

of bromine to the double bond is the only method recorded for the synthesis of 2,3-dibromo-*p*-dioxane.<sup>5</sup>

Dry hydrogen bromide converts tetrahydrofuran to 1,4-dibromobutane readily whereas dry hydrogen chloride is unreactive.<sup>6</sup> The failure to obtain 2,3-dibromo-*p*-dioxane by direct bromination is probably due to a similar opening of the *p*-dioxane ring by the hydrogen bromide coproduct.

A refluxing mixture of *p*-dioxane and carbon tetrachloride, however, can be brominated to give 2,3-dibromo-*p*-dioxane readily in good yield. This is probably due to the low solubility of hydrogen bromide in warm carbon tetrachloride.<sup>7</sup> Good quality 2,3-dibromo-*p*-dioxane that is considerably more stable than material described previously<sup>5</sup> can be crystallized readily from the reaction mixture in 75% yield. Simple distillation of the crude reaction mixture gives similar yields of crystalline product that decompose rapidly at room temperature with evolution of hydrogen bromide unless washed well with ether. One possible explanation is that the ether removes traces of hydrogen bromide which trigger the autocatalyzed decomposition if not removed. This is suggested by the fact that in one run in which the ether wash was less thorough the product was considerably less stable than usual and began to decompose on standing at room temperature for one day. At the beginning of the decomposition dark specks appeared throughout the mass of colorless crystals. The specks increased in size with increasing speed and with evolution of heat and hydrogen bromide until the entire mass had decomposed.

Bromination in refluxing carbon tetrachloride has an additional advantage in that halogen loss is minimized since halogen in the off-gas is returned to the reaction mixture dissolved in the condensate. This method might be extended to the halogenation of other compounds (especially ethers) where evolved hydrogen halides produce undesirable side reactions.

#### EXPERIMENTAL<sup>8</sup>

*2,3-Dibromo-p-dioxane.* A refluxing solution of 88.1 g. (1.00 mole) of *p*-dioxane (Union Carbide Corp. commercial grade) and 100 ml. of reagent-grade carbon tetrachloride in a 500-ml. round-bottomed flask equipped with all-glass accessories including a dropping funnel, Trubore stirrer, and an efficient condenser connected to an off-gas scrubbing system, was treated with 291.0 g. (1.82 moles, 91% of theory) of bromine over a 4-hr. period with constant irradiation from two Hanovia SC 5041 ultraviolet lamps placed 1 cm. from the flask. Bromine was added at such a rate that the condensate and flask contents remained only slightly colored.

(5) R. K. Summerbell and L. N. Bauer, *J. Am. Chem. Soc.*, **57**, 2364 (1935).

(6) S. Fried and R. D. Kleene, *J. Am. Chem. Soc.*, **63**, 2691 (1941).

(7) J. J. Howland, D. R. Miller, and J. E. Willard, *J. Am. Chem. Soc.*, **63**, 2807 (1941).

(8) Melting points are corrected.

The mixture was irradiated for an additional 5 min. The resulting pale yellow solution was cooled, seeded with 2,3-dibromo-*p*-dioxane, and held at 0° for 0.5 hr. The heavy crop of crystals was collected on a sintered glass funnel, washed with cold carbon tetrachloride, and dried on an aspirator with the aid of a rubber dam. To keep the product free from moisture, it was allowed to warm to room temperature before removing the dam. The product was then transferred to a round-bottomed flask and dried further at 12 mm. to give 118.8 g. of colorless, irregular prisms, m.p. 73.0–74.5° (reported<sup>5</sup> 69–70° with previous softening).

*Anal.* Calcd. for C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>Br<sub>2</sub>: Br, 65.0%. Found: Br, 65.2, 64.9, 64.8%.

A small portion of the product was allowed to react with excess 2,4-dinitrophenylhydrazine in aqueous ethanol containing perchloric acid.<sup>9</sup> The yield of glyoxal 2,4-dinitrophenylosazone in four runs was 99.6 ± 0.2%.

The mother liquor was concentrated rapidly at aspirator pressure (water bath at 60°) and on working up as described above yielded 37.2 g. of colorless, irregular prisms, m.p. 71.5–73.5°. Repeating this operation gave 11.9 g. of colorless product, m.p. 70.5–73.0°, bringing the total yield to 167.9 g. (0.683 mole; 75.1% based on bromine consumed). The mother liquor was not investigated further.

Samples of product in polyethylene-capped bottles were stored for several weeks at room temperature and for 6 months at –8° with no change in appearance.

When the reaction was repeated exactly as described above and the crude product distilled rapidly through an 8-in. Vigreux column, there was obtained, after a forerun of solvent and unreacted dioxane, 72.4% (based on bromine consumed) of colorless liquid in four fractions, b.p. 123–133° (21 mm.). This material crystallized completely when cooled and seeded. A small portion of the third cut was washed several times with cold ether and dried under vacuum at room temperature to give colorless, irregular prisms, m.p. 73.0–74.5°, having the same stability as the material described above. The remainder of the distilled product turned dark and began to liquify on standing at room temperature for 1 hr.

When *p*-dioxane was brominated and distilled as described above, except that no solvent was employed and the bromination was carried out at 90–110°, none of the seven fractions obtained crystallized on cooling and seeding with 2,3-dibromo-*p*-dioxane.

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(9) C. L. Dunn, *J. Agr. Food Chem.*, in press.

#### Preparation and Properties of Some Aryl Esters of Phosphoric Acid<sup>1</sup>

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Diphenyl hydrogen phosphate (I) and its *p*-nitro derivative, bis(*p*-nitrophenyl) hydrogen phosphate (II) are convenient substrates for the investigation of phosphodiesterases. Rapp<sup>2</sup> has in-

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(2) M. Rapp, *Ann.*, **224**, 156 (1884).

licated that II is synthesized with difficulty, at least by nitration of I. Consequently, biochemists have followed the procedure of Yoshida<sup>3</sup> in which *tris(p-nitrophenyl) phosphate* (III) is hydrolyzed in alcoholic NaOH, and II precipitated from the reaction mixture as the calcium salt, the crude product being used as substrate for phosphodiesterase activity.<sup>4</sup> Inasmuch as the calcium salt of *p-nitrophenyl phosphate* (IV) is also water insoluble, the possibility arises that the crude material may be contaminated with IV and that this is responsible, in part, for the observation that II is attacked by certain phosphomonoesterases.<sup>5</sup> This question can be resolved by investigating the behavior of phosphomono- and diesterases against pure II. In this communication we describe a simple method for preparing II in good yield and discuss the preparation and properties of this and related esters of phosphoric acid, about which some erroneous statements appear in the literature.

#### EXPERIMENTAL

*Tris(p-nitrophenyl) phosphate.* Garihi and Laskowski<sup>4</sup> prepared this material by nitrating triphenyl phosphate and obtained a product which crystallized from acetone-water, 1:1, and had a m.p. of 130°. Following their procedure, we obtained a crude product, m.p. 138–145° which, after crystallization from 2-butanone, melted at 154–156°. This is the melting point given by Rapp<sup>2</sup>. An m.p. of 157–159° is reported by Corby, Kenner and Todd.<sup>6</sup>

While the yield of crude III is practically theoretical, the yield of the purified compound by crystallization from 2-butanone was unexpectedly low (15% of theory) in our initial preparation. Upon evaporation of the mother liquor, a large amount of material crystallized out, m.p. 175–176°, whose identity was unknown at the time. This will be referred to later.

*Bis(p-nitrophenyl) hydrogen phosphate.* Rapp<sup>2</sup> reported the melting point of this compound as 133.5°. Hoeflake<sup>7</sup> has corrected this misinformation and gives the m.p. as 175°. Corby *et al.*<sup>6</sup> record 176–178° for a preparation obtained by the phosphorylation of *p-nitrophenol*. It thus became apparent that the unknown compound, m.p. 175–176°, referred to above, was very likely II. This possibility was confirmed by a mixed melting point determination with II prepared according to Corby *et al.*<sup>6</sup> Investigation of the hydrolytic reaction which yielded II during the preparation of III led to a simple procedure for the preparation of II, illustrated in the following example: 2.4 g. (0.005 mole) *tris(p-nitrophenyl) phosphate*, m.p. 154–156, was completely dissolved in about 21 ml. of boiling 2-butanone, 2% (v/v) with respect to water, and refluxed for 3 hr. The solution was evaporated to dryness, first by a stream of air, and finally *in vacuo*. The cake was taken up in 15 ml. boiling chloroform (which did not dissolve all of the solid) and filtered. The crystalline material which separated from the solvent (0.64 g., m.p. 174–175°) was combined with the residue on the filter (0.76 g., m.p. 159–170°) and recrystallized from ethyl *n*-butyrate, yielding 1.1 g. (65% of theory) II, m.p. 175–177°.

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(4) M. P. de Garihi and M. Laskowski, *Biochim. et Biophys. Acta*, **18**, 370 (1955).

(5) G. Schmidt, *Methods in Enzymology* Colowick and Kaplan, Ed., Academic Press, New York, N.Y., 1955, II, p. 524.

(6) N. S. Corby, G. W. Kenner, and A. R. Todd, *J. Chem. Soc.*, 1234 (1952).

(7) J. M. A. Hoeflake, *Rec. trav. chim.*, **36**, 26 (1916).

The following comments are of interest. (1) The completeness of the hydrolytic reaction is indicated by the non-appearance of crystalline III which would otherwise separate out from the 2-butanone upon cooling. (2) The addition of mineral acids, *e.g.*, nitric acid, 0.01–0.1N with respect to 98% aqueous 2-butanone, did not appear to influence the rate of the reaction. The hydrolysis is, therefore, not strongly catalyzed, if at all, by hydrogen ions. (3) It is not essential to isolate purified III before preparing II. This may be accomplished directly from the crude product resulting from the nitration of triphenyl phosphate. (4) If, however, it is desired to prepare purified III in good yield, (60% or better) it is essential to dry the crude product before crystallizing it from anhydrous solvents. Even the theoretical amount of water may permit appreciable hydrolysis of III, depending upon time and temperature.

*Diphenyl hydrogen phosphate.* This was prepared according to Asakawa<sup>8</sup> as well as Brigl and Muller,<sup>9</sup> neither of whom report its melting point. It is given by Rapp<sup>2</sup> as 56°. Hoeflake<sup>7</sup> has corrected this to 70°. This is the melting point we also found for the anhydrous compound crystallized from water and dehydrated *in vacuo*.

It has been mentioned that Rapp<sup>2</sup> was unsuccessful in preparing II by the nitration of I. The following example illustrates that such a preparation is feasible: 500 mg. of diphenyl hydrogen phosphate (m.p. 69–70°) was treated with 1.6 ml. HNO<sub>3</sub> (sp. gr. 1.5) by adding increments of the former to the latter while maintaining the temperature at about 10°. The solution was then diluted with 5 ml. cold water and filtered. The precipitate was dried *in vacuo* over KOH and crystallized from *n*-butyl acetate, yielding 274 mg. of product, m.p. 175–176°. This method offers no advantage over the hydrolysis of III, especially as triphenyl phosphate (Eastman-Kodak P 1149) is commercially available whereas diphenyl hydrogen phosphate is not.

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### Some New Derivatives of Pentachlorophenol and Their Fungistatic Activities

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Pentachlorophenol is a fungistatic agent of well-known activity. It is used as a chemical preservative,<sup>1</sup> but is too toxic for use on plants, usually causing burns.

In view of the reported fungistatic activity of pentachlorophenoxyethanol<sup>2</sup> and related compounds, it seemed of interest to prepare and test other derivatives of pentachlorophenol. It was hoped that certain derivatives might be less phytotoxic than the parent substance and at the same time retain the fungistatic activity. In the present investigation, eight esters, two ethers, and six salts of pentachlorophenol have been synthesized, most of them novel compounds. These have

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