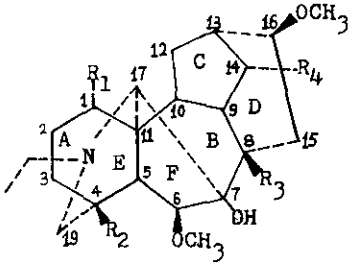
THE STRUCTURES OF FOUR NEW DITERPENOID ALKALOIDS FROM DELPHINIUM BONVALOTII FRANCH

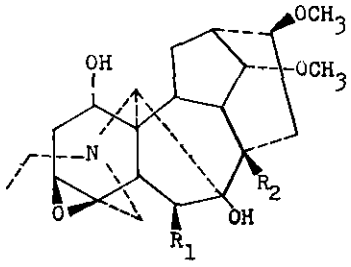
Qing Ping Jiang[1] and Wei Liang Sung*
The Institute of Materia Medica, Chinese Academy of Medical Sciences
1 Xiang Nong Tan Street, Beijing, China

Abstract - Continued investigation of the alkaloids of Delphinium bonvalotii Franch has led to the isolation and structural determination of four new diterpenoid alkaloids, delbotine (1), delboxine (3), delbonine (5) and delbine (6), together with two known bases, deltamine and deltaline. Structures 1 and 3 were confirmed by x-ray analyses. Delboxine (3) and delbine (6) are the first examples of C_{18}-diterpenoid alkaloids bearing C(6)-oxygenated substituent.

During our continued studies of the alkaloids from the root of Delphinium Bonvalotii Franch growing in China, we have isolated four more new diterpenoid alkaloids, delbotine (1), delboxine (3), delbonine (5) and delbine (6), together with two known alkaloids, deltamine and deltaline, in addition to the previously reported new bases bonvalotine, bonvalol and bonvalone.[2]



		R_1	R_2	R_3	R_4
1	Delbotine	OH	CH_2OCH_3	OCH_3	OCH_3
2		OH	CH_2OCH_3	OH	OCH_3
5	Delbonine	OH	CH_2OCH_3	OCH_3	OAc
6	Delbine	OH	OH	OH	OH
7		OAc	OH	OH	OAc
8		OH	CH_2OCH_3	OH	OAc



3 Delboxine $R_1 = R_2 = OCH_3$

4 R_1 = H, R_2 = OH

Delbotine, $C_{26}H_{43}NO_7$ (M^+ 481.3059, calc. 481.3039), mp 155-157°C, $[\alpha]_D^{18}$+13.6°(c 0.1, $CHCl_3$), showed spectra characteristic to lycoctonine-type alkaloid. IR indicated two hydroxyls (3430 (br); 3150 (br)). ^1H nmr showed an NCH_2CH_3 (δ1.05, 3H, t, J= 7.2 Hz) and five methoxyls (δ3.34, 6H, s; 3.39, 9H, s). The signal at δ3.62 (1H, m, $W\frac{1}{2}$= 7.0 Hz) was attributed to the hydrogen at C(1) bearing α-OH,[3] and this was substantiated by the finding that acetylation of delbotine with Ac_2O/Py afforded monoacetyldelbotine (M^+ 523) in which the signal of C(1)-βH shifted to δ4.69 (t, J= 9.0 Hz). The absorptions at δ3.78 (1H, br s) and δ3.42 (1H, t, J= 5.4 Hz) would indicate the existence of methoxyls at C(6)-β and C(14)-α positions, respectively, since no downfield shifts were observed on both signals by acetylation. One methoxyl was situated at C(18) based on the triplet at 79.1 ppm found in the ^{13}C nmr of delbotine, and another methoxyl was assigned to C(16) on account of the biogenetics. The position of the remaining methoxyl of delbotine could be either C(7) (with C(8)-OH) or C(8) (with C(7)-OH). When comparison was made, however, between the ^{13}C nmr (Table 1) of delbotine and that reported for delsoline (2),[4] it revealed that the chemical shift of C(15) in the former appeared at a higher field (29.9 ppm) than that of the latter (33.5 ppm), while no significant difference was observed for their C(6) chemical shift values. This was found to be in accordance with the case between ambiguine (with C(8)-OCH_3 and 28.5 ppm for C(15)) and browniine-14-acetate (with C(8)-OH and 33.7 ppm for C(15)).[5] It was thus feasible to postulate delbotine to have structure 1, with C(7)-OH and C(8)-OCH_3. Subsequently, this structure was confirmed by the X-ray analysis.[6]

Delboxine, $C_{24}H_{37}NO_7$ (M^+ 451. 2567, calc. 451.2569), mp 200-202°C, $[\alpha]_D^{18}$+43.5°(c 0.1, $CHCl_3$). Spectral data indicated two hydroxyls (3430 (br); 3180 (br) cm^{-1}), an NCH_2CH_3 (δ1.03, 3H, t, J= 7.2 Hz), and four methoxyls (δ3.34, 3.43, each 3H, s; 3.37, 6H, s). The signal at δ3.86 (1H, m, $W\frac{1}{2}$= 6.8 Hz) was attributed to C(1)-βH of ring A in boat form. Acetylation (Ac_2O/Py) of the base yielded monoacetyldelboxine (M^+ 493) in which C(1)-βH appeared as quadruplet (J= 3.6, 2.0 Hz) at δ5.07, indicating that ring A remained in boat form. This strongly suggested that delboxine, like monticoline (4),[7] possessed C(3),C(4)-epoxy group which requires ring A to exist in boat form regardless of C(1)-substituent being hydroxyl or acetyloxyl. The monoketone obtained by oxidation (CrO_3/Py) of delboxine demonstrated an absorption at 1740 cm^{-1}, accompanied with the disappearance of the inner hydrogen-bonded hydroxyl at 3180 cm^{-1}. The higher value (1740 cm^{-1}) than that for normal cyclohexanone also supported a boat form of ring A in which the keto group takes part of a strained boat-form

cyclohexanone. Carbons in rings B, C and D of delboxine, however, showed quite similar ^{13}C nmr values corresponding to that of delbotine (1), except for C(11) which shifted 3.0 ppm downfield as a result of the strain effect of the 3-membered ring (Table 1). The existence of C(6)-βOCH$_3$ in delboxine was similarly demonstrated by a one-proton broad signal at lower field (δ4.16) than that of delbotine (δ3.78). Based on the above reasoning, structure 3 was assigned to delboxine. This structure was subsequently confirmed by the X-ray analysis.[6]

Delbonine, $C_{27}H_{43}NO_8$ (M^+ 509.2931, calc. 509.2988), $[\alpha]_D^{16}$ +41.1° (c 0.1, $CHCl_3$), was a non-crystalline minor alkaloid. IR showed 3450 (br) and 3180 (br) cm^{-1} (2× OH). ^1H nmr spectrum, characteristic to lycoctonine-type alkaloid, showed signals of δ1.14 (3H, t, J = 8.0 Hz, $NCH_2\underline{CH}_3$), 2.04 (3H, s, $OCOCH_3$), 3.32 (3H, s, OCH_3). 3.38 (9H, s, 3×OCH_3), 3.72 (1H, m, $W_{\frac{1}{2}}$ = 7.2 Hz, HO-C(1)-$\beta\underline{H}$), 3.84 (1H, br s, CH_3O-C(6)-$\alpha\underline{H}$, and 4.80 (1H, t, J = 4.7 Hz, AcO-C(14)-$\beta\underline{H}$). MS gave 478.2827 (M^+-OCH_3) as base peak, indicating that delbonine possessed C(8)-OCH_3. One methoxyl was assigned to C(18) since no signal corresponding to C(4)-CH_3 was observed in ^1H nmr. One hydroxyl was required to be placed at C(7). Thus, considering the structures of its congeners 1 and 3, structure 5 was tentatively assigned for delbonine.

Delbine, $C_{22}H_{35}NO_7$ (M^+ 425.2465, calc. 425.2414), mp 116-118°C, $[\alpha]_D^{27}$+53.3° (c 0.1, CH_3OH). IR showed hydroxyls (3470, 3420 (br) cm^{-1}). ^1H nmr (C_5D_5N) displayed signals of an NCH_2CH_3 (δ0.80, 3H, t, J = 7.2 Hz), two methoxyls (δ3.02, 3.12, each 3H, s), C(1)-βH (δ3.50, 1H, m, $W_{\frac{1}{2}}$ = 7.2 Hz), C(14)-βH (δ4.03, 1H, t, J = 4.8 Hz) and C(6)-αH (δ4.38, 1H, br s). Acetylation of delbine with Ac_2O/Py afforded diacetyldelbine (7) in which the signals for C(1)-βH and C(14)-βH shifted downfield to δ4.71 (t, J = 9.0 Hz) and 4.84 (t, J = 5.0 Hz), respectively. This revealed that two hydroxyls in delbine were located at C(1) and C(14) in α-orientation. ^{13}C nmr of diacetyldelbine (7) showed a quaternary carbon signal at 69.3 ppm, indicating the existence of C(4)-OH.[4] Moreover, the ^{13}C nmr chemical shifts (Table 1) of C(6)~C(16) in diacetyldelbine (7) were very similar to that of 14-acetyldelcosine (8),[4] demonstrating that 7 possessed the same substituents at the same locations in rings B, C and D as 8. Thus, structure 6 was assigned to delbine.

It is interesting that both delboxine (3) and delbine (6) are C_{18}-diterpenoid alkaloids possessing a methoxyl at C(6), while no C(6)-substitution was found in the naturally occurring C_{18}-diterpenoid alkaloids reported so far.

Table 1. Carbon-13 Chemical Shifts and Assignments for Delbotine (1), Delsoline (2), Delboxine (3), Diacetyldelbine (7) and 14-Acetyldelcosine (8)[a]

	1	2	3	7	8
C(1)	72.5	72.6	77.0	76.1	72.6
C(2)	27.3	27.2	31.9	28.4	27.2
C(3)	29.6	29.3	52.3	37.0	29.9
C(4)	37.4	37.4	58.8	69.3	37.5
C(5)	39.5	43.9	39.2	55.9	43.5
C(6)	91.5	90.4	90.5	89.3	90.2
C(7)	91.4	87.8	92.7	88.6	87.6
C(8)	82.3	78.5	82.2	77.6	78.4
C(9)	49.4	44.9	50.8	44.9	44.9
C(10)	37.0	37.7	36.8	37.9	38.0
C(11)	51.0	49.3	54.0	49.6	49.2
C(12)	30.3	30.5	30.6	29.7	29.4
C(13)	45.2	43.3	43.7	42.7	42.6
C(14)	84.4	84.5	83.9	75.4	76.3
C(15)	29.9	33.5	29.6	33.7	33.8
C(16)	83.4	82.9	83.1	82.9	82.7
C(17)	66.2	66.0	67.0	62.9	66.1
C(18)	79.1	77.3	-	-	77.3
C(19)	57.5	57.2	54.4	58.5	57.2
N-CH_2	50.4	50.3	49.9	50.0	50.3
CH_3	13.7	13.5	14.0	13.6	13.6
C(6)'	59.4	57.2	60.3	58.5	57.2
C(8)'	57.7	-	57.5	-	-
C(14)'	57.7	57.9	57.9	-	-
C(16)'	56.4	56.3	56.2	56.2	56.3
C(18)'	59.4	59.1	-	-	59.1
C(1)-OCO	-	-	-	170.1	-
CH_3	-	-	-	21.8	-
C(14)-OCO	-	-	-	171.6	171.4
CH_3	-	-	-	21.4	21.4

a. Chemical shifts in ppm downfield from TMS. The solvent is $CDCl_3$

REFERENCES AND NOTES

1. Part of the M.S. thesis of Q. P. J.

2. Q. P. Jiang and W. L. Sung, Heterocycles, 1984, 22 (11), (in press).

3. A. G. Gonzaléz, G. de la Fuente and R. Diaz, Phytochemistry, 1982, 21, 1781.

4. T. A. Broadbent and E. G. Paul, Heterocycles, 1983, 20, 863.

5. S. W. Pelletier, R. S. Sawhney and N. V. Mody, Heterocycles, 1978, 9, 1241.

6. Lin Xiuyun and Zheng Qi-Tai, personal communication.

7. E. F. Ametova, M. S. Yunusov, V. E. Bannikova, N. D. Abdullaev and V. A. Tel'nov, Khim. Prir. Soedin., 1981, (4), 446.

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