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TRITERPENES OF THE FRIEDELANE SERIES.

A THESIS

Submitted in part fulfilment of
the requirements for admittance
to the degree of

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of the

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by

John Lawrence Courtney

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TABLE OF CONTENTS.

SUMMARY.

A scheme has been devised for the separation of the extract of the bark of Siphonodon australe Benth. into the following groups of compounds: (1) An acidic fraction, (2) a paraffin hydrocarbon, (3) a diterpene fraction, and (4) a triterpene fraction. The triterpene fraction has been resolved into groups consisting of ketones, monohydroxy-ketones, and polyhydroxy-compounds, and the ketonic portion has been shown to contain friedelin, two diketones, and a triketone. These three new ketones have been related to friedelin (friedelan-3-one) and to each other and are named friedelane-3:x-dione, friedelane-3:y-dione, and friedelane-3:x:y-trione. One of the monohydroxy-ketones has been shown to be y-hydroxyfriedelan-3-one and another has been shown to be x[eq]-hydroxyfriedelane-3:y-dione. In view of their relation to friedelin, the chemistry and stereochemistry of friedelin and cerin have been reviewed.

A review of skeletal rearrangements in triterpene chemistry is included since the method adopted for the location of the x- and y-oxo groups utilises the friedelene-oleanene rearrangement. Initial experiments indicated the possibility of intermediates in the friedelene-oleanene rearrangement and a study of this transformation was undertaken. It was discovered that alnus-5(10)-ene is an isolable intermediate and thus the rearrangement is not

fully concerted. The possibility of other intermediates in the rearrangement is discussed. Olean-12-one has also been isolated from the friedelene-oleanene rearrangement and this establishes the configuration of $C_{(18)}$ in friedelane. The mechanism of the formation of olean-12-one is discussed.

Evidence has been obtained which indicates that the x-oxo group is probably located at $C_{(22)}$ though $C_{(15)}$ and $C_{(21)}$ are possibilities which cannot be definitely excluded. The y-oxo group is most probably located in ring C.

THE CHEMISTRY OF FRIEDELIN AND CERIN.

An Outline of the Development of the Structure.

The chemistry of friedelin has had a slow and rather spasmodic development in spite of the fact that it may be obtained readily from a very common material --- cork. The explanation for this is that friedelin has only one reactive functional group, the carbonyl group at one end of a completely saturated carbon skeleton. Had it not been for the discovery of the conversion of friedelene to an equilibrium mixture of 18α-olean-12-ene and olean-13(18)-ene, the structure of friedelin might not be known for some considerable time.

A mixture of friedelin and a related compound, cerin, was first isolated from cork in 1807 by Chevreul[1] who thought he was dealing with a single substance. The purification of cerin was described by Thoms[2] in 1898, and in 1899 Istrati and Ostrogovich[3] demonstrated that cork extract consisted principally of two substances which could be separated by recrystallisation from chloroform. Istrati named the more soluble compound friedelin after Friedel who had found during his own studies that cerin possessed a carbonyl group.[3a]

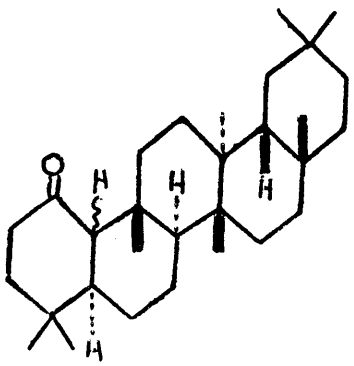
Thirty six years later Drake and Jacobsen[4] commenced their investigations on the chemistry of friedelin and cerin. They extracted cork with ethyl acetate and separated cerin from friedelin in the extract by virtue of the low solubility of cerin in chloroform. Their investigations revealed that cerin was a hydroxy-ketone with formula $C_{30}H_{50}O_2$ and that

friedelin was a ketone with formula $C_{30}H_{50}O$. It was found that friedelin formed the usual carbonyl derivatives (oxime, 2:4-dinitrophenylhydrazone etc.) and that various enol esters could be formed without difficulty. Both cerin and friedelin were reduced to the same hydrocarbon ($C_{30}H_{52}$) by the Clemmensen method[4] but Drake and Shrader[5] were unable to convert cerin to friedelin. The selenium dehydrogenation of friedelanol[6] yielded 1:8-dimethylpicene, 1:2:7-trimethylnaphthalene, 1:2:5:6-tetramethylnaphthalene and 1:2:8-trimethylphenanthrene which indicated that friedelin and cerin were pentacyclic triterpenes. It was shown later by surface film measurements[7] that the carbonyl group of friedelin was located near the end of the molecule and that the hydroxyl and carbonyl groups of cerin are not far removed from each other.

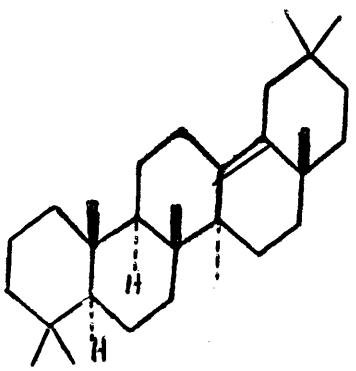
Ruzicka and his collaborators[8,9] repeated some of the work of Drake's school and carried it further. On the basis of a series of oxidative degradations which they carried out, they concluded that friedelin contained the grouping $-CH_2-CH_2-CO-\underset{|}{CH}-\underset{|}{CH}-$ and that cerin is the related α-hydroxy compound.

Six years later Spring and his associates[10] proposed a structure (I) for friedelin on the basis of the conclusion of the Swiss workers and the remarkable acid-catalysed rearrangement of friedelene to olean-13(18)-ene (II). (It was subsequently shown by Spring et.al.[12] that the substance obtained is an equilibrium mixture of olean-13(18)-ene and

18α-olean-12-ene, and that these two substances form a mixed crystal).

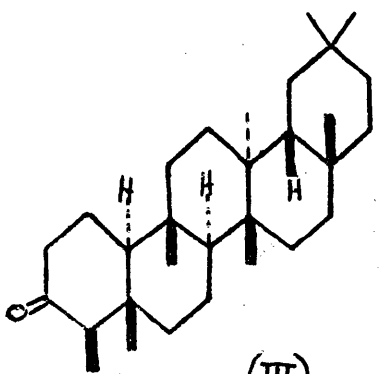


(I)



(II)

Ourisson and Takahashi[11,11a] pointed out that this structure could not be correct for their investigations indicated that friedelin possessed a methyl group adjacent to the carbonyl group. On the basis of this and other results obtained by Ourisson and Takahashi, Spring and his associates[13,16] modified their original structure and proposed a structure (III) which satisfactorily fitted the known facts. They also indicated that friedelin cannot possess the grouping $-CH_2-CH_2-CO-\overset{|}{C}H-\overset{|}{C}H-$ as suggested by the Swiss workers.



(III)

At about the same time, Corey and Ursprung[14] independently deduced the same structure for friedelin on the basis of a considerable amount of degradative work and converted it into the oleanene equilibrium mixture under different conditions.

Dutler, Jeger and Ruzicka[15] also announced that they had discovered the friedelene-oleanene rearrangement and used yet another set of conditions for the conversion.

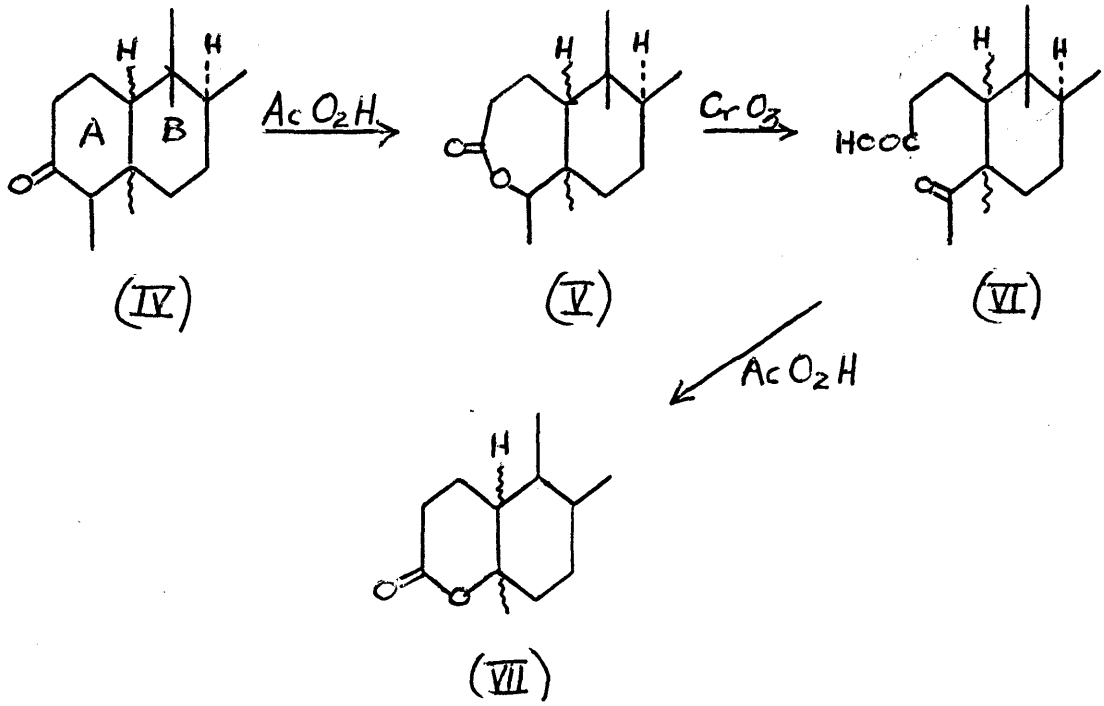
DETAILED EVIDENCE FOR THE STRUCTURE OF FRIEDELIN.

Evidence for the Presence of a Methyl Group and a Hydrogen Atom at $C_{(4)}$.

When Drake and Campbell[17] oxidised friedelin with chromic acid they obtained a keto-acid which they called friedonic acid. They were able to convert it to a lactone by reduction with sodium and alcohol or by hydrogenation, but were unsuccessful in their attempts to prepare carbonyl derivatives from either the acid or its ester. Ourisson and Takahashi[11,11a] demonstrated that friedonic acid is a methyl ketone by oxidising it with alkaline hypobromite to a dicarboxylic acid. This indicated that friedelin has a methyl group on the carbon atom adjacent to the carbonyl group.

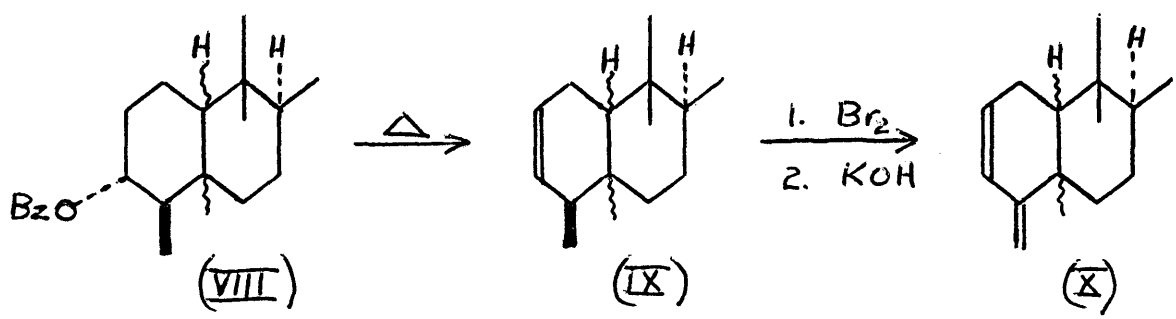
Further evidence for this was supplied by Corey and Ursprung's experiments.[14] They oxidised friedelin (IV) with peracetic acid and formed a lactone (V) which was converted to a keto-acid, friedonic acid (VI) by oxidation with chromic acid. This keto-acid was converted to a C_{28}-lactone(VII)

by oxidation with peracetic acid and lost two carbon atoms in the process.



(IV) (V) (VI) (VII)

Additional evidence for the presence of a hydrogen and methyl groups on $C_{(4)}$ was obtained as follows. Pyrolysis of friedelanyl benzoate (VIII) yielded friedel-2-ene (IX) which, after bromination and dehydrobromination of the product, formed an exomethylenic diene (X) the nature of which was indicated by its infrared and ultraviolet spectra.[14]



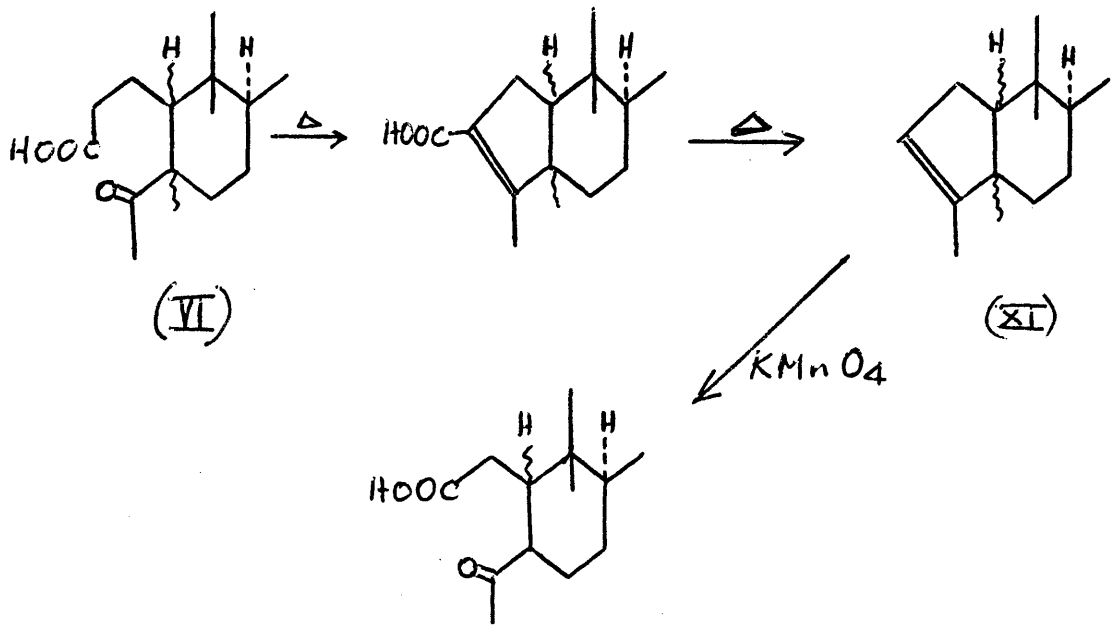
(VIII) (IX) (X)

Spring and his collaborators[16] described the preparation of friedel-3-ene by dehydration of epifriedelanol with phosphorus oxychloride and pyridine. Since oxidation of friedel-3-ene with osmic acid gave a saturated glycol which forms a monoacetate only, and this was stable to chromic-acetic acid at room temperature they concluded that the double bond in this compound was trisubstituted. They have also shown that the product of pyrolysis of friedelanyl benzoate is a mixture of hydrocarbons, the major component of which is friedel-3-ene since oxidation of this hydrocarbon mixture with osmic acid followed by acetylation, yielded the diol monoacetate of friedel-3-ene plus a small amount of a diol diacetate.

Evidence for the Presence of Two Methylene Groups in Ring A.

The pyrolysis of friedelanyl benzoate yielded an unsaturated hydrocarbon which upon oxidation with chromic acid gave an unsaturated ketone, friedelenone ($C_{30}H_{48}O$). From this Drake and Campbell[17] deduced the presence of the grouping $>CH\text{-}CO\text{-}CH_2\text{-}$.

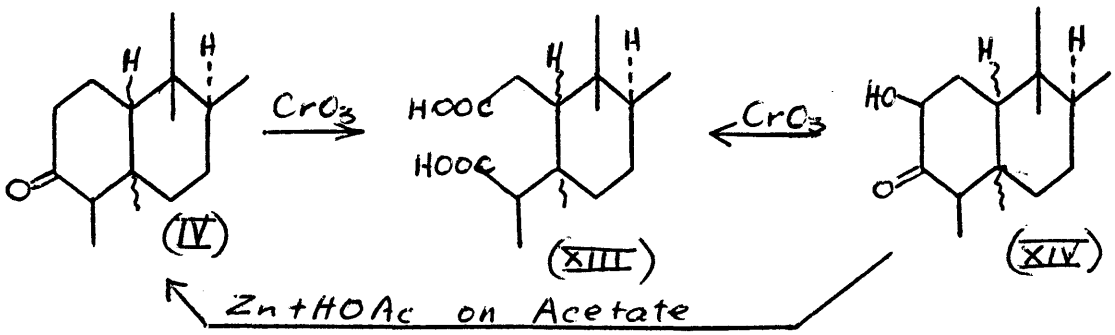
When friedonic acid (VI) was heated above its melting point it formed norfriedelene ($C_{29}H_{48}$) (XI) with the loss of carbon dioxide and water. Oxidation of norfriedelene with potassium permanganate afforded norfriedonic acid ($C_{29}H_{48}O_3$) (XII), a keto-acid which formed the usual carbonyl derivatives.[18]



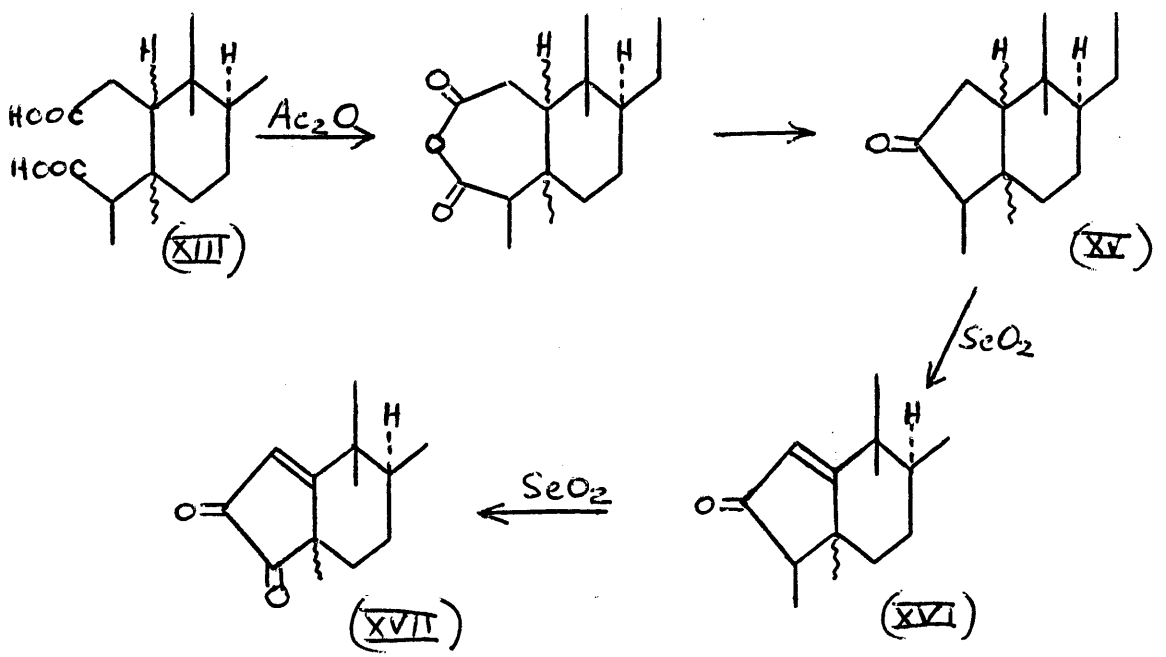
(VI) (XI) (XII)

These reactions proved the presence of a methylene group adjacent to the carbonyl group of friedelin.

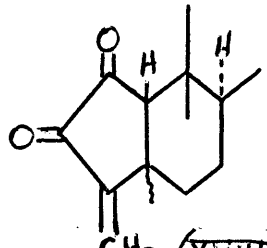
Ruzicka and his collaborators[8] obtained a dicarboxylic acid (XIII) as well as friedonic acid (VI) when they oxidised friedelin with, chromic acid. This also indicated the presence of a methylene group adjacent to the carbonyl group. The same dicarboxylic acid and a saturated α-diketone were formed by the oxidation of cerin with chromic acid.[8] Thus cerin must be either 2-hydroxyfriedelan-3-one or 3-hydroxyfriedelan-2-one and since Spring et al.[16] were able to convert cerin acetate to friedelin by the action of zinc and acetic acid, they concluded that cerin was 2-hydroxyfriedelan-3-one (XIV).



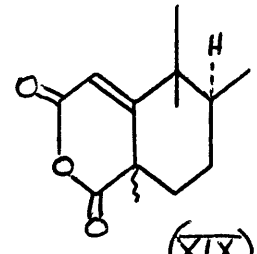
The dicarboxylic acid was converted by treatment with acetic anhydride to the acid anhydride and this upon heating yielded norfriedelanone (XV). Selenium dioxide oxidation of norfriedelanone yielded norfriedelenone (XVI) which was oxidised further with the same reagent to a compound which was eventually shown to be bisnorfriedelendione $C_{28}H_{42}O_2$ (XVII). Hence the formation of this compound by selenium dioxide oxidation of norfriedelanone involved the loss of one carbon atom.



On the basis of the infrared absorption of bisnorfriedelendione, ($>C = CH_2$ infrared max. 875 cm^{-1}) Corey and Ursprung[14] had suggested the C_{29} structure (XVIII). This was shown to be incorrect by Spring and his co-workers[13] who reasoned that since it is not enolisable it cannot have this structure and it must therefore be (XVII). Support for this view was supplied by the X-ray crystallographic determination of the molecular weight of norfriedelendioic anhydride(XIX).[11a]



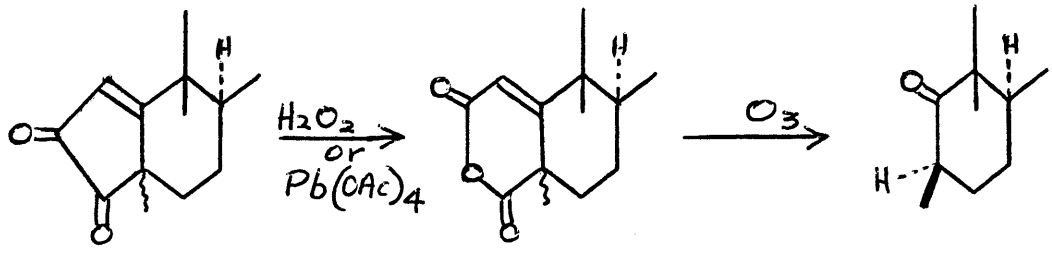
(XVIII)



(XIX)

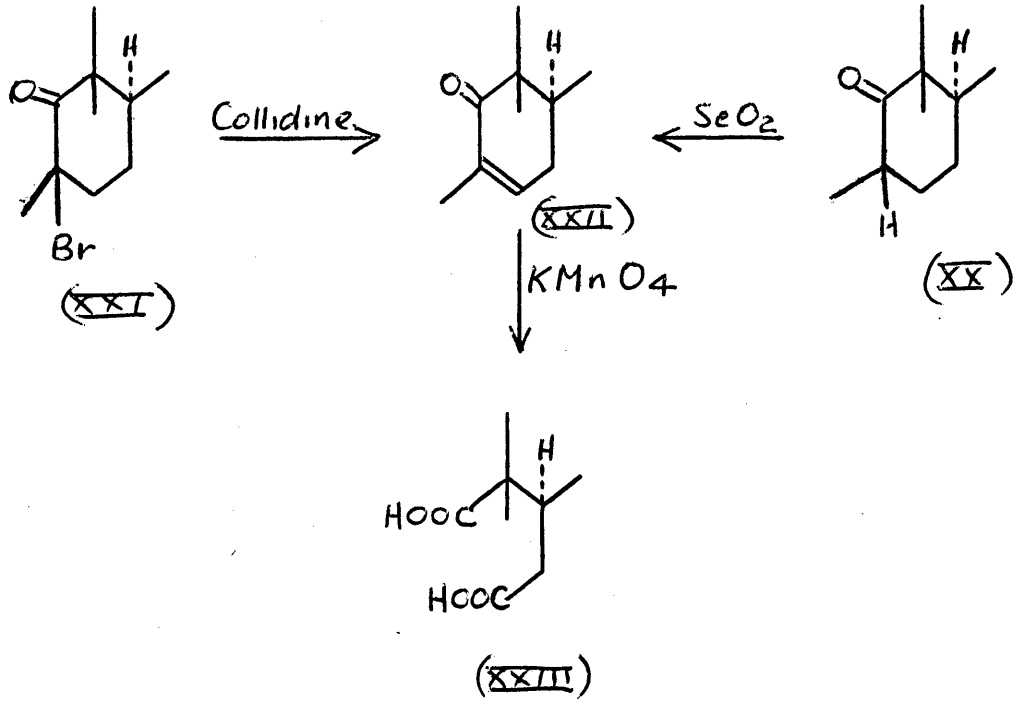
Evidence for the Presence of Methyl Groups at $C_{(5)}$ And $C_{(9)}$.

Bisnorfriedelendione (XVII) was converted by means of lead tetra-acetate or hydrogen peroxide in acetic acid to an acid anhydride (XIX) which formed a saturated tetracyclic ketone (XX) upon ozonolysis.[9] This ketone was shown to



(XVII) (XIX) (XX)

possess only one α-hydrogen atom by titration with bromine[11,11a] and by deuterium exchange with deuterium bromide.[14] Ourisson and Takahashi [11,11a] found that the axial monobromoketone (XXI) was readily dehydrobrominated to form an αβ-unsaturated ketone (XXII) which they also formed by selenium dioxide oxidation of the original tetracyclic ketone (XX). When the αβ-unsaturated ketone was oxidised with potassium permanganate a tricyclic dicarboxylic acid (XXIII) was formed involving the loss of two carbon atoms.

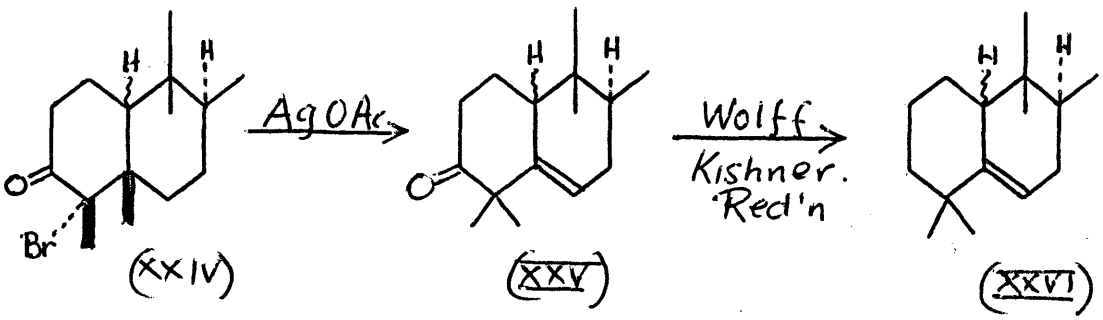


(XXI) (XXII) (XX) (XXIII)

This proved the presence of methyl groups at $C_{(5)}$ and $C_{(9)}$ in friedelin.

Further evidence for the presence of a methyl group

at $C_{(5)}$ was the formation of an unsaturated, unconjugated ketone by the dehydrobromination of 4-bromofriedelin (XXIV) with silver acetate.[14] This compound could not be isomerised to an αβ-unsaturated ketone and the hydrocarbon obtained by Wolff-Kishner reduction was neither friedel-2-ene nor friedel-3-ene. It was therefore assumed that the unsaturated ketone had structure (XXV), that the hydrocarbon derived from it was (XXVI) and that migration of a methyl group at $C_{(5)}$ had occurred during dehydrobromination.[14]



(XXIV) (XXV) (XXVI)

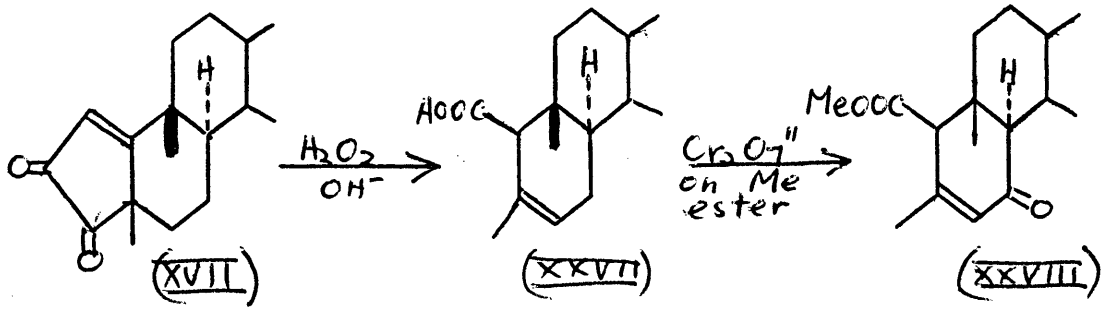
Recently it has been shown that the product of dehydrobromination of 4-bromofriedelin by silver acetate is a mixture of two unsaturated ketones (XXV) and (XXVa). These are produced in the ratio of 1 to 2 respectively and form a mixed crystal.[19] The hydrocarbon obtained by Wolff-Kishner reduction is therefore probably a mixture of the two isomers (XXVI) and (XXVIa).

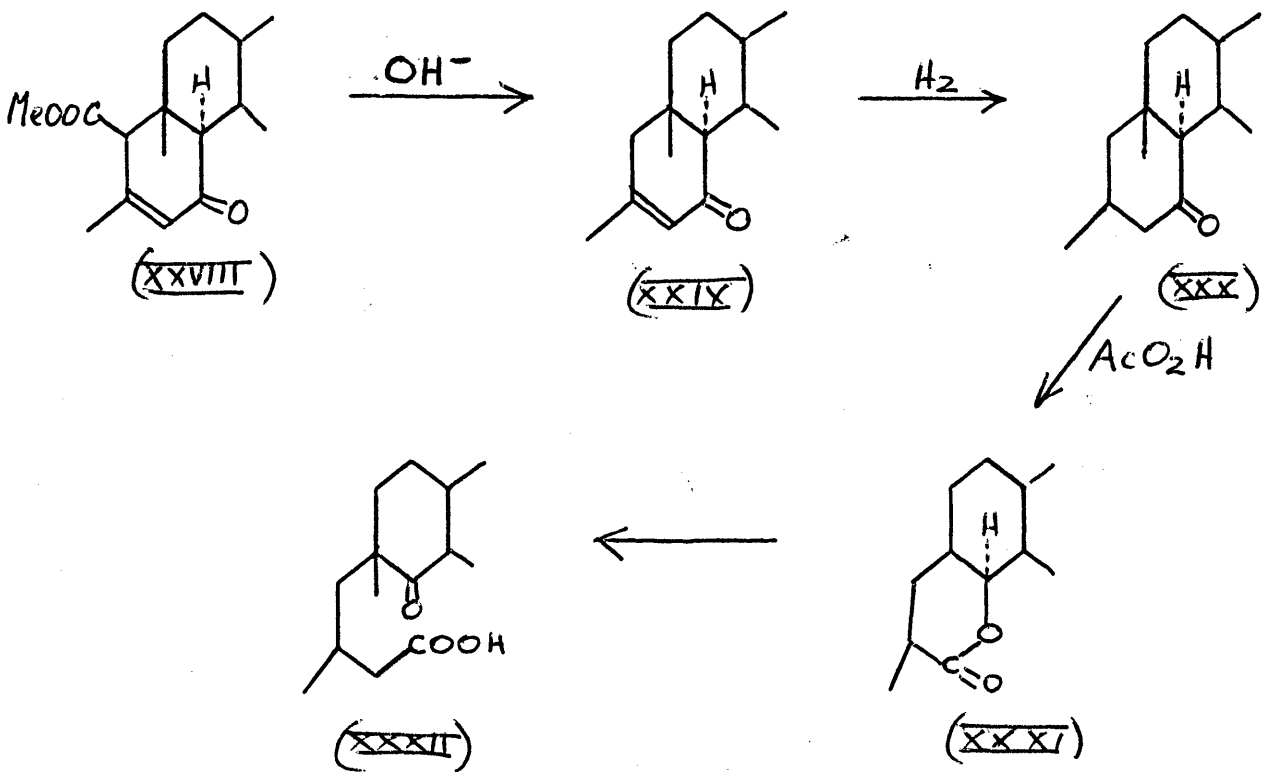
(XXVa) (XXVIa)

Evidence for the Presence of a Hydrogen Atom at $C_{(8)}$.

In 1949 Ruzicka and his co-workers[9] treated bisnor-friedelendione (XVII) with alkaline hydrogen peroxide and obtained an unsaturated acid $C_{26}H_{42}O_2$ (XXVII) which was readily decarboxylated to form a mixture of unsaturated hydrocarbons. Selenium dehydrogenation of the unsaturated acid yielded 1:2:5:6-tetramethylnaphthalene, a benzene derivative $C_{24}H_{36}$ or $C_{25}H_{38}$, a saturated hydrocarbon $C_{25}H_{44}$, and an alkylated chrysene $C_{20}H_{16}$ or $C_{21}H_{18}$.

Corey and Ursprung[14] prepared this unsaturated acid in the same way and oxidised the methyl ester with dichromate to form an unsaturated keto-ester (XXVIII). Hydrolysis and decarboxylation of this product gave an αβ-unsaturated ketone (XXIX) which was converted to a saturated ketone (XXX) by hydrogenation. Deuterium exchange of this ketone with deuterium bromide indicated the presence of a hydrogen atom at $C_{(8)}$. The oxidation of the ketone (XXX) by peracetic acid to a lactone (XXXI) which was then oxidised to a keto-acid (XXXII) was also proof of the presence of a hydrogen atom at $C_{(8)}$.





The Location of the Four Remaining Methyl Groups.

The products of the selenium dehydrogenation of friedelanol[6] and the conversion of friedel-3-ene to the equilibrium mixture of oleanenes[10,14,15] have indicated the presence of the four remaining methyl groups. Methyl groups must be present at $C_{(13)}$ and $C_{(14)}$ since 1:2:7-trimethylnaphthalene and 1:2:8-trimethylphenanthrene were formed by selenium dehydrogenation of friedelanol. The rearrangement of friedelene to a mixture of oleanenes proved the location of methyl groups at $C_{(17)}$ and $C_{(20)}$.

THE STEREOCHEMISTRY OF FRIEDELIN.

Evidence for the stereochemistry of friedelin has been derived from two types of sources: (a) the friedelene —— oleanene rearrangement, and (b) other physical and chemical investigations. The validity of some of the stereochemical deductions from the friedelene —— oleanene rearrangement is dependent on whether or not this rearrangement is fully concerted; consequently these deductions are discussed in a later section (p. 91) in which it is shown that the rearrangement is, in part at least, not concerted. Even though some of the deductions from the rearrangement are not applicable, the absolute configurations of all asymmetric centres in friedelin have been satisfactorily established with the exception of $C_{(18)}$. The situation may be summarised in the following chart.

Apart from the friedelene —— oleanene rearrangement, the only evidence for the stereochemistry of the C/D- and D/E- ring junctions has been derived from an X-ray analysis mentioned by Corey and Ursprung[14] in their preliminary note. The accuracy of deductions based on X-ray analysis is greatly dependent upon the degree of refinement of the various calculations employed. Deductions about the stereochemistry of friedelin based on X-ray analysis therefore cannot be taken as conclusive until full details of the analysis are published.

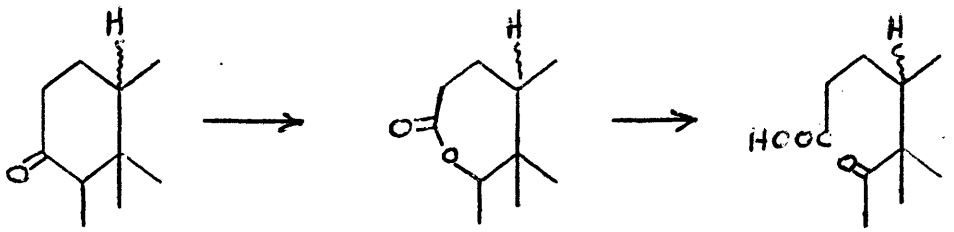
SUMMARY OF THE EVIDENCE FOR THE STEREOCHEMISTRY OF FRIEDELIN.

Ring Junction	Asymmetric Centre	Evidence from Friedelene-Oleanene Rearrangement	Evidence from other Methods
	$C_{(4)}$	No evidence	Configuration established by several methods
A/B	$C_{(5)}$ and $C_{(10)}$	No evidence since alnus-5(10)-ene is an intermediate (see p.92)	Configuration established by several methods
B/C	$C_{(8)}$	No evidence if the alnusene-oleanene rearrangement is not concerted (see p.91)	Configuration established by several methods
	$C_{(9)}$	Configuration established whether rearrangement is concerted or not	
C/D	$C_{(13)}$ and $C_{(14)}$	Configuration established whether rearrangement is concerted or not	Evidence entirely from X-ray analysis
D/E	$C_{(17)}$	Configuration established whether rearrangement is concerted or not	Evidence entirely from X-ray analysis
	C(18)	Configuration established in the present work (see p.93)	

EVIDENCE OTHER THAN THE FRIEDELENE — OLEANENE REARRANGEMENT.

The Configuration of $C_{(4)}$.

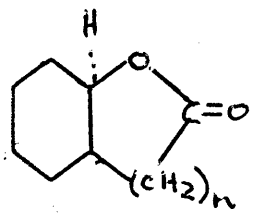
Ourisson and Takahashi[11a] oxidised friedelin (I) with perbenzoic acid and formed a lactone (II) whose structure was proved by oxidation to friedonic acid (III).



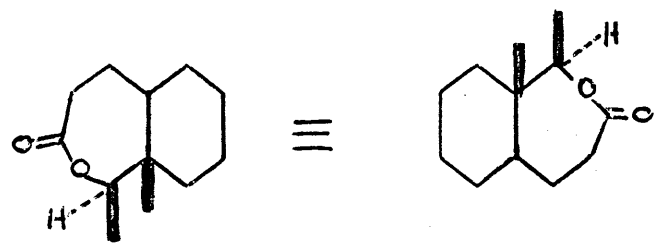
(I) (II) (III)

Using Klyne's modification of Hudson's lactone rule[20] and assuming its applicability to a seven-membered lactone ring, they were able to show that the hydrogen atom at $C_{(4)}$ was α-oriented and thus the methyl group at $C_{(4)}$ must be β-oriented. Klyne's modification of Hudson's rule states that if the hydrogen atom attached to the carbon atom carrying the potential hydroxyl group is below the plane of the lactone ring as in (IV), the difference between the molecular rotations of the lactone and the hydroxy acid, (or the deoxy acid, or hydrocarbon) will be positive. If the hydrogen is above the plane of the ring the $\triangle$ value will be negative. The molecular rotation of the lactone(II)

was found to be +170°, that of friedelin was -120° and friedelane had a molecular rotation of +90°. The molecular rotation difference in both cases was large and positive thus indicating that the lactone had the structure (V).



(IV)

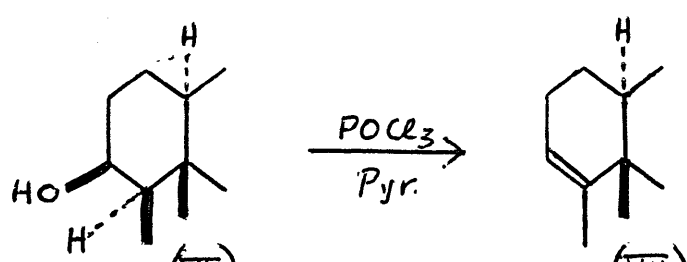


(V)

Hence the hydrogen atom at $C_{(4)}$ was shown to be α-oriented and the methyl group at $C_{(4)}$ must therefore be β-oriented.

Recently it has been shown that the equatorial configuration of an alkyl group in an α-alkylcyclohexanone is the more stable configuration[21]. Since friedelin has been shown to be stable to treatment with both acid and alkali, the methyl group at $C_{(4)}$ must be equatorial.

epiFriedelanol (friedelan-3β[ax]-ol) (VI) was readily dehydrated with phosphorus oxychloride to give friedel-3-ene (VII).[11a,16] This reaction is an ionic elimination involving two adjacent trans-diaxial groups.



(VI) (VII)

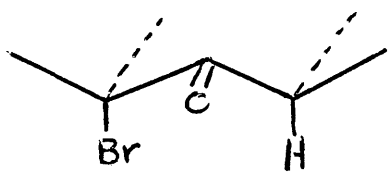
Hence the hydrogen atom at $C_{(4)}$ must be axial and the methyl group at $C_{(4)}$ must be equatorial and β-oriented.[11a,16]

The A/B Ring Junction.

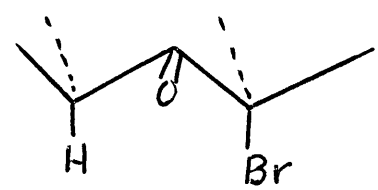
Various lines of evidence have led to the conclusion that the A/B ring junction of friedelin is enantiomorphic to the 5α-steroids and the usual triterpenes. One approach to the study of stereochemistry of the A/B ring junction utilised Klyne's principles of molecular rotation differences.[22] Klyne has shown that in polycyclic compounds such as steroids and triterpenes two enantiomorphic forms of a terminal ring have rotational contributions of opposite sign, often of the same order of magnitude. Ourisson and Takahashi[11a] demonstrated this enantiomorphic relationship in a most striking manner. By plotting the molecular rotation differences of various ring A derivatives of friedelin against those of the corresponding derivatives of several 5α-steroids and triterpenes, they demonstrated graphically the enantiomorphic relationship of the A/B ring junction of friedelin. Dutler, Jeger and Ruzicka[15] have observed that the molecular rotation differences of A-nor-friedelanone and A-norlanostanone are of opposite sign indicating that the A/B ring junction of friedelin is enantiomorphic to the A/B ring junction of lanosterol and the tetracyclic and pentacyclic triterpenes. An abundance of similar evidence has accumulated during the present work

to confirm the views of all of these workers. (see p.43)

A slightly different approach to the problem was used by Corey and Ursprung.[14] Since they were unable to epimerise 2-bromofriedelin by hydrogen bromide they concluded that rings A and B must be <u>trans</u>- locked and that there must be a hydrogen atom attached to $C_{(10)}$. If the A/B ring junction were <u>cis</u>, 2-bromofriedelin would be a strained and unstable structure due to steric congestion of the bromine with any substituent on $C_{(10)}$, and would therefore be epimerisable. If the A/B ring fusion were <u>trans</u> and a methyl group was attached to $C_{(10)}$ then steric hindrance between it and the bromine would make the compound epimerisable.[23] The absolute configurations of $C_{(5)}$ and $C_{(10)}$ were determined by these workers in the following manner. Using data obtained from steroidal bromo-ketones, they showed that the molecular rotation contributions of axial bromine atoms in α-bromo-ketones of type (A) and (B) are of opposite signs. The molecular rotation contributions



(A)



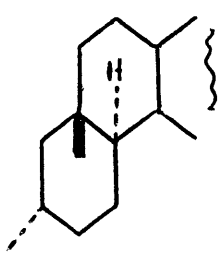
(B)

of axial bromine in 2-bromofriedelin and 4-bromofriedelin

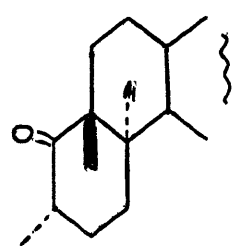
(the bromine in both compounds was shown to be axial by their ultraviolet and infrared absorption spectra[24]) were found to be -651° and +614° respectively hence the bromine atoms are α-oriented in both compounds. Since the A/B ring junction had been shown to be trans- locked the substituents at $C_{(5)}$ and $C_{(10)}$ must have axial conformations, and as the axial bromine in 4-bromofriedelin has been shown to be α-oriented, the axial methyl group at $C_{(5)}$ must be β-oriented. Thus the hydrogen atom at $C_{(10)}$ must have an α-orientation.

The B/C and C/D Ring Junction.

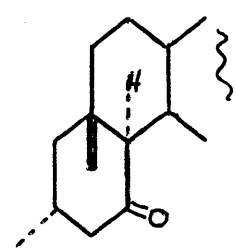
Ourisson and Takahashi[11a] deduced that the B/C ring fusion was trans on the basis of the molecular rotation contributions of the carbonyl groups in the isomeric C_{25} Tetracyclic ketones (VIII)[9] and (IX).[14] The molecular rotation of the ketone (VIII) was +135° and that of its isomer (IX) was +150° whilst the hydrocarbon (X)[9] had a molecular rotation of +51°.



(X)



(VIII)

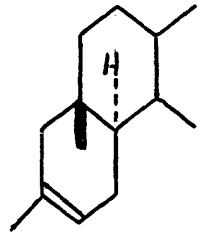


(IX)

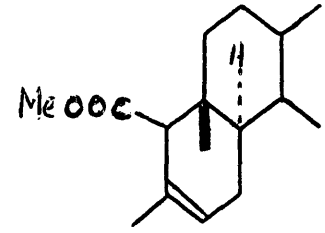
The molecular rotation contributions of both of the carbonyl

groups are thus positive. Applying Klyne's generalisations with respect to terminal rings[22] (see p.20) they concluded that the B/C ring junction was <u>trans</u>- locked analogous to the A/B ring junction of the 5α-steroids.

Corey and Sneen[25] have calculated by the method of vector analysis that <u>trans</u>- Δ^2-octalin should be more stable than <u>trans</u>- Δ^1-octalin because of differences in steric congestion in the molecules. They also point out that this has been confirmed by experiments on various steroidal compounds.[26] Because of the stability of the double bond in the Δ^2- position in the tetracyclic olefin (XI) and in the methyl ester of the tetracyclic acid (XII), Corey and Ursprung[14] have suggested that rings B and C are <u>trans</u>- locked.



(XI)



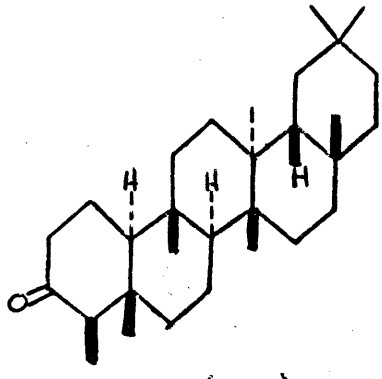
(XII)

An X-ray single crystal analysis of friedelanyl chloroacetate revealed that the molecule was flat and hence the B/C and C/D rings must be <u>trans</u>- locked.[14]

The D/E Ring Junction.

Reasoning from the friedelene-oleanene rearrangement and biosynthetic considerations, various workers[10,13,14,15,16] have expressed the opinion that the D/E ring junction is cis-fused on hypothetical grounds. These views have apparently been confirmed by a 2-dimensional Fourier X-ray analysis on friedelan-3α-ol chloro- and bromoacetates.[14] Until details of this examination are published it can hardly be taken as being conclusive. However, the configuration of $C_{(18)}$ has been definitely established by chemical evidence obtained in the present work.(see p. 93)

The evidence described, in conjunction with evidence from the friedelene-oleanene rearrangement, establishes that the constitution of friedelin is (XIII).

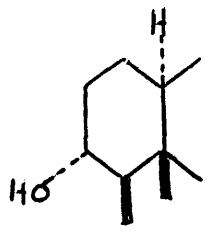


(XIII)

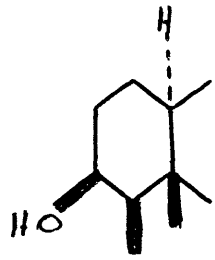
EVIDENCE FOR THE CONFIGURATIONS OF FRIEDELANOL, epiFRIEDELANOL AND CERIN.

Friedelanol and epiFriedelanol.

Friedelanol and epifriedelanol have been shown to be epimers since they were prepared from friedelin by different methods and were both oxidised back to friedelin. epiFriedelanol has been isolated from a lichen[27,28] and from Ceratopetalum apetalum D. Don.[28,29] Friedelanol was prepared by the reduction of friedelin with sodium and n-pentyl alcohol and since it is known that such reductions occur under equilibrating conditions, friedelanol must be the equatorial alcohol. Friedelanol is also formed when epifriedelanol is heated with sodium pentyloxide.[16] Thus epifriedelanol must be the axial alcohol. Since the ring structure of friedelane is in part a "skeletal enantiomorph" of the 5α-steroids and the usual triterpenes (see p.20), the 3-equatorial alcohol must be α-oriented and the axial alcohol is β-oriented. Thus friedelanol is friedelan-3α-ol (XIV) and epifriedelanol is friedelan-3β-ol (XV).



(XIV)

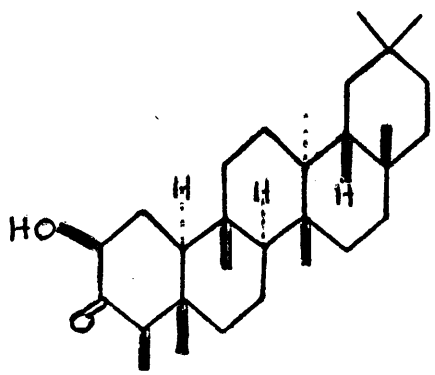


(XV)

Ourisson and Takahashi[11a] have pointed out that this is in accordance with the molecular rotation contributions of the hydroxyl and acetate groups at $C_{(3)}$; according to Klyne and Stokes,[30] the molecular rotation differences of hydroxyl and acetate groups at $C_{(3)}$ in triterpenes are negative when the groups are α-oriented, and positive when they are β-oriented; the molecular rotation differences of friedelanol and its acetate are negative whilst the corresponding properties of epifriedelanol are positive. Additional data in support of this view have been obtained in the present work (p.43).

Cerin.

Cerin has been shown to be 2β-hydroxyfriedelin (XVI)[11,11a] because of the characteristic influence of an equatorial alcohol group on the ultraviolet and infrared absorption spectra of an adjacent carbonyl group.[31] Corey and Ursprung[14] ascribe the equatorial configuration to the hydroxyl group of cerin because of the ease with which it is acylated and sulphonated.



(XVI)

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TRITERPENES OF THE FRIEDELANE SERIES FROM SIPHONODON AUSTRALE.

Apart from the compounds isolated in this work, the only representatives of the friedelane series of triterpenes which have been found in Nature are friedelin, epifriedelanol (friedelan-3β-ol)[1], and cerin. As is well known, friedelin and cerin occur together in cork,[2] and Sorm and Bazant[3] have isolated from cork wax a number of compounds in small amount including a triterpene diol, and a substance $C_{30}H_{50}O_3$ containing an unreactive hydroxyl group and a reactive keto group. These substances which are possibly triterpenes of the friedelane series are not identical with any of the compounds obtained in the present work.

This project was initiated by a gift of the triterpene fraction isolated from the bark of Siphonodon australe Benth. by Dr. J. R. Cannon, (the late) Dr. G. K. Hughes, and Dr. E. Ritchie of Sydney University during their investigations of the alkaloids of Australian flora.

Siphonodon australe Benth., known as ivorywood and sometimes as Native Guava, belongs to the family Celastraceae. It occurs in northern New South Wales and Southern Queensland and its slender trunk grows up to 130 feet in height. The bark is usually furrowed and wrinkled and brownish grey in colour.

Isolation.

Preliminary exploratory work by Dr. R. M. Gascoigne on the original specimen of the triterpene mixture revealed that it was an unusually complex mixture of ketones, hydroxy-ketones, and polyhydroxy compounds. In view of this complexity, a large amount of the bark was extracted and a method was devised to separate the triterpene constituents. During the course of these rather tedious operations a small amount of a paraffin hydrocarbon, probably $C_{28-30}H_{58-62}$, some gummy material which appears to be a mixture of ketonic diterpenes, and an acidic fraction were isolated. Mr. Szumer subsequently obtained lignoceric acid from the latter material. The triterpene mixture had selective absorption only in the 285 mu region ($E^{1\%}_{1\ cm}$ 3) thus indicating that none of the compounds contained a conjugated system. The triterpene mixture was chromatographed on a long column of alumina (approximately 8 feet high) and since such a complex mixture could not be expected to be sharply separated on the column into the pure components, it was decided to divide it into about sixty fractions of approximately equal weight. By means of this chromatogram and subsequent fractional crystallisations the following compounds were isolated. (For clarity in exposition the systematic names of the new compounds are used here; the evidence for these assignments is described in the sequel). The compounds are listed in the order in

which they came off the chromatographic column.

Compound.	Approx. % of the mixture.	
friedelin	0.2%	
friedelane-3:x-dione	15 %	
friedelane-3:y-dione	1 %	
friedelane-3:x:y-trione	10 %	
x[ax]-hydroxyfriedelan-3-one	1.6%	+
x[eq]-hydroxyfriedelan-3-one	2.7%	+
y-hydroxyfriedelan-3-one	-	+
x[eq]-hydroxyfriedelane-3:y-dione	5 %	+
y-hydroxyfriedelane-3:x-dione	1 %	+
polyhydroxy compounds derived from friedelane-3:x-dione	15%	+
polyhydroxy compounds derived from friedelane-3:y-dione		+
polyhydroxy compounds derived from friedelane-3:x:y-trione		+

\+ Isolated by Dr. Gascoigne and Mr. Szumer.

Since friedelin and friedelane-3:y-dione were present in small amount, they were obtained by rechromatographing the appropriate fractions and fractionally crystallising the products. Friedelin has been obtained in separations of various natural products when corks have been used in the apparatus;[4] however, in this work no corks were used. Most of the other compounds were isolated and purified by means of fractional crystallisation.

The three monohydroxy-ketones have been oxidised (two of them by Mr. Szumer) to one or other of the diketones and the two hydroxy-diketones have been oxidised by Mr. Szumer to the triketone obtained from the mixture.

INTER-RELATION OF FRIEDELANE-3:x-DIONE, FRIEDELANE-3:y-DIONE, AND FRIEDELANE-3:x:y-TRIONE.

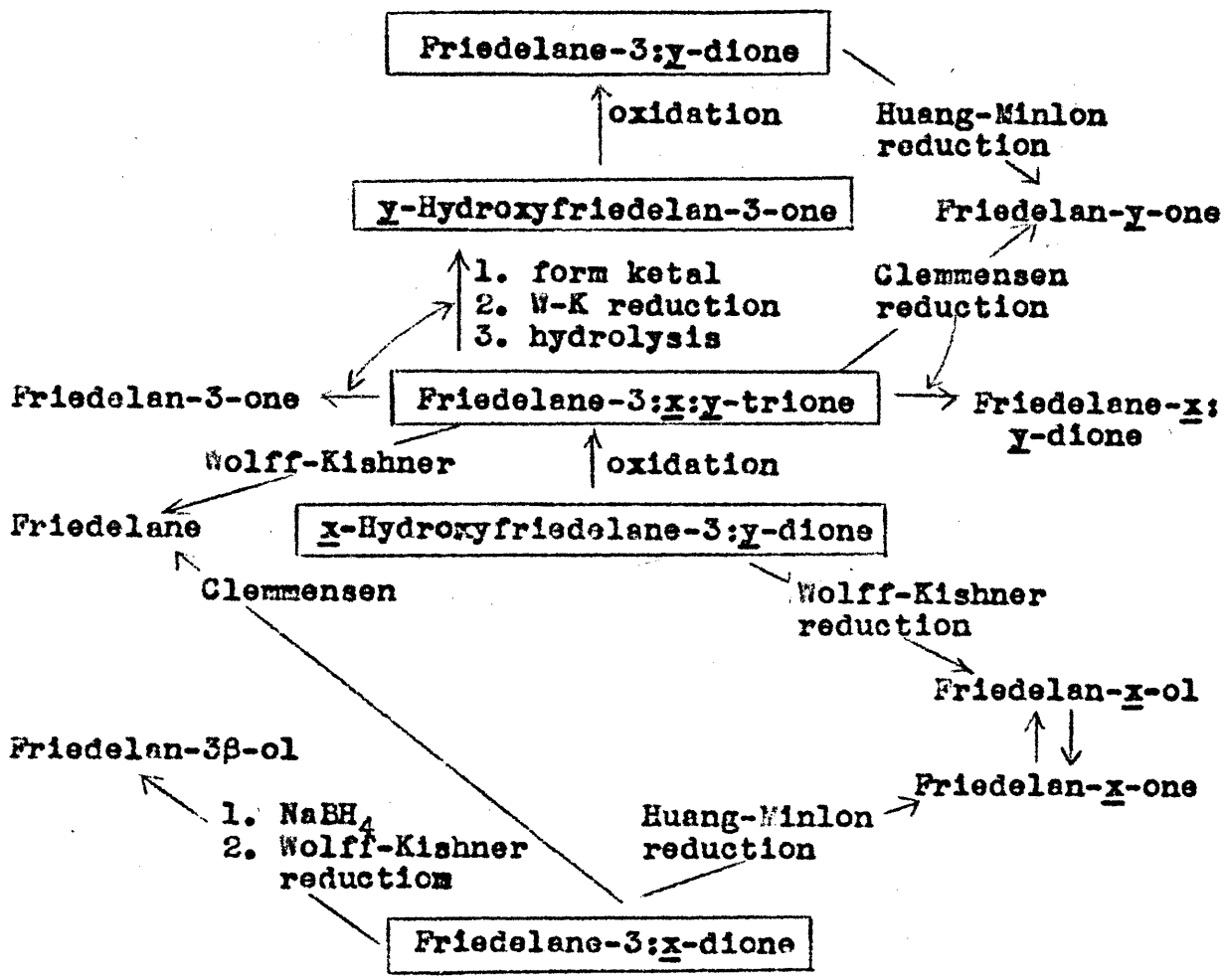
The method of exposition in the following account is an alternative to that used in the publication embodying this work.[5] Since the inter-relation of the ketonic triterpenes involves a complicated interweaving of experiments and facts, the position may be clarified by reference to the chart on page 33 .

Variations in the Steric Hindrance of the 3-, x-, and y-Oxo-Groups.

The inter-relation of the three ketonic triterpenes was based largely on the differences in steric hindrance of the three oxo-groups. The 3-oxo-group forms the usual carbonyl derivatives (oxime, semicarbazone, 2:4-dinitrophenylhydrazone) and is reduced by sodium borohydride to a mixture of epimeric alcohols, whilst the x-and y- carbonyl groups are unreactive to these reagents.* The steric hindrance of the x-oxo group is comparable to that of the

* It has been observed that the x-oxo-group can be reduced to a limited extent by sodium borohydride (see p.36).

INTER-RELATION OF THE TRITERPENES OF SIPHONODON AUSTRALE.



11-oxo-group in steroids for it cannot be reduced by the Huang-Minlon modification of the Wolff-Kishner method but may be reduced by the Clemmensen method and by the Wolff-Kishner method using anhydrous hydrazine.[6,7,8,9] The y-oxo-group is not reduced by the Clemmensen method but may be reduced by the Wolff-Kishner method using anhydrous hydrazine. It is thus even more hindered than the x-oxo-group.

Identification of the Parent Hydrocarbon.

The establishment of the identity of the hydrocarbon skeleton of the compounds was the initial problem. The negative tetranitromethane tests, and low end absorption in the ultraviolet spectra, indicated that these compounds were saturated and hence might be related to friedelin and cerin, the only saturated triterpenes then known. However, the specific rotation of the hydrocarbon obtained in this work ($[\alpha]_D$ +22°) did not correspond with that published for friedelane ($[\alpha]_D$ +41.8°).[10] Fortunately, soon after the parent hydrocarbon had been prepared, Bruun[11] published a new, correct value for the specific rotation of friedelane which corresponded with that of our own hydrocarbon which was subsequently shown to be identical with an authentic specimen. Reduction of friedelane-3:x-dione by the Huang-Minlon modification of the Wolff-Kishner method failed to yield any hydrocarbon, the main product being friedelan-x-one and large amounts of an azine. However when reduced by the

Clemmensen method (using heavily amalgamated zinc), friedelane-3-x-dione yielded friedelan-x-one and friedelane, which was identical with an authentic specimen obtained from friedelin.

Clemmensen reduction of friedelane-3:x:y-trione failed to yield a hydrocarbon; instead, two new ketones which were subsequently shown to be friedelan-y-one and friedelan-x:y-dione were obtained. However, when the triketone was reduced by the Wolff-Kishner method using anhydrous hydrazine at 200°, friedelane was obtained. An alcohol was also obtained from this reduction and was shown to be friedelan-y-ol by oxidation to friedelan-y-one. The formation of friedelan-y-ol can probably be attributed to the extreme steric hindrance of the y-oxo-group. Examples of the reduction of a carbonyl group to a hydroxyl group are known.[12] Reduction of friedelane-3:y-dione by the Huang-Minlon procedure yielded friedelan-y-one and no hydrocarbon.

Proof of the Presence of the 3-oxo-Group in Friedelane-3:x-dione, friedelane-3:y-dione and Friedelane-3:x:y-trione.

Friedelane-3:x-dione, friedelane-3:y-dione and friedelane-3:x:y-trione all formed monosemicarbazones and this was indicative of the presence of the 3-oxo-group; friedelin forms a semicarbazone. Proof of the presence of this group in friedelane-3:x-dione and friedelane-3:x:y-trione was established by converting them into epifriedelanol

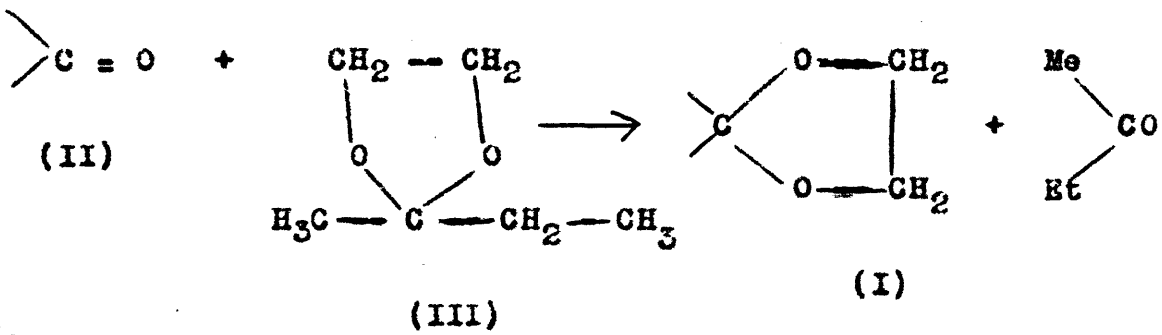
and friedelin respectively.

Reduction of friedelane-3:x-dione by sodium borohydride gave a mixture of two hydroxy-ketones. Chromatography only partially separated these compounds and it was necessary to repeatedly recrystallise the fractions in order to purify them. They were shown to be epimers by their infrared spectra, the infrared spectra of their acetates, and their molecular rotation differences (see p.43). One of these epimers, when reduced by the Wolff-Kishner method employing anhydrous hydrazine under pressure, formed epifriedelanol (friedelan-3β-ol), identical with an authentic specimen prepared from friedelin. The compound used in this reaction must have been 3β[ax]-hydroxyfriedelan-x-one, the other epimer must have been 3α[eq]-hydroxyfriedelan-x-one, and friedelane-3:x-dione must contain the 3-oxo-group.

A similar approach to prove the presence of the 3-oxo-group in friedelane-3:x:y-trione was unsuccessful. Sodium borohydride reduction of friedelane-3:x:y-trione yielded 3β-hydroxyfriedelane-x:y-dione and what appeared to be 3:x-dihydroxyfriedelan-y-one. These compounds were not readily separated by chromatography but repeated fractional crystallisation from several solvents was eventually successful. Wolff-Kishner reduction of the monohydroxy-diketone unexpectedly yielded only an alcohol which was shown to be friedelan-y-ol by oxidation to friedelan-y-one and its

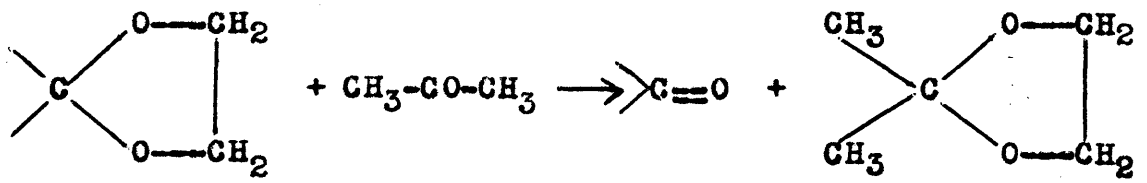
infrared spectrum. Clearly the formation of this compound must have involved reduction of the 3-hydroxyl group to methylene and the y-oxo group to hydroxyl group. Examples of both of these side reactions are known[12] and the reduction of the y-oxo-group to the hydroxyl group in high yield had previously been observed (see p. 35).

In view of the failure of the above method a new approach was employed. An ethylene ketal (I) was formed with the 3-oxo-group of friedelane-3:x:y-trione by the transfer procedure of Dauben, Löken and Ringold.[13] In this method the carbonyl compound (II) is refluxed with 2-methyl-2-ethyl-1:3-dioxolan (III) (the ethylene ketal of methyl ethyl ketone) and a catalytic amount of p-toluenesulphonic acid.



(II) (III) (I)

The ketal was reduced by the Wolff-Kishner method using anhydrous hydrazine under pressure, and the crude product (IV) was refluxed with acetone and a trace of p-toluenesulphonic acid to remove the ketal group. Careful chromatography of this crude reaction product followed by



(IV)

fractional crystallisation of the fractions, yielded as well as a small amount of friedelane, friedelin, and a hydroxy-ketone. The latter compound was shown to be y-hydroxy-friedelan-3-one by oxidation to friedelan-3:y-dione and by molecular rotation considerations. It was also shown to be identical with one of the hydroxy-ketones isolated from the triterpene mixture of Siphonodon australe. This series of reactions proved the presence of the 3-oxo-group in friedelane-3:x:y-trione and the 3- and y-oxo-groups in friedelane-3:y-dione.

Proof of the Presence of the x-oxo-Group in Friedelane-3:x:y-trione and Friedelane-3:x-dione.

As mentioned above, Huang-Minlon reduction of friedelane-3:x-dione yielded a new ketone which was named friedelan-x-one. Proof that the x-oxo-group was present in the trione was provided by the following experiments. Mr. Szumer had found that oxidation of one of the naturally occurring hydroxy-diketones gave the trione in question. Consequently this hydroxy-diketone was reduced by the Wolff-Kishner method with anhydrous hydrazine. The product was an alcohol which was identical with friedelan-x[eq]-ol which had been

prepared by reduction of friedelan-x-one with sodium and pentyl alcohol. It follows that the triketone contains the x-oxo-group and that the hydroxy-diketone was x-[eq]-hydroxyfriedelan-3:y-dione.

Proof of the Presence of the y-oxo-Group in Friedelane-3:y-dione and Friedelane-3:x:y-trione.

As previously mentioned, Huang-Minlon reduction of friedelane-3:y-dione yielded a new monoketone which was named friedelan-y-one. Since the same compound was obtained by Clemmensen reduction of friedelan-3:x:y-trione, the latter must contain the y-oxo-group.

CONFIRMATORY PHYSICAL EVIDENCE FOR THE RELATION OF THE KETONIC TRITERPENES OF SIPHONODON AUSTRALE.

The chemical evidence for the relation of the various ketones described above is substantiated by both their infrared absorption and the molecular rotation contributions of the carbonyl groups. The molecular rotation contributions are summarised in the following table.

Infrared Evidence.

Evidence of the presence of 3-, x- or y-oxo-groups may be provided by infrared spectroscopic properties. It has been observed that the 3- and x-oxo-groups, separately or together give rise to a single band in the region of 1732-1710 cm^{-1} (all infrared spectra were determined on

MOLECULAR ROTATION CONTRIBUTIONS OF CARBONYL GROUPS.

	$[M]_D$ with CO group	$[M]_D$ without CO group	ΔCO
3-Oxo-group			
Friedelan-3-one	-94°	+91°	-185°
Friedelane-3:x-dione	+506	+647	-141
Friedelane-3:x:y-trione	+327	+453	-126
Friedelane-3:y-dione	-273	-145	-128
x-Oxo-group			
Friedelan-x-one	+647	+91	+556
Friedelane-3:x-dione	+506	-94	+600
Friedelane-3:x:y-trione	+327	-273	+600
Friedelane-x:y-dione	+453	-145	+598
y-Oxo-group			
Friedelan-y-one	-145	+91	-236
Friedelane-3:y-dione	-273	-94	-179
Friedelane-3:x:y-trione	+327	+506	-179
Friedelane-x:y-dione	+453	+647	-194

The value of the specific rotation of friedelane observed in this investigation was that found by Bruun[11] and not the higher value recorded in the earlier literature.

nujol mulls because of the low solubility of the friedelane derivatives in organic solvents.) whereas the y-oxo-group shows carbonyl absorption at 1702-1696 cm^{-1}. The difference in the C=O stretching frequency of the 3- and x-oxo-groups on the one hand and that of the y-oxo-group on the other hand is most apparent in the infrared spectra of compounds containing the y-oxo-group together with either or both of the 3- or x- oxo-groups; in such cases two distinct bands occur in the C=O stretching region.

These characteristics do not occur in the spectra of the hydroxyfriedelanones but are present in the spectra of the acetyl derivatives of these compounds. Presumably, hydrogen bonding in the hydroxy-ketones causes the disappearance of these characteristics.

It has been observed that all compounds containing the x-oxo-group exhibit a weak to medium intensity band in the region of 696-687 cm^{-1} which is apparently characteristic of this group. The presence or absence of the x-oxo-group in the compounds so far examined can therefore be deduced from the presence or absence of this absorption band.

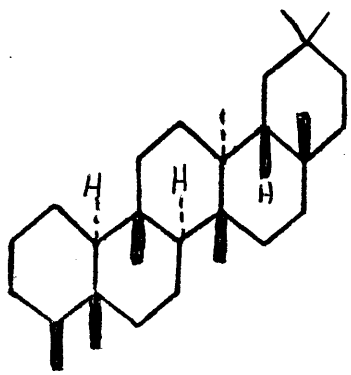
Stereochemical Course of the Reduction of the 3-oxo-Group.

For a variety of reasons it was necessary to prepare the 3β[ax]-hydroxy compounds derived from friedelin, friedelane-3:x-dione, friedelane-3:y-dione, and friedelane-3:x:y-trione. The reductions were carried out with sodium

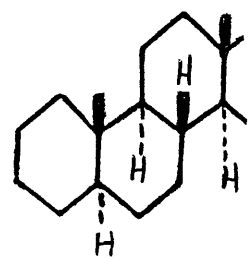
borohydride, and in all cases the axial epimer was obtained in predominant amount; in the case of friedelane-3:y-dione and friedelane-3:x:y-trione the equatorial (3α-) alcohol was not detected. It was observed during chromatographic separations that the equatorial epimer was more strongly adsorbed on alumina than the axial epimer. From mechanical considerations this is to be expected[14] but exceptions to this prediction have been noted.[15] Barton[16] pointed out that the predominant product of lithium aluminium hydride reduction of an unhindered alicyclic ketone is the equatorial alcohol; hindered ketones give predominantly the axial epimer. Dauben and his co-workers[17] have indicated that the two important factors influencing the stereochemistry of hydride reductions are: (1) the steric hindrance of the oxo-group, and (2) the thermodynamic stability of the two epimeric alcohols which may be formed. This is merely a re-statement of previous generalisations. Reduction of ketones with sodium borohydride yields more of the axial epimer than is obtained when lithium aluminium hydride is used.[17] Presumably this is due to the greater size of the sodium borohydride molecule which is affected more by steric hindrance than lithium aluminium hydride. Thus highly hindered oxo-groups which may be reduced by lithium aluminium hydride are unaffected by sodium borohydride.

Reduction of the 3-oxo-group of the usual triterpenes

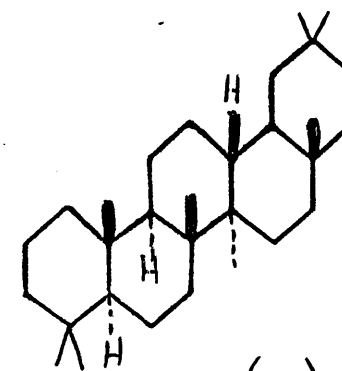
and the 5α-steroids with sodium borohydride or lithium aluminium hydride yields mainly the equatorial (3β-) alcohol;[18] presumably this is due to rear (α) attack of the reagent.[19] Rear attack of these reagents on the 3-oxo-group of the friedelane derivatives would be even more favoured by steric hindrance considerations. Thus the reduction of 3-oxo-friedelane derivatives by these reagents yields predominantly 3β-hydroxy-compounds. However, the 3β-hydroxyl group has an axial configuration in friedelane because of the "skeletal enantiomorphic" nature of friedelane (V) compared to the 5α-steroids (VI) and usual triterpenes (VII).[5]



(V)



(VI)



(VII)

This is confirmed by the molecular rotation differences of the 3-hydroxyl and 3-acetate groups of various friedelane derivatives (see table). According to Klyne and Stokes[20] the molecular rotation differences are negative for α-oriented groups and positive for β-oriented groups.

In accordance with the enantiomorphic relation of friedelane to the 5α-steroids and triterpenes, the 3β-hydroxyl group has an axial configuration whilst the 5α-hydroxyl is equatorial.

MOLECULAR-ROTATION CONTRIBUTIONS OF HYDROXYL AND ACETOXYL GROUPS.

Symbols and conventions are as used by Klyne and Stokes (J., 1954, 1979).

	$[M]_D$ CH_2	$[M]_D$ OH	$[M]_D$ OAc	ΔOH	ΔOAc	$[M]_D$OAc $-[M]_D$OH
3-Hydroxyl group (equatorial)						
Friedelan-3α-ol	+91°	+69°	-99°	-22°	-190°	-168°
3α-Hydroxyfriedelan-x-one .....,	+647	+641	+552	-6	-95	-89
3-Hydroxyl group (axial)						
Friedelan-3β-ol	+91	+90	+169	-1	+78	+79
3β-Hydroxyfriedelan-x-one	+647	+704	+764	+57	+117	+60
3β-Hydroxyfriedelane-x-:y-dione.	+453	+489	+564	+36	+111	+75
3β-Hydroxyfriedelan-y-one	-145	-142	-97	+3	+48	+45

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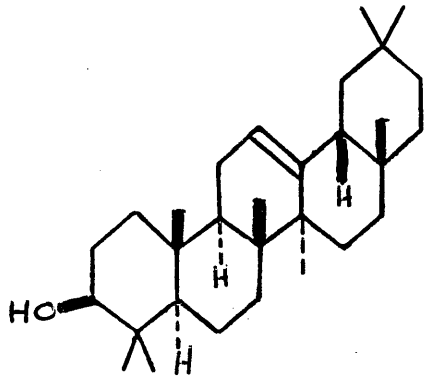
19. Cf. Cram and Elhafez, J. Amer. Chem. Soc., 1952, 74, 5828; Noyce and Denney, ibid., 1950, 72, 5743; Shoppee and Summers, J. Chem. Soc., 1950,687.

20. Klyne and Stokes, J. Chem. Soc., 1954, 1979.

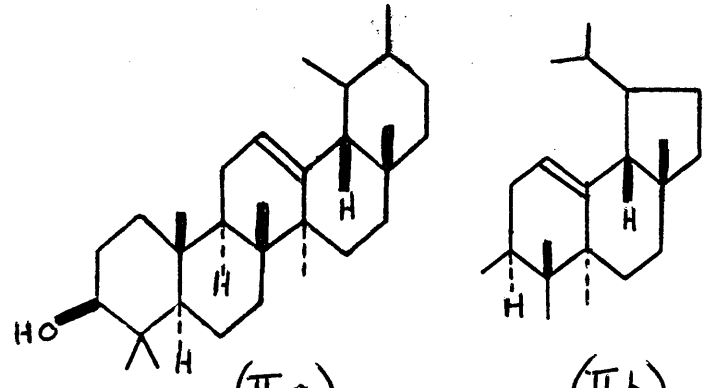
AN OUTLINE OF SKELETAL REARRANGEMENTS IN THE PENTACYCLIC AND TETRACYCLIC TRITERPENES.

The Pentacyclic Triterpenes.

The pentacyclic triterpenes may be divided into several groups of related compounds named after their parent saturated hydrocarbons. Each of these series comprises a number of compounds all with the same carbon skeleton but differing from each other in the number and position of oxygenated groups. Thus there is the oleanane or β-amyrin (I) series, the ursane or α-amyrin (II) series, the lupane or lupeol (III) series, the taraxastane series, e.g. taraxasterol (IV), the taraxerane series, e.g. taraxerol (V), the alnusane series, e.g. alnusenone (VI) and the friedelane series, e.g. friedelin (VII). All of these compounds are thought to be related biosynthetically and a scheme has been proposed to suggest the possible biosynthetic pathways of the conversions.[1] The biosynthesis of friedelin from β-amyrin or its biological equivalent by the reverse of the friedelene-oleanene rearrangement (discussed in detail, p. 7/), is an attractive hypothesis;[2,3,4] in this case, compounds with the carbon skeletons of taraxerol (V), the hydrocarbon (VIII) and alnusenone (VI) would presumably represent intermediate stages in the process. Compounds having the carbon skeleton (VIII) are the only ones in this series

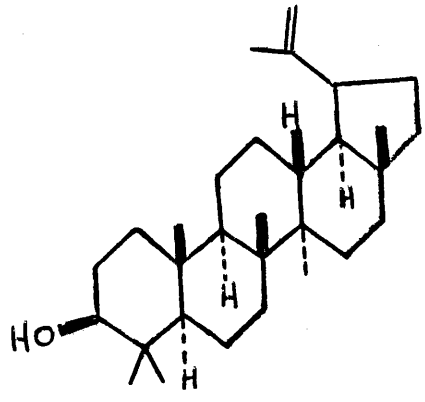


(I)

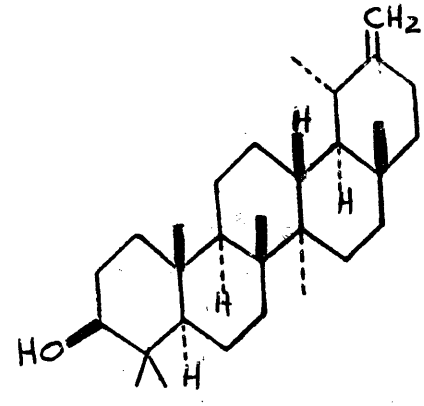


(IIa) (IIb)

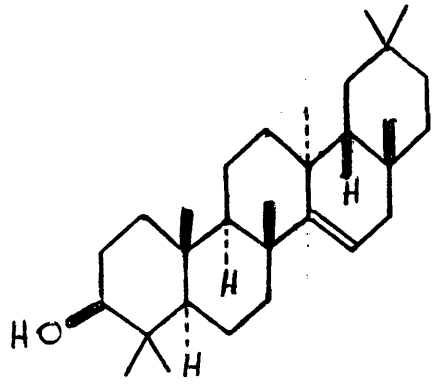
II



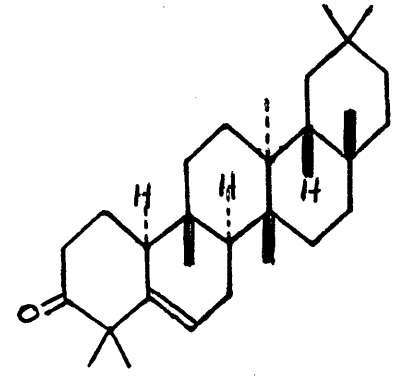
(III)



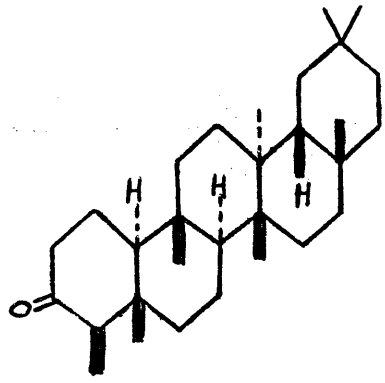
(IV)



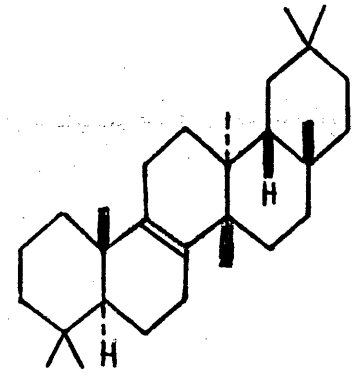
(V)



(VI)



(VII)



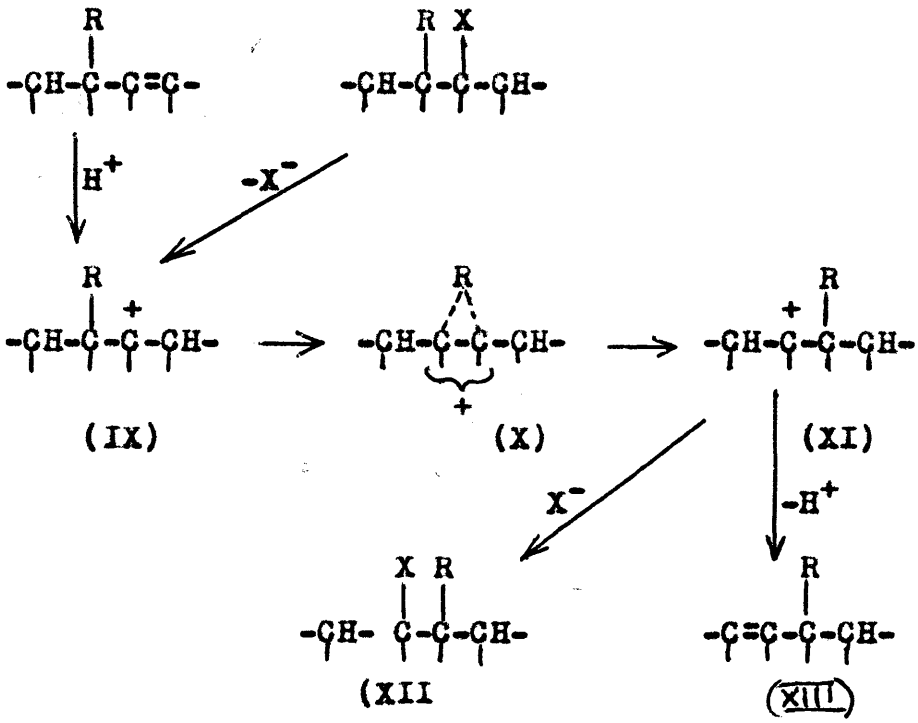
(VIII)

which have not been found in Nature but no doubt derivatives of this series will eventually be isolated from a natural source.

The interconversions of members of the various groups of triterpenes, and oxidative degradations of these compounds leading to their structures have been described in several reviews.[5] Selenium dehydrogenation and the application of the isoprene rule,[6] oxidative degradation experiments and the pyrolytic fission of a derivative of oleanolic acid to yield two fragments, one consisting of rings A and B and the other of rings D and E,[7,8] led to the establishment of the structure of β-amyrin. Similar experiments on α-amyrin yielded information from which Ruzicka, Jeger, and their co-workers[9] concluded that α-amyrin has structure (IIa). The alternative structure (IIb) has been proposed by

Spring and his collaborators.[10]

In recent years skeletal rearrangements resulting in the interconversion of different triterpenes have become increasingly important in the establishment of structure. These rearrangements are of the Wagner-Meerwein type[11] and may be considered to consist of three phases; (a) the formation of a carbonium ion, followed by (b) the migration of either a hydrogen atom, a substituent group (commonly methyl groups in triterpene chemistry), or a ring member. When the latter occurs ring contraction or expansion results. The final stage (c) is the discharge of the ion either by the elimination of a proton or the addition of an anion. These phases of Wagner-Meerwein rearrangements may take place stepwise or synchronously and the migrating atom or group is never detached from the molecule.



Thus the carbonium ion (IX) is formed and the substituent group migrates through the transition state (X) to form a new ion (XI) which may be discharged by: (a) the addition of an anion to form (XII) or by (b) the elimination of a proton to give an olefine (XIII). An important feature of Wagner-Meerwein type rearrangements is that the migrating group retains its orientation and its configuration (if it is asymmetric) during the rearrangement. This is in accordance with the theory that the rearrangement proceeds via the carbonium ion intermediate (X).

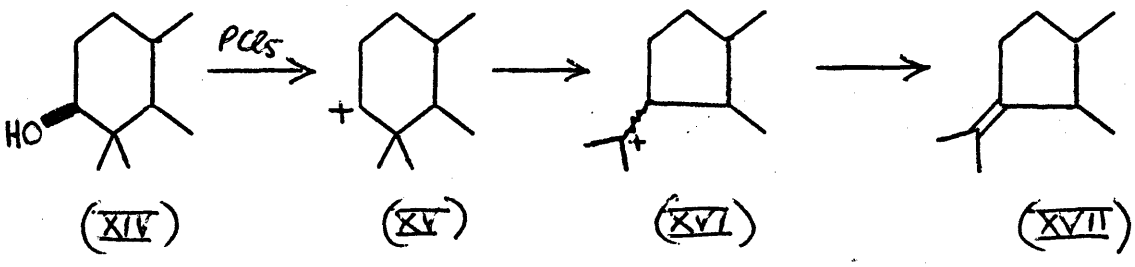
Biosynthesis and the Wagner-Meerwein Rearrangements.

The biosynthesis of steroids and triterpenes has received considerable attention in recent years. Ruzicka and his co-workers,[1] have proposed a general hypothesis for the biosynthesis of steroids and triterpenes starting from squalene. The various rearrangements visualised in this scheme proceed by the mechanism of Wagner-Meerwein rearrangements. It is thought that the rearrangements are concerted and evidence for this is found in the biological conversion of squalene to lanosterol.[12]

The Retropinacolinic Rearrangement of 3β-Hydroxytriterpenes.

This type of rearrangement is useful as a diagnostic test for a certain grouping in the tetracyclic and pentacyclic triterpenes. Thus the action of phosphorus pentachloride on

an equatorial alcohol group adjacent to a gem-dimethyl group in a terminal six membered ring (XIV) effects this change. This reaction presumably takes place by the formation of a carbonium ion (XV) which rearranges by the migration of a ring member to give ring contraction and a new ion (XVI). This eliminates a proton to form a compound having an iso-propylidene group attached to a five membered ring (XVII).

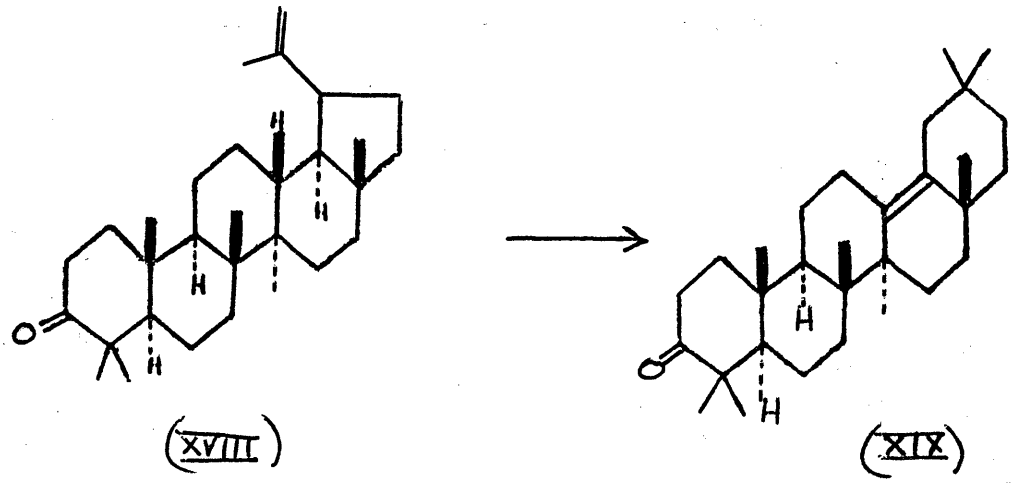


(XIV) (XV) (XVI) (XVII)

Oxidation of the olefine to acetone and a trisnorketone affords evidence that this rearrangement has occurred. This reaction has been applied in the present work as a diagnostic test (p. 105)

Rearrangements of Lupeol and Related Compounds.

The elucidation of the structure of lupeol (III) depends mainly on the conversion of α-lupene to olean-13(18)-ene (subsequently shown to be an equilibrium mixture of 18α-olean-12-ene and olean-13(18)-ene), and of lupen-3-one (XVIII) to olean-13(18)-en-3-one (XIX) under acidic conditions.[13,14]

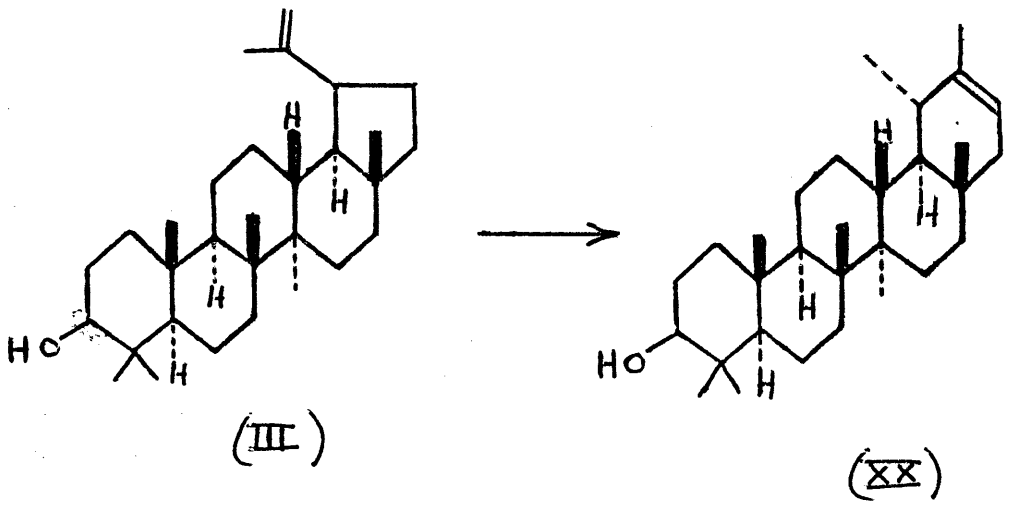


(XVIII) (XIX)

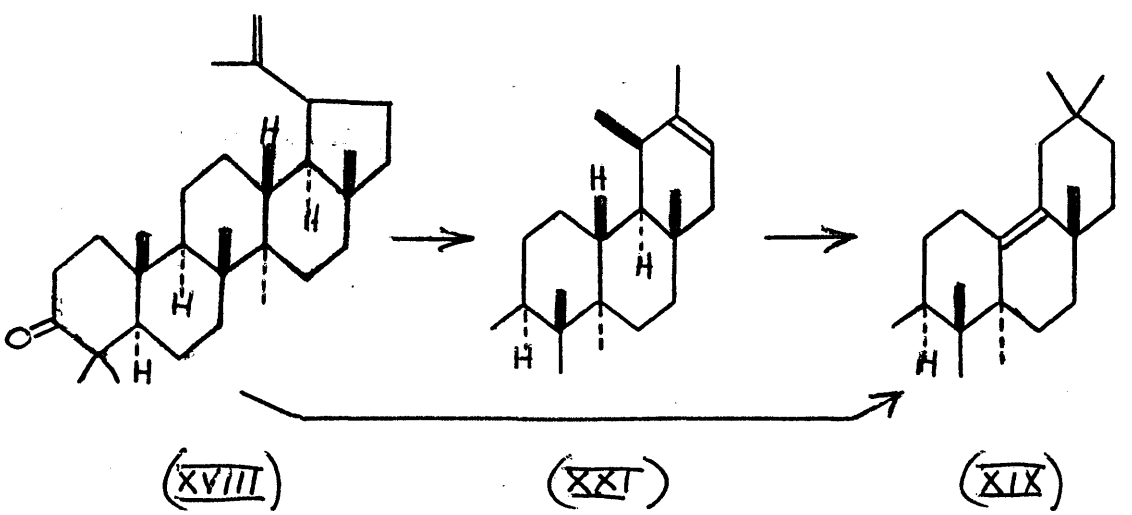
This rearrangement can be satisfactorily explained if lupeol has the structure (III). Thus lupeol has the same carbon skeleton and stereochemistry as oleanane in rings A, B and C; the two compounds differ only in ring E.

Jones and his co-workers[15] have carried out extensive investigations on the acid catalysed rearrangements and interconversions of several triterpenes. In this way they have elucidated the structure of taraxasterol, ψ-taraxasterol (heterolupeol) and lupenol-I. Lupeol (III) was converted into ψ-taraxasterol (heterolupeol)(XX) by boiling formic acid, and lupenone (XVIII) upon treatment with 6% sulphuric acid in acetic acid; formed lupenone-I (XXI). When 15% sulphuric acid in acetic acid was used, Lupenone (XVIII) was converted into olean-13(18)-en-3-one (XIX). Lupenone-I (XXI) also yielded this compound under more

strongly acidic conditions.

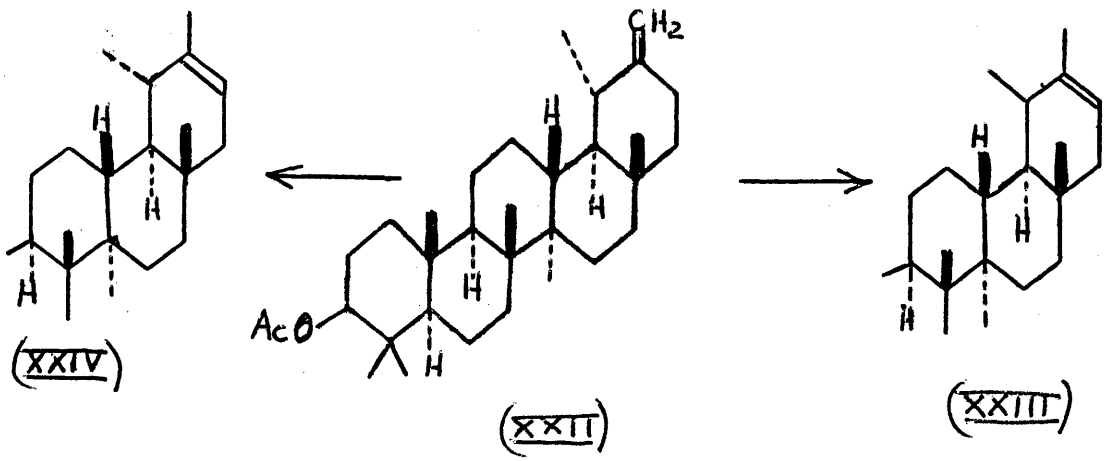


(III) (XX)



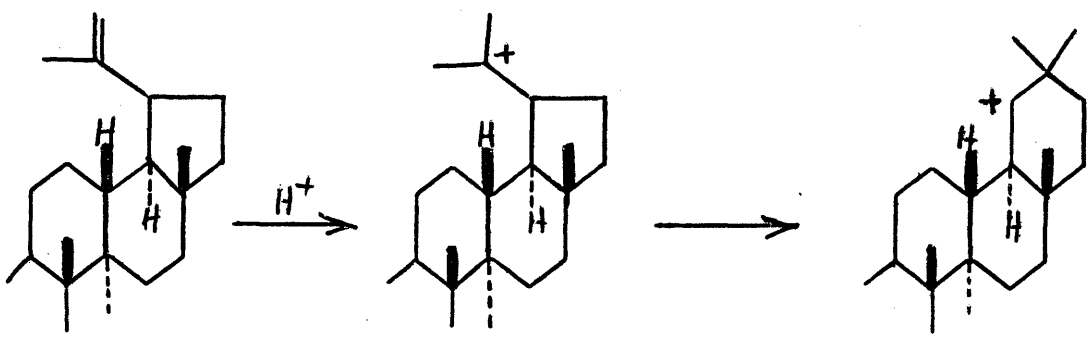
(XVIII) (XXI) (XIX)

Taraxasteryl acetate (XXII) has been converted to lupenyl-I acetate (XXIII) by 6% sulphuric acid in acetic acid and to ψ-taraxasteryl acetate (XXIV) by 10% ethanolic sulphuric acid in benzene.



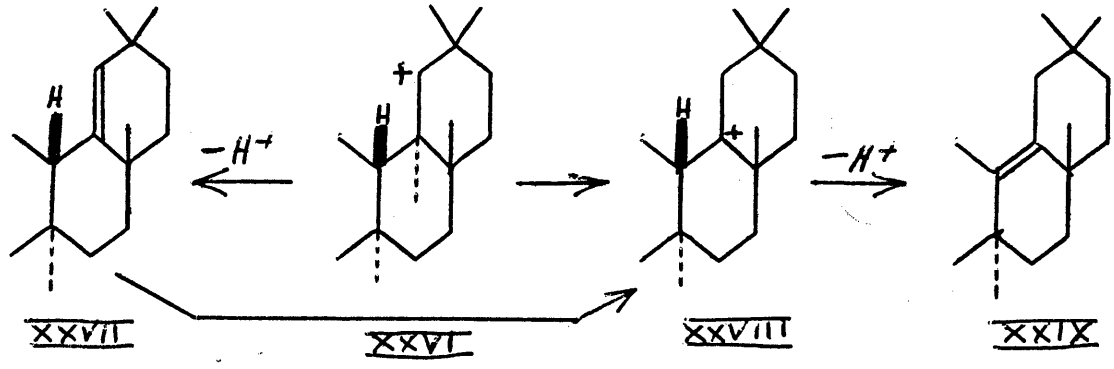
(XXIV) (XXII) (XXIII)

These transformations presumably proceed by the initial addition of a proton to the double bond to form a carbonium ion which may then undergo rearrangements of the Wagner-Meerwein type. Thus the action of acidic reagents on α-lupene (XXV) could take the following course to form a carbonium ion (XXVI) which Ruzicka and his collaborators[1] proposed as a key intermediate in the biogenesis of pentacyclic triterpenes.

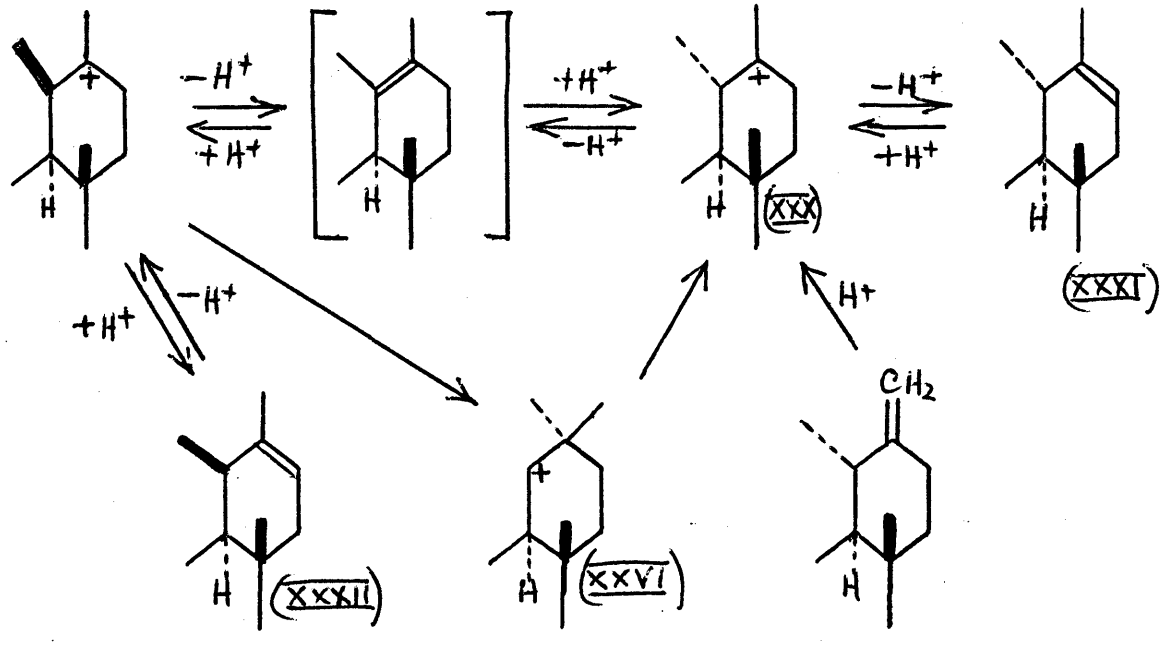


(XXV) (XXVI)

From this ion the formation of the various compounds may be postulated. Loss of a proton gives the germanicol structure (XXVII), whilst rearrangement of the carbonium ion involving a hydride shift would give an ion (XXVIII) which, upon losing a proton yields olean-13(18)-ene (XXIX).

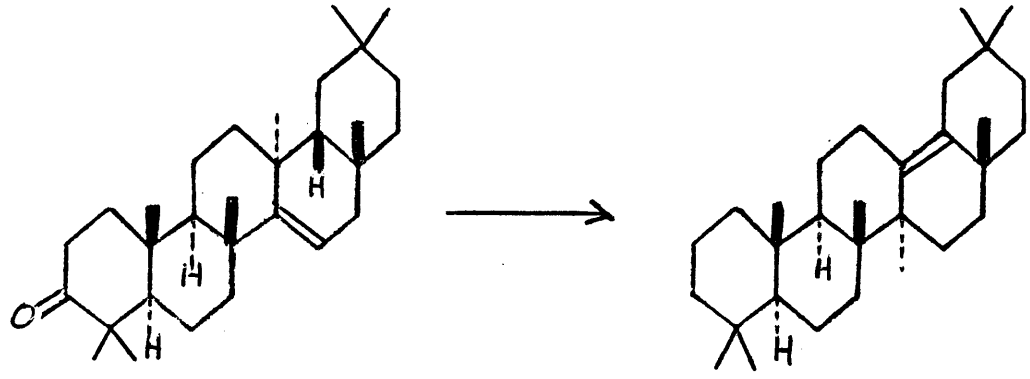


Rearrangement of the ion (XXVI) to another carbonium ion (XXX) which may lose a proton, results in the formation of ψ-taraxastene (XXXI). This latter reaction has been represented as an equilibrium reaction in order to satisfactorily explain the formation of lupene-I (XXXII).



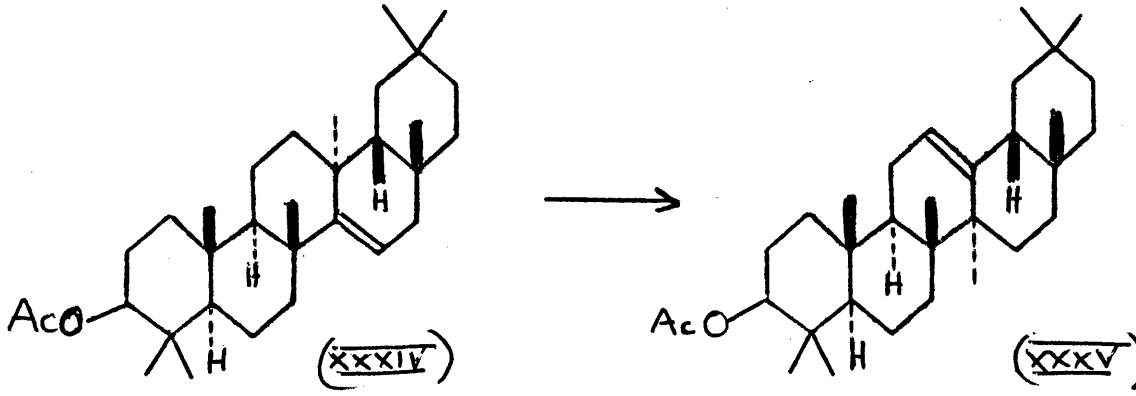
Interconversions of the Taraxarene and Oleanene Structures.

The conversion of taraxerol and its derivatives into the corresponding oleanene derivatives has been elucidated by Spring and his co-workers.[16] Takeda[17] converted taraxerone (XXXIII) into olean-13(18)-ene (XXIX) (now known to be an equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene) by the Clemmensen method of reduction.



(XXXIII) (XXIX)

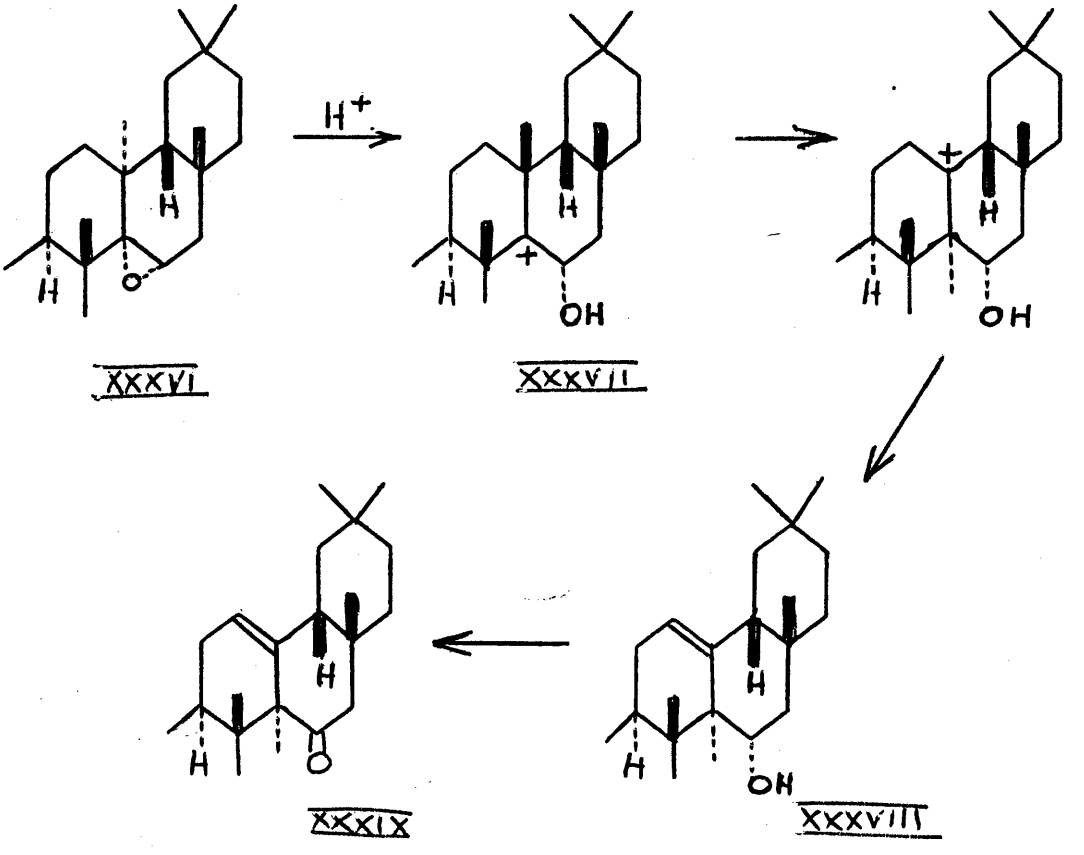
Spring and his collaborators[16] have effected the conversion of taraxeryl acetate (XXXIV) into β-amyrin acetate (XXXV) by treatment with a mixture of hydrochloric and acetic acids.



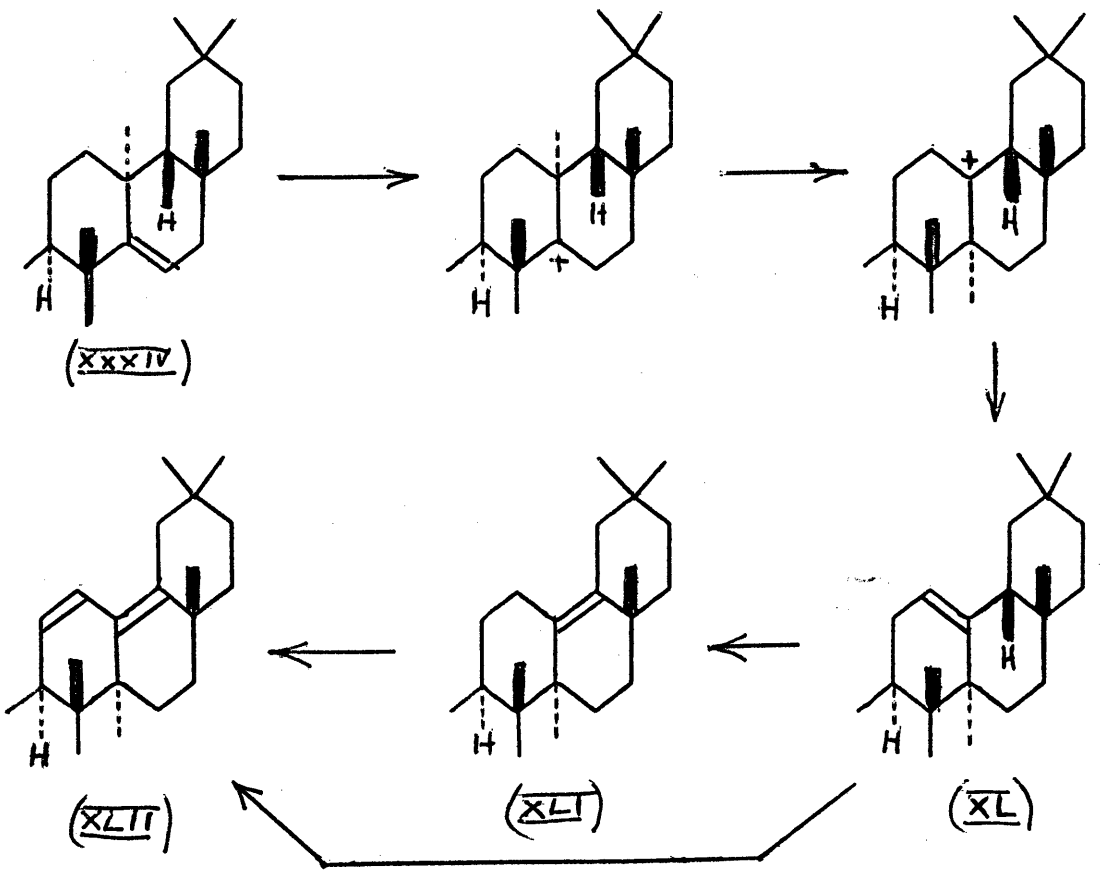
(XXXIV) (XXXV)

This rearrangement is of special interest in the present work because it represents the final stage in the friedelene-cleanene rearrangement (see p. 71).

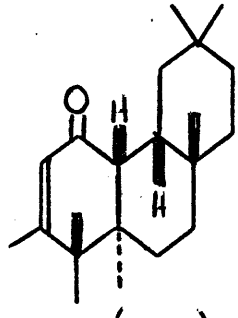
Some of Takedas'experiments have been re-examined and interpreted by Spring and his collaborators.[16] Taraxeryl acetate oxide (XXXVI) when treated with mineral acid, yielded an unsaturated diol monoacetate (XXXVIII). This latter compound formed an unsaturated keto-acetate (XXXIX) upon oxidation, and did not contain an αβ-unsaturated ketone chromophore. The fission of taraxeryl acetate oxide must have involved the formation of a carbonium ion (XXXVII), a molecular rearrangement and the elimination of a proton.



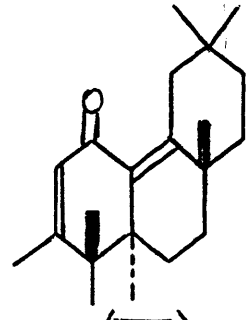
An interesting feature of the two previous rearrangements is that the elimination of the proton gave the thermodynamically less stable Δ^{12-} derivative rather than the more stable $\Delta^{13(18)-}$ derivative. This has been attributed to the geometry of the molecule[16]; the same phenomenon has been observed in the present work and is discussed on p. 90. The taraxerene-oleanene rearrangement also occurs in the condition of selenium dioxide oxidation experiments. Thus selenium dioxide oxidation of taraxeryl acetate (XXXIV) gave oleana-11:13(18)-dien-3β-yl acetate (XLII).[18] Rearrangement to the oleanene structure (XL), (XLI) must have occurred before dehydrogenation took place.



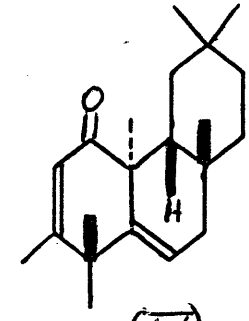
The reverse of the taraxerene-oleanene rearrangement occurs in the special case where the 12-oxo-group is present. Thus the oxidation of 12-oxo-olean-9(11)-en-3β-yl acetate (XLIII) by selenium dioxide or bromine gave, instead of the expected 12-oxo-oleana-9(11):13(18)-dien-3β-yl acetate (XLIV), 12-oxo-taraxera -9(11):14-dien-3β-yl acetate (formerly known as 12-oxo<u>iso</u>-oleana-9(11):14-dien-3β-yl acetate)(XLV).



(XLIII)



(XLIV)



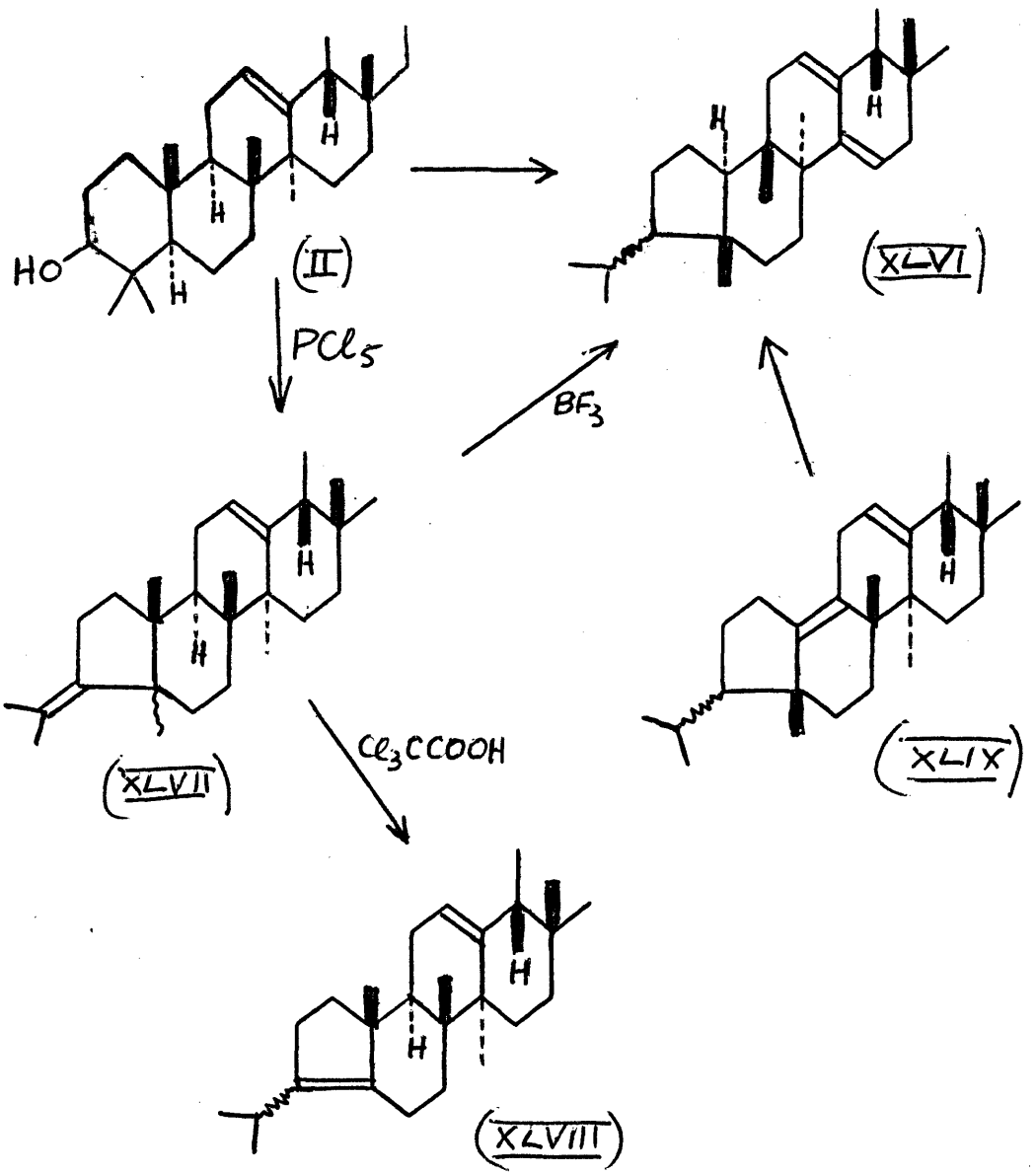
(XLV)

<u>"Backbone" Rearrangements in the Ursane and Oleanane Series.</u>

During their investigations on the structure of α-amyrin, Spring and his collaborators[19] have effected a number of extensive molecular rearrangements. They have referred to these as "backbone" rearrangements since they involve the migration of methyl groups and hydrogen atoms along the ring junctions (the "backbone") of the molecule.

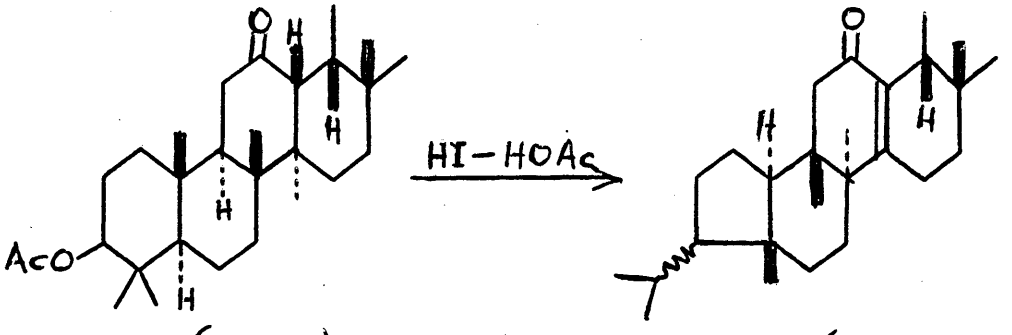
Treatment of α-amyrin (II) with phosphoric oxide at room temperature resulted in the formation of "1-α-amyradiene" (XLVI) in high yield. This conversion involved a retropinacolinic rearrangement in ring A, followed by migration of three axial methyl groups and one axial hydrogen atom, and was considered to be fully synchronous.

"1-α-amyradiene (XLVI) was also prepared by firstly carrying out the well known retropinacolinic rearrangement with phosphorus pentachloride and α-amyrin (II), and treating the product (XLVII) with boron trifluoride in acetic acid. By contrast, trichloracetic acid only effected isomerisation of the double bond (i.e. (XLVII) to (XLVIII)).



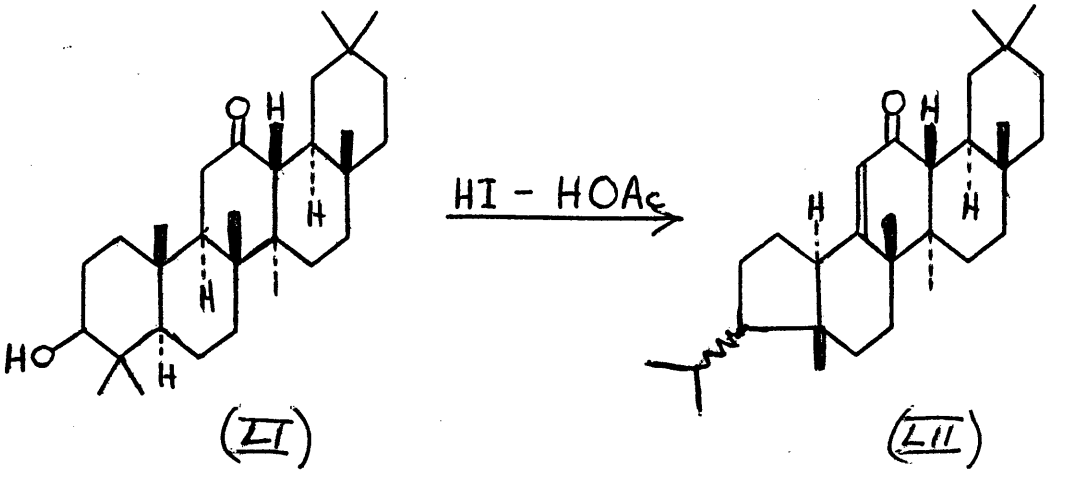
In the previous example, formation of a conjugated system of double bonds must provide at least part of the driving force for the rearrangement. That the formation of conjugated systems does not always occur by the most direct route is evidenced by the example above. When the compound (XLIX) was treated with hydrochloric-acetic acid it rearranged to the diene (XLVI).

Here the most direct route would give a homoannular conjugated diene which, however, would not be as thermodynamically stable as the product actually obtained. Thus this rearrangement involved the migration of two methyl groups in order to form the more stable product. Another example of a rearrangement proceeding by an indirect route to form a conjugated system has been described by Spring and his co-workers.[19] In this case, 3-acetoxy-12-oxoursane (XLIX) was treated with hydriodic acid-acetic acid and underwent ring contraction and isomerisation to yield an αβ-unsaturated ketone (L).



(XLIX) (L)

The conversion of (XLIX) to (L) shows that steric factors can lead to the rearrangement taking a more roundabout route than would be necessary merely to attain the conjugated system. Spring et.al.[19] were of the opinion that the driving force supporting the reactions of the ursane derivatives was the constraint imposed by a cis(β)-locking of rings D and E. Thus, when the corresponding 18α-oleanane derivative (LI) in which the D/E ring junction is trans was treated in the same manner, the αβ-unsaturated ketone (LII) was formed by the shortest possible route of the rearrangement.



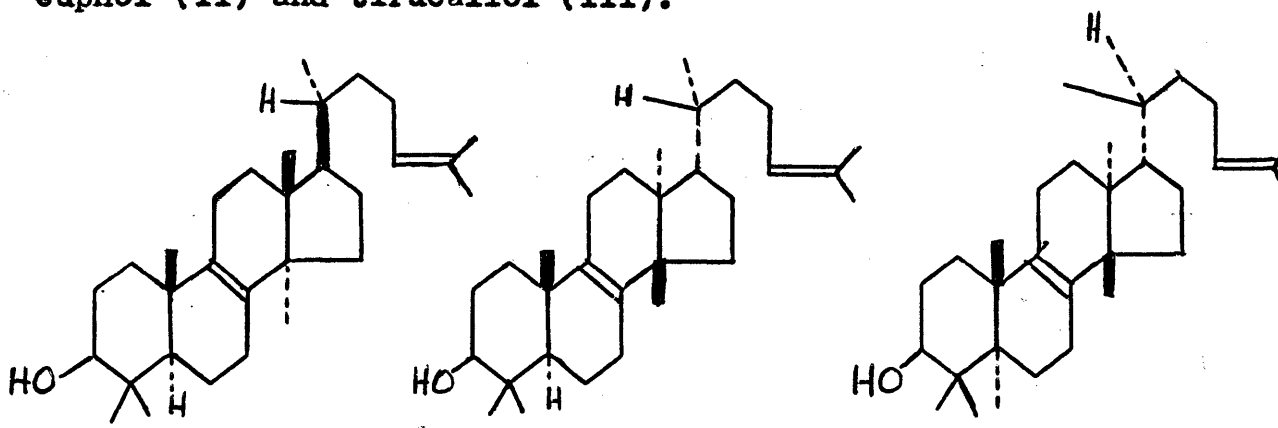
(LI) (LII)

The Friedelene-Oleanene Rearrangement.

This extensive rearrangement of the "backbone" type provided important evidence in the elucidation of the structure of friedelin.[2,3,4] A full discussion of this conversion is given in a later section of this thesis (see p. 71 et. seq.)

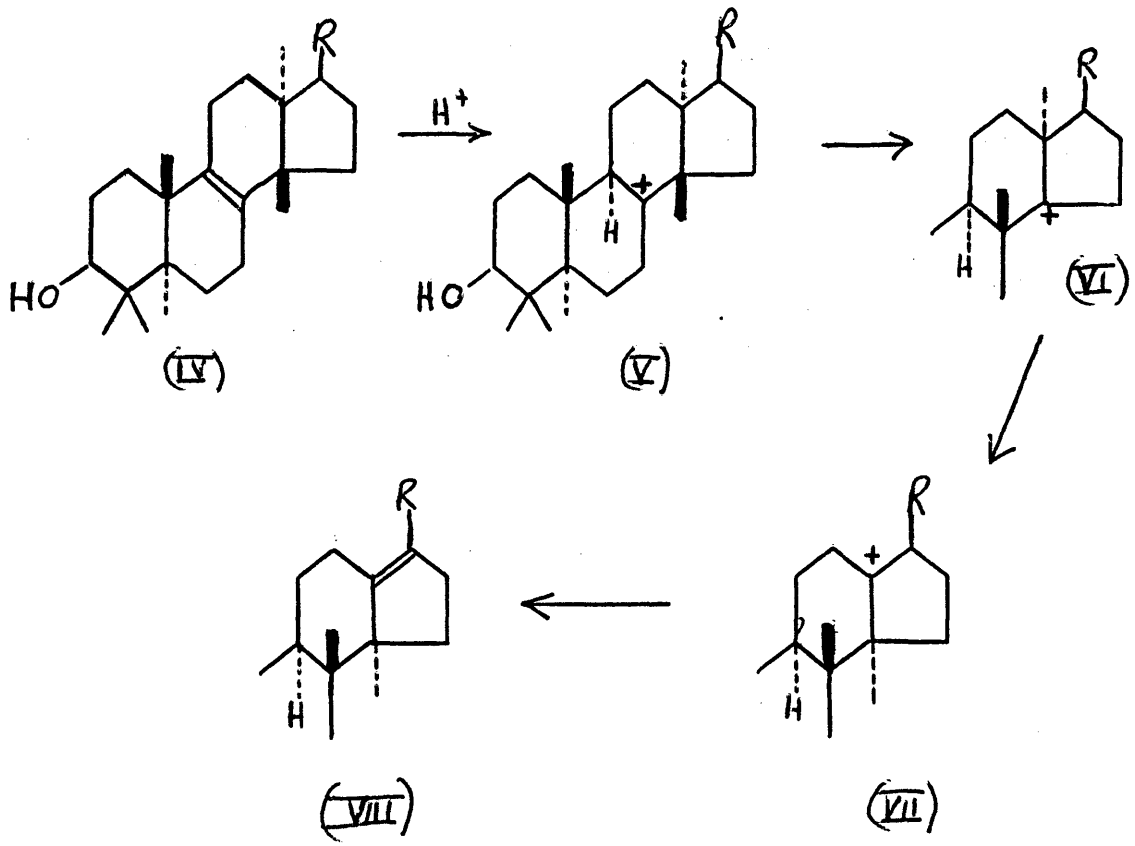
TETRACYCLIC TRITERPENES.

The three main classes of tetracyclic triterpenes are exemplified by the three stereoisomers lanosterol (I), euphol (II) and tirucallol (III).[20]



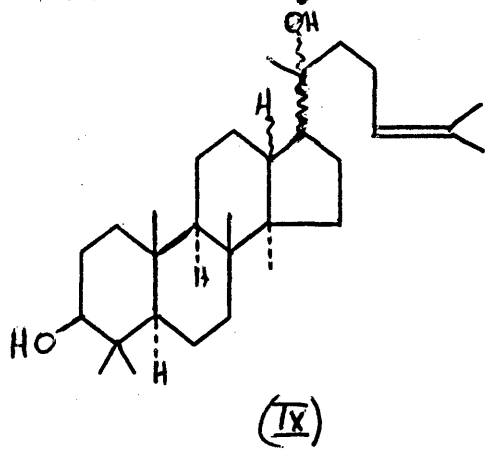
The Euphenol-isoEuphenol Rearrangement.

When euphenol (dihydroeuphol) (IV) was treated with acid it underwent a skeletal rearrangement which provided important evidence for the structure of euphol.[21,22] The rearrangement yields isoeuphenol (VIII) and involves the formation of a carbonium ion (V) which rearranges by the migration of two methyl groups, and finally eliminates a proton (V→VIII). Presumably this transformation takes place because of a "conformational driving force" resulting from rings B and C of euphenol existing in half-boat conformations.[21] Tirucallol, which has the same configuration at the C/D ring junction as euphol, undergoes the same



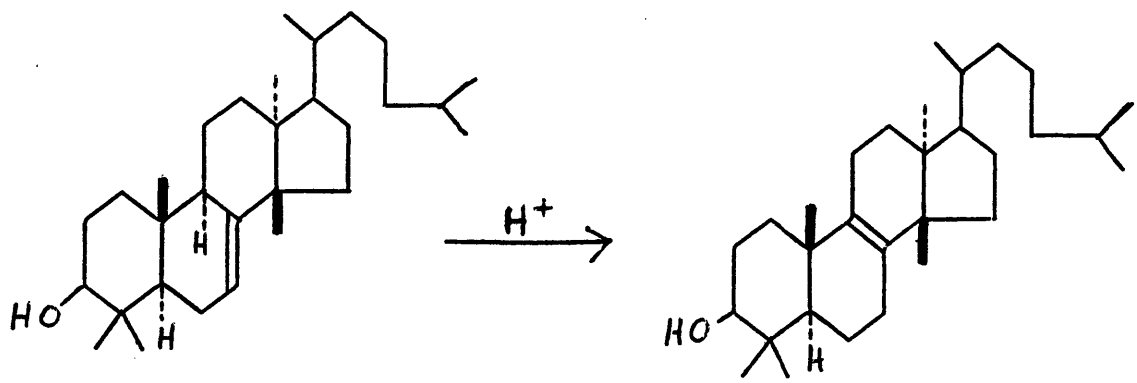
rearrangement but lanostenol, which has the opposite configuration at the C/D ring junction, does not.

It is of considerable interest that dammarenediol (IX) and related compounds which have the same carbon skeleton as <u>iso</u>euphenol have recently been found in Nature.[23]



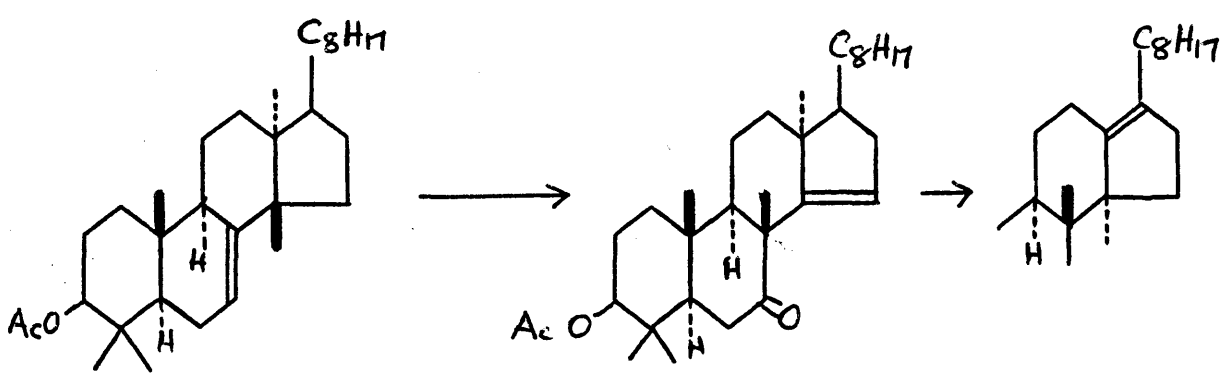
Rearrangements of Butyrospermol Derivatives.

When dihydrobutyrospermol (X) was treated with strong acid it yielded dihydroeuphol (IV) [24,25,26] This interconversion merely involves an isomerisation of a double bond without any skeletal changes.



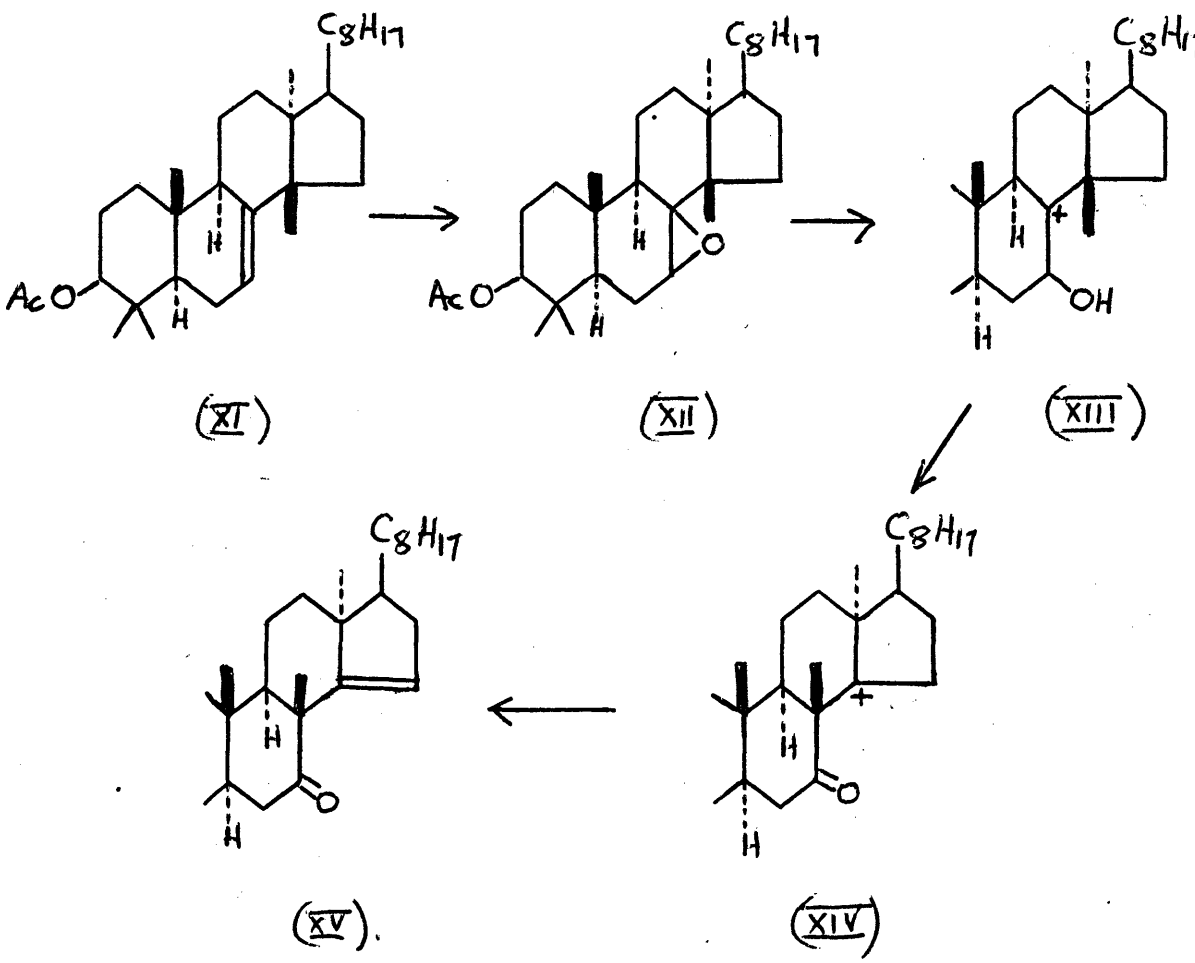
X IV

However, oxidation of dihydrobutyrospermol acetate (XI) with chromic acid afforded 7-oxoapoeuph-14-enyl acetate (XV). This, upon treatment with mineral acid, followed by Wolff-Kishner reduction and acetylation gave isoeuph-13(17)-enyl acetate(XVI).[27]



XI XV XVI

The preparation of the unconjugated enone (XII) by chromic acid oxidation presumably involved the initial formation of an epoxide (XII). This compound, under the influence of acid, would form a carbonium ion (XIII) which rearranged and was oxidised to a ketonic compound (XIV) which finally eliminated a proton to give 7-oxoapoeuph-14-enyl acetate (XV).



(XI) (XII) (XIII)

(XV). (XIV)

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    Cf. Meakins, Chem. and Ind., 1955, 1353.

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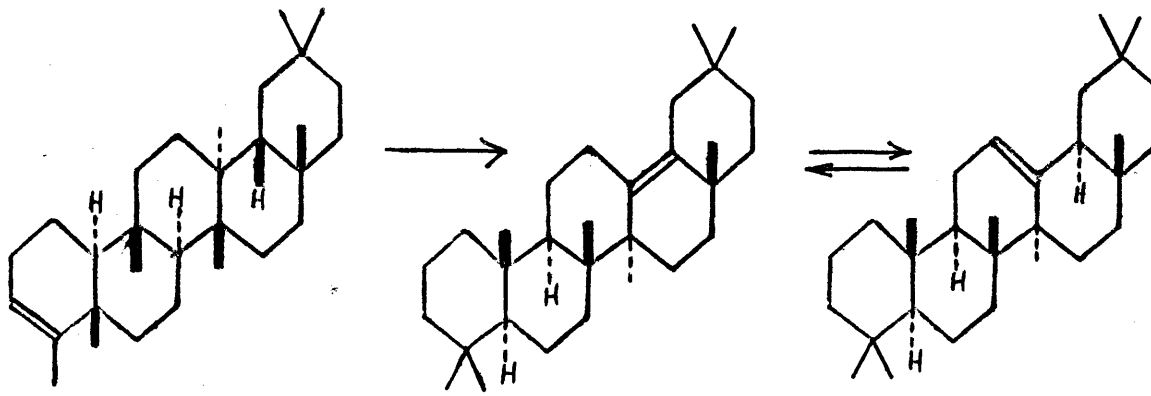
A STUDY OF THE FRIEDELENE-OLEANENE REARRANGEMENT.

With the inter-relation of the triterpenes of the friedelane series from Siphonodon australe Benth. established, (p. 32) the structural problem was reduced to locating the x- and y-oxo groups. The friedelene-oleanene rearrangement was employed as the most direct approach to the problem, and early experiments with friedel-3-en-x-one indicated the possibility of intermediates in the rearrangement. Because of this, a study of the friedelene-oleanene rearrangement was undertaken.

The rearrangement of friedelene to an equilibrium mixture of oleanenes is among the more spectacular of skeletal rearrangements in triterpene chemistry. It is of the "backbone" type and involves the migration of four methyl groups and two hydrogen atoms along the ring junctions of the pentacyclic molecule. In this respect, it is similar to a number of rearrangements in the oleanane and ursane series.[1]

It proceeds by the addition of a proton to the double bond of friedel-3-ene (I) to form a carbonium ion which rearranges by 1:2-shifts of four methyl groups and two hydrogen atoms. Elimination of a proton followed by double bond rearrangement yields finally an equilibrium mixture of olean-13(18)-ene (II) and 18α-olean-12-ene (III).[2] The rearrangement has generally been thought to be fully

concerted and if this were so no intermediates would exist.



I II III

THE COURSE OF THE FRIEDELENE-OLEANENE REARRANGEMENT.

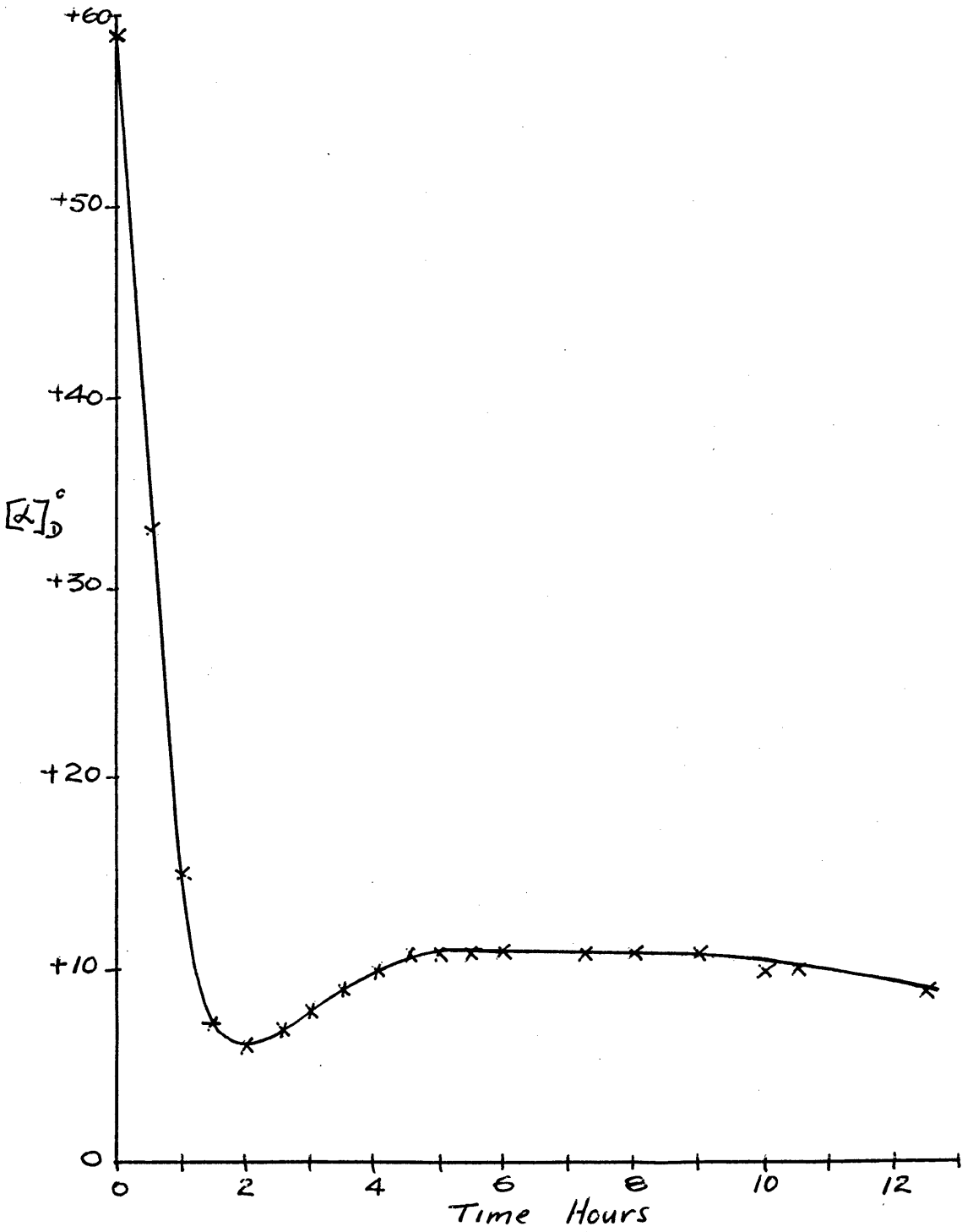
Since rearrangements of the Wagner-Meerwein type are influenced by the nature of the solvent (in particular the dielectric constant[3]), the course of the friedelene-oleanene rearrangement was studied in a variety of solvents. Progress of the rearrangement was followed polarimetrically.

Rearrangement in Chloroform Solution. Formation of Friedel-4(23)-ene.

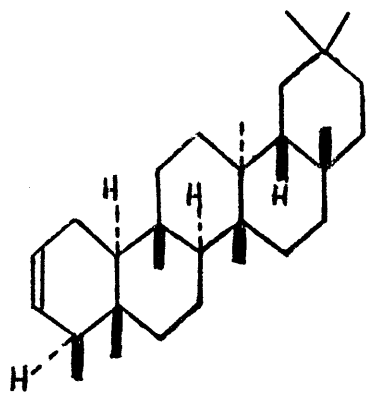
When a solution of friedel-3-ene in chloroform was saturated with dry hydrogen chloride at room temperature the specific rotation changed from $+59^{\circ}$ to $+6^{\circ}$ during two hours. After a rather tedious fractional crystallisation from hexane and then ethyl acetate, friedel-3-ene and an isomer, m.p. 217-218°, $[\alpha]_D$ -12° were obtained from the mixture. This isomer is most probably identical with the

Curve 1.

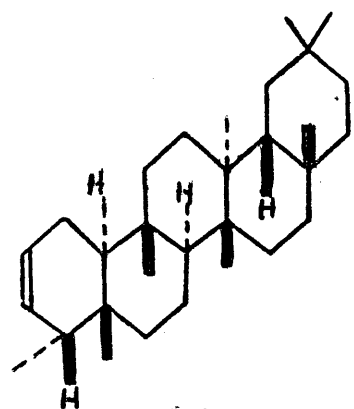
ISOMERISATION OF FRIEDEL-3-ENE WITH HYDROGEN CHLORIDE IN CHLOROFORM.



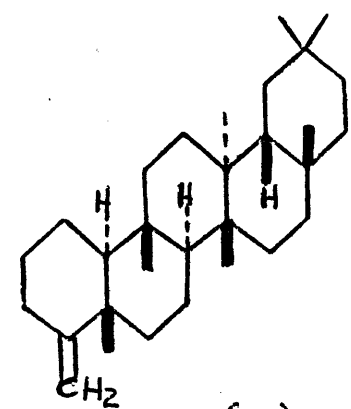
isofriedelene obtained by Corey and Ursprung[4a] by treating a solution of friedel-2-ene (IV) in chloroform with hydrogen chloride. These workers were of the opinion that their product was 4-epifriedel-2-ene (V). During an attempt to hydrogenate this compound they found that it was isomerised back to friedel-2-ene. The compound obtained in the present work was incompletely hydrogenated at atmospheric pressure. However, when high pressure and temperature (90 atmospheres, 60°) were used it was converted to friedelane. The infrared spectrum of the new compound had strong absorption bands at 1635 and 888 cm^{-1} showing the presence of a vinylidene group. Thus the compound must be friedel-4(23)-ene (VI).



(IV)



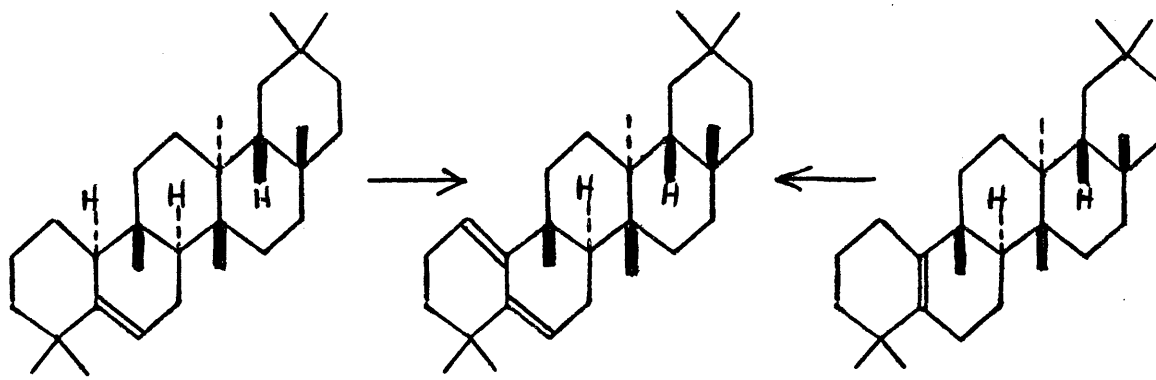
(V)



(VI)

The presence of other hydrocarbons in the isomerisation mixture prepared by treatment of friedel-3-ene with hydrogen chloride in chloroform was apparent from the results of an oxidation experiment. Selenium dioxide oxidation yielded

a mixture consisting predominantly of oxygenated compounds and a smaller amount of a conjugated diene. After chromatography and fractional crystallisation the purified diene had λ max. 239 mu and was identical with alnusa-1(10):5-diene (IX) obtained by selenium dioxide oxidation of alnus-5(10)-ene (VIII) (see p. 78). Assuming that no rearrangement is effected by the selenium dioxide,* the formation of this diene indicates the presence of either alnus-5-ene (VII) or alnus-5(10)-ene (VIII) or both in the isomerisation mixture since these compounds would both be oxidised to alnusa-1(10):5-diene (IX).



(VII) (IX) (VIII)

The infrared spectrum of the product obtained from the action of hydrogen chloride on a solution of friedel-4(23)-ene

* Friedel-3-ene does not give any hydrocarbon when oxidised with selenium dioxide.

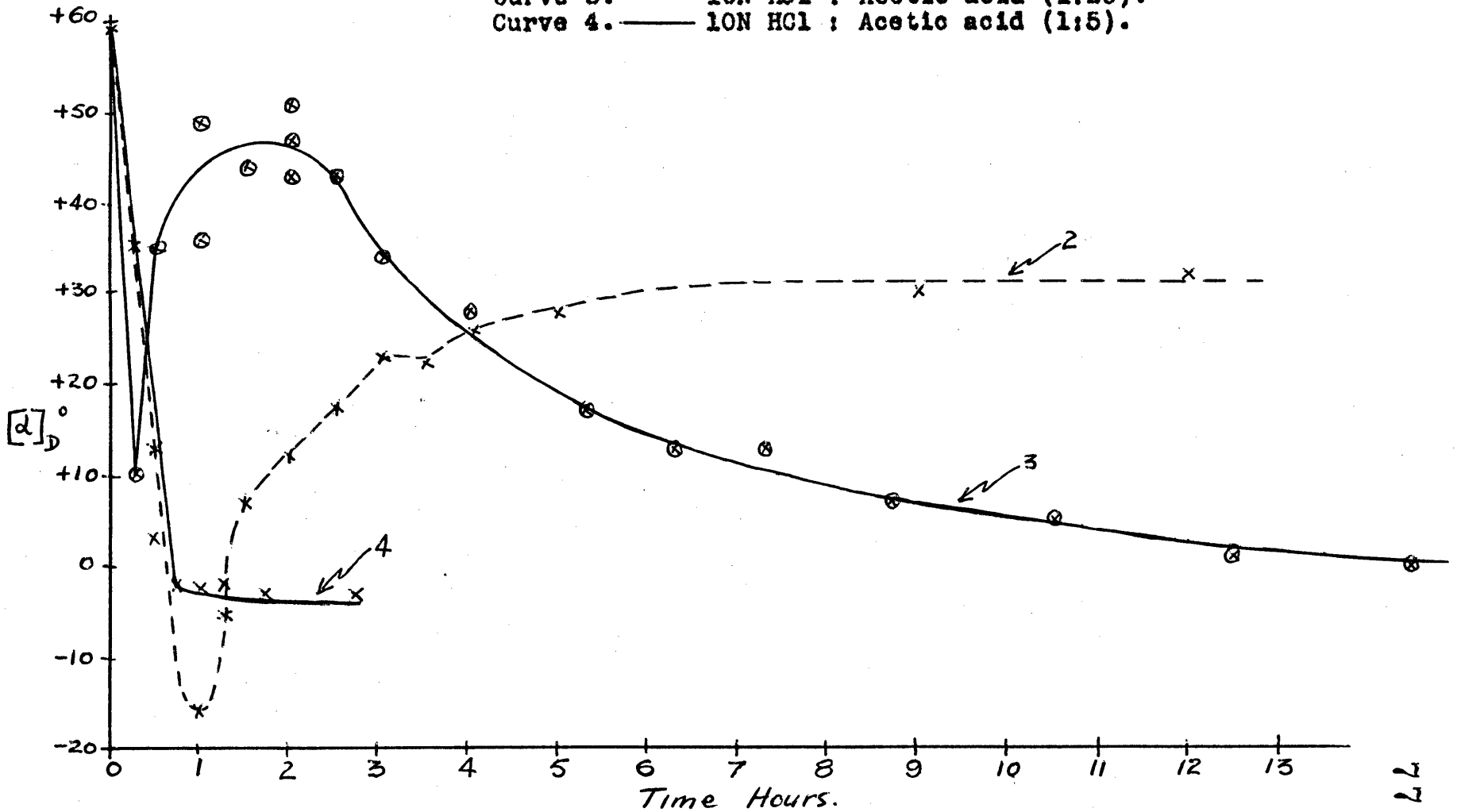
for three hours is quite different from that of the mixture obtained by the same treatment of friedel-3-ene. Presumably friedel-4(23)-ene undergoes rearrangement to a mixture of alnusenes under these conditions.

Rearrangement in Glacial Acetic Acid. Isolation of Alnus-5(10)-ene and its Conversion to Olean-12-ene.[5]

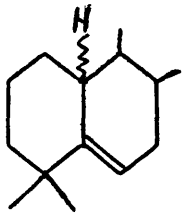
When dry hydrogen chloride was passed through a boiling solution of friedel-3-ene in glacial acetic acid, more extensive changes occurred (see curve 2). The shape of the curve indicates that two reactions take place; the first reaction is very rapid and forms a compound with a negative specific rotation, and this product is then converted into a compound with a positive specific rotation of at least +31°. Fractional crystallisation of the mixture obtained after one hour (the point of minimum specific rotation) yielded as the less soluble and major component, a hydrocarbon with $[\alpha]_D$ -42° and m.p. 226-227°. The infrared spectrum of this compound was identical with that of the hydrocarbon obtained by Corey and Ursprung[4a,4b] from the Wolff-Kishner reduction of an unsaturated ketone obtained from the dehydrobromination of 4-bromofriedelin. Admixture of the two samples of hydrocarbons caused no depression of their melting points. Corey and Ursprung[4b] had proposed the partial structure (X) for this compound but the absence of any absorption in the infrared spectrum typical of

REARRANGEMENT OF FRIEDEL-3-ENE.

Curve 2.----Hydrogen chloride in acetic acid.
Curve 3. ——10N HCl : Acetic acid (1:20).
Curve 4.—— 10N HCl : Acetic acid (1:5).

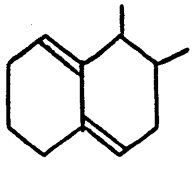


unsaturation indicated that the double bond was tetra-substituted as in (VIII). Confirmatory evidence was



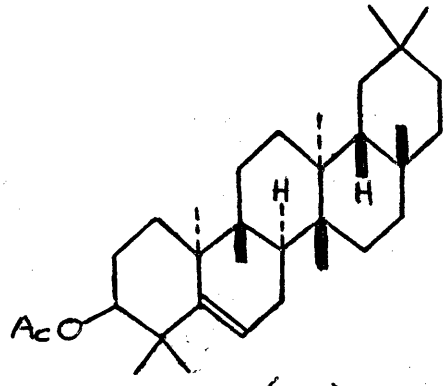
(X)

obtained by oxidising the compound with chromic acid. The ultraviolet spectrum of the crude oxidation product exhibited absorption in its ultraviolet spectrum (λ max. 252 mu.) indicating the presence of an $\alpha\beta$-unsaturated ketone with a tetrasubstituted double bond. Subsequently, Mr. Szumer chromatographed the mixture and obtained a keto-epoxide as the major product. Such compounds are often obtained by the oxidation of steroids possessing tetrasubstituted double bonds.[6] Selenium dioxide oxidation of the new hydrocarbon provided further evidence for its structure. From this oxidation Mr. Szumer obtained a conjugated diene with the characteristic ultraviolet absorption of a heteroannular diene (XI). When Spring and his co-workers[7] treated

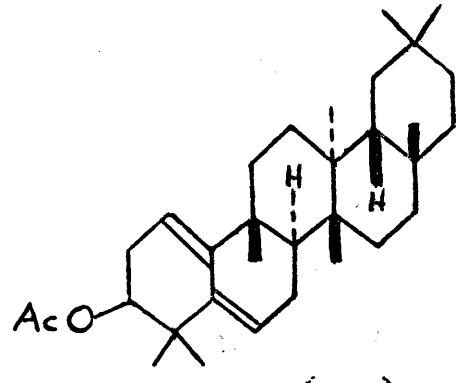


(XI)

alnus-5-en-3α-yl-acetate (XII) in a similar manner they obtained a diene (XIII) whose ultraviolet absorption characteristics were the same as the diene mentioned above.

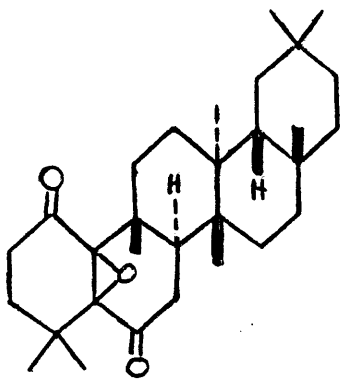


(XII)

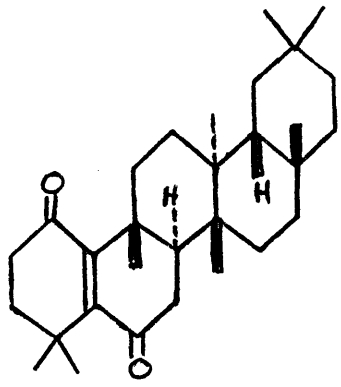


(XIII)

The diene obtained in the present work is therefore alnusa-1(10):5-diene (IX). Mr. Szumer oxidised alnusa-1(10):5-diene (IX) with chromic acid and obtained as the main product, a compound which was presumably 5(10)-epoxyalnus-2:6-dione (XIV). Accompanying this product was a small amount of a yellow substance having absorption in its ultraviolet spectrum (λ max. 259 mu.) characteristic of an ene-1:4-dione. Presumably this latter compound is alnus-5(10)-en-2:6-dione(XV). The oxidative reactions described indicate that the hydrocarbon formed by the rearrangement of friedel-3-ene is alnus-5(10)-ene.

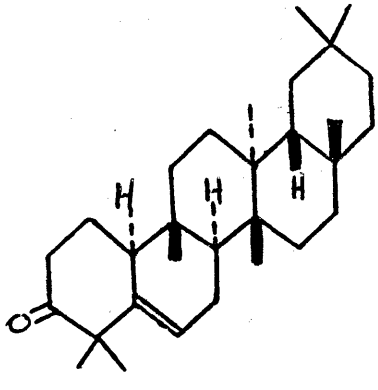


(XIV)

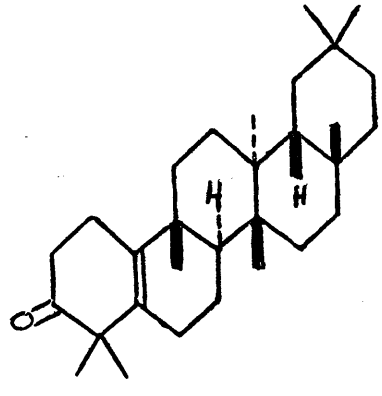


(XV)

Spring, Beaton, Stevenson and Stewart[7] have re-investigated the dehydrobromination of 4-bromofriedelin and have found that the product is a mixed crystal consisting of alnus-5-en-3-one (XVI) and alnus-5(10)-en-3-one (XVII) in the ratio of 1:2. Alnus-5(10)-en-3-one had previously been prepared by Chapon[8] by mild acid treatment of alnus-5-en-3-one.



(XVI)



(XVII)

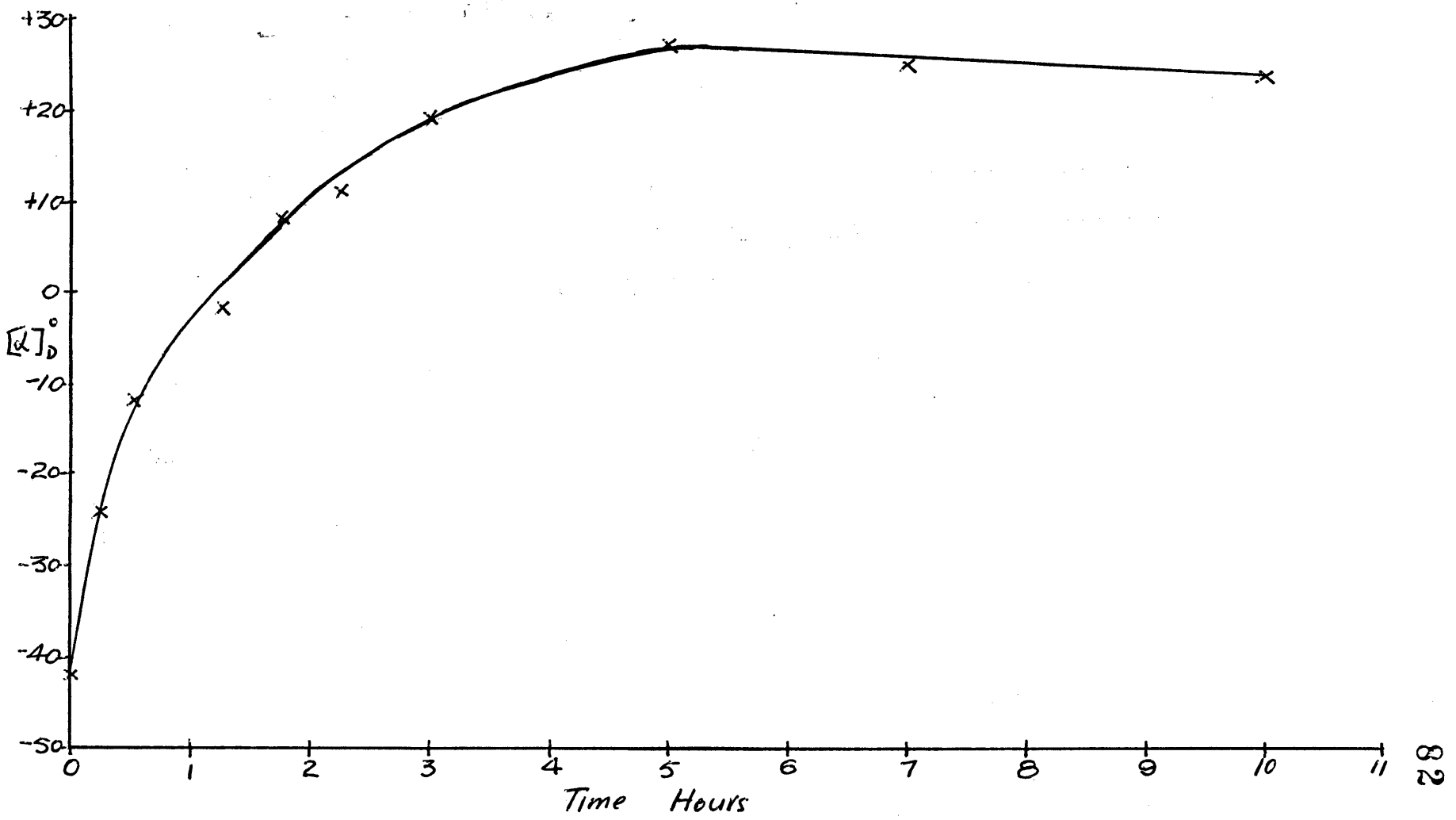
The product was then reduced by the Wolff-Kishner method to a hydrocarbon with $[\alpha]_D$ -38° and m.p. 226°. This compound is almost certainly identical with the hydrocarbon obtained by rearrangement of friedel-3-ene.

Since alnus-5(10)-ene was isomerised to the equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene by vigorous acid treatment, alnus-5(10)-ene must be an intermediate in the friedelene-oleanene rearrangement. Its isolation proves that the first stage of the friedelene-oleanene rearrangement is not concerted with the remainder of the rearrangement, at least in the conditions used.

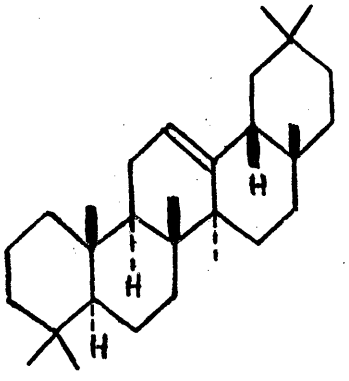
Isolation of Olean-12-ene.- After treating a boiling solution of friedel-3-ene in glacial acetic acid with dry hydrogen chloride for seven hours, the specific rotation attained a constant value of +31° (curve 2). The hydrocarbon mixture obtained from this treatment was subjected to an extensive fractional crystallisation from which alnus-5(10)-ene and olean-12-ene were obtained. The identity of olean-12-ene (XVIII) was proved by comparison of its infra-red spectrum with that of an authentic specimen and by oxidising it with selenium dioxide to oleana-11:13(18)-diene (XIX). Similar acid treatment of alnus-5(10)-ene (curve 5) for several hours resulted in the specific rotation rising rather rapidly to a roughly constant value of +27°. The hydrocarbon mixture obtained by this treatment was identical

Curve 5.

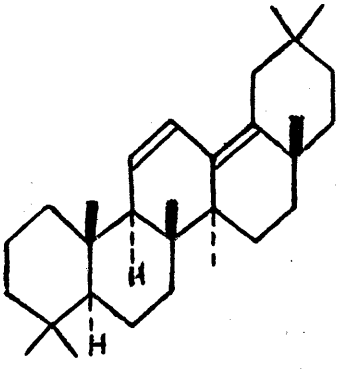
REARRANGEMENT OF ALNUS-5(10)-ENE WITH HYDROGEN CHLORIDE IN ACETIC ACID.



(infrared spectra) with the final mixture obtained by the same treatment of friedel-3-ene.



(XVIII)

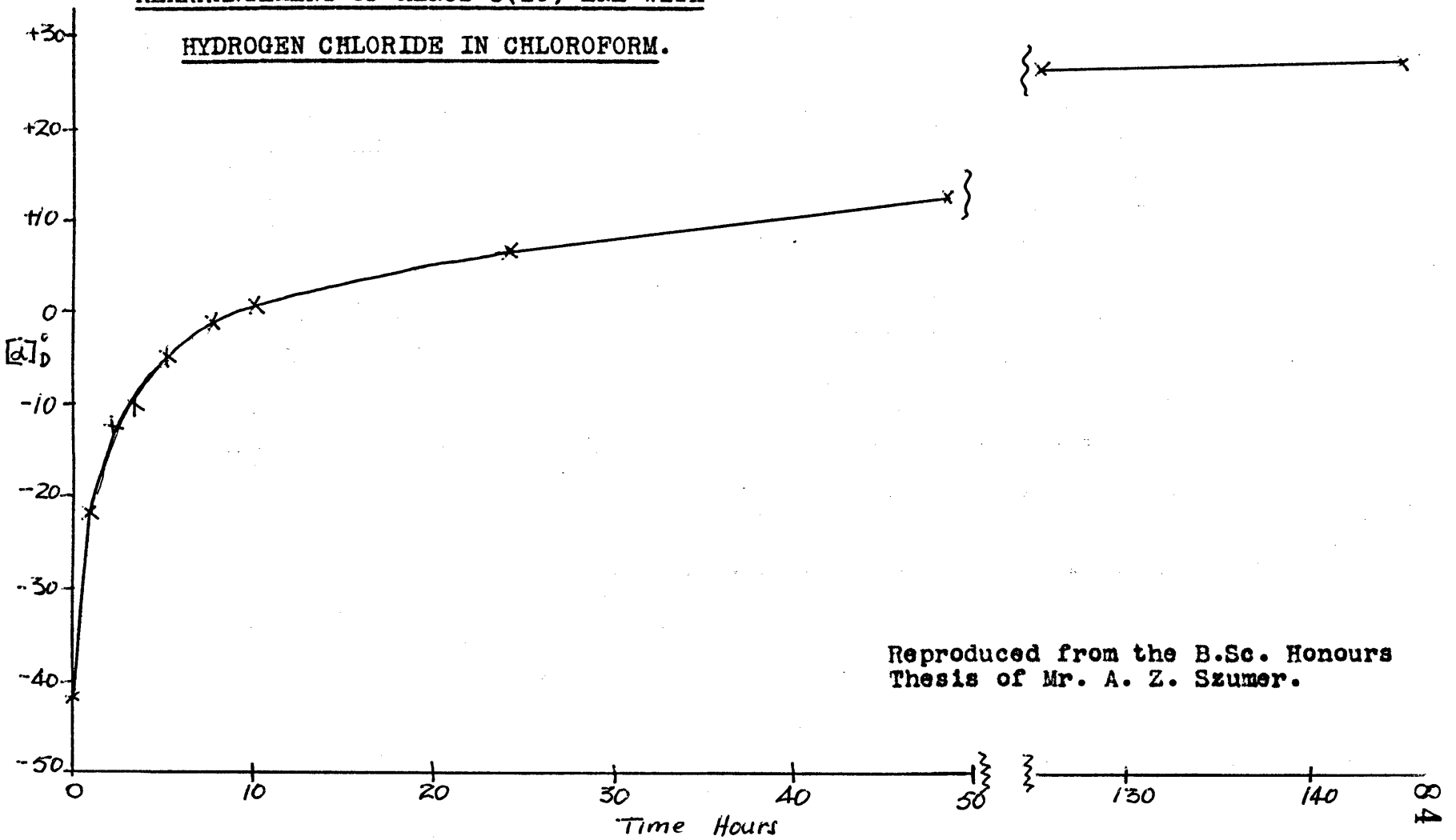


(XIX)

The infrared spectrum of the hydrocarbon mixture ($[\alpha]_D$ $+31^\circ$) resembled that of a synthetic mixture of equal proportions of alnus-5(10)-ene and olean-12-ene. The differences in the spectra suggested that the isomerisation mixture contained small amounts of olean-13(18)-ene and possibly 18α-olean-12-ene. These compounds are known to be formed by isomerisation of olean-12-ene.[2] Later, Mr. Szumer observed that specific rotation of a solution of alnus-5(10)-ene in chloroform saturated with hydrogen chloride at room temperature rose steadily during about 120 hours to a value of $+27^\circ$ (curve 6). The infrared spectrum of this product was very similar to that of the synthetic mixture of olean-12-ene and alnus-5(10)-ene and gave no indication of the presence of other compounds. Presumably, under

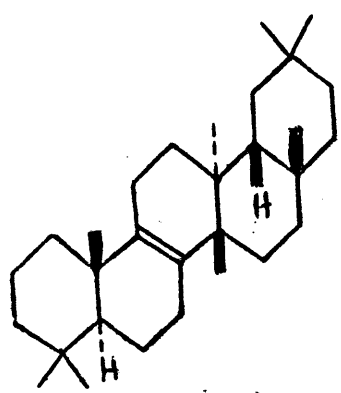
Curve 6.

REARRANGEMENT OF ALNUS-5(10)-ENE WITH HYDROGEN CHLORIDE IN CHLOROFORM.

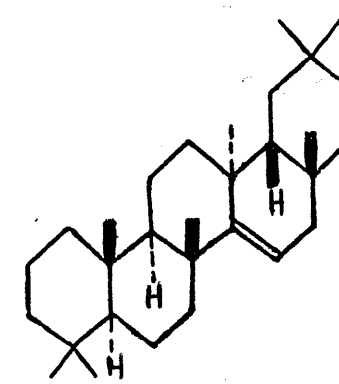


Reproduced from the B.Sc. Honours Thesis of Mr. A. Z. Szumer.

these conditions olean-12-ene is not isomerised further to olean-13(18)-ene and 18α-olean-12-ene. Since olean-12-ene was unchanged after treatment with hydrogen chloride in chloroform for about 20 hours its formation from alnus-5(10)-ene cannot be an equilibrium reaction. The specific rotation-time curves exhibited slight, reproducible irregularities which may possibly be due to the formation of double bond isomers such as alnus-5-ene. However, no other intermediates could be detected by the methods which were employed. It is conceivable that the hydrocarbon (XX) and taraxerene (XXI) could be intermediates in the friedelene-oleanene rearrangement. This point is discussed below.



(XX)



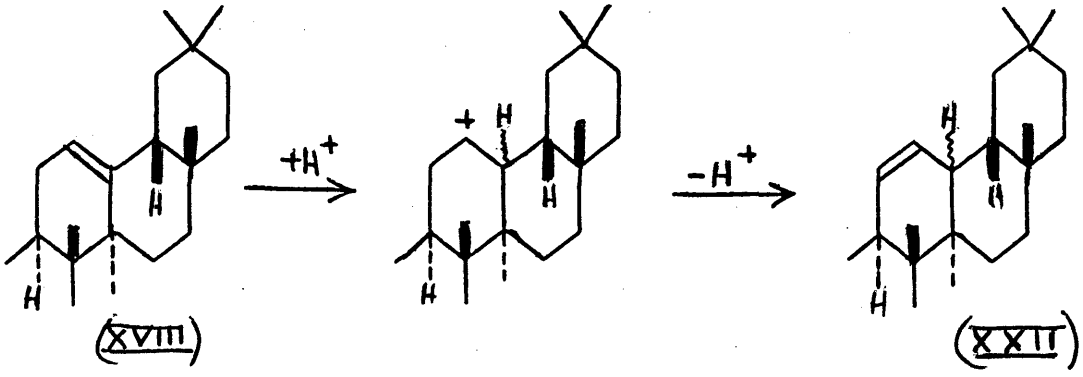
(XXI)

Rearrangement in Aqueous Acid Solution.

The polarimetric rate curve for a boiling solution of friedel-3-ene in glacial acetic acid — 10N hydrochloric acid (20:1) was more complex than those obtained from

previous experiments. As was the case when hydrogen chloride in acetic acid was used, the specific rotation dropped sharply to a minimum and then rose to a maximum value. However, in the more proton-rich solvent the specific rotation finally decreased steadily to a value of 0° after 14½ hours. The product obtained after this treatment was fractionally crystallised and yielded the mixed crystal of 18α-olean-12-ene and olean-13(18)-ene. The first part of the curve undoubtedly represents the conversion of friedel-3-ene to alnus-5(10)-ene. A substance with $[\alpha]_D$ $+56^{\circ}$ was isolated by fractional crystallisation of the product from the point of maximum specific rotation. On the basis of specific rotations it could not be 18α-olean-12-ene ($[\alpha]_D$ $+37^{\circ}$), olean-13(18)-ene ($[\alpha]_D$ -48°) or taraxerene ($[\alpha]_D$ $+3^{\circ}$). The possibility that it was impure olean-12-ene was eliminated because upon admixture with olean-12-ene it depressed its melting point. Since selenium dioxide oxidation of the mixture at this point ($[\alpha]_D$ $+43^{\circ}$) gave oleana-11:13(18)-diene (XIX) in good yield, the substance was most probably an oleanene isomer (assuming that no rearrangement took place during the oxidation). Thus olean-11-ene (XXII) could be formed by the addition and elimination of a proton from olean-12-ene (XVIII).

When the ratio of 10N hydrochloric acid to glacial acetic acid was raised to 1:5 the rearrangement proceeded



(XVIII) (XXII)

so rapidly that the equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene was evidently formed in one hour and the specific rotation-time curve (curve 4) gave no indication that there might be any intermediate stages.

The evidence outlined above suggests that the friedelene-oleanene rearrangement consists of three stages.

1. Friedel-3-ene rearranges rapidly to alnus-5(10)-ene.
2. Alnus-5(10)-ene rearranges to olean-12-ene by a concerted reaction, or, if intermediates are formed they are converted very rapidly to olean-12-ene.
3. Olean-12-ene isomerises to an equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene as shown by Spring et.al.[2]

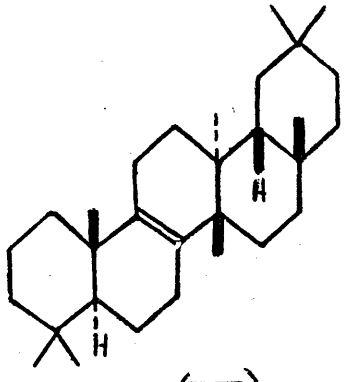
Conformational Driving Forces.

The ease with which friedelene is rearranged is undoubtedly due to its thermodynamic instability which is a result of various steric interactions. The conformational driving force for the friedelene-oleanene rearrangement has been attributed to the steric congestion in rings D and E as a consequence of their cis-fusion.[9,10] An examination

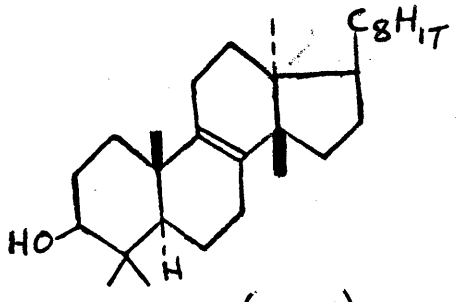
of models reveals that the cis-locking of rings D. and E in friedelene causes considerable congestion between axial α-oriented methyl groups at $C_{(13)}$ and $C_{(20)}$. As a consequence of this, ring E is distorted and cannot exist in either a pure chair or a pure boat conformation. This feature is also present in alnus-5(10)-ene (VIII), the hydrocarbon (XX), and taraxerene (XXI) but is absent in olean-12-ene (XVIII). This cannot be the factor causing the rearrangement of friedelene to alnus-5(10)-ene since it is present in both these compounds, but it is undoubtedly responsible for the final stage of the rearrangement. Presumably the driving force for the friedelene-alnusene rearrangement is a result of 1:3-interactions[11] between axial methyl groups at $C_{(5)}$ and $C_{(9)}$. The additional 1:3-interaction between axial methyl groups at $C_{(9)}$ and C(14) in friedelene may also aid the reaction. The formation of alnus-5(10)-ene removes the $C_{(5)}$-methyl group from the proximity of the $C_{(9)}$-methyl group resulting in a molecule of lower compression energy.

During this investigation neither the hydrocarbon (XX) nor taraxerene (XXI) could be isolated as intermediates in the rearrangement and no indication of their presence was obtained. This may be due to their very short life in the conditions used or to the rearrangement of alnus-5(10)-ene to olean-12-ene being concerted, in which case they do not exist as intermediates. Both of these compounds are conformationally less stable than alnus-5(10)-ene and friedel-3-ene

since they possess factors contributing to their instability other than the steric congestion in ring E already described. Thus the hydrocarbon (XX) is analogous to euphenol (XXIII)[11] in that both of these molecules possess boat conformations in rings B and C. Taraxerene has ring C in a boat conformation as well as 1;3-interactions between axial methyl groups at $C_{(4)}$, $C_{(10)}$ and $C_{(8)}$. One can therefore



(XX)



(XXIII)

predict that the hydrocarbon (XX) and taraxerene (XXI) would be very readily converted into olean-12-ene with the release of considerable compression energy. This theory is in accord with the experimental facts. Thus Mr. Szumer observed that taraxerene was converted almost instantly into olean-12-ene when it was dissolved in chloroform saturated with hydrogen chloride. The evidence indicates that the possibility of isolating taraxerene and the hydrocarbon (XX) from the friedelene-oleanene rearrangement is

most unlikely. However, conformational instability of these compounds does not necessarily mean that they cannot be intermediates in the friedelene-oleanene rearrangement and no conclusions can be made as to whether the alnusene-oleanene rearrangement is concerted or not.

The Mechanism of the Formation of Olean-12-ene.

An interesting feature of the alnusene-oleanene rearrangement is the initial formation of olean-12-ene rather than the thermodynamically more stable olean-13(18)-ene. Spring and his collaborators have commented on the similar formation of β-amyrin acetate from taraxeryl acetate by acid treatment and attributed it to the geometry of the molecule[12] (see p.59). The formation of the Δ^{12}-isomer rather than the $\Delta^{13(18)}$-isomer indicates that the proton elimination is concerted with migration of the methyl group from $C_{(13)}$ to $C_{(14)}$. The concerted process would be facilitated (and may only occur) by elimination of the proton in a direction anti-parallel to the movement of the methyl group; the process would thus resemble a bimolecular elimination reaction. This geometrical requirement is satisfied by the equatorial hydrogen atom at $C_{(12)}$ but not by the hydrogen atom at $C_{(18)}$ which is axial in friedelane and in related structures.[13]

The Bearing of the Friedelene-Oleanene Rearrangement on the Stereochemistry of Friedelin.

Much of the stereochemistry of friedelin has been deduced from the friedelene-oleanene rearrangement[9,10], the assumption being made that the rearrangement is fully concerted. Other methods have been used to determine the configuration of the asymmetric centres of friedelin, (see p. 16) and in all cases the results agree with the deductions based on the rearrangement.

Stereochemical deductions are based on the fact that such rearrangements involving 1:2-shifts are stereospecific in that the migrating atom or group retains its orientation (and its configuration). Thus a methyl group which was β-oriented before the rearrangement will remain so during and after the rearrangement. Hence, if the stereochemistry of the isomerisation product is known, then (with certain provisos) the stereochemistry of the precursor may be deduced. Ourisson and Takahashi[14] have stated that no conclusions can be drawn about the stereochemistry of friedelin if the rearrangement is not concerted, since the final products possess the most stable conformations. However, this is not entirely correct; whether the rearrangement is concerted or not certain conclusions may be drawn about the stereochemistry of friedelin. Thus deductions about the configurations of $C_{(9)}$, $C_{(13)}$ and $C_{(14)}$ based on the rearrangement are legitimate. This is because these

centres possess methyl groups which must retain their orientation during the rearrangement. The configuration of $C_{(17)}$ is apparent since the methyl group at $C_{(17)}$ does not take place in the rearrangement.

Since alnus-5(10)-ene (VIII) is an intermediate in the friedelene-oleanene rearrangement no conclusions can be drawn from the rearrangement about the configurations of $C_{(5)}$ and $C_{(10)}$. However, the stereochemistry of these positions has been established from other evidence (see p.20). No other intermediates have been detected in the friedelene-oleanene rearrangement but if the compound (XX) were an intermediate then deductions based on the rearrangement concerning the configuration of $C_{(8)}$ would be invalid. Here again the configuration of this centre has been established by other means.

The only centre about which no definite evidence had been obtained is $C_{(18)}$. On biosynthetic grounds Corey and Ursprung[4b] favoured the view that the D/E ring junction is cis- and the hydrogen atom at $C_{(18)}$ is therefore β-oriented. Spring and his collaborators[9,10] also ascribe the β-configuration to the hydrogen atom at $C_{(18)}$. Their conclusion is based on the observation that in a number of rearrangements resembling the friedelene-oleanene rearrangement the cis-locking of rings D/E was a common feature and is presumably essential for such transformations[1] (see p.63).

The isolation of olean-12-ene from the friedelene-oleanene rearrangement provides definite proof of the configuration of $C_{(18)}$ in friedelane. Since this compound is thermodynamically less stable than 18α-olean-12-ene (XI) or olean-13(18)-ene (X) to which it is readily converted, its formation during the rearrangement proves the β-configuration of the hydrogen atom at $C_{(18)}$.

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11. Cf. Barton and Cookson, Quart. Rev., 1956, 10, 44.

12. Beaton, Spring, Stevenson, and Stewart, J. Chem. Soc., 1955, 2131.

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14. Ourisson and Takahashi, Bull. Soc. Chim. Fr., 1956, 353.

LOCATION OF THE x- AND y-OXO GROUPS.

Since the triterpenes of Siphonodon australe Benth. have been inter-related,[1,2] (see p. 29 et. seq.) the structural problem is resolved into locating the x- and y-oxo groups.

Neither of these two groups can be located in ring A since the chemical and spectroscopic properties of friedelane-3:x-dione and friedelane-3:y-dione indicate the absence of an α- or β- diketone system. Also, since friedelan-x-one and friedelan-y-one (in which the D/E ring junction is cis) are unaffected by alkali, neither of these groups can be at $C_{(19)}$. The infrared spectra (in carbon tetrachloride) are confirmatory in this respect since they both exhibit absorption (a peak at 1424 cm^{-1}) characteristic of a methylene group adjacent to an oxo group.[3]

Consideration of molecular rotation differences should indicate possibilities of the positions of the x- and y-oxo groups. Friedelane is a skeletal enantiomorph with respect to rings A, B, C and D of the usual triterpenes and rings A, B, and C of the 5α-steroids (see p. 2o). Hence the molecular rotation contribution of an oxo group in the friedelane series should be opposite to that of an oxo group in the corresponding ring of the usual triterpenes and 5α-steroids. This is illustrated in the following table. The x-oxo group has a large positive value (+ 589°; see p.4o) and on this basis could be located in ring B or ring D.

Ring	Δ(CO) Triterpenes and 5α-steroids	Δ(CO) Friedelane series	
A	+	-	*
B	-	+	*
C	+	-	
D	- (triterpenes only)	+	

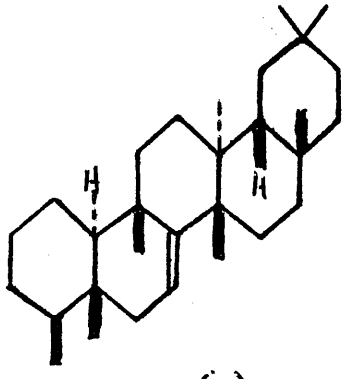
* Confirmed by experiment (see p.20,22)

The molecular rotation contribution of the y-oxo group is negative (-197; see p. 40) and it could therefore be located in ring C. Although ring E has not been considered (because of the cis- D/E ring junction[4]), it cannot of course be excluded as a possible location for one or other of these oxo groups.

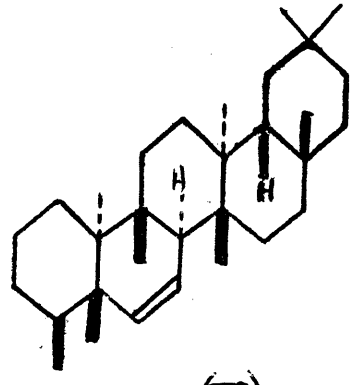
Location of the x-Oxo Group.

Interpretation of one of Mr. Szumers experiments leads to the probable elimination of $C_{(7)}$ as a possible location for the x-oxo group. He prepared an unsaturated hydrocarbon by treating friedelan-x[ax]-ol with phosphorus oxychloride. The infrared spectrum of this hydrocarbon indicates that the double bond is cis- disubstituted (absorption in the 1650 cm^{-1} region and a strong peak at 748 cm^{-1}) and that there is no methylene group adjacent to the double bond (i.e. no peak near 1438 cm^{-1}).[3] Dehydration of

friedelan-7β[ax]-ol by phosphorus oxychloride (proceeding by trans-elimination) would probably yield the unsaturated hydrocarbon (I). This compound however, possesses a trisubstituted double bond with an adjacent methylene group. The possibility that the alternative hydrocarbon (IA) would be formed cannot be excluded.



(I)



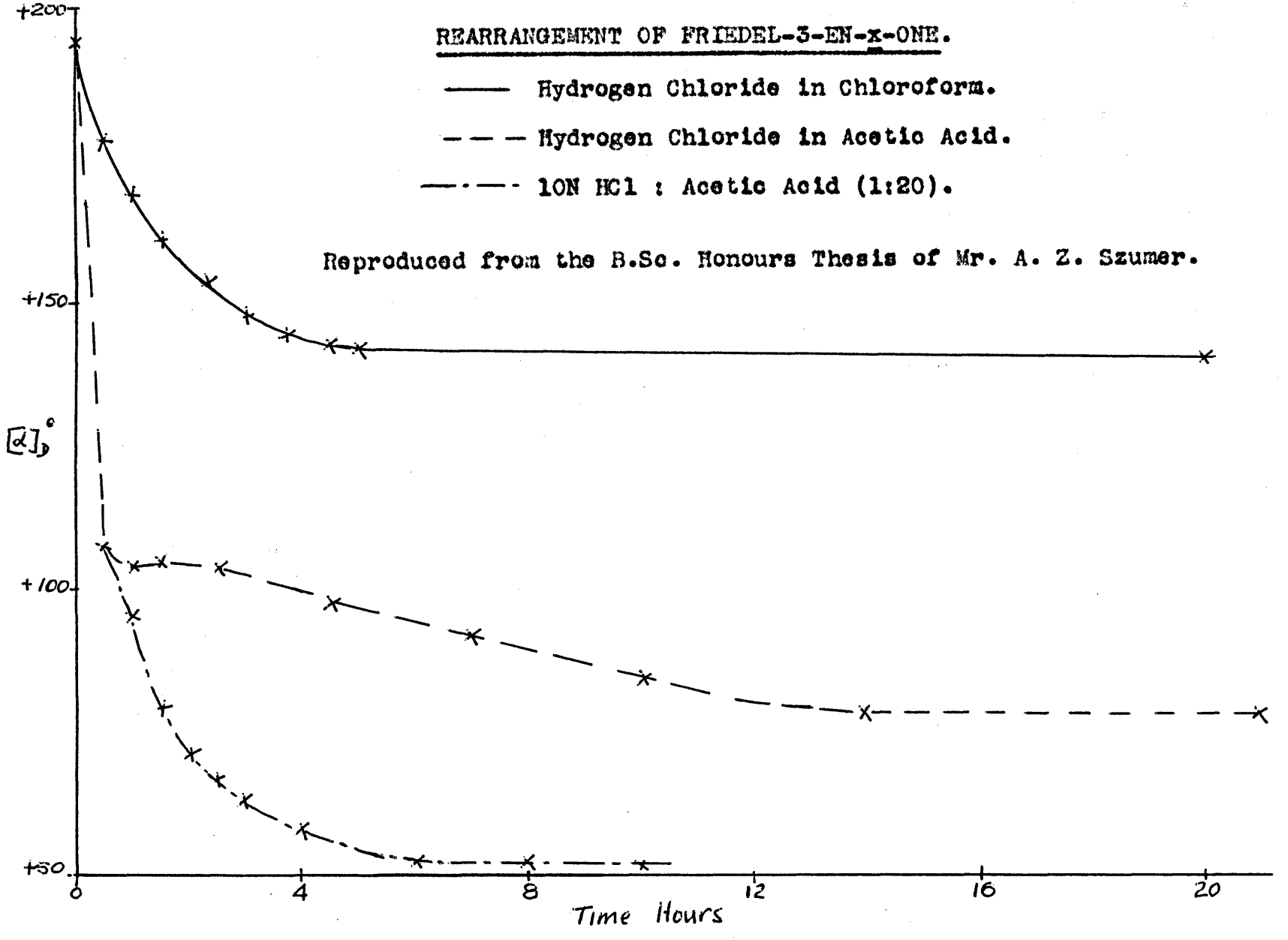
(IA)

If the x-oxo group were near the path of the friedelene-oleanene rearrangement it should be possible to form an αβ-unsaturated ketone by rearranging friedel-3-en-x-one. This compound was prepared by reducing friedelane-3:x-dione with sodium borohydride to a mixture of 3α and 3β-hydroxy-friedelan-x-one, and treating the axial (3β-) epimer with phosphorus oxychloride. When dry hydrogen chloride was bubbled through a boiling solution of friedel-3-en-x-one in n-butanol for 16 hours and the product fractionally crystallised, a new unsaturated ketone was obtained.

This compound had no absorption in its ultraviolet spectrum other than that of an isolated carbonyl group, and it did not react with 2:4-dinitrophenylhydrazine. Wolff-Kishner reduction with anhydrous hydrazine yielded alnus-5(10)-ene.* Thus this unsaturated ketone is alnus-5(10)-en-x-one. When friedel-3-en-x-one or 3β-hydroxyfriedelan-x-one was treated with a boiling mixture of glacial acetic acid and 10N hydrochloric acid (ratio 5:1) for 16 hours, the product obtained after repeated recrystallisations had $[\alpha]_D$ +66°. Wolff-Kishner reduction of this product yielded a hydrocarbon mixture whose melting point and infrared spectrum were identical with those of the mixed crystal of 18α-olean-12-ene and olean-13(18)-ene;[5] the melting points of these products were undepressed on admixture. There was however a difference of 15° in the specific rotation. These facts show that the two products were mixtures of the same two hydrocarbons in somewhat different proportions. Hence the product with $[\alpha]_D$ +66° is a mixture (presumably a mixed crystal) of 18α-olean-12-en-x-one and olean-13(18)-en-x-one. The mixed crystal of oleanen-x-ones formed a semicarbazone and 2:4-dinitrophenylhydrazone and had no selective

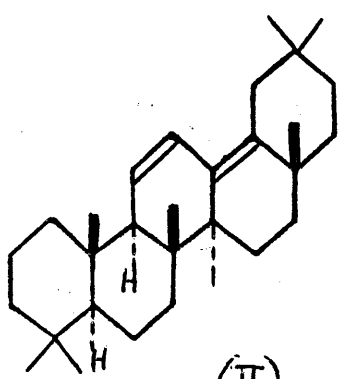
* This was the first discovery in this work of alnus-5(10)-ene and lead to the investigation of the friedelene-oleanene rearrangement described earlier.

absorption in its ultraviolet spectrum other than that of an isolated oxo group. Subsequently Mr. Szumer followed polarimetrically the rearrangement of friedel-3-en-x-one by hydrogen chloride in boiling glacial acetic acid (see curve). He isolated alnus-5(10)-en-x-one after one hour and olean-12-en-x-one after seven hours (and also after fourteen hours) treatment. Olean-12-en-x-one formed a semicarbazone and a 2:4-dinitrophenylhydrazone. More vigorous acid treatment gave the mixed crystal of oleanenones already described. Thus the course of this rearrangement is identical and the kinetics very similar to the rearrangement of friedelene. The difference in the shapes of the curves is a consequence of the different specific rotations of the products of the rearrangement. (The molecular rotational contribution of an oxo group in the various products will not necessarily have the same order or sign). At no stage in the rearrangement was there any absorption in the ultraviolet indicative of an αβ-unsaturated ketone. The x-oxo group must therefore be located at either $C_{(15)}$, $C_{(21)}$ or $C_{(22)}$ since these positions would not be favourable for the formation of an αβ-unsaturated ketone during the rearrangement. Although it cannot be conclusively eliminated, $C_{(15)}$ is not regarded as a likely position for the x-oxo group. This opinion is based on the fact that the kinetics of the friedelene-oleanene rearrangement is evidently unaffected


REARRANGEMENT OF FRIEDEL-3-EN-x-ONE.
Hydrogen Chloride in Chloroform.
Hydrogen Chloride in Acetic Acid.
10N HCl : Acetic Acid (1:20).
Reproduced from the B.Sc. Honours Thesis of Mr. A. Z. Szumer.
+200
+150
+100
+50
[α]D°
0
4
8
12
16
20
Time Hours

by the presence of the x-oxo group in the molecule. It seems reasonable to suppose that an oxo group at $C_{(15)}$ would considerably influence the rate and possibly the course of the friedelene-oleanene rearrangement.

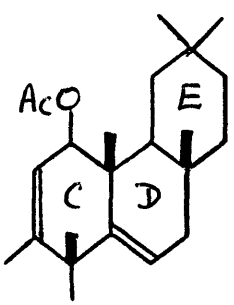
Additional evidence in support of the location of the x-oxo group at $C_{(21)}$ or $C_{(22)}$ was provided as follows. When Mr. Szumer treated diaxial friedelane-3:x-diol (prepared by lithium aluminium hydride reduction of friedelane-3:x-dione) or friedel-3:x-diene (prepared by the action of phosphorus oxychloride on the diol) with boiling 10N hydrochloric acid -- glacial acetic acid (ratio 1:5), he obtained a conjugated diene whose constants were very similar to those of oleana-11:13(18)-diene (II), and whose ultraviolet absorption spectrum indicated that it had the same chromophoric system. Comparison of X-ray diffraction powder photographs and infrared spectra established that this compound was not identical with an authentic specimen



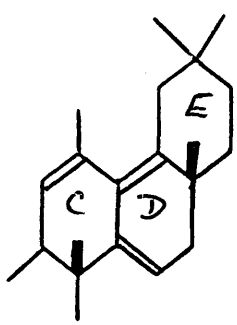
(II)

of oleana-11:13(18)-diene. Various schemes can be envisaged whereby this type of chromophore could be formed but the following appears most reasonable. Addition of a proton to the Δ^3 double bond of friedel-3:21-diene (III) would form a carbonium ion (IV) which would undergo the friedelene-oleanene rearrangement to form olean-12:21-diene (V). Isomerisation of this compound would give olean-13(18):21-diene (VI) which could form the carbonium ion (VII). This ion could undergo a retropinacolinic rearrangement to form the ion (VIII) which in turn could form the conjugated diene (IX).

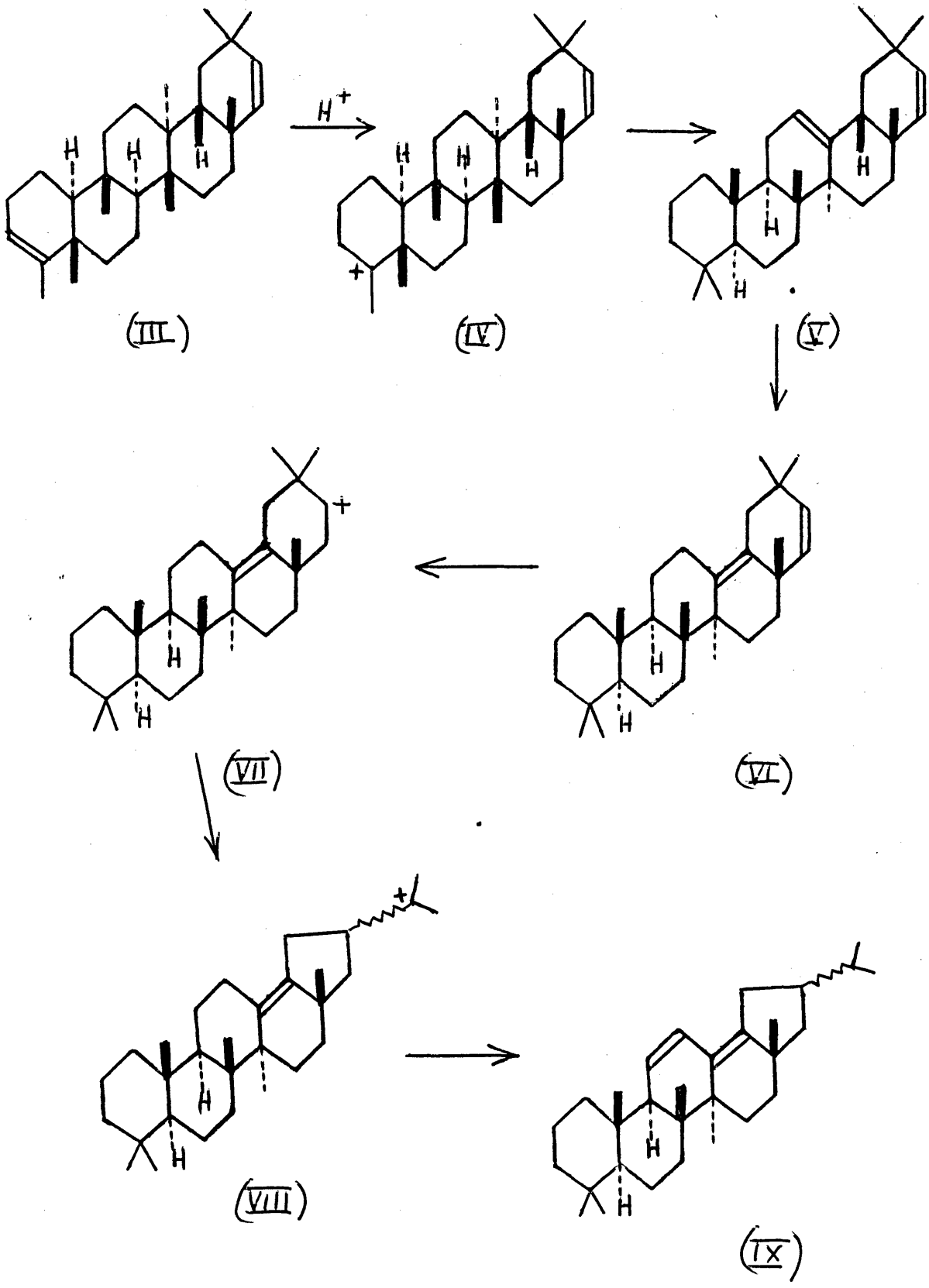
The formation of the conjugated diene does not eliminate the possibility of the x-group being at $C_{(15)}$. In this case however, the migration of a methyl group from a tertiary to a secondary position would be necessitated. Such migrations do not commonly occur although the taraxerene derivative (X) has been converted into a compound (XI) in which a methyl group is thought to have migrated from a tertiary to a secondary position.



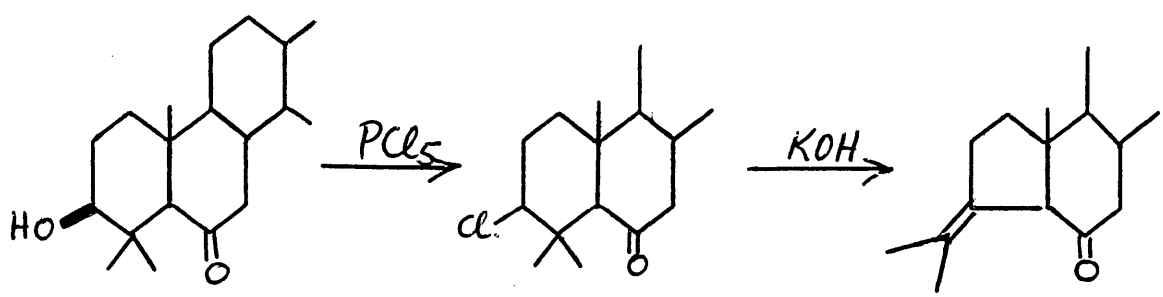
(X)



(XI)


H+
(III)
(IV)
(V)
(VI)
(VII)
(VIII)
(IX)

If the x-group were at $C_{(21)}$ then friedelan-x[eq]-ol and the x[eq]-hydroxyoleanenes should undergo the well known retropinacolinic rearrangement when treated with phosphorus pentachloride. The detection of an isopropylidene group would be indicative that the transformation had occurred. However, when friedelan-x[eq]-ol was treated with phosphorus pentachloride a complex mixture was obtained. The fraction not adsorbed on alumina contained chlorine and its elementary analysis indicated that it consisted of approximately equal parts of a hydrocarbon and a chloro-compound. Hydrogen chloride was evolved at the melting point of this mixture which was found to be inseparable. Usually the retropinacolinic rearrangement proceeds almost quantitatively though a derivative of sumaresinolic acid (XII) forms a chlorocompound, probably (XIII) when treated with phosphorus pentachloride.[6] This chlorocompound however, gave the expected product (XIV) when it was treated with methanolic potassium hydroxide. Similar treatment of the reaction product from friedelan-x[eq]-ol failed to remove the chlorine. Thus the evidence indicates that

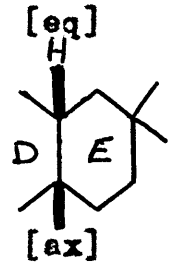


(XII) (XIII) (XIV)

the normal retropinacolinic rearrangement did not take place and the x-group is therefore not at $C_{(21)}$.

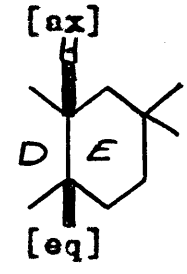
The oxo group in the oleanene-x-ones reacts with semicarbazide and 2:4-dinitrophenylhydrazine whereas in the friedelene and the alnusene series it is unreactive. This marked difference in the steric hindrance of the x-oxo group in the oleanenes on the one hand and in friedelene and alnus-5(10)-ene on the other is consistent with the location of this group in rings D or E. Examination of models reveals that $C_{(15)}$, $C_{(21)}$ and $C_{(22)}$ are all considerably hindered in friedel-3-ene and less hindered in olean-12-ene. However, no definite conclusions can be drawn.

A consequence of the friedelene-oleanene rearrangement is a conformational and configurational inversion of all rings in the structure even including the cis-fused ring E.



friedelane series

(XV)



olean-12-ene series

(XVI)

Consequently the Δ(CO) value for each ring should change its sign after the friedelene-oleanene rearrangement has taken place. This appears to be the case since the Δ(CO)

of the x-oxo group in the friedelane series is ca. +600° (see p. 40) whereas in the olean-12-ene series it is -152° (see table p.109). Also, the molecular rotation contribution of an oxo group in rings D and E in the olean-12-ene series is negative (see table p.109). This is confirmatory evidence for the location of the x-oxo group at either $C_{(15)}$, $C_{(21)}$ or $C_{(22)}$, but allows no discrimination to be made between these centres.

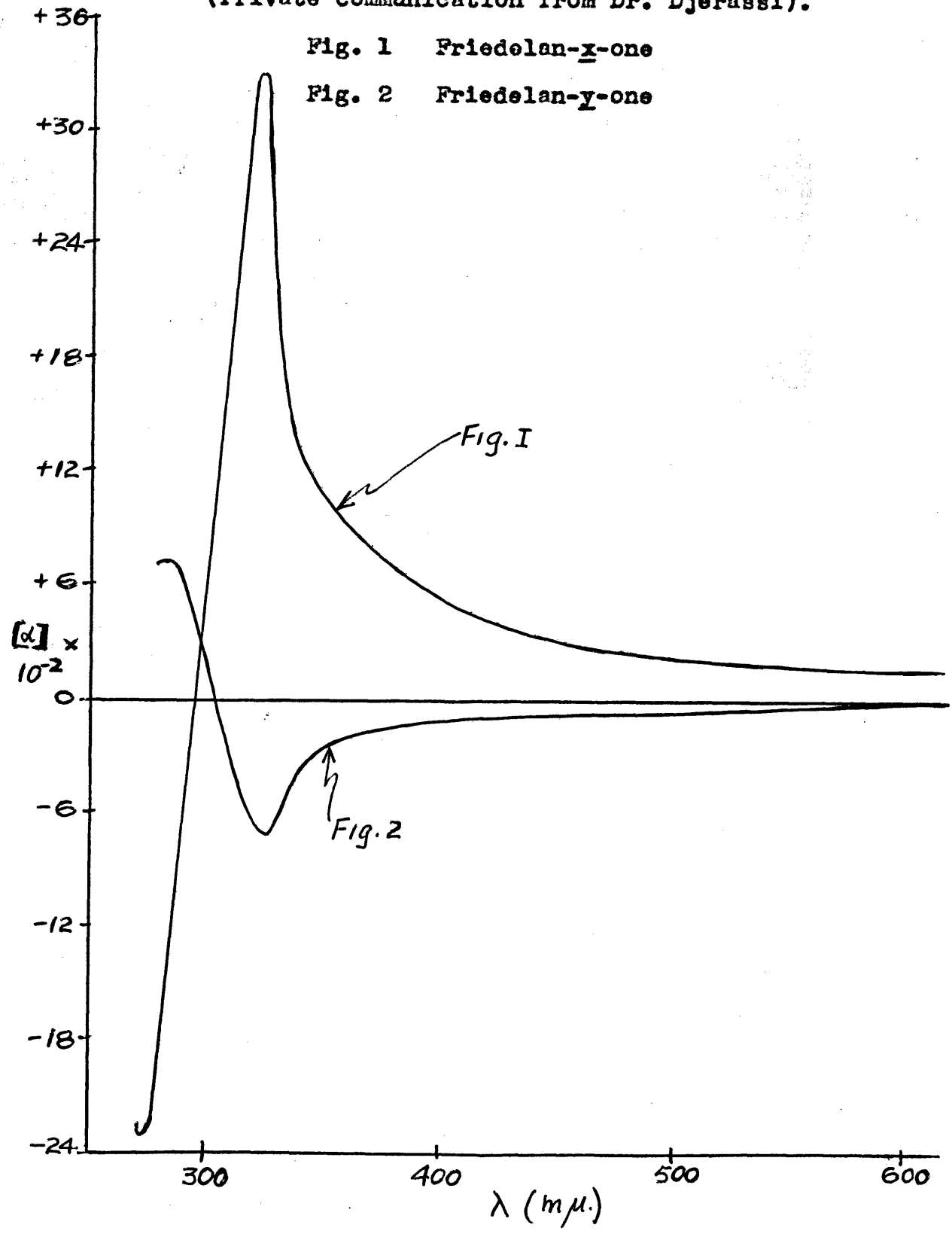
As part of his programme on the application of rotatory dispersion measurements on steroids and triterpenes, Professor Djerassi of Detroit requested specimens of friedelan-x-one and friedelan-y-one. The rotatory dispersion curves are reproduced in fig.162. Interpretation of these results involves comparison of the curves with those of suitable reference compounds (steroids or, if available, triterpene model compounds). Professor Djerassi writes, that as regards positions in rings B, C and D there is some uncertainty in the interpretations because of interaction with the axial methyl groups of which there are several more than in the steroid models. For $C_{(21)}$ a suitable triterpene model is available, namely methyl machaerate (methyl-21-oxo-oleanate); its rotatory dispersion curve is negative as is also the Δ(CO) value of the oxo group at $C_{(21)}$ in the olean-12-ene series (see table p.109). The rotatory dispersion curve of friedelan-x-one is positive as

ROTATORY DISPERSION CURVES.

(Private communication from Dr. Djerassi).

Fig. 1 Friedelan-x-one

Fig. 2 Friedelan-y-one



is also the Δ(CO) value for the x-oxo group in the friedelane series. Thus the rotatory dispersion curves are complementary to the molecular rotation results.

The evidence indicates that the x-oxo group is located at either $C_{(21)}$ or $C_{(22)}$, probably the latter, though $C_{(15)}$ cannot be definitely eliminated. It is hoped to obtain positive evidence for the location of this group later.

MOLECULAR ROTATION CONTRIBUTIONS OF OXO GROUPS IN RINGS D AND E IN THE OLEANENE SERIES.

	$[M]_D$ with oxo group	$[M]_D$ without oxo group	Δ(CO)
16 Oxo-Group			
Olean-12-en-3:16-dione	+226[1]	+454[2]	-228
3-Acetoxy-methyl olean-12-en-16-on-28-oate	-53[3]	+358[4]	-411
Methyl olean-12-en-3:16-dion-28-oate	+10[3]	+468[5]*	-358
21-Oxo-Group			
Methyl olean-12-en-3:21-dion-28-oate	+208[6]	+417[2]	-209
22-Oxo-Group			
Methyl olean-12-en-3:22-dion-28-oate	+193[8]	+417[2]	-224
28-norOlean-12-en-3:22-dione .	+208[8]	+454**	-246
x-Oxo-Group			
Olean-12-en-x-one	+242[7]	+394[7]	-152

* Oleanonic acid[5]

** Olean-12-en-3-one[2]

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6. Djerassi, et.al., J. Amer. Chem. Soc., 1955, 77, 1200.

7. Present work.

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Location of the y-Oxo Group.

If the x-oxo group is located at $C_{(21)}$ or $C_{(22)}$ then the y-oxo group cannot be in ring E and, on the basis of its molecular rotation contribution (see p.97), can only be in ring C. The rotatory dispersion curve for friedelan-y-one is negative as is the Δ(CO) value for the y-oxo group (see discussion p.107).

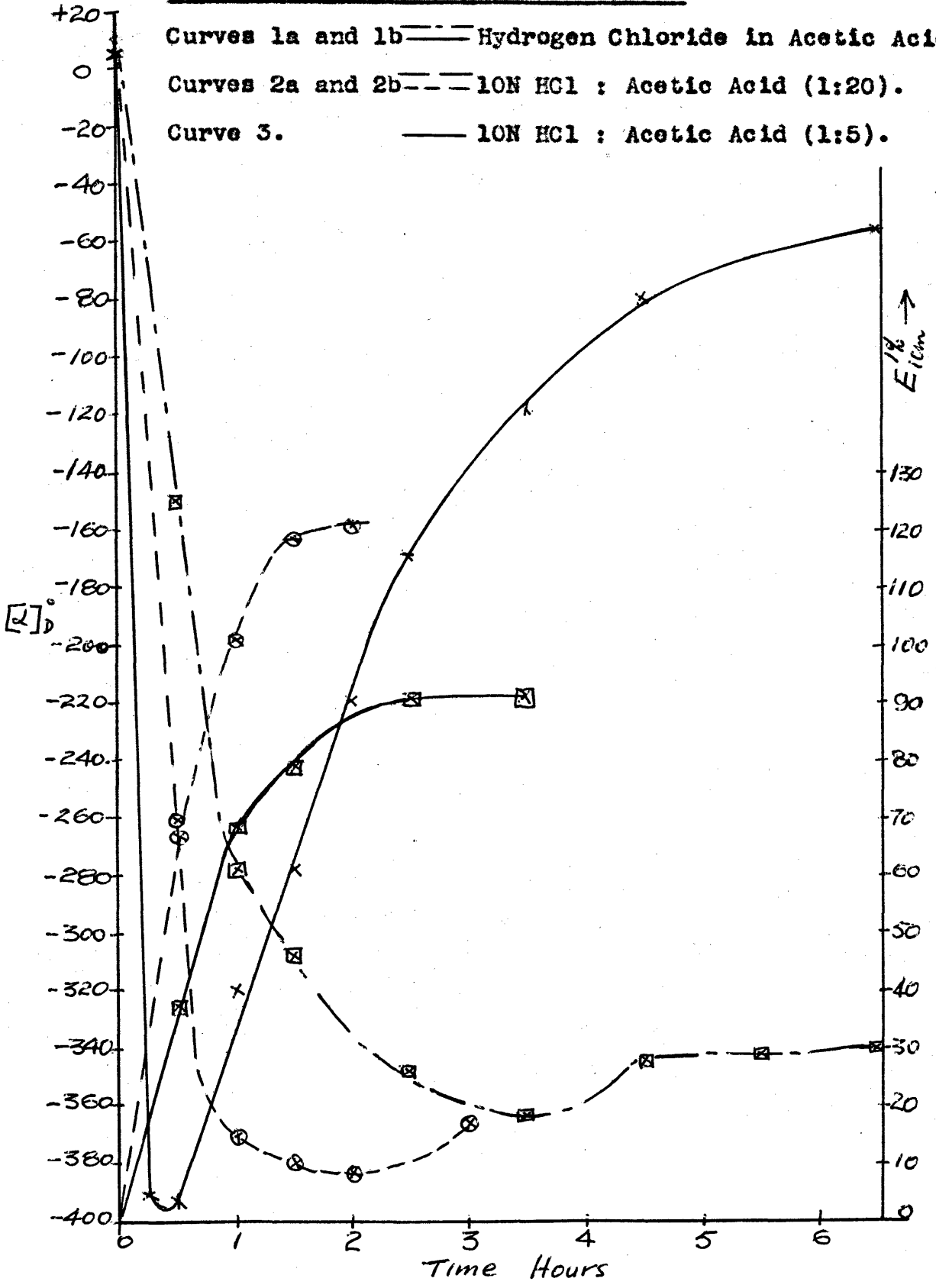
Initially the same approach was used for the location of the y-oxo group as was used in the location of the x-oxo group. Friedel-3-en-y-one was prepared by the action of phosphorus oxychloride on 3β-hydroxyfriedelan-y-one, and a kinetic study was made of its rearrangement in acid conditions. The rearrangement was followed polarimetrically and by ultraviolet absorption measurements. When friedel-3-en-y-one was treated with hydrogen chloride in boiling glacial acetic acid (curves 1a and 1b), the specific rotation changed from $+5^{\circ}$ to -363° in 3½ hours and then rose to a constant value of -340° during a further three hours. Absorption in the ultraviolet was detected (a broad band at 232-233 mu (hexane)) and the $E^{1\%}_{1cm}$ rose to a maximum of 102 after 4½ hours. The velocity of the rearrangement of friedel-3-en-y-one in a boiling mixture of 10N hydrochloric acid-acetic acid (ratio 1:20) was even greater (curves 2a and 2b). After two hours the specific rotation fell to -383° and the $E^{1\%}_{1cm}$ was 121. More drastic changes occurred when a mixture of

ISOMERISATION OF FRIEDEL-3-EN-y-ONE.

Curves 1a and 1b ——— Hydrogen Chloride in Acetic Acid.

Curves 2a and 2b – – – 10N HCl : Acetic Acid (1:20).

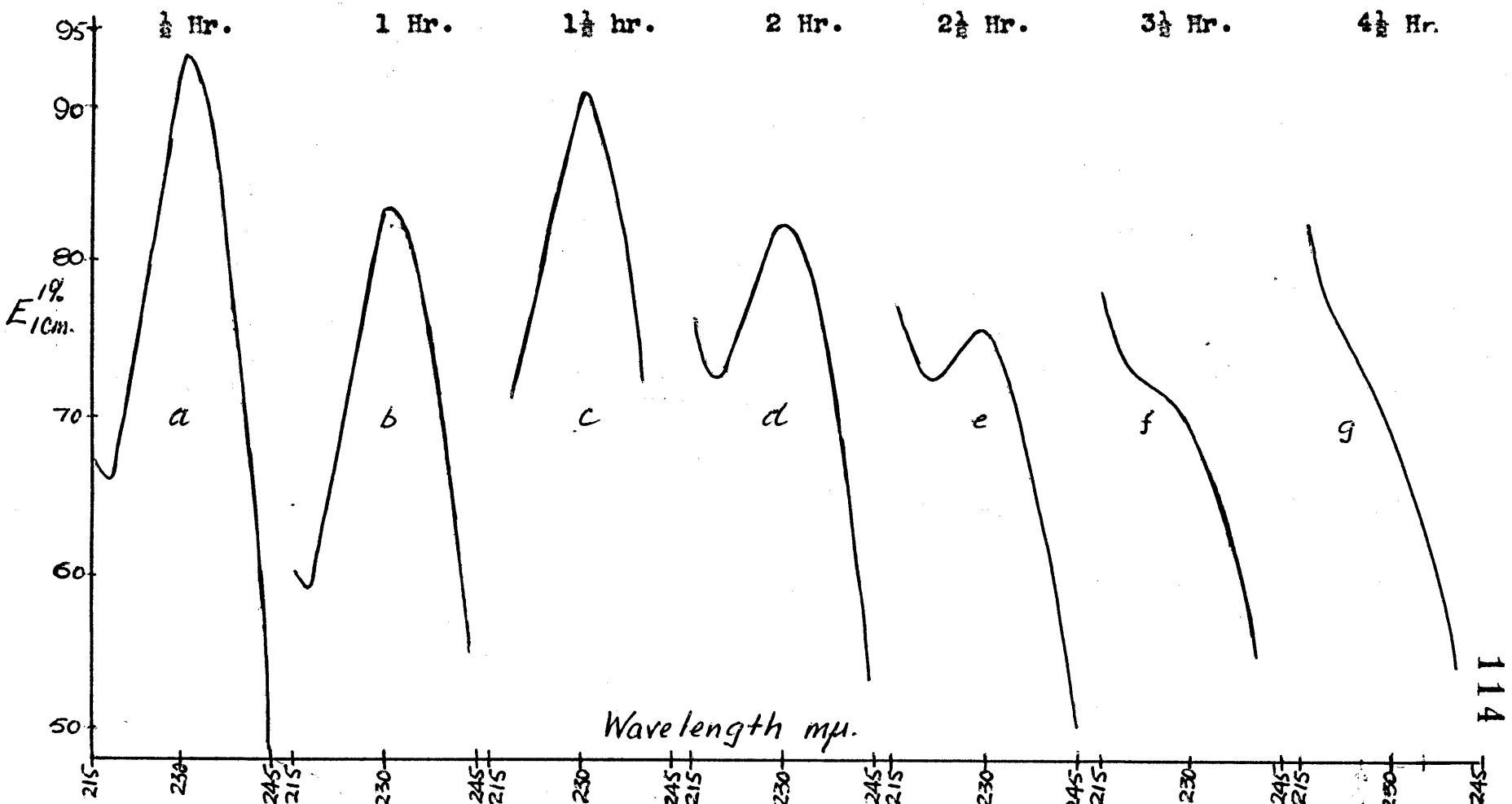
Curve 3. —— 10N HCl : Acetic Acid (1:5).



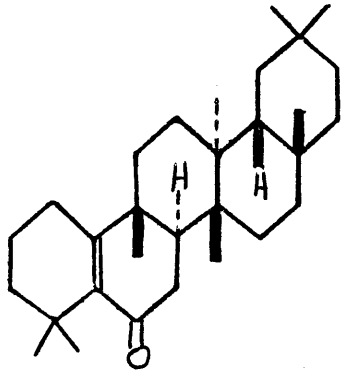
10N hydrochloric acid-acetic acid (1:5) was used (curve 3). The specific rotation fell to -392° in half an hour whilst the absorption peak at 232-233 mu. gradually disappeared as the time of treatment increased. (curves 4a to 4g). The ultraviolet absorption spectra (λ max. 232-233 mu. (hexane), λ max. 238 mu. (alcohol)) indicate that an αβ-unsaturated ketone of the type $>C=\underset{H}{C}-\underset{|}{C}=O$ is formed during the rearrangement and is converted into a product having no conjugation. From the intensity of its absorption it is apparent that about 30% of the αβ-unsaturated ketone was the maximum amount that was ever present in the isomerisation mixture. An attempt was made to prepare this compound using the optimum conditions determined in the kinetic study. Accordingly, friedel-3-en-γ-one was treated with 10N hydrochloric acid-acetic acid (1:20) for two hours. The infrared spectrum of the isomerisation product exhibited absorption (a strong band at 1693 cm^{-1} with flank absorption on the lower frequency side) indicative of an isolated ketone group and a smaller amount of an αβ-unsaturated ketone. The intensity of the ultraviolet absorption ($E^{1\%}_{1cm}$ 98) suggested that the product contained about 30% of an αβ-unsaturated ketone. This mixture proved to be inseparable. Although the αβ-unsaturated ketone could not be obtained pure, its formation (deduced from the ultraviolet spectrum) limits the number of possible positions of the γ-oxo group.

Curves 4a to 4g.

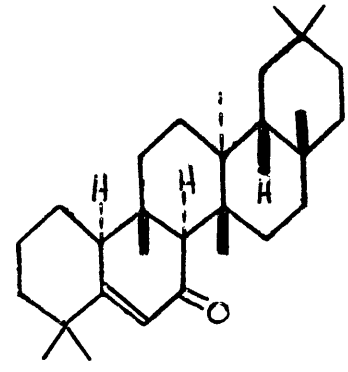
Ultraviolet Absorption Spectra of Various Stages of Isomerisation of Friedel-3-en-y-one with 10N HCl : Acetic Acid (1:5).



Assuming that the αβ-unsaturated ketone is formed as the result of the friedelene oleanene rearrangement taking its normal course,* then its formation excludes $C_{(15)}$, $C_{(19)}$, $C_{(21)}$, and $C_{(22)}$ as possible positions of the y-oxo group. Ring B can also be eliminated as a possible location of the y-oxo group. Thus if the y-oxo group were at $C_{(6)}$ or $C_{(7)}$ one would expect a much higher yield of an αβ-unsaturated ketone (I) or (II), since alnus-5(10)-ene can be formed in high yield (ca. 75%) by the rearrangement of friedel-3-ene (see curve p. 77). In any case $C_{(6)}$ would be eliminated since the αβ-unsaturated ketone (I) possesses a tetrasubstituted double bond.



(I)

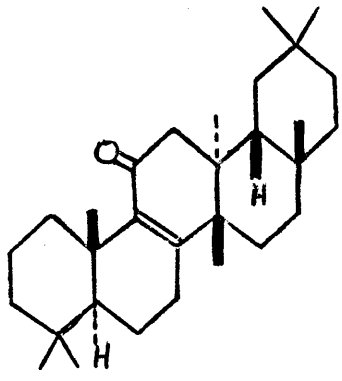


(II)

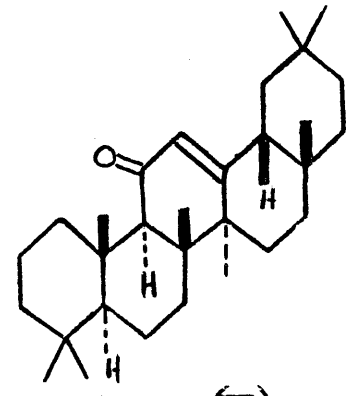
If the y-oxo group were at $C_{(11)}$ the expected product (III) would have a tetrasubstituted double bond. However examples

* This assumption may not be valid; other rearrangements may well be involved.

are known where the αβ-unsaturated ketone is formed by an indirect route (see p. 62) and should this happen the product (IV), possessing a trisubstituted double bond, could be formed. Thus $C_{(11)}$ cannot be eliminated on the evidence available. The location of the γ-oxo group at $C_{(16)}$

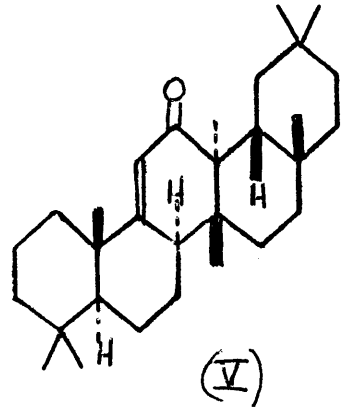


(III)



(IV)

appears unlikely since the molecular rotation contribution of the γ-oxo group is not compatible with its location in ring D. If the γ-oxo group were at $C_{(12)}$ then the rearrangement could presumably produce the αβ-unsaturated ketone (V). This possesses a trisubstituted double bond and hence the location of the γ-oxo group at $C_{(12)}$ is not impossible.



(V)

The evidence described is compatible with the view that the γ-oxo group is probably in ring C.

An interesting transformation occurs when friedel-3-en-γ-one is treated with a boiling mixture of 10N hydrochloric acid-acetic acid (1:5) for fourteen hours. The product, $[\alpha]_D$ +31°, obtained after repeated recrystallisation of the isomerisation mixture, exhibited no absorption in its infrared spectrum characteristic of either an oxo group or a hydroxyl group. A negative Beilstein test indicated the absence of chlorine and a negative test with tetranitromethane was indicative of no unsaturation. This was confirmed by the absence of end absorption in the ultraviolet spectrum. The elementary analysis of the compound showed that it was isomeric with friedel-3-en-γ-one. Thus it would appear that an unexpected cyclisation has occurred in the conditions used. Unfortunately, this conversion does not assist in the location of the γ-oxo group.

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EXPERIMENTAL.

Melting points are uncorrected and were determined on an electrically heated copper block. Since the melting points of many of the compounds described were dependent on the rate of heating, the capillary tube was always placed in the apparatus at about 30° below the melting point. All specific rotations were measured in chloroform solution and, unless otherwise specified, in a 1 dm. polarimeter tube. Ultraviolet absorption measurements were made with either the Carey or the Beckman D.U. spectrophotometer. The infrared spectra were determined with a double beam instrument and because of the low solubility of the compounds in organic solvents, nujol mulls were used. Alumina for chromatography had activity II, and the light petroleum had b.p. 40-60°.

Isolation of the Triterpene Mixture from Siphonodon australe.- The air-dried, finely-milled bark (23 kg.) was extracted by percolation with chloroform. The extract after removal of the chloroform was dissolved in alcohol (5 l.) and on standing the solution deposited amorphous material (ca. 110 g.). This was dissolved in benzene and the solution filtered through a column of alumina (600 g.). The filtrate, which contained black rubber-like material (10 g.) was discarded and the column was eluted with acetone yielding a crystalline solid (21 g.) which was recrystallized from benzene. The column was extruded and the alumina extracted repeatedly with boiling acetic acid to yield an amorphous acidic solid (28 g.).

The original alcoholic filtrate on concentration yielded crystalline material which was recrystallised from alcohol. Removal of alcohol from the concentrated filtrate left a resinous mass (ca. 450 g.) which was dissolved in benzene. This solution was extracted with 2N.NaOH and acidification of the aqueous alkaline extract yielded resinous acidic material (226 g.).

The benzene solution was concentrated to small volume and ethyl acetate was added. White crystalline material (12.5 g.) was deposited from the solution. The solvent was then removed by steam distillation, the residue dissolved in benzene (2 l.) and the solution was chromatographed on a

column of alumina (2.5 kg.) to give the following fractions:

Fraction	Solvent	Volume of solvent	Yield of eluate	Remarks
1.	Benzene	1.5 l.	27.1 g.	Pale yellow viscous liquid
2.	"	1.5 l.	21.9 g.	Yellow solid
3.	"	1.5 l.	5.6 g.	Crystalline solid
4.	"	5 l.	7.6 g.	Yellow solid
5.	5% Acetone in benzene	2 l.	9.2 g.	Dark yellow solid
6.	"	2 l.	8.2 g.	Dark yellow solid
7.	"	5 l.	8.3 g.	Dark yellow solid
8.	10% Acetone in benzene	4 l.	14.5 g.	Brown solid
9.	"	2 l.	9.6 g.	Brown solid
10.	"	4 l.	21.6 g.	Brown solid
11.	"	8 l.	18.9 g.	Brown solid
12.	Acetone	4 l.	20.3 g.	Dark brown resin

Fractions 2 to 5 were treated with light petroleum and yielded white crystalline material. Fractions 6 to 11 were treated with ethyl acetate and yielded white crystalline material. Total yield of crystalline material from chromatogram was 31.5 g.

Isolation of Paraffin Hydrocarbon and Diterpene Mixture:- Fraction 1 and the mother liquors from the treatment of fractions 2 and 3 of the previous chromatogram were

combined and chromatographed on alumina (1200 g.) to give the following fractions:-

Fraction	Solvent	Volume of eluate	Amount eluted	$[\alpha]_D$	n_D^{20}
1.	Petroleum ether	1.5 l.	1.13 g.	-	-
2.	" "	1.5 l.	1.78 g.	+70°	1.5143
3.	" "	1.5 l.	3.54 g.	+74	1.5137
4.	" "	1.5 l.	2.44 g.	+75	1.5136
5.	" "	3 l.	2.94 g.	+71	1.5133
6.	" "	9 l.	3.92 g.	+71	1.5150
7.	10% benzene in petroleum	2 l.	3.67 g.	+65	1.5152
8.	"	7.5 l.	3.23 g.	-	-
9.	20% benzene in petroleum	9 l.	2.75 g.	-	-
10.	Benzene	8 l.	4.71 g.	-	-
11.	10% acetone in benzene	3.5 l.	12.62 g.	-	-
12.	"	5 l.	5.07 g.	-	-
13.	Acetone	5 l.	-	-	-

Paraffin Hydrocarbon.- Fraction 1 was semisolid and had infrared absorption typical of a paraffin hydrocarbon and after recrystallisation from ethyl acetate yielded plates m.p. 62-63° (Found: C, 85.3; H, 14.5. $C_{30}H_{62}$ requires C, 85.2; H, 14.8%). The mother liquors contained a hydrocarbon which was recrystallised to constant melting point, m.p.55-57

(Found: C, 85.1; H, 14.5%).

Diterpenes.- The gums (fractions 2 to 7) could not be crystallised and the refractive indices indicated that there were at least two compounds in these fractions. The infrared spectra of the diterpene fractions indicated that they were ketonic and that fractions 2 to 6 were identical and fraction 7 differed negligibly from them. Fractions 8 and 9 had considerably different spectra from fractions 2 to 6 and fraction 10 was very different. Fraction 4 was distilled under high vacuum (10^{-3}mm.) for analysis (Found: C, 82.1; H, 11.6; $C_{20}H_{36}O$ requires C, 82.1; H, 12.4%). Perbenzoic acid titration indicated the absence of a double bond (0.1 atoms oxygen absorbed in 4 days) but tetranitromethane gave a strong positive test indicating unsaturation. The carbonyl group in the diterpenoid gum was unreactive to both 2:4-dinitrophenylhydrazine and semicarbazide hydrochloride.

Chromatography of the Triterpene Mixture.- All the triterpene fractions from the extraction were combined (140 g.), dissolved in benzene (about 3 l.) and chromatographed on alumina (4.11 kg. in a column 233 x 5 cm.) to give the following fractions:

Fraction	Solvent	Volume	Amount eluted	$[\alpha]_D$
1.	Benzene	6 l.	0.92 g.	-
2.	"	1 l.	2.07 g.	+55°

Fraction	Solvent	Volume	Amount eluted	$[\alpha]_D$
3.	Benzene	0.5 l.	2.14 g.	+97°
4.	"	0.5 l.	2.24 g.	+105
5.	"	0.5 l.	2.28 g.	+110
6.	"	0.5 l.	2.18 g.	+112
7.	"	0.5 l.	1.92 g.	+113
8.	"	0.5 l.	1.60 g.	+113
9.	"	0.5 l.	1.40 g.	+109
10.	"	0.5 l.	1.24 g.	+111
11.	"	0.5 l.	1.13 g.	+111
12.	"	0.5 l.	0.96 g.	+112
13.	"	1 l.	1.50 g.	+112
14.	"	2 l.	2.08 g.	+111
15.	"	2.5 l.	1.58 g.	+109
16.	"	3.5 l.	1.47 g.	+ 74
17.	"	5 l.	1.78 g.	+ 14
18.	2% chloroform in benzene	4 l.	1.55 g.	+ 31
19.	" " " "	3 l.	1.78 g.	+ 47
20.	" " " "	2.5 l.	1.50 g.	+ 57
21.	" " " "	2 l.	1.19 g.	+ 61
22.	5% " " "	3 l.	1.72 g.	+ 67
23.	" " " "	3 l.	1.46 g.	+ 71
24.	" " " "	3.5 l.	1.77 g.	+ 70
25.	" " " "	3.5 l.	1.57 g.	+ 67
26.	" " " "	3 l.	0.98 g.	+ 67

Fraction	Solvent	Volume	Amount eluted	$[\alpha]_D$
27.	5% chloroform in benzene	4.5 l.	1.32 g.	+69°
28.	" " " "	4.5 l.	1.12 g.	+67
29.	10% " " "	4.5 l.	1.20 g.	+51
30.	" " " "	5 l.	1.80 g.	+41
31.	" " " "	5 l.	1.34 g.	+36
32.	20% " " "	7.5 l.	1.68 g.	+28
33.	" " " "	7 l.	1.52 g.	+31
34.	50% " " "	6 l.	1.83 g.	+32
35.	" " " "	5.5 l.	1.72 g.	+42
36.	" " " "	1 l.	1.83 g.	+ 1
37.	" " " "	0.5 l.	1.66 g.	-11
38.	" " " "	0.5 l.	1.87 g.	-20
39.	" " " "	0.5 l.	2.22 g.	-27
40.	" " " "	0.5 l.	2.49 g.	-38
41.	" " " "	0.5 l.	3.90 g.	-50
42.	Chloroform	0.5 l.	4.64 g.	-42
43.	"	0.5 l.	5.10 g.	-29
44.	"	0.5 l.	4.24 g.	- 9
45.	"	0.5 l.	3.72 g.	+12
46.	"	0.5 l.	3.35 g.	+29
47.	"	0.5 l.	4.30 g.	+42
48.	"	0.5 l.	4.66 g.	+34
49.	"	0.5 l.	4.11 g.	+28
50.	"	0.5 l.	3.18 g.	+25
51.	"	0.5 l.	3.11 g.	+16

Fraction	Solvent	Volume	Amount eluted	$[\alpha]_D$
52.	Chloroform	0.5 l.	2.59 g.	+21°
53.	"	0.5 l.	1.89 g.	+19
54.	"	1.5 l.	1.62 g.	-
55.	"	5 l.	1.34 g.	-
56.	"	9 l.	0.96 g.	-
57.	"	3 l.	2.56 g.	- 8
58.	"	20 l.	1.45 g.	-
59.	10% methanol in chloroform	3.5 l.	3.01 g.	-

Friedelin.- Fractions 2 to 4 were combined and chromatographed on alumina (250 g.) to yield the following fractions:

Fraction	Solvent	Volume	Amount eluted	$[\alpha]_D$
1.	Petrol:benzene::4:1	3.5 l.	0.50 g.	-14°
2.	" " "	1 l.	0.42 g.	- 2
3.	" " "	1 l.	0.47 g.	+94
4.	" " "	1 l.	0.50 g.	+105
5.	" " "	1 l.	0.41 g.	+107
6.	" " "	1 l.	0.41 g.	-
7.	Chloroform	4 l.	2.78 g.	-

Fractions 1 and 2 were combined and recrystallised from alcohol-benzene to yield friedelin, needles, m.p. 261-264°, $[\alpha]_D$ -21° (c 2.5) (Found: C,84.3; H,11.7. Calc. for $C_{30}H_{50}O$: C,84.4; H, 11.8%). The product was shown to be identical with

an authentic specimen by comparison of infrared spectra and a mixed melting point determination. Fractions 4 to 7 were combined and recrystallised to yield friedelane-3:x-dione which was added to the next fractions.

Friedelane-3:x-dione.- Fractions 5 to 14 inclusive were combined and recrystallised from ethanol to give friedelane-3:x-dione, needles m.p. 248-250°, $[\alpha]_D$ +115° (c 2.4) (Found: C, 82.1; H, 10.7. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%). An additional amount was obtained from fractions 2 to 4 and 16 to 17 by chromatography (total, 22.5 g.). The monosemicarbazone was prepared by heating friedelane-3:x-dione (0.25 g.) with pyridine (5 ml.) and semicarbazide hydrochloride (0.25 g. dissolved in a few drops of water) on a steam bath for 15 minutes. The product was filtered off from the cooled reaction mixture and recrystallised from alcohol to give prisms m.p. 247° (decomp.) (Found: C, 74.2; H, 10.5; N, 8.4; $C_{31}H_{51}O_2N_3$, $\frac{1}{4}C_2H_5OH$ requires C, 74.4; H, 10.4; N, 8.3%).

Friedelane-3:y-dione.- Fractions 15 to 21 were fractionally crystallised to give friedelane-3:y-dione (1.6 g.) in the more insoluble fractions and friedelane-3:x-dione in the soluble fractions. Friedelane-3:y-dione formed laths from alcohol-benzene, m.p. 305-309°, $[\alpha]_D$ -62°, (c 2.3) (Found: C, 81.5; H, 10.9. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%). The Monosemicarbazone was prepared by heating friedelane-3:y-dione

(0.25 g.) with pyridine (5 ml.) and semicarbazide hydrochloride (0.25 g.) on a steam bath for 15 minutes and working the reaction mixture up in the usual manner. Recrystallisation from alcohol-chloroform gave plates m.p. 331° (decomp.) (Found: C, 74.8; H, 10.4; N, 8.6. $C_{31}H_{51}O_2N_3$ requires C, 74.8; H, 10.3; N, 8.4%).

Friedelane-3:x:y-trione.- Fractions 22 to 28 were combined and recrystallised from alcohol to yield friedelane-3:x:y-trione, needles or plates, m.p. 300-303°, $[\alpha]_D$ +72° (c 2.4) (Found: C, 79.4; H, 10.2. $C_{30}H_{46}O_3$ requires C, 79.2; H, 10.2%). An additional amount was obtained from fractions 18 to 21 and 29 to 35 by chromatography (total, 13.8 g.). The monosemicarbazone was prepared in the usual manner and recrystallised from alcohol to give needles m.p. 320° (decomp) (Found: C, 72.8; H, 9.5; N, 8.3. $C_{31}H_{49}O_3N_3$ requires C, 72.8; H, 9.65; N, 8.2%).

Hydroxy-ketones.- Subsequent fractions from the chromatogram were recrystallised by Dr. Gascoigne to give the following compounds:

x[ax]-Hydroxyfriedelan-3-one from fractions 30 to 35.

x[eq]-Hydroxyfriedelan-3-one from fractions 36 to 39.

y-Hydroxyfriedelan-3-one from another batch of the triterpene mixture.

x[eq]-Hydroxyfriedelane-3:y-dione from fractions 40 to 44.

y-Hydroxyfriedelane-3:x-dione from fractions 46 to 53.

Huang-Minlon Reduction of Friedelane-3:x-dione.- Friedelane-3:x-dione (5g.) was refluxed with hydrazine hydrate (7 ml of 87.5%) pulverised potassium hydroxide (4.5 g.) and diethylene glycol (32 ml) for 1½ hours. Excess reagent was removed and the temperature of the reaction mixture was raised to 190-200° for a further five hours. The mixture was then raised to the boiling point of diethylene glycol and refluxed for ten minutes.

After cooling, the mixture was acidified with hydrochloric acid (50 ml of 2.5N) and extracted with chloroform. The extract was washed with water, dried over sodium sulphate and the solvent removed. The reaction product (4.8 g.) was extracted with petroleum ether to leave a very insoluble, high-melting, nitrogenous substance which could be an azine. The extracted material (3.5 g.) was dissolved in petrol-benzene, 4 to 1 and filtered through a column of alumina (200 g.). Elution with petroleum ether-benzene 1:1 yielded friedelan-x-one which crystallised from alcohol as needles m.p. 241-243°, $[\alpha]_D$ +152° (6.2.2) (Found: C, 84.8; H, 12.1; $C_{30}H_{50}O$ requires C, 84.4; H, 11.8%). $E^{1\%}_{1cm}$ = 0.98 (dioxan) λmax. = 290 mμ. A 2:4-dinitrophenylhydrazone could not be formed under the usual conditions.

Clemmensen Reduction of Friedelane-3:x-dione.- Amalgamated zinc was prepared by covering zinc needles (80 g.) with a solution of $HgCl_2$ (80 g.) in 50% ethanol (575 ml.) for 15 mins.

The solution was poured off and the amalgamated zinc washed twice with distilled water. The majority of the remaining water was removed in vacuo.

The amalgamated zinc was added to a hot solution of friedelane-3:x-dione (2 g.) in dioxan (500 ml.) and 10N hydrochloric acid (290 ml.) and the mixture was heated on a steam bath for five hours. It was then cooled and the precipitate filtered off. Extraction of the filtrate yielded a small quantity (0.08 g.) of dark brown gum which was discarded. The reaction product was washed several times with water to remove any mineral acid and dried to yield a white solid (1.87 g.). This was dissolved in 3 to 1 petrol-benzene (2 l.) and filtered through a column of alumina (67 cm x 2.2 cm, 60 g.) to yield the following fractions:

Fraction	Solvent	Volume eluent	Wt. eluate, g.	$[\alpha]_D$
1.	Petrol-benzene;3 to 1	1.5 l.	0.20	$+22^\circ$
2.	" " "	2 l.	0.57	+137
3.	" " "	1 l.	0.38	+154
4.	" " "	1 l.	0.16	+149
5.	" " "	6 l.	0.13	+106
6.	Benzene	3.5 l.	0.07	-
7.	Alcohol	-	0.28	-

The fractions were purified further by fractional crystallisation. Fraction 1 when recrystallised from benzene-alcohol yielded friedelane, plates, m.p. $243\text{-}5^\circ$, $[\alpha]_D$ $+22^\circ$

(c 0.67 ; 2dm. tube) (Found: C, 87.05; H, 12.5. Calc. for $C_{30}H_{52}$: C, 87.3; H, 12.7%).

The melting point of an authentic sample of friedelane was not depressed on admixture with this material and their infrared spectra were identical. Fractions 3 and 4 were combined and recrystallised from alcohol to yield friedelan-x-one, needles, m.p. 242-245°, $[\alpha]_D$ +153° (c 2.1).

Sodium Borohydride Reduction of Friedelane-3:x:dione.- Friedelane-3:x-dione (2 g.) was dissolved in pyridine (100 ml.) and added to sodium borohydride (0.55 g.) dissolved in methanol (50 ml.) to which was added N-sodium hydroxide solution (0.25 ml.). The mixture was allowed to stand at room temperature for 24 hours after which it was acidified with 5N-hydrochloric acid (400 ml.). The mixture was extracted with chloroform and the extract washed with 10N-hydrochloric acid followed by water, then sodium bicarbonate solution and finally water. After removal of the solvent the product was dissolved in benzene (550 ml.) and chromatographed on alumina (100 g.) to give the following fractions:

Fraction	Solvent	Volume	Wt. eluted, g.	$[\alpha]_D$
1.	Benzene	1 l.	0.33	+109°
2.	"	1 l.	0.26	+126
3.	"	1 l.	0.32	+155
4.	"	1.5 l.	0.23	+150
5.	"	2 l.	0.21	+147
6.	"	3.5 l.	0.19	+147

Fraction	Solvent	Volume	Wt. eluted, g.	$[\alpha]_D$
7.	Benzene	2 l.	0.34	+142
8.	"	2.5 l.	0.12	+137

Fraction 1 was starting material.

Fraction 3 was recrystallised from ethanol to give 3β-hydroxyfriedelan-x-one, prisms, m.p. 288-291°, $[\alpha]_D$ +159° (c 1.0) (Found: C, 81.5; H, 11.1. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The acetate was prepared by heating the compound (66 mg.) on a steam bath for 3 hours with acetic anhydride (6 ml.) and pyridine (4 ml.). The reaction mixture was poured into water, the product filtered off and recrystallised from ethanol to give plates, m.p. 271-273°, $[\alpha]_D$ +158° (c 0.5; 2 dm. tube) (Found: C, 79.35; H, 10.8. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

Fractions 4 to 6 consisted of mixtures which could not be seperated by fractional crystallisation. Fraction 7 was recrystallised from ethanol to yield 3α-hydroxyfriedelan-x-one, plates, m.p. 307-311°, $[\alpha]_D$ +145° (c 1.0) (Found: C, 81.3; H, 11.2%). The acetate was prepared in the usual way and formed plates from alcohol, m.p. 305-307°, $[\alpha]_D$ +114° (c 0.7; 2 dm. tube) (Found: C, 79.3; H, 10.7%).

Attempted separation of 3α- and 3β-Hydroxyfriedelan-x-ones through their acetates.- The intermediate fractions and material recovered from mother liquors from the sodium borohydride reduction of friedelane-3:x-dione were combined and acetylated in the usual manner. The mixture of acetates was triturated

several times with ether to give two fractions:-

Ether soluble acetates which after recrystallisation several times from ethanol gave a product with $[\alpha]_D$ +142° (c 1.1).

Ether insoluble acetates which after recrystallisation several times from ethanol gave a product with $[\alpha]_D$ +128° (c 1.0).

This method clearly offers only a partial separation.

Chromatography of the Acetates on alumina did not afford any separation.

Wolff-Kishner Reduction of 3β-Hydroxyfriedelan-x-one.- A mixture of 3β-hydroxyfriedelan-x-one (1.0 g.) anhydrous hydrazine (6.5 ml.) and a solution of sodium (2.5 g.) in methanol (25 ml.) was heated at 200°C for 16 hours in a bomb. The product (0.87 g.) was extracted with chloroform after the mixture had been acidified and was dissolved in 3:1 petroleum: benzene (1 l.) and chromatographed on alumina (60 g.) as follows:-

Fraction	Solvent	Volume	Amount eluted, g.	$[\alpha]_D$
1.	3:1 petroleum:benzene	2 l.	0.20	-
2.	" " "	3 l.	0.19	+20°
3.	" " "	1.5 l.	0.16	+20
4.	" " "	4.5 l.	0.17	+28
5.	Benzene	8 l.	0.16	+52

Fraction 1 was dissolved in petroleum and filtered through alumina (20 g.) to give friedelane, plates from chloroform, m.p. 244-246°, $[\alpha]_D$ +22° (c 1.2). The melting point was not

depressed on admixture with an authentic specimen. Fractions 2 and 3 were combined and recrystallised from alcohol to give epifriedelanol, plates, m.p. 281-283°, $[\alpha]_D$ +21° (c 1.1) (Found: C,84.2; H, 12.1. Calc. for $C_{30}H_{50}O$: C, 84.0; H, 12.2%). Its infrared spectrum was identical with that of an authentic specimen. The acetate was formed in the usual manner and was recrystallised from alcohol-benzene to give plates, m.p. 290-293°, $[\alpha]_D$ +33° (c 1.1) (Found: C, 81.3; H, 11.5. Calc. for $C_{32}H_{54}O_2$: C, 81.6; H, 11.6%).

Ethylenedioxy Derivative of Friedelane-3:x:y-trione.- A solution of friedelane-3:x:y-trione (2.95 g.) in 2-methyl-2-ethyl-1:3-dioxolan (60 ml.) containing toluene-p-sulphonic acid (45 mg.) was refluxed for 7½ hours. The product was filtered off from the cooled reaction mixture and recrystallised from benzene to yield the ethylene ketal, prisms, m.p. 342-5°, $[\alpha]_D$ +76° (c 1.2) (Found: C, 77.3; H, 10.3. $C_{32}H_{50}O_4$ requires C, 77.1; H, 10.1%). The infrared spectrum had strong peaks at 1092, 1077, and 1067 $cm.^{-1}$ (Nujol mull).

Wolff-Kishner Reduction of the Ethylenedioxy Derivative of Friedelane-3:x:y-trione.- The derivative (1.28 g.) was mixed with anhydrous hydrazine (8.5 ml.) and a solution of sodium (3.2 g.) in methanol (51 ml.) and left overnight in a bomb at 200°. The reaction mixture was poured into water, acidified, and extracted with chloroform. The chloroform solution was washed free of acid with water and evaporated

dry to yield the crude product (1.12 g.).

Removal of the Ethylenedioxy group.- The crude product from the Wolff-Kishner reduction was refluxed with acetone (400 ml.) and toluene-p-sulphonic acid (75 mg.) for 14 hours. The acetone was distilled off until about 30 ml. of solution remained. The cooled residue was poured into water, filtered, and the product washed with water several times. The crude product (1.12 g.) was dissolved in 2:1 petroleum:benzene (1 l.) and chromatographed on alumina (112 g.) to yield the following fractions:-

Fraction	Solvent	Volume	Wt. eluted g.	$[\alpha]_D$
1.	2:1 petroleum:benzene	2 l.	0.06	-
2.	" " "	5 l.	0.08	-25°
	1:1 " "	3 l.		
	Benzene	3.5 l.		
	10% chloroform in benzene	3 l.		
3.	20% " " "	1 l.	0.09	-16
4.	" " " "	1 l.	0.15	-14
5.	" " " "	1 l.	0.13	-15
6.	" " " "	1 l.	0.08	-14
7.	" " " "	5.5 l.	0.07	
8.	50% " " "	7.5 l.	0.22	
	20% " " methanol	3.5 l.		

Fraction 1 was recrystallised from chloroform to yield

plates m.p. 246-8°, $[\alpha]_D$ +21 (c 0.6, 2 dm. tube). This is identical with friedelane.

Fraction 2 was recrystallised from benzene-alcohol to yield friedelin as needles m.p. 258-261°, $[\alpha]_D$ -25° (c 0.8) (Found: C, 84.3; H, 11.65. Calc. for $C_{30}H_{50}O$: C, 84.4; H, 11.8%). Its infrared spectrum is identical with that of an authentic specimen of friedelin. The melting point was undepressed on admixture with an authentic specimen.

Fractions 3, 4 and 5 had identical infrared spectra which corresponded with that of y-hydroxyfriedelan-3-one which was isolated from the original triterpene mixture. Recrystallisation from alcohol yielded laths m.p. 301-305°, $[\alpha]_D$ -20° (c 0.7, 2 dm. tube). (Found: C, 81.4; H, 11.3. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The melting point was undepressed on admixture with a specimen of the material isolated from the original triterpene mixture.

Chromic Acid - Pyridine Oxidation of y-hydroxyfriedelan-3-one.- y-hydroxyfriedelan-3-one (124 mg.) was dissolved in pyridine (10 ml.) and added to a solution of chromium trioxide (124 mg.) in pyridine (1.5 ml.) and left at room temperature overnight. The reaction mixture was diluted with benzene (20 ml.) and filtered. The precipitate was extracted twice with boiling benzene and the extracts combined with the first filtrate. This combined benzene solution was washed with water then concentrated hydrochloric acid (three times) and then with saturated sodium sulphite solution followed by water.

The reaction product was recrystallised from benzene-alcohol to yield prisms, m.p. 306-310°, $[\alpha]_D$ -60° (c 0.8). The infrared spectrum was identical with that of naturally occurring friedelane-3:y-dione.

Clemmensen Reduction of friedelane-3:x:y-trione.- Zinc needles (120 g.) were amalgamated in the same manner as before and added to a solution of friedelane-3:x;y-trione (2 g.) in dioxan (850 ml.) and 10N hydrochloric acid (435 ml.). This mixture was heated on a steam bath for six hours and then cooled. The precipitate (1.27 g.) was filtered off and washed with water. An additional amount (0.4 g.) of reaction product was obtained by concentrating the filtrate and extracting with chloroform. The product was dissolved in petroleum-benzene, 2:1 and chromatographed on alumina (250 g.) to give the following fractions:-

Fraction	Solvent	Volume	Wt. eluted, g.	$[\alpha]_D$
1.	Petroleum:benzene::3:1	3.5 l.	0.08	-
2.	" " "	5 l.	0.19	-28°
3.	" " "	5 l.	0.19	+42
4.	" " "	4 l.	0.19	+65
	" " 2:1	3 l.		
5.	" " "	2.5 l.	0.19	+64
6.	" " "	5.25 l.	0.20	+56
7.	" " 1:1	3 l.	0.18	+52
	Benzene	1 l.		
8.	"	6 l.	0.25	+68

Fraction 2 was recrystallised several times from alcohol-benzene to give friedelan-y-one, prisms, m.p. 287-290°, $[\alpha]_D$ -34° (c 1.6) (Found: C,84.7; H, 12.0 . $C_{30}H_{50}O$ requires C, 84.4; H, 11.8%).

Fractions 4 to 7 were recrystallised from alcohol-benzene to yield friedelane-x:y-dione as plates, m.p. 302-305°, $[\alpha]_D$ +103° (c 1.6).(Found: C, 81.7: H, 11.0. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%).

Fraction 8 yielded friedelane-3:x:y-trione as needles from benzene-alcohol, m.p. 299-303°, $[\alpha]_D$ +74° (c 1.5). The melting point was undepressed on admixture with an authentic sample.

Wolff-Kishner Reduction of Friedelane-3:x:y-trione.-

A mixture of friedelane-3:x:y-trione (1.64 g.), anhydrous hydrazine (10 ml.) and a solution of sodium (4 g.) dissolved in methanol (40 ml.) was heated at 200° for 18 hours in a bomb. The reaction mixture was cooled, acidified and extracted with chloroform. The product (1.5 g.) was dissolved in 2:1petroleum:benzene and chromatographed on alumina (150 g.) to give the following fractions:-

Fraction	Solvent	Volume	Amount eluted,g.	$[\alpha]_D$
1.	2:1 petroleum:benzene	350 ml.	0.13	+17°
2.	" " "	1.5 l.	0.49	+14
3.	" " "	6.5 l.	0.17	+ 2
4.	1:1 " "	1 l.	0.16	+18

Fraction	Solvent	Volume	Amount eluted, g.	$[\alpha]_D$
5.	1:1 petroleum:benzene	1 l.	0.13	+22°
6.	" " "	1.5 l.	0.11	+22
7.	" " "	2.5 l.	0.11	+19
8.	Benzene	8 l.	0.16	+22

Fractions 1 and 2 were combined, dissolved in petroleum and filtered through alumina. The filtrate contained friedelane which crystallised as plates from chloroform, m.p. 245-247°, $[\alpha]_D$ +22° (c 1.0).

Fractions 4, 5, 6 and 7 were combined and recrystallised from ethanol to give friedelan-y-ol plates, m.p. 223-226°, $[\alpha]_D$ +20 (c 1.8). The infrared spectrum was identical with a sample prepared from friedelan-y-one and the melting point was undepressed on admixture with it.

Huang-Minlon Reduction of Friedelane-3:y-dione.- Friedelane-3:y-dione (0.5 g.) was heated under reflux for 1½ hours with diethylene glycol (9 ml.), potassium hydroxide pellets (0.35 g.) and 100% hydrazine hydrate (1 ml.). The excess hydrazine hydrate was removed by distillation and the temperature was raised to 190-200° for 4 hours. The reaction mixture was worked up in the usual manner and the product (0.44 g.) was dissolved in 2:1 petroleum:benzene (0.5 l.) and chromatographed on alumina (50 g.), to yield friedelan-y-one (0.35 g.) which was recrystallised from alcohol to give prisms, m.p. 286-290°, $[\alpha]_D$ -32° (c 1.0). Its identity was confirmed by comparison of its infrared spectrumwith that of friedelan-

y-one obtained from friedelane-3:x:y-trione. Its melting point was undepressed on admixture with an authentic specimen.

Sodium Borohydride Reduction of Friedelane-3:x:y-trione.- Friedelane-3:x:y-trione (5 g.) was dissolved in pyridine (150 ml) and a solution of sodium borohydride (2.4 g.) in methanol (150 ml.) containing 2N sodium hydroxide (1 ml.) was added to it. The mixture was allowed to stand at room temperature for 24 hours after which it was poured into water and the resulting suspension extracted with chloroform. The chloroform solution was washed several times with water and then with concentrated hydrochloric acid, and finally with water. The crude reaction product (4.9 g.) was dissolved in benzene (2.5 l.) and chromatographed on alumina (500 g.) to give the following fractions:-

Fraction	Solvent	Volume	Wt. eluted, g.	$[\alpha]_D$
1.	Benzene	6 l.	-	-
	10% chloroform in benzene	4.5 l.	-	-
	20% " " "	2.5 l.	-	-
	50% " " "	3.5 l.	3.56	+81°
2.	50% " " "	0.5 l.	0.77	+48
3.	50% " " "	5.5 l.	0.28	+40
4.	20% methanol in chloroform	10 l.	0.20	-

Purification of fraction 1 was particularly difficult. Repeated crystallisation from benzene and then from alcohol yielded 3β-hydroxyfriedelan-x:y-dione, prisms, m.p. 314-318°,

$[\alpha]_D$ +107° (c 1.1) (Found: C, 78.8; H, 10.7%. $C_{30}H_{50}O_3$ requires C, 78.55; H, 11.0%). The acetate, prepared in the usual way formed plates from alcohol, m.p. 321-325° $[\alpha]_D$ +113° (c 1.1) (Found: C, 76.9; H, 10.0%. $C_{32}H_{50}O_4$ requires C, 77.1; H, 10.1%).

Fraction 2 was fractionally crystallised from benzene to give 3:x-dihydroxyfriedelan-y-one, prisms, m.p. 330-335°, $[\alpha]_D$ +24° (c 1.0) (Found: C, 79.1; H, 10.6 . $C_{30}H_{50}O_3$ requires C, 78.6; H, 11.0%). The diacetate crystallised from alcohol as needles, m.p. 324-326°, $[\alpha]_D$+1° (c 1.0). (Found: C, 75.0; H, 9.9 . $C_{34}H_{54}O_5$ requires C, 75.2; H, 10.0%). This name is assigned to this compound in view of the analytical results and since its molecular rotation differences do not fit that of 3α-hydroxyfriedelane-x:y-dione. The peak at 690 cm^{-1} in the infrared spectrum which is characteristic of the x-oxo-group is absent and in the infrared spectrum of the acetate there is only one peak due to carbonyl absorption (except the acetate peak) and this peak is at 1702 $cm.^{-1}$. The x-oxo-group shows a peak at about 1720 $cm.^{-1}$.

Wolff-Kishner Reduction of 3β-Hydroxyfriedelan-x:y-dione.- A mixture of 3β-hydroxyfriedelan-x:y-dione (0.64 g.), anhydrous hydrazine (5 ml.) and a solution of sodium (1.6 g.) in methanol (20 ml.) was heated in a bomb at 160° for 17 hours. The reaction mixture was worked up in the usual manner, dissolved in 3:1 petroleum:benzene and chromatographed on alumina (60 g.).

Fraction	Solvent	Volume	Wt. eluted, g.
1.	3:1 petroleum:benzene	0.5 l.	0.19
2.	3:1 " "	2 l.	-
	2:1 " "	1.5 l.	0.07
	1:1 " "	1.5 l.	-
	Benzene	0.75 l.	
3.	"	0.75 l.	0.07
4.	"	1 l.	0.07
5.	"	1 l.	0.07
6.	"	1 l.	0.05
7.	Alcohol	4 l.	0.10

Fraction 1 was recrystallised from chloroform to give friedelane, plates, m.p. 246-248°, $[\alpha]_D$ +21° (c 1.0). The infrared spectra of the fractions revealed that fractions 2, 3 and 4 were identical with friedelan-y-ol, fraction 5 was slightly different from fraction 2 and fraction 6 was considerably different from fraction 2 and showed some resemblance to friedelanol. Fractions 2, 3 and 4 were combined and recrystallised from alcohol to give friedelan-y-ol, plates, m.p. 224-226°, $[\alpha]_D$ +19 (c 1.0). The melting point was undepressed on admixture with friedelan-y-ol from another source.

Oxidation of Friedelan-y-ol with Chromium Trioxide-Pyridine.-- Friedelan-y-ol (1.59 g.) was dissolved in pyridine (100 ml.) and added to a solution of chromium trioxide (1.59 g.) dissolved in pyridine (30 ml.). A black precipitate formed and the mixture was allowed to stand at room temperature overnight. The reaction mixture was diluted with benzene and then filtered. The residue was boiled three times with fresh benzene and filtered. The filtrates were combined, washed with water, 10N hydrochloric acid, twice with water, then with sodium sulphite solution and finally twice with water. The benzene solution was evaporated to small volume to give friedelan-y-one. This was recrystallised twice from alcohol-benzene to give prisms, m.p. 288-290°, $[\alpha]_D$ -33° (c 1.1). The infrared spectrum was identical with that of a specimen of friedelan-y-one from another source, and the melting points of the two specimens were undepressed upon admixture.

Reduction of Friedelin with Sodium Borohydride.-- Friedelin (7 g.) was dissolved in hot pyridine (250 ml.), and the cooled solution was added to a solution of sodium borohydride (2.1 g.) in methyl alcohol (150 ml.) containing N-sodium hydroxide (1 ml.). The mixture was left for two days at room temperature and occasionally shaken. The mixture was then acidified with 5N-hydrochloric acid and the product

extracted with chloroform. The extract was washed several times with 5N-hydrochloric acid, then with water, sodium carbonate solution and finally with water. The solvent was removed and the crude product (6.9 g.) was dissolved in benzene (1 l.) and chromatographed over alumina (700 g.) to give the following fractions.

Fraction	Solvent	Volume	Amount eluted
1.	benzene	0.5 l.	1.03 g.
2.	benzene	1.0 l.	0.98 g.
3.	benzene	3.5 l.	0.27 g.
	10% chloroform in benzene	3.0 l.	0.06 g.
4.	20% " " "	5.5 l.	0.82 g.
5.	50% " " "	1.5 l.	0.48 g.
6.	" " " "	2.5 l.	1.05 g.
7.	" " " "	2.5 l.	1.11 g.
8.	" " " "	3.0 l.	0.94 g.
9.	20% methanol in chloroform	2.5 l.	0.14 g.

Fractions 1 and 2 consisted entirely of friedelin. Fractions 3 and 4 were mainly friedelin having almost identical infrared spectra and a band due to a carbonyl group. Fractions 5 to 7 had identical infrared spectra and were therefore combined and recrystallised from benzene to yield epifriedelanol, plates, m.p. 280-282°, $[\alpha]_D$ +21° (c 0.7;2 dm. tube).

The acetate was prepared in the usual way and crystallised from ethanol-benzene as plates, m.p. 290-293°, $[\alpha]_D$ +36° (c 1.1).

The infrared spectrum of fraction 8 was almost identical with that of an authentic specimen of friedelanol.

Wolff-Kishner Reduction of x[eq]-hydroxyfriedelan-3:y-dione.-- A mixture of x[eq]-hydroxyfriedelan-3:y-dione (2 g.), anhydrous hydrazine (13 ml.), and a solution of sodium (4 g.) in methyl alcohol (70 ml.) was heated in a bomb at 200° for sixteen hours. The reaction product was poured into water, acidified, and extracted three times with chloroform. After washing several times with water, the extract was dried, and the solvent removed. The crude product was dissolved in 3 to 1 light petroleum-benzene and was chromatographed on alumina (75 g.). Elution with benzene yielded friedelan-x[eq]-ol (1.7 g.), m.p. 260-262°, $[\alpha]_D$ +10° (c 1.2). This was shown to be identical with an authentic specimen (prepared by sodium and pentyl alcohol reduction of friedelan-x-one) by comparison of their infrared spectra and a mixed melting point determination.

The Relative Rates of Hydrolysis of Friedelanyl and epiFriedelanyl Acetates.-- Friedelanyl acetate (0.1128 g.) and epifriedelanyl acetate (0.1737 g.) were each refluxed

with benzene (25 ml.) and N/2 alcoholic potassium hydroxide solution (25 ml.). Samples were taken at intervals of ½ hour and one hour and the degree of hydrolysis determined. The results are as follows;-

Hydrolysis Time	% Hydrolysed	
	Friedelanyl acetate	epifriedelanyl acetate
½ hr.	54.2	29.8
1 hr.	71.0	35.2

The maximum error is calculated to be ± 1%.

Oxidation of Cerin to Friedelane-2:3-dione.-- A solution of chromium trioxide (1.5 g.) in acetic acid (50 ml. of 90%) was added to a suspension of cerin (4 g.) in carbon tetrachloride (150 ml.) and glacial acetic acid (340 ml.). The mixture was left at room temperature for sixteen hours and was occasionally shaken. The insoluble material (1.7 g., presumably cerin) was filtered off and methanol (5 ml.) was added to the filtrate which was then distilled under vacuum to small volume. The solution was poured into water and extracted with ether. The ether extract was washed three times with 2N sodium carbonate solution and finally three times with water. After removal of the solvent the product (1.46 g.) was recrystallised from ethanol-benzene to give needles, m.p. 256-261°. This product was given to Mr. Szumer for further treatment.

Preparation of epiFriedelanol.— Friedelin (5 g.) was dissolved in benzene (210 ml.) and added to a suspension of lithium aluminium hydride (10 g.) in ether (250 ml.). The mixture was refluxed for twelve hours and left to stand at room temperature during the week-end. It was then poured onto crushed ice and 5N-sulphuric acid and the product (2.5 g.) was extracted with benzene and then chloroform. A further quantity of epifriedelanol was obtained by filtering the mixture and boiling the precipitate several times with chloroform. Total yield of product 4.75 g. Recrystallisation from benzene gave plates, m.p. 277-281°, $[\alpha]_D$ +20° (c 0.5). The product was not purified further and was used as such to prepare friedel-3-ene.

Dehydration of epiFriedelanol with Phosphorus Oxychloride.— epifriedelanol (4.75 g.) was dissolved in pyridine (650 ml.) and phosphorus oxychloride (65 ml.) was added with cooling. The mixture was allowed to stand at room temperature overnight after which time it was poured into water and the product filtered off. The crude product was dissolved in hexane (100 ml.) and filtered through a column of alumina (500 g.) to give a filtrate containing friedel-3-ene (2.85 g.). It crystallised from benzene-ethanol as prisms m.p. 255-256°, $[\alpha]_D$ +59° (c 0.5 ; 2dm. tube). The low yield of hydrocarbon is probably due to the formation of some phosphate ester.

A large amount of the crude reaction product was insoluble in benzene and chloroform and hexane.

Attempts to Isomerise Friedelene with Various Acids.

The chloroform used in these experiments was thrice washed with water, dried and distilled from phosphorus pentoxide. Two percent by volume of alcohol (95%) was then added.

Treatment of Friedel-3-ene with Trichloracetic Acid.— Friedel-3-ene (124 mg.) Was dissolved in the minimum amount of chloroform, a solution of trichloracetic acid in chloroform (6 ml. of 43% W/V) was added and the volume made up to 25 ml. with chloroform. No change in specific rotation was observed after twenty hours. This experiment was repeated using chloroform containing five percent alcohol. During the first hour some of the friedelene crystallised out of solution and the specific rotation of the material in solution was not changed after twentyone hours.

Treatment of Friedel-3-ene with Formic Acid.— Formic acid could not be used as a catalyst since it precipitated friedelene from a chloroform solution.

Treatment of Friedel-3-ene with p-Toluenesulphonic Acid.— Friedel-3-ene (50 mg.) was dissolved in the minimum amount of chloroform and the solution was made up to 10 ml. with

a saturated solution of p-toluenesulphonic acid in chloroform. The specific rotation was unchanged after twentythree hours.

Treatment of Friedel-3-ene with Hydrogen Chloride in Chloroform at 17°.-- Hydrogen chloride was bubbled through a solution of friedel-3-ene (99 mg.) in chloroform (25 ml.) for fifteen minutes at room temperature (17°). The solution, saturated with hydrogen chloride, was placed in a polarimeter tube (4 dm.) and readings were taken at intervals.

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	+59°	5	+11°
½	+33	5½	+11
1	+15	6	+11
1½	+7	7½	+11
2	+6	8	+11
2½	+7	9	+11
3	+8	10	+10
3½	+9	10½	+10
4	+10	12½	+9
4½	+11		

Treatment of Friedel-3-ene with Hydrogen Chloride in Chloroform at 42°.-- A solution of friedel-3-ene (50 mg.) in chloroform (10 ml.) was saturated with hydrogen chloride at 42°, poured into a polarimeter tube and kept at that

temperature. The specific rotation was determined at intervals.

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	+59°	3	+4°
¼	+29	4	0
½	+29	5	-1
3/4	+23	6	0
1¼	+15	18½	0
2	+6		

Treatment of Friedel-3-ene with Hydrogen Chloride in Boiling Chloroform.— Friedel-3-ene (75 mg.) was dissolved in boiling chloroform (155 ml.). Hydrogen chloride was continuously passed through the boiling solution and samples were taken at intervals. No change in the specific rotation occurred after four hours. The material was recrystallised from chloroform-alcohol to give needles m.p. 255-256°. A mixed melting point with authentic specimen of friedel-3-ene was undepressed, and the infrared spectrum was identical with that of friedel-3-ene.

Preparation of Friedel-4(23)-ene.— Dry hydrogen chloride was bubbled through a solution of friedel-3-ene (1.58 g.) in chloroform (300 ml.) for 2¼ hours at room temperature (17°). At the end of this period the solution had $[\alpha]_D$ +8°. Repeated recrystallisation from chloroform-ethanol failed to effect any purification of the product. Recrystallisation

from ethyl acetate or hexane followed by recrystallisation from chloroform yielded needles, m.p. 254-256°, $[\alpha]_D$ +55° (c 0.5, 2 dm. tube). The infrared spectrum of this material was identical with that of friedel-3-ene.

Fractional crystallisation of the material in the mother liquors from hexane and then from ethyl acetate gave friedel-4(23)-ene, needles, m.p. 217-218°, $[\alpha]_D$ -12° (c 0.5, 2 dm. tube). The infrared spectrum had strong absorption bands at 888 cm^{-1} and 1635 cm^{-1}. (Found: C, 87.8; H, 12.15 $C_{30}H_{50}$ requires C, 87.7; H, 12.3%).

Hydrogenation of Friedel-4(23)-ene.-- Adam's catalyst (0.1g.) was suspended in a solution of friedel-4(23)-ene (80 mg.) in hexane (50 ml.) and the mixture was shaken under hydrogen at atmospheric pressure for two days and nights. Fractional crystallisation of the product ($[\alpha]_D$ +6°) from chloroform-ethanol yielded friedel-4(23)-ene.

The material was recovered, dissolved in glacial acetic acid, Adam's catalyst (0.1 g.) was added and the mixture was heated at 60° under hydrogen at 90 atmospheres pressure for twelve hours. The product ($[\alpha]_D$ +9°) was recrystallised three times from chloroform-ethanol to give friedelane, plates, m.p. 238-242°, $[\alpha]_D$ +21° (c 0.4, 2 dm. tube). Its identity was confirmed by comparison of its infrared spectrum with that of an authentic specimen. The melting points of

the two specimens were undepressed on admixture.

Treatment of Friedel-4(23)-ene with Hydrogen Chloride in Chloroform.-- Dry hydrogen chloride was bubbled through a solution of friedel-4(23)-ene (50 mg.) in chloroform (10 ml.) for three hours. After ½hour the specific rotation was +8° and after three hours, +9°. The infrared spectrum of the product was compared with that of the product from similar treatment of friedel-3-ene and was found to be quite different.

Selenium Dioxide Oxidation of the Product from the Treatment of Friedel-3-ene with Hydrogen Chloride in Chloroform.-- The isomerisation mixture (1.18 g.) was dissolved in boiling glacial acetic acid (30 ml.) and a solution of selenium dioxide (1.67 g.) in glacial acetic acid (8 ml.) was added. The mixture was refluxed for ½ hour after which it was cooled, diluted with hexane and filtered. The hexane solution was washed several times with water, dried over sodium sulphate and filtered through alumina (120 g.). After removal of the solvent from the filtrate, the product (0.289 g.) was recrystallised several times from acetone to give alnusa-1(10):5-diene, needles, m.p. 182-184°, $[\alpha]_D$ +118° (c 0.7). The melting point was undepressed on admixture with an authentic specimen.

Isomerisation of Friedel-3-ene by Hydrogen Chloride in Acetic Acid.-- Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (0.10 g.) in glacial acetic acid (100 ml.). After ½ hour the reaction mixture was poured into water (ca. 1 l. and extracted four times with chloroform. The extract was washed several times with water, the solvent was removed, and the specific rotation of the product determined. The procedure was repeated on this product for measured periods of treatment and the specific rotation was graphed against the time of treatment.

Time (hrs.)	$[\alpha]_D$	Time (hrs,)	$[\alpha]_D$
0	+59°	3	+23°
½	+3	3½	+22
3/4	-2	4	+26
1	-16	5	+28
1½	-2	7	+31
1½	+7	9	+30
2	+12	12	+32
2½	+17		

Conversion of Friedel-3-ene to Alnus-5(10)-ene.-- Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (1.6 g.) in glacial acetic acid (1500 ml.) for one hour. The reaction mixture was cooled somewhat, poured into water (ca. 3 l.) and extracted four times with chloroform.

The extract was washed several times with water, and was distilled to small volume. Alcohol was added and the mixture boiled down until crystallisation commenced. The product was recrystallised five times from chloroform-ethanol to give alnus-5(10)-ene, plates, m.p. 226-228°, $[\alpha]_D$ -41° (c 1.0).

Conversion of Alnus-5(10)-ene to the Equilibrium Mixture of Oleanenes.-- A solution of alnus-5(10)-ene (0.2 g.) in glacial acetic acid (150 ml.) and 10N hydrochloric acid (28 ml.) was refluxed for sixteen hours. The reaction mixture was cooled and the product which crystallised was filtered off. Repeated recrystallisation from ethanol-chloroform yielded the mixed crystal of 18α-olean-12-ene and olean-13(18)-ene, m.p. 186-187°, $[\alpha]_D$ -13° (c 0.7). Its infrared spectrum was identical with that of the mixed crystal prepared by similar treatment of friedel-3-ene and the melting points of the two specimens were undepressed on admixture.

Chromic Acid Oxidation of Alnus-5(10)-ene.-- Alnus-5(10)-ene (0.186 g.) was dissolved in boiling glacial acetic acid (120 ml.) which had previously been distilled from chromium trioxide. The solution was cooled to about 90° and a solution of chromium trioxide (0.123 g.) in glacial acetic acid

(2.5 ml.) and water (0.5 ml.) was added. The mixture was heated on a steam bath for one hour after which it was poured into a large volume of water. The product (0.174 g.) was filtered off and recrystallised several times from ethanol to give pale yellow needles. The ultraviolet spectrum had a peak at 252 mu. and $E^{1\%}_{1cm}$ 57 (alcohol). A previous small scale experiment gave a product with exactly the same ultraviolet spectral characteristics. At this stage the experiment was passed on to Mr. Szumer who chromatographed the product.

Treatment of Alnus-5(10)-ene with Hydrogen Chloride in Acetic Acid.-- Dry hydrogen chloride was bubbled through a boiling solution of alnus-5(10)-ene (0.1 g.) in glacial acetic acid (100 ml.) for ¼ hour. The reaction mixture was poured into water, extracted with chloroform, and the extract washed several times with water. When the specific rotation of the product was determined the procedure was repeated for further measured periods and the specific rotation was graphed against time of treatment.

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	-42°	2¼	+11°
¼	-24	3	+19
½	-12	5	+27
1¼	-2	7	+25
1¾	+8	9¼	+24

Conversion of Friedel-3-ene to Olean-12-ene.-- Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (3 g.) in glacial acetic acid (2 l.) for seven hours. The solution was concentrated to about 500 ml. and allowed to cool when the first crop of material crystallised from the solution. After filtering the crystalline material off, the filtrate was concentrated to about 200 ml. when a second crop of crystalline material was obtained. A third crop of crystals was obtained when the solution was concentrated to very small volume. The first crop had $[\alpha]_D$ +23° and was discarded. The second crop, $[\alpha]_D$ +42°, was recrystallised twice from acetic acid to give a product with $[\alpha]_D$ +35° which was discarded. The third crop of crystals was recrystallised first from the mother liquors of the second crop and then six times from glacial acetic acid to give olean-12-ene, needles, m.p. 161-163°, $[\alpha]_D$ +95° (c 0.5, 2 dm. tube). Its infrared spectrum was identical with that of an authentic specimen showing characteristic bands at 822 and 813 cm^{-1}.

In another experiment friedel-3-ene was treated with hydrogen chloride and acetic acid in the same way but the fractional crystallisation procedure was different. In this case the isomerisation mixture was recrystallised twice from chloroform-ethanol and then four times from acetone to give alnus-5(10)-ene, m.p. 222-225°, $[\alpha]_D$ -32°. Though the specific rotation was low, there can be no doubt that

this material was alnus-5(10)-ene since its infrared spectrum was identical with that of an authentic specimen and a mixed melting point determination showed no depression. Olean-12-ene could not be obtained pure from this experiment.

Selenium Dioxide Oxidation of Olean-12-ene.-- Olean-12-ene (0.161 g.) was dissolved in boiling glacial acetic acid (40 ml.) and a solution of selenium dioxide (0.228 g.) in glacial acetic acid (10 ml.) containing water (1 ml.) was added. After refluxing for ½ hour the solution was cooled, filtered and diluted with hexane (ca. 100 ml.). The hexane solution was washed four times with water and then dried with anhydrous sodium sulphate and filtered through a column of alumina (ca. 20 g.). Evaporation of the eluate gave the crude product (0.14 g.), $[\alpha]_D$ -21° (c 1.4). After three recrystallisations from chloroform-ethanol, oleana-11:13(18)-diene was obtained as needles, m.p. 215-217°, $[\alpha]_D$ -66° (c 0.7). Its ultraviolet spectrum had peaks at 242, 251 and 260 mu (hexane) and molar extinction coefficients:
ϵ_{242} = 26,400, ϵ_{251} = 30,600, ϵ_{260} = 19,800.

This was shown to be identical with an authentic specimen by comparison of their X-ray diffraction powder photographs and infrared spectra.

Treatment of Friedel-3-one with 10N Hydrochloric Acid-Acetic Acid (1:20).— A stream of dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (0.1 g.) in glacial acetic acid (150 ml.) and 10N hydrochloric acid (7.5 ml.) for ¼ hour. The reaction mixture was poured into water, and extracted with chloroform. The extract was washed several times with water and the solvent was then removed. The specific rotation of the product was determined and graphed against the time of treatment. This procedure was repeated for measured periods of treatment on the recovered product.

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	+59°	4	+28°
¼	+10	5¼	+17
⅓	+35,+36	6¼	+13
3/4	+41	7¼	+13
1	+49,+36	8¾	+7
1⅓	+44	10⅓	+5
2	+51,+43,+47	12⅓	+1
2⅓	+43	14⅓	0
3	+34		

Treatment of Friedel-3-one with 10N Hydrochloric Acid-Acetic Acid (1:20).--

Product from Two Hour Treatment. A stream of dry hydrogen

chloride was bubbled through a boiling solution of friedel-3-ene (1 g.) in glacial acetic acid (1500 ml.) and 10N hydrochloric acid (75 ml.) for two hours. The reaction mixture was poured into water (500 ml.) and extracted four times with chloroform. The extract was washed several times with water and the solvent removed to yield a gum, $[\alpha]_D$ +47°. After ten recrystallisations from glacial acetic acid and chloroform-ethanol a product, needles, $[\alpha]_D$ +56° (c 1.6), m.p. 161-164° was obtained. The melting point was depressed on admixture with an authentic specimen of olean-12-ene.

Selenium Dioxide Oxidation of the Product.-- The isomerisation product (489 mg.) was dissolved in boiling glacial acetic acid (20 ml.) and a solution of selenium dioxide (76 mg.) in glacial acetic acid (3 ml.) containing water (0.5 ml.) was added. After refluxing for ½ hour the solution was cooled, filtered and diluted with hexane (ca. 100 ml.). The hexane solution was washed four times with water and after drying over anhydrous sodium sulphate, was filtered through a column of alumina (50 g.). Removal of the solvent from the filtrate gave the product (384 mg.) which, after several recrystallisations from ethyl acetate gave oleana-11:13(18)-diene, needles, $[\alpha]_D$ -64° (c 1.1), m.p. 203-204°. The melting point could not be raised by

subsequent recrystallisations. The identity of this compound was confirmed by comparison of its infrared spectrum with that of an authentic specimen of oleana-11:13(18)-diene. Also the ultraviolet spectrum of the product had peaks at 242, 251 and 260 mu (hexane) characteristic of the oleana-11:13(18)-diene chromophore.

Treatment of Friedel-3-ene with 10N Hydrochloric Acid-Acetic Acid (1:20).--

Product From 14½ Hour Treatment. Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (0.5 g.) in glacial acetic acid (750 ml.) and 10N hydrochloric acid (37.5 ml.) for 14½ hours. The mixture was poured into water (2 l.), extracted with chloroform and the extract was washed several times with water. After removal of the solvent the product was recrystallised from acetone and then chloroform-ethanol to give the mixed crystal of olean-13(18)-ene and 18α-olean-12-ene, needles, m.p. 186-188°, $[\alpha]_D$ -19° (c 1.4). The infrared spectrum was identical with that of an authentic specimen of the mixed crystal.

Treatment of Friedel-3-ene with 10N Hydrochloric Acid-Acetic Acid (1:5).-- Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (0.1 g.) in glacial acetic acid (150 ml.) and 10N hydrochloric acid (30 ml.) for ¼ hour. The reaction mixture was worked up

as usual, the specific rotation of the product determined, and the process repeated for further measured intervals. The specific rotation was graphed against time of treatment.

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	$+59^\circ$	1	-2.5°
$\frac{1}{4}$	+35	$1\frac{1}{4}$	-5
$\frac{1}{2}$	+13	$1\frac{3}{4}$	-3
3/4	-2	$2\frac{3}{4}$	-3

Conversion of Friedel-3-ene to Alnus-5(10)-ene with Hydrogen Chloride and Butanol.-- Dry hydrogen chloride was bubbled through a boiling solution of friedel-3-ene (0.5 g.) in n-butanol (150 ml.) for fifteen hours. The reaction mixture was concentrated to a small volume, cooled, and the precipitate filtered off. Repeated recrystallisation from ethanol-benzene yielded alnus-5(10)-ene, needles, m.p. 224-226°, $[\alpha]_D$ -41° (c 0.7, 2 dm. tube). The infrared spectrum was identical with that of a specimen prepared by the action of hydrogen chloride and acetic acid on friedel-3-ene.

Dehydration of 3β-Hydroxyfriedelan-x-one with Phosphorus Oxychloride.-- 3β-Hydroxyfriedelan-x-one (0.87 g.) was dissolved in pyridine (100 ml.) and phosphorus oxychloride (10 ml.) was added with cooling. The mixture was allowed to stand at room temperature for four days after which it was boiled for five minutes. The reaction mixture was cooled, poured into water and the precipitate (0.76 g.) was filtered off. Recrystallisation from benzene-ethanol gave friedel-3-en-x-one, prisms, m.p. 252-255°, $[\alpha]_D$ +197° (c 1.1) (Found: C, 85.1; H, 11.6. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%). Friedel-3-en-x-one gave a positive test with tetranitromethane and its ultraviolet spectrum exhibited no selective absorption other than that due to an isolated oxo group.

Conversion of Friedel-3-en-x-one to Alnus-5(10)-en-x-one.— A stream of dry hydrogen chloride was bubbled through a boiling solution of friedel-3-en-x-one (100 mg.) in n-butanol (80 ml.) for fifteen hours. Most of the solvent was removed by distillation and the product crystallised from the cooled solution. Repeated recrystallisation from benzene-ethanol gave alnus-5(10)-en-x-one, needles, m.p. 221-222°, $[\alpha]_D$ +123° (c 1.0), (Found: C, 85.1; H, 11.7. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%). Neither the crude product nor alnus-5(10)-en-x-one had any selective absorption in its ultraviolet spectrum apart from that due to an

isolated oxo group. Alnus-5(10)-en-x-one gave a positive tetranitromethane test and did not react with 2:4-dinitrophenylhydrazine.

Wolff-Kishner Reduction of Alnus-5(10)-en-x-one.--

Alnus-5(10)-en-x-one (0.5 g.) was heated at 200° for eighteen hours in a bomb with anhydrous hydrazine (4 ml.) and sodium (1.6 g.) which had previously been dissolved in methanol (15 ml.). The reaction mixture was cooled, neutralised and extracted with chloroform. The crude product (0.48 g.) was dissolved in hexane and filtered through alumina (50 g.). The eluate contained an unsaturated hydrocarbon, alnus-5(10)-ene which crystallised from ethanol-benzene as prisms, m.p. 226-227°, $[\alpha]_D$ -42° (c 1.0) (Found: C, 87.7; H, 12.3. $C_{30}H_{50}$ requires C, 87.7; H, 12.1%). The infrared spectrum was identical with that of a specimen of alnus-5(10)-ene obtained from the rearrangement of friedel-3-ene. The melting points of these two samples were undepressed upon admixture.

Lithium Aluminium Hydride Reduction of Alnus-5(10)-en-x-one.--

Alnus-5(10)-en-x-one (1 g.) was dissolved in dry ether (250ml.), lithium aluminium hydride was added, and the mixture was refluxed for eleven hours. The reaction mixture was poured onto a mixture of crushed ice and 5N sulphuric acid and the

product was extracted with ether. The ethereal solution was washed twice with water then with sodium carbonate solution and finally with water. Recrystallisation from ethanol-benzene yielded alnus-5(10)-en-x-[ax]-ol, needles, m.p. 247-250°, $[\alpha]_D$ -25° (c 1.0) (Found: C, 84.7; H, 11.6. $C_{30}H_{50}O$ requires C, 84.4; H, 11.8%).

The acetate, formed in the usual way, crystallised as plates from ethanol-benzene, m.p. 243-244°, $[\alpha]_D$ -26° (c 0.9) (Found: C, 81.6; H, 11.1. $C_{32}H_{52}O_2$ requires C, 82.0; H, 11.2%).

Dehydration of Alnus-5(10)-en-x[ax]-ol with Phosphorus Oxychloride.-- Alnus-5(10)-en-x[ax]-ol (0.65 g.) was dissolved in pyridine (100 ml.) and phosphorus oxychloride (10 ml.) was added with cooling. The mixture was allowed to stand at room temperature for seventy hours. It was then poured into water and the product filtered off, dissolved in hexane and filtered through alumina (50 g.). The crude product (a gum) had no selective absorption in the ultra-violet spectrum in the range 200 - 300 mu , indicating the absence of a conjugated diene. The product was recrystallised from chloroform-ethanol to give needles, m.p. 122-124°, $[\alpha]_D$ -3° (c 1.0).

Treatment of 3β-Hydroxyfriedelan-x-one with Hydrochloric Acid-Acetic Acid (1:5).— 3β-Hydroxyfriedelan-x-one (5.47 g.) was dissolved in boiling glacial acetic acid (650 ml.), 10N hydrochloric acid (140 ml.) was added and the mixture was boiled under reflux for twenty hours. The solution was then boiled down to small volume (100 ml.) and cooled when the product (3.36 g.) crystallised as needles, m.p. 211-216°. When the mother liquors were poured into water a further quantity (1.9 g.) of the product was obtained. Recrystallisation from ethanol-benzene or acetone gave a mixed crystal of 18α-olean-12-en-x-one and olean-13(18)-en-x-one, m.p. 222-225°, $[\alpha]_D$ +66° (c 1.1). (Found: C, 85.0; H,11.55. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%). The product gave a positive test with tetranitromethane and formed a 2:4 dinitrophenylhydrazone. It exhibited no selective absorption in its ultraviolet spectrum other than that due to an isolated oxo group.

The semicarbazone was formed in the usual manner and was recrystallised from ethanol-chloroform to give needles, m.p. 273-275° (decomp.) (Found: C, 77.5; H, 10.7; N, 8.87. $C_{31}H_{51}ON_3$ requires C, 77.3; H, 10.7; N, 8.72%).

Rearrangement of Friedel-3-en-x-one to a Mixture of Olean-13(18)-en-x-one and 18α-Olean-12-en-x-one.— Friedel-3-en-x-one (1.4 g.) was dissolved in boiling glacial acetic acid

(500 ml.) and 10N hydrochloric acid (100 ml.) was added. The mixture was boiled under reflux for eighteen hours during which time a stream of hydrogen chloride was bubbled through it. The reaction mixture was boiled down to small volume (ca. 50 ml.) and the product crystallised on cooling. Recrystallisation from chloroform-ethanol and then from acetone gave the mixed crystal of 18α-olean-12-en-x-one and olean-13(18)-en-x-one, $[\alpha]_D$ +66° (c 1.0) m.p. 222-225°.

Wolff-Kishner Reduction of the Mixed Crystal of 18α-Olean-12-en-x-one and Olean-13(18)-en-x-one.— The mixed crystal of oleanenones (0.5 g.) was heated with anhydrous hydrazine (5 ml.) and a solution of sodium (1.6 g.) in methanol (20 ml.) for seventeen hours at 200° in a bomb. The crude product (0.48 g.), obtained after neutralising the reaction mixture and extracting with chloroform, was dissolved in hexane and filtered through alumina (50 g.). The filtrate contained a hydrocarbon mixture with $[\alpha]_D$ +7° (c 1.1), m.p. 175-177°. Numerous recrystallisations from chloroform-ethanol and then from acetone gave a mixture of 18α-olean-12-ene and olean-13(18)-ene, needles, m.p. 187-188°, $[\alpha]_D$ ± 0° (c 1.0). Its infrared spectrum was identical with that of an authentic specimen of the mixed crystal of 18α-olean-12-ene and olean-13(18)-ene prepared by the rearrangement of friedel-3-ene. The melting points of these two specimens

were undepressed upon admixture.

Sodium-Pentyl Alcohol Reduction of the Mixed Crystal of Oleanen-x-ones.— The mixed crystal of 18α-olean-12-en-x-one and olean-13(18)-en-x-one (1.14 g.) was dissolved in boiling isopentyl alcohol (60 ml.) and sodium (4.8 g.) was added. The mixture was refluxed until all the sodium had dissolved (ca. two hours) and the pentyl alcohol was then removed by steam distillation. Fractional crystallisation of the product from methanol-chloroform was successful in partially separating the two alcohols. One was obtained as plates with $[\alpha]_D$ -15° (c 1.1), m.p. 218-219°. The other component of the mixture was not obtained pure but its specific rotation is at least +82°.

Treatment of Oleanen -x[eq]-ol with Phosphorus Pentachloride.— Oleanen -x[eq]-ol (0.212 g. of material $[\alpha]_D$ -15°) was suspended in hexane (5 ml.), phosphorus pentachloride (0.15g.) was added and the mixture was shaken for ½ hour. After filtering off the excess phosphorus pentachloride the hexane solution was washed several times with water and finally dried over anhydrous sodium sulphate. The hexane solution was then filtered through alumina (22 g.) and the eluate contained a crystalline product (0.119 g.). This product gave a positive Beilstein test and so must have contained

chlorine. Recrystallisation from ethanol-chloroform yielded a chlorine-containing substance as needles, m.p. 137-139°, $[\alpha]_D$ -8° (c 0.6).

Sodium-Pentyl Alcohol Reduction of Friedelan-x-one.—

Friedelan-x-one (0.54 g.) was dissolved in boiling pentyl alcohol (50 ml.) and sodium (4 g.) was added. The mixture was refluxed until all of the sodium had dissolved after which the pentyl alcohol was removed by steam distillation. The product was filtered off and recrystallised several times from hexane to give friedelan-x[eq]-ol, needles, m.p. 276-279°, $[\alpha]_D$ +26° (c 1.4).

Treatment of Friedelan-x[eq]-ol with Phosphorus Pentachloride.—

Friedelan-x[eq]-ol (1.1 g.) was suspended in hexane (25 ml.) and phosphorus pentachloride (0.82 g.) was added. The mixture was shaken for six hours and allowed to stand during the week-end. It was then filtered and the hexane solution was washed several times with water and dried over anhydrous sodium sulphate. The dried hexane solution was filtered through alumina (110 g.) and removal of the solvent from the filtrate gave a gum (0.53 g.). This product gave a positive Beilstein test and hence contained chlorine. Several recrystallisations from ethanol-chloroform gave a substance, plates, m.p. 204-207° (decomp.; hydrogen chloride

evolved.), $[\alpha]_D$ +3° (*c* 1.2) (Found: C, 84.7; H, 11.7. $C_{30}H_{51}Cl$ requires C, 80.6; H, 11.5%). The substance is probably a mixture of a chloro-compound and a hydrocarbon in roughly equal proportions.

The Action of Alkali on the Chlorocompound.— The substance obtained from the action of phosphorus pentachloride on friedelan-*x*[eq]-ol (32 mg.) was dissolved in benzene (5 ml.), a solution of potassium hydroxide in methanol (50 ml. of 5%) was added and the mixture was refluxed for 5½ hours. After standing overnight the reaction mixture was poured into water (*ca.* 300 ml.) and extracted three times with benzene. The product gave a positive Beilstein test, and evolved hydrogen chloride on melting. Thus, it was not affected by alkali.

Pyrolytic Dehydrohalogenation of *x*-Chlorofriedelane.— The material from the previous experiment (25 mg.) was heated in a test tube immersed in an oil bath at 230° for six minutes. Hydrogen chloride was evolved and a dark brown resin was obtained. The product was dissolved in hexane and filtered through alumina (2 g.). A colourless, chlorine-free gum was obtained from the filtrate. This was crystallised from acetone to give colourless needles (14 mg.), the infrared spectrum of which exhibited very weak peaks at 852 and 1650 cm^{-1}.

Selenium Dioxide Oxidation of Friedelan-y-one.—

Friedelan-y-one (0.4 g.) was dissolved in boiling glacial acetic acid (300 ml.) and selenium dioxide (o.6 g.) was added. The mixture was refluxed for four hours during which time no selenium was deposited. The solution was distilled to small volume, water was added and the starting material was recovered by filtration.

The recovered material was refluxed in freshly distilled nitrobenzene (30 ml.) with selenium dioxide (0.6 g.) for two hours. After filtering off the selenium and washing it with ether, the total filtrates were steam distilled to remove the nitrobenzene. The product was extracted with benzene and chromatographed on alumina (40 g.). Careful chromatography and fractional crystallisation failed to yield anything but a minute amount of crystalline material. The ultraviolet spectrum of the crystalline material exhibited an absorption maximum at 255 mu.

Sodium Borohydride Reduction of Friedelane-3:y-dione.—

Friedelane-3:y-dione (5 g.) was dissolved in hot pyridine (200 ml.), and the cooled solution was added to a solution of sodium borohydride (2.4 g.) in methanol (150 ml.), containing 2N sodium hydroxide (1 ml.). The mixture was allowed to stand at room temperature for twentyfour hours with occassional shaking. After acidification with 5N

hydrochloric acid the product was extracted with chloroform and the extract was washed several times with 5N hydrochloric acid and finally water. The solvent was removed and the crude product was dissolved in benzene (3 l.) and chromatographed on alumina (500 g.). Elution with 20% chloroform in benzene gave firstly starting material and then elution with 50% chloroform in benzene gave one product, 3β-hydroxyfriedelan-y-one which crystallised from ethanol-benzene as prisms, m.p. 319-322°, $[\alpha]_D$ -32° (c 1.1) (Found: C, 81.2; H, 11.3. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The acetate, prepared in the usual way, formed needles from ethanol-benzene, m.p. 329-333°, $[\alpha]_D$ -20° (c 1.1) (Found: C, 79.6; H, 10.9. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

Dehydration of 3β-Hydroxyfriedelan-y-one with Phosphorus Oxychloride.-- Phosphorus oxychloride (10 ml.) was added with cooling to a solution of 3β-hydroxyfriedelan-y-one (1 g.) in pyridine (100 ml.). After standing at room temperature during the week-end, the mixture was boiled for five minutes, cooled and poured into a large volume of water. The product was filtered off and recrystallised from ethanol-benzene to yield friedel-3-en-y-one, prisms, m.p. 296-299°, $[\alpha]_D$ +5° (c 1.1) (Found: C, 84.6; H, 11.5. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%). This compound gives a positive tetranitromethane test and its ultraviolet

spectrum exhibits no selective absorption other than that due to an isolated carbonyl group.

Isomerisation of Friedel-3-en-y-one with Hydrogen Chloride in Acetic Acid.— Friedel-3-en-y-one (0.15 g.) was dissolved in boiling glacial acetic acid (100 ml.) and dry hydrogen chloride was bubbled continuously through the solution to maintain saturation. After refluxing for half an hour, the reaction mixture was cooled somewhat and poured into a large volume of water (ca. 700 ml.). The mixture was extracted four times with chloroform and the extract was washed three times with water to remove mineral acid. After the specific rotation and ultraviolet absorption spectrum were determined the product was submitted to the same treatment for further periods of time. All of the ultraviolet absorption spectra had λ max. 233 mu (hexane), 238 mu (alcohol).

Time (hrs.)	$[\alpha]_D$	$E^{1\%}_{1cm}$	Time (hrs.)	$[\alpha]_D$	$E^{1\%}_{1cm}$
0	+5°	0	2½	-347°	90.5
½	-149	37.1	3½	-363	91.3
1	-277	68.6	4½	-344	102.2
1½	-307	78.4	5½	-342	86.5
2	-337	88.6	6½	-340	-

Isomerisation of Friedel-3-en-y-one with Acetic Acid: 10N Hydrochloric Acid (20/1). Friedel-3-en-y-one (0.15 g.) was dissolved in boiling glacial acetic acid (150 ml.), 10N hydrochloric acid (7.5 ml.) was added and dry hydrogen chloride was bubbled through the boiling solution continuously. The reaction mixture was treated in the usual manner and specific rotations and ultraviolet spectra were determined after various times of treatment. All of the ultraviolet spectra had λ max. 233 mu (hexane), 238 mu (alcohol).

Time (hrs.)	$[\alpha]_D$	$E^{1\%}_{1cm}$	Time (hrs.)	$[\alpha]_D$	$E^{1\%}_{1cm}$
0	+5°	0	1½	-379°	119
½	-261	67	2	-383	121
1	-370	101	3	-366	-

Isomerisation of Friedel-3-en-y-one with Glacial Acetic-10N Hydrochloric Acid (5/1). Friedel-3-en-y-one (0.10 g.) was dissolved in boiling glacial acetic acid (150 ml.), 10N hydrochloric acid (30 ml.) was added and the mixture was refluxed whilst a stream of dry hydrogen chloride was bubbled through it. The product was examined at various intervals in the same way as previous experiments. As well as the specific rotation, the ultraviolet absorption spectra were determined and it was observed that the shape of the curves

varied considerably with time though the $E^{1\%}_{1cm}$ at 230 mu decreased only slightly (93-69). These spectra are shown in the discussion.(see p. 114).

Time (hrs.)	$[\alpha]_D$	Time (hrs.)	$[\alpha]_D$
0	+5°	2½	-168°
¼	-391	3½	-118
½	-392	4½	-79
1	-320	6½	-55
1½	-278	14	-30
2	-219		

Attempted Preparation of Conjugated en-y-one.— A solution of friedel-3-en-y-one (0.53 g.) in glacial acetic acid (750 ml.) and 10N hydrochloric acid (37.5 ml.) was refluxed for two hours. During this time a stream of hydrogen chloride was bubbled through the solution. The isomerisation mixture was poured into water (ca. 1.5 l.), extracted three times with chloroform and the extract washed three times with water. After removing the solvent the crude product (0.53 g.) was dissolved in hexane (300 ml.) and chromatographed on neutral alumina (106 g.). The isomerisation mixture proved to be inseparable by this method. Fractional crystallisation also failed to separate the substances. The infrared spectrum of the isomerisation mixture had a band at 1693 cm^{-1} with flank absorption on the lower

frequency side. A negative Beilstein test indicated the absence of chlorine.

Sodium-Pentyl Alcohol Reduction of the Ketonic Mixture.-- Because of the failure to separate the αβ-unsaturated ketone from the other component of the mixture by the usual physical methods, the mixture was reduced with sodium (12 g.) and pentyl alcohol (150 ml.) in the usual way. The products should be an unsaturated alcohol and an allylic alcohol which might readily dehydrate to give a conjugated diene. However no hydrocarbon was separated by chromatography on alumina. The mixture of alcohols was therefore acetylated and hydrolysed and the product chromatographed. A small amount of hydrocarbon was obtained (ca. 6% of the mixture) which had λ max. 230 mu hexane, $E^{1\%}_{1cm}$ 8.

Treatment of Friedel-3-en-y-one with 10N Hydrochloric Acid-Glacial Acetic Acid (1:5) for Fourteen Hours.-- A solution of friedel-3-en-y-one (0.5 g.) in glacial acetic acid (750 ml.) and 10N hydrochloric acid (150 ml.) was refluxed for 14 hours. A current of hydrogen chloride was passed through the solution during thie time. The isomerisation mixture was reduced to small volume (ca. 100 ml.) by distillation, poured into water (ca. 2 l.) and extracted several times with chloroform. The chloroform solution was washed several

times with water and the solvent then removed to yield a dark brown product (0.49 g.). This was dissolved in petrol: benzene (2 to 1) and filtered through a short column of alumina. The material obtained from the filtrate was recrystallised twice from acetone and seven times from chloroform-ethanol to give a product, needles, m.p. 236-238°, $[\alpha]_D$ +31° (c 1.0) (Found: C, 84.7; H, 11.2. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%).

The compound gave a negative Beilstein test, a negative tetranitromethane test, and had absolutely no absorption in the ultraviolet spectrum. The infrared spectrum of this compound exhibited no absorption characteristic of either a carbonyl or hydroxyl group or unsaturation.

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414. *Triterpenes of the Friedelane Series. Part I. Ketones.*

By J. L. COURTNEY and R. M. GASCOIGNE.

The bark of *Siphonodon australe* Benth. contains a mixture of over a dozen triterpenes of the friedelane series. The ketonic fraction of this mixture consists of friedelin, two diketones, and a triketone. These new ketones have been related to friedelin (friedelan-3-one) and to each other and are named friedelane-3 : *x*-dione, friedelane-3 : *y*-dione, and friedelane-3 : *x* : *y*-trione.

The hindrance of the *x*-oxo-group is comparable to that of the 11-oxo-group in steroids, and the *y*-oxo-group is even more hindered.

As part of an extensive investigation of alkaloids of the Australian flora Dr. J. R. Cannon, (the late) Dr. G. K. Hughes, and Dr. E. Ritchie of the University of Sydney examined the bark of the tree *Siphonodon australe* Benth. From it they isolated dulcitol and a crystalline mixture of neutral triterpenes which they very kindly passed on to us. The mixture contains over a dozen triterpenes of the friedelane series; it can be divided into three main fractions containing respectively ketones, monohydroxy-ketones, and polyhydroxy-compounds. This paper describes the ketonic constituents and the following paper the monohydroxy-ketones. The polyhydroxy-compounds will be dealt with later.

The ketonic fraction consists of friedelin (*ca.* 0·2% of the whole mixture), two diketones (*ca.* 15% and 1%), and a triketone (*ca.* 10%). None of the last compounds has the properties of an α- or β-diketone. The structure and configuration of friedelin (friedelan-3-one) have recently been elucidated.[1] We assign the name friedelane-3 : *x*-dione to one of the diketones on the following grounds. When reduced by the Clemmensen method it yielded friedelane and a new ketone friedelan-*x*-one. Reduction by sodium borohydride afforded two epimeric hydroxy-ketones,* one of which, when reduced by the Wolff–Kishner method with anhydrous hydrazine, yielded *epi*friedelinol (friedelan-3β-ol). It follows that the two epimeric hydroxy-ketones are 3α- and 3β-hydroxyfriedelan-*x*-one and that the diketone contains a 3-carbonyl group.

Friedelan-*x*-one was formed also on reduction of friedelane-3 : *x*-dione by the Huang-Minlon modification of the Wolff–Kishner reduction, with 85% hydrazine hydrate. In this case, however, no friedelane was obtained. The *x*-oxo-group is considerably hindered: thus friedelan-*x*-one does not react with semicarbazide or 2 : 4-dinitrophenylhydrazine. Friedelane-3 : *x*-dione yields a monosemicarbazone which must be formed by the 3-oxo-group. The reduction experiments described above indicate that the hindrance of the *x*-oxo-group is comparable to that of the 11-oxo-group in steroids. Thus it is not reduced by sodium borohydride (at ordinary temperature) or by the Huang-Minlon procedure (with aqueous hydrazine); these methods do not reduce 11-oxo-steroids.[2,3] On the other hand it is reduced by the Clemmensen method (with heavily amalgamated zinc) and by the Wolff–Kishner method (with anhydrous hydrazine), both of which also reduce 11-oxo-steroids.[4,5]

The triketone is friedelane-3 : *x* : *y*-trione. It formed a monosemicarbazone and so contains two unreactive carbonyl groups. The reactive carbonyl group was identified as the 3-oxo-group in the following way. The group was protected by formation of the ethylene ketal (by the transfer procedure [6]) which was then reduced by the Wolff–Kishner method (anhydrous hydrazine). Removal of the protecting group and chromatography of the product yielded friedelin accompanied by a small amount of friedelane and a hydroxy-ketone which is discussed below. Proof of the presence of the *x*-oxo-group is given in the following paper.

Clemmensen reduction of the triketone under vigorous conditions (heavily amalgamated zinc) yielded a new ketone, friedelan-*y*-one, and a new diketone, friedelane-*x* : *y*-dione; no

* Evidence that these two compounds are epimers is provided by their molecular rotation differences (given in the following paper) and their infrared absorption.

friedelane was obtained. It is evident from this result that the *y*-oxo-group is even more hindered than the *x*-oxo-group. Probably as a consequence of this marked hindrance, the *y*-oxo-group is partially converted into a hydroxyl group in the conditions of the Wolff–Kishner reduction with anhydrous hydrazine. Thus, when friedelane-3 : *x* : *y*-trione was reduced by this method it yielded friedelane and an alcohol which was shown to be friedelan-*y*-ol by oxidation to friedelan-*y*-one. Similarly the hydroxy-ketone obtained along with friedelin from the reduction of the ethylene ketal of friedelane-3 : *x* : *y*-trione is *y*-hydroxy-friedelan-3-one.

The second diketone is friedelane-3 : *y*-dione. It formed a monosemicarbazone and on reduction by the Huang-Minlon procedure yielded friedelan-*y*-one. Proof of the presence of the 3-oxo-group is provided by the oxidation of *y*-hydroxyfriedelan-3-one which yielded the diketone.

The relations summarised in the names assigned to the several ketones described are substantiated by their infrared absorption, which will be discussed in a later paper, and by the molecular-rotation contributions of the carbonyl groups (Table).

Molecular rotation contributions of carbonyl groups.

	$[M]_D$ with CO group	$[M]_D$ without CO group	ΔCO
3-Oxo-group			
Friedelan-3-one	−94°	+91°	−185°
Friedelane-3 : *x*-dione	+506	+647	−141
Friedelane-3 : *x* : *y*-trione	+327	+453	−126
Friedelane-3 : *y*-dione	−273	−145	−128
x-Oxo-group			
Friedelan-*x*-one	+647	+91	+556
Friedelane-3 : *x*-dione	+506	−94	+600
Friedelane-3 : *x* : *y*-trione	+327	−273	+600
Friedelane-*x* : *y*-dione	+453	−145	+598
y-Oxo-group			
Friedelan-*y*-one	−145	+91	−236
Friedelane-3 : *y*-dione	−273	−94	−179
Friedelane-3 : *x* : *y*-trione	+327	+506	−179
Friedelane-*x* : *y*-dione	+453	+647	−194

The value of the specific rotation of friedelane observed in this investigation was that found by Bruun [7] and not the higher value recorded in the earlier literature.

Experimental

Analyses by Dr. E. Challen and Mr. D. Weedon, and infrared spectra by Mr. I. Reece.

Specific rotations were measured in $CHCl_3$ solution and, unless otherwise stated, in a 1 dm. tube. The m. p. of many of the compounds described was dependent on rate of heating, so the capillary tube was always placed in the apparatus at *ca.* 30° below the m. p. Identity of specimens was established by comparison of their infrared spectra. Alumina for chromatography had activity II, and the light petroleum had b. p. 40—60°.

Oxidation of hydroxyl to keto-groups was carried out with the chromium trioxide–pyridine reagent [8] as follows: a 5—10% solution of the compound to be oxidised, in dry pyridine, was added to an equal weight of chromium trioxide in pyridine (10% solution; prepared by slowly adding the chromium trioxide to the pyridine with cooling [8]). The mixture was occasionally shaken and left overnight. It was then diluted with benzene and filtered; the solid material was extracted twice with boiling benzene. The benzene filtrate and extracts were combined and washed with water, then with 5N-hydrochloric acid until the pyridine was removed, and then with sodium hydrogen sulphite solution. Evaporation of the benzene yielded the product, generally in almost quantitative yield.

Isolation of the Triterpene Mixture from Siphonodon australe (with Mr. A. Z. Szumer).—The air-dried, finely milled bark (55 kg.) was extracted by percolation with chloroform, and the extract, after removal of chloroform, was dissolved in hot alcohol (12 l.) and left for several days. Amorphous material which was deposited was filtered off and extracted twice with hot alcohol; the extracts were added to the alcoholic filtrate.

The amorphous material was extracted with hot N-sodium hydroxide (the extract yielded

black acidic material which was discarded) and then with hot benzene which extracted crystalline triterpenes (79 g.). The undissolved material consisted of a mixture of sodium salts (70 g.) insoluble in sodium hydroxide solution.

The alcoholic filtrate on concentration yielded a mixture of triterpenes (339 g.) which was recrystallised from alcohol. Removal of alcohol from the concentrated filtrate with steam left a resin which was dissolved in benzene (10 l.). The benzene solution was extracted with 2N-sodium hydroxide [acidification of the extract yielded resin (764 g.)] and then filtered through a column of alumina (2 kg.); the filtrate contained a clear gum (214 g.). Elution of the column with benzene and then with chloroform–benzene gave a series of fractions from which crystalline triterpene material (39 g.) was obtained by treatment with light petroleum (lower fractions) and ethyl acetate (higher fractions).

The combined triterpene mixture (457 g.) had selective ultraviolet absorption only in the 285 mμ region ($E^{1\%}_{1\,cm.}$ 3).

Chromatography of the Triterpene Mixture.—The mixture (140 g.) was dissolved in benzene (3 l.) and adsorbed on a column of alumina (4·1 kg.; 5 × 233 cm.). The column was eluted with benzene, then with increasing concentrations of chloroform in benzene, and finally with chloroform to give 58 fractions, each of *ca.* 2 g. All the fractions except the first were crystalline and had the following specific rotations (*c* 2 to 3):

Fraction	$[\alpha]_D$	Fraction	$[\alpha]_D$	Fraction	$[\alpha]_D$	Fraction	$[\alpha]_D$
2	+55°	21	+61°	36	+1°	45	+12°
3	+97	22—28	+67—71	37	−11	46—53	+42—19
4	+105	29	+51	38	−20	54	+38
5—15	+110—113	30	+41	39	−27	55	+26 *
16	+74	31	+36	40	−38	56	−8 *
17	+14	32	+28	41	−50	57	+12
18	+31	33	+31	42	−42	58	−18
19	+47	34	+32	43	−29		
20	+57	35	+42	44	−9	* *c* 0·6, 2 dm. tube	

Each fraction (except 2—4, 5—15, and 22—28) was examined separately, initially by recrystallisation from alcohol.

Friedelin.—Fractions 2—4 were combined, dissolved in 4 : 1 light petroleum–benzene, and chromatographed over alumina (200 g.). The first fraction (0·9 g.) had $[\alpha]_D$ −9° and after three recrystallisations from alcohol–benzene yielded friedelin (0·28 g.), m. p. 261—264°, $[\alpha]_D$ −21° (*c* 2·5) (Found: C, 84·3; H, 11·7. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%). The product was identical with an authentic specimen (infrared spectra). Corks were not used in the extraction or the separation of the triterpene mixture.

Friedelane-3 : x-*dione.*—Fractions 5—15 were combined and recrystallised from alcohol, yielding *friedelane*-3 : x-*dione* in needles, m. p. 248—250°, $[\alpha]_D$ +115° (*c* 2·6) (Found: C, 82·1; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). An additional amount was obtained from fractions 2—4 and 16—17 by chromatography (total, 22·5 g.). The *monosemicarbazone* formed prisms (from alcohol), m. p. 247° (decomp.) (Found: C, 74·2, 74·2; H, 10·5, 10·4; N, 8·3, 8·5. $C_{31}H_{51}O_2N_3,\frac{1}{4}C_2H_5{\cdot}OH$ requires C, 74·4; H, 10·4; N, 8·3%).

Friedelane-3 : y-*dione.*—By virtue of its low solubility in alcohol, *friedelane*-3 : y-*dione* was isolated from fractions 16 and 17. An additional amount was obtained from fractions 18—21 by chromatography (total, 1·6 g.). It crystallised from alcohol–benzene in laths, m. p. 305—309°, $[\alpha]_D$ −62° (*c* 2·3) (Found: C, 81·5; H, 10·9%). The *monosemicarbazone* formed plates (from alcohol–chloroform), m. p. 331° (decomp.) (Found: C, 74·8; H, 10·4; N, 8·6. $C_{31}H_{51}O_2N_3$ requires C, 74·8; H, 10·3; N, 8·4%).

Friedelane-3 : x : y-*trione.*—Fractions 22—28 were combined and recrystallised from alcohol, yielding *friedelane*-3 : x : y-*trione* in needles or plates, m. p. 300—303°, $[\alpha]_D$ +72° (*c* 2·4) (Found: C, 79·4; H, 10·2. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). An additional amount was obtained from fractions 18—21 and 29—35 by chromatography (total, 13·8 g.). The *monosemicarbazone* formed needles (from alcohol), m. p. 320° (decomp.) (Found: C, 72·8; H, 9·5; N, 8·3. $C_{31}H_{49}O_3N_3$ requires C, 72·8; H, 9·65; N, 8·2%).

Clemmensen Reduction of Friedelane-3 : x-*dione.*—A hot solution of friedelane-3 : *x*-dione (2 g.) in dioxan (500 ml.) was diluted with 10N-hydrochloric acid (290 ml.) and added to amalgamated zinc [prepared by leaving zinc needles (80 g.) in a solution of mercuric chloride (80 g.) in 50% aqueous alcohol (600 ml.) for 15 min.]. The mixture was heated on the steam-bath for 5 hr. and then cooled, whereupon the product separated out. Filtration of a solution of the product in 3 : 1 light petroleum–benzene through alumina (60 g.) yielded friedelane (0·2 g.), plates (from alcohol–benzene), m. p. 243—245°, $[\alpha]_D$ +22° (*c* 0·7; 2 dm. tube) (Found: C, 87·05;

H, 12·5. Calc. for $C_{30}H_{52}$: C, 87·3; H, 12·7%). Its identity was established by comparison (mixed m. p. and infrared spectra) with an authentic specimen.

Elution of the column with 3 : 1 light petroleum–benzene yielded *friedelan*-x-*one* (1·1 g.), needles (from alcohol), m. p. 241—243°, $[\alpha]_D$ +152° (*c* 2·1) (Found : C, 84·4; H, 11·95. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

Huang-Minlon Reduction of Friedelane-3 : x-*dione*.—A solution of friedelane-3 : *x*-dione (5 g.), potassium hydroxide (4·5 g.), and hydrazine hydrate (7 ml. of 85%) in diethylene glycol (32 ml.) was refluxed for 1½ hr. Hydrazine hydrate was then removed by distillation and the mixture was kept at 200° for 5 hr.; it was then cooled and acidified. The product, isolated with chloroform, was extracted with light petroleum which left high-melting nitrogen-containing material. The light petroleum extract was filtered through alumina (200 g.) which was eluted with 1 : 1 light petroleum–benzene, yielding friedelan-*x*-one (1·3 g.), m. p. 241—243°, $[\alpha]_D$ +152° (*c* 2·2).

Reduction of Friedelane-3 : x-*dione with Sodium Borohydride*.—A solution of friedelane-3 : *x*-dione (2·0 g.) in pyridine (100 ml.) was added to a solution of sodium borohydride (0·55 g.) in methyl alcohol (50 ml.) containing N-sodium hydroxide (0·25 ml.). The solution was left for 24 hr. and then acidified with 5N-hydrochloric acid (400 ml.). The product, isolated with chloroform, was dissolved in benzene and chromatographed over alumina (100 g.). Elution with benzene gave eight fractions (each *ca.* 0·25 g.). Fraction 1 was starting material. Fraction 3 was recrystallised from alcohol, yielding 3β-*hydroxyfriedelan*-x-*one*, prisms, m. p. 288—291°, $[\alpha]_D$ +159° (*c* 1·0) (Found : C, 81·5; H, 11·1. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The *acetate* formed plates (from alcohol), m. p. 271—273°, $[\alpha]_D$ +158° (*c* 0·5; 2 dm. tube) (Found : C, 79·35; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

Fractions 4—6 consisted of mixtures which could not be separated. Fraction 7 was recrystallised from alcohol, yielding 3α-*hydroxyfriedelan*-x-*one*, plates, m. p. 307—311°, $[\alpha]_D$ +145° (*c* 1·0) (Found : C, 81·3; H, 11·2%). The *acetate* formed plates (from alcohol), m. p. 305—307°, $[\alpha]_D$ +114° (*c* 0·7; 2 dm. tube) (Found : C, 79·3; H, 10·7).

When the reduction was repeated on a larger scale a 53% yield of the 3β(axial)-epimer was isolated.

Wolff–Kishner Reduction of 3β-*Hydroxyfriedelan*-x-*one*.—A mixture of 3β-hydroxyfriedelan-*x*-one (1·0 g.), anhydrous hydrazine (6·5 ml.), and a solution of sodium (2·5 g.) in methyl alcohol (30 ml.) was heated at 200° for 16 hr. The product, isolated with chloroform after the mixture had been acidified, was dissolved in 3 : 1 light petroleum–benzene and filtered through alumina (60 g.). The filtrate contained friedelane (0·20 g.), m. p. 244—246°, $[\alpha]_D$ +22° (*c* 1·2). Elution with 3 : 1 light petroleum–benzene yielded *epi*friedelinol (0·35 g.), plates (from much alcohol), m. p. 281—283°, $[\alpha]_D$ +21° (*c* 1·1) (Found : C, 84·2; H, 12·1. Calc. for $C_{30}H_{52}O$: C, 84·0; H, 12·2%). Its infrared spectrum was identical with that of an authentic specimen. The acetate formed plates (from alcohol–benzene), m. p. 290—293°, $[\alpha]_D$ +33° (*c* 1·1) (Found : C, 81·3; H, 11·5. Calc. for $C_{32}H_{54}O_2$: C, 81·6; H, 11·6%).

Conversion of Friedelane-3 : x : *y-trione into Friedelin and Friedelane*-3 : *y-dione*.—A solution of friedelane-3 : *x* : *y*-trione (2·95 g.) in 2-ethyl-2-methyl-1 : 3-dioxolan [6] (60 ml.) containing toluene-*p*-sulphonic acid (45 mg.) was refluxed for 7 hr. The product, obtained by filtering the cooled reaction mixture, was recrystallised from benzene, yielding the ethylene *ketal*, prisms, m. p. 342—345°, $[\alpha]_D$ +76° (*c* 1·2) (Found : C, 77·3; H, 10·3. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%). It had strong infrared peaks at 1092, 1077, and 1067 cm.$^{-1}$ (Nujol mull; cf. Page, *J.*, 1955, 2017).

A mixture of the ketal (1·3 g.), anhydrous hydrazine (8·5 ml.), and a solution of sodium (3·2 g.) in methyl alcohol (50 ml.) was heated at 200° for 16 hr. The product, isolated from the acidified mixture with chloroform, was dissolved in acetone (400 ml.) containing toluene-*p*-sulphonic acid (75 mg.), and the solution was refluxed for 14 hr., to remove the ketal group. The product, isolated by pouring the concentrated solution into water, was dissolved in 2 : 1 light petroleum–benzene and filtered through alumina (100 g.). The filtrate contained friedelane (30 mg.), m. p. 245—247°, $[\alpha]_D$ +21° (*c* 0·3; 2 dm. tube). Elution with benzene gave friedelin (80 mg.), m. p. 261—264°, $[\alpha]_D$ −25° (*c* 0·8) (Found : C, 84·3; H, 11·65%).

Elution with 20% chloroform in benzene yielded y-*hydroxyfriedelan*-3-*one* (450 mg.), laths (from alcohol), m. p. 301—305°, $[\alpha]_D$ −20° (*c* 0·7; 2 dm. tube) (Found : C, 81·4; H, 11·3%). The *acetate* formed needles (from aqueous alcohol), m. p. 175—176°, $[\alpha]_D$ −25° (*c* 1·2) (Found : C, 79·1; H, 10·7%).

Oxidation of *y*-hydroxyfriedelan-3-one with chromium trioxide in pyridine yielded friedelane-3 : *y*-dione, m. p. 306—310°, $[\alpha]_D$ −60° (*c* 0·8).

Clemmensen Reduction of Friedelane-3 : x : y-trione.—Friedelane-3 : *x* : *y*-trione (2 g.) was reduced in the same way as friedelane-3 : *x*-dione, and the product was chromatographed over alumina (100 g.). Elution with 3 : 1 light petroleum–benzene yielded *friedelan-y-one* (0·2 g.), prisms (from alcohol–benzene), m. p. 287—290°, $[\alpha]_D$ −34° (*c* 1·6) (Found : C, 84·7; H, 12·0%). Elution with 2 : 1 light petroleum–benzene yielded *friedelane-x : y-dione*, plates (from alcohol–benzene), m. p. 302—305°, $[\alpha]_D$ +103° (*c* 1·6) (Found : C, 81·7; H, 11·0%).

Wolff–Kishner Reduction of Friedelane-3 : x : y-trione.—Friedelane-3 : *x* : *y*-trione (1·64 g.) was reduced in the same way as 3β-hydroxyfriedelan-*x*-one, and the product was dissolved in 2 : 1 light petroleum–benzene and filtered through alumina (100 g.). The filtrate contained friedelane (0·61 g.), m. p. 245—247°, $[\alpha]_D$ +22° (*c* 1·0). Elution with 1 : 1 light petroleum–benzene yielded *friedelan-y-ol* (0·67 g.), plates (from alcohol), m. p. 223—226°, $[\alpha]_D$ +20° (*c* 1·8) [Found (after vacuum-sublimation) : C, 84·3; H, 12·2. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%]. The *acetate* formed prisms (from aqueous alcohol), m. p. 143—145°, $[\alpha]_D$ +13° (*c* 1·0) (Found : C, 81·6; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%).

Oxidation of friedelan-*y*-ol with chromium trioxide in pyridine yielded friedelan-*y*-one, m. p. 290—292°, $[\alpha]_D$ −30° (*c* 1·0).

Huang-Minlon Reduction of Friedelane-3 : y-dione.—Friedelane-3 : *y*-dione (0·5 g.) was reduced in the same way as friedelane-3 : *x*-dione, and the product was chromatographed over alumina (50 g.). Elution with 2 : 1 light petroleum–benzene yielded friedelan-*y*-one (0·35 g.), m. p. 286—290°, $[\alpha]_D$ −32° (*c* 1·0).

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415. *Triterpenes of the Friedelane Series. Part II.* Hydroxy-ketones and Alcohols.*

By J. L. COURTNEY, R. M. GASCOIGNE, and A. Z. SZUMER.

Three hydroxy-ketones and two hydroxy-diketones have been isolated from the triterpene mixture from *Siphonodon australe* Benth. These compounds have been related to the ketones described in Part I and, where possible, configurations have been assigned to the hydroxyl groups. The five compounds can consequently be named *x*[eq]- and *x*[ax]-hydroxyfriedelan-3-one, *y*-hydroxyfriedelan-3-one, *x*[eq]-hydroxyfriedelane-3:*y*-dione, and *y*-hydroxyfriedelane-3 : *x*-dione.

Reduction of friedelan-*x*-one by two different methods gives two epimeric alcohols, but reduction of friedelan-*y*-one by the same two methods gives only one alcohol.

Molecular-rotation differences observed with these compounds support the absolute configuration assigned to friedelane.[1] This configuration is a partial " skeletal enantiomorph " of the 5α-steroids and the usual triterpenes; consequently reduction of 3-oxo-derivatives with sodium borohydride yields mainly axial (3β-)alcohols.

THREE hydroxy-ketones and two hydroxy-diketones have been isolated from the triterpene mixture from *Siphonodon australe* Benth. and, as described in the sequel, have been related to the ketones discussed in Part I.* It may be of biological significance that the nine friedelane derivatives so far isolated from this source all contain the 3-oxo-group.

To provide reference compounds for this investigation friedelan-*x*-one and friedelan-*y*-one were reduced with sodium and pentyl alcohol and also with lithium aluminium hydride. Friedelan-*x*-one yielded two different alcohols, one by each method. The alcohol obtained by reduction with sodium and pentyl alcohol must, from its method of preparation, be the more stable of the two epimers and can consequently be assumed to have the equatorial configuration. It is therefore friedelan-*x*[eq]-ol, and the alcohol obtained by reduction with lithium aluminium hydride is friedelan-*x*[ax]-ol. (It should be noted, however, that in some special cases the more stable of a pair of epimers has the axial configuration; see below.) In the case of friedelan-*y*-one by contrast, both methods of reduction gave the same alcohol, friedelan-*y*-ol. Such a result, with a hindered ketone, is unusual but an analogy is provided in the reduction of the very hindered 18α-oleanan-19-one which yielded 18α-oleanan-19β[ax]-ol by both methods of reduction;[2] in this case the axial epimer is more stable than the equatorial epimer.[2] Consequently we do not yet assign any configuration to friedelan-*y*-ol; it happens that it is not necessary to do so for present purposes.

Friedelan-*x*-one, friedelan-*y*-one, and evidently also 18α-oleanan-19-one were readily reduced by sodium and pentyl alcohol in spite of their very hindered nature. 11-Oxosteroids are also reduced by sodium and alcohols[3] and it appears that this method of reduction is not appreciably affected by steric hindrance. As is well known, the stereochemical course of the reduction is determined by thermodynamic rather than by kinetic factors.

Of the three hydroxy-ketones isolated from *Siphonodon australe* one is identical with *y*-hydroxyfriedelan-3-one, described in Part I,[4] whilst the other two on oxidation yielded friedelane-3 : *x*-dione. Since these two compounds are not identical with the epimeric 3-hydroxyfriedelan-*x*-ones described in Part I they must be the epimeric *x*-hydroxyfriedelan-3-ones. Both formed semicarbazones thus confirming the presence of the reactive 3-oxo-group. To complete the identification of these compounds it was necessary to determine which of them was the equatorial and which the axial epimer. Accordingly one of them was reduced by the Huang-Minlon procedure; it yielded friedelan-*x*[ax]-ol and consequently must be *x*[ax]-hydroxyfriedelan-3-one. The possibility of epimerisation during the reduction is eliminated since the product was the less stable of the epimeric friedelan-*x*-ols.

The two hydroxy-diketones on oxidation gave friedelane-3 : *x* : *y*-trione and both formed

* Part I, preceding paper.

semicarbazones, indicating the presence of the 3-oxo-group. One of them, when reduced by the Wolff–Kishner method (anhydrous hydrazine), yielded friedelan-*x*[eq]-ol and is therefore *x*[eq]-hydroxyfriedelane-3 : *y*-dione. This conversion also provides proof for the presence of the *x*-oxo-group in friedelane-3 : *x* : *y*-trione. For the other hydroxy-diketone three possibilities remain : *x*[ax]-hydroxyfriedelane-3 : *y*-dione and the two epimers of *y*-hydroxyfriedelane-3 : *x*-dione. The first of these can be eliminated by molecular rotations : the observed $[M]_D$ is +498° whereas the calculated $[M]_D$ for *x*[ax]-hydroxyfriedelane-3 : *y*-dione is −249° {the sum of the observed $[M]_D$ of friedelane-3 : *y*-dione (−273°) and the ΔOH value for the *x*[ax]-hydroxyl group (+24°; see Table 1)}. The compound

TABLE 1. *Molecular-rotation contributions of hydroxyl and acetoxyl groups.*

Symbols and conventions are as used by Klyne and Stokes (*J.*, 1954, 1979).

	$[M]_D$ CH_2 *	$[M]_D$ OH	$[M]_D$ OAc	ΔOH	ΔOAc	$[M]_D$OAc −$[M]_D$OH
3-Hydroxyl group (equatorial)						
Friedelan-3α-ol †	+91°	+69°	−99°	−22°	−190°	−168°
3α-Hydroxyfriedelan-*x*-one *	+647	+641	+552	−6	−95	−89
3-Hydroxyl group (axial)						
Friedelan-3β-ol ‡	+91	+90	+169	−1	+78	+79
3β-Hydroxyfriedelan-*x*-one *	+647	+704	+764	+57	+117	+60
3β-Hydroxyfriedelane-*x* : *y*-dione	+453	+489	+564	+36	+111	+75
3β-Hydroxyfriedelan-*y*-one	−145	−142	−97	+3	+48	+45
x-Hydroxyl group (equatorial)						
Friedelan-*x*[eq]-ol	+91	+51	+24	−40	−67	−27
x[eq]-Hydroxyfriedelan-3-one	−94	−142	−193	−48	−99	−51
x[eq]-Hydroxyfriedelane-3 : *y*-dione	−273	−328	−344	−55	−71	−16
x-Hydroxyl group (axial)						
Friedelan-*x*[ax]-ol	+91	+111	+113	+20	+22	+2
x[ax]-Hydroxyfriedelan-3-one	−94	−66	−58	+28	+36	+8
y-Hydroxyl group						
Friedelan-*y*-ol *	+91	+90	+61	−1	−30	−29
y-Hydroxyfriedelan-3-one *	−94	−89	−121	+5	−27	−32
y-Hydroxyfriedelane-3 : *x*-dione	+506	+498	+439	−8	−67	−59

* Compounds described in Part I.[4]

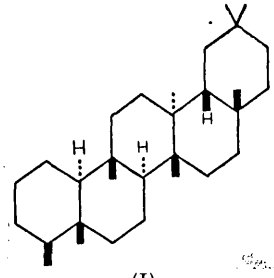
† Friedelinol; the constants are given in the Experimental section.

‡ *epi*Friedelinol; our constants (Experimental) are in agreement with those of Bruun and Jefferies (*Acta Chem. Scand.*, 1954, **8**, 1948).

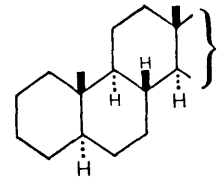
is named *y*-hydroxyfriedelane-3 : *x*-dione since its molecular rotation differences (Table 1) indicate that the hydroxyl group has the same configuration as in the other *y*-hydroxy-compounds.

The molecular-rotation differences set out in Table 1 provide supporting evidence for the names assigned to the various compounds, and further confirmation is available from the molecular-rotation contributions of the carbonyl groups (*e.g.*, the 3-oxo-group; Table 2) and from the infrared spectra which will be discussed in a later paper.

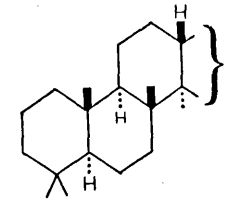
The molecular-rotation differences also support the absolute configuration (I) deduced for the friedelane structure.[1] Klyne [5] has shown that in polycyclic compounds such as steroids and triterpenes two enantiomorphic forms of a terminal ring have rotational



(I)



(II)



(III)

contributions of opposite sign, often of the same order of magnitude. On the basis of formula (I), if methyl groups are neglected (an admissible procedure [5]), friedelane is enantiomorphic with respect to ring A (also rings B and C) with androstane (II) and with oleanane, ursane, and lupane (III). Consequently the rotational contribution of the 3-oxo-group in the friedelane series should be opposite in sign to the contribution of this group in the various series represented by (II) and (III). We have determined the rotational contribution of the 3-oxo-group with ten sets of friedelane derivatives [six in this paper (Table 2) and four in Part I [4]] and the average value is −170°. Klyne [5] records the

TABLE 2. *Molecular-rotation contribution of the* 3-*oxo-group.*

	$[M]_D$ with 3-oxo-group	$[M]_D$ without 3-oxo-group	ΔCO
x[eq]-Hydroxyfriedelan-3-one	−142°	+51°	−193°
x[eq]-Acetoxyfriedelan-3-one	−193	+24	−217
x[ax]-Hydroxyfriedelan-3-one	−66	+111	−177
x[ax]-Acetoxyfriedelan-3-one	−58	+113	−171
y-Hydroxyfriedelan-3-one	−89	+90	−179
y-Acetoxyfriedelan-3-one	−121	+61	−182

rotational contribution of the 3-oxo-group in several triterpenes of the oleanane, ursane, and lupane series; the values range from +64° to +144°. For steroids of the 5α-series the average value [6] is +71°. Similarly Dutler, Jeger, and Ruzicka [1d] have observed that a molecular-rotation difference for an A-nor-ketone derived from friedelin is negative whereas for an analogous compound from lanosterol it is positive.

The conclusion that, in ring A, friedelane is a " skeletal enantiomorph " of the 5α-steroids and the usual triterpenes rationalises the stereochemical course of reduction of its 3-oxo-derivatives. We have had occasion to reduce four such derivatives (friedelin, friedelane-3 : *x*-dione, friedelane-3 : *y*-dione, and friedelane-3 : *x* : *y*-trione) with sodium borohydride and in all cases the axial (3β-)alcohol was formed in predominant amount; in the last two cases the equatorial (3α-)alcohol was not detected. It is well established that reduction of the 3-oxo-group in 5α-steroids and in triterpenes of the type (III) with sodium borohydride (or lithium aluminium hydride) yields mainly the equatorial (3β-)-alcohol [7] and it seems likely, at least with the triterpenes, that the β-orientation of the hydroxyl group in the reaction product is determined by rear (α) attack of the reagent.[8] This would be the determining factor also in the friedelan-3-one series, again causing β-orientation in the reaction product. That friedelan-3β-ol and its congeners have the axial rather than the equatorial configuration is a consequence of the " skeletal enantiomorphic " nature of friedelane * and is presumably not relevant to the course of the reaction. Reduction of friedelan-3-one with lithium aluminium hydride [1a, b] and by hydrogenation (in acetic acid solution) [9] also yields friedelan-3β-ol.

The 3-oxo-group is somewhat more hindered in the friedelane series than in the usual triterpenes : thus 3-ketones of the latter type give a positive Zimmermann colour test [10] whereas friedelan-3-one does not; it does, however, form a semi-carbazone. It is possible, but seems unlikely, that the course of reduction is not determined by rear attack in the case of the usual triterpene 3-ketones but is so determined in the case of the friedelan-3-ones.

EXPERIMENTAL

Analyses by Dr. E. Challen and Mr. D. Weedon. Infrared spectra by Mr. I. Reece.

General experimental conditions are given in Part I.[4] Fraction numbers refer to the chromatogram of the triterpene mixture described in Part I.

x[*ax*]-*Hydroxyfriedelan*-3-*one*.—By virtue of its low solubility in alcohol, x[*ax*]-*hydroxyfriedelan*-3-*one* (2·3 g.) was isolated from fractions 30—35. It crystallised from benzene in tetrahedra, m. p. 272—275°, $[\alpha]_D$ −15° (*c* 2·2) (Found : C, 81·5; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The *acetate* formed needles (from alcohol), m. p. 265—270°, $[\alpha]_D$ −12°

* If bonds at corresponding carbon atoms in the two " skeletal enantiomorphs " are to have the same orientation (α or β) they must necessarily have different configurations (axial or equatorial). Orientation, in the sense used here, does not necessarily have any absolute significance but is defined by the direction of the exocyclic bond at $C_{(10)}$ which is α in the friedelane series [1a] and β in the series represented by structures (II) and (III).

(*c* 2·9) (Found : C, 79·3; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The *semicarbazone* formed laths (from alcohol–benzene), m. p. 322—327° (decomp.; frothing at 281—284°) (Found : C, 72·7; H, 10·9; N, 7·9. $C_{31}H_{53}O_2N_3,C_2H_5{\cdot}OH$ requires C, 72·6; H, 10·9; N, 7·7%).

When oxidised with chromium trioxide in pyridine it yielded friedelane-3 : *x*-dione, m. p. 250—252°, $[\alpha]_D$ +116° (*c* 2·5).

x[*eq*]-*Hydroxyfriedelan*-3-*one*.—Fractions 36—39 were combined with the alcohol-soluble material from fractions 40—43 and recrystallised repeatedly from alcohol, yielding x[*eq*]-*hydroxyfriedelan*-3-*one*, needles, m. p. 264—268°, $[\alpha]_D$ −32° (*c* 2·6) (Found : C, 81·2; H, 11·25%). An additional amount was obtained by chromatography of the material from the mother-liquors (total, 3·8 g.). The *acetate* formed needles (from alcohol), m. p. 236—238°, $[\alpha]_D$ −40° (*c* 2·2) (Found : C, 79·1; H, 10·8%). The *semicarbazone* formed needles (from aqueous alcohol), m. p. 259—262° (decomp.) (Found : C, 74·7; H, 10·7; N, 8·2. $C_{31}H_{53}O_2N_3$ requires C, 74·5; H, 10·7; N, 8·4%).

When oxidised with chromium trioxide in pyridine it yielded friedelane-3 : *x*-dione, m. p. 248—252°, $[\alpha]_D$ +114° (*c* 1·8).

y-*Hydroxyfriedelan*-3-*one*.—This compound was not detected in the present separation but was obtained in small amount in the separation of another batch of the triterpene mixture. It was eluted from alumina after *x*[eq]-hydroxyfriedelan-3-one and crystallised from benzene in laths, m. p. 305—308°, $[\alpha]_D$ −20° (*c* 0·5; 2 dm. tube). It was identical (infrared spectra and mixed m. p.) with the product prepared from friedelane-3 : *x* : *y*-trione (Part I).[4]

x[*eq*]-*Hydroxyfriedelane*-3 : y-*dione*.—By virtue of its low solubility in alcohol x[*eq*]-*hydroxy-friedelane*-3 : y-*dione* (7 g.) was isolated from fractions 40—44. It crystallised from benzene in prisms, m. p. 289—292°, $[\alpha]_D$ −72° (*c* 2·0) (Found : C, 79·0; H, 10·5. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The *acetate* formed needles (from alcohol), m. p. 276—278°, $[\alpha]_D$ −69° (*c* 1·2) (Found : C, 76·8; H, 10·0. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%). The *monosemi-carbazone* crystallised from alcohol in plates, m. p. 282° (decomp.) (Found : C, 70·7; H, 9·95; N, 7·9. $C_{31}H_{51}O_3N_3,C_2H_5{\cdot}OH$ requires C, 70·8; H, 10·25; N, 7·5%).

When oxidised with chromium trioxide in pyridine it yielded friedelane-3 : *x* : *y*-trione, m. p. 300—303°, $[\alpha]_D$ +70° (*c* 1·2).

y-*Hydroxyfriedelane*-3 : x-*dione*.—This compound could not be obtained pure in the present separation although it was present in considerable amount in fractions 46—53. From chromatography of a previous batch of the triterpene mixture (which had been extracted from the bark with light petroleum and probably did not contain the polyhydroxy-triterpenes which interfere with the purification) a fraction was obtained with $[\alpha]_D$ +94° (corresponding in position to fractions 46—53 in the present chromatogram). Rechromatography of this material (1·4 g.) over alumina (100 g.) and recrystallisation of the higher fractions from alcohol yielded y-*hydroxy-friedelane*-3 : x-*dione* in needles, m. p. 304—310° (decomp.), $[\alpha]_D$ +109° (*c* 2·4) (Found : C, 78·9; H, 10·6%). The *acetate* formed rods (from methyl alcohol), m. p. 205—207°, $[\alpha]_D$ +88° (*c* 1·6) (Found : C, 77·1; H, 9·8%). The *monosemicarbazone* was obtained microcrystalline from aqueous alcohol, with m. p. 270° (decomp.) (Found : C, 70·5; H, 10·1; N, 7·9. $C_{31}H_{51}O_3N_3,C_2H_5{\cdot}OH$ requires C, 70·8; H, 10·25; N, 7·5%).

When oxidised with chromium trioxide in pyridine it yielded friedelane-3 : *x* : *y*-trione, m. p. 300—303°, $[\alpha]_D$ +65° (*c* 0·7; 2 dm. tube).

Reduction of Friedelan-x-*one*.—(*a*) Sodium (2 g.) was added to a boiling solution of friedelan-*x*-one (0·5 g.) in pentyl alcohol (25 ml.); when the reaction was complete the alcohol was removed with steam. The product was chromatographed over alumina (50 g.) from solution in 3 : 1 light petroleum–benzene. Elution with benzene yielded *friedelan*-x[*eq*]-*ol* (0·4 g.), needles (from *cyclo*hexane), m. p. 261—264°, $[\alpha]_D$ +12° (*c* 0·8; 2 dm. tube) [Found (after vacuum-sublimation) : C, 84·3; H, 12·3. $C_{30}H_{52}O$ requires C, 84·05; H, 12·2%]. The *acetate* formed prisms (from alcohol–chloroform), m. p. 239—242°, $[\alpha]_D$ +5° (*c* 1·1) (Found : C, 81·8; H, 11·6. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%).

(*b*) A solution of friedelan-*x*-one (0·7 g.) in benzene (25 ml.) was added to a suspension of lithium aluminium hydride (2 g.) in ether (60 ml.), and the boiling mixture was stirred under reflux for 8 hr. and then poured into ice-cold 3N-sulphuric acid. Recrystallisation of the product from alcohol–benzene yielded *friedelan*-x[*ax*]-*ol*, plates, m. p. 276—279°, $[\alpha]_D$ +26° (*c* 1·4) (Found : C, 83·8; H, 12·0%). The *acetate* formed plates, m. p. 258—261°, $[\alpha]_D$ +24° (*c* 0·6; 2 dm. tube), from alcohol–benzene (Found : C, 81·9; H, 11·7%).

Reduction of Friedelan-y-*one*.—(*a*) Reduction of friedelan-*y*-one (1 g.) with sodium and pentyl alcohol and purification of the product as described above yielded friedelan-*y*-ol (0·75 g.), m. p. 224—226°, $[\alpha]_D$ +23° (*c* 1·4).

(*b*) Reduction with lithium aluminium hydride as described above also yielded friedelan-*y*-ol, m. p. 224—226°, $[\alpha]_D$ +21° (*c* 1·6).

Huang-Minlon Reduction of x[*ax*]-*Hydroxyfriedelan*-3-*one*.—A solution of *x*[ax]-hydroxyfriedelan-3-one (2·15 g.), potassium hydroxide (1·4 g.), and hydrazine hydrate (4 ml. of 100%) in diethylene glycol (20 ml.) was refluxed for 1½ hr. Hydrazine hydrate was then removed by distillation and the mixture was kept at 200° for 4 hr. The product, isolated from the acidified mixture with chloroform, was dissolved in 3 : 1 light petroleum–benzene and chromatographed over alumina (60 g.). Elution with the same solvent gave friedelan-*x*[ax]-ol (1·7 g.), m. p. 276—279°, $[\alpha]_D$ +26° (*c* 1·1).

Wolff–Kishner Reduction of x[*eq*]-*Hydroxyfriedelane*-3 : y-*dione*.—A mixture of *x*[eq]-hydroxyfriedelane-3 : *y*-dione (2 g.), anhydrous hydrazine (13 ml.), and a solution of sodium (4·9 g.) in methyl alcohol (70 ml.) was heated at 200° for 16 hr. The product, isolated with chloroform after the mixture had been acidified, was chromatographed in 3 : 1 light petroleum–benzene over alumina (75 g.). Elution with benzene yielded friedelan-*x*[eq]-ol (1·7 g.), m. p. 260—262°, $[\alpha]_D$ +10° (*c* 1·2).

Reduction of Friedelin with Sodium Borohydride.—Friedelin (7 g.) was dissolved in hot pyridine (250 ml.), and the cooled solution was added to a solution of sodium borohydride (2·1 g.) in methyl alcohol (150 ml.) containing N-sodium hydroxide (1 ml.). The mixture was left for 2 days and then acidified. The product, isolated with chloroform, was chromatographed in benzene over alumina (700 g.) to give 8 fractions. Fractions 1 and 2 (2·0 g.) consisted entirely, and fractions 3 and 4 (1·15 g.) mainly, of friedelin. The infrared spectra of fractions 5—7 were identical; they were combined (2·64 g.) and recrystallised from benzene, yielding *epi*friedelinol, plates, m. p. 280—282°, $[\alpha]_D$ +21° (*c* 0·7; 2 dm. tube). The acetate crystallised from alcohol–benzene in plates, m. p. 290—293°, $[\alpha]_D$ +36° (*c* 1·1). The infrared spectrum of fraction 8 (0·94 g.) indicated that it consisted mainly of friedelinol, an authentic specimen of which was prepared by reduction of friedelin with sodium and pentyl alcohol, having m. p. 303—306°, $[\alpha]_D$ +16° (*c* 0·4; 2 dm. tube). The acetate had m. p. 316—318°, $[\alpha]_D$ −21° (*c* 1·1). Drake and Campbell [11] record m. p. 301—304° and for the acetate m. p. 315—316°.

Reduction of Friedelane-3 : y-*dione with Sodium Borohydride*.—Reduction of friedelane-3 : *y*-dione (5 g.) and chromatography of the product (8 fractions) was carried out as described for friedelin. Fractions 1—4 (2·0 g.) consisted mainly of starting material. Fractions 4—8 (2·2 g.) all had the same infrared spectra and were combined and recrystallised from alcohol, yielding 3β-*hydroxyfriedelan*-y-*one*, prisms, m. p. 319—322°, $[\alpha]_D$ −32° (*c* 1·1) (Found: C, 81·2; H, 11·3%). The *acetate* formed needles, m. p. 329—333°, $[\alpha]_D$ −20° (*c* 1·1), from alcohol–benzene (Found: C, 79·6; H, 10·9%).

Reduction of Friedelane-3 : x : y-*trione with Sodium Borohydride*.—The reduction and the chromatography of the product were carried out as described for friedelin. Chromatographic separation was not successful, consequently the product was fractionally crystallised from benzene and then from alcohol, yielding 3β-*hydroxyfriedelane*-x : y-*dione*, prisms, m. p. 314—318°, $[\alpha]_D$ +107° (*c* 1·1) (Found: C, 78·8; H, 10·7%). The *acetate* formed plates (from alcohol), m. p. 321—325°, $[\alpha]_D$ +113° (*c* 1·1) (Found: C, 76·9; H, 10·0%).

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AN INTERMEDIATE IN THE FRIEDELENE-OLEANENE REARRANGEMENT

By J.L.Courtney, R.M.Gascoigne and A.Z.Szumer.

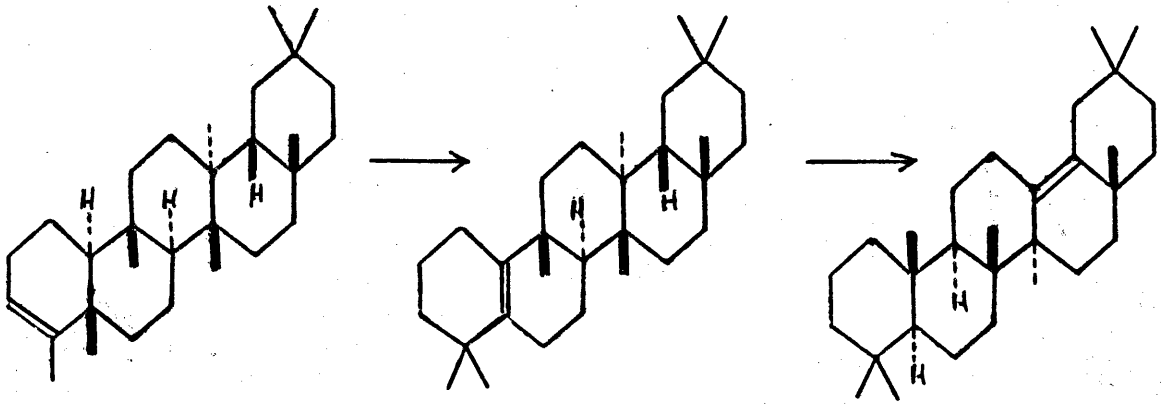
The acid-catalysed rearrangement of friedel-3-ene (I) to an equilibrium mixture of olean-13(18)-ene (III) and 18α-olean-12-ene[1,2,3] has been generally thought to be a fully concerted rearrangement. However, when friedel-3-ene, in boiling glacial acetic acid solution, is treated with a stream of hydrogen chloride for one hour it is converted in good yield into a hydrocarbon, m.p. 226-227°, $[\alpha]_D$ -42° (all rotations in chloroform) (Found: C, 87.7; H, 12.1. Calc. for $C_{30}H_{50}$: C, 87.7; H, 12.3%). This compound, in turn, is converted by a boiling mixture of acetic and hydrochloric acids into the equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene isolated as the mixed crystal, m.p. 186-187°, $[\alpha]_D$ -15°, identical with a specimen prepared directly from friedel-3-ene by use of the same conditions.

The hydrocarbon, m.p. 226-227°, is thus an intermediate in the friedelene-oleanene rearrangement. It is identical (infrared spectra and mixed m.p.) with the hydrocarbon, m.p. 221-222°, obtained by Corey and Ursprung[2] from Wolff-Kishner reduction of a ketonic product resulting from dehydrobromination of 4-bromofriedelin. (We are indebted to Dr. E.J.Corey for a specimen of his hydrocarbon). Corey and Ursprung

formulate the ketonic product with a trisubstituted double bond as in (IV); however, the infrared spectrum of the hydrocarbon exhibits no absorption typical of unsaturation thus indicating that the double bond is tetrasubstituted as in (II).

Recently Spring, Beaton, Stevenson and Stewart[4] have established the constitution (IV) of the naturally-occurring ketone alnusenone (glutinone); They found that the ketonic product obtained by dehydrobromination of 4-bromofriedelin is a mixed crystal consisting of alnus-5-en-3-one (IV) and alnus-5(10)-en-3-one (V) in the ratio 1:2. Previously, Chapon[5] had observed that the latter ketone can be obtained from the former (alnusenone) by relatively mild treatment with mineral acid and had reduced it by the Wolff-Kishner method to a hydrocarbon, m.p. 226°, $[\alpha]_D$ -38°, which must be alnus-5(10)-ene (II). The hydrocarbon now obtained by isomerisation of friedel-3-ene is undoubtedly identical with this compound; a number of oxidation reactions, to be described in full later, confirm the structure (II).

Since alnus-5(10)-ene exists as an isolable intermediate in the friedelene-oleanene rearrangement (at least in the conditions used here) no definite conclusions can be drawn from the rearrangement concerning the configurations of $C_{(5)}$ and $C_{(10)}$ in the friedelane structure. The absolute configurations of these centres have however been established



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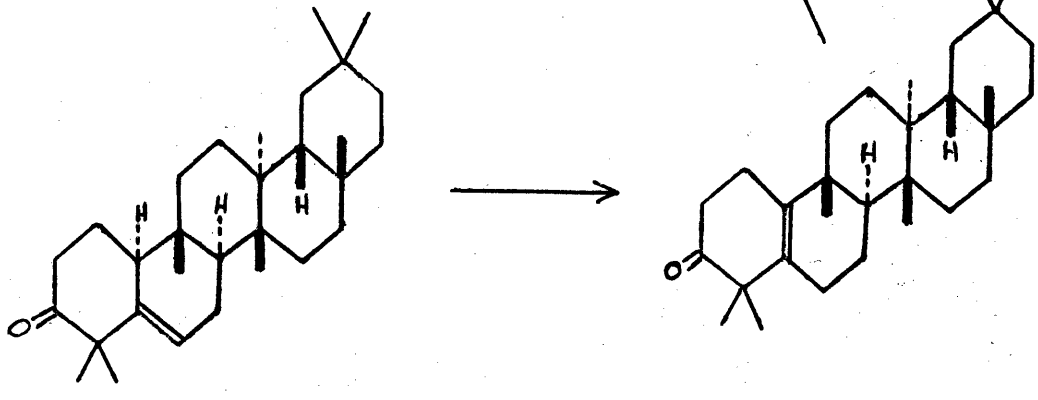

IV V

from other considerations.[2,6]

The driving force for the friedelene-oleanene rearrangement has been attributed to steric congestion in the ring E area of friedelene occasioned by the (postulated) cis-fusion of rings D and E.[1] No doubt this is the cause of the final stage of the rearrangement but it is now apparent that it cannot be the cause of the initial stage, i.e. the friedelene-alnusene rearrangement. In this case the conformational driving force is presumably due to the proximity (1:3 interaction) of the axial methyl groups at $C_{(5)}$ and $C_{(9)}$ (also the group at $C_{(14)}$) in friedelene (I).

Investigation of other intermediates in the friedelene-oleanene rearrangement is in progress.

Added in Proof:- Treatment of friedel-3-ene or alnus-5(10)-ene, in boiling glacial acetic acid solution, with hydrogen chloride for seven hours yields olean-12-ene, m.p. 160-161°, $[\alpha]_D$ +96°. This conversion establishes that the configuration of $C_{(18)}$ in friedelane is the same as in oleanane and that the D/E ring junction is cis.

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