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6-OXOCORUMDEPHINE AND 18-METHOXYELADINE, NEW NORDITERPENE ALKALOIDS FROM THE AERIAL PART OF *Delphinium uralense*

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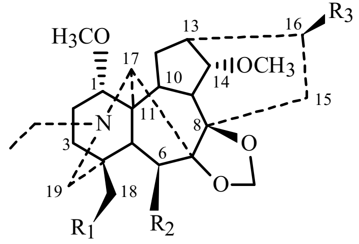
The new norditerpene alkaloids 6-oxocorumdephine and 18-methoxyeladine were isolated from the aerial part of Delphinium uralense *N. The structures 16β-hydroxy-7,8-methylenedioxy-6-oxo-1α,14α,18-trimethoxy-*N*-ethylaconitane and 6β,16β-dihydroxy-7,8-methylenedioxy-1α,14α,18-trimethoxy-*N*-ethylaconitane were proposed based on PMR, ^{13}C NMR, IR, and mass spectra.*

Key words: *Delphinium uralense*, norditerpene alkaloids, 6-oxocorumdephine, 18-methoxyeladine.

In continuation of studies of the alkaloids from the aerial part of *Delphinium uralense* N. collected during the start of budding in the Southern Urals (Zilair Plateau), two new bases **1** and **2**, called by us 6-oxocorumdephine and 18-methoxyeladine, respectively, were isolated from the moderately basic fraction (pH 6) [1, 2].



1 - 6

1: $R_1 = OCH_3$, $R_2 = O$, $R_3 = OH$; **2:** $R_1 = OCH_3$, $R_2 = R_3 = OH$
3: $R_1 = OCH_3$, $R_2 = H$, $R_3 = OH$; **4:** $R_1 = OCH_3$, $R_2 = O$, $R_3 = OCH_3$
5: $R_1 = H$, $R_2 = R_3 = OH$; **6:** $R_1 = R_3 = OCH_3$, $R_2 = OH$

The IR spectrum of **1** contained bands for hydroxyl (3300-3500 cm^{-1}) and ketone (1750). The high-resolution mass spectrum gave a molecular weight of 463.2570, which corresponded to $C_{25}H_{37}NO_7$. The PMR was consistent with three methoxyls (δ 3.26, 3.30, 3.38 ppm), an *N*-ethyl (1.02), and methylenedioxy (5.07, 5.50). The mass sepctrum was characteristic of C_{19}-diterpene alkaloids. The fact that the base peak in the mass spectrum of **1** was the ion $[M - 31]^+$ indicated that one of the three methoxyls was located on C-1 [3]. The presence in the PMR spectrum of a 1H triplet (J = 4.5 Hz) at δ 3.69 ppm was consistent with an α-methoxyl on C-14 and the lack of substituents on C-9, C-10, and C-13 [4]. The presence of the third methoxyl on C-18 was confirmed by the presence in the ^{13}C NMR spectrum of a triplet at δ 76.6 ppm in addition to doublets for C-14 (82.8) and C-1 (83.2) [5].

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TABLE 1. Chemical Shifts in ^{13}C NMR Spectra of 6-Oxocorumdephine (**1**), 18-Methoxyeladine (**2**), Corumdephine (**3**) [8], 6-Dehydrodelcorine (**4**) [9], Eladine (**5**) [10], and Delcorine (**6**) [5]

C atom	δ, ppm					
	1	**2**	**3**	**4**	**5**	**6**
1	83.2	83.7	83.8	82.7	82.8	83.1
2	26.0	27.2	26.2	26.5	26.9	26.4
3	32.3	32.0	31.9	32.2	36.8	31.8
4	38.8	38.6	38.4	38.6	34.2	38.1
5	56.1	52.0	44.0	56.5	55.7	52.6
6	217.1	78.7	32.5	216.7	79.1	78.9
7	91.8	93.2	92.1	90.4	93.0	92.7
8	81.4	82.2	79.7	81.5	82.3	83.9
9	47.7	48.2	47.8	47.8	47.9	48.1
10	41.3	39.8	42.3	41.8	39.9	40.3
11	45.9	49.7	50.3	46.1	49.8	50.2
12	26.6	29.8	26.9	27.7	27.1	28.1
13	39.6	39.0	39.9	38.7	38.9	37.9
14	82.8	83.8	84.7	82.4	83.8	82.5
15	35.4	36.0	36.2	32.9	36.1	33.3
16	71.3	72.1	72.0	82.3	71.9	81.8
17	63.6	64.1	62.3	63.0	63.5	63.9
18	76.6	79.0	78.9	76.8	25.3	78.9
19	53.4	54.1	52.6	53.4	57.6	53.7
CH_2O_2	95.3	93.9	93.4	95.3	93.8	92.9
$\underline{C}H_3$-CH_2-N	13.8	14.2	14.0	13.7	13.9	14.0
CH_3-$\underline{C}H_2$-N	50.3	50.9	50.7	50.2	50.4	50.7
C-1-O$\underline{C}H_3$	56.0	56.1	55.9	55.9	56.1	55.5
C-14-O$\underline{C}H_3$	58.3	58.4	58.1	58.1	58.2	57.8
C-16-O$\underline{C}H_3$	-	-	-	56.5	-	56.3
C-18-O$\underline{C}H_3$	59.2	59.7	59.4	59.2	-	59.6

Weak-field 1H singlets in the PMR spectrum at δ 5.07-5.50 ppm were consistent with methylenedioxy on C-7 and C-8 and an oxygen-containing substituent on C-6 [6].

For C-6-OH, the resonance of H-6*α* should be observed as a 1H singlet or 1H doublet (J ~ 2 Hz) at δ 4.14-4.25 ppm [7]. The absence of this and the large difference in the chemical shifts of the methylenedioxy protons (0.43 ppm) in addition to the singlet at 217.1 ppm in the ^{13}C NMR spectrum suggested that C-6 was a ketone. This was confirmed by the IR spectrum, which was consistent with it being located in a five-membered ring (1750 cm^{-1}).

Because three resonances from methine C atoms, two of which, as shown above, belonged to C-1 and C-14, were observed in the ^{13}C NMR spectrum in JMODCH mode at weak field (65-85 ppm), which is characteristic of C atoms with methoxyl and hydroxyl substituents, the hydroxyl should have been located on methine C-16, as indicated by the doublet at 71.3 ppm. Thus, **1** was 6-oxocorumdephine. Alkaloids corumdephine (**3**) and 6-dehydrodelcorine (**4**) have similar structures.

The ^{13}C NMR spectrum of **1** compared with those of **3** [8] and **4** [9] confirmed this hypothesis (Table 1). Exchanging the methoxyl on C-16 in **4** by hydroxyl in **1** and **3** led to a strong-field shift of the resonance for C-16 to 71-72 ppm.

Thus, **1** had the structure 16*β*-hydroxy-7,8-methylenedioxy-6-oxo-1*α*,14*α*,18-trimethoxy-*N*-ethylaconitane (6-oxocorumdephine) based on PMR, ^{13}C NMR, IR, and mass spectral data.

The IR spectrum of **2** was consistent with hydroxyls (3200-3400 cm^{-1}). The high-resolution mass spectrum gave a molecular weight of 465.2608, corresponding to $C_{25}H_{39}NO_7$. The PMR spectrum showed three methoxyls (δ, 3.26, 3.35, 3.48 ppm), *N*-ethyl (1.06), and methylenedioxy (5.08, 5.17). The mass spectrum was also characteristic of C_{19} diterpene alkaloids. The base peak in the mass spectrum of **2** was $[M - 31]^+$, which placed one of the three methoxyls on C-1 [3].

The presence in the PMR spectrum of a 1H triplet (J = 4.5 Hz) at δ 3.72 ppm indicated that the second OMe was located on C-14 and that C-9, C-10, and C-13 were unsubstituted [4]. A triplet at δ 79.0 ppm in the ^{13}C NMR spectrum in JMODCH mode indicated that the third methoxyl was located on C-18 [5].

1H singlets at weak field in the PMR spectrum (δ 5.08-5.17 ppm) indicated that the methylenedioxy bridged C-7 and C-8 and that C-6 had an oxygen-containing substituent [6].

Because the molecule lacked ketone and ester groups according to spectral data (IR, PMR, ^{13}C NMR), the three methoxyls and methylenedioxy and the empirical formula suggested the presence of two hydroxyls. The appearance of a 1H singlet at δ 4.27 ppm was consistent with a *β*-OH on C-6 [7]. This was confirmed by the chemical shifts of the methylenedioxy protons [6]. If it is assumed that the second OH was located on C-16, the structure of **2** should be similar to that of **1**, eladine (**5**) [10], and delcorine (**6**) [5].

The observed strong-field shifts in the ^{13}C NMR spectra (Table 1) of C-16 on going from **6** to **2** and of C-18 on going from **2** to **5** and the similarity of the chemical shifts for the other C atoms of **2**, **5**, and **6** confirmed the proposed structure of **2** as 18-methoxyeladine. Thus, **2** had the structure 6*β*,16*β*-dihydroxy-7,8-methylenedioxy-1*α*,14*α*,18-trimethoxy-*N*-ethylaconitane (18-methoxyeladine) based on PMR, ^{13}C NMR, IR, and mass spectral data.

EXPERIMENTAL

Chromatographic separations were carried out on a Du Pont Instruments liquid chromatograph using a semi-preparative column (μ-Bondapak^{TM}NH$_2$, 10 μm, 300 × 7.8 mm) with a Waters 484 variable wavelength UV detector. The mobile phase was hexane:isopropanol (90:10), isocratic, flow rate 4.0 mL/min, 18°C, UV detection at 230 nm. IR spectra in mineral oil were recorded on a Specord M-82 spectrometer. Mass spectra (EI, 70 eV) were obtained in a Thermo Finnigan MAT 95 XP mass spectrometer using a peak overlap method. PMR and ^{13}C NMR spectra in $CDCl_3$ were recorded on a Bruker AMX III-300 instrument with Me_4Si internal standard.

Isolation of Alkaloids. The fraction obtained by chromatography of the moderately basic total alkaloids (pH 6) (0.984 g) using benzene:methanol (2%) over a SiO_2 column (50/160) [2] was separated again by HPLC. Several fractions were isolated, two of which were pure alkaloids 6-oxocorumdephine (**1**, 0.006 g, amorph.) and 18-methoxyeladine (**2**, 0.007 g, amorph.).

6-Oxocorumdephine (1). IR spectrum (ν, cm^{-1}): 3500-3300 (OH), 1750 (C=O). High-resolution mass spectrum: *m/z* 463.2570 [M]$^+$, $C_{25}H_{37}NO_7$.

Mass spectrum (*m/z*, I_{rel}, %): 463 (6) [M]$^+$, 432 (100) [M - 31]$^+$.

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 1.02 (3H, t, J = 7.2, $C\underline{H}_3$–CH_2–N), 3.01 (1H, d, ^{2}J = 9.0, H-18a), 3.19 (1H, d, ^{2}J = 9.0, H-18b), 3.26, 3.30, 3.38 (3H each, all s, 3×OMe), 3.69 (1H, t, J = 4.5, H-14*β*), 5.07, 5.50 (1H each, all s, CH_2O_2).

18-Methoxyeladine (2). IR spectrum (ν, cm^{-1}): 3400-3200 (OH). High-resolution mass spectrum: *m/z* 465.2608 [M]$^+$, $C_{25}H_{39}NO_7$.

Mass spectrum (*m/z*, I_{rel}, %): 465 (15) [M]$^+$, 434 (100) [M - 31]$^+$.

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 1.06 (3H, t, J = 7.2, $C\underline{H}_3$–CH_2–N), 3.20 (1H, d, ^{2}J = 7.1, H-18), 3.26, 3.35, 3.48 (3H each, all s, 3×OMe), 3.72 (1H, t, J = 4.5, H-14*β*), 4.27 (1H, s, H-6*α*), 5.08, 5.17 (1H each, all s, CH_2O_2).

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