
New heterocycles on the basis of 2,5-dimercapto-1,3,4-thiadiazole

3. 3,4-N,N-disubstituted derivatives of 1,3,4-thiadiazole

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The 3,4-N,N-aminomethylated derivatives of 1,3,4-thiadiazole have been obtained as a result of interaction between 2,5-dimercapto-1,3,4-thiadiazole and benzotriazole, 2-mercaptobenzothiazole, 2-mercaptobenzoxazole, phthalimide, benzoic sulphimide and N-aminorhodanine under the Mannich reaction conditions. The 3,4-di(methylenoxo)-substituted derivatives of 1,3,4-thiadiazole are thermally resistant.

Key words: 2,5-dimercapto-1,3,4-thiadiazole, synthesis, Mannich reaction, 3,4-N,N-disubstituted derivatives of 1,3,4-thiadiazole

INTRODUCTION

When continuing our investigations in the field of the synthesis of new heterocycles on the basis of 2,5-dimercapto-1,3,4-thiadiazole [1–4] with the aim to investigate them as brighteners-levellers in electrolytes of copper plating and to study their anticancer activity, in the present work we have synthesized 3,4-N,N-disubstituted derivatives of 1,3,4-thiadiazole to investigate them as inhibitors of steel corrosion and to study their antimicrobial properties.

METHODS, RESULTS AND DISCUSSION

Two methods were used to synthesize 3,4-di(chloromethylene)-1,3,4-thiadiazole-2,5-dithion (III): starting from 3,4-di(hydroxymethylene)-1,3,4-thiadiazole-2,5-dithion (II) and sulfinyl chloride with the yield of 86%, as well as during interaction of 2,5-dimercapto-1,3,4-thiadiazole (I) with formaldehyde and conc. hydrochloric acid with the yield of 65%. Derivative III interacts with butyl or benzyl alcohols when heated for 5 h at a temperature of 80 °C and forms corresponding 3,4-di(methylenoxo)-substituted derivatives of 1,3,4-thiadiazole IV, V. The yield amounted to 67–78%.

Derivatives IV, V are thermally resistant, *i.e.* capable of retaining a constant chemical constitution at a temperature rise. This determines the strength of chemical bonds in them. The maximum temperature at which a substance does not change chemically characterizes quantitatively its thermal resistan-

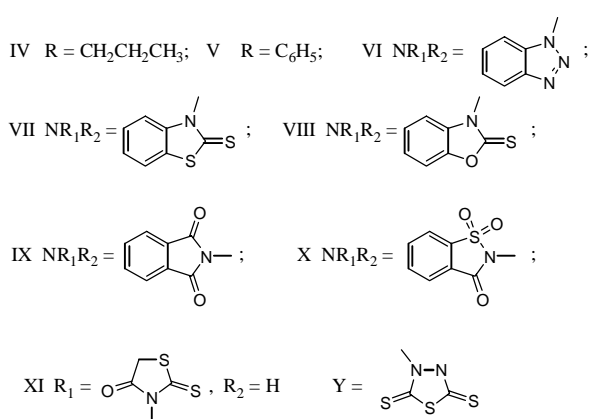
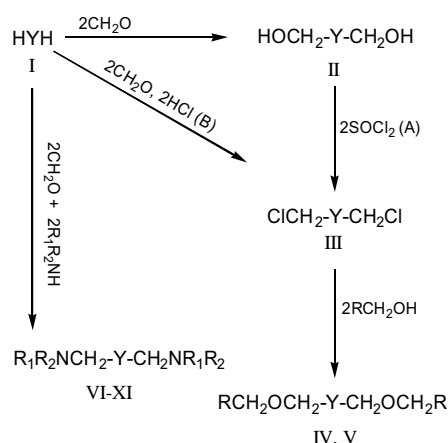
ce. In our case, compounds IV, V are melted with decomposition just at a temperature of 235 °C and 258 °C, respectively.

In work [4] we have investigated the Mannich reaction of 2,5-dimercapto-1,3,4-thiadiazole with diethylamine, morpholine, piperidine, carbamide, thiocarbamide, semicarbazide and thiosemicarbazide. Interesting data have been obtained there, because N,S-aminomethylated thiadiazoles have been developed in the first three cases and N,N-aminomethylated thiadiazoles have been formed in the latter four cases. This was determined with the help of IR and ¹H NMR spectra.

Therefore, it was of interest to carry out the Mannich reaction in 2,5-dimercapto-1,3,4-thiadiazole and with other aromatic and heterocyclic compounds which had a labile hydrogen atom, and to clear up the structure of the Mannich bases developed. For this purpose, benzotriazole, 2-mercaptobenzothiazole, 2-mercaptobenzoxazole, phthalimide, benzoic sulphimide and N-aminorhodanine have been chosen. It has been found with the aid of IR spectra that 3,4-N,N-aminomethylated derivatives of 1,3,4-thiadiazole VI–XI have been obtained in absolutely all cases with a yield of 40–91% (Scheme).

Strong absorption lines have been detected in IR spectra of compounds II–XI within the range of 1210–1200 cm⁻¹, which correspond to valency oscillation (ν) of C=S groups, and strong absorption lines within the range of 1490–1470 cm⁻¹ which correspond to ν groups -N-C=S [5].

Scheme



The absence of intense absorption lines within the range of 3067–2860 cm⁻¹ is indicative of the disappearance of NH groups and of the formation of 3,4-N,N-disubstituted derivatives of 1,3,4-thiadiazole.

EXPERIMENTAL

The reactions were controlled by TLC method and performed on a Silufol UV-254 silica gel plates. Spots were visualized with a UV hand lamp or iodine vapour. The melting points were determined in open capillaries and were uncorrected. The IR spectra were taken with a Specord IR-75 in KBr disks.

The data on the synthesized compounds II–XI are summarized in Table.

3,4-Di(hydroxymethylene)-1,3,4-thiadiazole-2,5-dithione (II). 2,5-Dimercapto-1,3,4-thiadiazole (I) (3.8 g, 0.025 mol), conc. hydrochloric acid (1 ml), methyl alcohol (20 ml) and 28% formaldehyde (10 ml) were boiled up, methanol was distilled, the mixture was filtered, distilled water (25 ml) was added, the formed crystals of II were filtered off and washed with methanol and ether.

3,4-Di(chloromethylene)-1,3,4-thiadiazole-2,5-dithione (III). **Method A.** Derivative II (2.1 g, 0.01 mol) was dissolved in chloroform (20 ml), and sulfinyl chloride (2.4 g, 0.02 mol) was added dropwise to the solution so that the temperature should not exceed 40 °C; then the mixture was mixed for 2 h at 45 °C. Chloroform was distilled, the deposited

Table. Constants and elemental analysis data on the synthesized compounds II–XI

Compound	Yield, %	M.p., °C	Molecular formula	Found/Calculated, %			Method
				C	H	N	
II	85	111–112	C ₄ H ₆ N ₂ O ₂ S ₃	22.75	2.78	13.16	
				22.85	2.87	13.32	
III	86.2	205(dec.)	C ₄ H ₄ Cl ₂ N ₂ S ₃	19.68	1.76	11.44	A
				19.44	1.63	11.33	
III	64.8	206 (dec.)	C ₄ H ₄ Cl ₂ N ₂ S ₃	19.52	1.58	11.51	B
				19.44	1.63	11.33	
IV	78.3	235 (dec.)	C ₁₂ H ₂₂ N ₂ O ₂ S ₃	44.49	6.62	8.91	
				44.69	6.88	8.69	
V	67.4	258 (dec.)	C ₁₈ H ₁₈ N ₂ O ₂ S ₃	55.49	4.42	7.35	
				55.35	4.64	7.17	
VI	39.6	136–137	C ₁₆ H ₁₂ N ₈ S ₃	46.32	3.15	27.04	
				46.59	2.93	27.16	
VII	62.9	109–110	C ₁₈ H ₁₂ N ₄ S ₇	42.23	2.51	11.29	
				42.49	2.38	11.01	
VIII	66.7	103–104	C ₁₈ H ₁₂ N ₄ O ₂ S ₅	45.18	2.42	11.63	
				45.36	2.54	11.75	
IX	56.6	212–213	C ₂₀ H ₁₂ N ₄ O ₄ S ₃	51.17	2.34	11.88	
				51.27	2.58	11.96	
X	59.3	117–119	C ₁₈ H ₁₂ N ₄ O ₆ S ₅	40.13	2.38	10.24	
				39.99	2.24	10.36	
XI	91.2	130 (dec.)	C ₁₀ H ₁₀ N ₆ O ₂ S ₇	25.62	2.32	17.67	
				25.52	2.14	17.85	

crystals of product III were filtered off and recrystallized from benzene.

Method B. Derivative I (3.8 g, 0.025 mol), formaldehyde of 36% (4 g, 0.05 mol) and conc. hydrochloric acid (1.8 g) were heated for 15 min at 40 °C, filtered and left over night. The formed crystals of III were filtered off and recrystallized from benzene.

3,4-Di(butyloxomethylene)-1,3,4-thiadiazole-2,5-dithione (IV). Derivative III (2.5 g, 0.01 mol) and butyl alcohol (16.2 g, 4.6 mol) were heated for 5 h at 80 °C, the mixture was filtered, butyl alcohol was distilled, the formed crystals of IV were filtered off and washed with acetone and ether.

3,4-Di(benzyloxomethylene)-1,3,4-thiadiazole-2,5-dithione (V). Derivative III (2.5 g, 0.01 mol) and benzyl alcohol (5.4 g, 0.05 mol) were heated for 5 h at 80 °C, the mixture was filtered, benzyl alcohol was distilled, the formed crystals of V were filtered off and washed with acetone and ether.

3,4-Di(benzotriazolilmethylene)-1,3,4-thiadiazole-2,5-dithione (VI). 2,5-Dimercapto-1,3,4-thiadiazole (I) (1.8 g, 0.0125 mol), formaldehyde of 28% (5 ml, 0.025 mol), benzotriazole (3.0 g, 0.025 mol), cuprous chloride (0.2 g) and 1,4-dioxane (50 ml) were boiled for 5 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of VI were filtered off and washed with ethanol.

3,4-Di(2-thiobenzothiazolil-3'-methylene)-1,3,4-thiadiazole-2,5-dithione (VII). Derivative I (1.8 g, 0.0125 mol), formaldehyde of 28% (5 ml, 0.025 mol), 2-mercaptobenzothiazole (4.2 g, 0.025 mol), cuprous chloride (0.2 g) and 1,4-dioxane (100 ml) were boiled for 4 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of VII were filtered off and washed with ethanol.

3,4-Di(2-thiobenzoxazolil-3'-methylene)-1,3,4-thiadiazole-2,5-dithione (VIII).

2,5-Dimercapto-1,3,4-thiadiazole (I) (1.8 g, 0.0125 mol), formaldehyde of 28% (5 ml, 0.025 mol), 2-mercaptobenzoxazole (3.7 g, 0.025 mol), cuprous chloride (0.2 g) and 1,4-dioxane (100 ml) were boiled for 4 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of VIII were filtered off and washed with ether.

3,4-Di(phthalimidilmethylene)-1,3,4-thiadiazole-2,5-dithione (IX). Derivative I (3.7 g, 0.025 mol), formaldehyde of 28% (10 ml, 0.05 mol), phthalimide (7.4 g, 0.05 mol), cuprous chloride (0.2 g) and 1,4-dioxane (100 ml) were boiled for 5 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of IX were filtered off and washed with ethanol.

3,4-Di(benzoic sulphimidilmethylene)-1,3,4-thiadiazole-2,5-dithione (X). Derivative I (1.8 g, 0.0125 mol), formaldehyde of 28% (5 ml, 0.025 mol), benzoic sulphimide (4.6 g, 0.025 mol), cuprous chloride

(0.2 g) and 1,4-dioxane (100 ml) were boiled for 5 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of X were filtered off and washed with acetone and ether.

3,4-Di(aminorhodanilmethylene)-1,3,4-thiadiazole-2,5-dithione (XI). Derivative I (1.8 g, 0.0125 mol), formaldehyde of 28% (5 ml, 0.025 mol), N-aminorhodanine (3.7 g, 0.025 mol), cuprous chloride (0.2 g) and 1,4-dioxane (100 ml) were boiled for 5 h, the mixture was filtered, 1,4-dioxane was distilled, the formed crystals of XI were filtered off and washed with ethanol and ether.

CONCLUSIONS

1. 2,5-Dimercapto-1,3,4-thiadiazole interacts with benzotriazole, 2-mercaptobenzothiazole, 2-mercaptobenzoxazole, phthalimide, benzoic sulphimide and N-aminorhodanine into Mannich reaction and gives 3,4-N,N-aminomethylated derivatives of 1,3,4-thiadiazole.

2. 3,4-Di(methylenoxo)-substituted derivatives of 1,3,4-thiadiazole, thermally resistant, were synthesized during interaction of 3,4-di(chloromethylene)-1,3,4-thiadiazole-2,5-dithion with butyl or benzyl alcohols.

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NAUJI HETEROCIKLAI 2,5-DIMERKAPTO-1,3,4-TIADIAZOLO PAGRINDU

3,4-N,N-DIPAVADUOTI 1,3,4-TIADIAZOLO DARINIAI

S a n t r a u k a

Ištirta 2,5-dimerkapto-1,3,4-tiadiazolo Manicho reakcija su benzotriazolu, 2-mercaptobenzotiazolu, 2-mercaptobenzoxazolu, ftalimidu, benzoilo sulfimidu bei N-aminorodaninu ir IR spektrų pagalba nustatyta, kad visais atvejais susidaro 3,4-N,N-aminometilinti 1,3,4-tiadiazolo dariniai.

3,4-Di(chlormetilen)-1,3,4-tiadiazol-2,5-ditionas buvo gautas dviem būdais: 3,4-di(hidroksimetilen)-1,3,4-tiadiazol-2,5-ditioną veikiant sulfinilchloridu, taip pat 2,5-dimerkapto-1,3,4-tiadiazolui sąveikaujant su formaldehidu ir konc. druskos rūgštimi.

3,4-Di(chlorometilen)-1,3,4-tiadiazol-2,5-ditionui reaguojant su butilo arba benzilo alkoholiais susidarė 3,4-di(metilenokso)-pavaduoti 1,3,4-tiadiazolo dariniai, kurie pasižymi termostabilumu.

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НОВЫЕ ГЕТЕРОЦИКЛЫ НА ОСНОВЕ 2,5-ДИМЕРКАПТО-1,3,4-ТИАДИАЗОЛА

3. 3,4-N,N-ДИЗАМЕЩЕННЫЕ 1,3,4-ТИАДИАЗОЛЫ

Резюме

Исследована реакция Манниха 2,5-димеркапто-1,3,4-тиадиазола с бензотриазолом, 2-меркаптобензотиазолом,

2-меркаптобензоксазолом, фталимидом, бензоилсульфимидом, а также с N-аминороданином и с помощью ИК спектров установлено, что во всех случаях образуются 3,4-N,N-аминометилированные производные 1,3,4-тиадиазола.

3,4-Ди(хлорметил)-1,3,4-тиадиазол-2,5-дитион был получен двумя способами: исходя из 3,4-ди(гидроксиметил)-1,3,4-тиадиазол-2,5-дитиона и сульфенилхлорида, а также при взаимодействии 2,5-димеркапто-1,3,4-тиадиазола с формальдегидом и конц. соляной кислотой.

3,4-Ди(хлорметил)-1,3,4-тиадиазол-2,5-дитион при взаимодействии с бутиловым или бензиловым спиртами образует 3,4-ди(метиленоксо)-замещенные производные 1,3,4-тиадиазола, которые проявляют термостойкость.