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CRYSTAL STRUCTURE OF 5-CHLOROSALICYLIC ALDEHYDE ISONICOTINOYL HYDRAZONE

Yu. M. Chumakov, B. Ya. Antosyak, V. I. Tsapkov, and N. M. Samus

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Isonicotinoyl hydrazide (tubazid) is the chief derivative of isonicotinic acid, possessing high bacteriostatic activity against microbacteria of tuberculosis and used for treatment and localization of all forms of tuberculosis [1-3]. Recent evolution of drug-resistant strains of this pathogen, however, calls for development of new bactericidal and bacteriostatic pharmaceuticals. Among these are hydrazones (phthivazide, saluzide, etc.) [4-6], obtained by condensation of isonicotinoyl hydrazide with substituted aromatic aldehydes. Therefore acquisition and systematization of experimental data on synthesis and structure of this class of compounds is of both scientific and practical interest.

Here we report on the results of synthesis and X-ray diffraction study of 5-chlorosalicylic aldehyde isonicotinoyl hydrazone (I).

Experimental. *Synthesis*. Azomethine I was prepared by boiling equimolar amounts of isonicotinoyl hydrazide and 5-chlorosalicylic aldehyde. Recrystallization from ethanol gave light yellow crystals with t_m = 237-238°C (ν(NH) 3300, 3220, 3100; ν(C=O) 1660; ν(C=H) 1620; δ(N–H) 1570; δ(C–N) 1340; δ(OH) 1255, 1255, 1245; δ(NCH) 1240; ν(C–O) 1180 cm^{-1}). Found, %: C 56.48, H 3.42, Cl 12.69, N 15.17. Calculated for $C_{13}H_{10}ClN_3O_2$, %: C 56.62, H 3.63, Cl 12.89, N 15.25.

X-ray diffraction study. An X-ray diffraction experiment was carried out on a DAR-UMB diffractometer (MoK_α radiation, graphite monochromator, room temperature, ω-θ/2θ scan mode). An absorption correction was not applied. The structure was solved by direct methods using SHELX-86 software [7]. The least-squares refinement was performed with SHELX-93 [8] anisotropically for nonhydrogen atoms and isotropically for hydrogens. The latter were placed geometrically and refined as atoms rigidly bound with the respective nonhydrogen atoms. In the case of the hydroxyl group, the most probable orientation of H atoms for the respective OH group was determined from difference Fourier maps and then refined by the least-squares procedure.

Crystal data and refinement parameters for compound I are listed in Table 1. The atomic coordinates are presented in Table 2, and the bond lengths and angles are given in Table 3.

TABLE 1. Experimental Information and Crystal and Refinement Data for I

1	2
Molecular formula	$C_{13}H_{10}ClN_3O_2$
Mol. wt.	275.69
Temperature, K	293(2)
Wavelength, Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1/n$
Cell parameters	
a, Å	8.710(2)
b, Å	15.776(3)

Institute of Applied Physics, Moldavian Academy of Sciences, Kishinev. Moldavian State University, Kishinev. Translated from *Zhurnal Strukturnoi Khimii*, Vol. 42, No. 2, pp. 400-404, March-April, 2001. Original article submitted February 24, 2000.

TABLE 1 (Continued)

1	2
c, Å	9.294(2)
β, deg	100.95(3)
Volume, Å^3	1253.8(5)
Z	4
Density (calc.), g/m^3	1.460
Absorption coeff., mm^{-1}	0.305
Crystal dimensions, mm	0.3×0.2×0.2
θ range for data collection, deg	2.58-26.39
Reflections collected	1402
Unique reflections	1298 [R_{int} = 0.0344]
GOOF on F^2	1.030
Final *R* indices [$I > 2\sigma(I)$]	$R1$ = 0.0475, $wR2$ = 0.1172
R indices (all data)	$R1$ = 0.0483, $wR2$ = 0.1252
Residual peaks in difference synthesis (eÅ^{-3})	0.235 and –0.168

TABLE 2. Atomic Coordinates (×10^4) and Equivalent Isotropic Thermal Parameters (Å^2×10^3) for I

Atom	*x*	*y*	*z*	U_{eq}	Atom	*x*	*y*	*z*	U_{eq}
Cl(1)	1967(1)	3988(1)	9555(1)	64(1)	C(5)	734(4)	3898(2)	7844(4)	41(1)
O(1)	–2175(3)	3639(2)	3791(3)	56(1)	C(6)	–247(4)	4561(2)	7311(4)	38(1)
O(2)	–5464(4)	4906(2)	1880(3)	65(1)	C(7)	–2284(4)	5205(2)	5404(3)	37(1)
N(1)	–3275(3)	5123(2)	4201(3)	39(1)	C(8)	–5339(4)	5614(2)	2421(4)	42(1)
N(2)	–4248(3)	5782(2)	3662(3)	40(1)	C(9)	–6351(3)	6336(2)	1757(3)	35(1)
N(3)	–8378(3)	7603(2)	375(3)	42(1)	C(10)	–6669(4)	7052(2)	2518(4)	39(1)
C(1)	–1244(4)	4504(2)	5938(3)	33(1)	C(11)	–7684(4)	7659(2)	1794(4)	41(1)
C(2)	–1223(4)	3755(2)	5120(3)	38(1)	C(12)	–8059(4)	6910(2)	–339(4)	42(1)
C(3)	–218(4)	3101(2)	5680(4)	45(1)	C(13)	–7075(4)	6272(2)	293(4)	42(1)
C(4)	756(4)	3164(2)	7045(4)	43(1)					

TABLE 3. Bond Lengths *d* and Angles ω for I

1	2	3	4
Bond	*d*, Å	Bond	*d*, Å
Cl(1)–C(5)	1.747(3)	C(1)–C(7)	1.455(5)
O(1)–C(2)	1.363(4)	C(2)–C(3)	1.389(5)
O(2)–C(8)	1.220(4)	C(3)–C(4)	1.390(5)
N(1)–C(7)	1.282(4)	C(4)–C(5)	1.377(5)
N(1)–N(2)	1.375(4)	C(5)–C(6)	1.383(5)
N(2)–C(8)	1.374(4)	C(8)–C(9)	1.500(5)
N(3)–C(12)	1.336(4)	C(9)–C(10)	1.388(5)
N(3)–C(11)	1.345(4)	C(9)–C(13)	1.390(4)
C(1)–C(6)	1.403(4)	C(10)–C(11)	1.387(5)
C(1)–C(2)	1.408(4)	C(12)–C(13)	1.379(5)

TABLE 3 (Continued)

1	2	3	4
Angle	ω, deg	Angle	ω, deg
C(7)–N(1)–N(2)	120.5(3)	C(4)–C(5)–Cl(1)	119.3(3)
C(8)–N(2)–N(1)	116.1(3)	C(6)–C(5)–Cl(1)	119.7(3)
C(12)–N(3)–C(11)	116.3(3)	C(5)–C(6)–C(1)	120.7(3)
C(6)–C(1)–C(2)	118.4(3)	N(1)–C(7)–C(1)	119.6(3)
C(6)–C(1)–C(7)	120.0(3)	O(2)–C(8)–N(2)	121.1(3)
C(2)–C(1)–C(7)	121.6(3)	O(2)–C(8)–C(9)	121.7(3)
O(1)–C(2)–C(3)	118.1(3)	N(2)–C(8)–C(9)	117.2(3)
O(1)–C(2)–C(1)	122.3(3)	C(10)–C(9)–C(13)	117.4(3)
C(3)–C(2)–C(1)	119.6(3)	C(10)–C(9)–C(8)	124.6(3)
C(4)–C(3)–C(2)	121.4(3)	C(13)–C(9)–C(8)	118.0(3)
C(5)–C(4)–C(3)	119.0(3)	C(11)–C(10)–C(9)	119.0(3)
C(4)–C(5)–C(6)	120.9(3)	N(3)–C(11)–C(10)	123.9(3)
N(3)–C(12)–C(13)	123.9(3)	C(12)–C(13)–C(9)	119.5(3)

The geometrical parameters of compound I were analyzed with the aid of the Cambridge Structural Database (version 5.15) [9].

Description of structure. Figure 1 shows the structure of compound I. It contains a pyridine ring (*A*) and a nearly planar salicylaldimine fragment, which is benzoid like most azomethines [9]. The dihedral angle between ring *A* and the chlorophenol fragment *B* is 169.2°. The torsion angles between each of these fragments and the mean plane of the atoms of the hydrazide chain *C* (it is nearly planar, the torsion angle C(7)N(1)N(2)C(8) is 175.7°), *A*/*C* and *B*/*C*, are 158.5 and 169.0°, respectively. Analogous angles *A*/*C* and *B*/*C* in *para*-dimethylaminobenzaldehyde isonicotinoyl hydrazone monohydrate [10], furfuralacetone isonicotinoyl hydrazone larusamonohydrate [11], and salicylalisonicotinoyl hydrazone [12] are 136.8 and 173.6°, 155 and 175°, 152.6 and 172.4°. Thus in compound I, rotation of the pyridine ring relative to the hydrazide chain is the smallest, and that of the chlorophenol fragment is the largest compared to the cited structures. The bond lengths and angles agree with the literature data [9-17]. In compound I as well as in molecules investigated in [13-16], the oxygen and nitrogen atoms of the salicylaldimine fragments form an intramolecular hydrogen bond: O(1)...N(1) 2.584(4), H(1)...N(1) 1.87(2) Å; the O(1)H(1)N(1) angle is 146(2)°. Note that in N-phenylsalicylaldimine-5-sulfomate [6], where the proton lies at the azomethine nitrogen atom, the O–C distance (1.298 Å) in the phenyl ring is shorter than the analogous distances in I and in the compounds reported in [13-16] (1.334-1.380(6) Å).

In crystal, the molecules related by a symmetry operation (0.5+*x*, 1.5–*y*, 0.5+*z*) form intermolecular hydrogen bonds (IHB) N–H...N(Py) (Fig. 2). The geometrical parameters of this bond: the distances N(2)...N(3)′ 3.023(4) Å and H(2)...N(3)′ 2.18 Å and the N(2)H(2)N(3)′ angle 165° permit one to regard the bond as slightly linear [17]. However, for an analogous

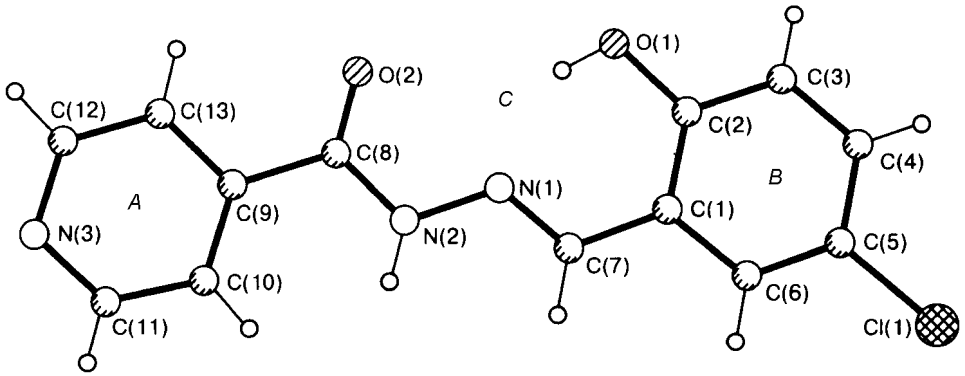

Fig. 1. Structure of compound I.

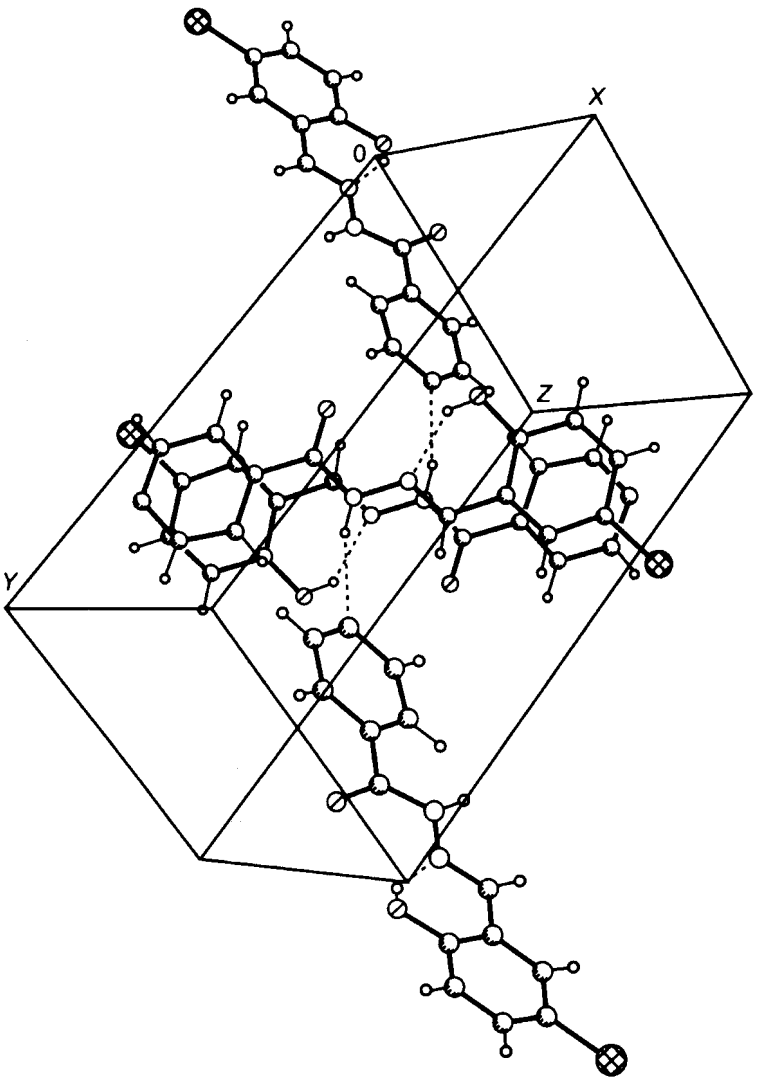

Fig. 2. Fragment of the packing of compound I.

IHB in the crystal structure of N′-(5-nitrofurfurylidene)isonicotine hydrazide (N...N′ 3.003(3), H...N′ 2.24 Å, NHN′ angle is 169°), the low frequency of N–H vibrations (3120 cm^{-1}) indicates that the interaction energy of N–H...N(Py) is high enough [17]. Molecules I linked by this IHB are packed in crystal in such a way that the chlorophenol ring of one pair of molecules lies over the pyridine ring of the neighboring pair related to the initial pair by a symmetry center, thus forming infinite chains (Fig. 2). The distances between these rings are from 3.26 to 3.55 Å and are characteristic of a stacking interaction of molecules in crystal [18]. The chains are linked by van der Waals interactions.

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