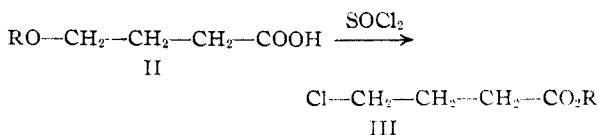
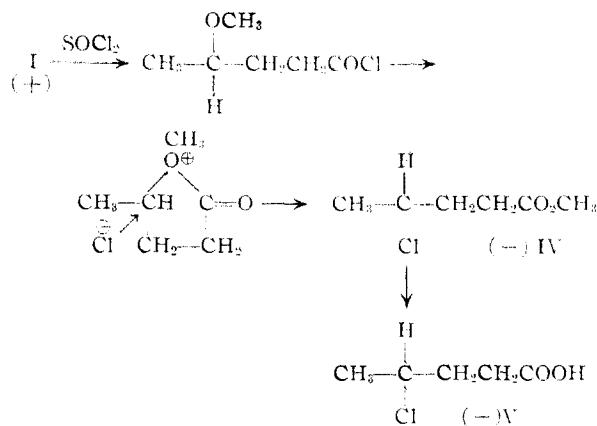


butyric esters (III) when treated with warm thionyl chloride.²



Levene and Haller³ have shown that (+)-2-hexanol has the same configuration as (+)- γ -chlorovaleric acid (V), the acid derived from the expected ester (IV). Since it has now been found that (+)-I gives the ester of (-)-V, it is apparent that the reaction produced an inversion at the optically active center, thus confirming the mechanism previously suggested.^{2b}



Experimental⁴

Methyl 4-Chlorovalerate (IV).—To 26 g. (0.2 mole) of (+)-I, $[\alpha]_D^{25} +1.53^\circ$, neat, $l = 1$) was added 30 g. of thionyl chloride, and the mixture was heated to reflux for one hour. After cooling, the mixture was added to water and extracted with ether. The ether extract was washed with 10% sodium carbonate solution, dried over sodium sulfate and distilled giving 20 g. (67%) of methyl 4-chlorovalerate, b.p. 73–75° at 15 mm., $n_D^{25} 1.4298$, $d_4^{25} 1.063$, $[\alpha]_D^{25} -2.07^\circ$ (neat, $l = 1$); M_D , calcd. 36.53, found 36.68.

Anal. Calcd. for $\text{C}_6\text{H}_{11}\text{O}_2\text{Cl}$: C, 47.85; H, 7.36; Cl, 23.54. Found: C, 47.77; H, 7.34; Cl, 23.25.

IV was hydrolyzed by the procedure of Levene and Mori⁵ giving 4-chlorovaleric acid (V) having b.p. 120–122° at 20 mm., $\alpha_D^{25} -2.36^\circ$ (neat, $l = 1$).

A sample of (\pm)-IV,⁶ prepared by the interaction of γ -valerolactone, methanol and hydrogen chloride according to the method of Levene and Mori⁵ was found to have b.p. 73–75° at 15 mm., $n_D^{25} 1.4299$, $d_4^{25} 1.061$. The infrared spectra of IV prepared by the two procedures were identical.

Anal. Calcd. for $\text{C}_6\text{H}_{11}\text{O}_2\text{Cl}$: C, 47.85; H, 7.36; Cl, 23.54. Found: C, 47.68; H, 7.31; Cl, 23.40.

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(2) (a) F. F. Blicke, W. B. Wright and M. F. Zienty, *THIS JOURNAL*, **63**, 2488 (1941); (b) V. Prelog and S. Heimbach-Juhasz, *Ber.*, **74B**, 1702 (1941).

(3) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **83**, 591 (1929). On the basis of our present knowledge of the Walden inversion, their work must be corrected to state that the reaction between an aliphatic secondary alcohol and a phosphorus halide gives inversion rather than retention of configuration.

(4) Analyses were performed by O. Schwarzkopf and T. Hinton.

(5) P. A. Levene and T. Mori, *J. Biol. Chem.*, **78**, 1 (1928).

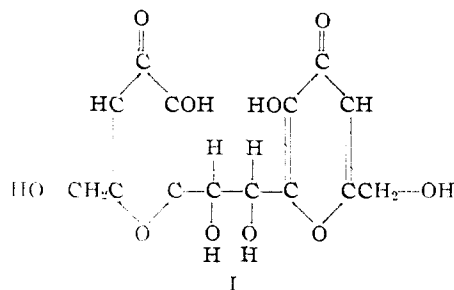
(6) Kindly supplied by Dr. R. W. Young.

The Condensation of Kojic Acid with Glyoxal¹

By L. L. Woods

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The easy condensation of kojic acid with glyoxal produces a compound which exhibits more promise of becoming an important chemical intermediate than any other produced in this series of experiments.^{2,3} The fact that 1,2-bis-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-ethylene glycol (I) formed during the reaction is sensitive to strong acidic reagents and undergoes a 1,2-shift typical of the pinacol rearrangement⁴ was expected; as was the



fact that thionyl chloride would convert the hydroxy methyl groups to stable chloromethyl groups, whereas the glycolic hydroxyls when removed by chlorine exhibited no such stability in the presence of water. A similar observation has been made before² and an explanation has been advanced by Stodola.⁵

Experimental⁶

1,2-Bis-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-ethylene Glycol (I).—A mixture of 10 ml. of 30% glyoxal, 50 ml. of absolute ethanol and 7.1 g. of kojic acid was heated to boiling—cooled slightly—and 1 g. of potassium bicarbonate was added. The stoppered flask was set aside and the mixture allowed to react overnight. The next day the flask was filled with yellow-orange crystals which when recrystallized from ethanol produced 4.5 g. of yellow needles which melted at 147–149°. During the melting point determination some sublimate was formed which melted at 155.5–156.5°. The sublimate was probably due to thermal rearrangement of (I) to form a small amount of (II). Compound (I) gave a very deep red coloration to dilute solutions of ferric chloride. The compound gave no test with Schiff reagent.

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_{10}$: C, 49.12; H, 4.09. Found: C, 49.40; H, 4.30.

1-Oxy-1,2-bis-(2-hydroxymethyl-5-hydroxy-4-pyrone-6)-ethane (II).—Three grams of (I) was placed in 10 g. of cold concentrated sulfuric acid and allowed to stand 24 hours. The viscous mass was diluted with 100 ml. of water and neutralized with sodium bicarbonate. The rearranged compound was obtained by repeated extractions with ethyl acetate. The extract was dried with anhydrous sodium sulfate and the solvent evaporated, giving 0.8 g. of yellow prisms. Recrystallization from ethanol produced crystals

(1) The author wishes to express his gratitude to the Corn Products Sales Corporation for the kojic acid used in these experiments and to the Research Corporation for a Frederick Cottrell Grant-in-aid to continue this investigation.

(2) L. L. Woods, *THIS JOURNAL*, **72**, 4322 (1950).

(3) L. L. Woods, *ibid.*, **74**, 1106 (1952).

(4) G. W. Wheland, "Advanced Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 452; E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 45.

(5) F. H. Stodola, *THIS JOURNAL*, **73**, 5912 (1951).

(6) All analyses were performed by Dr. Carl Tiedcke. All melting points were made on a Fisher-Johns melting point assembly.

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 $C_{14}H_{12}O_5$: 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 Acid¹

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 hydroxy 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

Experimental³

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

(1) The author wishes to express his thanks to the Research Corporation for a Frederick G. Cottrell Grant-in-Aid. The kojic acid used in these experiments was furnished through the courtesy of the United States Department of Agriculture Northern Regional Laboratory, Peoria, Illinois.

(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.

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 $C_{17}H_{18}O_7Br$: 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 acids¹ were esterified with methanol and sulfuric acid to furnish the esters desired as starting materials. The aluminum-amalgam reduction² 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-

(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)