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SYNTHESIS OF INTERMEDIATES FOR
STEROID ELABORATION

DISsertation
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By
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The Ohio State University
1960

Approved by

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INTRODUCTION

The potentiality of the Diels-Alder reaction for steroid elaboration was recognized following the discovery\(^1\) that 1-vinyl-6-methoxynaphthalene, I, can serve as the diene in a Diels-Alder reaction. Subsequent efforts to utilize the Diels-Alder reaction for the synthesis of aromatic steroids have been

\[
\begin{align*}
\text{CH}_3\text{O} & \quad + \quad \begin{array}{c} \text{O} \\
\text{O} \end{array} \\
\text{I} \\
\text{CH}_3\text{O} & \quad \rightarrow \quad \begin{array}{c} \text{O} \\
\text{O} \end{array} \\
\text{II} & \quad \rightarrow \quad \text{ESTRONE}
\end{align*}
\]

summarized in a review. A recent synthesis of estrone utilized the Diels-Alder adduct II as an intermediate.

Our interest in the Diels-Alder approach for the synthesis of the hydroaromatic steroids was stimulated by communication with Professor W. S. Johnson, University of Wisconsin. As a result a joint steroid synthetic program was agreed upon. In this agreement workers at the Ohio State University were to try to develop a good method for preparing a diene component suitable for synthesis of steroids containing the \( \alpha, \beta \)-unsaturated carbonyl moiety in ring A (e.g. \( \Delta^4 \)-androstenedione-3,17) while the group at Wisconsin were to concentrate on the subsequent steps in the steroid elaboration.

\[
\Delta^4\text{-Androstenedione-3,17}
\]

---


OBJECTIVE

The objective of this investigation was the synthesis of 1-(1'-methoxyvinyl)-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, IV and/or 1-vinyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, V, from 1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, III.

In order to attain the objective in the fewest steps we arbitrarily decided to retain the $\alpha,\beta$-unsaturated carbonyl moiety in ring A while carrying out necessary reactions. For blocking purposes conversion
of the $\alpha,\beta$-unsaturated ketone function to a dienol ether or ester was considered satisfactory, since the unsaturated ketone system can be readily regenerated by mild acid hydrolysis.
HISTORICAL

The preparation of the diketone III and 1-ethynyl-1-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, VI have been reported. The conversion of the ethynylalcohol VI to 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII, has been claimed.

The methods employed for the synthesis of these compounds are described in this section.

2-Methyl-1,3-cyclohexanедione, VIII, the starting material for the bicyclic diketone III, has been made

\[\text{III}\]
\[\text{VI}\]
\[\text{VII}\]

---


by base-catalyzed cyclization of methyl 5-oxoheptanoate\(^1\) and by methylation of dihydroresorcinol.\(^2\)

![Chemical structure](image)

\(\text{CO}_2\text{CH}_3\) \(\rightarrow\) \(\text{O}\) \(\text{C}\) \(\text{O}\) \(\text{C}\) \(\text{H}\) 

\(1,6\)-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, III, m.p. 49-50\(^\circ\), was first prepared\(^3\) in poor yield in impure state (m.p. 41.5-42.5\(^\circ\)) from acetonedicarboxylic acid, formaldehyde and dione VIII under physiological conditions. Improved yields of diketone III were obtained\(^4\) by reacting dione VIII with diethylamino-3-butanone in the presence of pyridine. Treatment of the dione VIII with methyl vinyl ketone in the presence of traces of base followed by cyclization of the Michael adduct IX in the presence of aluminum t-butoxide\(^5\) or piperidine-phosphate\(^6\) also furnished diketone III in improved yields.

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\(^1\)Ref. 1, page 5.
\(^4\)Ref. 1, page 5.
\(^6\)Ref. 2, page 5.
In earlier attempts failure to obtain the diketone III from diethylamino-3-butanoic methiodide and dione VIII
was traced\(^1\) to the ready conversion of the trione IX to the acid X under the conditions employed. Diketone III also suffers facile cleavage to the acid XI in presence of alkali\(^1\) or cleavage followed by cyclization in a new direction to give the isomeric ketone XII in presence of methoxide\(^2\).

Condensation at the saturated carbonyl of the ketone XIII or III with metal acetylides followed by acid hydrolysis can lead to two epimeric ethynylalcohols differing in configuration at C\(_1\). While reaction of III with ethynyllithium in liquid ammonia gave\(^3\) one ethynylalcohol, VI B, m.p. 171-172\(^0\), in 70\% yield as the sole product, reaction of XIII with ethynylpotassium in ether was reported\(^4\) to give the same ethynylalcohol VIB in 32\% yield in addition to an isomeric solid, m.p. 145-147\(^0\), in 8\% yield. The latter material, obtainable also by treatment of VIB with hot 90\% formic acid, was considered\(^4\) to be the epimer of VIB but was later shown\(^5\) to be a

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\(^1\)Ref. 5, page 6.
\(^3\)Ref. 3, page 5.
\(^5\)Ref. 4, page 5.
mixture, m.p. 145-155°, of VIB, m.p. 171-172° and an isomeric solid, m.p. 181-182° of unknown structure. In this investigation the material, m.p. 181-182°, is shown to be an impure sample of the epimeric ethynylalcohol, VIA, m.p. 184-185°. Epimeric configurations have been assigned\(^1\)\(^2\) to the ethynylalcohol VIB and will be described in a later section (page 16).

\[ \text{C} = \text{C} \text{H} \]

\[ \text{O} \]

\[ \text{OH} \]

\[ \text{C}_2\text{H}_5 \]

\[ \text{XIII} \]

\[ \text{III} \]

\[ \text{VIB + VIA} \]

Conversion of VIB to 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII, has been described.\(^3\)

By treatment of the ethynylalcohol, VIB, m.p. 171-172°, with mercuric sulfate in aqueous methanol an isomeric compound, m.p. 122-123°, \( \lambda_{\text{max}} 257 \text{ m} \mu \) (\( \epsilon = 10,900 \)) was

\(^1\)Ref. 4, page 8.

\(^2\)Ref. 3, page 5.

\(^3\)C. A. Friedmann and R. Robinson, Chem. and Ind., 777, 1117 (1951) have described compounds VI and VII as liquids and compound IX as a solid, m.p. 47.0-48.5°. Since VIA and VIB have been obtained as high melting solids and IX as a liquid the English authors must have had compounds of other structures.
obtained¹ in 25% yield. Structure VII was assigned¹ to this product. When diketone III was reacted with ethynylsodium in liquid ammonia for 24 hours the expected alcohol VI was obtained in only 5% yield. The

major product (50%) was an isomeric liquid diketone, \( \lambda_{\text{max.}} 246 \text{ m}\mu (\epsilon = 8128) \), I.R. absorption peaks at 5.85, 6.00 and 6.17 \( \mu \). This liquid has also been assigned² structure VII and was presumed to arise by isomerisation of ethynylalcohols VIA and VIB during work-up with acid. Since the authentic compound VII, m.p. 97-98°, has been prepared in this investigation, the materials for which structure VII were assigned require reexamination.

¹Ref. 4, page 5.
²Ref. 1, page 5.
RESULTS AND DISCUSSION

The attempted preparation of 1-vinyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, V, is described first. The successful preparation of 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII, followed by an account of the attempted preparation of 1-(1′-methoxyvinyl)-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, IV, is given later.

2-Methyl-1,3-cyclohexanedione, VIII

The preparation of the dione VIII from resorcinol was simplified by avoiding isolation of the intermediate dihydroresorcinol. Hydrogenation of an aqueous solution of the mono sodium salt of resorcinol followed by methylation of the enolate of dihydroresorcinol in 50% aqueous methanol or 25% aqueous dioxane with methyl iodide gave the dione VIII in 55-60% overall yield. The use of a dioxane-water medium for methylation proved superior to aqueous methanol from the point of view of isolation and quality of the product. This modification of the earlier preparation\(^1\) of dione VIII

obviates difficulties attending isolation of dihydrosorcinol\(^1\) without affecting the overall yield.

\[\text{1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, III}\]

The dione VIII furnished a 40-46% yield of the diketone III, by treatment with diethylamino-3-butanone alone or in the presence of pyridine\(^2\) or triethylamine.\(^3\) A simplified procedure was then developed to obtain the diketone III in improved yield. The dione VIII was condensed with methyl vinyl ketone in the presence of traces of potassium hydroxide to yield the crude 2-methyl-2-(3'-oxobutyl)-1,3-cyclohexanedione, IX, which cyclized readily when treated with catalytic amounts of pyrrolidine or piperidine to give the diketone III in 60-65% overall yield.

\[\text{1-Oxo-6-ethoxy-8a-methyl-1,2,3,7,8,8a-hexahydronaphthalene, XIII}\]

The ketone XIII was obtained in 92% yield by

\[\text{III} \quad \rightarrow \quad \text{C}_2\text{H}_5\text{O} \quad \text{XIII}\]

\(^1\text{R. B. Thompson, Organic Syntheses, Coll. Vol. 3, 278 (1955).}\)

\(^2\text{Ref. 1, page 5.}\)

\(^3\text{Ref. 2, page 8.}\)
reacting diketone III with triethyl orthoformate in ethanol in the presence of traces of dry hydrogenchloride. XIII was characterized by its known monoxime.¹

Reaction of Ketones III and XIII with Grignard Reagents

The diketone III as well as the ketone XIII reacted readily with one equivalent of either vinylmagnesium bromide or ethynylmagnesium bromide in tetrahydrofuran by an enolization mechanism since the sole product of each reaction, after acid hydrolysis, was the diketone III (75 to 90% recovery).

Reaction of Ketone XIII with Ethynylpotassium

At the beginning of this investigation the best procedure available for the synthesis of ethynylalcohol VI was the reported¹ formation of an epimeric mixture of VIB and VIA (4:1) in 40% yield by treatment of the ketone XIII with ethynylpotassium in ether. In our efforts to improve the yield of VI the above results were confirmed. But the same mixture of alcohols was obtained in 76% yield when tetrahydrofuran was used instead of ether. A better procedure for the synthesis of VIB is described below.

¹Ref. 1, page 5.
1-Ethynyl-1-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7.8,8a-octahydronaphthalene, VIB

At this stage details of the successful preparation\textsuperscript{1} of the ethynylalcohol VIB in 70\% yield, by treating the diketone III with ethynyllithium in liquid ammonia, became available. In our experiments the reaction period was found to be a critical factor for optimum yields of VIB. When the reaction mixture obtained by rapid addition of the diketone III to a solution of ethynyllithium in ammonia was hydrolyzed after 1 hour VIB was obtained as the sole product in 80-85\% yield. Longer reaction periods under identical conditions led to a liquid product\textsuperscript{2} which was not investigated. Whereas the addition of acetylene to the ketone XIII gave the epimeric ethynylalcohols VIB and VIA only VIB could be obtained from the reaction with diketone III.

\textsuperscript{1}Ref. 3, page 6.

\textsuperscript{2}On the basis of insufficient data structure VII has been erroneously assigned to a liquid diketonic material obtained by reacting diketone III with ethynylsodium in ammonia for 24 hours. Ref. 1, page 5.
Epimerization of VIB to VIA

When a methylenechloride solution of the ethynylalcohol VIB, m.p. 172-173°, $\lambda_{\text{max}}$ 242 m$\mu$ ($\varepsilon = 13,800$) was treated with boron trifluoride-etherate, an isomeric ethynylalcohol, VIA, m.p. 184-185°, $\lambda_{\text{max}}$ 242 m$\mu$ ($\varepsilon = 15,500$) was isolated in about 25% yield. The residual material (57%), m.p. 149-175°, was found to consist of VIB (4 parts) and VIA (1 part) by chromatography.

Under the same isomerizing conditions VIA, m.p. 184-185°, furnished 18.5% of VIB and 69% of the starting material. The interconversion of VIB and VIA considered along with their I. R., U. V. and N. M. R. spectral data leave no doubt that VIB and VIA are the epimeric ethynylalcohols.

The reported isomerization of ethynylalcohol VIB, m.p. 172-173°, by treatment with hot 90% formic acid has been shown to give traces of two isomeric solids (m.p.

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1The presence of small amount of ethanol was found necessary for this isomerization. A similar observation was made in the hydrogenchloride-catalyzed isomerization of $6\beta,21$-diacetoxy-$\Delta^4$-pregnene-3,20-dione to the $6\alpha$-epimer. P. Th. Herzig and M. Ehrenstein, J. Org. Chem., 16, 1050 (1951).

2We wish to thank Dr. G. V. D. Tiers, Minnesota Mining and Manufacturing Co., Minneapolis, Minn. for the N. M. R. analysis.

3Ref. 4, page 8.

4Ref. 4, page 5.
94-95° and 181-182° respectively) of unknown nature. On repeating this experiment materials having similar melting ranges were obtained and were found to be impure samples of the ethynylalcohol VIA, m.p. 184-185° and the diketone VII, m.p. 97-98°, described later.

Configuration of Ethynylalcohols VIB and VIA

The only remaining question regarding the structure of the epimeric ethynylalcohols is the configuration at C₁. We prefer the β-hydroxy¹ structure VIB for the ethynylalcohol, m.p. 172-173°, since we assume that the attack of the acetylide ion at C₁ of diketone III will occur from the direction away from the angular methyl group. This mode of addition of metal acetylides to 17a-keto function of D-homosteroids is known.² The epimeric ethynylalcohol, m.p. 184-185°, should then have the α-hydroxy structure VIA.

¹ The prefix α- and β- are used in the same sense as in the steroid series.

The configuration shown above for the ethynyl-alcohol, m.p. 172-173°, is just the reverse of the assignment given by earlier workers¹ who noted a difference in the stereochemistry of addition of metal acetylides to the ketones III and XIV. This difference in the mode of addition was shown by the fact that the hydrogenated alcohols XV, XVI and XVII were different from one another. These authors studied the metal acetylide addition to the ketone XIV prior to their work on diketone III. They assigned the β-hydroxy structure to the product from ketone XIV assuming attack by acetylide ion at C₁ of XIV from the α-side. The alcohol XVI differs from XVII only in the configuration

¹Ref. 3, page 5.
at C₁ and was therefore assigned the α-hydroxy structure.

The mode of addition of metal acetylides to ketones III and XIV is obviously opposed to each other. Further study is necessary to find out which of the two ketones undergoes attack by acetylide from the α-side. When a mixture of VIA and VIB were chromatographed on alumina, the ethynylalcohol VIB, m.p. 172-173°, was eluted first and hence¹ should be assigned the axial hydroxy structure VIA, as proposed by the Russian authors. However, since factors responsible for adsorption of the epimeric alcohols VIA and VIB might be complicated by the proximity of the α,β-unsaturated carbonyl function, a definite conclusion cannot be drawn.

Attempted Dehydration of the Ethynylalcohol VIB

Attempts to dehydrate the ethynylalcohol VIB to the corresponding enyne were of no avail. Treatment of VIB with collidine and phosphorous oxychloride or with collidine and thionylchloride led to water soluble colored resinous material. No reaction occurred between VIB and pyridine-thionylchloride at room temperature.

Partial Hydrogenation of Ethynylalcohol VIB to Vinylalcohol XVIIIB

Partial hydrogenation of the ethynylalcohol VIB in

pyridine over a Pd-CaCO\textsubscript{3} catalyst furnished 1-vinyl-1\(\beta\)-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, XVIIIB, m.p. 77-78\(^\circ\), \(\lambda\) max. 242 m\(\mu\) (\(\varepsilon = 13,000\)) in 90\% yield.

**Attempted Dehydration of Vinylalcohol XVIIIB to the Trienone V**

The preparation of the trienone V was attempted by (a) dehydration of the vinyl alcohol XVIIIB under acid conditions and (b) pyrolysis of the acetate. In this section attempts at dehydration of the free alcohol XVIIIB is described.

The vinylalcohol XVIIIB behaved similar to the ethynylalcohol VIB when treated with pyridine and thionyl chloride. At room temperature no reaction occurred and at reflux temperature only resinous water soluble material was obtained. XVIIIB was recovered after treatment with iodine in toluene at reflux temperature for 48 hours.

By treating XVIIIB with potassium bisulfate at
150-160°, a liquid (80-90% yield), \( \lambda \) max. 242 m\( \mu \), I. R. absorption peaks at 5.85 (s), 6.00 (s), and 6.17 (m)\( \mu \), was obtained. The I. R. bands for -OH and -CH = CH\(_2\) functions were absent. The band at 5.85\( \mu \) is not present in the starting material. This liquid was not further examined. Unlike XVIIIB, the vinylalcohols XIX and XX gave the corresponding dienes when heated with potassium bisulfate. The sensitivity of the vinylalcohol XVIIIB towards acidic reagents and the behaviour of ethynylalcohol VIB during its preparation in basic medium may be attributed to the complicating side reactions of the vinylogous \( \beta \)-hydroxy ketone function present in VIB and XVIIIB. The preparation of the trienone V was then attempted by the acetate pyrolysis method.

**Attempted synthesis of V by Pyrolysis of Acetate XXIII**

The desired acetate XXIII could not be prepared by acetylation of the vinylalcohol XVIIIB with pyridine and acetic anhydride. XXIII was then prepared as described below.

Acetylation of the ethynylalcohol VIB with acetic anhydride under acid catalysis gave the diacetae XXIB (92%), m.p. 92-93°, \( \lambda \) max. 235 m\( \mu \) (\( \varepsilon = 19,950 \)).

---

The acetate XXIII remained unchanged under pyrolytic conditions up to 400°C. Pyrolysis at 450°C furnished a liquid that showed the absence of the acetoxy group in the infra-red but failed to react with either N-phenylmaleimide or p-benzoquinone. The liquid product from pyrolysis gave a red mono-2,4-dinitrophenylhydrazone in poor yield indicating that pyrolysis resulted in a mixture of products. No further attempts were made to obtain V.

**Attempted Preparation of Diketone VII According to Literature**

Since the synthesis of the trienone V proved difficult, attention was turned to the synthesis of 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII, for use as an intermediate for the trienone IV. The compound described in the literature as VII was prepared and the structure assigned was found to be incorrect as shown below.

![Chemical Structures](attachment:chemical_structures.png)

Treatment of the ethynylalcohol VIB, m.p. 172-173°C, with mercuric sulfate in aqueous methanol was reported
Partial hydrogenation of XXIB in alcohol over palladium on calcium carbonate furnished the diacetate $^1$ XXIIB, $\lambda_{\text{max.}}$ 235 m\(\mu\) ($\epsilon = 18,800$), in 90% yield.

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

Mild acid hydrolysis of the diacetate XXIIB at room temperature gave the liquid monoacetate XXIII, $\lambda_{\text{max.}}$ 242 m\(\mu\). Both XXIIB and XXIII exhibit the characteristic I. R. absorption for the vinyl group at 10.1 and 10.9\(\mu\) (995 and 910 cm$^{-1}$).$^2$

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

$^1$XXIB and XXIIB have been assigned the heteroannularenal diene structures shown, on the basis of the similarity in their U. V. absorption to the enolacetates derived from $\Delta^4$-3-ketosteroids. L. F. Fieser and M. Fieser, "Steroids", Reinhold Publishing Corporation, New York, 1959, p 310.

to give an isomeric solid, XXIV, m.p. 122-123°, $\lambda_{\text{max.}}$ 257 ($\epsilon = 10,900$) for which structure VII was assigned.\(^1\)

We have repeated this experiment and obtained a compound, m.p. 124.4-126.0°, which was undoubtedly the same compound previously described.\(^1\) While the U. V. data agreed with that quoted, the I. R. spectrum, not reported earlier, revealed the presence of an hydroxyl group. This fact alone rules out structure VII for the compound XXIV. N. M. R. analysis\(^2\) revealed the presence of $-\text{OH}, \overset{1}{\text{C}} - \text{CH = C} -$, and $\overset{1}{\text{C}} = \overset{1}{\text{C}}$ functions. The ethynyl and acetyl groups were absent. XXIV does not give a ferric chloride test and the U. V. spectrum is not changed by alkali. This excludes an enol or a phenol. Acid-catalyzed reaction with acetic anhydride gave a mono acetate, $\lambda_{\text{max.}}$ 256 m\(\mu\) ($\epsilon = 15,000$). No further attempts were made to elucidate the structure of XXIV. The synthesis of the diketone VII was then attempted by a different route.

**Synthesis of 1-Acetyl-6-oxo-8a-methyl-2,4,6,7,8,8a-hexahydonaphthalene, VII**

Treatment of the diacetate XXII\(B\), already described, with hot 90% formic acid gave a crystalline product, m.p. 97-98°, (in about 40% yield) which furnished I. R.,

\(^1\)Ref. 4, page 5.

\(^2\)Ref. 2, page 15.
U. V., N. M. R.\(^1\) and analytical data consistent with structure VII. The same compound was obtained in 32\% yield by formic acid treatment of the epimeric diacetate \(\text{XXIA}\), obtained by acid-catalyzed acetylation of ethynyl-alcohol \(\text{VIA}\) in 55\% yield. VII has an absorption maximum at 235 m\(\mu\) (\(\varepsilon = 19,900\)). This wavelength is about that to be expected as \(\Delta^4,16\)-pregnadiene-3,20-dione, \(\text{XXV}\), absorbs\(^2\) at 234 m\(\mu\) (\(\varepsilon = 25,100\)), the intensity being about the sum of the intensities for the unsaturated ketone systems in \(\text{XXVI}\) (\(\varepsilon = 15,850\)) and in \(\text{XXVII}\) (\(\varepsilon = 8,900\)) at 234 m\(\mu\). The fact that \(\text{XXVIII}\) absorbs\(^3\) at 233 m\(\mu\) (\(\varepsilon = 8,930\)) shows that the intensity of absorption of the chromophore in both \(\text{XXVII}\) and \(\text{XXVIII}\) is the same whether the unsaturation is in a 5- or 6- membered ring. The intensity of

\[\text{XXI B} \quad \text{VII} \quad \text{XXI A}\]

\(^1\)Ref. 2, page 15.

\(^2\)A. Butenandt and J. Schmidt-Thomé, Ber., 72, 182 (1939).

absorption of VII ($\epsilon = 19,900$) is less than expected ($\epsilon = \text{Ca. } 25,000$). Possibly the proximity of the two $\alpha,\beta$-unsaturated ketone systems in VII is responsible for the lower intensity. The infra-red absorption at $6.0 \mu$ of VII is also that to be expected since XXV has a single peak$^1$ at $5.98 \mu$. Compound VII furnished a red mono-2,4-dinitrophenylhydrazone which still retains the I. R. peak at $6.0 \mu$ characteristic of VII but of

relatively low intensity. VII was further characterized by its crystalline 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene-6-trimethylenethio-ketal, XXIX,

\[ \lambda \text{max. } 230 \text{ m}\mu \left( \epsilon = 12,300 \right), \text{I. R. peaks at } 6.00 \text{ (s)} \]
and 6.18\( \mu \). Reduction of VII with sodium borohydride gave 1-acetyl-6\( \beta \)-hydroxy-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, \(^1\) XXX, \[ \lambda \text{max. } 231 \text{ m}\mu \left( \epsilon = 11,900 \right), \]
I. R. peaks at 2.86 (s), 6.03 (s) and 6.16 (m)\( \mu \).

We believe that the methylketonic function in XXIX and XXX is free for two reasons: (a) the absorption maximum for the cyclohexenone chromophore in III, VIB, VIA, and XVIIIIB is at 242 m\( \mu \) and (b) the \( \lambda \) max. for 1-acetyl-1-cyclohexene types\(^2\) is at 232 m\( \mu \). Since XXIX and XXX absorb at 230 and 231 m\( \mu \) respectively, the structures indicated seem correct.

\[ \text{CH}_3 \]

\[ \text{HO} \]

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


\(^2\) J. D. Chanley, J. Am. Chem. Soc., 70, 244 (1948).
Attempted Conversion of 1-Acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII, to Enol Ether IV

When the diketone VII was treated at room temperature with trimethyl orthoformate in methanol in the presence of p-toluenesulfonic acid extensive resini-fication occurred over several hours and the expected product XXXI could not be obtained. Treatment of VII with acetic anhydride or isopropenyl acetate under the drastic condition employed for enol acetylation of 11-ketosteroids gave a liquid acetoxy compound that still retained the \( \alpha,\beta \)-unsaturated carbonyl bands in the I. R. This liquid material failed to react with either N-phenylmaleimide or p-quinone but furnished the starting material VII on acid hydrolysis at room temperature.

![Chemical structures](image)

Judging from the ease of enol acetylation of 3,11-diketosteroids the liquid product probably has the structure XXXII. No further attempts were made to obtain the diene IV.
to the allylic primary bromide XXXV by treatment with anhydrous hydrogenbromide. When XVIIIIB was treated with hydrogen bromide in ether, an isomeric diketone (20%), m.p. 59-61°, λ max. 247 mμ (ε = 13,000), I. R. peaks at 5.86 (s), 6.00 (v.s) and 6.18 (s), was obtained. Structure XXXVI is consistent with the I. R., U. V. and N. M. R.¹ spectral data for this rearranged product but no attempt was made to prove the structure.

We thank Dr. George Slomp, the Upjohn Co., Kalamazoo, Michigan, for suggesting structure XXXVI from N. M. R. analysis.

¹We thank Dr. George Slomp, the Upjohn Co., Kalamazoo, Michigan, for suggesting structure XXXVI from N. M. R. analysis.
Two experiments of a miscellaneous nature are included for purposes of record.

**Action of Base on the Diketone VII**

Extensive decomposition of VII observed during attempted chromatographic purification on neutral "Aluminum oxide Woelm", prompted study of the action of base on VII. When VII was treated with sodium hydroxide in methanol for 12 hours at room temperature an isomeric dicarbonyl compound, XXXIII, m.p. 116-117°, \( \lambda \text{max.} 279 \text{ m} \mu \ ( \varepsilon = 25,600)\), I. R. peaks at 5.82 (s), 6.02 (s), 6.14 (v.s), 6.26 (s) \( \mu \), was obtained in 33\% yield after purification on acid-washed alumina. The obvious structures involving migration of a double bond to give an extended conjugated system were eliminated on the basis of N. M. R. analysis. The presence of two olefinic hydrogens located on different double bonds, a methyl group and an acetyl group were indicated. Compound XXXIII was not further studied.

**Action of Hydrogenbromide on 1-Vinyl-1\( \beta \) -hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, XVIII**

The tertiary vinylalcohol XXXIV was rearranged\(^3\)


\(^2\)Ref. 2, page 15.

SUMMARY

Starting from resorcinol, 1-ethynyl-1-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydroronaphthalene, m.p. 172-173° was prepared in 29% overall yield by a lithium acetylide condensation on the intermediate 1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydroronaphthalene. This ethynylalcohol has been provisionally assigned the β-hydroxy structure VIB.

The ethynylalcohol VIB undergoes epimerization in the presence of boron trifluoride-etherate and traces of ethanol to give approximately equal mixture of epimers (in 80% yield) from which the pure epimer VIA, m.p. 184-185° could be isolated in 25% yield by fractional crystallization. Pure VIA also undergoes epimerization under the same conditions.

The epimeric alcohols VIA and VIB were converted into epimeric diacetates, XXIA, m.p. 113-114° and XXIB, m.p. 92-93° respectively. Treatment of either acetate with hot 90% formic acid gave 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydroronaphthalene, VII, which could not be converted into the desired diene IV. VII was found to be sensitive to base giving an isomeric diketone XXXIII of unknown structure.
Treatment of ethynylalcohol VIB with mercuric sulfate in methanol gave the compound XXIV, m.p. 124.5-126.0°, for which structure VII had been assigned by previous workers. While the structure of XXIV was not elucidated evidence has been presented to disprove the earlier assignment to this compound.

The ethynylalcohol VIB and its diacetate XXIB were partially hydrogenated to their vinyl analogs XVIIIB, m.p. 77-78° and XXIIB, m.p. 81-82° respectively. The diacetate XXIIB was hydrolyzed to 1-vinyl-1β-acetoxy-6-oxo-8α-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, XXIII, a liquid. Attempted dehydration of the vinylalcohol XVIIIB or the pyrolysis of its monoacetate XXIII did not give the desired trienone, V. Thus neither objective of this investigation could be realized within the limitations stated in the "objective".
EXPERIMENTAL

General

Melting points recorded are uncorrected and were taken in a Hershberg apparatus.

Microanalyses carried out by Galbraith Microanalytical Laboratories, Knoxville, Tenn. and by Schwarzkopf Microanalytical Laboratory, N. Y., are indicated by superscripts g and s.

U. V. spectra were obtained in 95% alcohol. I. R. spectra of solid compounds were obtained using potassium bromide pellets and peaks reported in microns with the usual notation to indicate intensity.

The phrase "treated as usual" means the organic layer was washed with 5% hydrochloric acid or 5% sodium bicarbonate solution as indicated, water, saturated brine and dried by dripping through a funnel containing magnesium sulfate. The solvent was then removed by distillation at atmospheric or reduced pressure.
2-Methyl-1,3-cyclohexanedione, VIII

A freshly prepared solution of 384 g. (9.6 moles) of sodium hydroxide and 880 g. (8 moles) of resorcinol in 1500 ml. of water was placed in a 3.5 l. hydrogenation bomb together with 160 g. of powdered nickel catalyst.¹ The hydrogenation was carried out under a pressure of 1800 lbs. psi. of hydrogen for about 16 hr. without application of external heating until the drop in pressure due to hydrogen uptake was negligible. After cooling to room temperature the catalyst was removed by filtration and washed with 2 x 125 ml. portions of water. The filtrate and washings were transferred to a 5 l. round-bottomed flask and treated with 130 ml. of conc. hydrochloric acid (for neutralizing the excess base used), 450 ml. of dioxane and 1193 g. (8.4 moles) of methyl iodide. The reaction mixture was held at mild reflux using an efficient condenser for 10 hr. during which time the product crystallized out with the simultaneous disappearance of the methyl iodide layer. The suspension was cooled in ice-bath for 1 hr. and the product collected by filtration and washed with 3 x 200 ml. portions of water to remove sodium iodide which otherwise discolored the product on drying. The filtrate and washings were

¹Grade 0104T 1/8 Harshaw Nickel catalyst supplied by the Harshaw Chemical Co., Cleveland 6, Ohio, was used.
concentrated to half volume and a second crop of product collected and washed as before. The colorless dione VIII, 585 g. (58%), m.p. 205-208°, obtained in this manner was used as such in the next step.

1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydonaphthalene, III

(A) A mixture of 88.2 g. (0.7 mole) of dione VIII and 114.6 g. (0.8 mole) of diethylamino-3-butanone\(^1\) sus­pended in 600 ml. of benzene in a 2 l. flask fitted with a phase separating head, was refluxed for 8 hr. until the separation of water ceased. The dark reaction mixture was cooled, diluted with equal volume of ether, washed with 5% aqueous hydrochloric acid and treated as usual. The residual crude liquid (89 g.) was distilled at 0.4 mm. pressure and distillate collected in two fractions; fraction (a) 66 g., b.p. 123-133° and fraction (b) 8 g., b.p. 134-155°. Fraction (a) was diluted with 10 ml. of ether and after cooling overnite in an ice-box, the crystals were collected by filtration and washed with 25 ml. of ether. The mother liquor and washings were redistilled and treated as before to obtain additional solid product. The

\(^1\)Prepared by treating technical grade methyl vinyl ketone (supplied by Matheson, Coleman and Bell Co., Cincinnati, Ohio) with slight excess of diethylamine at 20° for 24 hr. followed by distillation. (88% yield; b.p. = 70-72° at 11 mm.).
diketone III, 57.5 g. (46% on VIII), m.p. 47-50°, was obtained as colorless crystals.

Fraction (b) deposited crystals after long storage in the freezer. The crystals were collected and re-crystallized from ether to obtain 4.2 g. (3%) of the acid X, m.p. 46-48°. This material gave a semicarbazone¹ which after one crystallization from methanol melted at 203-205°.

(B) Improved Procedure for the Diketone III

A mixture of 63.1 g. (0.5 mole) of dione VIII, 52.6 g. (0.75 mole) of technical grade methyl vinyl ketone, about 0.25 g. (3 pellets) of potassium hydroxide and 250 ml. of absolute methanol was placed in a 500 ml. round-bottomed flask fitted with a reflux condenser and a drying tube. The dione completely dissolved on refluxing for 3 hr. At the end of this period methanol and the excess methyl vinyl ketone were removed by distillation under reduced pressure. The residual liquid² was dissolved in 250 ml. of benzene and 20 ml. of solvent was removed by distillation at atmospheric pressure.

¹ M. P.s reported for the acid X and the semicarbazone are 46-48° and 204-205° respectively, Ref. 5, page 6.

pressure via a phase separating head to remove traces of methanol and water. Addition of 3 ml. of pyrrolidine or piperidine to the reaction mixture at this stage resulted in a vigorous reaction and 9 ml. of water collected in the trap in $\frac{1}{2}$ hr. After refluxing for additional 15 minutes the crude reaction mixture was worked up as in (A) to obtain 57-58 g. (64-65% on VIII), of colorless III, m.p. 47-50°.

1-Oxo-6-ethoxy-8a-methyl-1,2,3,7,8,8a-hexahydronaphthalene, XIII

A solution of 18 g. (0.1 mole) of diketone III and 20 g. (0.135 mole) of triethyl orthoformate in 75 ml. of absolute alcohol was treated with 1 ml. of alcohol saturated with dry hydrogen chloride and left at room temperature for 36 hr. The greenish reaction mixture was concentrated under aspirator pressure. An ether solution of the residue was washed with 5% aqueous sodium bicarbonate and treated as usual to obtain 19 g. (92%) of the crude liquid product. Distillation of the crude liquid gave 17.7 g. (85%) of XIII as an yellow liquid, b.p. 114-116°/0.5 mm. Since the I. R. spectrum of the crude liquid was identical with that of the distilled product, the crude liquid was used as such in later preparations. Compound XIII gave an oxime, m.p. 133-135° (lit. 1 132.5-134.0°).

1Ref. 1, page 5.
Attempted Grignard Reactions on Diketone III and Ketone XIII

Vinylmagnesium bromide\(^1\) and ethynylmagnesium bromide\(^2\) reagents were prepared according to directions in the literature.

(A) To a solution of 7 g. (0.034 mole) of ketone XIII in 150 ml. of dry tetrahydrofuran in a 500 ml. three-necked flask equipped with a stirrer, an addition funnel and a condenser connected via drying train to a gas trap, a solution of 0.0375 mole of vinylmagnesium bromide in 100 ml. of tetrahydrofuran was added dropwise over 50 minutes. During this addition about 1 l. of a gas was collected in the trap. The reaction mixture was refluxed for \(\frac{1}{2}\) hr., cooled and hydrolyzed with 6 ml. of saturated aqueous ammonium chloride. The solid was collected by filtration and washed with 50 ml. of ether. Filtrate and washings were evaporated and the residue dissolved in ether was treated as usual to obtain 6.3 g. (90\%) of a liquid which furnished an oxime, identified as the dioxime of diketone III by mixed m.p. 199-200\(^\circ\). Distillation of the crude liquid followed by crystallization gave 4 g. of diketone III.


(B) To a solution of 6 g. (0.034 mole) of diketone III in 100 ml. of tetrahydrofuran, a solution of 0.0345 mole vinylmagnesium bromide in 100 ml. of same solvent was added over ½ hr. under the usual conditions for a grignard reaction. A pink solid that separated on adding the grignard reagent did not dissolve after refluxing for 2 hr. The reaction mixture was worked as in (A) above to obtain 5.2 g. (86%) of a liquid that was found to be the starting material by oximation.

(C) A standard solution of ethynylmagnesium grignard was prepared. An aliquot portion was tested by reaction with 13.5 g. (0.1 mole) of cinnamaldehyde to obtain 12 g. (76%) of 1-ethynyl-1-hydroxy-3-phenyl-2-propene, m.p. 66-67° (lit. m.p. 67-68°). Under the conditions employed for the above reaction, diketone III was recovered in 60 and 72% yields when the ketone XIII and diketone III were used.

1-Ethynyl-1-hydroxy-6-oxo-8a-methyl-
1,2,3,4,6,7,8,8a-octahydronaphthalene, VIA and VIB

A solution of potassium t-amyloxide prepared from 1.31 g. (0.033 g. atom) of potassium and 25 ml. of t-amylalcohol was added to 150 ml. of tetrahydrofuran saturated with acetylene at dry ice temperature. A solution of 5.8 g. (0.028 mole) of the ketone XIII in 25 ml. of tetrahydrofuran was added over 1 hr. to the
potassium acetylide solution with stirring. The reaction mixture was hydrolyzed with dilute hydrochloric acid after stirring for an additional hr., the solvent removed by distillation under reduced pressure and the residue dissolved in 200 ml. of methylene chloride was treated as usual. The crude solid product after one crystallization furnished 4.4 g. (76.5%) of crystals, m.p. 140-169°, in two crops. Fractional crystallization of this material from 20 ml. of methylene chloride gave 3 g. (52%) of VIB, m.p. 172-173°, and 1.1 g. of a mixture, m.p. 145-160°. The latter material was chromatographed on acid-washed alumina and separated into 0.6 g. of VIB and 0.4 g. of another solid, m.p. 184-185°, identified as the epimer VIA by mixed m.p. with the authentic sample, the preparation of which is described later.

1-Ethynyl-1β-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, VIB

A solution of ethynyllithium from 7.35 g. (1.05 g. atom) of lithium in 1 l. of liquid ammonia was formed in a 3 l. three-necked flask equipped with a dryice condenser, stirrer, inlet for acetylene and cooled in acetone-dryice bath. To this solution, a solution of 180 g. (1.01 mole) of diketone III dissolved in 1 l. of dry ether was added in a rapid stream (in 5 minutes) with stirring. After stirring the thick yellow suspension for 3/4 hr. at dryice-acetone temperature, 200 ml. of
by 15 mg. of a third crystalline material that proved to be VIA. These compounds were found to be identical with the corresponding authentic samples, as checked by mixed m.p. determination and I. R. spectral analysis. 

(B) A solution of 42 g. of VIB, m.p. 172-173°C, in 1 l. of methylene chloride, 22 ml. of boron trifluoride-etherate and 15 ml. of ethanol was refluxed for 6 hr. The dark solution was washed with saturated aqueous sodium bicarbonate, treated as usual and concentrated to a volume of about 250 ml. A first crop of 12 g. of light yellow crystals, m.p. 182-184°C, after charcoal treatment of an ethyl acetate solution gave 11.3 g. (27%) of VIA, m.p. 184-185°C, mixed m.p. with VIB, 145-180°C, \( \lambda \text{ max.} 242 \text{ m} \mu \) (\( \epsilon = 15,500 \)), I. R. peaks 2.99 (s), 3.09 (s), 4.80 (w), 6.00 (s), 6.18 (m). 

Anal. Calcd. for C\( \text{I}_{13} \text{H}_{16} \text{O}_{2} \): C, 76.4; H, 7.9

\[\text{Found:} \quad C, 76.2; \quad H, 7.8\]

From the mother liquor of the crude product a further 24 g. (57%) of solid, m.p. 149-175°C, was obtained. This mixture could not be separated into individual components by fractional crystallization. Chromatography of 1 g. of this mixture on acid-washed alumina\(^1\) and elution with ether and methylene chloride gave 0.75 g. of VIB, m.p. 172-173°C, followed by 0.18 g.

\(^1\)When the neutral "aluminum oxide Woelm" was used extensive loss due to decomposition occurred.
saturated aqueous ammonium chloride was added and the ammonia evaporated. The crude product collected by filtration, washed with 2 x 200 ml. of water followed by 500 ml. of methylene chloride. The yellow product, after drying in an oven at 110° melted at 169-172°.
The filtrate was worked separately to obtain a further crop of product. The combined product, m.p. 169-172°, weighed 182 g. (88%). One crystallization from methylene chloride or ethylacetate after charcoal treatment furnished crystalline VIB, m.p. 172-173°, $\lambda_{\text{max}}$ 242 m$\mu$ ($\varepsilon = 13,800$), I. R. 2.96 (s), 3.06 (s), 4.80 (w), 6.00 (s) and 6.16 (m). Longer reaction periods (4 to 24 hr.) gave lower yields (65% to 8%) of product along with a liquid which was not studied. In runs larger than 1 mole the yield (60-70%) was lower.

1-Ethynyl-1α-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, VIA

(A) A solution of 1 g. of VIB in 12 ml. of 90% formic acid was refluxed for 1½ hr. and the formic acid removed under vacuum. A methylene chloride solution of the residue was washed with 5% aqueous sodium bicarbonate and treated as usual. The crude product dissolved in a small volume of methylene chloride was chromatographed on acid-washed alumina. Elution with a 3:2 mixture of Skellysolve F and benzene gave 10 mg. of VII. Further elution with ether gave 25 mg. of VIB followed
of VIA, m.p. 184-185°. Thus 24 g. of the mixture consists of VIB (4 parts) and VIA (1 part). Estimated net yield, 15.6 g. (37%) of VIA and 18 g. (43%) of VIB.

The remaining crude reaction product was chromatographed to obtain 6 g. of a liquid that shows absorption bands for saturated and α,β-unsaturated carbonyls in the I. R. The absorption bands for -OH and -C=CH were absent. This liquid was not studied further.

While 1 g. of pure VIA could be obtained from 4.2 g. of VIB under conditions described in (B), the starting material was recovered when ethanol was omitted in another experiment. When 1 g. of 17α-ethynyltestosterone,1 m.p. 264-266° was treated as in (B) the starting material was recovered.

Epimerisation of VIA to VIB

Treatment of 2.16 g. of pure VIA, m.p. 184-185°, as in (B) above yielded 0.4 g. (18.5%) of VIB, m.p. 172-173° and 1.5 g. (69.4%) of VIA, m.p. 184-185°, by crystallization and chromatography.

1-Vinyl-1β-hydroxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, XVIII

A solution of 31 g. (0.152 mole) of VIB in 125 ml. of C. P. pyridine was hydrogenated at 28 lbs. pressure

1We wish to thank the Upjohn Co., Kalamazoo, Mich., for this sample.
of hydrogen over 0.5 g. of Pd-CaCO$_3$ catalyst.\(^1\) Hydrogen absorption ceased after an uptake of one equivalent of hydrogen. The catalyst was filtered through a bed of supercel, washed with 20 ml. of pyridine and the filtrate concentrated under vacuum. The residue dissolved in 250 ml. of ether was washed with 5% aqueous hydrochloric acid and treated as usual. The crude product was crystallized from ether to obtain 28.8 g. (92%) of crystals, m.p. 77-78\(^0\). One crystallization afforded pure XVIIIB, m.p. 77-78\(^0\), \(\lambda\) max. 242 m\(\mu\) (\(\epsilon = 13,000\)), I.R. peaks 2.90 (s), 6.00 (v.s), 6.18 (s), 10.18 (s), 11.05 (s).

Anal. Calcd. for C$_{13}$H$_{18}$O$_2$: C, 75.7; H, 8.8
Found\(^\circ\): C, 75.6; H, 8.7

**Attempted Dehydration of VIB and XVIIIB**

(A) A mixture of 3 g. of vinylalcohol VIB and 1.5 g. of powdered potassium bisulfate was heated under 55 mm. pressure at 155-160\(^0\) for \(\frac{1}{2}\) hr. and the cooled mixture extracted with 4 x 50 ml. portions of ether and the extract treated as usual to obtain 2.8 g. of crude liquid, I.R. peaks 5.85 (s), 6.00 (s), 6.17 (s). The absorption bands for -OH and -CH = CH$_2$ were absent. The liquid gave a 2,4-dinitrophenylhydrazone, m.p. 253-255\(^0\)

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\(^1\)Catalyst was prepared according to D. A. Shirley, "Preparation of organic Intermediates", John Wiley and Sons, Inc., N. Y. (1951), p. 243.
after recrystallization from ethyl acetate. Treatment of XVIIIB with either phosphorous pentoxide in benzene at reflux temperature for 1 hr. or with boron trifluoride-etherate in benzene at room temperature for 10 hr. gave the same liquid as identified by I. R. spectra and confirmed by mixed m.p. determination of the 2,4-dinitrophenylhydrazone derivative.

(B) After treatment of either VIB or XVIIIB with one equivalent of thionylchloride in pyridine solutions at room temperature for 24 hr., the starting materials were recovered in 90 and 70% yields respectively. At reflux temperature the dark reaction mixtures obtained were concentrated but the water soluble residues could not be extracted into ether or methylene chloride. The same results were obtained when pyridine was replaced by collidine.

1-Ethynyl-1β,6-diacetoxy-8a-methyl-1,2,3,7,8,8a-hexahydronaphthalene, XXIB

(A) Attempted acetylation of ethynylalcohol VIB with pyridine and acetic anhydride or pyridine and acetyl chloride at room temperature for 48 hr. failed and the starting material was recovered.

(B) A mixture of 5 g. of VIB, 25 ml. of acetic anhydride and 0.5 g. of p-toluenesulfonic acid was left at room temperature for 16 hr. On pouring the dark-green solution into iced-water an oil that separated solidified in
and was collected by filtration, washed with water and dried. Yield 6.5 g. (92%). Reproducible yields were obtained in larger runs. One crystallization from ethanol afforded with negligible loss colorless crystals of XXIB, m.p. 92-93°, λ max. 235 mμ (ε = 19,950), I. R. peaks 3.09 (s), 4.80 (w), 5.70 (s), 5.76 (s), 6.00 (m), 6.10 (m).

Anal. Calcd. for C₁₇H₂₀O₄: C, 70.8; H, 7.0.

Found: C, 70.7; H, 7.1.

1-Ethynyl-1α,6-diacetoxy-8α-methyl-1,2,3,7,8,8α-hexahydronaphthalene, XXIA

Treatment of 2,3 g. of the epimeric ethynylalcohol VIA, m.p. 184-185°, at room temperature with 15 ml. of acetic anhydride containing 100 mg. of p-toluenesulfonic acid yielded 2.0 g. of product, m.p. 110-114°, after a work-up as above. One crystallization from ether-skelleysolve F afforded 1.8 g. (55.4%) of XXIA, m.p. 113-114°, λ max. 234.5 mμ (ε = 18,600), I. R. peaks 3.04 (s), 4.80 (w), 5.70 (s), 5.76 (s), 6.00 (m), 6.10 (m).

Anal. Calcd. for C₁₇H₂₀O₄: C, 70.8; H, 7.0.

Found: C, 71.0; H, 7.1.

1-Vinyl-1β,6-diacetoxy-8α-methyl-1,2,3,7,8,8α-hexahydronaphthalene, XXIB

A solution of 7.2 g. (0.025 mole) of XXIB in 40 ml. of absolute methanol was hydrogenated over 250 mg. of
Pd-CaCO$_3$ and the hydrogenation stopped at the end of theoretical drop in pressure for one equivalent of hydrogen. (Unlike VIB which undergoes hydrogenation to the vinylalcohol smoothly in pyridine solution, XXIB could not be hydrogenated in pyridine). The catalyst was removed, washed with 25 ml. of alcohol and the filtrate concentrated to obtain 6.7 g. (92%) of product, m.p. 77-81°. Two crystallizations from ether furnished pure XXIIB, m.p. 81-82°, $\lambda$ max. 235 m$\mu$ ( $\epsilon$ = 18,800), I. R. peaks 5.7 (shoulder), 5.75 (s), 6.00 (m), 6.1 (m), 8.0-8.4 (s), 10.1 (m), 10.86 (s).

Anal. Calcd. for C$_{17}$H$_{22}$O$_4$: C, 70.3 ; H, 7.6.

Found$^8$: C, 70.2, 70.4 ; H, 7.7, 7.6.

Attempted Pyrolysis of 1-Vinyl-1$\beta$-acetoxy-6-oxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene, XXIII

A solution of 10 g. of XXIIB in 50 ml. of ethanol was treated with 5 ml. of 5% hydrochloric acid and left at room temperature for 18 hr. The solvent was removed under reduced pressure and the residue dissolved in ether was treated as usual to obtain 8.0 g. (95.8%) of a liquid, $\lambda$ max. 242 m$\mu$ , I. R. peaks 5.76 (s), 6.00 (s), 6.18 (s), 8.2 (s), 9.9 (s), 10.9 (m). XXIII is distinguished from XXIIB readily in the I. R. The heteroannular trans diene system in XXIIB shows two equal, medium intensity bands at 6.0 and 6.1$\mu$ while
XXIII shows a strong band at 6.0 and a medium intensity band at 6.18/μ due to the α,β-unsaturated carbonyl function.

The pyrolysis of the monoacetate, XXIII was carried out in a column1 of vycor glass tubing (2.5 cm. O. D.) packed (45 cm.) with glass helices and provided with an external heating jacket and two thermocouples, one at the top and another at the exit end of the column, to measure the temperature.

A solution of 8 g. of XXIII in 100 ml. of p-ethyl-toluene (b.p. 161°) was dropped in 1 hr. at the rate of 10 drops per 15 seconds through the column maintained at 400°C. The column was cooled and washed with 25 ml. of the same solvent. The combined condensate and washings were washed with water and treated as usual. The residue (6.4 g.) had an I. R. spectrum identical with that for the starting material. The operations were repeated with the recovered material at a column temperature of 450°. The crude product (6 g.) was distilled to obtain 4.7 g. of a liquid, b.p. 120-140°/1 mm., λ max. 236 m/μ, I. R. peaks 6.0 (shoulder), 6.2 (s), no peaks at 8-8.4, 10 and 11/μ. A sample of this liquid (200 mg.) when treated with 200 mg. of

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1I wish to thank Dr. K. Greenlee and Mr. V. G. Wiley of the Petroleum Research Laboratory, the Ohio State University, for their kind permission to use the facilities of their laboratory.
2,4-dinitrophenylhydrazine gave a crude mixture of derivatives, m.p. 70-110°, which after chromatography on alumina and elution with benzene furnished 80 mg. of an orange-red 2,4-dinitrophenylhydrazone, m.p. 136-137°. The analysis is difficult to interpret. The pyrolysate failed to react with N-phenylmaleimide or p-quinone in benzene solutions.

**Action of Hydrogenbromide on XVIIIB (compound XXXVI)**

Into a solution of 8.4 g. (0.04 mole) of XVIIIB in 100 ml. of ether, cooled in ice-bath, dry hydrogenbromide was passed until the weight increased by 5 g. A gummy mass that separated was allowed to warm to room temperature over 1 hr. The mixture was washed with saturated aqueous sodium bicarbonate and treated as usual. The crude liquid (8.7 g.) on distillation furnished 3.8 g. of distillate, b.p. 137°/0.03 mm., that partially solidified. Crystallization from ether-skellysolve F afforded 1.75 g. (20.6% by weight) of a product, m.p. 52-57°. Two crystallizations furnished the analytical sample, m.p. 59-61°, \( \lambda_{max} \) 247 m\( \mu \) (\( \epsilon = 13,000 \)), I. R. peaks 5.86 (s), 6.00 (v.s), 6.17 (s), 10.94 (m). Sodium fusion test for bromide was negative. N. M. R. spectrum revealed absence of olefinic hydrogen \( \alpha \) to the carbonyl and structure XXXVI was suggested by Dr. George Slomp.
Anal. Calcd. for C\textsubscript{13}H\textsubscript{18}O\textsubscript{2}:  C, 75.7 ;  H, 8.8.

Found\textsuperscript{6}:  C, 75.2, 75.0 ;  H, 8.8, 9.0.

Conversion of VIB to XXIV

Treatment of 4 g. of VIB with mercuric sulfate in aqueous methanol as described\textsuperscript{1} furnished 600 mg. of product, XXIV, m.p. 124-126°. The same compound was obtained in 35% yield by using a boron trifluoride-mercuric oxide catalyst. Two crystallizations from ether-skellysolve F furnished pure XXIV, m.p. 124.5-126.0°, λ\textsubscript{max}. 257 m\textsubscript{λ} (ε = 11,000), I. R. peaks 2.86 (s), 6.00 (s), 6.06 (s), 6.12 (s), 6.24 (m).

N. M. R. spectrum confirmed the presence of -OH, \( \text{O} = \text{C} - \text{CH} = \text{C} - \text{H} \), \( \text{C} = \text{C} - \text{H} \), groups. Ethynyl and acetyl groups were absent.

Anal. Calcd. for C\textsubscript{13}H\textsubscript{16}O\textsubscript{2}:  C, 76.4 ;  H, 7.9.

Found\textsuperscript{6}:  C, 76.4, 76.6 ;  H, 8.0, 8.1.

XXIV does not give a ferric chloride test. The U. V. spectrum is not changed by alkali. Acid-catalyzed reaction with acetic anhydride gave a mono acetate, m.p. 122.0-122.6°, λ\textsubscript{max}. 256 (ε = 15,000), I. R. peaks 5.76 (s), 6.00 (s), 6.06 (s), 6.12 (s), 6.24 (m), 8.05 (s).

\textsuperscript{1}Ref. 4, page 5.

\textsuperscript{2}The catalyst was prepared according to R. A. Raphel, "Acetylenic Compounds in Organic Synthesis", Butterworths Scientific Publications Ltd., London, 1955, page 204.
Anal. Calcd. for C$_{15}$H$_{18}$O$_3$: C, 73.1; H, 7.4.

Found: C, 72.8, 72.7; H, 7.6, 7.7.

XXIV furnished a 2,4-dinitrophenylhydrazone, m.p. 222-223° (reported for the mono derivative 218.5-219.5°).

1-Acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene, VII

A solution of 90 g. of XXIB in 200 ml. of 90% formic acid was refluxed under nitrogen for 2 hr. After removal of formic acid under aspirator pressure, the residue was dissolved in methylene chloride, washed free of acid with a minimum quantity of 5% aqueous sodium bicarbonate and treated as usual. The crude product on cooling yielded 17.3 g. of light yellow crystals of VII, m.p. 90-96°. Chromatography of the mother liquor on acid-washed alumina and elution with skellysolve F and benzene gave another 11.8 g. of VII, m.p. 92-96°. Further elution of the column with ether gave about 20 g. of a liquid which has not been studied besides 0.75 g. of VIB and 0.7 g. of VIA eluted in that order. One crystallization of crude VII from ether gave 28.3 g. (43.4%) of product, m.p. 94-96°. The persistent light yellow color could not be removed by charcoal treatment. The analytical sample was pre-

\(^{1}\)In preliminary experiments chromatography on neutral grade "Aluminum oxide Woelm" resulted in complete loss of product due to decomposition on the column.
pared by rechromatography on alumina and crystallization from ether to obtain colorless plates of VII, m.p. 97-98°, \( \lambda \text{ max. } 235 \text{ m} \mu (\epsilon = 19,500) \), I. R. peaks 6.00 (v.s), 6.10 (s), 6.17 (s). The N. M. R. spectrum was consistent with structure VII as no unexpected peaks were present.

Anal. Calcd. for \( \text{C}_{13}\text{H}_{16}\text{O}_{2} \) : C, 76.4 ; H, 7.9.

Found : C, 76.6, 76.7 ; H, 8.2, 8.2.

VII gives a red mono-2,4-dinitrophenylhydrazone.

Two crystallizations from ethanol furnished the analytical sample, m.p. 198.6-199.6°.

Anal. Calcd. for \( \text{C}_{19}\text{H}_{20}\text{N}_{4}\text{O}_{5} \) : C, 59.4; H, 5.2; N, 14.6.

Found : C, 59.6, 59.6; H, 5.4, 5.2; N, 14.8, 14.9.

Conversion to XXIA to VII

A solution of 1.43 g. of XXIA in 5 ml. of 90% formic acid was refluxed for 1½ hr. and worked as described in the preceding experiment. Chromatography of the crude liquid yielded 330 mg. (32.6%) of VII, m.p. and mixed m.p. with the product from XXIB, 97-98°.

1-Acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene-6-trimethylenethioketal, XXIX

To a suspension of 1.8 g. of VII in a mixture of 5 ml. of ether and 2 ml. of boron trifluoride-etherate cooled in ice-bath 1 ml. of propane-1,3-dithiol was added dropwise. The suspension soon turned to a clear solution
Attempted Preparation of XXXI

A solution of 1.02 g. (5 molea) of VII, 1.2 g. (11 molea) of trimethyl orthoformate in 5 ml. of dry methanol was treated with 2 drops of saturated methanolic hydrogenbromide and left at room temperature for 12 hr. The initially colorless solution turned to a dark red suspension over a few hours. The solvent was removed under aspirator to obtain dark resinous matter insoluble in most solvents. Repeating the experiment under nitrogen led to the same results.

Enol Acetylation of VII to XXXII

Treatment of VII with excess acetic anhydride at room temperature or at reflux temperature or with isopropenylacetate at reflux temperature in the presence of p-toluenesulfonic acid resulted in 80-90% yield of a liquid that showed absorption peaks in I. R. at 5.72 (s), 6.00 (v.s), 6.18 (m) and 8.2-8.5 (s). This liquid failed to react with N-phenylmaleimide or p-quinone in benzene solutions at reflux temperature but could be hydrolyzed in 85% yield to the starting material VII. From the I. R. spectrum the liquid material is believed to be XXXII. No further work was done with it.

Action of Base on Diketone VII

To a solution of 1.1 g. of VII in 10 ml. of dry methanol was added 0.13 g. of sodium hydroxide. The
and in 2 hr. set to a mass of needles. The mixture was dissolved in ether, washed with 10% aqueous sodium bicarbonate and treated as usual. The crude liquid deposited 2.2 g. of crystals which on recrystallization from ether afforded 2 g. (75%) of XXIX, m.p. 119.5-120.0°, \( \lambda_{\text{max}} 230 \text{ m\(\mu\)} ( \varepsilon = 12,300), \) I. R. peaks 6.00 (s), 6.18 (s) both of relatively diminished intensity as compared to same peaks for VII.

**Anal. Calcd.** \( C_{16}H_{22}O_2 \) : C, 65.3; H, 7.5; S, 21.8.

**Found** : C, 65.1, 65.3; H, 7.6, 7.6; S, 21.6, 21.8.

1-Acetyl-6\( \beta \)-hydroxy-8a-methyl-3,4,6,7,8,8a-hexahydonaphthalene, **XXX**

A solution of 1 g. (5 mmoles) of VII 200 mg. (5.3 mmoles) of sodium borohydride and 1 ml. of water in 10 ml. of t-butyl alcohol was stirred for 1 hr. at room temperature. The excess borohydride was destroyed by adding a few drops of glacial acetic acid and the mixture evaporated to dryness. After the usual treatment the crude liquid residue gave 0.5 g. of crystals, m.p. 111-114° and the mother liquor on chromatography afforded a further 120 mg. of crystals. Two crystallizations from ether-methanol yielded 0.58 g. (58%) of colorless XXX, m.p. 115-117°, \( \lambda_{\text{max}} 231 \text{ m\(\mu\)} ( \varepsilon = 11,900), \) I. R. peaks 2.86 (s), 6.03 (s), 6.16 (m).

**Anal. Calcd.** for \( C_{13}H_{18}O_2 \) : C, 75.7 ; H, 8.8.

**Found** : C, 75.8, 75.8 ; H, 8.9, 9.0.
initially colorless solution turned dark red instantaneously on adding the alkali. After 12 hr. at room temperature the reaction mixture was acidified with acetic acid and evaporated to dryness under aspirator pressure. The residue dissolved in methylene chloride was treated as usual. The crude liquid was chromatographed on acid-washed alumina and eluted with 1:1 ether-benzene mixture to obtain 490 mg. of crystals, m.p. 115-116.5°. Charcoal treatment of an ether solution furnished 370 mg. (33.6%) of colorless XXXIII, m.p. 116-117°, λ max. 279 mμ (ε = 25,600), I. R. peaks 5.82 (s), 6.02 (s), 6.14 (v.s), 6.26 (s). N. M. R. spectrum revealed the presence of one -CH₃ and -CH₃ group each and two olefinic hydrogens located α and β to carbonyl on different double bonds.

Anal. Calcd. for C₁₃H₁₆O₂ :  C, 76.4 ;  H, 7.9.

Found:  C, 76.3, 76.4 ;  H, 7.7, 7.6.
I, Sambasiva Ramachandran, was born in Madras, India, June 10, 1929. I received my early education in the private schools in Sirkali, Madras State, and my undergraduate training at Annamalai University, Annamalainagar, Madras State, India, and obtained the Bachelor of Science degree in 1949. From the Indian Institute of Sugar Technology, Kanpur, India, I received the Associateship diploma of that institute in 1952. During 1952-1955, I worked as a process chemist in the cane sugar factories in India. I joined the Graduate School, Ohio State University, in September, 1955, and held a teaching assistantship from September, 1957, through March, 1958.