

Crystal Structures of Hydrochlorides of 2,3-Pentamethylene-3,4-dihydroquinazolin-4-one

K.K. TURGUNOV*, A.G. TOJIBOEV, B. TASHKHODJAEV,
and KH.M. SHAKHIDOYATOV

S. Yunusov Institute of Chemistry of Plant Substances, H. Abdullaev Str., 77, Tashkent, 700170, Uzbekistan

(Received: 22 September 2004; in final form: 6 January 2005)

Key words: disordered water molecules, quinazoline, X-ray crystallography

Abstract

The crystal structures of hydrate (**1**) and anhydrate (**2**) forms of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one hydrochloride have been determined by X-ray structure analysis. Crystal data of **1** are $2(\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}) \cdot 3(\text{HCl}) \cdot 4.5(\text{H}_2\text{O})$, triclinic $P\bar{1}$, $Z = 2$, $a = 8.004(5)$, $b = 13.129(7)$, $c = 15.725(7)$ Å, $\alpha = 106.45(4)$, $\beta = 92.61(4)$, $\gamma = 97.98(5)$, $R = 0.0652$ and **2** are $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O} \cdot \text{HCl}$, monoclinic $C2/c$, $Z = 8$, $a = 21.360(4)$, $b = 5.954(1)$, $c = 21.263(4)$, $\beta = 117.89(3)$, $R = 0.0556$. The crystal of the hydrate form **1** is unstable. This form collapses easily with evaporation of H_2O and part of HCl molecules from crystals. By recrystallizing destroyed form has been obtained stable crystal form **2**.

Introduction

The condensed tricyclic 3,4-dihydroquinazolin-4-ones have a wide spectrum of biological activity, and in medical practice they are used as water-soluble salts [1–4]. They easily form hydrochlorides, and for this reason, this research is of practical importance.

In earlier studies, the crystal structure of tricyclic quinoxaline hydrochlorides has been shown that the crystals are formed as a stable system of molecules and ions which are connected by H-bonding. Changing a number of atoms in the third cycle of quinazoline molecule did not influence architecture of crystals [5–8]. In order study of structure formation and comparison of crystal packing with packing, observed in the last investigated crystals, has been carried out crystallization of titled compound. Unexpectedly has been received unstable crystal form, that after recrystallization is received expected crystal form. The present paper is devoted to X-ray analysis of the obtained unstable and stable forms of hydrochlorides of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one.

Experimental

Preparation of 2,3-Pentamethylene-3,4-dihydroquinazolin-4-one hydrochlorides

To a suspension of 20 mg 2,3-pentamethylene-3,4-dihydroquinazolin-4-one in ~2 ml water was dripped excess

quantity of concentrated hydrochloric acid under stirring until the compound was dissolved. Then the solution was allowed to evaporate slowly at room temperature. A few days later, the transparent crystals **1** were formed, but crystal destruction began within a few hours. A crystal suitable for X-ray analysis was selected, covered with epoxy glue and mounted on a glass fiber. By recrystallizing the destroyed crystals of form **1** in a water solution at temperature 80 °C, stable crystal **2** was obtained.

Crystal structure solution

The unit cell parameters and space group of crystals **1** and **2** were determined on a Stoe Stadi-4 diffractometer. Final cell parameters determined from 25 reflections ($15 < 2\theta < 25^\circ$) are given in Table 1, along with other information regarding data collection and refinement. The intensities of the reflections were measured with graphite monochromatized $\text{MoK}\alpha$, radiation, $T = 295$ K. Though crystal **1** was covered with epoxy glue (because of instability in air), it exhibited significant decay, as observed from three standard reflections monitored after each hour. During data collection (~30 h) the intensity of control reflections reduced by half. Data were corrected for Lorentz and polarization effects but not for absorption.

The structures **1** and **2** were solved by direct methods with the program SHELX-86 [9]. The structures were refined by a least-squares method using the program SHELX-93 [10] using initially isotropic and later anisotropic thermal parameters for non-hydrogen

* Author for correspondence. E-mail: qambarr@yahoo.com, rentgen@uzsci.net

Table 1. Crystal data, experimental and refinement parameters for the 2,3-pentamethylene-3,4-dihydroquinazolin-4-one hydrochlorides

	1	2
Formula	2(C ₁₃ H ₁₄ N ₂ O)*3(HCl)* 4.5(H ₂ O)	C ₁₃ H ₁₄ N ₂ O*HCl
Formula weight	618.09	250.72
Crystal system	Triclinic	Monoclinic
Space Group	P-1	C2/c
Z	2	8
a, Å	8.004(5)	21.360(4)
b, Å	13.129(7)	5.954(1)
c, Å	15.725(7)	21.263(4)
α(°)	106.45(4)	90
β(°)	92.61(4)	117.89(3)
γ(°)	97.98(5)	90
V, Å ³	1563.1(14)	2394.1(8)
Dx, g/cm ³	1.313	1.391
Crystal dimension (mm)	0.80 × 0.60 × 0.45	0.80 × 0.35 × 0.20
Range scanned 2θ (°)	3 ≤ θ ≤ 45°	3 ≤ θ ≤ 55°
μ _{exp} (cm ⁻¹)	0.339	0.304
No. of unique reflection	4069	2760
No. of reflection with I > 2σ(I)	2818	2071
R1 (wR2), (I > 2σ(I))	0.0652 (0.1035)	0.0556 (0.0835)
R1 (wR2)	0.1664 (0.2330)	0.1587 (0.2306)
Largest diff. peak and hole	0.279 and -0.239 e/Å ³	0.268 and -0.303 e/Å ³

atoms. At the initial stage of determination of structure **1**, two molecules of water and three chlorine atoms were discovered. After several stages of refinement of structure **1**, other guest molecules were elucidated – 2.5 molecules of water in six statistically disordered positions. In both structures, N(1)⁺-H hydrogens were included in the refinement at the position found from a difference Fourier maps and its coordinates were refined. C–H and O(w)–H hydrogens fixed at idealized geometry and all hydrogens treated isotropically. Final atomic coordinates of structures **1** and **2** with other crystallographic data are found in Supplementary Data.

Results and discussion

Crystal structure

The asymmetric unit of crystal **1** consists of two protonated (on N(1)) molecules 2,3-pentamethylene-3,4-dihydroquinazolin-4-one, three Cl⁻ anions and 4.5 molecules of water (Figure 1). One of water molecule must be protonated. In structure **1**, 2.5 molecules of water (oxygen atoms of O(3w), O(4w) and O(5w)) occupy six disordered positions (each oxygen occupies two unequivalent positions with different site occupation factors). The occupation factors of atom O(5w) in

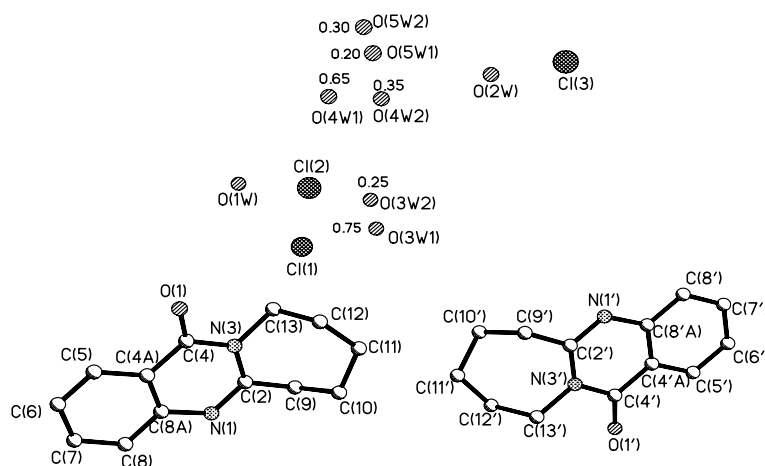


Figure 1. The asymmetric unit and the numbering scheme of structure **1** (for oxygens of O(3w), O(4w), O(5w) of water molecule are given site occupation factors, hydrogen atoms have been omitted).

the sum of two positions do not exceed 0.5 and allocated closely to center of inversion.

One of protonated quinazolone molecule linked with chlorine ion, other molecule linked with water molecule by means of H-bonding: the distances Cl(3) ... N(1) and O(1w)...N(1') are 3.11 and 2.69 Å respectively. Consequently, each water molecules and Cl⁻ ions takes part in hydrogen bonds. If we omit the each one of disordered water molecules the resulting hydrogen bonded chain arrangements will be as illustrated in Figure 2. (Disordered positions are not far from each other, therefore can be described structure using one position.)

The analysis of the packing of molecules in structure **1** shows that the cations (protonated molecules of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one) form a column in the direction of crystallographic axis *b*. Between columns a channel is formed, inside which 'guests' – Cl⁻ ions and H₂O are located (Figure 3a). It is visible from Figure 3a that the 'walls' of the channel are interacting by means of H-bonds only with species Cl(3) and O(1w). Other species Cl(1), Cl(2), O(w2) and disordered water molecules participate in the formation of chains of H-bonding directed along axis *b*. Thus, the formation of the channel with packing of the host molecules (cations) are favorable to the desorption of guest molecules (HCl and H₂O), therefore to the destruction of crystals of form **1** when exposed to air.

The crystals **2** obtained by recrystallizing the destroyed crystals **1** from water are stable. The asymmetric unit of the crystal **2** consists of a cation – protonated 2,3-pentamethylene-3,4-dihydroquinazolin-4-one - connected with a Cl⁻ ion by hydrogen bonding. Such formation of salt was observed in deoxyvazicinone hydrochloride – 2,3-trimethylene-3,4-dihydroquinazolin-4-one [8]. In Figure 3b the packing in the crystal is

shown. As it is visible from a Figure 3b the packing of host molecules in structure **2** is similar to this in form **1** and channel formation is still observed. However, inside the channels there are Cl⁻ anions interacting with protonated atom N(1). The short distance Cl(1) ... N(1) (3.05 Å) in comparison to the H-bonding distances in structure **1** proves the presence of a strong H-bond.

Molecular structure

In structures **1** and **2** the quinazoline nucleus of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one is planar within ± 0.08 Å, and the hepta-membered ring has a chair conformation. In condensed tricyclic 3,4-dihydroquinazolines the length of N(1) = C(2) and C(2)-N(3) bonds readily vary depending on the condition of atom N1. The geometric analysis of the –N(1)-C(2)-N(3)– fragment of the pyrimidine ring has shown, that in structure **1** the average length of the N(1) = C(2) and C(2)-N(3) bonds in two independent cations is 1.309(7) and 1.335(7) Å, respectively. In structure **2** corresponding bonds are 1.314(4) and 1.338(4) Å, respectively. These bond lengths within the limits the experimental error, are close to the earlier found values in nitrate of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one (1.311(4) and 1.340(4) Å) [11]. On the unprotonated molecules of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one length of these bonds are 1.296(9) and 1.389(8) Å [12]. These facts show that conjugation in salts occurs more strongly than in bases. The reason of such change is the delocalization of a positive charge on the system N(1)–C(2)–N(3). The lengths of other valent bonds in cations essentially do not differ from observed in the earlier investigated crystal forms of 2,3-pentamethylene-3,4-dihydroquinazolin-4-one [8,9].

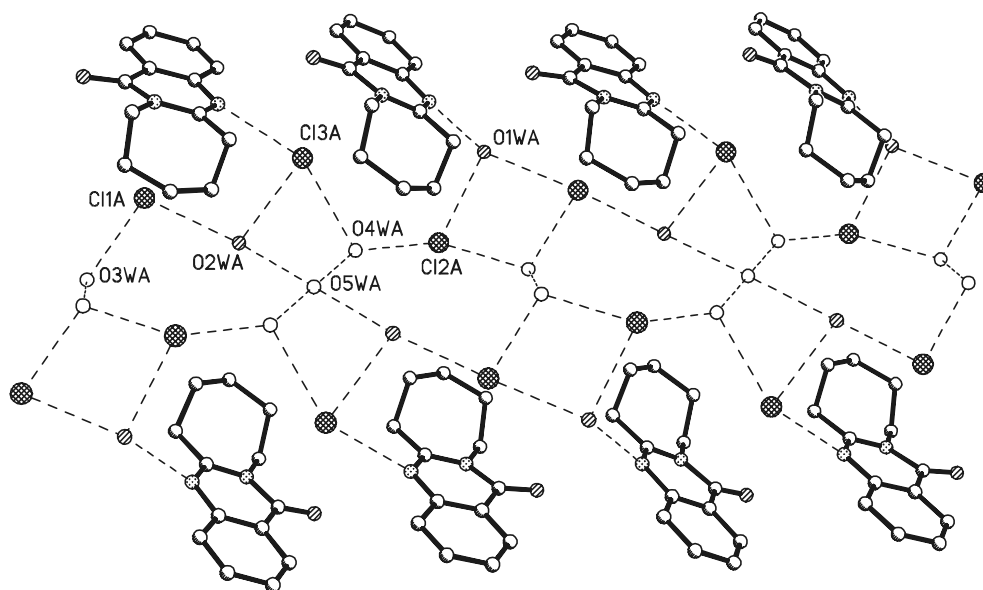


Figure 2. The observed H-bonds in structure **1**. Each disordered water molecules are shown in one position and they are indicated as open circle. (Hydrogen atoms have been omitted.)

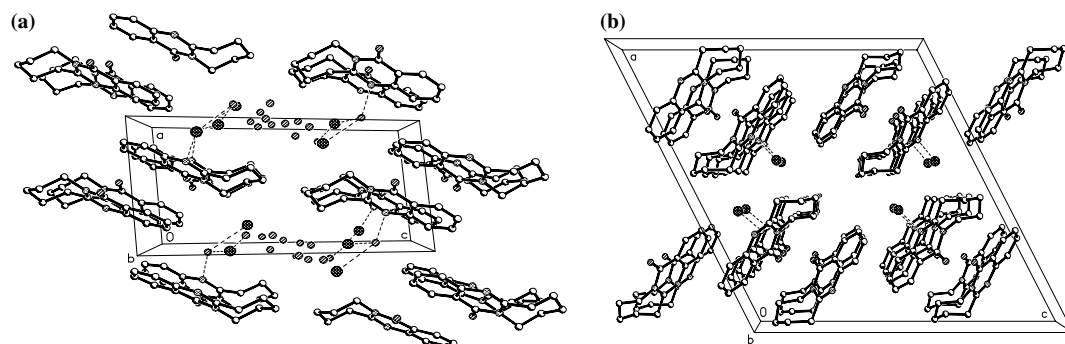


Figure 3. Crystal packing in **1**(a) and **2** (b).

Supplementary Data relating to this article has been deposited at the Cambridge Crystallographic Data Centre as supplementary publication and allocated the deposition number 223752 and 223753.

Acknowledgements

The authors wish to thank Dr. L.B. Molchanov for the preparation of the samples and Prof. B.T. Ibragimov for their interest in the work. The financial assistance from 'Latoxan' is gratefully acknowledged.

References

1. K.D. Sargazakov, Kh.N. Aripov, and L.V. Molchanov: *Khimija prirod. soedin.* 456 (1990).
2. Kh.M. Shakhidoyatov, A. Irisbaev, and Ch.Sh. Kadirov: *Khimija prirod.soedin.* 681 (1974).
3. Kh.M. Shakhidoyatov, A. Irisbaev, and L.M. Yun: *Khimija geterozikl.soedin.* 1564 (1976).
4. S.Yu. Yunusov, and N. Tulaganov et al. Certificate of authorship 605614 (USSR).
5. K.K. Turgunov, B. Tashkhodzhaev, L. V. Molchanov, and Kh.M. Shakhidoyatov: *Chem. Nat. Comp.* **39**, 379 (2003).
6. K.K. Turgunov, B. Tashkhodzhaev, L.V. Molchanov, G.V. Musaeva, and Kh.N. Aripov: *Chem. Nat. Comp.* **34**, 300 (1998)
7. B. Tashkhodzhaev, L.V. Molchanov, K.K. Turgunov, M.K. Makhmudov, and Kh.N. Aripov: *Chem. Nat. Comp.* **31**, 349 (1995).
8. K.K. Turgunov, B. Tashkhodzhaev, L.V. Molchanov, and Kh.N. Aripov: *Chem. Nat. Comp.* **31**, 714 (1995).
9. G.M. Sheldrick: SHELX-86. *Acta Crystallogr.* **A46**, 467 (1990).
10. G.M. Sheldrick: *Acta Crystallogr.* **A49**, 53 (1993).
11. K.K. Turgunov. B. Tashkhodjaev, L.V. Molchanov, and Kh.M. Shakhidoyatov: *Zh. Strukt. Khim.* **43**, 1021 (2002).
12. B. Tashkhodjaev, K.K. Turgunov, A.L. Dyakonov, G.A. Belova, and Kh.M. Shakhidoyatov: *Khimija prirod.soedin.* 410 (1995).