3-Phenyl-5-nitro-1,2,3-thiadiazolium-4-olate (Va, $C_8H_5N_3O_3S$). A solution of 1 g (0.012 mole) of sodium nitrite in 10 ml of water was added to a hot solution of 2.7 g (0.01 mole) of 3-phenyl-4,5-dichloro-1,2,3-thiadiazolium chloride in 20 ml of 50% ethanol. The dark-yellow precipitate was filtered, and recrystallized from a benzene–heptane (1:1) mixture. Yield, 81%, mp 175-176°C [4]. Mass spectrum: M^+ 223. IR spectrum: 1660 cm^{-1} (C=O), UV spectrum, λ_{max} ($\log \varepsilon$): 228 (3.82), 280 (3.4); 425 nm (4.03).

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DISULFIDES OF THE BENZO-2,1,3-THIADIAZOLE SERIES

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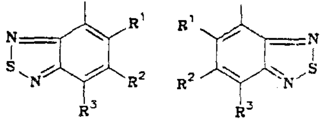
Disulfides of the benzo-2,1,3-thiadiazole series were obtained by reduction of benzo-2,1,3-thiadiazolesulfonyl chlorides (by hydriodic acid or by sulfur dioxide) or by the reaction of benzo-2,1,3-thiadiazolesulfinic acids with hydrogen bromide in acetic acid. Convenient methods for the synthesis of the starting compounds were found, and the fungicidal activity of the disulfides obtained was studied.

We have previously described a convenient method for the preparation of mercapto derivatives of benzo-1,2,3-thiadiazole from disulfides [1]. However, little is known about the syntheses and transformations of disulfides of the benzo-2,1,3-thiadiazole series [1-4]. In the present work these investigations are continued.

We showed that 4,4'-di(benzo-2,1,3-thiadiazolyl) disulfide (I), which we obtained previously [1] by the reaction of benzo-2,1,3-thiadiazole-4-sulfinic acid (II) with hydrogen bromide in glacial acetic acid, can be synthesized by the action of hydriodiodic acid on 4-chlorosulfonylbenzo-2,1,3-thiadiazole (III) in glacial acetic acid or by reduction of sulfonyl chloride III by sulfur dioxide in acetic acid in the presence of iodine.

Disulfides IV-VIII were synthesized in a similar way as disulfide I. The IR spectra of all these compounds contain the absorption band of the S–S group at 473-499 cm^{-1} (Table 1).



I, IV–VIII

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TABLE 1. Characteristics of Disulfides I, IV-VIII

Compound	R^1	R^2	R^3	Empirical formula	mp, °C*	IR spectrum, cm^{-1}**	R_f***	Yield, %		
								A	B	C
I	H	H	H	$C_{12}H_6N_4S_4$	181...182	483	0,45	63	85	70
IV	Cl	H	Cl	$C_{12}H_2Cl_4N_4S_4$	227...229	483	0.89	60	56	51
V	H	H	Br	$C_{12}H_4Br_2N_4S_4$	214...216	473	0.82	80	90	81
VI	H	H	Cl	$C_{12}H_4Cl_2N_4S_4$	120...122	486	0,85	63	—	—
VII	CH_3	H	H	$C_{14}H_{10}N_4S_4$	168...170	488	0,70	36	77	69
VIII	H	CH_3	Br	$C_{14}H_8Br_2N_4S_4$	271...273	499	0,78	36	—	—

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*Compounds I, IV, V, VII were recrystallized from benzene, and VI and VIII from toluene.

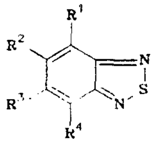
**The spectrum of compounds I, VI, VII, VIII was recorded in KBr tablets, and that of compounds IV and V in a $CHCl_3$ solution.

***The TLC of compounds I, V-VIII was carried out in $CHCl_3$, and that of compound IV in a benzene–acetone–acetic acid (100:50:1) mixture.

Reduction of sulfonyl chloride III by red phosphorus and iodine in glacial acetic acid gives a mixture of disulfide I and 4-mercaptobenzo-2,1,3-thiadiazole (IX) in a 4:1 by weight ratio. Compound I is readily separated from compound IX by treating the mixture with a 10% solution of sodium hydroxide. It should be noted that disulfide I converts into mercaptan IX by the action of sodium sulfide or glucose in an alkaline medium, but the reaction does not proceed to completion. The yields of mercaptan IX are 40 and 30%, respectively. Mercaptan IX required for comparison was synthesized by the method described in [1].

Disulfide I by the action of chlorine and mercaptan IX by the action of sulfuryl chloride convert in acetic acid medium into the initial sulfonyl chloride III.

Sulfonyl chlorides III, X, XII, XIV, XVI, XVIII and sulfinic acids II, XI, XIII, XV, XVII, XIX of the general formula:



II, III, X-XXI

	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
II	SO_2H	H	H	H	XV	SO_2H	Cl	H	Cl
III	SO_2Cl	H	H	H	XVI	SO_2Cl	CH_3	H	H
X	SO_2Cl	H	H	Br	XVII	SO_2H	CH_3	H	H
XI	SO_2H	H	H	Br	XVIII	SO_2Cl	H	CH_3	Br
XII	SO_2Cl	H	H	Cl	XIX	SO_2H	H	CH_3	Br
XIII	SO_2H	H	H	Cl	XX	—	H	—	H
XIV	SO_2Cl	Cl	H	Cl	XXI	—	Cl	—	Cl

were obtained either according to [5-9] (II-III, X, XI, XVI) or by the reaction of the corresponding benzo-2,1,3-thiadiazoles with chlorosulfonic acid and thionyl chloride (XII, XIV, XVIII) or by the reduction of the corresponding sulfonyl chlorides by sodium sulfite in an alkaline medium (XIII, XV, XVII, XIX), whereby the sulfinic acids were not isolated in an analytically pure state, because of high losses during recrystallization from water.

The starting benzo-2,1,3-thiadiazole (XX) and its 5,7-dichloro derivative (XXI) required for the synthesis of sulfonyl chlorides III and XIV were obtained through a new method, the condensation of the corresponding ortho-phenylenediamines with thionyl chloride in the presence of concentrated H_2SO_4.

Addition of 0.34 mole of concentrated H_2SO_4 to the above reaction mixture increased the yield of benzo-2,1,3-thiadiazole from 7 to 80-90%.

We found that disulfides I, IV, V, VII have moderate fungicidal activity.* Compound I in a concentration of 0.01% suppresses the intergrowth spores of smut spores in a millet to the extent of 68%, disulfide IV in a concentration of 0.1% inhibits the development of phytophthora infection of tomatoes on green plants to the extent of 67%, compound V in a concentration of 0.1% inhibits grey mold in beans to the extent of 60%, and disulfide VII in a concentration of 0.05% inhibits the development of powdery mildew of cucumbers on green plants to the extent of 74%.

EXPERIMENTAL

The course of the reactions was monitored and the individual state of the compounds was evaluated by means of TLC on Silufol UV-254 plates in chloroform (a), in a benzene—acetone—acetic acid (100:50:1) mixture (b) and in an alcohol—chloroform (1:3) mixture (c). The IR spectra were run on a Perkin-Elmer 577 spectrophotometer. The mass spectra were measured on a Varian MAT-112 mass-spectrometer at a ionization energy of 70 eV.

The characteristics of compounds I, IV-XIII are given in Table 1. The data of the elemental analysis for Cl, N, S of the newly synthesized compounds correspond to the calculated values.

Benzo-2,1,3-thiadiazole Disulfides (I, IV-VIII). A) Hydrogen bromide was passed for 25-30 min into a solution of 7.45-7.50 mmoles of the corresponding sulfinic acids II, XI, XIII, XV, XVII, XIX in 35 ml of glacial acetic acid. After 15-30 min, the reaction mixtures was diluted with water, the precipitate of the corresponding disulfide I, IV-VIII was filtered, washed with water, dried and recrystallized.

B) A 5 ml portion of a 57% of hydriodic acid was added rapidly at 80° to 3.5-3.6 mmoles of the corresponding sulfonyl chlorides III, X, XIV, XVI in 5 ml of glacial acetic acid, and the mixture was allowed to stand for 12 h at room temperature. A 10 ml portion of water and 6.5 ml of a 40% aqueous solution of sodium bisulfite, prepared according to [10] were added to the reaction mixture. The precipitate that separated out was filtered off, washed with water to a neutral reaction, dried and crystallized. Disulfides I, IV, V, VII were obtained.

C) A mixture of 7.5 mmoles of the corresponding sulfonyl chloride III, X, XIV, XVI, 15 ml of glacial acetic acid and 0.314 mmole of iodine was heated to 60°C, sulfur dioxide was passed into it for 3 h, and simultaneously 3 ml of water were added dropwise, while the reaction temperature was maintained at 70-80°C. The reaction mixture was evaporated to one half of its volume and diluted with water. The precipitate of the corresponding disulfide I, IV, V, VII was filtered off, washed with water, dried, and crystallized.

4,4'-Di(benzo-2,1,3-thiadiazoline) Disulfide (I) and 4-Mercapto-2,1,3-thiadiazole (IX). A 4.7 g portion (20 mmoles) of compound III was added to a boiling mixture of 1.5 g (48.38 mmoles) of red phosphorus, 0.08 g (0.628 mmole) of iodine, and 6 ml of glacial acetic acid. The reaction mixture was boiled for 2 h, 3 ml of water was added, and the mixture was boiled for another 1 h, and then allowed to stand overnight. The precipitate that separated out was filtered off, washed with water, and dried. Thus, 3.2 g of a mixture consisting, according to the TLC data, of disulfide I and mercaptan IX was obtained. The mixture was stirred for 5 min with 20 ml of a 10% solution of sodium hydroxide at room temperature. The precpitate of the disulfide I was filtered off, washed with water to neutral reaction, and dried. Yield, 2.56 g (38.3%) of disulfide I, mp 180-182°C (from benzene), R_f 0.45 (a). The filtrate was acidified with hydrochloric acid, the precipitate of mercaptan IX was filtered off, washed with water, and dried. Yield, 0.64 (19%) of mercaptan IX, mp 45-47°C (from isopropanol); the R_f 0.76 (the system of solvents and development are described in [1]) coincided with the R_f value of mercaptan IX obtained in [1]. IR spectrum (KBr): 2579 cm^{-1} (SH). An aqueous solution of sodium nitroprusside with an alkaline solution of mercaptan IX gave a dark-pink coloration.

4-Mercaptobenzo-2,1,3-thiadiazole (IX). A) A mixture of 0.5 g (1.5 mmole) of disulfide I, 0.12 g (1.5 mmole) of sodium sulfide and 30 ml for a 10% sodium hydroxide solution was boiled for 1 h, and then cooled. The unreacted disulfide was filtered off, the filtrate was

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*The tests was carried out by Zh. S. Dyachina.

acidified with hydrochloric acid to pH 1, and the precipitated mercaptan IX was filtered off, washed with water, and dried. Yield, 0.2 g (40%) of compound IX, mp 46-48°C (from isopropanol); the R_f 0.76 coincided with the R_f value of mercaptan IX obtained according to [1].

B) A mixture of 0.5 g (1.5 mmole) of disulfide I, 0.27 g (0.98 mmole) of glucose and 30 ml of a 10% sodium hydroxide solution was boiled for 1 h. The mixture was cooled and treated as in method A to yield 0.15 g (30%) of mercaptan IX*, mp 46-48°C (from isopropanol); the R_f 0.76 coincided with the R_f value of mercaptans obtained by method A and according to [1].

4-Chlorosulfonylbenzo-2,1,3-thiadiazole (III). A) Chlorine was passed for 3 h into a suspension of 0.2 g (0.598 mmole) of compound I in 5 ml of glacial acetic acid and 1 ml of water. The mixture was then diluted to twice its volume with water, the preicpitate was filtered off, washed with water, and dried. Yield, 0.2 g (71.4%) of compound III which after crystallization from a mixture of cyclohexane and benzene melted at 147-149°C; according to the data in [8], mp 149.0-150.5°C; the R_f 0.67 (a), coincided with the R_f value of the compound obtained according to the literature data.

B) A 0.72 ml portion (8.88 mmoles) of sulfuryl chloride was added to 0.6 g (3.57 mmoles) of mercaptan IX in 3 ml of glacial acetic acid. The mixture was heated for 20 min at 55-65°C, cooled and the precipitate that separated out was filtered off, washed with water, and dried. Yield, 0.54 g (64.5%) of compound III, mp 145-147°C; the R_f 0.67 (a) coincided with the R_f value of compounds obtained by method A and according to [8]. A peak of molecular ion with m/z 235 (M^+) was observed in the mass spectrum.

4-Chloro-7-chlorosulfonylbenzo-2,1,3-thiadiazole (XII, $C_6H_2Cl_2N_2O_2S_2$). A 3.41 g portion (12 mmoles) of 4-chlorobenzo-2,1,3-thiadiazole, obtained according to [5], was added with stirring to 15 ml of chlorosulfonic acid (d 1.7666 g/cm^3). The mixture was held for 4 h at 140°C, cooled and 5 ml of thionyl chloride was added. The reaction mixture was boiled for 1 h, then cooled to 30-40°C, and poured onto ice. The precipitate was filtered off, washed with cold water, and dried. Yield, 3.78 g (70.2%) of sulfonyl chloride XII, after crystallization from petroleum ether or toluene, mp 116-118°C, R_f 0.63 (a).

5,7-Dichloro-4-chlorosulfonylbenzo-2,1,3-thiadiazole (XIV, $C_6HCl_3N_2O_2S_2$) [yield, 5 g (67.5%), mp 123-125°C (from toluene), R_f 0.62 (a)] and 5-methyl-7-bromo-4-chlorosulfonyl-2,1,3-thiadiazole (XVIII, $C_7H_4BrClN_2O_2S_2$ [yield, 2.7 g (68.5%), mp 130-132°C (from toluene), R_f 0.71 (a)] were obtained in a similar way.

Benzene-2,1,3-thiadiazole-4-sulfinic Acids (XIII, XV, XVII, XIX). A 10 mmole portion of the corresponding sulfonyl chloride XII, XIV, XVI, XVIII and 8 ml of a 10% solution of sodium hydroxide were added to a solution of 15-20 mmoles of sodium sulfite in 35 ml of water. The mixture was heated for 1 h 30 min on a boiling water bath, then was cooled and acidified by dilute sulfuric acid to pH 6. The precipitation that separated was filtered, washed with a small amount of water, and dried. Yield, 50-60% of sulfinic acids XIII, XV, XVII, XIX. Compound XIII, mp 129-131°C, R_f 0.8 (c). Compound XV, mp 122-124°C, R_f 0.89 (c). Compound XVII, mp 138-140°C, R_f 0.97 (c). Compound XIX, R_f 0.79 (c).

Benzo-2,1,3-thiadiazole (XX). A) A 54 g portin (0.5 mmole) of ortho-phenylenediamine was mixed together with 145-175 ml (2015-2434 mmoles) of thionyl chloride, and 9.0-10.5 ml (169-197 mmoles) of conc. H_2SO_4. The mixture was boiled for 1 h, cooled and poured into 500 ml of ice water. The precipitate that separated out was filtered off, washed with water to a neutral reaction, and dried. Yield, 55-65 g (80.9-95.6%) of compound XX, mp 42-44°C; the R_f 0.77 (a) coincided with the R_f value of the compound obtained according to [12].

B) A mixture of 5.4 g (50 mmoles) of ortho-phenylenediamine and 14.5 ml (201.5 mmoles) of thionyl chloride was boiled for 1 h, then live steam was passed into the reaction mixture, and compound XX was distilled off. Yield, 0.47 g (6.9%), mp 42-44°C; the R_f 0.77 (a) coincided with the R_f value of the compound obtained by method A and according to [12].

5,7-Dichlorobenzo-2,1,3-thiadiazole (XXI). A 27 g portion (108 mmoles) of 2,4-dichloro-6-aminoaniline was mixed together with 96.5 ml (1342 mmoles) of thionyl chloride and 4.7 ml (88.2 mmoles) of conc. H_2SO_4. The mixture was boiled for 1 h, and treated in a similar way as compound XX (method A). Yield, 26.5 g (85.2%) of compound XXI, mp 96-98°C; according to

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*Mercaptan IX is not formed from disulfide I, when the latter is heated with a 10% solution of sodium hydroxide without reducing agents.

the data in [11], mp 97.0-97.7°C; the R_f 0.89 (a) coincided with the R_f value of compound XXI, obtained according to [1].

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SYNTHESIS OF MACROHETEROCYCLES — ANALOGS OF DIBENZO-CROWN COMPOUNDS.

4.* 15-18-MEMBERED PYRIDINE-CONTAINING CROWN COMPOUNDS

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By condensation of bridged, aromatic diamines, derivatives of o-aminophenol or o-aminothiophenol, with the diacyl chloride of 2,6-pyridinedicarboxylic acid under high dilution, 15-18-membered macrocyclic diamides containing a pyridine nucleus have been synthesized. The synthesized compounds were characterized by IR and PMR spectroscopy.

At the present time, a number of synthetic paths are known for obtaining macrocyclic polyamines and their metal complexes [2, 3]. Attempts to modify the structure of crown ethers so as to form macrocycles possessing the ability to selectively bind different metal cations led to the incorporation of various heterocyclic fragments in the macrocyclic ring. The most widespread methods of synthesizing such compounds are the condensation of heteroaromatic dialdehydes and diketones with primary diamines in the presence of a template ion [4] as well as the use of the technique of high dilution [3] with the formation of the corresponding macrocyclic Schiff base.

One of the most useful heterocyclic fragments that can be incorporated in a macrocyclic structure is the pyridine fragment. To obtain macrocyclic cryptands and diamines, primary diamines [5], diaza-crown ethers [6] and thioethers [7] are acylated with 6,6'-bis(chlorocarboxyl)-2,2'-dipyridyl. A porphyrin-like macrocycle was obtained by the high-temperature cyclization of 6,6'-dichloro-2,2'-dipyridyl in the presence of ammonium tetrachlorozincate [8]. The usual method of synthesizing aza-crown compounds is to condense sodium salts of sulfonyl derivatives of primary polyamines with 6,6'-bis(chloromethyl)-2,2'-dipyridyl [9].

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*See [1] for Communication 3 in this series.

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