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THE SYNTHESIS OF THE GEOMETRICALLY ISOMERIC TRIMETHYLCYCLOHEXANES

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By
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*****

The Ohio State University
1962

Approved by

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I. INTRODUCTION

The synthesis, purification and study of properties of pure hydrocarbons has long been in progress at The Ohio State University. Since 1938, this work has been under the sponsorship of the American Petroleum Institute whose program originally called for an extended series of motor tests on each hydrocarbon included in gasoline.

In more recent years, the emphasis has been on the preparation of very pure hydrocarbons on which physical and thermodynamic property determinations are made. These standard samples are also made available widely for calibration of analytical instruments such as ultraviolet, infrared and mass spectrometers and, more recently, gas chromatographs. Such physical and thermodynamic data and rapid analyses on these hydrocarbons are needed for controlling refining processes and for designing future refining and petrochemical plants.

Cyclohexane and its polyalkyl derivatives are some of the many hydrocarbons that occur in petroleum and have long been recognized as important constituents of light naphtha. The need for their identification and characterization has prompted the work on the synthesis of the geometrically isomeric trimethylcyclohexanes.
There are six possible positional isomers of the trimethylcyclohexanes: 1,1,2; 1,1,3; 1,1,4; 1,2,3; 1,2,4; and 1,3,5. Only the last three will be discussed in this dissertation as the others do not occur in geometrically isomeric forms. Of the non geminal isomers, synthesis and characterization has been completed satisfactorily only in the case of the 1,3,5-trimethylcyclohexanes.\(^1,2\) In this case, there are only two possible geometric isomers, the \(ccg\) and \(cct\).

Synthesis of the three 1,2,3-trimethylcyclohexanes\(^3,4\)

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the purity of some of these isomers was later found to be so low that a reinvestigation of the problem was deemed to be necessary.
II. STATEMENT OF THE PROBLEM

The purpose of this research was the synthesis and identification of the geometrical isomers of the 1,2,3- and the 1,2,4-trimethylcyclohexanes and some of their unsaturated derivatives by methods suitable for their subsequent preparation by the American Petroleum Institute.
III. HISTORICAL

Undesignated geometrical isomers of the 1,2,3- 1,2,4- and 1,3,5-trimethylcyclohexanes have been isolated from petroleum fractions 7-11 and were also noted in rearrangement

(7) V. Grignard, Compt. rend., 178, 2149 (1924).

In none of these instances have the authors attempted to designate the geometry of their products.
The first attempt to synthesize 1,2,3-trimethylcyclohexane was by Zelinsky\(^{17}\) and no mention was made of the possibility of the formation of various isomers. Eisenlohr\(^ {18}\) was the first worker to recognize the existence of two isomers but he apparently overlooked the possibility of a third. The 3 possible isomers are:

\[
\begin{align*}
&\text{cis,trans,cis} \\
&\text{cis,cis,trans} \\
&\text{cis,cis,cis}
\end{align*}
\]

It is to be noted that the \text{cis, cis, trans} isomer will actually exist as a d,l pair.

Eisenlohr carried out his synthesis by hydrogenating 1,2,3-trimethylbenzene over platinum catalyst to give a \text{cis}-trimethylcyclohexane and over nickel catalyst to give a \text{trans}-trimethylcyclohexane. However, the question arises which of the two possible \text{trans} isomers was obtained here, the \text{ctt} or the \text{ctc}?
The literature contains numerous references to the 1,2,4-trimethylcyclohexanes. Here again the earliest workers were either unaware of or ignored the possibility of geometrical isomers. The 4 possible isomers are:

Table I shows the isomers listed by the respective authors together with their respective physical constants. Where no specific isomer is designated the investigator failed to specify. From consideration of Table I, it is evident that most of the data are questionable, the possible exception being those from Skita's work. He was the first to postulate the proposition that hydrogenation of alkylbenzenes over a platinum catalyst gives the cis isomer, whereas von Auwers had previously suggested that hydrogenation over a nickel catalyst at high temperatures yielded the trans isomer. Interestingly, Eisenlohr, a few years later, found that hydrogenation of 1,2,4-trimethylbenzene gave two 1,2,4-trimethylcyclohexanes the physical properties of which did not agree with any of those reported by Skita.

White and Glasgow reported isolating a geometrical isomer of 1,2,4-trimethylcyclohexane in 94% purity from
a petroleum fraction with the following physical properties; b.p. 141.22°C., m.p. 86.4°C., \( d_4^{20} 0.7720 \), \( n_D^{20} 1.4266 \) and was designated later\(^{28} \) as the ctt isomer.


Recently\(^3,4,6 \) an attempt was made to synthesize each of the 1,2,3-trimethylcyclohexanes stereospecifically; however, re-examination of the products by gas-liquid partition chromatography revealed that two of the isomers, the cct and ccc, were mixtures. The same workers\(^5,6 \) attempted to prepare the 1,2,4-trimethylcyclohexanes, but subsequent analysis of the products obtained revealed that only one of them was pure. The present research has proved that even the assignment of configuration was wrong in two cases.
<table>
<thead>
<tr>
<th>Investigator</th>
<th>Isomer</th>
<th>B.p. °C./760 mm.</th>
<th>d$_4^{20}$</th>
<th>n$_D^{20}$</th>
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<td>Markonikow$^{19}$</td>
<td></td>
<td>135-136</td>
<td>.7652</td>
<td></td>
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<tr>
<td>Zelinski$^{20}$</td>
<td></td>
<td>142-144</td>
<td>.7807/18°C.</td>
<td></td>
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<tr>
<td>Konowalow$^{21}$</td>
<td></td>
<td>135-138</td>
<td>.7667</td>
<td></td>
</tr>
<tr>
<td>Sabatier$^{22}$, $^{23}$</td>
<td>Fraction 1</td>
<td>141.5-143/759</td>
<td>.7850</td>
<td></td>
</tr>
<tr>
<td>Eykman$^{24}$</td>
<td>Fraction 2</td>
<td>143-144/759</td>
<td>.7848</td>
<td></td>
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<tr>
<td>Gadaskin$^{25}$</td>
<td></td>
<td>140</td>
<td>.778</td>
<td>1.429</td>
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<tr>
<td>von Auwers$^{26}$</td>
<td></td>
<td>140-141</td>
<td>.7799/16.9°C</td>
<td>1.43056/16.6°C</td>
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<td>Skita$^{27}$</td>
<td>ccc</td>
<td>146</td>
<td>.790</td>
<td>1.43314</td>
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<tr>
<td></td>
<td>ctt</td>
<td>142</td>
<td>.786</td>
<td>1.43209</td>
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<tr>
<td></td>
<td>ctc</td>
<td>140</td>
<td>.774</td>
<td>1.42916</td>
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<tr>
<td>Eisenlohr$^{18}$</td>
<td>cis</td>
<td>141.5</td>
<td>.7850</td>
<td>1.43341 n$_{He}^{20}$</td>
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<tr>
<td></td>
<td>trans</td>
<td>138.5-139.5/755</td>
<td>.7813</td>
<td>1.43121 n$_{He}^{20}$</td>
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(20) N. D. Zelinski and A. Reformatsky, Ber., 29, 214 (1896).
(22) P. Sabatier and J. B. Senderens, Compt. rend., 122, 506 (1901).
(23) P. Sabatier and J. B. Senderens, Compt. rend., 132, 1254 (1901).
(27) A. Skita and A. Sneck, Ber., 55, 144 (1922).
IV. THEORETICAL

A. Discussion of the Axial and Equatorial Positional Isomers of the Trimethylcyclohexanes

Considering first the 1,2,3-trimethylcyclohexanes, three geometrical isomers are possible:

One can see that isomer I (ctc) may be either eee or aee (e=equatorial, a=axial). The eee configuration is the one most likely to exist at room temperatures since this trans isomer is the least strained as evidenced by its physical constants (i.e., lowest boiling point, refractive index, density) seen in Table IV, page 34. Isomer II (cct) may be either aee or eea and isomer III (ccc) may be either eea or aea. This assignment would follow logically from the premise that axial positions are the positions affording the molecule a higher potential energy. Since II (cct) and isomer III (ccc) have somewhat similar physical constants (Table IV) it is likely that they both have either one or two axial substituents. At room temperature, the
lower energy tautomers are most likely to be present, thus the more stable tautomeric configuration of isomer III is probably (eae) rather than (sea) and the more stable tautomeric configuration for isomer II is probably (ae) rather than (eaa).

The case of the 1,2,4-trimethylcyclohexanes is treated in the same fashion. The planar representation of the four expected isomers is as follows:

Each of these may exist in either a high energy form, containing at least two axial substituents or a corresponding low energy form having at least two equatorial substituents. Once again the low energy forms with a maximum number of equatorial methyls is preferred rather than the alternative high energy forms with a maximum number of axial methyls.
The 1,3,5-trimethylcyclohexanes include only two isomers, the ccc and the cct shown as follows:

\[
\begin{array}{cc}
\text{ccc (eee)} & \text{cct (eee)} \\
\text{VIII} & \text{IX}
\end{array}
\]

Seeing that the physical constants exhibited by a molecule are manifestations of its spatial geometry and electrical effects, prediction of the boiling points can be made. The geometric isomers of the dimethylcyclohexanes have been characterized and definite physical properties have been assigned to them.\(^{29}\)


The first three members of Table II exhibit higher spatial requirements since each necessarily has one axial substituent and conversely the latter three members presumably have no axial substituent. It is also noted that when two methyl groups are vicinal, there is an additional degree of steric hindrance as seen in the case of cis-1,2-dimethylcyclohexane, which has the highest internal energy of the last three members. The small difference between
the trans-1,3 and cis-1,4-isomers; and the cis-1,3- and trans-1,4-isomers is probably due to considerations of symmetry of the molecule.

Correlating the trimethylcyclohexanes to the above facts, one would predict on the basis of spatial requirements of the methyl groups in the dimethylcyclohexane series, that the physical constants i.e., boiling point, refractive index and density, for the 1,2,3-trimethylcyclohexanes would be in the order of:

\[ \text{ccc} \succ \text{cct} \succ \text{ctc} \]
\[ (\text{eae}) \ (\text{see}) \ (\text{eee}) \]

and for the geometrical isomers of the 1,2,4-trimethylcyclohexanes to be in the order of:

\[ \text{ccc} \succ \text{cct} \succ \text{ctc} \succ \text{ctt} \]
\[ (\text{eee}) \ (\text{eae}) \ (\text{eea}) \ (\text{eee}) \]

This prediction of order for the several physical constants agrees very closely with the observed values in Tables IV and VII.

B. The Diels-Alder Reaction

The stereospecificity of the Diels-Alder reaction carried out under mild conditions has been amply demonstrated in studies reported in the literature.\(^{30-33}\)

\[ \text{(30) J. A. Norton, Chem. Reviews, 238 (1942).} \]
| Configuration | cis-1,2 | trans-1,3 | cis-1,4 | trans-1,2 | cis-1,3 | trans-1,4 |
|---------------|—————|—————|—————|—————|———|—————|
| B.p. °C./760 mm | 129.84 | 124.7 | 124.34 | 123.39 | 120.7 | 119.33 |
| n^20          | 1.43591| 1.4310 | 1.42965| 1.42693| 1.4230 | 1.42080 |
| d^20          | .79637 | .78453 | .7827 | .77606 | .7660 | .76257 |


In the addition of a 1,4-disubstituted diene to a 1,2-disubstituted olefin, for example, no less than eight racemic products could conceivably be formed; the number is doubled by considering, in addition, the alternate structural orientation. Yet the usual result of the reaction is that one, or at the most, two stereoisomers are obtained. Empirical rules which govern the selection of isomers were formulated and are believed to be general.

1. The cis rule. — Cis additions of the diene component take place at the original olefinic or acetylenic linkage of the dienophile. This rule reflects the influence of the non-participating electrons on the ease of forming the complex with the highest overlap of electron density.
2. **Diene configuration rule.**—The diene always reacts in the quasicyclic (cisoid) rather than the elongated (transoid) form.

3. **Stereochemical orientation.**—The product formed will be the one that results from the maximum overlap of electron densities of the reactants in the transition state, i.e., that transition state which is best stabilized by spatial orbital overlap and simultaneously least destabilized by unfavorable steric repulsions has the lowest free energy of all possible transition states, and consequently predominates in the kinetically determined form.

However, cases have been reported in which the initial adduct was epimerized to a more stable stereoisomer by sufficiently high temperature conditions.\(^{34}\) At such temperatures, the initial adduct may even dissociate into its components and recombine again to form the thermodynamically more stable adduct at the expense of the kinetically favored one.\(^{35,36}\)

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In the present work, the Diels-Alder reaction was shown to be useful in the preparation of intermediates for the synthesis of trimethylcyclohexanes. However, the temperature dependence of the reaction imposed serious limitations to its stereospecificity.
V. DISCUSSION AND RESULTS

The stereospecific synthesis of the 1,2,3- and 1,2,4-trimethylcyclohexanes was first attempted in a manner involving the Diels-Alder rules discussed previously as a rationale.

A. Synthesis of 1,2,3-Trimethylcyclohexanes.

2,3- and 2,6-Dimethyl-4-cyclohexene-1-carboxaldehydes (X-XIII) trans-Piperylene was condensed with crotonaldehyde and expected to give a mixture of adducts, as follows:

![Chemical structure diagram]

On the basis of electronic effects and the noted steric preference for cis-1,2-compounds when piperylene is used, the predominant isomer was assumed to be X with substantially lesser amounts of the other three cyclic aldehydes. However, as will be apparent in the following, the reaction was even less stereospecific than assumed.
3,4,5-Trimethylcyclohexenes.—The mixture of the ad-
ducts was reduced via Wolff-Kishner reaction and the product
was distilled to give two virtually constant boiling
fractions. They were designated as the ctc-3,4,5-trimethyl-
cyclohexene for the low boiling fraction and the oct-3,4,5-
trimethylcyclohexene for the high boiling fraction and they
occurred in a 2:1 ratio (Figure I).

1,2,3-Trimethylcyclohexanes

In the previous work, hydrogenation of the low boiling
fraction was expected to give pure ctc-trimethylcyclohexane
I, but the product actually obtained was found to be only
55% pure due (presumably) to isomerization under the severe
conditions used. The other 45% was found to be the cct-
trimethylcyclohexane II which was free from the ccc-trimethyl-
cyclohexane III. Why the supposed isomerization did not pro-
duce about equal amounts of II and III was not explained.

The hydrogenation product of the high boiling fraction
was found to contain 2% of I while the remainder was II,
96.4% pure. Assuming the impurity in the II to be III, the
ratio occurrence becomes 2.0/94.5/3.5 for I, II, and III
respectively. Since the hydrogenation conditions were
about as severe as before, it was not clear why the degree
of isomerization was less and why, in the case, III pre-
dominated (3.5/2) over I in the part isomerized. This
ratio seems especially queer since I is considered the most stable isomer.

In the present work, numerous attempts were made to resolve these anomalies. Both low and high boiling trimethylcyclohexenes were hydrogenated over various catalysts, Raney-nickel, Harshaw-nickel and platinum-on-charcoal under various conditions, some considered too mild to provide any rearrangement. The low-boiling fraction still gave a mixture of I and II, 45:55 ratio, and the high-boiling fraction gave 95% pure II with no I present at all. It appeared that each of these fractions might contain two cyclo-olefins, i.e., that all four of the possible geometric isomers of the 3,4,5-trimethylcyclohexene, ctc, ctt, cct and ccc, might be present in the original mixture. This situation could result if the crotonaldehyde to some extent rearranged to its cis form before or after reaction with 1,trans-3-pentadiene. To check this possibility, a sample of adduct was analyzed by G.L.C. and found to contain at least 6 components in significant amount (Figure II). A total of eight isomers, structural and geometric, are possible if the crotonaldehyde moiety may be partly cis, though only four if it must be entirely trans. Since at
Fig. 1
3,4,5—Trimethylcyclohexenes.
least 6 of the 8 possible isomers are present in the adduct mixture, it is likely that the other 2 are also present though not resolved in the chromatogram. In fact, the largest peak observed, representing 51% of the adduct, must include 2 or more isomers since in the derived cycloolefin, the most abundant species comprised but 37% of the whole. The several minor components may include all the isomers having the -CHO group in the not favored 5-position.

![Chemical structures](image)

\[X, \text{ cct; XI, ctc; XIV, ctt; XV, ccc}\]

\[XII, \text{ cct; XIII, ctc; XVI, ctt; XVII, ccc}\]

It seems probable that the bulk of the product, first formed, is \((X)\) which then undergoes a partial equilibration, with the formyl group swinging from one side of the ring to the other with relative ease. Thus, about half of \((X)\) might rearrange to the \text{ctt} (XIV) form since, in either case, the steric hindrance is approximately the same. Isomerization of either form by reorientation of a methyl group must occur very slowly, if at all, else the \text{ctc} forms of the adduct (and derived trimethylcyclohexenes) would surely predominate over all others. It was found that at 250°C., the mixture of adducts \((X-XVII)\) undergoes further change; after 3 hours, its chromatogram is similar to Figure II, but different proportions of the components are indicated.
Fig. II
Gas-Liquid Chromatogram of Adduct of 1, trans-3-Pentadiene and Crotonaldehyde.
For the crotonaldehyde itself, a separate chromatogram of freshly distilled material indicated one major and one minor component (ratio, 97:3) assumed to be the *trans* and *cis* isomers, respectively. This substantially confirms the results of Young\(^38\) who oxidized crotonaldehyde and found

\[ *\text{trans}*-\text{crotonic acid as the only product.} \]

The mixture of trimethylcyclohexenes obtained by Wolff-Kishner reduction of the adduct was also analyzed by G.L.C. and four components were found (Figure III). At moderate resolution only 3 components were indicated in the proportion of 67.7/24.8/7.5. At very high resolution, the major peak was split in the approximate ratio of 45:55. Combination of these figures gives for the four, in the order of their elution, the approximate percentages:

\[ A = 31\% ; \quad B = 37\% ; \quad C = 25\% ; \quad D = 7\% \]

The mixture of cyclo-olefin was hydrogenated over platinum at room temperature and re-examined by G.L.C. (Figure IV). The product consisted of three trimethylcyclohexanes which could be identified by comparison of their retention times and infrared spectra with known samples, etc, 31.0\%, oco, 61.5\% and occ, 7.5\%. From their relative percentages it is seen that the etc cycloparaffin was
Fig. III. G. L. Chromatogram of mixtures of four 3,4,5-trimethylcyclohexenes. Lower curve: obtained with 200' of .01" capillary (with squalane); 15 psi; 80°; argon detector. Upper curve: with 200' of .01" capillary (squalane) plus 100' (polar mixture); 25 psi; 30°; argon detector. The polar mixture comprised equal parts of iso-octyl phthalate, 3,3'-oxydipropionitrile and Triton X-100.
Fig. III. GCL Analysis of 3,4,5-Trimethylcyclohexenes.
Fig. IV. G. L. Chromatogram of mixture of three 1,2,3-trimethylcyclohexanes. Column, 200' of .01" capillary (squalane); 15 psi; 50°; argon detector.
Fig. IV

GLC Analysis of a Mixture of All Three 1,2,3-Trimethylcyclohexanes.
derived from cyclo-olefin A, which must itself be a \textit{ctc} variety, and similarly for the \textit{ccc} cycloparaffin and cyclo-olefin D. Moreover, it is seen that the \textit{ctt} cycloparaffin derives from both cyclo-olefins B and C (61.5\% = 37\% + 25\%) one of which must be of the \textit{ctt} variety and the other of the \textit{ctt}.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{diagram.png}
\end{figure}

\underline{3,\textit{cis}-4,\textit{cis}-5-Trimethylcyclohexene (XXVIII)}

In order to establish more conclusively the identity of I, it was synthesized by the following sequence involving pure cyclo-olefin D, \textit{ccc} (Figure III).
This sequence was essentially the same as Bussert's for making III except that the originally present double bond was retained. The adduct of 1,trans-3-pentadiene and maleic anhydride was reduced to a diol in 70% yield. The diol was then converted to the tosylate in 90.5% yield which was then reduced by a combination of lithium aluminum hydride and lithium hydride to XXVIII. The derived cyclo-olefin was found to be 99% pure, and to have the same retention time as D (Figure III) and to boil at 149.41°/760 mm. Its boiling point explains why it was previously overlooked as a minor impurity in XIX, b.p. 148.30° (Table III).

1, cis-2, cis-3-Trimethylcyclohexane (III)

A portion of the synthesized cco isomer (XXVIII) was hydrogenated to yield a product which was 99.5% pure and had the same retention time as the major component of the best previous sample of III. The improvement in purity is reflected in the physical properties of the new sample (Table IV).

3, trans-4, cis-5-Trimethylcyclohexene (XXI) and 3, cis-4, trans-5-Trimethylcyclohexene (XIX)

Cyclo-olefin A (ctc) and C (cct) were prepared as a mixture by a similar series of reactions, commencing with the adduct of 1,trans-3-pentadiene and fumaroyl chloride which is known to condense in the trans configuration.\textsuperscript{39,40}


The adduct (XXIX) was converted through the diol and ditosylate stages to mixture (approx. 1:1) of two cyclo-olefins.
The cyclo-olefins were easily separated by distillation into pure A (ctc), b.p. 144.36° and pure (cct), b.p. 148.30°. The correspondence was shown by G.L.C. retention times and infrared spectra. The two can be identified as XIX and XXI, respectively, on the basis of their genesis, hydrogenation products and relative boiling points.

1,trans-2,cis-3-Trimethylcyclohexane (I) and 1,cis-2,trans-3-Trimethylcyclohexane (II)

Hydrogenation of these two cyclo-olefins gave cycloparaffins which were shown by G.L.C. and infrared spectra to be pure and virtually identical with previous concentrates of I and II, respectively. Their physical properties (Table IV) suggest the same conclusion.

3,trans-4,trans-5-Trimethylcyclohexene (XX)

Cyclo-olefin B also was prepared from the adduct of 1,trans-3-pentadiene and maleic anhydride undergoing the following sequence:

\[
\begin{align*}
\text{CH}_3 & \quad \text{CO} & \quad \text{R}_3\text{N} & \quad \text{CO} \\
\text{CO} & \quad \text{CH}_3 & \quad \text{CO} & \quad \text{CO} \\
\end{align*}
\]

3 steps →

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 & \quad \text{ctt} \\
\text{CO} & \quad \text{CO} & \quad \text{ctt} \\
\text{XX} & \quad & \quad \text{ctt}
\end{align*}
\]
The all cis adduct VIII was partially converted to the ctt adduct by heating it in a bomb in the presence of diethyl-aniline in a 70% conversion. The mixture of anhydrides was hydrolyzed and the two acids were separated from one another by crystallization. By processes of esterification, lithium aluminum hydride reduction, tosylation and hydrogenolysis, the pure acid was converted to a pure trimethyl-cyclohexene which must be the ctt isomer (XX) according to its genesis. Its boiling point (Table III) corresponds closely to the prediction for cyclo-olefin B (ctt) based on data from distillation of the mixture of A + B (ctc + ctt). Moreover, the G.L.C. retention time and infrared spectra of this cyclo-olefin and of the synthetic sample of A were found almost identical. On the other hand, hydrogenation of the new cyclo-olefin gave pure II whereas A had given pure III.

A practical conclusion can be drawn about the mixture of the four cyclo-olefins XVIII, XIX, XXX and XXI. They can be easily separated into two pairs, ctc + ctt and ctt + ccc. The second pair can be further separated into pure individuals by the use of high efficiency stills (100 – 200 theoretical plates). The first pair cannot be

split by any practical laboratory still, but can be hydrogenated to yield an easily separable mixture of the cis and cct 1,2,3-trimethylcyclohexanones.

**TABLE III**

**PROPERTIES OF 3,4,5-TRIMETHYLCYCLOHEXANES**

<table>
<thead>
<tr>
<th>Isomer</th>
<th>B.p., °C./760 mm.</th>
<th>n$_D^{20}$</th>
<th>Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis, trans, cis</td>
<td>144.36</td>
<td>1.4472</td>
<td>99.5</td>
</tr>
<tr>
<td>cis, trans, trans</td>
<td>144.45</td>
<td>1.4481</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>(144.47)$^a$</td>
<td>(1.4478)$^a$</td>
<td></td>
</tr>
<tr>
<td>cis, cis, trans</td>
<td>148.30</td>
<td>1.4508</td>
<td>99.5</td>
</tr>
<tr>
<td>cis, cis, cis</td>
<td>149.42</td>
<td>1.4524</td>
<td>99</td>
</tr>
</tbody>
</table>

$^a$ Estimated from properties of 70% concentrate from distillation of mixture. See Figure I.

**TABLE IV**

**PHYSICAL PROPERTIES OF 1,2,3-TRIMETHYLCYCLOHEXANES**

<table>
<thead>
<tr>
<th>Isomer</th>
<th>B.p., °C./760</th>
<th>n$_D^{20}$</th>
<th>d$_4^{20}$</th>
<th>F.p., °C.</th>
<th>t$_1$</th>
<th>α</th>
<th>Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>c,t,c</td>
<td>145.60</td>
<td>1.4333</td>
<td>0.7870</td>
<td>-66.94</td>
<td>-66.79</td>
<td>0.033</td>
<td>99.5</td>
</tr>
<tr>
<td></td>
<td>145.61$^a$</td>
<td>1.4333</td>
<td>0.7870</td>
<td>-66.86</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>c,c,t</td>
<td>151.22</td>
<td>1.4399</td>
<td>0.8025</td>
<td>-85.73</td>
<td>-85.60</td>
<td>0.033</td>
<td>99.7</td>
</tr>
<tr>
<td></td>
<td>151.21$^a$</td>
<td>1.4401</td>
<td>0.8029</td>
<td>-86.73</td>
<td>--</td>
<td>--</td>
<td>96.4</td>
</tr>
<tr>
<td>c,c,c</td>
<td>151.66</td>
<td>1.4403</td>
<td>0.8027</td>
<td>-85.0</td>
<td>--</td>
<td>--</td>
<td>99.5$^b$</td>
</tr>
<tr>
<td></td>
<td>151.43$^a$</td>
<td>1.4403</td>
<td>0.8021 (glass)</td>
<td>--</td>
<td>--</td>
<td>95$^c$</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Values in second line in each case are from literature (reference $b$). $^b$ Estimated from G.L.C. $^c$ Estimated value in reference 3, now corrected to 88% by G.L.C. analysis.
B. Synthesis of 1,2,4-Trimethylcyclohexanes

2,4- and 2,5-Dimethyl-4-cyclohexene-1-carboxaldehydes (XXII)

Isoprene and crotonaldehyde were condensed together to give a mixture of adducts. Since G.L.C. analysis of the product revealed only two components comprising 80% and 14% in order of elution, it was concluded that the major component included the two possible trans forms and the minor the two cis forms.

\[ \text{cis+trans} \quad \text{XXII} \]

Adducts XXII were reduced as a mixture to a mixture of cyclo-olefins and analysis revealed only two very close boiling components which were impossible to separate by distillation. The cyclo-olefinic mixture was hydrogenated at room temperature over platinum catalyst and analysis showed the presence of all four possible cycloparaffinic isomers (Figure V), labelled both cryptically, IV, V, VI and VII, and specifically (by hindsight). The G.L.C. analysis indicated that IV and V would be isolable by
Fig. V
GLC Analysis of a Mixture of All Four 1,2,4-Trimethylcyclohexanes.
fractional distillation but that VI and VII would not, for it appeared that they would boil only 0.60° apart. Distillation afforded IV and V in the pure state and VI and VII as a mixture.

**TABLE V**

<table>
<thead>
<tr>
<th>1,2,4-TRIMETHYLCYCLOHEXANES FROM DISTILLATION OF MIXTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.p./760 mm.</td>
</tr>
<tr>
<td>F.p.</td>
</tr>
<tr>
<td>nD20</td>
</tr>
<tr>
<td>d420</td>
</tr>
</tbody>
</table>

Only component IV could be readily identified, its relatively low boiling point fixing it as the ctt isomer. This hydrocarbon has been found to be a component of petroleum and later was recognized as such. In fact, this compound has become available as standard samples for
calibration of analytical equipment.

Syntheses described previously were suitable for the preparation of token amounts of the 1,2,3-trimethylcyclohexanes and for their identification. Others proved to be practical syntheses for large amounts of the ctc and cct 1,2,3-trimethylcyclohexanes and ctt and cto 1,2,4-trimethylcyclohexanes but contributed nothing toward proof of the configuration of any of these paraffins. The 1,2,4-trimethylcyclohexanes remained unidentified except for the ctt isomer which was distinguished by its physical properties.

In the study of the 1,2,4-trimethylcyclohexanes, an attempt was made to isolate the 1,4,5-trimethylcyclohexanes, at a stage in which the geometric complexity is reduced. However, separation of the cyclo-olefinic isomers failed due to their close boiling points (page 37). Had these been separable, hydrogenation of the two individually would have yielded pairs of cycloparaffins which might have been separable. Thus, all four of the isomers would have been obtained.

Three other cyclo-olefinic isomers are possible in
which the geometric complexity is similarly reduced, as follows:

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

However, no attempt was made to synthesize them, because good syntheses were not available and because it was felt that in these cases also, the olefinic mixtures would be close boiling and inseparable.

A new approach to the problem was devised and outlined in Figure VI, in which an exomethylene group is present on the cyclohexane ring in place of one methyl. One of the three intended methyl groups is removed from the geometric pattern, forming a compound with only two geometric isomers. If these two are separable, their hydrogenation will result in pairs of trimethylcyclohexanes each of which may be separable. Furthermore, the makeup of these pairs could help identify the individuals as only certain olefins would give certain paraffins or combinations of paraffins.

C. *Synthesis of 1,2,4-Trimethylcyclohexanes*

The mixture of the cyclic aldehydes XXII was hydrogenated to the corresponding saturated alcohols in 95-98% yield.
Figure VI.
Synthesis of 1,2,4 - Trimethylcyclohexanes

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\begin{align*}
&\text{CH}_3\text{CHO} \\
&\text{CH}_3\text{CHO} \\
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\end{align*}
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2 Steps

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\end{align*}
\]
The cyclic alcohols XXIII were acetylated with acetic anhydride to give the corresponding mixture of acetates in 93% yield. The acetates were purified and pyrolyzed to a mixture of dimethylmethylene cyclohexanes in 70-80% yield. Chromatography revealed the presence of four components A, B, C and D, Figure VII. Distillation of the olefinic mixture separated A and B as a close boiling mixture and C and D as pure compounds. Properties are given in Table VI.

**TABLE VI**

**DIMETHYLMETHYLENECYCLOHEXANES RELATED TO THE 1,2,4-TRIMETHYLCYCLOHEXANES**

<table>
<thead>
<tr>
<th></th>
<th>A+B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative amount</td>
<td>53</td>
<td>14</td>
<td>33</td>
</tr>
<tr>
<td>B.p./760 mm.</td>
<td>141.91</td>
<td>144.46</td>
<td>135.96</td>
</tr>
<tr>
<td>nD²⁰</td>
<td>1.4497</td>
<td>1.4485</td>
<td>1.4497</td>
</tr>
<tr>
<td>Purity %</td>
<td>--</td>
<td>98</td>
<td>99</td>
</tr>
</tbody>
</table>

1. **Hydrogenation of cyclo-olefins A+B (XXV+XXVI)**

Hydrogenation of A+B under mild conditions gave a mixture of cycloparaffins V, VI and VII in a 45:25:30
Fig. VII
GCL Analysis of Dimethylmethylenecyclohexanes Related to 1,2,4-
Trimethylcyclohexanes.
ratio showing the A+B must be a mixture of cis-2,4-dimethylmethylene-cyclohexane XXV and trans-2,5-dimethylmethylene-cyclohexane XXVI.

```
CH₃       CH₃
CH₂CH₃ + CH₃CH₃ H₂/Pt → ctc+cct+ccc
XXV      XXVI

V       VI VII
```

The ctc isomer V was separated by distillation while the cct and ccc isomers, VI and VII remained as a mixture.

2. Hydrogenation of Cyclo-olefins C (XXVII) and D (XXVIII)

Hydrogenation of cyclo-olefin C, cis-2,4-dimethylmethylene-cyclohexane, gave two cycloparaffins in a 28:72 ratio corresponding to components IV and VII that were separated and characterized; physical properties in Table VI.

Cyclo-olefin D, trans-2,5-dimethylmethylene-cyclohexane, on hydrogenation also gave two cycloparaffins in a 30:70 ratio corresponding to components IV and VI that were separated and characterized (Table VI).

This provided the final proof that V is the ctc isomer, since it is the only one which, according to the scheme on page 40, cannot be paired with IV (the ctt isomer).
Thus, it was also proved that the remaining two, VI and VII, were the \textit{cct} and \textit{ccc} isomers but not which was which.

\textbf{Structure proof of C (XXVII) and D (XXVIII)}

\textbf{Oxidation}.--To differentiate between VI and VII, the pure olefins, C (XXVII) and D (XXVIII) were individually oxidized by aqueous permanganate solution to the corresponding dimethylcyclohexanones. Thus, C yielded \textit{cis}-2,4-dimethylcyclohexanone XXIX and D yielded \textit{trans}-2,5-dimethylcyclohexanone XXX which are well known compounds\(^{43}\) easily characterized by their semicarbazones.

\textbf{Reduction of XXIX and XXX}

A great number of authors have used the Wolff-Kishner method of reduction, yet no reference is made in the literature as to its stereochemical aspect, i.e., whether there is maintenance or loss of steric configuration on going from the ketone to the hydrocarbon.

The Clemmensen reduction\(^{44}\) can also be used to reduce


\(^{44}\) E. L. Martin, Org. Reactions I, 155.
ketones by means of zinc amalgam and hydrochloric acid but no mention of its stereospecificity is found in the literature. A proposed mechanism\(^{45}\) is based on the dehydration of the alcohol first formed followed by hydrogenation. The experimental facts found here tend to corroborate this and thus making this mode of reduction non stereospecific except perhaps for compounds that do not have a group \(a\) to the carbonyl.

XXIX and XXX were reduced to the dimethylcyclohexanes by both methods. By the Wolff-Kishner method XXIX gave \textit{cis}-1,3-dimethylcyclohexane and XXX gave \textit{trans}-1,4-dimethylcyclohexane in better than 98\% purity. Clemmensen reduction of XXIX and XXX gave, in both cases, a mixture of geometric isomers along with olefin, presumably obtained from the alcohol which is first formed.

\begin{center}
\begin{tikzpicture}

\node (XXVII) at (0,0) {XXVII};
\node (XXIX) at (2,0) {XXIX};
\node (cis) at (4,0) {\textit{cis}};

\draw[->] (XXVII) -- (XXIX) node[midway,above] {[O]};
\draw[->] (XXIX) -- (cis) node[midway,above] {W.K.};

\end{tikzpicture}
\end{center}

\(^{(45)\text{ D. M. Cowan, G. H. Jeffery, and A. I. Vögel, J. Chem. Soc., 1862 (1939).}}\)
This fixed the identity of the olefins, C being the cis-1,3-dimethylmethylene cyclohexane and D being the trans-1,4-dimethylmethylene cyclohexane. Therefore their hydrogenated products must be the ctt and ccc isomers from C, and ctt and cct isomers from D.

| TABLE VII |
| 1,2,4-TRIMETHYLCYCLOHEXANES |
| (VI)ctt | (V)ctc | (VI)cct | (VII)ccc |
| B.p./760 mm. | 141.29 | 144.56 | 146.65 | 146.57 |
| n_d^0 | 1.4274 | 1.4344 | 1.4345 | 1.4340 |
| d_4^0 | 0.7743 | 0.7908 | 0.7908 | 0.7916 |
| F.p.(m.p.), °C | -85.17 | -85.53 | -91.86 | -78.31 |
| F.p., 100% | -84.89 | -- | -- | -77.45 |
| A | 0.0392 | -- | -- | 0.048 |
| Purity mole % | 98.9 | 98+ | 99+ | 95.9 |
Figure VIII
Synthesis of 1,2,3-Trimethylcyclohexanes.
D. Synthesis of 1,2,3-Trimethylocyclohexanes

For the preparation of the 1,2,3-trimethylocyclohexanes a similar scheme was followed, as outlined in Figure VIII.

The Diels-Alder adduct (X-XVII) can take any of eight forms, as shown in Figure II. The mixture obtained was hydrogenated to a presumed total of 7 saturated cyclic alcohols which were converted to their corresponding acetates. The acetate mixture was pyrolyzed by the same procedure as before. Analysis of the mixture readily revealed 3 components as shown in Figure IX. Higher resolution showed the middle peak to actually consist of 2 components. The four were arbitrarily designated A, B, C and D. Distillation of the olefinic mixture yielded 3 fractions; A, B+C and D having properties shown in Table VIII.

TABLE VIII
DIMETHYL METHYLENE CYCLOHEXANES RELATED TO THE 1,2,3-TRIMETHYLCYCLOHEXANES

<table>
<thead>
<tr>
<th>Relative amount %</th>
<th>A</th>
<th>B+C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>9</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>B.p./760 mm.</td>
<td>145.64</td>
<td>147.78</td>
<td>152.7°C</td>
</tr>
<tr>
<td>nD²⁰</td>
<td>1.4552</td>
<td>1.4562</td>
<td>1.4560</td>
</tr>
<tr>
<td>Purity %</td>
<td>99</td>
<td>98</td>
<td>99</td>
</tr>
</tbody>
</table>
Fig. IX

GLC Analysis of Dimethylmethylenecyclohexanes Related to 1,2,3-Trimethylcyclohexane.
E. Synthesis of 1,3,5-Trimethylcyclohexanes

In order to apply this method to the 1,3,5-trimethylcyclohexanes, the cis and trans-dimethylmethylenecyclohexanes were prepared by the following scheme.

\[
\frac{\text{cis}}{\text{trans}} \quad \text{dimethylmethylenecyclohexane} \quad \text{on hydrogenation} \quad \text{should afford two paraffins, the ccc and the cct-1,3,5-trimethylcyclohexanes and the trans-dimethylmethylenecyclohexane should afford only one isomer, the cct-1,3,5-trimethylcyclohexane thereby proving the identity of the paraffins according to their genesis.}
\]

\text{cis and trans-3,5-dimethylcyclohexanones}

Purified 3,5-xylenol hydrogenated to a mixture of cyclohexanols was fractionally distilled and all the

\[\text{ cis alcohol was separated out and recrystallized several times. Following, in Table IX, are the constants for the alcohols as listed by Skita and Faust who worked out the configuration from chemical and dipole moment studies.}\]
1. Hydrogenation of Cyclo-olefin A (trans-2,6-Dimethylmethylene cyclohexane).

Hydrogenation of A under mild conditions afforded only one cycloparaffin, which thereby identified itself as the cct isomer (II) according to the reaction scheme outlined in Figure VIII. Moreover, its properties checked closely with those previously given for this cycloparaffin.

2. Hydrogenation of Cyclo-olefin D (cis-2,6-Dimethylmethylene cyclohexane)

Hydrogenation of D gave a 25:75 mixture of two easily separable cycloparaffins neither of which was identical with the one derived from A. On this basis, one could identify the lower boiling of these two as the ctc isomer and the remaining one, by elimination, as the ccc isomer. Moreover, when separated by distillation and compared with previous samples they proved identical with I and III.

3. Hydrogenation of Cyclo-olefin B+C (cis and trans-2,3-Dimethylmethylene cyclohexanes)

Hydrogenation of B+C gave a mixture of all three of the cycloparaffins; proving itself to include both B and C cyclo-olefins.
Attempts to obtain a pure sample of the \textit{cyclo}-3,5-dimethylcyclohexanol free from the \textit{cyclo} isomer failed, and only a 65\% concentrate of it could be obtained.

Oxidation\textsuperscript{48} of the all \textit{cis} alcohol gave a 99\% pure \textit{cis}-3,5-dimethylcyclohexanone in 90\% yield and oxidation of the \textit{cyclo}-concentrate gave 35:65 \textit{cis-trans} mixture of 3,5-dimethylcyclohexanones.

\textbf{cis and trans-3,5-Dimethylmethylene cyclohexanes}

Both ketones were subjected to the Wittig reaction with triphenylphosphinemethylene hydrobromide and sodium amide in glyme to produce the corresponding dimethylmethylene cyclohexanes in about 70\% yield.
The cis-dimethylmethylenecyclohexane gave on hydrogenation two cycloparaffins, cis and trans-1,3,5-trimethylcyclohexane in a 65:35 ratio which were characterized by G.L.C. and compared with authentic samples.

The trans-concentrate gave on hydrogenation a predominance of cis-1,3,5-trimethylcyclohexane with a small amount of cis which can be accounted for by the presence of the cis-ketone in the original starting material.
A. Determination of Physical Constants

1. Cryoscopic constants

The hydrocarbons which showed a definite freezing point were assigned calculated purities on the basis of their respective freezing and melting point curves. The apparatus used in these determinations was essentially that developed at the National Bureau of Standards.\(^{49}\) Temperatures were measured by a platinum resistance thermometer (calibrated by the National Bureau of Standards) reading through a Mueller resistance bridge (Leeds and Northrup, Type G-2). With this apparatus temperature differences of less than 0.01°C. can be accurately measured.

The purities of the compounds for which no cryoscopic constants are available were determined by essentially the same method as that described by Mair, Glasgow and Rossini,\(^{50}\) in which the theoretical freezing point of


100% pure material \(T_{fo}\) was determined from the melting point \(T_f\) or the freezing point \(T_f\) of the substance and the midpoint temperature \(T_{\Delta/2}\) on a time-temperature freezing curve. One assumes that at the midpoint, exactly one-half of the liquid phase is crystallized and that the midpoint temperature \(T_{\Delta/2}\) represents the melting point of the liquid phase when it contains exactly twice the impurity that it does at the actual melting or freezing point. This assumption is reasonably valid if the solution is sufficiently dilute, if the impurities form an ideal solution with the solvent and if the impurities are insoluble in the solid phase. The true freezing point \(T_{fo}\) can then be calculated by adding the temperature differences between the freezing point and the midpoint \(T_{\Delta/2}\) to the freezing point \(T_f\). This can be expressed by the following equation,

\[
T_{fo} = T_f + (T_f - T_{\Delta/2})
\]

A value for the cryoscopic constant \(K_f\) in terms of degrees lowering per mole percent impurity is then determined experimentally by adding to a known weight of the material being investigated, having a known melting point \(T_f\), a weighed amount of a suitable impurity and measuring the melting point \(T_{fm}\) of the mixture. Another useful form of the cryoscopic constant is represented by \(\gamma\), in terms of mole fraction per degree of freezing point lowering.
Both may be expressed as follows:

\[ K_f = \frac{T_f - T_{fm}}{\text{mole \% impurity}} \quad A = \frac{1}{K_f \times 100} \]

Then, the purity (P) of the compound under investigation can be calculated from the following equation

\[ \log_{10} P = 2.00000 - \left(\frac{A}{2.30259}\right)(T_{fo} - T_f) \]

2. Gas-Liquid Chromatography (G.L.C.)

The G.L.C. studies were all done on a Barber-Colman IDS Model 20 gas chromatograph with capillary columns. As used with an argon ionization detector, this system was found to give results not strictly linear with concentration. Thus, the indicated percentage of minor component of a mixture may be as high as 1-1.5%. However, similar chromatograms should be comparable.

3. Cottrell Boiling Points

The boiling points reported in this dissertation as "Cottrell b.p.'s" were those determined in a modified Cottrell ebulliometer, described by Quiggle, Tonberg and Fenske,\(^{(51)}\) which was attached to an electronically con-


...trolled manostat that maintained a constant pressure of
760 mm. in the ebulliometer. The actual temperatures were measured with the same platinum resistance thermometer and Mueller bridge used for the cryoscopic determinations, and are accurate to about ±0.01°C.

4. Refractive Indices

Refractive indices were determined with a Valentine Precision Refractometer, manufactured by the Industro-Scientific Company, connected to an electronically controlled constant temperature bath. The refractive indices are accurate to about ±0.0001.

5. Densities

The densities were determined using a 20 ml. pycnometer which was accurately calibrated using pure benzene and certified isooctane. The water bath used for these measurements was electronically controlled to maintain the temperature at 20.00±0.02°C. The densities obtained are believed accurate to ±0.0001 g./ml.

6. Infrared Spectra

All of the infrared absorption spectrograms reported herein were determined by means of a Perkin Elmer Model 21 double beam spectrometer.
B. Synthesis of 1,2,3-Trimethylcyclohexanes - Method I

2,3- and 2,6-Dimethyl-4-cyclohexene-1-carboxaldehydes X-XIII

In a typical run, 350 g. (5 moles) of freshly distilled crotonaldehyde, 400 g. (5.88 moles) of commercial piperylene52 and 1 g. of hydroquinone were charged to a three liter steel bomb, sealed under 500 p.s.i. nitrogen pressure and heated to 200-225°C. In this temperature range, an exothermal reaction commenced, causing a quick rise to 250-275°C. As soon as this maximum was passed, the autoclave was chilled by a stream of cold water, pressure was released and the product was removed. Unreacted 1,3-pentadienes and crotonaldehyde were stripped off and the residue was fractionally distilled at about a 10-plate efficiency under reduced pressure. The cyclic aldehyde (b.p. 90-93°/30 mm, n°D 1.4675-1.4700) was obtained in 66% average yield, based on 1, trans-3-pentadiene, as well as pentadiene dimers (b.p. 75-80°/30 mm.) and higher polymers in yields of 25% and 8% respectively, based on total pentadienes used.

(52) Obtained from the Enjay Co., Inc. as a 66% trans concentrate.
G.L.C. analysis of the adduct, Figure II, on an 100' of .01" (i.d.) capillary column with squalane; press., 20 p.s.i., temp., 80°, revealed 6 components.

3,4,5-Trimethylcyclohexanones

The reaction was carried out in a 5-liter, 3-neck flask equipped with an electric heating mantle, stirrer, dropping funnel and (initially) with a thermometer and reflux condenser. The stirrer was of the Hershberg type,53


mercury sealed, and driven by a powerful variable-speed motor. The reflux condenser was attached to the flask through a 35/25 spherical joint and could be replaced in a few seconds by a wide-bore (i.d. 25 mm.) delivery tube of inverted U shape leading to a condensing system. This system comprised of a 2-necked, 5-liter flask bathed by cold water, a multibulb reflux condenser mounted over the flask, and a Dry Ice-cooled trap connected at the top of the condenser. A bubbler was provided at the outlet of the trap to indicate when nitrogen was being evolved.

The vessel was charged with diethylene glycol (100 ml.), dihydrazine sulfate (5.0 moles) and commercial flake sodium hydroxide (10.0 moles). This mixture was heated and stirred until homogeneous; at 95-110°, the
cyclic aldehyde 690 g. (5.0 moles) was added rapidly and the mixture was stirred under reflux for 2-3 hours. Then, additional sodium hydroxide (8.0 moles) and 10 ml. of n-octanol (anti-foam) were added, the condensing system was attached and the product was distilled from the reactor with vigorous stirring. Most of the product condensed in the received flask, along with about a half volume of water, but some was swept into the trap by the escaping nitrogen. During the period of most vigorous evolution, foaming occurred, some solids were deposited in the delivery tube which did not plug however due to its wide bore. In 2-3 hours, distillation had nearly stopped and temperature of the reaction mixture reached 190°. At this point, 200 ml. of water were added slowly and the formed steam flushed the last part of the product into the receiver.

The organic product from the receiver and trap were combined, washed three times with 5% sulfuric acid and dried by quick percolation through a 40-200 mesh activated silica gel. The average yield of crude cyclo-olefin was 3.9 moles. Preliminary fractionation at about 15-plates efficiency returned 3.0 moles of trimethylcyclohexenes (b.p. 144-148°) or 72% yield from the cyclic aldehyde. This mixture was analyzed by G.L.C. (Figure III). Lower curve: obtained with 200' of .01" capillary with squalene; 15 p.s.i., 80°C. Upper curve: with 200' of .01" capillary
(squalane) plus 100' (polar mixture), 25 p.s.i., 30°. The polar mixture comprised of equal parts of isocetyl phthalate, 3,3'-oxydipropionitrile and Triton X-100. A 7 kilo lot of the mixture was further fractionated at over 100-plate efficiency and two flats were defined: b.p. 144.30-144.44°, 63%; b.p. 148.20-149.30°, 37%. The final fraction of the low flat was found to be enriched to about 70% of the ctt cyclo-olefin.

1,2,3-Trimethylcyclohexanes

Low-flat cyclo-olefin material, 62 g. (0.5 mole) was mixed with ethanol (80 ml.) and 5% platinum-on-charcoal catalyst (2.0 g.) and was hydrogenated to saturation in a Burgess-Parr apparatus at 50 p.s.i.g. The product was washed free of ethanol and percolated through a 1 x 10 cm. tube of silica gel. The yield was 62 g. (.49 mole) of product which was analyzed by capillary G.L.C. (200 ft. of squalane at 50°C., with 15. p.s.i.g. argon pressure). It was found to consist of 1,trans-2,cis-3- and 1,cis-2, trans-3-trimethylcyclohexane, 45 and 55% respectively.

High-flat cyclo-olefin was similarly hydrogenated and the product similarly analyzed indicating, 1,cis-2,trans-3-trimethylcyclohexane, 80%; 1,cis-2,cis-3-trimethylcyclohexane, 20%.

A portion of the original mixture of trimethylcyclohexanes was hydrogenated. Presence of all three
1,2,3-trimethylcyclohexanes was indicated: \textit{etc}, 31.0\%, \textit{cct}, 61.5\%, \textit{acc}, 7.5\% (Figure IV). Identity of these components with known samples was shown by additional chromatograms with small amounts of the knowns added.

**Hydrogenation experiments on "low flat" 3,4,5-trimethylcyclohexene**

"Low flat" olefin, 20 ml., in 100 ml. of absolute ethanol was hydrogenated under various conditions. After hydrogenation, the products were filtered, washed with water and dried by passing through a column of silica gel.

<table>
<thead>
<tr>
<th>Run</th>
<th>Catalyst</th>
<th>Temp. °C</th>
<th>Pressure p.s.i.g.</th>
<th>Solvent</th>
<th>Time/Hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Raney-nickel</td>
<td>100</td>
<td>1000</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>B</td>
<td>Raney-nickel</td>
<td>100</td>
<td>1650</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>Raney-nickel</td>
<td>150</td>
<td>1000</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>Raney-nickel</td>
<td>27</td>
<td>40</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>E</td>
<td>Raney-nickel</td>
<td>30</td>
<td>1200</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>F</td>
<td>Harshaw-nickel</td>
<td>50</td>
<td>1000</td>
<td>EtOH</td>
<td>2</td>
</tr>
<tr>
<td>G</td>
<td>Platinum/charcoal</td>
<td>50</td>
<td>50</td>
<td>EtOH</td>
<td>2</td>
</tr>
</tbody>
</table>

All the different runs gave very comparable results in the ratio of \textit{etc}/\textit{cct} isomers produced. Determinations of their relative amount was made on the basis of boiling points, refractive indices and G.L.C.
Run G.L.C. Refractive Cottrell
          Index b.p.
A    45/55    44/56    48.2/51.8
B    45.2/54.8 45.3/54.7  44.8/55.2
C    45.1/54.9 44.9/55.1  45.2/54.8
D    44.1/55.8 42.6/57.4  44.6/55.3
E    45.4/54.6 44.7/55.3  48.1/51.9
F    46.5/53.5 47.0/53.0  46.4/53.6
G    45.3/54.7 45.1/54.9  45.4/54.6

Sample calculations used in all experiments.

Gas-Liquid Chromatography

Area under curve = width at half height x height

Curve A = 123 x 36 = 4428
Curve B = 143 x 38 = 5434
A + B = 100% = 9862
% A = \frac{4428}{9862} x 100 = 45%
% B = \frac{5434}{9862} x 100 = 55%

Refractive index

using \( n^D_0 \) 1.4399 for oct = 1,2,3-trimethylcyclohexane

\( n^D_0 \) 1.4333 for ctc = 1,2,3-trimethylcyclohexane

Reaction product \( n^D_0 \) = 1.4370

cct = 1.4399            reaction product = 1.4370
ctc = 1.4333

cct-ctc = .0066              Index due to cct .0037
\[
\frac{37}{66} \times 100 = 56.0\% \text{ cct present}
\]

\[
\text{cct} = 1.4399
\]

reaction product = \( \frac{1.4370}{1.4399} \)

Index due to cct present = .0029

\[
\frac{29}{66} \times 100 = 44.0\% \text{ ctc present}
\]

Cottrell b.p.

Using 151.2°C for cct-1,2,3-trimethylcyclohexane

and 145.6°C for ctc-1,2,3-trimethylcyclohexane

Reaction product b.p. = 148.5°C.

\[
\begin{align*}
\text{cct} &= 151.2°C. \\
\text{ctc} &= 145.6°C. \\
\text{reaction} &= 148.5°C. \\
\text{cct-ctc} &= 5.6 \\
\text{b.p. due to ctc present} &= 2.7
\end{align*}
\]

\[
\frac{2.7}{5.6} \times 100 \times 48.2\% \text{ ctc present}
\]

Reaction product = 148.5

\[
\text{ctc} = 145.6°C
\]

b.p. due to cct present = 2.9

\[
\frac{2.9}{5.6} \times 100 = 51.8\% \text{ cct present}
\]

\( \text{cis-3-Methyl-4-cyclohexene-cis-1,cis-} \)

2-dicarboxylic anhydride

This adduct was prepared from piperylene and maleic

anhydride as previously described. The yield of the crude
adduct was 97%; m.p. 61-63°C. One recrystallization from ether raised the m.p. to 63-64°C.

cis-3-Methyl-4-cyclohexene-cis-1,cis-2-dimethanol

Lithium aluminum hydride 95.0 g. (2.5 moles) was suspended in 2 liters of sodium-dried ether contained in a 5-liter, 3-necked flask equipped with a motor driven Hershberg stirred, dropping funnel, electric heating mantle and an efficient aluminum coil reflux condenser connected to an overflow trap and a nitrogen reservoir. To this solution was added the cyclic anhydride 332 g. (2.0 moles) dissolved in dry ether, 700 ml. at such a rate as to maintain a steady spontaneous reflux. The reaction mixture was stirred under reflux for 12 hours longer, then hydrolyzed with cold water and 10% hydrochloric acid. The ether-product layer was separated, combined with 3 ether extracts (250 ml. each) of the aqueous layer, and washed with cold water followed by 5% sodium bicarbonate before drying by percolation through a column of magnesium sulfate and magnesium carbonate (7:1). The ether solution was concentrated to 500 ml. and the diol was crystallized out by cooling in a Dry Ice-isopropanol bath. The crude
dial was recrystallized from ether as a white solid, yield 218 g. or 70%; m.p. 51.5-52°C.

**Anal.** Calcd. for C₉H₁₆O₂: C, 69.19; H, 10.25.

Found: C, 68.90; H, 10.04

**cis-3-Methyl-4-cyclohexene-cis-1,cis-2-dimethanol-di-p-toluenesulfonate**

The pure diol, 312 g. (2.0 moles) and pyridine, 949 g. (12.0 moles), freshly distilled from barium oxide, were placed in a 3-liter, 3-necked flask equipped with a motor-driven Hershberg stirrer and a low temperature thermometer. The solution was cooled to -15°C. by a Dry Ice-isopropanol bath and a 10% excess of finely powdered p-toluenesulfonyl chloride, 838 g. (4.4 moles) was added portionwise at such a rate that the observed temperature never exceeded -5°C. After the addition (requiring 1.5-2 hours), the pasty reaction mixture was stirred for 2 hours longer, then stored overnight in a refrigerator. It was then poured into 2.5 liters of cracked ice and hydrochloric acid, whereupon the ditosylate separated out as a viscous oil. The oily product was combined with 3 ether extracts of the water layer and the whole was washed with water and sodium bicarbonate solution, then dried by percolation through a column of magnesium sulfate. The solution was evaporated to about 300 ml. whereupon the ditosylate precipitated
as a white solid. It was filtered on a Buchner funnel, washed several times with cold water, air dried, recrystallized from methanol and vacuum desiccated. There was obtained 840 g. (90.5%) of the ditosylate, m.p. cl-62 °C. An analytical sample recrystallized from methanol, melted at 62.5-63.0 °C.

Anal. Calcd. for C_{23}H_{28}O_{6}S: C, 59.47; H, 6.08; S, 13.80. Found: C, 59.15; H, 6.06; S, 13.84.

3,cis-4,cis-5-Trimethylcyclohexene (XXVIII)

Lithium aluminum hydride 8.0 g. (0.2 mole) and 100 mesh lithium hydride, 24 g. (3.0 moles) were placed under nitrogen in a 3-necked, 5-liter flask equipped with a mechanical stirrer, reflux condenser and a dropping funnel. Sodium-dried tetrahydrofuran (3.5 liters) was added and the mixture was refluxed for an hour. Then, the ditosylate, 96 g. (1.5 moles) dissolved in tetrahydrofuran (500 ml.) was added slowly through the funnel and the mixture was refluxed for 10 hours after completion of the addition. The tetrahydrofuran was stripped from the reaction mixture under reduced pressure and condensed in Dry Ice-cooled traps. The stripped solvent was replaced with 1.5 liters of ether and the excess hydrides and inorganic residues were decomposed with cold water and 10% hydrochloric acid. The ether-hydrocarbon layer was separated, combined with
three (300 ml.) ether extracts of the aqueous layer, washed with 5% sodium bicarbonate solution and dried over magnesium sulfate. The ether was stripped off and the product was distilled on a Nester and Faust spinning band fractionating column operating at about 20-plates efficiency. The yield of trimethylcyclohexene was 86.8 g. (0.69 mole) or 46% from ditosylate; b.p. 149.41-42°, n_D^20 1.4524. G.L.C. analysis indicates a 99+ purity.

**Analytical Data:**
- **Calc:** C, 87.03; H, 12.97
- **Found:** C, 87.06; H, 13.15

1,cis-2,cis-3-Trimethylcyclohexane (III)

The cyclo-olefin, 62.0 g. (0.5 mole), absolute ethanol (50 ml.) and platinum oxide (0.2 g.) were mixed in a magnesia bottle which was connected to a Parr hydrogenation apparatus. At 50 p.s.i.g. absorption was rapid at first, then slowed to a halt at 97% of the theoretical uptake. Some rise in temperature was evident. The product, after filtration, washing with water to remove the ethanol and percolation through activated silica gel, was found to be saturated by bromine test. It was fractionated on the spinning band column, and the constant boiling distillate (b.p. 151.83-84°/760) amounted to 52 g. or 83% yield from the cyclo-olefin. G.L.C. analysis indicated this to be a single compound, 99.5% pure or better.
Anal. Calcd. for C_{19}H_{18}O; 85.63; H, 14.37.
Found: C, 85.56; H, 14.41.

Dimethyl cis-3-methyl-4-cyclohexene-trans-1,trans-2-dicarboxylate

The all-cis adduct of 1,trans-3-pentadiene and maleic anhydride, 332 g. (2.0 moles) was heated with 10 ml. of diethylamiline in a glass-lined bomb for 4 hours at 175° to rearrange it to cis-3-methyl-4-cyclohexene-trans-1,trans-2-dicarboxylic anhydride. Vacuum distillation of the reaction mixture gave 289 g. of product (b.p. 125-139°/4 mm.) which was shown by G.L.C. to contain 70% of the desired isomer.

The anhydride mixture was boiled with 350 ml. of water for 25 minutes and chilled to 0°C. The crystalline product was filtered, washed with water and recrystallized four times from water, yielding 212 g. (1.1 moles) of diacid, m.p. 160-162, (literature 39) m.p. 162°.

The diacid was esterified by refluxing for 3 hours with methanol (20 moles) containing 3% of dissolved hydrogen chloride. The solution was cooled, diluted with ether (250 ml.) washed with water and dilute sodium bicarbonate solution and dried over anhydrous magnesium sulfate. On distillation 200 g. (92%) of the dimethyl ester, b.p. 132-138°/4 mm. was obtained.
Dimethyl-trans-3-methyl-4-cyclohexene-
trans,1,trans-2-ditosylate

The diester 200 g. (0.94 mole) was reduced by lithium aluminum hydride to the diol which (as crude) was converted to the ditosylate, by procedures described before. The ditosylate water-washed and air-dried, m.p. 91-93°C., was obtained in 98% yield.

Anal. Calcd. for C_{23}H_{28}O_6S_2: C, 59.47; H, 6.08; S, 13.80.
Found: C, 59.57; H, 6.15; S, 13.91

3,trans-4,trans-5-Trimethylcyclohexene (XX)

Hydrogenolysis of the ditosylate 35 g. (0.92 mole) was effected by treatment with lithium hydride and lithium aluminum hydride to obtain the corresponding cyclo-olefin. The product, as a solution in tetrahydrofuran, was filtered from the formed lithium tosylate and distilled. Unfortunately, some lithium compounds remained dissolved and decomposed violently near the end of the distillation. This caused some loss of material, but 39 g. of crude product (b.p. 140-145°) was obtained. By redistilling it at about 20-plate efficiency, 25 g. (20% yield) of nearly constant boiling material was obtained, b.p. 144.44-144.45°, n_H^2 1.4481, d_4^20 0.9129. Infrared spectra, Plate I.

Anal. Calcd. for C_{9}H_{16}: C, 87.03; H, 12.97
Found: C, 86.92; H, 13.07
1, cis-2, trans-3-Trimethylcyclohexane (II)

A small amount of the **cis** cyclo-olefin, 5 g., was hydrogenated to saturation (as before) and examined by G.L.C. This revealed it as a single compound, 99% pure or better, with the same retention time as previous samples of **cis** cycloparaffins, II. Infrared spectra, Plate II.

**cis-3-Methyl-4-cyclohexene-cis-1,trans-2-dicarboxyl chloride and cis-3-Methyl-4-cyclohexene-trans-1,cis-2-dicarboxyl chloride (XXIX)**

In a 3-liter, 3-necked flask fitted with a stirrer, reflux condenser and dropping funnel was placed 136 g. (2.0 moles) of pentadiene mixture estimated to contain 1.2 moles of **1,trans-3-pentadiene**. Fumaryl chloride, 153 g. (1.0 mole) was then added dropwise at such a rate so as to maintain a gentle reflux (~2 hrs.). The reaction mixture was stirred another hour, then fractionally distilled at about 3-plate efficiency. The product, b.p. 89-93°/3 mm. nD^20 1.5039 was a liquid; yield 100.5 g. (90%).

**Anal.** Calcd. for C_{9}H_{10}O_{2}Cl_{2}: C, 49.00; H, 4.54; Cl, 31.81. Found: C, 49.33; H, 4.68; Cl, 31.80.

**cis-3-Methyl-4-cyclohexene-cis-1,trans-2-dicarbinol and cis-3-Methyl-4-cyclohexene-trans-1,cis-2-dicarbinol**

To a 5-liter, 3-necked flask fitted with a stirrer, reflux condenser and separatory funnel were added lithium
aluminum hydride 65 g. (1.7 moles) and 2 liters of dry ether. After these were stirred at reflux for 3 hours, the dicarboxylic chloride, 330 g. (1.5 moles) in 600 ml. of ether, was added slowly. The reaction mixture was refluxed for 12 hours longer, then hydrolyzed with 15% sulfuric acid. The ether and product layer was separated, combined with three ether extracts (250 ml. each) of the aqueous layer, washed with water followed by 5% sodium bicarbonate solution and dried over magnesium sulfate. The ether solution was evaporated to a volume of about one liter and cooled, whereupon the diol mixture separated in a semi-crystalline state; yield, 187 g. (80%). It was used in the next step without further purification.

3, trans-4, cis-5-Trimethylcyclohexene and 3, cis-4, trans-5-Trimethylcyclohexene
(XIX and XXI)

The crude diol mixture 134.3 g. (0.86 mol) was converted to crude mixture of ditosylates in 87% yield by the procedure used previously. The detosylation (reduction by LiH and LiAlH₄) was carried out as before, and 352 g. of ditosylate gave 74.5 g. of trimethylcyclohexenes (60% yield). G.L.C. analysis showed the mixture to consist almost entirely of two components occurring in 1:1 ratio separable by distillation. The separation was done at about 30-plate efficiency on the spinning band column and 90% of
the distillate occurred on two flats, center cuts of which boiled at 144.36° and 148.30° respectively. These center cuts both appeared as 99.5% pure by G.L.C. and were used for other properties (Table I) and for hydrogenation.

**Anal.** Calcd. for C₉H₁₆: C, 87.03; H, 12.97

Found for the ctc isomer: C, 87.28; H, 12.79

Found for the cct isomer: C, 86.86; H, 13.17

Their infrared spectra were consistent with the assigned structures. Plate No. I.

1,trans-2,cis-3-Trimethylcyclohexane (II)

The two cyclo-olefins (25 g. each) were hydrogenated over platinum oxide in 50 ml. of ethanol at 50 p.s.i.g. The product in each case was found to be saturated and was distilled on a small spinning band column about 15 g. of pure material being recovered in each case. The common physical properties of both are given in Table II. G.L.C. examination showed them to be 99.5% pure or better and identical in retention times with the major components of the corresponding known sample. Infrared spectra, Plate II.
C. Synthesis of 1,2,4-Trimethylcyclohexanes

Method I

2,4- and 2,5-Dimethyl-4-cyclohexene-1-carboxaldehyde (XXI)

In a typical run, 350 g. (5 moles) of freshly distilled crotonaldehyde, 352 grams (5.15 moles) of freshly distilled isoprene and one gram of hydroquinone were charged to a 3-liter steel bomb. The bomb was pressurized to 500 p.s.i.g. with nitrogen and heated to 180° with shaking. An exothermic reaction set in at 180° raising the temperature to 250-275° for 10 minutes before dropping again to 180°. The bomb was left 20 minutes at this temperature then chilled and vented to the atmosphere. Unreacted isoprene and crotonaldehyde were stripped off and the residue was fractionally distilled at 10-15 plates efficiency at reduced pressure to give 510 g. (3.7 moles) of good adduct b.p. 92-95°/30 mm., n\textsuperscript{20} D 1.4688-1.4693 in 74% yield, together with 21% of isoprene dimer, b.p. 82-85°/30 mm., n\textsuperscript{20} D 1.4702-1.4734. G.L.C. analysis of the good adduct showed two peaks in an 86:14 ratio.

1,4,5-Trimethylcyclohexënes

690 g. (5 moles) of the adduct was reduced via a modified Wolff-Kishner reaction described previously. The resulting crude olefinic mixture, 590 g. (95% yield) was steam distilled and the product of several runs was
combined and fractionated at about 50-plate efficiency. The purified product, b.p. 148.1-148.4°C, \( n_\text{D}^{20} = 1.4495-1.4496 \), G.L.C. showed the presence of two close boiling components.

1,2,4-Trimethylcyclohexanes

126 g. (1 mole) of the mixture of olefins above was hydrogenated at room temperature with platinum-on-charcoal (1 g.) in a 3-neck flask equipped with a fast stirrer and a condenser. The theoretical amount of hydrogen was taken up after 1.5 hours but a slight unsaturation was still present. The catalyst was filtered off and the material was treated exhaustively with an aqueous solution of potassium permanganate, steam distilled and dried. G.L.C. showed the presence of all four possible isomers, IV, V, VI and VII, Figure V. A 7.3 kilo batch was distilled at about 120-plate efficiency separating out the first two isomers from each other but the last two remained as an inseparable mixture.

Component I (cct)

b.p. 141.29, \( n_\text{D}^{20} = 1.4274, d_4^{20} = 0.7743 \). F.p. (M.p.), °C -85.17, F.p., 100% -84.89, Purity, 99%.

Component II (cgc)

b.p. 144.56, \( n_\text{D}^{20} = 1.4344, d_4^{20} = 0.7908 \), F.p. (M.p.), -85.53, Purity, 98%.
Component III and IV (cct + cac)

b.p. 146.41 - 146.45, $n_D^{20}$ 1.4342 - 1.4345.

D. Synthesis of 1,2,4-Trimethylcyclohexanes

Method II

2,4- and 2,5-Dimethylcyclohexylmethanols (XXIII)

Isoprene-crotonaldehyde adduct 1382 g. (10 moles) was hydrogenated in a 3.5 liter rocking hydrogenator over 10% of its weight of 20% nickel-on-kieselguhr catalyst. The first absorption of hydrogen occurred at 110-125°, corresponding to saturation of the double bond. The temperature was then raised to 180-190° and hydrogenation of the aldehyde group started and was complete in about 6 hours. The crude alcohol was filtered and used in the next step without purification; it gave no qualitative test for unsaturation or for free aldehyde. Average yields were 95-98%.

2,4- and 2,5-Dimethyl-1-acetoxyethylcyclohexanes (XXIV)

A mixture of crude XXIII, 2350 g. (17 moles) was added slowly to boiling acetic anhydride (16.5 moles) and 10 g. of a sulfonic acid type ion-exchange resin. Reflux occurred spontaneously during the addition and was maintained for 2 hours after the addition was complete. The crude ester was then cooled, washed free of acetic acid and dried over anhydrous magnesium sulfate. Upon vacuum distillation the desired mixtures of acetates, b.p.
96-98°/12 mm., $n^D_{20} 1.4473-1.4479$, was obtained in 93% yield.

**Anal.** Calcd. for C$_{11}$H$_2$O$_2$: C, 71.69; H, 10.94.
Found: C, 71.74; H, 10.85

**Pyrolysis of Acetates and Purification of Olefins**

The mixture of acetates was pyrolyzed at 525° in a 2.2 x 100 cm. electrically heated vertical Vycor tube packed with 1/4" glass helices. The feed was introduced at the top of the tube at a rate of 3 ml. per minute by a Corson-Cerveny bellows pump, and the pyrolysate was condensed by a glass coil condenser. The pyrolysate was washed free of acetic acid and distilled to obtain 70-80% of olefinic product and 20-30% of unchanged ester which was recycled. By gas-liquid chromatography the product was found to contain 5% of low molecular weight "fragments" while the remainder was represented by four major peaks A, B, C and D in Figure V. A and B were only slightly separated under highly resolved conditions but appeared to be roughly equal. $A + B$, 53%; C, 14%; D, 33%.

Distillation of an 11.0 kilo lot of the olefinic mixture at about 120-plate efficiency separated "A + B" as a mixture, b.p. 141.91°, $n^D_{20} 1.4497$, pure "C", b.p. 144.46°, $n^D_{20} 1.4485$ and pure "D", b.p. 145.96, $n^D_{20} 1.4497$. 
Anal. Calcd. for C₉H₁₆ : C, 87.03; H, 12.97
Found for olefins "A+B" : C, 87.20; H, 12.77
Found for olefin "C" : C, 86.92; H, 13.07
Found for olefin "D" : C, 87.18; H, 13.11
Infrared spectra, Plate No. III.

Oxidation of Olefin "C" (XXVII)

To an ice cooled solution of 50 g. (0.4 mole) of (XXVII) in 1.5 liters of water and 0.5 g. of sodium carbonate, a solution of 140 g. (0.88 mole) of potassium permanganate in 3.5 liters of water was added slowly with rapid stirring. The excess permanganate was destroyed with sodium bisulphite solution and on steam distilling a clear solution 35 g. (70%) of ketone was obtained, b.p. 176.5-177° (uncorr.), lit. 175-176°. The semicarbazone derivative had a m.p. 192-193°, lit. 193° and the oxime m.p. 97.5-98.0°, lit. 97-97.5°.

Found : C, 58.93; H, 9.50; N, 23.01

Oxidation of Olefin "D" (XXVIII)

Similarly 50 g. (0.4 mole) of XXVIII was oxidized to a ketone in 75% yield, b.p. 172-175°. The semicarbazone had a m.p. 174-175°, lit. 175-176° and an oxime m.p. 110°, lit. m.p. 110°.

Found: C, 58.90; H, 9.55; N, 23.04

Reduction of cis-2,4-Dimethylcyclohexanone (XXIX)

a. Wolff-Kishner method

A one-liter 3-neck flask equipped with an electric treating mantle, stirrer, dropping funnel, thermometer and reflux condenser was charged with 40 ml. of diethylene glycol, 25.0 g. (.16 mole) of dihydrazine sulfate and 12.0 g. (.30 mole) of sodium hydroxide flakes. This mixture was stirred and heated until homogeneous, at 98° the dihydrazine dissolved with vigorous effect, liberating hydrazine and raising the temperature to 120°. The reaction was cooled to 95° and 19.0 g. (.15 mole) of XXIX was added rapidly. The mixture was refluxed for 1 hour and an additional 8.0 g. (.2 mole) of sodium hydroxide was added and again refluxed for 15 minutes. The condenser was removed and replaced by a side-arm tube and the product was distilled while stirring vigorously. The product was washed with 5% sulphuric acid followed by sodium bicarbonate and water and dried over silica gel. Distillation afforded a saturated product, b.p. 120.5°, \( \mu_N \) 1.4231, which was 99+% pure by G.L.C. Its infrared spectra (Plate IV) and other physical properties are identical with those for 1,6,11-3-dimethylcyclohexane.
components in the resulting hydrocarbon which on distillation gave no pure product, b.p. 118-125°. Bromine test showed unsaturation to the extent of 24%.

**Hydrogenation of Olefins "A+B"**

The mixture of olefins, 1.5 liters, was hydrogenated over 120 g. of powdered Harshaw nickel at 90° until saturation. The catalyst was filtered off and the mixture of paraffins was fractionated at 60-plate efficiency to yield 3 components in a ratio of 45:25:30. G.L.C. showed the presence of three components V, VI and VII in Figure V. The lower separable component had the following physical constants:

**Component V (cte)**

<table>
<thead>
<tr>
<th>Cottrell b.p. °C./760 mm</th>
<th>n²⁰</th>
<th>d⁴</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>144.56</td>
<td>1.4344</td>
<td>0.7908</td>
<td>-85.53</td>
</tr>
</tbody>
</table>

**Anal.** Calcd. for C₉H₁₈: C, 85.63; H, 14.37

Found: C, 85.60; H, 14.29

The two remaining higher boiling paraffins remained as a mixture, b.p. 146.40-146.46, n²⁰ 1.4341-1.4345.

**Hydrogenation of Olefin "C"**

Hydrogenation of olefin "C" under the same conditions as before gave 2 cycloparaffins in the ratio of 28:72. G.L.C. showed that they corresponded to compounds IV and
b. Clemmensen method

Mossy zinc 100 g., 200 ml. of 5% warm solution of mercuric chloride and 50 ml. of 10% hydrochloric acid agitated for an hour. The solution was decanted and replaced with 50 ml. of concentrated hydrochloric acid, 10 ml. of water and 20 g. of XXIX. This mixture was stirred and heated to reflux for 15 hours while adding 10 ml. of concentrated hydrochloric acid, every two hours. On cooling, the organic layer was separated, washed, neutralized and distilled yielding 10.9 g. (65%) of hydrocarbon, b.p. 118-125°. G.L.C. shows this to be a mixture of 3 products, 70% 1,cis-3-dimethylcyclohexane, 20% 1,trans-3-dimethylcyclohexane and 10% 1,3-dimethylcyclohexene-1.

Reduction of trans-2,5-Dimethylcyclohexanone (XXX)

a. Wolff-Kishner method

The reduction was done as before on 20 g. (.15 mole) of XXX. G.L.C. showed only the presence of one component in a purity of 99+%. The hydrocarbon was distilled affording 11 g. (.65 mole) of material, b.p. 119.5°, \( n^D_{20} \) 1.4209. Its infrared spectra was identical to that for 1,trans-4-dimethylcyclohexane. Plate No. IV.

b. Clemmensen method

The same procedure as before was used on 20 g. (.16 mole) of XXX. G.L.C. showed the presence of 3
VII (Figure V). They were fractionated apart on a 50-plate efficiency column and had the following physical constants:

Component IV (cTT)

<table>
<thead>
<tr>
<th>Cottrell b.p.</th>
<th>mD</th>
<th>d4</th>
<th>F.p.</th>
<th>Purity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>141.29</td>
<td>1.4274</td>
<td>0.7743</td>
<td>-85.17</td>
<td>99</td>
</tr>
</tbody>
</table>

Component VII (cGC)

<table>
<thead>
<tr>
<th>Cottrell b.p.</th>
<th>mD</th>
<th>d4</th>
<th>F.p.</th>
<th>Purity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>140.57</td>
<td>1.4340</td>
<td></td>
<td>-78.31</td>
<td>99+</td>
</tr>
</tbody>
</table>

Anal. Calcd. for C$_9$H$_{18}$: C, 85.63; H, 14.37

Found for IV: C, 85.65; H, 14.32

Found for VII: C, 85.68; H, 14.23

Infrared spectra, Plate No. V.

Hydrogenation of Olefin "D"

Hydrogenation of olefin "D" under the same conditions as before gave 2 cycloparaffins in the ratio of 30:70.

G.L.C. showed that they corresponded to compounds IV and VI (Figure V). Fractionation afforded the components in high purity (99+), the lower boiling components being identical in physical properties to the previously described cTT isomer and the higher boiling component having the following physical properties.


Component VI (cct)

<table>
<thead>
<tr>
<th>Cottrell b.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>°C./760 mm</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>146.65</td>
</tr>
</tbody>
</table>

Anal. Calcd. for C_{9}H_{18}: C, 85.63; H, 14.37

Found for VI: C, 85.47; H, 14.25

Infrared spectrogram Plate No. V.

E. Synthesis of 1,2,3-Trimethylcyclohexanes
Method II

Diels-Alder Condensation

The adduct of 1,trans-3-pentadiene and crotonaldehyde was prepared and purified as described previously (page 58).

2,3- and 2,6-Dimethylcyclohexylmethanols

Piperylene-crotonaldehyde adduct, 1382 g. (10 moles) was hydrogenated as described previously (page 76) and the crude alcohol obtained in a 98% yield was used in the subsequent step without further purification.

2,3- and 2,6-Dimethyl-1,acetoxydimethylcyclohexanes

A mixture of 2350 g. (17 moles) of the above adduct was acetylated as described previously (page 76) to give 85% of the corresponding acetate mixture, b.p. 114-119/20 mm., n^20 1.4503-1.4513.

Anal. Calcd. for C_{11}H_{20}O_{2}: C, 71.69; H, 10.94

Found: C, 71.57; H, 10.73
**Pyrolysis of Acetates and Purification of Olefins**

The pyrolysis of the acetates was carried out under the same conditions as described previously to give comparable yields of olefin. G.L.C. analysis of the product revealed the presence of 3 components, Figure IX, but at high resolution the middle peak was split into two. They were designated as A, B+C and D and were found to be in a ratio of 57:9:34. Distillation of a 9.8 kilo lot of the olefinic mixture at about 120-plate efficiency afforded a clean-cut separation, "A", b.p. 145.64°, n°D 1.4552, "B"+"C", b.p. 147.78°, n°D 1.4562 and "D" b.p. 152.17°, n°D 1.4560.

**Anal.** Calcd. for C₉H₁₆: C, 87.03; H, 12.97

Found for "A": C, 87.21; H, 13.07

Found for "B"+"C": C, 87.10; H, 13.02

Found for "D": C, 87.19; H, 13.04.

Infrared spectra, Plate No. VI.

**Hydrogenation of Cyclic Olefins and Identification of Cyclopentanafins**

Hydrogenation was carried out on 1 ml. samples in 10 ml. of ethanol and 0.1 g. of platinum oxide catalyst in a Burgess-Parr hydrogenation under 50 lbs. of hydrogen pressure.

**Hydrogenation of Olefin "A"**

Only one cyclopentanafin was obtained which was identified as the oot isomer by means of G.L.C.
Hydrogenation of Olefins "B" and "C"

Three cycloparaffins were obtained, the \textit{cte} and \textit{occ} in a 25:75 ratio.

F. Synthesis of 1,3,5-Trimethylcyclohexanes

Method II

\textit{cis} and \textit{trans}-3,5-Dimethylcyclohexanols

A mixture of \textit{occ}, \textit{ctt} and \textit{cte}-3,5-dimethylcyclohexanols, 450 g. (3.5 moles) was distilled on a column at 20-plate efficiency. The all \textit{cis} alcohol 145 g. (1.1 moles), b.p. 177.5-178°, n^20 1.4509-145.15, m.p. 39°, distilled over first and the rest of the material was fractionated under vacuum, b.p. 83-85°/17 mm., n^20 1.540-1.4572 with no definite flat in the distillation. The all \textit{cis} alcohol was recrystallized from ethanol 5 times to give a white solid, m.p. 40-40.3°.

The end fraction of the distillate, 100 g., composed of the \textit{ctc} and \textit{ctt} isomers were combined and chilled in the refrigerator overnight. A small amount of the solid that formed, 16 g. was filtered off and the filtrate was distilled on a Nestor-Faust spinning band under vacuum, b.p. 84-85/17 mm., n^20 1.4557-1.4570. G.L.C. analysis showed that all fractions were mixtures of two components ranging from ratios of 80:20 to 35:65.
105 g. (1.1 moles) was added while stirring. A voluminous precipitate developed after 3 hours which was filtered and washed with a little cold petroleum ether and dried in a desiccator under vacuum. A nearly quantitative yield of triphenylphosphinemethylene hydrobromide was obtained.

To a nitrogen filled 3-necked flask fitted with a reflux condenser, stirrer and addition funnel was placed 40 g. (.11 mole) of triphenylphosphinemethylene hydrobromide, 250 ml. of sodium dried glyme and 13 g. (.3 mole) of sodium amide. The mixture was heated to reflux for three hours at which time the color changed to deep orange. cis-3,5-dimethylcyclohexanone 12.8 g. (.1 mole) in 15 ml. of glyme was added very slowly and after the addition, a reflux was maintained for 10 hours. The mixture was cooled and the precipitated triphenylphosphite was filtered off. The filtrate was then distilled to one third its volume, washed 3 times with water and dried over anhydrous magnesium sulfate. Distillation gave 9.2 g. (72%) of pure 1,cis-3,cis-5-dimethylmethylene cyclohexane, b.p. 139.4°.

Anal. calcd. for C₉H₁₆: C, 87.03; H, 12.97

Found: C, 87.20; H, 12.89.

Trans-3,5-dimethylmethylene cyclohexane

The predominantly trans ketone mixture (35:65) was similarly subjected to a Wittig reaction to give a 35:65 mixture of cis and trans-3,5-dimethylmethylene cyclohexane.
Oxidation of cis-3,5-dimethylcyclohexanol

Ethyl ether, 400 ml. and 128 g. (1 mole) of cis-3,5-dimethylcyclohexanol were placed in a one-liter, 3-necked flask fitted with a stirrer, condenser and addition funnel. The chromic acid solution, prepared from 100 g. (1 mole) sodium dichromate dihydrate and 75 cc. (1.3 moles) of 96% sulfuric acid diluted to 500 ml., was added to the stirred solution over 30 minutes, maintaining the temperature at 25°C. After two hours, the upper layer was separated and the aqueous phase extracted 3 times with 50-ml. portions of ether. The combined extracts were washed with saturated sodium bicarbonate, then water. G.L.C. analysis on a squalane column showed 99% ketone and 1% alcohol. Distillation gave 114.1 g. (90.6%) yield of ketone, b.p. 181.1-181.3, \( n_D^{20} \) 1.4423.

Oxidation of a mixture of trans-3,5-dimethylcyclohexanols

A 35:65 ctc-concentrate of the alcohol 70 g. (.5 mole)' oxidized under the same conditions as above gave 58.5 g., (93% yield) of ketone, b.p. 82-85/30 mm., \( n_D^{20} \) 1.4428-1.4447. G.L.C. analysis showed this to be a mixture of cis and trans ketones in a 35:65 ratio.

cis-3,5-dimethylmethylenecyclohexane

a. Triphenylphosphinemethylene hydrobromide

To an ice cooled solution of triphenyl phosphine, 262 g. (1 mole) in 2 liters of benzene, methyl bromide,
The pure trans compound was isolated by quantitative G.L.C., b.p. 140.2, $n_D^{20} 1.4267$.

Anal. Calcd. for C$_9$H$_{16}$: C, 87.03; H, 12.97

Found: C, 87.17, H; 12.95

1, cis-3, cis-5-Trimethylcyclohexane

Ten ml. of cis-3,5-dimethylmethylenecyclohexane was hydrogenated to saturation at room temperature over 5% platinum catalyst. The product was saturated to bromine and G.L.C. indicated the presence of two components in a 65:35 ratio. They could not be separated apart by distillation but quantitative G.L.C. separated out enough pure sample for physical determinations. A first component, b.p. 138.5, $n_D^{20} 1.4266$, and a second component b.p. 141.2, $n_D^{20} 1.4308$. Infrared spectra and G.L.C. retention times showed them to be ccc and cct-1,3,5-trimethylcyclohexane respectively.

The trans olefin concentrate gave on hydrogenation a mixture with a predominance of the cct isomer.

1. 30/70 (cis/trans) olefins gave 20/80 cycloparaffins (theoretical 19/81)
2. 60/40 (cis/trans) olefins gave 37/63 cycloparaffins (theoretical 39/61)

The paraffins were identified by G.L.C. retention times and I.R. spectra.
SUMMARY

1. The condensation of isoprene and piperylene with maleic anhydride or fumaroyl chloride has been shown to be stereospecific and to follow the Diels-Alder rule for configuration.

2. The condensation of isoprene and piperylene with crotonaldehyde was found to be non stereospecific and to be temperature dependent.

3. The reduction of cis-3-methyl-4-cyclohexene-cis-1, cis-2-dicarboxylic anhydride; cis-3-methyl-4-cis-3-methyl-4-cyclohexene-cis-1, trans-2, dicarbonyl chloride and cis-3-methyl-4-cyclohexene-trans-1, cis-2-dicarbonyl chloride by lithium aluminum hydride to their corresponding diol was found to be stereospecific.

4. The tosylation of these diols was found to be nearly quantitative under low temperature conditions.

5. A method of detosylation using lithium hydride-lithium aluminum hydride mixture was developed and was also found to be stereospecific.

6. All four geometric isomers of the 3,4,5-trimethylcyclohexenes, the ctt, ctc, act and ccc were synthesized and their physical constants determined.

7. Hydrogenations of the 3,4,5-trimethylcyclohexenes were
performed under a variety of conditions using different catalysts, Harshaw nickel, Raney nickel, platinum oxide and platinum-on-charcoal and an evaluation of their stereospecificity was made.

8. The three geometric isomers of the 1,2,3-trimethylcyclohexanes, ctc, cct and ccc have been synthesized, characterized and their physical constants determined.

9. A new large scale scheme for the synthesis of the 1,2,3-trimethylcyclohexanes was devised using readily available starting materials.

10. The synthesis of eight new dimethylmethylene cyclohexanes has been described. They were characterized and their physical constants determined.

11. The stereospecificity of the Wolff-Kishner reduction of some ketones was demonstrated as opposed to that of the Clemmenson method.

12. The four geometric isomers of the 1,2,4-trimethylcyclohexanes, ctt, ctc, cct and ccc, were synthesized, characterized and their physical constants determined.

13. A novel scheme for the preparation of the 1,3,5-trimethylcyclohexanes is presented.

14. The Wittig reaction of triphenylphosphinemethylene hydrobromide and 3,5-dimethylcyclohexanone in sodium amide as a base and glyme as a solvent has been described. The stereospecificity of the reaction is demonstrated.
15. The two dimethylmethylene cyclohexanes pertaining to
the 1,3,5-trimethylcyclohexanes have been synthesized and
characterized.

16. Additional proof for the configuration of the geo-
metrical isomers of the 1,3,5-trimethylcyclohexanes is
given.
AUTOBIOGRAPHY

I, Bahram H. Mahmoud, was born May 26, 1932, in Tanta, Egypt, U.A.R. I received my secondary school education at the El-Nasr School, Heliopolis, Egypt, and my undergraduate training at Cairo University, which granted me the Bachelor of Science degree in 1954. I was appointed on the teaching staff of the El-Nasr Secondary School in June, 1954. I held this position until April, 1955 at which time I joined the graduate school at the Imperial College of Science and Technology, London, England. In February, 1957, I joined the General Petroleum Authority, Cairo, as a research chemist and was granted a four year study leave in August, 1958. In September, 1958, I was appointed as a Teaching Assistant in the Department of Chemistry at The Ohio State University. I held this position until June, 1959 at which time I joined the American Petroleum Institute, Project 58, as a Research Assistant.