

The melting and boiling points of methyl chloride are 175.44 and 248.94°K. respectively (0°C. = 273.16°K.).

The heat of fusion is 1537 cal./mole and the heat of vaporization is 5147 cal./mole at the boiling point.

The vapor pressure of methyl chloride is represented from the triple point to the boiling point by the equation, $\log_{10} P_{\text{mm.}} = -(1822.60/T -$

$9.287119 \log_{10} T + 0.00555556 T + 31.07167.$

The triple point pressure is 6.57 int. mm.

The entropy of methyl chloride in the ideal gas state has been found from calorimetric data to be 54.27 e. u. and 55.94 e. u. at 284.94 and 298.16°K., respectively. The corresponding values calculated from spectroscopic and molecular data are 54.31 e. u. and 55.98 e. u.

STATE COLLEGE, PA.

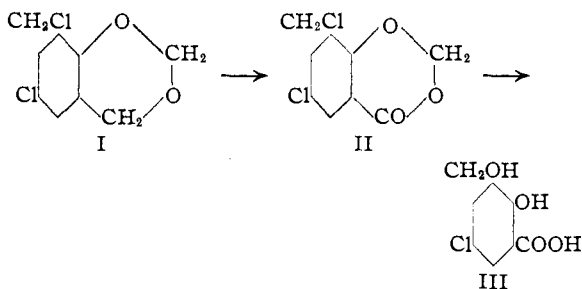
RECEIVED JANUARY 12, 1940

[CONTRIBUTION FROM THE DABNEY CHEMICAL LABORATORY, UNIVERSITY OF TENNESSEE]

Proof of Structure of 6-Chloro-8-chloromethyl-1,3-benzodioxane by Oxidation¹

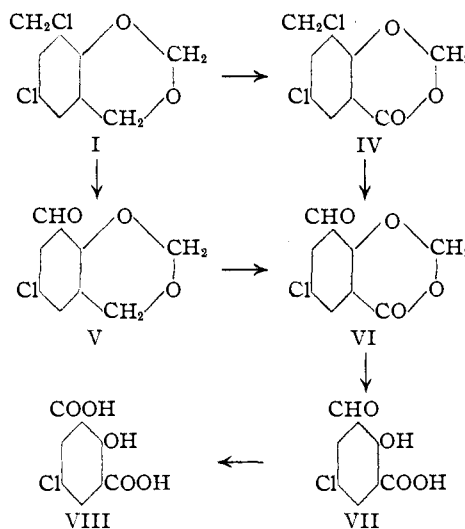
BY C. A. BUEHLER, B. CALVIN BASS, ROBERT B. DARLING AND MILTON E. LUBS

In studying the action of formaldehyde on *p*-chlorophenol² in the presence of hydrochloric acid, a compound (I) thought to be 6-chloro-8-chloromethyl-1,3-benzodioxane was obtained. That the condensation product was a dioxane was shown by oxidation with chromium trioxide in acetic acid by the method of Borsche and Berkhout.³ The 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, II, thus obtained gave, on alkaline hydrolysis, 2-hydroxy-3-methylol-5-chlorobenzoic acid, III.



To prove the structure of the original dioxane, I, a new oxidizing mixture, potassium permanganate in acetic acid, was tried and it was found that complete disruption of the dioxane ring was possible in one step. In this oxidation five products, IV, V, VI, VII and VIII, were isolated. Considering the effect of time and concentration of oxidizing agent on the amounts of the products obtained, we are inclined to support the oxidation sequence as indicated below. Of the first-formed products, IV appears in greater amounts than V

although the former apparently is consumed more rapidly as the oxidation proceeds.



The 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, IV, and 6-chloro-8-aldol-1,3-benzodioxane, V, were isolated only in small quantities. The former, identical with II, gave the corresponding alcohol on alkaline hydrolysis while the latter was identified by conversion into its phenylhydrazone.

Of all the oxidation products, perhaps 6-chloro-8-aldol-1,3-benzodioxane-4-one, VI, is the most interesting because of the ease with which the dioxanone ring is broken. Not only does this opening occur on standing and on titration with standard alkali, since the neutral equivalent is fairly satisfactory and 2-hydroxy-3-aldol-5-chlorobenzoic acid, VII, may be recovered from the titration mixture, but catalytic reduction, in which

(1) Presented at the 99th meeting of the American Chemical Society, Cincinnati, Ohio, April, 1940.

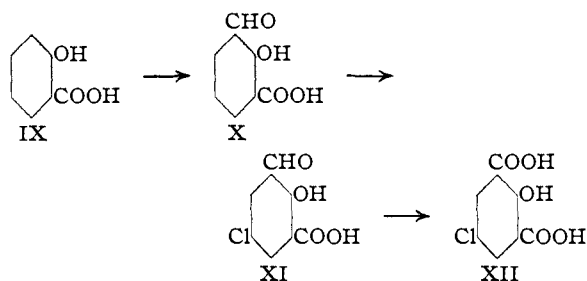
(2) For a similar reaction of phenol, see *Chem. Zentr.*, **103**, I, 2997(1932).

(3) Borsche and Berkhout, *Ann.*, **330**, 92 (1904).

the product is purified from slightly acidified water, gives 2-hydroxy-3-methylol-5-chlorobenzoic acid, III, rather than the expected 6-chloro-8-methylol-1,3-benzodioxane-4-one. Of indefinite melting point, this unstable dioxanone reacts positively with Tollens' reagent, a test which serves to distinguish it clearly from its decomposition product, 2-hydroxy-3-aldo-5-chlorobenzoic acid, VII, which does not affect this reagent.

2-Hydroxy-3-aldo-5-chlorobenzoic acid, VII, formed an oxime and could be oxidized readily to 2-hydroxy-5-chloroisophthalic acid, VIII, a compound which is fluorescent in ultraviolet light. The latter formed a diethyl ester.

None⁴ of the oxidation products is recorded in the literature. To establish their constitution the synthesis below was carried out



Salicylic acid, IX, was converted into the known 2-hydroxy-3-aldo-5-chlorobenzoic acid, X, by the Reimer-Tiemann reaction. On chlorination X gave a chloro derivative, XI, identical with VII. From an examination of the oxidation and synthetic series of reactions it is apparent that this identity could occur only if the formula for VII and XI was that of 2-hydroxy-3-aldo-5-chlorobenzoic acid. As further proof of structure, XI was oxidized with potassium permanganate in acetic acid to give the dicarboxylic acid, XII, which proved to be identical with VIII.

Experimental

Preparation of 6-Chloro-8-chloromethyl-1,3-benzodioxane.—To a mixture of 500 cc. of concentrated hydrochloric acid and 15 cc. of concentrated sulfuric acid warmed to 40°, 20 g. of Eastman Kodak Co. practical *p*-chlorophenol and 80 cc. of U. S. P. 40% formaldehyde were added. Hydrogen chloride was bubbled rapidly through the stirred mixture, kept at 40°, for one and one-half hours, at which point the solution had clarified with the separation of some solid. This crude solid, 30 g., was crystallized three times from methanol and gave 18.5 g. melting at 103°.

Anal. Calcd. for $C_8H_8O_2Cl_2$: Cl, 32.37; mol. wt.,

(4) German Patent 216,924 refers to a product, melting at 201°, which was thought to be 2-hydroxy-3-aldo-5-chlorobenzoic acid.

219.1. Found: Cl, 32.31, 32.42; mol. wt. (cryoscopic, benzene), 217, 218.

Oxidation of 6-Chloro-8-chloromethyl-1,3-benzodioxane to 6-Chloro-8-chloromethyl-1,3-benzodioxan-4-one.—The dioxane, 3 g., was oxidized by the method of Borsche and Berkhout.² The crude benzodioxanone, washed with water until free from color, was crystallized from 95% ethanol, on the addition of water, in white, glistening plates, 1 g., melting at 181–182°. The compound gave a positive test for chlorine with aqueous silver nitrate, but no coloration was produced with ferric chloride nor was there any fluorescence in ultraviolet light.

Anal. Calcd. for $C_8H_6O_3Cl_2$: Cl, 30.43; mol. wt., 233.1. Found: Cl, 30.48, 30.22; mol. wt. (cryoscopic, acetic acid), 238, 242.

Hydrolysis of the Benzodioxanone to 2-Hydroxy-3-methylol-5-chlorobenzoic Acid.—6-Chloro-8-chloromethyl-1,3-benzodioxane-4-one, 1 g., was warmed with sodium hydroxide solution and then acidified as recommended by Borsche and Berkhout. The crude product when crystallized from 95% ethanol, upon the addition of water, gave a white powder, 0.5 g., melting at 165.5–166°. The pure acid produced a mulberry-purple color with ferric chloride and a bluish-green fluorescence in ultraviolet light.

Anal. Calcd. for $C_8H_7O_4Cl$: Cl, 17.50, neut. equiv., 202.6. Found: Cl, 17.61, 17.64; neut. equiv., 206.

Oxidation of 6-Chloro-8-chloromethyl-1,3-benzodioxane with Potassium Permanganate.—To a solution of 3 g. of 6-chloro-8-chloromethyl-1,3-benzodioxane in 100 cc. of glacial acetic acid there was added 160 cc. of distilled water, which causes considerable precipitation, and 9 g. of potassium permanganate. This mixture was refluxed vigorously for two hours while a stream of air was introduced to prevent bumping. After partial cooling, sulfur dioxide was bubbled through the solution to remove the color and dissolve the suspended material. To prevent resinification the resulting amber colored solution, having a greenish-blue fluorescence, was evaporated in a stream of air to one-half its volume or until organic material began to separate. Twice the volume of distilled water was then added, and the mixture was allowed to stand for three to four hours when about 0.2 g. of 6-chloro-8-aldo-1,3-benzodioxane, usually mixed with a smaller amount of 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, separated out. The total solid was dissolved in about 10 cc. of methanol and then thrown out by the addition of 50 to 75 cc. of cold water as 6-chloro-8-aldo-1,3-benzodioxane, a white solid melting at 138–138.5°.

After the removal of the crude 6-chloro-8-aldo-1,3-benzodioxane, concentrated hydrochloric acid was added to the filtrate until the amber color just disappeared. At the same time the solution became cloudy, and the fluorescence changed to blue-violet. This mixture was allowed to stand, usually twelve hours or more, until about 0.3 g. of 2-hydroxy-3-aldo-5-chlorobenzoic acid separated out. This product, when crystallized from water three or four times, gave 0.1 g. of long needles melting at 213.5–215.5°. More of the compound may be recovered by the addition of hydrochloric acid to the filtrate.

The filtrate obtained on removing the aldo acid was extracted with about 75-cc. portions of ether four times, the aqueous layer being discarded. On evaporating the com-

bined ether extractions to dryness, a mixture of about 1 g. of 6-chloro-8-aldo-1,3-benzodioxan-4-one and 2-hydroxy-5-chloroisophthalic acid, containing small amounts of 2-hydroxy-3-aldo-5-chlorobenzoic acid, was recovered. This residue was extracted with two 75-cc. portions of chloroform, and the combined chloroform solutions were then evaporated to about 90 cc., during which process some solid separated. This solid was removed and added to that remaining from the two chloroform extractions.

The chloroform filtrate was evaporated to about 25 cc., and the solid separating, about 0.4 g., which was removed by filtration, was crude 6-chloro-8-aldo-1,3-benzodioxan-4-one. This compound proved to be difficult to purify by the usual methods. Our best product was obtained by recrystallization twice from chloroform, in which process the first crystals, consisting largely of 2-hydroxy-5-chloroisophthalic acid, were discarded. The fact that 2-hydroxy-5-chloroisophthalic acid was fluorescent in ultraviolet light was of great assistance in this purification. Because of its instability the melting point of the 6-chloro-8-aldo-1,3-benzodioxan-4-one obtained, about 0.3 g., was indefinite. If heated rapidly, it melted in the neighborhood of 165–170°, then solidified, and finally sublimed around 190–200°. If heated slowly, the compound did not melt, but began to sublime around 175°, the process being complete near 200°.

The residue, about 0.3 g., remaining from the chloroform extractions was crude 2-hydroxy-5-chloroisophthalic acid. It was purified by solution in hot water followed by cooling in an ice-bath. After removing some 2-hydroxy-3-aldo-5-chlorobenzoic acid, which separated out first as an impurity, by filtration, concentrated hydrochloric acid was added to the filtrate and 2-hydroxy-5-chloroisophthalic acid precipitated. This compound, after five crystallizations, gave about 0.1 g. of a white, hair-like product melting at 238–240°.

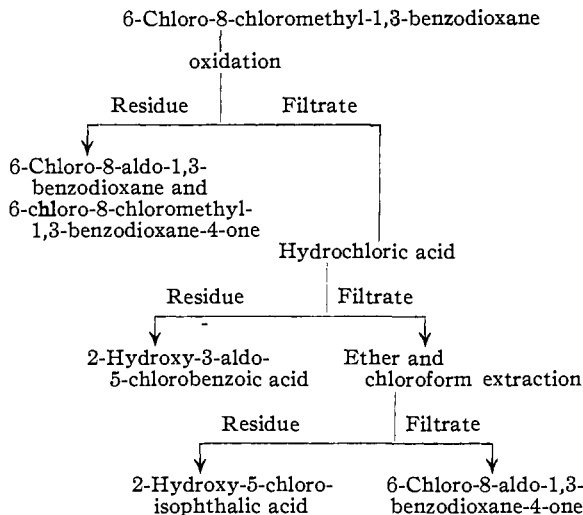
Either varying the time or concentration of oxidizing agent exerted an influence on the amounts of the oxidation products. For instance, in a forty-five minute oxidation, fairly pure 6-chloro-8-chloromethyl-1,3-benzodioxan-4-one separated at the point at which impure 6-chloro-8-aldo-1,3-benzodioxane normally appeared. This dioxanone, after crystallization from methanol, weighed 0.25 g. and melted at 178–181°. A three-hour oxidation, in which the 6-chloro-8-aldo-1,3-benzodioxane-4-one produced was converted into 2-hydroxy-3-aldo-5-chlorobenzoic acid during the purification of 2-hydroxy-5-chloroisophthalic acid, gave 0.4 g. of the aldo acid. Likewise, a five and one-half hour oxidation gave 0.3 g. of 2-hydroxy-5-chloroisophthalic acid.

The scheme of separation employed for the oxidation products of 6-chloro-8-chloromethyl-1,3-benzodioxane may be represented diagrammatically as shown

Oxidation Products and Derivatives

(1) **6-Chloro-8-chloromethyl-1,3-benzodioxan-4-one.**—This dioxanone, m. p. 178–181°, was identical with that previously described as melting at 181–182°. On hydrolysis it gave 2-hydroxy-3-methylol-5-chlorobenzoic acid also previously described.

(2) **6-Chloro-8-aldo-1,3-benzodioxane.**—This compound, a white powder, m. p. 138–138.5°, gave negative



tests with aqueous silver nitrate, ferric chloride, litmus and ultraviolet light.

Anal. Calcd. for $C_9H_7O_2Cl$: Cl, 17.85. Found: Cl, 17.82, 17.96.

(a) The phenylhydrazone separated from an alcoholic solution on the addition of water as pale yellow needles, m. p. 152.5–155°.

Anal. Calcd. for $C_{15}H_{13}O_2ClN_2$: Cl, 12.28. Found: Cl, 12.31, 12.21.

(3) **6-Chloro-8-aldo-1,3-benzodioxan-4-one.**—The melting point of this dioxanone is of little significance as has been indicated above. The compound did not affect aqueous silver nitrate nor fluoresce in ultraviolet light, but it gave a mulberry-purple color with ferric chloride and a deposit of silver with Tollens reagent. In hot alkali it was sufficiently soluble for a neutral equivalent determination. Conversion to 2-hydroxy-3-aldo-5-chlorobenzoic acid was accomplished on standing or by heating in neutral or alkaline solution.

Anal. Calcd. for $C_9H_7O_4Cl$: Cl, 16.68; neut. equiv., 212.6. Found: Cl, 16.71, 16.88; neut. equiv., 202, 198.

(a) The oxime of 2-hydroxy-3-aldo-5-chlorobenzoic acid was obtained from the dioxanone and hydroxylamine hydrochloride in 10% sodium hydroxide solution. By the addition of water to an ethanol solution, it crystallized as a white, needle-like solid, m. p. 199.5–200.5°.

Anal. Calcd. for $C_9H_6ClNO_4$: Cl, 16.45; neut. equiv., 215.6. Found: Cl, 16.48; neut. equiv., 207.

(b) By reduction of the dioxanone in ethyl acetate with hydrogen (Raney catalyst) at 39 lb. (2.5 atm.) pressure followed by evaporation of the solvent and taking up the residue in warm water, 2-hydroxy-3-methylol-5-chlorobenzoic acid separated as the solution, slightly acidified with hydrochloric acid, cooled for several hours. Purification by the same process gave a product of m. p. 166.5–167°. The identity of this acid with that previously described was established by analysis and mixed melting point.

(4) **2-Hydroxy-3-aldo-5-chlorobenzoic Acid.**—This aldo acid, one of the most abundant oxidation products, crystallized easily though not with a sharp melting point from

aqueous solution. The crude product, m. p. 208–214°, rose in melting point to 217–221° after ten crystallizations. The crystals separated in clusters from a dilute and in a hair-like mat from a concentrated solution. Aqueous silver nitrate reacted negatively, but ferric chloride gave a cherry-red coloration. In solution the substance gave a green fluorescence in reflected light, but there was no effect in the ultraviolet except on standing when fluorescence developed slowly due to the formation of 2-hydroxy-5-chloroisophthalic acid. Potassium permanganate in acetic acid converted the aldo acid to the corresponding dicarboxylic acid in good yield. The compound first formed was a monohydrate.

Anal. Calcd. for $C_8H_5ClO_4 \cdot H_2O$: Cl, 16.27; neut. equiv., 218.6. Found: Cl, 16.57, 16.49; neut. equiv., 208, 212.

Heating at 115–120° for three hours gave the anhydrous form.

Anal. Calcd. for $C_8H_5ClO_4$: Cl, 17.68; neut. equiv., 200.6. Found: Cl, 17.66, 17.80; neut. equiv., 201.

(a) The oxime, m. p. 199.5–200.5°, prepared in the usual manner, was shown by analysis and mixed melting point to be identical with that previously described. It gave a dark purple color with ferric chloride; its aqueous solution in reflected light produced a blue, while the solid in ultraviolet gave a yellowish-green, fluorescence.

(5) **2-Hydroxy-5-chloroisophthalic Acid.**—This dicarboxylic acid separated from water as a white mat resembling filter paper. When heated it shrank at about 225°, darkened at about 235°, and then melted with slight decomposition at 238–240°. Its aqueous solution in reflected light possessed a blue-violet, while the solid in ultraviolet gave a bright greenish-blue, fluorescence. Silver nitrate did not affect a solution of the acid, but ferric chloride produced a dark red color. The compound separating from water was a monohydrate.

Anal. Calcd. for $C_8H_5ClO_5 \cdot H_2O$: Cl, 15.11; neut. equiv., 117.3. Found: Cl, 15.23, 15.38; neut. equiv., 116, 115.

By heating for five hours at 115–120°, the anhydrous acid resulted.

Anal. Calcd. for $C_8H_5ClO_5$: Cl, 16.37; neut. equiv., 108.3. Found: Cl, 16.40, 16.42; neut. equiv., 115, 116.

(a) The diethyl ester was produced from ethanol and hydrogen chloride. By the addition of cold water to an ethanol solution, it crystallized as white needles, m. p. 50–51°. In ultraviolet light the solid produced a bluish-green fluorescence.

Anal. Calcd. for $C_{12}H_{13}ClO_5$: Cl, 13.00. Found: Cl, 13.04, 13.11.

Synthetic Products and Derivatives

(1) **2-Hydroxy-3-aldobenzoic Acid.**—This acid was prepared by the Reimer–Tiemann reaction⁶ modified as follows. A solution of 200 g. of sodium hydroxide in 450 cc. of water was prepared and to 300 cc. of it at room temperature, containing 50 cc. of chloroform, there was added slowly, with constant stirring, 90 g. of salicylic acid. The resulting solution was placed in a three-necked,

round-bottomed flask in which it was stirred while being refluxed on a water-bath at 80°. After the initial foaming and refluxing had subsided somewhat, another 50 cc. of chloroform and the remainder of the sodium hydroxide solution were added gradually through the condenser over a period of three hours. After another hour of stirring at 80°, the mixture was allowed to cool. Any chloroform layer was siphoned off, and 1:1 hydrochloric acid was added cautiously to the remainder of the reaction mixture until it became neutral, a fact indicated by its light, almost transparent appearance. After filtering off any resinous material present, 150 cc. more of 1:1 hydrochloric acid was added and a voluminous tan precipitate formed. This solid was permitted to settle while being cooled to about 20°, and then it was filtered off in a Büchner and washed five times with about 50-cc. portions of cold water.

The residue was now dissolved in an amount of 1:10 ammonium hydroxide sufficient to produce an orange to red solution. To this solution about 100 cc. of a 20% copper sulfate solution was added, with constant stirring, until the suspension which formed assumed a pea-green color. More 1:10 ammonium hydroxide, about 100 cc., was then added until the color became a much darker green.⁶ After warming at 60° with constant stirring, the mixture was filtered, the green residue being washed three or four times with cold water.

In a solution of 15 cc. of concentrated sulfuric acid in 1200 cc. of water, the above residue was dissolved and, on stirring, the free 2-hydroxy-3-aldobenzoic acid separated as a flocculent white to yellow precipitate. So much resinous material was present, however, that the precipitate was redissolved in the mother liquor by heating barely to boiling, to avoid additional resinification, and the mixture was filtered rapidly. On cooling, tan crystals, melting at 167–173°, separated from the filtrate. For purification, the crude product was dissolved at room temperature in the least possible quantity of methanol, and this solution was poured several times through boneblack. Crystallization occurred after adding 3 volumes of water and cooling to 20°. Two more crystallizations from methanol gave 3 g. of tan needles melting at 178–179° (Reimer and Tiemann give 179°).

(2) **2-Hydroxy-3-aldo-5-chlorobenzoic Acid.**—Into a solution of 3.0 g. of 2-hydroxy-3-aldobenzoic acid in 75 cc. of glacial acetic acid surrounded with ice, dry chlorine was bubbled at the rate of 60 to 70 bubbles per minute until 1.3 g. of the gas had dissolved. After standing at room temperature for twenty-four hours, the reaction mixture was diluted with approximately three times its volume of distilled water. Upon cooling in a refrigerator for two hours, 2-hydroxy-3-aldo-5-chlorobenzoic acid had precipitated as a white, fluffy solid. By crystallization three times from water the acid, 2.7 g., melted at 226°. An analysis, as shown below, indicated that the compound was isomeric with the hydrated oxidation acid melting at 217–221°.

Anal. Calcd. for $C_8H_5ClO_4 \cdot H_2O$: Cl, 16.27; neut.

(6) The success of the experiment depends largely on the skill in arriving at the proper shade of color. Since the copper salts of 2-hydroxy-3-aldobenzoic and 2-hydroxy-5-aldobenzoic acids have different solubilities in ammonium hydroxide, a satisfactory separation is possible at the proper concentration. However, if the alkali is excessive, both isomeric salts dissolve.

(5) Reimer and Tiemann, *Ber.*, **10**, 1563 (1877).

equiv., 218.6. Found: Cl, 16.41, 16.61; neut. equiv., 212, 219.

That the two acids were identical was shown by a mixed melting of the oximes (synthetic aldoxime, m. p. 202°; oxidation aldoxime, m. p., 199.5–200.5°).

(3) **2-Hydroxy-5-chloroisophthalic Acid.**—To a solution of 1.2 g. of synthetic 2-hydroxy-3-aldo-5-chlorobenzoic acid in 40 cc. of glacial acetic acid, 64 cc. of distilled water and 4 g. of potassium permanganate were added. The mixture was stirred about a minute, until a noticeable reaction began, and then it was allowed to stand for two hours. After clarification with sulfur dioxide, evaporation to about half its volume, and then cooling, the crude 2-hydroxy-5-chloroisophthalic acid, which had separated, was removed. Upon purifying and heating as before, the anhydrous synthetic dicarboxylic acid melted at 245–246°. The analysis, as given below, indicated that the compound was isomeric with the anhydrous oxidation dicarboxylic acid whose hydrate melted at 238–240°.7

Anal. Calcd. for $C_8H_5ClO_5$: Cl, 16.37; neut. equiv., 108.3. Found: Cl, 16.48, 16.17; neut. equiv., 113, 113.

That the two dicarboxylic acids were identical was

(7) For both 2-hydroxy-3-aldo-5-chlorobenzoic and 2-hydroxy-5-chloroisophthalic acids the melting points of the hydrates do not differ appreciably from those of the anhydrous forms.

shown by a mixed melting point of the two diethyl esters (synthetic ester, m. p. 50°; oxidation ester, m. p. 50–51°).

Summary

1. 6-Chloro-8-chloromethyl-1,3-benzodioxane has been obtained by the action of formaldehyde on *p*-chlorophenol in the presence of hydrochloric acid.

2. Oxidizing the above dioxane with potassium permanganate in acetic acid gave five products: 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, 6-chloro-8-aldo-1,3-benzodioxane, 6-chloro-8-aldo-1,3-benzodioxane-4-one, 2-hydroxy-3-aldo-5-chlorobenzoic acid and 2-hydroxy-5-chloroisophthalic acid.

3. The structure of 6-chloro-8-chloromethyl-1,3-benzodioxane was established through the identity of 2-hydroxy-3-aldo-5-chlorobenzoic and 2-hydroxy-5-chloroisophthalic acids with two isomeric acids synthesized from salicylic acid.

KNOXVILLE, TENN.

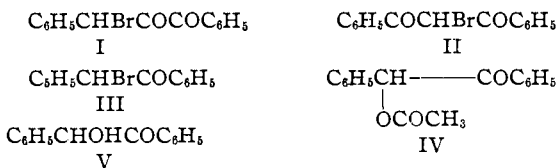
RECEIVED FEBRUARY 1, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, HOWARD UNIVERSITY]

The Acetylation of alpha-Bromo Ketones and their Derivatives

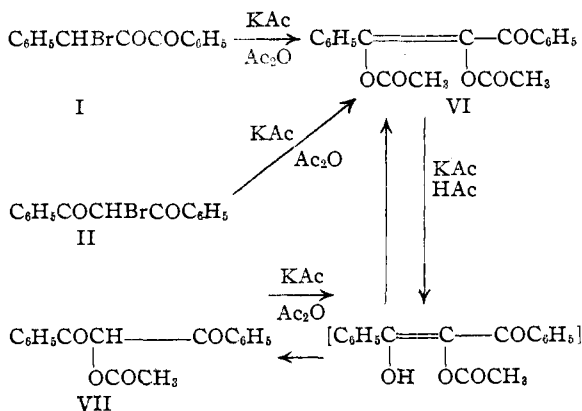
BY R. P. BARNES AND VICTOR J. TULANE

In an attempt to obviate certain difficulties experienced with glacial acetic acid solutions of freshly fused potassium acetate as an acetylating agent for alpha haloketones, we turned to acetic anhydride solutions of the acetate instead. The results were so surprising that we decided to test further the power of this acetylating combination. Thus the following compounds were investigated: phenyl bromobenzyl diketone (I), bromodibenzoylmethane (II), desyl bromide (III), acetylbenzoin (IV) and benzoin (V).



We have found that both bromo ketones (I) and (II) upon refluxing with a solution of freshly fused potassium acetate in acetic anhydride lead to the diacetate of phenylbenzoyl acetyleneglycol (VI). This diacetate, upon treatment with a solution of freshly fused potassium acetate in

glacial acetic acid with subsequent distribution of the acetic acid by pouring into a large volume of water, is changed quantitatively into dibenzoylcarbinol acetate (VII). While other methods of acetylation fail,¹ dibenzoylcarbinol acetate is acetylated quantitatively by means of acetic anhydride-fused potassium acetate, giving the diacetate (VI).



(1) A. H. Blatt and W. Lincoln Hawkins, *THIS JOURNAL*, **58**, 81 (1936).