Macrocyclic Budmunchiamine Alkaloids from *Albizia lebbek*†

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Received January 23, 1996⊗

A MeOH extract of the seeds of *Albizia lebbek* gave three new macrocyclic alkaloids, named as budmunchiamines L4, L5, and L6 (**1**−**3**). The known budmunchiamines A, B, C, and F have also been found. The structures of **1**−**3** have been determined, by the use of spectroscopic methods and by comparison with budmunchiamines L1−L3, reported earlier from this plant.

In continuation of our studies on the chemistry of Indian medicinal and aromatic plants,[1−4] we have recently reported the presence of macrocyclic alkaloids (budmunchiamines L1−L3) in the seeds of *Albizia lebbek* (L.) Benth. (Leguminosae).[5] Further separation of the complex mixtures of alkaloids present in the remaining fractions has yielded three new budmunchiamine derivatives (**1**−**3**) whose isolation and structural characterization are the subject of this paper.

Structurally unique budmunchiamines have been reported earlier from *Albizia amara* by Pezzuto *et al.*[6−9] and recently from *Albizia gummifera* by Rukunga and Waterman.[10] Earlier we reported the *N*-demethylbudmunchiamine derivatives L1−L3 from a MeOH-soluble extract of *A. lebbek* seeds.[5] Further work has indicated the presence of a complex mixture of amines possessing *N*-methyl groups as reported from *A. amara*.[6] These amine-containing fractions upon chromatographic separation have yielded the known budmunchiamines A, B, C, F, and G, whose spectral data were comparable to those reported in the literature.[6] Fraction 11, after rigorous purification, gave subfractions III and IV, which showed a positive test with Dragendorff's reagent.

Subfraction III, after further purification, afforded budmunchiamine L4 (**1**), which showed bands in the IR spectrum at 3550−3150 and 1651 cm^{-1} for OH and amide groups, respectively. As in the case of budmunchiamines L1−L3, the mass spectrum of **1** also showed an ion at *m*/*z* 255 and the absence of *N*-methyl signals at δ 2.30−2.10 in its ^{1}H-NMR spectrum, which clearly indicated that it was also devoid of any *N*-methyl group. The ^{1}H-NMR spectrum of **1** showed a large, broad singlet at δ 1.22 and a triplet at δ 0.88, indicating the presence of a straight-chain alkane substituent. Overlapping multiplets at δ 3.40−3.00 and a broad singlet at δ 8.20 suggested the presence of a $-CONHCH_2-$ system in **1**. The overlapping multiplets at δ 2.80−2.60 and 2.45−1.85 for $-CH_2NHCH_2-$ and H-3 and H-4, together with another set of multiplets at δ 1.64−1.50 for CH_2 at H-7, H-11, H-12, and H-16, clearly supported the presence of a macrocyclic compound, analogous to budmunchiamines L1−L3.[5]

The high-resolution mass spectrum of **1** showed a $[M - H_2O]^+$ fragmentation at *m*/*z* 478.4622 for $C_{29}H_{58}ON_4$. The presence of a fragment at *m*/*z* 255 in the mass spectrum for the $C_{13}H_{27}ON_4$ macrocycle indicated the attachment of a side-chain represented by $C_{16}H_{33}O$. In the ^{13}C-NMR spectrum of **1**, the signal for −CONH− appeared at δ 172.8, along with the usual signals as given in Table 1, which were largely comparable with the ^{13}C-NMR spectra of the known budmunchiamines L1−L3. The additional signals at δ 64.5 and 65.0, along with the stronger multiplet at δ 3.60 in its ^{1}H-NMR spectrum, suggested that **1** possessed a hydroxyl group in the molecule. On acetylation, **1** gave compounds having signals at δ 4.50 and 2.11 supporting the above observation. The presence of typical signals of a terminal alkane for C-1 to C-3 at δ 14.0, 22.5, and 39.0 indicated the possibility of OH being present at the carbon next to C-3 from the terminal methyl of the alkane chain. This was further supported by the ions formed due to the α-fission of −CHOH at *m*/*z* 365 and 393 along with the appearance of a $[M - H_2O]^+$ ion at *m*/*z* 478. These data, when compared with budmunchiamines L1−L3, supported the structure of budmunchiamine L4 as **1**.

Table 1. ^{13}C-NMR Spectral Data of Budmunchiamines L4−L6 (**1**−**3**) (20 MHz, $CDCl_3$)

carbon	**1**	**2**	**3**
2	172.8	172.0	172.0
3	40.9	39.3	39.3
4	55.5	55.5	55.5
6	46.0	46.0	46.0
7	29.0[a]	28.8[a]	28.8[a]
8	52.0[b]	51.3[b]	51.3[b]
10	51.3[b]	51.0[b]	51.0[b]
11	26.0[c]	26.8[c]	26.8[c]
12	24.5[c]	25.0[c]	25.0[c]
13	52.5[b]	51.3[b]	51.3[b]
15	52.0[b]	51.3[b]	51.3[b]
16	28.8[a]	28.8[a]	28.8[a]
17	37.6	37.6	37.6
1′	33.5	33.5	33.5
2′	25.9	25.0	25.0
3′	29.6	29.6	29.6
4′	29.6	29.6	29.6
5′	29.6	29.6	29.6
6′	29.6	29.6	29.0
7′	29.6	29.6	29.0
8′	29.6	29.0	29.0
9′	29.6	29.0	31.2
10′	29.6	29.0	57.2
11′	31.9	31.2	132.0
12′	38.5	35.7	129.8
13′	64.5	132.0	36.2
14′	39.0	129.8	22.1
15′	22.5	36.2	13.2
16′	14.0	22.1	
17′		13.6	

[a−c] Assignments within the same column may be reversed.

Subfraction IV on further separation gave budmunchiamines L5 (**2**) and L6 (**3**), which, in their IR spectrum, showed bands at 3400−3100 and 1648 cm^{-1} for

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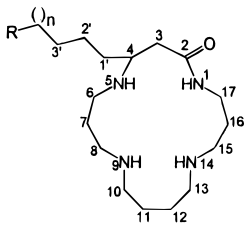
† CIMAP publication no. 95-59J.

⊗ Abstract published in *Advance ACS Abstracts,* September 1, 1997.

amide groups. Their high-resolution mass spectra gave molecular ions at *m*/*z* 492.4765 and 464.4464, respectively, consistent with the molecular formulas $C_{30}H_{60}ON_4$ and $C_{28}H_{56}ON_4$. The presence of ions at *m*/*z* 255 in the EIMS of **2** and **3** again indicated that the macrocyclic rings were devoid of any *N*-methyl groups, as in case of **1**. These observations were further supported by the absence of *N*-methyl signals in the region δ 2.30−2.10 in the ^{1}H-NMR spectra of **2** and **3**. The remaining ^{1}H-NMR signals of **2** and **3** were comparable to those of **1**, except that multiplets occurred at δ 5.30 for vinylic protons. The presence of a double bond in both **2** and **3** was further indicated by the appearance of signals at δ 129.8 and 132.0 in their ^{13}C-NMR spectra (Table 1) and was also supported by the molecular ion peaks in their mass spectra at *m*/*z* 492 and 464, respectively. The position of the double bond was ascertained in the side-chain between carbons 4 and 5 (numbered from the terminal methyl) from their mass spectra, because clear fragments formed by α- and β-fission were evident at *m*/*z* 449, 423, 421, and 395. These data were clearly in support of budmunchiamines L5 and L6 possessing structures **2** and **3**, respectively.



1 R = $CH_2CH(OH)CH_2CH_2CH_3$ n = 5
2 R = $CH{=}CHCH_2CH_2CH_3$ n = 9
3 R = $CH{=}CHCH_2CH_2CH_3$ n = 7

Experimental Section

General Experimental Procedures. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian FT 80A spectrometer at 80 and 20 MHz, respectively. HRMS were recorded on a Kratos MS 80 RFA instrument; and FT-IR spectrum, on a Perkin-Elmer 1710B instrument. UV were recorded on a Pye Unicam SPS-100 instrument; and optical rotations, on a JASCO DIP-181 digital polarimeter.

Plant Material. The collection of the plant material and the extraction procedure have already been described.[5]

Extraction and Isolation. Fractions 5−9, obtained after column chromatography of the MeOH extract,[5] gave a complex mixture of alkaloids that, after further separation, yielded a mixture dominated by budmunchiamines A, B, C, and F, reported earlier from *A. amara*.[6] Fraction 11 on further column chromatography afforded **1** (50 mg) ($CHCl_3$−MeOH−Et_2NH, 8:1:1; R_f 0.45), and isolate IV after further column chromatography over $AgNO_3$-impregnated Si gel with hexane−EtOAc−MeOH as mobile phase, yielded **2** (40 mg) ($CHCl_3$−MeOH−Et_2NH, 8:1:1; R_f 0.60) and **3** (20 mg) ($CHCl_3$−MeOH−Et_2NH, 8:1:1; *Rf* 0.58).

Budmunchiamine L4 (1): obtained as a viscous liquid; $[\alpha]^{27}_D$ +13.5° (*c* 0.02, MeOH); UV (MeOH)λ_{max} (log ϵ) 208 (4.01) nm; IR ($CHCl_3$) ν_{max} 3550−3150 (OH and NH), 2927, 1651 (CONH), 1457, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.88 (3H, t, J = 6.5 Hz, Me), 1.22 [16H, br s, $(CH_2)_8$], 1.70−1.45 (4H, m, H-7, H-11, H-12, H-16), 3.40−3.00 (4H, overlapping m, $CONHCH_2$ and H-3, H-4), 3.60 (1H, m, CHOH), 8.20 (1H, br s, CONH); ^{13}C-NMR data, see Table 1; HRMS (70 eV) *m*/*z* [M − H_2O]$^+$ 478.4622 ($C_{29}H_{58}ON_4$) (2), [*m*/*z* 478 − 43]$^+$ 435 (2) [*m*/*z* 478 − 71]$^+$ 407 (2), 255 (2), 148 (100), 84 (25), 58 (45).

Budmunchiamine L5 (2): obtained as viscous liquid; $[\alpha]^{27}_D$ +13.2° (*c* 0.01, MeOH); UV (MeOH)λ_{max} (log ϵ) 209 (4.00) nm; IR ($CHCl_3$) ν_{max} 3400−3100 (NH), 2925, 1648 (CONH), 1640 (C=C), 1542, 1458, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.95 (3H, t, J = 6.5 Hz, Me), 1.22 [22H, br s, $(CH_2)_{11}$], 1.85−1.45 (4H, m, H-7, H-11, H-12, H-16), 3.50−3.00 (4H, overlapping m, $CONHCH_2$ and H-3, H-4), 5.30 (2H, m, both vinylic H), 8.51 (1H, br s, CONH); ^{13}C-NMR data, see Table 1; HRMS (70 eV) *m*/*z* [M]$^+$ 492.4765, ($C_{30}H_{60}ON_4$) (2), [*m*/*z* 492 − 43]$^+$ 449 (2), [*m*/*z* 492 − 69]$^+$ 423 (2), 255 (2), 148 (35), 85 (85), 83 (100), 47 (25).

Budmunchiamine L6 (3): obtained as viscous liquid; $[\alpha]^{27}_D$ +11.2° (*c* 0.01, MeOH); UV (MeOH)λ_{max} (log ϵ) 209 (3.98) nm; IR ($CHCl_3$) ν_{max} 3400−3100 (NH), 2925, 1648 (CONH), 1640 (C=C), 1542, 1458, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.95 (3H, t, J = 6.5 Hz, Me) 1.22 [18H, br s, $(CH_2)_9$], 1.85−1.45 (4H, m, H-7, H-11, H-12, H-16), 3.50−3.00 (4H, overlapping m, $CONHCH_2$ and H-3, H-4), 5.30 (2H, m, both vinylic H), 8.51 (1H, br s, CONH); ^{13}C-NMR data, see Table 1; HRMS (70 eV) *m*/*z* [M]$^+$ 464.4464 ($C_{28}H_{56}ON_4$) (2) [*m*/*z* 464 − 43]$^+$, 421 (2), [*m*/*z* 464 − 69]$^+$ 395 (2), 255 (2), 148 (35), 85 (85), 83 (100), 47 (25).

Acknowledgment. The authors thank Dr. Sushil Kumar, Director, CIMAP, Lucknow, for his keen interest and encouragement in the work and Dr. R. P. Sharma, Head, Phytochemical Technology Division, for valuable discussions. Prof. H. Wagner, Institute for Pharmaceutical Biology, Munich, is thanked for kindly arranging for samples of budmunchiamines from Prof. J. M. Pezzuto, University of Illinois at Chicago.

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NP9602067