solution and then with 10% hydrochloric acid. The neutral and base-soluble fractions contained only traces of material. The acid-soluble fraction was recovered and treated with methyl iodide to give 0.87 g. (50%) of the methiodide of β-dimethylaminopivalophenone; m. p. 122–123°. No melting point depression occurred on admixture of authentic IV to this salt.

Reaction of Methiodide of β-Dimethylaminopivalophenone with Sodium Hydroxide.—The methiodide (IV) (1.04 g.) was heated under reflux with 8 ml. of 5% sodium hydroxide for forty-eight hours. A basic gas was evolved rapidly during the first few hours. The cooled solution was filtered, the filtrate acidified, and the precipitated benzoic acid was collected in benzene; m.p. (and mixed m.p.) 122–122.5°, after recrystallization from water; yield 0.21 g. (57%).

Summary

β-Dimethylaminopivalophenone has been prepared by the Mannich reaction of isobutyrophenone. This β-aminoketone cannot suffer amine elimination, is sterically hindered to amine displacement, and cannot form a resonance-stabilized "carbonium ion." It failed to undergo amine exchange and replacement reactions; it was stable to strong base, but it readily underwent the reverse Mannich reaction in weakly basic or acidic medium.

The methiodide of this Mannich base reacted with sodium cyanide by demethylation rather than by amine replacement. Hot aqueous alkali caused cleavage of the methiodide to benzoic acid.

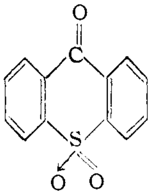
URBANA, ILLINOIS RECEIVED JULY 29, 1948

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA AND SWARTHMORE COLLEGE]

The Thiaxanthone Dioxide–Thiaxanthenol Dioxide–Thiaxanthene Dioxide Oxidation–Reduction System: A Sulfone Series Analog of the Anthraquinone–Anthrahydroquinone–Anthrone System[1]

BY EDWARD A. FEHNEL[2]

Several investigators have called attention to the peculiar color reactions of thiaxanthone-5-dioxide and substituted thiaxanthone-5-dioxides in the presence of zinc dust and alkali,[3] but no detailed study of these reactions has previously been reported and the nature of the chromogen has remained a subject for speculation.[3] Our interest in the physico-chemical properties of the sulfone function[4] led us to investigate the color reactions of thiaxanthone-5-dioxide in some detail, and we are now able to report the isolation and characterization of the substance responsible for color formation and to suggest a mechanism for the reactions involved.[5]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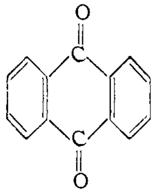
II

On treatment with zinc dust or sodium hydrosulfite and alkali, alcoholic solutions of thiaxanthone-5-dioxide (I) give an intense blue color, which is discharged on shaking with air. The striking similarity of this behavior to that shown by anthraquinone[6] (II) under the same conditions immediately suggests that the color is to be attributed to the formation of a sulfone anion analogous to the deeply colored, readily oxidizable anthrahydroquinone anion formed in the familiar vatting reaction.[7] Our data on the oxidation–reduction reactions in the thiaxanthone dioxide series are in accord with this interpretation. The demonstration of a close parallelism in the reactions of the thiaxanthone dioxide and anthraquinone series of compounds is of particular interest in view of the fact that the formulation of a sulfone oxidation–reduction system analogous to the anthraquinone–anthrahydroquinone system requires

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(1) Presented at the Meeting-in-Miniature of the Philadelphia Section of the American Chemical Society, January 20, 1949.

(2) American Chemical Society Postdoctoral Fellow at the University of Pennsylvania, 1946-1948. Present address: Department of Chemistry, Swarthmore College, Swarthmore, Pa.

(3) (a) Graebe and Schulthess, *Ann.*, **263**, 1 (1891); (b) Ullmann and Lehner, *Ber.*, **38**, 729 (1905); (c) Ullmann and Glenck, *ibid.*, **49**, 2487 (1916); (d) Amstutz, Fehnel and Hunsberger, THIS JOURNAL, **70**, 133 (1948).

(4) Fehnel and Carmack, *ibid.*, **71**, 231 (1949).

(5) NOTE ADDED IN PROOF.—While the present paper was in press, Heymann [*ibid.*, **71**, 260 (1949)] reported a closely related study of the thiaxanthone dioxide-thiaxanthenol dioxide oxidation-reduction system, in which essentially the same conclusions were reached with regard to the reaction mechanism.

(6) For a detailed discussion of the chemistry of anthraquinone and its reduction products, see Houben and Fischer, "Das Anthracen und die Anthrachinone," Georg Thieme, Leipzig, 1929, esp. pp. 143-172 and 197-206. An excellent concise summary of the more important oxidation-reduction reactions has been given by Fieser and Fieser, "Organic Chemistry," D. C. Heath, Boston, 1944, pp. 798-802.

(7) NOTE ADDED IN PROOF.—Strictly speaking, it is not entirely accurate to attribute the color to the simple ion, since the colored species is undoubtedly the semiquinone ion-radical which results from the loss of one electron by the doubly-charged anion (*cf.* Heymann, ref. in footnote 5). This idea is, of course, implicit in the present discussion of the thiaxanthone-enol dioxide oxidation–reduction system, since it follows from the analogy with the anthraquinone-anthrahydroquinone system, in which the blood-red color of the "anthrahydroquinone anion" is almost certainly due to the presence of the corresponding semiquinone ion-radical (see, however, Dufraisse and Priou, *Bull. soc. chim.*, [5] **6**, 1649 (1939), who postulate a biradical anion).

the assumption of an expanded valence shell for sulfur.[4]

The reactions in the thiaxanthone dioxide system are best described by reference to Fig. 1.

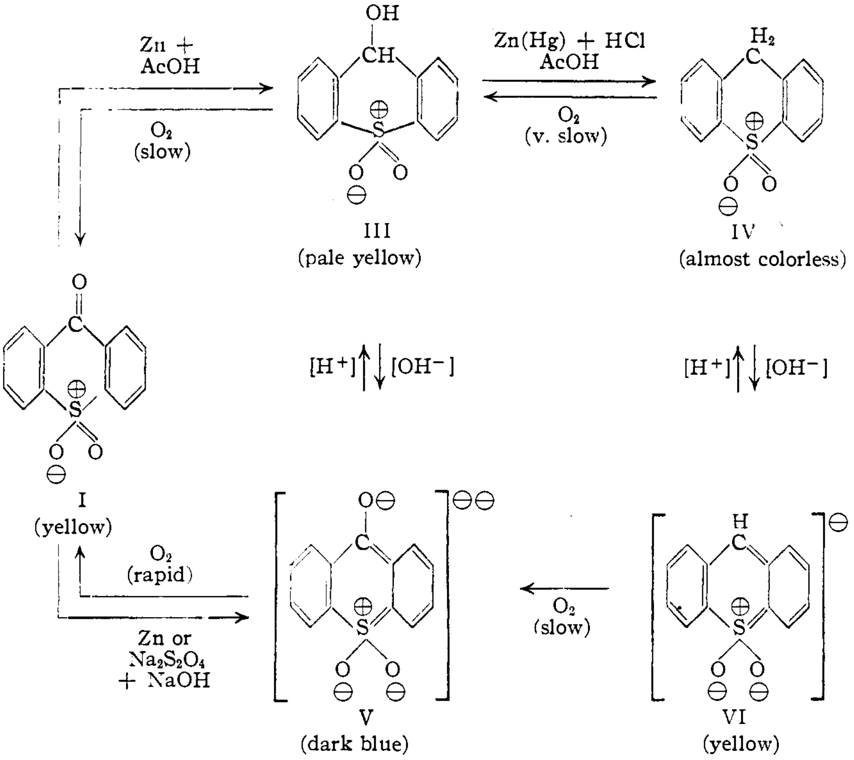
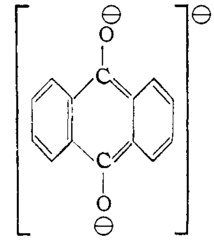


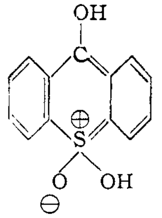
Fig. 1.

Reduction of thiaxanthone-5-dioxide (I) with zinc dust in dilute acetic acid affords a pale yellow crystalline compound, $C_{13}H_{10}O_3S$, which readily forms a monoacetyl derivative on treatment with acetic anhydride in the presence of sulfuric acid. This compound, which is undoubtedly thiaxanthenol-5-dioxide (III), dissolves in aqueous or alcoholic alkali with the production of a deep blue color. On shaking with air, the color is rapidly discharged and thiaxanthone-5-dioxide (I) precipitates from the solution. Neutral alcoholic solutions of thiaxanthenol-5-dioxide (III) also undergo oxidation on prolonged exposure to air, but the rate of reaction, as evidenced by the slow precipitation of the slightly soluble thiaxanthone-5-dioxide (I) is much lower under these conditions than in the presence of alkali. A slow autoxidation of crystalline thiaxanthenol-5-dioxide (III) is indicated by the gradual development of a deep yellow color when the solid is allowed to stand in contact with air for several weeks; no such change is observed with samples stored under nitrogen.

The crystalline product obtained on acidification of the deep blue solution from the alkaline sodium hydrosulfite reduction of thiaxanthone-5-dioxide (I) was shown, by the method of mixed melting points, to be identical with the thiaxanthenol-5-dioxide (III) obtained from the acid reduction. An oxidation–reduction cycle analogous to the anthraquinone–anthrahydroquinone system is thus established. The ground-state structure (V) assigned to the resonating anion responsible for the intense blue color is the sulfone series counterpart of the ground-state structure of the anthrahydroquinone anion (VII).[7] While structure V very probably represents the most stable electronic configuration for the sulfone anion, the addition of protons to the system is represented in Fig. 1 as resulting in the formation of the sulfone analog, not of anthrahydroquinone, but of its tautomer, oxanthrone. It seems likely, however, that the compound characterized as thiaxanthenol-5-dioxide (III) is at all times in equilibrium with a small but significant amount of the tautomeric form (VIII) corresponding to anthrahydroquinone. This assumption seems necessary to account for the autoxidation of the compound in the crystalline state and in neutral solutions,[8] and it is strongly supported by the observation that thiaxanthenol-5-dioxide exhibits a blue fluorescence, since in the anthraquinone series the phenomenon of fluorescence is regarded as evidence for the presence of an *o*-quinonoid structure.[9]



VII (blood-red)



VIII

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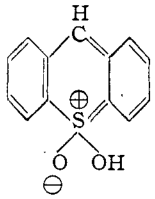
[8] Thus, in the anthraquinone series, the ketonic forms of the reduction products (oxanthrone, anthrone) are resistant to air oxidation, while the enolic forms (anthrahydroquinone, anthranol) are very sensitive to oxidation by air (see ref. 6).

[9] Houben and Fischer, ref. 6, pp. 13-14.

With a reducing agent of sufficiently high potential, such as amalgamated zinc in the presence of hydrochloric acid, it is possible to complete the reduction of thiaxanthenol-5-dioxide (III) and thus to obtain thiaxanthene-5-dioxide (IV).[10,11] The identity of the nearly colorless crystalline product (m. p. 171–172°) obtained in this way was established by its failure to depress the melting point of authentic thiaxanthene-5-dioxide (m. p. 170–171°) prepared by the oxidation of thiaxanthene. Attempts to prepare the same compound (IV) by alkaline reduction of thiaxanthenol-5-dioxide have thus far been unsuccessful, possibly because the anion V undergoes ring cleavage at the sulfonyl group on prolonged treatment with hot alkali.

Although thiaxanthene-5-dioxide (IV) is much less sensitive to oxidation than thiaxanthenol-5-dioxide (III), its ability to undergo gradual oxidation in the presence of air, particularly in alkaline solutions, was demonstrated by treating solutions of the pure compound, after prolonged exposure to air, with zinc dust or sodium hydrosulfite and alkali. The appearance of a deep blue color indicated the presence of thiaxanthone-5-dioxide (I) in the solutions exposed to air; control solutions which were kept under nitrogen gave no color reaction.[12] As was anticipated, the thiaxanthenol-5-dioxide (III) (or, in alkaline solutions, its anion V) which was presumably formed as an intermediate in the oxidation could not be detected in these solutions, since the much greater susceptibility of these molecules to oxidation prevents their accumulating in the mixture.

Like anthrone, of which it is the sulfonyl analog, thiaxanthene-5-dioxide (IV) appears to be the more stable member of a tautomeric pair of isomers. The existence of an equilibrium system involving at least traces of the enolic form (IX) is indicated both by the tendency of alcohol solutions of thiaxanthene-5-dioxide to undergo autoxidation and by the blue fluorescence which this compound exhibits on exposure to ultraviolet light.



IX

Acknowledgment.—The author wishes to express his appreciation to Dr. Marvin Carmack for many helpful suggestions and valuable discussions during the course of this work.

Experimental[13]

Preparation of Compounds.—**Thiaxanthone**, prepared according to the directions of Graebe and Schulthess,[3a] was oxidized to **thiaxanthone-5-dioxide** by treatment with excess 30% hydrogen peroxide in acetic acid.[3d] The crude product (48% over-all yield based on anthranilic acid) was recrystallized from ethanol (Norit) to give yellow needles, m. p. 185.5–186° (reported[3a] m. p. 185°). **Thiaxanthene**, which has previously been prepared by reduction of thiaxanthone with hydrogen iodide and red phosphorus,[3a,14] was conveniently obtained in the present investigation by the Huang-Minlon modification[15] of the Wolff–Kishner reduction; from 1.80 g. of thiaxanthone there was thus obtained 1.15 g. (69%) of pale yellow microcrystalline powder, which afforded colorless needles melting at 127–127.5° (reported[3a] m. p., 128°) after recrystallization from ethanol (Norit). Oxidation of this product with excess hydrogen peroxide in acetic acid[12] yielded 97% of the theoretical amount of **thiaxanthene-5-dioxide** as almost colorless needles, which melted at 170–171° (reported[14] m. p., 170°) after recrystallization from ethanol (Norit).

Reduction of Thiaxanthone-5-dioxide (I) to Thiaxanthenol-5-dioxide (III): (a) With Zinc Dust and Acetic Acid.—A mixture of 12.2 g. (0.050 mole) of thiaxanthone-5-dioxide, 10 g. of zinc dust (activated by washing with dilute hydrochloric acid), and 150 ml. of 80% acetic acid was refluxed under nitrogen for thirty minutes, after which it was cooled, filtered, and diluted with 800 ml. of water. The resultant yellow precipitate was collected, washed with water and dried *in vacuo* over calcium chloride; yield, 8.6 g. (70%) of yellow powder, m. p. 165–168°. Recrystallization of this material from chloroform afforded pale yellow crystals, m. p. 184–185°, which exhibited a blue fluorescence on exposure to ultraviolet light; mixed m. p. with thiaxanthone-5-dioxide, *ca.* 146–152°. On treatment with aqueous or alcoholic sodium hydroxide, this product gave a dark blue solution from which the color was discharged on shaking with air.

Anal. Calcd. for $C_{13}H_{10}O_3S$: C, 63.39; H, 4.09. Found: C, 63.10; H, 4.11.

When a suspension of 0.50 g. of the above product in 2 ml. of acetic anhydride was treated with 1 drop of concentrated sulfuric acid and allowed to stand for fifteen minutes, a semicrystalline paste was obtained from which 0.58 g. of the acetyl derivative was separated by diluting the mixture with water and filtering off the insoluble product. Recrystallization from ethanol gave almost colorless crystals, m. p. 155.5–156°, which dissolved slowly in aqueous or alcoholic sodium hydroxide with the production of a deep blue color.

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[10] The compound prepared by Amstutz and Neumoyer [THIS JOURNAL, **69**, 1925 (1947)] by brief treatment of 2,8-diaminothiaxanthone-5-dioxide with zinc dust in dilute acetic acid and designated 2,8-diaminothiaxanthene-5-dioxide monohydrate was in all probability *2,8-diaminothiaxanthenol-5-dioxide* (*Anal.* Calcd. for $C_{13}H_{12}N_2O_3S$: S, 11.60. Found: S, 11.57, 11.73). This possibility has been called to Dr. Amstutz' attention and is now being checked in the light of the results described in the present paper.

[11] NOTE ADDED IN PROOF.—The reference in Heymann's paper (see "Preparative Part" of ref. in footnote 4) to the previously reported zinc dust–acetic acid reduction of substituted thiaxanthone-5-dioxides to thiaxanthene-5-dioxides apparently refers to the above paper by Amstutz and Neumoyer (footnote 10), not to that by Amstutz, Fehnel and Hunsberger (footnote 3d) as erroneously indicated.

[12] The recent report (ref. 3d) that certain substituted thiaxanthene-5-dioxides give colored solutions on treatment with aqueous-alcoholic alkali is almost certainly in error. The color reactions observed with these compounds must in all probability be ascribed to the presence of traces of the corresponding thiaxanthenol-5-dioxides, formed either during the preparation of the compounds by hydrogen peroxide oxidation of the thiaxanthenes or by subsequent autoxidation of the pure thiaxanthene-5-dioxides. The problem of completely freeing samples of thiaxanthene-5-dioxide from thiaxanthenol-5-dioxide was overcome in the present investigation only by repeated, rapidly conducted recrystallizations, until the product no longer gave a blue color with aqueous-alcoholic alkali.

[13] Microanalyses were performed by Mrs. Sarah M. Woods. All melting points are corrected.

[14] Hilditch and Smiles, *J. Chem. Soc.*, **99**, 145 (1911).

[15] Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

Anal. Calcd. for $C_{15}H_{12}O_4S$: C, 62.49; H, 4.20. Found: C, 62.27; H, 4.17.

(b) **With Sodium Hydrosulfite and Alkali.**—A solution of 1.0 g. of sodium hydrosulfite and 1.0 g. of sodium hydroxide in 10 ml. of water was added to a suspension of 0.60 g. of thiaxanthone-5-dioxide in 10 ml. of ethanol, and the mixture was warmed to *ca.* 50° under a nitrogen atmosphere for ten minutes. The resultant dark blue solution was cooled to room temperature, acidified with hydrochloric acid, and diluted with 100 ml. of water. The yellow precipitate was collected, washed with water, and dried *in vacuo* over calcium chloride; yield, 0.40 g. (66%) of yellow powder, m. p. 167–171°. Recrystallization of this material from chloroform afforded pale yellow crystals which melted at 181–183° and showed no depression in melting point when mixed with the acid-reduction product described above.

Reduction of Thiaxanthone-5-dioxide (I) to Thiaxanthene-5-dioxide (IV).—A mixture of 1.22 g. (0.0050 mole) of thiaxanthone-5-dioxide, 3 g. of amalgamated zinc dust, 15 ml. of acetic acid, and 3 ml. of hydrochloric acid was refluxed under nitrogen for three hours. Another 1 ml. of hydrochloric acid was added during the refluxing, and at the end of the three-hour period the unreacted zinc was filtered off and the filtrate as diluted with 100 ml. of water. The precipitate was collected, washed with water, and dried; yield, 1.08 g. (94%) of pale yellow microcrystalline powder, m. p. 150–155°, which gave a blue color on treatment with aqueous-alcoholic sodium hydroxide. After repeated recrystallization from ethanol, the pure product was obtained as almost colorless crystals, m. p. 171–172°, which gave *no color* on treatment with aqueous-alcoholic sodium hydroxide and which failed to depress the melting point of authentic thiaxanthene-5-dioxide prepared by the oxidation of thiaxanthene. This product exhibited a blue fluorescence on exposure to ultraviolet light.

Reduction of Thiaxanthenol-5-dioxide (III) to Thiaxanthene-5-dioxide (IV).—When an acetic acid solution of 1.23 g. (0.0050 mole) of thiaxanthenol-5-dioxide was treated with amalgamated zinc and hydrochloric acid in the same manner as in the preceding example, 0.85 g. (74%) of pale yellow powder, m. p. 139–144°, was obtained, which crystallized from ethanol in the form of almost colorless needles melting at 169–171°. No depression of the melting point was observed when this material was mixed with authentic thiaxanthene-5-dioxide.

Air Oxidation of Thiaxanthenol-5-dioxide (III).—A suspension of 0.62 g. of thiaxanthenol-5-dioxide in 10 ml. of ethanol was treated with 10 ml. of 10% aqueous sodium hydroxide, and air was blown into the mixture through a sintered glass gas-dispersion tube until the blue color was completely discharged (five to ten minutes). The resultant yellow suspension was diluted with water and filtered, thus affording 0.55 g. (90%) of yellow microcrystalline powder, m. p. 185–186°, which gave a blue color with aqueous-alcoholic alkali only after the addition of zinc dust or sodium hydrosulfite. This product failed to depress the melting point of thiaxanthone-5-dioxide prepared by the oxidation of thiaxanthone.

When a saturated solution of thiaxanthenol-5-dioxide in 95% ethanol was shaken with air for ten days in a mechanical shaker, a small amount of yellow insoluble material was precipitated which melted at 182–185° and showed no melting point depression when mixed with authentic thiaxanthone-5-dioxide.

Air Oxidation of Thiaxanthene-5-dioxide (IV).—A suspension of 0.20 g. of freshly purified thiaxanthene-5-dioxide in 10 ml. of 10% aqueous sodium hydroxide was refluxed for ten minutes while a stream of air was bubbled through the boiling mixture. Although the thiaxanthene-5-dioxide used in this experiment gave no color with alkali and sodium hydrosulfite, the yellow solid filtered out of the above suspension gave the characteristic blue color test for thiaxanthone-5-dioxide on treatment with these reagents.

When neutral, saturated solutions of pure thiaxanthene-5-dioxide in 95% ethanol were similarly aerated and refluxed for periods of several hours, addition of aqueous sodium hydroxide and sodium hydrosulfite resulted in the formation of a dark blue color. If the refluxing was carried out under nitrogen and no air was bubbled through the solution, no color test could be obtained even after four hours.

Summary

The color reactions of thiaxanthone-5-dioxide in the presence of alkaline reducing agents have been studied and shown to be similar to the familiar vatting reactions of anthraquinone. The intermediate reduction product responsible for the characteristic color reactions has been isolated and identified as thiaxanthenol-5-dioxide, which dissolves in alkali with the formation of a highly colored, readily oxidizable anion analogous to the anthrahydroquinone anion. On the basis of the assumption that sulfur is capable of expanding its valence shell, the thiaxanthone dioxide–thiaxanthenol dioxide–thiaxanthene dioxide oxidation–reduction system is formulated as the sulfone series counterpart of the anthraquinone–anthrahydroquinone–anthrone system.

SWARTHMORE, PA. RECEIVED SEPTEMBER 8, 1948

[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Reactions of Vanillin and its Derived Compounds. VII.[1] Some New Esters of Vanillic Acid and Related Acids[2,3]

BY IRWIN A. PEARL AND DONALD L. BEYER

Several esters of vanillic acid were recently shown[4,5] to have high toxicity toward representative microörganisms and to be of value as food preservatives. These results led to the synthesis of the new esters of vanillic acid, orthovanillic acid, and 5-chlorovanillic acid described in Table I.

The new esters of vanillic acid reported herein comprise esters of polyhydric alcohols, their chlorohydrins, and their ethers. Most of these were prepared by the various methods described earlier.[4] The chlorohydrin esters were prepared by reaction of the chlorohydrin with vanillic

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[1] For paper VI of this series, see THIS JOURNAL, **70**, 2008 (1948).

[2] Presented before The Division of Organic Chemistry at the 113th meeting of The American Chemical Society, Chicago, Illinois, April 19–23, 1948.

[3] This paper represents a portion of the results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

[4] Pearl and McCoy, THIS JOURNAL, **69**, 3071 (1947).

[5] Pearl and McCoy, *Food Industries*, **17**, 1458 (1945).