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NEW CYCLOPEPTIDE ALKALOIDS FROM *ZIZIPHUS LOTUS*

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ABSTRACT.—Two new 14-membered frangulanine-type cyclopeptide alkaloids, lotusanines A [**1**] and B [**2**], have been isolated from the aerial parts of *Ziziphus lotus*, together with the known alkaloids sanjoinenine [**3**], sanjoinine F [**4**], and frangufoline [**5**].

Ziziphus lotus Lam. (Rhamnaceae) is a small tree that is widely distributed in the Jordan Valley. The genus *Ziziphus* comprises several species that are used in indigenous medicine for the treatment of various diseases (1–5). We report here the first chemical investigations of *Z. lotus*, yielding two new 14-membered frangulanine-type (6) cyclopeptide alkaloids from an extract of the aerial parts of *Z. lotus*. The new compounds, lotusanine A [**1**] and lotusanine B [**2**] were isolated along with the known alkaloids, sanjoinenine [**3**] (7), sanjoinine F [**4**] (7), and frangufoline [**5**] (8) (Table 1). Characterization of these compounds was achieved with the help of spectroscopic studies, especially mass spectrometry, which permitted conclusions to be drawn about the structural units (amino acids and styryl moiety) present in the compound and the manner in which they are linked (6,9).

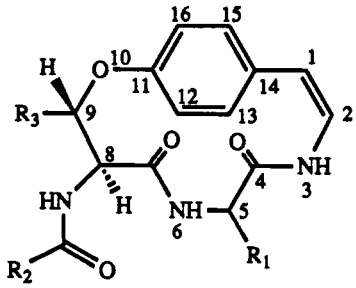
RESULTS AND DISCUSSION

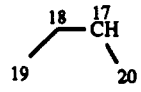
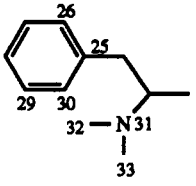
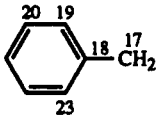
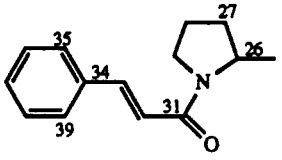
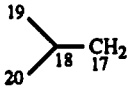
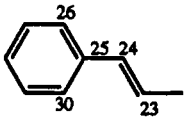
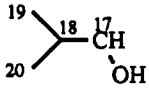
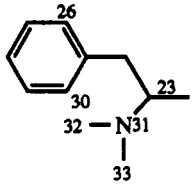
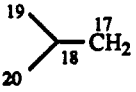
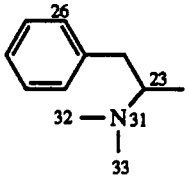
Cc of an alkaloidal fraction of the C_6H_6 extract of *Z. lotus* (see Experimental) gave an amorphous solid, lotusanine A [**1**]. The uv spectrum of **1** showed only terminal absorption. The ir spectrum exhibited bands for NH- (3260 cm^{-1}), amide carbonyls (1622 cm^{-1}), and an ether linkage (1219 cm^{-1}).

The molecular ion was not observed by ei or hreims; however, it was located at *m/z* 534 by field-desorption mass spectroscopy and was further confirmed by fab (negative-ion) and linked-scan mass spectroscopy. The highest peak observed in the hreims was at *m/z* 489.2629 which corresponded to the molecular formula $C_{29}H_{35}N_3O_4$, ion **a** (Scheme 1). This ion was formed by a facile deamination, well known in cyclopeptide alkaloids bearing an *N,N*-dimethylphenylalanine group. This conclusion was confirmed by the appearance of a base peak at *m/z* 148.1182 ($C_{10}H_{14}N$), ion **f**. Other important fragments were at *m/z* 443.2715 and 91.0585 which corresponded to ions **g** and **h**, respectively. The fragments at *m/z* 135.0684 (C_8H_9NO), 131.0523 (C_9H_7O), and 86.0960 ($C_5H_{12}N$) indicated the presence of hydroxystyrylamine, cinnamoyl, and decarbonyl leucine or isoleucine groups, ions **d**, **o**, and **m**, respectively (Scheme 1). The linkage between substituents on the cyclopeptide ring was confirmed from fragment **c** at *m/z* 189.1186 ($C_{12}H_{15}NO$), which showed that leucine is linked to styrylamine through an ether linkage, and from fragment **l** at *m/z* 214.1050 ($C_{14}H_{16}NO$), which indicated that leucine is linked to the cinnamoyl moiety. Therefore, considering the results of fd, ei, hrei, fab (negative-ion), and linked-scan mass spectroscopy, the molecular formula was deduced to be $C_{31}H_{42}N_4O_4$, indicating the presence of 13 double bond equivalents in the molecule.

The ^{1}H-nmr spectrum of **1** showed the presence of a 6-H singlet at δ 2.42 due to the *N,N*-dimethyl group. There were only two methyl doublets at δ 0.73 (J=6.6 Hz) and 0.97 (J=6.6 Hz) and one methyl triplet at δ 0.45 (J=7.1 Hz). This indicated the

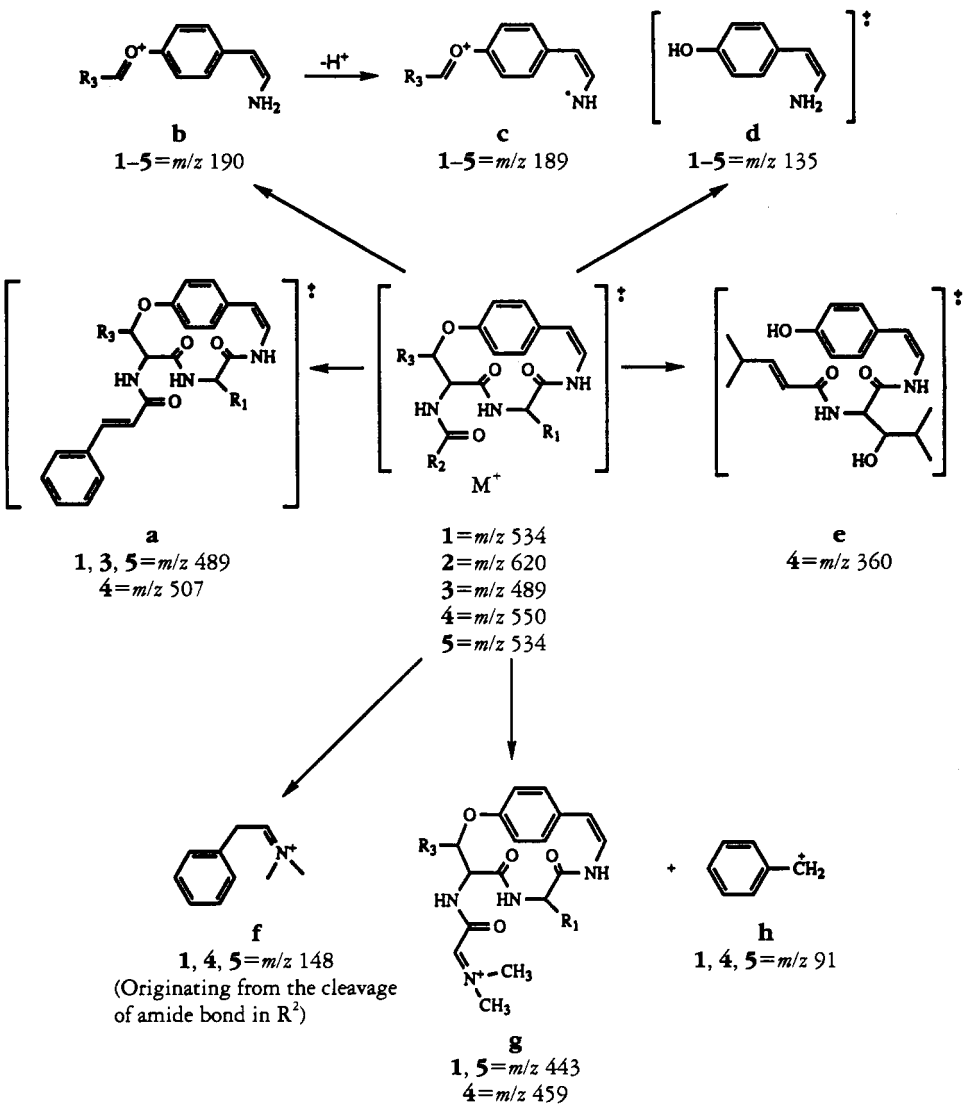
TABLE 1. Cyclopeptide Alkaloids of *Ziziphus lotus*.



Cyclopeptide alkaloid	R_1	R_2	R_3
Lotusanine A [1] $C_{31}H_{42}N_4O_4$			
Lotusanine B [2] $C_{37}H_{40}N_4O_5$			
Sanjoinenine [3] $C_{29}H_{35}N_3O_4$			
Sanjoinine F [4] $C_{31}H_{42}N_4O_5$			
Frangufoline [5] $C_{31}H_{42}N_4O_4$			

presence of one leucine and one isoleucine group in compound **1**. The ^{13}C-nmr spectrum provided further evidence for the presence of both an isoleucine and leucine group by comparison of the ^{13}C-nmr chemical shifts with literature values (12). The H-H and H-C correlations were determined using COSY 45°, HMBC, and HMQC experiments and by comparison with data reported for similar compounds.

The stereochemistry of leucine in the 14-membered ring can be deduced from the

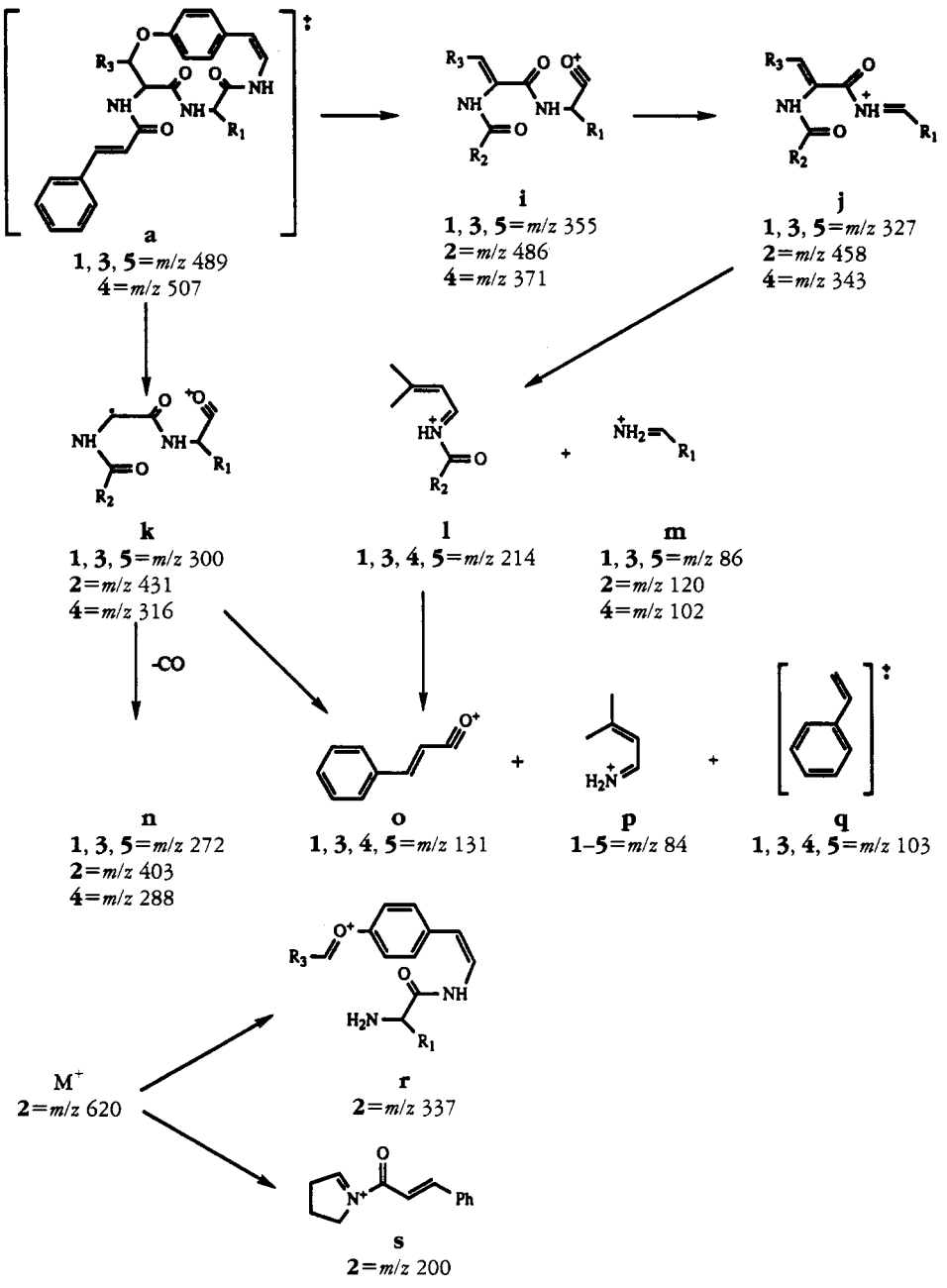


SCHEME 1. Mass spectral fragmentations of compounds **1–5**.

^{13}C-nmr chemical shift at C-9 as L-erythro-β-hydroxyleucine, because C-9 resonated at 80.2 ppm (in the D-erythro compounds C-9 resonates at about 87 ppm) (13). The stereochemistry of the leucine moiety in the 14-membered ring was also confirmed from the J value of the methyls ($J_{9\beta\text{-}8\alpha}$=6.6 Hz pseudoaxial/equatorial coupling) typical of L-erythro-β-hydroxyleucine (6,15). The data led to the assignment of structure **1** for lotusanine A.

Lotusanine B [**2**] was isolated by cc of fraction 6 (C_6H_6 extract of *Z. lotus*). The compound was further purified by prep. tlc on glass plates coated with Si gel using Me_2CO-C_6H_6 (20:80) as the developing solvent. The uv spectrum of **2** showed characteristic absorptions of cyclopeptide alkaloids with λ max at 280 nm and λ min at 224 nm, which are typical for 14-membered cyclopeptide alkaloids (10,11). The ir spectrum showed bands for NH (3450 cm^{-1}), amide carbonyl (1660 cm^{-1}), and ether (1100–1000 cm^{-1}) functionalities.

The hreims of compound **2** showed the molecular ion peak (M^+) at *m/z* 620.3180



SCHEME 1. Continued.

($C_{37}H_{40}N_4O_5$), which was further confirmed by fdms. The high M^+ value suggested the presence of an additional amino acid between the terminal amino acid and the 14-membered ring. Other major fragments were at *m/z* 486.2412 ($C_{29}H_{32}N_3O_4$, **i**), 458.2461 ($C_{28}H_{32}N_3O_3$, **j**), 431.1827 ($C_{25}H_{25}N_3O_4$, **k**), 190.1193 ($C_{12}H_{16}NO$, **b**), 189.1146 ($C_{12}H_{15}NO$, **c**), 135.0714 (C_8H_9NO, **d**), and 131.0520 (C_9H_7O, **o**) (Scheme 1). The fragments at *m/z* 337.1935 ($C_{21}H_{25}N_2O_2$, **q**) and *m/z* 200.1054 ($C_{13}H_{14}NO$, **s**) indicated that proline was the additional amino acid located between the deaminated phenylalanine moiety and the 14-membered ring, leading to structure **2**.

This conclusion was further supported by comparison of the ^{1}H- and ^{13}C-nmr chemical shifts of the proline methylene groups at the C-27 and C-29 positions in similar structures to **2** (12,14). The ^{1}H- and ^{13}C- (DEPT) nmr data for lotusanine B [**2**] are given in Tables 2 and 3. The ^{1}H-nmr spectrum showed the presence of two methyl doublets at δ 0.66 and 1.22 (J=6.6 Hz) suggesting that the stereochemistry of leucine is L-erythro (6,15). Lotusanine B was assigned structure **2** on the basis of the above spectroscopic data.

The molecular formula of sanjoinenine [**3**] was determined by hreims as $C_{29}H_{35}N_3O_4$ (*m/z* 489.2665) and confirmed by fdms. The fragments at *m/z* 135.0684 (C_8H_9NO), 131.0523 (C_9H_7O), and 86.0960 ($C_5H_{12}N$) indicated the presence of hydroxystyrylamine (d), cinnamoyl (o), and decarbonyl leucine or isoleucine (m) groups, respectively. Fragment **c** at *m/z* 189.1186 ($C_{12}H_{15}NO$) showed that leucine/isoleucine is attached to styrylamine through an ether linkage and fragment **l** at *m/z* 214.1050 ($C_{14}H_{16}NO$) showed that the same leucine is linked to the cinnamoyl moiety on the other side which, on linked-scan ms measurement, gave two daughter peaks at *m/z* 131 and 84 (ions **o** and **p**). Fragment **i** (*m/z* 355.2034, $C_{21}H_{27}N_2O_3$) showed the linkage to be between the two leucine groups and the cinnamoyl moiety.

The ^{1}H-nmr spectrum of **3** showed the presence of four methyl doublets at δ 0.59, 0.73, 1.01, and 1.28, each coupled to a methine proton. This indicated the presence of two leucine units. The two doublets at δ 6.30 ($J_{23,24}$=15.5 Hz) and 7.61 ($J_{24,23}$=15.5 Hz) were assigned to the *trans* olefinic protons of the cinnamoyl group. The data led to

TABLE 2. ^{1}H-Nmr Spectral Data of Compounds **1–5**.[a]

Proton(s)	Compound				
	1	**2**	**3**	**4**	**5**
H-1	6.01 (br s)	6.02 (d, 7.8)	6.50 (m)	6.70 (d, 7.4)	6.38 (d, 7.7)
H-2	6.43 (d, 7.2)	6.32 (d, 7.6)	6.66 (m)	6.20 (m)	—
H-3	6.00 (m)	—	5.96 (d, 9.6)	—	—
H-5	4.20 (m)	4.30 (dd, 9.2,6.7)	4.05 (m)	4.40 (m)	4.05 (m)
H-6	6.77–7.01 (m)		5.90 (d, 7.8)		
H-8	4.18 (d, 8.1)	4.60 (m)	4.69 (dd, 7.4,2)	4.66 (m)	4.65 (m)
H-9	4.64 (d, 7.9)	4.91 (dd, 6.6,1.9)	5.00 (dd, 7.4,2)	4.87 (d, 7.9)	4.92 (dd, 7.5,1.9)
H-12–16 ..	6.77–7.01 (m)	7.38–7.54 (m)	7.00–7.50 (m)	7.00–7.50 (m)	7.05–7.50 (m)
H-17	1.40 (m)		1.38 (d, 7.3)	4.05 (m)	3.1 (m)
H-18	1.79 (m)	7.38–7.54 (m)		2.05 (m)	2.02 (m)
H-19	0.43 (t, 7.2)	"	0.59 (d, 6.5)	1.17 (d, 6.5)	0.57 (d, 6.6)
H-20	0.40 (d, 6.6)	"	0.73 (d, 6.5)	1.22 (d, 7.4)	1.14 (d, 6.8)
H-21	6.77–7.01 (m)	"	6.38 (d, 7.2)	—	—
H-23	3.54 (t, 1.8)	"	6.30 (d, 15.5)	3.44 (t, 1.8)	3.34 (br d, 14.8)
H-24			7.61 (d, 15.5)	3.04 (d, 2.0)	
H-26–30 ..	6.77–7.01 (m)	3.39–3.55 (m)	7.00–7.50 (m)	7.00–7.50 (m)	7.00–7.50 (m)
H-31	—	—	—	—	—
H-32	2.42 (s)	6.68 (d, 15.4)	1.01 (d, 6.8)	2.88 (s)	2.85 (s)
H-33	2.42 (s)	7.72 (d, 15.4)	1.28 (d, 6.8)	2.91 (s)	2.97 (s)
H-34	1.8 (m)	—		2.05 (m)	2.05 (m)
H-35	0.73 (d, 6.6)	7.38–7.54 (m)		0.89 (d, 6.6)	0.71 (d, 6.6)
H-36	0.98 (d, 6.6)	—		0.76 (d, 6.6)	1.24 (d, .68)
H-37					
H-38					
H-39					
H-40		1.80 (m)			
H-41		0.66 (d, 6.6)			
H-42		1.12 (d, 6.6)			

[a]Recorded in $CDCl_3$. Chemical shift values are reported as δ values (ppm) from TMS at 500 MHz, with multiplicities and J values (Hz) in parentheses.

TABLE 3. ^{13}C-Nmr Spectral Data of Compounds **1–5**.[a]

Carbon	Compounds				
	1	**2**	**3**	**4**	**5**
C-1	130.2[b]	130.9[b]	130.0	131.0[b]	130.3[b]
C-2	130.9[b]	131.8[b]	132.7	134.0[b]	131.6[b]
C-4	169.2	166.6	165.6	165.0	159.0
C-5	55.4	53.9	52.9	56.9	55.4
C-7	170.1	167.7	171.9	168.0	166.0
C-8	58.0	55.2	55.6	68.0	55.7
C-9	80.2	81.9	81.6	80.7	79.0
C-11	155.7	156.0	156.0	156.1	150.0
C-12	118.4	117.1	118.8	118.0	118.9
C-13	121.1	123.4	123.0	126.0	122.5
C-14	130.8[b]	130.1[b]	131.6[b]	129.5	131.6[b]
C-15	129.7	126.6	125.7	125.8	123.0
C-16	125.2	123.5	122.3	121.5	126.1
C-17	35.7	36.0	40.0	77.2	40.0
C-18	23.9	131.8	24.5	28.9	28.0
C-19	10.6[c]	128.8	23.2[c]	11.2[c]	15.3
C-20	14.7[c]	129.0	20.6[c]	20.3[c]	19.4
C-21	—	125.5	—	—	—
C-22	171.2	129.0	—	167.1	—
C-23	—	128.8	127.8	—	—
C-24	39.4	—	143.3	42.3	38.7
C-25	141.9	171.1	—	129.5	—
C-26	128.5	59.1	127.8	—	127.9
C-27	129.3	59.1	130.4	—	—
C-28	126.4	28.6	127.9	127.7	128.7
C-29	129.3	47.2	130.4	127.5	130.4[b]
C-30	128.6	—	127.8	—	—
C-31	—	171.4	29.5	—	—
C-32	39.7	128.2	20.0[c]	42.0	42.0
C-33	41.4	144.1	14.7[c]	42.0	42.0
C-34	28.7	136.7	—	28.9	28.0
C-35	19.9	128.1	—	14.9[c]	14.7[c]
C-36	14.2[c]	130.9[b]	—	19.3[c]	20.3[c]
C-37	—	126.6	—	—	—
C-38	—	130.9[b]	—	—	—
C-39	—	128.1	—	—	—
C-40	—	28.9	—	—	—
C-41	—	14.0[c]	—	—	—
C-42	—	19.7[c]	—	—	—

[a]Recorded in $CDCl_3$. Chemical shift values (ppm) at 125 MHz.
[b,c]Assignments bearing the same superscript in each column are interchangeable.

assignment of structure **3** to sanjoinenine, previously isolated by Han *et al.* (7) from the seeds of *Z. vulgaris*.

Sanjoinine F [**4**] was isolated from the ninth fraction of the alkaloidal portion through repeated cc (Si gel, 70–230 mesh), and tlc (Si gel) using Me_2CO-C_6H_6 (30:70) as the developing solvent. The resulting amorphous solid had $[\alpha]^{25}D$ −107° in $CHCl_3$. The uv and ir spectra of **4** were similar to the reported data (7). The eims of **4** showed a weak molecular ion peak at *m/z* 550, confirmed by the fd and fab (negative-ion) mass spectra. Other major fragments were at *m/z* 507, 459, 360, 316, 190, 189, 148 (base peak), 135, and 102 (fragments **a**, **g**, **e**, **k**, **b**, **c**, **f**, **d**, and **m**) (Scheme 1). The exact formula of each fragment was determined by hreims. The ^{1}H-nmr spectrum of **4** showed

a downfield shift for the protons of the leucine moiety attached at position R_1 due to the presence of a hydroxy group at the β-position of leucine (Table 1). The number of methyl, methylene, and methine carbon atoms was confirmed by DEPT experiments, and the presence of a *N,N*-dimethyl unit by a signal at δ 42.0, and of a methylene carbon at δ 42.3, which was assigned to C-24. The data led to structure **4** for sanjoinine F, previously isolated by Han *et al.* from the seeds of *Z. vulgaris* (7).

Frangufoline [**5**] was isolated from the MeOH extract of *Z. lotus* by repeated cc on Si gel. Elution with MeOH-$CHCl_3$ (15:85) afforded frangufoline [**5**]. The uv and ir spectra were similar to those of the reported compound (10,11). The eims of this compound showed a weak molecular ion peak at *m/z* 534. The molecular ion was confirmed by the daughter-to-parent linked-scan mass spectrum for the fragment at *m/z* 148. Other major fragments appeared at *m/z* 489.2660 ($C_{29}H_{35}N_3O_4$, $M^+-C_2H_7N$) and 443.2670 ($C_{24}H_{35}N_4O_4$, $M^+-C_7H_7$). The base peak appeared at *m/z* 148.1128 ($C_{10}H_{14}N$), which indicated the presence of an *N,N*-dimethylphenylalanine unit at the terminal end of the cyclopeptide alkaloid. The ^1H- and ^{13}C-nmr spectra of frangufoline [**5**] were similar to those of sanjoinenine [**3**] except for the presence of the *N,N*-dimethylamino group and the absence of the olefinic protons of the cinnamoyl moiety. This led to structure **5** for the compound, which was also confirmed by comparing the spectral data reported for frangufoline isolated previously from *Rhamnus frangula* (8).

All the compounds isolated were racemic except **4**, which showed a negative rotation.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ir spectra were generally measured in $CHCl_3$ and uv spectra were measured in MeOH. The ^1H-nmr spectra were recorded at 400 MHz or 500 MHz with TMS as internal standard. The ^{13}C-nmr spectra were measured at 100 or 125 MHz also with TMS as an internal standard. The COSY 45°, DEPT, HMBC, and HMQC nmr spectra were recorded at 400 MHz. Tlc was preformed on Merck precoated Si gel GF-254 plates; cc was carried out on Merck Si gel 60 (70–230 mesh size).

PLANT MATERIAL.—The whole plant of *Ziziphus lotus* (except the roots), about 70 kg, was collected from the Jordan Valley and was identified at the Biology Department, University of Jordan, Amman, Jordan, by Dr. Dawood Al-Esawi. A voucher specimen was deposited at the herbarium of the University of Jordan.

EXTRACTION AND ISOLATION.—The plant material was soaked in NH_4OH-MeOH-C_6H_6 (1:1:100) for about 3 weeks. The extract was filtered and concentrated under high vacuum, giving an amorphous residue, which was then taken up in 5% citric acid solution (10 liters). This was then basified with NH_4OH to pH 9–10 and extracted with $CHCl_3$ (5 liters). The $CHCl_3$-soluble fraction (13 g) gave a positive alkaloidal test with Dragendorff's reagent. The crude alkaloidal fraction was chromatographed over Si gel (1 kg, 70–230 mesh) and eluted with increasing polarities of MeOH/$CHCl_3$ mixtures. The eluate fractions (100 ml each) were followed by tlc and combined into 14 fractions, out of which the fifth fraction afforded lotusanine A [**1**] on elution with MeOH-$CHCl_3$ (5:95), while lotusanine B [**2**] was isolated from the sixth fraction (Si gel 70–230) using MeOH-$CHCl_3$ (10:90) as the eluting solvent system, and it was repurified by tlc using Me_2CO-C_6H_6 (20:80) as the developing solvent. Sanjoinenine [**3**] was also isolated from the fifth alkaloidal fraction, while sanjoinine F [**4**] was obtained from the ninth fraction on elution with MeOH-$CHCl_3$ (20:80). It was repurified by tlc (silica precoated plates) using Me_2CO-C_6H_6 (30:70) as the developing solvent. Frangufoline [**5**] was isolated from the MeOH extract of *Z. lotus* by repeated cc (Si, 70–230 mesh). It was eluted from the column using MeOH-$CHCl_3$ (15:85) as the solvent system.

Lotusanine A [**1**].—Colorless amorphous solid: uv (MeOH) λ max (log ε) 208 (4.20) nm; ir ($CHCl_3$) ν max 3260 (N-H), 1622 (amide), 1219 (C-O-C)- cm^{-1}; ^1H nmr data ($CDCl_3$, 500 MHz), see Table 2; ^{13}C-nmr data ($CDCl_3$, 125 MHz), see Table 3; eims (70 eV) *m/z* 443 ($[M]^+-C_7H_7$, 6), 189 (5), 148 (100), 103 (8), 86 (38), 83 (58); fdms *m/z* $[M]^+$ 534; hreims *m/z* found 489.2629 (calcd for $C_{29}H_{35}N_3O_4$, $[M]^+-C_2H_7N$, 489.2627), 443.2652 ($C_{24}H_{35}N_4O_4$, 443.2658), 355.2035 ($C_{21}H_{27}N_2O_3$, 355.2022), 327.2050 ($C_{20}H_{27}N_2O_2$, 327.2072), 300.1490 ($C_{17}H_{20}N_2O_3$, 300.1474), 189.1115 ($C_{12}H_{15}NO$, 189.1154), 148.1182 ($C_{10}H_{14}N$, 148.1126), 135.0640 (C_8H_9NO, 135.0684), 131.0533 (C_9H_7O, 131.0498), 91.0585 (C_7H_7, 91.0547), 86.1005 ($C_5H_{12}N$, 86.0970), 56.0475 (C_3H_6N, 56.0500).

Lotusanine B [**2**].—Amorphous solid: uv (MeOH) λ max (log ε) 280 (3.12) λ min 244 (3.74) nm; ir ($CHCl_3$) ν max 3450 (NH), 1660 (amide), 1610 (C=C), 1100–1000 (C-O-C) cm^{-1}; ^{1}H-nmr data ($CDCl_3$, 500 MHz), see Table 2; ^{13}C-nmr data ($CDCl_3$, 125 MHz), see Table 3; eims (70 eV) *m/z* $[M]^+$ 620 (25), 486 (20), 458 (18), 432 (10), 228 (38), 200 (25), 190 (10), 189 (47), 135 (25), 131 (100), 103 (18), 70 (15); fdms *m/z* $[M]^+$ 620; hreims *m/z* found 620.3180 (calcd for $C_{37}H_{40}N_4O_5$, 620.2999), 486.2412 ($C_{29}H_{32}N_3O_4$, 486.2393), 458.2461 ($C_{28}H_{32}N_3O_3$, 458.2444), 432.1922, ($C_{25}H_{26}N_3O_4$, 432.1922), 337.1935 ($C_{21}H_{25}N_2O_2$, 337.1915), 228.0977 ($C_9H_{14}N_3O_4$, 228.0984), 200.1054 ($C_{13}H_{14}NO$, 200.1075), 190.1193 ($C_{12}H_{16}NO$, 190.1232), 189.1146 ($C_{12}H_{15}NO$, 189.1154), 135.0714 (C_8H_9NO, 135.0684), 103.0514 (C_8H_7, 103.0548), 97.0650 (C_6H_9O, 97.0653), 70.0665 (C_4H_8N, 70.0656).

Sanjoinenine [**3**].—Colorless amorphous solid: uv (MeOH) λ max (log ε) 277 (3.13), 252 (3.83) nm; ir ($CHCl_3$) ν max 3251 (N-H), 3100 (Ar-H), 1652 (carbonyl amide), 1610 (C=C), 1100 (C-O-C) cm^{-1}; ^{1}H-nmr data ($CDCl_3$, 500 MHz), see Table 2; ^{13}C-nmr data ($CDCl_3$, 125 MHz), see Table 3; eims (70 eV) *m/z* 489 $[M]^+$ (44), 356 (8), 355 (32), 327 (16), 303 (15), 242 (6), 215 (6), 214 (11), 190 (21), 189 (100), 136 (6), 135 (53), 134 (12), 132 (11), 131 (92); fdms *m/z* $[M]^+$ 489; hreims *m/z* found 489.2665 (calcd for $C_{29}H_{35}N_3O_4$, 489.2627), 355.2034 ($C_{21}H_{27}N_2O_3$, 355.2022), 327.2072 ($C_{20}H_{27}N_2O_2$, 327.2072), 300.1506 ($C_{17}H_{20}N_2O_3$, 300.1474), 285.1592 ($C_{17}H_{21}N_2O_2$, 285.1603), 242.1164 ($C_{15}H_{16}NO_2$, 242.1181), 190.1224 ($C_{12}H_{16}NO$, 190.1232), 189.1186 ($C_{12}H_{15}NO$, 189.1154), 135.0684 (C_8H_9NO, 135.0684), 131.0523 (C_9H_7O, 131.0497), 103.0555 (C_8H_7, 103.0548), 86.0960 ($C_5H_{12}N$, 86.0970).

Sanjoinine F [**4**].—Amorphous solid: $[\alpha]^{25}D$ −107° (*c*=0.050, $CHCl_3$); uv (MeOH) λ max (log ε) 280 (sh) (4.40) nm; ir ($CHCl_3$) ν max 3400–3300 (OH and NH), 1699 (amide), 1597 (C=C), 1100–1025 (C-O-C) cm^{-1}; ^{1}H-nmr data ($CDCl_3$, 500 MHz), see Table 2; ^{13}C-nmr data ($CDCl_3$, 125 MHz), see Table 3; eims (70 eV) *m/z* $[M]^+$ 550 (4), 535 (7), 507 (20), 505 (5), 460 (35), 459 (98), 445 (4), 387 (4), 186 (6), 148 (100), 135 (25), 97 (10), 57 (7); fdms *m/z* $[M]^+$ 550; hreims *m/z* found 535.2967 (calcd for $C_{30}H_{39}N_4O_5$, 535.2920), 507.2598 ($C_{28}H_{35}N_4O_5$, 507.2607), 459.2618 ($C_{24}H_{35}N_4O_5$, 459.2607), 360.2036 ($C_{20}H_{28}N_2O_4$, 360.2049), 190.1199 ($C_{12}H_{16}NO$, 190.1232), 189.1120 ($C_{12}H_{15}NO$, 189.1154), 148.1126 ($C_{10}H_{14}N$, 148.1126), 135.0703 (C_8H_9NO, 135.0684), 103.0584 (C_8H_7, 103.0548), 97.0676 (C_6H_9O, 97.0653).

Frangufoline [**5**].—Colorless amorphous solid: uv (MeOH) λ max (log ε) 280 (4.49) nm; ir ($CHCl_3$) ν max 3255 (NH), 1622 (amide), 1110 (C-O-C) cm^{-1}; ^{1}H-nmr data ($CDCl_3$, 500 MHz), see Table 2; ^{13}C-nmr data ($CDCl_3$, 125 MHz), see Table 3; eims (70 eV) *m/z* $[M]^+$+1 535 (2), 489 (20), 443 (15), 420 (10), 353 (7), 255 (15), 190 (5), 189 (30), 148 (100); hreims *m/z* found 489.2660 (calcd for $C_{29}H_{35}N_3O_4$, 489.2627), 443.2670 ($C_{24}H_{35}N_4O_4$, 443.2658), 303.2068 ($C_{18}H_{27}N_2O_2$, 303.2072), 190.1219 ($C_{12}H_{16}NO$, 190.1232), 189.1172 ($C_{12}H_{15}NO$, 189.1154), 148.1128 ($C_{10}H_{14}N$, 148.1126).

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