## [Contribution from the Research Laboratories of the Goodyear Tire & Rubber Co. and the Department of Chemistry of The University of Texas]

# REACTIONS IN THE THIAZOLE SERIES. II. THE REACTION OF 2-CHLOROBENZOTHIAZOLE WITH THIOUREA IN AQUEOUS MEDIA

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It has been shown previously<sup>1</sup> that reactions between organic halides and thiourea lead to the formation of stable addition compounds, mercaptans, sulfides, or disulfides. It was shown that 2-chlorobenzothiazole and thiourea react quantitatively in alcoholic solution to form 2-mercaptobenzothiazole,



Further study has shown that when these substances react in aqueous media (in which the chloro compound is practically insoluble), there is obtained both 2-mercaptobenzothiazole and 2,2'-dibenzothiazyl sulfide. The formation of the latter may be explained by assuming that the intermediate addition compound postulated in equation 1 reacts with another molecule of the 2-chloro compound:<sup>2</sup>



<sup>&</sup>lt;sup>1</sup> Scott and Watt, J. Org. Chem., 2, 148-56 (1937).

<sup>&</sup>lt;sup>2</sup> Cf., ROSENHAUER, HOFFMAN, AND HEUSER, Ber., 62B, 2730-6 (1929).

By altering the experimental conditions, it was found possible to cause the formation of either the mercaptan or sulfide to predominate. A somewhat detailed study was made of the influence of concentration, time, temperature, and the nature of the reaction medium upon the course of this reaction.

No evidence of the formation of either mercaptan or sulfide was obtained when 2-chlorobenzothiazole and thiourea were brought together in liquid ammonia at  $-33.5^{\circ}$  or at room temperature either in the presence or absence of ammonium bromide (an acid in liquid ammonia). However, it was found that both thiourea and the thiazole enter into reaction with the solvent at room temperature. These reactions are being studied in more detail.

#### EXPERIMENTAL

*Materials.*—2-Chlorobenzothiazole was prepared and purified as previously described.<sup>1</sup> The thiourea used was a commercial product purified by repeated recrystallization from water.

Procedure.—One-tenth mole each of 2-chlorobenzothiazole (17 g.) and thiourea (7.6 g.) and 50 cc. of water contained in a 250 cc. flask\* were stirred rapidly and continuously for 80 hours by means of an air-driven stirrer. The resulting white precipitate was filtered and washed twice with small portions of water. (In all cases involving the use of mixtures of water and organic solvents, the reaction mixture was diluted with 200 cc. of cold water and allowed to stand for one-half hour prior to filtration.) The solid product was extracted twice with 50 cc. portions of cold 10 per cent sodium hydroxide solution and filtered. The alkali-insoluble solid was washed twice on the filter with small portions of petroleum ether to remove any unchanged 2-chlorobenzothiazole. When dry, this product weighed 5.8 g. Recrystallization from alcohol gave fine needle-like crystals of 2,2'-dibenzothiazyl sulfide, m.p. 98.7-99.1° (corr.). The melting point of a mixture with a sample of the sulfide prepared by an independent method gave no depression.

Anal., Calc'd for C14H8N2S3: N, 9.33; S, 32.00.

Found: N, 9.48; S, 32.13.

The combined alkaline extracts and washings were extracted with ether, following which the aqueous layer was acidified with dilute hydrochloric acid. The precipitated 2-mercaptobenzothiazole was filtered, washed with cold water, dried, and found to weigh 0.55 g. The mercaptan thus obtained was of a high degree of purity and melted at 179.2–180° (corr.). The melting point of this product was not depressed by mixing with a specimen of the mercaptan prepared by another method.

In Table I are presented data obtained as described above. Data given in Table II relate to reactions which occurred in acid media,<sup>†</sup> while results obtained using water-alcohol and water-acetone mixtures are given in Table III. Unless otherwise specified, each experiment involved reaction at room temperature between one-tenth mole each of 2-chlorobenzothiazole and thiourea in the indicated volume of solvent

<sup>\*</sup> Reactions effected above room temperature were carried out in a 3-necked flask equipped with an air-driven stirrer, a thermometer, and a reflux condenser.

<sup>†</sup> No reaction occurs between 2-chlorobenzothiazole and thiourea in the presence of aqueous alkali at room temperature.

and over the given period of time. Repeated experiments under representative sets of experimental conditions showed that the yield data are subject to variation within the range,  $\pm 4$  per cent.

### DISCUSSION

The experimental data presented in Table I show: (1) that the yields of both mercaptan and sulfide are decreased with decrease in concentration; (2) that at any particular concentration the yields increase with increase in time of reaction; and (3) that the rate at which these reactions approach completion is increased by the presence of an excess of either thiourea or of

EXPT. NO.			YIELD (%)		
	102. (00.)	IIIE (ARS.)	Sulfide	Mercaptar	
13	50	52	_	9	
30ª	50	52	39	19	
48	25	80	65	28	
10	50	80	39	3	
42 <sup>5</sup>	50	112	8	92	
49	75	80		5	
12	75	112	35	1	
11	75	148	70	24	
51	50	112	42	44	
28°	50	112	56	35	
34 <sup>d</sup>	50	112	19	73	
52	50	148	. 33	50	
<b>7</b> °	50	4	32	66	

TABLE IReactions in Water at 25°.

<sup>a</sup> Reaction in presence of 0.05 mole of 2-mercaptobenzothiazole.

<sup>b</sup> Reaction in presence of excess thiourea (0.1 mole).

• Reaction in presence of 0.1 mole of 2-mecaptobenzothiazole.

<sup>d</sup> Reaction in presence of excess thiourea (0.05 mole).

• Reaction at 95°.

2-mercaptobenzothiazole. The influence of temperature upon the velocity of the reactions is shown by the data of experiment 7.

Preliminary experiments showed that the sulfide is not formed by the direct interaction of 2-chlorobenzothiazole and 2-mercaptobenzothiazole either in alcohol at its boiling point or in water at room temperature. Hence, some intermediate substance must be involved in the formation of the sulfide. The earlier work of Rosenhauer, Hoffman, and Heuser<sup>2</sup> on the reactions of chloroquinolines with thiourea demonstrated that either sulfide or mercaptan may be formed from addition compounds of the type postulated as an intermediate in equation 1. They obtained addition

compounds which were sufficiently stable to permit isolation. However, in the case of the reactions presently under consideration, all attempts to

NYDE NO	BEAGTAN MEDITING		YIELD (%)		
BAIT: NO.	ASACITON MEDICIA	IIME (ERS.)	Sulfide	Mercaptan	
	Sulfuric acid:				
38	0.01N	88		48	
39	0.1N	40		<b>25</b>	
37	0.5N	16		41	
44	2.0N	3	_	92	
	$Hydrochloric \ acid:$				
41	0.05N	49	57	12	
5	0.5N	24	73	6	
68	0.5N	4	19	73	
8°	0.5N	4	36	61	
43	2.0N	3	2	89	

TABLE II							
REACTIONS	IN	SULFURIC	AND	Hydrochloric	Acids	АТ	$25^{\circ}$

<sup>a</sup> Fifty cubic centimeters used in all cases.

<sup>b</sup> Reaction at 60°.

• Reaction at 95°.

### TABLE III

# Reactions in Water-Alcohol and Water-Acetone Mixtures at $25^{\circ}$

EXPT. NO.	PRACTION MEDITING	MINE (HPE )	VIELD (%)		
	REACTION REDICE		Sulfide	Mercaptan	
	Aqueous alcohol: <sup>b</sup>				
21	12.5%	112	30	54	
55	25.0	40	—	18	
20	25.0	90	26	44	
18	50.0	16		19	
54	50.0	24		51	
16	50.0	40		59	
25	50.0	112	4	90	
	Aqueous acetone: <sup>b</sup>				
27	25.0%	80	19	75	
22	50.0	24	_	38	
23	50.0	40	9	56	
53	50.0	80	11	89	

<sup>a</sup> Fifty cubic centimeters used in all cases.

<sup>b</sup> Concentration of organic solvent given in per cent. by volume.

isolate such compounds met with failure. Whether mercaptan or sulfide is formed in any given case appears to be dependent upon the stability of either the addition compound or of its dissociation products. If the addition compound itself is relatively unstable, it should be expected to decompose rapidly, yielding mercaptan in accordance with equation 1. A more stable addition compound, or a stable ion formed therefrom, however, might be expected to react as shown by equation 2, yielding the sulfide. The greater stability required in the formation of sulfide is probably due to the fact that the reaction involved occurs only very slowly.

The data of Table II show that the rate of conversion of the chloro compound to either the mercaptan or sulfide is increased markedly with increase in hydrogen-ion concentration. This increase in rate of reaction is probably due to the influence of the acids upon the solubility of the chloro compound, since thiazoles are known to be soluble in mineral acids by virtue of salt formation on the nitrogen atom in the thiazole ring.<sup>3</sup> It is of interest to note that all reactions involving the use of sulfuric acid led to the formation of mercaptan almost exclusively.<sup>‡</sup> When hydrochloric acid was used, the product predominating was dependent upon the temperature at which the reaction was effected. The marked increase in reaction velocity observed in reactions carried out at elevated temperatures and the predominance of mercaptan over sulfide in the product are probably due to the effect of temperature upon the stability of the addition compound. Earlier work has shown that compounds of this type are unstable under comparable conditions.<sup>2, 4</sup>

The manner in which the formation of the observed products may be determined by the ionization of the addition compound must also be considered. Goldschmidt and co-workers<sup>5</sup> have measured the conductance of a large number of addition compounds of alkyl halides with thiourea and substituted thioureas. They have shown that the degree of ionization in aqueous solutions is such that these substances may be considered as being relatively strong electrolytes. In alcoholic solutions, however, the degree of ionization is low, but is progressively increased by the addition of water.

The data of Table III indicate that the formation of sulfide is dependent upon the ionization of the addition compound. The formation of sulfide in water-alcohol and water-acetone mixtures occurs only when a low percentage of organic solvent is present or in reactions allowed to proceed over long periods of time. Hence it appears that the degree of ionization

<sup>3</sup> HOFMANN, Ber., 13, 15 (1880).

‡ Although no yield data for sulfide are given, traces of this product were formed in nearly every case.

<sup>4</sup> CLAUS, *ibid.*, **8**, 41-4 (1875).

<sup>5</sup> GOLDSCHMIDT AND GRINI, Z. Elektrochem., **19**, 226-34 (1913). GOLDSCHMIDT AND HOUGEN, *ibid.*, **22**, 339-49 (1916).

of the addition compound is decreased as the percentage of organic solvent is increased and this results in the formation of mercaptan rather than sulfide.

The foregoing evidence, although not wholly conclusive, indicates that the formation of 2,2'-dibenzothiazyl sulfide from 2-chlorobenzothiazole and thiourea may occur only in a medium which permits the 2-chlorobenzothiazole-thiourea addition compound to ionize to form an ion which is more stable than the addition compound itself and which is capable of reacting with 2-chlorobenzothiazole in a relatively slow reaction in which the sulfide is formed.

#### SUMMARY

1. The reaction between 2-chlorobenzothiazole and thiourea in aqueous media has been shown to result in the formation of 2-mercaptobenzo-thiazole and 2,2'-dibenzothiazyl sulfide.

2. It has been shown that the formation of the sulfide is dependent upon the formation and ionization of an intermediate addition compound.