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STIPANOVIC, Robert Douglas, 1939-
STUDIES IN THE SYNTHESIS OF KAURENE.

Rice University, Ph.D., 1966
Chemistry, organic

University Microfilms, Inc., Ann Arbor, Michigan
RICE UNIVERSITY

STUDIES IN THE SYNTHESIS

OF KAURENE

by

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A THESIS SUBMITTED
IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF

Doctor of Philosophy

Thesis Director's signature:

Houston, Texas
June, 1966
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ACKNOWLEDGEMENT

I wish to express my appreciation to Professor Richard B. Turner, who directed this research, for his advice, assistance, and criticism.

I want to thank my wife for her encouragement and aid in the preparation of this work, as well as my parents for their moral and financial support of my undergraduate work.

My thanks to my associates and colleagues for their suggestions and help.

Acknowledgement is also made to Rice University, The Robert A. Welch Foundation, and the National Aeronautics and Space Administration for financial support of this work.
I. INTRODUCTION

In recent years, a great deal of research has been applied to the structural determination and synthesis of the diterpenes, phyllocladene and kaurene, and the structurally related diterpene alkaloids atisine (1), garryfoline (2), and veatchine (3).

![Chemical Structure 1](image1)

![Chemical Structure 2](image2)

Kaurene was first isolated in 1928 by Hosking\textsuperscript{1} as a crystalline compound from the leaf of the kauri pine (\textit{Agathis australis}), which is
native to New Zealand. The hydrocarbon, $C_{20}H_{32}$, was found to have one double bond, since on catalytic hydrogenation one mole of hydrogen was absorbed to give dihydrokaurene, $C_{20}H_{34}$, and thus it was shown to be tetracyclic. Three years later, in 1931, Nishida and Uota\textsuperscript{2} isolated a $C_{20}H_{32}$ hydrocarbon from the essential oil of *Podocarpus macrophylla* which they termed $\alpha$-podocarpene. Reinvestigation of these two compounds, however, demonstrated that they were identical.\textsuperscript{3,4}

At an early date, the chemical behavior (Chart I) of kaurene (4) was noted to closely resemble that of phyllocladene (5), whose structure has been determined unambiguously by degradation\textsuperscript{5,6} and synthesis.\textsuperscript{7,8} The double bond of kaurene was shown to possess a terminal methylene group by infrared and NMR studies and it isomerizes in the presence of acid to yield isokaurene. Both kaurene and isokaurene yield the same hydrochloride and dicyclo derivative which suggests that the isomerization may be the same as that in phyllocladene and isophyllocladene (6).

On dehydrogenation, pimanthrene (7) was the only product isolated from both kaurene and isokaurene,\textsuperscript{9} as opposed to the case of phyllocladene which gives both pimanthrene (7) and retene (8).\textsuperscript{5} However, on prolonged dehydrogenation over selenium followed by oxidation with chromium trioxide in acetic acid, small amounts of retene quinone (9) were obtained from kaurene,\textsuperscript{10} and thus its basic ring structure may be assigned. The fourth ring was shown to be bridged in the same manner as that in phyllocladene.

Ozonolysis of kaurene (Chart II) yielded formaldehyde and a norketone (10) the infrared spectrum of which indicated that it was a 5-ring
Chart I

(4)  

(5)  

(6)  

(7)  

(8)  

(9)
Chart II

(10) → (11) → (12)

(13) → (14) → (15) → (16)

(17) → (18)
ketone. On treatment of isokaurene with permanganate the diol (11) and the keto acid (12) were formed, analogous to the behavior of phyllocladene.5

A great deal more evidence may be cited concerning the stereochemistry of kaurene including optical rotatory dispersion studies.11,12 The most critical argument, however, concerns the direct correlation of kaurene with phyllocladene (Chart II) by comparison of the keto ester (16) obtained from kaurene13 and the keto ester (18) obtained from phyllocladene12 as well as by synthesis.13

Baeyer-Villiger oxidation of kaurene norketone (10) affords a δ-lactone (13), which is converted into the diol (14) on treatment with lithium aluminum hydride. The diol on oxidation yields a lactol (15), which may be converted to the keto ester (16) on treatment with potassium carbonate and methyl iodide or to the keto ester (18) by treatment with sodium methoxide and methyl iodide. Phyllocladene norketone, however, on Baeyer-Villiger oxidation yields the δ-lactone (17) which provides by alkaline hydrolysis, methylation and oxidation, the keto ester (18). The skeletal structure, as well as the stereochemistry of the A/B ring junction, is thus established. The stereochemistry at C.13 and C.14 is not established by this evidence, however, due to the possibility of a reverse Michael reaction, followed by double bond migration as in the intermediate (19). The remaining uncertainties are resolved by synthesis.

Recently two syntheses of kaurene have appeared in the literature. The work by Ireland et al.14,15 resulted in the first total synthesis
of dl-kaurene (Chart III). The starting material was the \( \alpha,\beta \)-unsaturated tricyclic ketone (20) which upon reduction afforded two epimeric alcohols of which the quasi-equatorial alcohol (21) predominated. The alcohol (21) was converted to the vinyl ether (22) by treatment with ethyl vinyl ether in the presence of mercuric acetate. Upon pyrolysis the vinyl ether (22), by Claisen rearrangement, was converted into the aldehyde (23a), which in turn was converted to the ethylene acetal (23b). Since the aldehyde (23a) had been converted into the phyllocladene degradation product (18) by an unambiguous route,\(^{14}\) the stereochemistry at C.13 and C.14 is rigorously established.

Hydroboration of the ethylene acetal yielded a mixture of 13- and 14-hydroxy acetals, of which the minor product (26%) was the desired 14-hydroxy acetal which could be oxidized to the keto acetal (24). Upon cleavage of the acetal in aqueous acid a hydroxy ketone (25) was obtained by an internal aldol condensation, which on oxidation yielded a dione (26) of which one of the carbonyls was a 5-ring ketone. The 5-ring keto- tone was converted into the corresponding methylene derivative (27) by a Wittig reaction and under Wolf-Kishner forcing conditions dl-kaurene (4) was obtained.
Chart III

(20) → (21) → (22)

(23a) \( R=0 \)

(23b) \( R=\bigcirc \)

(24) → (25)

(26) → (27) → (4)
The second and more recent synthesis of kaurene\textsuperscript{16} (Chart IV) begins with the acid (28) which is treated in successive steps with oxaly chloride, diazomethane, and hydrobromic acid thus affording the bromoketone (29). The bromoketone on reduction with sodium borohydride yields a mixture of epimeric bromohydrins which are converted to the tetrahydropyranyl ethers (30a). Hydrogenolysis of (30a) gives the phenol (30b), which upon base treatment cyclizes to yield one isomer (31a). The tetrahydropyranyl ether was cleaved and the resulting hydroxyl group was protected as the benzoate (31b). Catalytic hydrogenation afforded two isomeric tetrahydro compounds of which (32) was carbomethoxylated and methylated to give (33). Ring A was introduced by standard methods, and by conventional reductive and oxidative methods kaurene norketone was synthesized.

In addition to the work reported here, another attempt to synthesize kaurene\textsuperscript{17} in this laboratory should be mentioned. In an attempt to convert a derivative of phyllocladene to kaurene, an acyloin condensation of the keto ester (18) was undertaken. On treatment of this substance with sodium in liquid ammonia a crystalline compound whose properties consistent with the glycol (34) was obtained. On treatment with acid it was hoped that rearrangement might take place as shown below to yield
Chart IV

(28) $\xrightarrow{\text{COOH}}$ (29) $\xrightarrow{\text{C}_6\text{H}_5\text{O}}$

(30a) $R=\text{C}_6\text{H}_5$  
(30b) $R=\text{C}$  

(31a) $R=\text{C}_6\text{H}_9\text{O}$  
(31b) $R=\text{Bz}$

(32) $\xrightarrow{\text{CH}_3\text{OO}}$ (33) $\xrightarrow{\text{OBz}}$
kaurene norketone (10). On acid treatment, however, a mixture of products was obtained which showed both 5-ring and 6-ring ketone absorption in the infrared and which therefore may contain some kaurene norketone. Further work in this regard is being actively pursued.

That such a rearrangement is possible was subsequently demonstrated by Japanese work\textsuperscript{18} in which such a device was employed in the synthesis of the diterpene alkaloids garrying and veatchine. The more recent acid isomerization\textsuperscript{19} of stachene (35) to kaurene (4) constitutes a further example of such an isomerization.
II. DISCUSSION

The first approach to the kaurene synthesis which was undertaken as part of the present investigation was based on observations of Wenkert and his collaborators. In standard reactions from podocarpic acid (36), O-methylpodocarpane (37) was obtained (Chart V). Lithium and ammonia reduction of (37) followed by treatment with acid yielded the unsaturated ketone (38). Ozonization of (38) with an oxidative work up afforded the keto acid (39). The keto acid and its derivatives were treated with methyl vinyl ketone and various bases in the hope of obtaining compound (40). However, under no circumstances was condensation observed. It should be noted, however, that the initial Michael addition reaction is readily reversible and that steric interference by the C.10 methyl group might well account for the failure of the reaction leading to intermediate (41). Therefore, the possibility of accomplishing such a
Chart V

(37) \rightarrow (38) \rightarrow (39) \rightarrow (40)
condensation under irreversible conditions was considered to be a desirable objective.

The starting material for this investigation (Chart VI) was the commercially available 2,7-dihydroxynaphthalene (42) which was converted to the 2,7-dimethoxynaphthalene (43) on treatment with dimethyl sulfate in base. The dimethoxynaphthalene was smoothly reduced with sodium in alcohol to the enol ether (44), which cleaved readily in acid to 7-methoxy-2-tetralone (45). The ketone was methylated via the pyrrolidine enamine to 7-methoxy-1-methyl-2-tetralone (46). The A-ring was added by the Cornforth-Robinson method through the quaternary ammonium salt of diethylaminobutanol to yield the unsaturated ketone (47).

Dimethylation (Chart VII) of (47) was accomplished by the Woodward-Patchett method to give compound (48). All attempts to crystallize (48) failed but the equatorial alcohol (49) obtained by lithium aluminum hydride reduction was crystalline. The double bond was hydrogenated over palladium-on-charcoal to yield 3-hydroxy-0-methylpodocarpane (50). The tosylate (51) was prepared, but all attempts to displace tosylate by the use of lithium aluminum hydride in ether or refluxing tetrahydrofuran led to starting material. Under more drastic conditions an oil of unknown composition was obtained. A colorless oil was eluted from a chromatographic column by petroleum ether, but no crystalline material could be isolated. That the oil did not contain considerable quantities of 0-methylpodocarpane (37) cannot be immediately concluded, however, since the compound melts at 31-32°C and is reported to crystallize only with difficulty. However, products of the type (52) may also be
Chart VI

(42) → (43)

(44) → (45)

(46) → (47)
Chart VII

(48) \[ \rightarrow \] (49)

(50) \[ \rightarrow \] (51)

(37)
present since rearrangements to the type shown are well known. 25

In order to overcome these difficulties, the hydroxyl group in
the crystalline derivative (50) was left for removal at a later stage.
Compound (50) was subjected to Birch reduction by lithium in liquid
ammonia and alcohol (Chart VIII). No attempt was made to isolate the
intermediate enol ether (53), but it was hydrolyzed directly to the
β,γ-unsaturated ketol (54), which in turn was smoothly isomerized to
the α,β-unsaturated ketol (55a). The hydroxyl group was acetylated
and the resulting product (55b) was ozonized to the keto acid (56).

The keto acid (56) was treated with allyl bromide in the presence
of potassium t-butoxide at room temperature. The acid fraction was
esterified with diisoxethane and chromatographed. Only small quantities
of oily material were obtained, the infrared spectrum of which indicated
no terminal methylene absorption, and this oil resisted all attempts at
crystallization.

Since the oil accounted for less than one tenth of the entire pro-
duct and could not be crystallized, alkylation of the conjugated ketone
(55b) was attempted. Compound (55b) in the presence of potassium t-
Chart VIII

(53) → (54)

(55a) R=H
(55b) R=Ac

→ (56)
butoxide was treated with allyl bromide at room temperature. On chromatography an oily material was obtained, the infrared spectrum of which indicated that some alkylation had taken place. This result was not completely encouraging, however, since this material accounted for only about one sixth of the total product. Furthermore, the exact point or points of alkylation were unknown.

With these results in hand, a re-evaluation of the problem was undertaken. The keto acid (56) appeared to alkylate but in poor yield. It was believed that the yield might be increased by the use of a different base (e.g., sodium hydride) and by masking the alcohol as the t-buty1 ether, since some cleavage of the acetate had occurred.

While considering alternate reaction conditions, an interesting series of transformations appeared in the literature. Birch reduction of anisole (Chart IX) yielded 2,5-dihydroanisole (57) which could be equilibrated with the conjugated 2,3-dihydro isomer (58) on treatment with potassium t-butoxide in dimethyl sulphoxide. The conjugated diene was then observed to undergo a Diels-Alder reaction with benzoquinone (59) which in turn opened in the presence of acid to yield (60).

The fact that such a scheme could be utilized to synthesize kaurene (Chart X) was recognized and it was found that the enol ether (53), which had not been isolated heretofore, could be crystallized, and when treated with potassium t-butoxide in dimethyl sulphoxide, the conjugated isomer (61) was obtained.

If the adduct (62) could be obtained through the reaction of the dieneophile, methyl vinyl ketone, with (61), its treatment with acid
should yield (53), which might be utilized to synthesize kaurene. However, on treatment of (61) with methyl vinyl ketone under reflux or in an autoclave at 140-155°C no products recognizable as (62) were obtained on chromatography. Since a considerable amount of polymerization had occurred, any of the desired product that had formed might have been concealed in this fraction. To avoid the problem of polymerization, methyl vinyl ketone was replaced by maleic anhydride. The acetate (64) of compound (61) was treated with maleic anhydride in refluxing xylene. A compound with a melting point of 220-235°C was obtained which may have been the adduct (65), but since the yield was less than 3% the reaction was not investigated further.

Attention was next focused on a new synthetic approach. The enol ether resulting from Birch reduction of the ethylene ketal of 0-methyl estrone (66) had been successfully converted into the 3,3-dimethoxyester-5(10)-ene 17-ketal (67).

\[
\begin{align*}
\text{(66)} & \quad \xrightarrow{\text{Birch reduction}} \quad \text{(67)} \\
\text{CH}_3\text{O} & \quad \text{CH}_3\text{O}
\end{align*}
\]

In a similar manner the acetate of (53) was converted into the dimethoxy ketal (68). Conversion of (68) to (69) was then attempted by adding ethyl diazoacetate in the presence of copper-bronze powder to the carbon-carbon double bond of (68). Preparation of (70) would
then be attempted by cleavage of the ketal and opening of the cyclopropane ring with acid or base by $\beta$-elimination. However, on treatment of (68) with ethyl diazoacetate under various conditions, only starting material was obtained.

Since the addition of the carbenoid intermediates to double bonds in the presence of copper-bronze powder or copper salts is known to be subject to steric interference, a series of model compounds was studied.

Anisole was reduced (Chart XI) under standard conditions to the enol ether (57) which was smoothly converted to the ketal (71). The NMR of the ketal showed a 2-proton multiplet centered at $\delta 5.53$, a 6-proton singlet at $\delta 3.11$, and a multiplet between $\delta 2.2$ and $\delta 1.5$ integration of which indicated six protons. The infrared spectrum of the ketal had lost the peaks at 5.91 and 6.04 $\mu$, characteristic of the enol ether (57), and instead gave several peaks in the 8.8 to 9.5 $\mu$ region. Analysis confirmed this structure. The ketal (71) was treated with ethyl diazoacetate and the crude material was distilled. The NMR spectrum of the product (72), boiling between 95-105$^\circ$C at 0.05-0.06 mm Hg, has no vinyl hydrogens. A 2-proton quartet centered at $\delta 4.05$, indicative of a methylene of an ethyl ester was observed, along with the 6-proton singlet of the ketal.
Chart XI

(57) \[ \xrightarrow{\text{反应}} \] (71)

(72) \[ \xrightarrow{\text{反应}} \] (74)

(75) \[ \xrightarrow{\text{反应}} \] (76a) \( R = C_2H_5 \)
(76b) \( R = H \)
The methyl group of the ester was a triplet centered at δ 1.21. The mass spectrum of (72) yielded a parent peak of mass 197. The ketal ester itself had a mass of 228. The difference is readily accounted for by the loss of a methoxy group (mass 31), the loss of which is expected for such ketals.

The vapor phase chromatography of the compound on an SE-30 column showed two peaks with retention times of 19 and 26 minutes at 230°C. The latter peak was determined to be (72) while the former peak was shown to be (73), a mixture of enol ethers with the carbon-carbon double bond α,β and β,γ to the cyclopropane ring. Its formation is easily accounted for by the loss of methanol. Its NMR exhibits two peaks in the vinyl proton region at δ 4.41 and δ 4.92 which together integrate for one proton; the methoxy singlet has shifted to δ 3.48 and integrates for three protons. The infrared possesses the characteristic enol ether peaks at 5.93 and 6.0 µ. Carbon-hydrogen analysis agrees with structure (73).

The ketal (72) was cleaved by exchange with acetone in the presence of p-toluenesulfonic acid to afford (74) which when treated with p-toluenesulfonic acid in refluxing benzene yielded the conjugated keto ester (75). On treatment of (75) with palladium-on-charcoal in refluxing xylene p-hydroxyphenyl ethyl acetate (76a) was produced, which on hydrolysis yielded
p-hydroxyphenyl acetic acid (76b) whose infrared, melting point, and mixed melting point agreed with that of an authentic sample.

The same general set of reactions was then carried out on p-methyl anisole (Chart XII). The expected 2,5-dihydro-4-methylanisole (77) was obtained on Birch reduction. The enol ether was smoothly converted to the ketal (78). On treatment of the ketal with ethyl diazoacetate as above, the norcarane ester (79) was obtained in good yield. On cleavage of the ketal the keto ester (80) was obtained.

Compound (80) was dissolved in dry benzene, treated with a catalytic amount of p-toluenesulfonic acid, and refluxed in the same manner as above. On vapor phase chromatography only one peak was apparent. Its infrared spectrum possessed the expected peaks at 5.78 and 5.92μ for the ester and conjugated ketone groups respectively. But in addition to these bands, there were strong absorptions at 5.32 and 5.87μ. On refluxing for a longer period of time, the infrared spectrum did not change. The NMR of the product was very complex, and if it is assumed that the quartet at 84.08 represents two hydrogens, the other peaks gave fractional values. The carbon-hydrogen analysis, however, proved that the product was isomeric with the starting material. It is believed that the product is a mixture of the expected compound (81) and one or more of the

```
\begin{align*}
\text{(81)} & \quad \text{(82)} \\
\end{align*}
```

![Chemical Structures](image-url)
Chart XII

(77) \rightarrow (78)

(79) \rightarrow (80)

(81)
isomers (82), which arise as shown below.

This difficulty presumably arises in the present case but not in the unsubstituted example (74) owing to the formation of the stabilized tertiary carbonium ion (83).

This problem was surmounted by treating the keto ester (80) with sodium acetate in refluxing dry ethanol. In this manner compound (81) was obtained in good yield and none of the isomeric product (82) could be observed by infrared or NMR methods.

Since the disubstituted carbon-carbon double bond as well as the trisubstituted one had reacted in good yield, it was reasonable to examine a case involving a tetrasubstituted double bond. To obtain such a compound (Chart XIII) 3,4-dimethylanisole (84) was reduced in the customary fashion to the enol ether (85). The dimethoxy ketal (86), obtained as described above was treated with ethyl diazoacetate and afforded the adduct (87). The ketal was smoothly exchanged with acetone to yield the keto ester (88), which in turn opened cleanly to the conjugated keto ester (89) on treatment with sodium acetate.

Thus the addition of ethyl diazoacetate to a tetrasubstituted carbon-carbon double bond, and its subsequent opening, was clearly demonstrated.
Chart XIII

(84) → (85)

(86) → (87)

(88) → (89)
It was also shown that the hindrance to addition did not arise from the methoxy groups alone, and that the reaction could take place with the ketal present. The factors responsible for the failure of ethyl diazoacetate to add to compound (68) remained to be determined.

To investigate this problem more fully, the ketal (90) was prepared from the methyl 8-tetralone (46). Following Birch reduction to the enol ether (91), the ketal (92) was prepared in the customary manner. The addition of the diazoacetate was attempted neat and in refluxing n-octane in the presence of copper-bronze powder. However, no addition to the tetrasubstituted double bond occurred as judged by chromatographic examination of the total crude product.

In view of this failure, further simplification of the molecule was undertaken. The 8-tetralone (45) was reduced by Clemmenson reduction, and the methoxy tetralin (93) obtained was subjected to a Birch reduction.
The enol ether (94) was treated with p-toluenesulfonic acid in methanol and ether as above. The resulting dimethoxy ketal (95) was heated in the presence of copper-bronze powder and ethyl diazoacetate was added. The dark oily product was chromatographed and the ketal (95) was obtained unchanged in almost quantitative yield.

Since the dimethoxy ketal (86) (in which the double bond was tetra-substituted) had readily undergone addition with ethyl diazoacetate, and the bicyclic dimethoxy ketal (95) had not, it appeared that the most serious hindrance must arise from the bicyclic ring system itself. In order to test this hypothesis, 9,10-octalin (96) was prepared according to the method of Campbell and Harris. 31

\[ \text{(96)} \rightarrow \text{COOEt} \text{ (97)} \]

The product from the reaction of 9,10-octalin with ethyl diazoacetate was the customary dark oil. On vapor phase chromatography through an SE-30 column at 242°C two products in addition to starting material were obtained. One substance had a retention time of 17 minutes and its NMR indicated that it was a polymeric material. The second product, with a retention time of 20.5 minutes, however, appeared to be compound (97). Its NMR had a quartet at δ4.16, a multiplet between δ2.4 and δ1.0. The area between δ2.4 and δ1.4 closely resembled that of the starting material, but centered at δ1.28 a definite triplet was superimposed. If
it is assumed that the quartet integral equals two hydrogens, the multiplet correctly integrated for twenty hydrogens. However, the compound (97) was obtained in only 17% yield.

Thus it appeared that the steric hindrance resulted from a combination of the steric factors associated with the bicyclic system, and to a lesser extent from the dimethoxy ketal. Some steric interference was expected due to the bulky copper complex. However, the high degree of interference was totally unexpected, since in the 9,10-octalin system the rings are somewhat planar and thus leave the carbon-carbon double bond rather exposed.

The 9,10-octalin system was treated with ethyl diazoacetate under both photolytic and thermal conditions. However, no material corresponding to compound (97) was observed by chromatographic methods.

Since the cyclopropane ring could not be formed in the bicyclic case, a plan was devised whereby, starting with a monocyclic system, the second ring would be introduced after formation of the cyclopropane ring had been accomplished.

To this end, p-methoxy anisaldehyde (98) was condensed (Chart XIV) with methyl ethyl ketone in the presence of base. The conjugated ketone (99) which was obtained was hydrogenated over palladium-on-charcoal to afford compound (100). The ketone was protected as the ethylene ketal (101). Compound (101) was reduced by lithium in liquid ammonia to the enol ether (102), which in turn was converted to the ketal (103). On treatment of compound (103) with ethyl diazoacetate the adduct (104) was obtained in 43% yield (based on recovered starting material). On
Chart XIV

(98) \[ \rightarrow \] (99) \[ \rightarrow \] (100)

(101) \[ \rightarrow \] (102) \[ \rightarrow \] (103)

(104) \[ \rightarrow \] (105) \[ \rightarrow \] (106)
treatment of compound (104) with p-toluenesulfonic acid in acetone for 25 hours at room temperature, the diketo ester (105) resulted with no opening of the cyclopropane ring. Compound (105) was treated with base under a variety of conditions. It was believed that the cyclopropane ring would open to yield an unsaturated ketone, and through an internal Michael reaction compound (106) would be produced. However, under a variety of conditions no product corresponding to the bicyclic compound (106) was observed. Instead a dark oily product was obtained, which on chromatography yielded no recognizable products.

This reaction sequence was designed to produce the trans-decalin system. Another possibility existed for preparing the cis-decalin compound which could possibly be converted into the trans compound.

To accomplish this, the enol ether (102) (Chart XV) was treated with oxalic acid affording the unconjugated ketone (107). The ketone was reduced with sodium borohydride to the epimeric alcohol (108a) without migration of the double bond. The acetate (108b) was obtained in the customary manner and on treatment with ethyl diazoacetate in the presence of copper-bronze powder the adduct (109) was obtained. The ketal was successfully exchanged with acetone in the presence of p-toluenesulfonic acid to yield compound (110). The product was treated with sodium ethoxide in refluxing alcohol.33

It was hoped that a cis-decalin system would be obtained, and on reduction with lithium aluminum hydride the triol (111) would be formed. The diketo acid (112) should be obtained by oxidation with the Jones
Chart XV

(102) → (107)

(108a) R=H
(108b) R=Ac

(109)

(110) → (111)
reagent. On treatment with base compound (112) may rearrange through a reverse Michael reaction to the more stable trans diketo acid (106).

However, the reaction of compound (110) with sodium ethoxide produced an intractable oil of unknown composition. The failure of the reaction was demonstrated by the NMR of the product. The methyl group in the side chain of the starting material exhibited a triplet in the NMR centered at \( \delta 1.02 \). This methyl group in the product (111) should be a doublet. However, the triplet remained intact.

Unfortunately time does not permit further investigation of these reactions. It is possible that by varying the reaction conditions the desired product may be obtained, but further study will be required to establish this point with certainty.
III. EXPERIMENTAL*

Preparation of 2,7-Dimethoxynaphthalene (43). 2,7-Dihydroxynaphthalene (100 g.) was dissolved in 560 ml. of 2 N sodium hydroxide. Dimethyl sulfate (125 ml.) was added in one portion. The solution was shaken and prevented from actually boiling by cooling in cold water as necessary. When the reaction had subsided another 280 ml. of 2 N sodium hydroxide was added followed by an additional 62.5 ml. of dimethyl sulfate. The flask was shaken until the second reaction had subsided. The flask was heated on the steam bath for one hour in order to destroy any remaining dimethyl sulfate. The crystalline precipitate was filtered and washed with dilute sodium hydroxide until white. The product was then washed free from base with water, and was finally washed with cold ethanol. A yield of 90% (105 g.) was thus obtained, m.p. 139-140°C, (Lit.34: m.p. 139°C).

$$\lambda_{\text{max}}^{\text{CCl}_4}: \ 3.45, 6.15, 6.82, 7.20, 8.50, 8.60, 8.65, 8.80, 8.95, 9.65, 10.50, 11.53, 11.70 \mu.$$
Preparation of 7-Methoxy-2-tetralone (45). A solution of 100 g. of
2,7-dimethoxynaphthalene in 1200 ml. of refluxing 95% ethanol was pre-
pared. To the refluxing ethanol solution 100 g. of sodium metal was
added over a 45 minute period. At the end of this time another 200 ml.
portion of ethanol was added and refluxing continued for another 45 min-
utes. Most of the solvent was removed leaving a thick slurry, to which
water was added. The resulting crystals were filtered and washed with
water until neutral. The gray crystals were recrystallized from 250 ml.
of ethanol, m.p. 115-120°C. These crystals were found to decompose
slowly on standing.

The 1,4-dihydro-2,7-dimethoxynaphthalene from the above reaction
was dissolved in 850 ml. of methanol and 750 ml. of ether. The organic
solution was poured into 160 ml. of a 1:3 HCl-H₂O solution into which
nitrogen was bubbled throughout the course of the reaction. The solu-
tion was stirred for 70 minutes, and the solvent was then evaporated.
The resulting crystals were dissolved in methylene chloride and washed
with water, saturated sodium chloride solution, and dried over magnesium
sulfate. The solvent was evaporated and the resulting brown crystals
were recrystallized from ether-petroleum ether. White crystals of 7-
methoxy-2-tetralone weighing 18.5 g. were obtained, m.p. 26-27°C. The
remaining dark oil was distilled under reduced pressure and yielded
another 68.1 g. of the desired product, b.p. 98-110°C/0.03 mm Hg pressure,
(lit.35: b.p. 123-124°C/0.25 mm) for a total yield of 86.6 g. (91%).

Preparation of 1-Methyl-7-methoxy-2-tetralone (46). A solution of
50 g. of 7-methoxy-2-tetralone (45) in 500 ml. of benzene was refluxed
with 105 ml. of freshly distilled pyrrolidine in the presence of a catalytic amount of p-toluenesulfonic acid. The reaction was allowed to proceed over night under a water separator. Most of the solvent was removed under vacuum and 400 ml. of oxygen-free methanol was added. The solution was cooled below room temperature and 65 ml. of methyl iodide was added. After refluxing for 45 minutes and cooling, an additional 200 ml. of methyl iodide was added and the mixture refluxed for one hour. Most of the solvent was removed under vacuum and a solution of 105 g. of sodium acetate, 105 ml. of acetic acid, and 210 ml. of water (pH 5) was added along with enough methanol to give a homogeneous solution. After a one hour reflux period the solvent was removed under vacuum. Water and ether were added and the aqueous layer was extracted several times with ether. The combined organic layers were washed with dilute sodium hydroxide until the aqueous layer was no longer blue. The ether solution was then washed with water until neutral and after washing with saturated sodium chloride solution, was finally dried over magnesium sulfate. The ether was removed, and the remaining viscous oil was distilled under reduced pressure; yield 45 g. (85%), b.p. 98-110°C/0.04 mm. (Lit.\textsuperscript{36}: 125-126°C/0.8 mm).

**Preparation of 2-Keto-12-methyl-6-methoxy-2,3,4,9,10,12-hexahydrophenanthrene** (47). In a one liter flask 17.38 g. of diethyl aminobutanone-2\textsuperscript{37} was cooled to 0°C. Methyl iodide (17.3 g.) was added slowly with simultaneous swirling of the flask so that the quaternary ammonium salt deposited as a white salt on the walls of the flask. This addition
was carried out under a nitrogen atmosphere. The flask was allowed to stand in the ice bath an additional half hour under a rapid flow of nitrogen. The flask was then allowed to warm to room temperature. A solution of 1-methyl-2-tetralone (23.1 g.) in 100 ml. of dry benzene was added. The flask was cooled in an ice bath, and a solution of 7.5 g. of potassium in 100 ml. of ethanol was added over a five minute period while the flask was swirled. The swirling was continued until the ammonium salt had all dissolved and been replaced by a precipitate of potassium iodide. The reaction was kept at 0°C for an additional hour with occasional swirling and was then refluxed gently for twenty-five minutes. The solution was acidified with 2 N sulfuric acid. The flask was then washed with water and ether, and the organic layer separated and washed with water and saturated sodium chloride solution and dried over anhydrous sodium sulfate. The resulting dark oil was distilled under reduced pressure, b.p. 165-180°C/0.11mm, (Lit.39: b.p. 115-120°C/0.0004mm), to yield 11.8 g. (40%) of the desired product. On seeding the oil crystallized, m.p. 70-72°C (Lit.39: m.p. 73°C).

Preparation of 1,1,12-Trimethyl-2-keto-6-methoxy-1,2,3,4,9,12-hexahydrophenanthrene (48). Compound (47) was methylated by the Woodward-Patchett procedure.40 A solution of 10.0 g. of compound (47) in 150 ml. of dry t-butanol was prepared. To it was added a solution of 4.9 g. of potassium in 150 ml. of dry t-butanol. Methyl iodide (17 ml.) was added immediately, and the reaction stirred at room temperature under dry purified nitrogen for 2 hours. At the end of this time dilute
(10%) sulfuric acid was added with enough water to dissolve the potassium sulfate and potassium iodide that had precipitated. Ether was then added, and the organic layer was washed with dilute sodium hydroxide followed by several washings with large quantities of water. After drying, the solvent was evaporated. No attempt was made to purify the crude yellow oil, but instead it was carried directly to the next step.

\[
\lambda_{\text{CH}_2\text{Cl}_2}^{\text{max}}: 3.4-3.6, 5.84\mu.
\]

Preparation of 1,1,12-Trimethyl-2-hydroxy-6-methoxy-1,2,3,4,9,12-hexahydrophenanthrene (49). The yellow oil obtained above was dissolved in 200 ml. of absolute ether and was added dropwise to a stirred suspension of 10.4 g. of lithium aluminum hydride in 200 ml. of absolute ether. The solution was stirred for one hour at the end of which time the remaining lithium aluminum hydride was destroyed. After separating and washing the organic layer, it was dried and the solvent evaporated. Upon standing crystallization set in. A total of 5.85 g. of crystalline material was obtained, m.p. 117-118°C, (Lit. \(^41\): m.p. 120-121°C) for an overall yield of 52% for the two reactions.

Preparation of 1,1,12-Trimethyl-2-hydroxy-6-methoxy-1,2,3,4,9,10, 11,12-octahydrophenanthrene (50). The unsaturated alcohol (49) (1.00 g.) was dissolved in 30 ml. of glacial acetic acid and 500 mg. of 10% palladium-on-charcoal was added. The mixture was stirred in a hydrogen atmosphere and when the uptake of hydrogen had nearly ceased the palladium was filtered off and most of the acetic acid evaporated under vacuum. Ether
was then added, and the organic layer was washed with dilute sodium
hydroxide until the wash water was basic. It was then washed with water
and saturated sodium chloride solution and dried over anhydrous magnesium
sulfate. The solvent was then evaporated, and the resulting oil was
crystallized from ether-petroleum ether yielding 650 mg. (65%) of white
crystals, m.p. 110-110.5°C.

$\lambda_{\text{max}}^\text{CS}_2: 2.79, 3.4-3.5, 5.81 \mu$

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.78; H, 9.55.

Found: C, 79.00; H, 9.54.

The tosylate (51) of the alcohol (50) was prepared by standard methods
from pyridine and $p$-toluensulfonfyl chloride, m.p. 132-134°C (with some
decomposition).

**Preparation of 1,1,12-Trimethyl-2-hydroxy-6-methoxy-1,2,3,4,5,8,9,
10,11,12-decahydrophenanthrene (53).** A solution of 1.49 g. of compound
(50) in 100 ml. of absolute ether, 24 ml. of dry ethanol, and 300 ml. of
distilled liquid ammonia was treated with lithium metal, added in portions,
so that the solution remained blue a total of 45 minutes. The ammonia
was then allowed to evaporate under a nitrogen atmosphere. Ice water
and ether were added to the remaining mass until solution was complete.
The ether layer was separated and the water layer was extracted several
times with ether. The combined ether layers were then washed with cold
water until neutral. The ether layer was then washed with saturated sodium
chloride solution and dried over anhydrous sodium sulfate. Upon evapora-
tion of the solvent, crystals appeared. On recrystallization from ether-
petroleum ether 1.16 g. (78%) of (53) was obtained, m.p. 142-143°C.
\( \lambda_{\text{max}}^\text{CH}_2\text{Cl}_2: \) 2.81, 5.90 (medium), 6.01 (weak), 9.70 \( \mu \).

**Anal.** Calcd. for \( \text{C}_{15}\text{H}_{28}\text{O}_2 \): C, 78.21; H, 10.21.

Found: C, 78.39; H, 10.22.

Preparation of 1,1,12-Trimethyl-2-hydroxy-6-keto-1,2,3,4,5,6,7,8, 2,10,11,12-dodecahydrophenanthrene (54). A solution of 200 mg. of compound (53) in 16 ml. of 95% ethanol was prepared. The solution was stirred at room temperature under nitrogen, and 750 mg. of oxalic acid dihydrate was added. After 1.5 hours the reaction mixture was poured into ice water and the aqueous layer was extracted several times with ether. The combined organic layers were washed with cold dilute sodium hydroxide followed by several washings with water. The ether layer was finally washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. After evaporation of the solvent the resulting oil was crystallized from ether-petroleum ether. A yield of 125 mg. (69%), m.p. 135-136°C, of the \( \beta,\gamma \)-unsaturated ketone was obtained.

\( \lambda_{\text{max}}^{\text{CSO}}: \) 2.79, 3.4-3.5, 5.81 \( \mu \).

**Anal.** Calcd. for \( \text{C}_{17}\text{H}_{26}\text{O}_2 \): C, 77.82; H, 9.99.

Found: C, 77.94; H, 10.06.

Preparation of 1,1,12-Trimethyl-2-hydroxy-6-keto-1,2,3,4,5,6,7,8, 10,11,12,14-dodecahydrophenanthrene (55a). The \( \beta,\gamma \)-unsaturated ketone (100 mg.) was dissolved in 6.25 ml. of 95% ethanol and heated to 54°C. Sodium hydroxide (1 ml. of 1 N) was added and the reaction was held between 54°C and 56°C for 17 minutes under nitrogen. The reaction mixture
was then poured into ice and extracted with ether and methylene chloride. The organic solution was washed with water and saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the resulting product was crystallized from ether-petroleum ether and yielded 59.6 mg. (59.6%) of a crystalline compound, m.p. 160.5-161°C.

\[ \lambda_{\text{max}}^\text{CH}_2\text{Cl}_2: 2.79, 5.98, 6.21 \mu. \]

**Anal.** Calcd. for C\(_{17}\)H\(_{26}\)O\(_2\): C, 77.82; H, 9.99.

**Found:** C, 77.65; H, 9.94.

**Preparation of the Acetate of (55a).** The \(\alpha,\beta\)-unsaturated ketone (55a) (25.8 mg.) was dissolved in 4 ml. of dry pyridine and 1 ml. of acetic anhydride was added. The reaction mixture was stirred for 14 hours at room temperature. The solution was then poured into ice water and extracted with ether. The ether layer was washed with cold dilute sodium hydroxide followed by water and saturated sodium chloride solution. The solution was dried over anhydrous magnesium sulfate, and the solvent was evaporated, which operations yielded 24.2 mg. (81%) of the crystalline acetate, m.p. 139.5-140°C.

\[ \lambda_{\text{max}}^\text{CH}_2\text{Cl}_2: 5.78, 5.99, 6.21 \mu. \]

**Anal.** Calcd. for C\(_{19}\)H\(_{28}\)O\(_3\): C, 74.96; H, 9.27.

**Found:** C, 75.21; H, 9.48.

**Preparation of 1-Keto-5,5,9-trimethyl-6-acetoxy-decahydrodronaphthyl-2-(2-propanic acid) (56).** The \(\alpha,\beta\)-unsaturated keto acetate (55b) (87.3 mg.) was dissolved in a 1:1 mixture of acetic acid and ethyl acetate.
Ozone (3.25 equivalents) was slowly bubbled through the solution. Water (1 ml.) and 30% hydrogen peroxide (0.1 ml.) was added. The reaction was then allowed to stand for 24 hours in the hood. At the end of this time the reaction was poured into ice water. Ether and dilute base were added. The aqueous layer was separated, acidified, and extracted with ether. The organic solution was washed with water and saturated sodium chloride solution and was dried over anhydrous magnesium sulfate. The solvent was evaporated and 83.7 mg. (90%) of crystalline material were obtained, which was recrystallized from ether-petroleum ether, m.p. 137.5-138°C.

\[ \lambda_{\text{max}}^{\text{CH}_2\text{Cl}_2}: 2.72, 2.89, 3.1-3.6, 5.68(\text{sh}), 5.78, 5.86\mu. \]

**Anal.** Calcd. for C_{18}H_{25}O_5: C, 66.64; H, 8.70.

Found: C, 66.81; H, 8.71.

**Attempted Alkylation of Compound (56).** Freshly distilled allyl bromide (1 ml.) was added to a solution of 50 mg. of the keto acid (56) in 2.5 ml. of dry t-butanol containing 51 mg. of potassium. The solution was protected from light and was stirred under nitrogen at room temperature for 4 hours. The solution was then poured into cold dilute sodium hydroxide solution. The aqueous layer was extracted with ether and acidified. The acidified aqueous layer was then extracted with ether. The ether layer was washed with water and saturated sodium chloride solution and dried over magnesium sulfate. Upon evaporation of the solvent an intractable oil was obtained that yielded no identifiable product on chromatography.
Preparation of 1,1,12-Trimethyl-2-hydroxy-6-methoxy-1,2,3,4,7,8,9,10,11,12-decahydrophenanthrone (61). The enol ether (53) (200 mg.) was dissolved in 5 ml. of dimethyl sulfoxide and 150 mg. of sublimed potassium tert-butoxide was added. The solution was stirred at room temperature under nitrogen. Small samples were removed at about 3 hour intervals. The ultraviolet spectrum was taken, and at the end of 13.5 hours the \( \lambda_{\text{max}} \) 270\text{nm} reached an \( \varepsilon = 4770 \). The entire solution was then poured into ether, acidified and washed with cold water and saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The crude material was used directly in the next experiment.

Attempted Preparation of (62). The crude product from the above experiment was dissolved in 30 ml. of methyl vinyl ketone to which 26 mg. of methylene blue had been added. The mixture was heated in an autoclave at 140-150\textdegree C for 11 hours. The mixture was dissolved in ether and extracted with water (to remove the methylene blue), washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. After evaporation of the solvent the crude material was chromatographed. No material corresponding to (62) could be identified.

Preparation of Compound (64). The crude mixture of enol ethers (53) and (61) (200 mg.) was dissolved in 2 ml. of dry acetic anhydride and 0.8 ml. of dry pyridine. After standing at room temperature for 20 hours, ice water and ether were added. The ether solution was washed several times with water and dried, m.p. 161.5-163.5\textdegree C.
Anal. Calcd. for C$_{20}$H$_{30}$O$_{3}$: C, 75.43; H, 9.50.

Found: C, 75.73; H, 9.03.

Attempted Preparation of Compound (65). The crude material from the preceding experiment and 80 mg. of sublimed maleic anhydride were dissolved in 7 ml. of dry xylene and stirred at room temperature for 8 hours and heated to 135-145° C for 8 hours. The solvent was evaporated under vacuum. A small amount of ether was added to the oily residue, and after standing overnight in the cold, a small amount of crystalline material was obtained, m.p. 208-235° C.

Preparation of the Acetate of (53). A solution of 633 mg. of compound (53) in 1.2 ml. of dry pyridine was treated with 3 ml. of acetic anhydride. The solution was protected from light and stirred under a nitrogen atmosphere for 21 hours. The solution was then poured into ice water-ether, and dilute sodium hydroxide was added. The ether layer was separated, and the water layer was extracted with ether. The combined ether layers were washed with ice water and saturated sodium chloride solution and dried over anhydrous sodium sulfate. On crystallization 561 mg. (77%) of the desired compound was obtained, m.p. 152-153° C.

$\lambda_{\text{max}}^{\text{CHCl}_3}$: 5.80 (strong), 5.90 (medium), 6.01 (weak), 9.71 μ.

Anal. Calcd. for C$_{20}$H$_{30}$O$_{3}$: C, 75.43; H, 9.50.

Found: C, 75.37; H, 9.46.

Preparation of Compound (68). To a solution of 206 mg. of the above compound in 8 ml. of absolute ether, 0.2 ml. of dry methanol was added.
The resulting solution was cooled to 0°C. A catalytic amount of p-toluenesulfonic acid monohydrate was added. The solution was kept at 0°C for 2 hours and was then refluxed for 30 minutes. The solution was then poured into cold dilute sodium bicarbonate solution and shaken well. The ether layer was then washed with water and saturated sodium chloride solution and dried over sodium sulfate. Crystallization from ether-petroleum ether yielded 165 mg. of compound (68) (75%), m.p. 120-121°C.

\[
\lambda_{\text{max}}: 5.80, 8.94, 9.50, 9.70\mu.
\]

Anal. Calcd. for C\textsubscript{21}H\textsubscript{34}O\textsubscript{4}: C, 71.96; H, 9.78.

Found: C, 71.95; H, 9.70.

Preparation of 2,5-Dihydroanisole (57). A solution of 100 g. of anisole (0.93 moles), 100 ml. of absolute ether, and 200 ml. of dry ethanol was prepared. The solution was cooled in a dry ice-acetone bath and to it was added 550 ml. of liquid ammonia. Lithium metal was added slowly until a blue color persisted for a total of 45 minutes. At the end of this time ammonium chloride was added until the blue color disappeared. The ammonia was then allowed to evaporate and 1.5 liters of cold water was added. The water layer was extracted several times with ether. The ether layer was then washed repeatedly with cold water until neutral, followed by saturated sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate.

\[
\lambda_{\text{max}}: 5.91, 6.04, 10.42\mu.
\]

Preparation of 1,1-Dimethoxy-3-cyclohexene (71). The dried ethereal enol ether solution from the above experiment (approx. 800 ml.) was added
to 125 ml. of dry methanol and a catalytic amount of p-toluenesulfonic acid monohydrate. The solution was stirred at room temperature for 8 hours and was refluxed for an additional 8 hours under nitrogen. At the end of this time it was washed with cold concentrated sodium bicarbonate solution, ice water, and saturated sodium chloride and dried over sodium sulfate. The solvent was evaporated carefully through a Vigreux column. The clear product was then purified by vapor phase chromatography (automatic injection) with a yield of 71% for the two reactions (93.4 g.).

\( \lambda_{\text{max}} \) : 8.85, 8.95, 9.43, 9.55 \( \mu \).

NMR in CDCl\(_3\):

- \( \delta \) (ppm) 5.53 multiplet (2H)
- \( \delta \) (ppm) 3.11 singlet (6H)
- \( \delta \) (ppm) 1.5-2.2 multiplet (6H)


Found C, 67.52; H, 9.87.

**Preparation of Ethyl 7-Norcaran-4,4-dimethoxy Carboxylate (72).**

Approximately 6.7 g. of the unsaturated ketal was heated between 120° and 130°C, and a solution of 13.5 g. of ethyl diazoacetate and 6.7 g. of the unsaturated ketal was added dropwise over a 7 hour period. It was then heated for an additional 2 hours and the resulting dark oil was distilled. No attempt was made to recover the starting material, but 9.86 g. of the ketal ester was obtained, b.p. 95-105°C at 0.05-0.06 mm., which was shown by vapor phase chromatography to be 83% pure, for a total
yield of 43%.

$\lambda_{\text{max}}^\text{Film}$: 5.78μ.

NMR in CCl₄

$\delta$ (ppm) 4.05  quartet  (2H)
$\delta$ (ppm) 3.07  singlet  (5H)
$\delta$ (ppm) 2.2-1.4  multiplet  (9H)
$\delta$ (ppm) 1.21  triplet  (3H)

Found:  C, 63.63; H, 8.75.

Isomeric Mixture (73). Vapor phase chromatography of compound (72) yielded two peaks with retention time of 41 and 58.5 minutes at 200°C.
The latter peak was found to be compound (72). The former peak, however, was found to be the isomeric mixture (73).

$\lambda_{\text{max}}^\text{Film}$: 5.78, 5.93, 6.0μ; $\lambda_{\text{max}}^{\text{EtOH}}$: 225μ, ε =1770.

NMR in CCl₄

$\delta$ (ppm) 4.92-4.41  multiplet  (1H)
$\delta$ (ppm) 4.15  quartet  (2H)
$\delta$ (ppm) 3.48  singlet  (3H)
$\delta$ (ppm) 2.67-1.44  multiplet  (7H)
$\delta$ (ppm) 1.25  triplet  (3H)

Found:  C, 67.34; H, 8.20.

Preparation of Ethyl 7-Norcaran-4-one Carboxylate (74). To a solution of 6.00 g. of the ketal ester (72) and 300 ml. of acetone was added
1 g. of p-toluenesulfonic acid monohydrate. The solution was stirred at room temperature for 18 hours. At the end of this time the solution was added to 300 ml. of dilute cold sodium bicarbonate solution and 100 ml. of ether. The organic layer was separated and the aqueous layer was extracted several times with small portions of ether. The combined organic layers were washed three times with cold water and once with saturated sodium chloride solution and dried over magnesium sulfate. Evaporation of the solvent yielded 6.02 g. of crude material which proved to be 75% pure by vapor phase chromatography, for a total yield of 94%.

$\lambda_{\text{film}}^{\text{max.}}$: 5.78, 5.83 µ.

**Anal. Calcd. for C_{10}H_{14}O_{3}:**  C, 65.91; H, 7.74.

**Found:**  
  C, 65.97; H, 7.77.

The 2,4-dinitrophenylhydrazone prepared as a derivative melted at 129-132°C, on crystallization from 95% ethanol.

**Anal. Calcd. for C_{16}H_{18}O_{6}N_{4}:**  C, 53.03; H, 5.01; N, 15.46.

**Found:**  
  C, 53.01; H, 5.03; N, 15.50.

**Preparation of Ethyl (2-Cyclohexene-4-one) Acetate (75).** A solution of 3.72 g. of the unsaturated keto ester was dissolved in 125 ml. of dry benzene. A small quantity of p-toluenesulfonic acid monohydrate was added, and the solution refluxed for 8 hours. It was then cooled and poured into dilute sodium bicarbonate solution and ether. The organic layer was washed with cold water, saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. After evaporation of most of the solvent, 4.34 g. of a clear liquid remained. Vapor phase chromatography
indicated this to be 80% pure, for a total yield of 94%.

\[ \lambda_{\text{max}}: 5.78, 5.92 \mu. \]

**Anal.** Calcd. for C<sub>10</sub>H<sub>14</sub>O<sub>3</sub>: C, 65.91; H, 7.74.

**Found:** C, 65.92; H, 7.61.

**Preparation of p-Hydroxyphenylacetic Acid Ethyl Ester** (76a). The unsaturated keto ester (300 mg.) was dissolved in 1 ml. of xylene and 300 mg. of 10% palladium-on-charcoal was added. The reaction mixture was heated for 5 hours in an oil bath at 180°C. After cooling, ether was added, and the catalyst was removed by filtration. The ether solution was extracted with 2 N sodium hydroxide to remove the phenol. The aqueous layer was acidified and extracted with ether. The organic layer was washed with water and saturated sodium chloride solution and dried over magnesium sulfate. Upon evaporation of the solvent 55 mg. of crude material were obtained.

**Preparation of p-Hydroxyphenyl Acetic Acid** (76b). The crude ester from the above experiment was dissolved in 1.5 ml. of 10% potassium hydroxide and refluxed for 50 minutes. The reaction mixture was cooled and 1 ml. of concentrated hydrochloric acid was added. The reaction mixture was then extracted with ether and the organic layer was washed with water and saturated sodium chloride solution and dried over magnesium sulfate. Upon evaporation 27 mg. of crystalline material were obtained that sublimed at 115°C and 0.01 mm of Hg pressure. The resulting crystals were recrystallized from ether-petroleum ether and melted at 153-154.5°C and
demonstrated no depression upon mixed melting with an authentic sample, whose infrared spectrum was identical.

**Preparation of 2,5-Dihydro-4-methylanisole (77).** A solution containing 60 g. of \( p \)-methylanisole, 200 ml. of absolute ether, 140 ml. of dry ethanol and 600 ml. of distilled dry liquid ammonia was prepared. Lithium metal was added, and the solution was kept blue for a total of 45 minutes. The ammonia was then allowed to evaporate. Ice water was added until solution was complete. The aqueous solution was extracted several times with ether, and the combined ether layers were washed with water until neutral and then with saturated sodium chloride solution and dried over anhydrous sodium sulfate.

\[ \lambda_{\text{max}}^{\text{film}}: \quad 5.91, 6.00, 6.85, 6.97, 7.24, 7.33, 8.26, 8.55, 8.70, 9.34, 9.62, 9.95, 10.47, 10.74, 12.98, 14.31 \mu. \]

**Preparation of 1-Methyl-4,4-dimethoxycyclohexene (78).** The crude material from the above reaction, after evaporation of the solvent, was dissolved in 800 ml. of absolute ether. Dry methanol (80 ml.) was added, and the solution was cooled to 0°C. A catalytic amount of \( p \)-toluenesulfonic acid was added. The solution was kept cold for 2 hours and was refluxed for a total of 1.5 hours. The solution was poured into cold dilute sodium bicarbonate solution and was washed several times with water and finally with saturated sodium chloride solution. After drying over anhydrous sodium sulfate, the solvent was evaporated, and the resulting oil distilled on a spinning band column under reduced pressure; yield
39.3 g. (52%), b.p. 82-84°C/20-21 mm.

λ\text{Film max.}: 3.42-3.68, 6.9-7.1, 7.45, 8.02, 8.62, 8.92, 9.36, 9.50, 9.79, 10.04, 11.80, 12.52 μ.

NMR in CCl₄

δ (ppm) 5.23  broad singlet (1H)
δ (ppm) 3.15  singlet (6H)
δ (ppm) 2.23-1.55  multiplet (9H)

Found: C, 69.23; H, 10.15.

Preparation of Ethyl i-Methyl-4,4-dimethoxynorcaran-7-carboxylate (79). The unsaturated ketal (78) (14.8 g.) was heated to 120°C and 11.4 g. of ethyl diazoacetate was added dropwise in the presence of copper-bronze powder. The resulting dark oil was distilled. The distillation yielded 4.65 g. of starting material and 10.36 g. (66% based on recovered starting material) of the desired product, b.p. 78-79°C/0.007 mm.

λ\text{Film max.}: 3.4-3.6, 5.77, 6.80-7.00, 7.22, 7.47, 7.63, 7.90, 8.00, 8.20, 8.50, 8.80, 9.10, 9.42, 10.15, 10.85, 11.61, 11.78 μ.

NMR in CCl₄

δ (ppm) 4.12  quartet (2H)
δ (ppm) 3.12  singlet (6H)
δ (ppm) 2.23-1.45  multiplet (8H)
δ (ppm) 1.21  triplet (3H)
δ (ppm) 1.19  singlet (3H)
Anal. Calcd. for $\text{C}_{17}\text{H}_{22}\text{O}_4$: C, 64.34; H, 9.15.

Found: C, 64.31; H, 8.90.

**Preparation of Ethyl 1-Methyl-4-keto-norcaran-7-carboxylate (80).**

To a solution of 6.33 g. of the ketal ester in 250 ml. of dry acetone was added a catalytic amount of $p$-toluenesulfonic acid. After stirring for 16 hours, the solution was poured into cold dilute sodium bicarbonate solution and ether. After separation, the aqueous layer was extracted several times with ether. The combined organic extracts were then washed with water and saturated sodium chloride solution. The solution was dried over anhydrous sodium sulfate, and the solvent was evaporated. A light yellow oil was obtained (5.3 g.), which, by vapor phase chromatography, was shown to be 81% of the desired compound, thus an overall yield of 84% was obtained.

$\lambda_{\text{film}}^\text{max.}$: 3.3, 3.5, 5.78, 5.82 $\mu$.


Found: C, 67.00; H, 8.16.

**Preparation of the Isomeric Mixture (82).** The keto ester (80) (5.0 g.) was dissolved in 150 ml. of dry benzene. A catalytic amount of $p$-toluenesulfonic acid was added, and the solution was refluxed for 15 hours. On cooling, the solution was poured into cold dilute sodium bicarbonate solution and extracted with ether. The ether solution was washed with water and saturated sodium chloride solution and was dried over anhydrous magnesium sulfate and evaporated. The resulting oil gave
only one peak on vapor phase chromatography.

\[ \lambda_{\text{max}}^{\text{Film}} : 5.78, 5.82, 5.87, 5.92 \mu \).

NMR in CCl₄

\[
\begin{align*}
\delta (\text{ppm}) & \quad \text{multiplet} \\
6.79 & \quad \text{doublet} \\
5.77 & \quad \text{quartet} \\
4.08 & \quad \text{singlet} \\
2.6-1.6 & \quad (6.6H) \\
1.28 & \quad \text{triplet} \\
1.22 & \quad \text{singlet} \\
\end{align*}
\]


Found: C, 67.13; H, 8.12.

Preparation of Ethyl (1-Methyl-cyclohex-2-en-4-one) Acetate (81).

A solution containing 1.00 g. of the keto ester (80), a catalytic amount of sodium acetate, and 40 ml. of dry ethanol was refluxed under nitrogen for 5 hours. The solution, after cooling, was poured into cold water and extracted several times with ether. The ether layer was washed with water, saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated leaving 0.87 g. of a yellow oil which was found to be 97% pure by vapor phase chromatography, thus an overall yield of 87% was obtained.

\[ \lambda_{\text{max}}^{\text{Film}} : 5.78, 5.92 \mu \).

NMR in CCl₄

\[
\begin{align*}
\delta (\text{ppm}) & \quad \text{broad doublet} \\
6.82 & \quad (1H) \\
5.80 & \quad (1H) \\
\end{align*}
\]
δ (ppm) 4.16 quartet (2H)
δ (ppm) 2.6-1.6 multiplet (6H)
δ (ppm) 1.29 singlet & triplet (6H)

Anal. Calcd. for C_{11}H_{16}O_3:  C, 67.32; H, 8.22.
Found: C, 66.61; H, 7.92.

The 2,4-dinitrophenylhydrazone prepared as a derivative melted at
116-117.5°C on crystallization from 95% ethanol.

Anal. Calcd. for C_{17}H_{20}O_6N_4:  C, 54.25; H, 5.26; N, 14.89.
Found: C, 54.07; H, 5.52; N, 15.09.

Preparation of 2,5-Dihydro-3,4-dimethylanisole (85). A solution
of 26 g. of 3,4-dimethylanisole (84) (b.p. 91-93°C/19 mm) in 150 ml. of
absolute ether and 60 ml. of dry ethanol was cooled in a dry ice-acetone
bath and 700 ml. of distilled liquid ammonia was added. Lithium metal was
added to the solution in such a way that the solution remained blue for a
total of 45 minutes. The ammonia was then allowed to evaporate and ice
water was added to the white solid residue until solution was complete.
The ether was separated and the aqueous solution was extracted several
times with ether. The combined organic layers were washed with water
until neutral and then with saturated sodium chloride solution and dried
over anhydrous sodium sulfate. The solvent was carefully evaporated and
the resulting colorless liquid was used in the next reaction.

λ_{max}^* Film: 5.85 (medium), 5.96 (strong), 6.79, 6.80, 7.15, 7.25, 8.07,
8.20, 8.43, 8.71, 8.90, 9.44, 9.76, 11.12, 12.71, 14.91µ.
Preparation of 4,4-Dimethoxy-1,2-dimethylcyclohexene (86). The crude product from the preceding reaction was dissolved in 350 ml. of absolute ether and 35 ml. of dry methanol. The solution was cooled to 0°C, and a catalytic amount of p-toluenesulfonic acid monohydrate was added. The reaction was allowed to stand for 2 hours at 0°C. It was then refluxed for 30 minutes and cooled and a portion taken out. After work up, an infrared spectrum was taken and the decrease in the peaks at 5.85 and 5.96μ was noted. The 30 minute reflux period was continued again until these two peaks had disappeared. The ether solution was then washed with cold dilute sodium bicarbonate solution and then with water and saturated sodium chloride solution. The solution was dried over anhydrous sodium sulfate and the solvent carefully evaporated. The resulting liquid was then distilled under reduced pressure; yield 25.5 g. (78%), b.p. 70-71°C/7mm.

\[
\lambda_{\text{max}} \quad \text{Film}: \quad 6.90, 7.11, 7.31, 7.50, 7.76, 7.90, 8.08, 8.18, 8.40, 8.49, 8.62, 9.16, 9.26, 9.44, 9.71, 10.12, 10.78, 10.92, 11.39, 11.90, 13.48, 14.20, 15.50\mu.
\]

NMR in CCl₄

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NMR in CCl₄

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Anal. Calcd. for $\text{C}_{10}\text{H}_{18}\text{O}_2$: C, 70.54; H, 10.66.

Found: C, 70.67; H, 10.64.

Preparation of Ethyl 1,2-Dimethyl-4,4-dimethoxy-7-norcarancarboxylate (82). A flask containing 11.5 g. of the unsaturated ketal (86) was heated in the presence of copper-bronze powder between 125° and 135°C while 16.7 g. of ethyl diazoacetate was added dropwise. When the evolution of nitrogen was complete the flask was allowed to cool, and the crude dark oil was distilled under vacuum. The distillation yielded 2.3 g. of starting material and 10.2 g. of compound (87) (78% based on recovered starting material), b.p. 76-96°C/0.02-0.05 mm.

$\lambda_{\text{max}}$: 5.78 μ.

NMR in $\text{CCl}_4$

$\delta$(ppm) 4.05 quartet (2H)

$\delta$(ppm) 3.12 & 3.09 singlets (6H)

$\delta$(ppm) 1.32-1.00 multiplet (16H)

$\delta$(ppm) 1.24 singlet & triplet

Anal. Calcd. for $\text{C}_{14}\text{H}_{24}\text{O}_4$: C, 65.59; H, 9.44.

Found: C, 65.62; H, 9.25.

Preparation of Ethyl 7-Norcaran-4-one-1,2-dimethylcarboxylate (88). A solution of 1.8 g. of the ketal ester (87) was dissolved in 90 ml. of dry acetone and was treated with a catalytic amount of $\text{n}$-toluenesulfonic acid monohydrate. The solution was protected from light and was stirred under a nitrogen atmosphere at room temperature for 17 hours. The solvent
was evaporated under reduced pressure at room temperature. Ether was added, and the solution poured into cold dilute sodium bicarbonate solution and shaken. After separation of the basic solution, the organic layer was washed with cold water followed by saturated sodium chloride solution. The ether solution was dried over anhydrous sodium sulfate, and the solvent was evaporated. Attempted purification of this crude material by vapor phase chromatography resulted in partial decomposition on an SE-30 column, thus an exact determination of the yield of this reaction was not possible.

\[ \lambda_{\text{Film max.}}: 5.78, 5.81\mu. \]

NMR in \( \text{CCl}_4 \)

\[ \delta (\text{ppm}) \quad 4.05 \quad \text{quartet} \quad (2\text{H}) \]
\[ \delta (\text{ppm}) \quad 2.45 \& 2.12 \quad \text{broad singlets} \quad (6\text{H}) \]
\[ \delta (\text{ppm}) \quad 1.32 \quad \text{triplet} \]
\[ \delta (\text{ppm}) \quad 1.26 \quad \text{singlet} \quad (10\text{H}) \]
\[ \delta (\text{ppm}) \quad 1.11 \quad \text{singlet} \]

**Anal. Calcd. for \( \text{C}_{12}\text{H}_{18}\text{O}_3 \):** C, 68.54; H, 8.63.

**Found:** C, 68.86; H, 8.41.

**Preparation of Ethyl (1,2-Dimethylcyclohex-2-en-4-one) Acetate (89).**

The crude material from the above reaction (1.37 g.) was dissolved in 50 mL. of dry ethanol and a catalytic amount of \( p \)-toluenesulfonic acid monohydrate was added. The solution was refluxed for 3 hours under a nitrogen atmosphere. Most of the solvent was evaporated under reduced pressure, and ether was added. The organic solution was washed with water and
saturated sodium chloride solution and dried over anhydrous sodium sulfate. Upon evaporation of the solvent 1.24 g. of crude material was obtained. The vapor phase chromatography of this material indicated that 75% was the desired material, thus an over all yield for the two reactions was 63%.

Film 
A. max.: 5.78, 5.99, 6.25µ.

NMR in CCl₄

δ(ppm) 5.65  broad singlet  (1H)
δ(ppm) 4.08  quartet   (2H)
δ(ppm) 2.45 & 2.28 broad singlets (6H)
δ(ppm) 1.90  singlet  (3H)
δ(ppm) 1.22  singlet & triplet (6H)

Anal. Calcd. for C₁₂H₁₈O₃:  C, 68.54; H, 8.63.
Found:    C, 68.41; H, 8.66.
The 2,4-dinitrophenylhydrazone prepared as a derivative melted at 119.5-120°C on crystallization from 95% ethanol.

Found:    C, 55.21; H, 5.91; N, 14.42.

Preparation of Compound (90). A solution containing 44.4 g. of 1-methyl-7-methoxy-2-tetralone, 500 ml. of benzene, 100 ml. of ethylene glycol, and a catalytic amount of p-toluenesulfonic acid was refluxed for 6 hours with a Barrett distillation receiver. After cooling to room temperature, dilute sodium hydroxide, ether, and water were added. The aqueous layer was separated and washed with ether. The combined organic layers were washed with water, saturated sodium chloride solution and
dried over anhydrous magnesium sulfate. The product crystallized on evaporation of the solvent. The crystals were sublimed (65°C/0.004 mm Hg) and recrystallized from ether-petroleum ether, m.p. 73.5-74°C.

$\lambda_{\text{max}}^\text{film}$: 3.5-3.6, 6.22, 6.28, 6.39, 6.7-7.0, 7.32, 7.54, 7.65, 7.78, 8.00, 8.21, 8.51, 8.93, 9.08, 9.30, 9.44, 9.61, 9.96, 10.57, 10.92, 11.06, 11.58, 11.98, 12.27, 12.85, 13.35, 14.28, 14.82 µ.

NMR in CCl₄

\begin{align*}
\delta (\text{ppm}) & \quad 6.92-6.40 & \text{multiplet} & (3\text{H}) \\
\delta (\text{ppm}) & \quad 3.81 & \text{singlet} & (4\text{H}) \\
\delta (\text{ppm}) & \quad 3.62 & \text{singlet} & (3\text{H}) \\
\delta (\text{ppm}) & \quad 2.79 & \text{broad triplet} & (3\text{H}) \\
\delta (\text{ppm}) & \quad 2.0-1.6 & \text{multiplet} & (2\text{H}) \\
\delta (\text{ppm}) & \quad 1.10 & \text{doublet} & (3\text{H})
\end{align*}

\textbf{Anal. Calcd. for } C_{14}H_{18}O_{3}: \quad C, 71.77; \text{ H, 7.74.}

\text{Found:} \quad C, 71.89; \text{ H, 7.69.}

\textbf{Preparation of Compound (91). } Lithium metal was added to a solution containing 1.00 g. of the aromatic ketal (90), 20 ml. of dry ethanol, 60 ml. of absolute ether, and 120 ml. of liquid ammonia in such a manner that the solution was kept blue for a total of 45 minutes. The ammonia was then allowed to evaporate. Water and ether were added and the aqueous layer was separated and extracted several times with ether. The combined organic layers were washed with water until neutral and dried over anhydrous sodium sulfate. The crude oil resisted all attempts at crystallization.
\[ \lambda_{\text{max}}^\text{Film}: \ 5.87, 5.96\mu. \]

NMR in CCl₄

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<td>(9H)</td>
</tr>
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<td>1.00</td>
<td>doublet</td>
<td>(3H)</td>
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</tbody>
</table>

**Preparation of Compound (92).** The crude enol ether (91) from the above experiment was dissolved in 50 ml. of absolute ether and 2 ml. of dry methanol. The solution was cooled to 0°C and a catalytic amount of p-toluenesulfonic acid was added. The solution was kept cold for 4 hours and refluxed for 30 minutes. After cooling, the ether solution was washed with cold dilute sodium bicarbonate solution, water, and saturated sodium chloride solution. The ether layer was dried over anhydrous sodium sulfate and the solvent was evaporated. The crude material was distilled, b.p. 98-111°C/0.01 mm Hg, and yielded 1.08 g. (95%) of compound (92).

\[ \lambda_{\text{max}}^\text{Film}: \ 3.4-3.6, 6.8-7.0, 7.28, 7.30, 8.29, 8.50, 8.60, 8.90, 9.13, 9.78, 10.57, 10.79\mu. \]

NMR in CCl₄

<table>
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<th>Number of Protons</th>
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<tr>
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**Anal. Calcd. for C_{15}H_{24}O_{4}:**

C, 67.13; H, 9.02.

**Found:**

C, 68.03; H, 8.97.
Preparation of 7-Methoxytetralin (93). A 50% solution (180 ml.) of hydrochloric acid containing 60 g. of zinc amalgam and 12.35 g. of 7-methoxy-2-tetralone was refluxed for 24 hours. After cooling, the reaction mixture was extracted several times with ether. The combined organic extracts were washed with water and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvent was evaporated. The crude material was distilled, b.p. 121-123°C/10 mm Hg (Lit.: 129-133°C/11 mm Hg), to yield 6.00 g (53%) of compound (93).

λ_{max}^film: 3.3, 3.6, 6.18, 6.30, 6.62, 6.8-7.0, 7.35, 7.56, 7.75, 7.86, 7.94, 8.08, 8.30, 8.59, 8.87, 8.97, 9.32, 9.56, 10.57, 11.00, 11.53 μ.

NMR in CCl₄

δ (ppm) 6.9-6.4 multiplet (3H)
δ (ppm) 3.56 singlet (3H)
δ (ppm) 2.62 broad singlet - (4H)
δ (ppm) 1.66 multiplet (4H)

Preparation of 2-Methoxy-1,4,5,6,7,8-hexahydronaphthalene (94). Lithium metal was added to a solution containing 6.0 g. of 7-methoxytetralin, 250 ml. of absolute ether, 120 ml. of dry ethanol, and 630 ml. of liquid ammonia in such a manner that the solution remained blue for a total of 45 minutes. The ammonia was then allowed to evaporate. Ether and water were added and the aqueous layer was separated and extracted several times with ether. The combined organic extracts were washed with water and saturated sodium chloride solution. The solvent was evaporated
and the crude material was used directly in the next experiment.

\[ \lambda_{\text{max}}: 5.85, 5.96 \mu. \]

**Preparation of 2,2-Dimethoxy-1,2,3,4,5,6,7,8-octahydronaphthalene** (95). The crude material from the experiment above was dissolved in 300 ml. of absolute ether and 12 ml. of dry methanol. The solution was cooled to 0°C and a catalytic amount of p-toluenesulfonic acid was added. After standing at 0°C for 5 hours the solution was refluxed for 70 minutes. After cooling it was washed with cold dilute sodium bicarbonate solution, water, and saturated sodium chloride solution. The solvent was evaporated to yield 5.66 g. of crude material, which was shown by NMR to be 85% of compound (95), giving an over all yield for the two reactions of 66%.

\[ \lambda_{\text{max}}: 3.4-3.5, 6.8-7.0, 7.30, 7.50, 7.90, 8.14, 8.47, 8.70, 9.02, 9.17, 9.38, 9.46, 9.82, 9.96, 10.48, 11.15, 11.67, 12.25 \mu. \]

**NMR in CCl₄**

- \( \delta (\text{ppm}) 3.10 \) singlet (6H)
- \( \delta (\text{ppm}) 2.1-1.6 \) multiplet (14H)

**Preparation of 9,10-Octalin** (96). Polyphosphoric acid (84 g. phosphorous pentoxide in 840 g. of 85% phosphoric acid) was added to 84 g. of decahydro-2-naphthol. The temperature was raised to 150°C and held at this temperature for 10 minutes. Water was added slowly and the octalin was steam distilled. The water layer was separated and extracted with ether. The combined organic layers were washed with water and saturated sodium chloride solution. After drying over magnesium sulfate,
the solvent was evaporated. The crude material was distilled from sodium metal, b.p. 184°-189°C. The product was then heated to 140°C for two hours in the presence of 16 g. of phosphorous pentoxide. Ice water and ether were added and the aqueous layer was separated and extracted with ether. The combined organic layers were washed with water and saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the crude material distilled through a spinning band column. A product was obtained (10.0 g.), b.p. 191-192°C/760 mm Hg (Lit.31: 190-192°C/760 mm Hg), which showed no vinyl hydrogens in the NMR.

$\lambda_{\text{film max.}}$: 3.45-3.55, 6.90μ.

NMR in CCl₄

$\delta$ (ppm) 2.2-1.3 multiplet (16H)

Preparation of Compound (97). One gram of 9,10-octalin was heated between 126°C and 134°C in the presence of copper-bronze powder. Ethyl diazoacetate (1.5 g.) was added dropwise. When the evolution of nitrogen had ended, the material was cooled and flash distilled. The resulting liquid was passed through a gas chromatograph (SE-30 column), which indicated a yield of 17% of the desired compound.

$\lambda_{\text{film max.}}$: 3.4-3.5, 5.78, 6.35, 7.25, 7.75, 8.3-8.7, 9.60μ.

NMR in CCl₄

$\delta$ (ppm) 4.16 quartet (2H)

$\delta$ (ppm) 2.4-1.4 multiplet (20H)

$\delta$ (ppm) 1.28 triplet (20H)
Preparation of Compound (99). Methyl ethyl ketone (55 g.), \( \beta \)-anisaldehyde (100 g.), water (2.5 l.), and 10\% sodium hydroxide (1 l.) were mixed together and stirred for 44 hours. During this time a yellow crystalline precipitate formed, which was filtered from the aqueous solution. The yellow crystals were washed with water followed by cold 95\% ethanol. The light yellow crystals were then recrystallized from ether-petroleum ether, yielding 71 g. (51\%) of compound (99), m.p. 58-59°C, (lit. \(^{43}\): m.p. 61°C).

\( \lambda_{\text{max}}^{\text{CHCl}_2} \): 5.91, 6.02, 6.28, 6.34, 6.61\(\mu \).

Preparation of Compound (100). The unsaturated ketone (99) (71 g.) was dissolved in 250 ml. of 95\% ethanol and 1.0 g. of 10\% palladium-on-charcoal was added. The mixture was hydrogenated at room temperature and atmospheric pressure. At the end of two days slightly more than 1 molar equivalent of hydrogen had been absorbed, and the uptake of hydrogen had ceased. The catalyst was filtered off and the solvent was evaporated. The product was not purified at this time but the 2,4-dinitrophenylhydrazone was prepared which melted between 103\(°\) and 105°C when recrystallized from 95\% ethanol, (lit. \(^{43}\): m.p. 103°C).

\( \lambda_{\text{film}}^{\text{max}} \): 3.4-3.6, 5.83, 6.19, 6.30, 6.60, 6.82, 6.89, 7.07, 7.31, 7.67, 8.00, 8.45, 8.98, 9.62, 10.11, 12.10\(\mu \).

NMR in CC\(_4\)

\( \delta \) (ppm) 7.1-6.5 multiplet (4H)
\( \delta \) (ppm) 4.11 singlet (3H)
\( \delta \) (ppm) 2.8-2.05 multiplet (6H)
\( \delta \) (ppm) 0.98 triplet (3H)
Preparation of Compound (101). The unsaturated ketone (100) (71 g.) from the above experiment was dissolved in 1250 ml. of benzene, and 200 ml. of ethylene glycol was added together with a catalytic amount of p-toluenesulfonic acid. The reaction was refluxed over night under a Barrett distillation receiver. Approximately 800 ml. of benzene was distilled off under vacuum. The residue was dissolved in ether and washed with dilute sodium bicarbonate solution, water, and saturated sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated. The product was distilled, b.p. 92-95°C, yielding 84 g. of compound (101) giving a total yield for the hydrogenation and ketalization of 89%.

\[ \lambda_{\text{max}} : 3.4-3.5, 6.18, 6.59, 6.79, 6.81, 7.63, 7.99, 8.42, 9.32, 9.58, 10.48, 11.10, 12.10 \mu \]

NMR in CCl₄

\[ \delta (\text{ppm}) \]

- 7.28-6.60 multiplet (4H)
- 3.79 singlet (3H)
- 3.60 singlet (4H)
- 2.82-1.20 multiplet (6H)
- 0.90 triplet (3H)

Preparation of Compound (102). Compound (101) (30 g.) was dissolved in 40 ml. of dry ethanol, 150 ml. of absolute ether, and 600 ml. of dry liquid ammonia. Lithium metal was added in small pieces so that the solution remained blue for a total of 45 minutes. The ammonia was allowed to evaporate. Water and ether were added. The aqueous layer was separated
and extracted with ether. The organic extracts were combined and washed with water and saturated sodium chloride solution. After drying over anhydrous sodium sulfate the solvent was evaporated. The crude material was used directly in the next experiment.

\[ \lambda_{\text{max}}: \ 3.4-3.6, \ 5.88, \ 5.98, \ 6.8-7.0, \ 7.16, \ 8.18, \ 8.50, \ 9.32, \ 10.50, \ 11.14. \]

NMR in CCl₄

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**Preparation of Compound (103).** The crude material from the experiment above was dissolved in 375 ml. of absolute ether and 40 ml. of dry methanol. The solution was cooled to 0°C and a catalytic amount of p-toluenesulfonic acid was added. The solution was kept at 0°C for 1.25 hours and refluxed for one hour. After cooling, the solution was washed with dilute cold sodium bicarbonate solution, water, and saturated sodium chloride solution. The organic fraction was dried over anhydrous sodium sulfate and the solvent was evaporated. The product was distilled, b.p. 98-106°C/0.02 mm Hg, yielding 29.2 g of compound (103). This gives a total yield for the two reactions of 85%.
\lambda_{\text{max}}: 3.4-3.6, 6.8-7.0, 7.3-7.5, 7.24, 8.20, 8.31, 8.73, 8.92, 9.3-9.5, 10.50, 10.9-11.1, 11.62\mu.

NMR in CCl₄

δ (ppm) 5.20 multiplet (1H)
δ (ppm) 3.85 singlet (4H)
δ (ppm) 3.12 singlet (6H)
δ (ppm) 2.2-1.3 multiplet (12H)
δ (ppm) 0.83 triplet (3H)

Found: C, 66.60; H, 9.65.

Preparation of Compound (104). The unsaturated ketal (103) (10.38 g.) was heated between 125° and 132°C in the presence of copper-bronze powder. Ethyl diazoacetate (7.02 g.) was added dropwise. When the evolution of nitrogen had ceased, the starting material was distilled off under vacuum to yield 5.23 g. of compound (103). The residue was flash distilled yielding 5.145 g. (46% based on recovered starting material) of compound (104). The product was further purified by chromatography on Florisil.

\lambda_{\text{max}}: 3.3-3.5, 5.78, 6.8-7.0, 8.20, 8.50, 8.90, 9.05, 9.30, 10.50 11.00, 11.65\mu.

NMR in CCl₄

δ (ppm) 4.08 quartet (2H)
δ (ppm) 3.83 singlet (4H)
δ (ppm) 3.10 broad singlet (6H)
δ (ppm) 2.3-1.5 multiplet
δ (ppm) 1.22 triplet (20H)
δ (ppm) 0.88 triplet

Preparation of Compound (105). Compound (104) (238 mg.) was dissolved in 9 ml. of dry acetone. A catalytic amount of p-toluenesulfonic acid was added. The reaction was protected from light and stirred at room temperature for 25 hours. The solution was washed with dilute cold sodium bicarbonate solution, water, and saturated sodium chloride solution. After drying over anhydrous sodium sulfate the solvent was evaporated yielding 168 mg. (95%) of crude material.

λmax: 3.3-3.5, 5.78, 5.82, 6.8-7.0, 7.22, 8.50μ.

NMR in CCl4
δ (ppm) 4.12 quartet (2H)
δ (ppm) 2.8-1.5 multiplet
δ (ppm) 1.27 triplet (20H)
δ (ppm) 1.03 triplet

Preparation of Compound (107). The crude enol ether (102) obtained from the Birch reduction of 20 g. of compound (101) was dissolved in 90 ml. of 95% ethanol and added to a solution of 2.0 g. of oxalic acid dihydrate in 20 ml. of water. The reaction was stirred at room temperature for 45 minutes. The clear solution was poured into cold dilute sodium bicarbonate solution and extracted several times with ether. The combined ether extracts were washed with water and saturated sodium chloride
solution and dried over anhydrous sodium sulfate. A crude yield of 19.37 g. (99%) of compound (107) was obtained. No attempt was made to purify the product at this point.

\[ \lambda_{\text{max}}^{\text{Film}}: 5.81 \mu. \]

NMR in CDCl₃

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Preparation of Compound (108a). The crude β,γ-unsaturated ketone (107) was dissolved in 150 ml. of methanol and cooled to 0°C. Sodium borohydride (11.0 g.) which had been dissolved in 150 ml. of methanol was added dropwise. The solution was stirred for 17 hours at 0°C. Water and dilute sodium hydroxide were added, and most of the solvent was removed under vacuum at room temperature. The viscous residue was dissolved in water and ether, and shaken for an extended period of time with dilute sodium hydroxide in order to destroy the boron complex. The ether layer was separated and the aqueous layer was washed several times with ether. The combined ether extracts were washed with water and saturated sodium chloride solution. After drying over anhydrous sodium sulfate, the solvent was evaporated and the product distilled, b.p. 105-114°C/0.03 mm Hg. A yield of 13.5 g. of the epimeric alcohol (108a) was obtained for an overall yield, starting from the aromatic compound (101), of 71%.

\[ \lambda_{\text{max}}^{\text{Film}}: 2.96, 3.4-3.5, 6.8-7.0, 7.32, 7.75, 8.26, 8.71, 9.32, 10.26, 10.50, 11.03 \mu. \]
NMR in CCl₄

δ (ppm) 5.25  multiplet   (1H)
δ (ppm) 3.82  broad singlet   (5H)
δ (ppm) 3.52  singlet   (1H)
δ (ppm) 2.2-1.1  multiplet   (12H)
δ (ppm) 0.87  triplet   (3H)

Found:  C, 69.07; H, 9.74.

Preparation of Compound (108b). The alcohol (108a) (2.15 g.) was dissolved in pyridine and treated with acetic anhydride in the customary manner. After work up 2.18 g. (97%) of the acetate (108b) was obtained.

λ<sub>max</sub>: 3.3-3.5, 5.76, 6.8-7.0, 7.28, 8.00, 8.72, 9.31, 9.61, 10.22, 10.49, 11.05μ.

NMR in CCl₄

δ (ppm) 5.25  multiplet   (1H)
δ (ppm) 4.75  multiplet   (1H)
δ (ppm) 3.85  singlet   (4H)
δ (ppm) 2.3-1.2  multiplet   (15H)
δ (ppm) 1.95  singlet   (15H)
δ (ppm) 0.86  triplet   (3H)

Preparation of Compound (109). The acetate (108b) (1.07 g.) was heated in the presence of copper-bronce powder to 125-134°C. Ethyl diazoacetate (1.00 g.) was added dropwise. When the addition was complete and
the evolution of nitrogen had ceased, the product was cooled and chromato-
graphed on basic alumina. Starting material (650 mg.) eluted from the
column first, followed by 480 mg. of the adduct (109). A yield of 86%
based on recovered starting material was thus obtained.

\[ \lambda_{\text{max}}^\text{Film}: \quad 3.4-3.5, \ 5.78, \ 6.8-7.0, \ 7.25, \ 8.00, \ 8.55, \ 9.33, \ 9.62, \ 10.50, \]
\[ \quad 11.00, \ 11.70 \mu. \]

**NMR in CCl₄**

- \( \delta \) (ppm) 5.25 multiplet (1H)
- \( \delta \) (ppm) 4.18 quartet (2H)
- \( \delta \) (ppm) 3.92 singlet (4H)
- \( \delta \) (ppm) 2.00 split singlet (3H)
- \( \delta \) (ppm) 1.9-1.1 multiplet
- \( \delta \) (ppm) 1.25 triplet (20H)
- \( \delta \) (ppm) 0.87 triplet

**Preparation of Compound (110).** Compound (109) (753 mg.) was dissolved
in 25 ml. of dry acetone and a catalytic amount of p-toluenesulfonic acid
was added. The reaction was protected from light and stirred under nitro-
gen for 26 hours. The reaction was poured into cold dilute sodium bicar-
bonate solution. The sodium bicarbonate solution was extracted several
times with ether. The combined organic extracts were washed with water
and saturated sodium chloride solution. After drying over anhydrous sodium
sulfate, the solvent was evaporated, yielding 600 mg. (91%) of compound (110).

\[ \lambda_{\text{max}}^\text{Film}: \quad 3.4-3.5, \ 5.78, \ 5.81, \ 6.8-7.0, \ 7.25, \ 8.00, \ 8.50, \ 9.32, \ 9.62 \mu. \]

**NMR in CCl₄**

- \( \delta \) (ppm) 4.16 quartet (2H)
<table>
<thead>
<tr>
<th>δ (ppm)</th>
<th>Multiplet Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.4 - 1.4</td>
<td>Multiplet</td>
</tr>
<tr>
<td>2.00</td>
<td>Singlet</td>
</tr>
<tr>
<td>1.27</td>
<td>Triplet</td>
</tr>
<tr>
<td>1.03</td>
<td>Triplet</td>
</tr>
</tbody>
</table>
IV. REFERENCES


17. J. D. Tauber, unpublished results.


30. A. Serini and H. Koster, Ber., 71, 1766 (1938).
34. H. Buezsky and H. Decker, Ber., 38, 3268 (1905).
41. J. D. Tauber, unpublished results.