Synthesis and Crystal Structure of 2-Aminoacetyl-1,3,4-thiadiazole

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Abstract—2-Aminoacetyl-1,3,4-thiadiazole was synthesized, and its structure was studied. In crystal, the thiadiazole molecules form hydrogen-bonded endless one-dimensional chains related by the glide reflection plane.

Proceeding with our research into 1,3,4-thiadiazole derivatives [1–3] we synthesized 2-aminoacetyl-1,3,4-thiadiazole that belongs to compounds known to exhibit a broad-range biological and pharmacological activity [4]. A series of 1,3,4-thiadiazole derivatives was synthesized and studied mostly by means of ¹H and IR spectroscopy [5].

Here we present the results of single-crystal X-ray analysis of 2-aminoacetyl-1,3,4-thiadiazole (II) prepared by the reaction of 2-amino-1,3,4-thiazole (I) with acetic anhydride. The synthesis of acetyl derivative II was performed by the procedure in [6] by heating compound I in acetic anhydride. Therewith, the yield of the final product was 76%.



The IR spectrum of compound **II** contains characteristic absorption bands at 1543 [v_s (C=N)] and 1439 cm⁻¹ [v_{as} (C=N)] and =N-N=, N=C-N, C=O, and C-S absorption bands at 1040, 1564, 1684, and 634 cm⁻¹, respectively [7].

The ¹H NMR spectrum of compound **II** shows downfield multiplet signals centered at δ 9.08 ppm, that were assigned to the thiadiazole ring proton. Methyl protons give a broadened singlet at δ 2.14 ppm and the imino group, a singlet at δ 12.4 ppm.

The X-ray analysis showed that single crystals of compound II belong to the orthorhombic syngony. Figure 1 presents the molecular structure of II, and the table lists the interatomic distances and bond angles. Compound II (Fig. 1), like previously studied 2-amino-5-phenyl- and 2-amino-5-(m-nitrophenyl)-1,3,4-thiadiazoles [1, 2], have the N^1 , N^2 , and S^1 lone electron pairs conjugated with the double bonds of the thiadiazole ring, as evidenced by the N^1-C^1 , N^2-C^2 , and $N^{1}-N^{2}$ bond lengths of 1.283(5), 1.302(4), and 1.387(4) Å, respectively. The endocyclic N-C bond lengths are intermediate between the standard single and double bond lengths. The imino N^3-C^2 and $N^{3}-C^{3}$ [1.372(4) and 1.362(4) Å] and $C^{3}=O^{1}$ [1.218(4) Å] bond lengths are normal values. In whole the molecule is planar, which is evidenced by the fact that the molecule in crystal is in a special position, viz. in the glide reflection plane.

In the crystal structure of thiadiazole II, as noted above, the molecules are in special positions, i.e. glide reflection planes perpendicular to the y axis. The



Fig. 1. Molecular structure of compound II and atom numbering scheme.

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Fig. 2. Association of molecules II via H bonds and shortened contacts.



Fig. 3. Crystal structure of compound II.

molecules form endless one-dimensional chains running along the *x* plane, by means of the N^3 –H···O¹ bond with a length 2.848(4) Å and an angle of 165(3)° [N^3 –H 0.79(4), H···O¹ 2.07(3) Å], related to each other by the glide reflection plane. A shortened contact between sulfur and nitrogen [3.225(3) Å] in molecules related to each other by the glide reflection plane is observed. Thus, these contacts make possible formation of a layer on the reflection plane (Fig. 2). Molecules related by the inversion center form a layer antiparallel to the mentioned layer (Fig. 3). Therewith, the distance between the two layers is 3.307 Å. The distance between the C^2 atoms of opposite molecules is close to this value (3.365 Å). These data suggest dipole interactions between molecules of opposite layers, which makes the crystal packing tight (packing coefficient 0.732).

EXPERIMENTAL

The IR spectra were measured on an Avatar instrument at 400–4000 cm⁻¹. The ¹H NMR spectra were obtained on XL-100 and XL-200 spectrometers (solvent DMSO- d_6 , internal reference HMDS).

The single-crystal X-ray analysis of 2-aminoacetyl-1,3,4-thiadiazole (II) was performed on an STOE Stadi-4 diffractometer (λ MoK_{α} radiation, graphite monochromator, $\theta/2\theta$ scanning, $2\theta_{max}$ 560). The C₄H₅N₃OS crystals have orthorhombic syngony. Unit cell parameters: *a* 9.2610, *b* 6.6130, *c* 9.6350 Å; *V* 590.1(5) Å³, *Z* 4, *d*_{calc} 1.612 g cm⁻³, space group *Pnma*. Data collection was performed at 293±2 K. Crystal dimensions $0.2 \times 0.2 \times 0.4$ mm, μ (MoK_{α}) 0.456 mm⁻¹, and *F*(000) 296. Angle range 3.05 $\leq \theta \leq$ 25°. The structure was solved by the direct method using the SHELXS-97 program package [8] and refined by the SHELXL-97 program package [9]. Hydrogen atoms were located geometrically and refined by the rider model. The divergence factor *R* after

Interatomic distances and bond angles in structure II

Bond	<i>d</i> , Å	Bond	<i>d</i> , Å
$ \begin{array}{c} S^{1}-C^{1}\\ S^{1}-C^{2}\\ C^{3}-C^{4}\\ N^{1}-C^{1}\\ N^{3}-C^{2} \end{array} $	1.717(3) 1.726(3) 1.493(5) 1.283(5) 1.372(4)	$\begin{matrix} N^{3}-C^{3} \\ O^{1}-C^{3} \\ N^{1}-N^{2} \\ N^{2}-C^{2} \end{matrix}$	1.362(4) 1.218(4) 1.387(4) 1.302(4)
Angle	ω, deg	Angle	o, deg
$\begin{array}{c}\\ C^{1}S^{1}C^{2}\\ N^{2}N^{1}C^{1}\\ N^{1}N^{2}C^{2}\\ C^{2}N^{3}C^{3}\\ C^{2}N^{3}H^{2}\\ C^{3}N^{3}H^{2}\\ S^{1}C^{1}N^{1} \end{array}$	85.90(16) 112.0(3) 111.6(3) 124.0(3) 118.0(2) 118.0(2) 115.7(2)	$\begin{matrix} O^1C^3N^3 \\ O^1C^3C^4 \\ S^1C^2N^3 \\ N^2C^2N^3 \\ S^1C^2N^2 \\ N^3C^3C^4 \end{matrix}$	121.0(3) 122.3(3) 124.0(2) 121.2(3) 114.8(2) 116.7(3)

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the final step of refinement of positional and thermal parameters was 0.0389. The molecular drawings were performed using the XP program in SHELXTL-Plus [10].

The structures were registered in the Cambridge structural database.

2-Aminoacetyl-1,3,4-thiadiazole (II). A solution of 1.01 g of 2-amino-1,3,4-thiazole (I) in 20 ml of acetic anhydride was stirred for 1.5 h at 100°C and then cooled to 0°C. The precipitate that formed was filtered off and recrystallized from ethanol. Yield 76%, mp 242–244°C. The single crystals of compound II for X-ray analysis were obtained by recrystallization from hot ethanol.

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