The following compounds connected with the acridine syntheses have been characterized: 2-ethoxy-2-carboxylic-diphenylamine, 4-ethoxy-acridone, 4-hydroxy-acridone, 4-ethoxy-acridine, 4-hydroxy-acridine, 4-hydroxy-acridine-1-sulfonic acid and 3-iodo-4-hydroxy-acridine-1-sulfonic-acid.

TOKYO, JAPAN

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

THYMOLBENZEIN, 4-HYDROXY-3-ISOPROPYL-6-METHYLBENZOPHENONE AND SOME OF THEIR DERIVATIVES

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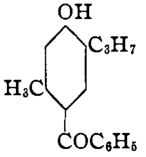
RECEIVED OCTOBER 16, 1926 PUBLISHED MARCH 9, 1927

In connection with the investigation of the phthaleins and related substances underway in this Laboratory it seemed desirable to study thymolbenzein, the mother substance of thymolphthalein,[2] thymoltetrachlorophthalein[3] and thymolsulfonephthalein.[4] Since thymolbenzein had not been made, the purpose of this investigation was to prepare it, to study it and to make derivatives of it characteristic of the benzeins.

Thymolbenzein was made by the action of benzotrichloride upon thymol with the subsequent decomposition of the hydrochloride thus formed. A benzophenone derivative, 4-hydroxy-3-*iso*propyl-6-methylbenzophenone (I), was also obtained. The benzotrichloride probably first reacts with



I

one molecule of thymol to form 4-hydroxy-3-*iso*propyl-6-methyldiphenyldichloromethane, which gives the ketone (I) on hydrolysis. The diphenyldichloromethane derivative then reacts with another molecule of thymol, or benzotrichloride reacts with two molecules of thymol to form the unstable chloride of the carbinol form of thymolbenzein, which immediately rearranges to form the stable hydrochloride of thymolbenzein. The latter is either a carbonium (II) or an oxonium (III) salt. It de-

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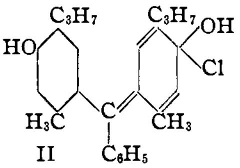
[1] From a dissertation presented by H. T. Lacey, Grasselli Fellow in Chemistry for 1925–1926, to the Faculty of the Graduate School of Cornell University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Traube, *Arch. Pharm.*, [3] **23**, 536 (1887). Sørensen, *Ergebnisse Physiol.*, **12**, 383 (1912).

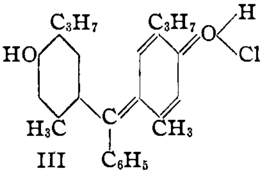
[3] Cornwell and Esselstyn, THIS JOURNAL, **49**, 826 (1927).

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

composes when boiled with water or dilute solutions of the alkalies and also when heated alone to set free thymolbenzein (IV).



II



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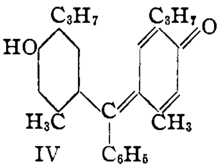

IV

Other benzeins[5] have been prepared in a similar manner.

The ketone (I) was also made from benzoyl chloride and thymol by the Friedel-Crafts reaction. Its structure was proved by fusion with potassium hydroxide. *p*-Thymotic acid[6] was isolated from the products of hydrolysis and, therefore, the hydroxyl group occupies the *para* position to the carbonyl group. The acetate of the benzophenone derivative was also made.

Thymolbenzein is a highly *colored* substance and is therefore given the *quinoid* structure (IV). It has basic properties, which was proved by making salts with acids (the hydrochloride, the sulfate and the perchlorate). Ammonia is not taken up by thymolbenzein. The sodium salt, the methyl ether and its hydrochloride, and the acetate were made. On bromination, dibromothymolbenzein was obtained. The acidifying influence of the bromine atoms was shown by the fact that while the dibromo derivative absorbs hydrogen chloride, the latter is easily given off and a stable hydrochloride is not formed. The dibromo derivative absorbs dry ammonia, which also is given off easily. Dinitrothymolbenzein was made. The tinctorial powers of the dinitro compound are very weak in comparison with the benzein and its dibromo derivative. These derivatives of thymolbenzein are *colored* and are, therefore, represented as having the *quinoid* structure. Attempts to prepare the colorless carbinol form or derivatives of it failed. On reduction thymolbenzein forms a colorless triphenylmethane derivative, 4,4′-dihydroxy-3,3′-di-*iso*propyl-6,6′-dimethyltriphenylmethane (V), $[HO.C_6H_2(C_3H_7)(CH_3)]_2$:$CH.C_6H_5$. The dimethyl ether of this reduction product resulted when thymolbenzein was boiled with methanol containing 3% of hydrogen chloride.[7] The acetate of the reduction product was prepared by boiling a solution of thymolbenzein in acetic anhydride in which zinc dust was suspended, and by boiling a solution of the reduction product (V) in acetic anhydride in an atmosphere of carbon dioxide. Phenylhydrazine also reduced the thymolbenzein to the triphenylmethane (V) derivative.

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[5] Doebner and Stackmann, *Ber.*, **9**, 1918 (1876). Doebner, *Ber.*, **12**, 1467 (1879). Meyer and Gerloff, *Ber.*, **56**, 98 (1923). Orndorff and McNulty, paper accepted for publication in THIS JOURNAL; Orndorff and Wang, *ibid.*, **47**, 290 (1925), and unpublished work.

[6] Kobek, *Ber.*, **16**, 2102 (1883).

[7] Kauffmann and Pannwitz, *Ber.*, **45**, 766 (1912).

Both thymolbenzein and dibromothymolbenzein exhibit color changes. Since both are insoluble in water the *P*H values at which the color changes take place could not be determined by means of buffer solutions. Therefore, these data were determined electrometrically in 50% alcoholic solutions by means of a Leeds and Northrup Type K potentiometer, using a saturated calomel electrode and a hydrogen electrode.[8] The values obtained are recorded in Table I,[9] which also shows the influence of substituents in thymolbenzein upon the *P*H values at which the color changes take place.

TABLE I

HYDROGEN-ION CONCENTRATION RANGES (*P*H) AND COLOR CHANGES OF THYMOLBENZEIN AND RELATED SUBSTANCES

*P*H	1	2	3	4	5	6	7	8	9	10	11
Thymolbenzein	r	(1.5–2.5)	y	y	y	y	y	(7.6–9)	b	b	b
Dibromothymolbenzein	y	y	y	y	y	(5.6–7.2)		b	b	b	b
Thymolsulfonephthalein	r	(1.2–2.8)	y	y	y	y	y	y	(8–9.6)	b	b
Dibromothymolsulfonephthalein	y	y	y	y	y	y	(6–7.6)	b	b	b	b
Thymolphthalein	c	c	c	c	c	c	c	c	(9.3–10.5)		b
Dibromothymolphthalein	Unknown										
Thymoltetrachlorophthalein	c	c	c	c	c	c	c	c	c (9.2–10)	b	b
Dibromothymoltetrachlorophthalein	c	c	c	c	c	c	c	c	(8.4–9.6)	b	b

b = blue, c = colorless, r = red, y = yellow.

Experimental Part

The 1925 atomic weights[10] were used in the computations. The melting points recorded are uncorrected.

Reaction of Benzotrichloride with Thymol.—For the preparation of thymolbenzein the following procedure was found to be the best.

Fifty g. (2 molecular proportions) of melted thymol was added dropwise with constant stirring to a mixture of 85 g. (2 molecular proportions) of stannic chloride and 33.5 g. (1.03 molecular proportions) of benzotrichloride. Hydrogen chloride was vigorously evolved and a dark red color developed. When the reaction had apparently ceased the pressure was reduced until hydrogen chloride was again vigorously given off. The reaction stopped again after a short time and then the mixture was heated at 60–65° in an electrically heated oil-bath for 15 hours. A hard, brittle, bright red mass was

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

[9] We are indebted to Mr. A. J. Esselstyn for the preparation of this table and to Dr. G. H. Brandes for aid in determining the *P*H values.

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

obtained, which was treated with dil. hydrochloric acid to remove the stannic chloride, and the unchanged thymol and benzotrichloride were removed by distillation in steam. During the steam distillation green crystals of thymolbenzein hydrochloride separated, together with the benzophenone derivative. The material was filtered off, air-dried, powdered and extracted with ether. The benzophenone derivative is soluble in ether, whereas the thymolbenzein hydrochloride is not; yields, thymolbenzein hydrochloride, 57.5%; benzophenone derivative, 20.5%.

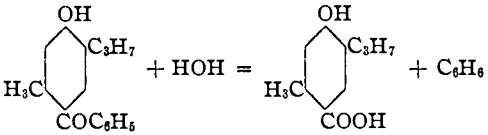
4-Hydroxy-3-*iso*propyl-6-methylbenzophenone.—An equal amount of petroleum ether was added to the ethereal extracts and the solution boiled with bone black, filtered and concentrated to crystallization. This process was repeated until colorless crystals were obtained which melted at 150–150.5°.

Anal. Subs., 0.2256, 0.2247: CO_2, 0.6618, 0.6620; H_2O, 0.1449, 0.1401. Calcd. for $C_{17}H_{18}O_2$: C, 80.27; H, 7.14. Found: C, 80.01, 80.35; H, 7.19, 6.98.

The substance is insoluble in water, petroleum ether, an aqueous solution of sulfur dioxide and aqueous sodium bisulfite solution; very soluble in methanol, ethanol, ethyl acetate and acetone. It dissolves in 10% aqueous sodium hydroxide solution and in concd. ammonium hydroxide with development of a yellow color.

4-Hydroxy-3-*iso*propyl-6-methylbenzophenone was also made by the Friedel-Crafts reaction from benzoyl chloride and thymol. The product was analyzed and found to be identical with the benzophenone derivative obtained from benzotrichloride and thymol. It gave large crystals[11] which separated from 98% ethanol and lost no weight at 110°.

Fusion with Potassium Hydroxide.—Five g. of 4-hydroxy-3-*iso*propyl-6-methylbenzophenone was dissolved in 50 cc. of 20% aqueous potassium hydroxide solution and 25 g. of powdered potassium hydroxide was then added. The mixture was heated to 200° and the pressure reduced until the solution boiled gently. From time to time the water which boiled off was replaced. After 30 hours' heating the material was dissolved in water. Upon acidifying the solution, a precipitate was obtained which was filtered off and dried at 50°. The material was extracted with ether and petroleum ether was added to the combined ethereal solutions. The solution was concentrated to crystallization and the substance thus obtained recrystallized from water. The crystals were identified as *p*-thymotic acid;[6] m. p., 156–156.5°. Therefore, the hydroxyl group in the benzophenone derivative is *para* to the carbon atom of the carbonyl group.



ACETATE.—Four g. of 4-hydroxy-3-*iso*propyl-6-methylbenzophenone obtained from thymol and benzotrichloride was dissolved in 20 cc. of acetic anhydride and the solution was boiled for two hours. The crude acetate separated when the cooled solution was poured into ice water. It was filtered off, air-dried and crystallized from 95% methanol. Flake-like, colorless crystals separated which melted at 73°.

Anal. Subs., 0.2378, 0.2685: CO_2, 0.6719, 0.7554; H_2O, 0.1423, 0.1589. Calcd. for $C_{17}H_{17}O_2(COCH_3)$: C, 76.99; H, 6.81. Found: C, 77.06, 76.73; H, 6.70, 6.62.

This acetate was also made in the same manner from the benzophenone derivative obtained from benzoyl chloride and thymol by the Friedel-Crafts reaction and was found to be identical.[11]

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[11] These crystals have been described by Professor Gill. See Lacey, *Thesis*, Cornell University Library, 1926.

It is very soluble in glacial acetic acid, acetone, ether, ethanol and ethyl acetate and insoluble in water. It is readily hydrolyzed by boiling water, hot 10% aqueous sodium hydroxide solution or cold 10% alcoholic potassium hydroxide solution.

Thymolbenzein.—Thymolbenzein was obtained as a bright red powder when pure, crystalline thymolbenzein hydrochloride was completely hydrolyzed with 2-3% aqueous sodium hydroxide solution. It was crystallized from 90% ethanol.[11] At 110° the loss in weight was negligible. The melting point of thymolbenzein is 184°.

Anal. Subs., 0.1829, 0.1840: CO_2, 0.5600, 0.5652; H_2O, 0.1260, 0.1253. Calcd. for $C_{27}H_{30}O_2$: C, 83.88; H, 7.83. Found: C, 83.51, 83.78; H, 7.72, 7.61.

It is very soluble in formic acid, acetic acid, methanol and acetone, and soluble in ether and benzene. The concentrated solutions are red and the dilute solutions are orange-yellow. It is insoluble in water and petroleum ether. It is slightly soluble in aqueous sodium hydroxide solutions with development of a blue color. Thymolbenzein dissolves in warm concd. sulfuric acid with a dark red color.

Thymolbenzein shows two color changes; one in the acid range from red to yellow at $P_H = 1.5–2.5$ and the other in the alkaline range from yellow to blue at $P_H = 7.6–9$. Because of the insolubility of thymolbenzein in water these values had to be determined electrometrically,[8] using 50% alcoholic solutions and the results could not be checked by buffer solutions.

Dry thymolbenzein does not take up dry ammonia.

Action of Dry Hydrogen Chloride.—Dry thymolbenzein takes up about 2 molecules of dry hydrogen chloride. The excess of hydrogen chloride was given off in a desiccator over potassium hydroxide and a stable hydrochloride was formed.

Anal. Subs., 0.3748, 0.3481: gain in wt., 0.0353, 0.0326. Calcd. for $C_{27}H_{30}O_2.HCl$: HCl, 8.62. Found: 8.61, 8.56.

The Hydrochloride.—The crude thymolbenzein hydrochloride obtained above was purified by hydrolyzing with 2 to 3% of aqueous sodium hydroxide solution, dissolving the thymolbenzein thus formed in methanol, ethanol or glacial acetic acid and adding an excess of concd. hydrochloric acid to the hot, concentrated solutions. On cooling, crystals of the pure hydrochloride separated[11] which decompose in an open melting-point tube at 225–235° and in a sealed tube at 235–250°.

Anal. Subs. (dried at 100–110°), 0.3430, 0.2395, 0.1621: AgCl, 0.1156, 0.0804, 0.0553. Calcd. for $C_{27}H_{30}O_2.HCl$: Cl, 8.39. Found: 8.34, 8.31, 8.44.

The hydrochloride is soluble in methanol, ethanol, acetic acid and acetone. It is very slightly soluble in benzene; insoluble in ether, petroleum ether and water. The solutions are dark red.

Hydrolysis of the Hydrochloride with Water.—A sample of the hydrochloride was finely ground and dried to constant weight at 110°. It was then boiled with 800 cc. of distilled water for two hours in a Pyrex Erlenmeyer flask connected with a reflux condenser. The supernatant liquid was then decanted through a tared Gooch crucible. This process was repeated until the filtrate gave no test for chlorine. The thymolbenzein in the Gooch crucible was dried at 110° to constant weight and the hydrogen chloride in the filtrate determined as silver chloride. The results of the analyses prove that thymolbenzein hydrochloride is completely hydrolyzed by boiling water.

Anal. Subs., 0.3560: loss of wt., 0.0301; AgCl, 0.1188. Calcd. for $C_{27}H_{30}O_2.HCl$: HCl, 8.62; Cl, 8.39. Found: HCl, 8.46; Cl, 8.26.

THE SULFATE.—Twenty g. of concd. sulfuric acid was added to a solution of 4 g. of thymolbenzein in 50 cc. of glacial acetic acid. On concentration, the sulfate crystallized.[11] The air-dried material lost no weight at 110°; m. p., 242–243°.

Anal. Subs., 0.2064, 0.2385: $BaSO_4$, 0.0983, 0.1157. Calcd. for $C_{27}H_{30}O_2$ + H_2SO_4: S, 6.62. Found: 6.54, 6.66.

Hydrolysis of the Sulfate with Water.—The sulfate was completely hydrolyzed with water in the same way as the hydrochloride.

Anal. Subs., 0.3050: loss of wt., 0.0614; $BaSO_4$, 0.1460. Calcd. for $C_{27}H_{30}O_2.H_2SO_4$: H_2SO_4, 20.25; S, 6.62. Found: H_2SO_4, 20.13, S, 6.57.

THE PERCHLORATE.—A slight excess of 72% aqueous perchloric acid was carefully added to a warm solution of 3 g. of thymolbenzein in 100 cc. of glacial acetic acid. Crystals of the perchlorate, which lost no weight at 120°, separated when the solution was concentrated in a boiling water-bath under reduced pressure.[11] The perchlorate decomposed between 265° and 272°.

Anal. Subs., 0.2873, 0.4106: AgCl, 0.0870, 0.1226. Calcd. for $C_{27}H_{30}O_2.HClO_4$: Cl, 7.29. Found: 7.49, 7.39.

The perchlorate is soluble in methanol, ethanol and acetone, and insoluble in ether, benzene, petroleum ether and water. The solutions are red.

SODIUM SALT.—Seven g. of thymolbenzein was dissolved in 100 cc. of absolute ethanol in which had been dissolved 7 g. of sodium. The solution was boiled and when cool it was poured into 500 cc. of cold 5% aqueous sodium hydroxide solution. A tar slowly separated. After filtration, the filtrate was concentrated over concd. sulfuric acid in a partially evacuated desiccator. Small, dark blue needles with a bronze surface color separated which proved to be the sodium salt of thymolbenzein with 2 moles of water of crystallization. It softens at 235–245° but does not melt under 310°.

Anal. Subs., 0.2861, 0.3541: loss of wt. at 120°, 0.0243, 0.0292. Calcd. for $C_{27}H_{29}O_2Na.2H_2O$: H_2O, 8.11. Found: 8.49, 8.29.

Subs. (dry), 0.2611, 0.2821: Na_2SO_4, 0.0454, 0.0482. Calcd. for $C_{27}H_{29}O_2Na$: Na, 5.63. Found: 5.63, 5.53.

Solutions of the sodium salt in absolute ethanol, methanol and acetone are blue. When these solutions are diluted with the dry solvent the color changes from blue through green to yellow. It is slightly soluble in ether, ethyl acetate and chloroform with development of an orange-yellow color and is very slightly soluble in petroleum ether and carbon tetrachloride with the development of a light yellow color. The sodium salt is slightly soluble in water with development of a light blue color. Upon standing, the aqueous solution becomes colorless and thymolbenzein separates from the solution as the salt hydrolyzes.

METHYL ETHER.—This was made by the Claisen method.[12] Six g. of thymolbenzein was dissolved in 200 cc. of acetone and 3 g. of potassium carbonate and 2.4 g. of methyl iodide were added to the solution. The mixture was boiled on a water-bath for 2.5 hours. After filtration, orange-colored crystals separated[11] from the concentrated filtrate; they were filtered off and dried in a desiccator over sulfuric acid. Analyses proved the substance, which melted at 132–133° and lost no weight at 110°, to be the methyl ether of thymolbenzein.

Anal. Subs., 0.3019, 0.2277: AgI, 0.1787, 0.1377. Calcd. for $C_{27}H_{29}O(OCH_3)$: OCH_3, 7.75. Found: 7.82, 7.99.

Solutions of the methyl ether in acetone, ether, benzene, methanol and ethanol are yellow.

Action of Hydrogen Chloride on the Ether.—The methyl ether of thymolbenzein absorbs about 3 moles of dry hydrogen chloride. The color changes from orange to a

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[12] Claisen and Eisleb, *Ann.*, **401**, 29 (1913).

dark, reddish-purple. The excess of hydrogen chloride is lost over potassium hydroxide with the formation of a stable hydrochloride.

Anal. Subs., 0.1211: gain in wt., 0.0111. Calcd. for $C_{28}H_{32}O_2.HCl$: HCl, 8.35. Found: 8.40.

The hydrochloride melts at 85–95° in a sealed tube. Solutions of it in methanol, ethanol and acetone are dark red. Upon adding an excess of aqueous sodium hydroxide to these solutions the color changes to yellow.

THE MONO-ACETATE.—A solution of 0.67 g. (1 molecular proportion) of acetyl chloride in acetone was added slowly to 3.5 g. (1 molecular proportion) of the sodium salt of thymolbenzein dissolved in 200 cc. of acetone. The mixture was warmed to 40–45° for two hours. When cool it was filtered and the filtrate poured into 200 cc. of ice water. The acetate which solidified was filtered off and dried. Small, orange-colored needles, m. p. 143–144°, were obtained by recrystallization from a mixture of ether and petroleum ether.

Anal. Subs., 0.3015, 0.3323: CO_2, 0.8996, 1.0487; H_2O, 0.2005, 0.2414. Calcd. for $C_{27}H_{29}O_2(OCCH_3)$: C, 81.26; H, 7.53. Found: C, 81.36, 81.18; H, 7.44, 7.67.

The acetate is very soluble in acetone, methanol, ethanol and ether, slightly soluble in petroleum ether and insoluble in water. It is slowly hydrolyzed by boiling water, readily hydrolyzed by hot, 10% aqueous sodium hydroxide solution and by a cold 10% alcoholic potassium hydroxide solution.

Dibromothymolbenzein.—Two molecular proportions (8.25 g.) of bromine dissolved in a mixture of 25 cc. of glacial acetic acid and 25 cc. of formic acid was added to a cold solution of 1 molecular proportion (10 g.) of thymolbenzein in 200 cc. of formic acid. After standing for several hours, the solution was concentrated to crystallization under reduced pressure at 90°. Large red crystals separated[11] which were filtered off, washed and air-dried; m. p., 96–97°. Analyses proved this substance to be dibromothymolbenzein with one molecule of formic acid.

Anal. Subs., 0.4006, 0.3152: AgBr, 0.2521, 0.2003. Calcd. for $C_{27}H_{28}O_2Br_2.CH_2O_2$: Br, 27.09. Found: 26.76, 27.04.

The formic acid was removed by boiling with a large volume of water. The resulting solution gave an acid reaction with litmus, but a negative test for bromine. The dibromothymolbenzein, freed from formic acid and dried at 50°, melted at 89–90°.

Anal. Subs., 0.2662, 0.3223: AgBr, 0.1831, 0.2198. Calcd. for $C_{27}H_{28}O_2Br_2$: Br, 29.38. Found: 29.27, 29.02.

Solutions of dibromothymolbenzein in acetone, ether, methanol and ethanol are orange or orange-red. It is very slightly soluble in petroleum ether and insoluble in water. It is slightly soluble in 5 to 10% aqueous sodium hydroxide solution and in concd. ammonium hydroxide with development of a blue color. It was found electrometrically[8] that the color change of solutions of dibromothymolbenzein from yellow to blue takes place at P_H = 5.6–7.2.

ACTION OF HYDROGEN CHLORIDE.—A sample of dry dibromothymolbenzein absorbed about 2.5 moles of dry hydrogen chloride, but all of the hydrogen chloride was given off in a desiccator over solid potassium hydroxide.

ACTION OF DRY AMMONIA.—A sample of dry dibromothymolbenzein absorbs a little more than one molecule of dry ammonia which is given off in a desiccator over concd. sulfuric acid.

Dinitrothymolbenzein.—Two g. of nitric acid (d., 1.5) in 50 cc. of glacial acetic acid was added to a cool solution of 5 g. of thymolbenzein in 400 cc. of glacial acetic acid. The solution was warmed to 60° for three hours and stirred mechanically. The cooled solution was then poured into a cold solution of 50 g. of sodium acetate and 100 g. of sodium chloride in 2 liters of water. A precipitate formed which was filtered off and dried. Small yellow needles of dinitrothymolbenzein were obtained by crystallization from a mixture of ether and petroleum ether.

Anal. Subs., 0.1930, 0.2316: N_2, 9.7 (22°, 734.2 mm.), 12.0 cc. (20°, 735.7 mm.). Calcd. for $C_{27}H_{28}O_6N_2$: N, 5.88. Found: 5.62, 5.86.

Dinitrothymolbenzein darkens at 100–110° and carbonizes at 150–160°, but does not melt under 310°. It is very soluble in methanol, ethanol, ether, acetone, slightly soluble in water and insoluble in petroleum ether. It dissolves in 5 to 10% aqueous sodium hydroxide solution with development of a red color.

4,4'-Dihydroxy-3,3'-di-*iso*propyl-6,6'-dimethyltriphenylmethane. (The Reduction Product of Thymolbenzein.)—Ten g. of zinc dust was slowly added to a boiling solution of 5 g. of thymolbenzein in 50 cc. of glacial acetic acid and the boiling was continued until the solution became colorless. After filtration the filtrate was concentrated and poured into 800 cc. of ice water. The material which separated was filtered off, dried in a desiccator over concd. sulfuric acid and crystallized from ether. Small, cream-colored crystals, m. p. 158–159°, were obtained. All of this work was done in an atmosphere of carbon dioxide.

Anal. Subs., 0.1739: CO_2, 0.5301; H_2O, 0.1297. Calcd. for $C_{27}H_{32}O_2$: C, 83.45; H, 8.31. Found: C, 83.13; H, 8.35.

The substance is soluble in methanol, ethanol, acetic acid, ether, acetone, benzene, toluene, xylene and petroleum ether, and insoluble in water. It is oxidized to the benzein upon warming with concd. nitric or sulfuric acid. The solutions are colorless.

DIMETHYL ETHER.—A solution of 5 g. of thymolbenzein in 700 cc. of absolute methanol containing 3% of hydrogen chloride was boiled for 150 hours.[7] It was then boiled with bone black, filtered and concentrated to crystallization. On recrystallization from absolute methanol, light cream-colored crystals,[11] m. p. 105°, were obtained which proved to be the dimethyl ether of 4,4'-dihydroxy-3,3'-di-*iso*propyl-6,6'-dimethyltriphenylmethane.

Anal. Subs., 0.0948, 0.2229: AgI, 0.1065, 0.2480. Calcd. for $C_{27}H_{30}(OCH_3)_2$: OCH_3, 14.91. Found: 14.81, 14.70.

Solutions of the ether in ethanol, acetone, ether, petroleum ether and benzene are colorless. It is insoluble in water.

This dimethyl ether was also made in an atmosphere of hydrogen by the action of dimethyl sulfate on the hot acetone solution of the reduction product of thymolbenzein, to which had been added twice its volume of 20% aqueous sodium hydroxide solution.[11]

DIACETATE.—A solution of 5 g. of thymolbenzein in 100 cc. of acetic anhydride was boiled for three hours, during which time 10 g. of zinc dust was slowly added. The filtered solution was poured into 1 liter of ice water. The diacetate which separated was filtered off and recrystallized first from absolute methanol and then from acetic anhydride. Small, colorless prisms were obtained; m. p., 121°.

Anal. Subs., 0.1692, 0.2247: CO_2, 0.4900, 0.6477; H_2O, 0.1164, 0.1528. Calcd. for $C_{31}H_{36}O_4$: C, 78.76; H, 7.68. Found: C, 78.98, 78.61; H, 7.70, 7.61.

The diacetate is soluble in ethanol, acetone, acetic acid and insoluble in water.

It was also made by boiling a solution of the reduction product in acetic anhydride in an atmosphere of carbon dioxide.[11]

ACTION OF PHENYLHYDRAZINE.—When a solution of 1 g. of thymolbenzein in 10 cc. of phenylhydrazine was boiled, reduction took place and 4,4'-dihydroxy-3,3'-di-*iso*propyl-6,6'-dimethyltriphenylmethane was isolated.

Attempts to prepare the colorless carbinol forms of thymolbenzein and of dibromothymolbenzein or their derivatives failed.

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 PH 1.5–2.5 and from yellow to red at PH 7.6–9.0, and that dibromothymolbenzein shows one color change from yellow to blue at PH 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 PH range at which the color changes take place.

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

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THYMOLTETRACHLOROPHTHALEIN AND SOME OF ITS DERIVATIVES

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RECEIVED OCTOBER 18, 1926 PUBLISHED MARCH 9, 1927

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).