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FURTHER CONSTITUENTS OF NIM OIL: THE CONSTITUTION OF MELDENIN

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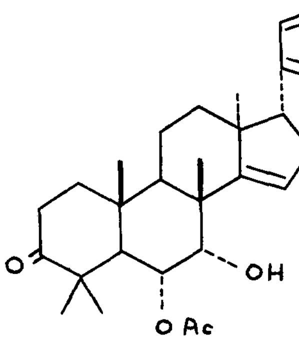
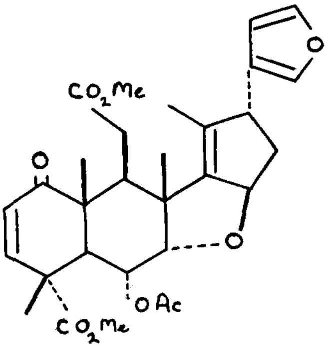
Recent publications[1, 2, 3] on further constituents of Nim oil, the seed oil of Melia azadirachta, prompt us to record the results of our own investigations. We have isolated from the oil in very small yield (∿ 0.0005%) a new tetranortriterpenoid, meldenin, which may be a nimbin[4, 5] precursor. Meldenin (I), $C_{28}H_{38}O_5$, m.p. 240-244°, has absorption in the i.r. attributable to a cyclohexanone, acetate and hydroxyl group (1716, 1747 and 3587 $cm.^{-1}$ respectively). Its n.m.r. spectrum reveals the presence of a β-substituted furan (τ 2.62, 2.74, 3.70, 1H each), five tertiary methyl groups (τ 8.72, 8.78, 8.90, 9.12, 9.17, 3 H each), a trisubstituted double bond (τ 4.42, 1 H), a secondary hydroxyl group (τ 5.91, 1H, doublet, J = 2 c./sec.) and a secondary acetate group (τ 7.86, 3H; τ 4.68, 1H, quartet, J = 2, 12 c./sec.). The sequence $>CH.CHOAc.CHOR-\overset{|}{\underset{|}{C}}-$ in nimbin (II) is duplicated here and is readily confirmed by double resonance experiments. The ketonic carbonyl group is placed at C-3 on the basis of o.r.d. measurements, $[\Phi]_{400}$ + 1805°; $[\Phi]_{303}$ + 9300°; $[\Phi]_{269}$ ± 0°; $[\Phi]_{239}$ + 4130°, which are consistent with those of a 3-keto-8β-methyl triterpenoid although the amplitude is unusually large. The above evidence leads to the structure (I) for meldenin as the most acceptable biogenetically. The presence of an oxygenation pattern in ring B identical to that in nimbin (II) suggests that meldenin may be converted into nimbin in the plant by further modification including cleavage of ring C and eventual closure of the C-7 hydroxyl group to C-15.

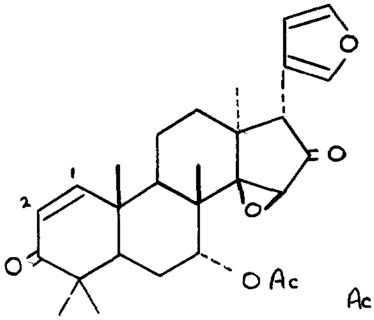
We have also isolated from Nim oil a compound m.p. 198-200°, $[\alpha]_D$ + 39° ($CHCl_3$) which from spectral data appears to be identical with nimbinin[1] (III), m.p. 202-204°, $[\alpha]_D$ + 45° ($CHCl_3$), the constitution of which has been recently determined by Narayanan and his colleagues.



I

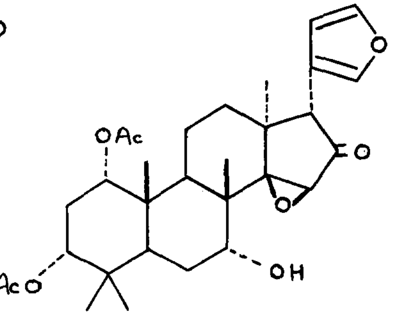


II



III

IV 1, 2-dihydro III



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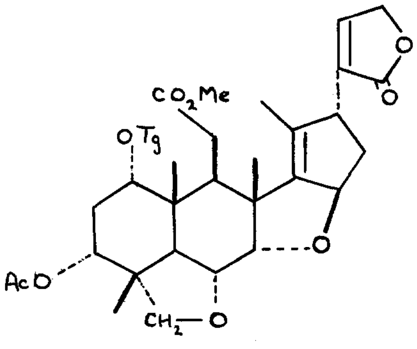
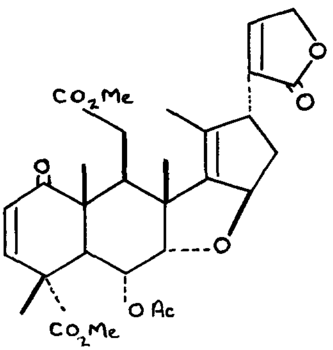


VI



VII

Nimbinin may be identical with epoxyazadiradione[2], m.p. 199-200°, $[\alpha]_D$ -75° ($CHCl_3$), although there is a discrepancy in the recorded specific rotations. The chemical shift values for the enone protons in nimbinin (τ 2.88, 4.15, J = 10 c./sec.) remove the residual uncertainty[1,2] as to the orientation of the enone in ring A. These values accord[6] with those of a Δ^1-3-ketone rather than a Δ^2-1-ketone. This conclusion is reinforced by comparison of the o.r.d. curves of dihydronimbinin (IV), ($[\Phi]_{400}$ -725°; $[\Phi]_{322}$ -5060°; $[\Phi]_{286}$ + 12300°; $[\Phi]_{266}$ + 12300°) and grandifolione (V)[7] ($[\Phi]_{400}$ -560°; $[\Phi]_{311}$ -8070°; $[\Phi]_{278}$ + 8610°; $[\Phi]_{249}$ + 6130°). A small positive contribution from the 3-ketone is apparent in the former.

From salannin[8] mother liquors we have obtained a compound, $C_{34}H_{44}O_{10}$, m.p. 244-246°, $[\alpha]_D$ + 126° ($CHCl_3$) which has an n.m.r. spectrum remarkably similar to that of salannin except that the resonances arising from the β-furan moiety in salannin are replaced by those of a vinyl proton at τ 2.75 (1H, broad singlet) and a methylene group at τ 5.30 (2H, broad singlet). This together with the i.r. absorption at 1765 $cm.^{-1}$ (αβ-unsaturated γ-lactone) leads to the structure (VI) for this compound. From nimbin mother liquors we have isolated the corresponding lactone (VII), $C_{30}H_{36}O_{10}$, m.p. 184-186°, $[\alpha]_D$ + 88° ($CHCl_3$). These two lactones could not be detected in fresh Nim oil and it is probable that they derive from light-induced oxygen attack on the furan ring. This type of auto-oxidation of furans has been reported[9] previously.

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