[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

THE FORMATION OF A PHENAZINE COMPOUND FROM A DIPHENYL ETHER DERIVATIVE

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I. Nitration of Diphenyl Ether.—On treating diphenyl ether with concentrated sulfuric acid and potassium nitrate in exactly the same manner as that described for the preparation of 2,4,8,10-tetranitrodiphenylmethane,[1] tetranitrodiphenyl ether (m. p. 195–197°) was obtained, as was expected, in 80% yield. The melting point and other properties of this substance are in close agreement with those of 2,4,8,10-tetranitrodiphenyl ether (m. p. 195°) which was prepared by C. Willgerodt by the reaction of potassium dinitrophenolate and chlorodinitrobenzene,[2] and differing from tetranitrodiphenyl ether (m. p. 216°) which was isolated by W. Borsche as a by-product when he prepared *m*-dinitrophenol from *m*-dinitrochlorobenzene.[3] The structure of this compound was further confirmed by the fact that on alkaline hydrolysis it gave 2,4-dinitrophenol in quantitative yield.

The nitration of diphenyl ether has been studied previously by Mailhe and Murat[4] and recently by Suter[5] but no satisfactory method of preparing this compound has been indicated.

II. Reduction of 2,4,8,10-Tetranitrodiphenyl Ether.—According to M. Schöpff, on reduction by stannous chloride and concentrated hydrochloric acid, 2,4,8,10-tetranitrobenzophenone gave 3,6-diamino-acridone in good yield.[6] This was also confirmed by the author.[7] In the hope of forming diaminophenoxazine in an analogous way, 2,4,8,10-tetranitrodiphenyl ether was reduced in exactly the same manner that was described for tetranitrobenzophenone. But this is not the case, and 2,4,8,10-tetraminodiphenyl ether, which was identified as such by its analysis, insolubility in caustic soda and the determination of molecular weight for its tetrabenzoyl derivative, was formed nearly exclusively, accompanied by a small quantity of a phenazine compound as a by-product. Special efforts to convert the tetraminodiphenyl ether to the corresponding phenoxazine compound were all fruitless.

To return to the problem of the phenazine compound, whose method of isolation will be given in the experimental part, this substance formed

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[1] Matsumura, THIS JOURNAL, **51**, 815 (1929).

[2] Willgerodt, *Ber.*, **13**, 887 (1880).

[3] Borsche, *ibid.*, **50**, 1349 (1917).

[4] Mailhe and Murat, *Compt. rend.*, **154**, 715 (1912); Mailhe, *Bull. soc. chim.*, [IV] **11**, 1011 (1912).

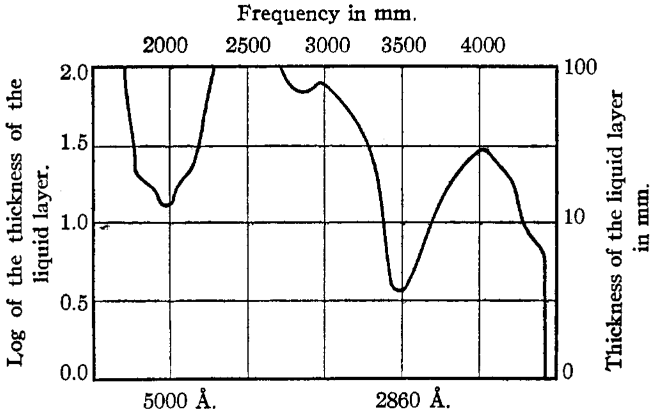
[5] Suter, THIS JOURNAL, **51**, 2581 (1929).

[6] Schöpff, *Ber.*, **27**, 2318 (1894).

[7] Matsumura, THIS JOURNAL, **51**, 815 (1929).

dark red crystals from alcohol, and it is characterized by a beautiful green color reaction with concd. sulfuric acid, this being a common color reaction of amino derivatives of phenazine compounds.

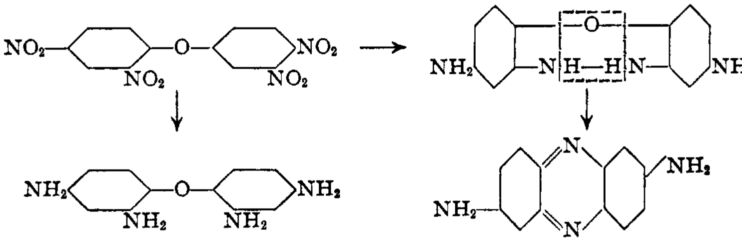
The analytical figures of this compound and its sulfate showed the compound to have a molecular formula agreeing with diaminophenazine. Finally, a phenazine base (m. p. 171°) was isolated from it by the diazo method, and the absorption maxima in visible and ultraviolet spectra were found to be in close agreement with those given for several amino derivatives of phenazine by F. Kehrmann and M. Sandoz[8] (Fig. 1 and Table I). From these facts, it may be concluded that the compound in question must be diaminophenazine.



1/10,000 mole alcoholic solution of diaminophenazine.

Fig. 1.

Concerning the problem of the positions of two amino groups, the following proposed interpretation for the mode of formation of this compound may serve in the solution of this problem. According to this explanation, the reaction involves formation of an intermediate seven-membered ring, dehydration and subsequent intramolecular rearrangement.



III

On the basis of this reaction, the substance must have the structure

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[8] Kehrmann and Sandoz, *Helv. Chim. Acta*, 3, 109 (1920).

of 2,6 diaminophenazine (III), an unknown isomer of diaminophenazine.[9] A further fact of value in the elucidation of the structural problem is found in comparisons of the characteristic constants given by earlier investigators with the known phenazine compounds and those of the compound in question.

TABLE I

COMPARISON OF THE CONSTANTS OF PHENAZINE COMPOUNDS

Compound	Crystal	M. p., °C.	Absorption max. Visible spectra	Absorption max. Ultraviolet
3,6-Diaminophenazine	Dark yellow needles	280	447	265
2,3-Diaminophenazine	Brown-yellow needles	265	454	265–285
Author's diaminophenazine	Dark red columns	> 320	506	285
2-Aminophenazine	Red needles	290–291	472	265

All compounds give a green color reaction with concd. sulfuric acid.

Experimental Part

2,4,8,10-Tetranitrodiphenyl Ether.—One hundred and thirty grams of finely-powdered potassium nitrate was dissolved in 700 g. of concd. sulfuric acid below 30° during about three-quarters of an hour; 50 g. of diphenyl ether (m. p. 28–29°, b. p. 253°) was introduced into the solution under constant stirring during one and one-half hours at 10–25°. The mixture was then gradually warmed to 70° on the sand-bath and kept at that temperature for half an hour with stirring and then allowed to stand. After being cooled, it was poured into 5 liters of ice water, when a light yellow precipitate was obtained which was filtered and washed. After being dried, it was boiled with 200 cc. of alcohol, filtered while hot and recrystallized from 600 g. of boiling glacial acetic acid, giving small prisms of light yellow color; m. p. 195–197°; yield, 80 g. (about 80%) after recrystallization. After three further recrystallizations from glacial acetic acid, no change of melting point was seen.

Anal. Calcd. for $C_{12}H_6O_9N_4$: C, 41.14; H, 1.71; N, 16.00. Found: C, 40.92; H, 2.04; N, 16.05, 16.10.

Hydrolysis of 2,4,8,10-Tetranitrodiphenyl Ether.—A mixture of 2 g. of finely powdered 2,4,8,10-tetranitrodiphenyl ether and 50 g. of potassium hydroxide solution (20%) was heated at 100° for two hours. After being cooled, water was added and it was filtered from a small quantity of insoluble white prisms (0.4 g.), which was identified as the initial substance by its melting point (195–197°) and the mixed melting point method. On acidifying with dilute hydrochloric acid, the filtrate gave 1.1 g. of yellow flat prisms; m. p. 113–114°; 0.3 g. of an additional yield was obtained by shaking the mother liquor with ether. After one recrystallization from hot water, no change of melting point was seen. Its mixed melting point with 2,4-dinitrophenol (m. p. 111–112°) of Kahlbaum was 112–113°.

Anal. Calcd. for $C_6H_4O_5N_2$: N, 15.22. Found: N, 15.30.

Reduction of 2,4,8,10-Tetranitrodiphenyl Ether.—On the gradual addition of 35 g. of 2,4,8,10-tetranitrodiphenyl ether to the solution of 270 g. of stannous chloride in the same quantity of concd. hydrochloric acid (sp. gr. 1.9) at 100°, a vigorous reaction took place with spontaneous elevation of temperature to 115–120°, and the main reduction

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[9] The study of absorption spectra of sulfate of 2,6-diaminophenazine has been reported by Kehrmann, Ref. 8, but so far as I am aware the description of its synthesis has not been given in the literature.

appeared to be finished after a few minutes. The violet colored viscous fluid obtained was heated for a further half hour at the same temperature with a constant agitation. On being cooled, after the addition of water, tin was removed by repeated treatments with hydrogen sulfide. The earlier portion of the precipitates of tin sulfide assumed a violet color, on account of being admixed with phenazine compound (perhaps in the form of quinhydrone salt).

The filtered liquid, after being concentrated to a small volume under reduced pressure, was saturated with hydrogen chloride gas, when the liquid became filled with colorless crystals of the hydrochloride of tetraminodiphenyl ether.

The crystalline material was dried in a vacuum over sodium hydroxide; yield, 25 g. It forms colorless prisms and is extremely hygroscopic. It became light gray at 230° and dark violet at 280°, ammonium chloride subliming to the upper part. It does not melt at 310°. The aqueous solution, on the addition of ferric chloride, assumed a dark red color and afterward gave a dark brown precipitate. The aqueous solution, in contact with air, became brown after two days, and sooner on warming. The aqueous solution, on the addition of ammoniacal silver solution or gold chloride solution in the cold, gave precipitates of the corresponding metals. The aqueous solution, on the addition of concd. ammonia, assumed a beautiful blue color; the color faded after some time and brown precipitates appeared.

Anal. Calcd. for $C_{12}H_{14}ON_4 \cdot 4HCl$: Cl, 38.83. Found: Cl, 39.32.

The free base was best prepared in the following way. On the addition of an excess of caustic soda solution (10%) to 1 g. of the hydrochloride, in a separating funnel, light colored oil drops separated out. It was quickly shaken with a large quantity of chloroform. On concentrating the solvent, after drying with sodium sulfate, light brown crystals separated out. As it is extremely sensitive to air and alkali, treatment of more than 1 g. at a time is not desirable. It gives a colorless prism with light brown surface from benzene; m. p. 129°. The sample thus purified keeps well in the air for a long time. It is moderately soluble in hot chloroform, hot alcohol and hot benzene, but almost insoluble in ether, and somewhat soluble in cold water.

Anal. Calcd. for $C_{12}H_{14}ON_4$: C, 62.61; H, 6.09; N, 24.35. Found: C, 62.44; H, 6.40; N, 24.39.

2,4,8,10-Tetrabenzoylaminodiphenyl Ether.—To the solution of 1 g. of 2,4,8,10-tetraminodiphenyl ether hydrochloride in 10 g. of pyridine, 4 g. of benzoyl chloride was added gradually with stirring. After being allowed to cool, water was added and the solution acidified with dilute hydrochloric acid, when the reaction product separated in a colorless and resinous form. The water was decanted and the material repeatedly washed. The resinous matter, on repeated treatment with ether, turned to white crystals. It gives colorless needles from nitrobenzene; m. p. 232–233°. It is easily soluble in hot chloroform, hot alcohol and cold acetone but difficultly in boiling benzene and almost insoluble in ether.

Anal. and mol. wt. Subs., 1.261 mg. in 9.445 mg. of camphor: Δt, 8.0°. Calcd. for $C_{40}H_{30}O_5N_4$: mol. wt., 646; C, 74.30; H, 4.64; N, 8.67. Found: mol. wt., 668; C, 74.68; H, 4.86; N, 8.84.

Various efforts to convert the tetraminodiphenyl ether to the corresponding oxazine compound were fruitless; for instance, (1) heating the hydrochloride alone or in the presence of fused zinc chloride in carbon dioxide atmosphere at 200° for twenty hours, or (2) heating it with glacial acetic acid at 140° for six hours, gave no definite substance, (3) heating it with hydrochloric acid (13%) at 160° appeared to have caused hydrolysis of the phenolic ether and gave, on further working, nothing but a black tar.

Diaminophenazine.—The first portion of the precipitate of tin sulfide which assumed a violet color, after thoroughly washing, was treated with an excess of caustic soda to complete dissolution of the tin sulfide, when a red substance remained undissolved. This was dissolved in dilute hydrochloric acid and the filtered bluish-violet solution, on making alkaline with ammonia, gave a dark red precipitate. It was recrystallized from alcohol; yield, 1.5 g. It forms hexagonal plates or columns of dark red color with a metallic luster. No change was seen at 320°. The absorption spectra of its 1/10,000 molar alcoholic solution is given in Fig. 1.

It is moderately soluble in boiling and cold alcohol, with orange-red color and yellow fluorescence, sparingly soluble in water and insoluble in benzene. It is fairly soluble in cold acetone with orange-yellow color and yellowish-green fluorescence, somewhat difficultly in warm chloroform with intense green fluorescence and sparingly soluble in ether with yellowish-green fluorescence. The solution in concd. sulfuric acid is bright green and on the addition of water becomes bluish-violet, and orange on the addition of a great excess of water. It dissolves in dilute hydrochloric acid with a purple-red color and on the addition of water the color becomes bluish-violet.

Anal. Calcd. for $C_{12}H_{10}N_4$: C, 68.57; H, 4.76; N, 26.67. Found: C, 68.60, 68.60; H, 4.84, 4.92; N, 26.24, 26.39.

Sulfate.—On addition of sulfuric acid (50%) to the alcoholic solution of the base violet needles of the sulfate ($C_{12}H_{10}N_4 \cdot H_2SO_4$) separate.

Anal. Calcd. for $C_{12}H_{10}N_4 \cdot H_2SO_4$: H_2SO_4, 31.82. Found: H_2SO_4, 32.35.

When it was recrystallized from hot water, after being allowed to stand for several days, large black-violet crystals of the sulfate ($(C_{12}H_{10}N_4)_2 \cdot H_2SO_4$) separated. The water of crystallization was removed at 130° in a vacuum.

Anal. Water of crystallization. Calcd. for $(C_{12}H_{10}N_4O_2)_2 \cdot H_2SO_4 \cdot 7.5H_2O$: H_2O, 20.67; C, 55.60; H, 4.63. Found: H_2O, 20.77; C, 55.83; H, 4.80.

Triacetyldiaminophenazine.—A mixture of 0.2 g. of diaminophenazine, 1.2 g. of acetic anhydride and 0.2 g. of fused sodium acetate was heated for two hours on the boiling water-bath. On cooling, water was added and the yellow crystals obtained were collected. It forms yellow prisms from alcohol; no change was observed at 320°. It is soluble in alcohol and acetone with yellow color and green fluorescence, very difficultly in hot chloroform, and almost insoluble in hot benzene and ether. The solution in concd. sulfuric acid is Bordeaux red; the color fades after a few minutes and a pure green color develops. Contrary to the expectation of obtaining a diacetyl compound, the analysis shows the presence of three acetyl groups.

Anal. Calcd. for $C_{18}H_{17}O_3N_4$: C, 64.09; N, 5.04; N, 16.62. Found: C, 64.14; H, 5.27; N, 16.92.

Phenazine.—On the gradual addition of an excess of finely powdered sodium nitrite to the cooled solution (−5°) of 0.4 g. of diaminophenazine in 24 g. of concd. sulfuric acid with vigorous agitation, the initial green solution became a dark violet, viscous mass. Then 120 cc. of alcohol was added and the clear brown solution obtained was refluxed for two hours on the water-bath. After evaporating the alcohol, the reaction mixture was made alkaline with caustic soda solution (25%) and shaken with ether. On evaporating the solvent, 0.2 g. of a yellow crystalline mass was obtained. It was sublimed in Kemp's apparatus under a diminished pressure; yield, 0.1 g. It gives yellow needles from alcohol, m. p. 170–171°. The solution in concd. sulfuric acid is blood red and on the addition of water becomes clear yellow.

Anal. Calcd. for $C_{12}H_8N_2$: N. 15.56. Found: N. 15.49.

I hereby desire to express my hearty thanks to Professor Hata for the interest which he has kindly taken in this work.

Summary

1. The preparation of 2,4,8,10-tetranitrodiphenyl ether by the nitration of diphenyl ether has been described.
2. In connection with the reduction of 2,4,8,10-tetranitrodiphenyl ether by stannous chloride and concd. hydrochloric acid, the formation of diaminophenazine and 2,4,8,10-tetraminodiphenyl ether has been observed.

TOKYO, JAPAN

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF WASHINGTON]

SOME REACTIONS OF QUINOL AND A CONTRIBUTION TO THE CONSTITUTION OF QUINHYDRONE

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When an iodate reacts with quinol,[2] quite diverse effects are produced when the solutions are acid, neutral or alkaline. In general, quinhydrone or a dye or a mixture of these two is obtained.

In equal aqueous solutions the following products were obtained

Quinol, g.	$NaIO_3$, g.	CH_3COOH, g.	NaOH, g.	Product
10	6	5	0	7 g. of quinhydrone
10	6	0	0	9 g. of quinhydrone
10	6	0	5	Only the dye
40	25	0	0	39 g. of quinhydrone

Preparation of Quinhydrone.—The following is the most convenient and satisfactory method for the preparation of quinhydrone. To 40 g. of quinol suspended or dissolved in 200 cc. of water, add a cold saturated solution of 25 g. of sodium iodate. The mixture is shaken and kept cold by tap water. Almost immediately long glistening prisms begin to separate and in less than one-half hour a 90% yield and in 2–3 hours practically a quantitative yield can be filtered off as brassy black prisms melting at 171°. The reaction is in accordance with

$$6C_6H_6O_2 + 2NaIO_3 \longrightarrow 3C_6H_4O_2{\cdot}C_6H_6O_2 + 2NaI + 6H_2O$$

Since hydriodic acid[3] reduces quinone to quinol, acid solutions give smaller yields.

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[1] The material presented in this paper is from part of a thesis submitted by Theodore W. Evans, du Pont fellow for 1929–1930, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1930.

[2] For the oxidation of quinol to oxalic acid, see Hesse, *Ann.*, **114**, 300 (1860); nitrogen oxides to nitranilic acid, Nietzki, *ibid.*, **215**, 138 (1883); silver sulfate and persulfuric acid to maleic and formic acid, Kempf, *Ber.*, **39**, 3717, 3726 (1906); by other oxidants, Wöhler, *Ann.*, **51**, 151 (1844).

[3] Wöhler, Ref. 2. For the reaction of iodine in $KHCO_3$ solutions, see Valeur, *Ann. chim.*, [7] **21**, 529 (1900).