A Thesis

submitted to

The University of Glasgow

in fulfilment of the
requirements for the

Degree of Doctor of Philosophy

by

George Graham Allan.

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The author wishes to here record his sincere appreciation and gratitude for the guidance, material and spiritual, extended unfailingly to him by Professor F. S. Spring, F.R.S.

He also wishes to acknowledge his indebtedness to Dr. R. Stevenson for advice and helpful discussion and to the Department of Scientific and Industrial Research for a Maintenance Award.

The Oleanane and Ursane Triterpenoids.

Contents.

General Summary.

The work described in this thesis is conveniently considered in three independent sections.

Section (1).

The constitution of iso-β-amyradienonyl acetate has been critically examined by reductive methods and confirmed, and it is now systematically named 12-oxotaraxera-9(11):14-dien-3β-yl acetate as a result of its relationship to the naturally occurring taraxerol. Mechanisms for the conversion of several taraxerane derivatives to oleanane derivatives are proposed.

Catalytic hydrogenation of iso-β-amyradienonyl acetate proceeds via a new trienyl acetate, neo-β-amyratrienyl acetate, to yield an isomer of β-amyrin acetate, neo-β-amyrin acetate. These compounds belong to a series which have a new type of triterpenoid carbon skeleton formed as a result of multi-methyl group migration. Possible structures for compounds in this series and reaction mechanisms for their formation are discussed.

Section (2).

A general investigation of the chemistry of 18α-oleanane derivatives and a comparison with the oleanane and ursane analogues under the subsections,

(A). Oxidation of 11-oxo-12-en-3β-yl acetates.

(B). Dehydrations of 11β-hydroxy-12-en-3β-yl acetates.

(C). Oxidation of 12-en-3β-yl acetates.

(D). Bromination of 12-oxo-an-3β-yl acetates.

(E). Acid rearrangements of -9(11):12-dien-3β-yl acetates.

(F). Ultra-violet absorption spectra.

(G). Reactions of 12-oxo-9(11)-en-3β-yl acetates.

shows that rings D and E in α-amyrin are cis-β-fused.

Section (3).

The structures of the well known dehydration products of α-amyrin and related alcohols, d-α-amyradiene, l-α-amyradie α-amyradienone-III, d-α-amyratriene, dichloro-α-amyradiene and l-α-amyratriene, have been examined and elucidated.

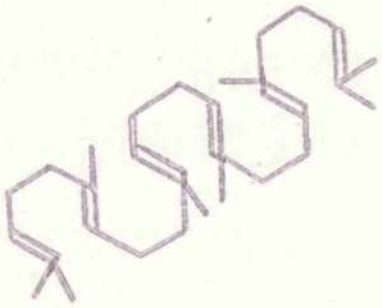
Reduction of α-amyradienone-I yields d-α-amyradiene which has been converted to l-α-amyradiene, also obtained from α-amyradienone-III. Reduction and dehydration of α-amyradienone-I gives d-α-amyratriene and demonstrates the constitution of dichloro-α-amyradiene. α-Amyradienone-III has been prepared stepwise from α-amyradienone-I via α-amyradienone-II, and has been converted to l-α-amyratriene.

Some analogous reactions in the oleanane series have been investigated.

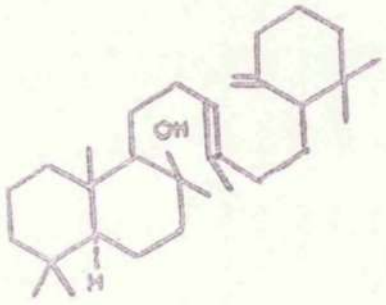
General Introduction.

The triterpenoids are widely distributed in nature, largely in the plant kingdom where they occur in saps and resins, either in the free state, or as esters or saponins. Relatively few occur in the animal kingdom. Comprehensive reviews of the occurrence, structures and inter-relationships of the triterpenoids are available (Barton, Progress in Organic Chemistry, Vol.II. ; Barton, Chemistry of Carbon Compounds, Vol.IIB. ; Elsevier Encyclopaedia, Vols. 14 and 14S.)

Apart from squalene (I), ambrein (II) and onocerin (III) (Barton and Overton, Chem. and Ind., 1955,654), which comprise the 'Squalene Group', the triterpenoids which have been the most extensively investigated are either tetra- or penta-cyclic



(I)



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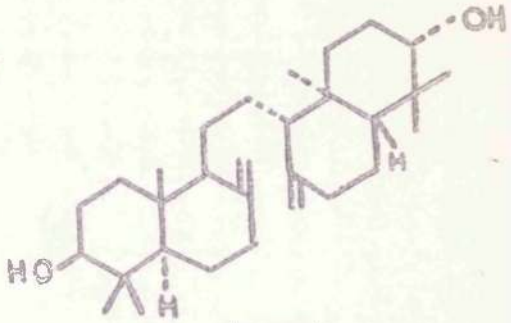
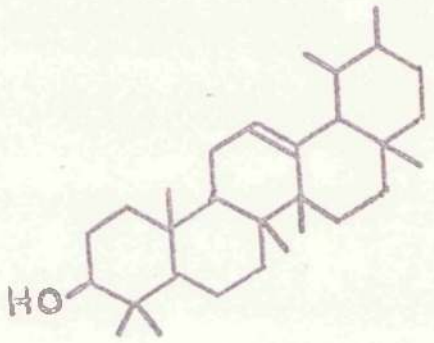


(III)

The pentacyclic triterpenoids may be conveniently sub-classified into three principal groups: the α-Amyrin (Ursane) Group, the β-Amyrin (Oleanane) Group and the Lupeol Group. (The cyclopropanoid pentacyclic compounds, cycloartenol and cyclo-laudenol are classified with the tetracyclic triterpenoid group). Since the work described in this thesis was concerned only with the α-Amyrin and β-Amyrin Groups, and excellent reviews of the chemistry of these groups are available (Barton, loc.cit.), the members of these groups are only mentioned briefly, and references are given only to those triterpenoids

whose chemistry has recently been described.

The α-Amyrin Group of triterpenoids are derivatives of the unsaturated alcohol, α-amyrin, for which the structure (IV), proposed by Meisels, Jeger and Ruzicka (Helv.Chim.Acta, 1949,32, 1075), was generally accepted (cf. Tschesche and Fugmann, Chem. Ber.,195,84,810) when this research was initiated.



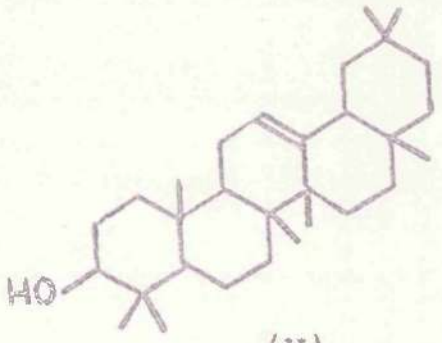
(IV)

The other members of this group are, brein, uvaol, ursolic acid, β-boswellic acid, asiatic acid and quinovic acid. (The cyclopropanoid hexacyclic alcohol, phyllanthol, is also considered to be a member of this group). These triterpenoids have been converted to known ursane derivatives, thus showing identity of location of the ethylenic linkage and stereochemical similarity in all these compounds. Accounts of these interconversions have been described in reviews (Barton, loc.cit.). More recently, phyllanthol has been synthesized from quinovic acid (Zürcher, Jeger and Ruzicka, Helv.Chim.Acta, 1954,2145) and from α-amyrin (Beaton, Easton, Macarthur, Spring and Stevenson, J.,1955, in press).

The β-Amyrin Group of triterpenoids are derivatives of the unsaturated alcohol, β-amyrin (V). Other members of the group are erythrodiol, maniladiol, genin A, α-boswellic acid, quillaic acid, oleanolic acid, hederagenin, sumaresinolic acid, δ-amyrin,

echinocystic acid, siaresinolic acid, gypsogenin, glycyrrhetic acid, germanicol, morolic acid and the soy sapogenols A, B, and C. Interconversions of members of this group have been summarized in reviews (Barton, loc.cit.).

Recently, triterpenoids have been isolated from cacti sources. Three of these, gummisogenin, longispinogenin and machaeric acid have been related to β-amyrin derivatives (Djerassi, Geller and Lemin, Chem. and Ind., 1954,161; Djerassi and Lipmann, ibid.,p.960).



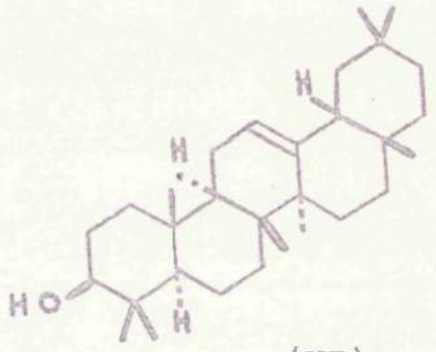
(V)

Other β-Amyrin Group members of recently established structure, which are not described in reviews are rehmannic acid and icterogenin (Barton and de Mayo, J., 1954,887;900), and lantadene-B (Barton, de Mayo, Warnhoff, Jeger and Perold, J., 1954, 3689) while terminolic acid (King, King and Hoss, J., 1955, 1333), of yet undefined structure, appears also to belong to this group.

Taraxerol, formerly considered to be an oleanane triterpenoid (Brooks, Chem. and Ind., 1953,1178) becomes a member of a group of triterpenoids with displaced methyl groups, which when treated with acid under suitable conditions afford a β-amyrin derivative by methyl group migration (Beaton, Spring,

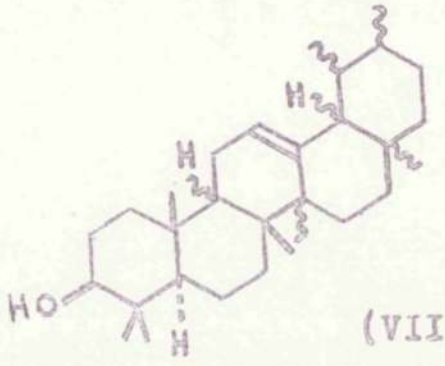
Stevenson and Stewart, Chem. and Ind., 1954,1454). Friedelin and Cerin have also been related to oleanane triterpenoids by acid treatment involving methyl group migration (Brownlie, Spring, Stevenson and Strachan, ibid., 1955,686).

When this work was commenced in September 1952, the structure proposed by Haworth (Ann. Reports, 1937,34,32), for β-amyrin had been confirmed and the stereochemistry elucidated as (VI)(Barton, Tilden Lecture, J., 1953,1027)

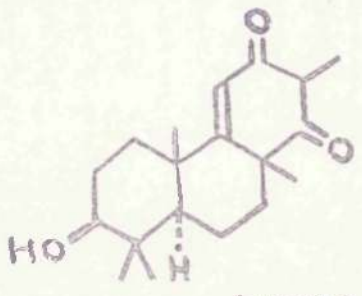


(VI)

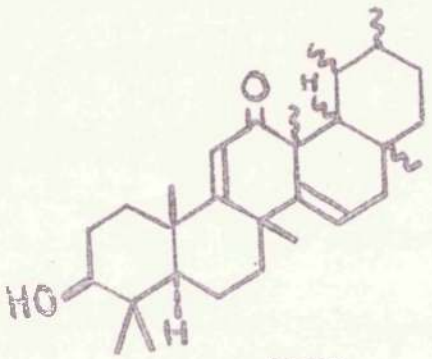
The situation with regard to α-amyrin was not so satisfactory and the stereochemistry had not been completely elucidated. The most complete stereochemical representation (VII) for α-amyrin was that of Meisels et al. (loc.cit.) who showed that the stereochemistry at positions C_3, C_5, C_8 and C_{10} was identical with that at the corresponding centres in β-amyrin (VI) since the same tricyclic pyrolysis fragment (VIII) had been obtained from both triterpenoids via iso-α-amyradienonol (IX) and iso-β-amyradienonol (X) respectively.



(VII)



(VIII)



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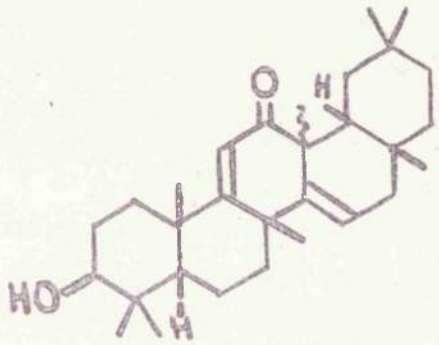


(X)

Meisels et al. (Helv. Chim. Acta, 1950, 33, 700) further suggested that the stereochemistry of C_9 and C_{14} in α- and β-amyrin was identical, to explain the similar formation of (IX) and (X).

The structure (VII), accepted for α-amyrin, does not give a satisfying explanation for the inert character of the double bond, or for the heavily hindered nature of carbonyl groups situated at position-12 in α-amyrin derivatives, when compared with the corresponding β-amyrin compounds.

The general terms of reference of the author's problem were therefore, to investigate certain aspects of these triterpenoids, with a view to resolving the more outstanding differences between. This investigation is described in the following pages in three sections:

Section (1). An investigation of the structure of iso-β-amyradienonol (X).

Section (2). A comparison of oleanane, 18α-oleanane and ursane derivatives.

Section (3). A structure elucidation of dehydration products of α-amyrin and its derivatives, and a comparison with some oleanane analogues.

Section (1).

Summary.

The structure of iso-β-amyradienonyl acetate has been critically examined and its validity tested by reduction methods. Wolff-Kishner reduction yields two isomeric non-conjugated dienyl acetates, isomerized by mineral acid to normal oleanane derivatives. Mechanisms for these isomerizations and others in oleanane chemistry are suggested.

It is concluded that iso-β-amyradienonyl acetate has a different carbon skeleton from that of oleanane, and its stereochemistry is defined.

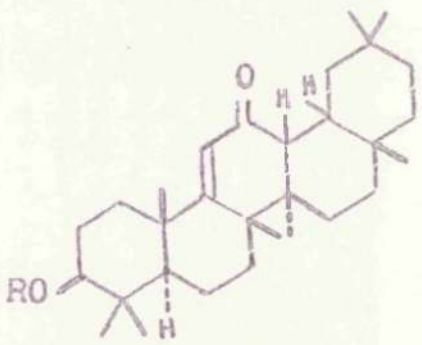
Lithium aluminium hydride reduction of iso-β-amyradienonyl acetate, followed by acid rearrangement, yields a new trienyl acetate; reduction affords an isomer of β-amyrin acetate and oxidation yields a trienonyl acetate.

Possible structures for these compounds, and reaction mechanisms for their formation, are discussed.

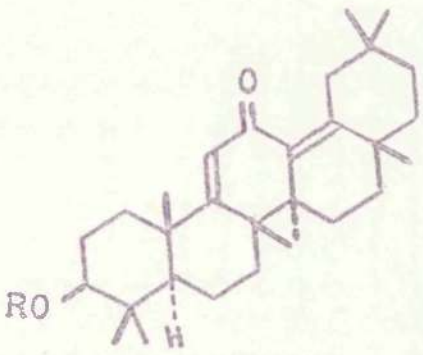
In all formulae in Section (1), R = Ac unless otherwise stated.

Iso-β-amyradienonyl acetate is obtained by the oxidation of 12-oxo-olean-9(11)-en-3β-yl acetate (I) with either bromine (Green, Mower, Picard and Spring, J., 1944,527), or selenium dioxide (Jeger and Ruzicka, Helv.Chim.Acta, 1945,28,209), and it contains an isolated ethylenic linkage in addition to the αβ-unsaturated ketone chromophore. Iso-β-amyradienonyl acetate and its ursane analogue, iso-α-amyradienonyl acetate, are important since they are key degradation intermediates on which the structures of α- and β-amyrin are based. Any dubiety as to the validity of their structures reflects on those of the parent triterpenoids, and a reinvestigation of iso-β-amyradienonyl acetate by reductive methods was therefore undertaken.

Green et al. (loc.cit.) suggested structure (II) for iso-β-amyradienonyl acetate, whereas Jeger and Ruzicka proposed the structure (III), in which it is represented as being formed from (I) by the migration of the angular methyl group from C_{14} to C_{13} with consequent introduction of a 14:15-double bond. Structure (II) can now be discarded since (II) has been prepared from β-amyrin by an unambiguous route (Beaton, Johnston, McKean and Spring, J., 1953,3660), and differs from iso-β-amyradienonyl acetate.



(I)



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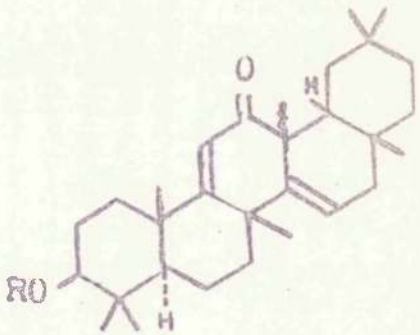
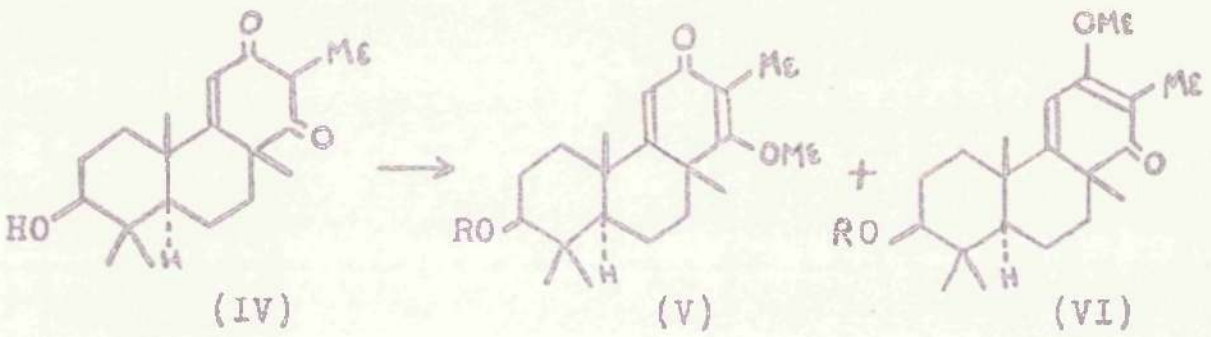
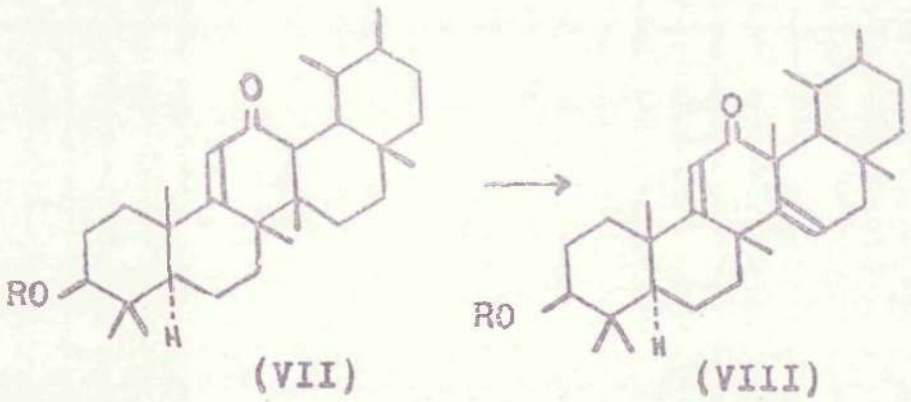


(III)

Meisels, Jeger and Ruzicka (Helv.Chim.Acta, 1950,33,700) have degraded iso-β-amyradienonyl acetate to a hydroxydiketone (IV), characterized by acetylation and methylation, which gave two isomeric compounds formulated as (V) and (VI). These were identical with two compounds obtained by the same route, from the corresponding ursane derivative, 12-oxours-9(11)-en-3β-yl acetate (VII), via iso-α-amyradienonyl acetate, formulated as (VIII)(Meisels et al., loc.cit.)





This conversion of the iso-α- and the iso-β-amyradienonyl acetate into two common degradation products which apparently include rings A to C of the triterpenoids was of considerable importance since it established identity in rings A, B and C in (I) and (VII).

Doubts were expressed as to the validity of formulae (III) and (VIII) since Budziarek, Johnston, Manson and Spring (J., 1951,3019) showed that Clemmensen reduction of iso-β-amyradienonyl acetate yielded oleana-11:13(18)-dien-3β-yl acetate (X) which contains the same carbon skeleton as β-amyrin, and McLean

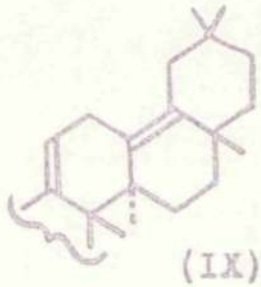
Ruff and Spring (J., 1951,1093) have emphasized the fact that catalytic hydrogenation of iso-α-amyradienonyl acetate gave 12-oxours-9(11)-en-3β-yl acetate (VII)(Ruzicka, Rüegg, Volli and Jeger, Helv.Chim.Acta, 1947,30,140) a normal ursane derivative. Both these reactions would require the remigration of the C_{13}-methyl group to C_{14} in (III) and (VIII).

Budziarek et al. (loc.cit.) demonstrated that whilst 12-oxo-olean-9(11)-en-3β-yl acetate (I) yielded enol esters, iso-β-amyradienonyl acetate (III) under drastic conditions, did not. These observations support the view that (III) carries a methyl substituent at C_{13}. Since the strong acid conditions involved in the Clemmensen reduction may cause skeletal rearrangement, attention was turned to reduction of iso-β-amyradienonyl acetate by the Wolff-Kishner method, in the expectation of obtaining the corresponding dienyl acetate by conversion of the carbonyl group to a methylene group under basic conditions.

Johnston (Ph.D. Thesis, Glasgow, 1953) had by this method obtained two homogeneous dienyl acetates of undetermined constitution, which were re-examined. The major product, $C_{32}H_{50}O_2$, m.p. 231°, obtained in 50% yield, showed an apparent absorption maximum in the 2000-2250 Å region, and on treatment with hydrochloric acid in acetic acid gave oleana-9(11):12-dien-3β-yl acetate (XI), in good yield. The acetate, m.p. 231°, is therefore a non-conjugated dienyl acetate. The three possible non-conjugated oleanadienyl acetates, in which the double bonds are in the C_9-C_{19} system, are oleana-9(11):18- (XII), -9(11):13(18)- (IX) and -11:18-dien-3β-yl acetate (XIII).

The acetate, m.p. 231°, differs from (IX) and (XII), each of which has been prepared from β-amyrin (Beaton et al., loc. cit.) and each of which yields oleana-11:13(18)-dien-3β-yl

acetate (X) when treated with mineral acid. Furthermore, the conversion of the acetate, m.p. 231°, into oleana-9(11):12-dien-3β-yl acetate (XI) shows that it is not the unknown oleana-11:18-dien-3β-yl acetate (XIII), since in analogy with oleana-9(11):18-dien-3β-yl acetate (XII), oleana-11:18-dien-3β-yl acetate would be expected to yield the stable oleana-11:13(18)-dien-3β-yl acetate (X) on treatment with mineral acid.



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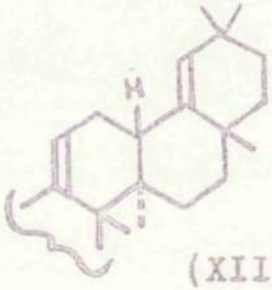
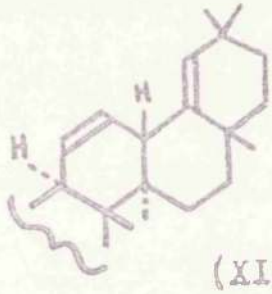
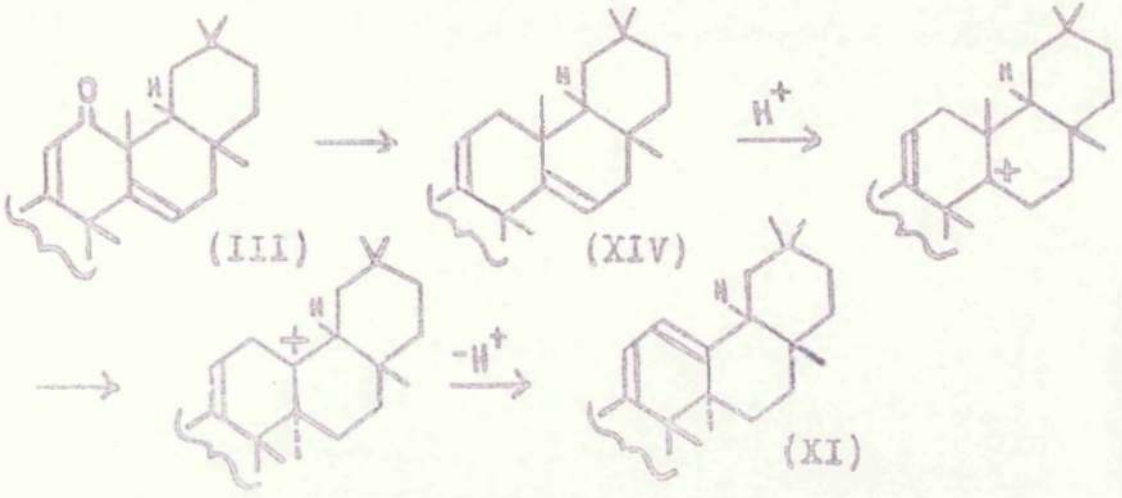


(XII)



(XIII)

These considerations support the view that the acetate, m.p. 231°, has a different carbon skeleton from that of β-amyrin, i.e., that the formation of iso-β-amyradienonyl acetate from 12-oxo-olean-9(11)-en-3β-yl acetate (I) must have involved a molecular rearrangement. The structure (III), proposed for iso-β-amyradienonyl acetate by Jeger and Ruzicka, affords a satisfactory explanation for the formation and properties of the dienyl acetate, m.p. 231°. The mechanism (III) ⟶ (XIV) ⟶ (XI) for the isomerization of the acetate, m.p. 231°, which is formulated as (XIV), is proposed.



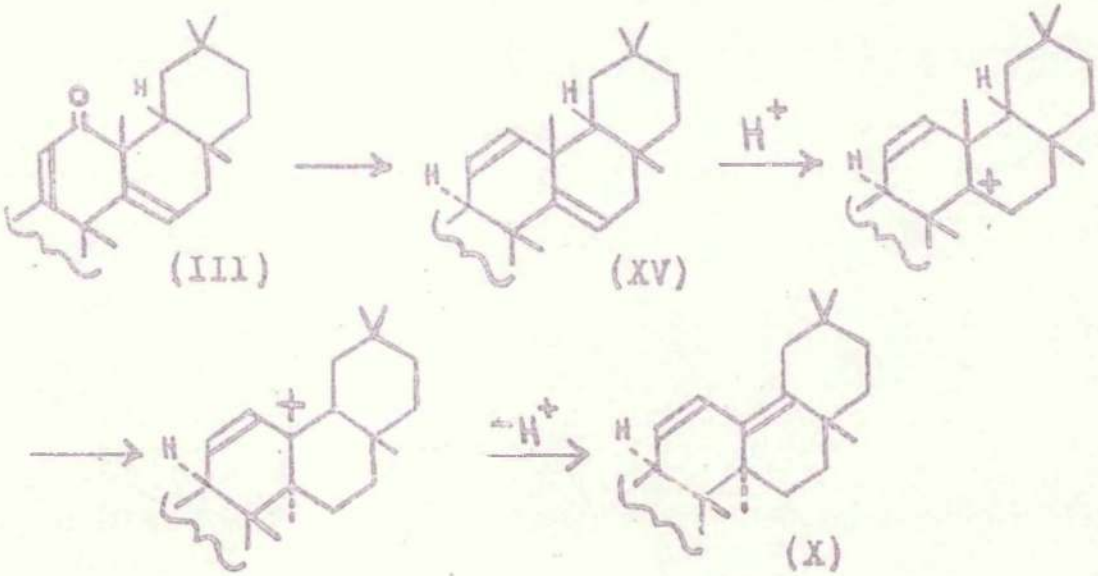
(III)

(XIV)

(XI)

The retention of the less stable 18β configuration in preference to the more stable 18α configuration provides a proof that C_{18} is not involved in the formation of iso-β-amyradienonyl acetate (III) from 12-oxo-olean-9(11)-en-3β-yl acetate (I).

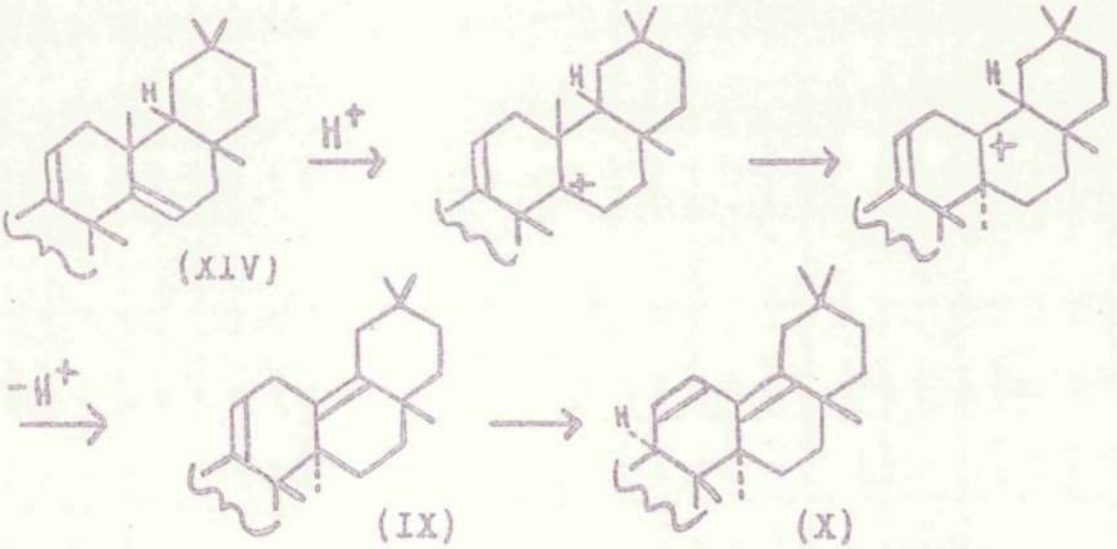
The minor reaction product, m.p. 203°, from the Wolff-Kishner reduction of iso-β-amyradienonyl acetate is also a non conjugated dienyl acetate, $C_{32}H_{50}O_2$, since it shows ethylenic absorption in the region 2000-2250 Å, and on treatment with hydrochloric acid in acetic acid affords olean-11:13(18)-dien 3β-yl acetate (X). The acetate, m.p. 203°, differs from olean 9(11):13(18)- (IX) and -9(11):18-dien-3β-yl acetate (XII), is formulated as (XV) in agreement with its properties and metho of formation, and a mechanism for its conversion into (X) is proposed.



The formation of (XIV) from (III) is by simple reduction of the carbonyl group to a methylene group, while the genesis of (XV) from (III) involves reduction of the carbonyl group wi double bond migration; similar double bond movements during Wolff-Kishner reductions are well known (Lardelli and Jeger,

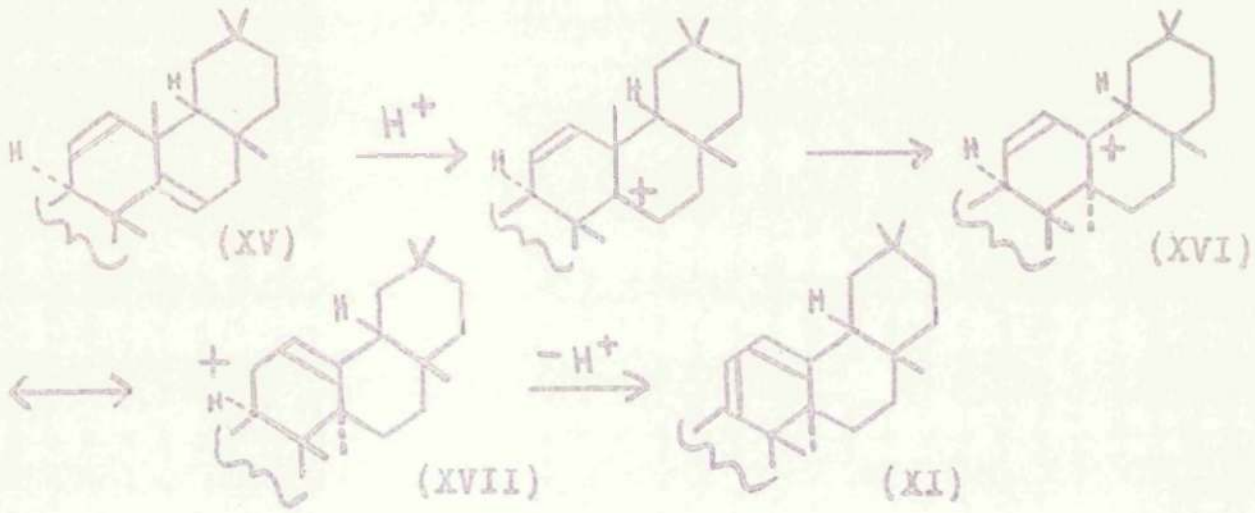
Helv.Chim.Acta,1949,32,1817; Fischer, Lardelli and Jeger, ibi 1950,33,1335).

The possibility that the acetate, m.p. 231°, (XIV), had the structure (XV), and the acetate, m.p. 203°, (XV), had the structure (XIV) has been considered, since an alternative mechanism for the acid rearrangement of (XIV), sketched in (XIV) → (IX) → (X) leads to oleana-11:13(18)-dien-3β-yl aceta (X); the last stage in this sequence has been described (Beat et al., loc.cit).

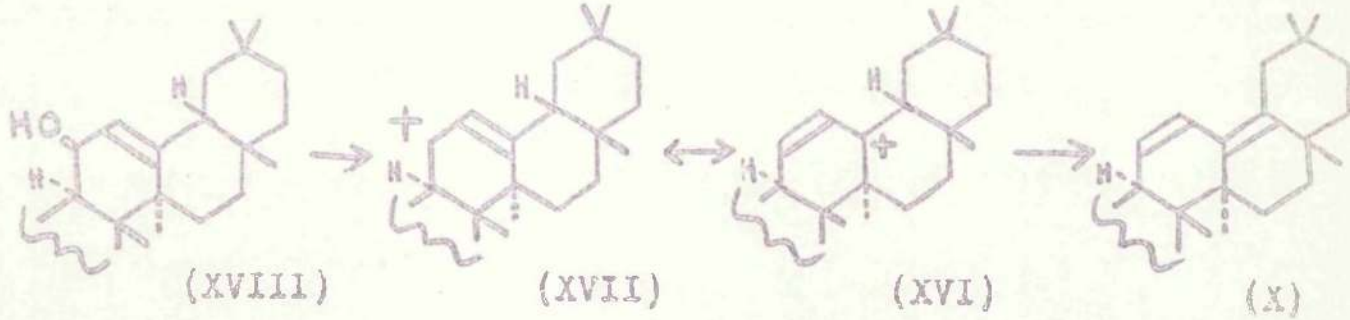


This possibility was rejected, however, by showing the reaction mechanism for the acid rearrangement, using the consequent formulation of the other acetate, to be demonstrab incorrect, i.e. acid rearrangement of (XV) would then require to furnish oleana-9(11):12-dien-3β-yl acetate. For (XV) to do this it would require to rearrange by the mechanism (XV) → (XV → (XVII) → (XI). This mechanism (sketched overleaf) contains a stage which is incorrect, as the following shows; reduction of 11-oxo-olean-12-en-3β-yl acetate with lithium aluminium hydride, followed by acetylation, yields 11β-hydroxyolean-12-e -3β-yl acetate (XVIII). The β-(axial)-configuration is ascribe

to the 11-hydroxyl group because it is not acylatable, and because on treatment with sodium acetate-acetic anhydride the diol monoacetate (XVIII) is readily dehydrated (trans-diaxial elimination) to oleana-9(11):12-dien-3β-yl acetate (XI).



Mild treatment of (XVIII) with mineral acid yields oleana 11:13(18)-dien-3β-yl acetate (X) and not oleana-9(11):12-dien-3β-yl acetate (XI).



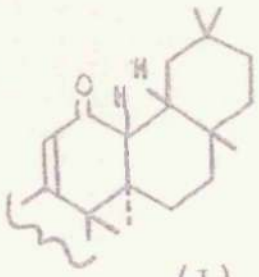
This demonstrates that the carbonium ion (XVII) stabilizes itself by loss of a proton yielding (X) and not (XI) as suggested in the mechanism (XV) → (XVI) → (XVII) → (XI). The acetate, m.p. 203°, therefore rearranges to (X) and is correctly formulated as (XV) whilst the acetate, m.p. 231°, is confirmed as (XIV).

A consideration of ultra-violet spectra in the region 2000-2250 Å did not allow of differentiation between formulat (XIV) and (XV) for the two non-conjugated dienyl acetates. Since (XIV) contains two trisubstituted ethylene linkages , whereas (XV) has one di- and one tri-substituted ethylene bon it was expected that (XIV) would show more intense absorption in the ethylenic region. The differences were in fact trivial and inconclusive. However, molecular rotation differences further support the choice of (XIV) for the acetate, m.p. 231 thus, the conversion of 12-oxo-olean-9(11)-en-3β-yl acetate (into iso-β-amyradienonyl acetate (III) is accompanied by a change in $[M]_D$ of approximately -480°, and the comparable change from olean-9(11)-en-3β-yl acetate to the acetate, m.p. 231°, is accompanied by a $[M]_D$ change of -410°. The corresponding $[M]_D$ value for the change, olean-9(11)-en-3β-yl aceta to the acetate, m.p. 203°, is -810°.

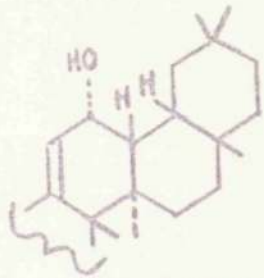
The behaviour of the two non-conjugated dienyl acetates with mineral acid raised the question of the mechanism of the conversion of iso-β-amyradienonyl acetate into oleana-11:13(18 dien-3β-yl acetate by Clemmensen reduction. It is known that such reduction of 12-oxo-olean-9(11)-en-3β-yl acetate (I) proceeds without double bond migration (Budziarek et al., loc. cit.). If this is the case with iso-β-amyradienonyl acetate (I the non-conjugated dienyl acetate (XIV) would be expected as an intermediate, and this in the presence of mineral acid has been shown to give oleana-9(11):12-dien-3β-yl acetate (XI). Since the reaction in fact leads to oleana-11:13(18)-dien-3β-y acetate (X), either the mechanism of the Clemmensen reduction of (III) does not follow the simple course suggested, or oleana-9(11):12-dien-3β-yl acetate (XI) isomerizes to oleana-11:13(18)-dien-3β-yl acetate under the conditions of reduction

Experiments to test the latter premise were initiated. Although (XI) is stable to relatively vigorous treatment with hydrochloric-acetic acid mixture, as shown by its formation fr the acetate, m.p. 231°, (XIV), prolonged refluxing with minera acid as obtains in the Clemmensen reaction medium, converted (XI) to (X). This accounts for the formation of oleana-11:13(1 dien-3β-yl acetate (X) rather than oleana-9(11):12-dien-3β-yl acetate (XI) by the Clemmensen reduction of iso-β-amyradienony acetate (III). It does not invalidate either the structure of the acetate, m.p. 203°, (XV), or the conversion of it into oleana-11:13(18)-dien-3β-yl acetate (X) since the acid conditi which convert (XV) to (X) do not isomerize oleana-9(11):12-die 3β-yl acetate (XI). In addition, the reaction conditions which convert 11β-hydroxyolean-12-en-3β-yl acetate (XVIII) into olea 11:13(18)-dien-3β-yl acetate are without effect on oleana-9(11 12-dien-3β-yl acetate.

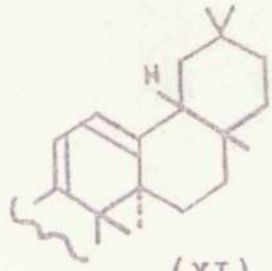
A related reaction leading to the formation of oleana-9(1 12-dien-3β-yl acetate in acid conditions, illustrating its stability, was investigated. Reduction of 12-oxo-olean-9(11)-e 3β-yl acetate (I) with lithium aluminium hydride, followed by acetylation, gave 12α-hydroxyolean-9(11)-en-3β-yl acetate (XIX The configuration of the 12-hydroxyl group is considered to be α (axial) because (XIX) undergoes simple dehydration (trans-diaxialelimination) when heated with pyridine- or sodium aceta acetic anhydride, yielding oleana-9(11):12-dien-3β-yl acetate. When (XIX) is treated with hydrochloric-acetic acid mixture under conditions which convert 11β-hydroxyolean-12-en-3β-yl acetate (XVIII) into oleana-11:13(18)-dien-3β-yl acetate (X), affords oleana-9(11):12-dien-3β-yl acetate (XI).



(I)

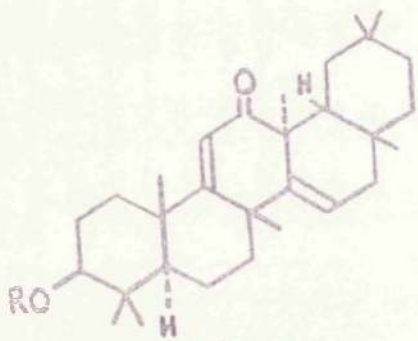


(XIX)

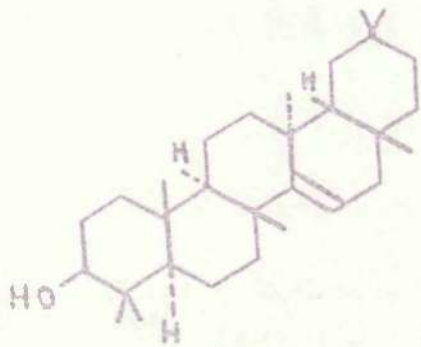


(XI)

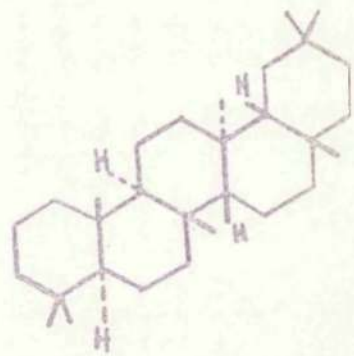
The reactions of iso-β-amyradienonyl acetate so far described are therefore consistent with the view that it is correctly formulated as (III) and is formed from (I) by the migration of the C_{14}-methyl group to C_{13}. The configuration of the C_{13}-methyl group in (III) is considered to be α since the transfer of this group from C_{14} to C_{13} during the conversion of (I) to (III) must involve its movement across the α-face. Iso-β-amyradienonyl acetate is now therefore represented stereochemically as (IIIA).



(IIIA)



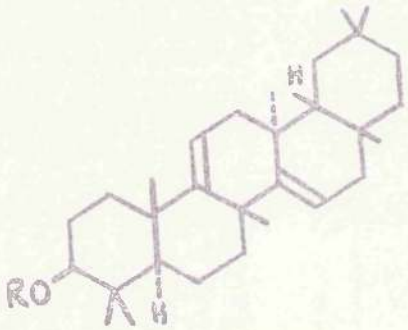
(XX)



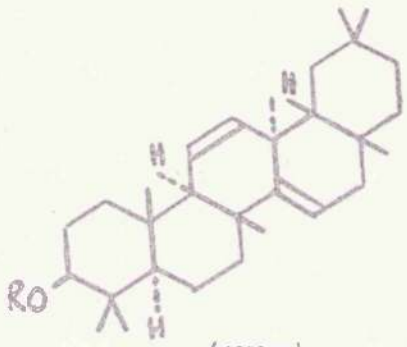
(XXI)

The structure of taraxerol (XX) has recently been established and confirmed by partial synthesis from iso-β-amyradienonyl acetate (IIIA)(Beaton, Spring, Stevenson and Stewart, Chem. and Ind., 1954,1454; 1955,35). Since (XX) has the same basic carbon skeleton as (IIIA), nomenclature is now systematized by reference to the parent hydrocarbon, formerly isooleanane (Johnston and Spring, J., 1954,1556) now named taraxerane (XXI) (Beaton, Spring, Stevenson and Stewart, J., 1955, in press).

Iso-β-amyradienonyl acetate (IIIA) therefore becomes 12-oxotaraxera-9(11):14-dien-3β-yl acetate and the dienyl acetates (XIV) and (XV), obtained by the Wolff-Kishner reducti of 12-oxotaraxera-9(11):14-dien-3β-yl acetate (IIIA) become taraxera-9(11):14-dien-3β-yl acetate (XIVA) and taraxera-11:14 dien-3β-yl acetate (XVA) respectively.



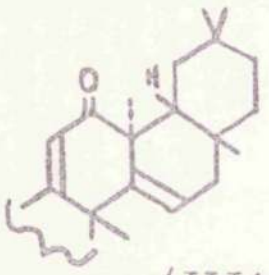
(XIVA)



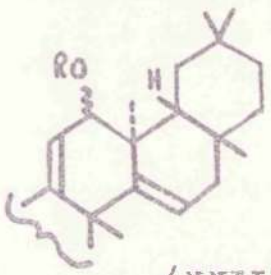
(XVA)

A facet of the chemistry of iso-β-amyradienonyl acetate (IIIA) which appeared anomalous, was its catalytic reduction in acetic acid to a compound called iso-β-amyradienyl acetate (Budziarek et al., loc.cit.). The same authors also obtained iso-β-amyradienyl acetate by catalytic hydrogenolysis of the product obtained by treatment of iso-β-amyradienonyl acetate with lithium aluminium hydride with subsequent acetylation. Budziarek et al. also reported that iso-β-amyradienyl acetate did not show selective absorption in the ultra-violet region, but gave an intense red colour with tetranitromethane in chloroform and suggested that it was a non-conjugated dienyl acetate. If iso-β-amyradienonyl acetate is correctly represent by (IIIA), 12-oxotaraxera-9(11):14-dien-3β-yl acetate, an explanation of these reactions in terms of (IIIA) must be forthcoming. To provide such an explanation, a reinvestigation of these reactions was initiated.

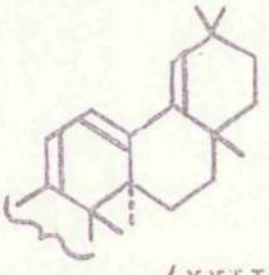
Reduction of 12-oxotaraxera-9(11):14-dien-3β-yl acetate (IIIA) with lithium aluminium hydride afforded a diol, $C_{30}H_{48}O$ formulated as 12ξ-hydroxytaraxera-9(11):14-dien-3β-ol (XXII, R = H) which on acetylation yielded a diacetate, $C_{34}H_{52}O_4$, identical with that described by Budziarek et al. (loc.cit.). The diol was further characterized by preparation of a dibenzo The diacetate and dibenzoate are now formulated as 12ξ-acetoxy taraxera-9(11):14-dien-3β-yl acetate (XXII) and 12ξ-benzoxy-taraxera-9(11):14-dien-3β-yl benzoate (XXII, R = Bz). The diacetate (XXII) shows strong ethylenic absorption between 200 2250 Å. In an attempt to conjugate the ethylenic linkages, 12ξ-acetoxytaraxera-9(11):14-dien-3β-yl acetate was treated with hydrochloric-acetic acid mixture. This resulted in the in the loss of the elements of acetic acid from (XXII) and the format of an acetate, $C_{32}H_{48}O_2$, which shows the absorption maxima (in ethanol) [2280 (E = 18,500), 2820 (E = 16,000) and 2940 Å (E = 12,500)] characteristic of a conjugated trienyl acetate; it is different, however, from oleana-9(11):12:18-trien-3β-yl acetate (XXIII), the only conjugated trienyl acetate in the oleanane series, and henceforth is designated neo-β-amyratrien acetate. Possible arrangements of the double bonds in neo-β-amyratrienyl acetate are shown in (XXIVa), (XXIVb) and (XXIVc). (The location of methyl groups will be discussed later).



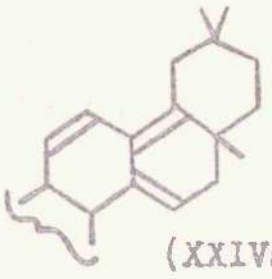
(IIIA)

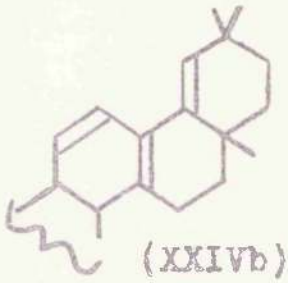


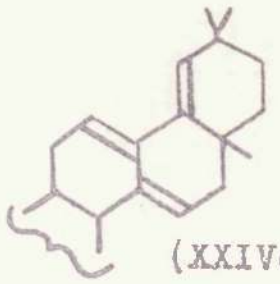
(XXII)



(XXIII)

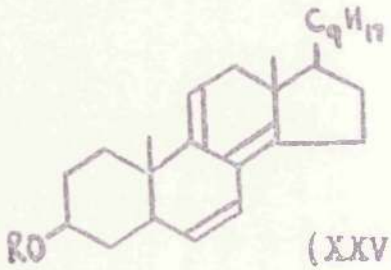

(XXIVa)


(XXIVb)

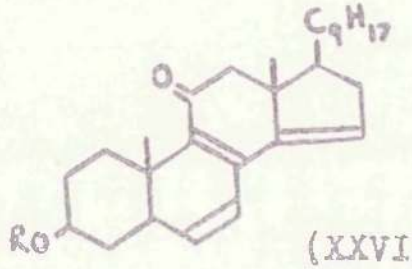

(XXIVc)

Neo-β-amyratrienyl acetate has an ultra-violet absorption spectrum similar to that of ergosta-6:8(14):9(11):22-tetren-3β yl acetate (XXV) which shows absorption maxima (in ether) at 2325 (log E = 4.25) and 2870 Å (log E = 3.82)(Laubach, Schreib Agnello, Lightfoot and Brunings, J. Amer. Chem. Soc., 1953, 75, 151 and this appears to exclude (XXIVc) in view of its dissimilari to (XXV).

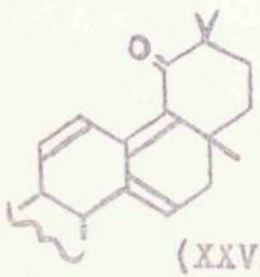
In an attempt to obtain further evidence as to the nature of neo-β-amyratrienyl acetate, its oxidation products were examined. Chromic acid oxidation of neo-β-amyratrienyl acetate yielded neo-β-amyratrienonyl acetate, which shows absorption maxima (in ethanol) at 2320 (E = 12,000) and 3400 Å (E = 11,00 Possible formulations of this chromophore are shown in (XXVIa) and (XXVIb)(derived from XXIVa),(XXVIc)(derived from XXIVb) an (XXVId) and (XXVIe)(derived from XXIVc). (The location of the methyl groups will be discussed later).



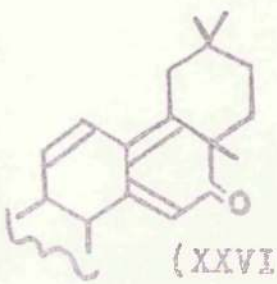
(XXV)



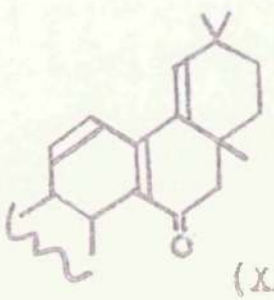
(XXVII)



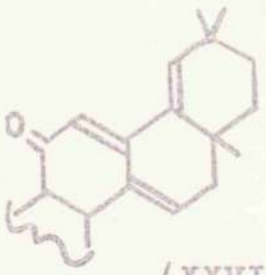
(XXVIa)



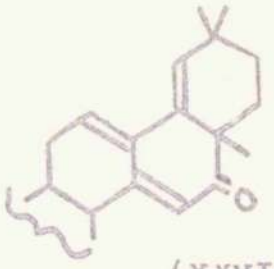
(XXVIb)



(XXVIc)

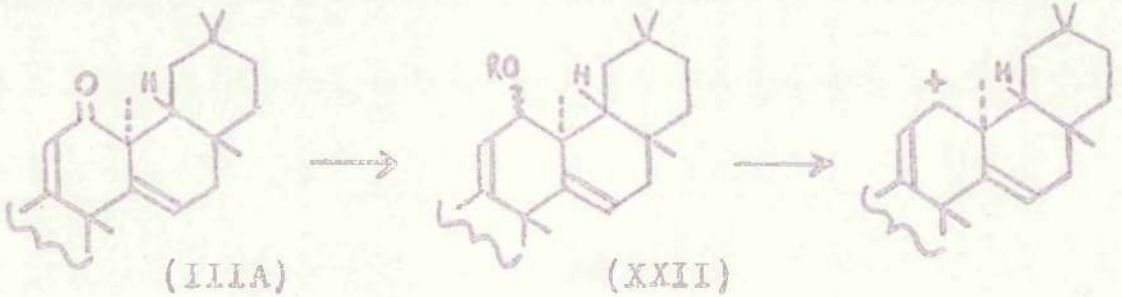


(XXVId)

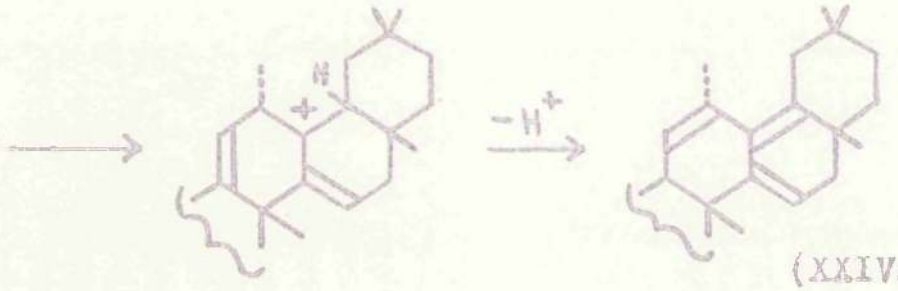


(XXVIe)

Representations (XXVIa) and (XXVIc) are preferred since they contain chromophores very similar to that of 11-oxoergost 6:8:14:22-tetraen-3β-yl acetate (XXVII), which exhibits light absorption maxima (in ether) at 2330 (log E = 3.95) and 3260 Å (log E = 4.18)(Laubach et al., loc.cit.), and consequently part-structure (XXIVa) is favoured for neo-β-amyratrienyl acetate. Mechanistically the genesis of neo-β-amyratrienyl acetate has been represented as below (Allan, Johnston and Spring, J., 1954,1546).

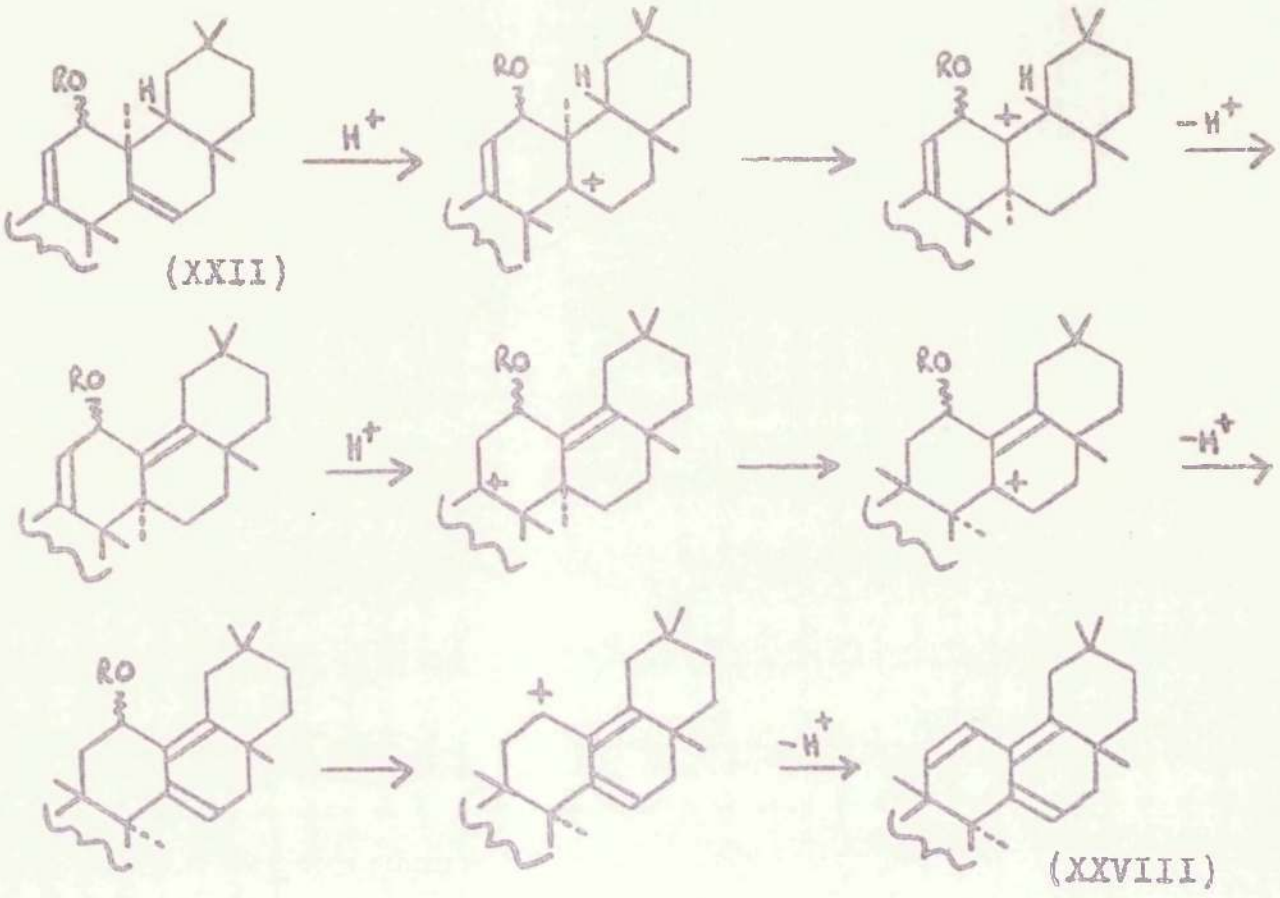


(IIIA) (XXII)



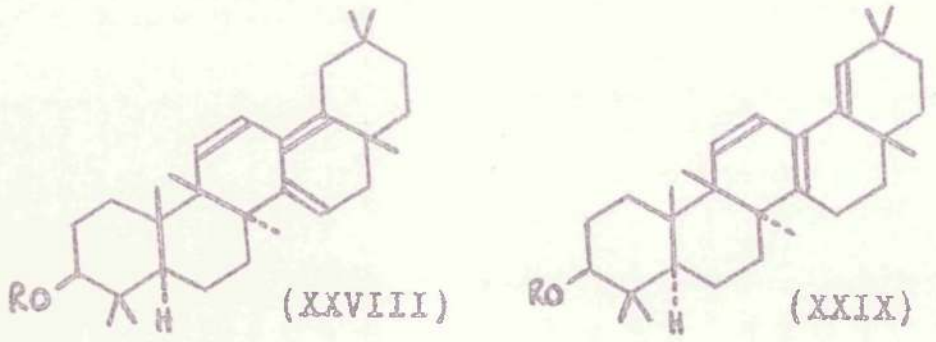
(XXIVa)

In the light of new information available on methyl group migrations (cf. Section 3.), and on the correlation of the ultra-violet light properties, the following mechanism is now preferred,

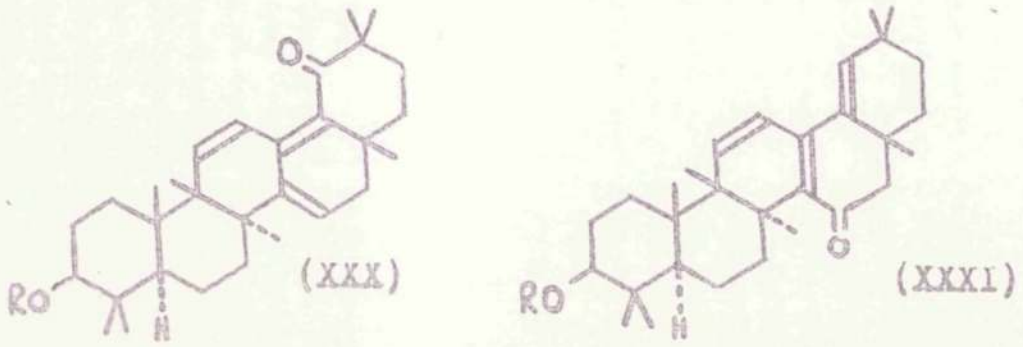


(XXII) (XXVIII)

and neo-β-amyratrienyl acetate is represented as (XXVIII) or (XXIX) and similarly neo-β-amyratrienonyl acetate becomes (XXX or (XXXI). A final decision between these alternatives cannot be made on the evidence so far available.

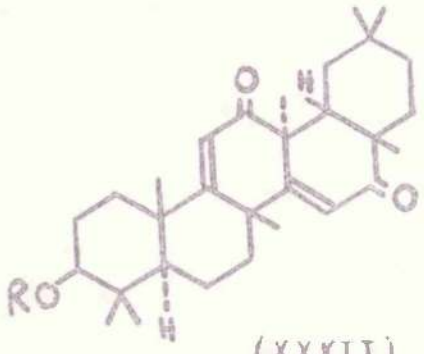


(XXVIII) (XXIX)

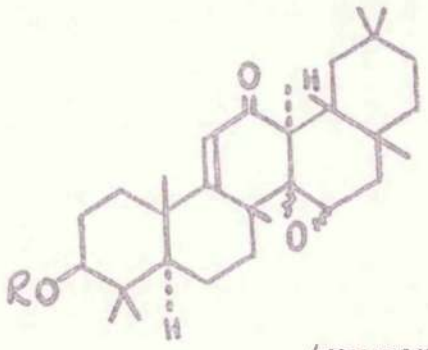


(XXX) (XXXI)

Hydrogenation of neo-β-amyratrienyl acetate proceeds very rapidly and 2 mols. of hydrogen are absorbed to yield an isome of β-amyrin acetate, now named neo-β-amyrin acetate. This is identical with the compound, iso-β-amyradienyl acetate, described by Budziarek et al., (loc.cit.), who obtained it by catalytic reduction of either 12-oxotaraxera-9(11):14-dien-3β- acetate (IIIA) or 12ξ-acetoxytaraxera-9(11):14-dien-3β-yl acetate (XXII). Attempts to repeat these reactions in highly purified acetic acid were unsuccessful, but addition of a trac of mineral acid led to rapid absorption of hydrogen. These facts are best explained by the conclusion that neo-β-amyra- trienyl acetate is an intermediate in these reactions. Hydrogenolysis of 12:16-dioxotaraxera-9(11):14-dien-3β-yl acetate (XXXII) or 14:15-epoxy-12-oxotaraxer-9(11)-en-3β-yl acetate (XXXIII) also yielded neo-β-amyrin acetate.

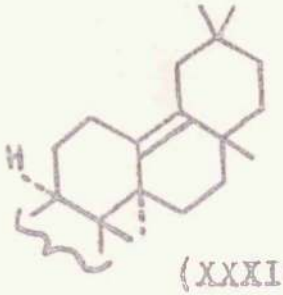


(XXXII)

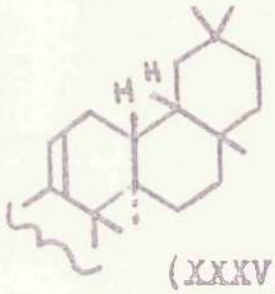


(XXXIII)

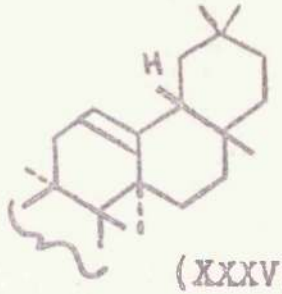
Since neo-β-amyrin acetate shows absorption between 2000- 2250 Å, it was compared, under similar conditions, with olean- 13(18)-en-3β-yl acetate (XXXIV), olean-9(11)-en-3β-yl acetate (XXXV) and olean-12-en-3β-yl acetate (XXXVI); the conclusion reached was that it is tetra- rather than trisubstituted, in view of its similarity to (XXXIV).(cf. Allan et al., loc.cit.)



(XXXIV)



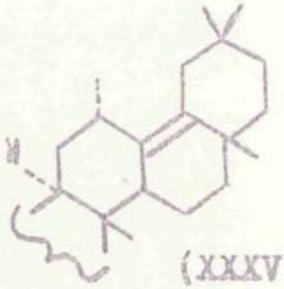
(XXXV)



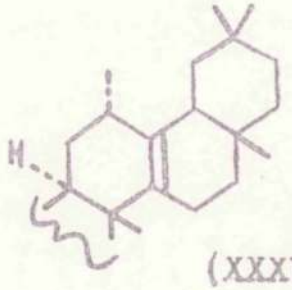
(XXXVI)

To prove the invalidity of the assumption of Budziarek et al. (loc.cit.) that iso-β-amyradienyl acetate (neo-β-amyrin acetate) was diethenoid, based on the remarkable red colour obtained with tetranitromethane in chloroform, it was oxidized with perbenzoic acid. The product was an oxide, $C_{32}H_{52}O_3$, whic did not give a colour with tetranitromethane in chloroform and did not show absorption between 2000-3500 Å. When treated with hydrochloric acid, neo-β-amyrin acetate oxide gave a conjugate dienyl acetate which is different from the known conjugated oleanadienyl acetates.

The properties of neo-β-amyrin acetate show that it contains a fully substituted double bond, and it has been represented by Allan et al. (loc.cit.) as (XXXVIIa) or (XXXVII



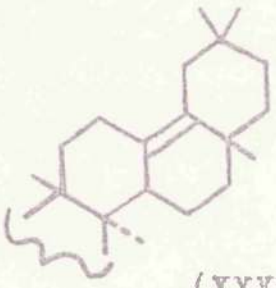
(XXXVIIa)



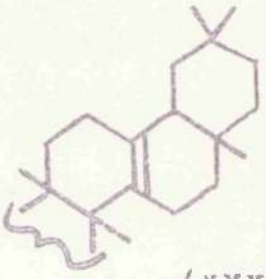
(XXXVIIb)

More probable structures, derived from those postulated for neo-β-amyratrienyl acetate, are (XXXVIIIa) or (XXXVIIIb), the latter of which might be construed as giving some explanation of the peculiar colour reaction with tetranitromethane

by virtue of an endocyclic tetrasubstituted ethylenic linkage between rings C and D.



(XXXVIIIa)



(XXXVIIIb)

In conclusion, it may be said that the products resulting from an extensive investigation of the reduction reactions of iso-β-amyradienonyl acetate, endorse the structure first proposed by Jeger and Ruzicka and illustrate the remarkable methyl group migrations possible in the triterpenoid field.

Experimental

Section (I).

Melting points were determined using a standardised N.P.L. thermometer.

Specific rotations were measured in chloroform solution in a 1 dm. tube at approximately 15°.

Ultra-violet absorption spectra were determined in ethanol solution with a Unicam SP.500 spectrophotometer and (E) denotes intensity of absorption.

Colour reactions with tetranitromethane were done in chloroform solution.

For chromatography, alumina (Brockmann Grade II) was used, in the ratio 30:1 of substance chromatographed, and light petroleum refers to that fraction of b.p. 40-60°.

The phrase 'in the usual way' implies, in general, dilution with water, extraction with ether, washing consecutively with aqueous sodium hydroxide, water, aqueous hydrochloric acid and aqueous sodium bicarbonate, followed by drying of the ethereal extract over anhydrous sodium sulphate, filtration and evaporation to dryness under reduced pressure.

Hydrogenations were carried out, at room temperature, in glacial acetic acid which had been refluxed over and distilled from chromium trioxide.

Acetylations were carried out using acetic anhydride in pyridine solution at 100° for 30 mins., unless otherwise specified.

12-Oxotaraxera-9(11):14-dien-3β-yl Acetate.

A mixture of 12-oxo-olean-9(11)-en-3β-yl acetate (27 g.), selenium dioxide (27 g.) and acetic acid (900 c.c.) was refluxed for 48 hrs. and filtered. The filtrate was refluxed with zinc (15 g.) for 16 hrs. and filtered. Concentration of the filtrate and dilution with water gave a crystalline solid (18 g.), which was recrystallised from chloroform-methanol to yield 12-oxotaraxera-9(11):14-dien--3β-yl acetate as colourless prisms (14 g.), m.p. 224-225°, $[\alpha]_D$ - 38° (c,2.8). Light absorption: Max. at 2090 (E = 3,000) and 2450 Å. (E = 10,000). Budziarek, Johnston, Manson and Spring (J., 1951,3019) give m.p. 220-221°, $[\alpha]_D$ - 38°.

Taraxera-9(11):14-dien-3β-yl Acetate.

A mixture of 12-oxotaraxera-9(11):14-dien-3β-yl acetate (2 g.), methanolic sodium methoxide (from 2 g. of sodium and 25 c.c. of methanol) and hydrazine hydrate (100%, 10 c.c.) was kept at 200° (autoclave) for 13 hrs. after the method of Allan, Johnston and Spring (J., 1954, 1546). The crude product was isolated and acetylated in the usual manner. The acetylated product crystallised from chloroform-methanol to yield taraxera-9(11):14-dien--3β-yl acetate as plates (1 g.), m.p. 230-231°, $[\alpha]_D$ - 9°

(c,2.0). Concentration of the mother liquor yielded a second crop of plates (500 mg.) m.p. 175-195°, two recrystallisations of which from chloroform-methanol gave more taraxera-9(11):14-dien-3β-yl acetate (160 mg.), m.p. and mixed m.p. 230-231°.

Taraxera-11:14-dien-3β-yl Acetate.

Concentration of the mother liquor from the second crop of the previous experiment gave a third crop of plates (270 mg.), which after five recrystallisations yielded taraxera-11:14-dien-3β-yl acetate as plates, m.p. 202-203°, $[\alpha]_D$ - 95° (c,1.0).

Conversion of Taraxera-9(11):14-dien-3β-yl Acetate to Oleana-9(11):12-dien-3β-yl Acetate.

A solution of taraxera-9(11):14-dien-3β-yl acetate (150 mg.) in acetic acid (25 c.c.) was heated with concentrated hydrochloric acid (1 c.c.) on the steam-bath for 4 hrs. The product was isolated in the usual way and crystallised from chloroform-methanol to give oleana-9(11):12-dien-3β-yl acetate as needles (70 mg.), m.p. and mixed m.p. 219-220°, $[\alpha]_D$ + 337° (c,1.5). Light absorption: Max. at 2820 Å. (E = 9,000).

Conversion of Taraxera-11:14-dien-3β-yl Acetate to Oleana-11:13(18)-dien-3β-yl Acetate.

A solution of taraxera-11:14-dien-3β-yl acetate (60 mg.) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (1 c.c.) on the steam-bath for 7 hrs. The product isolated in the usual way, crystallised from chloroform-methanol to yield oleana-11:13(18)-dien-3β-yl acetate as plates (35 mg.), m.p. and mixed m.p. 227-228°, $[\alpha]_D$ - 62° (c,0.6). Light absorption: Max. at 2420 (E = 22,000) 2510 (E = 27,200) and 2600 Å. (E = 17,000). The same treatment of oleana-9(11):12-dien-3β-yl acetate (m.p. 219-220°, $[\alpha]_D$ + 337°) gave, after two recrystallisations from aqueous acetone, a 70% return of starting material, m.p. 215-217°, $[\alpha]_D$ + 336° (c,0.7). Light absorption: Max. at 2820 Å. (E = 9,000)

Rearrangement of Oleana-9(11):12-dien-3β-yl Acetate to Oleana-11:13(18)-dien-3β-yl Acetate.

A solution of oleana-9(11):12-dien-3β-yl acetate (200 mg.) in acetic acid (100 c.c.) was treated with a solution of concentrated hydrochloric acid (10 c.c.) in acetic acid (50 c.c.). The mixture was refluxed for 6 hrs. with the addition of concentrated hydrochloric

acid (5 c.c.) after 2, 4 and 6 hrs. The mixture was set aside overnight and the product, isolated in the usual way, crystallised from chloroform-methanol to yield oleana-11:13(18)-dien-3β-yl acetate as plates (100 mg.), m.p. and mixed m.p. 224-225°, $[\alpha]_D$ - 63° (c,0.6). Light absorption: Max. at 2420 (E = 21,000), 2500 (E = 26,000) and 2600 Å. (E = 16,000). Oleana--9(11):12-olean-3β-ol was recovered unchanged after refluxing with ethanolic potassium hydroxide (20%, 100 c.c.) for 52 hrs.

11β-Hydroxyolean-12-en-3β-yl Acetate.

A solution of 11-oxo-olean-12-en-3β-yl benzoate (1 g.) (Budziarek, Manson and Spring, J., 1951,3336) in dry ether (250 c.c.), was treated with lithium aluminium hydride (1 g.) and kept overnight at room temperature. The product was isolated and acetylated in the usual manner. The acetylated product separated from chloroform-methanol as needles (900 mg.), m.p. 200-205°, which gave a yellow colour with tetranitromethane. Four recrystallisations gave 11β-hydroxyolean--12-en-3β-yl acetate, m.p. 209-210°, $[\alpha]_D$ + 29° (c,2.2) (Found: C,79.1; H,11.2. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%) Light absorption: Max. at 2100 Å. (E = 5,600).

Dehydration of 11β-Hydroxyolean-12-en-3β-yl Acetate to Oleana-9(11):12-dien-3β-yl Acetate.

A mixture of 11β-hydroxyolean-12-en-3β-yl acetate (250 mg.), anhydrous sodium acetate (400 mg.) and acetic anhydride (30 c.c.) was refluxed for 2 hrs. The product was isolated in the usual way and crystallised from aqueous acetone to yield oleana-9(11):12-dien-3β-yl acetate as fine needles (120 mg.), m.p. and mixed m.p. 214-217°, $[\alpha]_D$ + 338° (c,0.9). Light absorption: Max. at 2820 Å. (E = 9,000).

Acid dehydration of 11β-Hydroxyolean-12-en-3β-yl Acetate to Oleana-11:13(18)-dien-3β-yl Acetate.

A solution of 11β-hydroxyolean-12-en-3β-yl acetate (200 mg.) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (0.5 c.c.) on the steam-bath for 5 hrs. The product, isolated in the usual way, crystallised from chloroform-methanol to yield oleana-11:13(18)-dien-3β-yl acetate as plates (120 mg.), m.p. and mixed m.p. 228-230°, $[\alpha]_D$ - 62° (c,0.8). Light absorption: Max. at 2500 (E = 29,000) 2420 (E = 24,000) and 2600 Å. (E = 19,000).

12α-Hydroxyolean-9(11)-en-3β-yl Acetate.

A solution of 12-oxo-olean-9(11)-en-3β-yl acetate (1 g.) (Budziarek, Johnston, Manson and Spring, loc.cit.) in dry ether (250 c.c.), was treated with lithium aluminium hydride (1 g.) and the mixture kept overnight. The product was isolated by means of ether (avoiding the use of mineral acid), and acetylated by acetic anhydride-pyridine at room temperature overnight. The acetylated product crystallised from aqueous acetone, to give 12α-hydroxyolean-9(11)-en-3β-yl acetate as needles (750 mg.), m.p. 177-178°, $[\alpha]_D$ + 36° (c,0.6) (Found: C,79.5; H,11.2. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%).

Dehydration of 12α-Hydroxyolean-9(11)-en-3β-yl Acetate to Oleana-9(11):12-dien-3β-yl Acetate.

(a) A mixture of 12α-hydroxyolean-9(11)-en-3β-yl acetate (200 mg.), anhydrous sodium acetate (400 mg.) and acetic anhydride (30 c.c.) was refluxed for 2 hrs. The product was isolated in the usual way and crystallised from aqueous acetone to yield oleana-9(11):12-dien-3β-yl acetate as needles (100 mg.), m.p. and mixed m.p. 216-217°, $[\alpha]_D$ + 335° (c,0.7). Light absorption: Max. at 2820 Å. (E = 9,000).

(b) A solution of 12α-hydroxyolean-9(11)-en-3β-yl acetate (200 mg.) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (0.5 c.c.) on the steam-bath for 3 hrs. The product isolated in the usual manner, crystallised from aqueous acetone to give oleana-9(11):12-dien-3β-yl acetate as needles (110 mg.), m.p. and mixed m.p. 218-219°, $[\alpha]_D$ + 338° (c,0.6). Light absorption: Max. at 2820 Å. (E = 9,000). Oleana-9(11):12-dien-3β-yl acetate was isolated in similar yield when the solution in acetic acid containing hydrochloric acid was kept overnight at room temperature.

12ξ-Acetoxytaraxera-9(11):14-dien-3β-yl Acetate.

A solution of 12-oxotaraxera-9(11):14-dien-3β-yl acetate (400 mg.) in dry ether (100 c.c.) was refluxed with lithium aluminium hydride (300 mg.) for 4 hrs. The product, isolated in the usual way (avoiding the use of mineral acid), was crystallised from aqueous methanol from which 12ξ-hydroxytaraxera-9(11):14-dien-3β-ol separated as felted needles (300 mg.), m.p. 202-204°, $[\alpha]_D$ - 17° (c,0.8), which gave a yellow colour with tetranitromethane (Found: C,81.8; H,11.1. $C_{30}H_{48}O_2$ requires C,81.8; H,11.0%). Acetylation of 12ξ-hydroxytaraxera-9(11):14-dien-3β-ol gave 12ξ-acetoxytaraxera-

-9(11):14-dien-3β-yl acetate which separated from methanol as plates, m.p. 167-168°, $[\alpha]_D$ + 25° (c,1.0) undepressed in m.p. with the 'diacetate' m.p. 167-168°, described by Budziarek, Manson, Johnston and Spring (loc.cit.) Light absorption: Max. at 2110 Å. (E = 7,800) Benzoylation of 12ξ-hydroxytaraxera-9(11):14-dien-3β-ol by pyridine-benzoyl chloride gave 12ξ-benzoxytaraxera--9(11):14-dien-3β-yl benzoate which crystallised from chloroform-methanol as needles, m.p. 233-234°, $[\alpha]_D$ + 70° (c,1.0) (Found: C,81.6; H,8.8. $C_{44}H_{56}O_4$ requires C,81.4; H,8.7%).

neo-β-Amyratrienyl Acetate.

A solution of 12ξ-acetoxytaraxera-9(11):14-dien-3β--yl acetate (1 g.) in acetic acid (80 c.c.) was treated with concentrated hydrochloric acid (4 c.c.). After 1 hr. a crystalline solid separated from the yellow mixture. After 20 hrs. the product was isolated and acetylated in the usual way. A solution of the acetylated product (900 mg.) , in light petroleum (100 c.c was filtered through alumina (25 g.) and the column washed with light petroleum (200 c.c.). Elution with light petroleum-benzene (5:1; 750 c.c.) yielded a crystalline solid (550 mg.) which was recrystallised

from methanol to yield neo-β-amyratrienyl acetate as plates, m.p. 168-169°, $[\alpha]_D$ + 58° (c,1.0) which gave a purple colour with tetranitromethane (Found: C,82.8; H,10.2. $C_{32}H_{48}O_2$ requires C,82.7; H,10.4%) Light absorption: Max. at 2280 (E = 18,500), 2820 (E = 16,000 and 2940 Å.(E = 12,500). neo-β-Amyratrienyl acetate in benzene was recovered unchanged after shaking with hydrogen and, Raney Nickel, palladised barium sulphate or palladised strontium carbonate. It did not form an adduct with maleic anhydride when refluxed in benzene solution, and was recovered unchanged after refluxing, with zinc in ethanol or acetic acid solution, and with sodium in n-pentanol.

neo-β-Amyrin Acetate.

(a) A solution of neo-β-amyratrienyl acetate (1 g.) in acetic acid (100 c.c.) was added to a suspension of freshly reduced platinum (from 500 mg. of PtO_2) in aceti acid (25 c.c.) and the mixture shaken with hydrogen. Absorption was complete after 30 mins. (approx. 110 c.c. of hydrogen at N.T.P.). The product, isolated in the usual manner, crystallised from chloroform-methanol to yield neo-β-amyrin acetate as needles (450 mg.), m.p. 225-227°, $[\alpha]_D$ + 5° (c,0.7), which gave an intense

orange-red colour with tetranitromethane and which was undepressed in m.p. on admixture with iso-β-amyradienyl acetate as prepared by Budziarek, Johnston, Manson and Spring (loc.cit.). Light absorption: Max. at 2110 Å. (E = 5,000) (Found: C,82.0; H,11.2. $C_{32}H_{52}O_2$ requires C,82.0; H,11.2%). neo-β-Amyrin acetate (200 mg., m.p. 224-226°, $[\alpha]_D$ + 6°) was also obtained by hydrogenation of neo-β-amyratrienyl acetate (250 mg.) in ethanol over palladized strontium carbonate (2% PdO_2).

(b) A solution of 12β-acetoxytaraxera-9(11):14-dien-3β-yl acetate (1 g.) in acetic acid (75 c.c.) was added to a freshly reduced suspension of platinum (from 700 mg. of PtO_2) in acetic acid (50 c.c.) and the mixture shaken with hydrogen when the uptake was extremely slow. After 18 hrs. one drop of concentrated hydrochloric acid was added and shaking with hydrogen continued. Hydrogen uptake was then rapid. After 6 hrs. the product was isolated in the usual way and crystallised from chloroform-methanol to yield neo-β-amyrin acetate as needles (600 mg.), m.p. and mixed m.p. 226-227°, $[\alpha]_D$ + 5° (c,1.1).

(c) A solution of 12-oxotaraxera-9(11):14-dien-3β-yl acetate (200 mg.) in acetic acid (50 c.c.) was added to a freshly reduced suspension of platinum (from 100 mg. of

PtO_2) in acetic acid (25 c.c.) and the mixture shaken with hydrogen when reduction proceeded slowly being complete after 4 days. Addition of one drop of hydrochloric acid to an acetic acid solution led to rapid absorption of hydrogen, the reaction being complete in 4 hrs. The product isolated in the usual way crystallised from chloroform-methanol to yield neo-β--amyrin acetate as needles (120 mg.), m.p. and mixed m.p. 224-225°, $[\alpha]_D$ + 5° (c,0.7).

(d) A solution of 12:16-dioxotaraxera-9(11):14-dien--3β-yl acetate (250 mg.) (Jeger and Ruzicka, Helv.Chim. Acta, 1945,28,209) in acetic acid (100 c.c.) was shaken with platinum (from 200 mg. of PtO_2), concentrated hydrochloric acid (0.5 c.c.) and hydrogen for 24 hrs. The product, isolated in the usual way, crystallised from chloroform-methanol to yield neo-β-amyrin acetate as needles (100 mg.) m.p. and mixed m.p. 224-225°, $[\alpha]_D$ + 5° (c,0.8).

(e) A solution of 14:15-epoxy-12-oxotaraxer-9(11)-en-3β--yl acetate (1 g.) (Johnston and Spring, J., 1954, 1556) in acetic acid (200 c.c.) was added to a freshly reduced suspension of platinum (from 600 mg. of PtO_2) in acetic acid (30 c.c.) and the mixture shaken with hydrogen for 48 hrs. The product, isolated in the usual way,

crystallised from chloroform-methanol to yield neo-β-amyrin acetate as needles (400 mg.), m.p. and mixed m.p. 223-225°, $[\alpha]_D$ + 4° (c,1.1).

(f) A solution of 12ξ-benzoxytaraxera-9(11):14-dien-3β-yl benzoate (1 g.) in acetic acid (250 c.c.) was shaken with platinum (from 200 mg. of PtO_2), concentrated hydrochloric acid (1 c.c.) and hydrogen for 24 hrs. The product, isolated in the usual manner, crystallised from methylene chloride-methanol to yield neo-β-amyrin hexahydrobenzoate as plates (800 mg.), m.p. 170-171°, $[\alpha]_D$ + 1° (c,2.0), which gave an orange-red colour with tetranitromethane. Light absorption: Max. at 2080 Å. (E = 4,050) (Found: C,83.0; H,11.2. $C_{37}H_{60}O_2$ requires C,82.8; H,11.3%). Hydrolysis by refluxing in ethanolic potassium hydroxide (15%, 100 c.c.) for 8 hrs. gave a gum, acetylation of which yielded neo-β-amyrin acetate, crystallised from chloroform-methanol as needles (400 mg. m.p. and mixed m.p. 224-225°, $[\alpha]_D$ + 5° (c,3.1). Hydrolysis of neo-β-amyrin acetate in ether solution with lithium aluminium hydride gave a gum, benzoylation of which yielded neo-β-amyrin benzoate which crystallised from chloroform-methanol as needles, m.p. 186-187°, $[\alpha]_D$ + 26° (c,3.7) (Found: C,83.3; H,10.4. $C_{37}H_{54}O_2$ requires C,83.7; H,10.3%).

neo-β-Amyratrienonyl Acetate.

A solution of neo-β-amyratrienyl acetate (500 mg.) in acetic acid (25 c.c.) maintained at a temperature of 44-55° was treated with a solution of chromic acid (150 mg.; 2.2 mol.) in acetic acid (20 c.c.) added dropwise with stirring during 30 mins. Stirring was continued for a further 30 mins, and the product isolated in the usual way, was a gum (550 mg.), which was dissolved in benzene (50 c.c.) and chromatographed on alumina. Washing with benzene (1 l.) eluted only gum (60 mg.). Elution with ether-benzene (1:9) (200 mls.) gave a fracti which crystallised from methanol to yield neo-β-amyratrienonyl acetate as yellowish square plates (60 mg.), m.p. 209-210°, $[\alpha]_D$ + 21° (c,0.7), which gave a bright orange-yellow colour with tetranitromethane. (Found: C,79. H,9.8. $C_{32}H_{46}O_3$ requires C,80.2; H,9.7%) Light absorption Max. at 2320 (E = 12,000) and 3400 Å. (E = 11,000).

neo-β-Amyrin Acetate Oxide.

A solution of neo-β-amyrin acetate (350 mg.) in chloroform (20 c.c.) was treated with perbenzoic acid (120 mg.) in chloroform (2 c.c.) and allowed to stand for 48 hrs. at 0°. The product, isolated in the usual way, crystallised from methanol to yield neo-β-amyrin acetate oxide as prisms (180 mg.), m.p. 207-209°, $[\alpha]_D$

-5° (c,0.9), which showed no selective absorption in range 2000-3500 Å. (Found: C,79.3; H,10.9. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%).

Section (2).

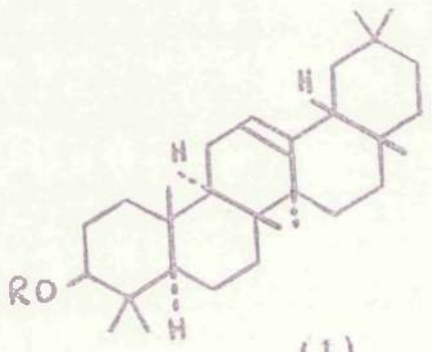
Summary.

A general investigation of the chemistry of 18α-oleanane derivatives and a comparison with the oleanane and ursane analogues shows that rings D and E in α-amyrin are cis-β-fused.

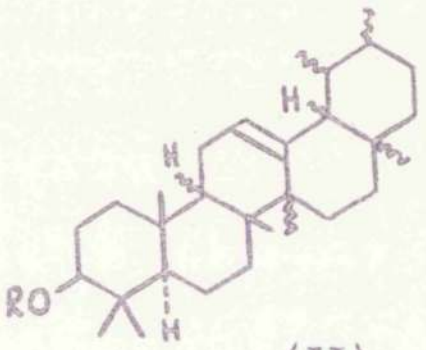
In all formulae in Section (2), R = Ac unless otherwise stated

Introduction.

The stereochemistry of olean-12-en-3β-ol (β-amyrin) (I, R=H) has been elucidated, mainly by Barton and his collaborators (cf. Barton, J., 1953,1027).



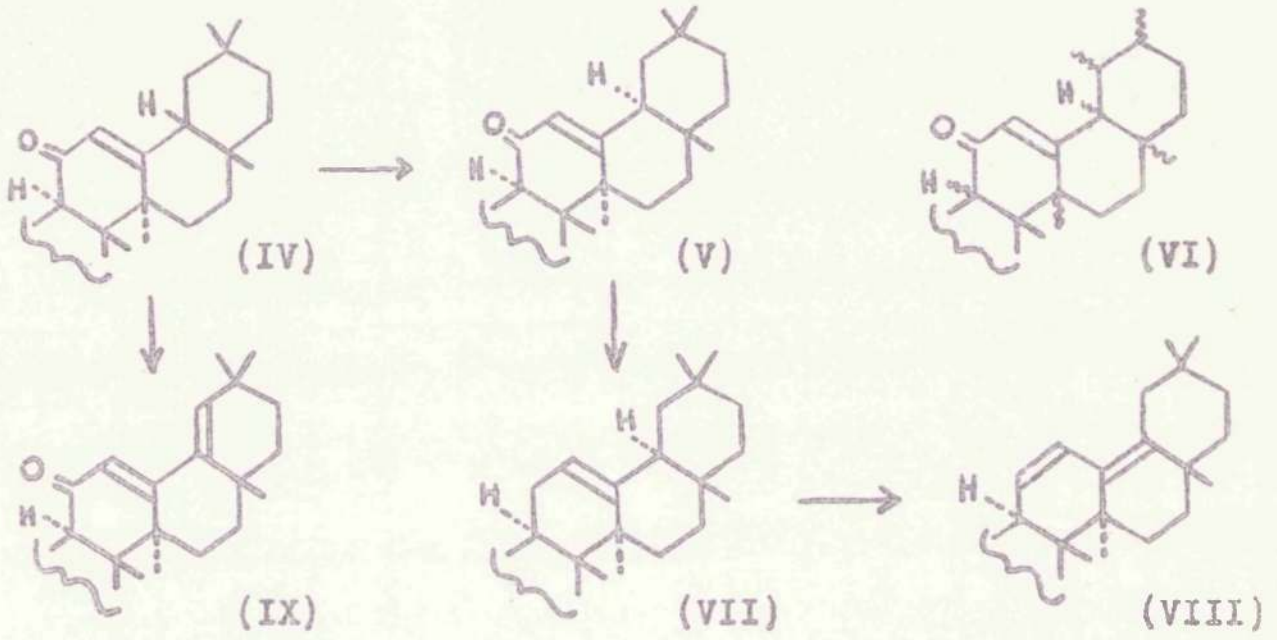
(I)



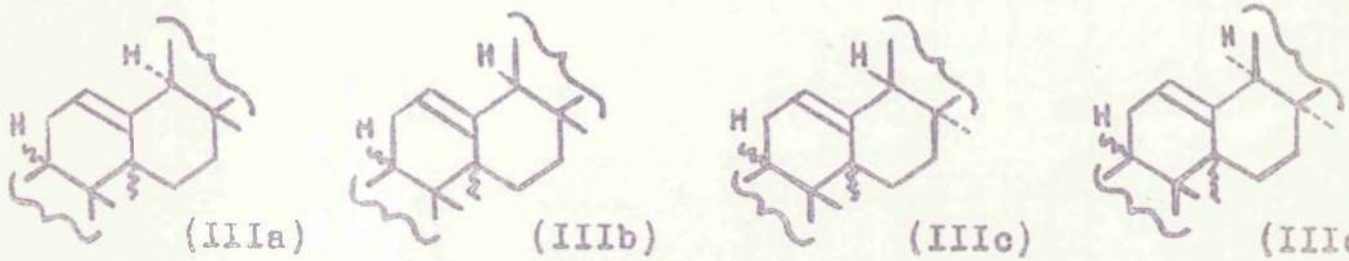
(II)

Rings D and E are cis-β-fused (Budziarek, Manson and Spring, J., 1951,3336 ; Barton and Holness, Chem. and Ind., 1951,233) and it has been demonstrated moreover, that the 18β-configuration is unstable since prolonged alkali treatment of 11-oxo-olean-12-en-3β-ol (IV, R=H) affords an isomer (Picard and Spring, J., 1940,1198 ; Ruzicka, Müller and Schellenberg, Helv.Chim.Acta, 1939,22,758), shown to be 11-oxo-18α-olean-12-en-3β-ol (V, R=H) (Budziarek et al., loc.cit.). That the isomerization had involved C_{18} and not C_9 was established by catalytic hydrogenolysis of the epimeric αβ-unsaturated ketone (V) to the deoxo-compound (VII), which was oxidized by seleniu dioxide to oleana-11:13(18)-dien-3β-yl acetate (VIII).

Thus, the β-configuration at C_{18} in the natural oleanane triterpenoids can be inverted to the more stable α-configurati where rings D and E are trans-fused.



The constitution (II, R=H) for α-amyrin (urs-12-en-3β-ol) was proposed by Meisels, Jeger and Ruzicka (Helv. Chim. Acta., 1949, 32, 1075) and the configurations at C_3, C_5, C_8 and C_{10} have been established (Jeger, Rüegg and Ruzicka, ibid., 1947, 30, 129; Meisels, Jeger and Ruzicka, ibid., 1950, 33, 700). Varying opinions have been expressed concerning the configurations at C_{17}, C_{18}, C_{19} and C_{20} in (II) and all four possible stereochemical combinatons involving C_{17} and C_{18} have been proposed. These are (IIIa) (Ruzicka, Experientia, 1953, 9, 357), (IIIb) Corey and Ursprung, Chem. and Ind., 1954, 1387), (IIIc) (Beton and Halsall, ibid., p.1560) and (IIId) (Zürcher, Jeger and Ruzicka, Helv. Chim. Acta, 1954, 37, 2149, footnote).



Unlike the oleanane triterpenoids, the stereochemistry at C_{18} in the ursane series is stable under the same conditions which cause isomerization in the oleanane series, since prolonged alkali treatment of 11-oxours-12-en-3β-yl acetate (V did not cause isomerization.

Since little was known of the chemistry of the 18α-oleana derivatives, a general investigation of this series was undertaken with the object of comparing them with oleanane and ursane analogues to elucidate some aspects of the chemistry of the Ursane Group and, in particular, the nature of the D/E ring fusion in α-amyrin. For clarity of exposition, a comparis of the reactions of the three classes (oleanane, 18α-oleanane and ursane) is conveniently subdivided into the following sections;

(A). Oxidation of 11-oxo-12-en-3β-yl acetates.

(B). Dehydrations of 11β-hydroxy-12-en-3β-yl acetates.

(C). Oxidation of -12-en-3β-yl acetates.

(D). Bromination of 12-oxo-an-3β-yl acetates.

(E). Acid rearrangements of -9(11):12-dien-3β-yl acetates

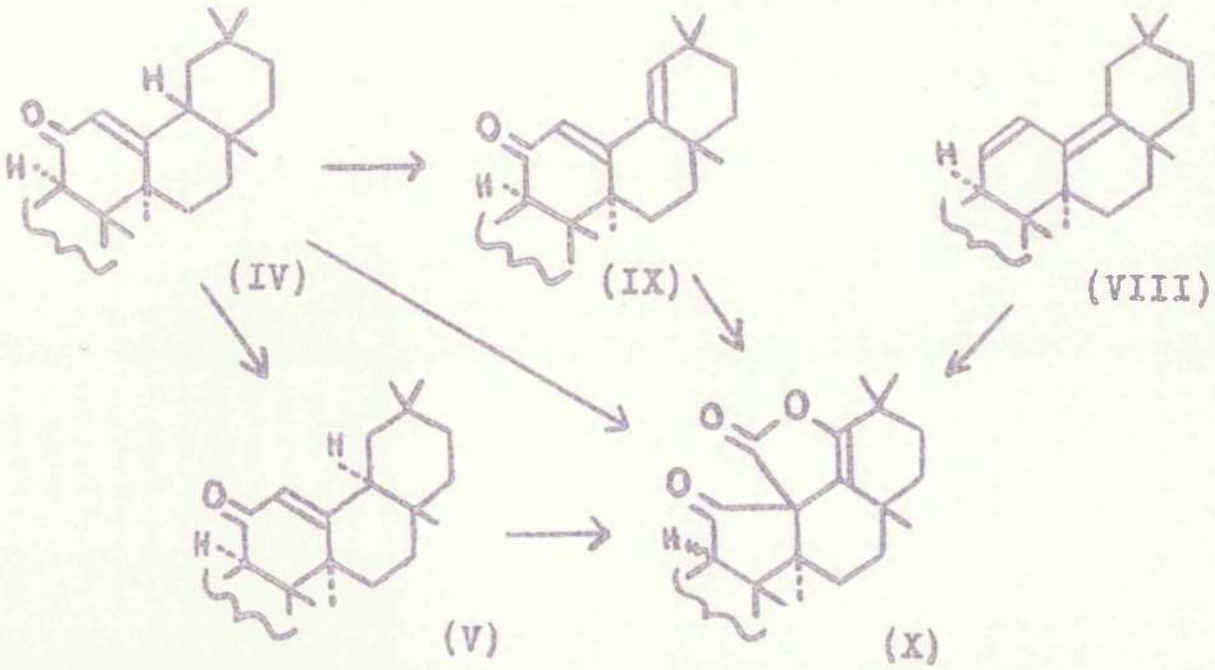
(F). Ultra-violet absorption spectra.

(G). Reactions of 12-oxo-9(11)-en-3β-yl acetates.

(A). Oxidation of 11-oxo-12-en-3β-yl acetates.

11-Oxo-18α-olean-12-en-3β-yl acetate (V), was prepared by the epimerization of 11-oxo-olean-12-en-3β-yl benzoate (IV, R=Bz) using the conditions of Budziarek et al. (loc.cit.) and isolated in 75% yield (acetylation without purification of intermediate alcohol). It was found that the remaining 25% could not be purified by crystallization, but retreatment with alkali under the same conditions afforded more pure (V), increasing the overall yield to 82.5% of the theoretical value 11-Oxo-18α-olean-12-en-3β-ol was further characterized by conversion to 11-oxo-18α-olean-12-en-3β-yl benzoate (V, R=Bz).

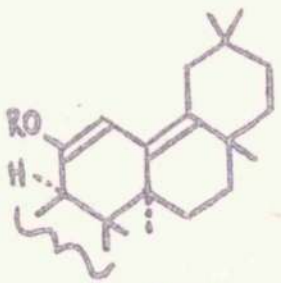
Oxidation of the oleanane derivatives, oleana-11:13(18) dien-3β-yl acetate (VIII) (Ruzicka and Jeger, Helv.Chim.Acta, 1941,24,1236), 11-oxo-olean-12-en-3β-yl acetate (IV) and 11-ox oleana-12:18-dien-3β-yl acetate (IX) (Mower, Green and Spring, J., 1944,256) yield the 'O_5-acetate' (X), the structure of which has been established by McKean and Spring (J., 1954,1989



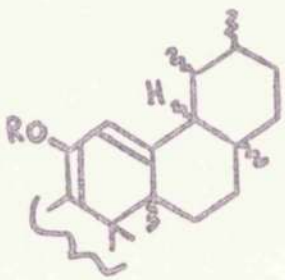
Similar oxidations in the ursane series do not yield an analogue of (X) and in an endeavour to ascertain the influence of configuration at C_{18} on the formation of (X), 11-oxo-18α-olean-12-en-3β-yl acetate (V) was oxidized with selenium dioxide. The product isolated was the known 'O_5-acetate'. It follows from the formation of (X) from (IV) and (V) that a specific fusion of rings D and E is not the determining factor for reaction. It is possible that the formation of the enol lactone (X) from the isomers (IV) and (V) proceeds via 11-oxo-oleana-12:18-dien-3β-yl acetate (IX). An attractive mechanism based on a closely related reaction has recently been proposed (Yates and Stout, J. Amer. Chem. Soc., 1954, 5112). In terms of formula (VI) for the α-amyrin derivative, a possible reason for the non-formation of an 'ursane-O_5-acetate' would be the presence of the C_{19}-methyl group.

Oxidation of 11-oxo-olean-12-en-3β-yl acetate (IV) with bromine yields 11-oxo-oleana-12:18-dien-3β-yl acetate (IX) (Picard and Spring, J., 1941, 35). Both 11-oxours-12-en-3β-yl acetate (VI) and 11-oxo-18α-olean-12-en-3β-yl acetate (V), however, were recovered unchanged after treatment with bromine using conditions which successfully lead to the formation of (I from (IV). The similarity in behaviour of (V) and (VI) does not necessarily indicate an identity of the D/E ring fusion in thes compounds since bromination proceeds via the enol form and the fact that enolization is directed toward C_{18} in (V) and (VI) ha not been demonstrated.

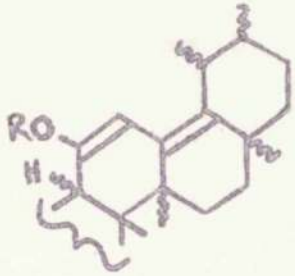
In an attempt to find an alternative route to 11-oxo-18α-olean-12-en-3β-yl acetate (V), it was proposed to form the enol acetate (XI) of 11-oxo-olean-12-en-3β-yl acetate (IV), and obtain (V) by hydrolysis of (XI).



(XI)



(XII)

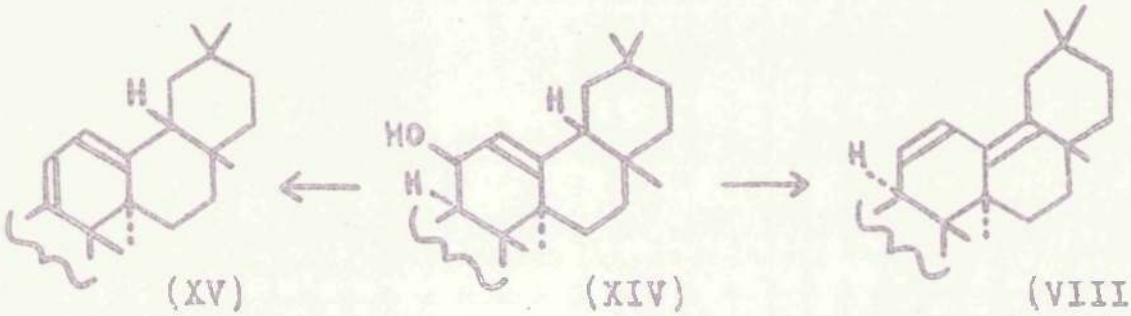


(XIII)

Neither (IV) or (V), however, gave 11-acetoxyoleana-11:13 (18)-dien-3β-yl acetate (XI) under standard conditions of enol acetylation. Forcing enol acetylation of 11-oxours-12-en-3β-yl acetate (VI) (Beaton, Spring, Stevenson and Strachan, J., 1955, in press) did not yield the heteroannular enol acetate (XIII), but 11-acetoxyursa-9(11):12-dien-3β-yl acetate (XII), hydrolysi and acetylation of which reaffords (VI) showing that rings B ar C are fused in the more stable form. These differences in enol- ization behaviour afford an explanation of the differences in bromination behaviour of (IV), (V) and (VI) described above.

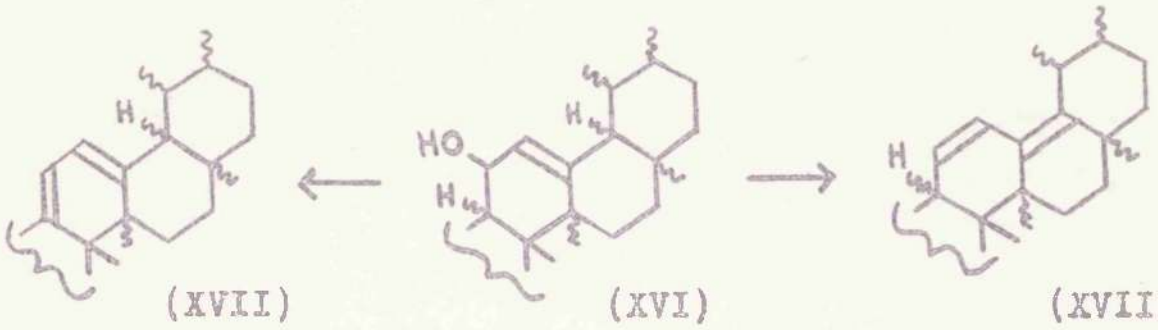
(B). Dehydration of 11β-hydroxy-12-en-3β-yl acetates.

Reduction of 11-oxo-olean-12-en-3β-yl benzoate (IV, R=Bz with lithium aluminium hydride, followed by acetylation, gives 11β-hydroxyolean-12-en-3β-yl acetate (XIV), which may be dehydrated with acetic anhydride-sodium acetate to yield oleana 9(11):12-dien-3β-yl (XV), and which on treatment with mineral acid affords oleana-11:13(18)-dien-3β-yl acetate (VIII).



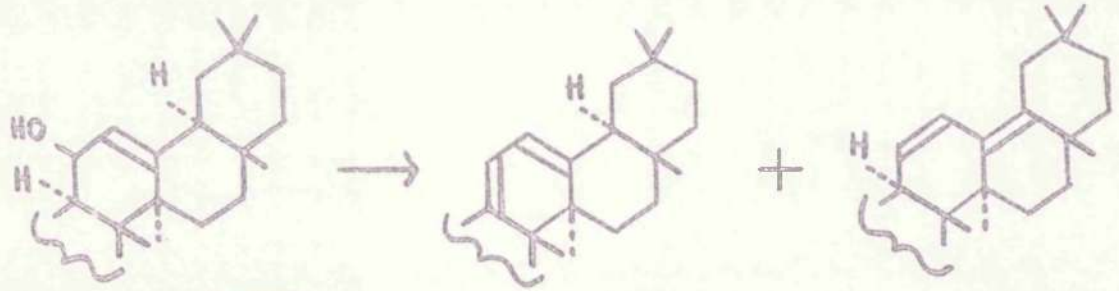
(XV) (XIV) (VIII)

It was considered that a comparison of the behaviour of 11-oxours-12-en-3β-yl acetate (VI) and 11-oxo-18α-olean-12-en-3β-yl acetate (V), under the same conditions, might throw some light on their relative configurations in rings C, D and E particularly at C_{18}. 11-Oxours-12-en-3β-yl acetate (VI) was therefore reduced with lithium aluminium hydride to yield 11β-hydroxyurs-12-en-3β-yl acetate (XVI). The β-(axial)-configuration is ascribed to the hydroxy group in (XVI) because it is not acylatable and readily dehydrates (trans-elimination) with acetic anhydride-pyridine to yield ursa-9(11):12-dien-3β-yl acetate (XVII). Treatment of (XVI) with mineral acid in an attempt to obtain ursa-11:13(18)-dien-3β-yl acetate (XVIII) (Easton, Manson and Spring, J., 1953,943), under the conditions which yield oleana-11:13(18)-dien-3β-yl acetate from (XIV), afforded only (XVII).



(XVII) (XVI) (XVIII)

From these observations and the formation of the homo-annular type enol acetate (XII), rather than a heteroannular type (XIII), it appeared that there existed some conformationa restraint to the introduction of an ethylenic linkage between C_{13} and C_{18} in the ursane series. Under the same conditions, 11-oxo-18α-olean-12-en-3β-yl acetate (V) was reduced with lithium aluminium hydride and acetylated to give 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX). The β-(axial)-configurati is ascribed to the hydroxyl group in (XIX) because it is not acylatable.



(XIX) (XX) (VIII)

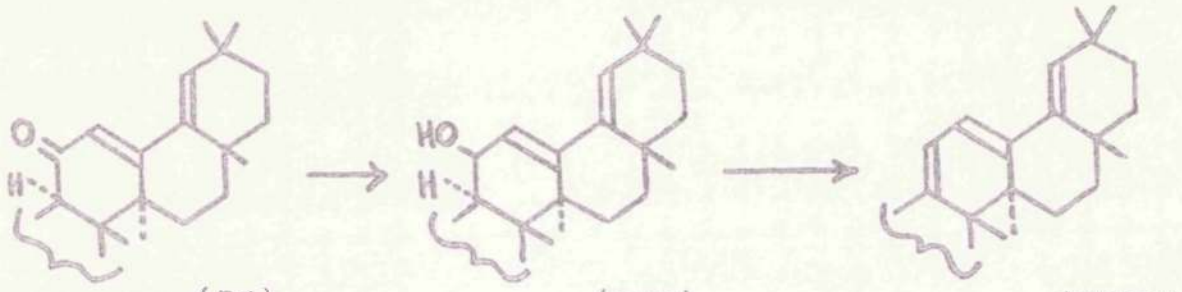
Unlike (XIV) and (XVI), (XIX) is not unilaterally dehydrated with acetic anhydride-sodium acetate to yield a homoannular dienyl acetate but affords mixed crystals of what is considered to be 18α-oleana-9(11):12-dien-3β-yl acetate (XX and oleana-11:13(18)-dien-3β-yl acetate (VIII). The specific rotation and ultra-violet absorption spectrum of the mixed crystals show that they consist of approximately 70% hetero-annular dienyl acetate and 30% homoannular dienyl acetate.

Similar mixed crystals were obtained by (a) treatment of 11-oxo-18α-olean-12-en-3β-yl acetate (V) with sodium-amyl alcohol followed by acetylation, and (b) refluxing 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX) with dimethylaniline. Treatment of the mixed crystal with hydrochloric acid in aceti acid converted it into pure heteroannular dienyl acetate (VIII) and this was obtained directly from (XIX) by similar treatment.

Thus, since both 11β-hydroxyolean-12-en-3β-yl acetate (XI and its 18α-isomer (XIX) give oleana-11:13(18)-dien-3β-yl acetate (VIII) on treatment with mineral acid then the configuration at C_{18} does not affect the acid rearrangement. The explanation for the non-formation of ursa-11:13(18)-dien-3β-yl acetate (XVIII) from 11β-hydroxyurs-12-en-3β-yl acetate (XVI), must therefore be sought elsewhere in the molecule. The difference in dehydration behaviour of (XIX) was initially assumed to be due to the extreme ease of isomerization of the then unknown 18α-oleana-9(11):12-dien-3β-yl acetate (XX) to oleana-11:13(18) dien-3β-yl acetate (VIII), but subsequent preparation of (XX) (to be discussed later) showed that it was only slightly less stable to mineral acid treatment than its 18β-isomer (XV).

Since differences existed in the ease of dehydration of 11β-hydroxyolean-12-en-3β-yl acetate (XIV) and 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX), it was of interest to examine the case where no hydrogen atom was present at C_{18} and the compound selected for comparison was 11-oxo-oleana-12:18-dien-3β-yl acetate (IX). Reduction of (IX) with lithium aluminium hydride yields 11β-hydroxyoleana-12:18-dien-3β-ol (XXI, R = H) which, on refluxing with acetic anhydride-sodium acetate for prolonged periods, undergoes no dehydration and affords 11β-hydroxyoleana-12:18-dien-3β-yl acetate (XXI) as the sole produc

no trace of oleana-9(11):12:18-trien-3β-yl acetate (XXII) being observed. The β-(axial)-configuration is ascribed to the hydrox in (XXI) since it is not acylatable. To demonstrate that oleana 9(11):12:18-trien-3β-ol (XXII, R = H) could in fact be obtained from (XXI, R = H), 11β-hydroxyoleana-12:18-dien-3β-ol was treate with hydrochloric-acetic acid mixture. Oleana-9(11):12:18-trien 3β-ol was obtained in good yield and further characterized by conversion to its acetate (XXII).



(IX) (XXI) (XXII)

Thus, on comparing the dehydrating action of acetic anhydride-sodium acetate on 11β-hydroxyurs-12-en-3β-yl acetate (XVI) with the behaviour of the allylic alcohols (XIV), (XIX) and (XXI), the similarity in behaviour of (XVI) and 11β-hydroxy olean-12-en-3β-yl acetate (XIV) leads to the conclusion that the configurations at C_{18} in (XVI) and (XIV) might be the same.

(c). Oxidation of -12-en-3β-yl acetates.

In an attempt to obtain more information to support the view that the configurations at C_{18} in oleanane and ursane might be identical, the oxidations of olean-12-en-3β-yl acetat (I), urs-12-en-3β-yl acetate (II) and 18α-olean-12-3β-yl aceta (VII) were compared. 18α-Olean-12-en-3β-yl acetate was prepare from 11-oxo-18α-olean-12-en-3β-yl acetate (V), using the method of Budziarek et al. (loc.cit.), or by the hydrogenolysis of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX), and was fully characterized by hydrolysis to the alcohol, and by the preparation of various esters.

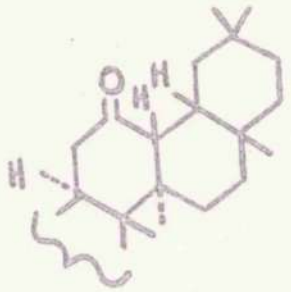
Olean-12-en-3β-yl acetate (I) on oxidation with selenium dioxide yields oleana-11:13(18)-dien-3β-yl acetate (VIII) (Ruzicka, Müller and Schellenberg, Helv.Chim.Acta,1939,22,767; Barton and Brooks, J., 1951,257) and urs-12-en-3β-yl acetate (under comparable conditions gives a small yield (1%) of ursa-11:13(18)-dien-3β-yl acetate (Easton et al., loc.cit.). Simila treatment of 18α-olean-12-en-3β-yl acetate (VII) yields oleana-11:13(18)-dien-3β-yl acetate (VIII) (Budziarek et al., loc.cit. Thus the configuration at C_{18} in no way influences the formati of the heteroannular dienyl acetate, though in the ursane seri the conformational resistance to the introduction of a C_{13}:C_{18} double bond appears to operate.

Olean-12-en-3β-yl acetate (I) on oxidation with N-bromo-succinimide yields oleana-9(11):12:18-trien-3β-yl acetate (XXI (Ruzicka, Jeger and Redel, Helv.Chim.Acta, 1943,26,1235) whils urs-12-en-3β-yl acetate affords ursa-9(11):12-dien-3β-yl aceta (XVII) (idem, loc.cit.). In view of this definite difference, the action of N-bromosuccinimide on 18α-olean-12-en-3β-yl acetate (VII) was examined in the expectation that since

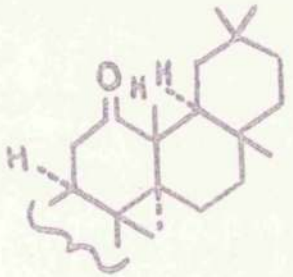
11-oxo-18α-olean-12-en-3β-yl acetate (V) and 11-oxours-12-en-3β-yl acetate (VI) were indifferent to bromination, (VII) might be expected to yield 18α-oleana-9(11):12-dien-3β-yl acetate (X only. In fact, oxidation of 18α-olean-12-en-3β-yl acetate (VII) yielded oleana-9(11):12:18-trien-3β-yl acetate (XXII), which shows that the βα-configurations at C_{17} and C_{18} of (IIIa) (Ruzicka, Experientia, 1953, 9, 357) in urs-12-en-3β-yl acetate (II) is not the factor which prevents the formation of an ursatrienyl acetate. The failure of (II) to form an analogue of oleana-9(11):12:18-trien-3β-yl acetate (XXII) could possibly be ascribed to a steric influence of the substituent at C_{19}, absent in the oleanane series.

(D). Bromination of 12-oxo-an-3β-yl acetates.

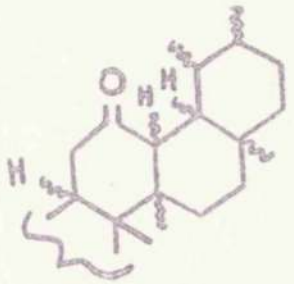
A comparison of the behaviour of the saturated ketones (XXIII), (XXIV) and (XXV) on bromination, was undertaken.



(XXIII)



(XXIV)

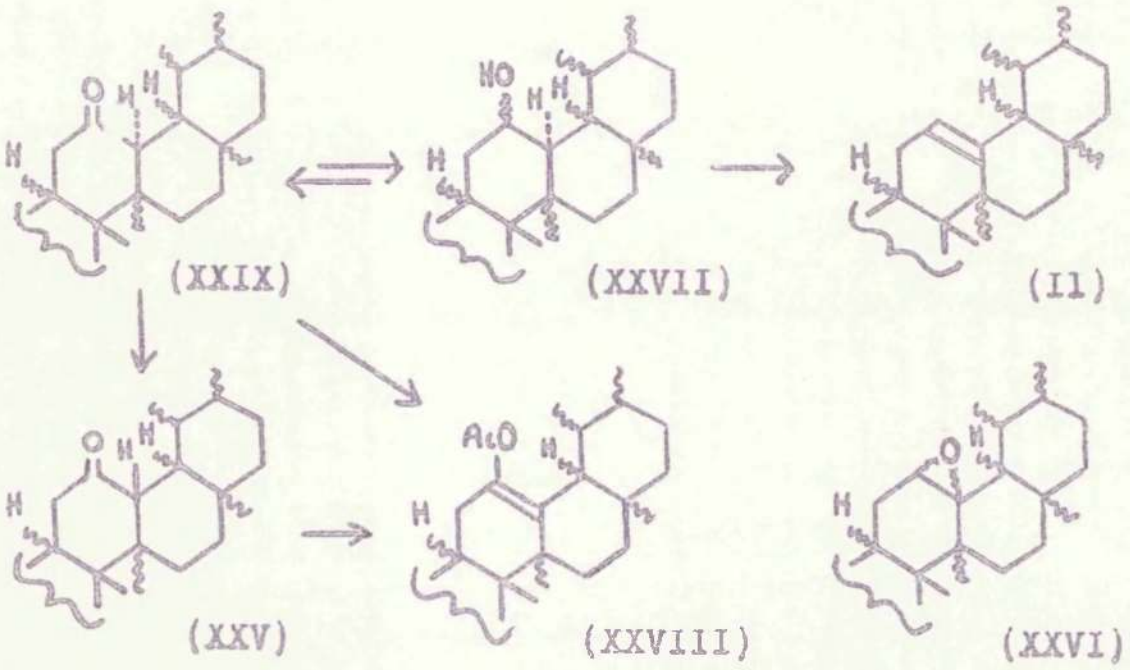


(XXV)

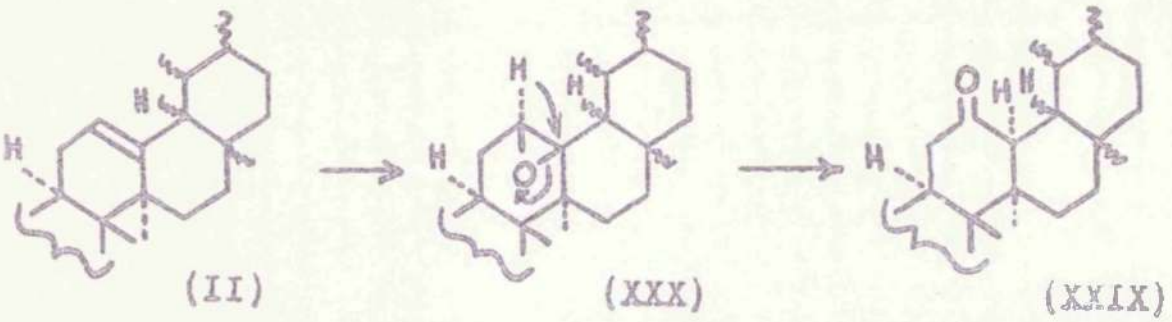
12-Oxo-oleanan-3β-yl acetate (XXIII) is obtained by the hydrogen peroxide oxidation of olean-12-en-3β-yl acetate (I) in acetic acid (Picard, Sharples and Spring, J., 1939,1045). Similar oxidation of urs-12-en-3β-yl benzoate (II, R = Bz) gives a product, $C_{37}H_{54}O_3$, $[\alpha]_D$ +132°, which was considered to be a saturated ketone (Seymour, Sharples and Spring, J., 1939,1075). The corresponding acetate, $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, was obtained by oxidation of urs-12-en-3β-yl acetate (II) with either ozone (Ruzicka, Jeger, Redel and Volli, Helv.Chim.Acta, 1945,28,199), or hydrogen peroxide in acetic acid (McLean, Silverstone and Spring, J., 1951,935), and since this oxidation product is isomerized by mineral acid to 12-oxoursan-3β-yl acetate (XXV), $[\alpha]_D$ +11°, and carbonyl absorption was not observed in its ultraviolet absorption spectrum, it was considered to be 12:13-epoxyursan-3β-yl acetate (XXVI). The structure of the related benzoate was revised to 12:13-epoxyursan-3β-yl acetate (XXVI, R = Bz), and a compound $C_{30}H_{50}O$, $[\alpha]_D$ +135°, obtained by oxidation of urs-12-ene with hydrogen peroxide, was described as 12:13-epoxyursane.

Treatment of the benzoate, $C_{37}H_{54}O_3$, and the compound $C_{30}H_{50}O$, with hydrochloric acid gave 12-oxoursan-3β-yl benzoate (XXV, R = Bz), $[\alpha]_D$ +25°, and 12-oxoursane, $[\alpha]_D$ 0°, respectively.

A consideration of this data leads to the conclusion that a ketone structure for the oxidation products of α-amyrin ester had not rigorously been excluded and experiments were therefore initiated to determine unequivocally, the nature of the new oxygen function. Treatment of the acetate $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, with lithium aluminium hydride yielded a product, acetylation of which, either at room temperature or at 100°, gives 12ξ-hydroxyursan-3β-yl acetate (XXVII). This product could originate from either an epoxide or a ketone. To differentiate between these possibilities, the diol monoacetate (XXVII) was oxidized with chromic acid at room temperature. The oxidation product was identical with the acetate $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, and hence the epoxide structure is eliminated and the oxygen function is present as a carbonyl group. This conclusion was confirmed by the infra-red spectrum of the acetate $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, which shows a well defined carbonyl band at 1707 cm^{-1}.



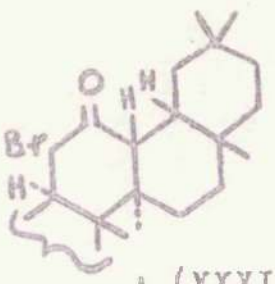
The conversion of the acetate $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, into 12-oxoursan-3β-yl acetate must therefore be represented as a simple inversion at C_{13} since treatment of the diol monoacetate (XXVII) with phosphoryl or benzoyl chloride in pyridine yields urs-12-en-3β-yl acetate (II), and both 12-oxoursan-3β-yl acetat (XXV) and the acetate $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, give the same enol acetate, 12-acetoxyurs-12-en-3β-yl acetate (XXVIII). The acetat $C_{32}H_{52}O_3$, $[\alpha]_D$ +114°, is therefore 12-oxo-13α-ursan-3β-yl aceta (XXIX), [The assignment of the β-configuration to the C_{13} hydrogen in 12-oxoursan-3β-yl acetate (XXV) is based on the oxidation of 12-oxours-9(11)-en-3β-yl acetate (XXXV), shortly to be discussed.], and the related compounds obtained by the oxidation of urs-12-en-3β-yl benzoate and urs-12-ene with hydrogen peroxide are 12-oxo-13α-ursan-3β-yl benzoate and 12-ox 13α-ursane respectively. The conversion of urs-12-en-3β-yl acetate (II) into 12-oxo-13α-ursan-3β-yl acetate (XXIX) may include the formation of an unstable β-epoxide (XXX), which rearranges by the transfer of the C_{12}-hydrogen across the α-fac to C_{13}. The ketone used in comparison studies was the stable ketone (XXV) in which the C_9-hydrogen has the α-configuration. [The assignment of the α-configuration is based on the acid isomerization of urs-9(11):12-dien-3β-yl acetate (XVII), short to be discussed.]



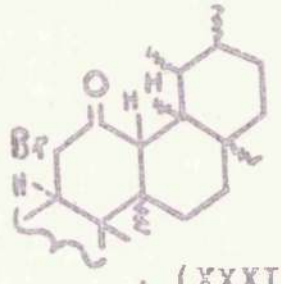
(II) (XXX) (XXIX)

The third saturated ketone, 12-oxo-18α-oleanan-3β-yl aceta (XXIV) had been prepared by Budziarek *et al.* (*loc.cit.*) in poor yield. In an endeavour to improve this yield, 18α-olean-12-en-3β-yl acetate (VII) in ethyl acetate solution was oxidized usin hydrogen peroxide in formic acid. The yield was doubled and the product (XXIV) was hydrolysed to the corresponding alcohol and further characterized by the preparation of the related benzoat In general, for the oxidation of an ethylene to a saturated ketone, this method gives enhanced yields. The ketones (XXIII) and (XXIV) were further characterized by reduction with lithium aluminium hydride to the diols, 12ξ-hydroxyoleanan-3β-ol and 12ξ-hydroxy-18α-oleanan-3β-ol.

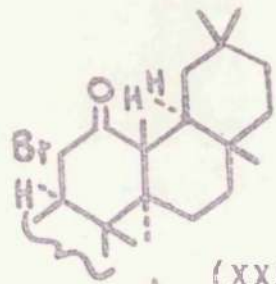
With regard to the bromination of the ketones (XXIII), (XXIV) and (XXV), it had previously been shown that 12-oxo-oleanan-3β-yl acetate (XXIII) and 12-oxoursan-3β-yl benzoate (XXV, R = Bz) yield the bromoketones (XXXI) and (XXXII, R = Bz) which, on heating with acetic acid containing a trace of hydro-bromic acid, readily lose hydrogen bromide and yield 12-oxo-olean-9(11)-en-3β-yl acetate (XXXIV) and 12-oxours-9(11)-en-3β-benzoate (XXXV, R = Bz) respectively (Seymour and Spring, J., 1941,319). In contrast, it was found that the action of bromine on 12-oxo-18α-oleanan-3β-yl acetate (XXIV) gives a bromoketone which under similar conditions did not dehydrobrominate (Budziarek *et al.*, *loc.cit.*). It was decided to investigate thi aspect of the chemistry of the 18α-saturated ketone (XXIV), sin it seemed allied to the difficulties of dehydration of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX) already discussed.



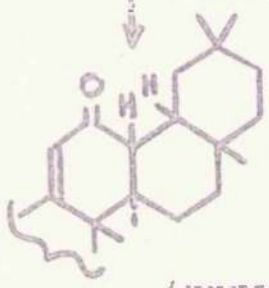
(XXXI)



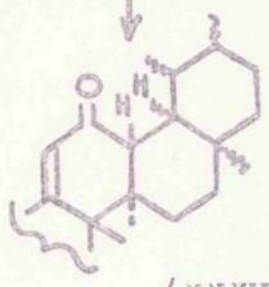
(XXXII)



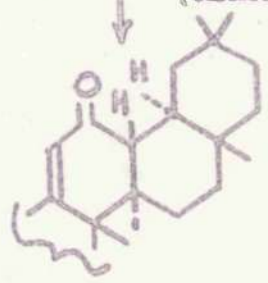
(XXXIII)



(XXXIV)



(XXXV)



(XXXVI)

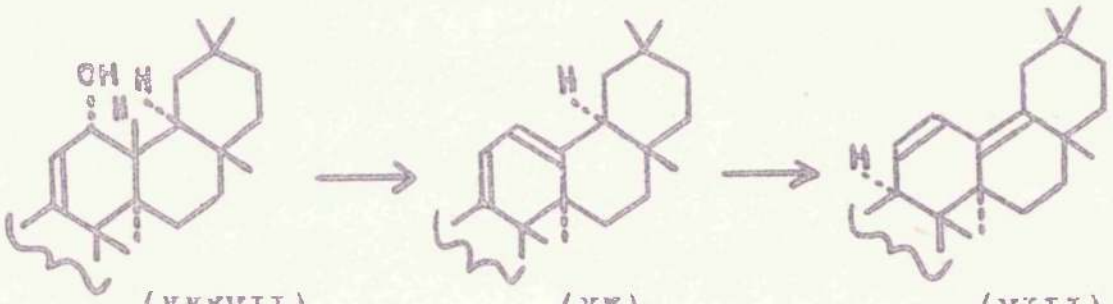
Bromination of the 18α-saturated ketone (XXIV) in a quart: flask, with ultra-violet irridiation, gave more consistent yields of the bromoketone than did the method of Budziarek et al. (loc.cit.). An examination of the infra-red absorption spectrum, to determine the configuration of the Br-atom, showe a band at 1706 $cm.^{-1}$ characteristic of an axial Br-atom (Corey, J.Amer.Chem.Soc., 1953,2301). The 18α-bromoketone is therefore 11β-bromo-12-oxo-18α-oleanan-3β-yl acetate (XXXIII), and in spite of the fact that the geometry of (XXXIII) is favourable for easy elimination of hydrogen bromide, the bromoketone prov to be very stable. The ease of dehydrobromination of (XXXI) an (XXXII) indicates the β-(axial)-configuration of the Br-atom i both these bromoketones, and the difference between this behaviour and that of (XXXIII) leads to the conclusion that th 18α-configuration causes this difference, and if C_{17} in the ursane bromoketone (XXXII) has the β-configuration, then consequently the ursane ketone (XXV) has not an α-configuration at C_{18}.

(E). Acid rearrangements of -9(11):12-dien-3β-yl acetates.

Oleana-9(11):12-dien-3β-yl acetate (XV) is isomerized by vigorous treatment with acid to oleana-11:13(18)-dien-3β-yl acetate (VIII) (cf. Section 1.) and ursa-9(11):12-dien-3β-yl acetate (XVII) can be also isomerized to (VIII), *via* ursa-11:13(18)-dien-3β-yl acetate (XVIII) (Beaton, Spring, Stevenson and Strachan, *loc. cit.*). From the observations on the dehydrati of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (XIX), it seemed that 18α-oleana-9(11):12-dien-3β-yl acetate (XX) would be very unstable to mild acid treatment, and it was desired to examine and compare the effect of acid treatment of the homoannular dienyl acetates. Since oleana-9(11):12-dien-3β-yl acetate (XV) can be easily prepared from 12-oxo-olean-9(11)-en-3β-yl acetate (XXXIV) (cf. Section 1.), an analogous route for the preparatio of the 18α-isomer (XX) appeared feasible. Dehydrobromination of the 18α-bromoketone (XXXIII), by prolonged refluxing in pyridin gave 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI), which was further characterized by the preparation of the related alcohol and benzoate. The configuration at C_{13} in (XXXVI) is the more stable since (XXXVI) was recovered unchanged (after reacetylati from prolonged treatment with alkali.

Reduction of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI) with lithium aluminium hydride, followed by acetylation of the product, yielded 12α-hydroxy-18α-olean-9(11)-en-3β-yl acetate (XXXVII). The α-(axial)-configuration is ascribed to the hydroxyl group in (XXXVII) because of its hindered nature and because of its relatively simple elimination by treatment with acetic anhydride-sodium acetate yielding 18α-oleana-9(11):12-dien-3β-yl acetate (XX), which shows an absorption maximum at 2780 Å. (E = 9,400) and is strongly dextrorotatory. It was furth

characterized by conversion into the parent alcohol and corresponding benzoate.



(XXXVII) (XX) (VIII)

A comparative hydrochloric-acetic acid isomerization of oleana-9(11):12-dien-3β-yl acetate (XV) and its 18α-isomer (XX was followed spectroscopically and did not show the marked differences expected. At intervals, the reaction solutions were worked up and the solid residues examined. Without exception, the intensities of absorption at 2500 Å, due to the formation of oleana-11:13(18)-dien-3β-yl acetate (VIII), were always higher for the material derived from the 18α-dienyl acetate than for that derived from the 18β-dienyl acetate (cf. Experimental Section 2.) showing that 18α-oleana-9(11):12-dien 3β-yl acetate (XX) is slightly less stable than oleana-9(11):1 dien-3β-yl acetate (XV). 18α-Oleana-9(11):12-dien-3β-yl acetat like (XV), was recovered unchanged from hydrochloric-acetic acid mixture after standing at room temperature for 80 hours.

(F). Ultra-violet absorption spectra.

The rather low wavelength of the absorption maximum of 18α-oleana-9(11):12-dien-3β-yl acetate (XX) prompted a comparison of the position of such maxima in the oleanane and 18α-oleanane series. The results allow of the formulation of the general rule, that the change from the higher energy of a cis ring fusion to the lower energy of a trans ring fusion, (18β → 18α), causes a hypsochromic shift of circa 4 mμ. (see Table I.); an observation which may prove of considerable diagnostic significance in the recognition of 18α-oleanane triterpenoids.

The application of this rule to α-amyrin, using a comparison of oleanane, 18α-oleanane and ursane derivatives, does not lead to a definite conclusion, since an insufficient number of suitable ursane derivatives are available. Those available have absorption maxima which, in position, lie nearer to the oleanane rather than to the 18α-oleanane analogu (see Table I.).

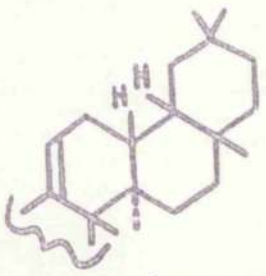
Table I.

C/D/E-chromophores.	18β.	18α.	$-\Delta\lambda$	Ursane.
12-oxo-9(11)-en-	248mμ.	242mμ.	6mμ.	251mμ.
12:19-dioxo-9(11)-en-	246	243	3	-
-9(11):12-dien-	282	278	4	280
11-oxo-12-en-	250	245	5	248
19-oxo-9(11)-en-	302	298	4	-
11-oxo-12-en-28-COOMe	250	248	2	250
11-oxo-12-en-30-COOH	248	243	5	-

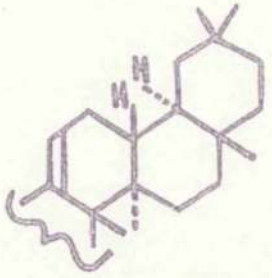
(G). Reactions of 12-oxo-9(11)-en-3β-yl acetates.

To investigate the nature of the D/E ring fusion in α-amyrin, the reactions of 12-oxo-olean-9(11)-en-3β-yl acetate (XXXIV), 12-oxours-9(11)-en-3β-yl acetate (XXXV) and 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI) were examined and compared.

Hydrogenation of (XXXIV) affords olean-9(11)-en-3β-yl acetate (XXXVIII), while (XXXV) could not be reduced by the same method (Jeger and Ruzicka, Helv.Chim.Acta, 1945,28,209). Hydrogenation of (XXXVI) yields a new stereoisomer of β-amyrin acetate, 18α-olean-9(11)-en-3β-yl acetate (XXXIX), further characterized by the preparation of the related alcohol. The trans-fusion of rings D and E thus does not introduce any steric effect toward catalytic hydrogenolysis of a carbonyl group at C_{12}, and hence an explanation for the hindered nature of such a group in the ursane derivative (XXXV) must be sought elsewhere in the molecule.



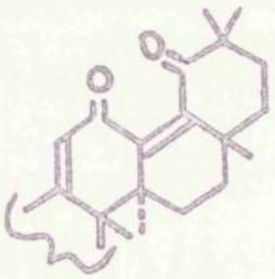
(XXXVIII)



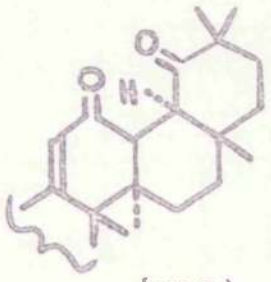
(XXXIX)

12-Oxo-olean-9(11)-en-3β-yl acetate (XXXIV) or 12-oxo-urs-9(11)-en-3β-yl acetate (XXXV) are recovered unchanged after treatment with selenium dioxide in dioxan at 200° (Ruzicka, Jeger and Norymberski, Helv.Chim.Acta, 1942,25,457). Oxidation of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI), using these conditions, gives a mixture of 12:19-dioxo-oleana-9(11):13(18)-dien-3β-yl acetate (XL) as the major product, together with 12:19-dioxo-18α-olean-9(11)-en-3β-yl acetate (XLI). The formati

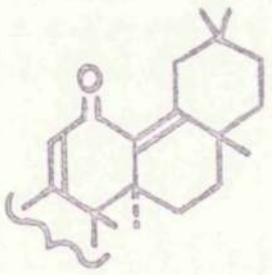
of the 18α-diketone (XLI) by oxidation of (XXXVI) is remarkable (XLI) is not an intermediate in the oxidation of (XXXVI) to (XL since the 18α-diketone (XLI) is recovered unchanged after treatment with selenium dioxide in dioxan at 200°. The formatio of (XLI) is possibly due to a reduction of 12:19-dioxo-oleana-9(11):13(18)-dien-3β-yl acetate (XL) by 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI), which is thereby oxidized to 12-oxo-oleana-9(11):13(18)-dien-3β-yl acetate (XLII). Further oxidatio of (XLII) by selenium dioxide gives (XL), a reaction which has been described (Beaton, Johnston, McKean and Spring, J., 1953, 3660). Attempts to oxidize (XXXVI) to (XLII) by bromination and dehydrobromination were unsuccessful.



(XL)



(XLI)

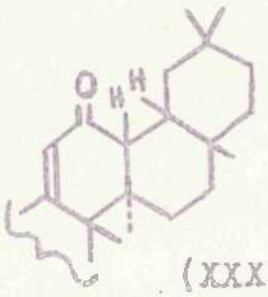


(XLII)

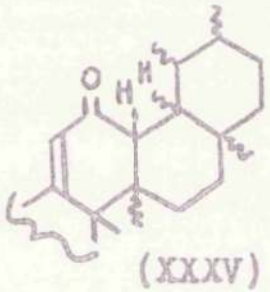
The similarity in behaviour of the α-amyrin derivative (XXXV) and the natural D/E cis-β-fused β-amyrin derivative (XXXIV) with selenium dioxide in dioxan and the marked contrast of the comparable 18α-oleanane derivative (XXXVI), under the same conditions, strongly suggests that rings D and E in α-amyrin are cis-fused.

The establishment of the nature of the D/E ring fusion in ursane drivatives was finally accomplished by a consideration of the oxidation of the αβ-unsaturated ketones (XXXIV), (XXXV) and (XXXVI) with selenium dioxide in acetic acid. Such an oxidation of 12-oxo-olean-9(11)-en-3β-yl acetate (XXXIV) yield

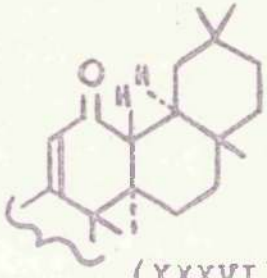
iso-β-amyradienonyl acetate (XLIII) (cf. Section 1.) and similar oxidation of 12-oxours-9(11)-en-3β-yl acetate (XXXV) yields iso-α-amyradienonyl acetate, which has conclusively been shown to have the structure (XLIV) (Easton and Spring, J., 1955, in press).



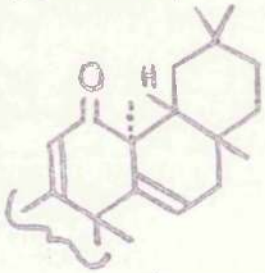
(XXXIV)



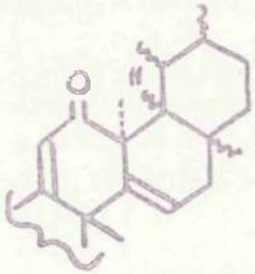
(XXXV)



(XXXVI)



(XLIII)



(XLIV)

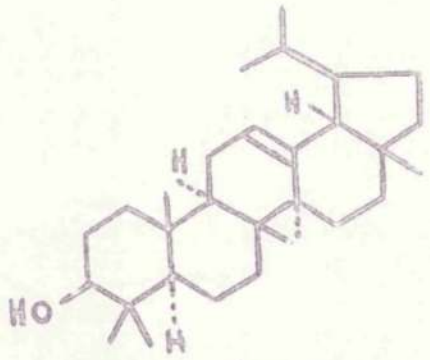
When 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI) is treated with selenium dioxide in acetic acid under the same reaction conditions, it is recovered unchanged.

The difference in behaviour between the isomers (XXXIV), (XXXV) and (XXXVI) suggests that the formation of the new carbon skeleton requires specific relative configurations at C_{13}, C_{14} and C_{18} before methyl group migration can occur from C_{14} to C_{13}. The configurations in 12-oxo-olean-9(11)-en-3β-yl acetate (XXXIV) at C_{13}, C_{14} and C_{18} are β,α,β respectively, and permit a synchronous reaction, including the removal of the C_{13} hydrogen (β), and leading to a favourable conformation in the resulting iso-β-amyradienonyl acetate (XLIII) in which the C_{13}-methyl group (α) and the C_{18}-hydrogen (β) are anti-related.

This reaction mechanism is not possible with 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XXXVI) because the configurations at C_{14} and C_{18} cannot lead to the stable anti-relationship betwee C_{13} and C_{18} by C_{14}-methyl (α) group migration, which must occu by migration across the α-face.

Since such a migration is observed with 12-oxours-9(11)-en-3β-yl acetate (XXV), it follows that the configurations at C_{13}, C_{14} and C_{18} in (XXXV) must be the same as in (XXXIV), i.e., β, α, β. This confirms the indications already discussed that the configuration of the hydrogen at C_{18} is the same in the oleanane and ursane series, and as a sequel it follows tha rings D and E in α-amyrin are cis-β-fused.

Recently a structure (IIA), embodying a cis-β-fusion for the D/E ring junction, has been proposed for α-amyrin (Allan, Beaton, Shaw, Spring, Stevenson, Stewart and Strachan, Chem. and Ind., 1955,281),



(IIA)

and this is the formulation which will be used in Section (3) of this thesis.

Experimental

Section (2).

Melting points were determined using a standardised N.P.L. thermometer.

Specific rotations were measured in chloroform solution in a 1 dm. tube at approximately 15°

Ultra-violet absorption spectra were determined in ethanol solution with a Unicam SP.500 spectrophotometer and (E) denotes intensity of absorption.

Colour reactions with tetranitromethane were done in chloroform solution.

For chromatography, alumina (Brockmann Grade II) was used, in the ratio 30:1 of substance chromatographed, and light petroleum refers to that fraction of b.p. 40-60°

The phrase 'in the usual way' implies, in general, dilution with water, extraction with ether, washing consecutively with aqueous sodium hydroxide, water, aqueous hydrochloric acid and aqueous sodium bicarbonate, followed by drying of the ethereal extract over anhydrous sodium sulphate, filtration and evaporation to dryness under reduced pressure.

Hydrogenations were carried out, at room temperatur in glacial acetic acid which had been refluxed over and distilled from chromium trioxide.

Acetylations were carried out using acetic anhydrid in pyridine solution at 100° for 30 mins., unless otherwis specified.

11-Oxo-18α-olean-12-en-3β-yl Acetate.

A solution of 11-oxo-olean-12-en-3β-yl benzoate (15 g.) in ethanolic potassium hydroxide (15%, 1200 c.c.) was treated under reflux for 52 hrs. The brown solution was concentrated to half bulk and diluted with water. The solid was collected, washed with water and dried. A solution in pyridine (100 c.c.) was treated with acetic anhydride (20 c.c.) and heated on the steam-bath for 1 hr. The product, isolated in the usual way, crystallised from chloroform-methanol as prisms (10 g.), m.p. 276-278°, $[\alpha]_D$ + 74° (c,1.9) undepressed in m.p. on admixture with 11-oxo-18α-olean-12-en-3β-yl acetate, m.p. 278-279°, prepared by the method of Budziarek, Manson and Spring (J., 1951,3336). Concentration of the crystallisation mother liquors afforded plates (3 g.), m.p. 245-255°, $[\alpha]_D$ + 95° (c,2.0). Light absorption: Max. at 2450 Å. (E = 10,000). This material could not be purified by further crystallisation and its solution in ethanolic potassium hydroxide (15%, 250 c.c.) was refluxed for 52 hrs. Isolation of the product and acetylation and crystallisation as before, gave 11-oxo--18α-olean-12-en-3β-yl acetate as prisms (1 g.) m.p. and mixed m.p. 275-277°, $[\alpha]_D$ + 72° (c,1.1), which were recovered unchanged after refluxing with acetic anhydride

and sodium acetate for 80 hrs. Hydrolysis using 5% ethanolic potassium hydroxide for 2 hrs. gave 11-oxo-18α-olean-12-en-3β-ol, m.p. and mixed m.p. 252-254°, $[\alpha]_D$ + 82° (c,0.5). Benzoylation in the usual manner gave 11-oxo-18α-olean-12-en-3β-yl benzoate, which crystallised from chloroform--methanol as plates m.p. 263-264°, $[\alpha]_D$ + 86° (c,1.8) (Found: C,81.2; H,9.6. $C_{37}H_{52}O_3$ requires C,81.6; H,9.6%).

Oxidation of 11-oxo-18α-olean-12-en-3β-yl Acetate with selenium dioxide.

A solution of 11-oxo-18α-olean-12-en-3β-yl acetate (500 mg.) in acetic acid (20 c.c.) was refluxed with selenium dioxide (500 mg.) for 20 hrs. The product isolated in the usual way, was crystallised from methanol to give the 'O_5-acetate' as needles (300 mg.), m.p. and mixed m.p. 267-269°, $[\alpha]_D$ + 33° (c,1.1) (Found: C,75.1; H,9.0. Calc. for $C_{32}H_{46}O_5$: C,75.3; H,9.1%). Light absorption: Max. at 2300 Å. (E = 3,600) and an inflexion at 3000 Å. (E = 340).

11β-Hydroxyurs-12-en-3β-yl Acetate.

A solution of 11-oxours-12-en-3β-yl acetate (1 g.) (Spring and Vickerstaff, J., 1937,249) in ether (500 c.c. was refluxed with lithium aluminium hydride (1 g.) for 2 hours. The product, isolated avoiding the use of mineral acid, was treated with pyridine-acetic anhydride at room temperature for 20 hrs. The acetylated product, isolated in the usual way, was crystallised from chloroform-methanol to yield 11β-hydroxyurs-12-en-3β-yl acetate as plates (650 mg.), m.p. 170-172°, $[\alpha]_D$ - 14° (c,1.5) (Found: C,79.7; H,10.8. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%) Light absorption: Max. at 2100 Å. (E = 5,550).

Dehydration of 11β-Hydroxyurs-12-en-3β-yl Acetate.

(a) A mixture of 11β-hydroxyurs-12-en-3β-yl acetate (250 mg.) acetic anhydride (30 c.c.) and anhydrous sodium acetate (250 mg.) was refluxed for 2 hrs. The product, isolated in the usual way, crystallised from chloroform-methanol to yield ursa-9(11):12-dien-3β-yl acetate as needles (150 mg.), m.p. and mixed m.p. 165-167°, $[\alpha]_D$ + 318° (c,1.2).

(b) A solution of 11β-hydroxyurs-12-en-3β-yl acetate (250 mg.) in acetic acid (250 c.c.) was heated on the

steam-bath with concentrated hydrochloric acid (5 c.c.) for 2 hrs., was allowed to stand at room temperature for 16 hrs. and again heated for 6 hrs. The product, isolated in the usual way crystallised from chloroform--methanol to yield ursa-9(11):12-dien-3β-yl acetate as needles (100 mg.), m.p. and mixed m.p. 165-167°, $[\alpha]_D$ + 317° (c,0.9).

11β-Hydroxy-18α-olean-12-en-3β-yl Acetate.

A solution of 11-oxo-18α-olean-12-en-3β-yl acetate (4 g.) in ether (500 c.c.) was refluxed with lithium aluminium hydride (2 g.) for 2 hrs. and the reaction product acetylated. The acetylated product was isolated in the usual manner and crystallised from chloroform-methanol to give 11β-hydroxy-18α-olean--12-en-3β-yl acetate as needles (3.5 g.), m.p. 238-239°, $[\alpha]_D$ + 46° (c,1.3) (Found: C,79.4; H,11.0. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%). Light absorption: Max. at 2060 Å. (E = 5,600).

Sodium/n-Pentanol reduction of 11-Oxo-18α-olean-12-en--3β-yl Acetate.

A solution of 11-oxo-18α-olean-12-en-3β-yl acetate (500 mg.) in boiling n-pentanol (20 c.c.) was treated with sodium (900 mg.) added portionwise during 1 hr.

and the mixture refluxed for 1 hr. The solvent was removed and the product acetylated for 1½ hrs. with acetic anhydride (10 c.c.) and anhydrous sodium acetate (500 mg.). The acetylated product crystallised from chloroform-methanol as plates (370 mg.) m.p. 216-217°, $[\alpha]_D$ + 21° (c,1.1), which gave a red-brown colour with tetranitromethane and no m.p. depression with oleana-11:13(18)-dien-3β-yl acetate, m.p. 227-229°, $[\alpha]_D$ - 63°. Light absorption : Max. at 2420 (E = 19,000), 2510 (E = 22,000) and 2600 Å. (E = 15,100).

Treatment of 11β-Hydroxy-18α-olean-12-en-3β-yl Acetate with sodium acetate-acetic anhydride.

A mixture of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (250 mg.) anhydrous sodium acetate (500 mg.) and acetic anhydride (30 c.c.) was refluxed for 2 hrs. The product, isolated in the usual way, crystallised from chloroform-methanol as plates (150 mg.), m.p. 214-215° $[\alpha]_D$ + 29° (c,1.7) which gave a red-brown colour with tetranitromethane and no m.p. depression with (a) oleana-11:13(18)-dien-3β-yl acetate, m.p. 227-229°, $[\alpha]_D$ - 63°, or (b) the product of previous experiment, m.p. 216-217°, $[\alpha]_D$ + 21°. Light absorption: Max. at 2420 (E = 21,600)

2500 (E = 23,000) and 2600 Å. (E = 16,000).

Acid dehydration of 11β-hydroxy-18α-olean-12-en-3β-yl Acetate to oleana-11:13(18)-dien-3β-yl Acetate.

A solution of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (270 mg.) in acetic acid (150 c.c.) was heated with concentrated hydrochloric acid (1 c.c.) on the steam-bath for 72 hrs. The product was crystallised from chloroform-methanol to yield oleana-11:13(18)--dien-3β-yl acetate as plates (150 mg.), m.p. and mixed m.p. 227-228°, $[\alpha]_D$ - 63° (c,1.1) (Found: C,82.4; H,10.9. Calc. for $C_{32}H_{50}O_2$. C,82.3; H,10.8%) Light absorption: Max. at 2420 (E = 27,000) 2500 (E = 29,000) and 2600 Å. (E = 20,000).

Rearrangement of mixed crystal from sodium acetate--acetic anhydride dehydration of 11β-Hydroxy-18α-olean--12-en-3β-yl Acetate.

A solution of the mixed crystal (100 mg., m.p. 214-215°, $[\alpha]_D$ + 29°, Light absorption: Ratio of intensities at 2500 and 2800 Å., 6.75) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (0.5 c.c.) on the steam-bath for 80 hrs. The product, isolated in the usual way, crystallised from

chloroform-methanol to yield oleana-11:13(18)-dien--3β-yl acetate as plates (50 mg.), m.p. and mixed m.p. 224-225°, $[\alpha]_D$ - 59° (c,0.6). Light absorption: Max. at 2500 Å. (E = 27,500). No absorption at 2800 Å.

11β-Hydroxyoleana-12:18-dien-3β-ol.

A solution of 11-oxo-oleana-12:18-dien-3β-yl acetate (1 g.) (Picard and Spring, J., 1941,35) in ether (100 c.c.) was treated with lithium aluminium hydride (0.5 g.) and allowed to stand overnight at room temperature. The product, isolated in the usual way, crystallised from methanol to yield 11β-hydroxy-oleana-12:18-dien-3β-ol as needles (400 mg.), m.p. 207-208°, $[\alpha]_D$ - 72° (c,2.5) (Found: C,82.0; H,11.0. $C_{30}H_{48}O_2$ requires C,81.8; H,11.0%). Light absorption: Max. at 2410 (E = 24,400) 2500 (E = 26,800) and 2580 Å. (E = 17,600). Acetylation with pyridine-acetic anhydride yielded 11β-hydroxyoleana-12:18-dien-3β-yl acetate which crystallised from chloroform-methanol as prismatic needles, m.p. 211-212°, $[\alpha]_D$ - 53° (c,1.2) which gave an orange colour with tetranitromethane (Found: C,79.6; H,10.8. $C_{32}H_{50}O_3$ requires C,79.3; H,10.8%). Light absorption: Max. at 2410 (E = 25,600) 2500 (E = 28,000) and 2580 Å. (E = 17,600).

Treatment of 11β-Hydroxyoleana-12:18-dien-3β-ol with sodium acetate-acetic anhydride.

A mixture of 11β-hydroxyoleana-12:18-dien-3β-ol (250 mg.) anhydrous sodium acetate (500 mg.) and acetic anhydride (30 c.c.) was refluxed for 4 hrs. The product, isolated in the usual way, crystallised from chloroform-methanol to yield 11β-hydroxyoleana-12:18--dien-3β-yl acetate as needles (230 mg.), m.p. and mixed m.p. 210-211°, $[\alpha]_D$ - 54° (c,0.9).

Acid dehydration of 11β-Hydroxyoleana-12:18-dien--3β-ol to Oleana-9(11):12:18-trien-3β-ol.

A solution of 11β-hydroxyoleana-12:18-dien-3β-ol (200 mg.) in acetic acid (50 c.c.) was treated with concentrated hydrochloric acid (0.5 c.c.) on the steam--bath for 10 hrs. The product isolated in the usual way crystallised from methanol to yield oleana-9(11):12:1 -trien-3β-ol as plates (50 mg.), m.p. 183-185°, $[\alpha]_D$ + 530° (c,0.5) which gave a deep brown colour with tetranitromethane. Light absorption: Max. at 3100 Å. (E = 12,800). Acetylation using pyridine-acetic anhydride gave oleana-9(11):12:18-trien-3β-yl acetate as plates (40 mg.) from methanol, m.p. and mixed m.p. 183-184°, $[\alpha]_D$ + 540° (c,0.4) which gave a deep brown

colour with tetranitromethane.

18α-Olean-12-en-3β-yl Acetate.

(a) A solution of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (200 mg.) in purified acetic acid (150 c.c.) (free from mineral acid) was shaken with platinum (from 100 mg. of PtO_2) and hydrogen for 16 hrs. The product was crystallised from chloroform-methanol to yield 18α-olean-12-en-3β-yl acetate as plates (150 mg.), m.p. and mixed m.p. 243-244°, $[\alpha]_D$ + 50° (c,0.8). Light absorption: Max at 2080 Å. (E = 4,600). Hydrolysi using 5% ethanolic potassium hydroxide gave 18α-olean-12-en-3β-ol which crystallised from chloroform-methanol as long needles, m.p. 213-214°, $[\alpha]_D$ + 50° (c,1.9) (Found: C,84.3; H,11.9. $C_{30}H_{50}O$ requires C,84.4; H,11.8% Benzoylation gave 18α-olean-12-en-3β-yl benzoate which crystallised from chloroform-methanol as plates, m.p. 223-225°, $[\alpha]_D$ + 64° (c,3.5) (Found: C,83.4; H,10.4 $C_{37}H_{54}O_2$ requires C,83.7; H,10.3%). Hydrolysis for 16 hrs. using 10% ethanolic potassium hydroxide gave 18α-olean-12-en-3β-ol, m.p. and mixed m.p. 212-214°, $[\alpha]_D$ + 49° (c,1.2).

(b) A solution of 11-oxo-18α-olean-12-en-3β-yl benzoate (800 mg.) in acetic acid (300 c.c.) was shaken with

platinum (from 300 mg. of PtO_2) and hydrogen for 48 hrs. The reaction product separated as plates after 30 hrs. Isolation of the product in the usual manner and crystallisation from chloroform-methanol yielded 18α-olean-12-en-3β-yl hexahydrobenzoate as plates (600 mg.), m.p. 210-211°, $[\alpha]_D$ + 48° (c,2.3) (Found: C,82.4; H,11.1. $C_{37}H_{60}O_2$ requires C,82.8; H,11.3%). Hydrolysis of the hexahydrobenzoate by using 10% ethanolic potassium hydroxide for 16 hrs., followed by crystallisation of the product from chloroform-methanol gave 18α-olean-12-en-3β-ol as needles, m.p. and mixed m.p. 211-213°, $[\alpha]_D$ + 48° (c,0.8). Acetylation by pyridine-acetic anhydride yielded, 18α-olean-12-en-3β-yl acetate as plates from chloroform-methanol, m.p. and mixed m.p. 245-246°, $[\alpha]_D$ + 52° (c,1.0).

Oxidation of 18α-olean-12-en-3β-yl Acetate to Oleana-9(11):12:18-trien-3β-yl acetate with N-bromosuccinimide.

A solution of 18α-olean-12-en-3β-yl acetate (500 mg.) in carbon tetrachloride (50 c.c.) was refluxed with N-bromosuccinimide (400 mg.) and anhydrous calcium carbonate (1 g.) for 3 hrs. After filtration, the solution was washed with 10% sodium thiosulphate and the product isolated in the usual way. Crystallisation from acetone gave olean-9(11):12:18-trien-3β-yl acetate as plates (300 mg.), m.p. and mixed m.p. 184-185° , $[\alpha]_D$

+ 525° (c,0.7). Light absorption: Max. at 3100 Å. (E = 12,000).

12-Oxo-oleanan-3β-yl Acetate.

A solution of olean-12-en-3β-yl acetate (40 g.) in ethyl acetate (2.8 l.) was treated at 50-60° with a solution of hydrogen peroxide (30%, 200 c.c.) in formic acid (98%, 600 c.c.) added, with stirring over 2 hrs. The mixture was stirred for a further 4 hrs. and evaporated under reduced pressure to small bulk. The product crystallised as prismatic needles (36 g.), m.p. 294-296°, $[\alpha]_D$ - 7° (c,3.3). Recrystallisation from chloroform methanol yielded 12-oxo-oleanan-3β-yl acetate as plates, m.p.293-300°, $[\alpha]_D$ - 15° (c,1.9).

12-Oxo-13α-ursan-3β-yl Acetate.

A solution of urs-12-en-3β-yl acetate (5 g.) in acetic acid (250 c.c.) was treated at 100° with a mixture of hydrogen peroxide (30%, 30 c.c.) and acetic acid (30 c.c.) added dropwise during 30 mins. with vigorous stirring. Stirring was continued for 2 hrs. at 100° when the solution was again treated with hydrogen peroxide (30%, 20 c.c.) in acetic acid (20 c.c.) during 15 mins. The solution was maintained at 100° for a further hour and then diluted with hot water until the

mixture became faintly opalescent. The crystalline solid which separated on cooling was recrystallised from chloroform-methanol to yield 12-oxo-13α-ursan-3β-yl acetate as blades (3.0 g.), m.p. 209-211°, $[\alpha]_D$ + 112° (c,1.5). Infra-red absorption in carbon tetrachloride solution. Bands at 1732 (acetate) and 1707 $cm.^{-1}$ (6 ring ketone). 12-Oxo-13α-ursan-3β-yl benzoate, obtained from urs-12-en-3β-yl benzoate (5 g.) in a similar manner, crystallised from chloroform--methanol as needles (2.7 g.) m.p. 218-219°, $[\alpha]_D$ + 132° (c,1.5).

12ξ-Hydroxy-13α-ursan-3β-yl Acetate.

A solution of 12-oxo-13α-ursan-3β-yl acetate (1.5 g.) in ether (750 c.c.) was treated with lithium aluminium hydride (1.5 g.) and allowed to stand at room temperature for 20 hrs. The product, isolated in the usual way, was acetylated by heating with pyridine-acetic anhydride for 15 mins. at 100°. The product obtained was crystallised from chloroform-methanol to yield 12ξ-hydroxy-13α-ursan-3β-yl acetate as plates (900 mg.), m.p. 234-235°, $[\alpha]_D$ + 68° (c,2.5) (Found: C,78.7; H,11.1. $C_{32}H_{54}O_3$ requires C,79.0; H,11.2%).

Oxidation of 12ξ-Hydroxy-13α-ursan-3β-yl Acetate with Chromic Acid.

A solution of chromium trioxide (75 mg.) in acetic acid (15 c.c.) was added dropwise over 15 mins. with vigorous stirring to a solution of 12ξ-hydroxy-13α-ursan-3β-yl acetate (500 mg.) in acetic acid (300 c.c.) at room temperature. After standing overnight at room temperature the reaction mixture was worked up in the usual way and the product crystallised from chloroform-methanol to yield 12-oxo-13α-ursan-3β-yl acetate as plates (400 mg.), $[\alpha]_D$ + 115° (c,2.3), m.p. and mixed m.p. 209-211°.

Dehydration of 12ξ-Hydroxy-13α-ursan-3β-yl Acetate

(a) A mixture of 12ξ-hydroxy-13α-ursan-3β-yl acetate (200 mg.) phosphoryl chloride (5 c.c.) and pyridine (20 c.c.) was refluxed for 2 hrs. The product isolated using benzene, was crystallised from chloroform-methanol to yield urs-12-en-3β-yl acetate as plates (100 mg.), m.p. and mixed m.p. 225-227°, $[\alpha]_D$ + 80° (c,1.1)

(b) A solution of 12ξ-hydroxy-13α-ursan-3β-yl acetate (500 mg.) in pyridine (15 c.c.) was refluxed with benzoyl chloride (2 c.c.) for 20 hrs. The product (400 mg.)

isolated in the usual way, was dissolved in benzene--petrol (1:4, 100 c.c.) and chromatographed on alumina. Elution with petrol (500 c.c.) gave urs-12-en-3β-yl acetate which crystallised from chloroform-methanol as plates (160 mg.), $[\alpha]_D$ + 80° (c,0.9) m.p. and mixed m.p. 226-227°. Elution with benzene (1000 c.c.) gave unchanged 12ξ-hydroxy-13α-ursan-3β-yl acetate which crystallised from chloroform-methanol as plates (150 mg.) $[\alpha]_D$ + 65° (c,1.1) m.p. and mixed m.p. 233-235°.

12-Acetoxyurs-12-en-3β-yl Acetate.

(a) A mixture of 12-oxoursan-3β-yl acetate (1 g.) anhydrous sodium acetate (1 g.) and acetic anhydride (30 c.c.) was refluxed for 40 hours. The product, isolated in the usual way, crystallised from chloroform--methanol as needles (850 mg.), m.p. 257-259°, $[\alpha]_D$ + 49° (c,2.3).

(b) A mixture of 12-oxo-13α-ursan-3β-yl acetate (1 g.) anhydrous sodium acetate (1 g.) and acetic anhydride (30 c.c.) was refluxed for 40 hrs. The product, isolated in the usual way, was crystallised from chloroform-methanol to yield 12-acetoxyurs-12-en-3β-yl acetate as needles (900 mg.), m.p. and mixed m.p. 256-258°, $[\alpha]_D$ + 50° (c,1.7).

12-Oxo-18α-oleanan-3β-yl Acetate.

A solution of 18α-olean-12-en-3β-yl acetate (7 g.) in ethyl acetate (500 c.c.) was treated at 50-60° with a solution of hydrogen peroxide (30%, 30 c.c.) in formic acid (98%, 100 c.c.) added with stirring, over 1 hr. The mixture was kept for 24 hrs. and evaporated under reduced pressure to small bulk. The crystalline solid was collected and the filtrate evaporated to dryness. The residual gum (4 g.) in benzene (100 c.c.) was chromatographed on a column of Grade II/III alumina and the column washed with benzene (1000 c.c.). Evaporation of the eluate gave a crystalline solid (1 g.) Recrystallisation of this solid and of the original crystalline product gave 12-oxo-18α-oleanan-3β-yl acetate as plates (3 g.) from chloroform-methanol, m.p. 286-287°, $[\alpha]_D$ + 77° (c,1.5) (Found: C,79.1; H,10.8. Calc. for $C_{32}H_{52}O_2$: C,79.3; H,10.8%). Hydrolysis of the acetate by using 5% ethanolic potassium hydroxide followed by crystallisation from methanol yielded 12-oxo--18α-oleanan-3β-ol as rods, m.p. 305-307°; $[\alpha]_D$ + 89°, (c,0.7). Benzoylation, and isolation in the usual manner, gave 12-oxo-18α-oleanan-3β-yl benzoate as plates from chloroform-methanol, m.p. 294-295°, $[\alpha]_D$ + 90° (c,2.5) (Found: C,80.9; H,9.8. $C_{37}H_{54}O_3$ requires C,81.3; H,9.95%). Hydrolysis for 16 hrs. using 10% ethanolic

potassium hydroxide gave 12-oxo-18α-oleanan-3β-ol, m.p. and mixed m.p. 307-309°, $[\alpha]_D$ + 91° (c,0.7).

18α-Oleanan-3β-yl Benzoate.

Benzoylation of 18α-oleanan-3β-ol (m.p. 229-230°) (Budziarek, Manson and Spring, loc. cit.) yielded 18α--oleanan-3β-yl benzoate which crystallised from chlorofor--methanol as plates, m.p. 277-278°, $[\alpha]_D$ + 60° (c,0.7) (Found: C,83.3; H,10.4. $C_{37}H_{56}O_2$ requires C,83.4; H,10.6%).

12ξ-Hydroxy-18α-oleanan-3β-ol.

A solution of 12-oxo-18α-oleanan-3β-yl acetate (200 mg.), in ether (300 c.c.) was refluxed with lithium aluminium hydride (500 mg.) for 4 hrs. Crystallisation of the product from methanol yielded 12ξ-hydroxy-18α-oleanan-3β-ol as needles (50 mg.), m.p. 278-279°, $[\alpha]_D$ + 56° (c,0.5) (Found; C,80.9; H,11.7. $C_{30}H_{50}O_2$ requires C,81.0; H,11.8%). Benzoylation and isolation in the usual way gave 12ξ-benzoxy-18α--oleanan-3β-yl benzoate as plates from chloroform--methanol, m.p. 288-289°, $[\alpha]_D$ + 105° (c,0.8) (Found: C,80.7; H,9.6; $C_{44}H_{60}O_4$ requires C,80.9; H,9.3%).

12ξ-Hydroxyoleanan-3β-ol.

A solution of 12-oxo-oleanan-3β-yl acetate (1 g.) in ether (300 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 1 hr. After 48 hrs. the product was isolated and crystallised from methanol to yield 12ξ--hydroxyoleanan-3β-ol as needles (700 mg.), m.p. 244-246°, $[\alpha]_D$ + 42° (c,1.2) (Found: C,80.6; H,11.6. $C_{30}H_{52}O_2$ requires C,81.0; H,11.8%).

11β-Bromo-12-oxo-18α-oleanan-3β-yl Acetate.

A solution of 12-oxo-18α-oleanan-3β-yl acetate (800 mg.) in acetic acid (100 c.c.) containing hydrobromic acid (40%, 1 c.c.) was treated in a quartz flask at 80° with bromine (320 mg.) in acetic acid (10 c.c.) added over 1 hr. with stirring. The mixture was exposed to radiation from an ultra-violet lamp during the addition and for a further period of 4 hrs. The reaction mixture was allowed to stand for 20 hrs., the product isolated in the usual manner and crystallised from chloroform-methanol to give 11β-bromo-12-oxo-18α--oleanan-3β-yl acetate as plates (400 mg.), m.p. 246-247°, $[\alpha]_D$ + 19° (c,0.7). The bromoketone was recovered unchanged after treatment with bromine in acetic acid, the mixture being exposed to ultra-violet light.

12-Oxo-18α-olean-9(11)-en-3β-yl Acetate.

A solution of 11β-bromo-12-oxo-18α-oleanan-3β-yl acetate (250 mg.) in pyridine (30 c.c.) was refluxed for 16 hrs. The product, isolated in the usual way, crystallised from methanol to yield 12-oxo-18α-olean--9(11)-en-3β-yl acetate as plates (125 mg.) m.p. 261-263 $[\alpha]_D$ + 145° (c,0.7) which gave no colour with tetranitromethane (Found: C,79.6; H,10.7. $C_{32}H_{50}O_3$ requires C,79.6; H,10.4%). Light absorption: Max. at 2420 Å. (E = 9,500). Hydrolysis by using 5% ethanolic potassium hydroxide afforded 12-oxo-18α-olean-9(11)--en-3β-ol which crystallised from methanol as blades, m.p. 318-320°, $[\alpha]_D$ + 138° (c,1.3) (Found: C,81.6; H,10.8. $C_{30}H_{48}O_2$ requires C,81.8; H,11.0%). Benzoylation and isolation of the product in the usual way, yielded 12-oxo-18α-olean-9(11)-en-3β-yl benzoate, which crystallised from chloroform-methanol as fine needles, m.p. 254-256°, $[\alpha]_D$ + 147° (c,0.7) (Found: C,81.4; H,9.4. $C_{37}H_{52}O_3$ requires C,81.6; H,9.6%). Hydrolysis for 16 hrs. using 10% ethanolic potassium hydroxide gave 12-oxo-18α-olean-9(11)-en-3β-ol, m.p. and mixed m.p. 317-319°, $[\alpha]_D$ + 137° (c,0.4), acetylation of which yielded 12-oxo-18α-olean-9(11)-en-3β-yl acetate,

m.p. and mixed m.p. 260-262°, $[\alpha]_D$ + 143° (c,0.5). 12-Oxo-18α-olean-9(11)-en-3β-yl acetate was recovered unchanged from (a) treatment in acetic acid solution at 80°, with bromine in acetic acid, the mixture being exposed to ultra-violet light; (b) refluxing for 52 hrs. with 15% ethanolic potassium hydroxide, followed by reacetylation and (c) after refluxing in acetic acid solution with selenium dioxide for 24 hrs.

12α-Hydroxy-18α-olean-9(11)-en-3β-yl Acetate.

A solution of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (1 g.) in ether (500 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 3 hrs. The product was isolated in the usual manner (avoiding the use of mineral acid) and kept with pyridine-acetic anhydride at room temperature overnight. The acetylated product was crystallised from aqueous acetone to yield 12α-hydroxy-18α-olean-9(11)-en-3β-yl acetate as needles (660 mg.) m.p. 192-193°, $[\alpha]_D$ + 140° (c,1.4) which gave a yellow colour with tetranitromethane (Found: C,79.0; H,10.9. $C_{32}H_{52}O_3$ requires C,79.3; H,10.8%). Light absorption: Max. at 2060 Å. (E = 5,600).

Dehydration of 12α-Hydroxy-18α-olean-9(11)-en-3β-yl Acetate to 18α-Oleana-9(11):12-dien-3β-yl Acetate.

A mixture of 12α-hydroxy-18α-olean-9(11)-en-3β--yl acetate (400 mg.), acetic anhydride (20 c.c.) and anhydrous sodium acetate (400 mg.) was refluxed for 3 hrs. The product was isolated in the usual way and crystallised from aqueous acetone to yield 18α-oleana--9(11):12-dien-3β-yl acetate as plates (150 mg.), m.p. 217-218°, $[\alpha]_D$ + 255° (c,1.5) (Found: C,81.9; H,10.7. $C_{32}H_{50}O_2$ requires C,82.3; H,10.8%). Light absorption: Max. at 2780 Å. (E = 9,400). Hydrolysis by using 5% ethanolic potassium hydroxide gave 18α-oleana-9(11):12--dien-3β-ol which crystallised from acetone as square plates, m.p. 203-204°, $[\alpha]_D$ + 262° (c,1.7) (Found: C,84.8 H,11.3. $C_{30}H_{48}O$ requires C,84.8; H,11.4%). Benzoylation and isolation of the product in the usual way yielded 18α-oleana-9(11):12-dien-3β-yl benzoate which crystallised from chloroform-methanol as fine needles, m.p. 238-239°, $[\alpha]_D$ + 250° (c,0.5) (Found: C,83.7; H,9.8. $C_{37}H_{52}O_2$ requires C,84.05; H,9.9%). Hydrolysis for 16 hrs. using 10% ethanolic potassium hydroxide gave 18α-oleana-9(11):12-dien-3β-ol, m.p. and mixed m.p. 200-203°, $[\alpha]_D$ + 259° (c,0.5), acetylation of which

yielded 18α-oleana-9(11):12-3β-yl acetate, m.p. and mixed m.p. 215-216°, $[\alpha]_D$ + 253° (c,0.7).

Comparative acid rearrangement of 18α-Oleana-9(11):12-dien-3β-yl Acetate and Oleana-9(11):12-dien-3β-yl Acetate.

Solutions of each acetate (100 mg.) in acetic acid (50 c.c.) were treated with concentrated hydrochloric acid (0.5 c.c.) and heated on the steam-bath. After 2 hrs. the solutions were diluted with water and the products, isolated in the usual way. The residues obtained were crystalline solids and ultra-violet spectroscopic examination showed the appearance of the characteristic 3-peak curve of a transoid heteroannular diene chromophore. The intensity of absorption in ethanol solution was determined for both residues and the isomerisation continued under the same experimental conditions for further periods of time to afford the following results.

Time (hrs.)	Intensity of absorption at 2500 Å. of material derived from	
	18α-acetate	18β-acetate
2	5300	3200
3½	6000	5300
5	9650	7025
6½	10800	8100

In another experiment using higher concentrations of mineral acid (2 c.c. of concentrated hydrochloric acid in 50 c.c. of glacial acetic acid) the following results were obtained.

Time (hrs.)	Intensity of absorption at 2500 Å. of material derived from	
	18α-acetate	18β-acetate
5	14,600	10,900
10	22,500	18,700

After a further 20 hrs. heating under the same conditions the residues were crystallised from chloroform-methanol to give plates, [50 mg. from 18α--acetate, m.p. 224-226°, $[\alpha]_D$ - 59° (c,0.4)] [40 mg. from 18β-acetate, m.p. 224-226°, $[\alpha]_D$ - 60° (c,0.5)]. Both were undepressed in m.p. on admixture with authentic oleana-11:13(18)-dien-3β-yl acetate m.p. 227-228°. 18α-Oleana-9(11):12-dien-3β-yl acetate was recovered unchanged from the same mineral acid treatment for 80 hrs. at room temperature.

18α-Olean-9(11)-en-3β-yl Acetate.

A solution of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (125 mg.) in acetic acid (200 c.c.) was shaken with hydrogen and platinum (from 100 mg. of PtO_2) for 48 hrs. The product was isolated in the usual manner

and crystallised from chloroform-methanol to yield 18α-olean-9(11)-en-3β-yl acetate as plates (110 mg.), which gave a yellow colour with tetranitromethane m.p. 248-249°, $[\alpha]_D$ + 120° (c,1.2) (Found: C,82.4; H,11.5. $C_{32}H_{52}O_2$ requires C,82.0; H,11.2%). Light absorption: Max. at 2080 Å. (E = 4,550). Hydrolysis by using 5% methanolic potassium hydroxide yielded 18α-olean-9(11)--en-3β-ol which crystallised from methanol as fine needles, m.p. 215-217°, $[\alpha]_D$ + 123° (c,1.1) which gave a yellow colour with tetranitromethane. (Found: C,84.0 H,12.0. $C_{30}H_{50}O$ requires C,84.4; H,11.8%). Acetylation reafforded 18α-olean-9(11)-en-3β-yl acetate, m.p. and mixed m.p. 249-250°, $[\alpha]_D$ + 121° (c,0.8).

Oxidation of 12-Oxo-18α-olean-9(11)-en-3β-yl Acetate with selenium dioxide in dioxan.

A mixture of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (200 mg.) and selenium dioxide (400 mg.) in dioxan (100 c.c.) was kept at 200° for 18 hrs. The reaction product was isolated in the usual manner and crystallised from methanol to yield a top crop, recrystallisation of which gave 12:19-dioxo-18α-olean--9(11)-en-3β-yl acetate as needles (25 mg.) m.p. and

mixed m.p. 279-281°, $[\alpha]_D$ + 95° (c,0.5) Light absorption: Max. at 2420 Å. (E = 10,000). Dilution of the combined mother liquors with water gave a second crop, recrystallisation of which from aqueous methanol yielded 12:19-dioxo-oleana-9(11):13(18)-dien-3β-yl acetate as plates (100 mg.), m.p. and mixed m.p. 240-241°, $[\alpha]_D$ - 83° (c,0.3). Light absorption: Max. at 2780 Å. (E = 11,200).

Summary.

The structures of several well-known dehydration products of α-amyrin and its derivatives have been elucidated and some analogous reactions in the oleanane series have been investigated.

Introduction.

Several dehydration products of α-amyrin, or its derivatives, have been described. These can be conveniently subdivided into three groups.

Group I. consists of four α-amyradienes derived from α-amyrin (by the action of various dehydrating agents. The physical constants of these dienes are shown in Chart I.

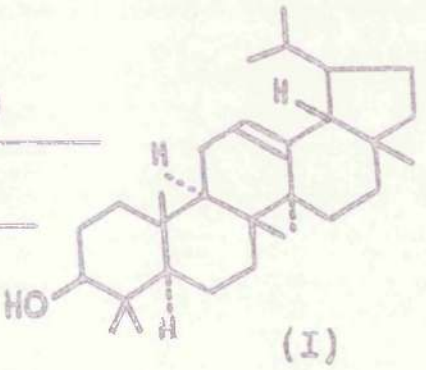
Chart I.

α-amyradiene-IV,
m.p. 131°, $[\alpha]_D$ +148°

α-amyrilene-II, or
α-amyradiene-II,
m.p. 120°, $[\alpha]_D$ +137°

mesylate + pyridine (2)

(1) benzoate pyrolysis



(I)

PCl_5 (3),(5)

(4),(5) P_2O_5 or HI

d-α-amyrilene-I, or
d-α-amyradiene,
m.p. 135°, $[\alpha]_D$ +110°,
λ_{2100} (E = 4,600)

l-α-amyrilene, or
l-α-amyradiene, m.p. 19
$[\alpha]_D$ -110°, $\lambda_{2360;2410}$
(E = 13,300;14500), Inf
λ_{2500} (E = 8,550).

(1). Winterstein and Stein (Annalen, 1933,502,223).
(2). Noller and Hearst (J.Amer.Chem.Soc., 1950,72,625).
(3). Vesterberg and Westerlind (Annalen, 1922,428,250).
(4). Vesterberg (Ber., 1891,24,3835).
(5). Ewen, Gillam and Spring (J., 1944,28).

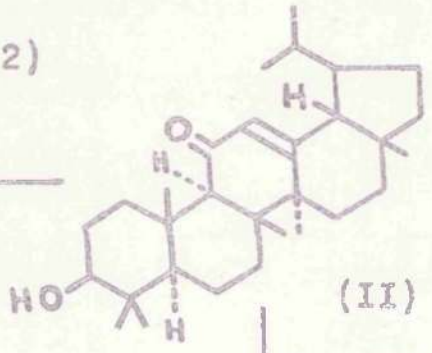
Group II. consists of three α-amyradienones derived from 11-oxours-12-en-3β-ol (II) by dehydration. The physical constar of these dienones are shown in Chart II.

Chart II.

α-amyradienone-I,
m.p. 197°, $[\alpha]_D$ +163°,
λ_{2490} (E = 14,000)

α-amyradienone-II,
m.p. 163°, $[\alpha]_D$ +158°,
λ_{2520} (E = 13,000)

PCl_5 (1),(2) (2),(3) P_2O_5 or PCl_5



(II)

HI (3)

α-amyradienone-III,
m.p. 171°, $[\alpha]_D$ +171°,
$\lambda_{2040;2580;2900}$ (E = 9,900;11,000;10,200).

(1). Spring and Vickerstaff (J., 1937,249).
(2). Ruzicka, Jeger and Volli (Helv.Chim.Acta, 1945,28,767,162
(3). Ewen, Gillam and Spring (J., 1944,28).

Group III. comprises two α-amyratrienes derived from ursa-9(11):12-dien-3β-ol (III) by dehydration. The physical constant of these trienes and of a related dichloro-α-amyradiene are shown in Chart III.

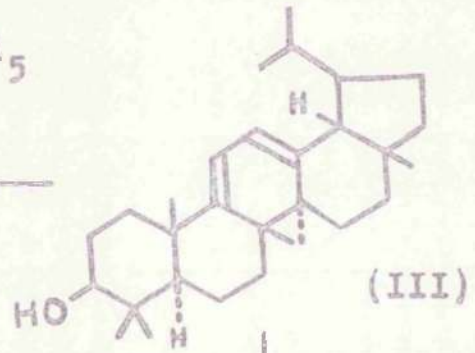
Chart III.

dichloro-α-amyradiene,
m.p. 129°, $[\alpha]_D$ +407°,
λ_{2800} (E = 11,800)

$\xrightarrow[Zn]{(1)}$

d-α-amyratriene,
m.p. 133°, $[\alpha]_D$ +439°,
λ_{2810} (E = 11,000)

(1) PCl_5 ↑



(III)

↑ PCl_5

(1) ↓ P_2O_5

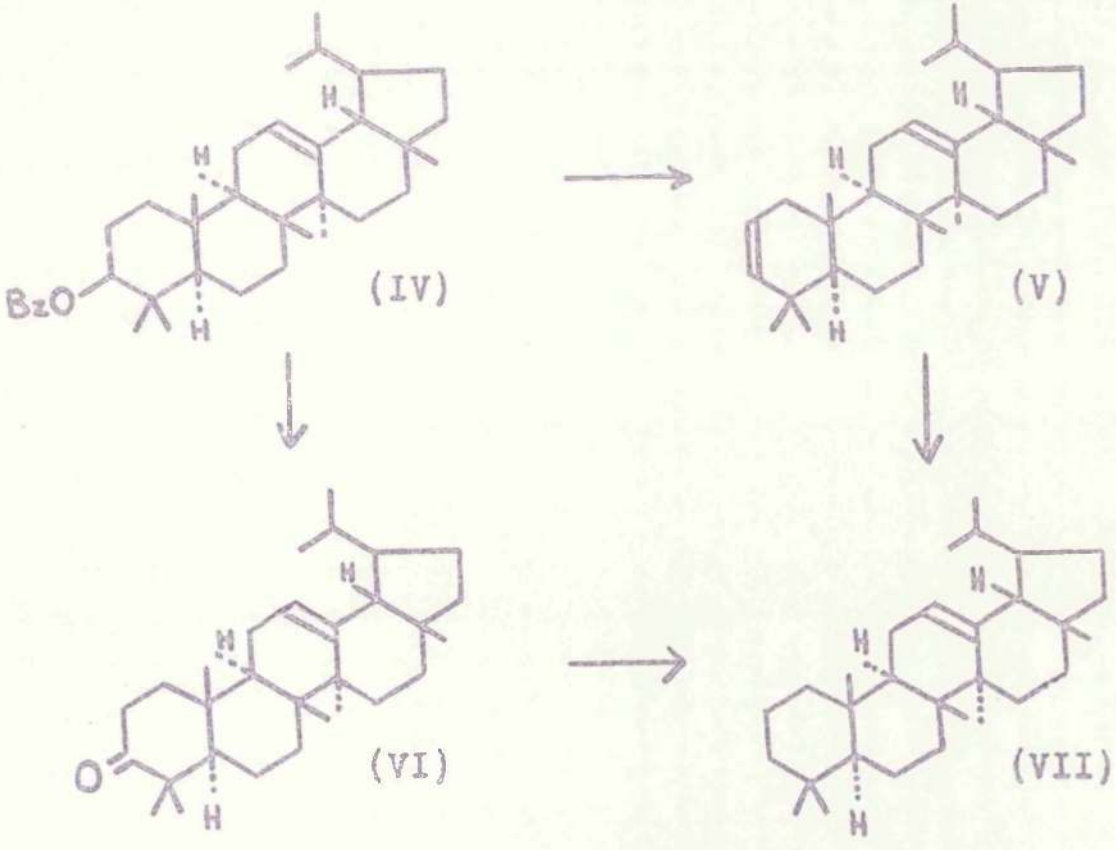
l-α-amyratriene,
m.p. 142°, $[\alpha]_D$ -450°,
λ_{2950} (E = 35,500)

(1). Ewen, Gillam and Spring (J., 1944,28).

Despite the almost complete elucidation of the parent triterpenoid structure, only the constitutions of α-amyradiene-α-amyradienone-I and α-amyradienone-II, of the ten dehydration products described above, had been determined. The purpose of this investigation was therefore, to determine the constitution of these dehydration products.

Group I. α-Amyradiene-II.

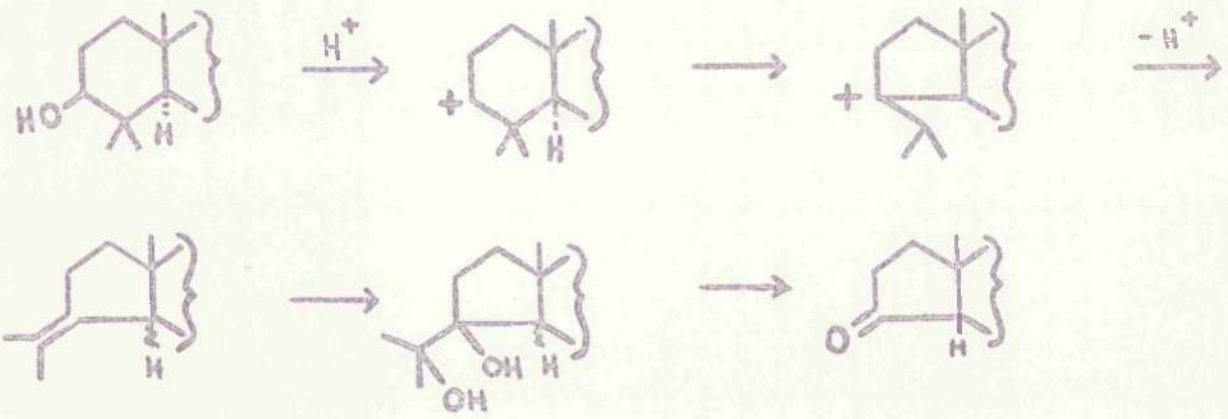
Thermal decomposition of α-amyrin benzoate (IV) gave a diene, which was initially called α-amyrilene-II and latterly α-amyradiene-II (Winterstein and Stein, Annalen, 1933, 502, 223) This has been formulated in terms of the accepted structure fo α-amyrin (II), the double bond being introduced by a cis-elimination of the elements of benzoic acid. Catalytic hydrogenation of α-amyradiene-II yielded α-amyrene-III (VII) (idem, loc.cit.) which is identical with the Clemmensen or Wolff-Kishner reduction product of α-amyrenone (VI) (idem, loc cit.; Ruzicka, Müller and Schellenberg, Helv.Chim.Acta, 1939, 22, 758, 767). α-Amyradiene-II is therefore formulated as ursa-2:12-diene (V).



d-α-Amyradiene.

Dehydration of α-amyrin with phosphorus pentachloride yields d-α-amyradiene (Vesterberg, Ber., 1887,20,1245; Vesterberg and Westerlind, Annalen, 1922,428,250; Ruzicka, Silbermann and Furter, Helv.Chim.Acta, 1932,15,482) which does not show selective absorption of high intensity above 2200 Å. (Ewen, Gillam and Spring, J., 1944,28).

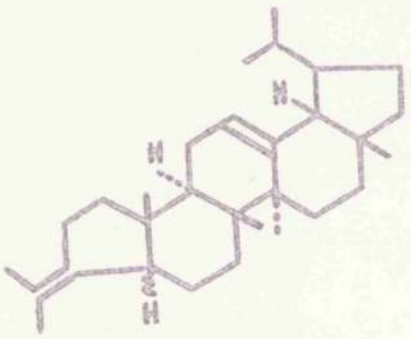
Treatment of a triterpenoid 3β-alcohol with phosphorus pentachloride has since become an important reaction sequence in triterpenoid chemistry to determine the presence of a gem-dimethyl group at the C_4-position. Ring A contraction occurs and a five-membered ring results with the formation of an isopropylidene side chain. The presence of an isopropylidene side chain can be established by osmium tetroxide oxidation of the ethylenic linkage to a glycol system which on subsequent cleavage affords acetone and a saturated ketone. The entire sequence is represented as follows:-



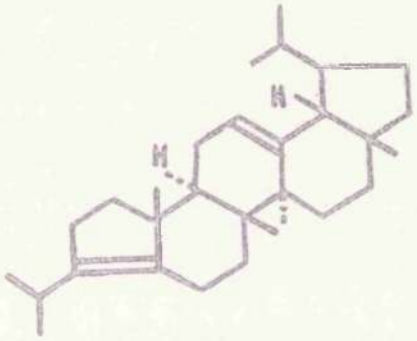
This procedure has been applied inter alia to lupanol (Ruzicka, Jeger and Huber, Helv.Chim.Acta, 1945,28,767), oleanolic acid 18α-lactone (Ruzicka, Rudowski, Norymberski and Jeger, ibid., 1946,29,210), quinovic acid dimethyl ester

(Ruzicka, Szpilfogel and Jeger, ibid., 1948, 31, 499) and dihydrolanosterol (Ruzicka, Montavon and Jeger, ibid., p.819).

It therefore seemed probable that d-α-amyradiene might have structure (VIII) though (IX) was equally feasible from a consideration of the above mechanism.



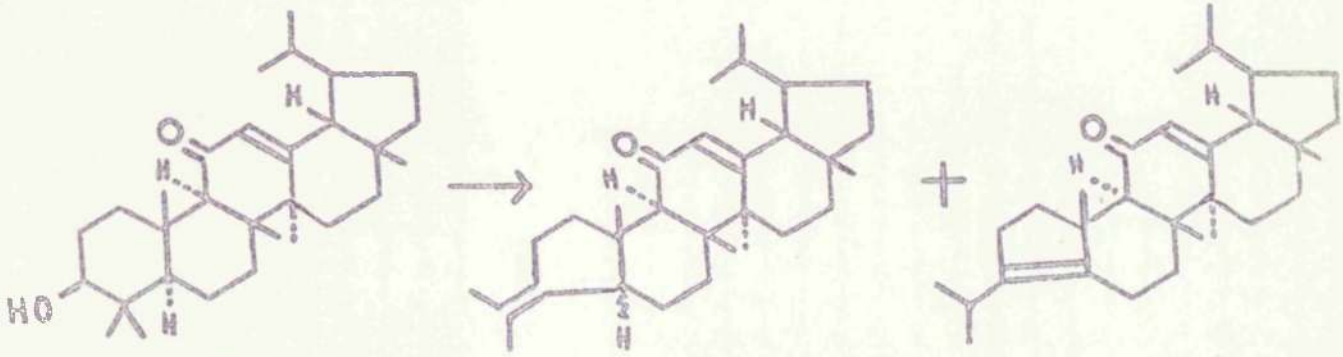
(VIII)



(IX)

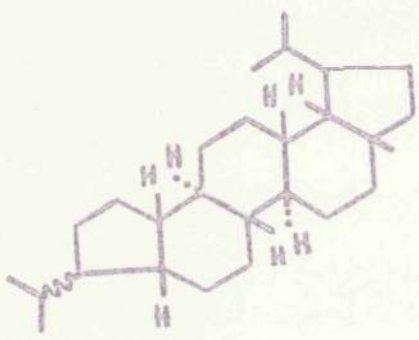
In an endeavour to distinguish between these possibilities a relationship was sought with α-amyradienone-I and the isomeric α-amyradienone-II.

Dehydration of 11-oxours-12-en-3β-ol (II) with phosphorus pentachloride gives a mixture of α-amyradienone-I (X) and α-amyradienone-II (XI) (Spring and Vickerstaff, J., 1937, 249), the structures of which have been elucidated (Ruzicka, Jeger and Volli, Helv. Chim. Acta, 1945, 28, 767, 1628; Klyne, J., 1952, 2916).

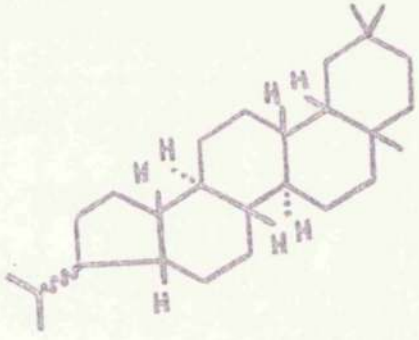


(II) (X) (XI)

As a basis for a rational nomenclature for these and other dehydration products described in this thesis, it is proposed that the hydrocarbon $C_{27}H_{46}$ with the constitution and stereochemistry represented by formula XIIA shall be considered as the parent compound and shall be called novursane. The isomeric hydrocarbon related to the oleanane series should, by analogy, be represented by formula XIIB and called novoleanane.



(XIIA)

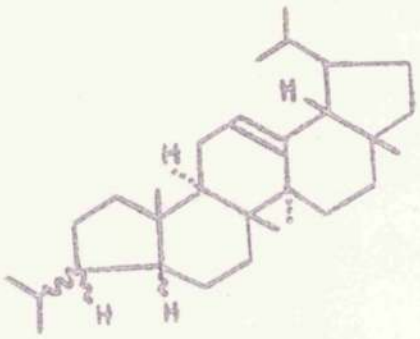


(XIIB)

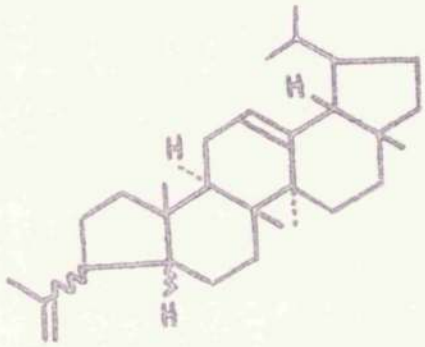
Using this system, α-amyradienone-I (X) is 8:10:14-trimethyl-11-oxo-5ξ-novursa-3:12-diene and α-amyradienone-II (XI) is 8:10:14-trimethyl-11-oxonovursa-3(5):12-diene.

To establish a relationship between d-α-amyradiene and the oxodienes (X) and (XI), it was decided to reduce the carbonyl group of the oxodienes (X) and (XI), by the Wolff-Kishner metho and to compare the products with d-α-amyradiene. The reduction product from 8:10:14-trimethyl-11-oxo-5ξ-novursa-3:12-diene (X) was identical with d-α-amyradiene, which is therefore now identified as 8:10:14-trimethyl-5ξ-novursa-3:12-diene (VIII). Catalytic hydrogenation of d-α-amyradiene yields α-amyrene-I (Ruzicka, Silbermann and Furter, loc.cit.; Ruzicka, Silbermann, and Pieth, Helv.Chim.Acta, 1932,15,1285; Winterstein and Stein, loc.cit.) which can now be formulated. Since the double bond of α-amyrin is resistant to catalytic hydrogenation (Ruzicka,

Huyser, Pfeiffer and Seidel, Annalen, 1929,471,21), α-amyrene-I must be formed by saturation of the side chain double bond and hence is considered to be 8:10:14-trimethyl-3ξ:5ξ-novurs-12-ene (XIII).



(XIII)



α-Amyradiene-IV.

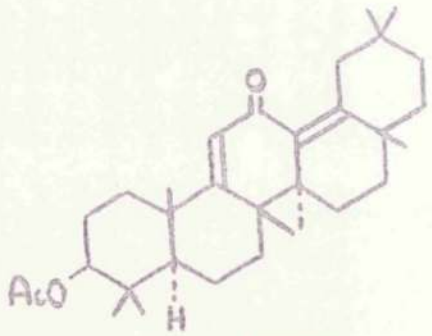
The Wolff-Kishner reduction product from 8:10:14-trimethyl-11-oxonovursa-3(5):12-diene (XI) is formulated as 8:10:14-trimethylnovursa-3(5):12-diene (IX), which differs from d-α-amyradiene and consequently the possibility of migration of the 3(4)-ethylenic linkage of (X) to the 3(5)-position during Wolff-Kishner reduction of (X) is discounted.

8:10:14-Trimethylnovursa-3(5):12-diene (IX) also differs from α-amyradiene-IV, which is obtained by the treatment of mesyl-α-amyrin with pyridine (Noller and Hearst, J.Amer.Chem.Soc 1950,72,625). α-Amyradiene-IV therefore cannot be represented as (IX) and it has since been shown to be 8:10:14-trimethyl-novursa-4(23):12-diene (Fayez, Ph.D. Thesis, Glasgow, 1955).

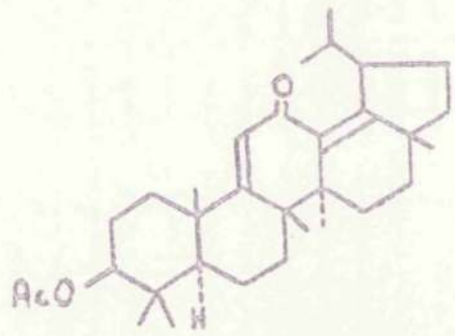
A discussion of the structure of l-α-amyradiene is deferred until after a consideration of the constitution of α-amyradienone-III.

Group II. α-Amyradienone-III.

As stated previously, the structures of α-amyradienone-I and α-amyradienone-II have been rigorously established (Ruzicka Jeger and Volli, loc.cit.). The third dienone, α-amyradienone-I which differed from (X) and (XI) was isolated by Ewen et al. (loc.cit.) by the dehydration of 11-oxours-12-en-3β-ol (II), with hydriodic-acetic acid mixture. The ultra-violet absorption spectrum of this compound, as reported by these authors, was not examined below 2200 Å. and it was therefore re-examined, th showing three maxima, at 2040, 2580 and 2900 Å. (E = 9,900, 11,000 and 10,200). In this respect, it resembles 12-oxo-oleana 9(11):13(18)-dien-3β-yl acetate (XIV)(Beaton, Johnston, McKean and Spring, J., 1953,3660) and 12-oxoursa-9(11):13(18)-dien-3β-acetate (XV)(Beaton, Shaw, Spring, Stevenson, Stewart and Strachan, J., 1955, in press), the characteristic absorption of which have been related to the geometry of the cisoid-transoid -C=C-CO-C=C- chromophore.

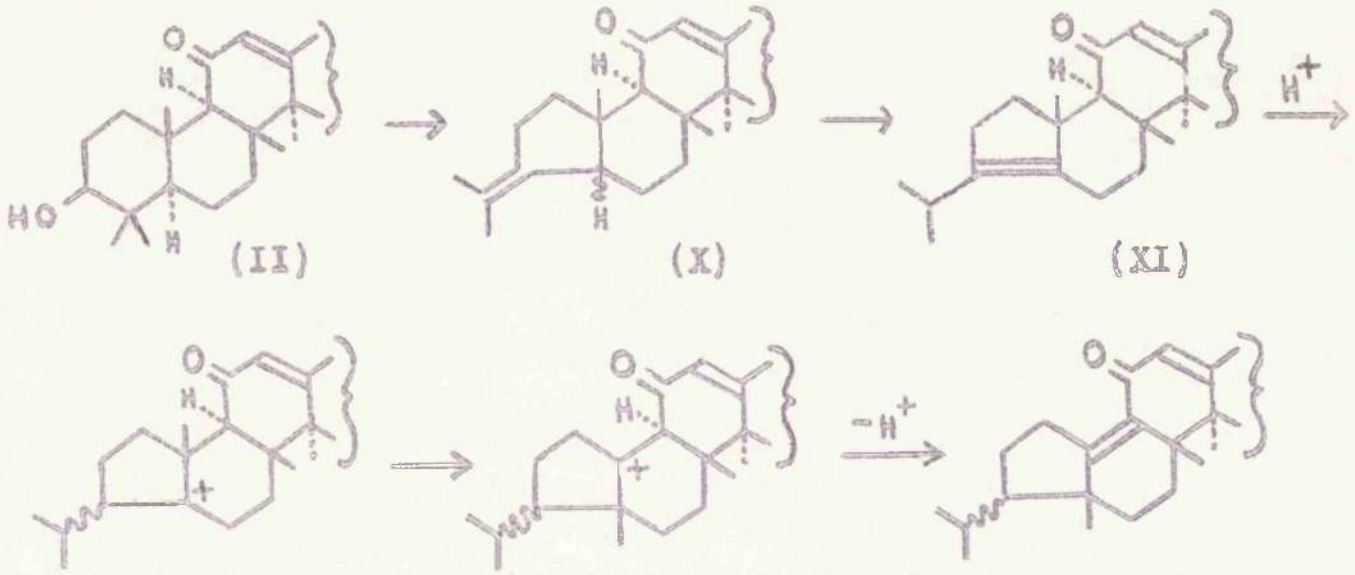


(XIV)



(XV)

For this reason it appeared that α-amyradienone-III contained a similar chromophore and it is therefore formulated as 5:8:14-trimethyl-11-oxonovursa-9:12-diene (XVI) and its formation from 11-oxours-12-en-3β-ol (II) is represented mechanistically as shown overleaf.



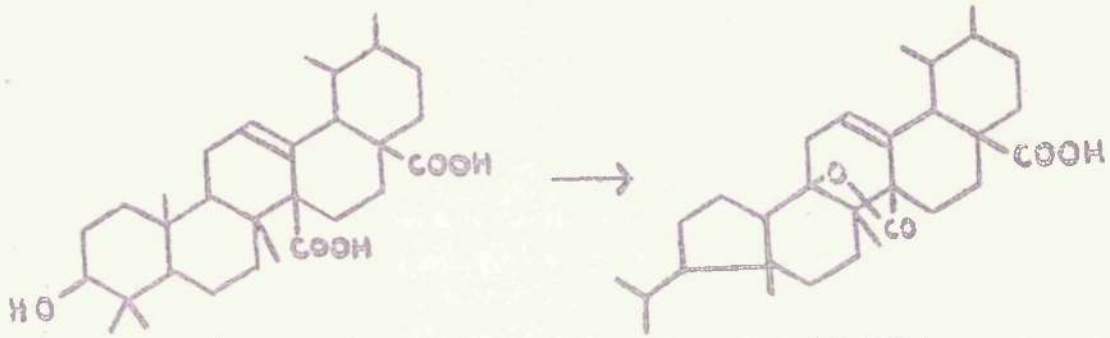
(II) (X) (XI) (XVI)

If this mechanism is correct, (X) must be capable of isomerization to (XI) under acid conditions. Ruzicka, Jeger and Volli (loc.cit.) had already shown that in neutral conditions the oxodiene (X) in ethanol solution is isomerized to (XI) by shaking with hydrogen and a palladized catalyst. To test the proposed mechanism, (X) was treated with refluxing hydrochloric-acetic acid mixture when 8:10:14-trimethyl-11-oxonovursa-3(5):1[illegible] diene (XI) was obtained as the sole product, and thus the mechanism is substantiated as far as (XI) in the above sequence.

In order that stages (XI) → → → (XVI) should be valid, (XI) should isomerize to 5:8:14-trimethyl-11-oxonovursa-9:12-diene (XVI) on treatment with hydriodic-acetic acid mixture. Treatment of 8:10:14-trimethyl-11-oxonovursa-3(5):12-diene (XI) under the conditions which lead to the formation of (XVI) from (II), gave the conjugated dienone (XVI) as the only product.

Barton and de Mayo (J., 1953,3111) have suggested the structure (XVII) for novic acid, a dehydration product of quinovic acid (XVIII), and in the formation of (XVII) from

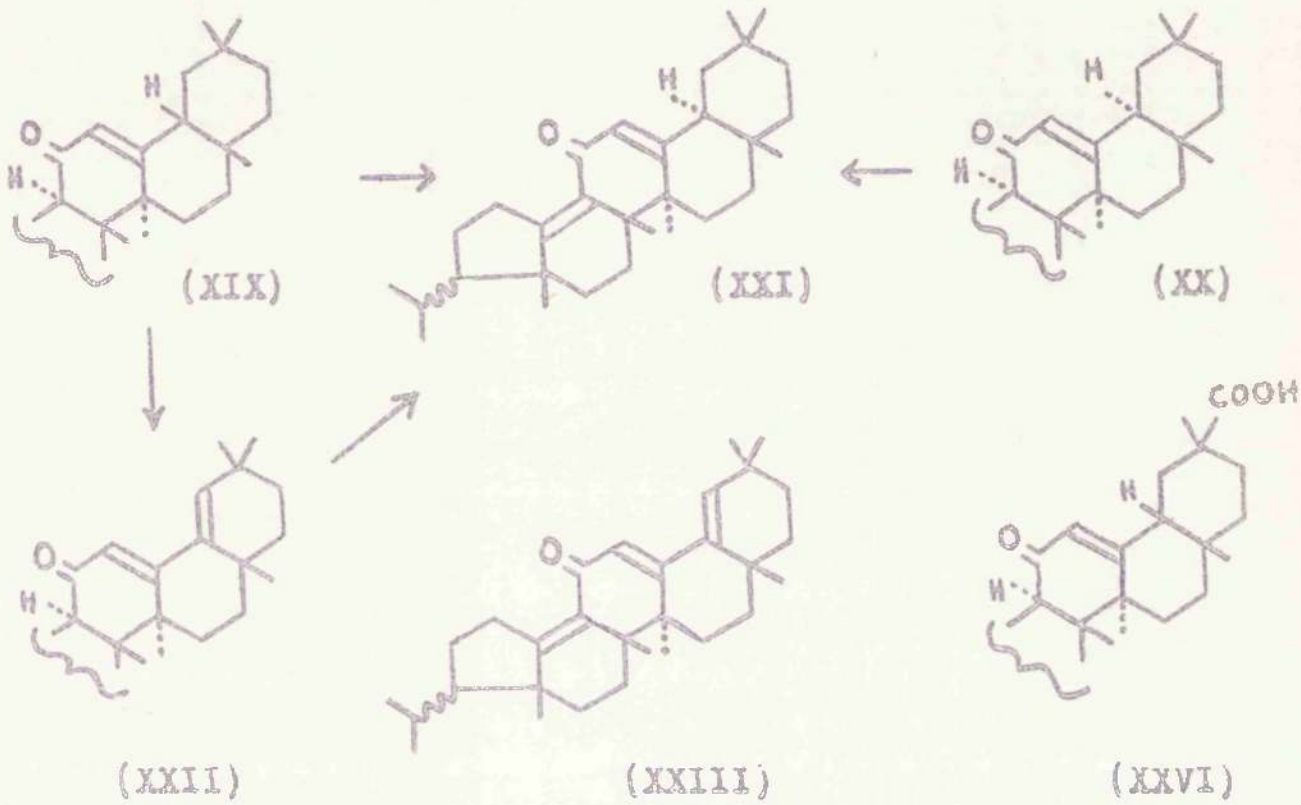
(XVIII) an analogous methyl group migration from C_{10} to C_5 has occurred.



(XVIII) (XVII)

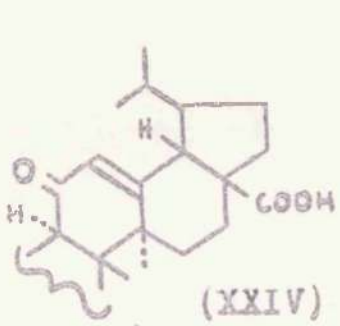
Prior to the elucidation of the structure of α-amyradienone-III, only one example (XIV) of the characteristic cisoid-transoid dienone chromophore had been described and it was of interest to obtain and compare the oleanane analogue of α-amyradienone-III. Treatment of 11-oxo-olean-12-en-3β-yl acetate (XIX) under similar conditions gave β-amyradienone-III which exhibits a comparable light absorption spectrum having maxima at 2060, 2560 and 2870 Å. (E = 7,800 , 10,000 and 9,600). The slight hypsochromic shift observed relative to the ursane analogue, α-amyradienone-III (cf. Section 2.) suggested that inversion had occurred at C_{18} in (XIX) during ring contraction. To test this hypothesis, 11-oxo-18α-olean-12-en-3β-yl acetate (XX) was treated with hydriodic-acetic acid and β-amyradienone-I was again the sole product. β-Amyradienone-III is therefore formulated as 5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-diene (XXI).

It was of further interest to prepare 5:8:14-trimethyl-11-oxonovoleana-9:12:18-triene (XXIII) from 11-oxo-oleana-12:18-dien-3β-yl acetate (XXII) to examine its light absorption characteristics.

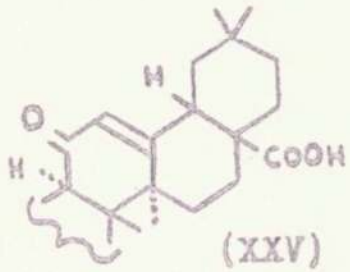


Treatment of (XXII) with hydriodic-acetic acid, however, gave as the only product, β-amyradienone-III, reduction of the $C_{18:19}$ ethylenic linkage having occurred.

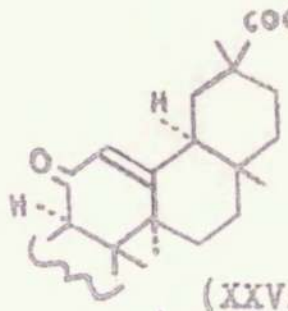
Treatment of 11-oxours-12-en-3β-yl-28-oic acid acetate (XXIV), 11-oxo-olean-12-en-3β-yl-28-oic acid acetate (XXV), 11-oxo-olean-12-en-3β-yl-30-oic acid acetate (XXVI) and 11-oxo-18α-olean-12-en-3β-yl-30-oic acid acetate (XXVII) with hydriodic-acetic acid mixture yielded three new dienone acids, 5:8:14-trimethyl-11-oxonovursa-9:12-dien-28-oic acid (XXVIII), 5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-dien-28-oic acid (XXIX), and 5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-dien-30-oic acid (XXX) which contain the characteristic cisoid-transoid chromophore first observed in 12-oxo-oleana-9(11):13(18)-dien-3β-yl acetate (XIV).



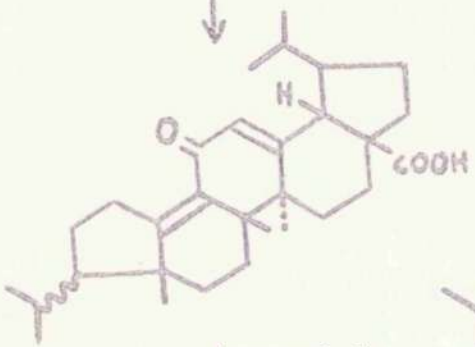
(XXIV)



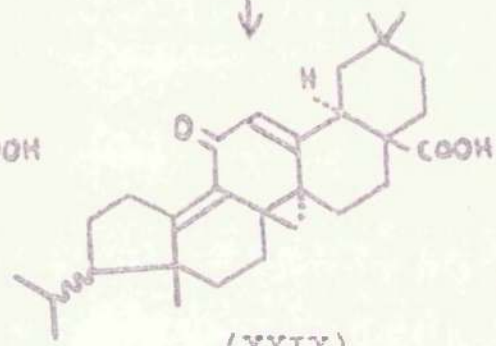
(XXV)



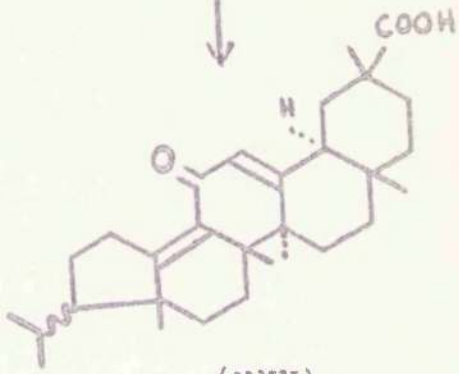
(XXVII)



(XXVIII)

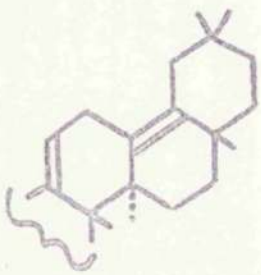


(XXIX)

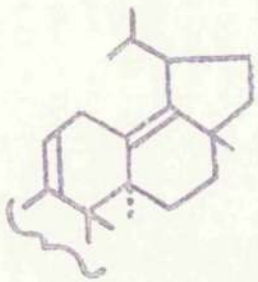


(XXX)

In comparing the behaviour of the ring contracted dienones (XVI) and (XXI) with the oleanane and ursane dienones (XIV) and (XV), the catalytic hydrogenation of α-amyradienone-III (XVI) was examined in the expectation that simple hydrogenolysis of the carbonyl group would occur. Unlike 12-oxo-oleana-9(11):13(18 dien-3β-yl acetate (XIV) and 12-oxoursa-9(11):13(18)-dien-3β-yl acetate (XV), which yield the corresponding non-conjugated dienyl acetates (XXXI) and (XXXII) on hydrogenation, α-amyradienone-III absorbed 3 mols. of hydrogen to yield a monoene, the optical properties of which suggest that it is 5:8:14-trimethyl-9ξ:10ξ-novurs-12-ene (XXXIII). In view of this observation, hydrogenation of β-amyradienone-III (XXI) was not attempted.

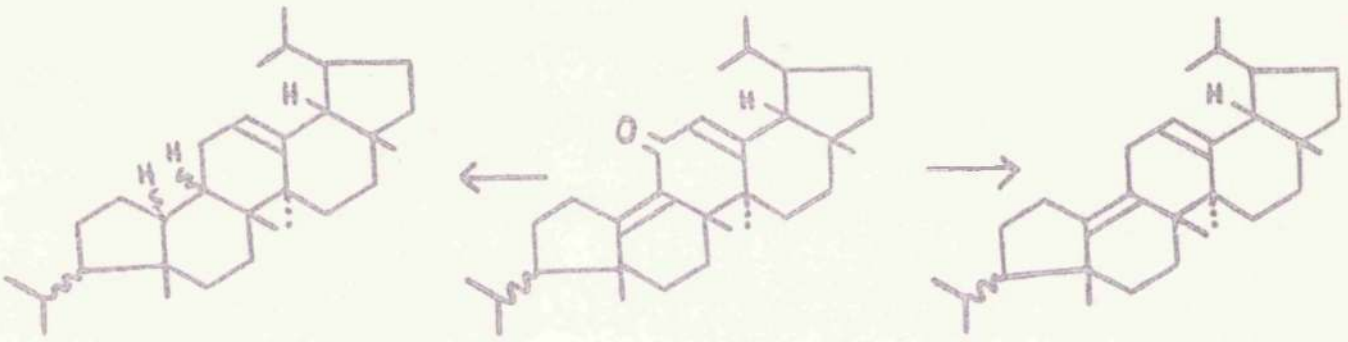


(XXXI)



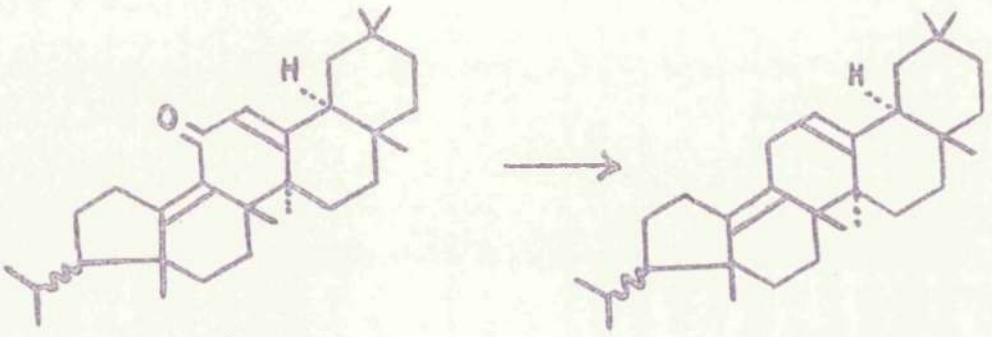
(XXXII)

The dienyl acetate (XXXI) can be obtained from the dienone (XIV) by hydrogenolysis using lithium aluminium hydride (Beaton, Johnston, McKean and Spring, loc.cit.) and this treatment of 5:8:14-trimethyl-11-oxonovursa-9:12-diene (XVI) also affords a non-conjugated diene formulated as 5:8:14-trimethylnovursa-9:12-diene (XXXIV). The diene (XXXIV) can also be obtained by the Wolff-Kishner reduction of (XVI).



(XXXIII) (XVI) (XXXIV)

The 18α-novoleanane analogue of (XXXIV) was obtained by similar treatment of the 18α-dienone (XXI) with lithium aluminium hydride and is formulated as 5:8:14-trimethyl-18α-novoleana-9:12-diene (XXXV). It can also be obtained by Wolff-Kishner reduction of the 18α-dienone (XXI)(Fayez, loc.cit.).



(XXI) (XXXV)

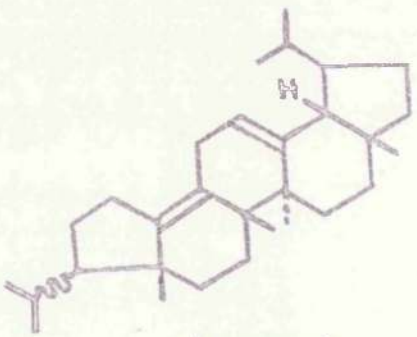
Both the dienes (XXXIV) and (XXXV) show strong ethylenic absorption in the region 2100-2200 Å. and give a strong positive reaction with tetranitromethane in chloroform.

The behaviour of the dienones (XVI) and (XXI), and the formation of the non-conjugated dienes (XXXIV) and (XXXV) is therefore closely analogous to that of 12-oxo-oleana-9(11):13(1 dien-3β-yl acetate (XIV) and is an endorsement of the proposed structures (XVI) and (XXI) for the dienones, and (XXXIV) and (XXXV) for the dienes.

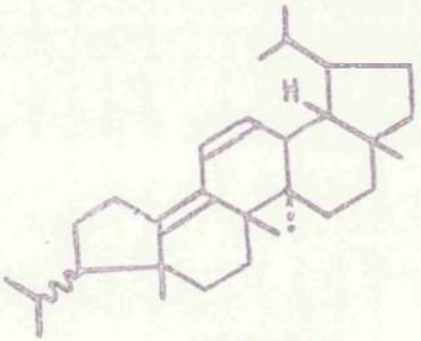
Group I. The Structure of 1-α-Amyradiene.

Treatment of α-amyrin with phoshoric oxide (Vesterberg, Ber., 1891, 24, 3835) or hydriodic-acetic acid mixture (Ewen et al., loc.cit.) gives the conjugated diene, 1-α-amyradiene. It seemed most probable that the double bonds in this diene were located in hindered positions since 1-α-amyradiene was indifferent to reducing agents, did not form a maleic anhydride adduct (Ewen et al., loc.cit.) and was unaffected by selenium dioxide or osmic acid (Manson, Ph.D. Thesis, Glasgow, 1950).

An important clue to the elucidation of the structure of 1-α-amyradiene was the observation that acid isomerization of the non-conjugated diene (XXXIV), obtained from α-amyradienone-III, (XVI), yielded 1-α-amyradiene. The most obvious conclusion was that 1-α-amyradiene had the structure (XXXVI)



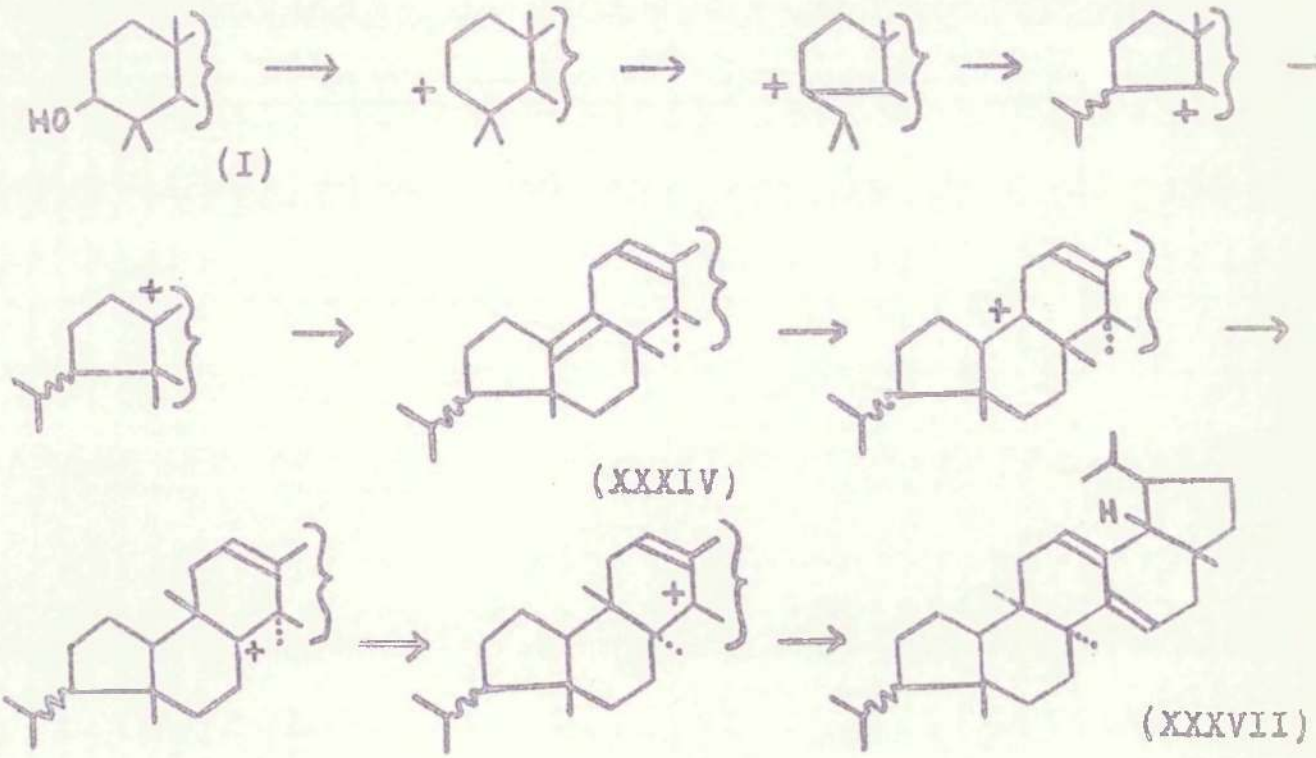
(XXXIV)



(XXXVI)

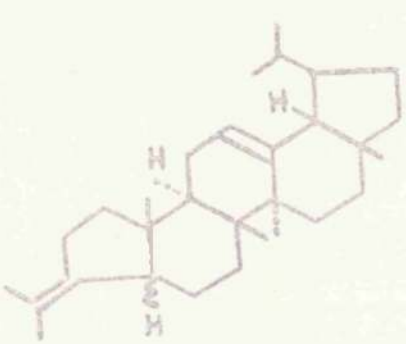
This formulation, however, is not satisfactory, as such a diene would be expected to show light absorption at circa 2500 Å. (E = 25,000) whereas 1-α-amyradiene has a principal max. at 2410 Å. (E = 14,500). Further, structure (XXXVI) would presumably readily hydrogenate at $C_{11:12}$ and would be expected to react with osmic acid or N-bromosuccinimide, reactions which do not proceed with 1-α-amyradiene.

Accordingly some further investigation of l-α-amyradiene was required to express these properties which cannot be accommodated in the basic skeleton of (XXXIV). Some expression for l-α-amyradiene involving a rearrangement of the methyl groups of the non-conjugated diene (XXXIV) so that the double bonds of (XXXIV) could attain stable hindered positions, therefore appeared necessary. The formation of l-α-amyradiene from the non-conjugated diene (XXXIV) would therefore seem to require a methyl group migration followed by conjugation rather than simple conjugation and a mechanism considered for the formation of l-α-amyradiene from α-amyrin, incorporating these views, was as follows, where l-α-amyradiene is represented as (XXXVII).

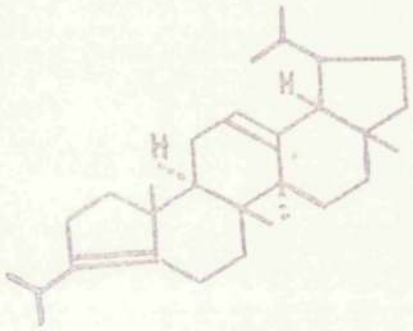


The structure (XXXVII) would therefore be systematically named 5:8α:9β-trimethyl-10α-novursa-12:14-diene and the correctness of this structure has been established (Fayez,

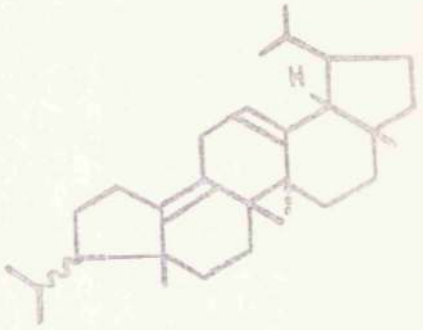
Grigor, Spring and Stevenson, J., 1955, in press). In this sequence 8:10:14-trimethyl-5ξ-novursa-3:12-diene (VIII), 8:10:14-trimethylnovursa-3(5):12-diene (IX) and 5:8:14-trimethylnovursa-9:12-diene (XXXIV) are presumably not discret intermediates since each is recovered unchanged after treatmen in benzene with phosphoric oxide under conditions which lead to the formation of l-α-amyradiene from α-amyrin.



(VIII)



(IX)

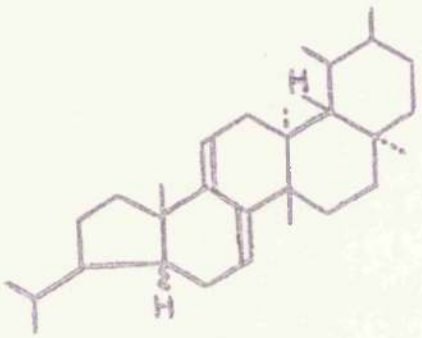


(XXXIV)

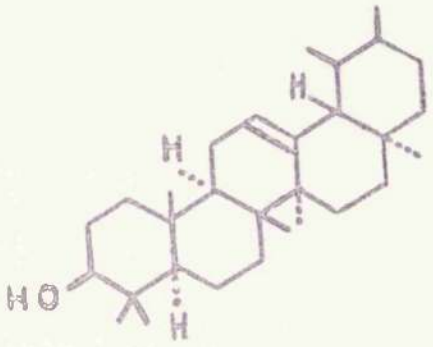
These observations, however, are not contrary to the proposed mechanism which is only intended to represent what is probably a largely concerted reaction. Conversion of the diene (VIII) to l-α-amyradiene can however be effected by treatment of 8:10:14-trimethyl-5ξ-novursa-3:12-diene (VIII) with boron trifluoride-acetic acid complex, and 8:10:14-trimethylnovursa-3(5):12-diene (IX), presumably an intermediate, can be obtaine by isomerization of (VIII) with trichloroacetic acid in chloroform.

Beton and Halsall (Chem. and Ind., 1954,1560) have proposed a structure for α-amyrin, (XXXVIII), based on a consideration of l-α-amyradiene, to which they assign structur (XXXIX). On the basis of the structure of α-amyradienone-III (XVI), and its conversion to l-α-amyradiene, the structure

(XXXIX) cannot represent 1-α-amyradiene, and this invalidates the conclusions leading to structure (XXXVIII) for α-amyrin.



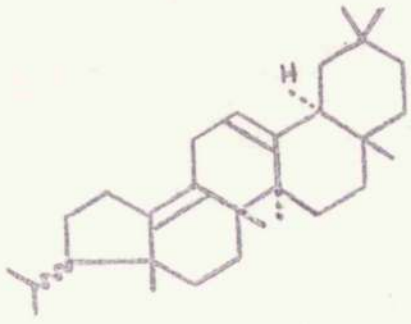
(XXXIX)



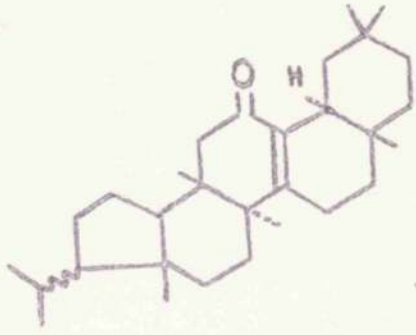
(XXXVIII)

Beton and Halsall (loc.cit.) further suggested that the non-formation of an oleanane analogue of 1-α-amyradiene from β-amyrin was determined by a conformational driving force due to the nature of the D/E ring junction, trans in α-amyrin as compared to cis in β-amyrin. In an endeavour to prepare 1-β-amyradiene, 5:8:14-trimethyl-18α-novoleana-9:12-diene (XXXV) was treated with acid under the conditions which convert 5:8:14-trimethylnovursa-9:12-diene (XXXIV) to 1-α-amyradiene. A gum was obtained which showed low intensity absorption at 2500 Å. This difference, in behaviour between the dienes (XXXIV) and (XXXV), can be ascribed to the inability of the 18α-oleanane derivative (XXXV) to undergo a reaction involving migration of the methyl groups attached to C_8 and C_{14} to C_9 and C_8 respectively.

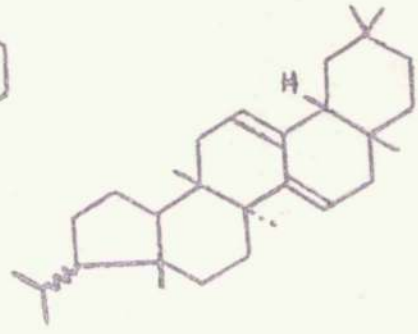
This difference has been fully resolved by a coworker (Fayez, loc.cit.) who has prepared 1-β-amyradiene from 5:8α:9β-trimethyl-12-oxonorolean-13-ene (XL) by reduction to the corresponding alcohol, mineral acid treatment of which yields 1-β-amyradiene (XLI).



(XXXV)



(XL)



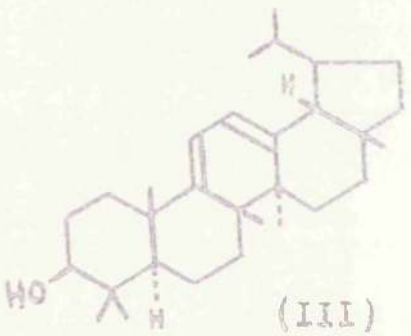
(XLI)

These observations in no way conflict with the structure proposed for α-amyrin in Section (2) of this thesis.

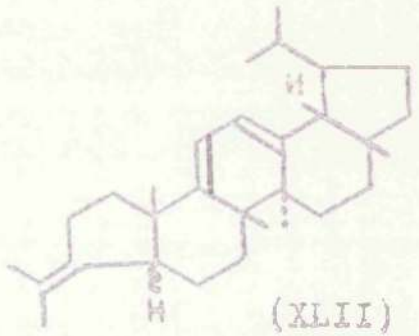
Group III. d-α-Amyratriene.

Dehydration of ursa-9(11):12-dien-3β-ol (III) with phosphorus pentachloride gives a dichloro-α-amyradiene, which with zinc dust yielded d-α-amyratriene, the ultra-violet absorption spectrum of which shows that the double bond introduced by dehydration is remote from the conjugated system in ring C (Ewen et al., loc.cit.).

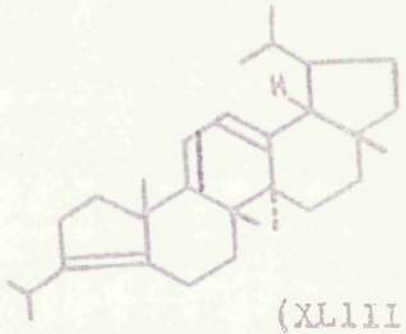
Two structures were considered for d-α-amyratriene, 8:10:14-trimethyl-5ξ-novursa-3:9(11):12-triene (XLII) and 8:10:14-trimethylnovursa-3(5):9(11):12-triene (XLIII), and of these (XLII) seemed the most probable.



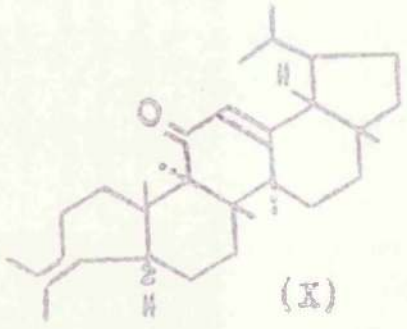
(III)



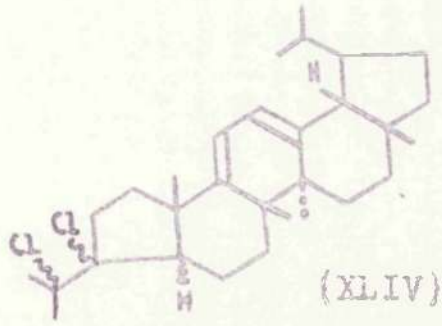
(XLII)



(XLIII)



(X)



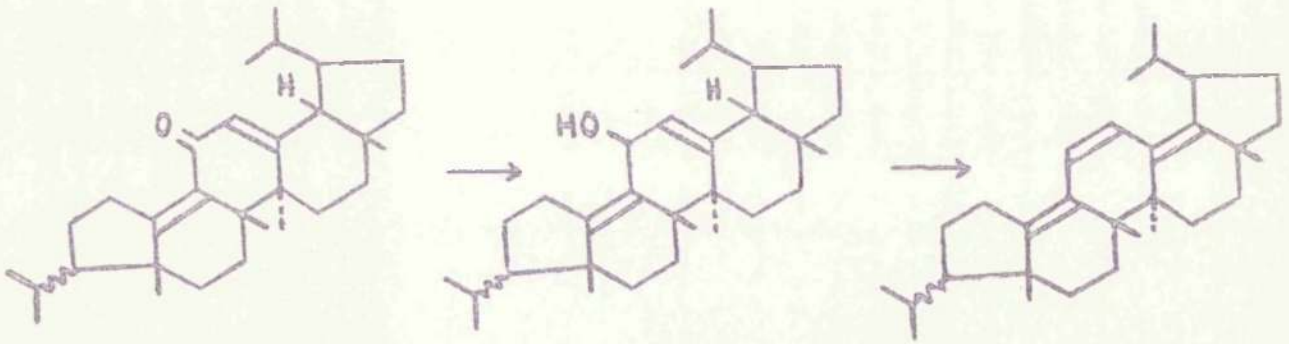
(XLIV)

The constitution of d-α-amyratriene was established as (XLII) by its formation from 8:10:14-trimethyl-11-oxo-5ξ-novursa-3:12-diene (X) by reduction with lithium aluminium hydride followed by treatment of the reaction product with phosphoryl chloride in pyridine. Dichloro-α-amyradiene is consequently 3ξ:4ξ-dichloro-8:10:14-trimethyl-5ξ-novursa-9(11):12-diene (XLI

1-α-Amyratriene.

Dehydration of ursa-9(11):12-dien-3β-ol (III) using phosphoric oxide gives a different triene, 1-α-amyratriene, which exhibits a triple maxima absorption with principal maximum at 2950 Å. (E = 35,500) and consequently contains a conjugated triene chromophore (Ewen et al., loc.cit.). An attempt to prepare 1-α-amyratriene by treatment of (III) with hydriodic-acetic acid mixture gave 1-α-amyradiene in 10% yield as the only isolable product.

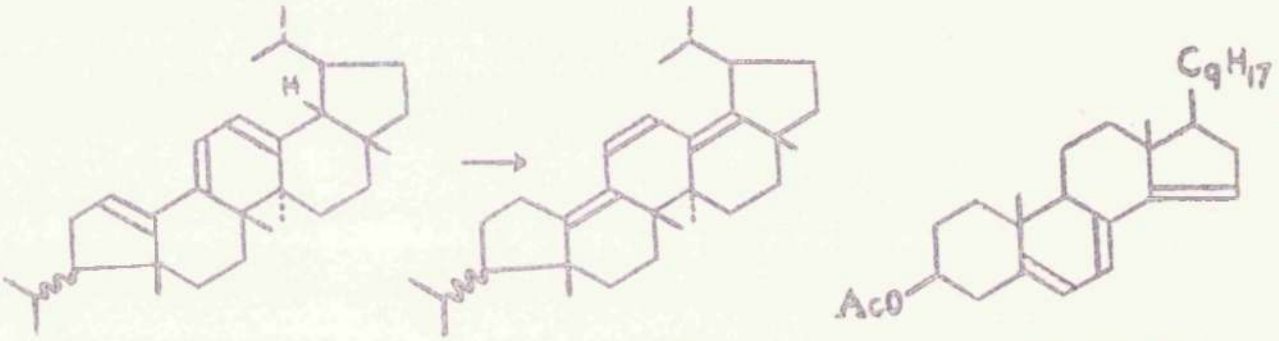
A structure considered tentatively for 1-α-amyratriene was 5:8:14-trimethylnovursa-9:11:13(18)-triene (XLV). In an endeavour to confirm this structure, it was proposed to reduce α-amyradienone-III (XVI) with sodium borohydride to the corresponding alcohol (XLVI), which with mineral acid was expected to afford 1α-amyratriene. 5:8:14-Trimethyl-11-oxonov-ursa-9:12-diene (XVI), however, was recovered unchanged after prolonged treatment with sodium borohydride.



(XVI) (XLVI) (XLV)

Treatment of (XVI) with lithium aluminium hydride in ether at 0° to obtain (XLVI) gave instead a strongly laevorotatory triene which exhibits an absorption maximum at 3200 Å. (E = 15,000) and which is considered to be 5:8:14-trimethylnovursa-

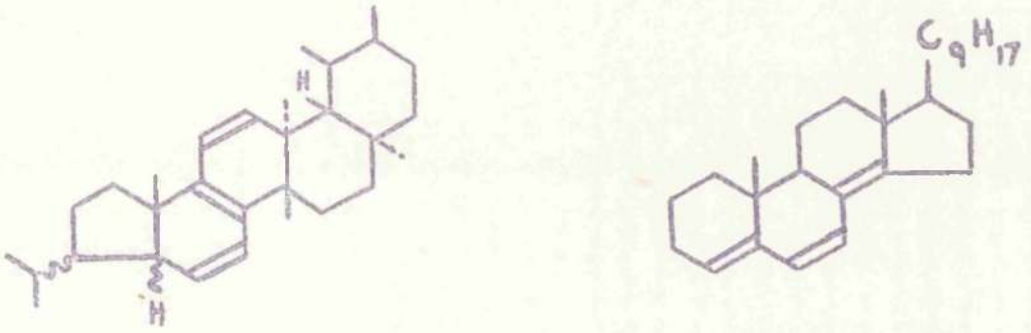
1(10):9(11):12-triene (XLVII). Treatment of (XLVII) with mineral acid causes isomerization and yields l-α-amyratriene.



(XLVII) (XLV) (XLVIII)

Comparison of the light absorption of (XLVII) with that (3190 Å., E = 15,000) of ergosta-5:7:14:22-tetraen-3β-yl acetate (XLVIII)(Barton and Bruun, J., 1951,2728), which has the same chromophoric system and is in agreement with the calculated value of 3230 Å. lends strong support to the structural assignation of (XLVII).

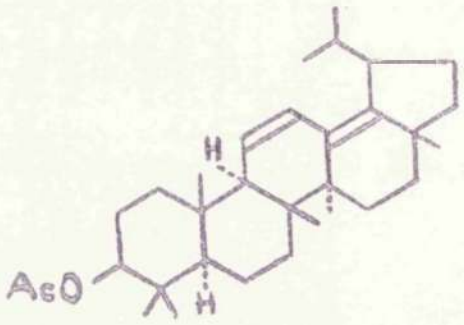
Beton and Halsall (loc.cit.) have proposed structure (XLI) for l-α-amyratriene which must be rejected since it does not account for its light absorption characteristics or for its formation from α-amyradienone-III (XVI).



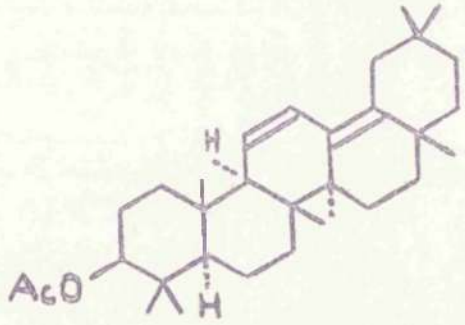
(XLIX) (L)

The light absorption characteristics of 1-α-amyratriene are those of an extended transoid triene system and the high intensity agrees well with the intensity (2830 Å., E = 33,000) found for the analogous chromophore of ergosta-4:6:8(14):22-tetraene (L)(Feiser, Rosen and Feiser, J.Amer.Chem.Soc., 1952, 74,5397). The maximal position is in excellent agreement with the calculated value (2940 Å.). This data, and the method of formation from 5:8:14-trimethyl-11-oxonovursa-9:12-diene (XVI) lead to the formulation of 1-α-amyratriene as 5:8:14-trimethyl-novursa-9:11:13(18)-triene (XLV).

Since the isomerization of ursa-11:13(18)-dien-3β-yl acetate (LI) to oleana-11:13(18)-dien-3β-yl acetate (LII) had been described (Beaton, Spring, Stevenson and Strachan, J., 19[illegible] in press), it was desired to prepare 1-β-amyratriene, the oleanane analogue of 1-α-amyratriene, in order to confirm that 1-α-amyratriene still contained an ursane ring E and that in its formation from α-amyradienone-III (XVI) a transformation to a novoleanane derivative had not occurred.



(LI)

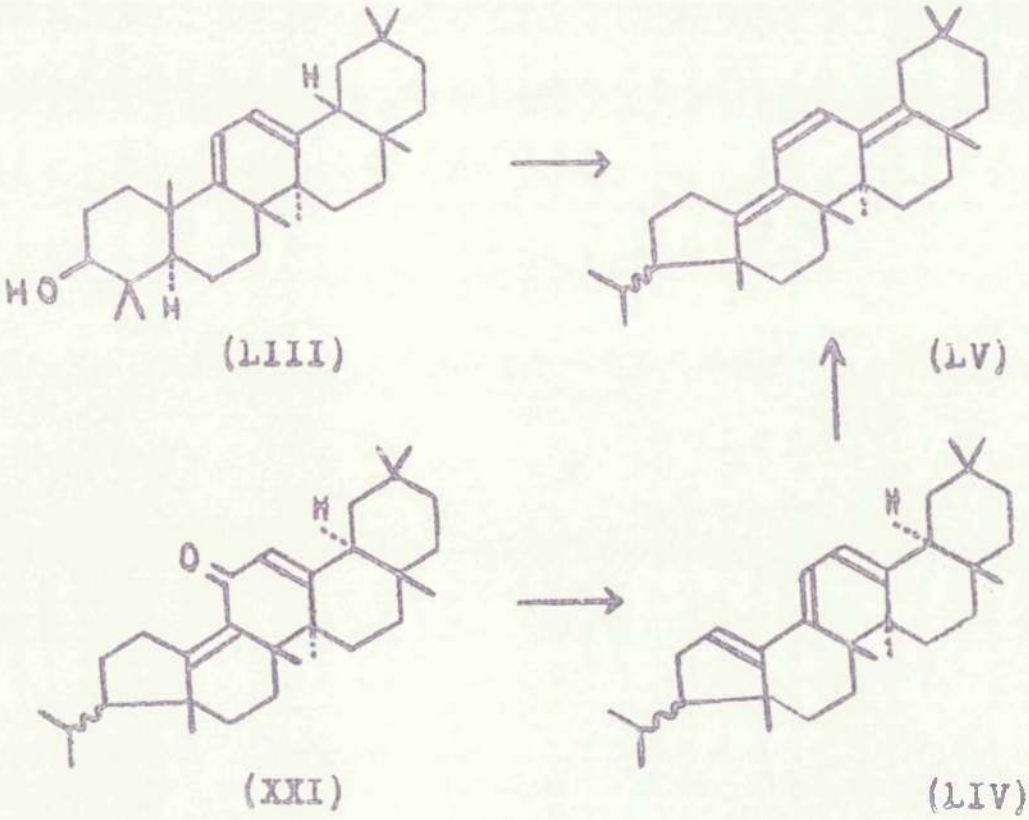


(LII)

1-β-Amyratriene was prepared by analogous methods. Treatment of oleana-9(11):12-dien-3β-ol (LIII) with phosphoric oxide gave 1-β-amyratriene which showed similar, crystalline

form, m.p., specific rotation and light absorption to 1-α-amyratriene. A mixture of the two trienes, however, gave a well defined m.p. depression.

Reduction of β-amyradienone-III (XXI) with lithium aluminium hydride in ether at 0° gave a strongly laevorotatory triene, which showed maximum light absorption at 3150 Å. (E = 14,000) and which is considered to be 5:8:14-trimethyl-18α-novoleana-1(10):9(11):12-triene (LIV). The hypsochromic shift of the absorption maximum from 3200 Å. in the case of (XLVII) which has a cis-β-fusion of rings D and E, to 3150 Å. in (LIV) which has a trans-fusion of rings D and E, further exemplifies the rule discussed in Section (2), p.61. Mineral acid rearrangement of the triene (LIV) gave 1-β-amyratriene which is formulated as 5:8:14-trimethylnovoleana-9:11:13(18)-triene (LV).



The ring contraction reactions of α-amyrin and its derivatives have been compared with the corresponding reactions in the β-amyrin series (Allan, Fayez, Spring and Stevenson, J., 1955, in press).

These authors conclude that steric identity prevails at all ring junctions in the α-Amyrin and β-Amyrin groups of triterpenoids, and thus the cis-β-fusion for the D/E ring junction in α-amyrin, proposed in Section (2) of this thesis, has been confirmed.

Experimental

Section (3).

The preliminary notes to Experimental Sections (1) and (2) apply in full to this section and the hydriodic acid (d,1.7) used was freshly distilled from hypophosphorus acid. The phrase 'in the usual way' in these particular experiments, involving this reagent, implies in general, dilution with water, extraction with ether, washing consecutively with sodium thiosulphat solution, water, aqueous sodium hydroxide, aqueous hydrochloric acid, aqueous sodium bicarbonate, followed by drying of the ethereal extract over anhydrous sodium sulphate, filtration and evaporation to dryness under reduced pressure.

The microanalyses in Sections (1), (2) and (3) were carried out by Mr. Wm. McCorkindale and determinations of ultra-violet spectra were by Misses, P. Adams, N. Caramando and S. MacKenzie under the direction of Dr. A. C. Syme, to whom are due best thanks. Infra-red spectra were determined by Dr. G. Eglinton.

Conversion of 8:10:14-Trimethyl-11-oxo-5ξ-novursa-3:12--diene to 8:10:14-Trimethyl-5ξ-novursa-3:12-diene.

A mixture of 8:10:14-trimethyl-11-oxo-5ξ-novursa--3:12-diene (800 mg.), sodium methoxide (from 800 mg. of sodium) in methanol (15 c.c.) and 100% hydrazine hydrate (5 c.c.) was heated at 200° (autoclave) for 15 hrs. The product, isolated in the usual way, was dissolved in petrol (100 c.c.) and percolated through a column of alumina (20 g.). The column was washed with petrol (100 c.c.) and the combined eluates were evaporated to dryness. The residue crystallised from methanol to yield 8:10:14-trimethyl-5ξ-novursa-3:12-diene as prisms (350 mg.), m.p. 134-135°, $[\alpha]_D$ + 109° (c,1.3). Light absorption: Max. at 2100 Å. (E = 4,600). A specimen on admixture with authentic d-α-amyradiene m.p. 134-135°, showed no m.p. depression.

8:10:14-Trimethylnovursa-3(5):12-diene.

(a) A solution of 8:10:14-trimethyl-5ξ-novursa-3:12--diene (700 mg.) in chloroform (7 c.c.) was treated with trichloroacetic acid (700 mg.) and allowed to stand at room temperature for 1 hr. The chloroform was removed by heating on the steam-bath for 15 mins. Isolation of the product from the violet residue in the

usual way gave a gum which crystallised from acetone to yield 8:10:14-trimethylnovursa-3(5):12-diene as hexagonal prisms (200 mg.), m.p. 70-72°, $[\alpha]_D$ + 123° (c,1.4) (Found: C,87.8; H,11.9. $C_{30}H_{48}$ requires C,88.2; H,11.8%). Light absorption: Max. at 2080 Å.(E = 4,500). (b) A mixture of 8:10:14-trimethyl-11-oxonovursa-3(5):12--diene (1 g.), sodium methoxide (from 1 g. of sodium) in methanol (15 c.c.) and 100% hydrazine hydrate (5 c.c.) was kept at 200° (autoclave) for 15 hrs. The product was isolated in the usual way, dissolved in light petroleum (50 c.c.) and chromatographed on alumina (30 g. The fraction eluted by light petroleum (200 c.c.) was crystallised from acetone to yield 8:10:14-trimethylnovursa-3(5):12-diene as prisms (200 mg.), m.p. 68-69°, $[\alpha]_D$ + 120° (c,2.1) undepressed in m.p. on admixture with the specimen described above.

Acid isomerisation of 8:10:14-Trimethyl-11-oxo-5ξ-novursa--3:12-diene to 8:10:14-Trimethyl-11-oxonovursa-3(5):12--diene.

A solution of 8:10:14-trimethyl-11-oxo-5ξ-novursa--3:12-diene (500 mg.) in acetic acid (50 c.c.) was treated with concentrated hydrochloric acid (5 c.c.) and the mixture refluxed for 16 hrs. with the addition of

concentrated hydrochloric acid (2 c.c.) every 4 hrs. The product, isolated in the usual way, crystallised from methanol as prisms (300 mg.), m.p. 153-154°, $[\alpha]_D$ + 158° (c,1.7) which gave a yellow colour with tetranitromethane. Light absorption: Max. at 2520 Å. (E = 13,000). A specimen on admixture with authentic 8:10:14-trimethyl-11-oxo-novursa-3(5)-diene, m.p. 159-160°, showed no m.p. depression.

Acid isomerisation of 8:10:14-Trimethyl-11-oxonovursa--3(5):12-diene to 5:8:14-Trimethyl-11-oxonovursa-9:12--diene.

A solution of 8:10:14-trimethyl-11-oxonovursa--3(5):12-diene (2 g.) in acetic acid (10 c.c.) was refluxed with hydriodic acid (5 c.c.) for 8 hrs. The product, isolated in the usual way, crystallised from methanol as laminae (1.2 g.), m.p. and mixed m.p. 170-17[illegible] $[\alpha]_D$ + 172° (c,2.1). Light absorption: Max. at 2040 (E = 9,900) 2580 (E = 11,000) and 2900 Å. (E = 10,200)

5:8:14-Trimethyl-11-oxo-18α-novoleana-9:12-diene.

(a) A mixture of 11-oxo-18α-olean-12-en-3β-yl acetate (5 g.) acetic acid (50 c.c.) and hydriodic acid (15 c.c.) was refluxed for 16 hrs. The product, isolated in the usual way, crystallised from methanol to yield

5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-diene as needles (1.5 g.), m.p. 191-192°, $[\alpha]_D$ + 125° (c,3.1) which gave no colour with tetranitromethane. Light absorption: Max. at 2060 (E = 7,800) 2560 (E = 10,100) and 2870 Å. (E = 9,600) (Found: C,85.3; H,11.3. $C_{30}H_{46}O$. requires C,85.25; H,11.0%).

(b) A mixture of 11-oxo-olean-12-en-3β-yl acetate (5 g.), acetic acid (50 c.c.) and hydriodic acid (15 c.c was refluxed for 16 hrs. The product, isolated in the usual manner, crystallised from methanol as needles (1.3 g.), m.p. 191-192°, $[\alpha]_D$ + 122° (c,2.3) which on admixture with the specimen described above showed no m.p. depression.

(c) A mixture of 11-oxo-oleana-12:18-dien-3β-yl acetate (4 g.), acetic acid (40 c.c.) and hydriodic acid (12 c.c.) was refluxed for 16 hrs. The product crystallised from methanol as needles (1 g.) m.p. and mixed m.p. 191-192°, $[\alpha]_D$ + 124° (c,1.7)

5:8:14-Trimethyl-11-oxonovursa-9:12-dien-28-oic Acid.

A mixture of 11-oxours-12-en-3β-yl-28-oic acid acetate (2 g.), acetic acid (20 c.c.) and hydriodic acid (6 c.c.) was refluxed for 16 hrs. The product was isolated in the usual way and crystallised from acetone-hexane to yield 5:8:14-trimethyl-11-oxonovursa-9:12-dien-

-28-oic acid as plates (600 mg.), m.p. 280-282°, $[\alpha]_D$ + 133° (c,2.6) (Found: C,79.8; H,9.9 $C_{30}H_{44}O_3$ requires C,79.6; H,9.8%). Light absorption: Max. at 2080 (E = 6,5 2590 (E = 10,400) and 2920 Å. (E = 9,350).

5:8:14-Trimethyl-11-oxo-18α-novoleana-9:12-dien-28-oic Acid.

A solution of 11-oxo-olean-12-en-3β-yl-28-oic acid acetate (1 g.) in acetic acid (100 c.c.) was refluxed wit hydriodic acid (5 c.c.) for 16 hrs. The product, isolat in the usual way, crystallised from chloroform-hexane to yield 5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-dien-28--oic acid as prisms (310 mg.), m.p. 312-314°, $[\alpha]_D$ + 120° (c,0.7) (Found: C,79.2; H,9.4. $C_{30}H_{44}O_3$ requires C,79.6; H,9.8%). Light absorption: Max. at 2080 (E = 7,250), 2570 (E = 10,800) and 2880 Å. (E = 9,750).

5:8:14-Trimethyl-11-oxo-18α-novoleana-9:12-dien-30-oic Acid.

(a) A solution of 11-oxo-18α-olean-12-en-3β-yl-30-oic acid acetate (800 mg.) in acetic acid (100 c.c.) was refluxed with hydriodic acid (5 c.c.) for 16 hrs. The product was isolated in the usual way and crystallised from methanol-hexane to yield 5:8:14-trimethyl-11-oxo--18α-novoleana-9:12-dien-30-oic acid as prisms (250 mg.),

m.p. 324-326°, $[\alpha]_D$ + 147° (c,0.3) (Found: C,79.4; H,10.2 $C_{30}H_{44}O_3$ requires C,79.6: H,9.8%). Light absorption: Max. at 2060 (E = 6850), 2540 (E = 10,200) and 2870 Å. (E = 8,800).

(b) A solution of 11-oxo-olean-12-en-3β-yl-30-oic acid acetate (2 g.) in acetic acid (150 c.c.) was refluxed with hydriodic acid (10 c.c.) for 16 hrs. The product crystallised from methanol-hexane to yield prisms (500 mg.) m.p. 324-326°, $[\alpha]_D$ + 145° (c,0.2) which was undepressed in m.p. on admixture with the dienone acid described above.

Catalytic hydrogenation of 5:8:14-trimethyl-11-oxonovursa-9:12-diene.

A solution of 5:8:14-trimethyl-11-oxonovursa-9:12-diene (600 mg.) in acetic acid (100 c.c.) was added to a suspension of freshly reduced platinum (from 250 mg. of PtO_2) in acetic acid (100 c.c.) and the mixture shaken with hydrogen at room temperature for 24 hrs. Absorption was then complete (3 mols. approximately). Isolation of the product gave a gum which crystallised from acetone-methanol to yield 5:8:14-trimethyl-9ξ:10ξ-novurs-12-ene as plates (350 mg.), m.p. 95-96°, $[\alpha]_D$ + 140° (c,1.4) which gave a yellow colour with tetranitromethane. (Found: C,87.7; H,12.3 $C_{30}H_{50}$ requires

C,87.9; H,12.5%). Light absorption: Max. at 2060 Å. (E = 2,750), (E_{2150} = 2050) (E_{2150} = 500).

5:8:14-Trimethylnovursa-9:12-diene.

(a) A solution of 5:8:14-trimethyl-11-oxonovursa-9:12--diene (1 g.) in ether (500 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 7 hrs. and allowed to stand overnight at room temperature. The product isolated in the usual way, crystallised from acetone--methanol to yield 5:8:14-trimethylnovursa-9:12-diene as plates (560 mg.) m.p. 98-99°, $[\alpha]_D$ + 120° (c,2.8) which gave an orange brown colour with tetranitromethane. (Found: C,88.2; H,11.8 $C_{30}H_{48}$ requires C,88.0; H,11.9%) Light absorption: Max. at 2080 Å. (E = 13,200).

(b) A mixture of 5:8:14-trimethyl-11-oxonovursa-9:12--diene (1 g.), methanolic sodium methoxide (from 1 g. of sodium and 15 c.c. of methanol and 100% hydrazine hydrate (5 c.c.) was kept at 200° (autoclave) for 15 hrs. The product, isolated in the usual way, crystallised from methanol as plates (250 mg.), m.p. 94-96°, $[\alpha]_D$ + 118° (c,0.9) which showed no m.p. depression on admixture with the specimen, m.p. 98-99°, described above. Light absorption: Max.at 2080 Å. (E = 12,000).

5:8:14-Trimethyl-18α-novoleana-9:12-diene.

A solution of 5:8:14-trimethyl-11-oxo-18α--novoleana-9:12-diene (800 mg.) in ether (500 c.c.) was treated with lithium aluminium hydride (1 g.) and refluxed for 7 hrs. The product, isolated in the usual way, crystallised from methanol-chloroform to yield 5:8:14-trimethyl-18α-novoleana-9:12-diene as matted needles (400 mg.), m.p. 160-162°, $[\alpha]_D$ + 103° (c,0.7) which gave a yellow colour with tetranitromethane (Found: C,88.0; H,12.0. $C_{30}H_{48}$ requires C,88.2; H,11.8%). Light absorption: Max. at 2080 Å. (E = 10,500).

Acid isomerisation of 5:8:14-Trimethylnovursa-9:12-diene.

A solution of 5:8:14-trimethylnovursa-9:12-diene (150 mg.) in chloroform (5 c.c.) and acetic acid (50 c.c.) containing concentrated hydrochloric acid (10 c.c.) was refluxed for 16 hrs. with the addition of concentrated hydrochloric acid (2 c.c.) every 2 hrs. The product was isolated in the usual way and crystallised from chloroform-methanol to give 5:8α:9β-trimethyl-10α--novursa-12:14-diene (1-α-amyradiene) as plates (50 mg.) m.p. and mixed m.p. 193-194°, $[\alpha]_D$ - 110° (c,1.9) Light absorption: Max. at 2360 (E = 13,200) and 2410 Å. (E = 14,500). Inflexion at 2500 Å. (E = 8,550).

Acid Isomerisation of 8:10:14-Trimethyl-5ξ-novursa--3:12-diene.

A solution of 8:10:14-Trimethyl-5ξ-novursa-3:12--diene (250 mg.) in acetic acid (100 c.c.) and boron trifluoride-acetic acid complex (3 c.c.) was refluxed for 80 hrs. The product was isolated through ether and crystallised from chloroform-methanol to yield 5:8α:9β-trimethyl-10α-novursa-12:14-diene (l-α--amyradiene) as plates (130 mg.), m.p. and mixed m.p. 193-194°, $[\alpha]_D$ - 104° (c,1.5). Light absorption: Max. at 2360 (E = 13,000), 2410 (E = 14,500). Inflexio at 2500 Å. (E = 8,500).

8:10:14-Trimethyl-5ξ-novursa-3:9(11):12-triene.

A solution of 8:10:14-trimethyl-11-oxo-5ξ-novursa--3:12-diene (500 mg.) in ether (200 c.c.) was refluxed with lithium aluminium hydride (500 mg.) for 3 hrs. The reaction product (isolated in the usual way), was dissolved in pyridine (50 c.c.) and refluxed for 15 hrs with phosphoryl chloride (20 c.c.). The product was crystallised from methanol from which 8:10:14-trimethyl--5ξ-novursa-3:9(11):12-triene (d-α-amyratriene) separated as needles (200 mg.) m.p. and mixed m.p. 132-133°, $[\alpha]_D$ + 445° (c,2.1). Light absorption: Max. at 2060 (E = 11,500) and 2800 Å. (E = 10,300)

Treatment of Ursa-9(11):12-dien-3β-yl Acetate with Hydriodic Acid.

A solution of ursa-9(11):12-dien-3β-yl acetate (3 g.) in acetic acid (30 c.c.) was refluxed with hydriodic acid (15 c.c.) for 16 hrs. The product was a gum and the only crystalline product isolable from it was 5:8α:9β-trimethyl-10α-novursa-12:14-diene (1-α-amyradiene) which crystallised from chloroform--methanol as plates (300 mg.), m.p. and mixed m.p. 192-194°, $[\alpha]_D$ - 110° (c,0.9).

5:8:14-Trimethylnovursa-1(10):9(11):12-triene.

A solution of 5:8:14-trimethyl-11-oxonovursa-9:12--diene (500 mg.) in ether (200 c.c.) was treated with lithium aluminium hydride (500 mg.) at 0° and kept at that temperature for 72 hrs. The product was isolated avoiding the use of mineral acid and crystallised from methanol to yield 5:8:14-trimethylnovursa-1(10):9(11):1-triene as needles (300 mg.) m.p. 145-146°, $[\alpha]_D$ -358° (c,1.6) which gave a strong yellow colour with tetranitromethane (Found: C,88.8; H,11.4. $C_{30}H_{46}$ requires C,88.6; H,11.4%) Light absorption: Max. at 3200 Å. (E = 15,000).

Acid isomerisation of 5:8:14-Trimethylnovursa-1(10):9(11):12-triene to 5:8:14-Trimethylnovursa-9:11:13(18)-triene

A solution of 5:8:14-trimethylnovursa-1(10):11:13(18)-triene (80 mg.) in acetic acid containing concentrated hydrochloric acid (2 c.c.) was heated at 100° for 2 hrs. and then kept at room temperature for 48 hrs. The mixture was again heated on the steam-bath for 3 hrs and the product isolated in the usual way. Crystallisation from methanol yielded 5:8:14-trimethylnovursa-9:11:13(18)-triene (1-α-amyratriene) as needles (50 mg.), m.p. and mixed m.p. 140-142°, $[\alpha]_D$ - 455° (c,3.1) which gave a brown colour with tetranitromethane. Light absorption: Max. at 2950 Å. (E = 35,500). Inflexions at 2860 (E = 30,200) and 3080 Å. (E = 25,500).

5:8:14-Trimethylnovoleana-9:11:13(18)-triene.

A solution of oleana-9(11):12-dien-3β-ol (2 g.) in benzene (60 c.c.) was shaken with phosphoric oxide (3 g.) for 20 hrs. The product, isolated through benzene, crystallised from methanol to yield 5:8:14-trimethylnovoleana-9:11:13(18)-triene as needles (600 mg.) m.p. 135-136°, $[\alpha]_D$ -400° (c,1.8) which gave a brown colour with tetranitromethane. (Found: C,88.9; H,11.7 $C_{30}H_{46}$ requires C,88.6; H,11.4%). Light absorption: Inflexion at 2860 Å. (E = 31,000); Max. at 2950 (E = 36,200) and 3080 Å. (E = 25,400).

5:8:14-Trimethyl-18α-novoleana-1(10):9(11):12-triene.

A solution of 5:8:14-trimethyl-11-oxo-18α-novoleana-9:12-diene (400 mg.) in ether (200 c.c.) was treated with lithium aluminium hydride (500 mg.) and allowed to stand at 0° for 72 hrs. The product, isolated avoiding the use of mineral acid, crystallised from methanol to yield 5:8:14-trimethyl-18α-novoleana--1(10):9(11):12-triene as plates (250 mg.), m.p. 140-142 $[\alpha]_D$ - 450° (c,0.9), which gave a strong yellow colour with tetranitromethane. (Found: C,88.6; H,11.5. $C_{30}H_{46}$ requires C,88.6; H,11.4%). Light absorption: Max. at 3150 Å. (E = 14,000).

Acid isomerisation of 5:8:14-Trimethyl-18α-novoleana-1(10):9(11):12-triene to 5:8:14-Trimethylnovoleana-9:11:13(18)-triene.

A solution of 5:8:14-trimethyl-18α-novoleana-1(10):9(11):12-triene (50 mg.) in acetic acid (50 c.c.) was treated with concentrated hydrochloric acid (2 c.c.) and allowed to stand at room temperature for 70 hrs. The product, isolated in the usual way, crystallised from methanol to yield 5:8:14-trimethylnovoleana-9:11:13(18)--triene as needles (20 mg.), m.p. and mixed m.p. 132-135 $[\alpha]_D$ - 407° (c,0.4).