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ALKALOIDS OF *Nitraria schoberi*. N-METHYLNITRARINE

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Nitrarine, isonitrarine, schoberidine, isoschoberidine, nitramidine, nitraroxine, nitraraine, schoberine, dehydroschoberine, tetramethylenetetrahydro-β-carboline, dl-vasicinone, deoxypeganine, deoxyvasicinone, dihydronitraraine, nitraramine, nitraramine N-oxide, tetramethylenetetrahydro-β-carboline N-oxide, tryptamine, and a new alkaloid N-methylnitrarine were isolated from the aerial part of Nitraria schoberi *L. Spectral data and chemical transformations were used to establish the structure of the last, which was found in nature for the first time.*

Key words: alkaloid, *Nitraria*, nitrarine, isonitrarine, schoberine, N-methylnitrarine, nitraramine, schoberidine, nitraroxine, nitraraine.

We investigated alkaloids from the aerial part of *Nitraria schoberi* L. collected near the village Ayakhagitma of Bukhara region in the Republic of Uzbekistan during flowering in June, 1995.

The raw material was extracted as usual. The total alkaloids consisted of 0.41% of the air-dried mass. Schoberine [1a], nitraraine [1b], tetramethylenetetrahydro-β-carboline [1c], dihydronitraraine [1d], nitraramine [1e], nitraroxine [1e], tryptamine [2], *dl*-vasicinone [3], deoxypeganine [3], deoxyvasicinone [3], dehydroschoberine [2], nitraramine N-oxide [3], and tetramethylenetetrahydro-β-carboline N-oxide [4] were isolated from the benzene extract of the total alkaloids by column chromatography.

The $CHCl_3$ extract of the total alkaloids yielded nitrarine [1e], isonitrarine [1f], schoberidine [1a], isoschoberidine [1g], nitramidine [1h], and **1** in addition to an additional amount of nitraramine and nitraroxine.

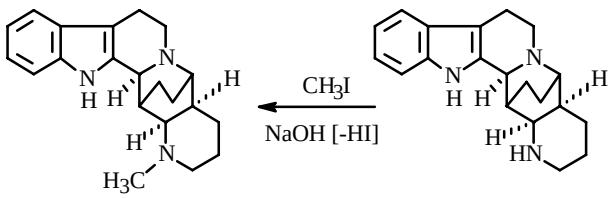
Compound **1**, mp 263-264°C (alcohol), $C_{21}H_{27}N_3$, optically inactive, molecular weight 321 (mass spectrometry).

The UV spectrum of **1** has maxima (λ_{max}, C_2H_5OH) at 220, 266-272, 280 (sh), 288 nm (4.68, 3.88, 3.85, 3.52) that are characteristic of a nonconjugated indole chromophore [5].

The IR spectrum of **1** contains absorption bands due to vibrations of *o*-disubstituted benzene (740 cm^{-1}), substituted indole (1451, 1473, 1572, and 1623 cm^{-1}), saturated C–H bonds (2855, 2949 cm^{-1}), and others.

The PMR spectrum exhibits signals at 2.32 ppm from the N-methyl protons. Four aromatic protons appear at 7.13 (2H), 7.45 (2H) ppm as multiplets.

The spectral data indicate that **1** is an indole alkaloid. Direct comparison of the alkaloid with an authentic sample of N-methylnitrarine obtained via methylation of nitrarine (**2**) with methyl iodide in ethanol indicates that they are identical. N-methylnitrarine was found for the first time in nature.



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EXPERIMENTAL

UV spectra were recorded in alcohol on a Lambda 16 UV/Vis spectrometer; IR spectra, on a Perkin—Elmer System 2000 FT-IR as KBr pellets; mass spectra, on a Kratos MS-25 RF GC—MS and an MX-1310 spectrometer. PMR spectra were recorded in a $CDCl_3$—CD_3OD mixture on a Tesla BS 567 A/100 MHz spectrometer with HMDS as an internal standard.

The purity of the compounds was checked by TLC using KSK and L 5/40 silica gel. Solvent systems have been described [3, 6, 7]. Dragendorff's solution and iodine vapor were used as developers.

Extraction of the Aerial Part of *Nitraria schoberi*. Finely ground raw material (6.7 kg) was wetted with aqueous ammonia (8%), left for 2 h, and extracted 12 times with $CHCl_3$. The concentrated $CHCl_3$ extracts were extracted with H_2SO_4 (10%). The acid extract was basicified with NaOH (10%) and extracted with benzene and then $CHCl_3$. The basic solution was treated with ammonium chloride. The phenolic part was extracted with $CHCl_3$.

The following total alkaloids were obtained. Nonphenolic part: benzene, 14.26 g; $CHCl_3$, 12.61 g. Phenolic part: $CHCl_3$ 0.6 g. Total yield, 24.47 g, 0.41% of the dry mass.

Separation of Total Alkaloids. The benzene extract of the total alkaloids was separated by chromatography on a silica-gel column with elution by $CHCl_3$—ethanol mixtures of various ratios (20:1, 15:1, 10:1, 5:1, and 4:1). Schoberine, dehydroschoberine, nitraraine, dihydronitraraine, tetramethylenetetrahydro-β-carboline, deoxyvasicinone, *dl*-vasicinone, nitraroxine, deoxypeganine, tetramethylenetetrahydro-β-carboline N-oxide, nitraramine, nitraramine N-oxide, and tryptamine were isolated from different fractions. The isolated compounds were identified by direct comparison of their physicochemical and spectral data with those of authentic samples.

The $CHCl_3$ total alkaloids (12.61 g) were boiled with acetone. The solution was discarded. The solid was dissolved in ethanol (50 ml) and treated with alcoholic HCl until the pH was 3-4. A crystalline precipitate (mp 238-239°C, alcohol) formed after the solution stood for 4-5 h and was isolated. Then crystals (mp 265-266°C, alcohol) formed after 13-14 h. These were identified as isonitrarine and nitrarine, respectively. Decomposition of the salts produced the corresponding free bases.

Crystals (0.1 g, mp 253-254°C) formed in the mother liquor after prolonged standing. These were identified as nitramidine dihydrochloride.

The solvent was evaporated under vacuum after separation of nitrarine, isonitrarine, and nitramidine. The solid was dissolved in $CHCl_3$. Alkaloids were isolated from the $CHCl_3$ solution with H_2SO_4 (10%). The acid extract was basicified with NaOH (10%) and extracted with $CHCl_3$. The purified total alkaloids were dissolved in alcohol (15 ml). The solution was treated dropwise with H_2ClO_4 until the pH was 3-4. The volume was reduced to one half. Yellow crystals formed upon standing. Recrystallization from alcohol gave schoberidine perchlorate (0.12 g, mp 340-342°C).

The acetone-soluble part of the total alkaloids (8.68 g) was separated by chromatography on a silica-gel column with elution by $CHCl_3$—ethanol mixtures (10:1 and 4:1) and $CHCl_3$—CH_3OH—NH_3 (4:1:0.1). Fractions of 40-50 ml were collected. Nitraroxine, nitraramine, schoberidine, and isoschoberidine were isolated from different fractions.

N-Methylnitrarine. Chromatographic fractions 40-46 were combined. Crystallization occurred in ethanol. Yield of **1**, 57 mg, mp 263-264°C.

Synthesis of N-Methylnitrarine. A solution of nitrarine (**2**, 0.2 g) in absolute ethanol (5 ml) was treated with methyl iodide (2 ml) and heated to 90°C for 1.5 h. The solvent was removed. Water was added. The solution was basicified with NaOH (10%) and extracted with $CHCl_3$. The $CHCl_3$ was removed. The solid was crystallized from alcohol. Yield, 0.16 g of N-methylnitrarine, mp 263-264°C.

Mass spectrum, *m*/*z* (%): 321 (M^+) (50), 306 (2), 293 (11), 292 (27), 239 (4), 238 (2), 224 (20), 223 (24), 197 (10), 196 (10), 195 (11), 184 (7), 182 (7), 171 (15), 170 (16), 169 (20), 156 (15), 144 (100), 98 (60).

IR spectrum (ν_{max}, cm^{-1}): 746, 766, 845, 900, 983, 1006, 1097, 1141, 1151, 1212, 1240, 1299, 1332, 1374, 1427, 1451, 1473, 1572, 1623, 2776, 2855, 2949, 3028, 3179, 3441.

PMR (δ, ppm): 1.21 (m), 1.76 (m), 2.25 (m), 2.32 (3H, s, N-Me), 2.86 (m), 3.45 (m), 3.71 (m), 3.96 (m), 4.48 (m), 4.76 (m), 7.13 (2H, m), 7.45 (2H, m).

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