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Original Scientific Paper

## Contribution to the Structure of 2,5-Dimercapto-1,3,4-thiadiazole and Related Compounds<sup>\*, \*\*</sup>

B. Stanovnik and M. Tišler

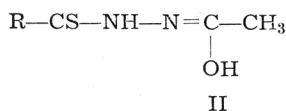
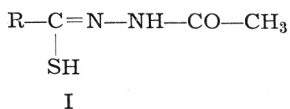
Department of Chemistry, University of Ljubljana, Ljubljana, Slovenia,  
Yugoslavia

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The structure of 2,5-dimercapto-1,3,4-thiadiazole and some derivatives was studied from the dependence of UV spectra on pH and  $H_0$  and a monomercapto monodipolar structure is proposed. Evidence was presented that addition reactions of 2,5-dimercapto-1,3,4-thiadiazoles on unsaturated systems proceed with the formation of *S*-alkylated derivatives involving thus the mercapto group.

Among the features of sulfur compounds is undoubtedly the complexity of the electronic structure of the chemical bond, especially where bonds can be formed either by non-charged structures or where participation of an adjacent group or atom to form charged structures due to a shift of electrons is possible. This is also true for thioamides where the dipolar character is predominant (see ref.<sup>1,2</sup> and references quoted therein).

In the preceding papers of this series<sup>2-6</sup> the structure of different cyclic thioamides was investigated. The main feature of these investigations was that such compounds exist predominantly in the dipolar form. As an extension of this work we have recently investigated different pyridazines<sup>1</sup> having the system —CS—NH—NH—CS— or its iminothiol forms incorporated in the molecule. The obtained results were interpreted in terms of a structure with a monomercapto group present and while the other is non-enolized with an important contribution of the dipolar character. A similar, but non-cyclic system was investigated recently by Sandström<sup>7</sup> when examining the structure of acetyl thiohydrazides. He found no indication for the existence of the possible tautomeric forms I or II.

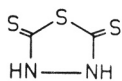


Considerable controversy has surrounded the assignment of the structure to 2,5-dimercapto-1,3,4-thiadiazole and related compounds. Theoretically,

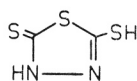
\* Presented in part at the XIth Colloquium Spectroscopicum Internationale, Beograd, 1963.

\*\* Here and elsewhere terms »mercapto« and »dimercapto« are used for the sake of simplicity.

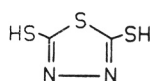
this compound could exist in three alternative tautomeric forms as III, IV or V.



III

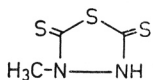


IV

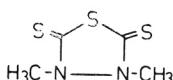


V

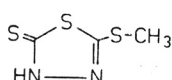
There exist different approaches to the determination of this structure and consequently some authors prefer either the bis-thioamide form III<sup>8</sup> or the monomercapto thioamide form IV<sup>9</sup>. Recently Thorn tried to resolve this problem on the basis of spectroscopic evidence. The correlation of UV spectra of the parent compound with those of different on ring nitrogen or *exo*-cyclic sulfur substituted derivatives led Thorn to postulate that the parent compound as well as VI and VII exist in the dithione form as present in III and that the possibility of enethiolization does not exist.



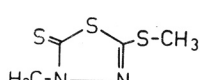
VI



VII



VIII



IX

In compounds where one thioamide group is fixed in the iminothiol form the second thioamide group was considered as non-enolized (c.f. VIII and IX). However, further examination of IR spectra led Thorn to conclude that the structure assignments are not as conclusive as given above. He supplemented his statement so far that the parent compound and VI exist in concentrated solutions in chloroform primarily in their monomercapto form, but in alcoholic solution the bis-thioamide structure should be predominant.

Accordingly we undertook the study of this system, particularly to investigate the dependence of the UV spectra on pH and  $H_0$ . The acidity function  $H_0$ <sup>11</sup> has found wide application in the determination of basicity of very weak acids.

In the present investigation we have used a similar technique as in previous communications. The spectrophotometrically determined  $pK$  values are collected in Table I and changes in UV spectra in dependence on pH and  $H_0$  are presented in Table II and Figs. 1—3.

TABLE I

Compound	$pK_{II^+}$	$pK_1$	$pK_2$
2,5-Dimercapto-1,3,4-thiadiazole	—5.40	—1.36	7.53
2-Mercapto-4-phenyl-1,3,4-thiadiazoline-5-thione	—6.50	—1.59	
2-Mercapto-4-methyl-1,3,4-thiadiazoline-5-thione	—5.30	—1.40	

A comparison of the  $pK$  values of the parent compound with those of both on the ring nitrogen substituted derivatives clearly demonstrates that

TABLE II  
Changes in UV spectra in dependence on pH and  $H_0$

$H_0$	pH	2,5-Dimercapto-1,3,4-thia- diazole		2-Mercapto-4-phenyl-1,3,4- thiadiazoline-5-thione	
		$\lambda_{\max}$	$\epsilon$	$\lambda_{\max}$	$\epsilon$
-8.98	}	2940	9.100	2250, 2970	7.700 7.750
-8.27				~2750	7.400
-6.97				2350 3000	8.900 7.300
				~2670	6.100
-5.65		2960	8.400	~2350 3120	10.000 7.800
-4.89		3100	10.900	~2350 3180	11.500 8.300
-3.87		3140	13.000	3200	8.800
-2.76		3150	13.300	3220	9.400
-1.85		2550 3160	4.200 12.500	3230	9.100
-0.84		~2500 3270	4.400 12.100	3310	8.800
	1	~2500 3270	4.500 11.950	~2550 3330	11.300 10.700
	2	~2500 3270	4.550 11.550		
	3	~2500 3270	4.800 11.100		
	4-5	~2500 3270	5.100 11.000	}	12.200 10.200
	6	~2500 3230	5.100 11.200		
	7	~2500 3230	4.960 11.120		
	8	3150	11.280		
	9-12	3120	11.350		

~ = inflexion

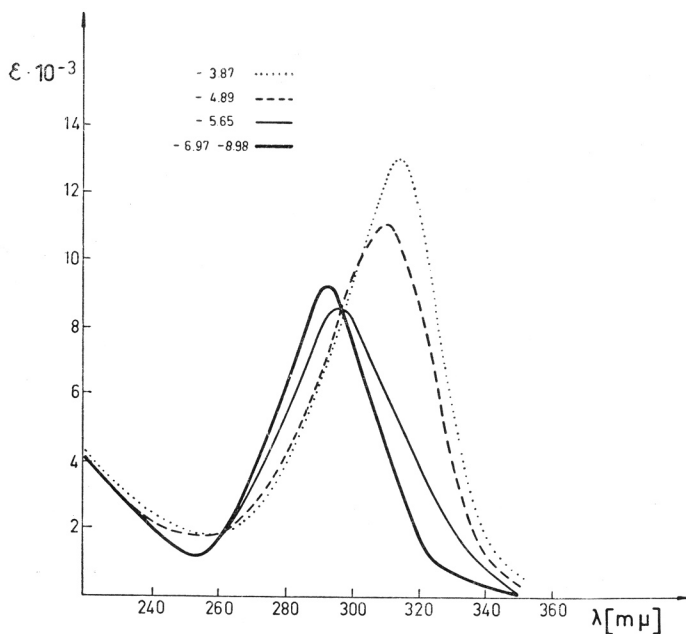


Fig. 1: UV spectrum of 2,5-dimercapto-1,3,4-thiadiazole at  $H_0$  -8.98 to -3.87.

the  $pK_1$  value corresponds to the dissociation of the mercapto group whereas the  $pK_2$  value of the parent compound is in the range characteristic for the

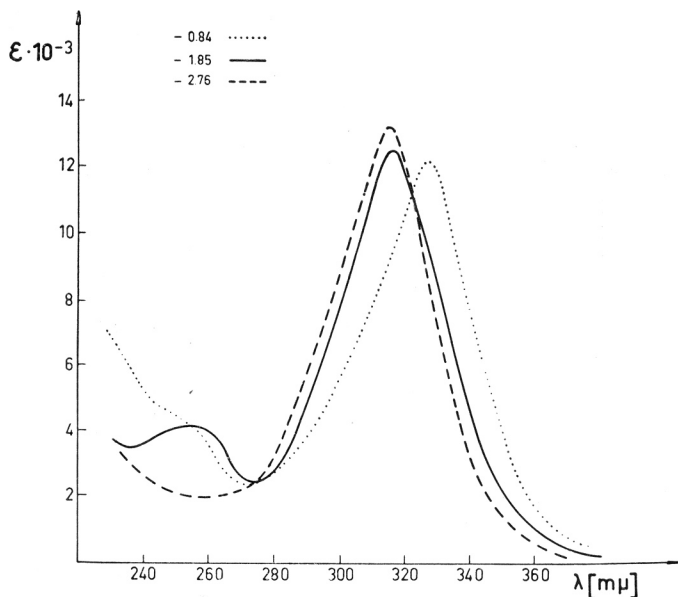


Fig. 2: UV spectrum of 2,5-dimercapto-1,3,4-thiadiazole at  $H_0$  -2.76 to -0.84.

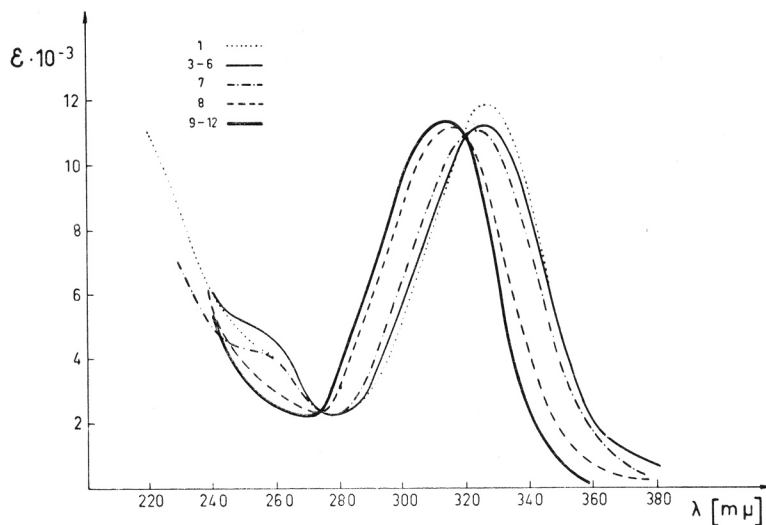
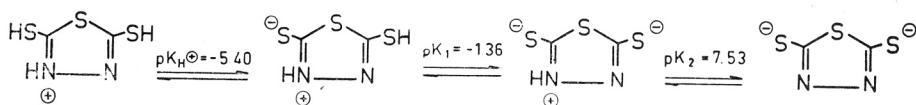


Fig. 3: UV spectrum of 2,5-dimercapto-1,3,4-thiadiazole at pH 1 to 12.

dissociation of simple thioamides. There can be little doubt about the site of proton loss or gain in these compounds and the assignment of the  $pK_{H^+}$  values which corresponds to the protonation of the second sulfur of the dipolar thioamide group. This evidence arises from the comparison of  $pK_{H^+}$  values of derivatives where half of the molecule is fixed in the iminothiol form (cf.

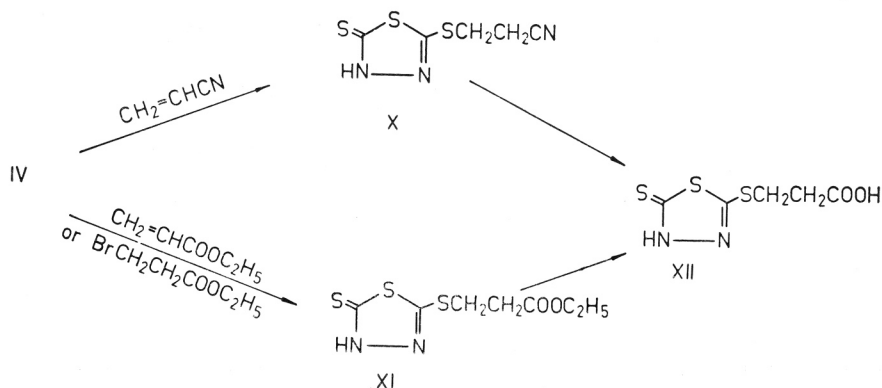
2-mercapto-5-methylmercapto-1,3,4-thiadiazole,  $pK_{H^+} = 4.85$ ; 2-methylmercapto-4-phenyl-1,3,4-thiadiazoline-5-thione,  $pK_{H^+} = -5.44$ ). The presence of one true mercapto group in compounds such as the parent compound and all derivatives monosubstituted only on the ring nitrogen cannot be disputed as all these compounds exhibit in the infrared spectrum bands characteristic for the presence of SH groups. Furthermore, the parent compound is susceptible to changes of the solvent polarity whereas other simple thioamides are not. Accordingly, the various protonated and deprotonated species are shown in following equations.



The monomercapto monodipolar form of 2,5-dimercapto-1,3,4-thiadiazole seems to be most adequate also in view of the fact that the planar ring system permits a greater resonance stabilization.

If one accepts the above evidence for the structure, the addition reactions which are characteristic for mercaptans should proceed similarly in the case of compounds under investigation. We have performed addition reactions with acrylonitrile and ethyl acrylate. As already pointed out, such additions to compounds containing thioamide groups are liable to proceed on nitrogen, but with 3-mercapto-6(1H)-pyridazinethione it was shown to proceed on the sulfur<sup>1</sup>.

Thus, acrylonitrile reacted with 2,5-dimercapto-1,3,4-thiadiazole to form a monocyanoethyl derivative X and a similar reaction course was observed with ethyl acrylate XI. Both products were hydrolyzed to the corresponding acids which were found to be identical XII. The IR spectra of all these compounds exhibited no absorption bands characteristic for the presence of an SH group and the site of addition was ascertained through the reaction with ethyl  $\beta$ -bromopropionate. In this case there is no doubt that the reaction proceeds on the *exo*-cyclic sulfur<sup>12</sup> and the product was identical with that from the reaction with ethyl acrylate.



An analogous reaction takes place with 2-mercapto-4-phenyl-1,3,4-thiadiazoline-5-thione. Contrarily to the observations with similar compounds in the

pyridazine series the cyanoethyl or carbethoxy-ethyl groups are here not eliminated during hydrolysis which may be attributed to the influence of the *endo*-cyclic sulfur.

#### EXPERIMENTAL

Melting points were determined on a Kofler heating microscope, UV spectra in ethanol were measured with a Beckman model DU spectrophotometer and were recorded as described previously<sup>1,2</sup>. The spectrophotometrically determined pK values were calculated in the usual manner<sup>13,14</sup>. For the determination of pK<sub>H</sub><sup>+</sup> values the following concentrations of sulfuric acid were used: 1,2,4,6,8 and 10 moles/liter and 70, 80, and 96% sulfuric acid corresponding to the H<sub>0</sub> values<sup>15</sup> presented in Table II.

*2,5-Dimercapto-1,3,4-thiadiazole* was prepared according to the procedure of Lo-sanitch<sup>16</sup>, a modification of the Busch synthesis<sup>17</sup>. UV spectrum:  $\lambda_{\max}$ , 3360 Å,  $\epsilon$  13,500; infl. at 2600 Å,  $\epsilon$  5,400; in CHCl<sub>3</sub>:  $\lambda_{\max}$ , 3230 Å,  $\epsilon$  12,700. From the IR spectrum the presence of a SH group (2490 cm<sup>-1</sup>) and NH group (3075 cm<sup>-1</sup>) is evident.

*2-Mercapto-4-methyl-1,3,4-thiadiazoline-5-thione* and *2-mercapto-4-phenyl-1,3,4-thiadiazoline-5-thione* were prepared by an analogous procedure as the parent compound starting with the corresponding substituted hydrazines<sup>16,17</sup>. Both compounds exhibit in their IR spectra the presence of SH groups (2247 and 2300 cm<sup>-1</sup> respectively) and no NH groups.

*2-Mercapto-5-methylmercapto-1,3,4-thiadiazole* was prepared following the procedure of Thorn and Ludwig<sup>18</sup> and *2-methylmercapto-4-phenyl-1,3,4-thiadiazoline-5-thione* was synthesized according to Bush<sup>17</sup>. UV spectrum:  $\lambda_{\max}$ , 3250 Å,  $\epsilon$  12,400.

#### *2-(2'-Cyanoethylmercapto)-5-mercapto-1,3,4-thiadiazole (X)*

To a solution of 2,5-dimercapto-1,3,4-thiadiazole (1.52 g.) in 10 ml. of dioxane acrylonitrile (0.53 g.) and few drops of triethylamine were added. The mixture was heated on water bath at 70° for 15 min., cooled to room temperature and poured in cold water. The separated yellow crystals were crystallized from ethanol. Yield: 52% m.p. 140°. The iodine-azide reaction<sup>19</sup> was positive. UV spectrum:  $\lambda_{\max}$ , 2430 and 2860 Å,  $\epsilon$  3.240 and 12.150.

*Anal.* C<sub>5</sub>H<sub>5</sub>N<sub>3</sub>S<sub>3</sub> (203.11) calc'd: C 29.57; H 2.48; N 20.69; S 47.27%  
found: C 29.23; H 2.65; N 20.78; S 47.43%

#### *2-(2'-Carbethoxyethylmercapto)-5-mercapto-1,3,4-thiadiazole (XI)*

a) A mixture of 2,5-dimercapto-1,3,4-thiadiazole (1.52 g.), 10 ml. of dioxane, 1.0 g. of ethyl acrylate and few drops of triethylamine was heated on a water bath at 70° for 15 min. The cooled reaction mixture was poured in water and the separated crystals were recrystallized from chloroform and petroleum ether. Yield: 34%. M.p. of colorless crystals 63°. UV spectrum:  $\lambda_{\max}$ , 3200 Å,  $\epsilon$  12,300.

*Anal.* C<sub>7</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S<sub>3</sub> (250.37) calc'd: C 33.60; H 4.02; N 11.20%  
found: C 33.63; H 4.39; N 11.34%

b) 2,5-Dimercapto-1,3,4-thiadiazole (1.52 g.) was dissolved in an ethanolic solution of sodium ethoxide (prepared from 0.23 g. sodium in 15 ml. of absolute ethanol), ethyl  $\beta$ -bromopropionate added and the mixture heated to reflux on a water bath for 10 min. The reaction mixture was treated as above and the purified product was identical with the compound obtained by procedure (a).

#### *2-(2'-Carboxyethylmercapto)-5-mercapto-1,3,4-thiadiazole (XII)*

The compound XI (0.41 g.) was hydrolyzed with 10% aqueous hydrochloric (or sulfuric) acid with heating on a water bath for 3 hrs. Upon cooling the deposited crystals were crystallized from ethanol. Yield: 44%, m.p. 118°.

*Anal.* C<sub>5</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>S<sub>3</sub> (222.11) calc'd: C 27.04; H 2.72; N 12.61; S 43.22%  
found: C 26.82; H 2.95; N 12.31; S 43.41%

## 2-(2'-Cyanoethylmercapto)-4-phenyl-1,3,4-thiadiazoline-5-thione

2-Mercapto-4-phenyl-1,3,4-thiadiazoline-5-thione (2.26 g.) was suspended in 10 ml. of acrylonitrile and the mixture was gently refluxed on a water bath for 45 min. Thereafter it was filtered hot and upon cooling the separated crystals were crystallized from acrylonitrile. M.p. 100°, yield: 2.1 g. UV spectrum:  $\lambda_{\max}$ . 3320Å,  $\epsilon$  11,920; (in dioxane):  $\lambda_{\max}$ . 3330 Å,  $\epsilon$  11,280.

Anal.  $C_{11}H_9N_3S_3$  (279.41) calc'd: C 47.32; H 3.25; N 15.05%  
found: C 47.21; H 3.52; N 14.90%

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## IZVLEČEK

## Prispevek k strukturi 2,5-dimerkapto-1,3,4-tiadiazola in sorodnih spojin

B. Stanovnik in M. Tišler

Obravnavana je struktura 2,5-dimerkapto-1,3,4-tiadiazola in nekaterih derivatov na podlagi študija odvisnosti ultravijoličnih spektrov od pH in  $H_0$ , ter je predlagana struktura kot monomerkapto monodipolarna. Ugotovljeno je, da potekajo reakcije adicije pri 2,5-dimerkapto-1,3,4-tiadiazolih na nekatere nenasičene spojine s tvorbo S-alkiliranih spojin pri čemer reagira merkapto skupina.

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LJUBLJANA

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