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ISOLATION AND CONSTITUTION OF OBLONGIFOLIOL, A NEW DITERPENE OF CROTON OBLONGIFOLIUS L.

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The seeds, roots and bark of C. oblongifolius (Euphorbiaceae) are drastic purgatives and are poisonous in larger doses. The air-dried powdered bark (900 g.) was extracted with light petroleum; after washing with aqueous alkali the neutral fraction (22.5 g.) of the extract was obtained as a viscous oil and column chromatography on neutral alumina afforded three crystalline compounds besides oily matter. Compound-1 obtained in poor yields from the earlier eluates with benzene crystallised from light petroleum as colourless plates, m.p. 143-4°, $[\alpha]_D^{32}$ +45.2° (C, 1.2 in $CHCl_3$). It is a new diterpene alcohol but its study could not be completed for lack of material. Compound-2 (0.1 g.) obtained from later eluates with benzene crystallised from methanol as colourless needles, m.p. 136°, $[\alpha]_D^{32}$ -33° (C, 1.8 in $CHCl_3$). Its identification as β-sitosterol, was confirmed by direct comparison with an authentic sample.

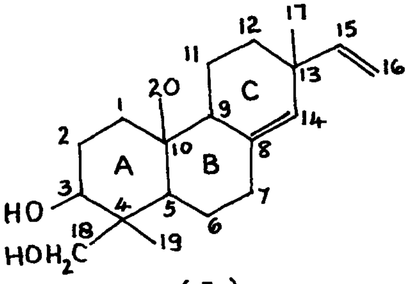
Compound-3 (oblongifoliol) was new and obtained from the benzene: ethyl acetate (95:5) eluate in 0.36% yield and it crystallised from light petroleum as colourless plates, m.p. 147-8°, $[\alpha]_D^{32}$ +27.4° (C, 4.9 in $CHCl_3$); it gave red colour in Liebermann-Burchard test and had molecular formula, $C_{20}H_{32}O_2$ (M^+ 304). IR (KBr) showed hydroxyls (3630 and 1088 cm^{-1}) and vinylic unsaturation (3080, 1640, 990 and 910 cm^{-1}). It had no UV absorption (absence of conjugation). NMR (δ, $CDCl_3$): 0.80, 0.83 and 1.22 (9H, 3 tertiary methyls), 3.67-4.30 (3H, $-C\underline{H}-OH$ and $-C\underline{H_2}-OH$), 5.35 (1H, singlet, proton on a triply substituted double bond), 4.69-6.10 (3H, ABX pattern of vinylic type[1], δ_A, 4.85, δ_B, 4.91; δ_X, 5.83; J_{AB} 1.5 c/s; J_{AX} 10 c/s, and J_{BX} 18 c/s). Its mass spectrum had strong peaks with m/e 304 (M^+), 286, 271, 245, 171, 169, 159 and 157. It did not consume periodate.

Oxygen functions: Oblongifoliol readily formed a diacetate (Ac_2O -Py; r.t., 24 hr.) $C_{24}H_{36}O_4$ (M^+ 388), m.p. 134-5°, $[\alpha]_D^{32}$ +17.81° (C, 1.9 in $CHCl_3$); the two oxygens are thus unhindered hydroxyls. NMR (δ, $CDCl_3$): 0.85, 0.97 (9H, 3 tertiary methyls), 2.01 (6H, 2 $O-CO.C\underline{H_3}$), 4.20 (2H, AB quartet, J_{AB} 17.5 c/s, $-C-\overset{|}{\underset{|}{C}}\underline{H_2}-O-CO.CH_3$), 4.58 (1H, singlet, $CH_3.CO.O.\overset{|}{\underset{|}{C}}-\underline{H}$), 5.30 (1H, singlet, proton on a triply substituted double bond next to quaternary carbon, $-\overset{|}{\underset{|}{C}}-C\underline{H}=\overset{|}{\underset{|}{C}}$), 4.73-6.07 (3H, ABX pattern of vinylic type[1]). Mass spectrum: marked peaks with m/e 388 (M^+), 328, 268, 255, 187, 170, 159 and 157. These data indicate that one hydroxyl of oblongifoliol is secondary and the other primary attached to a tertiary carbon atom.

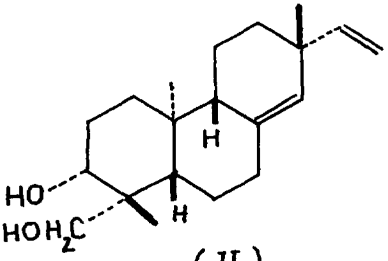
Nature of double bonds: NMR spectra of oblongifoliol and its diacetate indicated two double bonds, one being triply substituted and connected to a quaternary carbon atom and the other being vinylic. By catalytic hydrogenation oblongifoliol absorbed 2 moles of hydrogen yielding a tetrahydroderivative, $C_{20}H_{36}O_2$, m.p. 119-20° whose IR and NMR spectra indicated absence of unsaturation.

Gross Structure (I): Oblongifoliol should be tricyclic and this is supported by its selenium dehydrogenation yielding pimanthrene (1,7-dimethyl phenanthrene). Its oxidation with CrO_3-Py yielded a keto aldehyde giving Zimmermann colour test[2] for 3-keto compound[3] fixing 3-position for the secondary hydroxyl. Pyrolysis of oblongifoliol or its tetrahydro derivative with copper powder at 270-280° yielded formaldehyde indicative of 3,18(19)-diol system[4]; a hydroxy methyl at C-4 agrees with NMR of oblongifoliol and acetate. Further, the mass spectrum of oblongifoliol having a fairly prominent peak with m/e 169 supports location of both the hydroxyls in ring A[5]. Hence gross structure (I) can be proposed for oblongifoliol.

Configuration: The assignment of configuration at C-4 rests upon NMR data. In diterpenes containing a methyl and a hydroxy (or acetoxy) methyl at C-4, the protons of the oxygenated methylene appear as quartet or a singlet at a much lower field in an axial configuration than in the equatorial[6,7,8]. The quartet centred at δ 4.2 recorded for oblongifoliol diacetate is close to that recorded for psiadiol diacetate[9] (δ 4.14) and beyerol triacetate[8] (δ 4.4) both having axially placed CH_2OAc at C-4. An equatorial acetoxy methyl would show methylene protons as a quartet at δ 3.8. The axial configuration is further supported by the keto aldehyde obtained by the oxidation of oblongifoliol having high formyl proton signal[10] at δ 9.86. The configuration of the 3-hydroxyl was determined by IR spectrum of oblongifoliol which clearly indicated intramolecular hydrogen bonding and had absorptions at 3630 and 3550 cm^{-1} with $\Delta\nu$ 80 cm^{-1}. This compares well with data for similar 3,24-dihydroxy triterpenes[11] and the diterpene beyerol[12]. Since oblongifoliol has an axial hydroxy methyl group at C-4, the 3-hydroxyl should be equatorial. The ABX pattern of vinylic proton resonance closely resembled those of isopimaric and sandaracopimaric acids[1] and hence a β-methyl and α-vinyl groups are present at C-13 of oblongifoliol.



(I)



(II)

The configuration of the A/B ring fusion of oblongifoliol could be deduced from molecular rotation differences. The majority of the triterpenes have the 5α, 10β configuration and have positive molecular rotation difference between their 3β acetates and alcohols[13] and the same is true for triterpenes having 3β, 24-dihydroxy system. This correlation is applicable to diterpenes also, e.g., 3β-hydroxy-8,15-sandaracopimaradiene. Compounds with the opposite unusual 5β, 10α ring junction show negative rotation differences (Cf. darutigenol[14]). Oblongifoliol belongs to the latter type, the rotation difference being -14.3°. Though there is no direct evidence regarding the configuration of the hydrogen at C-9, based on the analogy with darutigenol and other similar diterpenes having the above A/B ring fusion (e.g., steviol, stachenol, beyerol) it could be assigned a β configuration. The complete structure has therefore, been proposed for oblongifoliol as 3α, 18-dihydroxy darut-8(14),15-diene (II) and it forms the second pimaroid diterpene having an unusual A/B trans ring junction with 5β, 10α configuration.

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