3. The facts that the halogen becomes affected in this manner only when it is in Rings B or C, and therein only when in Position 3, are interpreted as indicating that of the four rings in the acridyls only these two are capable of undergoing a tautomeric change from benzenoid (VII) to the more reactive quinonoid state (VIII). The conclusion is drawn that in the acridyls, in common with other free radicals, the acquisition of the property of selective absorption on the one hand, and on the other, their capacity to exist tautomerically in the quinonoid state, are concomitant phenomena.

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENTS OF PHARMACOLOGY AND TROPICAL MEDICINE, HARVARD MEDICAL SCHOOL]

SOME DERIVATIVES OF GALLIC ACID AND PYROGALLOL

BY WALTER G. CHRISTIANSEN

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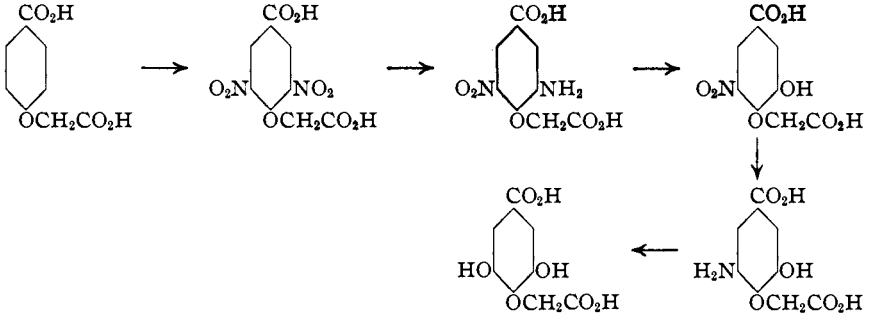
Studies which are being made in this Laboratory necessitated the preparation of a number of polyhydric phenols of the gallic acid and pyrogallol series. Some of these compounds are new and are reported in this paper together with a few general observations.

Esterification of gallic acid by the alcohol-hydrogen chloride process proceeds very smoothly when methyl[1] and *n*-butyl alcohols are employed; excellent yields are obtained and unchanged gallic acid is not recovered. However, in the case of the *iso*propyl compound 40% of the gallic acid remains unesterified.

Gallic acid reacts with chloro-acetic acid in aqueous solution containing three molecular equivalents of sodium hydroxide to form a dihydroxy-carboxyphenoxyacetic acid. That the condensation involves one of the hydroxyl groups and not the carboxyl group of the gallic acid molecule is evinced by the facts that the reaction product is not hydrolyzed by boiling sodium hydroxide and does yield a dimethyl ester when treated with absolute methyl alcohol and hydrogen chloride. If the product were a trihydroxybenzoyl-glycolic acid, gallic acid would be obtained by alkaline hydrolysis, and the only ester obtainable would be a monomethyl ester.

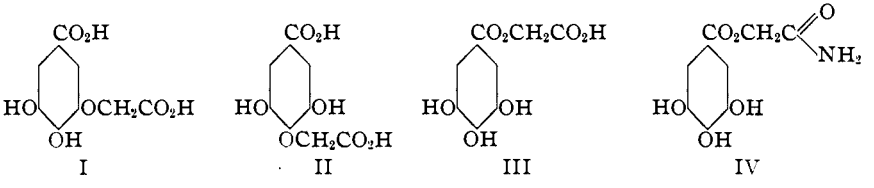
In an attempt to determine whether one of the hydroxyl groups in the *meta* positions to the carboxyl group of gallic acid or the one in the *para* position takes part in this reaction, the preparation of 2,6-dihydroxy-4-carboxyphenoxyacetic acid was undertaken by the process represented by the following reactions.

[1] Methyl gallate was prepared according to the directions of Will, *Ber.*, **21**, 2022 (1888).



This failed because, when a second nitro group is introduced into 2-nitro-4-carboxyphenoxyacetic acid, the main reaction is one in which the carboxyl group is replaced by a nitro group to form 2,4-dinitro-phenoxyacetic acid; only a trace of 2,6-dinitro-4-carboxyphenoxyacetic acid[2] could be isolated. Moreover, reduction of 2-nitro-4-carboxyphenoxyacetic acid or its dimethyl ester does not yield the corresponding amino compounds; an internal anhydride is the sole product.[3]

However, the behavior of an aqueous sodium hydroxide solution of the reaction product at room temperature in contact with air indicates that this compound is 2,3-dihydroxy-5-carboxyphenoxyacetic acid (I) and not 2,6-dihydroxy-4-carboxyphenoxyacetic acid (II). Compounds represented by Formulas I and II are substitution products of catechol and resorcinol,



respectively. If the substance under discussion has Structure I, it will undergo atmospheric oxidation in aqueous alkaline solution more rapidly than resorcinol does,[4] but less rapidly than catechol.[5] On the other hand, if Structure II were correct, an alkaline solution of the material would remain practically colorless.[4,5] When a sodium hydroxide solution of the material in question is agitated gently in the presence of air it becomes brown; the rate of oxidation is less than when gallic acid or catechol is used but many times greater than when resorcinol is employed. Structure I is, therefore, correct.

When gallic acid is treated with ethyl chloro-acetate, in the presence of one molecular equivalent of sodium hydroxide, much unchanged gallic

[2] Christiansen, THIS JOURNAL, **47**, 1158 (1925).

[3] Christiansen, *ibid.*, **48**, 461 (1926).

[4] Aqueous sodium hydroxide solutions of resorcinol become yellow very slowly.

[5] The introduction of a carboxyl group into a polyhydric phenol decreases the rate of oxidation; alkaline solutions of gallic acid oxidize more slowly than those of pyrogallol.

acid and an isomer of I are obtained. The latter is either II or 3,4,5-trihydroxybenzoyl-glycolic acid (III). When this compound is hydrolyzed in boiling aqueous sodium hydroxide, gallic acid is secured; when it is exposed in alkaline solution to the air at room temperature, it oxidizes at about the same rate as the alkyl gallates, that is, faster than I does. Therefore, the reaction product is represented by Formula III.

Gallic acid reacts with chloro-acetamide in the presence of one molecular equivalent of sodium hydroxide to yield mainly 3,4,5-trihydroxybenzoyl-glycol amide, IV. Hydrolysis of IV yields ammonia and gallic acid; in aqueous alkaline solution IV oxidizes more rapidly than the alkyl gallates.

In the presence of two molecular equivalents of sodium hydroxide, gallic acid reacts with one molecular equivalent of benzoyl chloride to give a mixture of gallic acid and its mono- and dibenzoyl derivatives; the yield of the dibenzoyl derivative is greater than that of the mono- substitution product. The fact that the second benzoyl group enters the molecule at least as readily as the first indicates that the two hydroxyl groups in the *meta* positions to the carboxyl group are those which are involved in this reaction, and that the products are 3-benzoyl- and 3,5-dibenzoyl-gallic acid.

2,3-Dihydroxyphenoxyacetic acid is obtained when pyrogallol is treated with either chloro-acetic acid or chloro-acetamide in the presence of two or one molecular equivalents of sodium hydroxide, respectively. When the amide is used, ammonia is evolved throughout the experiment, and the melting point of the product is about 5° higher than when the acid is used. The two specimens of this compound give the same methyl ester. Alkaline solutions of this dihydroxyphenoxyacetic acid and its methyl ester oxidize more rapidly in the air than a similar solution of catechol but less rapidly than does one of pyrogallol. The acid is, therefore, 2,3-dihydroxyphenoxyacetic acid and not the 2,6-isomer.

2,3,4-Trihydroxybenzaldehyde reacts readily with sulfanilic acid, anthranilic acid, 2-methyl-5-sulfo-aniline, and arsphenamine to give benzylidine compounds.

Experimental Part

***iso*Propyl Gallate.**—A suspension of 25 g. of powdered gallic acid in 105 cc. of anhydrous *iso*propyl alcohol is cooled and saturated with dry hydrogen chloride. The major part of the solid dissolves, and then a white precipitate forms. After the reaction mixture has stood at room temperature overnight, it is refluxed for four hours; the solid dissolves completely. When the solution is cooled and resaturated with hydrogen chloride, the precipitate reappears. The following morning the solvent is removed by evaporation, the residue is suspended in 25 cc. of water and extracted thrice with 50cc. portions of ether. The extract is treated with a small quantity of barium carbonate, clarified and evaporated to dryness. By refluxing the crude reaction product with chloroform and removing the insoluble material by filtration of the hot mixture,

10 g. of gallic acid is recovered. The chloroform extract yields 6 g. of crystalline *iso*-propyl gallate when it is cooled in the ice box. An additional 5.5 g. of the ester may be secured by evaporating the chloroform mother liquor; this crop is slightly impure (m. p., 118–120°).

*iso*Propyl gallate is a white solid, melts at 123–124.5° and is soluble in water, alcohol, ether, amyl acetate, acetone, glacial acetic acid and hot chloroform but insoluble in benzene.

Anal. Calcd. for $C_{10}H_{12}O_5$: C, 56.6; H, 5.7. Found: C, 56.6; H, 6.1.

n-Butyl Gallate.—The esterification is performed as in the case of the *iso*propyl compound. When the ether solution of the reaction product is treated with barium carbonate and evaporated to dryness, 30 g. (90%) of nearly pure *n*-butyl gallate is obtained, which after purification from chloroform forms white crystals; m. p., 133–134°. It is insoluble in benzene, slightly soluble in cold water and chloroform but very soluble in ether, alcohol, acetone and amyl acetate.

Anal. Calcd. for $C_{11}H_{14}O_5$: C, 58.4; H, 6.2. Found: C, 58.6; H, 6.3.

2,3-Dihydroxy-5-carboxyphenoxyacetic Acid.—A solution of 25 g. of gallic acid and 12.5 g. of chloro-acetic acid in 150 cc. of water and 44 cc. of 10 *N* sodium hydroxide solution is refluxed for three hours in an atmosphere of nitrogen. After the solution has been acidified with 45 cc. of hydrochloric acid, it is placed in the ice box and stirred occasionally for 48 hours. The crude product (17.4 g.) is recrystallized twice from water; 11.9 g. of pure material is obtained.

2,3-Dihydroxy-5-carboxyphenoxyacetic acid is a white, microcrystalline solid which melts at 262° when it is heated very gradually; if the temperature is raised rapidly a pasty mass is formed at 193–195° which quickly changes to a solid that melts at 270°. When this compound has been dried at 105°, it sinters at 246–250° and melts at 266–268°. It is soluble in alcohol, acetone, warm glacial acetic acid and methyl acetate, slightly soluble in ether and cold water and insoluble in chloroform, benzene and petroleum ether.

Anal. Calcd. for $C_9H_8O_7$: C, 47.4; H, 3.54. Found: C, 47.1; H, 3.73.

Boiling 2.5 *N* sodium hydroxide solution does not hydrolyze this substance; 91% of the material is recovered unchanged by the addition of acid. The product, after being dried at 105°, sinters at 245–246° and melts at 265–272°; it contains 47.1% of carbon and 3.71% of hydrogen.

Methyl 2,3-Dihydroxy-5-carbomethoxyphenoxyacetate.—A solution of 5 g. of 2,3-dihydroxy-5-carboxyphenoxyacetic acid in 50 cc. of absolute methyl alcohol is treated with hydrogen chloride according to the procedure adopted for the preparation of *iso*propyl gallate. The crude ester (5.2 g.) is dissolved in 50 cc. of absolute methyl alcohol and reprecipitated with dry hydrogen chloride. When the resulting paste has stood in an ice-bath for two hours, the white solid is collected on a filter, washed thrice with cold methyl alcoholic hydrochloric acid, dried in a vacuum over sodium hydroxide and then at 70° for two hours. The yield of pure ester is 2 g.; an additional 2.4 g. of slightly impure material is obtained by evaporating the alcoholic mother liquor to dryness.

Methyl 2,3-dihydroxy-5-carbomethoxyphenoxyacetate is a white, microcrystalline solid which melts at 143–145°; it is soluble in methyl and ethyl alcohols, ether, glacial acetic acid, acetone, methyl acetate, hot benzene and water, slightly soluble in cold water and insoluble in chloroform, petroleum ether and cold benzene.

Anal. Calcd. for $C_{11}H_{12}O_7$: C, 51.6; H, 4.72. Found: C, 51.3; H, 5.00.

3,4,5-Trihydroxybenzoyl-glycolic Acid.—A solution of 25 g. of gallic acid in 150 cc. of water and 14 cc. of 10 *N* sodium hydroxide solution is refluxed in an atmosphere

of nitrogen with 16.5 g. of ethyl chloro-acetate. The latter remains as an insoluble oil which gradually disappears; at the end of one and a half hours, the solution is homogeneous. The refluxing is continued for an additional one and a half hours, and then the reaction mixture is acidified with 15 cc. of hydrochloric acid and placed in the ice box for several days. The white solid (11.5 g.) which separates is slightly impure gallic acid; by recrystallization from water, 10 g. of pure gallic acid is recovered.

The mother liquor from the crude gallic acid is evaporated to 50–60 cc. on a steam-bath and placed in the ice box for four days. The white precipitate is collected on a filter and washed with cold water; 10.5 g. of material (m. p., 205–207°) is obtained. The latter is extracted by boiling with four 50cc. portions, one 30cc. portion and one 100cc. portion of ethyl *n*-butyrate. By evaporating the last extract to dryness 0.85 g. of pure 3,4,5-trihydroxybenzoyl-glycolic acid is obtained. When the first extract stands at room temperature overnight, it deposits 0.7 g. of crude gallic acid; the remaining four extracts remain homogeneous. The mother liquor from the small quantity of gallic acid and the remaining extracts are combined, evaporated to about 80 cc. and left at room temperature overnight; 5 g. of practically pure benzoyl compound (m. p., 214.5–215.5°) crystallizes. Only 0.75 g. of impure material could be isolated from the mother liquor from the benzoyl compound.

3,4,5-Trihydroxybenzoyl-glycolic acid is a white solid which melts at 216°; it is soluble in water, alcohol, acetone and methyl acetate, slightly soluble in ether and glacial acetic acid and insoluble in chloroform and benzene. When sodium bicarbonate solution is added to an aqueous solution of this substance, carbon dioxide is evolved.

Anal. Calcd. for $C_9H_8O_7$: C, 47.4; H, 3.54. Found: C, 47.8; H, 3.82.

By hydrolyzing this compound with alkali in an atmosphere of nitrogen, a 57% yield of crude gallic acid is obtained. After recrystallization from water, the hydrolysis product contains 49.1% of carbon and 3.87% of hydrogen as against 49.4% and 3.56%, respectively.

3,4,5-Trihydroxybenzoyl-glycolamide.—A solution of 25 g. of gallic acid and 12.5 g. of chloro-acetamide in 150 cc. of water and 14 cc. of 10.4 *N* sodium hydroxide solution is refluxed for three hours in an atmosphere of nitrogen, acidified with 15 cc. of hydrochloric acid and cooled to room temperature overnight. The white solid (9 g.) which separates is recrystallized from water; 7.7 g. of pure 3,4,5-trihydroxybenzoyl-glycolamide is obtained.

This substance is a white, crystalline solid which melts at 231–232°; it is soluble in alcohol, acetone and hot water, but insoluble in ether, chloroform, amyl acetate and cold water.

Anal. Calcd. for $C_9H_9O_6N.1.5H_2O$: H_2O, 10.6. Found: 11.5. Calcd. for $C_9H_9O_6N$: C, 47.6; H, 4.00; N, 6.21. Found: C, 47.6; H, 4.38, 4.22; N, 6.66, 6.37, 6.44.

Alkaline hydrolysis of this compound in an atmosphere of nitrogen produces gallic acid; ammonia is evolved immediately and the yield is 68%. After recrystallization from water, the hydrolysis product contains 48.9% of carbon and 3.85% of hydrogen as against 49.4% and 3.56%, respectively.

When a solution of 0.3263 g. of this benzoyl-glycolamide (dried) and 40 g. of sodium hydroxide in 300 cc. of water is distilled into hydrochloric acid, 0.0220 g. of ammonia is evolved as against 0.0244 g.

3-Benzoyl- and 3,5-Dibenzoyl-gallic Acid.—A solution of 15 g. of gallic acid in 135 cc. of water and 15.75 cc. of 10.4 *N* sodium hydroxide solution is stirred mechanically with 10.5 g. of benzoyl chloride in an atmosphere of nitrogen for six and a half hours; the reaction flask is kept in a water-bath at 30°. After 14 cc. of hydrochloric acid has been added, the reaction mixture is cooled in the ice box overnight. The crude product (19.9 g.) is a mixture of gallic acid and its mono- and dibenzoyl derivatives.

It is extracted with 75 cc. of boiling alcohol, and the residue is washed with 25 cc. of hot alcohol. After the combined filtrates have been cooled in ice, 100 cc. of cold water is added gradually during stirring, and the mixture is left in the ice box overnight. The white precipitate is collected on a filter and washed with 30 cc. of cold 50% alcohol; this fraction (9 g.) is crude 3,5-dibenzoyl-gallic acid. An additional 100 cc. of water is added to the alcoholic mother liquor and washings, and the cloudy solution is cooled in the ice box overnight. The solid which separates is a mixture of the mono- and dibenzoyl compounds; after it has been washed with 50 cc. of 30% alcohol and dried, it weighs 6.3 g. By evaporating the alcoholic filtrate and washings from the second fraction to dryness, 3.2 g. of slightly impure gallic acid is recovered; when this fraction is recrystallized from water 2.4 g. of pure gallic acid is obtained.

The first fraction is purified by extracting with 60 cc. of chloroform at room temperature, 75 cc. of boiling chloroform and 50 cc. of boiling 50% alcohol. When the insoluble material (5.7 g.) is recrystallized from 25 cc. of alcohol, 4.5 g. of 3,5-dibenzoyl-gallic acid is obtained as stout, colorless needles. This substance melts gradually at 218–221° without darkening; it is soluble in ether and acetone, slightly soluble in alcohol and insoluble in water and chloroform.

Anal. Calcd. for $C_{21}H_{14}O_7$: C, 66.7; H, 3.73. Found: C, 66.3; H, 4.00.

By hydrolyzing 2.5 g. of the dibenzoyl-gallic acid with alkali in an atmosphere of nitrogen 1.35 g. of benzoic acid and 0.3 g. of gallic acid are obtained

The second fraction, that is, the mixture of mono- and dibenzoyl compounds, is dissolved in 40 cc. of hot alcohol; the solution is filtered, evaporated to 20 cc., treated with 30 cc. of hot water and cooled gradually. After the mixture has been in the ice box overnight, the white precipitate is collected on a filter and washed with water; this material (2.8 g.) is still impure. When more water is added to the alcoholic filtrate, 2.8 g. of 3-benzoyl-gallic acid is obtained as a white solid. The monobenzoyl compound melts at 224–227° with darkening and evolution of a gas; when it is mixed with the dibenzoyl compound, the melting point is 206–216°. It is very soluble in alcohol but insoluble in water.

Anal. Calcd. for $C_{14}H_{10}O_6$: C, 61.3; H, 3.67. Found: C, 61.9; H, 4.01.

HYDROLYSIS.—When 1.25 g. of the monobenzoyl-gallic acid is hydrolyzed by the method described for the dibenzoyl compound, 0.5 g. (90%) of pure benzoic acid and 0.2 g. of pure gallic acid are obtained.

2,3-Dihydroxyphenoxyacetic Acid.—A. A solution of 17 g. of pyrogallol and 12.5 g. of chloro-acetic acid in 150 cc. of water and 30 cc. of 10 *N* sodium hydroxide solution is refluxed in an atmosphere of nitrogen for three hours, acidified with 30 cc. of hydrochloric acid and placed in the ice box. Six g. of slightly impure 2,3-dihydroxyphenoxyacetic acid is obtained; by recrystallization from water this substance is secured as slender needles (m. p., 147.5–149°). It is soluble in alcohol, acetone, glacial acetic acid, methyl acetate and hot water, slightly soluble in ether and cold water, and insoluble in chloroform, benzene and petroleum ether.

Anal. Calcd. for $C_8H_8O_5$: C, 52.2; H, 4.38. Found: C, 51.6; H, 4.40.

B. The procedure is identical with that described above except that 12.5 g. of chloro-acetamide and only 15 cc. of 10 *N* aqueous sodium hydroxide are used; only 15 cc. of hydrochloric acid is used for the acidification. Ammonia is evolved during the entire experiment. Only 4.3 g. of crude reaction product is obtained; the yield of pure, white needles is 3.7 g. The material obtained by this method melts at a slightly higher temperature than that obtained by Method A_1 that is, at 153–155.5°.

Anal. Found: C, 52.3; H, 4.49.

Methyl 2,3-Dihydroxyphenoxyacetate.—Two g. of 2,3-dihydroxyphenoxyacetic

acid (prepared by Method **B**) is esterified with absolute methyl alcohol and hydrogen chloride. The ester crystallizes from the cold alcoholic solution; it is collected on a filter and washed with 25 cc. of cold absolute methyl alcohol. Thus, methyl 2,3-dihydroxyphenoxyacetate is obtained as white, microscopic plates which melt at 156–157.5°; the yield is 0.93 g. The starting material melts at 153–155.5°, but a mixture of the acid and the ester melts at 138–147°. This compound is soluble in methyl alcohol at room temperature but insoluble in cold water or dilute, aqueous sodium bicarbonate; it crystallizes well from warm aqueous solutions in the form of needles.

Anal. Calcd. for $C_9H_{10}O_5$: C, 54.5; H, 5.09. Found: C, 54.1; H, 5.24.

One g. of the dihydroxyphenoxyacetic acid which has been prepared by Method **A** gives 0.25 g. of the methyl ester; the latter melts at 154.5–157° and a mixture of it with that described above melts at 154.5–158.5°.

2,3,4-Trihydroxybenzylidine-2'-methyl-5'-sulfo-aniline.—A boiling solution of 1.87 g. of 2-methyl-5-sulfo-aniline in 250 cc. of water is added to a boiling solution of 1.54 g. of 2,3,4-trihydroxybenzaldehyde in 250 cc. of water; the solution becomes yellow immediately and yields 2.9 g. of microscopic, transparent, yellow prisms when it is cooled in the ice box overnight.

This benzylidine compound does not melt below 304°; it is soluble in aqueous alkalies, hot water and hot alcohol, but insoluble in glacial acetic acid, ether, carbon disulfide, ethyl acetate, acetone, benzene, carbon tetrachloride, petroleum ether, cold water and cold alcohol. The sodium bicarbonate solution of this compound is orange.

Anal. Calcd. for $C_{14}H_{13}O_6NS$: N, 4.33; S, 9.92. Found: N, 4.66; S, 9.64.

2,3,4-Trihydroxybenzylidine-sulfanilic Acid.—This compound (2.3 g.) is prepared from 1.73 g. of sulfanilic acid and 1.54 g. of the aldehyde by the method described above. It consists of microscopic, transparent, yellow plates which do not melt below 300° and which dissolve in sodium bicarbonate to give an orange solution.

Anal. Calcd. for $C_{13}H_{11}O_6NS$: N, 4.53; S, 10.4. Found: N, 4.53; S, 10.9.

2,3,4-Trihydroxybenzylidine-anthranilic Acid.—A dull yellow powder (2.9 g.) is obtained from 1.37 g. of anthranilic acid and 1.54 g. of the aldehyde. The reaction product is extracted by refluxing for 30–45 minutes with water and filtering the hot solution. The filtrate deposits 1.35 g. of the benzylidine compound as a dull yellow powder which darkens above 200° and melts with decomposition at 252°. It is soluble in hot alcohol and glacial acetic acid and in dil. hydrochloric acid. The pale yellow acid solution gives yellow needles when an excess of hydrochloric acid is added. A sodium bicarbonate solution of the material is red.

Anal. Calcd. for $C_{14}H_{11}O_5N$: C, 61.5; H, 4.06; N, 5.13. Found: C, 60.7; H, 4.00; N, 4.89.

N,N' - Di - 2,3,4 - trihydroxybenzylidine - 3,3' - diamino - 4,4' - dihydroxy - arsenobenzene.—A slightly warm solution of 0.7 g. of 2,3,4-trihydroxybenzaldehyde in 50 cc. of water is added to a solution of 1 g. of arsphenamine in 200 cc. of water during mechanical stirring. The yellow solution becomes red rapidly and gradually changes to a jelly. After the mass has been stirred for an hour, it is allowed to stand for one and a half hours. The addition of 5 cc. of saturated aqueous sodium bicarbonate solution causes the transparent, red jelly to change to a suspension of a gelatinous, red solid in a colorless liquid. The solid is collected by centrifuging, washed thrice with water and twice with alcohol and dried in a vacuum; the yield is 1.25 g. of a brick-red powder. This dibenzylidine derivative of arsphenamine is insoluble in water, alcohol and ether; it dissolves readily in aqueous sodium hydroxide, but the solution oxidizes rapidly; it is insoluble in dil. hydrochloric acid but the color of the solid changes from red to yellow.

Anal. Calcd. for $C_{26}H_{20}O_8N_2As_2$: N, 4.39; As, 23.5. Found: N, 4.50; As, 23.4.

The assistance of Henry W. George in the preparation of the alkyl gallates is gratefully acknowledged.

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Summary

The following derivatives of gallic acid and pyrogallol are described: *iso*propyl gallate; *n*-butyl gallate; 2,3-dihydroxy-5-carboxyphenoxyacetic acid; methyl 2,3-dihydroxy-5-carbomethoxyphenoxyacetate; 3,4,5-trihydroxybenzoyl-glycolic acid; 3,4,5-trihydroxybenzoyl-glycolamide; 3-benzoyl-gallic acid; 3,5-dibenzoyl-gallic acid; 2,3-dihydroxyphenoxyacetic acid; methyl 2,3-dihydroxyphenoxyacetate; 2,3,4-trihydroxybenzylidine-2′-methyl-5′-sulfo-aniline; 2,3,4-trihydroxybenzylidine-sulfanilic acid; 2,3,4-trihydroxybenzylidine-anthranilic acid; N,N′-di-2,3,4-trihydroxybenzylidine-3,3′-diamino-4,4′-dihydroxy-arsenobenzene.

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[CONTRIBUTION FROM THE DEPARTMENTS OF PHARMACOLOGY AND TROPICAL MEDICINE, HARVARD MEDICAL SCHOOL]

THE REACTION OF SOME POLYHYDRIC PHENOLS WITH SODIUM ANTIMONYL TARTRATE

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Although antimony derivatives of polyhydric phenols are fairly well known, they have been ignored almost completely in chemotherapeutic investigations. In a brief discussion of antimonials derived from hydroxy compounds, Thomson and Cushny[1] dismiss them with a few words. While the studies reported herein were in progress, indications have appeared that the chemotherapeutic properties of antimony derivatives of compounds of the catechol series are being examined elsewhere;[2] in this Laboratory, attention has been concentrated on trihydroxybenzene derivatives.

Gallic acid and pyrogallol both react with alkali antimonyl tartrates in aqueous solution to give antimony derivatives of these phenols,[3] and they also afford excellent opportunities for the preparation of other polyhydric phenols by the introduction of different organic groups. Evidently, therefore, a means is at hand whereby the relation between the structure of the phenol and its reactivity with respect to an alkali antimonyl tartrate

[1] Thomson and Cushny, *Proc. Roy. Soc.* (*London*) **82B**, 252 (1910).

[2] (a) U. S. pat. 1,549,154 (1925); Brit. pat. 213,285 (1923). (b) Uhlenhuth, Kuhn and Schmidt, *Deut. med. Wochschr.*, **50**, 1288 (1924); *Arch. Schiffs-Tropen-Hyg.*, **29**, 623 (1925).

[3] (a) Rosing, *Compt. rend.*, **46**, 1140 (1858). (b) Causse, *Ann. chim. phys.*, (7) **14**, 551, 560 (1898).