REACTION OF 5-MERCAPTO-1,2,3-TRIAZOLE-4-CARBOXAMIDES WITH PHOSPHORUS DECASULFIDE

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The reaction of 5-mercapto-1,2,3-triazole-4-carboxamide with P_4S_{10} was studied; the mechanism of this reaction is discussed. The effect of the donor-acceptor properties of the substituents on the direction of cyclization of the intermediate malonic acid α-diazodithioamide was investigated. A new rearrangement in the 5-mercapto-1,2,3-triazole series was observed.

We have previously shown in two examples that recyclization of the 1,2,3-triazole ring with the formation of 5-amino-1,2,3-thiadiazoles IIa,b occurs in addition to conversion of the carboxamido group to a thiocarbamoyl group in the thionation of 5-mercapto-1,2,3-triazole-4-carboxamides Ia,b with phosphorus decasulfide (P_4S_{10}) [1]. In this case the sulfur atom of the mercapto group enters into the thiadiazole system. However, the possibility that the sulfur atom of the resulting carbothioamido group may also participate in the construction of the 1,2,3-thiadiazole ring when other substituents are introduced into the carbamoyl function is not excluded.

In order to determine the limits of this method for obtaining 5-amino-1,2,3-thiadiazoles, which are of interest as intermediates in the synthesis of biologically active compounds [2], investigate the effect of the donor-acceptor properties of the substituents attached to the nitrogen atom of the carboxamido group on the method of recyclization, and ascertain the mechanism of the reaction we studied the reaction of 5-mercapto-1,2,3-triazole-4-carboxamides that contain alkyl, aryl, and hetaryl substituents in the amido group with P_4S_{10}.

In contrast to amides Ia,b, mixtures of thiadiazoles IIc-g and IIIc-g are formed from triazoles Ic-g in this reaction. The structures of the substances obtained were proved by comparing them with compounds with known structures [3]. The amounts of isomers in the mixtures were determined on the basis of the integral curves in the ^1H and ^{13}C NMR spectra as in [3] (IIa/IIIa = 100:0, IIb/IIIb = 100:0, IIc/IIIc = 70:30, IId/IIId = 30:70, IIe/IIIe = 35/65, IIf/IIIf = 33:67, IIg/IIIg = 0:100). It is apparent from the data presented above that the electronic properties of the substituents attached to the nitrogen atom of the carboxamido group of triazole I affect the ratio of thiadiazoles II and III. The presence of electron-donor substituents — methyl and cyclohexyl groups — promotes the formation of thiadiazoles IIb,c, while the presence of aryl groupings promotes the formation of IIId-g. Individual thiadiazole IIIh is formed when the markedly electron-acceptor α-pyridyl radical is introduced.

Two pathways for the conversion of triazoles I to II and III are possible. In the case of mechanism A the thionation of the carboxamido group precedes opening of the triazole ring with the formation of diazodithioamide IV and its subsequent conversion to a 5-amino-1,2,3-thiadiazole system. When the reaction takes place via mechanism B, the rearrangement and thionation processes occur in the reverse sequence.

According to our data, a mixture of isomers II and III is also obtained in the thionation of thiadiazoles Va-g under conditions similar to the transformation of triazoles Ia-h discussed in this research [3]; this constitutes evidence in favor of mechanism B. However, thiadiazole IIa is also formed when triazole VIa with a known structure [1] is treated with P_4S_{10}. Since there is already a thiocarbamoyl function in VIa, P_4S_{10} in this reaction evidently acts not as a thionating agent but rather as an acidic recyclization catalyst. On the basis of this it is legitimate to replace P_4S_{10} by its model P_4O_{10}. In fact, thiadiazole IIa was also obtained when triazole VIa was treated with P_4O_{10}. Consequently, the second steps of mechanisms A and B are equally probable. In order to verify the possibility of recyclization of triazole I to thiadiazole V under conditions that model the thionation reaction

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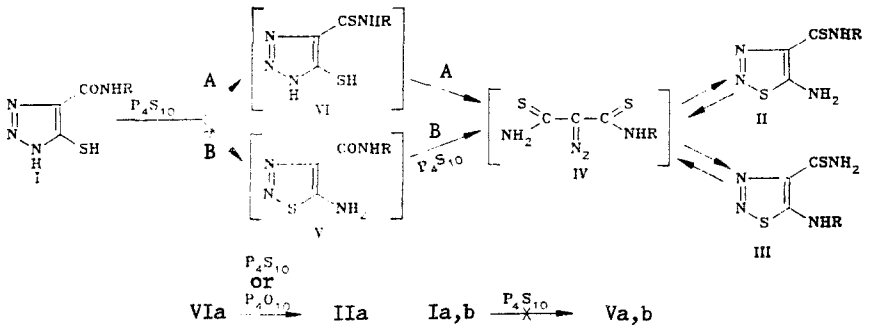
TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}			m/z (I_{rel}, %)*	PMR spectrum, δ, ppm	Yield, %
			NH	CH	C=O			
Ic	$C_9H_{14}N_4OS$	177...179	3370, 3210, 3060	2935, 2860	1640	M+ 226 (64), 145 (100), 144 (41), 128 (70), 98 (45)	0,9...2,1 (11H, m, C_6H_{11}), 8,2 (H, d J=8 Hz, NH), 11,8 (H, s NH)	80
Id	$C_9H_8N_4OS$	195...196	3060, 3015	2930, 2870	1630	M+ 220 (40), 128 (16), 93 (100), 92 (12), 77 (18)	7,0...7,9 (5H, m, C_6H_5), 10,5 (H, c, NH), 11,8 (H, s, NH)	89
Ie	$C_{10}H_{10}N_4OS$	191...192	3180, 3065	2930, 2795	1630	M+ 234 (100), 128 (30), 127 (15), 65 (17), 36 (20)	2,3 (3H, s, CH_3), 7,0...7,9 (4H, m, C_6H_4), 10,4 (H, s, NH), 11,8 (H, s, NH)	87
If	$C_{10}H_{10}N_4O_2S$	209...210	3240, 3185, 3040	2910	1605	M+ 250 (100), 128 (28), 123 (67), 122 (42), 108 (55)	3,8 (3H s, CH_3), 7,0...7,9 (4H, m, C_6H_4), 10,4 (H, s, NH), 11,8 (H, s, NH)	88
Ig	$C_9H_7BrN_4OS$	213	3085	2960, 2830	1670	M+ 300 (100), 172 (95), 145 (10), 128 (80), 91 (36)	7,4...8,0 (5H, m, NH, C_6H_4), 12,5 (H, s, NH)	93
Ih	$C_8H_7N_5OS$	285	3130, 3065	2985	1650	M+ 221 (45), 128 (10), 73 (47), 59 (75), 28 (100)	6,4 (H, s, NH), 6,9...8,1 (4H, m, C_5H_4N), 12,4 (H, s, NH)	81
IIh	$C_8H_7N_5S_2$	235	3450, 3280, 3170	3000		M+ 237 (6), 209 (20), 176 (100), 165 (26), 78 (60)	7,0...8,5 (4H, m, C_5H_4N), 7,4 (H, s, NH), 9,9 (2H, s, NH_2)	35

*The five most intense peaks are presented. The most intense peaks of multiplets correspnding to the ^{81}Br isotope are presented for Ig.

we studied the reaction of Ia,b with P_4O_{10}. In this reaction the starting triazole remained unchanged, and the product of its recyclization was not detected.



I—VI a R=H, b R=CH_3, c R=C_6H_{11}, d R=C_6H_5, e R=C_6H_4—CH_3-*p*, f R=C_6H_4—OCH_3-*p*, g R=C_6H_4--Br-*p*, h α-pyridyl

Thus our experiments provide evidence for the easier conversion of 5-mercaptol-1,2,3-triazole-4-carbothioamides VI to thiadiazoles as compared with -4-carboxamides I and , consequently, the greater probability of mechanism A.

The complete coincidence of the effect of the properties of the substituents on the ratios of isomers II and III obtained in the thionation of both triazoles I and thiadiazoles V [3] constitutes evidence that these processes take place with the formation of a common intermediate — the corresponding diazodithioamide VI.

The observed new transformation includes as one step the recyclization of triazole VI to thiadiazole III, which is similar to the Cornforth rearrangement previously described in the oxazole series [4].

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with UR-20 and Specord IR-20 spectrometers. The PMR spectra of solutions in d_6-DMSO were obtained with Perkin—Elmer 12B (60 MHz) and Bruker WP-80 (80.13 MHz) spectrometers with tetramethylsilane (TMS) as the internal standard. The ^{13}C NMR spectra of solutions in d_6-DMSO were recorded with a Bruker WP-80 spectrometer (20.13 MHZ) with TMS as the internal standard. The mass spectra were recorded with an MAT-311A spectrometer. Monitoring of the reactions and verification of the individuality of the compounds were carried out by means of TLC on Silufol UV-254 plates in the following solvent systems: proponal—3% ammonium hydroxide (3:1), ethanol— , chloroform (1:10), and ethanol—chloroform (1:15). The results of elementary analysis of I and III for C, H, N, and S were in agreement with the calculate values.

The characteristics of the synthesized compounds are presented in Table 1.

5-Mercapto-1,2,3-triazole-4-N-R-carboxamides (Ic-h). A 1-mole sample of thiadiazole Vc-h was suspended in 1.5 liters of 25% ammonium hydroxide, and the suspension was refluxed until the solid material had dissolved completely. The reaction mass was evaporated to one third of its original volume, and the precipitate that formed after the concentrate was acidified to pH 1 was removed by filtration and crystallized from water.

5-N-Pyridylamino-1,2,3-thiadiazole-4-carbothioamide (IIIh). A 2-g (9 mmole) sample of 1h was suspended in 150 ml of absolute dioxane and 15 ml of dry pyridine, 2 g (4.5 mmole) of P_4S_{10} was added with vigorous stirring at 50°C, and the mixture was maintained for 1 h at 100°C. It was then cooled, and the liquid phase was decanted. The residue was triturated with water and crystallized several times from ethanol.

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