STUDIES IN SOME TRITERPENOIDS

THESIS

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INTRODUCTION
INTRODUCTION

The triterpenes\(^{(1)}\) have been defined as a class of natural products containing thirty carbon atoms divisible into isoprene units. This divisibility into isoprene units, and their head to tail union, may conveniently be referred to as isoprene rule. This rule, which has several exceptions, can only be used as a guiding principle and not as a fixed rule.

Triterpenes are very widely distributed in the vegetable kingdom; their occurrence in the animal kingdom is, however, much more limited. Conforming to the isoprene rule we have in the animal kingdom the acyclic hydrocarbon, squalene (VII) and the alcohol am\^{}rein (VIII), whilst in wool fat the alcohols, lanosterol (of XII) and agnosterol\(^{(2)}\) which do not conform to the rule. Ruzicka prefers to regard these alcohols, the ketone cycloartenone\(^{(3)}\) and the related secondary alcohol, cycloartenol\(^{(4)}\) as C\(_{30}\) steroids. But they are more logically included in the triterpene series. In plants the triterpenes have been found to occur in all parts of the plant, in the free state and in combination with sugars as glycosides and with acids as esters. One widely distributed group is the saponins which yield on acid hydrolysis their aglycones, the sapogenins.
Isolation of a crude specimen of triterpene is an easy task; but the purification is a process which has to be tailored to individual cases according to the nature of impurities present. Usually, triterpenoids are extracted with petroleum ether or alcohols and then purified by a particular method such as fractional crystallization, chromatography, sublimation, or acetylation followed by deacetylation. Very often a combination of two or more methods may be necessary. The homogeneity of a triterpene may be tested by paper chromatography or thin layer chromatography (TLC).

Although triterpenes were isolated very early in the study of plant materials, it is only within the last three decades that their structures have been determined. Prior to this many triterpenes had been characterized and their degradation products investigated but knowledge of their carbon skeleton was completely lacking. The experimental difficulties encountered in the study of triterpenes were also considerable. Their tendency to crystallize with the solvent of crystallization made the determination of their composition difficult, whilst the ethylenic linkage, which was present in the majority of them, was inert and its presence could only be shown, in the earlier investigation, by colour reactions with tetranitromethane.
In 1929 Ruzicka, Huyser, Pfeiffer and Seidel reported the dehydrogenation of a mixture of \( \alpha \)- and \( \beta \)-amyrins with sulphur when they obtained a trimethyl naphthalene. But the structure of this hydrocarbon was not determined until 1933, when Ruzicka and Ehmann showed by its synthesis that it was 1,2,7-trimethylnaphthalene. Its isolation stimulated further investigations of fundamental importance in this field of research. Detailed studies in triterpenoids have been carried out by Noller, Marker, Djerassi, Wall etc., in U.S.A., Barton, Spring, Halsall etc., in England, Tschesche, Hagedorn etc., in Germany, Sannie, Lapin, Lederer, Ourisson, etc., in France, Ruzicka and Jeger in Switzerland and Kitasato in Japan.

Systematic chemical investigation of Indian medicinal plants was undertaken as it afforded a wide scope for isolation and characterisation of several interesting plant products which could also possess marked biological activity. Moreover, only very few of the innumerable Indian plants have so far been properly investigated.

This thesis records studies in some pentacyclic triterpenoids isolated from Anisomeles malabarica (R.Br.), Vallaris
solanacea (Ktze), Glochidion hohemackeri (Bedd) and Asterolcantha longifolia (Nees.) belonging to the families Labiatae, Apocynaceae, Euphorbiaceae and Acanthaceae respectively.
THEORETICAL
THEORETICAL

Constitution:

The initial breakthrough as regards the constitution was achieved by dehydrogenation experiments of Ruzicka. Of the various methods of dehydrogenation using zinc, sulphur, selenium and palladised carbon, selenium dehydrogenation was found to lead to better yields and involved fewer side reactions, inspite of the use of high temperatures (320-350°). In utilizing dehydrogenation products for the determination of the carbon skeleton of the triterpenes, Ruzicka made two primary assumptions, (i) that they followed the isoprene rule and (ii) that their colour reactions with tetranitromethane indicated unsaturation. In support of the first assumption Ruzicka pointed to the analogy with the monocyclic terpenes, e.g. (I), the sesquiterpenes, e.g. (II) and the diterpenes, e.g. (III).
On the basis of dehydrogenation studies triterpenoids and steroids could also be distinguished. The former yield principally sapotalene (1,2,7-trimethyl naphthalene, IV) or 1,8-dimethyl picene (V) and the latter Diel's hydrocarbon (3'-methyl 1,2-cyclopentenophenanthrene VI). Even though the dehydrogenation studies provide a fool proof method of classification of the triterpenoids and steroids, the large quantity of material necessary, the low yield of hydrocarbons and the difficulty of separating them makes this method less attractive. Hence the following methods have also been used to differentiate between the two classes.

1. Colour reactions.

Colour reactions

Some of the colour reactions cited below can be carried out on filter paper as well and hence can be used in paper chromatography.

(i). Liebermann - Burchard reaction

A solution of the substance in cold acetic anhydride is treated with a few drops of conc. sulphuric acid; the substance is dissolved in chloroform and treated with acetic anhydride and sulphuric acid. It gives crimson, violet, blue and green colours. The triterpenes give green colour directly or through crimson, violet and blue colours.

(ii). Holler reaction \(^{(7,8)}\)

0.2 g of the substance with 0.5 ml of the reagent (0.01% pure stannic chloride in pure thionyl chloride) is kept corked in a test tube for several hours. A series of shades run through but red persists. Oxyacids containing at least one free hydroxyl group give a dark positive colouration. This reaction is highly specific for triterpenes.

(iii). Zimmerman reaction \(^{(9)}\)

An alcoholic solution of a keto steroid with meta dinitro-benzene in caustic potash gives a violet colour and is characteristic of a 3-keto group. 17-keto steroids also answer this test but is negative when the ketogroup is at 6,7 or 12
positions. Only 3-keto triterpenes give a positive reaction\(^{(10)}\). 1,3-dinitronaphthalene has also been used in which case steroids give a red colour\(^{(11)}\).

**Molecular rotation** :

Though the determination of the rotation of optically active compounds have been practised for very many years, it is only within the last 15 years or so that it has been realised that such values are a source of much information. Callow and Young\(^{(12)}\) first observed that all naturally occurring sterols having a double bond at the 5:6 position are laevorotatory. They also noted that the presence of a double bond at 4:5 positions increased dextro rotation. The applications of this method were further extended by Wallis and collaborators\(^{(13)}\) and finally Barton\(^{(14)}\) developed a method by which rotation became an important tool in the elucidation of the structure of steroids and triterpenes. An examination of the molecular rotation data of the steroids and triterpenoids revealed that there is a well defined and characteristic difference in the molecular
rotation values of the two groups of compounds\textsuperscript{(15)}. This
difference is attributed to the presence of the gem dimethyl
group at C\textsubscript{4} in the triterpenes.

Comparison of molecular rotation differences for many
olefinic, ketonic and conjugated groups in the two series shows
that, in all but two cases the $\Delta$ values in the triterpenoid
series are of the sign which would be predicted from the
known $\Delta$ values for steroids. Often the $\Delta$ values in the two
series are of the same order of magnitude. It was found that
the triterpene carboxylic acids and their methyl esters have
practically same molecular rotations\textsuperscript{(16)}.

A simple and direct application of this has been the
classification of cycloartenol as a triterpene, which was
previously believed to be a steroid\textsuperscript{(16)}. There is at present
no explanation for the anomalous $\Delta$ values for 11- and 12-keto
triterpenoids.
Classification of triterpenes:
The triterpenes can be classified into the following four groups:

1. Acyclic
2. Tricyclic
3. Tetra cyclic
4. Penta cyclic

Acyclic triterpenes:
Squalene, initially isolated from shark liver oil, is the only member of this group.

Tsujiimoto\(^{(17)}\) suggested an acyclic structure for squalene on the basis of the presence of six ethylenic linkages as indicated by catalytic hydrogenation. Heilbron and collaborators\(^{(18)}\) showed it to be a derivative of isoprene and gave a conclusive proof of its structure (VII).

\[ \text{(VII)} \]
The gross constitution of squalene was proved by synthesis by Karrer and Helfenstein (19).

**Tricyclic Triterpenes:**

Ambrein (VIII) the sole member of this group was first isolated from ambregris. Ruzicka and collaborators (20) as the result of extensive experimentations have characterised it as a triterpene alcohol containing two double bonds which are not conjugated and a tertiary hydroxyl group.

Oxidation of ambrein with ozone gave a lactone (IX), a diketone (I) and formic acid, the latter suggesting the presence of an oxomethylene group. The lactone ambreinolide (IX)

was found to be identical with the lactone obtained from manool by permanganate oxidation followed by potassium bromite oxidation and lactonisation (21). Later, from amongst the permanganate oxidation products of ambrein a C$_{15}$ hydroxy acid was isolated which was converted to an acid, (XI) earlier obtained from oleanolic acid (22).
The correlation of these results led to the structure of ambrein as (VIII).

**Tetracyclic triterpenes:**

This group consists of several C-30 alcohols and C-31 acids. The two main families in this group of compounds are lanosterol and euphol. Most of the members of this group are similar in structure and the main points of difference lie in their stereochemistry. Thus lanostane (XII) and euphane (XIII) series differ in the stereo-chemistry of the fusion of the ring C and D (C-13 and C-14) and in the configuration of the side chain.

**Lanostadienol (lanosterol):**

Perbenzoic acid titration indicated the presence of two double bonds in lanostadienol (23) and this coupled with the
molecular formula $C_{30}H_{50}O$ readily suggested a tetracyclic formulation. Selenium dehydrogenation of lanostadienol led to 1,2,8-trimethylphenanthrene (XIV) as the main product\(^{(24)}\).

![Diagram](XIV)

The oxygen function was identified as a secondary alcohol by oxidation to a ketone. Catalytic hydrogenation of lanostadienol gave only a dihydroderivative indicating the difference in nature of the two double bonds present in the molecule.

The dehydration of lanostenol (XV) with phosphorous pentachloride\(^{(25)}\) yielded a doubly unsaturated hydrocarbon, characterised as isolanostadiene (XVI). This rearrangement

![Diagram](XIV) → ![Diagram](XVI)
is analogous to that in pentacyclic triterpenes, which carry a hydroxyl group adjacent to the carbon carrying the gem dimethyl group. Thus, by analogy, ring A can be pictured as carrying a hydroxyl group at position 3 and a gem dimethyl group at position 4.

The infra red spectra suggested the inert double bond to be tetra substituted\(^{(26)}\), which was further confirmed by selenium dioxide oxidation of lanosteryl acetate (XVII) to a heteroannular diene (XVIII) showing the characteristic ultraviolet absorption. The study of the oxidation products of lanosteryl acetate finally fixed the position of the double bond at C\(_{8-9}\)\(^{(27)}\).

The formation of 1,2,8-trimethyl phenanthrene (XIV) by selenium dehydrogenation, coupled with the fact that the
hydrocarbon lanostene (XIX) gave a greater yield of
1,2,8-trimethyl phenanthrene than did the corresponding
alcohol, fixed the positions of the angular methyl groups
at C-13 and C-14. These evidences led to a partial structure
of lanostadienol (XX) indicating the points of attachments
of ring D. The size of the ring D was proved to be five
membered by a study of the ketone formed by the complete
removal of the side chain\(^{(28,29)}\).

Vigorous oxidation of lanostenyl acetate yielded 6-methyl
heptan-2-one as one of the products, showing thereby that the
side chain comprised of eight carbon atoms. The isolation
of acetone as one of the oxidation products of lanostadienol
derivatives carrying the reactive double bond indicated the
presence of an isopropylidene group\(^{(30)}\). The final picture
of the side chain (XXI) was provided by Ruzicka and
Collaborators\(^{(31)}\) who carried out a stepwise degradation
of the side chain and found the arrangement to be identical
with the arrangement in cholesterol. A detailed degradation
study of the C-27 acid (XXII), by them\(^{(32)}\) led to the

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} & \quad \text{H} \\
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{H} \\
\text{H} & \quad \text{H} & \quad \text{H} & \quad \text{H} \\
\end{align*}
\]

(XXI)
ABSTRACT

of "Studies in some Triterpenoids"

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ABSTRACT

Anisomeles malabarica R. Br. (Labiatae)

An unsaturated monobasic hydroxy acid of the triterpene series, isolated from hot petroleum ether extract of the air-dried powdered plant has been shown to be identical with betulinic acid. The identity of the product has been confirmed by comparison of its derivatives namely the acetyl, the methyl ester and the acetyl methyl ester. Also its reduction product (betulin) with lithium aluminium hydride and an oxidation product (~an α,β-unsaturated aldehyde) with selenium dioxide in glacial acetic acid have been prepared and their melting points, elemental composition and spectroscopic data were verified.

Vallaris solanacea o.ktze (Apocynaceae)

From the cold ethanol extract of the air-dried leaves of this plant another known triterpene has been isolated and characterised as ursolic acid. The identity was established by comparing the melting points, elemental compositions and spectroscopic details of its derivatives.

Glochidion hohenackeri Bedd. (Euphorbiaceae)

The bark and root of this plant were examined. The hexane extract of the bark yielded a gum which on acetylation followed by chromatography over neutral alumina gave three crystalline compounds, glochidone, 3-epilupeol acetate and glochidiol diacetate. From the roots of the plant glochidiol and glochidone were obtained. The structure of these two new triterpenes have been established by relating them to a known compound, lupan-3-one.
The stereochemistry of the hydroxyl groups in glochidiol has also been determined by the partial synthesis of three of the four possible stereoisomers of the dihydrodiol diacetate (CXII, CXIII and CXIV) which all differ from dihydroglochidiol diacetate (CXVIII).

_Asteranthra longifolia_ Hees. (Syn. Hygrophila spinosa T. Anders (Acanthaceae)

Lupeol has been isolated from the hexane extract of this plant and in an attempt to modify its structure to induce biological activity, oxidation in ring A in lupeol has been studied. Lupeone and lupanone on autoxidation yielded the corresponding diophenols. Catalytic hydrogenation of the diophenol from lupanone yielded a ketoalcohol which when acetylated, rearranged to lupan 3-acetoxy 2-one.

Diosphenol from lupanone when ozonised and worked up with sodium bicarbonate and hydrogen peroxide gave a neutral compound C_{29}H_{48}O_{3} which has no selective absorption in the U.V., \( \nu_{\text{max}} \) 3600 cm\(^{-1}\) (OH), 1730 cm\(^{-1}\) (\( \delta \)-lactone). Based on its mode of formation, spectral characteristics and elemental composition, it has been assigned structure (CCXVIII).

In another series of reaction diophenol from lupeone was cleaved by alkaline hydrogen peroxide to a dicarboxylic acid (CCXIX), C_{30}H_{48}O_{4} the methyl ester of which on refluxing with alcoholic alkali yielded a nor-ketone (CCXII), C_{29}H_{46}O in excellent yield, \( \nu_{\text{max}} \) 1740 cm\(^{-1}\) (cyclopentanone).
conclusion that the point of attachment of the side chain is at C-17. Just before this final chemical evidence of the position of the side chain was put forward by Ruzicka the complete structure and stereochemistry of lanostenol (XXIII) was determined by X-ray diffraction analysis\(^{(33)}\) of lanostanyl iodoacetate. The conclusive proof of the constitution and stereochemistry of lanostadienol was provided by the conversion of cholesterol to 14-methyl cholestanol\(^{(34)}\) which was also obtained from lanosterol and lanostanol\(^{(35)}\).

\(\alpha\)-O nocerin (XXIV) is a novel tetracyclic triterpenoid.

Pentacyclic triterpenes:

The classification of pentacyclic triterpenes is based on three different types of hydrocarbons, (1) Oleanane (XXV), (2) Ursane (XXVI) and (3) Lupane (XXVII) and are accordingly
classified to belong to (1) $\beta$-amyrin, (2) $\alpha$-amyrin and (3) lupeol respectively.

This classification stands good with respect to the reactivity of double bond also. To facilitate the classification of a new triterpene certain diagnostic reactions have been devised (Table I). However, these reactions are not strictly followed in all cases. Thus dumortierigenin, a member of the $\beta$-amyrin group does not react with selenium dioxide to form 11, 13 diene and $\alpha$-amyrone oxide is formed by the action of perbenzoic acid on the corresponding olefin. Also the results obtained from the reactions involving N-bromosuccinimide have been questioned and it has been suggested that this reaction is very much dependent on the reaction conditions employed. Thus, in general, a triterpene belonging to any of these groups will be found to respond to a majority of the specific tests listed.
### Table I

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Oleanane</th>
<th>Ursane</th>
<th>Lupane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bromine (on a compound with COOH at C-17)</td>
<td>12-Bromo-lactone</td>
<td>No appreciable bromolactone</td>
<td>Brominated product.</td>
</tr>
<tr>
<td>2. Catalytic hydrogenation</td>
<td>--</td>
<td>--</td>
<td>Double bond reduced.</td>
</tr>
<tr>
<td>3. Cold perbenzoic acid</td>
<td>12,13 oxide which readily isomerises to the 12 ketone</td>
<td>12,13 oxide which readily isomerises to the 12 ketone</td>
<td>20, 29 oxide</td>
</tr>
<tr>
<td>4. Ozone</td>
<td></td>
<td>12,13 oxide which readily isomerises to the 12 ketone</td>
<td>29 nor ketone</td>
</tr>
<tr>
<td>5. SeO₂ in HAC</td>
<td>11,13 (18) diene</td>
<td>--</td>
<td>Unsaturated aldehyde</td>
</tr>
<tr>
<td>6. N-bromo-succinimide</td>
<td>9(11),12,18 triene</td>
<td>9(11), 12 diene</td>
<td>**</td>
</tr>
<tr>
<td>7. Strong acid conditions</td>
<td>Migration of double bond to 13 (18) or 18 isolactone</td>
<td>--</td>
<td>Expansion of ring E.</td>
</tr>
</tbody>
</table>

*Ozone is seldom used in the oleanane series where the milder perbenzoic acid is preferred.

**No sufficient data.
Determination of the carbon skeleton

The determination of the carbon skeleton is the first step in elucidating the structure of pentacyclic triterpenes. The dehydrogenation experiments with selenium have been of great value in fixing the carbon skeleton of this type of compounds\(^{40}\). Pentacyclic triterpenes undergo rupture during dehydrogenation and only a minor quantity of aromatic products characteristic of the skeleton are formed.

The usual dehydrogenation products of pentacyclic triterpenes are the following:

1) 1,2,3,4-tetramethyl benzene (XXVIII)
2) 2,7-dimethyl naphthalene (XXIX)
3) 1,2,7-trimethyl naphthalene (XXX)
4) 1,2,5,6-tetramethyl naphthalene (XXXI)
5) 6-hydroxy-1,2,5-trimethyl naphthalene (XXXII)
6) 1,8-dimethyl picene (XXXIII)
7) 2-hydroxy-1,8-dimethyl picene (XXXIV)
Formation of these products from \( \beta \)-amyrin can be shown as above. The origin of (XXVIII) and (XXXI) is believed to be due to the migration of one of the methyl groups by a Wagner-Meerwein shift from the geminal position to the adjacent hydroxyl at position 3.
The β-amyrin group:

A clear picture of the chemistry of this group was obtained by studying the reactions of oleanolic acid (XXXV). The relative positions of the double bond and the carboxyl group in oleanolic acid was fixed initially. Then the oxidative degradation studies led to the constitution of the acid. Once the structure of the oleanolic acid was elucidated, the structures of other compounds were determined by transforming them into known compounds.

The double bond and the carboxyl group in oleanolic acid:

The nonformation of an ester by normal acid catalysed esterification and the difficulty in hydrolysing the methyl ester prepared by reacting the acid with diazomethane indicated the tertiary nature of the carboxyl group in oleanolic acid.

... /-
Positive tetranitromethane test and formation of an epoxide (XXXVI) which subsequently rearranges to a ketone (XXXVII) showed the presence of a double bond. Oleanolic acid acetate (XXXVIII) led to the formation of (XXXIX) a bromelactone and a ketolactone (XL) in reactions involving the double bond and the carboxyl group.
Ruzicka and collaborators located the double bond in ring C at C_{12-13} by a series of reactions involving the fission of ring C.

Acetyl derivative ofoleanolic acid (XXXVIII) on chromic acid oxidation gave a dihydroxy carboxylic acid (XLI) which on further oxidation yielded progressively a hydroxy lactone (XLII), a ketolactone (XLIII) and finally a lactone dicarboxylic acid (XLIV). The monomethyl ester (XLVI) of the derived ketodicarboxylic acid (XLV) was pyrolysed to yield a ketone (XLVII) and an ester (XLVIII).
The ketone (XLVII) on reduction gave a hydrocarbon (XLIX) which by selenium dehydrogenation yielded 1,6-dimethyl naphthalene (L).

The ester (XLVIII) was hydrolysed to an acid (LI) and the acid subjected to selenium dehydrogenation to yield 2,7-dimethyl-naphthalene (LII).

The dimethyl ester (LIII) of the keto dicarboxylic acid (XLV) was also pyrolysed to give two fractions, ketonic and non-ketonic. This ketene (LIV) on reduction gave an ester (LV), a substance
also obtained by the degradation of ambrein$^{(22)}$ (VIII). This established the structure of rings A and B of oleanolic acid.

The nonketonic fraction, considered to be a mixture of esters, was hydrolysed to the corresponding acids. These on selenium dehydrogenation gave 2,7-dimethyl naphthalene (LII). The structure of rings D and E was thus established.

The above mentioned reactions clearly showed that the double bond was present in ring C. The formation of lactones (XXXIX and XL) described earlier$^{(45)}$ confines the double bond to a $\beta$ or an $\gamma$ position with respect to the carboxyl group. $\beta$unsaturated acids undergo easy decarboxylation on pyrolysis with a shift of the double bond to the corresponding $\alpha,\beta$ position, and the absence of this type of decarboxylation indicated that the double bond was to the C-17 carboxyl group. On the basis of these studies structure (XXXV) can be assigned to oleanolic acid.

**Interconversions:**

After establishing the basic skeleton and structures of a few compounds belonging to this group by degradative methods, the structures of other new compounds could be easily determined by relating them with the known compounds.
Tomentosic acid (LVI, R = H) has recently been isolated from Terminolia tomentosa in which it occurs along with oleanolic acid, arjunolic acid (LVII) and baringtogenol (LVIII). Preliminary studies indicated that it belonged to \( \beta \)-amyrin group. Methyl tomento\( \beta \)ate (LVI, R = CH\(_3\)) and the anhydrolactone (LIX) readily gave isopropylidene derivatives, suggesting the presence of a 1,3-diol system. Copper pyrolysis yielded small amount of formaldehyde which confirmed the presence of a 3, 23-diol in the system\(^{(47)}\).
Periodic acid and leadtetraacetate oxidation of the methyl tomentosate and anhydrolactone require one mole of either reagent and it was presumed that it contains an α-glycol system\(^{48}\). The isopropylidene derivatives of both the compounds were inert to lead tetraacetate, which indicated that the remaining two hydroxyl groups were not present as α-glycol system and that one of the hydroxyls is common to α, β and to the 3, 23 diols. Hence, tomentosic acid must possess a 2α, 3β, 23(24) trihydroxy system as in arjunolic acid.

After establishing the relative positions of the two hydroxyl groups, attempts were made to relate tomentosic acid with arjunolic acid. Oxidation of 2-acetyl-3,23 isopropylidene methyl tomentosate (LX) gave a ketone (LXI). The ketone is then reduced by forced Wolf Kishner method, the isopropylidene group removed and the resulting product methylated to give methyl arjunolate (LXII).
This correlation left the position of one hydroxyl group to be fixed further in tomentosic acid. The ketone (LXI) was inert towards ketonic reagents showing that the keto-group is sterically hindered. The ketone also did not give a benzylidene derivative indicating the absence of a methylene group to the carbonyl.

Triacetyl methyl keto tomentosate (LXIII) isomerises in the presence of alkali to an $\alpha,\beta$-unsaturated ketone (LXIV) ($\lambda_{\text{max}}$ 248 m$\mu$) reminiscent of the isomerisation of 19-keto oleanolate (LXV) under the same conditions.
The facile dehydration of tomentosic acid (LVI, R = H) to give the anhydrolactone (LIX) could be expected only with hydroxyl groups at positions 6, 11 or 19. Tomentosic acid is not an epimer of terminolic acid (LXVI) and because the ketone (LXI) does not form a benzylidene derivative, the hydroxyl group cannot be at position 6 or 11. Thus the hydroxyl group should be at position 19\(^{(49)}\) which again relates tomentosic acid to siaresinolic acid (LXVII). If it were so, the 19-OH group should
undergo dehydration as in siaresinolic acid to give triacetyl-
methyl dehydroarjunolate (LXVIII)\(^{(50)}\).

\[ \text{POCl}_3/\text{pyridine dehydration of triacetyl methyl tomentosate (LXIX) did not give (LXVIII). However, treatment of the same (LXIX) with selenium dioxide in acetic acid led to (LXVIII).} \]

\[ \text{POCl}_3/\text{Pyridine} \]

Similar dehydration of the pentol tetraacetate (LXX) yielded tetraacetyl dehydrobarringtogenol (LXXI) also obtained by selenium dioxide dehydrogenation of barringtonol tetra-
acetate (LXXII).
The formation of dehydro arjunolate and dehydrobarringtogenol thus conclusively established the position of the fourth hydroxyl group. The failure of triacetyl methyl tomentosate to undergo dehydration to form (LXXII) indicated that the orientation of the OH group is different from that in siaresinolic acid, in which it is axial, trans to the $\beta$-hydrogen. Therefore the 19-OH in tomentosic acid must have the $\beta$-equatorial orientation. This led to the structure (LVI) for tomentosic acid.
Taraxerol (LXXIII)\(^{(51)}\), multiflorenol (LXXIV)\(^{(52)}\) and arundoin (LXXV)\(^{(53)}\) are three examples of few other penta-cyclic triterpenes which could be included in the \(\beta\)-amyrin group wherein double bonds and methyl groups have rearranged.

\begin{align*}
\text{(LXXIII)} & \\
\text{(LXXIV)} & \\
\text{(LXXV)} & 
\end{align*}

\(\alpha\)-amyrin group:

This group is comparatively small and only a few members are known. On the basis of the close resemblance of \(\alpha\) and \(\beta\) amyrins and the formation of identical products on dehydrogenation it was suggested that the two amyrins were stereoisomers\(^{(54)}\). But Ruzicka and collaborators\(^{(55)}\) proved by a series of reactions on \(\alpha\)-amyrin acetate, largely parallel to the reactions on oleanolic
acid described earlier, that the above suggestion was wrong. However molecular rotation studies\(^{(56)}\) indicated that ring A and B were similarly constituted in both \(\beta\) and \(\alpha\)-amyrins. It was also found that the molecular rotation values can be used to distinguish between the members belonging to the \(\beta\) and \(\alpha\)-amyridine groups on one hand and Lupeol on the other hand. Barton and Jones\(^{(16,56)}\) were the first to show that each of the three main groups of triterpenoids \(\alpha\)amyridine, \(\beta\)-amyridine and lupeol showed very characteristic rotation values for acetylation, benzoylation and oxidation at \(C_5\).

\(\alpha\)-amyridine acetate (LXXVI) was converted to the saturated ketone (LXXVII) by the action of formic acid and hydrogen peroxide or by the action of ozone followed by acid treatment.
The ketone on oxidation gave a dicarboxylic acid (LXXXVIII) which formed the dimethyl ester (LXXIX). On pyrolysis (LXXIX) yielded two products (LXXX) and (LXXXI). The ketonic fraction (LXXX) on reduction gave an ester (LXXXII) identical with that obtained by the degradation of oleanolic acid. This proved that rings A and B are similar in \( \alpha \) and \( \beta \)-amyrins.
The non-ketonic fraction (LXXXI) was subjected to selenium dehydrogenation to yield 1,2,7-trimethyl naphthalene (LXXXIII). Since the equivalent product from $\beta$-amyrin was 2,7-dimethyl naphthalene, this suggested that $\alpha$ and $\beta$ amyrins differ in the position of one methyl group in ring E. On the basis of the above evidences $\alpha$-amyrin has been assigned structure (LXXXIV) which also would explain the more inert nature of the double bond, compared with $\beta$-amyrin, because of the shielding effect of the 29-methyl group.

A detailed study of the infra red spectra of the penta-cyclic triterpenes in the methyl bending absorption region led Cole and collaborators\(^{(57)}\) to support this structure (LXXXIV). The N.M.R. spectrum\(^{(58)}\) also support this formula, originally proposed by Ruzicka. Again this was confirmed by the synthesis of $\alpha$-amyrin acetate from methyl glyceritate, a $\beta$-amyrin derivative\(^{(59)}\).

An interesting member of $\alpha$-amyrin group is phyllanthol (LXXXV) which carries a cyclopropane ring. This compound undergoes acid induced isomerisation to $\alpha$-amyrin\(^{(60)}\).

$\text{Arborinol}\(^{(61)}\)$ (LXXXVI), isolated from the leaves of Glycosmis arborea has been shown to have a carbon skeleton
different from \( \alpha \)-amyrrin in the disposition of double bond, size of the ring E and methyl groups in ring E.

\[(\text{LXXXV})\]

\[(\text{LXXXVI})\]

\textbf{Lupeol group:}

The parent compound of this group is lupeol, first isolated from the seeds of Lupinus albus\(^{62}\).

Selenium dehydrogenation of lupeol led to the products originating from the rings A and B only. The absence of picene, 2,7-dimethyl naphthalene and 1,2,7-trimethyl naphthalene indicated that lupeol has a skeleton different from those of both amyrins. Lupeol differed also in that the double bond is easily hydrogenated\(^{63}\). Based on degradation experiments lupeol has been assigned the structure \((\text{LXXXVII})\).

The envirornment of the isopropenyl group was shown by the oxidation of lupeol to an \( \alpha \)-unsaturated aldehyde with
SeO₂ (65) and by infra red spectra (66). The structure of lupeol was finally established as (LXXXVIII) by the conversion of lupeol into β-amyrene (67). This was further confirmed by the conversion of lupeol to germanicol acetate (LXXXIX), a β-amyrin derivative by the action of acetic anhydride on hydrogen chloride adduct of lupeol (68).

An interesting reaction of lupane group is the mercuric acetate dehydrogenation (69). This reaction leads to cyclic ethers or Δ12, 13 compounds. Thus lupeol gives rise to Δ12, 13 compound (XC).
Betulin (XCI, R = H) yields the 13, 28-epoxy derivative (XCII) whereas betulin diacetate (XCI, R = Ac) gives rise to \( \Delta^{12,13} \) betulin diacetate (XCIII). Similarly betulinic acid acetate (XCVI, R = H) leads to a lactone (XCV) whereas acetate-methylbetulinate (XCVI, R = CH\(_3\)) leads to a \( \Delta^{12,13} \) derivative (XCVII).
Lupeol group is the smallest of the three and one of the most interesting compounds belonging to this series is ceanothic acid (XCVII), a nor-lupane derivative(70).

Other types:-

Certain other types of pentacyclic triterpenes are also known. But as each type consists of very few members a systematic classification becomes difficult.

Friedelin (XCVIII) isolated from cork has been shown to be a triterpene ketone(71). An interesting feature in the structure of friedelin is the absence of the gem dimethyl group at position 4, in contrast with all other types of
triterpenes. Cerin (XCIX), a ketoalcohol is another member belonging to this group.

Glutinone or alusenone (C) is another type, the structure of which was determined by Spring and collaborators (72). Zeorin (CI) (73) and hydroxyhopanone (CII) (74) are two other types, both having five membered terminal ring E. Serratenediol (CIII), a novel pentacyclic triterpene having 7 membered ring C was recently reported (75) and its structure was established by Rowe and coworkers (76).
Adipematol (CIV) and filicenal (CV) are two other recently reported new triterpenoids, both having five membered ring E. Their structures were established by Ageta and Iwata (77).

Cedrelone (CVI), a bitter principle of cedrela toona, has been characterised (78,79) as a polyfunctional C26 compound of euphol type. The natural product presumably is derived from an isoprenoid precursor having four more carbon atoms in the side chain. The presence of a methyl group at C8 suggests a precursor of the squalene type.
Stereochemistry:

The stereochemistry of the pentacyclic triterpenes can also be considered on the basis of the three groups; \( \beta \)-amyrin, \( \Delta \)-amyrin and Lupeol.

\( \beta \)-amyrin :-

The formation of the bicyclic carboxylic ester (CVII) from the degradation of oleanolic acid derivatives and its correlation with ambrein, manool and abietic acid established that rings A and B are transfused. The action of phosphorous pentachloride on oleanolic acid derivatives involving the retropinacolic change further confirmed the part structure (CVIII).

(CVII)

(CVIII)

The next piece of evidence concerns the fusion of rings D and E involving positions 17 and 18. Siareasinolic acid (CIX) has an axial hydroxyl group at position 19 and as it undergoes easy elimination, the 18 hydrogen should be transferred to it. But as the hydroxy group and the carboxyl group are both axial
and do not undergo lactonisation they should be on the opposite sides of the molecule. Therefore, the carboxyl group at position 17 and the hydrogen at position 18 are on the same side indicating that the D/E junction is cis in nature.

![Chemical structures](image)

The relationship of the centres C\textsubscript{17} and C\textsubscript{18} to the adjoining centres was established by the study of reactions involving morolic acid (CX) and siaresinolic acid (CIX). The diol acetate (CXI) derived from morolic acid (CX) has been converted to the epoxide (CXII) and further to norolean 16, 18-dienyl acetate (CXIII). In this series of reactions the configuration at C-13 is unaffected and thus should be as in morolic acid. Norolean 16,18-dienyl acetate (CXIII) has also been obtained from siaresinolic acid. The decarboxylation of \(\Delta_{13} \) (18), 19 keto acid (CXIV) undergoes through a cyclic state (CXV) and hence the hydrogen at C-13 should be on the same side of the molecule as was the carboxyl group; i.e. \( \beta \). Siaresinolic acid (CIX) has been

---

80. cis

81. CXIII
converted into morolic acid (CX) through the ketone (CXVI)\textsuperscript{82}. This conversion involves the treatment of the ketone (CXVI) with strong base and it follows that the configuration at C-13 which is $\beta$ is stable, and hence the C-14 angular methyl group should be $\alpha$. 

\[ \text{(CX I)} \quad \text{CH}_2\text{OAc} \longrightarrow \quad \text{(CXII)} \quad \text{CH}_2\text{OAc} \]
Methyl keto-oleanolate acetate (CXVII) on treatment with alkali gave an isomer (CXVIII). Reduction of (CXVIII) removes the keto group and this product as well as the acetyl methyl oleanolate, on selenium dioxide oxidation, gave the same dehydro derivative (CXIX). This indicated that of the two possible positions, isomerisation took place only at C-18 and not at C-9. Hence it was concluded that the configuration at C-9 was stable and that rings B and C are fused in a stable configuration.

\[
\text{(CXVII)} \quad \text{(CXVIII)} \quad \text{(CXIX)}
\]

In the following sequence of reactions in which C-13 remains stable, the compound (CXX) has been converted into
(CXXI) which carries an axial hydroxyl group at C-11. The product (CXXI) has the 13 hydrogen axial and since the 11 hydroxyl is also axial, the hydroxyl should be β. This axial alcohol (CXXI) undergoes easy elimination to (CXXII) and therefore the hydrogen at C-9 should be α and axial.
This suggests the structure (CXXIII) for oleanalic acid\textsuperscript{83}.

Correlation of rings A and B of the molecule with (CXXI) led to two possibilities (CXXIV) and (CXXV) which could not be distinguished by chemical means. Molecular rotation\textsuperscript{84,85} arguments supported the formulation (CXXIV). X-ray studies of methyl oleanolate iodoacetate have revealed its structure and stereochemistry to be as in (CXXVI) which is typical of $\beta$-amyrin skeleton\textsuperscript{86}.
Molecular rotation studies also show that the A/B ring area in the triterpenoids and steroids is very similar; in each case the ring union is trans, the angular methyl group is in a similar position, and the only difference is the gem-dimethyl group at C4 in the triterpenoids.

Among the numerous results obtained by the application of molecular rotations are the support for the correct stereochemistry of the 3-amyrin series, a correlation of the stereochemistry of the triterpenes with that of the steroids and the fixation of the configuration of the hydroxyl group at position 3 in boswellic acid (CXXVII).

![Chemical structure of 3-amyrin]

(CXXVII)

3-amyrin group:

Oxidative degradation of 3-amyrin derivatives led to the same bicyclic ester (CVII) as obtained from oleanolic acid derivatives. This indicated that rings A and B were similarly
constituted in $\beta$ and $\alpha$ amyrins. Also, both $\beta$ and $\alpha$ amyrins have been converted into two isomeric methyl ethers (CXXVIII) and (CXXIX). This conversion proved the identity of the configuration at C-3, C-5, C-8 and C-10 in both the series.

\[ \text{(CVII)} \]

\[ \text{(CXXVIII)} \]

\[ \text{(CXXIX)} \]

$\Delta_{11, 13} (18)$ Ursadiene 3 ol (CXXX) was converted into $\Delta_{11, 13}(18)$ oleadiene 3 ol by vigorous acid treatment of the former. Since this transformation does not involve
C-9, C-14 or C-17, it could be presumed that the configuration at these centers are the same as in $\beta$-amyrin. Further both $\alpha$ and $\beta$ amyrins undergo rearrangements to the corresponding isodienoyl structure with selenium dioxide, but not 18-iso(18$\alpha$) amyrin$^{90}$, and hence the hydrogen at C-18 in $\alpha$-amyrin may be taken to be $\beta$ by analogy. This formulation has been also supported by study of optical rotations and stabilities of the lactones of ursolic acid and oleanolic acid$^{91}$.

The evidence recorded above, proves the configuration of all relevant points except those of the methyl groups at C-19 and C-20. Ruzicka and collaborators$^{92}$ isolated a hydrocarbon (CXXXIII) by pyrolysis of isoamyradienonyl acetate (CXXXII), which was converted to a ketone (CXXXIV). This ketone was also obtained by degradation on D(+)-pulegone (CXXXV) which established the structure of the ketone as well as the configuration of the methyl group at C-20 as $\alpha$.$^{92}$
The methyl group at C-19 was assigned an equatorial configuration for maximum hindrance of the double bond. These evidences led to structure (CXXXVI) as representative of \( \alpha \)-amyrin.

The diequatorial substituents in ring E may explain the relative stability of the cis D/E fusion, since an epimerisation at C-18 should make them axial\(^93\).

**Lupeol group**

Under acidic conditions lupeone. (CXXXVII) was transformed into \( \beta \)-amyrenone (CXXXVIII) of known constitution. This transformation allowed the stereochemistry of lupeol to be written
as (CXXXIX), in which the configuration at C-13, C-18 and the isopropenyl group were still to be determined.

(CXXXVII)  (CXXXVIII)

Betulinic acid (CXL) belongs to lupeol group and it differs from lupeol in that it carries a carboxyl group at position 17. Betulonic acid (CXLI) derived from betulinic acid, on treatment with acid, isomerised to a ketolactone

(CXXXIX)
Reduction of this with LiAlH$_4$ gave a triol (CXLIII). The triol on acetylation with boron trifluoride and acetic anhydride furnished moro-diol acetate (CXLIV) obtained from morolic acid.

Since the centre C-13 is not involved in this series of reactions the hydrogen at C-13 should have the same configuration as in the morolic acid; i.e. $\beta$. 

\[ \text{(CXLII)} \]
The ease of dehydration of the 19 hydroxyl group in (CXLIII) indicated that it had an axial configuration and also that the C-18 hydrogen was axial and trans to the 19 hydroxyl. Since the triol (CXLIII) was formed by the reduction of the lactone (CXLII) the 19 hydroxyl group and the C-17 primary hydroxyl should be $\beta$ and cis with respect to one another, and hence it followed that the 18-hydrogen was and that the rings D and E were trans locked$^{83}$.

The configuration of the isopropenyl group was determined by Halsall and collaborators$^{95}$ by reactions on lupeol. Lupeol (CXXXIX) formed a hydrochloride; which on treatment with silver acetate regenerated lupeol, where as on treatment with acetic anhydride gave the acetate of germanicol (CXLV). The hydrochloride on boiling with inert solvents was recovered unchanged but on boiling with an inert ionising solvent it gave germanicol. The hydrochloride may therefore have the structure (CXLVI) or (CXLVII). Reduction of the hydrochloride with sodium and isopropyl alcohol or by catalytic hydrogenation gave 18 iso $\beta$-amyranol (CXLVIII) indicating the structure (CXLVII) for the hydrochloride. This also indicated that the hydrogen at C-18 is $\alpha$ as in 18 isoamyranol (CXLVIII).
A consideration of the probable mechanistic path indicates that the chlorine atom in the hydrochloride is \( \alpha \). Thus germanicol is obtained from the hydrochloride by \( \text{SE}_1 \) mechanism and the regeneration of lupeol from the hydrochloride by \( \text{SN}_2 \) reaction shown in (CXLIX) where the chlorine atom, C-19, C-20 and C-21 are coplanar. This requires the chlorine atom to be \( \alpha \) and also for the configuration of the isopropenyl group to be trans to the methyl group at C-17. The stereochemistry of lupeol
can thus be represented as (CL).

\[
\begin{align*}
\text{(CXLIX)}
\end{align*}
\]

**BIOGENESIS**

Simultaneously with the chemical developments described above knowledge of the biogenesis of steroids and triterpenoids grew rapidly, leading to the proposal of Woodward and Bloch\(^96\) that these compounds came from squalene (CLVI) with its terminal isoprenoid units forming their terminal rings (or side-chain). Subsequent work, especially of Bloch\(^97\), Cornforth and Popjak\(^98,99\), has established the detailed pathway of the biogenesis of squalene and its subsequent transformation into lanosterol and the the steroids.
The problem of biosynthesis is usually considered at three levels. Firstly it is the creation of the 5 carbon isoprene (C5LI) units, secondly the combination of these units to form the theoretical precursors of the various groups of terpenes and finally the mechanism of cyclisation and rearrangement of these precursors to form the individual terpenes.

The five carbon fragment postulation has probably its origin in a two carbon fragment. Thus cholesterol has been biosynthesised from acetic acid\textsuperscript{100}. It was later found that \( \beta \)hydroxy \( \beta \)methyl \( \delta \)valerolactone (the lactone of mevalonic acid) (CLII) is utilised in the biosynthesis of cholesterol and squalene\textsuperscript{98}. It was also found that the carboxyl group of mevalonic acid was the carbon lost in the formation of the five carbon units\textsuperscript{101}. 
It has been postulated that each of the terpene group could be derivable from simple precursors; the precursors themselves being formed by the combination of five carbon fragments. Thus geraniol (CLIII) can give rise to monoterpens, farnesol (CLIV) to sesquiterpenes, geranyl-geraniol (CLV) to diterpenes and squalene (CLVI) to triterpenes.

\[
\text{(CLIII) CH}_2\text{OH} \quad \text{(CLIV) CH}_2\text{OH} \quad \text{(CLV) CH}_2\text{OH}
\]

A comprehensive scheme for the biogenesis of triterpenes was put forward independently by Rusicka and collaborators\textsuperscript{102} and by Stork and Burgstahler\textsuperscript{103}. According to Eschenmoser\textsuperscript{102} squalene is folded into a series of incipient chair or boat rings, and attack by the equivalent of HO\textsuperscript{+} then initiates a
completely concerted process leading to the triterpene and elimination of a proton. Thus cyclisation of squalene (CLVI) can lead to euphol (CLVII).

When the coiling pattern is chair, chair, chair, boat (CLVIII) the intermediates (CLIX) and (CLX) can result. Elimination of a proton from C-29 then affords lupeol (CLXI).
If, however, concerted ring E enlargement occurs to give the ion (CLXII) and a proton is then lost from C₁₈, germanicol (CLXIII) results. Further concerted Wagner-Meerwein shifts beginning with the ion (CLXII) lead to β-amyrin (CXXVI), mulifluorenol (LXXIV), friedelin (XCVIII) etc. α-amyrin (LXXXIV) can also be derived via the ion (CLX).

A different pattern of folding (chair, chair, chair, chair, chair) leads to the hopane ring system, exemplified by hydroxyhopanone (CLXIV), biogenetically the simplest of the pentacyclic triterpenes. A slightly different pattern (chair, chair, chair, chair, boat) accounts for adiantoxide (CLXV) and fernene (CLXVI), if these are formed by a completely concerted process.

\[(\text{CLXIV})\]  
\[(\text{CLXV})\]  
\[(\text{CLXVI})\]
Onocerin (XXIV) can be pictured as a product of cyclisation of squalene from both ends and ambrein (CLXVII) by cyclisation from one end as far as the first ring only.

It has been found that the oxygen in the hydroxyl group incorporated in the molecule is derived from the atmosphere and not from water$^{105}$.

One result of the development of the biogenetic theory is that it is now possible, with sufficient imagination and chemical insight, to predict the type of carbon skeletons which may be found. If a new parent $C_{30}H_{50}O$ alcohol or derivative thereof is isolated, the possibility should be considered whether it has one of the potential biogenetic structures found in nature. However, structural determination of this type is now, in a sense, filling in predictable gaps and the question arises as to what lies ahead.
PRESENT WORK
PRESENT WORK

Discussion:

India possess a very rich flora and this work was taken up with the idea that the chemical investigation of various Indian medicinal plants may lead to the isolation and characterisation of many interesting new plant products which could also have marked biological activity. Triterpenoids are one of the several groups of compounds very widely distributed in the vegetable kingdom. They are encountered in various parts of the plants.

In the present work recorded in this thesis four plants belonging to different families have been examined and their triterpenoid components studied. From the first two plants only known triterpenes could be isolated and characterised. From the third plant, in addition to the known 3-epi-lupeol, two new triterpenes were isolated and their structure and stereochemistry have been studied. From the fourth plant another known triterpene, lupeol was isolated in good yield. In an attempt to modify its structure oxidation in ring A in lupeol have been studied.
Anisomeles malabarica R. Br. (Labiatae)

Abstract: From petroleum ether extract of Anisomeles malabarica a triterpenic hydroxy acid, characterised as betulinic acid, was isolated.

Anisomeles malabarica R.Br. commonly known as 'Karithumba' in Malayalam is a member of Labiatae family. It occurs in Deccan, North Kanara, South Carnatic and throughout Kerala.

Although this plant is widely used internally for rheumatism and a variety of diseases, an infusion of the leaves for dyspepsia, and an essential oil distilled from leaves as an embrocation in rheumatic arthritis, little is known of its chemistry. An earlier investigation of this plant showed that it contains small amounts of alkaloid, citral, geranic acid and some essential oil. A reinvestigation of this plant showed that it also contains a triterpenoid characterised and identified as betulinic acid. The identity of the acid has been confirmed by comparison of a number of its derivatives and finally
by converting its methyl ester into betulin by lithium aluminium hydride reduction. Betulinic acid was earlier isolated from Cornus forida, Linn. Zizyphus vulgaris, Lamark, Cabbage and other sources (108-110).

The petroleum ether extract of the air dried powdered plant obtained from Kerala yielded a yellowish green substance which was crystallised from benzene as a persistent gel probably due to impurity. This on further purification by sublimation at reduced pressure gave a purer product which was crystallised from methanol as colourless crystalline needles (m.p. 315-320). It gave positive Liebermann-Burchard test, characteristic of triterpenes. It also showed a yellow colour with tetranitromethane indicating the presence of carbon-carbon double bond. In the infra red spectrum of this compound (CLXVIII) the presence of the hydroxyl and carbonyl groups were shown clearly by the bands at 3637 and 1714 cm\(^{-1}\) respectively. The compound was analysed for the molecular formula C\(_{30}\)H\(_{48}\)O\(_{3}\). With acetic anhydride and pyridine the crude acid gave an acetyl derivative which was purified by chromatography on a column of magnesium trisilicate in benzene. The monoacetate (CLXIX) after crystallisation from aqueous ethanol melted at 289-290° (reported m.p. of the acetate 289-291)\(^{107}\).

The infra red spectrum of the acetate showed bands at 1714 cm\(^{-1}\) (carboxyl) and 1249 cm\(^{-1}\)(acetyl). It also gave positive
tetramethylmethane test. Methylation of the original acid with
diazomethane furnished a methyl ester which was chromatographed on
neutral alumina column in benzene. The pure crystalline methyl ester
(CLXX) thus obtained melted at 225–226 °C (m.p. reported for methylester
of betulinic acid 223-224\textsuperscript{0}\textsuperscript{109}. Acetylation of the methyl ester with acetic anhydride and pyridine readily yielded a crystalline monoacetate (CLXXI), m.p. 206\textsuperscript{0}. This melting point did not agree with the reported m.p. 290-292\textsuperscript{0} in the "Dictionary of Organic compounds" (page 391) for the acetyl methyl ester of betulinic acid. However a search of the original literature revealed that the correct m.p. reported for the acetyl methyl ester of betulinic acid is 201-202\textsuperscript{0}\textsuperscript{110,111}. Selenium dioxide oxidation of the acetyl methyl ester readily gave a crystalline \(\alpha,\beta\)-unsaturated aldehyde (CLXXII) \(\lambda_{\text{max}} 228\), m.p. 253-254\textsuperscript{0}.

These findings suggested that the acid isolated was identical with betulinic acid. This was confirmed by a mixed melting point determination with an authentic sample of betulinic acid and the conversion of the methyl ester of the acid into betulin (CLXXXIII) by lithium aluminium hydride reduction.

**Vallaris solanacea, O.Ktze (Apocynaceae)**

**Abstract**: A triterpenoid hydroxy acid, identified as ursolic acid, was isolated from ethanolic extract of the leaves of vallaris solanacea.

Vallaris solanacea is commonly cultivated throughout India. Milky juice of the plant is applied to old wounds and sores. The only work on the chemical investigation of Vallaris solanacea Ktze. reported in literature is that of Kuwada and Matsukawa\textsuperscript{112} who
isolated two strophanthus - digitalis glycosides. The leaves
of Vallaris solanacea obtained from the state of Jammu and Kashmir
have now been examined and the result reported here\textsuperscript{113}.

Air-dried leaves of the plant were exhausted with cold
ethanol in a percolorator. The crude substance left after the
recovery of the solvent was treated under reflux with boiling
petroleum ether. The undissolved residue thus obtained was
dissolved in acetone and filtered. The filtrate on concentration
gave a product which on repeated crystallisation from aqueous
ethanol yielded fairly good crystalline needles of ursolic acid
(CLXXIV), m.p. 278-280°. In acetic anhydride and chloroform it
gave fairly strong and stable crimson colour with Liebmann-
Burchardt reaction. Tetranitromethane also gave a positive test
with the compound. Infra red spectrum of the compound showed bands
at 3637 and 1714 cm\textsuperscript{-1} indicating the presence of hydroxyl and
carbonyl functional groups.

With acetic anhydride and pyridine the crude acid gave an
acetyl derivative (CLXXV) which was purified by chromatography
using magnesium trisilicate and benzene. The acetate (m.p. 289-
292°) also showed a pale yellow colour with tetranitromethane.
It analysed for the molecular formula C\textsubscript{32}H\textsubscript{50}O\textsubscript{4}. Infra red
spectrum of the acetate showed bands at 1714 cm\textsuperscript{-1} (carboxyl) and
1240 cm\(^{-1}\). The acetate on hydrolysis with 7% methanolic potassium hydroxide yielded pure acid which after crystallisation from aqueous ethanol melted at 284-285°. With diazomethane the original acid gave a monomethyl ester (CLXXVI) which after chromatographic purification and crystallisation melted at 171°. The methyl ester on acetylation with acetic anhydride and pyridine yielded a crystalline acetyl methyl ester (CLXXVII), m.p. 244-245°.

These physical constants indicated that the acid isolated was identical with ursolic acid\(^{114}\). Mixed melting point of the
acid isolated with an authentic sample of ursolic acid showed no depression.

**Glochidion hohenackeri** Bedd. (Euphorbiaceae)

Abstract: From the bark and roots of Glochidion hohenackeri (Euphorbiaceae), in addition to the known 3-epi-lupeol, two new triterpenes glochidone and glochidiol have been isolated and assigned the structures (CLXXVIII) and (CXCVI) respectively. The stereochemistry of the hydroxyl groups in glochidiol has been determined by the partial synthesis of three of the four possible stereoisomers of the dihydrodiol diacetate (CXI, CXII and CXIII) which all differ from dihydroglochidiol diacetate (CXIV).

Glochidion hohenackeri (Euphorbiaceae) is a tree grown in W. Peninsula, Chota, Nagpur and Orissa. It is very common on the West Coast of India especially in Konkan. The bark of the tree is given medicinally when the stomach revolts against food. In this thesis studies on the triterpene constituents of the bark and roots of plant obtained from Mahabeleshwar (Maharashtra State) are reported.

The hexane extract of the bark yielded a gum which on chromatography on neutral alumina in hexane gave a crystalline ketone, m.p. 164-165, \[ [\alpha]_D + 73.4 \] , which we have named glochidone. The gummy material in the polar fractions was found to consist of a mixture of two triterpene alcohols. Acetylation of this mixture
and chromatography of the product on neutral alumina in benzene yielded two crystalline acetates. One was found to be a monoacetate, m.p. 163°, $\left[\alpha\right]_D^0 - 6.91$; the other a diacetate, m.p. 253-256°, $\left[\alpha\right]_D^0 + 20.82$. The alcohol corresponding to the latter acetate has been named glochidiol. In subsequent isolations, instead of initial chromatography, it was found more convenient to acetylate first the gum obtained by evaporation of the hexane extract and then to chromatograph the acetylated product. From the hexane extract of the roots of the plant after acetylation and chromatography yielded glochidone and glochidiol diacetate in somewhat lower yield. All these compounds gave a positive Liebermann-Burchardt test.

Glochidone has the molecular formula $C_{30}H_{46}O$ (molecular weight by mass spectrum 422). The ultra violet spectrum (Fig.I) of the glochidone has a maximum at 228 μ (log ε 4.00) and its infra red spectrum (Fig.II) in methylene chloride shows bands at 1660 cm$^{-1}$. These indicates that glochidone is an $\alpha$, $\beta$-unsaturated ketone. The infra red spectrum also shows a band at 885 cm$^{-1}$ which indicates the presence of a = CH$_2$ system in the molecule. Its NMR spectrum (Fig.III) shows the presence of six tertiary C-CH$_3$, one vinyl C-CH$_3$, a two-proton doublet at $\delta$ 4.65 (=CH$_2$, $J = 6$ c/s) and a pair of one-proton doublets each at $\delta$ 5.75 ($J = 10$ c/s) and $\delta$ 7.09 ($J = 10$ c/s) indicating the presence of the grouping.
Fig. I

Fig. II
Catalytic hydrogenation of glochidone yielded lupan-3-one (CLXXXIV)\textsuperscript{116-118} identical in all respects with an authentic sample. Glochidone hence possesses the structure and stereochemistry shown in (CLXXXVIII).

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

(CLXXXVIII)

The monoacetate, m.p. 163\textdegree, obtained by chromatography has the molecular formula C\textsubscript{32}H\textsubscript{52}O\textsubscript{2} (molecular weight by mass spectrum 468). On alkaline hydrolysis it gave an amorphous alcohol (CLXXX). Oxidation of this alcohol with Jones reagent furnished lupen-3-one (CLXXXI)\textsuperscript{117-118}. Mixed melting point with an authentic sample showed no depression. Its infra red spectrum was superimposable with that of the authentic sample.
Catalytic reduction of the acetate gave a dihydroderivative (CLXXXII). This was hydrolysed to the alcohol (CLXXXIII) and then oxidised with chromium trioxide to yield lupan-3-one (CLXXXIV). The acetate is hence 3-epi-lupeol acetate (CLXXIX). 3-epi-lupeol has previously been obtained from plants of the Burseraceae family. 

![Chemical structures](CLXXXI, CLXXXII, CLXXXIII, CLXXXIV)
Glochidiol diacetate (CLXXXV) has the molecular formula \( \text{C}_{34}\text{H}_{54}\text{O}_{4} \) (molecular weight by mass spectrum 526). Its I.R. spectrum (Fig.IV) shows bands at 1725 cm\(^{-1}\) (ester), 1630 and 880 cm\(^{-1}\) (=CH\(_2\)). Catalytic reduction of the diacetate yielded a dihydroderivative (CLXXXVI). Alkaline hydrolysis of glochidiol diacetate gave an amorphous diol (CLXXXVII) which could not be cleaved by periodic acid showing that it was not a 1,2 diol. On being subjected to Jones oxidation the diol yielded a 1,3-diketone (CLXXXVIII), m.p. 197-200\(^{\circ}\), \( [\alpha]_{D}^{c} + 101.7^{\circ} \).
Its ultra violet spectrum (Fig. V) shows a $\lambda_{\text{max}}$ at 256 m$\mu$ ($\log \epsilon$ 3.97), and infra red spectrum (Fig. VI) has bands at 1718 and 1696 cm$^{-1}$. 
Fig. V

Fig. VI
Oppenauer oxidation of glochidiol yielded an $\alpha',\beta$-unsaturated ketone (CLXXXIX) $C_{30}H_{46}O$, which was found to be identical with glochidone (CLXXVIII). This suggests that glochidiol has the structure (CLXXXVII). Formation of glochidone from glochidiol would involve oxidation of the $C_3$-OH followed by $\beta$-elimination of the OH at $C_1$.

The stereochemistry of the OH groups in (CLXXXVII) remained to be settled. Stereospecific synthesis of three (CXC, CXCI and CXCII) of the four possible stereoisomers (CXC, CXCI, CXCII and CXCIII) of the dihydrodiol diacetates showed that they are to be different from dihydroglochidiol diacetate (CXCIII). Dihydroglochidiol diacetate hence possesses the stereochemistry shown in (CXCIII), glochidiol itself being represented by (CXCIV).
Treatment of glochidone with alkaline hydrogen peroxide
gave the epoxide (CXCIII), m.p. 181-183°, which on catalytic
hydrogenation yielded the dihydroepoxide (CXCIV), m.p.223-225°.
Lithium aluminium hydride reduction of (CXCVI) yielded a mixture of diols (CXCVII and CXCVIII) which were separated by chromatography on neutral alumina. The less polar fraction of the column afforded the 1α, 3α-diol (CXCVII), m.p. 250°, which on acetylation with acetic anhydride and pyridine yielded the 1α, 3α-diacetate (CXCIX), m.p. 158-160°. The more polar fraction afforded the 1α, 3β-diol (CXCVIII), m.p. 236-238° which yielded on acetylation the 1α, 3β-diacetate (CC), m.p. 238-242°.

Lithium aluminium hydride reduction of glochidone epoxide (CXCV) similarly gave two diols (CCI and CCII), namely 1α, 3α and 1α, 3β which yielded the corresponding diacetates (CCIII and CCIV).
The diketone (CLXXXVIII) on reduction with lithium aluminium hydride or sodium borohydride yielded the 1α, 3β-diol (CCII). However, on reduction with sodium and propanol, it yielded the 1β, 3β-diol-(CCV) acetylation of which furnished 1β, 3β-diacetate (CCVI).
Catalytic hydrogenation of $1\beta$, $3\beta$-dil (CCV) gave amorphous $1\beta$, $3\beta$-dihydrodiol (CCVII); a similar reduction of $1\beta$, $3\beta$-diacetate (CCVI) yielded $1\beta$, $3\beta$-dihydrodiacetate (CCVIII), m.p. 223-226°.
Catalytic reduction of glochidiol diacetate (CCIX) readily yielded $1\beta, 3\alpha$-dihydrodioldiacetate (CCX), m.p. 210-211°. This acetate on hydrolysis furnished the corresponding $1\beta, 3\alpha$-dihydrodiol, (CCXI), m.p. 262-263°.

![Chemical structures](image)

The melting points and optical rotations of the glochidiol, glochidioldiacetates and their stereoisomers are summarised (Table II). The melting points and optical rotations of the stereoisomeric dihydrodiol, and their diacetates are also tabulated (Table III).
<table>
<thead>
<tr>
<th>Compound</th>
<th>Diol m.p.</th>
<th>[α]D</th>
<th>Compound</th>
<th>Acetate m.p.</th>
<th>[α]D</th>
</tr>
</thead>
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<tr>
<td>1β, 3α</td>
<td>Oxidation</td>
<td></td>
<td>1β, 3α</td>
<td>253-256°</td>
<td>+20.82°</td>
</tr>
<tr>
<td>(Glochidiol)</td>
<td>amorph</td>
<td></td>
<td>Oxidation</td>
<td>256-257°</td>
<td>+28.03°</td>
</tr>
<tr>
<td>1α, 3α</td>
<td>Acetylation</td>
<td></td>
<td>1α, 3β</td>
<td>124-126°</td>
<td>-</td>
</tr>
<tr>
<td>1α, 3β</td>
<td>Acetylation</td>
<td></td>
<td>1α, 3β</td>
<td>230-234°</td>
<td>+46.57°</td>
</tr>
<tr>
<td>1β, 3β</td>
<td>Acetylation</td>
<td></td>
<td>1β, 3β</td>
<td>212-214°</td>
<td>+31.5°</td>
</tr>
<tr>
<td>Compound</td>
<td>Dihydrodiol m.p.</td>
<td>$[\alpha]_D$</td>
<td>Compound</td>
<td>Dihydrodiacetate m.p.</td>
<td>$[\alpha]_D$</td>
</tr>
<tr>
<td>----------</td>
<td>----------------</td>
<td>-------------</td>
<td>----------</td>
<td>-----------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>1$\alpha$, 3$\alpha$</td>
<td>CXCIX</td>
<td>250°</td>
<td>-16.0°</td>
<td>CXCIX</td>
<td>158-160°</td>
</tr>
<tr>
<td>1$\alpha$, 3$\beta$</td>
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<td>238-242°</td>
<td>9.80°</td>
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<tr>
<td>1$\beta$, 3$\beta$</td>
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</tr>
<tr>
<td>1$\beta$, 3$\alpha$</td>
<td>262-263°</td>
<td>-29.39°</td>
<td>CCX</td>
<td>210-211°</td>
<td>-30.68°</td>
</tr>
</tbody>
</table>

The NMR spectra of the dihydrodiol diacetates (CXCIX, CC, CCVIII and CCX) are presented in Fig. VII to Fig.X.
Fig. VII

Fig. VIII
Fig. IX

Fig. X
As reported by Williams and Bhacca\(^{(120)}\), the \(J_{ax}\) values denoting the coupling of an axial proton on the carbon atom bearing the electro negative substituent to an equatorial proton were observed to be of the order of 6 cycles per second (Fig. IX) whereas \(J_{ae}\) values denoting the analogous coupling in which the proton on the electro negatively substituted carbon atom is equatorial were of the order of 2-3 cycles per second second (Fig. VII).


**Abstract** : Lupeol has been isolated from this plant and in an attempt to modify its structure to induce biological activity, oxidation in ring A in lupeol have been studied. Lupeone and lupanone on autoxidation yielded the corresponding diosphenols in almost quantitative yield. Hydrogenation of lupanone diosphenol yielded dihydro derivative which on acetylation yielded 3\(\beta\)-acetoxy lupan 2-one.

Astercantha longifolia. Nees is a very common plant throughout India in moist places. The decoction of roots of this plant are said to be used as diuretic. The seeds are given for gonorrhoea and spermatorrhoea. The leaves, roots and seeds of this plant are also employed for jaundice, dropsy, rheumatism and diseases
of the urinogenital tract.

Although some work has been reported\(^{(121)}\) no reference was available in the literature about the triterpene constituent of the plant. However, the presence of a sterol was indicated\(^{(122)}\) by earlier workers. So a systematic reinvestigation of this plant was undertaken.

The whole plant obtained from Borivili, Bombay, was air-dried, powdered and extracted with cold petroleum ether. The solvent was removed by evaporation. The residue was dissolved in minimum benzene and adsorbed on a column of neutral alumina in benzene. The hexane eluate of the column gave nothing but a waxy material. The later fractions of benzene eluate as well as benzene : acetone \(19:1\) eluate on evaporation gave solids which are identical and single by TLC. So, they are combined and crystallised from methanol \((m.p. 213-215)\). It gave an acetyl derivative \((m.p. 217-218^\circ)\) with acetic anhydride and pyridine. The parent compound as well as the acetate gave positive Liebermann-Burchard test. They also showed a yellow colour with tetranitromethane. In the infra red spectrum of the parent alcohol the presence of hydroxyl was shown clearly by the band at \(3637 \text{ cm}^{-1}\).
These physical data indicated that the alcohol isolated was identical with lupeol. Mixed melting point of the alcohol isolated with an authentic sample of lupeol showed no depression.

As the yield of lupeol was sufficiently good an attempt to modify its structure was undertaken and in this attempt oxidation in ring A in lupeol have been studied\(^{(123)}\). Lupeone (CCXII) and Lupanone (CCXIII), obtained by chromium trioxide and pyridine oxidation of lupeol and lupanol, in dry tertiary butyl alcohol containing potassium tertiary butoxide were rapidly autoxidised to the corresponding diosphenols (CCXIV) and (CCXV) having characteristic \( \lambda_{\text{max}} \) at 272 and \( \nu_{\text{max}} \) at 3440, 1660, 1640 cm\(^{-1}\) and gave positive ferric chloride reaction.
When hydrogenated with palladium charcoal the diosphenol (CCXV) yielded a non-crystalline keto alcohol which afforded a crystalline keto acetate when treated with acetic anhydride and pyridine. Based on the following observations the ketoacetate have been assigned structure (CCXVI). It gave a positive Zimmermann test for \(-\text{COCH}_2\)-group and in the NMR spectrum it had a sharp singlet at $\delta 4.95$ ascribed to the C\textsubscript{3} proton.

![Diagram of CCXVI and CCXVII](image)

The alternative structure (CCXVII) for the keto acetate would have a triplet or quartet for the C\textsubscript{2}-proton. Formation of (CCXVI) from (CCXV) could be explained as follows:
Diosphenol (CCXV) when ozonised and worked up with sodium bicarbonate and hydrogen peroxide gave a neutral compound C_{29}H_{48}O_{3} which had no selective absorption in U.V.; but its infra red spectrum showed bands at 3600 cm\(^{-1}\) (hydroxyl) and 1730 cm\(^{-1}\) (\(\delta\)-lactone). Based on its mode of formation, spectral characteristics and elemental composition, it has been assigned
In another series of reactions diosphenol (CCXIV) was cleaved by alkaline hydrogen peroxide to the dicarboxylic acid (CCXIX), $C_{30}H_{48}O_4$ which on methylation with diazomethane yielded a dimethyl ester (CCXX). On refluxing with methanolic potassium hydroxide it (CCXX) yielded a neutral crystalline compound (CCXXI), $C_{29}H_{46}O$. Its infra red spectrum showed a band at 1740 cm$^{-1}$ indicating the presence of cyclopentanone system.
EXPERIMENTAL
EXPERIMENTAL

All the melting points recorded in this thesis were determined on Kofler block and they are uncorrected. The micro analysis were carried out in Dr. Zimmermann's micro analytical laboratory, Australia and also in CIBA Research Centre, Goregaon, Bombay 63.

The ultra violet spectra were taken in alcohol using a Beckmann DB model spectrophotometer and the infra red spectra were taken in methylene chloride using a Perkin-Elmer Model 421 spectrophotometer. Optical rotations refer to 2-3 percent solutions in chloroform at 24°. NMR spectra were determined in CDCl₃ on a varian A-60 spectrometer. The mass spectra and some of the NMR spectra were taken through the courtesy of Drs. R. Zurcher and H. Hürzler of CIBA Limited, Basle.

Hexane used had b.p. 60-80°. Magnesium trisilicate and neutral alumina were used for column chromatography and silica gel G (E. Merck) was used for thin layer chromatography.
ANISOMELES MALABARICA R. Br.

Isolation of betulinic acid:

Air dried powdered plant (2 kg) was extracted thrice with hot petroleum ether (40-60°C). The combined extract was concentrated under reduced pressure and cooled when a yellowish green solid separated. It was crystallised once from benzene and then purified by sublimation under reduced pressure. The sublimate was washed with petroleum ether and crystallised from methanol as colourless needles, m.p. 315-320°C. In sealed capillary m.p. 250°C with sublimation (Found: C, 78.43; H, 10.73. C$_{30}$H$_{48}$O$_{3}$ requires C, 78.89; H, 10.59%).

Acetylation of betulinic acid:

The crude acid (0.5 g) was treated with acetic anhydride (5 ml) and pyridine (.25 ml), the mixture left overnight at room temperature and then poured into crushed ice with constant stirring. The solid that separated out was filtered, washed free from pyridine and dried. This was dissolved in benzene and adsorbed on a column of magnesium trisilicate (15 g) in benzene. The column was eluted with benzene and removal of the solvent yielded a colourless solid which was crystallised from aqueous ethanol, m.p. 289-290°C (Davy, Halsall and Jones$^{110}$) reported 289-291°C for the acetate of betulinic acid).
Methylation of the acid :-

A solution of the crude acid (2 g) in the minimum volume of methanol was added to an ethereal solution of diazomethane prepared from nitrosomethyl urea (5 g) and left overnight in a refrigerator. Then the solvent was removed by evaporation and the product dried in vacuo. The crude methylated product (2 g) was dissolved in small amount of benzene and adsorbed on a column of neutral alumina (20 g) suspended in benzene. Benzene eluate on evaporation gave a colourless solid (0.6 g) which was crystallised from methanol, m.p. 225-226° (m.p. reported for methyl ester of betulinic acid 223-224°). (Found : C, 78.69; H, 10.47; OCH₃, 6.56; active H, 0.24. \(\text{C}_{31}\text{H}_{50}\text{O}_3\) requires C, 79.10; H, 10.71; OCH₃, 6.59; active H, 0.21%).

Acetylation of methyl ester :-

The methyl ester (0.5 g) was treated with acetic anhydride (5 ml) and pyridine (2 ml) in the usual way and the acetyl methyl ester was crystallised from methanol as colourless heavy needles, m.p. 206° (m.p. reported \(110-111°\) for the acetyl methyl ester 201-202°). (Found : C, 77.42; H, 10.13. \(\text{C}_{33}\text{H}_{52}\text{O}_4\) requires C, 77.29; H, 10.22%).
Selenium dioxide oxidation of the acetyl methyl ester:

The acetyl methyl ester (0.3 g) was dissolved in hot glacial acetic acid (6 ml), freshly sublimed selenium dioxide (0.3 g) was added and the mixture refluxed gently for 2 hrs., over a small flame. The selenium was filtered off and the acetic acid was removed by evaporation under reduced pressure. Water (10 ml) was added to the residue and extracted with ether. The ether extract was washed with aqueous sodium bicarbonate, then with water, dried over sodium sulphate and evaporated to dryness. The residual solid was crystallised several times from methanol, m.p. 253-254°.

Lithium aluminium hydride reduction of methyl betulinate:

A solution of the methyl-ester (500 mg) in anhydrous ether (50 ml) was added dropwise to a stirred ethereal suspension of excess of lithium aluminium hydride at room temperature. Stirring was continued for an additional three hours and then the mixture was carefully decomposed with water. The ether solution was decanted, the inorganic hydroxide sludge washed well with ether, the combined ether extracts dried (sodium sulphate), the solvent was removed and the residue crystallised from methanol as colourless needles, 0.4 g., m.p. 251-252°. m.p. and m.m.p. with an authentic sample of betulin showed no depression.
**VALLARIS SOLANACEA**

**Isolation of ursolic acid:**

Air-dried leaves (2 kg) of the plant were extracted thrice with cold ethanol and the combined extract was evaporated to dryness under reduced pressure. The crystalline substance left after the removal of the solvent was washed well with hot low boiling petroleum ether. The residue was then refluxed with acetone, filtered hot, concentrated and cooled; a solid material separated out (m.p. 260–265°). This was repeatedly crystallised from aqueous ethanol to yield colourless needles, m.p. 275–285°.

**Acetylation of ursolic acid:**

The acid (200 mg) was treated with acetic anhydride (5 ml) and pyridine (1 ml) and allowed to stand overnight at room temperature. Then it was poured into ice-cold water with constant stirring. The solid that separated out was taken up in ether. The ether extract was washed with cold dilute hydrochloric acid (2N), water, dried over sodium sulphate, filtered and evaporated. The solid residue (200 mg) was dissolved in minimum benzene and adsorbed on a column of magnesium trisilicate (10 g) suspended in benzene. Benzene eluate of the column on evaporation gave a solid which was crystallised as needles from methanol, m.p. 289–292°. (Found: C, 77.36; H, 10.40. \( \text{C}_{32}\text{H}_{50}\text{O}_4 \) requires C, 77.06; H, 10.11).
Hydrolysis of the acetate:

The acetate (200 mg) was refluxed with methanolic potassium hydroxide (7%, 25 ml) for 3 hrs. over a water-bath. Water was added, the methanol removed by evaporation and filtered. The filtrate was acidified and extracted with ether. The residue was triturated well with acid and extracted with ether. The combined ether extract was washed with water, dried over sodium sulphate and evaporated. The solid obtained was crystallised from aqueous ethanol, m.p. 284-285°. (Found: C, 78.67; H, 10.46. C_{30}H_{48}O_{3} requires C, 78.89; H, 10.59%).

Methylation of ursolic acid

The acid (1 g) in minimum methanol was added to an ethereal solution of diazomethane prepared from nitrosomethyl urea (5 g) and allowed to stand overnight in refrigerator. The solvent was evaporated and the material dried in vacuo. The crude methylated product (1 g) was chromatographed on a column of neutral alumina (30 g) in benzene. Benzene eluate of the column on evaporation left behind a solid which was crystallised from ethanol to yield the methyl ester (700 mg.), m.p. 169-171°. (Found: C, 79.30; H, 11.08, active H, 0.30. C_{31}H_{50}O_{3} requires C, 79.10, H, 10.71%).
Acetylation of the methyl ester

The methyl ester (300 mg) was acetylated with acetic anhydride (4 ml) and pyridine (2 ml) and worked up in the usual manner. The acetyl methyl ester thus obtained was crystallised from methanol, m.p. 244-245°.

GLOCHIDION HOKENACKERI.BEDD

Isolation of the components:

The dried ground bark (5 kg) of Glochidion hohenackeri was extracted three times with hexane. The combined hexane extract was evaporated to dryness, treated with acetic anhydride (120 ml) and pyridine (50 ml) and left overnight at room temperature. The mixture was poured into cold water and kept for 5 hrs., with occasional stirring. The sticky product thus obtained was extracted with chloroform. The chloroform solution was washed with dilute hydrochloric acid, water, sodium bicarbonate again with water, dried over sodium sulphate and evaporated. The residue (70 g) thus obtained was dissolved in chloroform and adsorbed on a column of neutral alumina (700 g) suspended in hexane. The column was successively eluted with hexane, benzene-hexane (1:1), benzene and chloroform - 10% methanol.
The hexane eluate on evaporation to dryness yielded a solid (9 g). It was dissolved in chloroform, filtered, concentrated. Methanol was added to it and cooled, when crystalline needles of glochidone separated, m.p. 164-165°, $\left[\alpha\right]_D + 73.41^\circ$, $\lambda_{max} 228 \ \text{m} \ (\log e = 4.00)$. (Found C, 84.72; H, 10.65. $C_{30}H_{46}O$ requires C, 85.24; H, 10.97%).

Benzene-hexane (1:1) and initial benzene eluates of the column on evaporation to dryness gave some solid (0.8 g) which was dissolved in methanol, filtered and concentrated when crystals of 3-epi-lupeol acetate separated out, m.p. 163°, $\left[\alpha\right]_D -6.91^\circ$, $\nu_{max} 1720, 1635, 880 \ \text{cm}^{-1}$. (Found : C, 82.06; H, 11.25. $C_{32}H_{52}O_2$ requires C, 81.99; H, 11.18%).

Later fractions of the benzene eluate on evaporation to dryness yielded a solid (8.5 g) which was dissolved in chloroform, filtered, concentrated, methanol was added and cooled when crystalline needles of glochidiol diacetate separated out, m.p. 253-256, $\left[\alpha\right]_D + 20.82^\circ$, $\nu_{max} 1725, 1630, 880 \ \text{cm}^{-1}$. (Found : C, 77.34; H, 10.21. $C_{34}H_{54}O_4$ requires C, 77.52; H, 10.33%). The chloroform-methanol eluate of the column on evaporation yielded only gums.

The bark was then extracted with methanol and the methanol extract was evaporated to dryness. The crude material obtained,
after removal of tannins, was chromatographed over neutral alumina. Benzene eluate on evaporation to dryness gave more glochidiol diacetate (3 g).

When the residue from the hexane extract was chromatographed without being acetylated, the only crystalline compound obtained was glochidone since the free alcohols epi-lupeol and glochidiol were both amorphous.

The hexane extract of the roots (5 kg) was evaporated to dryness and acetylated with acetic anhydride and pyridine. The acetylated product was adsorbed on neutral alumina in hexane. The column was eluted first with hexane and then with benzene. Hexane eluate on evaporation to dryness gave glochidone while benzene eluate afforded glochidiol.

**Dihydroglochidone (Lupan-3-one)**

Glochidone (0.25 g) in acetic acid (10 ml) was reduced with hydrogen at atmospheric pressure in the presence of 10% palladium-charcoal (50 mg) as catalyst. The catalyst was filtered off, the solvent evaporated in vacuo and the residue crystallised from chloroform-methanol to give dihydroglochidone.
(0.2 g), $[\alpha]_D^{14.41} + 14.41$, m.p. 208-209°. Mixed melting point with an authentic sample of lupan-3-one showed no depression. The I.R. spectra of the two samples were also superposable. (Found : C, 84.48; H, 11.85. C$_{30}$H$_{52}$O requires : C, 84.04; H, 12.23%).

**Hydrolysis of 3-epi-lupeol acetate**

A solution of the acetate (1 g) in dioxan (30 ml) was refluxed with 7% methanolic potassium hydroxide (50 ml) for four hours. The solution was evaporated in vacuo, the residue diluted with water and extracted with chloroform. The chloroform extract was washed with water till it was free from alkali, dried over sodium sulphate and the solvent was removed in vacuo. The gummy material obtained (0.9 g) could not be crystallised.

**Jones oxidation of 3-epi-lupeol**

3-Epi-lupeol (0.4 g) was dissolved in aldehyde free acetone (50 ml) and cooled in an ice-bath. Jones reagent (0.8 ml) was added drop by drop, to the cold solution with constant shaking. After the addition the reaction mixture was kept for three minutes with constant shaking. Excess of chromic acid was decomposed by the addition of saturated solution of sulphur dioxide in acetone, followed by aqueous potassium carbonate and extracted with ether. The ether extract was washed with
aqueous potassium carbonate, water, dried over sodium sulphate
and evaporated to give lupen-3-one which was crystallised from
chloroform-methanol (m.p. 170°). Mixed melting point with an
authentic sample showed no depression. The I.R. spectra of the
two samples were also identical.

**Dihydro-3-epi-lupeol acetate**

3-Epi-lupeol acetate (0.2 g) in glacial acetic acid (10 ml)
was hydrogenated in presence of Adam's Catalyst (40 mg). The
catalyst was filtered off, the solvent evaporated in vacuo and
the residue (0.19 g) crystallised from methanol to give the
dihydro-3-epi-lupeol acetate, m.p. 164°, $\left[\alpha\right]_D^{20} = 46.32°$. (Found:
C, 81.24; H, 11.27. $C_{32}H_{54}O_2$ requires: C, 81.64; H, 11.56%).

**Chromic acid oxidation of dihydro-epi-lupeol**

The dihydroacetate (1.5 g) was refluxed with 5% methanolic
potassium hydroxide (100 ml) for five hours. Water was added to
the solution, methanol removed under reduced pressure and extracted
with ether. The ether extract was washed with water till free
from alkali, dried over sodium sulphate and evaporated to dryness
to give dihydro-epi-lupeol (1.3 g) as a gel.

The alcohol (1.3 g) in acetic acid (10 ml) was treated with
a solution of chromium trioxide (0.4 g) in acetic acid (10 ml)
and left overnight at room temperature. The reaction mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried over sodium sulphate and evaporated to dryness. The solid material (0.8 g) obtained was crystallised from chloroform-methanol to yield needles of dihydrolupeone (m.p. 207-208°). The m.p. was undepressed by admixture with authentic lupan-3-one.

**Dihydroglochidiol diacetate**

A solution of glochidiol diacetate (1 g) in glacial acetic acid (30 ml) was reduced with hydrogen at atmospheric pressure in presence of platinum oxide (0.1 g). The catalyst was filtered off, the solvent evaporated *in vacuo* and the residue crystallised from chloroform-methanol to give needles, m.p. 210-211°, \([\alpha]_D^{20} = 30.68°\). (Found : C, 77.77; H, 10.38. \(\text{C}_{34}\text{H}_{56}\text{O}_4\) requires C, 77.22; H, 10.67%).

**Hydrolysis of glochidiol diacetate**

The diacetate (2 g) was refluxed for two hours with 7% methanolic potassium hydroxide (40 ml). The methanol was removed under reduced pressure, the residue diluted with water and extracted with methylene chloride. The methylene chloride extract was washed with water till free from alkali, dried
over sodium sulphate and evaporated to dryness to yield glochidiol (1.7 g) as an uncrystallised gum.

**Hydrolysis of dihydroglochidiol diacetate**

Dihydroglochidiol diacetate (500 mg) was refluxed for three hours with 7% methanolic potassium hydroxide (30 ml). The methanol was removed under reduced pressure, diluted with water and extracted with chloroform. The chloroform extract was washed with water, dried over sodium sulphate, filtered and concentrated. To the concentrated solution, methanol was added, concentrated further and cooled when crystalline needles of dihydroglochidiol (0.45 g) separated out, m.p. 262-63°, $[\alpha_\text{D}]_D = 29.39°$. (Found: C, 81.24; H, 11.77. $\text{C}_{30}\text{H}_{52}\text{O}_2$ requires C, 81.02; H, 11.79%).

**Jones oxidation of glochidiol**

A solution of glochidiol (2 g) in aldehyde free acetone (30 ml) was cooled to zero degree in a freezing mixture and treated with excess of Jones reagent (4 ml). After five minutes excess of chromic acid was decomposed by adding saturated solution of sulphur dioxide in acetone followed by aqueous potassium carbonate and extracted with ether. The ether extract was washed with water, dried over sodium sulphate and
evaporated to yield the diketone (1.1 g) which was crystallised as needles from hexane, m.p. 196-200, $\left[ \alpha \right]_D + 101.71^\circ$, $T_{\text{max}}$ 256 mp (log $\epsilon$ 3.97) (Found: C, 82.58; H, 10.52. $C_{30}H_{48}O_2$ requires C, 82.13; H, 10.57%).

**Oppenauer oxidation of dihydroglochidiol**

A solution of dihydroglochidiol (0.53 g) in dry and distilled toluene (70 ml) was refluxed with freshly distilled cyclohexanone (7 ml) over an oil-bath kept at 120°C. Freshly distilled aluminium isopropoxide (2.5 g per 5 ml of toluene) (5 ml) was added, dropwise, to the refluxing solution. The solution was refluxed for one hour longer after the addition of aluminium isopropoxide. The toluene was distilled off, the reaction mixture was cooled, decomposed with water and extracted with ether. The ether extract was washed twice with 20% sodium hydroxide (30 ml each time), then with water till free from alkali and the ether removed by evaporation under reduced pressure. Excess of cyclohexanone was removed by steam distillation. The residue, after steam distillation, was extracted with chloroform, washed with water, dried over sodium sulphate and evaporated. The solid obtained was crystallised from chloroform-methanol mixture to give lup-1-ene-3-one (0.35 g), m.p. 177-179°,
\[ \lambda_{\text{max}} \text{ 228 } \mu\text{m} \text{. (Found: } \text{C, 84.63; H, 11.67. } \text{C}_{30}\text{H}_{48}^0 \text{ requires C, 84.84, H, 11.39%).} \]

**Oppenauer oxidation of glochidiol**

Glochidiol (1 g) in dry and distilled toluene (100 ml) was refluxed with cyclohexanone (14 ml) on an oil-bath at 120°. Aluminium isopropoxide (5 g per 10 ml of toluene) (10 ml) was added dropwise at a slow rate. After the addition the reaction mixture was refluxed for another hour and the product worked up as described in the above experiment. The material obtained (420 mg) was dissolved in benzene and adsorbed on neutral alumina (12 g) column set up with hexane. The column was eluted initially with hexane and then with benzene. Hexane eluate on evaporation left no residue. The first 25 ml of benzene eluate on removal of solvent gave a solid (0.3 g) which was crystallised from chloroform–methanol as fine needles, m.p. 165–166°, undepressed by admixture with a sample of glochidone. The U.V. and I.R. spectra of the two samples were identical.

**Glochidone epoxide**

A solution of glochidone (2 g) in pure dioxan (80 ml) was treated under vigorous stirring with sodium hydroxide (1N, 30 ml) and 30% hydrogen peroxide (15 ml) and the stirring continued
for 2 days. The reaction mixture was then diluted with excess of water and stirred for two hours. The solid that separated out was filtered, washed with water, dried *in vacuo* and crystallised from methanol to yield the epoxide (2 g), m.p. 181-183°, $[\alpha_C^\circ]_D + 107.15^\circ$. (Found: C, 82.27; H, 10.71. \(\text{C}_{30}\text{H}_{46}\text{O}_2\) requires C, 82.13; H, 10.57\%).

**LiAlH\(_4\)** reduction of glochidone epoxide

Glochidone epoxide (2 g) in dry and distilled tetrahydrofuran (25 ml) was added drop by drop during 30 minutes to a stirring suspension of Lithium aluminium hydride (2 g) in dry and distilled tetrahydrofuran (50 ml). When the addition was over the mixture was stirred at 60° over an oil bath for four hours. The reaction mixture was then cooled and the LiAlH\(_4\) was carefully decomposed by adding ice cold ethyl acetate followed by saturated sodium sulphate. The clear solution was decanted from the inorganic hydroxides and evaporated to dryness. The material obtained was taken in ether, washed with water, dried over sodium sulphate and ether removed by evaporation. The solid obtained was crystallised once from methanol and thrice from chloroform–methanol to yield needles (CCI, 600 mg),
This compound was acetylated with acetic anhydride and pyridine and the acetylated product was worked up in the usual manner. The solid obtained was crystallised from methanol to yield CCI\text{III}, m.p. 124-126°. (Found: C, 77.49; H, 10.20.
C_{34}H_{54}O_{4} requires C, 77.52; H, 10.33%).

The methanol mother liquor (before acetylation) was evaporated to dryness and the residue (1 g) was dissolved in benzene and adsorbed on a column of neutral alumina (30 g) suspended in benzene. The column was eluted with benzene and then with chloroform. Benzene eluate on evaporation left no residue. Fractions (20 ml) of chloroform eluate were collected and followed by T.L.C. The fractions which were alike and pure were mixed, evaporated and the solid obtained was directly acetylated with acetic anhydride and pyridine. The acetate (CCI\text{IV}) was worked up in the usual manner and crystallised from methanol to yield needles (800 mg), m.p. 230-234°, [\alpha]_{D}^{25} + 46.57°. (Found: C, 77.82; H, 10.19. C_{34}H_{54}O_{4} requires C, 77.52; H, 10.33%).
**LiAlH₄ reduction of lup-29-ene-1,3-dione**

A solution of the diketone (CLXXVIII, 100 mg) in dry and distilled tetrahydrofuran (10 ml) was added drop by drop to a stirring suspension of lithium aluminium hydride (100 mg) in tetrahydrofuran (50 ml). The reaction mixture was refluxed on an oil-bath at 60° for 5 hours. Then it was cooled and the lithium aluminium hydride was carefully decomposed by dropwise addition of a saturated solution of sodium sulphate. The solution was filtered and evaporated. The material obtained was taken in ether, washed with water, dried over sodium sulphate, filtered and evaporated to dryness.

The amorphous product thus obtained (100 mg) was treated with acetic anhydride (3 ml) and pyridine (1 ml) and the mixture was left overnight at room temperature. It was then poured into ice cold water and stirred well. The solid obtained was filtered, washed free from pyridine and dried. It was dissolved in minimum amount of benzene and adsorbed on a column of neutral alumina (3 g) suspended in benzene. Benzene eluate of the column on evaporation gave a solid which was repeatedly crystallised from methanol to yield needles, m.p. 230-234°. Mixed m.p. with the acetate (CCIV) mentioned above showed no depression.
Sodium borohydride reduction of lup-29-ene-1,3-dione

A solution of sodium borohydride (100 mg) in methanol (5 ml) was added to a solution of diketone (CLXXXVIII, 300 mg) in methanol (30 cc) at room temperature. The reaction mixture was allowed to stand for three hours at room temperature and then refluxed for twelve hours. The solution was filtered and the solvent evaporated. The product was extracted with ether, washed thrice with water, dried over anhydrous sodium sulphate, filtered and evaporated to dryness. The solid material obtained was acetylated as such with acetic anhydride and pyridine and worked up in the usual manner. The acetate was purified by chromatography over neutral alumina. Benzene eluate of the column on evaporation gave a solid which was crystallised as colourless needles from chloroform-methanol mixture, m.p. 234-235°, undepressed by admixture with the acetate (CCIV) obtained by the LiAlH₄ method.

Dihydroglochidone epoxide

A solution of glochidone epoxide (1 g) in acetic acid (50 ml) was hydrogenated at atmospheric pressure using platinum oxide as catalyst. The catalyst was filtered off, the solvent evaporated in vacuo and the solid obtained was crystallised from chloroform-methanol to give the dihydroepoxide, m.p. 223-225°,
120

\[ \begin{array}{c}
\text{C} + 67.52^\circ. \text{(Found: C, 81.38; H, 11.26. } C_{30}H_{48}O_2 \text{ requires C, 81.76, H, 10.98\%).}
\end{array} \]

**LiAlH₄ reduction of dihydroglochidone epoxide**

The above dihydroepoxide (2 g) in dry and distilled tetrahydrofuran (25 ml) was added drop by drop to a stirring suspension of LiAlH₄ (2 g) in tetrahydrofuran (75 ml) and the product was refluxed on an oil-bath at 60° for 5 hours. The mixture was cooled and the LiAlH₄ was decomposed in the usual manner. The solution was filtered and evaporated. It was taken up in ether, washed with water, dried over sodium sulphate, filtered and evaporated to dryness. Thin layer chromatography (on silica using chloroform : ethyl acetate = 19:1) of the product showed two spots which were wide apart and different from the spot corresponding to the starting material. These were separated by column chromatography.

The solid mixture (1.8 g) was dissolved in minimum chloroform and adsorbed on a column of neutral alumina (60 g) suspended in benzene. The column was eluted with chloroform and 10 ml fractions collected. Like fractions were combined after being checked by thin layer chromatography. Fractions 2–6 gave 878 mg of a diol (CXCVII) which was crystallised from chloroform-methanol as needles (740 mg.), m.p. 250°, \[ \begin{array}{c}
\left[ \alpha \right]_D^{20} -16.06 \text{ (Found: C, 81.10;}
\end{array} \]
compound was acetylated with acetic anhydride and pyridine in the usual manner and the acetate (CXCIX), crystallised from methanol, had m.p. 158-160°. (Found: C, 77.79; H, 10.86. C₃₄H₅₆O₄ requires C, 77.72; H, 10.67%).

Fractions 8 to 25 in the chromatography on evaporation gave 741 mg of a second diol (CXCVIII) which was crystallised from methanol, m.p. 236-238°, [α]D₂₄ = -6.4. (Found: C, 81.18; H, 12.16. C₃₀H₅₀₂ requires C, 81.02; H, 11.79%). This was also acetylated with acetic anhydride and pyridine in the normal way and the acetate, (CC)(680 mg), was crystallised from chloroform-methanol mixture, m.p. 238-242°, [α]D₂₄ = +9.80°. (Found: C, 77.10, H, 10.69. C₃₄H₅₆O₄ requires C, 77.22; H, 10.67%).

**Sodium and propanol reduction of lup-29-ene-1,3-dione**

A solution of (CLXXXVIII) (0.3 g) in boiling normal propanol (50 ml) was treated with sodium (3.5 g) portionwise over a period of 40 minutes. Heating was continued for 30 minutes more during which time all sodium went into solution. Water was added to the reaction mixture and the propanol removed by distillation under reduced pressure.
The solution was cooled and extracted with ether. The ether extract was washed with water, dried over sodium sulphate, filtered and evaporated to dryness.

The product was acetylated with acetic anhydride and pyridine in the usual manner. The solid obtained (240 mg) was dissolved in minimum benzene and adsorbed on a column of neutral alumina (10 g) suspended in hexane. The column was successively eluted with hexane and benzene. Hexane eluate on evaporation gave no material. Further elution with benzene gave a solid which was crystallised from methanol to yield needles of (CCVI), m.p. 212-214°, \([\alpha]_D^0 = 31.53\). (Found: C, 77.72; H, 10.42. C\(_{34}\)H\(_{56}\)O\(_4\) requires C, 77.22; H, 10.67%).

**Catalytic hydrogenation of the above acetate**

The above acetate (180 mg) was hydrogenated in glacial acetic acid solution using platinum oxide as catalyst and worked up in the usual manner. The solid obtained was crystallised thrice from methanol to yield needles of (CCVIII), m.p. 223-226°, \([\alpha]_D^0 = -6.48°\). (Found: C, 77.04; H, 10.97. C\(_{34}\)H\(_{58}\)O\(_4\) requires C, 76.93; H, 11.01).
Isolation of lupeol

Air dried powdered plant (50 kg) was extracted three times with cold petroleum ether (40–60°). The combined extract was evaporated to dryness under reduced pressure. The viscous residue (102 g) was dissolved in minimum amount of benzene and adsorbed on a column of neutral alumina (1 kg) in hexane. The column was eluted successively with hexane, benzene and benzene:acetone (19:1). The later fractions of benzene eluate as well as the benzene-acetone eluate on evaporation gave some solids. They were combined after checking melting points and TLC. The combined fraction (40 g) was crystallised from methanol to give lupeol, m.p. 213-215°.

Acetylation of lupeol

Lupeol (0.5 g) was treated with acetic anhydride (5 ml) and pyridine (2 ml) and left overnight. It was worked up in the usual manner. The solid acetate (0.5 g) was crystallised as needles from methanol, m.p. 217-218°.

Autoxidation of lupeone and lupanone

Lupeone (1 g), obtained by Jones oxidation of lupeol, was suspended in a solution of potassium (3 g) in freshly distilled
tertiary butanol (80 ml) and shaken with oxygen at atmospheric pressure for two hours (uptake of 1 mole of oxygen). Water (80 ml) was added, cooled in ice-bath and acidified with cold 6N hydrochloric acid. The solid separated was extracted with chloroform, washed with water, dried over sodium sulphate and evaporated to dryness. The solid residue was crystallised from acetone-methanol mixture as colourless needles (0.9 g), m.p. 187-190°, λ 272 μν, ν_{max} 3440, 1660, 1640 cm⁻¹, [α]_D + 70.9°. (Found: C, 81.86; H, 10.58. C_{30}H_{46}O_{2} requires C, 82.13; H, 10.57%). It gives positive ferric chloride colour reaction.

Similarly, lupanone (CCXIII) (0.9 g) yielded the diosphenol (CCXV) (0.85 g), m.p. 210-213°, λ_{max} 272 μν, ν_{max} 3440, 1660, 1640 cm⁻¹, [α]_D + 24.75. (Found: C, 82.19; H, 11.27. C_{30}H_{48}O_{2} requires C, 81.76; H, 10.98%).

**Ketoacetate (CCXVI)**

Diosphenol (CCXV) when hydrogenated (Pd/C) in benzene, yielded a dihydro derivative which was acetylated as such using acetic anhydride and pyridine at room temperature. The ketoacetate (CCXVI) crystallised from acetone as cubes, m.p. 260-263°, ν_{max} 1700, 1725 cm⁻¹. (Found: C, 79.69; H, 10.41, C_{32}H_{52}O_{3} requires C, 79.28; H, 10.81%).
**Ozonolysis of dihydrodisphenol (CCXV)**

Chloroform solution of dihydrodisphenol (0.75 g) was ozonised at zero degree till completion. Crude ozonide was heated on a water-bath for three hours with aqueous sodium bicarbonate solution and hydrogen peroxide (30%). It was then extracted with chloroform. The bicarbonate solution on acidification did not yield anything.

The chloroform extract was washed with water, dried over sodium sulphate and evaporated to yield (CCXVIII) which was crystallised from methanol, m.p. 205-209°, \( \nu_{\text{max}} \) 3600, 1730 cm\(^{-1}\).

(Found: C, 78.32; H, 11.06. \( \text{C}_{29}\text{H}_{48}\text{O}_3 \) requires C, 78.32; H, 10.88%).

**Alkaline hydrogen peroxide oxidation of disphenol (CCXIV)**

A solution of disphenol (CCXIV) (1.36 g) in 2.5% methanolic potassium hydroxide (200 ml) was treated with 30% hydrogen peroxide (15 ml). After refluxing the reaction mixture on a water-bath for 1½ hours, methanol was removed under vacuum, water was added and the solution filtered. The clear filtrate was acidified and extracted with ether. The ether extract was washed with water, dried over sodium sulphate and evaporated to yield a solid (1.25 g) which was crystallised from ether-hexane,
Conversion of the acid (CCXIX) to the ketone (CCXI)

The dicarboxylic acid (CCXIX) (1.2 g) yielded a methyl ester with diazomethane which was refluxed with 10% methanolic potassium hydroxide (30 ml) for 15 hrs. Water was added and it was extracted with ether. The ether extract was washed with water, dried over sodium sulphate and the solvent removed to yield the ketone (CCXI) (1.16 g) which was crystallised from methanol, m.p. 194-196°, λ$_{max}$ 1740 cm$^{-1}$, $\left[\alpha\right]_D^0 + 132.7°$ (Found C, 84.79; H, 11.21. $C_{29}H_{46}O$ requires C, 84.81; H, 11.29%).
SUMMARY
compounds, glochidone, 3-epilupeol acetate and glochidiol diacetate. From the roots of the plant glochidiol and glochidone were obtained. The structure of these two new triterpenes have been established by relating them to a known compound, lupan-3-one.

The stereochemistry of the hydroxyl groups in glochidiol has also been determined by the partial synthesis of three of the four possible stereoisomers of the dihydrodiol diacetate \( \text{CXC, CXI and CXCII} \) which all differ from dihydroglochidiol diacetate \( \text{CXCIII} \).

*Astercantha longifolia* Nees. (Syn. *Hygrophila spinosa* T. Anders (Acanthaceae)

Lupeol has been isolated from the hexane extract of this plant and in an attempt to modify its structure to induce biological activity, oxidation in ring A in lupeol has been studied. Lupeone and lupanone on autoxidation yielded the corresponding diosphenols. Catalytic hydrogenation of the diosphenol from lupanone yielded a ketoalcohol which when acetylated, rearranged to lupan 3-acetoxy 2-one.

Diosphenol from lupanone when ozonised and worked up with sodium bicarbonate and hydrogen peroxide gave a neutral compound \( \text{C}_{29}\text{H}_{48}\text{O}_3 \) which has no selective absorption in the U.V.,
$\nu_{\text{max}}$ 3600 cm$^{-1}$ (OH), 1730 cm$^{-1}$ ($\delta$-lactone). Based on its mode of formation, spectral characteristics and elemental composition, it has been assigned structure (CCXVIII).

In another series of reaction diosphenol from lupeone was cleaved by alkaline hydrogen peroxide to a dicarboxylic acid (CCXIX), $C_{30}H_{48}O_4$ the methyl ester of which on refluxing with alcoholic alkali yielded a nor-ketone (CCXXI), $C_{29}H_{46}O$ in excellent yield, $\nu_{\text{max}}$ 1740 cm$^{-1}$ (cyclopentanone).
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