SYNTHESIS AND STEREOCHEMISTRY OF
SOME 9,10-DISUBSTITUTED cis-DECALINS

by

WILLIAM BRUCE SCOTT
B. Sc. (Hons.) University of British Columbia, 1961

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF
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DOCTOR OF PHILOSOPHY

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of
CHEMISTRY

We accept this thesis as conforming to the
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FACULTY OF GRADUATE STUDIES

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SYNTHESIS AND STEREOCHEMISTRY OF SOME 9, 10 - DISUBSTITUTED DECALINS

ABSTRACT

The application of low temperature nuclear magnetic resonance (n.m.r.) spectroscopy to the determination of the barrier heights to interconversion in compounds which contain one and two flexible six-membered rings is reviewed. Although the barrier heights in cyclohexane and its derivatives have been experimentally determined, similar studies in the cis-decalin system have (until very recently) not been successful. Consideration is given, therefore, to the preparation of a number of cis-9,10-disubstituted decalin derivatives, which will act as model compounds for a further study in the problem of the barrier height to ring interconversion in the cis-decalin system.

Various attempts to synthesize a novel model compound, tricyclo[4.4.4.0]tetradecane, are described. Partial success has been achieved in that a small but demonstrable amount of tricyclo[4.4.4.0]-3,8-tetradecadiene has been synthesized in a ten step reaction sequence, starting from acetylenedicarboxylic acid. A Diels-Alder condensation of this compound with two mole-equivalents of 1,3-butadiene gave $\Delta_2^2,6$-hexalin-9,10-dicarboxylic anhydride. Lithium aluminum hydride reduction of this compound gave cis-9,10-bis(hydroxymethyl) $\Delta_2^2,6$-hexalin, which was converted to its dimesylate derivative on treatment with methanesulfonyl chloride in pyridine. Reaction of the dimesylate derivative with sodium cyanide in N-methyl-2-pyrrolidinone gave cis-9,10-bis(carboxymethyl) $\Delta_2^2,6$-hexalin, which was converted to its dimethyl ester on treatment with methanesulfonyl chloride in pyridine. Reaction of the dimesylate derivative with sodium cyanide in N-methyl-2-pyrrolidinone gave cis-9,10-bis(cyanomethyl) $\Delta_2^2,6$-hexalin. Alkaline hydrolysis of the latter gave cis-9,10-bis(carboxymethyl) $\Delta_2^2,6$-hexalin, which was converted to its dimethyl ester on treatment with diazomethane in 1,2-dimethoxyethane. Lithium aluminum hydride reduction of the dimethyl ester gave cis-9,10-bis(2-hydroxyethyl) $\Delta_2^2,6$-hexalin. Treatment of the dialcohol with methanesulfonyl chloride in pyridine gave cis-9,10-bis(2-mesyloxyethyl) $\Delta_2^2,6$-hexalin. Reaction of the dimesylate with sodium iodide in acetone gave cis-9,10-bis(2-iodoethyl) $\Delta_2^2,6$-hexalin. Treatment of this compound with n-butyllithium in diethyl ether and in heptane gave a mixture of cis-9-ethyl-10-vinyl $\Delta_2^2,6$-hexalin and tricyclo[4.4.4.0]-3,8-tetradecadiene (minor product). Attempts to improve the yield of the tricyclic compound, using zinc and magnesium as coupling reagents, were unsuccessful.
The syntheses of other desired model compounds are described. Thus, cis-9,10-dimethyl-Δ²-octalin and -Δ²,6-hexalin were prepared from their cis-9,10-bis(mesyloxymethyl)-analogs on treatment of the latter compounds with sodium iodide in N₂N-dimethylformamide, followed by the treatment of the respective product iodides with lithium aluminum hydride in 1,2-dimethoxyethane. cis-9,10-Dimethyldecalin was prepared from cis-9,10-dimethyl-Δ²,6-hexalin by catalytic hydrogenation of the latter. In addition, treatment of cis-9,10-bis(hydroxymethyl)decalin and -Δ²-octalin with p-toluenesulfonic acid in benzene yielded 12-oxatricyclo[4.4.3.0]tridecane and -3-tridecene, respectively. 12-Oxatricyclo[4.4.3.0]-3,8-tridecadiene was isolated as a by-product from the reaction of cis-9,10-bis(mesyloxymethyl)-Δ²,6-hexalin with sodium cyanide in N-methyl-2-pyrrolidinone, as was 12-amino-11-cyanotricyclo[4.4.3.0]-3,8,11-tridecatriene. All of the new compounds have been characterized by means of infrared, ultraviolet, and n.m.r. spectroscopy, mass spectrometry, and microanalysis, where applicable.

Preliminary investigations of the barrier heights to interconversion in cis-9,10-dimethyldecalin and 12-oxatricyclo[4.4.3.0]tridecane are described. Quantitative kinetic data could not be obtained from the low temperature (0 to -60°C) n.m.r. spectra of the former, since no broadening of the ring proton resonance peak was observed. On the other hand, the latter compound gave n.m.r. spectra in which the ether ring proton resonance peak broadened considerably as the sample temperature was lowered. From these spectra a value of the energy of activation (E_a) of 8.4 + 2 kcal./mole was calculated for the interconversion process in 12-oxatricyclo[4.4.3.0]tridecane.
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W. Bruce Scott and Richard E. Pincock

SOME 9,10-DISUBSTITUTED DERIVATIVES OF CIS-DECALIN,
CIS- $\Delta^2$-OCTALIN AND CIS- $\Delta^{2,6}$-HEXALIN

In press.
ABSTRACT

Supervisor: Dr. R. E. Pincock

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ACKNOWLEDGEMENTS

I should like to thank Dr. R. E. Pincock most sincerely for his encouragement and expert guidance during the course of this research project.

I should like to thank also the other members of the physical-organic group for their helpful suggestions and interesting discussions.
Recent advances in the technology of nuclear magnetic resonance (n.m.r.) spectroscopy have enabled chemists to investigate more directly the nature and scope of hindered rotations about single bonds in organic molecules. Of particular interest to this thesis is the work which has been reported on the stereochemistry of cyclohexane and its derivatives, with regard to the barrier to interconversion of the ground state conformations of these compounds. Comprehensive recent reviews are available, which discuss the stereochemistry of cyclohexane and the application of n.m.r. spectroscopy to problems of stereochemistry; therefore, only brief discussions of these subjects will be given here. The results of current theoretical and experimental investigations will be presented, followed by an outline of the research proposal on which this thesis is based.

Cyclohexane has been found to exist almost exclusively in the chair conformation (Fig. 1a) at room temperature (a conformation is any spatial arrangement of the atoms of a molecule which arises from the rotation of substituent groups about a single bond). The chair conformation has a six-fold axis of alternating symmetry; hence, all the methylene groups are structurally equivalent. The two hydrogen atoms on each methylene group, however, are not. One is aligned parallel to the principal symmetry axis and is termed "axial", while the other extends out radially from this axis and is termed "equatorial".
On considering a model of cyclohexane in the chair conformation, it can be seen that when a rotation of the methylene groups about the carbon-carbon single bonds is effected, another chair conformation is produced in which all of the originally axial hydrogen atoms now occupy equatorial positions, and vice versa. The difference in the environments of the axial and equatorial hydrogen atoms results in a difference of about 27 c.p.s. between their corresponding chemical shifts in the n.m.r. spectrum of cyclohexane ⁷ at -100° (the chemical shift of a hydrogen atom in a molecule is the difference between the n.m.r. frequencies of that atom and a specified standard).

The n.m.r. spectrum of a group of atoms in a molecule may be modified ⁸ if that group is taking part in a rate process such as internal rotation. This variation of spectrum with rate of rotation is a result of the Heisenberg uncertainty principle, which may be written in the form:

\[ \tau \Delta \nu \approx \frac{1}{2} \pi \]

where \( \Delta \nu \) is the separation between the corresponding resonance lines, and \( \tau \) is the shortest lifetime of the hydrogen atoms in each environment. Hence, for a sufficiently rapid rate of chair-chair interconversion in cyclohexane, the lifetimes of the hydrogen atoms in the axial and equatorial positions will become less than this value, giving rise to a time-averaged spectrum. On the other hand, a sufficiently slow rate of interconversion should produce a distinct resonance peak for the hydrogen atoms in each environment.

Jensen ⁷ has observed experimentally that the shape of the n.m.r. spectrum of cyclohexane does change with temperature. The spectrum at room temperature consists of a single sharp line corresponding to a rapid rate of interconversion. As the temperature of the cyclohexane sample is lowered, the resonance peak broadens until at about -66° (termed the coalescence temperature, \( T_c \)) the peak separates into two main components corresponding
to the axial (higher field) and equatorial protons. These two components are themselves broadened due to spin-spin coupling of adjacent hydrogen atoms. The two components continue to separate as the temperature is lowered further, until at about -100° no further increase is observed. The maximum separation is about 27 c.p.s. The employment of deuterium substitution plus double irradiation gives better spectra, since the complications due to spin-spin coupling are eliminated.

Two general methods have been developed for calculating thermodynamic values for the rotation barrier from the observed n.m.r. spectra. One method, outlined by Pople, involves the calculation of the mean lifetimes of the hydrogen atoms in their two environments from the shapes of the n.m.r. spectra at various temperatures. The rate constant of interconversion is the reciprocal of the lifetime. The thermodynamic parameters can then be calculated graphically using Eyring's equation in the form:

$$\log \tau_T = \Delta H^*/4.59T - 10.320 - \Delta S^*/4.59$$

where \( \tau \) is the mean lifetime of the proton in either environment, \( H^* \) is the enthalpy of activation and \( \Delta S^* \) is the entropy of activation. The free energy of activation (\( \Delta F^* \)) can then be obtained from the equation:

$$\Delta F^* = \Delta H^* - T \Delta S^*$$

where \( T \) is the absolute temperature (°K). The other method, developed by Piette and Anderson, gives the value of the energy of activation (\( E_a \)) from a plot of a function of the width at half-height of the resonance peak against \( 1/T \).

A summary of the published experimental thermodynamic values for the chair-chair interconversion of cyclohexane is given in Table I.
### TABLE I

Activation Parameters for the Ring Interconversion in Cyclohexane

<table>
<thead>
<tr>
<th>ΔF⁺ (kcal/mole)</th>
<th>ΔH⁺ (kcal./mole)</th>
<th>ΔS⁺ (cal./deg.mole)</th>
<th>Reference</th>
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<td>10.1 ± 0.1</td>
<td>11.5 ± 2</td>
<td>4.9</td>
<td>7</td>
</tr>
<tr>
<td>10.3</td>
<td>9.0 ± 0.2</td>
<td>-7.9 ± 1.0</td>
<td>13</td>
</tr>
<tr>
<td>10.3</td>
<td>9.1 ± 0.5</td>
<td>-5.8 ± 2.4</td>
<td>14</td>
</tr>
<tr>
<td>10.7</td>
<td>11.4</td>
<td>4.0</td>
<td>15</td>
</tr>
<tr>
<td>10.3a</td>
<td>10.9 ± 0.6b</td>
<td>2.9 ± 2.3</td>
<td>9</td>
</tr>
<tr>
<td>10.2a</td>
<td>10.5 ± 0.5</td>
<td>1.4 ± 1.0</td>
<td>10</td>
</tr>
<tr>
<td>10.3a</td>
<td>9.1 ± 0.1</td>
<td>-5.8 ± 0.4</td>
<td>14</td>
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a - experimental values for undecadeuteriocyclohexane
b - this value has been corrected to 9.9 kcal./mole

The substitution of alkyl and halogen moieties into the cyclohexane ring can affect the rate of interconversion in either of two ways. Harris and Sheppard have observed no significant changes in the n.m.r. spectra of 1,1-, cis-1,2-, and trans-1,2-dimethylcyclohexane down to -120°. They conclude that these compounds are still rapidly interconverting at this temperature. Other derivatives, however, give approximately the same value for the barrier as for cyclohexane itself. Ultrasonic relaxation measurements give values of ΔH⁺ of 8.3 kcal./mole and 10.8 kcal./mole and of ΔS⁺ of -11 cal./deg.mole for methylcyclohexane. For chloro- and bromocyclohexane a value of ΔH⁺ of 12 kcal./mole has been reported. Published barrier heights for substituted cyclohexanes using n.m.r. methods are: ΔF⁺ = 10.9 kcal./mole for bromocyclohexane, 19 11.9 kcal./mole for 1,2 dibromo- and 1,2-dichlorocyclohexane, 18 and ΔH⁺ = 7.5 kcal./mole and ΔS⁺ = 10.7 cal./deg.mole for perfluorocyclohexane 20 (fluorine, like hydrogen, has a nuclear spin of one-half and therefore gives analogous n.m.r. spectra).

The effect of introducing hetero-atoms into the cyclohexane ring has been measured. Using the low temperature n.m.r. technique, a value of ΔF⁺ of 11.6 kcal./mole has been obtained for 1,2-dithiane 21 (1,2-dithiacyclohexane).
addition, the values of $\Delta H^*$ of 16.1 and 18.5 kcal./mole and of $\Delta S^*$ of 6.7 and 14.4 cal./deg. mole for 3,3,6,6-tetramethyl-1,2-dithiane and -1,2-dioxane, respectively, were reported.

The presence of the double bond in cyclohexene has the effect of lowering the barrier to interconversion, relative to cyclohexane. Anet has recently reported a value of $\Delta F^*$ of 5.3 kcal./mole (at -164°C) for the barrier to ring inversion in cyclohexene-$\text{cis}-3,3,4,5,6,6$-$d_6$. Jensen has reported a value of $\Delta F^*$ of 5.93 kcal./mole (at -148°C) for the barrier in 4-bromocyclohexene.

The magnitude of the barrier to interconversion in flexible bicyclic compounds containing the cyclohexane ring has been investigated. Analysis of the low temperature n.m.r. spectra of $\text{cis}$-hydrindan (cis-bicyclo[4.3.0]nonane) gives a value of $\Delta F^*$ = 6.4 kcal./mole at -133°C. The relatively low barrier is presumed to be due to ring-fusion strains. Similar measurements on $\text{cis}$-decalin (cis-bicyclo[4.4.0]decane) have shown that no broadening of the n.m.r. line occurs, even at -121°C. Three explanations have been put forward to account for this result. First, although no ring-fusion strain exists, there is a considerable amount of steric interaction possible between the hydrogen atoms at C-1, C-3, C-5, and C-7 in the double chair conformation (Fig. 2). This interaction may have the effect of raising the ground state energy more than that for the transition state. Secondly, the existence of a large positive entropy of activation could overshadow a normal value for the enthalpy of activation. Thirdly, the difference in chemical shifts for the axial and equatorial protons in the ground state may be smaller than expected; therefore, any separation of the resonance lines could be overshadowed by the presence of spin-spin coupling.

On considering a model of $\text{cis}$-decalin it can be seen that, in the double chair conformation, the molecule has one two-fold axis of rotation (Fig. 2). In addition, the two possible double-chair conformations are non-superimposable
mirror images; hence, cis-decalin exists as a 1:1 mixture of enantiomers in dynamic equilibrium (Fig. 2).

Figure 2. Ring interconversion in cis-decalin.

Some very recent reports have produced values for the barrier to interconversion in derivatives of cis-decalin. Riddel and Robinson give a value of \( \Delta F^* = 12.5 \text{ kcal./mole at } -67^\circ \) for the barrier in 3,3-ethylenedioxy-10-methyl-cis-decalin. Roberts has investigated the temperature dependent \(^{19}\)F n.m.r. spectra of 2,2-difluoro-cis-decalin, together with its 1,1,3,3-tetradeutero- and 9-methyl- derivatives, and gives values of the energy of activation (\(E_a\)) of about 10.5, 11, and 13 kcal./mole, respectively. In contrast, 1-methyl- and 6-methyl-2,2-difluoro-cis-decalin show temperature independent \(^{19}\)F n.m.r. spectra.

The exact physical origin of the barrier to internal rotation in molecules is not known with certainty. In order to gain some insight into the origin, a number of quantum mechanical calculations have been applied to the case of ethane, which has an experimentally determined \(^{27,28}\) barrier of about 3 kcal./mole. Pitzer and Lipscomb calculated a value of 3.3 kcal./mole, but could not say what interactions actually contributed to the barrier. Eyring, Grant, and Hecht calculated the barrier heights for a number of possible interactions and found that a calculation based on the interactions between the hydrogen orbitals gave the best value, 2.88 kcal./mole.
A less rigorous but more practical method of calculating barrier heights has been used, which is based on the non-bonded interactions between neighbouring atoms due to van der Waal's repulsions. With the aid of a computer, one can calculate the relative stabilities of the various conformations of cyclohexane, through which the interconversion proceeds, assuming particular transition states and intermediates. Hendrickson's calculations show the chair conformation of cyclohexane to be the most stable—the boat (Fig. 1b) and twist (Fig. 1c) conformations being 6.93 and 5.33 kcal./mole less stable, respectively. The experimental value for the difference between the chair and twist conformations is 5.5 - 5.9 kcal./mole. Hendrickson's results also show that a transition state for the interconversion consisting of a half-chair (Fig. 1d) conformation (12.66 kcal./mole less stable than the chair conformation) is more economical than one consisting of five planar carbon atoms (14.13 kcal./mole). These values are slightly higher than the experimental barrier height of about 11 kcal./mole (Table I).

Geneste and Lamaty have applied this van der Waal's interaction approach to cis-decalin. They were primarily concerned with trying to determine the most stable conformation of the molecule. Their results showed that the double-chair (Fig. 3a) and double-twist (Fig. 3c) conformations had comparable interaction energies (6 - 10 kcal./mole), while the chair-boat conformation (Fig. 3b) had a somewhat higher value (12 - 16 kcal./mole).

(a) double-chair      (b) chair-boat      (c) double-twist
Figure 3. Conformations of cis-decalin.
The postulation that non-bonded interactions of the van der Waal's type contribute in some measure to the barrier to internal rotation in cyclohexane systems, forms the basis for this thesis. In order to assess the validity of this postulate, it was decided to investigate a number of derivatives of cis-decalin using the technique of variable-temperature n.m.r. spectroscopy.

As mentioned earlier, the double-chair conformation of cis-decalin has severe hydrogen-hydrogen interactions not present in the chair conformation of cyclohexane. These localized interactions could be minimized if the molecule adopted a more planar conformation, e.g., a double-twist type, thus spreading the extra interaction energy throughout the whole system. These interactions, then, could lower the barrier to internal rotation by making the molecule adopt a conformation similar to that for a predicted transition state. A lower temperature than in the case of cyclohexane would be required, in order to observe a decrease in the rate of the interconversion using n.m.r. spectroscopy. The changes in the n.m.r. spectra, however, may not be seen at all, if the new ground state conformation causes the ring protons to be in more or less identical environments, thus decreasing the difference between their chemical shifts.

In order to ensure the presence of a double-chair ground state conformation in the cis-decalin molecule, it was decided to synthesize a number of derivatives of cis-decalin, which contained substituent groups in the C-9 and C-10 positions. Two kinds of substituent groups were considered. The first kind consisted of methyl and mono-substituted methyl groups. These groups would tend to arrest any decrease in the dihedral angle between themselves at C-9 and C-10, due to a flattening of the rings, thus increasing the stability of the double-chair conformation. During the process of ring interconversion, however, these groups must necessarily eclipse one another; hence, the barrier to interconversion should be higher in the derivative than in cis-decalin itself.
The substitution of equal groups into the C-9 and C-10 positions does not change the optical isomerism and symmetry properties of the derivatives from those of cis-decalin. The presence of these groups, however, does eliminate the spin-spin coupling which existed between the bridgehead and ring protons in cis-decalin. Because of this, any changes in the n.m.r. spectra of the ring protons of the cis-decalin derivatives as the temperatures of the samples are lowered should be more readily observable than in the case of cis-decalin. A change in the shape of the resonance peak of the ring protons, as in the case of cyclohexane, will indicate a change in the rate of interconversion between the two ground state double-chair conformations.

The second kind of substituent group involves the attachment of a third ring across the C-9 and C-10 positions in cis-decalin. This group is exemplified by the attachment of a butano moiety, thus forming a third six-membered ring. The resulting compound is tricyclo[4.4.4.0^4.9]tetradecane (TTD).

TTD

The symmetry in TTD is characterized by a three-fold axis of rotation along the C-1 - C-6 bond and three two-fold axes passing through the midpoints of the bonds C-3 - C-4, C-8 - C-9, and C-12 - C-13, each through the midpoint of the C-1 - C-6 bond. The molecule is in point group D_3.
The most stable conformation of TTD is assumed to be the triple-chair (Fig. 4). Although there are now three sets of extra hydrogen-hydrogen interactions of the cis-decalin type present in the molecule, these interactions are symmetrically disposed around the molecule and should tend to cancel one another. Figure 4 shows the two triple-chair conformations of TTD as seen looking down the C-1 - C-6 bond. The two interconverting conformations are non-superimposable mirror images (enantiomers) existing in a 1:1 equilibrium mixture, as in cis-decalin.

![Figure 4. Ring interconversion in tricyclo[4.4.4.0]tetradecane.](image)

The barrier to internal rotation in TTD is predicted to be higher than that for cyclohexane, since, from the consideration of a molecular model, it appears that the interconversion must take place through a simultaneous "flipping" of all three cyclohexane rings. The low temperature n.m.r. spectra of this compound and other 9,10-cyclic derivatives of cis-decalin, therefore, should exhibit the same kind of changes as those found for cyclohexane.

A search of the chemical literature revealed that only a few derivatives of the tricyclo[4.4.4.0]tetradecane system had been prepared (the parent compound, itself, is not known). Fieser and Dunn \(^{36}\) reported the isolation of adducts from Diels-Alder condensations of 5, 6, 11, 12-naphthacenediquinone with 1,3-butadiene.
and 2, 3-dimethyl-1, 3-butadiene:

\[
\begin{align*}
\text{R} = & \text{H}, \text{-CH}_3
\end{align*}
\]

Inhoffen and co-workers,\(^{37}\) using the same method, obtained an adduct from 1, 4, 9, 10-anthradiquinone and 1-methoxy-1, 3-butadiene:

One possible route to tricyclo[4.4.4.0]tetradecane, therefore, is a Diels-Alder condensation of 1, 4, 5, 8-naphthodiquinone (III) with 1, 3-butadiene, followed by a multi-step reduction of the adduct to the parent hydrocarbon:
A second possible way of synthesizing TTD might be simply a Diels-Alder condensation of $\Delta^9$-octalin (VII) with 1,3-butadiene, followed by hydrogenation of the adduct:

A parallel synthetic route was considered in which photo-sensitized 1,3-butadiene is added to $\Delta^9$-octalin to give the same product as in the Diels-Alder reaction. Hammond and co-workers\textsuperscript{38, 39, 40} had reported the photo-sensitized cyclic dimerization of a number of conjugated dienes, the products from which could be explained by the initial excitation of \textit{cis-} and \textit{trans-} oriented dienes to their corresponding triplet states, followed by cyclo-addition to other unexcited dienes. In particular, it was found that \textit{cis}-1,3-butadiene in the triplet state gave a 1,4-cyclo-addition product with another molecule of 1,3-butadiene:
It was considered possible, therefore, that under suitable conditions 1,3-butadiene would give a 1,4-cyclo-addition product with $\Delta^9$-octalin.

Finally, a synthetic route to TTD was considered, which involved the multi-step synthesis of cis-9,10-bis(2-iodoethyl)decalin from decalin-9,10-dicarboxylic anhydride (XXVIII), followed by ring closure using, say, a divalent metal such as zinc or magnesium:

A further search of the chemical literature revealed that no 9,10-dimethyl or 9,10-bis(mono-substituted methyl) derivatives of cis-decalin had been reported. In order to synthesize these compounds, suitable reactions were considered, using decalin-9,10-dicarboxylic anhydride as the basic starting material. In analogous ways, derivatives of cis-$\Delta^2$-octalin and cis-$\Delta^2,6$-hexalin could be prepared, using $\Delta^2$-octalin-9,10-dicarboxylic anhydride (XX) and $\Delta^2,6$-hexalin-9,10-dicarboxylic anhydride (XXXVII), respectively. The low
temperature n.m.r. spectra of these compounds could then be compared with the spectra obtained from the cis-decalin series.

\[ \text{XIX} \]

\[ \text{XXXVII} \]
RESULTS

The following section reviews the results of the various methods of synthesis employed in the preparation of cis-9,10-disubstituted decalins, Δ^2-octalins, and Δ^2,6-hexalins and outlines the characterization of the individual compounds. The methods are grouped into seven Schemes.

A. Synthesis

Scheme I.

\[
\begin{align*}
\text{OH} & \quad + \quad \begin{array}{c}
\text{C}=\text{O} \\
\text{C}=\text{O}
\end{array} & \xrightarrow{\text{NaCl/AlCl}_3, 210^\circ} \quad \begin{array}{c}
\text{OH} \\
\text{O}
\end{array} & \xrightarrow{\text{oxidizer}} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array}
\end{align*}
\]

\(-\text{OAc} = \text{acetate}
\]

\(-\text{N. R.} = \text{no reaction}
\]

\[
\begin{align*}
\text{OAc} & \quad \text{O} \\
\text{OAc} & \quad \text{O}
\end{align*}
\]

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

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

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]
Naphthazarin (I) was prepared by the method of Zahn and Ochwat, in which maleic anhydride was condensed with hydroquinone in an aluminum chloride - sodium chloride melt at 210°. The reported yield of naphthazarin of about 10% was obtained. A small amount of the pure product was acetylated with acetic anhydride, giving the known diacetate derivative (II), m. p. 192-193°, identical with the literature value.

The attempted oxidation of naphthazarin (I) to 1, 4, 5, 8-naphthodiquinone (III), also by the method of Zahn and Ochwat, using lead tetraacetate in glacial acetic acid, was unsuccessful. Attempted oxidations using manganese dioxide in benzene and potassium permanganate in acetone were equally unsuccessful.

The oxidation of quinizarin (IV) to 1, 4, 9, 10-anthradiquinone (V) was attempted using three different methods, none of which were successful. The first method employed lead tetraacetate in glacial acetic acid, as described by Dimroth, Friedmann, and Kammerer. The only material isolated from this attempt was a small amount of the starting material, quinizarin. Secondly, quinizarin was reacted with lead dioxide in glacial acetic acid, according to Dimroth and Schutze. The product from this reaction consisted of a few dark brown crystals, which did not give a definite melting point. The expected product, 1, 4, 9, 10-anthradiquinone, was reported to exist as a yellow crystalline solid with m. p. 211-213° (decomp.). The final attempt involved oxidizing a paste consisting of powdered quinizarin and water with oxides of nitrogen obtained from red fuming nitric acid. The product, a white solid with m. p. 194-195° (decomp.), was identified as phthalic acid (lit. m. p. 191° (decomp.)) by the comparison of infrared spectra.
A mixture consisting of 65% $\Delta^9$-octalin (VII), 25% $\Delta^{1,9}$-octalin, and 10% cis-decalin (shown by gas-liquid chromatography), was obtained from the dehydroacetylation of a commercial mixture of 2-acetoxydecalin isomers, according to the method of Hussey. Diels-Alder condensations of the $\Delta^9$-octalin (not isolated from the product mixture in the previous reaction) with 1,3-butadiene were carried out at 200° with and without the addition of anhydrous aluminum chloride as a catalyst. Analysis of the product mixture from each attempt by gas-liquid chromatography (g.l.c.) indicated that the expected reaction had not taken place. This conclusion was based on the assumption that the expected Diels-Alder adduct (VIII) would have a higher boiling point and hence a longer g.l.c. retention time than $\Delta^9$-octalin.

Scheme 3.
The possibility of forming a 1, 4-cyclo-addition product between a conjugated diene and an olefin under photochemical conditions was investigated. For the purpose of determining whether or not the reaction would take place, the photochemical 1, 4-cyclo-addition of 1, 3-butadiene to cyclohexene (more readily available than $\Delta^9$-octalin) was attempted. The reaction involved the slow passage of butadiene gas into an ultraviolet irradiated solution of cyclohexene, containing benzil as the photo-sensitizer. In this way the concentration of butadiene was kept low so as to minimize cyclo-dimerization, thus maximizing the probability of encounters between butadiene molecules in the triplet state and the molecules of cyclohexene. The g.l.c. analysis of samples withdrawn hourly from the reaction mixture showed that, in spite of the relative concentrations of butadiene and cyclohexene, only the cyclo-dimerization products of butadiene - 4-vinylcyclohexene and cis,cis-1, 5-cyclooctadiene were being formed:

![Chemical structure diagram]

These two butadiene dimers were identified by the comparisons of their n.m.r. spectra with those published by Varian Associates, Ltd.

Since the boiling point of the desired product, cis-$\Delta^2$-octalin (IX), (lit. b.p. 197-199°) is higher than that of 4-vinylcyclohexene (lit. b.p. 128°) and cis, cis-1, 5-cyclooctadiene (lit. b.p. 150-155°), it was expected that the g.l.c. retention time of cis-$\Delta^2$-octalin, under the conditions used, would be longer than the retention times of the latter compounds. The absence of a longer retention time component in the g.l.c. tracings of the hourly samples inferred that the desired product had not been prepared or that the concentration of the
desired product was too low to be detected. The reaction mixture was partly distilled, therefore, and the residue analysed by g. l. c. The g. l. c. tracing showed, in addition to the peaks for 4-vinylcyclohexene and cis, cis-1, 5-cyclooctadiene, two longer retention time components. Neither of the latter components could be isolated in a quantity sufficient for characterization, however.

Another photochemical product was isolated through the g. l. c. separation of the distillate. This product was identified as trans-1, 2-divinylcyclobutane (a 1, 2-cyclo-addition dimer of butadiene) from its n. m. r. spectrum, which showed multiplets at τ3. 8-4. 4 (two olefinic protons), 4. 8-5. 3 (four terminal vinyl protons), 7. 1-7. 6 (two allylic protons), and 7. 9-8. 4 (four methylene protons).

Scheme 4.
The isomerization of cis-4-cyclohexene-1,2-dicarboxylic anhydride (X) to cyclohexene-1,2-dicarboxylic anhydride (XI), m.p. 72-73°C (lit. 71-72°C), was accomplished using phosphorus pentoxide, according to the method of Bailey and Amstutz. The absence, in the n.m.r. spectrum of (XI), of any resonance peaks due to olefinic protons proved the purity of the product, i.e., it contained no starting material or intermediate isomers. The n.m.r. spectrum of the product anhydride (XI) showed multiplets at 7.6 (four allylic protons) and 8.2 (four homoallylic protons). The infrared spectrum of (XI) showed the characteristic absorption bands for a 1,2-cyclic dicarboxylic anhydride system at 1820 and 1770 cm\(^{-1}\).

The fusion of anhydride (XI) with urea at 160°C, according to the method of Ficken and Linstead, gave the cyclic imide analog (XII), m.p. 171-172°C (lit. 170.5°C). A Diels-Alder condensation of this compound with 1,3-butadiene yielded \(\Delta^2\)-octalin-9,10-dicarboximide (XIII), m.p. 173-174°C (lit. m.p. 176°C). Conversion of the imide (XII) to cyclohexene-1,2-dicarboxamide (XIV) was carried out using concentrated aqueous ammonia at room temperature. After isolation of the product, the reaction mixture was acidified with concentrated hydrochloric acid, giving back 36% of unreacted (XII) in the form of the cyclic anhydride (XI). The diamide (XIV) gave a melting point of 210-212°C (decomp.), (lit. m.p. 208°C (decomp.)). The infrared spectrum of (XIV) showed characteristic absorption bands at 3400 and 3200 cm\(^{-1}\) (–NH\(_2\)), 1650 (carbonyl Amide I), and 1620 (carbonyl Amide II).

Dehydration of the diamide (XIV), using phosphorus pentoxide and triethylamine in benzene, gave a lower yield than expected of 1,2-dicyanocyclohexene (XV), m.p. 95-96°C (lit. m.p. 96-97°C). The infrared spectrum of (XV) showed an absorption band at 2200 cm\(^{-1}\), characteristic of an \(\alpha,\beta\)-unsaturated nitrile.

* N.m.r. spectra were interpreted according to reference 48, Vol. 1 and 2, and reference 68, Chapters 4, 5, and 6.
The unusually low yield was probably due to an incomplete mixing of the components during the reaction.

Although the two cyano groups should activate the carbon-carbon double bond in (XV) towards a Diels-Alder condensation with 1,3-butadiene, none of the expected Diels-Alder product (XVI) could be obtained by experiment. Both mild (room temperature) and vigorous (120°C) conditions were employed. In each case the starting material (XV) was recovered. There was no depression in the mixed melting point of the recovered material and the authentic 1,2-dicyano-cyclohexene (XV).

Scheme 5.

The chemical and physical evidence for the establishment and retention of the cis-Δ^2-octalin ring system in this series is summarized as follows. First, the Diels-Alder condensation of cyclohexene-1,2-dicarboxylic anhydride (XI) with 1,3-butadiene-involved the stereospecific cis-addition of a diene to a dieneophile having a cis-oriented functional group; therefore, the product (Δ^2-octalin-cis-9,10-dicarboxylic acid) must necessarily have cis-oriented functional groups. The preparation of the tricyclic compounds (XIX) and (XXI) supported this fact. Secondly, the retention of the Δ^2-octalin ring system throughout this series of compounds was shown by n.m.r. spectroscopy, which gave the expected ratio of 1:2:4 for the olefinic, allylic, and saturated-ring protons in each case. Thirdly, the fact that the n.m.r. spectra of the compounds (XXI) to (XXIV) showed no coupling of the side-chain methylene protons with other protons indicated that the methylene groups were in quaternary positions, i.e., at C-9 and C-10.

The Diels-Alder condensation of cyclohexene-1,2-dicarboxylic anhydride (XI) with 1,3-butadiene gave Δ^2-octalin-cis-9,10-dicarboxylic acid (XVII), m.p. 187.5-188°C (foaming, sealed tube). (lit. m.p. 190°C (decomp.)). Although
Figure 5. Reaction sequence for the preparation of cis-9,10-disubstituted derivatives of cis-Δ⁴²-octalín (Scheme 5).
the actual Diels-Alder product is the octalin anhydride (XIX), the work-up involved extracting the reaction mixture with boiling aqueous sodium hydroxide solution, followed by acidification of the combined extracts with hydrochloric acid, thus yielding the diacid. A quantitative yield of the corresponding dimethyl ester (XVIII) was obtained from the treatment of the acid with diazomethane in ether-glyme. The dimethyl ester, m. p. 52.5–54.5°, showed characteristic infrared absorption bands at 3030 cm.⁻¹ (olefinic hydrogen), 1730 (ester carbonyl), and 1660 (carbon-carbon double bond).

Dehydration of the octalin diacid (XVII) in acetyl chloride at room temperature gave the corresponding cyclic anhydride (XIX), m. p. 67–68° (lit. 53, 55 m. p. 68°). The infrared spectrum of (XIX) showed the characteristic two absorption bands at 1860 and 1780 cm.⁻¹, indicative of a 1,2-cyclic dicarboxylic anhydride. The n. m. r. spectrum of (XIX) showed a triplet at 4.28 (two olefinic protons), a multiplet at 7.30–8.10 (four allylic protons) and a multiplet at 8.39 (eight saturated-ring protons). The number and kind of protons illustrated by this spectrum served to characterize the cis-Δ²-octalin ring system.

Reduction of the octalin anhydride (XIX) with lithium aluminum hydride in 1,2-dimethoxyethane (glyme) afforded a 64% yield of cis-9,10-bis(hydroxymethyl)-Δ²-octalin (XX), m. p. 147–149°. The expected structure of this compound was confirmed by its n. m. r. spectrum, which showed a triplet at 4.46 (two olefinic protons), a triplet at 5.58 (two hydroxyl protons, J = 5.0 c. p. s.), a doublet at 6.57 (two -CH₂O- groups, J = 5.0 c. p. s.), a singlet at 8.03 (four allylic protons), and a singlet at 8.57 (eight saturated-ring protons). The infrared spectrum of (XX) showed a broad absorption band at 3300 cm.⁻¹, characteristic of a hydroxyl function, and a weak band at 1660 cm.⁻¹ for the carbon-carbon double bond.
Cyclodehydration of the octalin dialcohol (XX), using p-toluenesulfonic acid in refluxing benzene, gave a nearly quantitative yield of 12-oxatricyclo[4.4.3.0]3-tridecene (XXI). The cyclic ether was purified by g.l.c., \( \delta^D_{1.5122} \). That the product (XXI) contained a five-membered cyclic ether moiety was inferred by the presence of strong infrared absorption bands at 1060, 1040, and 915 cm\(^{-1}\). The n.m.r. spectrum showed the compound to have the correct ratio (1:2:4) of olefinic, allylic and saturated-ring protons for a \( \Delta^2 \)-octalin derivative, in addition to having four protons in the form of two \(-\text{CH}_2\text{O}-\) groups.

The diacetate derivative (XXII) of the octalin dialcohol (XX) was prepared by reacting the alcohol with acetic anhydride containing a catalytic amount of sulfuric acid. The diacetate was sublimed at 75\(^0\)/mm., m.p. 57.5-59.0\(^0\). The diacetate was characterized by its infrared spectrum, which gave strong absorption bands at 1745 and 1240 cm\(^{-1}\) for the acetate function, and by its n.m.r. spectrum, which gave the correct ratio of ring protons for a \( \Delta^2 \)-octalin derivative, in addition to showing the presence of four protons in the form of two \(-\text{CH}_2\text{O}-\) groups and six protons in the form of two acetate groups.

Treatment of the octalin dialcohol with two mole-equivalents of methanesulfonyl chloride in dry pyridine at -5\(^0\) gave an 85\% yield of the dimesylate\(^*\) derivative (XXIII), m.p. 125-126\(^0\). The infrared spectrum of this compound showed strong absorption bands at 1340 and 1180 cm\(^{-1}\), characteristic of a mesylate group. The n.m.r. spectrum of (XXIII) showed distinct resonance peaks for each kind of proton in the correct ratio.

Nucleophilic displacement of the two mesylate groups in (XXIII) with sodium iodide in refluxing dry N,N-dimethylformamide afforded a low yield (9\%) of cis-9,10-bis(iodomethyl)-\( \Delta^2 \)-octalin (XXIV), m.p. 101-102\(^0\) (needles from methanol).

* mesylate is a contraction of methanesulfonate.
The infrared spectrum of (XXIV) showed only five major absorption bands; however, the bands at 1200 and 1160 cm$^{-1}$ were indicative of a primary iodomethyl group (by comparison of a number of published infrared spectra of aliphatic iodides). The n.m.r. spectrum of (XXIV) showed the expected ratio of ring protons for a 9,10-disubstituted $\Delta^2$-octalin system, together with an AB quartet centered at $\tau$ 6.46 for four protons in the form of two iodomethyl groups. The reasons for the appearance of this AB quartet will be discussed later.

Treatment of the octalin diiodide (XXIV) with lithium aluminum hydride in glyme gave cis-9,10-dimethyl-$\Delta^2$-octalin (XXV) in low yield (18%), purified by g.l.c., m.p. 51-53°C (sealed tube). The low yield was primarily due to losses in the work-up of the reaction mixture, caused by the moderate volatility of the waxy compound. The infrared spectrum of (XXV) showed medium absorption bands at 3030 and 1660 cm$^{-1}$, indicating the presence of a partly substituted carbon-carbon double bond. The n.m.r. spectrum showed the expected ratio of ring protons for a $\Delta^2$-octalin system, plus a single sharp resonance peak at $\tau$ 9.10 for six protons in the form of two methyl groups in quaternary positions.

Scheme 6.

The chemical and physical evidence for the cis-9,10-disubstituted decalin structures of the compounds prepared in this scheme may be summarized as follows: First, the preparation of the decalin diacid (XXVI) from the Diels-Alder adduct (XVII), through catalytic hydrogenation of the latter, inferred that the decalin diacid also had cis-oriented carboxyl groups at the C-9 and C-10 positions. The preparation of the tricyclic compounds (XXVIII) and (XXXIII) supported this idea. Secondly, the n.m.r. spectra of most of the compounds in this series showed single unsplit resonance peaks for the ring protons (as is the case
Figure 6. Reaction sequence for the preparation of cis-9,10-disubstituted derivatives of cis-decalin and the attempted synthesis of tricyclo[4.4.4.0^1]tetradecane (Scheme 6).
for cis-decalin) and showed the expected ratios of these protons to the protons in other environments, e.g., on the side-chains. Thirdly, the appearance of unsplit resonance peaks for the side-chain methylene protons in compounds (XXXII) to (XXXIV) indicated that these methylene groups were in quaternary positions, i.e., at C-9 and C-10.

Catalytic hydrogenation of the octalin diacid \(^{53}\) (XVII) in glacial acetic acid, using platinum oxide (Adam's catalyst), gave the corresponding decalin-cis-9,10-dicarboxylic acid (XXVI), m.p. 190-191\(^0\) (foaming) (lit. \(^{53}\) m.p. 192\(^0\) (decomp.)). Treatment of this acid with diazomethane in ether-glyme gave the known dimethyl ester derivative (XXVII), m.p. 60-62.5\(^0\) (lit. \(^{53}\) m.p. 63\(^0\)).

The decalin diacid (XXVI) was dehydrated with concentrated sulfuric acid giving a nearly quantitative yield of the dicarboxylic anhydride (XXVIII), m.p. 94-96\(^0\) (lit. \(^{55}\) m.p. 95-96\(^0\)). The n.m.r. spectrum of this compound consisted simply of a partly resolved doublet at \(\tau\) 8.40 for the ring protons. The infrared spectrum of (XXVIII) showed the two characteristic absorption bands for the five-membered cyclic anhydride at 1850 and 1785 cm.\(^{-1}\).

Two attempted preparations of decalin-cis-9,10-dicarbonyl chloride (XXIX) from the decalin anhydride (XXVIII) by (a) fusion with phosphorus pentachloride and anhydrous zinc chloride at 150\(^0\), and (b) reaction with dichloromethyl dimethylamine in N,N-dimethylformamide \(^{59}\) at 75\(^0\), were unsuccessful. In each case the starting decalin anhydride was recovered, m.p. and mixed m.p. with authentic material 93-95\(^0\).

Decalin-9,10-dicarboximide (XXX) was prepared by fusing the decalin anhydride (XXVIII) with urea at 180\(^0\). The imide gave a melting point of 187-188\(^0\) (lit. \(^{53}\) m.p. 188-189\(^0\)). The infrared spectrum of this compound showed absorption bands at 1780 and 1720 cm.\(^{-1}\), characteristic \(^{51f}\) of a cyclic imide function. The urea fusion method used here was considered to be an improvement over the literature preparation, \(^{53}\) which involved the use of concentrated ammonia
at 150° in a closed system.

Reduction of the decalin anhydride (XXVIII) with lithium aluminum hydride in glyme gave a 93% yield of the decalin dialcohol (XXXI), m. p. 183-184°. The infrared spectrum of (XXXI) showed a characteristic absorption band at 3250 cm. \(^{-1}\) for the hydroxyl group, while the n. m. r. spectrum showed a triplet at 5.78 (J = 5.0 c. p. s.) a doublet at 6.60 (J = 5.0 c. p. s.), and a singlet at 8.60 in the ratio of 1:2:8. The first two sets of peaks indicated a hydroxymethyl group, while the high field singlet corresponded to the ring protons of the cis-decalin system.

Treatment of the decalin dialcohol with acetic anhydride and a catalytic amount of sulfuric acid gave the diacetate derivative (XXXII), m. p. 80.0 - 80.5°. The diacetate was characterized by its infrared spectrum, which gave absorption bands at 1740 and 1240 cm. \(^{-1}\), characteristic of an acetate function. The n. m. r. spectrum confirmed the structure of (XXXII).

Further evidence for the absence of rearrangement during the acetylation of (XXXI) was obtained by reducing a small amount of the diacetate derivative (XXXII) with lithium aluminum hydride in refluxing glyme. The white solid product was identified as the decalin dialcohol (XXXI) by its m. p., 183-184°, undepressed on admixture with authentic material. In addition, the infrared spectra of the reduction product and the decalin dialcohol (XXXI) were identical.

The decalin dialcohol (XXXI) was converted to 12-oxatricyclo[4.4.3.0]tridecane (XXXIII) by two methods. First, the dialcohol was treated with p-toluenesulfonic acid in refluxing benzene giving a nearly quantitative yield of the cyclic ether. Secondly, the dialcohol was reacted with one mole-equivalent of methanesulfonyl chloride in dry pyridine at 0°, giving the same product in 26% yield. The cyclic ether was purified by gas-liquid chromatography, m. p. 61-62°, and existed as a waxy white solid. The infrared spectrum showed
strong absorption bands at 1060 and 925 cm.⁻¹, characteristic of a five-membered ring ether, while the n.m.r. spectrum showed singlets at 56.38 (-CH₂O⁻) and 8.54 (-CH₂⁻) in the ratio of 1:4.

The treatment of the decalin dialcohol (XXXI) with two mole-equivalents of methanesulfonyl chloride in dry pyridine at -5° gave a 90% yield of cis-9,10-bis(mesyloxymethyl)decalin (XXXIV), m.p. 126.5 - 128°. The infrared and n.m.r. spectra of this compound gave the required evidence for its structure. In addition, treatment of the decalin dimesylate (XXXIV) with lithium aluminum hydride in dry glyme gave the tricyclic ether (XXXIII), identified by its infrared spectrum and g.l.c. tracing.

The preparation of cis-9,10-bis(cyanomethyl)decalin (XXXV) by the reaction of the decalin dimesylate (XXXIV) with a metal cyanide in an aprotic dipolar solvent was unsuccessful. The preparation was attempted using sodium cyanide in dry dimethyl sulfoxide at 130°, cuprous cyanide in refluxing pyridine, and sodium cyanide in diethylene glycol dimethyl ether at 120°. Each reaction was run under anhydrous conditions. In each case some unreacted decalin dimesylate was recovered (identified by comparison of infrared spectra and melting points). In addition, the cuprous cyanide-pyridine method gave a small amount of the tricyclic ether (XXXIII), identified by its infrared spectrum.

Scheme 7.

A Diels–Alder condensation of acetylenedicarboxylic acid with two moles of 1,3-butadiene gave Δ₂,⁶-hexalin-9,10-dicarboxylic anhydride (XXXVII), which necessarily had a cis-orientation of functional groups at the C-9 and C-10 position. The preparation of other tricyclic compounds in this series inferred that the cis-orientation was being retained throughout. The retention of the Δ₂,⁶-hexalin system throughout the series was also shown by a ratio of 1:2 for the olefinic and allylic protons in the n.m.r. spectra of the various compounds. The n.m.r.
Figure 7. Reaction sequence for the preparation of cis-9,10-disubstituted derivatives of cis-Δ
2,6-hexalin and the synthesis of the tricyclo [4. 4. 4. 0]tetradecane ring system (Scheme 7).
spectra of compounds (XLII) to (XLIV) showed single unsplit resonance peaks for the side-chain methylene protons, indicating that these methylene groups were in quaternary positions, i.e., at C-9 and C-10.

Treatment of the monopotassium salt of acetylenedicarboxylic acid with dilute sulfuric acid, followed by extraction of the product with diethyl ether, gave a 79% yield of acetylenedicarboxylic acid (XXXVI), m. p. 178-180° (lit. 62 m.p. 175-176°).

The Diels-Alder condensation of (XXXVI) with two mole-equivalents of 1,3-butadiene in glyme at 190° gave a 31% yield of $\Delta^2,6$-hexalin-9,10-dicarboxylic anhydride (XXXVII), m. p. 99.5-101° (lit. 55 m.p. 102-103°). The crude hexalin anhydride could best be isolated through a direct distillation of the reaction mixture, b. p. 140-145°/3 mm. Any mono-adducts, which were present in the product, were removed on extraction of a diethyl ether solution of the crude product with aqueous 10% sodium carbonate solution. The hexalin anhydride was not hydrolyzed under these conditions. The infrared spectrum of (XXXVII) showed two strong absorption bands at 1840 and 1770 cm$^{-1}$, characteristic of a 1,2-cyclic dicarboxylic anhydride 51a. The n. m. r. spectrum showed a multiplet at 74.10 (olefinic H) and a complex quartet centered at 7.62 (allylic H) in the ratio of 1:2. The reasons for the appearance of a complex quartet for the allylic protons will be discussed later.

Fusion of the hexalin anhydride (XXXVII) with urea at 180° led to the cyclic imide analog (XXXVIII), m. p. 218-219° (sealed tube). The infrared spectrum of this compound showed the two strong absorption bands at 1750 and 1700 cm$^{-1}$, characteristic 51f of a cyclic imide function, while the n. m. r. spectrum showed the olefinic and allylic protons to be in a ratio of 1:2.
The hexalin anhydride (XXXVII) was hydrolyzed in a refluxing aqueous 10% sodium hydroxide solution, containing 10% ethanol, to give an 86% yield of the corresponding hexalin diacid (XXXIX), m. p. 226-227° (foaming) (lit. m. p. 226° (decomp.)). The known dimethyl ester derivative (XL) was obtained from the treatment of the diacid with diazomethane in ether-glyme. The dimethyl ester had m. p. 96.5 - 98° (lit. m. p. 100°).

Reduction of the hexalin anhydride (XXXVII) with lithium aluminum hydride in refluxing glyme gave a nearly quantitative yield of cis-9,10-bis(hydroxymethyl)-Δ²,6-hexalin (XLII), m. p. 174.5 - 176° (sealed tube). The infrared spectrum showed absorption bands at 3300 cm⁻¹ (hydroxyl group) and 1660 cm⁻¹ (carbon-carbon double bond). The n. m. r. spectrum showed a triplet at δ 5.43 coupled with a doublet at 6.60 (J = 5.0 c. p. s.), indicating a hydroxymethyl group in a quaternary position, in addition to a 1:2 ratio for the olefinic and allylic protons at δ 4.48 and 8.07, respectively. The diacetate derivative (XLII) of the hexalin dialcohol (XL) was prepared by heating the alcohol with acetic anhydride, containing a catalytic amount of sulfuric acid. The diacetate was purified by sublimation at 80°/1 mm., m. p. 65.5 - 67.0°. The infrared and n. m. r. spectra confirmed the structure of (XLII).

Treatment of the hexalin dialcohol (XL) with two mole-equivalents of methanesulfonyl chloride in pyridine at -5° gave a 92% yield of the corresponding dimesylate (XLIII), m. p. 115-116°. The infrared spectrum of (XLIII) showed absorption bands at 3020 and 1650 cm⁻¹, indicating a partly substituted carbon-carbon double bond, and at 1340 and 1175 cm⁻¹ characteristic of a mesylate group.

The reaction of (XLIII) with sodium iodide in refluxing N,N-dimethylformamide, under anhydrous conditions, gave a 59% yield of cis-9,10-bis(iodomethyl)-Δ²,6-hexalin (XLIV), m. p. 98-99°. The progress of this reaction was followed
by thin-layer chromatography. Periodic samples of the reaction mixture were spotted on glass plates coated with silica gel G (Stahl), developed with chloroform, dried, and sprayed with a basic potassium permanganate solution. Samples of the authentic hexalin dimesylate (XLIII) and tricyclic ether (L) were run concurrently in order to establish their presence or absence in the samples of the reaction mixture. It was shown that a small amount of (L) probably did form during the reaction, although it was not isolated in the work-up. The reaction usually went only to 90% completion; 10% of the starting hexalin dimesylate was usually recovered. The reaction of quantities of the dimesylate larger than 10 g. led to much lower yields of the product hexalin diiodide (XLIV) even though the quantities of the various starting reagents were scaled up proportionately. The hexalin diiodide was characterized by its infrared and n. m. r. spectra. The latter showed a 1:2 ratio of the olefinic and allylic protons in addition to a sharp singlet at \( \tau 6.34 \), which indicated four protons in the form of two -CH\(_2\)I groups in quaternary positions.

The treatment of (XLIV) with lithium aluminum hydride in refluxing glyme gave a 40% yield of cis-9,10-dimethyl-\( \Delta^2,6 \)-hexalin (XLV). The crude product was purified by g. l. c., which showed the presence of a small amount of by-product from the reaction. The dimethyl hexalin was a volatile, waxy solid, m. p. 69-71° (sealed tube). In addition to the infrared and n. m. r. spectra of this compound, its mass spectrum* was also obtained. This spectrum showed a parent ion peak at m/e 162, corresponding to a molecular weight of 162 for (XLV) (calc. mol. wt. 162.3). The principal fragmentation reactions were (a) loss of methyl radical, (b) loss of butadiene, (c) consecutive loss of both methyl radical and butadiene, and (d) formation of the cycloheptatrienyl cation.

Figure 7. (continued)
The n.m.r. spectrum of the by-product (amounting to about 5% of the total product, from analysis of the g.l.c. tracing) showed singlets at $\tau$ 8.16 (allylic H) and 8.55 (saturated-ring H). This compound was tentatively identified as tricyclo[4.4.2.0\textcircled{3}]3,8-dodecadiene (XLVI), assuming that the resonance peak for the olefinic protons was lost in the high background noise (the n.m.r. sample was very dilute – about 2%). The compound was not analysed for its elemental composition due to scarcity of material.

The dimethylhexalin (XLV) was observed to take up two mole-equivalents of hydrogen, on quantitative catalytic hydrogenation over platinum oxide (Adam's catalyst), and give a 78% yield of cis-9,10-dimethyldecalin (XLVII). The comparatively low yield in this reaction was primarily due to the moderate volatility of the product. The product was shown to be pure by g.l.c., m.p. 89-91° (sealed tube). The n.m.r. spectrum of this compound showed a broad singlet at $\tau$ 8.50 (saturated-ring H) and a sharp singlet at 9.12 (CH$_3$-) in the ratio of 8:3. The mass spectrum of (XLVII) showed a parent ion peak at m/e 166, corresponding to a molecular weight of (XLVII) of 166 (calc. 166.3). The principal fragmentation reactions were the loss of methyl, C$_4$H$_9$, C$_5$H$_{11}$ and C$_6$H$_{11}$ radicals.

The addition of a second carbon atom onto the side-chains of the $\Delta^2,6$-hexalin system was accomplished by reacting the hexalin dimesylate (XLIII) with an excess of a metal cyanide in a dipolar aprotic solvent. The best yield of the corresponding bis(cyanomethyl)hexalin (XLVIII), 21%, was obtained by the reaction of (XLIII) with excess sodium cyanide in N-methyl-2-pyrrolidinone at 175° for four hours. The tricyclic ether (L) was isolated as a by-product in 13% yield. The crude product obtained from this reaction was treated with diethyl ether and petroleum ether (b.p. 30-60°) to induce crystallization of the dinitrile. Recrystallization from benzene-petroleum ether (b.p. 65-110°) gave the pure material, m.p. 152-153°. The remainder of the crude product was distilled at 60°/1 mm. to give the tricyclic ether (L), which on further purification by g.l.c., gave $n_{20}^D$ l. 5312. An appreciable amount of intractable material remained after the distillation,
The hexalin dinitrile (XLVIII) was characterized by a nitrile absorption band at 2260 cm.\(^{-1}\) and a carbon-carbon double bond band at 1660 cm.\(^{-1}\) in the infrared. The n.m.r. spectrum showed a 1:2 ratio for the olefinic and allylic protons in addition to a singlet at \(\tau 7.54\) indicating four protons in the form of two -CH\(_2\)CN groups at quaternary positions. The tricyclic ether (L) was also characterized by its infrared and n.m.r. spectra.

Lower yields of the hexalin dinitrile (XLVIII) were obtained using sodium cyanide in N,N-dimethylformamide (DMF) and in dimethyl sulfoxide (DMSO), cuprous cyanide in pyridine and in DMF, and mercuric cyanide in DMF. The sodium cyanide-DMF method gave a 13% yield of (XLVIII), a trace of (L), and a 10% yield of the tricyclic aminonitrile (XLIX), while the sodium cyanide-DMSO method gave yields of 8 and 11.5% of (XLVIII) and (XLIX), respectively. The reactions employing cuprous cyanide and mercuric cyanide failed to produce any nitrile product, as shown by the infrared spectra of their corresponding product mixtures.

The tricyclic aminonitrile (XLIX) had a melting point of 157-158\(\circ\)C; mixed m.p. with its dinitrile isomer (XLVIII), 125-140\(\circ\)C. The structure of (XLIX) was inferred from its infrared, ultraviolet, and n.m.r. spectra. The infrared spectrum showed absorption bands at 3450 and 3380 cm.\(^{-1}\) (primary amine), 2190 (conjugated nitrile), 1650 (carbon-carbon double bond plus NH deformation), and 1600 (conjugated carbon-carbon double bond). The n.m.r. spectrum (13% in DMSO) showed singlets at \(\tau 3.63\) (\(-\text{NH}_2\) at a quaternary position), 4.45 (four olefinic protons), and 8.09 (ten allylic protons). The ultraviolet spectrum (ethanol solution) showed an absorption band at 269 m\(\mu\) (\(\epsilon = 10,800\)), which shifted to 264 m\(\mu\) (\(\epsilon = 1340\)) on addition of sulfuric acid. These ultraviolet characteristics were indicative of a 3-cyano-eneamine function.

Treatment of the hexalin diiodide (XLIV) with sodium cyanide in DMF, under anhydrous conditions, resulted in a 59% yield of the dinitrile (XLVIII). None of the
isomeric nitrile (XLIX) was found in the crude product. Although this preparation of (XLVIII) gave a good yield, its use was precluded by the low yields experienced when trying to prepare large quantities of the hexalin diiodide (XLIV).

Alkaline hydrolysis of the hexalin dinitrile (XLVIII) gave an 81% yield of the corresponding diacid (LI), m.p. 230-233°. A quantitative yield of its dimethyl ester derivative (LII) was obtained by treating the acid with diazomethane in ether-glyme. The dimethyl ester was distilled at 152°/1.5 mm.; its purity checked by g.l.c. The n.m.r. spectrum of (LII) showed a triplet at τ 4.45 (olefinic H), and singlets at 6.39 (CH₂O₂C⁻), 7.64 (-CH₂CO⁻), and 7.90 (allylic H), in the ratio of 2:3:2:4.

Reduction of the dimethyl ester (LII) with lithium aluminum hydride in refluxing glyme gave a rather low yield (62%) of cis-9,10-bis(2-hydroxyethyl)-Δ²,₆-hexalin (LIII), m.p. 149.5 - 150.5°. No other products were isolated from the reaction. The infrared spectrum of (LIII) showed the characteristic broad absorption band at 3300 cm⁻¹, indicative of a hydroxyl group.

Treatment of the dialcohol (LIII) with freshly distilled phosphorus tribromide in glyme gave a very low yield (16%) of the corresponding dibromide (LIV), m.p. 132-133°. The n.m.r. spectrum of (LIV) showed the expected coupled triplets (J = 8.5 c.p.s.) for the side chain 2-bromoethyl groups. The dibromide was converted to its diiodide analog (LVI) on reaction with sodium iodide in dry acetone. The yield of (LVI) from this reaction was 76%, m.p. 147-148° (decomp). Just as for the case of the dibromide, the n.m.r. spectrum of the diiodide analog showed two triplets for the two different methylene groups in each of the 2-iodoethyl side-chains (J = 9.0 c.p.s.).

A larger overall yield of the bis(2-iodoethyl)hexalin was obtained from the dialcohol (LIII) by first treating the dialcohol with excess methanesulfonyl chloride.
Figure 7. (continued)
in pyridine at -10°, thus forming the dimesylate derivative (LV), yield 70%, m.p. 124-125° (decomp.). Treatment of this compound with sodium iodide in dry acetone gave a 46% yield of diiodide (LVI).

The coupling of the two iodoethyl groups in cis-9,10-bis(2-iodoethyl)-
\[\Delta^2,6\]-hexalin (LVI) to form a third six-membered ring, and hence tricyclo
[4.4.0]3,8-tetradecadiene (LVIII), was attempted using n-butyllithium in
diethyl ether and in heptane. Two products were obtained from each reaction
and were tentatively identified as cis-9-ethyl-10-vinyl-\[\Delta^2,6\]-hexalin (LVII)
and the expected product, tricyclo[4.4.0]3,8-tetradecadiene (LVIII). The yields
of (LVII) and (LVIII) were 37 and 9%, respectively, from the reaction in diethyl
ether and 35 and 4%, respectively, from the reaction in heptane.

The evidence for the structure of (LVII) may be summarized as follows. The infrared spectrum of (LVII) showed absorption bands at 3030 and 1660 cm.\(^{-1}\), characteristic of a 1,2-disubstituted cis-olefin. The absorption bands at 3080, 1640, and 912 cm.\(^{-1}\) indicated the presence of a terminal vinyl group. A quantitative elemental analysis of (LVII) gave a formula of C\(^{14}\)H\(^{20}\), which corresponds to a molecular weight of 188. This value was supported by the analysis of the mass spectrum of (LVII), which showed a parent ion peak at m/e 188. In addition, the mass spectrum showed strong fragment peaks corresponding to the facile loss of ethyl radical and butadiene. The loss of butadiene inferred the presence of a cyclohexene ring which was partly or wholly substituted at its homoallylic positions only. The absence of an absorption peak in the ultraviolet spectrum of (LVII) ruled out the presence of a conjugated diene function. The n.m.r. spectrum of (LVII) showed resonance peaks at 7.4, 4.0, 8.10, 8.71 and 9.25, which were interpreted as being due to the expected presence of olefinic, allylic, acyclic methylene, and methyl protons, respectively. The methyl resonance peak was actually a triplet, which suggested the presence of an ethyl group; however, the corresponding quartet structure for the adjacent methylene protons
was not readily distinguishable. The n. m. r. data which did not correspond to the assigned structure of (LVII) were (a) the absence of a resonance peak (or peaks) at around 5.2 for the methylene protons of the terminal vinyl group and (b) an observed ratio of 4:8:4:4, respectively, for the four previously mentioned kinds of protons, which did show up in the n. m. r. spectrum, instead of the expected ratio of 4:8:2:3. These apparent discrepancies were probably caused by the moderate amount of background noise in the n. m. r. spectrum - the spectrum was obtained from a dilute microsample.

Evidence for the assigned structure for (LVIII) was based on the analysis of its infrared, n. m. r. and mass spectra. The infrared spectrum showed absorption bands at 3030 and 1660 cm$^{-1}$, indicating the presence of a 1,2-disubstituted cis-olefin. The rest of the absorption bands were characteristic of an otherwise saturated hydrocarbon. The expected molecular weight of 188 for (LVIII) was shown by the mass spectrum, which contained a parent ion peak at m/e 188. The facile loss of butadiene was shown by a strong fragment peak at m/e 134. This loss of butadiene inferred the same type of ring structure as in (LVII). The losses of other simple fragments from the parent ion were small, indicating that the molecule had no terminal alkyl groups. Two very dilute n. m. r. microsamples of (LVIII) - one from the reaction in diethyl ether and the other from heptane - gave weak spectra which were only somewhat similar. Each spectrum showed a resonance peak for the olefinic protons; however, the allylic and saturated-ring proton resonance peaks were not reproducible.

Attempted cyclizations using zinc and magnesium in various solvents failed to yield any of the expected tricyclic compound (LVIII) as the major product. The reaction of the diiodide (LVI) with zinc in refluxing glyme gave (LVII) in a 27% yield, together with three minor products which could not be separated by g. l. c. The reaction of (LVI) with magnesium in tetrahydrofuran gave a 15% yield of (LVII) and a 7% yield of a compound whose infrared spectrum showed absorption
CH₂CH₂I → Zn, glyme → CH₂CH₃ + 3 minor products

CH₂CH₂I → Mg, THF → CH₂CH₃ + 1 minor product

CH₂CH₂I → Mg, heptane → + 3 minor products

LVI → mixture of at least 4 components

Figure 7. (concluded)
bands characteristic of an unsaturated hydrocarbon. Half of the starting material was recovered unreacted.

The attempted cyclization of the diiodide (LVI) using magnesium in heptane resulted in the thermal decomposition of (LVI) - the reaction solvent evaporated during the overnight reflux. The subsequent work-up of the reaction mixture and separation of the crude product oil by g. l. c. gave a 12% yield of a compound tentatively identified as tetracyclo[4.4.2.1.8.2.3.6.0]tetradecane (LIX). The g. l. c. tracing also showed the presence of three minor components, which were too small to be collected.

The evidence for the structure of (LIX) may be summarized as follows. The infrared spectrum showed the absence of any absorption bands characteristic of an olefinic group, but did show bands characteristic of an aliphatic hydrocarbon. The n. m. r. spectrum (dilute microsample) showed a single resonance peak at \( \tau 8.4 \), characteristic of a saturated cyclic hydrocarbon. The mass spectrum showed a parent ion peak at m/e 190, as expected, indicating that (LIX) contained two more hydrogen atoms than the diiodide (LVI). The fragmentation pattern showed a negligible loss of methyl radical, a moderate loss of ethyl radical, and small equal losses of C\(_3\) to C\(_6\) fragments. The peak at m/e 136, which would correspond to a loss of butadiene, was conspicuously absent.

The final cyclization attempt using magnesium in glyme gave very small amounts of four products (separated by g. l. c.). The infrared spectra of these products were different from the infrared spectra of the products isolated from the other cyclization attempts.

B. N. M. R. Spectra - AB Systems

In the course of characterizing the compounds in the cis-\( \Delta^2 \)-octalin and cis-\( \Delta^2,6 \)-hexalin series by means of their n. m. r. spectra, it was found that for
some compounds the side-chain and allylic methylene protons exhibited multi-fold splittings. Simple AB-quartet spectra were exhibited by the side-chain methylene protons in the octalin derivatives (XXII) to (XXIV), inclusive, and by the ether ring methylene protons in (XXI).

\[
\text{XXI}
\]

\[
\text{XXII, } X = -\text{OAc} \\
\text{XXIII, } X = -\text{OMs} \\
\text{XXIV, } X = -\text{I}
\]

The following resonance parameters were calculated using the equations presented by Jackman\(^68\) for the analysis of an AB system; the chemical shifts of protons A and B, the coupling constant \(J_{\text{AB}}\), and the ratio of the intensities of the outer to the inner lines. The latter parameter was also obtained experimentally from the integrated areas of the corresponding lines.
TABLE II

AB Quartet Parameters Calculated from the
N.M.R. Spectra of Some cis-Δ²-Octalin Derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shift (τ)</th>
<th>J&lt;sub&gt;AB&lt;/sub&gt; (c.p.s.)</th>
<th>Intensity Ratio</th>
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<tr>
<td></td>
<td>A</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>XXI</td>
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<td>6.51</td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>XXIII</td>
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</tr>
<tr>
<td>XXIV</td>
<td>6.40</td>
<td>6.52</td>
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</tr>
<tr>
<td></td>
<td>7.8</td>
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</tr>
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<tr>
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<tr>
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<td>0.12</td>
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<tr>
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</table>

The allylic protons in each of Δ²-Octalin-9,10-dicarboxylic anhydride (XIX) and -dicarboximide (XII), together with the Δ²,6-hexalin analogs (XXXVII) and (XXXVIII), exhibited a group of resonance peaks having the general shape of an AB system. The spectra of these protons were complicated, however due to spin-spin coupling with the neighbouring olefinic proton(s), which caused additional splittings to appear in the four main resonance peaks. For the two octalin derivatives, each of the AB peaks was split into a partly resolved doublet. The concurrent splitting of the olefinic proton resonance peak into a partly resolved triplet indicated that the allylic protons formed the AB part of an ABX system.
For the two hexalin derivatives, the two higher field peaks (B protons) were relatively sharp singlets, while the two lower field (A protons) peaks were partly resolved multiplets containing at least five lines each. The corresponding olefinic proton resonance peak was also a multiplet containing at least five lines.

C. Low Temperature N.M.R. Spectra - Kinetic Studies

In order to investigate the effect on the rate of interconversion, of substituting alkyl groups into the C-9 and C-10 positions of cis-decalin, low temperature n.m.r. spectra were obtained for cis-9,10-dimethyldecalin (XLVII) and 12-oxatricyclo[4.4.3.0]tridecane (XXXIII). Low temperature spectra of cis-decalin were also obtained for comparison purposes. The spectra were recorded on a Varian A-60 n.m.r. spectrometer, fitted with a Varian V-6040 temperature controller assembly and a Varian V-6031 variable temperature probe assembly. The samples used were 15% (w./v.) solutions of the decalin derivative in chloroform placed in 5 mm. o.d. thin-walled glass capillary tubes. The spectra of these samples were obtained at successively lower temperatures. About twenty minutes was considered to be sufficient time for the probe to reach thermal equilibrium after each change in temperature. The lowest temperature, to which the sample probe was taken, was -60°, in accordance with the manufacturer's specifications. The spectra were obtained with sweep widths of 50 or 100 c.p.s. and a sweep time of 250 sec.

The n.m.r. spectra of cis-decalin (Fig. 8) taken at 0 and -50°, each showed two main resonance peaks - the small one due to the two bridgehead protons, the large one due to the sixteen protons in the eight methylene groups. The spectrum at 0° showed the peaks to be centered at τ8.39 and 8.57, respectively, giving a separation of 11 c.p.s. The width at half-height of the larger peak was 9 c.p.s. The spectrum at -50° showed a more defined peak for the bridgehead protons together with small undulations on either side of the main resonance group. This peak had
Figure 8. N.m.r. spectra of cis-decalin taken at 0 and $-50^\circ$ with a sweep width of 100 c.p.s. and a sweep time of 250 sec.
also shifted 2 c.p.s. further down-field from the methylene proton peak. The width at half-height of the methylene proton peak increased to 10 c.p.s.

N.m.r. spectra of cis-9,10-dimethyldecalin were taken at +25, 0, -20, and -50°. The resonance peak for the methylene protons (Fig. 9) showed no fine structure at 25° and had a width at half-height of 10 c.p.s. At 0° the peak had broadened somewhat at its apex and showed some splitting. A number of small peaks appeared on the low-field side of this peak. At -20° the methylene proton peak was partly resolved into four lines of more or less equal intensity. No further splitting of this peak took place at -50°. In addition, the width at half-height of the methylene proton peak remained constant at 10 c.p.s. throughout the temperature range. No change in the resonance peak for the methyl protons was noticed. This peak was a sharp singlet in each spectrum, having a width at half-height of about 1.5 c.p.s. In each spectrum a sharp, resolved resonance peak (width at half-height about 0.5 c.p.s.) was obtained for the internal standard, tetramethylsilane (TMS).

The effect on the rate of interconversion of adding a third ring across the C-9 and C-10 positions in cis-decalin was investigated by obtaining the n.m.r. spectrum of 12-oxatricyclo[4.4.3.0]tridecane at a series of temperatures between 0 and -60°. The spectra showed a twelve-fold increase in the width at half-height of the resonance peak for the methylene protons in the five-membered ether ring (Fig. 10) as the sample temperature was decreased from 0 to -60°. On the other hand, the width at half-height of the resonance peak for the six-membered ring protons increased from 2 c.p.s. at 0° to only 4 c.p.s. at -60°, i.e., this resonance peak remained as a relatively sharp singlet. In each spectrum a sharp, resolved resonance peak (width at half-height about 0.5 c.p.s.) was obtained for the TMS internal standard. The broadening of the resonance peak for the ether ring protons, therefore, indicated that the rate of interconversion of the molecule
Figure 9. N.m.r. spectra of the ring methylene protons of cis-9,10-dimethyl-decalin taken at 25, 0, -20 and -50° with a sweep width of 100 c.p.s. and a sweep time of 250 sec.
Figure 10. N.m.r. spectra of the ether ring protons of 12-oxatricyclo[4.4.3.0]tridecane taken at 0, -40, and -60° with a sweep width of 50 c.p.s. and a sweep time of 250 sec.
was decreasing. The still rather pointed shape of this resonance peak at -60° indicated that the spectra had been obtained in the region above the coalescence temperature (this temperature is usually associated with a flattened resonance peak); hence, the activation energy (Ea) for the interconversion was calculated from the "fast exchange region" equation developed by Piette and Anderson: 12

\[ \log (\pi \Delta \nu T_2 - 1) = \log \left( \frac{V_T}{2V_0} \right) + \frac{E_a}{2.303RT}, \]

where \( \Delta \nu \) = full width at half-height (c.p.s.)

\( T_2 \) = transverse relaxation time (sec.)

\( V \) = second moment

\( V_0 \) = Arrhenius frequency factor.

The value of \( T_2 \) was not experimentally determined for the ether methylene proton resonance; however, it was assumed to be of the order of 1 sec. The data from the n.m.r. spectra of the tricyclic ether together with the parameters calculated from Piette and Anderson's equation (assuming \( T_2 \approx 1 \) sec.) are given in Table 3.

**TABLE III**

<table>
<thead>
<tr>
<th>Temperature (°K)</th>
<th>( 10^3/T )</th>
<th>( \Delta \nu ) (c.p.s.)</th>
<th>( \log (\pi \Delta \nu T_2 - 1) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>273</td>
<td>3.66</td>
<td>0.80</td>
<td>0.18</td>
</tr>
<tr>
<td>253</td>
<td>3.95</td>
<td>1.35</td>
<td>0.51</td>
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<tr>
<td>243</td>
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<td>223</td>
<td>4.48</td>
<td>4.20</td>
<td>1.10</td>
</tr>
<tr>
<td>213</td>
<td>4.70</td>
<td>10.3</td>
<td>1.50</td>
</tr>
</tbody>
</table>

The plot of \( \log (\pi \Delta \nu T_2 - 1) \) against \( 1/T \) (Fig. 11) gave a slope of 1.83 x \( 10^3 \), from which a value of the energy of activation (Ea) of 8.4 kcal./mole was calculated. Errors in the measurement of the temperatures (\( \pm 1 \)°) at which the spectra were taken and of the widths at half-height (\( \pm 0.2 \) c.p.s.) of the
Figure 11. Plot of a function of $\log k$ for the ring interconversion in 12-oxatricyclo[4.4.3.0]tridecane against $1/T$. 
resonance peaks contributed to a calculated deviation of $\pm 2 \text{ kcal.}/\text{mole}$ for the value of $E_a$. 
A. Synthesis

The syntheses of cis-9,10-dimethyl-Δ^2-octalin (XXV) and Δ^2,6-hexalin (XLV) were carried out using analogous two-step sequences starting with the dimesylates (XXIII) and (XLIII), respectively.

In the first step each dimesylate was treated with sodium iodide in refluxing DMF, giving yields of 9% of the octalin diiodide (XXIV) and 59% of the hexalin diiodide (XLIV), respectively. The difference in the yields reflected the difference in the steric environments of the side-chain methylene groups in the two dimesylates (this idea will be discussed later). The diiodide derivatives were then treated with lithium aluminum hydride in glyme, giving the corresponding dimethyl derivatives (XXV) and (XLV). The reaction involving the hexalin diiodide also produced a small amount of by-product, which was tentatively identified as tricyclo[4.4.2.0]4,8-dodecadiene (XLVI). The compound probably resulted from the attack of the hydride ion complex (ZH^-) on one iodine atom, followed by nucleophilic displacement of the iodine atom on the remaining iodomethyl group by the intermediate carbanion.
The dimethyldecalin (XLVII) was easily prepared through catalytic hydrogenation of the dimethylhexalin (XLV).

The two-step sequences used here were made necessary by the fact that the attempted direct displacement of the mesylate groups in the decalin dimesylate (XXXIV) with hydride ion gave the tricyclic ether (XXXIII) rather than the dimethyl derivative (XLVII). This result has been explained by Stork to be due mainly to steric hindrance to attack of the hydride ion complex at the side-chain methylene carbon atom.

The most direct method, which was considered to be feasible for the synthesis of the tricyclo[4.4.4.0]tetradecane ring system, consisted of the addition of a four carbon atom moiety across the 9,10-double bond in $\Delta^9$-octalin or a derivative. The experimental approaches to this method (Schemes 1, 2 and 3) involved the attempted 1,4-addition of 1,3-butadiene to $\Delta^9$-octalin (VII) or a derivative, both thermally (Diels-Alder reaction) and photochemically. Thus, Scheme 1, which was based on the work of Fieser and Dunn and Inhoffen and co-workers, consisted of the preparation of 1,4,5,8-naphthodiquinone, to be followed by a Diels-Alder condensation with 1,3-butadiene and subsequent reduction.
of the adduct. This synthetic route was ruled out, however, when repeated attempts to oxidize naphthazarin (I) to 1, 4, 5, 8-naphthodiquinone (III), according to the method of Zahn and Ochwat, were unsuccessful.

Some unconjugated olefins such as ethylene and norbornadiene (bicyclo[2. 2. 1]-2, 5-heptadiene) had been reported to give albeit low yields of Diels-Alder adducts from reactions with 1, 3-butadiene at about 200°. Although the analogous reaction between \( \Delta^9 \)-octalin (VII) and 1, 3-butadiene (Scheme 2) was expected to give a low yield of adduct also, this result would have been offset by the simplicity of the synthetic route. Hence, mixtures of the two starting materials, some-containing anhydrous aluminum chloride as a catalyst, were sealed in Carius tubes and heated at 200° for up to forty hours. It was hoped that the isolation of the desired product, tricyclo[4. 4. 4. 0]-3-tetradecene (VIII), could be carried out by g.l.c.; however, no compound with the expected chromatographic characteristics (e.g., long retention time) was detected in the various product mixtures.

The attempted photo-sensitized 1, 4-addition of butadiene to cyclohexene (Scheme 3) was based on work published on the photo-sensitized cyclo-dimerization of both cyclic and acyclic dienes. Cyclohexene was used in the initial attempt because it was more readily available than \( \Delta^9 \)-octalin. The result of the attempted addition was the formation of cyclo-dimers of butadiene, indicating that triplet state butadiene molecules were being formed; however, none of the expected adduct, \( \text{cis-} \Delta^2 \)-octalin (IX), could be isolated. At the same time as this work was being carried out, Hammond and Liu reported that attempts to react cyclohexene photochemically with 1, 3-cyclohexadiene and cyclopentadiene had also been unsuccessful.

The failure of the short reaction sequences to yield any compounds containing the tricyclo[4. 4. 4. 0]tetradecane ring system resulted in attempts to synthesize this ring system by the longer but potentially more secure routes outlined in
Schemes 4, 6, and 7. These schemes were based on the idea of preparing cis-9,10-bis(2-iodoethyl)decalin, cis-2,2'-octalin, and cis-2,6'-hexalin, followed by ring closure to the desired tricyclic ring system.

The failure to obtain cis-9,10-dicyano-2'-octalin (XVI) in Scheme 4 ruled out the possibility of synthesizing the tricyclo[4.4.4.0]tetradecane ring system through a series of 2'-octalin derivatives.

In Scheme 6 the preparation of decalin-9,10-dicarboxylic anhydride (XXVIII) served to establish the cis-decalin ring system. It remained now to carry out reactions using this anhydride so as to convert the two carbonyl groups into two 2-iodoethyl groups. The unsuccessful attempt to prepare the acid chloride (XXIX) from the anhydride ruled out the possibility of adding a carbon atom onto each carbonyl group through the reaction of the acid chloride with diazomethane, followed by thermal rearrangement in anhydrous methanol to form cis-9,10-bis(carbomethoxymethyl)decalin (Arndt-Eistert reaction):
A second attempt to add a carbon atom onto each of the carbonyl groups in the anhydride involved the two-step synthesis of cis-9,10-bis(mesyloxymethyl)decalin (XXXIV) from the anhydride, followed by an attempted nucleophilic displacement of the mesylate groups by cyanide ion. An examination of a molecular model of (XXXIV) showed that each of the side-chain methylene groups was in an environment similar to that for the methylene group in neopentyl p-toluensulfonate. This kind of compound is normally quite resistant to nucleophilic displacement, due to steric hindrance by the methyl groups towards a concerted "back-side" attack (S_N2 mechanism) of the nucleophile. Sugihara and co-workers, however, had reported a 56% yield of the corresponding nitrile from the reaction of neopentyl p-toluensulfonate with sodium cyanide in refluxing DMF. The enhanced rate of nucleophilic substitution (S_N2) in dipolar aprotic solvents over that in protic solvents has been recently reviewed. The employment of various dipolar aprotic solvents and metal cyanides, together with high reaction temperatures, failed to produce any of the desired decalin dinitrile (XXXV) from the decalin dimesylate (XXXIV). This result indicated that the side-chain methylene group in (XXXIV) was even more hindered than that in neopentyl p-toluensulfonate.

The steric hindrance to "back-side" attack was partly alleviated by the introduction of two carbon-carbon double bonds into the cis-decalin ring system, giving the cis-\( \Delta^2 \) hexalin system (Scheme 7). In addition to removing four interfering hydrogen atoms, the presence of the double bonds resulted in each of the rings adopting a half-chair conformation, thus flattening the rings. These changes in molecular structure and conformation resulted in a yield of 21% of the hexalin dinitrile (XLVIII) from the reaction of the hexalin dimesylate (XLIII) with sodium cyanide in N-methyl-2-pyrrolidinone (NMP) at 175°. Other solvent and metal cyanide combinations gave lower yields.

The yield of the hexalin dinitrile might have been higher but for the formation of two by-products. The first one, 12-oxatricyclo[4.4.3.0]3,8-tridecadiene (L),
was produced in small amounts in the sodium cyanide-DMSO and -DMF reactions but was isolated from the sodium cyanide-NMP reaction in a 13% yield. This compound was formed probably from the attack of the cyanide ion on one of the sulfur atoms in the hexalin dimesylate side-chain, displacing the alkoxide group, which subsequently displaced the mesylate group on the other side-chain:

![Chemical structure diagram]

The reason for this side-reaction was probably steric hindrance to the attack of the nucleophile at the side-chain methylene carbon atom. The nucleophilic attack at the sulfur atom is unfavourable (mesylate ion is a better leaving group than alkoxide ion); however, a highly reactive nucleophile, such as cyanide ion, would tend to become indiscriminate when confronted with steric hindrance at the favoured reaction site. This mechanism is similar to one presented by Stork to explain the formation of a tetrahydrofuran ring system in an attempted lithium aluminum hydride reduction of a related compound containing a 1,4-ditosylate moiety.

The second by-product, 12-amino-ll-cyano-tricyclo[4.4.3.0^3,8]tridecatriene (XLIX), was obtained in relatively moderate yields in the sodium cyanide-DMSO and -DMF reactions but was not isolated in the sodium cyanide-NMP reaction. This compound most likely resulted from a base catalysed internal condensation of the cyanomethyl groups (Thorpe reaction) in the initially
formed hexalin dinitrile (XLVIII), followed by tautomerization of the imino group to give the conjugated enamine function:

\[
\text{H} \quad \text{CHCN} \quad \text{C-CN} \quad \text{C=NH} \quad \text{C-CN} \\
\text{CH}_2\text{-C=N} \quad \text{XLIX}
\]

The subsequent conversion of cis-9,10-bis(cyanomethyl)-Δ²,⁶-hexalin (XLVIII) to cis-9,10-bis(2-iodoethyl)-Δ²,⁶-hexalin (LVI) was carried out in a five-step sequence. The best overall yield of the bis(idoethyl)hexalin from the corresponding bis(hydroxyethyl)hexalin (LIII) was obtained through the preparation of the dimesylate derivative (LV) of (LIII), followed by the nucleophilic displacement of the mesylate groups using sodium iodide in refluxing acetone. The relatively mild conditions, under which this nucleophilic displacement took place, contrasted sharply with the extreme conditions which had to be employed in the reactions of cis-9,10-bis(mesyloxymethyl)-Δ²,⁶-hexalin (XLIII) with sodium cyanide in NMP at 175° and sodium iodide in refluxing DMF.

The methods used for the attempted coupling of the two 2-idoethyl groups in (LVI) to give tricyclo[4.4.0]-3,8-tetradecadiene (LVIII) were modifications of two general methods, which had been used to prepare three-, four-, and six-membered ring systems. The two methods involved the Wurtz coupling of appropriate dihalide functions using (a) aryllithium compounds and (b) divalent metals such as zinc and magnesium. The reaction of the bis(idoethyl) hexalin (LVI) with one mole-equivalent of n-butyllithium in diethyl ether and in
heptane gave (in each solvent) two compounds, which were tentatively identified as cis-9-ethyl-10-vinyl-$\delta^2,6$-hexalin (LVII) and tricyclo[4.4.4.0$^{3,8}$]-3,8-tetradecadiene (LVIII), the expected product. The total yield of the two products in each reaction was about 40-50%. The ratio of the yield of (LVII) to (LVIII) was 4:1 in diethyl ether and 9:1 in heptane.

The reaction probably proceeded through the formation of the monolithium derivative of the hexalin diiodide (LVI) (in a 1:1 equilibrium with unreacted n-butyllithium). The ethyllithium side-chain then reacted with the remaining iodoethyl side-chain by displacing the iodine atom with (a) a transferred hydride ion to give (LVII) or (b) the partly formed carbanion to give (LVIII):

$$
\begin{align*}
\text{CH}_2\text{CH}_2\text{I} + n\text{-BuLi} & \rightleftharpoons \text{CH}_2\text{CH}_2\text{Li} + n\text{-BuI} \\
\text{CH}_2\text{CH}_2\text{I} & \xrightarrow{\text{(a)}} \text{CH}_2\text{CH}_2\text{CH}_3 + \text{LiI} \\
\text{CH}_2\text{CH}_2\text{I} & \xrightarrow{\text{(b)}} \text{CH}_2\text{CH}_2\text{Li} + \text{LiI}
\end{align*}
$$
The higher yield of the disproportionation product (LVII) than the coupling product (LVIII), in both diethyl ether and heptane, was probably due to steric hindrance to the close approach of the terminal methylene groups of the mono-lithium intermediate - the preferred conformation (in a molecular model) consists of the two side-chains pointing outwards from the rings in opposite directions, thus favouring mechanism (a). The increase in the yield of the coupling product (LVIII) in diethyl ether over that in heptane was probably due to a greater charge separation in the ethyllithium side-chain, which was brought about by the higher dielectric constant of diethyl ether.

The attempted cyclizations of cis-9,10-bis(2-iodoethyl)-Δ2,6-hexalin (LVI) using zinc in glyme and magnesium in THF, diethyl ether-glyme, and in heptane, each gave multi-component product mixtures. Of the products which were separated and isolated by g.l.c., none gave an infrared spectrum identical to that for the coupling product (LVIII). The principal product, isolated from most of the attempts, was the disproportionation product (LVII). The reason for the formation of this product was probably the existence of a preferred conformation similar to that mentioned in the case of the n-butyllithium reaction. In fact mechanism (a) probably holds true for the magnesium reaction (replacing -Li with -Mgl), since this mechanism is analogous to one put forward to explain the disproportionation reaction between ethyl magnesium bromide and n-propyl bromide.

The isolation of a small amount of tricyclo[4.4.4.0]3,8-tetradecadiene (LVIII) from the cyclization of cis-9,10-bis(2-iodoethyl)-Δ2,6-hexalin (LVI) demonstrates that the tricyclo[4.4.4.0]tetradecane ring system can be synthesized by the eleven step route outlined in Scheme 7. The catalytic hydrogenation of (LVIII) to give tricyclo[4.4.4.0]tetradecane, itself, was precluded, however, by a scarcity of (LVIII). A possibly more productive route, which had been previously considered, involves the cyclization of the dimethyl ester (LII) by means of an
acyloin condensation (using sodium in liquid ammonia) to form the desired tricyclic ring system. This route was not investigated initially, because the actual route followed (Scheme 7) was considered to lead more directly to (LVIII) and hence to tricyclo[4.4.4.0]tetradecane.

Two independent investigations into the synthesis of the tricyclo[4.4.4.0]tetradecane ring system have been reported in the recent literature. In the first paper, Snatzke and Zanati report the syntheses of the following compounds, which have also been described in this thesis: in the decalin series, compounds (XXXI), (XXXIII), and (XXXIV); in the cis-Δ^2,6-hexalin series, compounds (XXXVIII), (XL), (XLIII) and (L). The physical and spectral data for each of these compounds, which have been presented both in their paper and in this thesis, are in excellent agreement, except for the melting points of the dialcohols (XXXI) and (XLII). The values presented in this thesis are 18 and 50° higher, respectively. It appears that Snatzke and Zanati had prepared these compounds in order to add two two-carbon atom groups onto the C-9 and C-10 positions of cis-decalin and cis-Δ^2,6-hexalin in an attempt to synthesize the third six-membered ring by an acyloin condensation, i.e., by the route mentioned previously. This plan was ruled out due to the failure to obtain the dinitriles (XXXV) and (XLVIII) from the corresponding dimesylates, using reaction methods similar to those reported in this thesis. Unsuccessful attempts to synthesize the tricyclo[4.4.4.0]tetradecane ring system through the base-catalyzed condensation of compounds (XXVII) and (XL) with diethyl succinate, succinonitrile, and tetraethyl 1,1,2,2-ethanetetracarboxylate were reported to be due to steric hindrance. A very small but demonstrable yield of tricyclo[4.4.4.0]-2-tetradecane was obtained through a ten step preparation of cis-9-carbomethoxypropyl-10-carbomethoxydecalin, followed by a Dieckmann condensation (using sodium hydride in benzene) and treatment of the crude product with a hydrochloric-acetic acid mixture (hydrolysis and decarboxylation).
An acyloin condensation of cis-9-carbomethoxyethyl-10-carbomethoxydecalin gave tricyclo[4.4.4.02,3]tetradecadione in only 1.7% yield. The unsuccessful attempts by Snatzke and Zanati to prepare the diacid chloride of (XXXIX) by treating (XXXIX) with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, or oxalyl chloride, parallels the unsuccessful attempts described in this thesis to prepare the diacid chloride (XXIX).

In a preliminary communication the second group of workers, Nerdel, Janowsky and Frank, report the successful preparation of tricyclo[4.4.3.0]tridecane in a seven step synthesis from cis-9,10-bis(hydroxymethyl)decalin (XXXI). The synthesis consists of treating (XXXI) with t-butyl chromate to give the tricyclic \( \gamma \)-lactone (A), followed by a cleavage of the lactone ring using potassium cyanide to give the cyano-acid (B). Hydrolysis of the cyano group followed by methylation of the two acid functions gives the dimethyl ester (C), which undergoes an acyloin condensation (sodium in liquid ammonia) to give a mixture of acyloins (D). Acetylation of this mixture and a subsequent Clemmensen reduction gives a 1:2 mixture of tricyclo[4.4.3.0]tridecane and -11-tridecanone.
These workers report that an analogous route is currently being followed for the preparation of tricyclo[4.4.4.0^4]tetradecane, starting with the dialcohol obtained from a hydride reduction of the diacid corresponding to the dimethyl ester (C).
B. N. M. R. Spectra - AB Systems

The appearance of simple AB quartets for the side-chain methylene protons in the room temperature n. m. r. spectra of the cis-$\Delta^2$-octalin cyclic ether (XXI), diacetate (XXII), dimesylate (XXIII), and diiodide (XXIV) can be accounted for by considering both the environmental symmetry of the methylene groups and the rate of interconversion of the ring systems.

XXI

The latter three compounds each exist as a pair of interconverting enantiomers, whose geometries are shown in the following diagram (looking down the C-9 - C-10 bond):

XXII, $X = \text{OAc}$

XXIII, $X = \text{OMs}$

XXIV, $X = \text{I}$
In each case the conformation of the cyclohexane ring is a chair and the cyclohexene ring is a half-chair. It can be seen that the two methylene groups in each enantiomer are not equivalent; however, they do become equivalent when the rate of interconversion is rapid.

The methylene protons are themselves non-equivalent, due to the fact that the adjacent bridgehead carbon atom is asymmetrically substituted. The three possible rotational isomers are as follows:

where R, S, and T are differently substituted carbon atoms attached to the adjacent bridgehead carbon atom, i.e., the other bridgehead, the cyclohexane, and the cyclohexene carbon atoms, respectively. Since the order of the relative sizes of these groups is $R >> S \approx T$, the order of relative conformational stability should be $(ii) > (iii) \approx (i)$. It has been shown that, depending on the rate of rotation of a $\text{-CH}_2\text{X}$ group about an asymmetric carbon atom, different numbers of AB quartets may appear for the $\text{-CH}_2\text{X}$ protons; however, both a fast rate, in which the populations of the three rotational isomers are equal, and a slow rate, in which one isomer predominates almost exclusively, will give only one AB quartet. The latter situation appears to be the more favourable one in the three compounds, based on the steric environments involved.
The rate of interconversion of the $\Delta^2$-octalin ring systems is relatively independent of the rate of rotation of the $\text{-CH}_2\text{X}$ groups. The appearance of a single AB quartet for the latter groups, therefore, infers that the rate of interconversion of the $\Delta^2$-octalin ring system is fast, thus averaging out the two positions of the $\text{-CH}_2\text{X}$ groups. A slow rate would be expected to give rise to two different AB quartets, due to the presence of two non-equivalent $\text{-CH}_2\text{X}$ groups, each having two non-equivalent protons.

The appearance of a single AB quartet for the ether ring methylene protons in the octalin cyclic ether (XXI) can be explained in a similar manner. In this case, however, the geometry of the ether ring constrains the methylene protons to only two possible conformations, (i) and (iii), where $\text{X}$ is the ether oxygen. In addition, the rate of change of the two possible environments of both protons is directly coupled with the rate of interconversion of the enantiomeric forms of the whole molecule (in contrast to the acyclic derivatives mentioned previously, in which the two motions are independent). The most stable conformation of the molecule is probably the one in which the cyclohexane ring is a chair and the cyclohexene and ether rings are half-chairs.

On considering one enantiomer it is seen that the two methylene groups are in different environments. On conversion to the other enantiomer, however, the environments of the two groups are reversed. At a slow rate of interconversion, therefore, there should be two different AB quartets present in the n.m.r. spectrum. At a fast rate the two methylene groups will become equivalent, thus leading to the appearance of a single AB quartet, due to the inherent non-equivalence of the germinal protons. The experimentally observed appearance of a single AB quartet, therefore, can be explained only by the existence of a fast rate of interconversion of the whole molecule at room temperature.
The appearance of AB quartets for the allylic methylene protons in the \( \Delta^2 \)-octalin dicarboxylic anhydride (XIX) and dicarboximide (XIII) and in the \( \Delta^2,6 \)-hexalin analogs (XXXVII) and (XXXVIII) can be explained as being due to the influence of the adjacent, asymmetrically substituted bridgehead carbon atoms. A complete discussion of the origins of the fine structure in the AB spectra, based on spectra obtained at only one temperature, however, is not possible, since the contributions from the interconversions of the molecules and the added spin-spin couplings between the neighbouring olefinic protons cannot be unequivocally separated.

C. Low Temperature N. M. R. Spectra - Kinetic Studies

Preliminary investigations have been carried out in order to determine the effect on the rate of interconversion in \( \text{cis} \)-decalin of substituting both cyclic and acyclic groups into the C-9 and C-10 positions. To this end, n.m.r. spectra of \( \text{cis} \)-9,10-dimethyldecalin (XLVII) and 12-oxatricyclo[4.4.3.0]tridecane have been obtained at various temperatures between -60 and +25°. For the purpose of comparison, the n.m.r. spectra of \( \text{cis} \)-decalin have also been obtained under the same conditions. The room temperature n.m.r. spectrum of \( \text{cis} \)-decalin consisted of two resonance peaks, which were identified as the methylene proton peak (8.57 \( \tau \), large) and the bridgehead proton peak (8.39 \( \tau \), small). The latter assignment was based on the fact that this peak did not appear in the n.m.r. spectra of the \( \text{cis} \)-9,10-disubstituted decalins. The \( \text{cis} \)-decalin spectrum (Fig. 8) at -50° showed small but significant changes from that obtained at 0° (and at 25°). In particular the bridgehead proton peak had become more clearly defined and small peaks had begun to appear on both the low-field and high-field sides of the main peaks. These changes could be reflecting a decrease in the rate of interconversion in \( \text{cis} \)-decalin. The width at half-height of the methylene resonance peak remained virtually constant throughout the temperature range employed, thereby preventing a determination of the barrier height or rate constant by the usual methods.
The low temperature n.m.r. spectra of cis-9,10-dimethyldecalin (Fig. 9) showed the appearance of partly resolved fine structure in the ring methylene proton peak, together with small peaks on the low-field side of this peak. The small low-field peaks were thought to be part of an unsymmetrical A₂B₂ system, which could arise from the coupling between each of the four sets of methylene groups (A protons) in the α-position relative to the bridgehead carbon atom and the methylene groups (B protons) in the β-position. No satisfactory agreement could be obtained, however, between the experimental spectra obtained here and published experimental \(^5\) and theoretical \(^9\) A₂B₂ spectra. Nevertheless, if the changes in the appearance of the ring proton peak do reflect a decrease in the rate of interconversion, then the fact that changes in the dimethyldecalin spectra occurred at a higher temperature than those in the cis-decalin spectra suggests that the barrier to interconversion is higher in the former compound. No quantitative determination of this barrier height could be carried out, since there was virtually no change in the width at half-height of the methylene proton peak throughout the temperature range employed. It should be mentioned that the methyl resonance peak remained constant as a sharp singlet as expected, since, during the interconversion process, the methyl groups oscillate between two identical positions, with respect to the rings.

The appearance of an increasingly broader resonance peak for the ether ring protons in 12-oxatricyclo[4.4.3.0]tridecane (XXXIII), as the temperature of the n.m.r. sample of this compound was lowered, was assumed to be due to a decrease in the rate of interconversion of the molecule. That this assumption is correct can be shown from a consideration of a molecular model. The most stable conformation of the molecule is probably the one which contains the two cyclohexane rings as chair conformations and the ether ring as a half-chair. The interconversion between the two enantiomers can be shown as follows (looking down the C-1–C-6 bond):
It can be seen that the two ether ring methylene groups are always in identical environments (in contrast to the octalin analog). The geminal protons of these methylene groups, however, are non-equivalent. The two conformations of these protons may be illustrated as follows (looking down the methylene carbon−bridgehead carbon bond):

where R is the other bridgehead group and S is the cyclohexane methylene group.

Depending on the rate of change of the above conformations, it is expected that the n.m.r. spectrum of the protons will be either an AB quartet (slow rate) or an $A_2$ singlet (fast rate resulting in the time-averaging of the two environments of each proton). Due to the geometry of the molecule, however, this rate of change will be identical to the rate of interconversion of the two enantiomeric forms of
the molecule. The transition between the singlet and quartet spectra would be expected to involve a broadening of the singlet line followed by the appearance of the quartet as the temperature of the n.m.r. sample is lowered. The shapes of the experimental spectra (Fig. 10), therefore, did indicate that the molecules were interconverting at a relatively fast rate. That the observed broadening of the ether ring protons was due to a decrease in the rate of interconversion, and not to a viscosity or sample freezing effect, was shown by the appearance of sharp, resolved TMS signals at each temperature.

The application of the "fast exchange region" equation, derived by Piette and Anderson, gave a value of the energy of activation (Ea) of 8.4 ± 2 kcal./mole. This value of Ea should be considered as only a qualitative estimate, since (a) an assumed value of the transverse relaxation time (T₂) was used and (b) the spectra of the regions of intermediate and slow rates of interconversion were not obtained. A more complete investigation of these factors should lead to an accurate determination of not only Ea but also the enthalpy (ΔH*), entropy (ΔS*) and free energy of activation (ΔF*).

Qualitatively speaking, the value of Ea obtained here for the barrier height in 12-oxatricyclo[4.4.3.0]tridecane is lower than the values of Ea obtained by Roberts for some derivatives of 2,2-difluoro-cis-decalin. Thus, the addition of a third ring to cis-decalin (at the 9,10-positions) appears to have a negative effect on the barrier to interconversion rather than a positive one. The full effect of substituent groups, however, should be considered only from a comparison of the relative free energies of activation of the various derivatives, since both the enthalpy and entropy of activation may be affected by substitution.
EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer Model 137B Infracord spectrophotometer (sodium chloride optics), unless otherwise stated (e.g., Perkin-Elmer Model 21). Relative absorption band intensities are given as w = weak, m = medium and s = strong. Absorption band positions are given in wave numbers (cm$^{-1}$).

Nuclear magnetic resonance (n.m.r.) spectra were recorded by Mrs. A. Brewster of this department on a Varian Model A-60 60 Mc. spectrometer. Resonance peak positions are given in $\tau$ units, relative to tetramethylsilane (TMS, internal standard) at 10 $\tau$. The n.m.r. samples were 15% (w./v.) solutions (total volume 350 $\mu$l) placed in 5 mm. o.d. glass capillary tubes, unless otherwise specified. Integrated peak areas are given as a ratio.

Ultraviolet spectra were recorded on a Bausch and Lomb Spectronic 502 spectrophotometer.

Mass spectra were recorded by Mr. F. G. Bloss of this department on an Atlas Model CH4 spectrometer.

Microanalyses were performed by Dr. A. Bernhardt and his staff at the Max Planck Institute, Mulheim, Ruhr, West Germany.

Melting points (uncorrected) were obtained using an electrically heated, circulating oil bath.

Gas-liquid chromatography (g.l.c.) tracings were recorded on Wilkens Model A-90 Aerograph and A-700 Autoprep chromatographs. Standard commercial 1/4 in. diameter columns were used. Retention times of components are given in minutes.

The following solvents and reagents were purified and dried, as indicated, for use in particular reactions.
Acetonewas stirred over potassium permanganate crystals for two days, filtered, and distilled, collecting the middle fraction, b.p. 56°. This material was then fractionally distilled from Drierite, again collecting the middle fraction, b.p. 56° (lit. 56.2°).

Diethyleneglycol dimethyl ether (diglyme, Eastman) was refluxed over and distilled from sodium metal, collecting the middle fraction, b.p. 164°.

Diethyl ether (Mallinckrodt anhydrous) was used without further treatment.

N,N-Dimethylformamide (DMF) was stirred over potassium hydroxide pellets for one day, filtered, then refluxed over and distilled from calcium oxide, b.p. 154° (lit. 153°).

Dimethyl sulfoxide was distilled from powdered calcium hydride, b.p. 188° (lit. 189°).

1,2-Dimethoxyethane (glyme, Eastman) was refluxed over and distilled from sodium wire. The distillate was then treated with powdered lithium aluminum hydride and distilled, collecting the middle fraction, b.p. 85° (lit. 85°).

Heptane was refluxed over and distilled from molecular sieves Type 5a (Eastman), collecting the middle fraction, b.p. 98° (lit. 98.4°).

N-methyl-2-pyrrolidinone (NMP, Eastman) was stirred over potassium hydroxide pellets for one day, filtered, then refluxed over and distilled from calcium oxide, b.p. 202-203° (lit. 202-202°).

Pyridine was refluxed over and distilled from barium oxide, b.p. 114° (lit. 115.5°).

Tetrahydrofuran (THF) was stirred over potassium hydroxide pellets for one day then distilled. The distillate was refluxed over and distilled from powdered
lithium aluminum hydride, b. p. 65° (lit. \textsuperscript{44} b. p. 64-65°).

Sodium cyanide (Merck, 95\%) was washed with small amounts of 95\% ethanol, then dried at 120° for 24 hrs.

Sodium iodide (Mallinckrodt analytical reagent grade) was dried at 120° for 24 hr.

5,8-Dihydroxy-1,4-naphthoquinone (Naphthazarin) (I)

The procedure used was that reported by Zahn and Ochwat.\textsuperscript{95} A mixture of 10.0 g. (0.10 mole) of maleic anhydride and 11.0 g. (0.10 mole) of hydroquinone was pulverized in a mortar and pestle, then added in small portions to a stirred melt of 100 g. of anhydrous aluminum chloride and 20 g. of sodium chloride. The temperature of the reaction mixture during the addition was maintained at 180°, then raised to 210° and maintained until the reaction mixture became solid (about 2 hr.). During the addition of the reagents the color of the reaction mixture progressed from bright orange to a reddish-blue to black. Excessive foaming of the reaction mixture was controlled by a slow addition of the reagents and fairly vigorous stirring.

The black bubbly mass was cooled to room temperature, crushed up into small lumps and added carefully to 800 g. of ice. Stirring helped to break the lumps down into fine particles. The reddish-violet mixture was heated to boiling, then 400 ml. of concentrated hydrochloric acid were added in small portions. The mixture turned a brown color and a black precipitate of crude naphthazarin separated out. The mixture was cooled to 0° and filtered. The black precipitate was washed with 300 ml. of water and dried. Yield of crude product 22.4 g.
The black solid was extracted with benzene in a Soxhelet apparatus until the extract from the thimble was no longer colored. The benzene was evaporated, leaving a dark red powder. This material was then sublimed at 90°/0.01 mm. and crystallized from petroleum ether (b.p. 65-110°) yielding 2.0 g. (10.5%) of naphthazarin (dark green needles), m.p. 195° (decomp.), (no lit. m.p.).

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm. $^{-1}$) at 2920 (s), 1630 (s), 1570 (m), 1460 (s), 1410 (m), 1380 (m), 1340 (m), 1260 (m), 1230 (m), 1145 (m), 1105 (w), 950 (w), and 870 (m).

Naphthazarin diacetate (II) was prepared as follows. A mixture of 0.5 g. of naphthazarin, 3 ml. of acetic anhydride and 3 drops of concentrated sulfuric acid was heated gently until all the naphthazarin dissolved. The orange solution was cooled to room temperature, poured into 15 ml. of water, and filtered. The yellow precipitate was washed with water, dried, and recrystallized from acetone-water yielding long yellow needles, m.p. 192-193° (lit. 95 m.p. 192-193°).

Lead Tetraacetate

Lead tetraacetate was prepared according to Vogel. The white crystalline material was stored under vacuum with a small amount of glacial acetic acid. The product was assayed to be 87% lead tetraacetate by iodometry.

1, 4, 5, 8-Naphthodiquinone (III)

Method 1. A mixture of 250 mg. (1.32 mmoles) of naphthazarin (I) and 5 ml. of glacial acetic acid was heated until all the naphthazarin dissolved, then cooled quickly to room temperature. The resulting mixture of fine red crystals and glacial acetic acid was added to 590 mg. (1.33 mmoles) of lead tetraacetate in a mortar. This mixture was ground slowly with a pestle. The red mixture slowly turned brown. The reaction mixture was filtered. The dark yellow filtrate yielded no product material on cooling. The solution slowly turned brown during the
attempted crystallization.

The dark brown precipitate, which had been filtered off, contained no product (Zahn and Ochwat reported the precipitate to be yellow crystals of the naphthodiquinone).

This procedure was repeated three more times without success.

Method 2. Activated manganese dioxide (100 mg.), prepared according to Attenburrow, et al., was added to a solution of 10 mg. of naphthazarin (I) in 15 ml. of dry benzene. No decolorization was noted after stirring at room temperature for 20 hr. The reaction mixture was filtered and the filtrate evaporated to dryness leaving a red solid, m. p. 194-195° (decomp.), mixed m. p. with naphthazarin 194-195° (decomp.).

Method 3. To a solution of 10 mg. of naphthazarin (I) in 10 ml. of acetone was added a solution of 10 mg. of potassium permanganate in 10 ml. of acetone. The resulting solution was stirred at room temperature for about 2 hr. The acetone was evaporated off and the dark residue extracted with diethyl ether. The ether extract was washed once with water, dried over anhydrous magnesium sulfate, and evaporated. The residue consisted of a small amount of a clear oil.

The procedure was repeated once again without success.

1, 4, 9, 10-Anthradquinone (V)

Method 1. A mixture of 2.0 g. (8.3 mmoles) of dry quinizarin (IV), 4.0 g. (9.1 mmoles) of lead tetraacetate and 5 ml. of glacial acetic acid was stirred in a mortar and pestle. The red mixture coagulated after 1 min. of stirring. Stirring was continued for 20 min., at which time no further color change from red to brown was noticed. The mixture was filtered and the dark residue washed with water and dried. The dry residue was crystallized from
dry nitrobenzene (heated to 90°). The yield was 0.5 g. of orange crystals, m.p. 194-195°, mixed m.p. with quinizarin, 194-195°.

This procedure was repeated four more times without success.

Method 2. To a fine suspension of 0.80 g. of quinizarin (IV) in 16 ml. of glacial acetic acid was added 4.0 g. of lead dioxide. The resulting mixture was stirred at room temperature until a sample, when added to an excess of water, remained clear. Petroleum ether (b.p. 65-110°) was then added in small portions to the reaction mixture in order to precipitate out the crude product. The dark brown precipitate was filtered off and extracted with 20 ml. of benzene. Petroleum ether (b.p. 65-110°) was added to promote crystallization of the product. Only a few milligrams of dark brown crystals were obtained, which did not give a definite melting point.

Method 3. A paste made from adding a small amount of water to 0.5 g. of powdered quinizarin (IV) was placed on a watch glass and suspended over 2 ml. of red fuming nitric acid in a vacuum desiccator. The desiccator was evacuated slightly, then left at room temperature for 3 days. During this time the red paste turned to a colorless solution. The reaction mixture was then evaporated to dryness by vacuum desiccation over potassium hydroxide pellets. The residue was a yellow-orange tacky substance. A small sample of the residue added to water gave an orange solution which was acidic (turned Hydrion paper red).

The residue was found to be insoluble in benzene, chloroform, and carbon tetrachloride and soluble in ethanol and acetone. Attempted crystallizations of the residue using various combinations of these solvents were unsuccessful.

A small amount of a white solid, m.p. 194-195° (decomp.) was obtained from the crystallization of the residue using nitrobenzene. This white solid was soluble in water, giving a colorless, acidic solution.
The infrared spectrum (KBr pellet, PE2I) of this compound showed
\( \nu_{\text{max}} \) (cm\(^{-1}\)) at 3000 (m, broad), 2650 (m, shoulder), 2520 (m, shoulder), 1685 (s), 1585 (m), 1520 (m), 1495 (w), 1405 (s), 1350 (m), 1275 (s, doublet), 1150 (w), 1138 (w), 1070 (s), 1005 (w), 972 (w), 905 (s), 825 (w), 795 (s), 735 (s), 705 (w), and 670 (s).

\( \delta^9 \)-Octalin (VII)

A commercial isomeric mixture of 2-acetoxydecalin (VI, 25.0 g.) was reacted with 80 g. of 100% phosphoric acid according to Hussey to yield 17.8 g. of crude product. The crude product was distilled through a column of perforated steel plates yielding 12.3 g. of a middle fraction, b. p. 184-189\(^\circ\). Quantitative analysis, by gas-liquid chromatography on a 6 ft. acid-washed Carbowax 20M on firebrick column at 105\(^\circ\) with a helium flow rate of 40 ml./min., showed that the middle fraction contained 65\% \( \delta^9 \)-octalin (VII), 25\% \( \delta^{1,9} \)-octalin and 10\% cis-decalin. Their retention times were 24, 21.5 and 17.5 min., respectively.

The n. m. r. spectrum of \( \delta^9 \)-octalin (15% in CCl\(_4\)) showed multiplets at \( \tau8.19 \) (allylic H) and 8.34 (-CH\(_2\)-) in the ratio of l:l. The n. m. r. spectrum of \( \delta^{1,9} \)-octalin showed a resonance peak at \( \tau4.5 \) for the olefinic proton, while that of cis-decalin showed singlets at \( \tau8.39 \) (bridgehead H) and 8.57 (-CH\(_2\)-).

Tricyclo[4.4.0.0\(^3\)]-3-tetradecene (VIII)

Method 1. A Carius tube was partly filled with 3.0 g. of the octalin mixture and 7 ml. of liquid 1,3-butadiene, then sealed. The tube was heated at 200\(^\circ\) for 40 hr. After cooling the tube, the viscous liquid product was removed and analysed by gas-liquid chromatography on a 6 ft. acid-washed Carbowax 20 M on firebrick column at 190\(^\circ\) with a helium flow rate of 40 ml./min. The tracing for the product mixture showed peaks between 3 and 10 min. which were also present in a sample of the starting material run under the same chromatography conditions.
No significant amount of a longer retention time component was observed.

Method 2. A Carius tube was partly filled with 3.0 g. of the octalin mixture, 8.0 ml. of 1,3-butadiene and 0.4 g. of anhydrous aluminum chloride, then sealed. On shaking the tube at room temperature, the aluminum chloride coagulated into an orange mass. The mixture was heated at 200° for 24 hr. After cooling the tube, the black lumpy mixture was removed and added to 100 ml. of ice and water. The mixture was extracted three times with 50 ml. portions of benzene. The combined benzene extracts were washed with 50 ml. of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated. A sample of the residue, analysed by gas-liquid chromatography as in method 1, showed only peaks corresponding to those in the Δ⁹-octalin mixture.

Method 3. A Carius tube, partly filled with 2.0 g. of the Δ⁹-octalin mixture, 5 ml. of liquid 1,3-butadiene, and 0.2 g. of anhydrous aluminum chloride, was allowed to stand at room temperature for 20 hr. The reaction mixture was then filtered to remove the excess aluminum chloride. The residue was washed with benzene. The product filtrate and the benzene washings were combined and evaporated to constant weight. Analysis of this product mixture by gas-liquid chromatography as in method 1 showed no components other than those in the Δ⁹-octalin mixture.

cis-Δ²-Octalin (IX)

A mixture of 100 ml. of cyclohexene and 0.5 g. of benzil was placed in a Pyrex photochemical reaction vessel and purged with helium. The reaction vessel consisted of a double-walled cylinder (internal diameter 8 cm., external diameter 10 cm.) about 11 cm. in height, fitted with two vertical Bl9 outlets, two 4 mm. diameter inlets for bubbling gases into the reaction mixture, and a pressure operated 4 mm. diameter reaction sample collector.
The reaction mixture was stirred with a small teflon-coated bar magnet. The apparatus was cooled by an external carbon tetrachloride - Dry ice bath, maintained at -5 to -10°. Both 1,3-butadiene and helium were bubbled into the reaction mixture while the mixture was being irradiated by a water-cooled G. E. AH-6 immersion type ultraviolet lamp placed in the center of the reaction vessel.

Small samples were withdrawn hourly from the reaction mixture and analysed by gas-liquid chromatography on a 6ft. acid-washed Carbowax 20 M on firebrick column at 120° with a helium flow rate of 40 ml./min. Two peaks with retention times of 2.5 and 6.0 min. appeared in the g.l.c. tracing of the 4 hr. sample. The two compounds were identified as 4-vinylcyclohexene and cis, cis-1,5-cyclooctadiene, respectively by comparison of their n.m.r. spectra with those published by Varian Associates, Ltd. No longer retention time components were observed in the g.l.c. tracing of the 8 hr. sample.

The reaction was then stopped. The reaction mixture was removed and distilled until the boiling point of the distillate reached 115°. The residue was analysed by g.l.c. using the Carbowax column at 85°. In addition to the peaks for 4-vinylcyclohexene and cis, cis-1,5-cyclooctadiene (retention times 7 and 18 min., respectively), there were two very small, longer retention time components (retention times 24 and 28.5 min.). An attempted collection of these latter two components was unsuccessful.

Cyclohexene-1,2-dicarboxylic Anhydride (XI)

4-Cyclohexene-cis-1,2-dicarboxylic anhydride (X, 300 g.) and 4.5 g. of phosphorus pentoxide were heated together at 195° for 48 hr. Distillation of the resulting dark mass afforded 233 g. (78%) of the rearranged anhydride, b.p. 129-134°/5mm. On crystallization from diethyl ether the anhydride (XI) melted at 72-73° (lit. m.p. 71-72°). The infrared spectrum (Nujol mull) showed max (cm.⁻¹) at 2920 (s), 1820 (s), 1770 (s, broad), 1660 (s), 1450 (s), 1430 (s), 1370 (s), 1265 (s), 1230 (m), 1175 (m), 1075 (m), 1040 (m), 960 (m), 890 (s, broad), 730 (s), and 700 (s). The n.m.r. spectrum (15% in CCl₄) showed multiplets at 7.6 (allylic H) and 8.2 (-CH₂-) in the proton ratio of 1:1.
Cyclohexene-1,2-dicarboximide (XII)

An intimate mixture of 61.0 g. (0.40 mole) of the cyclohexene anhydride (XI) and 12.5 g. (0.21 mole) of urea was heated at 155-160° until effervescence ceased and most of the reaction mixture had turned solid (2 hr.). The mixture was cooled to room temperature and crystallized from benzene yielding 47.9 g. (80%) of the imide, m.p. 166-167°. On recrystallization from methanol the melting point of the imide rose to 171-172° (lit. m.p. 170.5°).

The infrared spectrum (solution in CHCl₃) showed ν_max (cm⁻¹) at 3400 (m), 3250 (m), 2950 (m), 1770 (s), 1720 (s), 1650 (m), 1440 (m), 1420 (s), 1340 (s), 1260 (w), 1175 (w), 1125 (w), 1080 (s), 1020 (s), and 943 (m).

△²-Octalin-9,10-dicarboximide (XIII)

Cyclohexene-1,2-dicarboximide (XII, 42 g., 0.28 mole), 0.25 g. of hydroquinone, and 100 ml. of benzene were placed in the autoclave, followed by a solution of 100 ml. (65 g., 1.2 moles) of liquid 1,3-butadiene (chilled to -50°) in 200 ml. of benzene. The mixture was stirred and heated at 110° for 13 hr., then 130° for 9 hr. After cooling the product mixture to room temperature, the crystalline solid was filtered off, washed with benzene, and dried, m.p. 135-140°. On crystallization from diethyl ether, 5 g. of the cyclohexene imide (XII) were obtained, m.p. 170-171°, mixed m.p. with authentic imide 170.5 - 171.5°. The filtrate was evaporated to dryness yielding 28 g. of product, m.p. 135-136°. Further recrystallizations from benzene-petroleum ether (b.p. 65-110°) failed to separate the product mixture.

In order to purify this material the following procedure was used: the crude product (5 g.) was refluxed in a solution of 100 ml. of 5% aqueous sodium hydroxide and 50 ml. of ethanol for 8 hr. The solution was cooled to room temperature and filtered to remove the coagulated butadiene polymers. The ethanol was evaporated off.
and concentrated hydrochloric acid added in small portions with stirring until the filtrate became distinctly acid. The white precipitate was filtered off, dried, and crystallized from 95% ethanol yielding 2.26 g. of the octalin imide, m.p. 173-174° (lit. m.p. 176°).

The infrared spectrum (KBr pellet, P. E. 21) showed \(\nu_{\text{max}}\) (cm.\(^{-1}\)) at 3150 (s), 3030 (s), 2940 (s), 2870 (s), 2760 (s), 1760 (s), 1700 (s, broad), 1655 (m), 1460 (m), 1440 (s), 1395 (m), 1370 (s), 1345 (s), 1330 (s), 1310 (s), 1220 (m), 1185 (s), 1125 (s), 1020 (m), 955 (m), 860 (s, broad), 770 (m), 755 (m), 710 (m), and 660 (s, broad).

The n.m.r. spectrum (15% in CDCl\(_3\)) showed a very broad singlet at \(\tau 1.3\) (-CONHCO-), a multiplet at 4.18 (olefinic H), a complex quartet with maxima at 7.27, 7.55, 7.88, and 8.17 (allylic H), and a multiplet at 8.42 (-CH\(_2-\)) in the ratio of 1:2:12 (the quartet and high-field multiplet were not resolved in the area integral).

Cyclohexene-1,2-dicarboxamide (XIV)

A mixture of 55.0 g. of the cyclohexene imide (XII) in 300 ml. of concentrated aqueous ammonia was stirred at room temperature for 24 hr. The white precipitate was filtered off, washed with water, then methanol, and dried. Yield of diamide, 31.9 g. (53%), m.p. 210-212° (decomp.) (lit. m.p. 208° (decomp.)).

The infrared spectrum (Nujol mull) showed \(\nu_{\text{max}}\) (cm.\(^{-1}\)) at 3400 (s), 3200 (s), 2920 (s), 2850 (s), 1650 (s), 1620 (s), 1460 (m), 1400 (m), 1380 (m), 1340-1260 (w, broad multiplet), 1165 (m), 1135 (w), 1120 (w), 965 (w), 900 (w), 810 (w) and 670 (s).

The aqueous filtrate and washings were combined and made distinctly acid by adding concentrated aqueous hydrochloric acid. The resulting white precipitate was
filtered off, washed with water and dried. Yield of cyclohexene-1, 2-dicarboxylic anhydride (XI), 20.0 g. (36%), m. p. 69-70°, mixed m. p. with authentic material 69-70°.

1, 2-Dicyanocyclohexene \(52,99\) (XV)

Phosphorus pentoxide (80 g.) was added to a mixture of 34.0 g. (0.20 mole) of the dry cyclohexene diamide (XIV), 84.0 g. of dry triethylamine and 160 ml. of dry benzene. The reaction mixture was refluxed gently for 2 hr. The triethylamine and benzene were distilled off. Ice and water (300 g.) were stirred carefully into the dark residue and the whole was allowed to stand overnight. The resulting precipitate was filtered off, boiled for 1 min. in 100 ml. of IN-aqueous potassium hydroxide solution, cooled to 0°, and filtered off again. After washing with water and drying, the crude product was crystallized from petroleum ether (b. p. 65-110°), yielding 0.75 g. (2.8%) of the dinitrile, m. p. 95-96° (lit. \(52\) m. p. 96-97°).

The infrared spectrum (hexachloro-1, 3-butadiene mull) showed \(\nu_{\text{max}}\) (cm.\(^{-1}\)) at 2950 (s), 2880 (m), 2200 (s), 1450 (s), 1430 (s), 1350 (w), 1330 (w), 1260 (m), 1240 (w), 1140 (m), and 1070 (w).

cis-9,10-Dicyano-\(\Delta^2\)-octalin (XVI)

Method 1. A mixture of 0.53 g. (4.0 mmoles) of the cyclohexene dinitrile (XV), 5 ml. of benzene and 1 ml. (0.65 g., 12 mmoles) of liquid 1,3-butadiene was sealed up in a Carius tube and allowed to stand at room temperature for 4 days. Evaporation of the excess butadiene and benzene yielded 0.52 g. of a compound, m. p. 96-97°, mixed m. p. with the cyclohexene dinitrile (XV), 96-97°.

Method 2. To 0.60 g. (4.6 mmoles) of the cyclohexene dinitrile (XV), dissolved in 35 ml. of dry benzene and placed in the autoclave, was added a solution
of 10 ml. (6.5 g., 0.12 mole) of liquid 1,3-butadiene (chilled to -20°) in 50 ml. of dry benzene. The mixture was stirred for 1.5 hr. at 150°, then 2.5 hr. at 120°. The resulting brown solution was removed from the autoclave, treated with activated charcoal and evaporated, leaving about 3 ml. of a dark brown oil. Addition of anhydrous ether produced crystallization. The crystals were filtered off, washed with diethyl ether and dried. Yield 313 mg., m. p. 98-99°, mixed m. p. with starting material 96-98°.

\[ \Delta^2 \text{-Octalin-cis-9,10-dicarboxylic acid} \] (XVII)

To a mixture of 64 g. (0.42 mole) of cyclohexene-1,2-dicarboxylic anhydride (XI), 100 ml. of benzene, and 0.25 g. of hydroquinone in the autoclave, was added a solution of 200 ml. (130 g., 2.4 moles) of liquid 1,3-butadiene (chilled to -50°) in 100 ml. of benzene. After stirring and heating the mixture at 160-170° for 13 hr., the system was cooled to room temperature. The product mixture was removed from the autoclave and the benzene and butadiene dimers evaporated at 50°/10 mm. The residue was then boiled with three separate 250 ml. portions of 10% aqueous sodium hydroxide solution. The combined alkali extracts were treated with activated charcoal, extracted three times with 100 ml. portions of diethyl ether, then acidified carefully with concentrated hydrochloric acid. After cooling the mixture to 0°, the white precipitate was filtered off and dried, yielding 34 g. (36%) of the diacid. On crystallization from ethanol-water the diacid melted at 187.5 - 188° (foaming, sealed tube), lit. m. p. 190° (decomp.)).

The infrared spectrum (Nujol mull) showed \( \nu_{\text{max}} \) (cm.\(^{-1}\)) at 2920 (s, broad), 2650 (m, broad), 1700 (s), 1460 (s), 1405 (m), 1375 (m), 1300 (s), 1255 (m), 1220 (m), 1175 (m), 1155 (w), 950 (m, broad), 738 (m), and 678 (m, broad).
cis-9,10-Bis(carbomethoxy)-\(\Delta^2\)-octalin (XVIII)

The procedure used was as for the preparation of the analogous decalin dimethyl ester (XXVII). The crude product (quantitative yield) was sublimed at 55°/1mm., m.p. 52.5 - 54.5°.

Analysis. Calculated for C\(_{14}\)H\(_{20}\)O\(_4\): C, 66.65; H, 7.99

Found: C, 66.99; H, 7.79.

The infrared spectrum (Nujol mull) showed \(\nu_{\text{max}}\) (cm.\(^{-1}\)) at 3030 (m), 2920 (s), 1730 (s), 1660 (w), 1450 (s), 1375 (m), 1280 (s), 1250 (s), 1230 (s), 1210 (s), 1195 (s), 1160 (s), 1140 (s), 1090 (m), 1070 (s), 1040 (m), 1020 (s), 970 (w), 940 (w), 865 (w), 820 (w), 800 (w), 760 (w), and 680 (w).

The n.m.r. spectrum (15% in CCl\(_4\)) showed a triplet at \(\tau\) 4.50 (olefinic H), a sharp singlet at 6.39 (CH\(_3\)O-), a broad multiplet with maxima at 7.66 and 8.30 (allylic H) and a singlet at 8.54 (-CH\(_2\)-) in the ratio of 1:3:6 (the multiplet and high field singlet were not resolved in the area integral).

\(\Delta^2\)-Octalin-9,10-dicarboxylic Anhydride \(\textnormal{(XIX)}\)

The octalin acid (XVII, 5.0 g.) was added in small portions to 25 ml. of stirred acetyl chloride cooled to 0°. The mixture was allowed to warm up to room temperature and stirred for 0.5 hr. The final solution was poured into 100 ml. of ice and water. The white precipitate was filtered off and washed with water to remove any occluded acetic acid. On crystallization from petroleum ether (b.p. 65-110°), the yield of anhydride was 3.5 g. (70%), m.p. 67-68° (lit. \(53,55\) m.p. 68°).

The infrared spectrum (Nujol mull) showed \(\nu_{\text{max}}\) (cm.\(^{-1}\)) at 3030 (w), 2940 (s), 1860 (m), 1780 (s), 1660 (w), 1450 (s), 1375 (m), 1300 (w), 1255 (m), 1220 (m),
1185 (m, doublet), 1140 (w), 1080 (w), 1055 (w), 1035 (w), 1000 (w), 980 (w), 940 (m, shoulder), 915 (s, broad), 880 (m), 840 (m), 785 (w), 738 (m), and 688 (m).

The n.m.r. spectrum (15% in CCl₄) showed a triplet at τ 4.28 (olefinic H), a complex quartet with maxima at 7.30, 7.58, 7.82 and 8.10 (allylic H) and a multiplet at 8.39 (-CH₂-) in the ratio of 1:2:4.

\textit{cis-9,10-Bis(hydroxymethyl)-8-octalin (XX)}

The procedure used was as for the preparation of the analogous hexalin dialcohol (XLI). The yield of octalin alcohol was 12.5 g. (64%) from 20 g. (0.10 mole) of the octalin anhydride (XXIX). On crystallization from ethanol-water the dialcohol melted at 147-149°.

Analysis. Calculated for C₁₂H₂₀O₂: C, 73.43; H, 10.27. Found: C, 73.51; H, 10.42.

The infrared spectrum (Nujol mull) showed ν max (cm⁻¹) at 3300 (s), 2940 (s), 1660 (w), 1500 (m), 1460 (m), 1380 (m), 1100 (m), 1080 (m), 1055 (m), 1020 (s), 1000 (m), and 980 (m).

The n.m.r. spectrum (23% in DMSO) showed a triplet at τ 4.46 (olefinic H), a triplet at 5.58 (-OH, J = 5.0 c.p.s.) a doublet at 6.57 (-CH₂O-, J = 5.0 c.p.s.), a singlet at 8.03 (allylic H), and a singlet at 8.57 (-CH₂-) in the ratio of 1:1:2:2:4.

\textit{12-Oxatricyclo[4.4.3.0]3-tridecene (XXI)}

The procedure used was as for the preparation of the tridecane analog (XXXIII) by method I. The octalin dialcohol (XX, 2.0 g., 10 mmoles) yielded 1.70 g. (95%) of the cyclic ether as a clear colorless oil. The ether was obtained pure by gas-liquid chromatography using a 10 ft. Carbowax 20 M on firebrick column at 200° with a helium flow-rate of 60 ml./min., retention time 16 min., n^20 D 1.5122.
Analysis. Calculated for \( \text{C}_{12}\text{H}_{18}\text{O} \): C, 80.85; H, 10.18.

Found: C, 80.62; H, 10.37.

The infrared spectrum (film) showed \( \nu_{\text{max}} \) (cm\(^{-1}\)) at 3020 (m), 2920 (s), 1660 (m), 1490 (m), 1445 (s), 1145 (m), 1110 (m), 1090 (m), 1060 (s), 1040 (s), 990 (m), 955 (m), 915 (s), 845 (m), 810 (w), 770 (w), and 725 (s).

The n.m.r. spectrum (48% in CCl\(_4\)) showed a singlet at \( \tau \) 4.47 (olefinic H), an AB quartet with maxima at 6.23, 6.34, 6.47 and 6.59 (\(-\text{CH}_2\text{O}-\), \( J_{\text{AB}} = 7.5 \) c.p.s.), a singlet at 8.05 (allylic H) and a singlet at 8.53 (\(-\text{CH}_2\)) in the ratio of 1:2:2:4.

\( \text{cis-9,10-Bis(acetoxymethyl)}\Delta^2\text{-octalin (XXII)} \)

The procedure used was as for the preparation of the decalin diacetate analog (XXXII). The octalin dialcohol (XX, 1.0 g., 5mmoles) yielded 1.36 g. (97%) of the diacetate, m.p. 57.5 - 59.0\(^\circ\). The diacetate was sublimed at 75\(^\circ\)/1 mm., m.p. unchanged.

Analysis. Calculated for \( \text{C}_{16}\text{H}_{24}\text{O}_4 \): C, 68.55; H, 8.63.

Found: C, 68.89; H, 8.70.

The infrared spectrum (Nujol mull) showed \( \nu_{\text{max}} \) (cm\(^{-1}\)) at 3030 (m), 2940 (s), 1745 (s), 1460 (s), 1380 (m), 1360 (m), 1280 (m), 1240 (s, broad), 1030 (m, broad), and 972 (m).

The n.m.r. spectrum (15% in CCl\(_4\)) showed a triplet at \( \tau \) 4.44 (olefinic H), an AB quartet with maxima at 5.68, 5.87, 5.99, and 6.17 (\(-\text{CH}_2\text{O}-\), \( J_{\text{AB}} = 11.0 \) c.p.s.), a singlet at 7.94 (allylic H), a singlet at 8.02 (\( \text{CH}_3\text{CO}_2^- \)), and a singlet at 8.50 (\(-\text{CH}_2\)) in the ratio of 1:2:2:3:4.
**cis-9,10-Bis(mesyloxymethyl)-Δ²-octalin (XXIII)**

The procedure used was as for the preparation of the hexalin dimesylate analog (XLIII). The yield of dimesylate from 3.0 g. (15 mmoles) of the octalin dialcohol (XX) was 4.5 g. (85%), m. p. 124-125° on crystallization from methanol. On recrystallization from benzene-petroleum ether (b. p. 65-110°), the m. p. was 125-126°.

**Analysis.** Calculated for C₁₄H₂₀O₆S₂: C, 47.71; H, 6.87; S, 18.19

Found: C, 47.85; H, 6.78; S, 18.26.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm⁻¹) at 3030 (m), 2920 (s), 1660 (w), 1460 (s), 1380 (m), 1340 (s), 1180 (s), 1070 (w), 1050 (w), 980 (s), 950 (s, broad), 910 (m), 850 (s), 830 (m), 765 (m), 732 (w), and 670 (m).

The n. m. r. spectrum (15% in CHCl₃) showed a triplet at τ 4.29 (olefinic H), an AB quartet with maxima at 5.50, 5.67, 5.72, and 5.89 (-CH₂OSO₂⁻, $J_{AB} = 10.0$ c. p. s.), a singlet at 6.92 (CH₃SO₃⁻), a singlet at 7.80 (allylic H), and a singlet at 8.37 (-CH₂-) in the ratio of 1:2:3:2:4.

**cis-9,10-Bis(iodomethyl)-Δ²-octalin (XXIV)**

A solution of 5.0 g. (14.2 mmoles) of the dry octalin dimesylate (XXIII) and 6.0 g. (40 mmoles) of dry sodium iodide in 80 ml. of dry N,N-dimethylformamide (DMF) was stirred and refluxed for 5.5 hr. The progress of the reaction was followed by thin-layer chromatography as follows: a micro-sample, withdrawn periodically from the reaction mixture, was spotted on a glass plate (heated to 120°) coated with a 0.25 mm. thickness of silica gel G (Stahl). The plate was developed with chloroform, dried, and sprayed with an aqueous solution containing 1% potassium permanganate and 2% sodium carbonate. The octalin dimesylate had an $R_f$ of about 0.1, while the product iodide had an $R_f$ of about 0.9.
During the course of the reaction, the mixture turned progressively darker in color and a crystalline precipitate appeared. After 5.5 hr. the dark mixture was cooled to room temperature, 30 ml. of water were added and the whole was poured into 150 ml. of benzene. The aqueous layer was separated off. The organic layer was extracted six times with 70 ml. portions of aqueous hydrochloric acid (10% by weight) in order to remove the DMF as its hydrochloride salt. The resulting organic layer was extracted once with 50 ml. of aqueous 10% sodium carbonate solution, once 40 ml. of aqueous 10% sodium thiosulfate solution (to remove any free iodine) and once with 60 ml. of aqueous saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the benzene layer was evaporated to dryness. The black residue was eluted through a silica gel column with petroleum ether (b.p. 30-60°), yielding 0.54 g. (9.2%) of the octalin diiodide, m.p. 101-102° (needles from methanol).

Analysis. Calculated for C_{12}H_{18}I_{2}: C, 34.64; H, 4.36; I, 61.00.

Found: C, 34.75; H, 4.51; I, 61.00.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 3030 (m), 2920 (s), 1460 (s), 1375 (m), 1200 (m), 1160 (m), 845 (w), 795 (w) and 740 (w).

The n.m.r. spectrum (15% in CCl$_4$) showed a triplet at $\delta$4.40 (olefinic H), an AB quartet with maxima at 6.28, 6.44, 6.48 and 6.75 (–CH$_2$I, $J_{\text{AB}}$ = 10.0 c.p.s.), a singlet at 7.83 (allylic H), and a singlet at 8.45 (–CH$_2$–) in the ratio of 1:2:2:4.

**cis-9,10-Dimethyl-$\Delta^{2}$-octalin (XXV)**

A solution of 1.0 g. (2.4 mmoles) of the dry octalin diiodide (XXIV) in 20 ml. of dry glyme was added dropwise to a stirred suspension of 0.25 g. (6.6 mmoles) of powdered lithium aluminum hydride in 20 ml. of dry glyme. The mixture was stirred and gently refluxed for 20 hrs. The reaction mixture was then cooled to
room temperature. Water was added dropwise to the stirred mixture until a white precipitate resulted. Aqueous sulfuric acid (10% by weight) was added in small portions to the mixture until the resulting mixture became distinctly acid. This mixture was extracted four times with 50 ml. portions of diethyl ether. The combined ether extracts were washed once with 50 ml. of aqueous 10% sodium carbonate solution, once with 40 ml. of aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulfate. The dry ether solution was concentrated to a thick oil on a rotary evaporator at 10°/20 mm. The crude product was purified by gas-liquid chromatography using a 10 ft. diethylene glycol succinate column at 95° with a helium flow rate of 40 ml./min., retention time 33 min. The yield of the dimethyloctalin was 71 mg. (18%), m.p. 51-53° (sealed tube). The compound is a waxy white solid and is quite volatile in the open air.

Analysis. Calculated for C_{12}H_{20}: C, 87.73; H, 12.27.

Found: C, 87.78; H, 12.01.

The infrared spectrum (film) showed $\nu_{\text{max}}$ (cm.\(^{-1}\)) at 3030 (m), 2900 (s), 1660 (m), 1450 (s), 1360 (m), 1320 (m), 1220 (m), 1180 (w), 1140 (w), 1020 (m), 1000 (m), 970 (w), 960 (m), 945 (w), 880 (w), 860 (w), 830 (m), and 795 (w).

The n.m.r. spectrum (22% in CHCl_3) showed a triplet at $\tau$4.44 (olefinic H), a multiplet at 8.10 (allylic H), a multiplet at 8.58 (-CH\(_2\)-), and a sharp singlet at 9.10 (-CH\(_3\)) in the ratio of 1:2:4:3.

Decalin-cis-9,10-dicarboxylic Acid\(^{53}\) (XXVI)

A solution of 22.5 g. (0.10 mole) of the octalin diacid (XVII) in 350 ml. of glacial acetic acid was hydrogenated in the autoclave for 5 hr. at room temperature using 0.28 g. of platinum oxide (Adam's catalyst), and hydrogen at 400 p.s.i. The catalyst was then filtered off. The volume of the reaction mixture was reduced to about one-third and the product allowed to crystallize out. The yield of decalin
diacid was 20.5 g. (90%), m.p. 190-191° (foaming) (lit. m.p. 192° (decomp.)).

The infrared spectrum (Nujol mull) showed $v_{\text{max}}$ (cm. $^{-1}$) at 3000 (m, broad), 2600 (m, broad), 1700 (s), 1460 (m), 1400 (m), 1325 (m, shoulder), 1305 (s), 1280 (m), 1250 (s), 1180 (w), 1160 (s), 1070 (m), 1000 (w), 940 (m, broad), 895 (w), 855 (w), 820 (w), 808 (w), 738 (w), and 678 (m).

cis-9,10-Bis(carbomethoxy)decalin $^{53}$ (XXVII)

A quantitative yield of the decalin dimethyl ester (XXVII) was obtained by adding small portions of an ethereal solution of diazomethane $^{74}$ to 1.0 g. of the decalin diacid (XXVI) in 25 ml. of dry glyme at 0°. The solution was allowed to warm up and stand at room temperature for 3 hr. After driving off the excess diazomethane by gentle heating, the solution was evaporated to dryness. The resulting solid dimethyl ester was sublimed at 63°/1 mm., m.p. 60-62.5° (lit. m.p. 63°).

The infrared spectrum (Nujol mull) showed $v_{\text{max}}$ (cm. $^{-1}$) at 2940 (s), 1730 (s), 1450 (s), 1295 (m), 1250 (m), 1220 (s), 1190 (w), 1160 (m), 1140 (s), 1090 (w), 1070 (m), 1015 (m), 970 (w), 950 (w), 880 (w), 855 (w), 810 (w), 770 (w), and 750 (w).

The n.m.r. spectrum (15% in CCl$_4$) showed a sharp singlet at 6.39 (CH$_3$O–) and a broad doublet with maxima at 8.24 and 8.50 (–CH$_2$–) in the ratio of 3:8.

Decalin-9,10-dicarboxylic Anhydride (XXVIII)

The decalin diacid (XXVI, 10.0 g., 44 mmoles) and 70 ml. of concentrated sulfuric acid were stirred together until a clear solution resulted (about 30 min.). The solution was then poured into 500 g. of ice. The white precipitate was filtered off, dried, and crystallized from petroleum ether (b.p. 65-110°) yielding 8.4 g.
(91%) of the anhydride, m.p. 94–96° (lit. 53, 55 m.p. 95–96°).

The infrared spectrum (Nujol mull) showed ν max (cm.−1) at 2900 (s), 2840 (s), 1850 (m), 1785 (s), 1450 (m), 1280 (w), 1250 (m), 1180 (m), 1140 (w), 1080 (w), 1035 (w), 995 (m), 970 (m), 890 (s, broad doublet), 850 (w), 820 (m), 733 (m), and 678 (w).

The n. m. r. spectrum (15% in CCl₄) showed a partly resolved doublet at T 8.40 (–CH₂).  

Decalin-cis-9,10-dicarbonyl Chloride (XXIX)

Method 1. A mixture of 1.0 g. (4.8 mmoles) of the decalin anhydride (XXVIII), 2.0 g. (9.6 mmoles) of phosphorus pentachloride, and 0.50 g. (3.7 mmoles) of anhydrous zinc chloride was heated to 140–150° and stirred for 30 min. The dark mass which formed was cooled to room temperature, broken up into small pieces, and extracted with 30 ml. of diethyl ether. The ether solution was extracted twice with 10 ml. portions of water, dried over anhydrous magnesium sulfate, and evaporated to dryness. The residue was a white solid, yield 0.54 g., m.p. 93–95°, mixed m.p. with the decalin anhydride 93–95°.

Method 2. Dichloromethyl dimethylamine (1.5 g., 11.6 mmoles), prepared according to Bosshard, 59 was added to a solution of 1.0 g. (4.8 mmoles) of the decalin anhydride (XXVIII) in 30 ml. of N,N-dimethylformamide. The reaction mixture was stirred at room temperature for 30 min., then at 75° for 4 hr. The bright orange solution was cooled to room temperature, poured into 100 ml. of water and filtered. The white solid residue was washed with water and dried, yield 0.65 g., m.p. 93–95° mixed m.p. with the decalin anhydride 93–95°.
Decalin-9,10-dicarboximide (XXX)

The decalin anhydride (XXVIII, 2.0 g., 9.8 mmoles) and 2.0 g. (33 mmoles) of urea were powdered in a mortar and mixed intimately. The mixture was heated to 180° and stirred until the effervescence stopped and a solid formed (about 2 hr.). After cooling to room temperature the solid was pulverized, mixed with 75 ml. of water and extracted twice with 50 ml. portions of chloroform. The chloroform layers were combined, dried over anhydrous magnesium sulfate and evaporated to dryness. Crystallization from 95% ethanol yielded 1.6 g. (80%) of the imide, m. p. 187-188° (lit. 53 m. p. 188-189°).

The infrared spectrum (Nujol mull) showed v max (cm. -1) at 3180 (m), 2940 (s), 1780 (m), 1720 (s), 1450 (m), 1340 (m, quintet), 1230 (m), 1130 (s), 1090 (w), 955 (w), 820 (m, broad), and 678 (w).

The n. m. r. spectrum (15% in CDC13) showed a very broad singlet at δ 1.3 (-CONHCO-) and a multiplet at δ 8.45 (-CH2-) in the ratio of 1:16.

cis-9,10-Bis(hydroxymethyl)decalin (XXXI)

The procedure used was as for the preparation of the analogous hexalin dialcohol (XLI). The yield of the decalin dialcohol from 2.0 g. (9.62 mmoles) of the decalin anhydride (XXVIII) was 1.77 g. (93%). On crystallization from ethanol-water the alcohol melted at 183-184°.

Analysis. Calculated for C12H22O2: C, 72.68; H, 11.18
Found: C, 72.66; H, 10.86.

The infrared spectrum (Nujol mull) showed v max (cm. -1) at 3250 (s), 2920 (s), 1500 (m), 1460 (s), 1380 (m), 1080 (m), 1060 (m), 1045 (s), 1020 (s), 1005 (s), 970 (s), 910 (w), and 880 (w).
The n.m.r. spectrum (18% in DMSO) showed a triplet at 5.78 (-OH, \( J = 5.0 \) c.p.s.), a doublet at 6.60 (-CH\(_2\)O-, \( J = 5.0 \) c.p.s.), and a singlet at 8.60 (-CH\(_2\)-) in the ratio of 1:2:8.

cis-9,10-Bis(acetoxy methyl) decalin (XXXII)

The decalin dialcohol (XXXI, 0.4 g., 2.0 mmoles), 3 drops of concentrated sulfuric acid, and 15 ml. of acetic anhydride were heated together on a steam bath for 30 min. The resulting solution was cooled to room temperature, poured into 100 ml. of crushed ice and water, and neutralized by adding small portions of solid sodium carbonate. The mixture was extracted three times with 30 ml. portions of diethyl ether. The ether extracts were combined, dried over anhydrous magnesium sulfate and evaporated to dryness, yielding 0.43 g. (75%) of the diacetate. On crystallization from acetone-water the diacetate melted at 80.0 - 80.5°.

Analysis. Calculated for \( \text{C}_{16}\text{H}_{26}\text{O}_4 \): C, 68.06; H, 9.28

C, 68.14; H, 9.18.

The infrared spectrum (Nujol mull) showed \( \text{max} \ (\text{cm.}^{-1}) \) at 2940 (s), 2850 (s, shoulder), 1740 (s), 1455 (m), 1360 (m, doublet), 1270 (m, doublet), 1240 (s), 1020 (s), 970 (m), 950 (w), 880 (w), 869 (w), and 785 (w).

The n.m.r. spectrum (15% in CHCl\(_3\)) showed singlets at 5.82 (-CH\(_2\)O-), 7.93 (CH\(_3\)CO\(^-\)) and 8.46 (-CH\(_2\)-) in the ratio of 2:3:8.

A small sample of the decalin diacetate (XXXII) was reduced using lithium aluminum hydride in glyme. The product gave a melting point of 183-184°, mixed m.p. with the decalin dialcohol (XXXI) 183-184°. The infrared spectra of the reduction product and the decalin dialcohol (XXXI) were identical.
12-Oxatricyclo[4.4.3.0]tridecane (XXXIII)

Method 1. A solution of 1.75 g. (8.84 mmoles) of the decalin dialcohol (XXXI) and 1.50 g. (8.72 mmoles) of p-toluenesulfonic acid in 70 ml. of benzene was refluxed for 24 hr. in an apparatus fitted with a Dean-Stark water trap. The mixture was then extracted three times with 50 ml. portions of 5% aqueous sodium carbonate solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The yield of tricyclic ether was 1.50 g. (95%). The ether was obtained pure by gas-liquid chromatography (g.l.c.) using a 10ft. Carbowax 20 M on firebrick column at 200° with a helium flow rate of 60 ml./min., retention time 11 min., m.p. 61-62° (lit. 62-64°). The tricyclic ether sublimed at 30°/1 mm. as a waxy white solid.

Analysis. Calculated for C_{12}H_{16}O: C, 79.94; H, 11.18


The infrared spectrum (Nujol mull) showed ν max (cm.⁻¹) at 2940 (s), 2850 (s), 1490 (w), 1455 (m), 1380 (w), 1200 (w), 1085 (w), 1060 (s), 1040 (m), 970 (w), 940 (w), 925 (s), 893 (w), 850 (w), 793 (w), and 720 (w).

The n.m.r. spectrum (15% in CCl₄) showed singlets at δ 6.38 (-CH₂O-) and 8.54 (-CH₂-) in the ratio of 1:4.

Method 2. Methanesulfonyl chloride (0.19 ml., 2.52 mmoles) was added dropwise to a stirred solution of 0.50 g. (2.52 mmoles) of the decalin dialcohol (XXXI) in 13 ml. of dry pyridine maintained at 0°. The mixture was allowed to stand at 0° overnight. Chloroform (100 ml.) was added and the solution extracted with aqueous sulfuric acid (10% by weight) to remove the pyridine. The chloroform layer was dried over a mixture of anhydrous sodium carbonate and magnesium sulfate, then evaporated to dryness. Sublimation of the crude product at 25°/1 mm yielded 0.116 g. (26%) of a waxy solid, m.p. 61-62°. The infrared spectrum and g.l.c. tracing of this compound
were identical with those obtained for the tricyclic ether in method 1.

Method 3. A solution of 0.50 g. (1.41 mmoles) of the decalin dimesylate (XXXIV) in 15 ml. of dry glyme was added dropwise to a stirred suspension of 0.15 g. (3.95 mmoles) of powdered lithium aluminum hydride in 15 ml. of dry glyme. The mixture was stirred and refluxed for 16 hr. in a hume hood, then cooled to room temperature. Water was added to the mixture until a white precipitate formed. Aqueous sulfuric acid (50 ml., 5% by weight) was added. The oily mixture was extracted three times with 30 ml. portions of diethyl ether. The ether layers were combined, dried over a mixture of anhydrous sodium carbonate and magnesium sulfate, and evaporated to dryness. Sublimation at 25°/1 mm. yielded 0.10 g. (40%) of a waxy solid m. p. 61-62°. The infrared spectrum and g.l.c. tracing of this compound were identical with those obtained for the tricyclic ether prepared by method 1.

**cis-9,10-Bis(mesyloxymethyl)decalin (XXXIV)**

The procedure used was as outlined for the preparation of the analogous hexalin dimesylate (XLII). The decalin dialcohol (XXXI, 3.3 g., 17 mmoles) yielded 5.2 g. (90%) of the decalin dimesylate, m. p. 126.5 - 128° (crystallized from benzene-petroleum ether (b. p. 65-110°)).

**Analysis.** Calculated for $C_{14}H_{26}O_6S_2$: C, 47.43; H, 7.40.

Found: C, 47.85; H, 7.32.

The infrared spectrum (KBr pellet, P. E. 2l) showed $v_{\text{max}}$ (cm. $^{-1}$) at 2940 (m), 2860 (m), 1475 (m), 1450 (m), 1335 (s), 1165 (s), 985 (s), 950 (s, broad), 835 (s), and 750 (m).

The n. m. r. spectrum (15% in CHCl$_3$) showed singlets at $^\tau$5.68 (-CH$_2$OSO$_2$-), 6.92 (CH$_3$SO$_3$-), and 8.40 (-CH$_2$-) in the ratio of 2:3:8.
cis-9,10-Bis(cyanomethyl)decalin (XXXV)

Method 1. A mixture of 1.0 g. (2.8 mmoles) of the dry decalin dimesylate (XXXIV), 2.0 g. (41 mmoles) of dry sodium cyanide, and 40 ml. of dry dimethyl sulfoxide was stirred and heated at 130° for 24 hr. The reaction mixture was cooled to room temperature and filtered. The white solid residue dissolved completely in cold water. The filtrate was poured into 300 ml. of water and extracted four times with 100 ml. portions of 9:1 diethyl ether - petroleum ether (b.p. 30-60°). The combined organic extracts were washed once with 100 ml. of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated. Petroleum ether (b.p. 30-60°) was added to the oily residue. The white precipitate which formed was filtered off and dried, yield 0.5 g., m.p. 112-120°. An infrared spectrum of this material showed the characteristic bands for the decalin dimesylate, but showed no nitrile band around 2250 cm. \(^{-1}\).

Method 2. A solution of 1.0 g. (2.8 mmoles) of the decalin dimesylate (XXXIV) in 25 ml. of dry pyridine was added dropwise to a stirred solution of 1.02 g. (11.2 mmoles) of dry cuprous cyanide in 25 ml. of dry pyridine at 100°. No increase in temperature was noticed during the addition. The mixture was then heated to reflux and stirred.

A sample (2 ml.) of the reaction mixture was withdrawn daily, poured into 30 ml. of benzene, and extracted with dilute aqueous ammonia until the aqueous layers remained colorless. The organic layer was then washed successively with two 25 ml. portions of dilute aqueous hydrochloric acid, two 25 ml. portions of water, and one 20 ml. portion of aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulfate and evaporated to dryness. In each case the white solid product had a melting point and mixed melting point of 122-126° with starting decalin dimesylate.
At 48 hr. two 5 ml. samples of the reaction mixture were sealed in Carius tubes and heated at 198°. The tubes were removed after 6 and 30 hr. and the contents worked up as for the daily samples. In both cases small amounts of a clear oil were obtained which gave infrared spectra identical to that for 12-oxatricyclo[4.4.3.0]tridecane (XXXIII).

After 6 days the remainder of the reaction mixture was worked up as for the samples. The crude product melted at 111-115°, mixed m. p. with the decalin dimesylate 119-125°. An infrared spectrum of the material indicated starting material and a trace of the tricyclic ether (XXXIII) present. No nitrile band was observed.

Method 3. A mixture of 0.50 g. (1.4 mmole) of the dry decalin dimesylate (XXXIV), 0.20 g. (4.1 mmole) of dry sodium cyanide and 25 ml. of dry diethylene glycol dimethyl ether (diglyme) was stirred and heated at 100° for 1 hr., then 120° for 22 hr. The reaction mixture was then cooled to room temperature, poured into 100 ml. of water, and filtered. The white residue was washed thoroughly with water and dried, yield 0.47 g., m. p. 124-126°, mixed m. p. with the decalin dimesylate 124-126°. An infrared spectrum of the product was identical with that for the decalin dimesylate. No nitrile band was present.

Acetylenedicarboxylic Acid (XXXVI)

The monopotassium salt of acetylenedicarboxylic acid (110 g.) was added in small portions to a stirred solution of 125 ml. of concentrated sulfuric acid in 1000 ml. of water. The resulting solution was extracted six times with 200 ml. portions of diethyl ether. The combined ether extracts were washed once with 100 ml. of saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The yield of acid was 65 g. (79%), m. p. 178-180° (lit. 62 m. p. 175-176°).
Acetylenedicarboxylic acid (XXXVI, 65 g., 0.57 moles) and 0.5 g. of hydroquinone were placed in the autoclave. Glyme (100 ml.), chilled to -50°, was then added followed by 300 ml. (195 g., 3.6 moles) of liquid 1,3-butadiene, chilled to -70°. The reaction mixture was heated to 190° and stirred for 8 hr. The system was allowed to cool to room temperature overnight. The reaction mixture was removed from the autoclave and distilled at 50°/15 mm. to remove the glyme, water, and butadiene dimers. The partly solidified residue was quickly heated to 230°/15 mm. in order to convert any diacid product to its anhydride. The dehydration was complete when no solid material remained visible in the residue. The residue was then distilled at 140-145°/3 mm. yielding the crude anhydride product as a pale yellow solid. An appreciable amount of intractable polymeric material remained in the stillpot.

The crude product was dissolved in 600 ml. of diethyl ether and extracted four times with 100 ml. portions of 10% aqueous sodium carbonate solution. The ether layer was then washed once with 100 ml. of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. Crystallization from petroleum ether (b.p. 65-110°) gave 36 g. (31%) of the hexalin anhydride, m.p. 99.5 - 101° (lit. m.p. 102-103°).

The infrared spectrum (KBr pellet, P.E. 2I) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 3040 (m), 2940 (m), 1840 (s), 1770 (s), 1630 (w), 1455 (m), 1440 (m), 1380 (m), 1340 (s), 1285 (m), 1225 (s), 1195 (m), 975 (s, broad), and 700 (s, multiplet).

The n.m.r. spectrum (12% in CCl$_4$) showed a multiplet at $\tau$4.10 (olefinic H) and a complex quartet with maxima at 7.20, 7.47, 7.78 and 8.03 (allylic H) in the ratio of 1:2.
$^{2,6}$-Hexalin-9,10-dicarboximide (XXXVIII)

The procedure used was as for the decalin imide analog (XXX). The yield of the hexalin imide from 2.0 g. (9.9 mmoles) of the hexalin anhydride (XXXVII) was 1.27 g. (64%) after crystallization from methanol. Recrystallization from chloroform-petroleum ether (b.p. 65-110°) gave the hexalin imide with m.p. 218-219° (sealed tube).

Analysis. Calculated for C$_{12}$H$_{13}$NO$_{2}$: C, 70.92; H, 6.45; N, 6.89.

Found: C, 70.87; H, 6.58; N, 7.00.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 3130 (s), 3030 (m), 2900 (s), 2750 (w), 1750 (s), 1700 (s), 1440 (s), 1420 (m), 1360 (s), 1320 (m, doublet), 1180 (s), 1100 (s), 1080 (m), 1035 (w), 1005 (w), 840 (m, broad), 720 (m), and 695 (m).

The n.m.r. spectrum (10% in CDCl$_3$) showed a multiplet at $\tau$4.08 (olefinic H) and a complex quartet with maxima at 7.20, 7.46, 7.81, and 8.06 (allylic H) in the ratio of 1:2. The peak at $\tau$1.3, expected for the imido proton, was absent.

$^{2,6}$-Hexalin-cis-9,10-dicarboxylic Acid (XXXIX)

A mixture of the hexalin anhydride (XXXVII, 1.5 g., 7.4 mmoles) in 20 ml. of 10% aqueous sodium hydroxide solution, containing 2 ml. of ethanol, was stirred and refluxed for 16 hr. After cooling to room temperature, the reaction mixture was extracted three times with 8 ml. portions of diethyl ether. Concentrated hydrochloric acid was then added carefully to the stirred aqueous layer until complete precipitation of the hexalin diacid resulted. The precipitate was filtered off, washed with water, and dried, yield 1.4 g. (86%). On crystallization from ethanol-water the hexalin diacid melted at 226-227° (foaming) (lit.$^{55}$ m.p. 226° (decomp.)).
The infrared spectrum (Nujol mull) showed $\nu_{\max}$ (cm.$^{-1}$) at 3030 (s), 2920 (s), 2650 (s, broad), 1700 (s), 1660 (m), 1460 (s), 1440 (m), 1400 (m), 1380 (m), 1340 (w), 1270 (m), 1220 (s), 1190 (m), 1020 (w), 1000 (m), 950 (m, broad), 880 (w), 860 (w), 785 (w), 740 (m), and 672 (m).

cis-9,10-Bis(carbomethoxy)-$\Delta^{2,6}$-hexalin (XII)

The procedure used was as for the preparation of the decalin dimethyl ester analog (XXVII). The product (quantitative yield) was crystallized from petroleum ether (b.p. 65-110°), m.p. 96.5 - 98° (lit. m.p. 100°).

The infrared spectrum (Nujol mull) showed $\nu_{\max}$ (cm.$^{-1}$) at 3030 (w), 2920 (s), 1735 (s), 1660 (w), 1460 (s), 1430 (m), 1380 (m), 1290 (m), 1270 (s), 1235 (m), 1190 (s, broad doublet), 1100(m), 1085 (m), 1045 (m), 1000 (m), 975 (w), 938 (m), 920 (w), 885 (w), 860 (m), 845 (w), 795 (w), 750 (m), and 675 (s, doublet).

The n.m.r. spectrum (15% in CCl$_4$) showed a triplet at $\delta$4.51 (olefinic H), a singlet at 6.38 (CH$_3$CO$^-$) and a complex quartet with maxima at 7.21, 7.50, 7.72 and 8.01 (allylic H) in the ratio of 2:3:4.

cis-9,10-Bis(hydroxymethyl)-$\Delta^{2,6}$-hexalin (XIII)

A solution of dry hexalin anhydride (XXXVII, 30 g., 0.15 mole) in 150 ml. of dry glyme was added dropwise to a stirred suspension of 7.3 g. (0.19 mole) of powdered lithium aluminum hydride in 100 ml. of dry glyme. The mixture was refluxed and stirred for 20 hr. After cooling the reaction mixture to room temperature, water was added dropwise with stirring until a white precipitate formed. Aqueous sulfuric acid (10% by weight) was added in small portions until the mixture became distinctly acidic. Water was added to make the total volume 1500 ml. After cooling the mixture to 0°, the white crystalline solid was filtered off and dried. The yield of the hexalin dialcohol was 27 g. (94%), m.p. 174.5 -
176° (sealed tube), on crystallization from ethanol-water (lit. m. p. 130-134°).

Analysis. Calculated for $\text{C}_{12}\text{H}_{18}\text{O}_{2}$: C, 74.19; H, 9.34.

Found: C, 73.79; H, 9.35.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm$^{-1}$) at 3300 (m), 3030 (w), 2940 (s), 1660 (w), 1450 (m, broad), 1070 (m), 1015 (s), 980 (s), and 660 (s).

The n.m.r. spectrum (23% in DMSO) showed a triplet at $\tau$ 4.48 (olefinic H), a triplet at 5.43 ($-\text{OH}$, $J = 5.0$ c.p.s.), a doublet at 6.60 ($-\text{CH}-\text{O}$, $J = 5.0$ c.p.s.), and a singlet at 8.07 (allylic H) in the ratio of 2:1:2:4.

**cis-9,10-Bis(acetoxymethyl)-Δ$_{2,6}$-hexalin (XLII)**

The procedure used was as for the preparation of the analogous decalin diacetate (XXXII). The yield of hexalin diacetate from 1.0 g. (5.2 mmoles) of the hexalin dialcohol (XLI) was 1.36 g. (95%). The diacetate was purified by sublimation at 80°/1mm., m.p. 65.5 - 67.0°.

Analysis. Calculated for $\text{C}_{16}\text{H}_{22}\text{O}_{4}$: C, 69.04; H, 7.97.

Found: C, 69.08; H, 8.02.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm$^{-1}$) at 3030 (w), 2940 (s), 1735 (s), 1650 (w), 1460 (m), 1380 (m), 1240 (s, multiplet), 1075 (m), 1040 (m), 1000 (w), 985 (m), 940 (w), 910 (w), 840 (w), 680 (m), and 670 (m).

The n.m.r. spectrum (15% in CCl$_4$) showed a triplet at $\tau$ 4.46 (olefinic H), a singlet at 5.91 ($-\text{CH}_2\text{O}$), a singlet at 7.98 (allylic H), and a singlet at 3.02 ($\text{CH}_3\text{CO}_2$) in the ratio of 2:2:7 (the singlets at 7.98 and 8.02 were not resolved in the area integral).
cis-9,10-Bis(mesyloxymethyl)-Δ²,⁶-hexalin (XLIII)

To a stirred solution of 25 ml. (0.33 mole) of methanesulfonyl chloride in 100 ml. of dry pyridine was added dropwise a solution of 27 g. (0.14 mole) of the dry hexalin dialcohol (XLI) in 125 ml. of dry pyridine. The reaction mixture temperature was maintained between -5 and -10° throughout the addition in order to eliminate formation of the hexalin cyclic ether (L). The reaction mixture was then stirred for 2 hr. at -5° and allowed to stand overnight at 0°. The resulting mixture was poured onto 100 g. of crushed ice. Aqueous hydrochloric acid (10% by weight) was added in small portions with stirring until the mixture became distinctly acid. The mixture was cooled to 0°. The precipitate was filtered off, washed with water, and dried, yield 45 g. (92%). On crystallization from benzene-petroleum ether (b. p. 65-110°) the hexalin dimesylate melted at 115-116°.

Analysis. Calculated for C_{14}H_{22}O_{4}S_2: C, 47.98; H, 6.33; S, 18.30.

Found: C, 48.13; H, 6.07; S, 18.25.

The infrared spectrum (KBr pellet, P. E. 21) showed ν_{max} (cm.⁻¹) at 3020 (m), 2940 (s), 1650 (w), 1450 (m), 1425 (m), 1340 (s, doublet), 1175 (s, doublet), 1080 (m), 950 (s, multiplet), 850 (s, multiplet), 760 (m), and 670 (m, multiplet).

The n. m. r. spectrum (15% in CDCl₃) showed a triplet at ¼ 4.38 (olefinic H) and singlets at 5.72 (-CH₂O⁻), 6.98 (CH₃SO₃⁻), and 7.87 (allylic H) in the ratio of 2:2:3:4.

 cis-9,10-Bis(iodomethyl)-Δ²,⁶-hexalin (XLIV)

A mixture of 10 g. (26.5 mmoles) of the dry hexalin dimesylate (XLIII), 13 g. (87 mmoles) of dry sodium iodide and 150 ml. of dry purified N,N-dimethylformamide was stirred and refluxed for 10 hr. The progress of the reaction was followed by
spotting microsamples of the reaction mixture after 3, 5, 7 and 9 hr. on heated (120°) thin-layer chromatography plates coated with a 0.25 mm. thickness of silica gel G (Stahl). The plates were developed with chloroform, dried, and sprayed with an aqueous solution of 1% potassium permanganate and 2% sodium carbonate. The order of elution was the hexalin diiodide (XLIV) at $R_f$ 0.9, the hexalin cyclic ether (L) at 0.3, and the hexalin dimesylate (XLIII) at 0.1. No change in the composition of the reaction mixture was noted after 7 hr.

The dark reaction mixture was cooled to room temperature, 50 ml. of water were added, and the whole was poured into 400 ml. of benzene. The aqueous layer was separated off. The organic layer was extracted six times with 100 ml. portions of aqueous hydrochloric acid (10% by weight), once with 100 ml. of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The crude product was boiled in 150 ml. of petroleum ether (b.p. 30–60°), treated with charcoal, and filtered. On cooling the hexalin diiodide crystallized out as fine needles, yield 6.5 g. (59%), m.p. 98–99°. The diiodide was then recrystallized from 95% ethanol giving colorless needles, m.p. 98–99°.

The residue from the petroleum ether extraction was taken up in boiling methanol and filtered. On cooling 1.0 g. of unreacted hexalin dimesylate (XLIII) was obtained, m.p. 117–118.5°, mixed m.p. with authentic material 117–118°.

Analysis. Calculated for $C_{12}H_{16}I_2$: C, 34.81; H, 3.90; I, 61.30.

Found: C, 34.76; H, 4.00; I, 61.37.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm. $^{-1}$) at 3030 (m), 2920 (s), 1650 (w), 1460 (s), 1440 (m), 1420 (m), 1380 (m), 1260 (w), 1215 (m), 1180 (s), 1020 (w), 1000 (m), 930 (w), 895 (m), 855 (w), 805 (w), 725 (w), and 673 (s).
The n. m. r. spectrum (15% in CDCl₃) showed a triplet at τ 4.42 (olefinic H) and singlets at 6.34 (-CH₂I) and 7.87 (allylic H) in the ratio of 1:1:2.

cis-9,10-Dimethyl-\(\Delta^{2,6}\)-hexalin (XLV)

For this reaction the hexalin diiodide (XLIV) must be free of any hexalin dimesylate (XLIII) impurity (accomplished by several crystallizations from petroleum ether (b. p. 30–60°)).

A solution of 4.0 g. (9.6 mmoles) of the dry pure hexalin diiodide (XLIV) in 50 ml. of dry glyme was added dropwise to a stirred suspension of 1.1 g. (29 mmoles) of powdered lithium aluminum hydride in 50 ml. of dry glyme. The mixture was stirred and refluxed for 16 hr., then cooled to 0°. Small pieces of ice were added carefully to the stirred mixture until a white precipitate formed. Aqueous sulfuric acid (10% by weight) was added in small portions until the mixture became distinctly acid. The mixture was extracted three times with 50 ml. portions of dichloromethane. The combined organic extracts were washed once with 50 ml. of aqueous 10% sodium carbonate solution, once with 25 ml. of aqueous 10% sodium thiosulfate solution (to remove any free iodine), then dried over anhydrous magnesium sulfate. The crude product was isolated as an oil by carefully evaporating off the dichloromethane and glyme on a rotary evaporator at 10°/20 mm.

The dimethylhexalin was obtained pure by gas-liquid chromatography using a 10 ft. Carbowax 20M on firebrick column at 150° with helium flow rate of 60 ml./min., retention time 22 min. A minor component (about 5%) in the crude product had a retention time of 26 min.

The yield of the dimethylhexalin (waxy solid, quite volatile in the open air) was 0.63 g. (40%), m. p. 69–71° (sealed tube).
Analysis. Calculated for C_{12}H_{18}: C, 88.82; H, 11.18; mol. wt. 162.3.

Found: C, 88.72; H, 11.45; mol. wt. 162 (mass spec.).

The mass spectrum showed a parent peak M at m/e 162. The principal fragmentation peaks were M-15 (loss of methyl radical), M-54 (loss of butadiene), M-55, M-56, M-57, M-69 (loss of methyl radical plus butadiene), and M-71 (formation of the cycloheptatrienyl cation).

The infrared spectrum (film) showed \( \nu_{\text{max}} \) (cm\(^{-1}\)) at 2900 (s, broad), 1650 (m), 1430 (s, broad), 1365 (s), 1320 (m, doublet), 1235 (s), 1220 (m), 1180 (w), 1150 (m), 1130 (m), 1085 (m), 1010 (s), 960 (m), 920 (m), 910 (m), 875 (m), 852 (m), 830 (s), 718 (m), and 660 (s).

The n.m.r. spectrum (15% in CCl\(_4\)) showed a triplet at \( \delta 4.53 \) (olefinic H), a broad singlet at \( \delta 8.15 \) (allylic H), and a singlet at \( \delta 9.10 \) (CH\(_3\)) in the ratio of 2:4:3.

An n.m.r. spectrum of the minor component (about 2 mg. in 90 \( \mu \)l of CCl\(_4\)) showed singlets at \( \delta 8.16 \) (allylic H) and \( \delta 8.55 \) (\(-\text{CH}_2\)). Due to a high noise level in the spectrum, the resonance due to any olefinic hydrogen atoms could not be detected.

cis-9,10-Dimethyldecalin (XLVII)

A stirred mixture of 250 mg. (1.54 mmols) of the dimethylhexalin (XLV) and 22 mg. of platinum oxide (Adam's catalyst) in 11 ml. of 95% ethanol was hydrogenated under a slightly positive pressure (i.e., a few centimeters of Hg. above atmospheric pressure). There was a linear uptake of 76 ml. of hydrogen in 80 min., corresponding to 2.05 moles of hydrogen/mole of the dimethyldecalin. The catalyst was then filtered off. The filtrate was carefully concentrated to a thick oil by evaporating off the ethanol at 25\(^\circ\)/20 mm. on a rotary evaporator.
The pure dimethyldecalin was obtained by gas-liquid chromatography using a 10 ft. Carbowax 20M on firebrick column at 145° with a helium flow rate of 60 ml./min., retention time 12 min. The yield of the dimethyldecalin (waxy solid, quite volatile in the open air) was 200 mg. (78%), m. p. 89-91° (sealed tube). The compound could be sublimed at 25°/1 mm.

Analysis. Calculated for C₁₂H₂₂: C, 86.67; H, 13.33; mol. wt. 166.3.

Found: C, 86.84; H, 13.07; mol. wt. 166 (mass spec.).

The mass spectrum showed a parent peak M at m/e 166. The principal fragmentation peaks were M-15 (loss of methyl radical), M-57, M-71, M-83, and M-84.

The infrared spectrum (film) showed ν (cm⁻¹) at 2940 (s, broad), 2680 (m), 1460 (s, broad), 1375 (m), 1350 (m), 1280 (m), 1200 (m), 1180 (m), 1145 (m), 1090 (w), 1038 (m), 1005 (m), 940 (m), 930 (m), 885 (m), 858 (w), 840 (m), 815 (w), 782 (w), and 755 (w).

The n.m.r. spectrum (15% in CHCl₃) showed a broad singlet at τ 8.50 (-CH₂-) and a sharp singlet at 9.12 (CH₃-) in the ratio of 8:3.

\textit{cis-9,10-Bis(cyanomethyl) Δ²,6-hexalin (XLVIII)}

A. From \textit{cis-9,10-bis(mesyloxymethyl) Δ²,6-hexalin (XLIII)}.

Method 1. A mixture of 23 g. (66 mmoles) of the dry hexalin dimesylate (XLIII), 19 g. (0.39 mole) of dry purified sodium cyanide and 300 ml. of dry N-methyl-2-pyrrolidinone (NMP) was stirred and heated at 175° for 4 hr. The initial light brown mixture turned progressively darker during the reaction. The initially suspended sodium cyanide slowly dissolved during the reaction and was replaced by a more crystalline suspension (probably sodium methanesulfonate).
The final reaction mixture was cooled to room temperature and poured into 1 l. of benzene. The black benzene mixture was extracted once with 500 ml. of aqueous 50% saturated sodium chloride solution, then four times with 200 ml. portions. The last two aqueous layers were almost colorless. The organic layer was then extracted five times with 300 ml. portions of aqueous hydrochloric acid (10% by weight) to remove the NMP as its hydrochloride salt. Again the last two aqueous layers were nearly colorless. The organic layer was finally extracted twice with 300 ml. portions of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to constant weight. The crude product mixture consisted of a partly crystallized oil, yield 13.5 g.

Diethyl ether (20 ml.) was added to the crude product. Petroleum ether (b.p. 30-60°) was then added in small portions until the mixture turned just turbid. After standing at 0° overnight the mixture was filtered and the crystalline residue washed with a solution of 1:1 diethyl ether-petroleum ether (b.p. 30-60°). The washings were added to the filtrate.

The yield of crude crystalline hexalin dinitrile was 3.06 g., m.p. 149-152°. After crystallization from benzene-petroleum ether (b.p. 65-110°), the dinitrile melted at 152-153°, yield 2.90 g. (21%). A small quantity for elemental analysis was sublimed at 115°/2 mm., m.p. 152-153°.

Analysis. Calculated for C_{14}H_{16}N_2: C, 79.21; H, 7.60; N, 13.20.


The infrared spectrum (Nujol mull) showed \( \nu_{\text{max}} \) (cm\(^{-1}\)) at 3050 (m), 2920 (s), 2880 (s), 2260 (m), 1660 (w), 1460 (s), 1435 (m), 1415 (m), 1380 (m), 1325 (w), 1245 (w), 1000 (m), 710 (m), and 680 (s).

The n.m.r. spectrum (14% in CDCl\(_3\)) showed a triplet at \( \tau 4.40 \) (olefinic H), a sharp singlet at 7.54 (-CH\(_2\)CN), and a broad singlet at 7.83 (allylic H) in the ratio of 1:1:2.
The filtrate containing the remainder of the crude product mixture was evaporated to constant weight. The resulting oil was distilled at 60°/1 mm. to yield 1.5 g. (13%) of 12-oxatricyclo [4.4.3.0]-3,8-tridecadiene (L). An appreciable amount of a viscous intractable oil remained in the stillpot. The cyclic ether was obtained pure by gas-liquid chromatography using a 10 ft. Carbowax 20M on firebrick column at 200° with a helium flow rate of 60 ml./min., retention time 11 min., 

\[ n^2 \text{D} 1.5312 \text{ (lit.} n^2 \text{D } 1.5195). \]

Analysis. Calculated for C_{12}H_{16}O: C, 81.77; H, 9.15.

Found: C, 81.68; H, 9.20.

The infrared spectrum (film) showed υ_{max} (cm.\(^{-1}\)) at 3030 (m), 2900 (s), 1660 (m), 1500 (m), 1425 (m), 1320 (w), 1270 (w), 1135 (m), 1120 (m), 1100 (m), 1080 (s), 1035 (s), 1005 (s), 907 (s), 872 (m), 760 (w), and 730 (s).

The n.m.r. spectrum (13% in CCl₄) showed a triplet at \( \tau 4.50 \) (olefinic H), a sharp singlet at \( \tau 6.39 \) (-CH₂O-), and a multiplet with maxima at 7.64, 7.96, and 8.28 (allylic H) in the ratio of 1:1:2.

Method 2. A mixture of 10 g. (29 mmoles) of the dry hexalin dimesylate (XLIII), 10 g. (0.20 mole) of dry purified sodium cyanide and 400 ml. of dry N,N-dimethylformamide (DMF) was stirred and refluxed for 48 hr. The appearance of the reaction mixture changed as in method 1. The progress of the reaction was followed by thin-layer chromatography. Periodically, a sample of the reaction mixture was spotted on a glass plate (heated to 120°), coated with a 0.25 mm. thickness of aluminum oxide G (Stahl). The cooled plate was developed with a mixture of 1:1 benzene-chloroform, then sprayed with an aqueous solution of 1% potassium permanganate and 2% sodium carbonate. The \( R_f \) values for the tricyclic aminonitrile (XLIX), the hexalin dimesylate and dinitrile were 0.38, 0.45, and 0.81, respectively.
The volume of the final reaction mixture was reduced to about 50 ml. by distilling off the excess DMF at atmospheric pressure. The residue was poured into 250 ml. of chloroform and extracted once with a 200 ml. portion, then four times with 70 ml. portions of aqueous 50% saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and evaporated to constant weight. The black oily residue was eluted through an alumina column, first with benzene, yielding 0.81 g. (13.5%) of the hexalin dinitrile, m.p. 151-152° (mixed m.p. with authentic material 151-152°) and a small amount of the hexalin cyclic ether (L) (identified by its infrared spectrum), then with chloroform, yielding 0.62 g. (10.2%) of the hexalin cyclic aminonitrile (XLIX), m.p. 152-155°.

On recrystallization from petroleum ether (b.p. 65-110°) the cyclic aminonitrile melted at 157-158.5°. A small amount for elemental analysis was sublimed at 130°/2 mm., m.p. 157-158°. A 1:1 mixture of this cyclic nitrile and the hexalin dinitrile melted over the range 125-140°.

Analysis of the cyclic nitrile (XLIX).

Calculated for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20.

Found: C, 79.03; H, 7.55; N, 13.16.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 3450 (m), 3380 (m), 3280 (w), 3040 (w), 2920 (s), 2880 (s), 2190 (s), 1650 (s), 1600 (s), 1460 (m), 1420 (m), 1380 (m), 1340 (w), 995 (w), 870 (w), 800 (w), and 730 (w).

The n.m.r. spectrum (13% in DMSO) showed singlets at 3.63 (-NH$_2$), 4.45 (olefinic H), and 8.09 (both kinds of allylic H) in the ratio of 1:2:5.

The ultraviolet spectrum showed $\lambda_{\text{max}}$ (EtOH) at 269 m$\mu$ ($\varepsilon = 10,800$). On addition of concentrated sulfuric acid, the spectrum shifted to 264 m$\mu$ ($\varepsilon = 1340$).
Method 3. A solution of 1.0 g. (2.9 mmoles) of the hexalin dimesylate (XLIII) in 15 ml. of dry dimethyl sulfoxide (DMSO) was added dropwise to a stirred solution of 2.0 g. (41 mmoles) of dry sodium cyanide in 30 ml. of DMSO (heated to 90°). No exothermicity was noted. The mixture was stirred and heated at 160° for 3 hr., then at 150° for 20 hr. The reaction mixture was cooled to room temperature, poured into 50 ml. of water and extracted four times with 30 ml. portions of a 4:1 mixture of diethyl ether – petroleum ether (b.p. 65-110°). The organic layer was washed once with aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. Fractional crystallization of the crude product from diethyl ether–petroleum ether (b.p. 65-110°) gave first 50 mg. (8.3%) of the hexalin dinitrile (XLVIII), m.p. 151-152° (mixed m.p. with authentic material 151-153°), and second 70 mg. (11.5%) of the hexalin cyclic aminonitrile (XLIX), m.p. 156-158° (mixed m.p. with authentic material 156-158°).

Method 4. A mixture of 1.0 g. (2.9 mmoles) of the dry hexalin dimesylate (XLIII), 1.02 g. (11.2 mmoles) of dry cuprous cyanide, and 50 ml. of dry pyridine was stirred and refluxed for 5 days. A 5 ml. sample of the reaction mixture was withdrawn periodically and poured into a solution of 10 ml. of diethyl ether in 80 ml. of benzene. The organic mixture was extracted with 30 ml. portions of dilute aqueous ammonia until all the copper salts had been extracted out as their blue ammonia complexes. The organic layer was then extracted four times with 20 ml. portions of aqueous hydrochloric acid (10% by weight) to remove the pyridine as its hydrochloride salt, once with 30 ml. of aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulfate and evaporated to dryness. The solid white residue melted at 115-120°, mixed m.p. with authentic hexalin dimesylate 116-120°. All the samples worked up during the 5 days gave the same result.
The remainder of the reaction mixture was worked up in the same manner as for the samples. The product was shown to be essentially pure hexalin dimesylate by mixed m.p. and a comparison of infrared spectra. No nitrile band around 2250 cm\(^{-1}\) was observed in the infrared spectrum of the product.

Method 5. A mixture of 1.0 g. (2.9 mmoles) of the dry hexalin dimesylate (XLIII), 1.02 g. (11.2 moles) of dry cuprous cyanide and 25 ml. of dry DMF was stirred and refluxed for 24 hr. The initial green mixture soon turned dark brown. The reaction mixture was cooled to 90\(^{\circ}\), poured into 250 ml. of dilute aqueous ammonia, stirred for 20 min., and filtered. The precipitate was washed with water and dried, yielding 0.70 g. of a white solid m.p. 115-118\(^{\circ}\). An infrared spectrum of this material was identical to that for the hexalin dimesylate. No nitrile band around 2250 cm\(^{-1}\) was observed.

Method 6. A mixture of 1.0 g. (2.9 mmoles) of the dry hexalin dimesylate (XLIII), 3.0 g. (11.9 mmoles) of dry mercuric cyanide, and 15 ml. of dry DMF was stirred and refluxed for 48 hr. The dark brown mixture was cooled to room temperature and poured into 100 ml. of benzene (the elemental mercury in the reaction flask excluded). The organic mixture was extracted four times with 50 ml. portions of aqueous 50% saturated sodium chloride solution, once with 30 ml. of aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulfate and evaporated to constant weight. An infrared spectrum of the dark oily residue contained no nitrile absorption band, but did exhibit bands characteristic of the hexalin dimesylate.

B. From cis-9,10-bis(iodomethyl)-\(\Delta^{2,6}\)-hexalin (XLIV)

A solution of 1.0 g. (2.4 mmoles) of the dry hexalin diiodide (XLIV) in 15 ml. of dry DMF was added dropwise to a stirred solution of 0.75 g. (15.3 moles) of dry purified sodium cyanide in 15 ml. of dry DMF (heated to 120\(^{\circ}\)). No exothermicity was noticed. The reaction mixture was stirred and heated at 120\(^{\circ}\) for 6 hr.
The progress of the reaction was followed by thin-layer chromatography. A sample was withdrawn periodically, spotted on a glass plate coated with a 0.25 mm. thickness of silica gel G (Stahl), developed with a 1:19 mixture of acetone-chloroform, then sprayed with an aqueous solution containing 1% potassium permanganate and 2% sodium carbonate. $R_f$ values for the hexalin diiodide and dinitrile were 0.8 and 0.65, respectively.

The reaction mixture was cooled to room temperature, poured into 100 ml. of benzene and extracted five times with 50 ml. portions of aqueous 50% saturated sodium chloride solution, four times with 50 ml. portions of aqueous hydrochloric acid (10% by weight) and once with 50 ml. of aqueous saturated sodium chloride solution. The benzene layer was then dried over anhydrous magnesium sulfate and evaporated, yielding 0.44 g. of crude product. This material was eluted through a silica gel column with a 1:19 mixture of acetone-chloroform, yielding 0.30 g. (59%) of the pure hexalin dinitrile, m.p. 152-153°, mixed m.p. with authentic material 152-153°.

No evidence for the formation of the isomeric hexalin cyclic aminonitrile (XLIX) was indicated by thin-layer chromatography.

cis-9,10-Bis(carboxymethyl)-$\Delta^2,6$-hexalin (LI)

A mixture of 2.95 g. (14 mmoles) of the hexalin dinitrile (XLVIII), 300 ml. of aqueous 10% sodium hydroxide solution, and 60 ml. of ethanol was stirred and refluxed for 34 hr. The initial suspension of the hexalin dinitrile slowly disappeared as the hydrolysis progressed (about 4 hr.). At the end of the reflux time the ethanol was removed by distillation and the aqueous residue cooled to room temperature. A small amount of precipitate usually appeared. In this case the aqueous mixture was extracted three times with 100 ml. portions of diethyl ether. The ether layers were combined, dried over anhydrous magnesium sulfate, and evaporated to dryness. The small amount of oily residue usually
consisted of the hexalin cyclic aminonitrile (XLIX) - by comparison of infrared spectra - plus other unidentified substances.

Concentrated hydrochloric acid was added dropwise to the stirred aqueous alkaline product mixture until precipitation of the product acid was complete. The white precipitate was filtered off, washed with water, and crystallized from ethanol-water, yield 2.82 g. (81%) of the diacid, m.p. 230 - 233° (decomp.).

Analysis. Calculated for $\text{C}_{14}\text{H}_{18}\text{O}_{4}$: C, 67.20; H, 7.20.

Found: C, 67.16; H, 7.31.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 2920 (s, broad), 1700 (s), 1650 (m), 1460 (s), 1400 (m), 1370 (m), 1340 (m), 1240 (m), 1190 (m), 1045 (w), 995 (w), 975 (w), 940 (m, broad), 720 (m), and 680 (m).

cis-9,10-Bis(carbomethoxymethyl)-$\Delta^{2,6}$-hexalin (LII)

A dry solution of diazomethane in diethyl ether was added in small portions to a stirred mixture of 2.32 g. (9.3 mmoles) of the hexalin diacid (LI) in 50 ml. of dry glyme until a yellow color (excess diazomethane) persisted in the reaction mixture. The reaction temperature was maintained at 0-5°. The initial suspension of the hexalin diacid slowly disappeared as the reaction progressed. The reaction mixture was allowed to warm up to room temperature and to stand overnight. The mixture was warmed gently to expel the excess diazomethane, then evaporated to constant weight. The yield of the dimethyl ester was 2.56 g. (99%), b.p. 152°/1.5 mm. The dimethyl ester had a retention time of 32 min. on a 5 ft. 20% Apiezon J on firebrick column at 230° with a helium flow rate of 40 ml./min.

Analysis. Calculated for $\text{C}_{16}\text{H}_{22}\text{O}_{4}$: C, 69.04; H, 7.97.

Found: C, 68.75; H, 7.72.
The infrared spectrum (film) showed ν_{max} (cm⁻¹) at 3030 (s), 2960 (s), 2900 (s), 2850 (s), 1730 (s), 1660 (m), 1460 (m, shoulder), 1440 (s), 1340 (s, broad), 1200 (s, broad), 1120 (s), 1090 (s), 1055 (m), 1020 (s), 1000 (s), 960 (w), 935 (w), 890 (w), 860 (w), 840 (w), 760 (m), 685 (s), and 665 (s).

The n.m.r. spectrum (15% in CCl₄) showed a triplet at 4.45 (olefinic H) and singlets at 6.39 (CH₃O₂C-), 7.64 (-CH₂CO₂-), and 7.90 (allylic H) in the ratio of 2:3:2:4.

 cis-9,10-Bis(2-hydroxyethyl)-Δ²,⁶-hexalin (LIII)

A solution of 2.50 g. (9.0 mmoles) of the hexalin dimethyl ester (LII) in 20 ml. of dry glyme was added dropwise to a stirred suspension of 0.70 g. (18.5 mmoles) of powdered lithium aluminum hydride in 20 ml. of dry glyme. The resulting mixture was stirred and refluxed for 24 hr. The mixture was then cooled to room temperature. Water was added dropwise with stirring until a white precipitate resulted. Aqueous sulfuric acid (10% by weight) was added in small portions until the reaction mixture became distinctly acid. The mixture was then cooled to 0° and filtered. The white solid residue was washed with water and dried, yield 1.50 g.

The filtrate was extracted three times with 50 ml. portions of diethyl ether. The combined ether extracts were washed with aqueous 10% sodium carbonate solution, followed by aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulfate and evaporated to dryness, yield 0.10 g.

The combined crude products were crystallized from ethyl acetate - petroleum ether (b.p. 65–110°) yielding 1.22 g. (62%) of the dialcohol, m.p. 149.5 - 150.5°.

Analysis. Calculated for C₁₄H₂₂O₂: C, 75.63; H, 9.97.  
Found: C, 75.67; H, 9.70.
The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 3300 (m), 3030 (w), 2920 (s), 1660 (w), 1460 (s), 1380 (m), 1020 (s), 1005 (m), 985 (w), 930 (w) and 700 (w).

**cis-9,10-Bis(2-bromoethyl)-$\Delta^2,6$-hexalin (LIV)**

Freshly distilled phosphorus tribromide (7.2 g., 26.5 mmoles) was added dropwise to a stirred suspension of 1.27 g. (5.7 mmoles) of the dry bis(2-hydroxyethyl) hexalin (LIII) in 20 ml. of dry glyme maintained at 0°. The mixture was stirred and allowed to warm up to room temperature, then refluxed for 5 hr. After 1 hr. an orange precipitate formed in the reaction mixture. The mixture was stirred for a further 20 hr. at room temperature, then poured into 100 ml. of water and shaken. Aqueous 10% sodium carbonate solution was added in small portions until the reaction mixture became basic. This mixture was extracted six times with 50 ml. portions of diethyl ether. The combined ether extracts were washed twice with 50 ml. portions of aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The residue was crystallized from acetone-water yielding 0.32 g. (16%) of the dibromide, m.p. 132-133°.

Analysis. Calculated for $\text{C}_{14}\text{H}_{20}\text{Br}_2$: C, 48.31; H, 5.79; Br, 45.91. Found: C, 48.40; H, 5.69; Br, 45.82.

The infrared spectrum (Nujol mull) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 2920 (s), 1660 (w), 1460 (s), 1375 (m), 1325 (w), 1260 (w), 1220 (w), 1200 (w), 1020 (w), 850 (w), and 672 (s).

The n.m.r. spectrum (10% in $\text{CCl}_4$) showed a triplet at $\tau_{4.46}$ (olefinic H), a triplet with maxima at 6.54, 6.68, 6.82 ($-\text{CH}_2\text{Br}$, J = 8.5 c.p.s.) and a triplet with maxima at 7.86, 8.02, and 8.13 (triplet for $-\text{CH}_2\text{CH}_2\text{Br}$, J = 8.5 c.p.s., superimposed on a singlet at 8.02 for allylic H) in the ratio of 1:1:3.
cis-9,10-Bis(2-mesyloxyethyl)-$\Delta^2,6$-hexalin (LV)

A solution of 1.35 g. (6.1 mmoles) of the dry bis(2-hydroxyethyl)hexalin (LIII) in 10 ml. of dry pyridine was added dropwise to a stirred solution of 1.1 ml. (1.65 g., 14.5 mmoles) of methanesulfonyl chloride in 10 ml. of dry pyridine. The temperature of the reaction mixture during the addition was maintained at $-10^\circ$ in order to eliminate ether formation. Pyridine hydrochloride began to precipitate out after 20 min. The resulting mixture was stirred for 1.5 hr. while the reaction mixture temperature was allowed to rise slowly to $0^\circ$. The mixture was allowed to stand at $0^\circ$ for 20 hr. Water (15 ml.) was then added and the resulting solution made acidic with aqueous hydrochloric acid (10% by weight). After cooling to $0^\circ$, the precipitate was filtered off, washed with water, dried, and crystallized from 95% ethanol yielding 1.6 g. (70%) of the dimesylate, m.p. 124-125° (decomp.).

Analysis. Calculated for $C_{16}H_{26}O_3S$: C, 50.77; H, 6.93; S, 16.94.

Found: C, 50.98; H, 6.86; S, 16.83.

The infrared spectrum (Nujol mull) showed $\nu_{max}$ (cm. $^{-1}$) at 2900 (s), 1660 (w), 1480 (s), 1385 (s, shoulder), 1320 (s), 1240 (m), 1210 (m), 1185 (s), 1110 (m), 1025 (s), 970 (s, broad), 895 (m), 860 (m, shoulder), 835 (s), 780 (m), 750 (m), 718 (m), 690 (s), and 680 (s).

The n.m.r. spectrum (15% in CHCl$_3$) showed a singlet at $\tau$ 4.39 (olefinic H), a triplet with maxima at 5.55, 5.68, and 5.80 ($-\text{CH}_2\text{OSO}_2^-$, $J = 7.5$ c.p.s.), a singlet at 6.96 ($-\text{OSO}_2\text{CH}_3$), and a triplet with maxima at 7.97, 8.09, and 8.21 (a triplet for $-\text{CH}_2\text{CH}_2\text{OSO}_2^-$, $J = 7.5$ c.p.s. superimposed on a singlet at 7.97 for the allylic H) in the ratio of 2:2:3:6.
cis-9,10-Bis(2-iodoethyl)-Δ²,⁶-hexalin (LVI)

Method 1. A solution of 0.31 g. (0.89 mmole) of the dry bis(2-bromoethyl)-hexalin (LIV) and 400 mg. (2.7 mmoles) of dry sodium iodide in 10 ml. of dry purified acetone was stirred and refluxed for 5 hr. Within 30 min. of refluxing, precipitation of sodium bromide resulted. The reaction mixture was cooled to room temperature, 20 ml. of water were added, and the whole was extracted three times with 20 ml. portions of diethyl ether. The combined ether layers were washed with aqueous saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The solid residue was crystallized from 95% ethanol yielding 300 mg. (76%) of the diiodide, m.p. 147-148° (decomp.).

Analysis. Calculated for C_{14}H_{20}I₂: C, 38.03; H, 4.56; I, 57.41.

    Found: C, 38.22; H, 4.50; I, 57.53.

The infrared spectrum (Nujol mull) showed \( \nu_{\text{max}} \) (cm\(^{-1}\)) at 3030 (w), 2930 (s), 1660 (w), 1460 (m), 1375 (w), 1320 (w), 1255 (w), 1220 (w), 1180 (m), and 670 (m).

The n.m.r. spectrum (10% in CDCl₃) showed a triplet at \( \delta \) 4.46 (olefinic H) and triplets with maxima at 6.70, 6.85 and 7.00 (\(-\text{CH}_2\)I, \( J = 9.0 \) c.p.s.) and at 7.80, 7.95, and 8.07 (a triplet for \(-\text{CH}_2\text{CH}_2\)I, \( J = 9.0 \) c.p.s., superimposed on a singlet at 8.07 for the allylic H) in the ratio of 1:1:3.

Method 2. A solution of 2.4 g. (6.35 mmoles) of the dry bis(2-mesyl-oxyethyl)hexalin (LV) and 3.0 g. (20 mmoles) of dry sodium iodide in 100 ml. of dry purified acetone was stirred and refluxed for 8 hr. After 30 min. a white precipitate of sodium methanesulfonate appeared. The progress of the reaction was followed, using thin-layer chromatography, by spotting periodic samples of the reaction mixture on glass plates coated with a 0.25 mm. thickness of silica gel G (Stahl). The plates were developed with chloroform, then dried and sprayed with...
an aqueous solution containing 1% potassium permanganate and 2% sodium carbonate. The diiodide had an $R_f$ of 0.8, while the dimesylate ran at $R_f$ 0.2.

The reaction mixture was cooled to room temperature and 150 ml. of water were added. Solid sodium thiosulfate (0.5 g.) was added to reduce the free iodine which was present. The white precipitate was then filtered off, washed with water, dried, and crystallized from benzene-petroleum ether (b.p. 65-110$^\circ$) yielding 1.3 g. (46%) of the diiodide, m.p. 147-148$^\circ$ (decomp.). The infrared spectra of this material and the diiodide from method 1 were identical.

**Cyclization of cis-9,10-bis(2-iodoethyl)-A$^1$-hexalin (LVI)**

**Method 1.** A 150 µl. solution of n-butyllithium in hexane (Foote Chemicals, 15.05%) was added dropwise from a syringe to a suspension of 120 mg. (0.27 mmoles) of the dry bis(2-iodoethyl)hexalin (LVI) in 15 ml. of anhydrous diethyl ether in a nitrogen atmosphere and maintained at -70 to -80$^\circ$. The mixture was stirred for 1 hr. at this temperature range. The temperature was slowly raised (about 1 hr.) to -5$^\circ$ and maintained there for a further 5 hr. After 2 hr. a sample was withdrawn, spotted on a glass TLC plate coated with a 0.25 mm. thickness of silica gel G (Stahl), developed with petroleum ether (b.p. 30-60$^\circ$), and sprayed with an aqueous solution containing 1% potassium permanganate and 2% sodium carbonate. Two small spots at about $R_f$ 0.5 and 0.7 appeared, in addition to a large diiodide spot at about $R_f$ 0.3.

After the 5 hr. at -5$^\circ$ the reaction mixture was cooled to -75$^\circ$ and 5 ml. of diethyl ether and 250 µl. of n-butyllithium were added. The temperature of the reaction mixture was slowly increased (about 1.5 hr.) to room temperature. A sample of the reaction mixture, analysed by the TLC method, showed the spot at $R_f$ 0.7 to be more intense than the one at 0.6 but still weak compared to the spot for the starting material. A sample of the reaction mixture, taken after 17 hr. of
stirring at room temperature revealed no change in the composition of the mixture.

The reaction mixture was cooled to \(-10^\circ\) and 10 ml. of anhydrous diethyl ether and 250 μl of the n-butyllithium solution were added. The reaction mixture was stirred and refluxed for 1 hr. A sample of this mixture, analysed by the TLC method, showed a further increase in the intensity of the fastest spot relative to the others.

A further 400 μl of the n-butyllithium solution were added at 0°. After stirring and refluxing the reaction mixture for 1 hr., a sample was withdrawn. Analysis by TLC showed a very intense spot at \(R_f 0.7\), a weak spot at about \(R_f 0.5\), and no spot for the starting material.

Aqueous saturated ammonium chloride solution was added to the cooled reaction mixture until an aqueous layer became visible. The ether layer was drawn off with a pipette, dried over anhydrous magnesium sulfate, and evaporated, leaving about 50 mg. of a clear oil. Analysis of the oil by g.l.c. on a 10 ft. Carbowax 20 M on firebrick column at 210° with a helium flow rate of 60 ml./min. showed the oil to be a mixture of two compounds, (LVII) and (LVIII), retention times 13 and 20 min., respectively. Analysis of the oil on a 10 ft. diethylene glycol succinate on firebrick column at 165° with a helium flow rate of 70 ml./min. again showed two components with retention times of 11 and 18 min. In both cases the larger component had the shorter retention time. Separation of the oil under the latter g.l.c. conditions gave yields of 20 mg. (37%) and 5 mg. (9%) for (LVII) and (LVIII), respectively.

(a) Spectral analysis of (LVII).

The infrared spectrum (film) showed \(\nu_{\text{max}} (\text{cm}^{-1})\) at 3080 (w), 3030 (m), 2920 (s), 1660 (w), 1640 (w), 1460 (m), 1425 (m), 1380 (w), 1320 (w), 1225 (w),
n. m. r. spectrum (dilute microsample in CHCl₃) showed a triplet at τ 4.40 (olefinic H), a singlet at 8.10 (allylic H), a multiplet at 8.71 (-CH₂-) and a triplet at 9.25 (-CH₃) in the approximate ratio of 1:2:1:1.

(b) Spectral analysis of (LVIII).

The infrared spectrum (film) showed ν_max (cm⁻¹) at 3030 (m), 2920 (s), 1660 (w), 1455 (m), 1420 (m), 1380 (w), 1320 (w), 1230 (w), 1110 (m, broad), 1090 (m), 1000 (m), 944 (w), 862 (w), 848 (w), 822 (w), 795 (w), and 714 (w).

The n. m. r. spectrum (very dilute microsample in CHCl₃) showed resonance peaks at τ 4.65 (olefinic H), 8.50 (allylic H), and 8.80 (-CH₂-) in the ratio of 1:7.5 (the two high field resonance peaks were not distinguished in the area integral).

Method 2. A solution of n-butyllithium in petroleum ether (fraction with b.p. 36-40° on distillation of commercial material, b.p. 30-60°, after treatment with concentrated sulfuric acid) was prepared from 0.71 g. (0.10 g. -atom) of lithium (containing 1% sodium) and 4.63 g. (0.05 moles) of n-butyl chloride, according to the method of Gilman. After standing in the fridge overnight, all the insoluble material settled out of the product mixture leaving a clear colorless solution of n-butyllithium. This solution was used without further purification. Analysis of the n-butyllithium solution gave a total base concentration of 0.29 N and an n-butyllithium concentration of 0.11 N.

A suspension of 0.30 g. (0.68 mmole) of the dry bis(iodoethyl)hexalin (LVI) in 20 ml. of dry heptane, under a nitrogen atmosphere, was cooled to -75°. The n-butyllithium solution (7 ml., 0.77 mmole) was added dropwise to the stirred suspension. The reaction mixture was stirred for 3 hr. at -70°, then 16 hr.
at room temperature. Samples were withdrawn at 1.5, 3.5 and 19 hr. and analysed by TLC as in method 1. The analyses indicated no reaction after 1.5 hr., two weak product spots ($R_f$ 0.4 and 0.6) after 3.5 hr., and complete reaction giving one spot ($R_f$ 0.6) after 19 hr.

The reaction mixture was worked up as in method 1. The crude product was a mixture of an oil and a white solid. This mixture was separated by extraction with petroleum ether (b.p. 30–60°C). Evaporation of the petroleum ether extracts gave the clear colorless oil, free of any solid material. Separation of the oil by g.l.c., using a 5 ft. Carbowax 20 M on firebrick column at 150°C with a helium flow rate of 100 ml./min., gave two components.

(a) Analysis of the first component (retention time 17 min., yield 45 mg. (35%)).

This component gave an infrared spectrum identical to that of (LVII), isolated in method 1.

Elemental analysis. Calculated for $C_{14}H_{20}$: C, 89.29; H, 10.71.

Found: C, 89.01; H, 10.56.

The mass spectrum showed a large parent ion peak M at m/e 188, indicating a molecular weight of 188 for (LVII). The principal fragmentation peaks were M–29 (loss of ethyl radical), M–83 (consecutive loss of ethyl radical and butadiene), and M–99 (formation of the cycloheptatrienyl cation).

The ultraviolet spectrum (heptane solution) showed no absorption peaks in the range 210 – 300 μm.

(b) Analysis of the second component (retention time 25 min., yield 5 mg. (3.9%)).

This component gave an infrared spectrum identical to that for (LVIII),
isolated in method 1.

The n.m.r. spectrum (very dilute microsample in CHCl₃) showed a singlet at τ 4.48 (olefinic H), and a multiplet centered at 8.42 (allylic H and -CH₂-) in the ratio of 1:5.

The mass spectrum gave a parent ion peak M at m/e 188, indicating a molecular weight of 188 for (LVIII). The principal fragmentation peaks were M-54 (loss of butadiene), M-96, and M-97 (formation of the cycloheptatrienyl cation).

(c) Analysis of the white solid (yield 16 mg.)

The infrared spectrum (Nujol mull) showed no prominent absorption peaks. The n.m.r. spectrum (dilute microsample in CHCl₃) showed no resonance maxima. The material decomposed on heating at 220° and was not soluble in water.

Method 3. A mixture of 170 mg. (0.39 mmoles) of the dry bis(iodoethyl) hexalin (LVI), 100 mg. (1.5 mmoles) of acid-washed zinc, and 25 ml. of dry glyme was refluxed and stirred for 10 hr. A sample withdrawn after 3 hr. and analysed by TLC as in method 1 showed a weak spot at Rₐ 0.6 in addition to an intense spot at Rₐ 0.3 for the starting material. A sample of the reaction mixture at 10 hr. was shown by TLC analysis to consist only of the product, i.e. there was no spot present for the starting material.

The reaction mixture was cooled to room temperature, filtered, and evaporated, leaving a brown residue. This residue was eluted through a silica gel column with petroleum ether (b.p. 30–60°). Evaporation of the eluate gave a small amount of a clear colorless oil. Analysis of the oil by g.l.c., using a 10 ft. Carbowax 20 M on firebrick column at 205° with a helium flow rate of 20 ml./min., showed the oil to contain one major component (retention time 21 min., yield 20 mg. (27%)) together with four very small, longer retention time components (retention times 24–38 min.). These small components were not isolated.
The infrared and n.m.r. spectra of the major component were identical to those of (LVII), isolated in method 1.

Method 4. A mixture of 300 mg. (0.68 mmoles) of the dry bis(iodoethyl) hexalin (LVI), 18.0 mg. (0.75 mmoles) of magnesium turnings and 10 ml. of dry tetrahydrofuran was stirred and refluxed for 48 hr. under a nitrogen atmosphere. An addition of 5 ml. of tetrahydrofuran was made after 24 hr. to replace some of the reaction mixture solvent which had evaporated. At the 34 hr. mark 5 mg. of magnesium were added to the reaction mixture.

Samples were withdrawn periodically from the reaction mixture and analysed by TLC as in method 1. These analyses showed that some reaction had taken place after 7 hr. (two product spots, \( R_f 0.4 \) and 0.6) and that no change in the relative intensities of the product and starting material spots had taken place after 34 hr.

After 48 hr. of reflux the reaction mixture was cooled to room temperature, filtered, and evaporated, leaving a small amount of an oil and a white solid. The oil was isolated free of the solid by washing the mixture with petroleum ether (b.p. 30-60°), then evaporating off the solvent. This oil was shown to consist of three components (retention times of 13 (major component), 17 and 22 min.) by g.l.c. using a 5 ft. Carbowax 20 M on firebrick column at 155° with a helium flow rate of 100 ml./min.

(a) Analysis of the first component (yield 40 mg.).

The infrared spectrum (film) showed \( \nu_{\text{max}} \) (cm.\(^{-1}\)) at 3500 (m), 2980 (m), 2900 (m), 1770 (s), 1460 (m), 1420 (m), 1370 (s), 1270 (m), 1240 (m), 1180 (s, broad), 1080 (m), 1035 (s), 990 (s), 930 (m), 870 (m), 800 (m), and 675 (m).
The n. m. r. spectrum (10 mg. in 90 uL of CHCl₃) showed multiplets at τ 5.64 and 7.60 in the ratio of 1:2.

(b) Analysis of the second component (yield 10 mg.).

The infrared spectrum was identical to that of (LVII), isolated in method 1.

(c) Analysis of the third component (yield 5 mg.).

The infrared spectrum (film) showed v_max (cm⁻¹) at 3030 (m), 2920 (s), 1650 (w), 1450 (s), 1300 (w), 1175 (w), 1010 (w), 945 (w), 912 (w), 758 (m), and 710 (m).

The n. m. r. spectrum (very dilute microsample in CHCl₃) showed one broad multiplet at τ 8.1-8.8.

(d) Analysis of the white solid (yield 150 mg.).

The infrared spectrum of this material was identical with that for the bis(iodoethyl)hexalin (LVI).

Method 5. A mixture of 200 mg. (0.45 mmoles) of the dry bis(iodoethyl) hexalin (LVI), 12 mg. (0.50 mmoles) of magnesium turnings, and 5 ml. of dry heptane was stirred and refluxed under a nitrogen atmosphere. After 2 hr. a sample was withdrawn and analysed by TLC as in method 1. The analysis showed that no reaction had taken place. The reaction mixture was allowed to reflux overnight. During this time, however, the solvent evaporated leaving a dark mass in the reaction flask. This material was worked up by adding water and diethyl ether. The ether layer was separated off, washed successively with 20 ml. volumes of aqueous 10% hydrochloric acid, sodium carbonate solution, and sodium thiosulfate solution, dried over anhydrous magnesium sulfate, and evaporated, leaving a clear oil. Analysis of this oil by g. l. c., using a 5 ft. Carbowax 20 M on
firebrick column at $170^\circ$ with a helium flow rate of 70 ml./min., showed a group of three minor components with a retention time of 8 - 11 min. and one major component (LIX) at 15 min, yield 10 mg. The minor components were not collected.

The infrared spectrum (film) of (LIX) showed $\nu_{\text{max}}$ (cm.$^{-1}$) at 2900 (s), 2850 (s), and 1440 (m, multiplet). No other absorption bands could be distinguished.

The n. m. r. spectrum (dilute microsample in CHCl$_3$) of (LIX) showed a multiplet at $\tau8.4$.

The mass spectrum showed a large parent peak $M$ at m/e 190, indicating a molecular weight of 190 for (LIX). The principal fragmentation peaks were $M-29$ (loss of ethyl radical) and $M-99$ (formation of the cycloheptatrienyl cation).

Method 6. A mixture of 200 mg. (0.45 mmoles) of the dry bis(iodoethyl) hexalin (LVI), 12 mg. (0.50 mmoles) of magnesium turnings, and 5 ml. of anhydrous diethyl ether was stirred and refluxed for 4 hr. under a nitrogen atmosphere. Very little of the diiodide seemed to dissolve up during this period of time. A sample of the reaction mixture was withdrawn after 4 hr. and analysed by TLC as in method 1. No spots indicating the formation of products were observed.

The reaction solvent was replaced with 5 ml. of dry glyme. The reaction mixture was then stirred and refluxed for an additional 68 hr. Samples withdrawn after 20, 48, and 68 hr. and analysed by TLC as in method 1, showed two product spots ($R_f$ 0.4 and 0.6) together with a large spot for the starting material.

The reaction mixture was cooled to room temperature, and 20 ml. of aqueous 5% hydrochloric acid were added. After stirring this mixture for 15 min., 25 ml. of water were added, and the whole was extracted with three 25 ml. portions of diethyl ether. The combined ether extracts were washed once with 30 ml. of aqueous 10% sodium carbonate solution and 30 ml. of aqueous saturated sodium chloride.
solution, then dried over anhydrous magnesium sulfate and evaporated. The residue consisted of a white solid and a small amount of a clear oil. The oil was obtained free of the solid by extraction with petroleum ether (b.p. 30-60°), followed by evaporation of the solvent. Separation of the oil by g.l.c., using a 5 ft. Carbowax 20M on firebrick column at 160° with a helium flow rate of 100 ml./min., gave four components (yields about 5 mg. each) with retention times of 10.5, 13.5, 16.5, and 20 min. The g.l.c. tracing of the first component (a liquid) showed it to be a mixture of two compounds. The second and third components were partly crystallized oils, while the fourth component was a white solid. The four g.l.c. components (in order of elution) gave the following infrared spectra (ν<sub>max</sub> (cm<sup>-1</sup>):

- Component 1. 3050 (m), 2950 (s), 1650 (m), 1450 (m), 915 (m), 738 (w), 718 (m), and 700 (w).
- Component 2. 3050 (s), 2950 (s), 1650 (m), 1450 (s), 1300 (m), 1180 (m), 1100 (w), 1015 (m), 945 (w), 930 (w), 915 (m), 847 (m), 810 (w), 760 (s), 735 (m), and 710 (s).
- Component 3. 3050 (s), 2950 (s), 1650 (w), 1450 (s), 1330 (m), 1300 (m), 1270 (m), 1160 (w), 1120 (w), 1080 (w), 1060 (w), 918 (w), 887 (w), 840 (w), 790 (m), 760 (m), and 720 (m).
- Component 4. 3050 (m), 2950 (s), 1460 (s), 1380 (m), 1320 (m), 1300 (m), 1275 (m), 1110 (w), 912 (w), 845 (w), 780 (s), and 768 (s).

The white solid, which was part of the initial crude product material, gave an infrared spectrum identical to that of the bis(iodoethyl)hexalin (LVI), yield 62 mg.
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