INVESTIGATIONS OF THE SYNTHESIS OF
POLYCYCLIC AROMATIC HYDROCARBONS
CONTAINING SEVEN-MEMBERED RINGS

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By

DONALD FREDERIC BARRINGER, JR., B. S.

* * * *

The Ohio State University
1960

Approved by

[Signature]
Adviser
Department of Chemistry
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ACKNOWLEDGMENTS

The author would like to thank Dr. M. P. Cava for suggesting this study, and for advice and encouragement during the course of the research, The Ohio State University for financial assistance in the form of an assistantship, and The Standard Oil Company of Ohio and E. I. duPont de Nemours & Company for fellowship awards.
INTRODUCTION

A. The Heptalene System

Considerable theoretical interest centers on heptalene (I) and the other members of a class of hydrocarbons known as non-benzenoid or pseudo-aromatic hydrocarbons. Baker, in discussing non-benzenoid aromatic hydrocarbons, pointed out that while pentalene (II) possessed considerable strain (108° angles for a regular pentagon compared to 125° for the normal angle between a single and a double bond), heptalene, if planar, does not (128.6° angles for a regular heptagon). Furthermore, the angles in heptalene are less strained than those in the known hydrocarbon azulene (III).

Since the heptalene molecule can be planar without undue strain, and since it possesses a completely conjugated π-electron system, one might expect it to possess aromatic character. Both the valence bond and the molecular orbital approximations have been employed to calculate the resonance energy, and both

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methods predict a resonance energy comparable to normal aromatic hydrocarbons (molecular orbital calculations give 50 kcal/mole resonance energy for heptalene as compared to 54 kcal/mole for azulene and 63 kcal/mole for naphthalene).\textsuperscript{4}

In his discussion of pseudo-aromatic systems Craig\textsuperscript{5} points out several difficulties in applying these empirical methods derived from normal aromatic systems. While the two methods give essentially the same results when applied to normal aromatic systems, they do not when applied to pseudo-aromatic systems.

The most fundamental difference involves the nature of the ground state which the valence bond method predicts to be non-totally symmetrical (the $\pi$-electron cloud possesses a symmetry different from that of the carbon skeleton).

In order to avoid the difficulties of the empirical methods, Craig\textsuperscript{5} calculated the energy levels for the $\pi$-electrons of cyclobutadiene and bicyclobutadiene using the circular field model. These can be considered the simplest members of the series of monocyclic and bicyclic hydrocarbons containing 4 in $\pi$-electron centers all located in the periphery of the carbon skeleton. The results show that the members of these two series possess no more resonance energy than the open chain analogs.

As a final comment on the possibility of the existence of heptalene, it might be pointed out that heptalene can be

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puckered to accommodate normal bond angles. Thus if resonance is unimportant, the molecule might exist as a polyolefin with alternating single and double bonds.

All of the methods employed so far in attempted syntheses of heptalene have depended upon the aromatization of partially unsaturated [5.5.0] bicyclocodoceneanes. Horn and co-workers\(^6\),\(^7\) attempted the dehydrogenation of compounds IV and V over palladium-charcoal. Under the conditions usually employed dimethyl naphthalenes were the only products. Using a special apparatus to permit very short contact time, they isolated azulene-like products.

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Aspinwall and Baker\(^8\) were likewise unsuccessful in dehydrogenating \([5.5.0]\)bicyclododecane-3 (VI). On brominating, compound V gave a dibromide which, on elimination of hydrogen bromide, gave compounds with less ultraviolet absorption than the starting material. These were assumed to be benzenoid.

Barlow\(^9\) has prepared a mixture of \([5.5.0]\)bicyclododecandiones (predominantly the 1,6 isomer) (IX) by the action of nitrous acid on compound VIII. Compound VIII was prepared from trans decalin-1,5-dione (VII) by catalytic reduction of the bis cyanohydrin. He was unable to separate the isomeric diketones and was unable to isolate crystalline bromination products from the reaction of either the mixed diketones or the bis enol acetate


\(^{9}\) D. O. Barlow, Dissertation Abstracts, 13, 309 (1953).
with N-bromosuccinimide. The tetraketone (X) was prepared by oxidation of the mixed diketones, but it could not be converted to the bis tropolone (XI).

Hafner and Schneider\textsuperscript{10} have recently reported the synthesis of a heptalene derivative (XII) by treatment of XIII with sodium ethoxide. They report, however, that the visible light spectrum is similar to azulene. Thus the compound may not actually contain a truly heptalene-like $\pi$-electron system.

In the light of the previous attempts to synthesize heptalene,

\textsuperscript{10} K. Hafner and J. Schneider, Angew. Chem., 70, 702 (1958).
the procedure of introducing double bonds into a \([5.5.0]\) bicyclododecane system was not considered promising. It was considered desirable to devise a synthesis which would permit the introduction of all, or nearly all, of the double bonds during the ring closure. Of the known seven-carbon ring compounds possessing a high degree of \(\pi\)-electron conjugation, tropone (XIV) is most interesting.

\[
\begin{align*}
\text{XIV} & \quad \text{XV} & \quad \text{XVI} \\
\text{XVII} & \quad \text{XVIII} \\
\end{align*}
\]

because the as yet unknown bis tropones (XV-XVIII) can be considered heptalene quinones.

Thiele and Weitz\textsuperscript{11} have reported the synthesis of 2,7-diphenyl-4,5-benzotropone (XIX) by the alkaline condensation

\[
\begin{align*}
\text{XIX} & \quad \text{XX} & \quad \text{XXI} \\
\end{align*}
\]

\textsuperscript{11} J. Thiele and E. Weitz, Ann., \textbf{377}, 1 (1910).
of o-phthalaldehyde and dibenzyl ketone. If the proper tropone dialdehyde were available, this reaction should permit the synthesis of 2,4,7,9-tetraphenyl-3,8-heptalenequinone (XX) which could be subjected to reducing conditions in an attempt to prepare 2,4,7,9-tetraphenylheptalene-3,8-diol (XXI).

The above cyclic condensation also provides the key to a possible synthesis of the desired 2,7-diphenyltropone-4,5-dialdehyde (XXIV). If furan-3,4-dialdehyde could be substituted for o-phthalaldehyde

![Diagram](image)

XXII    XXIII    XXIV

in the condensation, compound XXII would result. If furan is brominated at -10° in methanol in the presence of potassium acetate, the product isolated is 2,5-dimethoxy-2,5-dihydrofuran. This compound is a cyclic acetal and can be hydrolized to malealdehyde. If compound XXII were subjected to these conditions, one should obtain the cyclic acetal XXIII and the dialdehyde XXIV. This compound could then be subjected to the condensation with dibenzyl ketone to obtain the quinone XX.

With the ultimate object of examining the above sequence of reactions, a synthesis for furan-3,4-dialdehyde was sought.

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B. The Pleiadene System

The other ring system dealt with in this dissertation is that of pleiadene (XXV).\textsuperscript{13} While this compound might be considered a distant relative of heptalene since it is an aromatic system containing a seven-carbon ring, it was primarily of interest because of its analogy to the quinodimethanes (XXVI) proposed as intermediates in the mechanism for the formation of benzocyclobutenes (XXVII).\textsuperscript{14-16} Pleiadene is very closely analogous to the $\alpha, \alpha'$-diphenyl-$\alpha$-quinodimethane (XXVI, $R = \phi$), which is the intermediate in the formation of 1,2-diphenylbenzocyclobutene (XXVII, $R = \phi$) reported by Jensen.\textsuperscript{17} The high degree of reactivity of

\begin{center}
XXV \quad XXVI \quad XXVII
\end{center}


this compound toward maleic anhydride and sulfur dioxide could be explained by assuming that it has considerable tendency to exist in the \( \alpha \)-quinodimethane form. One would expect that pleiadene (XXVa) would be at least as stable as \( \alpha, \alpha' \)-diphenyl-\( \alpha \)-quinodimethane (XXVI, \( R = \emptyset \)). It is therefore open to conjecture whether pleiadene would exist as the "open" form (XXVa) or the "closed" form (XXVb).

![XXVa](image)

![XXVb](image)

A. Reiche and Früwalt\(^{18}\) reported obtaining a condensation product \( C_{16}H_{10}O_3 \) from the condensation of phthalic anhydride and \( \beta \)-naphthol in the presence of sulfuric acid and boric acid. They assigned the compound the structure XXVIII, 1-hydroxyleiadene-7,12-dione. This compound had actually been prepared earlier by

![XXVIII](image)  ![XXIX](image)  ![XXX](image)

\(^{18}\) A. Reiche and E. Früwalt, Ber., 64, 1603 (1931).
Emma M. Dietz\textsuperscript{19} using aluminum chloride as the condensing agent, although she did not deduce the correct structure. Fieser\textsuperscript{20} improved upon the preparation used by Miss Dietz, and he also reported that the hydroxyl group in XXVIII could be replaced by chlorine using phosphorus pentachloride in the presence of phosphorus oxychloride to give 1-chloropleiadene-7,12-dione (XXIX, \(X = \text{Cl}\)). The correctness of structure XXVIII for 1-hydroxyleiadene-7,12-dione was established by an independent synthesis of its methyl ether (XXIX, \(X = \text{OCH}_3\)) via 1-methoxy-7-pleiadone (XXX, \(X = \text{OCH}_3\)).\textsuperscript{20-22}

This reaction sequence (Equation 1) is a general method for the preparation of compounds of the types XXIX and XXX where \(X = \text{CH}_3\) or \(\text{OCH}_3\), with or without other methyl or methoxy substituents at the free positions in the naphthalene ring.\textsuperscript{20-22} Phthalic anhydride (XXXI) is condensed with the appropriate \(\beta\)-substituted naphthalene (XXXII) in the presence of aluminum chloride in an ice bath. The resulting keto-acid (XXXIII) is reduced by heating with zinc dust in strongly alkaline solution to the corresponding naphthylmethylbenzoic acid (XXXIV). The acid (XXXIV) is converted to the acid chloride by treatment with thionyl chloride, and then cyclized using aluminum chloride at ice bath temperature. The resulting

\textsuperscript{19} Emma M. Dietz, dissertation, Bryn Mawr, 1929.


\textsuperscript{22} L. F. Fieser and Mary Fieser, J. Am. Chem. Soc., 55, 3010 (1933).
pleiadone (XXX) can be converted to the pleiadenedione (XXIX) by oxidation with chromic acid in acetic acid.

\[
\begin{align*}
\text{XXXI} & \quad + \quad \text{XXXII} & \quad \rightarrow & \quad \text{XXXIII} \\
\text{XXIX} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \ Quad
hydrate, potassium hydroxide, and palladium on calcium carbonate\textsuperscript{23} or by heating the chloro compound at 180–200\textdegree with the stoichiometric amount of tetralin in the presence of palladium on charcoal.\textsuperscript{24}

Reduction of 1-chloropleiadene-7,12-dione with sodium borohydride has been shown to afford 1-chloro-7,12-dihydropleiadene-7,12-diol (XXXIX).\textsuperscript{25} Dry distillation of pleiadene-7,12-dione

\textsuperscript{24} N. Doss, unpublished experiment.

or its 1-hydroxy- or 1-chloro-derivative with zinc dust in a hydrogen stream yields 7,12-dihydropleiadene (XL),\textsuperscript{23,26} and some substituted 7,12-dihydropleiadenes have been prepared by hydrogenating the corresponding pleiadones or pleiadenediones in alcohol over copper chromite at moderate pressure at 170°.\textsuperscript{27}

Since Jensen had reported that 1,2-diphenylbenzocyclobutene (XXVII, \(R = \varnothing\)) could be prepared either by the action of sodium iodide on \(\alpha,\alpha'\)-dibromo-\(\alpha,\alpha'\)-diphenyl-\(\varnothing\)-xylene (XLI) or by the action of a base on \(\alpha\)-bromo-\(\alpha,\alpha'\)-diphenyl-\(\varnothing\)-xylene (XLII), it was decided to investigate the applicability of these reactions to the analogous compounds in the pleiadene series (XLIII, XLIV). These compounds could conceivably be prepared either by transformation of the appropriate mono- or di-alcohol or by bromination of a 7,12-dihydropleiadene.

\textsuperscript{26} W. Knapp, Monatsh., \textbf{60}, 189 (1932).

DISCUSSION OF THE RESULTS

A. Furan-3,4-dialdehyde

In looking for a feasible route to furan-3,4-dialdehyde (I), it was decided that a logical starting point was furan-3,4-dicarboxylic acid (II). The method of Alder and Rickert,¹

![Chemical structures](image)

I

II

represented by Equation 1, appeared to be the best route for the synthesis of this acid. It was reinvestigated carefully as described below.

![Chemical structures](image)

III

IV

(1)

V

VI, R = CH₃

II, R = H

¹ K. Alder and H. F. Rickert, Ber., 70, 1354 (1937).
The commercially available mono-potassium salt of acetylene dicarboxylic acid was readily esterified with excess methanol in ethylene chloride solution in the presence of sulfuric acid. In working up this reaction, it is important to have the organic layer dry and free of acids before distillation. If it is not, hydrolysis during distillation will reduce the yield of ester. Since esters of acetylenedicarboxylic acid are powerful lachrymators, caution should be exercised in their handling.

Dimethyl acetylenedicarboxylate (III) readily undergoes the Diels-Alder Reaction with furan forming dimethyl 3,6-endoxy-3,6-dihydropthalate (IV). This reaction is carried out at atmospheric pressure using a slight excess of furan and benzene as solvent. This allows the reflux temperature to come to about 70° at the end of the reaction. The product (IV) may be isolated, but it is reported to be unstable, so the entire reaction mixture was dissolved in acetone and hydrogenated over palladium-charcoal to yield dimethyl 3,6-endoxy-3,4,5,6-tetrahydropthalate (V). This compound is the product of a hypothetical Diels-Alder Reaction between ethylene and dimethyl furan-3,4-dicarboxylate (VI), and on strong heating, the reverse Diels-Alder Reaction takes place. This decomposition begins as the dimethyl 3,6-endoxy-3,4,5,6-tetrahydropthalate (V) is heated above 100° in an open flask, but the temperature was slowly raised to 200° to ensure complete pyrolysis.

It is possible to eliminate the crystallization of the
intermediate (V) described in the experimental section by merely evaporating the solution from the hydrogenation and pyrolyzing the residue. However, this procedure generally yields a less pure product (VI). The ester (VI) was saponified with methanolic potassium hydroxide to yield furan-3,4-dicarboxylic acid (II).

Two general methods might be employed to convert furan-3,4-dicarboxylic acid (II) to furan-3,4-dialdehyde (I). One is to use one of the methods available to reduce carboxylic acid derivatives to aldehydes. The other is to reduce the acid to the corresponding dialcohol and oxidize this to I. Attempts to reduce either the ester (VI) or the acid (II) to 3,4-bis(hydroxymethyl)-furan (VII) with lithium aluminum hydride were not promising presumably because of isolation difficulties. The only product that could be isolated was an amorphous solid, in small amounts, which appeared to be polymeric in nature. There is a procedure described in the literature\(^2\) for converting dimethyl furan-3,4-dicarboxylate (VI) into 3,4-bis(hydroxymethyl)furan diacetate (VIII), (Equation 2). This is done by treating the complex from the hydride reduction with acetic anhydride to convert it directly to the diacetate.

\[
\begin{align*}
\text{II} & \quad R = H \\
\text{VI} & \quad R = CH_3 \\
\text{VII} & \quad R = H \\
\text{VIII} & \quad R = CH_3CO
\end{align*}
\]

\[\text{Equation 2}\]

Compound VIII was prepared by this method and subjected to oxidation by refluxing it in a slight excess of a 10 per cent sodium chromate solution buffered with sodium bicarbonate.\textsuperscript{3} No furan-3,4-dialdehyde was isolated, and the only product was an oily tar. Under the same conditions benzyl acetate is oxidized to benzaldehyde.

Since it appeared that the preparation of 3,4-bis(hydroxy-methyl) furan (VII) would be rather difficult at best, attention was turned toward possible methods of reducing a derivative of furan-3,4-dicarboxylic acid (II) directly to the aldehyde (I). At first, it appeared quite likely that the Rosenmund Reduction would not be applicable since it fails in the preparation of the seemingly analogous compound, o-phthalaldehyde (IX).\textsuperscript{4} However, closer examination reveals an important difference in the behavior of the two compounds. While o-phthalaldehyde derivatives undergo a variety of reactions which lead to the formation of a five-membered ring, functional groups in the 3 and 4 positions in the

\textsuperscript{3} L. Friedman, unpublished experiments.

\textsuperscript{4} K. W. Rosenmund and F. Zetzsche, Ber., 54, 2888 (1921).
furan ring show a marked tendency to behave independently.\textsuperscript{5}

It was felt, therefore, that the Rosenmund Reduction (Equation 3) might be a possible method for the preparation of furan-3,4-dialdehyde (I). The bis acid chloride (X) can be prepared using

\[
\begin{align*}
\text{II, } R &= \text{OH} \\
\text{X, } R &= \text{Cl}
\end{align*}
\]

either phosphorus pentachloride\textsuperscript{5} or thionyl chloride. The yields are about the same with either reagent, but the purification is somewhat simpler when thionyl chloride is used.

When the acid chloride was reduced under the usual Rosenmund conditions,\textsuperscript{6,7} using a palladium on barium sulfate catalyst poisoned with a quinoline and sulfur preparation, the reduction proceeded rather slowly. Omitting the catalyst poison did not seem to affect the rate appreciably. Nor did the method of preparation of the acid chloride appear to have much effect; although, it is reported that, in trace amounts, phosphorus compounds are very powerful inhibitors.\textsuperscript{7} The best yield of 22 per cent of a crude


dialdehyde was obtained in the reduction of a sample of acid chloride prepared with phosphorus pentachloride and using the catalyst poison.

In an effort to see whether the reaction would proceed more smoothly in the presence of a more active catalyst, the reduction was run once in the presence of palladium-charcoal in refluxing toluene. The rate of reduction was greatly increased, as evidenced by the rapid evolution of hydrogen chloride. However, the reduction did not stop at the aldehyde stage, and no aldehyde was isolated. The use of benzene as the solvent resulted in a considerably slower reaction, but still no aldehyde was formed. In general, the Rosenmund Reaction was quite unreliable for the preparation of furan-3,4-dialdehyde (I). The 22 per cent yield reported was the result of a single experiment. The reaction was run numerous times, and usually resulted in only a trace of aldehyde, or none at all.

Recently a general method was developed for the preparation of aldehydes by the reduction of substituted amides with lithium aluminum hydride. Both the bis anilide (XI) and the bis N-methylanilide (XII) were prepared by treating the acid chloride with the appropriate aniline. Preliminary investigations of the reduction of the compounds with lithium aluminum hydride

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were not promising in either case. Furan-3,4-dicarboxanilide (XI) was also subjected to the conditions of the Sonn and Müller Reduction, but reduction failed to occur.

In some previous investigations nitriles were reduced to aldehydes with lithium aluminum hydride. The secret of success appears to be careful selection of the proper temperature. With the investigation of this reaction in mind, the preparation of furan-3,4-dinitrile (XIV) was undertaken (Equation 4). The diamide (XIII) can be prepared by treating the acid chloride with concentrated aqueous ammonia, but somewhat better yields were obtained by adding a benzene solution of the acid chloride dropwise to liquid ammonia. The diamide (XIII) was dehydrated

\[
\begin{array}{c}
\text{XIII} \\
\text{XIV}
\end{array}
\]

---

to the dinitrile (XIV) by refluxing it for about 60-90 minutes in phosphorus oxychloride. Longer refluxing seemed to destroy the product, yielding gums. Long refluxing with thionyl chloride did not affect dehydration. If a dry mixture of the diamide (XIII) with phosphorus pentoxide is heated strongly under reduced pressure, the dinitrile sublimes out. This is probably the most convenient method for small scale preparations.

When furan-3,4-dinitrile (XIV) was treated with lithium aluminum hydride in ether solution for one-half hour at -20°, crude starting material was isolated. The infrared absorption spectrum of this crude material showed a slight absorption in the carbonyl region, which indicated that some reduction did occur. As the temperature and reaction time were increased, the extent of reduction also increased.

One reduction, carried out for 14 hours at 0°, yielded a complex mixture whose infrared absorption spectrum showed absorption corresponding to a carbonyl, a nitrile, and an amino or hydroxy group. Along with this mixture some unreacted starting material was also isolated. Reduction for one hour at 0° yielded a crude solid which melted at about 80°. This material showed absorption in the infrared corresponding to a nitrile and a carbonyl. The material was not investigated further to determine whether it was a mixture or a crude sample of 4-cyano-3-furaldehyde (XV).

The experience of this research has clearly shown that
furan-3,4-dicarboxylic acid derivatives are especially resistant to reduction. The reactions which can usually be employed to prepare aldehydes afford either a very slow reduction or no reaction at all. The Rosenmund Reduction produced the desired product only in small yield. When attempts were made to increase the rate of reaction and the yield by using a more active catalyst, overreduction apparently resulted.

Similarly, in the reduction of the dinitrile and the substituted diamides with lithium aluminum hydride, no set of conditions was found which would permit selective reduction of both functional groups to the aldehyde stage. The difficulty probably hinges on the solubility of the metal-organic complex (XVI or XVII) formed on reduction of the first functional group. If the solubility of the complex is too low, the second group
may not be reduced. Raising the temperature or increasing the reaction time may affect reduction of the second functional group, but it can also lead to reduction of the aldehyde functions.

Since only small amounts of impure furan-3,4-dialdehyde (I) were available, it was not possible to fully investigate the condensation reaction (5), but preliminary experiments indicated that it probably will not occur as easily as the analogous reaction with α-phthalaldehyde. In one small scale reaction

\[
\text{CHO} + \text{CHO} \xrightarrow{\text{OH}^-} \text{XVIII}
\]

(I) (XVIII)

carried out with methanolic potassium hydroxide, a very small yield (0.43%) of pale yellow leaflets was obtained. This material decomposed without melting at about 350°, and the infrared absorption spectrum indicated the presence of a carbonyl function. It is not known whether this material was the desired product (XVIII). Possibly the condensation could be successfully carried out in the presence of an organic base, but this possibility could not be fully investigated.

The work of Jeger et al.\textsuperscript{10} on the alkaline degradation

of the bitter principle limonin is interesting in connection with this reaction. They postulate that 3-furaldehyde is the primary degradation product, which is further degraded as in Equation 6 to the products isolated. Furan-3,4-dialdehyde would be expected to exhibit the same instability to strong alkali.

The failure to develop a satisfactory synthesis for furan-3,4-dialdehyde led to the abandonment of the attempt to synthesize a heptalene derivative at this stage.
B. Pleiadene

The condensation of phthalic anhydride and \( \beta \)-naphthol in the presence of aluminum chloride occurred readily as described in the literature\(^\text{11}\) and afforded a 72 per cent yield of 1-hydroxyleiadene-7,12-dione (XIX) (Equation 7). This is the result of one experiment and probably does not represent the optimum yield. During the work-up of this reaction the product is separated from water insoluble impurities by converting it to the sodium salt. This salt is only sparingly soluble in water, and the solid residues

\[
\begin{align*}
\text{CO} & \quad + \quad \text{HO} \quad \text{AlCl}_3 \\
\text{CO} \quad & \quad \rightarrow \quad \text{XIX, } X = \text{OH} \end{align*}
\]

must be extracted with a large volume of water to prevent the loss of a considerable amount of product.

The reaction of 1-hydroxyleiadene-7,12-dione (XIX) with phosphorus pentachloride proceeded smoothly but yielded 1-chloroleiadene-7,12-dione (XX) in only 30 per cent yield. This yield could undoubtedly be improved, but the best yield

reported is still only 48 per cent.\textsuperscript{12} The fate of the rest of the starting material is not known.

The conversion of the hydroxy compound (XIX) to the chloro compound (XX) is very much like the conversion of a carboxylic acid to an acyl chloride. To carry the analogy further, boiling with sodium hydroxide solution converts 1-chloropleiadene-7,12-dione (XX) into 1-hydroxypleiadene-7,12-dione (XIX).\textsuperscript{12} By comparing the partial structure XXI with structure XXII, it can be seen that 1-substituted pleiadenediones could be considered vinylogs of carboxylic acid derivatives.

The mechanism of these displacement reactions probably involves a 1-4 addition of the entering group (Y) to the unsaturated ketone system, followed by a reverse movement of the electrons to expel the leaving group (X) (Equation 8). In the conversion of

\[ \text{Equation 8} \]

the hydroxy compound to the chloro compound, the first step may be the formation of a chlorophosphate ester followed by a four-center transfer of a chlorine from phosphorus to carbon (Equation 9), with an assist from the conjugation. The reverse reaction probably follows the simple addition-elimination path (Equation 8).

1-Chloropleiadene-7,12-dione (XX), when heated with a slight excess of tetralin in the presence of palladium-charcoal, undergoes reduction as shown in Equation 10.

This reaction is best run using only a slight excess of tetralin and heating at about 200° until hydrogen chloride is no longer evolved. If the heating is continued after hydrogen chloride evolution ceases, or if an appreciable excess of tetralin is present, the pleiadene-7,12-dione (XXIII) will
be reduced further to 7,12-dihydropiadiene (XXIV). Water is produced as a by-product in this reduction, and at elevated temperatures this will hydrolyze 1-chloroplaadiene-7,12-dione (XX) to 1-hydroxypladiene-7,12-dione (XIX). This compound is difficult to remove from the product because it behaves very much like pladiene-7,12-dione in the recrystallization.
Finally, if the reduction is interrupted before completion, the resulting mixture of pleiadene-7,12-dione and 1-chloro-pleiadene-7,12-dione is also difficult to separate because of their similar properties. Thus it is desirable to operate as close as possible to the optimum conditions, not only to increase the yield, but also because the possible side products are difficult to remove. Even under the most favorable conditions, about 50-60 per cent was the best yield.

The hydrogenolysis of an aromatic halogen derivative under these comparatively mild conditions must depend upon the special activating effect of the carbonyl groups. Perhaps intermediates of the type XXV and XXVI are present on the catalyst surface.

Treatment of pleiadene-7,12-dione (XXIII) with excess sodium borohydride afforded an 86 per cent yield of 7,12-dihydro-pleiadene-7,12-diol (XXVII) (Equation 11).

$$\text{XXIII} \xrightarrow{} \text{XXVII}$$

(11)

When the solid diketone was added to the alcohol solution of sodium borohydride, an orange-red solution resulted, and this was left standing until the color faded. An amount of sodium
hydroxide equivalent to the hydrogen in the sodium borohydride was added, and the solution heated several hours to ensure hydrolysis of any borate esters. When the solution was diluted with an approximately equal volume of water and allowed to cool, the diol crystallized out. The hydrolysis of the intermediate borate esters is the most crucial part of the procedure. If this is not done properly, the yield obtained will be lowered by half or more.

The stereochemistry of the product is not known, but it is interesting to speculate on the probable situation. The pleiadene-7,12-dione molecule (XXIII) is probably flat, or nearly so, to allow for maximum \( \pi \)-orbital overlap, whereas the 7,12-dihydropleiadene molecule (XXIV) is bent into a strain-free quasi-boat conformation. If one pictures the first borohydride ion as approaching the 7-position of XXIII perpendicular to the plain of the molecule, one can see that the intermediate ketoalcohol must have a configuration intermediate between the extremes XXVIII and XXIX. Structure XXVIII represents one in which the molecule has bent to relieve angle strain, but in so doing the carbonyl group has been twisted out of the planes of both the
aromatic rings so that conjugation would be less effective. The planar structure XXIX retains the maximum conjugation, but also possesses the maximum angle strain.

If XXVIII most closely represents the actual situation, the clearest path of approach of the second borohydride ion is that indicated by the arrow. Models show that the other side of the carbonyl group is blocked by the hydrogen at position 7. This mode of attack will give the trans diol (XXX). If structure XXIX best represents the intermediate stage, the choice of the least hindered side for the approach of the second borohydride ion is less clear-cut. However, the side away from the oxygen at position 7 is probably the best choice. This would yield the cis diol (XXXI). The actual situation is probably intermediate between the extremes discussed here, and a mixture might be expected to result. The fact that the diol does not
crystallize well and does not give a sharp melting point tends to support this view.

When this diol is treated with p-toluenesulfonyl chloride in refluxing pyridine, one does not obtain a ditosylate even in the presence of an excess of the acid chloride. Instead, a 44 per cent yield of the cyclic ether (XXXII) is obtained (Equation 12).

![Chemical structure of XXVII and XXXII](image)

(12)

This does not offer any conclusive information about the stereochemistry, however. If the monotosylate is formed with a quasi-equatorial hydroxyl esterified (Equation 13), one can see that in the case of the trans diol the other hydroxyl is

![Chemical structure of XXXI and XXXII](image)

(13)
in a position to assist in the expulsion of the tosylate anion. This is not true with the cis diol where both hydroxyls are quasi-equatorial. However, these are benzhydryl type alcohols, and the reaction is run in refluxing pyridine. The reaction very probably proceeds by a $S_{N}1$ type mechanism. If that is the case, either isomer of the diol will yield the ether (XXXII).

The ether 7,12-endoxy-7,12-dihydropleiadene (XXXII) forms quite readily under a variety of conditions. It was the principle product isolated in all attempts to prepare 7,12-dibromo-7,12-dihydropleiadene (XXXIII) or 7,12-dichloro-7,12-dihydropleiadene (XXXIV). 7,12-Dihydropleiadene-7,12-diol (XXVII) was treated

![Diagram of molecular structure]

XXXIII \[X = \text{Br}\]

XXXIV \[X = \text{Cl}\]

with hydrogen bromide in a benzene suspension, thionyl bromide in benzene with a catalytic amount of pyridine, thionyl bromide in ether with an equivalent amount of pyridine and with no pyridine, and with thionyl chloride in ether with an equivalent amount of pyridine. In all runs but one the only products were the ether (XXXII) or gummy tars. In one run with thionyl bromide in benzene with a catalytic amount of pyridine a few
milligrams of a white crystalline solid, m.p. 181.5-183.0°, were isolated. This material was not identified, but the infrared spectrum was consistent with the dibromide (XXXIII).

Some preliminary attempts at brominating 7,12-dihydropleiadene (XXIV) were not successful. Only a small amount of this material was available, so a thorough investigation of the bromination was not possible.

Since the formation of the cyclic ether (XXXII) interfered with the preparation of 7,12-dibromo-7,12-dihydropleiadene, it was decided to switch to the monosubstituted series, and to attempt to prepare a mono bromide from which a pleiadene could be prepared by elimination of hydrogen bromide. The simplest readily available pleiadone is 1-methyl-7-pleiadone (XXXV) which has been synthesized by the route 14. 
2-(2'-Methyl-1'-naphthoyl) benzoic acid (XXVI) was prepared by the Friedel-Crafts condensation of phthalic anhydride and 2-methynaphthalene.\textsuperscript{13} This was reduced with zinc dust in alkaline solution to give 2-(2'-methyl-1'-naphthylmethyl) benzoic acid (XXVII). The conversion of this acid to the acid chloride and cyclization with aluminum chloride\textsuperscript{14} was quite cumbersome and gave a rather poor yield. Polyphosphoric acid was not effective, but the condensation proceeded smoothly in anhydrous hydrogen fluoride to give 1-methyl-7-pleiadone (XXV) in 61 per cent yield after purification.

The reduction of the ketone with sodium borohydride in alcohol solution proceeded smoothly, yielding 1-methyl-7,12-dihydropleiadene-7-ol (XXXVI) in 96 per cent yield (Equation 15).

\begin{equation}
\begin{array}{c}
\text{CH}_3
\end{array}\quad \begin{array}{c}
\text{NaBH}_4 \\
\text{EtOH}
\end{array}\quad \begin{array}{c}
\text{CH}_3 \\
\text{OR}
\end{array}
\end{equation}

\text{XXXV} \quad \text{XXXVI, } R = H \\
\text{XL, } R = \text{Et}

In one experiment the crude reaction mixture was diluted with

\textsuperscript{13} L. F. Fieser and Mary Peters, J. Am. Chem. Soc., \textbf{54}, 3742 (1932).

aqueous sodium hydroxide and heated overnight. After the product was isolated, it was recrystallized from aqueous alcohol which had been acidified with concentrated hydrochloric acid. In this case the product was not the alcohol (XXXVI) but its ethyl ether (XL). The infrared spectrum of this compound (Appendix, Figure 20) shows no absorption in the hydroxyl region around 3.0 \( \mu \), but it contains a strong band in the ether region just above 9.0 \( \mu \).

When this ether is treated with gaseous hydrogen bromide for one hour in benzene solution, 7-bromo-1-methyl-7,12-dihydropleiadene (XXXVII) is formed in 82 per cent yield (Equation 16). Similar treatment of the alcohol yielded the bromide in 89 per cent yield.

![Chemical Structures](image)

XXXVI, \( R = H \)  
XXXVII  

(16)

XL, \( R = Et \)

This bromide was treated overnight with potassium \( t \)-butoxide in \( t \)-butyl alcohol at room temperature. A benzene solution of the product was passed through a column of alumina, and the eluted material was recrystallized from ethanol. This yielded a compound with a melting point of 140-50\(^\circ\), which was still not analytically pure. The product is not a hydrocarbon, and the high percentage
of hydrogen (8.85%) plus the presence of strong infrared absorption bands in the vicinity of 3.3-3.5 \( \mu \), 7.0-7.5 \( \mu \), and 9.0 \( \mu \)

XXXVII \[ \xrightarrow{\text{KO-t-Bu, } t-\text{BuOH}} \] XXXVIII

seem to indicate that it is the \( t \)-butyl ether (XXXVIII). This is a rather surprising result since the use of \( t \)-butoxide as the base usually greatly favors elimination over substitution. Apparently with this substrate substitution is very much easier than elimination.

When the alcohol (XXXVII) is dissolved in pyridine with excess \( \rho \)-toluenesulfonyl chloride and the solution refluxed for two days, a hydrocarbon (XXXIX) is formed in 17 per cent yield. The nature of this hydrocarbon is not completely clear. It melts at 226-7\(^o\), and it is soluble in chloroform, moderately soluble in benzene, sparingly soluble in cyclohexane, and insoluble in ethanol and petroleum ether. The carbon and hydrogen analysis (C, 93.59; H, 6.36) is intermediate between 1-methylpleiaden (XLI; C, 94.18; H, 5.82) and 1-methyl-7,12-dihydropleiaden (XLII; C, 93.40; H, 6.60). It also would agree with that required for the coupling product, \( C_{38}H_{30} \) (XLIII; C, 93.79; H, 6.21). The molecular weight was determined using the
Rast method, and while the results were not very precise (195 and 263 for two determinations), the average value of 229 is not far from the value of 1-methylpleiadene (2β,2') or 1-methyl-7,12-dihydroleiadene (2β,4').

The hydrocarbons which would be expected to result from the treatment of the alcohol (XXXVI) with p-toluenesulfonyl chloride and pyridine are either 1-methylpleiadene in the "open" (XLIIa) or "closed" (XLIIb) form or a dimer or polymer if 1-methylpleiadene is very reactive at the 7 and 12 positions. It would not be easy to account for the formation of 1-methyl-7,12-dihydroleiadene (XLII) or the coupling product (XLIII). The molecular weight determination indicates that it is probably not a dimer or the coupling product.
The ultraviolet absorption spectrum of XXXIX was measured and compared with that of the alcohol (XXXVI) and the ethyl ether (XL) (Appendix, Figure 21). The three spectra are all very similar except that the peaks in XXXIX are shifted about 6 μm toward longer wavelengths. This would seem to exclude the "open" form of 1-methylpleiadene (XLIa), but it agrees well with the "closed" form (XLIb) or the dihydro compound.

The hydrocarbon (XXXIX) was recovered unchanged after standing overnight in the presence of N-phenylmaleimide in carbon tetrachloride solution. This is in contrast to 1,2-diphenylbenzocyclobutene which reacts under these conditions\(^{15}\) with maleic anhydride.

1-Methyl-7,12-dihydropleiadene is not known, and two attempts to prepare it failed (reduction of 1-methyl-7,12-dihydropleiadene-7-ol with phosphorus and iodine and Wolff-Kishner reduction of 1-methyl-7-pleiadone). However, 7,12-dihydropleiadene and 1,6-dimethyl-7,12-dihydropleiadene are known and they have melting points of 116.5\(^{16}\) and 133\(^{17}\) respectively. In view of this a melting point of 226-7\(^{0}\) would seem to be too high for 1-methyl-7,12-dihydropleiadene. It also seems rather high for the "closed" form of 1-methylpleiadene (XLIb), although there are no close analogies. This compound would not be planar, but it is a rigid


\(^{16}\) A. Reiche, H. Sauthoff, and O. Müller, Ber., 65, 1371 (1932).

system with some strain in the four- and five-membered rings, and this possibly could account for the high melting point. At this time XL Ib seems to be the structure which best fits the data available for the hydrocarbon (XXXIX), although it is not conclusively established.

An attempt to prepare 1-methylpleiadene by refluxing the bromide (XXXVII) with pyridine led to curious results. When the refluxing was carried out for three days, and the product isolated by pouring the solution into water, acidifying with excess hydrochloric acid, and extracting with benzene, a solid was obtained which upon recrystallization from benzene gave XXXIX in 11 per cent yield. When the refluxing was carried out for two days and the product isolated in the same manner except that it was recrystallized from benzene-ethanol, XXXIX was obtained in only 1.5 per cent yield, and 7-ethoxy-1-methyl-7,12-dihydropleiadene (XL) was obtained in a 31 per cent yield. This result was confirmed by running the experiment a second time.

It is not clear what sort of intermediate is present in the benzene extract which reacts with ethanol at room temperature or slightly above. The hydrocarbon XXXIX does not give the ether under the same conditions. It is hard to see how any benzhydryl type halide could be present after two days in refluxing pyridine unless it reforms when the aqueous pyridine solution is acidified. Pyridinium salts might very well be present in the reaction mixture, but they would probably not be extracted into benzene. At this time
there does not seem to be any satisfactory explanation for the formation of this ether.
EXPERIMENTAL

All melting points were taken on a Fisher melting point block and are reported uncorrected unless otherwise stated. Boiling points are also observed, uncorrected values. Elemental analyses were prepared by Galbraith Laboratories, Knoxville, Tennessee, and Schwarzkopf Microanalytical Laboratory, Woodside, New York.

**Dimethyl acetylenedicarboxylate (III).** This compound was prepared by the method of Stork.\(^1\) A mixture of 75 ml. of concentrated sulfuric acid and 25 ml. of fuming sulfuric acid was added cautiously with stirring to a solution of 400 ml. of methanol in 1000 ml. of ethylene chloride. To this solution was added 250 g. of the monopotassium salt of acetylenedicarboxylic acid. After 23.5 hours refluxing, the organic layer was separated and washed twice with water and twice with 10% sodium bicarbonate to remove all acid. The organic liquid was dried over magnesium sulfate and distilled in vacuo yielding 139.3 g. (60%) of clear liquid, b.p. 78-87\(^0\) at 10 mm. Hg.; reported, 98\(^0\) at 20 mm. Hg.\(^2\)

**Dimethyl 3,6-endooxy-3,4,5,6-tetrahydropthalate (V).**
This material was prepared by a modification of the method of Stork.\(^1\) A solution of 46.3 g. of dimethyl acetylenedicarboxylate and 30 ml. of furan in 50 ml. of benzene was refluxed for seven hours. This resulting oil was dissolved in 150 ml. of acetone

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and hydrogenated over 0.3 g. of 10% palladium on charcoal in a Parr hydrogenator. The amount of hydrogen consumed was 0.313 mole (96%). This procedure was repeated twice more using a total of 0.948 moles of material.

After removal of the catalyst by filtration, the solutions were combined and concentrated by evaporating the acetone. An equal volume of Skellysolve F was added, and the solution was cooled to dry ice temperature, which froze out the product along with the benzene still present. After allowing the benzene to melt, the product could be filtered out. The solution was further concentrated and the crystallization repeated. The residue was extracted once with Skellysolve F and once with Skellysolve B. The product can be crystallized from either Skellysolve B or Skellysolve F. The total yield was 100.7 g. (50%) of white prisms. The best fraction, crystallized from Skellysolve F, had a m.p. of 48.0-48.5°; reported, 52°.3

Anal. Infrared spectrum: Appendix, Figure 1.

**Dimethyl furan-3,4-dicarboxylate (VI).** Dimethyl 3,6-endoxy-3,4,5,6-tetrahydropthalate, 33.7 g., was heated at 100-200° until gas was no longer evolved. The oily product was distilled in vacuo yielding 29.0 g. (quantitative yield) of oil, b.p. 125-32° at 8 mm., which solidified in the refrigerator. This material was saponified without further purification.

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Anal. Infrared spectrum: Appendix, Figure 2.

**Furan-3,4-dicarboxylic acid (II).** Dimethyl furan-3,4-dicarboxylate, 12.6 g., was dissolved in 25 ml. of methanol and treated with a solution of 10 g. of potassium hydroxide in methanol. After standing for two hours, the resulting soap was dissolved in the minimum amount of water. The solution was strongly acidified with hydrochloric acid and extracted with ether. After evaporation of the ether, the product was recrystallized once from ethyl acetate yielding 6.5 g. (61%) of light tan crystals, m.p. 212°-5°; reported, 212°.⁴

**Furan-3,4-dicarboxylic acid chloride (X).** A. Furan-3,4-dicarboxylic acid, 22.0 g., and phosphorus pentachloride, 60.0 g., were mixed with 200 ml. of benzene, and left standing until gas evolution ceased. After evaporation of the benzene and phosphorus oxychloride, the product was recrystallized from benzene yielding 22.2 g. (82%) of pale yellow prisms, m.p. 74°-6°; reported, 76°.⁵

Anal. Infrared spectrum: Appendix, Figure 3.

B. Furan-3,4-dicarboxylic acid, 5.0 g., was mixed with 20 ml. of thionyl chloride, and allowed to stand until gas evolution ceased. Most of the excess thionyl chloride was evaporated, and the resulting oil treated with Skellysolve F to induce crystallization. The product was recrystallized

once from Skellysolve F yielding 5.2 g. (87%) of light tan prisms, m.p. 73-4.5°.

**Furan-3,4-dialdehyde (I).** Furan-3,4-dicarboxylic acid chloride, 4.2 g., was dissolved in 75 ml. of c. p. xylene and reduced with hydrogen at atmospheric pressure and reflux temperature over 3.0 g. of 5% palladium on barium sulfate with 0.3 ml. of special quinoline-sulfur catalyst poison. The hydrogen was bubbled through the vigorously stirred solution, and the hydrogen chloride in the exit gas was trapped and titrated. The reaction required two and one-half hours, and the hydrogen chloride evolved was equivalent to 3½ ml. of 1 N sodium hydroxide (78% of the theoretical amount). The solid material was filtered out, and the xylene distilled out of the solution. The residue solidified, and was further purified by sublimation, yielding 0.5 g. (22% based on unrecovered acid) of white needles, m.p. 65-8°. Crude furan-3,4-dicarboxylic acid, 0.5 g., was recovered by extracting the xylene insoluble material with ether.

**Anal.** Calcd. for \( \text{C}_6\text{H}_4\text{O}_3 \): C, 58.07; H, 3.25. Found: C, 56.60; H, 3.30. Infrared spectrum: Appendix, Figure 4.

**Bis-2,4-dinitrophenylhydrazone**, m. p. 221-6°, d. Calcd. for C\(_{18}\text{H}_{12}\text{N}_6\text{O}_9\): C, 44.63; H, 2.50; N, 23.14. Found: C, 44.41; H, 2.63; N, 23.16.

**Furan-3,4-dicarboxamide (XIII).** Furan-3,4-dicarboxylic acid chloride, 2.6 g., was dissolved in benzene, and added dropwise to liquid ammonia. The ammonia and benzene were allowed to evaporate, and the solid residue mixed with water. The water
insoluble material was filtered out and washed thoroughly with water. This yielded 1.9 g. (91%) of grayish white powder, m.p. 272-4°C (dec.); reported, 262°C (dec.).

Anal. Infrared spectrum: Appendix, Figure 5.

**Furan-3,4-dicarboxanilide (XI).** Furan-3,4-dicarboxylic acid chloride, 1.0 g., in 5 ml. of benzene was treated with 2.0 g. of aniline. The dianilide precipitated out and was collected by filtration. The product was washed thoroughly with water and recrystallized once from methanol yielding 1.1 g. (70%) of light tan prisms, m.p. 217-218.5°C.

Anal. Calcd. for C_{18}H_{14}N_{2}O_{3}: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.77; H, 4.65; N, 9.22.

**Furan-3,4-bis(N-methylcarboxanilide) (XII).** N-methyl-aniline, 9 ml., was poured onto 3.3 g. of furan-3,4-dicarboxylic acid chloride. The resulting solid was washed with water to remove amine hydrochloride. The solid residue was filtered out and recrystallized once from ethanol and once from methanol. The yield was 3.2 g. (56%) of white prisms, m.p. 150-151.5°C.

Anal. Calcd. for C_{20}H_{18}N_{2}O_{3}: C, 71.84; H, 5.43; N, 8.38. Found: C, 72.10; H, 5.58; N, 8.57.

**Furan-3,4-dinitrile (XIV).** A. Furan-3,4-dicarboxamide, 6.8 g., was treated with refluxing phosphorus oxychloride for 90 minutes. The excess phosphorus oxychloride was removed by heating with a steam bath at reduced pressure, and the residue treated cautiously with ice water. The solution was neutralized with saturated sodium carbonate and extracted continuously with
ether. The ether layer was evaporated, and the residue was re-
crystallized twice from methanol yielding 2.3 g. (35%) of crude
product. This was chromatographed on Fisher alumina using methy-
lene chloride as the developer. The eluent was evaporated, and
the residue recrystallized from methanol yielding 0.3 g. of white
prisms, m.p. 160-16°C.

Anal. Calcd. for C₆H₂N₂O: C, 61.02; H, 1.71; N, 23.72.
Found: C, 61.01; H, 1.86; N, 23.84. Infrared spectrum:
Appendix, Figure 6.

In another run a 53% yield of material with m.p. 149-54°C
was obtained.

B. Furan-3,4-dicarboxamide and phosphorus pentoxide,
4.0 g. each, were ground up together and heated in a sublimer
at 2 mm. pressure until no more material sublimed. The con-
denser collected 2.1 g. (68%) of white solid. Recrystalliza-
tion from methanol yielded 1.9 g. of white prisms, m.p. 149-54°C.

3,4-Bis(hydroxymethyl)furan diacetate (VIII). This com-
 pound was prepared by the method of Elming and Clauson-Kaas.6
Dimethyl furan-3,4-dicarboxylate, 17.8 g., in 125 ml. of dry
ether was added dropwise over a 1/2 hour period to a slurry of
7.3 g. lithium aluminum hydride in 80 ml. of dry ether. The
slurry was stirred during the addition of the ester and for an
additional 15 minutes. Acetic anhydride, 100 ml., was added
dropwise, and enough dry ether was added to maintain the

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liquid volume. The temperature was raised to evaporate the ether, and another 25 ml. of acetic anhydride were added. The mixture was maintained at 110-120° for three hours. After cooling the mixture was extracted with ether. The ether and excess acetic anhydride were distilled, and the residue distilled in vacuo yielding 12.0 g. (59%) of liquid, b.p. 113-114.5° at 4-5 mm.; reported 88-90° at 0.1 mm. 6

Anal. Infrared spectrum: Appendix, Figure 7.

Oxidation of 3,4-bis(hydroxymethyl)furan diacetate.

3,4-Bis(hydroxymethyl)furan diacetate, 0.5 g., was treated with 8 ml. of 1 M aqueous sodium chromate buffered with 2 ml. of 10% aqueous sodium bicarbonate. After 24 hours refluxing, the color change indicated oxidation had occurred, but no aldehydic product could be isolated. Only a tarry residue resulted.

1-Hydroxypleiadene-7,12-dione (XIX). This compound was prepared by the method of Fieser. 7 Aluminum chloride, 142 g., was added to 453.6 g. of molten phthalic anhydride at 180°. To this mixture was added slowly 71 g. of β-naphthol. The resultant thick, brown liquid was heated at 250° for 30 minutes and poured into 2.5 l. of water containing 20 ml. of concentrated hydrochloric acid. The solid material was filtered out and digested with dilute hydrochloric acid. The product was again recovered by filtration and heated in 20% sodium hydroxide. The sodium salt is sparingly soluble in water, and it must be extracted

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from the insoluble residues with a large volume of water. The alkaline solution is acidified, and the product is recovered by filtration. Yield, 99.0 g. (72%) of yellow powder, m.p. 201-4°; reported, 198°.7

Anal. Infrared spectrum: Appendix, Figure 8.

1-Chloropleiadene-7,12-dione (XX). This compound was prepared by the method of Fieser.7 1-Hydroxypleiadene-7,12-dione, 50 g., was heated on a steam bath with 57 g. of phosphorus oxychloride and 55 g. of phosphorus pentachloride. After the evolution of gas had ceased, the thick brown liquid was poured over ice and allowed to stand until the ice had melted. The solid material was filtered out and extracted with glacial acetic acid. After filtering out the insoluble material, the acetic acid solution was poured into twice its volume of water. The crude product was recovered by filtration and purified by vacuum distillation followed by recrystallization from ethanol yielding 14.0 g. (30%) of light yellow needles, m.p. 155-7°; reported, 165°.7

Anal. Infrared spectrum: Appendix, Figure 9.

Pleiadene-7,12-dione (XXIII). 1-Chloropleiadene-7,12-dione, 5.7 g., and 1.5 g. of tetralin were heated at about 200° over 0.5 g. of 10% palladium on charcoal until the evolution of hydrogen chloride could no longer be observed (about 90 minutes). After the reaction mixture had cooled, the organic material was extracted with acetone, and the catalyst filtered out. The acetone solution
was evaporated to dryness, and the product was recrystallized three
times from ethanol yielding: first crop, 2.3 g. (46%), m.p. 171-5°;
second crop, 0.6 g. (12%), m.p. 173-6°; reported, 178°.  

Anal. Calcd. for C₁₈H₁₀O₂: C, 83.71; H, 3.90. Found:
C, 83.85; H, 4.06. Infrared spectrum: Appendix, Figure 10.

Reduction of the ketone functions occurs as a side reaction.
Also, any water present, either from ketone reduction or as a con-
taminant, will tend to replace the chlorine in the starting material
with hydroxyl. Small amounts of both 1-hydroxypleiadene-7,12-
dione and 7,12-dihydropleiadene were isolated from the reaction
mixtures. The hydroxydiketone is only sparingly soluble in
ethanol, and it appears as a contaminant in the first crop from
the recrystallization. It was isolated in one case and purified
by recrystallization from a large volume of alcohol, m.p. 194.5-
197°; reported, 198°.  

Anal. Calcd. for C₁₈H₁₀O₃: C, 78.82; H, 3.68. Found:
C, 78.84; H, 3.63.

7,12-Dihydropleiadene (XXIV). This compound becomes a major
product in the above reduction if considerable excess of tetralin
is employed. After the reaction mixture has cooled, it is dis-
solved in acetone, and the catalyst is filtered out. The acetone
solution is evaporated to dryness, and the residue is chromato-
graphed on grade I alumina using benzene as a developer. The
product passes straight through the column along with some

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8 A. Reiche, H. Sauthoff, and O. Müller, Ber., 65, 1371 (1932).
naphthalene (a by-product from the reduction), which can be removed by trituration with Skellysolve F. The product is recrystallized from ethanol yielding white needles, m.p. 116.5-117.5°F (corrected); reported, 116.5°F.

Anal. Calcd. for C_{16}H_{14}: C, 93.87; H, 6.13. Found: C, 93.99; H, 5.85. This compound has been previously reported to crystallize from dilute ethanol solution with one molecule of water of crystallization. Infrared spectrum: Appendix, Figure 11.

7,12-Dihydropleiadene-7,12-diol (XXVII). To a solution of 0.34 g. of sodium borohydride in 10 ml. of ethanol was added 0.37 g. of pleiadene-7,12-dione. The resultant red-orange solution was allowed to stand for two days, then 0.5 g. of sodium hydroxide was dissolved in it, and the solution was heated on the steam bath for several hours. The addition of water precipitated a white gum which redissolved as more water was added. The solution was evaporated until crystallization began and allowed to cool. In this manner 0.11 g. of white leaflets, m.p. 217-210°F, were obtained. A second crop, 0.06 g., was obtained from the mother liquor. Total yield was 47%. The diol was not obtained analytically pure.

Anal. Calcd. for C_{18}H_{14}O_{2}: C, 82.42; H, 5.38. Found: C, 81.09; H, 5.57. Infrared spectrum: Appendix, Figure 12.

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9 W. Knapp, Monatsh., 60, 189 (1932).
The best yield in this reduction, obtained in a larger scale experiment, was 86%.

7,12-Endoxy-7,12-dihydropleiadene (XXXII). 7,12-Dihydropleiadene-7,12-diol, 300 mg., was dissolved in 5 ml. of pyridine and treated with 650 mg. of p-toluenesulfonyl chloride. After refluxing for 90 minutes, the solution was poured into water and the organic material extracted with ether. Evaporation of the ether solution yielded an oil which crystallized on standing. Recrystallization from methanol yielded 123 mg. (44%) of white plates, m.p. 138-90° (corrected).

Anal. Calcd. for C\(_{16}\)H\(_{12}\)O: C, 88.50; H, 4.95. Found: C, 88.72; H, 5.06. Infrared spectrum: Appendix, Figure 13.

2-(2'-Methyl-1'-naphthylmethyl)benzoic acid (XXXVII).

This compound was prepared by the method of Fieser.\(^\text{10}\) Phthalic anhydride, 16.5 g., and \(\beta\)-methylnaphthalene, 14.2 g., were dissolved in 100 ml. of \(\alpha\)-tetrachloroethane and cooled in an ice bath. Aluminum chloride, 30.0 g., was added with stirring over a one hour period. The solution was stirred overnight in the ice bath, and enough 18% hydrochloric acid added to hydrolyze the aluminum chloride. The product is best isolated by neutralizing the acid, steam distilling the tetrachloroethane, and extracting the residue with 10% sodium carbonate solution. This

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\(^{10}\) L. F. Fieser and Mary A. Peters, J. Am. Chem. Soc., 54, 3742 (1932).
solution is acidified to recover the crude 2-(2'-methyl-1'-naphthoyl)benzoic acid, 21.5 g. (74%). This compound is hard to purify, and it was reduced without further purification.

The crude product from above, 19.1 g., was dissolved in a solution of 30 g. of sodium hydroxide in 400 ml. of water. Zinc dust, 60 g., was added, and the solution was refluxed for 68 hours. After the solids had been filtered out of the solution, the solution was acidified to precipitate the crude 2-(2'-methyl-1'-naphthylmethyl)benzoic acid, which was recovered by filtration. The product was digested with hot water to remove any phthalic acid present, and dissolved in hot benzene. Skellysolve B was added to the hot solution until a permanent cloudiness was present, and then it was set aside to cool. The first crop of light tan powder, m.p. 185-90°, weighed 6.5 g. Further crops were obtained from the mother liquor. Total yield, 88%.

The best sample obtained by further recrystallizations had a m.p. of 188-90°; reported, 187°. 10

Anal. Infrared spectrum: Appendix, Figure 14.

1-Methyl-7-pleiadone (XXXV). To 7.5 g. of 2-(2'-methyl-1'-naphthylmethyl)benzoic acid about 500 ml. of anhydrous, liquid hydrogen fluoride were added. This solution was left standing for three days while the hydrogen fluoride evaporated. The residue was treated with 100 ml. of 10% sodium carbonate to neutralize any remaining acid. The solid residue and the alkaline solution were extracted with five 50 ml. portions of
benzene. The benzene solution was concentrated and chromatographed on grade I W&Lm neutral alumina (0% water) using benzene as the developer. The eluent solution was evaporated and the residue recrystallized from Skellysolve B to yield 3.1 g. of yellow needles. Further crops were obtained from the mother liquor. Total yield, 61%. An analytical sample was obtained by further recrystallization as pale yellow needles, m.p. 128.5-30°C; reported, 128°C.11

Anal. Calcd. for C<sub>19</sub>H<sub>14</sub>O: C, 88.34; H, 5.46. Found: C, 88.30; H, 5.49. Infrared spectrum: Appendix, Figure 15.

1-Methyl-7,12-dihydropleiadene-7-ol (XXXVI). A mixture of 1.737 g. of 1-methyl-7-pleiadone, 3.5 g. of sodium borohydride, and 50 ml. of absolute ethanol was heated on a steam bath until dissolution was completed. It was then allowed to stand overnight. The resulting mixture was dissolved in 50 ml. of water and heated one hour on a steam bath. The product crystallized on cooling and was collected by filtration. Recrystallization from aqueous ethanol yielded 1.407 g. of soft white needles, m.p. 153-5°C. A second crop of 0.280 g. was obtained giving a total yield of 96%.

Anal. Calcd. for C<sub>19</sub>H<sub>16</sub>O: C, 87.66; H, 6.19. Found: C, 87.63; H, 6.08. Infrared spectrum: Appendix, Figure 16. Ultraviolet spectrum: Appendix, Figure 21.

7-Bromo-1-methyl-7,12-dihydropleiadene (XXXVII). Gaseous hydrogen bromide was bubbled through a solution of 0.681 g. of 1-methyl-7,12-dihydropleiadene-7-ol in 20 ml. of benzene for one hour. The solution was allowed to stand for two hours and evaporated on a steam bath yielding 0.750 g. (89%) of crude bromide. Recrystallization from chloroform-Skellysolve B yields 0.603 g. of light brown needles, m.p. 160-30°.

Anal. Calcd. for C_{19}H_{15}Br: C, 70.60; H, 4.68; Br, 24.72. Found: C, 70.72; H, 4.67; Br, 24.60. Infrared spectrum: Appendix, Figure 17.

7-ß-Butoxy-1-methyl-7,12-dihydropleiadene (XXXVIII). 7-Bromo-1-methyl-7,12-dihydropleiadene, 0.202 g., was treated overnight with excess potassium ß-butoxide in 25 ml. of ß-butanol. The reaction mixture was diluted with water and extracted with benzene. The benzene solution was dried and passed through a column of Wulff neutral alumina, grade I (0% water). After evaporation of the eluent, the residue was recrystallized from absolute ethanol yielding 0.141 g. (71%) of a white solid, m.p. 140-50°. The compound was not obtained analytically pure.

Anal. Calcd. for C_{24}H_{24}O: C, 87.30; H, 7.65. Found: C, 87.84; H, 8.85. Infrared spectrum: Appendix, Figure 18.

Unknown hydrocarbon (XXXIX). A. 1-Methyl-7,12-dihydropleiadene-7-ol, 0.532 g., and p-toluenesulfonyl chloride, 0.50 g., were dissolved in 20 ml. of pyridine and refluxed for 45.5 hours. The resulting mixture was diluted with 50 ml. of water and extracted with benzene until all soluble material was removed.
Evaporation of the extract yielded a solid residue which was re-
crystallized from benzene yielding 0.085 g. (17%) of small white
prisms, m.p. 226-7°.

Anal. Calcd. for C\textsubscript{19}H\textsubscript{14}: C, 94.18; H, 5.82; M. W., 242.
Found: C, 93.59; H, 6.36; M. W. (Rast), 195, 263. Infrared
spectrum: Appendix, Figure 19. Ultraviolet spectrum: Appendix,
Figure 21. Trinitrofluorenone derivative, m.p. 230-30°, d.

B. 7-Bromo-1-methyl-7,12-dihydroleadiene, 0.706 g., was
dissolved in 20 ml. of pyridine and refluxed for 42 hours. The
solution was diluted with 30 ml. of water and 20 ml. of concen-
trated hydrochloric acid and extracted with four 25 ml. portions
of benzene. The extract was evaporated, and the residue was ex-
tracted with Skellysolve B. The insoluble material was recryst-
tallized from benzene yielding 0.006 g. (1.5%) of the hydro-
carbon. The Skellysolve B solution was evaporated, and the
residue dissolved in benzene. This solution was heated and di-
luted with an equal amount of absolute ethanol. On standing
overnight 0.195 g. of crystalline solid separated. Two re-
crystallizations from aqueous ethanol yielded 0.122 g. of light
yellow solid, m.p. 130-1°. Although not analytically pure, the
infrared absorption spectrum (Appendix, Figure 20) and the elemental
analysis indicate that the compound is probably 7-ethoxy-1-methyl-
7,12-dihydroleadiene, yield, 31%.

Anal. Calcd. for C\textsubscript{21}H\textsubscript{20}O: C, 87.46; H, 6.99. Found: C,
85.64; H, 7.10. Infrared spectrum: Appendix, Figure 20. Ultra-
violet spectrum: Appendix, Figure 21.
In another run 0.287 g. of 7-bromo-1-methyl-7,12-dihydropleiadene was dissolved in 20 ml. of pyridine and refluxed for 68 hours. The solution was diluted with 75 ml. of benzene, and then 25 ml. of water and 25 ml. of concentrated hydrochloric acid were added. The layers were separated, and the aqueous layer was extracted with 50 ml. of benzene. The combined benzene extracts were evaporated on a steam bath yielding 0.229 g. of crude residue. This residue was washed with benzene and then recrystallized from benzene yielding 0.023 g. (11%) of the hydrocarbon.

7-Ethoxy-1-methyl-7,12-dihydropleiadene (XII). This compound was isolated during an attempted preparation of 1-methyl-7,12-dihydropleiadene-7-ol. 1-Methyl-7-pleiadone, 3.1 g., was reduced with 3.0 g. of sodium borohydride in 100 ml. of absolute ethanol. After the solution had stood for 48 hours, 100 ml. of water and 3.0 g. of sodium hydroxide were added, and the solution was heated overnight on the steam bath. On cooling the product crystallized out of solution and was collected by filtration. This material was recrystallized from aqueous ethanol acidified with concentrated hydrochloric acid. A second recrystallization from aqueous ethanol yielded 2.5 g. (72%) of light orange needles, m.p. 125-7°C. A third recrystallization raised the melting point to 127.5-9°C. Although the orange color persisted, the infrared absorption spectrum and mixed m.p. (126-30°C) indicated that the compound was identical to the ether obtained during the dehydrobromination of 7-bromo-1-methyl-7,12-dihydropleiadene.
A benzene solution of 1.118 g. of 7-ethoxy-1-methyl-7,12-dihydroleiadene was treated with gaseous hydrogen bromide for one hour. The solution was dried over magnesium sulfate and evaporated yielding 1.032 g. (82%) of 7-bromo-1-methyl-7,12-dihydroleiadene (m.p. 157-61°, mixed m.p. 158-61°).
APPENDIX

Infrared and Ultraviolet Absorption Spectra
**Fig. 7**

3,4-bis(hydroxymethyl) furan diacetate

**Fig. 8**

1-Hydroxypleiadene-7,12-dione

Wave length in microns
Fig. 21. Ultraviolet absorption spectra
AUTOBIOGRAPHY

I, Donald Frederic Barringer, Jr., was born in Cleveland, Ohio, June 3, 1932. I received my secondary school education in the public schools of Fairview Park, Ohio, and my undergraduate training at Denison University, which granted me the degree Bachelor of Science With Departmental Honors in 1954. In September, 1954, I was appointed an Assistant at The Ohio State University in the Department of Chemistry. I held this position for three years and again in 1958-59 while working on the requirements for the degree Doctor of Philosophy. During the year 1957-58 I was Standard Oil Company of Ohio Fellow, and during the Summer Quarter of 1959 I was a Du Pont Fellow.