150° cyclopentenone and water began to distill at a head temperature of 40–45°. The temperature of the oil bath was raised as necessary up to 200° to maintain a slow distillation. After about 2 hr. only a small residue remained in the distilling flask, (*e.g.* 6 g. after one run). The yellow product was redistilled through a Vigreux column to give 23 ml. of aqueous forerun and 46.4 g. of pure cyclopentenone, b.p. 150–151°.[2] The forerun was continuously extracted with methylene chloride for 24 hr., the methylene chloride was stripped, and the remaining liquid was distilled to yield another 5.0 g. of cyclopentenone, a total of 51.4 g. of product. The yield of cyclopentenone, 61%, is representative of the yields from runs starting with 10 to 250 g. of diol mixture.

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7,2′,4′-Trimethoxyflavone

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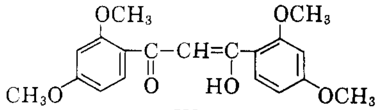
The synthesis of 2,2′-dihydroxy-4,4′-dimethoxydibenzoylmethane (V) was investigated to obtain the spectral characteristics of the compound. An attempt to prepare a similar compound, 2,2′-dihydroxy-5,5′-dimethyldibenzoylmethane, was reported recently by Thomas, Shamma, and Fernelius.[1] These workers, depending on a double Fries rearrangement of di-*p*-tolyl malonate, obtained instead 4-hydroxy-6-methylcoumarin.

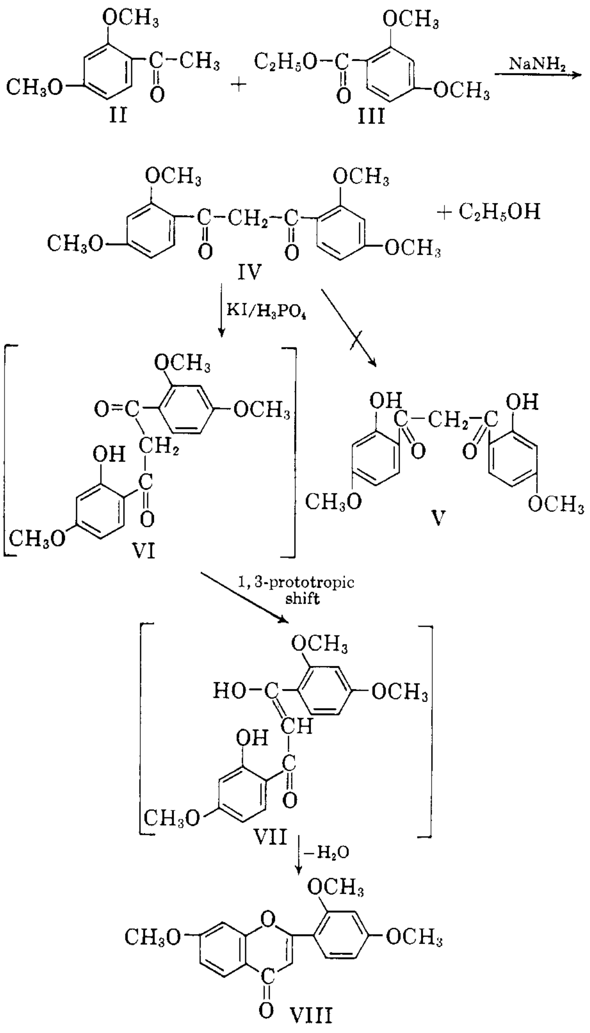
We attempted the synthesis of V by the reaction sequence indicated in the flow chart (II + III → IV → V). The Claisen condensation between 2,4-dimethoxyacetophenone (II) and ethyl 2,4-dimethoxybenzoate (III) was effected by means of sodamide. The structure of the resulting 2,2′,4,4′-tetramethoxydibenzoylmethane (IV) was established by elementary analyses (C and H), the method of synthesis involving reaction between selected functional groups, and its conversion to 7,2′,4′-trimethoxyflavone (VIII). The infrared spectrum of IV shows two strong bands at 1655 cm.$^{-1}$ (6.04 μ) and 1610 cm.$^{-1}$ (6.24 μ), respectively, indicative of a carbonyl double bond conjugated with an olefinic double bond.[2]

A conjugated system of this type can be accounted for by the tautomeric enol, IVa.



IVa

Flow Chart



Attempts to demethylate IV to V by means of aluminum chloride or 48% hydrobromic acid failed. A cleavage reaction with hydriodic acid, prepared *in situ* from orthophosphoric acid and potassium iodide, may be considered as being partially successful, since in yielding the flavone, VIII, it may well have formed the transitory 2-hydroxy-2′,4,4′-trimethoxydibenzoylmethane (VI). A 1,3-prototropic shift of a methylene hydrogen, followed by cyclodehydration, completes a plausible mechanism to VIII. It is also possible for IV to enolize first to IVa, as supported by the infrared spectrum; then to cyclize to VIII by the elimination of the elements of methanol.

The cyclization reaction of *o*-hydroxydibenzoylmethanes to flavones by means of concentrated sulfuric acid is a general method of synthesis.[3] It is of further interest to note that the cyclization of 2,4,6-trimethoxydibenzoylmethane to chrysin (*i.e.*, 5,7-

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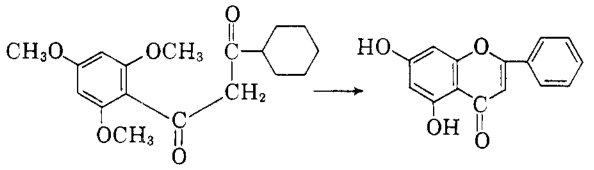
[1] F. D. Thomas II, M. Shamma, and W. C. Fernelius, *J. Am. Chem. Soc.*, **80**, 5864 (1958).

[2] 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, pp. 171–7.

[3] L. F. Fieser and M. Fieser, "*Organic Chemistry*," 3rd ed., Reinhold Publishing Corp., New York, 1956, pp. 820–2.

dihydroxyflavone) by means of aqueous HI also effects complete demethylation:[3,4]



On the other hand, our cyclization technique with potassium iodide in orthophosphoric acid constitutes an application of new materials to an old synthetic route, with the indicated bonus of maintaining the excess alkoxy groups intact. The structure of VIII was confirmed by elementary analyses, oximation to a mono-oxime, and the infrared spectrum for the carbonyl group.

EXPERIMENTAL

2,4-Dimethoxyacetophenone (II). This starting material was prepared by an adaptation of Gardner's technique[5] for the *C*-acetylation of aromatic compounds. A mixture of 41.4 g. (0.3 mole) of *m*-dimethoxybenzene (Eastman), 21.6 g. (0.36 mole) of glacial acetic acid, and 400 g. of polyphosphoric acid became homogeneous after the initiation of agitation, turning yellow, then red. The reaction mass was kept at 50–53° for 3 hr., then drowned in 1200 ml. of ice water. From the ether extract, after drying over anhydrous sodium sulfate, there was obtained 46.5 g. (86.1%) of 2,4-dimethoxyacetophenone: b.p., 134–137°/3 mm. m.p. 40–43°. A melting point given in the literature[6] is 44°.

2,4-Dimethoxybenzoic acid. This intermediate to the ethyl ester (III) was prepared by a modification of the procedure of Robinson and Venkataraman,[7] entailing treatment of β-resorcylic acid with 6 portions of dimethyl sulfate and concentrated aqueous alkali. Thus, from 154 g. (1.0 mole) of β-resorcyclic acid (Koppers), 1675 g. (13.3 moles) of dimethyl sulfate, and 612 g. (15.3 moles) of sodium hydroxide in 1.3 l. of water, there was obtained 146 g. (80%) of 2,4-dimethoxybenzoic acid, melting at 99–104° (lit. value, 108°).[7]

Anal. Calcd. for $C_9H_{10}O_4$: neut. equiv., 182.0. Found: neut. equiv., 180.0.

Ethyl 2,4-dimethoxybenzoate (III). A mixture of 126 g. (0.69 mole) of 2,4-dimethoxybenzoic acid, 127 g. (2.76 moles) of ethanol, 277 ml. of benzene, and 3 ml. of 100% sulfuric acid was reacted according to a modified procedure of Perkins and Schiess[8] to yield 89 g. (66%) of ethyl 2,4-dimethoxybenzoate, distilling at 143–147°/3.5 mm.

Anal. Calcd. for $C_{11}H_{14}O_4$: sapon. equiv., 210.0. Found: sapon. equiv., 205.0.

2,2',4,4'-Tetramethoxydibenzoylmethane (IV). A 0.5-mole batch of sodamide was freshly prepared in a reactor, consisting of a 250 ml., 3-necked, ground-glass flask, immersed in a Dry Ice bath and equipped with a Dry Ice condenser, dropping funnel, and thermometer. The excess ammonia was removed by distillation and replaced simultaneously with anhydrous ethyl ether. To the ethereal suspension of sodamide was added 45 g. (0.25 mole) of 2,4-dimethoxyacetophenone in 42 ml. of ether during a 10-min. period. Five min. later, a solution of 52.5 g. (0.25 mole) of ethyl 2,4-dimethoxybenzoate was added in the same manner. After refluxing overnight, the mass was drowned in ice water containing hydrochloric acid; the excess ether distilled off; and a red-yellow solid filtered off. Recrystallization of the latter gave 32 g. (37.2%) of a yellow, crystalline material melting at 131–134°; $\lambda_{max}^{CCl_4}$ 1655 cm.$^{-1}$ (6.04μ) and 1605 cm.$^{-1}$ (6.24μ).

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.2; H, 5.81. Found: C, 65.10, 65.32; H, 5.64, 5.79.

7,2',4'-Trimethoxyflavone (VIII). A small flask, fitted with an agitator, a reflux condenser, and a dropping funnel was charged with 1.2 g. of phosphorus pentoxide and 5.1 g. (0.045 mole) of 85% phosphoric acid. After the 100% phosphoric acid was cooled to room temperature, 5.0 g. (0.03 mole) of finely ground potassium iodide and 1.7 g. (0.005 mole) of 2,2',4,4'-tetramethoxydibenzoylmethane were added in sequence. The reaction mixture was agitated at 105–110° for 0.5 hr., drowned in ice water, and the precipitate filtered off. The latter, after recrystallization from aqueous ethanol, gave 1.4 g. (75%) of the white, crystalline flavone, melting at 143.5–145.5°; $\lambda_{max}^{CCl_4}$ 1635 cm.$^{-1}$ (6.11μ); $\lambda_{max}^{CH_3OH}$ 236 mμ (ε, 2200); $\lambda_{max}^{CH_3OH}$ 334 mμ (ε, 2450).

Anal. Calcd. for $C_{18}H_{16}O_5$: C, 69.23; H, 5.13. Found: C, 69.01, 69.18; H, 5.24, 5.19.

7,2',4'-Trimethoxyflavone oxime. The oxime was prepared by heating a mixture of 2 g. of the flavone and 3 g. of hydroxylamine hydrochloride and 3 ml. of pyridine on a steam bath for 4 hr. The reaction mixture was cooled and drowned in dilute acetic acid. The filtered product, after two recrystallizations from ethanol, yielded 1.7 g. (86%) of a white, crystalline material, melting at 204–207°.

Anal. Calcd. for $C_{18}H_{17}NO_5$: N, 4.28. Found: N, 4.14.

Attempted preparation of 2,2'-dihydroxy-4,4'-dimethoxydibenzoylmethane. The selective demethylation of the methoxy group ortho to the carbonyl in 2,4-dimethoxybenzophenone is known[9] and served as the basis for the attempted demethylations of IV to V. Reactions with aluminum chloride and 48% hydrobromic acid failed, yielding intractable gums or tars from which no crystalline material could be obtained.

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[4] T. Emilewicz, St. v. Kostanecki, and J. Tambor, *Ber.*, **32**, 2449 (1899).

[5] P. D. Gardner, *J. Am. Chem. Soc.*, **77**, 4674 (1955).

[6] F. Mauthner, *J. prakt. Chem.*, 119, 311 (1928).

[7] R. Robinson and K. Venkataraman, *J. Chem. Soc.*, 61 (1929).

[8] W. H. Perkins and E. Schiess, *J. Chem. Soc.*, 159 (1904).

[9] H. Kauffmann and P. Panwitz, *Ber.*, **43**, 1205 (1910).

Preparation of 2,6-Dialkoxy-3-(1-alkoxyalkyl)tetrahydropyrans

Kent C. Brannock

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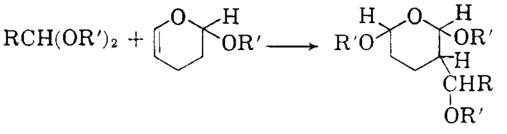
The acid-catalyzed addition of acetals to dihydropyran to give 2-alkoxy-3-(1-alkoxyalkyl)tetrahydropyrans is well known.[1] The purpose of this note is to report the extension of this reaction to include the addition of acetals to 2-alkoxy-3,4-dihydro-2*H*-



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[1] R. Paul and S. Tchelitcheff, *Bull. soc. chim. France*, 1155 (1950).