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URAPHINE, A NEW NORDITERPENE ALKALOID FROM THE AERIAL PART OF *Delphinium uralense*

T. M. Gabbasov,[1*] E. M. Tsyrlina,[1] L. V. Spirikhin,[1] N. I. Fedorov,[2] and M. S. Yunusov[1]

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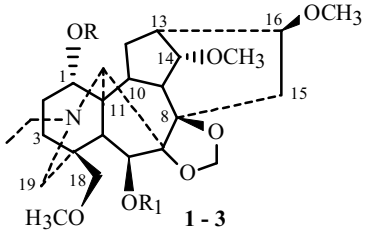
*The new norditerpene alkaloid uraphine, for which the structure 1α,6β-dihydroxy-7,8-methylenedioxy-14α,16β,18β-trimethoxy-*N*-ethylaconitane was proposed based on PMR, ^{13}C NMR, IR, and mass spectral data, was isolated from the aerial part of* Delphinium uralense *N. The known alkaloids dehydrodelcorine, delpheline, deltaline, deltamine, elasine, deacetylelasine, gigactonine, and lycoctonine were also isolated from the total alkaloids.*

Key words: *Delphinium uralense* N., norditerpene alkaloids, uraphine.

The plant *Delphinium uralense* Nevski has a limited distribution and belongs to the complex *D.* aggr. *dictyocarpum* DC. (section Delphinastrum DC) [1]. We reported previously on the isolation from the aerial part of this plant collected during the start of budding in the Southern Urals (Zilair Plateau) of methyllycaconitine, delcorine, and grandiflorine (uraline) [2].

In continuation of research on the alkaloid composition of the aerial part of *D. uralense*, we isolated from the benzene extract of the moderately basic fraction (A, pH 6) [2] by column chromatography and semi-preparative HPLC the known alkaloids dehydrodelcorine, delpheline, deltaline, deltamine, and elasine, and alkaloid **1**, which has not previously been described and which we called uraphine. We also isolated deacetylelasine, which was isolated by us for the first time from plant material and has been prepared previously via alkaline hydrolysis of elasine [3]. We isolated the known alkaloids gigactonine and lycoctonine from the strongly basic fraction (B, pH 12).

According to IR spectroscopy, **1** contained hydroxyls (3300-3500 cm^{-1}). The high-resolution mass spectrum gave molecular weight 465.2715 for **1**, which corresponded to the empirical formula $C_{25}H_{39}NO_7$. The fact that the peak for the ion $[M - 17]^+$ was the base peak suggested that C-1 had an OH group [4]. Peaks for ions $[M - 56]^+$ and $[M - 87]^+$ also suggested that there was a hydroxyl in the 1-position and a methoxyl in the 18-position [5, 6]. The location of one of the three methoxyls in the C-18 position was confirmed by the presencee in the ^{13}C NMR of **1** of a triplet at δ 78.5 ppm. The presence in the PMR of **1** of a 1H singlet for H-6α at δ 4.37 ppm placed a β-OH group on C-6 [7]. Furthermore, a 1H triplet (J = 4.5 Hz) was observed at δ 3.71 ppm, indicating that C-14 contained an α-methoxyl [8].



1 - 3

1: R = R_1 = H

2: R = CH_3, R_1 = H

3: R = H, R_1 = CH_3

1) Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, 450054, Ufa, prosp. Oktyabrya, 71, fax (347)-235-6066, e-mail: ivanov_sp@anrb.ru; 2) Institute of Biology, Ufa Scientific Center, Russian Academy of Sciences, 450054, Ufa, prosp. Oktyabrya, 71, fax (347) 235 62 47, e-mail: ib@anrb.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 380-382, July-August, 2008. Original article submitted April 30, 2008.

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TABLE 1. Table 1. Chemical Shifts of C Atoms in ^{13}C NMR Spectra of Delcorine (**2**) [8], Uraphine (**1**), and 7,8-Methylenedioxydelcoline (**3**)

C atom	δ, ppm			C atom	δ, ppm		
	2	**1**	**3**		**2**	**1**	**3**
1	83.1	71.9	71.8	15	33.3	33.7	35.8
2	26.4	27.1	26.9	16	81.8	82.2	82.6
3	31.8	30.3	29.5	17	63.9	65.5	65.7
4	38.1	37.2	37.1	18	78.9	78.5	78.0
5	52.6	47.8	45.5	19	53.7	58.1	57.7
6	78.9	79.0	88.8	CH_2O_2	92.9	93.3	94.0
7	92.7	92.0	91.8	$\underline{C}H_3$-CH_2-N	14.0	13.4	13.4
8	83.9	85.2	84.5	CH_3-$\underline{C}H_2$-N	50.7	51.3	49.9
9	48.1	45.2	46.6	O$\underline{C}H_3$-1	55.5	-	-
10	40.3	40.0	45.5	O$\underline{C}H_3$-6	-	-	58.1
11	50.2	50.0	51.2	O$\underline{C}H_3$-14	57.8	57.7	57.7
12	28.1	29.3	30.6	O$\underline{C}H_3$-16	56.3	56.3	56.2
13	37.9	37.0	37.4	O$\underline{C}H_3$-18	59.6	59.5	59.2
14	82.5	83.6	83.7				

The third OMe group may have been located on C-16. The presence of 1H singlets at δ 5.09 and 5.12 ppm were consistent with the presence of a methylenedioxy group between C-7 and C-8.

The structure of **1** was finally established based on a comparison of its ^{13}C NMR spectrum with analogous spectra of the known compounds delcorine (**2**) [9] and 7,8-methylenedioxydelcoline (**3**) [10] (Table 1).

Weak-field shifts observed on going from **1** to **2** for C-1 and from **1** to **3** for C-6 of 11.2 and 9.8 ppm, respectively, confirmed that **1** contained OH groups on C-1 and C-6. The hypothesis about a methoxyl on C-16 was also consistent with the experimental data.

Thus, the structure 1α,6β-dihydroxy-7,8-methylenedioxy-14α,16β,18β-trimethoxy-*N*-ethylaconitane was proposed for **1** based on PMR, ^{13}C NMR, IR, and mass spectra.

EXPERIMENTAL

Chromatographic separation was performed on a DuPont Instruments liquid chromatograph using a μ-Bondapak™ NH_2 semi-preparative column (10 μm, 300 × 7.8 mm) and a Waters 484 variable wavelength UV-detector. The mobile phase was hexane:isopropanol (90:10), isocratic elution at flow rate 4.0 mL/min, mp 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 on a Thermo Finnigan MAT 95 XP mass spectrometer by a peak displacement method. PMR and ^{13}C NMR spectra in $CDCl_3$ were recorded on a Bruker AMX III-300 instrument (300.13 MHz) with Me_4Si internal standard.

Isolation of Alkaloids. Total alkaloids from fraction A (0.984 g) were chromatographed over a column of SiO_2 (50/160) with elution by benzene:methanol with increasing concentration of the latter from 0 to 5% by volume to afford a series of fractions, several of which were enriched in pure alkaloids. Thus, elution by benzene:methanol (2%) produced dehydrodelcorine (0.120 g) [9] and fractions I (0.076 g) and II (0.085 g); by benzene:methanol (3%), fraction III (0.098 g); by benzene:methanol (5%), fraction IV (0.048 g). Repeated purification of fraction I by HPLC isolated delpheline (0.007 g) [11]; of fraction II, **1** (0.047 g).

Uraphine (1). IR spectrum (ν, cm^{-1}): 3500-3300 (OH). High-resolution mass spectrum: found 465.2715 *m/z* $[M]^+$, $C_{25}H_{39}NO_7$; calc. 465.2721. Mass spectrum (*m/z*, I_{rel}, %): 465 (63.5) $[M]^+$, 450 (32) $[M - 15]^+$, 448 (100) $[M - 17]^+$, 434 (11.5) $[M - 31]^+$, 409 (6) $[M - 56]^+$, 378 (6) $[M - 87]^+$.

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 1.11 (3H, t, J = 7.2, $C\underline{H}_3$–CH_2–N), 2.35 (1H, d, ^2J = 11.5, H-19α), 2.58 (1H, d, ^2J = 11.5, H-19β), 2.62-2.76 (1H, m, CH_3–$C\underline{H}\alpha$–N), 2.76-2.91 (1H, m, CH_3–$C\underline{H}\beta$–N), 3.20 (1H, d, ^2J = 8.9, H-18α), 3.28

(1H, d, ^2J = 8.8, H-18β), 3.36, 3.37, 3.42 (3H each, all s, 3 OMe), 3.71 (1H, t, J = 4.5, H-14), 4.37 (1H, s, H-6), 5.09, 5.12 (1H each, all s, CH_2O_2).

Alkaloid fraction III was repeatedly chromatographed over a column of SiO_2 (50/160) with elution by benzene:methanol with increasing concentration of the latter from 0 to 1.5% by volume. Additional purification by HPLC of the fraction eluted by benzene:methanol (1.5%) produced deltaline (0.007 g), the physical chemical properties of which were identical to those published [9].

Alkaloid fraction IV was repeatedly separated by HPLC to isolate three fractions that were the pure alkaloids deltamine (0.005 g), elasine (0.006 g), and deacetylelasine (0.005 g), the spectral properties of which (PMR and ^{13}C NMR spectra) were identical to those published [3, 9, 12].

Total alkaloids of fraction B (0.189 g) were chromatographed over a column of SiO_2 (50/160) using dichloroethane:methanol with increasing concentration of the latter from 3 to 30% by volume to produce chromatographically pure gigactonine (0.019 g); using dichloroethane:methanol (30%), lycoctonine (0.018 g). The spectral properties (PMR and ^{13}C spectra) of the isolated alkaloids were identical to those published [13, 14].

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