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CHAPTER I

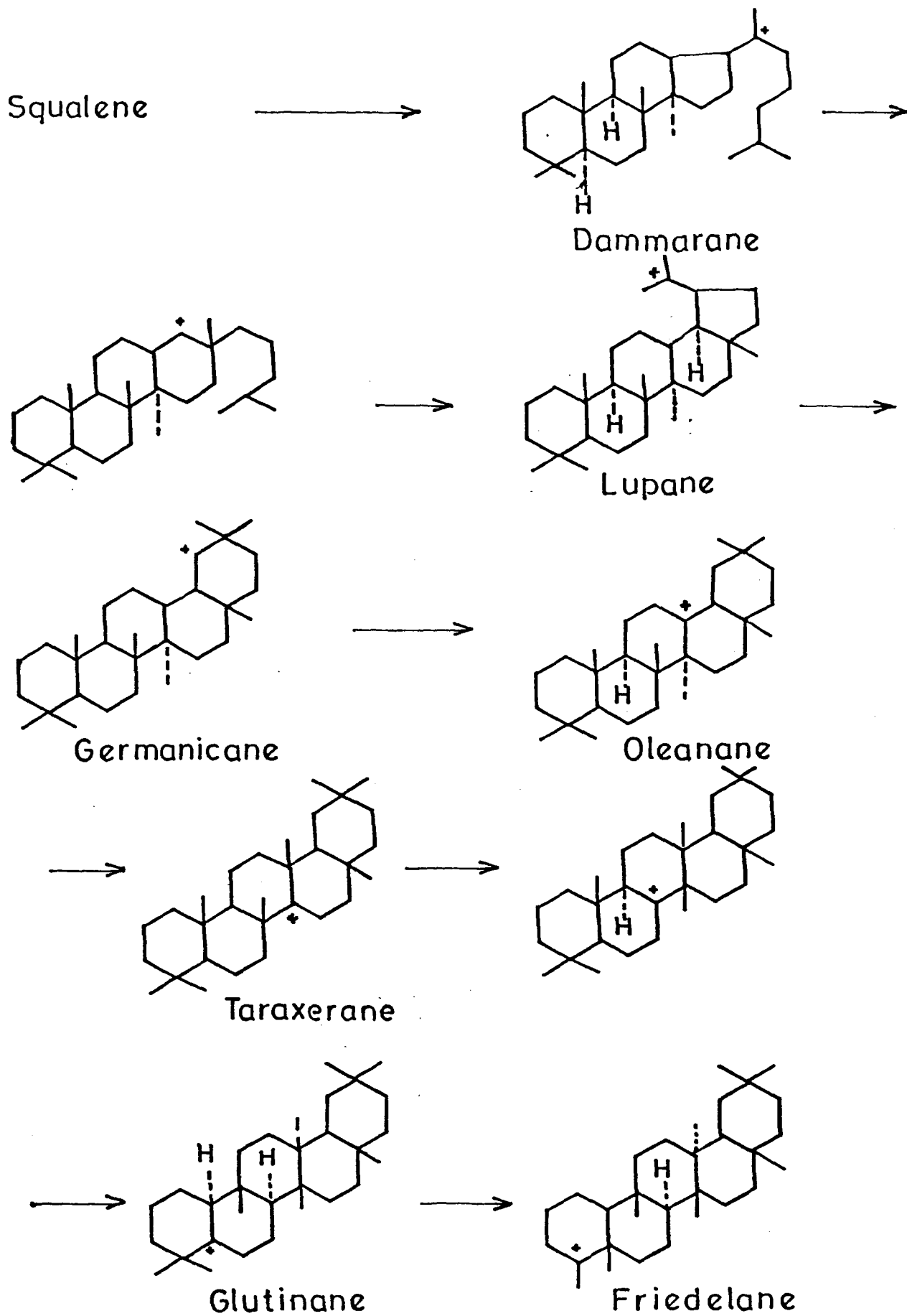
CHAPTER I

Δ^{18} OLEANE TRITERPENES

The term triterpenoids refers to a group of natural products containing thirty carbon atoms based on six isoprene units. They can be divided broadly into several classes such as oleanane, ursane, taraxastane, friedelane, strictane, hopane, lupane, serratane, fernane, dammarane, tirucallane, euphane, lanostane, cucurbitane, fusidane and tetranortriterpenoids. In oleanane series several triterpenes with double bonds at 12(13), 13(18) and 18(19) carbons are known. Biogenetically oleananes with 18(19) double bond (olean-18-enes) are believed to be derived from squalene (Scheme 1). While it has been well established that squalene is the biological precursor of all the triterpenes, olean-18-enes may be considered as the immediate precursors to olean-12-enes and olean-13-enes.

While most of the other triterpenes are abundant in nature olean-18-enes are relatively few in number. The advent of powerful analytical methods and their subsequent advancement resulted in the isolation and structural elucidation of more and more olean-18-enes during the past 15-20 years. The present chapter aims at a thorough review on the natural occurrence and chemistry of these triterpenes isolated so far. Table 1 gives a list of olean-18-enes reported in literature.

SCHEME 1



Biogenetic relationship of Δ^{18} Oleanes with other triterpenes

Table 1 : Natural occurrence of Δ^{18} Oleanane triterpenes

Sl. No.	Compound	Molecular formula	Part	Source	Family	m.p. °C	$[\alpha]_D^\circ$	Reference
1	Germanicol	$C_{30}H_{50}O$	Latex	<i>Lactucarium germanicum</i>	Compositae	176.7	+ 5.8	1 and Table 2
2	Epigermanicol	$C_{30}H_{50}O$	Latex	<i>Euphorbia candelilla</i>	Euphorbiaceae	221-2	-34.8	33
			Whole plant	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	-	-	24
3	Germanicone	$C_{30}H_{48}O$	-	<i>Euphorbia balsamifera</i>	Euphorbiaceae	-	-	15
4	Miliacin	$C_{31}H_{52}O$	Leaves and sheaths	<i>Chionochloa species</i>	Gramineae	280-2	+ 22	45 and Table 4
5	Anagadiol	$C_{30}H_{50}O_2$	Aerial parts	<i>Salvia broussonetii</i>	Labiatae	212-4	+ 5	66
6	Germanidiol	$C_{30}H_{50}O_2$	Whole plant and buds	<i>Rhododendron linearifolium</i>	Ericaceae	275	+36.8	69
				<i>Rhododendron macrocephalum</i>	Ericaceae	275-7	+15.4	70
7	Epigermanidiol	$C_{30}H_{50}O_2$	Buds	<i>Rhododendron macrocephalum</i>	Ericaceae	220-2	- 2.0	70
8	Nivadiol	$C_{30}H_{50}O_2$	Aerial parts	<i>Salvia broussonetii</i>	Labiatae	225-225.5	- 1	71
9	Compound 10	$C_{30}H_{48}O_3$	Aerial parts	<i>Salvia deserta</i>	Labiatae	229-33	+54	73
10	Compound 11	$C_{34}H_{54}O_4$	Aerial parts	<i>Schaefferia cuneifolia</i>	Celastraceae	230-2	+6.35	74
11	Compound 12	$C_{30}H_{50}O_2$	Aerial parts	<i>Schaefferia cuneifolia</i>	Celastraceae	237-8	+8.5	74
12	Compound 13 isolated as acetate	$C_{32}H_{50}O_3$	Aerial parts	<i>Schaefferia cuneifolia</i>	Celastraceae	208-10 acetate	+31.5 acetate	74
13	Compound 14 isolated as acetate	$C_{32}H_{50}O_3$	Aerial parts	<i>Schaefferia cuneifolia</i>	Celastraceae	210-2 acetate	+37 acetate	74

Table 1 (contd...)

Sl. No.	Compound	Molecular formula	Part	Source	Family	m.p. °C	$[\alpha]_D^0$	Reference
14	Moradiol isolated as diacetate	$C_{30}H_{50}O_2$	Leaves	<i>Buxus sempervirens</i>	Buxaceae	275 diacetate	-	14
15	3-Acetyl-moradiol	$C_{32}H_{52}O_3$	Wood bark	<i>Agauria salicifolia</i>	Ericaceae	285-6	-	75
16	3-Acetyl-moraldehyde	$C_{32}H_{50}O_3$	Wood bark	<i>Agauria salicifolia</i>	Ericaceae	274-5	-	75
17	Morolic acid	$C_{30}H_{48}O_3$	Heart wood	<i>Mora excelsa</i>	Moraceae	273	+31	76,78 and Table 5
18	Moronic acid	$C_{30}H_{46}O_3$	Aerial parts	<i>Roylea elegans</i>	Labiatae	222	+29	92
19	Semimoronic acid	$C_{30}H_{46}O_4$	Leaves	<i>Rhus semialata</i> <i>Rhus alata</i>	Anacardiaceae Anacardiaceae	260-1 260-1	+42 -	93 56
20	Compound 21	$C_{31}H_{48}O_4$	Aerial parts	<i>Orthopterygium huancuy</i>	Julianaceae	204-5	+7	96
21	Compound 22	$C_{31}H_{50}O_4$	Aerial parts	<i>Orthopterygium huancuy</i>	Julianaceae	-	-	89
22	Periandrin I	$C_{42}H_{62}O_{16} \cdot 4H_2O$	Roots	<i>Periandra dulcis</i>	Leguminosae	> 300	-23	97
23	Periandrin III	$C_{42}H_{64}O_{16} \cdot 2H_2O$	Roots	<i>Periandra dulcis</i>	Leguminosae	> 300	-24.5	98
24	Periandric acid I	$C_{30}H_{46}O_4$	Roots	<i>Periandra dulcis</i>	Leguminosae	260-3	+183.36	99
25	Compound 26	$C_{30}H_{44}O_4$	Roots	<i>Periandra dulcis</i>	Leguminosae	283-92	+1.52	100



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3-Oxygenated olean-18-enes

Germanicol (1)

Germanicol, the widely occurring 3-oxygenated olean-18-ene was first isolated by James et al in 1944 from the latex of *Lactucarium germanicum*¹. The structure of germanicol was first deduced by Serge David³ in 1949 by preparing from Germanicol, a dienol identical with a derivative of β -amyrin prepared earlier by Ruzicka. It was later confirmed by Meakins et al by its conversion from lupeol^{29,30}. Another method of converting lupeol to germanicol³¹ is by the action of formic acid on lupeol. When lupeol is treated with formic acid in benzene, formic acid adds on to the double bond with ring enlargement and the formation of 18α -oleanane- 3β , 19α -diol. This 19α -hydroxy compound was converted into 19β -hydroxy compound by the oxidation of 3-acetate and reduction with lithium aluminium hydride. Dehydration of the 3-acetate of 18α -olean- 3β , 19β -diol with phosphorus oxychloride in pyridine gives germanicol acetate. The structure 1 for germanicol was then confirmed by Serge David³². Germanicol occurs widely in nature and its occurrence in different plant species is recorded in Table 2.

Table 2 : Natural occurrence of Germanicol (1)

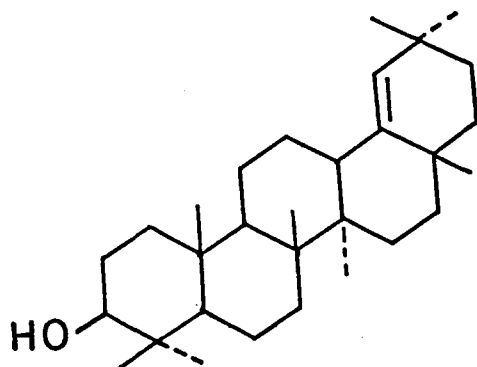
Sl. No.	Source	Family	Part	Reference
1	<i>Lactucarium germanicum</i>	Compositae	Latex	1
2	<i>Salvia officinalis</i> (Sage)	Labitae	Leaf	2
3	<i>Euphorbia balsamifera</i>	Euphorbiaceae	Latex	3,5,6,7,15
4	<i>Euphorbia balsamifera</i>	Euphorbiaceae	Resins	4
5	<i>Sonchus ortunoi</i> and <i>Sonchus leptcephalus</i>	Compositae Compositae	-	8
6	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	Latex, stems, bracts and flowers	9,16
7	<i>Youngia denticulata</i>	Compositae	Leaves	10
8	<i>Lactuca virosa</i>	Compositae	Latex	11
9	Gramineae plants	Gramineae	Leaves	12,13
10	<i>Buxus sempervirens</i>	Buxaceae	Leaves	14
11	<i>Hedyotis acutangula</i>	Rubiaceae	Stems	17
12	<i>Thea sinensis</i> (tea oil)	Theaceae	Seed	18

Table 2 (contd...)

Sl. No.	Source	Family	Part	Reference
13	<i>Sonchus asper</i>	Compositae	-	19
14	<i>Poinsettia pulcherrima</i>	Euphorbiaceae	Fruits	20
15	<i>Anthurus maellierianus</i>	-	Microorganism	21
16	<i>Salvia broussonetii</i>	Labiatae	Aerial parts	22
17	<i>Sarcostemma species</i>	Asclepiadaceae	Stems & leaves	23
18	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	Whole plant, leaves	24,26
19	<i>Ceropegia dichotoma</i>	Asclepiadaceae	Whole plant	25
20	<i>Cnidosculus urens</i>	Euphorbiaceae	Whole plant	27
21	<i>Ixeris debilis</i> and <i>I. dentata</i>	Compositae	Whole plant	28
22	<i>Lactuca sativa</i>	Compositae	Roots	36
23	<i>Camellia weiningensis</i>	Theaceae	Seed	40
24	<i>Maytenus horrida</i>	Celastraceae	Root bark	51
25	<i>Casuarina equisetifolia</i>	Casuarinaceae	Bark	52
26	<i>Euphorbia characias</i>	Euphorbiaceae	Leaf wax	53
27	<i>Euphorbia nicaeensis</i>	Euphorbiaceae	Leaf wax	53

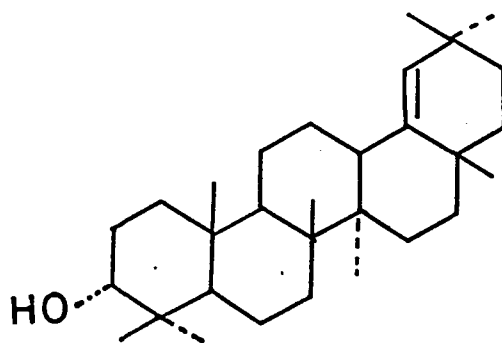
Table 2 (contd...)

Sl. No.	Source	Family	Part	Reference
28	<i>Euphorbia peplus</i>	Euphorbiaceae	Leaf wax	53
29	<i>Euphorbia supina</i>	Euphorbiaceae	Whole plant	54
30	<i>Trixis praestansis</i>	Compositae	Whole plant	55
31	<i>Salvia pratensis</i>	Labiatae	Aerial part	57
32	<i>Ixeris leavizate</i>	Compositae	-	58
33	<i>Vermonia incana</i>	Compositae	Aerial part	59
34	<i>Stevia alpina</i>	Compositae	Leaves and flowers	60
35	<i>Chrysanthemum indicum</i>	Compositae	Whole plant	61
36	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	Whole plant less root	62
37	<i>Colletia paradoxa</i>	Rhamnaceae	Epicuticular wax	63



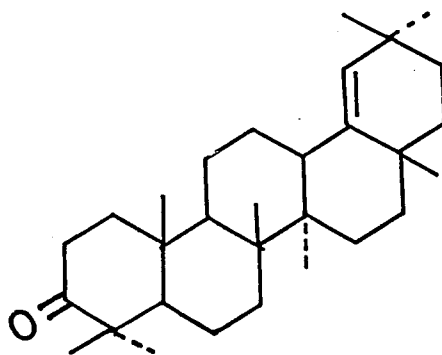
Epigermanicol (2)

It was first isolated from natural source in 1956 from the waxy cuticle of *Euphorbia condelilla* Var *Luxurians*³³. Oxidation of the above with chromium trioxide and pyridine gave germinacone, m.p. 189-9.5°, $[\alpha]_D + 39.3^\circ$. Germinacol⁶ (1) isolated from *Euphorbia balsamifera* was converted into epigermanicol by heating with 1% hydrochloric acid in acetic acid for three hours. It was also isolated from *Euphorbia pulcherrima*²⁴.



Germanicone (3)

It was isolated from the latex of *Euphorbia balsamifera*¹⁵ and identified on the basis of IR, NMR and MS. It was earlier synthesised from germanicol isolated from *Euphorbia candelilla* Var *Luxurians*³³. It was also isolated from *Euphorbia balsamifera*⁷ and *Poa huecu*⁷².

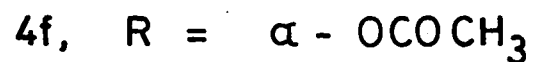
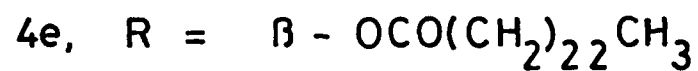
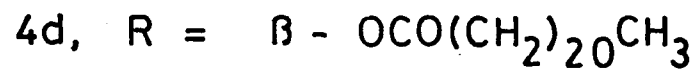
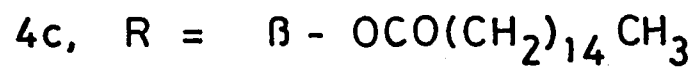
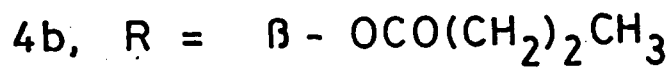
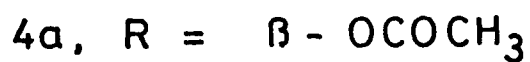
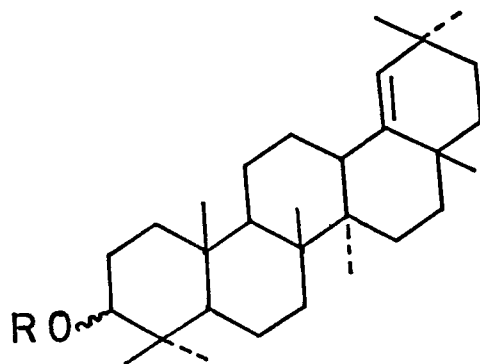


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Derivatives of germanicol and epigermanicol (4)

Several fatty acid esters of germanicol and epigermanicol were isolated from *Euphorbia pulcherrima*²⁴ and *Elaeagnospermum tapos*³⁵ and characterised by their IR, NMR and MS. Germanicol palmitate³⁵ (4c) $C_{46}H_{80}O_2$, m.p. 109-110°; butyrate²³ (4b) $C_{34}H_{56}O_2$, m.p. 238-9°; tetracosanoate²⁴ (4e) $C_{54}H_{96}O_2$, m.p. 84-87° $[\alpha]_D + 22.5^\circ$; behenate²⁴ (4d) $C_{52}H_{92}O_2$ and epigermanicyl acetate²⁴ (4f) m.p. 136-7° $[\alpha]_D -26^\circ$ were reported from *Elaeagnospermum tapos* bark, *Sarcostemma species* and *Euphorbia pulcherrima* respectively. Germanicol docosanoate

is a major constituent in the root of *Cryptolepis buchanani*⁶⁵.



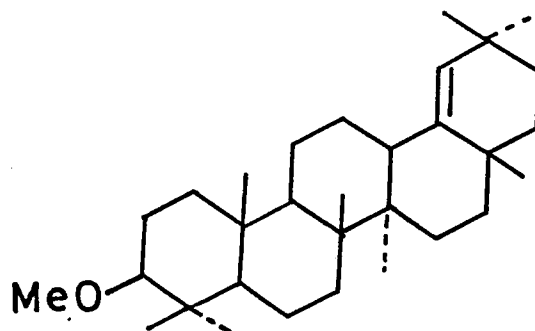
Germanicyl acetate (4a) occurs in several plant species and is listed in Table 3.

Table 3 : Natural occurrence of Germanicyl acetate

Sl. No.	Source	Family	Part	Reference
1	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	Whole plant	34
2	<i>Youngia denticulata</i>	Compositae	Leaves	10,39
3	<i>Elasterospermum tapos</i>	Euphorbiaceae	Bark	35
4	<i>Lactuca denticulata and Lactuca indica</i>	Compositae	Whole plant	11
5	<i>Sarcostemma species</i>	Asclepiadaceae	Stems and leaves	23
6	<i>Euphorbia pulcherrima</i>	Euphorbiaceae	Whole plant and leaves	16,24,26
7	<i>Sonchus asper</i>	Compositae	-	19
8	<i>Poinsettia pulcherrima</i>	Euphorbiaceae	Fruits	20
9	<i>Lactuca sativa</i>	Compositae	Root	36
10	<i>Cindosculus urens</i>	Euphorbiaceae	Whole plant	27
11	<i>Lagerstroemia lancasteri</i>	Lythraceae	Leaves and twigs	37
12	<i>Polypodium amanium</i>	Polypodiaceae	-	38

Miliacin (5)

Miliacin, the monomethyl ether of germanicol was isolated for the first time in millet in 1934⁴¹. Its structure was confirmed in 1960 by Shokichi Abe⁶⁴. The occurrence of miliacin from natural sources is recorded in Table 4.



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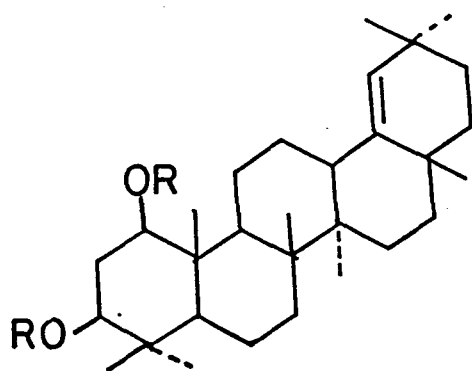
1-Oxygenated olean-18-enesAnagadiol (6)

The only 1-oxygenated olean-18-ene was isolated as its diacetate (6a) m.p. 247-255° by Gonzalez et al⁶⁶. The structure was established from chemical and spectral evidence. Jone's oxidation of 6 yielded a diketone (6b) m.p. 112-114°, $[\alpha]_D + 61^\circ$ (chloroform) IR: 1720, 1703 cm^{-1} .

Table 4: Natural occurrence of miliacin

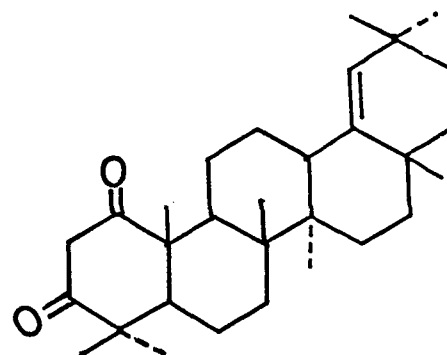
Sl. No.	Source	Family	Part	Reference
1	<i>Panicum miliaceum</i> (millet)	Gramineae	Seed	41,48,49,50
2	Gramineae plants	Gramineae	-	12,13,,42, 43,47,101
3	<i>Paspallum dilatatum</i>	Gramineae	Leaves	44
4	<i>Chionochloa crassiuscula</i> <i>Chionochloa flavescens</i> <i>Chionochloa oreophila</i> <i>Chionochloa rubra</i> <i>Chionochloa pallens</i> <i>Chionochloa pungens</i>	Gramineae	Leaf wax	45
5	<i>Chionochloa species</i>	Gramineae	-	46,102,103

The enolizable nature of β -diketone system in **6b** was established by the bathochromic shift to 293 nm from 260 nm in its UV spectrum. Final proof of its structure was obtained by Oppenauer oxidation of **6** to give an α,β -unsaturated ketone (**6c**) m.p. 163- 4°, $[\alpha]_D + 29^\circ$ (chloroform), IR: 1670, 1620 cm^{-1} , UV 232 nm and its catalytic reduction to germanicone **3**.

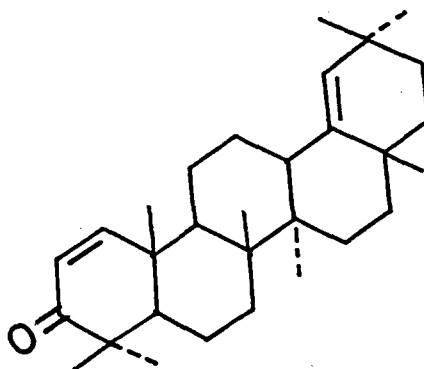


6, R = H

6a, R = Ac



6b



6c

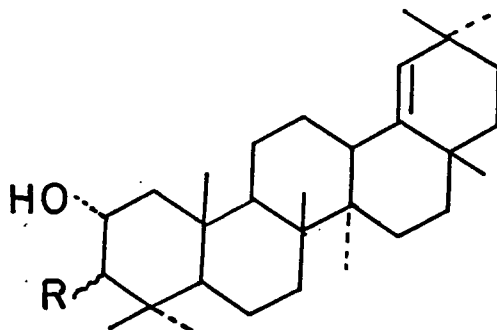
The structure of anagadiol was confirmed by synthesis starting from 19α -chloro- 18α -olean- 3β -ol⁶⁷ which was obtained by Wagner-Meerwein rearrangement of lupeol. Jones' oxidation of this compound yielded 19α -chloro- 18α -olean-3-one which was then treated with bromine in acetic acid. The brominated product was dehydrobrominated with lithium chloride in dimethylformamide to yield 1,18-oleanadien-3-one. This was epoxidised with hydrogen peroxide in alcoholic sodium hydroxide and $1\alpha,2\alpha$ -epoxy-18-oleanen-3-one formed was reduced with lithium aluminium hydride to give a mixture of 18-oleanen- $1\alpha,3\alpha$ -diol and 18-oleanen- $1\alpha,3\beta$ -diol which on Jones oxidation gave 18-oleanen-1,3-dione. Reduction of the dione with sodium in boiling propyl alcohol gave a product identical with natural anagadiol with the exception of a slight difference in optical rotation.

Anagadiol was also synthesised independently by Gonzalez et al⁶⁸ from germanicol. Germanicol on Jones oxidation gave germanicone, which on bromination, dehydrobromination, epoxidation and reduction gave the corresponding dione. The dione on reduction with sodium/propanol was found to give anagadiol.

Germanidiol and epigermanidiol (7 & 8)

Germanidiol was first isolated by Shiro Nakumura et al in 1965⁶⁹. That germanidiol has an 1,2-glycolic function

was suggested by consumption of periodate and lead tetracetate. Acetylation with pyridine and acetic anhydride gave two monoacetates, m.p. 204° and 233° and a diacetate, m.p. 264°, $[\alpha]_D + 36.8^\circ$. It formed an acetonide with acetone in presence of sulphuric acid, m.p. 201°. Reaction of germanidiol with p-toluenesulphonyl chloride in pyridine followed by reduction with lithium aluminium hydride gave a mono-hydroxy compound which was identified as germanicol. Germanidiol was thus shown to be 2 β -hydroxygermanicol. The structure was however revised as olean-18-ene-2 α ,3 α -diol (7) by Hiroyuki Ageta et al⁷⁰ based on its spectral characteristics and by comparison with spectral characteristics of the corresponding olean-12-enes and fern-7-enes. The structure of epigermanidiol as olean-18-ene-2 α ,3 β -diol (8) was also confirmed by the same workers⁷⁰



7, R = α -OH

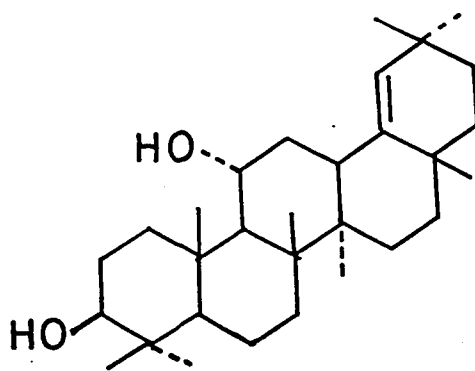
8, R = β -OH

11-Oxygenated olean-18-enes

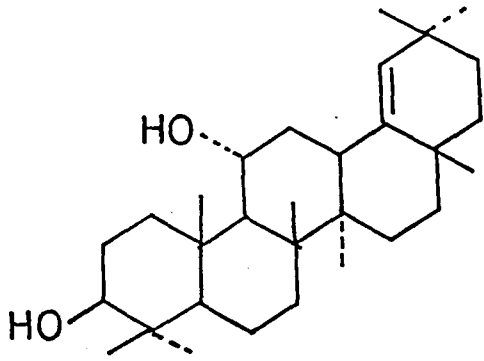
Nivadiol (9)

The structure of nivadiol was shown to be $3\beta,11\alpha$ -dihydroxyolean-18-ene by its NMR, MS and ORD spectra⁷¹. It formed two monoacetates (3β , m.p. $300-1^\circ$, $[\alpha]_D + 11^\circ$ and 11α) with pyridine and acetic anhydride. Chromium trioxide oxidation of nivadiol yielded a diketone which on Huang-Minlon reaction gave mono ketone (9b), m.p. $224-8^\circ$, $[\alpha]_D - 25^\circ$.

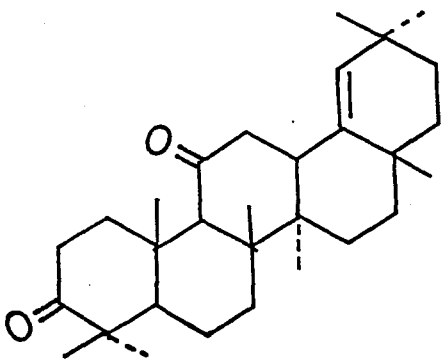
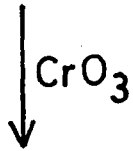
The monoacetate 9c gave 9b by similar set of reactions. A study of the NMR and Mass spectra of the two monoacetates as well as the original compound and the comparison of ORD spectra with those of sterioids having an oxygen function at C-11 confirmed the structure of nivadiol as 9. Later nivadiol was isolated from *Maytenus horrida* by Gonzalez et al⁵¹.



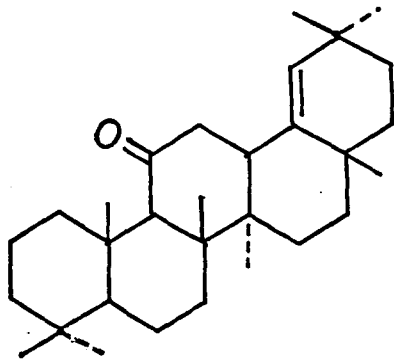
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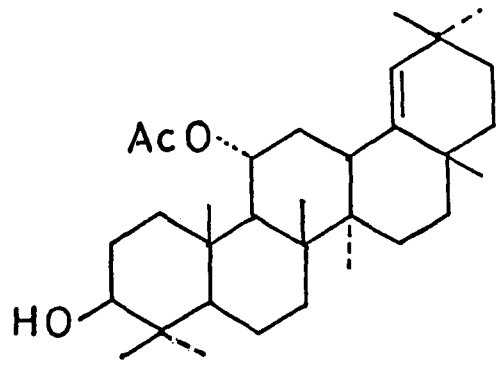
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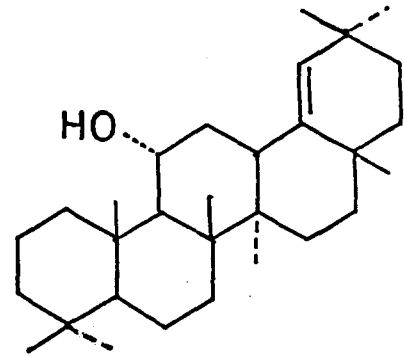
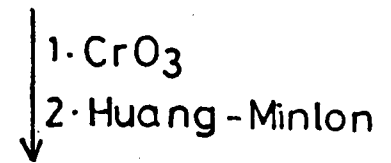
9a



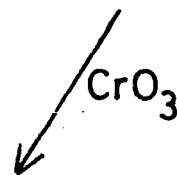
9b



9c

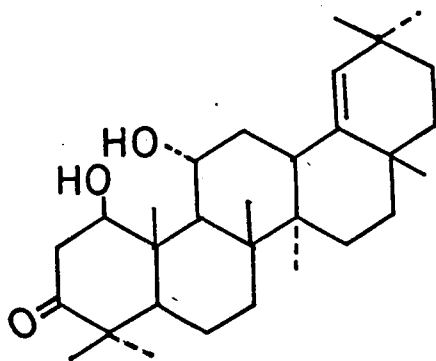


9d



Compound 10

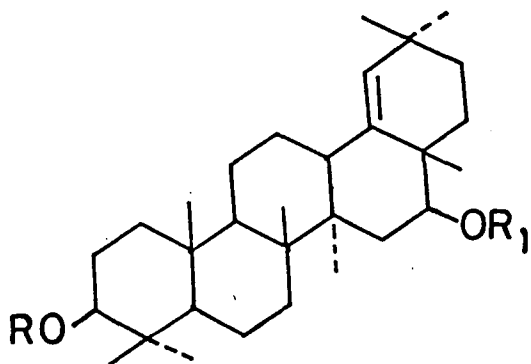
1 β ,11 α -Dihydroxyolean-18-ene-3-one (10) was isolated from the aerial parts of *Salvia deserta* by Rodriguez et al⁷³ and its structure was established by spectroscopic means.



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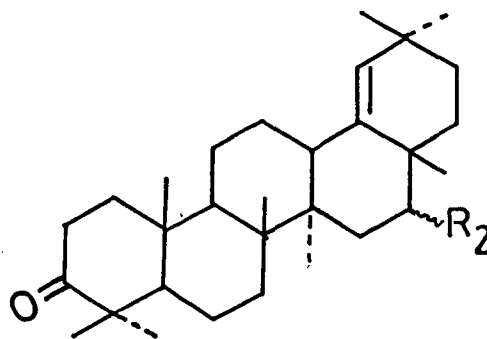
16-Oxygenated olean-18-enesCompounds 11-14

Four new 16-hydroxyolean-18-enes (11-14) were isolated from *Schaefferia cuneifolia* by Gonzalez et al⁷⁴. The latter two compounds were separated as their acetates. They were identified from their ¹H and ¹³C NMR data, DEPT experiments, chemical correlations and chemical shift values.



11, $R = R_1 = \text{Ac}$

12, $R = R_1 = \text{H}$



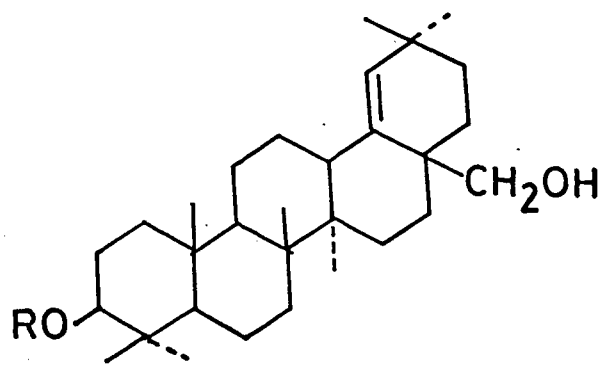
13, $R_2 = \beta\text{-OH}$

14, $R_2 = \alpha\text{-OH}$

28-Oxygenated olean-18-enes

Moradiol and 3-acetylmoradiol (15 & 16)

Moradiol was isolated as its diacetate, m.p. 275° from *Buxus sempervirens* by Abramson et al¹⁴. It was also isolated from *Planchonia careya*⁹⁵. 3-Acetylmoradiol was later isolated from *Agauria salicifolia* by Gregoire et al⁷⁵. The structures were established as 15 and 16 through their spectral characteristics.

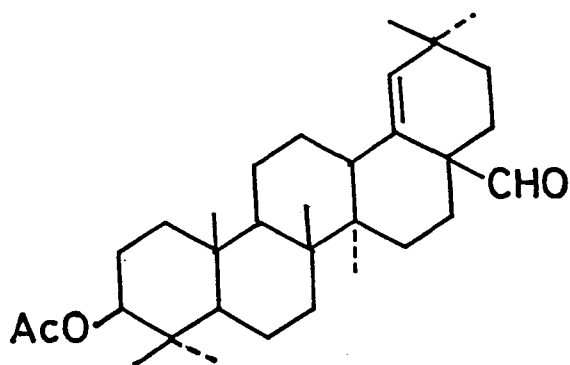


15, R = H

16, R = Ac

3-Acetylmoraldehyde (17)

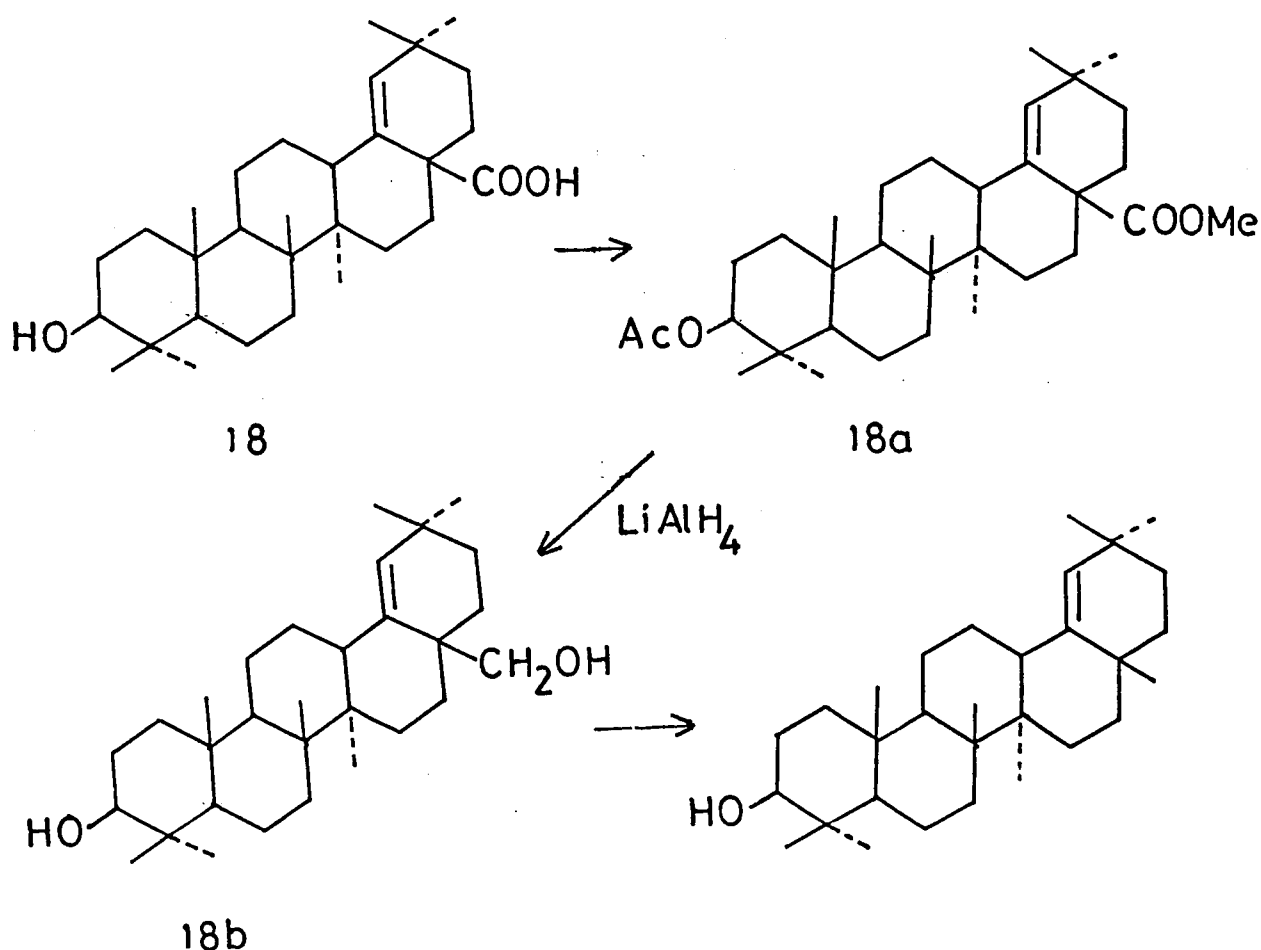
The structure of 3-acetylmoraldehyde (17) was established by spectral means⁷⁵.



17

Morolic acid (18)

Morolic acid was first isolated as its saponin from the heartwood of the Mora tree by Campbell et al⁷⁶. The structure was later established by Barton et al^{77,78}, by a series of chemical reactions. It formed a monoacetate, m.p. 256-7°, $[\alpha]_D + 44^\circ$ which was converted to methyl ester (18a) m.p. 263-4°, $[\alpha]_D + 38^\circ$. The acetate methyl ester on lithium aluminium hydride reduction gave the corresponding diol (moradiol, 18b) which contains one secondary and one primary hydroxyl group. By standard reactions the $-\text{CH}_2\text{OH}$ group was converted to $-\text{CH}_3$. The monohydroxy triterpenoids thus obtained was found to be identical with germanicol (1).



The final confirmation of the structure of morolic acid was obtained by its partial synthesis (Scheme 2) from siaresinolic acid (18c)⁷⁹. Treatment of methyl siaresinolate-3-acetate, m.p. 116-25° (18d) with perhydrol in acetic acid afforded, in a manner characteristic of the 12(13)-ethylenic linkage, methyl-12-keto oleananolate acetate (18e), m.p. 230-2°. Wolf-Kishner reduction of this ketone furnished after methylation and acetylation, methyldihydro-siaresinolate-3-acetate (18f) m.p. 205-6° $[\alpha]_D + 10^\circ$, which was smoothly dehydrated by phosphorus oxychloride in pyridine to give morolic acid acetate methyl ester (18a), m.p. 225-7° $[\alpha]_D + 24^\circ$. Morolic acid was later isolated from several plant species which is recorded in Table 5. 3-O-Arabinosylmorolic acid was also isolated from *Mimosa caesalpinifolia* by De Alancar et al⁸¹

Moronic acid (19)

The structure of moronic acid (19) was established by Majumder et al⁹² on the basis of its ¹H and ¹³C NMR spectra and confirmed by sodium borohydride reduction of moronic acid (19) and its methyl ester to morolic acid (18) and its methyl ester respectively.

SCHEME 2

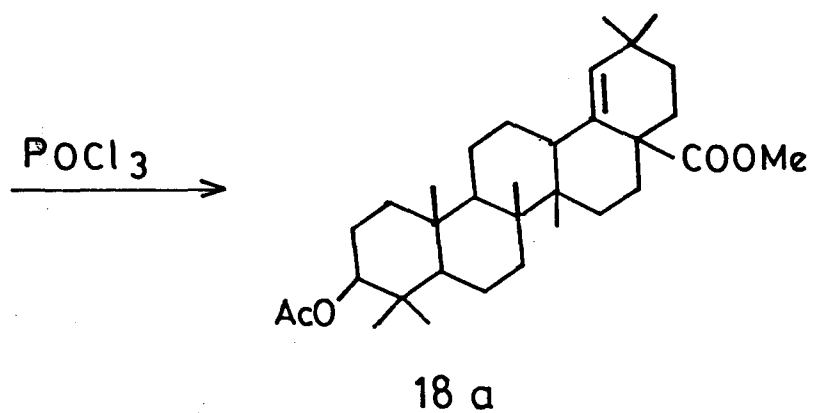
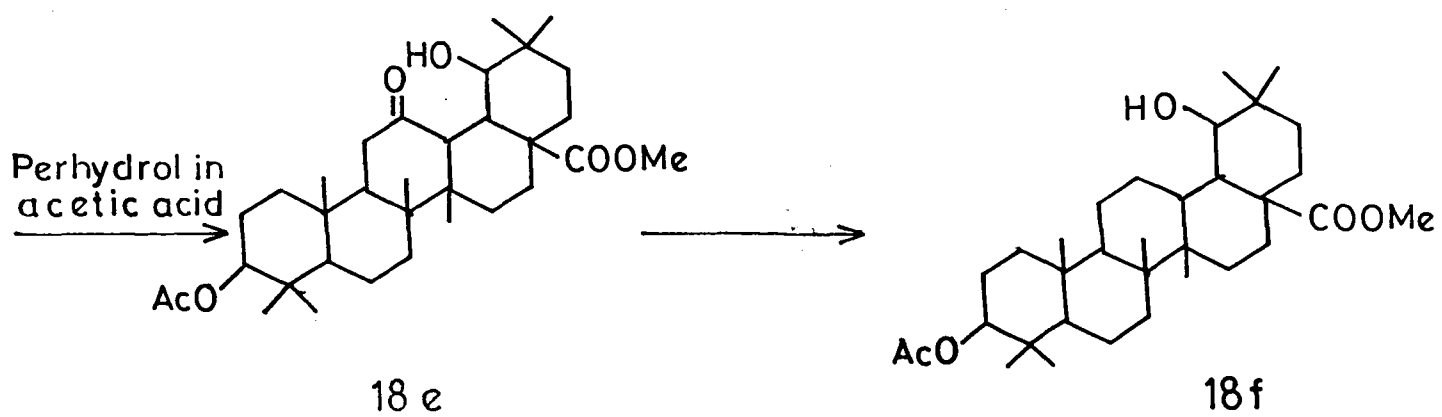
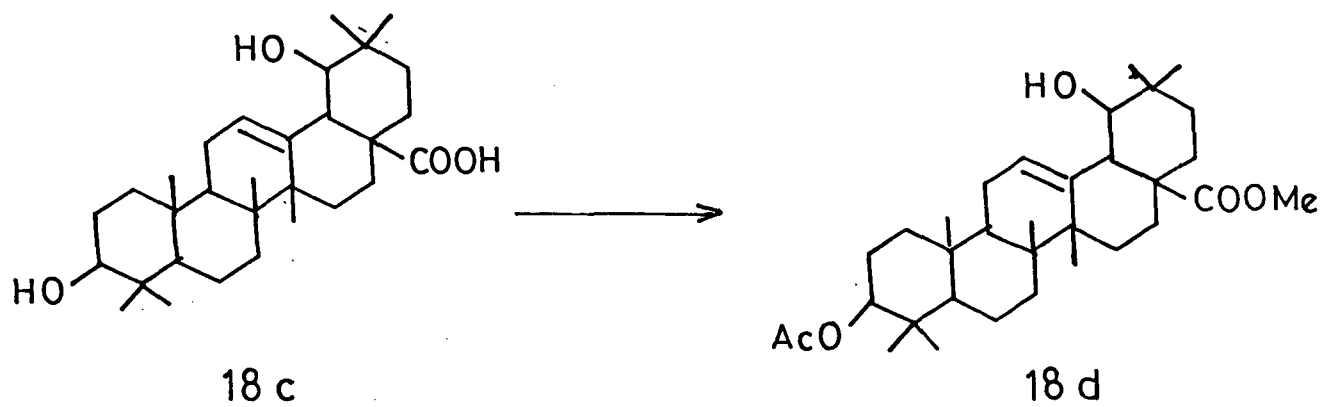
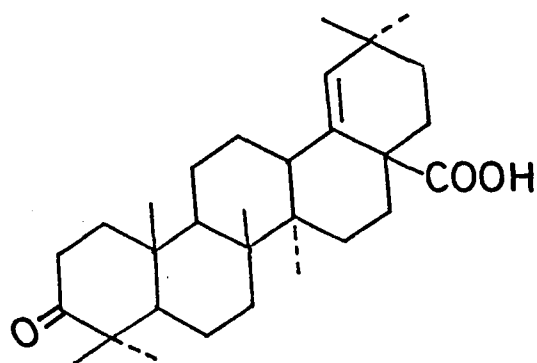


Table 5 : Natural occurrence of Morolic acid

Sl.No.	Source	Family	Part	Reference
1	<i>Mora exelsa</i>	Moraceae	Heartwood	76
2	<i>Mora gonggrijpii</i>	Moraceae	Heartwood	76
3	<i>Helichrysum diosmifolium</i>	Compositae	Leaves	82
4	<i>Mimosa caesalpiniaefolia</i>	Leguminosae	Heartwood	80
5	<i>Lithocarpus cornea</i>	Fagaceae	Stems	83
6	<i>Eucalyptus grossa</i>	Myrtaceae	Leaves	84
7	<i>Eucalyptus papuana</i>	Myrtaceae	Bark	85
8	<i>Orthopterygium huancy</i>	Julianaceae	Aerial parts	89
9	<i>Persimmon</i> (<i>diospyros malanonilan</i>)	Ebenaceae	Heartwood	90
10	<i>Dillenia pentagyna</i>	Dilleniaceae	Stem bark	91
11	<i>Agauria salicifolia</i>	Ericaceae	-	86,87
12	<i>Adina pilulifera</i>	Rubiaceae	Stems	88

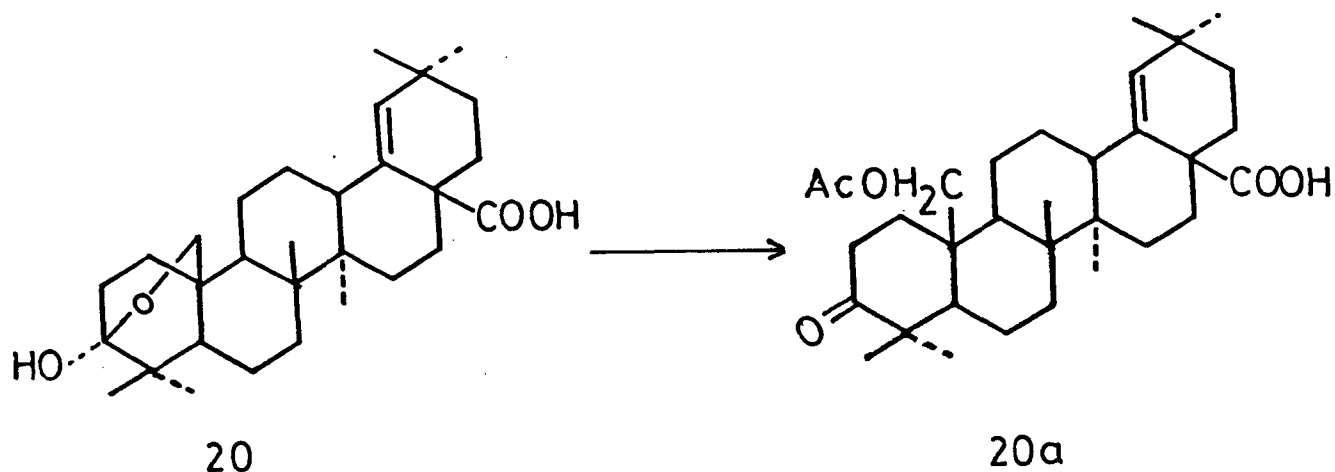


19

It was also isolated from *Ozoroa mucronata*¹⁰⁴, *Euonymus bungeanus*¹⁰⁵ and *Orthopterygium huancuy*⁹⁶.

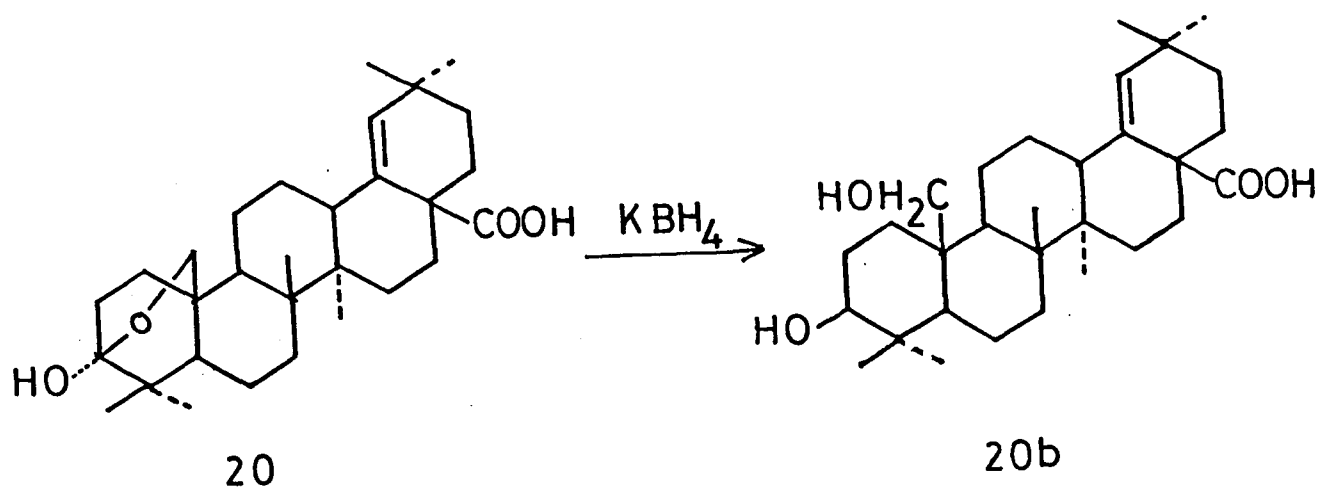
Semimoronic acid (20)

Semimoronic acid, the only hemiacetal triterpene olean-18-ene was shown to possess structure 20 on the basis of spectro-chemical evidence⁹³. Acetylation with pyridine and acetic anhydride was shown to give keto acetate 20a and potassium borohydride reduction yielded 3,25-dihydroxy-olean-18-ene-28-oic acid (20b). It was isolated from *Rhus alata*⁹⁴ also.



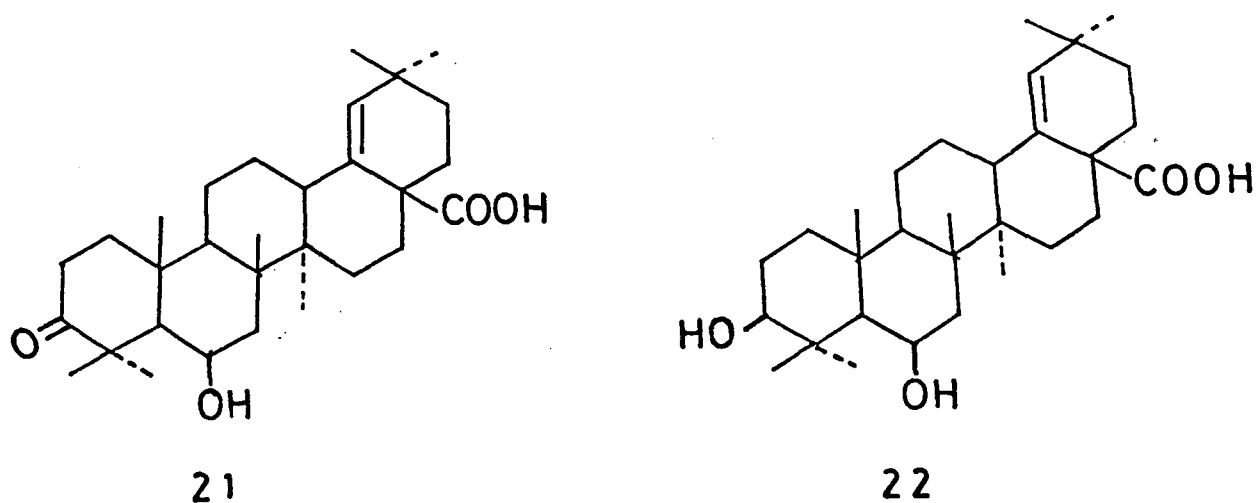
20

20a



Compounds 21 & 22

3-Oxo-6 β -hydroxyolean-18-ene-28-oic acid (21)⁹⁶ and corresponding 3 β -hydroxy compound (22)⁸⁹ were isolated from *Orthopterygium huancuy* by Gonzalez et al as their methyl esters. While the structure of 3-oxo compound was deduced from its spectral characteristics such as ¹H and ¹³C NMR, the structure of the latter compound 22 was established by single crystal X-ray crystallography.

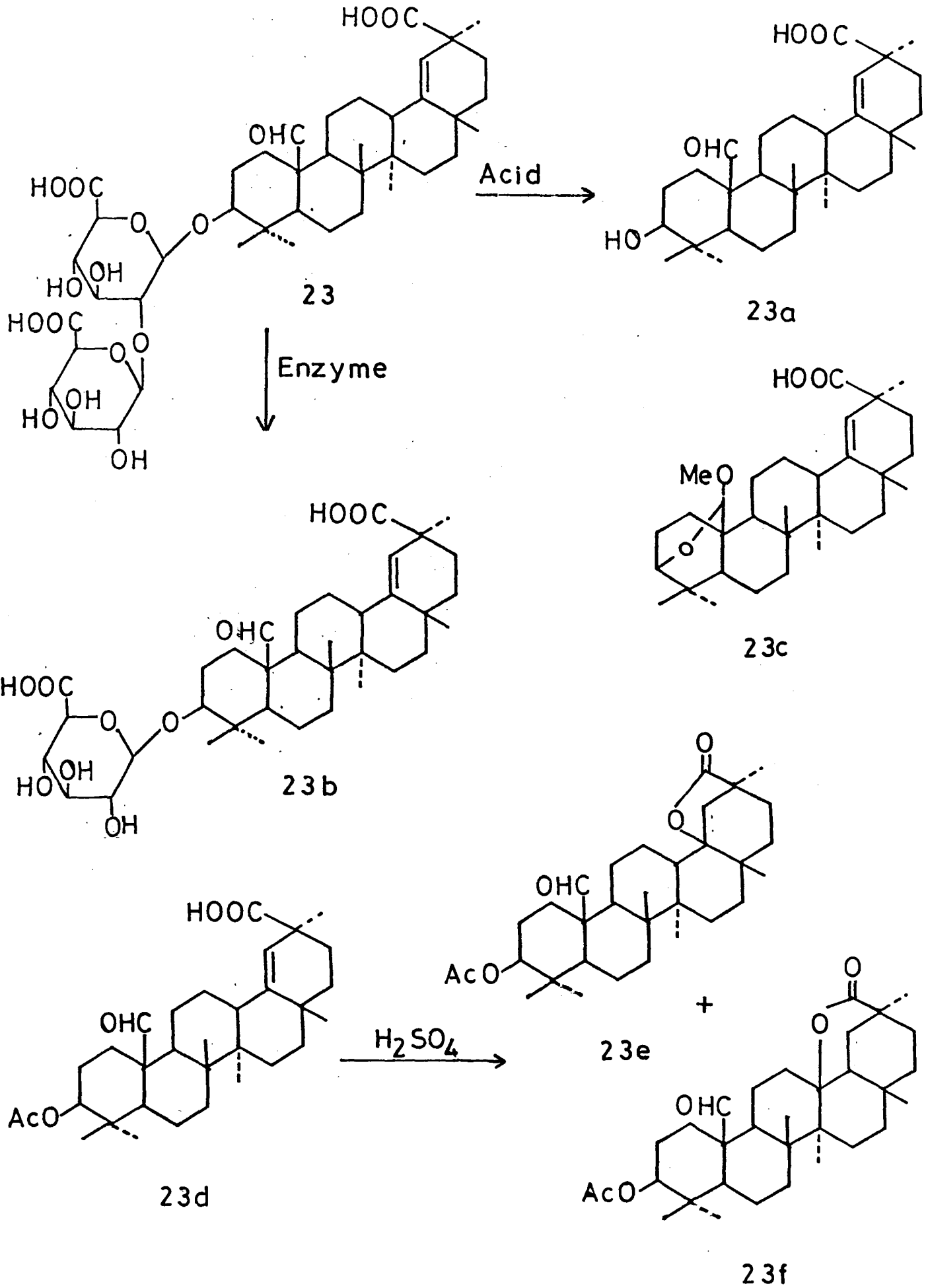


30-Oxygenated olean-18-enes

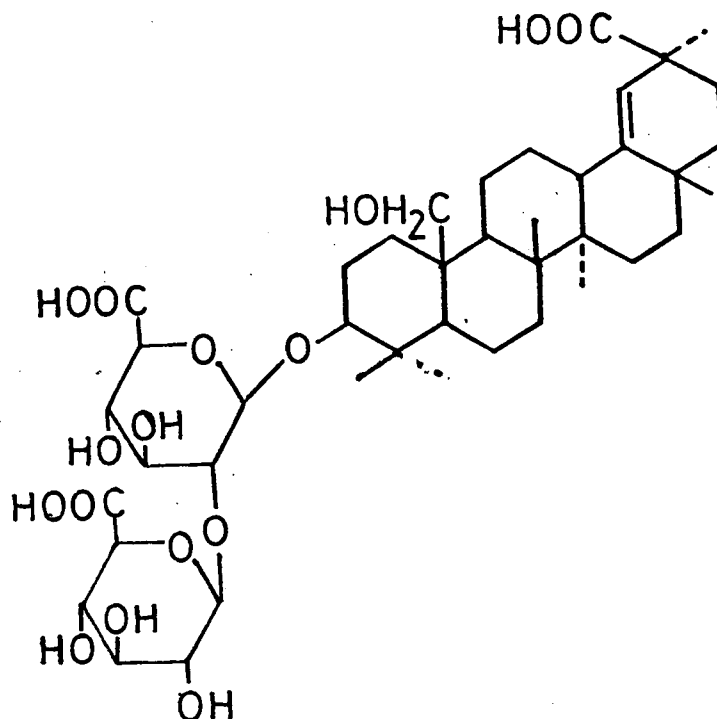
Periandrin I and periandrin III (23 & 24)

Periandrin I and periandrin III are the two natural sweeteners of *Periandra dulcis* isolated by Ogura et al^{97,98}. Acid hydrolysis of periandrin I yielded glucuronic acid and the aglycone periandric acid I (23a), m.p. 267-8°. Enzymatic hydrolysis with β -glucuronidase afforded periandric acid I, and prosapogenin which was identified as monoglucuronide (23b) of periandric acid. Periandric acid formed a monomethyl ester with diazomethane which formed acetate with pyridine and acetic anhydride. By dissolving in methanol periandric acid I was easily converted to acetal 23c which formed a monomethyl ester with diazomethane. Treatment of periandric acid I mono acetate 23d with sulphuric acid in chloroform afforded a γ -lactone 23e and δ -lactone 23f. The ¹H NMR and mass spectral studies of all these derivatives suggested structure 23 for periandrin I. The structure of periandric acid was also confirmed by single crystal X-ray crystallographic analysis of its p-bromobenzoate.

By similar reactions and by study of ¹H NMR and mass spectra of the derivatives, periandrin III was shown to be 3 β -O-[β -D-glucuronopyranosyl-(1 \rightarrow 2)- β -D-glucuronopyranosyl]-25-hydroxyolean-18-en-30-oic acid (24). Final confirmation



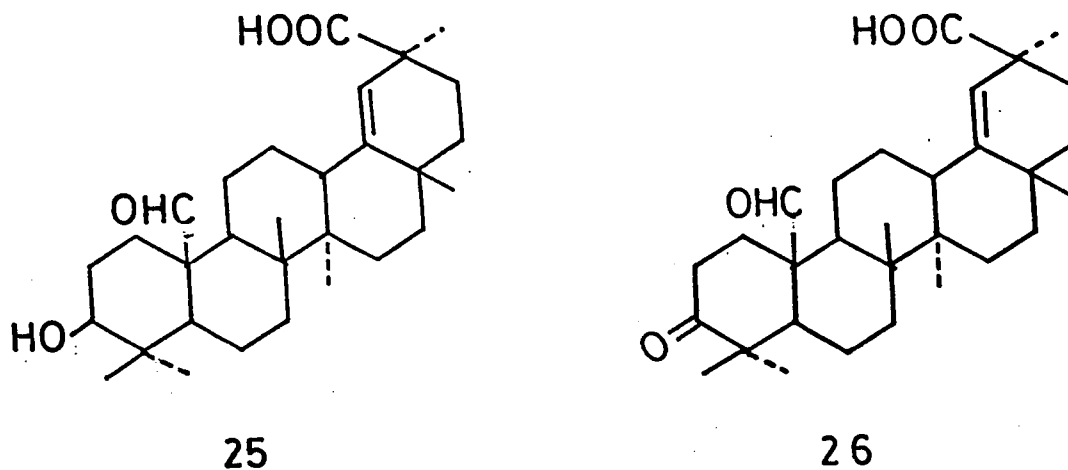
was accomplished by sodium borohydride reduction of periandrin I to the corresponding dihydro compound i.e. periandrin III.



24

Periandric acid I (25) and compound 26

The two aglycones, periandric acid I⁹⁹ and compound 26¹⁰⁰ were isolated from the same plant, *Periandra dulcis*. The structure of periandric acid I (25) was established by comparison of physical and spectral characteristics of its acetyl methyl ester with that obtained from the hydrolysis product of periandrin I. Sodium borohydride reduction of compound 26 gave a product identical with that obtained by the hydrolysis of periandrin III.



Nuclear magnetic resonance spectra of olean-18-enes

^1H NMR spectra:

The Δ^{18} oleanene triterpenes can be identified by the characteristic peak of the olefinic proton. The C-19 olefinic proton adjacent to a non-protonated carbon can be recognised by its non-splitting nature and is generally observed in the range δ 4.7 to δ 5.2. The presence of $-\text{COOH}$ group at C-17 or C-20 produces a downfield shift. For example in moronic acid⁹² and periandric acid I⁹⁹ proton singlets at δ 5.18 and δ 5.20 respectively are observed.

Gonzalez et al¹⁰⁶ studied methyl resonances of several olean-18-ene derivatives. Hydroxy constituent at C-3 position causes a shift in the resonances of 23,24 and

25 methyl group protons. Similarly introduction of 11-OH has substantial effect on the resonances of 25 and 26 methyl protons. The methyl protons in 29 and 30 positions give a double intensity signal at δ 0.94 which can be resolved in a high field and is characteristic of olean-18-enes. As an example the methyl resonances (100 MHz) of germani-diol⁷⁰ are given below:

23	24	25	26	27	28	29	30
1.004	0.848	0.938	1.066	0.742	1.014	0.938	0.938

α and β Orientations of the protons in triterpenes are deduced using the empirical rule $\delta H_{axial} < \delta H_{equatorial}$. The presence of a secondary hydroxyl group is deduced by the characteristic position and splitting pattern of the methine proton. The 3β -OH methine proton in olean-18-enes generally occurs at δ 3.13- δ 3.2 with the characteristic unresolved triplet ($J = \sim 10\text{Hz}$) which resolves into a doublet of a doublet with $J = 5-6\text{ Hz}$, 10 Hz in high resolution PMR. The chemical shift and its coupling constants for representative oxygenated olean-18-enes are tabulated (Table 6).

Table 6 : ^1H NMR spectral data of Olean-18-enes—chemical shift and coupling constant of hydroxymethine protons

Sl. No.	Compound	Proton	Chemical shift (JHz)	Reference
1	Germanidiol	2 β	3.99(ddd, 2.9, 4.0, 12.0)	70
		3 β	3.41(d, 2.9)	
2	Epigermanidiol	2 β	3.70(ddd, 4.7, 9.8, 10.7)	70
		3 α	2.98(d, 9.8)	
3	Lup-20(29)-ene*- 1 β , 3 β -diol	1 α	3.43(dd, 4.7, 11.3)	73
		3 α	3.24(dd, 4.4, 12.1)	
4	3-oxo-6 β -hydroxyolean- 18-en-18-oic acid methyl ester (21 methyl ester)	6 α	4.45(m)	96
5	Compound 10	11 β	3.94(td, 9 α ,11 β : 10.9 11 β ,12 α : 10.9 11 β ,12 β : 4.5)	73
6	Compound 11	3 α	3.20(dd, 5.8, 10.2)	74
		16 α	3.62(dd, 6.4, 9.8)	
7	16 β -Acetoxyolean- 18-ene-3-one (Compound 13 acetate)	16 α	4.90(dd, 6, 10.5)	74
8	16 α -Acetoxyolean- 18-ene-3-one (Compound 14 acetate)	16 β	4.79(dd, 4.0, 6.0)	74

* Since the data for Anagadiol is not available the corresponding data for lup-20(29)-ene-1 β ,3 β -diol is given.

^{13}C NMR spectra

The ^{13}C NMR spectra of several olean-18-enes have been studied by Gonzalez et al¹⁰⁷. C-18 and C-19 carbons occur at 142 ppm and 129 ppm respectively. The presence of -COOH group or -CH₂OH group at C-17 causes an upfield_λ ^{shift} of about 4-6 ppm on C-18 due to β-effect. Substitution effect of an equatorial hydroxyl group at C-1 and C-11, an equatorial acetoxyl or axial hydroxyl group at C-11 and a keto function at C-11 or C-16 can be calculated from the data presented by Gonzalez et al¹⁰⁷. The presence of the hydroxyl group at C-1 produced an upfield shift of 3-4 ppm on C-25 carbon. Keto or hydroxyl group at C-16 however had shown downfield shift on C-28 carbon. The methyl carbons in olean-18-enes have characteristic chemical shifts and compare well with other triterpenes such as olean-12-enes and lup-20(29)-enes. The chemical shifts of representative examples of olean-18-enes are given in Table 7.

Mass spectra of olean-18-enes

The mass spectral fragmentation pattern of four olean-18-enes were first studied by Djerassi et al¹⁰⁸. All other compounds showed similar mass spectral behaviour. Cleavage of ring C yields two fragments (x and y) for rings A, B and rings D, E respectively (Scheme 3). Fragment y suffers further loss of the C-17 substituent giving m/z 203. It

Table 7 : ^{13}C NMR spectral data of Olean-18-enes

	1	6	9	10	11	19a*	21a*
C-1	38.5	75.7	41.4	78.9	38.5	39.7	42.2
C-2	27.4	39.0	27.7	43.1	27.4	33.9	34.4
C-3	79.0	79.5	78.5	216.5	79.1	218.3	-
C-4	39.0	38.4	39.1	47.2	39.0	47.1	48.9
C-5	55.7	53.4	55.9	50.9	55.7	54.8	56.5
C-6	18.3	18.0	18.0	19.4	18.4	19.6	69.5
C-7	34.7	34.6	35.6	33.2	34.5	33.9	42.2
C-8	40.8	41.4	42.9	42.6	40.8	40.4	39.8
C-9	51.3	52.4	56.5	55.8	41.3	50.3	51.3
C-10	37.3	43.8	39.5	43.9	37.4	36.8	36.8
C-11	21.2	23.9	71.1	70.0	21.3	21.4	21.3
C-12	26.2	26.2	38.6	37.1	26.0	25.9	26.0
C-13	39.0	38.1	37.3	37.3	39.1	41.3	40.5
C-14	43.4	43.5	43.0	42.9	42.8	42.4	42.7
C-15	27.6	27.5	27.5	27.4	34.7	29.3	29.5
C-16	37.7	37.8	37.6	37.2	36.7	33.7	33.5
C-17	34.4	34.4	34.3	34.3	39.6	48.1	48.2
C-18	142.8	142.7	141.6	141.2	141.7	136.7	137.1
C-19	129.8	129.7	129.9	130.1	129.4	132.4	132.9
C-20	32.3	32.4	32.4	32.4	39.1	31.9	32.1
C-21	33.4	33.5	33.4	33.9	33.7	33.4	33.5
C-22	37.4	37.5	37.3	37.4	37.4	33.4	33.5

Table 7 (contd...)

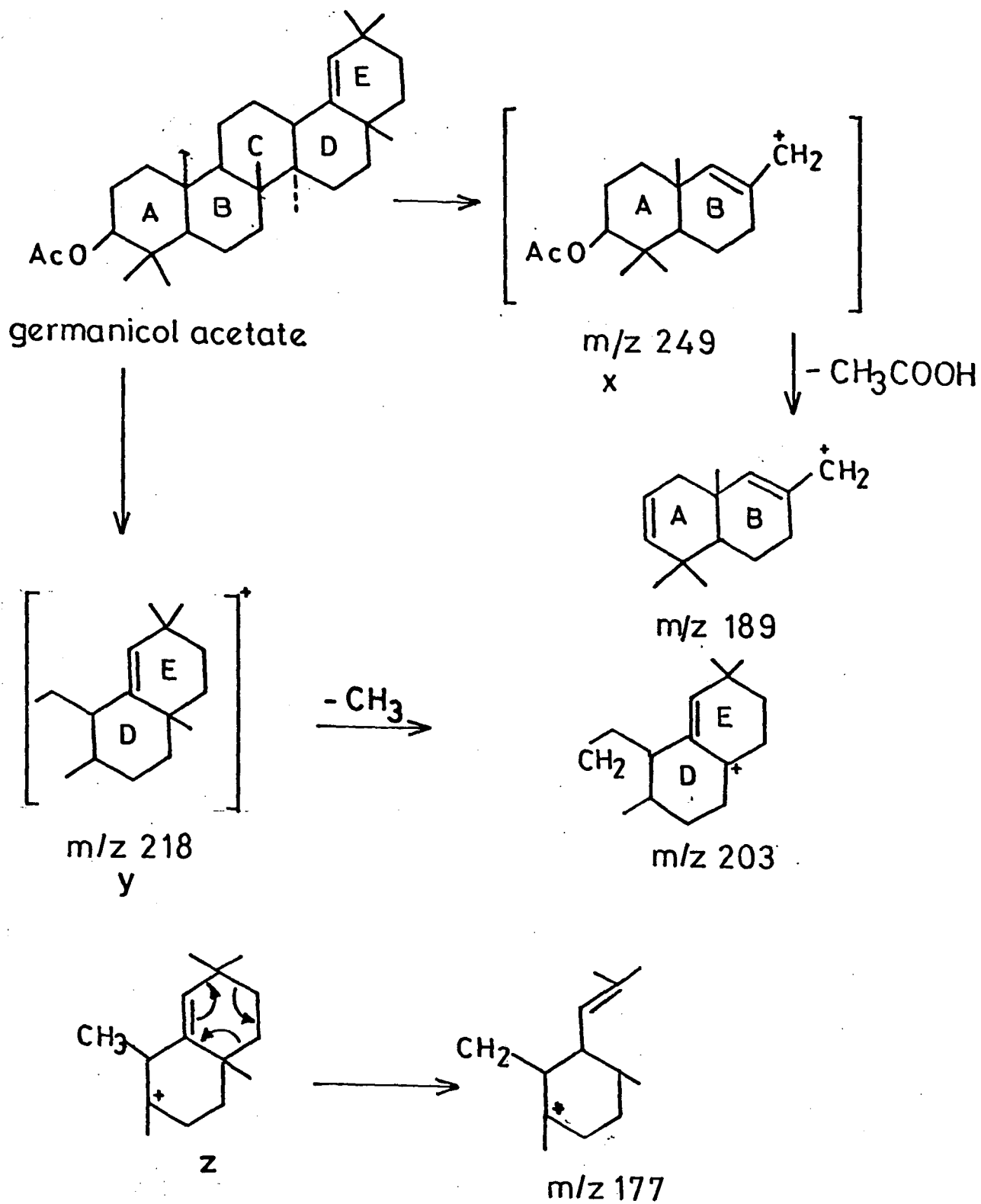
	1	6	9	10	11	19a*	21a*
C-23	28.0	28.0	28.2	28.9	28.1	20.9	23.6
C-24	15.4	15.1	15.6	19.3	15.5	26.8	25.0
C-25	16.1	12.5	17.4	14.1	16.3	15.8	17.3
C-26	16.7	16.5	16.9	17.4	16.9	16.4	17.5
C-27	14.6	14.5	14.3	14.2	13.8	14.8	15.1
C-28	25.3	25.4	25.3	25.2	27.4	176.8	177.1
C-29	31.3	31.3	31.3	31.3	31.9	30.3	30.4
C-30	29.2	29.3	29.2	29.1	30.9	29.1	29.1
<u>COCH</u> ₃						51.8	-

Ref.

1 Germanicol	107
6 Anagadiol	107
9 Nivadiol	107
10 Compound 10	73
11 Compound 11	74
19a Methylmoronate	92
21a Compound 21 methyl ester	96

SCHEME 3

38



is also observed that mass spectra of olean-18-ene and germanicol acetate exhibit a m/z 177 peak. Its formation was explained by Retro Diels Alder decomposition of species z and is influenced strongly by the nature of the C-17 substituent.