ARYLATION OF THIOUREA BY ARYLDIAZONIUM SALTS

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The reaction of thiourea with aryldiazonium salts has received little study. Based on the data given in [1], the reaction of thiourea with the phenyl- and p-nitrophenyldiazonium chlorides in acetone does not lead to S-arylisothiuronium compounds. Formamidine disulfide dihydrochloride $[H_2N(HN=)CS-]_2 \cdot 2HCl$ was obtained in the first case, while $H_2N(HN=)CSN=NC_6H_4NO_2 \cdot HCl$ was obtained in the second case. The latter is an unstable diazo compound, which decomposes when recrystallized from alcohol to give formamidine disulfide dihydrochloride. In the case of p-nitrophenyldiazonium chloride, together with the latter compound, a certain amount of p-nitrophenyl disulfide was obtained, which, in the opinion of the authors, is an indirect indication of the formation of the p-nitrophenylisothiuronium compound in this reaction.

We had previously [2, 3] shown that aryldiazonium fluoborates arylate thiourea in aqueous medium to give S-arylisothiuronium fluoborates, which were isolated as the picrates.

$$ArN_2BF_4 + SC(NH_2)_2 \rightarrow ArSC(=NH)NH_2 \cdot Picr$$

In the case of p-chlorophenyldiazonium fluoborate the main reaction product was the p-phenylenediisothiuronium compound, which was also isolated as the picrate.

$$p\text{-}ClC_6H_4N_2BF_4 + SC(NH_2)_2 \rightarrow NH_2(NH=)CSC_6H_4SC(=NH)NH_2 \cdot 2\ Picr$$

Taking into account the fact that copper compounds play a major role in the reactions of aryldiazonium salts [4], in the present paper we investigated the reaction of some aryldiazonium chlorides and fluoborates with thiourea in aqueous medium, both in the presence and in the absence of $CuCl_2$. The obtained S-arylisothiuronium compounds were isolated as the picrates. In the presence of $CuCl_2$ the aryldiazonium chlorides arylate thiourea to give S-arylisothiuronium compounds.

$$ArN_2Cl + SC(NH_2)_2 \xrightarrow{CuCl_2} ArSC(=NH)NH_2 \cdot Picr$$
$$Ar = C_6H_5,\ O_2NC_6H_4,\ p\text{-}CH_3C_6H_4$$

As in the case of the arylation of thiourea with aryldiazonium fluoborates [2], we investigated aryldiazonium chlorides that contain in the benzene ring either an electron-acceptor group (NO_2) or an electron-donor group (CH_3) and also phenyldiazonium chloride.

The yields of the S-arylisothiuronium picrates, obtained in the arylation of thiourea with aryldiazonium fluoborates and chlorides in the presence of $CuCl_2$ and in its absence, are compared in Table 1. From Table 1 it can be seen that the arylation of thiourea with aryldiazonium fluoborates in the absence of $CuCl_2$ gives better yields (68%) when the electron-acceptor NO_2 group is present in the benzene ring. The absence of a substituent or the presence of the electron-donor CH_3 group lowers the yield to 10-15%. On the example of the arylation of thiourea with the p-nitrophenyl and p-tolyldiazonium fluoborates it was shown that the addition of $CuCl_2$ to the reaction mixture has little effect on the yield of the arylation product.

When thiourea was arylated with aryldiazonium chlorides in the presence of $CuCl_2$ the presence of a substituent in the benzene ring failed to exert a marked effect on the yield of the S-arylisothiuronium salt. The arylation of thiourea with phenyldiazonium chloride in the absence of $CuCl_2$ failed to give the S-phenylisothiuronium salt; only a small amount (~ 9%) of formamidine disulfide dipicrate was isolated.

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TABLE 1. Arylation of Thiourea by Aryldiazonium Salts p-$XC_6H_4N_2Y$

X	Y	Catalyst	Yield of $XC_6H_4SC(=NH)$-NH_2·Picr, %
H	Cl	None	—
H	Cl	$CuCl_2$	20
CH_3	Cl	$CuCl_2$	10—18
NO_2	Cl	$CuCl_2$	30
CH_3	BF_4	$CuCl_2$	11
NO_2	BF_4	$CuCl_2$	63
H	BF_4	None	10 [2]
CH_3	BF_4	"	15 [2]
NO_2	BF_4	"	68 [2]

TABLE 2. Arylation of Thiourea by p-Chlorophenyldiazonium Salts p-$ClC_6H_4N_2Y$

Y	Catalyst	Yield of products, *%	
		(I)	(II)
BF_4 [2]	None	25	—
BF_4	$CuCl_2$	<1	15
Cl	None	12	—
Cl	$CuCl_2$	<1	35

* (I) — p-$H_2N(HN=)CSC_6H_4SC(=NH)NH_2$·2Picr; (II) — p-$ClC_6H_4SC(=NH)NH_2$·Picr.

Interesting results were obtained when p-chlorophenyldiazonium fluoborate and the chloride were used to arylate thiourea. As can be seen from Table 2, the arylation of thiourea with p-chlorophenyldiazonium fluoborate in the absence of a catalyst gave the p-phenylenediisothiuronium compound in 25% yield, which was isolated as the picrate. As a result, both the diazonium group and the chlorine atom were replaced by the isothiuronium moiety in the given case. The formation of a noticeable amount of the p-chlorophenylisothiuronium salt was not observed. When this reaction was run in the presence of $CuCl_2$ the p-chlorophenylisothiuronium compound was obtained in 15% yield, while the yield of the p-phenylenediisothiuronium compound was less than 1%.

The arylation of thiourea with p-chlorophenyldiazonium chloride proceeds in a similar manner. Only the p-phenylenediisothiuronium compound was obtained (12% yield) in the absence of $CuCl_2$, while in the presence of the catalyst the main product was the S-p-chlorophenylisothiuronium compound (35% yield). As a result, the aryldiazonium chlorides can be used for the arylation of thiourea provided the reaction is run in the presence of $CuCl_2$.

In some cases the reaction goes in different directions when run in the presence of $CuCl_2$ and in its absence. Thus, for example, p-chlorophenyldiazonium chloride (or the fluoborate) in the absence of $CuCl_2$ gives the p-phenylenediisothiuronium compound, and the p-chloroisothiuronium compound in the presence of $CuCl_2$, which compound can be used for the synthesis of isothiuronium compounds and thiols.

The fact that thiourea is arylated on the sulfur atom, and not on nitrogen, was proved by the identity of the p-tolyl- and p-nitrophenylisothiuronium picrates, obtained in this manner, with the authentic compounds. The same direction for the arylation of thiourea with p-chlorophenyldiazonium chloride in the presence of $CuCl_2$ was proved by the preparation of p-chlorothiophenol in good yield from p-chlorophenylisothiuronium chloride, with the intermediate formation of the bicarbonate, by the following scheme.

$$p\text{-}ClC_6H_4N_2Cl + SC(NH_2)_2 \xrightarrow{CuCl_2} p\text{-}ClC_6H_4SC(=NH)NH_2 \cdot HCl \rightarrow p\text{-}ClC_6H_4SC(=NH_2)NH_2 \cdot HCO_3 \rightarrow ArSH$$

The S-p-chlorophenylisothiuronium salts (chloride and bicarbonate) were not isolated from the reaction mixture.

EXPERIMENTAL METHOD

Reaction of Thiourea with Phenyldiazonium Chloride in the Presence of $CuCl_2$. With stirring, to a solution of 7.6 g of thiourea and 1.7 g of $CuCl_2 \cdot 2H_2O$ in 50 ml of water was added at 35-40°C a solution of phenyldiazonium chloride that had been prepared from 4.6 g of aniline and 3.7 g of $NaNO_2$. On conclusion of gas evolution the mixture was heated for another 1 h, and then it was extracted with $CHCl_3$ and the aqueous layer was separated. The addition of an alcohol solution of picric acid to an aliquot portion of the aqueous layer gave S-phenylisothiuronium picrate in 25% yield, mp 214-215° (from alcohol). The mixed melting point with an authentic specimen was not depressed.

The reaction of thiourea with the p-tolyl- and p-nitrophenyldiazonium chlorides was run in a similar manner. The reaction of thiourea with p-nitrophenyldiazonium chloride is exothermic and the temperature of the reaction mixture rises to 40-43°. The obtained S-arylisothiuronium compounds were isolated as the picrates and were identified by the fact that the mixed melting points with the authentic specimens [2] were not depressed. The yields of the S-arylisothiuronium picrates are given in Table 1.

Reaction of Thiourea with p-Chlorophenyldiazonium Chloride in the Presence of $CuCl_2$. The experiment was run the same as the preceding. For reaction we took 8 g of thiourea, 1.7 g of $CuCl_2 \cdot 2H_2O$ and the p-chlorophenyldiazonium chloride that was obtained from 6.4 g of p-chloroaniline and 3.7 g of $NaNO_2$. The S-p-chlorophenylisothiuronium picrate $p\text{-}ClC_6H_4SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH$ was obtained in 37% yield, mp 212° (from alcohol). The mixed melting point with an authentic specimen [2] was not depressed. Found: C 37.42; H 2.55; S 7.85; Cl 8.67; N 16.67%. $C_{13}H_{10}O_7N_5SCl$. Calculated: C 37.55; H 2.42; S 7.71; Cl 8.54; N 16.84%. The p-phenylenediisothiuronium dipicrate was also isolated in less than 1% yield. Found: C 34.86; H 2.45; N 19.22%. $C_{20}H_{16}O_{14}S_2N_{10}$. Calculated: C 35.08; H 2.35; N 20.46%.

Reaction of Thiourea with p-Chlorophenyldiazonium Fluoborate in the Presence of $CuCl_2$. A mixture of 2.3 g of p-chlorophenyldiazonium fluoborate, 1.52 g of finely ground thiourea, 0.34 g of $CuCl \cdot 2H_2O$ and 10 ml of water was heated at 50-60° until the gas evolution ceased. The obtained dark red solution was extracted with $CHCl_3$. The addition of an alcohol solution of picric acid to the aqueous layer gave a mixture of S-p-chlorophenylisothiuronium picrate and p-phenylenediisothiuronium dipicrate. The picrates could be separated by washing with hot alcohol, in which the dipicrate is insoluble. The yield of the p-chlorophenylisothiuronium picrate was 15%, mp 212°. The yield of the dipicrate was less than 1%.

Reaction of Thiourea with p-Chlorophenyldiazonium Chloride in the Absence of $CuCl_2$. With stirring, to a solution of 7.6 g of thiourea in 50 ml of water was added a solution of the p-chlorophenyldiazonium chloride that had been obtained from 6.4 g of p-chloroaniline and 3.7 g of $NaNO_2$. A rise in the temperature was not observed here. The mixture was heated at 40° for 2 h, after which it was extracted with $CHCl_3$ and the aqueous layer was separated. The addition of an alcohol solution of picric acid to an aliquot portion of the aqueous layer, followed by washing with hot alcohol, gave a 12% yield of p-phenylenediisothiuronium picrate, mp 245°.

Reaction of Thiourea with p-Tolyldiazonium Fluoborate in the Presence of $CuCl_2$. To a suspension of 2.06 g of p-tolyldiazonium fluoborate in 5 ml of water was added a solution of 1.52 g of thiourea and 0.34 g of $CuCl_2 \cdot 2H_2O$ in 5 ml of water. The reaction begins at 50-60°. At the end of gas evolution the mixture was allowed to stand overnight, after which it was diluted with water and extracted with benzene. The addition of an alcohol solution of picric acid to an aliquot portion of the aqueous solution gave S-p-tolylisothiuronium picrate in 11% yield, mp 211-212° (from a mixture of alcohol and DMF). The mixed melting point with an authentic specimen was not depressed.

S-p-Nitrophenylisothiuronium picrate was obtained in a similar manner in 63% yield, and it was identified by the fact that its mixed melting point with an authentic specimen was not depressed.

Preparation of p-Chlorothiophenol. The reaction of p-chlorophenyldiazonium chloride with thiourea was run in the presence of $CuCl_2 \cdot 2H_2O$, as described above. After neutralization with dry $NaHCO_3$, the obtained aqueous layer was treated with a conc. solution containing ~15 g of $NaHCO_3$. The reaction mixture was refluxed for 2 h, and then it was acidified with dilute HCl solution. The obtained oily precipitate was extracted with $CHCl_3$. After distilling off the $CHCl_3$ the p-chlorothiophenol [5] was vacuum-distilled, mp 54° (from alcohol). The yield was 20% (when based on p-chloroaniline), or 70% (when based on the S-p-chlorophenylisothiuronium salt). Found: C 49.98; H 3.50%. C_6H_5ClS. Calculated: C 49.81; H 3.46%.

CONCLUSIONS

1. In the presence of cupric chloride, aryldiazonium chlorides arylate thiourea to give S-arylisothiuronium compounds.

2. In the absence of $CuCl_2$, the reaction of the p-chlorophenyldiazonium fluoborate and chloride with thiourea gives the p-phenylenediisothiuronium compound, and the p-chlorophenylisothiuronium compound in the presence of $CuCl_2$.

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