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Structural Investigation Of 5-Amino-1,3,4-Thiadiazoles Containing Different Alkyl Groups

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***Abstract*—In the present work crystal structures of the 2-ethylthio-5-amino-1,3,4-thiadiazole (1) and 2-propylthio-5-amino-1,3,4-thiadiazoles (2) have been investigated. Single crystals of the compounds 1 and 2 were grown from solutions of methanol, ethanol, acetone, chloroform, DMF and acetonitrile by slow evaporation of the solvent at room temperature. By determination of the melting points and unit cell parameters of the crystals were found that in all cases form same crystals without inclusion of solvent molecules: so they are not clathrogens. Extension of terminal thioalkyl groups on one methylene group leads to a less dense packing of the molecules in the crystal and the changing nature of intermolecular interactions.**

Keywords- 5-Amino-1,3,4-thiadiazole-2-thione; 2-alkylthio-5-amino-1,3,4-thiadiazoles; X-ray analysis; Crystal structure

I. INTRODUCTION

The presence in the molecule of 5-amino-1,3,4-thiadiazole-2-thione pharmacophore sulfur- and nitrogen-containing fragments make it one of the most widely studying of five-membered heterocycles, which is of great interest for various chemical transformations. Among this class compounds are found many biological activities such as pharmacological, pesticide et al.[1-4]. Furthermore aminothiazolinthiones can exhibit multiple reactivity due to the presence of amino group in the fifth position, sulfur and nitrogen atoms in ambifunctional system NH-C=S.

Recently were studied reactions of 5-amino-1,3,4-thiadiazolin-2-thione with ethyl and propyl iodide to produce alkyl derivatives (**1**, **2**) and investigated their structure. The reactions were carried out in the presence of K_2CO_3 in acetone [5]:

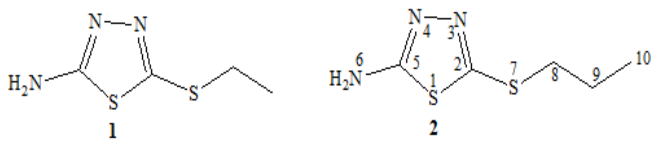

Fig.1. Schematic formula and numbering of the atoms in the structures **1** and **2**.

It was found that the reaction proceeds selectively on the sulfur atom to give 2-ethylthio-5-amino-1,3,4-thiadiazole (**1**) and 2-propylthio-5-amino-1,3,4-thiadiazoles (**2**) in high yield (91 %) [5]. It should be noted that the products of alkylation on the amino group or on the nitrogen atom in position 3 is not formed. The structures of the compounds were proved by spectral data (UV, IR and ^{1}H NMR) and X-ray diffraction analysis.

We have previously found that N-(3-methylthio and N-(3-ethylthio-5-acetamido-1,2,4-thiadiazole-2-thione) derivatives of the alkaloid cytisine exhibit clathratogen property including different solvent molecules in their crystal lattices [6-9]. Although the alkaloid cytisine [10] and other derivatives [11, 12] (for example, acetyl or benzyl derivatives of cytisine [13, 14]) have not such properties. For this reason, was interesting study of the crystal structures of related thiadiazoles: 2-ethylthio-5-amino- and 2-propylthio-5-amino-1,3,4-thiadiazole grown from different solvents.

II. Experimental

A. Crystal growth

Single crystals of the compounds 2-ethylthio-5-amino-1,3,4-thiadiazole (**1**) and 2-propylthio-5-amino-1,3,4-thiadiazole (**2**) were grown from solutions of methanol, ethanol, acetone, chloroform, DMF and acetonitrile by slow evaporation of the solvent at room temperature. By determination of the melting points and unit cell parameters of the crystals were found that in all cases form same crystals without inclusion of solvent molecules.

B. X-ray Structure Determination

The unit cell parameters of the crystals are determined and refined with CCD Xcalibur Ruby diffractometer (Oxford Diffraction) using CuKα-radiation, graphite monochromator (T = 293 K). The three-dimensional set of reflections received at the appropriate diffractometer. The amendment was introduced to the absorption by Multi-scan [15]. Table 1 shows the main parameters of the X-ray diffraction experiments and calculations clarify the structures of crystals **1** and **2**.

A three-dimensional data set of reflections was obtained on the same diffractometer. Absorption corrections were applied using a semi-empirical method in the SADABS program [15]. Table 1 presents the main crystallographic parameters and the characteristics of the X-ray diffraction experiments and crystal structure refinement calculations.

TABLE 1. The main crystallographic parameters and characteristics of the x-ray diffraction experiments and crystal structure refinement calculations

Compound	**1**	**2**
Molecular formula	$C_4H_7N_3S_2$	$C_5H_9N_3S_2$
Mr	161.25	175.27
Crystal symmetry	Monoclinic	Triclinic
Space group	P 2_1/c	P -1
Z	4	2
a, Å	7.7238(15)	5.6256(11)
b, Å	8.8629(18)	8.8779(18)
c, Å	10.875(2)	8.9419(18)
α, °	90	96.46(3)
β, °	93.52(3)	104.60(3)
γ, °	90	101.68(3)
V, Å^3	743.0(3)	416.86(16)
ρ, g/cm^3	1.441	1.396
Crystal dimension (mm)	0.35x0.48x0.55	0.40x0.45x0.55
Range scanned, 2θ°	5.74≤θ≤76.06°	5.16≤θ≤75.55°
μ_{exp} (cm^{-1})	5.826	5.236
No. reflection collected	1485	1653
No. reflection with I>2σ(I)	1171	1058
R_1 (I>2σ(I) and total)	0.0449 (0.0598)	0.0715 (0.1004)
wR_2	0.1104 (0.1230)	0.1786 (0.2103)
GOOF	1.029	1.034
Largest diff. peak and hole (e Å^{-3})	0.341 and –0.410	0.466 and –0.382
CCDC	1476419	1476420

The structures were solved by direct methods using SHELXS-2014 and refined using SHELXL-2014 programs [16]. All non-hydrogen atoms were refined by anisotropic full-matrix least-squares methods (over F^2). Positions of H atoms were found geometrically and refined with fixed isotropic thermal parameters Uiso = nUeq, where n = 1.5 for methyls and 1.2 for others and Ueq is the equivalent isotropic thermal parameter of the corresponding C atoms.

Results from the X-ray diffraction experiments were deposited at the Cambridge Crystallographic Data Centre (CCDC). Materials X-ray diffraction as a CIF file deposited at the Cambridge center of crystal data (CCDC), from which can be obtained free on request at the following link: www.ccdc.cam.ac.uk/data_request/cif

III. RESULTS AND DISCUSSION

Molecular structures of the compounds **1** and **2** comprise a flat (within ± 0.006 and ± 0.002 Å respectively) aromatic thiadiazole nucleus and movable thioethyl and thiopropyl fragments at position C2, respectively, which are also flat. Their location relative to the plane of the thiadiazole nucleus almost similar (the value of S1-C2-S7-C8 4.7 and 7.70 for the torsion angle **1** and **2**, respectively)

In the crystal structures of **1** and **2** N atom of thiadiazole ring and NH-group can form intermolecular H-bonds. In the crystal between molecules related centrosymmetrical and by 2_1 symmetry are formed N-H . N type H-bonded strands along *c* axis (Table 1). Within the strands are formed H-bond cycles with graph set motifs of $R_2^2(8)$ and $R_6^6(20)$ [17] (Fig. 2.).

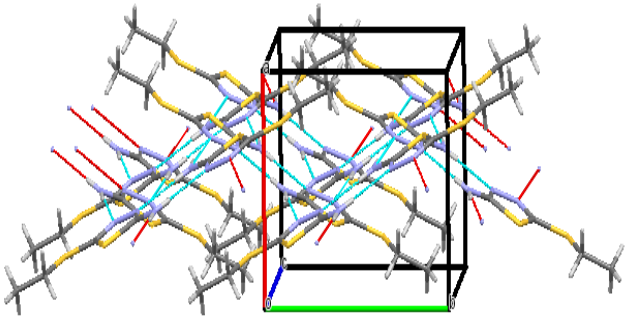

Fig.2. H-bonded strand in the structure of **1**.

The H-bonded tapes were formed in the crystal of **2**. In this case participates molecules translated by *a* axis and related centrosymmetrically. Within the tapes are formed H-bond cycles with graph set motifs of $R_2^2(8)$ and $R_4^4(10)$ [18]. H bond parameters are listed in Table 2 (Fig. 3.).

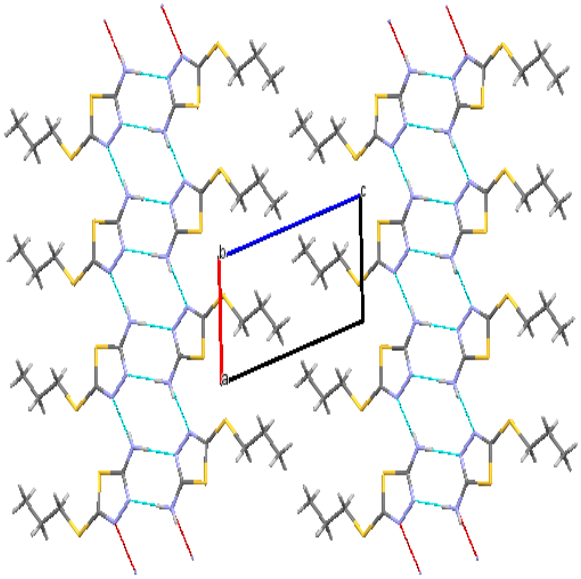

Fig.3 H-bonding in the structure of **2**.

Table 2 summarizes the geometric parameters H bonds in the structures **1** and **2**. From the table can be noted that the H-bonds distances were not significantly different in the two structures, but transformation elements (symmetry) of H-bonds are different, which in turn leads the formation of different H-bonded molecular systems for the two structures.

Table 2. Geometric parameters h bonds in the structures **1** and **2** (d: the distance, the d: donor a: acceptor)

D—H.A	*d*(D—H), Å	*d*(H.A), Å	*d*(D.A), Å	∠(DHA), °	Symmetry
1					
N6-HA.N4	0.80(4)	2.22(4)	3.014(4)	178(5)	*1-x,-y,1-z*
N6-HB.N3	0.88(4)	2.09(4)	2.958(4)	168(3)	*x,1/2-y,-1/2+z*
2					
N6-HA.N4	1.03(5)	1.98(5)	3.013(7)	179(5)	*1-x,1-y,-1-z*
N6-HB.N3	0.79(8)	2.21(7)	2.995(7)	170(7)	*-1+x,y,z*

In the structure **1** was observed weak π . π interaction between the aromatic rings (atoms S1, C2, N3, N4, C5) of molecules related by symmetry *1-x, 1-y, -z*, with centroid-centroid distance of 4.335 (2) Å. Also, there is observed C-H . π interaction between aromatic ring and C-H group, distance C9 . π 3.831 (5) Å, H9B . π 2.95 Å, angle C9-H9B . π 154, symmetry 1-*x, 1-y, 1-z*. Also in the crystal structure of **2** is observed π . π interaction between aromatic rings (atoms S1 C2 N3 N4 C5) of molecules, related by symmetry *1-x, 1-y, -z*, with centroid-centroid distance of 4.320(3) Å.

IV. CONCLUSIONS

In conclusion, it should be noted that the crystals grown from different solvents 2-ethylthio-5-amino- and 2-propylthio-5-amino-1,3,4-thiadiazole derivatives do not contain solvent molecules and they are not clathrogen. Extension of terminal thioalkyl groups on one methylene group leads to a less dense packing of the molecules in the crystal and the changing nature of intermolecular interactions.

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