2. Di-*n*-butylamine and diallylamine have been prepared by hydrolyzing the corresponding cyanamides.

CHICAGO, ILLINOIS

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RESEARCHES ON THIAZOLES. IV. THE SYNTHESIS OF BENZOTHIAZOLES FROM ORTHO-NITROCHLOROBENZENE

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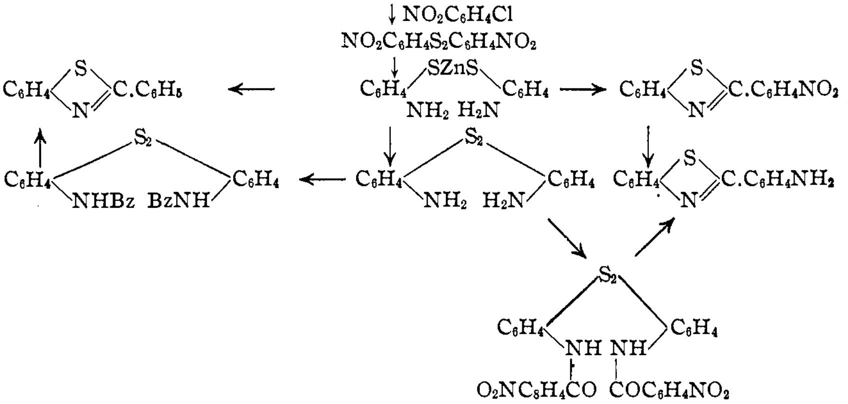
Introductory

Of the many methods which have been utilized from time to time for the preparation of benzothiazoles, one of the simplest and most satisfactory is that discovered many years ago by Hofmann,[1] which depends upon the condensation of acid halides or anhydrides with *o*-aminophenyl mercaptans. Such syntheses have been somewhat infrequent in application because of the non-availability or instability of the requisite thiophenol.

Due to our interest in the benzothiazoles, we have been led to devote some time to the study of methods by which such initial materials can be obtained more easily and used more conveniently, and this paper is a report upon some of the results already attained.

The ground which it covers is represented by the following schematic arrangement.



Free *o*-aminophenyl mercaptan is very sensitive to oxidation, even on standing in the air, rapidly changing to the disulfide. For this reason, the latter has been used often in synthetic work instead of the free thiophenol.[2] Möhlau, Beyschlag and Köhres[3] reduced the nitrophenyl di-

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[1] Hofmann, *Ber.*, **12**, 2362, 2365 (1879).

[2] Kehrmann and Nossenko, *Ber.*, **46**, 2812 (1913).

[3] Möhlau, Beyschlag and Köhres, *Ber.*, **45**, 134 (1912).

sulfide to the corresponding amino compound by hydrazine hydrate; while Claasz[4] employed a mixture of 50% acetic acid, concd. hydrochloric acid and tin, thereby obtaining the aminophenyl mercaptan hydrochloride, after de-tinning with hydrogen sulfide. Zincke and Siebert[5] dissolved the nitrophenyl disulfide in alcohol, reduced with tin and hydrochloric acid to the aminophenyl mercaptan, oxidized the latter by ferric chloride to the disulfide, and then treated the latter with sodium sulfide.[6]

We have found, however, that by dissolving the nitrophenyl disulfide in glacial acetic acid and reducing with zinc dust, the zinc salt of the aminophenyl mercaptan is readily obtained in excellent yield.

Further, it was ascertained that this zinc salt can be used in place of the unstable free thiophenol in many reactions, and benzothiazoles have been prepared from it easily and in good yield.

When the zinc salt is dissolved in ammonium hydroxide solution and air is passed through, the corresponding disulfide is obtained. This is readily acylated, and reduction of these acyl derivatives likewise gives benzothiazoles.

Through the courtesy of Captain Sidney M. Cadwell, of the research laboratories of the United States Rubber Company, the zinc *o*-aminophenyl mercaptide, and the *o*-nitro- and *o*-aminophenyl disulfide, were tested as accelerators for rubber vulcanization, but were found to have no advantage over other cheaper accelerators, the nitro derivative having but little action and the other two accelerating about as well as aniline.

Experimental Part

***o*-Nitrophenyl Disulfide,** $(O_2NC_6H_4)_2S_2$, was prepared from *o*-nitrochlorobenzene by the method of Blanksma,[7] as elaborated by Wohlfahrt;[8] m. p., 195° (corr.); yield, 75%.

o*-Aminophenyl Mercaptan** (o*-Aminothiophenol**).—To a solution of 3.1 g. of the above-mentioned disulfide in 350 cc. of warm glacial acetic acid, zinc dust was added slowly and in small amounts at a time. For rapid reduction (30 minutes), about 20 g. of zinc dust was required, but the reduction can be accomplished with much less by taking a longer time. The mixture was boiled until colorless, diluted with two volumes of water and filtered hot. As the filtrate cooled, the zinc salt of the aminothiophenol separated practically pure, as a colorless, microcrystalline solid; yield, 2.8 g., or 90%. If the original reduced solution was filtered and the filtrate allowed to crystallize, the product was impure and required much washing with water to free it from inorganic salts. The solution also became supersaturated unless stirred frequently.

For analysis, the samples were ignited to the oxide.

Analyses. Calc. for $C_{12}H_{12}N_2S_2Zn$: ZnO, 25.93. Found: 26.25, 26.11.

***o*-Aminophenyl Disulfide,** $(H_2NC_6H_4)_2S_2$.—To a mixture of 3.2 g. of finely powdered

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[4] Claasz, *Ber.*, **45**, 1029 (1912).

[5] Zincke and Siebert, *Ber.*, **48**, 1242 (1915).

[6] See also Schultz and Beyschlag, *Ber.*, **42**, 748 (1909).

[7] Blanksma, *Rec. trav. chim.*, **20**, 121 (1901).

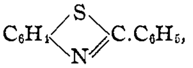
[8] Wohlfahrt, *J. prakt. Chem.*, [2] **66**, 553 (1902).

zinc *o*-aminophenyl mercaptide with 50 cc. of concd. ammonium hydroxide solution, was added an equal volume of water. Air was drawn through the mixture for two hours. The zinc salt gradually disappeared and its place was taken by a crystalline precipitate of the disulfide. This was purified by crystallization from 25% alcohol in the presence of a decolorizing carbon, and then appeared in lustrous, pale yellow plates; m. p., 93°; yield, 1.6 g., or 65%. The loss in recrystallization was large. Hofmann[1] prepared it by oxidation of the free aminothiophenol and found the same melting point.

***o*-Benzoylaminophenyl Disulfide,** $(C_6H_5CONHC_6H_4)_2S_2$.—A mixture of 2.5 g. of *o*-aminophenyl disulfide with 3 g. of benzoyl chloride was heated for an hour at 100°. The crude product was washed with *N* sodium hydroxide solution, decolorized by boneblack, and crystallized from 50% alcohol. Colorless, glassy needles were obtained; m. p., 142.6° (corr.); yield, 3.8 g., or 83%.

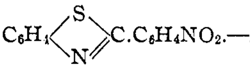
Analysis. Calc. for $C_{26}H_{20}O_2N_2S_2$: S, 14.03. Found: 14.32.

The compound was easily soluble in ethyl or *iso*-amyl alcohol, carbon tetrachloride, acetone or glacial acetic acid, hot and less readily cold. It was also easily soluble in chloroform or toluene, less soluble in carbon disulfide, and nearly insoluble in ether. It was obtained first by Möhlau, Beyschlag and Köhres,[3] who reported a melting point of 141°.

2-Phenylbenzothiazole,  was prepared both from the zinc salt of *o*-aminothiophenol and from *o*-benzoylaminophenyl disulfide.

A mixture of 3.2 g. of the zinc salt of *o*-aminothiophenol with 3 g. of benzoyl chloride was boiled for half an hour. The crude product was washed with warm *N* sodium hydroxide solution, decolorized by boneblack, and crystallized from 50% alcohol. There were thus obtained colorless crystals; m. p., 114° (corr.). Mixed with a sample of pure 2-phenylbenzothiazole prepared by a different method, the melting point remained unchanged; yield, 4 g., or 94%.

A mixture of 2.3 g. of *o*-benzoylaminophenyl disulfide, 5 cc. of concd. hydrochloric acid, 95 cc. of water and 10 g. of granular tin was boiled for 15 minutes. Solution occurred in about five minutes. The solution was made strongly alkaline with 4 *N* sodium hydroxide solution, kept warm for an hour, then cooled, the thiazole filtered out and recrystallized from 50% alcohol. The product melted at 114° (corr.), and mixed with a pure 2-phenylbenzothiazole of different origin still melted at the same point; yield, 1.9 g., or 90%.

2-(*p*-Nitrophenyl)benzothiazole, —A mixture of 3.2 g. of zinc *o*-aminophenyl mercaptide with 3.7 g. of *p*-nitrobenzoyl chloride was heated for an hour at 100°. The cooled melt was extracted with an excess of warm *N* sodium hydroxide solution, the undissolved material collected, washed with water, decolorized by a suitable carbon, and crystallized from alcohol. Nearly colorless, minute, felted needles were obtained, m. p., 231° (corr.); yield, 3.6 g., or 70%.

Analysis. Calc. for $C_{13}H_8O_2N_2S$: S, 12.50. Found: 12.47.

The compound dissolved readily in concd. hydrochloric acid, and on dilution separated as a pale yellow, flocculent precipitate. It was but slightly soluble in alcohol or acetone cold, somewhat more readily hot, and dissolved also in chloroform, *iso*-amyl alcohol or glacial acetic acid. In ether, carbon tetrachloride or benzene, it was practically insoluble.

2-(*p*-Aminophenyl)benzothiazole.—A mixture of 2.6 g. of the nitrophenyl derivative, described above 5 cc. of concd. hydrochloric acid, 95 cc. of water and 10 g. of granular tin was boiled for three hours. Complete solution was attained after two hours' boiling, but the heating was continued for another hour. Since the solution when filtered separated a precipitate on cooling, it was made strongly alkaline with 4 *N* sodium hydroxide solution, kept warm for an hour, then cooled, the precipitate removed, decolorized and crystallized from 50% alcohol. The product then appeared in minute, colorless, fluffy, felted needles; m. p., 155° (corr.). This melting point agrees with that given in French patent 216,086;[9] yield, 2 g., or 90%.

Analysis. Calc. for $C_{13}H_{10}N_2S$: S, 14.16. Found: 14.35.

Its alcoholic solution exhibited a blue fluorescence. In warm water, it dissolved slightly.

o-(*p*-**Nitrobenzoylaminophenyl) Disulfide,** $(ON_2C_6H_4NHC_6H_4)_2S_2$.—To a solution of 2.5 g. of *o*-aminophenyl disulfide in 100 cc. of dry ether was added a solution of 3.7 g. of *p*-nitrobenzoyl chloride in 40 cc. of dry ether. Precipitation occurred immediately. The mixture was allowed to stand for 15 minutes, after which the precipitate was collected, dried and crystallized from alcohol. There resulted 4 g., or 73%, of pale yellow, prismatic crystals, which melted with decomposition at 213° (corr.). Further recrystallization raised this decomposition point finally to 217° (corr.).

Analysis. Calc. for $C_{26}H_{18}O_6N_4S_2$: S, 11.72. Found: 11.58.

In solubilities, this product resembled the 2-(*p*-nitrophenyl)benzothiazole, except that it was practically insoluble in concd. hydrochloric acid.

A mixture of 2.8 g. of this compound with 10 cc. of concd. hydrochloric acid, 10 cc. of water and 10 g. of granulated tin was boiled for four hours, although everything had gone into solution at the end of three hours. The solution was diluted with 150 cc. of water and filtered. The filtrate was made strongly alkaline with 4 *N* sodium hydroxide solution, kept warm for an hour, then cooled and filtered. The precipitate so removed was crystallized from 50% alcohol, and then appeared in pale yellow needles, m. p. 155° (corr.), identical with the 2-(*p*-aminophenyl) benzothiazole obtained by reduction of the nitrophenylbenzothiazole. A mixture of the two likewise melted at 155° (corr.); yield, 2.1 g., or 80%.

Summary

1. *o*-Nitrochlorobenzene is readily converted into *o*-aminophenyl mercaptan and the corresponding disulfide.
2. 2-Phenylbenzothiazole results when the zinc salt of *o*-aminophenyl mercaptan is boiled with benzoyl chloride, or when the *o*-aminophenyl disulfide is benzoylated and then reduced.
3. Similarly, 2-(*p*-nitrophenyl)benzothiazole can be prepared from the zinc salt of the aminophenyl mercaptan and *p*-nitrobenzoyl chloride.
4. By reduction of the nitro derivative, 2-(*p*-aminophenyl)benzothiazole results; and this can be obtained also by the action of *p*-nitrobenzoyl chloride upon *o*-aminophenyl disulfide, followed by reduction.

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[9] French pat. 216,086. *Winther,* **3,** 379 (1910).