from acetone gave an analytical sample: m.p. 182–188°; n.m.r. spectrum at 73 (C-18 methyl), 226 (C-3 methoxyl), 233 and 240 (hydroxyl), 307 c.p.s. (multiplet, C-17β hydrogen); [α]D +78°.

*Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.33; H, 8.65.

**3,17α-Dimethoxy-17a-oxa-D-homoestra-1,3,5(10)-triene (7c).**—A mixture of 2.75 g. (9.1 mmoles) of **7b**, 100 ml. of methanol, and 100 mg. of *p*-toluenesulfonic acid was stirred for 1 hr., then concentrated to 40 ml. at room temperature. The product which separated was collected by filtration, washed on the filter with cold methanol, and dried to afford a crude product, weighing 2.4 g. (90%) and melting at about 116–120°. Crystallization of the crude product from methanol gave an analytical sample: m.p. 126–127°; n.m.r. spectrum at 72 (C-18 methyl), 208.5 (C-17α methoxyl), 227 (C-3 methoxyl), and 280.5 c.p.s. (multiplet, C-17β hydrogen); [α]D +126.5°.

*Anal.* Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 76.01; H, 8.75.

**17a-Oxa-D-homoestra-4,16-dien-3-one (6b) and 17α-Hydroxy 17a-oxa-D-homoestra-4-en-3-one (5b).**—To a mixture of 175 ml. of liquid ammonia, 20 ml. of *t*-butyl alcohol, and 125 ml. of tetrahydrofuran was added a solution of 4.5 g. (14.3 mmoles) of **7c** in 50 ml. of tetrahydrofuran. Approximately 2 g. of sodium was then added to the solution and the blue reaction mixture was allowed to stand for 1 hr. The reaction was quenched with methanol until the color was dissipated, and the mixture was then distilled to dryness under reduced pressure.

The residue was triturated with water. The crystalline product was collected by filtration, washed with water, and dried. The crude dihydro derivative, which melted at 139–140° and weighed 4.3 g., was not purified but was warmed with 55 ml. of methanol containing 8 ml. of 2 *N* hydrochloric acid for 30 min. The solution was cooled and neutralized with aqueous saturated sodium bicarbonate solution and stirred with 200 ml. of methylene chloride. The organic layer was separated, dried over anhydrous magnesium sulfate, and distilled to dryness. The residue, when triturated with hexane, yielded 2.75 g. (63%) of crude 17α-methoxy-17a-oxa-D-homoestra-4-en-3-one, m.p. 120–143°. A solution of this substance in 25 ml. of tetrahydrofuran, 30 ml. of water, and 2 ml. of 2 *M* hydrochloric acid was allowed to stand in a nitrogen atmosphere for 22 hr. The solution was then neutralized with aqueous sodium bicarbonate and extracted with chloroform. The chloroform extract was dried over magnesium sulfate and distilled to dryness. Crystallization of the crude product yielded 2.0 g. of an analytical sample: m.p. 170–173°; $\lambda_{max}$ 2.80, 2.95, 6.01 and 6.18 μ; n.m.r. spectrum at 72 (C-18 methyl), 305 (multiplet, C-17β hydrogen), 235 and 242 (hydroxyl), and 342 c.p.s. (C-4 hydrogen).

*Anal.* Calcd. for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.53; H, 9.20.

When 2.5 g. of the crude 17α-methoxy-17a-oxa-D-homoestr-4-en-3-one was instead hydrolyzed at reflux, 400 mg. of 17a-oxa-D-homoestra-4,16-dien-3-one (**6b**), m.p. 134°, was also obtained when the crude product was purified by chromatography on silica gel in benzene and elution with 5% ethyl acetate in benzene. The n.m.r. spectrum of **6b** exhibited maxima at 72 (C-18 methyl), 280 (multiplet, C-16 hydrogen), 352 (multiplet, C-4 hydrogen), and 372 and 378 c.p.s. (C-17 hydrogen).

*Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.36; H, 8.72.

**1- (or 4-) Methyl-17a-oxa-D-homoestra-1,3,5(10)-trien-17α-ol (10) and 17α-Hydroxy-17a-oxa-D-homoandrosta-1,4-dien-3-one (9).**—A solution of 5 g. (16.7 mmoles) of 17a-oxa-D-homoandrosta-1,4-diene-3,17-dione[1] (**8**, 1-dehydrotestololactone) in 450 ml. of toluene was distilled until anhydrous, then was cooled to about −70° by means of a Dry Ice–isopropyl alcohol bath. To that solution was then added, with stirring, 16 ml. of 1.4 *M* diisobutylaluminum hydride in toluene solution, dropwise over a period of about 5 min. Stirring of the light yellow solution at about −60° continued for an additional 40 min., after which time the reaction mixture was diluted with approximately 10 ml. of methanol. After that solution was allowed to warm to approximately 0°, about 300 ml. of concentrated aqueous sodium potassium tartrate was added and the organic layer was separated. That layer was washed successively with saturated aqueous sodium potassium tartrate and water, then was dried over anhydrous magnesium sulfate, and distilled to dryness under reduced pressure. The residual glass-like material was purified by chromatography on about 300 g. of silica gel in benzene. Elution of the column with 2% ethyl acetate in benzene afforded about 600 mg. (12%) of 1- (or 4-) methyl-17a-oxa-D-homoestra-1,3,5(10)-trien-17α-ol. Crystallization of the crude fraction from acetone and hexane gave an analytical sample: m.p. 153°; n.m.r. spectrum at 73 (C-18 methyl), 133 (methyl on A ring), and 310 (multiplet, C-17β hydrogen), 421–437 c.p.s. (multiplet, aromatic hydrogens); [α]D +119°.

*Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.63; H, 8.82.

Elution of the column with 25% ethyl acetate in benzene afforded a 170-mg. fraction which was triturated with ether to give 90 mg. (1.8%) of crude 17α-hydroxy-17a-oxa-D-homoandrosta-1,4-dien-3-one. Crystallization of the crude product from acetone and hexane gave an analytical sample: m.p. 161–164°; n.m.r. spectrum at 68 (C-19 methyl), 71 (C-18 methyl), 301 (multiplet, C-17β hydrogen), and 363, 377, 423, and 428 c.p.s. (multiplets, C-1, -2, -4 hydrogens); $\lambda_{max}^{MeOH}$ 243 mμ (ε 15,400); $\lambda_{max}$ 2.96, 5.98, 6.14, and 6.33 μ; [α]D 0°.

*Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.16; H, 8.54.

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## A Synthesis of Orsellinic Acid

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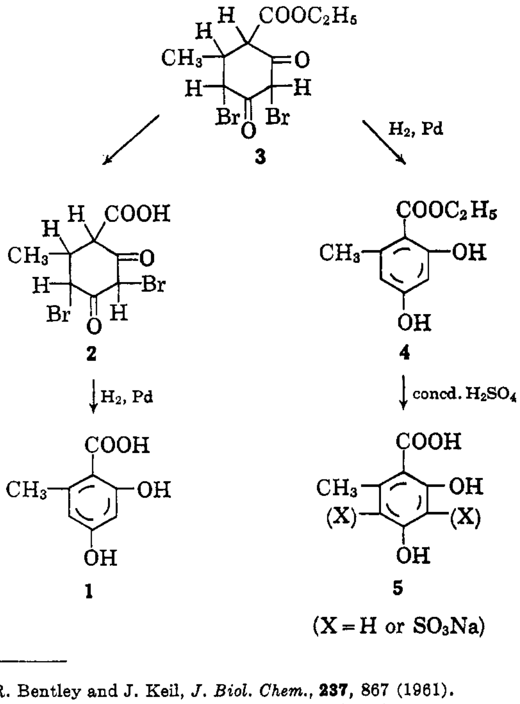
The role of orsellinic acid (**1**) in certain metabolic transformations has been established.[1,2] Investigation of the role of this compound in other transformations has created a need for a reliable synthesis.

The synthesis of Sonn[3] was not successful in this laboratory. Sonn's method, which uses a room temperature alkaline hydrolysis of ethyl orsellinate (**4**) as a final step, repeatedly resulted in decarboxylation upon acidification. Even when the acidification was done cautiously at 0° no product could be obtained. Variations on time and concentration of alkali and also an aqueous acid hydrolysis failed to yield **1**.



(X = H or $SO_3Na$)

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[1] R. Bentley and J. Keil, *J. Biol. Chem.*, **237**, 867 (1961).

[2] K. Mosbach, *Acta Chem. Scand.*, **14**, 457 (1960).

[3] A. Sonn, *Ber.*, **61**, 926 (1928).

The use of concentrated sulfuric acid for the hydrolysis of hindered esters is generally a useful method,[4] and it has been successful in the hydrolysis of certain compounds related to orsellinic acid ester.[5] When **4** was treated with concentrated sulfuric acid, a sulfonated product (**5**) was obtained even when the reaction period was as short as 15 min. This is not completely unexpected, since the ring is very highly activated toward electrophilic substitution. The product was obtained by salting out with sodium chloride. Carbon–hydrogen analysis of this compound indicates that a monosulfonation product is obtained and that the ester is converted to the acid (there is 1 mole of methyl alcohol/mole of compound in the crystalline product). No attempt was made to determine the position at which the substitution occurred. The compound gives a very intense violet ferric chloride test.

In order to avoid the sulfonation and still utilize the sulfuric acid method of hydrolyzing the ester to the acid, the hydrolysis was carried out on the dibromo ester **3** of Sonn. The corresponding acid **2** was obtained in 97% yield.

Using essentially the same method reported[3] for converting **3** to **4**, the new acid **2** was converted to orsellinic acid (**1**) in 70% yield. It should be noted that the melting point of the analytical sample reported in the Experimental Section is considerably higher than that reported in the literature.[6] The literature value apparently refers to the monohydrate; our recrystallized but undried product is also the monohydrate. Our analytical sample is the anhydrous compound.

### Experimental Section

**2,4-Dibromo-5-methyl-6-carboxycyclohexa-1,3-dione** (**2**).—The dibromo ester **3** (3.56 g., 10 mmoles) was prepared according to Sonn[1] and dissolved in 10 ml. of concentrated sulfuric acid. The reaction mixture was allowed to stand at room temperature for 30 min. When the solution was poured over ice, a heavy white precipitate formed. The complete reaction mixture was then extracted three times with 25-ml. portions of ethyl ether. The dibromo acid was separated from any unreacted ester by extraction of the ether with 0.5 *N* sodium bicarbonate.

The sodium bicarbonate solution was acidified to pH 3 using 3 *N* hydrochloric acid to yield 3.18 g. (97% yield) of the dibromo acid, m.p. 212–213°. This product gave an intense violet ferric chloride test; the starting ester did not. Recrystallization of crude product from methyl alcohol gave a white crystalline solid, m.p. 213–213.5°, $\lambda_{\max}^{\text{EtOH}}$ 265 m$\mu$ ($\epsilon$ 8650) and 313 (5850).

*Anal.* Calcd. for $C_8H_8Br_2O_4$ (328.98): C, 29.21; H, 2.40 Found: C, 29.68; H, 2.05.

**2,4-Dihydroxy-6-methylbenzoic Acid** (**Orsellinic Acid, 1**).—A mixture of 0.827 g. (252 mmoles) of dibromo acid **2**, 2.20 g. of palladium–calcium carbonate catalyst,[7] and 14 ml. of 2 *N* sodium hydroxide was shaken under 40 p.s.i. of hydrogen for 6 hr. A weight of catalyst two to three times the dibromo acid weight was found to give better results than when lesser amounts were used.

The mixture was filtered to remove the reduced catalyst and cooled to 0°. Acidification to pH 3 with 2 *N* hydrochloric acid to precipitate the orsellinic acid gave no evidence of carbon dioxide evolution. The solid removed by filtration, m.p. 186–187°, 0.32 g. (70% yield), gave a positive ferric chloride test. Recrystallization from acetone and water gave fine white crystals, m.p. 197–198°, when dried for at least 48 hr. at <1.0 mm. at 34°, $\lambda_{\max}^{\text{EtOH}}$ 260 m$\mu$ ($\epsilon$ 9450) and 298 (6500).[8]

*Anal.* Calcd. for $C_8H_8O_4$ (168.14): C, 57.17; H, 4.80. Found: C, 57.48; H, 5.04.

**Sodium Salt of Monosulfonated Orsellinic Acid** (**5**).—Concentrated sulfuric acid (2.0 ml.) was added to 0.60 g. of ethyl orsellinate. The reaction mixture was allowed to stand for 20 hr. and then poured over ice. The reaction mixture was then extracted three times with ethyl ether. Sodium bicarbonate was used to separate the acid from unreacted ester. Salting out with sodium chloride produced 0.25 g. (27% yield) of white solid. Recrystallization of the crude product from methanol gave a white crystalline solid.

*Anal.* Calcd. for $C_8H_7NaO_7S \cdot CH_3OH$ (302.24): C, 35.77; H, 3.67. Found: C, 36.00; H, 3.28.

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[4] M. Newman, *J. Am. Chem. Soc.*, **63**, 2431 (1941).

[5] K. Mosbach, personal communication.

[6] F. K. Beilstein, "Handbuch der organischen Chemie," Springer Verlag, Berlin, Vol. 10, 1927, p. 412; 1949, p. 272.

[7] M. Busch and H. Stöve, *Ber.*, **49**, 1063 (1916).

[8] *Cf.* C. A. Wachtmeister, *Acta Chem. Scand.*, **12**, 147 (1958).

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# Diels–Alder Reactions of Acrylic Acid Derivatives Catalyzed by Aluminum Chloride

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Remarkable acceleration of certain Diels–Alder reactions by aluminum chloride was first reported by Yates and Eaton.[1] Dienophiles tested by these workers were those activated by two carbonyl groups, for example, maleic anhydride, *p*-benzoquinone, and dimethyl fumarate. The scope of such catalyzed Diels–Alder reactions was extended to the cases of dienophiles with a single carbonyl function such as acrolein, methyl vinyl ketone, and acrylic acid, and also to the use of a variety of Friedel–Crafts catalysts for this type of reactions.[2,3] The general utility of these catalysts for preparation of the desired products is limited, however, owing to the instability of some dienes and dienophiles under the reaction conditions.[1,2]

We wish to report the aluminum chloride catalyzed diene syntheses with methyl acrylate, methyl methacrylate, and acrylonitrile as dienophiles and some observations relevant to such syntheses. The reaction between methyl acrylate and butadiene proceeds cleanly and smoothly at moderate temperatures in the presence of aluminum chloride to give methyl 3-cyclohexene-1-carboxylate in a high yield. Other Friedel–Crafts catalysts are of much less or practically no activity (Table I), in contrast to the general activity of these catalysts in the reactions with methyl vinyl ketone.[2,3] To carry out the reaction, a dienophile is mixed with aluminum chloride in a suitable solvent to form a complex[4] and the diene is then allowed to come into contact with the preformed complex, since undesirable side reactions may occur otherwise. Reactions of other combinations of diene and dienophiles are shown in Table II.

In all these cases resinous materials, which would be formed by the Friedel–Crafts reaction between butadiene and benzene (*vide infra*), or by the polymerization of diene, were not formed, presumably because aluminum chloride complexed with an ester group is not ca-

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[1] P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960).

[2] G. I. Fray and R. Robinson, *ibid.*, **83**, 249 (1961).

[3] R. Robinson and G. I. Fray, British Patent 835,840 (1960).

[4] Formation of a complex between aluminum chloride and an ester group has been shown, for example, by M. F. Lappert [*J. Chem. Soc.*, 817 (1961); 542 (1962)].