Anal. Calcd. for $C_{16}H_8SN_2$: C, 73.84; H, 3.07; S, 12.3; N, 10.76. Found: C, 73.63; H, 3.11; S, 12.32; N, 10.59.

Method B. A suspension of thiaxanthione (1 g.), malononitrile (0.4 g.), and yellow mercuric oxide (1 g.) in absolute alcohol (15 ml.) was heated under reflux on the water bath for 3 hr. while passing a stream of dry nitrogen. The reaction mixture was then filtered while hot and the black residue was extracted several times with boiling benzene. The benzene extracts were filtered while hot, concentrated, and then cooled to give IIIb (yield about 50%).

When the reaction was carried out in air, thioxanthone was mainly produced.

Preparation of Δ⁹,α-thiaxantheneacetic acid, α-cyanoethyl ester (IIId). 9,9-Dichlorothiaxanthene (from 2 g. of thiaxanthone), and ethyl cyanoacetate (3 ml.) were heated together as in the case of IIIc, and the reaction mixture was left to cool. The solid product obtained was extracted several times with boiling petroleum ether (b.p. 40–60°). The petroleum extracts were filtered while hot, concentrated, and then left to cool. The crystals obtained were recrystallized from methyl alcohol to give IIId in yellow crystals, m.p. 129–130°; yield about 60%. It is soluble in ether, acetone, and benzene and gives a blood red color with concentrated sulfuric acid.

Anal. Calcd. for $C_{18}H_{14}O_2SN$: C, 70.1; H, 4.54; S, 10.38; N, 4.54. Found: C, 69.92; H, 4.39; S, 9.96; N, 4.45.

Preparation of Δ⁹,α-cyano-α-thiaxantheneacetic acid (IIIg). The ester IIId was boiled with an alcoholic sodium hydroxide solution as in the case of IIIc. The reaction mixture was then cooled in ice, and the solid separated was filtered off and extracted with boiling water several times. The water-insoluble material was filtered off, dried, and crystallized from methyl alcohol to give thiaxanthone (undepressed when admixed with an authentic sample prepared according to Davis and Smiles[8]). The water extracts were left to cool, and acidified with dilute hydrochloric acid. The yellow precipitate formed was filtered off, dried and crystallized from benzene to give IIIg in orange crystals which melt with vigorous decomposition at about 187°. It dissolves readily in acetone, difficultly soluble in alcohol or ether. It gives a red color with concentrated sulfuric acid; (yield about 50%).

Anal. Calcd. for $C_{16}H_9O_2SN$: C, 68.81; H, 3.22; S, 11.46; N, 5.01. Found: C, 68.27; H, 3.79; S, 11.93; N, 5.00.

Preparation of Δ⁹α-thiaxantheneacetonitrile. Pyrolysis of the acid IIIg was carried out as in the case of IIIf. The crystalline product collected on the upper parts of the reaction vessel were crystallized from alcohol to give IIIi in pale yellow crystals, m.p. 158°. It is soluble in ether and acetone, and gives a blood red color with concentrated sulfuric acid; yield about 70%.

Anal. Calcd. for $C_{15}H_9SN$: C, 76.59; H, 3.82; S, 13.61; N, 5.95. Found: C, 76.20; H, 4.16; S, 13.43; N, 5.96.

Reaction of N¹-p-benzoquinonylidene-N²-xanthonylideneazine (IV) *with malononitrile.* A suspension of IV (2 g.) and malononitrile (0.5 g.) in absolute alcohol (50 ml.) was refluxed for 2 hr. The reaction mixture was cooled in ice, and the solid separated was filtered off and extracted with boiling acetone. The acetone extracts were filtered while hot, concentrated and left to cool. The yellow green crystals which separated (0.6 g.) were shown to be IIIa (melting point and mixed melting point). The residue left after acetone extraction was crystallized from xylene and was shown to be xanthone azine (undepressed when admixed with an authentic sample prepared according to Schönberg and Stolpp[9]). The alcoholic filtrate from the reaction mixture was poured onto a 2.5% sodium hydroxide solution (30 ml.), and the alkaline solution was acidified with dilute hydrochloric acid and extracted with ether. The ethereal extract was evaporated to dryness, and the oily residue was extracted with boiling water. The aqueous extracts were left to cool and then bromine water was added. The crystalline solid which separated was filtered off, dried, and recrystallized from petroleum ether (b.p. 40–60°) to give tribromophenol m.p. 95° (undepressed when admixed with an authentic sample).

Reaction of IV *with ethyl cyanoacetate.* A mixture of IV (1 g.) and ethyl cyanoacetate (2 ml.) in absolute alcohol (20 ml.) was heated under reflux for 10 hr. The reaction mixture was filtered while hot, and the filtrate was evaporated to dryness under reduced pressure. The oily residue was extracted several times with boiling petroleum ether (b.p. 40–60°), and the combined petroleum extracts were evaporated to dryness. The residue was recrystallized from methyl alcohol to give IIIc in yellow crystals, m.p. 117° (undepressed when admixed with an authentic sample prepared from 9,9-dichloroxanthene and ethyl cyanoacetate). The residue left after the petroleum ether extraction was dissolved in methyl alcohol, and the solution then poured onto a 2.5% sodium hydroxide solution. Phenol was isolated from the alkaline solution and identified as above.

DOKKI, CAIRO

(8) Davis and Smiles, *J. Chem. Soc.*, **97**, 1290 (1910).

(9) A. Schönberg and Th. Stolpp, *Ber.*, **63**, 3102 (1930).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY AND NEUROLOGY, COLUMBIA UNIVERSITY]

Synthesis of a Series of Organophosphorus Esters Containing Alkylating Groups[1]

ALLEN M. GOLD

Received April 24, 1961

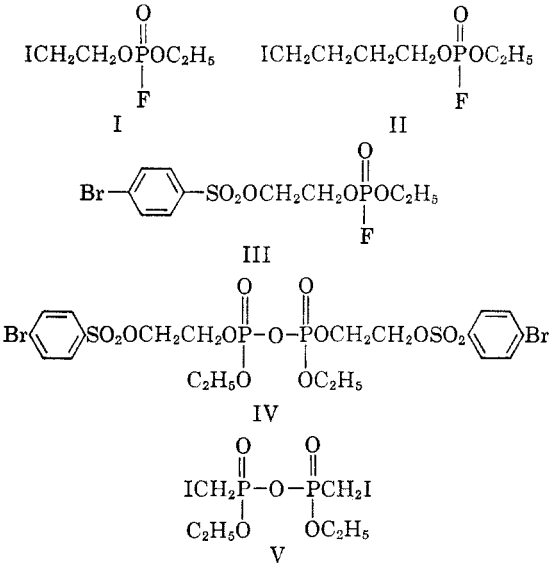
A series of bifunctional organophosphorus esters with alkylating groups in their side-chains was synthesized. These compounds differed in the number of atoms between phosphorus and the electrophilic carbon atom, in the nature of the leaving group, and in the identity of the electronegative group attached to the phosphorus atom. The compounds were: ethyl 2-iodoethyl phosphorofluoridate (I), ethyl 4-iodo-1-butyl phosphorofluoridate (II), ethyl 2-brosyloxyethyl phosphorofluoridate (III), ethyl 2-brosyloxyethyl phosphoric anhydride (IV), and ethyl iodomethylphosphonic anhydride (V).

The reaction of certain organophosphorus compounds, such as diisopropyl phosphorofluoridate and tetraethyl pyrophosphate, with a variety of enzymes has led to their use in the investigation of the active sites of these enzymes.[2–8] In the hope of producing

(1) This work was supported by a Special Fellowship BT-484 from the National Institute of Neurological Diseases and Blindness, Public Health Service.

(2) H. S. Jansz, C. H. Posthumus, and J. A. Cohen, *Biochim. Biophys. Acta*, **33**, 387, 396 (1959).

active phosphate esters which could yield information of a different nature from that already obtained, a series of bifunctional esters was prepared in which the alkyl chains carried alkylating groups. These substances differed in the number of atoms between phosphorus and the electrophilic carbon atom, in the identity of the leaving group, and in the type of electronegative group attached to the phosphorus atom.



In view of the potentially high toxicity[9] of compounds of this class, synthetic routes were chosen to avoid toxic intermediates and to permit the simplest possible isolation and purification of products. The direct reaction between substituted alcohols and ethyl phosphorodifluoridate[10] yielded substituted alkyl ethyl phosphorofluoridates which were isolated by distillation where possible. Because satisfactory analyses could not be obtained on liquid products the phosphorofluoridates were hydrolyzed and converted to barium salts for characterization. Saponification equivalents determined on the phosphorofluoridates gave an indication of the degree of purity.

Ethyl 2-iodoethyl phosphorofluoridate (I) was prepared by the reaction of iodoethanol with excess ethyl phosphorodifluoridate. The product, collected over a narrow boiling-point range, had a saponification equivalent of 152. The theoretical value is 141. This indicates a purity of 93%, assuming all impurities to be inert. When hydrolyzed by shaking the liquid with excess 4% sodium hydroxide, there was indeed a small amount of residual liquid which did not go into solution.

Similarly ethyl 4-iodo-1-butyl phosphorofluoridate (II) was synthesized from 4-iodobutanol-1. This alcohol was prepared from 4-bromobutanol-1 by treatment with sodium iodide in acetone. Neither the bromo nor the iodo alcohol was distillable, so the entire series of reactions was carried out without purification until the end product was reached. The phosphorofluoridate was distilled over a one degree range and had a saponification equivalent corresponding to 99% purity. It was shown by elementary analysis, however, that the compound was not pure. Apparently a small amount of saponifiable impurity was present.

2-Hydroxyethyl *p*-bromobenzenesulfonate[11] was prepared by allowing *p*-bromobenzenesulfonyl chloride to react with excess ethylene glycol. Treatment of the crystalline alcohol with ethyl phosphorodifluoridate resulted in production of nondistillable ethyl 2-brosyloxyethyl phosphorofluoridate (III). This product was clearly impure and, after hydrolysis, two barium salts could be isolated, due to the almost complete insolubility of one salt in water. The insoluble salt is presumed to be barium bis(2-brosyloxyethyl) phosphate on the basis of its partial elementary analysis, and its precursor may be the corresponding phosphorofluoridate. It can be calculated, from the saponification equivalent of the crude phosphorofluoridate and the neutralization equivalent of the crude acid mixture extracted after hydrolysis, that the product contains 60% of III and 20% of bis(2-brosyloxyethyl) phosphorofluoridate. The mechanism of formation of the latter compound is not clear.

The soluble barium salt, barium ethyl 2-brosyloxyethyl phosphate, exhibited instability in solution and some preparations yielded barium *p*-bromobenzenesulfonate on recrystallization. This is probably due to a reaction in which the phosphate anion displaces the sulfonate group in an intramolecular cyclization,[12] producing ethyl ethylene phosphate and barium sulfonate.

Infrared spectra[13] of the phosphorofluoridates I–III all show characteristic P=O stretching bands at *ca.* 1300 cm.$^{-1}$ There is also very strong absorption in the 1010–1060 cm.$^{-1}$ region, due to P—O—C (aliphatic) groupings, and weak bands at *ca.* 1170 cm.$^{-1}$, probably assignable to P—OC_2H_5 groups. The P—F bands do not appear at the ex-

(3) G. H. Dixon, D. L. Kauffman, and H. Neurath, *J. Biol. Chem.*, **233**, 1373 (1958).

(4) H. S. Jansz, D. Brons, and M. G. P. J. Warringa, *Biochim. Biophys. Acta*, **34**, 573 (1959).

(5) R. A. Oosterbaan, P. Kunst, J. van Rotterdam, and J. A. Cohen, *Biochim. Biophys. Acta*, **27**, 549, 556 (1958).

(6) F. Sanger and D. C. Shaw, *Nature*, **187**, 872 (1960).

(7) M. A. Naughton, F. Sanger, B. S. Hartley, and D. C. Shaw, *Biochem. J.*, **77**, 149 (1960).

(8) J. A. Gladner and K. Laki, *J. Am. Chem. Soc.*, **80**, 1263 (1958).

(9) R. D. O'Brien, *Toxic Phosphorus Esters*, Academic Press, New York, N. Y., 1960.

(10) B. C. Saunders, G. J. Stacey, F. Wild, and I. G. E. Wilding, *J. Chem. Soc.*, 699 (1948).

(11) The abbreviation "brosyl" will be used for "*p*-bromobenzenesulfonyl" in complex chemical names.

(12) J. Kumamoto, J. R. Cox, Jr., and F. H. Westheimer, *J. Am. Chem. Soc.*, **78**, 4858 (1956).

(13) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, second edition, John Wiley & Sons, Inc., New York, N. Y., 1958.

pected frequencies, but this may be caused by their being obscured by stronger neighboring bands; each of the latter absorption maxima is unsymmetrical and may conceal the lower frequency P—F band.

Another useful synthetic approach is the condensation of suitably substituted phosphoric or phosphonic acids to the symmetrical anhydrides by the use of dicyclohexylcarbodiimide. In this way ethyl 2-brosyloxyethyl phosphoric acid was converted to ethyl 2-brosyloxyethyl phosphoric anhydride (IV). The anhydride was a heavy oil which could not be distilled. The infrared spectrum has a clear P=O absorption maximum at 1282–1290 cm.$^{-1}$, but the region 910–1110 cm.$^{-1}$ is complex and no definite assignments are possible; the spectrum indicates a trace of dicyclohexylurea. The saponification equivalent, however, indicated a purity of 98%.

Ethyl iodomethylphosphonic acid was produced by alkaline hydrolysis[14] of diethyl iodomethylphosphonate[15] and converted to ethyl iodomethylphosphonic anhydride (V). This compound is a solid and could be readily purified by recrystallization. The infrared spectrum showed absorption maxima at the expected frequencies[13] for P=O, P—O—C (aliphatic), P—OC_2H_5, and P—O—P groups.

EXPERIMENTAL

Melting points were determined in a Thomas-Hoover melting point apparatus and are uncorrected; boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer, model 21 infrared spectrophotometer. Microanalyses were performed by Galbraith Laboratories, Inc.

Saponification equivalents. The general method was to dissolve an accurately weighed sample of about 0.6–0.7 meq. of test substance in 1 ml. of purified dioxane. This was then treated with 1.000 ml. of standard *N* sodium hydroxide, and the solution was titrated with standard 0.1 *N* hydrochloric acid within a few minutes. Phenolphthalein was used as indicator.

Ethyl phosphorodifluoridate. A modification of the method of Saunders *et al.*[10] was used. Sodium fluoride, 84 g. (2.0 mole), was placed in a 500-ml. flask fitted with a dropping funnel, sealed wire stirrer, and large Allihn reflux condenser with a drying tube. The contents were heated in vacuum to drive off traces of water, and ethyl phosphorodichloridate,[10] 135 g. (0.85 mole), was then added to the hot sodium fluoride. Addition was carried out at a rate that maintained refluxing at a convenient level. Finally, the mixture was refluxed for 30 min. and the product isolated by distillation. The crude product was redistilled, b.p. 84–85°, yield 46 g. (43%). This material could be best preserved in sealed glass ampoules.

2-Iodoethanol. The alcohol was synthesized according to the procedure of Wieland and Sakellarios.[16] The product was distilled at 71–72° (12 mm.). The saponification equivalent was 175 (theor. 172).

Ethyl 2-iodoethyl phosphorofluoridate (I). 2-Iodoethanol, 35 g. (0.20 mole), was added dropwise to 31.6 g. (0.24 mole) of ethyl phosphorodifluoridate over a period of 30 min. while the reaction mixture was stirred and cooled in ice. The mixture was stirred an additional 90 min. at 0° and washed with two 50-ml. portions of cold water containing a trace of sodium sulfite and enough sodium carbonate to neutralize the acid. The organic phase was washed with 50 ml. of saturated salt solution and distilled in vacuum. A crude fraction was collected at *ca.* 68° (0.10 mm.). The distillate was decolorized by shaking with metallic mercury and redistilled carefully, b.p. 62–63° (0.10 mm.). The saponification equivalent was 152 (theor. 141). Infrared absorption at 1303, 1167, 1010–1064, and 893–912 cm.$^{-1}$ (carbon tetrachloride).

Anal. Calcd. for $C_4H_9O_3PIF$: C, 17.03; H, 3.22; P, 10.99; I, 45.01. Found: C, 17.27; H, 3.23; P, 10.22; I, 43.76, 44.51.

Barium ethyl 2-iodoethyl phosphate. Ethyl 2-iodoethyl phosphorofluoridate (I), 1.2 g., was shaken briefly with 12 ml. of 4% sodium hydroxide. A small amount of oil failed to dissolve in the alkali. The aqueous solution was washed with three 10-ml. portions of chloroform (discarded), saturated with salt, and acidified with concentrated hydrochloric acid. The mixture was extracted with three 10-ml. portions of chloroform which were combined, dried over sodium sulfate, and evaporated in vacuum. The residual acid (1.073 g.) was titrated with standard 0.2*N* barium hydroxide, using phenolphthalein indicator; the neutralization equivalent was 284 (theor. for $C_4H_{10}O_4PI$ is 280). The barium salt was isolated by vacuum evaporation and recrystallized three times from ethanol-water mixture. This salt decomposed on heating above 200°.

Anal. Calcd. for $C_4H_9O_4PIBa_{1/2}$; C, 13.82; H, 2.61; P, 8.91; I, 36.50; Ba, 19.75. Found: C, 13.64; H, 3.18; P, 8.77; I, 36.21; Ba, 20.01.

4-Bromobutanol-1. Dry gaseous hydrogen bromide, 18.5 g. (0.23 mole) was passed rapidly into 100 ml. of pure dry tetrahydrofuran so that the solvent refluxed. The excess solvent was removed in vacuum below 35° and the residue was taken up in 100 ml. of benzene and washed with 25 ml. of water containing excess potassium bicarbonate. The organic phase was dried over magnesium sulfate and evaporated in vacuum. This product could not be distilled in vacuum without extensive decomposition, so it was used without further purification.

4-Iodobutanol-1. Crude 4-bromobutanol-1, 17.0 g. (0.11 mole), was dissolved in 200 ml. of acetone containing 19 g. (0.13 mole) of sodium iodide. The solution was allowed to stand at room temperature for 17 hr. and the precipitated sodium bromide removed by filtration. The acetone was evaporated in vacuum and the residue taken up in 100 ml. of carbon tetrachloride. This solution was washed with 25 ml. of water containing excess potassium bicarbonate and a little sodium sulfite. After drying over magnesium sulfate, the solvent was evaporated in vacuum below 35°, yielding 19.5 g. (88%) of undistillable dark oil.

Ethyl 4-iodo-1-butyl phosphorofluoridate (II). Crude 4-iodobutanol-1, 19.5 g. (0.098 mole), was dissolved in 100 ml. of dry ether and cooled in an ice bath. Ethyl phosphorodifluoridate, 15.3 g. (0.118 mole), was added, and the solution was allowed to stand at 0° for 2 hr. and at room temperature for 1 hr. The solution was shaken with 100 ml. of water and then with 100 ml. of water containing excess potassium bicarbonate and a little sodium sulfite. Most of the ether was evaporated in vacuum and replaced with 100 ml. of carbon tetrachloride. This solution was again washed with 100 ml. of water containing bicarbonate and sulfite. The organic phase was dried over magnesium sulfate and evaporated in vacuum. The crude material was distilled roughly between 74° (0.5 mm.) and 96° (0.1 mm.). On redistillation a pale yellow liquid was collected at 88–89° (0.05 mm.); saponification equivalent 156, 158 (theor. 155). Infrared absorption at 1299, 1164, 1020–1053, and 877–901 cm.$^{-1}$ (carbon tetrachloride). This product turned dark after a period of storage.

Anal. Calcd. for $C_6H_{13}O_3PIF$: C, 23.24; H, 4.23; P, 9.99; I, 40.93. Found: C, 24.70, 25.13; H, 4.69, 5.30; P, 10.43, 10.12; I, 42.22, 40.03.

Barium ethyl 4-iodo-1-butyl phosphate. The preparation, from II, was similar to that of barium ethyl 2-iodoethyl

(14) R. Rabinowitz, *J. Am. Chem. Soc.*, 82, 4564 (1960).

(15) A. H. Ford-Moore and J. H. Williams, *J. Chem. Soc.*, 1465 (1947).

(16) H. Wieland and E. Sakellarios, *Chem. Ber.*, 53B, 201 (1920).

phosphate. The neutralization equivalent obtained by titration with barium hydroxide was 302 (theor. 308). The salt congealed at *ca.* 210° but did not melt below 310°.

Anal. Calcd. for $C_6H_{13}O_4PIBa_{1/2}$: C, 19.18; H, 3.49; P, 8.25; I, 33.79; Ba, 18.28. Found: C, 19.03; H, 3.46; P, 8.41; I, 32.80; Ba, 17.80.

2-Hydroxyethyl p-bromobenzenesulfonate. A solution of 10 g. (0.13 mole) of pyridine in 35 g. (0.56 mole) of ethylene glycol was treated portionwise with 27.4 g. (0.106 mole) of powdered *p*-bromobenzenesulfonyl chloride. The reaction temperature was maintained below 30° by intermittent cooling during the addition, and the solution was then allowed to stand at room temperature for 90 min. The mixture was poured into 500 ml. of cold dilute hydrochloric acid, stirred well, and the acid decanted. The residue was taken up in 100 ml. of chloroform and washed well with water, dilute hydrochloric acid, and dilute potassium bicarbonate. After drying with sodium sulfate, the chloroform was completely evaporated and replaced with 100 ml. of dry ether. Upon standing overnight at 0° the solution deposited a quantity of finely crystalline ethylene bis-*p*-bromobenzenesulfonate. The mother liquor was concentrated and diluted with carbon tetrachloride to effect crystallization of the desired product. Recrystallization from ether-carbon tetrachloride gave 11.0 g. (37%) of massive crystals. The saponification equivalent was 283 (theor. 281). A sample was recrystallized for analysis; m.p. 45.8–47.6°.

Anal. Calcd. for $C_8H_9O_4BrS$: C, 34.18; H, 3.23; Br, 28.43; S, 11.41. Found: C, 33.96; H, 3.13; Br, 28.68; S, 11.62.

Ethyl 2-brosyloxyethyl phosphorofluoridate (III). Ethyl phosphorodifluoridate, 8.05 g. (0.062 mole), was added to an ice cold solution of 10.8 g. (0.038 mole) of 2-hydroxyethyl *p*-bromobenzenesulfonate in 50 ml. of dry ether. The solution was maintained at 0° for 30 min. and at room temperature for 3 hr. After dilution with 50 ml. of carbon tetrachloride, the mixture was washed with water and dilute potassium bicarbonate solution. The organic phase was filtered through sodium sulfate, dried over magnesium sulfate, and evaporated in vacuum. It proved impossible to distil or crystallize the crude product. The saponification equivalent was 264 (theor. 195.5). Infrared absorption was at 1301, 1175, 1048, 1011, and 917 cm.$^{-1}$ (carbon tetrachloride).

Barium ethyl 2-brosyloxyethyl phosphate. This preparation, from III, was similar to that of barium ethyl 2-iodoethyl phosphate. Considerable material failed to dissolve in the alkali. Titration of the crude acid with barium hydroxide gave a neutralization equivalent of 429 (theor. 389). The aqueous solution began to deposit a fluffy white solid shortly after titration, so the solution was set in a refrigerator for several hours before filtration. The filtrate was evaporated and the residue recrystallized four times for analysis. The salt did not melt below 270°.

Anal. Calcd. for $C_{10}H_{13}O_7PBrSBa_{1/2}$: C, 26.29; H, 2.87; P, 6.78; Br, 17.49; S, 7.02; Ba, 15.02. Found: C, 25.53; H, 2.80; P, 6.63; Br, 18.78; S, 7.35; Ba, 15.62.

The insoluble salt may be barium bis(2-brosyloxyethyl) phosphate.

Anal. Calcd. for $C_{16}H_{16}O_{10}PBr_2S_2Ba_{1/2}$: P, 4.48; Br, 23.10. Found: P, 4.90; Br, 23.12.

Ethyl 2-brosyloxyethyl phosphoric anhydride (IV). A solution of barium ethyl 2-brosyloxethyl phosphate, 1.5 g., in 20 ml. of water was acidified with concentrated hydrochloric acid. The oily acid precipitated and was extracted with chloroform, dried over sodium sulfate, and evaporated to dryness in vacuum. The free acid, 0.971 g. (2.50 mmoles), was dissolved in 20 ml. of ether-methylene chloride (1:1) and treated with a solution of 0.257 g. (1.25 mmoles) of dicyclohexylcarbodiimide in 10 ml. of ether. After standing at 25° for 1 hr. and at 0° overnight the solution was filtered to remove the crystallized dicyclohexylurea and evaporated to dryness in vacuum. The oily residue was dissolved in 15 ml. of methylene chloride and washed with dilute potassium bicarbonate solution. After drying with magnesium sulfate the solution was evaporated, leaving a thick oil with a little dispersed solid. The saponification equivalent was 388 (theor. 380). Infrared absorption at 1282–1290, 1184, 1174, 946, and 921 cm.$^{-1}$ (chloroform).

Anal. Calcd. for $C_{20}H_{26}O_{13}P_2Br_2S_2$: C, 31.59; H, 3.45; P, 8.15; Br, 21.02; S, 8.43. Found: C, 31.94; H, 3.87; P, 7.94; Br, 20.96; S, 8.56.

Diethyl iodomethylphosphonate. This substance was prepared by the method of Ford-Moore and Williams.[15] The product was a pale yellow liquid which soon darkened; b.p. 82–83° (0.15 mm.).

Anal. Calcd. for $C_5H_{12}O_3PI$: I, 45.64. Found: I, 44.88.

Barium ethyl iodomethylphosphonate. Diethyl iodomethylphosphonate, 1.00 g. (3.6 mmoles), was dissolved in 6 ml. of purified dioxane and treated with 6 ml. of 4% aqueous sodium hydroxide. The solution was held at 35° for 5 hr. and then extracted with several small portions of chloroform (discard). After acidification with concentrated hydrochloric acid and saturation with salt, the aqueous solution was extracted with six 5-ml. portions of chloroform. The chloroform extracts were combined, dried over sodium sulfate, and evaporated in vacuum. The oily acid was titrated with standard barium hydroxide solution; neutralization equivalent 249 (theor. 250). Evaporation of the solution in vacuum and crystallization of the salt from ethanol-water produced 0.712 g. (62%) of fibrous crystals. The salt was recrystallized twice for analysis; m.p. >300°.

Anal. Calcd. for $C_3H_7O_3PIBa_{1/2}$: C, 11.34; H, 2.22; P, 9.75; I, 39.94; Ba, 21.61. Found: C, 10.14; H, 3.02; P, 9.54; I, 39.23; Ba, 21.64.

Ethyl iodomethylphosphonic anhydride (V). A solution of barium ethyl iodomethylphosphonate, 0.712 g. (2.24 mmoles), in 5 ml. of water was acidified with concentrated hydrochloric acid, saturated with salt, and extracted with six 5-ml. portions of chloroform. The combined chloroform was dried over sodium sulfate and evaporated, leaving 0.515 g. (2.06 mmoles) of free acid. The acid was dissolved in 5 ml. of dry ether and treated with a solution of 0.223 g. (1.08 mmoles) of dicyclohexylcarbodiimide in 10 ml. of ether. The mixture was allowed to stand at room temperature for 70 min. before it was cooled in ice and filtered. The filtrate was evaporated; the crystalline residue was taken up in 15 ml. of methylene chloride, washed with 10 ml. of dilute potassium bicarbonate, dried over sodium sulfate, and evaporated. The residue crystallized readily from ether-petroleum ether (b.p. 30–60°), yielding 0.261 g. (49% on barium salt). After two recrystallizations the anhydride was analytically pure; m.p. 75–76.5°. The saponification equivalent was 243 (theor. 242). Infrared absorption was at 1267, 1160, 1037, and 940–944 cm.$^{-1}$ (chloroform).

Anal. Calcd. for $C_6H_{14}O_5P_2I_2$: C, 14.95; H, 2.92; P, 12.86; I, 52.66. Found: C, 14.82; H, 3.22; P, 12.68; I, 52.42.

Acknowledgment. I wish to express my gratitude to Professor David Nachmansohn for the encouragement and support that made this work possible.

NEW YORK 32, N.Y.