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ALKALOIDS OF *Nitraria komarovii* NITRARICINE AND NITRARIZINE

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Two new alkaloids — nitraricine and nitrarizine — have been isolated from the epigeal part of Nitraria komarovii.

Continuing investigations of alkaloids from the epigeal part of *Nitararia komarovii* Iljin et Lava [1], from the chloroform fraction of the total bases we have isolated two bases (**1**) and (**2**) by column chromatography.

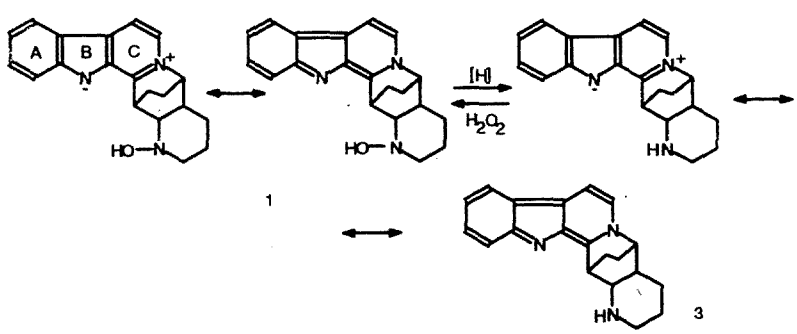
Base (**1**), mp 214-215°C, composition $C_{20}H_{21}N_3O$, $[\alpha]_D$ ±0. The UV spectrum of (**1**) had the following absorption maxima: λ_{max} (C_2H_5OH) 208, 253, 310, 365 nm (4.16, 4.13, 4.02, 3.41). On alkalinization a bathochromic shift was observed, λ_{max} ($C_2H_5OH + OH^-$) 216, 283, 330, 380 nm, which is characteristic for anhydronium bases. The mass-spectrometric fragmentation of (**1**) was similar to that of schoberidine and isoschoberidine, although, in contrast to these, the molecular composition of base (**1**) included one oxygen atom.

The presence in the IR spectrum of (**1**) of a characteristic band for N-oxides at 960 cm^{-1} [2], the presence in the mass spectrum of intense peaks of $(M - 16)^+$, $(M - 17)^+$, and (M — 18) ions and the ready solubility of the compound in water permitted the assumption that base (1) was an N-oxide.

When base (**1**) was reduced with sodium tetrahydroborate in methanol or was subjected to Adams hydrogenation, schoberidine (**3**) was obtained. On the other hand, oxidation of the latter with perhydrol in alcohol led to the formation of schoberidine N-oxide, identical with base (**1**).

The PMR spectrum of (**1**) (CD_3OD, 0 — HMDS, H_0 = 100 MHz) contained the following resonance signals (ppm): 0.66 (1H, m), 1.50 (3H, t), 1.84 (2H, m), 2.24 (2H, m), 2.64 (2H, dd), 3.54 (1H, dd, J = 9.2 and 2.5 Hz), 4.05 (1H, br.s), and 4.90 (1H, br.s), assigned to the protons of the saturated part of the compound under investigation. In the region of aromatic protons, the spectrum was characterized by the following lines (ppm): 7.40 (1H, m), 7.69 (1H, m), 7.74 (1H, m), 8.34 (1H, m), and 8.45 (2H, s). The first four signals related to the protons of the aromatic ring *A* [3]. In the PMR spectrum of (**1**) taken under the same conditions but at H_0 = 500 Hz, the above-mentioned two-proton signal at 8.45 ppm appeared in the form of two doublets of the *AB* type linked by spin–spin interaction with ^3J = 8.4 Hz. This fact showed that the molecule of (**1**) also contained two aromatic protons. The nature of the signals showed that they were located in ring *C*.

Thus, the results of chemical transformation and the spectral characteristics of schoberidine N-oxide given above, and also a correlation with schoberidine permitted the conclusion that this base had the structure of schoberidin-N_{16}-ol (**1**). A band corresponding to the hydroxy group appeared in the IR spectrum at 3400 cm^{-1}.



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Since the name of schoberidine N-oxide does not reflect the actual structure of the alkaloid, we considered it desirable to introduce a new name — nitrarizine:

Base (**2**) — mp 265-267°C (alcohol—acetone), composition $C_{20}H_{21}N_3O$, $[\alpha]_D$ ±0.

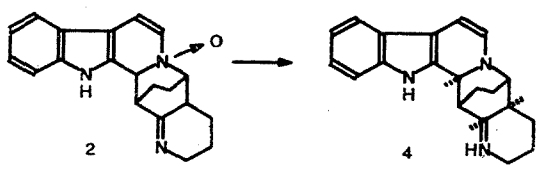
The UV spectrum of (**2**) taken in alcohol had the following absorption maxima: λ_{max} (C_2H_5OH) 208, 248, 356 nm (3.21, 3.69, 4.06), the spectrum being close to that of nitramidine [4]. On alkalinization the spectrum underwent a change: λ_{max}(C_2H_5OH + OH^-) 210, 250, and 372 nm.

In its molecular composition, the alkaloid differed from schoberidine and isoschoberidine by one oxygen atom, but otherwise their mass-spectral fragmentations were close.

The reduction of base (**2**) with sodium tetrahydroborate in methanol or Adams hydrogenation led to the formation of nitrarine (**4**). The presence in the IR spectrum of (**2**) of a band at 965 cm^{-1} that is characteristic for N-oxides [2], and the presence in the mass spectrum of intense peaks of the $(M - 16)^+$, $(M - 17)^+$, and $(M - 18)^+$ ions, and its ready solubility in water showed the N-oxide nature of the compound under investigation.

In general, the PMR spectrum of compound (**2**) was identical with that of (**1**). Resonance signals were shown at (ppm): 0.64 (1H, m), 1.61 (3H, m) 1.86 (2H, m) 2.26 (2H, m), 2.84 (2H, dd), 3.85 (1H, br.d, J = 8.8 Hz), 4.26 (1H, br.s), and 5.01 (1H, br.s). These signals were assigned to the protons of the saturated heterocyclic part. Aromatic protons resonated at (ppm): 7.39 (1H, m), 7.68 and 7.71 (1H each, br.s), 8.33 (1H, br.d, J = 8.0 Hz), and 8.50 (2H, br.s). As in the case of compound (**1**), in the spectrum taken at a working frequency of the spectrometer of 500 MHz the last signal appeared in the form of doublets with ^3J = 8.4 Hz, which enabled us to conclude that it related to the two aromatic protons of ring *C* [3].

The alkaloid has been named nitrarizine, and the information given permits us to propose structure (**2**) for it.



EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in tablets molded with KBr; mass spectra on MKh-1310 and Kratos instruments; UV spectra on an EPS-3T spectrophotometer (Hitachi); and PMR spectra on Tesla-567A (100 MHz) and Bruker WM-500 instruments.

For TLC we used types KSK and L 5/40 silica gel. The following solvent systems were used for chromatography: 1) chloroform—methanol (4:1); 2) chloroform—methanol—ammonia (8:2:0.1); 3) chloroform—ethanol (4:1); 4) chloroform—ethanol—ammonia (8:2:0.1); 5) chloroform—ethanol (1:1); 6) chloroform—methanol (6:3); and 7) chloroform—acetone—ethanol—ammonia (8:3:4:0.15). The spots were revealed with Dragendorff's reagent and with iodine vapor. The extraction and separation of the total bases has been described in detail previously [5, 6].

The chloroform fraction of the total bases (43.21 g) was chromatographed on a column of silica gel and was eluted by chloroform—acetone—ethanol (5:4:1) and then by chloroform—ethanol in various ratios (10:1; 10:2; 4:1; and 1:1). Fractions with a volume of 50-60 ml were collected. In addition to known bases, the following new ones were isolated:

Nitraricine (1). Fractions 31-37 were combined and rechromatographed on a column of silica gel with elution by system 3. Fractions with a volume of 15-20 ml were collected. On crystallization from a mixture of alcohol and acetone, fractions 19-27 yielded 96 mg of base (1) with mp 214-215°C.

The mass spectrum of (**1**) contained the peaks of ions with m/z 319 (3), 318 (11), 303 (60), 302 (31), 301 (23), 276 (19), 260 (23), 258 (7), 221 (41), 220 (69), 219 (100), 206 (27), 195 (19), 193 (15), 182 (57), 169 (31), 122 (80).

In the IR spectrum of (**1**) the following absorption bands were present (cm^{-1}): 770 (*o*-disubstituted benzene ring) 840, 960 (N→O), 1070, 1110, 1160, 1335, 1460, 1530, 1590, 1650, 2860, 2940, 3400.

Reduction of Nitraricine. Schoberidine (3). a) In portions, 100 mg of sodium tetrahydroborate was added to a solution of 32 mg of base (**1**) in 5 ml of methanol. The mixture was left for 12 h, the solvent was evaporated off in vacuum, and the residue was diluted with water. After extraction with chloroform, the solvent was distilled off, and the residue was chromatographed on a a column of silica gel. Elution with system 3 gave 11 mg of base (**3**) with mp 208-209°C (alcohol). M^+ 303.

b) A solution of 37 mg of base (**1**) in 10 ml of methanol was subjected to hydrogenation over Pt for 5 h. Then the catalyst was separated off, and the alcohol was driven off in vacuum. The residue was separated chromatographically on a column of silica gel, with elution by chloroform—ethanol (4:1). This gave 19 mg of base (**1**) with mp 208-209°C (alcohol). M^+ 303.

Oxidation of Schoberidine. Nitraricine (1). A solution of 67 mg of schoberidine in 7 ml of alcohol was treated with 2 ml of perhydrol and the mixture was left for five days. The solvent was distilled off and the residue was chromatographed on a column of silica gel with elution by system 3. Fractions with a volume of 5-7 ml were collected. By crystallization from a mixture of alcohol and acetone, fractions 13-21 yielded 23 mg of base (**1**) with mp 214-215°C.

Nitrarizine (2). Fractions 39-46 after the isolation of nitraricine were rechromatographed on a column of silica gel with elution by system 3. Fractions with a volume of 20-25 ml were collected. By crystallization from a mixture of alcohol and acetone, fractions 25-34 yielded 106 mg of base (**2**) with mp 265-267°C.

The mass spectrum of (**2**) showed the following ion peaks with m/z 319 (2), 318 (7), 303 (56), 302 (28), 301 (25), 276 (16), 274 (11), 220 (70), 219 (100), 206 (25), 193 (15), 182 (53), 169 (28), 133 (22), 122 (30).

The IR spectrum of (**2**) contained the following absorption bands (cm^{-1}): 770 (*o*-disubstituted benzene ring), 965 (N→O), 1010, 1050, 1110, 1140, 1160, 1230, 1280, 1340, 1380, 1410, 1450, 1510, 1580, 1600, 1620 (indole nucleus), 2840, 2960, 3030 and 3400.

Reduction of Nitrarizine. a) In portions, 100 mg of sodium tetrahydroborate was added to a solution of 43 mg of base (**2**) in 7 ml of methanol. Then the mixture was stirred at room temperature for 2 h. The solvent was distilled off, and the residue was decomposed with water and extracted with chloroform. The chloroform was distilled off and the residue was chromatographed on a column of silica gel with elution by system 3. Fractions with a volume of 10-12 ml were collected. This gave 12 mg of a base with mp 255-256°C (chloroform).

b) As a solution in 10 ml of alcohol, 52 mg of base (**2**) were hydrogenated over Pt for 2 h. The catalyst was separated off and the solvent was driven off in vacuum. The residue was separated chromatographically on a column of silica gel with elution by system 3. This gave 19 mg of a base with mp 255-256°C (alcohol).

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