The Meliacins (Limonoids). Nimbolin A and B, Two New Meliacin Cinnamates from *Azadirachta indica* L. and *Melia azedarach* L.

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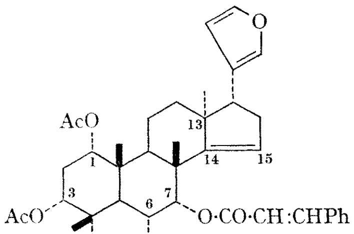
Summary Two new meliacins, nimbolin A (I) and B (II), as well as fraxinellone (previously reported from *Dictamnus albus* L., fam. Rutaceae) and gedunin, have been isolated from the trunk woods of *Azadirachta indica* L. and *Melia azedarach* L. (both, fam. Meliaceae).

PROTOMELIACINS, but so far no meliacins, have been reported[1] from *Melia azedarach* L., while the closely related species *Azadirachta indica* L. (syn. *Melia azadirachta* and *M. indica*) has furnished, besides one of the protomeliacins, mainly meliacins from the bark, seed oil, and leaves. We now report the isolation of two new meliacins, nimbolin A and B, from the trunk woods of both species. The petroleum extract from the ground wood of several samples of *A. indica* on chromatography afforded both compounds.

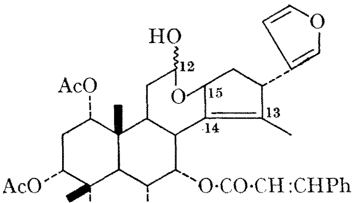
Nimbolin A, m.p. 180—183° $[\alpha]_D$ − 38·6°, $C_{39}H_{46}O_8$ (M^+ 642), for which we suggest structure (I), possesses three acyloxy-groups—two acetoxy- and one cinnamoyloxy-. Thus, alkaline hydrolysis afforded two moles of a volatile and one mole of a non-volatile acid identified as acetic and cinnamic acids, respectively, from the n.m.r. spectra of their sodium salts. This was supported by the n.m.r. spectrum of nimbolin A itself which showed signals attributable to two acetates (τ 7·87, 8·17) and a cinnamate [τ 2·67 (5 aromatic H) and two mutually coupled doublets at τ 2·38 and 3·70 (J 16 c./sec.) each corresponding to one hydrogen (CH=CH)]. Partial hydrolysis and double-resonance experiments† (to be discussed in the full paper) indicate that the two acetates are in a 1,3-relationship to one another. Three 1H signals [τ 4·35 (d, J 3 c./sec., 7-H); 5·79 (quartet, $J_{6,7}$ c./sec. and $J_{5,6}$ 12 c./sec., 6-H); and τ 7·33 (d, J 12 c./sec., 5-H)] are reminiscent of 7-, 6-, and 5-H in nimbin[2] and nimfolide[3] respectively. These assignments were supported by decoupling experiments.† The chemical shifts of these hydrogens show that in nimbolin A, 6-H is vicinal to an ether oxygen while 7-H is at the base of an acyloxy-group. Thus the cinnamate is placed at position 7. There are four tertiary methyls (τ 8·77, 8·80, 8·95, and 9·14), a fifth one having been oxidised to an oxymethylene, and being involved in an ether linkage to C-6 as in salannin[4] (τ 6·54, 2H; CH_2–O). A triplet at τ 4·50 is assigned to a vinyl 15-H by analogy with azadirone.[5] The presence of a β-substituted furan characteristic of the meliacins is indicated by absorptions at τ 2·83 and 3·83, and (i.r.) at 873 cm.$^{-1}$. These observations lead to the structure (I) for nimbolin A.

Nimbolin B (II), $C_{39}H_{46}O_{10}$ has m.p. 243—245° and $[\alpha]_D$ − 93·3°. Its spectral properties closely resemble those of nimbolin A and indeed indicate an identical structure in rings A and B as well as the presence of a β-substituted furan. There are, however, two significant differences in the n.m.r. spectra. While that of nimbolin A showed four tertiary methyls, the spectrum of nimbolin B showed only three, the fourth one being replaced by a sharp downfield methyl singlet at τ 8·20 which we assign to a vinyl methyl not involved in homoallylic coupling. Secondly, the vinyl 15-H signal present in nimbolin A is absent in nimbolin B and in its place is a 2H multiplet further upfield at τ 4·72. The vinyl methyl suggests cleavage of ring C such as has occurred in nimbin[2] and nimbolide.[3] Such a cleavage is an oxidative process and in the last two compounds has led to the formation of a carboxy-group. However, complete hydrolysis of nimbolin B gave a nucleus that had no carbonyl absorption in the i.r. spectrum. We suggest that in this case the cleavage has yielded a hydroxy-aldehyde, possibly *via* an intermediate such as (III). The hydroxy-aldehyde in turn forms nimbolin B as the internal hemiacetal (II). The signal at τ 4·72 is thus assigned to 15-H and the hydrogen vicinal to the hemiacetal hydroxy-group at C-12. This was supported by two further observations. Treatment of nimbolin B with methanol in the presence of an acidic catalyst (BF_3–methanol complex) afforded a methyl ether (τ 6·73) through the methylation of the hemiacetal hydroxy-group. Further, oxidation of nimbolin B with chromic oxide in pyridine (Sarrett's reagent) yielded a lactone (4 hydrolysable groups as compared with 3 in nimbolin B), the n.m.r. spectrum of which showed that one of the hydrogens at τ 4·72 had disappeared and the other had moved downfield to τ 4·33.

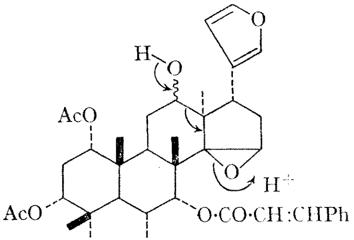
Three samples of *M. azedarach* were examined. Two of the samples gave 24-methylenecycloartanone and a non-furanoid compound, m.p. 258·5°, $[\alpha]_D$ − 38°, M^+ 676. In addition, one of them yielded nimbolin A and gedunin



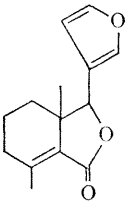
(I)



(II)



(III)



(IV)

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† Measurement at the Max Planck Institute, Heidelberg, Germany, by courtesy of Fräulein G. Taigel and Dr. J. C. Jochims, whom we thank.

while the other gave nimbolin B. The third sample was a younger tree and afforded fraxinellone (IV) m.p. 108—110° $[\alpha]_D$ − 41·7° ($CHCl_3$) {lit.[6] m.p. 105—115° and 116°, $[\alpha]_D$ − 44° (EtOH); n.m.r. and mass spectra identical with published[6] spectra} as well as two nonfuranoid compounds (a) m.p. 257—259° $[\alpha]_D$ − 66·5°, M^+ 454; and (b) m.p. 190—194°, $]\alpha]_D$ − 16°, M^+ 346. Fraxinellone was first reported[6] from *Dictamnus albus* L. (fam. Rutaceae) and is probably the first compound related to the meliacins (limonoids) to be isolated from both the families Meliaceae and Rutaceae.

The occurrence of nimbolin A and B in both *M. azedarach* and *A. indica* further underlines the close relationship between the two species.

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