SYNTHESIS OF AROMATIC ISOTHIOUREA COMPOUNDS CONTAINING SUBSTITUENTS IN THE BENZENE RING

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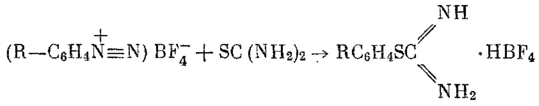
UDC 542.91+547.496.3

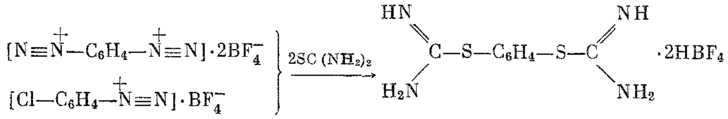
The only known method of synthesizing 5-arylisothiourea compounds is by the reaction of aryl mercaptans with cyanamide. S-Phenyl-, S-p-tolyl-, and 5-p-chlorophenylisothiourea [1] were synthesized in this way. The method cannot have broad application because of the difficultly accessible aryl mercaptans containing substituents in the benzene ring. Recently, two of us proposed a new method of synthesis of S-arylisothiourea compounds by arylation of thioureas with aryl diazonium borofluorides [2].



$$(R{-}C_6H_4\overset{+}{N}{\equiv}N)\,BF_4^- + SC(NH_2)_2 \rightarrow RC_6H_4SC\begin{smallmatrix}\diagup NH\\ \diagdown NH_2\end{smallmatrix}\cdot HBF_4$$

R=H, p-NO_2-, o-NO_2-, p-C_2H_5OOC-, CH_3O-, CH_3-,

In the same paper, diisothiourea compounds obtained in two ways, starting from p-phenylenebisdiazonium and p-chlorophenyldiazonium borofluorides, were described.

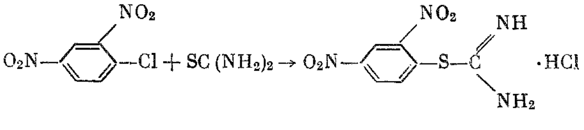


$$\left.\begin{matrix}[N{\equiv}\overset{+}{N}{-}C_6H_4{-}\overset{+}{N}{\equiv}N]\cdot 2BF_4^-\\ [Cl{-}C_6H_4{-}\overset{+}{N}{\equiv}N]\cdot BF_4^-\end{matrix}\right\}\xrightarrow{2SC(NH_2)_2}\begin{smallmatrix}HN\diagdown\\ H_2N\diagup\end{smallmatrix}C{-}S{-}C_6H_4{-}S{-}C\begin{smallmatrix}\diagup NH\\ \diagdown NH_2\end{smallmatrix}\cdot 2HBF_4$$

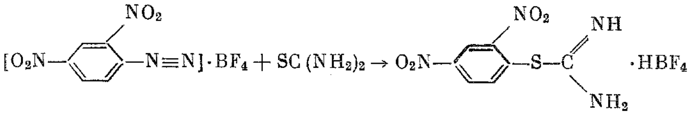
In the last case, the diazonium group (strong electron-accepting substituent) facilitates nucleophilic substitution of chlorine in the position para to it.

In this paper, the application of this method is described in synthesis of aromatic isothiourea compounds containing the following substituents in the ring: halogen atoms (one or two), two nitro groups, and the isothiourea group simultaneously with a halogen.

We found that upon reaction of thiourea with o-chlorophenyldiazonium borofluoride, the chlorine in the o-position is not substituted by an isothiourea residue under the studied conditions, which is evidently associated with steric hindrance. As, was also expected, the chlorine in the position meta to the diazonium group is not substituted by the isothiourea residue. The diisothiourea compound containing the isothiourea group and a halogen simultaneously in the ring was obtained upon reaction of thiourea and 2,4-dibromophenyldiazonium borofluoride. In addition, we found that under the effect of two nitro groups located ortho and para to the chlorine, the latter is substituted by the isothiourea residue.

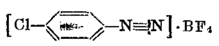
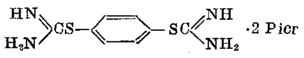
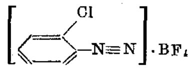
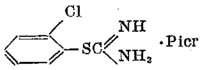
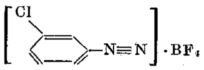
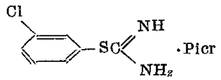
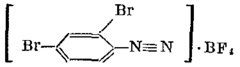
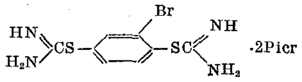
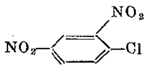
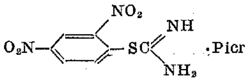
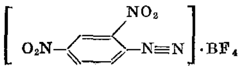
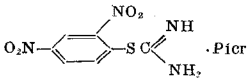


The structure of the obtained compound was demonstrated by direct synthesis by the reaction of 2,4-dinitrophenyldiazonium borofluoride with thiourea.



Institute of Heteroorganic Compounds, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk, Seriya Khimicheskaya, No. 8, pp. 1910-1913, August, 1968. Original article submitted February 28, 1968.

TABLE 1

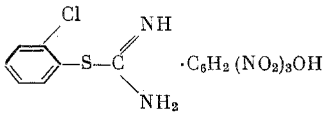
Starting borofluoride	Obtained materials	mp, °C	Yield, % of theor.	Found, %				Calculated, %			
				C	H	S	N	C	H	S	N
		253	30	35.22 34.96	2.45 2.48	9.13 9.23		35.08	2.35	9.36	
		225-226	90	37.64	2.47	6.34	16.89	37.55	2.42	7.71	16.84
		209-210	30	37.08	2.68	6.74		37.55	2.42	7.71	
		225	60	31.37	2.10	8.84		31.46	1.98	8.40	
		186-187	40	33.27	2.10	6.23		33.12	1.92	6.80	
		186-187	12								

Bis-2,4-dinitrophenyl sulfide was obtained as a by-product of the reaction of 2,4-dinitrochlorobenzene with thiourea.

Reactions were carried out in water at a temperature of 50-60°C. Increasing the reaction temperature to 100° did not lead to substitution of the halogen in the positions ortho and meta to the diazonium group. We showed on the examples of 3,4-dichlorophenyldiazonium and o-chlorophenyldiazonium borofluorides, that addition of catalytic amounts of zinc dust makes it possible to lower the reaction temperature and also facilitates the isolation of the isothiourea compound from the reaction mixture. The obtained S-arylisothiourea compounds were isolated in the form of picrates.

EXPERIMENTAL

Reaction of o-Chlorophenyldiazonium Borofluoride with Thiourea. To a mixture of 1 g of o-chlorophenyldiazonium borofluoride and 0.6 g of finely crushed thiourea was poured 3 ml of water. The reaction mixture was heated at 50-60° until evolution of gas ceased. The dark red solution was filtered from the tarry residue and extracted 2-3 times with benzene. From half of the filtrate by addition of an alcoholic solution of picric acid was obtained 0.8 g of the picrate of o-chlorophenylisothiourea.



The reactions of thiourea with m-chlorophenyldiazonium, 3,4-dichlorophenyldiazonium, and 2,4-dibromophenyldiazonium borofluorides were carried out analogously. The starting substituted aryldiazonium borofluorides, the obtained S-arylisothiourea compounds (isolated as picrates), their melting points, yields, and analysis are presented in Table 1.

Reaction of Thiourea with 2,4-Dinitrobenzene in Acetone. A mixture of 2 g of 2,4-dinitrochlorobenzene and 0.7 g of thiourea was dissolved in 20 ml of acetone. The reaction mixture was heated in a flask with a reflux condenser for 6 h. After evaporation of the solvent on a rotary evaporator, an oily material containing a precipitate remained. The oil was dissolved in alcohol, the solution was filtered from the precipitate, and the picrate of S-2,4-dinitrophenylisothiourea (yield, mp, and analysis presented in Table 1) was obtained from the alcoholic solution. The residue, bis-2,4-dinitrophenyl sulfide, was recrystallized from acetone, mp 193-195°. Literature data [3]: mp 193°. Found %: C 39.48; H 1.59; S 9.13. $C_{12}H_6O_8N_4S$. Calculated %: C 39.35; H 1.65; S 8.75. Direct synthesis of the picrate of S-2,4-dinitrophenylisothiourea by reaction of thiourea and 2,4-dinitrophenyldiazonium borofluoride was carried out as described in the preceding experiment. A mixed sample of both picrates did not give a melting point depression.

CONCLUSIONS

Arylation of thiourea with aryldiazonium borofluorides containing substituents in the benzene ring yielded isothiourea compounds containing halogen atoms, the nitro group, and the isothiourea group in the ring.

LITERATURE CITED

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2. R. Kh. Freidlina and B. V. Kopylova, Dokl. Akad. Nauk SSSR, 173, 839 (1967).
3. F. Beilstein and A. Kurbatow, Liebigs Ann. Chem., 197, 77 (1879).