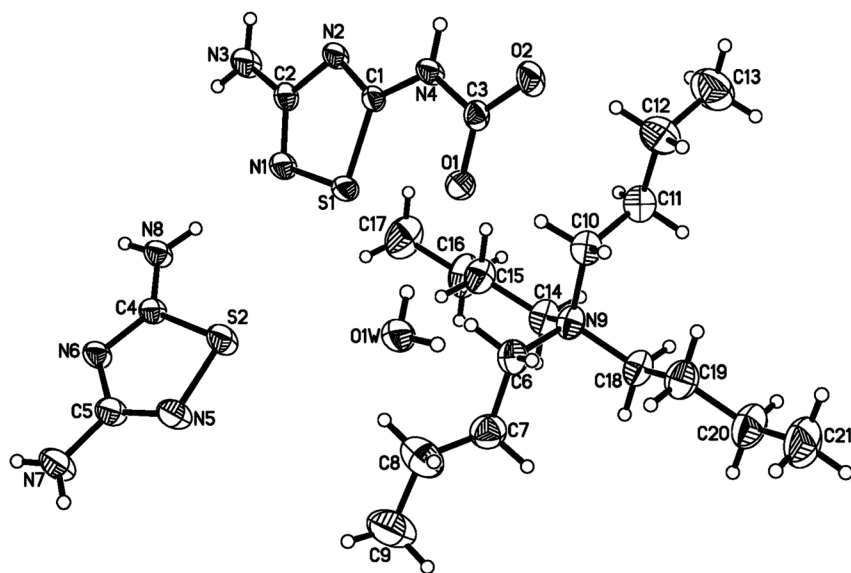


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Tetrabutylammonium 1,3,5-thiadiazole-5-amido-2-carbamate—1,2,4-thiadiazole-3,5-diamine—water (1/1/1), $C_{21}H_{45}N_9O_3S_2$



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Abstract

$C_{21}H_{45}N_9O_3S_2$, orthorhombic, *Pbca* (no. 61), $a = 9.5299(6)$ Å, $b = 16.5181(9)$ Å, $c = 36.886(2)$ Å, $\beta = 90^\circ$, $V = 5806.4(6)$ Å³, $Z = 8$, $R_{gt}(F) = 0.0568$, $wR_{ref}(F^2) = 0.1420$, $T = 296(2)$ K.

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.30 × 0.28 × 0.28 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.22 mm ^{−1}
Diffraction mode:	Bruker APEX-II, φ and ω
θ_{max} , completeness:	25.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int} :	27,778, 5110, 0.032
Criterion for I_{obs} , $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 4338
$N(param)_{refined}$:	322
Programs:	Bruker [1], SHELX [2, 3]

Source of materials

Amidinothiourea and tetrabutylammonium hydroxide (10% aqueous solution) were mixed in a molar ratio of 1:2. The mixture was dissolved in a minimum amount of ethanol/water, then the mixture was vigorously stirred for about 1.5 h. Subsequently the clean solution was set aside to allow it slow evaporation at room temperature. Colorless block crystals were obtained about 15 days later. It can be concluded that one part of amidinothiourea molecules

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.5290 (2)	0.04175 (15)	0.05309 (6)	0.0378 (5)
N1	0.7546 (2)	0.07756 (15)	0.08019 (6)	0.0521 (6)
O1	0.30458 (18)	0.05046 (12)	0.09974 (5)	0.0519 (5)
S1	0.58747 (7)	0.07287 (5)	0.09501 (2)	0.0488 (2)
O1W	0.3454 (2)	0.03028 (18)	0.17907 (6)	0.0728 (7)
H1WA	0.356 (4)	0.038 (3)	0.1562 (4)	0.109*
H1WB	0.2571 (14)	0.029 (3)	0.1837 (9)	0.109*
C2	0.7558 (3)	0.05466 (16)	0.04604 (7)	0.0446 (6)
N2	0.6314 (2)	0.03440 (14)	0.02957 (5)	0.0438 (5)
O2	0.16293 (17)	0.01508 (13)	0.05376 (5)	0.0552 (5)
S2	0.79275 (7)	0.07199 (6)	0.17583 (2)	0.0622 (2)
C3	0.2784 (2)	0.03095 (16)	0.06774 (7)	0.0411 (6)
N3	0.8734 (2)	0.05215 (16)	0.02551 (7)	0.0608 (7)
H3A	0.9528	0.0660	0.0347	0.073*
H3B	0.8687	0.0367	0.0033	0.073*
C4	0.9662 (2)	0.06170 (16)	0.16266 (7)	0.0418 (6)
N4	0.39442 (19)	0.02597 (14)	0.04410 (5)	0.0453 (5)
H4A	0.3780	0.0117	0.0221	0.054*
C5	0.9645 (3)	0.0350 (2)	0.22064 (7)	0.0546 (7)
N5	0.8299 (2)	0.04829 (18)	0.21880 (6)	0.0645 (7)
C6	0.3189 (3)	0.23839 (18)	0.15525 (8)	0.0600 (8)
H6A	0.2415	0.2036	0.1623	0.072*
H6B	0.3898	0.2042	0.1442	0.072*
N6	1.0471 (2)	0.04201 (15)	0.19002 (6)	0.0489 (5)
C7	0.3806 (4)	0.2754 (2)	0.18931 (10)	0.0749 (9)
H7A	0.4498	0.3158	0.1827	0.090*
H7B	0.3069	0.3022	0.2029	0.090*
N7	1.0269 (3)	0.0121 (2)	0.25208 (7)	0.0784 (9)
H7C	0.9774	0.0060	0.2714	0.094*
H7D	1.1159	0.0036	0.2527	0.094*
C8	0.4480 (5)	0.2126 (3)	0.21264 (11)	0.1010 (14)
H8A	0.3769	0.1736	0.2197	0.121*
H8B	0.5173	0.1841	0.1982	0.121*
N8	1.0093 (2)	0.07486 (14)	0.12864 (6)	0.0506 (6)
H8C	1.0968	0.0706	0.1233	0.061*
H8D	0.9495	0.0876	0.1121	0.061*
C9	0.5176 (5)	0.2432 (4)	0.24612 (12)	0.1217 (17)
H9A	0.5575	0.1986	0.2592	0.183*
H9B	0.5905	0.2806	0.2396	0.183*
H9C	0.4497	0.2701	0.2611	0.183*
N9	0.2659 (2)	0.29728 (13)	0.12659 (7)	0.0537 (6)
C10	0.2126 (3)	0.24676 (17)	0.09520 (8)	0.0575 (7)
H10A	0.2886	0.2121	0.0871	0.069*
H10B	0.1386	0.2118	0.1042	0.069*
C11	0.1567 (4)	0.2923 (2)	0.06262 (9)	0.0664 (8)
H11A	0.0902	0.3331	0.0705	0.080*
H11B	0.2332	0.3193	0.0502	0.080*
C12	0.0856 (4)	0.2340 (2)	0.03709 (10)	0.0854 (11)
H12A	0.0106	0.2067	0.0500	0.102*
H12B	0.1530	0.1932	0.0297	0.102*
C13	0.0256 (5)	0.2737 (3)	0.00366 (11)	0.1118 (16)
H13A	−0.0179	0.2334	−0.0113	0.168*
H13B	−0.0430	0.3132	0.0107	0.168*
H13C	0.0995	0.2998	−0.0096	0.168*
C14	0.3833 (3)	0.35338 (17)	0.11423 (9)	0.0604 (8)

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
H14A	0.3455	0.3903	0.0963	0.072*
H14B	0.4130	0.3856	0.1348	0.072*
C15	0.5110 (3)	0.31264 (19)	0.09831 (10)	0.0681 (9)
H15A	0.5528	0.2771	0.1162	0.082*
H15B	0.4835	0.2800	0.0776	0.082*
C16	0.6166 (4)	0.3748 (2)	0.08664 (13)	0.0893 (12)
H16A	0.6427	0.4073	0.1075	0.107*
H16B	0.5734	0.4104	0.0690	0.107*
C17	0.7477 (4)	0.3384 (3)	0.07029 (14)	0.1085 (15)
H17A	0.8109	0.3809	0.0634	0.163*
H17B	0.7924	0.3040	0.0878	0.163*
H17C	0.7230	0.3071	0.0493	0.163*
C18	0.1509 (3)	0.35124 (18)	0.14186 (9)	0.0630 (8)
H18A	0.1889	0.3806	0.1624	0.076*
H18B	0.1260	0.3908	0.1235	0.076*
C19	0.0182 (3)	0.3087 (2)	0.15396 (10)	0.0725 (9)
H19A	−0.0219	0.2791	0.1338	0.087*
H19B	0.0401	0.2704	0.1730	0.087*
C20	−0.0861 (4)	0.3700 (3)	0.16769 (13)	0.0932 (12)
H20A	−0.0446	0.3991	0.1878	0.112*
H20B	−0.1049	0.4089	0.1486	0.112*
C21	−0.2231 (4)	0.3337 (3)	0.17992 (14)	0.1152 (16)
H21A	−0.2843	0.3759	0.1883	0.173*
H21B	−0.2664	0.3059	0.1600	0.173*
H21C	−0.2060	0.2961	0.1993	0.173*

form 1,2,4-thiadiazole-3,5-diamine molecules under basic conditions, and another part of amidinothiourea molecules should absorb CO₂ of the atmosphere to convert to the corresponding 1,3,5-thiadiazole-5-amido-2-carbamate anions under basic conditions.

Comment

Amidinothiourea, which is a derivative of thiourea, is a key pharmaceutical intermediate of famotidine [4]. Observing the structure of amidinothiourea, it can be regarded as a plane molecule composed of two triangular parts, which can generate more than nine hydrogen bonds. As the related literatures [5–7] indicated, amidinothiourea is unstable and it can form heterocycle under specific conditions, such as 1,3,5-thiadiazole-5-amido-2-carbamate or 1,2,4-thiadiazole-3,5-diamine. In 2012, two compounds of 1,3,5-thiadiazole-5-amido-2-carbamate were reported with the existence of tetrapropylammonium and tetrabutylammonium [5]. In 2022, one dihydrate of tetraethylammonium 1,3,5-thiadiazole-5-amido-2-carbamate was reported [6]. As to 1,2,4-thiadiazole-3,5-diamine, it can be concluded that it is also a derivative of amidinothiourea under basic conditions, just like 1,3,5-thiadiazole-

5-amido-2-carbamate. Compared with 1,3,5-thiadiazole-5-amido-2-carbamate, 1,2,4-thiadiazole-3,5-diamine doesn't absorb extra CO_2 to further yield the additional carboxyl group to link with the heterocycle derived from amidinothiourea during the actual experimental process. It is noticeable that 1,2,4-thiadiazole-3,5-diamine is normally synthesized by amidinothiourea with the existence of H_2O_2 [7]. But in this manuscript, with the absence of H_2O_2 , 1,2,4-thiadiazole-3,5-diamine can also be obtained under basic conditions.

In the asymmetric unit of the crystal structure, there exist one tetrabutylammonium, one 1,3,5-thiadiazole-5-amido-2-carbamate, 1,2,4-thiadiazole-3,5-diamine and one water molecule. As the calculation implies, the carbamate anion and neutral diamine have qualified planarity with the mean deviation values from the least-square planes of 0.0050 Å and 0.0027 Å. In the carbamate, the bond lengths of the deprotonated carboxyl group tend to be average with the values of 1.249(3) Å and 1.244(3) Å. Analyzing the hydrogen bonds, it can be seen that one pair of 1,3,5-thiadiazole-5-amido-2-carbamate firstly connect with each other to form a hydrogen-bonded dimer by two $N-H\cdots N$ hydrogen bonds and two $N-H\cdots O$ hydrogen bond, then the adjacent dimers are further linked with $N-H\cdots O$ contacts to generate the extended ribbons along the a axis. Additionally, two neighboring 1,2,4-thiadiazole-3,5-diamine molecules are connected with $N-H\cdots N$ hydrogen bonding to yield a ziazag hydrogen-bonded chain along the a axis. Consecutively, the hydrogen-bonded chains interact with the anionic hydrogen-bonded ribbons mentioned above by the water molecules to finally construct the 2-dimensional layer. As to tetrabutylammonium cations, they are regularly contained between the layers to form the ultimate sandwich-like crystal structure. From this, it can be seen

that 1,3,5-thiadiazole-5-amido-2-carbamate and 1,2,4-thiadiazole-3,5-diamine, as two derivatives of amidinothiourea, both display excellent abilities of forming hydrogen bonds, which can be further explored in the related crystal structures.

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References

1. BRUKER. *SAINT, APEX2 and SADABS*; Bruker AXS Inc.: Madison, Wisconsin, USA, 2009.
2. Sheldrick G. M. SHELXTL – integrated space-group and crystal-structure determination. *Acta Crystallogr.* 2015, *A71*, 3–8.
3. Sheldrick G. M. Crystal structure refinement with SHELXTL. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Adane L., Bhagat S., Arfeen M., Bhatia S., Sirawaraporn R., Sirawaraporn W., Chakraborti A. K., Bharatam P. V. Design and synthesis of guanyltiourea derivatives as potential inhibitors of Plasmodium falciparum dihydrofolate reductase enzyme. *Bioorg. Med. Chem. Lett.* 2014, *A24*, 613–617.
5. Zhang W. H., Li K., Li Q., Mak T. C. W. Two inclusion compounds of guanyltiourea and 1,3,5-thiadiazole-5-amido-2-carbamate. *J. Inclusion Phenom. Macrocycl. Chem.* 2012, *74*, 353–359.
6. Tan X. K., Zhu X. Crystal structure of the dihydrate of tetraethylammonium 1,3,5-thiadiazole-5-amido-2-carbamate, $C_{11}H_{27}N_5O_4S$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 525–526.
7. Melenchuk T. V., Danilova E. A., Stryapan M. G., Islyaikin M. K. Synthesis and properties of diaminothiadiazoles. *Russ. J. Gen. Chem.* 2008, *78*, 480–484.