SECTION III

INTRODUCTION & DISCUSSION TO THE PREPARATION OF OPTICALLY ACTIVE TERTIARY ALCOHOLS CONTAINING TWO EQUAL GROUPS
INTRODUCTION AND DISCUSSION TO THE PREPARATION
OF
OPTICALLY ACTIVE TERTIARY ALCOHOLS CONTAINING TWO EQUAL GROUPS:

The esters of carboxylic acids react with Grignard reagents to form tertiary alcohols containing two equal groups introduced from Grignard reagent.

THE MECHANISM OF THE REACTION
BETWEEN A CARBOXYLIC ESTER AND A GRIGNARD REAGENT

"NORMAL" ADDITION TO CARBOXYLIC ESTERS:

Few synthetic processes of organic chemistry have been more extensively used than that which leads to the formation of tertiary alcohols by the action of magnesium alkyl, or aryl, halides upon ethereal salts. The mechanism of the process, however, is still in some respects obscure.

The reaction between a carboxylic ester of the type \( RCO_2R' \) and a Grignard reagent commonly regarded as the "normal" one, in which one molecule of the former reacts with two molecules of latter to form a halomagnesium tertiary-alkoxide and a halomagnesium alkoxide corresponding to the ester alcohol.
In his original papers dealing with this subject Grignard represented that the reaction most probably, taking place in three stages:

\[ RCO_2R' + 2 R''MgX \rightarrow RR_2''COMgX + R'OMgX \]

This representation is, of course, satisfactory from a stoichiometric point of view, but there is a reasonable question that it adequately describes the mechanism of the reaction.

An alternative view assumes that a ketone is formed as an intermediate product; and tertiary alcohol results from the action of the Grignard reagent upon the ketone. Hence equally satisfactory from a stoichiometric standpoint would be the sequence:

\[ R-C+R''MgX \rightarrow R-C-OR' \]
\[ R-C-OR' + R''MgX \rightarrow R-C-R'' + R'OMgX \]
\[ R-C-R'' + H_2O \rightarrow R-C-R'' + HO\cdot MgX \]
This mechanism was suggested by Reformatsky for the analogous case of an organo-zinc iodide reacting with an ethereal salt, and it has been advocated by several writers, notably Stadnikov.

The available evidence upon which to base a choice between the two reaction schemes is inconclusive, but, on the whole, would appear to favour the former except, possibly, in the case of "sterically hindered" esters.

Although it is true that ketones are among the final products of reaction of some esters with some Grignard reagents, it has not been demonstrated that they are present prior to hydrolysis; they may result from the hydrolysis of relatively stable products of the type postulated by Grignard.
Gomberg\textsuperscript{56} refers to Stadnikov's work as providing some evidence in support of the ketone hypothesis; but a consideration of Stadnikov's papers has led us to the conclusion that the evidence offered there is illusory.

Ketones have, it is true, been obtained by Blaise and Courtot\textsuperscript{57} by the action of water on the addition compounds which are formed on treating the esters of certain unsaturated acids with magnesium methyl iodide at $0^\circ$, e.g.

$$\text{CH}_3\cdot\text{C(CH}_3\text{)}\cdot\text{CO.OEt} \rightarrow \text{CH}_3\cdot\text{CH}_2\cdot\text{CH(CH}_3\text{)}\cdot\text{CO.CH}_3$$

These results, however, are not out of harmony with Grignard's views. The appearance of a ketone amongst the products of the reaction may be attributed to the stability, under the conditions of the experiment, of the magnesium addition compound arising in stage (1) of the Grignard scheme. The experiments of Blaise and Courtot provide no evidence in support of the hypothesis that the formation of a ketone is a necessary step in the production of a tertiary alcohol.

Boyd and Hatt\textsuperscript{58} found that if metallic magnesium is added to the reaction mixture the presence of a ketone is readily detected, e.g. in the presence of free magnesium, phenyl magnesium bromide reacts with ethyl $o$-toluate to form a diphenyl $di-o$-tolyl pinacol (38\%)
as well as a diphenyl o-tolyl carbinol (23%). They argue that pinacol formation is an evidence of the presence of free ketone from which the pinacol is derived by a Gomberg reaction.

Thus, the ester reacts with the Grignard reagent to form a ketone and some of the ketone escapes transformation to a tertiary alcohol by combining with metallic magnesium.

\[
\begin{align*}
2C\equiv O + Mg & \rightarrow R\overset{C\equiv C\overset{R}{\equiv}}{\equiv}R + Mg(OH)_2 \\
R & \overset{R}{\equiv}O & R\overset{C\equiv C\overset{R}{\equiv}}{\equiv}R & + Mg(OH)_2 \\
R' & \overset{O}{\equiv}Mg & R' & \overset{R}{\equiv}O & Mg
\end{align*}
\]

Also, Whitmore and Lewis found that, when treated with methyl magnesium bromide in the "Grignard-machine", the non-enolizable ethyl and butyl esters of \(\alpha\)-methyl-\(\alpha\)-ethyl butyric acid underwent apparent enolisation to the extent of 25% & 22% respectively. They attributed this phenomenon to intermediate ketone formation and enolisation of the ketone.
THE MECHANISM OF THE KETONE PRODUCED FROM THE ESTER:

On theoretical grounds, it appears probable that the Grignard reagent and the ethereal salt react in the first place to give an additive compound, and that the ketone results from the decomposition of this primary complex. Some experimental evidence in support of this view is on record. Stadnikov (loc. cit.) found that benzhydral acetate reacts, in the cold, with ethyl magnesium iodide to give an addition compound, from which the original ester can be recovered on treatment with water. Addition compounds of a somewhat similar character have been obtained from certain ketones by Klages. Stadnikov (loc. cit.) explains his observations by postulating the formation of an oxonium compound:

\[
R - CO.0R' + R''MgBr \rightarrow R-CO.0MgBr
\]

The groups \( R' \) and \( R'' \) in this complex are assumed by Stadnikov (loc. cit.) to be similarly situated, and the conclusion is drawn that two different ketones may result from its decomposition:

\[
\begin{align*}
R' & \quad \rightarrow \quad R - CO.R' \\
R'' & \quad \rightarrow \quad R - CO.R''
\end{align*}
\]
Stadnikov (loc. cit.) claims to have obtained experimental proof of the correctness of this hypothesis from the results of a study of the action of magnesium phenyl bromide upon (a) benzyl benzoate and (b) benzhydryl acetate.

The principal product of reaction (a) is triphenyl carbinol, but a small quantity of triphenylethylene is also formed. On this assumption, he argues that phenyl benzyl ketone must have been formed as an intermediate product:

$$\text{(i) } \text{Ph.CO.O.CH}_2\text{Ph} + \text{PhMgBr} \rightarrow \text{Ph.CO.O} - \text{MgBr}$$

$$\text{CH}_2\text{Ph}$$

$$\text{Ph.CO.CH}_2\text{Ph} + \text{Ph.O.MgBr}$$

$$\text{(ii) } \text{Ph.CO.CH}_2\text{Ph} + \text{PhMgBr} \rightarrow \text{Ph}_2\text{C} - \text{OMgBr}$$

$$\text{CH}_2\text{PH}$$

$$\text{Ph}_2\text{C(CH)_2Ph} \rightarrow \text{Ph}_2\text{C=CHPh}$$

On repeating this work by Boyd and Hatt, it was found that the final product is not the triphenyl ethylene but identified it as diphenyl.

Amongst the products of reaction (b), Stadnikov (loc. cit.) obtained a hydrocarbon which he assumed to
be methyltriphenylethylene. The formation of the compound is explained as due to a series of changes similar to those given for case (a), and involving the production of benzhydrylmethyl ketone as an intermediate step. Levy prepared methyltriphenylethylene, which is very different from the above compound.

Thus there is thus no experimental foundation for the view that an ester, \( R_\text{CO.}OR' \), can react with a Grignard reagent, \( R'MgBr \), to give a ketone with the formula \( R_\text{CO-}R' \). Hence Stadnikov's oxonium formula, in its original form, must be rejected, since it suggests possibilities of reaction which are not realised in practice. If, however, the Stadnikov formula is written in electronic fashion,

\[
\begin{align*}
+R' \\
\cdots \\
R : C : O : MgBr, : R'' \\
\cdots \\
: O:
\end{align*}
\]

it becomes apparent that the groups \( R' \) and \( R'' \) are not similarly situated. \( R'' \) is negatively charged and retained in the molecule by the electrostatic attraction of the positive oxonium oxygen atom; \( R' \), on the other hand, is attached by a covalency to the oxygen. The rearrangement of the oxonium compound will naturally take place by a movement of the radical \( R'' \), the radical \( R' \) retaining its original position. Hence only one ketone will be formed.
The magnesium complex (II) may be expected to break
down with extreme ease, giving free ketone and the aryloxy-
magnesium halide. The ketone thus liberated will be in a
highly reactive form, and rapid combination with a Grignard
reagent, or with activated magnesium may be anticipated.
This hypothesis appears to us to be the most satisfactory
way of interpreting the phenomena. It is possible, however,
that the formation of the primary addition compound may be
due to the residual affinity of the carbonyl oxygen, and
not to that of the ethereal oxygen:

Either view can be combined with the interesting suggestions
of Meisenheimer and Casper, who regard the Grignard
reagent as a magnesium complex compound containing two molecules of ether,

\[
\begin{align*}
\text{Et}_2\text{O} & \quad \text{Br} \\
\text{Mg} & \quad \text{Et}_2\text{O} \\
\text{R''} & \quad \text{Et}_2\text{O}
\end{align*}
\]

The primary reaction between this compound and an ethereal salt may be represented as follows:

\[
\begin{align*}
\left[\begin{array}{c}
\text{Et}_2\text{O} \\
\text{Br} \\
\text{Mg} \\
\text{Et}_2\text{O} \\
\text{R''}
\end{array}\right] + \text{O} = \left[\begin{array}{c}
\text{Et}_2\text{O} \\
\text{Br} \\
\text{Mg} \\
\text{Et}_2\text{O} \\
\text{R''}
\end{array}\right] + \left[\begin{array}{c}
\text{Et}_2\text{O} \\
\text{O} \\
\text{C} \\
\text{R'}
\end{array}\right]
\]

Considered as a practical method for the preparation of pinacols, the new process presents advantages in certain cases, since it starts from the ester, which is usually more accessible than the ketone. Indirectly it provides a method for the synthesis of ketones and secondary alcohols, pinacols being readily decomposed into these products. The yield of pinacol, however, varies greatly in different cases. It appears to be dependent upon the constitutions of both the ester and the Grignard reagent.

Thus, the above experiments show that the intermediate ketone formation takes place. Hence, Grignard's scheme cannot be reconciled with the above
phenomena and must therefore be rejected in favour of the ketone hypotheses. But there is a strong suggestion that the initial reaction product is an intermediate (possibly a hemiketal derivative) which is more susceptible to further Grignard reagent addition, and less susceptible to Grignard reagent enolisation, than is the corresponding free ketone.

The postulate that the initially formed intermediate is more reactive (with respect to further addition of the Grignard reagent) than is the corresponding ketone would necessarily imply that, in general, the second stage of addition is considerably more rapid than the first, for, although misdirected ingenuity may discover apparent exceptions (notably among the "hindered" ketones), it is generally true that a ketonic function is more reactive (with respect to Grignard reagent addition) than a reasonably comparable ester function. With regard to the more reactive esters at least this implication is consistent with experimental observation for the treatment of one molecular equivalent of ester with one molecular equivalent of Grignard reagent is much more likely to result in the formation of approximately one-half molecular equivalent of tertiary alcohol and the recovery of approximately one-half molecular equivalent of the ester than anything approaching the formation of one molecular equivalent of
Ivanoff and Spassoff on the other hand, although they accept in part the reaction scheme of Grignard, believe that the hemiketal-type intermediate first formed is unstable and decomposes spontaneously to liberate free ketone.

**PROBABLE MECHANISMS OF CARBOXYLIC ESTER REACTIONS:**

The direct experimental evidence appears insufficient to support a conclusion as to whether the first stage of the "normal" addition reaction is effected through complex rearrangement or through complex reaction with an additional molecule of Grignard reagent. The generally applicable and attractive concept of a quasi six-membered ring transition state may be invoked to propose a mechanism leading to the formation of a reasonably probable intermediate of the hemiketal-type.

If this choice of intermediate is correct it seems probable that the succeeding reaction stage resembles that
of an acetal or ketal or of an ortho ester. A slightly modified version of the quasi six-membered ring transition state concept may be employed without obvious violence to the "a priori" probabilities.

For most saturated esters of the type RCO₂R', it would appear that the second step of the Grignard reaction takes place even more readily than the first, for treatment of an ester with one equivalent of Grignard reagent usually leads, not to the formation of a ketone, but of a tertiary alcohol, and to the recovery of approximately half the ester used.

In this respect formic esters are exceptions to the general rule (probably because of their relatively greater
reactivity with respect to the first reaction step) as they usually yield secondary alcohols under ordinary Grignard reaction conditions. They can also be made to yield aldehydes as was discovered by Gattermann and Maffezzoli. As might be expected optimum yields of aldehydes are obtained by employing an excess of ester by reversing the usual order of reagent addition, and by operating at low temperature.

As regards "unhindered" saturated esters other than the formates it would appear from the available data. When the Grignard intermediate originally formed is reasonably ether-soluble the ability to form ketones is a function primarily of the Grignard reagent employed rather than of the ester. The branched-chain alkyl magnesium halides, the pyrryl magnesium halides, and the diorthosubstituted aryl magnesium halides appear to display a special tendency towards ketone formation. This suggests that the effect is primarily steric although in the case of the Grignard reagents derived from nitrogen heterocycles by hydrogen displacement this effect may be related to one of their typical properties. In extreme cases steric hindrance may, in itself, be sufficient to account for the inhibition of further addition. Probably, however, it is often in the case that such inhibition results, in part at least, from the
intervention of potentially competing reactions, such as enolisation or reduction of the intermediate formed in the first stage of the addition.

When the intermediate formed in the first stage of the Grignard reagent addition is virtually insoluble in the reaction medium, further reaction is necessarily slow as suggested by Long, Marshall and Gallagher.

MECHANISM OF THE REACTION BETWEEN HINDERED CARBONYL COMPOUNDS AND THE GRIGNARD REAGENTS:

Arnold, Bank and Liggett showed that esters of the type

\[ R - C = O \]

are cleaved abnormally by the Grignard reagent if in \( R^- \) there are substituents which sterically hinder additions to the carbonyl group of the ester, and if \( R'^- \) is of such a nature that it has considerable thermodynamic stability as a cation (\( R'^+ \)). The general reaction between such an ester and the Grignard reagent can be expressed by the equation:

\[ R - C = O + R''MgX \rightarrow R - C = O + MgX + R'R''. \]

If on the other hand, \( R'^- \) has little tendency to form
a cation and the group \(-\text{OR}'\) readily forms an anion (i.e. \(\text{Cl}^-, -\text{OC}_6\text{H}_5\), or \(\text{RCO}_2^-\)) then an entirely different reaction takes place and ketones are produced.

\[
\begin{align*}
R - \text{C}^0 \text{O} & \quad + \quad R''\text{MgX} \quad \rightarrow \quad R - \text{C}^0 \text{O} \quad + \quad R'O\text{MgX}.
\end{align*}
\]

When the magnitude of the steric factors about the carbonyl group is small, then simple esters of carboxylic acids react normally with the Grignard reagent to produce tertiary alcohols.

\[
\begin{align*}
R - \text{C}^0 \text{O} & \quad + \quad 2 R''\text{MgX} \quad \rightarrow \quad R - \text{C}^0 \text{O} \quad + \quad R''\text{OMgX} + R'O\text{MgX}.
\end{align*}
\]

From the above different suggestions, it is concluded that reaction change takes place in \(-\text{CO}_2\text{R}'\) part of the molecule \(\text{R.CO}_2\text{R}'\). It follows from this view of the mechanism of the reaction that when the reacting ester is derived from an optically active carboxylic acid the resulting tertiary alcohol will itself be optically active, since the four bonds of the asymmetric atom present in the radicle \(R\) remain undisturbed.
DISCUSSION

Frankland and Twiss for the first time studied the action of the ester of an optically active hydroxy acid on the Grignard reagent and prepared the optically active d-αδ-tetraphenyl erythritol by the interaction of methyl-d-tartarate and magnesium phenyl bromide.

However, later on it is stated by Bergmann and Hartrodt that when methyl ester of (-)-1-methyl butane-1-carboxylic acid reacts with phenyl magnesium bromide, the resulting 1:1-diphenyl-2-methyl-pentan-1-ol is optically inactive.

Now it is an axiom of stereochemistry that recemisation of a tetrahedral atom can only occur if (a) the tetrahedral atom participates in a substitution reaction or if (b) it loses temporarily its asymmetric structure. Obviously, the first alternative is inapplicable and only two possibilities can be contemplated in connection with (b): the ester undergoes enolisation before it reacts with the Grignard compound (or after the interaction with the first Grignard molecule in the form of the ketone CHMePr.CO.Phr or the reaction product is racemised. Since dialkylated ethyl acetates are not easily racemised (Conant and Carlson),
the loss of activity must occur in the end product.

To explain this they suggested that the carbinol (or its bromomagnesium derivative) when formed undergoes spontaneously reversible dehydration:

\[ \text{CHMePr.CPPh}_2.\text{OH} \rightleftharpoons \text{CHMePr.CPPh}_2 \]

which must be accompanied by racemisation.

But, on the other hand, Kenyon and Campbell\textsuperscript{72} have reported that when methyl magnesium iodide and phenyl magnesium bromide react with (-)-methyl hydratropate the resulting tertiary alcohols are optically active.

To study whether a similar condensation between other optically active esters like \( \alpha-(+)-2\)-methyl butane-ethyl acetate and the Grignard reagents afford optically active alcohols or not, this investigation is undertaken.

In the present work, the action of Grignard reagents on ester of optically active acid has been described. The action of alkyl magnesium halides on active \( \alpha-(+)-2\)-methyl-butyl-ethyl acetate produces tertiary carbinols and it may be noted that the optical activity is retained in spite of the molecular rearrangement.

For the preparation of the tertiary alcohols,
the method usually consists in the gradual addition of an ethereal solution of the ester to a stirred Grignard reagent solution. When the chosen reactant pair is unusually reactive the rate of reaction may be controlled by slow addition or by cooling of the reaction mixture or both.

However, here when the usual procedure, as described as above, is applied for the preparation of alcohols, the yield of the carbinols is poor. To the less active reaction mixtures, heat may be applied as required, so when the following procedure is adopted the yield of the carbinols is raised.

This procedure consists in the preparation of the Grignard reagent as usual in the ether. Later on, the ether was evaporated on steam-bath and the Grignard complex was taken up in dry benzene and to this complex, the ester in benzene was added. The contents were refluxed for two hours.

The tertiary alcohols obtained by the action of the ester $\alpha$-$(+)$-2-methyl-butyl-ethyl acetate and Grignard reagent $RMgX$, in which $R$ represents methyl, ethyl, $n$-propyl, iso-propyl, $n$-butyl and phenyl are $1:1$-dimethyl-1-ol-2- ($\beta$-methyl butyl) ethane $\alpha$ $^{35} + 3.054 (1, 0.5)$, $1:1$-diethyl-1-ol-2- ($\beta$-methyl-
-butyl) ethane $\alpha_D^{35} + 2.122$ (1, 0.5), 1:1-di-$n$-propyl-l-ol-2-(\(\beta\)-methyl-butyl) ethane $\alpha_D^{35} + 2.294$

(1, 0.5), 1:1-di-iso-propyl-l-ol-2-(\(\beta\)-methyl-butyl) ethane $\alpha_D^{35} + 3.186$ (1, 0.5), 1:1-di-$n$-butyl-l-ol-2-(\(\beta\)-methyl-butyl) ethane $\alpha_D^{35} + 2.004$ (1, 0.5), and 1:1-di-phenyl-l-ol-2-(\(\beta\)-butyl-methyl) ethane $\alpha_D^{35} + 3.59$ (1, 0.5) respectively.
REATIONS:

\[
\begin{align*}
\text{CH}_2\cdot\text{CH}_3 & \quad \text{H}^*\text{C} = \text{CH}_3 \\
\text{CH}_2 & \quad \text{OMgX} \\
\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 + \text{RMgX} & \quad \rightarrow \quad \text{CH}_2\cdot\text{CH}_3 \\
& \quad \text{H}^*\text{C} = \text{CH}_3 \\
& \quad \text{CH}_2 & \quad \text{OMgX} \\
& \quad \text{CH}_2 - \text{C} - \text{R} + \text{C}_2\text{H}_5\text{OMgX} \quad \text{Hydrolysis}
\end{align*}
\]

(1) \( R = \text{Methyl,} \)

\[
\begin{align*}
\text{CH}_2\cdot\text{CH}_3 & \quad \text{H}^*\text{C} = \text{CH}_3 \\
\text{CH}_2 & \quad \text{OH} \\
\text{CH}_2 - \text{C} - \text{R} & \quad \text{R} \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\cdot\text{CH}_3 & \quad \text{H}^*\text{C} = \text{CH}_3 \\
\text{CH}_2 & \quad \text{OH} \\
\text{CH}_2 & \quad \text{C} - \text{CH}_3 \\
\end{align*}
\]

1:1-\text{Dimethyl-1-ol-2-} (\alpha\text{-methyl-butyl}) \text{ ethane}
(2) \( R = \text{Ethyl,} \)
\[
\begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H-}^*\text{C-CH}_3 \\
\text{CH}_2 \text{OH} \\
\text{CH}_2 - \text{C-CH}_2\text{CH}_3 \\
\text{CH}_2\text{CH}_3
\end{align*}
\]
1:1-Diethyl-1-ol-2- (\( \beta \)-methyl-butyl) ethane

(3) \( R = \text{n-Propyl,} \)
\[
\begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H-}^*\text{C-CH}_3 \\
\text{CH}_2 \text{OH} \\
\text{CH}_2 - \text{C-CH}_2\text{CH}_2\text{CH}_3 \\
\text{CH}_2\text{CH}_2\text{CH}_3
\end{align*}
\]
1:1-di-n-propyl-1-ol-2- (\( \beta \)-methyl-butyl) ethane

(4) \( R = \text{iso-Propyl,} \)
\[
\begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H-}^*\text{C-CH}_3 \\
\text{CH}_2 \text{OH} \\
\text{CH}_2 - \text{C-CH}_2\text{CH}_3 \\
\text{H}_3\text{C} \text{CH}_3
\end{align*}
\]
1:1-di-iso-propyl-1-ol-2- (\( \beta \)-methyl-butyl) ethane
(5) R = \( \text{\text{\text{- Butyl,}} \)} \\
\[
\begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H}^*\text{C}\text{-CH}_3 \\
\text{CH}_2\text{OH} \\
\text{CH}_2\text{-C} - \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
\end{align*}
\]
1:1-di-\( \text{-Butyl-1-ol-2-} \) (\( \text{\text{-methyl-butyl}} \) ethane

(6) R = \( \text{Phenyl,} \) \\
\[
\begin{align*}
\text{CH}_2\text{CH}_3 \\
\text{H}^*\text{C}\text{-CH}_3 \\
\text{CH}_2\text{OH} \\
\text{CH}_2\text{-C} - \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 \\
\end{align*}
\]
1:1-di-\( \text{-phenyl-1-ol-2-} \) (\( \text{\text{-methyl-butyl}} \) ethane.

The physical constants of these alcohols such as boiling point, density, refractive index and optical rotation are shown in the table on the following page.
<table>
<thead>
<tr>
<th>No.</th>
<th>Tertiary Alcohols</th>
<th>Yield per cent</th>
<th>B.P. °C</th>
<th>$d_{35}^4$</th>
<th>$n_{34}^4$</th>
<th>$\alpha_{35}^D (1, 0.5)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1:1-Dimethyl-1-ol-2-</td>
<td>80.1</td>
<td>145-50</td>
<td>0.9851</td>
<td>1.420</td>
<td>+ 3.054</td>
</tr>
<tr>
<td></td>
<td>(β-methyl-butyl) ethane</td>
<td></td>
<td>10 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>1:1-Diethyl-1-ol-2-</td>
<td>66.4</td>
<td>175</td>
<td>0.9853</td>
<td>1.431</td>
<td>+ 2.122</td>
</tr>
<tr>
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<td>(β-methyl-butyl) ethane</td>
<td></td>
<td>15 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>1:1-di-n-propyl-1-ol-2-</td>
<td>67.5</td>
<td>194</td>
<td>0.9764</td>
<td>1.433</td>
<td>+ 2.294</td>
</tr>
<tr>
<td></td>
<td>(β-methyl-butyl) ethane</td>
<td></td>
<td>15 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>1:1-di-iso-propyl-1-ol-2-</td>
<td>33.3</td>
<td>175-76</td>
<td>0.9746</td>
<td>1.430</td>
<td>+ 3.136</td>
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<td>10 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>1:1-di-n-butyl-1-ol-2-</td>
<td>32.7</td>
<td>235</td>
<td>0.9827</td>
<td>1.434</td>
<td>+ 2.004</td>
</tr>
<tr>
<td></td>
<td>(β-methyl-butyl) ethane</td>
<td></td>
<td>15 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(β-methyl-butyl) ethane</td>
<td></td>
<td>10 mm.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
***************
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**
** EXPERIMENTAL **
**
**
** SECTION **
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***************
EXPERIMENTAL SECTION

Preparation of the Optically Active Ester

\( \alpha-(+)-2\text{-Methyl-Butyl-Ethyl Acetate} \)

Preparation of \( \alpha-(+)-2\text{-Methyl-Butyl Malonate} \):

Sodium (99.0 g.) was dissolved in absolute alcohol (1250 c.c.) in a flask fitted with a reflux condenser. This was maintained at 60° during the addition of di-ethyl malonate (630 g.; 585 c.c.). A white solid of sodio-ethyl malonate separated. The temperature was then raised to 80° and (+)-1-bromo-2-methyl butane (580 g.; \( \alpha \frac{31}{D} + 1.074 \)) was then added slowly from the dropping funnel (during three hours). The mixture was finally heated on a water bath until it no longer showed an alkaline reaction (2-3 hours). The alcohol was distilled off and the residue was treated with cooled water (750 c.c.) and extracted with ether. The ethereal layer was washed, dried (calcium chloride) and evaporated to get the \( \alpha-(+)-2\text{-methyl-butyl malonate} \) which was distilled under reduced pressure, collected the \( \alpha-(+)-2\text{-methyl-butyl malonate} \) at 160-210°/15 mm.; yield: 50 per cent. \( d_4^{32} 1.1275; \ n_0^{30} 1.422; \ \alpha \frac{35}{D} + 4.187 \).
Walden\textsuperscript{73} reports the constants of \textit{\textit{-(+)-2-methyl-butyl malonate}} as $d_2^{20} 0.9665$ and $\alpha^{20} + 7.19$.

\textbf{Preparation of $\alpha$-(-)-2-Methyl-Butyl Acetic Acid from $\alpha$-(-)-2-Methyl-Butyl Malonate:}

(1) \textbf{Hydrolysis and Decarboxylation:}

Into a three-necked flask, fitted with a separating funnel, a mechanical stirrer and a reflux condenser, was placed a hot solution of potassium hydroxide (475 g. of potassium hydroxide in 475 c.c. of water). To this was slowly added $\alpha$-(-)-2-methyl-butyl malonate (475 g.). After the addition, the solution was boiled gently till the hydrolysis was complete, the contents in the flask was diluted with water (475 c.c.) and distilled off: 475 c.c. of liquid.

To the cooled residue in the flask was added dilute sulphuric acid solution (413.5 c.c. in 1069 c.c. water). When all the acid was added, the mixture was refluxed for 3-4 hours, the upper layer of the organic acid was separated and the aqueous portion was extracted with ether and combined the acid layer with the ether extracts, washed with water, dried with sodium sulphate and ether evaporated. The acid obtained was distilled
under reduced pressure, b.p. 200°/16 mm.; yield: 75 per cent. $d_4^{35} 1.0637; n_4^{34} 1.417; \alpha_D^{35} + 4.494$.

Found, by rapid titration with sodium hydroxide solution, M 129.4. $C_7H_{14}O_2$ required M 130.0.

(ii) Preparation of Ester from Acid:

In a flask fitted with a condenser, containing distilled acid, $\alpha$-(-)-2-methyl-butyl acetic acid (200 g.) were added absolute alcohol (660 c.c.) and concentrated sulphuric acid (5 c.c.). The mixture was refluxed for 5-6 hours and the excess of alcohol was distilled off and the residue extracted with ether. The ethereal layer was washed with sodium carbonate solution (10%), water and dried (sodium sulphate). The evaporation of ether gave a crude ester, and was distilled under vacuum, b.p. 148-60°/10 mm.; yield: 74.4 per cent. $d_4^{35} 1.0146; n_3^{33} 1.413; \alpha_D^{35} + 3.237$.

Found: C, 66.12; H, 11.11 per cent.

$C_9H_{18}O_2$ requires: C, 68.34; H, 11.39 per cent.
Preparation of Tertiary Carbinols

1,1-Dimethyl-1-ol-2-(α-methyl-butyl) ethane:

To a flask, fitted with a mechanical stirrer, a reflux condenser and a dropping funnel, containing magnesium (8.4 g. : 0.35 mole) and ether (150 c.c.) was added drop by drop methyl iodide (49.7 g. : 0.35 mole) in ether (95 c.c.). Afterwards the contents were refluxed till the magnesium was dissolved.

The Grignard complex in ether thus obtained was heated on steam bath to evaporate the ether and then the complex was taken up in dry benzene (100 c.c.). To this complex was added the ester (α-(+)-2-methyl-butyl-ethyl acetate 27.6 g. : 0.175 mole) in benzene (60 c.c.). Afterwards, the contents were refluxed for two hours. Next day it was decomposed by ice and ammonium chloride. The benzene layer was washed with water, dried (sodium sulphate) and benzene evaporated. The crude product thus obtained was heated on a water bath with dilute solution of sodium hydroxide (5% : 100 c.c.) for three hours. When the hydrolysis was over, the crude tertiary carbinol was extracted with ether. The ethereal layer was washed with water, and dried (sodium sulphate). The ether was evaporated to get the tertiary carbinol.
This crude alcohol was distilled under reduced pressure, B.P. 145-50°/10 mm.; yield: 80.1 per cent.
\[ \text{Found: } C, 74.82; H, 13.67 \text{ per cent.} \]
\[ \text{C}_9\text{H}_{20}\text{O requires: } C, 74.99; H, 13.89 \text{ per cent.} \]

1:1-Diethyl-1-ol-2- (α-methyl-butyl) Ethane:

The Grignard complex, ethyl magnesium bromide, in ether (100 c.c.) was prepared from ethyl bromide (38.2 g.: 0.35 mole) and magnesium (8.4 g.: 0.35 mole). After the formation of the complex was complete, the ether was evaporated on steam bath and the complex was taken up in dry benzene (70 c.c.). To this was added the ester \( \alpha \)-(-)-2-methyl-butyl-ethyl acetate 27.6 g.: 0.175 mole. in benzene (58 c.c.). The contents were refluxed for two hours and on the next day were decomposed by ice and ammonium chloride. The benzene layer was washed, dried (sodium sulphate) and benzene evaporated. The crude product thus obtained was heated with dilute sodium hydroxide (5%: 100 c.c.) in a water bath for three hours. The mass was extracted with ether, washed with water, dried (sodium sulphate) and on evaporation of the ether the crude product tertiary carbinol obtained was distilled under reduced pressure, B.P. 175°/15 mm.;
yield: 66.4 per cent. $d_{35}^4 = 0.9853; n_{34} = 1.431; \\
\alpha = \frac{35}{D} + 2.122 (1, 0.5).

Found: C, 76.63; H, 13.73 per cent.

C_{11}H_{24}O requires: C, 76.76; H, 13.95 per cent.

lll-di-n-Propyl-1-ol-2- (a-Methyl-Butyl) Ethane:

In three necked flask fitted with a mercury seal stirrer, reflux condenser and a dropping funnel, were placed magnesium turnings (9.6 g.: 0.4 mole) and ether (100 c.c.). To this, n-propyl bromide (49.2 g.: 0.4 mole) in ether (90 c.c.) was added dropwise. After the addition was complete, the reaction mixture was refluxed till the magnesium had dissolved. From the Grignard complex, the ether was evaporated on the steam bath and the complex was taken in benzene (100 c.c.). To this Grignard complex in benzene, was added the solution of the optically active ester (\(\alpha-(+)-2\)-methyl-butyl-ethyl acetate 31.6 g.: 0.2 mole) in benzene (70 c.c.). The contents were refluxed for two hours after the addition of the ester was complete and kept overnight.

On the next day, the product in the flask was decomposed by ice and ammonium chloride. The benzene layer was washed, dried (sodium sulphate) and the
benzene was evaporated. The product was heated with dilute potassium hydroxide solution (5% : 100 c.c.) in a water bath for three hours. When the hydrolysis was complete, the mass was extracted with ether, the ethereal layer was washed, dried (sodium sulphate) and the ether evaporated. The tertiary carbinol thus obtained was distilled under reduced pressure, B.P. 194°/15 mm.; yield: 67.5 per cent. \( \alpha_3^{35} = 0.9764; \beta_3^{34} = 1.433; \alpha_D^{35} + 2.294 (1, 0.5). \)

Found: C, 77.66; H, 13.81 per cent. 

\( \text{C}_{13}\text{H}_{28} \) requires: C, 78.00; H, 14.00 per cent.

**1,1-di-iso-Propyl-1-ol-2- \( \alpha \)-methyl-butyl) Ethene:**

Magnesium turnings (7.2 g.: 0.3 mole) and ether (90 c.c.) were placed in a flask fitted with a reflux condenser, a stirrer and a dropping funnel. To this flask, was added dropwise a solution of iso-propyl bromide (32.7 g.: 0.3 mole) in ether (70 c.c.). When the addition was complete, the reaction mixture refluxed till the magnesium was dissolved, ether was evaporated on steam bath, and the complex was taken up in dry benzene (100 c.c.). To this complex, a solution of the ester (23.7 g.: 0.15 mole) in benzene (50 c.c.) was added drop by drop. Afterwards the contents were
refluxed for two hours. On the next day, the product in the flask was decomposed by ice and ammonium chloride. The benzene layer was washed, dried and the benzene evaporated. The crude carbinol was treated with dilute potassium hydroxide (5%: 100 c.c.) and heated for two hours. The mass was extracted with ether. It was washed with water, dried (sodium sulphate) and ether on evaporation gave a product which was distilled under reduced pressure, B.P. 175-76°/10 mm.; yield: 33.3 per cent. \( \delta_{4}^{35} \) 0.9746; \( n^{24} \) 1.430; \( \alpha_{D}^{35} + 3.186 \) (1, 0.5).

Found: C, 77.75; H, 13.6 per cent.

\( C_{13}H_{28}O \) requires: C, 78.00; H, 14.00 per cent.

**l,l-di-n-Butyl-1-ol-2- (\( \beta \)-Methyl-Butyl) Ethane:**

To a flask fitted with a reflux condenser, a stirrer and a dropping funnel, containing magnesium (9.6 g.; 0.4 mole) and ether (100 c.c.), was added drop by drop n-butyl bromide (55.8 g.; 0.4 mole) in ether (100 c.c.). After the magnesium had dissolved, the ether from the complex was evaporated and then the Grignard complex was taken up in dry benzene (100 c.c.). To this complex in benzene, was added the ester (\( \alpha \).-(+)-2-methyl-butyl-ethyl acetate 31.6 g.; 0.2 mole) in benzene (66 c.c.). Afterwards the contents were refluxed for two hours and
kept overnight.

On the next day, the mass in the flask was decomposed by ice and ammonium chloride. The benzene layer washed, dried and on evaporation of the solvent gave the crude product. This was heated with potassium hydroxide solution (5%) for three hours. The mass was then extracted with ether, the ethereal solution washed with water, dried (sodium sulphate) and on evaporation of ether gave the product which was distilled under reduced pressure and the carbinol 1:1-di-n-butyl-1-ol-2-(α-methyl-butyl) ethane was collected at B.P. 235°/15 mm.; yield: 32.7 per cent.  $d_4^{35}$ 0.9827;  $n_4^{34}$ 1.434;  $\alpha_D^{35} + 2.004 \left( 1, 0.5 \right)$.  

Found: C, 78.23; H, 13.61 per cent.

$C_{15}H_{32}O$ requires: C, 78.96; H, 14.04 per cent.

1:1-di-Phenyl-1-ol-2-(α-Methyl-Butyl) Ethane:

The Grignard complex, — phenyl magnesium bromide, — in ether was prepared from phenyl bromide (62.8 g.: 0.4 mole) and magnesium (9.6 g.: 0.4 mole).

The ether from Grignard complex was evaporated and was then taken up in dry benzene (100 c.c.). To this complex was added the optically active ester
(31.6 g.: 0.2 mole) in benzene (80 c.c.) and after the addition was complete the contents were refluxed for two hours.

On the next day, the mass in the flask was decomposed by ice and ammonium chloride, the separated benzene layer washed, dried and on evaporation of the solvent, the mass was heated with potassium hydroxide solution (5%: 100 c.c.) for two hours. Then after, the mass was extracted with ether. The ethereal layer was washed, dried (sodium sulphate) and the product was distilled under vacuum when the carbinol, 1:1-di-phenyl-1-ol-2- (β-methyl-butyl) ethane was collected at 270-80°/10 mm.; yield: 53.9 per cent. $d_4^{35} 1.1454$; $n_3^4 1.546$; $\alpha_0^{35} + 3.659 (l, 0.5)$.

Found: C, 84.22; H, 8.55 per cent.

$C_{19}H_{24}O$ requires: C, 85.07; H, 8.96 per cent.
**OPTICAL ROTATIONS**

**OF**

\[
\text{1:1-Dimethyl-1-ol-2- (\textit{\textalpha}-Methyl-Butyl) Ethane}
\]

**IN DIFFERENT SOLVENTS** (1, 1):

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation ([\alpha]_{D}^{35})</th>
<th>Concentration (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Chloroform</td>
<td>+ 1.936°</td>
<td>13.59</td>
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<tr>
<td>2.</td>
<td>Benzene</td>
<td>+ 1.952</td>
<td>15.41</td>
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<td>3.</td>
<td>Acetone</td>
<td>+ 2.332</td>
<td>8.06</td>
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<td>4.</td>
<td>Carbon tetrachloride</td>
<td>+ 2.443</td>
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<tr>
<td>5.</td>
<td>Ethyl-acetate</td>
<td>+ 2.910</td>
<td>12.66</td>
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<tr>
<td>6.</td>
<td>Methyl-acetate</td>
<td>+ 3.540</td>
<td>14.73</td>
</tr>
<tr>
<td>7.</td>
<td>Ethanol</td>
<td>+ 3.702</td>
<td>11.17</td>
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</tbody>
</table>
OPTICAL ROTATIONS
OF
1,l-Diethyl-1-ol-2-(α-Methyl-Butyl) Ethane
IN DIFFERENT SOLVENTS (1, 1):

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation [α]35°D</th>
<th>Concentration C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ethyl-acetate</td>
<td>+ 1.198°</td>
<td>14.95</td>
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<td>2.</td>
<td>Chloroform</td>
<td>+ 1.673</td>
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<td>3.</td>
<td>Benzene</td>
<td>+ 2.225</td>
<td>14.76</td>
</tr>
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<td>4.</td>
<td>Acetone</td>
<td>+ 2.250</td>
<td>13.27</td>
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<td>5.</td>
<td>Methyl-acetate</td>
<td>+ 2.823</td>
<td>19.03</td>
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<td>6.</td>
<td>Carbon tetrachloride</td>
<td>+ 2.633</td>
<td>11.34</td>
</tr>
<tr>
<td>7.</td>
<td>Dioxan</td>
<td>+ 2.783</td>
<td>12.34</td>
</tr>
<tr>
<td>8.</td>
<td>Ethanol</td>
<td>+ 3.332</td>
<td>13.44</td>
</tr>
</tbody>
</table>
OPTICAL ROTATIONS

OF

1:1-di-n-Propyl-1-ol-2-(\(\alpha\)-Methyl-Butyl) Ethan

IN DIFFERENT SOLVENTS (1, 1):

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation ([\alpha_c]^{35}_D)</th>
<th>Concentration (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ethyl-acetate</td>
<td>+1.938°</td>
<td>27.72</td>
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<td>2.</td>
<td>Carbon tetrachloride</td>
<td>+2.206</td>
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<tr>
<td>3.</td>
<td>Chloroform</td>
<td>+2.389</td>
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<td>4.</td>
<td>Acetone</td>
<td>+2.422</td>
<td>18.49</td>
</tr>
<tr>
<td>5.</td>
<td>Dioxan</td>
<td>+2.503</td>
<td>23.40</td>
</tr>
<tr>
<td>6.</td>
<td>Methyl-acetate</td>
<td>+2.575</td>
<td>30.14</td>
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<tr>
<td>7.</td>
<td>Benzene</td>
<td>+2.581</td>
<td>18.50</td>
</tr>
<tr>
<td>8.</td>
<td>Ethanol</td>
<td>+2.948</td>
<td>25.31</td>
</tr>
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</table>
OPTICAL ROTATIONS

OF

1:1-di-iso-Propyl-1-ol-2- ( β -Methyl-Butyl ) Ethane

IN DIFFERENT SOLVENTS ( l, l ) :

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation [α]_{D}^{25}</th>
<th>Concentration C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Carbon tetrachloride</td>
<td>+1.750°</td>
<td>7.24</td>
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<tr>
<td>2.</td>
<td>Ethyl-acetate</td>
<td>+2.462</td>
<td>13.34</td>
</tr>
<tr>
<td>3.</td>
<td>Benzene</td>
<td>+2.658</td>
<td>16.85</td>
</tr>
<tr>
<td>4.</td>
<td>Ethanol</td>
<td>+3.149</td>
<td>10.43</td>
</tr>
<tr>
<td>5.</td>
<td>Acetone</td>
<td>+3.339</td>
<td>19.67</td>
</tr>
<tr>
<td>6.</td>
<td>Dioxan</td>
<td>+3.349</td>
<td>6.24</td>
</tr>
<tr>
<td>7.</td>
<td>Chloroform</td>
<td>+3.526</td>
<td>21.17</td>
</tr>
<tr>
<td>8.</td>
<td>Methyl-acetate</td>
<td>+3.792</td>
<td>16.53</td>
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OPTICAL ROTATIONS
OF
1,1-di-\textit{n}-Butyl-1-ol-2- (\textit{\`{a}}-Methyl-Butyl) Ethane

IN DIFFERENT SOLVENTS (1, 1):

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation $[\alpha]_{D}^{25}$</th>
<th>Concentration C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Methyl-acetate</td>
<td>+ 1°568°</td>
<td>20°92</td>
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<tr>
<td>2.</td>
<td>Benzene</td>
<td>+ 2°004</td>
<td>20°81</td>
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<tr>
<td>3.</td>
<td>Acetone</td>
<td>+ 2°116</td>
<td>19°69</td>
</tr>
<tr>
<td>4.</td>
<td>Chloroform</td>
<td>+ 2°159</td>
<td>23°44</td>
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<tr>
<td>5.</td>
<td>Ethyl-acetate</td>
<td>+ 2°277</td>
<td>22°79</td>
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<td>6.</td>
<td>Ethanol</td>
<td>+ 2°342</td>
<td>20°34</td>
</tr>
<tr>
<td>7.</td>
<td>Dioxan</td>
<td>+ 2°367</td>
<td>17°61</td>
</tr>
<tr>
<td>8.</td>
<td>Carbon tetrachloride</td>
<td>+ 2°468</td>
<td>19°30</td>
</tr>
</tbody>
</table>
OPTICAL ROTATIONS
OF
1:1-di-Phenyl-1-ol-2- ( β-Methyl-Butyl ) Ethane
IN DIFFERENT SOLVENTS (1, 1):

<table>
<thead>
<tr>
<th>No.</th>
<th>Solvent</th>
<th>Specific Rotation $[\alpha]D^{35}$</th>
<th>Concentration C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dioxan</td>
<td>+1.092°</td>
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<td>2.</td>
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<td>Benzene</td>
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<td>Ethanol</td>
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<td>Acetone</td>
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<td>8.</td>
<td>Methyl-acetate</td>
<td>+4.826</td>
<td>34.25</td>
</tr>
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</table>