STUDIES IN THE ALKYL-OXYGEN FISSION

OF

CARBOXYLIC ESTERS.

being a thesis, submitted to the University Of London for the
Degree of Doctor of Philosophy,

by

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ABSTRACT OF THESIS.

Investigations of p-methoxybenzhydrol (Balfe, Doughty, Kenyon and Poplett: J.C.S. 1942, 605) showed that esters of this carbinol undergo hydrolysis mainly by the alkyl-oxygen fission mechanism. This led to the belief that the thio-methyl group would have a similar effect to that of the methoxy group in modifying the reactivity of the benzhydrol molecule. This expectation has been fully realised in thioanisylphenyl carbinol and its esters.

Accordingly, thioanisylphenyl carbinol has been prepared and resolved through its hydrogen phthalic ester by means of quinine. Reactions of this carbinol and its esters appear to be parallel with those of p-methoxybenzhydrol. Acid hydrolysis of the (-)-hydrogen phthalic ester of this carbinol proceeds by the alkyl-oxygen fission mechanism with production of the optically inactive carbinol; a mechanism for this type of acid hydrolysis is postulated.

(-)-thioanisylphenylcarbinol and its (-)-hydrogen phthalic ester undergo smooth oxidation with hydrogen peroxide to yield the (+)-p-methyl-sulphonylbenzhydrol and its (+)-hydrogen phthalic ester respectively. The electromeric displacement in the p-methylsulphonyl group is expected to take place in a direction opposite to that in the thioanisyl group, thus,
and, therefore, hydrolysis of esters of \( p \)-methylsulphonylbenzhydrol would be expected to proceed by the acyl-oxygen fission mechanism. That this is actually the case, is borne out by the experimental evidence recorded in this thesis.

Investigations by Konyon et al. (J.C.S. 1945, 609) on the esters of anisyl-\( \alpha \)-naphthylcarbinol, showed that these behave in a manner very much similar to that of esters of \( p \)-methoxybenzhydrol; a fact undoubtedly attributed to the presence of the anisyl group. In the case of phenyl-\( \alpha \)-naphthylcarbinol, we found the esters of this carbinol undergo various reactions mainly by the acyl-oxygen fission mechanism in a manner similar to that undergone by the esters of benzhydrol. Therefore, the presence of the methoxyl group appears to modify the reactivity, to a great extent, of the benzhydryl or the phenyl-\( \alpha \)-naphthylcarbinyl groups.
The work described in this thesis was carried out in the Research Laboratories of Battersea Polytechnic, London. The author wishes to express his thanks to Dr. J. Kenyon, F.R.S. for his inestimable guidance and help, and to Dr. M. P. Balfe for his advice and encouragement.
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HYDROLYSIS OF CARBOXYLIC ESTERS

The hydrolysis of carboxylic esters may be formulated in either of two ways:

(A) \( R\text{CO} \rightleftharpoons \text{OR}\ ^{+} + \text{H}^{+} + \text{CH}^{-} \)

(B) \( R\text{CO} \rightleftharpoons \text{OR}\ ^{+} + \text{HC}=\text{H} \)

for which the convenient terms acyl-oxygen fission and alkyl-oxygen fission were introduced by Day and Ingold (1). This question was first raised and discussed by van't Hoff (2) who suggested that hydrolysis proceeds by mechanism (A).

In the great majority of cases, mechanism (A) is operative as the following experimental results show:

a) The carboxylic esters of optically active saturated alcohols on hydrolysis yield the optically pure alcohols. Alkyl-oxygen fission implies the transitory existence of \( R^{\ominus} \), which would assume a planar configuration and result in the production of the alcohol in its dl-form (3). It was shown by Holmberg (4) that hydrolysis of \( \text{L}-\text{acetylmalic acid} \) by both acids and alkalis yields the optically pure acid; and by Olson and Miller (5) that hydrolysis of the optically active \( \beta \)-bromobutyric acid results in the formation of the optically active \( \beta \)-butyrolactone without change in sign.

b) Each of the two isomeric ester:

- crotyl acetate \( \text{Me.CH}=\text{CH-CH}_{2}:\text{OAc} \), and methylallyl acetate
methyllumallyl acetate  \[ \text{Me}_2\text{CH}-\text{CH}^-\text{CH}_2 \overset{\text{CAc}}{\longrightarrow} \]

on hydrolysis with aqueous alkalis (6) or acids (7) yields its own alcohol unmixed with the other alcohol. Had mechanism (B) been involved each ester would have given a mixture of the two alcohols, since both could give rise to the same mesomeric positive ion

\[ \text{Me}_2\text{CH}-\text{CH}^-\text{CH}_2 \]

It is interesting to note (8) that crotyl alcohol and \(-\text{methylallyl}\) alcohol, on esterification with acetic acid, each gives its own ester exclusively.

c) It has been shown by Whitmore and co-workers (9) that attempts at replacement of the \(-\text{CH}\) group of neopentyl alcohol, \(\text{Me}_3\text{C}-\text{CH}_2\text{CH}\), by a halogen atom leads to rearranged products with formation of tertiary amyl halide and olefines, and that hydrolysis of \text{neo-pentyl} halides yields \text{ter-amyl alcohol} along with unsaturated compounds. It can, therefore, be assumed that hydrolysis of \text{ter-esters} of \text{neo-pentyl alcohol}, if mechanism (B) were operative, would lead to rearranged products. That this is not the case, was shown by Quayle and Norton (10) who observed that \text{neo-pentyl alcohol} underwent smooth esterification with acetic acid and chloro-acetic acids, and that hydrolysis of the resulting esters yielded \text{neo-pentyl alcohol} without any evidence of rearrangement.

d) Ammonolysis of carboxylic esters may proceed by either of two ways:

(i) \[
\begin{array}{c}
\text{R.CO}^-\text{CR}^1 \\
\text{H}_4\text{N}^-\text{H}
\end{array}
\]

(ii) \[
\begin{array}{c}
\text{R.CO}^-\text{R}^2 \\
\text{H}^-\text{NH}_2
\end{array}
\]
Therefore, if mechanism (ii), involving alky-oxygen fission, were operative, the amine and acid would be produced, whereas mechanism (i) would lead to the formation of the amide and the alcohol. It has been shown (11) that ammonolysis of n-, iso-, and tert-butylacetate with alcoholic ammonia yields the amide and the corresponding alcohol; and by Betts and Hammett (12) that the influence of the structure of the acyl group on the rate of ammonolysis of phenylacetic esters in methanol solution is closely parallel to mechanism (i) but shows no relation to that in the reaction

\[ \text{R} \cdot \text{CO} \cdot \text{C} \rightarrow \text{Me} + \text{NM}_{3} \rightarrow \text{R} \cdot \text{COO}^{−} + \text{NM}_{3}^{+} \]

\[ 1 \]

The most conclusive demonstration in favour of acyl-oxygen fission was given by Polanyi and Szabo (13). They hydrolysed amyl acetate with sodium hydroxide dissolved in water containing an increased proportion of the isotope $^{18}O$, and showed that the resulting alcohol contained the normal proportion of $^{18}O$:

\[ C_{5}H_{11}^{18}O \rightarrow C_{5}H_{11} \cdot \text{CH}_{3} \]

They also showed that when amyl alcohol was subjected to prolonged treatment with a concentrated solution of caustic soda in heavy-oxygen water at 70°C, it did not exchange its hydroxyl group with that of the water.

Hydrolysis of methyl hydrogen succinate (14) in acid aqueous medium, enriched with $^{18}O$, yields methyl alcohol containing only the normal proportion of $^{18}O$.

In a work complementary to that discussed above, Roberts and Urey (15)
esterified methyl alcohol, containing an increased concentration of O\textsuperscript{18}, with benzoic acid, using hydrochloric acid as the catalyst; the water resulting from the reaction was shown to have ordinary isotopic composition and that its oxygen originated entirely from the benzoic acid.

Further evidence in favour of acyl-oxygen fission has not been lacking. Reid (16) has shown that the reaction between benzoic acid and mercaptan is reversible:

\[
\text{C}_6\text{H}_5\text{CO-CH} + \text{H-S-C}_2\text{H}_5 \rightleftharpoons \text{C}_6\text{H}_5\text{CO-S-C}_2\text{H}_5 + \text{H-CH}
\]

and recently by Iskander (17) that alkaline or acid hydrolysis of \(\alpha\)-benzoyl-benzhydryl thiobenzoate yields benzoic acid and the corresponding thiol:

\[
\begin{align*}
\text{Ph}_2\text{CO-S(Ph)}_2\text{Ph} & \quad \text{H-O-H} \\
\text{Ph}_2\text{CO-S(Ph)}_2\text{Ph} & \quad \text{Ph}_2\text{CO-CH} + \text{Ph}_2\text{CO-C(Ph)}_2\text{SH}
\end{align*}
\]

Nevertheless, alkyl-oxygen fission (process B) occurs more commonly than has been realised when the group \(R^1\) has electron-releasing properties, and the attention of Kenyon and co-workers was drawn to this subject during the preparation of some optically active \(\alpha\)-disubstituted allyl alcohols.

A convenient method of resolving \(\text{sec}\) alcohols into their optically active components is the fractional crystallisation of alkaloidal salts of their hydrogen phthalic (or succinic) esters followed by hydrolysis of the resulting \(d\)- or \(l\)-acid ester.
In the case of saturated aliphatic alcohols, there is no evidence whatever of the occurrence of any racemisation during the hydrolysis by either concentrated or dilute aqueous alkali, since the reformed esters possess their original rotatory powers. In the case of substituted allyl alcohols, however, as a result of the investigations of Burton and Ingold (18) and Prevost (5), it is now accepted that reversible isomeric change in systems of the type

\[
R_1\text{CHX-CH=CHR}_2 \rightleftharpoons R_1\text{CH=CHR}_2\text{CHX}
\]

involves an intermediate mesomeric ion

\[
\text{CHR}_1=\text{CH-CHR}_2
\]

It is, therefore, to be expected that hydrolysis of esters of optically active substituted allyl alcohols would yield racemic and, under certain favourable conditions, isomeric products according to the following scheme; where \(X = \text{OAc}\):

Kenyon and co-workers (19) have demonstrated that when (+)-\(\gamma\)-dimethyl
allyl hydrogen phthalate is hydrolysed using an excess of 5 N caustic soda, the liberated \( \alpha\gamma \)-dimethylallyl alcohol is almost optically pure, since this when reconverted to its hydrogen phthalic ester, gives an almost fully active product. On the other hand, when dilute alkali, in slight excess is used the alcohol is obtained in a highly racemised form. It seems likely, therefore, that mechanism (A) is operative in concentrated alkaline solution, but that mechanism (B) comes increasingly into play as the alkaline solution becomes more and more dilute. Since the postulated positively charged radical

\[
\text{Me}_2\text{CH-CH-CH}_2\text{Me}
\]

is symmetrical, the same racemic chemical individual is obtained whether the \( \text{CH} \) group becomes attached to the \( \alpha \) or \( \gamma \)-carbon atom. It has also been shown by the same investigators that the hydrogen phthalic ester of (+)-\( \alpha\gamma \)-dimethylallyl alcohol reacts with formic acid, acetic acid, methanol, \( \text{\textmu} \)-butyl alcohol and benzyl alcohol yielding the corresponding optically inactive formate, acetate, methyl or \( \text{\textmu} \)-butyl and benzyl ether; and that when these reactions are stopped before completion, the recovered hydrogen phthalic ester is found to be extensively racemised.

When, however, the di-substituted allyl alcohol molecule is not symmetrical, as in \( \alpha \)-phenyl-\( \gamma \)-methylallyl alcohol, a second possibility arises — and when the (+)-hydrogen phthalic ester of this alcohol is hydrolysed by diluted aqueous alkali, the product is the highly racemised form of the isomeric \( \alpha \)-methyl-\( \gamma \)-phenylallyl alcohol (20). This seems to indicate that the mesomeric positive radical becomes kinetically free at some stage of the reaction.
On the other hand, when hydrolysis is carried out with alcoholic alkali, the ester in question yields its own optically active alcohol exclusively and in an optically pure state.

γ-Phenyl-α-methylallyl alcohol is structurally more stable than the isomeric alcohol, and when its optically active hydrogen phthalic ester is hydrolysed by dilute aqueous alkali, the unisomerised alcohol is obtained in an almost optically inactive condition (21).

Perhaps the most interesting and novel example of alkyl-oxygen fission is the formation of neutral esters from the hydrogen phthalic esters of certain carbinols. The mode of formation of the neutral ester proceeds by the unimolecular mechanism and is promoted by the electron-release in the carbonyl radical, ionising effect of the solvent, and removal of the neutral ester as an insoluble product. Kenyon and co-workers (22) observed this to be particularly the case in the hydrolysis, in weak alkali, of the hydrogen phthalates or succinates of carbinols containing alkoxy groups which have high electron-releasing properties. Thus, when the hydrogen phthalic ester of (+)-p-methoxybenzhydryl is hydrolysed with 0.3 N caustic soda, the ester ionises yielding racemised p-methoxybenzhydryl cation and p-methoxybenzhydryl phthalate anion which combines with the former cation to form di-p-methoxybenzhydryl phthalate or the neutral ester, which on hydrolysis with
alcoholic caustic soda yields the carbinol with half its maximum rotatory power:

\[
\overset{\text{GOO}}{\text{COOR(+)}} \xrightarrow{\text{R}} \overset{\text{COO}^-}{\text{GOO}} \quad \overset{\text{H}_2\text{O} \xrightarrow{\text{H}^+}}{\text{GOOR(+)}} \xrightarrow{\text{COOR(dl)}} \overset{\text{COOR(dl)}}{\text{COOR(+)}} \xrightarrow{\text{H}_2\text{O}} \overset{\text{(dl)}}{\text{RCH}}
\]

When this reaction is allowed to proceed in a solution containing excess (5 mol.) of sodium phthalate, the dl-neutral ester is precipitated. In this case it seems probable that both groups R present in the neutral ester have been produced by alkyl-oxygen fission of the original (+)-hydrogen phthalic ester, and it may be postulated that the liberated cations react with the phthalic imino ions to yield the racemic hydrogen phthalic ester, which in turn slowly forms the dl-neutral ester which on hydrolysis yields the dl-carbinol:

\[
\overset{\text{CO}}{\text{COOR(+)}} \xrightarrow{\text{R}} \overset{\text{COO}^-}{\text{COONa}} \overset{\text{COONa}}{\xrightarrow{\text{COONa}}} \overset{\text{COOR(dl)}}{\text{COOR(dl)}} \xrightarrow{\text{H}_2\text{O}} \overset{\text{dl}}{\text{RCH}}
\]

Along with the neutral ester there is produced a very small proportion of almost racemic alcohol presumably by the interaction of p-methoxybenzhydryl cations with hydroxyl ions or water molecules of the solvent:

\[
\overset{\text{O}}{\text{R}} \xrightarrow{\text{CH}^-} \overset{\text{dl}}{\text{RCH}}
\]

Support for this view is found in the racemisation undergone by (+)-p-methoxybenzhydryl in aqueous solution at 100°C, when the rotatory power fell from +17.4° to 0° in 30 hours. No chemical decomposition had occurred since the recovered material carbinol melted sharply at 66°C.
Since this neutral ester is a viscous liquid, and therefore difficult to obtain in a highly purified condition, experiments were carried out with alcohols of higher molecular weight in the hope of obtaining a neutral phthalic ester which would be crystalline. This was successful in the case of anisyl-α-naphthylcarbinol:

\[
\text{CH(CHOH)\_6\_C\_6\_H\_4\_O\_CH\_3}
\]

and results parallel to those just described were obtained. It was also found that the optically active hydrogen succinic ester of the same alcohol behaves in an analogous way in yielding a crystalline half racemised neutral succinic ester (23°x) and it was similarly observed that in 0.3 N caustic soda, at room temperature, the hydrogen phthalic esters of anisylmethylcarbinol, p-methoxy-α'-methylbenzyldiol, p-methoxy-p'-isopropylbenzyldiol, and p-methoxyphenyl-α-naphthylcarbinol yield the respective neutral phthalic esters (24°).

That neutral esters can be obtained in other than alkaline media, has been demonstrated by Balfe, Evans and Kenyon (23°x) when they prepared the neutral phthalic ester of anisyl-α-naphthylcarbinol by heating the hydrogen phthalic ester of the latter in chloroform solution. The mechanism of this reaction is essentially the same as that described above. The phthalic acid which is formed, being insoluble in chloroform, is precipitated, and this favours the course of the reaction.

The structural similarity between the -COOH and -SOCH groups suggests that alkyl-oxygen fission may be expected to occur in
sulphinic esters of carbinols with electron-releasing groups. When the hydrogen phthalic esters of the optically active \( p \)-methoxybenzhydrol and anisyl-\( \alpha \)-naphthylcarbinol react with sodium \( p \)-toluenesulphinate in aqueous alkaline medium, the corresponding \( \text{dl} \)-sulphone separates rapidly from solution (22, 23):

\[
\text{COOR}^{(+)} + C_7H_7\text{SOO}_{\text{Na}} \rightarrow \text{C}_7\text{H}_7\text{S} - R(\text{dl})
\]

It was first observed by Kenyon and Phillips (26) that \( 1 \)-phenyl-methylcarbinyl-\( p \)-toluenesulphinate (liquid) changes spontaneously into the crystalline optically inactive \( p \)-tolyl-phenylmethylcarbinylsulphoxide:

\[
\begin{aligned}
\text{C}_6\text{H}_5\text{O}:\text{O}:\text{S}:\text{C}_6\text{H}_4\text{OCH}_3 & \rightarrow \left( \text{C}_6\text{H}_5\text{O}:\text{C}_6\text{H}_4\text{OCH}_3 \right)^+ \\
& \rightarrow \left( \text{C}_6\text{H}_5\text{O}:\text{C}_6\text{H}_4\text{OCH}_3 \right)^- & \rightarrow \text{C}_6\text{H}_5\text{S}:\text{C}_6\text{H}_4\text{OCH}_3
\end{aligned}
\]

\( 1 \)-
\( \text{dl} \)-

A rearrangement which is facilitated by formic acid (27); and when the \( 1 \)-sulphinate reacts with acetic acid, it forms the \( \text{dl} \)-acetate. Therefore, the reactions mentioned above indicate that under acid conditions, the sulphinate seems to undergo both isomerism and replacement reactions catalysed by hydrogen ions. On the other hand, the \( 1 \)-sulphinic ester undergoes alcoholysis in ethanol and potassium carbonate with complete retention of configuration. It, therefore, appears that esters of phenylmethylcarbinol do not undergo alkyl-oxygen fission readily. Such, however, is not the case with esters of substituted benzhydrols with strong electron-releasing groups.
That sulphones can be produced by the interaction of secondary alcohols with aromatic sulphinic acids, was first recorded by Hineberg (28) who observed that benzhydrol or Michler's hydrol condense with benzene-sulphinic acid or β-anthraquinonesulphinic acid to form the respective sulphone.

Kanyon and co-workers (22-25) prepared p-tolylsulphones of many secondary alcohols by the following methods:

a) By the interaction of the carbinyl hydrogen phthalic ester with p-toluene-sulphinic acid in an alkaline medium.

b) By the interaction of the carbinyl chloride with sodium p-toluene-sulphinat in aqueous acetone.

c) By heating the carbinyl hydrogen phthalic ester with p-toluene-sulphinic acid in dry chloroform.

d) By the interaction of the carbinyl hydrogen phthalic ester with sodium p-toluene-sulphinat in hot formic acid.

e) By the interaction of the carbinol or its acetate with sodium p-toluene-sulphinat in hot aqueous alcohol.

These methods have been used in the preparation of the sulphones of the following carbinols arranged according to their electron-releasing properties and the readiness with which they form the sulphone:

dianisylcarbinol > p-p-dimethoxybenzhydrol > p-methoxy-p'-isopropylbenzhydrol > p-methoxybenzhydrol > anisyl-α-naphthylcarbinol > p-phenoxybenzhydrol > ethylanisylcarbinol > anisyl alcohol > p-dimethylamino-benzhydrol > benzhydrol > phenylmethylcarbinol.

It was thus observed that the carbinols with strong electron-releasing groups, and whose esters undergo alkyl-oxygen fission readily,
form the sulphone by methods (a) and (b) rapidly and quantitatively.

Another interesting example of alkyl-oxygen fission has recently been demonstrated by the work of Cohen and Schneider (29). They suggested that the reaction between a carboxylic ester and an alcohol may proceed by either of two ways:

\[
\begin{align*}
R_\text{CO} + \text{OR'} & \quad \text{H-CR''} \quad \text{R_\text{CO} - CR''} + \text{H-CR'} \\
R_\text{COO} + \text{R'} & \quad \text{H-CR''} \quad \text{R_\text{COO} - H} + \text{R'}\text{O-R''}
\end{align*}
\]

and, therefore, these two mechanisms are parallel to those of mechanisms (A) and (B). They observed that when tert-butyl esters of acetic or 2,4,6-trimethylbenzoic acids react with methanol, tert-butyl methyl ether and the corresponding acid are formed; a reaction, which was shown to be catalysed by acids. On the other hand, tert-butyl benzoate in methanol and sodium methoxide results in the formation of tert-butyl alcohol and not the ether. It was, therefore, concluded that the uncatalysed and acid-catalysed alcoholysis of tert-butyl esters proceed by mechanism (ii) which involves alkyl-oxygen fission.

Mechanism (ii) is unimolecular and requires the separation of \( R' \) as a positive ion at one stage of the reaction, and when \( R' \) is asymmetric at the point of attachment, the d,l-ether is produced. That this is actually the case, was demonstrated by Kenyon and co-workers (22, 23, 24, 25). They observed that the hydrogen phthalic and succinic esters, and the neutral phthalic esters of optically active \( p \)-methoxybenzhydro and anisy-\( \alpha \)-naphthylcarbinol react readily with dry or aqueous methanol yielding the d,l-methyl ether; whereas, esters of
carbinols, which react by alkyl-oxygen fission, show no reaction with dry methanol, but when aqueous methanol is used, the methyl ether is produced. Thus the hydrogen phthalic ester of (+)-α-naphthylmethycarbinol shows no reaction with dry methanol, but with aqueous methanol it forms the dl-methyl ether. On the other hand, esters of (4)-phenylmethycarbinol, which react mainly by mechanism (A), show no reaction with anhydrous or aqueous methanol.

That carbinols, and not only their esters, can form ethers by their interaction with alcohols, has been demonstrated in many cases; the reaction appears to be favoured by acid catalysis. It shown by Norris and Rigby (30) that tertiarybutyl alcohol is converted into the ethyl ether by means of 15% sulphuric acid in excess ethanol; but under these conditions, the reactions are much slower if secondary alcohols are used instead of ethanol. It was also observed by Hatt (31) that triphenyl carbinol is unaffected by dry boiling methanol, whereas the presence of hydrogen chloride brings about the formation of the methyl ether. In the case of substituted benzhydrols, the presence of acids is not essential. Thus, p-methoxybenzhydrol and p-dimethylaminobenzhydrol form the corresponding methyl ethers when heated with an excess of methanol for few minutes (24).

Another interesting reaction that some carbinols undergo, in hot aqueous solution or by the action of heat, is the formation of di-ethers. This reaction may be formulated as follows:

\[
\text{R-OH} + \text{H-CH} \rightarrow \text{R-OH} \quad \text{R-OH}
\]

\[
\text{R} + \text{H-OH}
\]
Support for this view has been provided by Stolbe and Zeitschell (32) who observed that when benzhydryl is heated with a large volume of water for four days, is partly converted into di-benzhydryl ether. Therefore, the formation of the di-ether under these conditions, necessarily postulates the ionisation of the carbinol into \( R \) and \( -\text{OH} \) ions, and hence the possibility arises that the carbinol may interchange its hydroxyl ion with that of the water. That this is actually the case, has been demonstrated by Kenyon et al (22) who showed that when (\(+\))-benzhydryl is heated with water at 90° C for 30 hours, the di-carbinol is produced with no trace of the di-ether. On the other hand, when an ethereal solution of \( p \)-methoxybenzhydryl chloride is shaken with water, the carbinol together with di-ether are produced. In the latter case, the formation of the di-ether may have occurred by the interaction of the chloride and the carbinol (formed by the partial hydrolysis of the chloride), thus:

\[
\begin{align*}
\text{RO-H} \quad + \quad \text{R-Cl} \quad \rightarrow \quad \text{R,OR} \quad + \quad \text{HCl}
\end{align*}
\]

A similar reaction was first recorded by Friedel and Balschon (33) who observed that when benzhydryl bromide is heated with an excess of water, benzhydryl together with some di-benzhydryl ether are formed.

That di-ethers can be produced by the action of heat on carbinols, was first demonstrated by Mohlau and Heinze (34) who observed that when Michler's hydrol is heated at 105° C, it is converted into its di-ether. Later on, Kenyon and co-workers (22, 23 and 24) showed this to be generally the case with most substituted benzhydrols; they observed that each of the residues from the distillation of \( p \)-methoxybenzhydryl, anisylmethylc
anisylmethylicarbinol, p-methoxy-p'-methylbenzhydrol, p-methoxy-p'-isopropylbenzhydrol, and p-methoxyphenyl-<naphthylearbinol yield the respective di-ether; and when p-methoxy-p'-methylbenzhydrol, p-methoxy-p'-isopropylbenzhydrol, and anisyl-<naphthylearbinol heated at 140° until no more water evolved (10-25 mins.), each yields its di-ether. In the case of p-chloro- and p-dimethylaminobenzhydrol, however, no di-ether is produced under these conditions.

Another interesting feature of substituted benzhydrols and their esters, is the ease with which they react with phenol and p-thiocresol to form phenyl ethers and p-thiocresyl ethers respectively. When the hydrogen phthalic ester of p-methoxybenzhydrol or of anisyl-<naphthylearbinol is heated with phenol in chloroform solution, the corresponding phenyl ether is produced. The thio-ethers of p-methoxybenzhydrol, p-dimethylaminobenzhydrol, 3,4-diethoxybenzhydrol and of anisylmethylcarbinol can be obtained: a) by the action of p-thiocresol on the hydrogen phthalic ester in alkaline solution; b) by heating p-thiocresol with the carbinyl hydrogen phthalic ester in chloroform solution; and c) by heating p-thiocresol with the carbinol in chloroform solution (25). It seems clear that these reactions must proceed by mechanism (B).

Further evidence in support of alkyl-oxygen fission under special experimental conditions, has been revealed by recent work on the ammonolysis of carboxylic esters and hydrolysis of thio-esters, which contain a carbinyl radical R' which tends to separate as a cation.

It is well known that when ammonia, an amine or a hydrazine reacts with a carboxylic ester

\[
\begin{array}{c}
\text{R- CO- CR'} \\
\text{O} \\
\text{O}
\end{array}
\]
an amide or a hydrazide is formed together with the alcohol corresponding to the original ester. It thus appears that the ammonia molecule, owing to its nucleophilic nature, has a greater attraction for the cationoid carbon of the acyl group than for the electron-repelling group R', hence the reaction proceeds by alkyl-oxygen fission.

If, on the other hand, a powerful cationoid centre were introduced into the group R', then the ionic state of the resultant ester molecule could be reversed, with the result that the ammonia molecule might attack not only the acyl group but also the group R' to a greater or less extent. Under such conditions the rupture of the ester molecule would proceed by the alkyl-oxygen fission mechanism:

\[
\begin{align*}
\text{R-O-C-C}^+ & \quad \text{R-NO}_2 \quad \text{H-NH}_2 \\
\rightarrow & \quad \text{R-CO-H} + \text{H}_2\text{N-C}_2^+ \\
\end{align*}
\]

Such a condition has actually been realised by Chattaway (35) who observed that \( \gamma\gamma\gamma^-\text{trichloro-\&-nitro-\&-acetoxyp propane reacts with ammonia, p-toluidine or phenylhydrazine with production of the amine or the hydrazine}

\[
\begin{align*}
\text{CH}_3\text{-CO-CH-CCl}_3 & \quad \text{CH}_2\text{-NO}_2 \\
\text{H-NH}_2 & \quad \text{H-N-C}_2^+ \\
\rightarrow & \quad \text{CH}_3\text{-COOHH} + \text{H}_2\text{N-C}_2^+ \\
\end{align*}
\]

Here, the highly electron-attracting groups \(-\text{CCl}_3\) and \(-\text{CH}_2\text{-NO}_2\) would leave the \(\text{C}\) strongly positive and hence a centre of attack by nucleophilic reagents; and therefore the reaction proceeds by mechanism (B).
This was also found to be the case by Kenyon and co-workers (25) with the ammonolysis of substituted benzhydryl carboxylic esters. They observed that p-methoxybenzhydryl hydrogen phthalate reacts with concentrated ammonia solution at room temperature with formation of p-methoxybenzhydrylamine; and that the hydrogen phthalic esters of p-phenoxybenzhydrol and anisyl-α-naphthylcarbinol react with concentrated ammonia at 100°C in a sealed tube, producing the corresponding amine; but on the other hand, unsubstituted benzhydryl hydrogen phthalate, under similar conditions, undergoes hydrolysis with production of benzhydrol.

That hydrolysis of thio-carboxylic esters proceeds by mechanism (A) was proved by Raid (16) who also observed that hydrogen sulphide reacts with ethylbenzoate with formation of benzoic acid and mercaptan:

\[
\begin{align*}
C_6H_5CO_2C_2H_5 & \rightarrow C_6H_5COOH + C_2H_5SH \\
C_6H_5CO_2C_2H_5 & + H-SH & \rightarrow C_6H_5COOH + C_2H_5SH
\end{align*}
\]

This reaction, which is reversible, clearly involves alkyl-oxygen fission.

More recent work by Iskander (36) revealed that alkaline hydrolysis of triphenylmethylthiobenzoate yields benzoic acid and the corresponding thiol, whereas, acid hydrolysis by alcoholic HCl yields thiobenzoic acid and triphenylmethylcarbinol:

\[
\begin{align*}
\text{Ph}_2CO-S-C(\text{Ph})_3 & \xrightarrow{\text{alcohol}} \text{Ph}_2CO-\text{CH} + (\text{Ph})_3C-SH \\
\text{H}_2C\text{O} & \rightarrow \text{Ph}_2CO-S-C(\text{Ph})_3 \xrightarrow{\text{HCl}} \text{Ph}_2COS-\text{H} + (\text{Ph})_3C-\text{OH}
\end{align*}
\]
Here, the presence of the Ph-groups tends to promote the separation of the carbinyl radical as a positive ion, and this is facilitated by the acidic medium in which the reaction proceeds by mechanism (B). It will be of interest to study the hydrolysis of this ester in a weak alkaline medium, as it is known that hydrolysis, by weak alkali, of esters of carbinols, with strong electron-releasing properties, proceeds by mechanism (A), whereas hydrolysis with weak alkali proceeds by mechanism (B) (22).

Nevertheless, further references to secondary alcohols which react by alkyl-oxygen fission is not lacking in the literature. It is known that many aromatic sec. and tert. alcohols give intensely coloured salts (halochromic salts) when dissolved in concentrated sulphuric acid. These are ionic compounds with the positive charge appearing on the sec. or tert. carbon atom; for example, the halochromic salt produced by dissolving triphenylcarbinol in concentrated sulphuric acid may be represented as

\[
\text{[Ph}_3\text{C]}^+ \quad \text{[SO}_4\text{H]}^-
\]

In the case of optically active secondary alcohols, their halochromic salts are, therefore, expected to be optically inactive. This was found to be the case by Gomberg and Gordon (37) who showed that when the optically active phenylbiphenyl-α-naphthylmethylthioglycollic acid,

\[
(\text{C}_6\text{H}_5)(\text{C}_6\text{H}_5\text{C}_6\text{H}_4)(\text{α-C}_10\text{H}_7)\text{C-S-CH}_2\text{-COOH}
\]

is treated with concentrated sulphuric acid, the halochromic salt obtained is optically inactive.
Michler's hydrol and its derivatives undergo some remarkable reactions involving the rupture of the alkyl-oxygen bond. The hydrol reacts with aniline or α-naphthylamine or p-toluidine in alcoholic solution forming phenyl- or α-naphthyl or p-tolyl leucouramine respectively; and the leucouramine in acid solution reacts with hydrogen sulphide yielding the sulphide \([\mathrm{C}_6\mathrm{H}_4\mathrm{Me}_2\mathrm{CH}]_2\mathrm{S}\) (34). The hydrol, in alcoholic solution, reacts with phthalic or succinic anhydride forming phthalyl or succinyl leucouramine (38); and with sulphur dioxide to give the bisulphite derivative, \(\left(\mathrm{Me}_2\mathrm{C}_6\mathrm{H}_4\right)\mathrm{CH}_2\mathrm{HSO}_3\), or with hydrogen cyanide yielding the nitrile, \(\left(\mathrm{Me}_2\mathrm{C}_6\mathrm{H}_4\right)\mathrm{CH}_2\mathrm{CN}\) (39).

It was shown by Fesse that ββ-disubstituted propionic acid are readily obtained by the action of malonic acid on aromatic secondary alcohols containing the substituent groups -OMe or -OMe_2 according to the equation:

\[\text{CH}_2\text{CH} \text{CH}_2\text{COOH} \]

Thus, p-methoxybenzhydrol, anisyl-α-naphthylcarbinol, and p-dimethylaminobenzhydrol react readily with malonic acid to form ββ-disubstituted propionic acids (40). He also observed that malonic acid converts triphenylcarbinol quantitatively into ββα-triphenylpropionic acid (41).

It can, therefore, be concluded that in these reactions the rupture of the alkyl-oxygen bond is clearly indicated.
MECHANISMS OF HYDROLYSIS OF CARBOXYLIC ESTERS

The study of reaction-kinetics (of substitution or elimination) together with a detailed examination of the reaction products, in the hands of Ingold, Hughes and their co-workers, has contributed a great deal towards the elucidation of reaction mechanisms. The majority of substitution reactions appear to involve dissymmetric or heterolytic fission, and in the case of nucleophilic substitution (Sn), in which the attacking nucleophilic reagent Y transfers electrons to or shares electrons with a foreign nucleus, the reaction may proceed by either of two ways (42):

\[ Y: + R\cdot X \rightarrow Y:R + :X \quad \text{Bimolecular Sn2} \]

\[ R\cdot X \xrightarrow{\text{slow}} R + :X \]

\[ Y: + R \rightarrow Y:R \quad \text{Unimolecular Sn1} \]

The modern theory of displacement reactions, developed by London and Polanyi, postulates that the reaction \[ Y - RX \rightarrow YR + X \]
proceeds through the transition complex \[ Y\ldots R\ldots X \] in which the energy level is lowered, thus facilitating the breaking of the bond R-X.

The ease with which the fission of the bond R-X takes place depends upon many factors, such as the structure of R, effect of solvents, and presence of catalysts.

In the Sn1 mechanism, the reaction appears to proceed in two stages: first, a slow ionisation takes place and this has to pass over an energy maximum which may be reduced to a greater or less extent by solvation forces or by the structural nature of R, and lastly, a rapid reaction
between the carbonium ion and Y. This mechanism is promoted by sec. and
tert. alkyl groups with strong electron-releasing properties. Thus, in
the hydrolysis of alkyl esters in dilute alkaline solutions, it is
observed (43) that, when the alkyl or substituted alkyl groups are
placed in the order of increasing electron-releasing properties, the
bimolecular reaction-rate diminishes slowly, then passes through
a minimum, in the neighbourhood of which a mixture of first and second
order kinetics occur and either of which can be brought into prominence
by altering the concentration of -OH ions, and finally, the rate
rises sharply and the kinetics are of the first order, and the rate of
which is quite independent of the hydroxyl ion concentration.

The presence of a double bond in the alkyl radical appears to play
a prominent role in determining the mechanism by which substitution
reactions proceed. Thus, where a double bond is at the seat of substitu-
ion, as in vinyl halides \( \text{C} = \text{C}-\text{Hal} \) and phenyl halides

\[ \text{C} = \text{C}-\text{Hal} \quad \text{or} \quad \text{O} = \text{C} - \text{Hal} \]

an electromeric displacement is induced, strongly inhibiting mechanism
Sn1 and also retarding mechanism Sn2. Here, the dipolar structure of
phenyl halides reduces greatly the tendency for the halogen to separate as
an ion, and the increased electron density in the benzene nucleus
inhibits the approach of a nucleophilic reagent. Experiment shows that
substitution in these systems never occurs by mechanism Sn1 and only with
difficulty by mechanism Sn2.

But in the case of allyl and benzyl halides, where the double bond
is removed one carbon atom from the seat of substitution, electromeric
and mesomeric polarisations come into play. Thus, the electromeric polarisation $\text{C=C-Hal}$ has a strong facilitating influence on mechanism $\text{S}_\text{n1}$ and a much smaller effect on $\text{S}_\text{n2}$. These allyl halides are highly active under all conditions of nucleophilic substitutions; their hydrolysis and alcoholysis proceeds by $\text{S}_\text{n2}$ mechanism in dry alcohol and sodium ethoxide, and by $\text{S}_\text{n1}$ in neutral 50% alcohol (44). Similarly, in benzyl halides the mesomeric structure leads to incipient ionisation into a halide anion and benzyl cation:

$$\text{CH}_2\text{Br}^- \quad \text{or} \quad \text{CH}_2\text{C}=\text{O}^{-}$$

The introduction of electron-releasing groups in the $\pi$-position, greatly enhances the mesomeric polarisation, which lowers the energy level of the transition complex and simultaneously stretches the C-Br bond due to increased electron supply, and thus facilitating the attack by nucleophilic reagents:

$$\text{CH}_2\text{Br}^- \quad \text{NR}_3 \quad \text{CH}_2\text{Br}^- \quad \text{NR}_3$$

This is mostly marked where $X$ is a methoxy group, which has a powerful tautomeric effect:

$$\text{MeO}\text{CH}_2\text{Br}^-$$

hence the tendency for ionisation and reaction rates are greater. If, on the other hand, an electron-attracting group, such as $-\text{NO}_2$, is introduced into the $\pi$-position, the electron supply necessary for breaking the C-Br bond must be supplied to a greater extent by the attacking nucleophilic
reagent, hence retarding Sn2 mechanism:

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_2 & \quad \text{Br} \\
\text{CH}_3 & \quad \text{CH}_2 & \quad \text{CH}_2
\end{align*}
\]

Experiment shows that the reaction-rate of

\[
P^\text{-NO}_2 \text{ benzyl} < \text{benzyl} < P^\text{-Me} \text{ benzyl}
\]  (45).

Not only the structure of the alkyl group influences the course of reaction mechanism, but the influence of solvents appears to be very important, especially in cases where the transition state involves an increase or decrease in the magnitude of the charges. Thus, the reactions of benzhydryl halides with halogen ions are bimolecular in acetone and unimolecular in sulphur dioxide (46); and that the hydrolysis of the bromides of Me, Et, isopropyl and tertiary butyl shows, by changing the solvent to a more highly solvating one, not only the reaction rates of the whole series increases, but also the effect is very large for tertiary butyl, considerably smaller for isopropyl and still smaller for Et and Me bromides (47).

Another interesting factor influencing the rate of reactions is presence of salts with a common ion with that of the alkyl ester. If the reaction proceeds by mechanism Sn1, the presence of such salts should have a great effect on the rate of reaction, and, on the other hand, it would have no effect if the reaction proceeds by the Sn2 mechanism. Thus, in the hydrolysis of the following halides in presence of sodium halide, the mass-law effect is found to increase from left to right (48):

\[
(\text{CH}_3)_3\text{C}^- , (\text{C}_6\text{H}_5)_2\text{CH}^- , \text{P-ter-Bu.C}_6\text{H}_4^-\text{CH}^- , \text{P-Me.C}_6\text{H}_4^-\text{CH}^- , (\text{P-Me.C}_6\text{H}_4)^2\text{C}^+\text{H}_5^- , (\text{P-Me.C}_6\text{H}_4)^2\text{C}^+\text{H}_5^- \]

The most marked examples of reactions by the SnI mechanism have been found in the esters of secondary alcohols containing the anisyl radical which, as explained above, facilitates the formation of the positive carbinyl ion. Thus, (+)-p-methoxybenzhydrol, its (−)-hydrogen phthalic ester, its acetate, di-ether, methyl ether and benzoate react with concentrated hydrochloric acid with remarkable ease, yielding the dl-p-methoxybenzhydryl chloride. The readiness with which this carbinol tends to dissociate into a racemic cation, has been demonstrated by the formation of the dl-chloride by the reaction of (+)-p-methoxybenzhydrol with thionyl chloride in presence of pyridine, since this reaction is a standard method for preparing the optically active chlorides from optically active carbinols (22). Similarly, (+)-anisyl-α-naphthylcarbinol at room temperature, and p-phenoxybenzhydrol at 60° react smoothly with concentrated hydrochloric acid to form the dl-chloride (23, 25).

Other interesting reactions, by which optically active substituted benzhydrols and their esters undergo racemisation in organic acids, have been shown by Kenyon and co-workers. Thus, (+)-p-methoxybenzhydrol or its dl-methyl ether reacts with glacial acetic acid at 90° to yield the dl-acetate. Its (+)-hydrogen phthalic ester racemises completely in glacial acetic acid in 24 hours, and if the reaction is stopped before completion, the recovered hydrogen phthalic ester is found to be appreciably racemised (22). On the other hand, the (+)-hydrogen phthalic ester or (−)-benzoate of phenylmethylcarbinol shows no reaction with glacial acetic acid at 90°, but when the acid contains more than 20% water, the dl-acetate is produced, and the recovered hydrogen phthalic or benzoate ester is observed to be partially racemised (23).
It is well-known that the alkaline hydrolysis of the majority of esters of optically active carbinols proceeds by the Sn2 mechanism for which the bimolecular mechanism has been postulated by Datta, Day and Ingold (49). It involves three stages: a nucleophilic attack by \( \text{OH} \) on the carbonyl-carbon atom, elimination of \( \text{OR}^* \) and finally reaction of the latter with a water molecule with liberation of \( \text{OH} \) ion:

\[
\begin{align*}
R-C-OR^* + \text{OH} \quad \text{slow} & \quad \rightarrow \quad R-C-OH + \text{OR}^* \quad \text{fast} \\
\text{OR}^* + H_2O \quad \text{fast} & \quad \rightarrow \quad R'CH + \text{OH}.
\end{align*}
\]

This mechanism necessarily involves the transitory existence of the intermediate compound:

\[
\begin{align*}
\text{OR}^* + H_2O \quad \rightarrow \quad R'CH + \text{OH}.
\end{align*}
\]

It was demonstrated by von Pechmann (50) that the addition compound

\[
\begin{align*}
\text{C}_{6}H_{5},\text{C}-\text{CH}-\text{OEt}\\
\text{C}_6\text{H}_5,\text{C}-\text{OCH}_3
\end{align*}
\]

can be isolated from the interaction of ethyl benzoate and sodium methoxide.

If \( R' \) is asymmetric at the point of attachment, hydrolysis would yield the carbinol \( R'CH \) with complete retention of its optical activity.

Although the hydrolysis of a great majority of carboxylic esters appears to proceed by the bimolecular mechanism, quite a number of esters have been observed to undergo hydrolysis by the uni- and bimolecular mechanisms under different conditions. The course of the reaction mechanism appears to depend upon many factors, the most important of which are:
the nature and structure of $R'$, the ionising power of the solvent, temperature and the concentrations of the reactants. Thus the reaction-kinetics of the bimolecular hydrolysis of butyl acetates, in aqueous alkali at room temperature, show that the reaction rates follow this sequence (51): $n \rightarrow \text{iso} \rightarrow \text{sec} \rightarrow \text{tert}$, and that the rate of esterification and etherification of this series follows the opposite sequence (52). It is, therefore, obvious that the unimolecular mechanism becomes markedly operative in the hydrolysis of esters of tertiary-butyl alcohol.

It has been shown by Baljet (53) that the interaction of a variety of alcohols, in large excess, with a variety of esters in presence of a small amount of caustic soda, results in the higher alcohol being displaced by the lower, the extent of replacement being greater at higher temperatures; tertiary alcohols are displaced more readily than primary alcohols.

The unimolecular basic hydrolysis necessarily proceeds by alkyl-oxygen fission, a mechanism for which which has been postulated by Day and Ingold (54):

\[
\begin{align*}
\text{slow} & \quad \text{fast} \\
\text{R}-\text{O-O} & \quad \text{H}_2\text{O} \\
\text{R} & \quad \text{H} & \quad \text{CH}_2
\end{align*}
\]

This mechanism requires electron-release by $R'$ and electron withdrawal by $R$ and is not sensitive to steric hindrance (54); It involves the ionisation
of R' into a carbonium cation and its reaction-rate would be independent of the hydroxyl ion concentration. If R' is asymmetric at the point of attachment, hydrolysis would result in a racemic product.

That this is actually the case, is borne out by the researches of Kenyon and co-workers on the hydrolysis of esters of optically active carbinols containing the anisyl group. They showed that when the hydrolysis is carried out a) in absolute alcohol and sodium alcoholate, the carbinols are obtained with full retention of optical activity; b) in aqueous alcoholic caustic soda, the carbinols obtained are partially active, racemisation is proportional to the water content of the alcohol; and c) in aqueous sodium carbonate, the carbinols produced have lowest rotatory powers. The hydrolysis of esters of optically active p-methoxybenzhydrol, p-methoxy-p'-methylbenzhydrol, and anisyl-α-naphthylcarbinol in aqueous alkali yield the partially active carbinols even at high alkali concentrations (10 N). On the other hand, hydrolysis of esters of optically active phenylmethylcarbinol and anisylmethylcarbinol with 10 N caustic soda yields the fully active carbinols, whereas, when aqueous sodium carbonate is used, partially active carbinols are obtained (22, 23, 24). That ionisation of the ester precedes reaction, was proved by the fact that when the hydrolysis of the optically active ester is not carried out to completion, the recovered ester is observed to be extensively racemised. It can, therefore, be concluded that the unimolecular mechanism, involving alkyl-oxygen fission, is promoted to a greater or less extent by the presence of electron-releasing groups in the carbinyl radical, and that this effect is enhanced by the ionising power of the medium in which the reaction is effected.
PHENYL-α-NAPHTHYL CARBINOL

In view of the fact that esters of p-methoxybenzhydrol and anisyl-α-naphthylcarbinol show a great tendency to react by alkyl-oxygen fission in contrast to those of benzhydrol which show very little tendency to react by alkyl-oxygen fission, our attention has been drawn to the study of reactions of phenyl-α-naphthylcarbinol and its esters.

Phenyl-α-naphthylcarbinol can be prepared by two methods: i) by the action of benzaldehyde on α-naphthylmagnesium bromide, and ii) by the reduction of phenyl-α-naphthyl ketone obtained by the Friedläder and Crafts' reaction. The latter method is more economical and gives a higher yield of the carbinol. It is interesting to note that reduction of phenyl-α-naphthyl ketone proceeds smoothly and at a much faster rate than that of ketones with strong electron-releasing groups, such as p-methoxy-benzophenone.

The hydrogen phthalate, succinate, acetate and benzoate derivatives of this carbinol are obtained by the usual methods in presence of pyridine. But an attempt at resolution of the carbinol through its phthalic or succinic ester with various alkaloids failed, due to the fact that the stereoisomerides could not be fractionally crystallised from various solvents or their mixtures, due to the separation of the alkaloidal salts in the form of gums.

The hydrolysis of esters of this carbinol appears to proceed by acyl-oxygen fission mechanism. Thus, the hydrogen phthalic or succinic ester undergoes hydrolysis with caustic soda at various concentrations and temperatures yielding exclusively the carbinol without the formation
of a trace of the neutral ester. The hydrogen phthalic ester undergoes no dismutation when heated under reflux for 30 hours in dry chloroform solution, from which the ester can be recovered unchanged.

The hydrogen phthalic ester does not react with sodium p-toluene sulphinate in alkaline solution, but in formic acid solution at 90° it forms the corresponding sulphone. Therefore, the acid medium appears to promote the rupture of the alkyl-oxygen bond. It reacts with absolute alcohol at 90° to form the ethyl ether in 46% yield after 18 hours, whereas if 70% alcohol is used, the yield of the ethyl ether under similar conditions is 58%. The increased reaction-rate in the latter case is probably due to the increased dielectric constant and hence greater ionising power of the medium solvent.

Perhaps the most remarkable reaction that phenyl-α-naphthyl carbinol undergoes is its reaction with acetyl chloride at room temperature in the absence of pyridine, with formation of the chloride. It is quite probable that in this reaction the acetate may have been formed prior to its attack by hydrogen chloride. However, the carbinol is unaffected by concentrated hydrochloric acid at room temperature, but at 80° the chloride is formed.

Phenyl-α-naphthylchloromethane shows none of the ionic reactions of p-methoxybenzhydrylchloride. It does not react with water at room temperature, but it undergoes hydrolysis at 90° with formation of the carbinol. It does not react with sodium p-toluene sulphinate in aqueous acetone to yield the sulphone. But, on the other hand, it reacts with absolute alcohol or alcoholic potash at 90° forming the ethyl ether.
It may, therefore, be concluded that esters of phenyl-α-naphthylcarbinol, like those of benzhydrol, show considerably less tendency to react by alkyl-oxygen fission than those of p-methoxybenzhydrol or of anisyl-α-naphthylcarbinol in which the presence of the methoxyl group appears to have a deciding influence on the course of reactions.

A summary of some of the reactions of phenyl-α-naphthylcarbinol and its esters is given in the diagram below:
In view of the marked influence of a methoxyl group in the para position of the benzhydryl molecule in modifying the reactivity of this secondary alcohol and its esters, it was considered of interest to attempt to ascertain in what respects this degree of influence might be altered by replacing the methoxyl group by thio-methyl group. Accordingly, thioanisylphenyl carbinol has been prepared and its reactions, and those of its esters, examined and compared with those of the corresponding methoxyl compounds.

In the preparation of this carbinol, the starting material was thiophenol, which was methylated in two ways: i) by means of dimethylsulphate and caustic soda solution, and ii) by means of methyl iodide in absolute ethyl alcohol containing the requisite amount of sodium. The former method is not only more rapid and economical, but also gives a slightly higher yield. The thioanisole, thus obtained, underwent the Friedel and Crafts' reaction smoothly yielding thioanisylphenyl ketone, the reduction of which to the carbinol was effected by heating under reflux for few hours with sodium amalgam or zinc dust and caustic soda in alcohol. This reduction is analogous to that of ketones containing electron-releasing groups, whereas the reduction of benzophenones can be carried out at ordinary temperature. An identical carbinol was obtained by the Grignard reaction, from benzaldehyde and p-bromothioanisole (prepared by brominating thioanisole).

The resolution of the hydrogen phthalic ester was effected by
fractional crystallisation of its quinine salt from alcohol; and the fully active carbinol was obtained when the optically active hydrogen phthalic ester was hydrolysed by sodium ethoxide in absolute alcohol; on the other hand; when caustic soda was used in high or low concentrations the carbinol obtained was extensively racemised.

Not only in this respect is the hydrolysis of this ester of this carbinol parallel with that of \( \beta \)-methoxybenzhydrol, but the mode of formation of its neutral phthalic ester is also analogous. Thus, the \((-\))-hydrogen phthalic ester reacts with \( 0.3 \text{ M} \) caustic soda to form the neutral ester, which on hydrolysis by sodium ethoxide and absolute alcohol yields a half-fully active carbinol:

\[
\begin{align*}
\text{(-)R}_1 \text{OH} \quad -8.6^\circ & \quad \text{(-)R}_2 \text{OH} \quad -23.6^\circ \\
\text{Eton} \quad \text{EtOEt} & \quad \text{EtOEt}
\end{align*}
\]

It is, therefore, clear that alkaline hydrolysis of esters of this carbinol in absolute alcohol proceeds by the bimolecular mechanism with fission of the acyl-oxygen bond, whereas hydrolysis by aqueous alkali proceeds by the unimolecular mechanism with rupture of the alkyl-oxygen bond.
Our attention was next drawn to acid hydrolysis of esters of this carbinol, but first let us consider the important general mechanisms postulated for acid hydrolysis.

That acid hydrolysis is catalysed by hydrogen ions, and that the reaction-rate is of the second order, was shown by many investigators. The Lowry mechanism (55) postulates the addition of a proton to the "etheral" oxygen atom of the ester, and the compound produced reacts with a water molecule forming an intermediate compound which finally breaks down into acid and alcohol:

\[
\begin{align*}
\text{O} & \quad \text{R-C-OR}^+ + H^+ \rightarrow \text{R-C-O-R}^+ \quad \text{HCH} \quad \text{R-C-OR}^+ + H^+ \\
\text{H} & \quad \text{H} \\
\text{O} & \quad \text{H} \\
\text{R-C-OR}^+ & \rightarrow \text{R-COCH} + \text{R'-CH} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]

But as a result of their investigations on the acid hydrolysis of crotyl and methylallyl acetate, Ingold and Ingold (7) postulated the following mechanism:

\[
\begin{align*}
\text{O} & \quad \text{R-C-OR}^+ + H^+ \rightarrow \text{R-C-O-R}^+ \quad \rightarrow \text{R-C=O} + \text{HOR}^+ (\text{slow}) \\
\text{H} & \quad \text{H} \\
\text{R-C=O} + \text{HCH} & \rightarrow \text{R-COCH} + H^+ (\text{fast}) \\
\end{align*}
\]

This mechanism is essentially the same as that postulated by Datta, Day and Ingold (14) and it appears to be in harmony with the known facts.
The above two mechanisms involve a second order kinetics with fission of the acyl-oxygen bond. Therefore, if \( R' \) is asymmetric at the point of attachment, hydrolysis would result in retention of optical activity.

In the case of esters of optically active carbinols of substituted benzydrols, containing strong electron-releasing groups, we considered it feasible that acid hydrolysis would lead to racemic products. With this aim in view, we hydrolysed the hydrogen phthalic ester of \((-)\)-thianisyl-phenylcarbinol with dilute sulphuric acid and aqueous acetone; the carbinol produced was optically inactive. It is obvious that the rupture of the alkyl-oxygen bond is involved, and that the reaction could not have proceeded by either of the two mechanisms described above. Taking into account the fact that the esters of this carbinol ionise in various solvents, we suggest the following unimolecular mechanism, involving alkyl-oxygen fission, for this type of acid hydrolysis:

\[
\begin{align*}
0 & \xrightarrow{\text{fast}} R-C-\text{O}^- + H^+ \\
R-C-\text{O}^- + H & \xrightarrow{\text{fast}} R-COOH \\
R' + H-\text{OH} & \xrightarrow{\text{fast}} R'\text{OH} + H^+
\end{align*}
\]

That isomerisation of the hydrogen phthalic ester precedes hydrolysis, is shown by the fact that when the reaction is stopped before completion, the recovered ester is observed to have undergone extensive racemisation.

Under similar conditions, hydrolysis of the \((-)\)-neutral phthalic ester
yields the optically inactive carbinol.

Another interesting feature of the hydrogen phthalic ester of this carbinol is the readiness with which it forms the sulphones with aromatic sulphinic acids. Thus, the \((-\))-hydrogen phthalic ester reacts fairly rapidly with sodium \(p\)-toluenesulphinate in alkaline solution at room temperature yielding the corresponding optically inactive sulphone, the formation of which must have proceeded by the following stages: firstly, the ionisation of the phthalic ester yields a reactive \(+\) cation, which reacts more or less rapidly with the sulphinic anion to form the sulphinate, and finally, the latter undergoes instantaneous rearrangement into the sulphone:

\[
\begin{align*}
&\text{COOR}\rightarrow \text{COO}^+ \rightarrow \text{R(chloride)} + \text{CH}_3\text{CH}_2\text{SO}_3\text{Na} \\
&\text{CH}_3\text{CH}_2\text{SO}_3\text{Na} \rightarrow \text{CH}_3\text{CH}_2\text{SO}_3\text{OR}
\end{align*}
\]

An identical sulphone is also obtained much more rapidly, presumably in the same manner, when the carbinyl chloride reacts with sodium \(p\)-toluenesulphinate in aqueous acetone.

Perhaps the next interesting reaction, in which the rupture of the alkyl-oxygen bond takes place readily, is the action of acetyl chloride on the optically active hydrogen phthalic ester. This reaction may proceed by either of two ways:
Clearly, mechanism (a) involves acyl-oxygen fission with formation of the optically active acetate, whereas, mechanism (b) involves alkyl-oxygen fission with formation of the optically inactive chloride. Experiment shows that the hydrogen phthalic ester of the (+)-carbinol reacts readily with acetyl chloride yielding the racemic chloride.

Yet, on the other hand, the possibility that under mechanism (b) the acetate may have been formed as an intermediate product prior to its immediate attack by HCl to form the chloride is not excluded.

Aslo, the optically active carbinol reacts readily with acetyl chloride yielding the racemic chloride, but, on the other hand, in presence of pyridine, it forms the optically active acetate. The function of the pyridine in the latter reaction appears to promote the removal of the proton from the hydroxyl group rather than to cause ionic fission of the acid chloride (55).

Another notable example of the tendency of this carbinol to undergo alkyl-oxygen fission is the action of concentrated hydrochloric acid on the optically active carbinol, its esters and dl-ethyl ether to form the racemic chloride.
The hydrogen phthalic ester or the neutral phthalic ester of the (-)-carbinol react with cold concentrated sulphuric acid forming intensely coloured halochromic salts which rapidly hydrolyse in water yielding the racemic carbinol. A similar halochromic salt is formed by the action of cold concentrated sulphuric acid on the chloride with copious evolution of HCl gas.

Racemisation of the esters of the optically active carbinol in various solvents, is a clear evidence that alkyl-oxygen fission occurs. Thus, the rotatory power of the (-)-hydrogen phthalic ester in glacial acetic acid falls from -17° to 0° in 90 minutes at 100°C, and in 460 hours at room temperature with production of the dl-acetate. It also ionises in absolute alcohol at 90° with formation of the dl-ethyl ether. When the reactions are stopped before completion, the recovered hydrogen phthalic ester is observed to have undergone extensive racemisation. The optically active carbinol also racemises in glacial acetic acid, though at a much less rapid rate than that of the hydrogen phthalic ester.

Interesting ionic reactions are exhibited by the carbinyl chloride.
Thus, with potassium hydrogen phthalate or sodium benzoate in aqueous acetone it forms the hydrogen phthalic ester and the benzoate respectively. Its solution in aqueous acetone rapidly develops an acid reaction with formation of the carbinol. Hydrolysis of the chloride with caustic soda in aqueous acetone yields the carbinol, whereas, with alcoholic potash it forms the ethyl ether.

It can, therefore, be concluded that the influence of the thio-ethyl group in modifying the reactivity of the benzhydryl molecule is remarkably similar to that of the methoxy group. Therefore, the thio-ethyl group, like the methoxy group, has a powerful tautomer effect:

\[ \text{MeS} \rightleftharpoons \text{MeCH} \]

and hence the great tendency for ionisation and reaction-rates.
REASONS OF THIOANISYLPHENYL CARBINOL
p-METHYLSULPHONYLBENZHYDROL

Having established the close similarity between the thio-methyl and methoxyl groups in modifying the reactivity of the benzhydryl molecule, attention was next directed to the study of the influence of the methylsulphonyl group on the benzhydryl molecule.

In the case of the thioanisyl group, the electromeric displacement tends to increase the reaction-rates which proceed mainly by the alkyl-oxygen fission mechanism; but in the case of the p-methylsulphonylphenyl group, it was expected that the electromeric displacement would take place in the opposite direction, thus:

\[
\text{Me}_2\text{S}+\overset{\text{C}}{\text{O}} \quad \text{Me}_2\text{S}+\overset{\text{C}}{\text{O}}
\]

resulting in slower reaction-rates which would proceed mainly by the acyl-oxygen fission mechanism.

The first indication was provided by the non-reactivity of p-methylsulphonylbromobenzene,

\[
\text{Me}_2\text{S}+\overset{\text{Br}}{\text{C}}
\]

towards magnesium; no Grignard compound could be obtained. Also, p-methylsulphonylbenzophenone undergoes reduction much more readily than does thioanisylphenyl ketone; and when the reduction is carried out in an alkaline medium, unsubstituted benzhydrol and not the expected
carbinol is obtained. This indicates that the methylsulphonyl-
benzene bond, MeSO₂⁺, is much weaker than that of thio-
methyl - benzene bond, MeS⁻, and that its rupture is
promoted by the alkaline medium. On the other hand, reduction of
p-methylsulphonylbenzophenone, by means of zinc and acetic acid or
aluminium isopropoxide, takes place smoothly, yielding p-methylsulphonyl-
benzhydrol identical with that obtained by oxidation of thianisylphenyl
carbinol with hydrogen peroxide and acetic acid.

The hydrogen phthalic ester of this carbinol was obtained in
the usual manner. Its solution in 0.3 N caustic soda, after standing
at room temperature for several weeks, remained clear, showing no
evidence of hydrolysis nor of neutral water formation. Its alkaline
solution showed no reaction with sodium p-toluenesulphinate.

Hydrolysis of the (+)-p-methylsulphonylbenzhydrol hydrogen
phthalate with dilute alkali or with absolute alcohol and sodium
ethoxide, yields the optically active carbinol without any evidence of
racemisation. The results are recorded on the next page.
All determinations of rotatory powers in CHCl₂ solutions.

\[ \text{CH}_3\text{COO}\text{C}_\text{H}_3 \]
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EXPERIMENTAL
PHENYL-α-NAPHTHYL CARBINOL

Preparation Of Phenyl-α-Naphthyl Carbinol.

A) By The Grignard Reaction. α-Naphthylbromide (155 g or 0.75 mol.) was added slowly to a mixture of magnesium (18.8 g), iodine (0.5 g) and anhydrous ether (100 c.c.) placed in a three-necked flask provided with a condenser and a mechanical stirrer, and heated on a water-bath (55-60°C). After the complete addition (40 mins.) of α-naphthylbromide the mixture was stirred (2 hours) at room temperature. Benzaldehyde (73 g or 0.7 mol.) in ether (50 c.c.) was added slowly (2 hours) with stirring to the mixture cooled in ice. The cooled mixture was decomposed with a concentrated solution of ammonium chloride, and the liberated carbinol extracted with a further quantity of ether (300 c.c.). After washing the ethereal extract with dilute caustic soda, then with water, and drying over calcium chloride, phenyl-α-naphthyl carbinol crystallised from ether-light petroleum in rosettes of short needles, M.P. 84-5°C. It was recrystallised from carbon disulphide and formed colourless needles, M.P. 85°C. The carbinol distilled at 223°C/13mm. to a colourless viscous oil which on standing set to a white crystalline solid, M.P. 86°C.

Yield of the carbinol, 85 g : 53-55 % calculated on the benzaldehyde. (Acree: Ber. 1904, 37, 2757, gives the M.P. of phenyl-α-naphthyl carbinol as 85-6°C).
E. By The Reduction Of Phenyl-α-Naphthyl Ketone.

Preparation Of Phenyl-α-Naphthyl Ketone. Anhydrous aluminium chloride (100 g) was added slowly (20 mins.) to benzoyl chloride (57 c.c.) with shaking and cooling in an ice-bath until solution was complete. After adding carbon disulphide (150 c.c.), naphthalene (64 g) was added slowly (30 mins.) with continuous shaking and cooling. The mixture was left to react at room temperature (1 hour), and then heated under reflux (15 mins.). After cooling in a freezing mixture, the crystalline product was filtered off, washed with carbon disulphide (30 c.c.), and decomposed with ice-cold dilute hydrochloric acid. The dark brown product was extracted with ether, the solution washed with dilute caustic soda, heated under reflux with animal charcoal, and dried over calcium chloride. Phenyl-α-naphthyl ketone separated from ether-light petroleum in needles, M.P. 74.5°C; recrystallised from carbon disulphide it formed needles M.P. 76°C. Yield: 84 g, 70.3%. (Mers ; Ber. 1873, 6, 541, gives the M.P. of phenyl-α-naphthyl ketone as 75.5°C).

Reduction Of Phenyl-α-Naphthyl Ketone.

1) With Sodium Amalgam And Alcohol. Sodium amalgam (8 g of sodium in 50 g of mercury) was gradually added to a solution of phenyl-α-naphthyl ketone (12 g) in ethanol (100 c.c. of 96%) and the ensuing vigorous reaction was moderated by cooling. Next day, the decanted alcoholic solution was diluted with ice-cold water, and the precipitated material dried and crystallised from carbon disulphide, needles, M.P. 85.5°C (yield: 10 g). After an additional recrystallisation from the same solvent, the product had M.P. 85°C alone or when mixed with phenyl-α-naphthyl carbinol prepared
by the Grignard reaction.

2) With Zinc Dust, Caustic Soda, and Alcohol. Zinc dust (20 g) and sodium hydroxide (20 g) were added to a solution of phenyl-α-naphthyl ketone (11 g) in ethanol (75 c.c. of 96%), and the mixture heated under reflux for 3 hours and then filtered hot. The cooled filtrate was diluted with cold water, when the precipitated white semi-solid product solidified completely on standing. Yield: 10.7 g, M.P. 82-3°C. Crystallisation from carbon disulphide yielded needles of phenyl-α-naphthyl carbinol, M.P. 86°C. Yield of the pure carbinol: 10 g, 90%.

Phenyl-α-Naphthyl Carbinyl Hydrogen Phthalate.
The carbinol (23.43 g) was dissolved in a hot solution of phthalic anhydride (14.8 g) in pyridine (15 c.c.), and the homogeneous solution after heating (16 hours) on the water-bath (55-60°C) was mixed with an equal volume of acetone and decomposed with ice-cold dilute hydrochloric acid. The oily product turned on standing into a white solid, M.P. 153-4°C, which separated from methanol in prismatic needles, M.P. 158-158.5°C. Yield of phenyl-α-naphthyl carbinyl hydrogen phthalate: 35.5 g; 96%.

On titration with 0.0375 N caustic soda, the hydrogen phthalic ester (0.5 g) neutralised 13.36 c.c. (calc. 13.40 c.c.). Found, M.W. 384; C_{25}H_{18}O_{4} requires M.W. 382.4.

Preparation of Phenyl-α-Naphthyl Carbinyl Hydrogen Succinate.
The carbinol (7.03 g) was added to a solution of succinic anhydride (3 g) in pyridine (5 c.c.), and after heating (4 hours) the mixture on the steam-bath, it was mixed with an equal volume of acetone and decomposed with ice-cold dilute hydrochloric acid. The white solid product melted
at 116-8°C, and after crystallisation from methanol, was obtained in short needles, M.P. 122-3°C. Yield of phenyl-α-naphthyl carbaryl hydrogen succinate, 9.7 g: 97%. On titration with 0.0975 N caustic soda, the hydrogen succinic ester (0.531 g) neutralised 15.84 c.c. (calc. 16.00 c.c.)

Found M.W. 338; C_{21}H_{18}O_{4} requires M.W. 334.

Reactions Of Phenyl-α-Naphthyl Carbaryl Hydrogen Phthalate.

1) With Sodium Hydroxide.

a) A solution of the hydrogen phthalic ester (1 g) in an equivalent amount of caustic soda (9 c.c. of 0.3 N) was left to stand at room temperature in a closed vessel. After 2 months the carbinol began to separate as a white crystalline solid (0.54 g), M.P. 85-85.5°C, alone or mixed with an authentic specimen of the carbinol.

b) A solution of the hydrogen phthalic ester (1.0 g) in N/20 caustic soda (54 c.c.) after standing at room temperature (1 month), deposited the carbinol (0.55 g) in a finely divided crystalline state, M.P. 85-85.5°C.

c) A solution of the hydrogen phthalic ester (1.0 g) in 0.3 N caustic soda (9 c.c.), on heating at 80-85°C, became cloudy after 5 minutes. After heating for a further 25 minutes deposited an oil. This solidified on cooling and had M.P. 84-5°C. The carbinol crystallised from methanol in needles (0.5 g), M.P. 85.5°C.

d) A solution of the hydrogen phthalic ester (2.0 g) in 0.3 N caustic soda (180 c.c. - 10 equivalents), after heating at 80°C for 30 minutes yielded an oily product which solidified on cooling; and after crystallisation from methanol, the carbinol was obtained in needles (1.1 g), M.P. 85.5°C.
Under similar conditions a solution of the hydrogen succinic ester in N/1 or in 0.3 N caustic soda, on warming or standing at room temperature for few days, deposited the carbinol quantitatively. No neutral ester was formed.

2) By Heating In Chloroform Solution.
A solution of the hydrogen phthalic ester (2.0 g) in dry chloroform (20 c.c) was heated under reflux for 30 hours. A negligible amount of phthalic acid (M.P. 200°C) was deposited. The hydrogen phthalic ester (1.95 g) was recovered unchanged.

3) With Sodium p-Toluene Sulphinate.

a) A solution of the hydrogen phthalic ester (4.0 g) and sodium p-toluene sulphinic (2.24 g) in formic acid (50 c.c. of 98%) was heated on the steam-bath for 8 hours and then diluted with water; a yellowish brown solid was deposited. This after washing with dilute caustic soda, water, and then drying, was taken up in alcohol and heated (30 mins.) under reflux with animal charcoal. The alcoholic solution on concentrating, deposited almost colourless crystals of p-tolyl-phenyl-<naphthyl carbinyl sulphone (3.3 g; 82%), M.P. 120-1°C; recrystallised from the same solvent in colourless plates, M.P. 122°C. Found, S 8.3

C_{24}H_{20}O_{2}S requires S 8.5%.

b) A solution of the hydrogen phthalic ester (2.0 g) in 0.3 N caustic soda (18 c.c.) was filtered into a solution of sodium p-toluene sulphinate (1.12 g in 5 c.c. of water). Whilst standing in a closed vessel at room temperature for 4 months, the carbinol (1.0 g) was slowly deposited,
M.P. 85°C; it crystallised from ethanol in needles, M.P. 85.5-86°C, alone or mixed with an authentic specimen.

In a similar experiment, the reaction mixture after heating at 80°C for 15 minutes, deposited the carbinol.

4) With Ethyl Alcohol.

a) With Absolute Ethyl Alcohol. A solution of the hydrogen phthalic ester (5.0 g) in absolute ethyl alcohol (75 c.c.) after heating under reflux (18 hours) and concentrating to 30 c.c., was diluted with an equal volume of ether, washed twice with water and extracted with dilute ammonia. Decomposition of the alkaline extract with ice-cold dilute hydrochloric acid yielded unchanged hydrogen phthalic ester (2.2 g; M.P. 158°C). The ethereal extract, after drying over potassium carbonate and removal of solvent, yielded on distillation (B.P. 202-4°C/14 mm.) phenyl-α-naphthyl carbinal ethyl ether as a colourless heavy oil which solidified on cooling, M.P. 45-6°C. Yield, 1.6 g: 46%. It crystallised from ether-light petroleum in colourless needles, M.P. 47°C.

Found: C 87.2, H 7.1, C_{19}H_{16}O requires C 87, H 6.87%.

b) With 70% Ethyl Alcohol. A solution of the hydrogen phthalic ester (5 g) in 70% ethyl alcohol (100 c.c.) after heating under reflux (18 hours), was mixed with an equal volume of ether, washed with water and then extracted with dilute ammonia. The alkaline extract, after decomposition with ice-cold dilute hydrochloric acid, yielded unchanged hydrogen phthalic ester (1.8 g). The oily product obtained from the ethereal extract distilled at 202°C/13 mm., yielding phenyl-α-naphthyl carbinal ethyl ether as a colourless oil which solidified on cooling,
M.P. 44-5°C, Yield, 2.0 g: 58%. It crystallised from ether-light petroleum in clusters of short needles, M.P. 47°C.

Reactions Of Phenyl-K-Naphthyl Carbinol.

1) With Acetic Anhydride In Pyridine. A solution of the carbinol (2 g) in pyridine (2 c.c.) and acetic anhydride (1 c.c.) was heated on the steam-bath (4 hours). It was then mixed with an equal volume of acetone and decomposed with ice-cold dilute hydrochloric acid. The oily product solidified on standing, yielding phenyl-K-naphthylcarbinyl acetate, which crystallised from ether-light petroleum in prismatic needles, M.P. 80-80.5°C. Yield, 2.3 g: 98%. Found: C 82.5, H 5.9%

C₁₉H₁₆O₂ requires C 81.9, H 6.0%

A solution of phenyl-K-naphthylcarbinyl acetate (1.0 g) in alcoholic potash (60 c.c. of 0.9483 N) was heated under reflux. The excess potash neutralised 22.9 c.c. of 0.0269 N hydrochloric acid (calculated 22.78 c.c. of the acid). Found: M.W. 279, C₁₉H₁₆O₂ requires M.W. 267. The neutralised alcoholic solution on concentrating and adding water, deposited a white solid which on crystallisation from it ether-light petroleum, yielded the carbinol (0.8 g - calc. 0.84 g) in needles, M.P. 85.5°C, alone or mixed with an authentic specimen.

2) With Acetyl Chloride And Pyridine. Acetyl chloride (2 c.c.) was added dropwise to a cooled solution of the carbinol (2 g) in pyridine (2 c.c.). After warming the mixture gently for few minutes, it was dissolved in acetone (20 c.c.) and solution decomposed with ice-cold dilute hydrochloric acid. The oily deposit on standing changed into a
white solid which on crystallization from ether-light petroleum, yielded phenyl-α-naphthylcarbiny1 acetate in almost colourless needles, M.P. 80-80.5°C, alone or mixed with an authentic specimen. Yield: 2.2 g: 93%.

3) With Thionyl Chloride. Thionyl chloride (7 c.c.) was added slowly to a cooled solution of the carbinal (9 g) in benzene (50 c.c.). The mixture was heated under reflux (1 hour) until no more hydrogen chloride and sulphur dioxide were given off; the brown coloured solution produced was heated under reflux (30 mins.) with animal charcoal and then filtered. After removing the solvent from the filtrate, phenyl-α-naphthyl chloromethane crystallised from ligroin in clusters of short needles, M.P. 57-6°C. Recrystallised from ether-light petroleum in needles M.P. 59°C.

Yield: 7 g: 78%. Further recrystallisations of the chloride did not raise its M.P. (Norris & Blake: J.A.C.S. - 1928, 50, 1612 - give the M.P. of phenyl-α-naphthyl chloromethane as 64-64.5°C).

A solution of the chloride (1.50 g) in alcoholic potash (75 c.c. of 0.09483 N) was heated under reflux (3 hours). Potassium chloride was slowly deposited as a white crystalline powder (0.4 g - calc. 0.44 g), and the alkaline filtrate neutralised 10.10 c.c. of 0.11737 N hydrochloric acid (calc. 10.06 c.c.). Found, M.W. 254, C17H13Cl requires M.W. 252.8. The neutralised solution, after concentrating to 30 c.c., was mixed with an equal volume of ether, washed with water and dried over potassium carbonate. After concentrating the ethereal solution and addition of light petroleum, phenyl-α-naphthylcarbiny1 ethyl ether (1.42 g was deposited in short crystalline needles, M.P. 44-5°C. Recrystallised from the same solvents in short needles, M.P. 47°C, alone or mixed.
with an authentic specimen of the ethyl ether.

In the analysis of the chloride, Found: Cl 13.5; $C_{17}H_{13}Cl$ requires 14.0%.

4. With Concentrated Hydrochloric Acid.

a) At Room Temperature. No reaction took place when the carbinol was triturated with cold concentrated hydrochloric acid, even when the mixture was left standing in a closed vessel at room temperature for several days.

b) At 80°C. A solution of the carbinol (12 g) in acetone (15 c.c.) was gradually added to hot concentrated hydrochloric acid (100 c.c.). After heating (30 mins.) the mixture at 80°C, the supernatant liquid was decanted off, and the oily product washed with concentrated hydrochloric acid (10 c.c.) and dried in vacuo over caustic potash. The semi-solid product was extracted with hot light petroleum, and after evaporating the solvent, phenyl-α-naphthyl chloromethane distilled at 220°C/17 mm. as a heavy colourless oil which solidified on standing into a white crystalline solid, M.P. 58°C. Yield, 9 g: 75%. It crystallised from ligroin or carbon disulphide in colourless prismatc needles, M.P. 59°C, alone or mixed with an authentic specimen.

5. With Acetyl Chloride. Acetyl chloride (2 c.c.) was added to the carbinol (2 g) at room temperature; the latter went almost immediately into solution which developed an orange colour. After drying in vacuo over caustic potash, phenyl-α-naphthyl chloromethane distilled at 228°C/16 mm. as a colourless viscous oil which solidified on cooling, M.P. 56-6°C. It crystallised from ligroin in clusters of short needles, M.P. 59°C.
alone or mixed with an authentic specimen of the chloride. Yield, 1.2 g.

6) Action Of Heat. The carbinol (3 g) was heated at 150-5°C for 35 hours, when it developed a red-brown colour. The viscous product was extracted with ether (60 c.c.), and heated under reflux (30 mins.) with animal charcoal. After concentrating the filtrate and adding benzene, diphenyl-α-naphthylcarbinyl ether was deposited, M.P. 164-5°C; it crystallised from acetone in white glistening needles, M.P. 172-3°C.

Yield, 0.3 g. Found, C 90.0, H 5.72, C₁₄H₂₈O requires C 90.1, H 5.77%.

The ether-benzene filtrate on standing deposited the carbinol (2 g), M.P. 58.5°C.

In a separate experiment the carbinol was heated at 155-160°C for 6 hours, it developed a yellow colour, but practically all the carbinol was recovered unchanged.

Reactions Of Phenyl-α-Naphthyl Chloromethane.

1) With Water.

a) At Room Temperature. An ethereal solution of the chloride was mixed with water; the aqueous layer after standing at room temperature for several days, showed no acid reaction.

b) At 90°C. The chloride (0.50 g) was heated with water (50 c.c.) on the steam-bath; after few minutes the water developed an acid reaction. The mixture was titrated with 0.09783 N caustic soda solution at intervals of one hour. The titration values are recorded in the following table:


Hydrolysis of the chloride in water was complete in 8 hours, and the acidic solution neutralised 19.5 c.c. of 0.09783 N caustic soda solution (calc. 19.7 c.c.). The solid product after drying crystallised from methanol, yielding the carbinol (0.44 g - calc. 0.46 g) in needles, M.P. 85.5°C.

2) With Sodium p-Toluenesulphonate. A solution of equimolecular proportions of the chloride and sodium p-toluenesulphonate in aqueous acetone was left to stand at room temperature in a closed vessel for several days. No sulphone was formed.

In a separate experiment the solution of the chloride and sodium p-toluenesulphonate in aqueous acetone was heated under reflux for 3½ hours; no sulphone was obtained.

In each case, sodium p-toluenesulphonate and the chloride were recovered unchanged. A small amount of the carbinol was obtained due to partial hydrolysis of the chloride.

3) With Absolute Ethyl Alcohol. A solution of the chloride (2 g) in absolute alcohol (30 c.c.) was heated under reflux for 3 hours. After evaporating the solvent, the oily product solidified on cooling and scratching, M.P. 40-5°C. It crystallised from light petroleum, yielding phenyl-α-naphthylethynylcarbinyl ethyl ether in colourless needles, M.P. 47°C, alone or mixed with an authentic specimen of the ethyl ether. Yield, 2.05 g.
Attempted Resolution Of Phenyl-α-Naphthyl Carbinyl Hydrogen Pthalate

And Succinate.

When brucine, cinchonidine, quinine, quinidine, and strychnine were used for preparing the alkaloidal salts, the stereoisomericid could not be fractionally crystallised from various solvents and their mixtures, due to the separation of the alkaloidal salts in the form of gums.
Preparation Of Thianisole.

1) By The Action Of Methyl Iodide On Sodium Thiophenate In Absolute Alcohol.

To a solution of sodium (4.2 g) in absolute alcohol (100 c.c.) was added thiophenol (20 g), and after cooling, methyl iodide (25.5 g) was added slowly with shaking. The resulting solution was heated under reflux (30 mins.), and then poured into water (150 c.c.). The oil which separated was extracted with ether (200 c.c.), washed with caustic soda, then with water and finally dried over calcium chloride. After evaporating the solvent, thianisole distilled at 82°C/18 mm.

Yield, 19.7 g; 88%.

2) By The Action Of Dimethylsulphate On Sodium Thiophenate.

Thiophenol (110 g) was dissolved in a hot solution of caustic soda (40 g in 200 c.c. of water) forming a clear and slightly yellow solution. Dimethylsulphate (130 g) was added during 30 minutes with shaking to the externally cooled solution. The mixture was heated under reflux (30 mins.) to complete the reaction, then caustic soda (1.3 g in 20 c.c. of water) was added, and heating under reflux was continued for another 30 minutes to decompose any unreacted dimethylsulphate. After cooling, the reaction mixture was shaken with ether (200 c.c.), the extract washed with water and finally dried over calcium chloride. Thianisole distilled at
The boiling points of thianisole at various pressures are recorded in the following table:

<table>
<thead>
<tr>
<th>B.P. in °C</th>
<th>Pressure In mm.</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>195</td>
<td>751</td>
<td>(1)</td>
</tr>
<tr>
<td>187-8</td>
<td>760</td>
<td>(2)</td>
</tr>
<tr>
<td>96</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>82</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>76</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>58-60</td>
<td>6</td>
<td>(2)</td>
</tr>
</tbody>
</table>

(1) Bourgeois and Abraham: Rec. des. Trav. Chim. 1911 200, 413
(2) Suter and Hansen: J.A.C.S. 1932 54, 4101.

Oxidation Of Thianisole To Methyl Phenyl Sulphone.

1) By Means Of Potassium Permanganate In Glacial Acetic Acid. To a solution of thianisole (2 g) in glacial acetic acid (20 c.c.) potassium permanganate (4.5 g) was slowly added (10 mins.), and the mixture heated on the steam-bath for 1 hour. The resulting solution, after diluting it with acetone (10 c.c.) and decolourising it with sulphur dioxide, was poured into a cold concentrated solution of ammonium chloride (200 c.c.). Concentrated ammonia was added slowly until the clear solution was distinctly alkaline; Methyl phenyl sulphone was slowly deposited as a white glistening solid, M.P. 87-8°C. It separated from hot water in
white glistening plates, M.P. 88°C. Yield, 1 g. It is insoluble in light petroleum, sparingly soluble in ether, very soluble in acetone and alcohol.

( Brugnatelli : J. Pr. Chem. - 1884, (2), 40, 511—gives the M.P. of methyl phenyl sulphone as 88°C ).

2 ) By Means of Hydrogen Peroxide In Glacial Acetic Acid. To a solution of thioanisole ( 2 g ) in glacial acetic acid ( 15 c.c. ) hydrogen peroxide ( 16 c.c. of '50 vols.' ) was added. The clear solution, after standing room temperature for 1 week, was poured into cold dilute caustic soda solution ( 150 c.c. of 6 % ) ; methyl phenyl sulphone was deposited in short shiny needles; M.P. 84-5°C ; it crystallised from acetone in large colourless rhombs, and from methanol in white shiny plates; M.P. 88°C. Yield, 1.85 g .

p-Bromo-Thioanisole.

To a warm solution of thioanisole ( 12.4 g ) in carbon disulphide ( 20 c.c. ) a solution of bromine ( 16 g ) in carbon disulphide was gradually added ( 30 mins. ). The mixture was then heated ( 1 hour ) under reflux until no more hydrogen bromide was evolved. After evaporating the carbon disulphide the oily product was washed with dilute caustic soda, water, and extracted with ether and dried over calcium chloride. After evaporating the solvent, the oily product solidified on cooling yielding p-bromo-thioanisole as white shiny crystals, M.P. 36.5-37°C; it crystallised from methanol in white shiny plates, M.P. 37.5°C. Yield, 18.3 g .

p-Methylethanesulphonyl-Bromobenzene.

A solution of p-bromo-thianisole (2 g) in glacial acetic acid (25 c.c.) and hydrogen peroxide (10 c.c. of '90 vols.') after standing at room temperature for 1 week, was poured into an equivalent solution of cold dilute caustic soda, p-methylethanesulphonyl-bromobenzene (2.1 g) was deposited as white shiny crystals, M.P. 103-4°C; it crystallised from methanol in white shiny plates, M.P. 104.5°C. (van Hove: loc. cit. gives the M.P. of p-methylethanesulphonyl-bromobenzene as 102-102.5°C.)

It did not react with magnesium in presence of ether to form the Grignard compound.

Thianisylphenyl Ketone.

Thianisole (93 g), benzyl chloride (87 c.c.) and carbon disulphide (300 c.c.) were introduced into a 1-litre three-necked flask provided with a condenser and a mechanical stirrer. Powdered anhydrous aluminium chloride (112 g) was gradually added (45 mins.) with stirring. The vigorous reaction produced a reddish-brown solid with copious evolution of hydrogen chloride. During the addition of the aluminium chloride, the temperature was kept below 20°C by external cooling. After the complete addition of the aluminium chloride, stirring was continued for 1 hour at room temperature, and then for another hour at 40-5°C. The mixture was left to stand overnight at room temperature. The brown solid aluminium complex (sometimes bluish-purple, due mainly to aluminium chloride of inferior quality and to different temperature conditions) was filtered off, washed with carbon disulphide (30 c.c.), drained and then
decomposed with ice-cold dilute hydrochloric acid (60 c.c. of conc. acid in 100 c.c. of water). The acidified mixture was heated on the steam-bath (30 mins.) to complete the decomposition of the aluminium complex and to get rid of traces of carbon disulphide. The hot, oily product was poured into crushed ice, it rapidly set into a crystalline solid which after filtering, washing with water, dilute caustic soda, then with water, and drying, yielded 153 g (90%) of thioanisylphenyl ketone, M.P. 75-6°C. It separated from ether-light petroleum in almost colourless rhombic crystals, M.P. 76°C (sharp), and from methanol in prismic needles, M.P. 76°C. It distilled unchanged at 221°C/11 mm. It is moderately soluble in mixtures of cold ether and alcohol, very soluble in acetone, sparingly soluble in hot water. Found: C 73.3, H 5.4, S 13.4

C₁₄H₁₂O₃S requires C 73.6, H 5.3, S 14.0%.

Preparation of p-Methylsulphonylbenzophenone.

By The Oxidation Of Thioanisylphenyl Ketone

1) By Means Of Hydrogen Peroxide In Glacial Acetic Acid. To a solution of the ketone (1 g) in glacial acetic acid (25 c.c.) hydrogen peroxide (10 c.c. of '20-vols.') was added. The homogeneous mixture, after standing in a stoppered vessel for 1 week, was poured into ice-cold water (400 c.c.). p-Methylsulphonylbenzophenone was deposited as white shiny crystals, M.P. 135-6°C; it crystallised from alcohol in glistening plates, M.P. 141°C. Yield, 1 g. It is sparingly soluble in hot water.

Found: S 11.8. C₁₄H₁₂O₃S requires S 12.3%.
11) By Means Of Potassium Permanganate In Glacial Acetic Acid. To a solution of the ketone (2 g) in glacial acetic acid (25 c.c.), potassium permanganate (2.13 g) was added slowly with external cooling. After heating the mixture on the steam-bath (40 mins.) and decolourising the excess of potassium permanganate with sulphur dioxide, it was poured into cold water (400 c.c.). p-methylsulphonylbenzophenone separated as a white solid, M.P. 136-7°C. It crystallised from alcohol in small white glistening plates, M.P. 141°C. Yield, 2.1 g; 92%.

E) By The Oxidation Of Thianisylphenyl Carbinal.

A solution of potassium permanganate (2.5 g) in water (10 c.c.) was slowly added to a solution of the carbinal (1.0 g) in glacial acetic acid (25 c.c.). The homogenous mixture, after standing at overnight at room temperature and decolourising it with sulphur dioxide, was poured into cold water; p-Methylsulphonylbenzophenone separated as a white solid in a finely divided state; it crystallised from alcohol in shiny plates, M.P. 141°C, alone or mixed with a specimen prepared by the ether methods. Yield, 0.7 g.

Reduction Of Thianisylphenyl Ketone To The Carbinal.

1) By Means Of Sodium Amalgam And Alcohol. To a solution of thianisylphenyl ketone (57 g) in alcohol (250 c.c. of 96 %), sodium amalgam (30 g of sodium in 500 g mercury) was gradually added with external cooling. After standing overnight at room temperature, the mixture was heated under reflux (6-7 hours) and then the clear solution was decanted into ice-cold water (2 litres). Thianisylphenyl carbinal (54 g)
separated as a white solid, M.P. 92-3°C. It is moderately soluble in cold ether and carbon disulphide. It crystallised from ether-light petroleum ether and light carbon disulphide in white silky needles, M.P. 94°C (sharp). Yield, 96-7%.

2) By Means Of Zinc Dust, Caustic Soda And Alcohol. To a solution of thianisylphenyl ketone (46 g) in alcohol (300 c.c. of 96%) caustic soda (46 g) and zinc dust (46 g) were added. The mixture, after heating under reflux (5-6 hours), was filtered hot and the residue washed with hot alcohol (30 c.c. of 96%). The combined filtrate and washings were poured into ice-cold water (2 litres); thianisylphenyl carbinol separated as a white solid (46 g), M.P. 92-3°C. It crystallised from ether-light petroleum ether in white silky needles, M.P. 94°C. Yield, 96%.

Found: C 72.81, H 6.10, S 14.00, C₁₄H₁₄O₂S requires C 73.04, H 6.09, S 14.15%

Preparation Of Thianisylphenyl Carbinol By The Grignard Reaction.

p-Bromothianisole (2.1 g) in ether (10 c.c.) was added dropwise to magnesium (0.3 g) covered by dry ether and heated gently under reflux. The sluggish reaction was initiated by a crystal of iodine or a drop of methyl iodide. After addition of the bromide (1 hour), heating under reflux was continued for another hour. Benzaldehyde in (1 g) in ethereal solution was added slowly to the white Grignard product with external cooling and shaking. The Grignard complex was decomposed with cold dilute hydrochloric acid. After extraction with ether, drying over calcium chloride, evaporation of solution to a small bulk, and addition of light
petroleum, thianisylphenyl carbinol separated in needles, M.P. 94°C, alone or mixed with this a specimen of the carbinol prepared by the other method. Yield, 1 g; 44%.

A mixture of the carbinol and methyl iodide was kept in a closed vessel at room temperature for several days. In another experiment a solution of the carbinol in ether and methyl iodide was kept in a closed vessel at room temperature for several days. In both cases the carbinol was recovered unchanged. It was obvious that no sulphonium iodide derivative was formed.

The carbinol, after heating at 145°C for 1 hour, was recovered unchanged.

Thianisylphenylcarbinyl Hydrogen Phthalate.

To a solution of phthalic anhydride (37 g) in pyridine (40 c.c.) thianisylphenyl carbinol (57.5 g) was added, and the mixture was heated on the steam-bath until homogeneous (15 mins.). This solution was heated (3 hours) on the water-bath (50-60°C) and then left to stand overnight at room temperature. The oily product was dissolved in acetone (50 c.c.) and solution poured into ice-cold dilute hydrochloric acid (100 c.c. of conc. acid in 2 litres of water). The oily product was dissolved in acetone and again poured into ice-cold dilute hydrochloric acid in order to remove traces of pyridine. The oily product solidified (2-3 hours) into a white crystalline solid, M.P. 118-120°C. It crystallised from benzene-light petroleum in hemispherical clusters of white needles, M.P. 123-4°C, and from carbon disulphide in short silky needles, M.P. 123-4°C. Yield of the hydrogen phthalic ester, 85 g; 90%.
On rapid titration with 0.03851 N caustic soda, the hydrogen phthalic ester (0.534 g) neutralized 14.2 c.c. (calc. 14.3 c.c.). Found M.W. 382; C\textsubscript{22}H\textsubscript{18}O\textsubscript{4} requires M.W. 378.

When a solution of the hydrogen phthalic ester (0.50 g) in alcoholic potash (0.08696 N) was heated under reflux (30 mins.), the ester neutralised 30.28 c.c. of the alcoholic potash (calc. 30.23 c.c.). Found M.W. 378, C\textsubscript{22}H\textsubscript{18}O\textsubscript{4} requires M.W. 378. From the neutralised solution of the hydrolysed ester, the recovered carbinol (0.30 g - calc. 0.304 g) melted at 94°C.

(−)-Thioanisylphenylcarbinyl Hydrogen Phthalate.

Quinine (95 g) was added to a warm solution of the dl-hydrogen phthalic ester (95 g) in alcohol (200 c.c. of 96%), and the clear solution after standing overnight at room temperature, deposited the quinine salt of the laevorotatory hydrogen phthalate, which after three recrystallisations from the same solvent, yielded quinine (−)-thioanisylphenylcarbinyl hydrogen phthalate (40 g) as white shiny crystals, M.P. 116-7°C. This salt was dissolved in twice its weight of acetone, and the solution decomposed with cold dilute hydrochloric acid; it deposited (−)-thioanisylphenylcarbinyl hydrogen phthalate (19.5 g), M.P. 95-6°C; it separated from carbon disulphide in short fibrous needles, M.P. 96-7°C. Rotatory powers are recorded in Table I.
<table>
<thead>
<tr>
<th>Solvent</th>
<th>Carbon Disulfide</th>
<th>Benzene</th>
<th>Toluene</th>
<th>Acetone</th>
<th>Chloroform</th>
<th>Ethanol</th>
<th>Methyl Acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\eta$ (c, d)</td>
<td>-3.41 (0.0)</td>
<td>-2.98</td>
<td>-2.35</td>
<td>-1.82</td>
<td>-1.15</td>
<td>-0.16</td>
<td>-0.13</td>
</tr>
<tr>
<td>$\theta$ (c, d)</td>
<td>-26.6 (0.0)</td>
<td>-21.3</td>
<td>-10.9</td>
<td>-19.2</td>
<td>-15.0</td>
<td>-14.5</td>
<td>-13.0</td>
</tr>
<tr>
<td>$\phi$ (c, d)</td>
<td>-53.7 (0.0)</td>
<td>-32.0</td>
<td>-10.4</td>
<td>-13.8</td>
<td>-18.0</td>
<td>-16.0</td>
<td>-17.5</td>
</tr>
</tbody>
</table>
### TABLE II

Reacnonistion Of (−)-Thienyisylphenylcarbinyi Hydron Fathalate In
Glacial Acetic Acid At Room Tempetature.

<table>
<thead>
<tr>
<th>Time In Hours</th>
<th>0</th>
<th>3</th>
<th>25</th>
<th>51</th>
<th>71</th>
<th>103</th>
<th>187</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\alpha]_D^{20\circ})</td>
<td>-18.6°</td>
<td>-17.7°</td>
<td>-14.4°</td>
<td>-11.2°</td>
<td>-10.2°</td>
<td>-9.0°</td>
<td>-8.4°</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time In Hours</th>
<th>151</th>
<th>199</th>
<th>271</th>
<th>294</th>
<th>366</th>
<th>460</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\alpha]_D^{20\circ})</td>
<td>-7.7°</td>
<td>-6.3°</td>
<td>-3.9°</td>
<td>-3.4°</td>
<td>-2.0°</td>
<td>0°</td>
</tr>
</tbody>
</table>

(\(c, 5.012 \; 1, 2\)).

### TABLE III

Reacnstion Of (−)-Thienyisylphenylcarbinyi Hydron Fathalate In
Glacial Acetic Acid At 100°G.

<table>
<thead>
<tr>
<th>Time In Mins</th>
<th>0</th>
<th>45</th>
<th>60</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\alpha]_D^{20\circ})</td>
<td>-18.6°</td>
<td>-2.1°</td>
<td>-1.0°</td>
<td>0°</td>
</tr>
</tbody>
</table>

(\(c, 5.0231 \; 1, 2\)).
### TABLE IV

<table>
<thead>
<tr>
<th>Time In Hours</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[\alpha]_D^{20^\circ}$</td>
<td>-17.0$^\circ$</td>
<td>-11.2$^\circ$</td>
<td>-6.8$^\circ$</td>
<td>-5.9$^\circ$</td>
<td>-4.07$^\circ$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time In Hours</th>
<th>11</th>
<th>17.5</th>
<th>25</th>
<th>35</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[\alpha]_D^{20^\circ}$</td>
<td>-3.35$^\circ$</td>
<td>-2.35$^\circ$</td>
<td>-1.36$^\circ$</td>
<td>0$^\circ$</td>
</tr>
</tbody>
</table>

( $c$, 5.520 $1, 2$ ).

### TABLE V

<table>
<thead>
<tr>
<th>Days</th>
<th>0</th>
<th>3</th>
<th>10</th>
<th>19</th>
<th>46</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[\alpha]_D^{20^\circ}$</td>
<td>-17.0$^\circ$</td>
<td>-17.0$^\circ$</td>
<td>-16.56$^\circ$</td>
<td>-16.27$^\circ$</td>
<td>-14.61$^\circ$</td>
<td>-11.4$^\circ$</td>
</tr>
</tbody>
</table>

( $c$, 5.4491 $1, 2$ ).
(-)-Thianisylphenyl Carbinol.

(-)-Hydrogen phthalic ester (2 g, \([\alpha]_{D}^{15^\circ} = -30.4^\circ\) in carbon disulphide) was dissolved in a solution of sodium (0.5 g) in absolute alcohol (20 c.c.) and heated gently for a few minutes. On dilution with water, (-)-thianisylphenyl carbinol separated as a white solid, M.P. 5344°C; it crystallised from carbon disulphide in clusters of short needles, M.P. 55-7°C. Yield, 1.0 g. \([\alpha]_{D}^{20^\circ} = -13.5^\circ\) (c, 6.001 1, 1.5) in carbon disulphide.

Conversion Of (-)-Thianisylphenyl Carbinol Into Its (-)-Hydrogen Phthalic Ester.

The (-)-carbinol (0.575 g, \([\alpha]_{D}^{20^\circ} = -13.57^\circ\) in carbon disulphide) was added to a solution of phthalic anhydride (0.37 g) in pyridine (0.5 c.c.). The mixture, after heating on the water-bath (55-60°C) for 30 minutes and standing at room temperature overnight, was dissolved in an equal volume of alcohol and poured into ice-cold dilute hydrochloric acid. The oily deposit solidified rapidly. Yield of the hydrogen phthalic ester, 0.8 g, M.P. 90-1°C; it crystallised from carbon disulphide in short silky needles, M.P. 96-7°C. It had \([\alpha]_{D}^{19^\circ} = -29.0^\circ\) (c, 2.501 1, 2) in carbon disulphide.

The (-)-carbinol and its (-)-hydrogen phthalic ester racemised much more rapidly at 100°C than at room temperature. Rotatory powers at various intervals are recorded in tables II to V.
Preparation Of Thianisylphenylcarbinyl Acetate.

1) By The Action Of Acetic Anhydride On The Carbinol. A mixture of the carbinol (2.3 g), acetic anhydride (1.02 g) and pyridine (2 c.c) was warmed (3 min.) on the steam-bath until homogeneous. After standing at room temperature for 2 days, it was mixed with an equal volume of acetone and poured into cold dilute hydrochloric acid (10 c.c. of conc. hydrochloric acid in 300 c.c. of water). A slightly yellow oil was deposited, which after extraction with ether, drying over calcium chloride, and removal of solvent, gave thianisylphenylcarbinyl acetate, B.P. 221°C/15 mm. as a colourless oil. 

\[ \begin{align*}
\alpha^2_{D} & = 1.43^0 \\
n_2^D & = 1.5912
\end{align*} \]

\[
\text{Yield: 1.9 g. Found: C 70.26, H 6.22,}
\]

\[
\text{C}_{16} \text{H}_{16} \text{O}_3 \text{S requires C 70.58, H 5.88% .}
\]

The acetate (0.566 g) after heating (1 hour) under reflux with alcoholic potash, neutralised 23.81 c.c. of 0.08696 N alcoholic potash (calc. 23.81 c.c.). Found: M.W. 272, C.H.O.S requires M.W. 272.

The neutralised alcoholic solution yielded, after pouring it into cold water, the carbinol (0.45 g - calc. 0.48 g) M.P. 94°C, alone or mixed with an authentic specimen of the carbinol.

In a similar experiment, the thianisylphenylcarbinyl acetate (1.82 g), prepared as above, from a mixture of the carbinol (2.3 g, [\alpha]_D^{20^0} -3.6^0 in carbon disulphide), acetic anhydride (1.02 g) and pyridine (2 c.c.), had [\alpha]_D^{20^0} -29.4^0 (c, 3.756 l, 2) in carbon disulphide.

2) By The Action Of Acetyl Chloride On The Carbinol. To a cooled solution of the carbinol (2.3 g) in pyridine (1 c.c.) acetyl
chloride (0.8 g) was added dropwise. The vigorous reaction produced a yellowish-white solid, which after warming for few minutes on the steam-bath, was dissolved in acetone (20 c.c.) and then decomposed with ice-cold dilute hydrochloric acid. The yellow oil deposited, yielded after extraction with ether, drying over calcium chloride and removal of solvent, thianisylephenylcarbinyl acetate (1.8 g), B.P., 221°C/15 mm.

In a similar experiment, acetyl chloride (0.3 c.c.) was cautiously added to a cooled solution of the carbinol (0.8 g, [α]_D^20° = -8.6° in carbon disulphide) in pyridine. Thianisylephenylcarbinyl acetate was isolated as described above. Yield, ≈ 0.8 g. It had [α]_D^20° = 29.35° (c, 3.85 1, 2) in carbon disulphide.

3) By The Action Of Glacial Acetic Acid On The Carbinol. After heating a solution of the carbinol (2 g) in glacial acetic acid (20 c.c.) for 40 hours on the steam-bath, it was mixed with ether (50 c.c.), washed three times with water and dried over calcium chloride. After evaporating the solvent, thianisylephenylcarbinyl acetate (1.75 g) distilled at 221°C/15 mm. as a colourless oil.

n_D^20° 1.5912. The acetate (0.453 g), on hydrolysis with 0.08696 N alcoholic potash, neutralised 19.1 c.c. (calc. 19.5 c.c.). Found, M.W. 273, C_{16}H_{16}O_{2}S requires M.W. 272.

In a similar experiment a solution of the l-carbinol (1 g, [α]_D^20° = -8.6° in carbon disulphide) in glacial acetic acid (15 c.c.) yielded, after heating on the steam-bath for 35 hours, the dl-thianisylephenylcarbinyl acetate (0.9 g).
4. By the Action of Glacial Acetic Acid on the Neutral Phthalic Ester.

A solution of the neutral phthalic ester (2 g) in glacial acetic acid (15 c.c.) was heated on the steam-bath for 2 hours. Thianisylphenylcarbinyl acetate was isolated as described above. Yield, 1.72 g.

In a similar experiment, a solution of the (-)-neutral myd phthalic ester (2 g, $\left[\alpha\right]_D^{20} -23.6^\circ$ in carbon disulphide) in glacial acetic acid (15 c.c.), yielded the dl-thianisylphenylcarbinyl acetate (1.69 g).

Thianisylphenylcarbinyl Benzoate.

To a cooled solution of the carbinol (2.3 g) in pyridine (1 c.c.), benzoyl chloride (1.1 c.c.) was added slowly when a white crystalline solid immediately formed. The mixture, after heating on the steam-bath for few minutes to complete the reaction, was dissolved in acetone (20 c.c.) and decomposed with ice-cold dilute hydrochloric acid. The oily deposit solidified overnight. Thianisylphenylcarbinyl benzoate crystallised from ether-light petroleum in nodules of short white needles, M.P. 59°C. Yield, 3.3 g: 98%. Found: C 75.6, H 5.5

C_{21}H_{18}O_{8}S requires C 75.45, H 5.4%.

The benzoate (0.50 g) in alcoholic potash (25 c.c. of 0.08696 N) after heating under reflux for 1 hour, neutralised 17.10 c.c. of the alcoholic potash (calc. 17.13 c.c.). Found M.W. 334.8

C_{21}H_{18}O_{8}S requires M.W. 334. The neutralised alcoholic solution, after pouring into ice-cold water, yielded the carbinol (0.33 g - calc. 0.34 g), M.P. 94°C, alone or mixed with an authentic specimen.
Reactions Of Thioanisylphenylcarbinyl Hydrogen Phthalate.

1) With 0.3 N Caustic Soda Solution: Preparation Of Di-Thioanisylphenylcarbinyl Phthalate (The Neutral Phthalic Ester).

a) A solution of the hydrogen phthalic ester (5 g) in caustic soda (44.1 c.c. of 0.3 N) after standing at room temperature (40 mins.), became turbid with deposition of the neutral ester, the deposition of which as a glassy mass was complete in 3 days. The neutral ester, after washing with water and drying in vacuo, yielded an almost colourless glassy mass (3.75 g - calc. 3.9 g); it softened at 40°C and melted completely at 45°C. Efforts at crystallizing this neutral ester from various solvents and their mixtures failed, and resulted in the production of an oil which on drying produced the same glassy mass. The combined filtrate and washings, after concentrating, deposited colourless rhombs of phthalic acid (1.0 g - calc. 1.1 g) which sublimed at 195°C (the phthalic anhydride sublimate melted at 132-134°C).

A solution of the neutral ester (1.0 g) in alcoholic potash (50 c.c. of 0.08596 N) was heated under reflux for 1 hour; the unreacted alkali neutralised 9.2 c.c. of 0.1085 N hydrochloric acid (calc. 9.2 c.c.). Therefore; the neutral ester must have neutralised 38.38 c.c. of the alcoholic potash. Found, M.W. 596.4, C.H.O.S requires M 590.86 30 42

b) A solution of (-)-hydrogen phthalic ester (3 g, $[\alpha]_D^{18\circ} = -27^\circ$ in carbon disulphide) in caustic soda (27 c.c. of 0.3 N), after standing at room temperature (1 hour), became turbid with deposition
of the neutral ester, the deposition of which was complete in 5 days.
Yield: 2.1 g (calc. 2.3 g), M.P. 40-5°C. Found M.W. 598; 
C₃₀H₃₀O₈S requires M.W. 590. It had \([\alpha]_{D}^{20°} -23.6°\) (c, 2.50; 
1, 2) in carbon disulphide.
The (−)-neutral ester (1 g, \([\alpha]_{D}^{20°} -23.6°\) in carbon disulphide) was 
added to a solution of sodium (1 g) in absolute alcohol (40 c.c.).
After warming the mixture gently on the steam-bath (30 mins.) and 
pouring it into ice-cold water, the carbinol was deposited as a white 
solid (0.76 g - calc. 0.78 g), M.P. 85-8°C; it crystallised from 
carbon disulphide in short white needles, M.P. 90-1°C. It had 
\([\alpha]_{D}^{20°} -4.4°\) in carbon disulphide.
A specimen of the original hydrogen phthalic ester (2 g, \([\alpha]_{D}^{20°} -27.0°\) 
in carbon disulphide) was hydrolysed under similar conditions. The 
carbinol obtained (1.4 g - calc. 1.6 g) crystallised from carbon 
disulphide in short needles, M.P. 56-7°C; it had \([\alpha]_{D}^{20°} -8.6°\) 
in carbon disulphide.

2) With Sodium \(\pi\)-Toluene-sulphonate.
A solution of the hydrogen phthalic ester (1.9 g) in caustic soda 
(16.84 c.c. of 0.3 N) was rapidly filtered into a solution of sodium 
\(\pi\)-toluene-sulphonate (1.07 g) in water (8 c.c.). After standing 
at room temperature (30 mins.), the clear solution became turbid with 
deposition of the sulphone as a fine white powder, the deposition of 
which was complete in 24 hours, M.P. 165-8°C; it crystallised from 
methanol in short crystalline needles, M.P. 172°C. Yield of
p-tolyl-thiocamisylyphenylcarbinylsulphone, 1.65 g. Found, S 16.9
C\textsubscript{21}H\textsubscript{19}O\textsubscript{3}S\textsubscript{2} requires S 17.3%. The combined filtrate and washings, 
after acidifying and concentrating to small bulk, deposited phthalic 
acid (0.65 g - calc. 0.8 g), M.P. 200-2°C.

In a similar experiment, a solution of the (−)-hydrogen phthalic 
ester (0.5 g, [\alpha]\textsubscript{D}\textsuperscript{20} = -17.0° in carbon disulphide) in 0.3 N caustic 
soda (4.5 c.c.) and sodium p-toluenesulphinate (0.28 g in 5 c.c. of 
water) deposited the dl-p-tolyl-thiocamisylyphenylcarbinylsulphone 
(0.25 g), M.P. 172°C, alone or mixed with an authentic specimen 
prepared by the other method.

3 With Acetyl Chloride. To the hydrogen phthalic ester (1.9 g) 
acetyl chloride (0.73 c.c.) was added, and the mixture warmed gently 
for 2 minutes. The slightly yellow oily product solidified on cooling 
and was extracted with warm light petroleum (20 c.c.). The residue 
consisted of phthalic anhydride (0.7 g - calc. 0.74 g); M.P. 129- 
130°C; it crystallised from benzene in long needles, M.P. 130°C, 
alone or mixed with an authentic specimen. The petroleum extract 
deposited thioanisylphenylchloromethane (1.2 g - calc. 1.24 g), 
M.P. 56°C, alone or mixed with an authentic specimen of the chloride.

In a similar experiment (t)-hydrogen phthalic ester ([\alpha]\textsubscript{D}\textsuperscript{19} = +10.0 
in carbon disulphide) was rapidly dissolved in acetyl chloride on 
gentle warming. The product, isolated as described above, yielded the 
dl-thiocamisylyphenylchloromethane, M.P. 56°C, alone or mixed with 
an authentic specimen.
4) Dismutation Of The Hydrogen Phthalic Ester In Chloroform.

The hydrogen phthalic ester (3.78 g) in chloroform mix (25 c.c.) solution was heated under reflux. Phthalic acid immediately began to separate, and after 5 hours, the phthalic acid (0.55 g - M.P. 202°C) was removed by filtering, and the filtrate mixed with ether (100 c.c.) and shaken with dilute ammonia. From the alkaline extract, after acidification, unreacted hydrogen phthalic ester (1.5 g - M.P. 122-123°C) was recovered. The ethereal solution, after drying over calcium chloride and evaporation, yielded the neutral phthalic ester (1.5 g). This neutral ester (0.652 g) on hydrolysis with alcoholic potash (0.08596 N), neutralised 31.8 c.c. (calc. 32.0 c.c.). Found, M.W. 594, C₆H₈O₅S requires M.W. 590. Thus, dismutation of the hydrogen phthalic ester did occurred under these conditions upto 60%.

5) Acid Hydrolysis Of The Hydrogen Phthalic Ester.

a) To the hydrogen phthalic ester (0.5 g) dissolved in acetone (10 c.c.) and water (4 c.c.) three drops of concentrated sulphuric acid were added. The clear solution, after standing overnight at room temperature, deposited an oil, which was then dissolved in ether (30 c.c.) and extracted with dilute ammonia solution. The alkaline extract, after acidification, yielded unreacted hydrogen phthalic ester (0.14 g - M.P. 121-2°C). The ethereal solution, after drying, concentrating and adding light petroleum, deposited the carbino (0.2 g) in needles, M.P. 94°C, alone or mixed with an authentic specimen.
b) Dilute sulphuric acid (0.5 c.c. of conc. acid in 4 c.c. of water) was added to a solution of the (-)-hydrogen phthalic ester (1 g, [α]D20°-30°5° in carbon disulphide) in acetone (15 c.c.), and heated under reflux for 3 hours. To the cold clear solution ether (40 c.c.) was added, and the whole shaken with dilute ammonia solution. The alkaline extract, after acidifying, yielded no unreacted hydrogen phthalic ester. The ethereal extract, after drying over calcium chloride, concentrating to small bulk, and adding light petroleum, deposited the dl-carbinol (0.52 g) in silky needles, M.P. 94°C.

c) A solution of the (-)-hydrogen phthalic ester (1 g, [α]D20°-30°5° in carbon disulphide) in acetone (15 c.c.) and dilute sulphuric acid (0.5 c.c. of conc. acid in 4 c.c. of water), after standing at room temperature for 2 days in a closed vessel, was mixed with an equal volume of ether, washed with water and then shaken with dilute ammonia. The alkaline extract, after acidification, yielded unchanged hydrogen phthalic ester (0.75 g), M.P. 96-7°C; it had [α]D20°-24.6° (c 1, 513 1, 2) in carbon disulphide. The ethereal extract yielded the dl-carbinol (0.1 g), M.P. 94°C, alone or mixed with an authentic specimen.

d) The (-)-neutral phthalic ester (2 g, [α]D20°-23.6° in carbon disulphide) in acetone-dilute sulphuric acid solution, after heating under reflux for 2 hours, yielded the dl-carbinol (1.3 g), M.P. 94°C.
6) Reaction With Glacial Acetic Acid.

a) A solution of the hydrogen phthalic ester (5 g) in glacial acetic acid (40 c.c.) was heated at 100°C for 1 hour. The cold clear solution was mixed with ether (100 c.c.), washed three times with water, once with dilute ammonia, and finally with water and dried over calcium chloride. After evaporating the ether, thioanisylphenylcarbinyl acetate (3.2 g) distilled at 215-6°C/14 mm. as a colourless oil, \( d_20^\circ = 1.098 \), \( n_D^\circ 1.5912 \).

b) A solution of (+)-hydrogen phthalic ester (2 g, \( \left[\alpha\right]_D^{19^\circ} = +10.6^\circ \) in carbon disulphide) in glacial acetic acid (20 c.c.) was heated at 100°C for 30 minutes. The thioanisylphenylcarbinyl acetate (1.3 g) produced distilled at 216°C/14 mm. and was optically inactive.

c) A solution of the (-)-hydrogen phthalic ester (1 g, \( \left[\alpha\right]_D^{19^\circ} = -30.6^\circ \) in carbon disulphide) in glacial acetic acid (20 c.c.), after standing at room temperature for 1 hour, was mixed with ether (40 c.c.), washed twice with water and then shaken with dilute ammonia.

The alkaline extract, after acidification, yielded the unstable hydrogen phthalic ester (0.45 g - M.P. 95-6°C); it had \( \left[\alpha\right]_D^{20^\circ} = -21.83^\circ \) (c, 4.346 1, 2) in carbon disulphide. The ethereal extract yielded thioanisylphenylcarbinyl acetate (0.36 g), B.P. 216°C/14 mm. was again optically inactive.

7) Reaction With Absolute Ethyl Alcohol.

a) After heating under reflux a solution of the hydrogen phthalic ester
(4 g) in absolute alcohol (70 c.c.) for 1 hour, it was mixed with twice its volume of ether, washed twice with water, and then shaken with dilute ammonia solution. The alkaline extract, on acidification, yielded unreacted hydrogen phthalic ester 0.6 g, M.P. 123-4°C.

The ethereal extract, after washing with water, drying over anhydrous potassium carbonate, and evaporating the solvent, yielded on distillation thioanisylphenylcarbinyl ethyl ether (2.1 g), B.P. 212°C/20 mm., d₂⁴° 1.087; nD²⁰° 1.5910. Found, C 74.21, H 7.31, C₁₅H₁₈O₃ requires C 74.41, H 7.01%.

b) A solution of the (-)-hydrogen phthalic ester (4 g, [α]D¹⁹° -30.6° in carbon disulphide) in absolute alcohol (70 c.c.) was heated under reflux for 45 minutes, and then worked up as described above. The alkaline extract, after decomposition with dilute hydrochloric acid, yielded the hydrogen phthalic ester (1.4 g). It had [α]D¹⁹° -22.41° (c, 2.615 1, 2) in carbon disulphide. The ethereal extract yielded on distillation at 205-8°C/15 mm. thioanisylphenylcarbinyl ethyl ether (1.7 g) which was optically inactive.

c) A solution of the (-)-neutral phthalic ester (2 g, [α]D²⁰° -23.6° in carbon disulphide) in absolute alcohol (20 c.c.) after heating under reflux for 4 hours, was mixed with ether (50 c.c.) and washed three times with water. The dry ethereal extract yielded on distillation dl-thioanisylphenylcarbinyl ethyl ether (1.5 g).

8) Reaction With Concentrated Sulphuric Acid.

a) Hydrogen phthalic ester (1 g) was trititated with conc. sulphuric
acid (4 c.c.) and warmed gently for few minutes until all the ester went into solution, which developed a deep red colour. This was poured into ice-cold water, and the white solid produced crystallised from methanol-acetone solution in needles, yielding the carbinol (0.4 g), M.P. 93-4°C.

b) (+)-Hydrogen phthalic ester (0.6 g, $[\alpha]_D^{20} +10.0^\circ$ in carbon disulphide) was triturated with conc. sulphuric acid (2 c.c.) at 0°C. The deep red solution on pouring into ice-cold water, yielded the dl-carbinol as a slightly yellow solid, which crystallised from ether-light petroleum in needles, M.P. 93-4°C. Yield, 0.25 g.

c) In a similar experiment, the (-)-neutral phthalic ester (1 g, $[\alpha]_D^{20} -23.6^\circ$ in carbon disulphide) in conc. sulphuric acid solution on dilution with ice-cold water, yielded the dl-carbinol (2x50, 0.56 g), M.P. 93-4°C.

2) With Potassium Phthalimide.

A solution of the hydrogen phthalic ester (1 g) in caustic soda solution (9 c.c. of 0.3 N) was rapidly filtered into a solution of potassium phthalimide (0.5 g) in water (15 c.c.). The clear solution after standing at room temperature for 1 hour became turbid, depositing the neutral phthalic ester (0.78 g), the deposition of which was complete in 4 days. Potassium phthalimide was recovered unchanged from the filtrate.
Preparation Of Thianisylphenyl Chloromethane.

1) By The Action Of Concentrated Hydrochloric Acid On The Carbinol.

The carbinol (2 g) was triturated with conc. hydrochloric acid (40 c.c.) when it slowly changed into a greenish-white semi-solid. The reaction was completed by warming on the steam-bath for few minutes. The oily product was solidified after standing at room temperature overnight, was filtered, washed with conc. hydrochloric acid and dried in vacuo over potassium hydroxide. The chloride (2 g, M.P. 54-55°C) crystallised from light petroleum and little ether in needles, M.P. 56°C. Found, Cl 13.5

C₇H₅ClS requires Cl 14.2%.

A solution of the chloride (0.5 g) in alcoholic potash (25 c.c. of 0.06895 N) was heated under reflux for 1 hour. It neutralised 23.00 c.c. of the alcoholic potash (calc. 23.1 c.c.). Found, M.W. 253, C₇H₅ClS requires M.W. 248.5. The neutralised alcoholic solution was poured into cold water, and the turbid solution was extracted with ether, washed with water, and dried over calcium chloride. After evaporating the solvent, thianisylphenylcarbonyl ethyl ether (0.42 g, calc. 0.51 g) distilled at 213°C/20 mm.; d₄⁰ 1.06871, nₒ² 1.5310. It did not solidify after keeping in the ice-box for several days.

In a similar experiment, the (-)-carbinol (0.9 g, [α]_D²⁰ = -10.0° in carbon disulphide) was triturated with conc. hydrochloric acid. The chloride, isolated as described above, (0.9 g) melted at 56°C, alone or mixed with an authentic specimen of the chloride; it was optically inactive.
2) By The Action Of Thionyl Chloride On The Carbinol.

To a cooled solution of the carbinol (1.15 g) in pyridine (0.5 c.c.) thionyl chloride (0.7 c.c.) was added dropwise; the vigorous reaction produced an orange coloured oil. The mixture, after warming on the steam-bath for few minutes, was extracted with hot light petroleum. The chloride (1 g) crystallised in almost colourless needles, M.P. 56°C, alone or mixed with an authentic specimen.

3) By The Action Of Concentrated Hydrochloric Acid On The Hydrogen Phthalic Ester.

The hydrogen phthalic ester (1.9 g) was triturated with conc. hydrochloric acid (20 c.c.) — little or no reaction took place at room temperature. After warming for 5 mins. the mixture on the steam-bath, an oil was produced. This solidified overnight, and was dried in vacuo over sodium hydroxide. When extracted with warm light petroleum (20 c.c.), it left a residue of phthalic acid (0.8 g — calc. 0.83 g — M.P. 200°C). The petroleum extract, after concentrating and adding few drops of ether, deposited the chloride (1.10 g — calc. 1.24 g) in crystalline needles, M.P. 56°C.

In a similar experiment, the (+)-hydrogen phthalic ester (2 g, [α]_D^0 +10.40° in carbon disulphide) was triturated with hot conc. hydrochloric acid (10 c.c.); the oily product changed overnight into a greenish-white solid. When this was worked up as described above, it yielded phthalic acid (0.7 g) and the dl-chloride (1.1 g), M.P. 56°C, alone or mixed with an authentic specimen.
4) By The Action Of Acetyl Chloride On The Carbinol.

The carbinol (1 g) dissolved slowly in cold acetyl chloride (1 c.c.), more rapidly on slight warming, forming a greenish-white oil. This was dried in vacuo over sodium hydroxide, and then extracted with hot light petroleum (20 c.c.). After concentrating the petroleum extract and adding few drops of ether, the chloride (1 g) crystallised in short needles, M.P. 56°C.

In a similar experiment, when acetyl chloride (1 c.c.) was added to the (-)-carbinol (1 g, [α]_D^20° = -4.4° in carbon disulphide), the latter immediately reacted forming a yellow solution. The chloride (1 g, M.P. 56°C) isolated as described above, was optically inactive.

5) By The Action Of Concentrated Hydrochloric Acid On Thianisylphenylcarbinyl Acetate.

The acetate (0.67 g) was triturated with conc. hydrochloric acid (20 c.c.) when a white solid was formed overnight. This, after filtering, washing with conc. hydrochloric acid, and drying in vacuo over sodium hydroxide, yielded the chloride (0.6 g) which separated from light petroleum and little ether in needles, M.P. 56°C.

In a similar experiment, (-)-thianisylphenylcarbinyl acetate (1 g, [α]_D^20° = -29.35° in carbon disulphide) after titration with conc. hydrochloric acid (15 c.c.), yielded the chloride (0.9 g), M.P. 56°C, it was optically inactive.

6) By The Action Of Conc. Hydrochloric Acid On Thianisylphenylcarbinyl Ethyl Ether.
After trituration the ethyl ether (0.9 g) with conc. hydrochloric acid (15 c.c.) and keeping it in the ice-box for 2 days, the resultant chloride solidified, M.P. 55-55.5°C. It separated from light petroleum in needles, M.P. 56°C. Yield, 0.82 g.

7) By The Action Of Concentrated Hydrochloric Acid On The Neutral Phthalic Ester.

The oil produced by trituration the neutral phthalic ester (1 g) with conc. hydrochloric acid (15 c.c.) solidified overnight. This, worked up in the usual manner, produced phthalic acid (0.15 g - M.P. 201°C), and the chloride (0.5 g), M.P. 56°C.

In a similar experiment, when the (-)-neutral phthalic ester (0.8 g, \([\alpha]^{20}_D -23.6^\circ\) in carbon disulphide) was trituted with conc. hydrochloric acid, it yielded the dl-chloride (0.35 g), M.P. 56°C, alone or mixed with an authentic specimen.

Reactions Of Thioanisylphenyl Chloromethane.

1) With Sodium p-Toluenesulphonate.

To the chloride (1.23 g) in acetone (20 c.c.) a slight excess of sodium p-toluenesulphonate (1.15 g) in water (7 c.c.) was added. The homogeneous mixture almost immediately deposited the sulphone as a white crystalline solid; the deposition of which was complete in 20 minutes.

Yield of p-tolyl-thioanisylphenylcarbinylsulphone, 1.56 g, M.P. 168-170°C; it separated from alcohol (150 c.c.) in long silky needles, M.P. 172°C.
2) With Potassium Hydrogen Phthalate.

To the chloride (0.63 g) solution in acetone (10 c.c.) potassium hydrogen phthalate (0.6 g) solution in water (5 c.c.) was added. The clear solution deposited a yellow oil overnight. This was extracted with ether, washed with water and then shaken with dilute ammonia solution. The alkaline extract, on decomposition with ice-cold dilute hydrochloric acid, deposited thioanisylphenylcarbinyl hydrogen phthalate (0.45 g), M.P. 123-4°C, alone or mixed with an authentic specimen of the hydrogen phthalic ester. The remaining ethereal extract after washing with water, drying over calcium chloride and adding light petroleum, deposited the carbinol (0.18 g), M.P. 94°C.

3) With Sodium Benzoate.

To the chloride (0.6 g) dissolved in acetone (15 c.c.), sodium benzoate (0.8 g) solution in water (6 c.c.) was added. After standing at room temperature overnight, an oil deposited which set to a semi-solid on drying. Its solution in ether-light petroleum deposited thioanisylphenylcarbinyl benzoate (0.4 g) in clusters of hemispherical needles, M.P. 59°C, alone or mixed with an authentic specimen of the benzoate.

4) With Aqueous Acetone.

To the chloride (0.21 g) solution in acetone (10 c.c.), water was added dropwise until just turbid, few drops of acetone were added to render the solution clear. This immediately became acid to congo red, and when left overnight at room temperature in an open vessel, deposited colourless
crystals of the carbinol (0.2 g), M.P. 90-1°C; it separated from ether-light petroleum in needles, M.P. 94°C, alone or mixed with an authentic specimen of the carbinol.

5) **With Dilute Caustic Soda.**

To the chloride (0.5 g) solution in acetone (10 c.c.), caustic soda solution (1 c.c. of 0.3 N) was added, and after standing overnight at room temperature in an open vessel, deposited the carbinol in masses of crystalline needles (0.47 g), M.P. 92-3°C. It separated from ether-light petroleum in needles, M.P. 94°C, alone or mixed with an authentic specimen of the carbinol.

6) **With Absolute Ethyl Alcohol.**

A solution of the chloride (2 g) in absolute alcohol (20 c.c.) was heated under reflux for 2½ hours. After evaporating the solvent, thianisylphenylcarbinyl ethyl ether (1.58 g) distilled at 212°C/20 mm. as a colourless oil; $\alpha^{20}_D$ 1.5910.
**p-METHYLSULPHONYLBENZHYDROL**

Oxidation Of Thioanisylphenyl Carbinol.

To a solution of the carbinol (1.0 g) in glacial acetic acid (20 c.c.) hydrogen peroxide (3.3 c.c. of '90-vol.') was added, and the resultant clear solution, after standing for 2 days, was made alkaline, when a crystalline solid separated, M.P. 122-2°C. p-Methylsulphonylbenzhydrol separates from hot water, or methanol, or methylene chloride in glistening plates, M.P. 125-125.5°C. Yield, 1.0 g.

Found: C 63.66, H 5.50, S 12.17; C_{14}H_{14}O_{3}S requires C 64.12, H 5.34, S 12.23 %.

Reduction Of p-Methylsulphonylbenzophenone.

1) With Aluminium Isopropoxide. A mixture of dry isopropyl alcohol (30 c.c.), aluminium (0.5 g) and a trace of mercuric chloride was heated (3 hours) under reflux and left overnight at room temperature. To it p-methylsulphonylbenzophenone (4.0 g) was added, and the mixture was heated gently for 2 hours until acetone ceased to be evolved. The isopropyl alcohol was distilled off, and the residue, after heating on the steam-bath for few minutes with dilute sulphuric acid, yielded p-methylsulphonylbenzhydrol as a white solid which separated from ethanol or methylene chloride in shiny plates (3.7 g), M.P. 125-125.5°C, alone or mixed with an authentic specimen.
2) With Zinc Dust and Acetic Acid. Zinc dust (1.0 g) was added to solution of \( \text{p-} \)-methylsulphonylbenzophenone (1.0 g) in glacial acetic acid (20 c.c.), and the mixture heated on the steam-bath for 8 hours. After removing the unreacted zinc, the filtrate on dilution with water deposited an oily product, which after heating with caustic for few minutes, set to a solid mass on cooling. Its crystallisation from methylene chloride yielded \( \text{p-} \)-methylsulphonylbenzhydrol (0.6 g), shiny plates \( \text{M.P.} \ 125-125.5^\circ \text{C} \).

3) With Sodium Amalgam And Ethyl Alcohol. After slowly adding sodium amalgam (4 g of sodium in 80 g of mercury) to a solution of the ketone (4 g) in ethyl alcohol (150 c.c. of 96 %), the mixture was heated under reflux for 2 hours and then filtered. On diluting the filtrate with cold water, a white solid, free from sulphur, separated, \( \text{M.P.} \ 63-64^\circ \text{C} \). After two crystallisations from ether-light petroleum, benzhydrol separated as long silky needles, \( \text{M.P.} \ 66-70^\circ \text{C} \), alone or mixed with an authentic specimen. Yield, 1.7 g.

The benzhydrol, obtained as described above, was converted into its hydrogen phthalic ester by heating a mixture of the carbinol (1.3 g), phthalic anhydride (1.04 g) and pyridine (0.5 c.c.) on the steam-bath (2 hours); and when the resultant clear solution was decomposed with cold dilute hydrochloric acid, an oil separated which rapidly set to a white solid. This separated from methylene chloride-ligroin solution, yielding short silky needles of benzhydrol hydrogen phthalate (2.0 g), \( \text{M.P.} \ 157-8^\circ \text{C} \) (Balfe, Doughty, Kenyon and Poplett: J.C.S., 1942, 611, give the \( \text{M.P.} \) of benzhydrol hydrogen phthalate as 157-8°C).
On titrating this hydrogen phthalic ester (0.219 g) with 0.06196 N caustic potash, it neutralized 6.04 c.c. (calc. 6.05 c.c.). Found M.W. 332.3; \( \text{C}_2 \text{H}_4 \text{O}_4 \) requires M.W. 332.

4) With Zinc Dust, Caustic Soda And Alcohol. Zinc dust (5 g) and caustic soda (5 g) were added to a solution of the ketone (1.0 g) in ethyl alcohol (30 c.c. of 96 %); after standing overnight at room temperature, the solid product was removed by filtering. On dilution of the filtrate with cold water, a white solid, free from sulphur, separated, M.P. 62-3°C. It crystallised from light petroleum in colourless needles (0.4 g), M.P. 66-7°C, alone or mixed with an authentic specimen of benzhydrol.

p-Methylsulphonylbenzhydryl Hydrogen Phthalate.

p-Methylsulphonylbenzhydrol (2.0 g) was added to a solution of phthalic anhydride (1.13 g) in pyridine (1 c.c.); and after heating (2 hours) on the steam-bath and standing at room temperature overnight, the resultant homogeneous solution was diluted with an equal volume of alcohol and decomposed with ice-cold dilute hydrochloric acid, when a white solid separated. This after drying in vacuo, crystallised from methylene chloride-ligroin in white shiny plates, M.P. 103-4°C. Yield of p-methylsulphonylbenzhydryl hydrogen phthalate, 2.9 g.

On titration of the hydrogen phthalic ester (0.432 g) with 0.0925 N caustic soda, it neutralised 11.2 c.c. (calc. 11.4 c.c.). Found M.W. 415; \( \text{C}_9 \text{H}_9 \text{O}_6 \text{S} \) requires M.W. 410.

The hydrogen phthalic ester mixed with alkaline solutions of sodium p-toluenesulphinate at room temperature or at 100°C yielded no trace of
the corresponding p-tolylsulphone.

Oxidation Of Thiocarboxylcarvinyl Hydogen Phthaleate.

A homogeneous solution of thiocarboxylcarvinyl hydrogen phthaleate (2.0 g) and hydrogen peroxide (2 c.c. of 90-vols.) in glacial acetic acid (20 c.c.), after standing at room temperature for 2 days, was poured into ice-cold dilute hydrochloric acid, when p-methylsulphonylbenzhydryl hydrogen phthaleate separated. Crystallisation from methylene chloride-ligroin yielded shiny plates, M.P. 103-4°C. Yield: 1.5 g.

Hydrolysis Of p-Methylsulphonylbenzhydryl Hydogen Phthaleate With 0.3 M Caustic Soda.

1) At Room Temperature. A solution of the hydrogen phthalic ester (0.5 g) in caustic soda (4 c.c. of 0.3 M) after standing in a closed vessel for 2 months at room temperature remained clear. The hydrogen phthalic ester was recovered unchanged on acidifying this solution.

2) A 100°C. A solution of the hydrogen phthalic ester (1.0 g) in caustic soda (10 c.c. of 0.3 M) when heated on the steam-bath, deposited the carbinol slowly. After 1 hour, the deposited p-methylsulphonylbenzhydryl had M.P. 120-2°C; it separated from methanol in glistening plates, M.P. 125.5°C. Yield: 0.3 g. The mother liquor, on acidifying yielded unchanged hydrogen phthalic ester (0.4 g).

Oxidation Of (-)-Thiocarboxylcarvinyl Hydogen Phthaleate.
Oxidation Of (−)-Thioanisylphenylcarbinyl Hydrogen Phthalate.

The (−)-thioanisylphenylcarbinyl hydrogenphthalate used for this and the following experiments had $[\alpha]_D^{190} = 22.5^\circ$ in carbon disulphide and $[\alpha]_D^{120} = 16.3^\circ$ in methylene chloride. Its hydrolysis with absolute alcohol and sodium ethoxide yielded (−)-thioanisylphenylcarbinol with $[\alpha]_D^{190} = 8.9^\circ$ in carbon disulphide, and $[\alpha]_D^{190} = -4.5^\circ$ in methylene chloride.

To a solution of the (−)-thioanisylphenylcarbinyl hydrogen phthalate ( 3 g ) in glacial acetic acid ( 30 c.c. ), hydrogen peroxide ( 10 c.c. of ' 90-vols. ' ) was added. The clear solution, after standing at room temperature for 3 days, on diluting with cold water yielded p-methylsulphonylbenzhydryl hydrogen phthalate as a semi-solid, which separated from methylene chloride-ligroin in plates, M.P. 106-8°C; it had $[\alpha]_D^{190} = 36.6^\circ$ in methylene chloride. Yield, 2.9 g. On titration with standard alkali, found M.W. 416, $C_{22}H_{18}O_5$ requires M.W. 410.

Hydrolysis of (−)-p-Methylsulphonylbenzhydryl Hydrogen Phthalate.

1 ) With 0.3 N Caustic Soda. A solution of the (−)-hydrogen phthalic ester ( 1.5 g , $[\alpha]_D^{190} = 36.6$ in methylene chloride ) in caustic soda ( 10 c.c. of 0.3 N ), after being heating for 30 minutes on the steam-bath, was diluted with water, when p-methylsulphonylbenzhydryl separated as a white solid, M.P. 138-141°C; it separated from methylene chloride in plates, M.P. 146-7°C; it had $[\alpha]_D^{190} = 44.5^\circ$ in methylene chloride. Yield, 0.21 g. The mother liquor on acidifying yielded unchanged hydrogen phthalic ester ( 1.0 g ) with $[\alpha]_D^{150} = 36.5^\circ$ in methylene chloride.
2. With absolute Ethyl Alcohol and Sodium Ethoxide. The (+)-hydrogen phthalic ester (1.0 g, [α]_D^{190} +35.6° in methylene chloride) was dissolved in a solution of sodium (1.0 g) in absolute ethyl alcohol (35 c.c.) and after heating under reflux for 1 hour and diluting with cold water, (+)-p-methylsulphonylbenzhydrol was deposited. It separated from methylene chloride in shiny plates (0.6 g), M.P. 145-7°C with [α]_D^{190} +45.1° in methylene chloride.

**Oxidation of (-)-Thiocresyphenylcarbinol To (+)-p-Methylsulphonylbenzhydrol, And Conversion Of The Latter Into Its Hydrogen Phthalic Ester.**

To a solution of (-)-thioanisylphenylcarbinol (3.6 g, [α]_D^{190} -4.5° in methylene chloride) in glacial acetic acid (75 c.c.) hydrogen peroxide (15 c.c. of '90-vols.') was added. The homogeneous solution, after standing at room temperature for 6 days, was poured into excess of cold dilute caustic soda, when (+)-p-methylsulphonylbenzhydrol separated as a white solid, which separated from methylene chloride in glistening plates, M.P. 145-7°C, [α]_D^{190} +45.1° in methylene chloride. Yield, 3.0 g.

A solution of the (+)-p-methylsulphonylbenzhydrol (1.5 g, [α]_D^{190} +45.1° in methylene chloride) and phthalic anhydride (0.84 g) in pyridine (1 c.c.) after heating for 2 hours on the steam-bath and standing overnight at room temperature, was mixed with an equal volume of alcohol and poured into ice-cold dilute hydrochloric acid, when (+)-p-methylsulphonylbenzhydrol hydrogen phthalate separated as a semi-solid, which separated from methylene chloride - ligroin in plates, M.P. 105-7°C, [α]_D^{180} +37° in methylene chloride. Yield, 2.1 g.