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THE RICE INSTITUTE

Studies of Olefin Stability

I. The Acid-catalyzed Isomerization of Cholestanes
II. The Heats of Hydrogenation of Eight Unsaturated Hydrocarbons

by

William Ralph Meador

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PART I

THE ACID-CATALYZED ISOMERIZATION OF CHOLESTENES
INTRODUCTION

The steroids constitute a class of organic compounds which are structurally characterized by the presence of a more or less saturated 1,2-cyclopentenophenanthrene ring system (I). Among

![Diagram of steroid structure I]

the important steroids are those possessing the carbon skeleton of cholestane (II). The numbering of the carbon atoms and the

![Diagram of steroid structure II]

literal designations of the four rings are indicated. It is conventional to draw a full-line bond for a group which projects above the general plane of the rings and a dotted line for a group below the plane. Substituents on the nucleus are thus

-1-
distinguished as \( \beta \) and \( \alpha \), respectively. In Figure 1 are represented the arrangements in space of cholestane and of coprostan-ane, which differs from cholestane in the configuration of the

![Cholestane and Coprostan](image)

**Figure 1**

C.5 hydrogen (that is, the A/B ring fusion is cis rather than trans). The behavior of members of the cholestane and the coprostan series offers some interesting contrasts, of which some are examined briefly below.

The sense of the substitution reactions of a 3-ketosteroid is dependent upon the nature of the A/B ring fusion. For example, the bromination of cholan-3-one, which possesses a 5\( \alpha \) hydrogen, yields 2-bromocholestan-3-one, while bromination of coprostan-3-one, in which the fusion of the A/B rings is cis, gives the \( \beta \)-bromoketone (1). Similarly, the sulfonation, in acetic anhydride and sulfuric acid, of cholan-3-one gives the 2-sulfonic acid (2), but from coprostan-3-one the predom-
inant product is a $\alpha$-sulfonic acid (3). The degree of directional specificity in these reactions is attributable to energy differences between the two enols possible for each ketone. Acid-catalyzed brominations have been shown to proceed through the enolic form ($\alpha$). Many other reactions of these ketones and of steroids with other C,3 functions manifest a preference for reaction at C,2 in the A/B trans compound and at C,4 in the A/B cis series, which may often be ascribed ultimately to favorability of one or the other double bond. Bromination with N-bromosuccinimide (5) is a process which obeys such a rule. Enol acetates prepared with isopropenyl acetate (6) and enol ethers obtained by the pyrolysis of the ketone acetals (7, 8) possess double bonds in the positions which would thus be predicted. Especially noteworthy is the fact that the catalytic hydrogenation of the enol ether (III) of cholest-$\alpha$-en-3-one proceeds with bond migration and yields the enol ether (IV) rather than V.

\[\text{III} \quad \text{IV} \quad \text{V}\]

Acetolysis of the 3-chloro compounds yields, besides acetates, considerable olefinic material. Both 3$\alpha$- and 3$\beta$-chlorocholestane give cholest-2-ene (9), while the 3$\alpha$- and 3$\beta$-chloro-
coprostanones give coprostan-3-ene (10).* Pyrolysis of cholestane-3α-yl benzoate gives cholest-2-ene (11), but coprostan-3-ene is obtained by pyrolysis of coprostan-3α-yl benzoate (12).

The inference to be drawn from these illustrations is that pronounced stability differences exist among the monoolefinic steroids of a given series.

Steroid olefins with disubstituted double bonds have been examined with regard to their infra-red spectra by Henbest, Meakins, and Wood (13). The data appear in Table I. The strongest band in the region 1700-1600 cm.\(^{-1}\) was taken as the olefinic stretching frequency. In the region of the spectrum (800-650 cm.\(^{-1}\)) associated with olefinic C-H out-of-plane bend-

**TABLE I**

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Frequencies of Absorption Maxima</th>
<th>Average Frequency for 800-650 cm.(^{-1}) Region</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cm.(^{-1})</td>
<td>cm.(^{-1})</td>
</tr>
<tr>
<td>Cholest-1-ene</td>
<td>1614 748 (65) 718 (125) 700 (115)</td>
<td>710</td>
</tr>
<tr>
<td>Cholest-2-ene</td>
<td>1653 774 (35) 664 (145)</td>
<td>692</td>
</tr>
<tr>
<td>Cholest-3-ene</td>
<td>1647 773 (110) 671 (125)</td>
<td>718</td>
</tr>
<tr>
<td>Cholest-6-en-3β-ol</td>
<td>1633 772 (70) 729 (60)</td>
<td>738</td>
</tr>
<tr>
<td></td>
<td>739 (70) 710 (60)</td>
<td></td>
</tr>
<tr>
<td>Methyl 3α-hydroxycholesterol-11-ene</td>
<td>1620 832 (85) 751 (50)</td>
<td>771</td>
</tr>
<tr>
<td></td>
<td>794 (40) 725 (125)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>769 (45)</td>
<td></td>
</tr>
</tbody>
</table>

*Intensities of the bands in the 800-650 cm.\(^{-1}\) region are denoted by the figures in parentheses.

*The substance described by Bridgewater and Shoppee (10) as coprostan-2-ene has been shown to be actually coprostan-3-ene (12).
ing, each of the compounds displayed several bands of similar intensity, and a single frequency could not be assigned to this deformation. For the purpose of comparing frequencies, then, these authors computed for each substance an "average frequency," taking into account the relative intensities of the bands. The order of these average frequencies is the same as for the double bond stretching frequencies; namely, $2:3$, $3:4$, $1:2$, $6:7$, and $11:12$ olefins, increasing for the out-of-plane vibration, decreasing for the stretching vibration. In an earlier paper of the Manchester series on steroids Sladen and his associates (14) deduced from quantum-mechanical considerations by previous workers (15) that the double bond stretching frequency would decrease with increased steric strain in the ring, while the olefinic C-H out-of-plane bending frequency would increase. Thus the double bond positions should increase in strain in the order just given. The spectral results were judged to be in agreement with the order which could be predicted by consideration of the probable strains (13), except that the $1:2$ and $3:4$ double bonds could not be compared with any certainty on this basis.

The heats of hydrogenation of certain olefinic steroids have been measured in these laboratories (12). The data, given in Table II, furnish the following thermochemical stability order: $5:6 \approx 2:3 > 1:2 \approx 6:7 > 3:4 > 11:12$. The strain present in these molecules will be distributed over torsional strain of the double bond, angle strain in the tetrahedral and trigonal carbon atoms, and ring distortions which result in increased non-bonded interactions of substituent groups, in
TABLE II

HEATS OF HYDROGENATION OF STERIOD OLEFINS

<table>
<thead>
<tr>
<th>Olefin</th>
<th>-(\Delta H) (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholest-5-ene</td>
<td>25.85 ± 0.13</td>
</tr>
<tr>
<td>Cholest-2-ene</td>
<td>25.85 ± 0.17</td>
</tr>
<tr>
<td>Cholest-1-ene</td>
<td>27.30 ± 0.24</td>
</tr>
<tr>
<td>Cholest-6-ene</td>
<td>27.36 ± 0.10</td>
</tr>
<tr>
<td>Cholest-3-ene</td>
<td>27.97 ± 0.14</td>
</tr>
<tr>
<td>(\Delta^{11})-lithoclolemic acid</td>
<td>28.93 ± 0.5</td>
</tr>
</tbody>
</table>

such a way that the total energies of the molecules will be minimized. It is not surprising, therefore, that the heats of hydrogenation, which reflect total energies, should lead to a different stability order than the infra-red measurements, which are in the main concerned only with strain in the olefinic linkages.

The present study was carried out in connection with the hydrogenation work, and had as its objective the examination of various cholestenes with respect to their behavior under acid isomerizing conditions.

Acid catalyzed migration of double bonds is a common phenomenon. Ordinarily, the product of acid isomerization is expected to be more stable than the factor. By way of illustration may be mentioned butene-1, converted to butene-2 by aqueous solutions of any of a number of acids (16). The treatment of 2,6-dimethyl-2-dec-7-ene, dihydrotagatone (VI), with seventy per cent sulfuric acid gives methylmethylketone and methyliso- butylketone (17). The rationale of the reaction includes the
shifting of the double bond into the $\beta, 7^-$, and thence to the $\alpha, 7^-$-position, to form 2, 6-dimethyl-7-en-4-one (VII), followed by reverse aldol cleavage. An example of isomerization into a ring is the conversion of isopropenylcyclopentane by acids into 1-isopropylcyclopentene (18).

Although the general features of double bond migration are familiar, a detailed mechanistic study of the process has not been made, and much of the evidence necessary to a discussion of this phenomenon must thus be drawn from the somewhat related reactions of addition and elimination.

Several possible pathways for acid-catalyzed isomerization can be suggested, of which the following will serve as illustrations: (a) concerted 1,2 addition of the elements HX, followed by elimination from the 2,3 positions:

(b) concerted addition and elimination of protons through transition states of type VIII or IX. It is clear that in case VIII, involving the solvent as an external base, the approaching and departing protons will bear a trans relationship to one another, whereas in case IX, which is represented as proceeding through a cyclic transition state, a cis relationship will be preferred.
(c) non-concerted addition and elimination of protons involving a carbonium ion intermediate:

(d) initial protonation of the double bond, followed by proton loss:

Several variants of this scheme can, of course, be visualized.

In 1933 Whitmore and Johnston (19) provided evidence which indicates that mechanism (a) cannot be general. These investigators observed that addition of hydrogen chloride to 3-methyl-butene-1 (I) furnishes both 2-chloro-3-methylbutane (XI) and 2-chloro-2-methylbutane (XII), and furthermore, that XI is not

\[
\text{CH}_3
\]

\[
\text{CH}_2\text{CH} = \text{CH} - \text{CH}_3
\]

\[
\text{CH}_3\text{CH} = \text{CH} - \text{CH}_3 + \text{CH}_3\text{CH}_2\text{CHCl}_3
\]

X \quad XI \quad XII
converted into XII under the conditions of the experiment. Thus the second step (elimination) of mechanism (a) fails in this case, and the formation of XII must be explained in other terms. Mechanisms (b), (c), and (d) may be considered in this connection, as well as variations involving 1,2 hydrogen shift in a carbonium ion or its equivalent (cf. (c) and (d)).

Some evidence in support of transition state IX has been presented by Turkevich and Smith (20) in the special case of the isomerization of butene-1 to butene-2 in the presence of phosphoric acid. The rate of isomerization was found to be proportional to the pressure of butene-1 and to the concentration of phosphoric acid. When phosphoric acid was replaced by tritium phosphoric acid, hydrogen-tritium exchange was observed, exchange being slower than isomerization.

The results could be correlated with differences in zero-point energies of bonds involving hydrogen and tritium, respectively. It was further noted that the hydrogens of ethylene did not exchange with tritium phosphoric acid, but that exchange did occur with propylene and tritium phosphoric acid. On the basis of these and other observations a cyclic transition state, analogous to IX, was suggested.

With regard to mechanisms (c) and (d) a considerable body of evidence is accumulating which suggests that addition of HI to olefins, and carbonium ion reactions (e.g., solvolysis) of the addends do not necessarily involve the same intermediates. Thus, although the reaction of hydrogen bromide with 1,2-dimethylcyclohexene proceeds with predominant trans stereochemistry to yield trans-1-bromo-1,2-dimethylcyclohexane (XIII), the rates of
solvolyis of XIII and of cis-1-bromo-1,2-dimethylcyclohexane (XIV) are indistinguishable within the limits of experimental error (21). Hence, if solvolyis leads to a carbonium ion intermediate, a different species must be involved in the transition state leading to trans addition. Further arguments of the same type have recently been discussed by Winstein and Holness (22), who have proposed the following reaction scheme, in which B and C represent, respectively, intermediates formed in proton addition and in solvolyis.

Some evidence for the formation of the bridged ion (B) in reactions of olefins with acid is provided by the observation
that acid-catalyzed hydration of such substances appears to proceed through a transition state in which the water molecule is not involved. Such processes as

\[
\begin{align*}
 & \overset{\text{H}}{\text{C}} & \overset{\text{H}}{\text{C}} & \overset{\text{H}_2\text{O}^+}{\text{H}} & \overset{\text{H}}{\text{C}} \\
& \overset{\text{H}_2\text{O}}{\text{C}} & \overset{\text{H}_2\text{O}}{\text{C}} & \overset{\text{H}_2\text{O}}{\text{C}} & \overset{\text{H}_2\text{O}}{\text{C}}
\end{align*}
\]

are thus excluded in the rate-determining step, which is regarded as isomerization of the bridged ion B to C in the reaction sequence shown above (23). In this connection it is clear that if the process B $\rightarrow$ A is much faster than B $\rightarrow$ C, exchange of the hydrogen atoms of ethylene for tritium of an acid catalyst through intermediate C might escape detection under the experimental conditions employed by Turkevich and Smith (20). Exchange that was observed in the case of propylene can be accounted for by hydrogen shift in a form corresponding to the bridged ion B. A transformation of this type (XV $\rightarrow$ XVI) has in fact been proposed by Winstein and Holness

(22) to account for some of the products obtained in solvolysis of \textit{cis}-4-\textit{t}-butylcyclohexyl-$p$-toluenesulfonate.

Among the known examples of acid isomerization of steroid double bonds, probably the most familiar cases are those which consist of migration of a double bond from the 7:8 or 8:11 positions to the 14:15 position by treatment with hydrogen chloride
in chloroform. Such reactions have been reported for the cholestenes (24), cholesten-3-yl benzoates (25), ergosten-3-yl benzoates (26), apocholeic acid (27, 28), and others.

Acid isomerization has sometimes resulted in pure products when applied to steroidal diene systems. For example, cholesta-4,6-diene is converted by hydrogen chloride in chloroform to cholesta-3,5-diene (29). In general, homoannular steroid dienes are changed into heteroannular dienes by hydrochloric acid (30, 31). The treatment of ergosteryl acetate (XVII) with this reagent leads to a separable mixture of ergosteryl-\( \mathbf{B}_1 \), \( \mathbf{B}_2 \), and \( \mathbf{B}_3 \) acetates (XVIII, XIX, XX) (32, 33).
Hudgell, Turnbull, and Wilson (34) have obtained 86 per cent yields of ergosteryl-$B_1$ acetate from ergosteryl acetate or ergosteryl-$D$ acetate (XXI) by sealing these esters in Carius tubes with liquid sulfur dioxide for several hours, without rigorous exclusion of moisture.

The underlying causes of varying stabilities in steroid monoclefsins have been discussed elsewhere (12, 35, 36) and will be considered only briefly here. The preferred conformation adopted by cyclohexene is regarded by Barton, Cookson, Klyne, and Shoppes (37) as the "half-chair" configuration indicated in XXII with carbon atoms 1, 2, 3, and 6 in a single plane and

carbon atoms 4 and 5 out of the plane, one lying above and the other below the plane, as shown. In this arrangement the substituents attached to carbon atoms 4 and 5 are staggered with respect to each other (XXIII), and are hence considered to have the axial and equatorial properties associated with the similarly
situating substituents of the cyclohexane ring (XXIV). On the other hand, distortion of the molecule brought about by the introduction of a double bond forces the substituents on carbon atoms 3 and 6 into partial eclipse with those on carbon atoms 4 and 5 (XXIV), respectively, and thus the former substituents are neither truly axial nor truly equatorial. Atoms or groups attached to carbon atoms adjacent to the double bond are hence termed quasi-axial (a') or quasi-equatorial (e') as the case may be (see XXII). The application of these ideas to the steroid olefins (XXVI-XXX) permits the formulation of some general principles regarding relative stability in this series.

In cholest-2-ene (XXVI) the a' and e' bonds are all attached to hydrogen atoms and as a consequence the conformation
of ring B is essentially unaffected. On the other hand, in cholest-3-ene (XXVII) the C.5-C.6 bond must be quasi-equatorial if the olefinic linkage is planar, and the result will be a deformation of ring B with consequent increase in strain. This conclusion is in accord with the results obtained for these two substances by measurements of their heats of hydrogenation, and suggests that in general in a trans-fused octalin system a double bond will be more stable in a position opposite, than in a position adjacent to the ring fusion. Extension of this reasoning to cholest-6-ene (XXIX) leads to the prediction that this compound,

\[\text{XXX} \quad \text{XXX}\]

which possesses a double bond adjacent to two trans fusions, should be less stable than cholest-3-ene in which only one trans fusion is involved. A more detailed examination of the situation presented by cholest-6-ene, however, indicates a transmission of conformational effects* through the C.8-C.14

*The term "conformational transmission" was introduced by Barton in a lecture before the International Union of Pure and Applied Chemistry in Zurich in July, 1955.
quasi-equatorial bond to ring D, the net result of which is a reduction of the transoid character of the C/D fusion. Since trans-hydrindanes are highly strained (38), such an effect might be expected to lead to increased stability in the 6:7 olefin, and this conclusion is confirmed by comparison of the heats of hydrogenation of cholest-3-ene and cholest-6-ene.

$\Delta^{11}$-lithocholemic acid (XXX) cannot be directly compared with the other compounds of the series since it possesses the A/B cis, rather than the A/B trans, fusion. Nevertheless, it is clear from inspection of models that introduction of a quasi-equatorial bond in the C.13-C.17 position increases the transoid character of the C/D fusion, and the fact that XXX is thermodynamically the least stable of the steroid olefins that have been investigated thus far is consistent with this observation.

The difference in stability between cholest-1-ene (XXVIII) and cholest-3-ene (XXVII) is somewhat more difficult to rationalize. It will be observed, however, that direct transmission of conformational effects to ring C through a quasi-equatorial bond (C.9-C.10) can occur in XXVIII, but not in XXVII, and that the character of the C/D fusion may also be involved. It is of some interest in this connection that cholest-1-ene (XXX), which
likewise possesses a quasi-equatorial C.9-C.10 bond, is somewhat more stable than cholest-5-ene (XXXII), in which this bond is equatorial.

Double bond isomerizations in the steroid series are ordinarily carried out with hydrogen chloride in chloroform solution. Under these conditions chlorides are frequently obtained as by-products (39) and these derivatives are sometimes difficult to separate from the olefinic material. In order to avoid this complication, p-toluenesulfonic acid in acetic acid, or in acetic acid-cyclohexane, was employed in the present investigation, since the esters formed as by-products under these conditions are readily hydrolyzed to alcohols, which are easily removed. In practice it was found that the acetate esters, which constitute the principal source of contamination, could be separated from the olefinic products without difficulty by chromatography on alumina.
RESULTS AND DISCUSSION

When cholest-5-ene is treated with p-toluenesulfonic acid in a refluxing mixture of acetic acid and cyclohexane (temperature of the solution—85°C), it is rapidly converted into a poorly crystalline mixture, the infra-red spectrum of which (Fig. 2a) indicates the presence of both cholest-5-ene and cholest-4-ene. No other components, for example acetate esters or other double bond isomers, are spectrographically detectable, and the specific rotation of the product (α 17.5°) suggests the presence in the mixture of approximately 55 per cent of cholest-4-ene and 45 per cent of cholest-5-ene. For purposes of comparison the infra-red spectrum of a synthetic mixture of this composition is shown in Figure 2b. Similar treatment of cholest-4-ene leads to essentially the same results, and since the isomerization product is unaffected by further prolonged heating with acid under the conditions specified above, it is regarded as an equilibrium mixture.

Treatment of this equilibrium mixture, or of either pure olefin, with p-toluenesulfonic acid in refluxing acetic acid alone (solution temperature—120°C) for 2.5 hours, results in complete conversion into a colorless oil, which possesses the infra-red absorption characteristics shown in Figure 3d. This material, designated as olefin A, resisted all attempts at crystallization, and, although it appeared to be chromatographically homogeneous, it is not unlikely that the substance represents a mixture of two or more products. Unsaturation was demonstrated
by the tetranitromethane test (l0, l1), and ultra-violet examination of the tetranitromethane complex indicated the presence of a tetrasubstituted double bond (l2). Support for this conclusion is derived from the failure of the substance to undergo catalytic hydrogenation under normal conditions. Hydrogenation can, however, be accomplished under forcing conditions (l3), and the oily product obtained in this way proved to be saturated in the tetranitromethane reaction.

In intact cholestane or coprostone structures only three positions, 8:9, 8:11, and 17:20, can accommodate a tetrasubstituted double bond. The 17:20 position is unlikely in view of general knowledge concerning double bond isomerizations in the steroid series (l4), and would further appear to be excluded by the observation that cholest-7-ene and cholest-8:11-ene furnish a different isomerization product.

Examination of the infra-red spectrum of the hydrogenation product of olefin A reveals no detectable amounts of cholestane or of coprostone (Fig. l). Since forced hydrogenation of 8:9- and 8:11- cholestene and coprostone derivatives leads to the formation of the corresponding cholestanes (2l) and coprostanes (l3, l5), respectively, it follows that olefin A cannot possess the cholestane or coprostone nucleus and hence must be regarded as a product of skeletal rearrangement. The most reasonable suggestion that can be made regarding the structure of this material is that it represents the product of Wagner-Meerwein rearrangement involving intermediate formation of the C,5 carbocation ion followed by migration of the C,10 methyl group and loss of a proton from C,9, as indicated in the transformation XXXIII →
XXXIV. The resultant 9:10 olefin can, of course, equilibrate with the 8:9- and 8:10- unsaturated derivatives, XXXV and XXXVI,

respectively. An analogy for such a rearrangement is available in the observation that cholestane-3,5,6-triol 3,6-diacetate (XXXVII) undergoes rearrangement on acid-catalyzed dehydration (h6) to yield a substance (XXXVIII), the structure of which has been established with reasonable certainty (28, 47, h8). The possibility that dehydration of cholestane-5-ol with thionyl chloride and pyridine may result in partial rearrangement to a product of structure XXXIV has also been considered by Fudge, Shoppee, and Summers (h9), although the likelihood of rearrange-
ment under these conditions would appear to be relatively re-
more.

The alternate possibility of rearrangement of cholest-4-ene
and of cholest-5-ene by successive double bond migrations to
cholest-1-ene and Wagner-Meerwein rearrangement of the latter
compound to a product of type XXXIX would require the initial

XXXIX

formation of a secondary carbonium ion from cholest-4-ene in vi-
violation of Markownikoff’s Rule.

Cholest-1-ene, cholest-2-ene, cholest-3-ene, and cholest-6-ene, on treatment with p-toluenesulfonic acid in acetic acid-
cyclohexane at 85°, are unaffected, apart from the appearance of
small amounts of acetate ester formed by the addition of acetic
acid. These observations are consistent with the fact that
secondary carbonium ions, obtained by proton addition to the
four olefins noted above, are less stable than tertiary carbonium
ions (50, 51), formed from cholest-4-ene and from cholest-5-ene.
The appearance of acetate esters in the absence of isomerization
is in accord with the suggestion that olefin additions can occur
by a concerted mechanism without the intervention of carbonium
ion intermediates (52). The failure of cholest-4-ene and of
cholest-5-ene to yield acetate esters may be attributed to ster-
ic hindrance about C.5.

Under more vigorous conditions (p-toluenesulfonic acid in
refluxing acetic acid), cholest-1-ene, cholest-2-ene, cholest-3-ene, and cholest-6-ene are all slowly transformed into material with infra-red absorption characteristics identical with those of olefin A (Fig. 3).

In view of complications resulting from the intrusion of the rearrangement reaction, a quantitative study of equilibria involving the various cholestenes, which was the original objective of this investigation, was not possible. However, it has been possible to make a number of observations which display a qualitative agreement with results obtained by measurements of heats of hydrogenation in this series.

For example, interruption of the cholest-1-ene and cholest-3-ene isomerizations at an intermediate stage gives products, which, after removal of esters, consist very largely of cholest-2-ene (Fig. 5b, f). The starting olefins and olefin A are not detectable by examination of the infra-red spectrum. An exceptionally large proportion of the material (about two-thirds) is converted to acetates. The predominance of cholest-2-ene in the hydrocarbon thus obtained from cholest-1-ene and cholest-3-ene is not surprising, since the latter olefins are, respectively, 1.5 and 2.1 kcal/mole less stable than cholest-2-ene (Table II). Cholest-1-ene and cholest-3-ene are believed to be present as minor constituents of the hydrocarbon fractions, though not apparent in the rather dilute solutions examined spectroscopically.

In the isomerization of cholest-2-ene, olefin A appeared before other products were detected (Fig. 5d). Since the presence of olefin A precludes, by introducing interfering absorption
bands, the identification in cholest-2-ene of small amounts of cholest-1-ene or cholest-3-ene, the presence of these two cholestenes in the mixture cannot be definitely affirmed. However, if the cholest-2-ene is isomerized to cholest-4-ene by proton additions and abstractions, cholest-3-ene is necessarily an intermediate, and a steady state should be achieved in which some cholest-3-ene persists as long as cholest-2-ene is present.

Inasmuch as cholest-4-ene is slightly more stable than cholest-5-ene (see above), and hence, presumably, also slightly more stable than cholest-2-ene (Table II), it is interesting to note that cholest-2-ene, rather than cholest-4-ene (and hence olefin A) is first formed from cholest-3-ene. It is not inconceivable that cholest-4-ene may be actually less stable than cholest-2-ene, since the energy difference between cholest-4-ene and cholest-5-ene is of the same magnitude as the experimental errors in the hydrogenations.

The rates of disappearance of the individual olefins on acid treatment were studied in a very qualitative manner by interruption of the various isomerization reactions at specified time intervals and examination of the infra-red spectra of the partially rearranged products (Fig. 6). The rates of disappearance obtained by this rather crude method were in the order \( \Delta^1 > \Delta^3 > \Delta^2 > \Delta \), the rates of \( \Delta^1 \) and \( \Delta^2 \) differing by a factor of five to ten.

Although the rate differences are small and are hence not amenable to unequivocal interpretation, some discussion of the factors involved, and of possible pathways to the rearranged product, would appear to be appropriate.
Consideration of the reaction of an olefin with acid to give a carbonium ion, either directly or through an intermediate bridged ion, may be assumed to occur most readily in a coplanar system, yielding an axial C-H bond, in analogy with ethylene oxides and bridged bromonium ions, which are known to open in a \textit{trans} dihedral sense.\(^*\)

Addition of a proton to cholest-4-ene, with formation of the C-5 carbonium ion, can be represented as indicated in A. It will be noted that such an addition will be hindered to some extent by a 1,3 dihedral interaction involving the methyl group and the solvated proton, and that migration of the methyl group from C-10 to C-5 must occur in a second step since migration concerted with proton addition is unfavorable on geometric grounds. Similar arguments apply also to cholest-5-ene, and the rapid rearrangement of these olefins would therefore appear to be attributable to intermediate formation of a stable tertiary carbonium ion.

From the observations that cholest-1-ene and cholest-3-ene are slow to isomerize, it is possible that the initial step is hindered by the 1,3 dihedral interaction and that the rapid completion of the reaction is achieved by migration.\(^*\)

\(^*\)Equatorial attack cannot be rigorously excluded on the basis of present evidence, but presumably will involve a transition state of higher energy (cf. ref. 22, p. 5573). An interesting example of the involvement of equatorial bonds is the well-known isomerization of 5\(\alpha\)-6\(\alpha\)-dibromocholestane, for which a bromide-bromonium ion pair intermediate has been proposed by Winstein (5\(a\)).
isomerize to cholest-2-ene and olefin A, and that cholest-2-ene gives olefin A without accumulation of appreciable quantities of intermediates, it is surmised that the rearrangement involves establishment of a steady state amongst the three olefins in which cholest-2-ene predominates, and from which material is slowly converted through cholest-3-ene and cholest-4-ene to olefin A. The rapid rates of disappearance of cholest-1-ene and cholest-3-ene, as compared with that for cholest-2-ene, are quite consistent with this picture. The rate of disappearance of cholest-1-ene, which, despite this olefin's greater stability, is larger than that for cholest-3-ene, may be interpreted as a result due to the preference for the relatively unhindered process B, for the cholest-1-ene isomerization, over process C, for the cholest-3-ene reaction, which involves a 1,3 diaxial interaction (55) with the C10 methyl group. It will
also be noticed that the C.2 carbonium ion formed from cholesterol-1-ene has one less 1,3 diaxial interaction with the C.10 methyl group than the C.3 carbonium ion obtained from cholesterol-3-ene.

It has been mentioned that the isomerizations may be satisfactorily accounted for by a mechanism which requires only a succession of proton additions and abstractions. It is of some interest to note that mechanisms can be proposed which permit direct conversion of cholesterol-2-ene into olefin A without the intervention of any intermediate products.

Among the possible modes of rearrangement of cholesterol-2-ene is the completely concerted process D involving simultaneous addition of a proton at C.3, 1,3 hydride migration of the C.4 quasi-axial hydrogen, 1,2 hydride migration of the C.5 axial hydrogen, and 1,2 methyl migration. 1,3 hydride shifts have been proposed by Roberts (56, cf. 57) to account for the C\textsuperscript{14}\textsubscript{H} distribution in various rearrangement products of the C\textsuperscript{14}\textsubscript{H} labeled norbornyl cation, and a particularly interesting case of concurrent 1,2 hydride shifts and methyl migrations has been observed by Corey and Ursprung (58) in the conversion of friedelan-3β-ol into olean-13:18-ene. The divergent behavior of lan-
osterol (XII) and of euphol (XIII) on treatment with acid provides a notable example of the steric requirements of the concerted process (59, 60).

Another concerted mechanism, E, may be suggested for the rearrangement of cholest-2-ene. Mechanism E involves the 1,3 migration of an axial hydrogen, in contrast with the shift of the quasi-axial hydrogen in process D. Since the distance between carbon and a quasi-axial β-hydrogen (C.2-H.4 in D) is greater by approximately 0.6 Å units* than the corresponding distance between carbon and an axial α-hydrogen (C.3-H.5 in E),

* Determined by measurements on a scale model.
the energy of the transition state for D will be correspondingly increased over that for E. Process E, however, suffers the disadvantage of greater hindrance of the attacking solvated proton than D.

In the absence of any supporting experimental evidence, and in view of the fact that 1,3 hydrogen migrations have thus far been observed only in special systems, these suggestions must be regarded with considerable reserve.

Cholest-6-ene was not included in the qualitative rate study discussed in the preceding paragraphs, and its rearrangement into olefin A can be considered to proceed through cholest-5-ene. The particular point of interest that arises with regard to cholest-6-ene is its preference for rearrangement to olefin A, rather than to olefin B, the product of acid treatment of cholest-7-ene and of cholest-8:14-ene. An explanation for this observation may be found in the fact that proton addition (a), which furnishes the C.7 carbonium ion (XLIV), is hindered by the axial methyl group at C.10, whereas approach of a proton as in (b), leading to the C.6 carbonium ion (XLVI), is unencumbered. As a corollary to this argument it will be observed that XLVI, in which C.6 is trigonal and C.7 tetrahedral, is more stable
than XLIV (C.6 tetrahedral, C.7 trigonal) on steric grounds, in view of the occurrence in the latter structure of a 1,3 diaxial methyl-hydrogen interaction.

Treatment of cholest-7-ene with p-toluenesulfonic acid in acetic acid-c-clohexane at 85°C results in its rapid conversion into an oily mixture in which cholest-8:1h-ene predominates (see Fig. 7). Prolonged treatment of the mixture, or of pure cholest-8:1h-ene, under these conditions, furnishes a colorless oil, designated olefin B, with infra-red absorption characteristics shown in Figure 7d. The ultraviolet absorption spectrum of the tetrinitromethane complex (h2) suggests that the material consists primarily of tetrastubstituted olefin. Hydrogenation of this product under forcing conditions furnishes a non-crystalline saturated substance, in which the presence of traces of cholestan can be detected by infra-red measurements (Fig. 4). The cholestan, which presumably arises from unrearranged cholestene present in olefin B, persisted in the reduction product.
of material that had been heated with acid for a period of seven
days. However, since cholestane is a minor constituent of the
hydrogenated material, it would seem reasonable to assume that
olefin B consists mainly of rearrangement products of the type
illustrated in XLVII.

XLVII

Double bond isomerizations, particularly those involving
7:8, 8:9, 8:14, and 14:15 positions are well known and are
conventionally brought about by saturated solutions of hydrogen
chloride in chloroform. In no previous case, however, has the
intervention of skeletal rearrangement received attention, and
the observations that have been made in this investigation may
be taken as a warning that such rearrangement can occur under
relatively mild conditions. It seems not unlikely that the
poor yields encountered in hydrogen chloride-chloroform isom-
erisations that are allowed to reach temperatures appreciably
above -30° can be attributed to this cause.
EXPERIMENTAL

Each of the cholestenes employed was available by known reaction sequences.

**Cholest-1-ene** was contributed by Dr. R. E. Winkler, who prepared it according to the method of Henbest (61). Two samples were used, the melting point of one being 68-69°, and of the other 66-69°. The latter is believed to have contained a small amount of cholesta-1,3-diene. Infra-red spectrum of the former: Figures 5a, 6a.

**Cholest-2-ene** was prepared by the procedure of Fieser and Dominguez (62), except that the olefin was obtained from the bromohydrin and the dibromide by the use of zinc dust in ethanol (63) rather than in acetic acid.

Six grams of 2-bromocholestan-3-ol, m.p. 101-103°, prepared by sodium borohydride reduction of the ketone, was dissolved in about 100 ml. of ethanol and refluxed overnight with 12 g. of pulverized zinc. The zinc was then removed by filtration and washed with ether, the washings going into the filtrate. Upon removal of the ether and cooling of the remaining solution, 4 g. of cholest-2-ene, m.p. 67.5-72°, crystallized. The olefin thus obtained was dissolved in ether and treated, during a three-hour period, with 21.6 ml. of a carbon tetrachloride solution containing 0.5 mmoles of bromine per ml. The solution was washed with sodium sulfite, dilute sodium carbonate, dilute hydrochloric acid, and with water until neutral, then with
saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to dryness. Crystallization from ethyl acetate-ethanol gave 1.8 g. of dibromide, m.p. 124-125°. The olefin was regenerated with zinc and ethanol in the same manner in which it was obtained from the bromohydrin. M.p. 73.5-75°. Infra-red spectrum: Figures 5c, 6c.

Cholest-3-ene was supplied by Dr. R. E. Winkler, who prepared it by the method of Lardelli and Jeger (64). M.p. 73.5-74.5°. Infra-red spectrum: Figures 5e, 6e.

Cholest-4-ene was obtained through the procedure of Barton and Rosenfelder (65).

Fifteen grams of cholest-4-en-3-one, m.p. 78-81.5°, was dissolved in 15 ml. of freshly distilled benzyl mercaptan, b.p. 194-210°, with heating, then cooled in ice and treated with 1.5 ml. of 60% aqueous perchloric acid and 12 ml. of benzyl mercaptan. The mixture was then shaken until it solidified. After 25 min., water was added, and the product was extracted with ether and bensene. The ether-bensene extracts were washed successively with 2N sodium hydroxide, water, 2N hydrochloric acid, water, and saturated sodium chloride solution, dried with magnesium sulfate, and evaporated to small volume. Two recrystallizations from bensene-ethanol afforded 16 g. of the dibenzyl mercaptal of cholest-4-en-3-one, m.p. 126-128.5°. Two further recrystallizations raised the melting point to 127-129°.

Raney nickel catalyst was prepared from 20 g. of alloy according to Mosingo's procedure (66), except that the digestion was carried out at room temperature. The wet catalyst was washed first with alcohol, then with dioxane. Five grams of the di-
benzylmercaptal was dissolved in about 50 ml. of dioxane (dried and distilled over sodium), with heating. With 100 ml. of ethanol and 5 ml. of water sufficient dioxane was added to retain the steroid in solution at the boiling point. The Raney nickel was added and the mixture was refluxed for 7 hours. The solution was decanted from the Raney nickel through a filter. The nickel was washed with ether. Ether and water were added to the ethan-
ol-dioxane solution, the product being taken up in the ether layer, which was washed, successively, with 2N sodium hydroxide, water, 2N hydrochloric acid, water, and saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to dryness. The solid residue was dissolved in low-boiling petroleum ether and filtered through alumina. Recrystallization of the eluate from ethyl acetate-methanol gave 1.29 g. of cholest-
ene, m.p. 67-71°.

The crude cholest-4-ene was dissolved in 20 ml. of ether and treated with 4 ml. of a 2N solution of bromine in acetic acid. The dibromide was worked up as before. Three recrystal-
lizations from ether-methanol gave 787 mg. of dibromide, m.p.
114-116°.

The dibromide was dissolved in acetone by the addition of a little ether and treated with 1 g. of sodium iodide in 5 ml. of acetone. After several hours the solution was treated with sodium thiosulfate, water was added, and the product was worked up in the usual manner. The crystalline residue was dissolved in low-boiling petroleum ether and filtered through alumina. Cholest-4-ene, m.p. 80-83°, was obtained by recrystallization from ethyl acetate-methanol. Infra-red spectrum: Figure 2c.
Cholest-5-ene was prepared by the method of Mauthner and Suida (67), except that the reduction was accomplished with sodium in ethyl alcohol rather than in amyl alcohol.

To a boiling solution of 586 mg. of cholesteryl chloride, m.p. 92-94°, in 25 ml. of ethanol was added gradually 2 g. of clean sodium metal. An additional 10 ml. of ethanol was added after most of the metal had dissolved. Refluxing was continued for about one and one-half hours after the first addition of sodium. Water and ether were added, and the ether layer was washed with water, dilute hydrochloric acid, again with water until neutral, with saturated sodium chloride solution, and then dried with sodium sulfate, and evaporated to dryness. Recrystallization from ether-methanol afforded cholest-5-ene, m.p. 92-94°. Infra-red spectrum: Figure 2d.

Cholest-6-ene was supplied by Dr. R. E. Winkler from a preparation made according to the method of Cremlyn and Shoppee (12, 68). Infra-red spectrum: Figure 5g.

Cholest-7-ene was obtained by the method described by Cremlyn and Shoppee (68), who reported that the alumina chromatography of cholestan-7β-yl p-toluenesulfonate furnished pure cholest-7-ene by an $E_1$ mechanism. The hydrocarbon obtained in attempting to repeat this work contained, after several recrystallizations, about 6% of cholest-6-ene, according to the optical rotation ($[\alpha]_D^0 +6^0$). Alumina chromatography of this product gave pure cholest-7-ene.

Thirty grams of 7-ketocholesteryl acetate (69), m.p. 151-156°, was refluxed 7 hrs. under nitrogen with 15 g. of p-toluene-sulfonic acid hydrate in 750 ml. of reagent grade benzene. The
solution was cooled, diluted with ether, washed with 2N sodium carbonate, water, and saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to dryness. Recrystallization, first from ethanol and then from acetone, afforded 15 g. of 7-ketocholesta-3,5-diene, m.p. 107-111.5°.

Fifteen and one-half grams of 7-ketocholesta-3,5-diene was dissolved in 100 ml. of ether and 167 ml. of acetic acid. The solution was then stirred under hydrogen at one atmosphere with 1.5 g. of platinum dioxide catalyst. When hydrogen uptake ceased, the platinum was removed by filtration. Ether and water were added to the product. The ether layer was washed with water, dilute sodium hydroxide, water, and saturated sodium chloride solution, dried over magnesium sulfate and evaporated to dryness. The product was an oil in which some crystals appeared.

Cremlyn and Shoppée (68) reported the epimerization of cholestan-7β-ol to cholestan-7α-ol by sodium butylate. Since the oily product of the hydrogenation contains both isomers, an attempt was made to increase the yield of cholestan-7α-ol by means of this epimerization.

Forty and three-tenths grams of the oil containing the 7-hydroxycholestanes was dissolved in 500 ml. of reagent butanol and treated with 42.5 g. of sodium metal, added gradually to the refluxing solution. Heating was continued for 27 hours, at the end of which period no sodium remained. Water was added; the butanol was removed in vacuo. The product was taken up in ether and washed successively with water, dilute hydrochloric acid, water, and saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to dryness. From the residue
cholestan-7α-ol, 5 g., m.p. 110-113.5°C (ether-methanol), was separated on alumina.

From this point the procedure was repeated several times. The once-through yield of cholest-7-ene is low, but the by-product cholestan-7α-ol can be recovered and oxidized to cholestan-7-one (70). The latter, when reduced with sodium metal in butanol, yields cholestan-7β-ol.

A solution of 4 g. of cholestan-7α-ol, m.p. 110-113.5°C, in 20 ml. of dry pyridine, was cooled to 0°C. In it was dissolved rapidly by swirling 2 g. of p-toluenesulfonyl chloride. The solution was allowed to warm to room temperature. After 4 days it was chilled and poured into 100 g. of ice water containing 5 g. sodium bicarbonate. The aqueous layer, after standing 40 minutes, was extracted four times with benzene, and the combined extracts were worked up in the same manner as cholest-5-ene, but using ice-water solutions and adding a wash with saturated sodium bicarbonate. The benzene solution was then evaporated to dryness in vacuo. The product was redissolved, using a minimum amount of benzene, and passed, with added petroleum ether (b.p. 30-60°C), through a column of neutral alumina. The material eluted by 80-20 petroleum ether-benzene was reserved for combination with later batches of cholest-7-ene. The cholestan-7α-ol was stripped from the column with ether and recycled. Four batches of the olefin thus prepared were mixed and recrystallized once from acetone and twice from ether-methanol. M.p. 85.8-87°C, [α]D < 6°. The infra-red spectrum proved that this sample was contaminated with cholest-6-ene. Repeated chromatography on alkaline alumina using low-boiling petroleum ether
as the only eluent yielded a sample having $\delta_0^{1} = 11.7^\circ$. Alkaline alumina was employed in order to minimize the possibility of isomerization on the column. The spectrum (Fig. 7a) of the sample showed it to be free of cholest-6-ene (cf. Fig. 5g).

Inasmuch as recycling was intended, all the product of the tosylation was utilized for the reaction on alumina. In some of the preparations, however, samples of the ester were recrystallized from acetone. The melting points of such samples were varied and low, in comparison with product obtained by Cremlyn and Shoppee (see below), and the purity of the tosylate may be questioned. At the time of the experiments, before the character of the olefin produced on alumina had been fully examined, the unsatisfactory melting points were attributed to the presence of unesterified cholestan-7$\beta$-ol, which would not interfere in the process on alumina. However, in view of the difficulties encountered, another explanation might be sought.

One possibility which should not be overlooked is that the melting point may be in this instance a wholly unreliable test of purity. Nace (71) has reported the case of a steroid tosylate (cholestan-3$\beta$-yl tosylate) which possesses a variable melting point. Table III shows the melting points of several samples of cholestan-7$\beta$-ol and of the tosylates prepared from the samples. The tosylate reported by Karrer and his co-workers (72; Table III) was prepared from a 7-hydroxycholestane of unassigned configuration, and should be included in Table III only if it is a 7$\beta$ tosylate; however, Cremlyn and Shoppee report that cholestan-7$\alpha$-ol does not esterify with $p$-toluenesulfonyl chloride in pyridine. The Swiss workers mentioned that the melting point of their
ester after the first crystallization was as much as 40° higher than the temperature reported.

**TABLE III**

**MELTING POINTS OF CHOLESTAN-7α-OL SAMPLES AND THE CORRESPONDING TOSYLATES**

<table>
<thead>
<tr>
<th>Source</th>
<th>Alcohol</th>
<th>Melting Point</th>
<th>Tosylate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cremlyn and Shoppee</td>
<td>112-113°</td>
<td>158-159°</td>
<td></td>
</tr>
<tr>
<td>This thesis</td>
<td>110-113.5</td>
<td>below 105</td>
<td></td>
</tr>
<tr>
<td></td>
<td>110-113.5</td>
<td>121-122</td>
<td></td>
</tr>
<tr>
<td></td>
<td>108-112</td>
<td>110-111</td>
<td></td>
</tr>
<tr>
<td></td>
<td>114-118</td>
<td>(97-98)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>110-113</td>
<td>combined</td>
<td></td>
</tr>
</tbody>
</table>

Cholest-8:14-ene was prepared by the method of Eck and Hollingsworth (24).

Cholest-7-ene, [α]D +11.7°, was dissolved in ethyl acetate, and the solution obtained was stirred with palladium black in a hydrogen atmosphere for 12 hrs. The palladium was then separated by filtration and the solution was evaporated to dryness. Two recrystallizations from acetone-methanol gave cholest-8:14-ene, m.p. 53.5-55°. Infra-red spectrum: Figure 7b.

Some of the cholest-6-ene-containing fractions from the chromatograms of cholest-7-ene were combined and hydrogenated in ethyl acetate using ethanol-moist Raney nickel, a catalyst that does not promote double bond migration at atmospheric pressure. In the infra-red spectrum of the product, bands at 766 cm.⁻¹ and 972 cm.⁻¹, characteristic of cholest-6-ene and cholest-8:14-ene, respectively, were absent. The product was then
chromatographed, with the object of separating cholestane from cholest-7-ene. The alumina used was the alkaline material available from the Aluminum Ore Company, and was activated by heating in air for four hours at 400° and over. The first 28 fractions off the column represented 80% of the olefin put on. Fractions 1-10 were combined, and the resulting sample clearly showed the infra-red absorption at \(972 \text{ cm}^{-1}\) for cholest-8:14-ene, as did fractions 12, 22, and 28. The occurrence of cholest-8:14-ene in detectable amounts throughout such a large proportion of the eluate indicates that the 8:14 olefin was not an initial impurity which became concentrated on the column, but was rather formed from cholest-7-ene on the exceptionally active alumina.

**Acid Isomerization at 85°.** A solution of the olefin and an equal weight of \(p\)-toluenesulfonic acid hydrate in 1:1 acetic acid-cyclohexane, using about 6 ml. of solvent for 30 mg. of olefin, was refluxed by warming the flask in an electrically heated oil bath. The temperature of the solution under these conditions was about 85°. At the end of the heating period, which varied in length, the solution was poured into a dilute sodium hydroxide solution, and the aqueous layer was extracted three times with added petroleum ether. The combined extracts were washed twice with 2N sodium hydroxide, three times with water, and twice with saturated sodium chloride solution, dried with magnesium sulfate or sodium sulfate, and evaporated to dryness. To record the infra-red spectrum, the product was then twice dissolved in carbon disulfide and taken to dryness. Figure 2a shows the infra-red spectrum of a sample of cholest-
5-ene after treatment in this manner for 150 min. Figures 7c and 7d are the spectra of samples of cholest-7-ene treated 125 min. and 3 days, respectively. Esters have been removed from the latter sample.

**Acid Isomerization at 120°.** This procedure was like the one just described, except that after refluxing had begun a collar was attached to remove about 20% of the solvent. The cyclohexane and the water distilled off as an azeotrope; the temperature of the remaining solution rose to about 120°. Spectra of samples thus prepared from cholest-2-ene, cholest-4-ene, and cholest-6-ene are given in Figures 3b, d, and e; from cholest-1-ene, cholest-2-ene, and cholest-3-ene, in Figures 5b, d, and f; from cholest-5-ene, in Figure 7e. Figures 3b and 5b, d, and f represent hydrocarbon fractions.

**Qualitative Comparison of the Rates of Isomerization of Cholest-1-ene, Cholest-2-ene, and Cholest-3-ene at 112-121°.** In an experiment especially intended to show the relative rates of disappearance of cholest-1-ene, cholest-2-ene, and cholest-3-ene, an acetic acid solution of p-toluenesulfonic acid was prepared beforehand by dissolving 1.44 g. of the sulfonic acid hydrate in 230 ml. of acetic acid and 58 ml. of cyclohexane, and removing 62 ml. of distillate.

In the isomerizations, the three flasks containing the olefins and the acetic acid solution were immersed simultaneously in a paraffin heating bath, electrically stirred and heated to 112-121°. After refluxing for the planned period, the flasks were simultaneously removed from the bath, and immediately treated with 10 ml. 2N sodium hydroxide and cooled. The products were worked up
as in the other isomerizations.

In this manner 13 mg. of each olefin was treated, successively, for periods of 20 min., 30 min., 90 min., 60 min. (Figs. 6b, d, f), 5 hrs. (Figs. 3a, c), and 55 hrs. Two ml. of the acetic acid solution was used for each sample in the first heating period. For the other periods, 5 ml. each was used, to promote rapid solution. After each period the infra-red spectra of the samples were recorded. Acetates were removed on alumina before the 5 hr. heating period.

**Hydrogenation of Olefin A.** Olefin A (373 mg.) was dissolved in 40 ml. of 4:1 acetic acid-cyclohexane and stirred in a hydrogen atmosphere with 200 mg. of prereduced platinum oxide. No hydrogen was consumed, and the product remained unsaturated to tetranitromethane.

Two hundred milligrams of the product was dissolved in 35 ml. of 4:1 acetic acid-cyclohexane and stirred in a hydrogen atmosphere with 150 mg. of prereduced platinum oxide and 4 drops of 12N hydrochloric acid for 42 hrs., maintaining the solution between 40° and 65° by means of a water bath. Sixteen ml. of hydrogen, measured at 27°, was consumed. The product was worked up as before; it gave only a very faint color with tetranitromethane. The infra-red spectrum showed that neither cholestan nor coprostan was present (Fig. 4a, b, c).

**Hydrogenation of Olefin B.** When olefin B was reduced with hydrochloric acid and a prereduced platinum catalyst in acetic acid as described above, the infra-red spectrum of the product (Fig. 4d) indicated the presence of a small amount of cholestan (Fig. 4b).
Spectra. All infra-red spectra were recorded in carbon disulfide solution on a Perkin-Elmer Model 12C Infra-red Spectrometer. With the exceptions noted below, the solutions contained 40 mg. of the steroid per ml. of carbon disulfide. Figures 3a, c; 6b, d, f: 27 mg/ml. Figures 5b, f: 19 mg/ml.
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PART II

THE HEATS OF HYDROGENATION OF EIGHT UNSATURATED HYDROCARBONS
INTRODUCTION

A technique for the measurement of heats of catalytic hydrogenation in solution was described by R. B. Williams (1) in 1942, following the investigations by Kistiakowsky and his co-workers (2-8) of such reactions in the gas phase. The results obtained by these investigators have been of enduring interest, and application of the method to other unsaturated systems seemed desirable. Reported in this thesis are data for eight compounds, investigation of which was undertaken in connection with a more extensive study of heats of hydrogenation being carried on in these laboratories.

Williams measured directly the heats of the following reaction at 25\(^\circ\):

\[
\text{olefin (solid or liq) + H}_2 \text{ (g) = reduced product (solution)},
\]

and by measuring the heats of solution of the products was able to report the heats for the reaction at 25\(^\circ\):

\[
\text{olefin (solid or liq) + H}_2 \text{ (g) = reduced product (solid or liq)}.\]

The values given by Kistiakowsky are for the reaction at 82\(^\circ\):

\[
\text{olefin (g) + H}_2 \text{ (g) = reduced product (g)}.\]

The heats of hydrogenation presented herein are for the reaction at 25\(^\circ\):

\[
\text{olefin (solution) + H}_2 \text{ (g) = reduced product (solution)}.\]

The design of the calorimeter would permit the measurement of the heat of solution of the starting material immediately pre-
ceeding a hydrogenation run on the same sample, but inasmuch as
supplies of the reduced products were not always adequate for heat
of solution measurements, the data are given on a solution-to-
solution basis. It is not considered, however, that their value
is thereby greatly lessened, since energy differences in solution
are important for the consideration of many chemical reactions.
Gas-phase studies were precluded by the exceedingly low volatility
of many of the compounds of interest. The temperature of 25°C is
now standard for much thermal data.

Some of the compounds studied by Kistiakowsky have also
been included in the work of which this thesis is an initial
report. A rigorous comparison of the present results with
those of Kistiakowsky's group is not possible, due to the lack
of the necessary data on heat capacities and heats of solution
and vaporization. However, an approximate comparison has been
made (see Results and Discussion). None of the compounds examined
by Williams is among those reported in this thesis.
EXPERIMENTAL

Method

The calorimeter was employed as a transfer instrument; that is, approximately equal rises in temperature were induced successively by the heat of reaction and by a measured amount of electrical energy. The energy dissipated in the electrical heater was determined by measurement of the potential differences across the heater and across a standard resistor in the same circuit. Temperature changes were detected by means of a thermistor.

Apparatus

The reaction vessel, shown diagrammatically in Figure 1, is a Dewar flask of 470 ml. capacity having three standard taper outer joints inserted in its top. The two smaller openings, of which only one (A) is shown in the figure, are 19/38 joints, and each of these is fitted with a straight through-joint (B), called an ampoule tube in the sequel, extending about six inches above the joint where it terminates in a 14/20 joint. One ampoule tube extends a few millimeters below the surface of the solvent in the vessel, but the other (not shown) is cut off a little below the joint. The third opening in the Dewar is a 34/50 joint (C) fitted with an inner joint carrying the heater and thermistor walls (D) and (E), and through which pass the stirrer shaft (F) and the outlet (G) to the gas buret. This
Figure 1. Calorimeter.
assembly is termed the head, and also includes the binding posts (not shown) for electrical connections for leads to the resistance thermometer (thermistor) and the heater. The outlet to the gas buret terminates in a 10/30 inner joint. The stirrer, an integral part of the head, consists of a "Lew" magnetic stirrer (Scientific Glass Apparatus Co., Inc., Bloomfield, N. J.), having a glass shaft (H) attached to the stirring magnet (J) by means of a tight-fitting Teflon bushing in a cylindrical hole at the center of the magnet. The shaft passes through two loose-fitting Teflon guides (K). A bearing for the stirring assembly is provided by the glass surface (L).

The heater consists of a cylindrical shell of Teflon, 5/8 in. in diameter, threaded with 96 threads per inch, on which is wound a single layer of #36 enameled manganin wire, having a total resistance of about 100 ohms. The lower end of the resistance wire is brought up through a hole drilled in the wall of the Teflon cylinder to the upper edge of the cylinder where the manganin wires are soldered to thin copper leads from the binding posts on the head. The heating coil is immersed in mineral oil as a heat transfer medium, and is enclosed in a glass jacket (D).

The temperature sensitive element is a Western Electric #14B thermistor (Western Electric Co., 195 Broadway, New York, N. Y.), aged for two months at 105° to insure stability (9), and having a temperature coefficient of resistance of -3.9 per cent per degree at 25°, and nominal resistances of 5800 ohms at 0°, 2000 ohms at 25°, and 800 ohms at 50°. The thermistor is inserted in the well (E), consisting of a section of 3 mm.
glass tubing, sealed at one end. The slight lag introduced by the well facilitates observation of the galvanometer by eliminating undue oscillations.

During operation of the calorimeter the reaction vessel is immersed to a point just above the outlet to the gas buret in a water bath, which is maintained at 24.6° by a Model S Sargent Thermonitor (E. H. Sargent & Co., Chicago, Ill.). This device has as its temperature sensitive element a thermistor, and with care will maintain a water-bath temperature constant to about ±0.001\(^\circ\)\(\text{o}\). Operation at 25\(^\circ\) requires that the bath be constantly refrigerated. This is accomplished by a 1/3 h.p. Copeland compressor, the cooling coils for which are immersed directly in the bath.

The parts of the calorimeter which extend out of the bath are enclosed within a cylinder constructed of sheet copper, which dips into the bath and reaches nearly to the top of the stirring magnet. The top of the cylinder is closed by a flexible cover of neoprene cut in two pieces to fit around the stirrer and the ampoule tubes. Room temperature is maintained within a 1\(^\circ\) range with the aid of an air-conditioning unit. A centrifugal circulating pump utilizes water from the thermostated bath for circulation through copper coils soldered to the copper cylinder and through the jacket of the gas buret, which is calibrated for these conditions.

The thorough stirring which is necessary for the rapid progress of a hydrogenation reaction introduces a large quantity of heat which must be reproducible for the calibration. A constant and reproducible speed of stirring is obtained by
turning the driving magnet with a constant-speed D. C. motor
Model 6701 (Servospeed Division of Electro Devices, Inc., Pat-
erson, N. J.). The speed of stirring can be maintained fixed
within one per cent through a wide range of rpm by alteration
of the D. C. voltage by means of a rheostat, which is equipped
with a clamp stop permitting repetition of any given setting.
Inasmuch as the heat of stirring is proportional to the cube
of the speed (10), a variation of one per cent in the speed
will cause a variation of about three per cent in the heat of
stirring. However, this introduces an uncertainty of only 3
to 4 parts per thousand in the calculated temperature rise.

Flexibility in setting up the apparatus has been increased
by the use of universal joints in connecting the motor with the
driving magnet. The employment of a drive shaft two feet in
length permits permanent positioning of the motor at a con-
venient distance from the working space. The position of the
Dewar can also be changed to facilitate alignment of driving
and stirring magnets.

Electrical power for all of the apparatus except the heater
and the thermistor is supplied through a step-down transformer
from a 220-volt line which is free of large voltage fluctuations.
A diagram of the heater circuit is given in Figure 2. The
source of power for the heating coil consists of two six-volt
Willard storage batteries connected in series. The voltage
thus available is controlled by a 300-ohm Ohmite rheostat (Ohm-
ite Manufacturing Co., Chicago, Ill.). During the warm-up per-
iod the current is passed through a dummy resistance of 98 ohms.
The power input to the heater is measured by use of a Model DW-
Figure 2. Heater Circuit

111 Dekavider potential divider (Brown Electro Measurement Co., Portland, Ore.) in conjunction with a Leeds and Northrup #7651 student's potentiometer (Leeds and Northrup Co., Philadelphia, Pa.) and a standard wire-wound resistance of 10 ohms. The potentiometer circuit includes a Leeds and Northrup #2h20 galvanometer and a Shallcross #617B resistance box (Shallcross Manufacturing Co., Collingdale, Pa.), a five-decade box with maximum resistance of 1111.1 ohms.

The resistance of the thermistor is determined by including it in a Wheatstone bridge circuit, the diagram for which is given in Figure 3. The bridge is operated by a six-volt battery. The variable resistance in the bridge is a Shallcross #617B resistance box and the galvanometer is Leeds and Northrup #2h30. Knife-blade switches are employed exclusively in all electrical measuring circuits. The use of toggle switches introduces irregularities.

The timing device used is a Precision Time-it (Precision
Scientific Co., Chicago, Ill.). Switches are thrown manually as the operator notes the chronograph reading. The estimated accuracy of measurement of any time period is about one second or better. This is, of course, entirely sufficient for the measurement of a reaction period which extends typically over 2-3 thousand seconds.

![Wheatstone Bridge Circuit](image)

**Figure 3. Wheatstone Bridge Circuit**

**Procedure**

The calorimeter is assembled on the day before a scheduled run. The ampoule containing the catalyst is attached by a length of manganin wire to a small cylindrical magnet which is grooved at either end for this purpose. Another length of wire is fastened to the upper end of the magnet. Ampoule and magnet are then hung inside the shorter of the ampoule tubes and held in place by tying the upper wire to an ear on the outside of the tube. The ampoule which contains the olefin is similarly suspended in the other tube. The ampoule tubes are then put in place, using Lubrisal stopcock grease. Two hundred and twenty-five ml. of acetic acid are introduced into the Dewar, and the
head is put in position, using Lubrisal. The reaction vessel is then clamped to a vertical rod in the bath, and after connecting it to the buret system with a short length of Tygon tubing and a 10/30 outer joint, again greased with Lubrisal, the flask is immersed in the bath up to a point just above the joint connecting it with the gas buret. The copper cylinder is then placed in position, the driving magnet is centered over the stirrer, and the cover is taped over the cylinder.

With the assembly complete, small Alnico horseshoe magnets are placed outside the ampoule tubes to hold the cylindrical magnets in place, and the wires to the ears on the ampoule tubes are cut. The shorter ampoule tube is then stoppered, using a high-vacuum grease (as on all joints not submerged), and the other is fitted with a straight-through stopcock having a 10/30 joint on its upper end. This leads by means of a section of Tygon tubing through a second stopcock to the hydrogen tank. The reaction vessel, buret manifold, and the connection to the hydrogen cylinder (as far as the stopcock nearest to the needle valve) are then opened to each other and evacuated to a pressure of about 730 mm. The buret is also left under reduced pressure by lowering the leveling bulb. The stopcock between the buret manifold and the pump is closed. The system is allowed to stand thus overnight to test for leaks which might develop under reduced pressure.

At the beginning of the next day's run, the circulating pump and the bridge circuit are turned on. This allows about one and one-half hours for the circuit to warm up. The buret
is opened to the manifold, and the system is flushed three times with hydrogen by successive evacuations and fillings. After another evacuation, the stopcock between the manifold and the pump is closed, and the pump is disconnected. Hydrogen is now admitted to bring the pressure in the system to one atmosphere, the stirrer is turned on at its usual operating speed (about 600 rpm), and hydrogen is bubbled through the solvent for 10 minutes. This flushing ensures removal of dissolved air from the solvent. The stopcocks nearest the hydrogen cylinder and at the pump outlet are then closed. The system is then successively evacuated and filled twelve times, during which operation the heater is utilized to counteract the cooling effect of the solvent evaporation. Simultaneously with the last filling, the leveling bulb is raised to a convenient position so that the longer ampoule tube will contain hydrogen at the same pressure as in the Dewar. Both stopcocks in the hydrogen line are then closed, and the line is removed. The pressure in the system is set at 3 mm. above atmospheric, and maintained throughout the run so that air will not be introduced, even if small leaks should develop.

The calorimeter is warmed by use of the heater to a temperature slightly above bath temperature and then, while stirring as before, the time-temperature curve is recorded by noting the time at convenient values of the resistance, usually every 0.2 ohm drop. When the relationship becomes linear, the resist-

*Whenever the system is evacuated, the stopcock nearest the needle valve is closed, in order to avoid the introduction of air through that valve.*
ance declines about this much in a 100-130 second interval. At this temperature, this is approximately equivalent to a rise in temperature of 0.001 degrees per minute. When the buret reading is no longer changing, the ampoule containing the olefin is broken by removing the horseshoe magnet supporting it. The long stem of the ampoule prevents the cylindrical magnet from falling into the Dewar flask. The volume change which occurs upon breaking the evacuated ampoule is noted, along with a small temperature change due to the heat of solution.*

Again the time-temperature curve is followed until the temperature is rising at a constant rate. At a particular resistance reading, the same for every run if convenient, the catalyst ampoule is broken, and the time is recorded. Now the time interval is noted for each five-ohm change, for reaction proceeds very rapidly at the outset, the reduction of the catalyst being complete in about two minutes. A pressure of 3 mm. above atmospheric is maintained by manipulation of the leveling bulb. Soon after the reduction of the olefin is complete, the temperature begins to fall. The time-temperature relation is noted until it becomes linear.

In preparation for the calibration run, the calorimeter is cooled by slowing the stirrer, and allowing the bath temperature to drop about five degrees. Care is exercised that the pressure in the system does not fall below atmospheric during the cooling. When the calorimeter has cooled sufficiently, the bath is re-heated and the heater is used to reproduce the initial temper-

*It is possible to measure the heat of solution during a run but the error would be large for samples as small as were employed in this work.
ature conditions of the hydrogenation run. Between two and three hours are usually required to attain temperature equilibrium after the end of the hydrogenation run. The heater circuit is allowed to warm up for an hour before the calibration begins.

The stirrer speed is resumed, and the time-temperature curve is followed until it becomes linear. The buret reading, which is used in computing the volume of hydrogen taken up, is recorded as the temperature approaches the point at which the catalyst ampoule was broken. When that point is reached a voltage, calculated to give the same rate of temperature change that obtained during the hydrogenation, is applied across the heater. The time-temperature relationship is followed as before. Readings of the voltage across the heater and across a standard resistor are made at approximately uniform intervals. Near the maximum temperature attained during the hydrogenation, the heating circuit is opened. The rate of temperature change is observed to become constant. The system is then evacuated, air is admitted, and the calorimeter is disassembled and cleaned. Cleaning is done by the following standard procedure. The reaction vessel is emptied and washed with water. Chloroform is then used to remove grease. The chloroform is rinsed out with methanol, and the methanol with water. Trace amounts of catalyst are then removed by cleaning with aqua regia. Before this step was introduced, irregularities resulted from the premature reduction of the olefin. The flask is then washed with water, and rinsed successively with dilute ammonium hydroxide, distilled water, and methanol, and dried.
The total elapsed time required to complete the hydrogenation run and the calibration is about ten or twelve hours.

Calculations

The determination from the experimental data of the temperature rise during a reaction or an electrical calibration is carried out by the use of an improved form (11) of the Regnault-Pfaundler formula. The equation is:

$$\Delta T = \Delta T_x + V_t \cdot t_x + \frac{V_t - V_a}{\Phi_t - \Phi_a} (\Phi_x - \Phi_t) \cdot t_x,$$

wherein if

- $t_1 =$ time at beginning of the first rating period,
- $t_2 =$ time at the end of the first rating period, that is, at the beginning of the experimental process,
- $t_3 =$ time at beginning of the second rating period,
- $t_4 =$ time at the end of the second rating period, and
- $T_1...T_t$ are the temperatures at these times,

then:

$$\Delta T = \text{calculated temperature rise},$$

$$\Delta T_x = T_3 - T_2,$$

$$V_t = (T_3 - T_t)/(t_t - t_3),$$

$$t_x = t_3 - t_2,$$

$$\Phi_a = (T_1 + T_2)/2,$$

$$V_a = (T_1 - T_2)/(t_2 - t_1),$$

$$\Phi_t = (T_3 + T_t)/2,$$

$$\Phi_x = t_x^{-1} \int_{t_1}^{t_4} TdT = \text{mean temperature (with respect to time) during the experimental period.}$$

The integral is evaluated by cutting out and weighing a plot of thermistor resistance against time.*

The electrical energy input is obtained by use of the

*Resistances are used in place of temperatures throughout the calculations by prefixing the absolute values of resistance differences with the algebraic signs of temperature differences.
Energy input (in defined calories) = \( \frac{E_H E_S t_H}{R_S \times 1833} \),
wherein
\[ E_H \] = potential drop across the heater,
\[ E_S \] = potential drop across the standard resistor,
\[ t_H \] = duration of application of voltage across the heater, and
\[ R_S \] = resistance of the standard resistor.

The potential readings are the averages of measurements made at approximately uniform intervals during the heating period. At the conclusion of each electrical calibration run, the potential divider, used in measuring \( E_H \), is calibrated, and the factor thus obtained is employed in the calculation of the energy input. The amount of electrical energy supplied is corrected by subtraction of one-half the estimated heat dissipation in the copper leads to the heater. The correction has typically a value of about 0.4 calories. The remaining half of the heat dissipation in the leads is assumed to take place outside the calorimeter.

To determine from the temperature rise for the hydrogenation the increase in heat content for the reaction, a linear extrapolation is made from the electrical calibration. This procedure does not introduce any serious error if \( T_3 - T_2 \) is nearly the same for reaction and calibration. In this work the difference has rarely been greater than one ohm (out of about eighty).

From the total heat change for the reaction is subtracted the heat of hydrogenation for the amount of catalyst used (see Materials and Results and Discussion). A correction is also
applied for the heat given up upon condensation of acetic acid with decreasing volume of the system. Arbitrarily, one-half of the acetic acid is supposed condensed within the calorimeter and the other half is said to condense outside the calorimeter without affecting the results. An average value of this correction is of the order of 0.2 calories.

The molar heats of hydrogenation are computed on the basis of the volume of hydrogen absorbed. The volume of hydrogen absorbed is corrected for the opening of the evacuated catalyst ampoule and converted to standard conditions. The volume of free space within the ampoule is approximated before the run by noting the volume of water displaced by the ampoule upon immersion. The hydrogen pressure is computed from the mean of barometer readings at \( t_2 \) in the calibration and in the run, taking into account the vapor pressure of acetic acid and the 3 mm. pressure above atmospheric.

**Materials**

**Acetic acid.** J. T. Baker reagent grade acetic acid was stirred with platinum catalyst under hydrogenating conditions for a few hours, filtered, and distilled through a short column, discarding the forerun. The solvent was prepared in several large batches which were then mixed to ensure uniformity of the acetic acid throughout the work.

**Catalyst.** Baker and Company platinum dioxide, activity #380, was thoroughly mixed to ensure homogeneity. The heat of hydrogenation and hydrogen uptake were determined experimentally because of the indefinite composition of the catalyst. In order to avoid heating the unweighed samples of catalyst, the material
was weighed in open ampoules. All of the catalyst had been allowed to stand open to the air for 6 days to come to equilibrium with atmospheric moisture. The filled ampoules, each containing 100 ± 2 mg. platinum dioxide, were evacuated to a pressure of less than 1 mm. and sealed off. Before use the ampoule volume was determined approximately by displacement of water so that this amount could be subtracted from the apparent decrease in volume of the hydrogenation system. The heat of hydrogenation of the small amount of oxygen remaining in the ampoule is negligible.

**Hydrogen.** Houston Oxygen Company electrolytic hydrogen was used, after passing it through a Deoxo Purifier, a commercial palladium preparation, to remove oxygen.

**Olefins**

**Cis- and Trans-cyclodecenes.** These samples were generously donated by Professor V. Prelog.

**Bicycloheptene and Bicycloheptadiene.** These compounds were provided through the courtesy of Dr. S. J. Cristol.

**Bicyclooctene.** This sample was made available by Dr. J. Hine.

**Cis-cyclooctene.** This sample was very kindly supplied by Professor A. C. Cope. The hydrogen uptake amounted to about three per cent more than would have expected on the basis of the weight of the sample. The ultra-violet spectrum indicated the presence of a small amount of diene.

**Cyclooctatetraene-1,3,5,7.** The material obtained from General Aniline and Film Corporation, containing tertiary-butylcatechol as a preservative, was purified by conversion
to the complex $\text{C}_6\text{H}_8\cdot\text{AgNO}_3$, which was prepared according to the procedure of Cope and Hochstein (12), m.p. 173° (dec.). Upon regeneration and distillation, a fraction was chosen having b.p. 111-111.5° (19 mm.), and $n_\text{D}^{25}$ 1.5350. Examination of the infra-red spectrum for the styrene band at 11.08 µ gave no evidence of contamination with that substance.

Asulene. This compound was supplied through the generosity of Dr. W. von E. Doering. It was chromatographed on alkaline alumina before use. M.p. 99-100°.
RESULTS AND DISCUSSION

The results obtained for the heats of hydrogenation in acetic acid at 25° of the platinum oxide catalyst, and of eight olefins included in this investigation, are given in Table I. The heat evolved in reduction of the catalyst is expressed as calories per 100.0 mg., and that for the olefins as kilocalories per mole of hydrocarbon. The averages of individual determinations on the various compounds are listed, with the corresponding standard deviations. Since the heats of hydrogenation of the olefins were determined as the difference between the total heat evolved and that associated with reduction of the catalyst, the uncertainty in the latter value has been included in the deviations from the mean in these cases.

Inspection of the data for platinum oxide gives an indication of the precision of the measurements, which is of the order of ±0.5%, about the same as that reported by Williams (1). Since the temperature rise observed in catalyst reductions was approximately 0.3 to 0.4°, and that in olefin hydrogenation about 1°, it might be expected that a somewhat improved precision would be obtained in the latter. However, the precision for the hydrocarbon reductions, too, is about ±0.5%; probably the longer time required and the larger thermal head are responsible for increases in the indeterminate errors associated with heat loss. Some idea of the accuracy of the results can be gained by exam-
### TABLE I

HEATS OF HYDROGENATION IN ACETIC ACID AT 25°

<table>
<thead>
<tr>
<th>Compound</th>
<th>Amount of Olefin (millimoles)</th>
<th>Wt. of PtO₂ (mg.)</th>
<th>ΔH (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum oxide</td>
<td></td>
<td></td>
<td>31.06 (cal/100 mg.)</td>
</tr>
<tr>
<td></td>
<td>100.6</td>
<td>101.00</td>
<td>31.13</td>
</tr>
<tr>
<td></td>
<td>100.80</td>
<td>100.08</td>
<td>30.99</td>
</tr>
<tr>
<td></td>
<td>99.67</td>
<td>99.85</td>
<td>30.86</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>30.95 ± 0.13</td>
</tr>
<tr>
<td>Cis-cyclooctene</td>
<td>4.526</td>
<td>100.6</td>
<td>23.08</td>
</tr>
<tr>
<td></td>
<td>4.598</td>
<td>100.5</td>
<td>22.88</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>22.98 ± 0.10</td>
</tr>
<tr>
<td>Cis-cyclodecane</td>
<td>3.553</td>
<td>99.3</td>
<td>20.63</td>
</tr>
<tr>
<td></td>
<td>3.937</td>
<td>99.2</td>
<td>20.60</td>
</tr>
<tr>
<td></td>
<td>3.960</td>
<td>100.0</td>
<td>20.77</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>20.67 ± 0.08</td>
</tr>
<tr>
<td>Trans-cyclodecane</td>
<td>3.744</td>
<td>99.8</td>
<td>23.92</td>
</tr>
<tr>
<td></td>
<td>3.751</td>
<td>99.3</td>
<td>24.07</td>
</tr>
<tr>
<td></td>
<td>3.773</td>
<td>100.7</td>
<td>24.05</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>24.01 ± 0.09</td>
</tr>
<tr>
<td>Bicycloheptene</td>
<td>2.883</td>
<td>99.3</td>
<td>32.18</td>
</tr>
<tr>
<td></td>
<td>3.276</td>
<td>99.6</td>
<td>31.93</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>32.06 ± 0.13</td>
</tr>
<tr>
<td>Bicycloheptadiene</td>
<td>1.763</td>
<td>99.2</td>
<td>67.58</td>
</tr>
<tr>
<td></td>
<td>1.754</td>
<td>99.5</td>
<td>68.62</td>
</tr>
<tr>
<td></td>
<td>1.855</td>
<td>99.2</td>
<td>66.14</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>68.11 ± 0.41</td>
</tr>
<tr>
<td>Bicyclooctene</td>
<td>3.115</td>
<td>100.1</td>
<td>27.90</td>
</tr>
<tr>
<td></td>
<td>3.079</td>
<td>99.6</td>
<td>28.60</td>
</tr>
<tr>
<td></td>
<td>3.086</td>
<td>99.4</td>
<td>28.15</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>28.25 ± 0.20</td>
</tr>
<tr>
<td>Cyclooctatetraene</td>
<td>1.259</td>
<td>100.2</td>
<td>97.96</td>
</tr>
<tr>
<td></td>
<td>1.307</td>
<td>100.0</td>
<td>97.96</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>97.96 ± 0.04</td>
</tr>
<tr>
<td>Azulene</td>
<td>0.810</td>
<td>99.8</td>
<td>98.75</td>
</tr>
<tr>
<td></td>
<td>0.800</td>
<td>99.7</td>
<td>98.20</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td>98.98 ± 0.13</td>
</tr>
</tbody>
</table>
ination of the data of Table II, which includes besides cyclo-
octene, two substances, cycloheptene and cycloheptatriene, which,
though not fully reported herein, have been studied both in this
laboratory and by the Kistiakowsky group. Comparison of the two

TABLE II

COMPARISON OF HEATS OF HYDROGENATION
IN SOLUTION AND IN THE GAS PHASE

<table>
<thead>
<tr>
<th>Source</th>
<th>-\Delta H (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclooctene</td>
</tr>
<tr>
<td>This investigation</td>
<td>22.98</td>
</tr>
<tr>
<td>Gas phase data of Kistiakowski</td>
<td>23.53</td>
</tr>
<tr>
<td>Difference</td>
<td>0.55</td>
</tr>
</tbody>
</table>

sets of data for cyclooctene and for cycloheptene indicates a
correction term for monoolefins of approximately 0.6 kcal. for
conversion of the solution data at 25° to gas phase values at
82°. This term is of the same order of magnitude as the cor-
rection of 0.5 kcal, calculated by Williams for conversion of
his liquid phase data on heptene-1 at 29° to the gas phase con-
ditions of Kistiakowsky, and is in agreement with the expecta-
tion that the differences in heats of solution of olefin and
paraffin will be small. Correction terms for polyolefins should
be larger (see Williams' discussion of the basis of his calcu-
lation), and a comparison of the values for cycloheptatriene
can perhaps best be made in the following way. Calculation of
the resonance energy of cycloheptatriene in the usual way, and
subject to the usual approximations, from the gas phase heat of
hydrogenation of this substance and three times the gas phase
The heat of hydrogenation of cycloheptene gives a value of 6.7 kcal/mole. The corresponding result obtained in the same way from the solution data is 7.1 kcal/mole. If one assumes that interactions with the solvent are of no great consequence in the case of relatively non-polar hydrocarbons, the agreement would appear to be satisfactory. Although the overall accuracy of the present measurements is difficult to assess, it is felt, on the basis of the above comparisons, that the results are probably not in error by more than 1%.

Cis- and trans-cyclodecene

The heat of hydrogenation obtained for cis-cyclodecene (-20.67 ± 0.08) represents the lowest such value yet recorded for a compound possessing an isolated double bond, and is clearly the result of severe steric repulsions between non-bonded atoms in the product, cyclodecane. The problem of non-bonded interactions has been discussed previously by Conn, Kistiaakowsky, and Smith (8) in connection with the series: cyclohexene (-26.59), cycloheptene (-26.52), cis-cyclooctene (-23.53); cis-cyclodecene may now be added to this list. The remarkable transannular hydride shifts (e.g., I → II) which occur in derivatives of cyclooctane (13), cyclononane (14), and cyclodecane (15) have demonstrated the close proximity of hydrogen atoms and certain ring
carbon atoms. No such reactions have been observed in rings smaller
than 8-membered. If one assumes that the double bonds in the cy-
clic C_6 through C_{10} monoolefins are essentially unstrained, then
the downward trend in the heats of hydrogenation observed in pass-
ing from the lower to the higher homologues provides a quantita-
tive measure of increased internal crowding in the corresponding
cycloparaffins. Chemical evidence, particularly that relating to
the ease of formation of alicyclic compounds (16), supports this
hypothesis and suggests, moreover, that maximum crowding may be
encountered in the 9- and 10-membered cycles. Extension of the
present series to include at least the 9-, 11-, and 12-membered
cycloolefins would thus appear to be desirable.

Comparison of the result for cis-cyclodecene (-20.67) with
that for trans-cyclodecene (24.01) indicates that the cis isomer
is more stable than the trans by approximately 3.3 kcal/mole.
The relative stability of these isomers, which is the reverse of
that encountered in straight chain olefins (e.g., cis-butene-2:
-28.6; trans-butene-2: -27.6) (3), has been a matter of some
controversy in recent years. Kglomquist and his associates (17,
18) employed infra-red spectroscopy for the analysis of mixtures
resulting from acid treatment of the cis- and trans-cyclodecenes
and concluded that cis-cyclodecene predominates at equilibrium
to the extent of 70-80%. Similar results were obtained by Prelo-
og, Schenker and Günthard (19), who reported that in the pres-
ence of p-toluenesulfonic acid at 170° both cis- and trans-cy-
clodecene furnish the same equilibrium mixture consisting very
largely of cis-cyclodecene. Allinger (20), however, has recent-
ly suggested, on the basis of considerations of boiling point,
refractive index, and density, that \( \text{trans} \)-cyclodecene should represent the more stable isomer. The fundamental basis of Allinger's argument is questionable, and it is in any event certain from the hydrogenation data that the \( \text{cis} \) form is preferred. Instability of the \( \text{trans} \) form is to be attributed to strain accompanying the introduction of a \( \text{trans} \) double bond into the 10-membered ring.

**Bicycloheptene, bicycloheptadiene, and bicyclooctene**

These substances constitute a set of interesting bicyclic systems, for which hydrogenation data are now available. The heat evolved in hydrogenation of bicycloheptene (-32.06) is almost as high as that of ethylene (32.82) (2), if allowance is made for the somewhat lower values expected for solution calorimetry, and is higher by 4 kcal/mole than that of cyclohexene (-28.0)* (4), which possesses the same degree of substitution. The very large difference (11.4 kcal.) between the heats of hydrogenation of \( \text{cis} \)-cyclodecene and bicycloheptene provides a striking illustration of the profound influence of environment on the thermochemical properties of the carbon-carbon double bond.

In connection with recent interest (21, 22) in "homoconjugation," i. e., interaction of unsaturated functions separated by one or more saturated carbon atoms, there has been determined the heat of hydrogenation of bicycloheptadiene (III). This substance has been shown by Winstead (23) to undergo brom-

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*The underlined values for heats of hydrogenation represent gas phase data to which a correction term of 0.6 kcal. has been applied in order to make possible comparison with the solution results of this investigation.*
mination with double bond participation to give products of the type of IV.* This result, however, should not be interpreted as evidence for homoconjugation of the double bonds in III (cf. V), since bridging may be contingent upon attack upon the sys-

![Diagram](image)

III  IV

V  VI

em by a positively charged reagent. In this connection it should be noted that the orientation (nearly orthogonal) of the \(\pi\)-orbitals in bicycloheptadiene (cf. VI) is not conducive to efficient overlap, and exchange should hence be minimal (24).

The heat of hydrogenation of bicycloheptadiene determined in this investigation is \(-68.11 \pm 0.11\) kcal/mole. As a basis for estimating "resonance energy" in this system, twice the value for bicycloheptene, or \(-64.12\) kcal/mole, has been chosen. Since, however, hydrogenation of the first double bond of bicycloheptadiene results in the introduction of two hydrogen atoms (a and b of VII), which do not encounter the interactions

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*Similar attempts of van Tamelen (21) to demonstrate participation in reactions of 1,4-cyclohexadiene were unsuccessful.
a → c and b → d (VIII) introduced in the reduction of bicycloheptene, the value for the comparison standard should be revised upward by a term which probably does not exceed 1 kcal.

The "resonance energy" of bicycloheptadiene can then be expressed approximately as 65.1 - 68.1 or -3 kcal/mole. Although it is not impossible that electrostatic repulsions between the double bonds may contribute to this negative value, it appears more likely that this result and the unprecedentedly large heat (-36.05 kcal.) associated with the hydrogenation of the first double bond of bicycloheptadiene arise from relief of strain in a highly strained molecule. The existence of any appreciable homoconjugative resonance in bicycloheptadiene, however, would appear to be excluded.

Although the relatively strain-free bicyclooctadiene (22) was not available for the present investigation, we have determined the heat of hydrogenation of the corresponding monoolefin, bicyclooctene (IX). The results obtained with this substance
(-28.25 ± 0.20) are of some interest in that, in spite of a number of 1,2 and 1,3 eclipsed hydrogen interactions that appear in the reduction product, the heat of hydrogenation closely approximates that of cyclohexene (28.0), which furnishes a product in which all the hydrogen atoms are staggered.

Comparison of the heats of hydrogenation of cyclopentene and cyclohexene with those of the bicyclic analogues, bicycloheptene and bicyclooctene, provides an illustration of the relative importance of angle strain and conformational properties in such systems. The heat evolved on hydrogenation of cyclopentene is some 1.7 kcal. less than that produced in the hydrogenation of cyclohexene. This result, when first obtained, seemed to disprove the existence of strain energy in cyclopentene, although the bond angles in this substance must deviate from the normal values. It was noted subsequently, however (8), that since 5-carbon rings are planar, or nearly so, the hydrogen atoms of cyclopentene are all eclipsed, whereas in cyclohexene, owing to puckering of the ring, the hydrogen atoms are staggered. The lower energy of the staggered arrangement is now well established (25), and in this case the conformational factor appears to predominate. It will be noted further that, although the relative positions of hydrogen substituents on carbon atoms 3, 4, and 5 of cyclopentene are not appreciably altered by hydrogenation, the hydrogen atoms attached to C.3 and C.6 of cyclohexene (quasi-axial and quasi-equatorial) are partially eclipsed by the C.4 and C.5 hydrogens (26), and that these unfavorable interactions are relieved in passing to cyclohexane with consequent relative increase in the heat of hydrogenation.
The situation with respect to bicycloheptene and bicyclo-octene is somewhat different and can best be deduced from inspection of scale models. Both of these substances, as well as the corresponding hydrogenation products, are essentially rigid molecules. Apart from minor differences, the same interactions, namely, two 1,2 and four 1,3 opposed hydrogen-hydrogen repulsions, are introduced in the hydrogenation of either olefin.* The most conspicuous difference resides in the high degree of strain produced by one-carbon bridging in bicycloheptene. Bicyclooctene is virtually strain-free, and it is to this difference in strain that the large difference in the heats of hydrogenation of these two compounds is attributed.

**Cyclooctatetraene**

An important application of the hydrogenation method concerns the evaluation of resonance energies in aromatic and in other conjugated systems. Considerable work along these lines has been reported in the past by Kistiakowsky and his associates (5, 7). In this connection we have measured the heat of hydrogenation of cyclooctatetraene, which substance has been the subject of intensive study in recent years. Although a large body of evidence has been variously interpreted as favoring the "tub" structure on the one hand, and the "crown" structure on the other (27, 28), there is now general agreement that cyclooctatetraene exists in the "tub" form (X) (29, 30). This structure allows each olefinic double bond to assume a strainless

*It may be pointed out that as compared with cyclopentane, the 5-membered ring of bicycloheptane is incompletely eclipsed (cf. the bridge-head hydrogens) owing to its non-planar character.
planar configuration with C=C-C angles close to 120°, but with angles between adjacent double linkages of nearly 90° owing to rotation about the intervening C-C single bonds. This twisting should largely suppress conjugation between adjacent double bonds, and the resonance energy of cyclooctatetraene should, therefore, be small. This conclusion is in agreement with the chemical behavior of the substance, in particular with its facile rearrangement under certain conditions into derivatives of bicyclo(4:2:0)octadiene (XI \rightarrow \text{XII}) (31).

Following determination of the heat of formation of cyclooctatetraene by German workers shortly after World War II (32), Pink and Ubbelohde (33) calculated the resonance energy of this substance to be 25.3 kcal/mole. Person, Pimentel and Pitzer (29) have given a value of 10 kcal/mole, which they derived from the difference in heats of formation obtained from (a) the combustion data of Prosen, Johnson, and Rossini (3b), and (b) the summation of various bond energies proposed by Pitzer (35). A second calculation from the Rossini data, however, gives a smaller and
probably more reliable value. The heat of reaction, obtained from combustion experiments, for the isomerization of cyclooctatetraene to styrene is $-36.10 \pm 0.36$ kcal/mole (3h). Employing a value of 36.7 kcal, for the resonance energy of styrene (derived from hydrogenation data of Kistiakowsky (6)), the resonance energy of c-cyclooctatetraene may, as a first approximation, be expressed as the difference between these two numbers, or 0.6 kcal/mole. The basic assumption made in this calculation is that the total energies of hypothetical, non-resonating molecules of cyclooctatetraene and of styrene are identical. Since in each case the total energy can be represented by the sum of the individual bond energies, $\Delta E(C=C) = \Delta E(C-C) + 8E(C-H)$, the essential requirement is that the bond energies be independent of small changes in environment. Although this requirement is not fully satisfied (36), it will be noted that only variations in the bond energies, and not their absolute magnitudes, are involved. In the particular case under consideration, correction for this effect can be made on the basis of Franklin’s method of group equivalents (37).

Taking the value 72.5 kcal/mole for the heat of formation of non-resonating styrene calculated as indicated in Table III, and the resonance energy of styrene (36.7 kcal.), the heat of formation of resonating styrene can be expressed as 35.8 kcal/mole. From the heat of isomerization of cyclooctatetraene into styrene (-36.1 kcal/mole), it follows that the heat of formation of resonating cyclooctatetraene is 71.9 kcal/mole. The value calculated for non-resonating c-cyclooctatetraene (Table III) is 75.5 kcal., and the resonance energy of c-cyclooctatetraene is
-77-

TABLE III
CALCULATED HEATS OF FORMATION
OF "NON-RESONATING" STYRENE AND CYCLOOCTATETRAENE

<table>
<thead>
<tr>
<th>No.</th>
<th>Group</th>
<th>Styrene</th>
<th>Cyclooctatetraene</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td></td>
<td>37.8</td>
<td>....</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>20.2</td>
<td>....</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>15.0</td>
<td>....</td>
</tr>
<tr>
<td></td>
<td>C6 ring correction</td>
<td>-0.5</td>
<td>....</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>....</td>
<td>75.5</td>
</tr>
<tr>
<td></td>
<td>Totals</td>
<td>72.5</td>
<td>75.5</td>
</tr>
</tbody>
</table>

then 3.6 kcal/mole. This result is in good agreement with the most recent published value of 4.8 kcal/mole obtained by Springall, White and Cass (38), from a redetermination of the heat of combustion of cyclooctatetraene (-1084.9 ± 0.7 kcal/mole, as compared with Rossini's value of -1086.5 ± 0.22 kcal/mole) and various other thermodynamic data including the average bond energies: $E(C-C)$, 83.1 kcal.; $E(_{cis}-C=C)$, 118.2 kcal.; $E(C-H)$, 96.85 kcal.

The value for the heat of hydrogenation of cyclooctatetraene is $-97.96 ± 0.04$ kcal/mole. If one takes as the non-resonating comparison standard four times the cis-cyclooctene value (-23.0 kcal.) or 92.0 kcal., the resonance energy calculated for cyclooctatetraene is negative and equal to 6.0 kcal/mole.
It is clear, however, that since the heat of hydrogenation of a hypothetical, non-resonating cyclooctatetraene can be represented as the sum of the heats for the reduction of each of the four double bonds in turn, as follows:

\[ \text{cis-cyclooctene} \rightarrow \text{cis-cyclooctene} \rightarrow \text{cis-cyclooctene} \rightarrow \text{cis-cyclooctene} \rightarrow \text{cis-cyclooctene} \]

the use of the heat of hydrogenation of cis-cyclooctene for all four steps will lead to a low overall value if non-bonded interactions introduced in this last stage of hydrogenation are of greater consequence than corresponding repulsions introduced in earlier stages. In order to correct for this effect, the reduction of the first double bond of cyclooctatetraene has been assigned the cis-butene (or cyclohexene) value of \(-28.0\) kcal. \((3, 4)\), which has been taken as representative of a cis-substituted double bond whose hydrogenation is not seriously complicated by the steric repulsion problem. An average of this value and the experimental result for cis-cyclooctene \((-23.0\) kcal.) gives an average heat of hydrogenation for the four steps of the cyclooctatetraene reduction of \(25.5\) kcal., which leads in turn to a resonance energy for cyclooctatetraene of about \(4.0\) kcal/mole. This result is in reasonable agreement with that estimated from the heat of isomerization of cyclooctatetraene into styrene, and with that calculated by Springall, White, and Casss, if account is taken of the approximations involved in the three methods of calculation.
Azulene

As part of a more extensive investigation of resonance energies in non-benzenoid aromatic systems to be reported elsewhere, the heat of hydrogenation of azulene has been measured, the numerical value resulting being $-98.98 \pm 0.13$ kcal/mole. Simple calculation from twice the heat of hydrogenation of cyclopentene (-52.6) and three times that for cycloheptene (-77.7) gives a resonance energy for azulene of 31 kcal/mole. However, as in the case of cyclooctatetraene, discussed in the preceding section, certain corrections should be applied to compensate for undue magnification of steric interactions encountered in hydrogenation of the model compounds cyclopentene and cyclohexene, and further for the fact that two of the double bonds of azulene are tri- rather than disubstituted. To this end the cis-butene value of -28.0 kcal. has been assumed for $\Delta H_1$, and rather arbitrarily, the cycloheptene (-25.9) and cyclopentene (-26.3) values have been taken for $\Delta H_4$ and $\Delta H_5$, respectively. The heats of hydrogenation, $\Delta H_2$ and $\Delta H_3$, are difficult to estimate, and the values chosen, -24.4 for $\Delta H_2$ and -25.0 for $\Delta H_3$, founded upon con-

*The order in which the various double bonds are considered is not material to the present argument.
Consideration of the heats of hydrogenation of methylenecycloheptane, methylenecycloheptene, methylenecyclopentane, and methylenecyclopentene (39), and the correction term for substitution (1.5 kcal.) derived by Kistiakowsky (7), can be considered at best very crude approximations. They are, however, probably not in error by more than one or two kilocalories. The resonance energy calculated for agulene on the basis of these assumptions is, fortuitously, again 31 kcal/mole.

In 1947 Heilbronner and Wieland (40) reported a value of 46 kcal. for the resonance energy of agulene. This result was obtained from a consideration of the difference in heats of combustion of the isomers guaiasulene (XIII) and cadalene (XIV), 29.6 ± 2.1 kcal. (41) (which was taken also as the difference

![Chemical Structures](image)

between the heats of formation of the corresponding isomeric pair, agulene and naphthalene), the heat of formation of naphthalene, the heat of sublimation of carbon (for which the low value of 124.3 kcal. was selected), and bond energies given by Pauling. An equivalent, but more direct, calculation can be made from a knowledge of the resonance energy of naphthalene, and the heat of isomerization of agulene into naphthalene, for which the combustion value of -29.6 ± 2.1 kcal. may be assumed. Using the Pauling value of 75 kcal. for the naphthalene reso-
nance (42), the resonance energy obtained for azulene is 45.4 ± 2.1 (minimum deviation) kcal/mole. The constancy of bond energies* assumed in this calculation is, of course, implicit also in the calculation of Heilbronner and Wieland, and the accuracy of the result obtained by both methods depends ultimately on the validity of Pauling's value for the resonance energy of naphthalene. Experimental evidence is now available which suggests that this value is too high.

Linstead (43) has recently investigated the heats of dehydrogenation of a number of hydroaromatic systems by chloranil. From a comparison of the heat changes observed in the conversions XIV → XVI and XVII → XVIII, and from Kistiakowsky's

\[
\begin{align*}
\text{C}_6 \text{H}_6 + \text{C}_8 \text{H}_4 \text{Cl}_4 \rightarrow \text{C}_8 \text{H}_{10} + \text{C}_8 \text{H}_4 \text{Cl}_2 \\
\text{XIV} \quad \text{XVI}
\end{align*}
\]

\[
\begin{align*}
\text{C}_8 \text{H}_{12} + \text{C}_8 \text{H}_4 \text{Cl}_4 \rightarrow 2 \text{C}_8 \text{H}_{12} + \text{C}_12 \text{H}_6 \text{Cl}_2
\end{align*}
\]

\[
\begin{align*}
\text{XVII} \quad \text{XVIII}
\end{align*}
\]

value of 36 kcal. for the resonance energy of benzene, a tentative value of 68 ± 3 kcal. has been obtained for the resonance energy of naphthalene. A similar investigation of the dehydro-

*See the discussion of the resonance energy of cyclooctatetraene.
genation of dihydroanthracene furnished a value of 85 kcal. for
the resonance energy of anthracene, as opposed to Pauling's value
of 105 kcal. for this substance. It is of considerable interest
in this connection that Franklin has calculated resonance ener-
gies of 62 kcal. and 87 kcal., respectively, for naphthalene and
anthracene (37b).

Acceptance of Linstead's experimental value of 68 kcal. for
the naphthalene resonance gives 38.1 ± 5 kcal/mole as the re-
osonance energy of azulene, or a value of approximately 32.4 ± 2.1
kcal/mole when recalculated by the method of group equivalents
(see discussion of cyclooctatetraene). The agreement between
this result and the present experimental value is fortuitous in
view of the approximations involved in arriving at both figures.
It should, of course, be noted that since azulene is a polar
molecule (dipole moment = 1.0 ± 0.05 D) (44) the resonance en-
ergy calculated from heats of hydrogenation in solution includes
also a factor for stabilization of azulene by solvation. Un-
fortunately, insufficient amounts of material were available for
determination of the appropriate thermochemical quantities to
permit correction to the gas phase. The comparison between the
value for the resonance energy of azulene obtained from the hy-
drogenation data and that derived from Linstead's naphthalene
value is not, however, seriously compromised, since Linstead's
measurements were made in solution, and since the heats of com-
bustion of guaiazulene and of cadalene were presumably deter-
mined for the liquid phase.
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