

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

**2'-HYDROXY-3'-METHYLBENZOYL-3,4,5,6-
TETRACHLOROBENZOIC-2-ACID, ISO-ORTHO-
CRESOL-TETRACHLOROPHTHALEIN AND SOME OF THEIR
DERIVATIVES**

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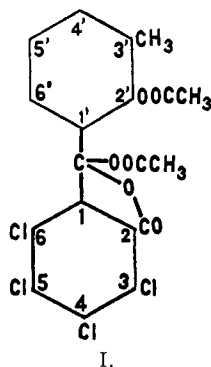
2'-Hydroxy-3'-methyl-benzoyl-3,4,5,6-tetrachlorobenzoic-2-acid was made by the method of Ullmann and Schmidt,² from *o*-cresol and tetrachlorophthalic acid anhydride and crystallized first from acetic acid and then from xylene and benzene. It melted sharply at 219–220°. As it gives *iso-o*-cresol-tetrachlorophthalein with *o*-cresol, it is called the intermediate acid.

*Anal.*³ Subs., 0.1958, 0.2015: AgCl, 0.2847, 0.2937. Calcd. for C₁₅H₈Cl₄O₄: Cl, 36.01. Found: 35.97, 36.06.

DIACETATE.—This was prepared by heating the pure acid with acetic anhydride and freshly fused sodium acetate. It was crystallized twice from acetone when the colorless crystals melted sharply at 182°.

Anal. Subs., 0.1453, 0.1899: AgCl, 0.1760, 0.2247. Calcd. for C₁₉H₁₂Cl₄O₆: Cl, 29.67. Found: 29.97, 29.27.

The analyses show that the substance is the diacetate and as it is colorless it is given the lactone formula (I).



The diacetate is insoluble in water, ether, ethanol, carbon tetrachloride and petroleum ether, but is readily soluble in acetone and chloroform. It is not hydrolyzed even on long continued boiling with water. It dissolves in cold 1% aqueous sodium hydroxide with the development of a yellow color owing to hydrolysis. When this solution is heated, the sodium salt of the trichloro-xanthone acid (see below) is formed.

¹ Work done in partial fulfilment of the requirements for the degree of Bachelor of Chemistry by Carlisle Schade, holder of the Grasselli Undergraduate Scholarship in Chemistry at Cornell University, 1924-1925.

² Ullmann and Schmidt, *Ber.*, **52**, 2098 (1919).

³ International Atomic Weights for 1925 are used in the calculations in this paper. *THIS JOURNAL*, **47**, 600 (1925).

ANHYDRIDE.—Once or twice when attempting to prepare the diacetate of the acid, by boiling it with acetic anhydride and a few drops of concd. sulfuric acid for about 15 minutes, this product was obtained. The solution became red, but on cooling colorless crystals separated. These were filtered off and recrystallized from benzene. The colorless crystals melted sharply at 242.5°.

Anal. Subs., 0.1308, 0.1320: AgCl, 0.2043, 0.2054. Calcd. for $C_{16}H_8Cl_4O_4 - H_2O$: Cl, 37.73. Found: 38.64, 38.47.

It was found to be soluble in methyl and ethyl acetates and readily soluble in chloroform. It is insoluble in water, ether, methanol and ethanol, carbon tetrachloride and petroleum ether (b. p., 60–70°).

The analyses show that water has been abstracted from the acid in the ratio of one molecule of water to one of the acid. The product is not an ordinary anhydride, however, since it is not hydrolyzed back to the acid when heated with solutions of alkalis. Further attempts to prepare this substance in larger quantity failed. The diacetate resulted in every case.

ZINC SALT.—This was prepared by boiling the acid and water with an excess of zinc carbonate and filtering the hot solution. The zinc salt crystallized out of the filtrate on cooling.

Anal. Subs., I, 0.3147; II, 0.2685; III, 0.2621; IV, 0.1260: loss at 105°, (I) 0.0190; AgCl, (II) 0.3373, (III) 0.3305; ZnSO₄, (IV) 0.0222. Calcd. for $C_{30}H_{14}Cl_8O_8 + 3H_2O$: H₂O, 5.97; Cl, 31.34; Zn, 7.22. Found: H₂O, 6.04; Cl, 31.08; 31.20; Zn, 7.14.

The anhydrous salt was also analyzed.

Anal. Subs., 0.1756, 0.1971: AgCl, 0.2373, 0.2645. Calcd. for $C_{30}H_{14}Cl_8O_8Zn$: Cl, 33.32. Found: 33.43, 33.20.

When powdered, the crystallized salt has a light yellow color, while the anhydrous salt is brilliant yellow. The salt is very soluble in ether, ethanol, methanol, acetone and chloroform, easily soluble in benzene, slightly soluble in water and insoluble in petroleum ether.

BARIUM SALT.—This was prepared in the same way as the zinc salt and crystallized from hot water.

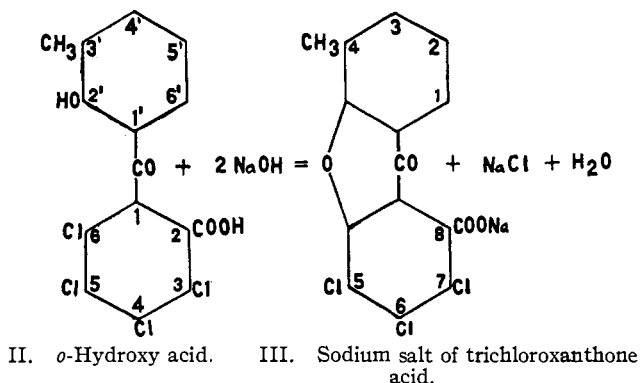
Anal. Subs., 0.2494: loss at 105°, 0.0385. Subs., 0.1754 (dry): BaSO₄, 0.0432. Calcd. for $C_{30}H_{14}Cl_8O_8Ba + 9.5 H_2O$: H₂O, 15.64. Found: 15.44. Calcd. for $C_{30}H_{14}O_8Cl_8Ba$: Ba, 14.88. Found: 14.49.

The results of the analyses of the zinc and barium salts show that the acid acts as a monobasic acid and that it has the normal molecular weight indicated by its simplest formula.

Sodium Salt of 4-Methyl-5,6,7-trichloro-xanthone-8-carboxylic Acid.—This salt was made by the method of Ullmann and Schmidt,² by heating the intermediate acid with a 7% aqueous sodium hydroxide solution. The solution became reddish-blue and the colorless sodium salt of the trichloro-xanthone acid separated. It was filtered off and washed with hot water until free from color and alkali. It was then recrystallized twice from a large volume of hot water.

Anal. Subs. (dry), 0.1448, 0.1769: Na₂SO₄, 0.0259, 0.0328. Calcd. for $C_{16}H_6O_4Cl_3Na$: Na, 6.06. Found: 5.79, 6.03.

The sodium salt crystallized in small, colorless crystals that are insoluble in methanol and ethanol, ether, chloroform and benzene. It is only slightly soluble in water. The reaction may be represented as follows.



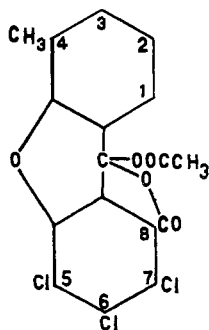
It was found that a 7% aqueous solution of sodium hydroxide was not required for this reaction, but that a 0.5% aqueous solution of sodium hydroxide or even a 10% aqueous solution of sodium carbonate will bring about the reaction on boiling. The formation of this salt of the trichloro-xanthone acid proves the *ortho* position of the hydroxyl group in the intermediate acid.

4-Methyl-5,6,7-trichloroxanthone-8-carboxylic Acid.—This acid was prepared by suspending some of the sodium salt in water, adding an excess of dil. hydrochloric acid and boiling the mixture until the sodium salt was decomposed. The free trichloro-xanthone acid was filtered off, dried and recrystallized thrice from 95% ethanol. The acid forms light, fluffy crystals melting at 269–270°. The crude acid melted at 285–287° and when recrystallized from a mixture of acetone and benzene or from methyl-ethyl ketone it melted at 286–289°.

Anal. Subs. (dry), 0.1601, 0.2176: AgCl, 0.1931, 0.2622. Calcd. for C₁₅H₇Cl₃O₄: Cl, 29.76. Found: 29.84, 29.81.

MONOACETATE.—The trichloro-xanthone acid gave a monoacetate when acetylated with acetic anhydride and sodium acetate. The product was crystallized by pouring its solution in methanol into ether. It melts with decomposition at 275–280°. The weight lost on heating to 120° was negligible.

Anal. Subs. (dry), 0.1555, 0.1320: AgCl, 0.1691, 0.1431. Calcd. for C₁₇H₉Cl₃O₅: Cl, 26.63. Found: 26.90, 26.82.



IV. Monoacetate.

It is soluble in methanol and in acetic acid and slightly soluble in ethyl and *n*-propyl alcohols, it is insoluble in other organic solvents.

The formation of a monoacetate shows that the trichloro-xanthone acid, like other γ -ketone acids, reacts in the tautomeric, lactone form.

We were unable to obtain the methyl ester of 4-methyl-5,6,7-trichloro-xanthone-8-carboxylic acid by the catalytic method of esterification. This is in accord with the Victor Meyer ester rule.

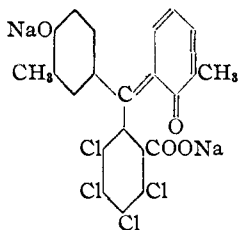
Iso-*o*-Cresol-tetrachlorophthalein.—This was prepared by the method of Orndorff and Patel⁴ and crystallized twice from methanol. The product melted with decomposition at 258–260°. It dissolved in dilute alkalis forming a deep blue solution. The reaction showing its formation has already been given by Orndorff and Patel.⁴

Anal. Subs., 0.1510, 0.2129: AgCl, 0.1803, 0.2521. Calcd. for C₂₂H₁₄Cl₄O₄: Cl, 29.31. Found: 29.53, 29.29.

DISODIUM SALT.—Six g. of the isophthalein dissolved in 400 cc. of absolute alcohol was added to a solution of 2 g. of sodium in 100 cc. of absolute alcohol and the solution boiled for several hours. When cold, the solution was poured into 2 liters of absolute ether and allowed to stand for several days. A dark blue mass of crystals separated. These were filtered off, dried at 120° and analyzed.

Anal. Subs., 0.1489, 0.1345, 0.1839: AgCl, 0.1291; Na₂SO₄, 0.0579, 0.0761. Calcd. for C₂₂H₁₂Cl₄O₄Na₂ + 2NaOC₂H₅: Cl, 21.36; Na, 13.85. Found: Cl, 21.44; Na, 13.94, 13.40.

The disodium salt dissolves in water forming a red solution which changes to blue on the addition of alkali. The salt is soluble in water and in ethanol. It is insoluble in ether. As it is a colored compound it is given the *o*-quinoid structure.⁵



V. Disodium salt.

DIACETATE.—Ten g. of the pure isophthalein was dissolved in 100 cc. of boiling acetic anhydride. After this solution had cooled, several drops of concd. sulfuric acid were added and the solution was again boiled. On standing overnight a mass of crystals separated. These were crystallized from a mixture of methanol and benzene and then from ethyl acetate; m. p., 224–227°.

Anal. Subs., 0.2397, 0.1380: AgCl, 0.2433, 0.1401. Calcd. for C₂₆H₁₈Cl₄O₆: Cl, 24.97. Found: 25.11, 25.12.

The diacetate is soluble in chloroform and in benzene, sparingly soluble in methanol and ethanol and in ether. It is insoluble in water and in 4% aqueous solution of sodium hydroxide and is only slightly hydrolyzed by the latter at room temperature. Concd. sulfuric acid hydrolyzes it at once with the development of a deep red color which changes

⁴ Orndorff and Patel, *THIS JOURNAL*, **47**, 863 (1925).

⁵ See Orndorff and Barrett, *ibid.*, **46**, 2483 (1924).

to the deep blue of the isophthalein on the addition of alkali. The diacetate is a colorless compound and it is given the lactone formula similar to that of the isophthalein.⁴

DIMETHYL ETHER.—Seven g. of the isophthalein was dissolved in 400 cc. of methanol. To the boiling solution was added slowly a solution of 2 g. of sodium in 100 cc. of methanol. The color changed to a light yellow, orange, red, green and finally to a deep blue. The mixture was boiled for several hours and then 100 g. of methyl iodide was added in small portions. After several hours' boiling the color changed to a light orange. About 100 cc. of methanol was distilled and the solution set aside. The dimethyl ether crystallized and was filtered off. It was purified by crystallization from benzene. It melted with decomposition at 261–264°.

Anal. Subs. (dry), 0.1807, 0.1492; AgCl, 0.2077, 0.1682. Calcd. for C₂₄H₁₃Cl₄O₄: Cl, 27.70. Found: 28.43, 27.89.

This dimethyl ether is a colorless substance, soluble in benzene, slightly soluble in methanol and ethanol and insoluble in ether, chloroform and water. It dissolves in warm, concd. sulfuric acid forming a red solution. When this solution is diluted with water and alkali is added, a deep blue color appears showing that the ether has been hydrolyzed. It is insoluble in cold, 4% aqueous sodium hydroxide and a hot alcoholic solution of sodium hydroxide hydrolyzes it but slowly. Since the dimethyl ether is colorless it is given the lactone structure similar to the isophthalein.⁴

Summary

1. 2'-Hydroxy-3'-methylbenzoyl-3,4,5,6-tetrachlorobenzoic-2-acid has been made. It has been shown that it combines with *o*-cresol to form iso-*o*-cresol-tetrachlorophthalein. It is hence called the intermediate acid.

2. Tautomeric derivatives of the 2'-hydroxy-3'-methylbenzoyl-4,3,5,6-tetrachloro-2-acid have been made. The diacetate is a derivative of the lactone form and the zinc and barium salts are derivatives of the ketone form.

3. In the preparation of the diacetate of the intermediate acid, a substance was obtained which seems to be an anhydride of the acid.

4. 4-Methyl-5,6,7-trichloro-xanthone-8-carboxylic acid was obtained by the action of boiling alkaline solutions on the intermediate acid.

5. The 4-methyl-5,6,7-trichloro-xanthone-8-carboxylic acid is a γ -ketone acid. The sodium salt is a derivative of the ketone form, and the monoacetate a derivative of the lactone form of the acid.

6. Iso-*o*-cresol-tetrachlorophthalein is a tautomeric substance, yielding *colored* and *colorless* derivatives. The disodium salt is blue and probably has the *o*-quinoid structure. The diacetate and the dimethyl ether are *colorless* derivatives and have the lactone structure like the isophthalein⁴ itself.