$[\alpha]^{27}_{D}$ +23° (c, 1.07 in methanol). λ_{max}^{Nujol} 3.20 (m), 3.78 (w), 3.88 (m), 3.95 (m), 5.75 (s), 7.94 (s), and 13.58 (s) μ.

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Phosphorus Acids in Organic Systems. III. Specific Pyrophosphoric Acid Catalysis in the Conversion of Resorcinol Dimethyl Ether to Coumarins[1]

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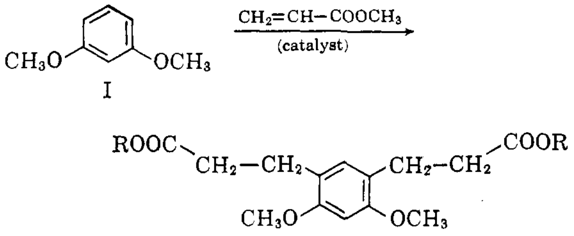
Studies on the composition of polyphosphoric acid[2-6] indicate that the components (H_3PO_4, $H_4P_2O_7$, $H_5P_3O_{10}$, etc.) comprise a spectrum of equilibria which is governed by concentration (% P_2O_5) and, presumably, by temperature. This would perhaps make it seem futile to look for specific catalysis by individual components of these equilibria except for the fact that equilibrium is established rather slowly.[4]

The condensation between pyrogallol trimethyl ether and benzoic acid is catalyzed by polyphosphoric acid and proceeds efficiently to give 2,3,4-trimethoxybenzophenone.[7] This reaction has now been studied semiquantitatively in a series of experiments in which the polyphosphoric acid was varied in composition (% P_2O_5) and the extent of conversion to the product determined after a reaction time of ten minutes. Good kinetic studies of polyphosphoric acid systems are precluded by the viscosity of the reagent but the data obtained are meaningful on a relative basis; these are shown graphically in Fig. 1. The change in slope at high phosphorus pentoxide concentrations is undoubtedly due to the increased viscosity of the solution where the already serious diffusion problem approaches the point of control. The most significant feature is the displacement of the pyrophosphoric acid point from the curve. It demonstrates that equilibration of pyrophosphoric acid among the various equilibrium components existent at that phosphorus pentoxide concentration[4] of polyphosphoric acid does not occur to an appreciable extent during ten minutes at 65° and, perhaps more significantly, that pyrophosphoric acid is almost certainly noncatalytic in this process.[8]



I

IIa. R = CH_3
IIb. R = H

It has been observed, on the other hand, that the reaction between resorcinol dimethyl ether (I) and methyl acrylate proceeds in good yield (77%) to give a bispropionate (IIa) when catalyzed by pyrophosphoric acid but in poor yield (34%) when catalysis is by polyphosphoric acid of about the same phosphorus pentoxide content. Identification of the product in each case was through the diacid (IIb).[11]

The most conspicuous catalyst specificity yet observed is that in the reaction of resorcinol dimethyl ether (I) with β-keto esters. It was found that I reacts with ethyl acetoacetate in the presence of pyrophosphoric acid to give 7-methoxy-4-methylcoumarin (III) and methyl *trans*-β-methyl-2,4-dimethoxycinnamate (IVa). Similarly with 2-carbethoxycyclohexanone, I in the presence of pyro-

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[1] Part II, P. D. Gardner, *J. Org. Chem.*, **77**, 4675 (1955).

[2] Victor Chemical Co.

[3] R. N. Bell, *Ind. Eng. Chem.*, **39**, 136 (1947); **40**, 1464 (1948).

[4] A. Huhti and P. A. Gartaganis, *Can. J. Chem.*, **34**, 785 (1956).

[5] V. E. Thilo and R. Sauer, *J. prakt. Chem.*, [4] **4**, 324 (1957).

[6] General applications of polyphosphoric acid in condensation reactions and rearrangements have been reviewed; F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 321 (1958).

[7] P. D. Gardner, *J. Am. Chem. Soc.*, **76**, 4550 (1954).

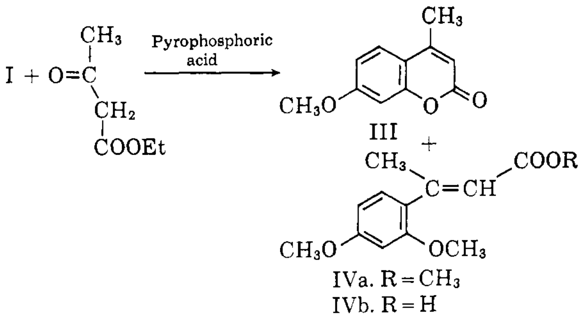
[8] Another illustration of difference is found in the rearrangement of the oxime of fluorenone. Horning, Stromberg, and Lloyd[9] observed that the reaction proceeds readily at 180° in polyphosphoric acid whereas Anet, Bavin, and Dewar[10] report the oxime to be stable at 190° in a 2:1 mixture of sirupy phosphoric acid and phosphorus pentoxide. This mixture contains 74.4% phosphorus pentoxide and corresponds approximately to a reported[4] polyphosphoric acid mixture of 68% orthophosphoric acid, 29% pyrophosphoric acid, and 3% tripolyphosphoric acid. It seems probable that equilibration to this composition occurred at 190° and therefore that orthophosphoric acid and pyrophosphoric acid are noncatalytic in the Beckmann rearrangement.

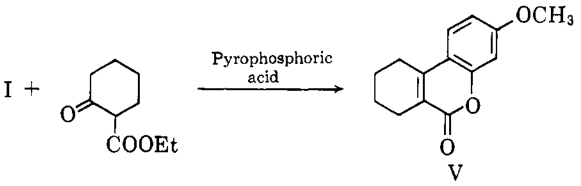
[9] E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Am. Chem. Soc.*, **74**, 5153 (1952).

[10] F. A. L. Anet, P. M. G. Bavin, and M. J. S. Dewar, *Can. J. Chem.*, **35**, 180 (1957).

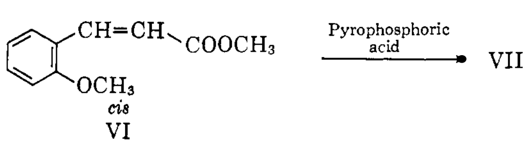
[11] The "addition" of aromatics to unsaturated esters has been reported with other Lewis acids. For examples, see "Anhydrous Aluminum Chloride in Organic Chemistry," C. A. Thomas, Reinhold Publishing Corp., New York, N. Y., 1941, pp. 477, 478.

phosphoric acid afforded 3-methoxy-7,8,9,10-tetrahydrodibenzo[*b*,*d*]pyran-6-one (V). These reactions were conducted at temperatures as low as 10° but attempts to effect them with polyphosphoric acid at 10° or 65° were unsuccessful; in each case an unresolvable mixture of liquid products was obtained.[12]





Several mechanisms appear reasonable for the conversion of I to III or V. To exclude some of these, samples of methyl *cis*-2-methoxycinnamate (VI) and methyl *trans*-2-methoxycinnamate were prepared and mixed with pyrophosphoric acid. From the former (30°) was obtained a 79% yield of coumarin (VII) while the latter gave a 95% recovery of starting material. Moreover, an attempted reaction of ethyl β-(2,4-dimethoxyphenyl)-propionate under the same conditions gave an 83% recovery (after distillation) of starting material. The reaction thus appears to be specific for coumarin formation and is not general for lactonization.



Perhaps the most interesting feature of these reactions is the facile cleavage of the methoxyl group associated with the ring closure. One example of coumarin formation from a methoxy acid has been reported (polyphosphoric acid),[13] but other work suggests that this is probably a singular case and unique to the molecule studied.[6,14] Phosphorus acids have also been reported to catalyze coumarin formation from the free phenol (polyphosphoric acid)[15] or aryl acetate (pyrophosphoric acid).[16] Other ether cleavages reported have required the use of aluminum chloride or hydrogen halides[17-19] or have been accelerated by other substituents on the aromatic ring.[17,19,20] The pyrolysis of alkoxycinnamoyl chlorides also gives coumarins.[14]

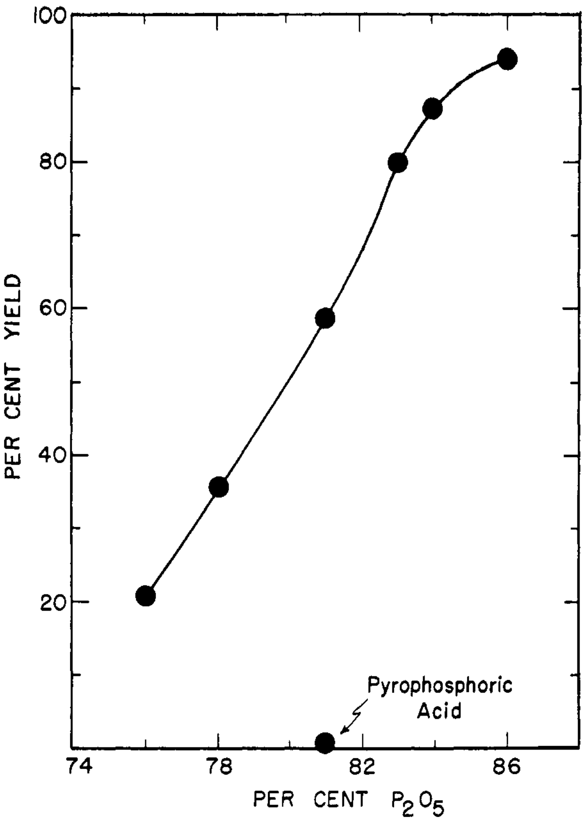


Fig. 1.—Yield data as a function of concentration of polyphosphoric acid (% P_2O_5) for the reaction of pyrogallol trimethyl ether with benzoic acid giving 2,3,4-trimethoxybenzophenone.

Experimental

Benzoylation of Pyrogallol Trimethyl Ether, Comparison of Polyphosphoric Acid Concentrations.—Several compositions of polyphosphoric acid were prepared from the commercial[2] product by the addition of calculated quantities of water or phosphorus pentoxide. To a 500-ml. round-bottom flask equipped with a large, sturdy impeller mounted on a powerful, constant-speed stirring motor was placed 100.0 g. of polyphosphoric acid of known composition. The system was equilibrated while stirring (drying tube) in an oil bath maintained at 64.5 ± 0.1°. To this was added (stirring) an intimately mixed reactant sample comprised of 1.00 g. of benzoic acid and 1.38 g. of pyrogallol trimethyl ether. Dissolution occurred almost instantaneously. After precisely 10 min., 250 ml. of ice and water were added. The mixture was extracted with carbon tetrachloride (4 × 50 ml.) and the combined extracts were washed with water. This solution was then diluted with 95% ethanol to a volume which placed the concentration of product (2,3,4-trimethoxy-

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[12] Pyrophosphoric acid is 81% phosphorus pentoxide and polyphosphoric acid samples used were 83% phosphorus pentoxide.

[13] H. Pan and T. L. Fletcher, *J. Org. Chem.*, **25**, 1106 (1960).

[14] F. D. Popp and W. Blount, *ibid.*, **26**, 2108 (1961).

[15] J. Koo, *Chem. Ind.* (London), 445 (1955).

[16] P. M. Bhargara and S. H. Zaheer, *J. Chem. Soc.*, 311 (1952).

[17] P. Hill and W. F. Short, *ibid.*, 1123 (1935).

[18] J. F. Garden, N. F. Hayes, and R. H. Thomson, *ibid.*, 3315 (1956).

[19] W. A. Hutchins and T. S. Wheeler, *Current Sci.*, **6**, 604 (1938); *Chem. Abstr.*, **32**, 8387 (1938).

[20] P. D. Gardner, W. J. Horton, and R. E. Pincock, *J. Am. Chem. Soc.*, **78**, 2541 (1956).

benzophenone)[7] in a range suitable for spectrophotometric analysis. Using a blank comparable with the solution solvent, the optical density at 290 mμ was measured and from this was calculated the concentration of product. Results are shown in Fig. 1.

Reaction of Resorcinol Dimethyl Ether with Methyl Acrylate.—A mixture of 15.0 g. of resorcinol dimethyl ether (I) and 150 g. of pyrophosphoric acid was placed in a flask equipped with a stirrer and drying tube and heated to 65°. While stirring, there was added during 1 hr. 18.8 g. of methyl acrylate. Ice and water (400 ml.) were added and the mixture was extracted with several portions of ether. The combined extract was washed twice with water and dried (sodium sulfate). Evaporation of solvent left 28.1 g. of liquid product (IIa) which was hydrolyzed by refluxing for 6 hr. in 200 ml. of 2 *M* potassium hydroxide in methanol. Water was added and the resulting mixture washed several times with ether. Acidification of the aqueous phase followed by ether extraction and processing as described above gave a crystalline residue. Recrystallization from ethyl acetate–petroleum ether gave 24.0 g. (77%) of 1,3-dimethoxy-4,6-bis(2-carboxyethyl)benzene (IIb), m.p. 120–121°.

Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.60; H, 6.38; neut. equiv., 286. Found: C, 59.90; H, 6.38; neut. equiv., 284.

A reaction identical with the preceding except for the substitution of commercial polyphosphoric acid for pyrophosphoric acid gave 10.5 g. (34%) of the diacid (IIb).

Condensation of Resorcinol Dimethyl Ether with Ethyl Acetoacetate.—A mixture was prepared comprised of 15.0 g. of resorcinol dimethyl ether (I) and 150 g. of pyrophosphoric acid. To this was added during 30 min., with stirring, (20°) 15.5 g. of ethyl acetoacetate. After 1 hr., 300 ml. of ice and water were added and the resulting mixture was extracted with three portions of ether. The combined extracts were dried and distilled through a short-path system. There was obtained 10.1 g. of liquid, b.p. 130–144° (0.3 mm.), and 4.0 g., b.p. 145–240° (0.3 mm.). Crystallization of the former from ethyl acetate–petroleum ether gave 7.2 g. (35%) of 7-methoxy-4-methylcoumarin (III), m.p. 155–156°. A sublimed sample had m.p. 157–158° (lit.,[21] m.p. 159°).

The smaller fraction was heated under reflux for 12 hr. in 50 ml. of 3 *M* methanolic potassium hydroxide. Processing in the usual way gave 1.5 g. (6%) of β-methyl-2,4-dimethoxycinnamic acid (IVb), m.p. 148–149° (lit.,[22] m.p. 145°).

An attempt to effect this condensation with commercial polyphosphoric acid failed; neither of the products described could be isolated from the mixture.

Condensation of Resorcinol Dimethyl Ether with 2-Carbethoxycyclohexanone.—A well stirred mixture of 15.0 g. of resorcinol dimethyl ether (I) and 150 g. of pyrophosphoric acid was heated to 65° and during 15 min. 20.5 g. of 2-carbethoxycyclohexanone was added. After an additional 5 min. the mixture was poured into 400 ml. of ice and water (stirring) and the product was extracted with several portions of ether. The combined extracts were washed twice with water and dried. The residue remaining from evaporation of solvent crystallized. Recrystallization from ethyl acetate–petroleum ether gave 12.8 g. (53%) of 3-methoxy-7,8,9,10-tetrahydrodibenzo[*b,d*]pyran-6-one (V), m.p. 119–120°. A sublimed sample melted sharply at 121°.

Anal. Calcd. for $C_{14}H_{14}O_3$; C, 73.04; H, 6.09. Found: C, 72.91; H, 5.98.

Methyl *cis*-2-Methoxycinnamate (VI).—This substance was prepared by a modification of the method described by Stoermer.[23] A solution of 20.0 g. of *trans*-2-methoxycinnamic acid in 1700 ml. of methanol was irradiated through a Pyrex filter with a 200-w. high-pressure mercury vapor lamp. The process was monitored by the periodic withdrawal of samples and a measurement of the ultraviolet spectrum of each. It was discontinued when no further spectral changes were observed (6 hr.). Methanol was removed at an aspirator and the residual solid fractionally crystallized from ethanol. There was obtained 12.0 g. of crude *cis* acid, m.p. 84–87°, and 6.0 g. of recovered *trans* acid, m.p. 181°. Several recrystallizations of the former gave 10.0 g. (50%) of colorless *cis* acid, m.p. 90° (lit.,[24] m.p. 88–89°).

cis-2-Methoxycinnamic acid (6.0 g.) was converted to the methyl ester by treatment of an ethereal solution with excess diazomethane. After 15 min., the excess was destroyed by the dropwise addition of acetic acid. Ether was removed under reduced pressure and the residue distilled through a short-path system to give 6.0 g. of the ester (VI), b.p. 84–88° (0.1 mm.), n^{23}_{D} 1.5646, $\lambda_{\max}^{\mathrm{EtOH}}$ 273 mμ, ε 14,800 (lit.,[24] b.p. 277°, n^{10}_{D} 1.5718).

Conversion of Methyl *cis*-2-Methoxycinnamate to Coumarin.—The ester (VI) (2.0 g.) was stirred into 15 g. of pyrophosphoric acid. The vessel was cooled during the early stages of reaction so as to maintain room temperature. After 3 hr. (occasional stirring) 25 ml. of water was added and the resulting mixture was extracted with three portions of ether. Evaporation of solvent from the dried solution left 1.20 g. (79%) of pale yellow solid, m.p. 65–70°. Recrystallization from ethanol raised the m.p. to 69–70°, undepressed with a sample mixed with authentic coumarin (VII).

An attempt to cyclize the *trans* ester under essentially identical conditions gave a 95% recovery of starting material. Similarly, ethyl β-(2,4-dimethoxyphenyl)propionate gave starting material.

Acknowledgment.—The authors are indebted to the Robert A. Welch Foundation for the financial support of this work.

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[21] H. von Pechmann and C. Duisberg, *Ber.*, **16**, 2119 (1883).

[22] H. von Pechmann and J. B. Cohen, *ibid.*, **17**, 2129 (1884).

[23] R. Stoermer, *ibid.*, **42**, 4865 (1909); **44**, 637 (1911).

[24] W. H. Perkin, *J. Chem. Soc.*, **31**, 388 (1877).

The Course of the Mannich Reaction with Isopropyl Methyl Ketone. Preparation of Isopropyl Vinyl Ketone

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In connection with another problem, the hitherto unknown isopropyl vinyl ketone was required. A potentially promising precursor of this substance, namely 1-(N,N-dimethylamino)-4-methylpentanone-3 (I), has been reported[1,2] as the product of the Mannich reaction between isopropyl methyl ketone, formaldehyde, and dimethylamine hydrochloride. Evidence for the structure of this product was provided by condensation of the amine with ethyl acetoacetate to afford 3-isopropyl Δ^2-cyclohexenone, but the yield was unspecified.

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[1] R. Jacquier, M. Mousseron, and S. Boyer, *Bull. soc. chim. France*, **23**, 1653 (1956).

[2] R. Jacquier and S. Boyer, *ibid.*, **21**, 442 (1954).