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ALKALOIDS OF *Nitraria sibirica*. STRUCTURES OF NITRARAMIDINE AND NITRARAIDINE

T. S. Tulyaganov and F. Kh. Allaberdiev

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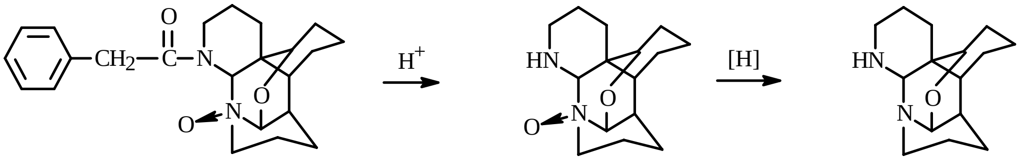
Two new alkaloids nitraramidine and nitraraidine were isolated from the aerial part of Nitraria sibirica. *Their structures were established using spectral data and chemical transformations.*

Key words: *Nitraria, Nitraria sibirica,* alkaloid, nitraramidine, nitraraidine.

In continuation of an investigation of the alkaloids of the aerial part of *Nitraria sibirica* Pall. [1], we isolated from the benzene part of the total bases by column chromatography nitramine and isonitramine [2], *l*-vasicinone [3], nitraramine [4], nitraroxine [5], sibirinine [6], and the new alkaloid **1**.



1 **3** **4**

We obtained by column chromatography from the $CHCl_3$ part of the total aklaoids the new alkaloid **2** in addition to **1**, *l*-vasicinone, sibirinine, nitraramine, and nitraroxine.

Compound **1**, $C_{23}H_{30}N_2O_3$, called by us nitraramidine, is very soluble in water, pyridine, and DMSO and difficulty soluble in CH_3OH and C_2H_5OH.

The UV spectrum of **1** exhibits absorption maxima at 209 and 245-253 nm. The IR spectrum contains bands due to vibrations of monosubstituted benzene ring (702 and 754 cm^{-1}), amide carbonyl (1642), saturated C–H bonds (2843 and 2947), and others.

The mass spectrum has a peak for the molecular ion with *m*/*z* 382 and peaks at 293, 292, 276, 275, 264, 263, and all sets of peaks belonging to nitraramine alkaloids [4, 5, 7].

The PMR spectrum of **1** contains multiplets for methylene and methine protons at 0.9-2.30 ppm. Furthermore, the following signals can be found: 3.48 (m), 4.09 (br.s, 1H), 4.31 (br.s, 1H), 4.44 (br.s, 1H), 4.81 (m), 7.31 (br.s, 5H, aromatic Ar–CH_2– protons).

The spectral data showed that the alkaloid belongs to the nitraramine group and contains a phenacetyl group.

Hydrolysis of nitraramidine in acidic medium produced phenylacetic acid and nitraramine N-oxide (**3**) [4, 7]. This is consistent with the mass spectrum of **1**, which contains a peak for the molecular ion with *m*/*z* 382 and a peak for $[M - 119]^+$, due to loss from $[M]^+$ of the phenylacetic acid, and a peak for the acyl ion of phenylacetic acid with *m*/*z* 119. Reduction of nitraramine N-oxide by Zn in HCl produced **4**, mp 85-86°C, identified as nitraramine [4].

Thus, nitraramidine is based on nitraramine N-oxide acylated by phenylacetic acid and is phenacetylnitraramine N-oxide.

Base **2**, mp 308-310°C, $C_{20}H_{25}N_2$, called by us nitraraidine, does not exhibit acidic or basic properties and is insoluble in ordinary organic solvents. It is optically inactive. $[M]^+$ is 293 (mass spectrometry).

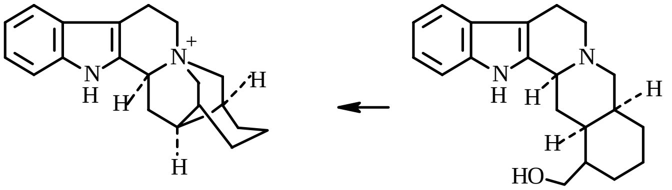
S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (99871)120 64 75, e-mail: cnc@icps.org.uz. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 479-481, November-December, 2002. Original article submitted November 18, 2002.

The UV spectrum exhibits absorption maxima at 224, 275, and 288 (sh) nm that are typical of the chromophore in tetrahydro-*β*-carboline compounds [8].

The IR spectrum contains absorption bands due to vibrations of *o*-disubstituted benzene ring (744), substituted indole (1456, 1495, 1571, 1599), saturated C–H bonds (2865, 2919, 2965), and active H (3273 and 3435 cm^{-1}).

The PMR spectrum of the alkaloid is complicated, showing multiplets for methine and methylene protons. The aromatic protons (4H) resonate at 7.13 (m, 2H), 7.42 (m, 1H), and 7.62 ppm (m, 1H) as a complicated four-spin system.

The spectral data are similar to those for yohimbine alkaloids [9-11] and coincide with those published for the product from the reaction of dihydronitraraine (**5**) with *p*-TsCl [12]. Compound **2** and that prepared by the literature method [12] were identical.



2 **5**

Thus, nitraraidine has the structure **2** and is isolated from natural sources for the first time. Alkaloids of this type have been obtained several times from natural sources [13-15].

EXPERIMENTAL

Instruments and spectral conditions, solvent systems used for TLC, and extraction and separation of total bases have been described in detail [1].

Column chromatography for separation of the benzene fraction of the total bases isolated from individual fractions nitramine, isonitramine, *l*-vasicinone, nitraramine, nitraroxine, and sibirinine.

Fractions 29-41 were combined and rechromatographed over a silica-gel column with elution by $CHCl_3$—CH_3OH mixtures (10:1 and then 4:1). Fractions of 8-10 mL were collected. Fractions 19-20 produced by crystallization from $CHCl_3$—C_2H_5OH (1:1) **1**, 39 mg, mp 225-226°C.

Nitraramidine (1), $[\alpha]_D$ ±0.

UV spectrum (EtOH, λ_{max}, nm): 209, 245-253 (log ε 4.02, 2.05).

IR spectrum (KBr, ν_{max}, cm^{-1}): 702, 754, 902, 1009, 1093, 1146, 1226, 1257, 1291, 1339, 1372, 1453, 1642, 2767, 2843, 2947, 3334.

Mass spectrum, *m/z* (I_{rel}, %): 383 $[M + 1]^+$ (11), 382 (20), 292 (100), 275 (20), 264 (13), 263 (21), 248 (9), 245 (33), 218 (11), 205 (17), 186 (13), 164 (10), 158 (18), 136 (16), 119 (17), 115 (28), 112 (42), 99 (16), 98 (21), 95 (28), 92 (52), 80 (70), 69 (68).

PMR spectrum (CD_3OD, δ, ppm): 1.75 (m), 2.27 (m), 2.57 (m), 309 (m), 3.48 (m), 4.09 (br.s, 1H), 4.31 (br.s), 4.44 (br.s), 4.81 (m), 7.31 (br.s, 5H); (Py-d_5, δ, ppm). 1.10 (m), 1.56 (m), 2.45 (m), 2.95 (m), 3.28 (m), 4.68 (m), 5.35 (br.s), 7.10 (m, 5H).

The $CHCl_3$ part (17.2 g) of the total bases were separated by chromatography over a silica-gel column with elution by $CHCl_3$—CH_3OH mixtures in various ratios (20:1, 10:1, and 4:1). Fractions of 30-40 mL were collected. *l*-Vasicinone, sibirinine, nitraramine, and nitraroxine were isolated from separate fractions.

Fractions 45-56 were combined and rechromatographed over a silica-gel column with elution by $CHCl_3$—CH_3OH (10:1). Fractions of 10-12 mL were collected. Fractions 15-21 were combined and recrystallized from C_2H_5OH—$CHCl_3$ (1:1). Yield of **2**, 31 mg, mp 308-310°C.

Fractions 28-34 afforded by crystallization from alcohol **1**, 47 mg, mp 225-226°C.

Nitraraidine (2).

UV spectrum (EtOH, λ_{max}, nm): 224, 275, 288 (sh) (log ε 4.05, 3.59, 3.47).

Mass spectrum, *m/z* (I_{rel}, %): 293 (3), 292 (5), 279 (45), 223 (9), 197 (13), 184 (16), 170 (38), 169 (49), 156 (14), 144 (13).

IR spectrum (KBr, ν, cm^{-1}): 744, 761, 817, 840, 860, 912, 948, 974, 1010, 1036, 1082, 1108, 1124, 1178, 1288, 1329, 1379, 1456, 1495, 1571, 1599, 2635, 2745, 2865, 2919, 2965, 3054, 3273, 3435.

PMR spectrum (DMSO + TCA, δ, ppm): 1.75 (m), 2.25 (br.s), 2.58 (m), 3.05 (m), 3.32 (m), 4.11 (m), 4.51 (m), 7.13 (m, 2H), 7.42 (m, 1H), 7.62 (m, 1H).

Hydrolysis of Nitraramidine. Compound **1** (0.03 g) was dissolved in HCl (5 mL, 10%) and heated at 90°C for 2 h. The acidic solution was washed with ether after the reaction was finished. The ether was removed. The solid was crystallized from petroleum ether. Yield of phenylacetic acid, 2 mg, mp 75-76°C. The acidic solution was basicified with KOH (10%) and shaken with $CHCl_3$. The solvent was removed. The solid was crystallized from ethanol—acetone. Yield of nitraramine N-oxide, 15 mg, mp 250-251°C.

Reduction of Nitraramine N-Oxide. Nitraramine. Compound **3** (11 mg) was dissolved in HCl (5 mL, 10%) and reduced by granulated Zn at room temperature for 16 h. The solution was basicified by KOH (10%) and extracted with $CHCl_3$. The solvent was removed. The solid was crystallized from petroleum ether. Yield of **4**, 7 mg, mp 85-86°C.

Quaternary Salt of Dihydronitraraine. Dihydronitraraine (35 mg) in dry purified pyridine (5 mL) was stirred by a magnetic stirrer and treated with *p*-toluenesulfonylchloride (67 mg) in pyridine (1.5 mL). The mixture was left for seven days in a refrigerator. The pyridine was vacuum distilled. The solid was dissolved in $CH_3OH—H_2O$ (4:1) and passed over anion exchanger. The solvent was removed. The solid was crystallized from CH_3OH. Yield, 29 mg, mp 310-312°C.

REFERENCES

1. T. S. Tulyaganov and F. Kh. Allaberdiev, *Khim. Prir. Soedin.*, 476 (2001).
2. A. A. Ibragimov, Z. Osmanov, B. Tashkhodzhaev, N. D. Abdullaev, M. R. Yagudaev, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 623 (1981).
3. M. V. Telezhenetskaya and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 731 (1977).
4. B. Tashkhodzhaev, A. A. Ibragimov, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 692 (1985).
5. A. A. Ibragimov and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 655 (1986).
6. A. A. Ibragimov, N. D. Abdullaev, Z. Osmanov, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 685 (1987).
7. T. S. Tulyaganov, *Khim. Prir. Soedin.*, 39 (1993).
8. A. W. Sangster and K. L. Stuart, *Chem. Rev.*, **65**, 69 (1965).
9. P. E. Aldrich, P. A. Diassi, D. F. Dickel, C. M. Dylion, P. D. Hance, C. F. Huebner, B. Korzun, M. E. Kuehne, L. H. Liu, H. B. MacPhillamy, E. W. Robb, D. K. Roychaudhuri, E. Schlittler, A. F. St. Andre, E. E. van Tamelen, F. L. Weisenborn, E. Wenkert, and O. Wintersteiner, *J. Am. Chem. Soc.*, **81**, 2481 (1959).
10. J. D. Albright, L. A. Mitcher, and L. Goldman, *J. Heterocycl. Chem.*, **7**, 623 (1970).
11. A. A. Ibragimov and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 536 (1985).
12. A. A. Ibragimov and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 544 (1985).
13. J. Penelle, P. Christen, J. Molgo, M. Tits, V. Brant, M. Frederich, and L. Angenot, *Phytochemistry*, **58**, 619 (2001).
14. T. Fujii, M. Ohba, and S. Seto, *Chem. Pharm. Bull.*, **43**, 49 (1995).
15. J. Penelle, M. Tits, P. Christen, J. Molgo, V. Brandt, M. Frederich, and L. Angenot, *Phytochemistry*, **53**, 1057 (2000).