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CRYSTAL AND MOLECULAR STRUCTURE OF 2,3-TETRAMETHYLEN-3,4-DIHYDROQUINAZOLINE

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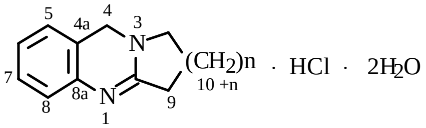
The crystal and molecular structure of the alkaolid 2,3-tetramethylen-3,4-dihydroquinazoline hydrochloride was solved by X-ray structure analysis. It was demonstrated that the crystal contains an aqua system similar to those in the isostructural 2,3-trimethylen-3,4-dihydroquinazoline (deoxypeganine), and 2,3-pentamethylen-3,4-dihydroquinazoline hydrochlorides.

Key words: quinazolines, aqua system, X-ray structure analysis.

Derivatives of quinazoline alkaloids typically have a wide spectrum of biological activity. They are widely distributed in plants and animals and play an important role in their life cycles [1].

We observed during an investigation of the crystal structures of two quinazoline hydrochlorides, 2,3-trimethylen-3,4-dihydroquinazoline (deoxypeganine) (**1**) and 2,3-pentamethylen-3,4-dihydroquinazoline (**3**) that they form crystal hydrates. The two water molecules in them form infinite chains through H-bonds [2, 3]. Such a phenomenon was not observed in the crystal structure of the quinazolone alkaloid deoxyvasicinone (2,3-trimethylen-3,4-dihydroquinazol-4-one) [4].



1: n = 1; **2:** n = 2; **3:** n = 3

Therefore, we assumed that formation of H-bonded chains involving water molecules is typical of compound **2** with the intermediate value n = 2. The crystal structure of 2,3-tetramethylen-3,4-dihydroquinazoline hydrochloride (**2**), which was obtained earlier from a *Mackinlaya* species [5] and synthetically [6-8], was investigated to confirm this by X-ray method.

Figure 1 shows the molecular packing in the crystal of **2**. Analysis of the geometry of the protonated alkaloid showed that the quinazoline part, including C9 and C12, is planar (within ±0.05 Å). Ring C has a slightly flattened half-chair conformation with C10 and C11 deviating from the plane to different sides (by 0.32 and 0.38 Å, respectively).

The lengths of the formally double N1=C2 and single C2–N3 bonds changed significantly on going from the base to the salt. They were 1.33(1) and 1.31(1) Å, respectively, in **2**. Changes were also observed in salts of **1** and **3** [2, 3] and in other salts of related quinazolines [9-10]. This is consistent with the presence of strong conjugation of π-electrons on the N1=C2 double bond and the unshared pair of N3 in the –N1=C2–N3 fragment of ring B.

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TABLE 1. H-Bond Distances in the Structures of **1-3**

Compound	Distance, Å				
	d_1	d_2	d_3	d_4	d_5
1	3.11	3.15	3.14	2.79	2.74
2	3.15	3.15	3.21	2.76	2.73
3	3.12	3.20	3.19	2.76	2.75

TABLE 2. IR Frequencies of Quinazoline Salts in the Range 2100-3500 cm^{-1} (Data for Deoxyvasicinone are Given for Comparison)

Compound	ν (N-H), cm^{-1} N^+-H...Cl	ν (H_2O), cm^{-1} O-H...Cl
1	2757-3075	3400
2	2825-2955	3409
3	2883-2989	3448
Deoxyvasicinone hydrochloride	2363-2600	-
Deoxyvasicinone complex with $CoCl_2$	2700-3075	-
Deoxypeganine complex with $ZnCl_2$	2985-3230	-
2,3-Pentamethylen-3,4-dihydroquinazoline complex with $CoCl_2$	3000-3250	-

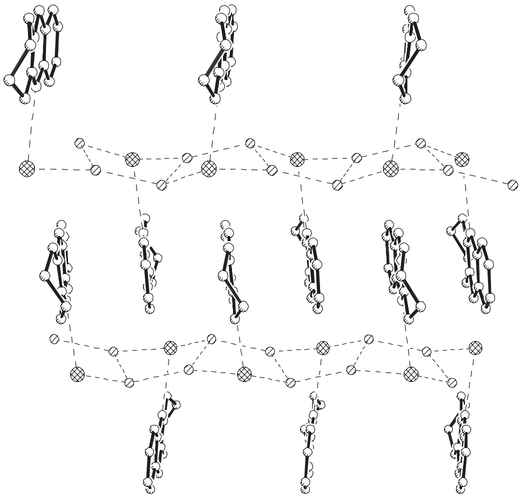

Fig. 1. Crystal structure of compound **2**.

Analysis of the crystal structure of **2** showed that it is similar to those of **1** and **3** (isostructural crystals). The independent part of the unit cell of **2** contains the protonated (cationic) base, Cl anion, and two waters of crystallization bonded by a H-bond. This pair of water molecules is coordinated to another pair transformed by the 2_1 screw axis. This leads to the formation of an infinite chain, to which Cl anions approach from two sides, forming O–H...Cl H-bonds. This forms an infinite ribbon consisting of fused "five-membered" rings. The Cl ions in the five-membered ring are bonded to protonated (at N1) 2,3-tetramethylen-3,4-dihydroquinazoline situated perpendicular to the plane of the ribbon (cations are linked to the ribbon from two sides). The crystal volume is filled by alternating protonated alkaloid from different ribbons transformed by the 2_1 symmetry elements (Fig. 1). The molecular cations are situated at Van-der-Waals distances from each other.

TABLE 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters U_{eq} for the structure of **2**

Atom	x	y	z	U_{eq}
N1	5830(6)	2806(10)	5915(4)	48(2)
C2	6911(8)	2781(12)	5716(6)	44(2)
N3	7180(6)	2594(10)	4926(4)	49(2)
C4	6359(7)	2506(14)	4195(5)	57(3)
C4a	5156(8)	2446(13)	4460(5)	51(3)
C5	4277(9)	2217(14)	3873(6)	69(3)
C6	3191(10)	2173(16)	4119(8)	81(4)
C7	2938(8)	2309(14)	4970(8)	71(3)
C8	3823(8)	2522(13)	5568(6)	62(3)
C8a	4930(8)	2587(12)	5310(6)	48(3)
C9	7792(7)	2924(14)	6419(5)	60(3)
C10	8944(7)	3436(17)	6137(7)	81(3)
C11	9215(8)	2314(18)	5384(7)	87(4)
C12	8360(7)	2579(16)	4661(6)	73(3)
CL1	364(2)	1594(4)	2847(2)	69(1)
Ow1	3615(6)	-65(11)	7744(5)	86(2)
Ow2	1665(5)	1217(10)	6906(4)	84(2)

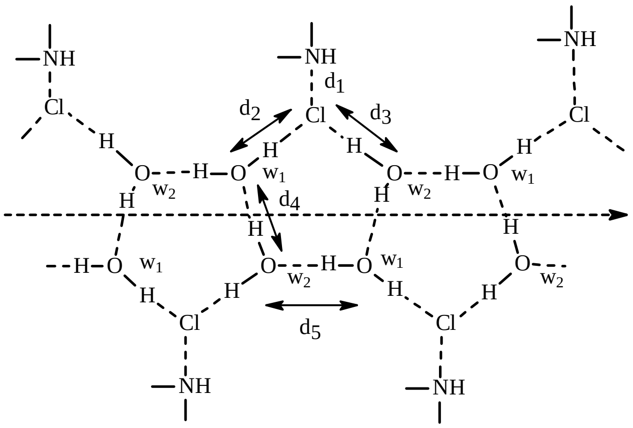

Fig. 2. H-bond formation along the 2_1 screw axis in crystal structures of **1-3** (distances between nonhydrogen atoms are given in Å; NH is a protonated N atom of the base).

Analysis of the crystal structures of **1-3** found that the infinite ribbon involving water molecules and Cl ions forms along the shortest unit-cell translation. The length of this translation (crystallographic parameter) determines the repeat distance (period) of the infinite ribbon. The geometries of the H-bonds in the chain forming the ribbon are almost identical. Therefore, the cell vector directed along the ribbon has practically the same value in **1-3**: 7.073(3) Å (**1**) [2], 7.075(7) (**2**), and 7.313(1) (**3**) [3]. The parameter corresponding to **3** is slightly elongated because of the presence of a nonplanar seven-membered ring in the molecule. Figure 2 shows schematically the part with the H-bonded chain in the crystals. Table 1 gives their numerical values.

The determination of crystal structures of salts of a rather large number of tricyclic quinazolines and quinazolones and the multifaceted study of their IR spectra [11] enabled strong absorption bands at 3200-3500 cm^{-1} to be assigned to O–H vibrations of water involved in intermolecular H-bonds OH...O and OH...Cl. Such a band is not observed in the IR spectra of quinazol-4-one salts (Table 2 was constructed using selected literature data [11, 12]). This indicates that there are no waters of crystallization. This is confirmed by the X-ray structure analysis (XSA) [4, 10].

EXPERIMENTAL

A prismatic crystal of approximate dimensions 0.35×0.25×0.08 mm was selected for the XSA. The unit-cell constants and space group of **2** were determined and refined on a Stoe Stadi-4 diffractometer. The principal parameters of the XSA and calculations of the structure of **2** are given below.

Empirical formula $C_{12}H_{14}N_2 \cdot HCl \cdot 2H_2O$
Monoclinic, space group, $P2_1/n$, Z = 4

a = 11/868 (7) Å α = 90.0
b = 7.075 (7) Å β = 92.74 (5)
c = 15.579 (9) Å γ = 90.0
V = 1321.7 (14) $Å^3$
d_{calc} = 1.30 g/cm^3

Number of reflections 1725 (I > 0), 912 ($I > 2\sigma$)
R[$I > 2\sigma(I)$] factor R1 = 0.096 wR2 = 0.149
R using all reflections, R1 = 0.199, wR2 = 0.213

A three-dimensional set of intensities was obtained on the same diffractometer by $\omega/2\Theta$-scanning using Mo $K\alpha$-radiation (graphite monochromator) for $2\Theta = 45°$. The intensity data were processed using the XRED program [13]. Absorption corrections were not applied.

The structure was solved by direct methods using the automated SHELX-86 program [14] and refined successively by isotropic and anisotropic least-squares methods using the SHELXL-93 program [15] for nonhydrogen atoms. Coordinates of H atoms were determined from a difference electron-density synthesis and refined isotropically. Table 3 contains coordinates of principal atoms from the final least-squares refinement cycle.

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