[Contribution from the Baker Laboratory of Chemistry at Cornell University]

THE OXIDATION OF 2-AMINOBENZOTHIAZOLES[1]

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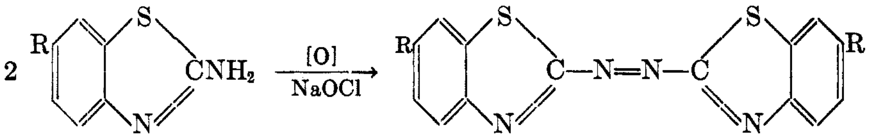
The so-called safety papers used in legal documents, checks, etc. are treated chemically during manufacture so as to prevent alteration by erasure and insertion. The 2-aminobenzothiazoles are an important group of substances which are used effectively in the protection of paper against forgery. Paper impregnated with a 2-aminobenzothiazole will develop a deep colored blot almost instantly when an ink eradicator (usually a hypochlorite solution) is applied. This action of a hypohalite (bleaching powder) on substituted 2-aminobenzothiazoles was first observed by Fischer and Besthorn (1) in 1882. However, neither they, nor subsequent investigators (2) determined the structure of the reaction products. Accordingly, the present study of the bright colored products of the sodium hypochlorite oxidation of various 2-aminobenzothiazoles was undertaken. Six different 2-aminobenzothiazoles were studied, particular attention being given to 2-amino-6-methylbenzothiazole and 2-amino-6-chlorobenzothiazole.

Oxidation was carried out by the addition of aqueous sodium hypochlorite to a solution of the 2-aminobenzothiazole in dioxane. Pure substances were isolated with difficulty from the crude reaction products by a procedure of extraction and sublimation in a high vacuum. The purified compounds were all bright red, insoluble, crystalline solids which melted with decomposition in the neighborhood of 300–350° and which exhibited red-yellow pleochroism. Elementary analyses indicated two atoms of hydrogen were removed from the 2-aminobenzothiazole in the oxidation. This suggested that the bright colored products were azo compounds formed by oxidation of the amino group as follows:



$R = H, CH_3, Cl, Br, \text{and } OC_2H_5$

That oxidation of the amino group had occurred was shown by attempting a hypochlorite oxidation of acyl derivatives of certain of the 2-aminobenzothiazoles. No reaction was observed when either 2-benzoylamino-6-methylbenzothiazole or 2-acetylamino-6-chlorobenzothiazole was treated with aqueous

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[1] This paper is an abstract of a portion of the doctoral dissertation of William Kirk, Jr., submitted to the Graduate Faculty of Cornell University in February, 1943.

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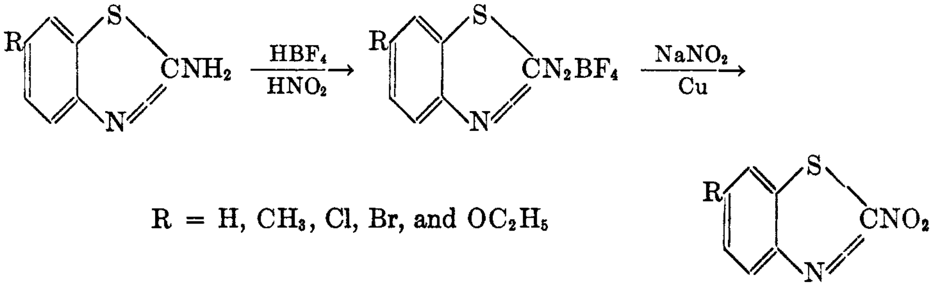
sodium hypochlorite. However, 2-acetylamino-6-methylbenzothiazole did give the characteristic red-brown precipitate when treated with the hypohalite. Presumably in this latter case the acetyl derivative was very readily hydrolyzed by the alkaline solution, liberating the free aminobenzothiazole.

In view of the fact that Bogert (3) has assigned an azo structure to the chloramine yellow type of dyes which are prepared by the action of sodium hypochlorite on substituted 2-(*p*-anilino)benzothiazoles, the azo structure for the compounds formed in the oxidation of the 2-aminobenzothiazoles appeared reasonable.

Confirmation of this postulation was obtained by an independent synthesis of the substituted 2-azobenzothiazoles.

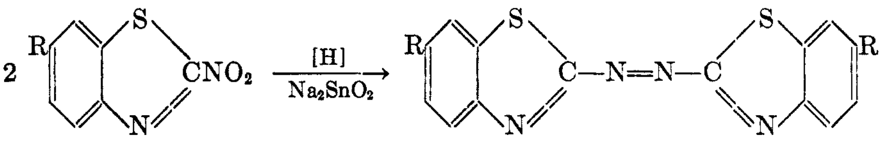
A series of substituted 2-nitrobenzothiazoles was prepared from the 2-aminobenzothiazoles through the diazonium fluoborates according to the following:



R = H, CH_3, Cl, Br, and OC_2H_5

The 2-nitrobenzothiazoles were identified by reduction to the corresponding 2-aminobenzothiazoles which in turn were converted to the acetyl derivatives. Mixed melting points of these derivatives with the acetyl derivatives of authentic specimens of 2-aminobenzothiazoles confirmed the identity. The 2-nitrobenzothiazoles which were prepared are listed in Table I.

The substituted 2-nitrobenzothiazoles were reduced readily by sodium stannite to the corresponding 2-azobenzothiazoles.



R = H, CH_3, Cl, Br, and OC_2H_5

The 2-azobenzothiazoles prepared in this manner (Table II) were identical with the products obtained by the hypochlorite oxidation of the corresponding 2-aminobenzothiazoles. There was exact agreement in melting point and mixed melting point. The identity of the compounds was also confirmed by microscopical examination.

Attempts to effect a reductive cleavage of the azo compound to 2-aminobenzothiazoles by chemical methods were unsuccessful. This was probably due to the extreme insolubility of the compounds in the usual solvents. Catalytic reduction

TABLE I

SUBSTITUTED 2-NITROBENZOTHIAZOLES

BENZOTHIAZOLE	AVERAGE YIELD, %[a]	M.P., °C (UNCORR.)	% NITROGEN	
			Calc'd	Found
2-Nitro-	33.3	157–158	15.56	15.82 15.79
2-Nitro-6-methyl-	8.5	131–132	14.43	14.28 14.39
2-Nitro-6-ethoxy-	2.6	151–152	12.50	12.56 12.56
2-Nitro-6-chloro-	11.2	160–161	13.05	13.19 13.07
2-Nitro-6-bromo-	4.4	179–180	10.81	10.86 10.75
2-Nitro-4-methyl-	16.9	152–153	14.43	14.23 14.48

[a] This is the average yield from three or more runs starting with 5 g. of the corresponding 2-aminobenzothiazole.

TABLE II

2-AZOBENZOTHIAZOLES FROM 2-NITROBENZOTHIAZOLES BY REDUCTION WITH SODIUM STANNITE[a]

2-AZOBENZOTHIAZOLE	COLOR	M.P., °C (UNCORR.)[b]	% YIELD[c]	ANALYSIS	
				Calc'd	Found
Unsubstituted	Dark red	295 decomp.	21	18.91 N	18.85 N 19.05 N
6,6′-Dimethyl-	Dark red	319 decomp.	24	17.26 N	17.22 N 17.22 N
6,6′-Dichloro-	Bright red	348 decomp.	20	19.42 Cl	19.30 Cl 19.20 Cl
6,6′-Dibromo-	Bright red	338 decomp.	16.5	12.33 N	12.18 N 12.19 N
6,6′-Diethoxy-	Dark purple	290 decomp.	25	14.58 N	14.53 N 14.60 N
4,4′-Dimethyl-	Bright red	301 decomp.	71.5	17.26 N	17.05 N 17.20 N

[a] Identical 2-azobenzothiazoles were obtained by the sodium hypochlorite oxidation of the corresponding 2-aminobenzothiazoles.

[b] All melting points taken on the Maquenne block.

[c] Starting with 0.2–0.3 g. of the 2-nitrobenzothiazole.

of 6,6′-dichloro-2-azobenzothiazole with a Raney nickel catalyst gave 2-amino-6-chlorobenzothiazole, identified as the acetyl derivative.

In order to demonstrate that the hypochlorite oxidation products of the 2-aminobenzothiazoles were azo compounds and not azoxy derivatives, reduction of the 2-nitrobenzothiazoles was carried out with dextrose. The resulting products were mainly the corresponding 2-azoxybenzothiazoles (Table III). However, dextrose reduction of the parent compound, 2-nitrobenzothiazole, produced only 2-azobenzothiazole. Like the azo compounds the 2-azoxybenzothiazoles were highly colored crystalline substances similar in properties to the corresponding azo derivatives. Their melting points were slightly lower and in some cases twinning of the crystals was prominent.

TABLE III

2-AZOXYBENZOTHIAZOLE FROM 2-NITROBENZOTHIAZOLES BY REDUCTION WITH DEXTROSE

2-AZOXYBENZOTHIAZOLE[a]	COLOR	M.P. °C[b] (UNCORR.)	% YIELD[c]	% NITROGEN	
				Calc'd	Found
6,6′-Dimethyl-...........	Bright red	314 decomp.	26	16.48	16.70[d] 16.80
6,6′-Dichloro-...........	Bright red	344 decomp.	20	14.70	15.19
6,6′-Dibromo-...........	Bright red	336 decomp.	12	11.92	11.80
6,6′-Diethoxy-...........	Dark purple	272 decomp.	38	14.00	13.99 14.07
4,4′-Dimethyl-..........	Bright red	293 decomp.	18.6	16.48	16.43 16.38

[a] Dextrose reduction of the unsubstituted 2-nitrobenzothiazole gave only the 2-azobenzothiazole described in Table II.

[b] All taken on the Maquenne block.

[c] Based on the amount obtained from 0.1–0.2 g. of the 2-nitrobenzothiazole.

[d] Also analyzed for carbon and hydrogen.

Anal. Calc'd for $C_{16}H_{12}N_4S_2O$: C, 56.43; H, 3.55
$C_{16}H_{12}N_4S_2$: C, 59.22; H, 3.72
Found: C, 57.90, 57.97

These calculations indicate that the product is probably a mixture of the azo and azoxy derivatives.

The chemical evidence given above indicating an azo structure for the hypochlorite oxidation products of 2-aminobenzothiazoles is also supported by the high color of these products. An azo structure affords the maximum conjugation of double bonds possible in the benzothiazole nucleus. Although a 2-nitrosobenzothiazole would have about the same amount of conjugation, such compounds would be expected to melt much lower than 300-350° (the observed melting point range for the 2-azobenzothiazoles).

The 2-azobenzothiazoles in the oxidation of the 2-aminobenzothiazoles could be isolated in yields of 15 to 17% of the theoretical. The nature of the remainder of the oxidation product remains to be considered. The crude red-brown oxidation products are reminiscent of the deeply colored mixture obtained when aniline is oxidized to bimolecular and polymolecular products. It is reasonable to suppose that the reaction products remaining after removal of the azobenzothiazoles consists of polymeric products of the aniline black type. The structure of these other products was not investigated.

EXPERIMENTAL

Preparation of the 2-aminobenzothiazoles. 2-Aminobenzothiazole was prepared by the method of Fischer and Besthorn (2), 2-amino-4-methyl- and 2-amino-6-methyl-benzothiazole were prepared according to the method of "Organic Syntheses" (4), and 2-amino-6-bromobenzothiazole according to the method of Kaufmann (5). 2-Amino-6-chlorobenzo thiazole and 2-amino-6-ethoxybenzothiazole were furnished through the courtesy of the E. I. du Pont de Nemours and Co. They were purified by recrystallization from a solvent consisting of equal parts (by volume) of dioxane, alcohol, and water. The 2-amino-6-chlorobenzothiazole then melted at 196–197° (uncorr.); the 2-amino-6-ethoxybenzothiazole melted at 163–164° (uncorr.).

Oxidation of the 2-aminobenzothiazoles. The sodium hypochlorite oxidation of the 2-aminobenzothiazoles was carried out in the same general way with all of the amino derivatives. The oxidation of 2-amino-6-methylbenzothiazole illustrates the general procedure.

A solution of 10 g. (0.061 mole) of 2-amino-6-methylbenzothiazole in 200 cc. of dioxane was added over a period of fifteen minutes to 200 g. of a well stirred solution of sodium hypochlorite ("Clorox") (0.134 mole) at room temperature. A red-brown, flocculent precipitate formed immediately upon addition. The temperature of the reaction mixture rose to 50° after one-half of the solution of the amine had been added, and no further increase in temperature occurred when the remainder of the reactant was added. Stirring was continued for ten minutes after addition was complete, 50 cc. of "Clorox" was added and stirring continued for half an hour. The precipitate was filtered and dried at 55°. The resulting amorphous powder was extracted with boiling 2-nitropropane and sublimed at 0.1 mm pressure and 250–260°.

Preparation of the 2-nitrobenzothiazoles. This series of compounds was prepared by a slight modification of the method of Starkey, which is now given in "Organic Syntheses" (6). Since all of the 2-nitrobenzothiazoles were prepared by the same method, only the procedure for 2-nitrobenzothiazole is described in detail.

In a 400-cc. beaker 5.0 g. (0.033 mole) of 2-aminobenzothiazole was dissolved in a solution of 100 g. of water and 20 g. of fluoboric acid solution (42%). This solution was cooled to 4° and maintained at this temperature with an ice-water bath during the addition of 2.3 g. (0.033 mole) of sodium nitrite dissolved in 10 cc. of water. The sodium nitrite solution was added under the amine solution, using moderate stirring. The diazotization required fifteen to twenty minutes. At the end of the diazotization, the reaction mixture contained some dissolved diazonium fluoborate as well as some of the precipitated salt. The mixture was added immediately to a boiling solution of 25 g. of sodium nitrite in 100 cc. of water containing 5 g. of copper powder (pure carbon copper which had been previously "wetted" with 10 cc. of alcohol to prevent foaming). This mixture was steam distilled at once and 1500 cc. of distillate was collected which contained the light yellow crystalline product. The 2-nitrobenzothiazole was purified by recrystallization from hot alcohol. The yield was 2.0 g. of the pure compound or 33%; m.p. 157–158° (uncorr.). The average yields, melting points, and analyses of the substituted 2-nitrobenzothiazoles are given in a preceding table (Table I).

The 2-nitrobenzothiazoles listed in the foregoing table were identified by reduction to the corresponding 2-aminobenzothiazoles with tin and hydrochloric acid. They were then acetylated and the melting points of the products were compared with authentic samples of substituted 2-acetylaminobenzothiazoles.

Reduction of the 2-nitrobenzothiazoles by sodium stannite. The substituted 2-azobenzothiazoles were all prepared in the same manner. The preparation of 4,4′-dimethyl-2-azobenzothiazole is described in detail.

In a 50-cc. flask were placed 0.20 g. (0.0010 mole) of 2-nitro-4-methylbenzothiazole and 20 cc. of ethyl alcohol. The solution was warmed to 50° on a water-bath and 0.464 g. (0.00206 mole) of stannous chloride dihydrate dissolved in 5 cc. of 10% sodium hydroxide was added all at once. The solution flashed bright red upon addition of the stannite solution and turned green in a few seconds. The flask was fitted with a reflux condenser and warmed over a water-bath at 80° for two hours. The warm solution was neutralized by dropwise addition of concentrated hydrochloric acid, which produced a bright red, flocculent precipitate. The mixture was filtered when cool and the precipitate was extracted with boiling 2-nitropropane and recrystallized from the same solvent. Long, dark red needles were obtained. The yield was 0.121 g. of pure 4,4′-dimethyl-2-azobenzothiazole, or 71.5%; m.p. 301° decomp. (uncorr.) on the Maquenne block. The melting points, etc., of the 2-azobenzothiazoles are given in Table II.

The melting points of the 2-azobenzothiazoles agreed exactly with the melting points of the oxidation products of the corresponding 2-aminobenzothiazoles. Mixed melting point determinations confirmed the identity of the compounds prepared by the two methods.

Reduction of the 2-nitrobenzothiazoles by dextrose. In a 50-cc. flask were placed 0.200 g. (0.00103 mole) of 2-nitro-4-methylbenzothiazole, 0.150 g. (0.00075 mole) of dextrose, and 20 cc. of water; 1 cc. of alcohol was added to "wet" the nitro compound. This mixture was warmed to 50° and 3 cc. of 10% sodium hydroxide was added. The flask was fitted with a reflux condenser and warmed to 60–70° for two hours. At the end of this time the red precipitate which formed was filtered off and dried at 55°. This crude reaction product was extracted with boiling 2-nitropropane and recrystallized from the same solvent. There was obtained 0.033 g. of bright red crystals of 4,4′-dimethyl-2-azoxybenzothiazole; m.p. 293° decomp. (uncorr.) on the Maquenne block.

The reduction of other 2-nitrobenzothiazoles by dextrose was carried out similarly. The results are given in Table III.

Catalytic reduction of 6,6′-dichloro-2-azobenzothiazole. In a thick-walled glass hydrogenation bottle were placed 0.30 g. of 6,6′-dichloro-2-azobenzothiazole (prepared by the sodium hypochlorite oxidation of 2-amino-6-chlorobenzothiazole), 50 cc. of dry ether, and 0.3–0.4 g. of Raney nickel. (Peroxide-free dioxane was also tried as a solvent; reduction apparently took place, but the difficulty of removing that solvent from a small amount of product made identification impossible.) The solution was shaken for two hours under a pressure of 43.5 pounds of hydrogen and at 26°. At the end of this time the Raney nickel was filtered off and the ether evaporated to dryness. About 0.1 g. of solid residue remained which was converted *in situ* to the acetyl derivative by adding 10 cc. of acetic anhydride and two drops of concentrated sulfuric acid to the flask and warming to 50–60° for ten minutes. Water was added dropwise with care until the sputtering subsided; 50 cc. of water was added and the unreacted anhydride allowed to hydrolyze. This gave a crystalline product which melted at 226–227° (uncorr.) when recrystallized from dilute alcohol. [Melting point of 2-acetylamino-6-chlorobenzothiazole is 227–228° (uncorr.)]. The mixed melting point was 227–228°.

SUMMARY

1. The action of sodium hypochlorite on a number of 2-aminobenzothiazoles has been studied. The highly colored products formed in the reaction have been isolated in a pure state and assigned an azo structure.

2. A new series of compounds, the 2-nitrobenzothiazoles, has been prepared. Reduction of the 2-nitrobenzothiazoles with sodium stannite produces 2-azo-

benzothiazoles, whereas reduction with dextrose yields mainly the 2-azoxybenzothiazoles.

ITHACA, N. Y.

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