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THE ACTION OF FORMALDEHYDE ON *ortho*-CHLOROPHENOL AND 2,4-DICHLOROPHENOL

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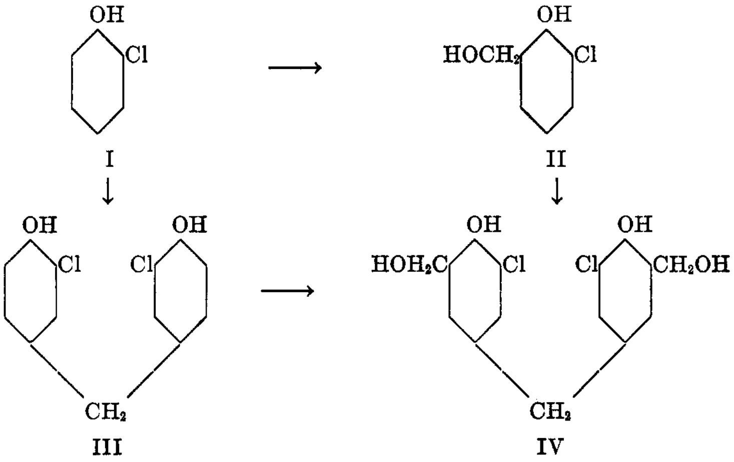
This investigation is one of a series on attempts to isolate and identify the simple condensation products obtained by treating substituted phenols with formaldehyde in acid media. In cases such as *p*-nitrophenol (1) and salicylic acid (2) it has already been shown that in hydrochloric acid the first-formed product, a hydroxybenzyl chloride, may be synthesized in good yield.

In the *o*-chlorophenol-formaldehyde condensation in hydrochloric acid medium, Stoermer and Behn (3) reported an unidentified chlorohydroxybenzyl chloride, m.p. 93°, while a German patent (4) indicated the formation of a benzyl chloride, m.p. 112°. Later another German patent (5) claimed that the higher-melting benzyl chloride was 5-chloro-(or 3-chloro-) 4-hydroxybenzyl chloride. The one other literature reference dealing with *o*-chlorophenol is that of Zinke, Hanus, and Ziegler (6). These investigators, produced the compounds shown below, II and III being obtained directly from the phenol:



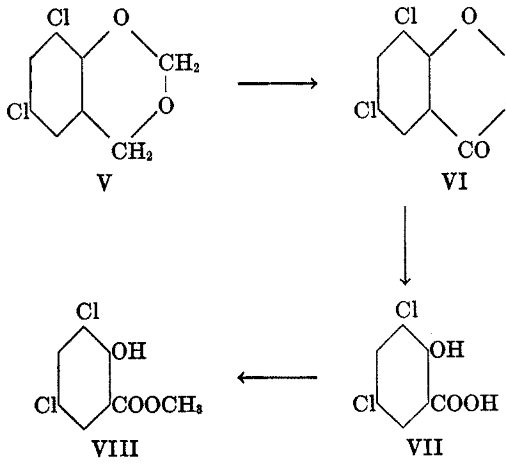
Apparently since I and II are known and IV may be obtained *via* II or III, they concluded that III was 3,3′-dichloro-4,4′-dihydroxydiphenylmethane.

Although the isolation of crystalline products was difficult from the *o*-chlorophenol reaction, two compounds, 3-chloro-4-hydroxybenzyl chloride and 3,3′-dichloro-4,4′-dihydroxydiphenylmethane were obtained. It was extremely difficult to convert the former into known derivatives. Melting at 92–93° in disagreement with the German patent (5) claim, it was shown to have the structure assigned by the identity of its alcohol with that obtained in the reduction of 3-chloro-4-hydroxybenzaldehyde. New evidence in support of the structure of 3,3′-dichloro-4,4′-dihydroxydiphenylmethane was acquired in two ways:

(a) Chlorination gave a tetrachloro derivative whose melting point and analysis agreed with that of 3,3′,5,5′-tetrachloro-4,4′-dihydroxydiphenylmethane.

(b) It was synthesized by the condensation of 3-chloro-4-hydroxybenzyl alcohol and *o*-chlorophenol.

The reaction of 2,4-dichlorophenol was much more favorable to the formation of crystalline products, in all probability because of the limited number of positions available for substitution in the benzene nucleus (7). Although what was regarded as 2,2′-dihydroxy-3,3′,5,5′-tetrachlorodiphenylmethane (8) is the only condensation product of this phenol referred to in the literature, our products in hydrochloric acid medium were 6,8-dichloro-1,3-benzodioxane, V, and 2-hydroxy-3,5-dichlorobenzyl chloride. The structure of this dioxane was established by the method of Borsche and Berkhout (9) by which it was converted through 6,8-dichloro-1,3-benzodioxan-4-one, VI, into the known compounds, 2-hydroxy-3,5-dichlorobenzoic acid, VII, and its methyl ester, VIII:



That the other product was 2-hydroxy-3,5-dichlorobenzyl chloride was shown by its conversion into an alcohol which agreed in melting point with the known 2-hydroxy-3,5-dichlorobenzyl alcohol, and which formed a dioxane with benzaldehyde (10).

EXPERIMENTAL

Products from o-*Chlorophenol and Derivatives*

1. *3-Chloro-4-hydroxybenzyl chloride.* A mixture of 6 g. of Eastman's C.P. *o*-chlorophenol, 40 cc. of 40% U.S.P. formaldehyde, and 500 cc. of concentrated hydrochloric acid was stirred at room temperature for 10 minutes while hydrogen chloride was bubbled rapidly through the mixture. The temperature was then raised to 45–50° in about 10 minutes and held at that point for 45 minutes. The reaction mixture was filtered rapidly through glass wool to prevent partial solidification and the heavy oil in the filtrate was separated from the aqueous portion. A second filtration was necessary to remove the last traces of oil from the aqueous portion. This oil was then mixed with 400 cc. more of concentrated hydrochloric acid and 30 cc. more of formaldehyde, and the mixture was stirred with hydrogen chloride passing through exactly as before, except that the final stirring at 45–50° was continued for only 30 minutes. In this way a second aqueous portion was obtained. The combined aqueous portions were allowed to stand overnight and the crystals which formed were washed several times with ice-water and dried in the open air. They weighed 2 g. and melted at 91–93°. Further purification by crystallization was exceedingly difficult due to the ease of resin formation. Our best product, m.p. 92–93°, [Stoermer and Behn's (3) unidentified chloride, 93°] was obtained by dissolving the crystals in petroleum ether (b.p. 35–60°), allowing the solution to evaporate at room temperature, and separating mechanically the last crystals which formed.

Anal. Calc'd for $C_7H_6Cl_2O$: Cl, 40.06. Found: Cl, 39.86.

The *alcohol* was obtained by heating, with frequent shaking, 0.5 g. of the chloride and a solution containing a crystal of silver nitrate in 50 cc. of water at 70° for 30 minutes. Upon extracting the cooled filtrate with ether and then allowing the solvent to evaporate, a clear oil was recovered. This product, which soon crystallized, was dissolved in 0.5 cc. of hot alcohol from which solvent it was thrown out by the addition of benzene. The dried, white needles, m.p. 122–123° [Stoermer and Behn's (3) unidentified alcohol, 123°] weighed about 0.05 g.

2. *Synthesis of 3-chloro-4-hydroxybenzyl alcohol.* Through a solution of Eastman's C.P. *p*-hydroxybenzaldehyde, 1.5 g., in 100 cc. of U.S.P. chloroform in an ice-bath, dry chlorine was bubbled at the rate of two to three bubbles per second for about 15 minutes. The evaporation of the chloroform with a stream of air and crystallization of the residue from water gave 1.6 g. 3-chloro-4-hydroxybenzaldehyde, m.p. 132–134°. [Biltz (11) gives 139° for a vacuum-distilled product]. The aldehyde, 1 g., in solution in C.P. ethyl acetate with 1 g. of Raney nickel catalyst was treated with hydrogen at 40 lbs. pressure for about 45 minutes. After filtration and evaporation to dryness in a stream of air, the residue, upon crystallization from benzene, gave 0.6 g. of 3-chloro-4-hydroxybenzyl alcohol, m.p. 127°.

Anal. Calc'd for $C_7H_7ClO_2$: Cl, 22.36. Found: Cl, 22.31, 22.32.

A mixed melting point with the alcohol obtained from 3-chloro-4-hydroxybenzyl chloride showed no appreciable depression.

3. *3,3'-Dichloro-4,4'-dihydroxydiphenylmethane.* To 53 g. of Eastman's C.P. *o*-chlorophenol was added 15 cc. of 40% U.S.P. formaldehyde and 325 g. of 60% sul-

furic acid and the mixture was stirred for 16 hours at 60–65°. Upon pouring into 1 liter of water, the mass solidified, after which the solid was separated and steam distilled to remove any unreacted *o*-chlorophenol. The oil remaining was vacuum distilled in an all-glass apparatus with ground joints, the fraction coming over at 230–240° (25 mm.) being collected. One crystallization from ligroin gave 18 g., m.p. 99–101°. A purer product, m.p. 103–104°, [Zinke, Hanus, and Ziegler (6) give 103°] was obtained by crystallization from water, although this solvent is unsatisfactory due to the limited solubility of the compound in it.

Anal. Calc'd for $C_{13}H_{10}Cl_2O_2$: Cl, 26.36. Found: Cl, 26.50, 26.62.

(a) *3,3′,5,5′-Tetrachloro-4,4′-dihydroxydiphenylmethane.* Through a solution of 0.5 g. of the dichlorodihydroxydiphenylmethane in 20 cc. of glacial acetic acid at room temperature, dry chlorine was bubbled for 10 minutes. The needles, 0.45 g., which separated were filtered off and after being washed with water and crystallized from dilute alcohol, gave light brown leaflets, m.p. 184–185°; [Zincke and Birschel (12) give 185–186°].

Anal. Calc'd for $C_{13}H_8Cl_4O_2$: Cl, 41.97. Found: Cl, 41.75.

(b) The dichloro compound, 0.5 g., and acetyl chloride gave 0.45 g. of a *diacetyl derivative*, white needles, m.p. 126.5–127.5°.

Anal. Calc'd for $C_{17}H_{14}Cl_2O_4$: Cl, 20.08. Found: Cl, 20.12, 20.18.

(c) The dichloro compound, 0.5 g., and benzoyl chloride gave 0.45 g. of a *dibenzoyl derivative*, white crystals, m.p. 116–116.5°.

Anal. Calc'd for $C_{27}H_{18}Cl_2O_4$: Cl, 14.86. Found: Cl, 15.07, 15.10.

4. *Synthesis of 3,3′-dichloro-4,4′-dihydroxydiphenylmethane.* This synthesis was accomplished by von Koebner's method (13) as follows: 3-chloro-4-hydroxybenzyl alcohol, 9 g., as synthesized above, was dissolved in 45 g. of *o*-chlorophenol by warming and 1.2 cc. of hydrochloric acid was added. The mixture was set aside for 2 days, at which time it was distilled in the all-glass apparatus, the fraction coming over at 235–240° (25 mm.) being collected. Upon solidification, the distillate was crystallized from water to give 3 g. of a product, m.p. 103–104°. A mixed melting point with 3,3′-dichloro-4,4′-dihydroxydiphenylmethane, m.p. 104–105°, showed no appreciable depression. Chlorination as described previously gave the tetrachloro derivative, m.p. 185.5–187°.

Products from 2,4-Dichlorophenol and Derivatives

1. *6,8-Dichloro-1,3-benzodioxane.* A mixture of 10 g. of Eastman's C.P. 2,4-dichlorophenol, 80 cc. of U.S.P. 40% formaldehyde, 450 cc. of concentrated hydrochloric acid, and 10 cc. of concentrated sulfuric acid was agitated at 35–40° for 2 hours while a rapid stream of hydrogen chloride was bubbled through the solution. Although a solid formed after about 1.75 hours, the reaction mixture was allowed to stand overnight to complete the separation. After filtration and washing with water to remove the acid present, the solid was steam distilled. The white solid, 6.8 g., which came over, was crystallized from methanol, m.p. 109–109.5°.

Anal. Calc'd for $C_8H_6Cl_2O_2$: Cl, 34.59; mol. wt., 205.0.
Found: Cl, 34.86; mol. wt. (crysoscopic, benzene), 194.

(a) *6,8-Dichloro-1,3-benzodioxan-4-one.* The dioxane, 13.5 g., was oxidized by the method of Borsche and Berkhout (9). The crude benzodioxanone, washed with water until free from color, was crystallized from ethanol to give 8 g. of a white compound, m.p. 114°.

Anal. Calc'd for $C_8H_4Cl_2O_3$: Cl, 32.38; mol. wt., 219.0.
Found: Cl, 32.44; mol. wt. (crysoscopic, benzene), 210.

(b) *3,5-Dichlorosalicylic acid.* The dioxanone, 8 g., was boiled in dilute sodium hydroxide solution and then acidified as recommended by Borsche and Berkhout. The crude product when crystallized from water gave a white solid, 4 g., m.p. 220° [Zincke (14) gives 219°].

(c) For verification the *methyl ester* was prepared by refluxing with methyl alcohol while dry hydrogen chloride was passed through the mixture. Two crystallizations from ethanol gave crystals, 2 g., m.p. 148–149° [Lassar-Cohn and Schultze (15) give 150°].

2. *3,5-Dichloro-2-hydroxybenzyl chloride.* A mixture of 10 g. of crushed Eastman's C.P. 2,4-dichlorophenol and 450 cc. of concentrated hydrochloric acid was stirred at near 50° until the phenol dissolved. Formaldehyde, 10 cc. of U.S.P. 40%, was added dropwise over a period of 20 to 30 minutes and then hydrogen chloride was bubbled rapidly through the stirred solution at 50° for 36 hours. By this time a white solid had formed and the flask was placed in the refrigerator for 12 hours. Filtering through empty Gooch crucibles followed by washing with cold water and drying gave 12 g. of a product, m.p. 81–84°. Crystallization from petroleum ether (b.p. 60–75°) produced long, white needles, m.p. 82–84°.

Anal. Calc'd for $C_7H_5Cl_3O$: Cl, 50.30. Found: Cl, 50.36, 50.36.

(a) *3,5-Dichloro-2-hydroxybenzyl alcohol.* This alcohol was always present in the liquor remaining from the steam distillation of 6,8-dichloro-1,3-benzodioxane. It was best prepared from 3,5-dichloro-2-hydroxybenzyl chloride as follows: Two grams of the chloride in 350 cc. of water was stirred at 50° for 4.5 hours, by which time only a trace of a yellow resinous substance remained undissolved. The clear solution was evaporated down to 100 cc. and, upon chilling, yielded 1.2 g. of white needles, m.p. 80–81°; [Mettler (16) gives 82°].

Anal. Calc'd for $C_7H_6Cl_2O_2$: Cl, 36.74. Found: Cl, 36.58, 36.51.

(b) *6,8-Dichloro-2-phenyl-1,3-benzodioxane.* This dioxane was prepared by the method of Adams (8). A mixture of 9 g. of the alcohol and 0.6 g. of freshly purified benzaldehyde was warmed over a steam-bath for two hours. Cooling gave a dark solid, which when crystallized from ethanol produced 0.7 g. of white, fluffy needles, m.p. 83.5–85.0°. This dioxane gives no color with ferric chloride while the original alcohol produces a deep purple.

Anal. Calc'd for $C_{14}H_{10}Cl_2O_2$: Cl, 25.22. Found: 25.30, 25.40.

SUMMARY

On condensing *o*-chlorophenol with formaldehyde in hydrochloric acid medium, moderate yields of 3-chloro-4-hydroxybenzyl chloride and 3,3′-dichloro-4,4′-dihydroxydiphenylmethane were obtained; under somewhat similar conditions 2,4-dichlorophenol gave good yields of 6,8-dichloro-1,3-benzodioxane and 3,5-dichloro-2-hydroxybenzyl chloride.

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