[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

p-Nitrophenyl Disulfide, *p*-Nitrophenyl Sulfide and *p*-Nitrothiophenol[1]

BY CHARLES C. PRICE* AND GARDNER W. STACY

Interest in a more satisfactory preparation of *p*-nitrobenzenesulfonyl chloride has been stimulated by its application to the synthesis of sulfanilamide derivatives. Procedures for the preparation of this compound, using *p*-nitrophenyl disulfide as an intermediate,[1a] have been adapted by Bell,[2a] Schreiber and Shriner[2b] and Barber.[2c] However, although *o*-nitrophenyl disulfide has been prepared smoothly in good yield by the reaction of sodium disulfide with *o*-nitrochlorobenzene,[1a] the corresponding reaction to prepare the *p*-nitro isomer has given material which was apparently a mixture. Thus, the crude disulfide forms appreciable sulfoxide and sulfone upon oxidation, detracting from the yield of sulfonyl chloride and causing some inconvenience in obtaining a pure product. Furthermore, Blanksma[1a] reported that it underwent a "transition" at 134° and melted at 170° whereas the pure disulfide, first obtained by Willegerodt[3] by oxidation of *p*-nitrothiophenol, had a melting point of 181°. This was confirmed by the work of Kehrmann and Bauer and Zincke,[4] and a similar melting point was observed for samples prepared by a number of other methods.[5]

As the result of attempts to improve the synthesis, the composition of the crude disulfide has been the subject of considerable investigation and there has been much speculation and controversy concerning the exact nature of the components of the mixture. Several investigators[6,7,8] have isolated samples from the disulfide which melted at about 135°. This material was ascribed the structure of an "angular" isomer (II) of the normal, linear disulfide (I) by Vorozhtzov and Kozlov[8] since they reported its sulfur analysis to check properly for such a substance. However, Bennett and Youle,[9] as well as Witte,[10] have expressed the belief that the impurity was the monosulfide (III), which was actually isolated from the crude material by the former investigators after laborious recrystallization.

$$\underset{\text{I, m. p. 181°}}{O_2NC_6H_4—S—S—C_6H_4NO_2} \qquad \underset{\text{II}}{(O_2NC_6H_4)_2S \longrightarrow S}$$

$$\underset{\text{III, m. p. 161°}}{(O_2NC_6H_4)_2S}$$

Since a complete elementary analysis of the various products was not reported by the previous investigators, crude *p*-nitrophenyl disulfide was separated into the samples of different melting points, which were then subjected to a complete elementary analysis. The composition of the sample melting at 180° was that expected for the pure disulfide. The material melting at 135° had the proper composition for a molecular compound containing two equivalents of monosulfide to one of disulfide. A melting point diagram for mixtures of pure mono- and disulfide (Fig. 1) showed that this system behaved as a simple binary system with a eutectic at 134–137°, corresponding to the composition of the analytical sample. Extrapolation from the melting curve indicated a monosulfide–disulfide composition for material melting at 170° which corresponded very closely to that estimated from the analytical data for the sample melting at that temperature (about 25% mono- and 75% disulfide).

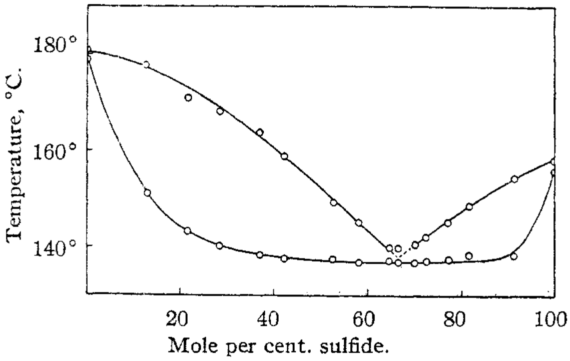

Fig. 1.—Melting curve for mixtures of *p*-nitrophenyl sulfide and disulfide.

These results thus seem ample substantiation of the conclusion of Bennett and Youle[9] that the properties of *p*-nitrophenyl disulfide, prepared by treating *p*-nitrochlorobenzene with sodium disulfide, could be attributed to the presence of monosulfide. To further substantiate this conclusion, a mixture of pure mono- and disulfides, of such a composition (about 25% monosulfide) as to correspond in melting point (170°) to that usually observed for crude disulfide, was subjected to the fractionation procedure used for the

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[1] The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Illinois.

(1a) Blanksma, *Rec. trav. chim.*, **20**, 125 (1901); "Organic Syntheses," Col. 6, Vol. I, 220 (1941).

(2) (a) Bell, *J. Chem. Soc.*, **2**, 2776 (1928); (b) Schreiber and Shriner, THIS JOURNAL, **56**, 114 (1934); (c) Barber, *J. Chem. Soc.*, 102 (1943).

(3) Willegerodt, *Ber.*, **18**, 331 (1885).

(4) (a) Kehrmann and Bauer, *ibid.*, **29**, 2362 (1896); (b) Zincke, *Ann.*, **400**, 1 (1913).

(5) (a) Fries and Schurmann, *Ber.*, **47**, 1199 (1914); (b) Bamberger and Kraus, *ibid.*, **29**, 282 (1896); (c) Challenger and Collins, *J. Chem. Soc.*, **125**, 1377 (1924).

(6) Hodgson and Wilson, *J. Chem. Soc.*, **127**, 440 (1925).

(7) Elgersma, *Rec. trav. chim.*, **48**, 752 (1929).

(8) Vorozhtzov and Kozlov, *J. Gen. Chem.*, *U. S. S. R.*, **2**, 939 (1932).

(9) Bennett and Youle, *J. Chem. Soc.*, 887 (1938).

(10) Witte, *Rec. trav. chim.*, **51**, 299 (1932).

crude material. By this means it was possible to isolate the eutectic and pure disulfide.

To test the possibility that the considerable proportion of monosulfide formed may have been due to the equilibrium of sodium disulfide with monosulfide and sulfur, samples of disulfide were

$$Na_2S_2 \rightleftarrows Na_2S + S$$

prepared from sodium disulfide containing 0.4, 0.8 and 1.2 equivalents of excess sulfur. If anything, this was found to increase the sulfoxide obtained on subsequent oxidation of the crude disulfide.

Another approach to the conversion of *p*-nitrochlorobenzene to *p*-nitrobenzenesulfonyl chloride would be to utilize *p*-nitrothiophenol instead of the disulfide as an intermediate. The preparation of this material by the direct route from *p*-nitrochlorobenzene and sodium sulfide is complicated by the reducing action of the sodium sulfide on the nitro groups.[11] It was possible, however, to apply successfully the observation of Brand[12] that disulfides are reduced to thiophenols by alkaline sodium disulfide. Thus *p*-nitrothiophenol could be obtained in 65% yield by heating an excess of sodium disulfide in an alcoholic solution of *p*-nitrochlorobenzene under reflux for a short period followed by addition of sodium hydroxide solution dropwise.

$$6O_2NC_6H_4Cl + 4Na_2S_2 + 6NaOH \longrightarrow 6O_2NC_6H_4SNa + 6NaCl + Na_2S_2O_3 + 3H_2O$$

Other methods of obtaining thiophenols, using potassium ethyl xanthate and thiourea, were applied to the case at hand. The yields of *p*-nitrothiophenol, however, were only 16 to 22% when *p*-nitrochlorobenzene and thiourea were boiled together in alcohol and the resulting complex subjected to hydrolysis.

Although S-(*p*-nitrophenyl)-ethyl xanthate was not obtained when an alcoholic solution of potassium ethyl xanthate and *p*-nitrochlorobenzene was boiled for two days, an 80 to 90% yield of *p*-nitrophenyl sulfide was obtained. The excellent yields of the sulfide are noteworthy in as much as no particularly satisfactory method of preparing this compound has been described in the literature.

Experimental

Preparation of Samples of *p*-Nitrophenyl Disulfide.—The preparation of the crude disulfide and the separation of various fractions was carried out by essentially the same procedure as that used by Vorozhtzov and Kozlov.[8] The crude product, obtained in 73% yield, melted at 115–146°. A sample was recrystallized four times from xylene and washed with boiling alcohol. The product (A) melted at 168.5°. A sample of this material was extracted a number of times with boiling alcohol, the supernatant liquid being filtered from the residue each time. When the combined filtrates were allowed to cool, a finely-divided crystalline precipitate settled, m.p. 138–144°. This was collected, recrystallized several times from xylene, twice from glacial acetic acid, and washed with boiling alcohol; m. p. 134–137° (B). The residue from the alcohol extractions was recrystallized from xylene and washed with boiling alcohol, m. p. 176–178° (C).

Anal. Calcd. for $C_{12}H_8O_4N_2S_2$: C, 46.75; H, 2.62; S, 20.80; N, 9.09. Found for compound melting at 176–178° (C): C, 46.52; H, 2.63; S, 20.67; N, 9.00. Found for compound melting at 134–137° (B): C, 50.55, 50.45; H, 2.78, 2.83; S, 14.73; N, 9.89, 9.99. Calcd. for $2C_{12}H_8O_4N_2S\cdot C_{12}H_8O_4N_2S_2$: C, 50.27; H, 2.81; S, 14.91; N, 9.77. Found for substance melting at 168.5° (A): C, 48.02; H, 2.88; S, 18.24; N, 9.38. By extrapolation from the melting-point diagram: C, 48.2; H, 2.70; S, 18.1; N, 9.37.

Melting Point Diagram for the System, *p*-Nitrophenyl Sulfide and Disulfide.—The disulfide, m. p. 181°, was prepared essentially according to directions outlined by Zincke,[4b] while the sulfide was obtained according to Nietzki and Bothof.[13] Mixtures totaling 0.400 g. were fused by heating in an oil-bath at 180–190° for ten to fifteen minutes. The samples were allowed to cool in a desiccator and a small portion of each was powdered on a clay plate. Samples in a capillary melting-point tube were heated so that the temperature increased a degree every half to three-quarters of a minute and two temperatures were recorded, the first appearance of liquid and the final disappearance of solid (see Fig. 1).

Separation of the Eutectic Compound and Pure *p*-Nitrophenyl Disulfide from an Artificial Mixture.—To show that the eutectic compound as well as the pure disulfide could be separated from an artificial mixture, a sample was made up containing 26.5% (1.38 g.) of monosulfide and 73.5% (3.68 g.) of disulfide. These were fused together in an evaporating dish and after cooling ground in a mortar. This material melted at 172°. It was extracted several times with portions of boiling alcohol. The filtrates were cooled and the crystalline precipitate collected, m. p. 135–140°. The residue from the alcohol extracts was recrystallized from glacial acetic acid, m. p. 179–181°.

***p*-Nitrothiophenol.**—To a solution of 157.5 g. (1 mole) of *p*-nitrochlorobenzene in 250 cc. of boiling alcohol, an alcoholic solution of sodium disulfide, prepared from 175 g. (0.720 mole) of sodium sulfide nonahydrate and 23.4 g. (0.729 mole) of sulfur, was added portionwise over a period of about ten minutes. Then an alcoholic solution of 40 g. (1 mole) of sodium hydroxide was added dropwise from the dropping funnel over a period of about twenty minutes as the reaction mixture was boiled under reflux. The mixture was cooled and then poured onto 1 kg. of ice and 1500 cc. of water. A precipitate was removed by filtration. The filtrate was acidified with hydrochloric acid, and the *p*-nitrophenol collected by filtration and washed with 500 cc. of water. The crude thiophenol was dissolved in 150 cc. of alcohol. After addition of 40 g. of sodium hydroxide in 1500 cc. of water, the solution was filtered and the *p*-nitrothiophenol was reprecipitated with hydrochloric acid collected by filtration, and dried in a vacuum desiccator. Yields of *p*-nitrothiophenol, melting at 75°, were 93–101 g. or 60–65%.

***p*-Nitrothiophenol from *p*-Nitrochlorobenzene and Thiourea.**—A suspension of 31.4 g. (0.20 mole) of *p*-nitrochlorobenzene and 15.2 g. (0.20 mole) of thiourea in 100 cc. of alcohol was boiled under reflux for three to six hours.

After addition of 24 g. (0.6 mole) of sodium hydroxide dissolved in 100 cc. of water, the mixture was boiled under reflux for one hour and poured into 360 cc. of water. A precipitate which formed was removed by filtration, the red filtrate was acidified with 18% hydrochloric acid and the thiophenol collected; m. p. 75–76°; yield 16 to 22%.

***p*-Nitrophenyl Sulfide.**—A solution of 32 g. (0.2 mole) of *p*-nitrochlorobenzene and 32 g. (0.2 mole) of potassium ethyl xanthate in 150 cc. of ethanol was boiled under reflux for forty-eight hours. The reaction mixture was cooled, and the crystalline product collected by filtration. The product was washed several times with hot water and hot alcohol, m. p. 158–161°. A mixed melting point of this

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[11] Kehrmann and Bauer, *Ber.*, **29**, 2362 (1896).

[12] Brand, *ibid.*, **42**, 3463 (1912); Zincke, *Ann.*, **400**, 1 (1913); Waldron and Reid, This Journal, **45**, 2399 (1923).

[13] Nietzki and Bothof, *Ber.*, **27**, 3261 (1894). This sample was kindly supplied by Dr. Sidney Melamed of this University.

material with *p*-nitrophenyl sulfide, prepared from sodium sulfide and *p*-nitrochlorobenzene,[13] showed no depression. The yield was 23.6 g. (87%). After the substance had been recrystallized several times from glacial acetic acid, it melted at 160-161° (lit. 154°[13]).

Anal. Calcd. for $C_{12}H_8N_2O_4S$: C, 52.16; H, 2.90; N, 10.14. Found: C, 52.19; H, 2.82; N, 10.23.

Summary

The low-melting material (m. p. *ca.* 135°) obtained from the crude product of the reaction of *p*-nitrochlorobenzene with sodium disulfide has been shown to be the eutectic mixture of two moles of *p*-nitrophenyl sulfide and one mole of the disulfide. There thus appears to be no basis for the suggestion of Vorozhtzov and Kozlov that this material is an "angular" disulfide.

p-Nitrophenyl sulfide can be obtained in good yield by refluxing an alcoholic solution containing equivalent amounts of *p*-nitrochlorobenzene and potassium ethyl xanthate.

A conveneient procedure for the preparation of *p*-nitrothiophenol has been described.

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The Higher Fatty Alcohol Esters of Gallic Acid

BY STEWARD G. MORRIS AND R. W. RIEMENSCHNEIDER

Direct esterification of gallic acid with the lower alcohols up to six carbon atoms has been accomplished by various workers.[2,3,4] In most cases the gallic acid was esterified by an excess of the alcohol in the presence of either concentrated sulfuric acid or anhydrous hydrogen chloride as a catalyst. Attempts in this laboratory to apply these procedures in the preparation of the higher alcohol gallates resulted in very low yields of impure products. It has been reported[5] that the higher esters of gallic acid cannot be prepared by ordinary means. A search of the literature failed to reveal any description of the higher fatty alcohol esters of gallic acid.[5a]

Esterification of gallic acid with the polyalcohols has been effected by using galloyl chloride in which the hydroxyl groups have been protected as the tricarbomethoxy[6] and triacetyl[7] derivatives. Benzylation as proposed by Schöpf and Winterhalder[8] offers an advantage over carbomethoxylation or acetylation, in that the benzyl groups can be more readily removed by hydrogenation.

In a preliminary study benzyl chloride, ethyl chloroformate and benzyl chloroformate were tried as a means of protecting the hydroxyl groups. The benzylated product was preferable because it could be more readily purified by crystallization. Clinton and Geissman[9] have shown that on benzylation better yields were obtained with methyl gallate than with gallic acid.

In the present work the hexyl, octyl, dodecyl, tetradecyl, hexadecyl and octadecyl gallates were prepared as follows: Gallic acid was esterified with methyl alcohol[8] and then benzylated.[9] The methyl tribenzyl gallate obtained was saponified to yield the free gallic acid tribenzyl ether. This was treated with thionyl chloride to form galloyl chloride tribenzyl ether, which was then esterified with the appropriate alcohol. The resulting ester was debenzylated.

Experimental

Galloyl Chloride Tribenzyl Ether.—Into a 1-liter, round-bottom flask were introduced 44.0 g. (0.1 mole) of gallic acid tribenzyl ether[9] and 122 g. (1.2 moles) of thionyl chloride (distilled over beeswax), and the mixture was heated on a water-bath at 60° for one hour.[8] Then the excess of thionyl chloride, at a bath temperature of 60°, was removed at the water pump and the residue taken to dryness. (The recovered thionyl chloride can be reused.) To remove the last of the thionyl chloride from the reaction product, the residue was dissolved in benzene and again evaporated to dryness under diminished pressure. The product crystallized from benzene-petroleum ether mixture to yield 41.1 g. (90%) of galloyl chloride tribenzyl ether in white cottony needles, m. p. 116-116.5°.[10] On recrystallizing from benzene-petroleum ether, the crystals melted at 116.5-117°.

Purification of Alcohols.—Alcohols, none of which had a distillation range greater than 1.5°, were further purified by distilling them through a 75-cm. column packed with glass helices. The hexyl and octyl alcohols were distilled at atmospheric pressure; the others at about 1 mm. pressure. Only the constant boiling, middle cut of each alcohol was reserved for esterification work.

Tribenzyl Gallate Esters.—A typical experiment will be described. Ten grams of galloyl chloride tribenzyl ether (0.022 mole) and 9.4 g. (0.044 mole) of *n*-tetradecyl alcohol were placed in a 250-cc. Erlenmeyer flask and heated in an oil bath at 120°. The flask was shaken occasionally and removed from the bath as soon as the reagents had melted (*ca.* fifteen min.). After the bath had cooled to 90°, the

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(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(2) McKenzie and Müller, *J. Chem. Soc.*, **95**, 544 (1909).

(3) Cristiansen, THIS JOURNAL, **48**, 1358 (1926).

(4) Russell and Tebbens, Jr., *ibid.*, **64**, 2274 (1942).

(5) Bergel, *Chemistry and Industry*, 127 (1944).

(5a) Since this paper was completed it has come to our attention that work is in progress on the evaluation of methyl, ethyl, propyl, amyl, hexyl, octyl, decyl and cetyl gallates as antioxidants for marine oils [see Editor's note, *Fishery Market News*, **7**, 7, 18 (1945)]. No method of preparation of these esters was given.

(6) Fischer, *Ber.*, **41**, 2882 (1908).

(7) Fischer, Bergmann and Lipschitz, *ibid.*, **51**, 45 (1918).

(8) Schöpf and Winterhalder, *Ann.*, **544**, 62 (1940).

(9) Clinton and Geissman, THIS JOURNAL, **65**, 85 (1943).

(10) The 76-mm. immersion thermometer used for all melting point determinations was calibrated against a 76-mm. immersion thermometer which had been certified by the U. S. Bureau of Standards.