

1955

Syntheses of hydrophenanthrene ketones

Travis E. Stevens
Iowa State College

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SYNTHESES OF HYDROPHENANTHRENE KETONES

by

Travis E. Stevens

**A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY**

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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Head of Major Department /

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Dean of Graduate College

Iowa State College

1955

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INTRODUCTION

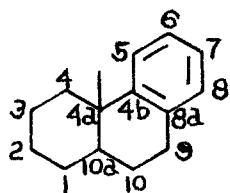
The synthesis of hydrophenanthrenes containing angular-methyl groups has been of considerable interest in recent years because of the structural relationship of these compounds to naturally occurring terpenes and steroids. However, most methods have led to intermediates of wrong stereochemistry, or to ones lacking the functional groups necessary for further synthetic progress.

The purpose of this work was to develop general hydrophenanthrene syntheses that would yield intermediates useful for the total synthesis of the tricyclic diterpenes.

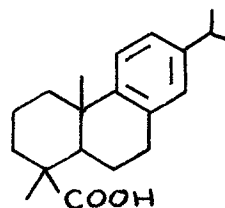
HISTORICAL

Syntheses of hydrophenanthrenes containing a 4a-methyl group

The formation of a 4a-methylhydrophenanthrene containing an aromatic ring (I) has been accomplished by several



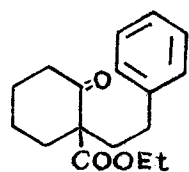
I



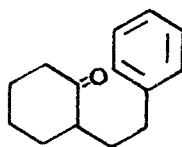
II

synthetic schemes. Some of the investigators sought a synthesis of dehydroabietic acid (II), or related diterpenes, while others were interested in intermediates for steroid syntheses.

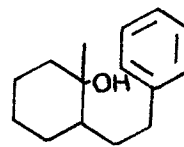
The phenanthrene synthesis of Bardhan and Sengupta (1) was used by Kon (2) to obtain 4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (I). The potassium salt of ethyl cyclohexane-2-carboxylate was alkylated with β -phenylethyl bromide to give the ketoester III. Alkaline hydrolysis



III



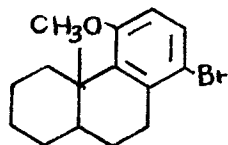
IV



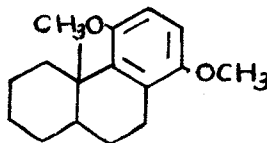
V

of the ketoester was accompanied by decarboxylation to the ketone IV, which was converted to the tertiary alcohol V with methylmagnesium iodide. Cyclodehydration of the alcohol with phosphorus pentoxide gave the hydrophenanthrene I.

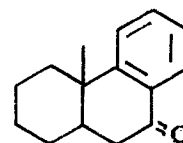
In their studies on the cyclization of various β -phenylethyl cyclohexanols, Barnes and co-workers (3) used the Bardhan-Sengupta method to synthesize several 4a-methylocta-hydrophenanthrenes, including the 5-methoxy-8-bromo (VI), the 5,8-dimethoxy (VII), and the 9-keto (VIII) compounds.



VI

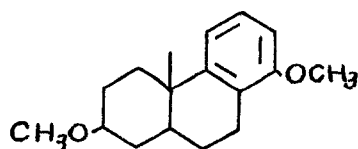


VII

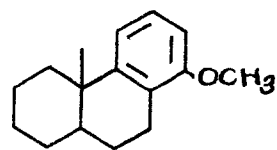


VIII

Using the same procedure, Renfrow (4) reported the synthesis of 4a-methyl-2,8-dimethoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IX), and Panizzi and Piattelli (5) synthesized the 8-methoxy compound X.

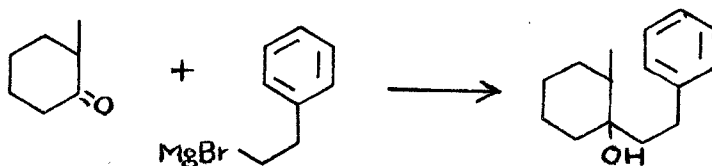


IX



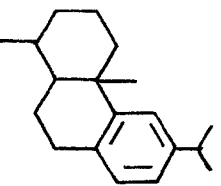
X

A shorter route to phenanthrenes involving some of the same steps as the Bardhan-Sengupta synthesis was discovered by Bogert (6), and by Cook (7). This method is illustrated by Bogert's synthesis (8) of the known (2) octahydrophenanthrene I. The tertiary alcohol XI, obtained by condensing the Grignard reagent of β -phenylethyl bromide with 2-methylcyclohexanone, yielded the hydrophenanthrene I on treatment with sulfuric acid.

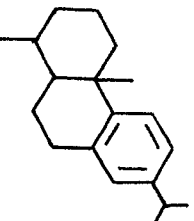


XI

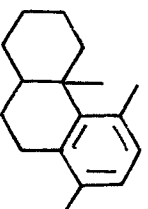
Using this same procedure, Slater (9) reported the synthesis of the hydrocarbon XII. Bogert (10) obtained



XII



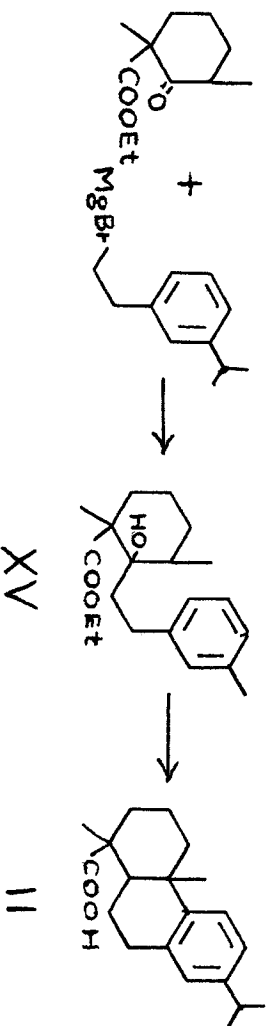
XIII



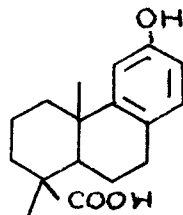
XIV

hydrocarbons XIII and XIV by similar means.

In 1939 Haworth and Barker (11) attempted to extend the Bogert-Cook method to the synthesis of dehydroabietic acid (II). The tertiary alcohol XV was dehydrated, and then cyclized, to give 1,4a-dimethyl-7-isopropyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (II). No resolution of the synthetic product has been reported.



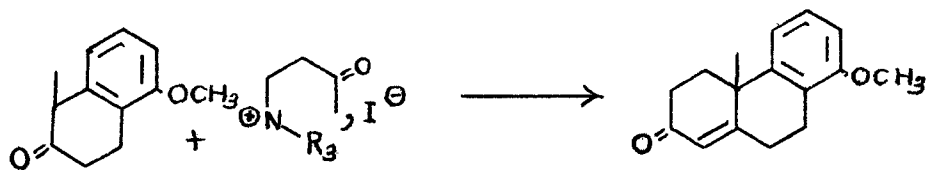
Attempts to synthesize podocarpic acid (XVI) in the same manner have been reported (12, 13). Again, no resolution of the synthetic acids has been reported.



XVI

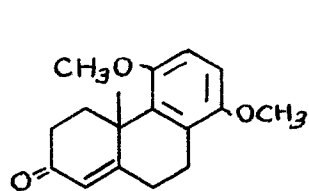
Barnes (3, 14) has obtained additional octahydrophenanthrenes from his studies of cyclizations of compounds of the type used in the Bogert-Cook synthesis.

Sir Robert Robinson (15) in 1946 synthesized the methoxy phenanthrone XVII by adding 4-diethylamino-2-butanone methiodide to 1-methyl-5-methoxy-2-tetralone.

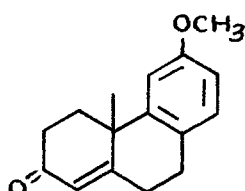


XVII

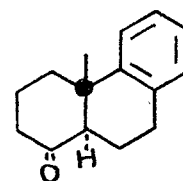
Using the same procedure, Grob and Jundt (16) prepared 4a-methyl-5,8-dimethoxy-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XVIII), and Stork (17) synthesized the methoxy ketone XIX.



XVIII

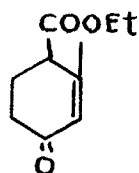


XIX

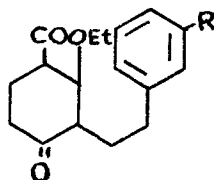


XX

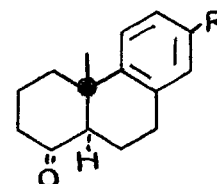
A general synthesis of hydrophenanthrene ketones of type XX has been reported (18). Condensation of Hagemann's ester (XXI) with the required β -phenylethyl bromide gave the corresponding substituted cyclohexenone XXII.



XXI



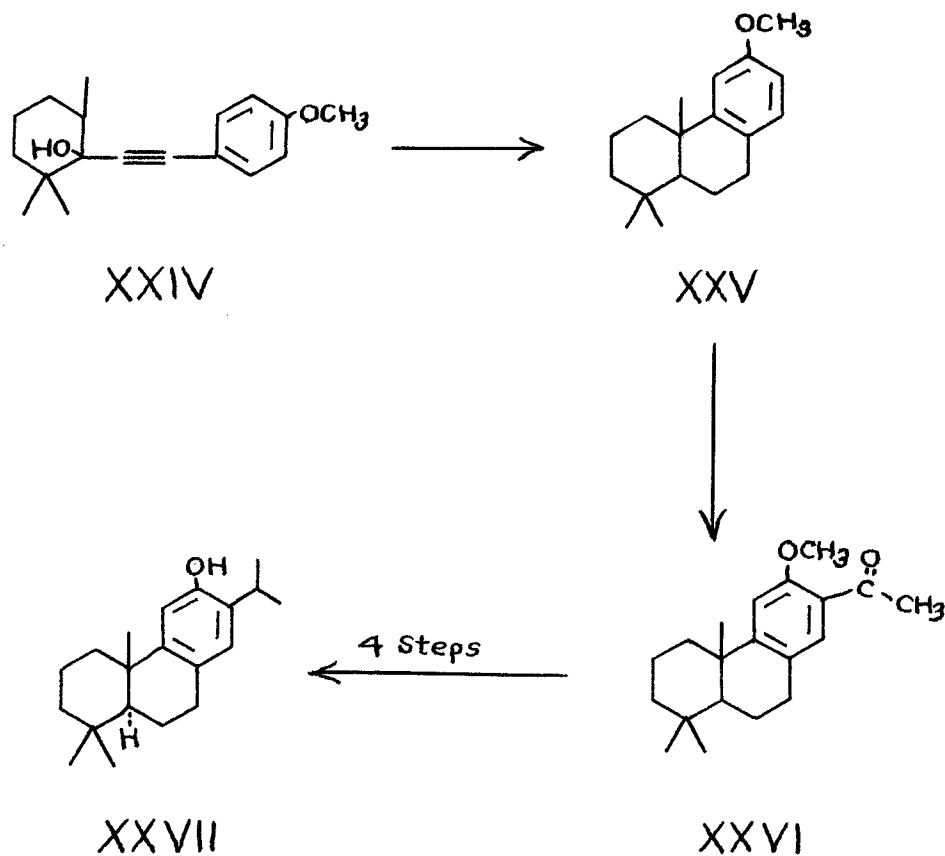
XXII



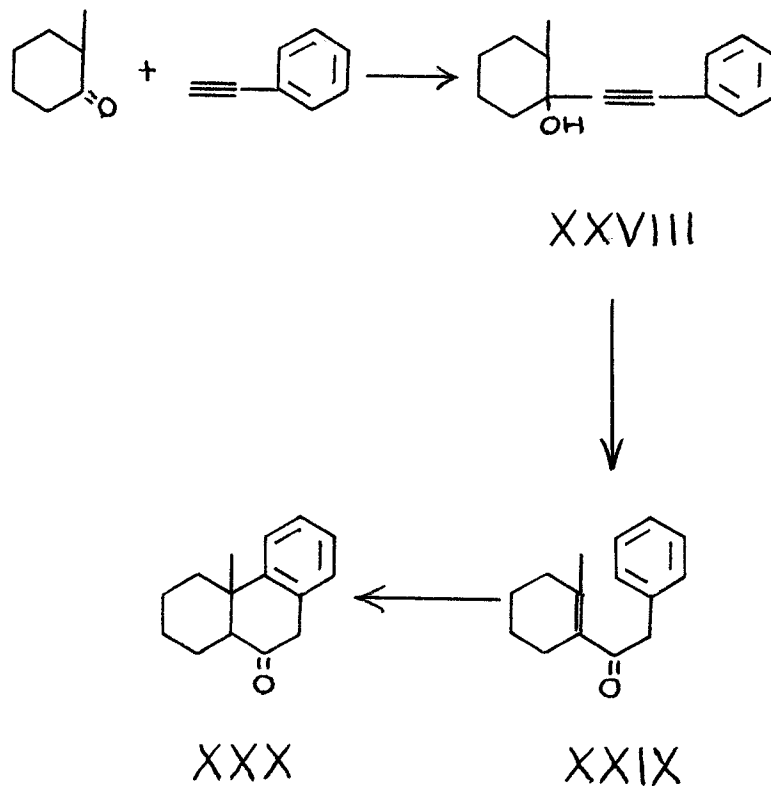
XXIII

Decarbethoxylation with alcoholic potassium hydroxide, followed by cyclization with phosphoric acid, gave the hydrophenanthrene ketones XXIII, with R representing hydrogen, methoxyl, and isopropyl groupings. A closely related synthesis has been published recently by Saha, Bagchi, and Dutta (19).

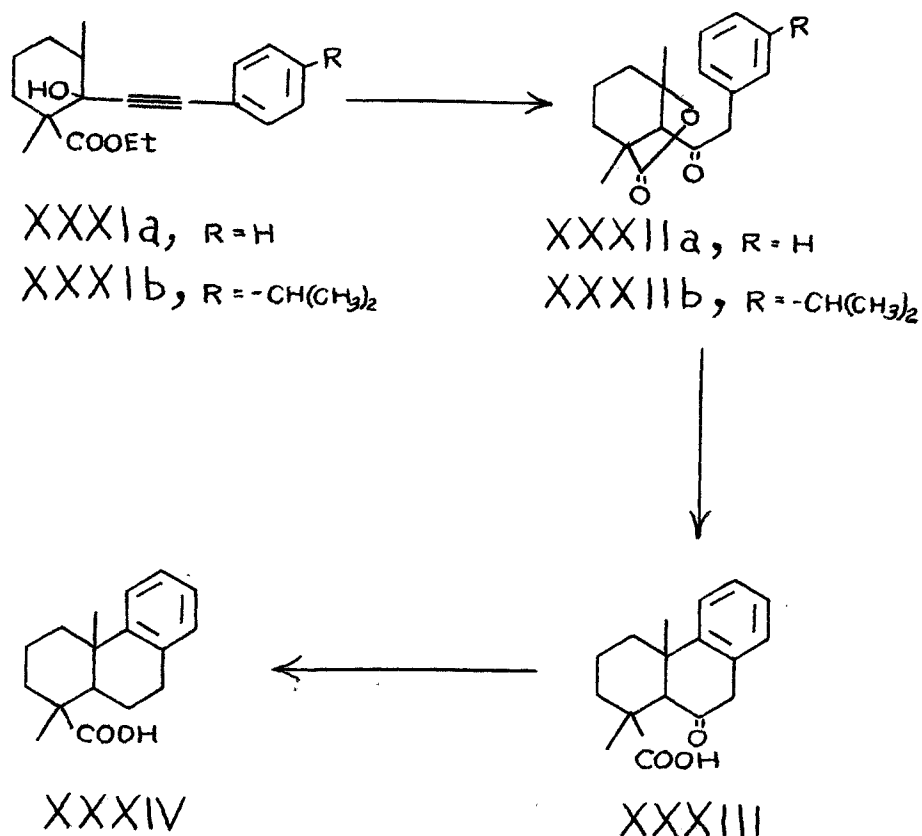
A phenylacetylene also can be condensed with a cyclohexanone to obtain the β -phenylethylcyclohexanol (or cyclohexene) needed for cyclization. By this means the synthesis of dl-ferruginol (XXVII) was accomplished (20). Addition of the sodio derivative of p-methoxyphenylacetylene to 2,2,6-trimethylcyclohexanone gave the acetylenic carbinol XXIV. This was reduced, and then cyclized to the methoxy hydrophenanthrene XXV. The acetyl compound XXVI was formed, and was converted to dl-ferruginol by the following four steps. Addition of methylmagnesium iodide to the ketone XXVI, followed by dehydration, hydrogenation, and cleavage of the ether linkage, gave the desired XXVII.



Dodson, Parham and Wheeler (21, 22) attempted the synthesis of dehydroabietic acid (II) in a similar manner. As a preliminary experiment they condensed potassium phenylacetylide with 2-methylcyclohexanone to obtain the acetylenic carbinol XXVIII. The action of formic acid on XXVIII gave a liquid ketone (XXIX), which was cyclized to give the phenanthrone XXX.

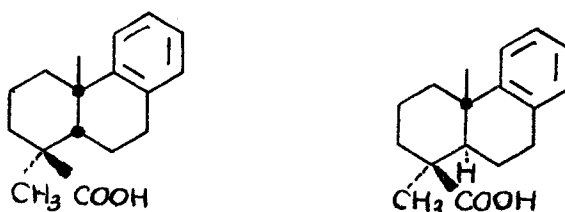


Similarly (21, 22), the acetylenic alcohols XXXIa and XXXIb were obtained by the reaction of the Grignard reagent, prepared from the corresponding phenylacetylene, with 2,6-dimethyl-2-carbethoxycyclohexanone. The Rupe rearrangement

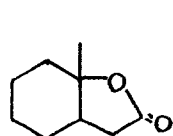


of each acetylenic carbinol gave as the principal product the corresponding ketolactone (XXXIIa and XXXIIb). When either of the lactones was cyclized under Friedel-Crafts conditions, the ketoacid XXXIII was obtained. Preliminary attempts to effect cyclization of XXXIIb with retention of the isopropyl group have been unsuccessful. Wolff-Kishner reduction of the ketoacid XXXIII gave two acids of structure XXXIV.

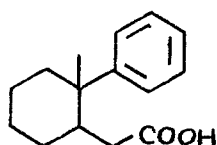
Neither of the isomeric acids (XXXIV) was identical with the des-isopropyldehydroabietic acid obtained by treating dehydroabietic acid (II) with aluminum chloride. It has been postulated (21) that the two synthetic acids of structure XXXIV have the stereochemistry shown below.



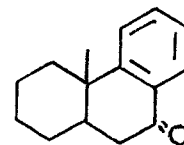
By reacting the lactone of 2-methylcyclohexeneacetic acid (XXXV) with benzene and aluminum chloride, Ghosh (23) has synthesized the acetic acid XXXVI. Cyclization of XXXVI to the phenanthrone XXXVII was accomplished with sulfuric acid.



XXXV

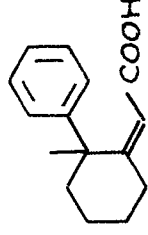
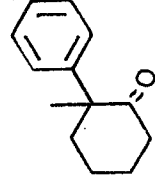
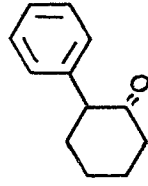


XXXVI



XXXVII

Newman and Farbman (24) accomplished a synthesis of the ketone XXXVII through the same acid XXXVI. Their synthesis consisted of methylating 2-phenylcyclohexanone (XXXVIII) to give XXXIX, and then introducing a two-carbon side chain at the ketonic carbon by means of a Reformatsky



XXXVIII

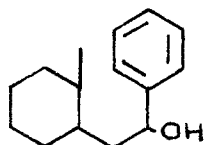
XXXIX

XL

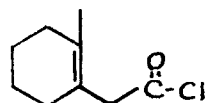
reaction. The unsaturated acid XL thus obtained was reduced catalytically to the acid XXXVI. The ketone XXXVII obtained by this synthesis was a mixture of stereoisomers.

Fry (25) also has reported the use of 2-hydroxycyclohexanecetic acid lactones in the synthesis of hydrophenanthrenes.

In 1941 Nenitzescu (26) reported that the carbinol XLI would cyclize to give the hydrocarbon I. The condensation of the acid chloride XLII and benzene, which it was hoped would give the precursor to the carbinol XLI, was not successful.

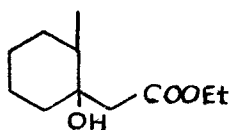


XLI

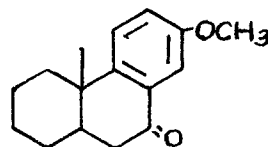


XLII

Deno and Chafetz (27), however, have reported the successful synthesis of the methoxy ketone XLIV by condensing anisole with the hydroxy ester XLIII in the presence of polyphosphoric acid. This reaction does not appear to be of general application (27).

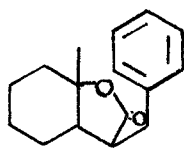


XLIII

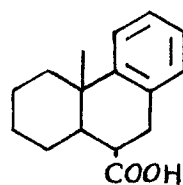


XLIV

Grewe (28) has obtained the acid XLVI by cyclization of the lactone XLV.

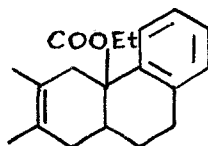


XLV

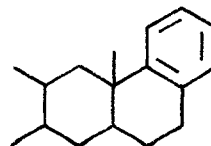


XLVI

Fieser (29) has used the Diels-Alder reaction to form hydrophenanthrenes. Addition of 2,3-dimethylbutadiene to 3,4-dihydro-1-naphthoic ester gave the tricyclic ester



XLVII



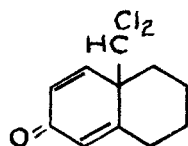
XLVIII

XLVII. Reduction of the ester to the alcohol, conversion to the chloride, and catalytic hydrogenolysis of the chloromethyl group, gave the octahydrophenanthrene XLVIII.

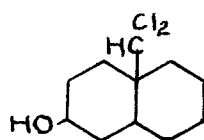
Use of the Reimer-Tiemann reaction for introduction of an angular-methyl group

It has been shown (30) that *o*- and *p*-alkyl substituted phenols, on treatment with chloroform and alkali under the conditions of the Reimer-Tiemann synthesis, were converted to phenolic aldehydes and to cyclohexadienones. The ratio of "normal" to "abnormal" product varied with the structure of the phenol.

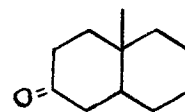
Woodward (31) made use of the "abnormal" Reimer-Tiemann reaction to synthesize 10-methyl-2-decalone (LI). The dichloromethyl ketone XLIX was reduced to the



XLIX



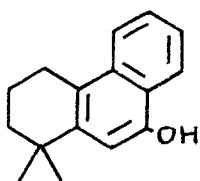
L



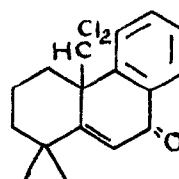
LI

dichloromethyl alcohol L, and this, after hydrogenolysis of the chlorine atoms, was oxidized to the decalone LI.

The introduction of a potential angular-methyl group in the form of a dichloromethyl group was reported by Gibson (32). The phenol LII containing the basic skeleton of ferruginol (XXVII) was converted to LIII by means of a Reimer-Tiemann reaction.

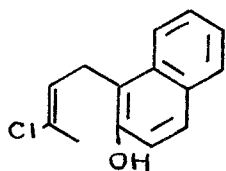


LII

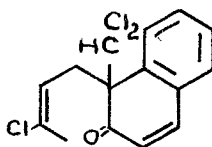


LIII

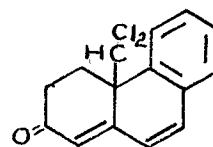
Dodson and Webb (33) attempted the synthesis of 4a-(dichloromethyl)-4,4a-dihydro-2(3H)-phenanthrone (LVI) from the "abnormal" Reimer-Tiemann product LV. The dichloromethyl ketone LV was readily obtained from the



LIV



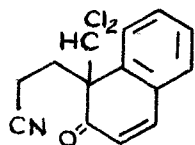
LV



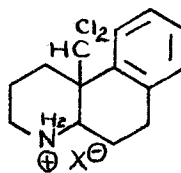
LVI

corresponding naphthol LIV, but the hydrolysis and cyclization of LV was unsuccessful.

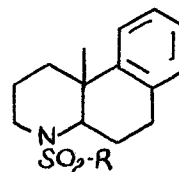
The cyano dichloromethyl ketone LVII, and what was assumed to be the diketone LX, have been prepared as intermediates for phenanthrene syntheses (34). However, LVII



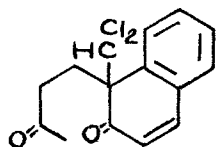
LVII



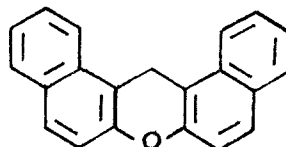
LVIII



LIX



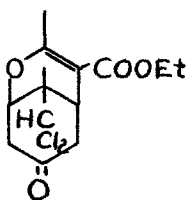
LX



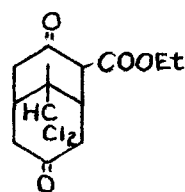
LXI

underwent reductive cyclization on reduction with platinum in acid to give the amine salt LVIII. The structure LIX has been proposed (34) for the sulfonamide of the amine obtained on Clemmensen reduction of LVIII. When the diketone LX was reduced with Raney nickel in basic solution, LXI was obtained (34).

Corley (35) attempted to use the dichloromethyl group introduced by a Reimer-Tiemann reaction as the point of attachment for a six-membered ring, and thereby introduce an angular-methyl directly. The "abnormal" product from



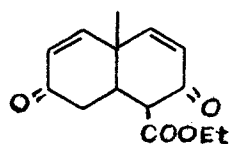
LXII



LXIII



LXIV



LXV

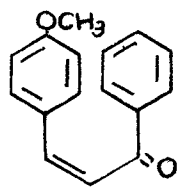
p-cresol and chloroform was reacted with ethyl acetoacetate, and the products examined for the presence of the expected diketoester LXV. The three products isolated (LXII, LXIII, and LXIV) were formed, however, by the initial product of the Michael addition undergoing a second addition to the unsaturated keto grouping present, instead of displacing the chlorine atoms of the dichloromethyl group.

C-Alkylation of phenols by α,β -unsaturated ketones

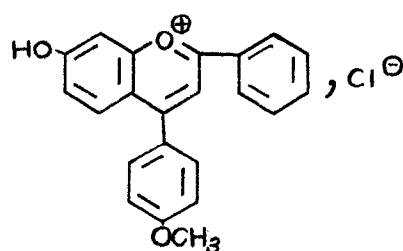
It is well known that a phenol may undergo alkylation reactions either at the oxygen atom, or at the ortho- or para-position. Several examples of C-addition of phenols to α,β -unsaturated ketones are cited here.

Robinson and Walker (36) have condensed resorcinol with several α,β -unsaturated ketones in the presence of

an acid and an oxidizing agent to obtain benzopyrylium salts. An illustration is the addition of resorcinol to the ketone LXVI to give 7-hydroxy-2-phenyl-4-p-methoxy-phenylbenzopyrylium chloride (LXVII).

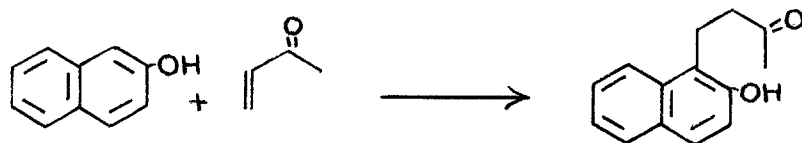


LXVI



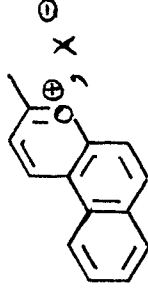
LXVII

The base-catalyzed addition of 2-naphthol to methyl vinyl ketone also was reported by Robinson (37). Using potassium ethoxide as the catalyst, the ketobutyl naphthol LXVIII was obtained.



LXVIII

When an α, β -ethynyl ketone was condensed with a phenol in acid solution it was not necessary to use an oxidizing agent to obtain the benzopyrylium salt. Johnson and Melhuish (38) condensed α, β -ethynyl ketones with several reactive phenols, and obtained the corresponding benzopyrylium salts. That C-alkylation, not O-alkylation, had taken place was shown by the condensation of β -naphthol and methyl ethynyl ketone to give the 2-methyl- β -naphthopyrylium salt LXIX (38).

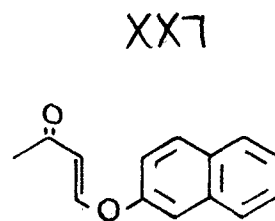
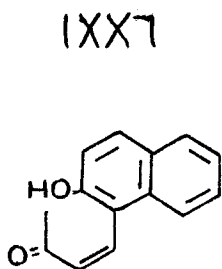
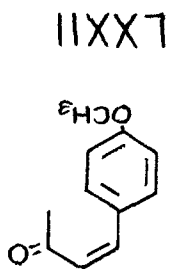


LXIX

It has been shown (39) that 4-chloro-3-buten-2-one gave the same product as methyl ethynyl ketone when condensed with a phenol in the presence of acid. The naphthopyrylium salt LXIX also was obtained by reacting β -naphthol with 4-chloro-3-buten-2-one.

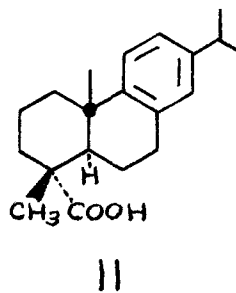
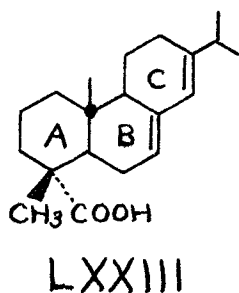
When 2-naphthol and 4-chloro-3-buten-2-one were condensed in basic media, the product was a mixture of the enol ether LXX and the C-alkylation product LXXI (40).

Other workers have observed (41) that anisole and 4-chloro-3-buten-2-one condense in a benzene-stannic chloride solution to give LXXII.



DISCUSSION

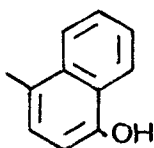
Since abietic acid (LXXIII) and its partly-aromatic counterpart, dehydroabietic acid (II), possess a trans A-B ring fusion (42), any synthetic approach to these natural products must introduce this trans ring system directly, or provide a means whereby it can be made to occur. The introduction of the methyl and carboxyl groups at C-1 also must be controlled stereochemically.



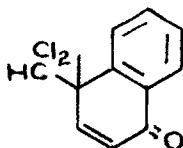
In this study attention was first focused on obtaining a 4a-methylhydrophenanthrene with trans fused A-B rings.

Had the synthetic scheme of Corley (35) been successful, a useful method of obtaining trans decalins would be available. However, the difficulties encountered by Corley (35) (see Historical section) could be overcome by using the known dichloromethyl compound LXXV (43) as the Michael acceptor. Here a second, internal Michael addition was

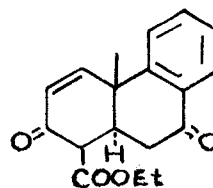
improbable, and reaction in the manner anticipated by Corley (35) would give the ketoester LXXVI. The carbethoxyl group



LXXIV



LXXV



LXXVI

at C-1 in the ketoester LXXVI could not be retained for the synthesis of deg-isopropyldehydroabiatic acid, for methylation at C-1 would occur mainly from the side opposite the angular-methyl, and a product of wrong stereochemistry would be obtained. However, the formation of a phenanthrone via intramolecular displacement of chloride ion from a dichloromethyl group appeared worthy of further study.

The dichloromethyl naphthalenone LXXV has been isolated previously (43) as a product of the "abnormal" Reimer-Tiemann reaction (30) on 4-methyl-1-naphthol (LXXIV). The yield of naphthalenone LXXV from the reaction with chloroform was low (reported as 13.8%) (43), but the naphthol LXXIV was easy to obtain.

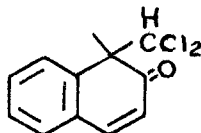
The preparation of the required 4-methyl-1-naphthol was accomplished by two methods. In the first, 1-methylnaphthalene was sulfonated with concentrated sulfuric acid

(44). The sodium salt of the sulfonic acid was isolated by partial neutralization of an aqueous solution of the acid with sodium carbonate, and by salting out the sodium sulfonate with sodium chloride (45). Fusion of the sulfonic acid salt with a KOH-NaOH (1:1) mixture (44, 46) gave crude 4-methyl-1-naphthol in overall yields of 20-50%.

Clemmensen reduction of the known 4-hydroxy-1-naphthaldehyde (47) using ethanol-water as the solvent (48) also yielded 4-methyl-1-naphthol. The slow addition of the aldehyde and the use of enough ethanol in the reaction mixture to keep the reactants in solution were necessary to prevent tar formation. While the purity of the product prepared by reduction of the aldehyde was better than that from the sulfonic acid fusion, the latter was more adaptable to large scale preparation.

The use of the crude naphthol (purified only by vacuum distillation) was satisfactory for the Reimer-Tiemann reaction. In addition to the expected 4-methyl-4-(dichloromethyl)-1(4H)-naphthalenone (LXXV), m.p. 109-110°, a 3-4% yield of the 2-naphthalenone LXXVII, derived from 1-methyl-2-naphthol, was isolated when the starting naphthol was prepared by sulfonation and alkaline fusion. The known 1-(dichloromethyl)-1-methyl-2(1H)-naphthalenone (LXXVII) (33)

was identified by reduction to 1-(dichloromethyl)-1-methyl-2-tetralone, m.p. 71-72° (33).

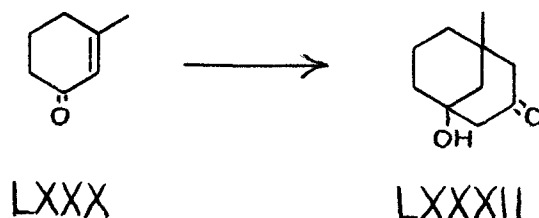


LXXVII

When ethyl acetoacetate was reacted with the Reimer-Tiemann product LXXV using 0.3 mole percent of sodium ethoxide as the catalyst and ethanol as solvent, only one product other than starting materials could be isolated. This compound, $C_{18}H_{20}Cl_2O_4$, m.p. 116-117°, was isolated in 94% yield based on recovered naphthalenone.

Since the dichloromethyl naphthalenone must have a planar, or nearly planar structure, addition of the ethyl acetoacetate anion to this system should occur predominantly on the side of the methyl group. The dichloromethyl moiety would be expected to offer considerably more steric hindrance. Isolation of only one product in high yield tended to verify this expectation.

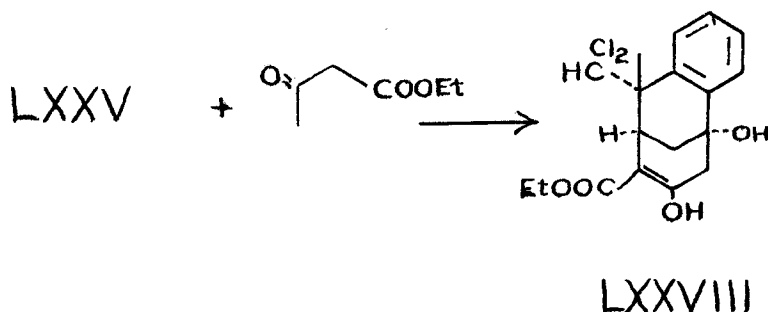
The Michael addition of ethyl acetoacetate to LXXV was carried out successfully using sodium ethoxide or potassium t-butoxide as the catalyst. The adduct was isolated



hydrolyzed and decarboxylated with aqueous base to give the bicyclo [3.3.1] nonanones LXXXI and LXXXII.

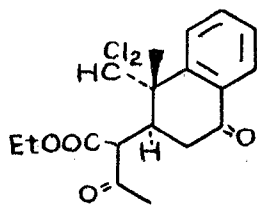
The infrared spectrum also indicated that the adduct was enolized completely. The absence of bands in the 1666-1800 cm.^{-1} region, and the presence of bands at 1640 cm.^{-1} and at 1605 cm.^{-1} , attributed (50) to carbonyl and to carbon-carbon unsaturation, respectively, in the conjugated, chelated enol form, were the basis for this assignment.

From the elemental analysis and the spectral characteristics mentioned above, the adduct was assigned the structure of the enol of ethyl 3-keto-5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo [3.3.1] nonane-2-carboxylate (LXXVIII).

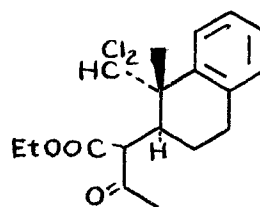


The complete absence in the infrared spectrum of LXXVIII of the bands at 1744 and 1718 cm.^{-1} found in ethyl cyclohexanone-2-carboxylate, and assigned to the ester and carbonyl groups (50), respectively, may be a consequence of the bicyclo[3.3.1]nonane ring system. The spectrum of Corley's compound LXIII, or of any related bicyclic β -ketoester, has not been compared to that of LXXVIII.

By using piperidine and benzene as catalyst and solvent, respectively, for the Michael addition of ethyl acetoacetate to the naphthalenone LXXV, it was possible to isolate the unaldolized adduct, ethyl 2-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-3-ketobutyrates (LXXXIII), m.p. 102-103°.



LXXXIII



LXXXIV

The infrared spectrum of LXXXIII exhibited the expected unconjugated carbonyl absorption with a shoulder at 1730 cm.^{-1} and a peak at 1715 cm.^{-1} . The conjugated carbonyl band was at 1680 cm.^{-1} .

The piperidine catalyzed addition was a slow reaction, and even though the reaction time was ten times that of the ethoxide runs (52 days against 5), 78% of starting material was recovered, and only an 18% yield of unaldolized adduct LXXXIII, and a 1% yield of aldolized adduct LXXVIII were obtained. Since a 20 day reaction gave a 15% yield of unaldolized adduct, the piperidine-benzene reaction may have proceeded to near equilibrium. Increasing the reaction temperature to that of refluxing benzene and shortening the reaction time to 3 days gave a 96% recovery of starting material, and only a 0.3% yield of unaldolized LXXXIII. However, when a similar reaction was conducted in refluxing ethanol (3 days), a 0.4% yield of aldolized adduct LXXVIII and a 94% recovery of starting material were obtained.

When the diketoeater LXXXIII was treated with sodium ethoxide at room temperature, the aldolized product LXXVIII was formed in 35% yield, and 62% of the original naphthalene LXXV was formed by reversal of the Michael addition.

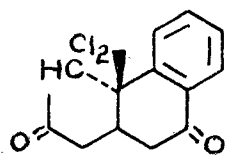
Hydrogenation of the keto group adjacent to the benzene ring in LXXXIII was accomplished readily in the presence of

palladium-on-charcoal catalyst and a small amount of acid. The resulting substituted acetacetic ester LXXXIV should be much more suitable for cyclization to a phenanthrone than would LXXXIII because of the inability of the former to undergo the reverse Michael and aldolization reactions.

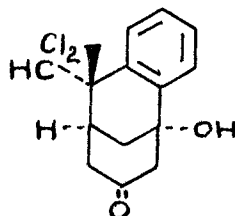
The hydrolysis and decarboxylation of the ethyl acetate adducts LXXVIII and LXXXIII was carried out in ethanolic hydrochloric acid. Basic hydrolysis was not attempted because of the observed tendency of the Michael adduct to revert to naphthalenone. The products isolated were considered to be 4-(dichloromethyl)-4-methyl-3-acetyl-1-tetralone (LXXXV), m.p. 147-148°, and 5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo [3.3.1] nonan-3-one (LXXXVI), m.p. 187-188°. The diketone had absorption bands in the infrared at 1715 cm.^{-1} (saturated carbonyl) and 1680 cm.^{-1} (conjugated carbonyl), while the hydroxy ketone exhibited carbonyl absorption at 1705 cm.^{-1} , as well as OH absorption in the 3500 cm.^{-1} region. The ultraviolet spectra of the diketone had a maximum at 252 $\text{m}\mu$ (ϵ 10,600) characteristic of the 1-tetralone system, while the hydroxy ketone exhibited only a low intensity maximum at 265 $\text{m}\mu$ (ϵ 200).

In the case of the aldolized adduct LXXVIII, the diketone and hydroxy ketone were isolated in 60 and 16%

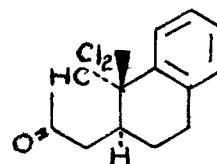
yields, respectively. Similarly, the unaldolized LXXXIII gave 58% of the diketone and 20% of the hydroxy ketone.



LXXXV



LXXXVI

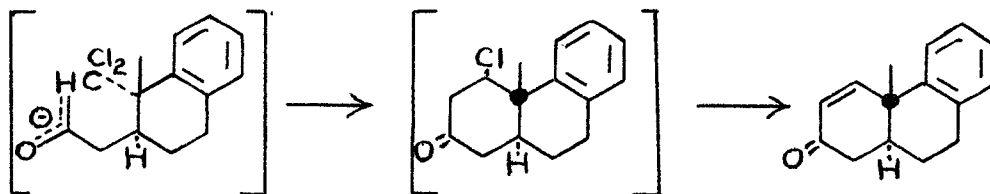


LXXXVII

Removal of the tetralone carbonyl in the diketone LXXXV was desirable, because otherwise on base treatment elimination of the acetone side chain or aldolization could occur. Hydrogenation of LXXXV over palladium-on-charcoal in acid solution gave 1-methyl-1-(dichloromethyl)-2-acetyl-1,2,3,4-tetrahydronaphthalene (LXXXVII), m.p. 82-83°.

As the hydroxy ketone LXXXVI and the diketone LXXXV apparently were in equilibrium in acid solution, it appeared possible to convert the hydroxy ketone LXXXVI to the acetyl compound LXXXVII by reduction in acid medium. The diketone LXXXV would be removed from the equilibrium by reduction to LXXXVII. This proved to be the case, as LXXXVI in acid solution and with 5% palladium-on-charcoal as the catalyst, slowly absorbed hydrogen to give LXXXVII in quantitative yield.

The cyclization of the acetyl compound was the key step in this phenanthrene synthesis. To be successful, the anion formed on the methyl group adjacent to the ketone would have to displace a chloride ion from the dichloromethyl group as shown below. After the initial displacement



LXXXVIII

of chloride ion, the dehydrochlorination to give 4a-methyl-4a,9,10,10a-tetrahydro-2(1H)-phenanthrone (LXXXVIII) would be expected to proceed readily in the β -chloroketo system.

Neopentyl halides are known to undergo bimolecular nucleophilic displacements with difficulty (51). The method of synthesis of the dichloromethyl compound LXXV showed that the abnormal Reimer-Tiemann product was no exception. Internal chloride ion displacement in LXXXVII to give the phenanthrone LXXXVIII should take precedent over displacement by an external base, especially if a strong base of weak nucleophilicity (such as the *t*-butoxide or triphenylmethide anions) was used to form the anion of the acetyl compound LXXXVII. Non-reversible anion formation, such as

occurs with sodium hydride, also should favor the internal displacement reaction.

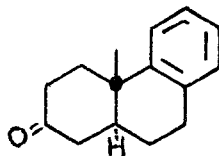
When potassium t-butoxide (3.0 mole/mole of LXXXVII) was used as the base for the cyclization of LXXXVII, no definite product could be isolated. Chloride ion displacement, as evidenced by the formation of potassium chloride in the reaction flask, occurred, but none of the crude material isolated had an infrared spectrum exhibiting the expected conjugated carbonyl band at about 1675 cm.^{-1} .

Similarly, a reaction occurred when sodium hydride was tried, but the infrared spectra of the crude products did not show unsaturated carbonyl absorption.

A 43% yield of 4a-methyl-4a,9,10,10a-tetrahydro-2(1H)-phenanthrone (LXXXVIII), m.p. $103-104^{\circ}$, was obtained when a four-fold excess of sodium triphenylmethyl was used as the base. Due to loss in transferring, the amount of base actually present in the reaction mixture may not have been as high as indicated by the preliminary titrations, but an appreciable yield of phenanthrone was not realized unless enough triphenylmethyl anion was present to keep the reaction mixture a deep red throughout the three-day reaction time. No product other than the phenanthrone was recovered from the mixture obtained on hydrolysis of the reaction, but the infrared spectra of various fractions obtained by

chromatography showed that a considerable amount of unreacted dichloromethyl compound LXXXVII still was present.

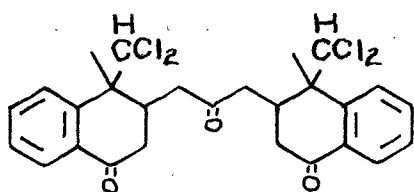
The phenanthrone LXXXVIII readily took up 1 mole of hydrogen to give trans-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (LXXXIX), m.p. 107-108°, in quantitative yield. The assignment of trans fusion to the A-B rings was predicated on the initial stereospecific addition of acetoacetic ester.



LXXXIX

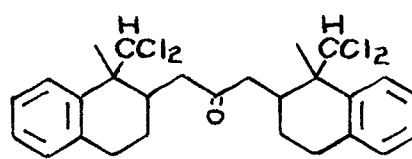
An attempt was made to synthesize the acetyl tetralone LXXXV, or its internal aldol product LXXXVI, by adding acetone to the dichloromethyl compound LXXV. The principal products (62%) of the reaction, run in the presence of potassium t-butoxide, were two high melting (227° and 240°) solids. A mixture of these compounds was isolated easily from the reaction mixture due to their relative insolubility in ethanol. Separation of the two compounds from one another was accomplished by fractional recrystallization from ethanol-ethyl acetate.

The ultraviolet spectra of the two were almost identical, but the infrared spectra (CHCl_3 and nujol mull) were different in the 8-16 μ region. These $\text{C}_{27}\text{H}_{26}\text{Cl}_4\text{O}_2$ compounds were considered to be isomeric 1,3-di-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-2-propanones (XCA and XCB). From the data at hand, no stereochemical assignments could be made. Apparently,



XCA , m.p. 227-228°

XCB , m.p. 240-241°



XCIA , m.p. 190-191°

XCIB , m.p. 186-188°

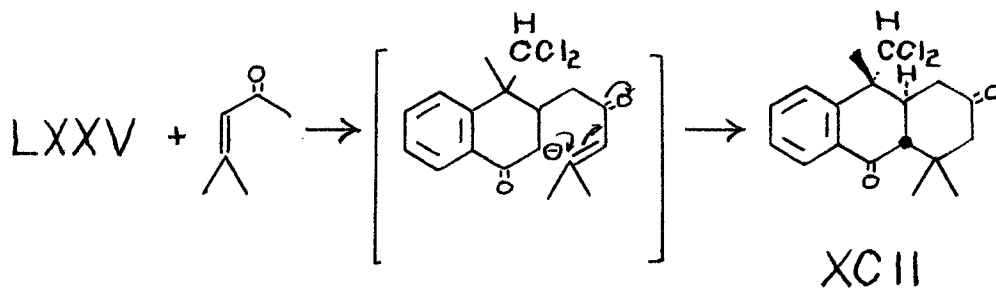
either the addition of acetone to LXXV, or the addition of the initial acetone adduct LXXXV to LXXV, was not stereospecific, with the result that at least one of the isomers had a side chain attached on the same side as the dichloromethyl group.

Both XCA and XCB absorbed 4 moles of hydrogen to give the isomeric propanones XCIA and XCIB. When XCIA, m.p.

190-191°, was admixed with XCIB, m.p. 188-190°, a mixture melting point of 171-174° was observed.

Only trace amounts of the desired products, LXXXV and LXXXVI, could be isolated from the reaction mixture. No sign of the stereoisomers of the acetone adducts could be found, but a complete product balance was not obtained.

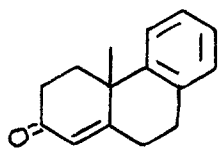
From a similar reaction employing excess acetone, a $C_{18}H_{20}Cl_2O_2$ compound was isolated. Because of the infrared spectrum (carbonyl bands at 1705 and 1675 $cm.^{-1}$), and because of the similarity of the ultraviolet spectrum (maxima at 252 and 290 $m\mu$) to that of LXXXV, it was assigned the octa-hydroanthracene structure XCII.



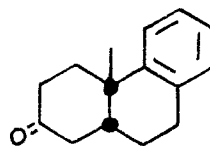
Mesityl oxide could form in the reaction mixture, and the formation of the intermediate shown above could occur by Michael addition of the anion derived from the α -methyl group of mesityl oxide to LXXXV. An internal Michael addition as indicated by the arrows (above) would account for the formation of XCII. The stereochemistry shown for XCII

was based on the assumption that the first addition occurred trans to the dichloromethyl group, and that the more stable trans ring fusion would result from the thermodynamic equilibrium possible in excess base.

Before any attempt was to be made to use the phenanthrone synthesis outlined above for the total synthesis of dehydroabietic acid (II), it was considered necessary to prove conclusively that the A-B ring fusion in LXXXIX was trans. One way to do this would be to obtain 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XCIII), and to reduce it to 4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XCIV or LXXXIX) both catalytically and with lithium in liquid ammonia. The catalytic reduction is known to result, in the case of steroidal Δ^4 -3-ketones and related systems (52), in predominantly cis A-B ring fusion. The



XCIII

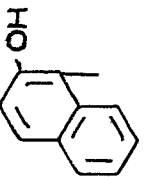


XCIV

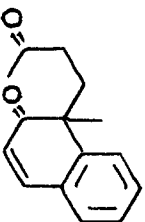
lithium-liquid ammonia reduction should result in the thermodynamically more stable trans fusion (53).

The phenanthrone XCIII should be obtained readily by the addition of methyl vinyl ketone to 1-methyl-2-tetralone (the classical method of Robinson (15)). It was decided, however, to investigate other methods of preparing the desired phenanthrone.

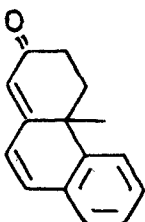
As mentioned in the Historical section, 2-naphthol reacted with methyl vinyl ketone to give 1-(γ -ketobutyl)-2-naphthol (37). If a similar reaction occurred with 1-methyl-2-naphthol (XCV), the γ -ketobutyl naphthalenone XCVI might result. This would be expected to undergo an aldol reaction to give 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (XCVII).



XCV



XCVI



XCVII

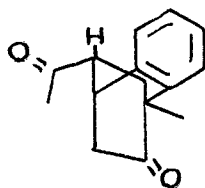
Reduction of 2-hydroxy-1-naphthaldehyde, prepared by the procedure of Adams (47), was accomplished with copper-coated zinc in acetic acid (54) to give 1-methyl-2-naphthol (XCV), m.p. 110-111°.

When the addition of methyl vinyl ketone to 1-methyl-2-naphthol was attempted under the reaction conditions used

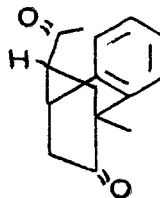
by Robinson (37) for the similar addition to 2-naphthol (sodium ethoxide in ethanol at 5°), 1-methyl-2-naphthol was recovered. There was no sign of any other product.

The addition of methyl vinyl ketone to 1-methyl-2-naphthol then was carried out using 0.1 equivalent of potassium *t*-butoxide as the catalyst. In addition to 1-methyl-2-naphthol, three products were obtained from the oily reaction mixture. Two of these were soluble in petroleum ether, and were separated readily by chromatography on Celite-silicic acid. Both were $C_{15}H_{16}O_2$ compounds, with the isomer of m.p. 103-104° being eluted from the column before the isomer of m.p. 108-109°. Low intensity maxima in the 264, 272 and 294 $m\mu$ regions of the ultraviolet were observed for both isomers. The intensity of absorption shown by the lower melting (ϵ 410, 410, 440) was greater than that of the higher melting isomer (ϵ 390, 360, 390), but no stereochemical assignment was attempted on this basis. The infrared spectra of both compounds possessed an unconjugated carbonyl band at 1715 $cm.^{-1}$, but definite differences appeared in the 7-11 μ region. Each gave a di-2,4-dinitrophenylhydrazone.

They were assigned structures XCVIIIA and XCVIIIB, the stereoisomeric 1-methyl-5,6-benzo-8-acetylbicyclo [2.2.2] octan-2-ones.



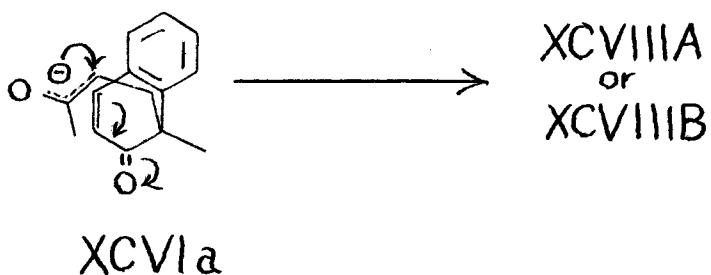
XCVIIIA



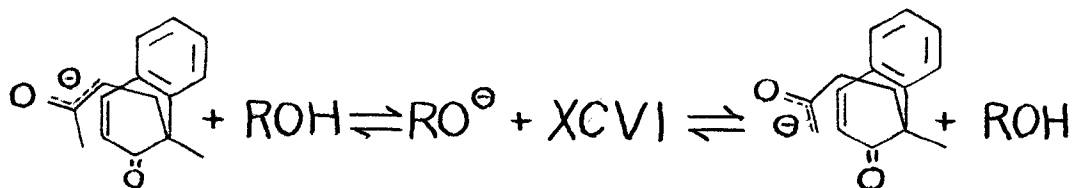
XCVIIIB

Evidence for postulating XCVIIIA and B as being C-8 epimers came from sodium ethoxide equilibration studies. Since C-8 has a hydrogen adjacent to a keto grouping, treatment with base should allow XCVIIIA and B to come to thermodynamic equilibrium via carbanion formation. As the two products were obtained from a potassium *t*-butoxide (mainly potassium naphthoxide) solution in which this equilibrium should have been attained, either XCVIIIA or B should equilibrate to the same mixture as was isolated originally. This was a ratio of 0.69 g. to 1.11 g., or 0.62. When XCVIIIA was treated with an equimolar quantity of sodium ethoxide in ethanol for 10 hours at room temperature, the ratio of XCVIIIA to XCVIIIB isolated was 0.67. Similar treatment of XCVIIIB gave a product ratio of 0.64, confirming that the compounds were epimeric at a carbon atom containing an acidic hydrogen.

The formation of XCVIIIA and XCVIIIB occurred when the initial adduct (XCVI) of methyl vinyl ketone and 1-methyl-2-naphthol underwent a second, internal Michael addition (XCVIa, arrows). The anion XCVIa, formed by the



addition of methyl vinyl ketone to 1-methyl-2-naphthol, may have undergone the second addition before it had any chance to equilibrate with solvent, and with the anion from the methyl group. Had the intermediate γ -ketobutyl compound XCVI existed in the solution for some time, and had the equilibrium shown below been attained, some aldol reaction



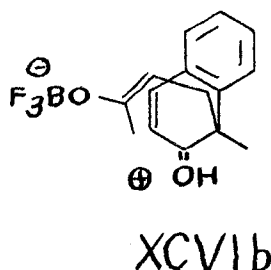
resulting in the phenanthrone XCVII (or the ketol precursor to it) should have occurred. No trace of the phenanthrone (later isolated under different conditions) was found.

The evidence for assigning the configurations of XCVIII A and B rests on three facts. Firstly, XCVIII A was eluted more readily from either an alumina or a silicic acid-Celite column. The two keto groups in these molecules are the only functional groups present that will be adsorbed, and therefore must be protected in one isomer more than in the other. When the acetyl group is on the same side of the two-carbon bridge as the C-2 keto grouping, this hindrance could well be greater than when it is on the side of the benzene ring.

The second observation, the results of ethoxide equilibration, correlated with the first. The more thermodynamically stable XCVIII B was the isomer more strongly adsorbed in chromatography. The interaction of the C-8 acetyl group and one of the C-3 hydrogens in XCVIII A, a 1-3 diaxial interaction in a boat-form cyclohexane ring, should be less favored than the alternative acetyl-benzene ring interaction of XCVIII B.

The third fact to be considered was the product ratio obtained when the reaction was conducted in ether solution using boron trifluoride as the catalyst. Here a definite

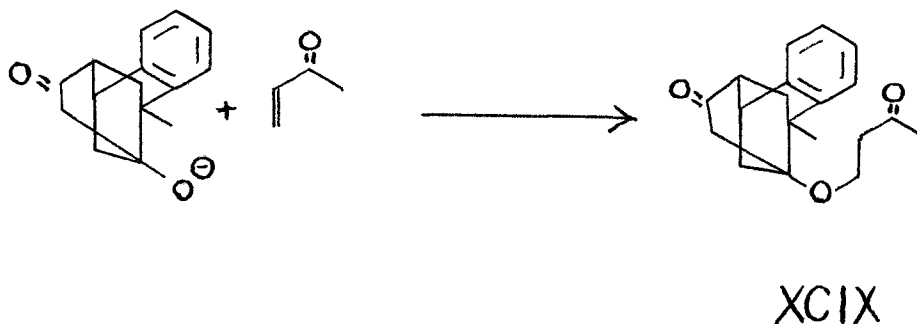
preponderance of XCVIIIA (7:1) was obtained. The boron trifluoride catalyst in this reaction undoubtedly complexed with the keto grouping of methyl vinyl ketone (55). The initial product of the addition (XCVIb) surely would



encounter unfavorable steric and electronic interactions with the benzene ring when it assumed the configuration leading to XCVIIIB. Orientation in the manner leading to XCVIIIA would lead to no such interference.

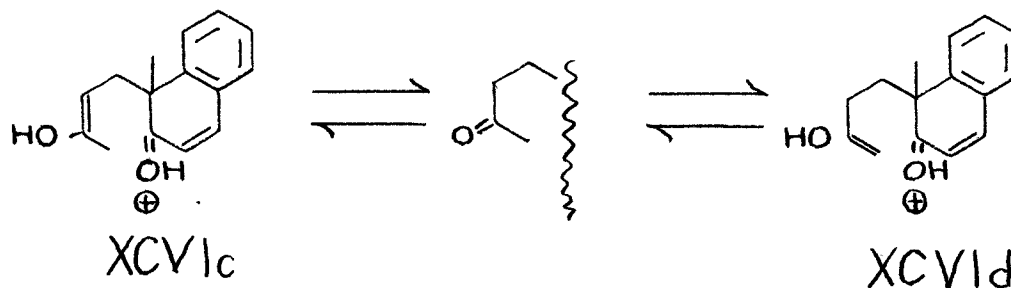
The third product, a $C_{19}H_{22}O_3$ compound melting at 244-245°, was isolated in 4% yield from the petroleum ether-insoluble residues of the reaction mixture. Only saturated carbonyl absorption (1710 cm.^{-1}) was present in the infrared 5-6 μ region, while the broad band at 1100 cm.^{-1} was attributed to the ether linkage. There was no indication of absorption in the 3200-3800 cm.^{-1} region. Only low intensity maxima at 265 and 295 $m\mu$ were present in the ultraviolet spectrum. The presence of two carbonyl groupings in the

molecule was confirmed by the formation of a di-2,4-dinitro-phenylhydrazone which did not exhibit carbonyl absorption in the infrared. On the basis of the data given above, it was formulated as 1-methyl-2-(3-keto-1-butoxy)-5,6-benzo-9-ketotricyclo[2.2.2.2^{2,8}]decane (XCIX).

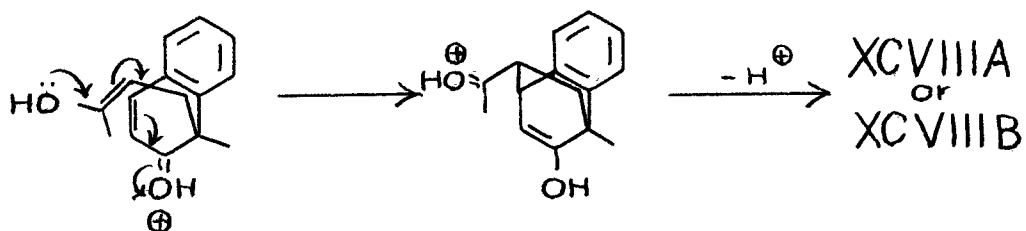


The tricyclic diketone XCIX was formed when XCVIII A underwent an internal aldol reaction to give the anion of the tricyclic ketol shown above. Addition of this alkoxide ion to methyl vinyl ketone resulted in XCIX.

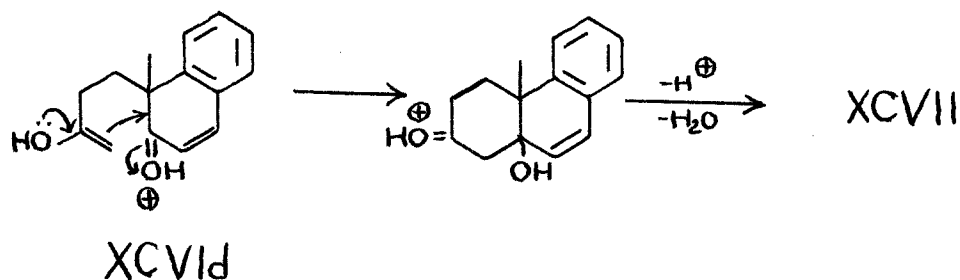
The use of a hydroxylic solvent for the addition reaction was considered next. A medium of this type might be more favorable for the equilibrium shown below. Reaction



of the enolic conjugate acid XCVIc in the manner shown below, and as observed in the boron trifluoride reaction, would give rise to XCVIIIA and XCVIIIB. The desired phenanthrone



(XCVII) would be obtained if XCVId underwent an aldol reaction as indicated below; therefore reaction conditions favorable to the formation of XCVId were sought.

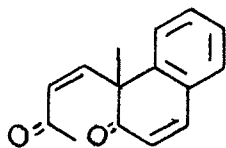


The addition of methyl vinyl ketone to 1-methyl-2-naphthol was carried out in glacial acetic acid, using *p*-toluenesulfonic acid as the catalyst. This led to a mixture of three products, whose separation was accomplished, though inefficiently, by repeated chromatography on silicic acid-Celite and alumina. Small amounts of the isomeric bicyclic diketones XCVIIIA and XCVIIIB were obtained, but the main product (26%) consisted of pale yellow needles melting at 97-98°.

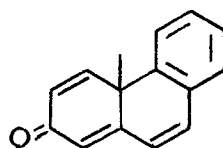
This was considered to be 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone. The ultraviolet spectrum exhibited maxima at 242 and 354 $m\mu$ (ϵ 16,800 and 14,900), and carbonyl absorption in the infrared was at 1655 cm.^{-1} .

The addition also was successful when ethanol saturated with gaseous hydrochloric acid was used as solvent and catalyst. However, an 89% recovery of naphthol and only a 6% yield of phenanthrone were realized.

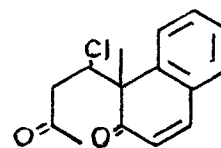
The base-catalyzed addition of methyl vinyl ketone to 1-methyl-2-naphthol failed to give a phenanthrene because of the occurrence of an internal Michael reaction (discussed above). This difficulty might be overcome by using an acceptor that would possess, after the initial addition, an α, β -unsaturated carbonyl system in the side chain (C). The double bond in the γ -ketobutyl side chain not only might prevent the system from attaining the geometry necessary for an internal Michael addition, but also would make



C



CI



CII

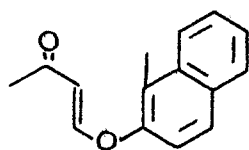
for an unfavorable anion on the double bond adjacent to the carbonyl group.

This assumption was tested using 4-chloro-3-buten-2-one. The C-alkylation adduct CII from this ketone and 1-methyl-2-naphthol was expected to undergo rapid β -elimination of chloride ion to give the γ -ketobutenyl naphthalenone C.

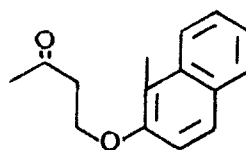
When 4-chloro-3-buten-2-one was reacted with 1-methyl-2-naphthol in the presence of 1.1 equivalent of potassium t-butoxide, a $C_{15}H_{14}O_2$ compound melting at $70-71^\circ$ was

isolated in 43% yield. A maximum in the ultraviolet was observed at $245\text{ m}\mu$ (ϵ 24,600), and carbonyl absorption in the infrared was found at 1675 cm.^{-1} . This product absorbed 1 mole of hydrogen when hydrogenated over 5% palladium-on-charcoal to give a product melting at $51\text{-}52^\circ$. The hydrogenation product exhibited an ultraviolet spectrum similar to a naphthol, with maxima at 230, 282, 322 and $335\text{ m}\mu$ (ϵ 69,000, 5,200, 1,700, 1,700, respectively). Saturated carbonyl absorption (1710 cm.^{-1}) was observed in the infrared spectrum.

The structure of the hydrogenation product, 4-(1-methyl-2-naphthoxy)-2-butanone (CIV), was established by base treatment. With methanolic sodium hydroxide, a 98% yield of 1-methyl-2-naphthol was obtained from the butanone CIV. The naphthol resulted from the facile β -elimination of 1-methyl-2-naphthoxide ion from the β -naphthoxy ketone CIV.



CIII



CIV

However, treatment with potassium t-butoxide gave, in addition to 1-methyl-2-naphthol, the three products (XCVIII A, XCVIII B and XCIX) isolated previously by the butoxide-catalyzed addition of methyl vinyl ketone to 1-methyl-2-naphthol. The ratio of XCVIII A to XCVIII B found here (0.63) agreed with the previous equilibration data.

The assignment of the naphthoxy butanone structure to CIV implied that the $C_{15}H_{14}O_2$ compound was 4-(1-methyl-2-naphthoxy)-3-buten-2-one (CIII).

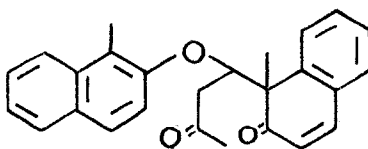
The same naphthoxy butenone CIII was isolated when the anhydrous sodium salt of 1-methyl-2-naphthol was reacted with 4-chloro-3-buten-2-one in acetonitrile or in dioxane. When methanolic sodium hydroxide was used, 1-methyl-2-naphthol was recovered cleanly.

Addition of 4-chloro-3-buten-2-one to 1-methyl-2-naphthol undoubtedly resulted in the formation of the O-alkylation product, 4-(1-methyl-2-naphthoxy)-4-chloro-2-butanone, and this product underwent dehydrochlorination to give CIII.

Failure to find any indication of a C-alkylation product from the base-catalyzed 4-chloro-3-buten-2-one reactions may be attributed to several factors. Apparently the dehydrochlorination of 4-(1-methyl-2-naphthoxy)-4-chloro-2-butanone proceeded readily, and the resulting naphthoxy butenone CIII

was stable under the reaction conditions. The butenone CIII theoretically could revert to starting material via chloride ion addition, and elimination of naphthoxide ion, but the weak nucleophilic properties of chloride ion preclude this reversion.

Formation of the desired C-alkylation product conceivably could occur by C-addition of a naphthoxide ion to the naphthoxy butenone CIII. If the resulting butanone CV underwent β -elimination of the naphthoxy portion of the



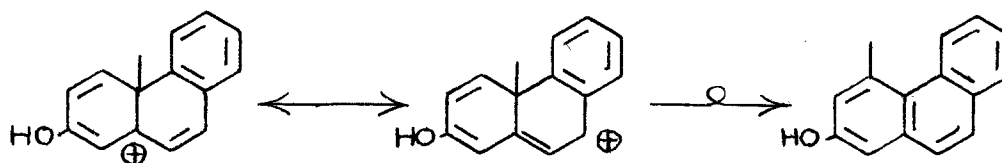
CV

molecule, the γ -ketobutenyl naphthalenone C would result. As a several-fold increase in the reaction time gave neither any indication of the desired product C, nor resulted in any decrease in the yield of CIII obtained, it was concluded that the formation of CIII was irreversible in this case.

The isolation of only CIII implied that the rate of O-alkylation of 4-chloro-3-buten-2-one was very much greater than the rate of C-alkylation.

The points discussed above contrast with the methyl vinyl ketone addition. Here O-alkylation was reversible via β -elimination of the naphthoxide ion; hence the compounds isolated were the slowly formed, but more stable, C-alkylation products. This assumption was confirmed by the rearrangement of the naphthoxy butanone CIV to the same products isolated by addition of 1-methyl-2-naphthol to methyl vinyl ketone.

Acid-catalyzed addition of 4-chloro-3-buten-2-one to 1-methyl-2-naphthol also was tried. If C-alkylation were to occur, and if the expected aldol reaction would take place to give CI, the chance that 4a-methyl-2(4aH)-phenanthrene (CI) actually could be isolated would be small. A dienone such as CI is known to undergo the dienone-phenol rearrangement (56) in acid to give a phenolic product. In this case, 2-hydroxy-4-methylphenanthrene (CVI) would be the expected product. Conventional methyl migration would probably occur when an aromatic ring and double bond are in conjugation with the dienone grouping, as contributing species to the resonance hybrid permit the 10,10a-bond to acquire some double bond character.



CVI

However, neither boron trifluoride in ether nor *p*-toluenesulfonic acid in glacial acetic acid gave the expected phenanthrol. When a catalytic amount of either acid was used, a 95% recovery of 1-methyl-2-naphthol, and a trace of a solid, m.p. 158-160°, was obtained. The trace of product had peaks at 1680, 1350 and 1420 cm^{-1} in the infrared, but no band in the OH region. This product was not investigated further.

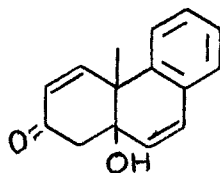
Use of excess boron trifluoride in ether gave a small amount of oily material, and a 50% recovery of naphthol. The oily product had a broad absorption band at 1660 cm^{-1} in the infrared, but the absorption bands in the 7-11 μ region were not the same as 4a-methyl-2(4aH)-phenanthrone. This oil also was not investigated further.

Another route to the γ -ketobutenyl adduct C would be via methyl ethynyl ketone. The addition of 1-methyl-2-naphthol to it could give, obviously, the naphthoxy butenone CIII, as well as the desired C-alkylation product.

When the reaction was tried using 0.1 equivalent of potassium t-butoxide as catalyst, a mixture of products was obtained. Separation of the mixture by chromatography on silicic acid-Celite gave a 25% recovery of 1-methyl-2-naphthol, a 25% yield of the naphthoxy butanone CIII, a small amount of a yellow oil and 26% of a $C_{15}H_{14}O_2$ compound melting at 132-134°.

The yellow oil was purified by chromatography on alumina, but apparently was not homogeneous. It could not be obtained crystalline at room temperature, but would solidify at -10°. When it was converted to a 2,4-dinitrophenylhydrazone, a mixture of purple and orange crystals was obtained. It probably was predominantly 4a-methyl-2(4aH)-phenanthrone (CI).

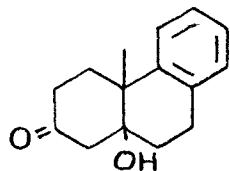
The $C_{15}H_{14}O_2$ compound exhibited the spectral characteristics expected of 4a-methyl-10a-hydroxy-4a,10a-dihydro-2(1H)-phenanthrone (CVII). The maxima in the ultraviolet were at 222 and 264 $m\mu$ (ϵ 28,000 and 7,500), and were attributed to the α, β -unsaturated ketone and styryl chromophores, respectively. The infrared had peaks at 1675 $cm.^{-1}$ (conjugated carbonyl), and at 3340 $cm.^{-1}$ (OH group).



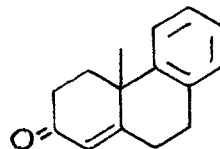
CVII

Elemental analysis of the 2,4-dinitrophenylhydrazone of CVII indicated that it, as anticipated, underwent dehydration during derivative formation. This derivative, m.p. 203-204° dec., did not depress the melting point of the purple 2,4-dinitrophenylhydrazone melting at 194-196° obtained from the oily CI.

Hydrogenation of CVII over palladium-on-charcoal led to 4a-methyl-10a-hydroxy-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (CVIII), m.p. 157-158°. The isolation of only one product in the case of CVII and CVIII indicated that only one diastereoisomer of CVII was produced by the addition reaction. This was probably the thermodynamically more stable product. A related condensation reaction led to a ketol that was assigned the cis configuration (57).



CVIII



XCIII

The hydroxy phenanthrone CVIII was dehydrated cleanly with *p*-toluenesulfonic acid in benzene to give 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XCIII), m.p. 89-90°.

Reduction of XCIII with lithium in liquid ammonia (57, 58) gave a 70% yield of trans-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (LXXXIX). This product was identical with the phenanthrone obtained through the cyclization of the acetyl dichloromethyl tetralin LXXXVII, confirming the trans structure originally assigned to the Δ^3 -phenanthrone LXXXVIII.

When 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (XCVII) was hydrogenated with palladium-on-charcoal catalyst, 2 moles of hydrogen were absorbed readily. The oily product was chromatographed on alumina, and an 11% yield of trans-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (LXXXIX) was obtained. The major product of the reduction was an oily, saturated ketone assumed to be

cis-4a-methyl-3,4,4a-9,10,10a-hexahydro-2(1H)-phenanthrone (XCIV). This oil could not be obtained crystalline at room temperature, but would crystallize on standing overnight at -10° , only to revert to an oil on slight warming. The infrared spectrum was different from that of the solid trans phenanthrone.

Attempts to prepare a 2,4-dinitrophenylhydrazone of the cis phenanthrone were not fruitful. Even after repeated recrystallizations from ethanol and ethanol-ethyl acetate, and after chromatography on alumina, an amorphous product melting at about $98-103^{\circ}$ was obtained. The same derivative from the trans phenanthrone also was difficult to purify. The melting point, after recrystallizations and chromatography, gradually rose from $162-170^{\circ}$ to $199-200^{\circ}$, but the elemental analysis did not check.

Semicarbazone and p-nitrophenylhydrazone formation on both the cis and trans products was more successful. The cis p-nitrophenylhydrazone, again difficult to purify, melted at $148-150^{\circ}$ dec., and that of the trans had a m.p. of $178-180^{\circ}$ dec. The semicarbazones were readily prepared, however. The cis derivative melted at $195-197^{\circ}$ dec., and the trans at $220-221^{\circ}$ dec. When the isomeric semicarbazones were admixed, no definite depression of melting points was

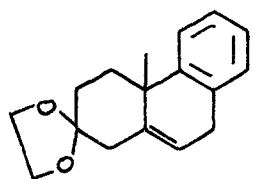
observed, but considerable preliminary darkening with a melting point of 199-201° dec. was noted.

The infrared spectra of the semicarbazones in nujol (not recorded in the Spectra section) showed definite differences. The bands at 1570 and 1088 cm.^{-1} in the cis were displaced to 1590 and 1077 cm.^{-1} in the trans. In addition, the sharp cis band at 764 cm.^{-1} was broadened in the trans, and a peak at 742 cm.^{-1} in the cis was missing in the trans.

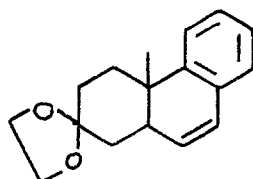
Hydrogenation of the Δ^1 -phenanthrone XCIII with palladium-on-charcoal also gave predominantly cis phenanthrone XCIV. The presence of some trans phenanthrone was indicated by the infrared spectra of fractions isolated by chromatography on alumina. The main fraction, purified by chromatography on alumina, gave a semicarbazone melting at 195-197°. This did not depress the melting point of the same derivative prepared from the oily reduction product of 4a-methyl-~~4~~,4a-dihydro-2(3H)-phenanthrone.

That the yellow oil obtained from the methyl ethynyl ketone addition to 1-methyl-2-naphthol was mainly 4a-methyl-2(4aH)-phenanthrone was indicated by reducing it over palladium-on-charcoal. It absorbed 3 moles of hydrogen to give a good yield of cis-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone, identified by infrared spectrum and semicarbazone formation.

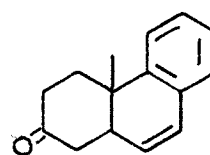
It has been shown that the formation of ethylene ketals of steroidal Δ^4 -3-ketones was accompanied by migration of the double bond to the 5,6-position (59). If similar double bond migration were to occur on formation of the ethylene ketal of XCIII (leading to CIX), it should be possible to effect the further migration of the double bond into conjugation with the benzene ring. Migration of the double bond from the 10,10a- to the 9,10-position in the ketal CIX would give the Δ^9 -ketal CX possessing the thermodynamically more stable A-B ring fusion. Hydrolysis of the ketal, and reduction of the double bond in the ketone CXI, would give either of the saturated phenanthrones, LXXXIX or XCIV. A somewhat analogous reaction of a steroid derivative led to a product with rings A-B trans fused (60).



CIX



CX



CXI

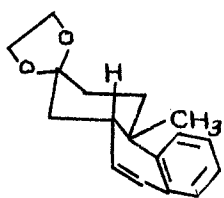
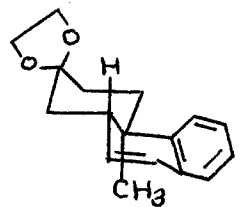
The ketal CIX was prepared in the usual manner (59), but was not purified or characterized. The infrared spectrum of the crude product showed no absorption in the 5-6 μ region, and the ultraviolet exhibited a maximum at

265 m μ (ϵ 400). The ketal was heated with KOH in ethylene glycol at 190°, and the crude product from this was hydrolyzed with acid. Chromatography of the hydrolysis residues gave a 16% yield of a ketone melting at 68-69°. This ketone (CXI) showed saturated carbonyl absorption in the infrared, and the ultraviolet had a maximum at 267 m μ (ϵ 9,800) characteristic of the styryl chromophore.

Hydrogenation of CXI over palladium-on-charcoal gave a clean yield of an oily product whose infrared spectrum was identical with that of the cis phenanthrone XCIV. Confirmation of the cis configuration for the reduction product was obtained from the melting point, mixed melting point, and infrared spectrum of the semicarbazone. This led to the assignment of cis A-B ring fusion in CXI.

The isolation of only a small yield (16%) of the Δ^9 -phenanthrone (CXI) from the ketal equilibration prevents any rigorous statement regarding the stability of cis and trans ring fusion in CX. However, as only cis was isolated, it can be assumed that cis is the more stable. This observation contrasted with that found in a related reaction (60), and was somewhat unexpected in view of the usual greater stability of the trans isomer in fused systems such as this (61).

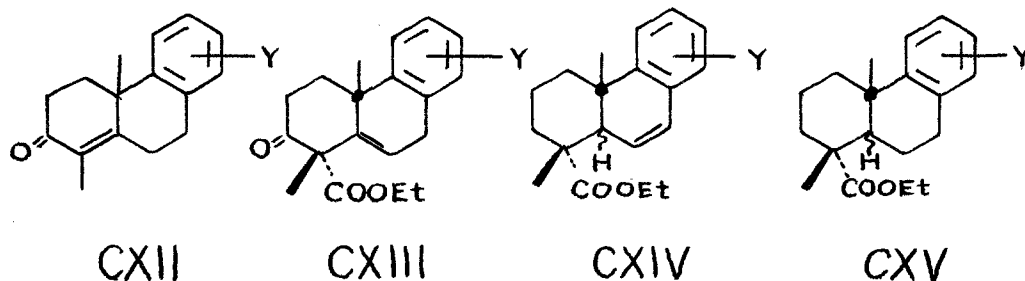
In the 9-methyldecalin system, the energy difference between cis and trans ring fusion is only about 0.8 kcal (61). However, the ketal CX does not possess a true decalin ring system due to the double bond at C-9 and the benzene ring attached at carbons 4b and 8a. The two double bonds in ring B require an almost planar structure for this ring. Thus, the energy differences between cis CX and trans CX (below) would be due essentially to the difference between the angular methyl being axial (trans fusion), and the

cis CXtrans CX

C-4a,4b-bond being axial (cis fusion). The methyl group might well encounter greater 1,3-diaxial interactions from the hydrogens at C-1 and C-3 than would the trigonal C-4b.

If it can be assumed that the cis ketal CX is thermodynamically favored over the trans, an attempt to use a Δ^1 -phenanthrene such as CXII for the synthesis of ring-C-aromatic tricyclic diterpenes could well be unsuccessful. (A phenanthrene such as CXII could be obtained using ethyl

vinyl ketone in the scheme of Robinson (15), or by using the appropriate 1-methyl-2-naphthol and ethyl ethynyl ketone in the manner outlined above.) Carbalkoxylation of CXII



should lead to CXIII. In an analogous case, Woodward and Barton (60) dimethylated cholestenone at C-4 (equivalent to C-1 in CXII). After reduction of the keto grouping in CXIII, migration of the double bond from C-10,10a to C-9,10 (giving CXIV) probably would be necessary, as reduction of CXIII to give trans ring fusion would present difficulties. If, however, CXIV possessed a cis ring fusion, and the result of the ketal equilibration indicates that such stereochemistry might obtain, the synthesis would produce a diastereoisomer of the desired product.

The possibility exists that CXII could be reduced to the saturated ketone via lithium and liquid ammonia to give the necessary trans ring fusion, but carboxylation of the saturated ketone might not occur at C-1.

Attempts to convert a compound of the CXII type to a tricyclic diterpene by methods other than those discussed above are in progress in another laboratory (17).

SPECTRA

All infrared absorption spectra were recorded using a Baird Double Beam infrared spectrophotometer. Ultraviolet spectra were run in 95% ethanol using a Beckman model DU quartz spectrophotometer. Special thanks are due the Institute for Atomic Research, Iowa State College, for the use of the infrared spectrophotometer.

Figure 1

Ultraviolet Spectra

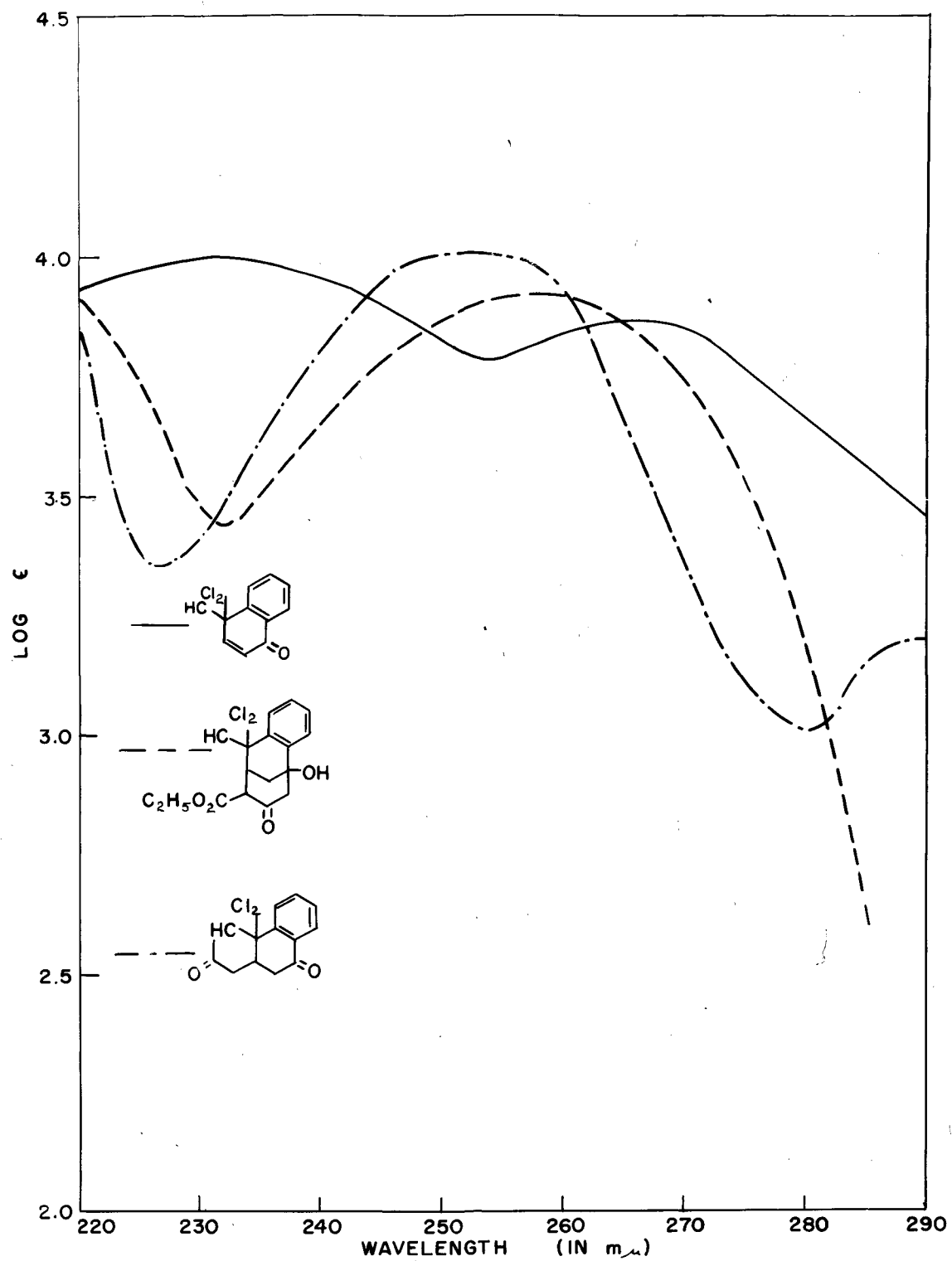


Figure 2

Ultraviolet Spectra

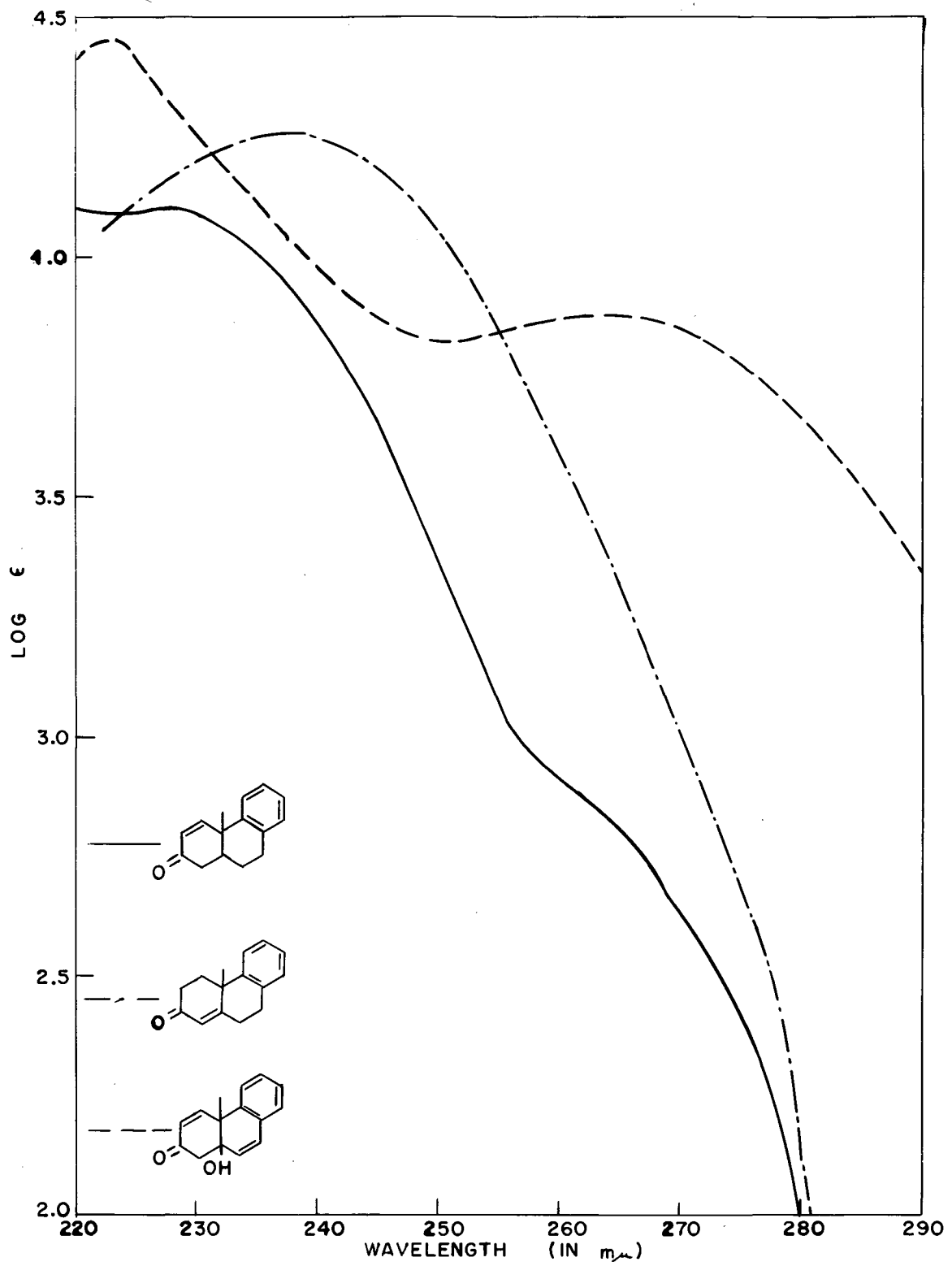


Figure 3

Infrared Spectra

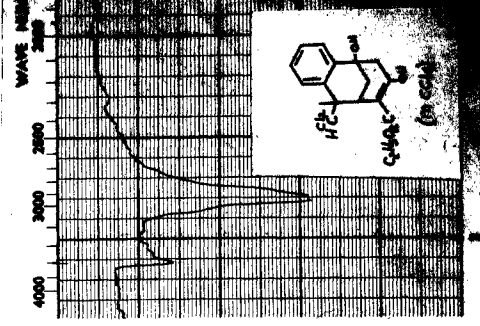
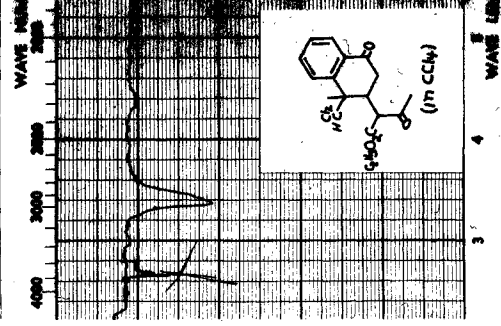
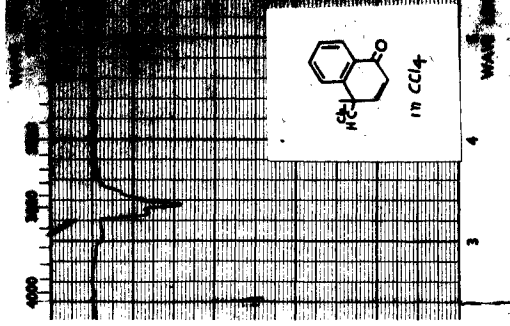


Figure 4

Infrared Spectra

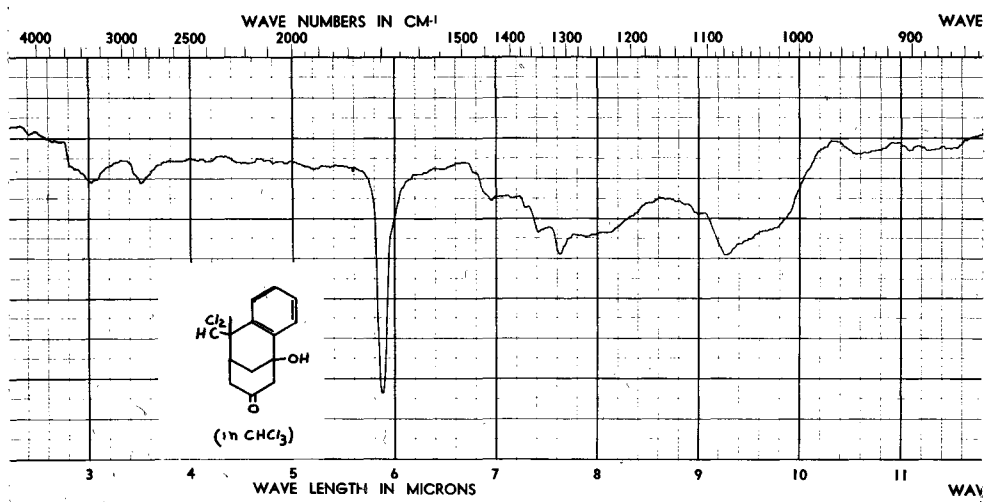
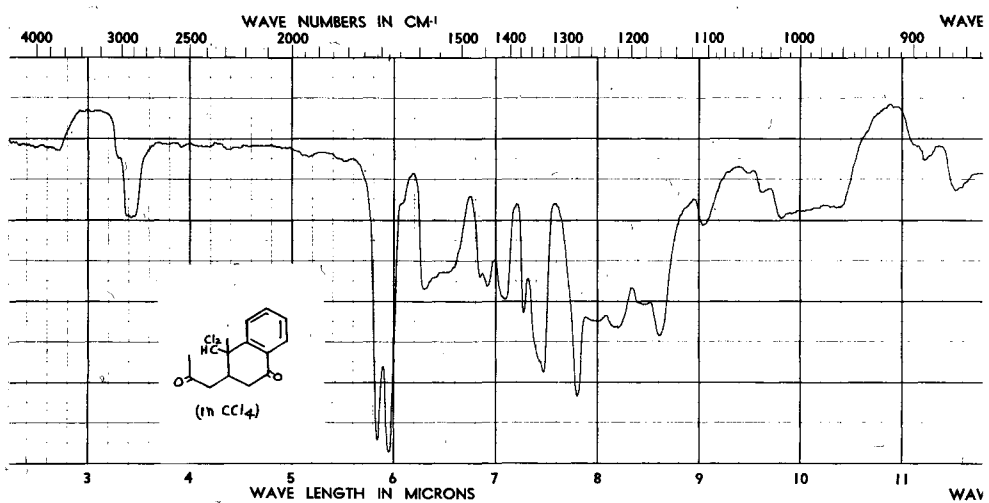
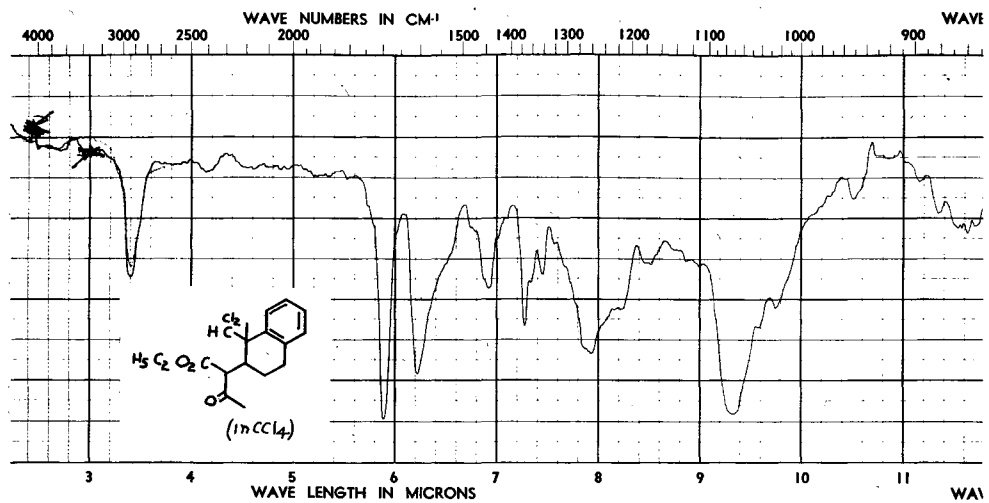


Figure 5

Infrared Spectra

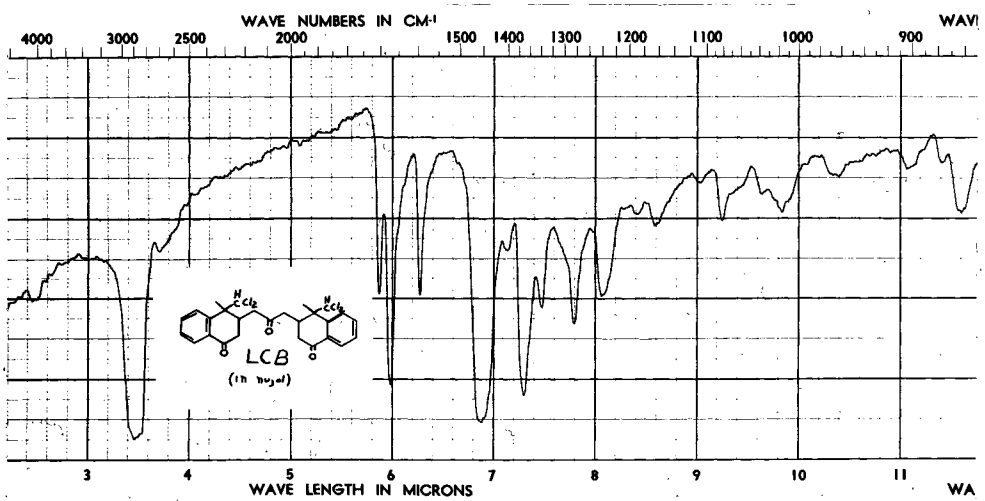
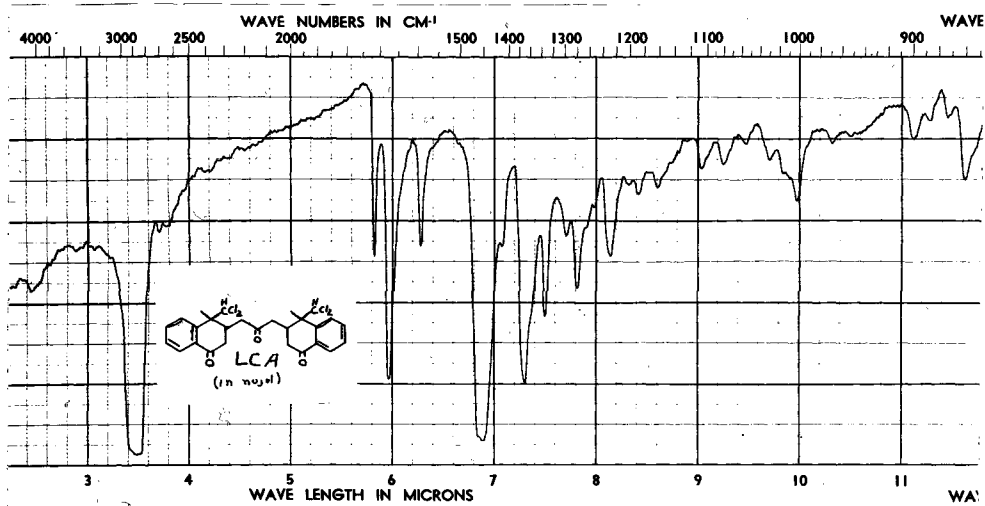
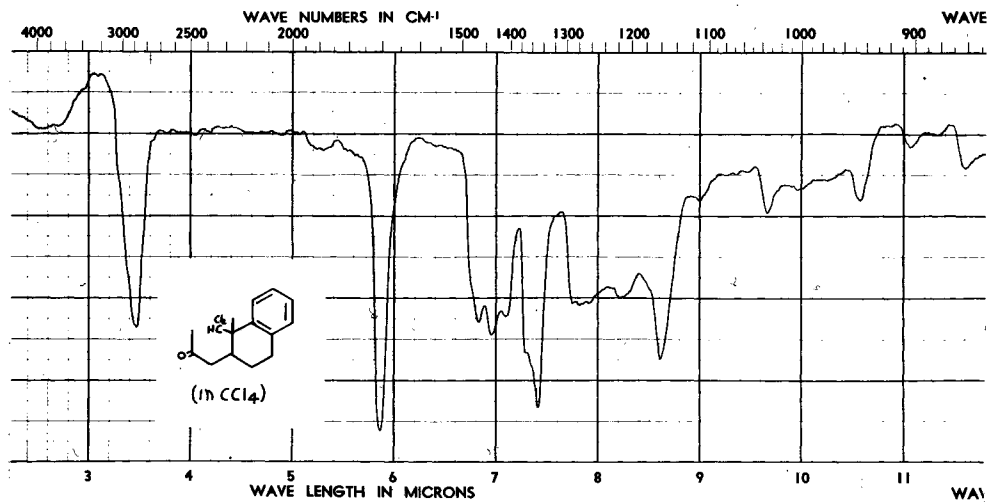


Figure 6

Infrared Spectra

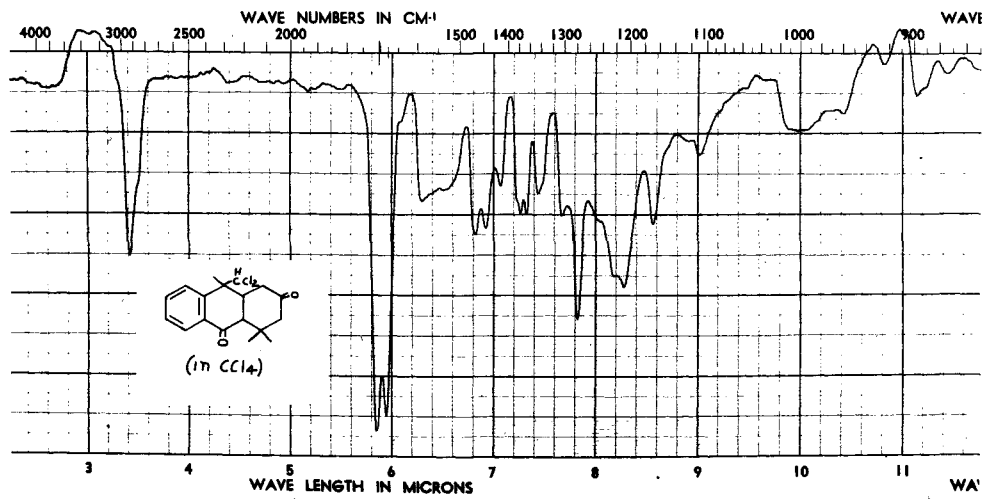
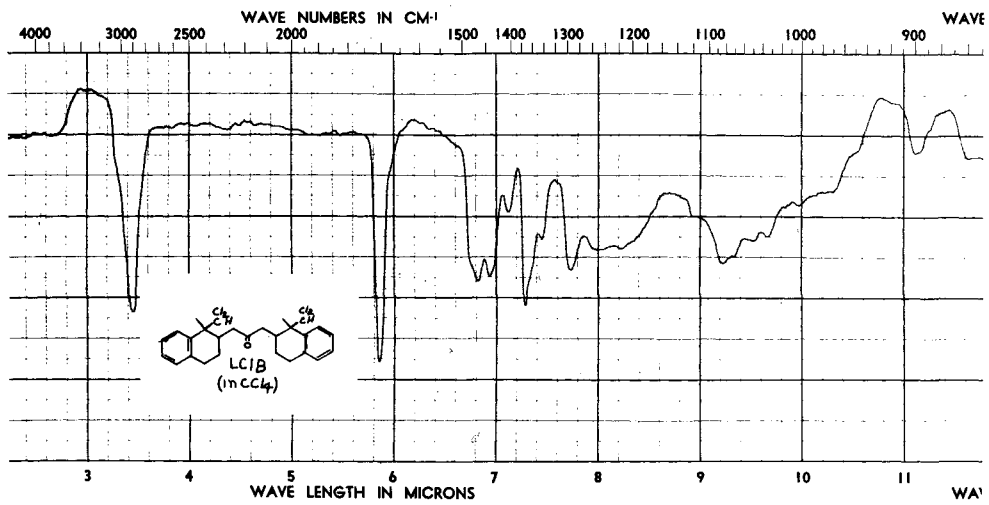
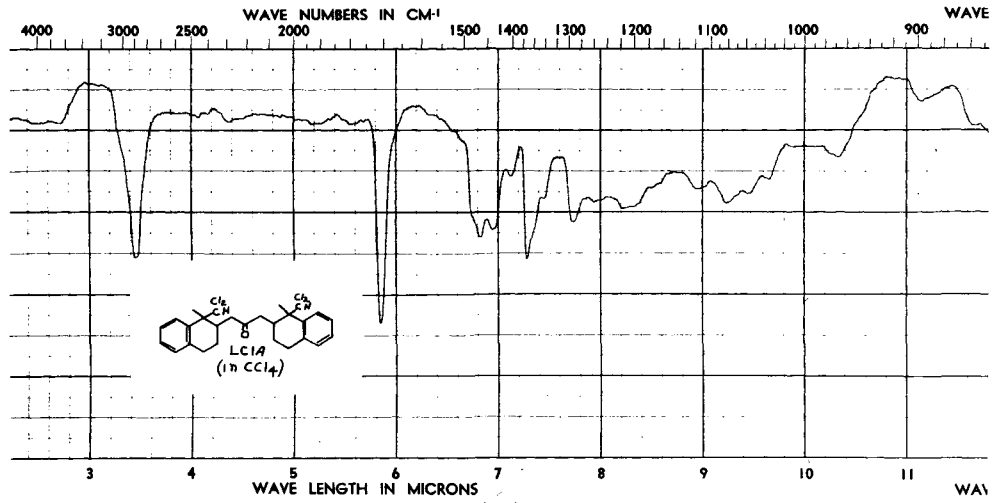


Figure 7

Infrared Spectra

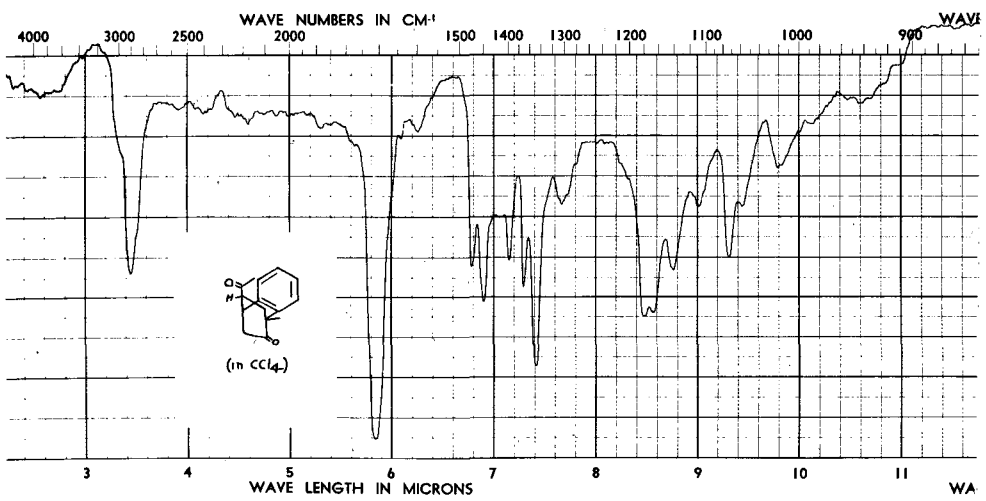
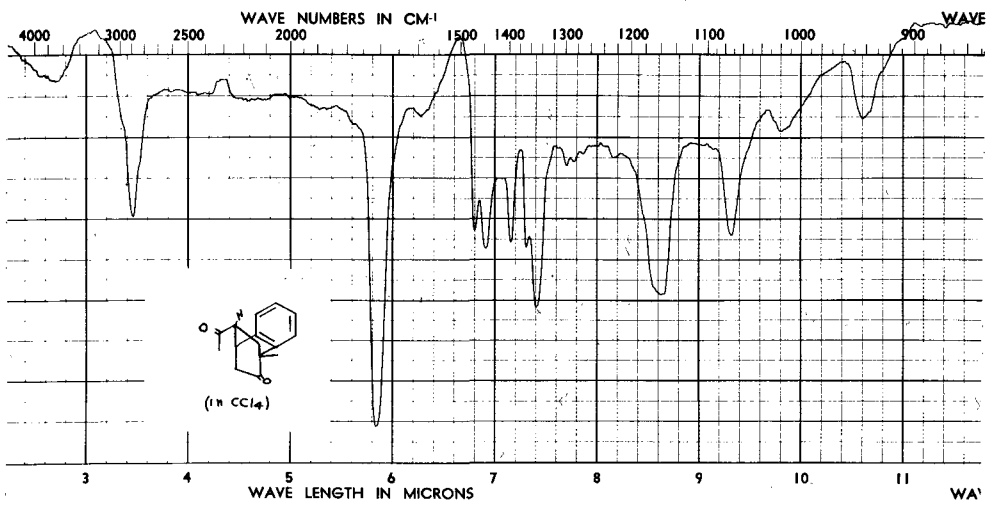
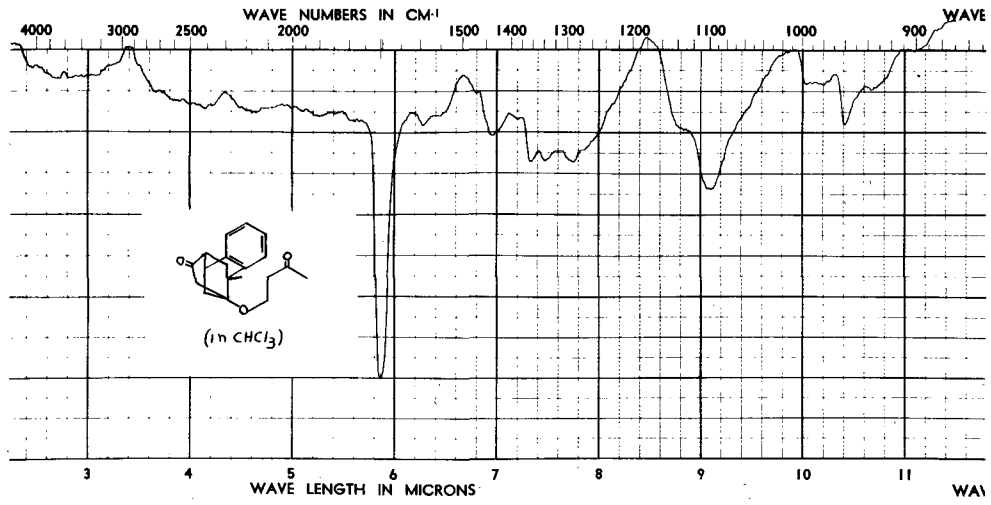


Figure 8

Infrared Spectra

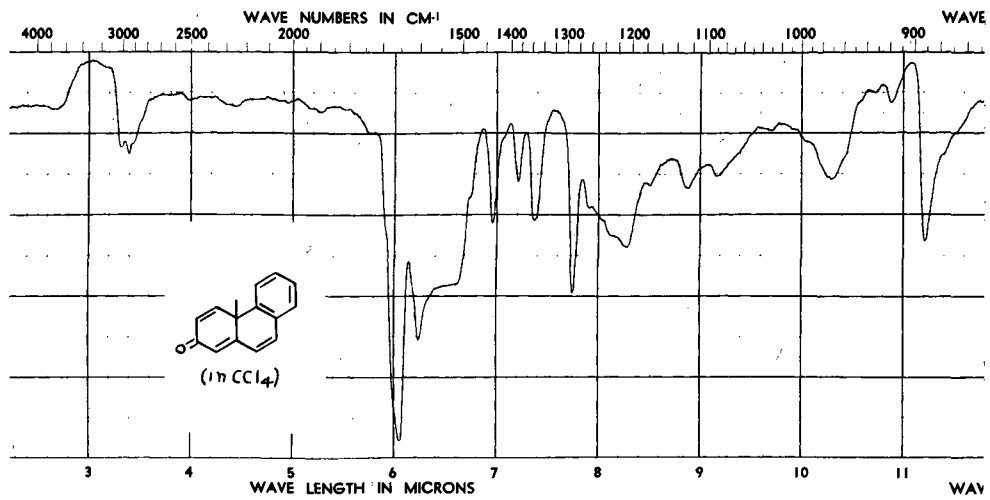
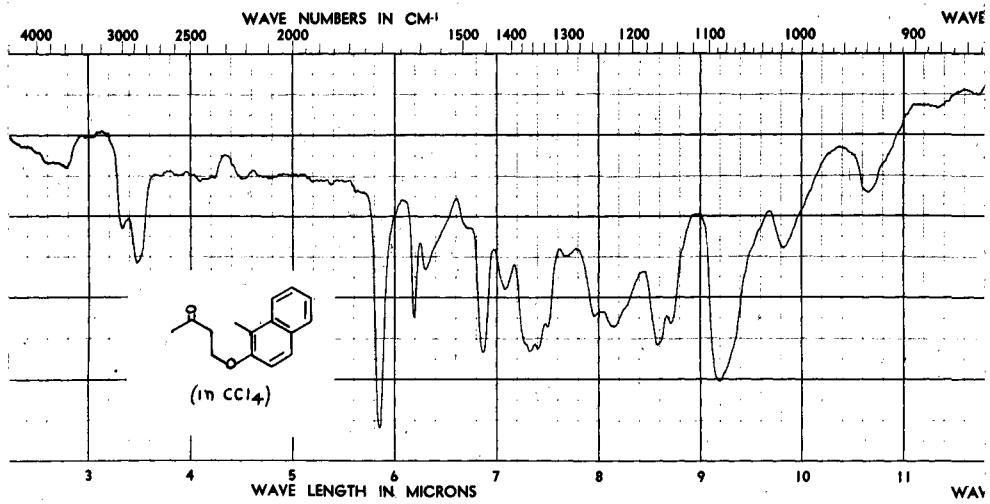
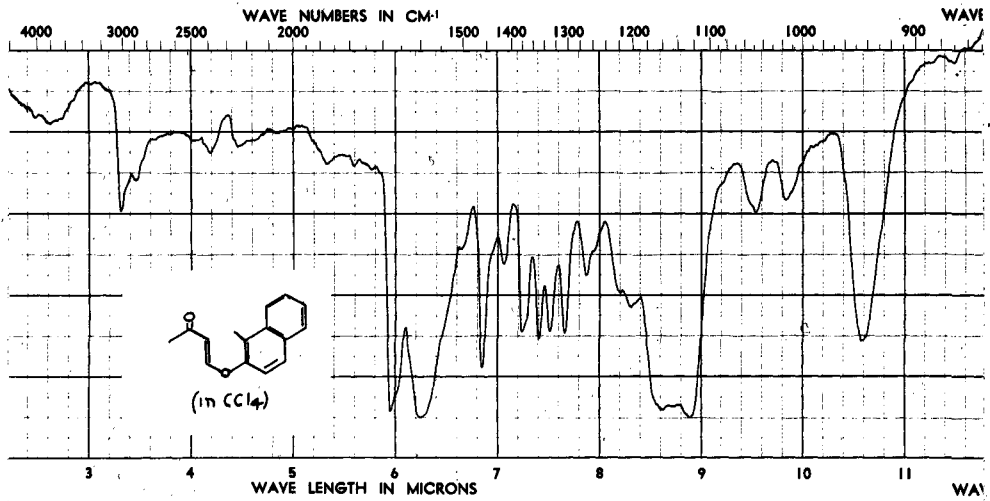


Figure 9

Infrared Spectra

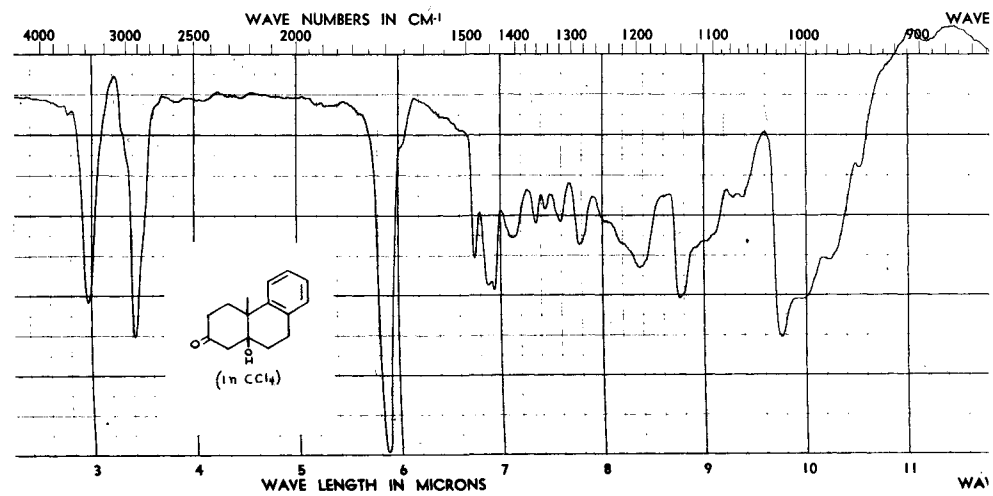
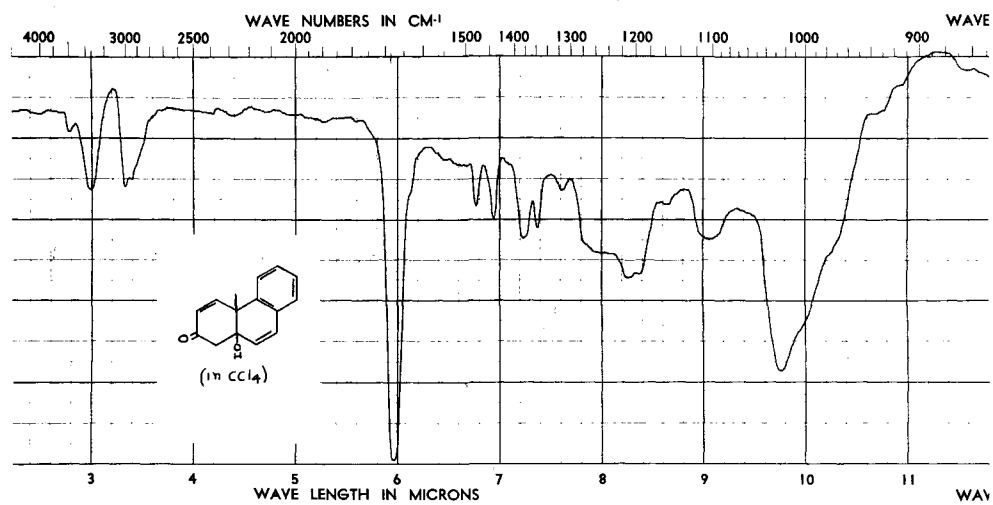
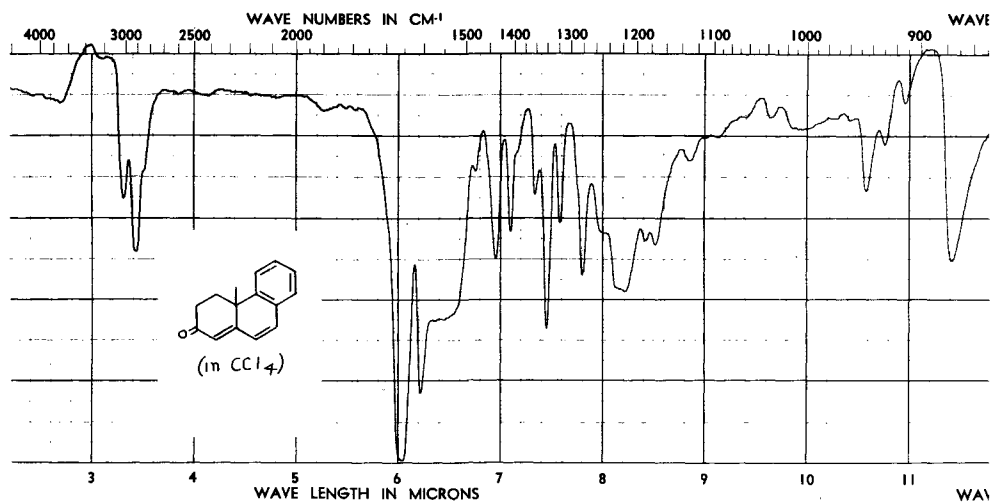


Figure 10

Infrared Spectra

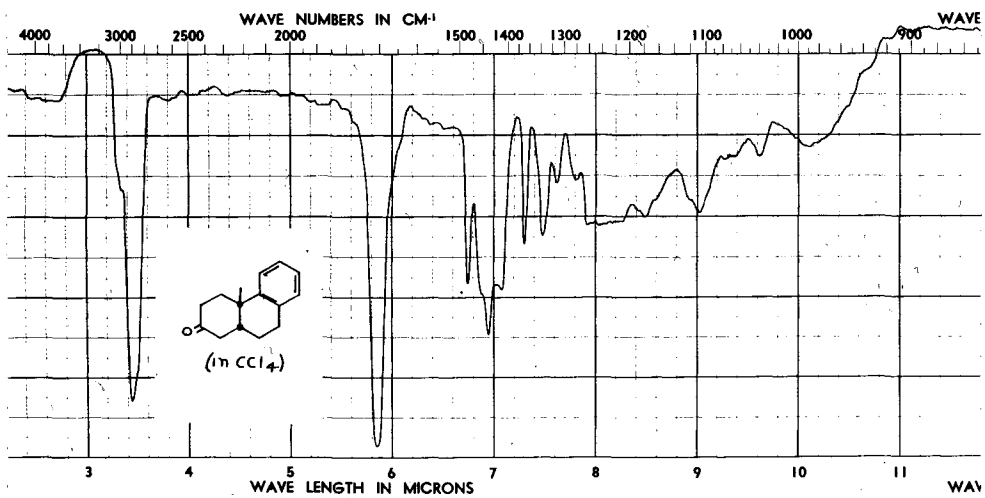
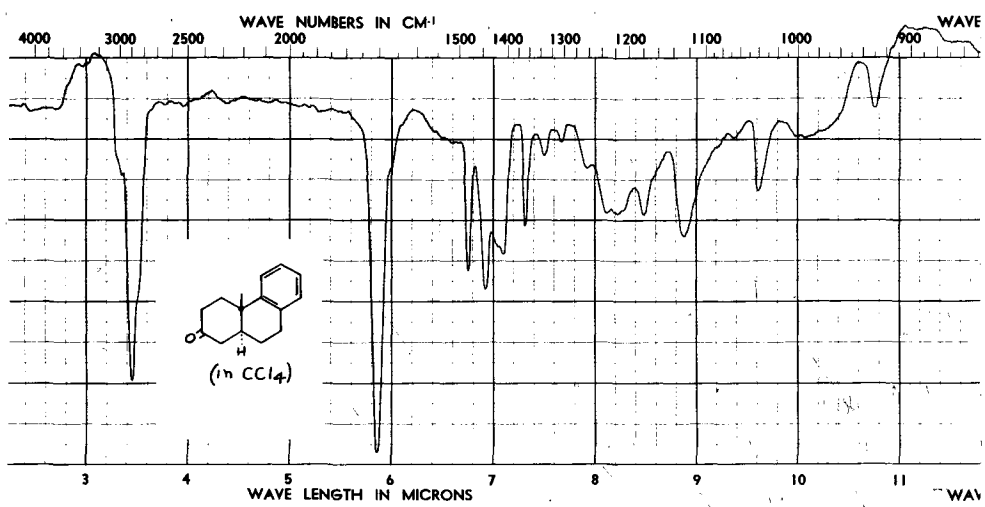
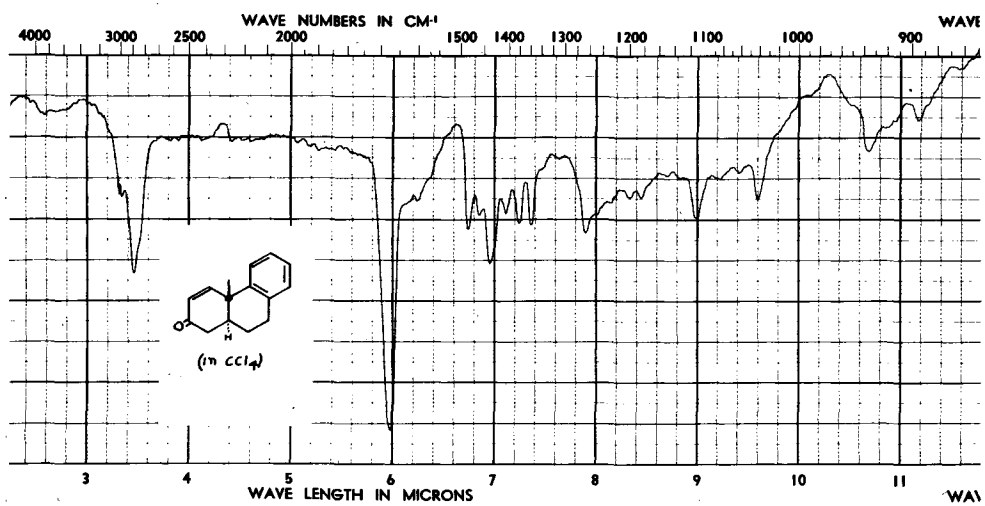
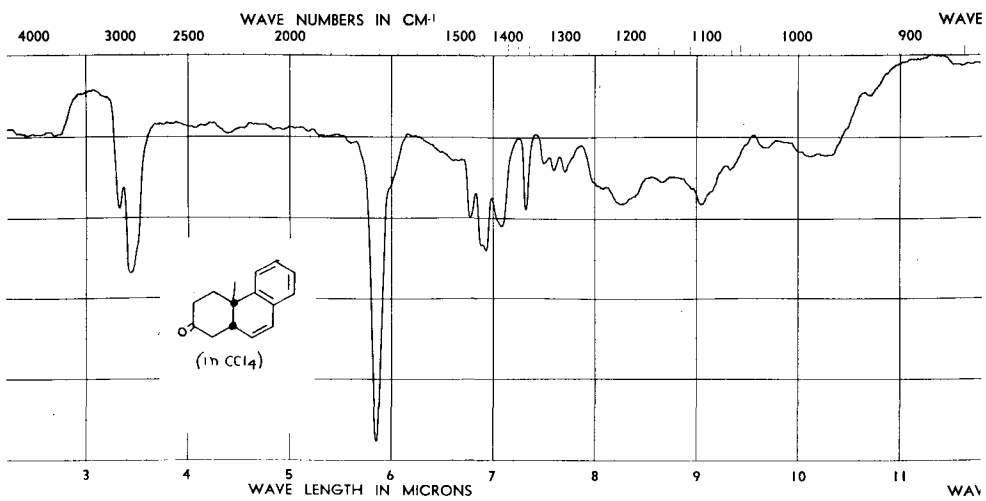
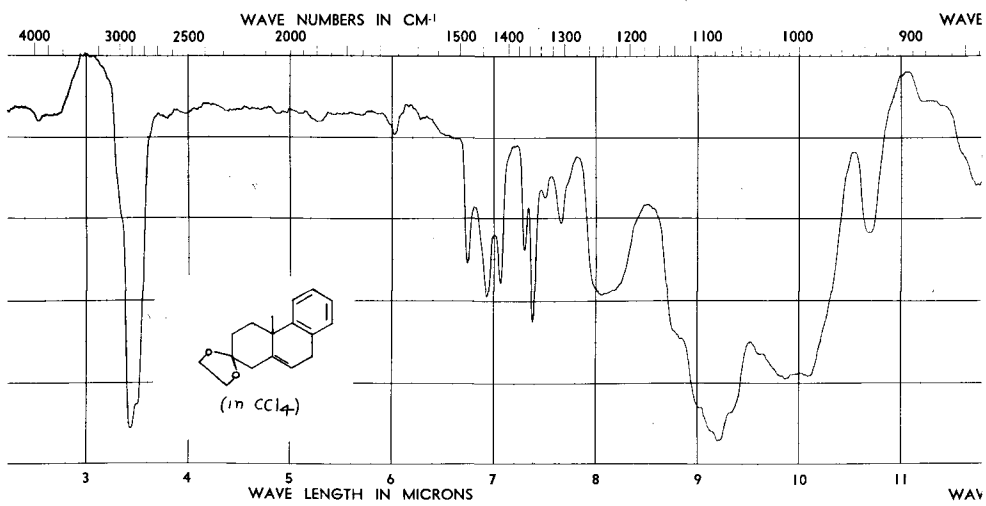
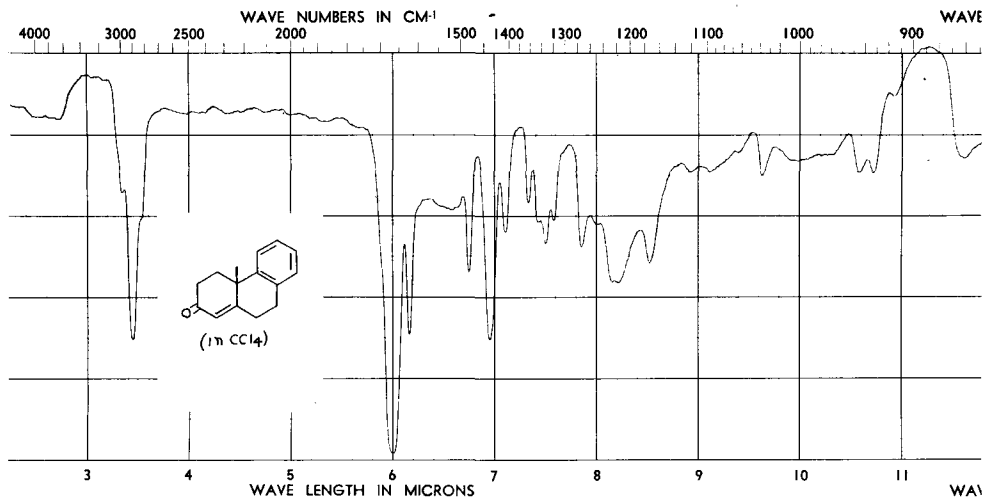


Figure 11

Infrared Spectra



EXPERIMENTAL

All melting points and boiling points are uncorrected. The term petroleum ether refers to the fraction b.p. 60-70°. Ultraviolet spectra were measured in 95% ethanol solution with a Beckman model DU quartz spectrophotometer. Microanalyses were carried out by the Strauss and Weiler Microanalytical Laboratory, Oxford, England.

Adsorbents for chromatography

Activated alumina, 80-200 mesh, was allowed to stand with ethyl acetate for 24 hours, then washed with water and methanol, and dried at 100° for 24 hours.

The Celite-silicic acid adsorbent was prepared by mixing equal weights of Celite and Mallinckrodt 100 mesh silicic acid.

Equal weights of Celite and Norit-A were mixed thoroughly to prepare the Celite-charcoal adsorbent.

4-Methyl-1-naphthol

Method A. 1-Methylnaphthalene was sulfonated by the method of Elbs and Christ (44), and the sodium 4-methyl-

naphthalene-1-sulfonate was isolated by salting out according to the procedure of Fieser (45). Fusion of the sodium salt with a mixture of equal weights of sodium and potassium hydroxide (44, 46) gave the naphthol in crude yields (based on 1-methylnaphthalene) varying from 20 to 50%.

Method B. The procedure of Adams and Levine (47) was used to prepare 4-hydroxy-1-naphthaldehyde, m.p. 170-172°. Clemmensen reduction of this aldehyde using ethanol-water as a solvent (48) gave crude 4-methyl-1-naphthol in 40-45% overall yield. Recrystallization from petroleum ether gave the naphthol as white crystals melting at 83-84°.

4-(Dichloromethyl)-4-methyl-1(4H)-naphthalenone (LXXV)

Crude 4-methyl-1-naphthol was reacted with chloroform and base according to the procedure of Fuson and Miller (43). The colored product obtained on distillation of the neutral fraction was purified by passing a petroleum ether-benzene (1:1) solution through an alumina column. Recrystallization from petroleum ether gave white needles melting at 109-110°. The yield, based on crude naphthol, varied from 7-9%.

The 2,4-dinitrophenylhydrazone melted at 212-213°.

The ultraviolet spectrum is shown in Figure 1.

1-(Dichloromethyl)-1-methyl-2(1H)-naphthalenone (LXXVII)

When the 1-naphthalenone LXXV was prepared using 4-methyl-1-naphthol from the fusion preparation, concentration of the petroleum ether filtrates gave the isomeric 2-naphthalenone LXXVII, m.p. 66-67°, in 3-4% yields.

Ultraviolet spectrum. λ_{\max} . 239 m μ (ϵ 13,300) and 315 m μ (ϵ 9,900). Reported (33): λ_{\max} . 239 m μ (ϵ 11,900) and 314 m μ (ϵ 9,200).

Hydrogenation of the 2-naphthalenone LXXVII using Adams catalyst gave the known (33) 1-(dichloromethyl)-1-methyl-2-tetralone, m.p. 71-72°.

Ethyl 3-keto-5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo[3.3.1]nonane-3-carboxylate (LXXVIII)

To 240 ml. of absolute ethanol in which 0.64 g. (0.036 mole) of sodium had been dissolved was added 10.8 g. (0.083 mole) of ethyl acetoacetate and 20.0 g. (0.083 mole) of the 1-naphthalenone LXXV. After standing at room temperature for 127 hours, the solution was poured into 1 l. of water, neutralized with acetic acid, and extracted with chloroform. The chloroform solution was washed with sodium bicarbonate solution and water, dried (MgSO₄), and evaporated. The

residual semi-solid was taken up in petroleum ether. From this solution 18.89 g. (61.4%) of the bicyclic ketoester LXXVIII, m.p. 114-116°, crystallized. The petroleum ether filtrate was chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (97:3) gave 4.31 g. (21.6%) of the naphthalenone LXXV. Further elution with petroleum ether-ether (9:1) gave an additional 3.81 g. (12.4%) of the bicyclic ketoester melting at 114-116°. No further products were obtained on continued elution of the column. The analytical sample of the bicyclic ketoester LXXVIII, white prisms melting at 116-117°, was obtained by crystallization from petroleum ether.

Anal. Calcd. for $C_{18}H_{20}Cl_2O_4$: C, 58.23; H, 5.43; Cl, 19.10. Found: C, 58.13, 58.19; H, 5.63, 5.58; Cl, 19.2, 19.05.

Ultraviolet spectrum. (Figure 1) λ_{max} . 258 m μ (ϵ 8,300); λ_{min} . 232 m μ (ϵ 2,800).

The ketoester LXXVIII also was obtained using sodium ethoxide (1 mole) or potassium *t*-butoxide (0.3 or 1.0 mole) as the base at either room temperature or reflux. However, the above procedure appeared to give the cleanest reaction.

When a solution of 60 ml. of ethanol, 0.40 ml. of piperidine, 2.75 g. of ethyl acetoacetate and 5.0 g. of the naphthalenone LXXV was refluxed for 3 days, a 94%

recovery of the starting ketone plus a 0.4% yield of the ketoester LXXVIII were obtained.

Ethyl 2-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-3-ketobutyrate (LXXXIII)

A solution containing 120 ml. of benzene, 15.0 g. (0.062 mole) of the 1-naphthalenone LXXV, 15.0 g. (0.115 mole) of ethyl acetoacetate and 1.2 ml. of piperidine was stoppered, shaken, and allowed to stand at room temperature for 52 days. The benzene solution was washed with dilute acetic acid and water, dried over $MgSO_4$, and evaporated to give a solid residue. The solid was dissolved in hot petroleum ether, and on cooling, 5.86 g. (39.1%) of the starting ketone LXXV, m.p. 107-108°, separated. The petroleum ether filtrate was chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave an additional 5.80 g. (38.7%) of starting material melting at 108-109°. Continued elution of the column with petroleum ether-ether (9:1) gave 0.24 g. (1%) of the bicyclic ketoester LXXVIII. The petroleum ether-ether (4:1) eluate gave 4.2 g. (18.3%) of white crystals, m.p. 98-100°. Recrystallization of this product from

petroleum ether gave the diketoester LXXXIII as white prisms melting at 102-103°.

Anal. Calcd. for C₁₈H₂₀Cl₂O₄: C, 58.23; H, 5.43; Cl, 19.10. Found: C, 58.32; H, 5.62; Cl, 19.18.

Ultraviolet spectrum. λ max. 252 m μ (ϵ 10,000) and 290 m μ (ϵ 1,400).

When a similar reaction was allowed to stand at room temperature for 20 days, a 15% yield of the diketoester LXXXIII was obtained.

Refluxing the reactants in the same proportions as above for 3 days gave a 0.3% yield of the desired product (LXXXIII), and a 96% recovery of starting material.

Ethyl 2-(1-(dichloromethyl)-1-methyl-1,2,3,4-tetrahydro-2-naphthyl)-3-ketobutyrate (LXXXIV)

To 20 ml. of ethyl acetate containing 0.30 ml. of 80% sulfuric acid was added 200 mg. of the diketoester LXXXIII and 50 mg. of 5% palladium-on-charcoal catalyst. Hydrogenation at one atmosphere was carried out while hydrogen absorption was measured volumetrically. Hydrogen absorption ceased at the end of 2 hours with an uptake corresponding to 2 moles of hydrogen. The solution was filtered to remove the catalyst, and washed with sodium bicarbonate solution

and water. Evaporation of the ethyl acetate under reduced pressure left an oily residue. Slow evaporation of a petroleum ether solution of this residue gave crystals melting at 125-127°. Recrystallization from petroleum ether yielded the ketoester LXXXIV as hard white crystals melting at 128-129°.

Anal. Calcd. for $C_{18}H_{22}Cl_2O_3$: C, 60.51; H, 6.21; Cl, 19.85. Found: C, 60.94; H, 5.89; Cl, 19.6.

Ultraviolet spectrum. λ_{max} . 250 $m\mu$ (ϵ 7,400);
 λ_{min} . 230 $m\mu$ (ϵ 5,200).

Hydrolysis and decarboxylation of ethyl 3-keto-5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo[3.3.1]nonane-2-carboxylate (LXXVIII)

To a mixture of 300 ml. of 95% ethanol and 300 ml. of concentrated hydrochloric acid was added 15.0 g. of the bicyclic ester LXXVIII. The solution was refluxed on the steam bath for 9 hours, cooled, and poured into 1200 ml. of water. The chloroform extract of this mixture was washed with sodium bicarbonate solution and water, dried ($MgSO_4$), and evaporated to give a gummy residue. Recrystallization of the residue from 95% ethanol gave 7.88 g. (65.2%) of 4-(dichloromethyl)-4-methyl-3-acetyl-1-tetralone (LXXXV),

m.p. 145-146°. Recrystallization of this material from petroleum ether-benzene gave hard white crystals melting at 147-148°.

Anal. Calcd. for $C_{15}H_{16}Cl_2O_2$: C, 60.21; H, 5.39; Cl, 23.70. Found: C, 60.29, 60.34; H, 5.40, 5.47; Cl, 23.6, 23.5.

The ultraviolet spectrum is shown in Figure 1.

Evaporation of the ethanolic filtrate under reduced pressure and recrystallization of the residue from benzene five times gave 0.77 g. (6.4%) of 5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo[3.3.1]nonan-3-one (LXXXVI) as white prisms melting at 187-188°.

Anal. Calcd. for $C_{15}H_{16}Cl_2O_2$: C, 60.21; H, 5.39; Cl, 23.70. Found: C, 60.14; H, 5.48; Cl, 23.8.

Ultraviolet spectrum. λ max. 265 m μ (ϵ 200);
 λ min. 250 m μ (ϵ 100).

All filtrates from the above recrystallizations were combined and evaporated under reduced pressure. A benzene solution of the residue was placed on an alumina column. Elution with benzene-chloroform (9:1) gave an additional 0.56 g. (4.6%) of the diketone LXXXV melting at 144-146°. When the eluent was changed to benzene-methanol (99:1), 1.15 g. (9.5%) of the hydroxy ketone LXXXVI, m.p. 186-187° was obtained.

Ethyl 2-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-3-ketobutyrate (LXXXIII) plus sodium ethoxide

To 10 ml. of absolute ethanol containing 0.00035 mole of sodium ethoxide was added 300 mg. (0.00081 mole) of the diketoeater LXXXIII. After 30 hours at room temperature the reaction mixture was poured into 100 ml. of water, neutralized with acetic acid, and extracted with chloroform. The chloroform extract was washed with water, dried over $MgSO_4$, and evaporated to leave a syrupy residue. A petroleum ether solution of the residue was placed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave 120 mg. (61.5%) of the naphthalenone LXXV, m.p. 107-108°. Further elution with petroleum ether-ether (9:1) gave 105 mg. (35%) of the bicyclic ketoester LXXVIII melting at 114-116°.

Hydrolysis and decarboxylation of ethyl 2-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-3-keto-butyrate

To a mixture of 10 ml. of 95% ethanol and 10 ml. of concentrated hydrochloric acid was added 500 mg. of the diketoeater LXXXIII. The mixture was refluxed on the steam

bath for 7 hours, poured into 100 ml. of water, and partially neutralized with a 10% sodium hydroxide solution. The chloroform extract of the aqueous solution was washed with sodium bicarbonate solution and water, dried over $MgSO_4$, and evaporated. The solid residue was taken up in benzene and chromatographed on an alumina column. Elution with benzene-ether (9:1) gave 235 mg. (58.4%) of 4-(dichloromethyl)-4-methyl-3-acetyl-1-tetralone (LXXXV) melting at 146-147°. Continued elution of the column with benzene-methanol (99:1) gave 80 mg. (19.8%) of 5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methylbicyclo[3.3.1]nonan-3-one (LXXXVI) melting at 184-186°.

Michael addition of acetone to 4-(dichloromethyl)-4-methyl-1(4H)-naphthalenone (LXXV)

To a solution of 0.80 g. of potassium in 25 ml. of anhydrous *t*-butanol was added 0.50 ml. of acetone and 2.00 g. of the naphthalenone LXXV. The mixture was warmed slightly to effect solution of the naphthalenone, shaken, and then allowed to stand at room temperature for 22 hours. A deep red color appeared soon after mixing the reactants. The solution was poured into 60 ml. of water, neutralized with acetic acid, and the aqueous suspension extracted with

chloroform. The organic extract was washed with water, dried (MgSO_4), and evaporated to give a red gum. Refluxing this gummy mass with 50 ml. of 95% ethanol led to crystallization. Filtration of the hot solution gave 0.90 g. of a tan solid melting at $200-204^\circ$. On cooling a further 0.37 g. of solid material melting at $214-217^\circ$ was obtained from the ethanolic filtrate. Repeated recrystallization (with charcoal decolorization) of this high melting material from ethanol-ethyl acetate gave 0.52 g. of 1,3 di-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-2-propanone (XCA) as white platelets melting at $225-226^\circ$. The analytical sample, recrystallized from ethanol-ethyl acetate, melted at $227-228^\circ$.

Anal.* Calcd. for $\text{C}_{27}\text{H}_{26}\text{Cl}_4\text{O}_3$: C, 60.02; H, 4.84; Cl, 26.25. Found: C, 60.05, 60.06; H, 5.03, 4.86; Cl, 26.0.

Ultraviolet spectrum. λ_{max} . $252 \text{ m}\mu$ (ϵ 21,200) and $292 \text{ m}\mu$ (ϵ 2,900).

When the mother liquors from the above recrystallizations of the triketone XCA were concentrated and the residue recrystallized from ethanol-water, 0.60 g. of 1,3-di-

*While this compound and its isomer (XCB) gave very good, duplicable C and H analyses, considerable difficulty was encountered in obtaining chlorine analyses that checked with one another.

(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-2-propanone (XCB) melting at 227-230° was obtained. Repeated recrystallization of this material from ethanol-water gave white needles melting at 240-241°. When admixed with the isomeric triketone XCA, a melting point of 207-209° was observed.

Anal. Calcd. for $C_{27}H_{26}Cl_4O_3$: C, 60.02; H, 4.84; Cl, 26.25. Found: C, 60.08, 60.06; H, 4.68, 5.12; Cl, 26.6.

Ultraviolet spectrum. λ_{max} . 252 $m\mu$ (ϵ 20,800) and 292 $m\mu$ (ϵ 3,200).

The ethanolic filtrate of the original reaction mixture was placed on a short (2 x 6 cm.) Celite-charcoal column, and eluted with 200 ml. of ethanol-ethyl acetate (1:1). The residue obtained upon evaporation of the eluent was recrystallized from 95% ethanol to give 40 mg. of 4-(dichloromethyl)-4-methyl-3-acetyl-1-tetralone (LXXXV) melting at 145-146°. A sample admixed with the diketone LXXXV from the hydrolysis of the bicyclic ketoester LXXVIII melted at 146-147°.

Dilution of the ethanolic filtrate from the above recrystallization, and recrystallization of the product from ethanol-water gave 60 mg. of the bicyclic ketone LXXXVI, m.p. 186-187°. It did not depress the melting point of the bicyclic ketone obtained from the hydrolysis of the bicyclic ketoester LXXVIII.

A similar reaction using a larger amount of acetone (1.20 ml.) also was attempted. Chromatography of the ethanol-soluble residue over alumina, and elution of the column with benzene, led to the isolation of a small amount of material m.p. 153-155°. Recrystallization from petroleum ether-benzene gave hard white crystals melting at 156-157°. This compound may be 2,10-diketo-4,4,9-trimethyl-9-(dichloromethyl)-1,2,3,4,4a,9,9a,10-octahydroanthracene (XCII). A mixture melting point with the diketone LXXXV, m.p. 146-147° depressed to 125-130°.

Anal. Calcd. for $C_{18}H_{20}Cl_2O_2$: C, 63.72; H, 5.95; Cl, 20.90. Found: C, 63.74; H, 6.29; Cl, 20.9.

Ultraviolet spectrum. λ max. 252 $m\mu$ (ϵ 10,000) and 290 $m\mu$ (ϵ 1,500). The diketone LXXXV (see Figure 1) exhibited λ max. 252 $m\mu$ (ϵ 10,600) and 290 $m\mu$ (ϵ 1,600).

Hydrogenation of the 1,3-di-(1-(dichloromethyl)-1-methyl-4-keto-1,2,3,4-tetrahydro-2-naphthyl)-2-propanones, (XCA) and (XCB)

A mixture containing 60 ml. of ethyl acetate, 200 mg. of the triketone XCA, 0.75 ml. of 80% sulfuric acid and 100 mg. of 5% palladium-on-charcoal was hydrogenated at one atmosphere while hydrogen absorption was measured

volumetrically. Hydrogen absorption ceased after 1 hour with an uptake corresponding to 4 moles of hydrogen. The solution was filtered to remove the catalyst, washed with sodium bicarbonate solution and water, and evaporated under reduced pressure. The solid residue remaining had a m.p. of 187-191^o. Repeated recrystallization from ethanol-ethyl acetate gave 1,3-di-(1-(dichloromethyl)-1-methyl-1,2,3,4-tetrahydro-2-naphthyl)-2-propanone (XCIA) as fluffy white needles melting at 190-191^o.

Anal. Calcd. for $C_{27}H_{30}Cl_4O$: C, 63.29; H, 5.90; Cl, 27.68. Found: C, 63.62; H, 6.02; Cl, 28.08.

Ultraviolet spectrum. λ_{max} . 265 m μ (ϵ 600);
 λ_{min} . 235 m μ (ϵ 100).

Similar reduction of the isomeric triketone XCB was complete in 1 hour. The solid residue, m.p. 183-186^o, was recrystallized from petroleum ether-benzene and 95% ethanol to give 1,3-di(1-(dichloromethyl)-1-methyl-1,2,3,4-tetrahydro-2-naphthyl)-2-propanone (XCIB) as soft white needles melting at 186-188^o.

Anal. Calcd. for $C_{27}H_{30}Cl_4O$: C, 63.29; H, 5.90; Cl, 27.68. Found: C, 62.94; H, 5.88; Cl, 28.54*.

*Only one chlorine analysis was run on this compound. As noted earlier, difficulty was encountered in getting reliable chlorine analyses on compounds of this type.

Ultraviolet spectrum. $\lambda_{\text{max.}}$ 265 $m\mu$ (ϵ 600);
 $\lambda_{\text{min.}}$ 235 $m\mu$ (ϵ 100).

The mixed melting point of these two isomers was 171-174°.

1-(Dichloromethyl)-1-methyl-2-acetyl-1,2,3,4-tetrahydro-naphthalene (LXXXVII)

From 4-(dichloromethyl)-4-methyl-3-acetyl-1-tetralone (LXXXV). A mixture containing 60 ml. of ethyl acetate, 1.0 ml. of 80% sulfuric acid, 200 mg. of 5% palladium-on-charcoal and 690 mg. of the tetralone LXXXV was hydrogenated at one atmosphere while hydrogen absorption was measured volumetrically. Hydrogen absorption ceased after 90 minutes with an uptake of hydrogen corresponding to 2 moles. The solution was filtered, washed with sodium bicarbonate solution and water, and evaporated to give white crystals melting at 75-77°. Recrystallization from aqueous ethanol gave 1-(dichloromethyl)-1-methyl-2-acetyl-1,2,3,4-tetrahydronaphthalene (LXXXVII) as white platelets melting at 82-83°.

Anal. Calcd. for $C_{15}H_{18}Cl_2O$: C, 63.17; H, 6.35; Cl, 24.87. Found: C, 63.50; H, 6.56; Cl, 24.4.

Ultraviolet spectrum. $\lambda_{\text{max.}}$ 265 $m\mu$ (ϵ 400);
 $\lambda_{\text{min.}}$ 240 $m\mu$ (ϵ 200).

The 2,4-dinitrophenylhydrazone crystallized from ethanol-ethyl acetate as yellow plates, m.p. 169-170°.

Anal. Calcd. for $C_{21}H_{22}Cl_2N_4O_4$: C, 54.20; H, 4.77; N, 12.04. Found: C, 54.06; H, 4.72; N, 12.2.

The keto tetrahydronaphthalene LXXXVII was sometimes isolated as prisms melting at 93-94°. The mixed melting point of the two forms was 92-94°. The infrared spectra of the two crystal forms were identical, and their 2,4-dinitrophenylhydrazones had the same melting point (169-170°) and did not depress on admixture.

From 5-hydroxy-6,7-benzo-8-(dichloromethyl)-8-methyl-bicyclo[3.3.1]nonan-3-one (LXXXVI). A mixture of 200 mg. of the bicyclic ketone LXXXVI, 25 ml. of ethyl acetate, 1.25 ml. of concentrated sulfuric acid and 100 mg. of 5% palladium-on-charcoal was hydrogenated at atmospheric pressure. After 24 hours uptake corresponding to 2 moles of hydrogen was complete. The solution was filtered, washed with sodium bicarbonate solution and water, and evaporated. Recrystallization of the residue from petroleum ether gave white crystals melting at 80-81°. This compound was identical with the keto tetrahydronaphthalene LXXXVII according to mixed melting point determination and infrared comparison.

4a-Methyl-4a,9,10,10a-tetrahydro-2(1H)-phenanthrone
(LXXXVIII)

Sodium triphenylmethyl was prepared by shaking 10 g. of triphenylchloromethane, 4.0 g. of sodium sand, 250 ml. of anhydrous ether and several pieces of jagged glass in a mechanical shaker until the solution turned deep red (usually 4 to 12 hours). After an additional 2 hours of shaking aliquots were hydrolyzed and titrated to determine the concentration of base present.

To 1 g. (0.0035 mole) of 1-(dichloromethyl)-1-methyl-2-acetyl-1,2,3,4-tetrahydronaphthalene was added (in an atmosphere of nitrogen) 200 ml. of ether containing 0.0286 mole of sodium triphenylmethyl. The solution was allowed to stand at room temperature for 3 days with occasional shaking. After a final 5 hour reflux on the steam bath the reaction mixture (still a deep red) was cooled, and then hydrolyzed with water containing a little acetic acid. This mixture was extracted with ether five times. The organic extract was washed with sodium bicarbonate solution and water, dried over $MgSO_4$, and evaporated. The residue was extracted five times with hot petroleum ether, and the cooled extract was placed on a Celite-silicic acid column. Elution of the column with petroleum ether containing increasing amounts

of ether gave, in the petroleum ether-ether (19:1) eluate, 230 mg. (31%) of the phenanthrone LXXXVIII melting at 98-100°. The non-crystalline fractions from the column shown by their infrared spectra to contain appreciable quantities of an unsaturated carbonyl compound were combined in petroleum ether and again chromatographed on Celite-silicic acid. Elution with petroleum ether-ether (19:1) yielded an additional 90 mg. of the phenanthrone. Three recrystallizations of the product from petroleum ether gave 4a-methyl-4a,9,10,10a-tetrahydro-2(1H)-phenanthrone as white crystals melting at 103-104°.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.96, 85.21; H, 7.38, 7.61

Ultraviolet spectrum. See Figure 2.

The 2,4-dinitrophenylhydrazone crystallized as red platelets from ethanol-ethyl acetate, m.p. 205-206°.

Anal. Calcd. for $C_{21}H_{20}N_4O_4$: C, 64.27; H, 5.14; N, 14.28. Found: C, 63.94; H, 5.20; N, 13.8.

The fractions immediately preceding the phenanthrone on elution of the column contained, as indicated by infrared spectra, considerable amounts of the unreacted acetyl compound LXXXVII.

4a-Methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone
(LXXXIX)

A mixture of 20 ml. of ethanol, 200 mg. of the phenanthrone LXXXVIII and 50 mg. of 5% palladium-on-charcoal was hydrogenated at one atmosphere. Hydrogen absorption was measured volumetrically. Uptake corresponding to 1 mole of hydrogen was complete in 15 minutes, and hydrogen absorption ceased. The solution was filtered, evaporated, and the residue recrystallized from petroleum ether to give the hydrophenanthrene ketone LXXXIX as white plates, m.p. 107-108°.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.06; H, 8.46. Found: C, 84.05; H, 8.58.

Ultraviolet spectrum. λ_{max} . 265 $m\mu$ (ϵ 400); λ_{min} . 240 $m\mu$ (ϵ 200).

The semicarbazone crystallized from aqueous ethanol as white platelets, m.p. 220-221° dec.

Anal. Calcd. for $C_{16}H_{21}N_3O$: C, 70.81; H, 7.80; N, 15.49. Found: C, 70.72; H, 7.76; N, 15.5.

The orange para-nitrophenylhydrazone was recrystallized from ethanol, m.p. 178-180° dec.

Anal. Calcd. for $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 71.97; H, 6.34; N, 11.9.

1-Methyl-2-naphthol

The method of Adams and Levine (47) was used to prepare 2-hydroxy-1-naphthaldehyde. This was reduced with copper-coated zinc according to Robinson (54), except that the reaction time was increased to 5 hours to give more complete reduction. The overall yield of 1-methyl-2-naphthol melting at 110-111° was 40%.

4-Chloro-3-buten-2-one

Acetylene was bubbled through a carbon tetrachloride solution of acetyl chloride and aluminum chloride for 8 hours as specified by Price (62). Two distillations of the product gave a 50% yield of 4-chloro-3-buten-2-one, b.p. (18 mm.) 39-41°, solidifying on standing in the refrigerator.

3-Butyn-2-one

3-Butyl-2-ol, b.p. 106-108° was prepared by standard methods (63), and was oxidized by the procedure of Bowden, et al., (64) to give 3-butyn-2-one, b.p. 84-86°.

Addition of methyl vinyl ketone to 1-methyl-2-naphthol

Depending on the catalyst and solvent used, different products or mixtures of products were obtained.

Potassium t-butoxide. To 60 ml. of t-butanol in which 0.13 g. of potassium had been dissolved was added 5.0 g. of 1-methyl-2-naphthol and 2.8 ml. of freshly distilled methyl vinyl ketone. The solution was swirled, and then allowed to stand at room temperature for 10 hours. The mixture was poured into 200 ml. of water, and neutralized with acetic acid. The aqueous mixture was extracted with ether, and the ether layer was washed with water, dried over $MgSO_4$, and evaporated to give an oily residue. Extraction of this residue with hot petroleum ether (5 x 100 ml.) left a gummy residue. The cooled petroleum ether extract was chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave 1.76 g. (35.2%) of 1-methyl-2-naphthol melting at $110-111^\circ$. From the petroleum ether-ether (5:1) eluate was obtained 1-methyl-5,6-benzo-8-acetylbicyclo[2.2.2]octan-2-one (XCVIII A) melting at $102-103^\circ$. Recrystallization of this material from petroleum ether gave 0.69 g. (9.6%) of white prisms melting at $103-104^\circ$.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.96; H, 7.03.

Ultraviolet spectrum. λ max. 264 $m\mu$ (ϵ 410), 272 $m\mu$ (ϵ 410), and 294 $m\mu$ (ϵ 440); λ min. 244 $m\mu$ (ϵ 130).

The yellow di-2,4-dinitrophenylhydrazone was recrystallized from ethanol-ethyl acetate, m.p. 238-239 dec.

Anal. Calcd. for $C_{27}H_{24}N_8O_8$: C, 55.11; H, 4.11; N, 19.04. Found: C, 54.96; H, 3.84; N, 18.6.

Continued elution of the column with petroleum ether-ether (3:1) gave the stereoisomeric 1-methyl-5,6-benzo-8-acetyl-bicyclo[2.2.2]octan-2-one (XCVIII B) melting at 104-106°. Recrystallization of this material from petroleum ether gave 1.11 g. (15.4%) of hard white needles melting at 108-109°.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.89; H, 7.07.

Ultraviolet spectrum. λ max. 264 $m\mu$ (ϵ 390), 270 $m\mu$ (ϵ 360) and 294 $m\mu$ (ϵ 390); λ min. 244 $m\mu$ (ϵ 150).

The yellow di-2,4-dinitrophenylhydrazone was recrystallized from chloroform-ethyl acetate, m.p. 277-278° dec.

Anal. Calcd. for $C_{27}H_{24}N_8O_8$: C, 55.11; H, 4.11; N, 19.04. Found: C, 54.77; H, 3.93; N, 18.8.

The mixed melting point of the isomeric bicyclic diketones XCVIII A and XCVIII B was 80-84°.

The gummy residue remaining behind after the extractions with petroleum ether was recrystallized (Norit-A decolorization) from ethanol to give 0.38 g. (4%) of crystalline material melting at 234-238°. This compound, assigned the structure of 1-methyl-2-(3-keto-1-butoxy)-5,6-benzo-9-ketotricyclo[2.2.2.2^{2,8}]decane (XCIX), was recrystallized three times from 95% ethanol to give white platelets melting at 244-245°.

Anal. Calcd. for C₁₉H₂₂O₃: C, 76.48; H, 7.43. Found: C, 76.56; H, 7.30.

Ultraviolet spectrum. λ_{\max} , 265 m μ (ϵ 300) and 295 m μ (ϵ 400); λ_{\min} , 248 m μ (ϵ 200).

The yellow di-2,4-dinitrophenylhydrazone was recrystallized from ethanol-ethyl acetate, m.p. 262-264° dec.

Anal. Calcd. for C₃₁H₃₀N₈O₉: N, 17.0. Found: N, 16.6.

Sodium ethoxide-ethanol. To 40 ml. of absolute ethanol in which 0.29 g. (0.0126 mole) of sodium had been dissolved was added 2.00 g. (0.0127 mole) of 1-methyl-2-naphthol. The solution was cooled in ice, and 1.2 ml. of freshly distilled methyl vinyl ketone was added. After remaining at 5° for 24 hours, the ethanolic solution was diluted with water, and extracted with ether. The ether extract was washed thoroughly with water, dried over MgSO₄, and evaporated to leave

a solid residue. This residue was taken up in refluxing petroleum ether, and on cooling deposited crystals of 1-methyl-2-naphthol, m.p. 110-111°. The petroleum ether filtrate was chromatographed on Celite-silicic acid. Elution with petroleum ether-ether (ratio increasing from 97:3 to 1:1) and with ether gave further quantities of 1-methyl-2-naphthol melting at 110-111°. No indication of any other product could be found.

Ether-BF₃. To a solution of 1.9 g. of boron trifluoride in 12 ml. of anhydrous ether was added dropwise, with ice cooling, a solution of 4.0 g. of 1-methyl-2-naphthol and 2.3 ml. of freshly distilled methyl vinyl ketone in 35 ml. of anhydrous ether. After 11 hours at room temperature the reaction mixture was poured into an ice water-hydrochloric acid mixture. The aqueous solution was made basic with sodium hydroxide solution, neutralized with acetic acid, and ether extracted. The ether extract was washed with sodium bicarbonate solution and water, and dried over MgSO₄. Evaporation of the ether left a dark oil. The oil was extracted with refluxing petroleum ether (6 x 80 ml.), and the cooled extract chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave 2.24 g. (56%) of 1-methyl-2-naphthol melting at 110-111°. Continued elution with petroleum ether-ether (7:1) gave

1.33 g. (23%) of the bicyclic diketone XCVIIIA, m.p. 102-103°. Further elution of the column with increasing amounts of ether gave only oily material. This was taken up in petroleum ether-ether (9:1) and chromatographed on a silicic acid-Celite column. Elution with petroleum ether-ether (2:1) gave, after recrystallization from petroleum ether, 60 mg. of the isomeric bicyclic diketone XCVIIIB melting at 107-108°. By rechromatographing the residues on another silicic acid-Celite column an addition 0.13 g. (total of 3.3%) of the bicyclic diketone XCVIIIB melting at 107-108° was obtained.

p-Toluenesulfonic acid. To 5.5 g. (0.026 mole) of p-toluenesulfonic acid hydrate in 80 ml. of glacial acetic acid was added 5.0 g. (0.0316 mole) of 1-methyl-2-naphthol and 7.0 g. (0.10 mole) of methyl vinyl ketone. The reaction was stoppered, swirled vigorously, and allowed to stand at room temperature for 11 hours. The reaction mixture was then poured into 500 ml. of water, partially neutralized with 10% sodium hydroxide, and extracted with chloroform. After being washed with sodium bicarbonate solution and water, and dried (MgSO_4), the chloroform solution was evaporated to leave a dark oil. The oil was extracted with hot petroleum ether (8 x 100 ml.), and the cooled extract chromatographed on a silicic acid-Celite column. Elution

with petroleum ether-ether (19:1) gave 2.36 g. (47.2%) of 1-methyl-2-naphthol melting at 110-111°. Further elution with petroleum ether-ether (9:1) gave a yellow oil which solidified after being taken up in petroleum ether. Thus 1.21 g. (18.3%) of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (XCVII) was obtained as hard yellow clusters melting at 95-97°. Recrystallization from petroleum ether gave pale yellow needles melting at 97-98°.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.72. Found: C, 85.67; H, 6.58.

Ultraviolet spectrum. λ max. 242 m μ (ϵ 16,800) and 354 m μ (ϵ 14,900).

The 2,4-dinitrophenylhydrazone, purple crystals melting at 213-215° dec., was recrystallized from ethanol-ethyl acetate.

Anal. Calcd. for $C_{21}H_{18}N_4O_4$: C, 64.61; H, 4.65; N, 14.35. Found: C, 64.30; H, 5.06; N, 14.7.

Continued elution of the column with petroleum ether-ether (2:1) gave 0.19 g. of the bicyclic diketone XCVIII B, m.p. 107-108°. The non-crystalline fractions were recombined in petroleum ether and again chromatographed on silicic acid-Celite. The column was eluted with petroleum ether containing increasing amounts of ether, and with ether. The infrared spectra of the fractions indicated an incomplete

separation of the phenanthrone XCVII from the two isomeric bicyclic diketones XCVIIIA and XCVIIIB. The fractions were recombined in petroleum ether-benzene (1:1), and chromatographed on alumina. Elution with benzene gave a major fraction shown by infrared spectrum to contain the phenanthrone XCVII and the bicyclic diketone XCVIIIA. Recrystallization from petroleum ether gave an additional 0.48 g. (7.3%) of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone, m.p. 95-97°. From the filtrate was obtained 20 mg. of the bicyclic diketone XCVIIIA, m.p. 98-100°. Elution of the column with benzene-ether (1:1) gave, after recrystallization from petroleum ether, an additional 0.13 g. of the bicyclic diketone XCVIIIB, m.p. 105-106°.

Ethanol-HCl. When methyl vinyl ketone and 1-methyl-2-naphthol were reacted under conditions identical to the *p*-toluenesulfonic acid-acetic acid run except that commercial absolute ethanol saturated with dry hydrochloric acid gas was used as solvent and catalyst, and 89.4% recovery of 1-methyl-2-naphthol and a 6.5% yield of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone was realized.

Sodium ethoxide equilibration of the 1-methyl-5,6-benzo-8-acetylbicyclo[2.2.2]octan-2-ones (XCVIIIA and XCVIIIB)

To 20 ml. of absolute ethanol containing 0.0022 mole of sodium ethoxide was added 500 mg. (0.0022 mole) of the bicyclic diketone XCVIIIA. After 10 hours at room temperature, the pale yellow mixture was poured into 100 ml. of water and neutralized with acetic acid. The chloroform extract of the aqueous solution was washed with water, dried over $MgSO_4$, and evaporated to leave a clear oil. A petroleum ether solution of the oil was chromatographed on a Celite-silicic acid column. Elution of the column with petroleum ether-ether (4:1) gave 195 mg. of the bicyclic diketone XCVIIIA, m.p. $103-104^\circ$, followed by 290 mg. of the isomeric diketone XCVIIIB, m.p. $107-108^\circ$.

When 500 mg. of the bicyclic diketone XCVIIIB was treated in a manner similar to that above, 185 mg. of XCVIIIA, m.p. $103-104^\circ$, and 290 mg. of isomeric XCVIIIB, melting at $107-108^\circ$ was isolated.

Addition of 4-chloro-3-buten-2-one to 1-methyl-2-naphthol

A variety of solvents and catalysts was used.

Potassium *t*-butoxide in *t*-butanol. To a cooled solution of 75 ml. of *t*-butanol in which 1.50 g. (0.0384 mole) of

potassium had been dissolved was added 5.00 g. (0.0316 mole) of 1-methyl-2-naphthol and 3.50 g. (0.0350 mole) of 4-chloro-3-buten-2-one. A red coloration formed on addition of the butenone. After 8 hours at room temperature the solution was poured into 300 ml. of water, neutralized with acetic acid, and extracted with chloroform. The organic extract was washed with sodium bicarbonate solution and water, dried over $MgSO_4$, and evaporated under reduced pressure to give a dark oil. Extraction of the oil with hot petroleum ether (5 x 80 ml.) left a small amount of a tarry residue. The cooled petroleum ether solution was chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (97:3) gave 2.15 g. (43%) of 1-methyl-2-naphthol, m.p. 110-111°. Continued elution of the column with petroleum ether-ether (19:1) gave 2.49 g. (34.8%) of 4-(1-methyl-2-naphthoxy)-3-buten-2-one (GIII), m.p. 68-70°. Several oily fractions from the chromatogram were taken up in petroleum ether and placed on another Celite-silicic acid column. Elution as above gave an additional 0.19 g. (3.8%) of 1-methyl-2-naphthol and 0.58 g. (8.1%) of the naphthoxy butenone melting at 68-70°. Recrystallization of 4-(1-methyl-2-naphthoxy)-3-buten-2-one from petroleum ether gave long white needles melting at 70-71°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.47; H, 6.26.

Ultraviolet spectrum. λ max. 245 m μ (ϵ 24,600);
 λ min. 240 m μ (ϵ 23,900).

Methanolic sodium hydroxide. To a cooled mixture of 15 ml. of water, 5 ml. of methanol and 1.0 g. of sodium hydroxide, was added 1.0 g. of 1-methyl-2-naphthol and 0.80 ml. of 4-chloro-3-buten-2-one. After 18 hours at room temperature the reaction was worked up as described above for the potassium t-butoxide run. A 96% recovery of 1-methyl-2-naphthol melting at 110-111° was obtained. There was no indication of any other product.

Sodium 1-methyl-2-naphthoxide in dioxane. Sodium 1-methyl-2-naphthoxide was prepared by dissolving a known amount of sodium hydroxide in methanol and adding an equimolar amount of 1-methyl-2-naphthol to the methanolic solution. The solution was evaporated to dryness under reduced pressure, and the residue dried at 80° and 1 mm. for 2 hours.

To 25 ml. of purified dioxane containing 1.20 g. (0.00667 mole) of sodium 1-methyl-2-naphthoxide was added 0.85 g. (0.0081 mole) of 4-chloro-3-buten-2-one. A red coloration and cloudiness formed in the solution. After 10 hours at room temperature the reaction mixture was

poured into 200 ml. of water, neutralized with acetic acid, and extracted with chloroform. After being washed with sodium bicarbonate solution and water, the chloroform extract was clarified with $MgSO_4$, and evaporated to leave an oily residue. A petroleum ether solution of the residue was chromatographed on a silicic acid-Celite column. Elution of the column with petroleum ether-ether (19:1) gave a recovery of 0.17 g. (16.1%) of 1-methyl-2-naphthol. Further elution with petroleum ether-ether (9:1) gave 0.84 g. (55.6%) of the naphthoxy butenone CIII melting at 68-70°. A small amount of material eluted by petroleum ether-ether (5:1) and melting at 205-208° dec. was not studied further.

Sodium 1-methyl-2-naphthoxide in acetonitrile. To a stirred mixture of 30 ml. of acetonitrile and 1.20 g. (0.00667 mole) of sodium 1-methyl-2-naphthoxide at 40° was added 0.85 g. (0.0081 mole) of 4-chloro-3-buten-2-one. Heating was discontinued for 1 hour, and the solution then warmed to 70° for 10 minutes. After an additional 9 hours at room temperature the reaction mixture was handled in the same manner as the corresponding dioxane run (above) to give 0.16 g. (15.2%) of 1-methyl-2-naphthol and 0.82 g. (54.3%) of the naphthoxy butenone CIII, m.p. 68-70°. A trace of material, m.p. 205-208°, isolated from the petroleum ether-ether (5:1) eluate and identical (by

mixed melting point and infrared comparison) with similar material from the dioxane run was not investigated.

Ether-BF₃. To a mixture of 1.50 g. of 1-methyl-2-naphthol, 20 ml. of ether and 1.1 g. of 4-chloro-3-buten-2-one was added 0.80 ml. of 47% boron trifluoride-etherate. The solution was poured into 100 ml. of water after standing at room temperature for 75 minutes. After making the aqueous solution basic with 10% sodium hydroxide solution, and neutralization with acetic acid, the ether layer was separated, and the aqueous layer extracted with chloroform. The ether-chloroform extract was washed with water, dried over MgSO₄, and evaporated to give a dark oil. The oil was extracted with hot petroleum ether, and this cooled extract was placed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave 1.43 g. of 1-methyl-2-naphthol. Continued elution of the column with petroleum ether containing increasing amounts of ether gave no material. Elution with ether gave a small amount (20 mg.) of material melting, after recrystallization from petroleum ether, at 158-160°. The infrared spectrum (in CCl₄) of this material showed absorption bands at 1350, 1420 and 1680 cm.⁻¹. There was no indication of absorption in the 3200-4000 cm.⁻¹ region. This fraction was not studied further.

A mixture of 500 mg. of 1-methyl-2-naphthol, 25 ml. of ether, 2.0 ml. of 4-chloro-3-buten-2-one and 5 ml. of 47% boron trifluoride-etherate was allowed to stand at room temperature for 7 hours, and then refluxed on the steam bath 1 hour. The reaction mixture was washed and extracted as described above, and a petroleum ether solution of the residue chromatographed on silicic acid-Celite. The first eluates contained 250 mg. of 1-methyl-2-naphthol. Further fractions contained material melting at 158-160° that was identical by infrared comparison with the product isolated previously, and a trace of a yellow oil which showed a peak at 1660 cm.^{-1} in the infrared. The infrared spectrum was not identical with that of the oily 4a-methyl-2(4aH)-phenanthrone. This oil was not investigated further.

Glacial acetic acid and p-toluenesulfonic acid. Glacial acetic acid and p-toluenesulfonic acid hydrate were used as solvent and catalyst, respectively, under conditions identical to the ether- BF_3 runs. The products obtained corresponded to those from the ether- BF_3 reactions, and were not studied further.

4-(1-Methyl-2-naphthoxy)-2-butanone (CIV)

A mixture of 25 ml. of ethyl acetate, 150 mg. of 5% palladium-on-charcoal and 500 mg. of 4-(1-methyl-2-naphthoxy)-3-buten-2-one was hydrogenated at one atmosphere and room temperature. The hydrogen absorption was measured volumetrically. Hydrogen absorption ceased after 3 hours with an uptake corresponding to 1 mole of hydrogen. The solution was filtered and evaporated to give a pale yellow oil. Recrystallization from petroleum ether gave white crystals melting at 45-47°. A petroleum ether solution of the crystals was chromatographed on a Celite-silicic acid column. Elution with petroleum ether-ether (19:1) gave 20 mg. of 1-methyl-2-naphthol, m.p. 110-111°. Further elution with petroleum ether-ether (9:1) gave 4-(1-methyl-2-naphthoxy)-2-butanone (CIV) melting at 50-51°. The analytical sample, after two recrystallizations from petroleum ether, melted at 51-52°.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07.

Found: C, 78.90; H, 7.07.

Ultraviolet spectrum. λ_{max} . 230 $m\mu$ (ϵ 69,000), 282 $m\mu$ (ϵ 5,200), 322 $m\mu$ (ϵ 1,700) and 335 $m\mu$ (ϵ 1,700).

Cleavage of 4-(1-methyl-2-naphthoxy)-2-butanone by methanolic sodium hydroxide

To a mixture of 5 ml. of water, 50 ml. of methanol and 0.75 g. of sodium hydroxide was added 500 mg. of the naphthoxy butanone CIV. The solution was refluxed in an atmosphere of nitrogen for 2 hours, then cooled, and poured into 200 ml. of water. The aqueous solution was neutralized with acetic acid, and extracted with chloroform. The organic extract was washed with sodium bicarbonate solution and with water. A benzene solution of the solid residue obtained on evaporation of the chloroform was filtered through a short (2 x 7 cm.) alumina column. A total of 0.34 g. (98%) of 1-methyl-2-naphthol melting at 109-110° was obtained.

Reaction of 4-(1-methyl-2-naphthoxy)-2-butanone with potassium *t*-butoxide

In an atmosphere of nitrogen, 1 ml. of *t*-butanol in which 0.0086 g. of potassium had been dissolved was added to 500 mg. of the naphthoxy butanone CIV dissolved in 10 ml. of *t*-butanol. The solution turned pale yellow on addition of the base. The mixture was allowed to stand

at room temperature for 15 hours with occasional shaking. The mixture was poured into water (100 ml.), neutralized with acetic acid, and extracted with chloroform. After being washed with sodium bicarbonate solution and water, and dried (MgSO_4), the chloroform solution was evaporated to leave a clear oil. This oily residue was extracted with petroleum ether, leaving a small amount of a gummy residue. This residue was recrystallized from 95% ethanol, and yielded 20 mg. of white crystals melting at $236-238^\circ$. The mixture melting point of this material and the tricyclic decane XCIX (m.p. $244-245^\circ$) was $241-242^\circ$. The petroleum ether extract was chromatographed on a silicic acid-Celite column. The petroleum ether-ether (19:1) eluate gave 160 mg. of 1-methyl-2-naphthol, m.p. $110-111^\circ$. Continued elution with petroleum ether-ether (9:1) gave 85 mg. of the bicyclic diketone XCVIIIA, m.p. $102-103^\circ$. From the petroleum ether-ether (4:1) eluate came 135 mg. of the isomeric bicyclic diketone XCVIIIB, m.p. $106-107^\circ$.

Addition of 3-butyne-2-one to 1-methyl-2-naphthol

To 60 ml. of t-butanol in which 0.13 g. (0.0033 mole) of potassium had been dissolved was added 5.00 g. (0.0316 mole) of 1-methyl-2-naphthol. The solution was cooled to

15°, and 2.40 g. (0.0354 mole) of 3-butyn-2-one was added in an atmosphere of nitrogen. The mixture was allowed to stand (occasional shaking) at room temperature for 24 hours. Water (250 ml.) was then added to the reaction mixture, and the aqueous solution was neutralized with acetic acid. The chloroform extract of the mixture was washed with sodium bicarbonate solution and water, and dried over MgSO₄. Evaporation of the chloroform solution left a dark, tarry residue. Extraction of the tar with petroleum ether (5 x 80 ml.) left a dark solid residue. The petroleum ether solution was chromatographed on a Celite-silicic acid column. The petroleum ether-ether (97:3) eluate contained 1.27 g. (25.4%) of 1-methyl-2-naphthol, m.p. 110-111°. From the petroleum ether-ether (19:1) eluate came 1.80 g. (25.4%) of 4-(1-methyl-2-naphthoxy)-3-buten-2-one, m.p. 68-70°. The petroleum ether-ether (4:1) eluate gave a yellow oil, and the 2:1 eluate gave 1.67 g. of 4a-methyl-10a-hydroxy-4a,10a-dihydro-2(1H)-phenanthrone (CVII) melting at 131-133°. Recrystallization of this material from petroleum ether-benzene gave white crystals melting at 132-134°.

Anal. Calcd. for C₁₅H₁₄O₂: C, 79.62; H, 6.24.
Found: C, 79.99; H, 6.26.

Ultraviolet spectrum. (Figure 2) λ_{max} , 222 m μ (ϵ 28,000) and 264 m μ (ϵ 7,500).

The purple 2,4-dinitrophenylhydrazone was recrystallized from ethanol-ethyl acetate, m.p. 202-203° dec.

Anal. Calcd. for $\text{C}_{21}\text{H}_{16}\text{N}_4\text{O}_4$ *: C, 64.94; H, 4.16; N, 14.43. Found: C, 64.92; H, 4.13; N, 14.7.

The dark residue remaining after petroleum ether extraction was taken up in ethanol and passed through a short (2 x 7 cm.) charcoal-Celite column. Elution with ethanol-ethyl acetate gave an additional 0.21 g. (total of 25.6%) of the hydroxy phenanthrone CVII melting at 131-133°.

The yellow oil from the chromatogram was taken up in petroleum ether-benzene and placed on an alumina column. Elution with benzene gave 300 mg. of a pale yellow oil considered to be 4a-methyl-2(4aH)-phenanthrone. This oil was again chromatographed on alumina, and eluted with benzene. It would crystallize on standing overnight at -10°, but on warming to 5° would revert to an oil. That it may have been contaminated with some other substance was indicated by the formation of a small amount of orange crystals along with the expected purple 2,4-dinitrophenylhydrazone.

*Dehydration took place on acid-catalyzed derivative formation.

The purple 2,4-dinitrophenylhydrazone, after two recrystallizations from ethanol-ethyl acetate, melted at 194-196° dec. Admixed with the similar derivative of m.p. 202-203° dec. from the hydroxy phenanthrone CVIII, a melting point of 194-196° dec. was observed.

4a-Methyl-10a-hydroxy-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (CVIII)

A mixture of 20 ml. of 95% ethanol, 50 mg. of 5% palladium-on-charcoal and 200 mg. of 4a-methyl-10a-hydroxy-4a,10a-dihydro-2(1H)-phenanthrone was hydrogenated at one atmosphere and room temperature while the hydrogen absorption was measured volumetrically. Hydrogen absorption was complete at the end of 1 hour; the uptake corresponded to 2 moles. The solution was filtered to remove the catalyst, and the ethanol was evaporated under reduced pressure. The white residue melted at 155-157°. Two recrystallizations from petroleum ether-benzene gave white prisms melting at 157-158°.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88.

Found: C, 77.97; H, 7.71.

Ultraviolet spectrum. λ max. 265 m μ (ϵ 400).

The bright red 2,4-dinitrophenylhydrazone crystallized as plates from ethanol-ethyl acetate, m.p. 204-205° dec.

Anal. Calcd. for $C_{21}H_{20}N_4O_4^*$: C, 64.27; H, 5.14; N, 14.28. Found; C, 64.16; H, 5.10; N, 14.4.

4a-Methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XCIII)

To 25 ml. of dry benzene containing 100 mg. of *p*-toluenesulfonic acid hydrate and 100 mg. of calcium chloride was added 200 mg. of the hydroxy phenanthrone CVIII. The solution was heated at 50° for 30 minutes, then allowed to cool and stand at room temperature with occasional swirling for an additional hour. The benzene solution was washed with sodium bicarbonate solution and with water, and dried ($MgSO_4$). On evaporation of the benzene a solid residue was obtained. A petroleum ether-benzene (1:1) solution of the solid was filtered through a short (2 x 6 cm.) alumina column to give 170 mg. of white crystals melting at 88-90°. Two recrystallizations from petroleum ether gave white prisms, m.p. 89-90°.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 84.56; H, 7.42.

*Based on the dehydrated compound.

The ultraviolet spectrum is shown in Figure 2.

The 2,4-dinitrophenylhydrazone, bright red plates melting at 203-204°, did not depress the melting point of the similar derivative prepared from 4a-methyl-10a-hydroxy-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone.

Hydrogenation of 4a-methyl-4,4a-dihydro-2(3H)-phenanthrone (XCVII)

A mixture of 40 ml. of 95% ethanol, 200 mg. of 5% palladium-on-charcoal and 800 mg. of the phenanthrone XCVII was hydrogenated at 740 mm. and 25° while hydrogen absorption was measured volumetrically. Hydrogen absorption ceased after 8 hours with an uptake corresponding to two double bonds. The catalyst was removed by filtration, and the ethanolic filtrate evaporated. The oily residue was dissolved in petroleum ether and chromatographed on alumina. Elution of the column with petroleum ether-benzene (3:1) gave a clear oil that did not solidify. Continued elution of the column with petroleum ether containing increasing amounts of benzene gave a solid fraction. Recrystallization of this solid material from petroleum ether gave 90 mg. of crystals melting at 104-106°. When this material was admixed with the trans phenanthrone LXXXIX (m.p. 107-108°) from

cyclization of the dichloromethyl acetyl tetralin LXXXVII, a melting point of 106-107° was observed. The infrared spectra (CCl₄) of the trans phenanthrones prepared by the different methods were identical.

The oil from the first fractions of the chromatogram was taken up in petroleum ether, and again chromatographed on alumina. The oil eluted by petroleum ether-benzene (2:1) had an infrared spectrum (CCl₄) different than the trans phenanthrone LXXXIX, and was considered to be cis-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XCIV). The material could not be obtained crystalline at room temperature. The oil would crystallize on standing at -10° overnight, but melted almost immediately when removed from the refrigerator.

The semicarbazone of the cis phenanthrone crystallized from aqueous ethanol as sparkling white platelets, m.p. 195-197° dec. When admixed with the trans phenanthrone semicarbazone, a melting point of 199-201° dec., preliminary darkening, was observed.

Anal. Calcd. for C₁₆H₂₁N₃O: C, 70.81; H, 7.80; N, 15.49. Found: C, 70.86; H, 7.90; N, 15.4.

The yellow para-nitrophenylhydrazone was recrystallized from aqueous ethanol, and melted at 148-150° dec.

Anal. Calcd. for $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 71.78; H, 6.73; N, 12.3.

Reduction of 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XCIII)

Depending on the conditions used, different products or mixtures of products were obtained.

Palladium-on-carbon. A mixture of 200 mg. of the phenanthrone XCIII, 15 ml. of 95% ethanol and 100 mg. of 5% palladium-on-charcoal was hydrogenated at 740 mm. and 25°. In an hour hydrogen absorption corresponding to one double bond had occurred, and uptake ceased. The ethanolic solution was filtered, and evaporated, and a petroleum ether solution of the residual oil was chromatographed on alumina. A total of ten fractions were eluted using petroleum ether-benzene (2:1) and (1:1). The infrared spectra of the fractions indicated the cis phenanthrone XCIV to be the main product, with about 10% trans present. The first two fractions were combined and converted to the semicarbazone, which, after two recrystallizations from aqueous ethanol, melted at 195-197° dec. When admixed with the cis semicarbazone from the reduction of the phenanthrene dienone XCVII, there was no depression of melting point.

Lithium in liquid ammonia. To a solution of lithium (100 mg.) in liquid ammonia (100 ml.) was added 200 mg. of the phenanthrone XCIII in 20 ml. of dry ether. After 30 minutes 2.0 g. of ammonium chloride was added, and the ammonia was allowed to evaporate. The residue was taken up in chloroform-water. After washing the aqueous extract with chloroform, the combined organic extract was washed with dilute hydrochloric acid, sodium bicarbonate solution, and with water. The chloroform was removed by evaporation, and the solid residue was taken up in benzene-petroleum ether (3:2), and chromatographed on alumina. Elution of the column with the same solvent gave 140 mg. of trans-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (LXXXIX), m.p. 104-106°.

Hydrogenation of 4a-methyl-2(4aH)-phenanthrone (CI)

A mixture of 15 ml. of ethanol, 100 mg. of 5% palladium-on-charcoal and 260 mg. of the phenanthrone CI was hydrogenated at atmospheric pressure and room temperature while hydrogen absorption was measured volumetrically. Hydrogen absorption corresponding to 3 moles was complete in 10 hours. The solution was filtered, and the ethanol evaporated under reduced pressure. A petroleum ether solution of the

residue was chromatographed on alumina. Elution with petroleum ether-benzene (3:2) gave 120 mg. of an oil whose infrared spectrum was identical with that of cis-4a-methyl-3,4,4a,9,10,10a-hexahydro-2(1H)-phenanthrone (XCIV). The semicarbazone of this oil melted at 193-195^o, and did not depress the melting point of an authentic specimen. Further elution of the column gave material whose infrared spectra indicated that it was a mixture of the cis and trans phenanthrones XCIV and LXXXIX.

cis-4a-Methyl-3,4,4a,10a-tetrahydro-2(1H)-phenanthrone (CXI)

A solution containing 150 ml. of benzene, 1.50 g. of 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone and 3.5 ml. of ethylene glycol was distilled until 120 ml. of benzene remained. After adding 40 mg. of p-toluenesulfonic acid hydrate and attaching a water trap, the solution was refluxed and stirred for 4 hours. The cooled mixture was washed with sodium bicarbonate solution and water, and the benzene layer dried over MgSO₄. Evaporation of the benzene gave 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone ethylene ketal (CIX) as a thick oil. The infrared spectrum indicated no ketone was present. The ketal was used in the next reaction without further purification or characterization.

The ultraviolet spectrum of the crude ketal exhibited a maximum at $265\text{ m}\mu$ (ϵ 400).

To 50 ml. of ethylene glycol containing 2.0 g. of potassium hydroxide was added 1.0 g. of the ketal CIX. The mixture was heated at 190° (bath temperature) for five hours in an atmosphere of nitrogen. After cooling, the mixture was poured into 250 ml. of water, neutralized with acetic acid, and filtered to remove an insoluble residue. The residue was washed with chloroform, and the aqueous mixture was extracted with chloroform. The organic layer was washed with sodium bicarbonate solution and water, dried with MgSO_4 , and evaporated. The residue obtained on evaporation of the chloroform was dissolved in 60 ml. of 95% ethanol containing 10 ml. of 10% sulfuric acid, and refluxed on the steam bath for 1 hour. The cooled reaction mixture was poured into 250 ml. of water. The chloroform extract of the aqueous mixture was washed with sodium bicarbonate solution and water, and dried over MgSO_4 . The residue obtained on evaporation of the chloroform was taken up in benzene-petroleum ether (3:2), and chromatographed on alumina. The infrared spectra of the first fractions (eluted with benzene-petroleum ether, (3:2)) showed a considerable amount of unhydrolyzed ketal. These fractions were combined in 40 ml. of 95% ethanol and 10 ml. of 10% sulfuric acid, and refluxed on the steam bath

for 1 hour. The residue isolated from this second hydrolysis was dissolved in 40 ml. of petroleum ether-benzene (1:1), and combined with the remaining fractions from the alumina column (further eluted with benzene and benzene-ether). This solution was chromatographed on alumina. Elution of the column with petroleum ether-benzene (1:1) gave 125 mg. of cis-4a-methyl-3,4,4a,10a-tetrahydro-2(1H)-phenanthrone (CXI), m.p. 65-67°. Two recrystallizations from petroleum ether gave white plates melting at 68-69°.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60.

Found: C, 84.87, 84.36; H, 8.01, 7.61.

Ultraviolet spectrum. λ_{\max} . 267 $m\mu$ (ϵ 9,800);
 λ_{\min} . 234 $m\mu$ (ϵ 3,000).

Further elution of the column with benzene gave a small amount of material whose infrared spectrum was identical with that of 4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (XCIII).

Reduction of cis-4a-methyl-3,4,4a,10a-tetrahydro-2(1H)-phenanthrone (CXI)

A mixture containing 55 mg. of the phenanthrone CXI, 15 ml. of 95% ethanol and 20 mg. of 5% palladium-on-charcoal was hydrogenated at atmospheric pressure and room temperature.

Hydrogen absorption, measured volumetrically, ceased in 45 minutes with an uptake corresponding to one double bond. The solution was filtered, and evaporated in a stream of nitrogen. The infrared spectrum of the residue was identical with that of the cis phenanthrone XCIV. A benzene solution of the oily residue was filtered through a short (1.5 x 3 cm.) alumina column. The infrared spectrum of the oil eluted with benzene was identical with that of the crude residue. The oil was converted to a semicarbazone, which, after one recrystallization from ethanol, melted at 191-193° dec. When admixed with an authentic specimen of the cis phenanthrone (XCIV) semicarbazone, a melting point of 192-194° dec. was observed. The infrared spectrum (nujol mull) of the semicarbazone was identical with that of the semicarbazone from the cis hexahydrophenanthrone XCIV.

SUMMARY

Two new syntheses of hydrophenanthrene ketones are outlined. The first is based on ring formation by intramolecular displacement of chloride ion from a dichloromethyl group by an adjacent acetone side chain. The novel addition of an unsaturated ketone to 1-methyl-2-naphthol to give a phenanthrone is utilized in the second method.

The stereochemistry of the intermediate compounds as well as that of the hydrophenanthrones is discussed.

Structures are proposed for several side-products isolated from the reaction mixtures.

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