

tions. The final product weighed 8.5 g. (75%), melted at 209–211° alone and did not depress the melting point of the same substance prepared above.

*Anal.* Calcd. for  $C_{17}H_{15}N_3O_2S$ : S, 9.86. Found: S, 9.96.

**4-Nitro-4'-(N-2-thiazolyl)-aminodiphenyl Sulfone (XI).**—A mixture of 27.8 g. (0.10 mole) of (X) and 20.8 g. (0.25 mole) of 2-chlorothiazole<sup>16</sup> was heated in an oil-bath at 100–105° until solidification occurred (about two and one-half hours). The product, after having been extracted with pyridine, treated with decolorizing charcoal and precipitated by the addition of water, was digested for three hours in 200 ml. of methanol, in which it is only slightly soluble. The suspension was cooled, and the product was collected and washed with 50 ml. of methanol and 50 ml. of water. After drying, it weighed 33 g. (91.4%) and melted at 247.5–249°.

*Anal.* Calcd. for  $C_{15}H_{11}N_3O_2S_2$ : S, 17.73. Found: S, 17.53.

**4-Amino-4'-(N-2-thiazolyl)-aminodiphenyl Sulfone (III).**—To a warmed (75°) suspension of 33 g. (0.091 mole) of (XI) in 500 ml. of glacial acetic acid in a one-liter 3-necked flask equipped with stirrer, thermometer

(16) Obtained from 2-aminothiazole in 60% yield by the method of Ganapathi and Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 362 (1945); *C. A.*, **40**, 4059 (1946).

and condenser was added a clarified solution of 98.5 g. (0.438 mole) of  $SnCl_2 \cdot 2H_2O$  in 265 ml. of glacial acetic acid. After a three-hour period of reaction at 75–85°, the solution was cooled and neutralized below 25° by the addition of a 50% solution of sodium hydroxide. After extraction with concentrated caustic solution, decolorization with charcoal and numerous recrystallizations from aqueous acetone there was obtained 11 g. (37.8%) of colorless crystals melting at 234–237°. A small portion was recrystallized again from aqueous methanol and then melted at 235.6–240.1°.

*Anal.* Calcd. for  $C_{15}H_{13}O_2N_3S_2$ : S, 19.33. Found: S, 19.85.

### Summary

4-Amino-4'-(2-pyrimidylamino)-diphenyl sulfone, 4-amino-4'-(2-pyridylamino)-diphenyl sulfone and 4-amino-4'-(2-thiazolylamino)-diphenyl sulfone have been synthesized for study as possible new antibacterial agents. In the course of this work several new 4,4'-disubstituted diphenyl sulfides and sulfones have been prepared and characterized.

BETHLEHEM, PENNA.

RECEIVED MARCH 8, 1947

[CONTRIBUTION FROM THE WM. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

## Studies in the Sulfone Series. III.<sup>1</sup> The Preparation and Properties of 2,8-Diaminothioxanthone- and 2,8-Thioxanthene-5-dioxides and Some Related Compounds

BY E. D. AMSTUTZ AND C. R. NEUMOYER<sup>2</sup>

In a previous paper<sup>3</sup> we reported the preparation of 2,8-diaminodibenzothiophene-5-dioxide which is the simplest of the *o,o'* bridged diamino-diphenyl sulfone derivatives.

The thioxanthenes and thioxanthenes which were of primary interest to us in this investigation may be considered to be derived from 4,4'-diaminodiphenyl sulfone by joining the 2,2' positions with methylene and carbonyl groups respectively. It was believed that one effect of methylene bridging should be to diminish the toxicity of the drug. Furthermore, it was thought that carbonyl bridging might increase the activity of the drug.

During the investigation we found it necessary to examine several possible routes to the desired 2,8-disubstituted heterocycle. These approaches all may be considered to be variants of a general process: namely, the ring-closure of substituted diphenyl sulfides and sulfones through some appropriate ortho-group. As work progressed it became abundantly clear that the state of oxidation of the sulfur has a profound effect on the ease of ring-closure. For example, we were unable in any case to bring about cyclization of sulfones al-

though a considerable variety of ortho-substituent groups was employed.

The following reaction sequence illustrates the method of synthesis found to be most satisfactory.

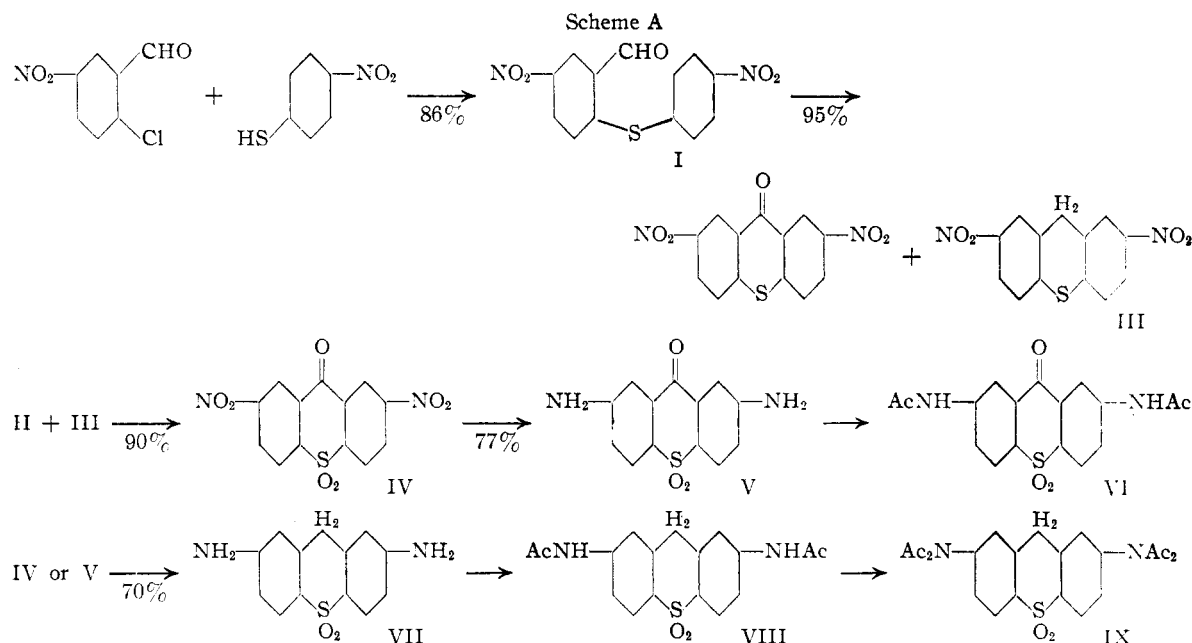
The condensation of 2-chloro-5-nitrobenzaldehyde with sodium *p*-nitrothiophenoxide was performed in refluxing aqueous ethanol solution. In ionic reactions of this and related sorts, the presence of water in the reaction mixture was of decided advantage. Dissolution of the aldehydodiphenyl sulfide (I) in concentrated sulfuric acid (60°) produced a deep red colored solution which developed a green fluorescence as cyclization proceeded. The product was recovered by pouring the solution onto ice and washing the solid with water. It appears probable from the work of Loudon<sup>4</sup> and from the character of the product that the carbinol which might be expected is either not produced or is unstable and undergoes disproportionation to the methylene and carbonyl groups. While we were not successful in separating, in pure condition, the present mixture we were able to show, in cases to be reported later, that both species are present and in substantially equal amounts. The mixture of thioxanthene and thioxanthone was smoothly converted by hydrogen peroxide in acetic acid to a single product,

(1) Paper II in this series, *THIS JOURNAL*, **69**, 1922 (1947).

(2) The William S. Merrell Co. Postdoctorate Fellow in Organic Chemistry, 1944–1946. Present address, Heyden Chemical Corp., Garfield, N. J.

(3) Neumoyer and Amstutz, *THIS JOURNAL*, **69**, 1920 (1947).

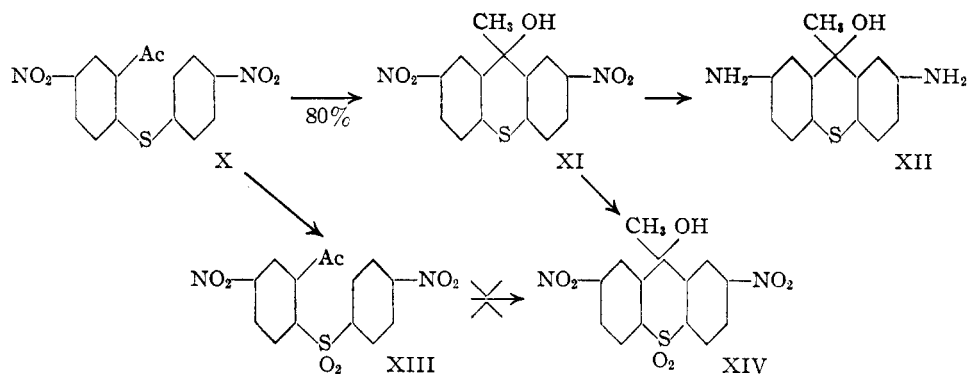
(4) Campbell, Dick, Ferguson and Loudon, *J. Chem. Soc.*, 747 (1941).



2,8-dinitrothiaxanthone dioxide. Reaction of the diamine with acetic anhydride yielded the diacetyl derivative and, with sodium formaldehyde sulfoxylate,<sup>5</sup> a water-soluble sodium salt. In general, however, the diamino compound proved to be quite unreactive and we were unable to force any

analogous to that with the corresponding xanthone.

The general method described above was applied also to the synthesis of the dinitro-10-methylthiaxanthanol, the reaction sequence appearing in the formula outline.



reaction with benzaldehyde or cinnamic aldehyde even under strenuous conditions.

The preparation of 2,8-diaminothiaxanthene dioxide (VII) was effected by a zinc metal and acetic acid reduction of either 2,8-dinitro- or 2,8-diaminothiaxanthone dioxide. This reduced derivative was found to be hygroscopic and resisted all attempts to render it anhydrous. For example, drying in a pistol over phosphorus pent oxide at 130° afforded only a monohydrate. The compound could be acetylated to either a diacetyl (VIII) or a tetraacetyl (IX) derivative depending upon the amount of acetic anhydride used. A water soluble sodium formaldehyde sulfoxylate derivative was prepared in a manner

The coupling of *p*-nitrothiophenoxide with 2-chloro-5-nitroacetophenone was carried out smoothly and in good yield in boiling ethanol or aqueous ethanol solution. When compound (X) was dissolved in concentrated sulfuric acid and the solution heated the usual dark red color developed. No greenish fluorescence was noted, however, as in the case of the corresponding aldehyde. Because of the tendency of the diamino compound (XIII) to produce tarry materials during the reduction with stannous chloride its isolation in a pure condition is more difficult than is the case with compound (V), for example. Indeed the amino derivatives of the thiaxanthenes as a whole appear to be much more labile substances than the aminothiaxanthenes. After preliminary attempts at purification by recrystallization and

(5) Raiziss, Clemeace and Freifelder, *J. Am. Pharm. Assn.*, **33**, 43 (1944).

extraction with various solvents, the pure amine was obtained by precipitation with dry hydrogen chloride from toluene solution. Under these conditions the colorless salt is first thrown down. On continued passage of dry hydrogen chloride gas through the suspension the solid assumes a definite blue color. This, we believe, may be associated with the formation of the thiaxanthonium ion by loss of the tertiary hydroxyl group of the carbinol.

Numerous attempts to oxidize the acetophenone-sulfide (X) led to only small yields of the sulfone (XIII), much material of undetermined structure and wide melting range being formed. The ring-closure of (XIII) to the xanthenol-dioxide (XIV) in sulfuric acid failed entirely but the required carbinol was obtained in small amounts by peroxide and chromic anhydride oxidation of (XI).<sup>6</sup> These oxidations likewise yielded much ill-defined material of indefinite melting points.

Another approach to the type of derivative represented by structures (IV) and (V) appeared to be by nitration of the readily available 2-nitrothiaxanthone (XVII). Mayer<sup>7</sup> had already prepared this substance by cyclization of (XVI) with phosphorus pentachloride (Route B). We found that the isomeric acid (XV) is more easily and

meric dinitro compounds (XVII) which resisted all attempts at complete separation. The partially separated mixture was reduced however and the resulting diaminothiaxanthones (XIX) recrystallized, acetylated and oxidized to the sulfone stage. After several recrystallizations a product was obtained which proved to be identical with (VI). Since the contaminant was not isolated, its structure is not certain but theoretical considerations point to the 2,6 configuration.

A report on the pharmacological and antibacterial properties of many of the compounds described herein will be made at a later time.

**Acknowledgment.**—The authors express their sincere thanks to The William S. Merrell Company for funds which permitted them to carry out this investigation. To Mr. I. Moyer Hunsberger the authors are especially grateful for some of the analyses and for technical assistance with the experiments on the xanthenols. The Heyden Chemical Corp. generously supplied the ortho chlorobenzoic acid and the ortho chlorobenzaldehyde used in the work.

### Experimental<sup>9</sup>

**5-Nitro-2-(*p*-nitrothiophenoxy)-benzaldehyde (I).**—5-Nitro-2-chlorobenzaldehyde (m. p. 81.2–82.7°) was prepared in 59% yield from *o*-chlorobenzaldehyde by the method of Erdmann<sup>10</sup> who reported a melting point of 80°. Sodium *p*-nitrothiophenoxide was prepared according to the directions of Waldron and Reid<sup>11</sup> in approximately the reported yield.

A hot solution of 21.3 g. (0.115 mole) of 5-nitro-2-chlorobenzaldehyde in 290 ml. of alcohol was diluted with 120 ml. of water after which 21.8 g. (0.123 mole) of sodium *p*-nitrothiophenoxide was added at one time. After refluxing for seventy-five minutes, the reaction mixture was cooled, filtered, washed once with cold alcohol and then with water. The product, obtained as yellow crystals, weighed 30.2 g. (86.5%) after drying and melted at 201–203°.

*Anal.* Calcd. for C<sub>13</sub>H<sub>8</sub>O<sub>6</sub>N<sub>2</sub>S: S, 10.54. Found: S, 10.44.

**2,8-Dinitrothiaxanthone (II) and 2,8-Dinitrothiaxanthene (III).**—The dinitrosulfide aldehyde (I) from the above condensation was added portionwise, over a period of fifteen minutes, to 300 ml. of concentrated sulfuric acid, the temperature rising to 35° in forty minutes. At the end of the spontaneous temperature rise, the mixture was heated slowly to 60° where it was kept for a short interval (fifteen minutes) and then allowed to cool for two hours. Pouring onto 600 g. of ice threw

down a precipitate which was filtered off, washed well with water and dried. The product, which had a bright yellow color, weighed 28.6 g. (94.5%).

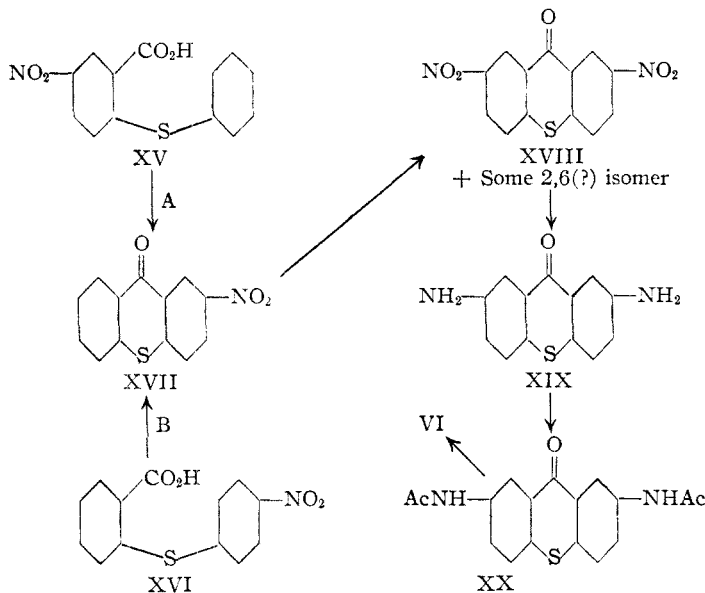
**2,8-Dinitrothiaxanthone Dioxide (IV).**—The filter cake from the above ring closure was refluxed for four hours in an oil-bath with 600 ml. of acetic acid and 91 g. (0.803 mole) of 30% hydrogen peroxide. The reaction mixture was then cooled and filtered and the solid washed with water, sodium bicarbonate solution and again with water.

(9) All melting points were corrected for stem emergence unless otherwise noted.

(10) Erdmann, *Ann.*, **272**, 153 (1892).

(11) Waldron and Reid, *This Journal*, **45**, 2399 (1923).

SCHEME B



more economically prepared and is also better adapted to ring closure (Route A). Nitration was accomplished readily enough by the method of Baeyer,<sup>8</sup> but the product was a mixture of iso-

(6) An alternative route to the 10-methylthiaxanthene (XI) which was of interest because of its possible flexibility involved the treatment of 2,8-dinitrothiaxanthone dioxide (IV) with methylmagnesium iodide. Unfortunately no reaction appeared to take place in either boiling diethyl ether or dibutyl ether even after several hours.

(7) Mayer, *Ber.*, **42**, 3–46 (1909).

(8) Baeyer, *Ann.*, **273**, 80 (1910).

Drying at 100° for several hours yielded 28.0 g. (89.5%) of light yellow powder melting at 302.0–307.5°.

*Anal.* Calcd. for  $C_{18}H_8O_7N_2S$ : N, 8.38; S, 9.59. Found: N, 8.75, 8.81; S, 9.37, 9.07.

**2,8-Diaminothioxanthone Dioxide (V).**—To a solution of 21 g. (0.0628 mole) of 2,8-dinitrothioxanthone dioxide (IV) in 84 ml. of acetic acid was added a solution of 107 g. (0.473 mole) stannous chloride dihydrate in 300 ml. of glacial acetic acid (solution clarified with dry hydrogen chloride hydrate in 300 ml. of glacial acetic acid (solution clarified with dry hydrogen chloride gas<sup>12</sup>), and the resulting mixture stirred at 80–90° for two hours. After cooling, the precipitate containing much tin was filtered off. Washing with water, potassium hydroxide solution and recrystallization from aqueous acetone yielded 13.3 g. (77%) of fine orange crystals, 11.5 g. of which melted at 291.0–293.0° (dec.) and the remaining 1.8 g. at 296.5–297.5° (dec.).

*Anal.* Calcd. for  $C_{12}H_{10}O_5N_2S$ : C, 56.92; H, 3.68; N, 10.21; S, 11.69. Found: C, 56.90; H, 3.95; N, 10.58, 10.54; S, 11.23, 11.71.

A small sample of the above diamino compound gave an almost quantitative yield of the cream colored **2,8-diacetamidothioxanthone dioxide (VI)** (m. p. above 348.0°) with acetic anhydride in acetic acid solution.

*Anal.* Calcd. for  $C_{17}H_{14}O_5N_2S$ : S, 8.95. Found: S, 8.63, 9.07.

Refluxing 1.4 g. (0.005 mole) of 2,8-diaminothioxanthone dioxide with 1.5 g. (0.00974 mole) of recrystallized sodium formaldehyde sulfoxylate in alcohol (60 ml. of absolute ethanol + 3 ml. of 99.5% methanol) for five hours, cooling, filtering and washing with acetone yielded 1.4 g. (51%) of the expected derivative which had a brownish mustard color and melted at 279.2° (dec.).

*Anal.* Calcd. for  $C_{15}H_{12}O_7N_2S_2Na_2 \cdot 2H_2O$ : S, 18.83;  $H_2O$ , 7.06. Found: S, 19.32;  $H_2O$ , 6.88, 8.33.

**5-Nitro-2-(p-nitrothiophenoxy)-acetophenone (X).**—A solution of 1.99 g. (0.01 mole) of 2-chloro-5-nitroacetophenone<sup>13</sup> (m. p. 63.6–65°), 1.9 g. (0.01 + mole) of sodium p-nitrothiophenoxide in 25 cc. of 95% ethanol was refluxed for several hours, after which the mixture was cooled, filtered and the solid washed with cold alcohol and water. After thorough drying in air the yellow crystals weighed 2.77 g. (88.3%) and melted at 190.2–190.9° with previous shrinking at 189°.

*Anal.* Calcd. for  $C_{14}H_{10}O_5N_2S$ : S, 10.07. Found: S, 9.87.

**2,8-Dinitro-10-methylthioxanthanol (XI).**—Two grams (0.0063 mole) of the above ketosulfide was stirred at room temperature with 25 ml. of concentrated sulfuric acid until complete solution had been effected. The dark red solution was then heated to 90° briefly and allowed to stand for about twelve hours. Pouring into water and working up in the usual manner yielded 1.6 g. (80%) of bright yellow powder which melted after recrystallization from glacial acetic acid at 210–213°.<sup>14</sup> Mixed with the original ketosulfide it melted at 164–180°. <sup>14</sup>

*Anal.* Calcd. for  $C_{14}H_{10}O_5N_2S$ : S, 10.07. Found: S, 10.47.

**2,8-Diamino-10-methylthioxanthanol (XII).**—A suspension of 1.3 g. (0.00406 mole) of 2,8-dinitro-10-methylthioxanthanol (XI) in 6 ml. of glacial acetic acid was reduced in the usual way with a solution of 8.5 g. (0.0387 mole) of stannous chloride dihydrate in acetic acid. Reduction was carried out for one and three-fourths hours at 85° after which the mixture was cooled to 10–15°. The precipitate was filtered off and on exposure to air it turned to a black tar. The residue was dissolved in cold water and precipitated by the addition of sodium bicarbonate solution. The amine proved to be too soluble to be recrystallized from acetone, ethanol, methanol and dioxane and too

insoluble in benzene although doubtless some purification was accomplished in these attempts. The crude material was then taken up as completely as possible in hot toluene, and the resulting cooled solution treated with dry hydrogen chloride. The first white precipitate which was formed became blue on continued passage of the gas. This solid was filtered off and dissolved in water to give a yellow solution which, after neutralization with aqueous sodium bicarbonate, deposited a yellow crystalline solid melting at 120.5–123.5°.

*Anal.* Calcd. for  $C_{14}H_{14}ON_2S$ : S, 12.41. Found: S, 12.37.

**5-Nitro-2-(p-nitrobenzene sulfonyl)-acetophenone (XIII).**—A solution of 2.127 g. (0.00669 mole) of X and 3 g. (0.0266 mole) of 30% hydrogen peroxide in 45 ml. of glacial acetic acid was boiled gently until the color changed from a yellow-brown to a light yellow (about fifteen minutes). It was set aside for about twelve hours and then gradually diluted with 400 ml. of water. The light yellow precipitate which formed was removed and extracted with hot, 10% aqueous sodium bicarbonate. Fractional precipitation from aqueous acetic acid yielded several colorless fractions whose melting extremes ranged from 148 to 189°. These were combined (wt., 1.6 g.) and reoxidized with hydrogen peroxide in acetic acid. The solid recovered from this oxidation was separated into several fractions of wide melting ranges and one (0.6 g.) which melted at 152–155°. When this fraction was recrystallized once again from acetic acid, it yielded shining white crystals which melted at 162.3–163.2°.

*Anal.* Calcd. for  $C_{14}H_{10}O_7N_2S$ : S, 9.15. Found: S, 9.36.

Ring closure was attempted by heating a solution of 0.142 g. (0.0004 mole) of the above sulfone in 2.5 ml. of concentrated sulfuric acid at about 90° for five minutes and then permitting the solution to stand ninety minutes without further heating before pouring onto ice. The precipitate was removed and washed with water, dilute bicarbonate and then with water. Drying yielded 0.123 g. of white crystals melting at 162.2–163.5°. When mixed with starting material the m. p. was 162.4–163.3°.

**2,8-Dinitro-10-methylthioxanthanol-5-dioxide (XIV).**—A solution of 2 g. (0.00629 mole) of XI in 55 ml. of glacial acetic acid was refluxed for three hours with 2.8 g. (0.025 mole) of 30% hydrogen peroxide. Some brown crystals which separated on standing overnight were removed and washed with water, dilute sodium bicarbonate and again with water. Recrystallization from acetic acid yielded a cream colored solid which was washed and dried at 100°. The dry powder weighed 0.141 g., melted at 302–303.5° and was completely insoluble in hot bicarbonate. The original filtrate from above yielded upon dilution a further 0.024 g. of material melting at 298–301.5°. The remainder of the solid recovered melted over wide ranges in the vicinity of 160° and could be made to yield no more of the high melting product.

*Anal.* Calcd. for  $C_{14}H_{10}O_7N_2S$ : S, 9.14. Found: S, 9.36.<sup>15</sup>

**4-Nitrodiphenyl Sulfide-2-carboxylic Acid (XV).**—A solution of 85.6 g. (0.421 mole) of 5-nitro-2-chlorobenzoic acid (m. p. 162.5–166°), 49.7 g. (0.476 mole) of thiophenol, 62.8 g. (1.12 moles) of potassium hydroxide and a trace of copper powder in 2710 ml. of alcohol was refluxed for eleven and three-fourths hours under a nitrogen atmosphere. After about two-thirds of the alcohol had been removed by distillation, the residue was diluted with water, acidified to congo red with concentrated hydrochloric acid, filtered and the solid washed with water. The crude product, which weighed 107 g. (92.5%) was recrystallized from about 80% alcohol, yielded 95.4 g. (81.5%) of dark yellow acid melting at 232.2–234.5°.

**2-Nitrothioxanthone (XVII).**—Nine and two-tenths grams (0.0335 mole) of 4-nitrodiphenylsulfide-2-carboxylic acid (XV) was added to about 80 ml. of concentrated sulfuric acid at 100° after which the temp. was maintained

(12) Cf. Cullinan, Davies and Davies, *J. Chem. Soc.*, 1435 (1936).

(13) Thorp and Brunsell, *This Journal*, 37, 1258 (1915).

(14) These melting points were run simultaneously on a block.

(15) Analysis by Dr. Carl Tiedcke.

at 100–105° for one hour. The solution was then poured onto about 100 g. of ice and the precipitate filtered, washed with water, sodium bicarbonate solution and water. Recrystallization from 50 ml. of nitrobenzene yielded 7.3 g. (85%) of 2-nitrothioxanthone melting at 226.8–229.0.<sup>16</sup>

**2,8-Dinitrothioxanthone (XVIII).**—To a cold solution of 73 g. of yellow fuming nitric acid (sp. gr. 1.49–1.50) in 73 cc. of concentrated sulfuric acid was added 7.3 g. (0.0267 mole) of 2-nitrothioxanthone. The mixture was allowed to stand with occasional stirring for one and three-fourths hours after which the product was precipitated by the addition of ice. Filtration and working up by the usual washings yielded 6.5 g. (80.5%) of crude dinitrothioxanthone which, after recrystallization from 25 ml. of nitrobenzene, weighed 3.4 g. (42%). The pale yellow crystals melted at 271.9–273.4°.

**2,8-Diaminothioxanthone (XIX).**—To a solution of 17.6 g. crude dinitrothioxanthone in 71 ml. glacial acetic acid was added a solution of 112 g. of tin salt in 326 ml. of acetic acid (which had been clarified with dry hydrogen chloride gas) at such a rate that the temperature rose spontaneously to 85°. When the exothermic phase of the reaction was over the temperature was maintained by applied heat for about two and one-fourth hours more. The product was removed and washed with water, dilute potassium hydroxide solution and water and dried over sulfuric acid and potassium hydroxide under diminished pressure. It then weighed 10 g. (71%) and after recrystallization from acetone amounted to 7 g. of orange crystals melting at 200–221°.<sup>17</sup>

**2,8-Diacetamidothioxanthone (XX).**—A small sample of the diamine was converted to the diacetyl derivative by refluxing in glacial acetic acid with acetic anhydride. Recrystallization from glacial acetic acid yielded crystals melting at 347.4–349.6°.

*Anal.* Calcd. for  $C_{17}H_{14}O_5N_2S \cdot 1\frac{1}{2}CH_3CO_2H$ : S, 7.70. Found: S, 7.64.

**2,8-Diacetamidothioxanthone-5-dioxide (VI).**—The diacetyl derivative from 6.7 g. of crude diamino compound was heated at 100° for two hours with 10 ml. 30% hydrogen peroxide in 60 ml. glacial acetic acid. During the reaction the starting material dissolved and shortly thereafter the product began to precipitate out. The pale yellow solid was filtered off, washed and dried *in vacuo* over potassium hydroxide and phosphorus pentoxide. Alone, it melted at 346.2–349.3° and admixed with unoxidized material at 318.5–340.1°.

*Anal.* Calcd. for  $C_{17}H_{14}O_5N_2S \cdot CH_3CO_2H$ : C, 54.5; H, 4.3; N, 6.68; S, 7.65. Found: C, 54.5; H, 5.1; N, 6.72, 6.50; S, 7.73.

After removal of the acetic acid of crystallization with bicarbonate the substance melted at 347.5 to above 350.0°.

*Anal.* Calcd. for  $C_{17}H_{14}O_5N_2S$ : N, 7.83. Found: N, 7.86, 8.06.

(16) Mayer, *Ber.*, **42**, 3046 (1909), reported a m. p. 219–221°.

(17) Melting point uncorrected.

**2,8-Diaminothioxanthene-5-dioxide (VII).** (A) From (IV).—A mixture of 13.7 g. (0.05 mole) of 2,8-dinitrothioxanthone dioxide and 10 g. (0.153 g. atom) of zinc dust (washed with hot dilute hydrochloric acid and water) was heated to incipient boiling with 200 ml. of 80% acetic acid. The mixture boiled spontaneously for twenty minutes after which it was heated at boiling for twenty-five minutes longer. Since the mixture had a dark color, an additional 5 g. of zinc was added and refluxing continued till the color was discharged (a few minutes). The hot filtrate from the reaction mixture was diluted with 800 ml. of water and the colorless precipitate removed, washed with sodium bicarbonate solution and water. After drying in a vacuum desiccator at room temperature over sulfuric acid, the dull yellow crystals weighed 9.7 g. (70%) and melted at 208.0° (dec.). Recrystallization twice from alcohol yielded material melting at 212° (dec.).

*Anal.* Calcd. for  $C_{13}H_{12}O_2N_2S \cdot H_2O$ : S, 11.52. Found: S, 11.57, 11.73.

(B) From 2,8-Diaminothioxanthone-5-dioxide (V).—A mixture of 1.4 g. (0.005 mole) of 2,7-diaminothioxanthone dioxide (V) and 1.0 g. (0.0153 g. atom) of zinc dust was refluxed with 20 ml. of 80% acetic acid for about three minutes at the end of which time the color had faded entirely. The unused zinc was filtered off and the product precipitated by the addition of water. Working up in the usual way yielded a material melting at 212° (dec.) and identical with that obtained by method (A).

The diacetyl derivative (VIII) was prepared in the usual way with acetic anhydride in acetic acid. The fine, almost colorless crystals melted, after washing with bicarbonate, at 292° (dec.).

*Anal.* Calcd. for  $C_{17}H_{16}O_4N_2S$ : S, 9.31. Found: S, 9.08, 9.20.

By the use of considerable excess of acetic anhydride in acetic acid a colorless derivative was obtained which melted at 293.0° (dec.) (284.0–286.0° when mixed with the diacetyl derivative) and analyzed correctly for 2,8-bis-(diacetylamido)-thioxanthene-5-dioxide (IX).

*Anal.* Calcd. for  $C_{21}H_{20}O_6N_2S$ : S, 7.48. Found: S, 7.75, 7.35.

## Summary

Interest in the 2,8-diaminothioxanthone- and thioxanthene-5-dioxides arises from their relationship to the powerful antibacterial agent 4,4'-diaminodiphenyl sulfone. Several possible synthetic routes to these xanthenes and xanthenes have been investigated, the most satisfactory of which is the ring-closure of substituted diphenyl sulfides by means of an ortho situated formyl group.

BETHLEHEM, PENNA.

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