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NEW CYCLOPEPTIDE ALKALOIDS FROM *MELOCHIA TOMENTOSA**

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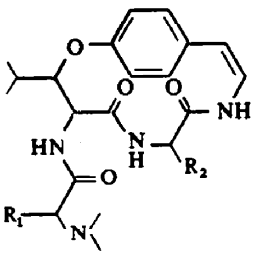
Abstract—Scutianine B and two new cyclopeptide alkaloids, melonovines A and B have been isolated from *Melochia tomentosa*.

INTRODUCTION

In a previous investigation [1] an extract of the roots of *Melochia tomentosa* was found to be tumorigenic; later two compounds were isolated and characterized as a novel quinolinone alkaloid, melochinone [2] and 6-methoxy-7,8-methylenedioxy coumarin [3]. The present publication reports the isolation of 3 cyclopeptide alkaloids from the roots of this plant. One alkaloid was identified as scutianine B; the other two, melonovines A and B are new compounds and their structures have been determined mainly by MS and corroborated by other physical and chemical methods.

RESULTS AND DISCUSSION

Three crystalline alkaloids were separated by column chromatography on silica gel. Scutianine B (**1**) mp 250° (d), M^+ 568 ($C_{34}H_{40}N_4O_4$) was identified by comparison with an authentic sample (MS, TLC, mmp). This alkaloid had been isolated previously from *Scutia buxifolia* (Rhamnaceae) [4] but never from a *Melochia* sp. (Sterculiaceae). Cyclopeptide alkaloids have, however, been previously isolated from other members of the Sterculiaceae viz.



1 scutianine B $R_1 = R_2 = CH_2C_6H_5$
2 melonovine A $R_1 = CH\text{-}(Me)_2$ $R_2 = CH_2CH(Me)_2$
3 melonovine B $R_1 = CH\text{-}(Me)_2$ $R_2 = CH_2C_6H_4OH$

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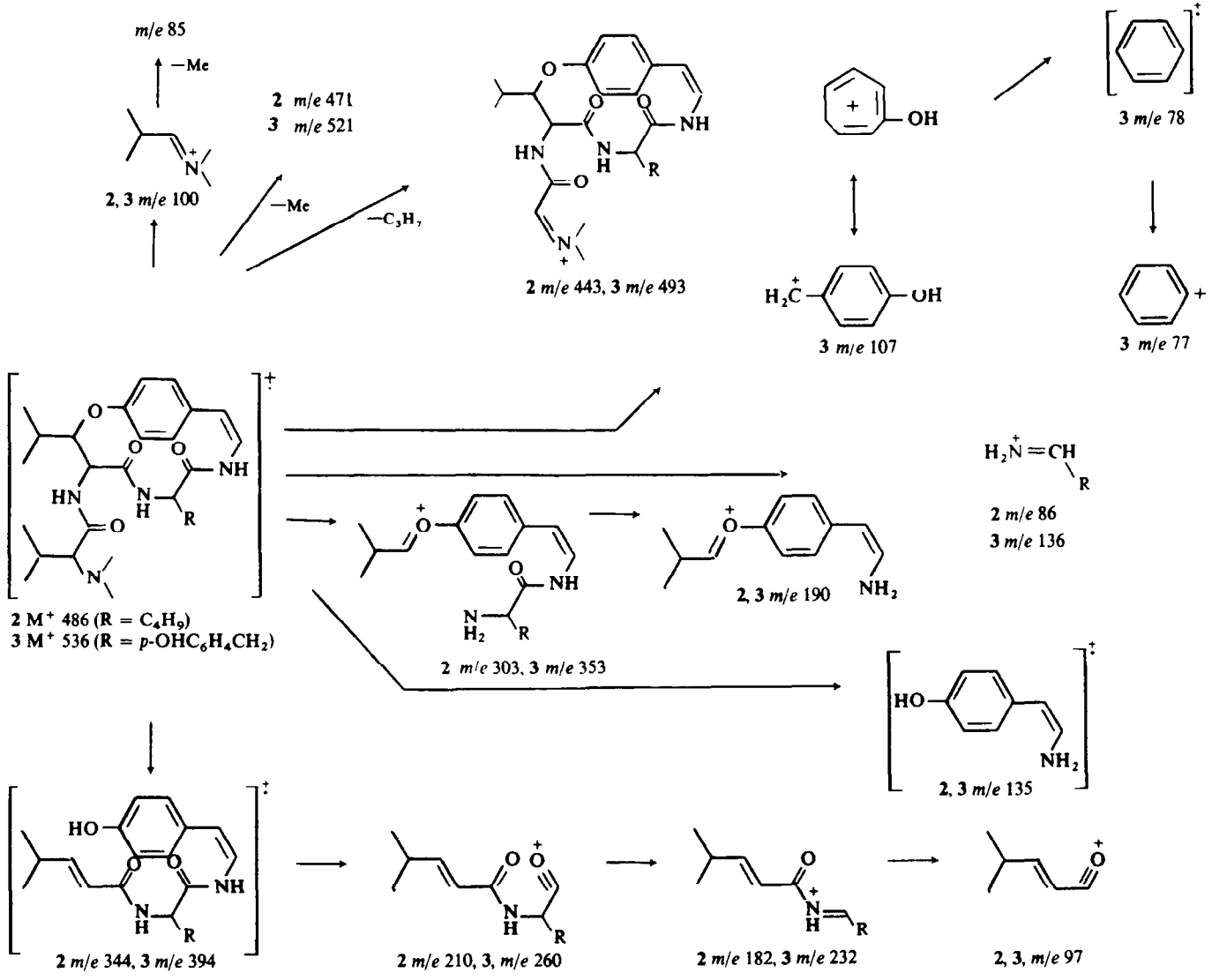
Waltheria americana [5, 6] and *Melochia corchorifolia* [7].

Melonovine A (**2**), mp 295° d, $[\alpha]_D$ − 285° showed an M^+ at *m/e* 486 suggesting a formula of $C_{27}H_{42}N_4O_4$. The IR spectrum exhibited bands corresponding to peptide linkages, phenol ether, *N*-methyl, aromatic and olefinic functions. Acid hydrolysis yielded *N*,*N*-dimethylvaline, leucine and β-hydroxyleucine. The MS fragmentation (Scheme 1) was typical of a frangulanine peptide alkaloid [8] and fitted structure **2** for melonovine A, the base peak at *m/e* 100 reflecting the basic terminal amino acid *N*,*N*-dimethylvaline and the main fragment ions at *m/e* 135, 97 and 86 originating from the hydroxystyrylamino unit, the hydroxyamino acid (hydroxyleucine) and the ring amino acid (leucine) respectively. The PMR spectrum ($CDCl_3$) supported this structure. The *N*,*N*-dimethylamino group appeared as a singlet at δ 2.2, the 4 aromatic protons as a multiplet centered at δ 7.15 and the α-proton of dimethylvaline as a doublet at δ 2.55 (J = 4 Hz). The α and β protons of the hydroxyleucine unit showed up as double doublets at δ 4.51 (J = 8 and 10 Hz) and 4.96 (J = 8, 2 Hz) respectively. After deuterium exchange the amido proton signal collapsed to a doublet (J = 8 Hz) and the two olefinic protons appeared as doublets at δ 6.45 and 6.60 (J = 8 Hz). The signals corresponding to the C—Me groups were situated between δ 0.74–1.32 (18 H) but could not be assigned unambiguously due to overlapping.

Melonovine B (**3**) mp 200–206°, $C_{30}H_{40}N_4O_5$ (MS), gave a positive test with the diazo reagent and exhibited IR bands for NH, phenolic OH, N–Me, CONH, C=C and C—O—C. On acid hydrolysis it gave *N*,*N*-dimethylvaline, β-hydroxyleucine and tyrosine. Examination of the MS (Scheme 1) showed that melonovine B possessed structure **3** and differed from melonovine A only in having tyrosine instead of leucine as the ring amino acid. Its PMR spectrum was consistent with the assigned structure. The dimethylamino group resonated as a sharp singlet at δ 2.18 and the olefinic and aromatic protons showed up in the region δ 6–7.15 (10 H). The C-Me groups of β-hydroxyleucine and dimethylvaline appeared as doublets at δ 1.23, 1.06 and 0.93 (J = 8Hz). The α proton of dimethylvaline occurred as a doublet at δ 2.51 (J = 4Hz) and the α and β methine protons of



Scheme 1. Mass spectral fragmentation of melonovines A and B.

hydroxyleucine were double doublets at δ 4.47 (J = 8 and 10Hz) and δ 4.94 (J = 8 and 2Hz) respectively. The double doublets at δ 2.6 (J = 14 and 6Hz) and δ 3.1 (J = 14 and 5Hz) and the multiplet at δ 4.3 corresponded to the two β protons and the α methine proton of the tyrosine unit respectively.

EXPERIMENTAL

Capillary mps are uncorr., $[\alpha]_D$ were determined in $CHCl_3$, IR in Nujol and 100 MHz NMR spectra in $CDCl_3$ with TMS as internal standard. TLC was done on Si gel.

Extraction and isolation. Air dried roots of *M. tomentosa* (collected at Curacao by Mr. W. P. Maal) (1.6 kg) were extracted continuously in turn with boiling petrol, C_6H_6 and CH_2Cl_2 (2 days, 5 l. each solvent). These extracts were set aside for later investigation. The residual material was combined with $Ba(OH)_2$ (50 g) and 50% aq. EtOH (1.2 l.), air dried and then continuously extracted with CH_2Cl_2 (2 days, 5 l.). Removal of solvent furnished a yellow powder (4.5 g) which was chromatographed on a Si gel column (300 g, >230 mesh). The column was eluted with mixtures of petrol, C_6H_6, $CHCl_3$, EtOAc and EtOH.

Scutianine B (4 mg) eluted with $CHCl_3$–EtOAc (3:1), crystallized from Me_2CO, mp 250° (d), MS: *m/e* 568 (M^+) 553, 477, 421, 378, 337, 308, 244, 216, 195, 190, 167, 148 (base peak) 135, 120, 97 and 91; identical with authentic sample (mp, mmp and TLC).

Melonovine A. Obtained from the $CHCl_3$–EtOAc (1:1) eluate (15 mg), crystallized from Me_2CO, mp 295° (d), $[\alpha]_D$ – 285°, IR: ν_{max} 3380 (NH), 2780 (N–Me), 1680 (CONH), 1605 (C=C) and 1240 cm^{-1} (COC), $C_{27}H_{42}N_4O_4$, MS: *m/e* 486 (M^+, 1), 471 (1.5), 443 (4.5), 344 (2), 303 (1.8), 210 (1.8), 190 (5), 182 (4.5), 135 (23), 100 (100), 97 (27), 86 (15) and 85 (39).

Amino acid analysis of melonovine A. The alkaloid (4 mg) was hydrolysed with 6 N HCl (2 ml, 100°, 15 hr) in a sealed tube. The hydrolysate was evapd to dryness and examined by GLC and PC (*n*-BuOH–HOAc–H_2O, 4:1:5). β-Hydroxyleucine, leucine and *N,N*-dimethylvaline were detected. For comparison authentic sample of *N,N*-dimethylvaline was prepared according to the method of ref. [9].

Melonovine B (10 mg) obtained from the EtOAc eluate was crystallized from Me_2CO–C_6H_6, mp 200–206°, IR: ν_{max} 3400 (NH), 3280 (phenolic OH), 2780 (N–Me), 1680 (CONH), 1610 (C=C) and 1250 cm^{-1} (C—O—C), $C_{30}H_{40}N_4O_5$, MS: *m/e* 536 (M^+, 1.7) 521 (1.3), 493 (6), 394 (2.1), 353 (0.9), 260 (0.9), 232 (2.1), 190 (6), 136 (20), 135 (30.4), 107 (27.8), 100 (100), 97 (26.9), 85 (45.2), 78 (4.3) and 77 (8.1). After acid hydrolysis, tyrosine, β-hydroxyleucine and *N,N*-dimethylvaline were detected.

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