"INFLUENCE OF ALKOXYL GROUPS ON THE REACTIVITY OF
BENZHYDROL AND 1- AND 2- NAPHTHYL METHYL CARBINOL"

A Thesis
Submitted to The University of London
for the Degree of
DOCTOR OF PHILOSOPHY

by
PANDEY RAGHURAJ SHARAN, M.Sc. (PATNA)

Chemistry Department,
Battersea College of Technology,
London, S.W.11.

The work described in this thesis was carried out at the Battersea College of Technology under the direction of the late Dr. J. Kenyon, F.R.S. The author wishes to thank and express his deep gratitude to the late Dr. Kenyon for his kindness and invaluable guidance.

The author also extends his deep gratitude and thanks to Dr. C. L. Arcus for his kind and invaluable advice and guidance after the death of Dr. Kenyon and to Dr. J. E. Salmon and Dr. L. A. Cort for their kind interest.

January 1962.
Abstract

This thesis describes an investigation of the influence of methoxy and ethoxy groups on the tendency of benzhydrol and naphthyl ethanols to undergo alkyl-oxygen fission during their reactions.

4-Ethoxybenzhydrol, α-(2-methoxy-1-naphthyl)ethanol, α-(2-ethoxy-1-naphthyl)ethanol, and α-(6-ethoxy-2-naphthyl)ethanol have been obtained by reduction of the corresponding ketones, which were prepared by Friedel-Crafts reactions. Optical resolution of each alcohol has been effected by conversion into the hydrogen phthalate, followed by fractional crystallisation of appropriate alkaloidal salts.

The incidence of alkyl-oxygen fission has been studied, for the hydrogen phthalate of each alcohol, by three reactions:

(a) Formation of the di-benzhydryl or di-naphthyl ethyl phthalate on keeping of the hydrogen phthalate in dilute alkali.

(b) Formation, by reaction with sodium-p-toluene sulphinic acid, of the p-tolyl sulphone.

(c) Formation of the methyl ether of the alcohol, by reaction with methanol, and the course of racemisation during this process.

The results are discussed, and it is concluded that, for the above reactions, the promotion of alkyl-oxygen fission, by electron-release, is greater for the ethoxy than for the methoxy group, and that the relay of this electronic effect is more effective from the 2- than from the 6-position of the naphthyl nucleus.
An index is provided, detailing the following sections:

- **General Notes**: Page 1
- **INTRODUCTION**: Page 2
- Discussion of preparation and resolution of \(\text{p-ethoxybenzhydrol}\): Page 23
- The function of pyridine and triethyl amine in acid phthalic ester formation: Page 24
- Influence of ethoxyl group on the reactivity of \(4\)-ethoxy-benzhydrol hydrogen phthalate: Page 30
- Dismutation of \((-\)\)-\(\text{p-ethoxybenzhydryl hydrogen phthalate}\) into \((\pm\)\)-\(\text{p-ethoxybenzhydryl hydrogen phthalate}\): Page 32
- Reaction of benzhydrol and its hydrogen phthalate with sodium-\(\text{p-toluene sulphinate}\): Page 36
- Reactions of methanol with \(4\)-ethoxy-benzhydryl hydrogen phthalate: Page 39
- Table I - IV: Pages 57-59
- Discussion of the preparation and resolution of alcohols containing \(1\)- and \(2\)-naphthyl groups: Page 60
- Influence of alkoxy groups on the reactivity of the hydrogen phthalates of alcohols containing the ethoxy- and methoxy-naphthyl radical: Page 70
- Alkyl-oxygen heterolysis in the reactions of acid esters of the alcohols containing the methoxy- and ethoxy-naphthyl radical: Page 73
- Table V - XVII: Pages 81-87

/Contd...
EXPERIMENTAL

Summary of preparation and resolution of 4-ethoxybenzhydrol. 89
Experimental Details 90
Reactions of 4-ethoxybenzhydrol and its hydrogen phthalate 98-104

Summary of preparation and resolution of α-(2-methoxy-1-naphthyl) ethanol 105
Experimental Details 106
Reactions of α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate 115-119

Summary of preparation and resolution of α-(2-ethoxy-1-naphthyl) ethanol 120
Experimental Details 121
Reactions of α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate 131-135

Summary of preparation and resolution of α-(6-ethoxy-2-naphthyl) ethanol 136
Experimental Details 137
Reactions of α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate 150-154
Reagents and solvents 155
The analyses were done by Dr. Alfred Bernhardt, Max Planck Institut, Mulheim, Germany.

The optically active hydrogen phthalates of the carbinols have been designated as (+)- or (-)- according to their sign of rotation in acetone. The corresponding optically active carbinols have been referred to as (+)- or (-)- irrespective of their actual sign of rotation, which is given in the appropriate place.

Purified and dried solvents were used for polarimetric observations, which were carried out in an air-thermostatted room unless otherwise mentioned.

Melting points are uncorrected.
The use of optically active compounds affords a convenient method for studying the course of certain organic reactions.

It is a well known fact that when a compound having an asymmetric centre in the molecule is synthesized, the racemic mixture is always obtained except in asymmetric synthesis. To obtain the dissymmetric compounds in optically active forms various methods of resolution, depending on the nature of the compound, are employed. An ingenious method for the resolution of alcohols has been devised by Pickard and Kenyon (J.C.S., 1913, 103, 1937), which consists in preparation of acid esters - hydrogen phthalates or hydrogen succinates - of the alcohol. These acid esters are then resolved by optically active alkaloidal bases.

Once the acid ester is obtained in a state of optical purity, the question of obtaining the corresponding optically pure active alcohol arises. This can only be done by hydrolysing the acid ester. Whether or not the process of hydrolysis of the acid ester is accompanied by any loss of optical activity of the alcohol thus obtained depends upon the mechanism and conditions of hydrolysis.

Various suggestions regarding the mechanism of hydrolysis have been put forward from time to time. Thus Ferns and Lapworth (J.C.S., 1912, 101, 273) suggested that alkyl esters of sulphonic and sulphuric acids react in a manner which is different from that of alkyl esters of carboxylic acids. They located the mode of rupture of the groups during the course of reaction as shown below:
But in the hydrolysis of carboxylic esters different mechanisms have been recognised — the classification of the mechanism depending on the following factors, Ingold (Structure and Mechanism in Organic Chemistry, Bell, London, 1957, p. 752).

1. Nature of the reagent, i.e. the hydrolyzing medium, viz, acidic, alkaline or neutral.

2. The position of rupture of the carboxylic compound.

3. Final and satisfactory elucidation of the nature of the mechanism is achieved by kinetic methods and optical and other relevant study of the reaction products — the basis of such classification of mechanism of hydrolysis being a series of experiments performed by Hughes-Ingold school, Kenyon and his school, and others (relevant reference given later on in this thesis).

Thus during the hydrolysis of a carboxylic ester in alkaline medium there are two feasible modes of rupture of the carboxylic compound. This can be formulated in either of the two ways:—

(A) \[ R\text{CO} \text{OR}' + H\text{OH} \rightarrow R\text{COOH} + R'\text{OH} \]

(B) \[ R\text{COO} \text{R}' + H\text{O} \rightarrow R\text{COOH} + R'\text{OH} \]

\[ [R' = \text{alkyl}] \]

Here it may be seen that in (A) the bond \(-C - \text{OR}'\) is broken, i.e. the ester molecule undergoes rupture on its acid side, the oxygen present
in the liberated alcohol is derived from the ester; whilst in (B) the bond between -CO -- R' is cleaved where the ester molecule is ruptured on its alcohol side, the liberated alcohol derives its oxygen from the aqueous medium. To distinguish between these two types of fission Day and Ingold (Trans. Farad. Soc., 1941, 37, 686) in a discussion on the mechanism of hydrolysis of carboxylic ester introduced the convenient terms acyl-oxygen fission (A) and alkyl-oxygen fission (B).

Further Day and Ingold showed that acyl-oxygen fission in alkaline hydrolysis is a second order reaction and involves the esters and a hydroxyl group. They (loc. cit.) designated the bimolecularity of the reaction by $B_{Ac}^2(B')^2$.

\[
\begin{align*}
\text{HO}^- & \quad \begin{array}{c} \text{slow} \\ \text{fast} \end{array} \quad \text{HO}^- \quad \begin{array}{c} \text{fast} \\ \text{slow} \end{array} \quad \text{HO}^- \\
\text{R'} & \quad \text{C} & \quad \text{OR} & \quad \text{RO}^- & \quad \text{C} & \quad \text{OR} & \quad \text{RO}^- & \quad \text{C} & \quad \text{OR} & \quad \text{RO}^- \\
\end{align*}
\]

\[
\begin{align*}
\text{R'}\text{CO}_2\text{OH} & \quad \text{OR} \quad \text{fast} \quad \text{R'}\text{CO}_2\text{O}^- & \quad \text{HOR} \\
\end{align*}
\]

However, they have indicated that hydrolysis by alkyl-oxygen fission mechanism (B) is a mono-molecular reaction which proceeds by initial ionisation of the ester to produce a carbonium ion, the rate of hydrolysis being
dependent on the rate of ionisation of the ester. This mechanism was termed \( B_{\text{all}} \) (B).
(ii) Further, when the isomeric crotyl acetate
\[ \text{Me} \cdot \text{CH} - \text{CH} - \text{CH}_2 \quad \xrightarrow{\text{Ac}} \quad \text{OAc} , \]
and 1-methyl allyl acetate
\[ \text{Me} \cdot \text{CH} - \text{CH} = \text{CH}_2 \]
\[ \xrightarrow{\text{OAc}} \]
are hydrolysed with 0.5N alkali each yields its own pure alcohol, C. Prévost, (Ann. Chim., 1928, 10, 147); Ingold and Ingold (J.C.S., 1932, 756). Had these reactions taken place by mechanism (B), i.e. alkyl-oxygen fission, the same positive mesomeric ion would have been set free at one stage giving rise to the mixture of the two alcohols
\[ \text{Me} \cdot \text{CH} - \text{CH} - \text{CH}_2 \]
\[ \xrightarrow{\text{OH}} \]
\[ \text{Me} \cdot \text{CH} - \text{CH} = \text{CH}_2 \]
\[ \xrightarrow{\text{OH}} \]
\[ \text{Me} \cdot \text{CH} = \text{CH} - \text{CH}_2 \]
\[ \xrightarrow{\text{OH}} \]

(iii) When neo-pentyl(tert-butylmethyl) halides are hydrolysed, tert-amyl alcohol along with some unsaturated compounds is formed. Whitmore and Rothrock (J.A.C.S., 1932, 54, 3431) and Whitmore, Rothrock and Popkin (ibid, 1939, 61, 1586).
These reaction products involve the formation of free neo-pentyl carbonium ion which undergoes rearrangement to the tert-pentyl cation and hence suggest that the hydrolysis took place by mechanism (B), i.e. by the alkyl-oxygen fission mechanism.

On the other hand, when X = -OAc, -O.C.H₂.Cl, -O.C.HCl₂, and -O.C.Cl₂, i.e. when neo-pentyl acetate and chloroacetates are hydrolysed, only neo-pentyl alcohol is recovered unchanged and unaccompanied by unsaturated compounds as was shown by Quayle and Norton (J.A.C.S., 1940, 62, 1170). Therefore, these reactions do not involve a free carbonium ion. Steric hindrance by the neo-pentyl group would furthermore preclude the B₂ mechanism, Hughes (Quart.Rev., 1948, 2, 107) leaving the B₄C₂ mechanism as the most probable alternative. Thus these hydrolyses were effected by mechanism (A), i.e. acyl-oxygen fission.

(iv) Betts and Hammett (J.A.C.S., 1937, 59, 1568) showed that the effect of the structure of the acyl group on the rate of hydrolysis of esters is closely parallel to that in the reaction

\[
\text{R. CO} + \text{OMe} + \text{NH}_3 \rightarrow \text{RCONH}_2 + \text{MeOH}
\]

but shows no relation to that in the reaction \[\text{R.CO.OMe} + \text{NMe}_3 \rightarrow \text{R.CO.} + \text{NMe}_4^+\].

(v) The most definite and conclusive demonstration in favour of mechanism (A)- acyl-oxygen fission - has been advanced by Polanyi and Szabo (Trans. Farad.Soc., 1934, 30, 508). They hydrolysed amyl acetate with aqueous sodium hydroxide having greater proportion of isotope O¹⁸, dehydrated the alcohol formed and determined the isotopic ratio of the oxygen in the water
thus produced. The ratio was normal showing that the oxygen in the alcohol came from the ester itself and not from the aqueous medium and thus proved that during the hydrolysis, the fission occurred in accordance with mechanism (A) i.e. acyl-oxygen fission as hydrolysis by mechanism (B), alkyl-oxygen fission, would give rise to $^{16}O^1H$ and $^{18}O^{18}H$.

$$\text{Me.CO} \rightarrow \text{O.C.H}_3 + \text{H} \rightarrow \text{Me.CO.OH} + \text{C}_5\text{H}_10 + \text{H}_2\text{O}$$

It was subsequently shown by Datta, Dey and Ingold (J.C.S., 1939, 838) that hydrolysis of methyl hydrogen succinate by acid aqueous ($^18O$ enriched) gives alcohol having only the normal proportion of $^18O$, thus proving that acyl-oxygen fission occurred in the hydrolysis. Roberts and Urey (J.A.C.S., 1938, 60, 2381) established a similar mechanism for the esterification of benzoic acid with labelled methyl alcohol.

Though in the majority of cases hydrolysis in alkaline medium is effected by alkoxy interchange (acyl-oxygen fission) by mechanism (A) in which the bonds of the alkoxy carbon atom are not disturbed, the alternative mechanism (B) - alkyl-oxygen fission - is more frequently operative particularly in esters of the type $R'\text{COOR}$, when the group $R''$ has sufficient electron repelling properties.

Arcus and Kenyon (J.C.S., 1938, 1912), Kenyon and his co-workers (J.C.S., 1936, 85; ibid 586) have shown that optical nature of the alcohol obtained by hydrolysing optically active ox-dimethyl-allyl hydrogen
phthalate and α-methyl cinnamyl hydrogen phthalate depends upon the strength of the aqueous alkaline solution.

Hills, Kenyon and Phillips (J.C.S., 1936, 576) and Balfie, Hills, Kenyon, Phillips and Platt (J.C.S., 1942, 556) have shown that the mechanism of fission of αγ-dimethyl allyl hydrogen phthalate during hydrolysis depends on the strength of the aqueous alkali used, as with 5 N aqueous alkali the alcohol obtained has greater $\alpha_D$ but with decreasing strengths of the alkali $\alpha_D$ of the alcohol obtained is progressively lower and almost racemized alcohol is obtained when dilute alkali is used.

It seems likely, therefore, that in concentrated alkaline solution bimolecular mechanism B'2 (acyl-oxygen fission) is mainly operative but mechanism (B), monomolecular mechanism (alkyl-oxygen heterolysis) comes increasingly into play as the alkaline solution becomes more and more dilute.

The mechanism (B) - alkyl-oxygen fission - is induced by the electron shift from the ethylenic bond, which is accelerated by the presence of adjacent methyl groups.

\[
\begin{align*}
\text{CH}_3\text{CH} & \rightarrow \text{CH} - \text{CH} = \text{CH}_2 \\
\text{CH} & \rightarrow \text{CH} = \text{CH}_2 \\
\frac{1}{2} + \text{CH} - \text{CH} & \rightarrow \text{CH}_3\text{CH} = \text{CH}_2 \\
\text{H}_2\text{O} & \rightarrow \text{CH}_3\text{CH} = \text{CH} - \text{CH}_3 \\
\text{OH} & \rightarrow \text{C}_6\text{H}_4\text{CO}_2^- \\
\text{C}_6\text{H}_4\text{CO}_2^- & \rightarrow \text{C}_6\text{H}_4\text{CO}_2^- \\
\end{align*}
\]

This marked tendency of optically active αγ-dimethyl allyl hydrogen phthalate to undergo hydrolysis by alkyl-oxygen heterolysis gets support in the following facts.
(i) When the isomeric α-methyl allyl acetate and crotyl acetate are hydrolysed separately by 0.5 N aqueous alkali (C. Prevost, Ann. chim., 1928, 10, 147) or in acid solution until upward of 90% hydrolysis and then forced to completion by alkaline saponification (Ingold and Ingold, J.C.S., 1932, 756), they yield the corresponding unisomerized pure alcohol. This strongly indicates that the crotyl and α-methyl allyl ions (carbonium ions) were never set free at any stage in course of the hydrolysis. Datta, Day and Ingold (J.C.S., 1939, 838) have arrived at the same conclusion by a heavy oxygen study of acid catalyzed ester hydrolysis.

(ii) Optically active α-methyl allyl hydrogen phthalate when hydrolysed by aqueous alkali (5 N approx.), yields α-methyl allyl alcohol in optically pure condition, (Kenyon and Snellgrave, J.C.S., 1925, 1169).

Vernon (J.C.S., 1954, 423) has shown that αα- and γγ- dimethyl allyl chlorides are hydrolysed nearly 100 times faster than the α- or γ-monomethyl allyl chlorides.

Thus the alkyl-oxygen fission in the substituted allyl alcohols requires the effect of an ethylenic bond to be reinforced not by only one methyl group rather by two.

Further, that the ionization is reversible is proved by the fact that when the hydrolysis is stopped before completion, partially racemized acid ester is obtained.

In hydrolysis of αγ-dimethyl allyl hydrogen phthalate the visualized positively charged radical, which assumes planar configuration,

\[ \text{Me} \quad \text{CH} \quad \text{CH} \quad \text{CH} \quad \text{Me} \]
is symmetrical, the same racemic chemical individual is obtained irrespective of the fact whether (OH) group links to the α- or γ- carbon atom. But when the molecule is not symmetrical, as in α-phenyl-γ-methyl allyl alcohol, a second possibility arises.

Kenyon, Partridge and Phillips (J.C.S., 1937, 216) have shown that when optically active γ-phenyl-α-methyl allyl hydrogen phthalate and α-phenyl-γ-methyl allyl hydrogen phthalate are hydrolysed with concentrated methyl alcoholic sodium hydroxide, almost optically pure corresponding unisomerized alcohols are formed; whereas when either ester is hydrolyzed by dilute aqueous alkali, highly racemized isomeric α-methyl-γ-phenyl allyl alcohol is the main product, Kenyon, Partridge and Phillips (J.C.S., 1937, 207).

This suggests that the mesomeric positive radical becomes kinetically free at some stage of the hydrolysis

\[ \text{Me. CH - CH - CH. Ph.} \]

The alcohol formed by nucleophilic attack of OH\(^-\) group on the planar mesomeric ion

\[ \text{Ph. CH - CH - CH. Me} \]

is γ-phenyl-α-methyl allyl alcohol, indicating that this alcohol is structurally more stable than α-phenyl-γ-methyl allyl alcohol. Kenyon, Partridge and Phillips (J.C.S., 1936, 85) have shown that when optically active hydrogen phthalic ester of γ-phenyl-α-methyl allyl
alcohol is hydrolysed by dilute aqueous alkali, the unisomerised alcohol is obtained in almost optically inactive condition.

Thus it seems that the alkyl-oxygen heterolysis in the esters of substituted allyl alcohols is promoted by the electromeric shift of electrons from ethylenic bond to the carbon atom carrying the hydroxyl group

Phenyl groups containing electron repelling substituents in ortho- or para- position possess identical electron releasing property and thus esters of such substituted phenyl carbinol would also facilitate alkyl-oxygen heterolysis
The experiment was thus extended to the esters of benzhydrol, 1-phenyl ethyl derivatives and to some naphthalene analogues. It was observed that the stability of the carbonium ion \( R^+ \) depended on the nature of the substituents on the carbinol carbon atom. Thus optically active \( p \)-methoxy benzhydrol hydrogen phthalate gave a racemic alcohol with 10 N aqueous sodium hydroxide, while for active \( p \)-phenoxybenzhydrol and \( l-p \)-anisyl-ethyl hydrogen phthalates, quite dilute alkali was required (Balfe, Evans, Kenyon, and Nandi, J.C.S., 1946, 803; Balfe, Kenyon and Wicks, J.C.S., 1946, 807), and for the unsubstituted 1-phenylethyl ester to yield racemic alcohol an almost neutral solution was required (Balfe, Bevan and Kenyon, J.C.S., 1951, 376). Thus it was shown that the influence of the substituents in stabilizing the carbonium ion \( R^+ \) is in the order

\[
\begin{align*}
\text{MeO} & \quad \text{PhO} \\
\text{Me-} & \quad \text{Me-}
\end{align*}
\]

Balfe, Doughty, Kenyon and Poplett (J.C.S., 1942, 605) have shown that hydrolysis of the (+)-\( p \)-methoxy benzhydrol hydrogen phthalate with 10 N sodium hydroxide results in extensive racemization; nearly optically pure alcohol was obtained by hydrolysis in 98% ethanol. When the water content is increased to 20 per cent, extensive racemization results, probably due to the high dielectric constant of water which causes ionization of the ester molecule to give a carbonium ion and hence formation of \( \text{dl} \)-alcohol.

The alcohol seems to ionise to give a carbonium ion (alkyl-oxygen fission) and hydroxyl ion more readily than by alkoxy-hydrogen fission.
This alkoxy-hydrogen fission of alcohols is similar to the acyl-oxygen fission of the carboxylic esters and is typical characteristic of primary and most secondary alcohols.

Thus optically active secondary alcohols will give optically active products in a chemical reaction by alkoxy-hydrogen fission and racemic products by the alkyl-hydroxyl fission.

The ease with which p-methoxy-benzhydrol and its derivatives give a carbonium ion (mechanism B) is shown by the following reactions (Balfe, Doughty, Kenyon and Poplett, loc.cit.):

1. p-Methoxy benzhydrol or its hydrogen phthalate, its benzoate, its acetate and its methyl ether on triturating with cold concentrated hydrochloric acid are instantly and completely converted into the corresponding chloro compound Ph.CHCl.C₆H₄.O.Me; when optically active compounds are used, the resulting phenyl anisyl chloromethane is completely racemic. The reaction of this (+)-alcohol with acetyl chloride furnishes a very notable example of its tendency to undergo alkyl-oxygen fission, the carbonium kation combining with chloride anion to give the racemic chloride.
However, in presence of pyridine the optically active alcohol reacts with acetyl chloride in the normal manner and yields the optically active acetate:

\[ (+) \text{ROH} + \text{H}^+ + \text{Cl}^- \xrightarrow{\text{Ac}} (+) \text{ROAc} + \text{C}_5\text{H}_5\text{N.HCl} \]

But in absence of pyridine the dL-RCl is formed, the alcohol ionises to give R⁺ carbonium ion which combines with chloride anion to form dL-RCl. The alternative mechanism of alkoxy-hydrogen fission of the alcohol would give the corresponding acetate.

2. When an aqueous solution of the sodium salt of the (+)-hydrogen phthalate of phenyl anisyl carbinol is mixed with a molecular proportion of an aqueous solution of sodium-p-toluene sulphonate, a crystalline precipitate of dL-p-tolyl-p-methoxy-benzhydryl sulphone separates - in theoretical yield within 20 minutes. The same compound is formed in theoretical yield by the interaction of phenylanisyl-chloromethane and the sodium-p-toluene sulphonate.

These reactions indicate the transitory existence of R⁺ (carbonium ion) by alkyl-oxygen fission, which goes to the sulphur atom having a lone pair of electrons.

\[ \text{COOR}(+) + \text{Me.C}_6\text{H}_4\text{SO}_2\text{Na} \xrightarrow{\text{Me.C}_6\text{H}_4\text{SO}_2} \text{Me.C}_6\text{H}_4\text{S}^\cdot - R(\pm) + \text{COONa} \]

\[ \text{R} \xrightarrow{\text{Cl}} + \text{Me.C}_6\text{H}_4\text{SO}_2\text{Na} \xrightarrow{\text{NaCl}^+} \text{Me.C}_6\text{H}_4\text{SO}_2\text{Na} \]
3. That (+)-p-methoxy benzhydrly hydrogen phthalate is hydrolysed by dilute alkali, by alkyl-oxygen fission to dl-p-methoxy benzhydrol, is further supported by the dismutation of the acid phthalic ester in dilute-alkaline solution.

The clear solution of the (+)-p-methoxy-benzhydrly hydrogen phthalate in the calculated amount of cold sodium hydroxide solution (0.15 N) begins to turn milky after standing a few minutes at room temperature, and after a day deposits the oily neutral ester. This neutral ester on hydrolysis gives p-methoxybenzhydrol whose rotatory power is one-half that of the p-methoxybenzhydrol obtained by hydrolysis of the parent acid phthalic ester under similar condition (98% alcoholic potash). About 50% of the total phthalic acid is obtained from the neutral ester and 50% from the aqueous layer on acidification.

The results can be shown by the following diagram:
When the reaction is carried out in a solution containing 5 molecular proportion of sodium phthalate, optically inactive neutral ester along with trace of almost racemic alcohol is formed. Here R present in the neutral ester and alcohol is formed by alkyl-oxygen fission.

Apart from the reactions mentioned above Kenyon and his co-workers have used the nature of the products to establish alkyl-oxygen fission for many carboxylic esters in the generalised reactions of ether and ester formation by solvolysis in alcoholic and carboxylic acid solvents.
Alcoholysis studies have a certain advantage over hydrolysis because in hydrolysis the same products are obtained irrespective of the fact whether the alkyl-oxygen or acyl-oxygen bond is fissioned; whereas in alcoholysis entirely different products are obtained as is shown by the following scheme:

\[
\begin{align*}
R - C & \quad \text{OR'} + H \quad \text{OR''} \quad \longrightarrow \quad \text{RCOOR''} + \text{HOR'} \\
R - CO & \quad \text{R'} + H \quad \text{OR''} \quad \longrightarrow \quad \text{R} - \text{C} - \text{OH} + \text{R''OR'}
\end{align*}
\]

Thus Arcus and Kenyon (J.C.S., 1933, 1912) observed that esters of optically active unsaturated alcohols, when warmed with carboxylic acids or with alcohols, yield esters or ethers with extensive loss of optical purity and, therefore, presumably by mechanism (B), i.e. by alkyl-oxygen fission. Further, Balfe, Hills, Kenyon, Phillips and Platt (J.C.S., 1942, 556) obtained racemic 1:3-dimethyl-allyl methyl ether by the action of methanol on 1:3-dimethyl-allyl hydrogen phthalate and this latter ester by treatment with acetic acid gave racemic 1:3-dimethyl-allyl acetate.

Balfe, Doughty, Kenyon and Foplett (J.C.S., 1942, 605) obtained racemic p-methoxy benzhydryl methyl ether by interaction of methanol and p-methoxy-benzhydryl hydrogen phthalate. Balfe, Downer, Evans, Kenyon, Foplett, Searle and Tarnoky (J.C.S., 1945, 797) obtained (+)1:1-naphthylethyl formate by the interaction of 1:1-naphthylethyl hydrogen
phthalate and formic acid. Balfe, Bevan and Kenyon (J.C.S., 1951, 376) observed that several esters of 1-phenylethyl and some analogous radicals, including formates, acetates, benzoates and hydrogen phthalates gave racemic ethers or esters on solvolysis with methanol or ethanol or with formic or acetic acid. Apparently these reactions proceed by alkyl-oxygen fission.

Evidence of alkyl-oxygen fission has been observed in the reactions of xanthrydrol, which may be regarded as an ortho-alkoxybenzhydrol, and Michler's hydrol too. Thus Fosse (Compt. rend., 1907, 145, 513) showed that xanthrydrol reacts with amides giving xanthyl derivatives. Fosse and Robyn (Compt. rend., 1906, 142, 239) prepared the condensation product of xanthrydrol with compounds having reactive methylene groups; Balfe, Kenyon and Thain (J.C.S., 1952, 790) prepared xanthrydyl-p-tolyl sulphone by the interaction of sodium-p-toluene sulphinate and xanthrydrol in acetic acid medium. Weil. (Ber., 1894, 27, 1048) prepared ammonia and hydroxylamine derivatives of Michler's hydrol. All these reactions presumably involve alkyl-oxygen fission.

Balfe, Evans, Kenyon, and Nandi (J.C.S., 1946, 803) have shown that hydrogen phthalate and hydrogen succinate of a-naphthyl anisyl carbinol yield half racemized neutral phthalic ester and racemic sulphone. It thus appears that the alkyl-oxygen fissions are in no way dependent on any special structural features of phthalic acid. Evidence of alkyl-oxygen fission has been obtained in sulphinic esters also. Thus Kenyon, Phillips and Taylor (J.C.S., 1933, 73) observed that optically active phenyl-methyl
carbinyl-p-toluene sulphinate reacts with acetic acid to give a racemic acetate and with ethyl alcohol to give a mixed ethyl ether with extensive loss of optical purity.

$\text{Me. } \text{C}_6\text{H}_4. \text{SO. } \text{O. } \text{CH. } \text{Me. } \text{Ph}$

$\text{H. } \text{OAcf}$

$\text{H. } \text{OEt}$

Balfe, Downer, Evans, Kenyon, Peplett, Searle and Tarnoky (loc. cit.) showed that carboxylic esters of phenylmethyl carbinol and of a-naphthyl methyl carbinol react with carboxylic acids and with alcohols by a mechanism which involves alkyl-oxygen fission.

Further Balfe and Kenyon (J.C.S., 1951, 381) have shown that acid esters of a-naphthyl methyl and $\beta$-naphthyl methyl carbinols yield racemic sulphone and half racemized neutral ester.

These reactions show that phenyl- and $\alpha$- and $\beta$-naphthyl radicals have enough electron releasing properties to permit this type of reaction to occur.

However, the tendency of these esters to undergo alkyl-oxygen fission is less pronounced than those of the esters of the allyl alcohols, aryl anisyl carbinols (described above), aryl phenetyl carbinol (this thesis), dimanisyl carbinol (Balfe, Kenyon and Thain, J.C.S., 1951, 386), anisyl phenetyl carbinol (Nurula, unpublished work, result personally communicated) and alkoxy substituted naphthyl methyl carbinols (this thesis).

Thus it seems certain that the carbonium ion formation in substituted
benzhydrols, and substituted naphthyl methyl carbinols is initiated by the conjugative electron release (Davies and Kenyon, Quart. Rev. 1955, Vol. IX, No.3) of the substituents (methoxy, ethoxy or dimethyl amino groups), and the carbonium cation formed is stabilized by resonance

\[
\begin{align*}
\text{OAlk} & \quad \text{OX} \\
\text{H} & \quad \text{C} \\
\text{C} & \quad \text{OAlk} \\
\text{OX} & \quad \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{Me} & \quad \text{C} \\
\text{C} & \quad \text{H} \\
\text{Me} & \quad \text{C} \\
\text{H} & \quad \text{OX} \\
\text{OX} & \quad \text{OX}
\end{align*}
\]

\[
\begin{align*}
\text{AlkO} & \quad \text{C} \\
\text{Me} & \quad \text{C} \\
\text{H} & \quad \text{H} \\
\text{C} & \quad \text{Me} \\
\text{OX} & \quad \text{OX}
\end{align*}
\]

\[X = H \text{ or } C_6H_4(COOH)CO.\]
Here we see that the electromeric effect of the electron releasing groups such as methoxy, ethoxy and dimethylamino, which facilitates the carbonium ion formation, involves only the lone pair of electrons of oxygen and nitrogen but not the alkoxy or amino groups. However, Robinson (J.C.S., 1947, 1299) has shown that ethoxyl group accelerates aromatic substitution more rapidly than the methoxyl group. Bradfield and Jones (J.C.S., 1928, 1006) have shown that the rate of bromination of alkyl-phenyl ethers is dependent on the nature of the alkyl group and is in the order —

\[
\text{iso-propyl} \succ \text{n-propyl} \succ \text{ethyl} \succ \text{methyl}.
\]

It thus seems probable that the electromeric effect is induced by the inductive release of electrons from the alkyl groups.
Discussion of preparation and resolution of \( p \)-ethoxybenzhydrol

\( p \)-Ethoxybenzhydrol was prepared by reducing \( p \)-ethoxybenzophenone. \( p \)-Ethoxybenzophenone was prepared by Friedel and Craft's method from phenetol and benzoyl chloride, using the procedure described in the experimental section which gave yields of the crude ketone of over 90%.

Preliminary experiments showed the desirability of keeping the temperature of the reaction mixture quite low; when this is not done some de-ethylation occurs as is shown by the liberation of 4-hydroxybenzophenone when the sodium hydroxide washings of the crude ketone are acidified.

4-Ethoxybenzhydrol is most conveniently prepared by reduction of \( 4 \)-ethoxybenzophenone in boiling ethanolic sodium hydroxide solution by means of zinc dust. The reaction seems somewhat slow in reaching completion but after some six hours an almost quantitative yield is obtained, and the alcohol rapidly sets to a crystalline mass. This is a considerable advantage because the slightly impure alcohol is pasty and its purification by crystallization is wasteful.

The process of reduction of the \( 4 \)-ethoxybenzophenone with magnesium and dry methanol proved to be extremely slow.

Generally, hydrogen phthalates of secondary alcohols are prepared by reacting equimolecular proportions of the alcohols and phthalic anhydride in presence of a slight excess of pyridine; Balfe, Doughty, Kenyon and Poplett (J.C.S., 1942, 605) prepared \( 4 \)-methoxybenzhydryl hydrogen phthalate in very good yield by using pyridine. But \( p \)-ethoxybenzhydrol reacts very
slowly with phthalic anhydride in the presence of pyridine alone. When
the carbinol was triturated with phthalic anhydride in a stronger base, cold
triethylamine with a few drops of pyridine, (necessary for complete solu­
tion), combination readily occurred with some evolution of heat resulting
in the production of solid \( p \)-ethoxybenzhydryl hydrogen phthalate in about
95% yield.

The function of pyridine and triethyl amine in acid
phthalic ester formation

Gerrard (J.C.S., 1940, 218) suggested that the function of pyridine
as a catalyst in the reaction between alcohol and acid chlorides or anhydride
might be to assist proton separation from the hydroxyl group, rather than
causing the ionic fission of the acid chloride or anhydride. Balfe,
Doughty, Kenvy, and Poplett (loc.cit.) confirmed this view by preparing
\( p \)-methoxy benzhydryl chloride from acetyl chloride and \( p \)-methoxy benzhydrol,
and \( p \)-methoxy benzhydryl acetate from the same two reactants in the presence
of pyridine. Later Baker and Gaunt (J.C.S., 1949, 13) showed that the
reaction might involve the formation of hydrogen bonding between the base
and alcohol. Thus it seems probable that the reaction is complex and
involves both mechanisms.

Hydrogen bonding between the hydroxyl group and the nitrogen of the
base would result in increased polarization and lengthening of the oxygen-
hydrogen bond, thus making alkoxy-hydrogen fission much easier. The
stronger the base the easier the formation of the hydrogen bond. As stated,
4-ethoxybenzhydrol reacts with phthalic anhydride more readily in the presence of triethylamine than in the presence of pyridine, the former \( [pK^b = 4.2] \) being a stronger base than the latter \( [pK^b = 8.8] \).

The aryl methyl alcohols containing more than one ortho- or para-alkoxy group seem to be the most reactive compounds known to undergo alkyl-oxygen heterolysis. As the tendency of an alcohol to yield a carbonium ion is increased, the tendency towards oxygen-hydrogen heterolysis \( (-O-H) \) decreases. Pyridine ceases to be a strong enough base to remove the proton and catalyse esterification by a \( B_{AC} \) mechanism, but a stronger base may be effective. (Davies and Kenyon, Quart. Rev., 1955, IX, No.3, p.226).

For example \( p \)-methoxy benzhydrol reacts with phthalic anhydride to give the acid ester in the presence of pyridine, Balfe, Doughty, Kenyon and Poplett \( (loc.cit) \) and Balfe, Kenyon and Wicks \( (J.C.S., 1946, 810) \). \( p \)-Ethoxybenzhydrol reacts with phthalic anhydride only slowly in the presence of pyridine but more readily in the presence of triethylamine (this thesis).

Di-\( p \)-methoxyphenyl carbinol is unreactive towards phthalic anhydride in the presence of pyridine but is esterified in the presence of triethylamine under similar conditions, yielding a mixture of the acid and the neutral phthalate \( (Balfe, Kenyon and Thain, J.C.S., 1951, 386) \). Dr. Nurula (unpublished work, result personally communicated) has prepared the hydrogen phthalic ester of anisyl-phenetyl-methanol by the interaction of this alcohol and phthalic anhydride in the presence of triethyl amine in dioxane-benzene mixture.

From these results it is inferred that the hydrogen-oxygen bond is
comparatively weaker in p-methoxybenzhydrol and gets stronger in other alkoxy substituted benzhydrols, the order of strength of the O - H bond being p-methoxybenzhydrol < p-ethoxybenzhydrol < di-4-methoxybenzhydrol < 4-ethoxy-4'-methoxybenzhydrol.

In order that the O - H bond may be stronger and consequently O and H atoms may be firmly bound, there should be an increased negative charge on the oxygen atom so that removal of the proton from the hydroxyl group might become difficult. This negative charge is due to the non-time variable factor of the electromeric effect, to which Ingold (J.C.S., 1926, 1310) gave the name mesomorphic effect, and later Ingold (J.C.S., 1933, 1124) showed that the weak acidity of anisic acid compared with benzoic acid is due to this property of the methoxyl group.

From a survey of the formation of acid phthalic esters of the alkoxybenzhydrols in the presence of pyridine and of triethylamine as described before, it can be seen that the mesomeric effect gets gradually stronger, in the tendencies of these alcohols in undergoing esterification by alkyl-oxygen fission rather than by alkoxy-hydrogen fission, the order being, p-methoxy-B < p-ethoxy-B < di-4-methoxy-B < 4-ethoxy-4'-methoxy-B. (B = Benzhydrol). In short, the O - H bond in these alcohols increases in strength due to increasing electron releasing influence of methoxy, ethoxy, di-methoxy, and ethoxy-methoxy groups in the p-positions of the benzene ring, which is relayed by conjugation to the alkyl-oxygen bond and, therefore formation of carbonium ion by alkyl-oxygen fission is more facilitated than alkoxy-hydrogen fission. However, Balfe, Kenyon, and Thain (loc.cit.) have
suggested that the stronger base like triethylamine overcomes the effect of the electron releasing substituents which hinder the separation of the proton from the hydroxyl group.

The course of reaction between \( p \)-ethoxybenzhydrol and phthalic anhydride in the presence of triethylamine can be represented as follows:

\[
\begin{align*}
\text{EtO} & \quad \text{H} \quad \text{C} \quad \text{C} \quad \text{H} + \text{Et}_3\text{N} \quad \text{EtO} \\
\text{H} & \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{H} \quad \text{C} \quad \text{O} \\
\text{O} & \quad \text{H} \quad \text{Ph} \quad \text{C} \quad \text{O} \quad \text{H} \quad \text{C} \quad \text{O}
\end{align*}
\]

The crude hydrogen phthalate was obtained in about 95% yield by using triethylamine. Attempts to purify the ester further by crystallisation from various solvents - polar or nonpolar - even at ordinary temperature, resulted in the quick separation of phthalic acid and the production of the neutral phthalic ester of the carbinol.

This illustrates the very marked influence of the \( p \)-ethoxy group in favouring alkyl-oxygen fission - greater than that of the corresponding \( p \)-methoxy group (Balfe, Doughty, Kenyon, and Poplett, \textit{loc.cit.}). When the
interaction of the carbinol with phthalic anhydride in the presence of pyridine was conducted at about 60 - 70° very little hydrogen phthalate could be isolated from the reaction mixture which consisted mainly of phthalic acid and the neutral ester.

Quinidine proved to be the most suitable alkaloid for effecting the resolution of the 4-ethoxybenzhydryl hydrogen phthalate. The hydrogen-phthalate failed to give a crystalline salt with brucine, cinchonidine, cinchonine, and strychnine. However, quinidine formed an insoluble crystalline salt with the hydrogen phthalic ester in acetone and the two diastereoisomeric salts differed considerably in their solubility in acetone at room temperature. After five crystallisations of the insoluble quinidine salt of the hydrogen phthalate from acetone the optically pure salt was obtained. Decomposition of a portion of this salt in acetone with dilute hydrochloric acid yielded the (-)-4-ethoxybenzhydryl hydrogen phthalate with \([\alpha]_D^{22} - 20.7°\) in acetone \((c, 5.005, 1,2)\). Decomposition of a portion of the alkaloidal salt which had been submitted to two further crystallisations yielded a hydrogen phthalic ester with \([\alpha]_D^{22} - 20.1°\) in acetone \((c, 2.85, 1,2)\). It thus appears highly probable that five recrystallisations of the salt had resulted in the complete separation of one of the diastereoisomeric salts.

Attempts to obtain the crystalline salt of (+)-4-ethoxybenzhydryl hydrogen phthalate with other alkaloids proved fruitless.

A suspension of the optically pure insoluble quinidine salt of the 4-ethoxybenzhydryl hydrogen phthalate when decomposed with hydrochloric acid and ice (Congo red) gave the (-)-4-ethoxybenzhydryl hydrogen phthalate in
crystalline form. The details of fractional crystallisation are shown on page 94 in the Experimental Section.

The specific rotatory powers of the (-)-4-ethoxybenzhydryl hydrogen phthalate were measured immediately after making up the solutions in different solvents, which are given in Table I, page 57.

As was found with the corresponding racemic hydrogen phthalic ester attempts to recrystallise this (-)-4-ethoxybenzhydryl hydrogen phthalate under the mildest conditions proved quite unsuccessful since dismutation to phthalic acid and the corresponding neutral ester rapidly supervened even in non-polar solvents.

The more soluble quinidine salt of the 4-ethoxybenzhydryl hydrogen phthalate on decomposition with hydrochloric acid - ice (Congo red) gave (+)-4-ethoxybenzhydryl hydrogen phthalate in crystalline form. The details are given in the Experimental Section.

Its specific rotatory power was measured immediately after making up the solution in methanol, which is given in Table IA, page 57.

As in the case of the corresponding (+)- and (-)-hydrogen phthalic esters attempts to recrystallise this (+)-isomeride resulted in its almost complete dismutation to phthalic acid and the neutral ester.

The details of the mechanism of ester hydrolysis are now known in considerable detail (Introduction). It has been observed by Kenyon and co-workers (J.C.S., 1942, 605; ibid, 1951, 386; etc.) that in concentrated aqueous-alcoholic alkaline medium the hydrolysis of the ester RC00R' proceeds by acyl-oxygen fission and, when R' has enough electron releasing properties,
as the strength of the aqueous alcoholic alkali is decreased, the carbinol obtained is highly racemized, in which case the hydrolysis takes place by a mechanism. Thus (+)-4-methoxybenzhydryl hydrogen phthalate gives (+)-4-methoxybenzhydrol with almost complete retention of optical activity when hydrolysis is carried out in ethanolic alkali containing 2% water, but much racemized alcohol is obtained when 20% water is present in the alcoholic alkali, whereas in 10 N aqueous sodium hydroxide extensive racemization takes place (Balfe, Doughty, Kenyon, and Poplett, loc.cit.).

However, when (-)-4-ethoxybenzhydryl hydrogen phthalate was hydrolyzed with alcoholic potash of different concentrations, only racemic 4-ethoxybenzhydrol was obtained in poor yield. But when the hydrolysis of (+)-4-ethoxybenzhydryl hydrogen phthalate was carried out with sodium ethoxide solution in 96% ethanol at almost the room temperature, optically pure (+)-or(-)-4-ethoxybenzhydrol respectively was obtained in almost quantitative yield. The details are given in the Experimental Section on pages 96/97.

The specific rotatory powers of (-)-4-ethoxybenzhydrol are given in Table II, page 57.

Influence of ethoxyl group on the reactivity of 4-ethoxybenzhydryl hydrogen phthalate

The hydrogen phthalic ester of the (+), (+)- or (-)-4-ethoxybenzhydrol decomposed rapidly when moist and impure. In the case of the optically active hydrogen phthalate a sticky mass having lower specific rotatory power than the optically pure hydrogen phthalate was obtained - it was presumably
due to formation of the neutral ester as a result of decomposition of the hydrogen phthalic ester.

(±), (+)- or (-)-4-ethoxybenzhydryl hydrogen phthalate on crystallisation from polar or non-polar solvents at ordinary temperature rapidly gives phthalic acid and neutral phthalic ester of the carbinol. The melting point of the hydrogen phthalate obtained from ether and light petroleum (b.p. 40-60°) altered after each subsequent crystallisations - some rise in m.p. was observed after each subsequent crystallisation and the proportion of the pasty mass increased considerably resulting in very poor yield of the hydrogen phthalate. The quantity of the pasty mass formed and variation of the m.p. of the crystals obtained depended on duration of contact of the hydrogen phthalate with the solvent. The optically active hydrogen phthalate racemised rapidly in solution in polar and non-polar solvents with separation of phthalic acid.

This illustrates the very marked influence of the p-ethoxyl group in favouring alkyl-oxygen fission - greater than that of the corresponding p-methoxy group: Balfe, Doughty, Kenyon, and Poplett (loc. cit.) having purified the 4-methoxybenzhydryl hydrogen phthalate by crystallisation from carbon disulphide.

The pronounced action of the p-ethoxyl group in promoting the alkyl-oxygen fission is further exhibited by the fact that the optically pure hydrogen phthalic ester decomposed a little even in dry and crystalline condition in several months resulting in the separation of a little phthalic acid (insoluble in dry chloroform) and formation of trace of neutral ester
(insoluble in aqueous sodium hydroxide solution).

The optically pure and dry hydrogen phthalic ester \([\alpha]_{\text{D}}^{\text{MeOH}} = 19.1^\circ\)
\((c, 2.75, 1, 2, t 22^\circ)\) and \([\alpha]_{\text{D}}^{\text{acetone}} = 20.9^\circ\)
\((c, 5, 1, 2, t 22^\circ)\) when examined after five months had \([\alpha]_{\text{D}}^{\text{MeOH}} = 15.6^\circ\)
\((c, 2.75, 1, 2, t 25^\circ)\) and had \([\alpha]_{\text{D}}^{\text{acetone}} = 15.7^\circ\)
\((c, 5.62, 1, 1, t 22^\circ)\) after 54 weeks. The optically pure
(-)-4-ethoxybenzhydryl hydrogen phthalate when freshly prepared had m.p. 82-
84° (decomp.). But after 54 weeks it had an indefinite m.p., softening at
84°. No such observation has been mentioned by Balfe, Doughty, Kenyon, and
Poplett (loc. cit.) for \(p\)-methoxybenzhydryl hydrogen phthalate, but Balfe,
Kenyon, and Thain (J.C.S., 1951, 386) have observed that di-(4-methoxyphenyl)
methyl hydrogen phthalate is unstable and both in the solid state or in solu-
tion disproportionates into phthalic acid and the neutral ester. Dr. Nurula
(unpublished work, result personally communicated) observed that 4-ethoxy-4'-
methoxybenzhydryl hydrogen phthalate was highly unstable and undergoes rapid
dismutation in solution to phthalic acid and corresponding neutral ester.

Dismutation of (-)-\(p\)-ethoxybenzhydryl hydrogen phthalate

\[
\text{into (±)-p-ethoxybenzhydryl (±)-p-ethoxybenzhydryl phthalate}
\]

The solution of (±)-4-ethoxybenzhydryl hydrogen phthalate in dilute
sodium hydroxide (equivalent amount of 0.3 N NaOH) turns milky within five
minutes. In about 4 - 5 hours a soft sticky mass of the neutral ester
settled at the bottom of the reaction vessel and the solution became clear.
The clear supernatant liquid when concentrated and decomposed with concen-
trated hydrochloric acid gave nearly half of the phthalic acid contained in
the parent hydrogen phthalic ester.

When the experiment was repeated with \((-\)-4-ethoxybenzhydryl hydrogen phthalate \([\alpha]_{D}^{CS2} = 61.5^\circ\) and equivalent quantity of 0.3 N sodium hydroxide, the solution became milky within 5 minutes and gradually deposited an oil which set to waxy solid in about 4 - 5 hours consisting mostly of \((\pm)\)-ethoxybenzhydryl\((-\)-ethoxybenzhydryl phthalate. Attempts to crystallise it from carbon-disulphide, benzene, ether-light petroleum \((b.p. 40-60^\circ)\) resulted in separation of thick viscous sticky mass - in methanol some phthalic acid was also obtained.

The neutral ester had \([\alpha]_{D}^{CS2} = 21.6^\circ\); it was washed with a little methanol to remove the adhering carbinol. It then had \([\alpha]_{D}^{CS2} = 20^\circ\) \((\bar{1}, 1, 0, 0.35)\). Nearly half of the phthalic acid contained in the parent hydrogen phthalate was obtained from the supernatant aqueous layer on acidification. The neutral ester \([\alpha]_{D}^{CS2} = 20^\circ; 21.6^\circ\) on hydrolysis gave the partially racemized carbinol, \([\alpha]_{D}^{CS2} = 15.7^\circ; a_{D}^{CS2} = 0.08^\circ\) \((\bar{a}, 0.51, 1, 1)\). Another sample of the neutral ester when hydrolyzed by heating on water bath for about 45 minutes gave the carbinol with \([\alpha]_{D}^{CS2} = 5^\circ\) \((a_{D}^{CS2} = 0.05^\circ, \bar{a}, 0.98, 1, 1)\).

The reaction is represented by the following scheme:

\[\]
One molecule of the hydrogen phthalate, by undergoing unimolecular alkyl-oxygen heterolysis, provides a carbonium ion, which can react with the hydroxyl ions to give the racemic alcohol or, as in this case, can be diverted to react with a second hydrogen phthalate molecule to give the dialkyl phthalate.

On a comparison of the disproportionation reaction of $p$-ethoxybenzhydryl hydrogen phthalate and $p$-methoxybenzhydryl hydrogen phthalate, (Balfe, Doughty, Kenyon and Poplett, loc.cit) into their respective neutral ester, we find that the former is quicker than the latter. This further shows the very marked influence of the $p$-ethoxy group in favouring alkyl-oxygen fission - greater than that of the $p$-methoxy group.

This disproportionation reaction is characteristic of acid esters, and indeed of most molecules whose electronegative group contains a
nucleophilic centre and which can undergo unimolecular alkyl-oxygen hetero-
lysis. However, the tendency of disproportionation of such acid esters
by unimolecular alkyl-oxygen fission increases as the electron releasing
power of the substituents in the phenyl ring increases. Thus $p$-ethoxy-
benzhydryl hydrogen phthalate disproportionates more quickly to the neutral
ester than the $p$-methoxybenzhydryl hydrogen phthalate. The di-(4-methoxy-
phenyl)methyl hydrogen phthalate disproportionates into its neutral ester
more quickly than $p$-ethoxybenzhydryl hydrogen phthalate since, as stated
before, the di-(4-methoxyphenyl)-methyl hydrogen phthalate was prepared
in very poor yield due to its strong tendency to form the neutral ester by
disproportionation either in solution or in dry state (Balfe, Kenyon and
Thain, loc.cit.).

As observed by Nurula (result personally communicated) the 4-ethoxy-4'-
methoxybenzhydryl hydrogen phthalate disproportionates into the neutral ester
still more quickly.

These neutral esters do not show any tendency of further quick decom-
position by unimolecular alkyl-oxygen heterolysis, and they are fairly
resistant to alkaline hydrolysis.

The (-)-$p$-ethoxybenzhydryl hydrogen phthalate is hydrolysed by
alcoholic sodium ethoxide solution almost at room temperature in about 3-5
minutes yielding optically active (-)-$p$-ethoxybenzhydrol in almost quanti-
tative yield; whereas the corresponding neutral ester takes a longer time
for hydrolysis by the ethanolic sodium ethoxide solution at higher
temperature. It is only after about 2-3 hours of vigorous refluxing
on a steam bath that the di-\(\text{p}\)-ethoxybenzhydryl phthalate is hydrolysed by 5 N ethanolic (96%) potassium hydroxide solution. A similar observation has been reported by Balfe, Kenyon and Thain (loc.cit.) in the case of the hydrogen phthalate and the neutral phthalate of di-(4-methoxyphenyl) methanol.

This peculiar stability of the neutral esters in comparison with the corresponding hydrogen phthalates has been attributed by Kenyon and Thain (Thain's thesis) to their symmetrical structure, in which the electrical forces (dipoles) are completely neutralised rendering the neutral ester less reactive. The reactivity of the hydrogen phthalates is ascribed to hydrogen bond formation, which facilitates the formation of a carbonium ion and thus the formation of neutral ester even in the dry state. This is shown in the diagram below.

\[
\begin{align*}
\text{Reaction of benzhydrol and its hydrogen phthalate with sodium-\(\text{p}\)-toluene sulphinate} \\
\text{Both (\(\pm\))- and (\(-\))-\(\text{p}\)-ethoxybenzhydrol and the corresponding hydrogen phthalic esters readily react with sodium-\(\text{p}\)-toluene sulphinate at room temperature, under conditions described in the Experimental Section, pages 101/102}
\end{align*}
\]
to yield 4-ethoxybenzhydryl-£-tolyl sulphone - the optically active carbinol and the optically active hydrogen phthalate always yielded racemic sulphone.

Thus when (-)-4-ethoxybenzhydrol, $[\alpha]^D_{22} - 13.7^\circ$ in benzene, was dissolved in 90% formic acid and the solution mixed with a solution of sodium-£-toluene sulphinate in 90% formic acid, turbidity appeared within 30 seconds and a flocculent crystalline mass of 4-ethoxybenzhydryl-£-tolyl sulphone separated within one minute. This sulphone had $[\alpha]^\text{CHCl}_3_{22} + 0^\circ$.

Similarly when the experiment was repeated with (±)-4-ethoxybenzhydryl hydrogen phthalate and (-)-4-ethoxybenzhydryl hydrogen phthalate, $[\alpha]^D_{22} - 41.4^\circ$ in benzene, in equivalent quantities of 0.3N sodium hydroxide and sodium-£-toluene sulphinate solution, the mixture became milky within 3-4 minutes due to separation of 4-ethoxybenzhydryl-£-tolyl sulphone. The sulphone formed from the optically active hydrogen phthalic ester had $[\alpha]^\text{D}_{22} + 0^\circ$ in acetone. This reaction seems somewhat quicker than the corresponding reaction of £-methoxybenzhydryl hydrogen phthalate and £-methoxybenzhydrol (Balfe, Doughty, Kenyon and Poplett, loc.cit.)

This furnishes a further support to the stronger influence of 4-ethoxy group than that of the 4-methoxy group in promoting alkyl-oxygen fission.

Formation of racemic sulphone from the optically active benzhydrol and (-)-4-ethoxybenzhydryl hydrogen phthalate implies the separation of the planar (4-ethoxybenzhydryl)$^+$ carbonium ion by unimolecular heterolysis which gives rise to racemic sulphone. The course of reaction is shown below.
(i) \[
\text{MeC}_6\text{H}_4\text{SO}_2\text{Na} + R^{\ominus}(\text{dl}) \rightarrow \text{MeC}_6\text{H}_4^- \text{S} \rightarrow R + \text{Na}^{\oplus}
\]

\[ R = \text{4-ethoxybenzhydryl group.} \]

(ii) \[
\text{MeC}_6\text{H}_4\text{SO}_2\text{Na} + \text{C}^{\ominus} + \text{OH} \rightarrow \text{MeC}_6\text{H}_4^- \text{S} \rightarrow \text{C} = R + \text{Na}^{\oplus}
\]

Balfe, Kenyon and Thain (loc. cit.) have prepared the di-(4-methoxy-phenyl) methyl-\(\text{p}\)-tolyl sulphone from di-(4-methoxyphenyl)methyl hydrogen phthalate and sodium-\(\text{p}\)-toluene sulphinate in aqueous acetone in 92% yield in about 1 minute. This further shows the strong influence of two methoxy groups in promoting alkyl-oxygen fission greater than the only one methoxy group and only one ethoxy group in the \(\text{p}\)-position of the benzene ring.

Another piece of evidence which goes to show the influence of the ethoxy group in inducing alkyl-oxygen fission to be greater than the
methoxy group is found in the rapid formation of di-4-ethoxybenzhydryl ether on treatment of 4-ethoxybenzhydrol with concentrated hydrochloric acid and subsequent washing with water. Thus the ethereal solution of (±)-4-ethoxy-benzhydrol when shaken with concentrated hydrochloric acid and subsequently washed with water until the aqueous washings were acid-free, gave rhombs of di-4-ethoxybenzhydryl ether on crystallisation from ether-light petrol (b.p. 40-60°). The course of reaction may be indicated in the following manner.

\[ \text{R} = \text{C}_6\text{H}_5; \quad \text{R'} = \text{EtO.C}_6\text{H}_4^- \]

Balfe, Doughty, Kenyon, and Poplett (loc.cit.) in a similar manner obtained the corresponding di-alkyl ether from 4-methoxy benzhydrol. Balfe, Kenyon, and Thain (loc.cit.) observed that the di-(4-methoxyphenyl) methanol under mildly acidic conditions readily decomposes into water and the dialkyl ether.

Reactions of methanol with 4-ethoxybenzhydryl hydrogen phthalate

When 4-ethoxybenzhydryl hydrogen phthalate is treated with dry methanol, 4-ethoxybenzhydryl methyl ether is rapidly formed. The reaction was followed by tracing the rate of racemization of the optically active hydrogen phthalate in dry methanol.
Thus when a solution of (-)-p-ethoxybenzhydryl hydrogen phthalate in dry methanol, having initially $[\alpha]_D^{25} = 15.6^\circ$, was examined after some three hours, the specific rotation was found to be, $[\alpha]_D^{25} = 11.3^\circ$. The rate of loss of optical activity was such that the solution had $[\alpha]_D^{25} = 0^\circ$ in about 24 hours. The specific rotatory powers of (-)-4-ethoxybenzhydryl hydrogen phthalate in methanol at different intervals are given in Table III on page 58. On further examination it was found that the solution had $[\alpha]_D^{25} = 0.2^\circ$ in about 25.5 hours, reaching to a maximum value $[\alpha]_D^{25} = 2.4^\circ$ in about 55 hours, the rotation remained constant for about 5 weeks after which it was not examined. The experiment was repeated with different specimens of (-)-4-ethoxybenzhydryl hydrogen phthalate and in each case the same result was obtained.

This result shows the reaction between the solvent methanol and the (-)-4-ethoxybenzhydryl hydrogen phthalate to give the (+)-4-ethoxybenzhydryl methyl ether and (+)-4-ethoxybenzhydryl methyl ether by alkyl-oxygen fission involving monomolecular nucleophilic substitution.

Substitution generally means the replacement of hydrogen by some other atom or group. But in a wider sense a substitution reaction means the replacement of any atom or group by any other. This can be demonstrated by the general example given below:

$$
A + R - X \longrightarrow R - A + X \\
A-B + R-X \longrightarrow R - B + X-A
$$

Lapworth (Nature, 1925, 115, 625) classed the chemical reagents into
two groups, namely (i) cationoid and (ii) anionoid. The cationoid reagents in a chemical reaction seek a point in the molecule where electron availability is high and the anionoid reagents go to a point in the molecule where there is deficiency of electrons. Ingold (J.C.S., 1933, 1120; Chem. Rev., 1934, 15, 265) introduced the convenient terms 'electrophilic' and 'nucleophilic' for cationoid and anionoid reagents respectively.

Substitution by electrophilic and nucleophilic reagents may be expressed by the following general equation:

\[
\begin{align*}
A^+ + R^- + X^+ &\rightarrow R - A + X^+ \quad \text{(Electrophilic substitution)} \\
A^+ + B^- + R^+ - X^- &\rightarrow R - B + AX \quad \text{(S$_B$)}
\end{align*}
\]

\[
\begin{align*}
A^- + R^- - X^- &\rightarrow R - A + X^- \quad \text{(Nucleophilic substitution)} \\
A^- + B^- + R^+ - X^- &\rightarrow R - B + X^-A \quad \text{(S$_N$)}
\end{align*}
\]

Any type of substitution may be either unimolecular or bimolecular. The unimolecular and bimolecular electrophilic substitutions are designated as S$_B$1 and S$_B$2 respectively, whereas the unimolecular and bimolecular nucleophilic substitution as S$_N$1 and S$_N$2 respectively.

The bimolecular substitution involves the addition of one group and the removal of another, both the processes occurring simultaneously. Thus in a bimolecular substitution of the type \( A + R - X \rightarrow RA + X \), the attacking reagent \( A \) will approach the molecule \( RX \) from the side of \( R \) which is opposite to \( X \) and \( X \) recedes simultaneously. Thus a transition
complex is formed, which involves the bringing up of the reagent and stretching of the bond which is to be broken, as for example:

\[ A + RX \longrightarrow A \ldots, R \ldots X \longrightarrow RA + X \]

If the seat of substitution be an asymmetric carbon atom, the net result of bimolecular substitution will be inversion of configuration, and that this does take place has been proved to a good degree of certainty by Kenyon and co-workers (J.C.S., 1923, 123, 44; ibid, 1925, 127, 399 and 2564; ibid, 1929, 1700; ibid, 1933, 173; ibid 1935, 1663) and Hughes and his collaborators (J.C.S., 1935, 1525; ibid, 1936, 1173; ibid, 1938, 209).

However, Ingold and Hughes (J.C.S., 1935, 244) and Hughes (Trans. Farad.Soc., 1938, 34, 165) have recognised another mechanism for substitution at a saturated carbon atom - aliphatic substitution - in solution only, in which the addition and removal processes are not simultaneous but the slow removal of X is followed by the rapid addition of A.

In a nucleophilic substitution at an asymmetric carbon atom by the unimolecular mechanism, first a +ve carbonium ion is formed, which loses its asymmetry and becomes flat thus giving rise to a racemic product (Wallis and Adams, J.A.C.S., 1933, 55, 3838).

However, Cowdrey, Hughes, and Ingold (J.C.S., 1937, 1208) and Cowdrey, Hughes, Ingold, Masterman, and Scott (J.C.S., 1937, 1252) have shown by hydrolysis and alcoholysis of α-halogenated acids and esters that when the carbonium ion is short-lived, the receding ion will be close enough
to produce a dissymmetric shielding of the carbonium ion, and substitution with inversion will be preponderant in the unimolecular mechanism.

The presence of unsaturated group such as phenyl, at the seat of substitution, would stabilise the ion by resonance.

\[
\text{\textopen怀抱符号} \quad + \quad \text{\textopen怀抱符号} \quad \rightarrow \quad \text{\textopen怀抱符号} 
\]

It would also flatten the ion. The net result is greater racemization. The formation of 4-ethoxybenzhydryl methyl ether is accompanied by much racemization with a little inversion.

That such ether formation must involve alkyl-oxygen fission has been shown by Hammond and Rudesill (J.A.C.S., 1950, 72, 2769), who obtained triphenylmethyl ethyl ether and benzoic acid by the solvolysis of triphenylmethyl benzoate in methanol. They further established the unimolecular nature of the reaction, which was kinetically of the first order, the rate of reaction being unchanged by the addition of small amounts of the ethoxide ion.

This is further supported by the fact that triphenylmethyl acetate in methanol is converted into triphenylmethyl - methyl ether and acetic acid, (Gomberg and Davies, Ber., 1903, 36, 3926). That this reaction is of first order has been shown by Bunton ("Structure and Mechanism in Organic Chemistry" by C.K.Ingold, Bell, London, 1953, p.764.

Alkyl-oxygen fission was established by Cohen and Schneider (J.A.C.S.,
in the acid catalyzed and uncatalyzed methyl alcoholysis of tert-butyl benzoate, tert-butyl methyl ether and benzoic acid being obtained. The mechanism proposed by Cohen and Schneider is shown below:

\[
\begin{align*}
R\cdot COOCMe_3 + H^+ & \quad \rightleftharpoons \quad R\cdot C \quad \rightleftharpoons \quad RCOOH + \cdot Me_3 \\
\cdot Me_3 + MeOH & \quad \rightarrow \quad Me - O\cdot CMMe_3 + H^+ \\
RCOOH + MeOH & \quad \rightleftharpoons \quad RCOOMe + H_2O.
\end{align*}
\]

Bunton (quoted by Ingold, "Structure and Mechanism in Organic Chemistry", p.780) observed when hydrogen chloride was added as catalyst, the reaction becomes faster and gives the same products as obtained by Cohen and Schneider (loc.cit.), and that the rate of reaction was proportional to the amount of catalyst present. He also obtained some substantial proportion of iso-butylene and thus showed that all the products obtained were the result of direct decomposition of the ester by alkyl-oxygen heterolysis.

Bunton further provided a second piece of evidence in support of this mechanism of etherification by obtaining triphenylmethyl methyl ether and acetic acid by the interaction of triphenylmethyl acetate and excess of methanol. He further showed that the rate of the reaction was accelerated in the presence of added hydrogen chloride.

It thus appears probable that this acid catalyzed etherification
must involve the unimolecular alkyl-oxygen fission \((A_{ul})\), which is shown below:

\[
\begin{align*}
\text{R.COOC Me}_3 & \rightarrow \text{R.COO}^- + \text{Me}_3^+ \\
\text{loses a proton} \\
\text{Me}^- & \rightarrow \text{CH}_2^- + \text{H}^+ \\
\end{align*}
\]

and in absence of the catalyzing acid, the weaker acid methanol might induce the reaction, resulting in a solvolytic reaction of the \(S_{cl}\) type.

In the reaction of 4-ethoxybenzhydryl-hydrogen phthalate and methanol, the 4-ethoxybenzhydrylmethyl ether is obtained in almost quantitative yield and no 4-ethoxybenzhydrol is formed. The reaction, therefore, is definitely of \(S_{cl}\) type which involves \(A_{ul}\) mechanism, because the solvent methanol can ionise to yield \(\text{CH}_2\overline{O}^-\) and \(\text{H}^+\) ions.

\[
\text{CH}_3\overline{OH} \rightarrow \text{CH}_2\overline{O}^- + \text{H}^+
\]

Formation of the mixed ether by \(A_{ul}\) mechanism is ruled out because no 4-ethoxybenzhydrol or methyl hydrogen phthalate is obtained as could be anticipated by this mechanism.

\[
\begin{align*}
\text{R'COOR} + \text{H}^+ & \rightarrow \text{R'COOH} \rightarrow \text{R'C} \rightarrow \text{HOR} \\
\text{R'C} + \text{MeO}^- & \rightarrow \text{R'COOMe} \\
\text{R} & = \text{EtO C}_6\text{H}_4\text{CH.Fh} \\
\text{R'} & = \text{C}_6\text{H}_4\text{COOH}
\end{align*}
\]
On the contrary almost quantitative yields of phthalic acid and the mixed ether are obtained. The chances of $A_{AC}^2$ mechanism being operative in the ether formation seem to be improbable for the same reasons.

$$R'CO.OR + H^+ \xrightarrow{\text{fast}} R'CO.OHR$$

$$R'CO.OHR + \text{MeOH} \xrightarrow{\text{slow, fast}} R'CO.OHMe + ROH$$

$R$ and $R'$ = same as above.

The probability of formation of the ether by acyl-oxygen fission mechanism demands the ionisation of the solvent methanol as $\text{CH}_3\text{OH} \rightarrow \text{CH}_3^+ + \text{OH}^-$, which is highly improbable.

The 4-ethoxybenzhydryl methyl ether obtained in the reaction is highly racemized, but contains a little optically active ether having the sign of rotation opposite from the parent hydrogen phthalate. This suggests that in the ether formation the mechanism $A_{AL}^1$ is mainly operative. But the possibility of $A_{AL}^2$ mechanism also being operative in the formation of the ether cannot altogether be ruled out because the relation of the absolute configuration of the 4-ethoxybenzhydryl methyl ether with its sign of rotation is unknown.

However, the probability that ether formation proceeded by mechanism $A_{AL}^1$ is supported by the following fact, quoted by Kenyon and Davies (Quart. Rev., 1955, IX, No.3, p.218-219).

It has been shown by Cowdrey, Hughes, Ingold, Mastermaan and Scott (J.C.S., 1937, 1252) that unimolecular heterolysis at the asymmetric centre
of an optically active compound will produce a carbonium ion, which will assume a planar trigonal configuration (unless this is prevented by steric strain or by intramolecular bonding.) If there is equal probability of attack by the nucleophilic reagent on either side of this planar ion, the product of reaction will be racemic. However, if the reagent attacks before the displaced electronegative group has receded by more than a few Angströms, this group may exert an asymmetric shielding effect upon the reaction centre directing the reagent's attack mainly on the side distant from the replaced group, with resultant inversion of configuration.

The resonance in carbonium ions containing phenyl groups at the reaction centre will (a) induce coplanarity at the ionic centre, and (b) prolong the life of the ions and permit their further separation from the displaced group before their reaction with the nucleophilic reagent; both these tend to increase the degree of racemization during reaction. The same factor of electron release which promotes alkyl-oxygen heterolysis thus promotes racemization in the resulting carbonium ions. Therefore, in general, the more readily an optically active compound undergoes alkyl-oxygen heterolysis, the more nearly racemic will be the products of such reaction.

Thus the rapid rate of racemization of the (-)-4-ethoxybenzhydryl hydrogen phthalate in methanolic solution suggests that the hydrogen phthalate ionises to give the (-)-4-ethoxybenzhydryl carbonium ion, which is stabilised by resonance and attains a coplanar trigonal form giving rise to racemic 4-ethoxybenzhydryl methyl ether by nucleophilic attack of methoxide \( \text{CH}_3\text{O}^- \) ion. However, the formation of the ether with the sign of rotation
opposite from the parent hydrogen phthalate suggests that the rate of ionisation of the hydrogen phthalate resulting in the complete separation of the alkyl carbonium ion $R^+$ from the receding electronegative carboxylate group is slower than the rate of attack by the methoxide, $\text{CH}_3\text{O}^-$ ion. Had there been complete ionisation of the hydrogen phthalate, giving the alkyl carboxonium ion $R^+$ before the nucleophilic attack by the methoxide ion, 50% of each configuration of the mixed methyl ether would have been formed. But faster attack by the methoxide ion, $\text{CH}_3\text{O}^-$, on the group $R^+$ from the other side before it is completely separated from the receding acidic component results in a greater proportion of the mixed ether with inversion. Thus the total product possesses some optical activity with the inverted configuration predominating. This can be shown by the following scheme:

\[
\begin{align*}
\text{Phthalic acid} & \quad \leftrightarrow \quad \text{COO}^- + R^+ \quad (1) \\
\text{R}^+(1) & \quad \rightarrow \quad \text{ROMe} \\
\end{align*}
\]
A similar inversion of configuration has not been recorded in the case of 4-methoxybenzhydryl hydrogen phthalate by Balfe, Doughty, Kenyon, and Poplett (loc.cit.), who obtained only racemic 4-methoxybenzhydryl methyl ether by the interaction of (+)-4-methoxybenzhydryl hydrogen phthalate and methanol.

This difference in nucleophilic attack by methoxide ion on (+)-4-methoxybenzhydryl hydrogen phthalate and 4-ethoxybenzhydryl hydrogen phthalate finds explanation in the following arguments. The formation of (+)-4-ethoxybenzhydryl methyl ether (Balfe, Doughty, Kenyon, and Poplett, loc.cit.) indicates that the rate of ionisation of the (+)-4-methoxybenzhydryl hydrogen phthalate furnishing R⁺ carbonium ion competes well with the rate of nucleophilic attack by the methoxide ion, CH₃O⁻. The
electromeric shift of electrons from methoxyphenyl group reinforced by the inductive release of electrons from the methyl group of the methoxyl substituent increases the electron density at the alkyl carbon atom but this is not strong enough to give complete hold of the bonding electrons of the \( \text{C}^{\delta+} \text{O}^{\delta-} \) bond to oxygen. Thus only a feeble electrostatic force is set up between \( \text{C}^{\delta+} \text{O}^{\delta-} \) group which is not strong enough to hold \( \text{C}^{\delta+} \text{O}^{\delta-} \) bond firmly and counteract the ionising power of methanol, which has appreciable dielectric constant \( (\text{D} = 33.7) \), and to slow the rate of separation of the carbonium ion from the phthalate group. This results in rapid formation of carbonium ion, which is stabilised by resonance and is long lived, and thus attains coplanarity, giving the racemic mixed ether by nucleophilic attack of methoxide ion, \( \text{CH}_3\text{O}^- \).

But in the case of the \((-\)-4-ethoxybenzhydryl hydrogen phthalate the electron releasing properties of ethoxyl group, being greater than that of the methoxyl group, increase the electron density at the alkyl carbon atom, which is enough to give greater hold of the \( \text{C}^{\delta+} \text{O}^{\delta-} \) bond electrons to oxygen atom which is manifested in a stronger electrostatic force between \( \text{C}^{\delta+} \text{O}^{\delta-} \) atoms. The negative charge at the oxygen atom combined with the negative charge of the second carboxylate ion in the phthalate group holds the carbonium carbon atom more firmly and thus the stronger electrostatic force opposes the ionising power of the solvent methanol to a fair extent and consequently slows down the rate of complete separation of the carbonium ion from the phthalate group, giving a chance for the methoxide ion, \( \text{CH}_3\text{O}^- \), to attack from the opposite side. This, and the shielding effect
of the phthalate group, result in the formation of the mixed ether with inversion.

The Hughes-Ingold group (J.C.S., 1946, 115, et seq.) have given evidence that the $S_N^2$ reaction can be completely suppressed by steric hindrance. Thus attack by the methoxide ion $\text{CH}_2\text{O}^-$, on the carbonium ion $R^+$ to give rise to the mixed ether with inversion by $S_N^2$, looks improbable for steric reasons. Also the formation of the mixed ether with retention of configuration seems improbable for steric factors and repelling effect of the free negative carboxylate group on the negative methoxide ion, $\text{CH}_2\text{O}^-$. The scheme of the reaction of the mixed ether formation is given below:

\[
\begin{align*}
\text{COO}^- \quad \text{OR}^{(dl)} & \quad \text{COO}^- - \delta^- 5^+ \quad \text{H}^{(+\text{MeOH})} \quad \text{COO}^- - 5^- \ldots R \\
\downarrow & \\
\text{COOH} & \quad \text{COOH} + R^+^{(dl)}
\end{align*}
\]

(i) $R^+^{(dl)} + \text{MeO}^- \quad \text{ROMe}^{(dl)}$

$R = \text{MeO}^-$
Further, on comparison of the rate of racemization of (+)-4-methoxybenzhydryl hydrogen phthalate (Balfe, Doughty, Kenyon, and Poplett, loc.cit.) and that of (-)-4-ethoxybenzhydryl hydrogen phthalate in methanol, vide Table III and IV, pages 58/59, we find that the former is much more rapid than the latter. This indicates that dissociation to the carbonium ion is more rapid with the electron-release of the ethoxy - than that of the methoxy - group.

To obtain a quantitative result, racemization has been assumed to be of the first order, and values of $K$, hr$^{-1}$ calculated.

Inspection of the values of $K$ for the racemization of (-)-4-ethoxybenzhydryl hydrogen phthalate show 0.086 hr$^{-1}$ to be a representative figure. For the (+)-4-methoxy compound (unfortunately without adequate control of temperature) a representative value is 0.011 hr$^{-1}$. The former is about 8
times as great as the latter, and provides a measure of the greater electron release of the ethoxy- as compared with the methoxy- group.

A summary of the influence of alkoxyl groups on the formation of hydrogen phthalic esters, and on the reactions of the hydrogen phthalic esters of the benzhydrols, is given in the attached table.

The alcohols compared are as follows:

A. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OH}
\end{array}
\] 

B. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OMe} \\
\text{OH}
\end{array}
\]

C. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OMe} \\
\text{OH}
\end{array}
\]

D. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OMe} \\
\text{OH}
\end{array}
\]

E. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OMe} \\
\text{OMe} \\
\text{OH}
\end{array}
\]

F. 
\[
\begin{array}{c}
\text{MeO} \\
\text{C} \\
\text{OMe} \\
\text{OH}
\end{array}
\]

G. 
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{OEt} \\
\text{CH}
\end{array}
\]

H. 
\[
\begin{array}{c}
\text{MeO} \\
\text{C} \\
\text{OEt} \\
\text{OH}
\end{array}
\]


<table>
<thead>
<tr>
<th>No. and name of alcohol</th>
<th>Formation of H.P.</th>
<th>Alkyl-oxygen fission reactions of H.P.</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Neutral Ester</td>
<td>Sulphone</td>
</tr>
<tr>
<td>A. Benzhydrol</td>
<td>H.P. formed in presence of pyridine at 60-70° for 5 hrs. Stable in methylene chloride.</td>
<td>Does not form neutral ester in dil. alkali.</td>
<td>Solution in dil. 0.3N NaOH remains clear for 2 weeks on heating for 10 hrs. on steam bath sulphone formed.</td>
</tr>
<tr>
<td>B. p-methoxy-benzhydrol</td>
<td></td>
<td></td>
<td>Forms sulphone in dil. alkali slowly during six days.</td>
</tr>
<tr>
<td>D. p-methoxy-benzhydrol</td>
<td>1. H.P. formed in presence of pyridine at 55-60° for 4-5 hrs. Crystallised from carbon disulphide. 2. H.P. formed in presence of pyridine at room temperature over several days.</td>
<td>Partially racemised neutral ester in 18 hrs. Turns turbid in a few minutes.</td>
<td>(+)-sulphone formed within 20 minutes in presence of one equivalent of 0.3N NaOH.</td>
</tr>
</tbody>
</table>

(Contd.)
<table>
<thead>
<tr>
<th>No. and name of alcohol</th>
<th>Formation of H.P.</th>
<th>Alkyl-oxygen fission reactions of H.P.</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Neutral Ester</td>
<td>Sulphone</td>
</tr>
<tr>
<td>E. 3:4-dimethoxy-benzhydrol</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Sulphone formed on refluxing the carbinol and p-toluene sulphinic acid in chloroform for several hrs.</td>
</tr>
<tr>
<td>F. Di-p-methoxybenzhydrol</td>
<td>H.P. in poor yield, in presence of triethyl amine in peroxide-free dioxane at room temperature. Unstable.</td>
<td>Forms neutral ester during crystallization from various solvents.</td>
<td>Sulphone formed in presence of aqueous acetone in 1 minute.</td>
</tr>
<tr>
<td>G. p-ethoxybenzhydrol</td>
<td>H.P. rapidly formed in good yield in presence of triethylamine and a little pyridine at room temperature. Unstable. Could not be purified by crystallisation.</td>
<td>Neutral ester formed in dil. alkali (0.3 N NaOH) turns turbid in 3-5 mins. Optically active H.P. gives partially racemized neutral ester.</td>
<td>1.(+)-sulphone formed in presence of dil. alkali in a few mins. 2.(+) -sulphone formed from carbinol in formic acid.</td>
</tr>
<tr>
<td>H. 4-ethoxy-4'-methoxybenzhydrol</td>
<td>H.P. rapidly formed at room temp. in good yield in presence of triethylamine in dioxane-benzene mixture unstable. Undergoes dismutation to neutral ester and phthalic acid during crystallization.</td>
<td>Formed neutral ester during crystallization of H.P. from carbon disulphide.</td>
<td>Not prepared</td>
</tr>
</tbody>
</table>
This comparison indicates that the introduction of the electron releasing groups such as MeO, EtO, etc. into the phenyl radical promotes alkyl-oxygen fission as is evident by the rate of formation of racemic sulphone, partially racemized neutral ester and alkoxybenzhydryl methyl ether from the benzhydrols and their respective hydrogen phthalates. It is also observed that the tendency of alkyl-oxygen fission of these alkoxy substituted benzhydryl compounds increases as the MeO-group is replaced by EtO-, or more MeO- or EtO-groups are introduced in the phenyl ring.

Further it can be noticed that in contrast to the 2- and 4-methoxy diphenyl compounds, 3-methoxydiphenyl hydrogen phthalate shows little or no tendency to react by alkyl-oxygen heterolysis, the (+c) conjugative electron releasing effect of the methoxy group is not relayed to the alkyl-oxygen bond from the meta-position, and hence cannot facilitate ionization.
TABLE I
Specific rotatory powers of (-)-£-ethoxybenzhydryl hydrogen phthalate in different solvents.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°C</th>
<th>(\alpha_{5893})</th>
<th>(\alpha_{5461})</th>
<th>(\alpha_{4358})</th>
<th>([\alpha]_{5893})</th>
<th>([\alpha]_{5461})</th>
<th>([\alpha]_{4358})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon disulphide</td>
<td>0.260</td>
<td>2</td>
<td>22</td>
<td>-0.32°</td>
<td>-0.40°</td>
<td>-0.68°</td>
<td>-61.5°</td>
<td>-77°</td>
<td>-131°</td>
</tr>
<tr>
<td>Benzene</td>
<td>2.715</td>
<td>2</td>
<td>22</td>
<td>-2.25°</td>
<td>-2.69°</td>
<td>-5.04°</td>
<td>-41.4°</td>
<td>-49.5°</td>
<td>-93°</td>
</tr>
<tr>
<td>Acetone</td>
<td>5.00</td>
<td>2</td>
<td>22</td>
<td>-2.09°</td>
<td>-2.52°</td>
<td>-4.8°</td>
<td>-20.9°</td>
<td>-25.2°</td>
<td>-48°</td>
</tr>
<tr>
<td>Methanol</td>
<td>2.75</td>
<td>2</td>
<td>22</td>
<td>-1.05°</td>
<td>-1.29°</td>
<td>-2.29°</td>
<td>-19.1°</td>
<td>-23.5°</td>
<td>-41.6°</td>
</tr>
</tbody>
</table>

TABLE IIA
Specific rotatory powers of (+)-£-ethoxybenzhydryl hydrogen phthalate.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°C</th>
<th>(\alpha_{5893})</th>
<th>(\alpha_{5461})</th>
<th>(\alpha_{4358})</th>
<th>([\alpha]_{5893})</th>
<th>([\alpha]_{5461})</th>
<th>([\alpha]_{4358})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>2.65</td>
<td>2</td>
<td>22</td>
<td>+0.70°</td>
<td>+0.76°</td>
<td>-</td>
<td>+13.2°</td>
<td>+14.3°</td>
<td>-</td>
</tr>
</tbody>
</table>

TABLE II
Specific rotatory powers of (-)-£-ethoxybenzhydryl in different solvents.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°C</th>
<th>(\alpha_{5893})</th>
<th>(\alpha_{5461})</th>
<th>(\alpha_{4358})</th>
<th>([\alpha]_{5893})</th>
<th>([\alpha]_{5461})</th>
<th>([\alpha]_{4358})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon disulphide</td>
<td>0.615</td>
<td>2</td>
<td>21</td>
<td>-0.54°</td>
<td>-0.65°</td>
<td>-1.15°</td>
<td>-43.9°</td>
<td>-53.2°</td>
<td>-94°</td>
</tr>
<tr>
<td>Benzene</td>
<td>1.525</td>
<td>2</td>
<td>22</td>
<td>-0.52°</td>
<td>-0.56°</td>
<td>-0.98°</td>
<td>-13.7°</td>
<td>-18.5°</td>
<td>-32.1°</td>
</tr>
</tbody>
</table>

TABLE IIIA
Specific rotatory powers of (+)-£-ethoxybenzhydryl.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°C</th>
<th>(\alpha_{5893})</th>
<th>(\alpha_{5461})</th>
<th>(\alpha_{4358})</th>
<th>([\alpha]_{5893})</th>
<th>([\alpha]_{5461})</th>
<th>([\alpha]_{4358})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>0.81</td>
<td>2</td>
<td>22</td>
<td>+0.1°</td>
<td>+0.13°</td>
<td>-</td>
<td>+12.0°</td>
<td>+15.4°</td>
<td>-</td>
</tr>
</tbody>
</table>
Racemization of (-)-4-ethoxybenzhydryl hydrogen phthalate in methanol: $G 2.75, 1 2; \ t 25^\circ$ in air-thermostatted room
"$\alpha_0$" = total change in rotation; "$\alpha_t$" = change in rotation after time $t$.

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>$\alpha_D$</th>
<th>$[\alpha]_D$</th>
<th>&quot;$\alpha_t$&quot;</th>
<th>$2.303 \times \log_{10}\frac{\alpha_0}{\alpha_t}$</th>
<th>Velocity coefficient $k$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>-0.86°</td>
<td>-15.6°</td>
<td>-17.8°</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>3.0</td>
<td>-0.61°</td>
<td>-11.3°</td>
<td>-13.5°</td>
<td>0.2766</td>
<td>0.0922</td>
</tr>
<tr>
<td>7.5</td>
<td>-0.38°</td>
<td>-6.8°</td>
<td>-9.0°</td>
<td>0.6822</td>
<td>0.091</td>
</tr>
<tr>
<td>8.5</td>
<td>-0.36°</td>
<td>-6.5°</td>
<td>-8.7°</td>
<td>0.716</td>
<td>0.0842</td>
</tr>
<tr>
<td>21.5</td>
<td>-0.03°</td>
<td>-0.6°</td>
<td>-2.8°</td>
<td>1.849</td>
<td>0.086</td>
</tr>
<tr>
<td>24</td>
<td>± 0°</td>
<td>± 0°</td>
<td>-2.2°</td>
<td>2.091</td>
<td>0.087</td>
</tr>
<tr>
<td>25.5</td>
<td>+0.01°</td>
<td>+0.2°</td>
<td>-2.0°</td>
<td>2.187</td>
<td>0.0866</td>
</tr>
<tr>
<td>30</td>
<td>+0.05°</td>
<td>+0.86°</td>
<td>-1.34°</td>
<td>2.586</td>
<td>0.0862</td>
</tr>
<tr>
<td>32.5</td>
<td>+0.06°</td>
<td>+1.1°</td>
<td>-1.1°</td>
<td>2.784</td>
<td>0.0857</td>
</tr>
<tr>
<td>48</td>
<td>+0.10°</td>
<td>+1.9°</td>
<td>-0.3°</td>
<td>4.0853</td>
<td>0.085</td>
</tr>
<tr>
<td>50</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>55</td>
<td>+0.13°</td>
<td>+2.4°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>97</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>128</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>247</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 days</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 days</td>
<td>+0.12°</td>
<td>+2.2°</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE IV

Racemization of (+)-4-Methoxybenzhydryl Hydrogen Phthalate in Methanol, Balfe, Doughty, Kenyon and Poplett (J.C.S., 1942, 608). § 2.5, ¶ 2; room temperature

"α_o" = total change in rotation; "α_t" = change in rotation after time t.

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>[α]_D</th>
<th>&quot;α_t&quot;</th>
<th>2.303 x log_{10}(\frac{α_o}{α_t})</th>
<th>Velocity Co-efficient K</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>+28°</td>
<td>28°(&quot;α_o&quot;)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>24.0</td>
<td>+21.8°</td>
<td>21.8</td>
<td>0.2503</td>
<td>0.0104</td>
</tr>
<tr>
<td>48.0</td>
<td>+17.2°</td>
<td>17.2</td>
<td>0.4875</td>
<td>0.0101</td>
</tr>
<tr>
<td>72.0</td>
<td>+13.1°</td>
<td>13.1</td>
<td>0.7598</td>
<td>0.0105</td>
</tr>
<tr>
<td>120.0</td>
<td>+7.6°</td>
<td>7.6</td>
<td>1.304</td>
<td>0.0108</td>
</tr>
<tr>
<td>144.0</td>
<td>+6.0°</td>
<td>6.0</td>
<td>1.540</td>
<td>0.0107</td>
</tr>
<tr>
<td>169.0</td>
<td>+3.4°</td>
<td>3.4</td>
<td>2.109</td>
<td>0.0125</td>
</tr>
<tr>
<td>192.0</td>
<td>+2.2°</td>
<td>2.2</td>
<td>2.542</td>
<td>0.0132</td>
</tr>
<tr>
<td>216.0</td>
<td>+1.6°</td>
<td>1.6</td>
<td>2.863</td>
<td>0.0132</td>
</tr>
<tr>
<td>240.0</td>
<td>+1.1°</td>
<td>1.1</td>
<td>3.235</td>
<td>0.0134</td>
</tr>
<tr>
<td>288.0</td>
<td>+0°</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Discussion of the preparation and resolution of alcohols containing 1- and 2-naphthyl groups.

Sultan Mahmud (Ph.D. thesis, 1959) carried out certain work on α-(2-methoxy-1-naphthyl) ethanol, indicated in the Experimental part, but it was decided to repeat and improve this investigation.

Considerable preliminary work on the preparation of 1-acetyl-2-methoxy-naphthalene was carried out with acetyl chloride as the acylating agent, following Gattermann (Ber., 1889, 22, 1130; ibid., 1890, 22, 1210), a poor yield of 1-acetyl-2-methoxy naphthalene was obtained.

When the reaction was conducted with ethylene chloride as solvent, a poor yield of 1-acetyl-2-methoxy naphthalene was obtained. The alkaline extract on acidification gave a phenolic ketone which had indefinite m.p., 62° onwards. This crude phenolic ketone, when recrystallized from hot 96% ethanol gave, in addition to 1-acetyl-2-naphthol, m.p. 62-63°, a crop-fine silky yellow needles - m.p. 162-165°. This on methylation with dimethyl sulphate yielded the corresponding methoxy derivative, which separated from aqueous ethanol in fine needles, m.p. 152-152.5°. Thus this phenolic ketone, m.p. 162-165° and the corresponding methylated product, m.p. 152-152.5° were different from the 1-acetyl-2-naphthol, m.p. 64° and 1-acetyl-2-methoxy naphthalene, m.p. 57-58°; their structures were not ascertained.

When the reaction was carried out with acetic anhydride and ice cooling, no evolution of hydrogen chloride took place and on gently warming on a
waterbath (Noller, J.A.C.S., 1924, 46, 1892) extensive dealkylation took place as was shown by the production of 1-acetyl-2-naphthol on acidification of the sodium hydroxide washings of the crude ketone.

Thus preliminary experiments showed the desirability of conducting the reaction at room temperature - controlling the temperature rise by cooling the reaction vessel with cold water just enough to prevent the boiling of the solvent. The final procedure for Friedel-Crafts acylation of 2-methoxy naphthalene by acetic anhydride with aluminium chloride in carbon disulphide is described in the Experimental part.

α-(2-methoxy-1-naphthyl) ethanol is not obtained by reduction of 1-acetyl-2-methoxy naphthalene by alcoholic sodium hydroxide and zinc dust but is not conveniently prepared in good yield by reduction of 1-acetyl-2-methoxy naphthalene by aluminium iso-propoxide.

The (+)-α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate was prepared in the usual manner by the interaction of equimolecular quantities of α-(2-methoxy-1-naphthyl) ethanol and phthalic anhydride in the presence of a slight excess of pyridine at 35-50°. This reaction seemed to be very slow at room temperature even when a stronger base, triethylamine, was used with pyridine. If more than a slight excess of the molecular proportion of pyridine was used in the reaction, on decomposition of the reaction mixture with dilute hydrochloric acid a pasty mass was obtained and gave lower yield of the hydrogen phthalate. A series of preliminary experiments showed the desirability of maintaining the reaction mixture at 35-50°, which gave good yield of the hydrogen phthalate.
This hydrogen phthalate showed a tendency to dismutate into the neutral ester and phthalic acid when crystallized from carbon disulphide, methylene chloride, and chloroform. Ethanol and methanol were found unsuitable as solvent for crystallization because in these solvents the corresponding mixed ether was formed and phthalic acid separated.

However, the hydrogen phthalate could be crystallized from ether-light petroleum (b.p. 40-60°) in which it was found to be fairly stable. As the hydrogen phthalate was only slightly soluble in ether, in order to avoid the use of large amount of ether for crystallization, the crude hydrogen phthalate was washed with a little ether to remove traces of unreacted carbinol and other impurities; this washed hydrogen phthalate was found satisfactory for resolution.

Brucine proved to be the most suitable alkaloid for effecting the resolution of the (±)-2-methoxy-1-naphthyl methyl carbinyl hydrogen phthalate. But the two diastereoisomeric brucine salts of the hydrogen phthalate differed very little in their solubility in acetone, chloroform, or ethylacetate either at low temperature or high temperature - other solvents such as ethanol and methanol being unsuitable for the purpose.

Preliminary experiment showed that for separation of 2 g. of the diastereoisomeric brucine salts of the hydrogen phthalate nearly 100 cc. of acetone was required for effecting complete and clear solution. In chloroform both were highly soluble. Thus a mixture of the two solvents, chloroform and acetone, was used for effecting the resolution. After 4
crystallizations of the less-soluble brucine salt of the hydrogen phthalate from chloroform-acetone mixture, and then leaching the salts with boiling acetone three times and filtering while warm, the optically pure less-soluble brucine salt was obtained.

The less-soluble optically pure brucine salt of the hydrogen phthalate, when decomposed with dilute hydrochloric acid and ice gave (+)-α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate \([\alpha]_{D}^{Me2CO} = 42.2^\circ; \quad [\alpha]_{D}^{CS2} = 135.1^\circ\).

Its specific rotatory powers were measured immediately after making up the solutions in different solvents, and are given in Table V, page 81. It is notable that hydrogen phthalate which is dextro-rotatory in acetone and methanol is laevorotatory in carbon disulphide and chloroform. Ultimately, phthalic acid was thrown out of the solution of the hydrogen phthalate in carbon disulphide, chloroform, or methanol.

The more-soluble brucine salt on decomposition with dilute hydrochloric acid as usual gave α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate having \([\alpha]_{D}^{CS2} = 83.6^\circ\).

The hydrogen phthalate during hydrolysis with dilute aqueous alkali is rapidly converted into the neutral ester which, owing to its insolubility, escapes hydrolysis. However, the hydrogen phthalate is easily hydrolysed with a solution of sodium in 96% ethanol by gently warming the mixture for 5 minutes on a steam bath. Thus the α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate of \([\alpha]_{D}^{CS2} = 135.1^\circ\) on hydrolysis gave α-(2-methoxy-1-naphthyl)
ethanol having \([\alpha]_{D}^{CS_2} = 27.2^\circ\). The specific rotatory powers are given in Table VI, page 81.

This carbinol \([\alpha]_{D}^{CS_2} = 27.2^\circ\) yielded a hydrogen phthalate \([\alpha]_{D}^{CS_2} = 73.5^\circ\).

\(\alpha\)-(2-ethoxy-1-naphthyl) ethanol was prepared by the reduction of 1-acetyl-2-ethoxy naphthalene. 1-acetyl-2-ethoxy naphthalene was prepared by Friedel-Crafts acylation by the action of acetic anhydride on 2-ethoxy naphthalene in presence of anhydrous aluminium chloride in carbon disulphide.

In preliminary works with acetyl chloride as the acylating agent (following Gattermann, Ber., 1890, 23, 1210) a poor yield of 1-acetyl-2-ethoxy naphthalene was obtained.

When the reaction was carried out at 40 - 45° with acetic anhydride as the acylating agent, extensive dealkylation took place as was shown by the production of 1-acetyl-2-naphthol on acidification of the sodium hydroxide washings of the crude ketone. This acetyl naphthol was re-ethylated with diethyl sulphate to give the required 1-acetyl-2-ethoxy naphthalene.

On cooling with ice to 3°, 2-ethoxy naphthalene and anhydrous aluminium chloride in carbon disulphide, on addition of acetic anhydride, very little hydrogen chloride evolved. Reaction was, therefore, conducted by moderate cooling with ice water to prevent the boiling of carbon disulphide and then keeping the reaction mixture at room temperature for 1 hour to ensure completion of reaction.

2-ethoxy-1-acetyl naphthalene is not reduced satisfactorily by zinc
dust and alcoholic sodium hydroxide, but most conveniently by aluminium iso-propoxide, to α-(2-ethoxy-l-naphthyl) ethanol in good yield.

The (+)-α-(2-ethoxy-l-naphthyl) ethyl hydrogen phthalate was prepared from the alcohol in the usual manner, in the presence of pyridine and phthalic anhydride. This acid ester failed to give a crystalline salt with cinchonidine, cinchonine, strychnine and quinidine. However, brucine proved to be a suitable alkaloid for effecting the resolution. But the two diastereoisomeric brucine salts of the hydrogen phthalate differed very little in their solubility in acetone, chloroform or ethyl acetate - other solvents such as ethanol and methanol being unsuitable for the purpose.

Preliminary experiment showed that for separation of 0.77 g. of the diastereoisomeric brucine salts of the hydrogen phthalate nearly 100 cc. of warm acetone was required for effecting complete and clear solution. In chloroform both the diastereoisomeric salts were highly soluble. Thus a mixture of the two solvents, chloroform and acetone, was used for effecting the resolution. After six crystallizations the less-soluble brucine salt was obtained in optically pure condition. The details of fractional crystallization are given in the scheme on page 128. This salt, on decomposition as usual with dilute hydrochloric acid, gave the α-(2-ethoxy-l-naphthyl)ethyl hydrogen phthalate having $[\alpha]_D^{\text{CO}} = +42.6^\circ$, $[\alpha]_D^{\text{CS2}} = 101.5^\circ$. Again a sign-change is notable.

Its specific rotatory powers in different solvents are given in
Table VII, page 82. Ultimately phthalic acid separated from the solutions of the hydrogen phthalate in carbon disulphide, chloroform and methanol.

The α-(2-ethoxy-1-naphthyl) ethanol was obtained by hydrolysing the hydrogen phthalate \([\alpha]_{D}^{20} + 42.6^\circ\) with a solution of sodium in 96% ethanol; it gave carbinol having \([\alpha]_{D}^{CS_2} - 31.2^\circ\).

The specific rotatory powers of the carbinol in different solvents are given in Table IX, page 82.

This carbinol \([\alpha]_{D}^{CS_2} - 31.2^\circ\), on interaction with phthalic anhydride in the presence of pyridine, gave a hydrogen phthalate of \([\alpha]_{D}^{CS_2} - 70^\circ\). Owing to the extremely reactive nature of the hydrogen phthalate it could not be obtained in optically pure form. However, this reaction establishes the identity of the carbinol and suggests that the hydrogen phthalate is mainly formed by alkoxy-hydrogen fission mechanism in the presence of pyridine.

The α-(6-ethoxy-2-naphthyl) ethanol was obtained by the reduction of 6-ethoxy-2-acetyl naphthalene. This was prepared by Friedel-Crafts acylation of 2-ethoxy naphthalene by acetyl chloride in presence of anhydrous aluminium chloride in dry nitrobenzene. The use of nitrobenzene as a solvent gives this ketone as the major product. However, definite indications have been obtained of the formation of an isomeric ketone, having the acetyl group in a position other than 6-position.

During acylation of 2-ethoxy-naphthalene, some dealkylation of the ketone took place presumably by the action of the hydrochloric acid produced (Zeisel reaction). 6-hydroxy-2-acetyl naphthalene, m.p. 171–173° was...
obtained as insoluble material when the decomposed reaction mixture was
being extracted with benzene. When the alkaline washings of the crude
ketone were acidified, a phenolic ketone 2-hydroxy-(x)-acetyl naphthalene,
m.p. 168-169.5° was obtained. The mixture of the 6-hydroxy-2-acetyl
naphthalene, m.p. 171-173°, with the 2-hydroxy-(x)-acetyl naphthalene, m.p.
m.p. 168-169.5° had m.p. 137-139°, thus showing that these two phenolic
ketones were structurally different.

Further the 6-hydroxy-2-acetyl naphthalene on methylation yielded
6-methoxy-2-acetyl naphthalene, m.p. 105-106°, while the phenolic ketone
2-hydroxy-(x)-acetyl naphthalene, m.p. 168-169.5° on methylation gave a
methylated ketone m.p. 95-96°. The mixed m.p. of these two methoxy-
acetyl naphthalenes was indefinite 93° onwards.

The 2-hydroxy-(x)-acetyl naphthalene on ethylation gave the corre­
sponding ethoxy derivative, m.p. 73-74.5°, which is different from the 6-
ethoxy-2-acetyl naphthalene, m.p. 82-83°.

As no reference to 6-ethoxy-2-acetyl naphthalene was found in the
literature, the structural identity of the 6-ethoxy-2-acetyl naphthalene was
established by dealkylating the ketone and re-methylating the phenolic
ketone obtained, when 6-methoxy-2-acetyl naphthalene was obtained, having
m.p. 105-106°. Haworth and Sheldrick (J.C.S., 1934, 865) give m.p. 104-
105°; Fries and Schimmelschmidt (Ber., 1925, 58, 2835) give m.p. 105°;
2-acetyl naphthalene.
α-(6-Ethoxy-2-naphthyl) ethanol is not obtained by the reduction of 6-ethoxy-2-acetyl naphthalene by alcoholic sodium hydroxide and zinc dust - the bimolecular reduction product (presumed) having m.p. 193.5 - 194.5° is formed. However, α-(6-ethoxy-2-naphthyl) ethanol is conveniently prepared in good yield by reduction of the ketone by aluminium iso-propoxide.

The hydrogen phthalic ester from α-(6-ethoxy-2-naphthyl) ethanol is obtained in over 90% yield by the use of pyridine as described in the Experimental section on page 144. This hydrogen phthalate, unlike the 2-ethoxy-1-naphthyl isomer, was found to be quite stable in chloroform and methanol and thus could be obtained in purified crystalline form from chloroform-benzene or ether-petroleum (b.p. 40 - 60°).

The α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate did not form crystalline salts with brucine, quinidine and strychnine even on long standing. However, the crystalline cinchonidine salt of the acid ester readily separated from acetone. After several recrystallizations the less-soluble cinchonidine salt of the acid ester was obtained optically pure. This, on decomposition with dilute hydrochloric acid as usual, yielded the optically pure hydrogen phthalate $[\alpha]_D^{\text{Me}_2\text{CO}} = -37°, [\alpha]_D^{\text{CHCl}_3} + 8.1°$, while the more soluble cinchonidine salt of the acid ester yielded hydrogen phthalate having $[\alpha]_D^{\text{Me}_2\text{CO}} + 32.9°$. It is notable that the hydrogen phthalate which is laevorotatory in acetone is dextrorotatory in chloroform.

The optically active hydrogen phthalate $[\alpha]_D^{\text{Me}_2\text{CO}} = -37°$ on hydrolysis with dilute aqueous sodium hydroxide solution yielded the racemic carbinol,
However, the optically active \( \alpha \)-\((6\text{-ethoxy-2-naphthyl})\) ethanol was obtained by hydrolyzing the optically active hydrogen phthalate \( [\alpha]_{D}^{MeCO} = 37^\circ \) with a solution of sodium (2 atom) in 96% ethanol; it had \( [\alpha]_{D}^{MeCO} = 36^\circ \).

This carbinol \( [\alpha]_{D}^{MeCO} = 36^\circ \), on interaction with phthalic anhydride in the presence of pyridine yielded the corresponding hydrogen phthalate having \( [\alpha]_{D}^{MeCO} = 36^\circ \), a value much nearer to that of the parent hydrogen phthalate than the corresponding values for the 2-ethoxy compounds.

This experiment establishes the chemical identity of the carbinol and suggests that the hydrogen phthalic ester is formed by alkoxy-hydrogen fission in the presence of the base, pyridine.

The rotatory powers of the hydrogen phthalates obtained from the two diastereoisomeric cinchonidine salts, and the rotatory powers of the optically active \( \alpha \)-\((6\text{-ethoxy-2-naphthyl})\) ethanol are given in Tables X, XII and XI respectively, page 83.

The specific rotatory powers of the carbinol and the hydrogen phthalates in different solvents are recorded for light of different wave-lengths. There are wide variations of rotatory powers in chloroform, carbon disulphide and acetone. The \((-\))-hydrogen phthalate gave \((+\))-carbinol on hydrolysis.

The optically active \( \alpha \)-\((6\text{-ethoxy-2-naphthyl})\) ethyl hydrogen phthalate shows some tendency to undergo alkyl-oxygen fission in its reactions, but this tendency does not seem to be as strong as that of the \( \alpha \)-\((2\text{-methoxy-1-naphthyl})\) ethyl hydrogen phthalate and \( \alpha \)-\((2\text{-ethoxy-1-naphthyl})\) ethyl phthalate. This is discussed later.
Influence of alkoxy groups on the reactivity of the hydrogen phthalates of alcohols containing the ethoxy- and methoxy-naphthyl radical

It has been shown by Kenyon and co-workers (relevant references given in the comparison chart on page 79) that the hydrogen phthalates of α-(1-naphthyl) ethanol and α-(2-naphthyl) ethanol are fairly stable, and show a tendency to undergo alkyl-oxygen fission only at higher temperatures.

However, the introduction of electron-releasing groups such as methoxyl and ethoxyl, in position 2- of the naphthalene ring of α-(1-naphthyl) ethanol, and position 6- of the naphthalene ring in α-(2-naphthyl) ethanol confers on these carbinols a stronger tendency to undergo reactions by alkyl-oxygen fission even at the ordinary temperature.

Thus racemic and optically active hydrogen phthalates of α-(2-methoxy-1-naphthyl) ethanol and α-(2-ethoxy-1-naphthyl) ethanol are too unstable to be crystallized from the solvents chloroform, carbon disulphide, methanol and ethanol - phthalic acid separates ultimately.

However, the (+)-hydrogen phthalates of α-(2-methoxy-1-naphthyl) ethanol and α-(2-ethoxy-1-naphthyl) ethanol differ from their respective optically active (+) or (-) isomerides in stability. The (+)- or (-)-hydrogen phthalates were found to be more unstable than the (+)-hydrogen phthalates. This was evident from the fact that when the ethereal solutions of (+) or (-)-hydrogen phthalates of 2-methoxy-1-naphthyl methyl carbinol or 2-ethoxy-1-naphthyl methyl carbinol were left for long, they tended to decompose giving phthalic acid. Further, these (+)- or (-)-
hydrogen phthalates tended to decompose even in the dry condition. For example, the optically active α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate of $\left[\alpha\right]_{D}^{\text{Me}_2\text{CO}} + 42.2^\circ$ after 12 weeks had $\left[\alpha\right]_{D}^{\text{Me}_2\text{CO}} + 7.3^\circ$, and the optically active α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate of $\left[\alpha\right]_{D}^{\text{CS}_2} - 101.5^\circ$, $\left[\alpha\right]_{D}^{\text{Me}_2\text{CO}} + 42.6^\circ$, when examined after 8 days had $\left[\alpha\right]_{D}^{\text{CS}_2} - 84.3^\circ$, and $\left[\alpha\right]_{D}^{\text{Me}_2\text{CO}} + 7.2^\circ$, after 9 weeks.

These hydrogen phthalates when freshly prepared were solid, and soluble in dry carbon disulphide and dry chloroform, but after a few weeks they changed to sticky masses which were not quite soluble in these solvents, presumably due to their dismutation into the corresponding neutral ester and phthalic acid. These hydrogen phthalic esters decomposed rapidly when moist and impure.

The chemical instability of the (+)- or (-)- acid esters of α-(2-methoxy- and 2-ethoxy-naphthyl) ethanol is in marked contrast with the stability of the corresponding racemic acid esters.

This curious difference is probably due to physical rather than to chemical causes. The (+)-hydrogen phthalates of both 2-methoxy-1-naphthyl methyl carbinol and 2-ethoxy-1-naphthyl methyl carbinol are obtained in crystalline form and are less soluble than their respective optically active isomerides; they can thus be purified easily, whereas the optically active isomerides are more soluble and can only be obtained in solid form by drying the original gums under vacuum. Further, the optically active hydrogen phthalates appear to be hygroscopic, leading to their decomposition with separation of phthalic acid.
The results described above illustrate the marked influence of ethoxyl and methoxyl groups in promoting alkyl-oxygen fission. Further, the optically active α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate racemizes more quickly in methanol (Table XIV, page 85) and chloroform (Table XVII, page 87) than the optically active α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate in these solvents (Table XIII, page 84 and Table XVI, page 86). The rate of formation of (±)-sulphone and partially-racemized neutral ester is faster for optically active α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate than for optically active α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate. This shows that the influence of the ethoxyl group in promoting alkyl-oxygen fission is greater than that of the methoxyl group, when these groups are substituted in position 2- of α-(1-naphthyl) ethanol.

In contrast to the above, the (±)-, (+)- or (−)-, α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate can be obtained in crystalline condition and appear to be quite stable both in the dry state and in solution, as is evident from the very slow rate of racemization of optically active α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate in methanol (Table XV, page 86) and chloroform (Table XVIII, page 87). The melting point of the hydrogen phthalate and its physical state and solubility in chloroform, did not alter in several weeks.

This stability of α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate may be due to the fact that the conjugative electron release from a methoxyl group (Dr. Sultan Mahmud, Ph.D. thesis 1959, London) or an ethoxyl group in position 6- is very ineffectively relayed to the alkyl carbon atom, and thus the oxygen atom linked to the alkyl carbon atom acquires only a feeble negative charge. The formation of an alkyl carbonium ion is therefore not strongly promoted.
Alkyl-oxygen heterolysis in the reactions of acid esters of the alcohols containing the methoxy- and ethoxy-naphthyl radical

The clear solutions of the optically active hydrogen phthalates of \( \alpha \)-(2-methoxy-1-naphthyl) ethanol and \( \alpha \)-(2-ethoxy-1-naphthyl) ethanol, in one equivalent of 0.3 N sodium hydroxide solution at room temperature, turn milky in about 5 minutes and on standing overnight yield the respective neutral esters, also phthalic acid in almost quantitative yield. Neutral ester formation involves an alkyl-oxygen fission mechanism, as is supported by the following.

The optically active \( \alpha \)-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate \([\alpha]_{D}^{MeCO} - 41.2^\circ\), gave crystalline neutral ester which had \([\alpha]_{D}^{22} - 46^\circ\) in acetone. This on hydrolysis with a solution of sodium in 96% ethanol gave the optically active \( \alpha \)-(2-methoxy-1-naphthyl) ethanol which had \([\alpha]_{D}^{CS} + 4.5^\circ\), a value half of that, \([\alpha]_{D}^{CS} + 9^\circ\), of the carbinol obtained by the hydrolysis of the original hydrogen phthalate of \([\alpha]_{D}^{MeCO} - 41.2^\circ\).

Similarly, the optically active \( \alpha \)-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate, \([\alpha]_{D}^{MeCO} + 22^\circ\), gave crystalline neutral ester which had \([\alpha]_{D}^{MeCO} + 20.5^\circ\). This, on hydrolysis with a solution of sodium in 96% ethanol, gave optically active \( \alpha \)-(2-ethoxy-1-naphthyl) ethanol which had \([\alpha]_{D}^{MeCO} - 8^\circ\), a value nearly half of that, \([\alpha]_{D}^{MeCO} - 16.2^\circ\), of the carbinol obtained by the hydrolysis of the original hydrogen phthalate of \([\alpha]_{D}^{MeCO} + 22^\circ\).

These results show that the neutral esters contain one alcoholic
radical in the racemic state.

The scheme of the reaction is shown below.

\[
\begin{align*}
\text{HOOCOR}^{(d)} & \quad \text{CO}_2^- \\
\text{CO}_2^- + \text{R}^{+}(dl) \quad & \text{CO}_2^- \\
\end{align*}
\]

Neutral phthalic ester

\[
\begin{align*}
\text{HOOCOR}^{(d)} + \text{R}^{+}(dl) & \quad \text{CO}_2^- \\
\end{align*}
\]

The optically active \(\alpha\)-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate and the \(\alpha\)-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate each formed the respective racemic sulphone on interaction with a molecular proportion of sodium-\(\pi\)-toluene sulphinate in 0.3 N aqueous sodium hydroxide solution at room temperature, the 2-ethoxy compound forming it more readily. Evidently these racemic sulphones are formed by the reactions, as mentioned in the introduction, involving an alkyl-oxygen fission mechanism.
The tendency of these 2-ethoxy- and 2-methoxy-1-naphthyl compounds to undergo alkyl-oxygen fission is further evidenced by the fact that the optically active \( \alpha \)-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate and \( \alpha \)-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate in methanolic solution in the course of a few days at room temperature, yield the corresponding (+) mixed methyl ether, and phthalic acid in quantitative yield.
First order constants for the course of racemization have been calculated (Tables XIII and XIV, pages 84/85). Inspection of the values of \( k \) for the racemization of \( \alpha -(2\text{methoxy}-1\text{-naphthyl}) \) ethyl hydrogen phthalate, and for the corresponding 2-ethoxy compounds, show 0.012 and 0.016 hr.\(^{-1}\) to be representative figures. Thus the electron-release from the ethoxy group is greater than that from the methoxy group to an extent leading to an increase of one third in the rate of racemization.

It is thus evident that the ethoxy- and methoxy- substituted-\( \alpha \)-naphthyl groups confer electron-releasing properties on the compounds described above. Further, the influence of the ethoxy group in conferring electron-releasing properties on the naphthyl compound is greater than that of the methoxy group, as is shown by the fact that the following reactions of optically active \( \alpha -(2\text{ethoxy}-1\text{-naphthyl}) \) ethyl hydrogen phthalate are faster than those of the 2-methoxy analogue: the formation of the partially racemized neutral ester, and of the \((+)\)-sulphone, and the rate of racemization of the hydrogen phthalate in chloroform and methanol.

However, for the \( \alpha -(6\text{ethoxy}-2\text{-naphthyl}) \) ethyl hydrogen phthalate the formation of sulphone, the mixed methyl ether (ROMe) and the neutral ester are slower than for the 2-ethoxy-1-naphthyl analogue, whence its
tendency to undergo alkyl-oxygen fission is not so strong as that of the latter compound.

The optically active \(\alpha\)-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate, \([\alpha]_{D}^{\text{Me}_2\text{CO}} = -37^\circ\), gave crystalline neutral ester which had \([\alpha]_{D}^{\text{Me}_2\text{CO}} = 21.7^\circ\). This, on hydrolysis with a solution of sodium in 96% ethanol, gave optically active \(\alpha\)-(6-ethoxy-2-naphthyl) ethanol which had \([\alpha]_{D}^{\text{Me}_2\text{CO}} = 16^\circ\), a value nearly half of that, \([\alpha]_{D}^{\text{Me}_2\text{CO}} = 36^\circ\), of the carbinol obtained by the hydrolysis of the original hydrogen phthalate of \([\alpha]_{D}^{\text{Me}_2\text{CO}} = 37^\circ\).

This result shows that the neutral ester contained one alcoholic radical in the racemic state. Thus the course of the reaction is the same as that given for the 2-ethoxy-1-naphthyl analogue, page 74, \(R\) being \(\alpha\)-(6-ethoxy-2-naphthyl) ethyl group.

The formation of the neutral ester takes place very slowly. Thus a solution of optically active \(\alpha\)-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate in 0.3 N sodium hydroxide turns milky only after several hours; the reaction reaches completion in the course of over a week. This suggests that the electron-releasing effect of the 6-ethoxy-2-naphthyl group is not so strong as that of the 2-ethoxy-1-naphthyl group.

A clear solution of optically active \(\alpha\)-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate in the equivalent quantity of 0.3 N sodium hydroxide solution reacted with one molecular proportion of sodium-p-toluene sulphinate
in the course of several days to give the racemic sulphone, which was con-
taminated with the neutral ester. However, in 90% formic acid, the
hydrogen phthalate reacted with sodium-\(\mathbf{p}\)-toluene sulphinate to give the
\((\pm)\)-sulphone after warming on steam bath for about 7 minutes. Apparently
the sulphone-formation involves alkyl-oxygen fission as follows:

\[
\begin{align*}
\text{Me}_3\text{C}_6\text{H}_4\cdot\text{SO}_2\text{Na} + R(\pm) \rightarrow & \text{Me}_3\text{C}_6\text{H}_4 - S - R(\pm) \\
\text{COOR}^{(d)} \rightarrow & \text{CO}_2^- + R^{(d1)} \\
\end{align*}
\]

\(R = \alpha-(6\text{-ethoxy}-2\text{-naphthyl})\text{ethyl group.}\)

The \(\alpha-(6\text{-ethoxy}-2\text{-naphthyl})\) ethyl hydrogen phthalate is fairly
stable in methanolic solution as is shown by its very slow rate of racemiza-
tion (Table XV, page 86); the mixed methyl ether is not formed in the
course of several days at the ordinary temperature. However, on prolonged
refluxing, a methanolic solution of optically active \(\alpha-(6\text{-ethoxy}-2\text{-naphthyl})\) 
ethyl hydrogen phthalate yielded the \((\pm)-\alpha-(6\text{-ethoxy}-2\text{-naphthyl})\) ethyl
methyl ether. Thus, this mixed ether formation also proceeded by alkyl-oxygen
fission mechanism, but somewhat forcing conditions proved necessary.

The influence of the methoxy and ethoxy group in promoting alkyl-
oxygen fission is evident from the comparison of the reactions of the hydro-
gen phthalates of the carbinols containing the unsubstituted naphthyl groups,
which have already been studied by Kenyon and co-workers, with the reactions
of the hydrogen phthalates of the carbinols containing methoxy- and ethoxy-
substituted naphthyl groups, as given in the adjacent table.
<table>
<thead>
<tr>
<th>Name of the Carbinol</th>
<th>Formation of the hydrogen phthalates</th>
<th>Reactions of the hydrogen phthalates</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. α-(1-naphthyl) ethanol</td>
<td>Forms H.P. in pyridine after heating on steam bath for several hrs. Kenyon, et al (J.C.S. 1946, 799)</td>
<td>Not reported</td>
<td>Kenyon et al (J.C.S. 1951, 381)</td>
</tr>
<tr>
<td>II. α-(2-naphthyl) ethanol</td>
<td>Forms H.P. in pyridine after heating on steam bath for several hrs. Collyer and Kenyon (J.C.S. 1940, 677)</td>
<td>Not reported</td>
<td>Balfe, Kenyon and Searle (J.C.S. 1951, 381)</td>
</tr>
<tr>
<td>III. α-(2-methoxy-1-naphthyl) ethanol</td>
<td>H.P. in pyridine at 35-50° for 90 minutes</td>
<td>Readily formed in 0.3N NaOH at room temp.</td>
<td>This thesis</td>
</tr>
<tr>
<td>IV. α-(2-ethoxy-1-naphthyl) ethanol</td>
<td>As in No. III</td>
<td>Readily formed in 0.3N NaOH at room temp.</td>
<td>This thesis</td>
</tr>
<tr>
<td>V. α-(6-methoxy-2-naphthyl) ethanol</td>
<td>H.P. in pyridine at 60-70° for 6 hours</td>
<td>Crystalline neutral ester half racemized formed in dilute alkali at room temp, very slowly</td>
<td>Not reported</td>
</tr>
<tr>
<td>VI. α-(6-ethoxy-2-naphthyl) ethanol</td>
<td>H.P. in pyridine at 45-50° for 1 hour</td>
<td>Crystalline neutral ester formed in dilute alkali very slowly</td>
<td>(±)ROMe very slowly at room temp or on refluxing for 30 hours</td>
</tr>
</tbody>
</table>
From this comparison it is inferred that the introduction of the methoxy and ethoxy group into the naphthyl radical promotes alkyl-oxygen fission, as is evident from the formation of (+) sulphone, partially racemized neutral ester, and (+) ROMe from the hydrogen phthalates of the carbinols containing such groups, more readily than from the hydrogen phthalates of the unsubstituted naphthyl ethanols.

Further, the methoxy and ethoxy groups in the 2-position of the naphthyl radical enhance the alkyl-oxygen fission to a greater extent than when they are in the 6-position, with respect to α-(2-naphthyl) ethanol, since the formation of sulphone, neutral ester and the mixed methyl ether is much more rapid with the former groups.

From these data, it can be inferred that the introduction of a methoxy or ethoxy group in the naphthyl radical reinforces the alkyl-oxygen heterolysis, especially when these groups are in the 2-position, and that the effect of the ethoxy group in promoting alkyl-oxygen fission is greater than that of the methoxy group. Further, when these alkoxy groups are in the other ring (position 6) of the 2-naphthyl compound, the conjugative electron release is only inefficiently relayed to the alkyl carbon atom.
**TABLE V**

Specific rotatory powers of α-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate obtained from less-soluble brucine salt

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°</th>
<th>α_{5893}</th>
<th>α_{5461}</th>
<th>α_{4358}</th>
<th>[α]_{5893}</th>
<th>[α]_{5461}</th>
<th>[α]_{4358}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>2.08</td>
<td>1</td>
<td>21.5</td>
<td>+0.68°</td>
<td>+1.15°</td>
<td>+2.7°</td>
<td>+42.2°</td>
<td>+55.3°</td>
<td>+129.8°</td>
</tr>
<tr>
<td>Methanol</td>
<td>2.06</td>
<td>1</td>
<td>21.5</td>
<td>+0.68°</td>
<td>+0.81°</td>
<td>+2.22°</td>
<td>+33°</td>
<td>+39.3°</td>
<td>+107.7°</td>
</tr>
<tr>
<td>Carbon disulphide</td>
<td>1.88</td>
<td>1</td>
<td>21.5</td>
<td>-2.54°</td>
<td>-3.13°</td>
<td>-5.57°</td>
<td>-135.1°</td>
<td>-166.5°</td>
<td>-296°</td>
</tr>
<tr>
<td>Chloroform</td>
<td>1.42</td>
<td>1</td>
<td>21.5</td>
<td>-0.56°</td>
<td>-0.61°</td>
<td>-0.92°</td>
<td>-39.5°</td>
<td>-42.6°</td>
<td>-64.5°</td>
</tr>
</tbody>
</table>

**TABLE VI**

Specific rotatory powers of (+)-α-(2-methoxy-1-naphthyl) ethanol

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°</th>
<th>α_{5693}</th>
<th>α_{5461}</th>
<th>α_{4358}</th>
<th>[α]_{5693}</th>
<th>[α]_{5461}</th>
<th>[α]_{4358}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon disulphide</td>
<td>1.97</td>
<td>1</td>
<td>22</td>
<td>-0.54°</td>
<td>-0.67°</td>
<td>-1.15°</td>
<td>-27.2°</td>
<td>-34.2°</td>
<td>-58.3°</td>
</tr>
<tr>
<td>Chloroform</td>
<td>2.3</td>
<td>1</td>
<td>22</td>
<td>-0.58°</td>
<td>-0.65°</td>
<td>-1.11°</td>
<td>-25.2°</td>
<td>-28.1°</td>
<td>-48.3°</td>
</tr>
</tbody>
</table>
### TABLE VII

Specific rotatory powers of α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate obtained from the less-soluble brucine salt.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l°</th>
<th>α\text{5893}</th>
<th>α\text{5461}</th>
<th>α\text{4358}</th>
<th>[α]\text{5893}</th>
<th>[α]\text{5461}</th>
<th>[α]\text{4358}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>1.55</td>
<td>22</td>
<td>+0.66°</td>
<td>+0.89°</td>
<td>+1.88°</td>
<td>+42.6°</td>
<td>+57.4°</td>
<td>+121.3°</td>
</tr>
<tr>
<td>Methanol</td>
<td>2.05</td>
<td>22.5</td>
<td>+1.36°</td>
<td>+1.77°</td>
<td>+3.97°</td>
<td>+33.2°</td>
<td>+43.1°</td>
<td>+96.8°</td>
</tr>
<tr>
<td>Carbon disulphide</td>
<td>2.02</td>
<td>22.5</td>
<td>-2.05°</td>
<td>-2.57°</td>
<td>-4.56°</td>
<td>-101.5°</td>
<td>-127.2°</td>
<td>-226°</td>
</tr>
<tr>
<td>Chloroform</td>
<td>1.79</td>
<td>22</td>
<td>-0.56°</td>
<td>-0.65°</td>
<td>-1.06°</td>
<td>-31.3°</td>
<td>-36.3°</td>
<td>-59.2°</td>
</tr>
</tbody>
</table>

### TABLE VIII

Specific rotatory powers of α-(2-ethoxy-1-naphthyl) ethyl hydrogen phthalate obtained from the more-soluble brucine salt.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l°</th>
<th>α\text{5893}</th>
<th>α\text{5461}</th>
<th>α\text{4358}</th>
<th>[α]\text{5893}</th>
<th>[α]\text{5461}</th>
<th>[α]\text{4358}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon disulphide</td>
<td>1.28</td>
<td>22</td>
<td>+0.55°</td>
<td>+0.65°</td>
<td>+1.17°</td>
<td>+43.4°</td>
<td>+50.8°</td>
<td>+91.4°</td>
</tr>
</tbody>
</table>

### TABLE IX

Specific rotatory powers of (+)-α-(2-ethoxy-1-naphthyl) ethanol.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l°</th>
<th>α\text{5893}</th>
<th>α\text{5461}</th>
<th>α\text{4358}</th>
<th>[α]\text{5893}</th>
<th>[α]\text{5461}</th>
<th>[α]\text{4358}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon disulphide</td>
<td>1.44</td>
<td>22.5</td>
<td>-0.45°</td>
<td>-0.52°</td>
<td>-0.98°</td>
<td>-31.2°</td>
<td>-36.1°</td>
<td>-68°</td>
</tr>
<tr>
<td>Chloroform</td>
<td>1.62</td>
<td>22.5</td>
<td>-0.36°</td>
<td>-0.47°</td>
<td>-0.83°</td>
<td>-22.2°</td>
<td>-29.0°</td>
<td>-51.2°</td>
</tr>
</tbody>
</table>
### TABLE X

Specific rotatory powers of α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate obtained from less-soluble cinchonidine salt.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°</th>
<th>α5893</th>
<th>α5461</th>
<th>α4358</th>
<th>[α]5893</th>
<th>[α]5461</th>
<th>[α]4358</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>2.02</td>
<td>1</td>
<td>22</td>
<td>-0.75°</td>
<td>-0.94°</td>
<td>-1.9°</td>
<td>-37°</td>
<td>-46.5°</td>
<td>-94°</td>
</tr>
<tr>
<td>Methanol</td>
<td>1.06</td>
<td>2</td>
<td>22</td>
<td>-0.62°</td>
<td>-0.82°</td>
<td>-1.66°</td>
<td>-29.2°</td>
<td>-38.7°</td>
<td>-79.3°</td>
</tr>
<tr>
<td>Chloroform</td>
<td>3.47</td>
<td>1</td>
<td>22</td>
<td>+0.28°</td>
<td>+0.33°</td>
<td>+0.36°</td>
<td>+8.1°</td>
<td>+9.5°</td>
<td>+10.4°</td>
</tr>
</tbody>
</table>

### TABLE XI

Specific rotatory powers of α-(6-ethoxy-2-naphthyl) ethanol obtained from the α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate [

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°</th>
<th>α5893</th>
<th>α5461</th>
<th>α4358</th>
<th>[α]5893</th>
<th>[α]5461</th>
<th>[α]4358</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroform</td>
<td>1.24</td>
<td>1</td>
<td>22</td>
<td>+0.55°</td>
<td>+0.60°</td>
<td>+1.02°</td>
<td>+44.6°</td>
<td>+48.3°</td>
<td>+82.2°</td>
</tr>
<tr>
<td>Acetone</td>
<td>0.31</td>
<td>1</td>
<td>22</td>
<td>+0.11°</td>
<td>+0.14°</td>
<td>+0.24°</td>
<td>+36°</td>
<td>+45°</td>
<td>+77°</td>
</tr>
</tbody>
</table>

### TABLE XII

Specific rotatory powers of α-(6-ethoxy-2-naphthyl) ethyl hydrogen phthalate obtained from more-soluble cinchonidine salt.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>C</th>
<th>l</th>
<th>t°</th>
<th>α5893</th>
<th>α5461</th>
<th>α4358</th>
<th>[α]5893</th>
<th>[α]5461</th>
<th>[α]4358</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>2.22</td>
<td>1</td>
<td>22</td>
<td>+0.73°</td>
<td>+0.87°</td>
<td>+1.9°</td>
<td>+32.9°</td>
<td>+39.4°</td>
<td>+86°</td>
</tr>
</tbody>
</table>
Table XIII
Rate of racemisation of (+)-α-(2-Methoxy-1-Naphthyl)Ethyl
Hydrogen Phthalate in Methanol, c 2.06, l 1, t 21.5-22°
in air-thermostatted room.
"α₀" = total change in rotation.

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>α₀</th>
<th>[α]₀</th>
<th>Change of rotation after time t &quot;αₜ&quot;</th>
<th>2.303x log₁₀ &quot;α₀/αₜ&quot;</th>
<th>Velocity coefficient K</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>+0.68°</td>
<td>+35°</td>
<td>33 (&quot;α₀&quot;)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10.0</td>
<td>+0.60°</td>
<td>+29.1°</td>
<td>29.1</td>
<td>0.1257</td>
<td>0.0126</td>
</tr>
<tr>
<td>25.0</td>
<td>+0.52°</td>
<td>+25.2°</td>
<td>25.2</td>
<td>0.2698</td>
<td>0.0108</td>
</tr>
<tr>
<td>34.5</td>
<td>+0.47°</td>
<td>+22.3°</td>
<td>22.3</td>
<td>0.3919</td>
<td>0.0113</td>
</tr>
<tr>
<td>48.0</td>
<td>+0.39°</td>
<td>+19°</td>
<td>19</td>
<td>0.5521</td>
<td>0.0115</td>
</tr>
<tr>
<td>56.5</td>
<td>+0.35°</td>
<td>+17°</td>
<td>17</td>
<td>0.6636</td>
<td>0.0117</td>
</tr>
<tr>
<td>72.0</td>
<td>+0.30°</td>
<td>+14.6°</td>
<td>14.6</td>
<td>0.8155</td>
<td>0.0113</td>
</tr>
<tr>
<td>79.5</td>
<td>+0.27°</td>
<td>+13.1°</td>
<td>13.1</td>
<td>0.9234</td>
<td>0.0116</td>
</tr>
<tr>
<td>96.0</td>
<td>+0.21°</td>
<td>+10.2°</td>
<td>10.2</td>
<td>1.174</td>
<td>0.0122</td>
</tr>
<tr>
<td>106.0</td>
<td>+0.19°</td>
<td>+9.2°</td>
<td>9.2</td>
<td>1.276</td>
<td>0.0120</td>
</tr>
<tr>
<td>168.0</td>
<td>+0.10°</td>
<td>+4.9°</td>
<td>4.9</td>
<td>1.907</td>
<td>0.0114</td>
</tr>
<tr>
<td>192.0</td>
<td>+0.07°</td>
<td>+3.4°</td>
<td>3.4</td>
<td>2.273</td>
<td>0.0118</td>
</tr>
<tr>
<td>216.0</td>
<td>+0.05°</td>
<td>+2.4°</td>
<td>2.4</td>
<td>2.607</td>
<td>0.0120</td>
</tr>
<tr>
<td>260.0</td>
<td>+0.01°</td>
<td>+0.5°</td>
<td>0.5</td>
<td>4.199</td>
<td>0.0161</td>
</tr>
<tr>
<td>271.0</td>
<td>±0°</td>
<td>±0°</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>333.0</td>
<td>±0°</td>
<td>±0°</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
**Table XIV**

Racemisation of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate in Methanol, c 2.06, λ 22-22.5° in air thermostatted room.

"α₀" = total change in rotation

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>α_D</th>
<th>[α]_D</th>
<th>change of rotation after time t = &quot;α₀&quot;</th>
<th>2.303x log₁₀ &quot;α₀&quot;</th>
<th>Velocity coefficient K</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>+1.36°</td>
<td>+33.2°</td>
<td>33.2 (&quot;α₀&quot;)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4.0</td>
<td>+1.28°</td>
<td>+31.2°</td>
<td>31.2</td>
<td>0.06195</td>
<td>0.0155</td>
</tr>
<tr>
<td>23.0</td>
<td>+0.96°</td>
<td>+23.9°</td>
<td>23.3</td>
<td>0.3540</td>
<td>0.0154</td>
</tr>
<tr>
<td>26.0</td>
<td>+0.89°</td>
<td>+21.6°</td>
<td>21.6</td>
<td>0.4297</td>
<td>0.0165</td>
</tr>
<tr>
<td>31.0</td>
<td>+0.83°</td>
<td>+20.2°</td>
<td>20.2</td>
<td>0.4967</td>
<td>0.016</td>
</tr>
<tr>
<td>33.5</td>
<td>+0.79°</td>
<td>+19.2°</td>
<td>19.2</td>
<td>0.5476</td>
<td>0.0163</td>
</tr>
<tr>
<td>48.0</td>
<td>+0.63°</td>
<td>+15.3°</td>
<td>15.3</td>
<td>0.7747</td>
<td>0.0162</td>
</tr>
<tr>
<td>55.0</td>
<td>+0.57°</td>
<td>+13.8°</td>
<td>13.8</td>
<td>0.8778</td>
<td>0.016</td>
</tr>
<tr>
<td>129.0</td>
<td>+0.17°</td>
<td>+ 4.1°</td>
<td>4.1</td>
<td>2.091</td>
<td>0.0162</td>
</tr>
<tr>
<td>144.5</td>
<td>+0.14°</td>
<td>+ 3.4°</td>
<td>3.4</td>
<td>2.279</td>
<td>0.0158</td>
</tr>
<tr>
<td>167.5</td>
<td>+0.07°</td>
<td>+ 1.7°</td>
<td>1.7</td>
<td>2.971</td>
<td>0.0177</td>
</tr>
<tr>
<td>177.0</td>
<td>+0.06°</td>
<td>+ 1.5°</td>
<td>1.5</td>
<td>3.097</td>
<td>0.0175</td>
</tr>
<tr>
<td>225.0</td>
<td>+0.02°</td>
<td>+ 0.5°</td>
<td>0.5</td>
<td>4.197</td>
<td>0.0186</td>
</tr>
<tr>
<td>334.5</td>
<td>± 0°</td>
<td>± 0°</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>358.5</td>
<td>± 0°</td>
<td>± 0°</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
### Table XV

**Racemisation of (-)-α-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate in Methanol**

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>α_D</th>
<th>[α]_D</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>-0.62°</td>
<td>-29.2°</td>
</tr>
<tr>
<td>3.0</td>
<td>-0.62°</td>
<td>-29.2°</td>
</tr>
<tr>
<td>46.0</td>
<td>-0.61°</td>
<td>-28.8°</td>
</tr>
<tr>
<td>192.0</td>
<td>-0.61°</td>
<td>-28.8°</td>
</tr>
<tr>
<td>243.5</td>
<td>-0.60°</td>
<td>-28.3°</td>
</tr>
<tr>
<td>434.0</td>
<td>-0.58°</td>
<td>-27.3°</td>
</tr>
<tr>
<td>550.0</td>
<td>-0.58°</td>
<td>-27.3°</td>
</tr>
</tbody>
</table>

### Table XVI

**Racemisation of (+)-α-(2-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate in Chloroform**

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>α_D</th>
<th>[α]_D</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>-0.56°</td>
<td>-39.5°</td>
</tr>
<tr>
<td>14.0</td>
<td>-0.42°</td>
<td>-29.6°</td>
</tr>
<tr>
<td>23.0</td>
<td>-0.36°</td>
<td>-25.3°</td>
</tr>
<tr>
<td>86.0</td>
<td>-0.06°</td>
<td>- 4.2°</td>
</tr>
<tr>
<td>110.5</td>
<td>-0.04°</td>
<td>- 2.8°</td>
</tr>
<tr>
<td>133.5</td>
<td>-0.02°</td>
<td>- 1.4°</td>
</tr>
<tr>
<td>157.5</td>
<td>± 0°</td>
<td>± 0°</td>
</tr>
</tbody>
</table>

Phthalic acid separates out of the solution.
Table XVII

Racemisation of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate in Chloroform a 1.79, f 1, t 22-22.5°

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>αD</th>
<th>[α]D</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>-0.56°</td>
<td>-31.3°</td>
</tr>
<tr>
<td>3.0</td>
<td>-0.50°</td>
<td>-27.9°</td>
</tr>
<tr>
<td>17.0</td>
<td>-0.28°</td>
<td>-15.6°</td>
</tr>
<tr>
<td>25.0</td>
<td>-0.18°</td>
<td>-10.1°</td>
</tr>
<tr>
<td>49.0</td>
<td>-0.04°</td>
<td>-2.2°</td>
</tr>
<tr>
<td>112.0 (after week-end)</td>
<td>± 0°</td>
<td>± 0°</td>
</tr>
</tbody>
</table>

Phthalic acid separates out of the solution.

Table XVIII

Racemisation of (-)-α-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate in Chloroform a 3.47, f 1, t 22°

<table>
<thead>
<tr>
<th>Time in hours</th>
<th>αD</th>
<th>[α]D</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>+0.28°</td>
<td>+8.1°</td>
</tr>
<tr>
<td>3</td>
<td>+0.28°</td>
<td>+8.1°</td>
</tr>
<tr>
<td>23</td>
<td>+0.27°</td>
<td>+7.8°</td>
</tr>
<tr>
<td>48</td>
<td>+0.27°</td>
<td>+7.8°</td>
</tr>
<tr>
<td>144</td>
<td>+0.27°</td>
<td>+7.8°</td>
</tr>
<tr>
<td>195.5</td>
<td>+0.27°</td>
<td>+7.8°</td>
</tr>
<tr>
<td>220.5</td>
<td>+0.26°</td>
<td>+7.5°</td>
</tr>
<tr>
<td>484</td>
<td>+0.26°</td>
<td>+7.5°</td>
</tr>
<tr>
<td>528</td>
<td>+0.25°</td>
<td>+7.2°</td>
</tr>
</tbody>
</table>
Summary

Preparation and resolution of 4-Hydroxybenzhydrol

\[
\begin{align*}
\text{EtO} & - \text{C} & \text{ClCO} - \text{C} \\
\text{Mw} & = 140.5 \\
\text{AlCl}_3 + \text{CS}_2 & \\
\text{EtO} & - \text{C} & \text{C} \\
\text{Mw} & = 226; \text{ m.p.} 47.5-48^\circ \\
\text{Zn} + \text{NaOH} & \\
96\% \text{EtOH} & \\
\text{EtO} & - \text{C} & \text{OH} \\
\text{Mw} & = 228; \text{ m.p.} 40-41^\circ \\
\text{Phthalic Anhydride} & \\
\text{triethylamine} & \\
\text{(±) H.P.} & \text{ m.p.} 109.5-111^\circ \text{ (decomp.)} \\
\text{Quinidine} & \text{in acetone} \\
\end{align*}
\]

- Insoluble quinidine salt m.p. 153.5-155^\circ \text{ (decomp.)}

- H.P. [\alpha]_\text{MeOH}^D = -19.1^\circ; \text{ m.p.} 82-84^\circ \text{ (decomp.)}

- Carbinol [\alpha]_{\text{C}_6\text{H}_6} = -13.7^\circ; \text{ m.p.} 41-42^\circ

- Filtrate

- H.P. [\alpha]_\text{MeOH}^D + 13.2^\circ

- Carbinol [\alpha]_{\text{C}_6\text{H}_6} + 12^\circ

- m.p. 40-41^\circ
Preparation of 4-ethoxybenzophenone
(Gattermann, Ber., 1889, 22, 1130).

To a solution of phenetole (30.5g.) and benzoyl chloride (36.2g.) in dried carbondisulphide (250cc) which was cooled in an ice-salt mixture and kept well stirred was added roughly powdered aluminium chloride (40g.) during not less than 3-4 hours. The stirring was continued until the evolution of hydrogen chloride had ceased - not less than 4-5 hours. The carbondisulphide was then decanted from the reddish-brown solid which had separated during the reaction. This solid, after washing with carbondisulphide to remove the unreacted phenetole and benzoyl chloride, was decomposed with ice and hydrochloric acid, and the liberated thick oil extracted with ether. The ethereal solution was shaken vigorously with sodium hydroxide solution (10%) to remove traces of benzoyl chloride - this alkaline extract, after acidification yielded only a trace of precipitate showing that very little de-ethylation had occurred during the reaction - then with water several times and finally dried with anhydrous potassium carbonate. Evaporation of the solvent left 4-ethoxy benzophenone as a faintly yellowish white mass of small crystals, m.p. 40-43°, yield 53.4g; 95%. It separated from slightly aqueous ethanol or acetic acid in thick irregular plates, m.p. 47.5-48°, yield 46.2 g; 82%.

Reduction of 4-Ethoxybenzophenone to 4-Ethoxybenzhydrol

A suspension of zinc dust (30 g.) in a solution of sodium hydroxide (25 g.) and the ketone (44.9 g.) in ethanol (200 cc., 96%) was heated under vigorous reflux for 5-6 hours and then filtered whilst hot; the unchanged zinc dust was washed twice with 25 ml. portions of boiling ethanol. The combined filtrates were evaporated to one third of their bulk and diluted with water and kept in an ice box overnight. The precipitated oil had set to a mass of crystals, m.p. 40-41°, yield 43.8 g., 97%. 4-Ethoxybenzhydrol separated from ether-light petroleum (b.p. 40-60°) or aqueous ethanol in clusters of small needles, m.p. 40-41° a value unchanged after crystallisation. Beilstein Organische Chemie Band VI, E 116, 965 records m.p. 40.75° (corr).

Preparation of (±)-4-Ethoxybenzhydrol Hydrogen Phthalate

A mixture of 4-ethoxybenzhydrol (41.6 g.), phthalic anhydride (27 g.), triethylamine (20 g.) and pyridine (3 cc., necessary for complete solution) was triturated - some heat was developed and the mixture changed to a clear thick gum. Next day the gum was dissolved in acetone and the solution rendered acid to Congo red by addition of hydrochloric acid containing powdered ice. The resultant solution was then mixed with ice and water until precipitation was complete. After about 30 minutes the
aqueous layer was decanted off and more crushed ice added, within 30 minutes the paste set to a hard solid mass. This was broken up, filtered, washed with much water – to dissolve any trace of phthalic acid – and dried, m.p. 104-105° (decomp.), yield 65.3g., 95%.

The dried hydrogen phthalate was washed with benzene, in which it was but sparingly soluble, to remove traces of unreacted carbinol and pyridine, when a white mass was obtained m.p. 109.5-111° (decomp.), yield 57g. Found on rapid tiration with 0.1N NaOH, M 372 (0.498g. of the hydrogen phthalate required 13.40cc. of N/10 NaOH); C\textsubscript{23}H\textsubscript{20}O\textsubscript{5} requires M 376.

This ester was found quite satisfactory for effecting the subsequent resolution. Attempts to recrystallise the hydrogen phthalate from benzene, methylene chloride, chloroform, ethanol and methanol resulted in separation of phthalic acid. A little of the hydrogen phthalate when recrystallised from ether - light petroleum (b.p. 40-60°) gave a very poor yield of the hydrogen phthalate contaminated with some sticky substance, probably the neutral ester. This was washed with more ether under suction and dried; it had m.p. 110.5-111.5° (decomp.). Found by rapid tiration with 0.1N NaOH, M 375 (0.352g. of the hydrogen phthalate required 9.40cc. N/10 NaOH); C\textsubscript{23}H\textsubscript{20}O\textsubscript{5} requires M 376.

In another experiment equimolecular amounts of the carbinol (11.4g.) and phthalic anhydride (7.5g.), in the presence of pyridine (9g.) were kept at 60-70° for 2 hours and the viscous mass was decomposed
with hydrochloric acid as usual. Very little hydrogen phthalate was obtained; crystallisation of the sticky mass from carbon disulphide gave material of m.p. 104–5°. This was further submitted to crystallisation from ether and petroleum ether (bp. 40–60°) when the m.p. became 107–108° and yet on further crystallisation the m.p. became 110–111°. The mother liquors on evaporation gave sticky mass of presumably, the neutral ester.

Resolution of (+)-p-Ethoxybenzhydryl Hydrogen Phthalate as its Quinidine Salt

To a mixture of (+)-p-ethoxybenzhydryl hydrogen phthalate (75.2g.) and quinidine (64.9g.) was added acetone (350 cc.) and the mixture stirred till a clear solution was obtained; the separation of the quinidine salt of the laboratory hydrogen phthalate set in within half an hour and gradually increased in amount. After 3 days the product was cooled in ice and filtered and the crystalline crop washed with cold acetone. It was then submitted to fractional crystallisation – as shown in the diagram on page 94 and after five recrystallisations was obtained optically pure, it had m.p. 153.5–155° (decomp.), yield 42.5g.

Decomposition of a portion of this salt with dilute hydrochloric acid and ice yielded the (−)-p-ethoxybenzhydryl hydrogen phthalate with \([\alpha]_{D}^{22} = 20.7^\circ\) (c 5.005, 1 2 in acetone). Decomposition of a portion of the alkaloidal salt which had been submitted to two further recrystallisations yielded a hydrogen phthalate with \([\alpha]_{D}^{22} = 20.1^\circ\) in acetone (c 2.85, 1 2).
Fractional Crystallisation of Quinidine Salt of (+)-4-Ethoxy Benshydryl Hydrogen Phthalate

(75.2g.) + Quinidine (64.9g.) in Acetone (350 cc.).

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Filtrate</td>
</tr>
<tr>
<td>B</td>
<td>Filtrate</td>
</tr>
<tr>
<td>C</td>
<td>Filtrate</td>
</tr>
<tr>
<td>D</td>
<td>Filtrate</td>
</tr>
<tr>
<td>E</td>
<td>Filtrate</td>
</tr>
<tr>
<td>A'</td>
<td>Filtrate</td>
</tr>
<tr>
<td>B'</td>
<td>Filtrate</td>
</tr>
<tr>
<td>C'</td>
<td>Filtrate</td>
</tr>
<tr>
<td>D'</td>
<td>Filtrate</td>
</tr>
<tr>
<td>E'</td>
<td>Filtrate</td>
</tr>
<tr>
<td>A''</td>
<td>Filtrate</td>
</tr>
<tr>
<td>B''</td>
<td>Filtrate</td>
</tr>
<tr>
<td>C''</td>
<td>Filtrate</td>
</tr>
<tr>
<td>D''</td>
<td>Filtrate</td>
</tr>
<tr>
<td>E''</td>
<td>Filtrate</td>
</tr>
</tbody>
</table>

- Bleached with 500 cc. acetone
- E (42.5g.) m.p. 253.5-155° (decomp.)
- H.P. E' (2.5g.) m.p. 200°
- [α] \text{D}^{acetone} = 20.9°
- [α] \text{D}^{McOH} = 19.1°
- m.p. 82-84° (decomp.)
- E'' (15g.) m.p. 102.5-104.5° (decomp.)
- H.P. (16.3g.)
- [α] \text{D}^{acetone} = 2.8°

The weights of the subsequent fractions A, B, C, & D were not taken as the salt when moist dissolved more quickly than when dry. In all crystallisations of the crops A, B, C, D, and E, acetone (350-500 cc.) was used and the filtrates were concentrated.
(--)-p-Ethoxybenzydryl Hydrogen Phthalate

The optically pure alkaloidal salt (37.5 g.) was suspended in acetone (75 cc.) and mixed with hydrochloric acid and ice until acid to Congo red, when a homogeneous solution was obtained. The resultant solution was mixed with more crushed ice and water until precipitation was complete. After about 15 minutes the aqueous layer was decanted off and the precipitated oil washed four times with ice-cold water to remove traces of quinidine hydrochloride. More ice and water were added to the thick oil when after about 3 hours the paste set to a hard crystalline mass. This was broken up, filtered, washed with much water – to remove traces of quinidine hydrochloride – and dried in a vacuum desiccator. It had m.p. 82-84° (decomp.); yield 18.5 g., 93%. Found on rapid titration with 0.1N NaOH, M 380, (0.445 g. of the hydrogen phthalate required 11.70 cc. of N/10 NaOH); C_{23}H_{20}O_{5} requires M 376.

Its specific rotatory powers were measured immediately after making up the solutions in different solvents, and are given in table I, page 57.

Attempts to recrystallise this (--)-p-ethoxybenzydryl hydrogen phthalate under the mildest conditions from benzene, methanol, ethanol, methylene chloride, chloroform, carbondisulphide and ether-light petroleum (bp 40–60°) proved unsuccessful since dismutation to phthalic acid and the corresponding neutral ester rapidly supervened.
(±)-4-Ethoxybenzhydryl Hydrogen Phthalate

The more soluble quinidine salt of the p-ethoxybenzhydryl hydrogen phthalate on decomposition with hydrochloric acid and ice (Congo red) gave (±)-p-ethoxybenzhydryl hydrogen phthalate in the form of a paste which did not turn hard even on keeping overnight in the refrigerator. Next day it was washed several times with water when it rapidly solidified. It was broken up, filtered, washed with much water and dried in a vacuum desiccator; it had m.p. 100.5-102.5° (decomp.). Found on rapid titration with 0.1N NaOH, M 381, (0.499g. of the hydrogen phthalate required 13.10cc. of N/10 NaOH); C_{23}H_{20}O_{5} requires M 376.

The specific rotatory power was measured immediately after making up the solution in methanol (table IA, page 57). As in the case of the corresponding (+)- and (-)- hydrogen phthalic esters attempts to recrystallise this (+)-isomeride resulted in its almost complete dismutation to phthalic acid and the neutral ester.

Hydrolysis of (-)-p-Ethoxybenzhydryl Hydrogen Phthalate

(-)-p-Ethoxybenzhydryl hydrogen phthalate (5.64g; [a]_{D}^{22} = 61.5° in carbondisulphide) was added to a solution of sodium (0.7g.) in ethanol (96%-15cc.); it dissolved on shaking and within 2-3 minutes the solution deposited a copious crystalline precipitate (of sodium phthalate). The mixture which was alkaline to litmus was very gently warmed on a water
bath for about 3-5 minutes. It was cooled and ice water added. The precipitate first dissolved and on addition of more ice and water an oil separated which solidified to a crystalline mass within 15 minutes. After about 5 hours the solid was filtered, washed free from alkali and dried in a vacuum desiccator, m.p. 40-41°, yield 3.2g; 94%. It separates from ether-light petroleum (b.p. 40-60°) in clusters of tiny needles m.p. 41-42°.

The specific rotatory powers are given in table II, page 57.

Hydrolysis of (+)-p-Ethoxybenzhydryl Hydrogen Phthalate with Alcoholic Potassium Hydroxide

(+)-p-Ethoxybenzhydryl hydrogen phthalate (1.88g., [α]D2 +5°) was dissolved in cold absolute alcohol and 2.5 cc. of alcoholic potassium hydroxide solution (prepared from lg. of potassium hydroxide dissolved in 1cc. water and absolute ethanol added to make the volume 4.2 cc.), 75 cc. of absolute ethanol was added and the mixture quickly warmed on a steam bath for about 3 minutes. A copious precipitate appeared. This was cooled and water added, when the precipitate dissolved. The mixture was then diluted with excess of water. After keeping overnight clusters of needles separated. These were filtered, washed and dried, and had m.p. 40-41° [α]D2 +0°, yield 0.2g.

In another similar experiment, when the water content of the alcoholic potassium hydroxide was slightly more than in the previous experiment (1.008g. of potassium hydroxide dissolved in 1cc. water and
15 cc. absolute ethanol added), (+)-p-ethoxybenzhydryl hydrogen phthalate (3.6 g., \([a]_D^{\text{Me}_2\text{CO}} + 5^\circ\)) gave thin needles of (±)-4-ethoxybenzhydrol \([a]_{\text{CS}_2}^0 + 0^\circ\) in poor yield (0.3 g.).

**Hydrolysis of (+)-p-Ethoxybenzhydryl Hydrogen Phthalate with Sodium Ethoxide Solution**

(+)-p-Ethoxybenzhydryl hydrogen phthalate (1.88 g., \([a]_{D}^{22} + 13.2^\circ\) in methanol) was added to a solution of sodium (0.25 g.) in ethanol (96% - 7 cc.): it dissolved on shaking and within 2-3 minutes the solution deposited a copious crystalline precipitate (of sodium phthalate). The mixture which was alkaline to litmus was very gently warmed on a water bath for about 5 minutes. It was cooled and ice-water added. The precipitate first dissolved and on addition of more ice and water an oil separated which solidified soon. Next day the solid was filtered, washed free from alkali, and dried in a vacuum desiccator; it had m.p. 40-41°, yield 0.95 g., 83%. It separated from ether-light petroleum (b.p. 40-60°) in clusters of tiny needles, m.p. 40-41°.

The specific rotatory powers are given in table IIA, page 57.

**Dismutation of (±)-4-Ethoxybenzhydryl Hydrogen Phthalate into (±)di-4-Ethoxybenzhydryl Phthalate and Phthalic acid**

(+)-4-Ethoxybenzhydryl hydrogen phthalate (5.64 g.) was added to sodium hydroxide solution (51 cc. of 0.3 N) and the mixture stirred until
a clear solution was obtained. Just as the last particle dissolved (5 minutes) the solution began to turn turbid. After about 20 minutes flocculent particles began to separate. In about 4-5 hours a crust of the neutral ester settled down. After about 24 hours the supernatant liquid was decanted off and the neutral ester washed three times with a little water. The combined aqueous washings and the decanted liquid on acidification with hydrochloric acid gave no precipitate showing that no free hydrogen phthalate was present in the solution. This was then concentrated to small bulk and concentrated hydrochloric acid added when phthalic acid was obtained. This was filtered and dried: m.p. 200° (decomp.), yield 1.18g., calculated yield 1.245g.

The soft mass of neutral ester was dried under reduced pressure in a vacuum desiccator at room temperature. It could not be obtained in solid form by crystallisation from ether-petrol (b.p. 40-60°) or carbon disulphide, yield 3.87g; calculated 4.395g.

Its molecular weight was determined by hydrolysing the neutral ester with 0.5 N alcoholic potassium hydroxide and back titration against 0.5 N sulphuric acid. Found M. 584.7 (0.497g. of the neutral ester required 3.40cc. 0.5 N KOH); \( C_{38}H_{34}O_6 \) requires M 586.

**Dissmutation of \((-\)-p-Ethoxybenzhydryl Hydrogen Phthalate into \((\pm\)-p-Ethoxybenzhydryl \((-\)-p-Ethoxybenzhydryl Phthalate**

\((-\)-4-Ethoxybenzhydryl hydrogen phthalate (0.714g; \([\alpha]_D^{22} = -61.5°\)
in carbondisulphide) was added to sodium hydroxide solution (6.6 cc. of 
0.3 N). Reaction proceeded exactly as described for the (±) hydrogen 
phthalate. Phthalic acid was obtained: m.p. 201-203° (decomp.), yield 
0.14g., calculated 0.157g.

The soft mass of the neutral ester was dissolved in ether. The 
ethereal solution was washed with water, dried over anhydrous sodium 
sulphate and filtered. Ether was evaporated at room temperature and the 
neutral ester dried under reduced pressure at room temperature: yield 
0.45g., calculated 0.556g. Its molecular weight was determined as above. 
Found M 583 (0.17g. of the neutral ester required 1.2 cc. approx. of 
0.5 N KOH); C_{38}H_{34}O_6 requires M 586.

The specific rotatory power of this neutral ester, measured 
immediately after preparing the solution, was \([\alpha]_D^{24} - 21.6°\) in carbondisulphide.

The pasty neutral ester was triturated with ice cold methanol 
(1 cc.) in which the neutral ester is sparingly soluble for about \(\frac{1}{2}\) minute 
and the methanol decanted. The neutral ester obtained after vacuum 
desiccation as a sticky mass had \([\alpha]_D^{24} - 20°\) in carbondisulphide 
(\(c 0.35; l 1\)).

The neutral ester (0.191g.) after removal of carbondisulphide in 
the above experiments was hydrolysed with sodium ethoxide solution in 96% 
ethanol prepared from 0.058g. of sodium and 2 cc. of 96% ethanol. The 
mixture was gently warmed on a water bath for about 15 minutes and cooled. 
It was then diluted with water and ice added. The carbinol was extracted
with ether. The ethereal extract dried over anhydrous potassium carbonate and ether evaporated at room temperature. The viscous oil obtained had \([\alpha]^2_D -15.1^\circ\) in carbondisulphide \((c 0.51, l 1)\); \([\alpha]^2_D -0.08^\circ\) 
On removal of the solvent carbondisulphide the carbinol dissolved in methanol thus proving that it was the 4-ethoxybenzhydrol but not the neutral ester, which is almost insoluble in cold methanol.

In another experiment \((-\))-4-ethoxybenzhydrol hydrogen phthalate 
\((0.51g; \ [\alpha]^2_D -61.5^\circ)\) was converted into neutral ester in the equivalent quantity of 0.3 N sodium hydroxide solution \((4.6 cc.)\). The neutral ester \((0.3g.)\) was hydrolysed by a solution of sodium \((0.03g.)\) in ethanol (3 cc., 96%) by warming on a water bath for 45 minutes. The carbinol so obtained had \([\alpha]^2_D -5^\circ; \ [\alpha]^2_D -0.05^\circ\) \((c 0.98, l 1, t 22^\circ)\).

Preparation of \((\pm)\) 4-Ethoxybenzhydryl-p-Tolyl Sulphone

(a) From \((\pm)\)-4 ethoxybenzhydryl Hydrogen Phthalate.

\((\pm)\)-4-Ethoxybenzhydryl hydrogen phthalate \((1.0g.)\) was quickly dissolved in sodium hydroxide solution \((10 cc. of 0.3 N)\) and the solution mixed with a solution of sodium-p-toluene sulphinate \((0.57g.)\) in 15 cc. water. Turbidity appeared in about 5 minutes. After about 5 hours the crystalline precipitate of the sulphphone was filtered, washed and dried; it had m.p. 153-156\(^\circ\), yield 0.85g., calculated yield 0.97g. It separated from acetone in prisms, m.p. 168\(^\circ\).
(b) From (-)-4-ethoxybenzhydryl hydrogen phthalate.

(-)-4-ethoxybenzhydryl hydrogen phthalate (0.543g., [a]$_D^{22}$ = 41.4° in benzene) was, after polarimetric examination, mixed with a solution of sodium-$p$-toluen sulphonate (0.32g.) containing sodium hydroxide solution (6 cc. of 0.3 N). The mixture became milky in 3-4 minutes. The crystalline precipitate formed was filtered off after 40 hours, washed and dried, and had m.p. 158.5-160°, yield 0.40g., calculated yield 0.528g. This sulphone had [a]$_D^{22}$ + 0° in acetone. It separated from acetone in prisms m.p. 168°, unchanged on further crystallisation. Found S 8.70% C$_{22}$H$_{20}$O$_5$S requires S 8.74%.

(c) From (-)-4-ethoxybenzhydrol.

(-)-4-Ethoxybenzhydrol (0.67g; [a]$_D^{22}$ = 13.7° in benzene) was dissolved in formic acid (90% - 3 cc.) and the solution mixed with a solution of sodium-$p$-toluen sulphonate (0.67g.) in 90% formic acid (5 cc.). Turbidity appeared within 30 seconds and a flocculent crystalline mass separated within 1 minute. The 4-ethoxybenzhydryl-$p$-tolyl sulphone was filtered off after 40 minutes, washed with water and dried: m.p. 163-164°, yield 1.03g., calculated yield 1.076g. The sulphone had [a]$_D^{24}$ + 0° in chloroform (c 3.58; l 1). It separated from acetone in prisms m.p. 168°, a value unchanged after further crystallisation.

The m.p's of mixtures of the sulphone prepared from different compounds were unaltered.
Preparation of di-p-Ethoxybenzhydryl Ether

An ethereal solution of (±)-4-ethoxybenzhydrol (11g.) was shaken with cone hydrochloric acid for about 10 minutes and then washed with water several times till the aqueous washings were free from acid. The ethereal layer was dried over calcium chloride, filtered and light petroleum (b.p. 40-60°) added to the ethereal solution. On slow crystallisation di-4-ethoxybenzhydryl ether separated in glassy rhombs, m.p. 99.5-100.5°. On recrystallisation from ether and light petroleum (b.p. 40-60°) it separated in rhombs, m.p. 104-105° a value which remained unchanged on further crystallisations. Found C 81.6; H 6.9; C₃₀H₃₀O₃ requires C 82.1; H 6.9%.

Reaction of (±)-p-Ethoxybenzhydryl Hydrogen Phthalate with Methyl Alcohol

(±)-p-Ethoxybenzhydryl hydrogen phthalate (9g.) was dissolved in excess of methyl alcohol (50 cc.) and the solution allowed to evaporate slowly at room temperature. After keeping overnight phthalic acid separated. After 5 days a little of the mixture was treated with sodium carbonate solution (0.3 N) and the aqueous layer separated. When the aqueous layer was made acid with dilute hydrochloric acid no precipitate was formed showing that the hydrogen phthalate had completely reacted with the methanol. Then the mixture was treated with sodium carbonate solution (0.3 N) till alkaline to litmus and extracted with
ether. The ethereal layer was washed three times with a little sodium carbonate solution and by water till aqueous washing was neutral to litmus. The ethereal extract was dried over anhydrous calcium chloride, ether removed by distillation and the (±)-4-ethoxybenzhydryl methyl ether distilled; it had b.p. 120°/0.2 mm., n_D^25 1.5568; yield 4g.

Found C 78.83; H 7.44; "-OMe" 24.69; C_{16}H_{18}O_2 requires C 79.3, H 7.48%. Found: O from the "methoxy" value, 12.73; calculated 13.2%.

The combined aqueous and alkaline washings on evaporation to small bulk gave phthalic acid on acidification with concentrated hydrochloric acid. This was filtered, washed with a few drops of cold water and dried: m.p. 198-200° (decomp.), yield 3.5g., calculated yield 3.97g.

**Reaction of (−)-p-Ethoxybenzhydryl Hydrogen Phthalate with Methanol**

When (−)-p-ethoxybenzhydryl hydrogen phthalate ([α]_D^{25} = 15.6° in methanol) was dissolved in methanol and its specific rotatory powers examined at frequent intervals, it was observed that the rotation falls rapidly, [α]_D ± 0° is reached in about 24 hours. After about 24 hours it becomes dextrorotatory, reaching to a maximum constant value in about 55 hours. The gradual change in rotatory powers is shown in table III, page 58.
Summary

Preparation and Resolution of \(a\)-(2-methoxy-1-naphthyl)ethanol

\[
\begin{align*}
\text{m.p. } 72^\circ & \quad \text{m.p. } 63.5-64.5^\circ \\
\text{m.p. } 63.5-64.5^\circ & \quad \text{m.p. } 57-58^\circ \\
\text{m.p. } 57-58^\circ & \quad \text{m.p. } 79.5-80^\circ \\
\text{m.p. } 79.5-80^\circ & \quad \text{m.p. } 132-132.5^\circ \text{ (decomp.)}
\end{align*}
\]

Less-Soluble Brucine Salt
m.p. 181-182\(^\circ\) (decomp.)

More-soluble Brucine Salt

\(\left[\alpha\right]_D^{\text{CS}_2} - 135.1^\circ\)

\(\left[\alpha\right]_D^{\text{CS}_2} - 27.2^\circ\)

m.p. 58.5-59\(^\circ\)
Preparation of 1-Acetyl-2-Methoxy Naphthalene

To a solution of dry 2-methoxy naphthalene (39.5 g., 0.25 mol.) in dried carbondisulphide (150 cc.) roughly powdered anhydrous aluminium chloride (74 g., 0.55 mol.) was added, and then acetic anhydride (26 g., 0.25 mol.) was slowly added during 15 minutes with vigorous mechanical stirring. Evolution of hydrogen chloride fumes soon started and carbon disulphide began to boil. (Noller, J.A.C.S. 1924, 46, 1892). The reaction flask was cooled by cold water just to prevent boiling of carbondisulphide. After the evolution of hydrogen chloride had ceased (about 1 hour), cold water was removed and the reaction mixture stirred at room temperature when evolution of more hydrogen chloride took place. After a further 1½ hours stirring at room temperature, when evolution of hydrogen chloride had completely ceased, the reaction mixture was decomposed with crushed ice and hydrochloric acid (75 cc.), with thorough stirring. This decomposed mixture was kept in a shallow basin for 48 hours to allow the carbondisulphide to evaporate. The mixture was then extracted with ether, the ethereal extract was shaken vigorously with sodium hydroxide solution (10% - 150 cc.) and then washed with water till washing was alkali free (litmus). The ethereal solution was dried over anhydrous potassium carbonate, decolourised with animal charcoal and filtered. Ether was removed by distillation and the crude product fractionated. The fraction b.p. 87-95°/0.1-0.3 mm. gave on cooling a crystalline substance m.p. 67-71°, yield 7 g. it was thus almost unreacted 2-methoxy naphthalene. The fraction b.p. 122-
126°/0.3 mm. gave a faintly yellowish liquid which set to needles on cooling; it had m.p. 52-53.5°. This on redistillation gave almost colourless liquid b.p. 126°/0.3 mm. - leaving only a trace of yellowish solid in the distillation flask - which set to crystalline mass, m.p. 57-58°; yield 18 g. This separated from aqueous ethanol in colourless prisms, m.p. 57-58°, a value unchanged by recrystallisation. Noller (loc cit) gives m.p. 57-58° for 1-acetyl-2-methoxy naphthalene.

During the acylation of 2-methoxy naphthalene, some of the reaction product was converted into 1-acetyl-2-naphthol by the action of hydrogen chloride (Ziesel reaction). The alkaline extract on acidification, with dilute hydrochloric acid to Congo red, gave a reddish brown crystalline mass of 1-acetyl-2-naphthol. This was filtered, washed with water, dilute sodium bicarbonate solution and finally by water and dried; it had m.p. 59-62°, yield 8 g. It separated from aqueous ethanol in yellowish brown prisms: m.p. 62.5-63.5°. This was subsequently converted into 1-acetyl-2-ethoxynaphthalene with diethylsulphate as described later on page 122.

**Reduction of 1-Acetyl-2-Methoxy Naphthalene**

1-Acetyl-2-methoxy naphthalene (38 g.) was added to a solution of aluminium **isopropoxide** in anhydrous isopropyl alcohol, prepared from aluminium (11 g.), anhydrous isopropyl alcohol (400 cc.), mercuric chloride 0.5 g. and carbontetrachloride (1 cc.). The resulting mixture was refluxed
for about 15 minutes on a steam bath and the acetone formed was removed by slow distillation. No acetone, as its 2,4 dinitrophenylhydrazone, was detected after about 2½ hours. The residual isopropyl alcohol was distilled off at slightly reduced pressure. The reaction mixture was cooled and decomposed by dilute sulphuric acid and crushed ice (45 cc. of concentrated sulphuric acid, ice and water 1000 cc.). The crystalline solid mass of 2-methoxy-1-naphthyl methyl carbinol was filtered, washed and dried under vacuum at room temperature; it had m.p. 57-62°, yield 37.5g. It separated from light petroleum (b.p. 40-60°) containing a little ether on slow evaporation in rosettes of white prismatic needles, m.p. 71-75°, yield 34g. It was submitted to further crystallisation, when it (32g., 84%) had m.p. 79.5-80°, a value unchanged after further crystallisation. Dr. Sultan Mahmud (Ph.D. thesis London, 1959, unpublished work) gives m.p. 77°.

This carbinol when mixed with a trace of the parent ketone had m.p. 34-36°.

Preparation of (+)-α-(2-Methoxy-1-Naphthylethyl) Hydrogen Phthalate

Phthalic anhydride (21.0g.) was dissolved in dry pyridine (20g.) by gently warming. This solution was cooled and mixed with (+)-α-(2-methoxy-1-naphthyl) ethanol (29g.) and the mixture triturated for about 10 minutes. The mixture was then kept in a water bath at 35-50° with frequent shaking.
for about 90 minutes during which time the mixture became homogeneously viscous.

Next day the mass was dissolved in acetone and decomposed as usual with dilute hydrochloric acid and ice. The resultant clear solution was then mixed with ice and water until the precipitation was complete, and thoroughly stirred. The precipitated oil set to a slightly yellow hard solid in about 25 minutes. This was broken up, filtered, washed with much water - to dissolve any traces of phthalic acid - and dried in vacuo at room temperature; it had m.p. 129-129.5° (decomp., giving phthalic acid, which has m.p. 200° decomp.), yield 41.6g., 83%.

Dr. Sultan Mahmud (unpublished work) gives m.p. 126-127°. The dried hydrogen phthalate was washed twice with 30 ml. portions of ether, in which it was very sparingly soluble, to remove traces of unreacted carbinol and other impurities, when an almost white mass of the hydrogen phthalate was obtained, m.p. 131° (decomp.), yield 37.7g. Found, on rapid titration with 0.1 N NaOH: M 351 (0.306g. of the H.P. required 8.70 cc. N/10 NaOH); C_{21}H_{18}O_{5} requires M 350.

This ester was found quite satisfactory for effecting the subsequent resolution. A little of the hydrogen phthalate was recrystallised from ether, in colourless irregular plates, m.p. 132-132.5° (decomp.)

Found, on rapid titration with 0.1 N NaOH: M 350 (0.154g. of the H.P. required 4.40 cc. of N/10 NaOH); C_{21}H_{18}O_{5} requires M 350. The m.p. remained unaltered after further crystallisation. Dr. Sultan Mahmud (unpublished work) gives m.p. 130°. Ethanol, methanol, methylene
chloride, chloroform and carbondisulphide were not suitable solvents for crystallisation of the hydrogen phthalate because in these solvents the acid ester was unstable.

Resolution of (±)-a-(2-Methoxy-1-Naphthyl)ethyl Hydrogen Phthalate as its Brucine Salt

A mixture of (±)-a-(2-methoxy-1-naphthyl)ethyl hydrogen phthalate (42g.) and brucine (47.4g.) was dissolved in dry chloroform (125 cc.) by gently warming, when a clear solution was obtained. To this clear solution warm acetone (125 cc.) was added. Crystallisation of the brucine salt soon occurred. The whole was kept overnight, cooled and filtered and the crystalline crop of the less-soluble brucine salt of the hydrogen phthalate washed with acetone. It was then submitted to fractional crystallisation - as shown in the diagram on page 111 - and after seven crystallisations was obtained optically pure. It had m.p. 181-182° (decomp.), yield 19.7g. Dr. Sultan Mahmud (unpublished work) gives m.p. 173°. After two further crystallisations from excess of hot acetone a little of this salt retained m.p. 181-182° (decomp.).

It thus appears highly probable that seven recrystallisations of the salt, had resulted in the complete separation of one of the diastereoisomeric salts in an optically pure form.
**Fractional Crystallisation of Brucine Salt of (+) (±)-α-(2-Methoxy-1-Naphthyl)ethyl Hydrogen Phthalate (42 g.)**

<table>
<thead>
<tr>
<th>Step</th>
<th>Reaction Details</th>
<th>Temperature</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Chloroform (60 cc.) + Acetone (50 cc.)</td>
<td>m.p. 171-172° (decomp.)</td>
<td>42 g.</td>
</tr>
<tr>
<td>B</td>
<td>Chloroform 60 cc. + Acetone 15 cc.</td>
<td>m.p. 172° (decomp.)</td>
<td>42 g.</td>
</tr>
<tr>
<td>C</td>
<td>Chloroform (50 cc.) + Acetone (5 cc.)</td>
<td>m.p. 175° (decomp.)</td>
<td>30.7 g.</td>
</tr>
<tr>
<td>D</td>
<td>Leached with boiling acetone (250 cc.) and filtered warm</td>
<td>m.p. 178-179° (decomp.)</td>
<td>21.5 g.</td>
</tr>
<tr>
<td>E</td>
<td>Leached with boiling acetone 250 cc. and filtered warm</td>
<td>m.p. 180° (decomp.)</td>
<td>20.3 g.</td>
</tr>
<tr>
<td>F</td>
<td>Leached 200 cc. with boiling acetone 250 cc. and filtered warm</td>
<td>m.p. 181-182° (decomp.)</td>
<td>20 g.</td>
</tr>
</tbody>
</table>

- Concentrated to 75 cc.
- Filt 200 cc.
- M (7 g.) m.p. 175° (decomp.)
- N (15 g.) m.p. 177° (decomp.)
- Concentrated to 75 cc.
- Filt 150 cc.
- Q (10 cc.) nearly.

<table>
<thead>
<tr>
<th>Optical Rotation</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>[α]D</td>
<td>135.1°</td>
</tr>
<tr>
<td>[α]D</td>
<td>+42.2°</td>
</tr>
<tr>
<td>[α]D</td>
<td>+38.6°</td>
</tr>
<tr>
<td>[α]D</td>
<td>+0.85°</td>
</tr>
</tbody>
</table>

- m.p. 159-160° (decomp.)
(-)-α-(2-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate

The optically pure alkaloidal salt - from the less-soluble brucine salt, m.p. 181-182° - (19g.) was suspended in acetone (40 cc.) and acidified with dilute hydrochloric acid and ice, when a homogeneous solution was obtained. The resultant solution was mixed with more crushed ice and water until precipitation was complete. After about 45 minutes the aqueous layer was decanted off and the mass was extracted with ether, washed with a little dilute hydrochloric acid and then with water till acid-free, and dried over anhydrous calcium chloride. Evaporation of the ether at room temperature, finally under reduced pressure, gave a white crystalline hydrogen phthalate, m.p. 100-103° (decomp.) (shrinks at 60°); yield 8g. Found on rapid titration with 0.1 N NaOH, M 351 (0.381g. of H.P. required 10.60 cc. N/10 NaOH); \( \text{C}_{21}\text{H}_{18}\text{O}_5 \) requires M 350.

Its specific rotatory powers were measured immediately after making up the solutions, and are given in table V, page 81.

No solvent was found suitable to crystallise this hydrogen phthalate.

Other crops of the insoluble brucine salt of the hydrogen phthalate and soluble brucine salt were decomposed in similar manner. Their respective specific rotation is given in the diagram on page 111.
Hydrolysis of (+)-a-(2-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate with Aqueous Sodium Hydroxide

(+)-a-(2-Methoxy-1-naphthyl)ethyl hydrogen phthalate (1.39g., $[\alpha]_D^{22} + 38.6^\circ$ in acetone) was dissolved quickly in dilute sodium hydroxide solution (0.4g. sodium hydroxide in 25 cc. water) and the solution quickly heated on steam bath. As soon as the solution was kept on a steam bath it turned milky and in about 1 minute an oil separated. This was heated for about 5 minutes and cooled. On cooling the oil solidified to a hard mass, which was broken up, filtered, washed, and dried under vacuum, m.p. (shrinks at $48^\circ$) indefinite, yield 0.74g, calculated yield 0.8g. It was sparingly soluble in ether, and hence it was not the required carbinol which is highly soluble in ether. This solid was triturated with ether and filtered. The insoluble crystalline solid had indefinite m.p. $88^\circ$ onwards and had $[\alpha]^2_2 + 22.7^\circ$ in acetone ($c 0.22$, $l 1$).

It is thus inferred that during hydrolysis by dilute aqueous alkali, the hydrogen phthalic ester is probably converted rapidly into neutral ester which owing to its insolubility escapes hydrolysis.

Hydrolysis of (+)-a-(2-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate with Sodium Ethoxide Solution

(+)-a-(2-Methoxy-1-naphthyl) ethyl hydrogen phthalate (2.8g., $[\alpha]_{acetone}^{22} + 42.2^\circ$, $[\alpha]_{D^2}^{1CS} - 135.1^\circ$) was added to a solution of sodium
(0.38g.) in ethanol (96% - 15 cc.) and triturated when it dissolved and within 2 minutes the solution deposited a copious crystalline precipitate (of sodium phthalate). The mixture which was alkaline to litmus was heated on a steam bath for about 5 minutes. It was then cooled, and a few drops of water added. The precipitate dissolved, and on addition of more water and ice an oil separated which solidified in about 45 minutes. After 7 hours the solid carbinol was filtered, washed free from alkali, and dried under vacuum; it had m.p. 54-56°, yield 1.38g., calculated yield 1.616g. It separated from light petroleum (b.p. 40-60°) containing a little ether in rosettes of prisms, m.p. 58.5-59°, a value unchanged after further crystallisation, yield 1.1g.

Its specific rotatory powers are given in table VI, page 81.

Preparation of (+)-α-(2-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate from the (+)-α-(2-Methoxy-1-Naphthyl)Ethanol

\[ [\alpha]_{D}^{Cs2} = 27.2° \]

(+)-α-(2-Methoxy-1-naphthyl) ethanol (0.254g, \([\alpha]_{D}^{Cs2} = 27.2°\)) was mixed with a cooled solution of phthalic anhydride (0.186g.) in warm pyridine (5 drops) and the mixture triturated for 5 minutes. The mixture was kept in warm water (35°) for about 3 minutes and then left at room temperature overnight. Next day it was dissolved in acetone and decomposed as usual with dilute hydrochloric acid. After 6 hours the supernatant liquid was decanted off and the sticky mass of the hydrogen phthalate extracted
with ether. The ethereal extract was washed, dried over anhydrous calcium chloride and filtered. Ether was removed at room temperature and the hydrogen phthalate solidified under vacuum, yield 0.3 g. This hydrogen phthalate had $[\alpha]_D^{22} = -73.5^\circ$, $\alpha_2^{22} = -1.25^\circ$ (c 1.7, 1 l) in carbondisulphide.

Dismutation of $(+)-\alpha-(2$-Methoxy-1-Naphthyl)Ethyl Hydrogen Phthalate to $(+)-\alpha-(2$-Methoxy-1-Naphthyl)Ethyl $(\pm)-\alpha-$

$(2$-Methoxy-1-Naphthyl)Ethyl Phthalate

$(+)-\alpha-(2$-Methoxy-1-naphthyl)ethyl hydrogen phthalate (2.1 g., $[\alpha]_D^{22} = +38.6^\circ$ in acetone) was dissolved in sodium hydroxide solution (20 cc. of 0.3 N). Just as the clear solution was obtained (in about 5 minutes) the solution began to turn turbid and gradually became milky due to separation of floculent particles. After keeping overnight, a white mass had settled to the bottom of the vessel. More water (75 cc.) was added and the mixture stirred. After about 20 hours it was filtered and washed with water. The combined filtrate and washing, about 100 cc., was concentrated to about 40 cc. and a couple of drops of dilute acid added to it, when no turbidity appeared. This showed the absence of sodium phthalic ester in the filtrate. It was further concentrated to small bulk and decomposed with concentrated hydrochloric acid, when crystalline phthalic acid was obtained. The whole was cooled in ice-water, and the acid filtered off, washed with a few drops of cold water and dried; it had m.p. 182-184° (decomp.), yield 0.434 g. (it was insoluble in dry chloroform), calculated yield 0.498 g.
The white, solid, neutral ester was dried under vacuum; m.p. 167-170° (decomp.) shrinks 145° onwards, yield 1.34g; calculated yield 1.6g. It was then washed with dry ether (10 cc.), in which it was almost insoluble, to remove traces of a-(2-methoxy-1-naphthyl) ethanol which might have been formed as a result of hydrolysis of the hydrogen phthalic ester in alkaline medium. It then had m.p. 167-169° (decomp.) shrinks 145° onwards, a value unchanged after further washing. The molecular weight was determined by saponifying the neutral ester with 0.5 N alcoholic caustic potash for 5 hours on a steam bath and titrating the unused alkali against 0.5 N sulphuric acid. Found: M 545 (0.419g. of the neutral ester required 1.54 cc. of N KOH); \( C_{34}H_{30}O_6 \) requires M 534. This neutral ester had \([\alpha]_{D}^{22} + 35.5°\) in acetone (c 1.47, l l).

In another experiment a-(2-methoxy-1-naphthyl) ethyl hydrogen phthalate (4.45g.), \([\alpha]_{D}^{acetone} + 41.2°\) (c 1.02, l l, t 22°) was dissolved in 0.3 N sodium hydroxide solution (42.5 cc.). The neutral ester formed (3g.) had \([\alpha]_{D}^{acetone} + 46°\), \([\alpha]_{D}^{acetone} + 0.53°\) (c 1.16, l l, t 22°). This neutral ester (1.6g.) on hydrolysis with sodium ethoxide solution (prepared from 0.14g. of sodium + 7 cc. 96% ethanol), by warming on steam bath for 20 minutes, gave the half racemised (-)-a-(2-methoxy-1-naphthyl) ethanol \([\alpha]_{D}^{CS} + 4.5°\), \([\alpha]_{D}^{CS} + 0.07°\) (c 1.57, l l, t 22°), m.p. 71-72.5°. The parent hydrogen phthalate \([\alpha]_{D}^{acetone} + 41.2°\) (0.7g.) on hydrolysis with sodium ethoxide (0.1g sodium + 7 cc. 96% ethanol) by gently warming on a steam bath for 5 minutes gave (-)-a-(2-methoxy-1-naphthyl) ethanol \([\alpha]_{D}^{CS} + 9°\), \([\alpha]_{D}^{CS} + 0.12°\) (c, 1.39, l l, t 22°).
Reaction of (−)-a-(2-Methoxy-1-Naphthyl)ethyl Hydrogen Phthalate with Methanol

(−)-a-(2-Methoxy-1-naphthyl)ethyl hydrogen phthalate (5g., [a]_{D}^{21.5} = 22° in methanol) was dissolved in excess of methyl alcohol (20 cc.) and the solution allowed to evaporate slowly at room temperature. After being kept for one day, phthalic acid separated. After 4 days a little of the mixture was treated with sodium carbonate solution (0.3 N) and the aqueous layer separated. When the aqueous layer was made acid with dilute hydrochloric acid, slight turbidity appeared which persisted on further dilution with water showing the presence of unreacted hydrogen phthalate in the original reaction mixture. The mixture was treated with a further quantity of methanol (20 cc.) and the solution allowed to evaporate slowly. After 10 days it was found that the hydrogen phthalate had completely reacted with methanol. Then the mixture was treated with sodium carbonate solution till alkaline to litmus and extracted with ether. The ethereal layer was washed twice with a little sodium carbonate solution and by water until the washing was neutral to litmus. The ethereal extract was dried over anhydrous calcium chloride, decolourised (charcoal), filtered, concentrated at room temperature and light petroleum (b.p. 40-60°) added. A crystalline mass separated on almost complete evaporation of the solvent; it had m.p. 39.5-41°, yield 2.98g; calculated yield 3.1g. It separated from light petroleum (b.p. 40-60°) in rosettes of crystals m.p. 40.5-41°, which remained unchanged after further crystallisations. This material had [α]_{D}^{22} ± 0° in acetone (c, 0.80, l 1). As this ether
was highly soluble in light petroleum (b.p. 40-60°) and other common organic solvents, it was difficult to obtain it in absolutely pure form for analysis and hence it was distilled under reduced pressure; it had b.p. 110°/0.4 mm, and gave a colourless liquid which set to a crystalline mass, m.p. 40.5-41°. When mixed with the undistilled α-(2-methoxy-1-naphthyl) ethyl methyl ether m.p. 40.5-41° the m.p. remains unaltered showing that no decomposition takes place during distillation. Found C 77.89, H 7.42, "OMe" 27.37%; C_14 H_16 O_2 requires C 77.75, H 7.45. (Found O from the "methoxy value" 14.11, calculated 14.72%)

The combined aqueous and alkaline washings on evaporation to small bulk gave phthalic acid on acidification with concentrated hydrochloric acid. This was filtered, washed with a few drops of cold water and dried, it had m.p. 182-184° (decomp.) yield 2.2g. (insoluble in dry chloroform), calculated yield 2.37g.

In a separate experiment, when (+)-α-(2-methoxy-1-naphthyl)ethyl hydrogen phthalate was dissolved in methanol and its rotatory powers examined at frequent intervals, it was observed that the rotation falls gradually, [α]_D = 0° being reached in about 271 hours. The change in rotatory power is shown in table XIII, page 84.

This solution, after a few days, on complete evaporation of the methanol gave a white crystalline solid which was extracted with light petroleum (b.p. 40-60°). The light petroleum extract on evaporation gave the crystalline ether, m.p. 40-41°. This when mixed with the analysed sample, m.p. 40.5-41°, had m.p. 40-41°.
Preparation of $(\pm)-\alpha-(2$-Methoxy-1-Naphthyl)
Ethyl-$p$-Tolyl Sulphone

$(\pm)-\alpha-(2$-Methoxy-1-naphthyl) ethyl hydrogen phthalate (0.7g.,
$[\alpha]_D^{21.5} + 42.2^\circ$ in acetone) was quickly dissolved in sodium hydroxide
solution (7 cc., 0.3 N) and mixed with a solution of sodium-$p$-toluene
sulphinate (0.43 g. in 5 cc. water). The mixture became turbid
immediately. After three days, the solution had deposited a crystalline
precipitate which was filtered off, washed and dried; it had m.p. 121-
125$^\circ$ (decomp.), yield 0.6g., calculated yield 0.752g. This crude
sulphone had $[\alpha]_D^{21.5} + 6.5^\circ$ in acetone ($c$ 2.16, 1 l) and was probably
contaminated with neutral ester. The sulphone separated from aqueous
acetone in colourless prisms, m.p. 141-141.5$^\circ$, yield 0.45g., $[\alpha]_D^{21.5} + 0^\circ$
in acetone ($c$ 2.1, 1 l). It was submitted to further crystallisation,
when the m.p. became 142-142.5$^\circ$, unchanged after further crystallisation.

Dr. Sultan Mahmud (unpublished work) gives m.p. 141$^\circ$, (found
$S$ 9.3%, $C_{20}H_{20}O_3$ $S$ requires $S$ 9.41%).
Summary

Preparation and Resolution of \( \alpha \)-(2-ethoxy-1-naphthyl)ethanol

\[
\begin{align*}
\text{m.p. } 37.5^\circ C & \quad \text{m.p. } 62-62.5^\circ C \\
\text{m.p. } 63.5-64.5^\circ C & \quad \text{m.p. } 61-62^\circ C
\end{align*}
\]

\[
\begin{align*}
\text{Comet} & \quad \text{Et}, \text{SO}_4 \\
\text{Phthalic anhydride} & \quad \text{Pyridine}
\end{align*}
\]

\[
\begin{align*}
\text{Less-Soluble Brucine Salt m.p. } & 159^\circ - 160^\circ C \\
\text{More-soluble Brucine salt } & 54-55^\circ C
\end{align*}
\]

\[
\begin{align*}
\text{Carbinol} & \quad \text{H.P.} \\
[a]_{D}^{\text{CS}_2} & 31.2^\circ \\
(+)[a]_{D}^{\text{CS}_2} & 101.5^\circ \\
(-)[a]_{D}^{\text{CS}_2} & 43.4^\circ
\end{align*}
\]
Preparation of 2-Ethoxy-1-Acetyl Naphthalene

To a solution of dry 2-ethoxy naphthalene (43g., 0.25 mol.) in dried carbon disulphide (200 cc.), cooled in ice and water, roughly powdered anhydrous aluminium chloride (73g., 0.55 mol.) was added; acetic anhydride (25.5g., 0.25 mol.) was then slowly added during 15 minutes with vigorous mechanical stirring. Hydrogen chloride was soon evolved; after 45 minutes, stirring at room temperature was started, when more hydrogen chloride was evolved. After 1 hour, when evolution of hydrogen chloride had completely ceased, the carbon disulphide was decanted from the deep green solid complex which was formed during the reaction. This after washing with carbon disulphide to remove unreacted 2-ethoxy naphthalene and acetic anhydride, was decomposed with ice and hydrochloric acid (concentrated hydrochloric acid 50 cc. + ice and water 500 cc.), with thorough stirring. The liberated oil, containing traces of solid, was extracted with ether. The ethereal solution was shaken vigorously with 10% sodium hydroxide solution (150 cc.) and then washed with water till washings were alkali-free. The ethereal solution was dried over anhydrous potassium carbonate, decolourised with animal charcoal and filtered. Ether was removed by distillation and the crude product fractionated. The fraction b.p. 80-90°/0.1-0.3 mm. gave on cooling a crystalline substance m.p. 36-37°, yield 6g.; its m.p. when mixed with an authentic specimen of 2-ethoxy naphthalene m.p. 37.5° remained unchanged (36-37°). The fraction b.p. 122-124°/0.1 mm. gave a faintly yellowish liquid which on cooling
set to a crystalline mass, m.p. 59.5-60.5°, yield 18g. This separated from aqueous ethanol in prisms m.p. 62-62.5°, yield 15.3g. The m.p. remained unchanged on further crystallisation. Gattermann (Ber., 1890, 23, 1210) gives m.p. 62-63°.

During acylation of 2-ethoxy naphthalene, some of the reaction product was converted into 1-acetyl-2-naphthol by the action of hydrogen chloride. The alkaline extract on acidification with dilute hydrochloric acid gave a yellowish brown crystalline mass of 1-acetyl-2-naphthol. This was filtered, washed with water, dilute sodium bicarbonate solution and finally by water and dried: m.p. 60-62.5°, yield 19.5g. It separated from aqueous ethanol in yellowish brown prisms m.p. 63.5-64.5°. This was subsequently converted into 1-acetyl-2-ethoxy naphthalene with diethyl sulphate.

**Ethylation of 1-Acetyl-2-Naphthol**

The dried crude 1-acetyl-2-naphthol (60g.) was dissolved in a solution of sodium hydroxide (14g.) in water (275 cc.). To the ice-cold solution of 1-acetyl-2-naphthol in sodium hydroxide, was added diethyl sulphate (42.5 cc., 49.7g.), slowly during 1 hour with vigorous mechanical stirring. The temperature of the reaction mixture was maintained at 3-5° for 1 hour. A solid mass of 1-acetyl-2-ethoxy naphthalene separated gradually during the addition of diethyl sulphate. After a further 1 hour's stirring at 3°, the reaction mixture was warmed
on a water bath (50-60°) for 1½ hours with mechanical stirring. The brown solid mass which separated on cooling was filtered, washed with sodium hydroxide solution (10%) and then liberally with water several times and dried: m.p. 55-58°, yield 50g. This after two crystallisations from aqueous ethanol gave faintly yellowish prisms m.p. 62-62.5°, yield 37g. This ketone when mixed with 1-acetyl-2-naphthol of m.p. 63.5-64.5° had m.p. 35-38° but when mixed with 1-acetyl-2-ethoxy naphthalene m.p. 62-62.5° had m.p. 61.5-62.5°, hence it was 2-ethoxy-1-acetyl-naphthalene.

To get rid of the yellowish tinge the 1-acetyl-2-ethoxy naphthalene (61g.) was distilled at reduced pressure, giving a colourless liquid b.p. 132-134°/0.5-0.6 mm., which set to a crystalline mass, m.p. 62-62.5° yield 60g.

**Reduction of 1-Acetyl-2-Ethoxy Naphthalene**

1-Acetyl-2-ethoxy naphthalene (52.6g.) was added to aluminium iso-propoxide solution in anhydrous iso-propyl alcohol, prepared from aluminium (20g.), anhydrous iso-propyl alcohol (400 cc.), mercuric chloride (0.5g.), and carbon tetrachloride (1 cc.). The resulting mixture was refluxed for about 15 minutes on a steam bath and the acetone formed was removed by slow distillation. The acetone test (2,4 dinitrophenyl hydrazine) became negative after about 2½ hours. The residual iso-propyl alcohol was distilled off at slightly reduced pressure. The reaction mixture was cooled and decomposed by dilute sulphuric acid (1000 cc., 3 N) and crushed ice. The crystalline solid mass of
α-(2-ethoxy-1-naphthyl) ethanol was extracted with ether. The ethereal solution was washed with dilute sulphuric acid, then with water until the aqueous washing was acid-free and dried over anhydrous potassium carbonate. It was concentrated to small bulk and then diluted with light petroleum (b.p. 40-60°). The carbinol separated in rosettes of small prisms, m.p. 60.5-62°, yield 44g., 84%. On recrystallisation from light petroleum (b.p. 40-60°) containing a little ether it had m.p. 61-62°, a value almost unchanged after crystallisation.

This carbinol when mixed with the parent ketone had m.p. 40-42°.

Preparation of (±)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate

Phthalic anhydride (17.8g.), dissolved in warm dry pyridine (12g.), was cooled and mixed with (+)-α-(2-ethoxy-1-naphthyl)ethanol (25.9g.) and the mixture triturated for about 10 minutes and then kept in a water bath at 35-50° with frequent shaking for about 90 minutes; during this time the mixture became homogeneously viscous.

Next day the viscous mass was dissolved in acetone and decomposed as usual with dilute hydrochloric acid and ice. The resultant clear solution was then mixed with more crushed ice and water until precipitation was complete, and thoroughly stirred. The precipitated oil set to a slightly yellowish hard mass in about 7 minutes. After 4 hours this was broken up, filtered, washed with much water – to dissolve any traces of phthalic acid – and dried in vacuo at room temperature; it had
m.p. 121.5-122.5° (it decomposed, giving phthalic acid which has m.p. 200°, decomp.); yield 39.5g., 90%. It separated from ether in colourless irregular plates m.p. 128° (decomp.), shrinking at 125°. Found on rapid tiration with 0.1 N NaOH, M 365 (0.402g. H.P. required 11.0 cc. of N/10 NaOH); C₂₂H₂₀O₅ requires M 364.

This hydrogen phthalate is very sparingly soluble in ether or benzene and thus large excesses of these solvents are required for crystallisation of a small amount of the hydrogen phthalate. Methanol, ethanol, chloroform and carbondisulphide were not suitable solvents for crystallisation because in these solvents the ester is unstable - phthalic acid separating ultimately.

Thus, for effecting the resolution, the dried crude hydrogen phthalate (73g.) was washed twice with 50 ml. portions of ether to remove traces of unreacted carbinol and other impurities when an almost white mass of the hydrogen phthalate was obtained; m.p. 125° (decomp.), yield 65g. Found on rapid tiration with 0.1 N NaOH, M 361 (0.397g. of H.P. required 11.0 cc. N/10 NaOH); C₂₂H₂₀O₅ requires M 364.

This ester was found satisfactory for resolution.

Resolution of (±)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate as its Brucine Salt

Brucine proved to be the most suitable alkaloid for effecting the resolution of the (±)-α-(2-ethoxy-1-naphthyl)ethyl hydrogen phthalate. But the two diastereoisomeric brucine salts of the hydrogen phthalate
differed very little in their solubility in acetone, chloroform, or ethyl acetate - other solvents such as ethanol, methanol being unsuitable for the purpose.

Preliminary experiment showed that for separation of 0.77g. of the diastereoisomeric brucine salts of the hydrogen phthalate nearly 100 cc. of warm acetone was required for effecting complete and clear solution. In chloroform both were highly soluble. A mixture of these two solvents was therefore used for effecting the resolution.

A mixture of (+)-α-(2-ethoxy-1-naphthyl)ethyl hydrogen phthalate (61.3g.) and brucine (66.5g.) was dissolved in dry chloroform (180 cc.) by gentle warming, when a clear solution was obtained. To this warm acetone (100 cc.) was added. Crystallisation of the brucine salt soon commenced. The whole was kept overnight, cooled and filtered and the crop of brucine salt washed with a little acetone. It was then submitted to fractional crystallisation - as shown in the diagram on page 128. - and after six crystallisations was obtained optically pure: m.p. 159-160°, yield 32.2g.

Decomposition of a portion of this salt in acetone with dilute hydrochloric acid and ice yielded optically active α-(2-ethoxy-1-naphthyl)ethyl hydrogen phthalate with \([\alpha]_{D}^{C_{2}} = 102.1° (c 0.93; l 1, t 22°)\).

Two further crystallisations of a little of this alkaloidal salt (2g.) from hot chloroform (5 cc.) and hot acetone (2 cc) gave no rise in m.p., 159-160°, and decomposition gave a hydrogen phthalate with \([\alpha]_{D}^{C_{2}} = 100.1° (c 1.1; l 1, t 22°)\). It is thus probable that six
The optically pure, less-soluble, brucine salt, m.p. 159-160°, (30 g.), was suspended in acetone (50 cc.) and acidified with dilute hydrochloric acid, when a homogeneous solution was obtained. The resultant solution was mixed with more crushed ice and water until precipitation was complete. After about 7 hours the aqueous layer was decanted off and the sticky mass washed several times with water containing a few drops of dilute hydrochloric acid with thorough stirring and then several times by water, to remove traces of hydrochloric acid. The sticky mass of the hydrogen phthalate was dried under vacuum at room temperature when it solidified: m.p. indefinite, 53-55° transparent solid, 95-110° opaque and 176-178° clear liquid, yield 12 g., calculated yield 14 g.

From an attempt to crystallise this hydrogen phthalate from ether, a pasty mass was obtained which solidified under vacuum at room temperature: the m.p. was indefinite, as above. Found, on rapid titration with 0.1 N NaOH, M 366.5; \( \text{C}_{22}\text{H}_{20}\text{O}_{5} \) requires M 364; (0.397 g. of H.P. required 10.90 cc. of N/10 NaOH).

Its specific rotatory powers were measured immediately after making up the solutions in different solvents, and are given in table VII, page 82.
m.p. 148-151° A (105g.)
chloroform 140 cc.
Acetone 40 cc.

m.p. 156-157° B (59.5g.)
chloroform (100 cc.)
Acetone (50 cc.)

m.p. 156-158° C (51.5g.)
chloroform (90 cc.)
Acetone (40 cc.)
filt. concentrated to 50 cc.
m.p. 135°

m.p. 159-160° D (42g.)
chloroform 65 cc.
Acetone 30 cc.
filt. 75 cc.
m.p. 145-148° C' (19g.)

m.p. 159-160° E (33g.)
filt. 50cc.
leached with boiling acetone (350cc.) and filtered at room temp.

m.p. 159-160° F (32.2g.)
filt. 350 cc.
conc. to 50cc.

F' (23.5g.) m.p. 156-159°

H. P. [a]_D^{Me_2CO} + 42.6°
[a]_D^{CS_2} - 101.5°
H.P. [a]_D^{Me_2CO} + 33.2°,
α_D + 0.87°
(α 2.62, 1 1, t 22)
Preparation of α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate from the more-soluble Brucine Salt

Solvent from A' filtrate, vide page 128, was removed by evaporation and the solid mass suspended in acetone and decomposed as above. About 0.5 g. of hydrogen phthalate, m.p. 112-116° (decomp.), shrinks at 110°, was obtained. It separated from ether in tiny plates m.p. 123-125° (decomp.). Its specific rotatory powers were measured immediately after making up the solution, and are given in table VIII, page 82.

Hydrolysis of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate with Sodium Ethoxide Solution

(+)-α-(2-Ethoxy-1-naphthyl)ethyl hydrogen phthalate (2.9 g., \([\alpha]_D^{acetone} + 42.6°; \:[\alpha]_D^{CS2} - 101.5°\) was added to a solution of sodium (0.38 g.) in ethanol (96% - 15 cc.) and triturated, when it dissolved; within 2 minutes the solution deposited a crystalline precipitate (of sodium phthalate). The mixture which was alkaline to litmus was heated on a steam bath for about 5 minutes when the precipitate increased in bulk. It was cooled and a few drops of water added. The precipitate first dissolved and on addition of more water and ice an oil separated which solidified in about 45 minutes. After 7 hours the white solid carbinol was filtered off, washed free from alkali, and dried under vacuum: m.p. 45-49°, yield 1.52 g.; calculated yield 1.72 g. It separated
from light petroleum (b.p. 40-60°) containing a little ether in glassy prismatic rods m.p. 53-54.5° and on further crystallisation the m.p. became 54-55°, a value unchanged on further crystallisation. The specific rotatory powers of this carbinol are given in table IX, page 82.

Preparation of (+)-a-(2-Ethoxy-l-Naphthyl)Ethyl Hydrogen Phthalate from the (+)-a-(2-Ethoxy-l-Naphthyl)Ethanol

(+)-a-(2-Ethoxy-l-naphthyl)ethanol (0.201 g., $[\alpha]_{D}^{\text{C}_{2}} - 31.2^\circ$) was mixed with a cooled solution of phthalic anhydride (0.14 g.) in warm dry pyridine (5 drops) and the mixture triturated for 5 minutes. The mixture was kept in warm water (35°) for about 3 minutes and then left at room temperature overnight. Next day it was dissolved in acetone and decomposed as usual with dilute hydrochloric acid. After 6 hours the supernatant liquid was decanted off and the sticky mass of the hydrogen phthalate extracted with ether. The ethereal extract was washed, dried over anhydrous calcium chloride and filtered. Ether was removed at room temperature and the hydrogen phthalate solidified under vacuum, (yield 0.27 g.). This hydrogen phthalate had $[\alpha]_{D}^{22} - 70^\circ$, $a_{D}^{22} - 0.38^\circ$ ($c$ 0.54, l 1) in carbondisulphide.
Dismutation of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate to (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl (−)-α-(2-Ethoxy-1-Naphthyl)Ethyl Phthalate and Phthalic Acid

(+)-α-(2-Ethoxy-1-naphthyl)ethyl hydrogen phthalate (2.13g; [α]_D^{22} + 42.6° in acetone) was dissolved in sodium hydroxide solution (20 cc. of 0.3 N). Just as the clear solution was obtained (about 5 minutes) the solution began to turn turbid and gradually became milky due to separation of flocculent particles. In about 4 hours a copious white precipitate was deposited in the vessel, when more water (50 cc.) was added to it. The precipitate settled at the bottom of the vessel and the supernatant liquid was clear. After keeping overnight the white solid precipitate of the neutral ester was filtered off and washed with water. The combined filtrate and washings on addition of a few drops of dilute hydrochloric acid gave no turbidity showing the absence of sodium phthalic ester in the filtrate.

The filtrate was concentrated by evaporation to small bulk and decomposed with concentrated hydrochloric acid, when crystalline phthalic acid was obtained. This was cooled in ice water, filtered, washed with a few drops of ice cold water and dried: m.p. 191-192° (decomp.), yield 0.45g. (insoluble in dry chloroform); calculated yield 0.50 g.

The white solid mass of the neutral ester was dried under vacuum: yield 1.44g; calculated yield 1.69g. It was washed with ether (15cc.) in which it was almost insoluble, to remove traces of α-(2-ethoxy-1-naphthyl) ethanol formed as a result of hydrolysis of the hydrogen
phthalic ester in alkaline medium during the process of disproportionation. The ethereal washing on evaporation at room temperature gave
only a trace of material. The neutral ester had m.p. 96° (decomp.)
indefinite, shrinks at 93°. It crystallised from acetone, and had
$[\alpha]_D^{22} + 11.9^\circ$ in acetone ($c 0.63, l 2$), $[\alpha]_D^{22} + 2.2^\circ$ in chloroform
($c 1.07, l 1$).

The molecular weight was determined by saponifying the neutral
ester with 0.5 N alcoholic caustic potash for 5 hours and titrating
the unused alkali against 0.5 N sulphuric acid. Found M 546 (0.266g.
of the neutral ester required 1.95 cc. of 0.5 N KOH); $C_36H_34O_6$
requires M 562.

In another experiment $\alpha$-(2-ethoxy-1-naphthyl)ethyl hydrogen
phthalate (4.175g., $[\alpha]_D^{22} + 22^\circ$ in acetone) was dissolved in 0.3 N
sodium hydroxide solution (38.3 cc.). The neutral ester formed
(2.9g.) had $[\alpha]_D^{22} + 20.5^\circ$, $\alpha_D^{22} + 0.53^\circ$ in acetone ($c 2.59, l 1$).
This neutral ester (1.87g.) on hydrolysis with sodium ethoxide solution
(prepared from 0.16g.) of sodium and 7cc. 96% ethanol) by warming on
a steam bath for 20 minutes gave the half racemised (+)-$\alpha$-(2-ethoxy-1-
naphthyl)ethanol $[\alpha]_D^{22} - 8^\circ$, $\alpha_D^{22} - 0.16^\circ$ in acetone ($c 2.08, l 1$),
m.p. 57.5 - 58.5°. The parent hydrogen phthalate $[\alpha]_{acetone}^{22} + 2.6^\circ$
(0.72g.) on hydrolysis with sodium ethoxide (0.1g. sodium + 7cc. 96%
ethanol by gently warming on a steam bath for 5 minutes gave (+)$\alpha$-
(2-ethoxy-1-naphthyl)ethanol $[\alpha]_D^{22} - 16.2^\circ$, $\alpha_D^{22} - 0.23^\circ$ in acetone
($c 1.45, l 1$).
Preparation of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl p Tolyl Sulphone

(+)-α-(2-Ethoxy-1-naphthyl)ethyl hydrogen phthalate (1.09g., [α]_D^{22} + 42.6° in acetone) was quickly dissolved in sodium hydroxide solution (10 cc., 0.3 N) and mixed with a solution of sodium p-toluene sulphinate (0.65g. in 10 cc. water). The whole operation was done in about 5 minutes. The mixture became turbid immediately with gradual separation of flocculent particles. After keeping overnight a white crystalline mass settled at the bottom of the vessel and the supernatant liquid became clear. The product was filtered off, washed and dried; m.p. 135-140° (decomp.), yield 0.81g; calculated yield 1.06g. The crude sulphone had [α]_D^{22} + 7° in acetone (c 3.5, l 2) and was probably contaminated with the neutral ester. The sulphone separated from acetone in colourless prisms m.p. 160.5-161.5°, yield 0.52g., [α]_D^{22} + 0° in acetone (c 1.345, l 2). It was submitted to further crystallisation when the m.p. became 161-161.5°, unchanged after further crystallisation.

Found S 8.31; C_{21}H_{22}O_3 S requires S, 9.0%.

Reaction of (+)-α-(2-Ethoxy-1-Naphthyl)Ethyl Hydrogen Phthalate with Methanol

(+)-α-(2-Ethoxy-1-naphthyl)ethyl hydrogen phthalate (6.2g., [α]_D^{22} + 33.2° in acetone) was dissolved in excess of methyl alcohol (40 cc.) and the solution allowed to evaporate slowly at room temperature. After keeping for seven days, when all the methanol had evaporated and
a white crystalline mass remained, a little was treated with sodium carbonate solution (0.3 N) and the aqueous layer was made acid with dilute hydrochloric acid. Slight turbidity appeared which became clear on shaking with a little more water showing that the hydrogen phthalate had completely reacted with the methanol. The whole was then treated with sodium carbonate solution till alkaline to litmus and extracted with ether. The ethereal layer was washed twice with a little sodium carbonate solution and by water until aqueous washing was neutral to litmus. The ethereal extract was dried over anhydrous calcium chloride, decolourised (animal charcoal), filtered, and concentrated at room temperature. The α-(2-ethoxy-1-naphthyl)ethyl methyl ether separated in white plates, m.p. 64-66°, yield 3.25g; calculated yield 3.9g. This ether had 
\[ \alpha \text{D} = 0° \text{ in acetone (c 2.7, l 1).} \] It separated from light petroleum (b.p. 40-60°) in white irregular plates, m.p. 67-67.5°; yield 2.85g. On further crystallisation the m.p. became 67.5-68° - unaltered after further crystallisation. Found C 78.57; H 7.75; "-O<sub>Me</sub>" 26.72%. C<sub>15</sub>H<sub>18</sub>O<sub>2</sub> requires C 78.23; H 7.87%; Found O from the methoxy value 13.77, calculated 13.90%. The combined aqueous and alkaline washings on evaporation to small bulk gave phthalic acid on acidification with concentrated hydrochloric acid. This was filtered, washed with a few drops of cold water and dried: m.p. 198-200° (decomp.), yield 2.35g. (insoluble in dry chloroform), calculated yield 2.8g.

In a separate experiment, (+)-α-(2-ethoxy-1-naphthyl) ethyl
hydrogen phthalate was dissolved in methanol and its rotatory powers examined at frequent intervals. It was observed that the rotation falls gradually, \([a]_D + 0^\circ\) being reached in about 330 hours as is shown in table XIV, page 85.

The solution on complete evaporation of the methanol gave a white crystalline solid which was extracted with light petroleum (b.p. 40-60°). The extract on evaporation gave a crystalline solid, m.p. 67-67.5°. When it was mixed with the analysed sample there was no depression in m.p., 67-67.5°.
Summary

Preparation and Resolution of \( \alpha \)-(6-Ethoxy-2-Naphthyl)Ethanol

\[
\begin{align*}
\text{OBt} & \quad \text{MeO} \\
\text{m.p. 37.5°} & \quad \text{COMe} \\
\text{AcCl, AlCl}_3, \text{C}_6\text{H}_5\text{NO}_2 & \quad \text{m.p. 105-106°} \\
\text{Methylation} & \quad \begin{align*}
\text{6 methoxy-(x)-acetyl} \\
\text{naphthalene m.p. 95-96°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{EtO} & \quad \text{EtO} \\
\text{m.p. 82-83°} & \quad \text{CHOHMe} \\
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \text{m.p. 113.5-114.5°} \\
\text{Ethylation} & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Phthalic anhydride} & \quad \text{AlCl}_3, \text{Pyridine} \\
\text{m.p. 171-173°} & \quad \text{EtO} \\
\text{m.p. 113-114°} & \quad \text{CHOHMe} \\
\end{align*}
\]

\[
\begin{align*}
\text{EtO} & \quad \text{EtO} \\
\text{m.p. 113.5-114.5°} & \quad \text{MeOH} \\
\text{Phthalic anhydride} & \quad \text{AlCl}_3, \text{Pyridine} \\
\text{m.p. 171-173°} & \quad \text{EtO} \\
\text{m.p. 113-114°} & \quad \text{CHOHMe} \\
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{EtO} & \quad \text{EtO} \\
\text{m.p. 113-114°} & \quad \text{MeOH} \\
\text{Phthalic anhydride} & \quad \text{AlCl}_3, \text{Pyridine} \\
\text{m.p. 171-173°} & \quad \text{EtO} \\
\text{m.p. 113-114°} & \quad \text{CHOHMe} \\
\end{align*}
\]

\[
\begin{align*}
\text{AlCl}_3, \text{Pyridine} & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 ethoxy-(x)-acetyl} \\
\text{naphthalene m.p. 73-74.5°}
\end{align*}
\end{align*}
\]

\[
\begin{align*}
\text{Al (i C}_3\text{H}_7\text{O)}_3 & \quad \begin{align*}
\text{6 hydroxy-(x)-naphthyl} \\
\text{methyl ketone m.p. 168-169.5°}
\end{align*}
\end{align*}
\]
Preparation of 6-Ethoxy-2-Acetyl Naphthalene

To an ice-cold (3°) solution of anhydrous aluminium chloride (33g., 1.25 mol.) in dry nitrobenzene (175 cc.) was added 2-ethoxy naphthalene (34.4g., 1 mol.) followed by the addition of acetyl chloride (20g., 1.25 mol.) during 15 minutes with vigorous mechanical stirring. During addition of acetyl chloride the reaction mixture turned reddish brown and evolution of hydrogen chloride fumes started. The reaction mixture was kept at 3-5° in ice for about 7 hours and then at room temperature over the week-end, when the mixture had turned green and evolution of hydrogen chloride had practically ceased. It was then decomposed with dilute hydrochloric acid (concentrated acid 75 cc. + water 150 cc.) with good stirring. The product was washed several times with water by decantation and the nitrobenzene was removed by steam distillation; towards the end a little faintly yellowish solid deposited on the walls of the condenser; it was found to be 6-ethoxy-2-acetyl naphthalene by mixed melting point with an authentic specimen.

After removal of nitrobenzene the sticky mass of the crude ketone was shaken with a mixture of benzene and a little very dilute hydrochloric acid, and filtered to remove some insoluble material - other solvents such as ether and chloroform were found unsuitable for the purpose. The insoluble material had m.p. 165-169°, yield, 4g. After two recrystallisations from 96% ethanol (charcoal) it gave a crystalline solid, m.p. 171-173°. This proved to be 6-hydroxy-2-acetyl naphthalene on identification by ethylation (below).
The benzene layer was separated from the aqueous layer of the filtrate, washed with water until acid-free (Congo red), then with 200 cc. of 0.2 N sodium hydroxide solution, and finally by water till the aqueous washing was alkali-free (litmus). The benzene solution was dried over anhydrous sodium sulphate, filtered, reduced to small bulk, and a little ligroin added to the product. Yellowish prismatic needles of 6-ethoxy-2-acetyl naphthalene separated on keeping over night: m.p. 79.5-81°. This on recrystallisation from aqueous ethanol separated in almost colourless tiny needles m.p. 82-83°, yield 12g. The m.p. remained unchanged on further crystallisation.

The combined mother liquors on distillation at reduced pressure gave a fraction, b.p. 152-168°/0.5 mm., a yellowish liquid, which solidified to a crystalline mass, m.p. 73-76°. This after two crystallisations from aqueous ethanol gave colourless prismatic needles, m.p. 82-83°, yield 5g. The m.p. of a mixture of the two samples remained unchanged. Thus the total yield of pure 6-ethoxy-2-acetyl naphthalene was 17g., 40%.

The mother liquor after crystallisation of the ketone gave a thick viscous yellowish oil which did not solidify.

The structure of 6-ethoxy-2-acetyl naphthalene, m.p. 82-83°, was proved by dealkylating the ketone and remethylating the phenolic ketone thus obtained. This procedure was adopted because no reference to 6-ethoxy-2-acetyl naphthalene was found in literature, but 6-methoxy-2-acetyl naphthalene has been prepared by Robinson and Rydon (J.C.S., 1939, 1399), Haworth and Sheldrick (J.C.S., 1934, 865), Fries and Schimmel-schmidt (Ber., 1925, 58, 2835), and Dr. Sultan Mahmud (unpublished work,
thesis London, 1959). The details of the procedure are given below.

The ketone, m.p. 82-83° (0.38g.), dissolved in glacial acetic acid (10 cc.), was mixed with concentrated hydrochloric acid (6 cc.) and the mixture refluxed in an oil bath (150°) for 4 hours. Next day the acid was neutralised with sodium bicarbonate solution and the precipitated phenolic ketone filtered, washed and dried, yield 0.2g. This was dissolved in sodium hydroxide solution (0.2g. sodium hydroxide + 25 cc. water) and filtered to remove the insoluble normal ketone (insoluble residue 0.06g.). The yellow solution (filtrate), which was alkaline to litmus, was mixed with about 1 cc. of dimethyl sulphate and the mixture shaken for ½ hour and then kept in warm water (40-50°) for ½ hour. After another hour the precipitated solid was filtered off, washed with dilute sodium hydroxide solution and then several times with water. The moist solid crystallised from 96% ethanol (charcoal) in colourless tiny plates m.p. 103.5-105°. This separated from slightly aqueous methanol in tiny plates m.p. 105-106°, a value unchanged after further crystallisation. Hence this was 6-methoxy-2-acetyl naphthalene. Haworth and Sheldrick (loc cit) give m.p. 104-105°; Fries and Schimmelschmidt (loc cit) give m.p. 105°; Dr. Sultan Mahmud (Ph.D. thesis, 1959, London) gives m.p. 107° for 6-methoxy-2-acetyl naphthalene. This preparation proves that the parent compound, m.p. 82-83° is 6-ethoxy-2-acetyl naphthalene.

Attempt to dealkylate the 6-ethoxy-2-acetyl naphthalene with anhydrous aluminium chloride resulted in the formation of violet resinous matter.
The alkaline washing of the benzene solution of the crude ketone on acidification with dilute hydrochloric acid (Congo red) gave a yellowish mass of 2-hydroxy-(x)-acetyl naphthalene m.p. 121° - indefinite, yield 4.5g. This on 4 recrystallisations from aqueous ethanol gave fine crystals of m.p. 168-169.5°, a value unchanged on further crystallisation. This compound differs from the 6-hydroxy-2-acetyl naphthalene (2-hydroxy-6-acetyl naphthalene), m.p. 171-173°, because a mixture of the two had m.p. 137-139°.

Further, the 2-hydroxy-(x)-acetyl naphthalene, m.p. 168-169.5°, when methylated and ethylated gave 2-methoxy-(x)-acetyl naphthalene m.p. 95-96° and 2-ethoxy-(x)-acetyl naphthalene m.p. 73-74.5° respectively. The details are given below.

Methylation of 2-Hydroxy-(x)-Acetyl Naphthalene

A solution of 2-hydroxy-(x)-acetyl naphthalene in sodium hydroxide solution prepared from the ketone (1.8g.) and sodium hydroxide (0.5g.) in 30 cc. water was filtered and mixed with dimethyl sulphate (1.5 cc.) and shaken at room temperature for about half an hour. The mixture was then kept in hot water (40-50°) for another half an hour. After 1 hour the solid separated was filtered, washed with dilute sodium hydroxide solution and then several times with water. The crude ketone had m.p. 92-96°. This separated in colourless tiny needles from slightly aqueous ethanol and after two crystallisations had m.p. 95-96° - unchanged on further
crystallisation. The mixed m.p. with 6-methoxy-2-acetyl naphthalene, m.p. 105-106° was indefinite; 93° onwards. Hence the 2-hydroxy-(x)-acetyl naphthalene was different from the 2-hydroxy-6-acetyl naphthalene.

**Ethylation of 2-Hydroxy-(x)-Acetyl Naphthalene**

2-Hydroxy-(x)-acetyl naphthalene (10g.) was dissolved in sodium hydroxide solution (2.5g. sodium hydroxide + 200 cc. water) - excess of water was used because the sodium salt of the phenolic ketone was not very soluble in water. To this ice-cold (3-5°) dark yellow solution, diethyl-sulphate (9g., 8 cc.) was added in about 30 minutes with thorough shaking. During addition of diethylsulphate, yellowish crystalline solid separated. The mixture was then warmed on a water bath for about 2 hours. On cooling yellowish brown solid separated. This was filtered off, washed with dilute sodium hydroxide solution and then several times with water, and crystallised from 96% ethanol. It separated in tiny yellowish needles, m.p. 70-72°, yield 4g. On two further crystallisations from aqueous methanol (charcoal) very faintly yellowish needles were obtained m.p. 73-74.5° - unchanged on further crystallisation.

These observations show that, during acylation of 2-ethoxy naphthalene in nitrobenzene, although the major product is 2-ethoxy-6-acetyl naphthalene (6-ethoxy-2-acetyl naphthalene) m.p. 82-83°, substitution at another position in the naphthalene ring also takes place.
Ethylation of 6-Hydroxy-2-Acetyl Naphthalene m.p. 171-173°

6-Hydroxy-2-acetyl naphthalene (7g.) was dissolved in sodium hydroxide solution (sodium hydroxide 2g., + 250 cc. water) and filtered to remove traces of insoluble impurities - excess of water was used because the sodium salt of the phenolic ketone was only slightly soluble in water. To the ice cold (3-5°) solution diethylsulphate (5 cc.) was added in about half an hour with good shaking. The mixture was then heated on water bath for about 2 hours. Brown solid separated on cooling, which was washed with 5% sodium hydroxide solution and then with water several times by decantation. It was then filtered, washed and dried, when a yellow crystalline mass was obtained, m.p. 73-77°. After two crystallisations from aqueous ethanol (charcoal) tiny needles of 2-ethoxy-6-acetyl naphthalene, m.p. 82-83° - unchanged on further crystallisation - were obtained, yield 2.5g.

The mixed melting point with the previously prepared 6-ethoxy-2-acetyl naphthalene, m.p. 82-83°, remained unchanged. This shows that the phenolic ketone, which was insoluble in benzene during extraction of the crude 6-ethoxy-2-acetyl naphthalene, is 6-hydroxy-2-acetyl naphthalene.

Reduction of 6-Ethoxy-2-Acetyl Naphthalene

(a) With zinc dust and alcoholic sodium hydroxide.

A suspension of zinc dust (2g.) in a solution of sodium hydroxide
(2g.) and the ketone (1.2g.) in ethanol (50 cc., 96%) was heated under vigorous reflux for 4 hours on a steam bath and then filtered whilst hot; the unchanged zinc dust being washed twice with 5 ml. portions of boiling ethanol. The combined filtrates were evaporated to small bulk and diluted with water. After keeping over the week-end, solid separated which was filtered off, washed and dried: m.p. 176-182°, yield 0.95g. It separated from 96% ethanol or acetone in colourless prisms and after two crystallisations had m.p. 193.5-194.5°, a value unchanged after further crystallisation.

This substance is probably the bi-molecular reduction product of 6-ethoxy-2-acetyl naphthalene because its m.p., 193.5-194.5°, differs from that of α-(6-ethoxy-2-naphthyl)ethanol, 113.5-114.5°. Found C 78.19, H 6.84%; C_{28}H_{30}O_4 requires C 78.11; H 7.02%.

(b) By aluminium isopropoxide

6-Ethoxy-2-acetyl naphthalene (30.0g.) was added to aluminium isopropoxide solution in anhydrous iso-propanol, prepared from aluminium (14g.), anhydrous iso-propyl alcohol (600 cc.), mercuric chloride (0.5g.), and carbontetrachloride (1 cc). The resulting mixture was refluxed for about 15 minutes on a steam bath, and the acetone formed was removed by slow distillation. The acetone test (2:4 dinitrophenyl hydrazine) became negative after about 2 hours. The residual iso-propyl alcohol was distilled off at slightly reduced pressure. The reaction mixture was cooled and decomposed by dilute sulphuric acid (700 cc., 0.3 N) and
crushed ice. After about 15 hours the crystalline solid \( \alpha \)-(6-ethoxy-2-naphthyl)ethanol was filtered off, washed and dried: m.p. 110-112\(^\circ\), yield 30g. It separated from ether (charcoal) and light petroleum (b.p. 40-60\(^\circ\)) in tiny white needles, m.p. 113.5-114.5\(^\circ\), yield 27g. The mother liquor gave 1g. of the carbinol, m.p. 112-113\(^\circ\). The carbinol on further crystallisation from methanol was obtained in tiny white needles, m.p. 113.5-114.5\(^\circ\), a value unchanged after recrystallisation.

**Preparation of \((\pm)\)-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate**

Phthalic anhydride (16.8g.) dissolved in warm dry pyridine (12g.) was cooled and mixed with \((\pm)\)-(6-ethoxy-2-naphthyl)ethanol (24.5g.) and the mixture triturated for about 10 minutes and then kept in a water bath at 45-50\(^\circ\) with frequent shaking for about 1 hour during which time the mixture became homogeneously viscous.

Next day the viscous mass was dissolved in acetone and decomposed as usual with dilute hydrochloric acid and ice. The resultant clear solution was then mixed with more crushed ice and water and thoroughly stirred. The precipitated oil set to a slightly yellowish solid in about 15 minutes. After 3 hours this was broken up, filtered off, washed with much water - to dissolve any traces of phthalic acid - and dried in vacuo at room temperature; m.p. 126-127\(^\circ\), yield 39.2g., 95\%. It separated from chloroform and benzene in clusters of small white needles, m.p. 130-130.5\(^\circ\). The melting point remained unchanged when a little of
the hydrogen phthalate was recrystallised from ether-light petroleum (b.p. 40-60°). Found, on rapid titration with 0.1 N NaOH, M 362 (0.326g. of H.P. required 9.00 cc. N/10 NaOH); $C_{22}H_{20}O_5$ requires M 364.

Resolution of (±)-a-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate as its Cinchonidine Salt

Cinchonidine proved to be the most suitable alkaloid for effecting the resolution of the (±)-a-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate. The two diastereoisomeric cinchonidine salts of the hydrogen phthalate differed considerably in their solubility in acetone in the cold, and more so in the warm.

Thus a mixture of (±)-a-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate (44g.) and cinchonidine (35.6g.) was dissolved in acetone (500 cc.). The less-soluble cinchonidine salt of the hydrogen phthalate began to separate soon. This was kept overnight, cooled and filtered off. The crop (A) was then leached with boiling acetone several times and collected on a filter; after repeating the process 7 times it was obtained optically pure, m.p. 186-187°, yield 36g. The details of the procedure are shown in the diagram, page 147.

Decomposition of a portion of this salt in acetone with dilute hydrochloric acid and ice yielded the a-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate having $[\alpha]_D^{22} = -32.2^\circ$ ($c$ 1.52, l 1) in acetone.
Two further crystallisations of a little of this cinchonidine salt from acetone gave no rise in m.p., 186-187°, and decomposition of this alkaloidal salt gave a hydrogen phthalate with $[\alpha]_D^{22} = 32.2^\circ$ ($c 1.4, l 1$) in acetone. It is thus probable that the less-soluble cinchonidine salt was obtained in optically pure condition.

**(-)-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate**

The optically pure, less-soluble, cinchonidine salt, m.p. 186-187°, (33g.), was suspended in acetone (100 cc.) and acidified with dilute hydrochloric acid, when a homogeneous solution was obtained. The resultant solution was mixed with more crushed ice and water until precipitation was complete. The precipitated oil on stirring immediately (within 3 minutes) set to hard white crystalline mass. After 4 hours this was broken up, filtered off, washed with much water, and dried in vacuo at room temperature; m.p. 130-132° (decomp.), yield 18g. This separated from chloroform and benzene, and from ether — light petroleum (b.p. 40-60°) in tiny white needles and after two crystallisations had m.p. 138-139° unchanged on further crystallisation. Found, on rapid titration with 0.1 N NaOH, $M$ 367; (0.528g. of H.P. required 14.40 cc. of N/10 NaOH); $C_{22}H_{20}O_5$ requires $M$ 354.

Its specific rotatory powers were measured immediately after making up the solutions in different solvents, and are given in table X, page 83. This hydrogen phthalate is too insoluble to allow any polarimetric observation in carbon disulphide.
### Fractional Crystallisation of Cinchonidine Salt of (+)-a-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate

#### (+)-a-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate (44g.) + Cinchonidine (35.6g.) in Acetone 500 cc.

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>m.p. 179-181°</td>
<td>A (46.4g.)</td>
<td>Leached with boiling acetone 350 cc. Filt. 500 cc. conc. to 100 cc. and seeded with crop A. No insoluble salt separated. H.P. (18g.) ([a]_D^{22} + 32.9°) in acetone.</td>
</tr>
<tr>
<td>m.p. 182-183°</td>
<td>B (43.7g.)</td>
<td>Filt. 350 cc. Leached with boiling acetone 400 cc. Conc. to 50 cc. and seeded with crop B. No insoluble salt separated. ([a]_D^{22} + 32°) in acetone (a_D^{22} + 0.72°) (c 2.24, 1 1)</td>
</tr>
<tr>
<td>m.p. 182-183°</td>
<td>C (42g.)</td>
<td>Filt. 400 cc. conc. Leached with boiling acetone 400 cc.</td>
</tr>
<tr>
<td>m.p. 182-183°</td>
<td>D (40.9g.)</td>
<td>Leached with boiling acetone 400 cc. and filtered warm. Filt. 400 cc. conc. to 50 cc.</td>
</tr>
<tr>
<td>m.p. 183-184°</td>
<td>E (40.1g.)</td>
<td>Leached with boiling acetone 400 cc. and filtered warm. Filt. 400 cc. conc. Concentrated to 100 cc. to 25 cc.</td>
</tr>
<tr>
<td>m.p. 185-186°</td>
<td>F (39g.)</td>
<td>Leached with boiling acetone 1000 cc. and filtered warm. Filt. 400 cc. conc. to 25 cc.</td>
</tr>
<tr>
<td>m.p. 186-187°</td>
<td>G (37g.)</td>
<td>Leached with boiling acetone 1000 cc. and filtered warm. Filt. 1000 cc. conc. to 50 cc. H.P. Cinchonidine recovered.</td>
</tr>
<tr>
<td>186-187°</td>
<td>Cinchonidine (36g. nearly)</td>
<td>M.p. 186-187° Filt. 1000 cc. conc. to 50 cc. H.P. H.P. ([a]_D^{22} - 37°) in acetone</td>
</tr>
</tbody>
</table>

Volumes of the filtrates are approximate.
Filtrate A was concentrated to about 100 cc. and seeded with the less-soluble cinchonidine salt of the hydrogen phthalate. After keeping over the weekend, the mixture set to a sticky mass which did not appear to contain the above salt. The whole was dissolved in acetone (50 cc.) and decomposed with dilute hydrochloric acid and ice as usual. On dilution with more ice and water an oil separated which solidified immediately. The solid was broken up, filtered off, washed with much water and dried: m.p. 135-136°. Yield 18g., \([\alpha]_D^{22} + 32.9^\circ (c 2.22, 1 l)\) in acetone. It separated from chloroform and benzene, and ether-light petroleum in clusters of tiny white needles, m.p. 137.5-138°, unchanged on further crystallisation. Found, on rapid titration with 0.1 N NaOH, M 368 (0.43 g. of H.P. required 11.70 cc. N/10 NaOH), \(C_{22}H_{20}O_5\) requires M 364.

Its specific rotatory powers are given in table XII, page 83.

Hydrolysis of Optically Active \(\alpha-\)\((6-\text{Ethoxy}-2-\text{Naphthyl})\)Ethyl Hydrogen Phthalate

(a) With dilute aqueous sodium hydroxide solution

Optically pure \(\alpha-\)(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate (0.50g., \([\alpha]_{D}^{\text{MeOH}CO} - 37^\circ\)) was dissolved in sodium hydroxide solution, prepared from sodium hydroxide (0.12g.) and water (10 cc.) and the solution heated on a steam bath. The solution became turbid in about
5 minutes. After being heated vigorously for 10 minutes, the mixture was diluted with water. Next day the gelatinous white precipitate of the \( \alpha-(6\text{-ethoxy-2-naphthyl})\)ethanol was filtered, washed and dried; m.p. 93-97\(^\circ\), yield 0.21g., calculated 0.30g. This carbinol had \([\alpha]_D^{22} + 0^\circ\) (c 1.12, l 1) in acetone. It separated from methanol in tiny needles; m.p. 110-113\(^\circ\) unchanged on further crystallisation.

(b) With sodium ethoxide solution

Optically pure \( \alpha-(6\text{-ethoxy-2-naphthyl}) \)ethyl hydrogen phthalate (0.72g., \( \alpha \quad \frac{100}{D} = 37^\circ \)) was added to a solution of sodium (0.092g.) in ethanol (96\% - 7 cc.) and stirred, when the hydrogen phthalate dissolved and a crystalline mass (of sodium phthalate) separated. The mixture which was alkaline to litmus, was heated on a steam bath for 20 minutes when the precipitate increased in bulk. It was then cooled and a few drops of water added. The precipitate first dissolved and on further dilution with water gave a gelatinous white precipitate. Next day the solid carbinol was filtered off, washed free from alkali and dried under vacuum; yield 0.33g; calculated 0.43g. It separated from aqueous methanol or light petroleum (b.p. 40-60\(^\circ\)) containing a little ether in tiny glistening needles; m.p. 94.2-94.8\(^\circ\), yield 0.25g. The rest of the carbinol was obtained from the mother liquor after completely evaporating the solvent (light petroleum, b.p. 40-60\(^\circ\)) at room temperature and had m.p. 94-94.8\(^\circ\). The m.p. of the carbinol remained unchanged on further crystallisation: 94.2-94.8\(^\circ\).

The specific rotatory powers of this carbinol are given in table XI, page 83.
Preparation of $\alpha$-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate from the optically active $\alpha$-(6-Ethoxy-2-Naphthyl)Ethanol $\alpha_D^{CHCl_3} + 44.6^\circ$

$\alpha$-(6-Ethoxy-2-naphthyl)ethanol (0.132g., $\alpha_D^{CHCl_3} + 44.6^\circ$) was mixed with a cooled solution of phthalic anhydride (0.091g.) in warm dry pyridine (4 drops) and triturated for 5 minutes. The mixture was kept at 45-50° in a water bath for about one hour, in which time the mixture became homogeneous. Next day the mixture was worked up as described in the preparation of (+)hydrogen phthalate. The hydrogen phthalate (0.17g.) was crystallised from chloroform-benzene, and m.p. 137-137.5°, unchanged on further crystallisation and, $[\alpha]^{22}_D + 36^\circ$, $\alpha_D^{24} = 0.17^\circ$ ($\alpha 0.467$, $\beta 1.1$, $t 24^\circ$) a value which is almost equal to that of the original optically pure hydrogen phthalate $[\alpha]^{22}_D + 37^\circ$.

A mixture of this hydrogen phthalate with the original optically pure hydrogen phthalate had m.p. 137°.

The above demonstrates the optical purity and chemical identity of the carbinol.

Formation of $(\pm)$-$\alpha$-(6-Ethoxy-2-Naphthyl)Ethyl-$p$-Tolylsulphone

$(+)$-$\alpha$-(6-Ethoxy-2-naphthyl)ethyl hydrogen phthalate (1.82g., $\alpha_D^{22} + 32.9^\circ$ in acetone) was dissolved in sodium hydroxide solution (16.7 cc., 0.3 N) and mixed with a solution of sodium-$p$-toluene sulphinate (1.1g. in 15 cc. water). The mixture remained clear for
several hours. After keeping overnight the solution became turbid and a few white crystalline particles settled at the bottom of the vessel in about 24 hours. The crystalline precipitate increased in bulk gradually, and after 5 days was filtered off, washed, and dried. The crude sulphone had m.p. 77-82°, yield 1.45g., calculated yield 1.76g; $[\alpha]_D^{22} + 11^\circ$, $\alpha_D^{22} + 0.11^\circ (c 1.04, 1 l)$ in acetone. It separated from methanol in tiny prisms m.p. indefinite 105-121°. On further crystallisation from methanol it had m.p. 111-120°, $[\alpha]_D^{22} + 4^\circ$, $\alpha_D^{22} + 0.04^\circ (c 1.02, 1 l)$ in acetone. The melting point remained unaltered on further crystallisation and it is considered that the sulphone was contaminated with the neutral ester from which it was not easily separated.

Accordingly the reaction was carried out in formic acid.

A mixture of (-)-a-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate (0.728g., $[\alpha]_D^{22} - 37^\circ$ in acetone) and sodium-p-toluene sulphinate (0.43g.) was mixed with formic acid (7 cc., 90%) and the mixture gently heated on a steam bath for 5 minutes when a clear solution was obtained. It was further heated for about 2 minutes when it became turbid. It was then diluted with water when a white crystalline precipitate was formed. This was filtered off, washed and dried, and had m.p. 118-120°, yield 0.62g., calculated yield 0.708g. This sulphone had $[\alpha]_D^{22} + 0^\circ (c 1.19, 1 l)$ in acetone. It separated from aqueous acetone in colourless prisms on slow evaporation of the solvent: m.p. 127-127.5°, unchanged after further crystallisation. Found S 8.6; $C_{21}H_{22}O_3$ S requires S 9.0%.
Dissmutation of (-)-α-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate to (±)-α-(6-Ethoxy-2-Naphthyl) Ethyl (-)-α-(6-Ethoxy-2-Naphthyl)Ethyl Phthalate

(-)-α-(6-Ethoxy-2-naphthyl)ethyl hydrogen phthalate (3.64g., \([\alpha]_{D}^{22} = 37^\circ\) in acetone) was dissolved in sodium hydroxide solution (33.4 cc. of 0.3 N). The solution remained clear for more than 5 hours. Next day the solution became turbid and flocculent particles separated. It was difficult to filter the neutral ester formed, due to its gelatinous nature. After 10 days a little water (25 cc.) was added to the mixture and the precipitate coagulated by centrifuge. The neutral ester was then filtered off, washed, and dried under vacuum at room temperature; yield 2.5g; calculated 2.81g. It separated from ether-light petroleum (b.p. 40-60°) in tiny white needles and after two crystallisations had m.p. 114.5-116.5° (shrinks at 90°). This neutral ester had \([\alpha]_{D}^{22} = 21.7^\circ; \alpha_{D}^{22} = 0.40^\circ (c 1.84, l 1)\) in acetone.

Its molecular weight was determined by saponifying the neutral ester with 0.5 N (approx.) alcoholic caustic potash for 5 hours and back titrating with 0.5 N sulphuric acid as usual. Found M 549 (0.500g. of the neutral ester required 3.65 cc. of 0.5 N alcoholic KOH); \(C_{36}H_{34}O_{6}\) requires M 562.

The neutral ester (0.7g., \([\alpha]_{D}^{22} = 21.7^\circ\) in acetone) was added to a solution of sodium (0.07g.) in ethanol (96° - 15 cc.) and the mixture stirred when the neutral ester almost dissolved. The mixture was then gently refluxed on a steam bath for 55 minutes. It was then cooled and a few drops of water added when the sodium phthalate dissolved and on
Further dilution with water a white gelatinous mass of the half-racemised carbinol separated. Next day it was filtered, washed, and dried. m.p. 106.5-108.5°; yield 0.48g., calculated 0.54g. It separated from ether-light petroleum (b.p. 40-60°) in fine needles and after two crystallisations had m.p. 111-112° (shrinks at 90°) - unchanged on further crystallisation.

This carbinol had $[\alpha]^2_D + 16^\circ$, $a^2_D + 0.23^\circ$ ($\gamma$ 1.49, $\Delta$ 1) in acetone.

A mixture of the neutral ester and this carbinol had m.p. 85-95° (indefinite).

The filtrate and washings of the neutral ester gave phthalic acid: m.p. 197-200° (decomp.) - insoluble in dry chloroform - yield 0.85g; calculated 0.83g.

The experiment was repeated with (-)-a-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate (1.82g., $[\alpha]^2_D + 22^\circ$ in acetone) and sodium hydroxide (16.7 cc., 0.3 N). The neutral ester $[\alpha]^2_D - 21^\circ$, $a^2_D - 0.10^\circ$ ($\gamma$ 0.487, $\Delta$ 1) in acetone obtained gave on hydrolysis as before, a carbinol, $[\alpha]^2_D + 20^\circ$, $a^2_D + 0.16^\circ$ ($\gamma$ 0.79, $\Delta$ 1) in chloroform.

**Reaction of (+)-a-(6-Ethoxy-2-Naphthyl)Ethyl Hydrogen Phthalate with Methanol**

(+)-a-(6-Ethoxy-2-naphthyl)ethyl hydrogen phthalate (7.2g., $[\alpha]^2_D + 32.9^\circ$ in acetone) was dissolved in hot methanol (100 cc., 90%). After keeping over the week-end some crystalline material had separated. A little was taken out and pressed over porous plate. It was then
treated with dilute sodium carbonate solution and filtered. The filtrate, which was alkaline to litmus, on acidification with dilute hydrochloric acid gave turbidity which persisted even on further dilution with water, showing the presence of the unchanged hydrogen phthalic ester in the reaction mixture. After another 3 days it was found that unchanged hydrogen phthalate was still present in the reaction mixture. Consequently the mixture was refluxed on a steam bath for 30 hours and after every 6 hours of refluxing, methanol was distilled off and the solid obtained tested for completion of the reaction as before. After 30 hours it was found that the hydrogen phthalate had completely reacted with the methanol. The reaction product was then treated with sodium carbonate solution till alkaline to litmus, filtered, and the (+)-α-(6-ethoxy-2-naphthyl)ethyl methyl ether so obtained washed till alkali-free, and dried; yield 3.3g; 

\[ \alpha^\circ_\text{D} = 0^\circ, (\alpha 2.5, 1.1) \] in acetone. This separated from hot methanol in prisms: m.p. 103.5-104.5°. On subsequent crystallisation it had m.p. 104-104.5° - unchanged on further crystallisation. Found C 77.74, H 7.71, "OMe" 26.82%; \( \text{C}_{15}\text{H}_{18}\text{O}_2 \) requires C 78.23; H 7.87%. Found 0 from the "methoxy" value, 13.82, calculated 13.90%.

The filtrate and washings were concentrated to small bulk and decomposed with concentrated hydrochloric acid, which gave phthalic acid; m.p. 200° (decomp.) - insoluble in dry chloroform - yield 2g.

In a separate experiment, when (-)-α-(6-ethoxy-2-naphthyl)ethyl hydrogen phthalate was dissolved in methanol and its rotatory powers examined at frequent intervals at room temperature, it was found to be constant for several days, as is shown in table XV, page 86.
Reagents and Solvents

Carbondisulphide was dried over anhydrous calcium chloride and distilled: the fraction, b.p. 46° was collected.

Chloroform was washed with water, dried with anhydrous calcium chloride and distilled: the fraction b.p. 61° collected and kept over anhydrous calcium chloride.

Benzene was dried with anhydrous calcium chloride, and distilled: the fraction b.p. 81-82° collected and kept over sodium wire.

Ether was dried with anhydrous calcium chloride, and distilled: the fraction b.p. 34-36° was collected and kept over sodium wire.

Pyridine was dried over caustic potash and distilled: the fraction b.p. 115-116° was collected and kept over caustic potash sticks.

Phenetole was dried over anhydrous calcium chloride, and distilled: the fraction b.p. 168-170°, was collected.

Carbon tetrachloride was dried over calcium chloride, distilled, and fraction b.p. 76.5-77° collected.

Acetone was dried over anhydrous potassium carbonate was distilled: and the fraction b.p. 56° collected.

Isopropyl alcohol ("Avantine") was dried over fused calcium oxide (previously heated in a muffle furnace to 500-600°), distilled over this reagent, and the fraction b.p. 82° collected.

Nitrobenzene was dried over anhydrous calcium chloride, and distilled: the fraction b.p. 210° was collected.
Methanol was dried over fused calcium oxide, then over anhydrous copper sulphate, and distilled: the fraction b.p. 65° was collected.

Acetic anhydride was fractionated, and the fraction b.p. 137.5-138° collected.