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CRYSTAL AND MOLECULAR STRUCTURE OF DEOXYPEGANINE HYDROCHLORIDE DIHYDRATE

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The crystal structure of deoxypeganine DOP chloride dihydrate (1) has been established by the x-ray structural method (diffractometer, CuK_α radiation, 671 reflections, direct method, $R = 0.094$). A comparative analysis has been made of the crystal structure of (1) with that of another complex of deoxypeganine (DOP) — DOP·$ZnCl_2$·2HCl.

The majority of alkaloids are used in medical practice in the form of water-soluble salts the composition of which includes water; however, even for compounds close in structure its amount differs [1]. Thus, the hydrochloride of 1,2,3,9-tetrahydropyrrolo[2,1−*b*]quinazoline (deoxypeganine hydrochloride) contains two molecules of water [2], while the hydrochloride of 1,2,3,4,5,11-hexahydroazepino[2,1−*b*]quinazoline contains no water [3].

Attempts to obtain deoxypeganine (DOP) hydrochloride containing no water by passing dry hydrogen chloride through a solution of DOP base in absolute chloroform or by azeotropic drying with toluene did not lead to the desired result. We therefore assumed that in solution deoxypeganine hydrochloride forms a kind of stable aqua complex, and the results of an investigation of the crystal structure of this are given in the present paper.

An x-ray structural investigation showed that the independent part of the unit cell of the (1) crystal contained a protonated molecule (cation) of deoxypeganine, a chloride anion, and two molecules of water of crystallization, i.e., DOP hydrochloride is actually a dihydrate.

In the crystal of the complex under investigation, the protonated DOP molecule forms a plane triclinic system (Fig. 1). The geometric parameters — bond lengths and valence angles — of DOP in structure (1) agree well with the corresponding standard magnitudes [4] and also with those observed in another complex of deoxypeganine, with $ZnCl_2$ [5] (Table 1). A lengthening of the N1═C2 double bond and a shortening of the N3−C2 bond in the quinazoline (1) shows the conjugation of the π-electronic system of the double bond with the unshared pair of the N3 atom. The lengths of the N1═C2 and N3−C2 bonds in (1) (1.32 and 1.29 Å, respectively) become equivalent within the limits of experimental error characteristic for quinazolines protonated at N1, since the same pattern is also observed in the structure of peganine hydrochloride (1.33 and 1.35 Å) [6] and that of peganine in a complex with $ZnCl_2$·2HCl (1.32 and 1.33 Å) [7] and also in the complex DOP·$ZnCl_2$·2HCl (1.290 and 1.314 Å). In quinazolines protonated at N1 the nature of the N1═C2 and N3−C2 bonds is averaged and approximates to that observed in the aromatic pyrimidine (1.336 Å) [4].

According to Bayer's scheme [8], in quinazolines protonated at N1 (literature results are included), the order of the π-bond in N1═C2 decreases and in C2−N3 it increases and becomes approximately 0.6-0.7.

At the present time, this pronounced change in the lengths of the N1═C2 and N3−C2 bonds in protonated quinazolines has found no explanation and requires additional investigations, including low-temperature x-ray experiments.

The packing in the (1) crystal is shown in Fig. 1. The molecules of the water of crystallization are linked with one another by H-bonds, the distance between the oxygen atoms of the water molecules being 2.82 Å. These pairs of water molecules, transformed by a 2_1 screw axis, form an infinite chain along the *c* axis, thanks to another H-bond (2.79 Å). To this chain, passing through 1/2, O, *z*, chloride ions approach from two sides, forming H-bonds of the O−H···Cl type, as is shown

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TABLE 1. Bond Lengths r (Å) and Valence Angles ω (degrees) in the Structure of (**1**)

Bond	r	Angle	ω
N1–C2	1.32(1)	C8a–N1–C2	119.0(9)
N1–C8a	1.42(1)	C9–C2–N1	124.4(1.0)
C2–N3	1.29(1)	C9–C2–N3	112.0(9)
C2–C9	1.50(2)	N1–C2–N3	123.4(10)
N3–C4	1.42(1)	C4–N3–C2	126.5(9)
N3–C11	1.49(1)	C2–N3–C11	112.7(9)
C4–C4a	1.53(2)	C4–N3–C11	120.6(9)
C4a–C5	1.35(2)	C4a–C4–N3	111.1(9)
C4a–C8a	1.39(2)	C5–C4a–C4	122.0(1.0)
C5–C6	1.34(2)	C8a–C4a–C4	118.9(10)
C6–C7	1.37(2)	C5–C4a–C8a	118.0(11)
C7–C8	1.37(2)	C6–C5–C4a	121.3(1.2)
C8–C8a	1.39(2)	C5–C6–C7	120.6(12)
C9–C10	1.52(2)	C6–C7–C8	120.1(1.3)
C10–C11	1.49(2)	C7–C8–C8a	118.2(11)
		C8–C8a–N1	118.3(10)
		C4a–C8a–N1	120.5(1.0)
		C8–C8a–C4a	119.5(1.1)
		C2–C9–C10	103.6(9)
		C9–C10–C11	107.3(9)
		C10–C11–N3	104.4(1.0)

TABLE 2. Coordinates (× 10^4) of the Nonhydrogen Atoms in the Structure of (**1**)

Bond	x	y	z	Ueq
N1	6201(4)	6564(9)	8979(31)	58(3)
C2	6429(6)	5315(11)	9099(34)	50(4)
N3	5982(5)	4241(9)	9147(31)	54(4)
C4	5455(5)	7007(11)	8867(36)	68(5)
C4a	4925(6)	5778(10)	8864(32)	52(4)
C5	4185(6)	5942(13)	8938(39)	76(6)
C6	3730(7)	4858(16)	8981(53)	90(6)
C7	4003(7)	3549(15)	8914(40)	85(6)
C8	4747(6)	3331(12)	8937(36)	68(5)
C8a	5208(6)	4465(11)	9132(36)	52(4)
C9	7252(6)	5221(11)	8983(43)	85(6)
C10	7494(6)	6709(13)	8842(40)	88(6)
C11	6815(5)	7569(13)	8796(51)	89(7)
Cl	6782(2)	1423(3)	8928(6)	82(1)
O_{w1}	5753(10)	47(20)	1964(27)	82(5)
O_{w2}	5708(15)	281(22)	5827(30)	125(8)

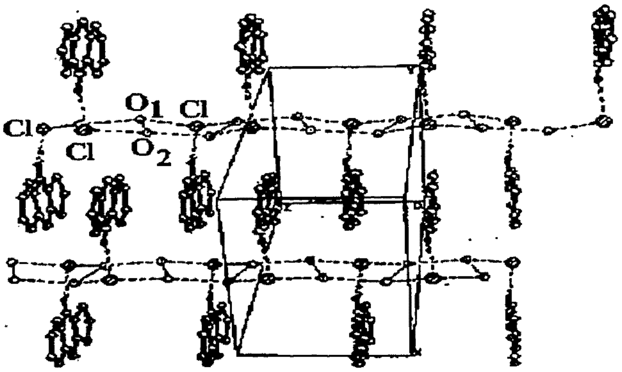

Fig. 1. Packing in the (**1**) crystal.

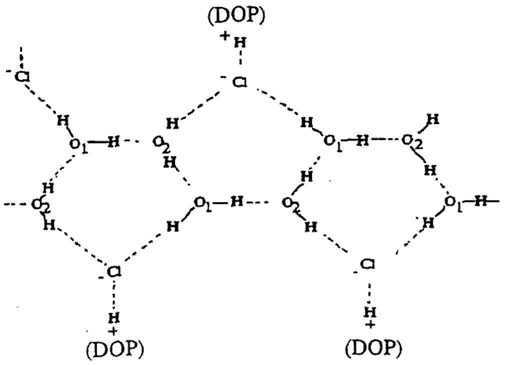

Fig. 2. Hydrogen bonds in the (1) structure. The distances (in Å) between the heavy atoms are shown [sic].

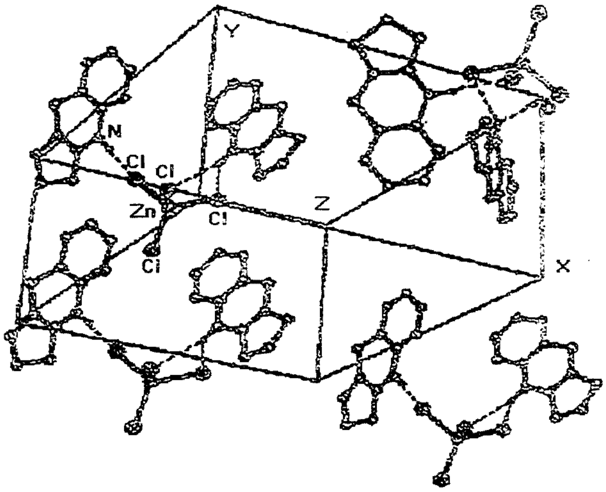

Fig. 3. Packing in the DOP·$ZnCl_2$·2HCl crystal.

by the Cl···O_{w1} and Cl···O_{w2} distances of 3.22 and 2.99 Å, respectively. The chloride ion, in its turn, is bound to the protonated (at the N1 atom) DOP molecule (Cl··N1 distance 3.11 Å). A section characterizing the intermolecular H-bonds in the (1) crystal is shown separately and schematically in Fig. 2. Here the positions of the hydrogen atoms in the water molecules were not found experimentally, but their presumable orientations fall logically within the proposed scheme.

Thus, in the DOP hydrochloride dihydate crystal, thanks to H-bonds with the participation of water molecules, infinite chains are formed, which is not the case in the crystal cell of the complex of DOP with $ZnCl_2$·2HCl, where H-bonds form closed islets (Fig. 3).

EXPERIMENTAL

Crystals of deoxypeganine hydrochloride dihydrate were obtained by the slow cooling of its isopropanol solution. The unit cell parameters and the space group were determined from precession x-ray diagrams and were refined on a Syntex $P2_1$ diffractometer: a = 18.163(5), b = 9.729(3), c = 7.073(3) Å, d_{calc} = 1.301 g/cm^3, space group $Pna2_1$, Z = 4. A three-dimensional set of intensities was obtained on the same diffractometer: $\theta/2\theta$ method of scanning using CuK_α radiation (graphite monochromator), $\sin\theta/\lambda < 0.55$, number of independent and nonzero reflections with $I > 2\sigma(I)$ 671.

The search for a model of the structure was made by the SHELXS-86 program [9] (PC DOS version), and we succeeded in finding a model of the molecule in the automatic regime. Subsequent Fourier syntheses enabled all the nonhydrogen atoms, including the atoms of the water of crystallization, to be localized. The structure was refined by the method of least squares (MLS) successively in the isotropic–anisotropic approximation by the SHELX-76 program [10]. The coordinates of the H atoms attached to carbon atoms were calculated and were refined isotropically. The final value of the divergence factor, R, was 0.094. The coordinates of the nonhydrogen atoms from the last stage of the MLS are given in Table 2.

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