[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF OREGON]

Syntheses of 3,3′-Dimethoxybenzophenone. *Para* Substitution in Acylation of the Organocadmium Reagent from *m*-Haloanisoles[1,2]

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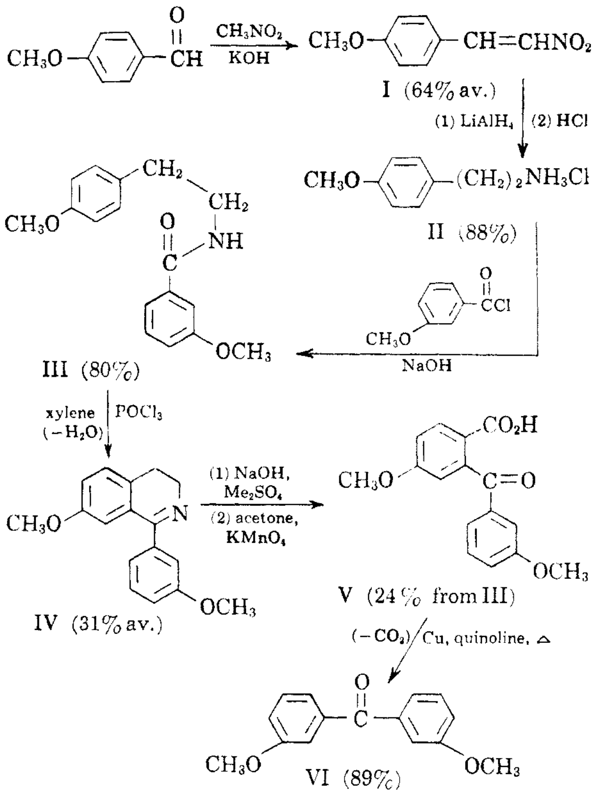
3,3′-Dimethoxybenzophenone (VI) has been prepared in 10% over-all yield from either (*a*) *p*-anisaldehyde (by the unequivocal Scheme I) or (*b*) benzophenone (Scheme II). The structure of the product from (*b*) was established by comparison of its 2,4-dinitrophenylhydrazone with that from procedure (*a*) and by Beckmann rearrangement of its oxime to 3-methoxy-*N*-(3-methoxyphenyl)benzamide (XI), identical with an authentic synthetic specimen.

Treatment of the organocadmium compound from either *m*-iodoanisole or *m*-bromoanisole with *m*-methoxybenzoyl chloride gave *ca.* 20% yield of liquid ketone from which was isolated the crystalline derivative of 3,4′-dimethoxybenzophenone 2,4-dinitrophenylhydrazone, identified by comparison with an authentic sample. Infrared analysis of the ketone (obtained from *m*-bromoanisole) showed it consisted of *ca.* 35% "normal product" (VI) and 65% "rearranged product," 3,4′-dimethoxybenzophenone.

For use in further studies we desired a convenient synthesis of 3,3′-dimethoxybenzophenone (VI) of unequivocal structure. Three alternative procedures were investigated in this regard. The first of these (Scheme I) was an adaptation of the method of Gensler and Samour[5] for a different series. Thus the ω-nitrostyrene I, formed by condensation of *p*-anisaldehyde with nitromethane, was reduced with lithium aluminum hydride in ether to the amine hydrochloride II. II was converted to the amide III by means of the Schotten-Baumann reaction. Bischler-Napieralski cyclization of III to the dihydroisoquinoline IV proved difficult (presumably because electrophilic substitution must occur meta to a deactivating methoxy group)[6,7] but could be effected in low yield using phosphorus oxychloride in refluxing xylene. More strenuous conditions proved even less suitable due to the formation of increased yields of tar. The crude liquid resulting from treatment of IV with alkaline dimethyl sulfate was oxidized directly to the crystalline acid V. Decarboxylation of V produced the desired ketone VI, b.p. 144–145° (0.3 mm.), in an over-all yield of 10% for the six-step process. As an added indication that the structural assignment for VI was appropriate for the final product, it was found that the 2,4-dinitrophenylhydrazone exhibited (*a*) an absorption maximum at 385–387 mμ (log ε 4.48), consistent with the values predicted (λ_{max} *ca.* 387 mμ, log ε *ca.* 4.5) on the basis of observations by Johnson,[8] and (*b*) a m.p. of 191–192°, the same as reported by Buchta and Weidinger[9] (whose prep-



Scheme I

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[1] This investigation was supported (in part) by research grant No. CY-3097 from the National Cancer Institute, Public Health Service. Presented at the Northwest Regional Meeting of the American Chemical Society, Spokane, Wash., June, 1957.

[2] Abstracted in part from the M.A. thesis of Roger Mann, University of Oregon, June, 1957.

[3] Research Fellow, 1957.

[4] Research Associate, 1956–1957.

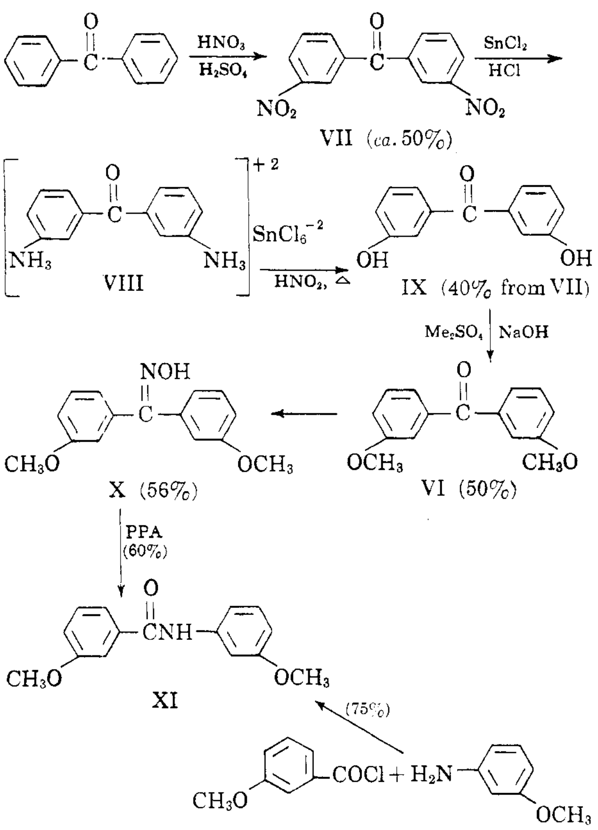
[5] W. J. Gensler and C. M. Samour, *J. Am. Chem. Soc.*, **73**, 5555 (1951).

[6] W. M. Whaley and W. H. Hartung, *J. Org. Chem.*, **14**, 650 (1949).

[7] See W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **VI**, Chap. 2 (1951); and discussion of the mechanism of the Morgan-Walls reaction (a special type of the more general Bischler-Napieralski reaction) by E. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **78**, 147 (1944).

[8] G. D. Johnson, *J. Am. Chem. Soc.*, **75**, 2720 (1953). Note the absence of an effect on the observed λ_{max} due to the presence of an unconjugated 3-methoxy group but the bathochromic shift caused by a conjugated 4-methoxy group in the series of 2,4-DNP's reported by Johnson: benzophenone $\lambda_{max}^{CHCl_3}$ 387 mμ (log ε 4.51); 3-methoxybenzophenone 387 (4.47); 4-methoxybenzophenone 396 (4.47); 4,4′-dimethoxybenzophenone 400 (4.46). It might also be noted that log ε is approximately 4.5 in all cases.

[9] E. Buchta and H. Weidinger, *Ann.*, **580**, 83 (1953).



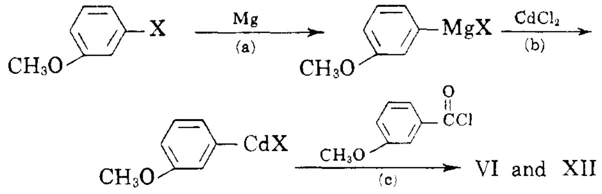
Scheme II

aration served only as a means of locating the positions of carbon-carbon double bonds in a tetra-anisylhexadiene and not as a suitable synthetic procedure for VI).

The second approach (Scheme II) was a modification of the method of Valette[10] by which he had produced a dimethoxybenzophenone of doubtful structure. This involved the successive steps of nitration according to the method of Barnett and Matthews,[11] reduction of the nitro compound with stannous chloride in hydrochloric acid, hydroxy-deamination of the crude salt VIII to give IX, and methylation of IX to form VI in *ca.* 10% over-all yield for the four-step process.

Two different procedures were used to establish the structure of the Valette dimethoxybenzophenone. First, it formed a 2,4-DNP identical (as based on melting point and mixture melting point) with that from Scheme I. Second, it was converted to a crystalline oxime which underwent Beckmann rearrangement in the presence of polyphosphoric acid to the amide XI, identical (as based on melting point, mixture melting point, and infrared spectrum) with an authentic specimen produced by Schotten-Baumann reaction between *m*-anisidine and *m*-methoxybenzoyl chloride.

Proof of the structure of the Valette dimethoxybenzophenone apparently also serves to establish the structures of VII, VIII, IX, X, and the free diamine obtainable from VIII. Since the Barnett and Matthews nitration procedure involves separation through crystallization of VII from other nitration products formed simultaneously, it is necessary to perform a careful fractionation before carrying out the reduction step in order to be assured of the isomeric purity of the resultant VI. Nonetheless as a preparative method for VI, Scheme II is much to be preferred over Scheme I on the bases of facility of carrying out the reactions as well as time and expense involved.



Scheme III

Scheme III was an adaptation of the method of Klemm and Largman[12] (for preparation of *m*-methoxybenzophenone) whereby *m*-methoxybenzoyl chloride would be reacted with the organocadmium compound from a *m*-haloanisole (rather than from bromobenzene). Use of *m*-iodoanisole in this fashion, however, yielded only 17% of liquid product from which no crystalline oxime could be obtained. Moreover, the dinitrophenylhydrazone A, m.p. 211–212° (dec.), λ_{max} 396 mμ (log ϵ 4.45), depressed the melting point of the *bona fide* derivative from Schemes I and II upon admixture therewith. Repetition of the synthesis using *m*-bromoanisole instead of *m*-iodoanisole gave similar results, *viz.* 20–24% yield of liquid which showed the expected percentage of methoxy groups for a dimethoxybenzophenone but gave a 2,4-DNP identical (as based on melting point, mixture melting point, and ultraviolet spectrum) with A. It thus appeared likely that our ketonic products from Scheme III contained at least an appreciable percentage of some isomer other than VI. On the basis of the λ_{max} found and the belief that no migration of the methoxy group should occur in the *m*-methoxybenzoyl moiety of the acid chloride, we tentatively assigned A the structure of *3,4'dimethoxybenzophenone 2,4-dinitrophenylhydrazone.* That this was indeed the correct assignment followed from the fact that *bona fide* 3,4'-dimethoxybenzophenone (XII), prepared in 60% yield by interaction of anisole and *m*-methoxybenzoic acid in the presence of polyphosphoric acid, formed a 2,4-dinitrophenylhydrazone derivative identical with A (as based on melting point, mixture melting point, ultraviolet and infrared spectra). Comparison of the infrared spectrum of the free ketone, B, from the *m*-bromoanisole reaction with the spec-

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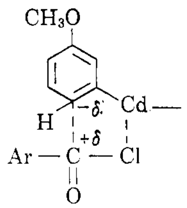
[10] M. Valette, *Bull. soc. chim. France,* [4] **47,** 289 (1930).

[11] E. deB. Barnett and M. A. Matthews, *J. Chem. Soc.,* **125,** 767 (1924).

[12] L. H. Klemm and T. Largman, *J. Am. Chem. Soc.,* **76,** 1688 (1954).

tra of standard mixtures of VI and XII indicated that B contained *ca.* 35% VI ("normal product") and 65% XII ("rearranged product").

Consideration of Scheme III for the organocadmium reaction of a *m*-haloanisole indicates there are three steps (*a*)-(*c*) in which a molecular rearrangement might plausibly occur. That step (*a*) is free of rearrangement is indicated by the results of Inagaki[13] and of Votocek and Matejka.[14] The former treated isatin with *o*-, *m*-, and *p*-methoxyphenylmagnesium iodides (respectively) and obtained three different crystalline products. Oxidation of these products by means of alkaline hydrogen peroxide gave *o*-, *m*-, and *p*-anisic acids, respectively. The latter workers reacted *m*-methoxyphenylmagnesium iodide with 4,4'-dimethylaminobenzophenone to give the carbinol which was reduced to bis(4-dimethylaminophenyl)-3-methoxyphenylmethane, identical with the product formed by condensation of *m*-methoxybenzaldehyde with *N*,*N*-dimethylaniline. Recent studies by Dauben and Collette[15] indicate that the rearrangement is associated with step (*c*) and not with step (*b*). Perhaps lending assistance to the consummation of such rearrangement would be the formation of a pseudo five-membered ring, as illustrated schematically by XIII. The donation of electronic charge by the methoxy group of the organocadmium reagent to the para position of the benzene ring is considered especially pertinent to this rearrangement.



XIII

EXPERIMENTAL[16]

3,3'-Dihydroxybenzophenone (IX). A mixture of 125 g. (0.46 mole) of 3,3'-dinitrobenzophenone,[11] 625 g. (2.76 moles) of C.P. stannous chloride dihydrate, and 835 ml. of concentrated hydrochloric acid was stirred at 70° for 6 hr. The yellow crystalline benzophenone-3,3'-diammonium chlorostannate was collected by filtration with a sintered glass funnel and suspended in 835 ml. of fresh concentrated hydrochloric acid. Beneath the surface of the cooled (3°) suspension was added over a period of 1 hr. a solution of 64 g. (0.93 mole) of sodium nitrite in 210 ml. of water. After an additional hr. of stirring at 0° the mixture was quickly filtered by means of a cold sintered glass funnel and the resultant bright yellow precipitate (tetrazonium salt) was added (cold) in small portions of 2.4 l. of boiling 1*N* sulfuric acid containing 10 drops of General Electric "Antifoam 60."[17] After the addition of 1 g. of Norit to the red solution the mixture was filtered hot. On cooling, the filtrate deposited a light tan powder, yield 39.6 g. (40%), m.p. 157.5–159.5°, reported[18] m.p. 163–164°.

Anal. Calcd. for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found: C, 72.70; H, 4.92.

3,3'-Diaminobenzophenone. For purposes of identification a small amount of the preceding chlorostannate was suspended in water, brought to *p*H 3, and treated with hydrogen sulfide. The filtered (to remove stannic sulfide) solution was basified with sodium hydroxide. The resultant precipitate was washed with water and recrystallized from 20% ethanol as light yellow, fine needles, m.p. 148–149°; reported[19] m.p. 150.5°.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.13; H, 5.82; N, 13.22.

4-Methoxy-β-nitrostyrene (I). This compound, m.p. 85–87.5°, prepared according to the method of Rosenmund,[20] showed strong allergenic properties[21] (contact dermatitis) toward Mr. Mann.

2-(4-Methoxyphenyl)ethylammonium chloride (II). In a manner similar to the second method described by Erne and Ramirez[22] for reduction of 2,3,4-trimethoxy-β-nitrostyrene there was added slowly (over a period of 3 hr.) a solution of 36 g. (0.201 mole) of I in 1.2 l. of anhydrous ether to a stirred refluxing mixture of 27 g. (0.71 mole) of lithium aluminum hydride in 2 l. of ether. After 2 more hr. of refluxing the reaction mixture was cooled thoroughly (ice-salt bath), and treated *very cautiously*[23] with 1.5 l. of 2*N* sulfuric acid, added in small portions over a period of 2 hr. by means of a long stem funnel reaching beneath the surface of the ether. The layers were separated and the ethereal layer was extracted with a slight excess of 2*N* sulfuric acid. The combined aqueous layer and extracts were basified cautiously with 33% aqueous sodium hydroxide until a milky emulsion resulted (*p*H > 10) and extracted thrice with ether. The white chalky precipitate which resulted from passing anhydrous hydrogen chloride into the dried (solid potassium hydroxide) combined ethereal extracts was collected and dried in air, yield 33.3 g. (88%), m.p. 203–210° (dec.), reported[20] m.p. 207°. For analysis a sample was recrystallized thrice from absolute ethanol to give silvery plates, m.p. 212–214° (dec.).

Anal. Calcd. for $C_9H_{14}ClNO$: Cl, 18.9. Found:[24] Cl, 19.2.

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[13] S. Inagaki, *J. Pharm. Soc. Japan*, **59**, 7 (1939).

[14] E. Votocek and J. Matejka, *Ber.*, **46**, 1755 (1913).

[15] In a private communication, Prof. W. G. Dauben reports that he and J. W. Collette "have shown that the cadmium reagent is normal and that the two products arise by competitive reactions of the acid chloride."

[16] Unless otherwise stated, all microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.; ultraviolet spectra were obtained by means of a Beckman DU instrument; and infrared spectra, by means of a Perkin-Elmer 112-C instrument.

[17] A preparation containing 30% silicone solids in aqueous suspension. In the absence of this agent considerable tar was produced.

[18] L. Gattermann and H. Rüdt, *Ber.*, **27**, 2293 (1894).

[19] P. J. Montagne, *Ber.*, **48**, 1027 (1915).

[20] K. W. Rosenmund, *Ber.*, **42**, 4778 (1909).

[21] I was identified as an active allergen through a series of patch tests made on the various compounds of Scheme I at the University of Oregon infirmary. The procedure is discussed by F. A. Patty, *Industrial Hygiene and Toxicology*, Interscience Publishers, Inc., New York, 1948, pp. 360–365.

[22] M. Erne and F. Ramirez, *Helv. Chim. Acta*, **33**, 912 (1950).

[23] Though this method of destroying unreacted lithium aluminum hydride was reported by Erne and Ramirez and gave no serious consequences in our hands, nonetheless we were unable to modify the manner of addition in such a way as to prevent violent reaction on contact of the acid with the hydride. It is *strongly recommended* that in future work a milder agent (perhaps ethyl acetate) be used to destroy at least a large part of the hydride before any acid is added.

[24] Analysis by R. Mann using the Mohr method.

N-(4-Methoxyphenylethyl)-3-methoxybenzamide (III). To a cooled, stirred mixture of 10 g. (0.25 mole) of sodium hydroxide, 250 ml. of water, and 18.8 g. (0.1 mole) of II was added dropwise (over a period of 1 hr.) 17.1 g. (0.1 mole) of freshly distilled *m*-methoxybenzoyl chloride. The reaction mixture was stirred overnight and filtered with suction. The white curdy precipitate was washed with water, aspirated for several hr., and dried in air, yield 22.7 g. (80%), m.p. 94–95°. For use in cyclization the product was dried further at room temperature *in vacuo* overnight in the presence of phosphorus pentoxide. A small sample, recrystallized four times from 60% ethanol, was obtained as platelets, m.p. 94.5–95°.

Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 72.17; H, 6.50; N, 4.61.

1-(3-Methoxyphenyl)-7-methoxy-3,4-dihydroisoquinoline (IV). (*a*) *Cyclization with phosphorus oxychloride in xylene.* A solution of 4.35 g. of preceding amide in 35 ml. of anhydrous reagent xylene (mixed isomers, Matheson Co.) was treated with 12 ml. of freshly distilled phosphorus oxychloride, refluxed for 5 hr., cooled in ice, and cautiously treated over a period of 2 hr. with *ca.* 350 g. of chipped ice. The aqueous phase was separated, washed with benzene (discarded), basified with 20% aqueous sodium hydroxide, and extracted twice with benzene. Evaporation of the combined, dried (magnesium sulfate) benzene extracts by means of an air blast left a pale yellow liquid; best crude yield 1.77 g. (43%), av. crude yield 31%. Two distillations of the combined crude products from several runs gave a yellow liquid, b.p. 172–173° (0.6 mm.).

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.08; H, 6.60; N, 5.70.

Treatment of 1.62 g. of the crude liquid with 10 ml. of methyl iodide[25a] gave 1.45 g. (25% from the amide) of *methiodide*, m.p. 228–235° (dec.). Five recrystallizations from absolute ethanol gave bright yellow needles, m.p. 226–230° (dec.).

Anal. Calcd. for $C_{18}H_{20}INO_2$: C, 52.81; H, 4.93; N, 3.42. Found: C, 53.03; H, 5.16; N, 3.70.

(*b*) *Cyclization by other methods.* Dropwise addition (over a period of 8 hr.) of a solution of 4 g. of amide in 750 ml. of anhydrous xylene to a refluxing solution of 25 ml. of phosphorus oxychloride in 500 ml. of xylene gave 0.83 g. (14%) of methiodide. Refluxing for 3.5 hr. a mixture of amide, reagent grade phosphorus pentoxide, phosphorus oxychloride, and xylene as per the general procedure of Whaley and Hartung[6] gave an 11% yield of methiodide. Attempts to use phosphorus oxychloride in toluene,[26] phosphorus oxychloride plus phosphorus pentachloride in benzene, or phosphorus oxychloride plus polyphosphoric acid[27] gave only minute quantities of liquid product.

2-(3-Methoxybenzoyl)-4-methoxybenzoic acid (V). A mixture of the crude dihydroisoquinoline resulting from cyclization of 28.1 g. of amide III by procedure (a), 570 ml. of 20% aqueous sodium hydroxide, and 41.5 ml. of dimethyl sulfate was stirred and heated on a steam bath for 24 hr. The ethereal extracts of the cooled mixture were combined and washed first with 4% hydrochloric acid and then with water, dried (magnesium sulfate), and evaporated *in vacuo* at room temperature. A solution of the residue [9.2 g., presumably of 2-(3-methoxybenzoyl)-4-methoxystyrene] in 700 ml. of acetone was refluxed for 1.5 hr., during which time 21.0 g. of C.P. potassium permanganate was added in 10 equal portions. Following dissipation of the permanganate color, the acetone was removed by distillation and a slurry of the residue in 360 ml. of water was treated with sulfur dioxide until the brown color of manganese dioxide had disappeared. The yellow-white precipitate remaining was collected by filtration and dissolved (by warming for 15 min.) in 120 ml. of 2% aqueous sodium hydroxide. Acidification with dilute hydrochloric acid of the filtered alkaline solution gave 6.7 g. (24% from the amide) of nearly white solid, m.p. 168–170°. A sample for analysis was obtained as small prisms, m.p. 172–173°, after three recrystallizations (one with Norit) from ethanol.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.12; H, 4.93. Found: C, 67.36; H, 5.08.

3,3'-Dimethoxybenzophenone (VI). (*a*) *From decarboxylation of* V. A mixture of 7.45 g. of the preceding ketoacid, 18.6 g. of fine copper powder (J. T. Baker, precipitated), and 140 ml. of synthetic quinoline was heated in a reflux apparatus (bearing an attachment for measurement of evolved carbon dioxide by displacement of dilute hydrochloric acid) to a temperature where evolution of gas was first noted. The temperature was maintained constant for 30 min. (94% completion as adjudged by gas evolution) and then raised to refluxing for 15 min. The filtrate from the cooled reaction mixture was diluted with 700 ml. of ether, washed first with excess 5% hydrochloric acid and then with excess 2% aqueous sodium hydroxide, dried (magnesium sulfate), and evaporated. Distillation of the residue gave 5.6 g. (89%) of pale yellow liquid, b.p. 145–160° (0.4 mm.). Redistillation gave an analytical sample, b.p. 144–145° (0.3 mm.).

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.30; H, 5.87.

The *2,4-dinitrophenylhydrazone*,[25b] recrystallized four times from ethyl acetate, was obtained as bright orange microcrystals, m.p. 191–192°, $\lambda_{max}^{CHCl_3}$ 385–387 mμ (log ϵ 4.48); reported[9] red-orange crystals, m.p. 191–192°.

Anal. Calcd. for $C_{21}H_{18}N_4O_6$: C, 59.71; H, 4.30; N, 13.27. Found: C, 59.46; H, 4.28; N, 13.61.

(*b*) *From methylation of* IX. A mixture of 3.43 g. of 3,3'-dihydroxybenzophenone (*vide supra*), 1.7 g. of sodium hydroxide, 30 ml. of water, and 8.0 g. of dimethyl sulfate was heated on a steam bath for 1 hr. The ethereal extract of the cooled mixture was washed with 5% aqueous sodium hydroxide, dried (magnesium sulfate), and evaporated. Distillation of the residue therefrom gave 1.94 g. (50%) of yellow liquid, b.p. 157–159° (0.5 mm.); reported[10] b.p. 230–235° (20 mm.).

The *2,4-dinitrophenylhydrazone*[25b] was recrystallized as in part (*a*), m.p. 190.5–191°, mixture melting point with 2,4-dinitrophenylhydrazone (m. p. 191–191.5°) from part (*a*) was 190.8–191.5°.

3,3'-Dimethoxybenzophenone oxime (X). Using the pyridine method of Shriner, Fuson, and Curtin[25c] 1 g. of 3,3'-dimethoxybenzophenone (from methylation) was converted to the oxime, recrystallized as tablets from 50% methanol, yield 0.59 g. (56%), m.p. 82–83°, reported[10] m.p. 86–87°.

Anal. Calcd. for $C_{15}H_{15}NO_3$: N, 5.44. Found: N, 5.15.

3-Methoxy-N-(3-methoxyphenyl)benzamide (XI). (*a*) *By Schotten-Baumann reaction.* A mixture of 4.6 g. (0.027 mole) of *m*-methoxybenzoyl chloride, 3.1 g. (0.025 mole) of *m*-anisidine, and 20 ml. of 10% aqueous sodium hydroxide (0.05 mole) were shaken vigorously in a stoppered flask for 10 min., diluted, and filtered. The collected solid was washed well with water and recrystallized from methanol to give 4.75 g. (75%) of needles, m.p. 91.5–93.5°. Recrystallization of a small sample from the same solvent gave a m.p. 92.5–93.5°.

Anal. Calcd. for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.20; H, 6.23; N, 5.61.

(*b*) *By Beckmann rearrangement.* A mixture of 0.5 g. of oxime X and 15 g. of polyphosphoric acid was stirred and heated on a steam bath for 10 min. and then poured into 75 ml. of water. The ethereal extract thereof was washed with water and evaporated. The residue was recrystallized from 70% methanol, yield 0.3 g. (60%) of needles, m.p. 91.5–

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(25) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1956, (a) p. 228, (b) p. 219, (c) p. 254.

(26) Method of R. D. Haworth, W. H. Perkin, and J. Rankin, *J. Chem. Soc.*, 125, 1686 (1924).

(27) Method of H. R. Snyder and F. X. Werber, *J. Am. Chem. Soc.*, 72, 2962 (1950).

92.5°, mixture melting point with crude compound from (*a*) 91.5–93°.

The infrared spectra (Nujol mulls) of compounds from parts (*a*) and (*b*) were identical.

3,4′-Dimethoxybenzophenone (XII). A mixture of 3.8 g. (0.025 mole) of *m*-methoxybenzoic acid, 2.7 g. (0.025 mole) of anisole, and 25 g. of polyphosphoric acid was stirred and heated at 65° for 2 hr. and then poured into 100 ml. of water. The ethereal extract thereof was washed with water, dried (magnesium sulfate), and evaporated. Distillation of the residue yielded 3.6 g. (60%) of pale yellow liquid, b.p. 158–164° (0.5 mm.), which partially solidified on standing.

The *2,4-dinitrophenylhydrazone*[25b] was obtained as bright orange microcrystals from ethyl acetate, m.p. 205.5–207° (dec.), $\lambda_{max}^{CHCl_3}$ 396 mμ (log ϵ 4.47).[28] The m.p. was raised to 214–215° (dec.) on repeated recrystallization from the same solvent.[29]

m-Iodoanisole. To the cold solution prepared by diazotization of 10.5 g. (0.085 mole) of *m*-anisidine in 6–8% sulfuric acid[30] was added dropwise (over 30 min.) a warm (40°) solution of 17.5 g. (0.105 mole) of potassium iodide in the same solvent. A small amount of sodium bisulfite was added and the mixture was steam distilled. The product was collected as a slightly pink liquid, b.p. 76–78° (0.5 mm.), yield 9.1 g. (46%).

Dimethoxybenzophenones via the organocadmium process. (*a*) *From m-iodoanisole.* Following the general procedure of Dauben and Tilles[31] the cold (ice bath) Grignard reagent from 17.3 g. (0.074 mole) of *m*-iodoanisole, 1.8 g. (0.075 g.-atom) of magnesium, 38 ml. of anhydrous ether, and 13 ml. of anhydrous benzene was treated with 7.33 g. (0.04 mole) of anhydrous cadmium chloride and then refluxed for 2.3 hr. until a negative Gilman test[32] was obtained. The ether was replaced by benzene, a solution of 10.2 g. (0.06 mole) of freshly distilled *m*-methoxybenzoyl chloride in 15 ml. of benzene was added, and the mixture was refluxed overnight and processed essentially according to published directions;[33] yield 2.4 g. (17%) of yellow liquid, b.p. 140–170° (0.3 mm.).

From treatment of the preceding distillate with 2,4-dinitrophenylhydrazine reagent[25b] and four recrystallizations of the resultant precipitate from ethyl acetate there were obtained bright red-orange microcrystals of *3,4′-dimethoxybenzophenone 2,4-dinitrophenylhydrazone*, (A) m.p. 211–212° (dec.); $\lambda_{max}^{CHCl_3}$ 396 mμ (log ϵ 4.45).

Anal. Calcd. for $C_{21}H_{18}N_4O_6$: C, 59.71; H, 4.30; N, 13.27. Found: C, 59.81; H, 4.34; N, 13.29.

A mixture m.p. of A with a sample of the DNP of XII (m.p. 210–211.6°) was 210–211.8°.

(*b*) *From m-bromoanisole.* In fashion similar to that of part (*a*) the Grignard reagent from 1.65 g. (0.069 g.-atom) of magnesium, 10.7 g. (0.057 mole) of *m*-bromoanisole,[34] 35 ml. of anhydrous benzene, and 35 ml. of anhydrous ether was treated at room temperature with 7.5 g. (0.041 mole) of anhydrous cadmium chloride and allowed to stand overnight, whereupon a Gilman test on the mixture was negative. After replacement of the ether by benzene and addition of 9.9 g. (0.058 mole) of *m*-methoxybenzoyl chloride, the mixture was stirred and refluxed for 2 hr. and then poured into 200 ml. of 10% aqueous ammonium chloride. The combined organic layer and benzene extracts of the aqueous phase were washed first with 10% aqueous sodium bicarbonate and then with water, dried (magnesium sulfate), and evaporated. Fractional distillation of the residue gave 6.0 g. of unreacted acid chloride and 2.7 g. (20%) of yellow liquid, b.p. 162–172° (1.2 mm.).

Anal. Calcd. for $C_{15}H_{14}O_3$: CH_3O, 25.6. Found:[35] CH_3O, 25.4.

Repetition of the procedure except with use of twice the amount of cadmium chloride gave a yield of 24%.

The infrared spectrum of the preceding distillate appeared to be a composite of those of VI and XII. Comparison of the first of these with spectra of synthetic mixtures of VI and XII containing 50%, 65%, and 75% (respectively) of XII showed virtual identity thereof only with the spectrum from 65% XII-35% VI.

From treatment of the distillate with 2,4-dinitrophenylhydrazine reagent[25b] and three recrystallizations of the resultant precipitate from ethyl acetate there were obtained brown-orange microcrystals of *3,4′-dimethoxybenzophenone 2,4-dinitrophenylhydrazone*, m.p. 205–207° (dec.),[29] identical with XII·2,4-dinitrophenylhydrazone (m.p. 205.5–207°) as based on mixture melting point, ultraviolet spectrum, and infrared spectrum.

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[28] Spectrum obtained by means of a Beckmann DK-2 instrument.

[29] The maximum value of the melting point for samples dried by an infrared lamp was 207°; while that for samples simply dried in air was 212° or 215°.

[30] *Cf.* diazotization procedure for *o*-anisidine by J. Cason and H. Rapoport, *Laboratory Text in Organic Chemistry*, Prentice-Hall, Inc., New York, N. Y., 1950, pp. 182–183.

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