PART - III

PARTIAL SYNTHESIS OF METHYL 2α, 3α-DIHYDROXY LUPAN - 28 - OATE FROM BETULINIC ACID

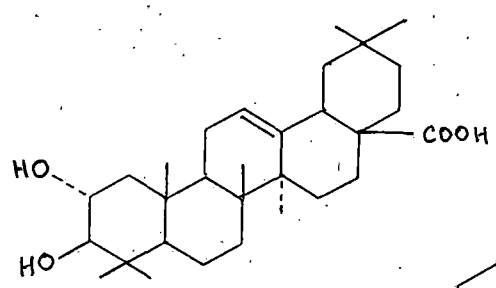
CHAPTER - I

A Short Review on the ~~Synthesis of Isomeric 2,~~ Triterpenoid 2,3 - dihydroxy 28- carboxylic acids. ~~3 - diols of Triterpenoids.~~

The 2α, 3β-dihydroxy olean-12-en-28-oic acid (Crategolic/ maslinic acid)

Bachler[1] was the first to isolate an amorphous acid "Crategus acid" from the leaves of Crategus Oxyacantha L. The acid was also observed in the leaves of Psidium guai java by Arthur and Hui[1]. However, a more detailed study of the acid was made by Tschesche et al[1,2]. They established the acid as crategolic acid ($C_{30}H_{48}O_4$) having a double bond and two hydroxyl groups. From a consideration of the behaviour of the acid towards acylation, decarboxylation and lactonisation Tschesche et al in a subsequent paper[3] correctly recognised crategolic acid 1 as a derivative of β-amyrin. They were also able to prepare a diacetate, a mono acetate and a keto-mono acetate from methyl ester of crategolic acid 1.

However, in the mean time, Caglioti et al[4] reported the isolation from the husks of Olean euvopa of a new acid, maslinic acid, which later proved identical with crategolic acid 1 of Tschesche et al[3].



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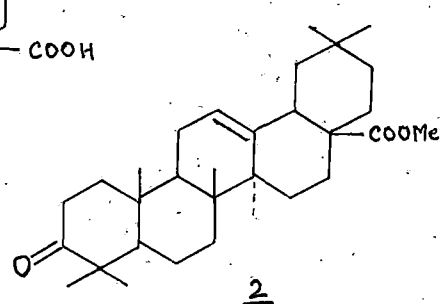

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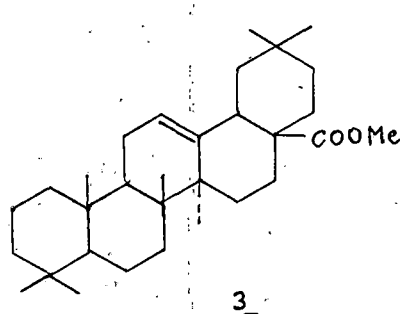
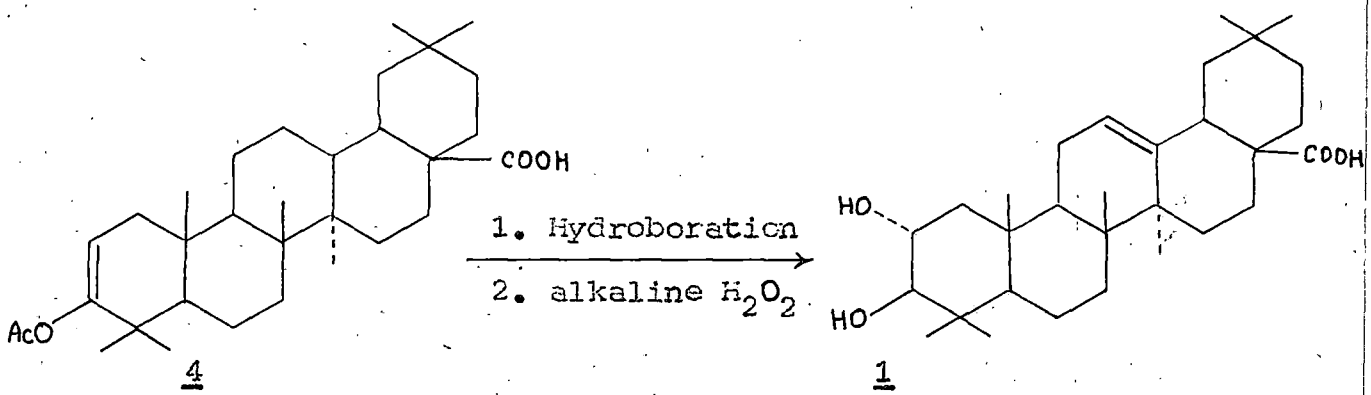


3

In their subsequent investigations[5,6] Caglioti et al were able to elucidate the complete structure of the acid as a 2,3-dihydroxy olean-12-en-28 oic acid. The correlation with the β-amyrin group was established by conversion of crategolic acid 1 into methyl oleanonoate 2 and methyl olean-12-en-28-oate 3. This conversion inter alia settled the position of the two hydroxyl group at C-2 and C-3. Subsequently, the configuration of the two hydroxyl groups was elucidated by Caglioti et al[7]. The 2α, 3β trans diequatorial configuration of diol moiety was proved by the formation of crategolic acid from the enol acetate 4 of oleanonic acid by hydroboration, which was known to be stereospecific process[8,9] supported also by the work of Tschesche et al[24].



4 1

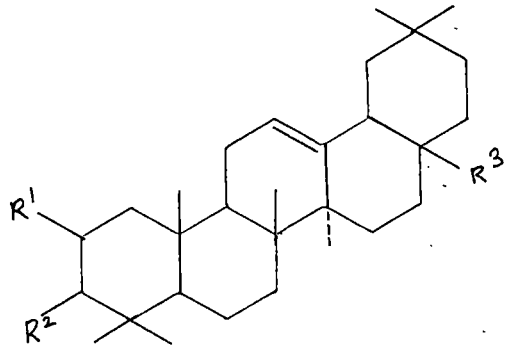
Sengupta et al[11] also isolated crategolic acid (maslinic acid) 1 from the flowers of Eugenia Jambolana Lam as its methyl ester along with oleanolic acid.

2α, 3β dihydroxy urs-12 en-28 oate from Rose-bay Willow herb

The leaf constituents of rose-bay willow herb were first examined by Puringer[13] who isolated an alcohol m.p. 256° - 260°, $[\alpha]_D$ + 72.75°. But later Glen et al[14] proved that Puringer's product was a complex mixture of five components four of which have already been identified by Glen et al as methyl oleanolate 5, methyl ursolate 6a and the 2α-hydroxy-derivatives of those esters.

The existence in nature of isomeric 2,3 dihydroxy acids of the oleanane series of triterpenes has already been shown by Caglioti[6,7] and Tschesche[15]. The 2,3 dihydroxy acid in the Lupane series viz. alphitolic acid, has been shown by Guise[16], while 2,3 dihydroxy acid of the ursane series was described by Glen et al[12].

Glen et al[12] isolated methyl 2α, 3β dihydroxy urs-12 en -28 oate 6b from the dried leaves of rose-bay willow-herb whose structure and stereochemistry were deduced from the observation described later.



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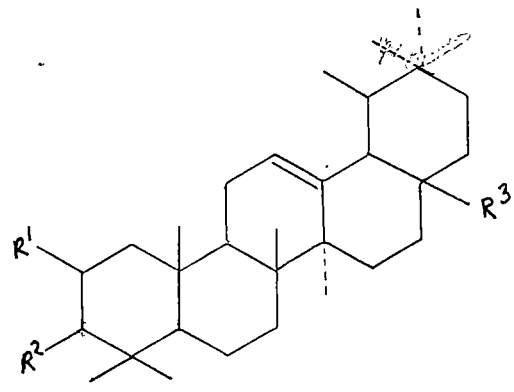
	R^1	R^2	R^3
b	H	β OH	COOMe



6

	R^1	R^2	R^3
a:	H	β-OH	CO_2Me
b	α-OH	β-OH	CO_2Me

The IR spectrum of the dihydroxy-methyl ester 6b indicated the presence of hydroxyl and ester groups, three peaks in region 1400-1350 cm^{-1} and two peaks in region 1330-1240 cm^{-1}, indicative of an ursane series. The n.m.r. spectrum revealed the presence of one olefinic hydrogen (τ4.73) and one methyl ester group (τ6.38). Mass spectrum examination indicated a molecular weight of 486 in agreement with the formula $C_{31}H_{50}O_4$. Mass fragmentation suggested that the compound was Δ^{12} triterpenoid.

The hydroxyl groups in the dihydroxy-ester 6b are primary or secondary follows from the ease with which they are acylated. Support for this point of view came from the n.m.r spectrum of the diacetate of 6b which showed twin distinct peaks at τ7.97 andτ8.04[17]. The presence of the ursane skeleton in the ester 6b was shown by Wolff-Kishner reduction of the diosphenol to give urs-12 en-28-oic acid identical with an authentic sample.

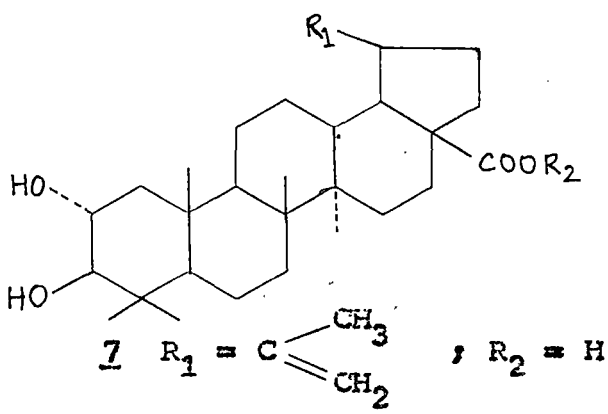
The configuration of the hydroxyl groups in the dihydroxy-ester 6b was determined by comparing the synthesised product of four possible 2,3 dihydroxy-isomers of the ester 6b.

The trans-diequatorial diol (methyl 2α, 3β-dihydroxy urs-12-en-28-oate) which was prepared from the enol acetate was identical with the dihydroxy-ester obtained from the natural dihydroxy acid.

Further support for the assignment of the α-configuration to the hydroxyl group at C-2 in the dihydroxy ester 6b was revealed by the n.m.r spectrum of the monoacetate, methyl 2α-acetoxy-3β-hydroxy urs-12-en-28-oate. The resonance due to the C-2 proton is in the region τ 4.9-5.4 although distinct peaks cannot be seen. The breadth of the resonance indicates at least two couplings of about 8 c/sec are present. This showed the proton at C-2 is axial. Therefore the acetoxy group at C-2 has the equatorial (α) conformation.

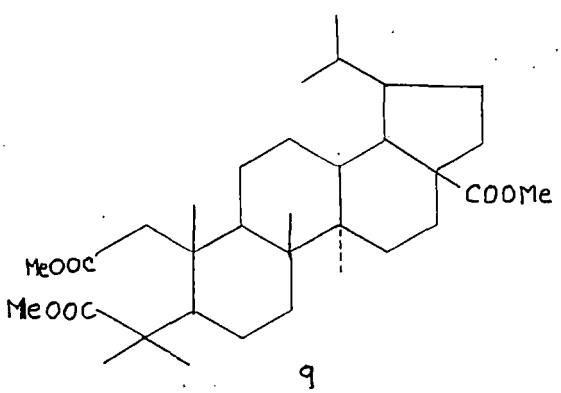
2α, 3β-dihydroxy lup 20(29)en-28-oic acid (alphitolic acid)

Guise et al[16] isolated alphitolic acid 7 as its methyl ester 8 from the wood of Alphitonia petrici Braid and white. IR spectrum showed the presence of two hydroxy groups and a double bond in the methyl alphitolate 8. Guise et al converted methyl alphitolate 8 to trimethyl ester 9 by subsequent treatment with hydrogen, sodium metaperiodate, chromic anhydride in acetic acid and methylation, which was identical with trimethyl ester of the seco-A-acid derived from dihydrobetulinic acid[18].



7 R_1 = C(CH$_3$)=CH$_2$; R_2 = H

8 R_1 = C(CH$_3$)=CH$_2$; R_2 = Me

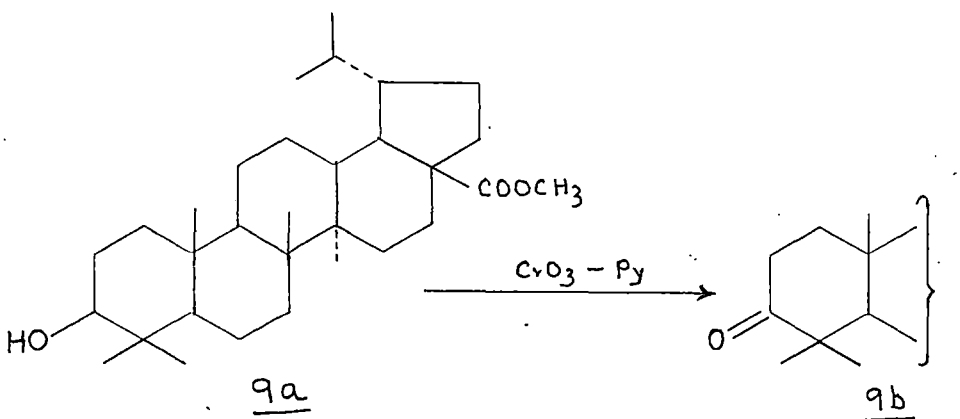


9

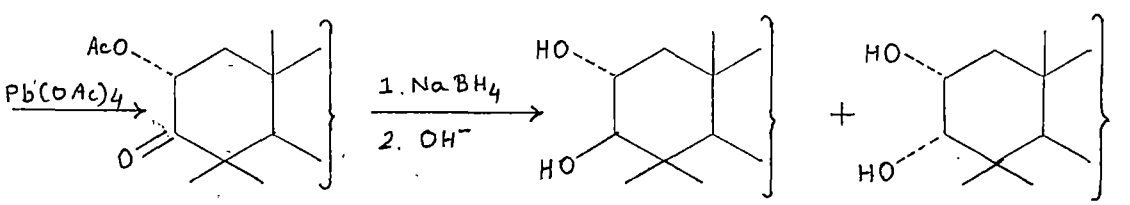
The stereochemistry of 1,2 glycol grouping in ~~2~~ 8 was based on quantitative lead-tetraacetate titrations under the defined conditions of Djerassi and Elrich[19] where a value $K = 2.7 \times 10^{-3}$ L mole^{-1}sec^{-1} was obtained, same for triterpene 2α, 3β-glycols. Thus the stereostructure of alphitolic acid was established as 2α, 3β-dihydroxy lup 20(29)en-28-oic acid ~~7~~.

The methyl 2α, 3β-dihydroxy lupan-28-oate (methyl dihydro alphitolate)

Row and co-workers[19a] attempted the synthesis of methyl dihydro alphitolate 9d starting from methyl dihydro betulinate 9a according to the following scheme:



9a 9b

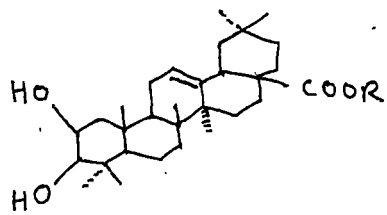


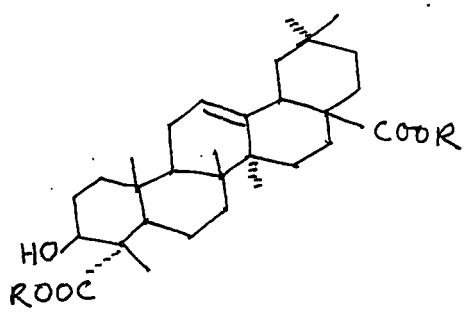
9c 9d 9e

The compound 9a was prepared by catalytic reduction of methyl betulinate in ethanol using Raney nickel-hydrogen at 100°/400 lb or Adams' catalyst. Oxidation of 9a with chromium trioxide-pyridine furnished 3-keto methyl ester 9b as colourless plates, m.p. 203-5°, $[\alpha]_D^{30}$ + 9° which was subjected to acetoxylation with lead tetraacetate under varying conditions and the best yield of 2α-acetoxy-3-keto ester 9c m.p. 215-16°, $[\alpha]_D^{30}$ + 4°. ν_{max} 1735 and 1720 cm^{-1} was obtained when 3-keto ester 9b was heated at 100° with freshly prepared lead tetraacetate in glacial acetic acid. Reduction of 9c with sodium borohydride followed by mild alkaline hydrolysis gave a mixture of glycols (9d and 9e) which was separated by chromatography on alumina. The minor fraction was found to be a mixture and the major fraction crystallised from methanol as colourless needles, m.p. 228-30°, $[\alpha]_D^{30}$ + 1.2°, ν_{max} 3600, 1720 cm^{-1}. It consumed 1.15 moles of lead tetraacetate within 8 hr indicating the presence of a trans 1, 2-glycol system. It was therefore, regarded to be methyl 2α, 3β-dihydroxy-lupan-28-carboxylate 9d. Row et al[19a] reported that the compound 9d showed no depression in melting point on admixture with an authentic sample but the IR comparison showed a significant difference.

In 1968 Cheung and Feng[19b] reported the partial synthesis of methyl dihydro alphitolate by following essentially the same sequence of reactions as described by Row et al[19a]. Although the melting point of their product was same as that recorded in

the literature[16] for naturally dihydro alphitolate but they have not recorded the IR spectra of the two compounds.





10 R = H

12 R = Me

11 R = H

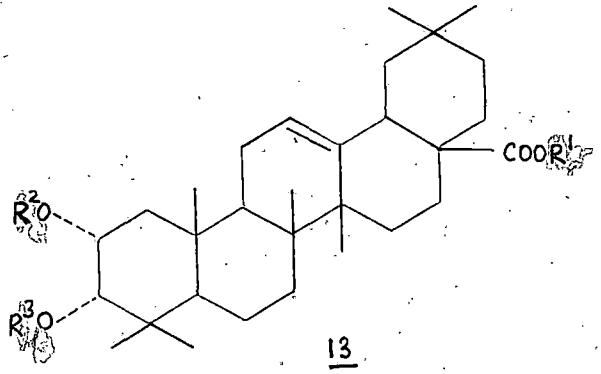
Isolation of a minor constituent as methyl 2β, 3β -dihydroxy olean-12-en-28-oate 12 from castanospermum australe and its stereospecific synthesis from methyl crategolate 1.

During reinvestigation of the sapogenin mixture, the bayogenin fraction was methylated and from the mixture of methyl esters, a less polar and minor fraction was separated by chromatography and has been shown to consist of methyl 2β, 3β -dihydroxy olean-12-en-28-oate along with hederagic acid 11. The structure of this minor sapogenin was suggested by its IR, NMR and mass spectra together with its occurrence with medicagenic acid and bayogenin. Its m.p. (276-80°) was in agreement with that previously published for the compound methyl 2β , 3β -dihydroxy olean-12-en-28-oate[21] (lit 278-82°) but its rotation $[\alpha]_D$ + 93° was different $[\alpha]_D$+65°. Bannon et al[20] compared the IR spectrum of their sample with

that of a sample previously described as methyl 2β, 3β dihydroxy olean-12-en-28-oate[21] and the two compounds were clearly different. NMR data have recently been used[22] to demonstrate that the structures originally assigned[10,21] to the two cis 2, 3 diols resulting from the osmium tetroxide oxidation of methyl oleana-2, 12-dien 28-oate should be reversed. Bannon et al[20] synthesized the methyl 2β, 3β-dihydroxy olean-12-en-28-oate from methyl crategolate. Partial acetylation of methyl crategolate (methyl maslinate) (methyl 2α, 3β-dihydroxyolean-12 en-28-oate) yielded the 2α-acetoxy 3β alcohol which was oxidized with dimethyl sulphoxide in acetic anhydride to give 2α-acetoxy 3 ketone. Isomerization on alumina yield 3β acetoxy 2 ketone which with sodium borohydride proceeded quantitatively to give a single product in which the introduced hydroxyl group at C-2 can be assigned the β-configuration on the assumption that attack has occurred from the less hindered α-side of the molecule. This monoacetate, methyl 3β-acetoxy 2β-hydroxy olean-12-en-28-oate [NMR δ 4.62 (1H, d, J 4 Hz; C 3 proton), δ4.10 (1H, m, $W_{1/2}$ 7 Hz; C 2 proton)] readily isomerized on acidic, basic or neutral alumina to methyl 2β-acetoxy-3β hydroxy olean-12-en-28-oate. Mild alkaline hydrolysis of the methyl 3β-acetoxy 2β-hydroxy olean-12-en-28-oate gave the corresponding diol, methyl 2β, 3β dihydroxy olean-12-en-28-oate 12. The NMR evidence for the synthetic product and the product isolated from C. australe ~~was~~, in fact, ~~support~~ supported the structure of the compound 2β, 3β-dihydroxy olean-12-en-28-oate 12.

2α, 3α Dihydroxy olean-12-en-28-oic acid (11a) from Shorea Accuminata.

Cheung and co-workers[23] isolated a new natural product 2α, 3α Dihydroxy olean-12-en-28-oic acid from Shorea accuminata resin of Dipterocarpaceae family. The structure of methyl 2α, 3α dihydroxy olean-12-en-28-oate (13) m.p. 296-299° was established by NMR and mass spectral measurements and on comparison basis. The methyl ester (ν_{max} 3340, 1725 cm^{-1}) has two hydroxy groups and forms a diacetate and a monoacetate. Each of the above compounds shows NMR signals due to a methyl ester group (3H, singlet, δ 3.6) and an olefinic proton (triplet, J 4 Hz, δ 5.3). The mass and NMR spectral measurements of the diol methyl ester indicated that the compound was a methyl 2,3-dihydroxy olean-12-en-28-oate 13.

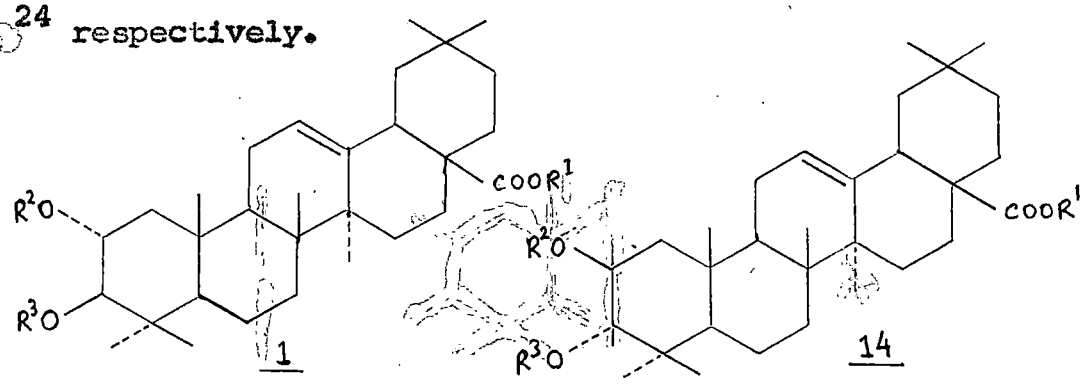


13

11a, $R^1 = R^2 = R^3 = H$

13, R^1 = Me, $R^2 = R^3 = H$

All four isomers with this structure are known. The two with trans hydroxyl groups 2α, 3β and 2β, 3α - are methyl ester of the naturally occurring maslinic acid 1[6,7] and bredemolic acid 14[24] respectively.



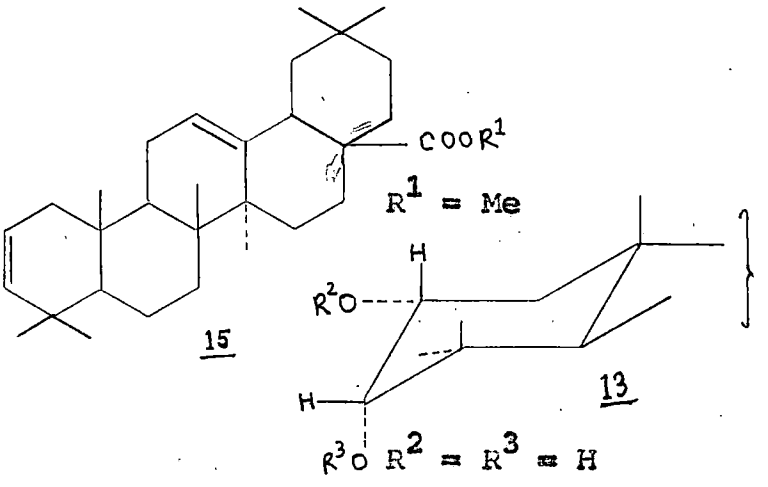
$R^1 = R^2 = R^3 = H$

The cis isomers, 2α, 3α- and 2β, 3β-, were first prepared[10] by osmium tetroxide oxidation of methyl oleana-2, 12-dien-28-oate 15. Cheung et al[23] found that of the two cis diols so obtained, the one with higher m.p. is identical to the methyl ester of m.p. 296-299°, isolated from Shorea accuminata. By considering the infrared absorption due to O-H stretching, Tschesche et al[24] assigned a 2β, 3β configuration to this diol, and an 2α, 3α-configuration to the one with lower m.p. (258-260°). Cheung et al[23] demonstrated that the configurations assigned should be reversed as described below:

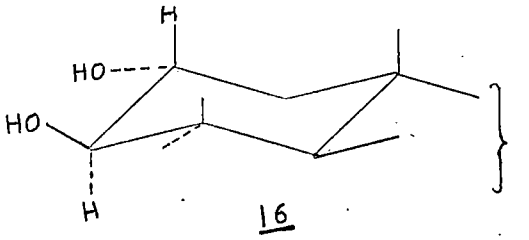
Configuration of cis-Diols from Methyl Oleana-2,12-dien-28-Oate 15.

N.M.R. frequencies of individual angular methyl groups in a triterpene framework showed that diol m.p. 296-299° has the 2α, 3α and diol m.p. 258-260° the 2β, 3β-configuration.

Support for the structural assignments came from analysis of the splitting pattern of signals due to protons at C-2 and C-3. It is generally accepted that as for lupane and 4,4 dimethyl cholestane analogues, ring A of the 2α, 3β and the 2α, 3α diols exists in a flattened chair conformation[25].



15 13



16

In contrast, ring A containing the 2β, 3α-diols adopts a twist conformation, resulting in equatorial orientation of hydroxyl groups. For the 2β, 3β-diol, a twist ring A would be less favourable, due to strong flagpole interactions involving substituents at position 3β and 10.

For methyl maslinate[1] the splitting pattern of the signals due to protons at C-2 and C-3 is readily interpreted in terms of

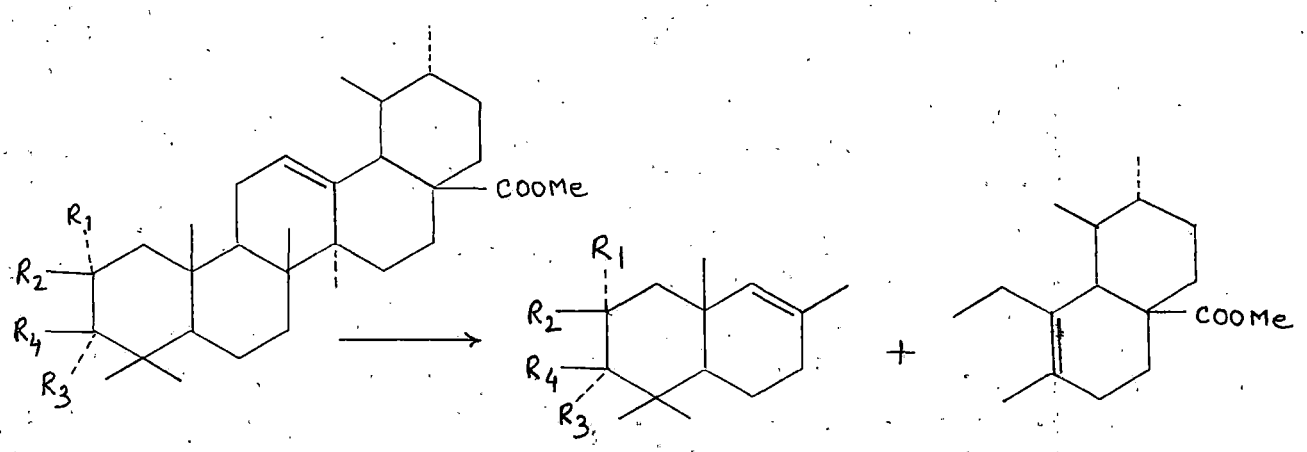
Chair ring A with axial protons at position 2 and 3 in 16. In the 2α, 3α-diol, also with a chair ring A (13), the 2β proton is axial and is expected to be subject to a large ax-ax coupling with the 1α-proton and to small ax-eq. couplings with the 3β and 1β protons. Of the two cis diols from osmium tetroxide oxidation only one, with m.p. 296-299°, shows a signal due to C-2 proton of sufficient width at half-height ($W_{1/2}$=21 Hz) to be compatible with a 2α, 3α-diol structure. In this diol the C-3 proton gives rise to a doublet (J=3 Hz) at δ3.35 due to vicinal coupling of equatorial and axial protons. All the forgoing evidence coupled with detailed NMR analysis of selective monoacetylated product of this diol led to the 2α, 3α-diol structure for this ester 13.

2α, 3α-dihydroxy Urs-12-en-28-oic acid

Biessels and co-workers[26] isolated the compound 2α, 3α-dihydroxy Urs-12-en-28 oic acid from Prunus Serotina and P. Lusitanica (Rosaceae). HRMS indicated the formula $C_{31}H_{50}O_4$ for methyl ester 17 whose fragmentation gave the characteristic pattern of a Δ^{12}-Ursene or a Δ^{12}-oleanene. IR spectrum in pyridine showed absorption at 1390, 1380, 1360 (weak), 1308, 1276 and 1238 cm^{-1} strongly resembling that reported by Snatzke and co-workers[27]. The PMR spectrum showed a doublet (J 11 Hz) at δ 2.22 which was attributed by Cheung and Yan[23] to the C-18 proton in a Δ^{12}-Ursene compound, corresponding

oleanene compound gave an AB-quartet at δ 2.8. A broad signal at δ 5.22 (1H) confirmed the presence of a double bond. Mass spectrum showed striking resemblance to that of methyl Ursolate 6a. In the spectra of both 17 and 6a, a base peak at m/z 262 appeared thus indicating that rings D and E of methyl Ursolate 6a also formed a part of 17 as well.

The appearance of a signal at m/z 223 in the mass of 17 and the absence of one at m/z 207 showed that the additional oxygen atom was present in ring A or B.



17 $R_1 = R_3 = CH$, $R_2 = R_4 = H$ m/z 223 m/z 262

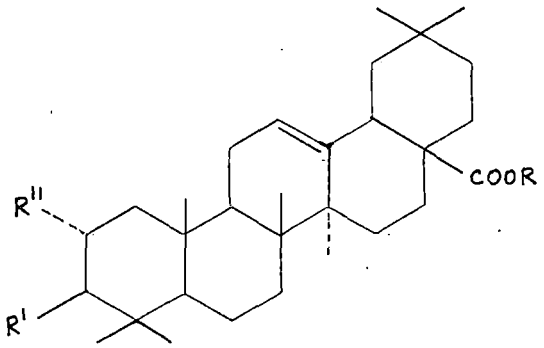
6a $R_1 = R_2 = R_3 = H$, $R_4 = OH$ m/z 207 m/z 262

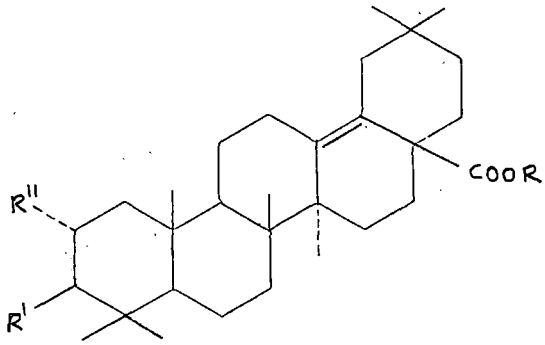
17 gave a diacetate which along with other peaks showed the prominent peaks at M^+ 570, 510 ($M^+ - CH_3COOH$), 450 m/z ($M-2CH_3CO_2H$). In the PMR spectrum of 17 the doublet at δ 3.39 indicated the two vicinal hydroxyl groups. They could only be placed at the position 1 and 2, 2 and 3 or 6 and 7. Based on MS analysis the authors excluded 6, 7-diol. They preferred 2,3-diol structure

for biogenetic reasons. 2α, 3α-diol structure was suggested by comparing the chemical shifts of the singlet methyl in the PMR spectra of the four possible methyl Urs-12-en-28-oate-2, 3-diols calculated according to Cheung[28] with the shifts of the methyl group of 17 and those of the two ursene diol 2β, 3β-diol and 2α, 3α diol synthesised by the authors. Thus the methyl ester 6a was established as methyl 2α, 3α-dihydroxy Urs-12-en-28-oate and the corresponding acid present in P. Serotina and P. Lusitanica as 2α, 3α-dihydroxy urs-12-en-28-oic acid.

2α, 3β dihydroxy Olean $\Delta^{13(18)}$-en-28-oic acid 19a from Olea europaea

Romualdo Caputo et al[29] reported oleanolic acid 18 and maslinic acid 1 from the leaves of Olea Europaea. The solid obtained from the mother liquors after crystallization of 1 followed by treatment with ethereal diazomethane, afforded a solid m.p. 183-7°, $[\alpha]_D$ -28°, $C_{31}H_{50}O_4$, isomeric with methyl maslinate. The compound was called methyl δ-maslinate, in analogy with δ-amyrin[30] which had the same tetra substituted double bond. The assignment of the structure 19 for this compound based on spectroscopic evidence and by conversion of methyl maslinate 16 into 19 according to the procedure used by Ruzicka et al[30a] for β-amyrin. Methyl maslinate was in fact acetylated and then refluxed with SeO_2 in acetic acid to afford the $\Delta^{11,13(18)}$ conjugate diene. Direct hydrogenation of this later on a pre-reduced PtO_2 catalyst, followed by alkaline





18 R, R'' = H, R' = OH

1 R = H, R', R'' = OH

16 R = Me, R', R'' = OH

19 R = Me, R', R'' = OH

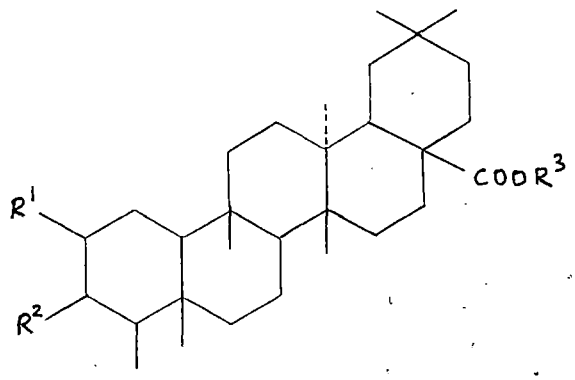
20 R = Me, R' = OAc, R'' = H

19a R = R' = R'' = H

hydrolysis and re-esterification of the carboxyl group, then led to a product m.p. 182-4° $[\alpha]_D$ -26°, identical with the natural sample. Again from the mother liquor of 18 a compound of tetra substituted double bond was found. The structure of this compound was established as 20.

2 , 3 - dihydroxy D : A friedooleanan-28-oic acid

Savitri Kumar et al[31] isolated the compound 2 α-hydroxy-3-oxo D:A friedooleanan-28-oic acid 21 from the stem bark of Euonymus revolutus Wight (Celastraceae). During their work on the structure elucidation of 21 they carried out $NaBH_4$ reduction of 21 and isolated a diol 22, this underwent quick oxidation with periodic acid suggesting the presence of a vicinal diol system.



21 $R^1 = \alpha$-OH, $R^2 = O$, $R^3 = H$

22 $R^1 = R^2 = \alpha$-OH, β-H, $R^3 = H$

23 $R^1 = R^2 = \alpha$-OAc, β-H, $R^3 = H$

The diol 22 on acetylation gave diacetate 23. The half-height width of the two CHOAc proton signal which appeared as a multiplet ($W_{1/2}$ 12.0 Hz) suggested the presence of one axial and one equatorial acetoxy group in the diacetate 23. No further work on the configuration of this diol has been reported.

2α, 3α -dihydroxy-lup-20(29)en-28-oic acid

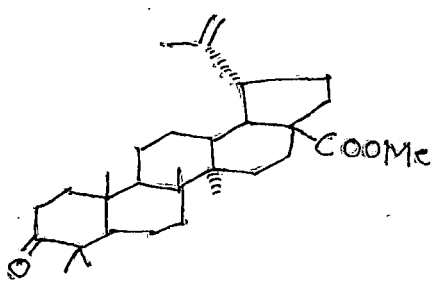
Savitri Kumar et al[32] reported the structure elucidation of a new lupene, 2α, 3α-dihydroxy-lup-20(29)en-28 oic acid 24 isolated from Euonymus revolutus.

Column chromatography and preparative TLC from the cold CH_2Cl_2 extract of the stem bark of Euonymus revolutus yielded a triterpene diol 24. IR spectrum showed the peaks at 3600-3100, 3400, 1690 cm^{-1} for hydroxyl and carboxylic acid groups.

The methyl ester 25 $C_{31}H_{50}O_4$ confirmed the presence of -COOH group. Acetylation of 24 gave a diacetate 26 [^{1}H NMR δ 5.21 (1H, m), δ 4.95 (1H, d), δ 2.12 (3H, s) and δ 1.95 (3H, s)] indicating two secondary hydroxyl groups in 24.

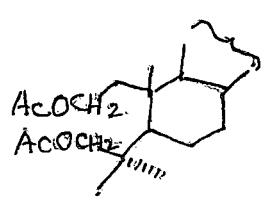
Two doublets in the ^{1}H NMR spectrum at δ 4.72 and δ 4.60 due to a single proton each and a broad singlet at δ 1.69 due to vinylic methyl showed lup-20(29)ene system in 24. The half height width of the multiplet at δ 3.92 ($W_{1/2}$ = 22 Hz) due to carbinol methine proton indicated axial orientation and hence -OH at this position was equatorial. Peak at δ 3.40 was a doublet with J = 4 Hz showing the presence of an axial hydroxyl group. The fragments at m/z 189 and at m/z 233 of the diacetate 26 suggested that lup-20(29)ene system and the two hydroxyl groups at rings A/or B were present.

The Lupene 24 was converted to seco diacetate 24a through periodic acid, sodium borohydride and acetylation respectively. The ^{1}H NMR spectrum showed two one proton doublets at δ 4.04 and δ 3.76 (J = 12 Hz) due to protons at C-3; at δ 4.22 and δ 4.10 multiplets for protons at C-2 for vicinal diol. The cis-vicinal diol was confirmed by formation of the isopropylidene derivative of lupene 24.

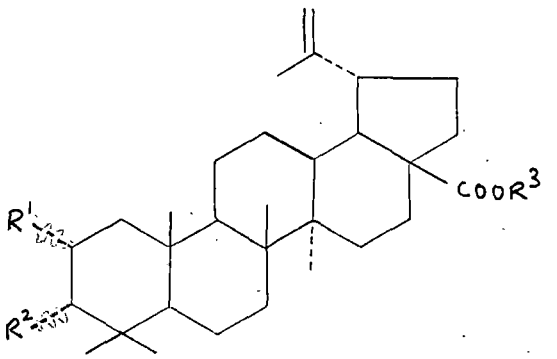


24b

24 ⟶



24a



24 $R^1 = R^2 = \alpha$-OH, H; R^3 = H

25 $R^1 = R^2 = \alpha$-OH, H; R^3 = Me

26 $R^1 = R^2 = \alpha$-OAc, H; R^3 = H

Partial acetylation of the methyl ester 25 showed in ^{1}H NMR that the -OH group with equatorial orientation was preferentially acetylated and the carbinol methine proton was shifted downfield to give a multiplet at δ 5.23 ($W_{1/2}$ = 20 Hz), while the chemical shift of the second carbinol methine proton remained unaltered.

Deacetoxylation of the keto derivative of mono acetate of 24 was effected with difficulty. It was previously reported[31] that the deacetoxylation of an axial acetoxy group situated α-to a keto group was complete easily. Hence it also confirmed the equatorial acetoxy group. The keto derivative was found to be identical with methyl betulonate 24b and therefore the axial -OH group must be at C-3 in 24.

The chemical shifts of the carbinol methine protons reported[33] for the Lup-20(29)ene-2, 3-diols and diacetates also supported the position and configuration assigned to these

protons. So the structure of Lupene 24 was thus established to be 2∝, 3∝ dihydroxy Lup-20(29)en-28-oic acid.

The ^{13}C NMR chemical shifts of 25 compared with methyl betulinate and lup-20(29)ene[34] at δ66.6 and δ78.9 confirm the presence of two secondary hydroxy groups. The ^{13}C NMR data also provide evidence of axial nature of -OH group at C-3 which gives rise to a γ-gauche interaction[35] with the C-5 carbon causing a shielding of 4 ppm compound to the hydroxyl group equatorial where such an interaction was not present.

Application of NMR spectroscopy on the stereochemical assignment of 2,3 diols in triterpenoids:

Very recently, Kojima and Ogura published a paper[44] on the application of ^{1}H NMR spectroscopy for the configurational assignment of 2, 3 diols of triterpenes. They have demonstrated that by analysing signal peaks of the protons on oxygen-bearing carbons atoms in ^{1}H NMR, unambiguous assignment of the stereochemistry of 2,3 -diols can be successfully achieved. They also suggested the revision of a few triterpene structures reported previously. The peak position of the proton signals on hydroxy- or acetoxy- bearing carbons, splitting pattern, coupling constant (or half - height width) give valuable information about the position and configuration of the hydroxy groups. Thus, detailed ^{1}H NMR spectra of the diol, particularly of the diacetate is necessary in order to arrive at an unequivocal assignment of the 2,3-diol stereochemistry.