ALKALOIDS OF *Nitraria komarovii*.

VI. STRUCTURE AND SYNTHESIS OF ISOKOMAROVINE AND OF KOMAROVIDININE

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Two new alkaloids, isokomarovine and komarovidinine, have been isolated from the epigeal part of the plant *Nitraria komarovii* Iljin et Lava. The passage from isokomarovine to komarovidinine has been performed. Their structures have been established on the basis of spectra and experimental facts: 1-(quinolin-5'-yl)-9H-pyrido[3,4-b]indole and indolo[3,2,1-de]quinolino[4,5-gh][1,5]naphthyridine, respectively. Their synthesis has been performed.

Continuing a study of the alkaloids of *Nitraria komarovii* Iljin et Lava [1], we have separated the combined ether-extracted alkaloids of the plant collected in August, 1979, according to solubilities in a Soxhlet apparatus. Two bases have been isolated from the benzene and ethyl acetate extracts by chromatography on a silica gel column. They have also been isolated from the combined ether-extracted material from the epigeal part of the plant collected in August, 1980.

The base with the composition $C_{20}H_{13}N_3$, mp 321-322°C (CH_2Cl_2), M^+ 295, we have called isokomarovine (I) [2]. The composition and UV spectrum of isokomarovine coincide with those of komarovine [1, 3]. Their mass-spectrometric fragmentations are also similar. There are differences in the IR and PMR spectra.

A base with the composition $C_{20}H_{11}N_3$ with mp 254-255°C, M^+ 293, M^{++} 146.5, we have called komarovidinine (II).

Chloroform solutions of the alkaloids fluoresce strongly. $\lambda_{max}^{ethanol}$ 242, 267, 295-308, 390, 406, 430 nm (log ε 4.70; 4.36; 4.02; 3.04; 3.30; 3.56). $\lambda_{max}^{ethanol+H^+}$ 246 (shoulder), 267, 396 (shoulder), 417, 440.

The presence of bands in the visible region of the UV spectrum of (II) shows that (II) is a condensed polycyclic aromatic compound. The PMR spectra of (I) and (II) lack strong-field signals characteristic for aliphatic and alicyclic compounds.

The composition of isokomarovine differs from that of komarovidine by two hydrogen atoms. When (I) was heated with Pd black, (II) was formed. It is obvious from what has been said above that (I) is an isomer of the alkaloid komarovine (III) [1, 3] with respect to the position of the β-carboline residue in the quinoline nucleus. Taking into account the fact that (II) with the properties given is formed on the dehydrogenation of isokomarovine, for the latter we have proposed the structure of 1-(quinolin-5'-yl)-9H-pyrido[3,4-b]indole. We have synthesized a compound of this structure from tryptamine and quinoline-5-carboxylic acid by a general method (see scheme).

However, in the last stage of the reaction under the conditions of dehydrogenation over palladium, the expected isokomarovine was converted almost completely into a substance identical with komarovodinine. The oxidation of the product (VII) by nitrobenzene permitted the reaction to be stopped at the stage of the formation of isokomarovine. The melting point of a mixture of the natural and synthetic samples showed no depression. Their spectral characteristics were also identical.

Thus, the alkaloid isokomarovine has the structure of 1-(quinolin-5'-yl)-9H-pyrido[3, 4-b]indole, and komarovidine is indolo[3,2,1-de]quinolino[4,5-gh][1,5]naphthyridine.

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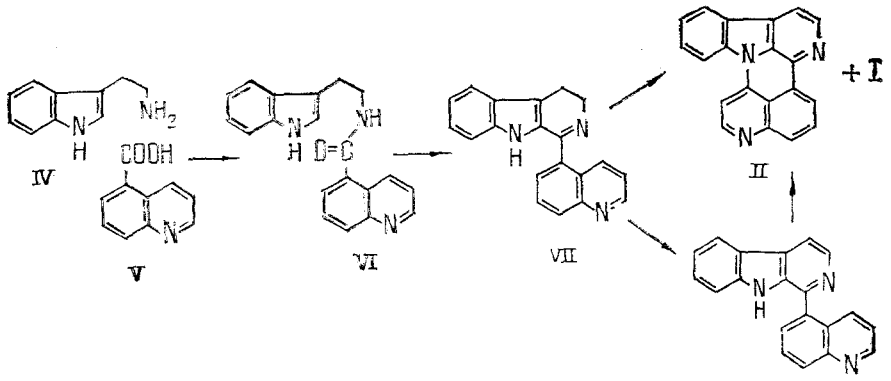

EXPERIMENTAL

UV spectra were taken in ethanol on a Hitachi spectrophotometer, mass spectra on an MKh-1310 mass spectrometer, PMR spectra on a JNM-4H 100/100 MHz instrument in $CDCl_3$–CD_3OD with HMDS as internal standard (δ scale), and IR spectra on a UR-20 spectrometer (KBr tablets). For TLC we used silica gel L 5/40 μm and the following solvent systems: 1) benzene–methanol (4:1); 2) chloroform–acetone–methanol (5:4:1); 3) benzene–ethyl acetate–diethylamine (7:2:1); and 4) chloroform–acetone–ethanol–ammonia (10:8:1:0.2).

Isokomarovine (I). The epigeal part of *N. komarovii* gathered in August, 1979 (17 kg) was extracted as described previously [1, 4]. This gave 36.5 g of total alkaloids (0.22% of the weight of the air-dried plant). A mixture of 20 g of the ether-extracted material and 40 g of alumina was made and the alkaloids were separated according to their solubilities in a Soxhlet apparatus using extraction with petroleum ether (40-70°C), benzene, ethyl acetate, ether, chloroform, and chloroform–methanol (1:1).

The epigeal part gathered in August, 1980 (8.7 kg) was extracted by the method described above. This gave 13.85 g (0.16%) of total alkaloids. The separation of 10 g of the ether-extracted material was carried out by the method described above. Chromatographically similar extracts (benzene and ethyl acetate) were combined and chromatographed on a column of silica gel. Elution was performed with chloroform and then with system 2 (10 ml portions). Fractions 10-17 yielded the technical base. Rechromatography in system 1 gave 45 mg (0.00017% of the weight of the dry raw material) of isokomarovine with the composition $C_{20}H_{13}N_3$, mp 321-322°C (petroleum ether–benzene, and CH_2Cl_2). Here and below the results of analyses corresponded to the calculated figures.

Komarovidinine. A. The subsequent fractions after the separation of the isokomarovine were combined and rechromatographed on a column of silica gel in system 1. After recrystallization from petroleum ether–benzene and then from CH_2Cl_2, 40 mg of komarovidinine was obtained with the composition $C_{20}H_{11}N_3 \cdot 2H_2O$, mp 254-255°C.

B. The combined petroleum ether fractions were chromatographed on a column of silica gel with elution by chloroform (10-ml fractions). Fractions 10-14 (strongly fluorescing solution) yielded komarovidinine. After recrystallization from petroleum ether–benzene and then from ethylene chloride, another 20 mg of (II) was obtained. The total yield was 60 mg (0.00023% on the weight of the dry raw material).

Passage from Isokomarovine to Komarovidinine. A round-bottomed flask with a carefully ground mixture of 20 mg of (I) and 20 mg of Pd black was immersed in a sand bath previously heated to 180°C. It was kept at a temperature of 180-200°C for 30 min. The cooled mass was dissolved in chloroform–methanol (1:1), the catalyst was filtered off, and the filtrate was evaporated. The residue was recrystallized from CH_2Cl_2, giving 9 mg (45%) of (II) with mp 254-255°C.

Quinoline-5-carboxylic Acid (V) [5]. In a round-bottoned flask with a reflux condenser were mixed 20 g of m-aminobenzoic acid, 10 g of m-nitrobenzoic acid, 45 ml of glycerol, and 30 ml of concentrated H_2SO_4. A rise in temperature first took place through the evolution of heat. Then the mixture was heated in a sand bath for 7 h. The cooled reaction mixture was dissolved in aqueous ammonia and the solution was boiled with activated carbon. Then it was filtered and the filtrate was treated with glacial acetic acid. The precipitate was filtered off and was crystallized from ethanol–acetic acid to give 10.2 g (40.3%) of (V), mp 340-342°C.

1-[β-(Quinoline-5'-carboxamido)ethyl]indole (VI). A ground mixture of 1.8 g (0.011 mole) of (IV) and 2.0 g (0.012 mole) of (V) was heated at 230-250°C (sand bath) for 1.5 h. After cooling, the fused mass was boiled with acetone. The precipitate that deposited was separated off and crystallized from methylene chloride, giving 1.75 g (50%) of technical (VI).

1-(Quinolin-5'-yl)-3,4-dihydro-β-carboline (VII). A. The reaction was carried out in a similar manner to that described in the synthesis of the 8'- isomer [1]. Yield 30% of theoretical, mp 253-254°C, composition $C_{20}H_{15}N_3 \cdot H_2O$.

B. A mixture of 1 g of technical (VI) and 5 ml of $POCl_3$ was boiled on a sand bath under a reflux condenser fitted with a calcium chloride tube for 1.5 h. After cooling, the excess of $POCl_3$ was decomposed carefully with ice. The acid solution was washed with ether and was decomposed with 15% caustic soda, and the product was extracted with ether and then with chloroform. This gave 400 mg (40%) of (VII).

Indolo[3,2,1-de]quinolino[4,5-gh][1,5]naphthyridine (II). A. A ground mixture of equal amounts (200 mg) of (VII) and Pd black in a round-bottomed flask was immersed in a sand bath previously heated to 180°C. It was kept at 180-200°C for 40 min. Then the cooled mass was dissolved in chloroform–methanol (1:1). The catalyst was filtered off, and the filtrate was evaporated. The residue was chromatographed on a column of silica gel in system 1. Recrystallization from petroleum ether–benzene and then from CH_2Cl_2 yielded 90 mg (45%) of (II) with mp 254-255°C.

B. A ground mixture of 200 mg of (VII) and 200 mg of selenium in a round-bottomed flask was placed in a sand bath heated to 290°C. The temperature was raised over 10 min to 300°C, and the reaction mixture was kept at this temperature for another 5 min. The cooled mass was then dissolved in 10% sulfuric acid and the acid solution was filtered and washed with ether. Then it was decomposed with 15% caustic soda and the product was extracted with ether and then with chloroform, giving 80 mg (40%) of (II).

C. The reaction was carried out with a mixture of 200 mg of (VII) and 100 mg of sulfur in a similar manner to experiment A. Then the product was worked up in a similar manner to experiment B. This gave 78 mg (40%) of (II).

1-(Quinolin-5'-yl)-β-carboline (I). A mixture of 0.5 g of (VII) and 12 ml of dry nitrobenzene was boiled for 45 min. Then the solution was diluted with an equal amount of chloroform. The substance was extracted from the mixture with 10% sulfuric acid solution, and the acid solution was washed with ether. Then it was decomposed with 15% caustic soda, the product was extracted with ether and then with chloroform. The solvents were evaporated off, the residue was boiled with methanol with the addition of activated carbon, and then the carbon was filtered off, and the filtrate was evaporated. The residue was recrystallized several times from methylene chloride, to give 0.24 g (50%) of (I) with mp 320-321°C.

SUMMARY

Two new alkaloids, isokomarovine and komarovidinine, have been isolated from the epigeal part of *Nitraria komarovii* Iljin et Lava. Their structures have been shown and their total syntheses have been performed. The 1-(quinolin-5'-yl)-3,4-dihydro-β-carboline obtained in the course of this synthesis, which has not been described in the literature, has been characterized.

LITERATURE CITED

1. T. S. Tulyaganov, A. A. Ibragimov, and S. Yu. Yunusov, Khim. Prir. Soedin., 192 (1981).
2. A. A. Ibragimov, T. S. Tulyaganov, and E. Osmanov, Vth Youth Conference on Synthetic and Natural Physiologically Active Compounds Devoted to the Sixtieth Anniversary of Soviet Armenia, Abstracts of Lectures [in Russian], Erevan (1980), p. 40.
3. T. S. Tulyaganov, A. A. Ibragimov, and S. Yu. Yunusov, Khim. Prir. Soedin., 732 (1980).
4. T. S. Tulyaganov, A. A. Ibragimov, and S. Yu. Yunusov, Khim. Prir. Soedin., 737 (1979).
5. L. Bradford, T. I. Elliott, and F. M. Rowe, J. Chem. Soc., 437 (1947).