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N-DEMETHYL BUDMUNCHIAMINES FROM *ALBIZZIA LEBBEK* SEEDS

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Key Word Index—*Albizzia lebbek*; Leguminoseae; seeds; macrocyclic spermine alkaloids; budmunchiamines L1–L3.

Abstract—A methanol extract of the seeds of *Albizzia lebbek* has yielded three new macrocyclic spermine alkaloids, budmunchiamines L1–L3. The structures have been determined by spectral analysis, chemical transformations and comparison with budmunchiamines A–I.

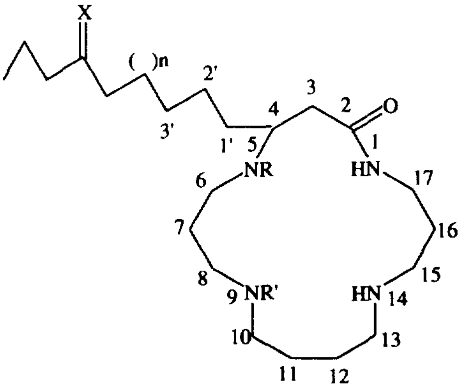
INTRODUCTION

Albizzia lebbek is a common tree occurring widely in the forests and roadsides of the plains of India. Its seeds, pods and leaves have been a subject of detailed chemical investigation and a variety of compounds, such as flavonoids, triterpenoids, saponins, lipids and amino acids [1–8] have been reported so far. Since the alcoholic extracts of its seeds have shown several biological activities [9–15], we studied the composition of its methanol extract which yielded a good concentration of a complex mixture of alkaloids, including budmunchiamine-G (**1**), earlier reported from *A. amara* seeds [16]. As this is the first report of the presence of alkaloids in *A. lebbek*, their detailed structure elucidation is discussed.

RESULTS AND DISCUSSION

Recently, the structurally unique budmunchiamines A–I have been isolated from the seeds of *A. amara* [16–18]; these contain an amide macrocycle invariably substituted by two or three *N*-methyl groups and a homologous side-chain. The seeds of *A. lebbek*, gave isolate-I which showed a positive test with Dragendorff's reagent and bands in the IR spectrum at 3300 and 1645 cm^{-1} for an amide group. In its mass spectrum, two peaks at *m/z* 480 and 452 were indicative of the presence of two compounds in isolate-I having a difference of C_2H_4 in their molecular formulae. An ion at *m/z* 255 in the mass spectrum and the absence of *N*-methyl signals at δ2.30–2.10 in their ^{1}H NMR spectra clearly indicated that isolate-I is devoid of *N*-methyl groups which had been invariably present in budmunchiamines A–I. Its ^{1}H NMR spectrum showed a large, broad singlet at δ 1.26 and a triplet at δ0.84, indicating the presence of a straight chain alkane. Two overlapping multiplets at δ3.40–3.00 and a broad *s* at δ8.50 suggested the presence of a $-CONHCH_2-$ system in isolate-I. The overlapping multiplets at δ2.80–2.60 and 2.45–1.85 for $-CH_2NHCH_2-$, H-3 and H-4, together with another set of multiplets at δ1.64–1.50 for CH_2 at H-7, H-11, H-12 and H-16 clearly supported the macrocycle analogous to budmunchiamines A–I, whose structures have been well established by HETCOR, COSY, selective INEPT and APT techniques [16–18].

The mass spectrum of isolate-I showed two $[M]^+$ with independent fragments at *m/z* 480 and 452 suggesting that



	R	R'	n	X
1	H	Me	5	H_2
2	H	H	8	H_2
3	H	H	6	H_2
4	H	H	3	O
5	H	H	3	H,OH

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Table 1. ^{13}C NMR spectral data of budmunchiamines L1–L3 from *A. lebbek* seeds (100 MHz, CDCl$_3$)

C	2	3	4
2	170.9	170.9	170.9
3	40.9	40.9	40.9
4	55.6	55.5	55.5
6	46.0	46.0	46.0
7	29.0^a	29.0^a	29.0^a
8	52.0^b	52.0^b	52.0^b
10	51.2^b	51.2^b	51.2^b
11	25.9^c	25.9^c	25.9^c
12	24.5^c	24.5^c	24.5^c
13	52.5^b	52.5^b	52.5^b
15	52.0^b	52.0^b	52.0^b
16	28.8^a	28.8^a	28.8^a
17	37.5	37.5	37.5
1′	33.4	33.4	33.4
2′	25.9	25.9	26.0
3′	29.2	29.2	29.1
4′	29.4	29.4	29.6
5′	29.6	29.6	29.6
6′	29.6	29.6	29.6
7′	29.6	29.6	42.6
8′	29.6	29.6	211.1
9′	29.6	29.6	44.6
10′	29.6	29.6	17.3
11′	29.6	29.6	13.9
12′	29.6	31.9	—
13′	29.6	22.5	—
14′	31.8	13.7	—
15′	22.5	—	—
16′	14.0	—	—

$^{a-c}$Assignments may be reversed within the same column.

there are two homologous chains, thereby, clearly indicating that it is a mixture of two compounds, **2** and **3**, having side-chains of $C_{16}H_{33}$ and $C_{14}H_{29}$, respectively. The chain length was further confirmed by the fragment at m/z 255 in their mass spectra for the macrocycle of $C_{13}H_{27}ON_4$. The ^{13}C NMR also supported the presence of **2** and **3** in isolate-I as carbon signals appeared in pairs in certain cases (Table 1) in the ratio of 13:7, respectively. The signal for CONH appeared at δ170.9, and for C-3 and C-4 at δ40.9 and 55.6, respectively. The typical signal for CONHCH$_2$ appeared at δ37.5, and for C-7, C-11, C-12, and C-16 at δ29.0, 25.9, 24.5 and 28.8, respectively, which were assigned on the basis of the values reported for budmunchiamines A–I [16]. The striking difference in the ^{13}C NMR of budmunchiamines A–I and **2** and **3** was observed by the absence of *N*-methyl signals at δ35.0 and 42.0–44.0 along with the 5 ppm upfield shift of C-4, C-6, C-8, C-10, C-13, C-15, and C-1′, a 2 ppm downfield shift of C-3, C-11, C-12 and C-16 and a 3 ppm downfield shift of C-7 owing to the demethylation of N. These observations were in conformity with those made for budmunchiamines A–I [16], and clearly suggested that all the four N of the ring are not methylated. This is the main difference in the structures of **2** and **3** from budmunchiamines reported from *A. amara*. The ^{13}C NMR spectrum also assisted in determining the structure of the *n*-alkane as it showed typical signals at δ14.0 (*q*), 22.5 (*t*), 31.8 (*t*), a large triplet at δ29.6, and other triplets at δ29.4, 29.2, 25.9 and 33.4. These data clearly confirmed the structures **2** and **3** for budmunchiamines L-1 and L-2 in isolate-I.

The second fraction, named as isolate-II, after purifications yielded **4** which gave similar bands in the IR spectrum except for an additional band at 1705 cm^{-1} indicating the presence of another carbonyl group in the molecule. The ^{1}H NMR signals were very similar to those of **2** and **3**, except for additional signals at δ2.28 for $-COCH_2-$. The ^{13}C NMR also showed a weak singlet at δ211.1 along with the triplets at δ44.6 and 42.6 for $-CH_2COCH_2-$. These data suggested the presence of a carbonyl group in the *n*-alkane side-chain. The position of the carbonyl group was fixed at C-8 since the typical signals for C-9 to C-11 at δ13.9, 17.3 and 44.6 were present in its ^{13}C NMR spectrum. The mass spectrum showed a $[M]^+$ at m/z 424 suggesting a side-chain of $C_{11}H_{24}O$. The position of the carbonyl group in the side-chain was further established at C-8 as **4** gave ions for $[M-43]^+$ and $[M-71]^+$ at m/z 381 and 353, respectively. Sodium borohydride reduction of **4** gave **5** with a multiplet at δ3.60 in its ^{1}H NMR spectrum and a $[M]^+$ at m/z 426. The ion at m/z 255 in **5** further indicated that carbonyl was present in the side-chain and not in the ring. These data established that budmunchiamine L3 has structure **4**.

EXPERIMENTAL

Mature dry seeds (2 kg) of *A. lebbek* were collected from Anurag Nursery and Agriculture farm, Kanwali, Dehradun, U.P., India, less mature green pods from Kukrail Reserve Forest, Lucknow, in November 1991, and dried in the shade to obtain seeds (1 kg). Seeds from these two sources were individually milled and extracted with MeOH by soaking overnight (×3). The extracts were compared by TLC using Dragendorff's reagent followed by 5% NaNO$_2$ as spray reagents. Since mature seeds showed a higher concentration of alkaloids, the extract of the less mature green seeds was discarded. The concd extract (400 g) was treated with 2% aq. HOAc and extracted (×3) with CHCl$_3$ for neutral compounds. The acidic aq. phase was treated with 25% NH$_4$OH to pH 9 and extracted (×3) with CHCl$_3$ to obtain the basic portion of the extract.

The basic substance after CC in CHCl$_3$–Et$_2$NH (9:1) was partitioned into 11 frs. Frs 1–4 yielded compounds in negligible amounts, while frs 5–10 gave viscous liquids. Fr. 10, after further CC in the above solvent system, gave 4 frs. Fr. 1 after prep. TLC (cyclohexane–Et$_2$NH–MeOH, 79:20:1) afforded **1** (15 mg), while fr. 2 after exhaustive TLC purifications (CHCl$_3$–MeOH–Et$_2$NH, 8:1:1) afforded isolate-I (R_f 0.73, **2** and **3**, 50 mg). Fr. 3 was discarded, while fr. 4, after rigorous purification (TLC, CHCl$_3$–Et$_2$NH–MeOH, 8:1:1, R_f 0.9) afforded isolate-II (**4**, 200 mg). NaBH$_4$ reduction of **4** (100 mg) after usual work-up afforded **5** (75 mg, TLC, CHCl$_3$–Et$_2$NH–MeOH, 8:1:1, R_f 0.45).

Isolate-I (**2**, **3**). Viscous liquid. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 3300 (NH), 2900, 1645 (CONH), 1556, 1460, 1380, 1060, 754. ^{1}H NMR (CDCl$_3$): δ0.84 (*t*, $J = 6.5$ Hz, Me), 1.26 (*br s*, $(CH_2)_n$) 3.40–3.0 (overlapping *m*, $CONHCH_2$), 8.50 (*br s*, CONH), 2.80–2.60, 2.45–1.85 (*m*, CH_2NHCH_2 and H-3, H-4), 1.64–1.50 (*m*, H-7, H-11, H-12, H-16). MS *m/z* (rel. int.): 480 ($[M]^+$, $C_{29}H_{60}ON_4$) (2), 452 ($[M]^+$, $C_{27}H_{56}ON_4$) (2), 465 $[480 - Me]^+$ (3), 437 $[452 - Me]^+$ (2), 451 $[465 - CH_2]^+$ (2), 423 $[437 - CH_2]^+$ (2), 409 (2), 395 (2), 381 (2), 255 (2), 112 (30), 58 (100), 45 (95).

Isolate-II (**4**). Viscous liquid. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (NH), 2950, 1730 (CO), 1645 (CONH), 1556, 1460, 1380, 1060, 754. ^{1}H NMR (CDCl$_3$): δ0.83 (*t*, $J = 6.5$ Hz, Me), 1.26 (*br s*, $(CH_2)_n$), 3.40–3.0 (overlapping *m*, $CONHCH_2$), 8.47 (*br s*, CONH), 2.80–2.60, 2.45–1.85 (*m*, CH_2NHCH_2, CH_2COCH_2 and H-3, H-4), 1.64–1.50 (*m*, H-7, H-11, H-12, H-16). MS *m/z* (rel. int.): 424 ($[M]^+$, $C_{24}H_{48}O_2N_4$) (1), 409 $[M - Me]^+$ (2), 395 $[409 - CH_2]^+$ (2), 381 $[M - CH_2CH_2Me]^+$ (2), 353 $[M - COCH_2CH_2Me]^+$ (2), 265 (10), 255 (5), 125 (10), 99 (15), 57 (100).

Reduction of compound **4**. Alkaloid **4** (100 mg) was taken up in MeOH and $NaBH_4$ (100 mg) added gradually at room temp. for 30 min. After usual-work up, **5** was obtained (75 mg) as a viscous mass. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550–3200 (OH, NH), 2950, 1660 (CONH), 1470, 1380, 1070, 755. ^{1}H NMR (CDCl$_3$): δ0.83 (*t*, $J = 6.5$ Hz, Me), 1.26 (*br s*, $(CH_2)_n$), 3.60 (*m*, CHOH), 3.40–3.0 (overlapping *m*, $CONHCH_2$), 8.47 (*br s*, CONH), 2.80–2.60, 2.45–1.85 (*m*, CH_2NHCH_2 and H-3, H-4), 1.64–1.50 (*m*, H-7, H-11, H-12, H-16). MS *m/z* (rel. int.): 426 ($[M]^+$, $C_{24}H_{50}O_2N_4$) (1), 408 $[M - H_2O]^+$ (1), 393 $[408 - Me]^+$ (2), 277 (5), 255 (4), 149 (10), 81 (55), 69 (55), 55 (100).

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