perature. The buffer consisted of HOAc–NaOAc to give an acetate concentration of 0.01 *M* in reaction mixture. The reactants were mixed, the *p*H checked, and a small amount of toluene added to prevent contamination by microörganisms. At termination of syntheses, reaction mixtures were steamed in an autoclave at 100 to 105° for 20 minutes, cooled and stored at 4° until analysis.

In all experiments reported, reactions achieved reducing values at least equal to that for complete conversion of sucrose to dextran and fructose. Hehre[32] has previously noted that reducing values slightly in excess of theory are obtained in enzymatic synthesis of dextran.

Paper Chromatography.—A major portion of dextran was precipitated with 50% ethanol and removed by centrifugation. Supernatant liquors were spotted on paper. The butanol–pyridine–water (3:2:1) solvent[33] was employed to develop chromatograms and ammoniacal silver nitrate was used as spray to detect reducing sugars and dilute urea–phosphoric acid solution[34] to detect fructose-containing oligosaccharides.

Molecular Weight Distribution and Yield of Dextran Synthesized.—Molecular weight distribution and yield of dextran were obtained from alcohol precipitation data. The alcohol concentration at which dextran precipitates from water–alcohol solutions decreases as molecular weight of dextran increases. The relation between precipitation behavior and molecular weight was established by precipitation of enzymatically synthesized, carefully fractionated dextran of known molecular weights. Either ethanol or methanol was employed as precipitant. Reaction mixtures, adjusted to *p*H 5.0, if necessary, were steamed at 105° in an autoclave for 20 minutes to redissolve any precipitated dextran. After mixtures had cooled to 25°, volumes were adjusted so that dextran content was 2.0%. Aliquots (generally 20 ml.) were transferred to test-tubes and warmed to 45–50°. Graded amounts of alcohol were added with shaking and test-tubes stoppered immediately. The mixtures were allowed to equilibrate in a constant temperature room at 25 ± 1.0° for 44–48 hours. After centrifugation, polarimetric measurements were made on supernatant liquors. The $[\alpha]^{25}\text{D}$ of dextran in mixtures of water and alcohol was taken to be +200°. Some solutions were opalescent but could be cleared by addition of formamide. In such cases, a correction was made for change in specific rotation on the basis that the $[\alpha]^{25}\text{D}$ of dextran in pure formamide is +215°. Weight of dextran precipitated was calculated from decrease in optical rotation. It is recognized that factors other than molecular weight affect alcohol precipitation characteristics of dextran, but the effects are minor under conditions used. Hence this method of analyzing molecular weight distribution was employed because of its relative simplicity.

Under our experimental conditions, it was found that dextran with average molecular weight of 50,000–100,000 precipitated in the methanol range of 44 to 50%.

Yields of dextran are reported as per cent. of dextran anticipated theoretically from sucrose converted, and where added, low-molecular-weight dextran.

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PEORIA, ILLINOIS

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[33] Allene Jeanes, C. S. Wise and R. J. Dimler, *Anal. Chem.*, **23**, 415 (1951).

[34] C. S. Wise, R. J. Dimler, H. A. Davis, and C. E. Rist, Abstracts of Papers, Am. Chem. Soc., 127th Meeting, 2D (1953).

[CONTRIBUTION FROM THE ROSS CHEMICAL LABORATORY, ALABAMA POLYTECHNIC INSTITUTE]

The Reaction of *m*- and *p*-Phenylene-bis-diazonium Fluoborates with Phosphorus Trichloride

BY GENNADY M. KOSOLAPOFF AND JOHN J. DUNCAN

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In an attempt to prepare the isomeric phenylenediphosphonic acids, none of which have been described in the chemical literature to date, we examined the reaction of the *meta* and the *para* isomers of phenylene-bis-diazonium fluoborates with phosphorus trichloride as one of the more promising routes to these acids. Neither the Friedel–Crafts nor the Grignard reactions afforded the desired compounds, although both these reactions are used advantageously in the synthesis of arylphosphonic acids.

Numerous preparations have been reported through the fluoborate route since the original publication by Doak and Freedman[1] but in all cases only the monodiazonium salts have been employed.

We found that the fluoborate route, as applied to the *m*- and the *p*-phenylene-bis-diazonium salts failed to yield the expected diphosphonic acids. Rather unexpectedly, the products isolated from the reactions were the corresponding isomers of the chloro- and the fluorophenylphosphonic acids. Evidently, while one of the diazonium groups reacted normally, the other one underwent not the Doak–Freedman reaction, but a form of the Sandmeyer reaction, and, in part, a Schiemann reaction.

Experimental Part

Reaction of *m*-Phenylene-bis-diazonium Fluoborate.—Since the available descriptions of the preparation of the bis-diazonium salts are devoid of some important experimental details, the preparation is given in some detail below; it follows that given by Täuber and Walder.[2] *m*-Phenylenediamine dihydrochloride (15 g.) was tetrazotized, according to Täuber and Walder, and the resulting solution was treated with 87.5 ml. of sodium fluoborate solution.[3] The resulting fluoborate was obtained in 45.3–52% yield in the form of light yellow powder which decomposed at 206°.

This (36.7 g.) was suspended in 250 ml. of anhydrous ethyl acetate, treated with 32.5 ml. of phosphorus trichloride, followed by 8 g. of cuprous chloride, and the stirred mixture was heated carefully to 50°, since no reaction was evident at room temperature after prolonged stirring. At approximately 50° the mixture acquired a transient violet color, which turned to gray, after which a vigorous reaction took place and the viscosity of the solution decreased. After 2.5 hr. at 55–60° the mixture was cooled, treated with 50 ml. of cold water and steam distilled. After the usual treatment[2] the copper-free, concentrated solution deposited a crop of colorless crystals which was augmented by saturation of the solution with dry hydrogen chloride. After nine recrystallizations from dilute hydrochloric acid the material showed a constant melting point (131–131.5°) and was appreciably hygroscopic after drying *in vacuo*. Further recrystallization of this product from concentrated hydro-

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[1] G. O. Doak and L. D. Freedman, THIS JOURNAL, **73**, 5658 (1951).

[2] E. Täuber and F. Walder, *Ber.*, **30**, 2901 (1897).

[3] A. Roe, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 203.

chloric acid revealed that the material was a mixture containing approximately 80% of *m*-chlorophenylphosphonic acid (m.p. 136°), which had been described previously,[4] while the remainder was the previously undescribed *m*-fluorophenylphosphonic acid, m.p. 129–130°, which was somewhat more soluble than the chloro analog. In view of the difficulties involved in the separation of mixtures of phosphonic acids with similar solubilities, the actual yield of the fluoro derivatives is uncertain, but appears to have been less than 10% (based on the original diamine). The yield of the above-described mixture of the chloro and fluoro acids was 45%. An authentic specimen of the fluoro derivatives was prepared in the usual manner[5] in 18% yield. This was found to be identical with the specimen obtained from the bis-diazonium salt.

Anal. Calcd. for $C_6H_6O_3PF$: P, 17.59; neut. equiv., 88. Found: P, 17.4, 17.5; neut. equiv., 87.88.

Curiously, the individual halophenylphosphonic acids are not hygroscopic, in contrast to the behavior of their mixture.

The filtrate obtained after the separation of the acid mixture, described above, was evaporated to a small volume, but the residual phosphorous acid prevented any further crystallization. This contaminant was removed as follows. The solution was treated with 30% hydrogen peroxide, added dropwise, until the oxidation was complete. The solution was then dehydrated by means of benzene azeotrope and the dry residue was treated with phosphorus pentachloride until no further reaction was evident. Distillation of the mixture yielded some unreacted phosphorus pentachloride, phosphorus oxychloride (removed under reduced pressure on a steam-bath) and a viscous residue weighing less than 0.5 g. After recrystallization of the latter from dilute hydrochloric acid there was obtained a small amount of a solid which was devoid of phosphorus. Thus, no indication of formation of a diphosphonic acid was obtained.

Reaction of *p*-Phenylene-bis-diazonium Fluoborate.—The preparation of the diazonium salt followed that described previously.[6] The yield of the yellow fluoborate was 78% and the material decomposed at 196°. This salt (19.8 g.) was allowed to react with 17.6 ml. of phosphorus trichloride, precisely as described above. The same treatment of the reaction mixture gave a crop of colorless needles, which showed a neutralization equivalent and a titration curve that were very close to those of *p*-fluorophenylphosphonic acid. However, this material failed to melt at 300° and contained a small amount of a sodium salt. Therefore the material was taken up in water and the solution was passed through a column of Dowex-50 ion-exchange resin on the hydrogen cycle and the solution was evaporated, yielding colorless plates which melted at 177–183°. Several recrystallizations of the material from concentrated hydrochloric acid gave a 10% yield (on fluoborate) of pure *p*-chlorophenylphosphonic acid, m.p. 188°, while the mother liquor gave a very small amount (about 0.1 g.) of *p*-fluorophenylphosphonic acid, m.p. 126–127°; this was reported previously with m.p. 125–127°.[5] The residual solution was treated as described for the *m*-isomer; the result was again negative.

Since the melting points of the *p*- and the *o*-chlorophenylphosphonic acids are rather close to each other, the identification of the above-described specimen of the *p*-isomer was performed both by a mixed melting point with an authentic *p*-chlorophenylphosphonic acid specimen, and by a mixed melting point with a specimen of the *o*-isomer, prepared conventionally from the fluoborate.[1] This specimen melted at 186.5–188° (somewhat above the previously reported 182–184°,[1] and gave a definite depression of melting point on mixing with the *p*-isomer or with the specimen prepared from the bis-diazonium salt.

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[5] R. W. Bost, L. D. Quin and A. Roe, *J. Org. Chem.*, **18**, 362 (1953).

[6] P. Ruggli and E. Caspar, *Helv. Chim. Acta*, **18**, 1416 (1935).

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Lanthanum Hydroxide Gel Promoted Hydrolysis of Phosphate Esters

BY W. W. BUTCHER AND F. H. WESTHEIMER

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Lanthanum hydroxide gel promotes the hydrolysis of methoxyethyl phosphate, of hydroxyethyl phosphate and of aminoethyl phosphate at *p*H 8.5 and 78°. 1-Methoxy-2-propyl phosphate is hydrolyzed at *p*H 4, or by $La(OH)_3$ at *p*H 8.5, with complete retention of stereochemical configuration and with cleavage of the P–O bond. In 1.8 *M* sulfuric acid, the hydrolysis is accompanied by extensive racemization. The mechanisms of these reactions are discussed.

E. Bamann[1] discovered that the hydroxides of lanthanum, cerium, thorium, etc., promote the hydrolysis of α-glyceryl phosphate (equation 1) in the region from *p*H 7–10, and suggested that the reaction serves as a model[2] for the metal-ion promoted alkaline phosphatases.[3] The present research was undertaken to elucidate further this metal-ion promoted hydrolysis.

$$\begin{aligned}&HOCH_2CHOHCH_2OPO_3^{=} + La(OH)_3 \longrightarrow\\&\qquad HOCH_2CHOHCH_2OH + LaPO_4 + 2OH^- \quad (1)\end{aligned}$$

Bailly[4] and Desjobert[5] have shown that (in the absence of heavy metal ions) a monoester of phosphoric acid is stable to alkali, and is moderately stable at a *p*H of 1 or 2, but it is readily hydrolyzed at *p*H 4 or in strong acid solution. (The region around *p*H 4 corresponds to a maximum in the concentration of the monoanion, $ROPO_3H^-$; see Fig. 1.) In view of these findings, the rate of hydrolysis of 1-methoxypropyl-2 phosphate was determined over a wide range of acidity, in the presence and in the absence of lanthanum hydroxide gel. The point of cleavage was determined by stereochemical and by O^{18} tracer experiments. Several other esters were tested with lanthanum hydroxide gel to determine the structural requirements for the metal-ion catalysis. A mechanism for the hydrolysis of phosphate esters, based on the new data is here advanced.

Experimental

Materials. Barium Ethyl Phosphate.—Phosphorous oxychloride (0.2 mole) and water (0.2 mole) were mixed in a

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[2] *Cf.* F. H. Westheimer, Abstracts of Papers, 120th Meeting, Am. Chem. Soc., N. Y., 1951, p. 7P.

[3] See A. Lehninger, *Physiol. Rev.*, **30**, 393 (1950).

[4] M. C. Bailly, *Bull. soc. chim.*, [5] **9**, 421 (1942).

[5] A. Desjobert, *Compt. Rend.*, **224**, 575 (1947); *Bull. soc. chim.*, [5] **14**, 809 (1947).