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Synthetic Studies
Utilising
Dehydroabietic Acid

A Thesis
presented to the University of Auckland
for the Degree of

Doctor of Philosophy.

by

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University of Auckland
June 1970
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This thesis is concerned with the utilisation of the natural product, abieta-8,11,13-trien-18-oic acid* (dehydroabietic acid) (1) for the synthesis of optically active steroids and diterpenoids. The work has been divided into three sections which describe transformations of rings A, B, and C of abieta-8, 11,13-trien-18-oic acid (1).

Selective epoxidation of the alkene mixture (3 - 5) derived from oxidative decarboxylation of abieta-8,11,13-trien-18-oic acid (1) with lead tetraacetate has given the epoxides (64), (65), a low yield of the epoxide (66), and the pure exocyclic alkene (3). The alkene (3) was oxidised to the ketone (6) which has been previously employed as an intermediate for the synthesis of the α,β-unsaturated ketone (10). The epoxides (64) and (65) have been converted to the unsaturated ketones (89), (107), and (67), and the saturated ketones (13), (99) and (100). A study of the boron trifluoride rearrangements of the three epoxides (64), (65) and (66)

* The numbering system used throughout this thesis is that proposed by J. W. Rowe (personal communication to Professor R. C. Cambie) in "The Common and Systematic Nomenclature of Cyclic Diterpenes" 3rd revision, Oct. 1968, to be submitted to the IUPAC Commission on Organic Nomenclature.
has been made using benzene and dimethyl sulfoxide as solvents, and pathways for the formation of the products are suggested.

Peracid oxidation of the enol acetate (155) derived from the C 7-ketone (18) provided a facile introduction of oxygen substituents into the hindered C 6 position of abieta-8,11,13-trien-18-oic acid (1). By hydrogenolysis of the C 7-hydroxy substituent of the compound (162), the C 6-acetate (172) was obtained. Hydrolysis of the latter compound, and methylation of the acid formed gave the C 6-alcohol (175) which was oxidised to the C 6-ketone (176).

The literature pertaining to the intramolecular functionalisation of aromatic alkyl groups has been surveyed, and, with the ultimate aim of synthesizing the aromatic steroids (237) and (249), the C 13-isopropyl group of abieta-8,11-13-trien-18-oic acid (1) has been functionalised by the application of two of the published procedures, viz. the lead tetraacetate oxidation of aromatic acids, and the thermolysis of diazomethyl ketones.

Nitration of methyl 12-acetylabieta-8,11,13-trien-18-oate (227) has given products of nitrodeacylation (44) and nitrodealkylation (266). The product of nitrodealkylation (266) has been converted to methyl 13-hydroxy-podocarpa-8,11,13-trien-18-oate (59) in 36% yield. Methylation of the phenol (59), and Birch reduction of the methyl ether (276) has given podocarp-8(14)-en-18-ol-13-one.
(281). Annelation of the α,β-unsaturated ketone (281) with bromoacetone was attempted in order to synthesize the steroid (284), but the only product identified was the furan (286).
INTRODUCTION

1.1 The work described in this thesis is an extension and development of previous work by the author, and is concerned with the utilisation of the diterpene resin acid, abieta-8,11,13-trien-18-oic acid (dehyroabietic acid) (1), for the synthesis of steroids and other diterpenoids. These synthetic efforts have been directed mainly towards the introduction of oxygen-containing substituents at C 3 and C 6, and towards the construction of a tetracyclic steroid nucleus. Its ready availability, and its possession of A, B, and C rings, with the required A/B bridgehead stereochemistry, make abieta-8,11,13-trien-18-oic acid (1) an attractive starting material for the synthetic aims proposed.

The following sections of this Introduction provide a brief background of previous work related to the synthetic problems under consideration.

1.2 Conversion of Abieta-8,11,13-trien-18-oic Acid (1) into 3-Oxygenated Tricyclic Steroid Analogues and Diterpenoids

Zeiss and Martin reported the degradation of abieta-8,11,13-trien-18-oic acid (1) to the hydrocarbon (3) and then its subsequent oxidation to the epimeric ketone mixture (6), in which the 5βH-epimer predominated. Translocation of the carbonyl group at C 4 of the ketone (6) via the intermediates (7) and (8), gave the steroid
analogue (10), in low overall yield. A recent reinvestigation of this synthetic sequence by the present author, employing in addition to 7 and 8, the intermediate (9), gave an improved overall yield of the enone (10). In this latter case, the ketone (6) was prepared by oxidation of the mixture of hydrocarbons (containing 40% of 3, 37% of 4 and 23% of 5), which was obtained from the oxidative decarboxylation of abieta-8,11,13-trien-18-oic acid (1) with lead tetraacetate. While oxidative decarboxylation of the acid (1) provided a direct route to the mixture containing the hydrocarbon (3), a serious disadvantage of this procedure was the fact that during the oxidation step to obtain the ketone (6), the isomers (4) and (5), constituting ca. 60% of the alkene mixture, were produced as unusable oxidised by-products. Thus, one part of this thesis is concerned with attempts to employ these alkenes as useful synthetic intermediates. The utilisation of the alkene (4) for the synthesis of 3-oxygenated compounds is an obvious choice for this aim, because it constitutes almost the same proportion of the alkene mixture as does the isomer (3), so that, with the alkene (3), almost 80% of the hydrocarbons obtained from the oxidative decarboxylation of abieta-8,11,13-trien-18-oic acid (1) would then be available as intermediates for the synthesis of 3-oxygenated steroid analogues and diterpenoids.

Since the initiation of this work, other syntheses of 3-oxygenated derivatives of abieta-8,11,13-trien-18-oic acid (1) have been reported. One, by hydroboration-oxidation of the alkene (4),
obtained pure by chromatography of the mixture of 3, 4, and 5 on silver nitrate-silica gel columns, afforded the alcohol (11). The latter was oxidized to the ketone (12), which in turn was epimerised to the ketone (13). 

Biellman and co-workers have reported that bacterial oxidation of abieta-8,11,13-trien-18-oic acid (1) gives the ketone (13), while others have studied a similar oxidation of the methyl ester (2) which yields the keto-ester (14). The hydroxy-ester (15) was obtained by microbial hydroxylation of the ester (2) with the fungus Corticium sasakii.

1.3 The Synthesis of 6-Oxygenated Derivatives of Abieta-8,11,13-trien-18-oic Acid (1)

Although a considerable volume of work has been published on the synthesis and subsequent transformations of 6-oxygenated derivatives of 10α-podocarpa-8,11,13-trien-18-oic acid (16), derived from the deisopropylation of abieta-8,11,13-trien-18-oic acid (1), little progress has been made in the preparation of similar compounds from abieta-8,11,13-trien-18-oic acid (1).

Defaye-Duchateau found that oxidation of methyl abieta-6,8,11,13-tetraen-18-oate (17) with perbenzoic acid did not give an epoxide, but rather gave the C 7-ketone (18) in 47% yield and an addition product, the hydroxy-benzoate (19) in 43% yield. The hydroxy-benzoate (19) could not be converted to the keto-
benzoate (20) by oxidation with active manganese dioxide or with chromic acid, which meant that the C 6 hydroxy group of 19 was too hindered for further transformation. The presence of the 4α-methoxycarbonyl group at C 4 was found to have considerable influence on the course of attack of the peracid on the 6,7-double bond, since peracid oxidation of abieta-6,8,11,13-tetraene (21) gave the C 6-ketone derivative (22) as the sole product. The C 6-ketone in these systems must also be highly hindered since Kupchan et al. found that the C 6-ketone (23), derived from the natural product, taxodione (24), failed to undergo Clemmensen reduction.

The course of peracid oxidation of other C 6,7-unsaturated diterpenoids appears to be similarly influenced by steric and electronic factors. Thus, the unsaturated phenol (25) has been shown to give the epoxide (26). With a 4β-methoxycarbonyl substituent, normal peracid oxidation occurred as was shown by the conversion of the unsaturated ester (28) to the epoxy-ester (29). However, the unsaturated ester (31) gave a mixture of hydroxy-benzoates (32). The compounds (26), (29) and (32) were all catalytically hydrogenolysed to the C 6-hydroxy compounds (27), (30), and (33), respectively. The C 6-ketones (34) and (35) were obtained by oxidation of the corresponding alcohols (27) and (33) with chromic acid.

Brannon et al. showed that microbial hydroxylation of methyl 7-oxo-abieta-8,11,13-trien-18-oate (18) gave the compound (36) with oxygen functions at both C 3 and C 6, while the metabolite (37) was similarly obtained from the diketone (38).
1.4 **Transformation of Abieta-8,11,13-trien-18-oic Acid (1) into Steroids**

To furnish the D-ring of an 18-norsteroid nucleus by addition of three carbon atoms across the C 13, 14 positions of abieta-8,11,13-trien-18-oic acid (1) requires firstly the removal, or modification of the three-carbon side-chain at C 13. The total removal of the C 13-isopropyl group has been the subject of several investigations.

The absorption of oxygen by abieta-8,11,13-trien-18-oic acid (1) has been studied, but only in one case was evidence obtained for a hydroperoxide having been formed at C 15. Autooxidation of methyl abieta-8,11,13-trien-18-oate (2) has been shown to proceed with attack of oxygen mainly at C 7 to form the C 7-oxo derivative (18) and the C 7-hydroperoxide (39), which was reduced to the alcohol (41), with only a small proportion of the product having a hydroperoxide function at C 15. When the C 7-ketone (18) was autooxidized, the hydroperoxide (40) was formed, which upon treatment with ferrous sulphate gave the diketone (38) in 10% yield, with sodium sulphide, the ketol (42) in 35% yield, and with mineral acid, recovery of the phenol (43) in 30-35% yield.

Oxidation of methyl 12,14-dinitro-abieta-8,11,13-trien-18-oate (44) and methyl 14-nitro-abieta-8,11,13-trien-18-oate (45) with chromic acid led only to products in which ring B had been ruptured. However, oxidation of methyl abieta-8,11,13-trien-18-oate (2) with chromic acid has been reported to give the diketone (38) in 17% yield and the keto-acetate (46), also in low yield. The keto-acetate (46) has also been converted to the phenol (59) by a multistage process.
A reverse Friedel-Crafts deisocrotylation of abieta-8,11,13-
trien-18-oic acid (1) gave a mixture of products which was found
by Ohta and Ohmori to contain podocarpa-8,11,13-trien-18-oic
acid (47) in 6% yield, and the 10α-podocarpa-8,11,13-trien-18-oic
acid (16) in 44% yield. An almost identical result was obtained by
Wenkert et al. who deisocrotylated the nitrile (48) with
aluminium chloride to give the product (49) in 9% yield, and the
epimer (50) in 43% yield.

Another study, on the radical bromination of the C 7α-acetoxy
derivative (51), gave the benzylic bromide (52). Acetolysis of
this compound resulted in the formation of the unsaturated ester
(53) which was further oxidised to the keto-ester (54), all in
unstated yields.

In 1966, Indian chemists reported a novel interaction of
abieta-7,13(14)-dien-18-oic acid (abietic acid) (55) with
tetrachloro-α-benzoquinone to form the quinol ether (56), which was
dehydrogenated with chloranil to the adduct (57). Later, in
1968, another publication by the same group describing the pyrolysis
of the ether (57) to the unsaturated acid (58), which was converted
to the phenol (59) in 10% overall yield, added impetus to the
present investigation.
DISCUSSION

2.1 The Reactions of Ring A Epoxides of Abieta-8,11,13-trien-18-oic Acid (1)

This work was undertaken in order to synthesize 3-oxygenated derivatives of abieta-8,11,13-trien-18-oic acid (1) utilising as intermediates the trisubstituted alkene (4), and the tetrasubstituted alkene (5), which together constitute ca. 60% of the alkene mixture from the lead tetraacetate oxidative decarboxylation of the acid (1). Previously, Denny found that selective epoxidation of the methoxy-alkene mixture (60) derived from the lead tetraacetate oxidative decarboxylation of 12-methoxy-podocarpa-8,11,13-trien-19-oic acid (61) with monoperphthalic acid afforded the epoxides (62) and (63), together with the less reactive exocyclic alkene of the mixture. This epoxidation was applied to the alkene mixture obtained from the oxidative decarboxylation of abieta-8,11,13-trien-18-oic acid (1). The reaction gave the pure exocyclic isomer (3) in 70% yield, together with the epoxides (64) and (65). A trace of the epoxide (66) was also produced during this reaction. Its presence was established by t.l.c. and g.l.c. comparisons with an authentic sample prepared by epoxidation of the pure hydrocarbon (3) with perbenzoic acid. The epoxides (65) and (66) were difficult to separate by chromatography of the reaction mixture on deactivated alumina, and they showed identical spots on t.l.c. They were distinguished from each other by g.l.c., and the oily
fractions which showed one main peak of 95%, or greater purity were combined. In this way, the tetrasubstituted epoxide (65) was isolated greater than 95% pure in 65% yield. Several small fractions of the epoxide (65) (homogeneous by g.l.c.) were obtained, and these were used for spectroscopic identification and analysis of the compound. The epoxide (64) derived from the trisubstituted alkene (4) was readily obtained pure in 82% yield. All the epoxides were assigned a configurations by analogy with the corresponding podocarpa-8,11,13-triene derivatives, and from the well-documented assumption of attack from the least hindered side of the molecule. The possibility that the third, and minor epoxide from the above reaction might have been a β-epoxy epimer of either of the epoxides (64) or (65), indistinguishable from the epoxide (66) by g.l.c. was discounted when the products arising from the boron trifluoride rearrangement of the pure epoxide (66) and of the g.l.c. impure fractions of the epoxide (65) (vide infra) were compared.

The exocyclic alkene (3) was oxidized by ozone employing a method developed for the ozonolysis of aromatic steroids, which involved the reaction of one equivalent of ozone with one equivalent of compound. While this method required the use of large quantities of solvents for preparing saturated solutions of ozone, the method was rapid, and the yield of the ketone (6) was high (70%) and consistent. As noted in the Introduction, the ketone (6) has been converted to the enone (10), and this compound has been C-methylated
to form the C 3-ketoditerpenoid (67). Attempts were made to prepare the C 3-oximino - C 4-ketone (68), as it was hoped that zinc-acetic acid reduction of this compound would form the C 3-keto-
C 4-hydroxy compound (69) by analogy with similar reduction of the steroid (70). Dehydration of the ketol (69) would then provide the enone (10) by a three-step non-oxidative route from the C 4-ketone (6). However, oximation of the C 4-ketone (6) with i-pentyl nitrite and dry hydrogen chloride in absolute methanol gave only a 50% yield of the crude oximinoketone (68), which underwent decomposition during attempts to purify it by chromatography on silica gel or on deactivated alumina. The crude oximinoketone (68) was too impure for further transformation. No products were isolated when the ketone (6) was treated with i-pentyl nitrite in t-butanol and potassium t-butoxide.

Attention was then directed towards opening the epoxide ring of 64 in order to obtain an oxygen function at C 3 directly. The opening of epoxides under neutral, acidic, and basic conditions has been the subject of numerous investigations, concerned with both the mechanism of the reactions, and their application to synthetic problems. These reactions give three classes of compounds:

i) trans disubstituted addition products, e.g. diols, halohydrins,
ii) elimination products, e.g. allylic alcohols, alkenes,
and iii) carbonyl compounds.
The nature of the products arising from a neutral (e.g. thermolytic) or an acid-catalysed epoxide opening reaction is governed by the direction of opening of the epoxide ring, and by the fate of the resulting carbonium ion intermediate (the term "carbonium ion" is used here to describe either a fully or partially developed positive centre). The direction of opening of the epoxide ring is determined by factors associated with the stabilisation of the resultant carbonium ion. With conformationally rigid epoxides, in the absence of overwhelming electronic effects, the dominant factor governing the epoxide ring opening is stereochemistry, with cleavage of the epoxide to the axial alkoxide being preferred, as this allows maximum orbital overlap of the negative charge with the vacant p orbitals of the positive centre in the transition state,\(^\text{34}\) e.g.:

![Equatorial Cleavage](image1)

![Axial Cleavage](image2)

**Fig. 1**

When other substituents capable of stabilisation of the carbonium ion by conjugative or inductive effects are close to the epoxide ring, the carbonium ion generated is that on the epoxide carbon atom closest to the electron-donating group.
The fate of the carbonium ion intermediate then determines which class of products is formed. In many cases of epoxide reactions, representatives of two or more of the classes are isolated. Direct trans attack of a nucleophile will give rise to the trans disubstituted products of class (i), viz. diols, halohydrins:

![Diagram](image)

Fig. 2

Compounds of class (ii) are obtained by elimination, which firstly yields an allylic alcohol, which may then undergo dehydration to form a conjugated diene, e.g.:

![Diagram](image)

Fig. 3

Carbonyl compounds of class (iii) arise by migration of a group, R, attached to the alkoxide-bearing carbon atom. If the migrating group is other than a hydride ion, products of rearrangement
of the carbon skeleton ensue, e.g.:

![Diagram of organic compounds](image)

Fig. 4

The relative migratory aptitudes of the R groups determine which will move with conformationally mobile epoxides, but with rigid epoxides, stereochemical factors are again dominant. It is the group perpendicular to the plane of the carbonium ion, and hence that which can attain maximum orbital overlap with the vacant p orbital, which will migrate. In exceptional circumstances, where formation of a transition state leading to a carbonium ion requires considerable energy, and the migrating R group is too far away for facile overlap with the vacant p orbital, Wagner-Meerwein rearrangements may occur by migration of a neighbouring group, rather than migration of the R group on the alkoxide-bearing carbon atom. Such is the case of the reaction of the epoxide (71) with boron trifluoride. Here it is suggested that formation of a carbonium ion at C 5 results in considerable distortion of both rings A and B, which necessitates the C 6 hydride ion to move a greater distance to C 5 to give rise to the ketone (72). Competing migration of the C 10 angular methyl group to C 5 initiated a chain of 1,2 shifts to afford the "backbone-rearranged" unsaturated alcohol (73) in low yield.
The opening of epoxides under basic conditions also gives rise to products of the three classes mentioned above. Nucleophilic opening of the epoxide ring by species such as $\text{OR}^-$ and $\text{NH}_3^-$ affords the trans disubstituted products of class (i).

![Diagram](image)

**Fig. 5**

In the presence of strong bases, the epoxide ring may open by an E2 elimination to give compounds of class (ii), such as allylic alcohols, e.g.:

![Diagram](image)

**Fig. 6**

The carbonyl compounds of class (iii) are formed by the removal of a proton from an epoxide carbon atom to give a carbenoid intermediate. Migration of an R group (as in Fig. 4) may occur to give ultimately the enolate of the ketone, i.e.
With large ring epoxides, transannular migrations have been shown to occur\(^\text{41}\) to give rise to bicyclic alcohols rather than ketonic products, \textit{viz}:

\[\text{Fig. 7}\]

In the present investigation, the 3\(\alpha,4\alpha\)-epoxide (64) was firstly committed to boron trifluoride etherate in benzene for a few minutes at 20\(^\circ\). Two products were formed. The major product (80\% yield) was the \(\alpha\)-noraldehyde (74) which was formed in a manner analogous to that of the aldehyde (75) from boron trifluoride rearrangement of 3\(\alpha,4\alpha\)-epoxy-12-methoxy-18-norpodocarpa-8,11,13-triene (62), \textit{viz}, by cleavage of the C 4–O bond to give the C 3 axial alkoxide and a C 4 tertiary carbonium ion. Migration of the C 2–C 3 \(\sigma\) bond gave the \(\beta\)-aldehyde. The minor product (10\% yield) was the exocyclic allylic alcohol (76), formed by loss of a C 19 methyl proton from the C 4 carbonium ion intermediate rather than by ring contraction which affords the aldehyde (74). The structure of
the allylic alcohol was assigned on the basis of its i.r. spectrum
($v_{\text{max}}$ 1650, 910 cm$^{-1}$, C=CH$_2$), and its n.m.r. spectrum, which showed
two broad signals at $\delta$ 4.72 and 5.05, characteristic of non-
equivalent exocyclic vinyl protons. The C 10 angular methyl signal
was shifted upfield ($\delta$ 0.96) from the normal position ($\delta$ 1.18 –
1.22) as a result of shielding by the double bond, while a signal
at $\delta$ 4.32 could be assigned to the C 3 proton since it was shifted
downfield to $\delta$ 5.37 in the n.m.r. spectrum of the derived acetate
(77). The C 3-hydroxy group was assigned an $\alpha$ configuration from
the diaxial mode of opening of the epoxide ring and from the
half-height peak width (6 Hz) of the C 3$\beta$ proton signal which
suggested the absence of axial-axial coupling of the C 2 and C 3
protons. Further evidence for the structure was obtained from the
deuteriopyridine-induced solvent shifts in the n.m.r. spectrum.
Observed shifts [$\delta$ (CDCl$_3$) – $\delta$ (C$_5$D$_5$N)] of -0.05 p.p.m. for the C 10
angular methyl group, of -0.24 p.p.m. for the C 3$\beta$ proton, and of
-0.08 p.p.m. for one of the exocyclic methylene protons (that
normally at $\delta$ 5.05) were in accord with the structure (76). It
is probable that the exocyclic methylene proton which experienced
the solvent-induced shift of its resonance signal is the one closer
to C 3, and hence closer to the deshielding environment of the
hydroxy-pyridine complex.

The allylic alcohol (76) was produced in better yield (52%)
by treatment of the 3$\alpha$,4$\alpha$-epoxide (64) with refluxing acetone-
aqueous sulphuric acid. The use of polar solvents for epoxide rearrangements generally assists the formation of class (i) and class (ii) products. This reaction also formed the A-noraledehyde (74) in 7% yield, and a hydrocarbon (20% yield), which was not investigated further.

The allylic alcohol (76) was produced more simply but in lower yield (20%) by chromatography of the epoxide (64) on activated alumina. Evidently, the isomerisation is initiated at active sites of the alumina, and one or more of the following reactions takes place:

(i) hydration to form a vicinal diol,
(ii) rearrangement to allylic alcohols, and
(iii) rearrangement to a carbonyl compound.

Similar production of allylic alcohols has been observed by Dev et al. and by Nigam and Levi. Thus limonene oxide (78) was isomerised by basic active alumina to the exocyclic allylic alcohol (79) in 33% yield, and to trans-carveol (80) in 28% yield, while α-pinene oxide (81) gave pinocarveol (82) in 63% yield, with very little of the other products having a rearranged carbon skeleton. That no isomeric allylic alcohols, or skeletally rearranged products were produced during the active alumina catalysed isomerisation of the epoxide (64) may be attributed to the specific activity of the alumina employed, and to the rigid shape of the epoxide molecule.
The epoxide (64) was inert towards sodium hydroxide and sodium methoxide, even in the base strength-enhancing solvent, dimethyl sulphoxide. However, treatment of the epoxide (64) with the strong base, lithium diethylamide, afforded the desired allylic alcohol (76) in quantitative yield. The very high stereoselectivity of this reaction is in agreement with the recent results of Rickborn and Thummel. The bulk of the relatively large lithium diethylamide base undoubtedly plays a major role in determining the course of the reaction with a conformationally rigid epoxide. The reaction is known to proceed by an $E_2$, and probably syn elimination. Electronic effects, i.e. the enhanced "acidity" of primary over secondary and tertiary hydrogen, may also contribute to the high specificity of the elimination reaction. Examination of a Dreiding model of the epoxide (64) in the light of these facts shows that of the possible hydrogen atoms available for an $E_2$ elimination, viz. those at C 2, C 5, or C 19, those at C 19 will be attacked preferentially, from either the $\alpha$ or $\beta$ face of the molecule, by the diethylamide anion to afford the exocyclic allylic alcohol (76) as the sole product.

A number of oxidations of the allylic alcohol (76) were attempted. In keeping with its axial conformation, oxidation of the C 3 hydroxy group was slow. Oppenauer oxidation with aluminium isopropoxide and cyclohexanone left the alcohol largely unaffected. The allylic C 3$\alpha$- and C 3$\beta$- alcohols (83) have been shown to be readily oxidised to the enone (84) with aluminium isopropoxide and acetone.
In the present case, with the exo-methylene function at C 4, it seems probable that steric hindrance inhibits the formation of an aluminium chelate of the alcohol (76) and cyclohexanone, rendering the transfer of the C 3β hydride ion difficult. Active manganese dioxide in chloroform also failed to oxidize the allylic alcohol (76), although numerous examples exist where this reagent has been employed for the oxidation of Δ⁴ C 3α- and C 3β- hydroxy steroids and other allylic alcohols. A similar result was observed when 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was used as the oxidant. Rate studies on the oxidation of steroidal Δ⁴ C 3α- and C 3β- alcohols with DDQ have shown that the equatorial epimer is oxidized faster than the axial epimer, a fact which has been attributed to favourable σ-π overlap of the departing axial hydride in the case of the former. Detailed analysis of the thermodynamic parameters showed that the cause of the rate difference appeared in the Δ S⁺ term, rather than in the Δ H⁺ term. The large negative entropy of activation was regarded as a measure of the need for a highly specific mutual orientation of the reactants in the activated complex. The lack of reactivity in the present case is thus, again, probably due to steric hindrance, where the favourable orientation of the quinone and the allylic alcohol cannot be achieved owing to the presence of the C 4 exomethylene function. A similar result has been reported by Djerassi et al., who found the axial allylic alcohol (85) to be inert towards 2,3-dichloro-5,6-dicyanobenzoquinone.
Stronger oxidants such as Jones reagent or chromium trioxide-pyridine complex in methylene dichloride gave complex mixtures from which only the starting alcohol (76), the cisoid enone (86), and the epoxy-ketone (87) were obtained in low yield after chromatography on alumina. The epoxy-ketone (87) was identified by direct comparison with the compound obtained by oxidation of the allylic alcohol (76) with m-chloroperbenzoic acid to give the cis-epoxy alcohol (88) followed by oxidation with Jones reagent or with chromium trioxide-pyridine complex. Formation of an epoxy ketone during oxidation of the alcohol (76) with Jones reagent is in accord with the results of Glotter et al., who suggest that during the oxidation of axial allylic alcohols which would normally give rise to cisoid enones, oxygen transfer from the chromate ester of the alcohol to the double bond occurs to give initially an epoxy alcohol in which the epoxide ring has the same configuration as the original hydroxy group. Further oxidation then leads ultimately to the epoxy ketone, viz:

![Chemical structure](image)

Fig. 9

Glotter et al. found that chromium trioxide can act as an epoxidising agent only under acidic conditions, i.e. the reactive
species is a mono-ester of "chromic acid". However, in the present case, the epoxy ketone (87) was isolated when the oxidation was carried out under acidic (Jones reagent) or weakly basic (dipyridine-chromium VI oxide in methylene dichloride) conditions. This means that a sufficiently electrophilic oxygen-containing species must have been formed to effect the cis-epoxidation of the double bond. One explanation is that the alcohol and the chromium trioxide-pyridine complex react to form a chromate ester, the proton of the hydroxy group being transferred to the chromium species, thus providing the necessary intermediate to effect the cis-epoxidation, viz:

![Diagram of molecular structures]

Fig. 10

When the oxidation of the allylic alcohol (76) was carried out with chromium trioxide in pyridine solution, the technical difficulties encountered during the work-up procedure forbade the isolation of any products. The other products which were formed during the chromium VI oxidations of the allylic alcohol (76) presumably arose by over-oxidation of the enone (86) or the epoxy ketone (87), or by decomposition of these during chromatography. Attempts were made to
reduce the epoxy ketone (87) with chromous chloride\textsuperscript{65} which gave low to moderate yields of the cisoid enone (86).

A number of oxidations of the allylic alcohol (76) were attempted with dimethyl sulphoxide in the presence of other reagents. No oxidation was found to occur when the reactions were carried out in the presence of acetic anhydride,\textsuperscript{66} phosphoric acid,\textsuperscript{67} or dicyclohexylcarbodiimide.\textsuperscript{68} In contrast to the above oxidations, treatment of the allylic alcohol (76) with dimethyl sulphoxide in combination with pyridine-sulphur trioxide complex and triethylamine\textsuperscript{69} gave the enone (86) in 90\% yield. The oxidation was extremely rapid. The reaction pathway which has been postulated\textsuperscript{69} involves the reaction of dimethyl sulphoxide with the sulphur trioxide complex to form dimethylsulphoxonium sulphate, which reacts with the allylic alcohol to form a complex sulphate. Attack at the C 3\& hydrogen by the base then displaces the complex sulphate to afford the enone (86). Dimethyl sulphide is also formed. The i.r. spectrum of the enone (86) showed a carbonyl peak at 1695 cm\textsuperscript{-1} corresponding to cisoid conjugation, while its n.m.r. spectrum still showed two vinyl proton signals of the exocyclic double bond (δ 5.20 and 5.95). However, the cisoid enone (86) was not particularly stable, and an attempt to convert it to the transoid enone (89) with anhydrous oxalic acid in absolute ethanol gave hydrocarbon and intractable products. It is probable that dimerisation rather than double bond isomerisation had occurred to some extent, as in the case for the reaction of 2-methylenecyclohexanone with oxalic acid.\textsuperscript{70}
In view of the preceding result, an attempt was made to isomerise the double bond of the allylic alcohol (76) to the C 4 endocyclic position before carrying out an oxidation. With oxalic acid this resulted, as expected, in rapid dehydration to an unstable unsaturated hydrocarbon while attempted isomerisation of the derived acetate (77) with dry hydrogen chloride in chloroform or with toluene-2-sulphonic acid in refluxing dioxane was unsuccessful. The alcohol (76) could be isomerised with N-lithioethylenediamine but after a reaction time of ca. 2 hr this afforded a 90% yield of the unsaturated alcohol (90) in which the double bond had become conjugated with the aromatic ring. Its structure followed from the n.m.r. spectrum which showed a C 4 methyl doublet at $\delta$ 1.22 ($J_7$ Hz), a doublet of doublets at $\delta$ 6.06 ($J_{6,7}$ 10 Hz, $J_{5,6}$ 6 Hz) corresponding to the C 6 vinyl proton and a doublet at $\delta$ 6.37 ($J_{6,7}$ 10 Hz) corresponding to the C 7 vinyl proton. The C 4 methyl group was assigned an $\alpha$ configuration since it showed an identical chemical shift in the n.m.r. spectrum with that of the C 4$\alpha$ methyl group of the saturated alcohol (91) (vide infra). Since no allylic coupling between the C 7 proton and the C 5 proton was observed, the A/B ring junction is almost undoubtedly cis. When the reaction time was reduced to 5 min, however, a new allylic alcohol (92) was obtained in almost quantitative yield. The i.r. spectrum of this alcohol showed a band at 980 cm$^{-1}$ due to the C - O stretch of an allylic alcohol [cf. $v_{max}$ 980 cm$^{-1}$ for compound (76)] but unlike its isomer (76) no
band in the 910 cm\(^{-1}\) region corresponding to an exocyclic double bond was observed. Its n.m.r. spectrum showed a deshielded C 10 angular methyl signal at \(\delta 1.32\), and a C 4 vinyl methyl signal at \(\delta 1.80\). Formation of the alcohols (90) and (92) from the compound (76) extends the application of N-lithioethylenediamine as a reagent not only for the migration of double bonds away from hydroxyl groups,\(^{74}\) but also for the isomerisation of exocyclic allylic alcohols to endocyclic allylic alcohols (vide infra). These results indicate that the isomerisation is a step-wise one, the double bond migrating one carbon atom at a time. The reaction pathway as proposed by the original investigators\(^{72}\) involved a nine-membered cyclic transition state, in which a proton was transferred from one end of the ethylenediamine anion bridge to the other, \textit{viz}:

\[
\text{LiO}^\cdot \\
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{N} \\
\text{N} \\
\text{H} - \text{N} - \text{CH}_2 - \text{CH}_2
\end{array} \rightarrow \text{LiO}^\cdot \\
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{N} \\
\text{N} \\
\text{H} - \text{N} - \text{CH}_2 - \text{CH}_2
\end{array} + \text{HNC}_2\text{H}_2\text{NH}_2
\]

\text{Fig. 11}

However, it is more likely that the strongly basic N-lithioethylenediamine firstly removes the allylic proton at C 5 to form a lithium alkyl (the hydroxy group also being converted to the lithium alkoxide). The lithium alkyl then reacts with a molecule of ethylenediamine to
form the N-lithioethylenediamine and the isomerised alkoxide, i.e.:

\[
\text{H - N - CH}_2\text{-CH}_2\text{-NH}_2
\]

Repetition of the process on the alcohol (92) would then form a lithium alkyl at C 6 which would ultimately give the compound with the double bond at C 5, and so on. The high isomeric purity of the allylic alcohol (92) obtained from the brief isomerisation reaction implies that all the compound present is converted to one isomer before the next isomerisation begins. That both the hydrogen atoms at C 5 and C 6 of the compound (90) have a \( \beta \) configuration indicates that the proton was transferred from the ethylenediamine molecule to the most hindered \( \beta \) face of the substrate molecule during the consecutive isomerisations. This was probably because the \( \alpha \) side of the molecule was occupied with solvent molecules solvating, by hydrogen bonding, the C 3a axial alkoxide.

Like the alcohol (76), the endocyclic allylic alcohol (92) was inert towards active manganese dioxide, but in contrast it was oxidised smoothly with Jones reagent to give the \( \alpha,\beta \)-unsaturated ketone (89)\(^7\) in 80% yield. This result is in agreement with those
from other chromic acid oxidations of allylic alcohols which yield transoid enones.\textsuperscript{55} No epoxy ketone was produced. The spectroscopic characteristics of the ketone ($v_{\text{max}}$ 1660 cm$^{-1}$; $\delta$ 1.54, deshielded C 10 methyl, and 1.88, vinylic C 4 methyl) were in accord with those expected for the structure (89). Methylation of the ketone (89) with methyl iodide-potassium t-butoxide\textsuperscript{76} in t-butanol or with methyl iodide-potassium 2-methyl-2-butoxide in benzene,\textsuperscript{77} followed by chromatography on alumina gave the $\beta$,Y-unsaturated ketone (67) in 68-74\% yield. The product was identical with that from similar methylation of the enone (10).\textsuperscript{1} The n.m.r. spectrum of the ketone (67) showed a C 10 angular methyl signal at $\delta$ 1.20, shifted considerably upfield from that of the enone (89), which implies that the C 10 methyl group has become shielded by the C 3 ketone, and that ring A has adopted a boat or half-boat conformation.\textsuperscript{78} This was verified by the rotatory dispersion curve which showed a positive Cotton effect. Application of the octant rule\textsuperscript{79} shows that a positive Cotton effect will be observed only if ring A adopts a boat, or near-boat conformation.

The ketone (67) was moderately air sensitive. A sample of the oily ketone which was kept at room temperature in contact with light and air for a period of one month became solid. The product was identified as the enedione (93). The compound undoubtedly arises by aerial oxidation of the activated C 7 position to form initially a hydroperoxide\textsuperscript{19} which spontaneously decomposes to the C 7- ketone
and water. A similar observation of the air sensitivity of the C 5-unsaturated diterpenoid (94) was made by Wenkert et al.\textsuperscript{80} but the autooxidation product was not isolated.

A number of catalytic hydrogenations of the \( \beta,\gamma \)-unsaturated ketone (67) were performed, employing both platinum and palladium catalysts. The catalytic hydrogenation of C 5 unsaturated diterpenoids has been found to give rise to trans A/B products.\textsuperscript{75,80,81} This is to be expected, since the diterpenoid skeleton is rigid, and the \( \beta \) face is too sterically crowded for the molecule to lie with the \( \beta \) face on the catalyst surface.\textsuperscript{82} Only two exceptions have been reported, viz. the catalytic hydrogenation of the keto-enol lactones (95)\textsuperscript{42a,83} and (96),\textsuperscript{84} which gave rise to cis A/B reduced products, although the catalytic hydrogenation of 95 was originally reported to have given a product with trans A/B stereochemistry.\textsuperscript{85} The ease of hydrogenation of different C 3 keto- C 5 unsaturated diterpenoids appears to be dependent on the actual diterpenoid. Thus Taylor\textsuperscript{81c} has stated that the compound (97) is hydrogenated rapidly over palladium on carbon, whereas Stork et al.\textsuperscript{81b} found that the compound (98) was hydrogenated over palladium on carbon only very slowly. In the present case, hydrogenation of the ketone (67) over 10\% palladium-carbon, or over platinum oxide barely proceeded at all. The oily products obtained still showed vinyl proton signals in the n.m.r. spectra. In contrast, hydrogenation over a 20\% palladium-carbon catalyst was fairly rapid, and two products were formed. The
total reduction product could be crystallized, but the two components
viz. the C 5αH and C 5βH ketones (99) and (100), repeatedly
crystallized together in the ratio of ca. 3:1 as a constant melting-
point mixture which could not be separated by chromatography. As
mentioned earlier, the ring A conformation of the β,γ-unsaturated
ketone (67) is a boat, or half-boat, as is apparent from its n.m.r.
spectrum and rotatory dispersion curve. This conformation of the
C 3-keto, C 5-unsaturated diterpenoid (67) is contrary to the chair
form depicted by Stork \(^{31b}\) for the compound (98). With a ring A
boat conformation, the ketone (67) has methyl groups both at C 10
and C 4 projecting perpendicularly from the plane of the molecule,
viz:

![Diagram](image)

Fig. 13

This shape of the molecule would make its adsorption on the catalyst
surface difficult, which could explain the reluctance of the double
bond to undergo hydrogenation using 10% palladium-carbon. The boat
conformation and the projecting methyl group at C 4 confer a concave
shape to the α face of the molecule, which may force it to lie with
the β face on the surface of the catalyst [cf. the compounds (95)
and (96)]. With larger metal atom clusters in the catalyst, (20%
palladium carbon), \(^{86}\) the reduction would be expected to be greatly
facilitated, which is observed. The cis A/B reduced product (100) may arise directly by hydrogenation from the β face of the compound (67), or, more likely, by isomerisation of the C 5 double bond to C 6 during the hydrogenation. This occurs by the adsorption of the α face of the molecule onto the catalyst surface. Transfer of a hydrogen atom to C 6 would generate a carbon-metal "bond" at C 5. Loss of a proton from C 7, and transfer of a hydride ion from C 6 to C 5 across the β face would then give rise to a C 6 unsaturated compound with the hydrogen atom at C 5 having a β configuration. All these processes occur while the molecule is adsorbed onto the surface of the catalyst. Hydrogenation of the C 6 double bond would then give rise to the ketone (100). Normal hydrogenation affords the expected ketone (99).

Fig. 14
An almost identical result was obtained for the hydrogenation of the enone (101) which gave an oily mixture of the two epimeric ketones (102).  

Brannon et al. claimed to have prepared the ketone (99) (\(^{13}C\) 284) by hydrolysis and decarboxylation of the keto-ester (14). Their ketone must be the monomethyl ketone (13), (\(^{13}C\) 270), as the gem dimethyl group cannot be formed during hydrolysis and decarboxylation of the keto ester (14). It appears that they have calculated the molecular weight from the wrong diagram for the structure (13).

An attempt was made to effect trans diaxial opening of the epoxide ring of the 3α,4α-epoxide (64) with methylmagnesium iodide. However, this reaction afforded as the major product (56%), a mixture of epimeric alcohols (103) which was the same as that produced by independent treatment of the A-noraldehyde (74) with methylmagnesium iodide. The intermediate A-noraldehyde clearly arose as a result of the opening of the epoxide ring by magnesium bromide etherate, a Lewis acid, present in the solution of the Grignard reagent. Attack of the carbonyl group by the Grignard reagent then affords the alcohols. Oxidation of the alcohol mixture with Jones reagent gave the C 4 methyl ketone (104) which was reconverted to the same alcohol mixture (103) on reduction with sodium borohydride. A further product (30%) from the reaction of the Grignard reagent on the epoxide (64) was identified as the allylic alcohol (92), arising by loss of a proton from C 5 rather than by C 2 - C 3 σ bond migration.
which leads to the A-noraldehyde (74).

Reduction of the epoxide (64) with lithium aluminium hydride in ether proceeded slowly to give the C 3α alcohol (91), which may be regarded as a trans disubstituted product of class (i). The slow rate of the above reaction is due to hindrance by the C 10 methyl to approach from the β face of the molecule by the AlH₄⁻ anion.⁹¹ Oxidation of the alcohol (91) with Jones reagent gave the ketone (13). The C 4α methyl group configuration of this ketone was confirmed by a positive Cotton effect in the rotatory dispersion curve, and from the fact that no epimerisation occurred on treatment of the compound with base.

With the aim of forming a C 4-hydroxy C 3-ketone, the 3α,4α-epoxide (64) was oxidised with dimethyl sulphoxide-boron trifluoride.⁹² Boron trifluoride etherate reacts with dimethyl sulphoxide (DMSO) to form a strongly bound complex.⁹³ This complex in its dissociated form, i.e. free BF₃ and DMSO, then opens the epoxide ring to form a boron alkoxide and a carbonium ion, which is attacked by the dimethyl sulphoxide to form an hydroxy ketone and dimethylsulphide.⁹⁴ Oxidation of terminal sugar epoxides with boron trifluoride-dimethyl sulphoxide has been shown to give aldehydes as products.⁹⁵

In the present case, a diverse range of products was formed. None of the desired hydroxy ketone (105) was obtained after separation of the products by chromatography. The first product was
an aromatic hydrocarbon (11%) which was identified as retene (106). Its formation may be explained as follows (see Fig. 15). The epoxide ring of 64 may be opened by boron trifluoride to give initially an allylic alcohol, which then dehydrates to form a conjugated diene, an example of a class (ii) reaction product. Dimethyl sulphoxide is known to decompose on heating for an extended period of time with a variety of other compounds, including acids and bases, to form formaldehyde and methyl thiol. French chemists have found that hydroaromatic systems undergo aromatisation when heated with thiols and sulphides. The reaction is believed to proceed by thermal homolysis of the thiol or sulphide to form radicals, which then abstract hydrogen atoms from the substrate. Thus, during the oxidation of the epoxide (64) with boron trifluoride-dimethyl sulphoxide, conditions exist for the formation of methyl thiol, and for the formation of MeS radicals. By successive removal of hydrogen atoms and the C 10 methyl group as a methyl radical, the diene would be ultimately converted to retene (106).

![Chemical structures](image)

**Fig. 15**

The second product obtained from the above reaction was the ketone (13). This compound arises by the electronic shifts as depicted in Fig. 4 (R = H).
A third product isolated from the above oxidation was a yellow ketonic oil (3%) for which the structure (107) is assigned on the basis of its i.r., n.m.r., and mass spectra. A dienone (109) was also obtained by Japanese chemists who studied the dimethyl sulfoxide-trifluoroacetic acid oxidation of the epoxy ketone (108). The dienone (107) may arise as follows. Opening of the epoxide ring of 64 firstly gives the cisoid diene as in Fig. 15. Since water is produced in these reactions, this can react with boron trifluoride in various proportions to form strong acids. Acid catalysed isomerisation of the cisoid diene to the more stable transoid diene (Fig. 16) can then occur, followed by oxidation at C 3 by dimethyl sulphoxide to initially form a C 3-allylic alcohol, which is then oxidised by another molecule of dimethyl sulphoxide to give the dienone (107).
Evidence for the intermediacy of the diene (111) in this oxidation was obtained by treating the hydrocarbon (111), obtained from the action of boron trifluoride in benzene on the 4α,5α-epoxide (65) (vide infra), with dimethyl sulfoxide, boron trifluoride etherate, and water at 100° for 22 hr. The t.l.c. and the i.r. spectrum of the product showed the presence of hydrocarbons [probably containing retene (106)], and the dienone (107).

The final product obtained from the above reaction was the allylic alcohol (76) (40%) formed by opening of the epoxide (64) ring to the C 3 alkoxide and loss of a proton from the C 4 methyl group.

It is evident that boron trifluoride rearrangement of epoxides is highly sensitive to the nature of the solvent in which the reaction is being conducted. A similar result to the above was reported recently by Hartshorn et al.¹⁰¹ who found that changing the solvent from benzene to diethyl ether for the boron trifluoride rearrangement of the epoxide (110) markedly affected both the rate of the reaction and the types of product isolated. The rearrangement in benzene was found to be fast, and ketonic products were isolated, while the rearrangement in diethyl ether was slow, and a fluorohydrin was formed as the major product.¹⁰¹

Three general properties of the boron trifluoride-dimethyl sulfoxide reagent are evident from the results detailed above.
These are:

i) Formation of the hydroxy ketone, the expected product, is dependent on the direction of opening of the epoxide ring, and of the fate of the carbonium ion intermediate formed. If elimination occurs faster than attack of dimethyl sulphoxide at the positive centre, then no hydroxy ketone is formed.

ii) Use of the polar reaction medium favours the formation of polar products, viz. allylic alcohols, and

iii) Skeletal rearrangements are fully suppressed, and proton and hydride ion shifts become dominant.

These properties are substantiated in the boron trifluoride-dimethyl sulphoxide rearrangements of the di- and tetra-substituted epoxides (66) and (65). It is important to add, that no reaction occurs between the epoxide (64) and boron trifluoride-dimethyl sulphoxide at 20°, since the BF₃ molecule is strongly coordinated to the solvent, and is unavailable for coordinating to the epoxide oxygen atom. By heating the reaction mixture to ca. 80-90°, the complex dissociates, and the reaction takes place.

Attention is now directed towards some rearrangements of the di- and tetrasubstituted epoxides (66) and (65). In particular, the aim here was to attempt to convert the tetrasubstituted epoxide (65) to 3-oxygenated compounds. The success of this transformation would mean that the total products from the lead tetraacetate oxidative decarboxylation of abieta-8,11,13-trien-18-oic acid (1) could be used
as relays for the synthesis of 3-oxygenated compounds.

The tetrasubstituted epoxide (65) was rearranged with boron trifluoride in benzene to give three products. The least polar product was a hydrocarbon, identified as the pentaene (111), and formed by opening of the epoxide ring to give a tertiary C 4 carbonium ion and a C 5 axial alkoxide. Loss of a proton and water affords the hydrocarbon (111). This hydrocarbon was unstable in air, and it is likely that it rapidly undergoes autooxidation in a fashion similar to that of the ketone (67) to the enedione (93), but no identifiable products were isolated.

Two ketones were also formed. It was difficult to decide whether the minor ketone had the structure (112) or (113). Hikino et al.\textsuperscript{102} were confronted with a similar uncertainty in deciding whether a ketone from the boron trifluoride rearrangement of the epoxideudesmane (114) had the structure (115) or (116). They decided on the structure (115) for their ketone on the evidence of small solvent-induced shifts of the methyl group signals in the n.m.r. spectrum. In the present case, the ketone in question showed a carbonyl band at 1700 cm\textsuperscript{−1} in the i.r. spectrum, indicative of a seven-membered ring ketone.\textsuperscript{103} The n.m.r. spectrum showed two methyl singlets at δ 1.17 and δ 1.35. The signal at δ 1.17 was assigned to the C 10 methyl group, and the one at δ 1.35 to the C 4/5 methyl group, the former being shielded, and the latter deshielded
by the carbonyl group, but these data cannot differentiate between the structures (112) and (113). The ketone showed a strong negative Cotton effect in its rotatory dispersion curve, but this result cannot be used to distinguish between the structures either, since the octant rule predicts a negative Cotton effect for the cycloheptanone (112)\(^{104}\) and the cyclohexanone (113). For this comparison, the conformation of ring B of the ketone (112) was assumed to exist in the skew-boat form, this being of lower energy than the chair form of cycloheptanones.\(^{105}\) Whitlock and Overman\(^{106}\) have synthesized the ketone (117) by alkylation of the enol benzoate (118). They found the chemical shifts of the C 10 methyl group, and the C 5 methyl group in the n.m.r. spectrum were \(\delta 1.10\) and \(1.25\). Since the ketone (117) showed methyl group resonances considerably different from those (\(\delta 1.17, 1.35\)) of the ketone in question, and since the ketones (113) and (117) would be expected to have almost identical signals in the n.m.r. spectra for their C 10 and C 5 methyl groups,\(^{42a}\) then it appears that the minor ketone obtained from the boron trifluoride rearrangement of the epoxide (65) can be assigned the structure (112).

It was hoped to synthesize the ketone (113) from the ketone (6) using the method of angular methylation described by Whitlock and Overman.\(^{106}\) A direct comparison between the ketone (113) and the ketone from the rearrangement reaction would then enable the structure to be unequivocally assigned. However, enol benzoxylation of the C 4 ketone (6) with benzoic anhydride gave a 1:1 mixture of the enol
benzoates (120) and (121), contrary to the findings of Whitlock and Overman who stated that enol benzylation of the ketone (119) gave solely the enol benzoate (118). An attempted alkylation of the enol benzoate mixture (120) and (121) with Simmon-Smith reagent unfortunately gave a complex mixture from which none of the desired ketone (113) could be obtained. Mechanistically, the ketone (112) arises from the C 4 carbonium ion - C 5 alkoxide with migration of the C 5,10 σ bond. Thus both the pentaene (111) and the ketone (112) are formed by the expected axial opening of the epoxide (65).

The major ketone from the boron trifluoride rearrangement of the epoxide (65) was identified as the indanone (122). This compound arises by equatorial opening of the epoxide to give the C 5 carbonium ion (see Fig. 17). Migration of the C 9,10 bond, either synchronous with or after the opening of the epoxide ring, then gives a rearranged carbonium ion. Loss of BF₃ by the electron shifts shown affords the unsaturated ketone (122).

![Diagram](image)

**Fig. 17**

The presence of the double bond in the compound (122) was demonstrated by its catalytic hydrogenation to the saturated ketone (123). Denny.
assigned to the ketones from the boron trifluoride rearrangement of the epoxide (63) the structures (124) and (125). Re-examination of the n.m.r. data for the ketone (125) has shown this structure to be incorrect. The correct structure has been shown to be (126), confirmed by its catalytic hydrogenation to the ketone (127). 88

It was of interest to examine the boron trifluoride-dimethyl sulfoxide reaction on the epoxide (65) to see if the extensive rearrangements which occurred with boron trifluoride in benzene would be suppressed. Indeed, this was found to be so. The reaction of the tetrasubstituted epoxide (65) with boron trifluoride-dimethyl sulfoxide gave retene (106), the dienone (107), and the allylic alcohol (128) as the only identifiable products. The dienone (107) was formed in 24% yield. This higher than expected yield [cf. the yield of dienone (107), (8%), from BF₃-DMSO on the epoxide (64)] of the dienone (107) is because the postulated intermediate, the diene (111), formed in 30% yield during the boron trifluoride in benzene rearrangement of the epoxide (65), would also be expected to be formed in comparable, if not higher yield in the dimethyl sulfoxide medium. The allylic alcohol (128) is formed by loss of a proton from the C 4 methyl group of the C 4 carbonium ion intermediate.

The allylic alcohol (128) was produced in 60% yield by reaction of the epoxide (65) with lithium diethylamide. Starting material was also recovered. The alcohol was formed in a manner entirely analogous with that of the allylic alcohol (76) from the epoxide (64),
i.e. by attack at C 19 by the diethylamide anion and displacement of the epoxide ring to the axial C 5 alkoxide. The n.m.r. spectrum of the allylic alcohol unexpectedly exhibited a deshielded C 10 angular methyl signal at $\delta \ 1.32$. In the chair conformation (see Fig. 18) for ring A of the allylic alcohol (128) the C 10 methyl group will lie within the shielding region of the double bond, and hence should show an upfield shift for the C 10 angular methyl group signal [cf. the n.m.r. spectrum of the allylic alcohol (76)].

Examination of a Dreiding model of the allylic alcohol (128) shows that in the chair form, the C 5 hydroxyl group suffers severe 1,3 interactions between the C 3 and C 7 hydrogen atoms. By twisting ring A into a flattened chair form, this unfavourable interaction is partially relieved, and the C 10 methyl group moves out of the shielding region of the C 4 double bond.

![Fig. 18](image)

The allylic alcohol (128) could not be deoxygenated to the hydrocarbon (129) by displacement of the pyridinium sulphate derivative $^{107}$ of the alcohol with lithium aluminium hydride. This is because the C 10 angular methyl group inhibits attack at C 5 from the $\beta$ face by the $\text{AlH}_4^-$ anion.
The double bond of the allylic alcohol (128) was isomerised with N-lithioethylenediamine to the C 3 position to give the allylic alcohol (130). The n.m.r. spectrum of this allylic alcohol (130) also showed a C 10 angular methyl signal at $\delta$ 1.32. Since the A ring of the alcohol (130) is flattened by the $sp^2$ centres in the ring, and since both the alcohols (128) and (130) show identically deshielded C 10 methyl signals in their n.m.r. spectra, this is further evidence for the flattening of ring A of the allylic alcohol (128).

The allylic alcohol (130) was treated with diborane, followed by chromic acid oxidation of the resulting borane$^{108}$ with the aim of preparing the ketol (131), which on dehydration would afford the enone (89). None of the desired ketol (131) was isolated. The product was identified as the diketone (132), formed by dehydration of the boron alkoxide$^{109a}$ of the allylic alcohol (130) to give initially the conjugated diene (111). Thus diborane behaves as a Lewis acid in a manner similar to that of boron trifluoride,$^{109b}$ and this dehydration parallels the reaction of the epoxide (65) with boron trifluoride to give initially the allylic alcohol (130) which dehydrates to the diene (111). Addition of diborane to the diene (111) would then give the C 3, C 6 di-borane, which on chromic acid oxidation gave the C 3,6-dione. Similar formation of 1,4-diketones has been reported during the hydroboration of other 1,4 difunctionalized systems.$^{108}$
The disubstituted epoxide (66) was rearranged with boron trifluoride in benzene to give as the main product a mixture of two epimeric aldehydes (133) and (134) in the ratio of ca. 1:3. The axial aldehyde (133) was epimerised to the equatorial aldehyde (134) during chromatography of the reaction product on deactivated alumina. The formation of the C 4-aldehydes indicates that the initial step in the reaction is cleavage of the C 4-O bond to give the more stable tertiary carbonium ion. The fact that a mixture of epimeric aldehydes is produced shows that the resulting hydride migration is non-stereospecific, and that the C 19-alkoxide is free to rotate during the reaction. This implies a discrete process involving a fully developed carbonium ion, as proposed by Hartshorn and coworkers to explain similar results from the reaction of exocyclic steroid epoxides. A minute amount of a 1:1 mixture of the allylic alcohols (135) and (136) was also produced during the rearrangement. These were formed by loss of the C 3 and C 5 axial protons rather than by migration of a C 19 hydride to form the aldehydes (133) and (134). The aldehyde (134) has been previously prepared by Huffman and Stockel, but it had not been fully characterised.

The epoxide (66) was also committed to the boron trifluoride-dimethyl sulfoxide reagent. This reaction gave, in addition to retene (106) (10%) and the dienone (107) (3%), the aldehyde (134), and the two allylic alcohols (135) and (136) (38%). Thus, as expected, changing the solvent from benzene to dimethyl sulfoxide gave a greater yield of the allylic alcohols and reduced the yield of the
aldehyde. The formation of retene (106) and the dienone (107) in this reaction is hard to explain, since opening of the epoxide ring to either a C 4 or C 19 alkoxide gives an intermediate which cannot immediately eliminate to a diene. It is essential to rearrange the epoxide (66) to a cisoid diene similar to that in Fig. 15, and this may be achieved by the following alternative pathways (see Fig. 19). Opening of the epoxide ring to give the tertiary carbonium ion, followed by a C 5 hydride shift would give the rearranged carbonium ion which can eliminate to give the cisoid diene (i). Otherwise, opening of the epoxide ring to give the primary carbonium ion, followed by a 1,3-hydride shift would give the more stable secondary carbonium ion which can eliminate to the cisoid diene (ii). Isomerisation of either of the cisoid dienes depicted will give the transoid diene (111).
In contrast to the allylic alcohols (76) and (92), the mixture of the allylic alcohols (135) and (136) was smoothly oxidized with active manganese dioxide to a 1:1 mixture of the α,β-unsaturated aldehydes (137) and (138). These aldehydes were unstable, as they could not be obtained entirely free from polar decomposition products (t.l.c.) after chromatography on deactivated alumina or silica gel.
Summary of the Reactions of the Epoxides (64), (65), and (66) with:

a) Boron Trifluoride in Benzene

b) Boron Trifluoride in Dimethyl Sulphoxide
2.2 The Synthesis of 6-Oxygenated Derivatives of Abieta-8,11,13-trien-18-oic Acid (1)

The work described in this section is concerned with the introduction of oxygen functions, and in particular, a ketone at the rather inaccessible C 6 position of abieta-8,11,13-trien-18-oic acid (1). Compounds functionalised as such could prove to be useful intermediates for the synthesis of other naturally occurring diterpenoids having oxygen substituents at C 6. One, the C 6-ketone (24) has recently been reported to possess anticarcinogenic properties. The introduction of a ketone at C 6 would also provide the molecule with a non-hindered, highly activated C 7 carbon for facile substitution, e.g., oximation, halogenation at that position.

The starting material chosen for these transformations was the C 7-keto ester (18). Abieta-8,11,13-trien-18-oic acid (1) was esterified quantitatively with diazomethane and the methyl ester (2) was oxidized with chromium trioxide in glacial acetic acid. After initial trials, the highest yield of the C 7-keto ester (18) realised was 68% by allowing the reaction to proceed at 0–4°C for several days. In this manner, although a small amount of the starting ester (2) was invariably recovered, the amount of the by-products (38) and (46) was minimised.

The first approach was via the C 5βH ester (139), since Wenkert et al. have shown that chromium trioxide-acetic acid oxidations of diterpenoid A/B cis systems give rise to C 6,7-diketones,
while A/B trans diterpenoids give only C 7-monoketones, although Grove and Riley\textsuperscript{113} have shown that vigorous chromic acid oxidation of methyl abiet-8,11,13-trien-18-oate (2) gave a low yield of methyl 5α-hydroxy-6,7-dioxo-abieta-8,11,13-trien-18-oate (140) together with some unidentified products. The oxidation of A/B cis diterpenoids to C 6,7-diketones by chromic acid appears to be highly sensitive to the stereochemistry of the molecule, since Ghatak et al.\textsuperscript{114} have recently shown that oxidation of the A/B cis 20-norditerpenoids (141) and (142) gave only the monoketones (143) and (144) in 67 and 72% yield.

Following the method described by Wenkert et al.\textsuperscript{85}, the C 7-keto ester (18) was oxidised with t-butylhydroperoxide to give the enol lactone (95). The reaction did not prove amenable to large scale preparations of the enol lactone (95), even when highly purified t-butylhydroperoxide was employed. Considerable amounts of tarry substances were often formed, from which only small yields of the lactone (95) could be obtained after extensive chromatography. The highest yield (80%) was obtained from 0.5 g scale reactions. Catalytic hydrogenation of the lactone (95) over palladium–carbon gave predominantly the A/B cis acid (145), which was not isolated as such, but was converted to the ester (139) with diazomethane. The course of the hydrogenation was found to be very sensitive to the pressure of hydrogen. Only when the reduction was carried out at atmospheric pressure were products obtained with the desired stereochemistry at C 5. At higher pressures, the main product was abiet-8,11,13-
trien-18-oic acid (1)

Oxidation of the A/B cis ester (139) [containing up to 30% of the A/B trans ester (2) impurity] with chromium trioxide in acetic acid unfortunately gave the enol lactone (95) as the only product. This result is undoubtedly the reason why Wenkert et al. prepared the acetate (146) before carrying out an oxidation to the C 6,7-diketone (147), although they did not say so. Inspection of a Dreiding model of the desired diketone (148) shows that there exists a strong non-bonded peri interaction between the C 4 equatorial and C 6 substituents. Evidently, in the acidic medium, the diketone (148) enolises readily with subsequent loss of methanol to give the lactone (95). This approach was therefore discontinued.

Next, the lactone (95) was opened with sodium methoxide in anhydrous methanol to give the diosphenol (149). As expected, in basic conditions, the diosphenol did not recyclise to the lactone (95), but the work-up procedure of the methanolysis was critical, since over-acidification of the sodium salt of the diosphenol (149) caused partial lactonisation. The diosphenol (149) was stable for a period of only a few days, since autocyclisation slowly occurred to regenerate the lactone (95). Hence, the crude diosphenol (149) was acetylated immediately after isolation with acetic anhydride-pyridine to form the enol acetate (150), together with some of the lactone (95), which could be separated by chromatography on silica gel. The enol acetate (150) showed the same metastability as did the diosphenol,
and it was used without delay for the next step.

Catalytic hydrogenation of the enol acetate (150) over palladium catalyst\textsuperscript{96} proceeded readily to give two products which were separated by chromatography. The major product was identified as methyl abiet-\textsuperscript{8,11,13}-trien-\textsuperscript{18}-oate (2), arising by reduction of the double bond and hydrogenolysis of both the C\textsubscript{6}-acetate and the C\textsubscript{7}-ketone functions. A low yield of the C\textsubscript{6}-acetate (151) must have been formed, since the minor product obtained from the chromatography was the unsaturated ester (17),\textsuperscript{143} resulting from deacetylation of the C\textsubscript{6}-acetate during the chromatography.

In view of these two previous results, it was decided to introduce the C\textsubscript{6} oxygen substituent by a longer route employing more reliable reactions.

Several methods of introducing an hydroxy or an acetoxy group in the position "\(\alpha\)" to a ketone are widely employed in organic synthesis.

Lead tetraacetate-boron trifluoride oxidation of ketones has been reported\textsuperscript{115} to give \(\alpha\)-acetoxy ketones in yields which can vary from ca. 20-90\%, depending on the nature of the substrate. The reaction proceeds by boron trifluoride-catalysed enolisation of the ketone, followed by formation of a lead triacetate ester of the enol. Decomposition of the lead ester then gives lead diacetate with intramolecular donation of an acetoxy group to the adjacent carbon
atom. A transition state (Fig. 1) may be involved.

\[
\begin{align*}
\text{C} & \quad \text{C} \\
\text{Ac} & \quad \text{O} \quad \text{Pb} \\
\text{OAc} & \quad \text{OAc}
\end{align*}
\]

**Fig. 1**

Lead tetraacetate oxidation of certain enol acetates has also given rise to α-acetoxy ketones in good yields. In contrast, the diterpenoid enol acetate (152) reacted rapidly with lead tetraacetate to afford the α,β-unsaturated ketone (153) in quantitative yield. A recent improvement on this type of oxidation was reported by Kuehne and Giacobbe. This involves oxidation of a solution of the ketone and morpholine in acetic acid with thallic triacetate to give the α-acetoxy ketone in a yield superior to that obtained by lead tetraacetate oxidation. The reaction evidently proceeds through the morpholine enamine of the ketone.

Indirect hydroxylation or acetoxylation by displacement of a halogen atom next to a ketone has been shown to have only a limited synthetic applicability in both the steroid and diterpenoid fields. Elimination reactions are normally encountered, and the yield of enone usually exceeds that of the desired α-hydroxy or acetoxy ketone.
Peracid oxidation of enol derivatives of ketones also provides a method of preparing α-hydroxy or acetoxy ketones, and this type of reaction has been much exploited in steroid synthesis. Peracid oxidation of enamines \(^{120}\) has been shown to give epoxy amines, which rearrange and hydrolyse under basic conditions to give α-hydroxy ketones. Similar oxidation and basic hydrolysis of enol acetates \(^{121}\) also gives α-hydroxy ketones.

Osmylation of vinyl halides \(^{122}\) and nitriles \(^{123}\) has given rise to α-hydroxy ketones, but these sequences are limited by the ease of dehydration of the cyanohydrins and halohydrins to the corresponding vinyl halides and nitriles.

The keto ester (18) was firstly oxidized with lead tetraacetate either alone, or in the presence of boron trifluoride etherate or morpholine. Very little reaction occurred, and the starting material was recovered from all attempts. It was subsequently found that the ketone (18) did not form an enamine with morpholine and toluene-\(\text{p}\)-sulphonic acid in refluxing toluene under a water separator. This accounts for the lack of reactivity in the lead tetraacetate oxidations, and reflects the hindrance of the C 6 position. The corresponding enol acetate (155) (\textit{vide infra}) was also inert to lead tetraacetate in refluxing benzene.

The keto ester (18) was brominated in glacial acetic acid to give methyl 6α-bromo-7-oxo-abieta-8,11,13-trien-18-oate (154) in 96% yield. An attempted acetylation \(^{124}\) did not bring about any change.
in the molecule, and reaction of the bromoketone (154) with freshly prepared silver tosylate\textsuperscript{125} also failed.

On refluxing with isopropenyl acetate and toluene-\textsubscript{p}-sulphonic acid\textsuperscript{126} for several days, the keto ester (18) was slowly converted into the enol acetate (155) in 78\% yield. Oxidation of the latter with perbenzoic acid in chloroform\textsuperscript{127} gave an almost quantitative recovery of material from which two products could be isolated by preparative t.l.c. The least polar compound was identified as the $\alpha$-acetoxy ketone (156), which was obtained in 53\% yield. The acetoxy group was assigned an $\alpha$ configuration from examination of the n.m.r. spectrum which showed a large value for the coupling constant of the C 5 and C 6 protons (12.5 Hz). The $\alpha$ configuration also follows from the postulated mode of formation of the acetoxy ketone, (\textit{vide infra}). It has recently been shown by x-ray methods,\textsuperscript{128} that the configuration of the bromine atom in the bromoketone (154) is $\alpha$, and that ring B is in an almost half-boat conformation, with C 6 slightly below the plane of C 7, 8, 9 and 10, imparting a dihedral angle of ca. 178° between the planes of the C 5 and C 6 protons. The coupling constant of the C 5 and C 6 protons of the bromoketone (154) is 12 Hz. Therefore, on the basis of the coupling constants of the C 5 and C 6 protons, the bromoketone (154) and the acetoxy ketone (156) must have almost identical conformations. Examination of a Dreiding model of the acetoxy ketone (156) shows that there exists considerable interaction between the C 4 and C 6 esters when ring B adopts a half-boat conformation (Fig. 2).
It has been shown, also by x-ray methods,\textsuperscript{129} that other diterpenoids, e.g. methyl 6α-bromo-7-oxo-12-methoxy podocarpa-8,11,13-trien-19-oate (157), have an almost classical boat conformation for ring B. This twisting of ring B into a boat on the introduction of a large substituent in the C 6α position has been attributed to the steric interaction between the C 6α substituent and the C 19 ester group.\textsuperscript{129} The dihedral angle between the planes of the C 5 and C 6 protons in this situation is ca. \(155^\circ\), and the coupling constant for the C 5 - C 6 protons is 7 Hz. It is surprising then, that ring B of the acetooxy ketone (158) does not twist into a boat form and thus remove some of the interaction between the C 4 and C 6 esters. However, if this happened, the dihedral angle between the planes of the C 5 and C 6 protons would diminish with a consequent reduction in the value of the coupling constant.\textsuperscript{130} An alternative structure, with the C 6 acetate having a \(\beta\) configuration and ring B in the boat form imparts a dihedral angle of ca. 0-10° between the C 5 and C 6 protons. A large C 5 - C 6 proton coupling constant would also be expected to be observed in the n.m.r. spectrum for this situation.\textsuperscript{130} Such a structure must be discounted, since inspection of models shows that the C 6 ester would suffer large interactions not only with the C 4 ester.
but also with the C 4 methyl group, resulting in a system of higher energy than that illustrated in Fig. 2.

The more polar product from the oxidation of the enol acetate (155) with perbenzoic acid was the ketol (158) which was formed in 43% yield. The n.m.r. spectrum of this compound also showed a coupling constant of 12.5 Hz for the C 5 and C 6 protons, and so its conformation is identical with that depicted for its acetate (156). The ketol (158) was readily acetylated with acetic anhydride and pyridine at 20° to the acetate (156). This is further evidence for the α configuration of the C 6 hydroxy group, since Denny has shown that acetylation of the C 6β, 7β diol (159) with acetic anhydride-pyridine at 20° gave only the monoacetate (160).

Just as in the case of the peracid oxidation of the unsaturated ester (17), no epoxides were isolated in the present reaction. The distinct difference between these two reactions is that with the present one, both the products isolated bear an oxygen substituent at C 6, whereas in the former, the major product isolated was the C 7 ketone (18). By acetylation of the crude product from the perbenzoic acid oxidation of the enol acetate (155), the acetoxy ketone (156) was isolated by direct crystallization in 95% yield.

The formation of compounds (156) and (158) can be rationalized as follows (see Figs. 3, 4). Attack of OH⁻ on the C 6,7 double bond, followed by cleavage of the C 7-O bond gives rise to the ketol.
Migration of the C7 acetate to give the C7 carbonium ion (Fig. 4) followed by loss of a proton and subsequent ketonisation of the enol gives the acetoxy ketone.

Hydrolysis of the acetoxy ketone (156) with methanolic sodium hydroxide was slow. After a reaction time of 2 hours, a considerable amount of the starting material remained, but none of the hydroxy ketone (158) was formed. The only products which were identified were the γ-lactone (95) and the α,β-unsaturated ketone (161). The enone (161) and the starting material (156) were difficult to separate, but t.l.c. and spectroscopic evidence was obtained for its presence by comparison with the authentic enone prepared by dehydrobromination of the bromoketone (154) with lithium bromide in refluxing dimethylformamide. The enone (161) is formed by an E2 elimination by attack
of the base at C 5 with loss of the C 6 acetate group. The γ-lactone (95) can arise by an \( E_1cB \) type pathway by attack of the base at the activated C 6 proton (see Fig. 5), to give the C 6 carbanion. Loss of an acetyl group by the electron shifts shown then affords the C 6,7-diketone. Further attack of the base at C 5 forms the anion of the diosphenol (149). The bright yellow colour formed during the hydrolysis supports this hypothesis. Evidently, the lactone (95) was formed by acidification of the diosphenol (149), as was noticed earlier.

![Diagram](image)

**Fig. 5**

Oxidation of the ketol (158) with bismuth oxide\(^{133}\) gave initially the diketone (Fig. 5) as shown by the yellow colour of the reaction mixture. The diketone readily enolised however, and the γ-lactone (95) was the sole product isolated. Thus it appears that the enolisation of C 6,7-diketo systems in the abiet-8,11,13-trien-18-oic acid series is a ready process, regardless of the stereochemistry at C 5.

The next step was to remove the ketone at C 7. Considering the behaviour of the acetoxy ketone (156) towards base, Wolff-Kishner reduction was not attempted, while Clemmensen reduction\(^{134}\) gave methyl
abieta-8,11,13-trien-18-oate (2) as the main product. Thioketalisation with ethanedithiol in boron trifluoride etherate gave a mixture of products as shown by t.l.c., although the i.r. spectrum of the total reaction product showed the absence of an aryl ketone band.

Reduction of the acetoxy ketone (156) with sodium borohydride in anhydrous methanol was rapid, and a high yield of the C 7β hydroxy compound (162) was obtained. It was of interest to examine the behaviour of this compound under hydrolysis conditions, and to compare the result with that of the hydrolysis of the acetoxy ketone (156) described previously. The hydrolysis of both the ester functions at C 4 and C 6 was rapid, and the dihydroxy acid (163) was obtained in high yield. An identical behaviour of the diester (19) under hydrolysis conditions was reported by Defaye-Duchateau, this reaction affording the dihydroxy acid (164) which is the C 7 epimer of 163. Wenkert et al. compared the rates of hydrolysis of the esters (2) and (165) with the C 7-keto counterparts (18) and (166) and observed an increase in the rate of hydrolysis of both the C 4-esters with the C 7-ketone substituents. While a properly oriented C 6 substituent would be expected to exert considerable influence on the rate of hydrolysis of the C 4-ester, little effect would be predicted from C 7 substituents in the rigid A/B trans ring system. This long-range phenomenon has been attributed to conformational transmission. In the present case, the result can be interpreted as a steric acceleration of the reaction rate.
Several attempts were made to dehydrate the hydroxy acetate (162) to the enol acetate (167). The results were generally disappointing. Reaction of the hydroxy acetate (162) with thionyl chloride in pyridine\(^{136}\) or with boron trifluoride etherate in acetic acid\(^{137}\) gave only the starting material. With phosphorus pentachloride in dry ether, the product obtained was the unstable 7α-chloroacetate (168). The chlorine atom was assigned an α configuration since the coupling between the C 6 and C 7 protons was different from that in the n.m.r. spectrum of the hydroxy acetate (162). It was difficult to determine the exact coupling constant as the C 6 and C 7 multiplets overlapped, but no lines having a 7 Hz separation were measured.

The reaction of the hydroxy acetate (162) with acetic anhydride with a trace of toluene-\(p\)-sulphonic acid was studied. Although the reaction was performed under identical conditions each time, different results were obtained from the various experiments. Sometimes, a low yield of the desired enol acetate (167) was obtained as the only identifiable product. The compound showed an i.r. band at 1760 cm\(^{-1}\), while in the n.m.r. spectrum, the C 5 and C 7 protons showed an allylic coupling constant of 3 Hz. This same coupling constant (3 Hz) was observed in the n.m.r. spectrum for the C 5 and C 6 protons of the enol acetate (155), but the two spectra were clearly different. On other occasions, the diacetate (170) was obtained as the major product, together with a minute amount of the enol acetate (167) as detected by t.l.c. On three other attempts to dehydrate the hydroxy acetate (162),
a new product was observed along with the enol acetate (167). This product was identified as the vinyl chloride (169). The only source of chlorine atoms was when the ether extract of the reaction mixture was washed with sodium chloride solution. Three pertinent observations about this reaction must be mentioned. Firstly, the reaction mixture which on work-up afforded the diacetate (170) as the major product was a colourless to pale yellow colour, while the reaction mixture which afforded the enol acetate (167) and/or the vinyl chloride (169) was a deep purple in colour, suggesting the formation of carbonium ion intermediates. Secondly, when the vinyl chloride (169) and the enol acetate (167) were formed, none of the diacetate (170) was detected, while when the diacetate (170) was isolated as the major product, together with a small amount of the enol acetate (167), none of the vinyl chloride was detected. Thirdly, the enol acetate (167) was the only product isolated when the ether extract of the reaction mixture was washed with sodium hydrogen carbonate solution only. The t.l.c. of the product isolated from this work-up procedure showed only the enol acetate (167) spot, together with a spot at the origin. Evidently, the other products formed did not survive the chromatography. The enol acetate (167) or the diacetate (170) were shown not to be the precursor of the vinyl chloride, since they were both unaffected by treating their ether solutions with sodium chloride solution, either alone, or with sodium acetate and sodium hydrogen carbonate solutions.
The precursor of the vinyl chloride (169) is probably the cis diacetate (171), formed by attack of acetic anhydride from the α face of the molecule on the C7 carbonium ion (see Fig. 6) rather than by loss of a C6 proton which forms the enol acetate (167), i.e. both these products are formed by benzyl C=O fission. The trans diacetate (170) is formed by attack of acetic anhydride on the protonated C7 hydroxyl, i.e. by acyl C=O fission.

To explain the very rapid conversion of the cis diacetate (171) to the vinyl chloride (169), it appears necessary to invoke a nucleophilic substitution reaction involving a neighbouring group participation. Displacement of the C7-benzylic acetate with participation by the C6-acetate affords initially the acetoxonium ion (Fig. 7). The positive charge could be stabilized by overlap of the p orbitals with the π orbitals of the neighbouring aromatic ring. Attack of Cl⁻ at C6 would initially form the trans-chloro acetate. In simple cyclohexyl systems, the substitution of acetate by halide proceeds with neighbouring group participation and leads to an
inversion of configuration, e.g. cis 1,2-diacetoxy cyclohexane with aqueous hydrochloric acid afforded trans-2-acetoxy cyclohexyl chloride. In the present case, loss of acetic acid from the intermediate benzyl acetate would give the vinyl chloride.

The reactivity of the intermediate C 6-chloro C 7-acetate (Fig. 7) may also explain the instability of the C 7-chloro C 6-acetate obtained by halogenation of the alcohol with phosphorus pentachloride in ether.

The difficulty experienced in controlling the course of the reaction of the hydroxy acetate with acetic anhydride and toluene-2-sulphonic acid led to the abandonment of this approach for preparing the desired enol acetate.

The saturated C 6-acetate was prepared by palladium-catalysed hydrogenolysis of the hydroxy acetate in virtually quantitative yield. The rate of the hydrogenolysis was found to be dependent on the scale on which the reaction was carried out. On a 1.0 g scale, the hydrogenolysis appeared to go to an extent of about 60%, and then slow down, but t.l.c. showed only the presence of the
starting hydroxy ester (162) and the desired C 6-acetate (172), which were easily separated by column chromatography. The starting material was then returned to the hydrogenation. On small scale reactions (0.1 g), the hydrogenolysis was complete. A similar observation was made by Baltzly and Buck during the palladium-catalysed hydrogenolysis of isopropyl phenyl ketone. They found that reduction to the alcohol was rapid, and that further hydrogenolysis of the alcohol to the hydrocarbon proceeded slowly, and did not go to completion. They have attributed this to the presence of a strong benzyl C=O bond, caused by alkyl substitution on the β carbon atom. In the present case, the electron-withdrawing acetate group should facilitate the hydrogenolysis of the benzyl C=O bond. Since the hydrogenolyses were observed to go to completion with small amounts of compound, but not with larger amounts, this may be due to a slow poisoning of the catalyst. More satisfactory results should be obtained by employing larger amounts of catalyst for the large scale reactions. This successful removal of the oxygen function at C 7 means that the C 6-acetate (172) can be prepared in 55% overall yield from methyl abiet-8,11,13-trien-18-oate (2). The peracid oxidation of diterpenoid C 7-enol acetates to C 6-oxygenated compounds appears to have a general synthetic application, since it has recently been shown that perbenzoic acid oxidation of the enol acetate (152) gave the acetoxy ketone (173) as the sole product.\(^{142}\) That no hydroxy ketone was isolated means that the initially formed "protonated epoxide" (cf Figs. 3,4) opens entirely in one direction (Fig. 4). Migration of
the C 7 acetate in this case is undoubtedly enhanced by the increased
electron density at C 7 due to the "para" methoxyl substituent of ring C.

As in the case of the hydroxy acetate (162), hydrolysis of both
the C 4 and the C 6 esters occurred when the acetate (172), in
methanol, was refluxed with dilute sodium hydroxide solution. The
hydroxy acid (174) which was formed was not characterised, but was
converted to the hydroxy ester (175) with diazomethane. The C 6-alcohol
(175) was obtained in 76% yield, together with small amounts of
elimination products, presumably mainly the C 6-unsaturated ester
(17).143

The C 6-alcohol (175) was smoothly oxidized with Jones reagent
to the desired C 6-ketone (176) in 80% yield. The pure ketone was a
colourless oil which very slowly turned yellow, possibly undergoing
autooxidation at the highly activated C 7 position.24 The i.r.
spectrum of the ketone showed a saturated six-membered ring ketone
band at 1715 cm\(^{-1}\), while in the n.m.r. spectrum, a singlet at \(\delta\) 2.26
was assigned to the C 5 proton, and two doublets at \(\delta\) 2.30, 3.26
(J 2.5 Hz) were assigned to the C 7 protons. It is difficult to make
individual assignments for these latter signals, but if ring B exists
in a half boat conformation, the most deshielded proton (\(\delta\) 3.26) will
then be the C 7\(\alpha\) one. That the C 10 methyl signal (\(\delta\) 1.18) is not
shifted to a very high field, and the C 4 axial methyl signal is
shifted considerably downfield to \(\delta\) 1.48, provides evidence that ring B
exists in a half-boat conformation with C 6 slightly below the plane
of the C 7, 8, 9 and 10 atoms. The ketone also showed a strong positive Cotton effect in its rotatory dispersion curve. This is predicted from the octant rule which indicates that the C 10 methyl group and ring A in the rear quadrants will make positive contributions to the Cotton effect. In the front quadrants, the C 4 methyl group will make a negative, and the C 4 ester a positive contribution.
2.3 The Synthesis of a Tetracyclic Steroid Skeleton from Abieta-8,11,13-trien-18-oic Acid (1)

Although much work has been directed towards the total synthesis of steroids, the use of diterpenes as starting materials for the synthesis of optically active steroids has met with varied success. Of the readily available diterpenoid resin acids, only 12-hydroxy-podocarpa-8,11,13-trien-19-oic acid (podocarpic acid) (177) has been converted by Friedel-Crafts acylations/cyclizations into the aromatic ring C steroids (178) and (179). Denny employed the ketone (180) as a starting material for the synthesis of the aromatic ring A steroid (181). This approach involved the conversion of the ketone (180) into the compound (182) by carboethoxylation, methylation, and Wittig addition of a CHCO₂Me group to the C 4 carbonyl group. The steroid (181) would then be obtained by an acyloin condensation of the diester (182). However, low yields and instability of some of the intermediates resulted in this synthesis being abandoned. Denny also attempted a saturated ring C approach wherein the hydroxy compound (183) was reduced to the hydroxy ketone (184) with a B/C trans ring junction. Other transformations of this latter compound led to a low yield of the unsaturated keto ester (185).

While other reduced ring C derivatives of 12-hydroxy-podocarpa-8,11,13-trien-19-oic acid (177), abieta-8,11,13-trien-18-oic acid (1), and 10α-podocarpa-8,11,13-trien-18-oic acid (16) which are of potential synthetic value e.g. the enones (186), (187), (188) have been prepared in varying yields, the elaboration of
a D ring of a steroid nucleus employing these as intermediates has yet to be accomplished.

As mentioned in the Introduction of this thesis, the task of synthesizing a tetracyclic steroid nucleus from abieta-8,11,13-trien-18-oic acid (1) must necessarily be centred initially on transformations of the C 13-isopropyl group. In the present investigation, the synthesis of a D ring was attempted from both aromatic ring C intermediates and reduced ring C intermediates.

In the aromatic ring C approach, it was planned to construct the D ring of the steroid nucleus by using the whole or part of the C 13-isopropyl group to furnish some of the three carbon atoms required to complete the five carbon ring at C 13,14. Thus the possibility of an intramolecular functionalisation of the isopropyl group was considered.

Whereas the intramolecular functionalisation of aliphatic alkyl groups by the photolysis of nitrite esters,\textsuperscript{153-155} the homolysis of hypohalites,\textsuperscript{156-163} and the oxidation of alcohols with lead tetraacetate\textsuperscript{164-169} has been considerably exploited in organic synthesis, especially in steroid transformations,\textsuperscript{170} the intramolecular functionalisation of aromatic alkyl groups is known to a much lesser degree.

Matsuura and Kitaura\textsuperscript{171} found that the photolysis of hindered benzophenones substituted in the ortho position with a methyl group,
led to good yields of aromatic cyclobutanols, e.g. the acetophenone (189) gave the cyclobutanol (190). The reaction occurs by excitation of the carbonyl group to give an oxygen radical, which abstracts a hydrogen atom from the ortho substituent, and is followed by radical combination to form the cyclobutane ring. Another photolytically-induced functionalisation of an aromatic t-butyl group was reported by Döpp. In this case, photo excitation of an aromatic nitro group in the compound (191) in methanol led to the N-methoxy lactam (192) which was reduced to the lactam (193) with triphenylphosphine.

Two closely related examples of an intramolecular transfer of a phenyl group to an ortho methyl group have been reported by Truce et al. and by Factor et al. In the former case, reaction of a phenyl sulphone (194) with strong base, e.g. an alkyllithium, forms a carbanion on the aromatic methyl group. Migration of the phenyl ring then affords the diphenyl methane sulphinic acid (195) after acidification. The related example of this type of migration is the pyrolysis of diphenyl ethers with ortho methyl groups to a diphenylmethane phenol, e.g. the ether (196) to the phenol (197), a reaction which is believed to involve benzyl radicals.

In a study on the intramolecular functionalisation of aromatic alkyl groups by hydrogen abstraction reactions, Baker found that thermolytic lead tetraacetate oxidation of the benzylic alcohols (198) and (199) gave fragmentation and polymerisation in the case of the former, and acylation of the C6 hydroxy group in the case of the latter.
He found that photolytic lead tetraacetate oxidation of the same benzylic alcohols gave solely polymeric products. Application of the proton abstraction reaction of Sneen and Matheny,\textsuperscript{177} \textit{viz.} the reaction of an alcohol with bromine and mercuric oxide to form the hypobromite which is decomposed with silver oxide, to the benzylic alcohols (200) and (201) afforded the furans (202) and (203) in 86\% and 30\% yields.\textsuperscript{176} The same reaction was performed on the benzylic alcohols (204) and (205), but in both cases, dehydration to the unsaturated derivatives (206) and (207) was the only reaction which occurred. From these results, Baker\textsuperscript{176} concluded that the reaction would only occur for tertiary benzylic alcohols and aromatic methyl groups.

Another interesting intramolecular cyclisation of the ortho \textit{t}-butyl benzylic alcohol (208) and its methyl ether was reported by Barclay and McDonald.\textsuperscript{178} Treatment of the alcohol, or its methyl ether, with hydriodic acid resulted in formation of the hydrocarbon (209) in high yield. This reaction is believed to proceed by a proton abstraction from the aromatic alkyl group of a highly hindered benzyl carbonium ion, \textit{viz.}:

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{fig1.png}
\caption{Fig. 1}
\end{figure}
Lansbury et al.\textsuperscript{179} have studied the intramolecular insertion of cationic nitrogen species into the CH bonds of proximate aromatic alkyl groups. These reactions are typified by the reaction of the sterically crowded indanone oxime (210) with polyphosphoric acid to afford mainly the amine (211), together with products arising from the normal Beckman rearrangement, and an abnormal Beckman rearrangement, wherein the group cis to the original hydroxy group of the oxime migrates. This reaction has been shown to proceed by dehydration of the oxime to a singlet positive nitrene (a nitrenium ion), which inserts into one of the methyl C - H bonds of the aromatic \textit{t}-butyl group.\textsuperscript{180} Aromatic nitrenes, generated by decomposition of aryl azides, insert into \textit{ortho} aromatic alkyl groups to form indole amines, e.g. thermolysis of the optically active azide (212) affords the optically active amine (213).\textsuperscript{181}

An intramolecular cyclisation process of high synthetic value is the thermolysis or photolysis of diazo derivatives of ketones and aldehydes, as these reactions lead to the formation of new carbon-carbon bonds. Formally, these reactions can be represented as involving carbene intermediates, which insert into carbon-hydrogen and carbon-carbon bonds, although evidence exists which suggests that free carbenes as such are not formed.\textsuperscript{182} The thermal decomposition of the diazo derivatives is catalyzed by the presence of transition metals, particularly copper and silver, or their salts, and the reactive species formed is probably a metal-carbenoid complex.\textsuperscript{182} Thus the photolysis of the diazo compound (214) gave a 30% yield of benzyllic
C–H insertion product (215), and a 9% yield of the aryl C–C insertion product (216).\(^{183}\) The copper-catalysed thermolysis of the sterically crowded diazoketone (217) gave rise to products of both C–H and C–C insertion, viz. the tetralone (218) and the indanone (219).\(^{184}\)

Two examples of the functionalisation of benzylic carbon by an intramolecular oxidative cyclization which show a high synthetic utility have been reported.

Dehydrogenation of the substituted naphthalene carboxylic acid (220) with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) gave an 85% yield of the δ-lactone (221).\(^{185}\) Oxidation of ortho-benzylbenzoic acid (222) with lead tetraacetate gave 3-phenylnaphthalide (223) as the sole product in 42% yield.\(^{186}\) The absence of any dimerisation products led Davies and Waring\(^{186}\) to suggest that this oxidative cyclization proceeds by a cyclic polar mechanism rather than by a pathway involving the benzhydryl radical, viz:

\[
\begin{align*}
\text{Ph} & \quad \text{H} \\
\text{H} & \quad \text{O} \\
\text{C} & \quad \text{Me} \\
\text{Ph} & \quad \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{Pb} & \quad \text{O} \\
\text{OAc} & \quad \text{O} \\
\text{Pb} & \quad \text{OAc}
\end{align*}
\]

\[
\text{Ph} \\
\text{H}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{H} \\
\text{O} & \quad \text{Ac}
\end{align*}
\]

Fig. 2

The application of one of these methods described above for the intramolecular functionalisation of the C 13-isopropyl group of abiet-8,11,13-trien-18-oic acid (1) requires firstly the introduction
of a reactive substituent in an ortho position. The most accessible position in the C ring of abieta-8,11,13-trien-18-oic acid (1) towards electrophilic substitution is C 12, and many compounds substituted in this position have been prepared. Only two compounds have been previously prepared with a substituent at the more hindered C 14 position. These are the C 14-acetyl compound (224), and the C 14-nitro derivative (45).

In the present study, the most promising compound to use for attempted intramolecular cyclisation of its C 13-isopropyl group was considered to be the diazo compound (225), prepared from the C 14-acetyl derivative (224), as this on photolysis would form the steroid skeleton, e.g. (226), directly. However, the C 14-acetyl derivative (224) could be obtained only in a very low yield by Friedel Crafts acetylation of methyl abieta-8,11,13-trien-18-oate (2) with acetyl chloride and aluminium chloride in sym-tetrachloroethane or nitrobenzene as solvent at 20°C. The C 14-acetyl substituent is also very hindered, and not very reactive. It was decided therefore to prepare the C 12-acetyl derivative (227), and attempt a cyclisation to the C 13-isopropyl group from C 12. While the compound (227) was isolated from the Friedel-Crafts acetylation of the ester (2) in sym-tetrachloroethane at 20°C, it was necessary to carefully chromatograph the reaction product in order to separate the starting material (2), the C 12-acetyl compound (227), and the C 14-acetyl compound (224). It was subsequently found that if the Friedel-Crafts acetylation was conducted in refluxing carbon
disulphide, the C 12-acetyl derivative (227) was obtained as the sole product in high yield. The compound (227) was reacted with iodine in pyridine\(^{187}\) to form a pyridinium iodide, which was cleaved with dilute base to form methyl 12-carboxy-abieta-8,11,13-trien-18-oate (228) in high yield.

Initially it was decided to attempt a cyclisation employing a hindered diazomethyl ketone as the reactive intermediate. The carboxylic acid (228) was reacted with oxalyl chloride\(^{191}\) in benzene to give a quantitative yield of the crude crystalline acyl chloride (229). The latter compound was converted into the diazomethyl ketone (230) by reaction with diazomethane in ether in the presence of triethylamine.\(^{192}\) The diazomethyl ketone (230) in cyclohexane was then added from a Herschberg addition funnel at an extremely slow rate to cuprous oxide in refluxing cyclohexane.\(^{193}\) The thermolysis period was varied from 11 hrs to 3 days, and yields of the indanone (231) varying between 36% and 50% were obtained.\(^{194}\) Several other products were formed along with the indanone (231). It is likely that one of these is the tetralone\(^ {184}\) (232), while others may be solvent insertion products.\(^ {193}\) A polar product obtained from the reaction was identified as the amino ketone (233). It is not clear whether this product is an artefact from the diazomethyl ketone (230) preparation, or if it arises during the thermolysis.

With the isopropyl group successfully functionalized the next task was to cleave the indanone ring of 231. The Baeyer-Villiger
oxidation of aryl ketones with peracids has been shown to give products arising solely from aryl migration,\textsuperscript{195} i.e., aryl methyl ketones give only aryl acetates. Oxidation of the indanone (231) with peracetic acid\textsuperscript{196} gave considerable amounts of polymeric materials, while oxidation using perbenzoic acid\textsuperscript{197} was so slow that it barely proceeded. The indanone (231) was oxidised to the δ-lactone (234) using pertrifluoroacetic acid,\textsuperscript{195} but the yield was only 40–50%, and some starting material was invariably recovered. A high yield of the desired δ-lactone (234) was obtained by oxidising the indanone (231) with meta-chloroperbenzoic acid with a trace of toluene-p-sulphonic acid in refluxing 1,2-dichloroethane.\textsuperscript{198}

Hydrolysis of the δ-lactone (234) with methanolic sodium hydroxide proceeded readily to afford initially the disodium salt of the hydroxy acid (235), which upon acidification, rapidly cyclized back to the δ-lactone (234). This problem was overcome by carrying out the hydrolysis with potassium t-butoxide in t-butanol, followed by addition of methyl iodide to effect methylation of the phenol. The carboxylic acid (236) was thus obtained in good yield, (68%).

The final step in this sequence involved the cyclization of the acid chloride derived from the acid (236) to give the aromatic steroid (237), following the example of Watkins\textsuperscript{150} who cyclized the acid chloride (238) to the steroid (179). Unfortunately, all efforts were vitiated, since attempted cyclisation of the acid chloride derived from the acid (236), with stannic chloride in benzéne\textsuperscript{199} or aluminium
chloride in carbon disulphide resulted in a very rapid formation of the δ-lactone as the sole product. A similar result has been reported by Hayes and Thomson who found that reaction of the acid chloride (239) with sodium aluminium chloride gave the δ-lactone (240). That the acid chloride did not cyclise to the steroid (237) may be due to the buttressing of the C 12-OMe group by the gem-dimethyl group in the side-chain, resulting in the acyl group being held too far above (or below) the plane of the aromatic ring, and hence too far away for overlap of the π electrons with the p orbital of the acylium cation, (Fig. 3).

![Fig. 3](image)

The demethylation of the phenyl methyl ether in this reaction was extremely rapid, and must involve a complex involving the acylium cation, the Lewis acid, and the methoxy group, (Fig. 4), since treatment of the acid chloride (241) with stannic chloride in benzene has been shown to give the tetralone (242) only, with no phenolic products.  

![Fig. 4](image)
In a further attempt to form a D ring, the carboxylic acid (228) was oxidised with a slight excess of lead tetraacetate in benzene. This effected a remarkably clean conversion to the γ-lactone (243) which was isolated in 93% yield. No other products were formed, which supports the hypothesis of Davies and Waring that the reaction proceeds through a polar mechanism (Fig. 2), rather than a radical one. The γ-lactone ring could not be hydrolysed to the hydroxy acid, presumably because the propinquity of the resultant hydroxy and carboxy groups led to rapid formation of the γ-lactone ring. The γ-lactone (243) was inert towards sodium borohydride, even when the latter was used in a large excess, but it was reduced quantitatively with lithium aluminium hydride to the triol (244). The triol (244) was oxidised to the aldehyde-lactone (245) with chromium trioxide in pyridine. Oxidation of the C 12 benzylic alcohol would initially form the aromatic aldehyde which reacts with the ortho tertiary alcohol to form a hemi-acetal, which is in turn oxidized to form the γ-lactone ring.

Several attempts were made to dehydrate the triol to the isopropenyl diol (246). With phosphoryl chloride in pyridine, the desired diol (246) was obtained on several occasions, but often only water soluble products were formed, and none of the diol was isolated. The water soluble products may have been cyclic phosphates. A more reliable dehydration, with concomittant acetylation, was effected by heating the triol (244) briefly with acetic anhydride and toluene-p-sulphonic acid to afford the unsaturated diacetate (247) in good yield, (63%).
Ozonolysis of the unsaturated ester (247) at -80° followed by destruction of the ozonide with aqueous potassium iodide-acetic acid gave the acetyl compound (248) in 22% yield. A better yield of the keto ester (248) was obtained from the oxidation of the unsaturated ester (247) with osmium tetroxide-sodium metaperiodate. Although a small amount of the starting material was recovered after a reaction period of 5 days, the keto ester (248) was isolated in 50% yield. Since the overall yield of the keto ester (248) from the ester (2) was only 20%, and since this yield is not much greater than those obtained from the oxidative degradations of the C13-isopropyl group described in the Introduction, further transformations on the keto ester (248) were not undertaken. The proposed following steps involving carboxylation of the ketone with magnesium methylcarbonate, hydrogenolysis of the benzyl groups and cyclisation of the acid via the acid chloride by a Friedel-Crafts reaction might provide a low overall yield of the aromatic ring C steroid (249).

An attempt was also made to oxidise the 12-methoxy derivative of methyl abietate-8,11,13-trien-18-oate (250) with peracid with the aim of obtaining a ring opened muconic acid208 of the type (251). In an extensive study on the peracid oxidation of methyl 12-methoxy-podocarpa-8,11,13-trien-18-oate (252) and some of its derivatives, Burkinshaw and Davis209 isolated quinones and para-quinols (hydroxy-dienones) from peracetic acid oxidations which had been allowed to proceed at 20° for 16 - 24 hr. By allowing the reaction to proceed for
an extended period of time, further oxidation occurs to give acidic products.

Methyl 12-acetylabieta-8,11,13-trien-18-oate (227) was oxidized with meta-chloroperbenzoic acid and toluene-p-sulphonic acid in refluxing 1,2-dichloroethane to afford the aryl acetate (253) in 85% yield. Hydrolysis of the acetate with sodium bicarbonate gave the phenol (254) which was methylated with potassium t-butoxide in t-butanol and methyl iodide to afford the methyl ether (250). This was oxidized at 20°C for a period of 10 days with peracetic acid. The product was separated into neutral and acidic fractions. T.l.c. examination of both these fractions showed that numerous products had been formed, and therefore this reaction was not pursued any further.

A study of the nitration of methyl abieta-8,11,13-trien-18-oate (2) and some of its derivatives was undertaken. It has been shown by Fieser et al.¹⁸⁸ that nitration of abieta-8,11,13-trien-18-oic acid (1) with mixed nitric-sulphuric acids gives the C 12,14-dinitro acid (255). No mono-nitro products could be obtained. The preparation of the C 14-nitro ester (45) was achieved by Campbell et al.¹⁸⁹ by converting the dinitro acid (255) into its methyl ester (44), and selectively reducing the C 12-nitro group with ammonium sulphide to give the nitro-amine (256). Diazotization of the amino group, and reduction of the resulting diazonium salt with zinc in ethanol gave the C 14-nitro ester (45). By dissolving abieta-8,11,13-trien-18-oic acid (1) in concentrated sulphuric acid, the C 12-sulphonic acid (257) was
Nitration of this compound was shown to give the C12,14-dinitro acid (255), the sulphonylic acid group being readily replaced by a nitro group. However, by careful control of the reaction conditions, Campbell et al. were able to isolate the nitro-sulphonylic acid (258). Unfortunately, this compound proved resistant to the hydrolysis conditions employed for removing the sulphonylic acid group from the compound (257). The sulphonylic acid (257), besides being hydrolysed with dilute sulphuric acid to abieta-8,11,13-trien-18-oic acid (1), was shown by Campbell et al. to react quantitatively with aqueous bromine to form the bromide (259). Reaction of the bromide (259) with aqueous sodium hydroxide in the presence of copper at a high temperature brought about replacement of the bromine, and after methylation of the acid, the C12-phenol (254) was obtained. By a similar procedure, but using concentrated ammonia solution as the base, Campbell et al. effected replacement of the bromine in the compound (259) by ammonia, thus affording the C12-amine derivative (260). Nitration of the latter compound with mixed sulphuric-nitric acids gave the nitro-amine (255).

Nitration of methyl abieta-8,11,13-trien-18-oate (2) using an acetic anhydride-cupric nitrate reagent was attempted in the present study. This reagent has been shown to form low concentrations of acetyl nitrate, which in turn slowly decomposes to give low concentrations of nitronium ion in solution. Furthermore, the reagent is more selective than nitric-sulphuric acids, and gives only mono-nitrated products, even with highly activated aromatic systems, e.g. the azulenes. On the 1.0 g scale, methyl abieta-8,11,13-trien-18-oate (2)
reacted with acetic anhydride-cupric nitrate to give the C 14-nitro ester (45) in excellent yield. No C 12,14-dinitro product was isolated. The nitro group was shown to be at C 14 by comparison of its m.p. with that reported,\textsuperscript{189} and by the presence of a pair of doublets due to the C 11 and C 12 protons in the n.m.r. spectrum. Evidently, the C 14-nitro ester (45) is the product arising from kinetic control, the ester (2) reacting rapidly with the small quantities of nitronium ion produced. However, when the reaction was carried out on a 10 g scale, a new effect was observed which was not evident with the small scale experiment. On adding the cupric nitrate crystals in small portions to a solution of the ester (2) in acetic anhydride, there was apparently an induction period in which no change was observed to take place. After \( \frac{1}{4} \) hr, crystals, presumably of cupric acetate, began depositing on the walls of the flask, and the temperature rose rapidly. This temperature rise must have increased the rate of decomposition of the acetyl nitrate resulting in a markedly higher concentration of nitronium ion. This then indiscriminately attacked either the C 12 or C 14 positions in the ester (2) to give a 1:1 mixture of the C 12- and C 14-nitro esters (261) and (45). Despite the loss of control of the reaction, no dinitro products were formed. The two nitro esters (261) and (45) crystallized together from methanol as a 1:1 complex which had a broad melting point. The individual esters could not be separated by chromatography but by seeding a solution of the complex in acetone with authentic C 14-nitro ester (45), a small quantity of the pure C 14-nitro ester slowly crystallized. The course of the large-scale nitration
experiments could not be altered by cooling the reaction mixture, or by an extremely slow addition of the cupric nitrate.

A photolysis of the C 14-nitro ester (45) was carried out in the hope of obtaining a lactam similar to that obtained by Döpp but the product was a red gum which was shown by t.l.c. to contain many compounds.

Reduction of the C 14-nitro ester (45) with stannous chloride-hydrochloric acid in boiling acetic acid followed by basic hydrolysis of the stannic chloride addition complex gave the C 14-amine (262), while similar reduction of the C 12- and C 14-nitro ester complex gave a 1:1 mixture of the amines. Fractional crystallization of the mixture gave the pure C 12-amino ester (263). The mother liquors from the crystallization contained mainly the C 14-amino ester (262), which could not be induced to crystallize, even after chromatography, and seeding with the authentic amine.

Bromination of the C 12- and C 14-amines was attempted using the modified procedure of Cadogan et al. which involves reaction of the aromatic amine with i-pentyl nitrite to form a diazonium derivative, which is thermally homolysed to form phenyl radicals. In the presence of a halocarbon solvent, e.g. bromoform, carbon tetrachloride, the phenyl radical abstracts a halogen atom from the solvent to form an aryl halide. In the present case, the solvent employed was bromoform. The C 12-amine (263) gave an 87% yield of the C 12-bromo ester (264), while under identical conditions, the pure C 14-amine (262) did not react, and
was recovered unchanged. It was thought that the bromination reaction might then be used to separate the C 12- and C 14-amines, by conversion of the C 12-amine (263) to the bromide, and chromatographic separation of the products. While this was achieved, the polarity of the solvent (benzene) required to elute the unreactive C 14-amine (262) from an alumina column was such that the deeply-coloured by-products which were produced during the conversion of the C 12-amine (263) to the bromide (264) were also eluted resulting in a product which was less pure than that obtained from fractional crystallization of the amine mixture. The difficulty encountered in obtaining pure products from these nitration-reduction sequences led to the examination of the nitration of a C 12-substituted derivative of methyl abieta-8,11,13-trien-18-oate (2).

Methyl 12-acetyl-abieta-8,11,13-trien-18-oate (227) was chosen as a starting material for this nitration study, as it was readily available, and the C 12-acetyl group is deactivating and meta directing so that the expected product would be the compound (265). The C 12-acetyl group could then be modified to the methyl ether by the procedure outlined previously (viz. 227 \rightarrow 253 \rightarrow 254 \rightarrow 250), and the nitro group modified to a suitable derivative for intramolecular cyclization from C 14 to the C 13 isopropyl group.

When methyl 12-acetyl-abieta-8,11,13-trien-18-oate (227) was nitrated using a mixture of fuming nitric acid containing a small quantity of sulphuric acid, an almost quantitative yield was obtained of a nitrated product which contained two compounds that were readily separated by chromatography. The minor product, (10% yield) was
identified as the dinitro ester (44). The major product (85% yield) was the nitro ketone (266). Thus, the products obtained from this reaction are those resulting from nitro-deacylation, and nitro-dealkylation processes,\textsuperscript{215} with none of the expected nitro-substituted product (265) having been formed. The i.r. spectrum of the nitro ketone (266) showed, in addition to a ring A ester band at 1725 cm\textsuperscript{-1}, an aryl ketone band at 1710 cm\textsuperscript{-1}. The high aryl C=O frequency is due to the presence of the strongly electron-withdrawing nitro group in the ortho position. Considerable interaction between the C 12-acetyl and C 13-nitro groups was evident from inspection of the n.m.r. spectrum which showed two singlets, each integrating for 1.5 protons, for the C 12-acetyl methyl signal. The two signals did not collapse to a single peak when the n.m.r. spectrum was measured at 60°. On the principle of simple mesomeric and steric arguments\textsuperscript{216} the nitro group should attain coplanarity, and hence maximum p-\pi overlap with the aromatic ring at the expense of conjugation of the carbonyl group with the aromatic ring. The carbonyl group is thus bent out of the plane of the aromatic ring, which can give two different orientations to the methyl group, one in which it lies closer to the deshielding environment of the nitro group and another in which it is remote from the nitro group, resulting in the two signals in the n.m.r. spectrum.

The formation of anomalous nitration products is influenced by such factors as the composition of the nitrating mixture, the temperature at which the reaction is conducted, and the number, orientation, structure, and types of groups attached to the aromatic ring.\textsuperscript{215} In general, it
has been found that the poly-alkylated benzenes undergo anomalous nitration reactions in favour of the normal nitro-deprotonation. Nitro-deacylation reactions have been found usually to occur only during the nitration of aromatic systems in which the acyl group is ortho or para to an activating methoxy group, but it is also conceivable that nitro-deacylation would occur in sufficiently sterically crowded systems, as is evident in the present case. The dinitro ester (44) arises by attack of \( \text{NO}_2^+ \) at C 12 with loss of an acetyl cation, followed by nitration at C 14 in accord with the usual mechanism of electrophilic substitution at unsaturated carbon.\(^{217}\) The nitro ketone (266) arises by attack of \( \text{NO}_2^+ \) at C 13 with loss of a propyl cation (Fig. 5).

\[
(44) \quad \text{[Diagram]} \quad (266)
\]

Fig. 5

The stereochemistry at C 10 of the compound (266) was still in doubt at this stage, since direct deisopropylation of abieta-8,11,13-trien-18-oic acid (1) with aluminium chloride led predominantly to inversion of configuration at C 10,\(^{11}\) and it was possible that a similar C 9,10 bond breaking may have occurred during the nitro-deisopropylation. The homogeneity (g.l.c., m.p., n.m.r. spectrum) of the compound (266) meant that the configuration at C 10 was entirely \( \beta \), or \( \alpha \). This uncertainty was removed by conversion of the nitro-ketone (266) to the
C 13-hydroxy compound (59) and by comparison of the compound obtained in this way with the known methyl 13-hydroxy-podocarpa-8,11,13-trien-18-oate (59) prepared by Wenkert et al.85

An attempt was made to oxidise the C 13-acetyl group with iodine-pyridine, and treat the product with sodium hydroxide in order to obtain the nitro acid (267) which would then be decarboxylated to the C 13-nitro compound (268). However, the nitro acid (267) was obtained as a dark gum, which would not crystallize, even after chromatography. In view of this result it was decided to modify the C 13 substituent first, and then remove the C 12 substituent.

Reduction of the nitro ketone (266) with stannous chloride-hydrochloric acid in acetic acid212 gave, after hydrolysis of the stannic chloride addition compound with sodium hydroxide solution, the amino ketone (269) in 68% yield. The i.r. spectrum of the amino ketone (269) showed an aryl carbonyl band at 1640 cm⁻¹, shifted to lower frequency by the electron donating ortho amino group. Significantly, the n.m.r. spectrum of the amino ketone (269) showed a single resonance for the C 12-acetyl methyl group. The amine formed a mono-acetate (270) with acetic anhydride-pyridine at 100°.

The amino ketone (269) was soluble in dilute hydrochloric acid, and was diazotized with sodium nitrite in an aqueous acid medium following the procedure of Wenkert et al.85 Decomposition of the diazonium salt with hot dilute sulphuric acid gave the phenol (271)
in 84% yield. The phenolic proton of this latter compound was strongly hydrogen bonded to the C 12-acetyl ketone, as shown by the aryl ketone i.r. band at 1640 cm$^{-1}$, and the phenolic proton signal at $\delta$ 11.90 in the n.m.r. spectrum.

Methylation of the phenol with sodium hydroxide-dimethyl sulphate$^{218}$ gave the phenyl methyl ether (272) in 82% yield. The next stage of this synthesis was to remove the C 12-acetyl substituent. Its conversion to the phenol by the Baeyer-Villiger oxidation-hydrolysis procedure as described previously for conversion of the compound (227) to the phenol (254) was carried out, since hydrogenolysis of phenyl tosylates has been shown to replace the phenol group with hydrogen.$^{219}$ Oxidation of the keto methyl ether (272) with meta-chloroperbenzoic acid and toluene-$p$-sulphonic acid in 1,2-dichloroethane gave the gummy phenyl acetate (273). The n.m.r. spectrum of the crude phenyl acetate showed two acetate methyl signals separated by 2 Hz indicative of restriction of rotation of the C 12 acetate group by the ortho C 13-methyl ether. Hydrolysis of the crude phenyl acetate (273) gave the methoxy phenol (274) in 70% overall yield from the aryl ketone (272). Tosylation of the phenol (274) with toluene-$p$-sulphonyl chloride in pyridine gave an almost quantitative yield of the tosylate (275) as a gum. Several attempts to hydrogenolyze the tosylate with Raney Nickel$^{219}$ to the phenyl methyl ether (276) resulted in partial recovery of the methoxy phenol (274). Almost half of the product must have been strongly adhering to the nickel, and attempts to remove it by boiling the metal with a variety of solvents failed.
Fétizon and Gramain removed the phenol group from the ortho-methoxy phenol (277) by forming the diethyl phosphate ester, and hydrolysing this with sodium in liquid ammonia. The methyl ether (278) was obtained in 45% yield, but considerable starting material remained, even although the reaction was conducted under optimum conditions. While other methods are available for the removal of aromatic hydroxy groups, all of these involve the hydrogenolysis of a derivative of the phenol. Musliner and Gates have developed an efficient process wherein the phenol is firstly converted to the ether of phenyl 1-chloro tetrazole. Hydrogenolysis of the phenyl tetrazole ether then affords the deoxygenated aromatic compound. The unavailability of the phenyl chloro tetrazole, and its relatively difficult synthesis precluded the application of this method for removing the C 12-hydroxy group from the methoxy phenol (274).

Methyl 12-acetyl-13-methoxy-podocarpa-8,11,13-trien-18-oate (272) was oxidised smoothly to the C 12-carboxylic acid (279) by the iodine-pyridine method described previously. In contrast to the acid (267), the acid (279) was readily obtained pure in 78% yield. Decarboxylation of the acid (279) in boiling quinoline using basic copper carbonate catalyst afforded methyl 13-hydroxy-podocarpa-8,11,13-trien-18-oate (59), which was eventually obtained in 98% yield. In initial trials, some 20% of the reaction product was lost during the work-up procedure. This material was identified as the hydroxy acid (280). By subsequent treatment of the crude decarboxylation product with an ethereal solution of diazomethane, the crude solid phenol (59)
was isolated in almost quantitative yield. Filtration chromatography removed a small amount of colour to give the pure phenol (59) in 98% yield. The acid (280) arises by hydrolysis of the ester group by the basic quinoline at the high reaction temperature. The demethylation of the C 13-phenyl methyl ether and the decarboxylation are probably synchronous, and proceed through a complexed copper carbonate, \textit{viz:}

\begin{center}
\includegraphics[width=0.5\textwidth]{fig6.png}
\end{center}

\textbf{Fig. 6}

The phenol (59), obtained by this eight step synthetic sequence in an overall yield of 26% from methyl abieta-8,11,13-trien-18-oate (2), had an identical melting point with that prepared by Wenkert \textit{et al.} \textsuperscript{85} Further confirmation of the structure was obtained by converting the phenol (59) to the methyl ether (276), which also had the same melting point as the ether prepared by Wenkert \textit{et al.} \textsuperscript{85} Thus the nitrodeisopropylation reaction, in contrast to the aluminium chloride-catalysed deisopropylation, does not alter the configuration of the C 10 asymmetric centre, and hence provides the most efficient, and simplest route to the phenol (59).
The ready preparation of the phenol (59) and its conversion to the methyl ether (276) provided an opportunity to study the Birch reduction of the methyl ether to the \(\alpha,\beta\)-unsaturated ketone (281). The podocarp-8(14)-en-13-one system, as represented by the compound (281) has been used for the synthesis of other diterpenoids,\(^{81b,225}\) but it was envisaged also as a useful intermediate for the synthesis of a saturated steroid skeleton.

When methyl 13-methoxy-podocarpa-8,11,13-trien-18-oate (276) was reduced with lithium in liquid ammonia, followed by the addition of ethanol,\(^{226}\) two compounds were produced (t.l.c.) which were presumably the unsaturated alcohol (282), arising from 1,2 reduction to give initially a 1,3-diene, which undergoes further reduction, and the dienol ether (283) arising from 1,4 reduction.\(^{228}\) The ring-A ester was hydrolysed and reduced to the alcohol, as has been proved previously.\(^{227}\) The crude product from the Birch reduction was treated with ethanolic hydrochloric acid to give the unsaturated alcohol (282) in 7% yield, and the desired enone (281) in 75% yield.

A number of attempts were made to carry out an annelation of the enone (281) using bromoacetone with a strong base, e.g. potassium t-butoxide in t-butanol, to form the steroid (284). In all these attempts, either starting material or polymeric products were obtained. The enone (281) was readily converted to the pyrrolidine enamine (285). The enamine was very unstable, and was reacted immediately with bromoacetone, followed by hydrolysis of the iminium salt with water\(^{229}\) to give a
mixture of products which were separated by chromatography on deactivated alumina. The least polar compound eluted from the column was identified as the furan (286). Further eluates gave mixtures of compounds which were not investigated, and finally a bright yellow band was eluted which was concentrated to a dark brown gum which appeared to be a quinone ($\nu_{\text{max}}$ 1670 cm$^{-1}$). None of the desired steroid (284) or diketone (287) was isolated. Although this final step failed, it is apparent that the most efficient route to a saturated steroid will be via the enone (281), and by employing better annelation procedures, such as those recently described by Corey et al. 230 the synthesis of optically active steroids from abieta-8,11,13-trien-18-oic acid (1) might be realized in the near future.
Microanalyses were carried out by Dr A. D. Campbell and associates, University of Otago, New Zealand. Melting points were determined on a Reichert Kofler block and are uncorrected.

Infrared (i.r.) spectra were measured on a Perkin-Elmer 237 spectrophotometer. Nuclear magnetic resonance (n.m.r.) spectra were measured on a Varian A 60 spectrometer. The n.m.r. data are expressed as parts per million downfield shift from tetramethylsilane as internal reference and are quoted as; position, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constant (J, Hz), and assignment. \( \frac{2}{2} \) signifies peak width at half-height. Mass spectra were determined by Dr R. Hodges, Massey University, New Zealand, on an A.E.I. MS 902 mass spectrometer. Optical rotations were measured with a Jasco ORD UV-5 spectropolarimeter.

Alumina for column chromatography was P. Spence and Co., Type H, and was deactivated with 5% \( \frac{\text{V/v}}{} \) of 10% aqueous acetic acid. Silica gel for column chromatography was Kieselgel S (Riedel de Haen). Analytical thin layer chromatography (t.l.c.) was conducted on plates of Kieselgel DG (Riedel de Haen), and the chromatograms were developed with iodine vapour. Preparative t.l.c. was conducted on plates of 1 mm thick Kieselgel PF\( \text{254 + 366} \) (Merck). Analytical gas-liquid chromatography (g.l.c.) was carried out on a Varian Aerograph 1868 using a 5 ft x \( \frac{1}{8} \) in. 3% SE 30 column and a flame ionisation detector. The carrier gas was nitrogen.
Light petroleum refers to the fraction boiling at 50–60°, and ether to diethyl ether. Exsiccate magnesium sulphate was used for drying organic solutions.
Abieta-8,11,13-trien-18-oic Acid (1)

Abieta-8,11,13-trien-18-oic acid (1) was obtained from disproportionated rosin (Hercules Resin 731 S) by extraction of the monoethanolamine salt into aqueous ethanol, followed by reacidification with hydrochloric acid. Recrystallization of the acid from aqueous ethanol gave flakes, m.p. 173-174° (lit. 231 173-174°).

$\nu_{max} (\text{CHCl}_3) 3600-2500 \text{ (OH), 1710 (acid C=O)}$.

Oxidative Decarboxylation of Abieta-8,11,13-trien-18-oic Acid (1)

with Lead Tetraacetate

A mixture of abieta-8,11,13-trien-18-oic acid (1) (30.0 g, 100 mmol), dry benzene (150 ml), and freshly crystallized lead tetraacetate (50.0 g, 100 mmol) was stirred under nitrogen at 20° for 1 hr, and then heated under reflux for 3 hr. The cooled mixture was filtered, and the filtrate was concentrated to yield a pale yellow oil (30.7 g) which was chromatographed on deactivated alumina.

Elution of the column with light petroleum gave, in initial eluates a mixture of alkenes (3), (4) and (5) (16.0 g) as a colourless mobile oil.¹

$\nu_{max} (\text{CCl}_4) 3080 \text{ (C=CH}_2\text{)}, 1610, 1500 \text{ (aromatic), 1640 (C=CH}_2\text{),}

900 \text{ cm}^{-1} \text{ (C=CH}_2\text{)}$.

N.m.r. δ (CCl₄) 0.96 (s, C 10 angular Me of 3), 1.00 (s, C 10 angular Me of 4), 1.18 (d, J 7 Hz, C 15 methyls of 3, 4, and 5), 1.30 (s, C 10 angular Me of 5), 1.64 (s, C 4 Me of 4 and 5), 2.72-2.88 (m, C 7 and C 15 protons), 4.56, 4.78 (2 singlets, W₂
5 Hz, C 18 protons of 3), 5.38 (s, W1 6 Hz, C 3 proton of 4),
6.70-7.25 (m, aromatic protons).

From the later light petroleum eluates was obtained 18-
norabieta-8,11,13-trien-4α-yl acetate (288) (3.5 g, 12%), m.p. 60-61°.
(lit.1 60-61°).

$\nu_{\text{max}}$ (CCl₄) 1735 (ester C=O), 1250 (OAc C=O).

N.m.r. δ (CCl₄) 1.14 (s, C 4 axial Me), 1.19 (d, J 7 Hz, C 15
methyls), 1.49 (s, C 10 angular Me), 1.87 (s, OAc), 2.68-2.75
m, C 7 and C 15 protons), 6.70-7.26 (m, aromatic protons).

**Epoxidation of the Alkene Mixture (3), (4) and (5)**

The alkene mixture (3), (4) and (5) (14.0 g, 55 mmol), was
dissolved in ether (100.0 ml), and the solution was added to an ethereal
solution of an excess of monoperphthalic acid at 0°. The mixture was
kept at 4° for 4 days, filtered, and the filtrate was washed successively
with dilute aqueous potassium iodide, sodium thiosulphate, and sodium
hydrogen carbonate, and then with water and finally with brine. The
ether solution was dried and concentrated to afford a pale yellow oil
which was chromatographed on deactivated alumina.

Initial light petroleum eluates gave 19-norabieta-4(18),8,11,13-
tetraene (3) [4.2 g, 75% based on the isomer (3) in the mixture] as an
oil, with an i.r. and n.m.r. spectrum identical with that of the authentic
hydrocarbon. ¹ From later light petroleum eluates were obtained various
mixtures of two epoxides as oils (2.5 g total). G.l.c. indicated that
the major component was 4α,5α-epoxy-18-norabieta-8,11,13-triene (65) (2.1 g, 65% estimated from n.m.r. and g.l.c. data of the various fractions), [α]D + 142° (± 0.34).

Found: C, 84.3; H, 9.6; 0, 5.8

C19H26O requires: C, 84.4; H, 9.7; 0, 5.9%.

νmax (CCl4) 925 and 860 cm⁻¹ (epoxide).

N.m.r. δ (CCl4) 1.18 (d, J 7 Hz, C 15 methyls), 1.30, 1.32 (C 4 axial and C 10 angular methyls), 2.55-2.95 (m, C 7 and C 15 protons), 6.75-7.05 (m, aromatic protons).

Elution of the column with light petroleum-benzene (4:1) afforded 3α,4α-epoxy-18-norabieta-8,11,13-triene (64) [4.3 g, 82% based on the alkene (4) in the mixture], which crystallized from chloroform-methanol as large flakes, m.p. 73-74°, [α]D + 170° (± 0.14).

Found: C, 84.2; H, 9.5; 0, 6.3

C19H26O requires: C, 84.4; H, 9.7; 0, 5.9%.

νmax (CCl4) 1250, 950 cm⁻¹ (epoxide).

N.m.r. δ (CCl4) 1.03 (s, C 10 angular Me), 1.26 (d, J 7 Hz, C 15 methyls), 1.29 (s, C 4 axial Me), 2.55-3.00 (m, C 3, C 7 and C 15 protons), 6.75-7.05 (m, aromatic protons).

4α,19-Epoxy-18-norabieta-8,11,13-triene (66)

A solution of the exocyclic alkene (3) (0.10 g) in chloroform (10.0 ml) was treated with an excess of perbenzoic acid in chloroform, and the mixture was kept at 4° for 12 hr. The solution was washed with
dilute aqueous potassium iodide, sodium thiosulphate, and sodium hydrogen carbonate, and then with water. Removal of the solvent from the dried solution gave 4α,19-epoxy-18-norabieta-8,11,13-triene (66) (83 mg, 85%) which was recrystallized from chloroform-methanol as needles, m.p. 63-64°, [α]D + 99° (c 0.14).

Found: C, 84.4; H, 9.6

C19H26O requires: C, 84.4; H, 9.7%.

νmax (CCl4) 3020, 1250, and 980 cm⁻¹ (epoxide).

N.m.r. δ (CCl4) 1.14 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 2.75-3.05 (m, C 19 protons, and C 7 and C 15 protons), 6.85-7.35 (m, aromatic protons).

This epoxide was also formed in low yield (ca. 10%) during the epoxidation of the alkenes (3), (4) and (5) with monoperphthalic acid. It showed a t.l.c. spot identical with that given by the 4α, 5α-epoxide (65), but was distinguished from the latter compound by g.l.c.

Ozonolysis of 19-Norabieta-4(18),8,11,13-tetraene (3)

The alkene (3) (0.25 g, 0.98 mmol), dissolved in methylene dichloride (5.0 ml), was added at -80° to methylene dichloride (125 ml) and pyridine (0.1 g) which had been saturated with ozone (ca. 0.2 mmol ozone per 25.0 ml). The solution was washed successively with aqueous solutions of potassium iodide containing 10% of acetic acid, and sodium metabisulphite, and then with water. The
organic phase was dried and concentrated to give an oil which was percolated through deactivated alumina in benzene to give 18,19-bisnor-5αH- and 5βH-abieta-8,11,13-trien-4-one (6) as an oil (0.18 g, 70%).

\[ \nu_{\text{max}} (\text{CHCl}_3) 1715 \text{ cm}^{-1} \text{ (ketone C=O).} \]

N.m.r. δ (CDCl₃) 0.98 (s, C 10 angular Me of 5α-epimer and/or of 5β-epimer, axial conformation), 1.18 (d, J 7 Hz, C 15 methyls), 1.28 (s, C 10 angular Me of 5β-epimer, equatorial conformation), 2.03-2.40 (m, C 3 and C 5 protons), 2.72-2.90 (m, C 7 and C 15 protons), 6.74-7.28 (m, aromatic protons).

**Rearrangement of 3α,4α-Epoxy-18-norabieta-8,11,13-triene (64)**

a) with Boron Trifluoride

Freshly distilled boron trifluoride etherate (0.2 ml) was added to a solution of the epoxide (64) (0.18 g, 0.67 mmol) in dry benzene (40.0 ml), and the mixture was kept at 20° for 3 min. Saturated aqueous sodium hydrogen carbonate (10 ml) was added, the mixture was shaken, and the benzene layer was separated and washed with water, dried, and concentrated to afford an oil which was chromatographed on deactivated alumina.

Light petroleum eluted A-norabieta-8,11,13-trien-19-al (74) (0.142 g, 80%) as an oil, [α]₅ + 27° (c 0.45).

Found: C, 84.4; H, 10.1

C₁₉H₂₆O requires: C, 84.4; H, 9.7%.
\[ v_{\text{max}} (\text{CHCl}_3) 2700 \text{ cm}^{-1} \text{ (aldehyde CH), } 1725 \text{ cm}^{-1} \text{ (aldehyde C=O).} \]

N.m.r. \( \delta (\text{CDCl}_3) 1.18 \text{ (s, C 4 and C 10 angular methyls), } 1.22 \text{ (d, J 7 Hz, C 15 methyls), } 2.60-3.15 \text{ (m, C 7 and C 15 protons), } 6.85-7.00 \text{ (s, } \frac{1}{2} \text{ 8 Hz, aromatic protons), } 9.06 \text{(s,CHO).} \]

Benzene eluted 19-norabieta-4(18),8,11,13-tetraen-3\(\alpha\)-ol (76) (20 mg, 10%) which formed a solid, m.p. 60-61° (from chloroform-light petroleum), \([\alpha]_D + 110^\circ \text{ (C 0.15).}\]

Found: \quad C, 84.3; H, 10.0

\( C_{19}H_{26}O \) requires: \quad C, 84.4; H, 9.7%

\[ v_{\text{max}} (\text{CHCl}_3) 3600 \text{ (OH), } 3080, 1650 \text{ (C=CH}_2\text{), } 980 \text{ (C=O)} \]

910 \text{ cm}^{-1} \text{ (C=CH}_2\text{).} \]

N.m.r. \( \delta (\text{CDCl}_3) 0.96 \text{ (s, C 10 angular Me), } 1.22 \text{ (d, J 7 Hz, C 15 methyls), } 1.83 \text{ (s, OH, exchanged with D}_2O\text{), } 2.60-3.18 \text{ (m, C 7 and C 15 protons), } 4.32 \text{ (s, } \frac{1}{2} \text{ 6 Hz, C 3 proton), } 4.72, 5.05 \text{ (2 singlets, } \frac{1}{2} \text{ 5 Hz, C 18 protons), } 6.86-7.32 \text{ (m, aromatic protons).} \]

Acetylation of the alcohol (76) with acetic anhydride-pyridine (20°, 12 hr) gave 19-norabieta-4(18),8,11,13-tetraen-3\(\alpha\)-yl acetate (77) as a colourless oil, \([\alpha]_D + 148^\circ \text{ (C 0.11).}\]

Found: \quad C, 80.7; H, 9.0

\( C_{21}H_{28}O_2 \) requires: \quad C, 80.7; H, 9.0%
\[ \nu_{\text{max}} (\text{CHCl}_3) \] 1725 (acetate C=O), 1250 (acetate C=O), 1655
and 910 cm\(^{-1}\) (C=CH\(_2\)).

N.m.r. 6 (CDCl\(_3\)) 1.00 (s, C 10 angular Me), 1.23 (d, J 7 Hz, 
C 15 methyls), 1.95 (s, OAc), 4.83, 5.18 (2 singlets, W\(_1/2\) 5 Hz, 
C 18 protons), 5.37 (s, W\(_1/2\) 6 Hz, C 3 proton), 6.90–7.38 (m, 
aromatic protons).

b) with Sulphuric Acid

A solution of the epoxide (64) (0.40 g, 1.48 mmol) in acetone 
(20.0 ml) was treated with 98% sulphuric acid (0.3 ml) and water (1.0 ml),
and the mixture was heated under reflux for 4 hr. The mixture was
diluted with water, extracted with ether, and the ether extract was
dried, and concentrated to give an oil which was chromatographed on
deactivated alumina.

Elution of the column with light petroleum gave an unstable
hydrocarbon fraction (80 mg, 20%) in the initial fractions. From the
later light petroleum eluates was obtained the A-noraldehyde (74) 
(30 mg, 7%) which had an identical t.l.c. spot and i.r. spectrum as
those of the authentic aldehyde (74).

From the benzene eluates was obtained 19-norabieta-4(18),8,11, 
13-tetraen-3α-ol (76) (0.21 g, 52%) as a semi-crystalline glass,
identical in all respects with the authentic compound.

Further material, eluted from the column with benzene was
obtained as an intractable brown gum.
c) with Activated Alumina

The epoxide (64) (80 mg, 0.3 mmol), dissolved in a small volume of light petroleum, was added to a column of active alumina (2.3 g, Spence, type H, activated at 110° for 12.0 hr), and the latter was left overnight.

Elution of the column with benzene gave the starting epoxide (64) (44 mg), identified by its t.l.c. spot and its i.r. spectrum. Elution of the column with ether gave 19-norabieta-4(18),8,11,13-tetraen-3α-ol (76) (18 mg, 20%), (identical i.r. and n.m.r. spectra).

d) with Lithium Diethylamide

An ethereal solution of n-butyllithium (1.57 m, 1.0 ml) was treated at 0° under dry nitrogen with redistilled diethylamine (1.0 ml) in dry ether (5.0 ml), and the mixture was stood at 0° for 10 min until the evolution of butane had ceased. The epoxide (64) (1.0 g, 3.7 mmol) in dry ether (18.0 ml) was slowly added at 0°, and the mixture was refluxed gently under nitrogen for 36 hr. The cooled mixture was poured into ice-water and extracted with ether. The ether extract was washed with 2N hydrochloric acid, water, and brine, and then dried and concentrated to give 19-norabieta-4(18),8,11,13-tetraen-3α-ol (76) (1.0 g, 100%), as a semi-crystalline glass which precipitated from chloroform-light petroleum as a solid, m.p. and m.m.p. 60–61°.

e) with Methylmagnesium iodide

A solution of the epoxide (64) (0.51 g, 1.9 mmol) in dry ether (35.0 ml) was added to a solution of methylmagnesium iodide, prepared
from magnesium (0.6 g), methyl iodide (3.45 ml), and ether (3.50 ml). The mixture was stirred and refluxed gently under nitrogen for 5 hr, cooled, poured into saturated aqueous ammonium chloride, and then extracted with ether. The ether layer was washed with water, dried, and concentrated to give an oily product which was chromatographed on deactivated alumina.

Elution of the column with light petroleum–benzene (4:1) gave the starting epoxide (64) (2 mg), identified by its t.l.c. spot and its i.r. spectrum.

The initial benzene eluates afforded a mixture of 19-methyl-A-norabieta-8,11,13-trien-19α-and 19β-ols (103) as a colourless oil (0.28 g, 56%).

Found: mol. wt., 286.2301 (mass spectrum)

C_{20}H_{30}O requires mol. wt., 286.2297

ν_{max} (CHCl_3) 3600 (OH) and 1105 cm^{-1} (secondary OH).

N.m.r. δ (CDCl_3) 1.00-1.27 (C 10, C 19 methyls), 1.22 (d, J 7 Hz, C 15 methyls), 1.69 (OH, exchanged with D_2O), 2.85-3.15 (m, C 7 and C 15 protons), 3.41 (q, J 7 Hz, C 19 proton), 6.75-7.00 (s, W 8 Hz, aromatic protons).

From the later benzene eluates was obtained 19-norabieta-4,8,11,13-tetraen-3α-ol (92) (0.15 g, 30%) which was recrystallized from light petroleum as needles, m.p. 120-121°, [α]_D + 264° (c 0.11).
Found: C, 84.7; H, 9.5

C_{19}H_{26}O requires: C, 84.4; H, 9.7%

ν_{max} (CHCl_{3}) 3600 (OH), 980 cm^{-1} (C=O).

N.m.r. δ (CDCl_{3}) 1.22 (d, J 7 Hz, C 15 methyls), 1.32 (s, C 10 angular Me), 1.80 (s, C 4 Me), 2.55-3.00 (m, C 7 and C 15 protons), 3.88 (s, W_{1/2} 6 Hz, C 3 proton), 6.80-7.28 (m, aromatic protons).

Treatment of the A-noraldehyde (74) (45 mg) with methylmagnesium iodide as above afforded a mixture of epimeric 19-methyl-A-norabieta-8,11,13-trien-19α- and 19β-ols (74%), with R_{P} value and the i.r. spectrum identical with those of the sample obtained above.

**48-Acetyl-19,A-bisnorabieta-8,11,13-triene (104)**

The mixed alcohols (103) (0.10 g, 0.35 mmol) in acetone (7.0 ml) were treated with Jones reagent (0.5 ml) at 0°, and the mixture was stirred for 30 min. The mixture was diluted with isopropanol and water, and then extracted with ether. The ether layer was washed with water, dried, and concentrated to afford 48-acetyl-19,A-bisnorabieta-8,11,13-triene (104) (75 mg, 74%) as an oil, [α]_{D} + 48° (c 0.25).

Found: C, 84.5; H, 10.1; 0.5.8

C_{20}H_{28}O requires: C, 84.5; H, 10.0; 0.5.6%

ν_{max} (film) 1695 cm^{-1} (ketone C=O).
N.m.r. δ (CDCl₃) 1.15 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.25 (s, C 4 Me), 2.12 (C 4 COMe), 2.65-3.15 (m, C 7 and C 15 protons), 7.00 (s, W₂ 8 Hz aromatic protons).


A solution of the ketone (104) (30 mg, 0.12 mmol) in absolute methanol (2.0 ml) was treated with sodium borohydride (13.0 mg) in methanol (4.0 ml) containing 2N aqueous sodium hydroxide (0.1 ml), and the mixture was stirred at 20° for 3 days. The mixture was diluted with water and extracted with ether. The ether layer was dried and concentrated to give the epimeric alcohols (103) (30 mg, 98%), which possessed i.r. and n.m.r. spectra identical with those of the mixed alcohols from rearrangement of the epoxide (64) with methylmagnesium iodide.

4α,19-Epoxy-18-norabieta-8,11,13-trien-3α-ol (88)

The allylic alcohol (76) (0.10 g, 0.37 mmol), dissolved in chloroform (10.0 ml), was treated with m-chloroperbenzoic acid (70 mg) in chloroform (2.0 ml) and the mixture was stood at 4° overnight. The chloroform solution was worked-up as described earlier for epoxidation, to give 4α,19-epoxy-18-norabieta-8,11,13-trien-3α-ol (88) (0.102 g, 100%), which crystallized from chloroform-light petroleum as needles, m.p. 96–97°, [α]₅₀ + 71° (c 0.085).
Found: \[ C, 79.4; H, 9.2 \]

\[ \text{C}_{19}\text{H}_{26}\text{O}_2 \text{ requires: } C, 79.7; H, 9.2\% \].

\[ \nu_{\text{max}} (\text{CHCl}_3) \text{ 3600 cm}^{-1} (\text{OH}). \]

N.m.r. \[ \delta (\text{CDCl}_3) \]

- 1.12 (s, C 10 angular Me),
- 1.22 (d, J 7 Hz, C 15 methyls),
- 1.70 (OH, exchanged with \( \text{D}_2\text{O} \)),
- 2.65-3.00 (m, C 19 and C 7, and C 15 protons),
- 3.45 (s, \( \frac{2}{3} \) 6 Hz, C 3 proton),
- 6.80-7.25 (m, aromatic protons).

**Oxidation of 4a,19-Epoxy-18-norabietta-8,11,13-triene (88)**

a) **with Jones Reagent**

A solution of the epoxy-alcohol (88) (80 mg, 0.28 mmol) in acetone (10.0 ml) was treated with Jones reagent (0.4 ml), and the mixture was stirred at 0° for 30 min. The mixture was diluted with isopropanol and water, and extracted with ether. The ether layer was washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina.

Elution of the column with benzene gave 4a,19-epoxy-18-norabietta-8,11,13-trien-3-one (87) (65 mg, 81%), as a pale-yellow oil.

Found: mol. wt., 284.1774 (mass spectrum)

\[ \text{C}_{19}\text{H}_{24}\text{O}_2 \text{ requires mol. wt., 284.1776.} \]

\[ \nu_{\text{max}} (\text{CHCl}_3) \text{ 1720 cm}^{-1} (\text{ketone C=O}). \]

N.m.r. \[ \delta (\text{CDCl}_3) \]

- 1.22 (d, J 7 Hz, C 15 methyls),
- 1.36 (s, C 10 angular Me),
- 2.60-3.15 (m, C 19, C 7 and C 15 protons),
- 6.80-7.35 (m, aromatic protons).
b) with Chromium Trioxide-Pyridine

The epoxy-alcohol (88) (40 mg, 0.14 mmol), dissolved in methylene dichloride (10.0 ml), was treated with chromium trioxide-pyridine complex (0.15 g), and the mixture was stirred at 20° for 3 days. The mixture was filtered through Celite and concentrated to afford an oil. T.L.C. of this oil showed the presence of the starting epoxy-alcohol (88) and the epoxy-ketone (87). The i.r. spectrum of the oil indicated only ca. 50% conversion to the epoxy-ketone (87).

Oxidation of 19-Norabieta-4(18),8,11,13-tetraen-3α-ol (76)

a) with Jones Reagent

A solution of the allylic alcohol (76) (60 mg, 0.45 mmol) in acetone (15.0 ml) at 0° was treated with Jones reagent (0.45 ml), and the mixture was stirred at 0° for 30 min. The mixture was diluted with isopropanol and water and extracted with ether. The ether layer was washed with water, dried, and concentrated to give a yellow gum, t.l.c. of which indicated the presence of five compounds plus starting material (76). Extraction of a solution of the oil in ether with 10% sodium hydroxide solution yielded a small amount of acidic material, \( \nu_{\text{max}} \) 3600-2500 (OH) and 1715 cm\(^{-1}\) (acid C=O), as a brown gum, while chromatography of the neutral fraction on deactivated alumina and elution of the column with light petroleum-benzene (4:1) gave a ketonic fraction (20 mg, 30%) containing the enone (86) \( \nu_{\text{max}} \) 1695 cm\(^{-1}\) (C=O), and the epoxy-ketone (87), \( \nu_{\text{max}} \) 1725 cm\(^{-1}\) (C=O), each identified by t.l.c. comparison with the authentic materials.
b) with Chromium Trioxide-Pyridine

The allylic alcohol (76) (25 mg, 0.11 mmol) in methylene dichloride (2.5 ml) was treated with chromium trioxide-pyridine complex (0.12 g), and the mixture was stirred at 20° for 24 hr. The mixture was filtered through Celite and the filtrate was concentrated to afford a brown gum which was chromatographed on deactivated alumina.

Light petroleum eluted the enone (86) (5 mg, 20%) as an oil, with a t.l.c. spot and i.r. spectrum identical with those of the authentic ketone.

Benzene eluted the epoxy-ketone (87) (10 mg, 40%) as a pale-yellow oil, having identical t.l.c. and i.r. spectra with the ketone previously obtained.

c) with Dimethyl Sulphoxide and Pyridine-Sulphur Trioxide Complex

A solution of pyridine-sulphur trioxide complex (68 mg) in dry dimethyl sulphoxide (0.5 ml) was added dropwise over a 15 min period at 20° to a solution of the allylic alcohol (76) (45 mg, 0.17 mmol) in dimethyl sulphoxide (0.5 ml) and freshly distilled triethylamine (0.15 ml). The mixture was diluted with water, acidified to pH 3 with 2N hydrochloric acid, and extracted with ether. The ether extract was washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (4:1) afforded norabieta-4(18),8,11,13-tetraen-3-one (86) (40 mg, 90%)
as an unstable pale-yellow oil, $\left[\alpha\right]_D + 146^\circ \leq 0.19$, identified from its spectroscopic properties.

$$\nu_{\text{max}} \quad \text{(CHCl}_3) \quad 1695 \text{ (cisoid } \alpha,\beta-\text{unsaturated ketone } C=O), \quad 1630, \quad 945 \text{ cm}^{-1} \quad (C=C).$$

$$\lambda_{\text{max}} \quad \text{(EtOH)} \quad 226 \text{ m}, \quad (\log \varepsilon 3.71).$$

N.m.r. $\delta$ (CDCl$_3$) 1.11 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 2.40-3.05 (m, C 2, C 7 and C 15 protons), 5.20, 5.95 (2 singlets, $\frac{1}{2} 5$ Hz, C 18 protons), 6.85-7.40 (m, aromatic protons).

R.d. $(\leq 0.19) \left[\varnothing\right]_{589} = 394^\circ, \left[\varnothing\right]_{450} = 788^\circ, \left[\varnothing\right]_{325} = 3790^\circ, \left[\varnothing\right]_{240} + 5380^\circ.$

**Reduction of 4α,19-Epoxy-18-norabieta-8,11,13-trien-3-one (87)**

A rapid current of carbon dioxide was passed for 30 min through a mixture of a solution of the epoxy-ketone (87) (60 mg, 0.047 mmol) in glacial acetic acid (7.0 ml) and chromous chloride solution [prepared from chromic chloride hexahydrate (0.12 g), zinc dust (0.24 g), and mercuric chloride (24 mg)]. The blue solution was diluted with water, extracted with ether, and the ether solution was washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina.

The $\alpha,\beta$-unsaturated ketone (86) (22 mg, 33%) was obtained from the light petroleum-benzene (4:1) eluates. It showed an identical t.l.c. spot and i.r. spectrum with those of the enone obtained previously.
Attempted Isomerisation of 19-Norabieta-4(18),8,11,13-tetraen-3-one (86)

The cis-cis enone (86) (25 mg, 0.09 mmol) in absolute ethanol (4.0 ml) was treated with anhydrous oxalic acid (1.5 mg), and the mixture was heated under reflux for 20 min. The cooled mixture was extracted with ether, and the ether extract was washed with saturated aqueous sodium hydrogen carbonate and then with water, dried, and concentrated to give a pale yellow oil. T.l.c. showed one spot with high Rf but with considerable streaking. The n.m.r. spectrum of the oil showed that the terminal vinyl protons had disappeared, but none of the desired transoid α,β-unsaturated ketone (89) could be isolated.

Isomerisation of 19-Norabieta-4(18),8,11,13-tetraen-3α-ol (76)

a) with Oxalic Acid in Absolute Ethanol

The allylic alcohol (76) (50 mg, 0.18 mmol) in absolute ethanol (5.0 ml), was treated with anhydrous oxalic acid (17 mg), and the mixture was refluxed under nitrogen for 30 min. The mixture was cooled, poured into water, and extracted with ether and worked-up to yield a yellow oil (45 mg), t.l.c. of which indicated the presence of one non-polar compound, probably a diene.

\[ \nu_{\text{max}} (\text{CCl}_4) \] 1600, 1495, 830 (aromatic) and 920 cm\(^{-1}\) (diene C=C).

The material rapidly discoloured in the air and was not investigated further.

Treatment of the derived acetate (77) of 19-norabieta-4(18),8,11,13-tetraen-3α-ol with hydrogen chloride in chloroform at -5\(^{\circ}\) for 4 hr,
or with toluene-\(p\)-sulphonic acid in refluxing dioxane for 4 hr gave quantitative yields of unchanged material.

b) with N-lithioethylenediamine for 2 hr

The allylic alcohol (76) (80 mg, 0.34 mmol) in anhydrous ethylenediamine (10.0 ml), was added to lithium (84 mg) in ethylenediamine (25.0 ml) at 100\(^\circ\) under nitrogen, and the purple solution was refluxed for \(\frac{1}{4}\) hr. The cooled solution was poured onto ice, extracted with ether, and the ether extract was washed, dried, and concentrated to give an oil.

Percolation of this oil in benzene through deactivated alumina, and recrystallization of the concentrate from light petroleum gave 19-nor-\(\Delta^8\)H-abieta-6,8,11,13-tetraen-3\(\alpha\)-ol (90) (75 mg, 90\%), as needles, m.p. 140-141\(^\circ\), \([\alpha]_D^0 + 234\) (c 0.06).

Found: C, 84.6; H, 9.9

C\(_{19}\)H\(_{26}\)O requires: C, 84.4; H, 9.7%.

\(\nu_{\text{max}}\) (CHCl\(_3\)) 3600 (OH), 1665 (disubstituted C=C), 1110 cm\(^{-1}\) (C-O).

N.m.r. \(\delta\) (CDCl\(_3\)) 1.04 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.22 (d, J 7 Hz, C 4 Me), 1.73 (OH, exchanged with D\(_2\)O), 2.76 (5 members of a septet, J 7 Hz, C 15 proton), 3.10 (s, \(\frac{7}{2}\) 6 Hz, C 3 proton), 6.06 (d of d, J 6,7 10 Hz, J\(_{5,6}\) 6 Hz, C 6 proton), 6.37 (d, J\(_{6,7}\) 10 Hz, C 7 proton), 6.85-7.20 (m, aromatic protons).
c) with N-lithioethylenediamine for 5 min

The allylic alcohol (76) (0.3 g, 1.1 mmol) in ethylenediamine (25.0 ml) was treated as above with lithium (0.35 g) in ethylenediamine (25.0 ml) for 5 min. The hot mixture was cautiously diluted with iced-water, and the mixture was extracted with ether. The ether extract was washed with water, dried, and concentrated to give 19-norabieta-4, 8,11,13-tetraen-3α-ol (92) (0.3 g, 98%), which was recrystallized from light petroleum as needles, m.p. and m.m.p. 121-122°.

Gas chromatography of the crude product showed one main peak (98%). Of three minor peaks, one corresponded to the alcohol (92) one to the starting material (76) and the other presumably to an isomeric C 5-unsaturated alcohol.

19-Norabieta-4,8,11,13-tetraen-3-one (89)

A solution of the allylic alcohol (92) (0.2 g, 0.75 mmol) in acetone (12.0 ml) was oxidised with Jones reagent (0.7 ml) at 0° for 30 min. The mixture was diluted with isopropanol and water and extracted into ether. The ether layer was washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (1:1) afforded 19-norabieta-4,8,11,13-tetraen-3-one (89) 75 (0.165 g, 81%) as a colourless oil, [α]D + 196° (c 0.23).

\[ \nu_{\text{max}} (\text{CHCl}_3) 1660 \text{ cm}^{-1} \] (transoid α,β-unsaturated ketone C=O).
N.m.r. δ (CDCl₃) 1.26 (d, J 7 Hz, C 15 methyls), 1.54 (s, C 10 angular Me), 1.88 (s, C 4 Me), 2.55-3.25 (m, C 2, C 7 and C 15 protons), 7.25-7.50 (m, aromatic protons).

Methylation of 19-Norabiet-a-4,8,11,13-tetraen-3-one (89)

a) with Potassium t-Butoxide, Methyl Iodide in t-Butanol

The enone (89) (0.3 g, 1.12 mmol) in dry t-butanol (10.0 ml) and potassium t-butoxide (0.55 g) was refluxed under nitrogen while methyl iodide (0.75 ml) in t-butanol (10.0 ml) was added over a 55 min period. The mixture was refluxed for a further 40 min, cooled, and poured into water. Extraction with ether, followed by chromatography of the oily product on deactivated alumina gave, from the light-petroleum-benzene (3:1) eluate, abiet-a-5,8,11,13-tetraen-3-one (67) (0.25 g, 68%), as a pale yellow oil, [α]D (c 0.18) + 83°.

Found: C, 84.8; H, 9.2

C20H26O requires: C, 85.0; H, 9.3%.

vmax (CHCl₃) 1710 (saturated ketone C=O), 1665 cm⁻¹ (C=C).

N.m.r. δ (CDCl₃) 1.20 (s, C 10 angular Me), 1.26 (d, J 7 Hz, C 15 methyls), 1.30, 1.34 (2 singlets, C 4 axial and C 4 equatorial methyls), 2.22-3.06 (m, C 2, C 7 and C 15 protons), 3.47 (d, J 4.5 Hz, C 7 protons), 5.97 (t, J 4.5 Hz, C 6 proton), 6.98-7.43 (m, aromatic protons).

R.d. (c 0.18) [α]589 + 234°, [α]500 + 375°, [α]400 + 826°, [α]355 + 1576°, [α]325 + 624°.
b) with Potassium 2-Methyl-2-Butoxide, Methyl Iodide in Benzene

A solution of the enone (89) (0.27 g, 1.1 mmol) in dry benzene (10.0 ml) and potassium 2-methyl-2-butoxide [from potassium (0.25 g) and t-pentanol (5.0 ml)] was prepared under nitrogen by heating at 50° for 30 min. The solution was cooled in ice, methyl iodide (0.75 ml) in benzene (2.0 ml) was added dropwise, and the mixture was refluxed for 2 hr. The cooled mixture was diluted with water, the benzene layer was separated, washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina.

Light petroleum-benzene (3:1) eluted the ketone (67) (0.21 g, 74%) as an oil, having identical i.r. and n.m.r. spectra with those of the product obtained in (a) above.

Catalytic Hydrogenation of Abieta-5,8,11,13-tetraen-3-one (67)

a) with 10% Palladium-Carbon

The β,γ-unsaturated ketone (67) (0.2 g, 0.70 mmol) in ethyl acetate (25.0 ml) was hydrogenated over 10% palladium-carbon (0.1 g) for 3 days at 55 p.s.i. The catalyst was filtered off and the filtrate was concentrated to afford an oil, the n.m.r. spectrum of which showed the presence of a predominance of the starting material (67). Attempted hydrogenation under identical conditions except for the addition of concentrated sulphuric acid (2 drops) as a co-catalyst, failed to give any reduced products.
b) with Platinum Oxide

The β,γ-unsaturated ketone (67) (0.2 g, 0.70 mmol) in ethyl acetate (25.0 ml) was hydrogenated over platinum oxide (25 mg) for 16½ hr at 50 p.s.i. The mixture was filtered, and the filtrate was concentrated to give an oil which was chromatographed on deactivated alumina. Elution of the column with light petroleum-benzene (9:1) afforded impure starting material (67) (0.18 g) with an n.m.r. spectrum similar to that of the product obtained in (a) above.

Elution of the column with benzene gave a mixture (t.l.c.) of oily alcohols (10 mg).

\[ \nu_{\text{max}} (\text{CHCl}_3) 3600 \text{ cm}^{-1} \text{ (OH)} \].

c) with 20% Palladium-Carbon

The β,γ-unsaturated ketone (67) (0.3 g, 1.06 mmol) in 95% ethanol (50.0 ml) and glacial acetic acid (2.0 ml) was hydrogenated over 20% palladium-carbon (0.5 g) at 20° and 55 p.s.i. for 13 hr. The catalyst was filtered off and the filtrate was concentrated to give a colourless gum which crystallised on standing. Recrystallization from chloroform-methanol afforded a constant melting point mixture of \( \text{5cH- and 5bH-abieta-8,11,13-trien-3-ones} \) (99) and (100) (0.15 g, 50%) as laths, m.p. 89–90°. Further recrystallisations from chloroform-methanol or acetone did not yield a homogeneous product.

Found: C, 84.5; H, 10.4

C\(_{20}\)H\(_{28}\)0 requires: C, 84.45; H, 9.9%. 
\( \nu_{\text{max}} (\text{CHCl}_3) \) 1715 cm\(^{-1}\) (ketone C=O).

N.m.r. \( \delta (\text{CDCl}_3) \) 0.95-1.45 (C 4 and C 10 methyls of 99 and 100), 1.22 (d, J 7 Hz, C 15 methyls), 2.42-3.08 (m, C 7 and C 15 protons), 6.80-7.45 (m, aromatic protons).

R.d. (c 0.14) [\( \phi \)\( \text{589 + 101}^\circ\), [\( \phi \)\( \text{400 + 205}^\circ\), [\( \phi \)\( \text{332}^\circ\), [\( \phi \)\( \text{315 - 470}^\circ\), [\( \phi \)\( \text{304}^\circ\), [\( \phi \)\( \text{288 + 1500}^\circ\).

An identical product was obtained if the hydrogenation was carried out employing concentrated sulphuric acid (2 drops) as a co-catalyst.

Auto-oxidation of Abieta-5,8,11,13-tetraen-3-one (67)

The \( \beta,\gamma \)-unsaturated ketone (67) (0.16 g, 0.57 mmol) was stood in contact with the air at 20\(^\circ\) for 1 month. The resulting product so formed was washed with light petroleum and recrystallized from light petroleum to give abieta-5,8,11,13-tetraen-3,7-dione (93) (0.1 g, 57%) as needles, m.p. 173-174\(^\circ\), [\( \alpha \)\( \text{D} + 55^\circ\) (c 0.11)

Found: C, 80.5; H, 8.1

C\(_{20}\)H\(_{24}\)O\(_2\) requires: C, 81.0; H, 8.2%.

\( \nu_{\text{max}} (\text{CHCl}_3) \) 1715 (saturated ketone C=O), 1655 cm\(^{-1}\) (\( \alpha,\beta \)-unsaturated aryl ketone C=O).

N.m.r. \( \delta (\text{CDCl}_3) \) 1.23 (s, C 10 angular Me), 1.27 (d, J 7 Hz, C 15 methyls), 1.40 (s, C 4 axial Me), 1.47 (s, C 4 equatorial Me), 2.88 (5 members of a septet, J 7 Hz, C 15 proton), 6.52 (s, C 6 proton), 7.45, 7.55 (2 doublets, J 9 Hz, C 11 and C 12 protons), 8.08 (s, \( \frac{1}{2} \) 4 Hz, C 14 proton).
R.d. (c 0.11) [φ]_{589} + 162°, [φ]_{400} + 830, [φ]_{342} + 2420°.

Rearrangement of 4α,19-Epoxy-18-norabieta-8,11,13-triene (66) with Boron Trifluoride

The epoxide (66) (0.46 g, 1.70 mmol) in dry benzene (20.0 ml) was treated with boron trifluoride etherate (0.1 ml, distilled from calcium hydride) and the solution was stood at 20° for 2 min. Saturated aqueous sodium hydrogen carbonate was added, the mixture was shaken, and the benzene layer was dried and concentrated to give an oil which was chromatographed on deactivated alumina. The initial light petroleum eluates afforded a hydrocarbon (40 mg, 9%) which was not investigated further. From later light petroleum eluates was obtained 19-norabieta-8,11,13-trien-18-al (134) (280 mg, 62%) as a colourless oil, [α]_{D} + 92° (c 0.24).

Found: C, 84.2; H, 9.5

C_{19}H_{26}O requires: C, 84.4; H, 9.7%.

v_{max} (CHCl_{3}) 2710 (aldehyde CH), 1735 cm^{-1} (aldehyde C=O).

N.m.r. δ (CDCl_{3}) 1.10 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 2.60-3.10 (m, C 7 and C 15 protons), 6.85-7.30 (m, aromatic protons), 9.50 (d, J 4 Hz, CHO).

From the benzene eluates was obtained an oil (20 mg) which showed two spots with similar R_{F} values on t.l.c. The spot with the highest R_{F} corresponded to that of the mixture of allylic alcohols (135) and (136).

v_{max} (CHCl_{3}) 3600 cm^{-1} (OH).
The n.m.r. spectrum of the crude product from the reaction showed in addition to the signals of the C 18 aldehyde (134), those of the C 19 aldehyde (133), viz \( \delta 1.02 \) (s, C 10 angular methyl) and \( 9.85 \) (s, \( \frac{W}{2} 1.5 \) Hz, CHO).

Rearrangement of 4α,5α-Epoxy-18-norabieta-8,11,13-triene (65) with Boron Trifluoride

Boron trifluoride etherate (0.1 ml, distilled from calcium hydride) was added to a solution of the epoxide (65) (0.44 g, 1.63 mmol) in dry benzene (20.0 ml). After the pink solution had stood at 20° for 5 min, saturated aqueous sodium hydrogen carbonate was added and the mixture was shaken. The benzene layer was dried and concentrated to afford an oil which was chromatographed on deactivated alumina. The initial light petroleum eluates gave 19-norabieta-3,5,8,11,13-pentaene (111) (140 mg, 30%) as an unstable oil.

\( \nu_{\text{max}} \) (film) 1645 cm\(^{-1}\) (C=C).

N.m.r. \( \delta \) (CCl\(_4\)) 1.13 (s, C 10 angular Me), 1.21 (d, J 7 Hz, C 15 methyls), 1.84 (d, J 2 Hz, C 4 Me) 2.87 (5 members of a septet, J 7 Hz, C 15 proton), 3.42 (d, J 5 Hz, C 7 protons), 5.55 (s, \( \frac{W}{2} 11 \) Hz, C 3 proton), 5.85 (t, J 5 Hz, C 6 proton), 6.70-7.40 (m, aromatic protons).

From the later light petroleum eluates was obtained 4β-methyl-18,19-bisnor-10(5→4) abeoabieta-8,11,13-trien-5-one (112) (40 mg, 9%) as a colourless oil, \([\alpha]_D - 29^\circ\) (c 0.24).

Found: C, 84.2; H, 10.1; 0.6.2

\( C_{19}H_{26}O \) requires: C, 84.4; H, 9.7; 0.5.9%. 
\( \nu_{\text{max}} \) (CHCl\(_3\)) 1705 cm\(^{-1}\) (7-membered ketone C=O)

N.m.r. \( \delta \) (CDCl\(_3\)) 1.17 (s, C 19 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.35 (s, C 4 angular Me), 2.20-3.00 (m, C 7 and C 15 protons), 6.76-7.35 (m, aromatic protons).

R.d. (c 0.24) \([\phi]_{589} - 77^\circ\), \([\phi]_{500} - 141^\circ\), \([\phi]_{400} - 282^\circ\), \([\phi]_{350} - 520^\circ\), \([\phi]_{312} - 1250^\circ\), \([\phi]_{280} - 118^\circ\).

From the light petroleum-benzene (9:1) eluates was obtained 1(1'-methylhex-1(1')-en-5'-one)-5-isopropylindane (122) (250 mg, 57%) as a colourless oil, \([\alpha]_D\) 0°.

Found: C, 84.2; H, 9.6
C\(_{19}\)H\(_{26}\)0 requires: C, 84.4; H, 9.7%.

\( \nu_{\text{max}} \) (CHCl\(_3\)) 1715 cm\(^{-1}\) (ketone C=O).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.22 (d, J 7 Hz, isopropyl methyls), 1.88 (s, C 1' Me), 2.10 (s, CH\(_3\)CO), 6.90-7.36 (m, aromatic protons).

1(1'-Methylhexan-5'-one)-5-isopropylindane (123)

1(1'-Methylhex-1(1')-en-5'-one)-5-isopropylindane (122) (0.2 g) in 95% ethanol (25.0 ml) was hydrogenated over 10% palladium-carbon (0.2 g) for 4 hr at 20° and 50 p.s.i. The catalyst was filtered off, and the filtrate was concentrated to afford the saturated ketone (123) (180 mg, 90%) as a colourless mobile oil.

Found: C, 84.0; H, 10.4; 0.6.4
C\(_{19}\)H\(_{28}\)0 requires: C, 83.8; H, 10.2; 0.5.9%.
\[ \nu_{\text{max}} \text{(CHCl}_3\text{)} 1715 \text{ cm}^{-1} \text{ (ketone C=O)} \].

N.m.r. \( \delta \text{(CDCl}_3\text{)} 0.88 \text{ (d, J 7 Hz, C1' Me)}, 1.20 \text{ (d, J 7 Hz, isopropyl methyls)}, 2.05 \text{ (s, CH}_3\text{CO)}, 6.80-7.20 \text{ (m, aromatic protons)} \).

Rearrangement of 4\(\alpha\),5\(\alpha\)-Epoxy-18-norabieta-8,11,13-triene (65) with Lithium Diethylamide

An ethereal solution of methyllithium (1.62 M, 6.4 ml) was treated at 0\(^0\) under dry nitrogen with redistilled diethylamine (3.0 ml) in dry ether (2.0 ml), and the mixture was stood at 0\(^0\) until the methane evolution had subsided. The epoxide (65) (1.1 g, 4.1 mmol) in dry ether (15.0 ml) was slowly added at 0\(^0\), and then the mixture was refluxed under nitrogen for 2 days. The mixture was cooled, and poured onto ice-water and extracted with ether. The ether extract was washed with 2N hydrochloric acid, water, and brine, and then dried and concentrated to give a gum which was chromatographed on deactivated alumina.

Light petroleum eluted the epoxide (65) (0.35 g), identified by its t.l.c. spot and i.r. spectrum.

Benzene eluted 19-norabieta-4(18),8,11,13-tetraen-5\(\alpha\)-ol (128) (0.6 g, 60%), which crystallized slowly from light petroleum as plates, m.p. 70-71\(^0\), \([\alpha]_D + 54^0 \) (c 0.43).

Found: C, 84.45; H, 9.7

\( \text{C}_{19}\text{H}_{26}\text{O} \) requires: C, 84.4; H, 9.7%.
\( \nu_{\text{max}} \) (CHCl\(_3\)) 3600 (OH), 3080, 1645 (C=CH\(_2\)), 1100 (C-O), and 905 cm\(^{-1}\) (C=CH\(_2\)).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.22 (d, J 7 Hz, C 15 methyls), 1.32 (s, C 10 angular Me), 1.68 (OH, exchanged with D\(_2\)O), 2.50-3.15 (m, C 7 and C 15 protons), 4.90, 5.14 (2 singlets, \( \frac{1}{2} \) 3 Hz, C 18 protons), 6.86-7.30 (m, aromatic protons).

Attempted De-oxygenation of 19-Norabieta-4(18),8,11,13-tetraen-5\( \alpha \)-ol (128)

The allylic alcohol (128) (0.1 g, 0.74 mmol) in dry tetrahydrofuran (5.0 ml) was treated at 0\(^{\circ}\) with pyridine-sulphur trioxide complex (90 mg), and the suspension was stirred at 4\(^{\circ}\) under anhydrous conditions for 9 hr. Lithium aluminium hydride (90 mg) in dry tetrahydrofuran (3.0 ml) was added and the mixture was stirred at 0\(^{\circ}\) for 1 hr, and then at 20\(^{\circ}\) for 5 hr. Concentrated aqueous sodium hydroxide was then added dropwise, and the mixture was filtered. Concentration of the filtrate gave the starting alcohol (128) (90 mg), which showed an identical t.l.c. spot and i.r. spectrum with those of the authentic alcohol.

19-Norabieta-3,8,11,13-tetraen-5\( \alpha \)-ol (130)

To a solution of lithium (0.45 g) in ethylenediamine (25.0 ml) was added a solution of 19-norabieta-4(18),8,11,13-tetraen-5\( \alpha \)-ol (128) (0.5 g, 1.85 mmol) in ethylenediamine (10.0 ml), and the purple mixture was refluxed in a nitrogen atmosphere for 5 min. Iced-water was then cautiously added, and the suspension was extracted with ether. The ether layer was washed with water, dried, and concentrated to give
a gum which was chromatographed on deactivated alumina.

Light petroleum-benzene (1:1) gave the starting allylic alcohol (128) (0.1 g), identified by its t.l.c. spot and i.r. spectrum.

Benzene eluted 19-norabieta-3,8,11,13-tetraen-5α-ol (130) (0.31 g, 62%) as a colourless gum.

Found: C, 83.8; H, 9.7

C₁₉H₂₆O requires: C, 84.4; H, 9.85%

νmax (CHCl₃) 3600 (OH), and 1010 cm⁻¹ (C=O).

N.m.r. δ (CDCl₃) 1.20 (d, J 7 Hz, C 15 methyls), 1.32 (s, C 10 angular Me), 1.57 (OH, exchanged with D₂O), 1.82 (s, W₂ 3 Hz, C 4 Me), 2.75 (m, C 7 and C 15 protons), 5.50 (s, W₂ 6 Hz, C 3 proton), 6.82-7.35 (m, aromatic protons).

Hydroboration-Chromic Acid Oxidation of 19-Norabieta-3,8,11,13-trien-5α-ol (130)

Diborane [generated from sodium borohydride (0.5 g) in dry diglyme, and boron trifluoride etherate (0.75 g) in dry diglyme] was diluted with a slow stream of nitrogen, and passed into a solution of the allylic alcohol (130) (0.3 g, 1.1 mmol) in dry tetrahydrofuran (40.0 ml) at 20°. After 2 hr, Jones reagent (2.50 ml) was added dropwise with stirring. After a further ½ hr, the mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried, and concentrated to give a gum. Percolation of the gum in benzene through deactivated alumina, and concentration of the eluates
gave 18-nor-abieta-8,11,13-trien-3,6-dione (132) (0.2 g, 63%) which crystallized from light petroleum as needles, m.p. 93-94°, [α]D + 113° (c 0.27).

Found: C, 80.7; H, 5.3

C19H24O2 requires: C, 80.2; H, 5.3%.

νmax 1710 cm⁻¹ (saturated ketone C=O)

N.m.r. δ (CDCl3) 1.22 (d, J 7 Hz, C 15 methyls), 1.26 (s, C 10 angular Me), 1.48 (d, J 2 Hz, C 4 Me), 2.50-3.10 (m, C 7 and C 15 protons), 6.85-7.15 (m, aromatic protons).

R.d. (c 0.27) [φ]589 + 320°, [φ]450 + 505°, [φ]350 + 1370°,

19-Norabieta-8,11,13-trien-3α-ol (91)

The epoxide (64) (0.5 g, 1.85 mmol) in dry ether (5.0 ml) was added slowly to a suspension of lithium aluminium hydride (40 mg) in dry ether (10.0 ml), and the mixture was heated under reflux in anhydrous conditions for 3 days. Saturated aqueous ammonium chloride was added dropwise to the cooled solution, the mixture was filtered, and the residue was washed with ether. The filtrate and the washings were concentrated to give an oil which was chromatographed on deactivated alumina.

Light petroleum eluted a small hydrocarbon fraction which was discarded.
Light petroleum-benzene (4:1) eluted the starting epoxide (64) (0.16 g), m.p. and m.m.p. 73-74°.

Benzene eluted 19-norabieta-8,11,13-trien-3α-ol (91) (0.29 g, 58%) as a colourless viscous gum, $[\alpha]_D + 60^\circ$ (c 0.20).

Found: C, 83.6; H, 10.6

$C_{19}H_{28}O$ requires: C, 83.8; H, 10.4%.

$\nu_{\max} (CHCl_3) 3600 \text{ cm}^{-1} (OH)$.

$\delta$ (CDCl$_3$) 1.08 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.22 (d, J 7 Hz, C 4 equatorial Me), 42 (OH, exchanged with D$_2$O), 2.60-3.15 (m, C 7 and C 15 protons), 3.82 (s, W 6 Hz, C 3 proton), 6.85-7.30 (m, aromatic protons).

19-Norabieta-8,11,13-trien-3-one (13)

A solution of the alcohol (91) (51 mg, 1.35 mmol) in acetone (5.0 ml) was treated with Jones reagent (0.2 ml) at 0°, and the mixture was stirred at 0° for 1 hr. The mixture was diluted with isopropanol and water, and extracted with ether. The organic phase was washed with water, dried, and concentrated to give an oil which was chromatographed on deactivated alumina. Elution of the column with light petroleum-benzene (1:1) afforded the oily 19-norabieta-8,11,13-trien-3-one (13) (45 mg, 80%), $[\alpha]_D + 52^\circ$ (c 0.14).

Found: C, 84.4; H, 9.7

$C_{19}H_{26}O$ requires: C, 84.8; H, 9.7%.
\( v_{\text{max}} \) (CHCl\(_3\)) 1710 cm\(^{-1}\) (ketone C=O).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.11 (d, J 7 Hz, C 4 equatorial Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.35 (s, C 10 angular Me), 2.45-3.11 (m, C 2, 4 and C 7, C 15 protons), 6.89-7.36 (m, aromatic protons).

R.d. \( \leq 0.139 \) [\( \phi \)]\(_{589} \) + \( 135^\circ \), [\( \phi \)]\(_{400} \) + \( 543^\circ \), [\( \phi \)]\(_{304} \) + \( 2175^\circ \) \( [\phi]_{284} \) + \( 427^\circ \).

The ketone (13) (25 mg) was recovered unchanged from refluxing in ethanol (2.0 ml) and potassium hydroxide (50 mg) in water (0.1 ml) for 1 hr under nitrogen.

Oxidation of 3\( \alpha \),4\( \alpha \)-Epoxy-18-norabieta-8,11,13-triene (64) with Boron Trifluoride-Dimethyl Sulphoxide

A solution of the epoxide (64) (0.5 g, 1.85 mmol) in dry dimethylsulphoxide (10.0 ml) was treated at 100\(^\circ\) with boron trifluoride etherate (1 drop), and the mixture was heated over a steam-bath for 23 hr. The mixture was poured into ice-water, extracted with ether, and the ether extract was washed with water, dried, and concentrated to give a black gum which was chromatographed on deactivated alumina.

Elution of the column with light petroleum gave 7-isopropyl-1-methylphenanthrene (106) (retene) (55 mg, 11%), m.p. and mixed m.p. 96-97\(^\circ\), (lit. \( \text{232} \) 98-99\(^\circ\)).

Found: mol. wt., 234.1405 (mass spectrum)

Calc. for C\(_{18}\)H\(_{18}\) mol. wt., 234.1408.

\( v_{\text{max}} \) (CCl\(_4\)) 3080, 3060, 3020, 1600 (aromatic).
N.m.r. δ (CDCl₃) 1.22 (d, J 7 Hz, C 15 methyls), 1.34 (s, C 10 angular Me), 1.88 (s, C 4 Me), 2.90 (5 members of a septet, J 7 Hz, C 15 proton), 6.58 (d, J 10 Hz, C 6 proton), 6.72 (d, J 10 Hz, C 7 proton), 6.95-7.30 (m, aromatic protons).

Elution of the column with benzene afforded 19-norabieta-4(18), 8,11,13-trien-3α-ol (76) (0.2 g, 40%) as a pale yellow, semi-crystalline glass, with a t.l.c. spot and i.r. spectrum identical with those of authentic compound.
The remainder of the material eluted from the column with benzene-ether (99:1) was obtained as a black intractable tar.

**Oxidation of 4α,19-Epoxy-18-norabieta-8,11,13-triene (66) with Dimethyl Sulphoxide-Boron Trifluoride**

The 4α,19-epoxide (66) (0.5 g, 1.85 mmol) was dissolved in hot dimethyl sulfoxide (10.0 ml, distilled from calcium hydride) and the solution was treated with boron trifluoride etherate (1 drop) and heated over the water bath for 23 hr. The black solution was cooled, diluted with water, and extracted with ether. The ether layer was washed with water, dried, and concentrated to afford a dark gum which was chromatographed on deactivated alumina. Elution of the column with light petroleum afforded, in the initial eluates, retene (106) (50 mg, 10%), with an identical t.l.c. and i.r. spectrum with those of an authentic sample. From later light petroleum eluates was obtained 19-norabieta-8,11,13-trien-18-ol (74) (65 mg, 13%), identical in all respects with the aldehyde obtained previously from rearrangement of the epoxide (66) with boron trifluoride.

Light petroleum-benzene (1:4) gave the dienone (107) (12 mg, 3%) as a pale yellow oil with t.l.c. behaviour and i.r. and n.m.r. spectra identical with those of the dienone obtained from the oxidation of the epoxide (64) with dimethyl sulfoxide-boron trifluoride.

Elution of the column with benzene gave a mixture of 19-norabieta-3,8,11,13-tetraen-18-ol (135) and 19-norabieta-4(5),8,11,13-tetraen-18-ol (136) as an oil (170 mg, 38%). G.l.c. (210°) showed
two main peaks at $R_v$ 5.2 and 6.1, with areas in the ratio of 1:1.

Found: C, 84.2; H, 10.1

C$_{19}$H$_{26}$O requires: C, 84.4; H, 9.7%.

$\nu_{\text{max}}$ (CHCl$_3$) 3590 cm$^{-1}$ (OH).

N.m.r. $\delta$ (CDCl$_3$) 1.03 (s, C 10 angular Me of 135), 1.23 (d, J 7 Hz, C 15 methyls), 1.39 (s, C 10 angular Me of 136), 1.58 (s, $\frac{1}{2}$ 6 Hz, OH exchanged with D$_2$O), 2.56-3.16 (m, C 7 and C 15 protons), 4.05, 4.25 (2 doublets, J 12 Hz, C 18 protons), 5.75 (s, $\frac{1}{2}$ 6 Hz, C 3 proton of 135), 6.84-7.35 (m, aromatic protons).

Oxidation of the Mixture of 19-Norabieta-3,8,11,13-tetraen-18-ol (135) and 19-Norabieta-4(5),8,11,13-tetraen-18-ol (136) with active Manganese Dioxide

The mixture of the allylic alcohols (135) and (136) (80 mg, 0.30 mmol) and active manganese dioxide (0.65 g) in chloroform (6.0 ml) was stirred overnight at 20°. The mixture was filtered and the filtrate was concentrated to afford a mixture of 19-norabieta-3,8,11,13-tetraen-18-al (137) and 19-norabieta-4(5),8,11,13-tetraen-18-al (138) (70 mg, 86%) as a pale yellow oil which could not be purified by chromatography on deactivated alumina or silica gel.

$\nu_{\text{max}}$ (CHCl$_3$) 1700 cm$^{-1}$ (a,ß-unsaturated aldehyde C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.03 (s, C 10 angular Me of 137), 1.22 (d, J 7 Hz, C 15 methyls), 1.50 (s, C 10 angular Me of 138), 2.55-3.20 (m, C 7 and C 15 protons), 6.82 (s, $\frac{1}{2}$ 9 Hz, C 3 proton of 137),
6.90-7.45 (m, aromatic protons), 9.55 (s, CHO of 137), 10.30 (s, CHO of 138).

**Oxidation of 4α,5α-Epoxide-18-norabieta-8,11,13-triene (65) with Boron Trifluoride-Dimethyl Sulphoxide**

The 4α,5α-epoxide (65) (0.5 g, 1.85 mmol) in redistilled dimethyl sulphoxide (10.0 ml) was heated on the water bath with boron trifluoride etherate (1 drop) for 23 hr. The cooled mixture was poured into water and extracted with ether. The ether extract was washed with water, dried, and concentrated to give a dark gum which was chromatographed on deactivated alumina.

Light petroleum eluted an oily hydrocarbon fraction which slowly crystallized, the i.r. spectrum of which indicated that the major component was retene (106) (55 mg, 11%).

Light petroleum-benzene (4:1) eluted the allylic alcohol (128) (0.2 g, 40%) as a pale yellow glass (identical t.l.c. behaviour and i.r. and n.m.r. spectra).

Light petroleum-benzene (1:1) afforded the oily dienone (107) (0.12 g, 25%) (identical t.l.c. behaviour and i.r. spectrum).

The remaining material, eluted with benzene, was obtained as an intractable brown gum.

**Enolbenzoylation of 18,19-Bisnorabieta-8,11,13-trien-4-one (6)**

The ketone (6) (0.55 g, 2.15 mmol) in methylene dichloride (10.0 ml) was stirred under nitrogen with freshly recrystallised
benzoic anhydride (1.02 g, 4.5 mmol) and 70% perchloric acid (5 drops) for 3 hr. The black solution was washed with water, dried, and concentrated to give a dark oil which was chromatographed on silica gel. Elution of the column with light petroleum-benzene (9:1) afforded a 1:1 mixture of 4-benzoyloxy-18,19-bisnorabieta-3,8,11,13-tetraene (121) and 4-benzoyloxy-18,19-bisnorabieta-4(5),8,11,13-tetraene (120) (0.15 g, 24%) as a colourless oil, identified from its spectroscopic properties.

$\nu_{\text{max}}$ (CHCl$_3$) 1725 (ester C=O) and 1270 cm$^{-1}$ (ester C-O).

N.m.r. $\delta$ (CDCl$_3$) 1.20 (d, J 7 Hz, C 15 methyls), 1.37 (s, C 10 angular Me of 121), 1.45 (s, C 10 angular Me of 120), 5.47 (s, W$^{1/2}$ 8 Hz, C 3 proton of 121), 6.72-7.25 (m, C 11,12 and 14 aromatic protons), 7.32-8.20 (m, benzoate aromatic protons).

**Attempted Methylation of the Mixture of Enolbenzoates (120) and (121)**

The enol benzoate mixture (120) and (121) (0.15 g, 0.42 mmol) was treated with an ethereal solution of methylolithium (1.6 M, 2.0 ml) in dry dimethoxyethane (10.0 ml) containing a few crystals of triphenylmethylene. The pink enolate solution was treated under nitrogen with an ethereal solution of Simonson-Smith reagent [prepared from methylene diiodide (2.34 g, 1.68 mmol), zinc-copper couple (0.57 g, 1.68 mmol) and a crystal of iodine], and was stirred for $\frac{1}{2}$ hr. The mixture was poured into saturated aqueous ammonium chloride and then taken up into ether. The ether extract was washed with water, dried, and concentrated to give an orange gum. T.l.c. of this gum showed a number of spots with high $R_p$ values. The mixture was too complex for
separation of the products.

Oximation of 18,19-Bisnorabieta-8,11,13-trien-4-one (6)

The C 4-ketone (6) (0.11 g, 0.43 mmol) and i-pentyl nitrite (freshly distilled, 0.2 ml, 1.55 mmol) in absolute methanol (5.0 ml) was saturated with dry hydrogen chloride at -15°, and the red solution was kept at -10° for 16 hr. The solution was partitioned between ether and water, and the ether layer was dried and concentrated to give a yellow oil which was chromatographed on silica gel. From benzene-ether (9:1) eluates was obtained the impure oximino ketone (68) (80 mg, 68%) as a yellow oil.

\[
\nu_{\text{max}} (\text{CHCl}_3) 3580, 3240, 975 (\text{-NOH}), 1725 \text{ cm}^{-1} \text{ (ketone C=O).}
\]

The oxime was too impure for further transformation.

Methyl Abieta-8,11,13-trien-18-oate (2)

Abieta-8,11,13-trien-18-oic acid (1) (20.0 g) in ether (50.0 ml) was treated at 0° with an ethereal solution of diazomethane (generated from N-methyl-N-nitroso-urea and aqueous potassium hydroxide), until a faint yellow colour persisted after \(\frac{1}{2}\) hr at 20°. The solution was concentrated and crystallised from methanol to give methyl abieta-8,11,13-trien-18-oate (2) (20.0 g, 95%) as needles, m.p. 57-58°, (lit.\(^{231}\) 59-61°).

\[
\nu_{\text{max}} (\text{CHCl}_3) 1725 \text{ (ester C=O), 1250 cm}^{-1} \text{ (ester C=O).}
\]
Methyl 7-oxo-abieta-8,11,13-trien-18-oate (18)

Methyl abieta-8,11,13-trien-18-oate (2) (18.0 g, 57 mmol) was dissolved in glacial acetic acid (260 ml) and the solution was cooled to 0°C. Chromium trioxide (22.0 g, 220 mmol) was dissolved in glacial acetic acid-water (4:1) (36.0 ml) and added dropwise with stirring to the solution of the ester (2). The mixture was stood at 0°C for 3 days, poured into water, and extracted with ether. The ether layer was washed with saturated aqueous sodium bicarbonate and then with water, dried, and concentrated to give a yellow gum which was chromatographed on deactivated alumina.

Elution of the column with light petroleum gave the starting ester (2) (0.5 g), while elution of the column with light petroleum-benzene (1:1) gave methyl 7-oxo-abieta-8,11,13-trien-18-oate (18) (15.5 g, 68%), which crystallised slowly from methanol as needles, m.p. 64-65°C (lit.20 68-69°C).

ν_max (CHCl₃) 1725 (ester C=O), 1250 (ester C-O), 1675 cm⁻¹ (aryl ketone C=O).

N.m.r. δ (CDCl₃) 1.22 (d, J 7 Hz, C 15 methyls), 1.23 (s, C 4 axial Me), 1.33 (s, C 10 angular Me), 2.55 (m, C 6 protons), 2.86 (5 members of a septet, J 7 Hz, C 15 proton), 3.60 (s, CO₂Me), 7.36 (m, C 11 and C 12 protons), 7.88 (d, J 2 Hz, C 14 proton).
Y-Lactone of 6-Hydroxy-7-oxo-abieta-5,8,11,13-tetraen-18-oic Acid (95)

Methyl 7-oxo-abieta-8,11,13-trien-18-oate (18) (0.55 g, 1.75 mmol) in glacial acetic acid (11.0 ml) was treated with 95% t-butylhydroperoxide (4.40 ml) and concentrated sulphuric acid (6 drops), and the mixture was heated under anhydrous conditions at 52° for 55 hr. The mixture was diluted with water and extracted into ether. The ether layer was washed with water, dried, and concentrated to give a yellow gum which was chromatographed on silica gel. Elution of the column with benzene-ether (1%) gave the enol-lactone (95) (0.44 g, 80%), which crystallized from ethanol as needles, m.p. 188-189° (with sublimation) and 216-217° (lit. 188-189°).

\[ \nu_{\text{max}} (\text{CHCl}_3) \text{ 1810 (enol-lactone C=O), 1675 (aryl ketone C=O)} \]

and 1660 cm\(^{-1}\) (C=C).

N.m.r. \( \delta (\text{CDCl}_3) 1.26 \text{ (d, } J 7 \text{ Hz, C 15 methyls), 1.62 \text{ (s, C 4 axial Me), 1.65 \text{ (s, C 10 angular Me), 3.03 \text{ (septet, J 7 Hz, C 15 proton), 7.47, 7.55 \text{ (2 doublets, J 8 Hz, C 11 and C 12 protons), 8.14 \text{ (s, W 4 Hz, C 14 proton).}}) \]

Methyl 6α-Bromo-7-oxo-abieta-8,11,13-trien-18-oate (154)

Methyl 7-oxo-abieta-8,11,13-trien-18-oate (18) (0.11 g, 0.34 mmol) in glacial acetic acid (6.30 ml) containing 48% hydrobromic acid (1 drop) was treated with bromine (0.35 ml) in glacial acetic acid (3.50 ml) and the mixture was stirred at 20° for \( \frac{1}{2} \) hr. The mixture was poured into water and the suspension was extracted with ether. The ether extract was
decolourized with dilute aqueous sodium metabisulphite, washed with water, dried, and concentrated to afford methyl 6α-bromo-7-oxo-abieta-8,11,13-trien-18-oate (154) (0.13 g, 96%), which crystallised from methanol as needles, m.p. 155-157° (lit. 159-160°).

\[ \nu_{\text{max}} (\text{CHCl}_3) 1725 \text{ (ester C=O)}, 1250 \text{ (ester C=O)}, 1690 \text{ (α-bromo aryl ketone C=O)}. \]

N.m.r. 6 (CDCl₃) 1.25 (d, J 7 Hz, C 15 methyls), 1.25 (s, C 4 axial Me), 1.50 (s, C 10 angular Me), 2.96 (5 members of a septet, J 7 Hz, C 15 proton), 3.22 (d, J 12 Hz, C 5 proton), 3.64 (s, CO₂Me), 4.99 (d, J 12 Hz, C 6 proton), 7.36 (m, C 11 and C 12 protons), 7.82 (d, J 2 Hz, C 14 proton).

Enol-acetylation of Methyl 7-Oxo-abieta-8,11,13-trien-18-oate (18)

Methyl 7-oxo-abieta-8,11,13-trien-18-oate (18) (6.75 g, 21.0 mmol) was refluxed in isopropenyl acetate (80.0 ml) containing toluene-2-sulphonic acid (0.5 g) for 72 hr. The cooled mixture was washed with water, dried, and concentrated to give a brown gum. Chromatography of the gum on silica gel and elution of the column with light petroleum benzene (1:1) afforded methyl 7-acetoxy-abieta-6,8,11,13-tetraen-18-oate (155) (4.8 g, 78%) which crystallised from light petroleum as needles, m.p. 76-77°, \([\alpha]_D - 139° (c 0.18)\).

Found: C, 73.9; H, 8.3

C_{22}H_{30}O_{4} requires: C, 73.7; H, 8.4%.

\[ \nu_{\text{max}} (\text{CHCl}_3) 1760 \text{ (enol acetate C=O)}, 1725 \text{ (ester C=O)}, 1660 \text{ cm}^{-1} \text{ (C=C)}. \]
N.m.r. δ (CDCl₃) 1.22 (d, J 7 Hz, C 15 methyls), 1.22 (s, C 4 axial Me), 1.38 (s, C 10 angular Me), 2.26 (s, OAc), 2.82 (5 members of a septet, J 7 Hz, C 15 proton), 2.97 (d, J 3 Hz, C 5 proton), 3.62 (s, CO₂Me), 5.44 (d, J 3 Hz, C 6 proton), 6.95 (s, W/₂ 4 Hz, C 14 proton), 7.10 (s, W/₂ 2.5 Hz, C 11 and C 12 protons).

**Perbenzoic Acid Oxidation of Methyl 7-Acetoxy-abieta-6,8,11,13-tetraen-18-oate (155)**

The enol-acetate (155) (1.30 g, 4.6 mmol) in chloroform (10.0 ml) was treated with a chloroform solution of perbenzoic acid (5.8 mmol/ml, 5.0 ml), and the mixture was stood at 0° for 1 day. The solution was washed successively with saturated aqueous potassium iodide, saturated aqueous sodium hydrogen carbonate, saturated aqueous sodium thiosulphate, and finally with water. The organic layer was dried and concentrated to afford a pale yellow gum, t.l.c. of which showed it to consist predominantly two compounds with similar spots at low Rₚ values. Chromatography on deactivated alumina did not separate the products, but this was achieved by preparative t.l.c. using benzene as the solvent.

From the upper band was obtained methyl 6α-acetoxy-7-oxo-abieta-8,11,13-trien-18-oate (156) (0.72 g, 53%), which crystallized from light petroleum as needles, m.p. 145-146°, [α]D - 66° (c 0.12).

Found: C, 71.6; H, 7.6

C₂₃H₃₀O₅ requires: C, 71.5; H, 7.8%.

νmax (CHCl₃) 1750 (acetate C=O), 1725 (ester C=O), 1695 cm⁻¹ (aryl ketone C=O).
N.m.r. δ (CDCl₃) 1.24 (d, J 7 Hz, C 15 methyls), 1.33 (s, C 4 axial Me), 1.42 (s, C 10 angular Me) 2.12 (s, OAc), 2.95 (5 members of a septet, J 7 Hz, C 15 proton), 3.27 (d, J 12.5 Hz, C 5 proton), 3.64 (s, CO₂Me), 5.78 (d, J 12.5 Hz, C 6 proton), 7.34 (m, C 11 and C 12 protons), 7.89 (d, J 2 Hz, C 14 proton).


From the lower band was obtained methyl 6a-hydroxy-7-oxo-abieta-8,11,13-trien-18-oate (158) (0.39 g, 43%) as a pale yellow oil, identified from its spectroscopic properties.

νₘₐₓ (CHCl₃) 3580, 3500 (OH), 1725 (ester C=O), 1680 cm⁻¹ (aryl ketone C=O).

N.m.r. δ (CDCl₃) 1.22 (d, J 7 Hz, C 15 methyls), 1.37 (s, C 4 axial Me), 1.50 (s, C 10 angular Me), 2.22 (s, OH, exchanged with D₂O), 2.88 (d, J 12.5 Hz, C 5 proton), 2.92 (5 members of a septet, J 7 Hz, C 15 proton), 3.58 (s, CO₂Me), 4.52 (d, J 12.5 Hz, C 6 proton), 7.33 (m, C 11 and C 12 protons), 7.85 (d, J 2 Hz, C 14 proton).

Acetylation of the ketol (158) with acetic anhydride-pyridine at 20° for 18 hr gave the keto-acetate (156) in quantitative yield, m.p. and m.m.p. 145-146°.

The keto-acetate (156) was obtained in 95% overall yield by acetylation (acetic anhydride-pyridine) of the crude product from the
perbenzoic acid oxidation of the enol-acetate (155), followed by
 crystallisation of the product from light petroleum.

Methyl 7-Oxo-abieta-5,8,11,13-tetraen-18-oate (161)

Methyl 6α-bromo-7-oxo-abeta-8,11,13-trien-18-oate (154)
(0.28 g, 0.69 mmol) in dry dimethylformamide (12.0 ml) was stirred and
heated at 150° with freshly fused lithium bromide (0.56 g) and dried
lithium carbonate (0.14 g) for 1 hr. The mixture was cooled and poured
into water. The precipitate was extracted with ether, and the ether
layer was washed with water, dried, and concentrated to give a gum, which
was filtered through a short column of deactivated alumina using benzene
as the solvent. Concentration of the filtrate gave methyl 7-oxo-abieta-
5,8,11,13-tetraen-18-oate (161) (195 mg, 88%) as a pale yellow oil.

\[ \nu_{\text{max}} (\text{CHCl}_3) 1725 \text{ (ester C=O)}, 1655 \text{ cm}^{-1} \text{ (a, \beta-unsaturated}
\]

\text{aryl ketone C=O).}

N.m.r. δ (CDCl₃) 1.27 (d, J 7 Hz, C 15 methyls), 1.52 (s, C 4
axial Me), 1.65 (s, C 10 angular Me), 3.00 (5 members of a
septet, J 7 Hz, C 15 proton), 3.70 (s, CO₂Me), 6.15 (s, C 6
proton), 7.43, 7.50 (2 doublets, J 10 Hz, C 11 and C 12 protons),
8.14 (s, W₂ 4 Hz, C 14 proton).

Hydrolysis of Methyl 6α-Acetoxy-7-oxo-abieta-8,11,13-trien-18-oate (156)

The keto-acetate (156) (200 mg, 0.52 mmol) in methanol (12.0 ml),
was treated with potassium hydroxide (80 mg) in water (1.0 ml) and the
bright yellow solution was refluxed under nitrogen for 2 hr, cooled,
added to water, and acidified to litmus with 2N hydrochloric acid. The
suspension was extracted with ether, and the ether layer was washed with water, dried, and concentrated to afford a gum which was triturated with ether to give the enol-lactone (95) (70 mg, 35%) m.p. and m.m.p. 188-189\degree (subl.) and 216-217\degree.

The mother liquors contained a mixture of methyl 6\alpha-acetoxy-7-oxo-abieta-8,11,13-trien-18-oate (156) and methyl 7-oxo-abieta-5,8,11,13-tetraen-18-oate (161) as shown by t.l.c. and the i.r. spectrum. Satisfactory separation of the products was not achieved by chromatography of the mixture on deactivated alumina.

**Oxidation of Methyl 6\alpha-Hydroxy-7-oxo-abieta-8,11,13-trien-18-oate (158) with Bismuth Oxide**

The ketol (158) (55 mg, 0.17 mmol) in glacial acetic acid (5.0 ml) was heated and stirred at 100\degree with bismuth oxide (80 mg, 0.21 mmol) for 2 hr. The mixture was cooled, diluted with ether, and filtered. The filtrate was washed with water, dried, and concentrated to give the enol-lactone (95) (50 mg, 90%) which was recrystallised from ethanol as needles, m.p. and m.m.p. 188-189\degree (subl.) and 216-217\degree.

**Attempted Thioketalisation of Methyl 6\alpha-Acetoxy-7-oxo-abieta-8,11,13-trien-18-oate (156)**

The keto-acetate (156) (0.55 g, 1.42 mmol) in ethanedithiol (0.2 g) and boron trifluoride-diethyl etherate (0.2 g) was stood at 20\degree for 2 days. The red mixture was extracted with ether, and the ether layer was washed with 5% aqueous sodium hydroxide followed by water. The ether extract was dried and concentrated to give a yellow oil. Although
the i.r. spectrum of this oil showed an absence of an aryl ketone band at 1690 cm\(^{-1}\), t.l.c. showed that many compounds had been formed.

Repetition of the experiment with glacial acetic acid as the solvent gave a quantitative recovery starting material (156) as shown by t.l.c. and the i.r. spectrum.

**Methyl 6α-Acetoxy-7β-hydroxy-abieta-8,11,13-trien-18-oate (162)**

Methyl 6α-acetoxy-7-oxo-abieta-8,11,13-trien-18-oate (156)

(0.6 g, 1.55 mmol) in methanol (25.0 ml) was treated with sodium borohydride (20 mg) and the solution was stirred at 20° for 2 hr. The solution was diluted with water, extracted with ether, and the ether layer was washed with water, dried, and concentrated to give a colourless gum which crystallised spontaneously. Recrystallisation from chloroform-light petroleum gave methyl 6α-acetoxy-7β-hydroxy-abieta-8,11,13-trien-18-oate (162) (0.6 g, 98%) as prisms, m.p. 150-151°, \([\alpha]_D^2 + 2^\circ\) (ε 0.19).

**Found:**

C, 71.1; H, 8.2

\(C_{23}H_{32}O_5\) requires: C, 71.1; H, 8.3%.

\(v_{\text{max}}\) (CHCl\(_3\)) 3585, 3450 (OH), 1740 (acetate C=O) and 1725 cm\(^{-1}\) (ester C=O).

**N.m.r. δ (CDCl\(_3\))** 1.23 (d, J 7 Hz, C 15 methyls), 1.25 (s, C 4 axial Me), 1.32 (s, C 10 angular Me), 2.06 (s, OAc), 2.77 (d, J 12.5 Hz, C 5 proton), 2.88 (5 members of a septet, J 7 Hz, C 15 proton), 3.37 (s, \(W_3^2\) 28 Hz, OH, exchanged with D\(_2\)O), 3.65 (s, CO\(_2\)Me), 4.72 (broadened d, J 7 Hz, \(W_2^2\) 5 Hz, C 7 proton), 5.32
(d of d, J \textsubscript{56} 12.5 Hz, J \textsubscript{67} 7 Hz, C 6 proton), 7.13 (s, W\textsubscript{2} 4 Hz, C 11 and C 12 protons), 7.37 (s, W\textsubscript{2} 5 Hz, C 14 proton).

6α,7β-Dihydroxy-abieta-8,11,13-trien-18-oic Acid (163)

Methyl 6α-acetoxy-7β-hydroxy-abieta-8,11,13-trien-18-oate (162) (0.15 g, 0.39 mmol) in methanol (20.0 ml), was treated with sodium hydroxide (0.2 g) in water (5.0 ml) and the yellow solution was heated under reflux for 1½ hr cooled, diluted with water, and acidified to litmus with the dropwise addition of concentrated hydrochloric acid. The flocculent precipitate was filtered, dried, and recrystallised from ethyl acetate to give 6α,7β-dihydroxy-abieta-8,11,13-trien-18-oic acid (163) (0.11 g, 86%) as needles, m.p. 202-203°, [α]_D + 2.5° (c 0.09).

Found: C, 72.5; H, 8.5

C\textsubscript{20}H\textsubscript{28}O\textsubscript{4} requires: C, 72.3; H, 8.5%.

ν\textsubscript{max} (CHCl\textsubscript{3}) 3600-2500 (H-bonded OH), 1690 cm\textsuperscript{-1} (acid C=O).

N.m.r. δ (CD\textsubscript{5}D\textsubscript{5}N). 1.20 (d, J 7 Hz, C 15 methyls), 1.29 (s, C 10 angular Me), 1.77 (s, C 4 axial Me), 2.85 (5 members of a septet, J 7 Hz, C 15 proton), 3.12 (d, J 12 Hz, C 5 proton), 4.64 (d of d, J\textsubscript{56} 12 Hz, J\textsubscript{67} 8 Hz, C 6 proton), 5.19 (d, J 8 Hz, C 7 proton), 7.23 (s, W\textsubscript{2} 5 Hz, C 11 and C 12 protons), 7.26-7.68 (CO\textsubscript{2}H and C 6 and C 7 OH, exchanged with D\textsubscript{2}O), 7.38 (s, W\textsubscript{2} 4 Hz, C 14 proton).

Dehydration of Methyl 6α-Acetoxy-7β-hydroxy-abieta-8,11,13-trien-18-oate (162).

a) with Thionyl Chloride-Pyridine

The hydroxy-acetate (162) (0.4 g, 1.04 mmol) in pyridine (7.50 ml) was cooled to 0° and treated with freshly distilled thionyl chloride...
(0.40 ml), and the mixture was kept at 20° for 1 hr. The red mixture was poured onto ice, and the suspension was partitioned between water and ether. The ether layer was washed with dilute aqueous copper sulphate followed by water, dried, and concentrated to give a red gum which was shown to contain a predominance of the starting material (162) by t.l.c. and the i.r. spectrum.

b) with Boron Trifluoride Etherate in acetic acid

The hydroxy-acetate (162) (0.1 g, 0.26 mmol) in glacial acetic acid (12.0 ml) was treated with freshly distilled boron trifluoride etherate (0.1 ml), and the pale-yellow solution was kept at 20° for 5 hr. The mixture was diluted with water, extracted with ether, and the ether extract was washed with water, dried, and concentrated to afford a gum which crystallised from light petroleum to give starting material, m.p. and m.m.p. 150-151°.

c) with Phosphorus Pentachloride in Ether

The hydroxy acetate (162) (0.1 g, 0.26 mmol) and phosphorus pentachloride (0.1 g, 0.46 mmol) in ether (10.0 ml) were stirred at 20° for 2 hr. The solution was partitioned between ether and water, and the ether layer was washed with water, dried, and concentrated to give a colourless gum which was chromatographed on deactivated alumina. Elution of the column with light petroleum-benzene (1:1) afforded methyl 6α-acetoxy-7α-chloro-abieta-8,11,13-trien-18-oate (168) (65 mg, 62%), m.p. (crude) 100-102°. The compound gave a positive Beilstein test.

\[ \nu_{\text{max}} (\text{CHCl}_3) 1745 \text{ (acetate C=O)}, 1725 \text{ cm}^{-1} \text{ (ester C=O)}. \]
N.m.r. δ (CDCl₃) 1.23 (d, J 7 Hz, C 15 methyls), 1.29 (s, C 4 axial and C 10 angular methyls), 2.05 (s, OAc), 2.85 (5 members of a septet, J 7 Hz, C 15 proton), 3.25 (d, J 11 Hz, C 5 proton), 3.70 (s, CO₂Me), 5.20-5.60 (m, C 6 and C 7 protons), 7.15 (s, W₂ 2.5 Hz, C 11,12 and 14 protons).

The compound decomposed during attempts to purify it for analysis.

d) with Acetic Anhydride and Toluene-p-sulphonic acid

The hydroxy acetate (162) (0.4 g, 1.04 mmol) in redistilled acetic anhydride (10.0 ml) and toluene-p-sulphonic acid (50 mg) was heated under reflux in a nitrogen atmosphere for ½ hr. The purple mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with saturated aqueous sodium bicarbonate, water, and brine. It was dried and concentrated to give a brown gum which was chromatographed on silica gel. Elution of the column with light petroleum-benzene (4:1) gave methyl 6-chloro-abieta-6,8,11,13-tetraen-18-oate (169) (0.152 g, 42%) which was recrystallised from chloroform-methanol as prisms, m.p. 131-132°, [α]D - 29° (c 0.24).

Found: C, 73.0; H, 8.0; Cl, 10.4
C₂₁H₂₇O₂Cl requires: C, 72.7; H, 7.8; Cl, 10.2%

Found: mol. wt., 348.1689, 346.1710 (mass spectrum)
C₂₁H₂₇O₂Cl (37) requires mol. wt., 348.1684
C₂₁H₂₇O₂Cl (35) requires mol. wt., 346.1704

The compound gave a positive Beilstein test.
\( \nu_{\text{max}} (\text{CHCl}_3) 1725 \text{ (ester C=O), } 1625 \text{ cm}^{-1} \text{ (C=C).} \)

N.m.r. \( \delta (\text{CDCl}_3) \)
- 1.17 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.59 (s, C 4 axial Me), 2.87 (septet, J 7 Hz, C 15 proton), 3.61 (d, J 3 Hz, C 5 proton), 3.68 (s, CO\(_2\)Me), 6.66 (d, J 3 Hz, C 7 proton), 6.87 (s, \( \frac{1}{2} \) 4 Hz, C 14 proton), 7.05, 7.14 (2 doublets, J 9 Hz, C 11 and C 12 protons).

From the light petroleum–benzene (1:4) eluates was obtained methyl 6-acetoxy-abieta-6,8,11,13-tetraen-18-oate (167) (50 mg, 13%) as a pale-yellow gum, identified from its spectroscopic properties.

\( \nu_{\text{max}} (\text{CHCl}_3) 1760 \text{ (enol acetate C=O), } 1725 \text{ (ester C=O), } 1650 \text{ cm}^{-1} \text{ (C=C).} \)

N.m.r. \( \delta \text{(CDCl}_3 \) )
- 1.16 (s, C 4 axial Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.47 (s, C 10 angular Me), 2.12 (s, OAc), 2.85 (5 members of a septet, J 7 Hz, C 15 proton), 3.50 (d, J 3 Hz, C 5 proton), 3.62 (s, CO\(_2\)Me), 6.42 (d, J 3 Hz, C 7 proton), 6.90 (s, \( \frac{1}{2} \) 4 Hz, C 14 proton), 7.02, 7.12 (2 doublets, J 9 Hz, C 11 and C 12 protons).

The above experiment was repeated, and the pale yellow mixture was worked-up as before. Chromatography of the oily product on silica gel, and elution of the column with light petroleum–benzene (1:4) gave methyl 6α,7β-diacetoxy-abieta-8,11,13-trien-18-oate (170) (75%), as a colourless gum.
Found: C, 69.9; H, 8.3  

$C_{23}H_{34}O_6$ requires: C, 69.7; H, 8.0%.  

$\nu_{\text{max}}$ (CHCl$_3$) 1745 (C 7 acetate C=O), 1735 (C 6 acetate C=O), 1725 cm$^{-1}$ (ester C=O).  

N.m.r. δ (CDCl$_3$) 1.20 (d, J 7 Hz, 15 methyls), 1.27 (s, 4 axial Me and C 10 angular Me), 1.97 (s, C 6 OAc), 2.06 (s, C 7 OAc), 2.85 (5 members of a septet, J 7 Hz, C 15 proton), 3.18 (d, J 13 Hz, C 5 proton), 3.65 (s, CO$_2$Me), 5.59 (d of d, J 5, 6 Hz, C 6 proton), 6.17 (d, J 7 Hz, C 7 proton), 6.96 (s, W$_2$ 4 Hz, C 14 proton), 7.14, 7.24 (2 doublets, J 5 Hz, C 11 and C 12 protons).  

**Methyl 6α-Acetoxy-abieta-8,11,13-trien-18-oate (172)**  

Methyl 6α-acetoxy-7β-hydroxy-abieta-8,11,13-trien-18-oate (162) (0.1 g, 0.29 mmol) was hydrogenolysed in 95% ethanol (25.0 ml) containing concentrated sulphuric acid (4 drops) and 10% palladium-carbon (0.1 g) at 50 p.s.i. for 18 hr. The catalyst was filtered off and the filtrate was extracted with ether. The ether layer was washed with water, dried, and concentrated to give methyl 6α-acetoxy-abieta-8,11,13-trien-18-oate (172) (95 mg, 99%) which was recrystallised from chloroform-methanol as needles, m.p. 132–133°, $[\alpha]_D + 95^\circ$ (c 0.19).  

Found: C, 74.4; H, 8.9  

$C_{23}H_{32}O_4$ requires: C, 74.2; H, 8.7%.
\[ \nu_{\text{max}} (\text{CHCl}_3) 1735 \text{ (acetate C=O)}, 1725 \text{ cm}^{-1} \text{ (ester C=O)}. \]

N.m.r. \( \delta (\text{CDCl}_3) \)
- 1.22 (d, J 7 Hz, C 15 methyls),
- 1.27 (s, C 4 axial Me and C 10 angular Me),
- 1.98 (s, OAc),
- 2.60-2.95 (m, C 7β and C 15 protons),
- 2.72 (d, J 11 Hz, C 5 proton),
- 3.35 (d, J 7 Hz, C 7α proton),
- 3.65 (s, CO₂Me),
- 5.30 (m, C 6 proton),
- 6.82-7.20 (m, aromatic protons).

Repetition of the experiment on the 1.0 g scale under identical conditions gave the C 6 acetate (172) and the starting hydroxy acetate (162) (0.4 g recovered) which were readily separated by chromatography on deactivated alumina.

**Methyl 6α-Hydroxy-abieta-8,11,13-trien-18-oate (175)**

Methyl 6α-acetoxy-abieta-8,11,13-trien-18-oate (172) (0.42 g, 1.25 mmol) in methanol (25.0 ml) was treated with sodium hydroxide (0.6 g) in water (1.0 ml) and the bright-yellow solution was heated under reflux for 1½ hr. The solution was cooled, diluted with water, and acidified to litmus by the dropwise addition of concentrated hydrochloric acid. The flocculent precipitate of the crude hydroxy-acid (174) was filtered off, suspended in methanol, and esterified with an excess of an ethereal solution of diazomethane. After removal of solvents, the resultant pale yellow gum was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (1:4) gave a mixture of non-polar gums, while elution of the column with benzene-ether (9:1) afforded methyl 6α-hydroxy-abieta-8,11,13-trien-18-oate.
(175) (0.28 g, 76%), m.p. 56-58° (from chloroform-light petroleum), 
\([\alpha]_D + 50^\circ (\leq 0.18)\).

Found: \( C, 76.35; H, 9.8 \)

\( \text{C}_{21}\text{H}_{30}\text{O}_3 \) requires: \( C, 76.3; H, 9.15\% \).

\( \nu_{\max} (\text{CHCl}_3) 3580, 3450 (\text{OH}), 1720 \text{ cm}^{-1} \) (ester \( \text{C}=\text{O} \)).

N.m.r. \( \delta (\text{CDCl}_3) 1.22 (\text{d}, J 7 \text{ Hz}, \text{C 15 methyls}), 1.22 (\text{s}, \text{C 4 \text{ axial} Me}), 1.42 (\text{s}, \text{C 10 angular Me}), 2.46 (\text{d}, J 11 \text{ Hz}, \text{C 5 \text{ proton}}), 2.55-3.05 (\text{m}, \text{C 7\beta and C 15 \text{ protons}}), 3.35 (\text{d}, J 7 \text{ Hz}, \text{C 7\alpha \text{ proton}}), 3.63 (\text{s}, \text{CO_2Me}), 4.62 (\text{m}, \text{C 6 \text{ proton}}), 6.82-7.18 (\text{m}, \text{aromatic \text{ protons}}).

**Methyl 6-oxo-abieta-8,11,13-trien-18-oate (176)**

Methyl 6\alpha-hydroxy-abieta-8,11,13-trien-18-oate (175) (0.21 g, 0.64 mmol) in acetone (25.0 ml) was cooled to 0° and stirred while Jones reagent (0.4 ml) was added dropwise. The mixture was stirred at 0° for 15 min and at 20° for 15 min. The mixture was treated with isopropanol and water and extracted with ether. The ether layer was washed with water, dried, and concentrated to afford a colourless gum which was chromatographed on deactivated alumina.

Elution of the column with benzene afforded **methyl 6-oxo-abieta-8,11,13-trien-18-oate (176)** (0.17 g, 80%) as a colourless oil, 
\([\alpha]_D + 100^\circ (\leq 0.16)\).

Found: \( C, 76.7; H, 8.6 \)

\( \text{C}_{21}\text{H}_{28}\text{O}_3 \) requires: \( C, 76.8; H, 8.6\% \).
\( \nu_{\text{max}} (\text{CHCl}_3) \) 1725 (ester C=O), 1715 cm\(^{-1}\) (saturated ketone C=O).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.18 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.48 (s, C 4 axial Me), 2.26 (s, C 5 proton), 2.30 (d, J 2.5 Hz, C 7 proton), 2.85 (septet, J 7 Hz, C 15 proton), 3.26 (d, J 2.5 Hz, C 7 proton), 3.62 (s, CO\(_2\)Me), 6.88-7.28 (m, aromatic protons).

R.d. (\( R < 0.16 \)) [\( \phi \)]\(_{589}^+ + 328^\circ\), [\( \phi \)]\(_{450}^- + 810^\circ\), [\( \phi \)]\(_{315}^\pm + 3280^\circ\), [\( \phi \)]\(_{298}^\circ\), [\( \phi \)]\(_{272}^- - 4750^\circ\), [\( \phi \)]\(_{252}^\circ\), [\( \phi \)]\(_{238}^\circ\).

Catalytic Hydrogenation of the \( \gamma \)-Lactone of 6-Hydroxy-7-oxo-abieta-5,8,11,13-tetraen-18-oic Acid (95)

The enol lactone (95) (0.5 g) in ethyl acetate (25.0 ml) and concentrated sulphuric acid (5 drops) was hydrogenated at atmospheric pressure and at 20\(^\circ\). The catalyst was filtered off and the filtrate was washed with water, dried, and concentrated to give an acidic gum, (\( \nu_{\text{max}} \) 3600-2800 cm\(^{-1}\)). Methylation of the gum with an ethereal solution of diazomethane and chromatography of the product on deactivated alumina afforded, from the light petroleum-benzene (4:1) eluates a mixture of methyl 5\( \beta \)H-abieta-8,11,13-trien-18-oate (139)\(^{42a}\) and methyl abieta-8,11,13-trien-18-oate (2) (0.2 g, 40\%) in a ratio of 7:3. The product was an oil which did not crystallize.

\( \nu_{\text{max}} (\text{CHCl}_3) \) 1725 cm\(^{-1}\) (ester C=O).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.20 (d, J 7 Hz, C 15 methyls), 1.26 (s, C 4 axial Me), 1.37 (s, C 10 angular Me), 2.50-3.22 (m, C 7 and
C 15 protons), 3.42 (s, CO₂Me of 139), 3.67 (s, CO₂Me of 2),
6.72-7.28 (m, aromatic protons).

Oxidation of Methyl 5βH-Abieta-8,11,13-trien-18-oate (139) with
Chromium Trioxide in Acetic Acid

The 5β-ester (139) (contaminated with ca. 30% of the 5α-epimer
(2) (134 mg, 0.46 mmol) in glacial acetic acid (2.0 ml) was treated
with chromium trioxide (200 mg) in glacial acetic acid (3.5 ml) and
water (0.5 ml) and the mixture was stood at 20°C for 16 hr. The mixture
was diluted with water and extracted with ether. The organic layer
was washed with saturated aqueous sodium bicarbonate, dried, and
concentrated to give a gum which on titration with ether gave the
enol lactone (95) (66 mg, 58%, based on the 5β epimer in the mixture),
m.p. and m.m.p. 198-199°C (subl.) and 216-217°C. The mother liquors
contained mixtures of the enol lactone (95) and the aryl ketone (18)
as shown by t.l.c.

Attempted preparation of Methyl 6β-Acetoxy-abieta-8,11,13-trien-18-oate

The enol lactone (95) (1.0 g, 3.3 mmol) in absolute methanol
(10.0 ml), was added to sodium methoxide (from sodium, 120 mg) in
absolute methanol (10.0 ml) and the bright yellow solution was refluxed
for 2 hr. The mixture was cooled, acidified to litmus with concentrated
hydrochloric acid, and extracted with ether. The organic layer was
washed with water, dried, and concentrated to give the crude
diosphenol (149) (1.0 g) as a pale-yellow gum.

\[ v_{\text{max}}^{\text(CHCl}_3) \] 3600-2500 (OH), 1725 (ester C=O) 1715 cm⁻¹

diosphenol C=O).
The crude diosphenol (1.0 g) was dissolved in acetic anhydride (10.0 ml) and pyridine (5 drops) and the mixture was stood at 20° for 18 hr. The mixture was poured onto ice, and extracted into ether. The ether layer was washed with water, dried, and concentrated to afford a pale yellow oil which was chromatographed on silica gel. Elution of the column with light petroleum-benzene (1:1) afforded the enol acetate (150) (0.3 g) contaminated with a trace of the enol lactone (95).

\[ \nu_{\text{max}} \ (\text{CHCl}_3) \ 1760 \ (\text{enol-acetate C=O}), \ 1725 \ (\text{ester C=O}), \ 1675 \ \text{cm}^{-1} \ (\text{aryl ketone C=O}). \]

The enol acetate (150) (0.3 g) in 95% ethanol (25.0 ml) was hydrogenated at 55 p.s.i. and 20° over 10% palladium-carbon for 13 hr. The catalyst was filtered off and the filtrate was concentrated to give a gum which was chromatographed on deactivated alumina. Elution of the column with light petroleum-benzene gave methyl abieta-8,11,13-trien-18-oate (2) (130 mg, 48%), m.p. and m.m.p. 58-60°. The i.r. spectrum was identical with that of the authentic ester (2).

Elution of the column with light petroleum-benzene (1:4) gave methyl abieta-6,8,11,13-tetraen-18-oate (17) (20 mg, 7%) as an oil. \[ \nu_{\text{max}} \ (\text{CHCl}_3) \ 1725 \ \text{cm}^{-1} \ (\text{ester C=O}). \]

N.m.r. δ (CDCl3). 1.23 (d, J 7 Hz, C 15 methyls), 1.25 (s, C 4 axial Me), 1.36 (s, C 10 angular Me), 2.46 (5 members of a septet, J 7 Hz, C 15 proton), 3.66 (s, CO₂Me), 7.05 (s, W₁ 4 Hz, C 6 and C 7 protons), 7.08-7.30 (m, aromatic protons).
Friedel-Crafts Acetylation of Methyl Abieta-8,11,13-trien-18-oate (2)

a) with Acetyl chloride-Aluminium chloride in 1,1,2,2-
Tetrachloroethane

Methyl abieta-8,11,13-trien-18-oate (2) (14.0 g, 44.5 mmol) and acetyl chloride (3.43 ml, 50.0 mmol) in 1,1,2,2-tetrachloroethane (75.0 ml) was treated at 20° with aluminium chloride (12.3 g, 90.0 mmol), added portionwise over 1 hr, and the resultant dark green solution was stood at 20° for 48 hr. The mixture was poured in a thin stream into ice (75 g) and concentrated hydrochloric acid (75.0 ml), and the organic phase was washed with water, dried, and concentrated with a rotatory evaporator to afford a deep green gum which was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (9:1) afforded the starting ester (2) (5.0 g, 35% recovery).

Elution of the column with light petroleum-benzene (4:1) gave methyl 12-acetylabieta-8,11,13-trien-18-oate (227) (6.2 g, 39%) which was recrystallised from methanol as prisms, m.p. 129-131° (lit. 188 133-134°).

$\nu_{\text{max}} (\text{CHCl}_3) 1725$ (ester C=O), 1675 (aryl ketone C=O) and 890 cm$^{-1}$ (isolated aromatic hydrogen).

N.m.r. δ (CDCl$_3$) 1.18, 1.22 (2 doublets, J 7 Hz, C 15 methyls), 1.20 (s, C 10 angular Me), 1.28 (s, 4 axial Me), 2.53 (s, CH$_3$CO), 2.87 (m, C 7 protons), 3.58 (septet, C 15 proton), 3.65
(s, CO₂Me), 7.02 (s, W₁/₂ 2 Hz, C 14 proton), 7.38 (s, W₁/₂ 2 Hz, C 11 proton).

Elution of the column with light petroleum–benzene (1:1) afforded methyl 14-acetylabieta–8,11,13-trien-18-oate (224) (0.75 g, 5%) as a gum which did not crystallise.

ν max (CHCl₃) 1725 (ester C=O), 1675 (aryl ketone C=O), and 820 cm⁻¹ (ortho aromatic hydrogens).

N.m.r. δ (CDCl₃) 1.18, 1.22 (2 doublets, J 7 Hz, C 15 methyls), 1.20 (s, C 10 angular Me), 1.27 (s, C 4 axial Me), 2.53 (s, CH₃CO), 2.92 (m, C 7 protons), 3.52 (5 members of a septet, J 7 Hz, C 15 proton), 3.65 (s, CO₂Me), 7.08 (d, J 8 Hz, C 12 proton), 7.68 (d, J 8 Hz, C 11 proton).

b) with Acetyl chloride-Aluminium chloride in Carbon Disulphide

Methyl abieta–8,11,13-trien-18-oate (2) (30.3 g, 97 mmol) and acetyl chloride (26.0 ml, 300 mmol) in dry carbon disulphide (300.0 ml) was added slowly to aluminium chloride (35.0 g, 260 mmol) in refluxing carbon disulphide (400.0 ml) and the crimson mixture was stirred and refluxed for 4 hr. The solvent was distilled off, and the viscous residue was treated with concentrated hydrochloric acid (25.0 ml) in ice-water (175 ml). The mixture was extracted with ether and the ether layer was washed with water, dried, and concentrated to give a crystalline black residue. This was filtered through a short column of deactivated alumina with light petroleum–benzene (1:1) as the solvent, and the
concentrate was recrystallized from methanol to give methyl 12-acetyl-
abieta-8,11,13-trien-18-oate (227) (29.5 g, 86%), m.p. and m.m.p.
130-131°.

**Methyl 12-Carboxy-abieta-8,11,13-trien-18-oate (228)**

Methyl 12-acetylabieta-8,11,13-trien-18-oate (227) (7.12 g, 20.0 mmol) in dry pyridine (14.0 ml) was treated with iodine
(5.08 g, 20.0 mmol) and the mixture was heated on the water-bath for
1½ hr. The solvent was removed under reduced pressure to give a dark
crystalline mass which was dissolved in 95% ethanol (110.0 ml) and
treated with sodium hydroxide (9.60 g) in water (55.0 ml). The solution
was refluxed for 2 hr and the cooled mixture was diluted with water
and extracted with ether. Concentration of the ether extract yielded
a black tar (0.7 g) which was discarded. The aqueous layer was
decolourised by warming it on the water bath with activated carbon for
5 min. The carbon was filtered off through a thin Celite pad, and
the aqueous solution was acidified to litmus by the dropwise addition of
concentrated hydrochloric acid. The flocculent precipitate was filtered
off and recrystallised from methanol to give methyl 12-carboxy-abieta-
8,11,13-trien-18-oate (288) (5.8 g, 81%) as fluffy needles, m.p.
185-190° (lit. 187 190-190.5°).

\[ \nu_{\text{max}} \text{ (CHCl}_3\text{)} 3520-2400 \text{ (carboxylic acid OH), 1725 (ester C=O),} \]
1690 (aryl acid C=O), and 890 cm\(^{-1}\) (isolated aromatic hydrogen).

N.m.r. \( \delta \) (CDCl\(_3\)) 1.18 (s, C 4 axial Me), 1.22 (d, J 7 Hz, C 15
methyls), 1.28 (s, C 10 angular Me), 2.92 (m, C 7 protons), 3.65
(s, CO\(_2\)Me), 3.89 (5 members of a septet, J 7 Hz, C 15 proton),
7.05 (s, $\frac{1}{2}$ Hz, C 14 proton), 7.84 (s, $\frac{1}{2}$ Hz, C 11 proton).

Oxidation of Methyl 12-Carboxy-abieta-8,11,13-trien-18-oate (228) with Lead Tetra-acetate

The aryl carboxylic acid (228) (3.0 g, 8.4 mmol) in dry benzene (255.0 ml) was treated under nitrogen with dried lead tetraacetate (3.75 g, 8.5 mmol), and the solution was refluxed under anhydrous conditions for 18 hr. Ethane-1,2-diol (2.0 ml) was added and the mixture was refluxed for a further 5 min. The mixture was filtered through a pad of Celite and the residue was washed well with benzene. The combined filtrate and washings were washed with water, dried, and concentrated to afford a gum which was chromatographed on silica gel.

Elution of the column with benzene-ether (99:1) afforded the Y-lactone of methyl 12-carboxy-15-hydroxy-abieta-8,11,13-trien-18-oate (243) (2.8 g, 93%), which was recrystallized from chloroform-light petroleum as needles, m.p. 198-199°, $[\alpha]_D^1 +77^0$ (C 0.43).

Found: C, 74.1; H, 7.9

C$_{22}$H$_{28}$O$_4$ requires: C, 74.0; H, 8.2%.

$\nu_{\text{max}}$ (CHCl$_3$) 1750 (aryl Y-lactone C=O), 1725 cm$^{-1}$ (ester C=O).

N.m.r. δ (CDCl$_3$) 1.19 (s, C 4 axial Me), 1.28 (s, C 10 angular Me), 1.59 (s, C 15 methyls), 3.00 (m, C 7 protons), 3.65 (s, CO$_2$Me), 7.05 (s, $\frac{1}{2}$ Hz, C 14 proton), 7.76 (s, $\frac{1}{2}$ Hz, C 11 proton).
Preparation and Copper I Oxide-Catalysed Thermolysis of Methyl 12-

Methyl 12-carboxy-abieta-8,11,13-trien-18-oate (228) (1.0 g, 2.8
mmol) was suspended in dry benzene (25.0 ml) and the mixture was
treated with oxalyl chloride (0.5 ml) in dry benzene (5.0 ml) at 0°.
The mixture was stood at 20° for 3/4 hr with occasional shaking. The
benzene was removed at 20° under reduced pressure to give the acyl
chloride (229) (1.05 g, 100%) as an oil which crystallised on scratching,
m.p. (sealed capillary) 114-116°.

\[ \nu_{\text{max}} (\text{CCl}_4) 1770 \text{ (aryl acyl chloride C=O), 1725 cm}^{-1} \]
(ester C=O).

The crude acyl chloride (229) (1.05 g, 2.8 mmol) was dissolved
in anhydrous ether (30.0 ml) and the solution was added very slowly
to an ethereal solution of diazomethane (0.32 mmol/ml, 15.0 ml) (which
had been distilled and then dried over sodium wire immediately before
use), containing triethylamine (0.1 ml, freshly distilled). The mixture
was then stood at 0° for 18 hr. The solution was filtered from the
precipitated triethylamine hydrochloride and the filtrate was concentrated
at 20° under reduced pressure to afford the crude diazoacetyl
derivative (230) (1.05 g) as a pale yellow, metastable gum.

\[ \nu_{\text{max}} (\text{CCl}_4) 2100 \text{ (-C=N=N allenic type stretching), 1725} \]
(ester C=O), and 1610 cm\(^{-1}\) (aryl diazomethyl-ketone C=O).
The crude diazomethyl ketone (230) (1.0 g, 2.8 mmol) was dissolved in dry cyclohexane (100.0 ml, spectroscopic quality), and the solution was filtered from a small quantity of polymethylene which had precipitated. The filtrate was transferred to a Hershberg addition funnel, and was added over a period of 3 days to a stirred suspension of dry copper I oxide in pure, refluxing cyclohexane (400.0 ml). The mixture was refluxed for a further 1 hr after the final addition. The cooled mixture was filtered, and the filtrate was concentrated to afford a brown gum which was chromatographed on deactivated alumina.

Light petroleum-benzene (4:1) eluted a pale yellow oil which showed only the ester absorption ($\nu_{\text{max}}$ 1725 cm$^{-1}$) in the i.r. spectrum, while the n.m.r. spectrum still exhibited an isopropyl doublet ($\delta$ 1.22, J 7 Hz). The mass spectrum indicated that this oil, t.l.c. one spot with high $R_F$ value, was a mixture. This fraction was not investigated further.

Elution with light petroleum-benzene (1:1) afforded methyl 12, 13 [3',3'-dimethyl-1'-oxopropano]-podocarpa-8,11,13-trien-18-oate (231) (0.52 g, 50%), which crystallized from chloroform-methanol as needles, double m.p. 125-127° and 136-137°, $[\alpha]_D + 60^\circ$ (c 0.15).

Found: C, 78.1 H, 8.5

$C_{23}H_{30}O_3$ requires: C, 77.9; H, 8.5%.

$\nu_{\text{max}}$ (CHCl$_3$) 1725 (ester C=O), and 1705 cm$^{-1}$ (aryl cyclopentanone C=O).
N.m.r. δ (CDCl₃) 1.19 (s, C 10 angular Me), 1.28 (C 4 axial Me),
1.38 (s, C 3' methyls), 2.52 (s, C 2' protons), 3.02 (m, C 7
protons), 3.64 (s, CO₂Me), 7.12 (s, W₁ 2 Hz, C 14 proton),
7.61 (s, W₁ 2 Hz, C 11 proton).

Benzene eluted a mixture of several compounds (t.l.c.) which
showed carbonyl absorptions at 1760, 1725, and 1675 cm⁻¹ in the i.r.
spectrum. This fraction was not investigated further.

From the benzene-ether (9:1) eluates was obtained a pale yellow
oil (80 mg) which contained methyl 12-aminoacetylabieta-8,11,13-trien-
18-oate (233) as the major component.

Found: mol. wt., 371 (mass spectrum)
C₂₃H₃₃O₃N requires mol. wt., 371.

ν_max (CHCl₃) 3460 (NH₂), 1725 (ester C=O), 1670 (aryl ketone
C=O), and the 1655 cm⁻¹ (NH₂).

N.m.r. δ (CDCl₃) 1.17 (s, C 10 angular Me), 1.22 (d, J 7 Hz,
C 15 methyls), 1.26 (s, C 4 axial Me), 2.90 (m, C 7 and C 15
protons), 3.64 (s, CO₂Me), 5.88 (s, W₁ 9 Hz, NH₂), 6.92 (s,
W₁ 2 Hz, C 14 proton), 7.10 (s, W₁ 2 Hz, C 11 proton).

Lithium Aluminium Hydride Reduction of the Y-Lactone of Methyl 12-

The Y-lactone (243) (2.10 g, 6.2 mmol) in absolute ether
(100.0 ml) was slowly added to a suspension of lithium aluminium hydride
(0.75 g, 18.5 mmol) in absolute ether (50.0 ml), and the mixture was
refluxed under anhydrous conditions for 5 hr. The mixture was cooled, treated dropwise with saturated aqueous ammonium chloride, and filtered. The residue was washed with ether, and the filtrate and washings were concentrated to afford 12-hydroxymethylabieta-8,11,13-trien-15,18-diol (244) (2.0 g, 100%) which crystallised from methanol chloroform as the methanol hemi-solvate, m.p. 210-211°, with loss of methanol at 132-135°, [α]_D + 200° (c 0.06).

Found: C, 74.5; H, 9.5

C_{21}H_{32}O_3 \cdot \frac{1}{2} \text{CH}_3\text{OH requires: C, 74.1; H, 9.8%}.

ν_{max} (CHCl_3) 3600, 3400 cm^{-1} (OH)

N.m.r. δ (CDCl_3) 0.97 (s, C 4 axial Me), 1.20 (s, C 10 angular Me), 1.23 (s, C 15 methyls), 2.08 (OH, exchanged with D_2O), 3.18, 3.48 (2 doublets, J 11 Hz, C 18 protons), 4.76 (s, δ_{1/2} 4 Hz, C 1' benzylic protons), 6.88 (s, δ_{1/2} 2 Hz, C 14 proton), 7.10 (s, δ_{1/2} Hz, C 11 proton).

Dehydration of the Triol (244)

a) with Phosphorus Oxychloride and Pyridine

The triol (244) (0.1 g, 0.3 mmol) was dissolved in pyridine (4.0 ml) and the solution was treated with phosphoryl chloride (1.0 ml) in pyridine (2.0 ml). The mixture was stood at 20° for 24 hr, added dropwise to ice-water, and the suspension was extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated to afford 12-hydroxymethylabieta-8,11,13,15-tetraen-18-ol (246) (82 mg, 75%) as a gum, identified from its spectroscopic properties.
\( v_{\text{max}} (\text{CHCl}_3) \) 3600 (OH), 910 cm\(^{-1}\) (C=CH\(_2\)).

N.m.r. \( \delta (\text{CDCl}_3) \) 0.83 (s, C 4 axial Me), 1.17 (s, C 10 angular Me), 2.03 (s, \( \frac{1}{2} \) 4 Hz, C 15 Me), 2.55 (OH, exchanged with \( \text{D}_2\)O), 3.12, 3.42 (2 doublets J 11 Hz, C 18 protons), 4.60 (s, \( \frac{1}{2} \) 6 Hz, C 1' benzyllic protons), 4.85, 5.19 (2 singlets, \( \frac{1}{2} \) 6 Hz, C 16 protons), 6.84 (s, \( \frac{1}{2} \) 2 Hz, C 14 proton), 7.30 (s, \( \frac{1}{2} \) 2 Hz, C 11 proton).

The crude unsaturated diol (246) was purified via its diacetate (247) formed by treatment with acetic anhydride-pyridine at 20\(^\circ\) for 16 hr. The product, isolated by water dilution of the reaction mixture, followed by ether extraction, was a gum which was chromatographed on deactivated alumina.

Elution of the column with benzene afforded 18-acetoxy-12-acetoxy methylabieta-8,11,13,15-tetraene (247) (80 mg, 74%), as a pale yellow oil, \([\alpha]_D + 10^\circ\) (C 0.21).

**Found:** C, 75.5; H, 8.7; O, 15.6

**C\(_{25}\)H\(_{34}\)O\(_4\) requires:** C, 75.3; H, 8.6; O, 16.0%.

\( v_{\text{max}} (\text{CHCl}_3) \) 1730 (acetate C=O), 910 cm\(^{-1}\) (C=CH\(_2\)).

N.m.r. \( \delta (\text{CDCl}_3) \) 0.93 (s, C 4 axial Me), 1.22 (s, C 10 angular Me), 2.00 (2 singlets, C 15 methyl and C 18 OAc), 2.02 (s, C 1' benzyllic OAc), 2.87 (m, C 7 protons), 3.67, 4.00 (2 doublets, J 11 Hz, C 18 protons), 4.87, 5.19 (2 singlets, \( \frac{1}{2} \) 6 Hz, C 16 protons), 5.07 (s, \( \frac{1}{2} \) 4 Hz, C 1' benzyllic
protons), 6.89 (s, W/2 2 Hz, C 14 proton), 7.28 (s, W/2 2 Hz, C 11 proton).

b) with Acetic Anhydride-Potassium Acetate

The triol (244) (0.2 g, 0.6 mmol) in acetic anhydride (12.0 ml) and potassium acetate (0.2 g), was stirred and heated on the water-bath for 20 hr. The cooled solution was poured into water, the mixture was extracted with ether, and the organic layer was washed with saturated aqueous sodium hydrogen carbonate, dried, and concentrated to give a yellow gum which was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (4:1) gave the unsaturated diacetate (247) (30 mg, 12%), identified by comparison of its t.l.c. behaviour and i.r. spectrum with those of authentic compound.

Elution of the column with light petroleum-benzene (1:4) afforded 15,18-diacetoxy-12-acetoxymethylnioba-8,11,13-triene (289) (85 mg, 30%), as a colourless oil, for which correct analyses could not be obtained.

\[ \nu_{\text{max}} (\text{CHCl}_3) = 1730 \text{ cm}^{-1} \] (acetate C=O).

N.m.r. δ (CDCl_3) 0.92 (s, C 4 axial Me), 1.18 (s, C 10 angular Me), 1.78 (s, C 15 methyls), 1.98 (s, C 18 OAc), 2.02 (C 1' benzylic OAc), 2.06 (s, C 15 OAc), 2.84 (m, C 7 protons), 3.65, 3.98 (2 doublets, J 11 Hz, C 18 protons), 5.28 (s, W/2 2 Hz, C 1' benzylic protons), 7.00 (s, W/2 2 Hz, C 14 proton), 7.25 (s, W/2 2 Hz, C 11 proton).
Elution of the column with benzene and benzene-ether (9:1) afforded mixtures (t.l.c.) showing both hydroxyl and acetate absorptions in the i.r. spectrum.

c) with Acetic Anhydride-Toluene-p-sulphonic acid

The triol (244) (0.6 g, 1.8 mmol) in acetic anhydride (25.0 ml) and toluene-p-sulphonic acid (10 mg) were refluxed under nitrogen for ½ hr. The purple mixture was cooled and poured onto ice-water. After the mixture had stood at 20° for 2 hr, the oil-water suspension was extracted with ether and the organic layer was washed with saturated aqueous sodium hydrogen carbonate, dried, and concentrated to give a brown gum which was chromatographed on deactivated alumina.

Elution of the column with light petroleum-benzene (1:1) afforded the unsaturated diacetate (247) (0.45 g 63%), as an oil, having an identical t.l.c. spot and i.r. spectrum with those of the compound obtained from previous dehydrations of the triol (244).

δ-Lactone of Methyl 15-Carboxymethyl-12-hydroxy-abieta-8,11,13-trien-18-oate (234)

The indanone (231) (0.52 g, 1.47 mmol), m-chloroperbenzoic acid (0.82 g, 4.7 mmol), and toluene-p-sulphonic acid (5 mg) were refluxed in 1,2-dichloroethane (35.0 ml) for 5 hr. The mixture was cooled, and washed successively with saturated aqueous potassium iodide, saturated aqueous sodium bicarbonate, aqueous sodium thiosulphate, and finally water. The organic layer was dried and concentrated to afford a brown solid which was chromatographed on silica gel.
Elution of the column with benzene-ether (9:1) gave the δ-lactone (234) (0.48 g, 85%), which was recrystallized from chloroform-light petroleum as needles, m.p. 198-199°, \([\alpha]_D^+ 75^\circ\) (c 0.08).

Found: C, 74.8; H, 8.2

\(C_{23}H_{30}O_4\) requires: C, 74.7; H, 8.2%.

\(\nu_{\text{max}}(\text{CHCl}_3)\) 1760 (aryl δ-lactone C=O), 1725 cm\(^{-1}\) (ester C=O).

N.m.r. δ (CDCl\(_3\)): 1.20 (s, C 10 angular Me), 1.28 (s, C 4 axial Me), 1.32 (s, C 15 methyls), 2.58 (s, C 1' protons), 2.85 (m, C 7 protons), 3.67 (s, \(CO_2\)Me), 6.95 (s, C 11 and C 14 protons).

**Attempted Hydrolysis of the δ-Lactone of Methyl 15-Carboxymethyl-12-hydroxy-abieta-8,11,13-trien-18-oate (234)**

The δ-lactone (234) (0.12 g, 0.31 mmol) in methanol (5.0 ml) was treated with sodium hydroxide (0.4 g) in water (0.5 ml) and the solution was refluxed under nitrogen for 2 hr. On cooling the mixture, yellow cubes of the bis-sodium salt of the phenol-acid (235) were deposited. The precipitate dissolved on dilution of the mixture with water, and the mixture was acidified to litmus with the dropwise addition of concentrated hydrochloric acid. The mixture was extracted with ether, and the ether extract was washed with water, dried, and concentrated to afford the δ-lactone (234) (100 mg recovered) as a brown solid, with a t.l.c. spot and i.r. spectrum identical with those of the authentic lactone (234).
Hydrolysis with Concomittant Methylation of the δ-Lactone (234)

The δ-lactone (234) (0.48 g, 1.30 mmol) in t-butanol (30.0 ml) was stirred at 20° under nitrogen with potassium t-butoxide (1.20 g) for 1/4 hr. Methyl iodide (0.6 ml) in t-butanol (15.0 ml) was then added, and the mixture was stirred at 20° overnight. The mixture was diluted with water, acidified with concentrated hydrochloric acid, and extracted into ether. The ether layer was washed with water, dried, and concentrated to afford a viscous gum which was filtered through silica gel in benzene. Concentration of the eluates afforded methyl 15-carboxymethyl-12-methoxy-abieta-8,11,13-trien-18-oate (236) (0.35 g, 68%) as a glass which did not crystallize, [α]D + 41° (c 0.29).

Found: C, 71.4; H, 9.0

C24H34O5 requires: C, 71.6; H, 8.5%

νmax (CHCl3) 3600–2500 (acid OH), 1725 (ester C=O), 1710 cm⁻¹ (acid C=O).

N.m.r. δ (CDCl3) 1.20 (s, C 10 angular Me), 1.25 (C 4 axial Me), 1.49 (s, C 15 methyls), 2.60–3.00 (m, C 7 protons and C1' protons), 3.64 (s, CO₂Me), 3.79 (s, OMe), 6.75 (s, W₁ 2 Hz, C 14 proton), 6.85 (s, W₁ 2 Hz, C 11 proton), 7.5–8.9 (CO₂H).

Attempted Cyclisation of Methyl 15-Carboxymethyl-12-methoxy-abieta-8,11,13-trien-18-oate (236)

a) with Stannic Chloride in Benzene

The carboxylic acid (236) (0.11 g, 0.27 mmol) in dry benzene (2.0 ml) was treated at 0° with oxalyl chloride (0.1 ml) in benzene
(1.0 ml), and the mixture was stood at 20° for 1 hr. The solvent was removed at 20° under reduced pressure to give the crude acid chloride as a pale yellow viscous oil.

\[ \nu_{\text{max}} (\text{CCl}_4) 1810 \text{ (acid chloride } C=O), 1725 \text{ cm}^{-1} (\text{CO}_2\text{Me } C=O). \]

The crude acid chloride (0.12 g) in dry benzene (5.0 ml) was cooled to 0° and treated with a solution of stannic chloride (0.1 ml) in dry benzene (1.0 ml). The purple mixture was stirred at 0° for 1 hr. Ice and concentrated hydrochloric acid were added, and the mixture was extracted with ether. The ether layer was washed with 10% hydrochloric acid and then water. The ether solution was dried and concentrated to afford the 8-lactone (234) as the sole product, m.p. and m.m.p. 197-199°, with a t.l.c. spot and i.r. spectrum identical with those of the authentic lactone (234).

b) with Aluminium Chloride in Carbon Disulphide

The acid chloride was prepared from 0.18 g of the acid (236) as in (a) above. The crude acid chloride (0.19 g) in dry carbon disulphide (2.0 ml) was treated with aluminium chloride (65 mg), and the crimson mixture was refluxed under anhydrous conditions for 15 min. The mixture was cooled, and worked-up as in (a) above to afford the lactone (234), identical in all respects with authentic compound.

18-Acetoxy-12-acetoxy methyl-13-acetyl-podocarpa-8,11,13-triene (248)

a) Ozonolysis of 18-Acetoxy-12-acetoxy methyl-abieta-8,11,13,15-tetraene (247)

The unsaturated diacetate (247) (0.46 g, 1.15 mmol) in dry methylene dichloride (200 ml) was treated at -80° with a slight excess
of ozone for 12 min. The solution was warmed to 20°, washed successively with potassium iodide in dilute aqueous acetic acid, aqueous sodium thiosulphate, saturated aqueous sodium hydrogen carbonate, and finally water. The solution was dried and concentrated to give a colourless oil which was chromatographed on deactivated alumina.

Elution with light petroleum-benzene (1:4) gave the keto-ester (248) (0.1 g, 22%) as a colourless gum, \([\alpha]_D + 50^0\) (c 0.26).

Found: \[\begin{align*} C, 71.8; \ H, 8.4 \\
C_{24}H_{32}O_5 \text{ requires: } C, 72.0; \ H, 8.05\%.
\end{align*}\]

\(\nu_{\text{max}}\) (CHCl\(_3\)) 1740 (acetate C=O), 1730 (acetate C=O), and 1680 cm\(^{-1}\) (aryl ketone C=O).

N.m.r. \(\delta\) (CDCl\(_3\)) 0.97 (s, C 4 axial Me), 1.22 (s, C 10 angular Me), 2.03 (s, C 18 OAc), 2.10 (s, C 1' OAc), 2.55 (s, CH\(_3\)CO), 3.68, 4.04 (2 doublets, J 11 Hz, C 18 protons), 5.38 (s, W\(_1\) 3 Hz, C 1' protons), 7.35 (s, W\(_1\) 2 Hz, C 14 proton), 7.49 (s, W\(_1\) 2 Hz, C 11 proton).

b) Osmium Tetroxide-Sodium Metaperiodate Oxidation of 18-Acetoxy-12-Acetoxyethyl-abieta-8,11,13,15-tetraene (247)

The unsaturated diacetate (247) (0.52 g, 1.30 mmol) was dissolved in a mixture of acetic acid (7.0 ml), water (5.0 ml), and dioxane (20.0 ml), and the solution was treated with osmium tetroxide (ca. 10 mg), and the solution was stirred at 20° for \(\frac{1}{4}\) hr. Finely powdered sodium metaperiodate (1.10 g, 5.1 mmol) was added in portions over a \(\frac{1}{2}\) hr period, and the mixture was stirred at 20° for 5 days.
The mixture was diluted with water and extracted with ether. The ether layer was washed with saturated aqueous sodium hydrogen carbonate, and then with water, dried, and concentrated to give a yellow gum which was chromatographed on deactivated alumina.

Light petroleum-benzene (4:1) eluted the starting ester (247) (80 mg), identified by its t.l.c. spot and i.r. spectrum.

From the light petroleum-benzene (1:4) eluates was obtained the keto-ester (248) (0.22 g, 50%), with an identical t.l.c. spot and i.r. spectrum as the compound obtained in (a).

**Methyl 12-Acetoxy-abieta-8,11,13-trien-18-oate (253)**

Methyl 12-acetylabieta-8,11,13-trien-18-oate (227) (1.0 g, 1.9 mmol), m-chloroperbenzoic acid (1.50 g), and toluene-2- sulphonic acid (2 mg) were refluxed in 1,2-dichloroethane (40.0 ml) for 5 hr. The mixture was cooled, and washed successively with dilute aqueous potassium iodide, sodium thiosulphate, sodium hydrogen carbonate, and finally water. The organic layer was dried and concentrated to give a red gum, which was filtered through silica gel using light petroleum-benzene (1:1) as solvent. Concentration of the eluates gave methyl 12-acetoxy-abieta-8,11,13-trien-18-oate (253) (800 mg, 75%) which recrystallised from chloroform-methanol as prisms, m.p. 113-114°, $[\alpha]_D + 45^\circ$ (c 0.22).

**Found:**
- C, 74.2; H, 8.8; O, 17.5
- $C_{23}H_{32}O_4$ requires: C, 74.2; H, 8.7; O, 17.2%. 


$v_{\text{max}}$ (CHCl$_3$) 1760 (phenyl acetate C=O), 1725 cm$^{-1}$ (ester C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.16 (s, C 10 angular Me), 1.18 (d, J 7 Hz, C 15 methyls), 1.25 (s, C 4 axial Me), 2.25 (s, OAc), 2.63-3.10 (m, C 7 and C 15 protons), 3.65 (s, CO$_2$Me), 6.85 (s, $\Omega_2$ 2 Hz, C 14 proton), 6.95 (s, $\Omega_2$ 2 Hz, C 11 proton).

**Methyl 12-Hydroxy-abieta-8,11,13-trien-18-oate (254)**

Methyl 12-acetoxy-abieta-8,11,13-trien-18-oate (253) (2.3 g, 6.2 mmol) in methanol-water (9:1) (150 ml), was treated with solid sodium hydrogen carbonate (4.0 g), and the mixture was refluxed gently for 1 hr. The cooled mixture was diluted with water and extracted with ether. The ether phase was washed with water, dried, and concentrated to give the phenol (254) (1.8 g, 90%) which crystallised from chloroform-methanol as diamond-shaped plates, m.p. 160-161$^\circ$ (lit.$^{74c}$ 162-163$^\circ$).

$v_{\text{max}}$ (CHCl$_3$) 3620, 3400 (phenol OH), and 1725 cm$^{-1}$ (ester C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.15 (s, C 10 angular Me), 1.18 (d, J 7 Hz, 1.26 (s, C 4 axial Me), 2.76 (m, C 7 protons), 3.06 (5 members of a septet, J 7 Hz, C 15 proton), 3.65 (s, CO$_2$Me), 5.45 (s, $\Omega_2$ 28 Hz, OH), 6.65 (s, $\Omega_2$ 2 Hz, C 14 proton), 7.00 (s, $\Omega_2$ 2 Hz, C 11 proton).

**Methyl 12-Methoxy-abieta-8,11,13-trien-18-oate (250)**

Methyl 12-hydroxy-abieta-8,11,13-trien-18-oate (254) (2.2 g, 6.7 mmol) dissolved in $t$-butanol (50.0 ml) was treated with potassium-
t-butoxide (4.5 g) and the mixture was heated under reflux in a nitrogen atmosphere for \(\frac{1}{2}\) hr. The solution was cooled in ice, and methyl iodide (2.9 g) in \(\text{t-butanol} \ (5.0 \text{ ml})\) was added, and the mixture was refluxed for a further 2 hr. The mixture was cooled, poured onto ice-water, and acidified to litmus by dropwise addition of concentrated hydrochloric acid. The suspension was extracted with ether, and the ether extract was washed with water, dried, and concentrated to give an orange gum which was filtered through deactivated alumina using light petroleum-benzene (4:1) as solvent. Concentration of the eluates gave the phenyl methyl ether (250) (1.2 g, 51%) as an oil which crystallized as needles, m.p. 60-64\(^\circ\) (lit.\(^\circ\) 65-65.5\(^\circ\)) on trituration with methanol.

\[v_{\text{max}} (\text{CHCl}_3) \ 1725 \ (\text{ester} \ C=O), \text{ and } 1040 \ \text{cm}^{-1} \ (\text{aromatic OMe}).\]

N.m.r. \(\delta (\text{CDCl}_3) \ 1.18 \ (d, J \ 7 \text{ Hz, C 15 methyls}), \ 1.23 \ (s, C 10 \text{ angular Me}), \ 1.27 \ (s, C 4 \text{ axial Me}), \ 2.78 \ (m, C 7 \text{ protons}), \ 3.22 \ (5 \text{ members of a septet, J 7 Hz, C 15 proton}), \ 3.65 \ (s, \text{CO}_2\text{Me}), \ 3.79 \ (s, \text{OMe}), \ 6.70 \ (s, \frac{W}{2} \text{ 2 Hz, C 14 proton}), \ 6.85 \ (s, \frac{W}{2} \text{ 2 Hz, C 11 proton}).\]

**Peracetic Acid Oxidation of Methyl 12-Methoxy-Abieta-8,11,13-trien-18-oate (250)**

The methyl ether (250) (1.20 g, 3.50 mmol) in acetic anhydride (10.0 ml) was cooled to 0\(^\circ\), and stirred while peracetic acid (25.0 ml, 7 M) was added dropwise. The mixture was stirred for a further 38 hr, and then kept in the dark for 10 days. The pale brown mixture was diluted with water, and the mixture was worked-up as for previous peracid
oxidations. The neutral fraction (0.7 g) showed many spots with considerable streaking on t.l.c. and was therefore not investigated further.

**Nitration of Methyl Abieta-8,11,13-trien-18-oate (2) with Copper II nitrate in Acetic Anhydride**

a) **small scale**

Powdered copper II nitrate trihydrate (0.78 g) was added in portions to a stirred solution of methyl abieta-8,11,13-trien-18-oate (2) (1.0 g, 3.10 mmol) in acetic anhydride (60.0 ml), and the blue solution was stirred at 20° for 1/2 hr. The mixture was poured onto ice and stirred for 2 hr. The pale yellow precipitate was filtered off, washed with water, dried, and recrystallised from chloroform-methanol to give methyl 14-nitro-abieta-8,11,13-trien-18-oate (45) (900 mg, 85%) as flakes, m.p. 193-194° (lit. 189 194-195°).

\[ \nu_{\text{max}}^{\text{CHCl}_3} \] 1725 (ester C=O), 1520, 1350 (aromatic NO₂), and 830 cm⁻¹ (ortho aromatic hydrogens).

\[ N . m . r . \delta (\text{CDCl}_3) \] 1.18 (s, C 10 angular Me), 1.20 (d, J 7 Hz, C 15 methyls), 1.26 (s, C 4 axial Me), 2.50-3.00 (m, C 7 and C 15 protons), 3.64 (s, CO₂Me), 7.16, 7.36 (2 doublets, J 9 Hz, C 11 and C 12 protons).

b) **large scale**

Methyl abieta-8,11,13-trien-18-oate (2) (10.0 g, 31.0 mmol) in acetic anhydride (250 ml) was treated as above with finely powdered copper II nitrate (8.0 g). The product, isolated as in (a) above,
crystallized as a 1:1 mixture of methyl 12-nitro-abieta-8,11,13-trien-18-oate (261) and methyl 14-nitro-abieta-8,11,13-trien-18-oate (45) with a wide melting point range (150-190°).

\[ \nu_{\text{max}} (\text{CHCl}_3) 1725 \text{ (ester C=O)}, 1520, 1350 \text{ (aromatic NO}_2\text{)}, \text{ and } 895 \text{ (isolated aromatic hydrogen)}, \text{ and } 830 \text{ cm}^{-1} \text{ (ortho aromatic hydrogens)}. \]

N.m.r. δ (CDCl\textsubscript{3}) 1.10-1.26 (C 4 axial and C 10 angular methyls), 1.22 (d, J 7 Hz, C 15 methyls), 2.60-3.50 (m, C 7 and C 15 protons), 3.64 (s, CO\textsubscript{2}Me), 7.10 (s, W\textsubscript{1/2} 2 Hz, C 14 proton of 261), 7.16, 7.36 (2 doublets, J 9 Hz, C 11 and C 12 protons of 45), 7.62 (s, W\textsubscript{1/2} 2 Hz, C 11 proton of 261).

A solution of the mixture in acetone, when seeded with authentic C 14-nitro-ester (45) slowly deposited the compound (45) (1.7 g), as diamond-shaped plates, m.p. and m.m.p. 193-195°.

**Photolysis of Methyl 14-nitro-abieta-8,11,13-trien-18-oate (45)**

The nitro-ester (45) (0.5 g, 1.25 mmol) in methanol (250.0 ml) containing sodium hydroxide (60 mg) in water (0.5 ml) was photolysed in a nitrogen atmosphere using a medium pressure mercury Hanovia arc lamp (125 W). The photolysis was terminated after 5 hr, and the methanol was removed using a rotatory evaporator. The residue was partitioned between ether and water, and the ether extract was washed with 1% aqueous sodium hydroxide. The ether layer was washed with water, dried, and concentrated to afford a red gum (0.3 g). T.l.c. of this gum showed seven spots with considerable streaking. The neutral fraction
was discarded.

The alkali extract was reacidified with 2N hydrochloric acid, extracted with ether, and the ether extract was washed with water, dried, and concentrated to give a brown gum containing many compounds (t.l.c.). This fraction was also not investigated further.

**Methyl 14-Amino-abieta-8,11,13-trien-18-oate (262)**

A solution of stannous chloride (1.5 g) in hot concentrated hydrochloric acid (10.0 ml) was added dropwise to methyl 14-nitro-abieta-8,11,13-trien-18-oate (45) (0.5 g, 0.14 mmol) in refluxing glacial acetic acid (20.0 ml), and the mixture was boiled for $\frac{1}{4}$ hr. The bulk of the solvents were removed under reduced pressure to give a semi-crystalline gum. This gum was treated with sodium hydroxide (6 g) in water (10.0 ml), and the mixture was extracted with ether. The ether layer was washed with water, dried, and concentrated to give a gum which was chromatographed on deactivated alumina.

From the benzene-ether (9:1) eluates was obtained methyl 14-amino-abieta-8,11,13-trien-18-oate (262) (0.35 g, 78%) which crystallised from chloroform-light petroleum as flat triangles, m.p. 104-105°, $[\alpha]_D + 92^\circ$ (c 0.13).

**Found:**

C, 76.75; H, 9.6; N, 4.3

$C_{21}H_{31}NO_2$ requires: C, 76.55; H, 9.5; N, 4.25%.

$\nu_{\text{max}}$ (CHCl$_3$) 3480, 3400 (NH$_2$), 1725 (ester C=O), and 1625 cm$^{-1}$ (NH$_2$).
N.m.r. δ (CDCl₃) 1.20 (s, C 10 angular Me), 1.21 (d, J 7 Hz, C 15 methyls), 1.26 (s, C 4 axial Me), 2.50–3.10 (m, C 7 and C 15 protons), 3.58 (s, W₁/₂ 19 Hz, NH₂), 3.65 (s, CO₂Me), 6.75, 7.00 (2 doublets, J 8 Hz, C 11 and C 12 protons).

Stannous Chloride–Hydrogen Chloride Reduction of the Mixture of Methyl 12-nitro– and 14-nitro-abieta-8,11,13-trien-18-oate (261) and (45)

The mixed nitro-esters (261) and (45) (7.0 g, 19.5 mmol) in glacial acetic acid (250 ml) were heated to boiling and treated with stannous chloride (42 g) in hot concentrated hydrochloric acid (140.0 ml), and the mixture was boiled for 1/4 hr. The solvents were removed using a rotatory evaporator, and the residue was treated with sodium hydroxide (84 g) in water (140.0 ml). The mixture was extracted with ether, washed with water, dried, and concentrated to give a brown gum which was chromatographed on deactivated alumina.

From the benzene-ether (9:1) eluates was obtained a mixture of the amino-esters (262) and (263). Fractional crystallisation from ether afforded methyl 12-amino-abieta-8,11,13-trien-18-oate (263) [2.4 g, 76%, based on the 12-nitro compound (261)], m.p. 134–135° (lit.¹⁸⁸ 137–137.5).

ν_{max} (CHCl₃) 3460, 3380 (NH₂), 1725 (ester C=O), and 1625 cm⁻¹ (NH₂).

N.m.r. δ (CDCl₃) 1.20 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.26 (s, C 4 axial Me), 2.65–3.00 (m, C 7 and C 15 protons), 3.55 (s, W₁/₂ 30 Hz, NH₂, exchanged with D₂O),
3.65 (s, CO$_{2}$Me), 6.53 (s, $\frac{W_1}{2}$ 4 Hz, C 11 proton), 6.50 (s, $\frac{W_1}{2}$ 4 Hz, C 14 proton).

The mother liquors from the crystallization contained the 14-amino-ester (262), which could not be obtained pure.

Sandmeyer Bromination of Methyl 12-Amino-abieta-8,11,13-trien-18-oate (263)

The amine (263) (0.4 g, 1.2 mmol) in bromoform (5.0 ml), was added slowly to a stirred solution of i-pentyl nitrite (0.2 g, freshly distilled) in bromoform (10.0 ml) heated on the water bath. The mixture was heated and stirred on the water bath for 2 hr. The solvents were removed under reduced pressure to afford a dark crystalline mass, which was filtered through deactivated alumina using light petroleum-benzene (4:1) as the solvent. Concentration gave methyl 12-bromo-abieta-8,11,13-trien-18-oate (264) (0.44 g, 87%), which crystallised from chloroform-methanol as needles, m.p. 137-138° (lit. 188 140-141°).

$\nu_{max}$ (CHCl$_3$) 1725 cm$^{-1}$ (ester C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.17 (s, C 10 angular Me), 1.22 (d, J 7 Hz, C 15 methyls), 1.27 (C 4 axial Me), 2.65-3.00 (m, C 7 and C 15 protons), 3.66 (s, CO$_{2}$Me), 6.92 (s, $\frac{W_1}{2}$ 2 Hz, C 14 proton), 7.35 (s, $\frac{W_1}{2}$ 2 Hz, C 11 proton).
Attempted Sandmeyer Bromination of Methyl 14-Amino-abieta-8,11,13-trien-18-oate (262)

The amine (262) (0.1 g, 0.3 mmol) in bromoform (2.0 ml) and i-pentyl nitrite (50 mg) in bromoform (2.0 ml) were reacted as above. After an identical work-up procedure the product was chromatographed on deactivated alumina.

From the benzene-ether (9:1) eluates was obtained the starting amine (262) (80 mg) as a dark brown gum, which showed a t.l.c. spot identical with the authentic compound. The amine could not be obtained pure, even after repeated chromatography and attempts at crystallisation.

Nitration of Methyl 12-Acetylabieta-8,11,13-trien-18-oate (227)

Finely powdered methyl 12-acetylabieta-8,11,13-trien-13-oate (227) (10.0 g, 28.2 mmol) was added in portions to a stirred mixture of red fuming nitric acid (50.0 ml) and concentrated sulphuric acid (2.5 ml) at -10°. The mixture was allowed to warm to 0° over a period of ½ hr, and then poured in a thin stream into rapidly stirred ice-water. The suspension was extracted into ether, and the ether extract was washed with water, dried, and concentrated to afford a yellow gum which was chromatographed on deactivated alumina.

From the light petroleum-benzene (4:1) eluates was obtained methyl 12,14-dinitro-abieta-8,11,13-trien-18-oate (44) (1.2 g, 10%) which crystallised from ether as needles, m.p. 189-190° (lit. 188 189-189.5°).
\( v_{\text{max}} (\text{CHCl}_3) \) 1725 (ester C=O), and 1630 cm\(^{-1}\) (NO\(_2\)).

N.m.r. \( \delta (\text{CDCl}_3) \) 1.23, 1.25 (2 singlets, C 4 axial and C 10 angular methyls), 1.32 (d, J 7 Hz, C 15 methyls), 2.58-3.20 (m, C 7 and C 15 protons), 3.67 (s, CO\(_2\)Me), 7.55 (s, C 11 proton).

From the light petroleum-benzene (1:1) eluates was obtained methyl 12-acetyl-13-nitropodocarpa-8,11,13-trien-18-oate (266) (8.5 g, 84%) which crystallized from chloroform-light petroleum as needles, m.p. 105-106\(^{\circ}\), [\( \alpha \)]\(_D\) +86\(^{\circ}\) (c 0.34).

Found: C, 67.0; H, 7.1; N, 4.3

C\(_{20}\)H\(_{25}\)O\(_5\)N requires: C, 66.8; H, 7.0; N, 3.9%.

\( v_{\text{max}} (\text{CHCl}_3) \) 1725 (ester C=O), 1710 (aryl ketone C=O), and 1550, 1350 cm\(^{-1}\) (aromatic NO\(_2\)).

N.m.r. \( \delta (\text{CDCl}_3) \) 1.28 (s, C 4 axial and C 10 angular methyls), 2.48, 2.55 (2 singlets, C 12 CH\(_3\)CO), 2.90 (m, C 7 protons), 3.68 (s, CO\(_2\)Me), 7.32 (s, \( \omega_1 \) 2 Hz, C 11 proton), 7.72 (s, \( \omega_1 \) 2 Hz, C 14 proton).

**Methyl 12-Acetyl-13-aminopodocarpa-8,11,13-trien-18-oate (269)**

A solution of stannous chloride (48.0 g) in hot concentrated hydrochloric acid (206.0 ml) was added dropwise to a solution of methyl 12-acetyl-13-nitropodocarpa-8,11,13-trien-18-oate (266) (8.7 g, 24.2 mmol) in boiling glacial acetic acid (340.0 ml). The mixture was boiled for a further \( \frac{1}{4} \) hr, and then the solvents were removed using a
rotary evaporator. The residue was treated with sodium hydroxide (80.0 g) in ice-water (200.0 ml), and the mixture was extracted with ether. The ether phase was washed with water, dried, and concentrated to give a brown gum which was chromatographed on deactivated alumina.

From the benzene-ether (9:1) eluates was obtained methyl 12-acetyl-13-aminopodocarpa-8,11,13-trien-18-oate (269) (5.3 g, 68%) as a pale yellow, viscous gum which slowly deposited prisms, m.p. 94-96°, $[\alpha]_D + 57^\circ$ ($c$ 0.35).

Found: C, 72.9; H, 8.4; N, 4.1

$C_{20}H_{27}O_3N$ requires: C, 72.9; H, 8.3; N, 4.25%.

$\nu_{\text{max}}$ (CHCl$_3$) 3480, 3340 (NH$_2$), 1720 (ester C=O), 1640 (aryl ketone C=O), and 1620, 1580 cm$^{-1}$ (NH$_2$).

N.m.r. 6 (CDCl$_3$) 1.18 (s, C 10 angular Me), 1.28 (s, C 4 axial Me), 2.54 (s, CH$_3$CO), 2.80 (m, C 7 protons), 3.67 (s, CO$_2$Me), 5.98 (s, $W_2$ 16 Hz, NH$_2^-$, exchanged with D$_2$O), 6.17 (s, $W_2$ 2 Hz, C 14 Proton), 7.56 (s, $W_2$ 2 Hz, C 11 proton).

The amine (269) (0.3 g) in acetic anhydride (10.0 ml) and pyridine (2 drops) was heated on the water bath for 3 hr. The cooled mixture was poured into water, extracted with ether, and the ether extract was washed with water, dried, and concentrated to afford a gum. Percolation of the gum in benzene through silica gel gave methyl 12-acetyl-13-acetylamino podocarpa-8,11,13-trien-18-oate (270) (0.32 g, 95%) as a pale yellow gum, $[\alpha]_D + 30^\circ$ ($c$ 1.04).
Found: C, 71.0; H, 8.2; N, 3.7

C_{22}H_{29}O_{4}N requires: C, 71.1; H, 7.9; N, 3.8%.

$\nu_{\text{max}}$ (CHCl$_3$) 3500, 3260 (amide NH), 1725 (ester C=O), 1690 (aryl ketone C=O), and 1650 cm$^{-1}$ (amide C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.20 (s, C 10 angular Me), 1.28 (s, C 4 axial Me), 2.18 (s, NAc), 2.62 (s, CH$_3$CO), 2.95 (m, C 7 protons), 3.67 (s, CO$_2$Me), 7.31 (s, $W_1^2$ 2 Hz, C 14 proton), 7.78 (s, $W_2^1$ 2 Hz, C 11 proton), 8.43 (s, NHAc).

**Methyl 12-Acetyl-13-hydroxy-podocarpa-8,11,13-trien-18-oate (271)**

Methyl 12-acetyl-13-aminopodocarpa-8,11,13-trien-18-oate (269) (5.0 g, 15.2 mmol) was stirred with 10% hydrochloric acid (250 ml) at 0° while sodium nitrite (3.25 g) in water (60.0 ml) was added dropwise. The solution was stirred at 0° for a further 20 min, and then urea (4.35 g) was added in portions. After a further 10 min period, the solution was filtered from a small quantity of insoluble material, and the filtrate was poured into 15% aqueous sulphuric acid (1.05 l). The solution was stirred and heated on the water bath at 80° for 20 min, and then stood overnight. The crude phenol was filtered off and dissolved in ether. The ether solution was washed with water dried, and concentrated to afford methyl 12-acetyl-13-hydroxy-podocarpa-8,11,13-trien-18-oate (271) (4.2 g, 84%), which crystallised from chloroform-methanol as prisms, m.p. 108-109°, $[\alpha]_D + 180^\circ$ (c 0.21).
Found: C, 72.4; H, 8.2

C_{20}H_{26}O_{4} requires: C, 72.7; H, 7.9%

v_{\text{max}} (\text{CHCl}_3) 3520-2400 (\text{H-bonded OH}), 1725 (\text{ester C=O}),
1640 \text{ cm}^{-1} (\text{H-bonded aryl ketone C=O}).

N.m.r. \delta (\text{CDCl}_3) 1.18 (s, C 10 angular Me), 1.27 (s, C 4
axial Me), 2.58 (s, CH$_3$CO) 2.94 (m, C 7 protons), 3.68 (s,
CO$_2$Me), 6.64 (s, W$^2_2$ 2 Hz, C 14 proton), 7.59 (s, W$^2_2$ 2 Hz, C 11
proton), 11.90 (s, OH).

**Methyl 12-Acetyl-13-methoxy-podocarpa-8,11,13-trien-18-oate (272)**

Methyl 12-acetyl-13-hydroxy-podocarpa-8,11,13-trien-18-oate
(271) (4.2 g, 12.7 mmol) was dissolved in ethanol (45.0 ml), and to
the gently refluxing solution was added dimethyl sulphate (17.5 ml)
and sodium hydroxide (5.9 g) in water (12.0 ml) in five equal alternate
additions over a period of 20 min. After the final addition, sodium
hydroxide (1.5 g) in water (3.0 ml) was added, and the mixture was heated
under reflux for 3 hr. The mixture was cooled, poured onto ice-water.
and the precipitate was taken up with ether. The ether extract was
washed with water, dried, and concentrated to give a solid. This solid,
in benzene was filtered through a short column of silica gel. Concentration
of the eluates afforded methyl 12-acetyl-13-methoxy-podocarpa-8,11,13-
trien-18-oate (272) (3.6 g, 82%), which crystallized from methanol as
flakes, m.p. 140-141°, [\alpha]_D + 55° (c 0.28).

Found: C, 73.1; H, 8.4

C$_{21}$H$_{28}$O$_{4}$ requires: C, 73.2; H, 8.2%.
$v_{\text{max}}$ (CHCl$_3$) 1725 (ester C=O), and 1665 cm$^{-1}$ (aryl ketone C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.18 (s, C 10 angular Me), 1.28 (s, C 4 axial Me), 2.50 (s, CH$_3$CO), 2.92 (m, C 7 protons), 3.67 (s, CO$_2$Me), 3.87 (s, OMe), 6.61 (s, $\frac{W_1}{2}$ 2 Hz, C 14 proton), 7.70 (s, $\frac{W_1}{2}$ 2 Hz, C 11 proton).

**Methyl 12-Hydroxy-13-methoxy-podocarpa-8,11,13-trien-18-oate (274)**

Methyl 12-acetyl-13-methoxy-podocarpa-8,11,13-trien-18-oate (272)

(2.8 mg, 10.7 mmol), m-chloroperbenzoic acid (4.2 g), and toluene-p-sulphonic acid (10 mg) were refluxed in 1,2-dichloroethane (200.0 ml) for 3 hr. The reaction mixture was worked-up by the procedure previously described for peracid oxidations to give the crude acetate (273) (3.2 g) as a red gum.

$v_{\text{max}}$ (CHCl$_3$) 1760 (phenyl acetate C=O), and 1720 cm$^{-1}$ (ester C=O).

N.m.r. $\delta$ (CDCl$_3$) 1.17 (s, C 10 angular Me), 1.25 (s, C 4 axial Me), 2.25, 2.26 (2 singlets, OAc), 2.75 (m, C 7 and C 15 protons), 3.64 (s, CO$_2$Me), 3.77 (s, OMe), 6.45 (s, $\frac{W_1}{2}$ 2 Hz, C 14 proton), 6.88 (s, $\frac{W_1}{2}$ 2 Hz, C 11 proton).

The crude acetate (273) (3.2 g) in methanol (180.0 ml) was treated with sodium bicarbonate (6.5 g) in water (20.0 ml), and the mixture was refluxed gently for 1 hr, cooled, and poured into water. The suspension was extracted with ether. The organic layer was washed with water, dried, and concentrated to give a dark gum, which was filtered through silica gel using benzene-ether (9:1) as solvent. Concentration of the eluates gave a solid, which was recrystallized from chloroform-
light petroleum to give methyl 12-hydroxy-13-methoxy-podocarpa-8,11, 13-trien-18-oate (274) (1.8 g, 70%) as needles, m.p. 173-174°, [α]D + 87° (c 0.31).

Found: C, 71.4; H, 8.1

C₁₉H₂₆O₄ requires: C, 71.8; H, 8.2%.

νmax (CHCl₃) 3525 (OH), and 1720 cm⁻¹ (ester C=O).

N.m.r. δ (CDCl₃) 1.17 (s, C 10 angular Me), 1.25 (s, C 4 axial Me), 2.80 (m, C 7 protons), 3.65 (s, CO₂Me), 3.82 (s, OMe), 5.50 (s, OH, exchanged with D₂O), 6.50 (s, W₁ 2 Hz, C 14 proton), 6.82 (s, W₁ 2 Hz, C 11 proton).

Attempted De-oxygenation of Methyl 13-Methoxy-12-tosyloxy-podocarpa- 8,11,13-trien-18-oate (274) with Raney Nickel

Methyl 12-hydroxy-13-methoxy-podocarpa-8,11,13-trien-18-oate (274) (0.14 g, 0.44 mmol) and freshly crystallised toluene-p-sulphonyl chloride (0.15 g) in dry pyridine (5.0 ml) were heated over the water bath for ½ hr, and the red solution was then stood at 20° for 12 hr. The solution was poured into water, and the suspension was extracted with ether. The ether layer was washed with 2N hydrochloric acid, water, and brine. After drying, the ether solution was concentrated to afford the tosylate (275) (0.16 g) as a pale yellow oil.

νmax (CHCl₃) 1725 (ester C=O), 1375 (tosylate S=O), 1130, 1110 and 890 cm⁻¹ (tosylate).

N.m.r. δ (CDCl₃) 1.13 (s, C 10 angular Me), 1.23 (s, C 4 axial Me), 2.42 (s, aromatic Me), 2.77 (m, C 7 protons), 3.52 (s,
CO₂Me), 3.67 (s, OMe), 6.48 (s, W₂ 2 Hz, C 14 proton), 6.87 (s, W₂ 2 Hz C proton), 7.30, 7.72 (2 doublets, J 8 Hz, aromatic protons).

The crude oily tosylate (275) (0.16 g) in ethanol (10.0 ml) was treated with freshly prepared Raney nickel²33 (3 spatulas full), and the suspension was stirred at 20°C under hydrogen at atmospheric pressure for 1 hr. The catalyst was filtered off and washed with ethanol. The combined filtrate and washings were concentrated to afford a solid (50 mg) which was identified as the starting phenol, m.p. and m.m.p. 165-168°C.

Methyl 12-Carboxy-13-methoxy-podocarpa-8,11,13-trien-18-oate (279)

Methyl 12-acetyl-13-methoxy-podocarpa-8,11,13-trien-18-oate (272) (3.31 g, 9.6 mmol) in dry pyridine (33.0 ml) was treated with iodine (2.45 g) and the dark mixture was heated on the water bath for 2 hr, and then kept at 20°C for 10 hr. The excess of pyridine was removed under reduced pressure to give a dark crystalline residue. This was dissolved in ethanol (66.0 ml) and the solution was treated with sodium hydroxide (2.20 g) in water (6.0 ml), and the mixture was refluxed for 2 hr, cooled, and poured into water. The dark solution was extracted with ether, and the ether layer was discarded. The aqueous layer was decolourised with activated carbon by heating it on the water bath for a few minutes. The carbon was filtered off, and the residue was washed with water. The filtrate and washings were combined, acidified to litmus by the dropwise addition of concentrated hydrochloric acid, and
the precipitate was extracted with ether. The ether extract was washed with water, dried, and concentrated to give a solid. Recrystallisation from chloroform-methanol afforded methyl 12-carboxy-13-methoxy-podocarpa-8,11,13-trien-18-oate (279) (2.4 g, 78%) as prisms, m.p. 204-205°, \([\alpha]_D + 56^\circ (c 0.43)\).

Found: C, 69.2; H, 7.6

C_{20}H_{26}O_5 requires C, 69.3; H, 7.6%.

\(\nu_{max} (\text{CHCl}_3) \) 3600-2400 (H-bonded acid OH), 1725 (ester C=O), 1720 cm\(^{-1}\) (acid C=O).

N.m.r. \(\delta (\text{CDCl}_3) \) 1.18 (s, C 10 angular Me), 1.26 (s, C 4 axial Me), 2.93 (m, C 7 protons), 3.67 (s, CO\(_2\)Me), 4.00 (s, OMe), 6.70 (s, \(\frac{2}{2}\) 2 Hz, C 14 proton), 6.40-7.90 (CO\(_2\)H), 8.05 (s, \(\frac{2}{2}\) 2 Hz, C 11 proton).

**Methyl 13-Hydroxy-podocarpa-8,11,13-trien-18-oate (59)**

The carboxylic acid (279) (2.20 g, 6.4 mmol) in quinoline (25.0 ml) was heated in an oil bath to 235° and the solution was treated in portions with basic copper carbonate (0.15 g). The temperature was held at 230-240° for \(\frac{1}{2}\) hr. The dark mixture was cooled, poured into 10% aqueous hydrochloric acid, and extracted with ether. The ether extract was washed with 2N hydrochloric acid, water, and then brine. After drying, the ether solution was concentrated to afford a yellow gum which was treated with an ethereal solution of diazomethane at 20° for \(\frac{1}{2}\) hr. Concentration of this solution gave a solid, which was chromatographed on silica gel. Benzene, and benzene-ether (99:1) eluted methyl 13-hydroxy-podocarpa-8,11,13-trien-18-oate (59) (1.8 g, 98%),
which crystallised from methanol as prisms, m.p. 145-146° (lit. 147.5-148.5°).

\[ \nu_{\text{max}} \text{(CHCl}_3\text{)} \] 3600, 3300 (OH), and 1720 cm\(^{-1}\) (ester C=O).

N.m.r. \( \delta \text{(CDCl}_3\text{)} \) 1.15 (s, C 10 angular Me), 1.25 (s, C 4 axial Me), 2.75 (m, C 7 protons), 3.65 (s, CO\(_2\)Me), 6.48 (d, J 2 Hz, C 14 proton), 6.60 (d of d, J\(_{11,12}\) 8 Hz, J\(_{12,14}\) 2 Hz, C 12 proton), 7.10 (d, J 8 Hz, C 11 proton), 7.56 (s, \( \delta \) 12 Hz, OH).

**Methyl 13-Methoxy-podocarpa-8,11,13-trien-18-oate (276)**

The phenol (59) (1.9 g, 6.6 mmol) was added to a solution of potassium (0.85 g) in dry t-butanol (70.0 ml) at 20°, and the solution was treated with methyl iodide\(^{224}\) (10.0 ml). The mixture was stirred at 20° in a nitrogen atmosphere for 2 hr. Water (25.0 ml) was added, and the mixture was acidified to litmus by the dropwise addition of concentrated hydrochloric acid. The bulk of the t-butanol was removed at 50° under reduced pressure. The residue was extracted with ether, and the organic layer was washed with water, dried, and concentrated to give a gum which was chromatographed on silica gel.

Light petroleum-benzene (1:1) gave methyl 13-methoxy-podocarpa-8,11,13-trien-18-oate (276) (1.5 g, 80%), which crystallised from ether-methanol as large prisms, m.p. 76-78° (lit.\(^{85}\) 79.5-80.5°).

\[ \nu_{\text{max}} \text{(CHCl}_3\text{)} \] 1720 (ester C=O), and 1185, 1030 cm\(^{-1}\) (aryl methyl ether).
N.m.r. δ (CDCl₃) 1.18 (s, C 10 angular Me), 1.25 (s, C 4 axial Me), 2.83 (m, C 7 protons), 3.65 (s, CO₂Me), 3.74 (s, OMe), 6.55 (d, J 2 Hz, C 14 proton), 6.67 (d of d, J₁₁,₁₂ 9 Hz, J₁₂,₁₄ 2 Hz, C 12 proton), 7.15 (d, J 9 Hz, C 11 proton).

Lithium in Liquid Ammonia Reduction of Methyl 13-Methoxy-podocarpa-8,11,13-trien-18-oate (276)

To a solution of lithium (4.0 g) in liquid ammonia (ca. 400 ml) was added a solution of methyl 13-methoxy-podocarpa-8,11,13-trien-18-oate (276) (2.0 g, 6.6 mmol) in absolute ether (150 ml). The blue solution was stirred for 20 min, and then absolute ethanol (ca. 150 ml) was cautiously added over a period of 45 min. The ammonia was allowed to evaporate, and the residue was partitioned between ether and water. Acidification of the aqueous extract with concentrated hydrochloric acid gave only a minute precipitate of acidic products, which was discarded. The ether extract was washed with water, dried, and concentrated to afford a colourless gum, which showed one major and one minor spot, both at low Rₚ values, on t.l.c. The gum, in ethanol (80.0 ml) was treated with a solution of concentrated hydrochloric acid (28.0 ml) and water (48.0 ml), and the mixture was stirred and heated at 65-67° in a nitrogen atmosphere for 35 min. The mixture was diluted with water and extracted with ether. The ether layer was washed with water, dried, and concentrated to give a pale yellow gum which was chromatographed on deactivated alumina.

Benzene eluted podocarp-8-en-18-ol (282) (0.1 g, 7%) as a colourless gum, [α]D + 59° (c 0.51), which failed to analyse correctly.
\( \nu_{\text{max}} (\text{CHCl}_3) 3620 \text{ cm}^{-1} \) (OH).

N.m.r. \( \delta (\text{CDCl}_3) 0.75 \) (s, C 4 axial Me), 0.97 (s, C 10 angular Me), 2.94 (OH, exchanged with D\(_2\)O), 3.02, 3.35 (2 doublets, J 11 Hz, C 18 protons).

Ether eluted podocarp-8(14)-en-18-ol-13-one (281) (1.3 g, 74%), which was recrystallised from acetone as prisms, m.p. 115-116\(^\circ\), \([\alpha]_D + 45^\circ\) (\(\leq 0.36\)).

Found: C, 77.55; H, 9.9

\( C_{17}H_{26}O \) requires: C, 77.8; H, 10.0%.

\( \nu_{\text{max}} (\text{CHCl}_3) 3620, 3420, \) (OH), 1665 (\(\alpha,\beta\)-unsaturated ketone C=O), and 1620 \text{ cm}^{-1} (C=C).

N.m.r. \( \delta (\text{CDCl}_3) 0.82, 0.83 \) (2 singlets, C 4 axial and C 10 angular methyls), 2.46 (OH, exchanged with D\(_2\)O), 3.10, 3.42 (2 doublets, J 11 Hz, C 18 protons), 5.90 (s, \( \frac{3}{2} \) 4 Hz, C 14 proton).

R.d. (\( \leq 0.36 \)) \([\phi]_{589} + 118^\circ, [\phi]_{460} + 155^\circ, [\phi]_{400} 0^\circ,\)

\([\phi]_{350} - 2296^\circ, [\phi]_{330} 0^\circ, [\phi]_{320} + 3540^\circ, [\phi]_{300} + 9440^\circ,\)

\([\phi]_{280} + 11,820^\circ.\)


The \(\alpha,\beta\)-unsaturated ketone (281) (0.55 g, 2.10 mmol) was dissolved in a mixture of dry methanol (5.5 ml) and dioxane (2.5 ml) and to the solution was added pyrrolidine (2.0 ml). The mixture was swirled, stoppered, and kept at 20\(^\circ\) for 3 hr. The bright yellow solution was
poured into water, and the gummy suspension was extracted with ether. The ether solution was washed with water, dried over anhydrous sodium carbonate, and concentrated to give the dienamine (285) (0.57 g) as an unstable, yellow gum.

\[ \nu_{\text{max}} (\text{CHCl}_3) ~3620 \,(\text{OH}), \,1630 \,(C=C), \,1600 \,(\text{enamine}) \text{ and } 1035 \,\text{cm}^{-1} \, (\text{C-O}). \]

N.m.r. \( \delta (\text{CDCl}_3) \) 0.93, 0.95 (2 singlets, C 4 axial and C 10 angular methyls), 3.00-3.60 (m, pyrrolidinyl \( \alpha \) protons and C 18 protons), 3.70 (OH), 4.88 (s, \( W_1^2 \) 3 Hz, C 14 proton), 5.30 (s, \( W_1^2 \) 12 Hz, C 7 proton).

**Attempted Annellation of 13-N-pyrrolidinylpodocarp-7,13-dien-18-ol (285) with Bromoacetone**

The crude dienamine (285) (0.57 g) in dry toluene (55.0 ml) was heated and stirred under reflux in an atmosphere of nitrogen while bromoacetone \( ^{234} \) (0.3 ml) in dry toluene (50.0 ml) was added dropwise. The mixture was stirred and heated under reflux for a further 2 hr. To the suspension of the resulting iminium bromide was added water (50.0 ml) and the mixture was stirred and refluxed for 3 hr. The mixture was cooled and the toluene layer was separated, washed with water, dried, and concentrated to give an orange gum. The gum, in methanol (20.0 ml) was heated under reflux in a nitrogen atmosphere with sodium hydroxide (0.2 g) and water (2.0 ml) for 3 hr. The cooled mixture was poured into water, acidified to litmus by the dropwise addition of concentrated hydrochloric acid, and extracted with ether. The ether layer was washed with water, dried, and concentrated to give a dark brown gum.
which was chromatographed on deactivated alumina.

The light petroleum-benzene (1:1) eluates afforded 4α-
hydroxymethyl-4β,16-dimethyl-18-nor-17-oxa-androsta-7,13-diene (286)
(0.1 g, 18%) as a pale yellow gum, identified from its spectroscopic
properties.

\[ \nu_{\text{max}} (\text{CICH}_3) \, 3620, \, 3400 \, (\text{OH}), \, 1610, \, 1490 \, (\text{aromatic}), \, \text{and} \]
\[ 1035 \, \text{cm}^{-1} \, (\text{furan C-O}). \]

N.m.r. \[ \delta (\text{CDCl}_3) \, 0.90 \, (s, \, C \, 10 \, \text{angular and C 4 axial methyls}), \]
1.86 (OH, exchanged with D_2O), 2.25 (s, C 16 Me), 3.13, 3.40
(2 doublets, J 11 Hz, C 4 methylene), 5.70 (s, W_2 \, 11 Hz, C 7
proton), 6.02 (s, W_2 \, 3 Hz, C 15 proton).

From the benzene, benzene-ether (9:1) eluates was obtained a
brown gum (0.18 g) which showed \[ \nu_{\text{max}} \, 3620 \, (\text{OH}) \, \text{and} \, 1660 \, \text{cm}^{-1} \, (\alpha, \beta \]
unsaturated ketone C=O). The gum was acetylated (acetic anhydride-
pyridine, 20°C) and chromatographed on deactivated alumina, but a
cleaner product could not be obtained.
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