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CONSTITUENTS OF *MELIA INDICA* - II*

NIMBIDIC ACID AND NIMBIDININ

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The total amorphous bitter from *Melia indica* (Syn. *Melia azadirachta*), nimbidin[1], on mild alkaline treatment (2 - 5 per cent KOH) has since yielded tiglic acid alongwith nimbidic acid[1](I), $C_{26}H_{34}O_7$, m.p. 228-30°, from the acidic fraction (*loc.cit*). The spectral studies with the tetra-nortriterpenoid, nimbidic acid and its methyl ester acetate (Ia) reveal the identity of the acid with salannic acid, the hydrolytic acid of salannin[2] (Ib), reported recently from *Melia dubia*[3]. An interesting feature noted with the nimbidic acid was the formation of a lactone acetate, 3-acetyl-nimbidic acid-1(12)-lactone (Ic), $C_{28}H_{34}O_7$ (M^+ 482), m.p. 226-28°, on attempted acetylation (Py/Ac_2O) of the acid.

The crystalline neutral constituent nimbidinin[4] m.p. 282-84° of the hydrolysate, a new tetra-nortriterpene belonging to Meliacin[5] series has been studied and its structure elucidated.

Nimbidinin (II) analysed for $C_{26}H_{34}O_6$ (M^+ 442) and showed UV absorption at λ_{max}^{alc} 225 nm. The IR spectra of nimbidinin showed the presence of both hydroxyl (3400 cm^{-1}) and carbonyl bands (1708 cm^{-1}). On acatylation (Py/Ac_2O) it yielded a triacetate (IIa) $C_{32}H_{40}O_9$ (M^+ 568), m.p. 222-24°, thus showing the presence of three hydroxyl groups in the molecule. The presence of the only

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*Part I, C.R. Mitra, Jour.Sci.Industr.Res., 16B, 477 (1957)

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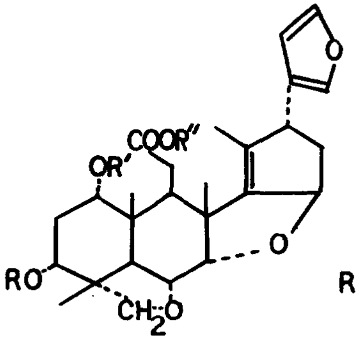
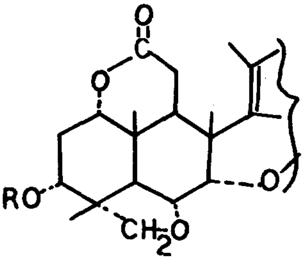
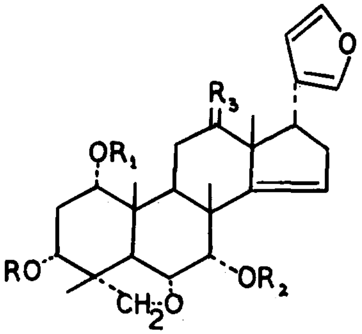
one carbonyl group was revealed by its formation of a mono-oxime (IIb), $C_{26}H_{35}O_6N$, m.p. 274-76°. The other significant features in the IR spectra of the nimbidinin and its acetate were the presence of a trisubstituted double bond (820 cm^{-1}) and ether linkage (1160 and 1070 cm^{-1}). These features were supported by the NMR and the mass spectral studies with nimbidinin and its acetate leading to its structure (II).



I R=R'=R"=H
Ia R=R'=Ac, R"=CH_3
Ib R=Ac, R'=Tg., R"=CH_3



Ic R=Ac



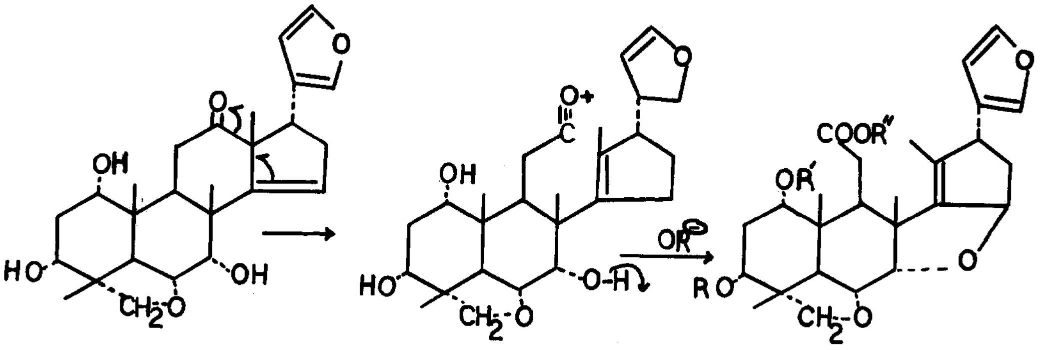
II R=R_1=R_2=H, R_3=O
IIa R=R_1=R_2=Ac, R_3=O
IIb R=R_1=R_2=H, R_3=NOH
IIc R=Ac, R_1=Tg., R_2=H, R_3=O

The presence of a β-substituted furan ring attached at C-17, a common feature of meliacins, in nimbidinin, was evident from its NMR spectra showing signals at δ 6.62 (1H) and δ 7.42 (2H) ppm. Thus all the six oxygen atoms in nimbidinin are accounted for by three hydroxyls, one carbonyl, one furan and an oxide.

The comparison of the NMR spectra of nimbidinin triacetate (IIa) with salannin diacetate[2] (Ia), revealed two interesting features; firstly, it showed the presence of two of the hydroxyl groups in nimbidinin at C-1 and C-3 in ring-A as both the corresponding protons <u>alpha</u> to the acetyl groups appeared as diffused triplets at δ 4.7 and δ 4.97 ppm due to their individual couplings with C-2 methylene protons appearing at δ 2.4 ppm ($J_{ax_2} = J_{bx_2}$ = 2.5 Hz), as in salannin diacetate, and secondly, the C-5, C-6, C-7 carbon chain resembled with that of salannin in the following manner: H-6 proton (double doublet centered at δ 4.24 ppm) is coupled as in salannin[2] and also in nimbin[6], to two neighbouring protons H-5 (J = 11 Hz) and H-7 (J = 2.5 Hz). The H-7 proton in turn appeared at δ 5.6 ppm as a doublet (J = 2.5 Hz). These observations confirmed the configuration of the protons attached at C-5, C-6 and C-7 as axial, axial, equitorial and the absence of protons at C-8 and C-10, and the location of oxygen functions at C-6 and C-7. Further, the presence of a methylene group adjacent to an oxide link was shown by the presence of two protons signal at δ 3.55 ppm. Thus the oxide link in nimbidinin was undoubtedly through C-23 and C-6 as reported in salannin (loc.cit). The third hydroxyl group could, therefore, be placed at C-7. However, some of the features in the NMR spectra of nimbidinin triacetate (IIa) distinguishing it from salannin diacetate (Ia) were the absence of the vinylic methyl and instead the presence of four angular methyl groups in (II) and the presence of a trisubstituted double bond at δ 5.7 ppm. Thus nimbidinin (II) did not have an oxide link at C-7(15) instead this oxide ring was open having the additional hydroxyl group at C-7 and a double bond at C-14(15). This was also in support of the fact that the carbonyl group was present as a six membered ketone in view of the absence of any aldehydic proton in its NMR spectra and that the ring-C is not open but a closed one as indicated by its molecular formula as well as the functional groups. The optical rotatory dispersion curve of nimbidinin showed a positive Cotton effect (peak at $(\alpha)_{267}$ - 14.4° and trough at $(\alpha)_{246}$ -23.2°) in agreement with C-11 and/or C-12 carbonyl sterols[7]. The placement of the carbonyl at C-12 is more probable in nimbidinin from its biogenetical possibility to give rise to nimbidic acid (I) vis-a-vis salannin (Ib) on further oxidation as shown in scheme-I.

Thus nimbidinin (II) appears to be an intermediatory product to salannin (Ib). This is in support of the coexistence of nimbidinin (II) and nimbidic acid (I), the hydrolytic acid from salannin (Ib), in the amorphous bitter of *M. indica*.

Since nimbidinin is obtained by step-wise mild alkaline hydrolysis of the amorphous bitter, the possibility of the presence of a tiglate and



II

Ib R=Ac,R'=Tg.,R"=CH_3

acetate at C-1 and C-3 respectively in the parent natural product (representing IIc) yielding nimbidinin (II), as in salannin (Ib), is not ruled out since tiglic acid was obtained from the acidic fraction of the hydrolysate.

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