

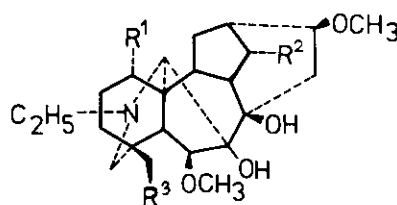
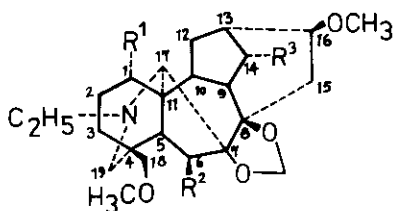
THREE NEW C₁₉-DITERPENOID ALKALOIDS, DELBRUNINE, DELBRULINE
AND DELBRUSINE FROM DELPHINIUM BRUNONIANUM ROYLE

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Abstract - The structure elucidations of delbrunine (1),
delbruline (2) and delbrusine (3) isolated from Delphinium
brunonianum Royle are presented.

In a previous paper we have reported the structure of brunonine, a C₂₀-diterpenoid alkaloid isolated from Delphinium brunonianum Royle¹. This paper presents the structure elucidations of three unreported C₁₉-diterpenoid alkaloids designated as delbrunine (1), delbruline (2) and delbrusine (3) obtained from the same plant. Four known alkaloids were also isolated and identified as delcosine (4), browniine (5), lycoctonine (6) and septentriodine (7).



- 1 $R^1 = R^3 = OH, R^2 = OCH_3$ Delbrunine
 2 $R^1 = R^2 = OCH_3, R^3 = OH$ Delbruline
 3 $R^1 = R^2 = R^3 = OCH_3$ Delbrusine
 8 $R^1 = OH, R^2 = OCH_3, R^3 = OAc$
 9 $R^1 = R^3 = OCH_3, R^2 = OH$
 10 $R^1 = R^2 = OCH_3, R^3 = OAc$

- 4 $R^1 = R^2 = OH, R^3 = OCH_3$
 5 $R^1 = R^3 = OCH_3, R^2 = OH$
 6 $R^1 = R^2 = OCH_3, R^3 = OH$
 7 $R^1 = R^2 = OCH_3, R^3 = OAr$
 Ar = $COC_6H_4-O-HNCOCH_2$
 CH_3OOCCH_2

Delbrunine, C₂₅H₃₉NO₇ (M⁺ 465.2665, calc. 465.2726), mp 178°C, (α)_D¹⁷ 0° (c 0.08, EtOH). Its ¹H-NMR showed the presence of an N-C₂H₅ group (δ 1.16, 3H, t, J = 7.2 Hz), three methoxyls (δ 3.37, 3.35, 3.33, 3H each, s) and a methylenedioxy group

(δ 5.12, 5.09, 1H each, s), demonstrating that the compound was a lycoctonine-type diterpenoid alkaloid². The signals δ 3.72 (1H, s) in $^1\text{H-NMR}$ and 88.3 ppm (d) in $^{13}\text{C-NMR}$ spectra indicated that an OCH_3 group was located at C(6) position with β -orientation^{3,4}. The existence of C(18)- OCH_3 was evidenced by the $^{13}\text{C-NMR}$ absorption at 77.9 ppm (t)⁴. One methoxyl group was assigned to C(16)- β -position on account of $^{13}\text{C-NMR}$ peak at 81.7 ppm (d)⁴ as well as the biogenetic considerations of those known naturally occurring lycoctonines⁵. IR of delbrunine exhibited the absorption of hydroxyls (3388 cm^{-1} , br), one of which would be placed at C(1) position because of the $^{13}\text{C-NMR}$ data: a methine doublet at 71.8 ppm together with the matching methylene triplets at 27.2 and 29.4 ppm assigned to C(2) and C(3), respectively⁴. Another hydroxyl group is situated at C(14)- α -position based on the peak δ 4.88 (1H, t, $J = 4.8\text{ Hz}$) in $^1\text{H-NMR}$ of delbrunine monoacetate (8)⁶. $^{13}\text{C-NMR}$ spectral data of delbrunine were found to be in agreement with its postulated structure 1 when comparison was made with that of known compounds delcosine (4)⁴ and delcorine (9)⁷ (Table 1). Thus, structure 1 was assigned to delbrunine. Since the structure of delbrunine (1) differs with that of delcosine (4) only in its C(7), C(8) substituents, cleavage of the methylenedioxy group of 1 in mineral acid was carried out², and the product in quantitative yield was proved to be identical (R_f , IR, MS and mmp) with 4. Consequently, the structure 1 for delbrunine is substantiated.

Delbruline, $\text{C}_{26}\text{H}_{41}\text{NO}_7$ (M^+ 479.2914, calc. 479.2883), mp 129-131°C, (α)_D²⁰ 0° (c 0.09, CHCl_3). $^1\text{H-NMR}$ (δ) indicated it was a lycoctonine-type alkaloid: 1.06 (3H, t, $J = 7.2\text{ Hz}$, NCH_2CH_3), 3.26, 3.32, 3.36, 3.36 (3H each, s, 4 X OCH_3) and 5.13, 5.16 (1H each, s, OCH_2O). The similarity between $^1\text{H-NMR}$ of delbruline and that of delbrunine (1) as well as the fact that the former possessed one more methoxyl group and 14 atomic-mass-unit higher than the latter implied that delbruline may be the C(1)-OH or C(14)-OH methylated derivative of delbrunine (1). Acetylation of delbruline gave a monoacetate (10) (M^+ 521) which showed in its $^1\text{H-NMR}$ spectrum (δ) a signal at 2.06 (3H, s, OAc) and a one-proton-triplet centered at 4.82 with $J = 4.6\text{ Hz}$, while the broad singlet at 4.08 found originally in the $^1\text{H-NMR}$ of delbruline disappeared. This indicated that there is a hydroxyl group situated at C(14)- α -position⁶, the same as in the case of delbrunine (1). Consequently, it is reasoned that it must be the hydroxyl group at C(1) of delbrunine being methylated to become delbruline, and the structure of the latter could be denoted as 2. This was then verified through correlation between delbruline and delbrunine (1). 1

Table 1. The Carbon-13 NMR spectra^a of delbrunine (1), delbruline (2), delbrusine (3), delcosine (4) and delcorine (9)

Carbons	1	2	3	4	9
1	71.8 (d)	83.2 (d)	82.1 (d)	72.7	83.1
2	27.2 (t)	26.7 (t)	26.7 (t)	27.5	26.4
3	29.4 (t)	31.9 (t)	31.6 (t)	29.4	31.8
4	37.1 (s)	37.9 (s)	39.0 (s)	37.6	38.1
5	42.0 (d)	51.0 (d)	52.3 (d)	44.0	52.6
6	88.3 (d)	88.5 (d)	89.5 (d)	90.1	78.9
7	92.1 (s)	93.7 (s)	92.5 (s)	87.9	92.7
8	83.4 (s)	80.7 (s)	84.0 (s)	78.1	83.9
9	45.7 (d)	48.0 (d)	48.7 (d)	45.3	48.1
10	46.6 (d)	42.1 (d)	40.2 (d)	45.3 ^b	40.3
11	50.7 (s)	49.0 (s)	50.7 (s)	48.9	50.2
12	29.0 (t)	25.7 (t)	28.3 (t)	29.4	28.1
13	38.6 (d)	36.0 (d)	37.9 (d)	39.4 ^b	37.9
14	74.7 (d)	74.2 (d)	82.1 (d)	75.8	82.5
15	36.5 (t)	32.1 (t)	35.0 (t)	34.5	33.3
16	81.7 (d)	81.8 (d)	81.9 (d)	82.0	81.8
17	65.8 (d)	64.4 (d)	64.3 (d)	66.3	63.9
18	77.9 (t)	78.3 (t)	79.0 (t)	77.4	78.9
19	57.4 (t)	53.4 (t)	53.9 (t)	57.1	53.7
N-CH ₂	50.1 (t)	50.4 (t)	50.7 (t)	50.4	50.7
CH ₃	13.5 (q)	13.9 (q)	13.4 (q)	13.7	14.0
1'	-	55.5 (q)	55.1 (q)	-	55.5
6'	58.1 (q)	58.1 (q)	58.5 (q)	57.4	-
14'	-	-	57.8 (q)	-	57.8
16'	56.2 (q)	56.2 (q)	56.2 (q)	56.4	56.3
18'	59.2 (q)	59.1 (q)	59.5 (q)	59.1	59.6
OCH ₂ O	94.1 (t)	93.7 (t)	94.0 (t)	-	92.9

a. Chemical shifts in ppm downfield from TMS; solvent CDCl₃.

b. These two values have been reversed as suggested by S.W. Pelletier, S.K.

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was acetylated ($\text{Ac}_2\text{O}/\text{CF}_3\text{CO}_2\text{H}$) under controlled condition to yield the 14-acetyl derivative (8)⁶, and the monoacetate in turn methylated at C(1) in the usual manner⁸ to afford a product which was demonstrated to be identical (R_f , IR and MS) with the acetylated compound of delbruline (10).

Delbrusine, $\text{C}_{27}\text{H}_{43}\text{NO}_7$ (M^+ 493.3032, calc. 493.3039), mp 141 C, $(\alpha)_D^{17} +16.8^\circ$ (c 0.057, CHCl_3). $^1\text{H-NMR}$ (δ) showed this compound was a lycoctonine-type alkaloid: 1.06 (3H, t, $J = 7.0$ Hz, NCH_2CH_3), 3.32, 3.33, 3.38, 3.42, 3.43 (3H each, s, OCH_3) and 5.11, 5.16 (1H each, s, OCH_2O)². Delbrusine exhibited close similarity with delbruline (2) in $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$, IR and MS except that the former showed no hydroxyl absorption in IR and an increment of 14 atomic-mass-unit (CH_2) in MS than that of the latter. Hence, it is reasonable to regard delbrusine as a methylated derivative of delbruline (2). To confirm this, delbruline (2) was methylated in the usual manner⁸, and the crystalline product so obtained was demonstrated to be identical with delbrusine in all respects including R_f , MS and mmp. Therefore the structure of delbrusine was determined as 3.

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