of (II) which changed at 153–154° with sublimation. The sublimate melted at 157°.

The compound reacted immediately with 2,4-dinitrophenylhydrazine reagent to form a yellow solution from which yellow-orange crystals slowly separated.

Anal. Calcd. for $C_{14}H_{12}O_9$: C, 51.85; H, 3.70. Found: C, 51.24; H, 3.97.

1,2-Bis-(2-chloromethyl-5-hydroxy-4-pyrone-6)-ethylene Glycol.—A purified sample of (I), treated with an excess of thionyl chloride, allowed to stand at room temperature until the reaction was complete, and the excess thionyl chloride decomposed with water, produced light tan crystals when recrystallized from alcohol. Sublimation of the compound gave white needles, m.p. 166–167°.

Anal. Calcd. for $C_{14}H_{12}O_8Cl_2$: C, 44.35; H, 3.16. Found: C, 44.00; H, 3.02.

Bis-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-diketone.—Three grams of (I), finely powdered, was added to an anhydrous mixture of 50 ml. of benzene and 50 ml. of acetone containing 6 g. of finely powdered aluminum isopropoxide. The resulting dispersion was vigorously refluxed for 8 hours, after which 50–60 ml. of the solvent mixture was removed under reduced pressure.

Following the addition of 150 ml. of approximately 3 *N* sulfuric acid a thin layer of benzene was formed which was separated and discarded. The aqueous layer was then extracted with ethyl acetate. Evaporation of the ethyl acetate left behind 0.9 g. of yellow crystals which were recrystallized from ethanol, m.p. 154.5°. The compound when tested with 2,4-dinitrophenylhydrazine reagent gradually reacted. A turbidity was definite in five minutes, and in ten minutes orange-red aggregates had separated.

Anal. Calcd. for $C_{14}H_{10}O_{10}$: C, 49.70; H, 2.95. Found: C, 50.02; H, 3.34.

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The Cyanoethylation of Kojic Acid[1]

BY L. L. WOODS

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Cyanoethylation has proved to be one of the reactions in which kojic acid participates, in good yield, with a surprising lack of side reactions, and in an unexpected position.

Experiments with the compound produced from the reaction leave no doubt but that C-alkylation has taken place rather than O-alkylation.

The fact that the product, β-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid, gives a red coloration with ferric chloride and forms a diacetylated derivative proves that neither of the hydroxyl radicals of kojic acid has been attacked during cyanoethylation.

It is, therefore, apparent from the reaction of kojic acid with acrylonitrile that the kojic acid, in this instance, acts more like a ketone than a phenol.[2]

Experimental[3]

A mixture consisting of 20 g. of kojic acid, 100 g. of dioxane, 5 g. of triton-R (trimethylbenzylammonium hydroxide) and 20 g. of acrylonitrile was heated by a glass heating mantle, under reflux (with a gradual increasing temperature) until all the kojic acid had dissolved. The temperature was then regulated so that very gentle refluxing was maintained for 19 hours. The reaction mass was evaporated to about one-half of its original volume over a steam-bath in the hood. The remaining material was treated with 100 ml. of dilute hydrochloric acid and refluxed for 16 hours. After the completion of the hydrolysis the solution was evaporated to dryness over a steam-bath.

Since ethylene chloride, benzene or ethyl acetate failed to act as favorable extractants, the dry crystals were taken up by refluxing with a mixture of absolute alcohol and ethyl acetate (approximately 50:50) treated with Norite, filtered and the solvents removed by evaporation. Reddish-brown crystals weighing 14 g. were obtained.

The analytical sample was obtained by refluxing a small quantity of the red crystals in a mixture consisting of 80 parts of absolute ethyl acetate and 20 parts absolute ethanol. The solution was decolorized with Norite, filtered, and chilled. Yellow crystals were obtained which melted at 155°, and gave a red coloration with dilute ferric chloride solution.

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.46; H, 4.67. Found: C, 50.63; H, 4.43.

The acetate was prepared in the usual manner from acetyl chloride and sublimed to a powder, m.p. 85–87°.

Anal. Calcd. for $C_{13}H_{14}O_8$: C, 52.34; H, 4.69. Found: C, 52.60; H, 4.69.

p-Bromophenacyl bromide formed a derivative with β-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-propionic acid by allowing 1 g. of the acid to react with 0.4 g. of sodium bicarbonate in a mixture of 5 ml. of water and 10 ml. of ethanol. After the effervescence had ceased 1 g. of *p*-bromophenacyl bromide and an additional 20 ml. of ethanol were added. The mixture was refluxed for 1 hour, filtered while hot, and cooled. The resulting crystals were filtered, washed with water, dried, and then recrystallized from absolute ethanol; m.p. 179–180.5°.

Anal. Calcd. for $C_{17}H_{15}O_7Br$: C, 49.63; H, 3.64. Found: C, 49.22; H, 3.39.

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NEW COMPOUNDS

cis- and *trans*-3,4-Bis-(*p*-methoxyphenyl)-cyclopentanone

meso- and *dl*-β,γ-bis-(*p*-methoxyphenyl)-adipic acids[1] were esterified with methanol and sulfuric acid to furnish the esters desired as starting materials. The aluminum–amalgam reduction[2] of methyl *p*-methoxycinnamate produced traces of the *meso*-ester only and was not a satisfactory preparative method.

***cis*-3,4-Bis-(*p*-methoxyphenyl)-cyclopentanone.**—A solution of 4 g. of methyl *meso*-β,γ-bis-(*p*-methoxyphenyl)-adipate, m.p. 142–153.0°, in 80 ml. of dry benzene was stirred at reflux with 1 g. of sodium, previously powdered under hot mineral oil, for 20 hours. Further treatment was carried out as described by Weidlich,[3] and, after the 19-hour hydrolysis in 80 ml. of 6 *N* hydrochloric acid, 2.5 g. (83%) of product was obtained in the form of a brown oil. Purification through Girard reagent "T"[4] afforded no crystalline product, although a semi-solid melting near room temperature was obtained on cooling an alcoholic solution of the oil. The oxime was prepared from 5.9 g. of the purified oil in 83% yield, using 5 g. of hydroxylamine hydrochloride, 25 ml. of pyridine and 25 ml. of ethanol. Purification from methanol gave white needles, m.p. 124.5–125°. *Anal.* Calcd. for $C_{19}H_{21}O_3N$: C, 73.29; H, 6.80. Found: C, 73.31; H, 6.70. Hydrolysis of this oxime gave back the same, uncrystallizable oil. The 2,4-dinitrophenylhydrazone was prepared and recrystallized from ethyl acetate; it crystal-

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(2) (a) H. A. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 79–135; (b) H. A. Bruson and T. W. Reiner, THIS JOURNAL, **64**, 2850 (1942).

(3) All analyses were made by Dr. Carl Tiedcke. All melting points were determined on a Fisher–Johns melting point assembly.

(1) C. L. Wilson and K. B. Wilson, *Trans. Electrochem. Soc.*, **84**, 153 (1943).

(2) G. R. Ramage and R. Robinson, *J. Chem. Soc.*, 607 (1933).

(3) H. A. Weidlich, *Ber.*, **71**, 1601 (1938).

(4) A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

lized as large, dark-orange needles, m.p. 190–191°. *Anal.* Calcd. for $C_{26}H_{24}N_4O_6$: C, 63.02; H, 5.08. Found: C, 63.02; H, 5.01.

***trans*-3,4-Bis-(*p*-methoxyphenyl)-cyclopentanone.**—Methyl *dl*-β,γ-bis-(*p*-methoxyphenyl)-adipate, m.p. 64–65°, 0.5 g. was subjected to ring closure as described above. The product, purified through Girard reagent and recrystallized from ligroin, was obtained in 66% yield; m.p. 110–111°. *Anal.* Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.85; H, 6.58.

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p-Fluorophenacyl Bromide Salts[1]

In order to obtain a variety of quaternary salts of heterocyclic nitrogen compounds all having the same quaternizing group attached to the nitrogen, so that correlations between structure and biological activity might be studied more conveniently, the salts listed in Table I were prepared for comparison with those previously reported.[2] The methods of preparation were in general the same as those described in the previous publications, care being taken to avoid altering any reactive substituent groups present on the rings. The solid heterocyclic bases which were insoluble in chloroform were treated with *p*-fluorophenacyl bromide in acetone or alcohol. The quinolinium and isoquinolinium salts were only slightly soluble in water, while the pyridinium and pyrazinium compounds were more soluble.

TABLE I

p-FLUOROPHENACYL BROMIDE SALTS

Salt from	Empirical formula	M.p.,[a] °C.	Ionic halogen, % Calcd.	Found
A. Substituted pyridines				
γ-Picoline	$C_{14}H_{13}BrFNO$	165–168	25.77	25.62, 25.64
2,6-Lutidine	$C_{15}H_{15}BrFNO$	248	24.65	24.30, 24.40
4-*n*-Amylpyridine	$C_{18}H_{21}BrFNO$	181	21.81	21.79, 21.80
2-*n*-Hexylpyridine	$C_{19}H_{23}BrFNO$	180	20.96	20.82, 20.78
2-Propanolpyridine	$C_{16}H_{15}BrFNO_2$	163	22.50	22.27, 22.41
3-Hydroxypyridine	$C_{13}H_{11}BrFNO_2$	223	25.61	25.36, 25.39
3-Aminopyridine	$C_{13}H_{12}BrFN_2O$	200–202	25.68	25.60, 25.70
3-Acetaminopyridine	$C_{15}H_{14}BrFN_2O_2$	177–179	22.63	22.88, 22.79
3-Acetylpyridine	$C_{15}H_{13}BrFNO_2$	172–173	23.62	23.51, 23.82
3-Cyanopyridine	$C_{14}H_{10}BrFN_2O$	212	24.88	24.87, 24.98
Ethyl nicotinate	$C_{16}H_{15}BrFNO_3$	90	21.70	21.31, 21.36
Nicotinamide	$C_{14}H_{12}BrFN_2O_2$	226–228	23.56	23.23, 23.42
B. Quinoline and isoquinolines				
Quinoline	$C_{17}H_{13}BrFNO$[b]	235	23.08	23.06, 23.54
Isoquinoline	$C_{17}H_{13}BrFNO$	202	23.08	23.04, 23.01
3-Methylisoquinoline	$C_{18}H_{15}BrFNO$	135–136	22.19	22.15, 21.98
C. Chloropyrazine				
2-Chloropyrazine[c]	$C_{12}H_9BrClFN_2O$	183		[d]

[a] In nearly all cases the compounds melted with decomposition. [b] The corresponding iodide, $C_{17}H_{13}FINO$, m. p. 190–191°, calcd. I, 32.28: found I, 31.91, 32.45. [c] The product may be either the 3-chloropyrazinium salt or the 2-chloropyrazinium salt, but the former seems more likely since 3-bromopyridine reacts more readily than 2-bromopyridine. [d] Calcd.: C, 43.46; H, 2.74. Found: C, 43.57; H, 2.87.

Samples of these compounds have been submitted to the National Cancer Institute or the Midwest Research Institute for screening against tumors and data showing the variations in biological activity are to be published elsewhere.

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(2) C. T. Bahner, W. K. Easley, M. D. Pickens, H. D. Lyons, L. L. Norton, B. G. Walden and G. E. Biggerstaff, THIS JOURNAL, **73**, 3499 (1951); C. T. Bahner and L. L. Norton, *ibid.*, **72**, 2881 (1950).

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Methyl Esters of Substituted Benzoic Acids[1]

Methyl *p*-phenoxybenzoate.—*p*-Phenoxybenzoic acid was prepared by carbonation of the Grignard reagent made in the usual way from 25 g. of *p*-bromodiphenyl ether. Pouring the Grignard solution onto crushed dry ice gave only very small amounts of the desired acid, but carbonation by the method of Hussey[2] yielded 7.5 g. (35%) of *p*-phenoxybenzoic acid, m.p. 158–160°. The methyl ester was prepared by boiling 5.15 g. of the acid with 70 ml. of methyl alcohol and 7 ml. of sulfuric acid for two hours, distilling off most of the methanol and washing the solid product with a solution of sodium bicarbonate and then with water. Recrystallization from methanol–water mixture yielded 4.0 g. (65%) of colorless crystalline methyl *p*-phenoxybenzoate, m.p. 59.5–60°. The ester is biaxial, crystallizing in the orthorhombic system, optically positive with 2V = 85°; α, 1.515; β, 1.573; γ, 1.667 (calculated), exhibiting prismatic habit and irregular cleavage.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.90; H, 5.34.

Methyl *p*-Ethoxybenzoate.—A similar esterification with *p*-ethoxybenzoic acid gave the methyl ester in 75% yield. Recrystallization was effected from methanol–water and from ligroin. This ester forms colorless crystals melting at 37.5–38° to a colorless liquid which boils at 260°. The crystals are orthorhombic, with 2V = 85–90°, showing prismatic habit and irregular fracture.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.71; H, 6.71.

Methyl anisate was found to have crystallographic properties similar to the two preceding esters. Microscopic examination showed crystals of this compound to be biaxial, orthorhombic, optically negative, with 2V = 70–75°, exhibiting irregular prismatic habit and platy cleavage.

Methyl 3,4-Dichlorobenzoate.—Although it has been mentioned in a patent,[3] no properties of this compound have been reported. It was prepared in 81% yield from the corresponding acid by a similar Fischer esterification, followed by recrystallization from methanol. The ester crystallizes in long colorless prismatic needles, also in the orthorhombic system; m.p. 46.5–47.5°; b.p. 248°.

Anal. Calcd. for $C_8H_6O_2Cl_2$: C, 46.86; H, 2.95. Found: C, 46.97; H, 3.15.

(1) All temperatures are corrected.

(2) A. S. Hussey, THIS JOURNAL, **73**, 1364 (1951).

(3) R. S. Long (to American Cyanamid Co.) U. S. Patent 2,392,167 (1946).

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Preparation of Cerous Ammonium Acetylacetonate

To 6 ml. (0.058 mole) of refluxing acetylacetone was added 6 ml. (0.091 mole) of concentrated ammonium hydroxide and the mixture refluxed for ten minutes. A solution of 500 mg. (0.0012 mole) of cerous nitrate hexahydrate in 3 ml. water was then introduced dropwise and the resulting solution refluxed for ten minutes. The solution was allowed to