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SCUTIANINE-J, A CYCLOPEPTIDIC ALKALOID ISOLATED FROM *SCUTIA BUXIFOLIA*

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Key Word Index—*Scutia buxifolia*; Rhamnaceae; peptide alkaloid; scutianine-J; FAB-MS.

Abstract—From the methanol extract of the bark of *S. buxifolia* Reiss (Rhamnaceae), a new cyclopeptidic alkaloid, together with the already known alkaloids scutianines-B–E, were isolated. On the basis of elemental analysis, mass spectroscopy (EI and FAB) and ^{1}H NMR spectroscopy, the molecular structure of scutianine-J has been elucidated.

INTRODUCTION

Cyclopeptidic alkaloids are poliamidic bases found in many families of plants, mainly in species that belong to the Rhamnaceae [1, 2]. These molecules are composed of 13-, 14-, or 15-membered macrocycles which as general structural elements bear two amino acids and a styrylamine unit. This class of compounds calls for special attention due to the different biological activities exhibited by many of them, e.g. hypotensive [3], anti-diarrhoeal and anti-dysenteric [4], anti-fungal and antibiotic [1, 2]. As a result of these interesting biological activities, the number of investigations concerning the isolation, structure determination and synthesis of these compounds is increasing [1, 2, 5, 6].

Plants from which these alkaloids were isolated have been applied as popular medicine in many parts of the world for centuries [7–10].

RESULTS AND DISCUSSION

The isolation and characterization of several cyclopeptidic alkaloids of 14-membered rings, from the methanolic extract of the bark of *Scutia buxifolia* and *Discaria febrifuga*, were described in former publications [1–6]. In continuation of this work, an exhaustive chromatographic analysis was done on a new extract of *Scutia buxifolia*, which furnished nine fractions of different R_fs, all of them giving a positive reaction with Dragendorff's reagent. In five of these fractions we found the formerly isolated alkaloids, scutianine-B(**1**), -C(**2**), -D(**3**), -E(**4**) and -H(**5**). The remaining fractions contained basic compounds of lower R_f. From these more polar fractions, one pure alkaloid could be isolated by TLC applying various solvent systems. The structure of the new alkaloid called scutianine-J, which is shown in structure **6**, was elucidated by fragmentation analysis (EI, low resolution) and FAB (Fast Atom Bombardment) mass spectra, elemental analysis and ^{1}H NMR spectra of **6**.

The molecular formula of scutianine-J was derived from mass spectroscopy and elemental analysis as $C_{34}H_{40}N_4O_6$. The FAB(+) spectrum of this alkaloid shows a [M + H] ion with *m/z* of 601 [14 amu more than (**3**) and (**4**)]. The EI mass spectrum (see Scheme) exhibits peaks that allow important conclusions for the elucidation of structure **6**. The base peak b at *m/z* 493, derived from initial cleavage, indicates the residues that form the macrocyclic system. Further decomposition of this fragment gives peak c at *m/z* 195, proving the presence of β-hydroxyleucine as the amino acid residue that forms the phenol–ether bond in the macrocyclic system. The peak d at *m/z* 387 appears due to the loss of C_7H_7O from b. This suggests β-phenylserine as α-amino acid in the peptide alkaloid. The ion i at *m/z* 135 $[C_8H_9NO]^+$ reveals the presence of a styrylamine unit characterizing the 14-membered ring. The fragment at *m/z* 106 $[C_6H_5C{=}O]^+$ and the ions at *m/z* 105 $[C_6H_5C{=}O]^{\ddagger}$ and *m/z* 107 $[C_6H_5CH{=}OH]^{\ddagger}$ can easily be assigned to β-phenylserine as the α-amino acid unit of the ring.

The ^{1}H NMR spectrum ($CDCl_3$, 250 MHz) of **6** shows, in addition to a resonance at δ2.20 ppm (*s*, -N[Me]), significant resonances at δ0.95 (3H, *d*, 19-Me) and 1.20 (3H, *d*, 18-Me). In the two dimensional COSY (^{1}H–^{1}H) spectrum, these two doublets have a cross-peak with the signal at 2.10 ppm (1H, *m*), which corresponds to H-17. In its turn, H-17 shows a cross-peak with H-3 at 4.80 ppm and this with H-4 at 4.35 ppm. H-4 exhibits another cross-peak with H-20 (NH-) which resonated at δ7.60. This spin system confirms the hydroxyleucine as the hydroxylated amino acid of the macrocycle ring. β-phenylserine, which is the α-amino acid of the macrocycle,

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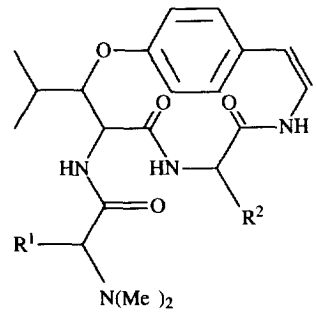

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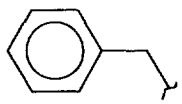
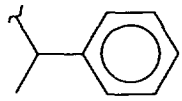
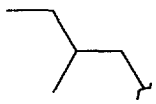
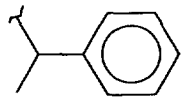
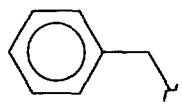
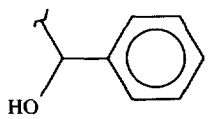
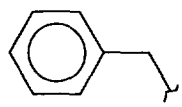
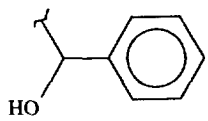
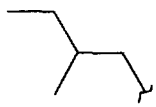
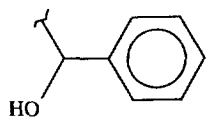
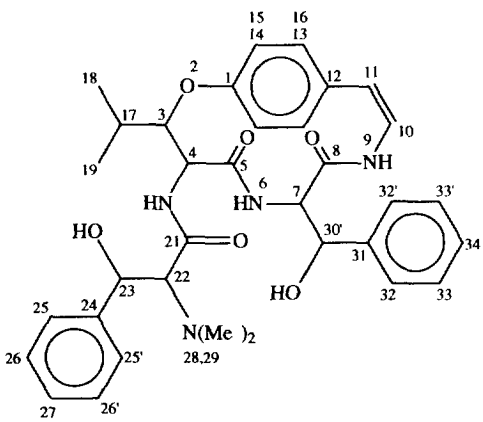
1			
2			
3			L-Erythro-β-hydroxyleucine L-Threo-β-phenylserine
4			D-Erythro-β-hydroxyleucine D-Threo-β-phenylserine
5			

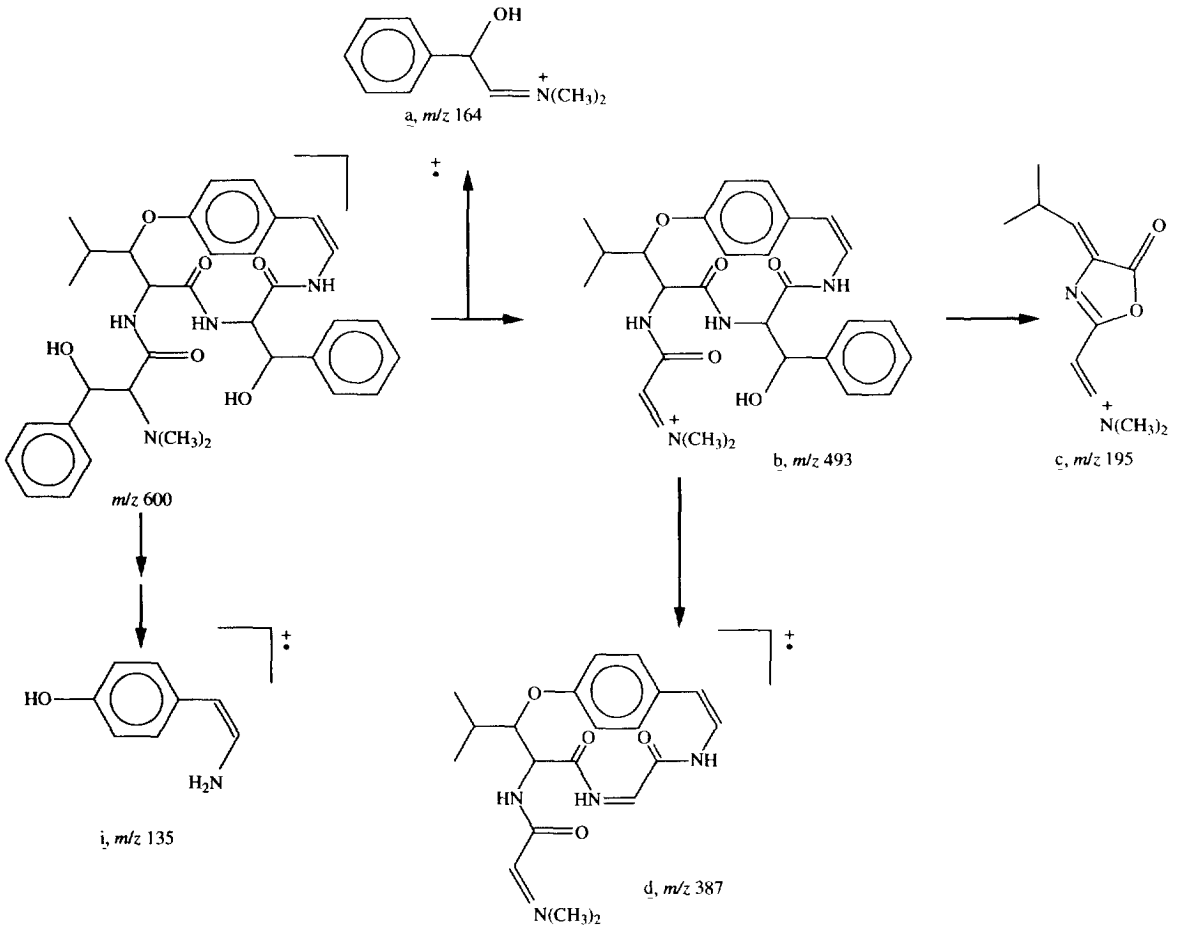


Scutianine-J (**6**)

was identified by cross-peaks between H-6 (NH-), H-7 and H-24. H-7 resonates at 4.35 ppm (superimposed by H-4) and shows cross-peaks with H-6 (NH) which absorb at 6.20 ppm and with H-23 resonating at 4.80 ppm (superimposed with H-3 and the OH-23). The two olefinic protons H-10 at 6.28 ppm and H-11 at 7.75 ppm show the expected coupling between themselves, H-10 having a second cross-peak with NH-9 at 6.55 ppm. This spin system indicates the presence of the styrylamine moiety. The 14 aromatic protons of **6** resonate in the range of 6.75–6.90 ppm and are difficult to assign due to heavy superimposition of the resonance lines. The foregoing evidence is in good agreement with structure **6** for scutianine-J.

EXPERIMENTAL

Extraction of Scutia buxifolia. The plant material was collected at Livramento (Rio Grande do Sul, Brazil) in



Scheme 1. Mass fragmentation of scutianine-J.

March 1993. The powdered bark (10 kg) was extracted exhaustively with MeOH, yielding a mixt. of alkaloids as a residue (9.6 g).

Isolation of the alkaloids. The alkaloid mixt. was fractionated on a SiO_2 chromatographic column using mixts of $CHCl_3$–MeOH as solvent and on TLC, as further purification was required.

Scutianine-J (**6**). Crystallization of the resultant solid (50 mg) from $CHCl_3$–Et_2O gave **6**, mp: amorphous. No UV absorption. IR ν cm^{-1}: 3600, 3280, 1650, 1625, 1250. MS *m/z* (rel. int.) 493 (1.5), 387 (3.6), 385 (4.7), 331 (3.1), 195 (2.1), 164 (100), 135 (30.0), 107 (26), 106 (60.0), 105 (61.0), 77 (73.6). ^{1}H NMR ($CDCl_3$): δ0.95 (3H, *d*, J = 6.4 Hz), 1.20 (3H, *d*, J = 6.4 Hz), 2.0 (1H, *m*), 2.20 (6H, *s*), 4.35 (2H, *m*), 4.80 (2H, *m*), 6.20 (1H, *d*, J = 9.5 Hz), 6.28 (1H, *m*), 6.55 (1H, *d*, J = 9.5 Hz), 7.60 (1H, *d*, J = 7.60 Hz), 6.75–6.90 (14H, Ar.).

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