Chemistry of Natural Compounds, Vol. 34, No. 3, 1998

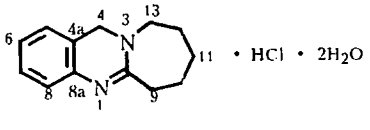
CRYSTAL AND MOLECULAR STRUCTURES OF PENTAZOLINE HYDROCHLORIDE DIHYDRATE

K. K. Turgunov, B. Tashkhodzhaev, L. V. Molchanov,
G. V. Musaeva, and Kh. N. Aripov*

UDC 548.737

The crystal structure of pentazoline hydrochloride dihydrate has been established by x-ray structural analysis. A comparative analysis has been made of the crystal structures of the dihydrates of the hydrochlorides of pentazoline and of deoxypeganine.

Pentazoline (2,3-pentamethylene-3,4-dihydroquinazoline) hydrochloride possesses a unique physiological property [1, 2] and can be used for the treatment of neurological diseases. In many cases, the preparative forms are used as salts, and therefore an investigation of the physicochemical properties and the determination of the crystal structure of pentazoline hydrochloride is urgent. In the present paper we give the results of an x-ray structural analysis of pentazoline hydrochloride.



The x-ray structural method showed that in the independent part of the unit cell of the crystals of this substance there was a protonated (at the N1 atom) molecule (cation) of pentazoline, a chloride anion, and two molecules of water of crystallization. A similar situation has been observed for the dihydrate of the hydrochloride of the closest analogue of pentazoline – deoxypeganine [3].

On the whole, the geometric parameters – bond lengths and valence angles – of the pentazoline molecule agree with the corresponding standard values [4] (Table 1). A lengthening of the formal N1=C2 double bond and a shortening of the N3–C2 bond in pentazoline show the conjugation of the π-electronic system of the double bond with the unshared pair of electrons of the N3 atom, as a result of which the lengths of these bonds are appreciably averaged. However, it is possible to note a tendency in the direction of a general shortening of these bonds as compared with what is observed in the bases deoxyvasicinone [5], tetrazolone, and pentazolone [6] – alkaloids related to it. This is explained by the fact that, in the pentazoline molecule, the N1 atom is protonated and the charge of the proton is transmitted through the bonds N1–C2–N3 to the N3 atom, which is positively charged, i.e., there is a drawing together of the unshared pair of electrons of the N3 atom to the N3–C2–N1 bonds. As a result, in N3–C2 the character of a multiple bond predominates.

On the whole, the quinazoline part of the molecule under investigation consists of a plane bicyclic system, and the seven-membered ring adopts a chair conformation.

The crystal packing is shown in Fig. 1. The molecules of the water of crystallization are linked to one another by H-bonds, the distance between the oxygen atoms amounting to 2.75 Å. These pairs of water molecules, transformed by a 2_1 screw axis, form an infinite chain around the X axis thanks to another H-bond (2.76 Å). Abutting this chain on both sides are chloride ions, forming H-bonds of the O–H···Cl type (Ow1···Cl 3.20 Å, Ow2···Cl 3.19 Å). The chloride ion, in its turn, is linked to a protonated (at the N1 atom) pentazoline molecule (Cl···N1 3.12 Å).

---

*Deceased.

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. 3, pp. 334-337, May-June, 1998. Original article submitted December 9, 1997.

0009-3130/98/3403-0300$20.00

TABLE 1. Bond Lengths r (Å) and Valence Angles ω (degrees) in the Pentazoline Cation

Bond	r	Angle	ω
N1–C2	1.30(1)	C(2)-N(1)-C(8)a	123.1(7)
N1–C8a	1.41(1)	N(1)-C(2)-N(3)	121.1(7)
C2–N3	1.33(1)	N(1)-C(2)-C(9)	118.5(7)
C2–C9	1.48(1)	N(3)-C(2)-C(9)	120.4(7)
N3–C4	1.45(1)	C(2)-N(3)-C(4)	123.8(7)
N3–C13	1.49(1)	C(2)-N(3)-C(13)	120.5(7)
C4–C4a	1.51(1)	C(4)-N(3)-C(13)	115.7(6)
C4a–C5	1.38(1)	N(3)-C(4)-C(4)a	112.8(7)
C4a–C8a	1.39(1)	C(4)-C(4)a-C(5)	120.8(8)
C5–C6	1.37(2)	C(4)-C(4)a-C(8)a	119.3(7)
C6–C7	1.41(2)	C(5)-C(4)a-C(8)a	119.9(8)
C7–C8	1.35(1)	C(4)a-C(5)-C(6)	120.0(10)
C8–C8a	1.40(1)	C(5)-C(6)-C(7)	121.0(9)
C9–C10	1.53(1)	C(6)-C(7)-C(8)	118.6(10)
C10–C11	1.52(1)	C(7)-C(8)-C(8)a	121.4(9)
C11–C12	1.50(1)	N(1)-C(8)a-C(4)a	119.2(7)
C12–C13	1.53(1)	N(1)-C(8)a-C(8)	121.7(7)
		C(4)a-C(8)a-C(8)	119.1(8)
		C(2)-C(9)-C(10)	113.8(8)
		C(9)-C(10)-C(11)	114.2(8)
		C(10)-C(11)-C(12)	114.6(7)
		C(11)-C(12)-C(13)	114.7(8)
		N(3)-C(13)-C(12)	113.6(7)

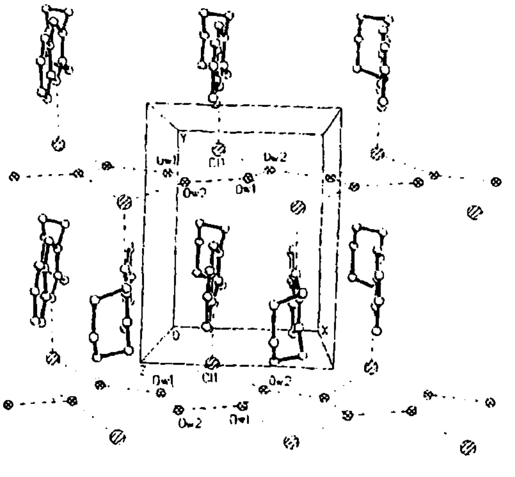


Fig. 1. Packing of the molecules in the crystal.

A section characterizing the intermolecular H-bonds in the crystal is shown schematically in Fig. 2a. The positions of the hydrogen atoms in the water molecules were not found experimentally. We may note that a similar infinite chain, consisting of nominal five-membered rings, around the Z axis has been observed in the crystal of peganine hydrochloride dihydrate [3] (see Fig. 2b). A comparison of intermolecular contacts witnesses their similarity in the formation of H-bonds.

EXPERIMENTAL

Pentazoline hydrochloride was obtained by reducing pentazolone with zinc in hydrochloric acid [7]. Crystals were grown from aqueous solution by slow cooling to room temperature.

The parameters of the unit cell and the space group were determined from precession x-ray photographs and were refined on a Syntex $P2_1$ diffractometer.

The crystals were orthorhombic, $a = 7.313(1)$ Å, $b = 9.932(2)$ Å, $c = 19.618(4)$ Å, $V = 1424.9(7)$ Å^3, $d_{calc} = 1.248$ g/cm^3, space group $P2_12_12_1$, $Z = 4$. A three-dimensional set of intensities was obtained on the same diffractometer: $\theta/2\theta$

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

Atom	x	y	z	U_{eq}
Cl	1926(4)	1166(2)	8360(1)	64(1)
N1	1908(12)	-1701(6)	9006(3)	50(2)
C2	1708(14)	-2713(8)	8588(4)	48(3)
N3	1662(11)	-3979(7)	8817(3)	51(3)
C4	1950(17)	-4349(8)	9525(4)	61(3)
C4a	1995(13)	-3144(9)	9996(4)	49(3)
C5	2027(15)	-3311(11)	10696(4)	66(4)
C6	2085(17)	-2212(13)	11113(5)	81(5)
C7	2104(15)	-894(13)	10841(5)	74(4)
C8	2031(14)	-740(9)	10156(5)	60(3)
C8a	1997(14)	-1854(8)	9718(4)	49(3)
C9	1545(14)	-2430(8)	7849(4)	56(3)
C10	3170(16)	-2933(9)	7428(5)	63(3)
C11	3095(17)	-4428(9)	7256(4)	63(3)
C12	3038(15)	-5341(9)	7862(5)	66(4)
C13	1410(13)	-5119(8)	8335(5)	61(4)
Ow1	-95(12)	2591(11)	621(4)	120(5)
Ow2	1358(11)	7153(10)	5687(4)	101(4)

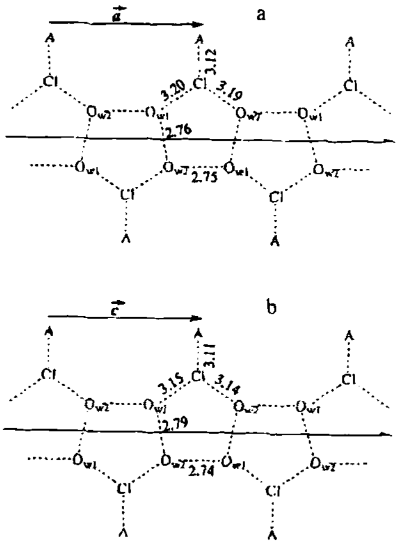


Fig. 2. Hydrogen bonds in crystal structures. Distances (Å) between heavy atoms are shown (A is a molecule of the base): a) in pentazoline salts; b) in deoxypeganine salts.

method of scanning, using CuK_α radiation (graphite monochromator), $\sin\theta/\lambda < 0.55$, number of independent and nonzero reflections with $I > 5\sigma(I) = 855$.

The search for a model of the structure was conducted by the SHELX-86 program (PC DOS version) [8]. We succeeded in finding a model of the molecule in the automatic regime. Subsequent Fourier syntheses permitted the localization of all the nonhydrogen atoms, including the molecules of water of crystallization. The structure was refined by the method of least squares (MLS) successively in the isotropic-anisotropic approximation by the SHELX-76 program [9]. The coordinates of the H atoms linked to carbon atoms were calculated and refined isotropically. The final value of the discrepancy factor R was 0.070. The coordinates of the nonhydrogen atoms for the last stage of the MLS are given in Table 2.

REFERENCES

1. A. K. Bogolepov, "Atherosclerotic Parkinsonism," in: Disturbance of the Cerebral Blood Circulation [in Russian], Lokhupin (ed.), Moscow, No. 1 (1978), p. 37.

2. N. Tulyaganov, "Influence of 2,3-pentamethylene-3,4-dihydroquinazol-4-one on the central nervous system," in: Questions of Pharmacology and Pharmacy [in Russian], No. IV, Tashkent (1976), p. 28.
3. K. K. Turgunov, B. Tashkhodzhaev, L. V. Molchanov, and Kh. N. Aripov, Khim. Prir. Soedin., 421 (1995).
4. F. N. Allen, O. Kennard, and D. G. Watson, J. Chem. Soc., Perkin Trans. II, No. 12, S1-S19 (1987).
5. K. K. Turgunov, B. Tashkhodzhaev, L. V. Molchanov, and Kh. N. Aripov, Khim. Prir. Soedin., 849 (1995).
6. B. Tashkhodzhaev, K. K. Turgunov, A. L. D'yakonov, G. A. Belova, and Kh. M. Shakhidoyatov, Khim. Prir. Soedin., 410 (1995)
7. G. V. Musaev, L. V. Molchanov, A. F. Mukminov, A. L. D'yakonov, and Kh. N. Aripov, Uzb. Khim. Zh., No. 6, 73 (1993).
8. G. M. Sheldrick, Acta Crystallogr., **A46**, 467 (1990).
9. G. M. Sheldrick, SHELX-76 Program for Crystal Structure Determination, Cambridge, England.