W. A. Sheppard for helpful discussions; to Drs. H. Foster, G. S. Reddy, and F. J. Weigert, Mrs. Jean L. Read, and Mr. C. B. Matthews for nmr consultations; to Misses Carol J Hermann, Naomi E. Schlichter, and Ellen Wallace for ir and uv spectra interpretations; and to Mrs. Adah B. Richmond for glpc separations.

Hydroxide Displacement of the Sulfone Linkage in Thioxanthen-9-one 10,10-Dioxides to Benzophenone-2′-hydroxy-2-sulfinic Acids. Intramolecular Cyclization to Xanthones

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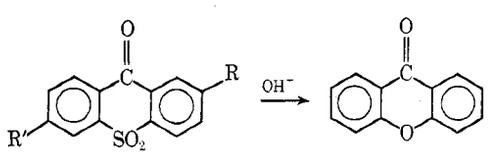
Received July 22, 1971

2-H, 2,6-diCOOH, 2-Cl, 2-CH_3, 2-CH_3O, and 2-NO_2 thioxanthen-9-one 10,10-dioxides were synthesized and treated, at reflux, with 2% NaOH–65% dioxane–H_2O. For these systems, facile hydroxide displacement of the sulfone linkage was found to occur exclusively on the more electrophilic ring to give the novel benzophenone-2′-hydroxy-2-sulfinic acids. Further, in alkaline media, these sulfinic acids generally undergo unique intramolecular cyclization to xanthones. The structures of the sulfinic acids were established by replacement of the sulfinic acid group with a chloromercury group followed by replacement of the latter with hydrogen to afford 2-hydroxybenzophenones.

Because thioxanthen-9-one 10,10-dioxides may possess some interesting physiologial properties, synthetic procedures leading to the preparation of a variety of substituted parent (**1**) systems have been reported.[3] Further, the well-known[4] colored solutions resulting from treatment of thioxanthen-9-one 10,10-dioxides with reducing agents in alkaline media have been investigated,[5] and epr data[6] have verified that formation of radical anions are responsible for the observed colors. While studying these color reactions in alkaline systems, the partial conversion of **1** to xanthone (**3**) was observed.[5a] Additional investigations relating to this transformation have not been reported and this interesting cleavage reaction has remained unexplained.



1, R = R′ = H
4, R = R′ = COOH

During the course of our recent studies[7] relating to the cyclization of diphenyl sulfone-2-carboxylic acids to thioxanthen-9-one 10,10-dioxides, we found that the heterocyclic moiety of the 2,6-dicarboxylic acid (**4**) of **1** was unstable to treatment with dilute aqueous sodium hydroxide. Since our results, along with those reported by Heymann, suggested a general lack of stability of the thioxanthen-9-one 10,10-dioxide nucleus in alkaline media, we undertook a more detailed investigation of this reaction system and report our findings in this paper.

For the purpose of this study, six thioxanthene-9-one 10,10-dioxides were prepared and refluxed with 2% sodium hydroxide–65% dioxane–water[8a] solution (Table I). All compounds underwent ring opening at the sulfone linkage[8b] under these conditions, and, following acidification, the corresponding novel hydroxybenzophenonesulfinic acids were obtained (Table II, A). In addition, except for the nitro compound **6**, xanthones were also isolated from the reaction mixtures (Table II, B). Nitro compound **6** gave only the 2′-hydroxy-5′-nitro-2-sulfinobenzophenone (**12**). Further, when the pure hydroxybenzophenonesulfinic acids were refluxed with 3% aqueous sodium hydroxide, all except **12** were converted to their corresponding xanthone products shown in Table III. Under these reaction conditions, the refractory nitro compound, **12**, remained unchanged even after reflux for 48 hr. The

TABLE I

THIOXANTHEN-9-ONE 10,10-DIOXIDES REACTED AT REFLUX IN 2% SODIUM HYDROXIDE–65% DIOXANE–H_2O

Reactant	mmol[a]	R′	R	Reaction time, hr	% Unreacted
1	16	H	H	4	61.5
4	6	COOH	COOH	0.25[b]	45.0
				5	7.5
5	14	H	Cl	4	50.2
6	14	H	NO_2	2	0.0
7	15	H	CH_3	18	23.0
8	15	H	CH_3O	18	28.8

[a] All reactions were run in 500 ml of solution except **4** which was run in 50 ml. [b] Yields in Table II were obtained for this reaction time.

(1) This investigation was supported in part by a National Science Foundation Undergraduate Research Grant No. GE 8888.

(2) (a) Taken in part from the M.S. theses of M. J. B. and R. M.; (b) the senior thesis of P. D.; (c) the Ph.D. dissertation of G. S.

(3) (a) E. D. Amstutz and C. R. Neumoyer, *J. Amer. Chem. Soc.*, **69**, 1925 (1947); (b) J. Blanz and F. A. French, *J. Med. Chem.*, **6**, 185 (1963).

(4) (a) C. Graebe and O. Schulthess, *Justus Liebigs Ann. Chem.*, **263**, 10 (1891); (b) F. Ullmann and O. Von Glenck, *Ber.*, **49**, 2509 (1916); (c) E. D. Amstutz, E. A. Fehnel, and I. M. Hunsberger, *J. Amer. Chem. Soc.*, **70**, 133 (1948).

(5) (a) H. Heymann, *J. Amer. Chem. Soc.*, **71**, 260 (1949); (b) E. A. Fehnel, *ibid.*, **71**, 1065 (1949).

(6) E. T. Kaiser and L. Kevan, Ed., "Radical Ions," Interscience, New York, N. Y., 1968, Chapter 8, and references cited therein.

(7) O. F. Bennett and P. Gauvin, *J. Org. Chem.*, **34**, 4165 (1969).

(8) (a) All of the thioxanthen-9-one 10,10-dioxides were completely soluble in this solvent system, while many exhibited limited solubility in only aqueous hydroxide. (b) One referee of this manuscript has observed base-induced ring opening of the thioxanthen-9-one (**2**) ring system using Huang-Minlon conditions. Unlike the sulfone systems, he reports that ring opening in the sulfides does not lead to new, ring-closed products.

TABLE II

PRODUCTS OBTAINED FROM REACTION OF THIOXANTHEN-9-ONE 10,10-DIOXIDES[f]

A

Reactant	Benzophenone product[a] (yield, %)	Product	Mp, °C
1	2′-OH-2-SO_2H (25.1)	9	119–120
4	4,5′-diCOOH-2′-OH-2-SO_2H (40.0)	10	189–191
5	5′-Cl-2′-OH-2-SO_2H (37.0)	11	118–119
6	2′-OH-5′-NO_2-2-SO_2H (89.5)	12	123–124
7	2′-OH-5-CH_3-2-SO_2H (72.4)	13	123–124
8	2′-OH-5-CH_3O-2-SO_2H (68.1)	14	105–106

B

Reactant	Xanthone product (yield, %)	Product	Mp, °C
1	Xanthone[b] (13.4)	3	174–175
4	2,6-diCOOH[c] (15.0)	15	407–412
5	2-Cl[b] (13.3)	16	170–171
7	2-CH_3[b,d] (4.6)	17	121–122
8	2-CH_3O[b,e] (3.1)	18	134–135

[a] Products 10 and 11 were purified by crystallization from aqueous methanol. All other products were crystallized from aqueous acetone. [b] Infrared and melting point comparisons with authentic samples were identical. [c] Infrared and melting point comparisons made with a sample prepared by an independent procedure proved identity; see Experimental Section. [d] F. Ulmann and M. Slokasow, *Ber.*, **38**, 2115 (1905). [e] A. Baeyer, *Justus Liebigs Ann. Chem.*, **372**, 102 (1910). [f] Satisfactory analytical values (±0.4% for C, H, S) for all new compounds were reported: Ed.

TABLE III

CYCLIZATION OF THE HYDROXYBENZOPHENONESULFINIC ACIDS TO XANTHONES BY REFLUX IN 3% AQUEOUS SODIUM HYDROXIDE

Reactant	mmol	Reaction time, hr	% Unreacted	Xanthone product	Yield, %
9	2	2	26.8	3	73.2
10	1.4	2	37.0	15	63.0
11	2	2	47.2	16	52.8
12	2	48	100.0		0.0
13	2	4	76.4	17	23.6
13	2	40	18.8	17	81.2
14	2	4	82.0	18	18.0
14	2	40	33.0	18	67.0

xanthone structures were confirmed by elemental analysis and by infrared and melting point comparison to known compounds. The structure of the new diacid xanthone, **15**, was established by comparison to a sample synthesized by an independent route (see Experimental Section).

All of the hydroxybenzophenonesulfinic acids immediately decolorize cold neutral permanganate and also give a positive Krishna test[9] indicating the presence of a sulfinic acid group. Their general structures were consistent with elemental analyses (Table II) as well as with ir and nmr data, but their absolute structures were established by synthetic procedures. Thus, for each hydroxybenzophenonesulfinic acid, the sulfinic acid group was replaced by a chloromercury group[10] to afford the corresponding solid hydroxychloromercuribenzophenones (Table IV). Removal of the chloromercury group was achieved in acid solution to give the respective 2-hydroxybenzophenones (Table V)

(9) S. Krishna and H. Singh, *J. Amer. Chem. Soc.*, **50**, 792 (1928).

(10) (a) W. Peters, *Ber.*, **38**, 2567 (1905). (b) I. L. Finar, "Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1955, p 522.

TABLE IV

PREPARATION OF HYDROXYCHLOROMERCURIBENZOPHENONES FROM THE HYDROXYBENZOPHENONESULFINIC ACIDS[b]

Reactant	mmol	Chloromercuri product[a] (yield, %)	Product	Mp, °C
9	15	2′-HgCl-2-OH (69.6)	19	185–187
10	3	2′-HgCl-4′,5-diCOOH-2-OH (70.3)	20	304–306 dec
11	13	5-Cl-2′-HgCl-2-OH (74.6)	21	206–208
12	13	2′-HgCl-2-OH-5-NO_2 (82.1)	22	255–256
13	14	2-HgCl-2′-OH-5-CH_3 (74.7)	23	203–204
14	14	2-HgCl-2′-OH-5-CH_3O (68.2)	24	203–204

[a] All products were purified by crystallization from aqueous acetone [b] Satisfactory analytical values (±0.4% for C, H) for all compounds were reported: Ed.

TABLE V

o-HYDROXYBENZOPHENONES FROM THE HYDROXYCHLOROMERCURIBENZOPHENONES[e]

Reactant	mmol	*o*-Hydroxy product (yield, %)	Product	Mp, °C	Recrystn solvent
19	18	2-OH[a] (91.8)	25	38–39	Distilled bp 136–138° (1.9 mm)
20	19	4′,5-diCOOH-2-OH[b] (89.0)	26	334–336 dec	Aqueous acetone
21	16	5-Cl-2-OH[b] (84.9)	27	93–94	Ethanol
22	16	2-OH-5-NO_2[c] (84.0)	28	123–124	Ethanol
23	15	2-OH-3′-CH_3[d] (82.4)	29	Liquid	Distilled, bp 140–141° (0.9 mm)
24	15	2-OH-3′-CH_3O[d] (83.6)	30	Liquid	Distilled, bp 148–149° (0.5 mm)

[a] The solid oxime was prepared, mp 132–134° [lit. mp 135°: E. P. Kohler and W. F. Bruce, *J. Amer. Chem. Soc.*, **53**, 1572 (1931)]. [b] Comparison made to Sadtler Research Laboratories, Standard Infrared Spectra, Grating 24374. [c] See F. Ulmann and J. H. Mallet, *Ber.*, **31**, 1696 (1898). [d] Comparisons made to structures prepared by independent procedures proved identity; see Experimental Section. [e] Satisfactory analytical values (±0.4% for C, H) for all compounds except **19**, **21**, and **22** were reported: Ed.

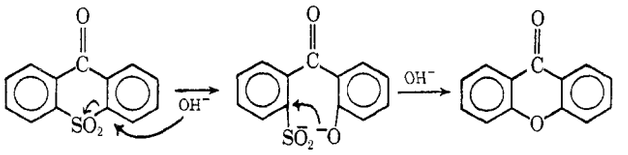
which were compared to known compounds or to structures synthesized by independent methods.

The reported[5a] finding of xanthone product following treatment of thioxanthen-9-one 10,10-dioxide in alkaline media can now be explained as the result of nucleophilic displacement of the sulfonyl linkage in the thioxanthen-9-one 10,10-dioxide moiety leading to the novel hydroxybenzophenonesulfinic acids. Further, in alkaline systems, the unique functionality of these sulfinic acids allows intramolecular displacement of the sulfinate group to afford xanthone products. Failure of the nitro compound **12** to undergo cyclization reaction may be attributable to the reduced nucleophilic strength of the phenoxy anion due to the strong electron-withdrawing influence of the *p*-nitro substituent.

Although for a given substituted thioxanthen-9-one 10,10-dioxide, two isomeric cleavage products are theoretically possible, we found no evidence to indicate that displacement reaction occurred other than exclusively on the more electrophilic aromatic ring.

Scheme I proposes a general mechanism that is con-

SCHEME I



sistent with the cleavage–cyclization reactions found in this investigation. Although some inorganic sulfite results from the cyclization reaction, the precise nature of the sulfinate displacement is not presently known.

Experimental Section[11]

Preparation of the Thioxanthen-9-one 10,10-Dioxides (1, 4–8).—The reported procedure[4b] for the oxidation of thioxanthen-9-one and 2-chlorothioxanthen-9-one in hydrogen peroxide (30%) and glacial acetic acid gave thioxanthen-9-one 10,10-dioxide[4b] (**1**) (84%) and 2-chlorothioxanthen-9-one 10,10-dioxide[12] (**5**) (85%). Thioxanthen-9-one 10,10-dioxide-2,6-dicarboxylic acid (**4**) was prepared (85%) according to the cyclization procedure reported by Bennett and Gauvin.[7] The condensation procedure reported by Roberts and Smiles[13] was utilized to obtain the 4′-nitro-[14] (72%), 4′-methyl-[15] (70%), and 4′-methoxydiphenyl sulfide-2-carboxylic acids[13] (78%). Cyclization of the 4′-methyl and the 4′-methoxydiphenyl sulfide-2-carboxylic acids was achieved in concentrated sulfuric acid at 100° and 50°, respectively, to afford 2-methylthioxanthen-9-one[16] (79%) and 2-methoxythioxanthen-9-one[17] (84%). The cyclization of 4′-nitrodiphenyl sulfide-2-carboxylic acid to 2-nitrothioxanthen-9-one (47%) was effected using the procedure of Mayer,[14] which involved reaction of the acid chloride with aluminum chloride. The oxidation of the 2-nitro-, 2-methyl-, and 2-methoxythioxanthen-9-ones in hydrogen peroxide and glacial acetic acid afforded the 2-nitro-[14] (**6**) (89%), 2-methyl-[18] (**7**) (70%), and 2-methoxythioxanthen-9-one 10,10-dioxides[19] (**8**) (73%).

All compounds synthesized were identified by satisfactory elemental analyses, melting points, and ir and nmr data.

Reaction of the Thioxanthen-9-one 10,10-Dioxides in 2% Sodium Hydroxide–65% Dioxane–Water.—The following typical examples illustrate the general procedures used to carry out the cleavage reactions. For each specific compound, changes in these procedures, as well as necessary product information, are noted in Tables I and II.

A. Reaction of Thioxanthen-9-one 10,10-Dioxide-2,6-dicarboxylic Acid (4).—In a typical reaction, **4** (2 g, 6 mmol) in 50 ml of 2% sodium hydroxide–65% dioxane–water was refluxed for 5 hr. The initial brown solution changed to a deep green as reflux began and this color persisted for 1 hr during the reaction time. Following addition of 150 ml of water, the dioxane was flash distilled and the cold, brown solution was acidified with 10% hydrochloric acid and filtered. The tan solid was washed with water, dried, and extracted with three 150-ml portions of cold acetone. The acetone-insoluble material, 1.56 g (92%), was identified as xanthone-2,6-dicarboxylic acid, **15** (Table II, B), by ir and melting point comparisons with a sample prepared by independent synthesis (*vide infra*).

The combined acetone extracts were evaporated to dryness, leaving 0.45 g of yellow powder. This solid was extracted with three 75-ml portions of ether, which left 0.15 g (7.5%) of unreacted **4**. Evaporation of the ether extracts afforded 0.29 g of 4,5′-dicarboxy-2′-hydroxy-2-sulfinobenzophenone, **10** (Table II, A).

B. Reaction of 2-Chlorothioxanthen-9-one 10,10 Dioxide (5).—A solution of **5** (4 g, 14 mmol) in 500 ml of 2% sodium hydroxide–65% dioxane–water was refluxed for 4 hr. The initial clear solution changed to a deep green as reflux began and this color persisted during the entire reaction time. Following the addition of 300 ml of water, the dioxane was removed by flash distillation and the solution was filtered. The white solid was washed with water, dried, and extracted with three 150-ml portions of cold ether. The ether-insoluble material, 1.99 g (50.2%), was unreacted **5**. The combined ether extracts were evaporated to dryness, leaving 0.45 g of white solid. Crystallization from methanol gave 2-chloroxanthone, **16**, which was identified by ir and melting point comparisons (Table II, B).

The remaining basic reaction solution was acidified with 10% hydrochloric acid to give a cloudy solution which was extracted with four 100-ml portions of cold ether. Evaporation of the ether extracts left a yellow oil which solidified on chilling to a light yellow solid. Two crystallizations from aqueous methanol afforded the white needles, 1.42 g, of 5′-chloro-2′-hydroxy-2-sulfinobenzophenone, **11** (Table II, A).

Cyclization of the Hydroxybenzophenonesulfinic Acids to Xanthones (Table III).—In a typical reaction, 0.5 g (2 mmol) of **13** was dissolved in 50 ml of 3% aqueous sodium hydroxide. The light yellow solution was refluxed for 4 hr with no color change. The white solid that formed was filtered from the cold solution, washed with water, and dried. This solid, 0.09 g, was 2-methylxanthone, **17**, as shown by ir and melting point comparison with an authentic sample. The remaining basic solution was acidified with 10% hydrochloric acid and filtered. The solid, 0.38 g, was washed with water and dried, and was shown to be unreacted **13**.

Preparation of Hydroxychloromercuribenzophenones from the Hydroxybenzophenonesulfinic Acids (Table IV).—The general procedure[10a] employed for the replacement of a sulfinic acid group with a chloromercury group was utilized in these preparations. In a typical reaction, 4 g (14 mmol) of **14**, 12 g (44 mmol) of mercuric chloride, and 80 ml of water were added to 80 ml of glacial acetic acid. The mixture was heated to reflux, giving a light yellow solution as **14** dissolved. After a 4-hr reflux period, the solid precipitate was filtered from the cold solution, washed with water, and dried. Crystallization from acetone afforded yellow needles (4.3 g) of 2-chloromercuri-2′-hydroxy-5-methoxybenzophenone, **24**.

Preparation of *o*-Hydroxybenzophenones from the Hydroxychloromercuribenzophenones (Table V).—The general procedure[20] employed for the replacement of a chloromercury group with hydrogen was utilized in these preparations. In a typical reaction, 8 g (16 mmol) of **22** and 200 ml of 95% ethanol was added to 200 ml of concentrated hydrochloric acid. The mixture was heated to reflux and after 2 hr a clear solution resulted. After 2 hr more at reflux, 300 ml of water was added to the cold solution and the ethanol was removed by flash distillation. The resulting acidic solution was extracted with five 100-ml portions of benzene and the benzene extracts were dried over anhydrous calcium carbonate. Evaporation of the benzene left 3.4 g of light tan solid. Crystallization from ethanol gave light tan needles of the known[21] 2-hydroxy-5-nitrobenzophenone, **28**.

Synthesis of Xanthone-2,6-dicarboxylic Acid (15). General.—Starting with 2-chloro-4-methylaniline, the reported procedure of Goldberg and Wragg[22] was used to prepare 3-chloro-4-cyanotoluene in 45% yield. This product was converted to 2-chloro-4-methylbenzoic acid, following the literature procedure,[22] in 86% yield. Reaction of the benzoic acid product with *p*-cresol using the method of Kobrich[23] gave the known 2-carboxy-4′,5-dimethyldiphenyl ether (75%).

A. Diphenyl Ether-2,4′,5-tricarboxylic Acid (31).—2-Carboxy-4′,5-dimethyldiphenyl ether, 0.5 g (2 mmol), was refluxed for 5 hr in 125 ml of water containing 2.2 g (14 mmol) of potassium permanganate. The cold reaction mixture was filtered and the purple filtrate was acidified with 5% hydrochloric acid. The solid, obtained by filtration, was washed with water, dried, and crystallized from aqueous methanol to give 0.45 g (72%) of white **31**, mp 314–318° dec.

Anal. Calcd for $C_{15}H_{10}O_7$: C, 59.58; H, 3.34. Found: C, 59.78; H, 3.32.

B. Xanthone-2,6-dicarboxylic Acid (15).—A stirred solution of **31** (0.2 g, 0.7 mmol) in 20 ml of concentrated sulfuric acid

(11) Melting points are corrected except for those compounds melting above 300°. Elemental analyses were performed by Dr. Carol K. Fitz, Needham Heights, Mass., and by Galbraith Laboratories, Inc., Knoxville, Tenn.

(12) H. Gilman and J. W. Diehl, *J. Org. Chem.*, **24**, 1914 (1959).

(13) K. C. Roberts and S. Smiles, *J. Chem. Soc.*, 867 (1929).

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(19) W. B. Price and S. Smiles, *J. Chem. Soc.*, 3159 (1928).

(20) T. Okamoto and J. F. Bunnett, *J. Amer. Chem. Soc.*, **78**, 5361 (1956).

(21) F. Ulmann and J. H. Mallet, *Ber.*, **31**, 1696 (1898).

(22) A. A. Goldberg and A. H. Wragg, *J. Chem. Soc.*, 4227 (1958).

(23) V. G. Kobrich, *Justus Liebigs Ann. Chem.*, **664**, 88 (1963).

was heated at 135° for 3 hr. The cool solution was poured onto ice and the solid, collected by filtration, was washed with water and several portions of hot methanol. The dry solid **15**, 0.15 g, was obtained in 83% yield, mp 407–412° dec, and was identical with the xanthone product obtained from cleavage of **4** (Table II, B) as shown by ir and melting point comparisons.

C. Dimethyl Xanthone-2,6-dicarboxylate (32).—Normal esterification of **15** could not be achieved due to its extreme insolubility. However, treatment of **15** with ethereal diazomethane gave **32**, mp 213–214°, from methanol. Similar treatment of **15** obtained from cleavage of **4** also afforded **32**.

Anal. Calcd for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87. Found: C, 65.10; H, 3.80.

Synthesis of 2-Hydroxy-3′-methylbenzophenone (29).—The position of hydroxide displacement of the sulfone linkage in compounds **1**, **5**, and **6** was established by ultimate conversion of cleavage products **9**, **11**, and **12** to the known *o*-hydroxybenzophenones **25**, **27**, and **28**, respectively. Similar conversion of cleavage products **10**, **13**, and **14** led to the unknown *o*-hydroxybenzophenones, **26**, **29**, and **30**. Thus, for comparative purposes, these latter compounds were prepared by independent procedures.

Nakazawa and Baba[24] have reported on the Fries rearrangement of *m*-phenyltoluate to obtain 4-hydroxy-3′-methylbenzophenone. Utilizing their procedure, we have also isolated the 2-hydroxy isomer, **29**, from the reaction mixture.

To a stirred mixture of 26.6 g (0.2 mol) of aluminum chloride in 200 ml of carbon disulfide was added 23.2 g (0.1 mol) of *m*-phenyltoluate in 50 ml of carbon disulfide at a rate sufficient to promote solvent reflux. Following complete addition, reflux was continued for 2 hr before distillation of the carbon disulfide. The remaining reaction mixture was heated at 150° for 3 hr, cooled, and treated with 200 ml of cold 5% hydrochloric acid. Filtration gave the known 4-hydroxy-3′-methylbenzophenone,[24] mp 165–166°. The oily filtrate was extracted with four 100-ml portions of ether. Distillation gave 4.7 g of light yellow oil, bp 142–144° (1 mm).

Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.38; H, 5.80.

Ir and nmr comparison of this compound with **29** showed the two to be identical.

2-Methoxy-3′-methylbenzophenone (33).—To a stirred solution of 50 ml of water, 50 ml of acetone, and 0.68 g (17 mmol) of sodium hydroxide was added 4 g (17 mmol) of **29**. After reflux for 30 min, 16.3 g (28 mmol) of iodomethane dissolved in 50 ml of acetone was added slowly to the hot solution. Following reflux for 8 hr, the acetone and unreacted iodomethane were removed by flash distillation and the solution was acidified with 10% hydrochloric acid. The oily solution was extracted with four 100-ml portions of ether and dried ($MgSO_4$). Distillation gave 3.1 g of light yellow oil, **33**, bp 161–162° (0.8 mm).

Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.64; H, 6.24. Found: C, 79.37; H, 6.15.

Synthesis of 2-Hydroxy-3′-methoxybenzophenone (30).—In similar manner to that described above for the synthesis of **29**, Nakazawa and Baba[24] prepared 4-hydroxy-3′-methoxybenzophenone by the Fries rearrangement of *m*-phenylanisate. Utilizing their procedure we also isolated the 2-hydroxy isomer, **30**, from the reaction mixture. Thus, the Fries rearrangement was conducted as described above to the point where the reaction mixture was treated with cold 5% hydrochloric acid. The waxy solid which formed was removed by extraction with four 100-ml portions of ether. The ether solution was extracted with three 50-ml portions of 10% sodium hydroxide. Acidification of the basic extracts afforded the known 4-hydroxy-3′-methoxybenzophenone,[24] mp 137–138°, from methanol. Distillation of the remaining ether solution gave 7.2 g of light yellow oil, bp 148–150° (0.4 mm).

Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.69; H, 5.30. Found: C, 73.65; H, 5.40.

Ir and nmr comparison of this compound with **30** showed the two to be identical.

2,3′-Dimethoxybenzophenone (34).—Following the procedure used for the preparation of **33** afforded **34** as a light orange oil, bp 151–152° (0.35 mm). This oil solidified upon chilling, mp 27–28°.

Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.38; H, 5.82. Found: C, 74.55; H, 5.91.

Conversion of 2-Hydroxybenzophenone-4′,5-dicarboxylic Acid (26) to 2-Methoxybenzophenone-4′,5-dicarboxylic Acid (35).—This methyl ether was prepared using the same general procedure that afforded methyl ethers **33** and **34**. Solid **35** was obtained in 70% yield, mp 306–309° dec, from aqueous methanol.

Anal. Calcd for $C_{16}H_{12}O_6$: C, 64.22; H, 3.71. Found: C, 63.87; H, 3.95.

2-Methoxydimethylbenzophenone-4′,5-dicarboxylate (36).—Treatment of **35** with ethereal diazomethane gave **36**, mp 138–139°, from aqueous methanol.

Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.87. Found: C, 65.70; H, 4.90.

Synthesis of 2-Methoxybenzophenone-4′,5-dicarboxylic Acid (35). A. 2-Methoxy-4′,5-dimethylbenzophenone (37).—The reported[25] synthesis of 2-hydroxy-4′,5-dimethylbenzophenone was used to obtain this compound in 78% yield. Its methyl ether was prepared using the same general procedure that gave methyl ethers **33**, **34**, and **35**. Solid **37** was obtained in 72% yield, mp 81–82°, from aqueous methanol.

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.00; H, 6.80.

B. Oxidation of 37 to 35.—A stirred mixture of **37** (1.4 g, 5.8 mmol), 7.7 g (43 mmol) of potassium permanganate, and 100 ml of 2% sodium hydroxide were heated at reflux for 3 hr and filtered. The cooled filtrate was acidified with dilute sulfuric acid, and 10% sodium bisulfite was added until the dark solution became clear. The solid was filtered, washed with dilute sulfuric acid and water, and dried. This product, 1.12 g (64%), was shown to be identical with **35** by melting point and ir comparisons. Further, diazomethane esterification of this compound gave **36**.

Registry No.—**3**, 90-47-1; **9**, 33886-18-9; **10**, 33785-48-7; **11**, 33785-49-8; **12**, 33785-50-1; **13**, 33785-51-2; **14**, 33785-52-3; **15**, 33872-64-9; **16**, 13210-15-6; **17**, 6280-45-1; **18**, 1214-20-6; **19**, 33785-56-7; **20**, 33785-57-8; **21**, 33785-58-9; **22**, 33785-59-0; **23**, 33785-60-3; **24**, 33785-61-4; **25**, 117-99-7; **26**, 33785-63-6; **27**, 85-19-8; **28**, 18803-19-5; **29**, 33785-66-9; **30**, 21554-73-4; **31**, 33785-68-1; **32**, 33785-69-2; **33**, 33785-70-5; **34**, 21554-74-5; **35**, 33785-72-7; **36**, 33785-73-8; **37**, 33785-74-9.

Acknowledgment.—We wish to thank Mr. James Johnson and Mr. Thomas Cigas for conducting several of the literature preparations.

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