358}^2 +308.3^\circ.\)

(+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl \(p\)-nitrobenzoate, leaflets,
m.p. 41°, from a mixture of ether and petroleum ether
Reduction of (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl alcohol to
(-)-\(\beta\)-Phenethyl methyl carbinol.

The alcohol (4.4g. with \([\alpha]_{5595}^\circ +23.65^\circ\) in carbon disulphide solution) was reduced with hydrogen in the presence of platinum catalyst prepared according to the method of Adams, Voorhees and Shriner. The calculated volume of hydrogen was absorbed within one hour. The resulting (-)-\(\beta\)-phenethyl methyl carbinol, which had no action on bromine solution, had b.p. 127/16mm., and \(\alpha_{5993}^{18^\circ} -3.42^\circ\); \(\alpha_{5780}^{18^\circ} -3.59^\circ\); \(\alpha_{5461}^{18^\circ} -4.04^\circ\); \(\alpha_{4353}^{18^\circ} -6.69^\circ (1,0.25)\). Its phenyl urethane (Found, N, 5.4; C_{17}H_{15}O_{2}N requires N, 4.7%) had m.p. 47-48° alone or admixed with a specimen prepared from the alcohol of Pickard and Kenyon. The values given by Pickard and Kenyon, for the rotatory powers of this alcohol prepared by direct resolution are \(\alpha_{5461}^{18^\circ} -4.10^\circ\); \(\alpha_{4353}^{18^\circ} -6.85^\circ\) (for 1,0.25). This specimen prepared by Pickard and Kenyon after keeping some 22 years was found to have (without redistillation) the following rotatory powers \(\alpha_{5461}^{19^\circ} -3.88^\circ\); \(\alpha_{4353}^{19^\circ} -6.52^\circ\) (1,0.25).

In view of the change in the sign of rotatory power
undergone by (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol after its conversion to (-)-\(\beta\)-phenethyl methyl carbinol it is interesting to note that whilst the less soluble cinchonidine salt of the hydrogen phthalic ester of the former gives rise to the (+)-alcohol and the less soluble brucine salt of the hydrogen phthalic ester to the (-)-alcohol, the converse is the case with the latter; the less soluble cinchonidine salt of the hydrogen phthalic ester yielding the (-)-alcohol and the corresponding brucine salt the (+)-alcohol.

\(\gamma\)-Phenyl-\(\alpha\)-methylallyl chloride could not be prepared by interaction of the alcohol with phosphorus trichloride in the presence of pyridine. Attempts led to the formation of a resinous mass; but it was found that if the reaction mixture contained a 50% excess of the alcohol a constant-boiling liquid could be isolated. (dl)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl alcohol (7.5g.) was mixed with pyridine (3g.) and ether (150c.c.) and slowly dropped into an ice-cold mixture of phosphorus trichloride (1.5g.) and ether (100c.c.). The ether solution was then poured off the viscous oil which separated, and was distilled, leaving a colourless oil, b.p. \(104^\circ/9\text{mm.}\), (3g.). The same product is formed when the alcohol (5g.) mixed with pyridine (2.7g.) and ether is dropped into thionyl chloride (3.5g.) and ether (2 vols.) in a freezing
mixture. Here the product (4g.) has b.p. 105°/10mm.,
$\rho_D^{15}$ 1.5846, soon became cloudy, and polymerised on
standing. It contained no chlorine, but on shaking with
silver nitrate gave a bulky white precipitate, which
(2.13g.) on igniting, left a residue of bright metallic
silver, (0.375g.); the organic material in it caught
fire during the ignition and burnt with a smoky flame.
The silver salt is soft, and retains a sweet smell even
after washing with ether. Its composition appears to
be variable. The same product resulted from attempts
to prepare $\alpha$-phenyl-$\gamma$-methylallyl chloride in a similar
way, and it was found that when optically active
alcohols were used, the product was always inactive.
On heating the product with alcoholic caustic soda,
followed by steam distillation, phenyl butadiene (b.p.
95°/15mm., m.p. 3°C., $\rho_D^{15}$ 1.6084) is formed. The product
from these reactions may possibly be an isomer of phenyl
butadiene formed by removal of the elements of hydrogen
chloride from an unstable intermediate chlorine compound.

\[
\begin{align*}
\text{PhCH(OH)CH:CH:Me} & \quad \rightarrow \quad \text{PhCH:CH:CH(OH)Me} \\
\text{PhCH(CH)CH:CH:Me} & \quad \rightarrow \quad \text{PhCH:CH:CH(Cl)Me}
\end{align*}
\]

\[
\begin{align*}
\text{PhC=CH:CH:Me} & \quad \rightarrow \quad \text{PhCH:CH:CH:Me} \\
\text{PhCH:CH:CH:CH}_2 & \quad \rightarrow \quad \text{PhC=CH:CH:Me}
\end{align*}
\]

$\alpha$-phenyl-$\alpha\beta$-butadiene

$\alpha$-phenyl-$\alpha\gamma$-butadiene
Like α-phenyl-α,β-butadiene the new product absorbs two atoms of bromine (calculated upon a molecular weight of 130) forming a dibromo-derivative $\text{PhCH} = \text{CH}.\text{CHBr}.\text{CH}_2\text{Br}$ m.p. 92° and mixed with a sample of the authentic material m.p. 92°, in characteristic aggregates of prismatic needles (Found, Br, 54.8%; $C_{10}H_{10}Br_2$ requires Br, 55.2%). It also decolourises acid permanganate solution. (Found: C, 84.5; H, 7.5%; $C_{10}H_{10}$ requires C, 92.3; H, 7.7%); the analysis shows that the product is not pure.
SECTION II.

The Unsymmetrical Addition of Bromine to Substituted Allyl Alcohols.

The addition of bromine to αγ-dimethylallyl alcohol and ethylvinylecarbinol has already been discussed in Chapter IV. and consequently the experimental details only are given here. In order to make a further investigation into the course of these reactions, the similarly constituted alcohol (+)γ-phenyl-α-methylallyl alcohol was chosen as being likely to afford crystalline dibromo-derivatives. This alcohol combines readily and completely with bromine at 18° to give a mixture of two methyl-αβ-dibromo-β-phenylethylcarbinols (II) which, without crystallisation or other form of separation, is smoothly oxidised to (-)methyl αβ-dibromo-β-phenylethyl ketone (III). By fractional crystallisation (II) can be separated into a (+) and

\[
\text{CHMe(OH).CH}_3\text{CHPh} \rightarrow \text{CHMe(OH).} \text{CHBr.CHBrPh} \rightarrow \text{COMe.CHBr.CHBrPh}
\]

\[
+45.7^\circ \text{ in CHCl}_3 \quad [\pi]_D \quad -31.3^\circ \text{ in CHCl}_3
\]

a (-)-isomeride, m.p. 112-113° (fine hairy needles from light petroleum) and 87-88° (large glassy prisms from light petroleum) respectively. The rotatory powers are given in Table X. Oxidation of the alcohol of higher
m.p. yields a (+)-ketone, and that of the other alcohol a (-)-ketone, both of m.p. 127°. Since the rotatory powers of these two ketones (Table X), although of opposite sign, are of equal magnitude, it is very probable that they are optically pure substances, and thus it is possible to calculate the degree of effectiveness of the asymmetric synthesis.

In a similar way the (-)-form of (I) afforded a (-)-methyl-αβ-dibromo-β-phenylethylcarbinol of m.p. 112-113°, which proved to be the optical enantiomorph of the less soluble dibromo-alcohol mentioned above, and on oxidation it was converted into optically pure (-)-methyl αβ-dibromo-β-phenylethyl ketone. These reactions are illustrated in different ways by Table X.
### ADDITION OF BROMINE TO (+)-PHENYL-α-METHYLALLYLALCOHOL

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Structure</th>
<th>Melting Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)-CHPhBr·CHBr·CH(OH)Me</td>
<td><img src="image1.png" alt="Structure 1" /></td>
<td>m.p. 112°</td>
</tr>
<tr>
<td>(-)-CHPhBr·CHBr·CH(OH)Me</td>
<td><img src="image2.png" alt="Structure 2" /></td>
<td>m.p. 127°</td>
</tr>
<tr>
<td>(+)-CHPh·CH·CH(OH)Me</td>
<td><img src="image3.png" alt="Structure 3" /></td>
<td>m.p. 61°</td>
</tr>
<tr>
<td>(-)-CHPhBr·CHBr·COMe</td>
<td><img src="image4.png" alt="Structure 4" /></td>
<td>m.p. 61°</td>
</tr>
<tr>
<td>(+)-CHPhBr·CHBr·CH(OH)Me</td>
<td><img src="image5.png" alt="Structure 5" /></td>
<td>m.p. 88°</td>
</tr>
<tr>
<td>(-)-CHPhBr·CHBr·CH(OH)Me</td>
<td><img src="image6.png" alt="Structure 6" /></td>
<td>m.p. 88°</td>
</tr>
<tr>
<td>(+)(+)(m.p. 112°)</td>
<td><img src="image7.png" alt="Structure 7" /></td>
<td>m.p. 112°</td>
</tr>
<tr>
<td>(+)(m.p. 127°)</td>
<td><img src="image8.png" alt="Structure 8" /></td>
<td>m.p. 127°</td>
</tr>
</tbody>
</table>
Each of the optically active dibromo-alcohols, since it contains three asymmetric centres, is theoretically capable of existing in four isomeric forms the mixture of which on oxidation should give rise to two isomeric dibromo-ketones. The dibromo-ketone, however, was homogeneous and obtained in good yield, showing that only two of the four possible isomeric dibromo-alcohols were present in the mixture. This is in harmony with the fact that \( \gamma \)-phenyl-\( \alpha \)-methylallyl alcohol behaves like a single geometrical isomeride and not as a mixture of cis- and trans-forms\(^5\).

The work of Soper and Smith\(^5\) and of Richelberger\(^5\) suggests that, in the addition of halogens at the ethylenic linkage, the attack is by the polarised molecule and not by either of its ions. The positive pole is assumed to enter before the negative pole, the latter, in ionising solvents being liberated as an anion after addition of the former has taken place. It is probable that in a relatively non-polar solvent such as chloroform, the anion does not actually separate, with the result that trans-addition to the double bond is inhibited, and the number of diastereoisomerides formed is consequently reduced.

As the energy of activation of a reaction frequently varies with the temperature at which it takes place,
The solution was obtained and the derived kinetic
constants determined.

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>Rate Constant (10^6 M⁻¹ s⁻¹)</th>
<th>Sign</th>
<th>Reaction (Species)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.00</td>
<td>-</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>100</td>
<td>-</td>
<td>+</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>200</td>
<td>-</td>
<td>-</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>300</td>
<td>-</td>
<td>+</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>400</td>
<td>-</td>
<td>-</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>500</td>
<td>-</td>
<td>+</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>600</td>
<td>-</td>
<td>-</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
<tr>
<td>700</td>
<td>-</td>
<td>+</td>
<td>CTOH⁻, CNO⁻, CBOH⁻</td>
</tr>
</tbody>
</table>

*Note: The reaction was carried out at room temperature.*
## Table XII

Specific Rotatory Powers of Methyl αβ-Dibromo-β-phenylethyl Ketones obtained by Oxidation of the Methylαβ-dibromo-β-phenylethylcarbinols prepared at Temperature t°.

<table>
<thead>
<tr>
<th>t°</th>
<th>Medium</th>
<th>$[\alpha]_{5893}$</th>
<th>$[\alpha]_{5710}$</th>
<th>$[\alpha]_{5461}$</th>
<th>$[\alpha]_{4350}$</th>
<th>In $\text{CHCl}_3$</th>
<th>Rotatory Power (1,2)c.</th>
<th>% of maximum rotatory power</th>
</tr>
</thead>
<tbody>
<tr>
<td>-15°</td>
<td>$\text{CHCl}_3$</td>
<td>-20.0°</td>
<td>-21.6°</td>
<td>-34.1°</td>
<td>2.13</td>
<td>41.1 of (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-6</td>
<td>-</td>
<td>-</td>
<td>16.5</td>
<td>17.9</td>
<td>30.3</td>
<td>5.15</td>
<td>34.0 &quot; (-)</td>
<td></td>
</tr>
<tr>
<td>+18</td>
<td>-</td>
<td>-</td>
<td>9.2</td>
<td>10.15</td>
<td>19.6</td>
<td>2.70</td>
<td>19.4 &quot; (-)</td>
<td></td>
</tr>
<tr>
<td>+60</td>
<td>-</td>
<td>+1.7</td>
<td>+1.84</td>
<td>+2.45</td>
<td>+4.75</td>
<td>3.27</td>
<td>4.7 &quot; (+)</td>
<td></td>
</tr>
<tr>
<td>+75</td>
<td>$\text{CCl}_4$</td>
<td>-</td>
<td>-</td>
<td>+3.50</td>
<td>+7.50</td>
<td>0.96</td>
<td>6.7 &quot; (+)</td>
<td></td>
</tr>
</tbody>
</table>
some variation in the composition of the mixture of dibromo-alcohols was to be anticipated when the addition of bromine to the unsaturated alcohol was made at different temperatures in the same solvent. Experiment proved that an unexpectedly wide variation in the rotatory powers of the ketones obtained by oxidation of the mixtures of dibromo-alcohols produced at different temperatures (Table XII) did actually occur, the (-)- or the (+)-ketone predominating according as the temperature was low or high.

The five values of \([\alpha]\) given in Table XIII lie on a curve, but attempts to extend these measurements were not very successful; at lower temperatures the reaction was very sluggish, and at higher temperatures it did not proceed smoothly. McKenzie (Chap. II, p.10) has been able to predict the sign of rotation of substituted glycollic acids formed by asymmetric synthesis from (-)-menthy1 benzoylformate and from (-)-menthy1 pyruvate. His prediction is based upon the sense of the contribution of the ketonic system to the total rotatory power of the ester in certain alcoholic solvents.

Clearly, in the above example no such prediction could be made, for the same initial material is able to give rise to either the dextro- or the laevo-rotatory dibromo-ketone according to the temperature of the reaction.
In order to show that the diastereoisomerides were not in a state of tautomeric equilibrium under the conditions of the reaction, a portion of the mixture prepared at a low temperature was heated under reflux in chloroform solution for 2 hours without any change in composition taking place.
EXPERIMENTAL DETAILS.

(+)-Methyl-αβ-dibromopropylcarbinol (8.3g.), prepared by addition of bromine (8g.) in chloroform (20c.c.) at room temperature to (-)-αγ-dimethylallyl alcohol (α\text{D}^0\text{L}^-\gamma = -1.40°; J,2) (4.5g.), has nD\text{D}^0 = 1.5336, b.p. 103/13 mm.,

α\text{D}^0 +2.04°, α\text{D}^0 +2.15°, α\text{D}^0 +2.46°, α\text{D}^0 +4.90° (1°0.5)

(Found: Br, 64.9. C\text{H}_10\text{OBr}_2 requires Br, 65.0%).

This (8.3g.) on oxidation with chromic anhydride (2.5g.) in glacial acetic acid (10c.c.) at 60° gave (+)-methyl αβ-dibromopropyl ketone (4.5g.), b.p. 90/13 mm.,

nD\text{D}^0 = 1.5195, α\text{D}^0 +5.06°, α\text{D}^0 +3.34°, α\text{D}^0 +3.95°,

α\text{D}^0 +8.25°(1°0.25) (Found: C, 35.4; H, 3.6. C\text{H}_8\text{OBr}_2 requires C, 34.6; H, 3.3%). In a similar manner the dextrorotatory αγ-dimethylallyl alcohol (α\text{D}^0\text{L}^-\gamma = +0.38°; J,0.5) obtained by hydrolysis of (+)-αγ-dimethylallyl chloride gave optically inactive methyl-αβ-dibromopropylcarbinol, b.p. 112/20 mm., which (12.3g.) on oxidation with chromic anhydride (3g.) gave inactive methyl αβ-dibromopropyl ketone (10g.) b.p. 90/13 mm.

Addition of bromine (8g.) in 50% chloroform solution to (+)-γ-phenyl-α-methylallyl alcohol (7.4g.) in chloroform (30c.c.) at room temperature yielded a mixture of two isomeric methyl-αβ-dibromo-β-phenylethylcarbinols, which, after removal of the chloroform, were obtained crystalline (Found: C, 39.1; H, 4.2. C\text{H}_12\text{OBr}_2 requires C, 41.3; H, 4.0%).
requires C, 39.0; H, 3.9%).

The solid residue (15g.) was dissolved in glacial acetic acid (15c.c.), and the solution at 60° mixed with chromic anhydride (3g.) in portions.

**Methyl-β-dibromo-β-phenylethyl ketone** separated on dilution with water, and crystallised from hot alcohol in glistening prismatic needles, m.p. 127°; $[\alpha]_{546}^\infty -10.15°$ (1,2; c,2.7 in chloroform) (Found: C, 39.4; H, 3.3; Br, 52.2. $C_{10}H_{10}OBr_2$ requires C, 39.2; H, 3.3; Br, 52.3%).

In a second experiment a mixture of dibromo-alcohols, prepared at -15° (9g.) (m.p. 65-70°), was recrystallised six times from hot light petroleum to constant m.p. (112-113°) and rotatory power, $[\alpha]_{584}^\infty +107.1°$, $[\alpha]_{5790}^\infty +115.9°$, $[\alpha]_{546}^\infty +128.0°$, $[\alpha]_{438}^\infty +261.0°$ (1,2; c,1.473 in chloroform). This homogeneous $\pm$-methyl-β-dibromo-β-phenylethyl carbinal (2g.) on oxidation in acetic acid solution with chromic anhydride (1.0g.) yielded (+)-methyl-β-dibromo-β-phenylethyl ketone (1.75g.) as prismatic needles, m.p. 127° (decomp.); $[\alpha]_{584}^\infty +42.8°$, $[\alpha]_{5790}^\infty +46.1°$, $[\alpha]_{546}^\infty +52.6°$, $[\alpha]_{438}^\infty +84.4°$ (1,2.0; c,3.70 in chloroform).

The light petroleum mother-liquors from the first three crystallisations of the mixed dibromo-alcohols, after standing for several days, deposited crystals of two distinct types: (1) fine hairy needles characteristic
of the (+ +)-methyl-αβ-dibromo-β-phenylethylcarbinol described above, and (ii) large regular hexagonal prisms. The former were readily removed by pouring off the mother-liquor, leaving the latter behind; these had m.p. 87–88°, and $[\alpha]_{58}^{193} = -97.6^\circ$, $[\alpha]_{57}^{193} = -115.4^\circ$, $[\alpha]_{54}^{193} = -119.7^\circ$, $[\alpha]_{55}^{193} = -224.0^\circ$ ($\lambda_2, \lambda_3, \omega_4, 6.42$ in chloroform).

This homogeneous (+ -)-methyl-αβ-dibromo-β-phenylethylcarbinol (0.8 g.) on oxidation with chromic anhydride in acetic acid yielded (−)-methyl αβ-dibromo-β-phenylethyl ketone (0.7 g.), m.p. 127° (decomp.), $[\alpha]_{57}^{193} = -40.7^\circ$, $[\alpha]_{54}^{193} = -45.5^\circ$, $[\alpha]_{54}^{193} = -51.7^\circ$, $[\alpha]_{45}^{193} = -90.7^\circ$ ($\lambda_2$, $\lambda_3$, $\omega_3, 3.02$ in chloroform). In a similar manner (−)-γ-phenyl-α-methylallyl alcohol yields the (− -)-carbinol, m.p. 112–113°, which on oxidation yields the (−)-ketone, m.p. 127°, and the (− +)-carbinol, m.p. 87–88°, which on oxidation yields the (+)-ketone, m.p. 127° (rotatory powers in Table XI).

The m.p. of the methyl αβ-dibromo-β-phenylethyl ketones is very susceptible to the rate of heating—rapid heating gives values as high as 131°. For this reason a specimen of the dl-ketone, which melts at 127° with a normal rate of heating, was always used for comparison.

The addition of bromine (1 mol.) to dl-γ-phenyl-α-methylallyl alcohol gave a mixture of isomeric
dl-dibromo-alcohols, m.p. 60-90°, which was much more difficult to separate by fractional crystallisation than mixtures of the corresponding optically active compounds. After seven recrystallisations from light petroleum (other solvents were tried), a fraction was obtained of m.p. 128-130°. A mixture of equal amounts of (+ +)- and (- -)-methyl-αβ-dibromo-β-phenylethyl carbinols had m.p. 134°, and this when mixed with the former product melted at 129-132°; hence it appears that the separation of the two isomeric racemic dibromo-alcohols has not been completely effected.

(+)Ethylvinylearbinal, prepared by decomposition of the strychnine salt of the hydrogen phthalic ester with subsequent steam distillation from caustic soda solution had α$_{546}$ +3.60° (1,0.25) b.p. 114-115°. The carbinol readily absorbed a molecular amount of bromine in chloroform solution, and on removal of the solvent, ethyl-αβ-dibromo-ethyl carbinol remained as an oil, b.p. 119/23 mm., n$^D$ 1.5546, α$_{546}$ +1.52; α$_{579}$ +1.34; α$_{546}$ 1.54; α$_{455}$ +2.16; (1,0.5). Another sample had [α]$_{546}$ +4.74°, [α]$_{546}$ +7.62° (1,2; α,11.8 in acetic acid). This (2.36g.) was dissolved in acetic acid (50c.c.) and chromic anhydride (1g.) added in small portions, with constant shaking, to the warmed solution (60-70°). The acetic acid solution was diluted with ice-water and extracted
with ether. The resulting ethyl-αβ-dibromo-ethyl ketone was a yellow oil which distilled without decomposition. (2.07g.), b.p. 95°/12mm., \( \mu_D \) 1.5340, \( \alpha_{5490} \) -0.75° (1, 0.25). Another sample had \( [\alpha]_{5490} \) -10.6°, \( [\alpha]_{5491} \) -12.2° (1, 2; \( \epsilon \), 10.4 in acetic acid). (Found: C, 25.42, 25.59; H, 3.17, 3.51; Br, 63.41, 63.50. \( \text{C}_9\text{H}_8\text{OBr}_2 \) requires C, 24.6; H, 3.28; Br, 65.6%).
SECTION III.

The (+) and (-) α-Phenyl-γ-methylallyl Alcohols.

By fractional crystallisation, firstly from methyl acetate and subsequently from acetone, the quinidine salt of (dl)-α-phenyl-γ-methylallyl hydrogen phthalate can be separated into the two salts dβA and dβA which on decomposition furnish (+) and (-) α-phenyl-γ-methylallyl hydrogen phthalate respectively. The latter ester when saponified with aqueous alkali gives rise to an almost completely racemic mixture of α-phenyl-γ-methylallyl alcohol and its isomeride γ-phenyl-α-methylallyl alcohol. Hydrolysis with sodium hydroxide in absolute alcohol however, yields 1-α-phenyl-γ-methylallyl alcohol; this alcohol on reduction is converted into (+)phenyl-n-propyl carbinol the rotatory power of which is in close agreement with that of the carbinol obtained by direct resolution, thus rendering it highly probable that optical purity has been reached in the resolution of both the unsaturated and the saturated alcohols.

It was found that if care in the avoidance of high temperatures and acid catalysts was taken, the acetic, hydrogen phthalic, p-nitrobenzoic esters and the p-xenyl urethane of α-phenyl-γ-methylallyl alcohol could be
prepared unmixed with the corresponding isomeric body, the isomerisation process being much slower at moderate temperatures than the esterification reaction. Attempts to prepare the methyl ether however proved unsuccessful, while the dibromide rapidly decomposed in chloroform solution, hydrobromic acid being evolved. As in the case of \( \gamma \)-phenyl-\( \alpha \)-methylallyl chloride, \( \alpha \)-phenyl-\( \gamma \)-methylallyl chloride could not be prepared by interaction of the alcohol with phosphorus trichloride or thiophenyl chloride, the major product of the reaction being phenylbutadiene in each case.

Both (+) and (-) \( \alpha \)-phenyl-\( \gamma \)-methylallyl hydrogen phthalates separate from a mixture of ether and light petroleum in clusters of long, prismatic needles, m.p. 81–82°, when freshly prepared. After keeping several days at room temperature, even in an evacuated desiccator, the crystals slowly form a matted mass which gradually becomes pasty but which resolidifies after some 20 days. (Table XIX) The surfaces of a crystal, which had been standing on a microscope slide for two days, appeared to have liquefied, the centre part remaining solid and the crystal, as a whole, retaining its shape. The liquid portion gradually travelled inwards and finally crystals of \( \gamma \)-phenyl-\( \alpha \)-methylallyl hydrogen phthalic ester, some fine hairs (d-) and some
rhombic (dl-) began to form and the whole became a mass of crystals still retaining the essential shape of the original crystal.

From this it would appear that transformation takes place on the surface of the crystal aided by traces of (moisture and) the solvent and the surface energy of the crystal. In marked contrast to this behaviour it was found that (a) dl-α-phenyl-γ-methylallyl hydrogen phthalate could be recovered unchanged after its (80%) solution in pyridine had been kept at room temperature for 3 weeks and (b) (−) α-phenyl-γ-methylallyl hydrogen phthalate dissolved in boiling cyclohexane crystallised unchanged from the cooled solution.

dl-α-Phenyl-γ-methylallyl hydrogen phthalate separates from a mixture of ether and light petroleum in small compact irregular crystals m.p. 93-94°; when mixed with the isomeric dl-γ-phenyl-α-methylallyl hydrogen phthalate, m.p. 92-93°, it melts at 92-93°. It is thus probable that 93-94° is not the true melting point of dl-α-phenyl-γ-methylallyl hydrogen phthalate - particularly in view of its less solubility - but rather the temperature at which it undergoes rapid isomeric change. This view is supported by the following experiment: dl-α-phenyl-γ-methylallyl hydrogen phthalate was melted and the resolidified material crystallised...
from ether and light petroleum. It, m.p. 93°, formed a crystalline salt with cinchonidine but not with quinidine, whereas the material before melting readily formed a crystalline salt with quinidine but not with cinchonidine.

The tautomeric change of α-phenyl-γ-methylallyl hydrogen phthalate proceeds smoothly at ordinary temperatures when the ester is dissolved in almost any neutral solvent. The reaction has therefore been followed polarimetrically, and the quantitative method has enabled both the degree of the reaction, and the energy of activation of the tautomeric change in benzene to be calculated.

(-)α-Phenyl-γ-methylallyl hydrogen phthalate has a low (+)-rotation when freshly dissolved in carbon disulphide. This value rapidly begins to rise, doubling itself within 5 or 6 hours, and finally reaching a maximum value in 10-14 days. These values, when plotted against time, lie on a smooth curve (Fig.VII) which proves to be a hyperbola, since, when a logarithmic function of the rotatory power is plotted against time, a straight line results (Fig.VIII). The rotatory powers of two solutions, (i) c, 1.5; (ii) c, 3.0 (1,2) of (-) α-phenyl-γ-methylallyl hydrogen phthalate in carbon disulphide are given in Table XIII.
FIGURE VIII.

Mutarotation of $d$-Phenyl-$d'$-methylallyl Hydrogen Phthalic Ester in Carbon disulphide Solution.

$$t = \frac{\log_{10} (A_0 - A_\infty) - \log_{10} (A_n - A_\infty)}{\log_{10} (A_0 - A_\infty) - \log_{10} (A_n - A_\infty)}$$
These values, when plotted against time give hyperbolas which apparently reach a maximum after about 180 hours. (Fig. II A). Applying the equation:

$$k = 2.305 \frac{\log_{10}(A_0 - A_{\infty}) - \log_{10}(A_n - A_{\infty})}{t_n}$$

$t_n$ was plotted against $\log_{10}(A_0 - A_{\infty}) - \log_{10}(A_n - A_{\infty})$ in each case, where $t_n$ = time in hours; $A_0$ the initial rotation; $A_{\infty}$ the final rotation and $A_n$ the rotation of the solution at time $t_n$.

It was found that (within the accuracy of the experiment) the values for both solutions lie on the same straight line. (Fig. II B). This shows that the velocity of the reaction is independent of the concentration of the solution, and the reaction is therefore monomolecular. The velocity of the reaction ($k$), calculated from the slope of the line, proved to be 0.017 (time units in hours). A similar experiment performed on a different sample of material when the temperature of the laboratory was lower (about 15 °C) gave two independent values of 0.008 for the velocity constant of the reaction. In order to obtain a value for the energy of activation of the reaction, the velocity constants at different temperatures (Ea) of the same reaction in benzene, were calculated from the rotation data given in Table XIV.
<table>
<thead>
<tr>
<th>Time in hours</th>
<th>$\alpha_{5461}$</th>
<th>$\alpha_{4358}$</th>
<th>$\alpha_{5461}$</th>
<th>$\alpha_{4358}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.10</td>
<td>0.21</td>
<td>0.20</td>
<td>0.43</td>
</tr>
<tr>
<td>19</td>
<td>0.18</td>
<td>0.38</td>
<td>0.39</td>
<td>0.61</td>
</tr>
<tr>
<td>43</td>
<td>0.26</td>
<td>0.57</td>
<td>0.59</td>
<td>1.10</td>
</tr>
<tr>
<td>67</td>
<td>0.39</td>
<td>0.76</td>
<td>0.90</td>
<td>1.63</td>
</tr>
<tr>
<td>94</td>
<td>0.47</td>
<td>0.86</td>
<td>1.00</td>
<td>2.01</td>
</tr>
<tr>
<td>111</td>
<td>0.52</td>
<td>0.89</td>
<td>1.12</td>
<td>2.27</td>
</tr>
<tr>
<td>163</td>
<td>0.56</td>
<td>1.14</td>
<td>1.18</td>
<td>2.50</td>
</tr>
<tr>
<td>212</td>
<td>0.56</td>
<td>1.08</td>
<td>1.18</td>
<td>2.50</td>
</tr>
</tbody>
</table>

1. ($17^\circ C - 34^\circ C$)

**TABLE XIII**

Transformation of $(-)$ $\alpha$-Phenyl-$\gamma$-methylallyl Hydrogen Phthalate to $(+)$ $\gamma$-Phenyl-$\alpha$-methylallyl Hydrogen Phthalate at Room Temperature in Carbon Disulphide (1,2).
FIGURE IX.

Monomolecular Character of the Isomeric Change of α-Phenyl-γ-methylallyl
Hydrogen Phthalate to γ-Phenyl-α-methylallyl γ-Hydrogen Phthalate in
Carbon disulphide Solution.

A (see Table XIV)

B

C

C, 1.5

× C, 3.0
The measurements were made by means of a jacketed polarimeter tube, through which water from a gas thermostat was passed. One example of the straight line produced by plotting \( \log_{10}(A_0 - A_{\infty}) - \log_{10}(A_n - A_{\infty}) \) against \( n \) is given in Fig. X. The velocity constants, when plotted against temperature, lie on a hyperbola rising rapidly towards infinity between 55° and 60°C. (Fig. XI).

Employing the equation:

\[
\log k_T = \frac{-E}{4.6T}
\]

where \( E \) is the energy of activation of the reaction and \( T \) the absolute temperature at which \( k_T \) was measured, \( \log k_T \) was plotted against \( \frac{1}{T} \), the points lying on a straight line (Fig. XIII), whose slope \( \frac{-E}{4.6} = \frac{2}{.00032} \).

Whence \( E = -28800 \) calories per gm. mol. (time units in minutes).
**TABLE XIV**

Influence of temperature on the rate of change of $(-)\alpha$-Phenyl-$\gamma$-methylallyl Hydrogen Phthalate into $(+)$-$\gamma$-Phenyl-$\alpha$-methylallyl Hydrogen Phthalate in Benzene Solution.

<table>
<thead>
<tr>
<th></th>
<th>At 18°</th>
<th>At 37°</th>
<th>At 47°</th>
<th>At 55°</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c$</td>
<td>3.06; 1,2</td>
<td>4.85; 1,2</td>
<td>5.0; 1,2</td>
<td>5.0; 1,2</td>
</tr>
<tr>
<td>$t$</td>
<td>$\alpha_{18^\circ}$</td>
<td>$\alpha_{37^\circ}$</td>
<td>$\alpha_{47^\circ}$</td>
<td>$\alpha_{55^\circ}$</td>
</tr>
<tr>
<td></td>
<td>Hours</td>
<td>mins.</td>
<td>mins.</td>
<td>mins.</td>
</tr>
<tr>
<td>0</td>
<td>-0.74</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>19.5</td>
<td>0.43</td>
<td>10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>72.5</td>
<td>0.12</td>
<td>30</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>91.5</td>
<td>+0.02</td>
<td>60</td>
<td>48</td>
<td>10</td>
</tr>
<tr>
<td>236</td>
<td>0.16</td>
<td>90</td>
<td>60</td>
<td>15</td>
</tr>
<tr>
<td>308</td>
<td>0.20</td>
<td>180</td>
<td>70</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>210</td>
<td>95</td>
<td>25</td>
</tr>
<tr>
<td>$k$</td>
<td>0.00039</td>
<td>0.00375</td>
<td>0.023</td>
<td>0.115</td>
</tr>
<tr>
<td>(time units in minutes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FIGURE X.

Mutarotation of \( \gamma \)-Phenyl-\( \gamma \)-methylallyl Hydrogen Phthalate in Benzene Solution at 55°C.

\[ k_{55} = 2.30 \times \frac{485}{10} = 0.115 \]
FIGURE XI.

Variation of Reaction Velocity with Temperature. (See Table XIV.)
Variation of $\log K$ with $1/T$
(-) $\alpha$-Phenyl-$\gamma$-methylallyl hydrogen phthalate dissolved in a saturated ethereal solution of ammonia had 
$[\alpha]_{\text{d}}^{20^\circ} +11.0^\circ$ ($c, 2.25; l, 2$); this value remained constant for 9 days after which the solution became slightly cloudy making accurate readings difficult. Under the same experimental conditions (+) $\gamma$-phenyl-$\alpha$-methylallyl hydrogen phthalate has $[\alpha]_{\text{d}}^{20^\circ} +44.0^\circ$ ($c, 1.80; l, 2$). Coupled with the non-occurrence of mutarotation in pyridine solution these experiments indicate that salts of $\alpha$-phenyl-$\gamma$-methylallyl hydrogen phthalate are more stable than the free acid ester. Moreover the quinidine salt after keeping for many months yields, on decomposition, the optically pure acid ester.

The alcohol is stable to $\frac{1}{10}$ NaOH for 14 days at room temperature and to boiling sodium hydroxide for a short time but undergoes complete isomeric change in presence of 0.5% aqueous acetic acid in 42 hours.

The neutral esters, are more stable than the acid esters; (-) $\alpha$-phenyl-$\gamma$-methylallyl acetate is recovered with unchanged rotatory power after (a) remaining at room temperature for 10 days in carbon disulphide, (b) 14 days in pyridine or (c) being heated in boiling benzene solution for 4 hours, while (-) $\alpha$-phenyl-$\gamma$-
methylylallyl- \( \alpha \)-nitrobenzoate is unchanged by similar treatment.

In considering the mechanism of the transformation it is interesting to bear in mind the following experimental results: 

\((-\)\( \alpha \)-phenyl-\( \gamma \)-methylylallyl alcohol and \( p \)-xenyl isocyanate mixed in molecular proportions

and heated 2\( \frac{1}{2} \) hours at 40-45\( ^\circ \) yield \( (+) \)-\( \alpha \)-phenyl-\( \gamma \)-methylylallyl \( p \)-xenyl urethane \([\alpha]_{54.1} +24.4^\circ\) in chloroform, a compound which can be maintained molten (m. p. 120\( ^\circ \)) for a few minutes, or kept in boiling benzene solution for 4 hours or kept in benzonitrile solution for 14 days at room temperature without its rotatory power \([\alpha]_{51.5} +5.4^\circ\),

\([\alpha]_{54.1} +7.3^\circ\) (c:1.30; l:2) undergoing any change. When, however, the original mixture of alcohol and isocyanate is heated on the steam bath for 0.5 hour only the solid product consists entirely of the isomeric \((+) \)-\( \gamma \)-phenyl-\( \alpha \)-methylylallyl \( p \)-xenyl urethane, which after one crystallisation from benzene has \([\alpha]_{54.1} +175.4^\circ\) in chloroform. Although it is possible that crystallisation may have resulted in the removal of some dl-urethane (which, however, is not very soluble in benzene) this reaction is remarkable for the very high proportion, 175.4/200\( ^\circ \) = 87.7%, of optical activity maintained through the isomeric change.
NOTE.

An examination by X-rays of (-)-α-phenyl-γ-methylallyl hydrogen phthalate and the dl-transformation product was kindly undertaken by Mr. J. D. Bernal of the University of Cambridge. In his report Mr. Bernal states: "The first ((-)-α-phenyl-γ-methylallyl hydrogen phthalate) has an extremely simple crystalline structure, an orthorhombic cell, a = 8.21, b = 6.29, c = 29.4. This is the typical orthorhombic arrangement for an aromatic hydrocarbon. We can only understand this if we write the structure out in the form I,

![Diagram of molecule](image)

which gives the molecule of length 14 A, fitting consequently in two layers into the cell. The dl variety of the other form has a totally different arrangement. It is monoclinic, with a = 14.7, b = 13.8, c sin \( \beta \) = 7.9, space-group \( P2_1/a \), also with four molecules in the cell. I have not yet succeeded in placing the molecules in this cell.

The main interest, however, lies in the transformation. I have followed it carefully both as it
occurs slowly at room temperatures, and on heating. It is a transformation of a typical dehydration type, that is, it proceeds from nuclei on the surface of the crystal; small pits appear, at first round, then subsequently of hexagonal outline, which gradually grow and are seen to be covered by a film of liquid. No internal transformation appears to take place. In fact, the whole process appears like very slow melting. As I visualise it, the chemical action consists merely in the transfer of the hydrogen atom from one side of the phthalic ion group to the other, and subsequent linking up of this with a group of a different molecule lying adjacent to it in the crystal structure."
EXPERIMENTAL DETAILS.

dl-α-Phenyl-γ-methylallyl alcohol (208g. = 78%), prepared by the interaction of pure crotonaldehyde (128g.) and the Grignard reagent from magnesium (48g.) and bromobenzene (366g.), had b.p. 121-122°/12mm., n_D^{25} 1.5525. Its phenyl urethane could only be obtained in the form of a gum after standing over a year. Its p-xenyl urethane (0.8g.), prepared by heating together for 2.5 hours at 40-45° p-xenyl isocyanate (1g.) and the alcohol (0.2g.), separated from ether and light petroleum in radiating clusters of prismatic needles, m.p. 124° (Found: N, 4.25. C_{25}H_{21}O_{4}N requires N, 4.1%).

dl-α-Phenyl-γ-methylallyl p-nitrobenzoate (20g.), prepared by the interaction of the alcohol (14.8g.) and p-nitrobenzoyl chloride (18.8g.) in the presence of pyridine (10g.), crystallised from a mixture of ether and light petroleum in radiating clusters of almost colourless prismatic needles, m.p. 99°. (Found: N, 4.8. C_{17}H_{15}O_{4}N requires N, 4.7%). Mixed with dl-γ-phenyl-α-methylallyl p-nitrobenzoate (m.p. 58-39°) it melts very indefinitely at 45-75°.

dl-α-Phenyl-γ-methylallyl acetate (6.8g.), b.p. 135-136°/21.5 mm., n_D^{25} 1.5087, (Found: C, 75.5; H, 7.7. C_{12}H_{14}O_{2} requires C, 75.8; H, 7.4%) was readily obtained by the action of acetic anhydride (5.4g., freed from
acetic acid by the method of Meisenheimer and Beulter on a warm mixture of the alcohol (6.0g.) and pyridine (5.0g.)

dl-α-Phenyl-γ-methylallyl hydrogen phthalate. A solution of phthalic anhydride (30g.) in hot pyridine (60g.) was rapidly cooled and mixed with α-phenyl-γ-methylallyl alcohol (30g.). The resultant mixture was maintained at 40-45° for 2 hours and occasionally shaken. The homogeneous liquid was dissolved in ether and washed repeatedly with ice-cold dilute hydrochloric acid until, as a result of the removal of much of the ether by the aqueous acid, the hydrogen phthalic ester began to crystallise. At this stage a large volume of cold water was added and the whole vigorously shaken when the hydrogen phthalic ester separated completely in small granules. These were finely triturated with very dilute cold hydrochloric acid, filtered, washed with water and dried in vacuo, m.p. 77-79°. Yield 54g. dl-α-Phenyl-γ-methylallyl hydrogen phthalate separates from a mixture of ether and light petroleum in small needles m.p. 95-94°. Mixed with dl-γ-phenyl-α-methylallyl hydrogen phthalate it softens and melts at 92-94°. (Found: C, 72.64, H, 5.4; C₁₈H₁₆O₄ requires C, 73.97, H, 5.4%). When this hydrogen phthalic ester was saponified with ethyl alcoholic sodium hydroxide the recovered alcohol distilled
sharply at 119-120/3.5mm., and could not be induced to solidify, from which it is evident that no considerable amount of isomeric change to dl-γ-phenyl-α-methylallyl hydrogen phthalate had occurred during the esterification. If the precautions described above, particularly the avoidance of high temperature, are not taken, the product is not homogeneous. When the reaction mixture of alcohol, phthalic anhydride and pyridine is heated on the steam bath for an hour the product consists entirely of the isomeric dl-γ-phenyl-α-methylallyl hydrogen phthalate m.p. and mixed m.p. 92-94°. This result was confirmed by saponification when dl-γ-phenyl-α-methylallyl alcohol, m.p. 30-51.5° was obtained. It is thus evident that α-phenyl-γ-methylallyl hydrogen phthalate and γ-phenyl-α-methylallyl hydrogen phthalate on saponification yield the alcohols from which they were respectively prepared.

**Quininidine Salt of (−)-α-Phenyl-γ-methylallyl Hydrogen Phthalate.**

Quininidine (24g.) was dissolved in a cold solution of dl-α-phenyl-γ-methylallyl hydrogen phthalate (22g.) in methyl acetate (3000c.c.) when there separated immediately a bulky mass of asbestose-like crystals. These, after recrystallisation from methyl acetate (2300c.c.) consisted of optically pure quininidine salt of (−)-α-phenyl-γ-methyl-
FIGURE XIII.

Normal Dispersion of $(-)\alpha$-Phenyl-$\gamma$-methylallyl Hydrogen Phthalate in Various Solvents. (See Table II.)
allyl hydrogen phthalate (16.5g.) m.p. 146-147° (decomp.).
(Rotatory powers in Table XV).

Quinidine Salt of (+)-α-Phenyl-γ-methylallyl Hydrogen Phthalate.
The filtrate from the quinidine salt described above, after removal of the solvent yielded a gum (16g.) which dissolved readily in hot acetone (60c.c.). After cooling this solution deposited bulky clusters of silky needles which, after recrystallisation from acetone (60c.c.), consisted of the quinidine salt of (+)-α-phenyl-γ-methylallyl hydrogen phthalate (4.3g.) m.p. 133-134° (decomp.). (Rotatory Powers in Table XV).

(-)-α-Phenyl-γ-methylallyl Hydrogen Phthalate. The quinidine salt of m.p. 146-147° (62g.), mixed with acetone (150c.c.), was decomposed with ice-cold dilute hydrochloric acid. The liberated hydrogen phthalic ester was precipitated by addition of ice-cold water and then extracted with ether. The dried ethereal solution, mixed with warm light petroleum, deposited (-)-α-phenyl-γ-methylallyl hydrogen phthalate as rosettes of long fine glistening needles (23g.) m.p. 81-82°. (Table XV).

(+) -α-Phenyl-γ-methylallyl Hydrogen Phthalate. The
quinidine salt of m.p. 133-134° (4.5g.), decomposed as described in the preceding paragraph, yielded (+)-α-phenyl-γ-methylallyl hydrogen phthalate (1.7g.) glistening needles, m.p. 80-81°. (Table XV).

(-)-α-Phenyl-γ-methylallyl alcohol was obtained by the addition of (-)-α-phenyl-γ-methylallyl hydrogen phthalate (19g.) to a hot solution of sodium hydroxide (6.8g.) in alcohol (300c.c.) and subsequently passing steam through the mixture. The steam distillate (900c.c.) on extraction yielded (-)-α-phenyl-γ-methylallyl alcohol (6.5g.) b.p. 126/20mm., nD 1.5525. Its rotatory powers (which lie on a smooth curves, Fig.XIV) and density are given in Table XV. Its p-xenyl urethane, hairy needles, m.p. 120°, from a mixture of methylene chloride and light petroleum, has [α]20° +20.0°; [α]576° +22.6°; [α]435° +24.4°; [α]435° +58.2° (α-2.25; l-2) in chloroform.

(-)-α-Phenyl-γ-methylallyl Acetate, b.p. 134-135/20mm., nD 1.5064; d25° 1.016; α25° 0.34°; α5875° -0.41°; α435° 1.23° (l-0.25); was prepared by gently heating on the steam bath for 1 hour at 60-70° a mixture of the (-)-alcohol (α20° -33.59°; l-0.5; 3g.) acetic anhydride (2.7g.) and pyridine (2.0g.).
Variation of Rotatory Power of \((-\alpha\)-Phenyl-\(\gamma\)-methyallyl Alcohol with Temperature \((1, 0.5)\). (See Table XVI).
### Variation of Rotatory Power of α-Phenyl-γ-methylallyl Alcohol with Temperature. (1, 0.5).

<table>
<thead>
<tr>
<th>$t^\circ$</th>
<th>$\alpha_{5643}$</th>
<th>$\alpha_{5780}$</th>
<th>$\alpha_{5661}$</th>
<th>$\alpha_{4356}$</th>
<th>$t^\circ$</th>
<th>$\frac{t^\circ}{4}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>16°</td>
<td>-</td>
<td>$-29.69^\circ$</td>
<td>$-34.17^\circ$</td>
<td>-</td>
<td>15.9</td>
<td>1.0110</td>
</tr>
<tr>
<td>20</td>
<td>$-27.66$</td>
<td>29.16</td>
<td>33.69</td>
<td>$-64^\circ$</td>
<td>25.8</td>
<td>1.0044</td>
</tr>
<tr>
<td>30.7</td>
<td>-</td>
<td>26.93</td>
<td>31.31</td>
<td>59.4</td>
<td>35.3</td>
<td>0.9954</td>
</tr>
<tr>
<td>34.8</td>
<td>-</td>
<td>26.07</td>
<td>30.21</td>
<td>57.0</td>
<td>46.8</td>
<td>0.9854</td>
</tr>
<tr>
<td>40.5</td>
<td>-</td>
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<td>28.74</td>
<td>54.28</td>
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<td></td>
</tr>
<tr>
<td>50.0</td>
<td>-</td>
<td>22.90</td>
<td>26.59</td>
<td>47.3</td>
<td></td>
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</tr>
<tr>
<td>62.5</td>
<td>-</td>
<td>20.62</td>
<td>23.71</td>
<td>45.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>66</td>
<td>-</td>
<td>20.07</td>
<td>23.13</td>
<td>44.15</td>
<td></td>
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</tr>
<tr>
<td>71</td>
<td>-</td>
<td>19.18</td>
<td>22.07</td>
<td>42.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 (after cooling)</td>
<td>-</td>
<td>29.16</td>
<td>33.69</td>
<td>$-64^\circ$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 (after cooling)</td>
<td>-</td>
<td>27.13</td>
<td>31.56</td>
<td>59.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FIGURE XV.

Variation of Specific Gravity of α-Phenyl-γ-methylallyl alcohol with Temperature. (Table XVI.)
(-)-α-Phenyl-γ-methylallyl p-Nitrobenzoate. A solution of p-nitrobenzoyl chloride (4g.) in chloroform (15c.c.) was added dropwise to a mixture of (-)-α-phenyl-γ-methylallyl alcohol (α$^{18}_{5844}$ = -34.17°, [α]$_D$ 0.5, 3g.) and pyridine (2g.). The reaction mixture, which had become warm, was left 24 hours and then worked up: the resulting p-nitrobenzoic ester was a mobile oil the rotatory powers of which are in Table XVII.
The Conversion of Derivatives of α-Phenyl-γ-methylallyl Alcohol into Derivatives of γ-Phenyl-α-methylallyl Alcohol.

(1) (a). Conversion of dl-α-Phenyl-γ-methylallyl acetate into dl-γ-Phenyl-α-methylallyl acetate. (i). The acetate b.p. 123°/11 mm. (5g.) and acetic anhydride (7.5g.) were heated together on the steam bath for 10 hours and then distilled. After removal of the acetic anhydride the main portion distilled at 133-133°/9 mm.; this product (2.5cc.) was heated under reflux for 1.5 hours with aqueous-alcoholic sodium hydroxide and the reaction mixture distilled in a current of steam. The volatile material, b.p. 123-124°/8.5 mm., crystallised completely when inoculated with dl-γ-phenyl-α-methylallyl alcohol and had m.p. 30-31°.

(ii). The acetate (5g.) was heated with glacial acetic acid (5g.) on the steam bath for 2 hours; the main portion (3.5g.) then had b.p. 133-134°/10 mm. and after saponification in a similar manner yielded dl-γ-phenyl-α-methylallyl alcohol (2cc.) b.p. 125-126°/9.5 mm., m.p. 30-31°.

Conversion of (-) -α-Phenyl-γ-methylallyl Acetate into (+) -γ-Phenyl-α-methylallyl Acetate.

(a). By the action of cold acetic acid. (-) -α-Phenyl-
Y-methylallyl acetate, $\alpha_{58^\circ}^\text{S} = 0.34^\circ$, $\alpha_{54^\circ}^\text{D} = -0.41^\circ$, $\alpha_{43^\circ}^\text{M} = 1.23^\circ$ (1.0.25) was dissolved in pure acetic acid when it had $[\alpha]_{58^\circ}^\text{S} = +2.6^\circ$, $[\alpha]_{54^\circ}^\text{D} = +3.0^\circ$, $[\alpha]_{43^\circ}^\text{M} = +4.2^\circ$ (c, 5.10, l, 2) in the freshly prepared solution. After standing 17 hours at the ordinary temperature the rotatory powers of this solution had changed to $[\alpha]_{58^\circ}^\text{S} = +25.5^\circ$, $[\alpha]_{54^\circ}^\text{D} = +28.9^\circ$, $[\alpha]_{43^\circ}^\text{M} = +56.8^\circ$ — values which had not changed after the solution had stood an additional 45 hours.

The isomeric (+)-Y-phenyl-α-methylallyl acetate prepared from the (-)-alcohol has $[\alpha]_{58^\circ}^\text{S} = +145.0^\circ$, $[\alpha]_{54^\circ}^\text{D} = +166.0^\circ$, $[\alpha]_{43^\circ}^\text{M} = +321^\circ$ (c, 1, 12; 1, 2) in acetic acid solution, hence the acetate formed by isomeric change in acetic acid solution possesses a rotatory power 17.3% of that of the optically pure (+)-Y-phenyl-α-methylallyl acetate.

After removal of the acetic acid the residual (+)-Y-phenyl-α-methylallyl acetate had b.p. 150-151°/22 mm., $n_D = 1.525$ and $\alpha_{58^\circ}^\text{S} = 10.15^\circ$, $\alpha_{54^\circ}^\text{D} = 11.69^\circ$, $\alpha_{43^\circ}^\text{M} = 22.86^\circ$ (1.0.5). The value $\alpha_{54^\circ}^\text{D} = 11.69^\circ$ (1.0.5) is 14.1% of that of optically pure (+)-Y-phenyl-α-methylallyl acetate.

Transformation of (-)-α-Phenyl-Y-methylallyl Alcohol to (+)-Y-Phenyl-α-methylallyl Alcohol.

A solution of (-)-α-phenyl-Y-methylallyl alcohol (1.5 c.c.
146.

After standing 42 hours at room temperature was rendered slightly alkaline and extracted with ether. The dried extract yielded (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol, b.p. 140°/20 mm., m.p. 33°, \(\alpha_{D}^{25} +0.51°\), \(\alpha_{D}^{35} +0.62°\), \(\alpha_{D}^{45} +1.36°\), (1,0.5).

Hydrolysis of (-)-\(\alpha\)-phenyl-\(\gamma\)-methylallyl hydrogen phthalate with alcoholic potash yields optically pure (-)-\(\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol (as is shown by its reduction to optically pure (+)-phenyl-\(\alpha\)-propylcarbinol) the rotatory power of which remains unchanged after standing 16 weeks at room temperature. Moreover dl-\(\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol undergoes no significant conversion to dl-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol when it is (a) left in contact with 20 vols. N/10 NaOH for 14 days, (b) boiled under reflux with aqueous sodium hydroxide or (c) heated with anhydrous potassium carbonate at 100° for 2 hours. Yet when (-)-\(\alpha\)-phenyl-\(\gamma\)-methylallyl hydrogen phthalate was saponified with a slight excess of aqueous 5N sodium hydroxide the liberated alcohol was a mixture b.p. 122-128.5/11 mm., from which, by fractional distillation (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl carbinol, m.p. 31°, \(\alpha_{D}^{25} +0.35°\), (1,0.25) was isolated. Similarly when aqueous alcoholic soda was used the liberated alcohols were separated by
distillation (i) b.p. 119-121.5°/11 mm., $\alpha^{15°}_{D} -4.35°$ (1, 0.25), (ii) b.p. 128-129°/10 mm., $\alpha^{15°}_{D} -2.14°$ (1, 0.25).

Fraction (ii), when inoculated with dl-γ-phenyl-α-methylallyl alcohol, deposited crystals of (+)-γ-phenyl-α-methylallyl alcohol, m.p. 33-34°, $[\alpha]^{54.1}_{D} +2.2°$ (c, 4.6; l, 2) in pyridine solution.

**Transformation of (-)-α-Phenyl-γ-methylallyl Alcohol to (+)-γ-Phenyl-α-methylallyl Acetate.**

A mixture of (-)-α-phenyl-γ-methylallyl alcohol (3g., $\alpha^{54.61}_{D} -14.98°$, l, 0.25) and acetic acid (10g.) after standing 4 days yielded (+)-γ-phenyl-α-methylallyl acetate b.p. 151°/34 mm., $\alpha^{20°}_{D} +1.74°$, $\alpha^{20°}_{215} +3.6°$ (l, 0.5).

A similar experiment using the inactive alcohol gave dl-γ-phenyl-α-methylallyl acetate, b.p. 151°/24 mm.

**Transformation of α-Phenyl-γ-methylallyl p-nitrobenzoate to γ-Phenyl-α-methylallyl p-nitrobenzoate.**

(a). In the homogeneous state.

A specimen of dl-α-phenyl-γ-methylallyl p-nitrobenzoate, m.p. 99°, after keeping in a closed vessel for a year had m.p. 96-97° but the amount of impurity (γ-phenyl-α-methylallyl p-nitrobenzoate ?) present was insufficient
<table>
<thead>
<tr>
<th>Solvent</th>
<th>Temp</th>
<th>Time</th>
<th>Conc</th>
<th>Initial Values</th>
<th>Final Values</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bensene</td>
<td>82°</td>
<td>3.5 hours</td>
<td>4.0</td>
<td>[α]_T=40° -59.7, [α]_T=28° -44.0, [α]_T=19° -</td>
<td>-30.6, -36.0, -</td>
<td>The recovered material remained liquid after keeping 2 months.</td>
</tr>
<tr>
<td>Chloroform</td>
<td>15-20</td>
<td>3 months</td>
<td>4.6</td>
<td>-59.4, -45.4, -63.4</td>
<td>± 0, ± 0, ± 0</td>
<td>The recovered material had m.p. 46-50°, and thus is largely dl-1-phenyl-1-methylallyl p-nitrobenzoate.</td>
</tr>
<tr>
<td>Pyridine</td>
<td>15</td>
<td>2 months</td>
<td>2.7</td>
<td>-46.5, -61.9, -</td>
<td>- changed</td>
<td></td>
</tr>
<tr>
<td>Ether</td>
<td>15</td>
<td>2 months</td>
<td>3.6</td>
<td>-54.0, -38.9, -73.6</td>
<td>- changed</td>
<td></td>
</tr>
<tr>
<td>Ether + 1 drop conc. HCl</td>
<td>15</td>
<td>2 days</td>
<td>3.6</td>
<td>-54.0, -38.9, -73.6</td>
<td>-39.4, -54.0, -</td>
<td></td>
</tr>
</tbody>
</table>
for separation by fractional crystallisation. The recrystallised ester after being kept molten for 0.5 hour, resolidifies to a crystalline mass of unchanged m.p., 98-99°; when, however, the molten material was kept at 100° for 2.5 hours, the cooled liquid did not solidify when inoculated with the original material, but did so immediately when inoculated with \( \text{dl-}\text{Y-phenyl-}\alpha\text{-methylallyl p-nitrobenzoate} \) and then had m.p. 46-48°; after recrystallisation from ether and light petroleum it had m.p. 58-59° alone and admixed with \( \text{dl-}\text{Y-phenyl-}\alpha\text{-methylallyl p-nitrobenzoate} \).

Liquid \((-\text{)-\text{Y-phenyl-}}\alpha\text{-methylallyl p-nitrobenzoate} \) after being kept at 100° for 2.5 hours readily solidified on cooling and had \([\alpha]_{578}^0 = -11.2°; [\alpha]_{584}^0 = -14.0°; [\alpha]_{435}^0 = -33.7° \) \((c,3.65; 1,2)\) in chloroform. Fractional crystallisation resolved this material into two fractions (i) m.p. 50-52° which when mixed with \( \text{dl-}\text{Y-phenyl-}\alpha\text{-methylallyl p-nitrobenzoate} \) (m.p. 58°) melted at 57-58° and (ii) a more soluble portion, m.p. 45°, which when mixed with \((-\text{-})\text{Y-phenyl-}\alpha\text{-methylallyl p-nitrobenzoate} \) (m.p. 41°) melted at 42-44° and showed \([\alpha]_{578}^0 = -13.8°; [\alpha]_{584}^0 = -15.7°; [\alpha]_{435}^0 = -38.5° \) \((c,1.07; 1,2)\) in chloroform.

Optically pure \((-\text{-})\text{Y-phenyl-}\alpha\text{-methylallyl p-nitrobenzoate} \) has \([\alpha]_{584}^0 = -27.52°; [\alpha]_{584}^0 = -33.48°; [\alpha]_{435}^0 = -87.4° \) \((c,5.00; 1,2)\) in chloroform.
(b). In solution.

By heating dl-α-phenyl-γ-methylallyl p-nitrobenzoate with 1.5 times its weight of acetic anhydride for 6 hours (3.5 hours are insufficient) on the steam bath it was converted into dl-γ-phenyl-α-methylallyl p-nitrobenzoate, m.p. and mixed m.p. 57-58°. About 5% of p-nitrobenzoic acid was isolated from the reaction mixture.

Conversion of α-Phenyl-γ-methylallyl Hydrogen Phthalate into γ-Phenyl-α-methylallyl Hydrogen Phthalate.

(a). dl-α-Phenyl-γ-methylallyl hydrogen phthalate was heated with an equal weight of pyridine on the steam bath for one hour and the cooled solution mixed with ice-cold dilute hydrochloric acid. The liberated oil soon crystallised, m.p. 94-95° either alone or admixed with authentic dl-α-phenyl-γ-methylallyl hydrogen phthalate: it crystallised from carbon disulphide and light petroleum in characteristic large, glassy rhombs.

(b). (−)-α-Phenyl-γ-methylallyl hydrogen phthalic ester (m.p. 83°) is insoluble in cold hexahydrobenzene, but dissolves in the boiling solvent. The ester (0.25g) [α]_22.0°_ETHRX was added to boiling hexahydrobenzene, and retained at 82°C for about 0.5 minute when it was
rapidly cooled. Long, flat, prismatic crystals, separated and had m.p. 82°, \([\alpha]_{{\text{sub}}}^{20.0°} (c,1.14,1.2)\) in ether solution, showing the material to be unchanged. The experiment was repeated retaining the temperature at 82° for 3 minutes, the hexahydrobenzene now being removed by exsiccation. The product had \([\alpha]_{{\text{sub}}}^{+10.0°} (c,2.5,1.2)\) in carbon disulphide solution showing that the reaction mixture contained about 22% (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate. (\(\alpha\)-Phenyl-\(\alpha\)-methylallyl hydrogen phthalic ester has \([\alpha]_{{\text{sub}}}^{+0.19°}\) in carbon disulphide solution).

It was found that if the heating was continued for 30 minutes the product was pure \(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate having \([\alpha]_{{\text{sub}}}^{+20.0°} (c,2.5,1.2)\) which represents 72% of the d-enantiomorph.

(c). (-)-\(\alpha\)-phenyl-\(\gamma\)-methylallyl hydrogen phthalic ester (\([\alpha]_{{\text{sub}}}^{22.4°}\) in ether solution) has \([\alpha]_{{\text{sub}}}^{-13.25°}\) in benzene. In 13 days this value changed to +3.12° (\(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate has \([\alpha]_{{\text{sub}}}^{+5.1°}\) in benzene). A small quantity of phthalic acid m.p. 200° was deposited on the sides of the polarimeter tube. The benzene was removed in a desiccator and the solid product had \([\alpha]_{{\text{sub}}}^{+13.6°}\) in carbon disulphide solution showing that the product contained 65% (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl hydrogen phthalate.
Another portion of the same sample of ester (0.5g.) was dissolved in benzene in a test tube and after being heated to boiling, was quickly cooled. The resulting ester had $[\alpha]_D^{25} +13.0^\circ$ in carbon disulphide solution. (dl)-$\gamma$-phenyl-$\alpha$-methylallyl hydrogen phthalate (m.p. 93-4$^\circ$) was isolated from the product.

(d) (-)-$\alpha$-Phenyl-$\gamma$-methylallyl hydrogen phthalate (0.64g) has $[\alpha]_D^{25} -3.0^\circ$ ($c, 3.25; 1, 2$) when freshly dissolved in pure acetic acid. In 2.5 hours this value changes to $[\alpha]_D^{25} +5.4^\circ$ when mutarotation ceases. On removing the solvent, phthalic acid (0.32g.), m.p. 198$^\circ$, was isolated, together with an oil possessing the characteristic smell of the acetic ester. A parallel experiment was carried out with dl-$\alpha$-phenyl-$\gamma$-methylallyl hydrogen phthalic ester, (64g.) in acetic acid (25c.c.). The oily product had b.p. 125/24m.m. $\beta_D^{25} 1.5320$ (Known $\gamma$-phenyl-$\alpha$-methylallyl acetate, b.p. 132-133/10mm., $\beta_D^{25} 1.5306$, had b.p. 151-152/24m.m. in the same apparatus.). (Optically pure $\gamma$-phenyl-$\alpha$-methylallyl acetate has $[\alpha]_D^{25} +166.0^\circ$ ($c, 1.12; 1, 2$) in acetic acid solution.).

In another experiment dl-$\alpha$-phenyl-$\gamma$-methylallyl hydrogen phthalate (64g.) was added to acetic acid (80c.c.) heated to 95$^\circ$ on a steam bath. The solution was immediately cooled and poured into ice-cold sodium
carbonate solution. The oil, (1.5 g.) which separated, was salted out, extracted, and distilled, and proved to be \( \gamma \)-phenyl-\( \alpha \)-methylallyl acetate, b.p. 145\(^\circ\)/21 mm. \( n_\text{D}^2 \) 1.5313.

(e) dl-\( \alpha \)-Phenyl-\( \gamma \)-methylallyl hydrogen phthalate (8 g.) was heated on a steam bath with acetic anhydride (150 c.c.) for 4 hours. The acetic anhydride was then removed by distillation under reduced pressure and light petroleum added to the remaining oil. Phthalic anhydride (4 g.) m.p. 128\(^\circ\), separated in long hairy needles. Petrol was removed from the filtrate, and the oil distilled under reduced pressure, (b.p. 135-140\(^\circ\)/20 mm.). However, more crystals of phthalic anhydride appeared in the distillate, and to remove these the oil was again diluted with light petroleum, plunged into ice, and filtered. The oil recovered from this filtrate proved to be \( \gamma \)-phenyl-\( \alpha \)-methylallyl acetate, b.p. 144-5\(^\circ\)/20 mm., \( n_\text{D}^2 \) 1.5310 (1.5 g.).
**TABLE XVII**

Transformation of (+)-\(\alpha\)-Phenyl-\(\gamma\)-methylallyl Hydrogen Phthalate into (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Hydrogen Phthalate at room temperature in Carbon Disulphide, \((g:3.00:1,2)\).

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>(\alpha_{514\text{nm}})</th>
<th>(\alpha_{566\text{nm}})</th>
<th>(\alpha_{435\text{nm}})</th>
<th>([\alpha]_{254\text{nm}})</th>
<th>([\alpha]_{544\text{nm}})</th>
<th>([\alpha]_{425\text{nm}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>+0.10°</td>
<td>+0.13°</td>
<td>+0.1°</td>
<td>+1.7°</td>
<td>+2.2°</td>
<td>+1.7°</td>
</tr>
<tr>
<td>21</td>
<td>0.28</td>
<td>0.28</td>
<td>0.3</td>
<td>4.6</td>
<td>4.6</td>
<td>5.0</td>
</tr>
<tr>
<td>27</td>
<td>0.30</td>
<td>0.40</td>
<td>0.68</td>
<td>5.0</td>
<td>6.6</td>
<td>11.3</td>
</tr>
<tr>
<td>42</td>
<td>0.40</td>
<td>0.53</td>
<td>0.97</td>
<td>6.6</td>
<td>8.8</td>
<td>16.1</td>
</tr>
<tr>
<td>89</td>
<td>0.61</td>
<td>0.78</td>
<td>1.42</td>
<td>10.1</td>
<td>13.0</td>
<td>23.6</td>
</tr>
<tr>
<td>99</td>
<td>0.62</td>
<td>0.80</td>
<td>1.60</td>
<td>10.2</td>
<td>13.3</td>
<td>26.6</td>
</tr>
<tr>
<td>114</td>
<td>0.70</td>
<td>0.84</td>
<td>1.61</td>
<td>11.6</td>
<td>14.0</td>
<td>26.8</td>
</tr>
<tr>
<td>141</td>
<td>0.82</td>
<td>0.99</td>
<td>1.89</td>
<td>13.6</td>
<td>16.5</td>
<td>31.5</td>
</tr>
<tr>
<td>165</td>
<td>0.88</td>
<td>1.02</td>
<td>2.00</td>
<td>14.6</td>
<td>17.0</td>
<td>33.3</td>
</tr>
<tr>
<td>194</td>
<td>0.96</td>
<td>1.10</td>
<td>2.20</td>
<td>16.0</td>
<td>18.3</td>
<td>36.6</td>
</tr>
</tbody>
</table>
Hence, for any given position of the bench and any given angle of projection, the range of the ball is determined by the horizontal distance traveled by the ball.

References:

XIX
Preparation of (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Methyl Ether
by a method unlikely to lead to Inversion of Configuration.

Potassium (3.9g.) was dissolved in an ethereal solution
of (optically impure) (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl alcohol,
\([\alpha]_{582}^\circ +10.7^\circ\) in carbon disulphide, and the resulting
solution mixed with methyl iodide (14.5g.) and gently
warmed. The resulting (+)-\(\gamma\)-phenyl-\(\alpha\)-methylallyl methyl
ether (1.5g.) had b.p. 102-103°/10.5m.m., and \(\alpha^\circ_{582} +6.61^\circ\),
\(\alpha^\circ_{577} +6.83^\circ\), \(\alpha^\circ_{545} +7.92^\circ\), \(\alpha^\circ_{436} +13.93^\circ\) (\(1,0.25\)), \(n_D^2 1.5327\).

Attempts to prepare the isomeric methyl ether from \(\alpha\)phenyl-\(\gamma\)-methylallyl alcohol by a similar procedure
were unsuccessful.

Conversion of (+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Hydrogen Phthalate
to (-)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl Ethyl Ether.

(+)-\(\gamma\)-Phenyl-\(\alpha\)-methylallyl hydrogen phthalate (14.9g.)
made up to 1000c.c. with absolute ethyl alcohol had
\([\alpha]_{577}^\circ -12.3^\circ\), \([\alpha]_{577}^\circ -12.9^\circ\), \([\alpha]_{545}^\circ -14.7^\circ\), \([\alpha]_{436}^\circ -28.2^\circ\) (\(1,14.9;\)
\(1,2\)) and after keeping 24 days at room temperature,
\([\alpha]_{545}^\circ -14.4^\circ\). After keeping at 25° for nine months the
rotatory power had reached the constant value \([\alpha]_{545}^\circ -1.5^\circ\)
half-life period about 60 days; on working up the
solution yielded (-)-\( \gamma \)-phenyl-\( \alpha \)-methylallyl ethyl ether (7g.), b.p. 114/11 mm., \( \alpha_D \)^15 -2.20, \( \alpha_{5893}^\circ \) -2.50, (1,2) (Found: C, 82.1; H, 9.1. \( \text{C}_{12} \text{H}_{16} \text{O} \) requires C, 81.8; H, 9.1%).

Conversion of (+)-\( \gamma \)-Phenyl-\( \alpha \)-methylallyl hydrogen phthalate to (-)-\( \gamma \)-Phenyl-\( \alpha \)-methylallyl methyl ether.

(+)-\( \gamma \)-Phenyl-\( \alpha \)-methylallyl hydrogen phthalate (14.60g.) made up to 100c.c. with methyl alcohol (dist. from calcium) had [\( \alpha \)]_{5893} -7.2°, [\( \alpha \)]_{5893} -7.4°, [\( \alpha \)]_{5461} -8.4°, [\( \alpha \)]_{435°} -15.3° (c, 14.60; l, 2) and after keeping 30 days at room temperature, [\( \alpha \)]_{5461} -6.3°. After a further 3 months the constant value [\( \alpha \)]_{5461} -0.72° was reached, half-life period about 34 days, and the solution — which contained no unchanged hydrogen phthalic ester — was worked up. The resulting (-)-\( \gamma \)-phenyl-\( \alpha \)-methylallyl methyl ether (7.5g.) b.p. 124°/25 mm., \( \alpha_D \)^15 1.5387 had \( \alpha_{5893}^\circ \) -0.34°, \( \alpha_{5461}^\circ \) -0.38°, \( \alpha_{435°}^\circ \) -0.59° (l, 0.25). A parallel experiment showed that when the original solution was heated under reflux the reaction was complete in 30 minutes; the resulting methyl ether having b.p. 106°/10 mm., \( \alpha_{5893}^\circ \) -0.48°(l, 0.5) \( \alpha_D \)^15 1.5385.
Conversion of \( \alpha \)-Phenyl-\( \gamma \)-methylallyl Hydrogen Phthalate to \( \gamma \)-Phenyl-\( \alpha \)-methylallyl Methyl Ether.

A solution of (\(-\)\( \alpha \)-phenyl-\( \gamma \)-methylallyl hydrogen phthalate in methyl alcohol (freshly distilled from calcium) gave the following changes in rotatory power (\( \alpha_{5892} = 1.2 \)) on standing at room temperature.

<table>
<thead>
<tr>
<th>Time</th>
<th>( \alpha_{5892} )</th>
<th>( \alpha_{5790} )</th>
<th>( \alpha_{5451} )</th>
<th>( \alpha_{4358} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-2.51°</td>
<td>-2.67°</td>
<td>-3.03°</td>
<td>-6.20°</td>
</tr>
<tr>
<td>20 mins.</td>
<td>-</td>
<td>-</td>
<td>2.95</td>
<td>-</td>
</tr>
<tr>
<td>45 &quot;</td>
<td>2.33</td>
<td>2.43</td>
<td>2.81</td>
<td>5.67</td>
</tr>
<tr>
<td>70 &quot;</td>
<td>2.23</td>
<td>-</td>
<td>2.72</td>
<td>-</td>
</tr>
<tr>
<td>165 &quot;</td>
<td>-</td>
<td>1.44</td>
<td>1.66</td>
<td>3.92</td>
</tr>
<tr>
<td>260 &quot;</td>
<td>-</td>
<td>1.38</td>
<td>1.51</td>
<td>3.00</td>
</tr>
<tr>
<td>320 &quot;</td>
<td>-</td>
<td>1.10</td>
<td>1.20</td>
<td>2.57</td>
</tr>
<tr>
<td>8 hours</td>
<td>0.72</td>
<td>0.75</td>
<td>0.85</td>
<td>1.72</td>
</tr>
<tr>
<td>27.7 &quot;</td>
<td>0.17</td>
<td>-</td>
<td>0.19</td>
<td>0.57</td>
</tr>
<tr>
<td>3 days</td>
<td>-</td>
<td>0.10</td>
<td>0.12</td>
<td>0.35</td>
</tr>
</tbody>
</table>

After evaporation of the solvent there was obtained phthalic acid and (\(-\)\( \gamma \)-phenyl-\( \alpha \)-methylallyl methyl ether b.p. 118/20 mm., \( \alpha_{5790}^{25^\circ} = -0.12 \); \( \alpha_{5451}^{25^\circ} = -0.20 \); \( \alpha_{4358}^{25^\circ} = -0.25 \) (1; 0.25); \( n_D^{19^\circ} = 1.5350 \).
Transformation of (-)-α-Phenyl-γ-methylallyl p-Nitrobenzoate to

(a). (-)-γ-Phenyl-α-methylallyl Acetate by the action of Acetic Acid at ordinary temperature.

A solution of (-)-α-phenyl-γ-methylallyl p-nitrobenzoate in glacial acetic acid had \([\alpha]_{5790}^\circ -41.1^\circ, [\alpha]_{5461}^\circ -46.7^\circ; [\alpha]_{4358}^\circ -93.2^\circ (c,1.445; l,2)\) when freshly prepared and, after standing 24 hours at room temperature, the constant values \([\alpha]_{5790}^\circ -7.1^\circ, [\alpha]_{5461}^\circ -7.5^\circ, [\alpha]_{4358}^\circ -18.4^\circ\). From a parallel experiment using a larger amount (4g.) of the dl-p-nitrobenzoate there was isolated dl-γ-phenyl-α-methylallyl acetate (1.5g.), b.p. 147°/18mm., \(n_D^{16} 1.534\). Since optically pure (-)-γ-phenyl-α-methylallyl acetate has \([\alpha]_{440}^\circ -165^\circ\) in acetic acid \((c,1.12; l,2)\) it follows that the replacement of the p-nitrobenzoyl group by the acetyl group has been effected with the maintenance of some 4.8% of the optical activity of the new ester.

(b). (-)-γ-Phenyl-α-methylallyl Methyl Ether by the action of Methyl Alcohol at ordinary temperature.

A solution of (-)-α-phenyl-γ-methylallyl p-nitrobenzoate in methyl alcohol had \([\alpha]_{5790}^\circ -40.25^\circ, [\alpha]_{5461}^\circ -47.0^\circ, [\alpha]_{4358}^\circ -90.3^\circ\)
when freshly prepared; after standing 6 days the constant value $[\alpha]_{D}^2 \approx -5.23^\circ$ was reached.

From a parallel experiment using the dl-p-nitrobenzoate (5g.) there was isolated p-nitrobenzoic acid (2.5g.) and dl-\(\gamma\)-phenyl-\(\alpha\)-methylallyl methyl ether (2.0g.), b.p. 112°/15 m.m., $n_D^21.5321$.

**Conversion of \((-\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol to \((+\alpha\)-phenyl-\(\alpha\)-methylallyl \(\gamma\)-xenylurethane.**

A mixture of \((-\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol (0.7g.) and \(\gamma\)-xenyl isocyanate (1g.) was heated on the steam bath for 0.5 hour. The resulting solid product gave, when crystallised from benzene, rosettes of hairy needles, m.p. 176° (0.8g.), $\left[\alpha\right]_{D}^{56.6} +147.6^\circ$; $\left[\alpha\right]_{D}^{56.6} +175.4^\circ$; $\left[\alpha\right]_{D}^{369} +368^\circ$ ($\alpha,2.25: \underline{1},2$) in chloroform; mixed with optically pure \((+\alpha\)-phenyl-\(\alpha\)-methylallyl \(\gamma\)-xenylurethane (m.p. 180°; $\left[\alpha\right]_{D}^{56.6} +200^\circ$, in chloroform) it melts at 182°.

\((+\alpha\)-phenyl-\(\alpha\)-propyl Caprinol from \((-\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol.\)

\((-\alpha\)-phenyl-\(\gamma\)-methylallyl alcohol ($\alpha_{D}^{56.6} -16.35^\circ$, $\underline{1},0.25$) (4.4g.) was dissolved in dry ether (50c.c.) in the
reaction vessel of a laboratory hydrogenation apparatus. Platino-
ous oxide catalyst prepared according to the method of Adams, Voorhees and Shriner \(^{50}\) (0.1g.) was added, and hydrogen under a pressure of two atmospheres passed in until absorption was complete. The product had b.p. 115°/14 m.m. and readily solidified, (m.p. 41°) having 

\[
\begin{align*}
\alpha_{554} & +40.9°, \quad \alpha_{574} +43.4°, \quad \alpha_{546} +49.3°, \quad \alpha_{435} +83.3°, \quad \alpha_{262} +84.9°
\end{align*}
\]

in benzene solution. (Richter, b.p. 117°/14 m.m.)

Levene and Marker \(^{56}\) obtained \((-\text{)-phenyl-\text{a-propyl}}

\text{carbinol with } [\alpha]_{554} -35.8° \text{ in benzene solution, and made no mention of its property of solidifying. It was therefore concluded that the carbinol described by these workers was not optically pure, and accordingly, steps were taken to repeat the resolution.}
FIGURE XVI.

Variation of Rotatory Power of (+) Phenyl-n-propyl carbinol (1, 0.5) (Table $\alpha_{435\AA}$)

- Graph showing the variation of rotatory power with temperature.
- Two curves are depicted, one labeled $\alpha_{435\AA}$ and the other $\alpha_{546\AA}$.
- Temperature range from 40° to 70° C.
SECTION IV.

The Resolution of Phenyl-n-propyl carbinol.

By fractional crystallisation of its quinidine salt, phenyl-n-propylcarbinyl hydrogen phthalate was readily obtained with $[\alpha]_{588}^{0} +9.8^\circ$ (in ether). When the highly laevorotatory hydrogen phthalic ester obtained from the more soluble fractions of the quinidine salt was converted into its strychnine salt, and this submitted to fractional crystallisation, the corresponding l-phenyl-n-propylcarbinyl hydrogen phthalate was obtained with $[\alpha]_{588}^{0} -10.0^\circ$ (in ether).

Saponification of the d-acid ester yielded d-phenyl-n-propylcarbinol, m.p. 49°, b.p. 115°/14 mm., the rotatory powers of which are recorded in Table XX. The rotatory powers of the various derivatives are given in Table XXI.
### TABLE XX.

**Rotatory Power (1,0.8) and Refractive Index of (+) Phenyl-n-propylcarbinol.**

<table>
<thead>
<tr>
<th>Temp.</th>
<th>43°</th>
<th>47.5°</th>
<th>50°</th>
<th>54°</th>
<th>56°</th>
<th>57°</th>
<th>60°</th>
<th>65°</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_{5750}$</td>
<td>+15.86°</td>
<td>-</td>
<td>+16.42°</td>
<td>-</td>
<td>+16.75°</td>
<td>+16.75°</td>
<td>-</td>
<td>+17.11°</td>
</tr>
<tr>
<td>$\alpha_{5261}$</td>
<td>+17.84°</td>
<td>-</td>
<td>+18.75°</td>
<td>-</td>
<td>+18.98°</td>
<td>+19.03°</td>
<td>-</td>
<td>+19.02°</td>
</tr>
<tr>
<td>$\alpha_{4385}$</td>
<td>+30.52°</td>
<td>-</td>
<td>+31.66°</td>
<td>-</td>
<td>+32.40°</td>
<td>+32.51°</td>
<td>-</td>
<td>+33.06°</td>
</tr>
<tr>
<td>$n^D$</td>
<td>-</td>
<td>1.5005</td>
<td>-</td>
<td>1.4889</td>
<td>-</td>
<td>-</td>
<td>1.4909</td>
<td>1.4945</td>
</tr>
</tbody>
</table>
Phenyl-n-propylcarbinol, b.p. 117-118°/18mm., m.p. 15°;
\[ \frac{d_{12}^2}{d_{12}^2} = 0.9822, \quad \frac{d_{25}^{12}}{d_{25}^{12}} = 0.9739, \quad \frac{d_{37}^{20}}{d_{37}^{20}} = 0.9654, \quad \frac{d_{40}^{23}}{d_{40}^{23}} = 0.9582, \]
\[ n_{D}^2 = 1.5166 \] (Grignard gives b.p. 113°/10mm., \[ d_{13}^{27} = 0.9861, \]
\[ n_{D}^2 = 1.5194 \]), obtained in 69% yield by the Grignard reaction, was smoothly converted into its hydrogen phthalic ester, which formed clusters of small needles, m.p. 90-91°, from carbon disulphide and light petroleum (Found by titration with sodium hydroxide: M, 297.6. C\textsubscript{18}H\textsubscript{18}O\textsubscript{4} requires M, 298).

Quinidine (200g.) was dissolved in a solution of the hydrogen phthalic ester (171g.) in acetone (1000c.c.). The salt, which separated at once, was only sparingly soluble in hot acetone and was recrystallised from ethyl acetate (9 l.), forming rosettes of woolly needles (132g.) m.p. 168-169°; a further crop (30g.) of the optically pure salt was obtained by concentration of the second mother-liquor.

The more soluble fractions of the quinidine salt yielded a somewhat pasty l+dl-hydrogen phthalic ester (35g.), which was combined with strychnine (38g.) in methyl-alcoholic solution (180c.c.). The strychnine salt, after two recrystallisations from methyl alcohol, was obtained in rosettes of needles (40g.), m.p. 164-185° (decomp.). d-Phenyl-n-propyl carbinyl hydrogen phthalate, from the less soluble quinidine salt,
separated from carbon disulphide - light petroleum in long needles, m.p. 53-54°; the corresponding l-phenyl-
\[\text{n-propylcarbimyl hydrogen phthalate}, \text{m.p. 52-53°}, \text{was obtained from the less soluble strychnine salt.} \]

\text{d-Phenyl-\[n\text{-propylcarbimyl, obtained by saponification of the d-hydrogen phthalic ester by aqueous-alcoholic sodium hydroxide, solidified with remarkable readiness to a mass of long needles, m.p. 49°, b.p. 115}/14\text{mm. The corresponding l-alcohol had m.p. 48-49°.} \]

\text{d-Phenyl-\[\text{n-propylcarbimyl acetate, b.p. 125}/16\text{mm. obtained by heating the d-alcohol with acetic anhydride in pyridine solution, had } n\text{D}^{20.5} 1.4869 \text{ and } \alpha^{26°}_{\text{D}} +26.96°, \alpha^{25°}_{\text{s}}+30.85°, \alpha^{26°}_{\text{s}}+55.35° (1,0.25) (\text{Grignard}^{57} \text{ gives b.p. 117-118}/13\text{mm.})).} \]
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