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SALANNIN

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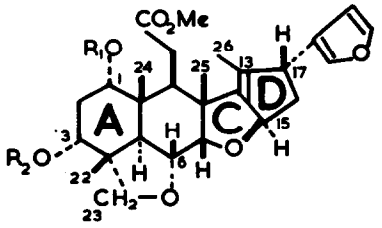
During the isolation of nimbin (1, 2) from nim oil, the seed oil of Melia Azadirachta, we have obtained as a minor constitutent a new related 'triterpenoid' which we name salannin and for which we propose the constitution and stereochemistry (I) on the following basis.



(I) R_1 = CO.C_4H_7 ; R_2=CO.CH_3
(II) R_1 = R_2 = CO.CH_3
(III) R_1 = CO.C_4H_7 ; R_2 = H
(IV) R_1 = R_2 = H
(V) R_1 = H ; C_3 carbonyl

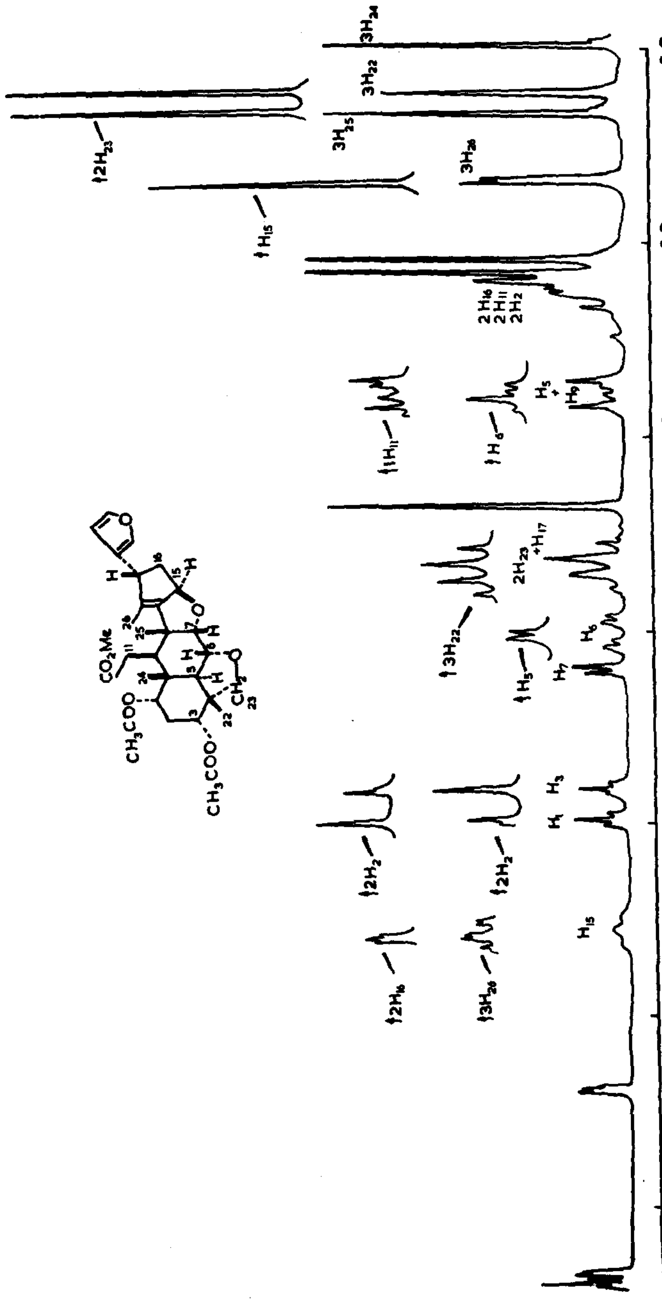


Fig. 1. Nuclear Magnetic Single and Double Resonance Spectra at 100 Mc.p.s. of the Diacetate II.

Salannin, m.p. 167 - 170°, $[\alpha]_D$ + 167° analysed for $C_{34}H_{44}O_9$. Its p.m.r. spectrum showed the presence of three quaternary methyls (τ 9.0, 8.77 and 8.67; 3 H each, singlets) and one vinyl methyl (τ 8.31; 3 H, doublet, J = 1.5 c.p.s.), one carbomethoxyl (τ 6.72; 3 H singlet), one acetate (τ 8.05, 3 H, singlet) and one tiglate ester (τ 3.0, 1 H, multiplet and τ 8.0 - 8.25; 6 H, characteristic multiplets at 100 Mc/s), one β-substituted furan ring (τ 2.65, 2 H, multiplet and τ 3.67; 1 H, diffuse singlet). In the infra red salannin showed $\nu_{max}^{CCl_4}$ 1710 (tiglate ester), 1743 (acetate and methyl esters), 1653 (olefinic linkage) $cm.^{-1}$. Salannin does not contain a hydroxyl group (absence of i.r. bands above 3000 $cm.^{-1}$) or a ketone or aldehyde function (quantitative evaluation of carbonyl absorption in the i.r.), so that the two remaining oxygen atoms are probably present as ethers.

The common botanical source and the similarity of several functional groups suggested a close structural relationship between salannin and nimbin.

Two features present in nimbin could be readily discerned from the p.m.r. spectrum at 100 Mc/s. (Fig.1) of the diacetate (II), $C_{31}H_{40}O_9$, m.p. 232 - 234° $[\alpha]_D$+ 126°, obtained from salannin by hydrolysis and acetylation. First, the structure of rings C and D (as I) were fully supported as follows: H_{15} is coupled equally with both protons at C_{16} ($J_{15,16}$ = 7 c.p.s.), with the vinyl (C_{26}) methyl group ($J_{15,26}$ = 2 c.p.s.) and with H_{17}($J_{15,17}$ = 2.5 c.p.s.) [the last two are homoallylic couplings (3)]. This follows from the observations (Fig. 1) that H_{15}, a diffuse multiplet centred at τ 4.52 (4.42 in nimbin), simplifies to a triplet of doublets upon irradiation at the C_{26} vinyl methyl group at τ 8.35 (8.4 in nimbin). Removal of the major (7 c.p.s.; $\theta H_{15}H_{\alpha\ 16}$ = 20°; $\theta H_{15}H_{\beta\ 16}$ = 140°) coupling by irradiation at τ 7.82 (C_{16} methylene) left H_{15} as a very narrowly spaced quartet. Second, the C_5 - C_6 - C_7 carbon chain resembles that of nimbin in the following manner. H_6 (τ 6.0) is coupled, as in nimbin (1, 2) to two neighbours:

H_5 (τ 7.22, J = 13 c.p.s.) and H_7 (τ 5.82, J = 3 c.p.s.), neither H_5 nor H_7 being otherwise coupled. These observations demonstrate the configurations of the protons attached to C_5, C_6, and C_7 (axial, axial, equatorial), the absence of hydrogen at C_8 and C_{10} and the location of ether oxygen functions at C_6 and C_7.

The second ether ring (that not present in nimbin), would terminate most probably at C_{23}. In fact, the C_{23} methylene group gives rise to an AB quartet (τ 6.25, 6.42, 2 H, J = 8.5 c.p.s.) at the expected position. The A branch (τ 6.25) has a small (<1 c.p.s.) ^4J coupling (4) with the C_{22} methyl group (τ 8.78).

On the assumption that ring C is cleaved as in nimbin to generate an acetate chain attached at C_9 [H_9 (τ 7.30) couples with one proton (τ 7.82) at C_{11}], the two ester functions (acetate and tiglate) must be located between C_1 and C_3 in salannin. They cannot be vicinal since the α protons (τ 5.05 and 5.20) are not mutually coupled, but instead couple individually with the intermediate methylene group at C2 (τ 7.56, $J_{AX_2} = J_{BX_2} = 3$ c.p.s.). The tiglate must be at C_1 and the acetate at C_3, rather than the reverse, for the following reason. Alkaline hydrolysis of salannin leads, after methylation, to a mixture of two compounds, a hydroxy-tiglate (III), $C_{32}H_{42}O_8$, m.p. 213 - 215°, $[\alpha]_D$ + 137° which has lost the acetate, and a diol (IV), $C_{27}H_{36}O_7$, m.p. 201 - 205°, $[\alpha]_D$ + 135° which has lost both acetate and tiglate esters. The methyl ester CH_3 resonances are abnormally high in salannin (τ 6.72) and the hydroxytiglate (τ 6.78), but normal (τ 6.40) in the diol, suggesting that the tiglate function shields the methyl ester protons and must therefore be at C_1. Confirmation comes from (i) the fact that the methyl ester carbonyl group is unbonded in dilute solution in the hydroxytiglate (III) ($\nu_{max.}^{CCl_4}$ 1742 cm.$^{-1}$), but is hydrogen-bonded in the diol (IV) ($\nu_{max.}^{CCl_4}$ 1718 cm.$^{-1}$), and (ii) the preferential hydrolysis of the less hindered acetate at C_3.

There remain for discussion the configurations at C_4, C_1 and C_3, and C_{15}.

The C_4 stereochemistry can be such as to produce either a cis - or a trans-fused ether ring with the α - (equatorial) oxygen at C_6, corresponding respectively to oxidation of the equatorial or axial methyl group at C_4. We prefer a cis-fusion (as in I) for the following reasons. The diol (IV) is oxidised by the Sarett reagent to a ketol (V), $C_{27}H_{34}O_7$, m.p. 253 - 255° $[\alpha]_D$ + 160° formed by oxidation of the C_3 hydroxyl group [$\nu_{max}^{CHCl_3}$ 1719 cm^{-1} (H - bonded methyl ester and clyclohexanone) in dilute solution]. Comparison of the methyl group resonances of this hydroxy-ketone with those in the diol (IV) shows that the newly introduced carbonyl group exerts a marked deshielding action on the C_{22} and C_{24} methyl groups. A trans-fused $C_6 \longrightarrow C_{23}$ ether ring would impose a quasi-boat conformation on ring A. In the most stable form of this (Dreiding models) the C_{24} methyl group would be strongly shielded (5) by the C_3 carbonyl group, contrary to observation. With a cis-fused ether ring, the C_{24} methyl group is in the plane of the C_3 carbonyl group and therefore negatively shielded, as observed. On this basis, and consequently assumption of a chair ring A, the ester groups at C_1 and C_3 must both be axially (α) attached, to account for the small width ($\sim$ 7 c.p.s.) (6) of the C_1 and C_3 proton multiplets in the p.m.r. spectrum of the diacetate (II) (Fig.1).

TABLE 1.

Resonances(τ) of Angular Methyl Groups in the P.M.R. Spectra of Salannin and its derivatives.

Compound	I	II	III	IV	V
C_{25}	8.67	8.70	8.70	8.72	8.62
C_{22}	8.77	8.80	8.85	8.89	8.70
C_{24}	9.01	9.06	9.05	9.11	8.88

The C_{15} configuration can be inferred from the C_{25} methyl group resonance in salannin and its derivatives. This is consistently the most deshielded (τ 8.62 - 8.72; Table 1) of the quaternary methyl groups and must owe its large paramagnetic shift to the isolated $C_{13} - C_{14}$ double bond (7). The optimum geometry for such a large shift (methyl group in plane of olefinic double bond) results when the C_{15} hydrogen has the α - configuration.

Rotations are in $CHCl_3$. P.m.r. spectra were recorded in $CDCl_3$ solution with internal T.M.S. at 100 Mc.p.s.

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