Communications to the Editor

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STRUCTURES OF PANICULIDINES A AND B: NOVEL PRENYLINDOLES FROM MURRAYA PANICULATA

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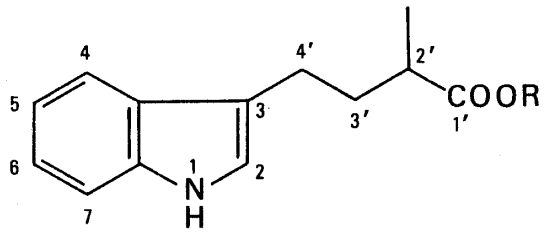
Two new indoles named paniculidines A and B were isolated from Murraya paniculata (Linn.) Jack., and their structures have been elucidated as methyl 2-methyl-4-(indol-3-yl)-butyrate and 2-methyl-4-(1-methoxyindol-3-yl)-1-butanol, respectively.

KEYWORDS ——Murraya paniculata; Rutaceae; prenylindole; 1-methoxyindole; Fischer indole synthesis; paniculidine A; paniculidine B

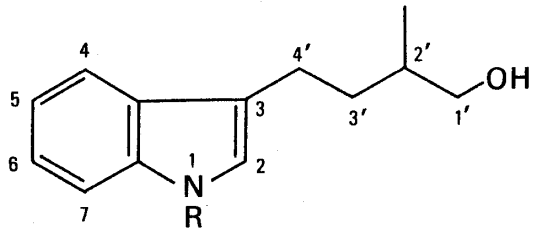
Murraya paniculata (Linn.) Jack. is a rutaceous shrub ranging widely from India, southeast Asia, and southern China to Taiwan and the Okinawa Islands. The leaves and bark of this plant are used as a folk medicine for the treatment of stomachache and toothache or as a stimulant and tonic throughout this area. In China the root bark is also used as an anodyne or local anesthetic for the treatment of gout, contusion and boneache. The leaves and bark of this plant have been the subject of extensive chemical investigations, and a number of coumarins, flavones, and essential oils have been isolated.[1] However, there have been no reports on chemical constituents of the root bark of this plant. The present communication deals with the isolation and structural elucidation of two new indoles from the root bark of this plant collected in Taiwan.

Paniculidine A (I) was obtained from chloroform extract as an optically active oil after repeated column chromatography over silica gel and identified



(I) R = Me paniculidine A

(II) R = H

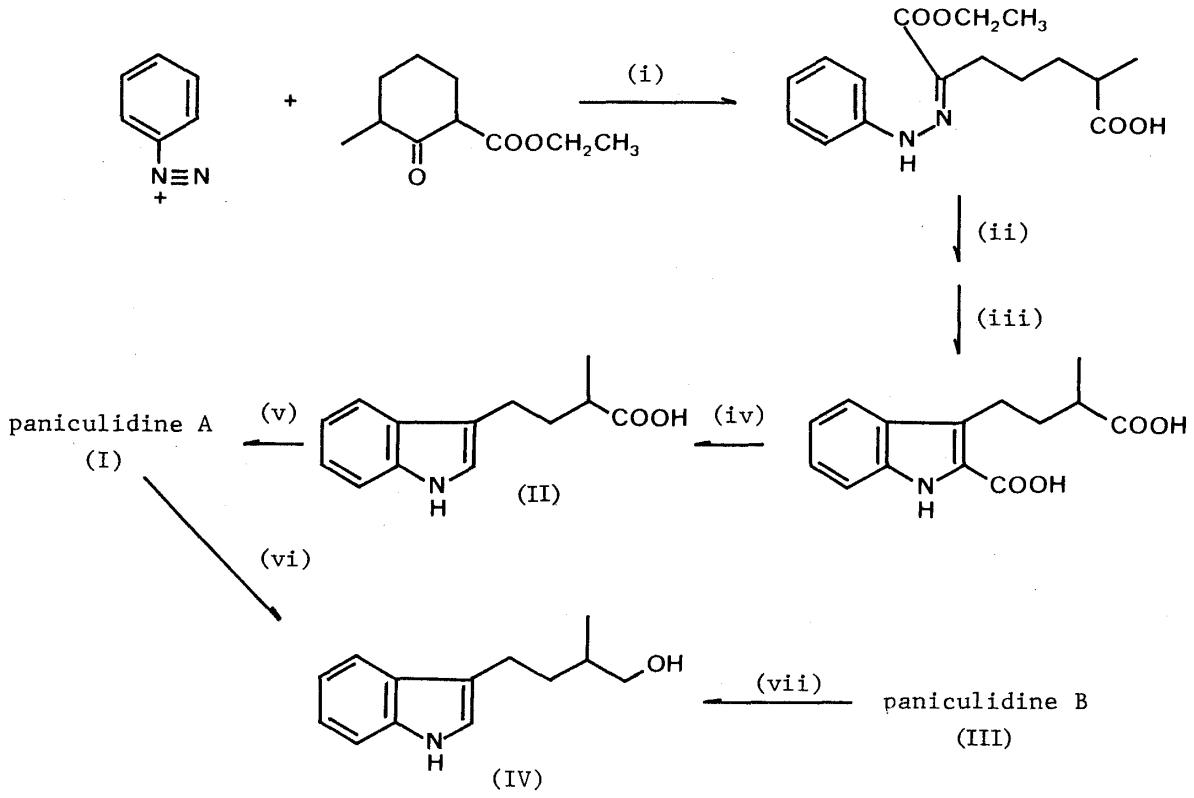


(III) R = OMe paniculidine B

(IV) R = H

as methyl 2-methyl-4-(indol-3-yl)-butyrate by spectral data analysis.[2] It showed a molecular formula $C_{14}H_{17}NO_2$ in high resolution mass spectrum.[3] The UV spectrum was typical of indole [4] and the presence of indole was further confirmed by the IR spectrum, in which the characteristic absorption band of NH group was observed at 3480 cm^{-1}. The IR spectrum also revealed the presence of ester, which was shown to be a carbomethoxy group by the ^{1}H-NMR spectrum.[5] Hydrolysis of paniculidine A with mild alkali yielded a racemic crystalline acid (II).[6] The ^{1}H-NMR spectrum of paniculidine A showed signals assignable to the protons of indole skeleton and signals due to the remaining $C_6H_{11}O_2$ moiety at the 3-position of indole,[5] and the ^{13}C-NMR spectrum and mass spectrum were also consistent with the proposed structure.[7] The elucidated structure was further confirmed by the synthesis of the free carboxylic acid (II) according to the Fischer indole synthesis as shown in Fig. 1.[8] The synthetic product was completely identical to the acid (II) derived from hydrolysis of paniculidine A.

Paniculidine B (III) was also obtained as an optically active oil from more polar fractions of silica gel chromatography.[9] The molecular formula $C_{14}H_{19}NO_2$ was determined by high resolution mass spectrometry.[10] Although the UV spectrum



conditions : (i) KOH, 0°C (ii) conc H_2SO_4, EtOH, 2.5 h reflux
(iii) 5% NaOH, 1 h reflux (iv) 220°C, 15 min
(v) CH_2N_2 (vi) $LiAlH_4$, ether, 0°C (vii) 5% Pd-C/H_2

Fig. 1. The Synthesis of Paniculidine A and Its Chemical Correlation to Paniculidine B

in ethanol showed absorption maxima at 279 nm (log ε 3.69) and 292 nm (log ε 3.71) which resembled those of indole, the IR spectrum showed no band around 3500 cm^{-1} where the NH band of indole is normally observed. The ^{1}H-NMR spectrum in lower field showed the presence of four protons and C-2 proton, whereas no D_2O-exchangeable signal was observed.[11] A sharp singlet (3 protons) observed at δ 3.99 was neither a carbomethoxy nor methoxy group on an aromatic ring since there was no absorption band in the region between 1650 and 1800 cm^{-1} in the IR spectrum. From these data paniculidine B was postulated as a 1-methoxyindole. The results of the approximate first order analysis of the ^{1}H-NMR spectrum depicted the remaining part of the compound (III) as $-CH_2CH_2CH(CH_3)CH_2OH$ that attached at the 3-position of indole.[11] The data of ^{13}C-NMR spectrum and mass spectrum support this structure.[12] The structure of paniculidine B (III) was finally confirmed by its chemical correlation to paniculidine A as shown in Fig. 1. It was also found that both paniculidines A and B had the same absolute stereochemistry at the 2'-position since both 2-methyl-4-(indol-3-yl)-1-butanols (IV) derived from paniculidines A and B showed the same $[\alpha]_D$ value. Four 1-methoxyindoles, all of which are tryptamine derivatives, have been known in nature.[13-16] Although the occurrence of indoles has been observed in numbers of plants belonging to the Rutaceae family, including Murraya species,[17] paniculidine B is the first 1-methoxyindole so far isolated from the rutaceous plants. A characteristic feature of both paniculidines A and B is the presence of isoprenoid units at the 3-position, and such a type of indole has not been reported.

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2) Paniculidine A (I): colorless oil, $[\alpha]_D^{24}$ -31.9°(c = 0.1, $CHCl_3$).

3) Calcd for $C_{14}H_{17}NO_2$: 231.1256. Found : 231.1208.

4) UV λ_{max}^{EtOH} nm (log ε): 277sh (3.75), 283 (3.78), 292 (3.71).

5) ^{1}H-NMR($CDCl_3$, 400 MHz) δ : 1.12(3H, d, J = 7 Hz, 2'-CH_3), 1.72(1H, ddt, J = 7, 14, and 8 Hz, 3'-CH(H)), 2.01(1H, ddt, J = 7, 14, and 8 Hz, 3'-CH(H)), 2.46(1H, ddq, J = 7, 7, and 7 Hz, 2'-CH-), 2.66(2H, t, J = 8 Hz, 4'-CH_2), 3.56(3H, s, $COOCH_3$), 6.80(1H, d, J = 2.5 Hz, 2-H), 7.01(1H, ddd, J = 8, 8, and 1.5 Hz, 5-H or 6-H), 7.07(1H, ddd, J = 8, 8, and 1.5 Hz, 6-H or 5-H), 7.19(1H, dd, J = 8 and 1.5 Hz, 4-H), 7.50(1H, dd, J = 8 and 1.5 Hz, 7-H),

7.95(1H, bs, NH, disappeared on deuteration).
6) The compound (II): mp 99-100°C (recrystallized from aqueous alcohol).
7) ^{13}C-NMR($CDCl_3$, 25 MHz) δ : 17.3(2'-CH_3), 23.0(3'-CH_2), 34.2(4'-CH_2), 39.2(2'-CH), 51.6(CH_3O), 111.1(7-C), 115.5(3-C), 118.7, 119.0, 121.3, 121.8(2-C and other aromatic carbons), 127.3(3a-C), 136.3(1a-C), 177.2(C=O). m/z: 231(M^+, 25%), 144(M^+-87, 15%, loss of $CH_3CHCOOCH_3$), 130(base peak, loss of $CH_2CH(CH_3)COOCH_3$).
8) R. W. Jackson and R. H. Manske, J. Am. Chem. Soc., **52**, 5029 (1930).
9) Paniculidine B (III): colorless oil, $[\alpha]_D^{20}$ +21°(c = 0.025, $CHCl_3$).
10) Calcd for $C_{14}H_{19}NO_2$: 233.1416. Found : 233.1419.
11) ^{1}H-NMR($CDCl_3$, 400 MHz) δ : 0.98(3H, d, J = 7.0 Hz, 2'-CH_3), 1.48(1H, dddd, J = 5.5, 8.0, 10.0, and 13.5 Hz, 3'-C<u>H</u>(H)), 1.69(1H, m, 2'-H), 1.81(1H, dddd, J = 5.5, 6.3, 10.0, and 13.5 Hz, 3'-CH(<u>H</u>)), 2.67(1H, dddd, J = 1.0, 6.3, 10.0, and 15.0 Hz, 4'-C<u>H</u>(H)), 2.78(1H, dddd, J = 1.0, 5.5, 10.0, and 15.0 Hz, 4'-CH(<u>H</u>)), 3.43(1H, dd, J = 6.5 and 11.0 Hz, 1'-C<u>H</u>(H)), 3.50(1H, dd, J = 5.5 and 11.0 Hz, 1'-CH(<u>H</u>)), 3.99(3H, s, OCH_3), 7.02(1H, bd, J = 1.0 Hz, 2-H), 7.08(1H, ddd, J = 8.5, 8.5, and 1.5 Hz, 5-H or 6-H), 7.21(1H, ddd, J = 8.5, 8.5, and 1.5 Hz, 6H or 5-H)), 7.37(1H, ddd, J = 8.5, 1.5, and 0.7 Hz), 7.56(1H, ddd, J = 8.5, 1.5, and 0.7 Hz, 7-H).
12) ^{13}C-NMR($CDCl_3$, 25 MHz) δ : 16.6(2'-CH_3), 29.8(3'-CH_2), 33.4(4'-CH_2), 35.5(2'-CH), 65.3(OCH_3), 68.0(1'-CH_2OH), 108.2(7-C), 112.9(3-C), 119.0, 119.2, 120.3, 123.2(2-C and other aromatic carbons), 123.9(3a-C), 132.7(1a-C). m/z: 233(M^+, 35%), 129(M^+-104, 31%, loss of CH_3 and $CH_2CH(CH_3)CH_2OH$).
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