## REACTION OF THIOUREA AND N,N'-DIPHENYLTHIOUREA WITH COMPOUNDS CONTAINING S-HALOGEN AND N-HALOGEN BONDS

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The reaction of thiourea with compounds containing a labile element-halogen bond has received very little study. It is recorded that alkylmercury bromides give alkylmercury isothiuronium bromides with thiourea [1].

$$RHgBr + SC(NH_2)_2 \rightarrow RHgSC(=NH)NH_2 \cdot HBr$$

A reaction of dialkylchlorothiophosphate with thiourea is described [2] in which an organophosphorus compound is obtained which according to the author's data has the thiourea group linked to the phosphorus atom

$$(\mathrm{RO})_{2}\mathrm{PSCl} + \mathrm{SC}\,(\mathrm{NH}_{2})_{2} \rightarrow (\mathrm{RO})_{2}\mathrm{PSSC}\,(=\mathrm{NH})\mathrm{NH}_{2}$$

In an example with butyl- and phenylsulfenyl chlorides it was shown that sulfenyl chlorides react with thiourea in acid medium to form alkyl(aryl)thioisothiuroniums [3]

$$RSCI + SC(NH_2)_2 \xrightarrow{HCOOH} RSSC(=NH)NH_2 \cdot HX$$

In the present paper the reaction of thiourea and N,N'-diphenylthiourea with compounds containing S-Hal and N-Hal bonds has been studied.

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For this we pursued a study of the reaction of thiourea with sulfenyl chlorides in acid medium. Ethylsulphenyl chloride and trichloromethylsulfenyl chloride were selected as examples. Ethylsulfenyl chloride, as was to be expected, gave with thiourea the S-ethylthioisothiuronium compound which was isolated as the picrate. The reaction of N,N'-diphenylthiourea with ethylsulfenyl chloride proceeded analogously and gave the nitrogen substituted S-ethylthioisothiuronium compound

$$C_2H_5SCl + SC(NHR)_2 \frac{CF_8COOH}{R=H, C_6H_5} C_2H_5SSC(=NR)NHR \cdot HCl$$

We failed to obtain the trichloromethylthioisothiuronium compound in the case of the reaction of trichloromethylsulfenyl chloride and thiourea. Trichloromethylsulfenyl chloride acts on diphenylthiourea as a free halogen [4] with the formation of N,N'-diphenylformamidine disulfide dihydrochloride

 $\begin{array}{c} C_{6}H_{5}NH \\ \hline \\ C_{6}H_{5}N \end{array} \\ \hline C-S-S-C \\ \hline \\ NC_{6}H_{5} \\ \hline \\ NC_{6}H_{5} \end{array} \\ \cdot 2 HCl$ 

Sulfur monochloride and sulfur dichloride were selected as other examples of compounds containing the S-Hal bond. It was shown that they also reacted with thiourea and N,N'-diphenylthiourea forming form-amidine disulfide or N,N'-diphenylformamidine disulfide.



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TABLI										
	S	tarting sub	stance							E
No. 111 series	formula	quantity,	formula	quantity.	Medium	ml	ature, °C	heating,	Substance obtained	vieia,%
Ŧ	C <sub>3</sub> H <sub>5</sub> SC1	2,5	SC (NH2)2	1,9	CF <sub>3</sub> COOH	15	~100	ىر س	C <sub>2</sub> H <sub>5</sub> SSC (=NH) NH <sub>2</sub> ·Picr	50
53	C2H.SCI	2,5	SC (NHC,H),	5,9	The same	15	~100	5	C <sub>2</sub> H <sub>5</sub> SSC (=NC <sub>6</sub> H <sub>6</sub> ) NHC <sub>6</sub> H <sub>5</sub> .Picr	64
ę	sci <sub>2</sub>	2,5	SC (NH <sub>2</sub> ) <sub>2</sub>	3,7	1	15	1820	2	[SC (=NH) NH2]2.2Picr	~100
4	sc1 <sub>2</sub>	2,0	SC (NHC <sub>6</sub> H <sup>s</sup> ) <sup>2</sup>	8,9	1	20	1820	63	[-S-C (-NC,Hs) NHC,Hs]2.2Pier	27
ۍ ۲	S2C12	2,5	The same	4,3	1	20	~100	6	The same	20
9	ccl,sci	2,5	в 2	3,1	2	15	~100	6		23
	0									
7	NBr	2,0	F E	2,5	нооон	30	70-80	9	2	16
	H <sub>2</sub> C-C		-							
80	The same	3,0	SC (NH <sub>2</sub> ) <sub>2</sub>	1,2	нсоон	20	~100	7	[SC (=-NH) NH2]2 '2Picr	10
6	r r	3,0	SC (NHC <sub>6</sub> H <sub>5</sub> ) <sub>2</sub>	3,8	CH3COCH3	50	65—70	∞	CH,C=CH	30
									C <sub>6</sub> H <sub>6</sub> N — C=NC <sub>6</sub> H <sub>6</sub> .HBr	
10	2 2	2,0	The same	2,5	CH3COC4H5	40	65—70	ø	CeH5C=CH	ਸ ਹ
									C,H,N-C-NC,H,HBr	3
11	C,H,SCI	2,0	. <b>F</b>	3,6	CH/COCH3	25	$\sim 100$	6	CH₃C=CSC,H₅	
		, 		; ;					C,He,NG=NC,Hs. Picr	07

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No. in series	Substance obtained	mp, °C	Recrystallization solvent	υ	H H	SS SS	ວ ບ	H	ß
1	C <sub>2</sub> H <sub>5</sub> SSC (=NH) NH <sub>2</sub> ··Picr	170-171	Alcohol	29,74	2,84	17,82	29,58	3,03	17,15
2	C <sub>2</sub> H <sub>5</sub> SSC (=NC <sub>6</sub> H <sub>5</sub> ) NHC <sub>6</sub> H <sub>5</sub> . Picr	143-144	*	49,06	3,63	11,92	48,73	3,70	12, 39
ന	[SC (=NH) NH <sub>2</sub> ] <sub>2</sub> ·2Picr *	165—166	Acetone + dimeth- ylformamide	27,37	1,97		27,63	1,98	
4	{SC (=-NC6H5) NHC6H5]3 · 2Picr <sup>†</sup>	223224	Alcohol + benzene	50,43 50,76	$^{2,74}_{2,89}$	6,38 6,91	49,99	3,09	7,02
ъ	CH <sub>s</sub> C=CH	243245	Acetone + alcohol	54,97	4,48	8,87	55,33	4,35	9,23
	Ś								
	C <sub>6</sub> H <sub>5</sub> NC-NC <sub>6</sub> H <sub>5</sub> . HBr								
9	CH <sub>3</sub> C=CH	187	Acetone	53,41 53,57	3,45	6,24 6,46	53,32	3,46	6,47
	C <sub>6</sub> H <sub>5</sub> N-C-NC <sub>6</sub> H <sub>5</sub> . Picr								
2	C <sub>6</sub> H <sub>5</sub> C==CH	276	Alcohoi	61,56 61,70	4,29 4,31	7,19 7,63	61,61	4,18	7,83
	S C <sub>6</sub> H <sub>5</sub> N C=NC <sub>6</sub> H <sub>5</sub> . HBr						·		
œ	CH <sup>s</sup> C=CSC <sub>4</sub> H <sub>9</sub>	157-158	Alcohol + benzene	53,57 53,50	4,44	10,78 10,40	53,50	4,31	10,93
	s, s				i.				
	G₀H₅N−Ć=NC₀H₅. Pier								
*The : men ok	specimen obtained from the reaction tained from the reaction	of SCl <sub>2</sub> and accinimide	SC(NH <sub>2</sub> ) <sub>2</sub> was an and SC(NH <sub>2</sub> ) <sub>2</sub> did 1	alyzed. not give	A mixe a depr	d sampl essed m	le with t elting p	he spec oint.	1

 $\dagger$  The specimen obtained from the reaction of CCl<sub>3</sub>SCl and SC(NH<sub>2</sub>)<sub>2</sub> was analyzed. A mixed sample with specimens obtained from the reaction of bromosuccinimide, SCl<sub>2</sub>, and S<sub>2</sub>Cl<sub>2</sub> with N,N'-diphenylthiourea did not give a depressed melting point.

The reaction of thiourea and N,N'-diphenylthiourea with compounds containing the N--Hal bond is studied with the example N-bromosuccinimide. The reactions were carried out in anhydrous formic acid and acetone. Bromosuccinimide in formic acid reacts both with thiourea and N,N'-diphenylthiourea forming formamidine disulfide and N,N'-diphenylformamidine disulfide. The reaction of bromosuccinimide with N,N'-diphenylthiourea in acetone led to quite different results. Acetone in this case is not an inert solvent but is involved in the reaction and 4-methyl-3-phenylthiazolone-2 anil hydrobromide is formed.



In the PMR spectrum of this substance a signal was detected for the  $CH_3$  protons ( $\delta = 1.85$  ppm), for the vinyl proton ( $\delta = 6.35$ ), for the phenyl protons ( $\delta_A = 7.12$ ,  $\delta_B = 7.41$ ), and for the HBr proton ( $\delta = 8.31$  ppm). The marked shift of the latter signal to weak field indicates the presence of a certain positive charge on the corresponding hydrogen atom. The assignment of the chemical shifts to rings A and B is made on the basis of a comparison of the donor properties of the nitrogen in respect to the phenyl ring. It is of course assumed that the imino nitrogen is a better electron donor and that the benzene ring adjacent to it will carry the greater negative charge; this will also determine the shift of the PMR signal to a stronger field relative to the usual position of the signal for aromatic protons. The position of the vinyl and methyl peaks agree with the usual values. These assignments are fully support by the measurements of the relative intensities of the peaks.

On substituting acetone by acetophenone we obtained the heterocyclic compound 4-phenyl-3-phenyl-thiazolone-2 anil hydrobromide

$$\begin{array}{c} C_6H_5C==CH\\ & \swarrow\\ C_6H_5N=-C==NC_6H_5\cdot HBr \end{array}$$

Its structure is also confirmed by the PMR spectrum in which signals are detected for the vinyl proton ( $\delta = 6.55$ ), for the phenyl protons ( $\delta = 7.02$ , 7.25, and 7.35), and for the HBr proton ( $\delta = 8.42$  ppm).

Evidently, the reaction of ketones with bromosuccinimide and thiourea is a general one-stage method of synthesis of thiazolone rings. This method of synthesis is similar to the known method of synthesis of thiazoles by the reaction of thiourea with ketones in the presence of such oxidizing agent as I or  $SO_2Cl_2$  [5]. The reaction of butylsulfenyl chloride with N,N'-diphenylthiourea in acetone medium also proceeded with the involvement of acetone in the reaction. The compound obtained presumably has the structure



## EXPERIMENTAL

<u>Reaction of Compounds Containing S-Cl and N-Br Bonds with Thiourea and</u> <u>N,N'-Diphenylthiourea in Acid Medium</u>. The reaction of the compounds containing S-Cl and N-Br bonds with thiourea and N,N'-diphenylthiourea in acid medium was carried out either in a flask with a stirrer or in sealed ampules (in the case of heating to ~100°C). After terminating the heating the reaction mixtures were concentrated under vacuum, the the corresponding picrates were obtained from an aliquot of the residues. The starting reactants, their quantity, the solvent and its quantity, temperature, period of heating, formula of compounds obtained, and the yield are given in Table 1 (experiments 1-8). The melting point and analysis of the compounds obtained are given in Table 2 (experiments 1-4).

<u>Reaction of Bromosuccinimide with N, N'-Diphenylthiourea and Acetone or</u> <u>Acetophenone</u>. To a solution of 3 g of bromsuccinimide in 20 ml of acetone was added dropwise with stirring a solution of 3.7 g of N, N'-diphenylthiourea in 30 ml of acetone. The reaction mixture was heated at 60-65° fro 8 h, then concentrated in vacuum. The residue was treated with hot water. After evaporation of the aqueous solution in vacuum 4-methyl-3-phenylthiazolone-2 anil hydrobromide was obtained with mp  $243-245^{\circ}$  (from acetone); the yield was 33% of theory. Found %: C 54.97; H 4.48; S 8.87. C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>SBr. Calculated %: C 55.33; H 4.35; S 9.23. The picrate had mp 187°. Found %: C 53.41; H 3.45; S 6.24. C<sub>22</sub>H<sub>17</sub>O<sub>7</sub>N<sub>5</sub>S. Calculated %: C 53.32; H 3.46; S 6.47. From the residue remaining after treatment with water there was isolated 2 g (54% of theory) of diphenylthiourea (the melting point of a mixture with authentic diphenylthiourea was not depressed) and 1.5 g (100% of theory) of succinimide (the melting point of a mixture with authentic succinimide was not depressed).

The reaction of bromosuccinimide with N,N'-diphenylthiourea in acetophenone was carried out similarly. After concentration in vacuum the residue was recrystallized from alcohol. 4-Phenyl-3-phenylthiazolone-2 anil hydrobromide (see Table 1, experiment 10 and Table 2, experiment 7) was obtained.

 $\frac{\text{Reaction of n-Butylsulfenyl Chloride with N, N'-Diphenylthiourea and Ace-}{\text{tone}}$ . The reaction was carried out in a sealed ampule as described above (see Table 1, experiment 11 and Table 2, experiment 8).

The PMR spectra were measured on a "Hitachi H-60" spectrometer. The samples were dissolved in 40% trifluoroacetic acid, measurements were carried out at a temperature of 35°, the internal standard was hexamethyldisiloxane.

The spectra were measured by E. I. Fedin and R. G. Gasanov, to whom the authors express their thanks.

## CONCLUSIONS

1. The reaction of thiourea and N,N'-diphenylthiourea with compounds containing S-Cl and N-Br bonds is studied in acid medium and in acetone or acetophenone.

2. Ethylsulfenyl chloride in trifluoroacetic acid reacts with thiourea and N,N'-diphenylthiourea forming S-ethylthioisothiuronium compounds.

3. Bromosuccinimide,  $SCl_2$ ,  $S_2Cl_2$ , and  $CCl_3SCl$  react with thiourea and N,N'-diphenylthiourea in acid medium similarly to free halogen forming adducts of structure  $[RHN(RN=)CS]_2 \cdot 2HX$ .

4. N,N'-Diphenylthiourea reacts with acetone or acetophenone forming the heterocyclic compounds.



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