SALTS OF 2,5-DIMERCAPTO-1,3,4-THIADIAZOLE

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Reaction of 2,5-dimercapto-1,3,4-thiadiazole with ammonia or pyridine gives monoammonium or monopyridinium salts, and the reaction with hydrazine hydrate gives both mono- and dihydrazine salts, which was confirmed by alkylation of the salts obtained. Difference in the chemical shifts of the SCH₂R groups was found in the ¹H NMR spectra of the mono- and dialkyl-substituted 2,5-dimercapto-1,3,4-thiadiazoles.

Keywords: monoammonium, monopyridinium, monohydrazine, and dihydrazine salts of 2,5-dimercapto-1,3,4-thiadiazole, mono- and dialkylation of salts of 2,5-dimercapto-1,3,4-thiadiazole.

The formation of monohydrazine salt of 2,5-dimercapto-1,3,4-thiadiazole is possible in the synthesis of 2,5-dimercapto-1,3,4-thiadiazole from carbon disulfide and hydrazine sulfate [1]. Monopyridinium salt of 2,5-dimercapto-1,3,4-thiadiazole is formed in the synthesis of 2,5-dimercapto-1,3,4-thiadiazole from carbon disulfide and hydrazine hydrate in pyridine [2]. Salts are also formed by 2-mercaptobenzothiazole [3] and 5-mercapto-2-methylthio-1,3,4-thiadiazole [4] with secondary amines. It was established [5] that the reaction of 2-mercaptobenzothiazole with hydrazine hydrate leads to hydrazine salt, which forms hydrazide at 80-100°C with the cleavage of hydrogen sulfide. The aim of the given work was to study reactions of 2,5-dimercapto-1,3,4-thiadiazole 1 with hydrazine hydrate, ammonia, and pyridine.

Q-HS S SH-Q
$$2Q$$
 HS S SH Q Sh Q Sh Q Sh Q S

The reaction of compound 1 with excess of hydrazine hydrate at room temperature leads to compound 2a, which melts with decomposition at 117°C. Similar reaction in boiling ethanol leads to compound 2b, which melts with decomposition at 168°C. The boiling of an ethanolic solution of compound 2a results in the release of gas and the formation of compound 2b. If it is assumed that compound 2a is hydrazine salt and 2b is hydrazide, then the last should form hydrazones by reaction with aldehydes. However, the reaction of compound 2b with 2-hydroxybenzaldehyde leads to a compound which corresponds in its physical parameters and ¹H NMR spectrum to the physical parameters and spectrum of 2,2'-dihydroxybenzalazine, obtained by the reaction of 2-hydroxybenzaldehyde with hydrazine hydrate [6]. On the basis of these data, the proposal is made that compound 2a is dihydrazine salt of 2,5-dimercapto-1,3,4-thiadiazole, and 2b is monohydrazine salt. Compound 1 formed salt 2c in the reaction with ammonia. Salt 2d was obtained by analogy [2].

The UV spectra of compounds **2a-d** show a strong absorption band at 336 nm, which is probably associated with electronic transitions of the thiadiazole ring.

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In order to show that salts **2b-d** are monobasic and **2a** is dibasic, their alkylation was performed using benzyl chloride, methyl bromoacetate, and 3-phenyl-2-propynyl chloride in ethanol at room temperature with the 1:1 and 1:2 molar ratios of the reagents.



3. 4 X = Cl, Br, a R = $CH_2C_6H_5$, b R = CH_2COOCH_3 , c R = $CH_2C\equiv CC_6H_5$

The reaction of compound 1 with the same alkyl halides in the presence of 1 or 2 equivalents of sodium hydroxide was chosen for comparison of the results obtained.

The chemical shift of protons of the methylene group in the compound obtained from thiadiazole 1, benzyl chloride, and sodium hydroxide in the 1:1:1 ratio comprised 4.31 ppm, whereas the chemical shift for the compound obtained from the same reagents in the 1:2:2 ratio was 4.41 ppm. Difference in the chemical shifts of the methylene groups was also noted for compounds synthesized from other halides. Such a difference can be explained by two reasons: the occurrence of alkylation at the S atom in one case and at the N atom in the other case, or by the difference in the chemical shifts of the methylene groups of the S-mono- and S,S'-dialkylated 2,5-dimercapto-1,3,4-thiadiazoles. In order to find out which of the reasons has preference, the alkylation of compound **3a** was performed with methyl bromoacetate in the presence of 1 equivalent of sodium hydroxide, which resulted in the isolation of compound **4d**.



Its ¹H NMR spectrum shows two signals of methylene groups, one of which has a chemical shift corresponding to the shift of the methylene groups of compound 4b (4.06 ppm), and the other corresponds to the chemical shift of the methylene groups of compound 4a (4.41 ppm). The signal with the chemical shift of the methylene group in compound 3a is absent.

According to published data [7], the unsubstituted S atom in S-monosubstituted 2,5-dimercapto-1,3,4-thiadiazole occurs in the thione form. Therefore, it can be concluded that, in our case, the signal of the methylene group in the ¹H NMR spectra of S-monosubstituted 2,5-dimercapto-1,3,4-thiadiazole is shifted to higher field ($\Delta\delta \sim 0.1-0.12$ ppm) due to the influence of the sulfur atom in the thione form in comparison with the signal of the methylene groups in S,S'-disubstituted 2,5-dimercapto-1,3,4-thiadiazole. The compounds **3a-c** are thereby S-monosubstituted, and **4a-c** are S,S'-disubstituted derivatives of 2,5-dimercapto-1,3,4-thiadiazole.

The UV spectra showed a difference between the heterocyclic rings of compounds 3 and 4, since the characteristic absorption bands of the thiadiazoline ring in compounds 3a-c occurred at 322-324 nm, and those of the thiadiazole ring in compounds 4a-d occurred at 287-294 nm.

Table 1 presents the percentage composition of mixtures of the products **3a-c** and **4a-c** obtained from salts **2a-d**, as well as compound **1** in the presence of sodium hydroxide and alkyl halides with different reagent ratios, calculated from integral intensities of signals of methylene groups in the ¹H NMR spectra. It can be seen from Table 1 that salts **2b-d** react with benzyl chloride by analogy with compound **1** in the presence of 1 equivalent of sodium hydroxide, and salt **2a** reacts similarly in the presence of 2 equivalents of sodium hydroxide. It can be concluded from this that salts **2b-d** were formed from 1 equivalent of the base, and salt **2a** was formed from 2 equivalents of the base. The application of salt **2b** in the synthesis of monosubstituted derivatives of 2,5-dimercapto-1,3,4-thiadiazoles, and the application of compound **1** in the presence of 2 equivalents of sodium hydroxide in the synthesis of the disubstituted derivatives of 2,5-dimercapto-1,3,4-thiadiazoles, give favorable conditions for the isolation of pure products.

The reaction of compound 1 with methyl bromoacetate using the 1:2 ratio in the presence of 1 equivalent of sodium hydroxide probably led to the formation of the mixture of the compounds 3b and 4b and their hydrolysis products, since the integral intensity of the OCH₃ signal is clearly lowered in comparison with the integral intensity of the signals of the methylene groups.

The boiling of compound **3a** with hydrazine hydrate in methanol led to the formation of salt **2e**, which underwent alkylation by methyl bromoacetate to give compound **4d**.

EXPERIMENTAL

¹H NMR spectra were obtained on Hitachi R-22 spectrometer (90 MHz), internal standard HMDS. UV spectra were recorded on Perkin-Elmer Lambda 20 UV/vis spectrometer in ethanol. Quantitative determinations were performed on the basis of the ¹H NMR spectra with the fivefold integration of signals of the methylene groups. The characteristics and data of the UV spectra of the compounds **2a-e**, **3a-c**, and **4a-d** are presented in Table 2, and those of the ¹H NMR spectra are presented in Table 3.

3-Phenyl-2-propynyl chloride was synthesized by the method [8].

Initial compound	Sumth winted again and	Composition of mixture, "a			
	- Synnesized compound	1:1*	1:2*		
I + NaOH	3a, 4a	99:1	86 : 14		
(1:1)	3b, 4b	80 : 20			
	3c, 4c	75:25	40 : 60		
1 + NaOH (1 : 2)	3a, 4a	33:67	0 : 100		
	3b, 4b	15:85	0:100		
	3c. 4c	20:80	0 : 100		
2a	3a, 4a	35:65	1:99		
2b	3a. 4a	100:0	88:12		
	3b. 4b	100:0	72 : 28		
	3c, 4c	100:0	75 : 25		
2c	3a, 4a	99:1	90:10		
	3b, 4b	90:10	45 : 55		
2d	3a, 4a	97:3	87:13		
	3b, 4b	91:9	45 : 55		

TABLE 1. Percentage Composition of Mixtures of Compounds **3a-c** and **4a-c** Synthesized Depending on the Ratio of Compounds **1**, **2a-d** and Alkyl Halides

* Molar ratio of the compounds 1, 2 and alkyl halides.

~		Found, %				UV	Yield	
Com- Empirical pound formula	Calculated, "u				mp. °C	spectrum,	00	
	C	н	N	S		A_{max} , nm (log ε)	(method)	
2a	$C_2H_{10}N_6S_3$	<u>11.42</u> 11.20	$\frac{4.45}{4.70}$	<u>38.87</u> 39.21	<u>45.26</u> 44.88	117 (dec.)	336 (4.11)	78
2b	C2H6N4S3	<u>13.42</u> 13.17	<u>3.18</u> 3.31	<u>31.01</u> 30.74	<u>52.39</u> 52.77	168 (dec.) (185 [1])	336 (4.12)	68 (A) 77 (B)
2c	$C_2H_4N_3S_3$	$\frac{14.50}{14.36}$	<u>3.14</u> 3.01	<u>24.88</u> 25.12	<u>57.52</u> 57.50	205	336 (4.07)	80
2d	C-H-N ₃ S ₃	<u>36.89</u> 36.66	$\frac{3.26}{3.08}$	$\frac{18.45}{18.32}$	$\frac{41.60}{41.94}$	75 (176-177 [2])	336 (4.12)	73
2e	$C_{10}H_{12}N_4S_3$	<u>42.15</u> 42.23	$\frac{4.41}{4.25}$	<u>19.52</u> 19.70	<u>33.92</u> 33.82	83	324 (4.22)	50
3a	C ₂ H ₈ N ₂ S ₃	<u>45.18</u> 44.97	<u>3.48</u> 3.35	$\frac{11.40}{11.65}$	<u>39.94</u> 40.02	128 (129 [9])	324 (4.15)	83
3b	C«H ₆ N ₂ O ₂ S ₃	$\frac{26.80}{27.01}$	$\frac{2.88}{2.72}$	$\frac{12.42}{12.60}$	$\frac{43.51}{43.27}$	100	322 (4.07)	72
3c	$C_{11}H_8N_2S_3$	<u>50.11</u> 49,97	$\frac{3.22}{3.05}$	$\frac{10.39}{10.60}$	$\frac{36.28}{36.38}$	125	244 (4.30) 324 (4.00)	77
4a	$C_{16}H_{14}N_2S_3$	<u>58.15</u> 47.96	$\frac{4.28}{4.43}$	<u>8.48</u> 8.25	<u>29.10</u> 29.36	87-88 (89[1])	294 (4.01)	85
4b	$C_xH_{10}N_2O_4S_3$	<u>32,41</u> 32.64	<u>3.61</u> 3.42	<u>9.33</u> 9.52	<u>32.85</u> 32.67	72-73 (72-73 [10])	287 (3.98)	61
4c	$C_{20}H_{14}N_2S_3$	<u>63.25</u> 63.46	<u>3.90</u> 3.73	7.18 7.40	<u>25.67</u> 25.41	91	245 (4.55) 294 (3.99)	58
4d	$C_{12}H_{12}N_2O_2S_3$	$\frac{45.86}{46.13}$	$\frac{4.02}{3.87}$	<u>8.75</u> 8.97	<u>31.03</u> 30.79	-	291 (4.01)	65 (A) 90 (B)

TABLE 2. Characteristics of the Compounds 2a-c, 3a-c, and 4a-d

TABLE 3. ¹H NMR Spectra of the Compounds **3a-c** and **4a-d** (Solvent $(CD_3)_2CO$)

Compound	Chemical shifts, ppm				
3a	4.31 (2H, s, CH ₂); 7.20 (5H, m, C (Hs)				
3b	3.60 (3H, s, CH ₃); 3.94 (2H, s, CH ₂)				
3c	4.00 (2H, s, CH ₂); 7.20 (5H, s, C ₆ H ₅)				
4a	4.41 (4H, s, CH ₂); 7.20 (10H, m, C ₅ H ₅)				
4b	3.60 (6H, s, CH ₃); 4.06 (4H, s, CH ₂)				
4c	4.12 (4H, s, CH ₂); 7.20 (10H, s, C ₆ H ₄)				
4d	3.60 (3H, s, CH ₁); 4.06 (2H, s, <u>CH</u> 2COOCH ₁); 4.41 (2H, s, <u>CH</u> 2C ₆ H ₂); 7.20 (5H, m, C ₆ H ₃)				

Dihydrazinium 1,3,4-Thiadiazole-2,5-dithiolate (2a). Hydrazine hydrate (5.0 g, 0.1 mol) in ethanol (20 ml) is added dropwise to a solution of compound 1 (4.5 g, 0.03 mol) in ethanol (50 ml) and DMF (5 ml), and the mixture is stirred for 2 h at room temperature. The crystals are filtered off and washed with ethanol.

Hydrazinium 5-Mercapto-1,3,4-thiadiazole-2-thiolate (2b). A. Hydrazine hydrate (30 g, 0.6 mol) is added dropwise to a solution of compound 1 (30 g, 0.2 mol) in ethanol (100 ml), and the reaction mixture is boiled for 2 h (until the release of gas ceased). The mixture is cooled, and the crystals are filtered off and washed with ethanol.

B. A solution of compound 2a (1.0 g, 5 mmol) in ethanol (20 ml) is boiled for 2 h. The solution is cooled, and the crystals are filtered off and washed with ethanol.

Ammonium 5-Mercapto-1,3,4-thiadiazole-2-thiolate (2c). Compound 1 (4.5 g, 0.03 mol) is dissolved in 25% solution of ammonia (20 ml). The solution is filtered, and water is distilled off *in vacuo* to dryness. The residue is washed with ethanol.

Pyridinium 5-Mercapto-1,3,4-thiadiazole-2-thiolate (2d). Compound 1 (4.5 g, 0.03 mol) is dissolved in solution of pyridine (4.7 g, 0.06 mol) in ethanol (50 ml) with heating. The mixture is cooled, and the crystals are filtered off and washed with ethanol.

2,2'-Dihydroxybenzalazine. 2-Hydroxybenzaldehyde (1.2 g, 10 mmol) is added to a solution of salt **2b** (0.9 g, 5 mmol) in dioxane (50 ml) and water (5 ml), and the mixture is heated for 2 h at 85°C. A portion of the solvent is distilled off, and the crystals are filtered off and recrystallized from ethanol. Yield of azine 1.0 g (83%); mp 214°C (according to [6], mp 214°C). ¹H NMR spectrum (DMSO-d₆): 8.84 (s, CH, 2H); 11.00 ppm (s, OH, 2H). Found, %: C 69.68; H 5.20; N 11.49. $C_{14}H_{12}N_2O_2$. Calculated, %: C 69.99; H 5.03; N 11.66.

5-Benzylthio-2,3-dihydro-1,3,4-thiadiazole-2-thione (3a). Salt **2b** (0.9 g, 5 mmol) is dissolved in ethanol (50 ml), benzyl chloride (0.6 g, 5 mmol) is added, and the mixture is left at room temperature for 24 h. The solvent is distilled off, and the crystals are washed with water and recrystallized from ethanol.

Methyl 2-(2-Thioxo-2,3-dihydro-1,3,4-thiadiazol-5-ylthio)acetate (3b) is obtained from salt 2b (0.9 g, 5 mmol) and methyl bromoacetate (0.77 g, 5 mmol) by the method described for compound 3a.

5-(3-Phenyl-2-propynylthio)-2,3-dihydro-1,3,4-thiadiazole-2-thione (3c) is obtained from salt **2b** (0.9 g, 5 mmol) and 3-phenyl-2-propynyl chloride (0.75 g, 5 mmol) by the method described for compound **3a**.

2,5-Di(benzylthio)-1,3,4-thiadiazole (4a). Compound **1** (0.75 g, 5 mmol) and sodium hydroxide (0.4 g, 10 mmol) are dissolved in ethanol (50 ml), benzyl chloride (1.2 g, 10 mmol) is added, and the mixture is left for 24 h at room temperature. The solvent is distilled off, and the residue is washed with water and recrystallized from ethanol.

Methyl 2-(5-Methoxycarbonylmethylthio-1,3,4-thiadiazol-2-ylthio)acetate (4b) is obtained from compound 1 (0.75 g, 5 mmol), sodium hydroxide (0.4 g, 10 mmol), and methyl bromoacetate (1.53 g, 10 mmol) by the method described for compound 4a.

2,5-Di(3-phenyl-2-propynylthio)-1,3,4-thiadiazole (4c) is obtained from compound **1** (0.75 g, 5 mmol), sodium hydroxide (0.4 g, 10 mmol), and 3-phenyl-2-propynyl chloride (1.5 g, 10 mmol) by the method described for compound **4a**.

Hydrazinium 5-Benzylthio-1,3,4-thiadiazole-2-thiolate (2e). Compound **3a** (1.2 g, 5 mmol) is dissolved in methanol (20 ml), hydrazine hydrate (0.5 g, 10 mmol) is added, and the mixture is boiled for 1 h. The solvent is distilled off, and the residue is recrystallized from acetonitrile.

Methyl 2-(5-Benzylthio-1,3,4-thiadiazol-2-ylthio)acetate (4d). A. Compound 3a (0.24 g, 1 mmol) and sodium hydroxide (0.04 g, 1 mmol) are dissolved in ethanol (20 ml), methyl bromoacetate (0.15 g, 1 mmol) is added, and the mixture is left for 24 h at room temperature. The solvent is distilled off, and the residue is dissolved in carbon tetrachloride. After filtration, the solvent is distilled off and the oily compound 4d is obtained.

B. Salt **2e** (0.28 g, 1 mmol) is dissolved in ethanol (20 ml), methyl bromoacetate (0.15 g, 1 mmol) is added, and the mixture is left for 24 h at room temperature. Compound **4d** is isolated by analogy with the method A.

General Method for Isolation of the Mixtures of the Compounds 3a-c and 4a-c. The corresponding salt 2a-d or compound 1 (5 mmol) and sodium hydroxide (5 or 10 mmol) are dissolved in ethanol (50 ml), the corresponding halide (5 or 10 mmol) is added, and the mixture is left for 24 h at room temperature. The solvent is distilled off, and the residue is washed with water. ¹H NMR spectrum is then taken.

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