ions which combine rapidly with hydrogen ion to form the nitro compounds.

The velocity constants of these second reactions have been measured at two temperatures for each of the substances. The heats of activation of these reactions have been calculated from the results.

The heats of activation have been found to differ very markedly for the three substances, that for phenylisonitromethane being more than 10,000 cal. greater than that for nitromethane.

The heat of activation in the case of *p*-isonitrophenol has been found to be very small, being less than 5000 cal.

BERKELEY, CALIFORNIA

[CONTRIBUTION FROM THE GOODYEAR TIRE AND RUBBER COMPANY]

RESEARCHES ON THIAZOLES. II. THE NITRATION AND REDUCTION OF 2-MERCAPTOBENZOTHIAZOLE AND ITS SUBSTITUTED DERIVATIVES

BY JAN TEPPEMA AND L. B. SEBRELL

RECEIVED FEBRUARY 21, 1927 PUBLISHED JULY 5, 1927

In a previous paper[1] a new method of preparation for 2-mercaptobenzothiazole was given. This method was extended to the preparation of several new 2-mercaptobenzothiazoles which had hitherto not been described.

It is the purpose of the present paper to outline the results obtained by nitration and subsequent reduction of 2-mercaptobenzothiazole and its derivatives as given in the first paper.

Bogert[2] has shown that the nitration of 2-phenylbenzothiazole gives 6-phenyl-2-mercaptobenzothiazole. We were unable to fix the position of the nitro group in nitro-2-mercaptobenzothiazole by use of the procedure followed by Bogert. However, we were able to prove by another way that the nitro group is in Position 6.

The work of Kwaysser[3] and Mylius[4] has made available 2-amino-5-nitrothiophenol. After reduction this compound, treated with sodium hydrosulfide and carbon disulfide according to our previously described method gave 6-amino-2-mercaptobenzothiazole; m. p., 263°. The reduction product of nitrated 2-mercaptobenzothiazole after purification melted at 260°. A mixed-melting-point determination gave no decrease in melting point. We, therefore, conclude that on nitration the nitro group enters the ring in 2-mercaptobenzothiazole in Position 6.

These reactions are

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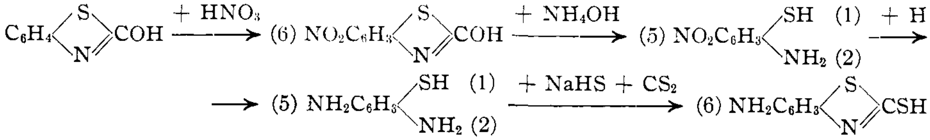
[1] Teppema and Sebrell, THIS JOURNAL, **49**, 1748 (1927).

[2] Bogert, *ibid.*, **44**, 826 (1922).

[3] Kwaysser, *Ann.*, **277**, 240 (1893).

[4] Mylius, *Dissertation*, University of Berlin, **1883**.



Another amido-2-mercaptobenzothiazole, m. p. 216°, was described by us in our previous paper. From its method of preparation it must be 5-amino-2-mercaptobenzothiazole.

Attempts to prepare 5-nitro-2-aminothiophenol by fusion of the nitration product of 2-mercaptobenzothiazole were unsuccessful. Heating under pressure with aqueous ammonia gave 6-nitro-2-aminobenzothiazole.

By diazotization and Sandmeyer reaction of 6-amino-2-mercaptobenzothiazole the corresponding 6-chloro-2-mercaptobenzothiazole is formed. Benzaldehyde condenses readily with the amino group to give 6-benzalamino-2-mercaptobenzothiazole.

A similar series of derivatives is formed by nitrating the 5-chloro-2-mercaptobenzothiazole. In this compound the position of the nitro group has not been definitely proved but it is believed to be in Position 6.

From 1,2,4-toluylenediamine and sulfur the corresponding disulfide was prepared according to Schultz and Beyschlag.[5] By reaction with sodium hydrosulfide and carbon disulfide the 5-amino-6-methyl-2-mercaptobenzothiazole is produced. It gives all the reactions characteristic of an aminomercaptobenzothiazole.

In this paper the melting points given are uncorrected.

Experimental Part

6-Nitro-2-mercaptobenzothiazole.—Fifty g. of 2-mercaptobenzothiazole was dissolved in 250 g. of sulfuric acid, and a mixture of 40 g. of fuming nitric acid and 55 g. of concd. sulfuric acid was slowly dropped in while cooling the reaction mixture with ice and salt. The solution was stirred during the addition of the acid mixture. After all the nitric acid solution is added, the solution is stirred in the cold for one hour more. The solution is then poured onto ice, the precipitate filtered, washed with water and dried; yield, 63 g.; calcd., 65 g. By boiling this compound with aqueous ammonia and repeating this with the residue most of this nitration product could be brought in solution.

From the red solution thus obtained, a yellow precipitate was formed by the addition of dilute acid. After filtering and drying, this material was crystallized from glacial acetic acid, giving yellow needles; m. p., 255–257°.

Anal. Calcd. for $C_7H_4O_2N_2S_2$: S, 30.19; N, 13.20. Found: S, 29.94; N, 13.48.

The crude nitration product which is obtained by pouring the nitric acid solution into ice water is a mixture of nitro-2-mercaptobenzothiazole and its disulfide. Aqueous ammonia dissolves in the cold only the free mercaptan. When the residue was heated with aqueous ammonia it also dissolved and gave the same nitro compound on addition of acid.

This is a remarkable case of the influence of the nitro group on the stability of the sulfur-to-sulfur bond. Whereas the disulfide of 2-mercapto-

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[5] Schultz and Beyschlag, *Ber.*, **42**, 743 (1909).

benzothiazole does not give the free mercaptan easily by boiling with alkalies, introduction of the nitro group loosens the bond between the sulfur atoms.

Amido-2-mercaptobenzothiazole.—The reduction of nitro-2-mercaptobenzothiazole can easily be accomplished by sodium hydrosulfide.

Fifty g. of the nitro compound was suspended in a solution of 75 g. of sodium sulfide, $Na_2S.9H_2O$, in 250 cc. of water which had previously been saturated with hydrogen sulfide. The mixture was then heated on a sand-bath under reflux for 24 hours while hydrogen sulfide was bubbled through the solution.

The solution was acidified with dil. acetic acid and heated on a steam-bath to complete the coagulation of the precipitate. The mixture of the amido compound and sulfur was filtered and the solid extracted with hot aqueous ammonia. Addition of dil. acetic acid yielded amido-2-mercaptobenzothiazole as a yellow-white precipitate which could be crystallized from aniline. It may also be purified by dissolving it in pyridine and reprecipitating with chloroform; m. p., 260°.

Anal. Calcd. for $C_7H_6N_2S_2$: S, 35.2; N, 15.35. Found: S, 34.82; N, 15.50.

This amino-2-mercaptobenzothiazole was diazotized as described below and coupled with β-naphthol. It gave a beautiful red dye.

The complete possibilities of utilizing the various amino-2-mercaptobenzothiazoles as intermediates in the synthesis of dyes have not been entirely developed. Further work is being done and will be reported in a separate communication.

A considerable improvement in the preparation of 6-amido-2-mercaptobenzothiazole could be made by omitting the isolation of the free nitro-2-mercaptobenzothiazole.

The crude nitration product of 2-mercaptobenzothiazole was reduced with sodium hydrosulfide and gave the corresponding amido-2-mercaptobenzothiazole in almost quantitative yield. It was purified as described above.

Position of Nitro Group.—The following experiments were carried out to prove the constitution of nitro-2-mercaptobenzothiazole, of which only the last method was successful.

(1) As already mentioned above, diazotized *p*-nitro-aniline did not react with amido-2-mercaptobenzothiazole according to the method described by Bogert[2] for amino-2-phenylbenzothiazole.

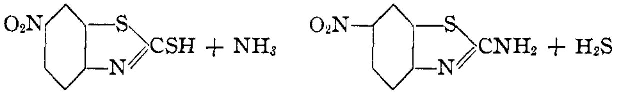
(2) The second method is the fusion of nitro-2-mercaptobenzothiazole with potassium hydroxide to give a nitro-aminothiophenol. However, through the formation of hydrogen sulfide during the fusion this compound seems to be reduced, and no definite compound could be isolated from the fusion.

(3) To avoid the strong action of potassium hydroxide, the nitromercaptobenzothiazole was heated with concd. aqueous ammonia under pressure.

Three g. was heated with 40 cc. of aqueous ammonia (d., 0.95) for four hours at 160° A red solution with crystals was obtained. The solution was filtered, diluted with twice the amount of water and neutralized. The precipitate formed was unchanged nitro compound.

The residue on the filter was crystallized from alcohol and treated with bone black; yellow needles were obtained; melting point, 249°. It proved to be different from nitro-2-mercapto-benzothiazole, as mixed with this compound the melting point was 218°.

This compound is soluble in acid and insoluble in alkali. The yield under these conditions was small and most of the final product was unchanged nitro compound. The analysis for sulfur and nitrogen showed it to be 2-amido-6-nitrobenzothiazole, and its formation can be formulated as follows.



Anal. Calcd. for $C_7H_3O_2N_3S$: S, 16.41; N, 21.5. Found: S, 16.48; N, 20.75.

(4) A fourth method consists in the preparation of 5-nitro-2-oxybenzothiazole and treating this compound with aqueous ammonia according to Kwaysser[3] to give 5-nitro-2-aminothiophenol. This compound is quite unstable when not dry, as it is easily oxidized to the corresponding disulfide.

It has been shown in a previous paper[1] that 2-mercaptobenzothiazole could be obtained from *o*-amidothiophenol with carbon disulfide in two ways. The new method described consisted in passing hydrogen sulfide, previously saturated with carbon disulfide, through an alkaline solution of the thiophenol.

This same procedure was applied to the reduction product of 5-nitro-2-amidothiophenol.

Reduction of 5-Nitro-2-amidothiophenol.—Four g. of 5-nitro-2-amidothiophenol was heated with 10 g. of granulated tin in 60 cc. of hydrochloric acid (1:1). The solution was boiled under reflux for three hours. The clear solution then obtained was diluted with much warm water and the tin precipitated with hydrogen sulfide. The filtrate from the tin sulfide was concentrated and neutralized with sodium hydroxide. Twenty g. of $Na_2S.9H_2O$ was then added and hydrogen sulfide, previously saturated with carbon disulfide, was passed through the solution, which was kept at 80° for ten hours.

On acidification with dil. acetic acid a colorless precipitate was formed. This was filtered, redissolved in aqueous ammonia and reprecipitated with dil. acetic acid; yield, 3 g.

The dried material was crystallized from aniline; m. p., 263°. It was 6-amino-2-mercaptobenzothiazole.

Mixed with the reduction product of nitro-2-mercaptobenzothiazole, no decrease in melting point was observed.

The conclusion is, therefore, that the nitration of 2-mercaptobenzothiazole under the conditions mentioned yields 6-nitro-2-mercaptobenzothiazole.

2-Mercapto-6-benzalamidobenzothiazole.—Nine and one-tenth g. of 2-mercapto-6-amidobenzothiazole was suspended in 100 cc. of alcohol and 7.5 cc. of freshly-distilled benzaldehyde was added. After heating for one and one-half hours the reaction mixture consisted of yellow needles. By addition of more alcohol these crystals dissolved in the hot solution and, on cooling, light yellow crystals separated; m. p., 226°.

Anal. Calcd. for $C_{10}H_{14}N_2S_2$: N, 10.37. Found: 10.13.

6-Chloromercaptobenzothiazole.—This compound was obtained from 6-amido-2-mercaptobenzothiazole by the well-known Sandmeyer reaction. As 6-amido-2-mercaptobenzothiazole is almost insoluble in water and does not form salts with acids, a modification of the usual way of diazotation was made. The following proved to be successful: 5 g. of 6-amido-2-mercaptobenzothiazole was dissolved in dil. sodium hydroxide (1:10) and this solution mixed with a solution of 3.8 g. of sodium nitrite in a little water.

The reason why twice the calculated amount of sodium nitrite is used is that part of the nitrous acid, set free, will oxidize the free mercaptan to its disulfide. In case the calculated amount of sodium nitrite is used, the diazotation will, therefore, be incomplete.

The solution was dropped slowly into 100 cc. of concd. hydrochloric acid, with ice cooling. If the solution was added carefully, the final solution did not contain any undissolved matter, but was slightly turbid. This solution was poured slowly into a dilute hydrochloric acid (1:1) solution of 12 g. of cuprous chloride, which was kept at 60–70°. A yellow-brown precipitate was formed. The reaction mixture was diluted with an equal volume of water and filtered, and the residue washed with water. The product obtained, being 6-chloro-2-mercaptobenzothiazole disulfide, was not isolated, but reduced with sodium hydrosulfide to the free mercaptan.

The solid, still wet, was mixed with 20 g. of $Na_2S.9H_2O$ and 250 cc. of water, and hydrogen sulfide was passed through for four hours with heating. The final solution was filtered from a little dark colored solid and the filtrate acidified with dil. acetic acid. The precipitate was filtered and washed. It was freed from sulfur by dissolving in dilute aqueous ammonia and reprecipitating with dil. acetic acid. After being dried it was crystallized from aniline; m. p. (unsharp), 245°.

Anal. Calcd. for $C_7H_4NS_2Cl$: Cl, 17.61. Found: 17.79.

Attempts to Obtain 6-Chloro-2-mercaptobenzothiazole by Chlorination of 2-Mercaptobenzothiazole.—When chlorine was passed through a solution of 2-mercaptobenzothiazole in carbon tetrachloride or *sym.*-tetrachloro-ethane, either at room temperature or at the boiling points of these solvents, no chlorinated 2-mercaptobenzothiazole was obtained.

In the first solvent only the disulfide of the mercaptan was formed. Chlorination in tetrachloro-ethane at the boiling point of this solvent gave an oil, b. p. 235–248°, with the characteristic odor of chlorophenyl mustard oil.

It was found, however, that 6-chloro-2-mercaptobenzothiazole is formed in a very small yield when 2-mercaptobenzothiazole reacts with chlorine in the presence of a small amount of iron.

Instead of 2-mercaptobenzothiazole, 2-mercaptobenzothiazole disulfide was used, as the latter product is produced as an intermediate compound. Ten g. of 2-mercaptobenzothiazole disulfide was dissolved in chloroform and 0.5 g. of iron powder added to the solution. Chlorine was passed through the boiling solution for five hours. After evaporation of the solvent at room temperature, the residue was extracted with chloroform to remove unchanged disulfide. The insoluble residue showed halogen present by qualitative test. The amount was small in comparison with unchanged disulfide.

One-half g. of this material was reduced with sodium hydrosulfide. A clear solution was obtained which, on acidification with dil. acetic acid, gave a white precipitate.

This compound was filtered, washed and redissolved in dil. aqueous ammonia. Dil. acetic acid precipitated a white material which, after filtering and drying, was crystallized from aniline, giving colorless needles; m. p., 230–235°. The amount of this compound was too small to be purified further.

To prove that it was identical with 6-chloro-2-mercaptobenzothiazole it was mixed with 6-chloro-2-mercaptobenzothiazole, m. p., 245°, previously obtained from 6-amino-2-mercaptobenzothiazole. The melting point was 235–240°, showing that it was identical with 6-chloro-2-mercaptobenzothiazole.

Nitro-5-chloro-2-mercaptobenzothiazole.—The same procedure as described for the nitration of 2-mercaptobenzothiazole was followed for 5-chloro-2-mercaptobenzothiazole.

Fifty g. of 5-chloro-2-mercaptobenzothiazole was dissolved in 175 cc. of concd. sulfuric acid and a mixture of 50 g. of fuming nitric acid and 70 g. of concd. sulfuric acid was dropped in gradually, cooling with ice and salt, while the solution was stirred mechanically.

After all of the mixed acid was added, stirring was continued for one hour and the mixture then poured into ice water. The yellow precipitate was filtered and digested with hot, aqueous ammonia. After repeating this thrice most of the nitro compound was dissolved and could be precipitated with acids; yield (dry), 50 g. It crystallized from acetic acid in yellow flakes; m. p., 190–192°.

Anal. Calcd. for $C_7H_3ClN_2O_2S_2$: N, 11.3; Cl, 14.4. Found: Cl, 14.30; N, 11.21.

Amido-5-chloro-2-mercaptobenzothiazole.—To prepare amido-5-chloro-2-mercaptobenzothiazole from nitro-5-chloro-2-mercaptobenzothiazole, sodium hydrosulfide could not be used as a reducing agent as it will not only reduce the nitro group but also substitute the chlorine atom to a certain extent.

Tin and hydrochloric acid were used as reducing agents. Fifty-five g. of nitro-5-chloro-2-mercaptobenzothiazole was added to a mixture of 100 g. of tin and 300 cc. of concd. hydrochloric acid. The solution was refluxed for four hours, whereby the yellow color of the suspended nitro-5-chloro-2-mercaptobenzothiazole disappeared. After dilution with water the solution was filtered and the residue digested with hot, aqueous ammonia.

The filtrate, acidified with dil. acetic acid, gave a white precipitate which crystallized from aniline, giving colorless needles; m. p., 240°.

Anal. Calcd. for $C_7H_5N_2S_2Cl$: S, 29.56; N, 12.93. Found: S, 29.17; N, 11.94.

Benzalamido-5-chloro-2-mercaptobenzothiazole.—Two g. of amido-5-chloro-2-mercaptobenzothiazole was boiled with 50 cc. of alcohol and 2 cc. of benzaldehyde for one hour. The solution was treated with bone black and filtered hot. Yellow needles were obtained; m. p., 242°.

Anal. Calcd. for $C_{14}H_9N_2S_2Cl$: S, 21.01. Found: 21.02.

5-Amido-6-methyl-2-mercaptobenzothiazole.—This compound can easily be prepared from *m*-toluylenediamine disulfide.[5]

Thirty-five and one-half g. of *m*-toluylenediamine was dissolved in 284 cc. of alcohol and 18.5 g. of sulfur was added. The solution was heated under reflux on a water-bath for four hours. After distilling off the alcohol the residue was treated with a solution of

100 g. $Na_2S.9H_2O$ in 200 cc. of water which had been previously saturated with hydrogen sulfide and carbon disulfide. The mixture was heated on a sand-bath while hydrogen sulfide (saturated with carbon disulfide vapor) was bubbled through for five hours. The red solution was acidified with dil. acetic acid. First a sticky, yellow precipitate was formed, from which the remaining solution was decanted. On further acidification a white, flocculent precipitate was formed, which was filtered off and washed with water. The crude material was treated with aqueous ammonia, leaving the sulfur behind. The ammoniacal solution was acidified (cold) with dil. acetic acid. The precipitate formed was filtered, dried and crystallized from freshly distilled aniline; yield, 15.5 g.; m. p., 205–213°. It was further purified by crystallizing it twice from alcohol, raising the melting point to 220°.

Anal. Calcd. for $C_8H_8N_2S_2$: S, 32.65. Found: 32.84.

This 5-amido-6-methyl-2-mercaptobenzothiazole is a starting material for a new series of derivatives which contain a methyl group in Position 6 and any other substituent in Position 5.

5-Chloro-6-methyl-2-mercaptobenzothiazole.—Ten g. of 5-amido-6-methyl-2-mercaptobenzothiazole was dissolved in dil. sodium hydroxide solution and this was mixed with a solution of 7 g. of sodium nitrite in a little water. This solution is then dropped slowly into 200 cc. of concd. hydrochloric acid, with cooling. After standing for half an hour in ice water the diazotized solution was added slowly to a solution of 24 g. of cuprous chloride in hydrochloric acid solution ($1HCl:1H_2O$) which was kept at 60–70°. After all had been added the solution was diluted with an equal amount of water. The precipitate was filtered off, washed and dried. It was crystallized from dil. alcohol; m. p. (unsharp), 221–223°. The analysis indicates an impure product.

Anal. Calcd. for $C_8H_5NS_2Cl$: S, 29.70; N, 6.49. Found: S, 30.64; N, 5.72.

Benzal-5-amido-6-methyl-2-mercaptobenzothiazole.—Five and nine-tenths g. of 5-amido-6-methyl-2-mercaptobenzothiazole was dissolved in 100 cc. of alcohol, and 3.18 g. of benzaldehyde was added to the warm solution. After 2 minutes' heating the solution solidified. Much alcohol was added, but apparently the benzal compound is very difficultly soluble in alcohol. The suspension was refluxed for ten minutes more and then cooled and filtered; yield, 7.5 g. of colorless crystals; m. p., 253°.

Anal. Calcd. for $C_{15}H_{12}N_2S_2$: S, 22.53; N, 9.86. Found: S, 22.48; N, 9.67.

Summary

1. The nitration products of 2-mercaptobenzothiazole and 5-chloro-2-mercaptobenzothiazole have been prepared and studied.

2. The position of the nitro group in nitro-2-mercaptobenzothiazole has been proved to be in the benzene ring in Position 6.

3. The reduction products of the above nitromercaptobenzothiazoles have been prepared, and from the amino compounds thus formed the aldehyde derivatives were prepared. By the Sandmeyer reaction the amino group was replaced by halogen.

4. From *m*-toluylenediamine disulfide a 5-amido-6-methyl-2-mercaptobenzothiazole was prepared. This gave also the corresponding aldehyde derivative, and by the Sandmeyer reaction the 5-chloro-6-methyl-2-mercaptobenzothiazole was obtained.

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