OXIDATIVE CYCLIZATION OF 4-ARYLTHIO-SEMICARBAZONES

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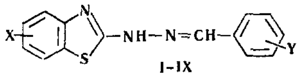
2-Benzothiazolylhydrazones were synthesized by the action of bromine on 4-arylthiosemicarbazones. The imino structure of the cyclization products was demonstrated by comparison of the UV spectra of the hydrazones and the methylation product. Cyclization to the thiadiazole derivative was noted when bromine was present in the aryl ring of the thiosemicarbazone. A dimethylamino group in the aldehyde portion of the molecule prevents cyclization.

In a letter to the editor [1], one of us reported a new method for obtaining 2-hydrazinobenzothiazoles and naphthothiazoles, which are produced by the action of bromine on the corresponding 4-arylthiosemicarbazides via the method proposed for the synthesis of aminobenzothiazoles from arylthioureas [2]. This reaction is accompanied by appreciable resinification during the cyclization of 4-phenylthiosemicarbazide. We were unable to obtain 6-bromo-2-hydrazinobenzothiazole from 4-(p-bromophenyl)thiosemicarbazide via this method.

Hydrazones of the benzothiazole series, the synthesis of which presents considerable difficulties, serve as the starting compounds for obtaining formazans which have benzothiazolyl substituents. It should have been expected that cyclization of 4-arylthiosemicarbazones by the action of bromine via the method in

TABLE 1



I-IX

Compound	X	Y	mp	Appearance*	λ_{max}	lg ε	Empirical formula	N, % found	N, % calc.	Yield, %
I	H	H	220—222[3]	Light-yellow needles	332	4,47	$C_{14}H_{11}N_3S$	16,9	16,6	99
II	6-CH_3	H	244—245	Light-yellow prisms	338	4,45	$C_{15}H_{13}N_3S$	15,5	15,7	99
III	4-CH_3	H	242—243	Colorless needles	340	4,42	$C_{15}H_{13}N_3S$	15,5	15,7	100
IV	6-OC_2H_5	H	194—196	Colorless plates	337	4,45	$C_{16}H_{15}N_3OS$	13,9	14,1	95
V	H	3-CH_3	199—200	Colorless needles	335	4,49	$C_{15}H_{13}N_3S$	15,5	15,7	100
VI	H	4-Br	270—271	Colorless prisms	345	4,52	$C_{14}H_{10}BrN_3S$	12,8	12,8	90
VII	H	4-NO_2	257—259	Yellow prisms	395	4,35	$C_{14}H_{10}N_4O_2S$	18,5	18,8	100
VIII	H	3-NO_2	250—251	Light-yellow needles	340	4,33	$C_{14}H_{10}N_4O_2S$	18,3	18,8	100
IX	H	4-$N(CH_3)_2$	238—239	Light-yellow prisms	360	4,63	$C_{16}H_{16}N_4S$	18,8	18,9	33

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*Compound III was crystallized from aqueous dimethylformamide, VII from dimethylformamide, VI and IX from butanol, and the rest from ethanol.

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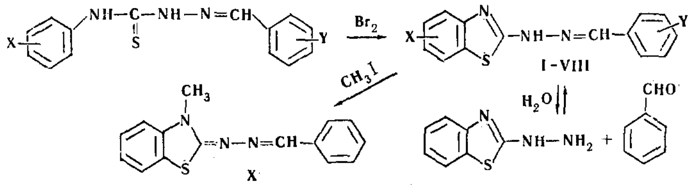
[2] would be suitable for the preparation of these compounds. In fact, we have established that cyclization of 4-arylthiosemicarbazones to the corresponding benzothiazolylhydrazones proceeds mildly with good yields (Table 1), during which absolutely no resinification of the reaction products occurs. A sample of benzaldehyde benzothiazolylhydrazone (I) synthesized by this method mixed with the compound obtained from 2-hydrazinobenzothiazole and benzaldehyde did not give a melting-point depression. Compound I is hydrolyzed to give a low yield of 2-hydrazinobenzothiazole on refluxing for many hours in hydrochloric acid.



Cyclization does not occur in the case of p-dimethylaminobenzaldehyde 4-phenylthiosemicarbazone; the nitrogen atom of the dimethylamino group probably complexes with bromine. Reaction between 2-hydrazinobenzothiazole and p-dimethylaminobenzaldehyde was accomplished to obtain p-dimethylaminobenzaldehyde benzothiazolylhydrazone (IX).

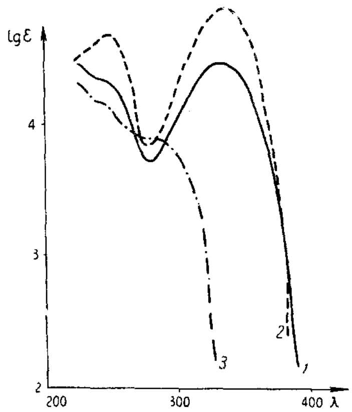


Fig. 1. UV spectra of 10^{-5} M solutions in ethanol: 1) benzaldehyde 2-benzothiazolylhydrazone (I); 2) benzaldehyde 3-methylbenzothiazolidene-2-hydrazone (X); 3) 2-(p-bromoanilino)-5-phenyl-1,3,4-thiadiazole (XI).

The UV spectra of hydrazones I-IX are similar and have long-wave maxima in the 330-340 nm region. Dimethylamino and nitro groups in the para position of benzaldehyde shift the absorption maximum appreciably to the long-wave side (Table 1); when alkali is added, the colorless alcoholic solutions of the hydrazones become yellow and the absorption maximum is shifted to 410-420 nm. Addition of acid to the alkaline solution results in decoloration. A methylation product at the cyclic nitrogen atom (X) was obtained by methylation of I with methyl iodide in alkaline medium. The UV spectrum of X recalls the spectrum of starting I, which indicates the imino structure of the benzothiazolylhydrazones of aromatic aldehydes.

A compound whose UV spectrum differs from the spectra of the hydrazones (Fig. 1) was obtained by cyclization of benzaldehyde 4-(p-bromophenyl)thiosemicarbazone. This product is insoluble in alkali and does not undergo hydrolysis on refluxing in hydrochloric acid; alkalation was not observed on heating with methyl iodide. On the basis of the results obtained, we consider that cyclization to a benzothiazolyl derivative is not accomplished, but that 2-(p-bromoanilino)-5-phenyl-1,3,4-thiadiazole (XI) is formed.

EXPERIMENTAL

Benzaldehyde Benzothiazolylhydrazone (I). Bromine [0.5 ml (0.01 mole)] in 10 ml of chloroform was added to a solution of 2.55 g (0.01 mole) of benzaldehyde 4-phenylthiosemicarbazone in 30 ml of chloroform, and the mixture was stirred for 30 min at room temperature and refluxed for another 30 min. The chloroform was distilled off, 20 ml of water was added, the residual chloroform was removed, and 2.5 g of I was filtered off (Table 1).

Hydrazones II-VIII were similarly obtained (Table 1).

Dimethylaminobenzaldehyde Benzothiazolylhydrazone (IX). 2-Hydrazinobenzothiazole [0.2 g (0.012 mole)] was dissolved in 5 ml of ethanol, 0.18 g (0.012 mole) of dimethylaminobenzaldehyde was added, and the mixture was refluxed for 10 min, cooled, and 0.12 g of IX was filtered off (Table 1).

Benzaldehyde 3-Methylbenzothiazolidene-2-hydrazone (X). Compound I [1.66 g (6.6 mmole)] was dissolved in 5 ml of 2 N sodium hydroxide, 10 ml of ethanol and 2 ml (32 mole) of methyl iodide were added, the mixture was refluxed for 30 min, and the alcohol and excess methyl iodide were removed in vacuo at room temperature after standing for 24 h. The residue was diluted with water and filtered to give 1 g (53%) of X with mp 119-120° (prisms from ethanol). Found %: C 67.8; H 5.1; N 15.3. $C_{15}H_{13}N_3S$. Calculated %: C 67.4; H 4.9; N 15.7.

2-(p-Bromoanilino)-5-phenyl-1,3,4-thiadiazole (XI). Benzaldehyde 4-(p-bromophenyl)thiosemicarbazone [3.34 g (0.01 mole)] was dissolved in 30 ml of chloroform, 0.5 ml (0.01 mole) of bromine in 10 ml of chloroform was added, and the mixture was stirred and refluxed for 30 min until hydrogen bromide evolution ceased. The chloroform was removed, 20 ml of water was added, and the residue was boiled until the chloroform was completely removed. The residue was filtered and crystallized from isopropyl alcohol to give 3.3 g (100%) of XI with mp 255-256° (colorless needles). Found %: C 50.4; H 3.3; N 12.8. $C_{14}H_{10}N_3S$. Calculated %: C 50.6; H 3.0; N 12.6.

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