

EXPERIMENTAL

Preparation of guanidinic sulfate and test of Beer's law. Eighteen grams (0.1 mole) guanidine carbonate, purified by recrystallization from water, was dissolved in 100 ml. of ice cold concentrated sulfuric acid. To this solution was added another composed of 27 g. (0.1 mole) potassium persulfate dissolved in 100 ml. of concentrated sulfuric acid. The resulting solution was allowed to warm up to room temperature and stand overnight for full color development. Aliquots were then diluted proportionately with concentrated and 20% fuming sulfuric acids. The per cent transmission at 613 $m\mu$ and 650 $m\mu$ was determined with a Beckmann DU Spectrophotometer.

Reversibility of the redox system. Aliquots of the above guanidinic sulfate solution were treated with tin, zinc, and anhydrous hydrogen sulfide until almost visually colorless. A brown-pink tint remained in the reduced solutions. The solutions were then reoxidized with excess solid potassium persulfate. The original solution transmitted 3.5% of the incident red light, the reduced solution 96%, and the reduced and reoxidized solution 2%. These measurements were made with a Leitz photoelectric colormeter using filter f-244.

Absorption spectra. To 5 ml. aliquots of a 0.185 molar guanidinous solution were added solid potassium persulfate in amounts equal to 0.103, 0.194, 0.382, 0.744, 0.937, 1.67, 1.85, 2.56, and 3.34 milliequivalents. The per cent transmission of these solutions at various wave lengths was measured with the Beckmann spectrophotometer. For the sake of clarity only three of the family of nine curves are shown in Fig. 1.

Stoichiometry. Weighed quantities of potassium persulfate were added to 5 ml. aliquot of 0.185 molar guanidinous solution. The percent transmission at 650 $m\mu$ was again determined with the Beckmann spectrophotometer.

Analytical test for guanidine and derivatives. About 10 mg. of substance were dissolved in 2 ml. of concentrated sulfuric acid. To the resulting solution was added about 30 to 40 mg. of potassium persulfate. On warming or standing at room temperature a blue or deep red-brown color developed.

Test for persulfate and permonosulfate ions.⁵ This was identical with the test for phenols with free para positions in which the diluted and neutralized solutions of the above ions were used as the source of oxidant.

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On the Oxidation of Desoxybenzoin

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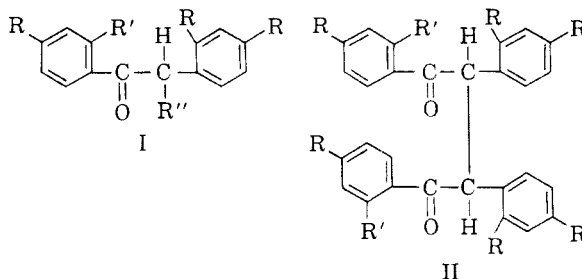
It has been shown¹ by A. Robertson *et al.*, that some desoxybenzoin can be oxidized by potassium permanganate to the corresponding benzoin. Further, it was found by these and other authors that oxidation of some derivatives of flavanone,²

(1) (a) G. G. Badcock, G. W. K. Cavill, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 2961 (1950). (b) After the present work had been completed, the writer received the July 1957 copy of *J. Chem. Soc.* in which Robertson *et al.* showed that the oxidation product of desoxybenzoin was a benzil and not a benzoin as they had previously considered.

(2) A. Robertson and W. B. Whalley, *J. Chem. Soc.*, 1440 (1954).

isoflavanone,³ and coumaranone⁴ by permanganate produced compounds having a hydroxyl group alpha to the carbonyl group.

In the course of investigation⁵ on the coloring matter of *Sophora japonica*, *L.*, potassium permanganate oxidation of 2-hydroxy-2',4',4'-trimethoxydesoxybenzoin (I, R = OCH₃, R' = OH, R'' = H) in refluxing anhydrous acetone produced a compound C₃₄H₃₄O₁₀, melting at 226–227°, in a moderate yield. It has now been confirmed that this compound is a bisdesoxybenzoin derivative having the formula (II, R = OCH₃, R' = OH).



The ultraviolet absorption spectrum (Figure 1, curve c) of this compound showed almost the same shape as that of the parent desoxybenzoin. The

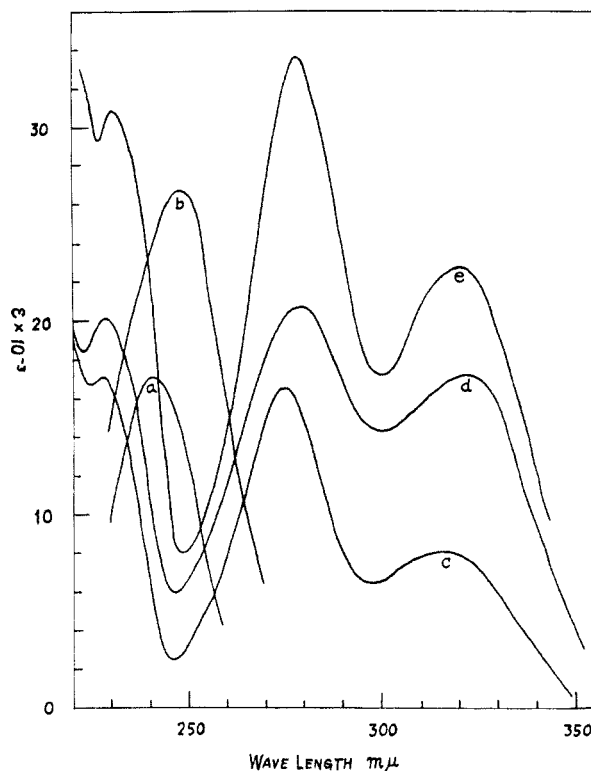


Fig. 1. Ultraviolet absorption spectra: a, Desoxybenzoin; b, Bisdesoxybenzoin; c, 2-hydroxy-2',4',4'-trimethoxydesoxybenzoin; d, 2-hydroxy-2',4',4'-trimethoxybenzil; e, Bis-2-hydroxy-2',4',4'-trimethoxydesoxybenzoin

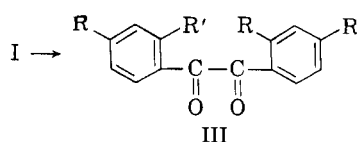
(3) V. B. Mahesh and T. R. Seshadri, *J. Chem. Soc.*, 2503 (1955).

(4) J. Gripenberg, *Acta Chem. Scand.*, 7, 1323 (1953).

(5) Unpublished paper.

molecular extinction coefficients of the bisdesoxybenzoin maxima, however, were approximately twice those of the latter. Though this compound is indifferent toward ketonic reagents the infrared spectrum showed a strong band of *o*-hydroxyacetophenone system at 1616 cm.^{-1} . Because this unexpected product which was not mentioned by the English investigators was obtained, the oxidation of desoxybenzoin by permanganate was examined under various conditions.

Thus, on treatment of (I), ($R = \text{OCH}_3$, $R' = \text{H}$, $R'' = \text{H}$) by aqueous potassium permanganate at room temperature another compound, $\text{C}_{17}\text{H}_{16}\text{O}_6$ (III), was produced in place of the expected 2-hydroxy-2',4,4'-trimethoxybenzoin.



The following facts indicate definitely that this compound is a derivative of benzil and not of benzoin. The infrared spectrum⁶ (Nujol or CS_2) showed no band attributable to a free alcoholic hydroxyl in the region $3000\text{--}3500\text{ cm.}^{-1}$. In the ultraviolet spectrum (Figure 1, curve d) the wave lengths of the maxima of compound III and the parent desoxybenzoin I are very similar. However, the extinction coefficients of the maxima of the former are considerably increased in comparison with those of the latter. (In the $332\text{ m}\mu$ maximum it is about twice as great.) This high intensity of the former is consistent with the benzil structure. According to Leonard⁷ *et al.* the dicarbonyl system in benzil has a skew configuration, in which the two benzoyl units line in planes approximately at right angles to each other and its excited structures giving the major contribution to the absorption are related to those which cause the absorption of the substituted benzaldehyde. The excited structures lead to a similarity in ultraviolet absorption of both compounds and intensify to approximately double the extinction coefficient of the symmetrical benzil in comparison with the corresponding benzaldehyde. Furthermore, in agreement with the above facts this compound gave a quinoxaline derivative. When the oxidation was conducted in refluxing aqueous acetone, the main product was the bis compound (II), accompanied by a small amount of the corresponding benzil (III).

(6) As in *o*-hydroxyacetophenone, the infrared spectrum (in nujol) of this alpha-diketone shows the absence of the clear band attributable to a chelated phenolic hydroxyl in the $3000\text{--}3500\text{ cm.}^{-1}$ region. [Cf. H. L. Hergert and E. F. Kurth, *J. Am. Chem. Soc.*, **75**, 1662 (1953)].

(7) N. J. Leonard, R. T. Rapala, H. L. Herzog, and E. R. Blout, *J. Am. Chem. Soc.*, **71**, 2997 (1949).

Furthermore, desoxybenzoin (I, $R = R' = R'' = \text{H}$) was oxidized with the same amount of permanganate. At room temperature in anhydrous or aqueous acetone benzil was obtained in good yield. At the reflux temperature, however, didesyl⁸ (a bisdesoxybenzoin) (II, $R = R' = \text{H}$), identified by its analyses and infrared and ultraviolet spectra (Figure 1 curve b), was obtained.

It is of interest that in those cases the temperature is the key factor for oxidative coupling although the yield depends partially upon the content of water. It may be considered that the oxidative coupling proceeds through the formation of intermediary aryloxy/methyl radicals.

A description of this type of oxidative coupling,^{8,9} using Fenton's reagent, can be found in the literature. However, in the case of permanganate oxidation, examples of dehydrogenative coupling and dehydrogenation are rather few.¹⁰ The formation of a bis-compound from 4,6-diacetoxy-5-methylcoumaran-2-one¹¹ and a dehydrogenation product¹² from 1,6-diduryl-2,5-dimesityl-1,5-hexadiene-1,6-diol were noted.

EXPERIMENTAL^{13,14}

Oxidation of 2-hydroxy-2',4,4'-trimethoxydesoxybenzoin (a) with powdered potassium permanganate in anhydrous boiling acetone. Finely powdered permanganate (1.08 g., 0.0068 mole) was added to a solution of 2-hydroxy-4,2',4'-trimethoxydesoxybenzoin (300 mg., 0.001 mole) in anhydrous acetone (14 ml.) in the course of 3 hr. After the removal of the solvent, water (6 ml.) was added to the residue. The aqueous solution was cleared with sulfur dioxide and extracted with three 50-ml. portions of ether. The combined ethereal extracts were washed with aqueous 5% sodium hydrogen carbonate (20 ml.) then with two 20-ml. portions of 2*N* sodium hydroxide and dried. On evaporation of the ether, the yellow oily bis compound (II), $R = \text{OCH}_3$, $R = \text{OH}$ which crystallized quickly, was obtained. The crystals were washed with a small volume of ether and recrystallized from dilute acetone, yielding colorless needles (60 mg.) of product melting at $226\text{--}227^\circ$.

Anal. Calcd. for $\text{C}_{24}\text{H}_{34}\text{O}_{10}$: C, 67.76; H, 5.69; Mol. wt., 603. Found: C, 67.97; H, 6.01; Mol. wt. 620 (Rast) [α_D^{20}].

Ultraviolet absorption (Figure 1, curve e) λ_{max} (alcohol) 230, 278, and $321\text{ m}\mu$ (ϵ 30900, 33600, and 22880).

An alcoholic solution of this compound exhibited a red-brown color with ferric chloride. It proved to be insoluble in aqueous 2*N* sodium hydroxide but dissolved in sulfuric acid producing a yellow color. In nitric acid, however, it developed a green color. The oximation was tried in pyridine-alcohol solution on the steam bath for 3 hr., but the original compound was recovered unchanged. The reaction of the

(8) E. Knoevenagel, *Ber.*, **21**, 1355 (1888).

(9) J. H. Merz and W. A. Waters, *J. Chem. Soc.*, 2427 (1949).

(10) T. Sakan in Jikkenkagakukoza, Ed., *Chem. Soc. Japan*, Maruzen Co., Ltd., Tokyo 17, 62 (1957).

(11) D. H. R. Barton and T. Bruun, *J. Chem. Soc.*, 603 (1953).

(12) R. C. Fuson and R. F. Heitmiller, *J. Am. Chem. Soc.*, **75**, 1494 (1953).

(13) Melting points uncorrected.

(14) Microanalyses by Miss N. Fujino, this laboratory.

compound with alcoholic 2,4-dinitrophenylhydrazine hydrochloride was negative.

(b) *With aqueous potassium permanganate at room temperature.* Potassium permanganate (375 mg., 0.0024 mole) in water (15 ml.) was gradually added in 3-ml. portions to a solution of (I) ($R = OCH_3$, $R' = OH$, $R'' = H$) (150 mg., 0.0005 mole) in acetone (23 ml.) in the course of 30 hr. On evaporation of the acetone, under reduced pressure, manganese dioxide separated, but redissolved on addition of sulfur dioxide. The solution was extracted with two 50-ml. portions of ether and the combined ethereal extracts were treated with two 20-ml. portions of 5% sodium hydrogen carbonate solution. Upon acidification of the combined sodium hydrogen carbonate extracts with dilute hydrochloric acid, a mixture of 2,4-dimethoxybenzoic acid and 2-hydroxy-4-methoxybenzoic acid was obtained. The ether layer, after removal of the acidic fraction, was dried. After removal of the ether 70 mg. of an oily substance remained. It was dissolved in ethanol and on cooling, 2-hydroxy-2',4,4'-trimethoxybenzil separated in pale yellow prisms. Repeated crystallization from alcohol gave faintly yellow crystals, m.p. 113–114°. On admixture with the parent ketone (m.p. 117–118°) it melted at about 90–95°.

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.29; 64.79; H, 5.21, 5.18.

The infrared spectrum showed doublet maximum at 1615 and 1595 cm^{-1} , which is attributable to the chelated conjugated dicarbonyl system. The spectrum was lacking in an alcoholic hydroxyl band. Ultraviolet absorption (Figure 1, curve d) λ_{max} (alcohol) 229, 279, and 322 $m\mu$ (ϵ : 20130, 20790, and 17300). The compound slowly dissolves in aqueous sodium hydroxide. In alcohol solution a red-brown color is produced with ferric chloride. The benzil (10 mg.) and *o*-phenylenediamine (4 mg.) in alcohol (0.5 ml.) were heated under reflux for 3 hr. On dilution of the reaction mixture the quinoxaline derivative separated from the dilute alcohol in yellow needles (4 mg.) melting at 170–171°.

Anal. Calcd. for $C_{23}H_{20}O_2N_2$: N, 7.21. Found: N, 7.11.

(c) *With aqueous potassium permanganate in boiling acetone.* Permanganate (300 mg., 0.0019 mole) in water (15 ml.) was added to 2-hydroxy-4,2',4'-trimethoxydesoxybenzoin (150 mg., 0.005 mole) in boiling acetone (23 ml.) during the course of 3 hr. After evaporation of the acetone under reduced pressure, the solution was cleared with sulfur dioxide and extracted with two 30-ml. portions of ether. The combined extracts were treated as in (b) above. Thus, 2-hydroxy-4-methoxybenzoic acid was obtained. It was purified by recrystallization from water forming needles melting at 153–154°. A mixed melting point with an authentic sample also melted at the same temperature. The yield of the acid obtained was 1 mg. Evaporation of the washed dried ethereal solution, freed from 2-hydroxy-4-methoxybenzoic acid, gave an oily residue which was crystallized from ethanol. Recrystallization from the same solvent gave 21 mg. of colorless needles melting at 226–227°.

This material was identical to compound (II), $R = OCH_3$, $R' = OH$) prepared according to procedure (a). The alcoholic filtrate from the crystallization gave a resinous residue which was redissolved in a small volume of alcohol. On dilution with water and keeping for a few days at room temperature 2-hydroxy-4,2',4'-trimethoxybenzil separated. On recrystallization from alcohol 12 mg. of material melting at 113–114° was obtained. This product was identical to the product isolated in procedure (b).

Oxidation of desoxybenzoin. (a) *At room temperature in anhydrous acetone.* Finely powdered potassium permanganate (3 g., 0.019 mole) was added to a solution of desoxybenzoin (1 g., 0.0051 mole) in anhydrous acetone (50 ml.) in the course of 25 hr. After removal of the solvent under reduced pressure, the residue was treated with water (18 ml.). After clearing the aqueous solution with sulfur dioxide, it was twice extracted with ether using 200 ml. and 100 ml., respectively. The combined ethereal extracts, freed from acidic substances (0.56 g.) by two extractions with 20 ml.

each of aqueous sodium hydrogen carbonate, were washed with a small volume of water and dried. On evaporation of the ether the residue remaining was crystallized from dilute methanol. Benzil (0.34 g.) was obtained. It was identified by admixture with an authentic specimen.

(b) *At room temperature in hydrous acetone.* Potassium permanganate (3 g., 0.019 mole) in water (120 ml.) was added in 10-ml. portions to a solution of desoxybenzoin (1 g., 0.0051 mole) in acetone (50 ml.) over 3 days. Needles of benzil separated gradually from the solution. After the evaporation of acetone under reduced pressure, the aqueous solution was treated with sulfur dioxide. The needles (0.63 g.) of benzil suspended in the aqueous solution, in almost pure condition, were collected by filtration. Upon treatment of the solution by aqueous sodium hydrogen carbonate benzoic acid (0.38 g., 0.0031 mole) only was obtained.

(c) *In anhydrous boiling acetone.* Powdered potassium permanganate (3 g., 0.019 mole) was added to a solution of desoxybenzoin (1 g., 0.0051 mole) in anhydrous boiling acetone (50 ml.) in the course of 4 hr. After the evaporation of the solvent, water (18 ml.) was added to the residue. The aqueous solution thus obtained was cleared with sulfur dioxide and twice extracted with a 200- and 100-ml. portion of ether. The combined ethereal solution was then treated with two 20-ml. portions of 5% sodium hydrogen carbonate. On acidification of the combined sodium bicarbonate extracts with dilute hydrochloric acid, pure benzoic acid (0.12 g.) was obtained. Evaporation of the dried ethereal solution left after the separation of the acidic fraction gave a brown resinous product which crystallized only partially. This residue was washed with ether and the extract on evaporation left a yellow amorphous powder. The ether insoluble fraction (0.2 g.) was purified from benzene, giving bisdesoxybenzoin in fine prisms, m.p. 250–251°. The infrared spectrum (in Nujol) showed a band at 1667 cm^{-1} (conjugated C = O). The compound is soluble with difficulty in alcohol and ether but is readily soluble in acetone.

Anal. Calcd. for $C_{28}H_{22}O_2$: C, 86.12; H, 5.68; mol. wt. 390. Found: C, 85.68; H, 5.88; mol. wt. 418 (Rast).

(Analytical sample dried under reduced pressure at 100–110° for 1 hour) ultraviolet absorption (Figure b) λ_{max} in dioxane 248 $m\mu$ (ϵ , 26500).

(d) *In hydrous boiling acetone.* Powdered potassium permanganate (3 g., 0.019 mole) in water (120 ml.) was added to a solution of desoxybenzoin (1 g., 0.0051 mole) in refluxing acetone (50 ml.) in the course of 1 hr. After the reaction mixture was treated as in the case of procedure (b), 0.38 g. of crude benzoic acid was obtained. The neutral fraction (0.9 g.) was washed with ether, leaving crude bisdesoxybenzoin (50 mg.). On recrystallization of this compound from benzene, pure bisdesoxybenzoin was obtained which was identical in every way with a specimen obtained by procedure (c).

Evaporation of the solvent from the above ethereal solution yielded 0.833 g. of product. When this was submitted to distillation at 30 mm., 50 mg. of benzaldehyde was obtained. It was identified through the 2,4-dinitrophenylhydrazone. Isolation of any other product from the residue left after distillation was unsuccessful.

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