CONVERSION OF 4-SUBSTITUTED BENZO-2,1,3-THIADIAZOLES TO 5-CHLORO-4,7-DIOXOBENZO-2,1,3-THIADIAZOLE BY ACTION OF HYDROGEN PEROXIDE AND HYDROCHLORIC ACID

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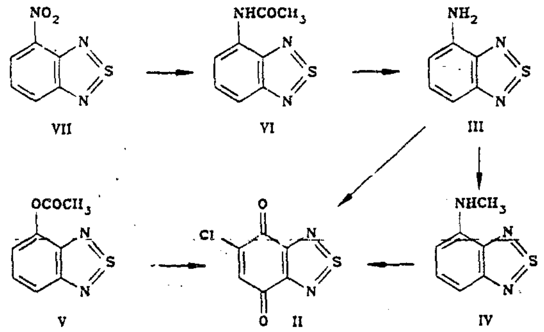
Under the influence of hydrogen peroxide and hydrochloric acid in acetonitrile 4-substituted benzo-2,1,3-thiadiazoles form 5-chloro-4,7-dioxobenzo-2,1,3-thiadiazole. 4-Alkoxy- and 4-[(alkoxycarbonyl)methoxy]benzo-2,1,3-thiadiazoles give, in addition, the corresponding 5,7-dichloro derivatives.

5-Chloro-4,7-dioxobenzo-2,1,3-thiadiazole (II) is formed in ~40% yield in the oxidation of 4-hydroxybenzo-2,1,3-thiadiazole (I) with 30% hydrogen peroxide in concentrated hydrochloric acid [1]. Since II has herbicidal activity and, in a dose of 5-10 kg/ha, suppresses the development of a green mass on garden radishes, flax, and beets by 87-100%,* it seemed expedient to examine other possibilities for obtaining quinone II and, for this purpose, to study the transformations of various 4-substituted benzo-2,1,3-thiadiazoles under the conditions indicated above.

Quinone II was isolated in 61%, 41%, and 54% yields, respectively, in the oxidation of 4-amino-, 4-methylamino-, and 4-acetoxybenzo-2,1,3-thiadiazole (III-V). An author's certificate was obtained for a method for obtaining quinone II from amine III [2].

Compound IV is formed by methylation of amine III with dimethyl sulfate by the method described in [3]. Amine III is readily obtained by hydrolysis of 4-acetamidobenzo-2,1,3-thiadiazole (VI) with 40% sulfuric acid. Acetamido derivative VI was obtained in high yield in the reaction of 4-nitrobenzo-2,1,3-thiadiazole (VII) with acetic anhydride, alcohol, and iron.

Acetoxy derivative V is readily obtained by heating I with acetyl chloride in dry pyridine and also by reaction of I with acetic anhydride in the presence of triethylamine or pyridine. Compound V is identical to the acetoxy derivative obtained by the method in [4].



Under the influence of a 30% solution of hydrogen peroxide and concentrated hydrochloric acid in acetonitrile 4-alkoxybenzo-2,1,3-thiadiazoles VIII-X are converted to mixtures of quinone II and products of chlorination of the corresponding ethers VIII-X. The chlorination products — 5,7-dichlorobenzo-2,1,3-thiadiazoles XI-XIII — are separated from quinone II by washing the mixtures with petroleum ether. However, they were not isolated in pure form

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*The tests were conducted by K. A. Abramova and T. D. Panasyuk.

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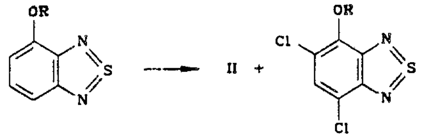
TABLE 1. Data on the Reagent Ratios, Refluxing Times, and Yields of Quinone II

Starting compound	Reagents				Method	Refluxing time, min	Compounds obtained	R_f of the reaction products (system)	Yield of quinone II, %
	Benzo-2,1,3-thiadiazole derivative, g (mmole)	Conc. HCl, ml	Acetonitrile, ml	30% hydrogen peroxide, ml					
III	4,8 (32)	83	150	160	A	20	II	0,88 (A)	61
IV	0,5 (3,1)	8	15	16	A	10	II	0,88 (A)	41
V	0,5 (2,6)	6,8	12	13,3	A	20	II	0,7 (C)	54
VIII	1,2 (7,2)	12,5	40	25	B	15	II+XI	0,88 and 0,92 (A) 0,70 and 0,89 (C)	38
IX	0,45 (2,5)	7	12	13	B	30	II+XII	0,88 and 0,93 (A)	20
X	0,9 (4,3)	6,3	19	12,5	B	10	II+XIII	0,88 and 0,95 (A)	39
XIV	0,84 (3,5)	5	20	10,0	B	30	II+XVI	0,89 and 0,60 (B)	
XV	0,5 (2,4)	6,3	11,7	12,3	B	30	II+XVI	0,89 and 0,60 (B)	

and were identified with authentic XI-XIII by means of TLC [5]. Ethers VIII-X were synthesized by alkylation of I with alkyl halides in DMF in the presence of anhydrous sodium carbonate.



VIII-X, XIV-XV XI-XIII, XVI

VIII, XI $R=CH_3$; IX, XII $R=C_2H_5$; X, XIII $R=C_4H_9$; XIV $R=CH_2COOC_2H_5$; XV, XVI $R=CH_2COOH$

Under the same conditions 4-[(ethoxycarbonyl)methoxy]- and 4-(carboxymethoxy)benzo-2,1,3-thiadiazole (XIV, XV) form mixtures of quinone II and 5,7-dichloro-4-(carboxymethoxy)-benzo-2,1,3-thiadiazole (XVI), which cannot be separated. Acids XV and XVI, which were necessary for the study of the oxidation and TLC comparison, were obtained by hydrolysis of ester XIV and 5,7-dichloro-4-[(ethoxycarbonyl)methoxy]benzo-2,1,3-thiadiazole (XVII) [6].

EXPERIMENTAL

Monitoring of the course of the reactions and evaluation of the individuality of the substances were accomplished by means of TLC on Silufol plates in the following three systems: acetone—chloroform—hexane (2:1:2) (A), benzene—acetone—acetic acid (100:50:1) (B), and chloroform (C). All of the compounds, with the exception of quinone II, were developed in UV light. Quinone II was developed with ammonia vapors. The IR spectra of KBr pellets of the compounds were recorded with a Perkin—Elmer 577 spectrometer.

5-Chloro-4,7-dioxobenzo-2,1,3-thiadiazole (II). A. A 6.8-ml sample of concentrated HCl and (dropwise) 13.3 ml of hydrogen peroxide were added successively at 50°C to a mixture of 0.5 g (2.6 mmole) of V in 12 ml of acetonitrile in such a way that violent foaming did not occur, after which the reaction mass was refluxed for 20 min, cooled, and poured over ice. The resulting precipitate was removed by filtration, washed with water, and dried to give 0.28 g (54%) of a product with mp 148-149°C (from dichloroethane) (no melting-point depression observed for a mixture with quinone II obtained by the method in [1]) and R_f 0.88 (A), 0.89 (B), and 0.7 (C). See Table 1.

B. A 12.5-ml sample of concentrated HCl and (dropwise) 25 ml of 30% hydrogen peroxide were added successively in the course of 30 min to a mixture of 1.2 g (7.3 mmole) of VIII in 40 ml of acetonitrile at 50°C, after which the reaction mixture was refluxed for 15 min and then poured without cooling over ice. The precipitate was removed by filtration, washed with water, and dried to give 1.2 g of a mixture with mp 127-129°C consisting of quinone II [R_f 0.70 (C)] and VII [R_f 0.89 (C)]. A 1.2-g sample of the mixture was suspended in 240 ml of petroleum ether, and the precipitate was removed by filtration, washed with 300 ml of petroleum ether, and dried to give 0.55 g (38%) of II, which was crystallized from dichloroethane (Table 1).

4-Aminobenzo-2,1,3-thiadiazole (III). A 1-g (5 mmole) sample of VI was refluxed in 7.5 ml of 40% sulfuric acid for 20 min, after which the mixture was cooled, and 25 ml of 20% sodium hydroxide solution was added. The precipitate was removed by filtration, washed with water, and dried to give 0.66 g (84%) of a product with mp 67-68°C (from water); no melting-point depression was observed for a mixture of this product with amine III obtained by the method in [7].

4-Acetoxybenzo-2,1,3-thiadiazole (V). A. A 1.22-ml (16.6 mmole) sample of acetyl chloride was added dropwise with vigorous stirring in the course of 20 min to a mixture of 2 g (13 mmole) of I [8] in 3.6 ml of dry pyridine, after which the reaction mixture was heated for 1.5 h at 90°C, cooled, and poured over ice. The precipitate was removed by filtration, washed with water, and dried to give 2.1 g (82%) of a product with mp 53-54°C (from ethanol) and R_f 0.86 (A); no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [4], and the R_f values of these substances were identical.

B. A 0.11-ml sample of triethylamine was added to a solution of 2 g (13 mmole) of I in 13.3 ml of acetic anhydride, and the reaction mixture was refluxed for 20 min. It was then cooled and poured into water, and the aqueous mixture was extracted with chloroform. The solvent was evaporated to give 2.23 g (87%) of a product with mp 53-54°C (from ethanol); no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [4].

C. A 0.04-ml sample of pyridine was added dropwise to a solution of 1 g (7 mmole) of I in 6.7 ml (71 mmole) of acetic anhydride, and the mixture was refluxed for 5 min. It was then cooled and worked up as described in method B to give 1.17 g (92%) of a product with mp 53-54°C; no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [4].

4-Acetamidobenzo-2,1,3-thiadiazole (VI). A mixture of 12.4 g (68.5 mmole) of VII [9], 24 g of reduced iron, 60 ml of acetic anhydride, and 20 ml of ethanol was refluxed for 30 min (in the case of vigorous foaming during refluxing 1 ml of water was added to the reaction mixture), after which 80 ml of DMF was added in portions, and the mixture was heated to 100°C and filtered hot. The precipitate on the filter was washed with 20 ml of hot DMF, and the filtrate was diluted with water in a ratio of 1:2. The precipitate was removed by filtration, washed with water, and dried to give 10.8 g (82%) of a product with mp 151-153°C (mp 150-151°C [7]). IR spectrum (KBr pellet): 1670 cm^{-1} (C=O). The product has R_f 0.70 (A). Found: N 21.6; S 16.3%. $C_8H_7N_3OS$. Calculated: N 21.7; S 16.6%.

4-Methoxybenzo-2,1,3-thiadiazole (VIII). A mixture of 10 g (66 mmole) of I, 4.2 ml (67 mmole) of methyl iodide, 20 g of anhydrous sodium carbonate, and 50 ml of DMF was heated on a boiling-water bath for 30 min, after which it was cooled and diluted with 500 ml of water. The precipitate was removed by filtration, washed with water, and dried to give 7.1 g (65%) of VIII with a pleasant odor and mp 65-66°C (from ethanol); no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [4]. The product had R_f 0.77 (A).

4-Ethoxybenzo-2,1,3-thiadiazole (IX). A mixture of 2 g (11 mmole) of I, 0.85 ml (11 mmole) of ethyl iodide, and 4 g of anhydrous sodium carbonate in 5 ml of DMF was heated and worked up as in the synthesis of IV to give 1.44 g (61%) of ether IX with a pleasant odor and mp 45-46°C (from ethanol); no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [4]. The product had R_f 0.9 (A).

4-Butoxybenzo-2,1,3-thiadiazole (X). This compound was similarly obtained from 2 g (11 mmole) of I, 1.48 ml (12.8 mmole) of butyl iodide, and 4 g of anhydrous sodium carbonate in 10 ml of DMF. Workup gave 2.23 g (82%) of a product with mp 48-50°C (from ethanol) and R_f 0.92 (A). Found: N 14.0; S 15.0%. $C_{10}H_{12}N_2OS$. Calculated: N 13.5; S 15.4%.

4-(Carboxymethoxy)benzo-2,1,3-thiadiazole (XV). A mixture of 0.5 g (2 mmole) of XIV, 10 ml of water, 11 ml of concentrated HCl, and 8 g of ferric chloride hexahydrate was refluxed for 10 min, after which it was cooled, and the precipitate was removed by filtration, washed with water, and dried to give 0.33 g (75%) of a product with mp 158-160°C (from toluene); no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [10]. The product had R_f 0.46 (B).

5,7-Dichloro-4-(carboxymethoxy)benzo-2,1,3-thiadiazole (XVI). A mixture of 0.21 g (0.68 mmole) of XVII, 3 ml of water, 4.6 ml of concentrated HCl, and 2.7 g of ferric chloride hexahydrate was refluxed for 10 min, after which it was worked up as in the synthesis of XV to give 0.19 g (91%) of a product with mp 174-175°C; no melting-point depression was observed for a mixture of this product with the substance obtained by the method in [10]. The product has R_f 0.6 (B).

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MASS SPECTRA OF 4,5-DISUBSTITUTED 1,2,3-THIADIAZOLES

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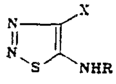
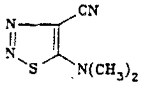
The schemes of the fragmentation of 4-substituted 5-arylamino-1,2,3-thiadiazoles were established on the basis of electron-impact mass spectra and high-resolution mass-spectrometric data, and the effect of substituents on the fragmentation pathways was analyzed. It is shown that the cyclization of the $[M - N_2]^+$ ions formed in the fragmentation of compounds that contain a thiocarboxamido group in the 4 position proceeds with the participation of the most nucleophilic heteroatom.

The 1,5-electrocyclization of diazo thioamides leads to 5-aminothiadiazoles or 5-mercaptotriazoles [1]. In [2] it was shown that mass spectrometry is the fastest and most reliable method for the identification of compounds of these classes.

In the present paper we present the results of a mass-spectrometric study of 4-cyano- and 4-thiocarboxyamido-5-aryl(alkyl)amino-1,2,3-thiadiazoles Ia-i.*



Ia-m



II

I a-d $X=CN$; e-g $X=CSNH_2$; h, i $X=CSNHCH_3$; a,e $R=C_6H_5$; b,f $R=4\text{-}CH_3C_6H_4$; c,g $R=4\text{-}CH_3OC_6H_4$; d $R=4\text{-}C_2H_5OC_6H_4$; h $R=H$; i $R=CH_3$

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*The mass spectrum of Ih was presented in [2]. For the purposes of our investigation it was rerecorded under conditions that were identical for the entire series.

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