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CRYSTAL AND MOLECULAR STRUCTURE OF KARAKOLINE

I. M. Yusupova, B. Tashkhodzhaev, and M. N. Sultankhodzhaev

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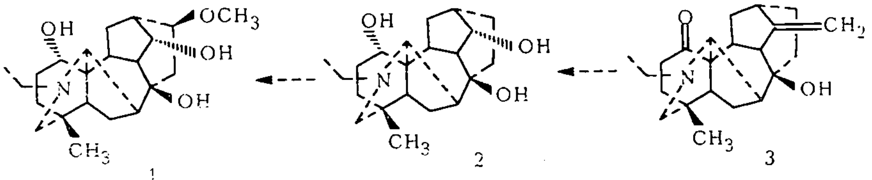
The structure and stereochemistry of the diterpene alkaloid karakoline (**1**), isolated from the tubers of *Aconitum karakolicum* Rapaics., have been shown by chemical and spectral methods [1, 2]. Transitions have been achieved between karakoline and a series of alkaloids close in structure, such as karasamine and 1-benzoylkarasamine [3], karakanine [4], and 14-acetylkarakoline [5]. This shows that these bases have a common carbon skeleton and the same stereochemistry of the substituents.

A possible mechanism of the biosynthesis of karakoline with the participation of cardiopetaline (**2**) and actaline (**3**) is shown in the scheme. Karakoline is one of the simplest representatives of the lycoctonine alkaloids and is of interest for biogenesis as a possible precursor of more complex bases of this series [6-8].



The above considerations have impelled us to determine the structure of karakoline in crystals. Figure 1 shows the spatial structure of the molecule, confirming that proposed previously. As can be seen from Fig. 1 and an analysis of torsional angles, the molecule contains a rigid lycoctonine skeleton of six rings with the following substituents: three OH groups (1α,14α,8β) and methyl (4β) and methoxy (16β) groups. The conformations and linkages of the rings in the karakoline molecule are the same as in the previously studied delcosine [9] and cardiopetaline [10]. The six-membered ring *A* (C1—C5,C11) has the boat conformation with C_S symmetry ($\Delta C_S(2) = 6.5°$), the C2 and C5 atoms departing from the plane of the other atoms by −0.66 Å. In this case, the boat conformation is stabilized, thanks to the presence in the molecule of an intramolecular hydrogen bond of the O—H···N type, as is shown by the distance between the O1 and N atoms (O1···N 2.67 Å, O—H···N angle 119°).

A characteristic pattern has been observed for the lycoctine alkaloids with an α-OH group at C1 studied previously [11]. The six-membered ring *C* adopts the form of a C9α,C17β chair (−0.51 and +0.87 Å, respectively), while *E* has the form of a distorted chair in which the C8,C9,C13,C16 atoms lie in one plane with an accuracy of ±0.02 Å, and the C14 and C15 atoms depart from the plane of the other atoms by 0.83 and 0.28 Å, respectively, which is characteristic for diterpene alkaloids with the lycoctonine skeleton [11] ($\Delta C_S(14) = 4.5°$). The conformation of the heterocycle *F* approximates to the ideal chair form C_S ($\Delta C_S(11) = 1.8°$). The five-membered ring *B* is a half-chair with C_2 symmetry ($\Delta C_2(6) = 7.9°$), the C11 and C17 atoms departing from the plane by −0.57 and +0.29 Å, respectively, while *D* is an envelope with C_S symmetry ($\Delta C_S(14) = 3.8°$), the C14 atom departing from the plane of the other four atoms by −0.71 Å.

The bond lengths agree with the usual ones [12] within the 3σ limits, and no anomalous deviations are observed in the valence angles (the mean square error does not exceed 0.5°).

Single crystals of karakoline were obtained by crystallization from methanol. The space group and the parameters of the unit cell were determined on a Syntex $P2_1$ diffractometer installed in the Institute of Bioorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan, using CuK$_\alpha$ radiation: $a = 10.822(1)$ Å, $b = 12.725(2)$ Å, $c = 14.144(2)$ Å; space

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Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 89 14 75. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 109-111, January-February, 1996. Original article submitted June 19, 1995.

TABLE 1. Coordinates (× 10^4) of the Nonhydrogen Atoms and Temperature Factors ($Å^2 \times 10^3$) in the Karakoline Structure

Atom	x	y	z	U
C1	2702(4)	12704(3)	1491(3)	44(1)
C2	3704(4)	13016(4)	806(4)	53(2)
C3	4964(5)	12733(4)	1180(4)	54(2)
C4	5064(4)	11574(4)	1511(3)	44(1)
C5	3892(4)	10951(3)	1237(3)	40(1)
C6	3896(4)	9850(3)	1696(4)	46(2)
C7	3122(4)	9979(3)	2611(3)	40(1)
C8	1866(4)	9469(3)	2499(3)	40(1)
C9	1299(4)	9826(4)	1551(3)	41(1)
C10	1512(4)	11012(3)	1350(3)	37(1)
C11	2737(4)	11484(3)	1679(3)	36(1)
C12	335(4)	11546(3)	1785(3)	42(1)
C13	−428(4)	10667(3)	2245(3)	39(1)
C14	−121(4)	9750(3)	1594(3)	43(1)
C15	1040(4)	9652(4)	3359(3)	44(1)
C16	−27(4)	10457(3)	3264(3)	41(1)
C17	2976(4)	11165(3)	2708(3)	34(1)
C18	6227(4)	11096(4)	1056(4)	61(2)
C19	5212(4)	11512(4)	2580(3)	44(1)
C20	−1937(5)	10738(5)	4047(4)	67(2)
C21	4198(5)	11592(4)	4114(3)	49(2)
C22	5105(5)	12325(4)	4572(4)	60(2)
O1	2778(3)	13321(2)	2342(2)	47(1)
O2	−491(3)	8724(2)	1890(3)	50(1)
O3	−1018(3)	10028(2)	3825(2)	53(1)
O4	2087(3)	8341(2)	2425(3)	54(1)
N	4056(3)	11753(3)	3095(2)	39(1)

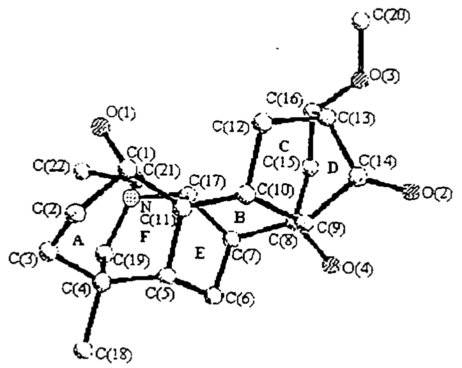

Fig. 1

group $P2_12_12_1$, $Z = 4$. The calculation made use of 1651 reflections. The structure was interpreted by the direct method by means of the SHELXS-86 program package [13]. Refinement was carried out by the full-matrix method of least squares in the isotropic-anisotropic approximation using the SHELX-76 program [14]. The final values of the divergence factors were: $R = 0.054$, $R_w = 0.055$. The coordinates of the atoms are given in Table 1.

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