

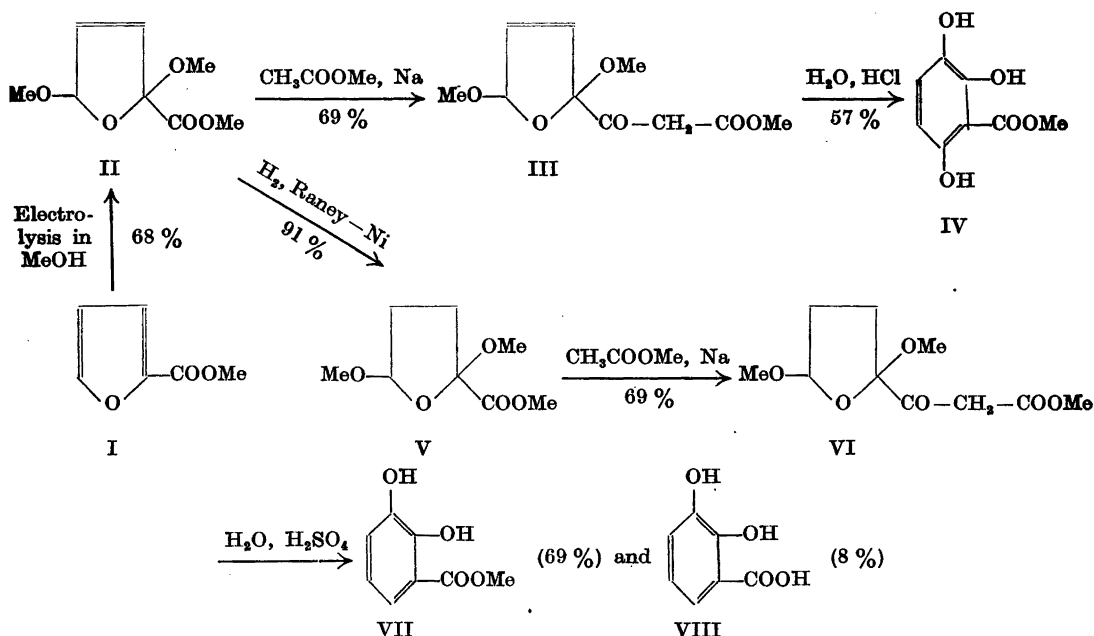
## Preparation of Certain Methyl Polyhydroxybenzoates from Methyl Furoate

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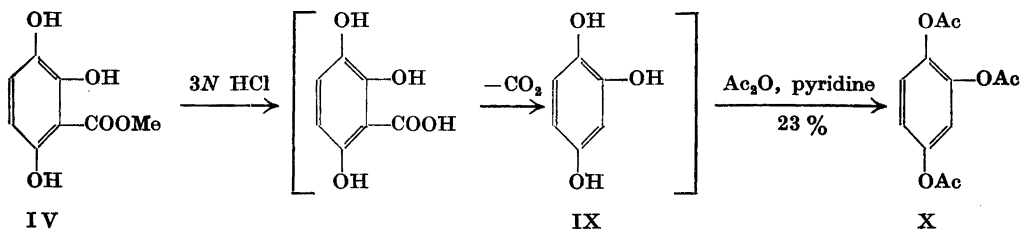
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The methyl esters of 2,3-dihydroxybenzoic acid (VII) and 2,3,6-trihydroxybenzoic acid (IV) have been prepared from methyl furoate (I).

Furans with suitable substituents in the 2-position may be transformed into other systems with aromatic character by methoxylation to cyclic acetals of 1,4-dicarbonyl compounds, followed by intramolecular condensation in acid solution<sup>1-4</sup>. Further application of this principle has led to the preparation of the methyl esters of 2,3-dihydroxybenzoic acid (VII) and of 2,3,6-trihydroxybenzoic acid (IV) from methyl furoate (I) by the reactions shown below. A small amount of the free 2,3-dihydroxybenzoic acid (VIII) was also isolated.



Compounds III, IV and VI are new. Their structures follow from the syntheses and from analyses. The structure of IV was confirmed further by transformation into the known triacetate (X) of hydroxyhydroquinone (IX). With the preparation of the methyl ester of 2,3,6-trihydroxybenzoic acid (IV), all the six theoretically possible trihydroxybenzoic acids have been prepared, either as esters or as free acids.



### EXPERIMENTAL

Microanalyses by Ernst Boss and Kirsten Glens

*2,5-Dimethoxy-2,5-dihydro-2-furoyl acetic acid methyl ester (III)* (cf.<sup>5</sup>). II<sup>6</sup> (51.7 g, 0.275 mole) is placed in a 0.5-liter three-necked flask fitted with a Hershberg stirrer, a dropping funnel and a reflux condenser and heated with stirring to 90°. 0.7 mm sodium wire (18.5 g, 0.81 mole) and methyl acetate (60.7 g, 0.82 mole) are added at 30–60 minute intervals in six portions of equal size. During each addition of sodium the stirrer is stopped. As the reaction mixture becomes more and more viscous, benzene (70 ml in all) is added. After the reaction, methanol (30 ml) is added dropwise to remove residual sodium and the mixture left standing with stirring and heating over-night. The solution is cooled to –10° and poured in one portion with efficient stirring into a mixture of concentrated hydrochloric acid (90 g, 0.89 mole) and 170 g of cracked ice. The dark brown mixture is extracted rapidly with cold ether (500 + 100 + 100 ml) and the ethereal solution washed with a 2 M solution of potassium hydrogen carbonate (300 ml) and dried with magnesium sulfate. The ether is removed by distillation and the residue distilled further under 0.1–0.2 mm from an oil bath (60–120°). After a fore-run of methyl acetoacetate, 43.4 g (69 %) of III is obtained [slightly yellow oil, b. p. 87–114° (main portion 104–114°),  $n_D^{25}$  1.4588]. (Found: C 52.6; H 6.3; OCH<sub>3</sub> 39.4. Calc. for C<sub>7</sub>H<sub>8</sub>O<sub>5</sub>(OCH<sub>3</sub>)<sub>2</sub> (230.2): C 52.2; H 6.1; OCH<sub>3</sub> 40.4).

*2,3,6-Trihydroxybenzoic acid methyl ester (IV)*. III (2.30 g) was shaken for 10 minutes with hydrochloric acid (0.1 N, 20 ml) under carbon dioxide. Hereby a homogeneous solution was obtained, which was left standing for 8 days. A light-violet precipitate was removed by filtration, washed with water and dried. The yield was 1.05 g (57 %) of IV [m. p. 131–135° (Hershberg apparatus, corr.)]. (Found: C 52.4; H 4.4; OCH<sub>3</sub> 16.8. Calc. for C<sub>7</sub>H<sub>8</sub>O<sub>4</sub>(OCH<sub>3</sub>) (184.1): C 52.2; H 4.4; OCH<sub>3</sub> 16.9).

The product gave a reddish-brown ferric chloride reaction. After two crystallizations from methanol-water the m. p. was raised to 138°. Further crystallization did not change the m. p.

*2,5-Dimethoxytetrahydro-2-furoyl acetic acid methyl ester (VI)*. This compound was prepared from 2,5-dimethoxy-2-carbomethoxy-tetrahydrofuran<sup>6</sup> (28.5 g) and methyl acetate (34.1 g) as described above for the preparation of III. The yield was 24.0 g (69 %) of VI (light-yellow liquid, b. p.<sub>0.1-0.2</sub> 98–99°,  $n_D^{25}$  1.4559). (Found: C 52.8; H 7.3; OCH<sub>3</sub> 38.8. Calc. for C<sub>7</sub>H<sub>8</sub>O<sub>5</sub>(OCH<sub>3</sub>)<sub>2</sub> (232.2): C 51.7; H 6.9; OCH<sub>3</sub> 40.1).

*2,3-Dihydroxybenzoic acid methyl ester (VII) and 2,3-dihydroxybenzoic acid (VIII)*. VI (1.00 g) was heated under reflux (15 min) with sulfuric acid (0.1 N, 5 ml). After cooling, a precipitate was removed by filtration, washed with water and dried. The yield was 500 mg (69 %) of VII (almost white crystals, m. p. 73–74°). (Found: C 56.9; H 5.0; OCH<sub>3</sub> 17.1. Calc. for C<sub>7</sub>H<sub>6</sub>O<sub>5</sub>(OCH<sub>3</sub>) (168.1): C 57.1; H 4.8; OCH<sub>3</sub> 18.5)

The product gave a blue ferric chloride reaction. After crystallization from benzene-petroleum ether the m. p. was raised to 77–78° (previously found<sup>7</sup> 78–79°).

The mother liquor was heated further under reflux (10 min) and continuously extracted with ether. Hereby 50 mg (8 %) of VIII was isolated (white crystals, m. p. 204–205°). (Found: C 54.7; H 4.1. Calc. for  $C_7H_6O_4$  (154.1): C 54.6; H 3.9).

The product gave a violet ferric chloride reaction. After crystallization from benzene the m. p. was raised to 207° (previously found<sup>8</sup> 206°).

*Hydroxyhydroquinone triacetate (X)*. IV (300 mg) was heated under reflux (3 hr) with hydrochloric acid (3 N, 10 ml) in an atmosphere of nitrogen. The solution was extracted with ether (15 + 15 ml), the ethereal solution dried with magnesium sulfate and the ether distilled. The oily residue was heated under reflux (10 min) with a mixture of acetic anhydride (3 ml) and pyridine (3 ml). The reaction mixture was evaporated to dryness under 0.5 mm on a water-bath (60°) and the oily residue dissolved in ether (15 ml). The ethereal solution was purified with carbon black and most of the ether removed by distillation. Hereby 95 mg (23 %) of X crystallized (white crystals, m. p. 86–88°). (Found: C 56.4; H 5.0;  $COCH_3$  51.0. Calc. for  $C_6H_3O_3(COCH_3)_3$  (252.2): C 57.1; H 4.8;  $COCH_3$  51.2).

The infrared spectrum of the product was identical with that of an authentic sample. After crystallization from benzene-petroleum ether the m. p. was raised to 95° (previously found<sup>9</sup> 96–97°).

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