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Structure of 6-Epiforsticine and Revision of the Stereochemistry of Forsticine

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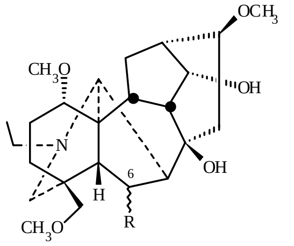
Abstract: A norditerpenoid alkaloid, 6-epiforsticine, has been isolated from the roots of the plants *Aconitum hemsleyanum* var. *pengzhouense and A. kuzsnezoffii* and its structure has been established as **1** on the basis of 2D-NMR and X-ray diffraction analysis. The structure of forsticine has accordingly been revised from **1** to **2**.

Keywords: Norditerpenoids alkaloid, 6-epiforsticine, forsticine.

In the course of our investigation on *Aconitum* and *Delphinium* species, we have isolated a number of norditerpenoid and diterpenoid alkaloids from *A. kuzsnezoffii* and *A. hemsleyanum* var. *pengzhouense*[1~6]. We have found that a norditerpenoid alkaloid, 6-epiforsticine isolated from both plants shows a great deal of similarity to forsticine[7] but significantly differed from the latter in its ^{13}C NMR spectrum (**Table l**), suggesting that the alkaloids were a pair of epimers at C-6. The present communication deals with elucidation of the structure of 6-epiforsticine as **1** by 2 D-NMR and X-ray diffraction analysis, as well as a revision of the structure of forsticine from **1** to **2**.

6-Epiforsticine[7] **1** was isolated as colorless needles with mp 114-116 ℃ (ether-hexane) and $[\alpha]_D^{24}$ +43.0 (c 0.73, $CHCl_3$)[5, 8]. Its molecular formula, $C_{24}H_{39}NO_6$, was established by MS, ^{1}H (^{13}C) NMR spectra. The FABMS of **1** showed distinctive fragment ion peaks at *m/z* 438 (M+1,100) and 406 (M-31, 10). The NMR spectra of **1** gave signals at δ_H 1.05 (3H, t, *J*=7.2 Hz), δ_C 49.0 t and 13.4 q for an *N*-ethyl group, δ_H 3.20, 3.22 and 3.28 (each 3H, s), δ_C 55.9 q, 56.2q and 59.0 q for three methoxyl groups. Its NMR spectra showed the connectivities of the signals at δ_H 4.12 (1H, t, *J*=4.8 Hz) and 4.80 (1H, s, *J*=6.8 Hz) with that at δ_C 75.1 d and 71.6 d (HMQC), respectively, and the signal at δ_C 73.7 s, indicating that it had two secondary hydroxyl groups and one tertiary hydroxyl group. The 1H triplet (*J*=4.8 Hz) signal at δ_H 4.12 (δ_C 75.1 d) was assigned to H-14β, suggesting the presence of an OH-14α group. Location of the hydroxyl group at C-8 was carried out due to two- and three-bond connectivities of C-8 with H-7 (δ_H1.96, 1H, m; δ_C 56.3 d), H_2-15 (δ_H 2.08, 1H, d, *J*=16.4 Hz and 2.41, 1H, dd, *J*=16.4, 9.2 Hz; δ_C 38.9 t), H-6 (δ_H 4.80 1H, d, *J*=6.8 Hz; δ_C 71.6 d), H-10 (δ_H 1.77, hidden; δ_C 45.5 d) and H-14 (δ_H 4.12, 1H, t, *J*=4.8 Hz; δ_C 75.1 d) signals in the HMBC spectrum of **1**. The 1H doublet (*J*=6.8 Hz) distinctive signal at δ_H 4.80 (δ_C 71.6 d) was assigned to H-6 when compared with forsticine **2**[7]. Comparison of these two alkaloids showed that they had similarities of NMR data except for some signals such as C-5, C-7, C-10, C-21 (*N*CH_2) (**Table l**) and H-6 (forsticine: δ 4.90, d, *J*=7.0 Hz)[8]. It is of interest to point out the difficulty of separating 6-epiforsticine and forsticine by TLC with a variety of solvent systems. Finally, the structure of 6-epiforsticine was established as **1** by an X-ray diffraction analysis (**Figure 1**). It is apparent that the structure of forsticine should be accordingly revised from **1** to **2**.

Figure 1 ORTEP drawing for 6-epiforsticine **1**



1 R=α-OH
2 R=β-OH

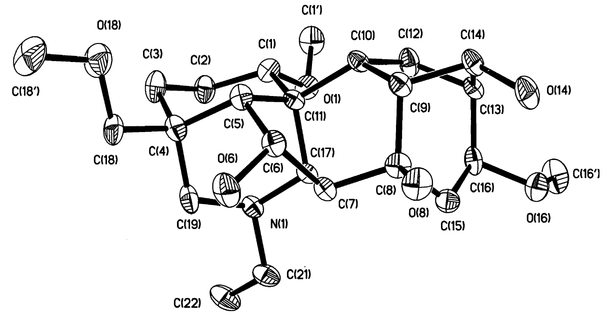


Table 1 ^{13}C NMR data of 6-Epiforsticine **1** and Forsticine **2**[8,9] ($CDCl_3$, 100 MHz)

	1	2		1	2		1	2
carbon	δ_C	δ_C	carbon	δ_C	δ_C	carbon	δ_C	δ_C
1	85.7 d	85.7	9	48.6 d	48.9	17	62.3 d	62.6
2	25.7 t	25.8	10	45.4 d	49.6	18	80.6 t	80.8
3	35.0 t	34.8	11	50.5 s	50.6	19	53.9 t	54.3
4	39.1 s	39.1	12	28.5 t	28.8	NCH_2CH_3	49.0 t	50.4
5	50.4 d	49.3	13	38.2 d	38.7	NCH_2CH_3	13.4 q	13.5
6	71.6 d	71.9	14	75.1 d	75.3	1'	56.2 q	56.1
7	56.3 d	54.3	15	38.9 t	39.4	16'	55.9 q	56.4
8	73.7 s	74.0	16	81.9 d	82.2	18'	59.0 q	59.2

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References and Notes

1. Z. B. Li., F. P. Wang, *Chin. Chem. Lett*, **1995**, *7*, 443.
2. Q. Y. Xu., Z. B. Li., F. P. Wang., C. T. Che, *Heterocycles*, **1996**, *43*, 1243.
3. Z. B. Li., F. P. Wang., C. T. Che, *J. Nat. Prod*, **1998**, *61*, 1555.
4. Z. B. Li., F. P. Wang., *J. Asian. Nat. Prod. Res*, **1998**, *1*, 87.
5. Z. B. Li., G. H. Lu., D. L. Chen., F. P. Wang., *Nat. Prod. R&D*, **1997**, *9* (1), 9.
6. C. S. Peng., X. P. Dai., D. L. Chen., F. P. Wang., *Nat. Prod. R & D*, **1999**, *11* (3), 23.
7. **1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.02 (1H, dd, *J*=10.4, 6.4 Hz, H-1β), 1.88 (1H, m, H-2β), 2.28 (1H, m, H-2α), 1.52 (1H, ddd, *J*=10.4, 10.4, 3.2 Hz, H-3β), 1.69 (1H, m, hidden, H-3α), 1.96 (1H, hidden, H-5), 4.80 (1H, d, *J*=6.8 Hz, H-6β), 1.96 (1H, m, hidden, 7-H), 2.23 (1H, t, *J*=5.2 Hz, H-9), 1.78 (1H, m, hidden, H-12β), 1.99 (1H, m, hiddem, H-12α), 2.28 (1H, m, hidden, H-13), 4.12 (1H, t, *J*=4.8 Hz, H-14β), 2.08 (1H, d, *J*=16.4 Hz, H-15α), 2.41 (1H, dd, *J*=16.4, 9.2 Hz, H-15β), 3.32 (1H, m, hidden, H-16), 3.06 (1H, s, H-17), 3.40, 3.80 (each 1H, ABq, *J*=8.4 Hz, H_2-18), 2.62, 2.79 (each 1H, ABq, *J*=10.8 Hz, H_2-19), 2.58 (2H,m, NCH_2-), 1.09 (3H, t, *J*=7.2 Hz, NCH_2CH_3), 3.34 (3H, s, OCH_3-1'), 3.24 (3H, s, OCH_3-16'), 59.0 (3H, s, OCH_3-18').
8. S. W. Pelletier., S. Y. Chen., B. S. Joshi., H. K. Desai., *J. Nat. Prod*, **1984**, *47*, 474.
9. B. S. Joshi, J. K. Wunderlich, S. W. Pelletier, *Can. J. Chem*, **1987**, *65*, 99.

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