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ALKALOIDS OF *Nitraria sibirica*. DIHYDROSCHOBERINE AND NITRABIRINE N-OXIDE

T. S. Tulyaganov and F. Kh. Allaberdiev

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Two alkaloids were isolated from the aerial part of Nitraria sibirca. *Their structures were determined using chemical transformations and spectral data.*

Key words: *Nitraria sibirca*, alkaloid, dihydroschoberine, nitrabirine N-oxide.

In continuation of research on alkaloids of the aerial part of *Nitraria sibirica* Pall., we isolated from the benzene part of the total bases by column chromatography the known alkaloids nitraramine N-oxide [1], nitrabirine [2], deoxyvasicinone [3], schoberine [4], dehydroschoberine [1], and two new alkaloids **1** and **2**. Dehydroschoberine is isolated from this species for the first time.

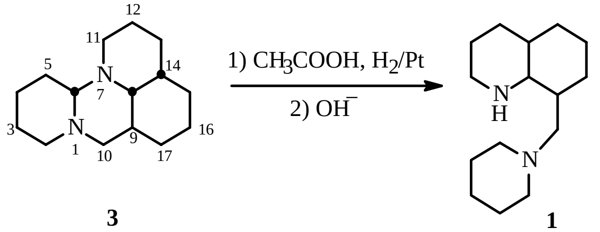
Base **1** is a light oil, $C_{15}H_{28}N_2$, $[\alpha]_D$ ±0. The alkaloid is transparent in the UV region. The mass spectrum exhibits peaks for ions with *m/z* 236 $[M]^+$ and 235 $[M - 1]^+$ and all ions characteristic of decahydroquinolines [5].

The PMR spectrum of **1** is complicated. It consists of three multiplets centered at 1.55, 2.78, and 3.50 (m) ppm.

The IR spectrum exhibits absorption bands for active H at 3363 and 3297 cm^{-1} and saturated C–H at 2943 and 2865 cm^{-1}.

The spectra showed that **1** is a schoberine-type alkaloid. The composition is two H atoms greater than schoberine (**3**).

Catalytic hydrogenation of **3** in acetic acid cleaves one C–N bond, as is characteristic of aminals [4, 6]. Schoberine is completely converted to dihydroschoberine.



3   **1**

Comparison of **1** and dihydroschoberine showed that they are identical.

Thus, dihydroschoberine has structure **1** and is found in nature for the first time.

Base **2** is optically inactive, mp 235-236°C (alcohol), $C_{12}H_{18}N_2O_2$, $[M]^+$ 222 (mass spectrometry). The UV spectrum contains one absorption band at 213 nm (log ε 3.81), indicative of the presence of an alkyl-substituted imidazole or pyrazole ring [7, 8].

The IR spectrum of **2** exhibits absorption bands typical of active H (3382 and 3327), saturated C–H (2972, 2942, and 2865), aromatic >C=C< and –C=N– bonds (1611, 1521), C–OH in alcohols (1266, 1087, 946 cm^{-1}), etc.

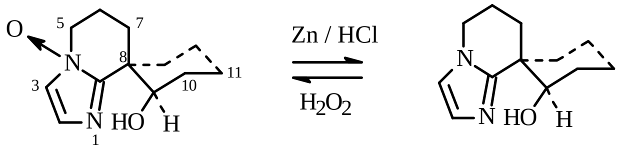
The composition of **2** is one H atom greater than nitrabirine. Otherwise, their mass spectral fragmentations are almost identical.

The presence in the mass spectrum of strong peaks for $[M - 16]^+$ and $[M - 17]^+$ and the free solubility in water indicate that **2** is an N-oxide.

S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (99871) 120 64 75, e-mail: cnc@icps.org.uz. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 476-478, November-December, 2001. Original article submitted November 23, 2001.

Reduction of **2** by zinc in HCl produced **4**, mp 184-185°C [2], PMR and mass spectra were identical to those of nitrabirine (**4**).

Oxidation of nitrabirine by perhydrol in methanol produced a base identical to **2**.



2 **4**

The signals for the two neighboring protons on the imidazole ring and the protons of the methylene group bonded to the imidazole N shift to weak field in the PMR spectrum of **2** compared with that of **4**. This indicates that **2** is nitrabirine N-oxide (on N-4).

Thus, the isolated base is nitrabirine N-oxide and has structure **2**.

EXPERIMENTAL

UV spectra were recorded in alcohol on a Perkin—Elmer Lambda-16 spectrometer; IR spectra, on a Perkin—Elmer System 2000 FT-IR in pressed KBr pellets; mass spectra, in a Kratos MS-25 RF GC-MS.

PMR spectra were recorded on a Tesla BS 567 A/100 MHz spectrometer with HMDS internal standard.

TLC used KSK and L 5/40 μ (Czech Rep.) silica gel and Silufol UV-254 plates.

Chromatography used the following solvent systems: C_6H_6—CH_3OH (4:1, 1), $CHCl_3$—$(CH_3)_2CO$—CH_3OH (5:4:1, 2), $CHCl_3$—CH_3OH (6:1, 3), $CHCl_3$—C_2H_5OH (5:1, 4), $CHCl_3$—$(CH_3)_2CO$—C_2H_5OH (5:4:1, 5), $CHCl_3$—C_2H_5OH (10:1, 6), C_6H_6—C_2H_5OH (9:1, 7), $CHCl_3$—$(CH_3)_2CO$—C_2H_5OH—NH_4OH (5:4:1:0.1, 8), $CHCl_3$—C_2H_5OH—NH_4OH (8:2:0.1, 9), and $CHCl_3$—CH_3OH—NH_4OH (7:3:0.1, 10).

Dragendorff's solution and iodine vapor were used as developers.

Extraction of the Aerial Part of *Nitraria sibirica* Pall. A) The finely ground aerial part (12.5 kg) of plants collected in June 1995 during flowering near Rybach′e (Republic of Kyrgyzstan) were wetted with aqueous ammonia (8%), left for 2 h, and extracted 13 times with $CHCl_3$. The condensed $CHCl_3$ extracts were extracted with H_2SO_4 (10%). The acid extract was made basic with NaOH solution (10%) and extracted with C_6H_6 and $CHCl_3$. The phenolic part was extracted by $CHCl_3$ by adding ammonium chloride to give total nonphenolic alkaloids in the C_6H_6 (19.7 g) and $CHCl_3$ (17.2 g) extracts and the phenolic ones (1.85 g). Total yield 38.75 g, 0.31% of the air-dried mass.

B) The aerial part of *N. sibirica* (2 kg) collected during flowering in June 1998 was extracted 10 times by the usual method described above to give benzene (3.1 g), $CHCl_3$ (2.8 g), and $CHCl_3$ phenolic (0.3 g) fractions. Total yield 6.2 g, 0.31% of the air-dried mass.

The benzene fraction (19.7 g) was separated by column chromatography over silica gel with elution by $CHCl_3$—CH_3OH mixtures (99:1, 98:2, 50:1, 20:1, 15:1, 10:1, 5:1, and 4:1). Fractions of 40-50 mL were collected. Schoberine, dehydroschoberine, deoxyvasicinone, nitrabirine, and nitraramine N-oxide were isolated from separate fractions.

Dihydroschoberine (1). Fractions 10-18 from the 98:2 eluates (0.81 g) were combined and rechromatographed over a silica-gel column with elution by $CHCl_3$—C_2H_5OH (20:1). Fractions of 10-15 mL were collected. Fractions 16-25 were combined. The solvent was removed to give base **1** (52 mg) as an oil, mp 251-252°C (ethanol). Dihydroschoberine was subsequently also isolated from the benzene fraction of bases from *N. sibirica* collected in June 1998.

Mass spectrum, m/z (I_{rel}, %): 236 (29), 219 (1), 206 (1.5), 194 (4), 192 (5), 179 (3), 178 (9), 149 (13), 148 (100), 138 (36), 137 (39), 136 (51), 124 (21), 123 (69), 122 (55), 112 (47), 99 (52), 98 (99), 97 (99), 89 (25), 88 (62), 70 (36), 69 (40).

IR spectrum (KBr, ν_{max}, cm^{-1}): 883, 910, 945, 995, 1018, 1048, 1065, 1089, 1142, 1175, 1202, 1284, 1314, 1456, 1479, 2553, 2578, 2634, 2698, 2813, 2865, 2934, 3297, 3363.

PMR spectrum (δ, ppm, DMSO): 1.55 (m), 2.78 (m), 3.50 (m).

Reduction of Schoberine. Dihydroschoberine. Schoberine (**3**, 49 mg) in an Ehrlenmeyer flask was treated with platinum oxide (22 mg) and glacial acetic acid (5 mL) and heated at 80°C with constant stirring under a H_2 atmosphere for 5 h. The catalyst was filtered off when the reaction was finished. The acid was removed in vacuum. The solid was treated with water and made basic with conc. NH_4OH. The product was extracted with $CHCl_3$. The $CHCl_3$ was removed to give **1** (35 mg) as a colorless oil. It forms a hydrochloride with mp 251-252°C (ethanol).

Nitrabirine N-Oxide (2). The next fractions 19-28 from the eluates (50:1) were combined and separated by column chromatography over silica gel with elution by $CHCl_3$—C_2H_5OH (10:1). Fractions of 8-10 mL were collected. Fractions 21-26 were combined. The solvent was distilled off. The solid was crystallized from ethanol to give **2** (48 mg), mp 235-236°C.

UV spectrum (EtOH, λ_{max}, nm): 213 (log ε 3.81).

IR spectrum (KBr, ν_{max}, cm^{-1}): 795, 854, 863, 1071, 1087, 1201, 1323, 1418, 1455, 1521, 1611, 2865, 2941, 2972, 3327, 3382.

Mass spectrum, *m/z* (I_{rel}, %): 222 (2), 206 (40), 189 (10), 178 (11), 161 (5), 160 (15), 148 (13), 136 (30), 135 (100), 123 (3), 121 (18), 95 (4), 90 (4), 89 (32), 88 (53), 67 (6).

PMR spectrum (CD_3OD, δ, ppm, J/Hz): 1.50 (m), 1.75 (m), 2.05 (m), 4.02 (3H, m), 7.39 (1H, d, J = 2.5), 7.47 (1H, d, J = 2.5).

Reduction of Nitrabirine N-Oxide. Nitrabirine (4). Base **2** (28 mg) was dissolved in HCl (5 mL, 10%) and reduced by granulated zinc at room temperature for 15 h. The solution was made basic with NaOH solution (10%) and extracted with $CHCl_3$. The $CHCl_3$ was distilled off. The solid was crystallized from ethanol to give **4** (13 mg), mp 184-185°C.

Mass spectrum, *m/z* (I_{rel}, %): 206 (99), 189 (35), 188 (20), 178 (43), 176 (22), 160 (48), 148 (44), 136 (80), 135 (100), 134 (40), 122 (59), 121 (63), 119 (27).

PMR spectrum (CD_3OD, δ, ppm, J/Hz): 1.45 (m), 1.63 (m), 1.95 (m), 3.90 (2H, m), 4.08 (1H, m), 6.82 (1H, d, J = 1.5), 6.87 (1H, d, J = 1.5).

Oxidation of Nitrabirine. Nitrabirine (33 mg) was dissolved in methanol (5 mL), treated with perhydrol (1.5 mL), and left for three days. The solvent was removed. The solid was separated by column chromatography over silica gel with elution by $CHCl_3$—C_2H_5OH (10:1). Fractions of 2-3 mL were collected. Fractions 15-22 afforded crystalline **2** (ethanol, 5 mg), mp 235-236°C.

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