Studies in the Geometrical and Optical Isomerism of the METHYL cyclo HEXANOLS

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

by

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The work described in this thesis was carried out by the Author in the Laboratories of Battersea Polytechnic, under the supervision of Dr J. Kenyon.

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NOTE: With the object of making this account more complete, two pieces of work, which were not performed by the writer, have been incorporated, viz,
i. The separation of the geometrical isomerides of 1\(^{-2}\)-methylcyclohexanol.
ii. The separation of the geometrical isomerides of 1\(^{-4}\)-methylcyclohexanol.

With these exceptions alone, the work detailed in this thesis is entirely due to the writer.
Introductory.

From previous work on isomerism in cyclic compounds, the existence of four 1:2, four 1:3, and two 1:4-isomeric methylocyclohexanols is to be expected. The relation between these isomeric bodies is seen best if reference is made to the d and l forms of the cis and of the trans-methylocyclohexanols, thus:

\[ \text{cis-} \]
\[ \text{trans-} \]

The above diagram represents the four isomeric 1:2 methylocyclohexanols: (1) and (2) and (3) & (4) are optical isomerides of each other, whilst (1) & (3) and (2) & (4) are geometrical isomerides, (1) & (3) will be related structurally in that they have a grouping of common configuration ( \(-\text{C-CH}_3\) ). Thus, both would be obtained from the optically active ketone (1:2-methylocyclohexanone) by reduction,
isomeride is identical with its mirror image.

Similar examples of combined geometrical and optical isomerism are frequently met in the terpene series, e.g. menthol and neo-menthol bornanol and iso-bornanol, and the isomeric fenchyl alcohols. Hence it was thought that the investigation of the relationships between existing between the isomeric methylocyclohexanols, might throw some light on the relative configurations of more complex substances.

Summary of previous work on the Methylocyclohexanols.

Previous work on the preparation of the cis- and trans- forms of the methylocyclohexanols, includes two more important investigations, in which the problem has been attacked from entirely different points.

Knoevenagel synthesized the unsaturated cyclic ketone corresponding with 1,3- methylocyclohexanol from formaldehyde and aceto-acetic ester.

\[
\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOEt} \quad \text{CH}_3\cdot\text{CO}\cdot\text{CH}\cdot\text{COOEt}
\]

\[
\text{CH}_2\text{O} \quad \text{CH}_2
\]

\[
\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOEt} \quad \text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOEt}
\]

\[
\text{CO} \quad \text{C(CH}_3) \quad \text{CO} \quad \text{C(CH}_3)
\]

\[
\text{CH}_2\text{O} \quad \text{CH}_2
\]

\[
\text{CO} \quad \text{C(CH}_3) \quad -2\text{CO}_2 \quad \text{CO} \quad \text{C(CH}_3)
\]

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

\[
-1,3- \text{ methylocyclohexanone}
\]
When, however, he attempted to prepare the saturated alcohol (1,3-methylcyclohexanol) from the supposed unsaturated alcohol by the addition of hydrogen iodide followed by reduction with zinc dust and glacial acetic acid, a substance, with such very similar properties, was obtained that he eventually concluded that the original was the saturated alcohol, mixed with a small quantity of the unsaturated. Nevertheless the two bodies showed slight differences and therefore Kröevenagel assumed tentatively that the substance produced directly by reduction with sodium and boiling alcohol was trans-1,3-methylcyclohexanol, and that the subsequent treatment converted this to the cis-modification. It would appear, at all events, that these bodies were not pure, since the phenyl urethanes prepared from them by Kröevenagel melted at 90°C and 91°C respectively; those prepared by Skita (vide infra) melted at 91°C and 96–97°C, and those prepared in the present work melt at 91°C and 101°C respectively.

SKITA\textsuperscript{2} claims to have prepared the six geometrical isomers of methycyclohexanol by varying the conditions under which the corresponding cresol or ketone can be hydrogenated in the presence of colloidal platinum. Thus he obtained substances having different characteristics, e.g.

1. By treating 0-cresol in aqueous solution with hydrogen under two to three atmospheres pressure in the presence of colloidal platinum, a 80% yield of 1,2-methycyclohexanone and a 5% yield of 1,2-methylcyclohexanol were obtained. This alcohol gave a phenyl urethane melting at 104.5°C.
Little certainty can be placed on the purity of these preparations, because the boiling points of the isomerides lie so close together that fractional distillation would effect little or no separation, and also because the solid derivatives of these products were not subjected to any test for homogeneity, such as fractional crystallisation.

Numerous investigators have prepared various derivatives of the methylocyclohexanols, generally assuming that the products of hydrogenation are pure substances, but since it is shown by the work described in this thesis that these preparations are invariably mixtures of the two geometrical isomerides, this assumption is inadmissible.
varying the mode of hydrogenation appears remote. There remain, however, at least two alternatives. Firstly it might be possible to destroy one isomeride in a mixture of the two by the use of a chemical reagent, towards which only one isomeride is stable. Such a method is employed to remove iso borneol from crude borneol. Or, secondly, a large amount of the mixture of isomerides could be prepared by some convenient method, converted into a crystalline derivative, and the resulting mixture separated by systematic fractional crystallisation.

Actually the second alternative was chosen as being more straightforward. The crude mixture of isomerides was obtained by reducing the corresponding cresol by the method of Sabatier and Senderens, after preliminary purification, converted into a solid ester. Acid phthalic esters were first tried, and by crystallising these esters, two sets of fractions of constant melting point were obtained in the case of 1,2- and of 1,4- methylcyclohexanyl hydrogen phthalates. The 1,2- methylcyclohexanyl ester, however, could not be crystallised satisfactorily, and no better success was obtained by the crystallisation of numerous salts produced by combining it with different bases. After trying several other esters, the p-nitro benzoate was found to crystallise extremely well, and to yield two sets of fractions each of constant melting point. In all instances the melting points of these fractions were unaltered by continued crystallisation from solvents other than those used in the original separation, and hence it is unlikely that the observed homogeneity was due to the occurrence of mixed crystals. The sets of pure crops were then hydrolysed and the resulting carbinols further characterised by conversion into other derivatives; these also were found to be unchanged by continued crystallisation.

Since it is not definitely known which isomeride corresponds to
of the $\beta^-$. This lends support to the view that the $\alpha$-form corresponds with the $\text{trans}$-form, but only in a tentative way. In the next section, however, other evidence is brought to bear on this point, and the conclusion arrived at above is found to be justified.

<table>
<thead>
<tr>
<th>Methylcyclohexanol</th>
<th>b.p. at 20 m.m.</th>
<th>$\mu \left(25^\circ\right)$</th>
<th>d $\left(25^\circ\right)$</th>
<th>$[\alpha]_D \left(25^\circ\right)$</th>
<th>$\Delta%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-1.2-</td>
<td>78-79°C</td>
<td>1.4506</td>
<td>9228</td>
<td>33.614</td>
<td>-0.1%</td>
</tr>
<tr>
<td>$\beta$-1.2-</td>
<td>77-78°C</td>
<td>1.4616</td>
<td>9228</td>
<td>33.933</td>
<td>+0.2%</td>
</tr>
<tr>
<td>$\alpha$-1.3-</td>
<td>78-79°C</td>
<td>1.4530</td>
<td>9104</td>
<td>33.871</td>
<td>+0.06%</td>
</tr>
<tr>
<td>$\beta$-1.3-</td>
<td>77-78°C</td>
<td>1.4554</td>
<td>9091</td>
<td>34.01</td>
<td>+0.47%</td>
</tr>
<tr>
<td>$\alpha$-1.4-</td>
<td>78-79°C</td>
<td>1.4544</td>
<td>9280</td>
<td>34.023</td>
<td>+0.5%</td>
</tr>
<tr>
<td>$\beta$-1.4-</td>
<td>78-79°C</td>
<td>1.4584</td>
<td>9180</td>
<td>33.908</td>
<td>+0.17%</td>
</tr>
</tbody>
</table>

Molecular refractivity calculated from Eisenlohr's figures = 33.851

Derivatives of the Methylcyclohexanols.

<table>
<thead>
<tr>
<th>Methylcyclohexanol</th>
<th>m.p. of Acid Phthalate</th>
<th>Phenyl Urethane</th>
<th>p-Nitrobenzoate</th>
<th>Acid succinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-1.2-</td>
<td>123-124°C</td>
<td>105-106°C</td>
<td>—</td>
<td>44.46°C</td>
</tr>
<tr>
<td>$\beta$-1.2-</td>
<td>89-90°C</td>
<td>78-80°C</td>
<td>34-35°C</td>
<td>oil</td>
</tr>
<tr>
<td>$\alpha$-1.3-</td>
<td>93-94°C</td>
<td>91-93°C</td>
<td>58°C</td>
<td></td>
</tr>
<tr>
<td>$\beta$-1.3-</td>
<td>82-83°C</td>
<td>101-103°C</td>
<td>65°C</td>
<td></td>
</tr>
<tr>
<td>$\alpha$-1.4-</td>
<td>119-120°C</td>
<td>124-125°C</td>
<td>67°C</td>
<td></td>
</tr>
<tr>
<td>$\beta$-1.4-</td>
<td>72-73°C</td>
<td>104°C</td>
<td>94°C</td>
<td></td>
</tr>
</tbody>
</table>
properties of any pair of geometrical isomerides differ only slightly. In order to characterise these isomerides more definitely, and to obtain some evidence which might give a clue to their relative configurations, a physical property was sought which would be more dependent on cis-trans isomerism and therefore exhibit larger variations. Reference to the literature showed a large number of possibilities

(i) MICHAEL\textsuperscript{3}, working on the fusibility and solubility of the different forms of some ethylenic isomers, found that generally the malenoid form is more fusible and more soluble than the fumaroid.

(ii) PERKIN\textsuperscript{4} showed that the fumaroid form has a slightly higher magnetic rotatory power than the malenoid.

(iii) TRAUBE\textsuperscript{5} concluded that the molecular volumes of sodium maleate, crotonate and citraconate were slightly smaller than those of the corresponding trans-forms.

(iv) MAGINI\textsuperscript{6} and STEWART\textsuperscript{7}, working on the absorption of light, showed that fumaric and mesaconic acids have a greater absorptive power than maleic and citraconic acids; the $\alpha$- and $\beta$-camphorquinone oximes were found to have the same absorption spectrum, but the $\beta$-form absorbed more light than the $\alpha$.

(v) STOHMANN and KLEBER\textsuperscript{8} have found that the heats of combustion of one gram molecule of the cis- and trans-forms of hexa-hydroterephthalic acid differ but slightly from one another: cis-acid 928.6 cal, trans-acid 929.5 cal.

The investigations described reveal only small variations in the particular physical property involved, which seems to show that these properties are only in small part dependent on configuration and hence cannot be usefully employed as criteria of configuration.

The work on the viscosity of geometrical isomerides was, however, much more promising - large and often erratic differences having been found to exist.
Sodium citraconate has a greater viscosity than sodium mesaconate (trans-).

These irregular results may be attributed to the fact that no account was taken of the degree of ionisation of the salts and also to the possibility of unequal combination between each of the two acids and the solvent.

Since Lauenstein's first investigation, other substances have been examined from this viewpoint, and it has been possible to frame a provisional hypothesis. Below is summarised in tabular form the work of BECK\(^1\) on the viscosity of oximes, and of THOLE\(^2\) on the viscosity of geometrically isomeric acids and their ethyl esters.

<table>
<thead>
<tr>
<th>Opposed form (trans-, syn- etc.)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acids</td>
<td>Greater viscosity than adjacent</td>
</tr>
<tr>
<td>Esters</td>
<td>Smaller Do.</td>
</tr>
<tr>
<td>Oximes</td>
<td>Greater Do.</td>
</tr>
<tr>
<td>Oxime ethers</td>
<td>Probably smaller Do.</td>
</tr>
</tbody>
</table>

Thus the opposed form (trans-, syn-) has sometimes a smaller, and sometimes a greater, viscosity than the corresponding adjacent form (cis-, anti-). These results seem a little difficult to understand, but the suggestions of BECK, and later of THOLE have provided a basis for their explanation. From his work on the viscosity of fused oximes, BECK concluded that viscosity was dependent in some way on the relative position of groups having residual affinity, and this idea was expanded by THOLE into the following postulates:

(a). When the groups responsible for geometrical isomerism, have smaller residual affinity, the opposed form has the lower viscosity value, because the proximity of the groups in the adjacent form leads to potential ring formation - a condition which is well known to enhance viscosity.

(The oxime ethers are extremely difficult to prepare in a pure condition)
depression in molecular association and hence in viscosity. In this case, then, the adjacent compound has the lower viscosity.

For example, in maleic acid and fumaric acid, where the carboxyl groups have large residual affinity, the effect due to the inhibition of molecular association in the cis-form is likely to be greater than the exalting effect due to the tendency to form a ring compound, and therefore maleic acid should be the less viscous form. The example of oleic and elaidic acids is of particular interest, for here the dominant groups are similar to those present in the methylcyclohexanols: carboxylic and hydroxylic groups of large residual affinity and the methyl group common. The large residual affinity of the hydroxylic group is well known, e.g. the formation of alcoholates and oxonium compounds. THOLE assumes that the methyl group has a small but definite residual affinity, and hence the viscosity of the trans-form (elaidic) will be greater than that of the cis-. Seeing that this reasoning applies to oleic and elaidic acids, it can be safely assumed to apply to the 1,2-methylcyclohexanols, since in both instances the dominant groups are in the 1,2-position, but it is questionable if it will apply to the 1,3-compound. The same phenomena may occur, but it seems probable that, owing to the difficulty with which meta-bridged rings are formed, there will be less intra-molecular neutralisation of the residual affinities and hence the viscosities of the cis- and trans-forms of 1,3-methylcyclohexanol will show a smaller difference than those of 1,2-methylcyclohexanols. Judging from the comparative ease with which para bridged rings are formed, the difference between the viscosity values for cis- and trans-1,4-methylcyclohexanol will be intermediate between the differences of the 1,2- and 1,3- compounds, i.e. greater than the difference between the 1,3-forms and approaching the difference between the 1,2-.
Sincerities© predictions are found to be true; the probability that the α-forms (those produced in larger proportion by hydrogenation of the corresponding cresol by the method of SABATIER and SANDEFERS) are the trans-form is raised to a high order.

With the object of strengthening this conclusion, the observations of viscosity were extended to the acetates of the methylecyclohexanols. In discussing the viscosity relationship of these compounds, it will be convenient to refer to the two distinct effects as:

Effect A, tending to make the cis-form more viscous, due to the ring-like structure of the cis-compound enhancing viscosity.

Effect B, tending to make the cis-form less viscous, due to intra-molecular neutralisation of residual affinities and a consequent reduction in inter-molecular association.

First, a general reduction in the magnitude of viscosity would be expected, because the residual affinity of an ester is generally much smaller than that of the parent alcohol - esters do not form addition products so readily as alcohols do. Therefore, since the residual affinity of the hydroxyl group has been reduced by conversion into acetoxyl, the Effect B should be less in the acetates than in the alcohols. What change, if any, will take place in the Effect A is difficult to determine, although an increase is to be expected owing to the substitution of the small hydroxyl chain by the longer acetoxyl chain.
By acetylation, the effect B has been reduced by a constant amount in each instance; for by acetylation the residual affinity of the hydroxyl group has been reduced to that of the acetoxyl. Denoting this reduction by \( K \), and assuming that the alteration in the effect A is negligible, we have

\[
[\text{effect} B]_{t} = R - K,
\]

\[
[\text{effect} A]_{t} = S - \Delta,
\]

therefore, \( r, s \) and \( t \) should be still in the same order of magnitude as \( R, S \) and \( T \), i.e., \( r > t > s \); but whether \( r, s \) and \( t \) will all be positive or not, depends on the size of \( K \). Four cases are possible:

(i) where \( K > R \); then \( r, s \) and \( t \) will be all negative;

(ii) where \( R > K > T \); then \( r \) will be positive and \( s \) and \( t \) negative;

(iii) where \( R > T > K \); then \( r \) and \( t \) will be positive and \( s \) negative;

(iv) where \( R > T > S > K \); then \( r, s \) and \( t \) will be positive.

Experiment shows that with the acetates we have case (iii), for the viscosity values are:

<table>
<thead>
<tr>
<th>Effect</th>
<th>( \eta^{25\circ} )</th>
<th>( \Delta )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha ) (-1.2) Methylocyclohexanyl Acetate</td>
<td>0.0174</td>
<td>-0.0021</td>
</tr>
<tr>
<td>( \alpha ) (-1.2) Do</td>
<td>0.0211</td>
<td>+0.0022</td>
</tr>
<tr>
<td>( \beta ) (-1.2) Do</td>
<td>0.0195</td>
<td></td>
</tr>
<tr>
<td>( \beta ) (-1.2) Do</td>
<td>0.0217</td>
<td>+0.0021</td>
</tr>
<tr>
<td>( \alpha ) (-1.4) Do</td>
<td>0.0196</td>
<td></td>
</tr>
<tr>
<td>( \beta ) (-1.4) Do</td>
<td>0.0233</td>
<td></td>
</tr>
</tbody>
</table>

and therefore the value of \( K \) lies between 0.142 and 0.054.
Although the equational form of representing the result of the two effects has been made rather to shorten the argument than to attempt a mathematical expression of the quantities, it is interesting to observe with what exactness the equations describe the phenomena. This may be done by calculating \( K \) in three ways, i.e.

\[
\begin{align*}
R - r &= K = 0.149 \\
S - s &= K = 0.056 \\
T - t &= K = 0.121
\end{align*}
\]

The variation in the value of \( K \) may be due to several causes; but the most probable of these is that the effect \( A \) is altered by different amounts in each of the three cases when the alcohol is converted into the acetate. Experimental investigation of this point is difficult to devise.

The same causes probably govern the order of differences between the melting points of derivatives of the isomeric methylcyclohexanols and also of other cyclic geometric isomerides, for one of the factors which determine a melting point is probably the inter-molecular attraction which tends to keep the compound in the solid state. Thus the same sort of variation is observed in the melting points of the acid phthalic esters as exists in the viscosities of the alcohols.

### Acid Phthalic ester of - Methylcyclohexanol

<table>
<thead>
<tr>
<th>( \alpha-12^- )</th>
<th>m.p. (123-124°)</th>
<th>( \Delta )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta-12^- )</td>
<td>89-90°</td>
<td>34°</td>
</tr>
<tr>
<td>( \alpha-13^- )</td>
<td>93-94°</td>
<td>11°</td>
</tr>
<tr>
<td>( \beta-13^- )</td>
<td>82-83°</td>
<td></td>
</tr>
<tr>
<td>( \alpha-14^- )</td>
<td>119-120°</td>
<td>47°</td>
</tr>
<tr>
<td>( \beta-14^- )</td>
<td>72-73°</td>
<td></td>
</tr>
</tbody>
</table>

Save that the last difference is greater than the first, but this is probably due to the fact that the carboxyl group is nearer the methyl group in the \( 1,4^- \) isomerides than in the \( 1,2^- \) isomerides.
Acid Phthalate  |  p-nitro benzoate  |  Phenyl Urethane

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>α-</td>
<td>93-94°C</td>
<td>91-93°C</td>
</tr>
<tr>
<td>β-</td>
<td>82-83°C</td>
<td>101-103°C</td>
</tr>
</tbody>
</table>

In these derivatives only where large residual affinity of the hydroxyl group has been replaced by the large residual affinity of the free carboxyl group, do the orders of the melting points follow the order of the viscosity values. The unusual results given by cyclic geometrical isomerides which contain the dominant groups in the 1,3 positions have already been noted by Stewart, who gives the following examples:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cis-m.p.</th>
<th>Trans-m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camphoric acid</td>
<td>187°C</td>
<td>171-172°C</td>
</tr>
<tr>
<td>Cyclohexane 1,3- dicarboxylic acid</td>
<td>161-163°C</td>
<td>118-120°C</td>
</tr>
<tr>
<td>Cyclopentane 1,3- dicarboxylic acid</td>
<td>120-121°C</td>
<td>67-68°C</td>
</tr>
</tbody>
</table>

In these instances, the effect A dominates, whereas in the instances tabulated below, where the groups are orientated in the 1,2- or 1,4- position, the effect B dominates (and therefore the trans-form has the higher melting point).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cis-m.p.</th>
<th>Trans-m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclopropane 1,2- dicarboxylic acid</td>
<td>139°C</td>
<td>175°C</td>
</tr>
<tr>
<td>Cyclopentane 1,2- Do</td>
<td>140°C</td>
<td>159-160°C</td>
</tr>
<tr>
<td>Cyclohexane 1,2- Do</td>
<td>192°C</td>
<td>215°C</td>
</tr>
<tr>
<td>Cyclohexane 1,4- Do</td>
<td>161-162°C</td>
<td>300°C</td>
</tr>
</tbody>
</table>
Hydrogenation of o-cresol by the method of SABATIER and SENDERS was found to give only a small amount of the 1,2-methylcyclohexanol compared to the α-form, and of this only a smaller quantity was obtained after the laborious process of purification. Since a large quantity of this isomeride was required for further examination of its properties, a method of preparation was sought, which, whilst convenient for large scale work, would yield a greater proportion of the desired isomeride. Although this investigation did not attain its end, the results are recorded because the influence of experimental conditions on the ratio of the amounts of two geometrical isomerides does not seem to have hitherto attracted attention.

The starting out material for these experiments - 1,2-methylcyclohexanone - was prepared by the oxidation, according to BECKMANN's method, of 1,2-methylcyclohexanol, which had been obtained from o-cresol by Sabatier & Sendern's method of reduction. This ketone was reduced easily by sodium and boiling ethyl alcohol and by sodium and moist ether, but was unattacked by zinc dust and glacial acetic acid, or by aluminium amalgam in moist ether. The ketone was also reduced catalytically by hydrogen in the presence of colloidal platinum, following closely the directions given by SKITA for the preparation of 1c-2c-oxy-methylcyclohexan.

The percentage proportions of the two isomerides in each of these mixtures - for they all proved to be mixtures - was found by observing the viscosity of a specially purified sample and comparing this value with those on a viscosity-composition diagram, which had been previously drawn by determining the viscosity of samples made by mixing the two pure isomerides.

The samples of the reduction products, after being purified in the usual manner, were subjected to a final purification. This
The solid ester was then precipitated by adding acid and the carbinol regenerated by hydrolysis. That no alteration in the proportions of the isomerides in the meantime took place during the various operations was shown by the fact that the viscosity of a mixture of the pure isomerides was the same before and after this treatment.

Since the method given by SKITA for the preparation of the cis-isomeride was followed exactly, any doubts as to the homogeneity of the product could now be settled finally. The product from the reduction (by the action of hydrogen on an acetic solution of the ketone containing colloidal platinum) after final purification, gave a phenyl urethane melting at the same temperature as that prepared by SKITA (Skita: 95°C, present work: 94-96°C) and was found to have a viscosity corresponding to a mixture of 62% of \( \beta \) and 38% of \( \alpha \)-isomerides.

By applying this procedure to the mixtures obtained by the various methods of reduction, the following results were obtained:

<table>
<thead>
<tr>
<th>Method of Preparation</th>
<th>( % \alpha )</th>
<th>( % \beta )</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a). Hydrogenation of o-cresol by Sabatier &amp; Sendern's method at 175°C</td>
<td>67</td>
<td>33</td>
</tr>
<tr>
<td>(b). Reduction of 1,2-Methylcyclohexanone by Sodium and boiling alcohol</td>
<td>77</td>
<td>23</td>
</tr>
<tr>
<td>(c). Ditto by Sodium and moist ether</td>
<td>81</td>
<td>19</td>
</tr>
<tr>
<td>(d). Ditto by Skita's method</td>
<td>33</td>
<td>62</td>
</tr>
<tr>
<td>(e). Hydrogenation of m-cresol by Sabatier &amp; Sendern's method at 100°C</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>(f). Ditto at 180°C</td>
<td>82</td>
<td>18</td>
</tr>
<tr>
<td>(g). Reduction of 1,3-Methylcyclohexanone by Sodium and boiling alcohol</td>
<td>86</td>
<td>14</td>
</tr>
</tbody>
</table>
Viscosity - Composition Diagrams.

\[
\begin{align*}
\text{AB} &: \alpha - 9 \beta - 12 - \text{methylcyclohexane} \\
\text{CD} &: \alpha - 9 \beta - 13 - 
\end{align*}
\]
large yield of \( \beta \)-1,2-methylcyclohexanol and at the same time suitable for large scale preparation, some other means was sought to attain this end.

Geometric inversion naturally suggested itself; but unfortunately in the vast majority of the instances of geometric inversion, the less stable, low melting isomeride is transformed into the stable high-melting isomeride, whereas the reverse was desired in the present work. Moreover, the methylcyclohexanols seem to be remarkably stable towards reagents which might be expected to produce inversion, e.g. heating with acid anhydrides followed by mild hydrolysis, heating with water under pressure at 120°C or prolonged keeping caused no change in the composition of a mixture of isomerides. Protracted boiling with alcoholic caustic soda, however, caused a slight increase in the amount of \( \alpha \)-1,4- methylcyclohexanol in a mixture of the \( \alpha \)- and \( \beta \)-forms, showing that the tendency is for \( \beta \)-to change to \( \alpha \)- (again pointing to the conclusion that the \( \alpha \)-corresponds to the trans-form.)

It is clear that if the configuration of the hydroxylic carbon atom be reversed, one isomeride will be changed into the other, thus:

\[
\begin{align*}
\text{d and l - } \alpha - & \quad \text{d - l - } \beta \text{-1,2 Methylcyclohexanol}
\end{align*}
\]

Therefore any reaction or reactions which would effect a Walden
and this ester is allowed to react with some salt of a carboxylic acid, such as potassium acetate,

when an ester of opposite configuration to that of the original alcohol is obtained (mixed with varying amounts of ester of the same configuration - according to conditions of experiment and reagents used). In the present instance the acetate of \( \beta \)-\( 1,2 \)-methylocyclohexanol should be produced by the action of potassium acetate on the toluene \( \rho \)-sulphonic ester of the \( \alpha \)-isomeride. To test this, the toluene \( \rho \)-sulphonate of \( \alpha \)-\( 1,2 \)-methylocyclohexanol was prepared by the action of toluene \( \rho \)-sulphonic chloride on \( \alpha \)-\( 1,2 \)-methylocyclohexanol in the presence of pyridine. This ester was then heated with an alcoholic solution of potassium acetate, and from the products of the reaction that occurred an ester was isolated, which gave on hydrolysis a hydroxylic body. This was identified, after special purification by analysis, by measurement of viscosity and by conversion into solid derivatives as \( \beta \)-\( 1,2 \)-methylocyclohexanol. The slope of the viscosity composition curve near the 100% \( \beta \)-point was too small to give a very accurate estimation of the extent to which this product was contaminated by the \( \alpha \)-isomeride, but at the maximum it did not amount to more than 1%.

This \( \beta \)-acetate was, however, only formed in a very poor yield.
action of the sulphonie ester on the ethyl alcohol, thus:

$$\text{CH}_2\text{CH}_2\text{O} - \text{CO}_2\text{C}_7\text{H}_7 + \text{H}\text{Et}$$

Judging from the work of Phillips on the ethers of benzyl-methyl-carbinol, this ethyl ether is probably a mixture of the $\alpha$- and $\beta$- forms; however this problem was attacked at a later stage when optically active substances were used. The unsaturated hydrocarbon is formed by a side reaction in which toluene $p$- sulphonie acid is eliminated from the ester. From the position of the double bond in the ring was not determined, but later work has shown that the compound is probably a mixture of isomerides.

The conversion of the sulphonie ester into a carboxylic ester was carried out under various conditions with different reagents and solvents and the percentage inversion estimated by the method already described. The results of these experiments are tabulated below. In those cases in which the yield of pure carbinol was too small to apply this method, the melting point of a solid derivative is given as furnishing some rough indication of the proportions of the two isomerides present.
<table>
<thead>
<tr>
<th>(ii). Ethyl Alcohol (l½ X volume of Sulphonic ester)</th>
<th>Potassium Acetate (4 X theoretical)</th>
<th>24 hours on the water bath</th>
<th>Inversion</th>
<th>99-100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylocyclohexanyl Acetate 25%</td>
<td>Methylocyclohexanyl Ethyl Ether 20%</td>
<td>Methylocyclohexene 40%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| (iii). Ethyl Alcohol (8 X volume of Sulphonic ester) | Potassium benzoate (2 X theoretical) | Do. | Methylocyclohexanyl Benzoate very small | Methylocyclohexanyl Ethyl Ether Ether 40% | Methylocyclohexene 50% | Phenyl urethane of carbinol from resulting benzoate m.p. 83-84°C α - m.p. 106°C | β - m.p. 78-80°C |

| (iv). Ethyl Alcohol (10 X volume of Sulphonic ester) | Sodium formate | Do. | Methylocyclohexanyl formate 9% | Methylocyclohexanyl Ethyl Ether 45% | Methylocyclohexene 40% | Phenyl urethane of carbinol m.p. 81-82°C |

| (v). Ethyl alcohol (10 X volume of Sulphonic ester) | Copper Acetate (Cu·Ac₂ H₂O l½ X weight of Sulphonic Ester) | Do. | Methylocyclohexanyl formate very small | Methylocyclohexanyl Ethyl Ether 12% | Methylocyclohexene 50% | Phenyl urethane of carbinol m.p. 84-85°C |

| (vi). Water added till turbid at 60°C | Formic acid (3½ X hours volume of Sulphonic ester) on the water bath | 3 | Methylocyclohexanyl formate 45% | Methylocyclohexene 40% | Inversion 49% of carbinol | β - 232 |

| (vii). Formamide (2/3rds volume of acid) | Formic acid (3½ X volume of sulphonic ester) on the water bath | 18 hours | Methylocyclohexanyl formate 45% | Methylocyclohexene 40% | Inversion 49% of carbinol | β - 232 |

<p>| (viii). Benzene (7½ X volume of Sulphonic ester) | Formic acid (3½ X volume of sulphonic ester) on the water bath | 12 hours | Methylocyclohexanyl formate 41% | Methylocyclohexene 40% | Inversion 41% of carbinol | β - 246 |</p>
<table>
<thead>
<tr>
<th>Reaction</th>
<th>Reactants</th>
<th>Conditions</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>(x)</td>
<td>Ammonium acetate (3 X weight of Sulphonic ester)</td>
<td>at 110-120°C</td>
<td>Methylcyclohexanyl acetate 65%</td>
</tr>
<tr>
<td>(xi)</td>
<td>Ammonium acetate (3 X weight of Sulphonic ester)</td>
<td>19 hours on the water bath with vigorous stirring</td>
<td>Methylcyclohexanyl acetate 70%</td>
</tr>
<tr>
<td>(xii)</td>
<td>Potassium acetate (equal to weight of Sulphonic ester)</td>
<td>24 hours on the water bath</td>
<td>Methylcyclohexanyl acetate 50%</td>
</tr>
<tr>
<td>(xiii)</td>
<td>Methylcyclohexanyl acetate</td>
<td>Boiled violently for 12 hours</td>
<td>Methylcyclohexene 15%</td>
</tr>
</tbody>
</table>

Similar reactions were carried out with the toluene p-sulphonic esters of some of the other isomerides of methylcyclohexanol -

(xiv) **α-1.3- Methylicyclohexanyl toluene p-sulphonate.**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Reactants</th>
<th>Conditions</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>(xiv)</td>
<td>Ethyl alcohol (2 X weight of Sulphonic ester)</td>
<td>Potassium acetate (4 X theoretical quantity)</td>
<td>Methylcyclohexanyl acetate 20%</td>
</tr>
<tr>
<td>(xv)</td>
<td>Ethyl alcohol (2 X weight of Sulphonic ester)</td>
<td>Potassium acetate (4 X theoretical quantity)</td>
<td>Methylcyclohexanyl acetate 30%</td>
</tr>
</tbody>
</table>

It may be pointed out in passing that these experiments furnish a considerable check on the purity of the isomerides, because in them...
experiment (ii) on page 21, was conducted, but the amount of material available did not permit any conclusive result to be drawn from it. The estimated inversion ($\beta \rightarrow \alpha$) was 85%, but since the product was probably slightly impure, the actual value was no doubt higher than this.

An experiment was also carried out with the toluene $p$-sulphonic ester of partially active $1,2$-methylcyclohexanol, and from it some interesting conclusions as to the relative configurations of $\alpha$- and of $1-\alpha$ and of $\beta$- and of $1-\beta$-methylcyclohexanol can be drawn. Theoretically the $\alpha$-isomeride would be expected to yield by the "sulphonate" method of inversion, the $\beta$-isomeride of related configuration, which may be dextro or laevo in sign of rotation.

It is difficult to imagine how any molecules (iii) corresponding to the mirror image of (ii) could be formed in this reaction, because their formation would necessitate, either a complete rupture of the ring, or the inter-change of the groups attached to both asymmetric carbon atoms - neither of which contingencies is at all probable.
Using the conditions under which it is known that practically full inversion takes place and working with a carbinol $\left[\alpha\right]_D = 16.32^\circ$ ($\left[\alpha\right]_D$ of optically pure carbinol = $32.25^\circ$) the following products were obtained:

1.2- Methylcyclohexanyl Ethyl Ether $\left[\alpha\right]_{17}^D = 7.91^\circ$

1.2- Methylcyclohexanyl Acetate $\left[\alpha\right]_{17}^D = 8.34^\circ$

Methylcyclohexene $\left[\alpha\right]_{17}^D = 17.10^\circ$

On hydrolysis the acetate gave a carbinol of $\left[\alpha\right]_{17}^D = 1.89^\circ$

Thus the d-$\alpha$ isomeride is similar in configuration to the 1-$\beta$ and, of necessity, the 1-$\alpha$ must be similar to the d-$\beta$ isomeride. In these respects the 1,2- methylcyclohexanols resemble the menthols, because PICKARD & LITTLEBURY$^{17}$ have shown that 1-menthol and d-nomenthol yield 1-menthone on oxidation, and therefore have the same configuration, saving for the asymmetric carbon atom to which the hydroxyl group is attached. This kind of relationship has also been observed between the optical isomerides of borneol and isoborneol, e.g. d-borneol and l-isoborneol each yield d-camphor when oxidised.

The formation of an ethyl ether possessing the same sign of rotation as the parent carbinol is somewhat curious at first sight, because the ethers formed by the action of sodium ethoxide or potassium carbonate and ethyl alcohol on sulphonic esters have an opposite sign of rotation and are opposite in configuration to the parent ester and carbinol$^{27}$. The possibility that d-$\beta$-methylocyclohexanyl ethyl ether corresponds to 1-$\beta$-methylocyclohexanol is very small, since menthyl ethyl ether has the same sign of rotation as the parent menthol$^{15}$.

It has been shown however that considerable racemisation takes place when an ether is produced from a sulphonic ester$^{27}$, and, if the
asymmetric carbon atom concerned is a member of a cyclic system is apparently new. Although there are numerous instances of the interconversion of cis- and trans- cyclic isomerides, none of these has been effected by a definite series of reactions, and hence it is doubtful if they and the Walden inversion are due to the same causes. The best known interconversion is described by GOODWIN & PERKIN\textsuperscript{19} who found that cis-1,2-cyclohexane dicarboxylic acid is converted into a mixture of the cis- and trans- forms on boiling with hydrochloric acid. HERMANS\textsuperscript{16} records one of the few examples of the interconversion of cis- and trans- cyclic alcohols, i.e. when the acetone compounds of cis-1,2- and of cis-1,3- tetrahydro-naphthalene diols are hydrolysed with hydrochloric acid, a mixture of the corresponding cis- and trans- diols is obtained. HERMANS was unable to detect any such change in the cyclohexane 1,2-diols.

In view of the unusual character of the inversions described it is of interest to examine the numerous hypotheses that have been advanced from time to time to explain the phenomenon of the Walden inversion, in order to find whether they would all embrace these new facts. The unsatisfactory nature of a large number of these hypotheses is due to the difficulty of their experimental verification or refutation.

In the light of the present results they are required to suggest a reason for the degree of inversion observed in any experiment, and also to admit the possibility that the asymmetric carbon atom concerned in the inversion may be a member of a cyclic system.

It is clear at the outset that these hypotheses which postulate the movement of only two groups will explain the inversion of a cyclic compound and most of them are sufficiently broad to allow any percentage inversion. Typical examples of this kind of hypothesis are those suggested by FISCHER and by PHILLIPS. The hypotheses which require more than two of the four groups of the
possible that the two groups held together in the ring may, one or each, move from one quadrant of the asymmetric atom to another. The presence of a cyclic structure could only hinder the process of a Walden inversion if the two groups held in the ring did not move at the same time, and, since there is no hypothesis which maintains that the groups -other than the group that is substituted- do not move at the same time, this point does not arise. Thus the hypotheses of WERNER, BJELMANN and GADAMER will describe the inversion of a cyclic compounds, and since none of them is sufficiently definite to predict the loss of rotatory power which will accompany an inversion they cannot be tested by the second alternative.

The ingenious hypothesis proposed by LOWRY differs from that those mentioned in that, can at least be subjected to experimental examination.

According to LOWRY, the Walden inversion takes place through the formation of an intermediate complex ion, composed of the sulphanic ester, split up into the sulphonoxy ion and the carbinyl ion, thus:

\[
\begin{align*}
\text{(i)} & \quad \begin{array}{c}
\text{C}_7\text{H}_7\text{S} - \text{O} - \text{C} - \text{R} \\
\text{R}_1
\end{array} \\
& \quad \xrightarrow[]{} \\
\text{C}_7\text{H}_7\text{S}^+ - \text{O} - \text{C} - \text{R}^+ \\
\text{R}_1
\end{align*}
\]

it being assumed that the carbinyl ion does not break away completely from the sulphonoxy ion (which would necessarily involve complete racemisation), but remains held near the electro static attraction.

\[
\begin{align*}
\text{(ii)} & \quad \begin{array}{c}
\begin{array}{c}
\text{C}_7\text{H}_7 - \text{S} - \text{O} \\
\text{R}_1
\end{array} \\
\text{C} - \text{R}
\end{array} \\
& \quad \xrightarrow[]{} \\
\begin{array}{c}
\begin{array}{c}
\text{C}_7\text{H}_7 - \text{S} - \text{O} \\
\text{R}_1
\end{array} \\
\text{C} - \text{CH}_3
\end{array}
\end{align*}
\]

In this complex the three groups attached to the asymmetric carbon
(iii). The sulphonyloxy ion now breaks away and the configuration of the asymmetric sulphonyloxy ester of an ester yielding a carboxylic ester of opposite configuration to that of the original sulphonic ester.

To explain the loss of rotatory power which often accompanies these inversions, LOWRY assumes that -

(i). Some of the molecules of the sulphonic ester ionise completely and hence racemisation of this part of the material takes place.

(ii) Direction action occurs by the displacement of the sulphonyloxy ion in the partially ionised form by the acyl ion.

The first is easy to conceive, but it is very difficult to imagine why the carbomyl ion should displace the sulphonyloxy ion, for one would expect that the carbomyl ion should displace the sulphonyloxy ion would be repelled from the part of the complex by the similar change in the sulphonyloxy ion and be attracted to the carbomyl ion to form the tri-ionic complex. Therefore it seems more logical to assume that loss of rotatory power proceeds by the first process.

If this be granted, it is clear that the amount of inversion can never be less than 50%. This, however, leads to difficulties, because experiment (viii) on page 21 gave an inversion undoubtedly below 50%

The present condition of the subject of the Walden inversion is somewhat confused and it seems that until we know more about the reactions involved e.g. which reactions are innate and what the order of each reaction is, we can only hope to conjecture the underlying causes.
first, because this geometrical isomeride is readily available in comparatively large quantities in the pure state.

The acid phthalate of this carbinol gave a crystalline salt only with strychnine, although numerous alkaloids were tried. By fractional crystallisation of this salt from acetone, a small amount of a phthalate having $[\alpha]_D^x = 52.2^\circ$ was obtained; but since the salt decomposed quickly and the crops diminished quickly in amount, it was not possible to attain optical purity in this manner. Ethyl alcohol was then substituted for the acetone as a solvent, but whilst this prevented the salt decomposing, the rapidity of the resolution was decreased enormously. After trying some other alternatives, the following process was adopted; the strychnine salt of the inactive ester was crystallised once from ethyl alcohol and the crop and mother liquor separately decomposed into strychnine and ester. The esters so obtained had $[\alpha]_D^x = 17^\circ$. These esters were then separately crystallised from glacial acetic acid, when the crops were found to be almost inactive and the mother liquors to yield esters of $[\alpha]_D^x = 48^\circ$ (approximately).

By a laborious repetition of this process - using the practically inactive esters from the previous separation for the following separation - about 100 grams of esters of $[\alpha]_D^x = 48^\circ$ and of $-48^\circ$ were obtained. Recombination of each of these esters with strychnine gave on repeated crystallisation from acetone, esters unaltered in rotatory power by crystallisation from solvents other than acetone. Altogether 130 crystallisations were necessary for the preparation of 25 grams of the $-\alpha$- and $\beta$- acid phthalates of $\alpha - 1.2$-methylcyclohexanol $[\alpha]_D^x = 63.3^\circ$ and $[\alpha] = 63.5^\circ$. Each of these esters was then hydrolysed and the specific rotatory powers of the resulting carbinols measured at different temperatures for different wave lengths of light. These values are given at the end of this section.

All rotations of acid phthalic esters were determined in benzene.

-23-
phthalic esters and from \( \alpha-1,2 \)-methylcyclohexanol by the 'sulphonate' method. A preliminary experiment showed that the strychnine salt of \( \beta-1,2 \)-methylcyclohexanyl hydrogen phthalate possessed the same characteristics as the \( \alpha \) salt—except that it was a less satisfactory substance to submit to fractional crystallisation. Numerous other alkaloidal salts of this ester were prepared, but none was so satisfactory as the strychnine salt. The \( 1 \)-hydroxy-hydrindamine salt is a glassy gum.

Systematic fractional crystallisation of the strychnine salt (prepared from 120 grs. of the ester) from acetone yielded two grams of a salt which gave on decomposition an ester \( [\alpha]_D = -38.4^\circ \). The previous crop yielded an ester \( [\alpha]_D = -36.1 \) and the mother liquor from the final crop, an ester \( [\alpha]_D = -23.4^\circ \).

The resolution of this isomeride has been accordingly abandoned until some more satisfactory method of procedure is found. It is noteworthy that in the resolution of the \( \alpha \)-isomeride the \( d \)-form separates out of solution first and that in the resolution of the \( \beta \)-isomeride the \( l \)-form separates out first. This would be expected, because the \( d-\alpha \)-form is similar in configuration to the \( l-\beta \)-form.

The Rotatory Dispersion of \( d-\alpha-1,2 \)-Methylcyclohexanol.

The rotatory powers of \( d-\alpha-1,2 \)-methylcyclohexanol were determined for ten different wavelengths of light ranging from \( \lambda = 6708 \text{ A.U.} \) to \( \lambda = 3820 \). The last five determinations were made photographically using the iron arc as illuminant. The observed rotatory powers ranged from \( 13^\circ \) to \( 47^\circ \).

Plotting \( \frac{1}{\lambda} \) against \( \lambda^2 \) (one of the tests suggested by Lowry for simplicity of rotatory dispersion) gave a straight line, from
Rupe made measurements of the dispersion of various terpene substances, and Lowry has examined the data on the basis of the Drude equation, finding that camphor, carvone, many derivatives of methylene camphor and the esters of myrtenol were all simple. Only pulegone he found complex. It is remarkable that such a class of substances, abounding with complex tautomeric changes and unstable ring systems, should exhibit generally simple dispersion. The ratio $\frac{\alpha_{vi}}{\alpha_{gr}}$ for d-\(\alpha\)-1.2-methylcyclohexanone is 1.63; at higher temperatures the value increases to 1.69, but this increase is within the limit of experimental error. The value is rather high compared with the average of 1.63 obtained by Pickard and Kenyon for the aliphatic alcohols and their esters.

Tschugaeff found that substances possessing an absorption band comparatively near the visible region of the spectrum had a higher $\frac{\alpha_{r}}{\alpha_{c}}$ than substances possessing a band in the remote ultraviolet. One would expect the methylcyclohexanols having a ring structure would possess a band of higher wavelength than the aliphatic alcohols.

<table>
<thead>
<tr>
<th>Substance</th>
<th>$\alpha_{r}$</th>
<th>$\alpha_{c}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylcyclohexanol</td>
<td>23.47</td>
<td>14.14</td>
</tr>
<tr>
<td>3112</td>
<td>19.16</td>
<td>13.13</td>
</tr>
<tr>
<td>3100</td>
<td>17.86</td>
<td>12.58</td>
</tr>
<tr>
<td>4641</td>
<td>22.12</td>
<td>15.76</td>
</tr>
<tr>
<td>4540</td>
<td>24.12</td>
<td>15.76</td>
</tr>
<tr>
<td>λ</td>
<td>μ_25</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>6408</td>
<td>1.4550</td>
<td></td>
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<td>6096</td>
<td>1.4564</td>
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<td>1.4569</td>
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<td>1.4603</td>
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<tr>
<td>5106</td>
<td>1.4611</td>
<td></td>
</tr>
<tr>
<td>4359</td>
<td>1.4682</td>
<td></td>
</tr>
</tbody>
</table>

Rotatory Power of 1-α-1,2-Methylcyclohexanol

Rotating Power of

\begin{align*}
\text{in } 50 \text{ m.m. tube at } 20^\circ C \\
d_{20^0} = .929 \\
\lambda \text{ in A.U.} & | \alpha_{20^0} | [\alpha]_{20^0} \\
6708 & 13.05 & 24.24 \\
5893 & 17.18 & 31.93 \\
5790 & 17.95 & 33.35 \\
5461 & 20.32 & 37.76 \\
4359 & 34.13 & 63.39
\end{align*}

Refractive Indices of 1-α-1,2-Methylcyclohexanol

<table>
<thead>
<tr>
<th>λ</th>
<th>μ_25</th>
</tr>
</thead>
<tbody>
<tr>
<td>6408</td>
<td>1.4550</td>
</tr>
<tr>
<td>6096</td>
<td>1.4564</td>
</tr>
<tr>
<td>5896</td>
<td>1.4566</td>
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<td>5106</td>
<td>1.4611</td>
</tr>
<tr>
<td>4359</td>
<td>1.4682</td>
</tr>
</tbody>
</table>

\text{Photographic determinations.}
$\alpha$-Methylcyclohexanol

$\frac{[\alpha]}{\lambda}$ at 20.5°C

$\frac{1}{[\alpha]} \lambda$ at 20.5°C

$\frac{1}{[\alpha]} \lambda^2$ at 69°C
The cresols were hydrogenated in the laboratories of Messrs Crossfields, Warrington by the method of SABATIER & SENDERRENS at 175°C. α-Cresol was found the most difficult to hydrogenate. Some m-cresol was also hydrogenated in the Laboratories of the Technical Research Works Ltd. London at 100°C and at 180°C; the special electrolytically prepared nickel catalyst described by LUSH was used.

The crude products were fractionally distilled several times under reduced pressure, using a fourteen inch rod-and-disk column. Three groups of fractions were collected: methylcyclohexanones, b.p. 62-64°C/20 m.m.; methylcyclohexanols, b.p. 77-80°C/20 m.m. and cresols, b.p. 85-100°C/20 m.m. The middle fractions were heated with phthalic anhydride (ten per cent excess) at 110°C for 12 hours. At the end of this time the product was poured, whilst still molten, into a slight excess of sodium carbonate solution, the resulting solution filtered, diluted with a large volume of water and extracted 10 times with benzene. The benzene was removed from the aqueous residue in a current of air and the ester precipitated by the addition of acid. The ester thus obtained was freed from phthalic acid by dissolving it in chloroform and drying and filtering this solution. The chloroform was removed first by distillation and finally over paraffin wax in vacuo.

**Acid Succinic Esters.**

These compounds were made by a similar method, the only difference being that they were freed from succinic acid by shaking the ethereal extract with water.

**p-Nitro benzoic Esters.**

To prepare these esters, p-nitro benzoyl chloride (1.05 mol), dissolved in benzene, was added to the methylcyclohexanol and dissolved in pyridine (1.2 mol). Considerable heat was developed, and the mixture was kept below 30°C by cooling in ice water. Crystals of
hydrochloric acid to remove pyridine, and twice with dilute sodium carbonate solution to remove any p-nitro benzoic acid.

Isolation of the Geometrical Isomerides.

(i) 1,2- and 1,4- Methylcyclohexanyl Hydrogen Phthalates.

Crystallisation of each of these esters from glacial acetic acid yielded finally crops of constant melting point of the less soluble component (α). The esters from each of the sets of mother liquors were removed and separately crystallised from light petroleum, when again crops of constant melting point finally resulted, but in this instance composed of the more soluble component (β). The pure crops were then crystallised from other solvents than those by means of which they were isolated, but in no instance was any change in melting point observed.

These esters were hydrolysed by dissolving them in a ten per cent excess of caustic soda solution and immediately distilling in a current of steam.

(ii). 1,3- Methylcyclohexanyl p-nitro-benzoate.

Crystallisation of this ester from methyl alcohol gave crops which, after several crystallisations, melted at either 59° (α') or 65° (β'). Generally two crops of the α'-ester separated first and then one β' followed by one or two α' crops. The α'-ester separated in round granules, whilst the β' ester separated in flat plates - quite distinct in appearance. About eight crops were generally worked up, each requiring about ten crystallisations to yield a product of constant melting point.

These esters were hydrolysed by re-fluxing for three quarters of an hour with a ten per cent excess of alcoholic caustic soda (alcohol ten times the weight of salt). About half the alcohol was removed by distillation and the residue poured into a large volume of water, and extracted with ether. The ethereal solution was dried with potassium carbonate, and after the removal of the ether, the residual alcohol was distilled under reduced pressure.
amounts of phenyl isocyanate and the methylcyclohexanol and allowing
the mixture to stand in a closed vessel for one day. The resulting
solid mass was crystallised from methylalcohol or petroleum (b.p.
40-60°C). Sometimes a small amount of the product was practically
insoluble in the petroleum; this proved to be diphenyl urea m.p.
230-232°C (correct 235°C).

The physical properties of the substances described in this
section are collected together on page 8.
½ SCALE.
glass sides and a copper bottom. A large toluene mercury thermo-
regulator kept the water in this within 0.02°C of 25°C. A standard
thermometer was used to check the thermo-regulator.

The water was kept in motion by a stirrer driven by a small
electric motor: the stirrer was specially designed to suck up the
warmed water from the spot on the copper sheet just above the burner
and mix it with the main volume in the middle of the tank.

Viscometers.

The viscometers used were a modification of the Ostwald type
designed by Thole for the measurement of the viscosity of liquids
when only a small quantity is available. One instrument, suitable
for measuring viscosities above 0.15, was presented to the Department
by Dr Thole, but for the measurement of the lower viscosities of the
acetates of the methylcyclohexanols, another viscometer was made by
the writer, because the times of flow in the first instrument were
very small, thereby involving considerable error in measurement and
danger of turbulent flow. In order to maintain a fairly large
capillary, and hence lessen the chance of blocking by dust, and also
to keep the time of flow high for a given quantity of liquid, a
slight alteration in the Thole pattern was made, i.e. spherical
containers were substituted for the usual cylindrical ones, thus
reducing the average head and increasing the time of flow. The
instruments were filled to the etched marks A and A\text{1} and the time
taken for the meniscus to pass from B to C.

Calibration of the Viscometers.

The first instrument was calibrated with cyclohexanol and
1-isopropyl-2-octyl carbinol.

(i). cyclohexanol

\[ \eta^{25^\circ} = 500^21 \]
\[ d^{25^\circ} = .9469 \]

average time of flow = 425.7 seconds.

\[ K^{25} = \frac{\eta^{25^\circ}}{d^{25^\circ}} = .00126 \]
Average time of flow = 139.5 seconds

The second instrument was calibrated with pure nitrobenzene and with ethyl alcohol.

(i) Nitrobenzene

\[ \eta_{25^\circ} = 0.018223 \]

Average time of flow = 193 seconds

(ii) Ethyl alcohol

\[ \eta_{25^\circ} = 0.010824 \]

Average time of flow = 178.6 seconds

Precautions taken in the measurement of viscosity.

The viscometers were cleaned with chromic acid solution after every two or three determinations and before use were rinsed with hot distilled water, absolute alcohol and absolute ether, and finally dried by the passage of hot dust-free air. The instruments were filled with a small pipette approximately to the graduation marks A and A', placed in the thermostat, adjusted by means of a plumb line and, after standing about half an hour, the excess liquid was removed by a capillary pipette. The open end of the viscometer was closed by a loose fitting glass cap during use.

In addition to these usual precautions, it was necessary to distil the alcohols before determining the viscosity and repeat this
In one instance the viscosity of a certain sample fell 30% after standing eight months in a stoppered bottle, but regained its normal value after distillation.

The acetates of the Methylecyclohexanols.

These esters were made by warming the corresponding alcohol with an excess of acetic anhydride for two hours on the water bath. Water was then added and the ester extracted with ether. The united ethereal extracts were washed with dilute sodium carbonate several times and dried with sodium sulphate. After removal of the ether the ester was fractionally distilled under reduced pressure until the viscosity was approximately constant.

<p>| Methylecyclo- | b.p. at 20 m.m. | $\beta_{25}^0$ | $\mu_{25}^0$ | $[R_\lambda]$ | $\Delta%$ |</p>
<table>
<thead>
<tr>
<th>hexanyl Acetate</th>
<th></th>
<th>$\alpha$</th>
<th>$\lambda$</th>
<th>D</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-1.2-</td>
<td>79-80°C</td>
<td>.9361</td>
<td>1.4389</td>
<td>43.57</td>
<td>+1.3</td>
</tr>
<tr>
<td>$\beta$-1.2-</td>
<td>79-80°C</td>
<td>.9434</td>
<td>1.4376</td>
<td>43.34</td>
<td>+0.4</td>
</tr>
<tr>
<td>$\alpha$-1.3-</td>
<td>81-82°C</td>
<td>.9385</td>
<td>1.4313</td>
<td>42.99</td>
<td>-0.7</td>
</tr>
<tr>
<td>$\beta$-1.3-</td>
<td>78-79°C</td>
<td>.9430</td>
<td>1.4369</td>
<td>43.38</td>
<td>+1.4</td>
</tr>
<tr>
<td>$\alpha$-1.4-</td>
<td>78-80°C</td>
<td>.9380</td>
<td>1.4398</td>
<td>43.78</td>
<td>+1.2</td>
</tr>
<tr>
<td>$\beta$-1.4-</td>
<td>78-79°C</td>
<td>.9337</td>
<td>1.4365</td>
<td>43.75</td>
<td>+0.9</td>
</tr>
</tbody>
</table>

$[R_\lambda]$, calculated = 43.32.
to 1-methylone was followed.

1.2-Methylcyclohexanol (35 grs obtained from the purified
acid phthalate by hydrolysis) was poured fairly with vigorous
stirring, into a mixture of potassium dichromate (60 grs)
sulphuric acid (50 grs) and water (200 grs). A black pasty
substance separated first, but this soon gave place to a light
brown oil. The temperature of the mixture tended to rise, but was
kept below 40°C by cooling. After stirring for one hour, the
ketone was separated, the residual liquid extracted with ether,
and the united extracts washed with water and dried by sodium
sulphate. On removal of the ether the product (32 grs) distilled
at 62-64°C at 20 m.m. and yielded a semi-carbazone of m.p.196-
196.5°C, ZELINSKY²⁵ gives 193-194°C

Reduction of 1.2-Methylcyclohexanone.

(i), by sodium and moist ether.
(ii) by sodium and boiling alcohol.

These reductions call for little note. The yields were above
90% and only a small quantity of non-volatile substance (pinacolone)
was produced; the first method gave slightly better results.

(iii) by hydrogen in the presence of colloidal platinum.

The directions given by SKITA (loc. cit) were closely
followed; a slight excess over the theoretical quantity of
hydrogen was absorbed during two hours. The carbinol was isolated
in 75% yield and gave an acid phthalic ester, m.p. 94-96°C.
toulene p-sulphonic chloride (1.02 mols) to a mixture of pyridine (1.05 mols) and the corresponding alcohol (1 mol). The acid chloride dissolved with an absorption of heat but after a few minutes the temperature rose and white crystals (pyridine hydrochloride) began to fill the liquid - at this point the mixture was cooled in ice. After standing overnight, the solid mass was ground up under water, filtered from the solution of pyridine hydrochloride and washed repeatedly with dilute hydrochloric acid and water. The ester so prepared was dried and recrystallised from light petroleum.

\[ \begin{array}{c|c|c}
\text{ester} & \text{m.p.} & \text{decomposition point} \\
\hline
\alpha-1.2- & 27-28^\circ & 156^\circ \\
\alpha-1.3- & 39-40^\circ & 155^\circ \\
\beta-1.3- & 45-47^\circ & 146-147^\circ \\
\alpha-1.4- & 71-72^\circ & 153^\circ \\
\end{array} \]

Analyses.

(a)\(\alpha-1.2-\) ester, 1.0081 grs. required, 149 grs of caustic soda for complete hydrolysis, exactly calculated amount .148(7) grs.

(b)\(\alpha-1.3-\) ester, 1.0092 grs required, .150 grs of caustic soda, calculated .149 grs.

(c)\(\alpha-1.4-\) ester, 1.0042 grs required, .149 grs of caustic soda, calculated .148(4) grs.

The conditions under which these esters were allowed to react with various reagents have already been dealt with (pages 21-22). It will be necessary to indicate here how the products of these reactions were separated. As a rule the mixture, after having been heated for the proper time, was mixed with three times its volume of water and neutralised to prevent any organic acid displaced from the salt of toluene p-sulphonic acid from being extracted. The liquor was then extracted with ether four times and the extracts dried. The ether was removed by distillation through a 20 pear column to prevent the highly volatile methylcyclohexene
from which the ethyl acetate was removed by washing twice with water; 104-115°C/760 m.m. this consisted of impure methylocyclo-
hexene; 65-70°C/20 m.m., ethyl methylocyclohexanyl ether fraction, 76-81°C/20 m.m., ester fraction. The ester fraction was
hydrolysed by alcoholic caustic soda, care being taken to reflux the reactants for the shortest possible time in order to minimise
risks of racemisation. The resulting carbinol was purified by the method already described and the viscosity determined.
The methylocyclohexanyl ethyl ethers formed in experiments in which ethyl alcohol was used, were identified by the comparison of the observed and calculated molecular refractivities:

\[
d_{20}^4 = 0.902, \quad \mu_D^{20} = 1.470
\]

\[
\left[ R_L \right]_D^{20} = 43.5 \quad \text{Calculated value 43.4}
\]

MURAT\textsuperscript{26} gives similar figures for methylocyclohexanyl ether prepared by the action of ethyl iodide on the sodium compounds of 1,2-methylocyclohexanol.

A nitrosate of the methylocyclohexene, formed in the experiments on \(\alpha\)-1,2-methylocyclohexanyl toluene \(\beta\)-sulphonate was prepared by the action of the nitric acid (.9 grs. S.G.1.4) on a solution of the hydrocarbon (1 gr) in glacial acetic acid (.5 c.c.) and amyl nitrite (1 gr), cooled in ice and salt. The colour of the mixture quickly changed to pale green, and after standing one hour some pale green solid separated. Water was then added and the whole thoroughly shaken to dissolve the reagents from the solid nitrosate. which was finally filtered off. The solid was crystallised from ethyl alcohol and then formed a white powder which melted, turned green and evolved gas at 107°C. MARKOWNIKOFF and TSCHIRDI\textsuperscript{23} gave the melting point of this substance as 104°C. Their methylocyclohexene was prepared from 1,1 methylocyclo-
hexanyl chloride. WALLACH\textsuperscript{29} gives the same figure for the
preparations of methylcyclohexene the existence of a nitrosate was confirmed in the present case by the preparation of the piperidine derivative of the nitrosate. This substance when first prepared, by addition of piperidine (1 mol) to a solution of the nitrosate (1 mol) in ethyl alcohol, had a m.p. 145-146°C which rose after one crystallisation from alcohol to 153°C, and after two to 157°C.

One experiment was made to ascertain whether methylcyclohexene would combine with acetic acid as camphene combines with acetic acid to give iso iso-bornyl acetate. The methylcyclohexene prepared in experiments in which \(-\alpha,\beta-\) methylcyclohexanyl toluene \(\beta\)-sulphonate was used was heated for 24 hours on the water bath with acetic acid (eight times the weight of unsaturated hydrocarbon) and 50% sulphuric acid (one tenth the weight of unsaturated hydrocarbon). In this way a 50% yield of a substance having the same boiling point as methylcyclohexanyl acetate was obtained. This ester was hydrolysed and the resulting carbinol oxidised to the ketone. This ketone yielded a semicarbazone softening at 156°C and becoming clear at 163°C. Upon recrystallisation from dilute ethyl alcohol the m.p. rose to 166°C (m.p. of \(\alpha,\beta-\) methylecyclohexanone semicarbazone, 193-194°C, \(\alpha,\beta-\); 191-200°C, \(\alpha,\beta-\); 199°C). This point has not been investigated further.

It was noticed that the methylcyclohexenes oxidised in the presence of air to viscid gums. This phenomenon is not due to mere polymerisation, because samples sealed in glass tubes retain their original properties.

The following are the observed physical properties of methylcyclohexene prepared from \(\alpha,\beta-\) methylcyclohexanyl toluene \(\beta\)-sulphonate:

- B.P. 105-108°C
- \(d^\circ_{40} = 0.8097\)
- \(d^\circ_{20} = 0.8052\)
- \(d^\circ_{26} = 0.8021\)
- \(\mu^\circ_{D} = 1.4409\)
advice and for the interest they have taken in the work.
5. Traube, Ann., (1886), 240, 43.
9. LAUENSTEIN, Zeit Physikal Chem. (1892), 9, 422.
15. Lander, ibid. (1900), 77, 731.
22. Dunston & Thole, J.C.S.
23. Prebani & Handel, Wien. Ber. (1878), 78, 80 and (1879), 80, 64.
32. Lowry, Meeting of Chemical Society (London), Nov. 1924.