PART - II

Synthetic approaches to tricyclo(3.2.1.0^2,7)octane ring system of trachylobane
THEORETICAL
Diterpenes with a complement of twenty carbon atoms in their molecular framework are biogenetically derived from geranylgeranyl pyrophosphate or geranylgeraniol pyrophosphate and these are remarkable for their fascinating skeletal variations as well as their occurrence in nature with normal as well as antipodal structural complexities. A few members of this family embrace wide range of biological activities represented by plant growth substances, tumour inhibitors, cytotoxic and hypotensive agents, cardiac-depressive substances, antibiotics, insecticides, cattle poisons etc. Another interesting activity shown by diterpenes is the bitter taste exhibited by many bicyclic compounds particularly with a lactonic function whereas the diterpenoid glycoside, stevioside is known as one of the sweetest substances.

Diterpenoids can be classified into open-(1), mono-(2), bi-(3), tri-(4), tetra-(5a-b) and pentacyclic-(6) systems (Chart - 1). Associated with these types of carbon framework, are a few functional groups e.g. hydroxyl, carbonyl, carboxyl, lactone, furan and the like. The tendency for migration of groups and of bonds culminating in novel types of molecular patterns has been remarkable and this is another fascinating chapter of diterpenoids chemistry. In fact, in the entire domain of terpenoid chemistry this phenomenon has been observed thereby adding elegance and beauty and also offers unique cases of mental gymnastics for an organic chemist.

During the last two decades, a vast amount of synthetic
experience has been acquired in this laboratory relating to terpenes, more particularly sesqui- and diterpenes, out of comprehensive studies towards developing methodologies for the total synthesis of various structural patterns encountered in these areas. Based on the success gained in this field, it was thought worthwhile to enter the more complicated pentacarbocyclic systems present in compounds related to trachylobanes. Before going into the details of our synthetic strategy for the trachylobane skeleton, a brief review of its chemistry may be presented at this stage.

Naturally occurring trachylobanes, from resins of *trachylobium verrucosum*, are a group of biogenetically important diterpenoids and these are characterised by tricyclo (3,2,1,0^2,7) octane system incorporated into ring C. This tricyclo (3,2,1,0^2,7) octane system is also found to be present in the sesquiterpenes, *ishwarone*¹ and *ishwarane*². Interesting postulations regarding the biogenesis of diterpenes have been associated with trachylobane skeleton. In 1955, Wenkert³ suggested a non-classical carbonium ion related to trachylobane skeleton as an intermediate during the biogenesis of tetracyclic diterpenes. A scheme for such rationalisation is depicted as follows (Chart - 2).

Cyclisation of properly oriented pimaradiene (7) leads to the formation of non-classical carbonium ion intermediate (8) which then collapses resulting in the formation of kaurene (9), *atisirene* (10), *stachene* (11) and pentacyclic trachylobane (12). With the eventual discovery of trachylobanes in nature, the theoretically conceivable array of diterpenoid skeleta
may be considered as complete so far as classical types are concerned.

In another communication it has been established by Wenkert et al. through isotopic labelling that the formation of tetracyclic hibaene-type skeleton proceeds through an eight-membered intermediate (Chart - 3).

Isolation and characterisation of compounds with trachylobane skeleton was reported first by Ourisson in 1965 and afterwards other members including the parent hydrocarbon have been reported. Several members of this pentacyclic family are known e.g., trachylobanic acid (13), 3-hydroxytrachylobanic acid (14), 18-hydroxytrachylobane (15), and the parent hydrocarbon (12). The presence of a "C-3 hydroxyl" substitution featuring in their molecular framework may be regarded as uncommon amongst diterpenoids, although it is frequently encountered in triterpenes and steroids.

\[ R_1 = \text{CH}_3; \quad R_2 = \text{H} \]
\[ R_1 = \text{COOH}; \quad R_2 = \text{H} \]
\[ R_1 = \text{COOH}; \quad R_2 = \text{OH} \]
\[ R_1 = \text{CH}_2\text{OH}; \quad R_2 = \text{H} \]

The total synthesis of methyl anti-trachylobanate (20) was first reported by Herz in 1968. The major adduct from methyl levopimarate with n-butyl crotonate was transformed into the keto-ester (16). Subsequent chemical transformations
resulted in the formation of keto-olefin (17) and this on reduction afforded the epimeric alcohols of which the major product was assigned the formula (18). Spontaneous cyclisation of (18) occurs during mesylation leading to the formation of trachylobane skeleton (19). Oxidation of (19) and subsequent reduction afforded methyl anti-trachylobanate (20).

In his ingenious syntheses of trachylobane, Kelly
reported three distinct approaches for incorporation of the cyclopropane ring in the trachylobane skeleton. Intramolecular cyclisation of tosyl ketone (21) leads to the formation of a cyclopropyl ketone (22) which under specific condition of reduction yielded trachylobane (12). Another route to trachylobane skeleton envisages homoallylic cyclisation of the mesylate (23) with dimethyl sulphoxide and sodium hydride. Oxidation and subsequent reduction of the resulting products (24) and (22) afforded the trachylobane (12).

The third route to trachylobane skeleton involves reduction of the mesylate (23) with lithium aluminium hydride under
During the last two decades in our laboratory, successful syntheses have been achieved of the four isomers of the tricarbo-cyclic diterpenoid resin acids (25)\textsuperscript{10,11} and three isomers of the corresponding isopropyl analogues of the acid (26)\textsuperscript{12}. One of these three isomers is designated as callistic acid (27), a naturally occurring compound\textsuperscript{13} and its identity with the synthetic racemic compound has been established through spectral studies. Synthesis of podocarpic acid (28)\textsuperscript{10}, four isomers of ring-C aromatic-10-nor acids (29a)\textsuperscript{14} and their 13-methoxy derivatives (29b)\textsuperscript{15} have been reported(Chart - 4). During the course of these synthetic studies, an interesting discovery pertaining to the conversion of cis A/B ring junction to trans-series of C-aromatic tricarbocyclic derivatives\textsuperscript{16} under mild dehydrogenation condition with palladium-charcoal may be regarded as a landmark in this direction. In continuation of further studies towards tricarbocyclic resin acids, relating to quaternisation of C-8, another interesting observation warranting some fascinating mechanistic interpretation of resin acid chemistry has been
CHART - 4

(25) [Chemical structure]

(26) [Chemical structure]

(27) [Chemical structure]

(28) [Chemical structure]

(29a) \( R = H \)

(29b) \( R = OCl_3 \)
observed and subsequently rationalised (loc. cit.). This will be detailed out later on in proper context.

An inspection of the systematic studies in tetracarbo-
cyclic systems reveals three approaches for the development of the D-ring viz. bicyclo(3.2.1)octane system, from the tricyclic skeleton and all these involve C-8 quaternisation, as the eventual target.

Stereospecific synthesis of the bridged bicyclo(3.2.1) -
octane ring system present in phyllocladene has been reported from our laboratory and this envisaged hydrocyanation of a suitable enone and cyclisation of the corresponding cyanoester (30).\textsuperscript{17} Synthesis of phyllocladene from the corresponding

\begin{center}
\begin{tikzpicture}
\node at (0,0) {{\includegraphics[width=0.3\textwidth]{comp1.png}}};
\node at (1.5,0) {{\includegraphics[width=0.3\textwidth]{comp2.png}}};
\node at (3,0) {{\includegraphics[width=0.3\textwidth]{comp3.png}}};
\end{tikzpicture}
\end{center}

(30)

tricyclic ketone (31) by Turner\textsuperscript{18} utilised the same route as above. However, the obvious difficulty of this approach is the

\begin{center}
\begin{tikzpicture}
\node at (0,0) {{\includegraphics[width=0.3\textwidth]{comp4.png}}};
\end{tikzpicture}
\end{center}

(31)

formation of mixture of stereoisomers as a result of non-
sterespecific hydrocyanation.
Quaternisation at C-8 from a vinyl ether (32) was based on the method developed by Burgstahler\textsuperscript{19} and the aldehyde\textsuperscript{20} (33) was prepared by Claisen rearrangement for the development of D ring of bicyclic (2.2.2) system (34). This approach was utilised by Ireland \textit{et al}.\textsuperscript{20} for the stereospecific synthesis of phyllocladene (35), kaurene (39) and atisirene (10). Another approach towards C-8 substituted tricyclic system envisages construction of (36)\textsuperscript{21} from a suitable substituted progenitor whose cyclisation would automatically lead to the correct stereochemistry at C-8. Thus the synthesis of 3-hydroxyphyllocladene (37) derivative with an additional oxygen function in ring D was reported\textsuperscript{22}.

An interesting chapter of tetracarbocyclic diterpenoid synthesis was opened up in our laboratory in the last decade and this highlighted extensive carbene addition studies with suitable precursors as the key step towards target skeleta.
This synthesis develops C-8 quaternisation. Compounds (39) and (40) have been synthesised through internal addition of \( \alpha \)-ketocarbenes to a double bond and subsequent cleavage of (38) under various conditions afforded the cyclopentanone derivatives. Copper catalysed decomposition of some suitable \( \gamma, \delta \)-unsaturated diazomethyl ketones and subsequent reduction of the resulting cyclopropyl ketones leads to the formation of some tetracyclic diterpene skeleta (41) and (42). These bridged intermediates represent relays towards complex tetracyclic diterpenes having the desired stereochemistry related to kaurene, phyllocladene, hibane and gibberellins.

These extensive experiences have been gainfully utilised towards developing methodologies for the construction of the ring system present in trachylobanes. In view of the novel and challenging aspects of chemistry associated with synthesising...
tricyclo(3.2.1.0^2^7)octane ring system present in trachylobanes we focussed our attention first on construction of the same as a model study. In this direction the construction of cyclopropane ring may be envisaged through carbene insertion process as depicted below.

Conjugate addition of hydrogen cyanide to the octalone (43) under acidic condition afforded the cyanoketone (44). The latter on hydrolysis with concentrated hydrochloric acid furnished the trans-keto acid (45a) in a fair yield which was found to be present in equilibrium with the lactol form (46). For the preparation of the lactone (47) and ultimately the unsaturated acid (48), considerable amount of experimental
modifications has been carried out to improve the yield. When the keto-ester (45b) was subjected to Grignard reaction with methylmagnesium iodide, it afforded the lactone (47) in 57\% yield. Previously the reported yield was as low as 9\% along with by-products. The lactone (47) thus obtained was purified by passing through silica gel column and found to be identical with the one reported earlier. This lactone (47) was isomerised with alkali at elevated temperature and under modified conditions to afford the unsaturated acid in 74\% yield, a distinct improvement on the previously reported 43\% yield. The identity of this unsaturated acid (48) was established with the known sample.

The acid chloride obtained from the reaction of the sodio salt of acid (48) with oxalyl chloride was treated with ethereal diazomethane solution to afford the diazoketone (49). Formation of the latter requires considerable period of time for the completion of reaction. The formation of (49) was evident from the characteristic bands at 2115 cm\(^{-1}\) in the i.r. spectrum. Intramolecular cyclisation of the diazoketone by refluxing in cyclohexane-tetrahydrofuran mixture in presence of "activated CuO catalyst" under illumination, requires five hours for completion of reaction as evident from the absence of diazoketone bands in the i.r. The product mixture after passing through neutral alumina column afforded the cyclopropyl ketone (50) and its structure was established from spectral properties. I.r. spectra indicated carbonyl absorption at 1710 cm\(^{-1}\). The absence of signals due to vinylic protons and vinylic methyl group in the n.m.r. spectrum points towards complete decomposi-
tion of diazoketone (49). On the other hand appearance of two
(1 H) doublets at δ 0.966 and 0.893 arising out of the two cyclo­
propyl bridge-head protons and a sharp singlet methyl signal at
δ 1.24 may be taken as a conclusive evidence in favour of struc­
ture (50). The M⁺ value at m/e 190 further corroborates the
structure (50).

With the eventual success already achieved in the model
studies, our attention was directed to the complicated tricyclo
(3.2.1.0²,7)octane ring system incorporated into ring C of the
trachylobane skeleton. The success of the total synthesis depends
entirely on the synthesis of olefinic acid (52) from any one of
the keto-esters (36) or (51).

\[
\text{(36)} \quad \text{(51)} \quad \text{(52) } R = \text{H, O\text{H}}
\]

The successful synthesis of olefinic acid (52) with
desired stereochemistry at each of the four asymmetric centres
associated with ring A, B and C constitutes the first programme
of studies. Copper catalysed decomposition of corresponding
diazoketone arising from olefinic acid (52) through acid
chloride will automatically lead to the formation of the ring
system with desired stereochemistry.

The synthesis of the keto-ester (36) has already been
reported from this laboratory. Grignard reaction on the
keto-ester (36) was expected to produce a γ-lactone which could be isomerised with alkali at elevated temperature to obtain the desired unsaturated acid (52) but preliminary investigation with (36) was unsatisfactory. The presence of hydroxyl function or its acetate creates difficulty with alkali at high temperature. So the synthetic strategy was modified and the synthesis of keto-ester (51) from podocarpic acid was sought for.

Synthetic studies in this direction necessitated quaternisation at C-8 of a suitable substituted podocarpa-8,11,13-triene nucleus. Following the method of Woodward and others for C-10 angular substitution of A-aromatic hydronaphthalene and hydrophenanthrene skeleton, methyl podocarpate (53) obtained by treating podocarpic acid with ethereal diazomethane solution, was subjected to Reimer-Tiemann reaction in presence of chloroform and alkali. The object was to isolate the substituted cyclohexadienone (54) which would have formed as an abnormal Reimer-Tiemann product by analogy. However, the reaction did not yield the desired ketone (54). In an attempt to modify the reaction condition, anhydrous sodio salt of methyl podocarpate (53), prepared from methyl podocarpate and methanolic sodium
methoxide, was treated with bromoform and the resulting mixture was refluxed for several hours. Even under this vigorous condition nothing except the starting compound could be isolated. The obvious hindrance to the C-8 substitution from the above reaction might have resulted from steric interactions between the incoming electrophile and the C-4 carboxymethyl group from one face and C-10 angular methyl group from other face. However, if this would have been the reason for non-occurrence of above reaction, the corresponding 12-hydroxypodocarpa-8,11,13 triene (59) under similar condition might be expected to yield the C-8 substituted cyclohexadienone (60). (59) was obtained by reduction of
methyl O-methylpodocarpate (55) with lithium aluminium hydride, oxidation of the resulting alcohol (56) to the corresponding aldehyde (57) and Wolff-Kishner reduction to (58) and subsequent demethylation. This hydroxypodocarpatriene (59) was subjected to Reimer-Tiemann condition in presence of chloroform and potassium hydroxide in aqueous ethanol (1:1) and a neutral product was obtained in a very poor yield by washing the ethereal solution of the reaction mixture with Claissen alkali. This product exhibited two characteristic peaks at 1660 and 1625 cm\(^{-1}\) in the i.r. and an absorption maximum at 230 nm (\(\varepsilon 11800\)) in the u.v. The n.m.r. spectrum revealed the presence of three vinyl protons in the range \(6.42 - 5.85\). Thus the spectral properties are suggestive of structure (60) for this neutral compound. However, further studies in this direction could not be effectively accomplished owing to the extremely poor yield from the above reaction. With the eventual limitation of this study, efforts were directed towards developing an alternative methodology for C-8 substitution. Use of hexamethylenetetramine in conjunction with trifluoroacetic acid was developed by Smith as a simple and pararegio-selective method for formylation of a-phenolic compound. This method was considered expedient for C-8 quaternisation of an appropriately substituted podocarpic acid (63). This was obtained from O-methylpodocarpane (58) by formylation followed by reduction of (61) and demethylation of the other (62) in good yield. The phenol (63) was subjected to hexamethylenetetramine-trifluoroacetic acid system with a view to
obtaining the dienone (64). However, a white crystalline solid was obtained from the resulting product mixture whose molecular weight was found to be 299 from the mass spectrum.

The structure (65) has been assigned to this neutral methylimine compound on the basis of its physical and chemical properties and this culminates in a new method of C-11 substitution instead of C-8 substitution. Absence of absorption in u.v. due to styrenoid conjugation, characteristic of structure (66) and the absence of signals due to -NCH₂ protons in n.m.r. rule out the possibility of imine to have structure (66). In contrast, the compound (65) exhibits in n.m.r. two vinyl protons at δ 4.7 and 5.57 resulting from geminal coupling of the terminal iminomethylene protons and a significant downfield
chemical shift by $\delta$ 0.36 of C-10 angular methyl proton in comparison to that in (63). Moreover, three other methyl signals remained unperturbed and the number of aromatic protons reduced to one. All these are highly suggestive of the proposed structure (65) for this imine. The transformation of the phenol (63) to the methylene imine (65) is indeed an interesting observation suggesting a new example of resistance to imine hydrolysis since (65) remained unchanged even on heating with alkali or water at elevated temperature for quite a long time.

By way of isolation of (65) from the reaction of (63), the suggestion of Smith relating to the intermediacy of methylimines and their genesis from the corresponding methyleneimines through rearrangement have been corroborated. In an alternative possibility, methyleneiminomethyl group might have entered at C-3 position resulting in the transformation of phenol (63) to a cyclohexadiene intermediate. Under the influence of trifluoroacetic acid this intermediate is expected to undergo spontaneous dienone-phenol rearrangement leading to the formation of (67). From stereoelectronic considerations (67) should again undergo facile hydrolysis to the corresponding aldehyde.
Analyses of spectral data rule out this possibility.

The hexamethylenetetramine-trifluoroacetic acid system provides sufficient energy to overcome the potential barrier for attack at C-11 in (63), because this position is hindered sterically by the axial proton at C-1 and C-10 angular methyl group. The possibility of rearrangement from (65) to (66) is again sterically prohibited (model study) because the steric repulsion between the angular C-10 methyl group and the developing sp²-imino carbon atom of (66) is increased enormously during this process. Although the rearranged imine (66) was expected to acquire more stability owing to styrenoid conjugation, the hydrolysis of either structures (65) or (66), to the corresponding primary amine or the aldehyde respectively requires attack of a molecule of water to the electron deficient imino carbon atom and this may not be possible from stereoelectronic considerations.

The next series of studies to build up the cyclopropane ring featuring in the trachylobane skeleton has been directed through free radical process generated from the related tetracyclic 1,3-dihalides. Before taking up the actual scheme for realising the total synthesis of trachylobane, it became necessary to carry out studies on model compounds because such types of reactions have analogies only in simple systems.

Formation of cyclopropane from 1,3-dihalopropane was envisaged long time back by reaction with zinc dust in ethanol.  

\[ \text{BrCH}_2 - \text{CH}_2 - \text{CH}_2\text{Br} \rightarrow \text{CH}_2 - \text{CH}_2 - \text{CH}_2 \]
Similarly\[31\]

\[
\begin{align*}
C_6H_5CH_2CH(CH_3)CH_2Br & \rightarrow C_6H_5 - \text{CH}_2 \text{CH}_2
\end{align*}
\]

Formation of cyclosteroid (68) was realised\[32\] following the same course of reaction.

This idea might be successfully exploited for the formation of cyclopropane of trachylobane and consequently investigations were directed to some model compounds.

Our immediate object is to obtain the dihalo compound (80) which can be achieved from the easily accessible tricyclic keto acid (70a) and the scheme is adumbrated below.
The kato-ester (69b) was obtained from α-tetralone by carbomethoxylation and alkylation with ethyl bromoacetate followed by hydrolysis and esterification. Annellation of the ethyl ester (69b) with methyl vinyl ketone in presence of an excess methanolic sodium methoxide afforded directly the unsaturated keto-acid (70a)\(^{33}\) in a high yield. On esterification with diazomethane it afforded (70b) which showed absorptions at 228 and 294 nm (\(\varepsilon\ 11, 230\) and 22,900) in the u.v. Catalytic hydrogenation of the keto-ester (70b) resulted in the uptake of two molar equivalents of hydrogen leading to the formation of epimeric hydroxy esters (71). The stereochemistry of the reduction process has been discussed fully later on (vide infra).
On oxidation with Jones reagent it afforded the keto-ester (72) in a good yield. Its homogeneity was tested through t.l.c. Its i.r. spectrum exhibited two peaks at 1735 and 1715 cm⁻¹. Our next strategy involved introduction of a methyl group at C-2 position. It was originally planned to carry out carboxymethylation and alkylation followed by decarboxylation on keto-ester (72). The course of reaction followed otherwise. With one molar equivalent of dimethyl carbonate and sodium hydride, the keto-ester (72) afforded a solid crystalline compound. The same compound was also obtained by treating the keto-ester (72) with sodium hydride. The compound was found to be homogeneous in t.l.c. It exhibited two peaks in i.r. at 1758 and 1715 cm⁻¹ showing thereby the presence of a five and a six-membered ketone. A tentative structure (73) has been assigned to it since the m.p. of the compound is same as that for a reported one having structure (73). Confirmation is being sought for through comparison with an authentic sample. The synthetic strategy was next modified and the keto-ester (69b) afforded the tricyclic unsaturated acid (74a) on treating the keto-ester (69b) with isopropyl methyl ketone in presence of an excess methanolic sodium methoxide. The keto-acid (74a) on esterification with diazomethane afforded the keto-ester (74b) on catalytic hydrogenation of (74a) resulted in the formation of epimeric saturated hydroxy acid in a good yield. Its i.r. spectrum exhibited two peaks at 1786 and 1715 cm⁻¹. The compound was found to be homogeneous in t.l.c. It exhibited two peaks in i.r. at 1798 and 1715 cm⁻¹. A tentative structure (74b) has been assigned to it since the m.p. of the compound is same as that for a reported one having structure (74b). Confirmation is being sought for through comparison with an authentic sample.
esters (75). The addition of hydrogen to the double bond during catalytic hydrogenation resulted from the opposite face of carboxylic side chain and thereby stereochemistry of B/C ring is trans. This also follows from well-known analogies. Reduction of hydroxy-ester (75) with lithium aluminium hydride

(69b) → (74a) \( R = H \)
(74b) \( R = Me \) → (75)

(76) → (77) → (78)

(79) → (80a) \( X = Br \)
(80b) \( X = I \) → (81)
afforded a solid dihydroxy compound (76). The dihydroxy compound (76) was oxidised with chromium trioxide pyridine complex in methylene chloride to afford a solid keto aldehyde (77) in a satisfactory yield. It exhibited a single spot in t.l.c.

The keto-aldehyde (77) was cyclised in presence of glacial acetic acid and afforded the ketol (78) in a fair yield in which one form will be in a major proportion. On reduction with lithium aluminium hydride the dihydroxy compound (79) was formed. The dihydroxy isomers were directly used in the next reaction without further separation.

In the syntheses of polyenes, Kuhn developed a method for introduction of double bond from 1,2-vicinal dihydroxy compound to the corresponding unsaturated compound through the conversion of dihydroxy compound to diiodo compound with diphosphorous tetraiodide and this simultaneously eliminated iodine. This idea has been utilised for the formation of the diiodo compound from the corresponding dihydroxy compound and elimination of iodine to form a new bond was envisaged from the behaviour of 1,3-dihalides under reducing condition.

Against this theoretical background, the dihydroxy compound (79) was treated with diphosphorous tetraiodide and the crude diiodo compound (80b) was refluxed with zinc dust in ethanol. The product isolated was found to contain iodine and no hydroxyl band in i.r. Attempt to isolate a product free from iodine was not successful.

Next attempt was made with dibromo compound (80a)
which was prepared from the dihydroxy compound (79) by treating with phosphorus tribromide in excess pyridine. The dibromo compound (80a) was refluxed with a mixture of zinc dust, sodium carbonate and sodium iodide in aqueous ethanol (80%) for a prolonged period. It afforded a liquid in a very poor yield and purified through column chromatography over activated neutral alumina. A liquid was isolated on elution with petroleum ether. In t.l.c. it was found to be a mixture of two components. The mass spectra of the compound reveals the presence of a molecular ion peak at 224 and this corresponds to that of hydrocarbon (81). Because of the extremely poor yield no pure compounds could be isolated from the reaction mixture and the formation of (81) could not be definitely established although its presence is evident from mass spectral analysis.
EXPERIMENTAL
M.p.s were taken for samples in open capillary tubes in a sulphuric acid bath. U.v. spectra were recorded with a Beckman DU spectrophotometer for solutions in 95% ethanol. N.m.r. spectra were measured for solutions in carbon tetrachloride with a Varian T-60 spectrometer, with tetramethylsilane as internal standard. I.r. spectra were taken with a Perkin-Elmer model 21 instrument. T.l.c. plates were coated (0.2 mm thickness) with silica gel G (200 mesh). Mass spectrum was measured with Hitachi RM-60 spectrometer. Gas chromatography was carried out by using Varian Aerograph model 1868-4 with columns, SE 30 on varaportzo and carbowax 20M on chromosorb W. Light petroleum refers to the fraction of b.p. 60 - 80°.
9-Methoxycarbonyl-trans-decal-2-one (45b)

To a mixture of octalone (43, 30g) in ethanol (200 ml) and acetic acid (12 ml), potassium cyanide (26 g) in water (30 ml) was added with stirring at -5°. The reaction mixture was left for 12 h at 6°. It was worked up in the usual way and the residue distilled to afford the cyanoketone (44, 24 g, 67.8%); b.p. 165-171° at 9 mm Hg (lit. 165 - 171° at 9 mm Hg).

The cyanoketone (44, 10 g) was refluxed with concentrated hydrochloric acid (800 ml) for 20 h. The mixture was concentrated (ca. 100 ml) under vacuum. The residue was saturated with sodium chloride and extracted with ether. The ethereal extract was washed with sodium bicarbonate solution till alkaline. The cooled alkaline extract was acidified with hydrochloric acid (6 N), extracted with ether, washed with water and dried. The solution was concentrated and residue on crystallisation afforded the pure acid (45a, 4.2 g, 38%), m.p. 117° (lit. 117°), $\nu_{\text{max}}$ 1705, 1765 cm$^{-1}$.

Esterification of the acid (45a, 2.1 g) with an excess of ethereal diazomethane and usual work-up afforded the keto-ester (45b, 2 g), b.p. 135 - 140° at 6 mm Hg (lit. 135 - 140° at 6 mm Hg), $\nu_{\text{max}}$ 1705, 1730 cm$^{-1}$.

3-Methyl-5α-carboxy-1,4,5,6,7,8,9,10β-octahydronaphthalene (48)

A solution of methylmagnesium iodide prepared from magnesium (1.2 g) and methyl iodide (7.2 g) in dry ether (100 ml) was added dropwise to the keto-ester (45b, 8 g) during
30 min. at \(-10^\circ\) and the reaction mixture kept at \(-10^\circ\) for 2.5 h. The product was decomposed with an excess of saturated ammonium chloride solution and left for 12 h. The mixture was extracted with ether, washed with water, sodium thiosulphate solution and then with water, dried and the solvent evaporated. The product was purified through column chromatography on silica gel (150 g). Fractions eluted with light petroleum afforded the lactone (47, 3.8 g, 57%), m.p. 67° (lit. 67°), \(\nu_{\text{max}}\) 1765 cm\(^{-1}\).

A mixture of the lactone (47, 3.1 g) and potassium hydroxide (4.5 g) in ethylene glycol (45 ml) was heated on a graphite bath at 200 - 210° for 2 h under nitrogen. It was cooled, diluted with water and extracted with ether. On evaporation of the solvent no organic residue was left behind. The alkaline mixture was acidified with ice-cold acetic acid and worked up in the usual way. On evaporation of the solvent the solid residue was crystallised to afford the olefinic acid (48, 2.3 g, 74%), m.p. 111 - 112° (lit. 111 - 112°), \(\nu_{\text{max}}\) 1690, 1602 cm\(^{-1}\), 6.66 (3 H, s, C-CH\(_3\)), 5.35 (1 H, s, olefinic proton), 3.75 (1 H, s), (Found : C, 74.2; H, 9.5. C\(_{18}\)H\(_{18}\)O\(_2\) requires C, 74.2; H, 9.3%)

**10-Methyl tetracyclo(6.2.2.0\(^3\),0\(^10\),12)dodecan-11-one (50)**

The olefinic acid (48, 200 mg) was dissolved in anhydrous methanol (2 ml) and converted to its sodio salt by neutralising the acid with a dilute solution of sodium methoxide (2%) in methanol using phenolphthalein as indicator. The solvent was removed and dried perfectly. Dry sodio salt was suspended
in dry benzene (20 ml) containing a catalytic amount of pyridine (ca. 0.1 ml) and cooled in the ice-bath. Oxalyl chloride (0.2 ml) was then added and stirred for 30 min. The reaction mixture was then allowed to attain room temperature and finally warmed at 60° for 1 h. It was filtered, concentrated and dried. The acid chloride was dissolved in dry ether (20 ml) and added very slowly to a magnetically stirred ice-cold ethereal solution of diazomethane containing dry triethylamine (0.2 ml). The reaction was left with stirring for 12 h and filtered. The solvent was concentrated to afford the diazoketone (49), ν max 2115, 1635 cm⁻¹.

The crude diazoketone in dry cyclohexane-tetrahydrofuran (210 ml, 20:1) was refluxed with stirring with activated CuO catalyst (600 mg) under illumination (200 W lamp). Refluxing was continued until the i.r. band at 2115 cm⁻¹ disappeared and it was found to be complete in 5 h. The reaction mixture was filtered and the solvent distilled off in vacuo. The residue was chromatographed over activated neutral alumina (15 g) and on elution with light-petroleum-benzene (9:1) a liquid was obtained. Evaporative distillation (75 - 80° at 0.1 mm Hg) afforded the ketone (50, 120 mg) homogeneous in g.l.c., ν max 1710, 1130, 1100, 1000, 900 cm⁻¹, (Found : C, 82.2; H, 9.5. C₁₃H₁₈O requires C, 82.1; H, 9.5%).

Methyl 12-methoxy-podocarpa-8,11,13-trien-19-oate (55)

Podocarpic acid (28, 10 g) was dissolved in a mixture of ethanol (50 ml) and sodium hydroxide solution (4.8 g, 50 ml water). To the reaction mixture dimethyl sulphate (13 ml) was
added dropwise with stirring at 50 - 55°. After the addition was over, the mixture was refluxed for 15 min. It was cooled, filtered and washed with water and dried. The solid residue was crystallised to afford (55, 8 g), m.p. 127 - 128° (lit. 128°), \( \nu_{\text{max}} \) 1710, 1605 cm\(^{-1}\).

12-Methoxy\textit{podocarpa-8,11,13-trien-19-ol} (56)

To a refluxing solution of lithium aluminium hydride (2.4 g) in ether-tetrahydrofuran (150 ml, 1:1), a solution of (55, 10 g) in tetrahydrofuran (20 ml) was added dropwise with constant stirring and the mixture refluxed for 3 h. On cooling the mixture was decomposed with saturated cold sodium sulphate solution. It was filtered, dried and concentrated. The residue was crystallised to afford (56, 9 g), m.p. 90° (lit. 90 - 91°).

12-Methoxy\textit{podocarpa-8,11,13-trien-19-al} (57)

To a stirred, cooled (0°) solution of pyridine (9.5 g) in methylene chloride (150 ml), chromium trioxide (6 g) was added portionwise and the mixture stirred for 30 min. A solution of (57, 8.22 g) in methylene chloride (10 ml) was added in one portion and the mixture stirred for 15 min. at room temperature. The solution was decanted and the residue washed with methylene chloride. The combined organic layer was washed successively with sodium hydroxide solution (5%), dilute hydrochloric acid (5%), sodium bicarbonate solution (5%), brine and finally dried over calcium chloride and the solution concentrated. The solid residue on crystallisation
gave (57, 6 g), m.p. 133 - 135° (lit. 133 - 135°), \( v_{\text{max}} \) 1705, 1600 cm\(^{-1}\).

\textbf{12-Methoxy\textit{p}odocarpa-8,11,13-triene (58)}

A mixture of (57, 5.44 g), hydrazine hydrate (70 ml, 95 - 100\%), hydrazine dihydrochloride (19.5 g) and diethylene glycol (280 ml) was heated under nitrogen for 2 h. It was cooled and potassium hydroxide (25 g) was added to it. The mixture was heated to 210° and kept for 2 h. The product was cooled and poured into ice-cold water. It was extracted with ether, washed with water and dried. The solvent was removed. The residue was distilled to afford (58, 2.5 g), b.p. 155 - 160° at 0.1 mm Hg (lit. m.p. 30.5 - 31.5°), \( v_{\text{max}} \) 1600 cm\(^{-1}\), δ 6.87 - 6.4 (3 H, m, Ar protons), 3.69 (3 H, s, -OCH\(_3\)), 1.17 (3 H, s, C-10 methyl), 0.96 (6 H, s, C-4 gem-dimethyl).

\textbf{12-Hydroxy\textit{p}odocarpa-8,11,13-triene (59)}

A mixture of (58, 5 g) hydrobromic acid (100 ml, 48\%) and glacial acetic acid (100 ml) was refluxed on an oil-bath for 12 h. The product was cooled and diluted with water. The product was extracted with ether and the ethereal solution washed with sodium hydroxide solution (5\%), water and finally dried. On removal of the solvent the residue was crystallised and it afforded (59, 4.5 g), m.p. 140° (lit. 140.5 - 141.5°), δ 6.8 - 6.26 (3 H, m, Ar protons), 5.43 (1 H, s, -OH), 2.7 (2 H, t, benzylic protons), 1.11 (3 H, s, C-10 methyl),
0.94 (6 H, s, C-4 gem-dimethyl).

**8-Dichloromethylpodocarpa-9 (11),13-dien-12-one (60)**

The phenol (59, 2.2 g) was dissolved in a mixture of ethanol (6 ml) and aqueous potassium hydroxide (3.5 g) in water (6 ml). To the stirred reaction mixture, distilled chloroform (2 g) was added slowly during 30 min. at 65 - 70°. After the addition was over the mixture was stirred for another 30 min. at that temperature. The product was cooled and diluted with cold water. The product was extracted with ether, washed with Claisen alkali, water and dried. The solvent was removed in vacuo and the residue on evaporative distillation (160 - 165°) at 0.01 mm Hg gave the dienone (60, 200 mg), $\lambda_{\text{max}}$ 230 nm ($\varepsilon$ 11,800), $\nu_{\text{max}}$ 1660, 1625 cm$^{-1}$.

**12-Methoxy 13-formylpodocarpa-3,11,13-triene (61)**

A mixture of (58, 4.3 g), hexamethylene tetramine (4.67 g) and trifluoroacetic acid (25 ml) was heated at 90° for 12 h. The product was concentrated and diluted with ice-water. The product was made alkaline with sodium carbonate solution and stirred for 15 min. It was extracted with ether, washed with water, dried and then concentrated. The residue on evaporative distillation (145 - 150° at 0.01 mm Hg) afforded the aldehyde (61, 3.35 g, 70%), $\lambda_{\text{max}}$ 1685, 1610 cm$^{-1}$, $\delta$ 9.33 (1 H, s, -CHO), 7.33 and 6.72 (2 H, Ar protons), 3.32 (3 H, s, -OCH$_3$), 1.18 (3 H, s, C-10 methyl), 0.97 (6 H, s, C-4 gem-dimethyl), (Found: C, 79.6; H, 9.1. C$_{19}$H$_{26}$O$_2$ requires C, 79.7; H, 9.1%).
12-Methoxy-13-methylpodocarpa-8,11,13-triene (62)

A mixture of the aldehyde (61, 2.62 g), hydrazine hydrate (20 ml, 95 - 100%) and diethylene glycol (50 ml) was heated at 130° under nitrogen for 2 h. It was cooled, potassium hydroxide (1.8 g) added and the temperature raised to 210° and maintained at that temperature for 2 h. The product was cooled, diluted with ice-cold water and extracted with ether. The ethereal extract was washed with water and dried. On removal of the solvent the residue was distilled to afford (62, 1.2 g), b.p. 145 - 150° at 0.05 mm Hg, \( \nu_{max} \) 1605 cm\(^{-1}\), \( \lambda_{max} \) 3600, 1600, 1380 cm\(^{-1}\), 6.62 (1 H, s, Ar proton), 6.42 (1 H, s, Ar proton), 2.71 (2 H, t, J = 5 Hz, benzylic protons), 2.1 (3 H, s, Ar methyl), 1.11 (3 H, s, C-10 methyl), 0.95 (6H, s, C-4 gem-dimethyl), \( (\text{Found: C, 83.7; H, 10.4. C}_{19}H_{23}O \text{ requires C, 83.8; H, 10.4%}).) \)

12-Hydroxy-13-methylpodocarpa-8,11,13-triene (63)

A mixture of (62, 2.8 g), hydrobromic acid (30 ml, 48%) and glacial acetic acid (30 ml) was refluxed in an oil-bath for 12 h. It was concentrated under vacuo and the product poured into ice-cold water. The mixture was extracted with ether, washed with water, sodium bicarbonate solution and water. The organic layer was dried and the solvent removed. It was chromatographed on neutral alumina (30 g). On elution with benzene a liquid was obtained. Evaporative distillation (140 - 145° at 0.01 mm Hg) afforded (63, 1.3 g), \( \nu_{max} \) 3600, 1600, 1380 cm\(^{-1}\), 6.62 (1 H, s, Ar proton), 6.42 (1 H, s, Ar proton), 2.71 (2 H, t, J = 5 Hz, benzylic protons), 2.1 (3 H, s, Ar methyl), 1.11 (3 H, s, C-10 methyl), 0.95 (6H, s, C-4 gem-dimethyl), \( (\text{Found: C, 83.7; H, 10.2. C}_{18}H_{26}O \text{ requires C, 83.7; H, 10.1%}).) \)
13-Methyl-12-hydroxy-11-methyleneimino-13-methyl-podocarpa-8,11,13-triene (65)

A mixture of phenol (63, 1 g), hexamethylene tetramine (1 g) and trifluoroacetic acid (5 ml) was refluxed for 12 h and the solution concentrated. The product was refluxed with alkaline sodium hydroxide solution for 8 h and cooled. The product was extracted with ether, washed with water and dried. On removal of the solvent a solid residue was obtained which on crystallisation gave the compound (65, 700 mg), m.p. 161 °C (light petroleum-benzene), \( \lambda_{\text{max}} \) 223, 230, 340 nm (\( \varepsilon \) 17950, 5214, 2675), \( \lambda_{\text{max}} \) 1625, 1595 cm\(^{-1}\), \( M^+ \) 299.64 (1 H, s, ArH), 5.57 (1 H, d, \( J = 12 \) Hz), 4.7 (1 H, d, \( J = 12 \) Hz), 2.1 (3 H, s, C-13 methyl), 1.47 (3 H, s, C-10 methyl), 0.98 (6 H, s, C-4 gem-dimethyl), (Found: C, 80.3; H, 9.7. \( C_{20}H_{29}O_2 N \) requires C, 80.2; H, 9.8%).

2-Carbomethoxy tetral-1-one (68a)

Sodium hydride (50% oil suspension, 10 g) was washed with dry light petroleum and kept under nitrogen. The flask was cooled in ice water and \( \alpha \)-tetralone (22 g) added dropwise with constant shaking. To the cooled mixture dimethyl carbonate (375 ml) was added slowly followed by addition of dry methanol (2 ml). It was allowed to rise to room temperature and then refluxed for 5 h. The excess solvent was distilled off. The product was cooled in ice and acidified with dilute hydrochloric acid (6 N). The residue was distilled to furnish (68a, 26.6 g, 86%), b.p. 133 - 140 °C at 0.8 mm Hg (lit. 115 °C at 0.5 mm Hg).
Ethyl 2-carbomethoxy tetral-1-one-2-acetate (68b)

Dry potassium t-amylate (from 4.4 g potassium) was suspended in thiophene-free benzene (150 ml) and the mixture cooled in ice. Compound (68a, 20.4 g) was added dropwise with constant stirring under nitrogen for 1 h followed by the addition of ethyl bromoacetate (20.04 g) and the mixture left 12 h. The mixture was refluxed for 8 h and then cooled. On acidification with cold dilute hydrochloric acid (6 N) the mixture was extracted with benzene. The extract was washed successively with brine, sodium bicarbonate solution (5%) and water. The solvent was removed and the residue distilled to afford the compound (68b, 25.9 g, 90%), b.p. 145 - 150° at 0.1 mm Hg.

Ethyl tetral-1-one-2-acetate (69b)

A mixture of the above compound (68b, 33.6 g), glacial acetic acid (300 ml), hydrochloric acid (230 ml, 12 N) and water (30 ml) was refluxed in an oil bath for 6 h. The product was concentrated under vacuo and cooled. It was extracted with ether and washed with sodium bicarbonate solution (10%) till alkaline. The cooled alkaline extract was acidified with cold dilute hydrochloric acid (2 N) and extracted with ether. The extract was washed with brine and dried. On removal of the solvent, the solid residue was crystallised and it gave the keto-acid (69a, 22 g, 93%), m.p. 99 - 103° (lit. 108 - 109°).

The above keto-acid (69a, 22 g) was refluxed with dry
ethanol (180 ml) and concentrated sulfuric acid (18 ml) for 12 h. The product was concentrated and the cooled mixture poured into ice-cold water and extracted with ether. The extract was washed with sodium bicarbonate solution (5%), brine and then dried. The solvent was evaporated and the residue distilled to afford the ketoester as a liquid (69b, 20.5 g, 82%), b.p. 130° at 0.5 mm, \( \lambda_{max} \) 1720, 1680, 1600 cm\(^{-1}\).

**Methyl 1,2,3,9,10,10a-hexahydro-3-oxo-phenanthrene-10a-acetate (70b)**

The keto-ester (69b, 6.02 g) dissolved in a minimum quantity of dry methanol was added at 0° under nitrogen to a solution of sodium methoxide (from 1.437 g sodium) in dry methanol (35 ml) followed by dropwise addition of methyl vinyl ketone (2.62 g) with constant stirring and the mixture stirred for 12 h at room temperature. The product was acidified with a slight excess of glacial acetic acid and concentrated. The residue was diluted with water and extracted with chloroform. The chloroform extract was washed with potassium carbonate solution (5%) till alkaline. The cooled alkaline extract was acidified with cold hydrochloric acid (2 N). It was extracted with chloroform, washed with water and dried, calcium chloride. The solvent was evaporated and the residue crystallised to afford the tricyclic unsaturated keto acid (70a, 5.3 g, 80%), m.p. 195° (lit. 195 - 195.5°), \( \lambda_{max} \) 212, 219, 297 nm (\( \epsilon \) 14,080, 12,960, 25,600), \( \nu_{max} \) 1715, 1660, 1580 cm\(^{-1}\).
Esterification of the above unsaturated keto-acid (70a, 1 g) with ethereal diazomethane gave the solid unsaturated keto-ester (70b, 1 g), m.p. 98° (lit. 98°), \( \lambda_{\text{max}} \) 228, 294 nm (\( \epsilon \) 11,230; 22,900), \( \nu_{\text{max}} \) 1735, 1660, 1590 cm\(^{-1}\).

Methyl 1,2,3,4,4\( \alpha \),9,10,10\( \alpha \)-octahydro-3-hydroxyphenanthrene-10\( \alpha \beta \)-acetate (71)

The unsaturated ketoc-ester (70b, 300 mg) in methanol (15 ml) was stirred under hydrogen in presence of palladium on charcoal (160 mg, 10%) till two equivalent amounts of hydrogen were consumed. It was filtered and the solution concentrated. The residue on evaporative distillation (160 - 170° at 0.01 mm Hg) afforded the hydroxy-ester (71, 800 mg), \( \lambda_{\text{max}} \) 1730 cm\(^{-1}\), (Found: C, 74.4; H, 7.4; \( \text{C}_{17}\text{H}_{22}\text{O}_3 \) requires C, 74.4; H, 7.4%).

Methyl 1,2,3,4,4\( \alpha \),9,10,10\( \alpha \)-octahydro-3-oxo-phenanthrene-10\( \alpha \beta \)-acetate (72)

To a cooled solution of the hydroxy-ester (71, 300 mg) in acetone, Jones reagent was added dropwise till the colour persisted for 1 min. It was diluted with cold water and extracted with ether. The extract was washed with water, sodium bicarbonate solution (5%), water and dried. The solvent was removed and the residue on evaporative distillation (140 - 145° at 0.01 mm Hg) afforded the keto-ester (72, 500 mg), \( \lambda_{\text{max}} \) 1735, 1715 cm\(^{-1}\), (Found: C, 75.2; H, 7.4; \( \text{C}_{17}\text{H}_{20}\text{O}_3 \) requires C, 75.0; H, 7.4%).
1,2,3,4,4a,9,10,10a-Octahydro-4,10a-ethano-phenanthrene-3,11-dione (73)

(i) Sodium hydride (50%, 150 mg) was washed with light petroleum and suspended under benzene (20 ml). The keto-ester (72, 500 mg) in benzene (5 ml) was added followed by dimethyl carbonate (400 mg) and the mixture allowed to stand with stirring for 12 h. It was refluxed for 3 h and cooled. The product was poured into excess of cold hydrochloric acid (2 N). The mixture was extracted with benzene, washed with water, sodium bicarbonate solution (5%) and water. It was concentrated and the residue crystallised to afford the diketone (73, 250 mg), m.p. 153° (lit. 152 - 152.5°), t.l.c. single spot, ν<sub>max</sub> 1760 (s), 1720 (w) cm<sup>-1</sup>, (Found: C, 79.9; H, 6.7. C<sub>16</sub>H<sub>16</sub>O<sub>2</sub> requires C, 79.6; H, 6.3%).

(ii) A mixture of the keto-ester (72, 500 mg) and oil-free sodium hydride (80 mg) in benzene (20 ml) was left with stirring for 12 h. It was refluxed for 8 h. The product was cooled and poured into excess cold hydrochloric acid (2 N). It was extracted with benzene, washed with water, sodium bicarbonate solution (5%) and water. The solvent was removed and a solid separated out. The solid product was crystallised and it afforded the diketone (73, 100 mg), m.p. 153°, mixed m.p. with the previous sample was 153°.

1,2,3,9,10,10a-Hexahydro-2-methyl-3-oxophenanthrene-10a-acetic acid (74a)

The keto-ester (69b, 6.02 g) dissolved in a minimum
volume of methanol was added at 0° under nitrogen to a solution of sodium methoxide (from 1.437 g sodium) in dry methanol (35 ml) followed by dropwise addition of isopropenyl methyl ketone (3.15 g) with constant stirring. When the addition was over the reaction mixture was allowed to rise to room temperature and left as such for 12 h. The reaction mixture was acidified with slight excess of acetic acid. The residue obtained after removal of the solvent was diluted with water and extracted with chloroform. The extract was washed with potassium carbonate solution (5%) till alkaline. The cooled alkaline mixture was acidified with cold hydrochloric acid (2 N) and a solid obtained. It was filtered and washed with water. It was crystallised to afford the unsaturated tricyclic keto-acid (74a, 6.3 g), m.p. 213° (lit. 213.5 - 214.5°), \( \lambda_{\text{max}} \) 212, 230, 296 nm (\( \epsilon 15660, 12350, 19970 \)), \( \lambda_{\text{max}} \) 1715, 1655, 1600 cm\(^{-1}\).

Methyl 1,2,3,9,10,10a-hexahydro-2-methyl-3-oxo-phenanthrene-10a-acetate (74b)

The above acid (74a) was esterified with cold ethereal solution of diazomethane. Distillation gave the unsaturated keto-ester as a colourless liquid (74b, 6.3 g), b.p. 155 - 160° at 0.01 mm Hg, \( \lambda_{\text{max}} \) 228, 290 nm (\( \epsilon 13490, 27210 \)), \( \lambda_{\text{max}} \) 1740, 1650, 1615, 1600 cm\(^{-1}\), (Found : C, 76.1; H, 7.2. C\(_{13}\)H\(_8\)O\(_3\) requires C, 76.0; H, 7.1%).

Methyl 1,2,3,4,4ax,9,10,10a-octahydro-2-methyl-3-hydroxy phenanthrene-10aβ-acetate (75)

The unsaturated keto-ester (74b, 1 g) in methanol (20 ml)
was stirred under hydrogen at room temperature under atmospheric pressure in presence of palladium-on-charcoal (10%, 200 mg) till two equivalents of hydrogen were consumed. The catalyst was filtered and washed with methanol. It was concentrated and the residue on evaporative distillation (165 - 170°C at 0.01 mm Hg) afforded the saturated hydroxy-ester (75, 1 g), \( \nu_{\text{max}}^{\text{IR}} 1725 \text{ cm}^{-1} \), (Found: C, 75.0; H, 8.4. \( \text{C}_{18}\text{H}_{24}\text{O}_3 \) requires C, 74.9; H, 8.4%).

1,2,3,4,4a\&,9,10,10a-Octahydro-2-methyl-3-hydroxy-phenanthrene-10a\&-ethanol (75)

To a stirred mixture of lithium hydride (4 g) in ether (150 ml) the saturated hydroxy-ester (75, 6 g) in ether (50 ml) was added dropwise. When the addition was over it was refluxed for 3 h. The mixture was cooled in an ice bath. The excess lithium aluminium hydride was decomposed with saturated sodium sulphate solution and filtered. On evaporation of the solvent the solid residue was crystallised and it gave the dihydroxy compound (76, 6.1 g) m.p. 125 - 130°C (light petroleum-ether), (Found: C, 78.3; H, 9.4. \( \text{C}_{17}\text{H}_{24}\text{O}_2 \) requires C, 78.4; H, 9.3%).

1,2,3,4,4a\&,9,10,10a-Octahydro-2-methyl-3-oxo-phenanthrene-10a\&-ethanol (77)

A stirred solution of pyridine (38 g) in methylene chloride (600 ml) was cooled in an ice-bath and dry chromium trioxide (24 g) was added portionwise. It was stirred at room temperature for 30 min. At the end of this period the dihydroxy compound (76, 5 g) dissolved in a small volume of methylene
chloride was added in one portion and the solution stirred for 15 min. The solution was decanted and the residue washed with methylene chloride (200 ml). The combined solution was washed successively with sodium hydroxide solution (5%), hydrochloric acid (5%), sodium bicarbonate solution (5%) and brine. It was next dried over calcium chloride. On evaporation of the solvent a solid residue was obtained which on crystallisation afforded the keto-aldehyde (77, 2.5 g), m.p. 114 - 115° (light petroleum ether), t.l.c. single spot, \( \nu_{\text{max}} \) 1710 cm\(^{-1}\), (Found: C, 79.5; H, 8.0. \( C_{17}H_{20}O_2 \) requires C, 79.6; H, 7.8%).

1,2,3,4,4ax,9,10,10a-Octahydro-2,10a-ethano-11-hydroxy-2-methylphenanthrene-3-one (78)

A mixture of the keto-aldehyde (77, 800 mg) and glacial acetic acid (30%, 20 ml) was heated on a steam bath for 8 h. The product was concentrated under vacuo. It was diluted with water and extracted with chloroform. The extract was washed with sodium bicarbonate solution (5%), water and dried. On evaporation of the solvent, a solid residue was obtained which on crystallisation afforded a mixture of ketols (78, 400 mg, 50%) m.p. 174 - 176° (methylen chloride-ether), \( \nu_{\text{max}} \) 1705 cm\(^{-1}\), \( \delta \) (CDCl\(_3\)), 1.15 (3 H, s, C-2 methyl), 2.1 (1 H, s, -OH), (Found: C, 79.7; H, 7.8. \( C_{17}H_{20}O_2 \) requires C, 79.6; H, 7.8%).

1,2,3,4,4ax,9,10,10a-Octahydro-2,10a-ethano-3,11-dihydroxy-2-methylphenanthrene (79)

The keto-hydroxy compound (78, 400 mg) dissolved in
tetrahydrofuran (15 ml), was added dropwise to a stirring mixture of lithium aluminium hydride (300 mg) in tetrahydrofuran ether (30 ml). When the addition was over the mixture was refluxed for another 3 h. The mixture was cooled in an ice bath and the excess lithium aluminium hydride was decomposed with saturated sodium sulphate solution. It was filtered and dried. On evaporation of the solvent, a viscous liquid was obtained which on evaporative distillation (180 - 190° at 0.01 mm Hg) afforded a mixture of dihydroxy compound (79, 400 mg), \( \nu_{\text{max}} \) 3250 cm\(^{-1}\), (Found : C, 79.0; H, 8.5. \( \text{C}_{17} \text{H}_{22} \text{O} \) requires C, 79.0; H, 8.5%).

1,2,3,4,4a,9,10,10a-Octahydro-2,10a-ethano-3,11-dibromo-2-methylphenanthrene (80a)

A solution of the dihydroxy compound (79) in ether (10 ml) and pyridine (2 g) was cooled in an ice bath, phosphorous tribromide (0.5 g) in ether (5 ml) was added dropwise and left stirring at room temperature for 12 h. The product was diluted with cold water and extracted with benzene. The extract was washed with cold hydrochloric acid (2 N), sodium bicarbonate solution (5%) and water. The solvent was dried and concentrated under vacuo. A solid residue (300 mg) was obtained. I.r. spectrum exhibited no hydroxyl band.

1,2,3,4,4a,9,10,10a-Octahydro-2,10a-ethano-3,11-diodo-2-methylphenanthrene (80b)

To a solution of the dihydroxy compound (700 mg) in dry ether (15 ml), a solution of diposphorous tetraiodide in dry carbon disulphide, prepared by gradually adding iodine
(1.6 g) to a solution of yellow phosphorous (200 mg) in dry carbon disulphide, was added slowly with constant stirring and the mixture left for 12 h. The product was poured into cold water and extracted with carbon disulphide. The extract was washed with water, sodium bicarbonate (5%), sodium thiosulphate solution and with water. It was dried over calcium chloride and concentrated under vacuo. A solid residue (400 mg) was obtained. I.r. spectrum exhibited absence of hydroxyl band.

**Attempted Cyclisation**

(i) The crude diiodo compound (80b, 400 mg) in ethanol (80%, 20 ml) and activated zinc dust (195 mg) were refluxed with constant stirring for 32 h. It was cooled, filtered and concentrated. The crude product exhibited the same i.r. spectrum as that of the starting material.

(ii) The crude dibromo compound (80a, 300 mg) in ethanol (80%, 40 ml), anhydrous sodium carbonate (100 mg), zinc dust (135 mg) and sodium iodide (30 mg) were refluxed with constant stirring for 48 h. The product was cooled and filtered. The filtrate was concentrated and the residue extracted with ether. The extract was evaporated and a pale yellow liquid was obtained. The liquid was purified by column chromatography. On elution with light petroleum, a liquid (ca8 - 10 mg) was obtained.
REFERENCES

   dron Letters, 1969, 133;
2. T. R. Govindachari, P. A. Mohamed, and P. C. Parthasa­
   rathy, Tetrahedron, 1970, 26, 615;
7. A. G. Gonzales, J. L. Breton, B. M. Fraga, and J. G.
8. W. Herz, R. N. Mirrington, H. Young, and Y. Y. Lin,


30. O. Freund, Monatsh., 1881, 3, 626;
   G. Gustavson, J. prakt. Chem., 1887, 2, 36, 300;


38. W. P. Campbell and D. Todd, J. Amer. Chem. Soc., 1942, 64, 928;