Communications to the Editor

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The Structure of Tsukushinamine, a New Type of Lupin Alkaloid in *Sophora franchetiana*[1)]

A new type of lupin alkaloid, tsukushinamine (I) was isolated together with six known alkaloid, (−)-cytisine, (−)-rhombifoline, (−)-N-formylcytisine, (−)-anagyrine, (−)-baptifoline and (±)-ammodendrine, from the epigeal parts of *Sophora franchetiana* Dunn (Leguminosae). The structure of I was presumed to be a new type of tetracyclic lupin alkaloid by spectral data.

Keywords——tsukushinamine; new type of lupin alkaloid; Leguminosae; *Sophora franchetiana*; rhombifoline; ammodendrine; anagyrine; baptifoline; N-formylcytisine; cytisine

In screening Leguminosae plants for lupin alkaloids, a new alkaloid (I, yield 110 mg), named tsukushinamine, was isolated from the basic fraction (1.8 g) of the 75% MeOH extracts of the fresh epigeal parts (320 g) of *Sophora franchetiana* (collected in Miyazaki prefecture in May) along with (−)-cytisine, (−)-rhombifoline, (−)-N-formylcytisine, (−)-anagyrine, (−)-baptifoline and (±)-ammodendrine by the method actually combined the ones described in previous papers.[2,3)]

Sophora franchetiana Dunn (Japanese name, Tsukushimuresuzume) is a perennial and ever green shrub, which is locally native and very rare in Japan.

Tsukushinamine (I), $C_{15}H_{20}N_2O$ (M^+, *m/e* 244.155, calcd. 244.158) is a colourless oil, $[\alpha]_D^{25}$ −72.3° (*c*=0.56, EtOH). Its mass spectrum revealed the prominent fragment ions at *m/e* 203 ($C_{12}H_{15}N_2O$, M^+–$CH_2CH{=}CH_2$, 73%), 160 ($C_{10}H_{10}NO$, 40) and 146 (C_9H_8NO, 25) in high mass range. The latter two coincided in elemental composition with the fragment ions characteristic of the lupin alkaloids having 3,4,5,6-tetradehydroquinolizidone moiety such as cytisine and its derivatives.[4)] However it was noted that the lactam carbonyl of the quinolizidone moiety, whose presence was also supported by the infrared spectrum absorption at 1640 cm^{-1}, was not conjugated in view of the lack of the ultraviolet absorption in the range above 210 nm. The ^{13}C nuclear magnetic resonance (^{13}C-NMR) spectrum of I (C_6D_6, Table 1) showed signals for one lactam carbonyl, four olefinic, three methin, six methylene and one sp^3-quarternary carbons. One of the four olefinic carbons was assigned to a terminal methylene, indicating a presence of a vinylic side chain. These data, and also the fact that it was produced in a *Sophora* plant, suggested that tsukushinamine (I) was a new type of tetracyclic C_{15}-lupin alkaloid different from matridine or sparteine type.

The proton magnetic resonance (PMR) spectrum of I (C_6D_6, Table I)[5)] revealed the mutually coupled signals at δ 4.00 (1H, dd, J=13.5 and 6 Hz, 10-H_α) and δ 3.24 (1H, d, J=13.5 Hz, 10-H_β),[6)] which could be assigned to the geminal protons of the methylene alpha to the lactam

1) This work was presented at the Meeting of Kanto Branch, Pharm. Soc. Japan, Tokyo, Nov. 11, 1978.
2) S. Ohmiya, H. Otomasu, J. Haginiwa and I. Murakoshi, *Phytochemistry*, **17**, 2021 (1978).
3) I. Murakoshi, K. Toriizuka, J. Haginiwa, S. Ohmiya and H. Otomasu, *Chem. Pharm. Bull.* (Tokyo), **27**, 151 (1979).
4) D. Schumann, N. Neuner-Jehle and G. Spiteller, *Monatsh. Chem.*, **99**, 390 (1968); N. Neuner-Jehle, H. Nesvadba and G. Spiteller, *Monatsh. Chem.*, **95**, 687 (1964).
5) All chemical shifts, multiplicities and coupling constants were obtainable either from direct inspection, employment of a shift reagent(Eu(fod)$_3$), or from appropriate decoupling experiments.
6) In the PMR spectrum of I in $CDCl_3$, the signals corresponding to 10-H_α and 10-H_β were observed at δ 4.00 and δ 3.41, respectively.

nitrogen in the quinolizidone moiety because of their low field chemical shifts.[7,8] Irradiation at δ 1.28 (1H, br.s, 9-H) caused the signal at δ 4.00 (10-H_α) to become a doublet (J=13.5 Hz). These data provided the presence of a $-CO-\underset{|}{N}-CH_2CH<$ unit in the molecule. Three signals revealed the prominent downfield shift by the addition of Eu(fod)$_3$ in comparison with other signals. Two of them were the signals above described of 10-H_α and 10-H_β, indicating the coordination of Eu(fod)$_3$ to the lactam C=O, and hence the third signal at δ 2.82 (2H, br.s, 3-H_2) was assigned to the methylene protons adjacent to the lactam C=O. The pair of double triplets centered at δ 4.92 (1H, J=10 and 1.5 Hz, 5-H) and δ 5.16 (1H, J=10 and 3 Hz, 4-H), both ascribable to olefinic protons, were collapsed to a sharp AB quartet (J=10 Hz) on irradiation at δ 2.82 (3-H_2), indicating that one end of the double bond neighbors with a quarternary carbon. The signal at δ 70.0 (s) in the ^{13}C-NMR spectrum (C_6D_6) can be assigned to a quarternary carbon bearing a nitrogen. These results suggested that I contained the partial structure **1**.

When a signal centered at δ 2.14 (2H, complicated octet, 15-H_2) ascribable to allylic methylene protons was irradiated, three signals due to terminal vinyl protons centered at δ 5.78 (1H, fourteen-peaks, J=17, 10, 7 and 6 Hz, 16-H), δ 5.05 (1H, fine split doublet, J=17 Hz, 17-H′) and δ 4.90 (1H, fine split doublet, J=10 Hz, 17-H) were transformed into three pairs of doublets (J=17 and 10 Hz, J=17 and 2 Hz, and J=10 and 2 Hz, respectively), and the signal at δ 2.64 (1H, t, J=7.5 Hz, 14-H) into a singlet. The PMR signal at δ 2.64 (14-H) was ascertained to correlate to the ^{13}C-NMR signal at δ 75.7 (*d*) by single frequency off resonance decoupling (SFORD) experiments, and the signal positions indicated that this methin carbon was bonded to a nitrogen. These data suggested the partial structure **2**. The partial structure **1** and **2** were expanded to **3** because the molecule had only one quarternary carbon as described above.

Table I. PMR and ^{13}C-NMR Data for Tsukushinamine (I) in C_6D_6

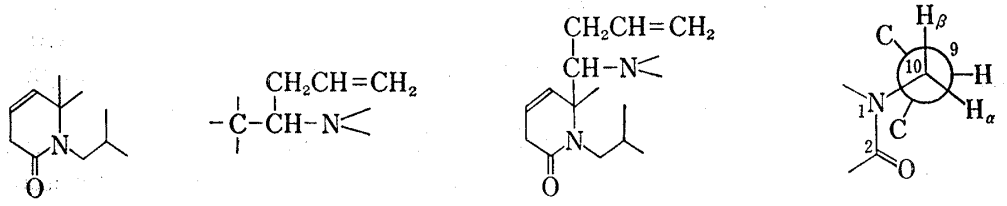
Chemical shifts[a] ^{13}C[b]	Chemical shifts[a] ^{1}H	No. of protons	Assignment	Multiplicity, J(Hz)
167.2(s) (CO–N)			2	
32.1(t) (–CH_2–)	2.82	2	3	br. s
119.2(d) (–CH=)	5.16	1	4	dt, $J_{4,5}$=10, $J_{3,4}$=3
129.6(d) (–CH=)	4.92	1	5	dt, $J_{4,5}$=10, $J_{3,5}$=1.5
70.0(s) (–$\underset{|}{C}$–N)			6	
46.8(d) (–CH<)	1.80	1	7	br. s
31.5(t) (–CH_2–)	1.22	2	8	br. s
28.6(d) (–CH<)	1.28	1	9	br. s
51.4(t) (–CH_2–N)	4.00	1	10(H_α)	dd, $J_{10,10'}$=13.5, $J_{10,9}$=6
	3.24	1	10′(H_β)	d, $J_{10,10'}$=13.5, $J_{10',9}\approx$0
52.4(t) (–CH_2–N)	2.62	2	11[c]	br. s
61.2(t) (–CH_2–N)	2.44	2	13[c]	br. s
75.7(d) (>CH–N)	2.64	1	14	t, $J_{14,15}$=$J_{14,15'}$=7.5
32.1(t) (–CH_2–)	2.14	2	15 and 15′	Complicated octet
135.8(d) (–CH=)	5.78	1	16	Fourteen peaks, $J_{16,17}$=10, $J_{16,17'}$=17, $J_{15,16}$=7, $J_{15',16}$=6
115.8(t) (=CH_2)	4.90	1	17	Fine split d, $J_{16,17}$=10
	5.05	1	17′	Fine split d, $J_{16,17'}$=17

a) δ Values in ppm from TMS as internal standard.
b) ^{13}C-^{1}H correlations are based on detailed single frequency off resonance decoupling (SFORD) experiments.
c) Assignment could be reversed.

7) F. Bohlmann and D. Schumann, *Tetrahedron lett.*, **1965**, 2435.
8) A. Ueno, K. Morinaga, S. Fukushima, Y. Iitaka, Y. Koiso and S. Okuda, *Chem. Pharm. Bull.* (Tokyo), **23**, 2560 (1975).

The PMR spectrum of I (C_6D_6) exhibited the remaining signals at δ 1.80 (1H, br.s, 7-H) due to a methin group, and δ 1.22 (2H, br.s, $W_{h/2}$=7.5 Hz, 8-H_2), δ 2.62 (2H, br.s, $W_{h/2}$= 6 Hz, 11 or 13-H_2) and δ 2.44 (2H, br.s, $W_{h/2}$=4 Hz, 11 or 13-H_2) for three methylene groups, which were consisted of magnetically equivalent geminal protons and not adjacent to one another as judged from their narrow band width. The latter two signals were assigned to methylene protons adjacent to a nitrogen because these signals were correlated to the ^{13}C-NMR signals at δ 52.4 (t) and δ 61.2 (t), respectively, by SFORD experiments.

Consideration of the above data allowed for two possible gross molecular structures, I and II.



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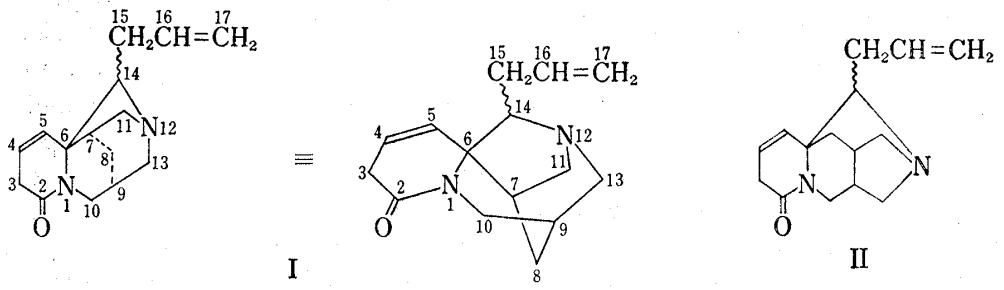

I II

The spatial structure **4** for the structural unit, $-CO-\overset{H}{\underset{H}{N}}-\overset{H}{C}_{10}-\overset{H}{C}_{9}-$, was elucidated from the chemical shifts and vicinal coupling constants of 10-H_α (δ 4.00, $J_{H_\alpha,9-H}$=6 Hz) and 10-H_β (δ 3.24, $J_{H_\beta,9-H}\approx 0$). Examination of molecular models revealed that this structural relationship could be explained reasonably for the structure I but not for the structure II.

From the above discussion, the structure of tsukushinamine was elucidated as the tetracyclic structure I.

Further investigation on the absolute configurations at the positions 7, 9 and 14 are being undertaken in our laboratories.

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