It is found that water formed by combustion of oxygen in an excess of hydrogen is 4 to 5 p. p. m. lower in density than that formed with an excess of oxygen. It is suggested that this observation may have some bearing on the interpretation of the results on apparent oxygen separation, reported by Washburn, Smith and Frandsen.

COLUMBUS, OHIO RECEIVED FEBRUARY 4, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Molecular Rearrangement of Sulfanilides. I

BY MAURICE L. MOORE[1] AND TREAT B. JOHNSON

In a previous paper,[2] the authors proposed a mechanism of reaction to explain the formation of aromatic amino-sulfides from aniline and similar amines by the action of sulfur in the presence of lead oxide. This mechanism is based on two reactions involving, first, the formation of an intermediate sulfanilide type of compound, which then under the conditions of the experiment undergoes rearrangement to an amino-sulfide. The isolation of such an intermediate from the reaction mixture seemed to present considerable experimental difficulty, so it was decided to prepare a series of analogous compounds containing the -S-NH-linkage within the molecule, and study the conditions controlling their molecular rearrangement.

Zincke[3] has described the preparation of certain compounds of the sulfanilide type. The *o*-nitro derivative, *o*-$NO_2C_6H_4$-S-NHC_6H_5, prepared by the action of *o*-nitrophenyl sulfur chloride upon aniline, is a typical representative. We have prepared this sulfanilide and the corresponding *o*- and *p*-sulftoluidides and studied their rearrangement. We found that *o*-nitrophenylsulfanilide I upon heating at a temperature of 150–160° for six hours gave a small yield of *o*-nitrophenyl *p'*-aminophenyl sulfide, II. This compound was identified by conversion to the corresponding *o*-nitrophenyl *p'*-hydroxyphenyl sulfide, which proved to be identical with the phenol derivative prepared by the action of *o*-nitrophenyl sulfur chloride on phenol.[3]

$NO_2C_6H_4SNHC_6H_5$ I

$NO_2C_6H_4SC_6H_4NH_2$ II

$NO_2C_6H_4SNHC_6H_4CH_3$ III

$NO_2C_6H_4SC_6H_3(CH_3)(NH_2)$ IV

Under similar treatment the *o*- and *p*-sulftoluidides underwent a corresponding rearrangement, the *p*-sulftoluidide III rearranging with substitution *ortho* to the amino group IV. Under the above conditions both compounds gave a dark colored mixture which presented considerable difficulty in purifying and the yield of the sulfide produced by rearrangement was low.

It has been shown previously that the benzidine, methylene[4] and sulfonyl[5] types of molecular rearrangements are greatly accelerated when heated in an acid solution. Here the conditions effecting rearrangement are much milder than when the compounds are heated alone, and are brought about with increased yields. Therefore, our sulfanilides were subjected to a similar treatment, but we found, on warming in a dilute hydrochloric acid solution, instead of undergoing a rearrangement, hydrolysis took place forming *o,o'*-dinitrophenyl disulfide and the hydrochloride of the amine. The same results were obtained if the sulfanilides were heated in the presence of the amine hydrochloride and also on long digestion in glacial acetic acid.

By heating the sulfanilides in the presence of an excess of the corresponding amine we found that it was possible greatly to increase the yield of our rearranged product and obtained it in a form which was much easier to purify. When *o*-nitrophenylsulfanilide, for example, was heated at a temperature of 180–190° for six hours with an excess of aniline, the *o*-nitrophenyl *p'*-aminophenyl sulfide was formed in a yield of 70%. Both the *o*- and *p*-sulftoluidides gave equally as good if not better results. In the case of the *o*-nitrophenylsulf-*o*-toluidide we were able to isolate two rearrangement products which reacted correctly for amino sulfides. The lower melting product was formed in yields about ten times as large as the higher melting material. Thus, it appears,

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(1) A. Homer Smith Research Fellow in Organic Chemistry, 1934–1935.

(2) Moore and Johnson, THIS JOURNAL, **57**, 1287 (1935).

(3) Zincke, *Ann.*, **391**, 57 (1912).

(4) (a) Braun and Kruher, *Ber.*, **45**, 2977 (1912); (b) Cohn and Fischer, *ibid.*, **33**, 2586 (1900); (c) Meyer and Rohmer, *ibid.*, **33**, 250 (1900); (d) Eberhardt and Welter, *ibid.*, **27**, 1804 (1894).

(5) Witt and Truttwin, *ibid.*, **47**, 2786 (1914).

at present, that we are dealing here with a double rearrangement with substitution in the *ortho* as well as in the *para* position. The differentiation between the two products has not been established as yet. This is the only case where we isolated two products in our rearrangement studies.

We have also prepared Zincke's *p*-nitrophenylsulfanilide[6] and rearranged it under the conditions described above into the corresponding amino sulfide. In conclusion, these results lead us to believe that our postulation calling for the primary formation of a sulfanilide type of compound in the reaction of aniline with sulfur is valid and that under the influence of heat this rearranges to an amino sulfide.

In an effort to obtain the amino sulfides directly, aniline hydrochloride and acetanilide were treated with *o*-nitrophenyl sulfur chloride in glacial acetic acid and also in the presence of sodium acetate but without success, the disulfide being formed in each case. The use of pyridine did not lead to better results and the disulfide was formed when *o*-nitrophenyl sulfur chloride was warmed with this reagent.

Experimental Part

o-Nitrophenylsulfur-o-toluidide.—The *o*-nitrophenyl sulfur chloride was prepared by allowing chlorine gas to react with *o,o'*-dinitrodiphenyl disulfide[7] according to the method of Zincke.[3] *o*-Nitrophenyl sulfur chloride (50 g.) dissolved in anhydrous ether (500 ml.) was allowed to interact with *o*-toluidine (55 g.) dissolved in ether (50 ml.), the toluidine solution being added slowly through a reflux condenser to the *o*-nitrophenyl sulfur chloride solution. A precipitate of *o*-toluidine hydrochloride immediately settled out and the solution began to reflux. After the final addition of *o*-toluidine the mixture was allowed to stand for thirty minutes. The *o*-toluidine hydrochloride was then removed by filtration and washed several times with ether. The combined filtrates were concentrated by slowly evaporating the ether, when the *o*-sulftoluidide crystallized as an orange reddish solid; yield, 60 g.; m. p. 119.5–120°. This is soluble in the ordinary organic solvents and insoluble in dilute hydrochloric acid.

Anal. Calcd. for $C_{13}H_{12}O_2N_2S$: S, 12.31; N, 10.77. Found: S, 12.36, 12.45; N, 10.71, 10.65.

o-Nitrophenylsulfanilide, m. p. 95°, and *p*-nitrophenylsulfanilide, m. p. 75°, were prepared as red solids by the same method. The *o*-nitrophenylsulf-*p*-toluidide was obtained as a yellow crystalline compound, m. p. 135° (Zincke,[3] m. p. 130°).

Anal. Calcd. for $C_{13}H_{12}O_2N_2S$: S, 12.31; N, 10.77. Found: S, 12.35, 12.40; N, 10.74, 10.68.

Rearrangement by Heating. (1) 2-Nitrophenyl-4'-aminophenyl Sulfide.—*o*-Nitrophenylsulfanilide (10 g.) was heated in an oil-bath for five hours at 150–160° with occasional stirring. The black oily liquid was cooled and treated with dilute hydrochloric acid by warming on the steam-bath for thirty minutes, forming a dark colored crystalline solid. This partially dissolved and by filtering and cooling the acid solution, a small quantity of glistening prismatic crystals was obtained. This was later shown to be the hydrochloride salt of *o*-nitrophenyl *p'*-aminophenyl sulfide, m. p. 225°. The remaining solid was dissolved in alcohol and decolorized by boiling several times with Norite. The solution was then made faintly alkaline with 10% sodium hydroxide and by recrystallizing several times from alcohol, a bright yellow crystalline solid was obtained; yield, 1.5 g.; m. p. 106°; mixed with the original starting material (94–95°), m. p. 70–76°. The sulfide was soluble in the ordinary organic solvents while the hydrochloride was difficultly soluble in water. The hydrochloric acid salt was readily obtained in crystalline form by dissolving the free base in ether solution and slowly adding a small amount of concentrated hydrochloric acid, m. p. 225°.

Anal. Calcd. for $C_{12}H_{10}O_2N_2S$: S, 13.01; N, 11.38. Found: S, 13.15, 13.08; N, 11.30, 11.50.

(2) 4-Nitrophenyl 4'-Aminophenyl Sulfide.—*p*-Nitrophenylsulfanilide (10 g.) gave a product which was quite soluble in hot dilute hydrochloric acid, although it was much darker and presented considerable difficulty in purifying. The *p*-nitrophenyl *p'*-aminophenyl sulfide was obtained as a yellow crystalline solid from warm alcohol; yield, 1 g.; m. p. 140–141°. The sulfide is soluble in dilute hydrochloric acid and in the ordinary organic solvents. The hydrochloride salt was obtained as a colorless crystalline solid, m. p. 200°.

Anal. Calcd. for $C_{12}H_{10}O_2N_2S$: S, 13.01; N, 11.38. Found: S, 13.20, 13.27; N, 11.20, 11.26.

(3) 2-Nitrophenyl 3'-Methyl-4'-aminophenyl Sulfide.—*o*-Nitrophenylsulf-*o*-toluidide (10 g.) gave about 1.5 g. of *o*-nitrophenyl *m'*-methyl-*p'*-aminophenyl sulfide under the same treatment as above. It crystallized in orange colored crystals from alcohol, m. p. 103°. When mixed with the original starting material (119.5–120°) the melting point was lowered to 80–84°. The amino sulfide hydrochloride is difficultly soluble in water. The hydrochloride salt was obtained as a green crystalline solid, m. p. 235°.

Anal. Calcd. for $C_{13}H_{12}O_2N_2S$: S, 12.31; N, 10.77. Found: S, 12.44, 12.50; N, 10.66, 10.52.

(4) 2-Nitrophenyl 5'-Methyl-2'-aminophenyl Sulfide.—*o*-Nitrophenylsulf-*p*-toluidide rearranged to *o*-nitrophenyl *p'*-methyl-*o'*-aminophenyl sulfide when heated as above. This crystallized from alcohol as an orange-red solid, m. p. 108°. Mixed with the original starting material (135°) it gave a depression to 88–90°. The amino sulfide hydrochloride is difficultly soluble in water. The hydrochloric acid salt formed as a slightly greenish crystalline powder, m. p. 190°.

Anal. Calcd. for $C_{13}H_{12}O_2N_2S$: S, 12.31; N, 10.77. Found: S, 12.16, 11.97; N, 10.40, 10.52.

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(6) Zincke, *Ann.*, **400**, 2 (1913).

(7) Bogert and Stull, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1928, Vol. VIII, p. 64.

Rearrangement by Heating in the Presence of an Excess of Amine

(1) **2-Nitrophenyl 3′-Methyl-4′-aminophenyl Sulfide.**—The *o*-sulftoluidide compound (10 g.) was suspended in 20 ml. of *o*-toluidine and the mixture heated on an oil-bath under a reflux condenser for six hours at 180–190°. Complete solution took place. The mixture was then cooled and 5 ml. of 20% sodium hydroxide solution added. The excess of *o*-toluidine was removed by steam distillation, leaving a dark black semi-solid mass. This was treated with dilute hydrochloric acid and the mixture warmed on the steam-bath for thirty minutes, when the reaction product partially dissolved, leaving behind a dark crystalline mass. The acid solution was neutralized with 10% sodium hydroxide, when a yellow colored oily solid was obtained. This was washed free of alkali, dissolved in alcohol, decolorized by boiling several times with Norite, and the solution then cooled. The product of rearrangement separated in crystalline form; yield, 0.8 g.; m. p. 129–130°. When mixed with the original material (135°), the m. p. was lowered to 95–97°. When mixed with the compound formed by direct heating of the *o*-sulftoluidide (103°) there was a depression in melting point to 76–81°. The sulfide is soluble in the ordinary organic solvents and in hot dilute hydrochloric acid.

Anal. Calcd. for $C_{13}H_{12}O_2N_2S$: S, 12.31; N, 10.77. Found: S, 12.60, 12.46; N, 10.61, 10.45.

The residual dark solid which was insoluble in the dilute hydrochloric acid above was dissolved in alcohol and decolorized by digestion with Norite. The solution was then made slightly alkaline with 10% sodium hydroxide and again further decolorized with Norite. Upon cooling a yellow crystalline substance was obtained, yield 5 g.; m. p. 101–103°.

It was later found that the excess of *o*-toluidine could be easily removed by pouring the warm mixture after heating into a cold solution of dilute hydrochloric acid. The *o*-toluidine formed the hydrochloric acid salt which readily dissolved whereas the hydrochloride of the amino sulfide was insoluble and could be separated by filtration. This was purified according to the above procedure. Five grams of the *o*-sulftoluidide gave 3.5 g. of the aminosulfide, m. p. 101–103°.

(2) **2-Nitrophenyl 4′-Aminophenyl Sulfide.**—The corresponding sulfanilide compound (10 g.) was heated with aniline (15 ml.) according to the above procedure and after standing overnight the solution was poured into dilute hydrochloric acid. The salt formed was dissolved in alcohol, and on decolorizing the solution with Norite the free amino sulfide base crystallized out; yield, 7 g.; m. p. 103–105°.

(3) **4-Nitrophenyl 4′-Aminophenyl Sulfide.**—Five grams of the sulfanilide (m. p. 75°) in 10 ml. of boiling aniline gave 3 g. of this sulfide, m. p. 128–140°.

(4) **2-Nitrophenyl 5′-Methyl-2′-aminophenyl Sulfide.**—The *p*-sulftoluidide compound (10 g.) when treated with *p*-toluidine (20 ml.) yielded the corresponding amino sulfide (6 g.), m. p. 106–108°.

All of the above sulfanilide type of compounds readily underwent hydrolysis when heated in a dilute hydrochloric acid solution or with the amine hydrochloride salt to give *o,o*′-dinitrodiphenyl disulfide instead of rearranging to the corresponding amino sulfides.

2-Nitrophenyl 4′-Hydroxyphenyl Sulfide.—This compound was prepared by diazotizing *o*-nitrophenyl *p*′-aminophenyl sulfide according to a modification of the method of Bass and Johnson.[8] The hydrochloride (5 g.) of the amino sulfide was suspended in 35 ml. of glacial acetic acid and treated with isoamyl nitrite (2.5 g.) at 0–5° over a period of thirty minutes with constant stirring. The reaction was continued for thirty minutes after the final addition of the nitrite. In the meantime, a solution of 100 ml. of concentrated sulfuric acid and 80 ml. of water was brought to boiling (160°) and the diazotized solution slowly added. The dark solution was then boiled for forty-five minutes, during which time an oil separated. The mixture was diluted with water and cooled. The oil which separated was dissolved in 5% sodium hydroxide solution and then decolorized by digestion with Norite. The free phenol was then precipitated as an oily solid with dilute hydrochloric acid. This was purified by dissolving in hot 50% alcohol, further decolorized with Norite and then allowed to crystallize; yield, 1.4 g.; m. p. 127–129°. The above compound was identical with the phenol sulfide, m. p. 129–130°, prepared by the action of *o*-nitrophenyl sulfur chloride upon phenol[3] in ether solution.

4-Nitrophenyl 4′-Hydroxyphenyl Sulfide.—This compound was prepared by the diazotization of *p*-nitrophenyl *p*′-aminophenyl sulfide by the above procedure, m. p. 148–150°. This was identical with the compound, m. p. 150–151°, prepared from phenol by the action of *p*-nitrophenyl sulfur chloride.[6,9]

Aniline hydrochloride and acetanilide were respectively treated with *o*-nitrophenyl sulfur chloride in glacial acetic acid and in the presence of sodium acetate by warming on the steam-bath, but *o,o*′-dinitrodiphenyl disulfide was obtained in each case instead of the corresponding amino sulfide. Pyridine was treated with the sulfur chloride in ether solution but instead of forming an addition compound, the disulfide was produced.

Summary

Certain amino sulfides have been prepared by the rearrangement of sulfanilides. This rearrangement was accomplished by heating the sulfanilide; but it was found possible greatly to increase the yields by heating sulfanilides in the presence of the corresponding amine. Sulfanilides do not rearrange to the isomeric amino sulfides in dilute acid solutions, but immediately undergo hydrolysis under such conditions to give a disulfide and an amine salt.

The rearrangement of sulfanilides by simple heating lends support to our explanation of the mechanism of the reaction between sulfur and aniline in the presence of lead oxide, leading us to conclude that there is an intermediate formation of a sulfanilide type of compound, which then undergoes rearrangement to give the resulting amino sulfide.

NEW HAVEN, CONN. RECEIVED JUNE 6, 1935

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[8] Bass and Johnson, THIS JOURNAL, 52, 1146 (1930).

[9] Foss, Dunning and Jenkins, *ibid.*, 56, 1978 (1934).