*nucifera.*[7] (+) And (−)-demethyl coclaurine were obtained by hydrolysis of (+) and (−)-7-O-benzyl coclaurine,[8] respectively. (−)-Demethyl coclaurine showed far greater cardiac activity than (+)-demethyl coclaurine in the frog's heart test. This represents the first reported instance in which the active (−) form of demethyl coclaurine has been found in natural products such as Higenamine, which also contained the less active or the inactive (+)-form.

Further studies on the biological activities of Higenamine on Mammalia are at present being carried out by a Pharmacologist.

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[8] T. Kametani, K. Sakurai, S. Kano, and H. Iida, *Yakugaku Zasshi*, **87**, 822 (1967).

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# The Structure of Arjungenin. A New Sapogenin from *Terminalia arjuna*

The structure of a new sapogenin, arjungenin, isolated from *Terminalia arjuna* was shown to be 2α,3β,19α,23-tetrahydroxyolean-12-en-28-oic acid (I).

The isolations and structure determinations of β-sitosterol, ellagic acid, D(+)-mannitol, (+)-leucocyanidin, (+)-leucodelphinidin, oleanolic acid, arjunic acid, arjunolic acid, and arjunetin from *Terminalia arjuna* have been reported.[1a,b,c,2] We have recently examined the methanol extract of the bark of the plant and isolated a new sapogenin which we named arjungenin. In this communication, we wish to report evidence leading to the structure I for arjungenin.

Arjungenin, mp 293—294° (decomp.), $[\alpha]_D +29°$ ($c$=2.6, EtOH) is crystallized from aqueous methanol and shows the infrared (IR) absorptions at $\nu_{max}^{KBr}$ 3400, 1690, and 1630 cm$^{-1}$. The mass spectrum and elemental analysis indicate the formula $C_{30}H_{48}O_6$ (M$^+$ at $m/e$ 504). The proton magnetic resonance (PMR) spectrum shows the absence of methoxyl and acetoxyl groups. Treatment of arjungenin with diazomethane gave a methyl ester (II), mp 162—165°, $C_{31}H_{50}O_6$ (M$^+$ at $m/e$ 518.3503, Calcd. 518.3604) $\nu_{max}^{KBr}$ 3430, 1720, and 1640 cm$^{-1}$. Acetylation of the ester (II) with acetic anhydride and pyridine at room temperature gave an ester triacetate (III), mp 137—138°, $[\alpha]_D +8.2°$ ($c$=1.82, EtOH), $C_{37}H_{56}O_9$ (M$^+$ at $m/e$ 644), $\nu_{max}^{Nujol}$ 3520, 1740, and 1630 cm$^{-1}$, PMR (Table I), which still shows an IR absorption due to a hydroxyl group. When treated with acetic anhydride in the presence of perchloric acid, III gave an ester

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[1] *a*) L.R. Row, P.S. Murty, G.S.R.S. Rao, C.S.P. Sastry, and K.V.J. Rao, *Indian J. Chem.*, **8**, 716 (1970); *b*) L.R. Row, P.S. Murty, G.S.R.S. Rao, C.S.P. Sastry, and K.V.J. Rao, *Indian J. Chem.*, **8**, 772 (1970); *c*) L.R. Row and G.S.R.S. Rao, *J. Indian Chem. Soc.*, 39, 89 (1962).

[2] F.E. King, T.J. King, and J.M. Ross, *J. Chem. Soc.*, **1954**, 3995.

tetraacetate (IV),[3] amorphous solid, $\nu_{\max}^{\text{Nujol}}$ 1730, and 1230 cm$^{-1}$ (no absorption due to a hydroxyl group), PMR (Table I). Therefore, the nature of all six oxygen atoms involved in arjungenin is characterized, showing the presence of a carboxyl and four hydroxyl groups in its molecule.

The mass spectra of arjungenin (I), II, III, and IV show characteristic peaks at *m/e* 264, 278, 278, and 320, respectively, due to a retro-Diels-Alder-type cleavage of the olean-12-ene skeleton[4,5] indicating the presence of a hydroxyl group at the D/E ring. On refluxing with phosphorus oxychloride in pyridine, III gave a mixture[6] of dienes (V and VI). The mixture was treated with dry hydrogen chloride in chloroform to give a single product [VI; mp 115—118°, $C_{37}H_{54}O_8$ ($M^+$ at *m/e* 626); $\lambda_{\max}^{\text{EtOH}}$ 243.5 nm (log $\varepsilon$ 4.41), 251.5 nm (4.47), and 260.5 nm (4.27); PMR ($CDCl_3$) $\delta$ 5.53 (d, $J$=11 Hz; $C_{(12)}$-H) and $\delta$ 6.43 (dd, $J$=11 and 2 Hz; $C_{(11)}$-H)] which was found to be identical with a diene (VI)[2] derived from methyl arjunolate triacetate (VII)[7] by treatment with selenium dioxide in boiling acetic acid. The optical rotatory dispersion (ORD) data ($[\Phi]_{315}+5170°$, $[\Phi]_{265}-4813°$; $c=0.57$ in EtOH) of the ketone (VIII), amorphous solid, $C_{37}H_{54}O_9$ ($M^+$ at *m/e* 642), obtained by Collins oxidation of III is almost identical with those ($[\Phi]_{315}+4781°$, $[\Phi]_{265}-5246°$; $c=0.43$ in EtOH) of the 19-keto derivative (IX)[1a] prepared from arjunic acid (X).[1a] These facts suggest that arjungenin is 2$\alpha$,3$\beta$,19$\xi$,23-tetrahydroxyolean-12-en-28-oic acid.

TABLE I. PMR Spectral Data ($\delta$ in ppm)[a]

| Compounds | t-$CH_3$ | -$OCOCH_3$ | -$CO_2CH_3$ | $C_{(18\beta)}$-H | $C_{(19\beta)}$-H | $-C\underline{H}_2OAc$ | $C_{(3\alpha)}$-H | $C_{(2\beta)}$-H | $C_{(12)}$-H |
|---|---|---|---|---|---|---|---|---|---|
| III | 0.69 s<br>0.91 s<br>0.99 s<br>0.99 s<br>1.10 s<br>1.25 s | 1.99 s<br>2.01 s<br>2.09 s | 3.62 s | 3.10[b] | 3.35m[c] | 3.58[d]<br>3.82[e] | 5.10m[f] | | 5.45 t |
| IV | 0.68 s<br>0.82 s<br>0.90 s<br>1.06 s<br>1.06 s<br>1.27 s | 1.99 s<br>2.01 s<br>2.08 s<br>2.10 s | 3.65 s | 3.35bd<br>$J$=4 | 4.92 d<br>$J$=4 | 3.58[d]<br>3.82[e] | 5.10m[f] | | 5.50 t |

a) Determined in $CDCl_3$ at 60 MHz. Coupling constants are expressed in Hz. s:singlet, d: doublet, bd: broad doublet, t: triplet, m: multiplet
b) broad signal
c) On addition of $D_2O$, this multiplet changes into a doublet ($J$=4 Hz).
d) A-part of AB-type quartet ($J$=12 Hz)
e) B-part of AB-type quartet
f) These signals are overlapped.

Tomentosic acid has been shown to be 2$\alpha$,3$\beta$,19$\beta$ (equatorial), 23-tetrahydroxyolean-12-en-28-oic acid (XI).[8] Physical constants of arjungenin and its methyl ester are not identical with those[8] of XI and its methyl ester, respectively. Therefore, the hydroxyl group at C-19 of arjungenin (I) was considered to be in $\alpha$ (axial) configuration. This is supported by the following evidences.

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[3] In the mass spectrum of IV, a molecular ion peak at *m/e* 686 ($C_{39}H_{58}O_{10}$) was not observed. A $[M\text{-}AcOH]^+$ ion peak was observed at *m/e* 626.

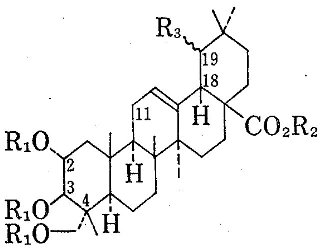
[4] H. Budzikiewicz, J.M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963).

[5] An alternative ursan-12-ene skeleton for these compounds (arjungenin (I), II, III, IV) can be eliminated as described later.

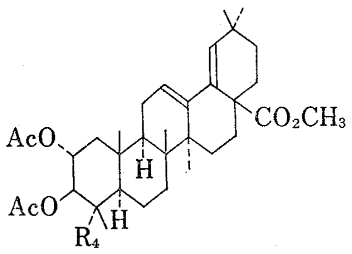
[6] The mixture shows the ultraviolet (UV) absorptions at $\lambda_{\max}^{\text{EtOH}}$ 243, 252, and 261 nm. The fact that the product is a mixture of dienes (V and VI) is suggested by the PMR spectrum. There appear signals at $\delta$ 5.40 (s) and $\delta$ 5.48 (m) due to olefinic protons of a 12,18-diene[1a] system, besides those at $\delta$ 5.53 and $\delta$ 6.43 due to olefinic protons of the 11,13(18)-diene (VI) (*vide infra*).

[7] F.E. King, T.J. King, and J.D. White, *J. Chem. Soc.*, **1958**, 2830.

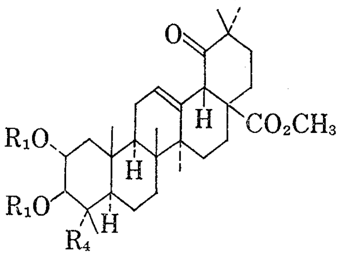
[8] L.R. Row and G.S.R. Rao, *Tetrahedron*, **18**, 827 (1962).



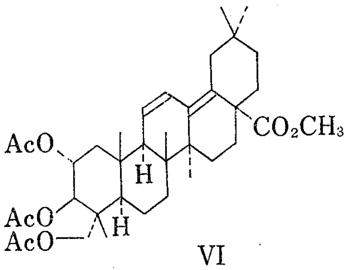
I : $R_1$=H, $R_2$=H, $R_3$=α-OH
II : $R_1$=H, $R_2$=$CH_3$, $R_3$=α-OH
III : $R_1$=Ac, $R_2$=$CH_3$, $R_3$=α-OH
IV : $R_1$=Ac, $R_2$=$CH_3$, $R_3$=α-OAc
VII : $R_1$=Ac, $R_2$=$CH_3$, $R_3$=H
XI : $R_1$=H, $R_2$=H, $R_3$=β-OH



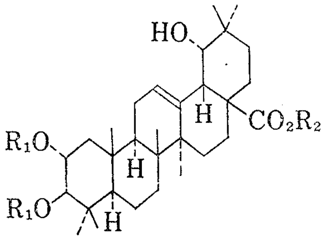
V : $R_4$=$CH_2OAc$
XV : $R_4$=$CH_3$



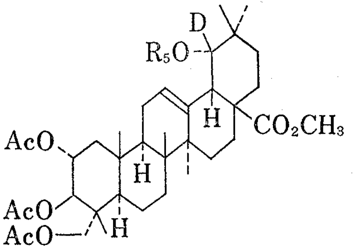
VIII : $R_1$=Ac, $R_4$=$CH_2OAc$
IX : $R_1$=Ac, $R_4$=$CH_3$
XII : $R_1$=H, $R_4$=$CH_3$



VI



X : $R_1$=H, $R_2$=H
XIII : $R_1$=H, $R_2$=$CH_3$
XIV : $R_1$=Ac, $R_2$=$CH_3$



XVI : $R_5$=H
XVII : $R_5$=Ac

It has been reported that the reduction of the ketone (XII) with sodium borohydride yields a 19α-ol (XIII; methyl arjunate) almost quantitatively,[1a] and that the dehydration of methyl arjunate diacetate [XIV; with a 19α (axial)-hydroxyl group] with phosphorus oxychloride in pyridine proceeds easily to form a 12,18(19)-diene (XV).[1a] The ketone (VIII) was reduced with sodium borohydride to give arjungenin ester triacetate (III) quantitatively. In the PMR spectrum of III, the protons on C-18 (β, axial) and C-19 resonate at δ 3.10 as a broad signal (1H; $W_{1/2}$ 6 Hz) and at δ 3.35 as a multiplet (1H), respectively. On addition of $D_2O$, this multiplet changes into a doublet ($J_{18\beta,19\beta}$=4 Hz) suggesting an equatorial (β) nature for the proton on C-19. When treated with sodium borodeuteride ($NaBD_4$; in dioxane, room temperature) VIII gave a 19β-deuteriated product (XVI). In the PMR spectrum of XVI, the multiplet at δ 3.35 is absent and the signal at δ 3.10 ($C_{(18)}$-H) appears as a broad singlet ($W_{1/2}$ 3 Hz). On acetylation with acetic anhydride in the presence of perchloric acid, XVI afforded a 19β-deuteriated tetraacetate (XVII). The signal due to a proton on C-18 of XVII is shifted and appears at δ 3.30 (determined at 100 MHz). These observations confirm the assignment for signals due to the protons on C-18 and C-19, and lead to an α(axial)-configuration for the hydroxyl group at C-19. Thus the structure including absolute configuration of arjungenin was shown to be 2α,3β,19α,23-tetrahydroxyolean-12-en-28-oic acid (I).

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