Chemistry of Natural Compounds, Vol. 29, No. 6, 1993

Oxytropis ALKALOIDS
II. STRUCTURE OF OXYTRIPHINE

V. I. Akhmedzhanova, D. Batsurén, and R. Sh. Shakirov

UDC 547.944/945

The new alkaloid oxytriphine, the parent of natural 2-oxazoline derivatives, has been isolated from the epigeal part of Oxytropis trichophysa*; and its structure has been established as (5S)-(+)-2,5-diphenyl-2-oxazoline. (−)-N-Benzoyl-2-phenyl-2-hydroxyethylamine and benzoic acid have been detected in this plant for the first time. A hypothesis of the possible biogenetic interrelationship of the compounds isolated is put forward.*

Continuing an investigation of the alkaloid composition of plants of the genus *Oxytropis* (fam. *Fabaceae*) [1], we have isolated two alkaloids (I and II) and a nitrogen-free substance (III) from the epigal part of *O. trichophysa* growing in the western part of Mongolia.

Substance (I) was an optically active compound exhibiting the characteristic properties of amide alkaloids [1, 2]. Its IR spectrum contained absorption bands of active hydrogen (3300 cm^{-1}) and of an amide carbonyl (1645 cm^{-1}), while its UV spectrum was typical for bases of the 2-(β)-phenylethylamine group.

The ^1H NMR spectrum of the alkaloid showed the signals of the protons of two monosubstituted benzene rings and of a hydroxylated ethylamine grouping. Under electron impact, (I) gave intense peaks of ions with m/z 135, 134, 105, and 77, while the peak of its molecular ion was observed in the LSIMS(+) mass spectrum.

These characteristics agree with those of (−)-N-benzoyl-2-hydroxy-2-phenylethylamine, isolated previously from *O. pseudoglandulosa* [3], but this is the first time that it has been found in *O. trichophysa*. Its optical antipode (IV) has been isolated from *O. trichophysa* growing in a different site [1]. Base (II), composition $C_{15}H_{13}ON$, was optically active and readily soluble in the usual organic solvents, and, in contrast to (I) gave the characteristic reactions for alkaloids with tungstosilicic acid and the Dragendorff reagent.

In the ^1H NMR spectrum of (II), just as for (I) the signals of 10 aromatic protons were observed, but the signals of a hydroxylated ethylamine grouping were absent. In addition to these, three one-proton doublets of doublets were observed at δ 3.91, 4.40, and 5.60 ppm, forming an ABX system. The chemical shifts of the signals and their multiplicities, and also their spin-spin coupling constants, were typical for the protons of the oxazoline ring in 2,5-disubstituted derivatives of 2-oxazoline [4-6]. This was confirmed by the mass spectrum of (II), which contained a weak peak of the molecular ion with m/z 223 and the maximum peak of an ion with m/z 117. The IR spectrum of the alkaloid showed an absorption band at 1655 cm^{-1}, confirming the presence of a C=N bond.

On the basis of the facts given and with consideration of its specific rotation it was possible to conclude that (II) had the structure (5S)-(+)-2,5-diphenyl-2-oxazoline, previously known as a synthetic compound [6] but now found in nature for the first time: we have called it oxytriphine.

It is known that many oxazole derivatives are unstable under the action of acids [7]. Since neither acids nor alkalis were used in the isolation of (II) (see the Experimental part) the native nature of oxytriophine is not a matter of doubt.

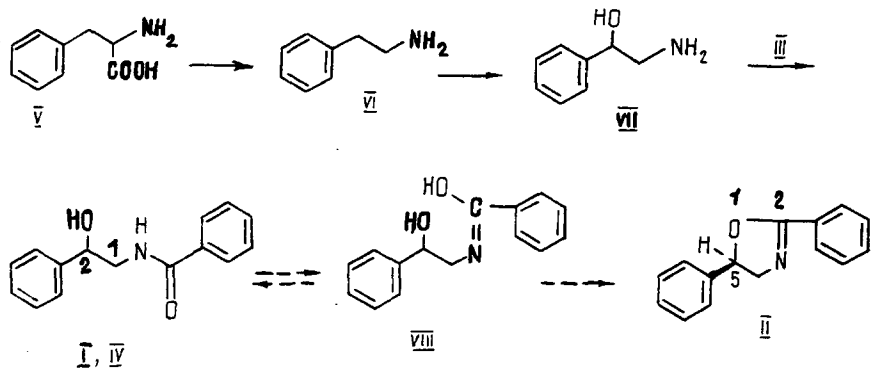
The 2-oxazoline ring is a component of several compounds isolated from microorganisms and belonging to hydroxamic acid derivatives (mycobactin [8]) and spermidine derivatives (agrobactin and parabactin [9]. However, this is the first time that oxazoline bases have been detected in the vegetable kingdom. Oxytriphine is the parent of a new group of natural 2-oxazolne derivatives.

By its mass and IR spectra and a mixed melting point, compound (III) was identified as benzoic acid, and this is the first time that it has been isolated from *O. trichophysa*.

Institute of the Chemistry of Plant Substances, Uzbekistan Academy of Sciences, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 873-876, November-December, 1993. Original article submitted April 29, 1993.

 0009-3130/93/2906-0778$12.50

It has been shown by experiments with compounds containing labeled carbon atoms that the common biogenetic precursor of alkamides of the 2-(β)-phenylethylamine group is phenylalanine [10]. This fact, and also the simultaneous presence of (I-III) in *O. trichophysa* permits us to put forward the hypothesis of a biogenetic interrelationship of the compounds mentioned in this plant (scheme). According to the scheme proposed, compounds (I) and (IV) are formed from phenylalanine (V) as the result of biological decarboxylation to (VI) followed by hydroxylation to (VII), and N-benzoylation. So far as concerns oxytriphine, it formation from N-benzoyl-2-hydroxy-2-phenylethylamine is possible as a result of the cyclization of a tautomeric form of the latter (VIII) with the splitting out of a molecule of water.



EXPERIMENTAL

UV spectra were taken on a Hitachi spectrophotometer, IR spectra on a UR-20, ^{1}H NMR spectra on a Tesla BS-567A spectrometer ($CDCl_3$, δ scale, 0 - HMDS), and mass spectra on a MKh-1310 instrument with a system for direct insertion into the ion source (a) and with a LSIMS(+) source (b), and also on a Kratos MS-25 chromato-mass spectrometer (c). The conditions for performing high-resolution mass spectrometry (HRMS) have been given in [11].

For column chromatography we used type KSK silica gel, and for thin-layer chromatography the same type of silica gel with 5% of gypsum, in the solvent system benzene–methanol (4:1); the revealing agents were iodine vapor and the Dragendorff reagent.

Isolation of (I-III). The air-dry epigeal part of *O. trichophysa* gathered in western Mongolia (0.3 kg) was extracted with methanol. The dry extract was treated with hexane. The hexane solution, after the evaporation of the solvent, was deposited on a column of silica gel (1:100) and was eluted with benzene–methanol (4:1). The first eluates yielded 50 mg of (II) and the following ones 25 mg of (III) and 3 g of (I).

(−)-N-Benzoyl-2-hydroxy-2-phenylethylamine (I), mp 151-152°C (from chloroform), $[\alpha]_D$ −21° (*c* 0.70, methanol).

UV spectrum, λ_{max}, nm: 210, 226 (shoulder).

IR spectrum (KBr), ν_{max}, cm^{-1}: 3300, 1645, 1568, 1490, 1460, 1310, 1200, 1060, 920, 760, 700.

Mass spectrum, m/z (%): 242 [(M + H)$^+$, 12] (b); 135 (100), 134 (90), 105 (97), 77 (40) (a).

^{1}H NMR spectrum: 3.35 (1H, br.s; OH); 3.50 (1H, m; H–C–H); 3.85 (1H, m; H–C–H); 4.90 (1H, m; H–C–OH); 6.58 (1H, br.s; NH); 7.38 (8H, m; Ar–H), 7.70 (2H, m; Ar–H).

Oxytriphine (II), $C_{15}H_{13}ON$ (HRMS), faint yellowish oily substance., $[\alpha]_D$ + 116° (c 1.34; chloroform).

IR spectrum, ν_{max}, cm^{-1}: 1655, 1500, 1455, 1340, 1260, 700.

Mass spectrum, m/z (%): 223 (M$^+$, 2.4), 118 (12), 117 (100), 105 (16), 91 (7), 90 (4), 78 (3), 77 (27) (c).

HRMS: $C_{15}H_{13}NO$. Calculated 223.10103. Found 223.09973.

^{1}H NMR spectrum: 3.91 (1H, dd, J = 8, 13 Hz, H-4), 4.40 (1H, dd, J = 10; 13 Hz; H-4), 5.60 (1H, dd, J = 8; 10 Hz; H-5), 7.32 (8H, m; Ar–H), 7.98 (2H, m; Ar–H).

Benzoic acid (III), mp 121-122°C (ether–hexane).

IR spectrum, ν_{max}, cm^{-1} 2800-3200 (OH), 1700 (C=O).

Mass spectrum, m/z (%): 122 (M$^+$, 70), 105 (100), 77 (80).

REFERENCES

1. D. Batsurén, S. Tsétségmaa, N. Batbayar, D. Dungérdordzh. V. I. Akhmedova, Yu. M. Mil'grom, Ya. V. Rashkes, and A. A. Ibragimov, Khim. Prir. Soedin., 388 (1992).
2 A. Chatterjee, M. Chakrabarty, and A. B. Kundu, Aust. J. Chem., **28**, 457 (1975).
3. S. Huneck, J. D. Connoly, and T. Khaidov, Fitoterapia, **57**, No. 6, 423 (1986).
4. O. Tsuge, S. Kanemasa, and K. Mamsuda, J. Org. Chem., **51**, 1997 (1986).
5. L. N. Pridgen, L. B. Killmer, and R. L. Webb, J. Org. Chem., **47**, 1985 (1982).
6. A. I. Meyers, M. A. Hanagan, L. M. Trefonas, and R. J. Baker, Tetrahedron, **39**, 1991 (1983).
7. P. Karrer, Organic Chemistry, 4th English ed., Elsevier, Amsterdam (1950).
8. G. A. Snow, J. Chem. Soc., 4080 (1954).
9. T. Peterson, K.-E. Falk, S. A. Leong, M. R. Klein, and J. B. Neilands, J. Am. Chem. Soc., **102**, 7715 (1980).
10. R. H. F. Manske, The Alkaloids, Academic Press, New York, Vol. 3 (1953), p. 315.
11. V. A. Raldugin, Yu. V. Gatilov, T. V. Rybalova, And Ya. V. Rashkes, Khim. Prir. Soedin., 688 (1986).