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ALKALOIDS FROM *Nitraria komarovii*. STRUCTURES OF NITRARIDINE, DIHYDRONITRARIDINE, AND TETRAHYDRONITRARIDINE

T. S. Tulyaganov

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*Three new alkaloids nitraridine (**1**), dihydronitraridine (**2**), and tetrahydronitraridine (**3**) were isolated from the aerial part of* Nitraria komarovii. *Their structures were established based on chemical transformations and spectral data. The compounds were synthesized. Spectral properties of the komarovine subgroup of alkaloids were discussed.*

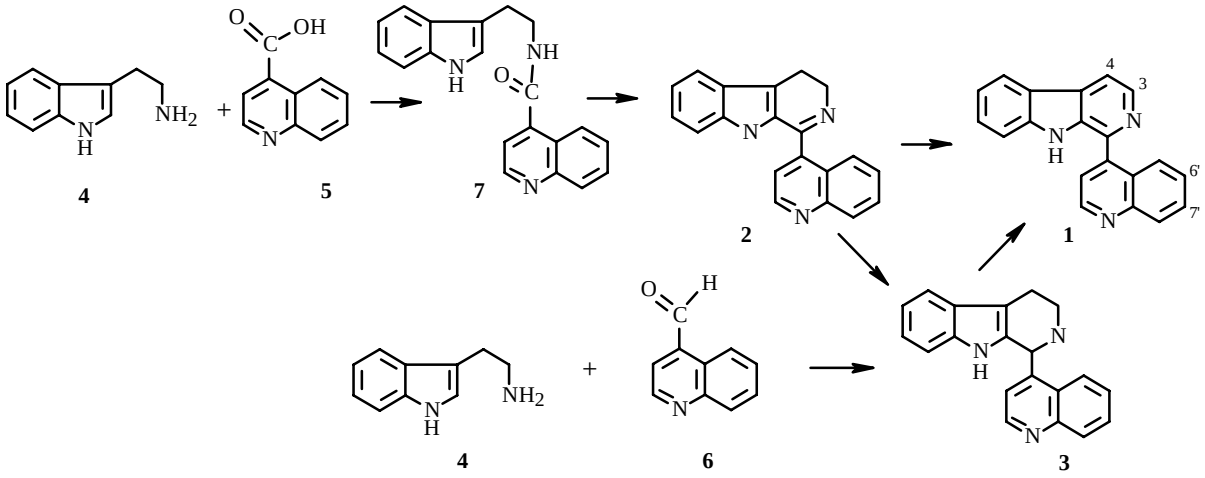
Key words: *Nitraria, N. komarovii*, alkaloid, nitraridine, dihydronitraridine, tetrahydronitraridine, komarovine.

The plant *Nitraria komarovii* Jljin et Lava that grows near Turkmanbashi (Krasnovodsk) in the Republic of Turkmenistan was studied.

Column chromatography of the benzene and ethylacetate extracts after isolation of isokomarovine and komarovidinine [1] produced a base with mp 272-273°C (CH_2Cl_2) of formula $C_{20}H_{13}N_3$ that we called nitraridine (**1**) [2].

The UV spectrum of **1** had the following absorption maxima (λ_{max}, EtOH): 211, 233, 252 (sh), 294, 317 (sh), 360 nm (log ε 4.65, 4.65, 4.32, 4.18, 3.93, 3.77). Upon acidification, they changed (λ_{max}, EtOH + H^+): 227, 242 (sh), 313, 385. The UV spectrum of the alkaloid is consistent with a conjugated chain of double bonds in the molecule. The change in acidic medium indicates that a β-carboline moiety may be present in **1** [3].

The mass spectrum of **1** had a peak for the molecular ion $[M]^+$ at 295 and a peak for the doubly charged molecular ion $[M]^{++}$ at 147.5. The mass spectrum of **1** was identical to those of the alkaloids komarovine, isokomarovine, komarovinine, and nitramarine.



The PMR spectrum of **1** exhibited the following signals characteristic of aromatic protons (δ, ppm, J/Hz): 7.30 (2H, m, H-6, H-3′), 7.48 (3H, m, H-7, H-8, H-6′), 7.52 (1H, m, H-7′), 7.62 (1H, m, H-5′), 7.94 (1H, dd, J = 8 and 2, H-8′), 8.10 (1H, d, J = 6, H-4), 8.19 (1H, dd, J = 9 and 2, H-5), 8.51 (1H, d, J = 7, H-3), 8.67 (1H, d, J = 5, H-2′).

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: tstulyaganov@rambler.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 370-372, July-August, 2006. Original article submitted September 27, 2004.

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The IR spectrum of **1** lacked absorption bands for methyls and methylenes but had bands characteristic of the indole nucleus (1460, 1510, 1570, 1630 cm^{-1}) and an *o*-disubstituted benzene ring (745 cm^{-1}).

The spectral data of the alkaloid indicated that nitraridine was an isomer of previously described alkaloids. A direct comparison of the physicochemical and spectral properties of **1** with synthetic samples of isomeric 1-(quinolinyl)-*β*-carbolines showed that nitraridine was identical to 1-(4-quinolinyl)-*β*-carboline. We synthesized a compound with this structure by two methods, as for komarovine [4].

Cinchoninic acid (**5**) was synthesized from isatin by the literature method [5]; quinoline-4-aldehyde (**6**), by oxidation of lepidine with selenous anhydride in boiling xylene.

Chromatography over a silica-gel column of the benzene part of the total bases from the aerial part of *N. komarovii* collected in May 1987 isolated two bases **2** and **3**.

Base **2**, mp 262-263°C had formula $C_{20}H_{15}N_3$ and molecular weight 297 (mass spectrometry).

The UV spectrum had absorption maxima (λ_{max}, EtOH): 218, 244 (sh), 307, 312 nm (log ε 4.51, 4.07, 3.93, 3.98).

The IR spectrum contained the following absorption bands (λ_{max}): 745, 770 (*o*-disubstituted benzene ring), 850, 910, 1185, 1280, 1325, 1370, 1450, 1465, 1510, 1560, 1600, 1620 (indole nucleus), 2840, 2950, 3070, and 3140 cm^{-1}.

The PMR spectrum of **2** exhibited signals characteristic of aromatic protons at 7.00-8.65 ppm and two triplets of neighboring methylenes at 3.04 and 4.07 ppm.

Base **3**, mp 176-177°C, $C_{20}H_{17}N_3$, was optically inactive, $[M]^+$ 299.

The IR spectrum contained absorption bands at 765 (*o*-disubstituted benzene ring), 1470, 1515, 1580, 1620 (indole nucleus), 2870, 2930, 2960, and 3240 cm^{-1}.

The UV spectrum had the following absorption maxima (λ_{max}, EtOH): 227, 275-286, 304, 316 nm (log ε 4.52, 4.01, 3.84, 3.72). The spectrum changed upon acidification (λ_{max}, EtOH + H^+): 236, 308, 317 nm.

The PMR spectrum exhibited the following signals (δ, ppm): 3.06 (t, 2H), 3.53 (t, 2H), 4.04 (br.s, 1H), 5.77 (t, 1H), 7.10-8.51.

Alkaloids with identical compositions and comparable spectral properties were isolated previously from this plant. Reduction of **2** by $NaBH_4$ formed **3**. Thermal dehydrogenation of **2** and **3** by Pd-black formed **1**.

Comparison of the spectral parameters and properties of **2** and **3** with those of the 3,4-dihydro- and 1,2,3,4-tetrahydro-derivatives of nitraridine that were prepared during the synthesis of nitraridine inducated that they were identical.

Thus, **2** had the structure 1-(quinolin-4-yl)-3,4-dihydro-*β*-carboline; **3**, 1-(quinolin-4-yl)-1,2,3,4-tetrahydro-*β*-carboline, which were called dihydronitraridine and tetrahydronitraridine, respectively.

EXPERIMENTAL

PMR spectra were recorded on a Tesla Bs 567 A spectrometer at 100 MHz and HMDS = 0; IR spectra, on UR-20 and Perkin—Elmer System 2000 FT-IR instruments in KBr disks; mass spectra, in MX-1310 and Kratos MS-25 RF GC—MS spectrometers; UV spectra, in alcohol on a EPS-3T (Hitachi) spectrophotometer and a Lambda 16 UV/Vis spectrometer.

The purity of compounds was checked by chromatography in a thin layer of KSK and L 5/40 silica gels. Chromatography used the following solvent systems: C_6H_6:CH_3OH (4:1, 1), $CHCl_3$:CH_3OH (1:1, 2), $CHCl_3$:CH_3OH:NH_4OH (4:1:0.05, 3), C_6H_6:$CHCl_3$ (5:1, 4), $CHCl_3$:$(CH_3)_2CO$:CH_3OH (5:4:1, 5), $CHCl_3$:$(CH_3)_2CO$:C_2H_5OH (5:4:1, 6), $CHCl_3$:$(CH_3)_2CO$ (4:1, 7), C_6H_6:$(CH_3)_2CO$ (9:1, 8).

The extraction and separation have been described in detail [1, 6, 7].

Isolation of Nitraridine. Mother liquors of the benzene and ethylacetate extracts after isolation of isokomarovine and komarovidinine were chromatographed over silica-gel columns with elution by $CHCl_3$ and then system 5, collecting 10-15 mL. Fractions 23-35 were combined and separated again over a silica-gel column with elution by system 7. Recrystallization from CH_2Cl_2 produced nitraridine (0.044 g, 0.00016% by weight of air-dried plant), mp 272-273°C.

Synthesis of Nitraridine [1-(Quinolin-4-yl)-*β*-carboline].

Quinolin-2,4-dicarboxylic Acid. Isatin (14.7 g, 0.1 mol) in KOH solution (110 mL, 33%) was treated with pyruvic acid (11.4 g, 0.11 mol). The mixture was kept at 35-40°C for 48 h. The precipitated potassium salt of quinolin-2,4-dicarboxylic acid was filtered off, washed with absolute alcohol, and dissolved in water. The solution was acidified with dilute HCl until the pH was 3-4. The precipitate was filtered off, washed with water, and dried to afford the acid (17.5 g, 80%), mp 245-246°C.

Cinchoninic Acid (5). Quinolin-2,4-dicarboxylic acid (10 g, 0.046 mol) was boiled in dry nitrobenzene (75 mL) for 20-25 min. The solution was cooled, filtered, and evaporated in vacuo. The solids on the filter and in the filtrate were combined and recrystallized from water to afford **5** (6.5 g, 81%), mp 253-254°C.

3-[β-(4-Quinolinylcarboxamido)ethyl]indole (7). A mixture of tryptamine (3 g, 0.018 mol) and **5** (3.6 g, 0.02 mol) was heated at 190-210°C for 1.5 h, cooled, and triturated with acetone to afford **7** (3 g, 56%), mp 236-237°C.

3,4-Dihydro-1-(quinolin-4-yl)carboline (2). Amide **7** (3 g, 0.01 mol) in PCl_3 (10 mL) was refluxed on a sand bath with a $CaCl_2$ trap for 1.5 h and cooled. The excess of the reagent was destroyed with water. The acidic solution was washed with ether and decomposed with aqueous NaOH (15%). The product was extracted with ether and then $CHCl_3$ to afford **2** (1.21 g, 40% of theoretical), mp 263-264°C.

PMR spectrum (100 MHz, $CDCl_3$ + CD_3OD, δ, ppm, J/Hz): 3.04 (2H, t, J = 8, H-4), 4.07 (2H, t, J = 8, H-3), 7.05 (1H, m, H-6′), 7.15 (2H, m, H-6, H-7), 7.38 (1H, d, J = 5.5, H-3′), 7.40 (1H, m, H-7′), 7.53 (2H, m, H-8, H-5′), 7.70 (1H, dd, J = 8 and 2, H-5), 7.94 (1H, d, J = 9, H-8′), 8.68 (1H, d, J = 6, H-2′).

Quinoline-4-aldehyde (6). Lepidine (20 g, 0.14 mol) and selenous anhydride (17 g) were boiled in xylene for 2 h, cooled, and filtered. The solid was washed with benzene and then $CHCl_3$. Solvent was removed in vacuo. The solid was recrystallized from water to afford **6** (13 g, 59%), mp 83-84°C.

1,2,3,4-Tetrahydro-1-(quinolin-4-yl)-β-carboline (3). A mixture of tryptamine hydrochloride (5 g, 0.025 mol), **6** (6 g, 0.038 mol), water (100 mL), and H_2SO_4 (20 mL, 2 N) was heated at 110°C for 2 h, cooled, washed with $CHCl_3$, and decomposed with NaOH solution (15%). The product was extracted with ether and then $CHCl_3$ and recrystallized from CH_2Cl_2 to afford **3** (4.5 g, 59%), mp 176-177°C.

PMR spectrum: 3.15 (2H, t, J = 7, H-4), 3.53 (2H, t, J = 8, H-3), 5.77 (1H, br.s, H-1), 7.15 (1H, d, J = 6, H-3′), 7.25 (2H, m, H-6, H-6′), 7.46 (3H, m, H-7, H-8, H-7′), 7.53 (1H, m, H-5), 7.83 (1H, m, H-5′), 8.44 (1H, d, J = 7, H-8′), 8.62 (1H, d, J = 6, H-2′).

1-(Quinolin-4-yl)-β-carboline (1). a) A mixture of 3,4-dihydro-1-(quinolin-4-yl)-β-carboline (1 g, 0.0035 mol) and sulfur (0.4 g) was heated at 180-200°C for 40 min, cooled, and dissolved in H_2SO_4 (10%). The acidic solution was filtered. The filtrate was washed with $CHCl_3$ and made basic with KOH solution (15%). The product was extracted with ether and then $CHCl_3$ to afford **1** (0.5 g, 52%), mp 272-273°C.

b) Compound **3** (1.5 g, 0.0051 mol) and sulfur (0.5 g) were dehydrogenated by the method described above to afford **1** (0.75 g, 53%), mp 272-273°C.

IR spectrum (KBr, ν, cm^{-1}): 3130, 3070, 1630, 1590, 1570, 1510, 1460, 1430, 840, 770, 745.

Mass spectrum (EI, 70 eV, *m*/*z*, I_{rel}, %): 295 (100) $[M]^+$, 147.5 (7) $[M]^{++}$.

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