Summary

1. Thymolbenzein has been made by the reaction of thymol with benzotrichloride. It is highly *colored* and, therefore, is given the *quinoid* structure. Derivatives of it were made.

2. 4-Hydroxy-3-*iso*propyl-6-methylbenzophenone was also obtained by the reaction of thymol with benzotrichloride and it was made by the Friedel-Crafts reaction from thymol and benzoyl chloride. It was proved that the hydroxyl group of this benzophenone derivative occupies the position *para* to the carbonyl carbon atom by isolating *p*-thymotic acid which resulted on fusion with caustic potash. The acetate of the benzophenone derivative was also made.

3. 4,4′-Dihydroxy-3,3′-di-*iso*propyl-6,6′-dimethyltriphenylmethane was made by the reduction of thymolbenzein. The diacetate and the dimethyl ether of this reduction product were also made.

4. It was determined electrometrically, using solutions in 50% ethanol, that thymolbenzein exhibits two color changes, from red to yellow at *P*H 1.5–2.5 and from yellow to red at *P*H 7.6–9.0, and that dibromothymolbenzein shows one color change from yellow to blue at *P*H 5.6–7.2. Because of the insolubility of these substances in water, the determination could not be checked with buffer solutions.

5. A table is given which shows the influence of substituents in thymolbenzein upon the *P*H range at which the color changes take place.

6. Attempts to prepare the carbinol forms of thymolbenzein and dibromothymolbenzein or derivatives of them failed.

ITHACA, NEW YORK

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

THYMOLTETRACHLOROPHTHALEIN AND SOME OF ITS DERIVATIVES

BY RALPH T. K. CORNWELL AND A. J. ESSELSTYN[1]

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Since thymolbenzein,[2] thymolphthalein[3] and thymolsulfonephthalein[4] have been investigated, the purpose of this work is to prepare and study the related substance, thymoltetrachlorophthalein.

Thymoltetrachlorophthalein was made by the reaction of thymol with the anhydride and with the chlorides of tetrachlorophthalic acid. The

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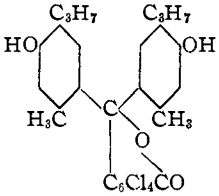
[1] From a thesis presented by A. J. Esselstyn to the Faculty of the Graduate School of Cornell University, in partial fulfilment of the requirements for the degree of Master of Science.

[2] Orndorff and Lacey, THIS JOURNAL, **49,** 818 (1927).

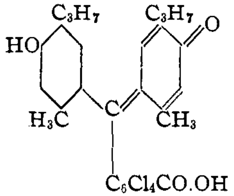
[3] Traube, *Arch. Pharm.,* [3] **23,** 536 (1887). Sørensen, *Ergebnisse Physiol.,* **12,** 393 (1912).

[4] Lubs and Clark, *J. Wash. Acad. Sci.,* **5,** 614 (1915); **6,** 481 (1916). Orndorff and Cornwell, THIS JOURNAL, **48,** 981 (1926).

latter method proved to be the better one. Thymoltetrachlorophthalein is a *colorless* substance and is, therefore, given the *lactoid* structure (I). However, like the other phthaleins it is a *tautomeric* substance and derivatives (salts) of the *colored, quinoid* form (II) were obtained as well as derivatives (diacetate, dibenzoate, etc.) of the *colorless, lactoid* form (I).



I



II

Thymoltetrachlorophthalein acts as an indicator, changing from colorless to blue at *P*H = 9.2–10.0. Dibromothymoltetrachlorophthalein also acts as an indicator, changing from colorless to blue at *P*H 8.4–8.8. These values were determined by means of buffer solutions.

Experimental Part

The chlorine determinations were made by means of the Parr bomb. The melting points recorded are uncorrected. The 1925 atomic weights[5] were used in the computations.

Condensation of Thymol with Tetrachlorophthalic Acid Anhydride.—Twenty-five g. (1 molecular porportion) of the anhydride,[6] 27 g. (2.1 molecular proportions) of thymol and 15 g. (0.6 molecular proportion) of fuming stannic chloride were heated at 108–113° for 68 hours. The unchanged thymol was then removed by distillation in steam and the crude phthalein washed with large quantities of hot water. The phthalein was then dissolved in dil. aqueous sodium hydroxide solution. The alkaline solution was filtered and the phthalein precipitated from the filtrate upon acidifying with dil. hydrochloric acid. The precipitate was filtered off, dried and extracted with ether to remove the last traces of thymol; yield, 6.2 g., or 12.4%. Zinc chloride, concd. sulfuric acid and fuming sulfuric acid were tried as condensing agents, without better results.

Reaction of the Dichlorides of Tetrachlorophthalic Acid with Thymol.—Sixty-eight g. (1 molecular proportion) of the dichlorides,[7] 75 g. of thymol (2.25 molecular proportions) and 50 g. (1 molecular proportion) of stannic chloride were heated at the temperature of the boiling water-bath for two hours. The pressure was then reduced and the heating continued until the evolution of hydrogen chloride ceased. The reaction mixture was then treated as described above. A substance insoluble in aqueous sodium hydroxide, which is probably dithymoltetrachlorophthalate, was obtained; yield, 39.2 g., or 34.6%.

Thymoltetrachlorophthalein.—When crystallized from benzene, the phthalein with one molecule of benzene separated in colorless, radiating clusters of needles; m. p., 266°.

Anal. Subs., 0.4506, 0.5433: loss at 120°, 0.0541, 0.0648. Calcd. for $C_{28}H_{26}O_4Cl_4.C_6H_6$, 12.08. Found: 12.01, 11.93.

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[5] Baxter, THIS JOURNAL, **47,** 600 (1925).

[6] Orndorff and Black, *Am. Chem. J.*, **41,** 359 (1909).

[7] Graebe, *Ann.*, **238,** 328 (1887).

Subs. (dry), 0.2206, 0.2616: AgCl, 0.2245, 0.2653. Calcd. for $C_{28}H_{26}O_4Cl_4$: Cl, 24.97. Found: 25.17, 25.09.

Thymoltetrachlorophthalein is easily soluble in acetone and ethanol, difficultly soluble in glacial acetic acid, very difficultly soluble in benzene and insoluble in water and ether. It dissolves in aqueous solutions of the alkalies with development of a deep blue color. The phthalein acts as an indicator and it was found, by means of buffer solutions,[8] that the change from colorless to blue takes place at P_H 9.2–10.0.

Monosodium Salt.—A carefully weighed sample of the pure, dry phthalein was dissolved in methanol and the calculated amount of a standard aqueous solution of sodium hydroxide was added. The solution was evaporated to *dryness* on the steam-bath. The residue was then crystallized from *absolute* methanol. Dark gray, crystalline aggregates were obtained.

Anal. Subs., 0.2147, 0.1670: Na_2SO_4, 0.0252, 0.0208. Calcd. for $C_{28}H_{25}O_4Cl_4Na$: Na, 3.90. Found: 3.80, 4.03.

When the monosodium salt is dissolved in water, hydrolysis takes place with the precipitation of some of the phthalein and the development of the blue color characteristic of solutions of the disodium salt. A similar hydrolysis takes place in 95% ethanol. Solutions of the salt in *absolute* ethanol or methanol are green.

Disodium Salt.—The calculated amount of a standard aqueous solution of sodium hydroxide was added to a weighed sample of the pure, dry phthalein. On concentration, the disodium salt separated in black, crystalline aggregates.

Anal. Subs., 0.3039, 0.2788: Na_2SO_4, 0.0696, 0.0655. Calcd. for $C_{28}H_{24}O_4Cl_4Na_2$: Na, 7.52. Found: 7.42, 7.61.

The disodium salt is very hygroscopic. It is extremely soluble in ethanol, methanol and acetone and insoluble in ether. The solutions are blue.

Barium Salt.—An aqueous suspension of the phthalein was boiled with 0.2 g. of pure barium hydroxide until all of the hydroxide had dissolved. The excess of phthalein was filtered off. On concentration of the deep blue solution the barium salt separated in black, crystalline aggregates.

Anal. Subs., 0.1738, 0.2539: $BaSO_4$, 0.0580, 0.0835. Calcd. for $C_{28}H_{24}O_4Cl_4Ba$: Ba, 19.53. Found: 19.64, 19.35.

It is very soluble in methanol and ethanol with development of a greenish-blue color, slightly soluble in acetone with development of a yellowish-green color and insoluble in benzene and ether.

Lead Salt.—The tan-colored lead salt was precipitated when a solution of lead nitrate was added to an alcoholic solution of the disodium salt of the phthalein.

Anal. Subs., 0.2125, 0.2155: $PbSO_4$, 0.0827, 0.0835. Calcd. for $C_{28}H_{24}O_4Cl_4Pb$: Pb, 26.80. Found: 26.59, 26.47.

It is slightly soluble in ether and acetone with development of a yellow color, and is insoluble in water.

Diacetate.—A solution of 10 g. of pure thymoltetrachlorophthalein in 50 g. of acetic anhydride was boiled for five hours. When cool, the solution was poured into a large volume of ice water. The acetate separated. It was filtered off and recrystallized from a concentrated solution in ether which was cooled in an ice-hydrochloric acid freezing mixture. Small, colorless crystals, m. p. 184–185°, were obtained.

Anal. Subs., 0.1848, 0.3326: AgCl, 0.1641, 0.2942. Calcd. for $C_{32}H_{30}O_6Cl_4$: Cl, 21.75. Found: 21.97, 21.88.

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[8] Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, 1922.

The diacetate is very soluble in benzene, acetone and ether, soluble in glacial acetic acid, very difficultly soluble in ethanol and insoluble in water. It is hydrolyzed in boiling, aqueous sodium hydroxide solution.

DIBENZOATE.—A solution of 5 g. of the phthalein in 15 g. of benzoyl chloride was boiled until it was light yellow in color. When cool it was poured into a 5% aqueous sodium carbonate solution. The benzoate separated. It was filtered off and crystallized from ethanol. Colorless prisms in radiating clusters, m. p. 177–178°, were obtained.

Anal. Subs., 0.2349, 0.1268: AgCl, 0.1721, 0.0940. Calcd. for $C_{42}H_{34}O_6Cl_4$: Cl, 18.27. Found: 18.12, 18.34.

It is very soluble in acetone and benzene, easily soluble in ether, soluble in glacial acetic acid, very difficultly soluble in ethanol and insoluble in water. It is slowly hydrolyzed by boiling, aqueous sodium hydroxide solution.

BISPHENYL CARBAMATE.—A mixture of 5 g. of the pure, dry phthalein and 10 g. of phenyl isocyanate was heated at 105° for three hours in a *dry* apparatus. On recrystallization from benzene, colorless needles, m. p. 234–235°, were obtained.

Anal. Subs., 0.1186, 0.1085: AgCl, 0.0854, 0.0769. Calcd. for $C_{42}H_{38}O_6N_2Cl_4$: Cl, 17.59. Found: 17.81, 17.53.

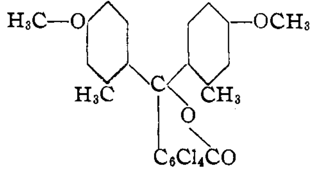
It is very soluble in acetone, soluble in ethanol and in ether, difficultly soluble in glacial acetic acid, very difficultly soluble in benzene and insoluble in water.

DIMETHYL ETHER.—Five g. of the pure, dry phthalein was dissolved in 400 cc. of absolute methanol and to this solution was added 50 cc. of absolute methanol in which 0.5 g. of sodium had been dissolved. Ten g. of methyl iodide was then added and the solution was boiled for 65 hours. From time to time more sodium methylate was added. On concentration small, bright yellow crystals were obtained; m. p., 208–210°. The color could not be removed by boiling a solution in methanol with bone black. Colorless crystals were obtained by recrystallization from acetic anhydride.

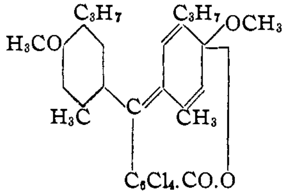
Anal. Subs., 0.1484, 0.1873: AgI, 0.1150, 0.1443. Subs., 0.2431, 0.2434: AgCl, 0.2343, 0.2360. Calcd. for $C_{28}H_{24}O_2Cl_4(OCH_3)_2$: OCH_3, 10.41; Cl, 23.80. Found: OCH_3, 10.24, 10.18; Cl, 23.84, 23.99.

The dimethyl ether is very soluble in glacial acetic acid, easily soluble in ethanol, acetone and benzene, soluble in ether, insoluble in water and aqueous solutions of the alkalies. It is not hydrolyzed by boiling with aqueous 10% sodium hydroxide solution. The solutions are yellow.

When viewed under a microscope the yellow crystals seem to be colorless with a yellow surface color. This color and the yellow color of the solutions are probably caused by the presence of small amounts of the colored form of the ether. The dimethyl ether may exist in the *colorless, lactoid* form (III) and in a *colored, quinoid* form which is an inner carbonium (IV) or oxonium salt.



III



IV

Dibromothymoltetrachlorophthalein.—A mixture of 5 g. of pure thymoltetrachlorophthalein and 1.6 g. of bromine in 100 cc. of glacial acetic acid was stirred mechanically for three hours. A colorless, crystalline substance separated which was filtered off and recrystallized from glacial acetic acid. After drying at 130° it melted at 223–225°.

Anal.[9] Subs., 0.2950, 0.1687: Ag halide, 0.3856, 0.2205; 24.35, 13.95 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{28}H_{24}O_4Br_2Cl_4$: Br, 22.02; Cl, 19.54. Found: Br, 22.18, 21.83; Cl, 19.43, 19.60.

The dibromothymoltetrachlorophthalein is very soluble in acetone, benzene and ether, easily soluble in ethanol, soluble in glacial acetic acid and insoluble in water. It acts as an indicator and it was found by means of buffer solutions[8] that the change from colorless to blue takes place at *P*H 8.4–8.8.

Summary

1. Thymoltetrachlorophthalein has been made. It is *colorless* and therefore has the *lactoid* structure.
2. Like other phthaleins it is *tautomeric,* and *colored* derivatives of the *quinoid* form were obtained as well as *colorless* derivatives of the *lactoid* form.
3. Thymoltetrachlorophthalein and dibromothymoltetrachlorophthalein act as indicators, changing from colorless to blue at *P*H 9.2–10.0 and *P*H 8.4–8.8, respectively.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF JOHNS HOPKINS UNIVERSITY]

SOME REACTIONS OF LEAD TETRA-ETHYL

BY OWENS HAND BROWNE[1] AND E. EMMET REID

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The recent discovery by Midgley and Boyd[2] of the "anti-knock" property of lead tetra-ethyl, and the subsequent manufacture on a commercial scale of this formerly little-known substance, have centered attention on it and also made it available in unlimited quantity for experimentation. This compound, although prepared by Löwig in 1853[3] has been but little studied. Its present importance seemed to justify a further investigation of its reactions.

Historical Part

Reference is made to an excellent summary of the chemistry of the organic derivatives of lead by Calingaert.[4] The first derivatives of lead tetra-ethyl were made by Löwig,[3] who obtained some of the carbonate, $[Pb(C_2H_5)_3]_2CO_3$, as a by-product. This was transformed into triethyl-

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[9] Ref. 6, p. 380.

[1] From a dissertation of O. H. Browne, June, 1926.

[2] Midgley and Boyd, *J. Ind. Eng. Chem.*, **14**, 896 (1922).

[3] Löwig, *Ann.*, **88**, 318 (1853).

[4] Calingaert, *Chem. Rev.*, **2**, 43 (1925).