warmed until a solution was obtained. The solution was stirred at 35° for 25 hr. During this time the product separated as an oily upper layer. The mixture was extracted with ether, the extract was dried over magnesium sulfate and the ether was removed. The oily base was dissolved in acetone and the solution was treated with hydrogen chloride. The solution was concentrated and cooled; the precipitated hydrochloride weighed 16.9 g.; m.p. 177–178° (dec.). After the filtrate had been concentrated and cooled, a further amount (2.5 g.) of product was obtained; total yield 66%; m.p. 176–177° (dec.).

Anal. Calcd. for $C_{15}H_{24}ONCl$: C, 53.98; H, 7.25; Cl, 10.62. Found: C, 53.86; H, 7.31; Cl, 10.51.

A solution of 3.2 g. (0.01 mole) of the oily base and 3 ml. (0.05 mole) of methyl bromide in 35 ml. of absolute ethanol was heated at 65° for 36 hr. in a pressure bottle. Ether was added; the precipitated methobromide weighed 3.0 g. (77%); m.p. 197–198° (dec.) after two recrystallizations from ethanol-ether.

Anal. Calcd. for $C_{16}H_{26}ONBr$: C, 48.99; H, 6.68; Br,

3-Methyl-3-azabicyclo[3.3.1]nonan-9-one-1,5-dicarboxylic acid hydrochloride dihydrate. A solution of 1.0 g. of dimethyl 3-methyl-3-azabicyclo[3.3.1]nonan-9-one-1,5-dicarboxylate hydrochloride in 5 ml. of 25% hydrochloric acid was refluxed for 1 hr. The solid which separated during this time weighed 0.6 g. (67%); m.p. 190–192° (dec.). After two recrystallizations from methanol, the product melted at 190–191° (dec.).

Anal. Calcd. for $C_{11}H_{16}O_5NCl.2H_2O$: C, 42.10; H, 6.43. Found: C, 42.04; H, 6.60.

In order to obtain the base, a solution of 1.5 g. of the hydrochloride dihydrate in 15 ml. of water which contained 10 drops of methanol was neutralized with 0.25 g. of sodium carbonate. The solution was cooled; the precipitate weighed 0.9 g. (72%); m.p. 136–137° (dec.). A sample, recrystallized from water, melted at 137° (dec.).

Anal. Calcd. for $C_{11}H_{15}O_5NCH_2O$: C, 50.95; H, 6.61; N, 5.40. Found: C, 50.73; H, 6.43; N, 5.22.

1,5-Bis(dimethylaminomethyl)-3-methyl-3-azabicyclo[3.3.1]-nonan-9-one trihydrochloride (I). To a stirred solution of 2.1 g. (0.031 mol.) of methylamine hydrochloride, 5.0 g. (0.062 mol.) of 37% formalin and 10 ml. of water there was added, dropwise, a solution of 2,6(bis.dimethylaminomethyl)-cyclohexanone dihydrochloride[2] in 15 ml. of water during a period of 15 min. The mixture was stirred for an additional 15 min., made alkaline with sodium hydroxide solution, and the base was extracted with ether. The solvent was removed from the dried extract and the residue was distilled; b.p. 80–82° (0.07 mm.); yield 2.0 g. (27%). The base, dissolved in ether, was treated with hydrogen chloride. The precipitated hygroscopic trihydrochloride, after recrystallization from methanol-ether, melted at 221–222° (dec.).

Anal. Calcd. for $C_{12}H_{32}ON_3Cl_3$: C, 47.81; H, 8.56; N, 11.16; Cl, 28.23. Found: C, 47.65; H, 8.30; N, 10.78; Cl, 27.90.

2,4-Bis(dimethylaminomethyl)-8-methyl-8-azabicyclo[3.2.1]-octan-3-one trihydrochloride (II). A mixture of 3.0 g. (0.013 mole) of tropinone hydrobromide,[4] 2.2 g. (0.027 mole) of dimethylamine hydrochloride, 0.82 g. (0.027 mole) of paraformaldehyde and 15 ml. of acetic acid was heated at 60–75° for 2 hr. The solvent was removed under reduced pressure, the oily residue was dissolved in water, and the solution was made alkaline with sodium hydroxide. After extraction with ether, the dried extract was treated with hydrogen chloride. The precipitate crystallized when it was heated with isopropyl alcohol; crude yield 1.4 g. (28%); m.p. 196–197° (dec.) after recrystallization from methanol ether.

Anal. Calcd. for $C_{14}H_{30}ON_3Cl_3$: C, 45.59; H, 8.20; N, 11.40, Cl, 28.84. Found: C, 45.95, H, 8.09; N, 11.25; Cl, 28.98.

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(4) Purchased from Winthrop Laboratories, New York, N. Y.

A Simple Large Scale Synthesis of Cyclopentenone

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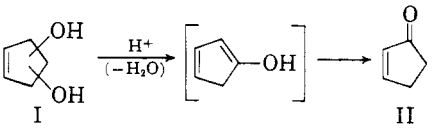
Although unsubstituted, cyclic, α-β-unsaturated ketones are among the most attractive starting materials for a variety of syntheses, they are not generally available in large quantities because of difficulties in their preparation. Cyclopentenone (II) is especially poor in this respect, the current methods of preparation involve allylic oxidation,[1] halogenation and dehydrohalogenation,[2] or pyrolysis of its cyclopentadiene adduct.[3] All of these methods are tedious and unsatisfactory for large scale synthesis.



I II

We wish to report a one step preparation of cyclopentenone by the distillation of the commercially available 3,4- and 3,5-cyclopentenediols[4,5] from a trace of *p*-toluenesulfonic acid. The distillate, a mixture of cyclopentenone and water, gives, after drying and redistillation, yields on the order of 60% and the product is free from impurities. This sequence makes cyclopentenone the most readily available of all cyclic enones and will make it an attractive starting material for further investigation of five-membered ring chemistry.

EXPERIMENTAL

In a vacuum distilling apparatus equipped with a short-path distilling head was placed 100 g. (1.0 mole) of the cyclopentenediol mixture and 0.2 g. of *p*-toluenesulfonic acid. The pressure was reduced to 10 mm., the receiver was cooled in a Dry Ice–acetone bath, and the diol mixture was heated. When the temperature of the oil bath reached about

(1) W. Triebs, B. Franke, G. Leichsenring, and H. Roder, *Ber.*, **86**, 616 (1953).

(2) E. J. Corey and K. Osugi, *Pharm. Bull. Japan*, **1**, 99 (1953).

(3) M. Rosenblum, *J. Am. Chem. Soc.*, **79**, 3179 (1957).

(4) Columbia Southern Chemical Co., One Gateway Center, Pittsburgh, Pa.

(5) In our experience the commercial material is 60–70% 3,5- and 40–30% 3,4- diol. Either of the pure diols or the mixture is converted to cyclopentenone under the conditions of the reaction.

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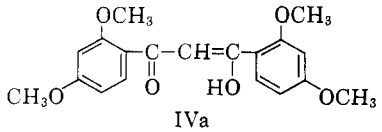
The synthesis of 2,2′-dihydroxy-4,4′-dimethoxydibenzoylmethane (V) was investigated to obtain the spectral characteristics of the compound. An attempt to prepare a similar compound, 2,2′-dihydroxy-5,5′-dimethyldibenzoylmethane, was reported recently by Thomas, Shamma, and Fernelius.[1] These workers,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

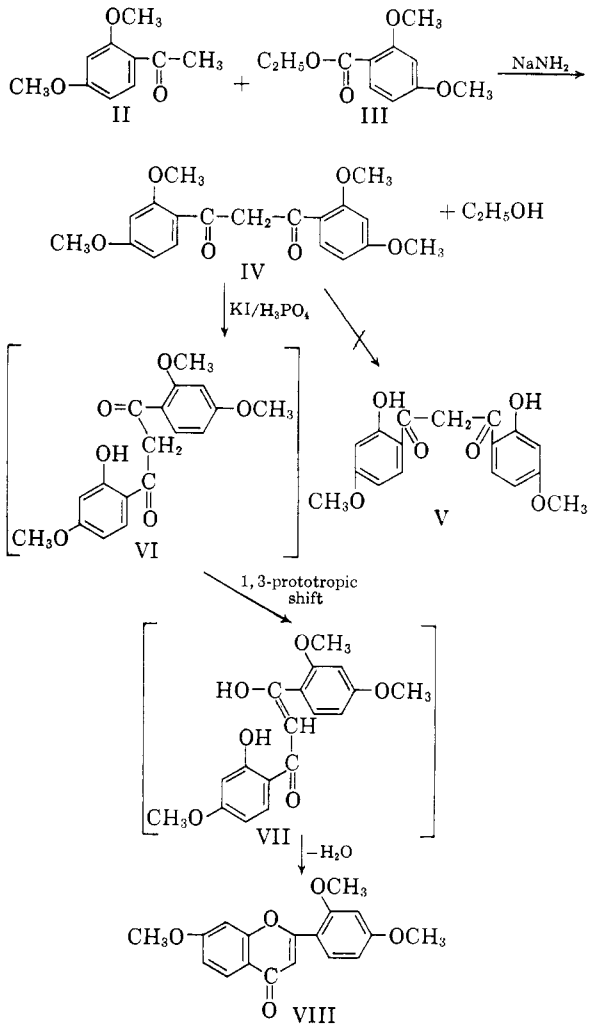
We attempted the synthesis of V by the reaction sequence indicated in the flow chart (II + III → IV → V). The Claisen condensation between 2,4-dimethoxyacetophenone (II) and ethyl 2,4-dimethoxybenzoate (III) was effected by means of sodamide. The structure of the resulting 2,2′,4,4′-tetramethoxydibenzoylmethane (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-

(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.