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CYCLOPEPTIDE ALKALOIDS FROM *MELOCHIA CORCHORIFOLIA**

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Key Word Index—*Melochia corchorifolia*; Sterculiaceae; aerial parts; cyclopeptide alkaloids; adouetine-y'; melofoline.

Abstract Adouetine-y' and a new cyclopeptide alkaloid, melofoline, have been isolated from *Melochia corchorifolia*. The latter was characterized mainly from its mass spectrum and hydrolysis products. Melofoline has *N,N*-dimethyl-β-hydroxyleucine as the terminal amino acid and 2-aminobutyric acid as the ring amino acid, neither of which has been found in these positions before.

INTRODUCTION

Melochia corchorifolia is one of the two species of the genus *Melochia* occurring throughout the hotter parts of India. A decoction of the plant has been reported in folk medicines as a cure for abdominal swelling, dysentery [1] and water snake bites [2]. Three flavonoids [3] and the cyclopeptide alkaloids, franganine (**1**), frangufoline (**2**) and adouetine-y' (**3**) [4] have been reported earlier from this plant. Since its aerial parts showed the presence of several compounds including alkaloids, a detailed investigation has now been undertaken.

RESULTS AND DISCUSSION

Two crystalline alkaloids were separated by CC on silica gel. Adouetine-y' (**3**) mp 290–292°, $[\alpha]_D$ −305° ($CHCl_3$), $[M]^+$ *m/z* 534 ($C_{31}H_{42}N_4O_4$) was identified by comparison with lit. data (IR, mass spectrum, NMR) [4, 5].

Melofoline (**4**) mp 305–307°, $[\alpha]_D$ −252° ($CHCl_3$) showed an $[M]^+$ at *m/z* 488 which together with elemental analysis suggested a formula of $C_{26}H_{40}N_4O_5$. The IR spectrum exhibited bands corresponding to peptide linkages, phenol ether, hydroxyl, *N*-methyl, aromatic and olefinic functions. Acid hydrolysis yielded 2-aminobutyric acid, β-hydroxyleucine and *N,N*-dimethyl-β-hydroxyleucine. The mass spectral fragmentation (Scheme 1) was typical of a frangulanine type 14-membered peptide alkaloid [6] suggesting structure **4** for melofoline, the base peak at *m/z* 130 reflecting the basic terminal amino acid, *N,N*-dimethyl-β-hydroxyleucine and the main fragment ions at *m/z* 135, 97 and 58 originating from the hydroxystyrylamino unit, the hydroxyamino acid (hydroxyleucine) and the ring amino acid (2-aminobutyric acid), respectively. The ions generated at *m/z* 246, 190 and 154 indicated the linkage of these units.

The ^{1}H NMR spectrum supported the structure assigned to **4**. *N,N*-dimethylamino group appeared as a singlet at δ2.17 and the four aromatic protons as a multiplet at δ7.10. Three NH protons resonated as broad singlets at δ8.25, 8.50 and 8.60 while the two olefinic protons appeared as doublets at δ6.62 and 6.45 (J = 8 Hz). The α and β protons of the hydroxyleucine unit appeared as double doublets at δ4.60 (J = 8 and 10 Hz) and 4.90 (J = 8 and 2 Hz), respectively [7]. The –CHOH proton of the terminal amino acid was seen as a multiplet at δ3.42 (shifted to δ4.24, *m*, in **5**) and the C-Me groups of β-hydroxyleucine and 2-aminobutyric acid appeared as doublets at δ1.04 and 0.84 (J = 7 Hz), and a triplet at δ0.75 (J = 6 Hz), respectively. In conformity with the presence of a free hydroxyl group, **4** formed a monoacetate **5**, mp 259–261°, ν_{max} 1725, δ2.05 (3H, *s*). It appears that **4** is the first cyclopeptide alkaloid carrying *N,N*-dimethyl-β-hydroxyleucine as the terminal amino acid and 2-aminobutyric acid as the ring amino acid.

EXPERIMENTAL

Capillary mps are uncorr. IR were determined in KBr and 80 MHz ^{1}H NMR spectra in $CDCl_3$ with TMS as int. standard. TLC was carried out on silica gel G. Plant material was collected from Pantnagar, Nainital and identified in our Botany Department where a voucher specimen has been deposited.

Extraction and isolation of alkaloids. Air dried aerial parts of *M. corchorifolia* L. (1 kg) were extracted with MeOH (5 × 2.5 l.) and the extracts concd to dryness *in vacuo*. The MeOH extract was treated with 2% HCl (3 × 50 ml), filtered and the filtrate extracted with *n*-hexane (2 × 150 ml). The acidic layer was then basified with NH_4OH (pH 9), extracted with $CHCl_3$ (5 × 150 ml) and dried (Na_2SO_4). Removal of solvent furnished a viscous residue (540 mg). Part of this residue (400 mg) was chromatographed over silica gel (25 g), eluting with increasing proportions of C_6H_6, $CHCl_3$ and MeOH. Fractions (15 ml) were monitored by TLC. A mixture of two alkaloids was obtained in early fractions of $CHCl_3$ which could not be separated. Latter fractions of $CHCl_3$ yielded adouetine-y' while melofoline was eluted in $CHCl_3$–MeOH (99:1).

Adouetine-y' (**3**). Yield 25 mg, mp 290–292° (MeOH), $[\alpha]_D$ −305° ($CHCl_3$) was identified by comparison of its IR, MS and NMR spectral data with those in lit.

Melofoline (**4**). Yield 17 mg, mp 305–307° (MeOH), $[\alpha]_D$ −252° ($CHCl_3$). IR ν_{max} cm^{-1}: 3400 (OH), 3260 (NH), 2790 (NMe), 1680 (CONH), 1618 (C=C), 1540, 1525, 1505, 1462 (aromatic), 1385 (C-Me), 1235 (C–O–C). MS *m/z* (rel. int.): 488 $[M]^+$ ($C_{26}H_{40}N_4O_5$) (17.6), 275 (1.5), 246 (1), 190 (82), 182 (2), 154 (1.5), 135 (45), 130

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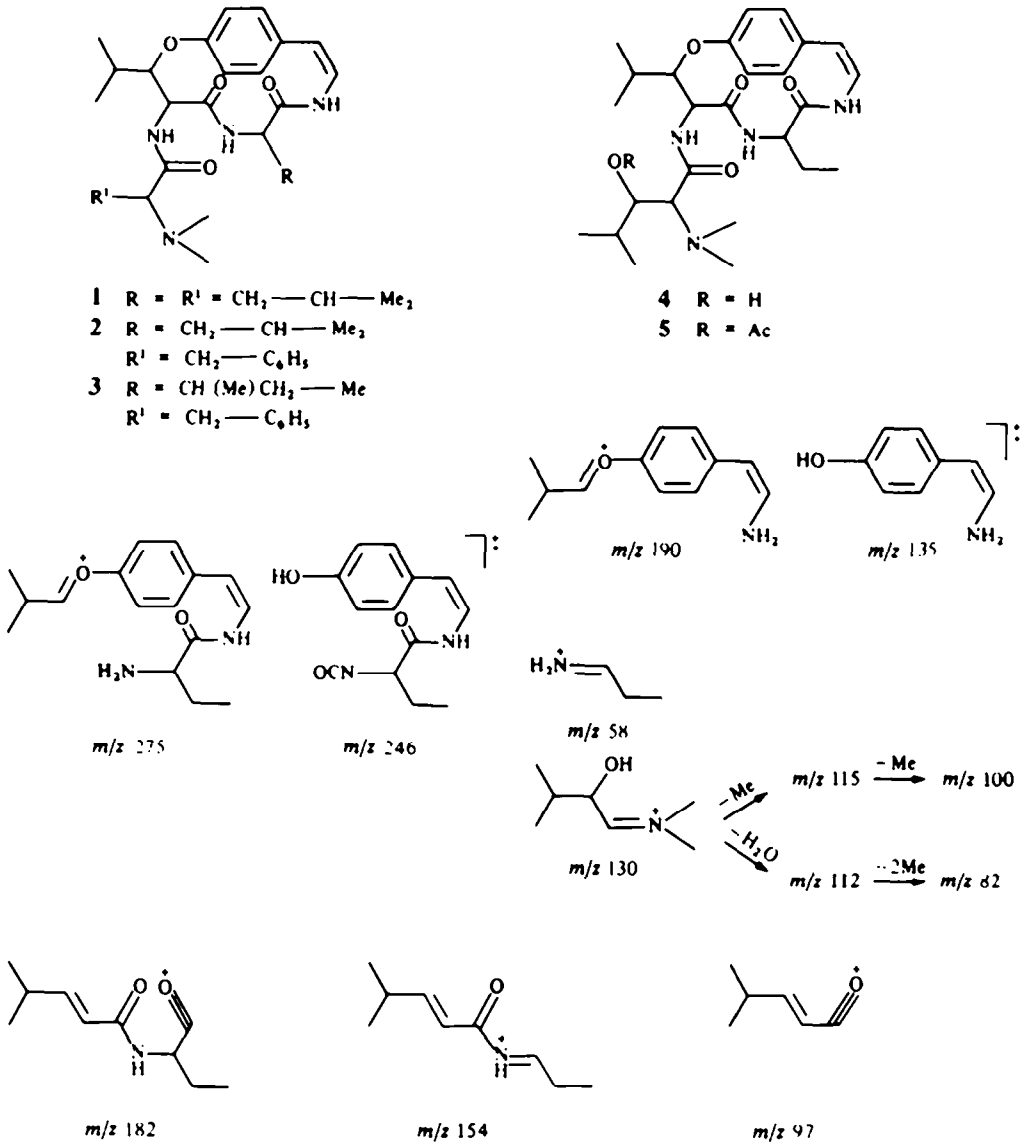

Scheme 1. Some important mass spectral fragment ions of melofoline (4).

(100), 115 (3), 112 (2), 100 (34), 97 (1.5), 82 (6), 58 (2.5). (Found: C, 64.14; H, 8.38; N, 11.40%. $C_{26}H_{40}N_4O_5$ requires: C, 63.93; H, 8.19; N, 11.47%.)

O-Acetylmelofoline (5). Compound 4 (5 mg) was treated with pyridine–Ac_2O (0.5 ml each) and left overnight at room temp. Usual work-up afforded a residue, mp 259–261° (MeOH). IR ν_{max}^{KBr} cm^{-1}: 3260 (NH), 2790 (NMe), 1725 (OAc), 1665 (CONH), 1610 (conjugated C=C), 1230 (aryl ether).

Hydrolysis. Compound 4 (5 mg) was hydrolysed with 6 N HCl (2 ml, 100°, 18 hr) in a sealed tube. The hydrolysate was evapd to dryness *in vacuo* and examined by PC (*n*-BuOH–HOAc H_2O, 4:1:5) [8]. 2-Aminobutyric acid, β-hydroxyleucine and *N,N*-dimethyl-β-hydroxyleucine were detected when sprayed with ninhydrin (co-PC with authentic samples).

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