

SOME INVESTIGATIONS ON AROMATIC STRUCTURES

- (1) Studies in Tropolone Chemistry.
 - (2) Synthesis of 4:5-Dimethylphenanthrene.
-

A THESIS FOR THE DEGREE OF Ph.D.

by

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September, 1952.

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A C K N O W L E D G M E N T S

The author wishes to express his thanks to Professor J. W. Cook, F.R.S. and Dr. R. A. Raphael for their constant advice and encouragement during this work.

Also, thanks are due to Mr. J. M. L. Cameron, Miss R. H. Kennaway and Miss Christie for micro-analyses, to Drs. E. A. Braude, F. Sondheimer, and G. D. Meakins for ultra-violet and infra-red absorption measurements, and to Professors H. Erdtman and V. Prelog for their kind provision of samples of the natural thujaplicins and of cyclooctadecane -1:10-dione respectively.

The author also expresses his indebtedness to the Department of Scientific and Industrial Research for a Maintenance Allowance during the period October, 1949 to October, 1952.

PART I

STUDIES IN TROPOLONE CHEMISTRY

S U M M A R Y

PART I.

By extension of the method of preparing tropolone dione to isopropylcycloheptanediones, α -, β - and γ -1:2-dione to isopropylcycloheptanediones, α -, β - and γ -isopropyltropolones have been prepared and have been shown to be identical with the naturally-occurring α -, β - and γ -thujaplicins.

Some reactions of tropolone have been examined, in particular, the Friedel-Crafts and Reimer-Tiemann reactions. The reduction of tropolone with lithium aluminium hydride has been studied. In the course of an attempt to prepare a γ -nitrotropolone, cyclodecane-1:2-dione was found to dimerise. The nature of this product has been examined and a structure proposed.

An attempted synthesis of γ -tropolone is also described.

I N D E X

PART I.

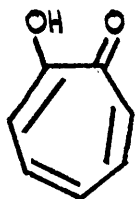
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STUDIES IN TROPOLONE CHEMISTRY

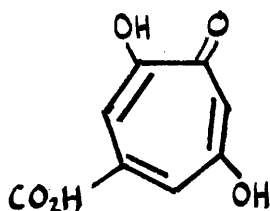
INTRODUCTION.

The postulate of the quasi-aromatic properties of the cycloheptatrien-2-ol-1-one (tropolone; I) system was first invoked by M. J. S. Dewar⁽¹⁾ to account for the properties of the naturally-occurring compound stipitatic acid (II). Since then, further natural products have been shown to derive from this system. These include (a) hinokitiol, isolated⁽²⁾ from the essential oil of Chamaecyparis taiwanensis and later shown⁽³⁾ to be identical with β -thujaplicin (VII) isolated along with α -(VI) and γ -(VIII) thujaplicins⁽⁴⁾ from the heartwood of Swedish and American Western Red Cedar; (b) purpurogallin (III), an oxidation product of pyrogallol;⁽⁵⁾ (c) the mould metabolites stipitatic acid (II),^{(1), (6)} puberulic acid (IV)⁽⁶⁾ and puberulonic acid (V)^{(7) (8)}; (d) colchicine, derived from the autumn crocus and almost certainly possessing structure (IX)⁽⁹⁾ containing a tropolone methyl ether system; and (e) nootkatin,⁽¹⁰⁾ $C_{15}H_{20}O_2$, a tropolone related to the sesquiterpenes, isolated from Chamaecyparis nootkatensis (Alaska Yellow Cedar) whose structure is at present under investigation by X-ray crystallographic methods⁽¹¹⁾ which

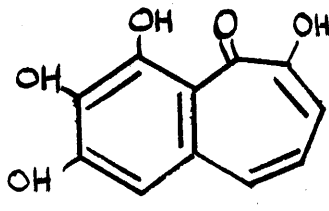
suggest structure (X) for this compound.



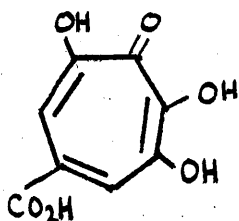
(I)



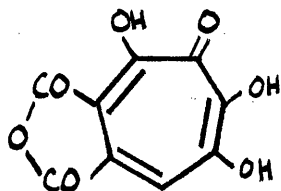
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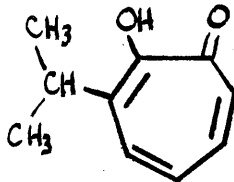
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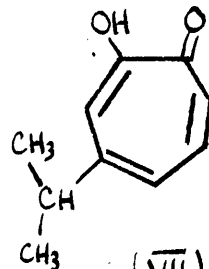
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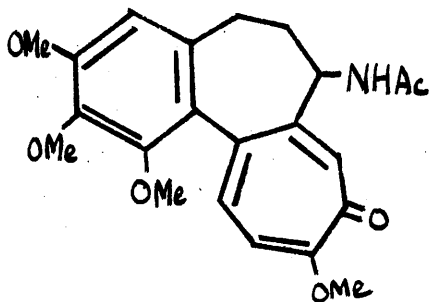
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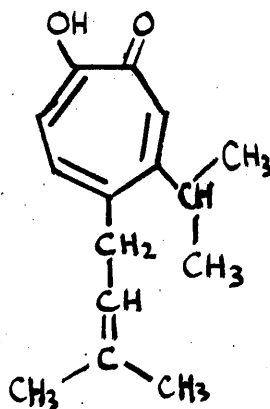
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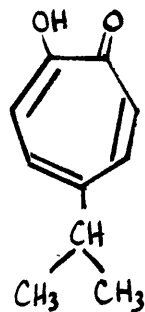
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(IX)



(X)

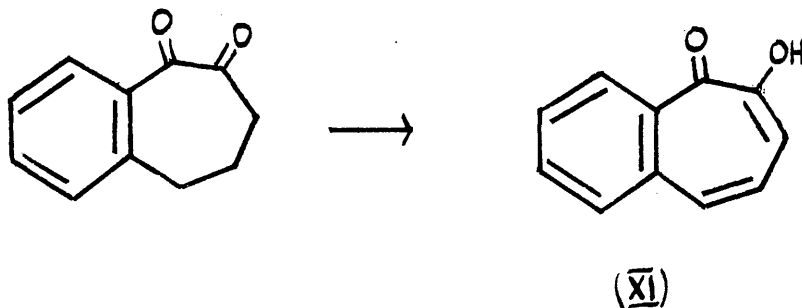


(VIII)

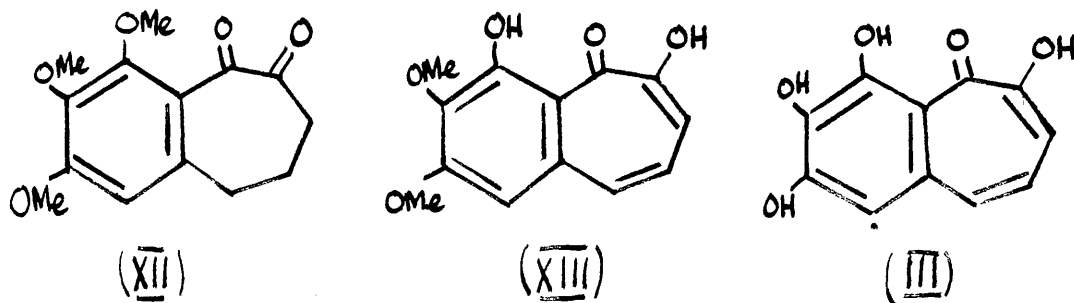
Several excellent reviews of the chemistry of the tropolones

have now appeared^(12,13,14) but a brief outline of the synthetic approaches to these interesting new compounds and an account of the more detailed chemistry of the thujaplicins have been included in this thesis.

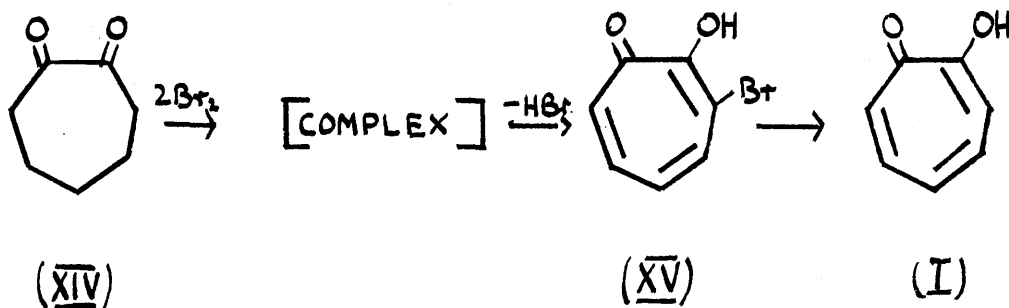
The first synthesis of the tropolone ring system was achieved by Cook and Somerville⁽¹⁵⁾ who prepared $\alpha\beta$ -benzotropolone (XI) by dehydrogenation of the appropriate benzocycloheptane-1:2-dione in boiling trichlorobenzene in presence of 10% palladised charcoal.



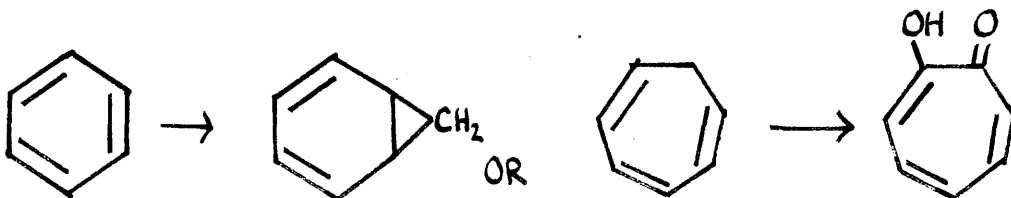
This method of dehydrogenation was also successful when applied to the trimethoxybenzosuberane-1:2-dione (XII) by Gaunt, Crow, Haworth and Vodoz⁽¹⁶⁾ who obtained the hitherto inaccessible purpurogallin dimethyl ether (XIII) readily convertible to purpurogallin (III).



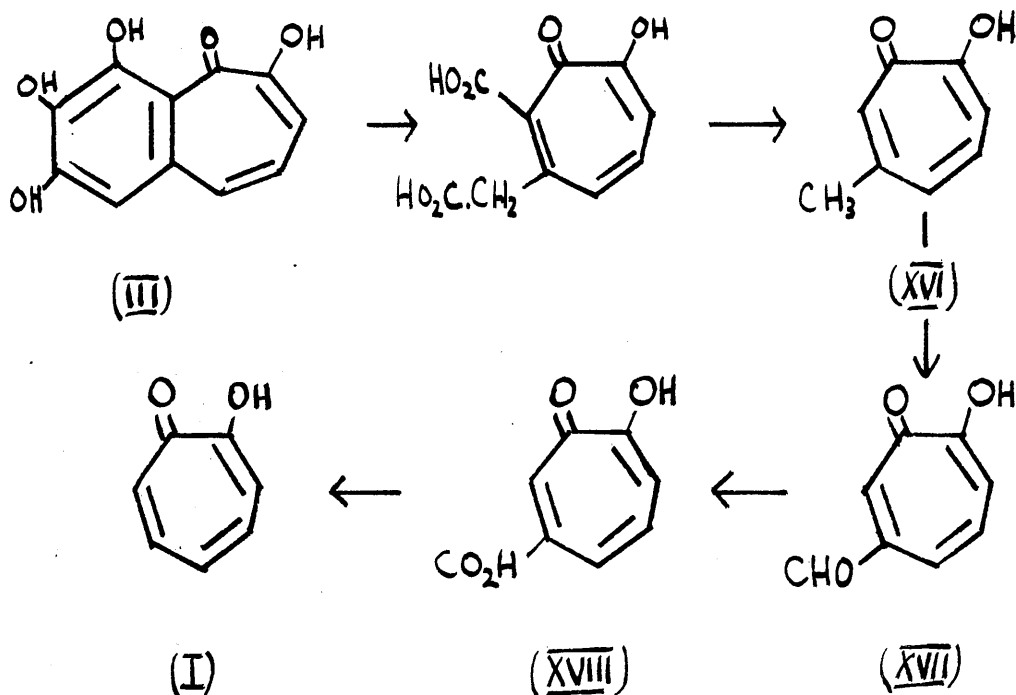
Tropolone itself (I) has now been synthesised by four different methods. Cook, Gibb, Raphael and Somerville⁽¹⁷⁾ showed that bromination of cycloheptane-1:2-dione (XIV) with two molecules of bromine followed by dehydrobromination yielded α -monobromotropolone (XV) whose sodium salt on hydrogenolysis afforded the parent tropolone (I) in good yield. Nozoe⁽¹⁸⁾ in Japan independently and almost simultaneously carried out a similar set of experiments to prepare tropolone.



About the same time two further independent syntheses of tropolone were announced. The first, due to Doering and Knox⁽¹⁹⁾ in the U.S.A., employed the photochemical ring expansion of benzene to cyclohepta-1:3:5-triene which on oxidation with potassium permanganate gave tropolone.



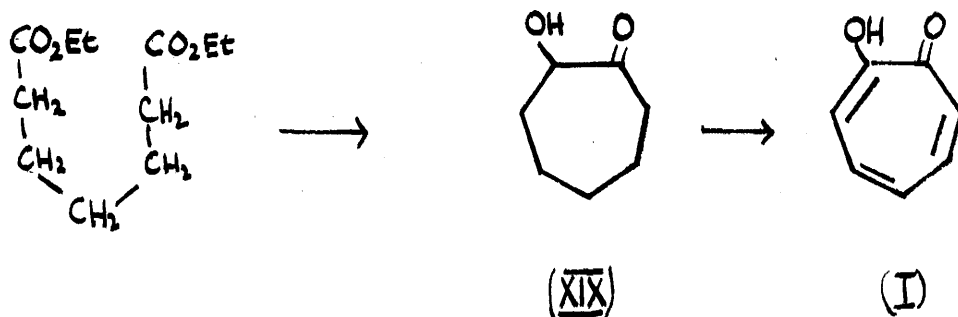
The second consisted in the stepwise degradation of purpurogallin (III) to β -methyltropolone (XVI).



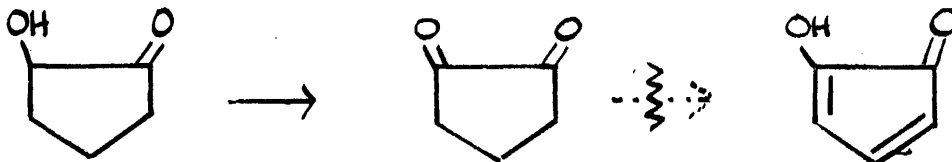
Oxidation of β -methyltropolone methyl ether gave β -formyltropolone (XVII) as its methyl ether which in turn was oxidised to tropolone β -carboxylic acid (XVIII) and finally decarboxylated to tropolone (I). In this way, Haworth et al.⁽²¹⁾ not only prepared tropolone but also a number of very useful intermediate substituted tropolone derivatives.

A fourth synthesis has recently been described by Knight and Cram⁽²⁰⁾ who utilised the acyloin condensation of diethylpimelate. The resulting 2-hydroxycycloheptanone

(XIX) underwent successive oxidation, bromination, and dehydrobromination on treatment with bromine to yield tropolone (I).

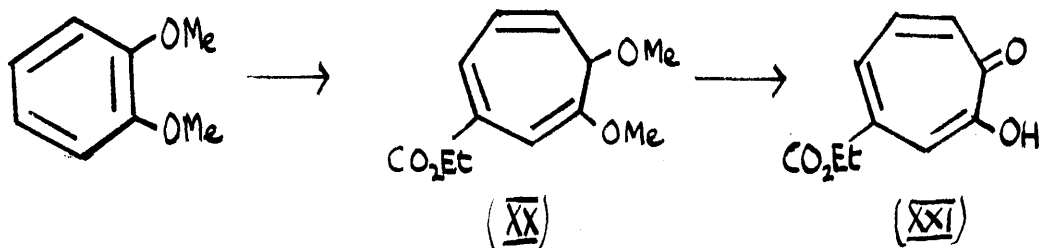


Analogous experiments with the five-membered acyloin did not yield an aromatic system:-



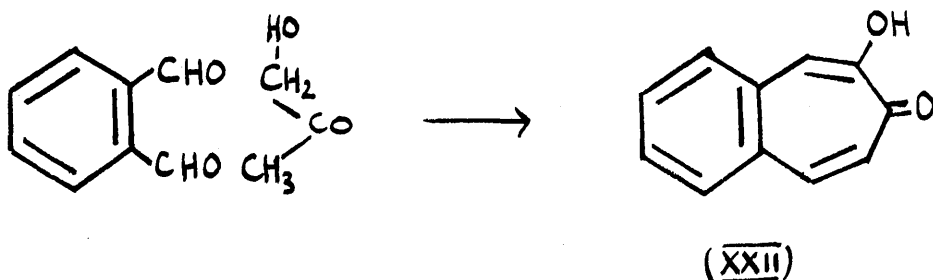
This lack of aromatic character has been attributed⁽²⁰⁾ to the availability in cyclopentadien-1-ol-2-one of only four $\bar{\pi}$ electrons, benzene and tropolone each having six $\bar{\pi}$ electrons available.

Bartels-Keith and Johnson⁽²²⁾ have obtained tropolone β -carboxylic ester (XXI) by ring expansion of veratrole with diazoacetic ester followed by



bromination of the resultant 1:2-dimethoxycycloheptatriene-4-carboxylic ester (XX). Hydrolysis and dehydrogenation afforded the β -carboxylic ester (XXI). By a similar procedure, starting from 1:2:4-trimethoxybenzene, stipitatic acid⁽²³⁾ has been synthesised.

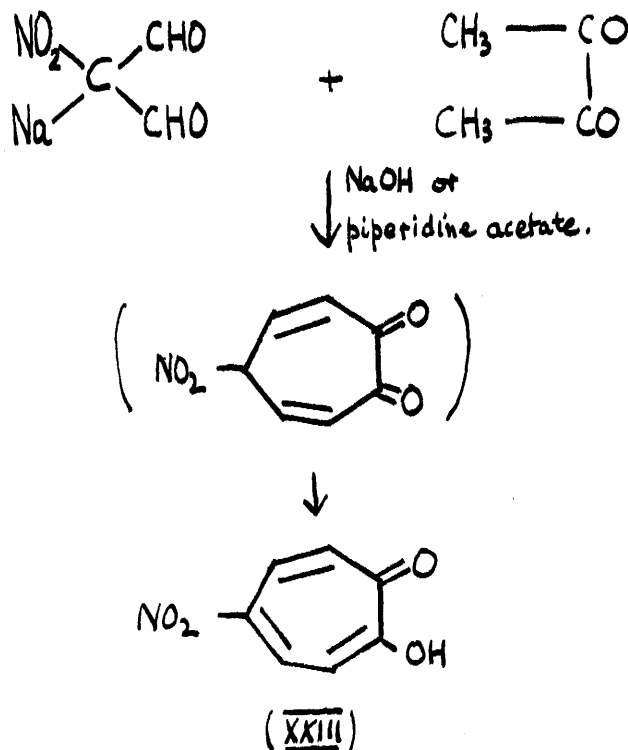
Scott and Tarbell⁽²⁴⁾ have prepared $\beta\gamma$ -benzotropolone (XXII) by the interesting double aldol condensation between o-phthalaldehyde and hydroxyacetone.



The method gives better yields when bromoacetone is employed.

Other attempts to produce the tropolone system by direct condensation reactions have not met with success. Dewar⁽¹⁾ described a fruitless reaction between mesityl oxide and ethyl oxalate in presence of potassium ethoxide. As reported elsewhere,⁽²⁵⁾ the present author has investigated the

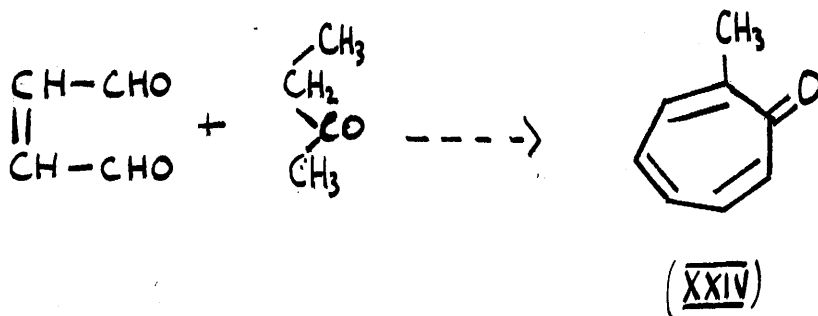
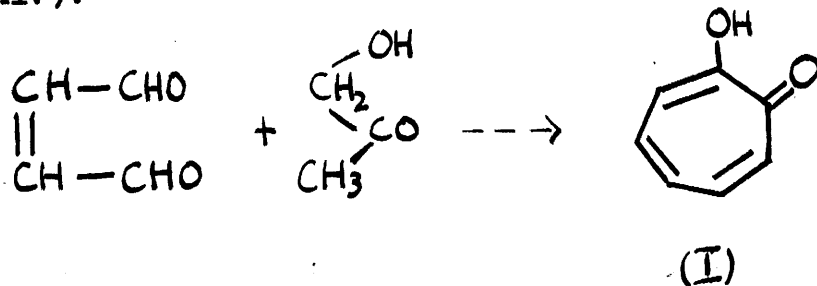
condensation between sodionitromalondialdehyde and diacetyl in an attempt to prepare γ -nitrotropolone (XXIII).



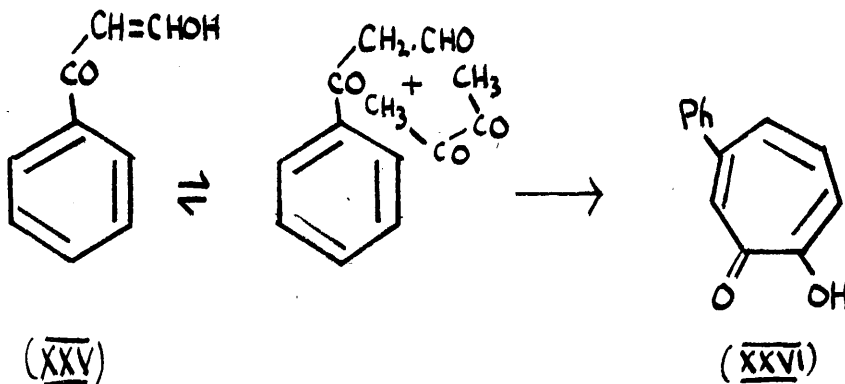
The failure of this reaction may be due to the transoid configuration of the carbonyl groups in diacetyl⁽²⁶⁾ which would force the methyl groups into a configuration unsuitable for the above condensation. The attempted condensation between nitromalondialdehyde and cyclodecane-1:2-dione is discussed below (p.29).

Several other abortive attempts to prepare tropolones were made by this author. Maleicdialdehyde failed to condense either with hydroxyacetone or methyl ethyl ketone to

furnish respectively tropolone (I) and 2-methyltropolone (XXIV).



In another experiment ω -hydroxymethyleneacetophenone (XXV) was treated with diacetyl in presence of piperidine acetate but no tropoloid material (e.g. XXVI) was isolable.

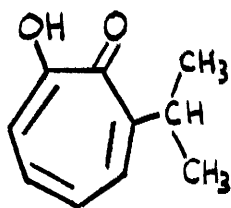


THE THUJAPLICINS.

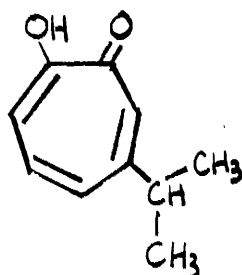
Of the known naturally-occurring tropolones, purpurogallin⁽¹⁶⁾(III) and stipitatic acid⁽²³⁾(II) have been synthesised. The object of the present work was the synthesis of the three isomeric thujaplicins (VI, VII, and VIII).

Mature trees contain "dead tissues" of which the central part of the trunk, the so-called heartwood is especially important. If the latter is devoid of preservatives it becomes easily destroyed. In the natural order Cupressales heartwood preservatives of terpenoid nature predominate. During a search for other phenolic constituents in this order, Blasdale⁽²⁷⁾ in 1907 isolated from the heartwood of Western Red Cedar (Thuja plicata D. Don) a compound $C_{10}H_{12}O_2$ m.p. 80° . In 1933 Anderson and Sherrard⁽²⁸⁾ described an acid $C_{10}H_{12}O_2$, m.p. 88° isolated from American grown Thuja plicata and named dehydroperillic acid because of a supposed connection (since proven mistaken^(29,30)) with perillic acid. Two phenolic isomers $C_{10}H_{12}O_2$ were also isolated along with the acid. One had m.p. 82° and was highly toxic to Fomes annosus; the other crystallised after sixteen years and melted at $52-52.5^\circ$. Erdtman and Gripenberg⁽³¹⁾ in 1948 described yet another isomer m.p. 32° found together with the isomer m.p. 82° and "dehydroperillic acid" in Thuja plicata grown in Sweden. The structures of the

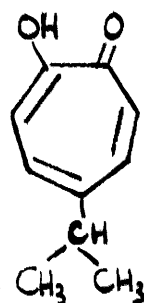
three phenolic isomerides have been rigidly established by Erdtman and Gripenberg.⁽⁴⁾ In increasing order of melting point they have been named α -, β -, and γ -thujaplicins (VI, VII, and VIII) and "dehydroperillic acid" which possesses structure (XXVII)^(29,30) has been renamed thujic acid.



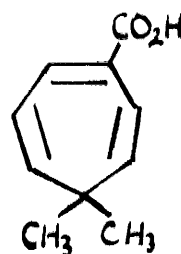
(VI)



(VII)



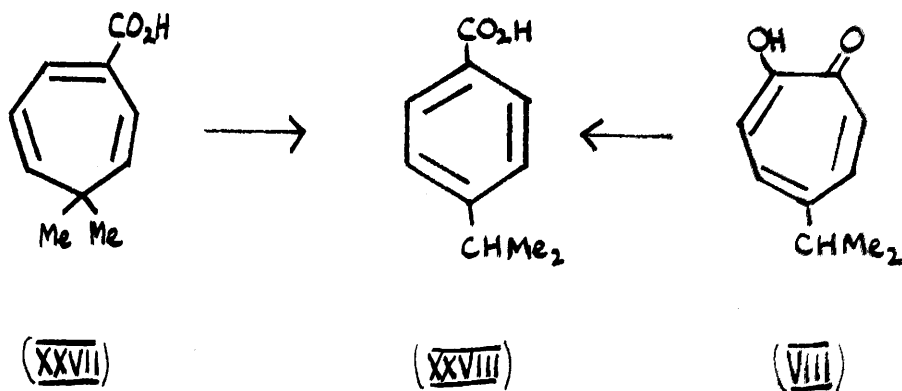
(VIII)



(XXVII)

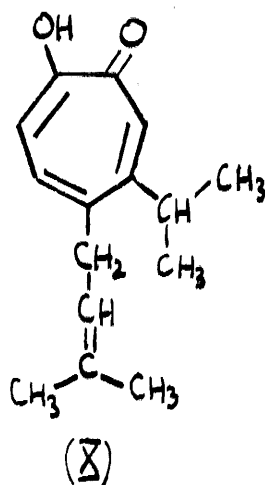
All three thujaplicins yielded isobutyric acid on chromic acid oxidation, and on catalytic hydrogenation octahydro-derivatives were obtained. Octahydro- γ -thujaplicin was shown to be an $\alpha\beta$ -diol by cleavage with periodic acid to a dialdehyde. α -thujaplicin on one occasion yielded a ketonic hexahydro-compound probably containing the grouping $-\text{CHOH}-\text{CO}-$ for it reacted with periodic acid and furnished α -isopropyl pimelic acid on oxidation with potassium permanganate. The octahydro- α -, β -, and γ -thujaplicins afforded on permanganate oxidation α -, β -, and γ -isopropyl pimelic acids respectively. By the synthesis

of these three substituted pimelic acids Erdtman confirmed the structures of the three compounds. The thujaplicins gave what are now known to be characteristic tropolone reactions, e.g. deep green colourations with ferric chloride and chloroform soluble copper salts; on fusion with potassium hydroxide at 230° , γ -thujaplicin underwent the benzylic type of rearrangement to furnish cuminic acid (XXVIII), which was also obtained when thujic acid (XXVII) was treated with mineral acid. The thujaplicins are soluble in caustic

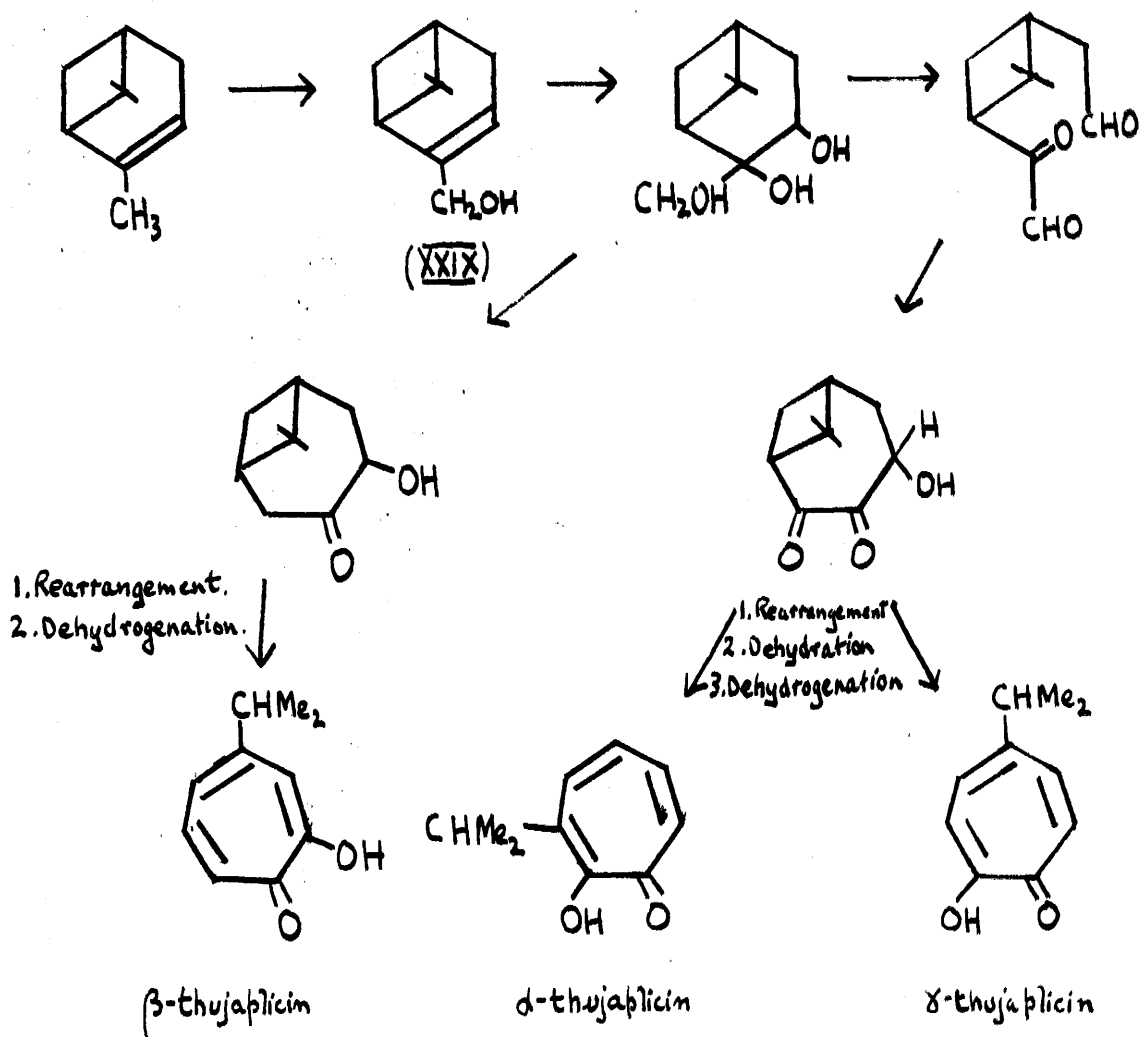


alkalis but insoluble in bicarbonate solution. β -thujaplicin (hinokitiol) has been studied extensively by Nozoe⁽³²⁾ who has described bromination, nitration, sulphonation, and diazo-coupling products. Hinokitiol was obtained from the heartwood of Japanese "hinoki" (Chamaecyparis obtusa Sieb. et Zucc.) by Nozoe.⁽²⁾ α - and β -thujaplicins and thujic acid have been isolated from Thuja occidentalis

by Gripenberg⁽³³⁾ and the α - and β -isomers also occur in the Thujaopsis species. The thujaplicins are strongly fungicidal^(34,35) and are also toxic to fish.^(33,4) Nootkatin, $C_{15}H_{20}O_2$, isolated from Chamaecyparis nootkatensis (Alaska yellow cedar) is related to the sesquiterpenes and its structure is being studied by Erdtman⁽¹⁰⁾ in Sweden and by J. M. Robertson in Glasgow. X-ray crystallographic analysis has suggested structure (X) for this compound.⁽¹¹⁾



Erdtman⁽³³⁾ has suggested the following type of reaction mechanism as a possible mode of biosynthesis of the thujaplicins with emphasis on the relationship with the terpene myrtenol (XXIX) found in Chamaecyparis obtusa.



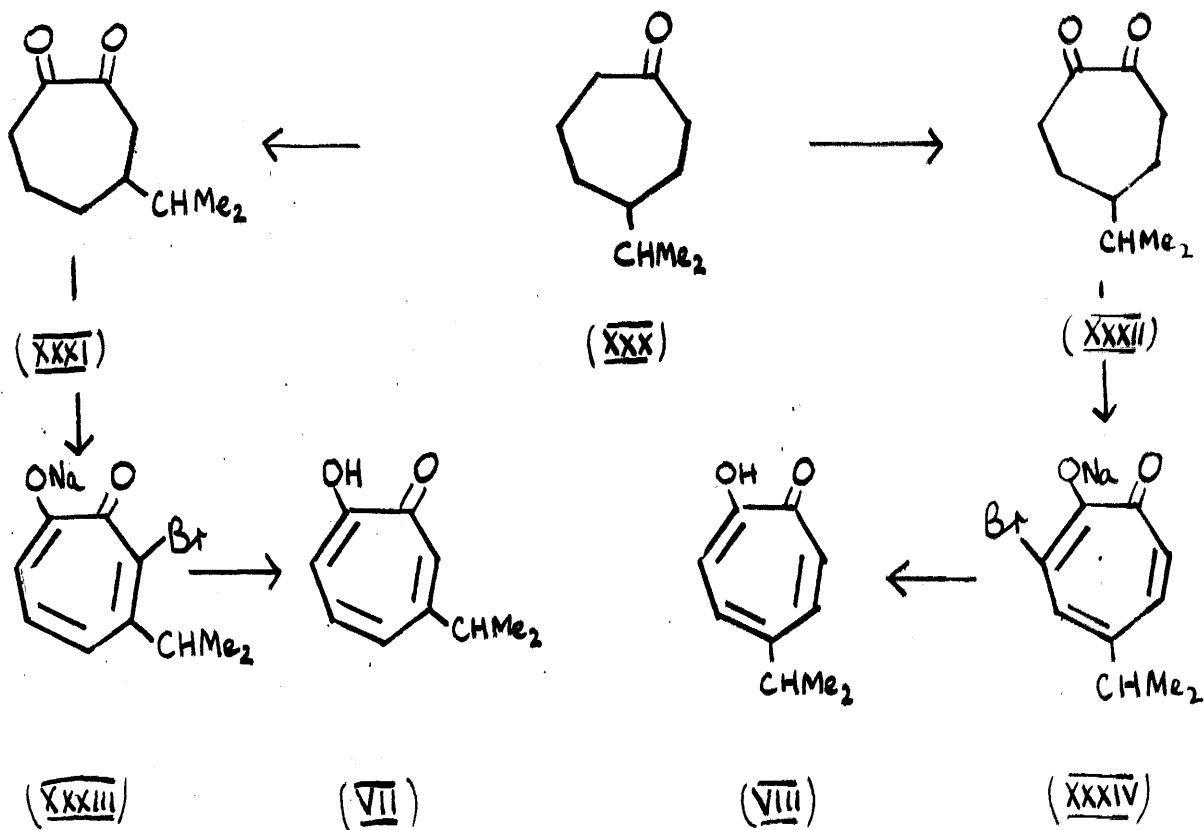
The ready conversion of cycloheptanone into tropolone suggested the synthesis of the thujaplicins from the appropriate isopropylcycloheptanones. One of these, 4-isopropylcycloheptanone (XXX) was obtained by ring enlargement of 4-isopropylcyclohexanone with diazomethane. From this

reaction were obtained (a) the initial ketone, identified by semicarbazone formation, (b) a fraction of non-ketonic material, presumably the methylene oxide, and (c) a main fraction of 4-isopropylcycloheptanone. This was converted to the semicarbazone which was found to exist in two isomeric forms, differing in solubility and melting point. Each form on regeneration yielded a sample of ketone which afforded only its own semicarbazone, i.e. the one from which it had been regenerated. The thiosemicarbazones of the two samples of ketone were also different, but, on the other hand, the 2:4-dinitrophenylhydrazones and bis-p-nitrobenzylidene compounds were identical. The infra-red absorption spectra of the two ketones were kindly determined by Dr. F. Sondheimer at Harvard University who reported that the curves were almost identical and gave the following band assignments; an intense C=O absorption occurs at 1694 cm^{-1} with an overtone at 3390 cm^{-1} ; the situation of the former band at a frequency rather lower than that exhibited by other examples of saturated ketones (ca. $1725\text{-}1710\text{ cm}^{-1}$) may be due to a steric property of the seven-membered ring. The expected methylene frequency occurs at 2874 cm^{-1} , and a doublet at 1387 and 1370 cm^{-1} is probably due to the C-Me grouping which is known in other compounds to give rise to absorption at ca. $1390\text{-}1370\text{ cm}^{-1}$.

The isomeric semicarbazones can only be ascribed to

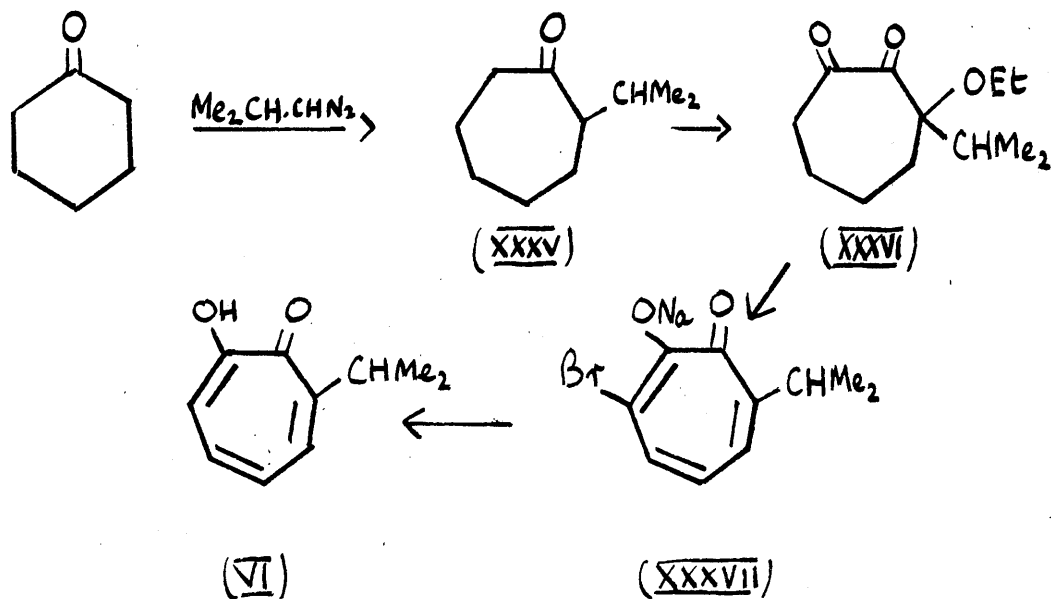
geometrical isomerism about the C=N bond, yet this cannot explain the exclusive formation of each semicarbazone from its parent ketone, or the non-interconvertibility of the two samples of ketone which still furnished their respective semicarbazones after heating to 150° in a sealed tube. A similar isomerism was observed in the case of the semicarbazones of 4-methylcycloheptanone by Qudrat-I-Khuda and Ghosh⁽³⁶⁾ who regarded them as derived from stereoisomeric forms of the parent ketones. However, the concept of the existence of such forms (analogous to boat and chair forms of cyclohexane) of the cycloheptane ring as separate compounds seems untenable, and this problem must remain, for the present, unexplained.

Oxidation of the ketone (XXX) with selenium dioxide afforded a mixture of the two α -diketones (XXXI and XXXII). These were not separated but brominated together to yield, after dehydrobromination and treatment with sodium hydroxide, a mixture of sodium bromo- β - and γ -thujaplicins (XXXIII and XXXIV). Hydrogenolysis of the purified mixture of the sodium salts over palladised charcoal yielded a mixture of β - and γ -thujaplicins (VII and VIII) which were separated by fractional crystallisation from light petroleum



α -Thujaplicin (VI) was synthesised by the following route. Cyclohexanone was treated with nitrosoisobutylurethane (cf. 37) to yield 2-isopropylcycloheptanone (XXXV). Selenium dioxide oxidation of (XXXV) in ethanol solution yielded 3-ethoxy-3-isopropylcycloheptane-1:2-dione (XXXVI). Such dual oxidations have been noted before, especially with compounds where a tertiary carbon atom is vicinal to the initial carbonyl group. (38) Treatment of (XXXVI) with bromine, dehydrobromination and hydrogenolysis of the sodium

salt of bromo- α -thujaplicin (XXXVII) in the manner described above furnished α -thujaplicin (VI). The ethoxyl group was presumably removed by the hydrogen bromide formed in the reaction.



The synthetic thujaplicins did not depress the melting points of the corresponding naturally occurring compounds and gave the same tropolone reactions (green colour with ferric chloride and chloroform-soluble copper salt formation). The α - and γ - isomers were further characterised by preparation of the (liquid) methyl ethers and hence the methyl ether picrates which had melting points of 110° and $148-149^\circ$ respectively.

Some practice was gained in the preparation of these derivatives by carrying out model experiments with tropolone

methyl ether which readily formed a picrate m.p. 119-120°. With a view to the preparation of the thujaplicin diphenylmethyl ethers, tropolone was treated with a solution of diphenyldiazomethane in benzene. There was obtained in good yield tropolone diphenylmethyl ether m.p. 142-143°. Repetition of this experiment with the thujaplicins afforded only diphenylazine however.

Since the publication of the above work⁽³⁹⁾ Professor Nozoe, who has been investigating the chemistry of hinokitiol (β -thujaplicin) since 1936⁽²⁾ has supplied us with a series of papers on tropolone chemistry recently published in Japan⁽⁴⁰⁾ and since reviewed by Birch,⁽⁴¹⁾ which include not only the synthesis of tropolone by an analogous route to that of J. W. Cook et al.⁽¹⁸⁾ but also of the α -⁽⁴²⁾, β -⁽⁴³⁾ and γ -⁽⁴⁴⁾ thujaplicins by a similar procedure to that described above. Comparison of the physical data of our synthetic intermediates with those of the Japanese authors reveals several small discrepancies e.g. differences in refractive indices and non-isolation of two isomeric semicarbazones of 4-isopropylcycloheptanone, only one being reported which melted at 155° (our semicarbazones had m.p.'s 135-137° and 180-182°). The ethoxylated dione (XXXVI) was presumed to be 3-isopropylcycloheptane-1:2-dione without supporting analytical evidence.

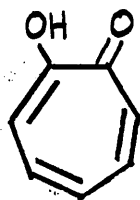
The success of this method obviously opens up the way for the preparation of numerous alkylated tropolones and this in fact has been realised by Nozoe who has synthesised methyl,⁽⁴⁵⁾ ethyl⁽⁴⁵⁾ and t-butyl⁽⁴⁶⁾ tropolones by application of procedures similar to those described herein.

SOME REACTIONS OF TROPOLONE

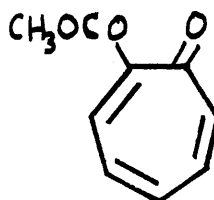
In view of the "phenolic" properties which have been associated with tropolone (I) and its derivatives (for example halogenation,⁴⁷ nitration,⁴⁸ diazo-coupling⁴⁹ and sulphonation⁵⁰) and in order to gain further insight into the aromatic character of the tropolone nucleus by chemical means, an investigation was undertaken of the behaviour of tropolone when subjected to some typical benzenoid reactions involving attack by electrophilic reagents. The tendency of tropolones towards salt formation with divalent metals⁽¹⁻¹⁰⁾ suggested that Lewis acid-catalysed reactions of the Friedel-Crafts type would be hindered by the great stability of the initially formed salt or complex towards substitution.

This was indeed borne out in practice. The iso-propylation of tropolone in presence of aluminium chloride and isopropyl chloride afforded a complex from which tropolone could be recovered. No trace of any of the three possible mono-substitution products (the thujaplicins) was isolated. An attempt to obviate this difficulty by the use of tropolone methyl ether under the same conditions resulted in the recovery of tropolone. Attempted C-acetylation of tropolone using acetyl chloride and aluminium chloride was attempted but only

tropolone could be recovered. Acetic anhydride and stannic chloride gave a similar result but on heating tropolone with acetic anhydride and syrupy phosphoric acid there was isolated in addition to the main part of starting material a small yield of O-acetyltropolone (XXXVIII). This acetate

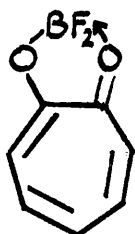
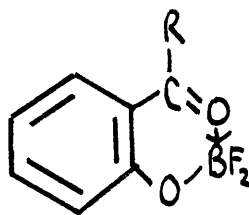
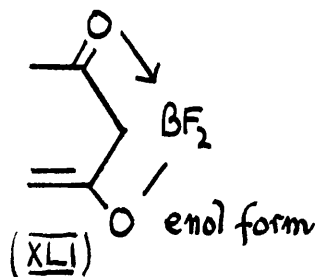


(I)

(XXXVIII)

has since been described by Doering and Knox⁽⁵¹⁾ who prepared it by heating a solution of tropolone in pyridine with acetic anhydride.

A further attempt at C-acetylation employing boron trifluoride and acetic acid yielded a complex for which structure (XXXIX) is suggested involving a five-membered chelate ring. Similar complexes have been obtained from both o-acylphenols (XL) and β -diketones (XLI) the ring in these latter cases being six-membered.⁽⁵²⁾

(XXXIX)(XL)(XLI)

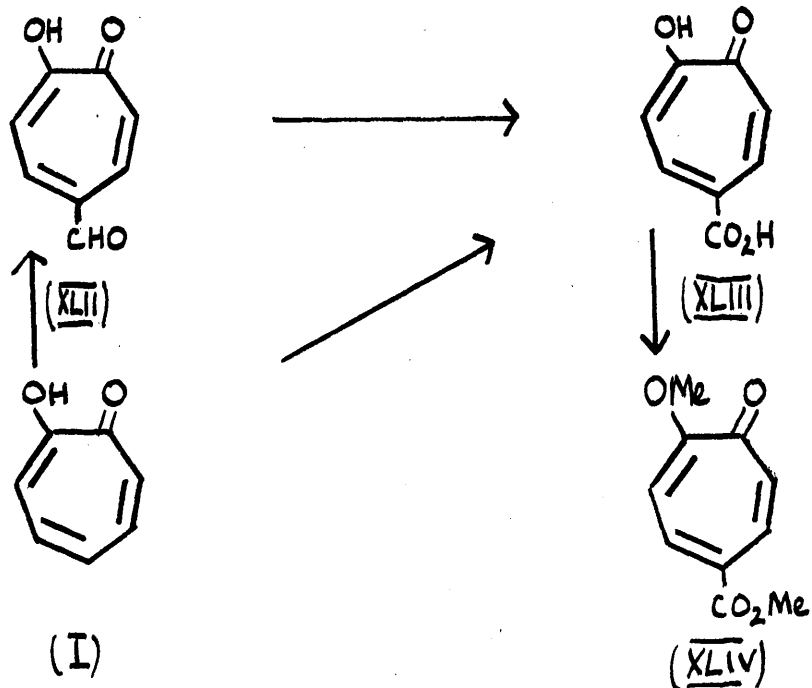
enol form

The Gatterman reaction with zinc cyanide and hydrogen chloride yielded only tropolone on decomposition of the white complex which was precipitated.

Attempted chloromethylation using both paraformaldehyde-hydrogen chloride and chloromethyl methyl ether techniques gave only tropolone hydrochloride.

Three procedures^(53,54) for the Kolbe-Schmidt reaction in an attempt to prepare a tropolone-carboxylic acid led only to the recovery of tropolone.

Some measure of success was however achieved in alkaline solution, for the Reimer-Tiemann reaction in presence of sodium hydroxide and chloroform furnished γ -formyl-tropolone (XLII) albeit in very small yield. This finding is in marked contrast with the results obtained in the case of the six-membered phenols. Thus phenol undergoes the Reimer-Tiemann reaction to yield salicylaldehyde and p-hydroxy-benzaldehyde in the proportion six to one.⁽⁵⁵⁾ The substitution of tropolone in the γ -position is however in accord with the predictions of Dewar⁽⁵⁶⁾ which indeed have accounted for most of the substitutions of tropolone hitherto reported, the only exception being halogenation⁽⁴⁷⁾ where the first step appears to be the formation of a complex.



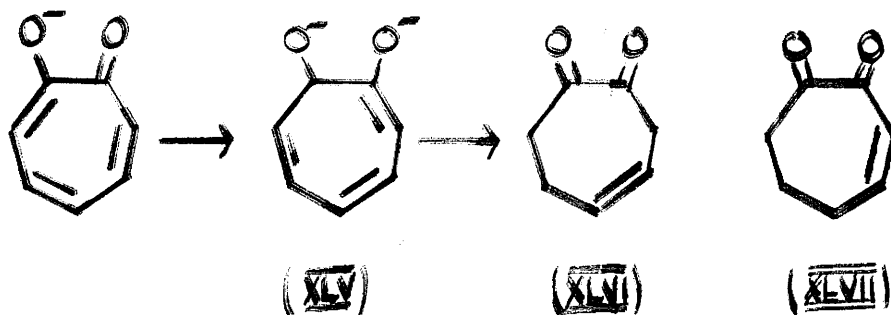
The structure of the aldehyde (XLII) was established not by alkaline fusion to the corresponding p-formylbenzoic acid which might have resulted in Cannizzaro products but by careful oxidation with silver oxide to tropolone- γ -carboxylic acid (XLIII) which had been prepared in this laboratory by Mr. D. K. V. Steel by an unambiguous synthesis. (57)

Direct comparison of the melting point data of this acid and its methyl ether methyl ester (XLIV) with our corresponding compounds (XLIII, XLIV) confirmed the structure of the latter unequivocally. The small yield of the aldehyde (XLII) discouraged further experiments with this potentially useful derivative.

The γ -acid (XLIII) was also obtained directly in minute yield when carbon tetrachloride potassium hydroxide and tropolone were heated in a sealed tube at 100°. By treating phenol similarly Reimer and Tiemann⁽⁵⁸⁾ obtained p-hydroxy-benzoic acid and for a series of phenols it has been shown that the principal product is the p-acid if the para position is free. The attempted preparation of a formyltropolone by the N-methylformanilide-phosphorus oxychloride procedure⁽⁵⁹⁾ resulted in one instance in a resinous product showing carbonyl activity. Analysis of the 2:4-dinitrophenyl-hydrazone of this crude product indicated that a formyltropolone had, in fact, been formed but constant repetition of this experiment failed to produce any compound other than the starting tropolone.

Cook, Gibb, Raphael, and Somerville⁽¹⁷⁾ had observed that tropolone reacted vigorously with lithium aluminium hydride. The nature of the product, however, was not investigated in detail at that time. Careful repetition of this work has shown that the reaction follows a complex route. On adding an ethereal solution of tropolone to a slurry of lithium aluminium hydride in ether, a bright yellow precipitate was initially formed. The colour disappeared on further heating and on addition of dilute sulphuric acid a deep reddish-brown colour developed. This

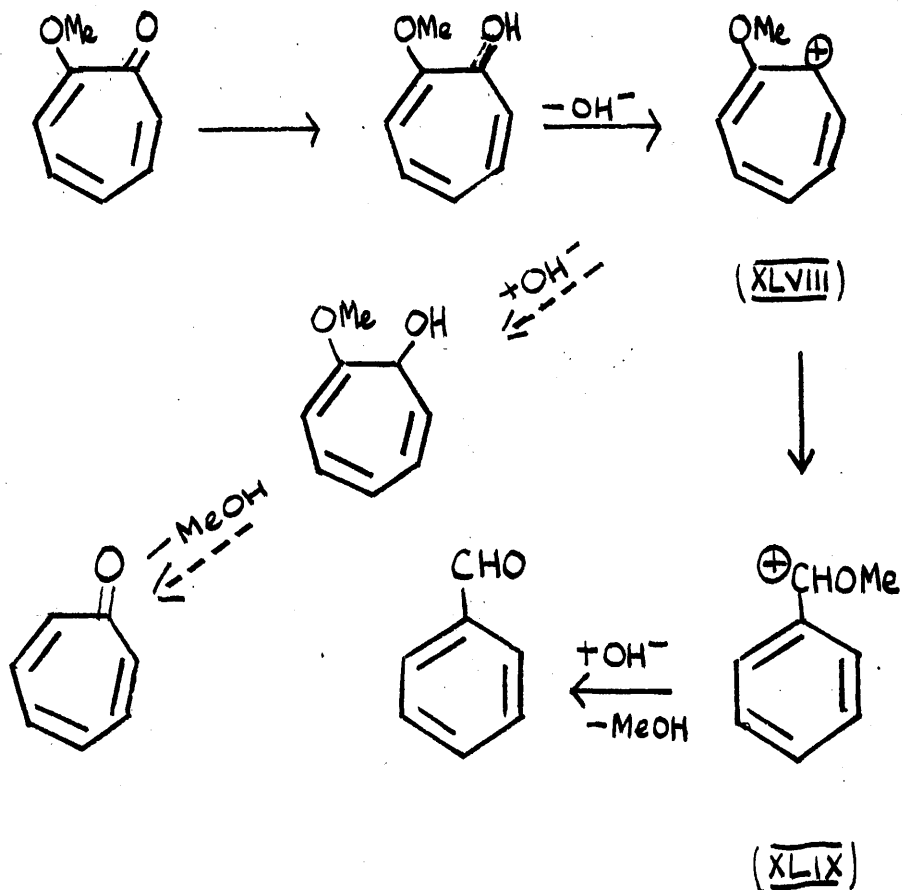
resinification could not be prevented either by working under nitrogen or by using ice to decompose the reaction mixture. Distillation of the tarry product gave mainly a resin but a small yield of a liquid was isolated which gave an immediate precipitate with (ethanolic) 2:4-dinitrophenylhydrazine sulphate. Analysis of the hydrazone indicated that it was the bis-2:4-dinitrophenylhydrazone of a cycloheptenedione. The ultra-violet absorption curve of this compound resembled very closely that of the bis-2:4-dinitrophenylhydrazone of cycloheptane -1:2-dione which was prepared for comparison, although the two compounds were clearly different. The liquid reduction product is therefore postulated as cyclohept-4-ene-1:2-dione (XLVI) produced by 1:4 or 1:6 addition of lithium aluminium hydride to the dienone system of the initially formed lithium tropolonate. Hydrolysis of the resulting dienolate (XLV) would give the dione (XLVI) by ketonisation.



A similar mechanism has been proposed to account for the formation of 1:4-diphenylbutan-2-ol-4-one by reduction of dibenzoyl ethylene.⁽⁶⁰⁾ Structure (XLVII) for the reduction product seems unlikely on the grounds that the expected bathochromic shift in the ultra-violet absorption associated with the conjugated double bond in this isomer was not observed.

It is of interest that the two bis-2:4-dinitrophenylhydrazones mentioned above display maximal absorption in the ultra-violet (3560 A) which corresponds to that of an unconjugated monoderivative, indicating that no conjugation has taken place between the hydrazone groups. This observation is in accord with the results of Leonard and Mader⁽²⁶⁾ who have shown that in 3:3:7:7-tetramethylcycloheptane-1:2-dione the inter carbonyl angle is 90°. The two hydrazone groupings thus behave as discrete chromophores.

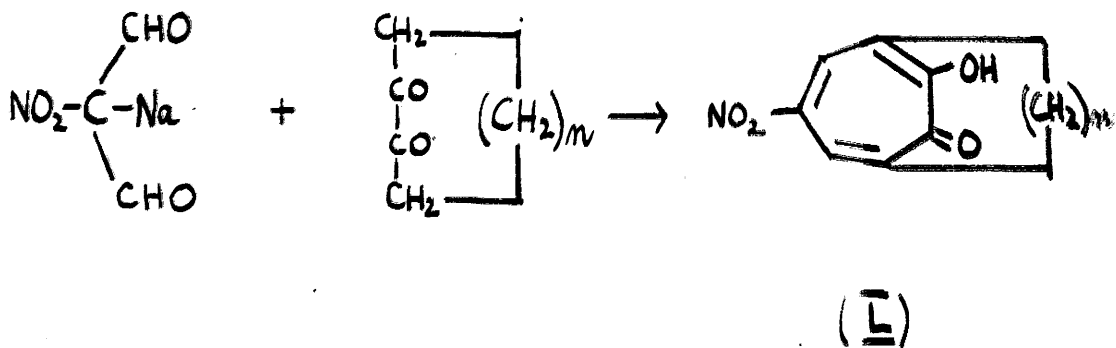
Reduction of tropolone methyl ether with lithium aluminium hydride gave a completely different and unexpected result, a good yield of benzaldehyde being produced. A possible explanation of this ring contraction is the formation of a carbonium ion (XLVIII) which rearranges by a Wagner-Meerwein type of reaction to the more stable benzenoid carbonium ion (XLIX). By similar anionotropy



it would seem possible that some cyclohepta-2:4:6-trien-1-one (tropone) would be formed but none of this latter could be isolated. This conversion to benzaldehyde recalls a similar rearrangement of tropolone to o-chlorobenzaldehyde on treatment with thionyl chloride.⁽⁶¹⁾

THE SELF-CONDENSATION OF cycloDECANE-1:2-DIONE

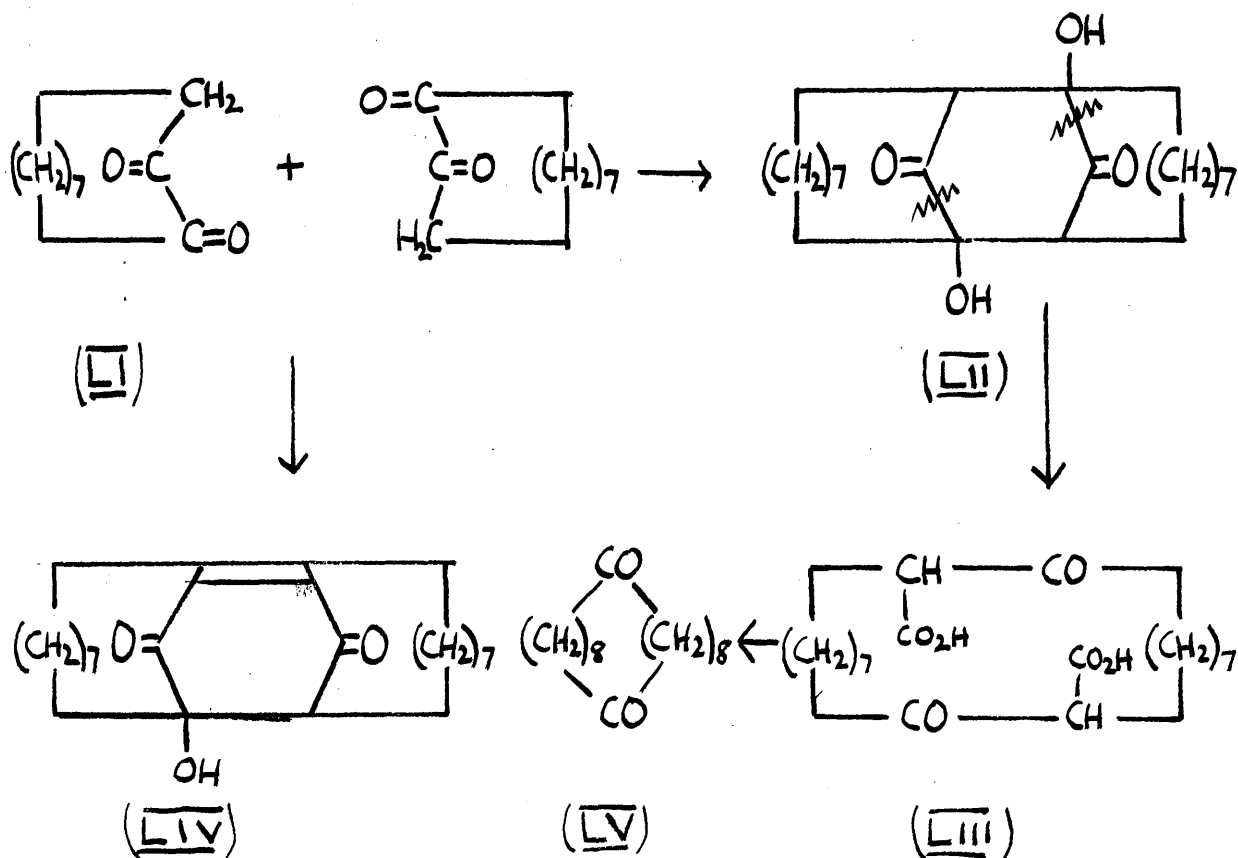
As has already been described (p. 8) an attempted preparation of γ -nitrotropolone by a condensation between sodionitromalondialdehyde and diacetyl failed because of the transoid configuration of the carboxyl groups of the diketone. The required cisoid α -diketone conformation is of course present when the grouping forms part of a small ring (e.g. cyclopentane-1:2-dione). However, any attempt to employ such a dione in this condensation to give a bridged ring tropolone of type (L) would be foredoomed to failure because of the tenets of the Bredt rule.⁽⁶²⁾




It has been shown, however, in similar reactions that the Bredt rule no longer remains valid if n be large enough.⁽⁶³⁾ On the other hand, for the above condensation to be favoured n must not be too large, since it is known that the carbonyl

groups in monocyclic α -diketones become progressively more transoid the bigger the ring.⁽²⁶⁾ In an attempt to steer a middle course between these two extremes a medium ring size α -diketone, cyclodecane-1:2-dione ($n = 6$), was employed in the condensation.

No tropoloid material could be isolated from the reaction mixture. The main product consisted of sebacic acid formed by oxidative fission of the dione, but a small amount of a neutral, non-nitrogenous, high-melting material was also obtained. This latter compound could be formed in much better yield by treatment of the dione alone with methanolic sodium methoxide, whereupon the product crystallised from the reaction mixture. Analysis and molecular weight determination showed that it was a dimer of cyclodecane-1:2-dione ($C_{20}H_{32}O_4$) exhibiting no carbonyl reactivity. Infra-red absorption measurements (Nujol mull) showed, however, the presence of strong bands at 1682 cm^{-1} ($C = O$ stretching frequency) and 3426 cm^{-1} (OH stretching frequency).



Prelog and his school have shown that the most stable configuration of cyclodecanone is that in which the oxygen atom of the carbonyl group is enclosed as far as possible by the polymethylene chain, the so-called "O-inside" configuration.⁽⁶³⁾ Thus in cyclodecane-1:2-dione the most stable configuration should be the "O-inside, O-outside" structure (formally represented by (LI)). The evidence for this structure gains support from the recent observations of the ultra-violet absorption data of alicyclic α -diketones made by Leonard and Mader.⁽²⁶⁾ Although highly unfavourable for the tropolone condensation the configuration

(LI) is very favourable for the occurrence in alkaline solution of a double-aldol type condensation between two molecules of the dione to form 2,6:3,5-bis (heptamethylene)-cyclohexane-2:5-diol-1:4-dione (LII). This postulated and, at first sight, rather surprising structure for the dimer $C_{20}H_{32}O_4$ was confirmed by oxidative degradation at 75° with sodium bismuthate whereby cyclooctadecane-1:10-dione (LV)⁽⁶⁴⁾ was produced and identified by mixed melting point determination. Such a product is readily derived from (LII) by fission of the bonds marked () and decarboxylation of the resulting cyclooctadecane-1:10-dione-2:11-dicarboxylic acid (LIII); this latter compound was isolated when the fission was carried out under milder conditions. Structure (LII) also accounts for the lack of carbonyl reactivity⁽⁶⁵⁾ and the resistance of the hydroxyl groups to acetylation, benzylation and replacement by halogen.

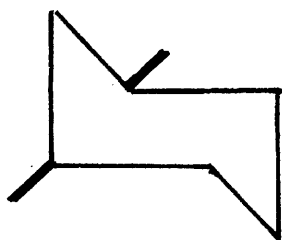
In attempts to convert the dimer (LII) to the corresponding substituted benzoquinone it was treated with a variety of dehydrating agents but in nearly every case the dimer crystallised from the reaction mixture. However, fusion with toluene-p-sulphonic acid gave an intense purplish-blue melt. Lack of time has prevented further investigation of this product.

Addition of water to the methanolic filtrate from the

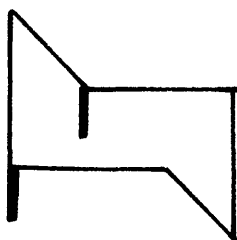
dimer preparation caused the precipitation of a second product with the molecular formula $C_{20}H_{30}O_3$. This also showed no carbonyl or hydroxylic reactions although its infra-red spectrum (carbon tetrachloride) exhibited the stretching frequencies of these groups at 1712 cm^{-1} and 3565 cm^{-1} respectively; in addition a weak C=C stretching frequency was observable at 1621 cm^{-1} . This indication of one double bond was confirmed by quantitative microhydrogenation. An ethanolic solution of the compound showed maximal absorption in the ultra-violet at 2450 Å ($\epsilon = 7,500$) with a marked inflection at 2520 Å ($\epsilon = 7,250$). This is in harmony with the chromophoric properties of a di-alkylated cyclohex-2-ene-1:4-dione.⁽⁶⁶⁾ All these properties point clearly to the structural formula (LIV) for this second product of the reaction. The fact that the dimer (LII) does not readily dehydrate even under drastic reaction conditions excludes it from being an intermediate in the production of (LIV) and it is thus very probable that the stereochemistry of the two molecules is different.

The production of the dimer (LII) from cyclodecane-1:2-dione involves the creation of four asymmetric carbon atoms and it is highly probable that the resulting six-membered ring is in the more stable chair configuration. In the various stereoisomeric modifications constructable on this basis it may readily be seen that there are three possible

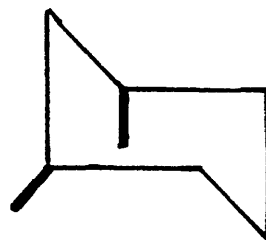
ways in which the heptamethylene chain may be attached to the six-membered ring, namely, equatorial-equatorial (e-e), polar-polar (p-p) and equatorial-polar (e-p).⁽⁶⁷⁾



(e-e)



(p-p)



(e-p)

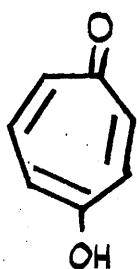
An assessment of the relative stability of the heptamethylene chain in these three configurations may be made by using the known relationship between the constellation of a polymethylene chain and its energy content which has been described by Prelog.⁽⁶³⁾ Construction of the three configurations by means of "Catalin" molecular models shows that in both the e-e and p-p modes of attachment the heptamethylene chain contains six energetically unfavourable c constellations while the e-p linking involves five c constellations and one favourable b constellation; this latter configuration represents a greater stability of ca 3 kcal.. Only three configurations (LVI, LVII, LVIII) of the dimer (LII) involving e-p linking of both polymethylene chains can be constructed.

One of these (LVIII) possesses adjacent hydrogen and

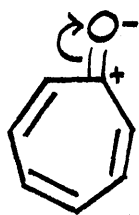
(LVII) as the configuration of the dimer (LII). Neither of these configurations have polar H and OH groups suitable for ionic dehydration which would explain the resistance of the dimer towards dehydration. Structure (LVI) however is energetically much more favourable as the hydroxyl groups occupy the less hindered and thermodynamically more stable equatorial positions. The finding that the yields of the two condensation products together constitute an almost quantitative conversion of cyclodecane-1:2-dione is in good accord with the prediction of only two favoured stereochemical structures.

THE ATTEMPTED SYNTHESIS OF γ -TROPOLONE

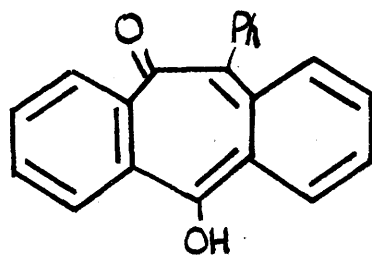
In view of the recent interest in compounds containing the tropolone ring system (p. 1 et seq.) a synthesis of an isomer of tropolone, γ -tropolone (4-hydroxycyclohepta-2:4:6-trien-1-one; LX) was devised with the purpose of comparing its properties with those of tropolone. γ -tropolone, although not possessing the characteristic hydrogen bonding and chelating properties associated with the 2-ol-1-one group of tropolone should nevertheless display some degree of aromatic stability since it is the 4-hydroxy-derivative of the aromatic parent tropone (LXI)⁽⁷⁰⁾ and should share in the latter's properties of salt formation, halogenation etc. Another interesting comparison which could be made between tropolone and its γ -isomer is the substitution by benzenoid-type reagents in presence of Lewis acid type catalysts which although hindered in the case of tropolone itself (p. 21) might proceed more smoothly with the γ -compound. Other points of comparison which, it was hoped, could be examined were the nature of the hydrogen bonding, if present, substitution by halogens, nitration, and rearrangement to benzenoid derivatives.



(IX)

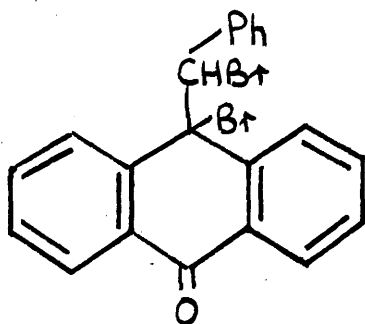


(LXI)

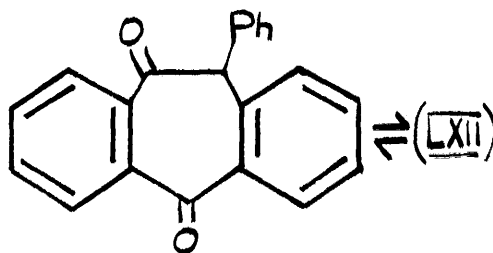
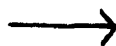


(LXII)

A dibenzo-derivative (LXII) of γ -tropolone has been described by J. W. Cook⁽⁷¹⁾ who prepared it by the hydrolytic rearrangement of benzylideneanthrone dibromide (LXIII); compound (LXII) furnished a red sodium salt.



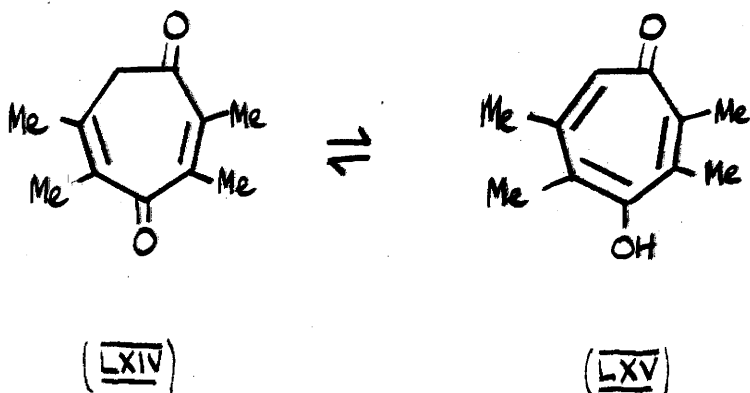
(LXIII)



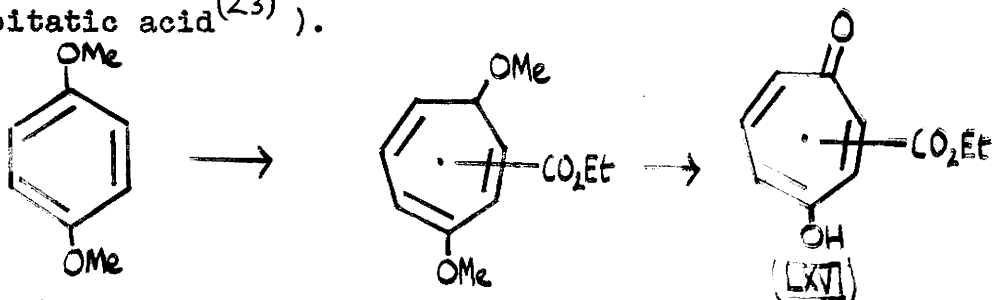
(LXII)

The preparation of a tetramethyl- γ -tropolone has been claimed by Smith and Pings⁽⁷²⁾ who assigned structure (LXIV) to one of the products of the ring enlargement of duroquinone with diazomethane. This should be readily

isomerisable to the more stable keto-enol system (LXV) but the American authors state that the product is insoluble in alkali and gives a dioxime.

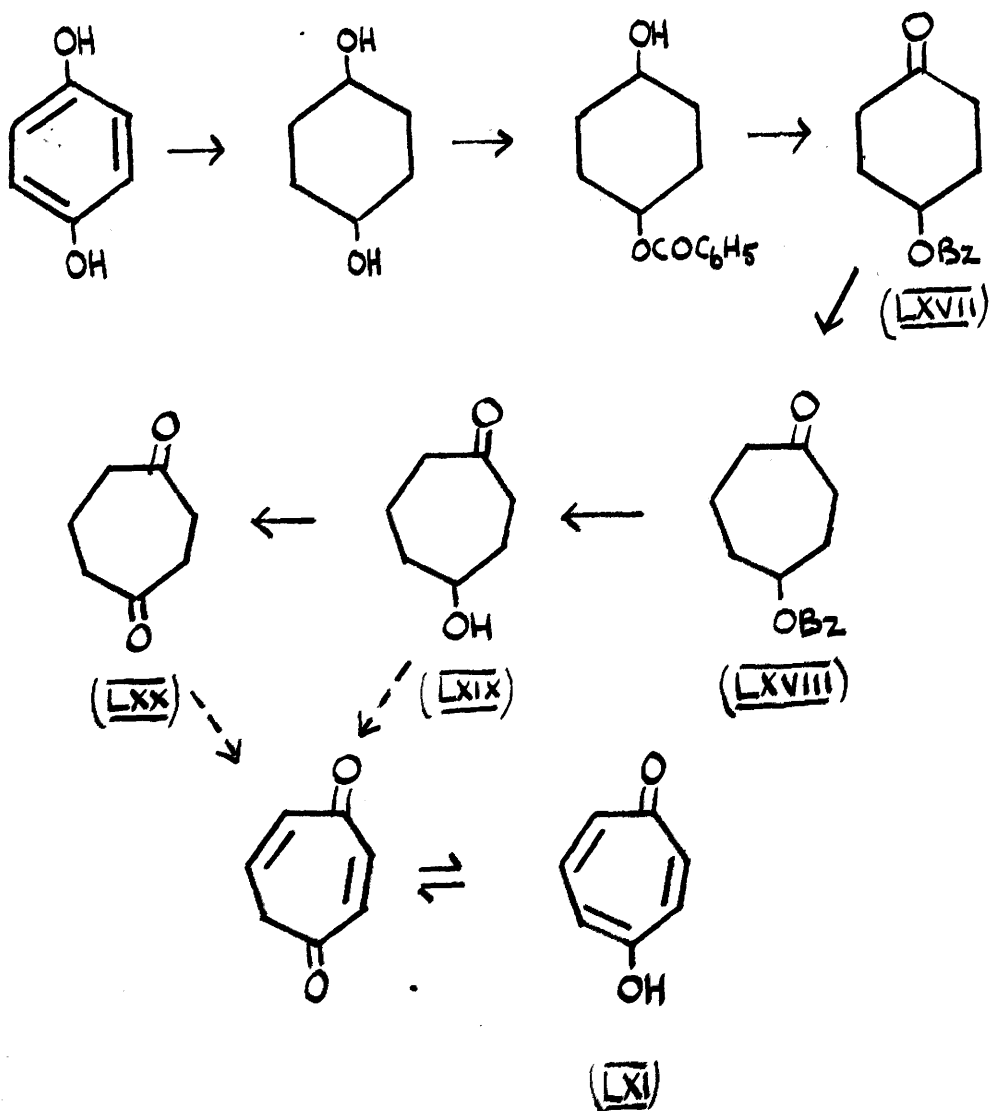


A. R. Todd⁽⁷³⁾ has recently made a brief report of the preparation of a carbethoxy- γ -tropolone (LXVI) obtained by the ring expansion of hydroquinone dimethyl ether with ethyl diazoacetate followed by bromination and dehydrobromination technique (cf. carbethoxytropolone p. 6 and stipitatic acid⁽²³⁾).



The recent success attending the dehydrogenation of cycloheptane-1:2-dione to tropolone^(17, 18) by the bromination-dehydrobromination technique suggested application of

the same procedure to cycloheptane-1:4-dione. The latter compound was synthesised from the known 4-benzoyloxycyclohexanone ^(74,75)(LXVII) in three steps. The first stage was the ring-enlargement of the ketone to 4-benzoyloxy-cycloheptanone (LXVIII) which proceeded in ca. 50% yield (cf. p. 14) in presence of diazomethane. Methanolysis of (LXVIII) yielded methyl benzoate and 4-hydroxycycloheptanone (LXIX). Jones and Sondheimer⁽⁷⁵⁾ observed that the separation of 4-hydroxycyclohexanone and methyl benzoate was extremely difficult and tedious by distillation and this was also found to be the case with the seven-membered hydroxyketone. The difficulty was resolved as in the six-membered series by shaking out the hydroxyketone in water and removing the last traces of ester by ether extraction. Chromic acid oxidation of the purified 4-hydroxycycloheptanone (LXIX) afforded cycloheptane-1:4-dione (LXX) which formed a bis-2:4-dinitrophenylhydrazone.



Application of the bromination-dehydro-bromination technique to the dione (LXX) using either bromine⁽¹⁷⁾ or N-bromosuccinimide⁽¹⁸⁾ failed to give a recognisable product. In one case an alkali-soluble oil was obtained from which a few milligrams of benzoic acid crystallised. This may

have been a rearrangement product of the initially formed γ -tropolone (LXI) or it may have arisen from traces of methyl benzoate still present in the starting material (vide supra).

The method of Knight and Cram⁽²⁰⁾ who prepared tropolone from 2-hydroxycycloheptanone by bromination and subsequent oxidation and dehydrobromination was then applied to 4-hydroxycycloheptanone (LXIX) but although derivatives corresponding to a dibromo- and a tribromo- substituted product were obtained, removal of the bromine by hydrogenolysis gave a very small yield of a gum which could not be characterised.

Direct dehydrogenation of the dione (LXX) by three methods left the starting material largely unaltered. These consisted of (a) heating alone with palladised charcoal (b) heating with palladised charcoal in trichlorobenzene solution and (c) distilling the vapour through palladised or platinised charcoal heated to 300°. Selenium dioxide has been used as a dehydrogenating agent for 2:5-hexanedione⁽⁷⁶⁾ (LXXI) which affords diacetylene (LXXII).

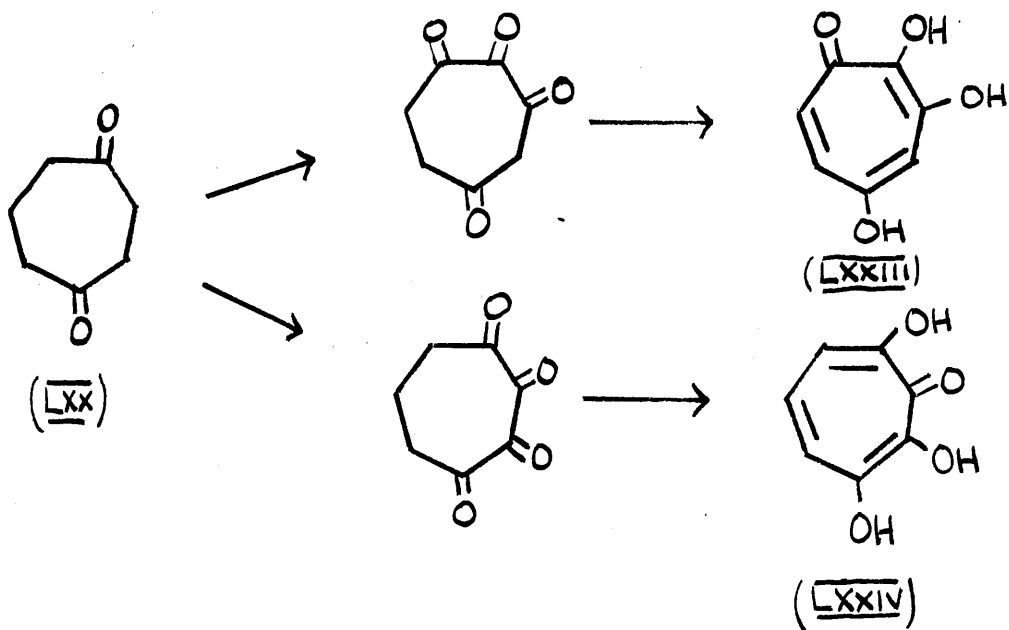


(LXXI)

(LXXII)

When applied to cycloheptane-1:4-dione (LXX) a minute yield

of a compound m.p. 270° giving an intense green colour with ferric chloride was obtained. This may be a polyhydroxy-tropolone e.g. (LXXIII) formed by oxidation and enolisation.



The possibility that the compound might have been $\alpha\alpha'$ -dihydroxytropolone (LXXIV) was excluded by the fact that the latter is known (decarboxylated puberulic acid⁽⁷⁷⁾) and has m.p. $237-238^{\circ}$.

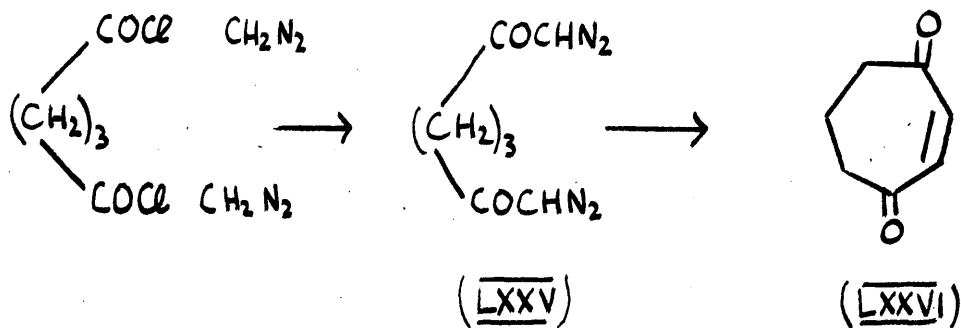
The failure of these methods to produce any trace of the required γ -tropolone was rather surprising. Treibs⁽⁷⁸⁾ has observed that certain hydroazulenes, which are extremely resistant to direct dehydrogenation by palladised charcoal catalysts, give the required azulenes on being heated alone or in nitrobenzene solution with iodine. When this procedure was applied to cycloheptane-1:4-dione (LXX) a small

yield of an oil possessing no carbonyl activity (no precipitate with alcoholic 2:4-dinitrophenylhydrazine sulphate) was obtained. Experiments are in progress to obtain this oil sufficiently pure for more detailed examination.

Grundmann⁽⁷⁹⁾ has described a preparation of diacyl-ethylenes which involved the treatment of a petrol solution of the relevant diazoketone with copper oxide, e.g.



In an attempt to carry out this reaction intramolecularly these conditions were applied to 1:7-bisdiazoheptane-2:6-dione (LXXV) but the yield of the required cyclohept-2-ene-1:4-dione (LXXVI) discouraged further work on this approach.



EXPERIMENTALTHE THUJAPLICINS.

2:2-Di(p-hydroxyphenyl) propane. - The method of Zincke⁽⁸⁰⁾ was used. A mixture of phenol (1050 g.), acetone (150 g.) and fuming hydrochloric acid (105 g.; S.G. 1.9) was kept at 30-40° until the whole mass became crystalline (2-3 days). The solid was stirred with acetic acid (35%; 1500 c.c.), filtered and washed with dilute acetic acid and then with water. The dried material, m.p. 145-150°, was used directly for the next step.

p - isoPropylphenol. - After Cook, Philip and Somerville.⁽⁸¹⁾

A mixture of the crude diphenol (380 g.) and copper chromite catalyst⁽⁸²⁾ (38 g.) was agitated with hydrogen for 5 hours in a stainless steel autoclave at 230°/180 atmos. The viscous product was distilled into (i) b.p. 88-100°/15 mm. (130 g.) and (ii) b.p. 100-125°/15 mm. (100 g.). Fraction (ii) crystallised affording colourless needles of p-isopropylphenol m.p. 62-63° (lit. 63°).

4-isoPropylcyclohexanol. - After Frank, Berry, and Shotwell.⁽⁸³⁾

A solution of p-isopropylphenol (200 g.) in ethanol (250 c.c.) was hydrogenated over Raney nickel catalyst at 190°/135 atmos. Fractional distillation of the product yielded (i) b.p. 90-104°/20 mm. (52 g.) and (ii) b.p.

104-110°/20 mm. (132 g.). Fraction (ii) was used for the next stage.

4-isopropylcyclohexanone. - To a solution of potassium dichromate (59 g.) in water (450 c.c.) was added 4-isopropylcyclohexanol (80 g.). Concentrated sulphuric acid (52 c.c.) was then added with stirring at such a rate that the temperature remained at 55-60°. The reaction mixture was cooled to room temperature, the oily layer separated and the aqueous layer extracted with ether. The oily layer and extracts were combined, washed with sodium hydroxide solution (5%; 100 c.c.) and then with water and dried (Na₂SO₄). Fractional distillation gave 4-isopropylcyclohexanone (61 g.) b.p. 97-99°/15 mm. (lit. 90-91°/13 mm.), semicarbazone m.p. 187-188° (lit. 187-188°).

4-isopropylcycloheptanone (XXX). - To a stirred mixture of 4-isopropylcyclohexanone (45 g.), methanol (50 c.c.) and powdered anhydrous sodium carbonate (1 g.) was added nitrosomethylurethane ⁽⁸⁴⁾ (1 c.c.). The reaction started almost immediately, and the temperature rose sharply. The nitroso compound (78 g.) was then added dropwise during 1.5 hours, the temperature being maintained at 20-25° by ice-water cooling. The mixture was stirred for 1 hour after the addition and then left at room temperature for 16 hours. The methanolic solution was filtered and distilled to yield (after

removal of solvent) (i) b.p. 80-100°/18 mm. (12g.); (ii) b.p. 100-110°/18 mm. (12g.); and (iii) b.p. 110-114°/18 mm. (22g.). 1 c.c. portions of (ii) and (iii) were treated with semicarbazide acetate solution. (ii) afforded a small amount of semicarbazone, plates m.p. 180-182° from aqueous ethanol. (iii) gave a substantial amount of the same semicarbazone. When mixed with the semicarbazone of 4-isopropylcyclohexanone (m.p. 187-188°) a depression of 30° was obtained.

A solution of crude 4-isopropylcycloheptanone (52g.) in ethanol (50 c.c.) was warmed to 50° and treated with warm ethanolic semicarbazide acetate solution [from semicarbazide hydrochloride (82g.), potassium acetate (120g.), and ethanol (400 c.c.)]. The crystals which separated on cooling were filtered off and crystallised from aqueous ethanol; semicarbazone-A (33g.) formed plates m.p. 180-182° (Found: C, 63.0; H, 9.7; N, 19.5. $C_{11}H_{21}ON_3$ requires C, 62.6; H, 9.95; N, 19.9%). The combined filtrate and mother liquors were diluted with water whereupon a further quantity of solid was precipitated. Repeated crystallisation from aqueous ethanol afforded the isomeric semicarbazone-B (24g.) as tiny plates m.p. 135-137° (Found: C, 62.8; H, 10.4; N, 19.7%). A mixture of the two semicarbazones melted indefinitely over the whole range between the m.p.s. of the individual constituents.

Semicarbazone-A (15g.) was heated at 100° for 4 hours

with oxalic acid (50g.) and water (50 c.c.). Water (100 c.c.) was added and the ketone recovered by distillation in steam followed by ether extraction. Distillation afforded the pure ketone (10g.) as a liquid with a pleasant odour b.p. 115-117°/18 mm. n_D^{18} 1.4708 (Found: C, 77.6; H, 11.6. $C_{10}H_{18}O$ requires C, 77.9; H, 11.7%). A small sample of the ketone on treatment with semicarbazide acetate gave only semicarbazone-A in good yield, with no detectable amount of the B-isomer. The thiosemicarbazone-A, prepared in the usual way, crystallised from aqueous ethanol in tiny platelets m.p. 156° (Found: C, 58.3; H, 9.5. $C_{11}H_{21}N_3S$ requires C, 58.15; H, 9.3%).

Similar regeneration from semicarbazone-B afforded the parent ketone b.p. 114-117°/18 mm., n_D^{19} 1.4690 (Found: C, 77.6; H, 11.9%) which yielded only semicarbazone-B on treatment with semicarbazide acetate, while the thiosemicarbazone-B crystallised from aqueous ethanol in plates, m.p. 174° (Found: C, 58.35; H, 9.5%). Both ketones regenerated from semicarbazones -A and -B gave the same 2:4-dinitrophenylhydrazone which crystallised in yellow plates m.p. 93-95° from ethanol and contained 4 molecules of water of crystallisation (Found: C, 47.7; H, 7.1; N, 13.6. $C_{16}H_{22}O_4N_4 \cdot 4H_2O$ requires C, 47.35; H, 7.4; N, 13.8%); on drying in vacuo the crystals lost water to give the anhydrous compound as a liquid which gradually resolidified to the hydrate in moist air. Both samples of the ketone when treated with p-nitrobenzaldehyde in presence

of ethanolic sodium methoxide (cf. Gripenberg)⁸⁵ furnished the same bis-p-nitrobenzylidene compound as prisms m.p. 151°, from n-butanol (Found: N, 7.1. $C_{24}H_{24}O_5N_2$ requires N, 6.7%). When separate samples of the ketones were heated in sealed tubes for 30 minutes at 250°, they gave only their respective semicarbazones as before.

Sodium Bromo- β - and γ -thujaplicins. XXXIII and XXXIV) - To a refluxing solution of 4-isopropylcycloheptanone (9.1g.) in ethanol (98%; 15 c.c.) was added dropwise over 1 hour a solution of selenium dioxide (7.2g.) in ethanol (98%; 45 c.c.). Heating under reflux was continued for 6 hours after the final addition and the mixture left at room temperature overnight. The selenium (3g.) was filtered off, the ethanol removed under reduced pressure and the resultant oil distilled to give a mixture of the diones (XXXI and XXXII) as a pale yellow liquid b.p. 135-145°/ 18 mm. (7.2g.).

A stirred solution of the diones (7.2g.) in glacial acetic acid (8c.c.) was cooled to 0° and treated dropwise with bromine (14.4g.) in acetic acid (9c.c.) during 1 hour. The resultant deep red solution was kept at room temperature overnight and then heated at 100° until evolution of hydrogen bromide had ceased (1.5 hours). The acetic acid was removed in steam together with a little unchanged dione. The tarry residue was extracted with ether and the extract filtered and

treated with sodium hydroxide solution (6N; 10c.c.); the resultant sodium salts (1.2g.) were filtered off and crystallised several times from water (yellow needles m.p. 300-305° dec.). They contained 2 molecules of water of crystallisation (cf. Cook, Gibb, Raphael and Somerville, loc. cit.) (Found: C, 39.0; H, 4.2. $C_{10}H_{10}O_2BrNa, 2H_2O$ requires C, 39.3; H, 4.6%).

The filtrate from the sodium salts was acidified with dilute sulphuric acid. Ether extraction afforded a small amount of dark brown oil which proved intractable even after distillation at 155-170° (bath temp.)/0.15 mm. followed by chromatography in benzene over alumina.

β - and γ -Thujaplicins (VII and VIII). - The mixture of isomeric sodium salts (626mg.) was dissolved in methanol (25c.c.) and stirred under hydrogen with palladium/charcoal (10%; 150mg.) until 1 mole of hydrogen had been absorbed. Removal of catalyst and solvent left a red oil which was extracted with boiling light petroleum (b.p. 40-60°). The extract (60 c.c.), after treatment with charcoal, was evaporated to small bulk (ca. 10 c.c.) and cooled to -15°. The sticky, crystalline solid thus obtained was sublimed at 80° (bath temp.)/ 0.001 mm. and the hard, cream-coloured sublimate was crystallised from light petroleum (b.p. 40-60°). The resulting prismatic needles (120 mg.) then had m.p. 79.5°,

undepressed on admixture with naturally-occurring γ -thujaplicin (m.p. 79°). Treatment with ethereal diazomethane yielded γ -thujaplicin methyl ether as a liquid, which yielded a picrate on treatment with saturated ethanolic picric acid solution. The picrate, after recrystallisation from ethanol formed yellow needles m.p. $148-149^{\circ}$ (Found: C, 50.3; H, 4.6. $C_{17}H_{17}O_9N_3$ requires C, 50.1; H, 4.2%).

The mother liquors from the above preparation after removal of petroleum afforded an oil which was distilled at 80° (bath temp.)/0.001 mm. The distillate was dissolved in light petroleum (b.p. $40-60^{\circ}$), cooled to -15° , and seeded with a trace of β -thujaplicin. The solution deposited prisms m.p. $46-47^{\circ}$ (12 mg.) which showed no depression when mixed with natural β -thujaplicin (m.p. 47°).

Both β - and γ -thujaplicin were formed in this way not only from the mixture of ketones from the ring-expansion of 4-isopropylcyclohexanone, but also from each of the samples regenerated from the pure semicarbazones (A and B).

N-Nitrosoisobutylurethane. - A mixture of ether (200 c.c.), isobutylamine (40 g.) and water (100 c.c.) was cooled to 5° with stirring. Ethyl chloroformate (60 g.) was added without allowing the temperature to rise above 5° . When half of the chloroformate had been introduced, a cold solution of sodium hydroxide (22g. in 30c.c. of water) was added at the same rate. Thirty minutes after the last addition the ether

layer was separated and the aqueous layer extracted with ether (200 c.c.). The combined ether layers were rapidly dried by shaking with potassium carbonate (8g.) in two portions. The ether was removed and the residue which consisted of isobutylurethane distilled at $110^{\circ}/30$ mm., n_D^{17} 1.4290 (67g.; 85%) (Found: N, 9.1. $C_7H_{15}O_2N$ requires N, 9.6%). To isobutylurethane (67g.) and ether (150c.c.) were added ice (46g.) and sodium nitrite (150g.) in cold water (230 c.c.). A solution of nitric acid (from concentrated acid - 100 c.c. - and ice - 150g. -) was added during 1 hour, with occasional shaking. The temperature was kept below 15° by the addition of ice. When the ethereal layer had become green, it was separated, washed with water and potassium carbonate solution, and dried (K_2CO_3); removal of the ether furnished N-nitrosoisobutylurethane (80g.) as a pink oil which was used without further purification for the next stage.

2-isoPropylcycloheptanone (XXXV). - A mixture of cyclohexanone (47g.), methanol (50c.c.), and sodium carbonate (1g.) was treated with N-nitrosoisobutylurethane (80g.) exactly as in the preparation of 4-isopropylcycloheptanone described above. Fractionation of the product yielded 2-isopropylcycloheptanone (23g.) b.p. $93-95^{\circ}/18$ m.m., n_D^{18} 1.4555 (Found: C, 77.4; H, 11.6. $C_{10}H_{18}O$ requires C, 77.9; H, 11.7%). The semicarbazone formed plates from aqueous ethanol m.p.

175-176° (Found: C,62.5; H,10.3, N,19.95. $C_{11}H_{21}ON_3$ requires C,62.6; H,9.95; N,19.9%).

3-Ethoxy-3-isopropylcycloheptane-1:2-dione (XXXVI). -

To a boiling solution of 2-isopropylcycloheptanone (23g.) in ethanol (98%; 30 c.c.) was added dropwise during 2 hours a solution of selenium dioxide (18g.) in ethanol (98%; 110 c.c.). After 6 hours' heating under reflux, the mixture was set aside overnight and worked up as described above. Fractionation yielded the ethoxy-dione (XXXVI) (13g.) as a pale yellow oil, b.p. 130°/22 mm., n_D^{15} 1.4785 (Found: C,68.3, 67.5; H,9.2,9.2; OEt,20.7. $C_{12}H_{20}O_3$ requires C,67.9; H,9.5; OEt,21.2%). The mono-2:4-dinitrophenylhydrazone after chromatography in benzene over alumina, crystallised from ethanol in orange rosettes m.p.118° (Found: N,15.0. $C_{18}H_{24}O_6N_4$ requires N,14.3%).

Sodium Bromo- α -thujaplicin (XXXVII). A solution of the ethoxy-dione (XXXVI) (10g.) in glacial acetic acid (10 c.c.) was treated with bromine (20g.) and worked up as described above. The sodium bromo- α -thujaplicin (2.1g.) thus obtained crystallised from water in yellow nodules dec.300° (Found: C,40.6; H,4.25. $C_{10}H_{10}O_2$ Br Na,1.5 H₂O requires C,40.5; H,4.4%). Heating the sesquihydrate at 150° in vacuo for 6 hours only removed half a molecule of water to leave the monohydrate (Found: C,42.6; H,4.1. $C_{10}H_{10}O_2$ Br Na,H₂O

requires C, 42.45; H, 4.25%).

α -Thujaplicin (VI). - A solution of the above sodium salt (400 mg.) in methanol (25 c.c.) was stirred under hydrogen in presence of palladium/charcoal (10%; 100 mg.) until 1 mole of hydrogen had been absorbed. Removal of catalyst and solvent followed by extraction with boiling light petroleum (b.p. 40-60°) and evaporation gave an oil which distilled at 80° (bath temp.)/0.001 mm. The distillate solidified to a feathery, frost-like mass on being cooled to 0°; crystallisation from a small volume of light petroleum (b.p. 40-60°) at -15° gave prisms of α -thujaplicin (78 mg.), m.p. 26-27°, undepressed on admixture with an authentic specimen (m.p. 27-28.5°). The oily methyl ether gave a poor yield of the picrate, yellow needles, m.p. 110° (dec.) (from ethanol) (Found: N, 10.6. $C_{17}H_{17}O_9N_3$ requires N, 10.3%). As the mother liquors gave much unchanged methyl ether, it is probable that only one of the two expected α -thujaplicin methyl ethers forms a picrate.

TROPOLONE METHYL ETHER PICRATE.

Tropolone (5 mg.) was treated with ethereal diazomethane (2%; 1 c.c.) when effervescence had ceased, the solvent was removed and the resultant oil treated with a saturated solution of picric acid in alcohol. The precipitated picrate was crystallised from methanol. It formed yellow needles

m.p. 119-120° (Found: C, 45.8; H, 3.25. $C_8H_8O_2$, $C_6H_3O_7N_3$ requires C, 46.05, H, 3.05%).

TROPOLONE DIPHENYLMETHYL ETHER.

Tropolone (100 mg.) in benzene (2 c.c.) was treated with a solution of diphenyldiazomethane in benzene (10%; 3 c.c.) (cf. Hardegger, El Heweihi and Robinet⁸⁶) and the solution heated on the steam bath until the red colour disappeared. Evaporation of the solvent afforded the ether as a yellow solid m.p. 120-130°. Recrystallisation from light petroleum (b.p. 100-120°) afforded tropolone diphenylmethyl ether as rosettes m.p. 142-143° (Found: C, 83.4; H, 5.6; $C_{20}H_{16}O_2$ requires C, 83.4; H, 5.6%).

SOME REACTIONS OF TROPOLONE.Attempted iso Propylation of Tropolone. -

(a) To a solution of tropolone (100 mg.) in isopropyl chloride (1 c.c.) was added aluminium chloride (20 mg.) and the mixture was kept at room temperature for 24 hours. The resulting red precipitate (25 mg.) m.p. $> 300^{\circ}$ was collected and boiled with dilute hydrochloric acid until dissolution was complete. Extraction with ether gave tropolone (10 mg.) m.p. 49° . Evaporation of the original mother liquor furnished a further quantity of tropolone.

(b) To a mixture of tetrachloroethane (3 c.c.), iso-propyl alcohol (80 mg.) and aluminium chloride (1 g.) heated to 80° was added dropwise a solution of tropolone methyl ether (150 mg.) in tetrachloroethane (1 c.c.). After two hours at 80° , the mixture was kept at room temperature for 16 hours. After being hydrolysed with dilute hydrochloric acid, the reaction mixture was basified with sodium carbonate solution and the tetrachloroethane removed in steam. Acidification with concentrated hydrochloric acid followed by isolation with ether afforded tropolone (110 mg.).

Attempted C-Acetylation of Tropolone. -

(a) To an ice-cold mixture of tetrachloroethane, (3 c.c.) acetyl chloride (205 mg.), and aluminium chloride (600 mg.) was added tropolone (240 mg.). The mixture was kept at 0°

for two hours, at 20° for 16 hours and then decomposed by pouring into 6N-hydrochloric acid (10 c.c.). Extraction with ether, shaking out with sodium hydroxide solution, re-acidification and isolation with ether gave only tropolone (150 mg.).

(b) A mixture of tropolone (180 mg.), stannic chloride (260 mg.) and acetic anhydride (102 mg.) was allowed to stand at room temperature for 45 minutes and the reaction product worked up as in (a). Tropolone (110 mg.) was again the sole isolable material.

(c) A mixture of tropolone (200 mg.) acetic anhydride (200 mg.) and syrupy phosphoric acid (40 mg.) was heated at 110° for 3 hours. Water was cautiously added to the cooled solution and the product isolated with ether. Evaporation gave a residue which sublimed under reduced pressure to yield (i) tropolone (110 mg.) and (ii) an oil b.p. 80° (bath temp.)/10 mm. The latter soon solidified and was crystallised from light petroleum (b.p. 60-80°) to give O-acetyl-tropolone (XXXVIII) (60 mg.) as prisms m.p. 67° (Kofler block) (Found: C, 65.1; H, 5.0. Calculated for $C_9H_8O_3$: C, 65.6; H, 4.9%).

(d) Tropolone (150 mg.) was dissolved in glacial acetic acid (1 c.c.) and borontrifluoride-ether (1 c.c.) added; an immediate precipitation occurred. The mixture was heated

in a sealed tube at 70° for 5 hours, the tube cooled and the crystalline precipitate filtered off. Crystallisation from acetic acid or light petroleum (b.p. 100-120°) yielded the complex (XXXIX) (115 mg.) as large plates m.p. 151° (Found: C, 49.7; H, 3.3. $C_7H_5O_2 \cdot BF_2$ requires C, 49.5; H, 2.95%). The complex gave no colouration with ferric chloride but was hydrolysed to tropolone with boiling dilute sulphuric acid. The complex was also formed in the absence of glacial acetic acid.

Attempted Gatterman Reaction. -

Dry hydrogen chloride was passed into a mixture of tropolone (240 mg.) dry ether (15 c.c.), zinc cyanide (300 mg.) and sodium chloride (6 mg.) until saturation was complete. The resulting white solid was separated from the ether by decantation and dissolved in boiling water. After cooling, extraction with ether furnished only tropolone (200 mg.)

Attempted Chloromethylation. -

A mixture of tropolone (100 mg.), glacial acetic acid (3 c.c.) and chloromethyl methyl ether (100 mg.) was shaken for two hours at room temperature. The solution deposited fine white needles of tropolone hydrochloride (80 mg.) m.p. 120-125° (dec.); these slowly passed into tropolone. A similar result was obtained when paraformaldehyde-hydrogen

chloride was employed.

Attempted Kolbe-Schmidt Reactions. -

(a) Sodium tropolonate (500 mg.) was dried in a stream of nitrogen at 150° for 3 hours; the temperature was then raised to 180° and dry carbon dioxide passed over the salt for 6 hours. The resulting sodium salt furnished only tropolone on acidification. Reaction temperatures ranging from 180-260° gave similar results.

(b) Powdered sodium (50 mg.) in Xylene (10 c.c.) was treated with tropolone (240 mg.) and the mixture heated under reflux for 5 hours while carbon dioxide was bubbled in. Acidification of the resulting yellow sodium salt gave a quantitative recovery of the tropolone.

(c) A mixture of tropolone (200 mg.) anhydrous potassium carbonate (600 mg.) and solid carbon dioxide (8 g.) in a pyrex tube was heated to 180° in an autoclave for 5 hours. Acidification of the product again led to quantitative regeneration of tropolone.

Reimer-Tiemann Reaction. -

A mixture of tropolone (500 mg.) water (12 c.c.) and 10-N sodium hydroxide solution (4 c.c.) was warmed until solution was complete and chloroform (0.5 c.c.) was then added. The resulting deep red solution was heated by steam and a further quantity (1 c.c.) of chloroform added during

one hour. After a further 2 hours' heating the cooled mixture was acidified to Congo red with dilute sulphuric acid and an amorphous brown precipitate (50 mg.) m.p. $> 300^{\circ}$ filtered off. The filtrate was continuously extracted with ether for 24 hours. Drying (Na_2SO_4) and removal of solvent furnished a yellow gum which, on being fractionally sublimed under reduced pressure, gave tropolone (100-200 mg.) subliming at $60-80^{\circ}$ (bath temp.)/18 mm. and a yellow solid (20-50 mg.) subliming at $100-120^{\circ}$ (bath temp.)/18 mm. Repeated crystallisation of this latter product from ethanol gave γ -formyltropolone (XLII) as bright yellow needles m.p. 181° (dec.) which slowly decomposed on exposure to light (Found: C, 64.0; H, 4.2. $\text{C}_8\text{H}_6\text{O}_3$ requires C, 64.0; H, 4.0%). The 2:4-dinitrophenylhydrazone crystallised in red prisms m.p. 226° (dec.) from ethyl acetate.

Tropolone- γ -carboxylic acid (XLIII). -

(a) γ -Formyltropolone (24 mg.) was added to a suspension of freshly precipitated silver oxide (68 mg.) in 4N sodium hydroxide solution (0.5 c.c.) and the mixture heated by steam for 30 minutes. The cooled filtered solution was acidified with dilute sulphuric acid and extracted continuously with ether for 16 hours. Evaporation gave a yellow solid (12 mg.) m.p. $250-270^{\circ}$ which on crystallisation from glacial acetic acid afforded tropolone- γ -carboxylic acid

as fine yellow needles m.p. 288° (dec.; sealed tube) undepressed on admixture with an authentic specimen m.p. 288° (Cook, Loudon and Steel⁵⁷). When crystallised from water the acid formed a monohydrate, yellow prisms m.p. $222-225^{\circ}$ (Found: C, 52.1; H, 4.4. $C_8H_6O_4 \cdot H_2O$ requires C, 51.65; H, 4.0%). Treatment of the acid with ethereal diazomethane gave the corresponding methyl ether methyl ester (XLIV) which crystallised from benzene as fine white needles, m.p. and mixed m.p. 184.5° .

(b) A mixture of tropolone (100 mg.), potassium hydroxide (300 mg.), ethanol (0.5 c.c.), water (0.5 c.c.), and carbon tetrachloride (100 mg.) was heated at 100° in a sealed tube for 16 hours. Cooling and acidification followed by continuous ether extraction and fractional sublimation gave tropolone (60 mg.) and a pale yellow solid subliming at 180° (bath temp.)/0.4 mm. Crystallisation of this latter from water gave tropolone- γ -carboxylic acid hydrate (3 mg.) m.p. and mixed m.p. $222-225^{\circ}$.

Attempted Reaction with N-Methylformanilide. -

A mixture of tropolone (200 mg.), N-methylformanilide (550 mg.), and phosphorus oxychloride (500 mg.) was kept at room temperature for 16 hours. The product was poured into water and extracted with ether. The extract was shaken out with dilute sodium hydroxide solution (1%). Acidification

and ether extraction furnished tropolone (100 mg.). In one experiment evaporation of the alkali washed extract gave an oil possessing carbonyl activity which gave a 2:4-dinitrophenylhydrazone, scarlet needles, m.p. 206° from n-butanol having the composition of the derivative of a formyltropolone. (Found: C, 50.8; H, 3.0. $C_{14}H_{10}O_6N_4$ requires C, 50.9; H, 3.0%). This result could not be repeated however.

Reduction of Tropolone with Lithium Aluminium Hydride.

A solution of tropolone (900 mg.) in dry ether (5 c.c.) was added to a slurry of $LiAlH_4$ (1 g.) in ether (40 c.c.). The initial yellow precipitate rapidly dissolved. The mixture was heated under reflux for 30 minutes, cooled and decomposed with ice-cold dilute sulphuric acid. The initial yellow colour of the solution rapidly darkened to a deep red-brown; this could not be prevented either by working under nitrogen or by carrying out the decomposition with ice alone. Isolation with ether yielded a dark red gum which on distillation at $80-100^{\circ}/18$ mm. gave a pale yellow oil (100 mg.) and a brown resin (600 mg.). The oil afforded a bis-2:4-dinitrophenylhydrazone which after chromatography over alumina in benzene crystallised from the latter solvent in red prisms m.p. $183-185^{\circ}$ (Found: C, 47.5; H, 3.35; N, 23.15. $C_{19}H_{16}O_8N_8$ requires C, 47.1; H, 3.35; N, 23.15%). Light absorption in chloroform: λ max. 3560 A ($\epsilon = 36,500$);

λ infl. 3960 A ($\epsilon = 29,000$).

The bis-2:4-dinitrophenylhydrazone of cycloheptane -1:2-dione, after chromatographic purification (benzene-alumina) crystallised from benzene as red needles which contained benzene of crystallisation (Found: C, 53.8; H, 4.4; N, 20.1. $C_{19}H_{18}O_8N_8$, C_6H_6 requires C, 53.2; H, 4.3; N, 19.85%). Drying at $140^\circ/18$ mm. gave the solvent free compound m.p. 213° (Found: C, 47.55; H, 4.1; N, 22.65. $C_{19}H_{18}O_8N_8$ requires C, 46.9; H, 3.75; N, 23.0%). Light absorption in chloroform: λ max. 3520 A ($\epsilon = 34,000$); λ infl. 3900 A ($\epsilon = 27,500$).

Reduction of Tropolone Methyl Ether with Lithium Aluminium Hydride.

A solution in ether of anhydrous tropolone methyl ether (1 g.) was added to $LiAlH_4$ (1 g.) in ether (20 c.c.). After the initial vigorous reaction, heating was continued for 30 minutes and the reaction mixture then decomposed with ice. Ether extraction gave an oil smelling strongly of benzaldehyde. Treatment of the product with excess ethanolic 2:4-dinitrophenylhydrazine sulphate gave a derivative which was washed with water and dried. The product (0.9 g.; m.p. ca 200°) was purified by chromatography (benzene-alumina) to yield benzaldehyde 2:4-dinitrophenylhydrazone, m.p. 236° undepressed on admixture with an authentic sample. The filtrate from the preparation of the derivative was neutralised

with ammonia and well extracted with ether. Evaporation gave a minute amount of an oil which did not give a picrate or a hydrochloride.

The Self-Condensation of cycloDecane-1:2-dione.

Melting points were determined on a Kofler block.

CycloDecan-1-ol-2-one. - This was prepared from diethyl sebacate by the method of Prelog, Frenkiel, Kobelt and Barman⁽⁸⁸⁾ in comparable yield. A higher boiling by-product b.p. 200-230°/0.1 mm. solidified on being triturated with methanol and crystallised from this solvent in needles m.p. 125-126°. Analysis showed it to be the bis-acyloin cycloecicosane-1:11-diol-2:12-dione derived from the condensation of two molecules of diethyl sebacate (Found: C, 70.45; H, 10.25. M.W. (ebull. in benzene) 351. $C_{20}H_{36}O_4$ requires C, 70.55; H, 10.65. M.W. 340)/cycloDecane-1:2-dione. - The oxidation procedure of Rigby⁽⁸⁷⁾ was used. A mixture of crude cyclodecan-1-ol-2-one (35 g.) bismuth oxide (35 g.) and acetic acid (150 c.c.) was stirred in a boiling water bath for 45 minutes. Bismuth compounds were then filtered off, the filtrate diluted with water and the dione extracted with light petroleum (b.p. 40-60°). Washing with water, drying and evaporation gave a low-melting solid; one crystallisation from a small volume of light petroleum (b.p. 40-60°) gave nearly pure cyclo-decane-1:2-dione (22 g.) as yellow prisms m.p. 41-43° (Prelog et al., loc. cit., give m.p. 44°).

Self-Condensation of cycloDecane-1:2-dione. - To a methanolic solution of sodium methoxide (from methanol, 50 c.c., and sodium, 2 g.) contained in a 100 c.c. flask was

added a solution of cyclodecane-1:2-dione (5.28 g.) in methanol (20 c.c.). The flask was then filled up to the stopper with methanol to exclude air. After 16 hours standing at room temperature, the resulting crystalline mass was filtered off, washed with methanol and water and dried (2.8 g.) This product (m.p. 242-248°) on being crystallised from a large volume of toluene gave the pure 2, 6:3, 5-bis (heptamethylene) cyclohexane-2:5-diol-1:4-dione (LII) as fine needles m.p. 255° (Found: C, 71.2; H, 9.4. M.W. (ebull. in benzene) 304. $C_{20}H_{32}O_4$ requires C, 71.4; H, 9.55%. M.W. 336). The substance was sparingly soluble in all the common organic solvents in the cold but slowly dissolved in hot dioxan, chloroform, toluene, pyridine and acetic acid. Heating the compound with potassium bisulphate at 200°, with phosphorus pentoxide in triethylamine-benzene, with phosphorus tribromide in toluene and with fused phthalic anhydride at 200° produced no change. It dissolved in warm concentrated sulphuric acid but was precipitated by water unchanged. Treatment with both boiling acetic anhydride and benzoyl chloride-pyridine left it unchanged. A blue melt obtained by fusion with toluene-p-sulphonic acid is under investigation.

The methanolic filtrate from the dimer was diluted with twice its volume of water and the turbid solution allowed to stand until crystallisation was complete. Filtration, washing

with water and drying gave the second product (LIV: 1.8g.) m.p. 150-158°. Crystallisation from light petroleum (b.p. 100-120°) furnished pure 2, 6: 3, 5-bis (heptamethylene) cyclo-hex-5-en-2-ol-1:4-dione as prismatic clusters m.p. 169-171° [Found: C, 75.7; H, 9.7. Microhydrogenation (Pd in acetic acid) 1.1 F. $C_{20}H_{30}O_3$ requires C, 75.45; H, 9.5% λ_{max} . (in ethanol) 2450 A ($\epsilon = 7,500$), λ_{infl} . 2520 A ($\epsilon = 7,250$)]. Treatment of this compound with the dehydrating agents mentioned above left it unchanged.

Sodium Bismuthate Oxidation of (LII). -

A. The dimer (LII; 1 g.) was dissolved in warm acetic acid (100 c.c.); phosphoric acid (8 c.c.; 3.3 M) and sodium bismuthate (AR; 4g.; 4 moles) were then added and the mixture stirred at 70-75° for 6 hours. The cooled reaction mixture was diluted with water (50 c.c.) and then shaken with three 250 c.c. portions of ether. A flocculent suspension in the ether was filtered and proved to be unchanged dimer (0.35 g.). The ether extract was well washed with water, dried ($MgSO_4$), and evaporated; residual acetic acid was removed by warming under reduced pressure. The resulting sticky solid was extracted with boiling light petroleum (b.p. 40-60°); evaporation of the extract gave a light yellow oil which solidified almost completely on standing. The solid was pressed on porous tile to remove

adhering oil and was then crystallised from a small volume of light petroleum (b.p. 40-60°) at 0° to furnish prismatic plates (80 mg.) m.p. 94-96°, undepressed on admixture with an authentic specimen of cyclooctadecane-1:10-dione (m.p. 96°).

B. The dimer (0.5 g.), sodium bismuthate (1 g.; 2 moles), acetic acid (10 c.c.) and phosphoric acid (2 c.c.) were shaken at 50° for 6 hours. On working up as in A the dimer (0.4 g.) was recovered unchanged together with an ethanol soluble product m.p. 125-128°, which crystallised from benzene in needles m.p. 128°. Analysis showed it to be cyclooctadecane-1:10-dione-2:11-dicarboxylic acid (LIII) (Found: C, 65.2; H, 8.6. $C_{20}H_{32}O_6$ requires C, 65.2; H, 8.75%). The acid was insoluble in cold but soluble in warm sodium bicarbonate solution. It showed no sign of decarboxylation on heating at 140° for 10 minutes.

Oxidation of the dimer with chromium trioxide in acetic acid at 80° furnished azelaic acid.

THE ATTEMPTED SYNTHESIS OF γ -TROPOLONE.

Cis-trans Quinitol was prepared by the catalytic hydrogenation of hydroquinone over Raney nickel in methanol solution at 150°/130 atmos. (cf. Owen and Robins ⁷⁴).

Quinitol Monobenzoate. - The method of Jones and Sondheimer (loc. cit.) was found to give a comparable yield. Quinitol (405 g.) was dissolved in chloroform (1250 c.c.; freed from alcohol by shaking with concentrated sulphuric acid) and dry pyridine (950 c.c.). A solution of benzoyl chloride (480 g.) in chloroform (1 litre) was added with stirring during 3 hours, the temperature being kept at 0-5° by external cooling. After standing overnight at room temperature the chloroform solution was freed from pyridine by washing with water (8 x 500 c.c.) and then with sulphuric acid (6N; 5 x 500 c.c.). Drying (Na_2SO_4) and removal of chloroform (bath temperature 80°/18 mm.) followed by fractionation of the residue gave the monobenzoate as a very viscous colourless oil b.p. 160-170°/0.6 mm. (400 g.). The residue solidified and consisted of the isomeric dibenzoates (m.p. 138-143°). / 4-Benzoyloxycyclohexanone (LXVII). - After Jones and Sondheimer ⁽⁷⁵⁾.

Chromium trioxide (50 g.) dissolved in a mixture of water (30 c.c.) and acetic acid (AR; 113 c.c.) was added to a stirred, cooled solution of the above monobenzoate (111 g.)

in acetic acid (190 c.c.) so that the temperature did not exceed 35°. On leaving overnight at room temperature, and adding ether (800 c.c.), the acetic acid was removed by washing with water and then 2N sodium hydroxide solution. Evaporation of the washed (H₂O) and dried (Na₂SO₄) ether layer gave 4-benzoyloxy-cyclohexanone (75 g.) m.p. 62° from ether-light petroleum (b.p. 40-60°) (lit. 63°, 62°).

4-Benzoyloxycycloheptanone (LXVIII). -

4-Benzoyloxycyclohexanone (LXVII) (50 g.) dissolved in methanol (150 c.c.) was treated drop-wise with N-nitrosomethylurethane (38 g.) in presence of powdered, anhydrous sodium carbonate (1 g.), the mixture being vigorously stirred and maintained at 25-30° by cooling in ice-water. After leaving overnight at room temperature, the filtered solution was evaporated and the residue distilled into three fractions - (a) b.p. 80-90°/0.4 mm. (5 g.); (b) b.p. 90-150°/0.4 mm. (9 g.); and (c) b.p. 150-151°/0.4 mm. (28 g.). Fractions (b) and (c) consisted mainly of 4-benzoyloxycycloheptanone b.p. 150-151°/0.4 mm., n_D^{15} 1.5321 (Found: C, 72.29; H, 7.23. C₁₄H₁₆O₃ requires C, 72.46; H, 6.90%). The 2:4-dinitrophenylhydrazone crystallised in orange prisms from n-butanol m.p. 178° (Found: C, 58.58; H, 4.50. C₂₀H₂₀O₆N₄ requires C, 58.38; H, 4.90%).

4-Hydroxycycloheptanone (LXIX). -

4-Benzoyloxycycloheptanone (15 g.) was heated under reflux with methanol (60 c.c.) containing sodium (0.2 g.) for 15 hours. Water (10 c.c.) was added to the cooled solution and carbon dioxide bubbled through the liquid until saturation was complete. The methanol was removed (steam bath) and the residue fractionated into (a) b.p. 60-80°/0.2 mm. (b) b.p. 80-90°/0.2 mm. and (c) b.p. 90-110°/0.2 mm.. (a) and (b) consisted mainly of methyl benzoate. (c) on redistillation had b.p. 95°/0.4 mm. (6 g.) n_D^{16} 1.4912 (Found: C, 65.42; H, 9.54. $C_7H_{12}O_2$ requires C, 65.62; H, 9.38%). As separation from methyl benzoate by distillation was very difficult, in later runs the crude mixture was shaken with water in which the hydroxyketone is very soluble and the ester removed by extraction with petroleum ether (b.p. 40-60°). Removal of water and distillation gave the pure hydroxyketone b.p. 95°/0.4 mm. The 2:4-dinitrophenylhydrazine formed yellow-orange prisms m.p. 137° from aqueous methanol (Found: C, 50.1; H, 5.12. $C_{13}H_{16}O_5N_4$ requires C, 50.6; H, 5.23%).

CycloHeptane-1:4-dione (LXX). - To the above hydroxyketone (LXIX) (3 g.) in water (10 c.c.) was added with stirring and ice-cooling, chromic acid (6 N solution in sulphuric acid; 12 c.c.) so that the temperature did not exceed 30°. The reaction was completed by allowing the mixture to stand over-

night at room temperature. Saturation with sodium chloride followed by continuous ether extraction yielded the dione b.p. $95^{\circ}/1 \text{ mm. } \frac{n_D^{15}}{D}$ 1.4822 (On microanalysis it was reported that the sample rapidly absorbed water as soon as it was weighed. Of 12 analyses performed two are reproduced here. The ready deliquescence of the compound explains the low carbon values. Found: C, 64.01, 63.0; H, 8.09, 7.50. $C_7H_{10}O_2$ requires C, 66.65; H, 7.99%). The bis-2:4-dinitro-phenylhydrazone formed orange needles m.p. 230° (dec.) from aqueous dioxan containing solvent of crystallisation after drying at $100^{\circ}/15 \text{ mm.}$ for 12 hours (Found: C, 48.1; H, 4.76. $C_{19}H_{18}O_8N_8$, $C_4H_8O_2$ requires C, 48.09; H, 4.56%). Chromatography in benzene over alumina and crystallisation from benzene yielded a sample m.p. 245° (dec.) from which the solvent could not be completely removed without decomposition of the compound (Found: C, 48.28; H, 3.71. $C_{19}H_{18}O_8N_8$ requires C, 46.9; H, 3.73%). Crystallisation of a sample from n-butanol gave orange needles m.p. 200° (dec.) (Found: N, 22.75. $C_{19}H_{18}O_8N_8$ requires N, 23.0%).

Attempted Bromination-Dehydrobromination of (LXX). -

(a) The dione (0.6 g.) was treated with bromine (2 mols.) in acetic acid (5 c.c.) at 0° . On leaving overnight at room temperature, heating at 100° for two hours and steam distilling, the residue was dissolved in ether and extracted with sodium

hydroxide solution. A brown amorphous solid m.p. 100-110° was obtained on acidification of the alkaline solution and recovery with ether, which defied attempts at purification. No recognisable material was obtained from the steam distillate.

(b) The diketone (1.0 g.) dissolved in acetic acid (10 c.c.) was treated at reflux temperature with bromine (2 mols.) in acetic acid. After 30 minutes hydrogen bromide was evolved and at the end of one hour the solvent was removed by heating the dark brown solution at 100°/15 mm. The resultant tar was extracted with boiling sodium bicarbonate solution which on acidification and ether extraction afforded a small amount (20 mg.) of an oil. Sublimation of this product at 50°/0.1 mm. yielded white needles of a bromo-compound m.p. 50°. Recrystallisation from light petroleum (b.p. 40-60°) did not change the melting point (Found: C, 31.98; H, 2.47. $C_7H_4O_2Br_2$ requires C, 30.0; H, 1.45%). Lack of material prevented further purification of this bromo-derivative.

(c) The dione (1.0 g.) was dissolved in a mixture of chloroform (5 c.c.) and carbon tetrachloride (5 c.c.). N-bromosuccinimide (2.8 g.; 2 mols.) was added and the mixture heated on the water bath. After five minutes a deep red colour developed. At the end of 30 minutes the colour

was suddenly discharged, a violent reaction took place, and hydrogen bromide was copiously evolved. The mixture was cooled, the succinimide removed by filtration and the solvent evaporated. The residue was heated at 100° for 3 hours to yield a black tar. Repeated extraction with carbon tetrachloride and washing of the extract with water followed by removal of acidic material by shaking with sodium hydroxide solution (2 N; 20 c.c.) afforded on acidification and ether extraction a yellow oil (200 mg.). When heated at 100° (bath temp.)/15 mm. a few milligrams of benzoic acid (m.p. and mixed m.p. 121°) sublimed from the product. The oil distilled at $100-120^{\circ}/15$ mm. but no analysis was possible due to insufficient material for fractional distillation.

Bromination of 4-Hydroxycycloheptanone (LXIX). -

To the hydroxyketone (1.9 g.) in boiling acetic acid (20 c.c.) was added dropwise bromine (1.95 c.c.; 2 moles) in acetic acid (8 c.c.). After 30 minutes' reflux, evolution of hydrogen bromide occurred. The acetic acid was removed in vacuo and residue extracted with boiling cyclohexane. Stout, colourless needles m.p. 86° crystallised from the cooled extract. Recrystallisation from cyclohexane afforded a compound m.p. 91° whose analysis indicated that of a tribromo derivative (Found: C, 22.0; H, 1.26. $C_7H_3O_2Br_3$ requires C, 23.45; H, 0.85%). Sublimation of this compound at 50° (bath temp.)/0.2 mm. yielded a dibromo-

derivative m.p. 85° whose analysis suggested either a hydroxydibromocycloheptatrienone (Found: C, 29.7; H, 2.2; Br, 57.6. $C_7H_4O_2Br_2$ requires C, 30.0; H, 1.45; Br, 57.1%) or a hydroxydibromocycloheptadienone ($C_7H_6O_2Br_2$ requires C, 29.8; H, 2.15; Br, 56.7%). Repetition of this experiment gave variable results, oils being frequently encountered.

Hydrogenolysis of the tribromo compound. -

The tribromide (300 mg.) and triethylamine (500 mg.) dissolved in ethanol (10 c.c.) were stirred under hydrogen in presence of palladised charcoal (10%; 50 mg.). Absorption of almost 3 mols. of hydrogen took place. Removal of solvent and catalyst left a pale yellow gum which on rubbing with cyclohexane deposited needles of benzoic acid (20 mg.) m.p. and mixed m.p. 121° . There was not sufficient of the residual oil (30 mg.) to distil fractionally for analysis.

Attempted Dehydrogenation of cycloHeptane-1:4-dione (LXX).

(a) The diketone (1 g.) dissolved in boiling trichlorobenzene (15 c.c.) was treated with palladised charcoal (10%; 0.9 g.) in an atmosphere of nitrogen and heating continued for 8 hours. The catalyst was removed by filtration and the trichlorobenzene extracted with potassium hydroxide solution (20%; 30 c.c.) On acidification and recovery with ether there was obtained an oil, presumably the starting ketone, b.p. $100-120^{\circ}/18$ mm. which gave a yellow precipitate with ethanolic 2:4-dinitrophenylhydrazine sulphate.

(b)

(b) The diketone (1 g.) was refluxed (bath temp. 200°) with palladium-charcoal catalyst (10%; 150 mg.) for 6 hours. The starting material was recovered almost quantitatively.

(c) When the diketone (2.5 g.) was distilled at 18 mm. through a 9-inch column of palladised or platinised charcoal (10%) on glass wool heated to temperatures ranging from $280-330^{\circ}$ it was recovered without change either in refractive index or in m.p. of its 2:4-dinitrophenylhydrazone.

(d) With Selenium Dioxide. - To a refluxing solution of the dione (0.5 g.) in acetic acid (5 c.c.) was added selenium dioxide (0.22 g.) in acetic acid (7 c.c.). After one hour the cooled, filtered solution was treated with water and extracted with ether. Evaporation of the dried (Na_2SO_4) extract furnished, after sublimation of the residue at 200° (bath temp.)/0.2 mm., tiny, white needles (2 mg.) m.p. 270° (dec.) giving an intense green colour with ferric chloride solution.

(e) With Iodine. - The dione (0.3 g.) was heated to reflux (metal bath temp. 200°) and one crystal of iodine added. The mixture became yellow in colour. After 20 minutes the residue was heated at $180^{\circ}/18$ mm. The oil which distilled had the same refractive index as the starting material and gave the identical 2:4-dinitrophenylhydrazone but the small (gummy) residue gave no carbonyl reactions and possessed a faintly phenolic smell.

(f) The dione (1.0 g.) was boiled in nitrobenzene (5 c.c.) with a crystal of iodine for $2\frac{1}{2}$ hours. Sodium hydroxide solution (2N; 30 c.c.) was added and the nitrobenzene removed in steam. Acidification of the residue and continuous ether extraction afforded a deep red gum from which was isolated by distilling at $100-120^{\circ}/0.4$ mm. a yellow oil (ca. 100 mg.) giving no precipitate with ethanolic 2:4-dinitrophenylhydrazine sulphate. Attempts to prepare a picrate, hydrochloride and diphenylmethyl ether were unsuccessful.

1:7-Bisdiazoheptane-2:6-dione (LXXV). -

Glutaryl chloride (5 g.) in benzene (20 c.c.) was added slowly with swirling and ice cooling to ethereal diazomethane (from 30 g. of N-nitrosomethylurea) and the mixture left overnight. Removal of ether at $30^{\circ}/18$ mm. left the diazoketone as a bright yellow solid (3.5 g.) m.p. 50° . Crystallisation from benzene-light petroleum (b.p. $60-80^{\circ}$) gave yellow plates m.p. 55° (dec.) (Found: C, 46.7; H, 4.82. $C_7H_8O_2N_4$ requires C, 46.67; H, 4.44%).

Reaction with cupric oxide - Cyclohept-2-ene-1:4-dione (LXXVI). -

The above diazoketone (2 g.) in benzene (20 c.c.) was added to cupric oxide (2 g.) in light petroleum (b.p. $60-80^{\circ}$; 80 c.c.) with efficient stirring. The mixture was heated on the water bath until evolution of nitrogen was complete.

Filtration, followed by evaporation of the solvent furnished an oil b.p. $90^{\circ}/0.4$ mm. (0.5 g.). The bi-2:4-dinitrophenyl-hydrazone after chromatography in benzene over alumina and crystallisation from benzene-light petroleum (b.p. $40-60^{\circ}$) formed red prisms m.p. 110° (Found: N, 22.8. $C_{19}H_{16}O_8N_8$ requires N, 23.1%).

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PART II

THE SYNTHESIS OF DIMETHYLPHENANTHRENE

S U M M A R Y

PART II.

4:5-Dimethylphenanthrene has been prepared from pyrene by a series of smooth reactions. Ozonolysis of pyrene gave 4-formylphenanthrene-5-carboxylic acid which was reduced to 4:5-bis-hydroxymethylphenanthrene. Replacement of the hydroxyl groups with bromine followed by the formation of phenanthrene -4:5-diisothiocoronium dibromide led to the production of 4:5-dimethylphenanthrene. The ultra-violet absorption data of the hydrocarbon and of its intermediates are discussed.

I N D E X

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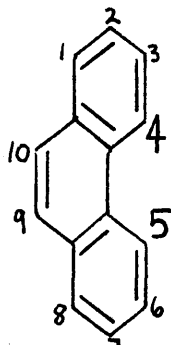
PART II.

SYNTHESIS OF DIMETHYLPHENANTHRENE.

Theoretical	1
Experimental	15

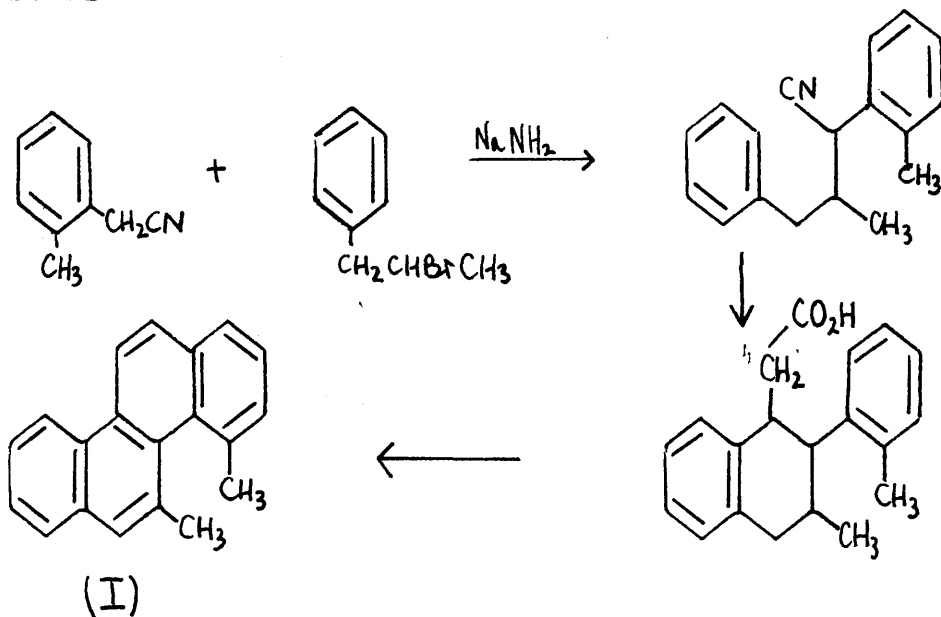
THE SYNTHESIS OF 4:5-DIMETHYLPHENANTHRENE

Interest in phenanthrene derivatives with methyl groups in the 4- and 5- positions arises from the possibility of steric hindrance in such compounds, for the relatively large methyl groups cannot be accommodated at positions



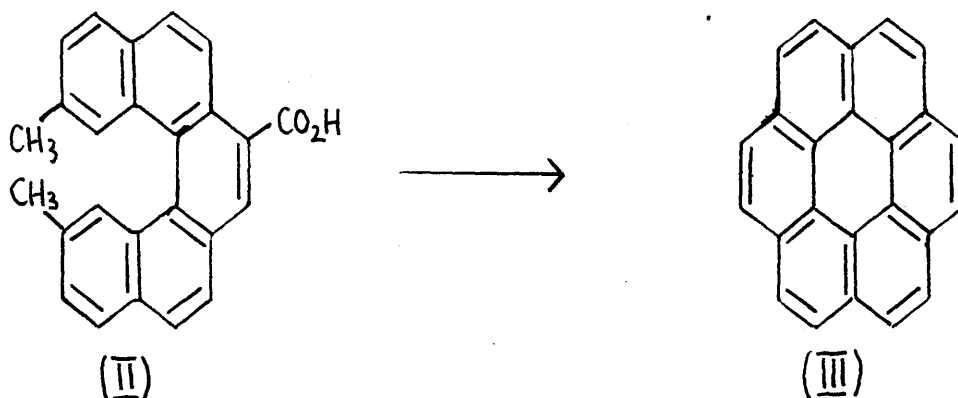
4 and 5 without overcrowding. That such compounds were capable of existence was demonstrated by Newman⁽¹⁾ who prepared the analogous 6:7-dimethylchrysene

(I) by the method outlined below and at the same time drew attention to the occurrence of similar systems

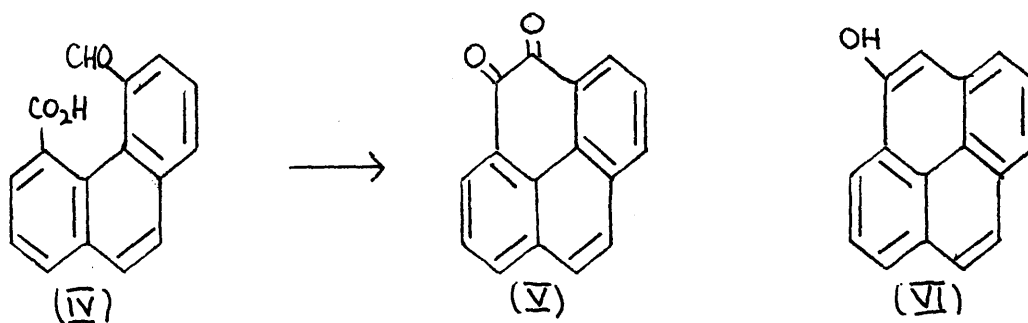


in 2:2'-dimethyl-meso-benzobianthrene⁽²⁾ and 2:2'-dimethyl-meso-naphthodianthrene⁽³⁾ where, however, the strain caused by the proximity of the methyl groups may be distributed more

easily throughout the large ring system. A somewhat similar situation obtains in the intermediate (II) in Newman's coronene synthesis ⁽⁴⁾ which readily loses six hydrogen atoms

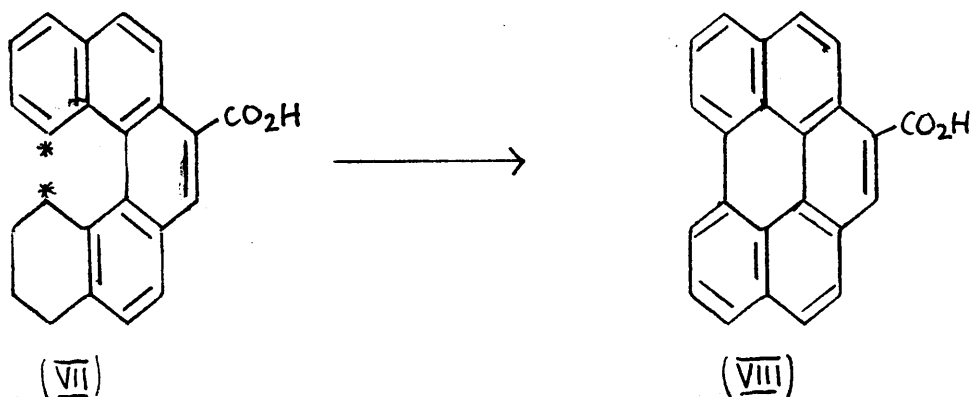


and decarboxylates to yield coronene (III). Another example of this steric effect on chemical behaviour is the ready conversion of 4-formylphenanthrene-5-carboxylic acid (IV) obtained by ozonisation of pyrene ⁽⁵⁾ back into derivatives of pyrene. Thus, treatment with alcoholic potash or potassium cyanide gives 1:2-pyrenequinone (V) whereas hydrazine hydrate gives 1-hydroxypyrene (VI).



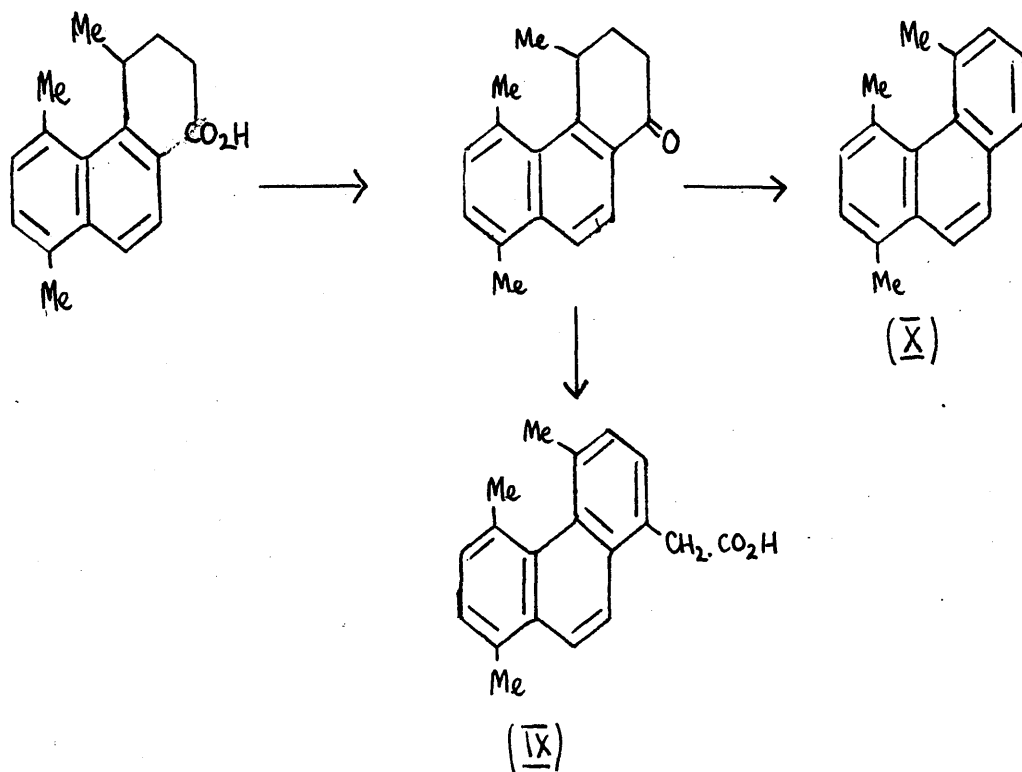
A similar example is provided by tetrahydro-3:4:5:6-dibenzophenanthrene carboxylic acid (VII) in which the hydrogen

atoms at the two starred positions interfere with each other.⁽⁶⁾
 Dehydrogenation takes place with the loss of six hydrogen atoms to yield the 1:12-benzoperylene carboxylic acid (VIII).

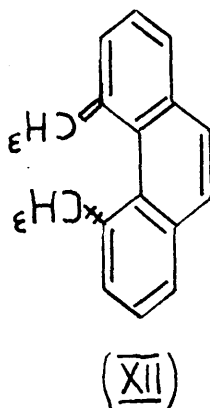
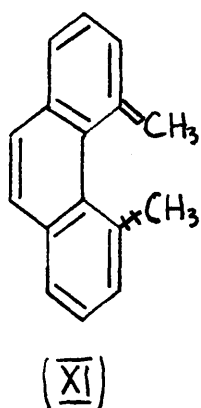


Newman^(6,7) considered three alternatives for the accommodation of two methyl groups at the 4:5-positions in phenanthrene as follows:-

(1) the methyl groups lie bent away from each other but in the same plane as the aromatic rings, (2) the aromatic ring system is distorted in some way and (3) the methyl groups lie bent out of the plane of the phenanthrene nucleus. The first possibility was excluded by the synthesis and optical resolution of 4:5:8-trimethyl-1-phenanthrylacetic acid (IX) by Newman and Hussey⁽⁷⁾ for condition (1) requires a planar molecule. 1:4:5-trimethylphenanthrene (X) was also prepared as indicated below and the ultra-violet absorption curves of (IX) and (X) were compared with that of phenanthrene which they resembled too closely for condition (2) to be satisfied. The third possibility accounts for the optical



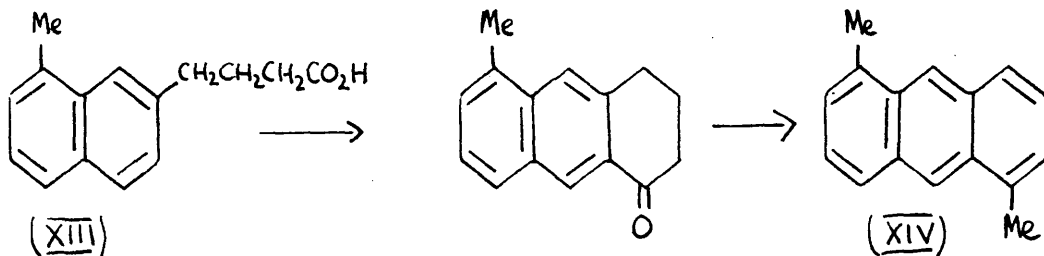
activity of (IX) in which the methyl groups in the 4 and 5 positions are on alternate sides of the phenanthrene nucleus. Newman suggested the term "optical isomerism of the 4,5 phenanthrene type" to describe this isomerism. The condition for optical activity is that there are two groups in the 4 and 5 positions which have effective volumes large enough to prevent rapid slipping past a position of coplanarity with the aromatic plane. The optical antipodes of 4:5-dimethylphenanthrene (XI and XII) when drawn or constructed in model form can be seen to be non-superposable mirror images. It was desirable, then, to prepare the hydrocarbon (XI) firstly to prove it capable of existence, for several projected



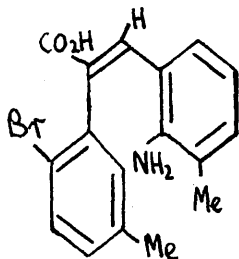
□ above } plane of paper
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syntheses had not met with success, and secondly in order to examine the steric effect of 4:5-substitution on the fine structure of the phenanthrene nucleus.

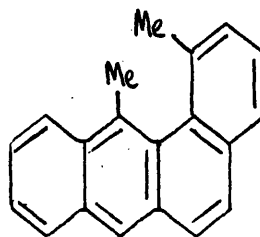
In an attempt to prepare 4:5-dimethylphenanthrene in 1934, Haworth and Sheldrick⁽⁸⁾ cyclised γ -(2-methyl-8-naphthyl) butyric acid (XIII) but obtained the anthracene instead of the desired phenanthrene structure. Treatment with methyl magnesium iodide followed by dehydrogenation afforded 1:5-dimethylantracene (XIV).



Another approach via the Pschorr ring closure reaction on α -(2'-bromo-5'-methylphenyl)-2-amino-3-methylcinnamic acid (XV) by Lewis and Elderfield⁽⁹⁾ proved impracticable.



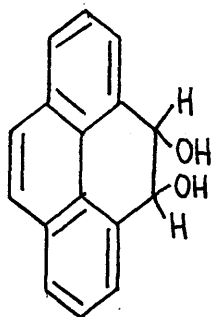
(XV)



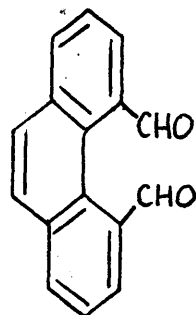
(XVI)

A fruitless attempt to prepare 1'-9-dimethyl-1:2-benzanthracene (XVI) a structure analogous to 4:5-dimethylphenanthrene has been reported by Fieser and Seligman.⁽¹⁰⁾

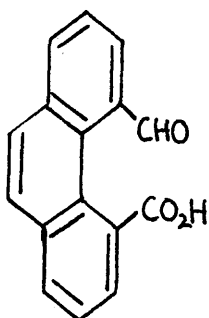
Campbell⁽¹¹⁾ treated pyrene with osmium tetroxide-pyridine to obtain 1:2-dihydro-1':2'-dihydroxypyrene (XVII) previously described by Criegee.⁽¹²⁾ Oxidation of (XVII) with lead tetraacetate by Criegee's method⁽¹³⁾ afforded a compound believed to be 4:5-diformylphenanthrene (XVIII). All attempts to reduce this compound by Huang-Minlon and Clemmensen procedures were unsuccessful. The same author⁽¹¹⁾ then made use of the facile production of 4-formyl-phenanthrene-5-carboxylic acid (XIX) from the ozonolysis of pyrene which had been studied by Vollman et al.^(5,14) Efforts to reduce the aldehyde group of (XIX) by Wolff-Kishner and Clemmensen methods, however, resulted only in the formation of 1-hydroxypyrene (XX).



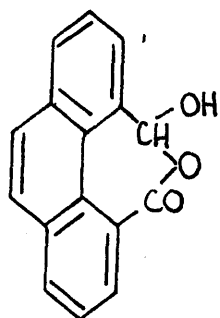
(XVII)



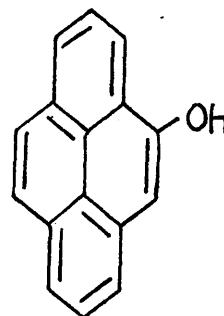
(XVIII)



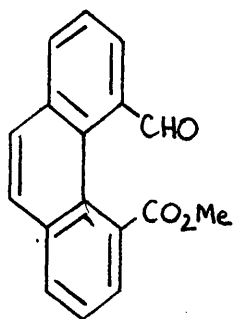
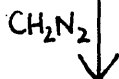
A



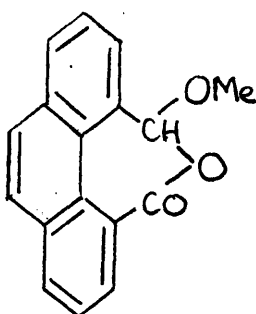
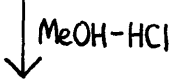
B



(XX)



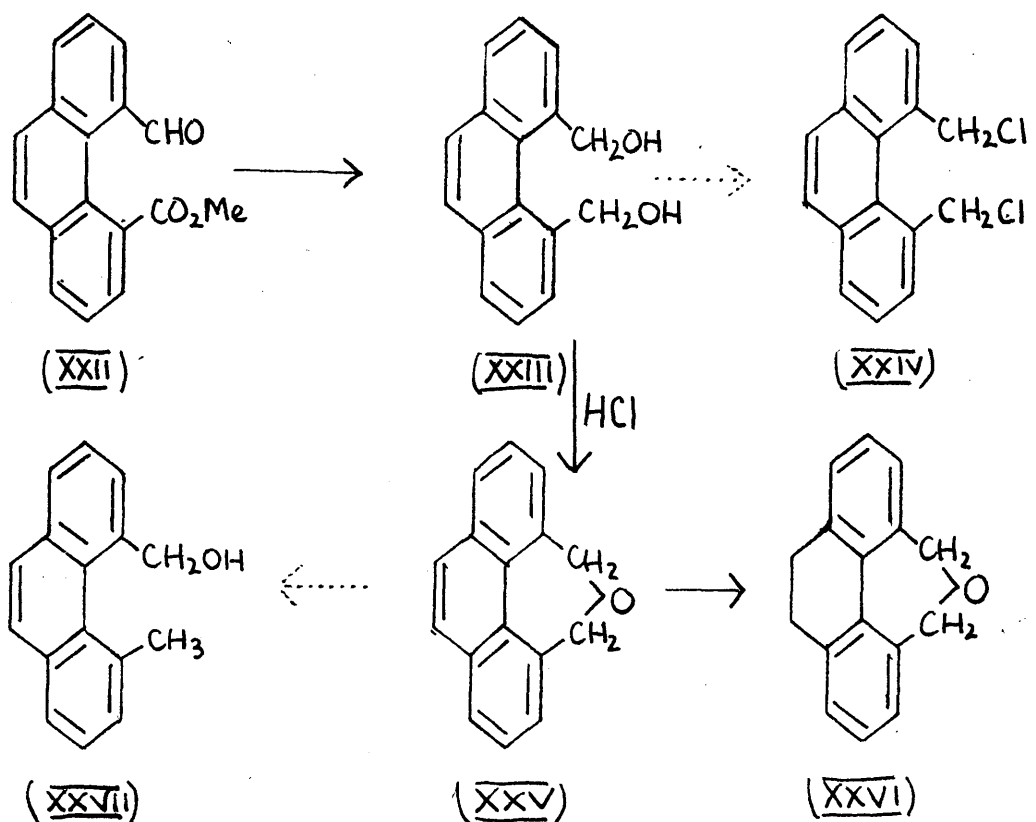
(XXII)



(XXI)

The aldehydo-acid (XIX) was found to give two methyl esters.
Treatment with methanol and hydrogen chloride yielded a

compound m.p. 176-177°, while the action of ethereal diazomethane furnished a compound m.p. 113-114°. Since these two products were isomeric (as indicated by analysis) it was assumed by Campbell that the treatment with methanol-HCl had resulted in the formation of the Ψ -ester (XXI) corresponding to the enol form of the acid (XIXB). A precedent for this assumption was found in the formation of methoxy- and acetoxy-lactones from β -keto-acids e.g. *o*-benzoylbenzoic acid described by Newman et al.⁽¹⁵⁾ The product obtained from diazomethane treatment was thus formulated as the normal methyl ester (XXII). Reaction of this latter ester with lithium aluminium hydride^(d.16) gave an excellent yield of 4:5-bishydroxymethylphenanthrene (XXIII). Reaction of this latter ester with HCl gave an excellent yield of 4:5-bis(chloromethyl)phenanthrene (XXIV). Reaction of XXIV with HCl gave 4:5-bis(hydroxymethyl)phenanthrene (XXV). Reaction of XXV with HCl gave 4:5-bis(methoxymethyl)phenanthrene (XXVI). Reaction of XXVI with HCl gave 4:5-bis(methyl)phenanthrene (XXVII).



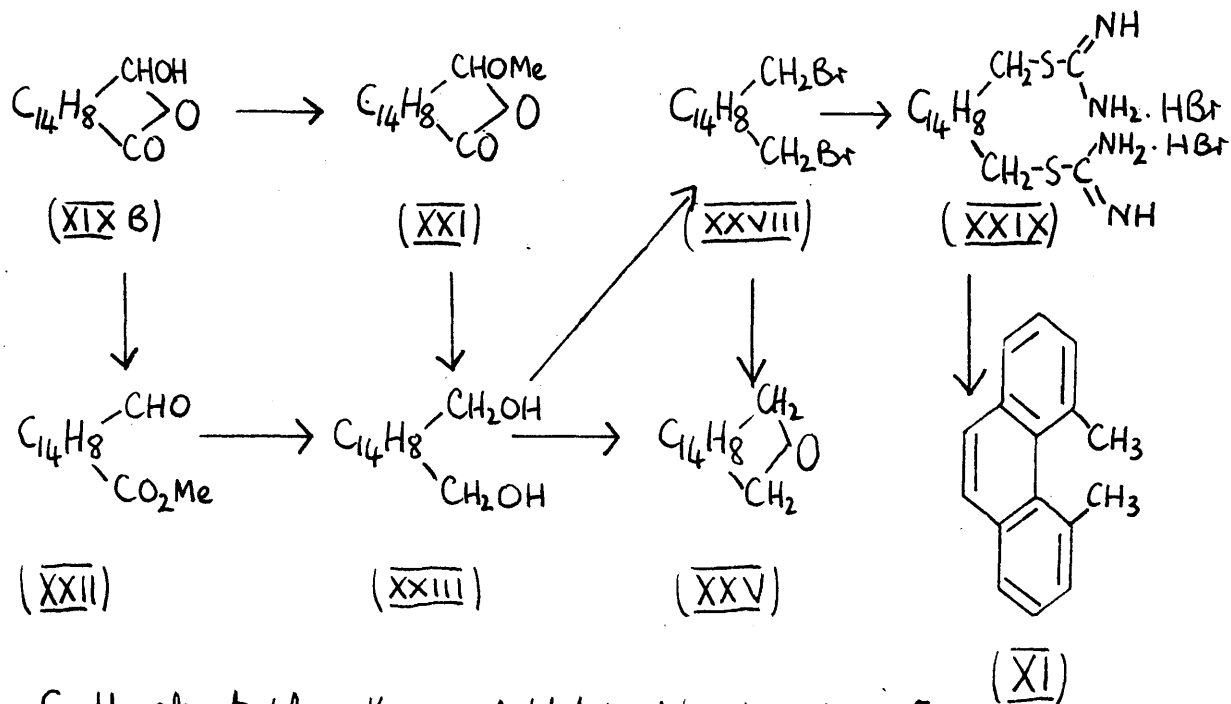
When the diol (XXIII) was reacted with hydrochloric acid in benzene solution, instead of the expected bischloromethyl compound (XXIV), the cyclic ether (XXV) was produced. Hydrogenation of this latter compound afforded the 9:10-dihydrophenanthrene epoxide (XXVI) rather than the hydrogenolysis product (XXVII). It was at this stage that the present author commenced work on the problem.

4-Formylphenanthrene-5-carboxylic acid (XIX) was prepared in improved yield by carrying out the ozonisation of pyrene in carbon tetrachloride solution rather than in acetic acid suspension, ^(cf 5) the precipitated ozonide thus being protected from further ozonisation. The acid showed no carbonyl reactivity and is best represented by the lactol formula (XIXB). The ψ -ester (XXI) gave no precipitate with ethanolic 2:4-dinitrophenylhydrazine sulphate whilst the isomeric methyl ester (XXII) gave the required 2:4-dinitrophenylhydrazone. These observations confirm Campbell's postulation of the structures of the acid and of its esters.

Reduction of either of the methyl esters with lithium aluminium hydride yielded 4:5-bishydroxymethylphenanthrene (XXIII). Treatment of this latter diol with phosphorus tribromide in benzene solution afforded an excellent yield of 4:5-bisbromomethylphenanthrene (XXVIII). It was hoped to reduce this compound directly to the required hydrocarbon,

but hydrogenation over palladised strontium carbonate catalyst led to the cyclic ether (XXV). This surprising result was again obtained when the bisbromomethyl compound was treated with lithium aluminium hydride. The formation of the cyclic ether (XXV) by these two reactions seems explicable only on the grounds of hydrolysis to the diol (XXIII) followed by dehydration, although rigorous measures were taken to exclude moisture in all of the experiments. That the dehydration of (XXIII) to (XXV) takes place readily had been demonstrated by Campbell when the epoxide was formed to the exclusion of the chloromethyl derivative (XXIV).

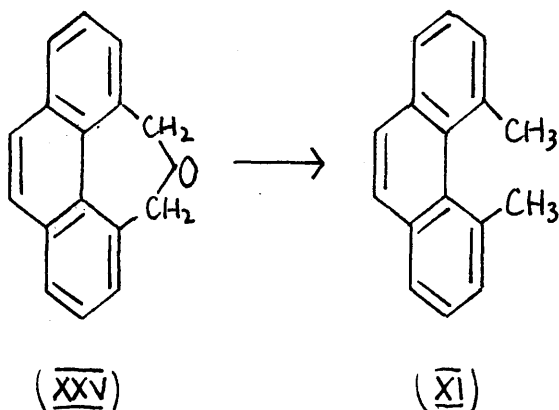
Accordingly, the bisbromomethyl compound (XXVIII) was treated with thiourea in acetone solution. Quantitative precipitation



C_{14}H_8 refers to phenanthrene substituted at positions 4 and 5

of the almost pure 4:5-di-isothiuronium dibromide (XXIX) took place. This compound underwent smooth hydrogenolysis with Raney nickel to give the required 4:5-dimethyl-phenanthrene (XI). The yields throughout are of the order of 80%. The hydrocarbon was characterised by formation of a picrate and a 2:4:7- trinitrofluorenone complex and by examination of its ultra-violet absorption spectrum.

The work was in its final stages⁽¹⁷⁾ at the time of the publication of the paper by Newman and Whitehouse⁽¹⁸⁾ who prepared 4:5-dimethylphenanthrene from the cyclic ether (XXV) in 17% yield by reductive fission of the latter compound at 165° in presence of phosphorus and hydriodic acid. The ether was prepared from the bishydroxymethyl derivative (XXIII) and the American authors observed how readily this dehydration occurred even in presence of traces of acid. The reaction conditions required for the production of the hydrocarbon (XI) from (XXV) were found to be extremely



critical and from the preparative point of view it would seem that the mild reaction conditions employed in our case lead to a smoother overall conversion of the diol to the hydrocarbon. The physical data of our hydrocarbon and of the intermediates in the synthesis are in good agreement with those of the American workers.

The ultra-violet absorption data (in ethanol) for the 4:5-disubstituted phenanthrenes were kindly determined by Dr. E. A. Braude and the results are tabulated below.

Compound	$\lambda_{\max.}, \text{A}$	ϵ	Compound	$\lambda_{\max.}, \text{A}$	ϵ
(XIXB)	2510	34,000	(XXIII)	2580	55,000
	2580	34,000		2920	9,000
	2650	34,000		3010	11,000
	<u>2760</u>	30,000		3120	11,000
	3480	1,500	(XXV)	2580	52,000
3650	1,500	2810		12,000	
(XXI)	2510	30,500		2910	10,000
	2580	33,000	3010	10,000	
	2670	30,500	(XI)	2580	38,000
	3460	1,000		2910	8,000
3640	1,000	3020		11,500	
		3140		11,500	
(XXII)	2720	25,000	(XXIX)	2700	36,000
	2800	24,000		<u>2770</u>	32,000
	<u>3560</u>	1,500		<u>3040</u>	10,000
(XXVIII)	<u>2600</u>	30,000			
	<u>2700</u>	34,000			
	2800	30,500			
	<u>3010</u>	13,000			
	<u>3130</u>	10,000			

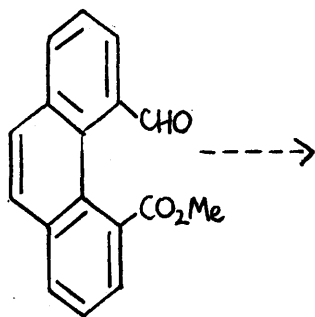
(Underlined wavelengths refer to inflections).

The spectra fall into two groups. The first, comprising the aldehydo-acid (XIXB), the ψ -ester (XXI), the bis-hydroxymethyl compound (XXIII), the cyclic ether (XXV), and 4:5-dimethylphenanthrene itself (XI), consists of absorption curves which are definitely "phenanthrenoid" in character, although some of the fine structure existing in the phenanthrene curve is absent. This may be taken as an indication that 4:5-substitution in these compounds has not affected the planarity and hence the resonance of the phenanthrene nucleus. The second group, containing the methyl ester (XXII), the bisbromomethyl compound (XXVIII), and the di-iso-thiouronium dibromide (XXIX) exhibits a single region of maximal absorption with practically no fine structure. This would seem to indicate that in these three compounds with very bulky substituents at positions 4 and 5 there is considerable distortion of the phenanthrene nucleus with consequent steric inhibition of resonance.

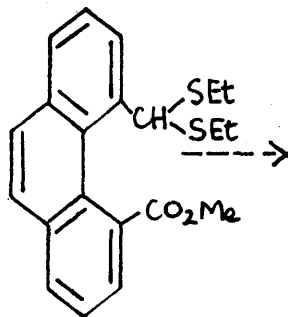
No resolution of the hydrocarbon was attempted but 4:5-bishydroxymethylphenanthrene was treated with (-)-menthoxyacetyl chloride in an attempt to prepare the diastereoisomeric dimenthoxyacetates. Dehydration occurred, however, and only the cyclic ether (XXV) was isolated.

A fruitless attempt was made to prepare 4-methyl-5-carbomethoxyphenanthrene (XXXI) via the intermediate

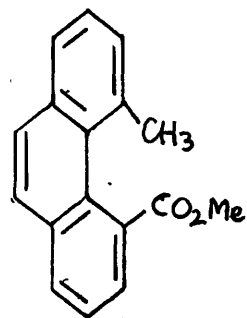
mercaptal (XXX).



(XXII)



(XXX)



(XXXI)

EXPERIMENTAL

4-Formylphenanthrene-5-carboxylic acid (XIX). - This was best prepared by a modification of the method of Vollmann et al. (loc. cit.). Pyrene (10 g.) was dissolved in carbon tetrachloride (250 c.c.) and ozonised oxygen (5% O₃) was passed through the solution for 16 hours. The precipitated ozonide was thus protected from further ozonisation. The mixture was poured into warm water (100 c.c.) and the solvent removed in steam. The resultant brown solid was filtered off, boiled twice with sodium hydroxide solution (1.6%; 150 c.c.) and the residue of unchanged pyrene (5.8 g.) filtered off. The dark brown filtrate was boiled with bleaching powder (12 g.) until the supernatant liquid became very pale yellow. On filtering and adding sodium hydroxide solution (50%; 40 c.c.) the sodium salt of the aldehydo-acid was precipitated. The next day the solid was filtered and then warmed with dilute hydrochloric acid to liberate the free acid. 4-formylphenanthrene-5-carboxylic acid (3.7 g.; conversion 42%; yield 71%) crystallised in felty needles from glacial acetic acid m.p. 271°. It showed no carbonyl activity (no reaction with 2:4-dinitrophenylhydrazine sulphate or semicarbazide acetate).

Methyl Ester (XXII). - The finely-powdered aldehydo-acid (3.6 g.) was suspended in acetone (50 c.c.) and treated with

excess ethereal diazomethane. The solution was kept at room temperature for 16 hours. The solvent was removed and the methyl ester crystallised from methanol in needles (2.9 g.) m.p. 113-114°, identical with the specimen prepared by Dr. Campbell. The 2:4-dinitrophenylhydrazone crystallised from methanol in orange prisms m.p. 250° (Found: N, 12.65. $C_{13}H_{16}O_6N_4$ requires N, 12.6%).

No recognisable product was obtained by the attempted Huang-Minlon reduction of the ester.

The ψ -methyl ester (XXI) like the parent acid gave no evidence of carbonyl reactivity.

4:5-Bishydroxymethylphenanthrene (XXIII). - This was prepared by the method of Campbell (loc. cit.). Lithium aluminium hydride (8 g.), the methyl ester (XII) (2.5 g.), and dry ether (200 c.c.) were heated under reflux for 30 minutes. The mixture was cooled and decomposition effected by the cautious addition of ice and dilute sulphuric acid. The solution was extracted with ether, the ether layer dried (Na_2SO_4), and evaporated to yield the diol (2.25 g.) m.p. 152-159° (from benzene) and mixed m.p. 152-159° with the specimen prepared by Dr. Campbell. The range in m.p. is probably due to the dehydrating effect of boiling benzene giving rise to the formation of some cyclic ether (XV) (cf. Newman and Whitehouse, loc. cit.). The diacetate was obtained by heating the diol

(45 mg.) for three hours with acetic anhydride (4 c.c.) and fused potassium acetate (5 mg.). The diacetate crystallised from light petroleum (b.p. 100-120°) in prisms m.p. 105° (Found: C, 74.6; H, 5.75. $C_{20}H_{18}O_4$ requires C, 74.55; H, 5.6%). The ψ -ester (XXI) (20 mg.) when treated with lithium aluminium hydride as described for (XXII) also gave the diol.

Cyclic ether (XXV). - In an attempt to prepare 4:5-bischloromethylphenanthrene (Campbell, loc. cit.) (XXV) was obtained almost quantitatively m.p. 77-78° from light petroleum (b.p. 60-80°). In view of later results obtained by this author it was of interest to prepare the 2:4:7-trinitrofluorenone complex which crystallised in orange prisms m.p. 190-191°, from alcohol (Found: N, 7.7. $C_{29}H_{17}O_8N_3$ requires N, 7.9%).

4:5-Bisbromomethylphenanthrene (XXVIII). - 4:5-Bishydroxymethylphenanthrene (280 mg.), benzene (20 c.c.), and pyridine (10 mg.) were treated with phosphorus tribromide (600 mg.) and the mixture warmed at 50° for 2 hours. The benzene solution was cooled and washed with water and then sodium hydrogen carbonate solution. Drying (Na_2SO_4) and removal of solvent on the steam bath left a crystalline residue of 4:5-bisbromomethylphenanthrene (370 mg., 85%). The compound crystallised in prisms m.p. 194° (dec.) from benzene (Found:

C, 52.6; H, 3.45; Br, 43.9. $C_{16}H_{12}Br_2$ requires C, 52.8; H, 3.3; Br, 43.8%).

Attempted reduction of (XXVIII). - (a) (XXVIII) (50 mg.) dissolved in acetone (10 c.c.) was shaken in an atmosphere of hydrogen with palladium/strontium carbonate catalyst (50 mg.; 2%). Filtration, followed by evaporation of solvent, gave a low-melting solid which sublimed at $80^{\circ}/10$ mm. to yield prisms m.p. $75-76^{\circ}$ undepressed on admixture with the cyclic ether (XXV).

(b) (XXVIII) (500 mg.) dissolved in benzene (20 c.c.) was slowly added to a refluxing solution of lithium aluminium hydride (2 g.) in ether (250 c.c.) (cf. Johnson⁽¹⁹⁾ et al.) and the heating continued under reflux for 16 hours. Cautious addition of ice and dilute sulphuric acid, followed by extraction and drying (Na_2SO_4) of the ethereal layer gave on evaporation a solid subliming at $70^{\circ}/10^{-3}$ mm. in prisms, m.p. $75-76^{\circ}$, undepressed on admixture with the cyclic ether (XXV) and trinitrofluorenone complex m.p. and mixed m.p. 190° .

Di-iso-thiouronium dibromide (XXIX). -4:5-bisbromomethylphenanthrene (XVIII) (100 mg.) and thiourea (64 mg.) were dissolved in dry acetone (10 c.c.) and heated under reflux for 30 minutes. The precipitated white solid (136 mg.) was filtered and washed with acetone. It crystallised from alcohol/acetone in rosettes of needles m.p. $200-201^{\circ}$ (Found: C, 41.9; H, 4.0. $C_{18}H_{20}N_4Br_2S_2$ requires C, 42.0; H, 3.9%).

4:5-Dimethylphenanthrene (XI). - A solution of the di-iso-thiuronium dibromide (XXIX) (340 mg.) in alcohol (15 c.c.) was heated under reflux with Raney nickel (ca. 500 mg.) for one hour. Filtration of catalyst and removal of solvent gave a low-melting solid which was dissolved in light petroleum (b.p. 40-60°) and chromatographed over alumina (B.D.H. - acid washed). The movement of the narrow band was easily followed by its intense blue fluorescence under ultra-violet light. The compound was eluted with light petroleum, the solvent removed, and the solid crystallised from methanol forming prisms m.p. 75-76° (150 mg.; 76%); it was 4:5-dimethyl-phenanthrene (Found: C, 93.4; H, 6.8. Calc. for $C_{16}H_{14}$: C, 93.2 H, 6.8%). The 2:4:7-trinitrofluorenone complex had m.p. 120-121° from alcohol (scarlet needles) (Found: N, 7.9. Calc. for $C_{29}H_{19}O_7N_3$: N, 8.1%). Regeneration of the hydrocarbon was effected by chromatography of the complex in benzene over alumina. The m.p. of the hydrocarbon was unchanged. The picrate formed orange prisms m.p. 109-110°, from alcohol (Found: N, 9.75. Calc. for $C_{22}H_{17}O_7N_3$: N, 9.7%).

Attempted resolution of the diol (XXIII). - The diol (476 mg.) was treated with (-)-menthoxyacetyl chloride (460 mg.) in anhydrous pyridine (5 c.c.) and the mixture left overnight. On pouring into water a solid m.p. 74-75° from ethanol was obtained. This proved to be the cyclic ether

(XXV) by direct comparison.

Attempted preparation of 4-methyl-5-carbomethoxyphenanthrene (XXXI). The methyl ester (XXII) (800 mg.) was treated with ethyl mercaptan (10 c.c.), freshly fused zinc chloride (1 g.), and anhydrous sodium sulphate (1 g.) and the mixture stored at 0° for 20 hours; then at 15° for 4 hours. Removal of excess ethylmercaptan in vacuo, followed by treatment with saturated sodium bicarbonate solution and extraction with ether, furnished (after drying and removal of solvent) a viscous oil (500 mg.). Treatment of this oil with Raney nickel in methanol afforded only an intractable tar.

B I B L I O G R A P H Y

PART II.

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- (2) Scholl and Tänyer, Annalen, 1923, 433, 172; Cf. Scholl and Meyer, Ber., 1934, 67, 1232.
- (3) German Patent 458,710; C.Z.1928, 99, II, 399.
- (4) Newman, J. Amer. Chem. Soc., 1940, 62, 1683.
- (5) Vollman, Becker, Corell and Streeck, Annalen, 1937, 531, 66; cf. Fieser and Novello, J. Amer. Chem. Soc., 1940, 62, 1855.
- (6) Hewett, J., 1938, 1286.
- (7) Newman and Hussey, J. Amer. Chem. Soc., 1947, 69, 3024.
- (8) Haworth and Sheldrick, J., 1934, 1950; cf. ibid., p. 456.
- (9) Lewis and Elderfield, J. Org. Chem., 1940, 5, 290.
- (10) Fieser and Selignan, J. Amer. Chem. Soc., 1938, 60, 170; ibid., 1939, 61, 136.
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- (12) Criegee, Annalen, 1935-1936, 521, 75; ibid., 1942, 550, 99.
- (13) Criegee, Craft and Rank, Annalen, 1933, 506-507, 194.
- (14) Vollman et al., Annalen, 1937, 531, 1.
- (15) Newman and McCleary, J. Amer. Chem. Soc., 1941, 63, 1537; ibid., 1950, 72, 5191; ibid., 1951, 73, 4627.
- (16) Nystrom and Brown, J. Amer. Chem. Soc., 1947, 69, 1197.
- (17) Badger, Campbell, Cook, Raphael and Scott, J., 1950, 2326.
- (18) Newman and Whitehouse, J. Amer. Chem. Soc., 1949, 71, 3664.
- (19) Johnson et al. J. Amer. Chem. Soc., 1948, 70, 3738.