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Dihydropyrogallol, A New Ene-diol and its Oxidation Product. 1,2,3-Cyclohexanetrione Dihydrate—A Ketonic Isomer of Pyrogallol

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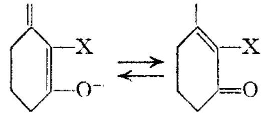
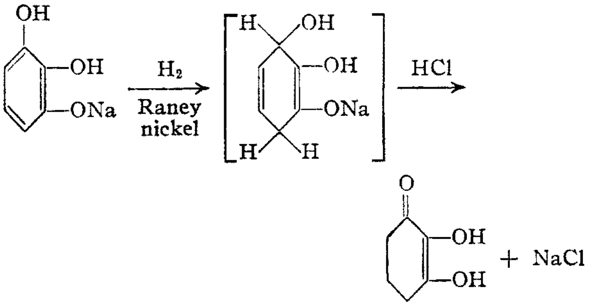
The ene-diols, compounds containing the group —COH=COH—, may be divided into two classes. The first class comprises about a dozen highly hindered stilbene diols which were studied by Fuson and his students[2] while the second class embraces those ene-diols containing a carbonyl group adjacent to the double bond. In the second group there are similarly a few well-defined members, which include ascorbic acid and its analogs,[3] reductone,[4] reductinic acid,[5] dihydroxymaleic acid, its salts and esters,[6] and hydroxytetronic acid.[7] To the second group may be added a miscellany of compounds such as 2,3-dihydroxy-1,4-benzoquinone, the corresponding naphthalene analog,[8] rhodizonic acid[9,10] and croconic acid.[9,10] A few other compounds containing the carbonyl group conjugated with the ene-diol group are mentioned in the literature, but if the further proviso is added that an ene-diol must react stoichiometrically with one molecule of iodine, then the rigid classification of these latter compounds is better deferred until this property has been demonstrated.

This paper describes a new ene-diol, dihydropyrogallol (I), prepared by the catalytic hydrogenation of pyrogallol in the presence of one mole of alkali. Previous workers[11,12,13,14,15] who studied the hydrogenation of pyrogallol obtained complex mixtures ranging from hexahydropyrogallols to cyclohexane, but the product after uptake of one mole of hydrogen has not been described previously. This method of reducing 1,3-dihydroxybenzenes, first used by Klingenfuss[16] for the preparation of dihydroresorcinol, works successfully for pyrogallol, but not for 4-substituted pyrogallols.[17] The success of this method is probably due to the formation of the resonating system



where X = H for resorcinol and X = OH for dihydropyrogallol.



I

Dihydropyrogallol is a typical ene-diol; it behaves as a monobasic acid and consumes two equivalents of iodine. With ferric chloride it gives a deep blue color which gradually fades. It has been further characterized by the preparation of a monoacetate and the bis- and tris-(phenylhydrazones) of 1,2,3-cyclohexanetrione.

Since dihydropyrogallol was originally prepared as a stabilizer for edible fats it was desirable to determine the nature of its oxidation products. Observations, recorded below, indicated that pyrogallol was not the primary oxidation product. On oxidation with iodine, using the method of Reichstein and Oppenauer[18] for reductinic acid, a white crystalline product melting at 106°, having the composition $C_6H_{10}O_5$, was obtained. This product was a neutral substance that did not decolorize iodine solution, slowly reduced silver nitrate, immediately reduced ammoniacal silver nitrate and gave a bis-(phenylhydrazone) identical with that obtained from dihydropyrogallol. Treatment with hydrogen sulfide gave dihydropyrogallol in high yield. These properties indicated the structure of a dihydrated 1,2,3-cyclohexanetrione (IIa or IIb).

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[2] Fuson, *et al.*, THIS JOURNAL, **61**, 975, 2010 (1939); **62**, 600, 2091, 2962 (1940); **63**, 1500, 1679, 2645, 2648 (1941); **64**, 2152, 2891 (1942).

[3] *Cf.* the excellent review by Haworth and Hirst in "Ergebnisse der Vitamin und Hormonforschung," Vol. II, Akademische Verlag., Leipzig, 1939, p. 160–191.

[4] v. Euler and Martius, *Ann.*, **505**, 73 (1933); *Svensk Kem. Tidskr.*, **45**, 73 (1933).

[5] Reichstein and Oppenauer, *Helv. Chim. Acta*, **16**, 988 (1933).

[6] Fenton, *et al.*, *J. Chem. Soc.*, **69**, 561 (1896); **73**, 71 (1898); **87**, 804 (1905); **101**, 1571 (1912); Fox, *J. Org. Chem.*, **12**, 535 (1947).

[7] Micheel and Jung, *Ber.*, **66**, 1291 (1933); Micheel and Haarhoff, *Ann.*, **545**, 28 (1941).

[8] This substance has been found to react quantitatively with one mole of iodine and therefore may be classed as a true ene-diol.

[9] Nietzki and Benckiser, *Ber.*, **19**, 293 (1886); Carpéni, *J. chim. phys.*, **35**, 193 (1938).

[10] Sprinson and Chargaff, *J. Biol. Chem.*, **164**, 433 (1946).

[11] Senderens and Aboulenc, *Compt. rend.*, **174**, 616 (1922); Senderens and Mailhe, *ibid.*, **146**, 1193 (1908).

[12] Somlo, *Z. Elektrochem.*, **35**, 769 (1929).

[13] Lindemann and de Lange, *Ann.*, **483**, 31 (1930).

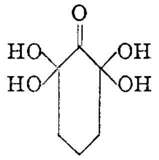
[14] Packendorff, *Ber.*, **68**, 1251 (1935).

[15] Thiele and Jaeger, *Ber.*, **34**, 2842 (1901).

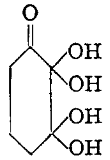
[16] U. S. Patent 1,965,499, *C. A.*, **28**, 5476 (1934); Barell Festschrift, Fredrick Reinhardt, Basel, 1936, p. 217.

[17] Unpublished work in this laboratory. Klingenfuss[16] states that 4-substituted resorcinols can be hydrogenated to dihydro derivatives.

[18] Reichstein and Oppenauer, *Helv. Chim. Acta*, **17**, 290 (1934).



IIa



IIb

Attempts to dehydrate or isomerize II yielded impure pyrogallol. Treatment with acetic anhydride gave pyrogallol triacetate in further support of structure II. Borsche[19] attempted to prepare a ketonic isomer of pyrogallol[20] from 1,3-dioximinocyclohexanone without success.

The absence of color in II is explained by the hydration which destroys the conjugation of the carbonyl groups. Although other 1,2,3-triones, such as tetramethyl-1,2,3-cyclopentanetrione[21] and 2,3,4-pentanetrione[22,23] form colorless hydrates which can be converted to colored anhydrous forms, it is unlikely that II can be dehydrated without isomerization to pyrogallol in view of the stabilization afforded by formation of the resonating benzene ring.

Reichstein and Oppenauer[18] oxidized reductinic acid, the next lower homolog of dihydropyrogallol to 1,2,3-cyclopentanetrione but failed to isolate a crystalline product. These workers noted the appearance of crystals during the isolation but on continued distillation, the crystals were converted to a sirup which yielded only the tris-(phenylhydrazone) of 1,2,3 - cyclopentanetrione. Whether their failure to isolate the crystalline trione is due to a lower stability is difficult to judge; however, in the present case, strict adherence to the procedure described below is necessary to obtain any crystalline product.

Attempts to use hydrogen peroxide for the oxidation of dihydropyrogallol showed that a trace of ferric ion was necessary for reaction to occur. From this reaction, an unexpected product, m. p. 169–170°, having the composition $C_6H_7O_3$ was isolated. This product was not reduced by hydrogen sulfide and gave no color with ferric chloride, but on the steam-bath yielded the same tris-(phenylhydrazone) obtained from I and II. Molecular weight determinations in acetone solution gave values corresponding to a monomer, but since the simple formula $C_6H_7O_3$ is unlikely, further work is necessary to elucidate the structure of this substance.[24]

Experimental[25]

Dihydropyrogallol (I).—This was prepared by the method of Klingenfuss[16,26] taking precautions to protect the alkaline pyrogallol solution from atmospheric oxygen with nitrogen.

One kg. of pyrogallol (E. K. Practical) (7.95 moles on a 100% basis) was dissolved in 2 liters of water containing 320 g. of sodium hydroxide (8 moles) and reduced at 60° under 1000 lb. hydrogen pressure using 50 g. of Raney nickel. The reduction was complete in about five hours. When cool, the catalyst was filtered off, and the filtrate acidified at −5° with 675 ml. of concentrated hydrochloric acid whereupon a light tan solid precipitated. After thirty minutes at −5°, the mixture was filtered and yielded 816 g. (80%) of material melting at 89–93°. Another 87 g. of product of the same m. p. was isolated after taking to dryness under nitrogen and extracting with benzene.

For purification, the dried material was recrystallized from dry benzene (550 ml. for 100 g.) using iron-free charcoal[27] to decolorize the solution. Dihydropyrogallol crystallizes from benzene in clusters of needles which are transformed to plates of m. p. 109–112° on drying. A sample after repeated recrystallization melted at 114°.

Anal. Calcd. for $C_6H_8O_3$: C, 56.22; H, 6.28. Found: C, 56.20; H, 6.16.

The substance behaves as a monobasic acid on titration with standard alkali. Fifty mg. of dihydropyrogallol consumed 0.782 milliequivalent of iodine; theory 0.780.

At room temperature, 100 ml. of benzene, ethanol, glycerol and ether dissolve 1.2, 20, 3 and 0.33 g., respectively.

The substance is stable in dry air for a few days after which decomposition sets in at an accelerated rate. In an inert atmosphere dihydropyrogallol has been stored for two years without deterioration.

Ferric chloride gives a blue color which fades in a short time. This "vanishing blue" color test can be repeated until all of the dihydropyrogallol has been consumed, but further additions give only the color of dilute ferric chloride solution. This observation indicated that an abnormal oxidation product was present.

Monoacetate of Dihydropyrogallol.—This derivative was prepared from 5 ml. of acetic anhydride and 4.0 g. of dihydropyrogallol in 10 ml. of pyridine. After two recrystallizations from ethyl acetate 3.05 g. of long prismatic crystals were obtained, m. p. 154–155.5°. The position of the acetyl group is uncertain; a red-purple color is obtained with ferric chloride.

Anal. Calcd. for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.78; H, 6.15. Calcd. for one CH_3CO: 25.3. Found: 26.1, 26.4.

1,3-bis-(Phenylhydrazone) of 1,2,3-Cyclohexanetrione.—This was prepared by treating dihydropyrogallol in dilute acetic acid solution with an excess of phenylhydrazine at 100°. Recrystallization from methanol gave bronze-red crystals, m. p. 131–132.5°. The position of the phenylhydrazone groups is inferred from the work of Henle and Schupp[28] who found that the reaction of mesoxalic aldehyde with phenylhydrazine gave a 1,3-bis-(phenylhydrazone).

Anal. Calcd. for $C_{18}H_{18}ON_4$: C, 70.56; H, 5.92. Found: C, 70.09; H, 5.63.

tris-(Phenylhydrazone) of 1,2,3-Cyclohexanetrione.—After heating the above bis-(phenylhydrazone) with phenylhydrazine at 130° for two hours, the cooled mixture deposited a dark oil on dilution with water. The aqueous layer was decanted and the oil dissolved in a minimum of hot ethanol. On cooling, yellow crystals were obtained which were filtered and washed with a little ether. After three recrystallizations from ethanol the m. p. was con-

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[19] Wallach Festschrift, 301 (1909); *C. A.*, **5**, 883 (1911).

[20] Phenylhydrazine does not react with pyrogallol under the conditions described in the Experimental Section.

[21] Shoppee, *J. Chem. Soc.*, 269 (1936).

[22] Sachs and Barschall, *Ber.*, **34**, 2047 (1901).

[23] Calvin and Wood, THIS JOURNAL, **62**, 3152 (1940).

[24] This will form the subject of a later communication.

[25] All melting points are uncorrected.

[26] One of the Referees has pointed out that a detailed procedure for the preparation of dihydroresorcinol has been published by Thompson, "Organic Syntheses," **27**, 21 (1947). This volume was received on January 20, 1947; this paper submitted on January 9.

[27] Charcoal containing iron imparts a blue color to the product.

[28] Henle and Schupp, *Ber.*, **38**, 1372 (1905), gave the first rigorous proof for structure of the reaction product of phenylhydrazine with a 1,2,3-tricarbonyl compound. A few years earlier Sachs and Röhmer, *ibid.*, **35**, 3308 (1902), assigned a 1,3 structure for the bis-(phenylhydrazone) of 2,3,4-triketopentanetrione, but their evidence is not convincing.

stant at 186°. Borsche,[22] who prepared this substance in another way, reported 182–183°.

Preparation and Properties of 1,2,3-Cyclohexanetrione Dihydrate (II).—To a stirred solution of 32 g. of dihydropyrogallol (0.25 mole) in 250 ml. of water at 3–5°, 63.1 g. of finely powdered iodine was added in portions of 1 or 2 g. over a period of one and one-half hours.[29] After 45.2 g. of iodine had been added the solution was brown but a test for free iodine was negative; the brown color disappeared however on dilution. Freshly precipitated and washed silver chloride (0.75 mole) was then added to convert the hydriodic acid to hydrochloric acid. As the conversion took place the dark brown color faded. Next the bulk of the hydrochloric acid was neutralized with silver carbonate (0.385 mole); removal of more acid will result in reduction of the silver carbonate to metallic silver. After the evolution of carbon dioxide became very slow (twenty to thirty minutes), the silver salts were filtered off and washed with several portions of cold water. The clear yellow filtrate was then evaporated *in vacuo* below 35° until the volume was 20–30 ml. whereupon the contents set to a mass of white crystals. At this point evaporation should be stopped or the crystals will disappear and be converted to a red sirup from which no crystalline material can be isolated.

The crystals were filtered and copious amounts of ether used to rinse out the flask and wash the precipitate. The product was then stored for a day or two *in vacuo* over calcium chloride and sodium hydroxide to remove traces of adherent acid. If traces of acid remain, indicated by the formation of a pink color, the product should be ground under ether which dissolves only the colored material.

The yield of dry material, m. p. 104–105°, averages about 20 g. Repeated recrystallization from dry ethyl acetate, which results in considerable loss, raises the m. p. to 106°.

Anal. Calcd. for $C_6H_{10}O_5$: C, 44.44; H, 6.22. Found: C, 44.28; H, 6.32.

The substance has the formula of a dihydrated pyrogallol, $C_6H_6O_3 \cdot 2H_2O$, and has the following properties: It is very soluble in water and alcohol, but insoluble in ether and benzene. Silver nitrate solution gives no turbidity but is slowly reduced. Ammoniacal silver nitrate is reduced immediately. A five per cent. aqueous solution has a *p*H of 5 and gives no color with ferric chloride.

From 100 mg. of II and phenylhydrazine, 95 mg. of a red crystalline compound was obtained, m. p. 134–135°; mixed m. p. with a sample of the 1,3-bis-(phenylhydrazone) of 1,2,3-cyclohexanetrione, 131–133°.

A stream of hydrogen sulfide was passed into a solution of 0.5 g. of the substance in 10 ml. of water. Free sulfur was precipitated, and from the filtrate 0.44 g. of dihydropyrogallol, m. p. 108–110°, was recovered.

Attempts to dehydrate the substance by azeotropic distillation were unsuccessful but indicated that dehydration was accomplished by isomerization to pyrogallol.

A few mg. of II in pyridine gave a purple gray flash when heated to about 80° and after evaporation of the solvent a little impure pyrogallol, m. p. 125–130°, could be sublimed from the residue. Control experiments with pyrogallol gave about 50% recovery of impure pyrogallol of m. p. 132–135°.

Preparation of Pyrogallol Triacetate from II.—One and eighteen-hundredths g. of II was suspended in 5 ml. of acetic anhydride at 0°, and a drop of sulfuric acid added. The solution assumed a momentary pink color and warmed to about 35°. After standing overnight, the mixture was diluted with water whereupon a mass of fine white needles separated. The crystals were filtered off, washed with water and recrystallized from ethanol. The crystalline product, m. p. 160.5–162°, weighed 0.5 g.

One gram of pyrogallol treated similarly gave 1.49 g. of the triacetate, m. p. 162–163°.[30] The mixed melting point was 160.5–162°.

The Preparation of $(C_6H_7O_3)_n$.—Sixty-four grams of dihydropyrogallol (0.5 mole) was dissolved in 1 liter of water containing 2 drops of ferric chloride solution (10%). To the stirred solution 54 ml. of "30% hydrogen peroxide" (0.3164 g. of hydrogen peroxide per ml.) was added dropwise, whereupon the color of the dihydropyrogallol-ferric ion-complex reappeared. Considerable heat was evolved, but the rate of addition was so adjusted that the internal temperature was 45°. The pale yellow solution (*p*H 2) was concentrated *in vacuo* at 30° to about 75 ml. whereupon the residue set to a crystalline mass, which was filtered off and dried *in vacuo*. Twenty-six g. of slightly yellow product, m. p. 85–88°, was obtained. Recrystallization from ethyl acetate-ether gave 10 g. of white crystals, m. p. 169–170°, dec.

Anal. Calcd. for $C_6H_7O_3$: C, 56.68; H, 5.51. Found: C, 56.55, 56.62; H, 5.57, 5.61. Molecular weight, calcd.: 127. Found: 120 (by isothermal distillation against azobenzene in acetone).

Treatment of this product with phenylhydrazine and a few drops of acetic acid gave a red precipitate *immediately*. The mixture was warmed overnight on the steam-bath and worked up in the usual manner. On recrystallizing from ethanol orange crystals, m. p. 187°, were obtained that gave no depression with the tris-(phenylhydrazone) of 1,2,3-cyclohexanetrione.

The new product does not react with iodine nor hydrogen sulfide, but has not been investigated further.

Acknowledgment.—We are indebted to Dr. Al Steyermark and his staff for the microanalyses and molecular weight determination reported in this paper.

Summary

The preparation of a new ene-diol, dihydropyrogallol, is described.

Oxidation of dihydropyrogallol with iodine yields 1,2,3-cyclohexanetrione dihydrate, a ketonic isomer of pyrogallol; while oxidation with hydrogen peroxide in the presence of a trace of ferric ion yields a product ($C_6H_7O_3$) of unknown constitution.

Nutley, N. J. Received January 12, 1948

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(29) Addition of a few ml. of carbon tetrachloride, or any other indifferent organic solvent, accelerates the reaction. This is probably due to the better solubility of iodine in the organic solvent.

(30) The literature records melting points of 162–163, 165, and 172–173° for pyrogallol triacetate.