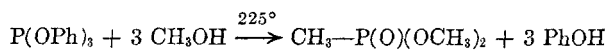


[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF CALIFORNIA]

Reaction of Trialkyl Phosphites with Methanol¹JAMES CASON AND WARREN N. BAXTER²*Received March 3, 1958*

At 210–215° in a sealed glass tube, *n*-butyl alcohol reacts with triethyl phosphite to give only transesterification; ethyl alcohol reacts slowly to give phosphonates; and methyl alcohol reacts more rapidly to give phosphonates. Under the most favorable conditions found, there was obtained an 85% yield of a phosphonate mixture which consisted of about 60% diethyl methylphosphonate, 25% diethyl phosphonate, and 15% triethyl phosphate. Evidence is presented that the latter two compounds do not arise by simple hydrolysis and oxidation of a part of the triethyl phosphite by moisture and air. Significant amounts of ethylphosphonates or mixed esters such as methyl ethyl methylphosphonate were shown to be absent. Transesterification is the most rapid reaction between methyl alcohol and triethyl phosphite; subsequent rearrangement may proceed in a manner analogous to the Arbuzov reaction. Reaction of trimethyl phosphite with less than 0.1 mole equivalent of methyl alcohol gave a 92% yield of pure dimethyl methylphosphonate. In pentavalent phosphorus compounds, such as dialkyl methylphosphonates, absorption in the infrared for the CH₃—P structure was found to occur at 7.65 ± 0.02μ, in contrast with the trivalent phosphorus compounds where absorption for this structure was observed at about 7.75μ, as has been previously reported.

In a recent investigation,³ it has been found that heating of trialkyl phosphites with aliphatic alcohols results in transesterification to yield mixed trialkyl phosphites. It had been reported earlier⁴ that heating of triaryl phosphites with alcohols boiling above 100° results in transesterification with replacement of one or more aryl groups; however, there is a single older report⁵ that heating of triphenyl phosphite at 225° with an excess of methyl or *n*-propyl alcohol results not only in transesterification but also in formation of an alkylphosphonate. The net conversion to form alkylphosphonate was represented as in the following equation. Since



such a rearrangement represents a potential synthesis of alkylphosphonic esters, the present investigation has been devoted to examination of similar conversions of triethyl phosphite and trimethyl phosphite.

In preliminary experiments, it was observed that heating of triethyl phosphite in a sealed glass tube with about 1.1 mole equivalent of *n*-butyl alcohol at 210° for 15 hr. resulted only in transesterification; no product was obtained which exhibited infrared absorption at 8μ, characteristic⁶ of the P → O bond in phosphates and phosphonates. In contrast, sim-

ilar heating of triethyl phosphite with ethanol resulted in only about 60% recovery of the triethyl phosphite, and there was obtained about 35% yield of a higher boiling product which exhibited absorption in the infrared for the P → O bond. When methanol was used in the reaction, little phosphite was recovered, and yields of 50–70% of pentavalent phosphorus compounds were observed. The latter material was found to consist in part of triethyl phosphate. The amount of phosphate was increased when 10 mole % of water was added to the methanol, but its amount could not be reduced below about 5% when the sealed tube was filled with nitrogen, and methanol dried over magnesium was employed. Since methanol exhibits such a facile reaction with triethyl phosphite, the principal investigations have been concerned with reactions of this alcohol.

The best conditions found for conversion of triethyl phosphite to diethyl methylphosphonate involved heating the phosphite with 1.15 mole equivalents of methanol in a sealed glass tube⁷ at 210–215° for 5 hr. Ethyl alcohol was a product of the reaction; about 10% of the phosphite was recovered; and about 85% yield of the "phosphonate fraction," b.p. 103–108°/48 mm., was received. Analysis of the latter fraction by gas phase chromatography and infrared spectroscopy showed it to consist almost entirely of three compounds: about 60% diethyl methylphosphonate, about 25% diethyl phosphonate [(C₂H₅O)₂P(O)H], and about 15% triethyl phosphate. One is tempted to rationalize appearance of the latter two compounds on the basis of simple hydrolysis and oxidation of a part of the triethyl phosphite; however, present evidence indicates that these compounds arise by more devious routes.

When a reaction was carried out in a tube filled with nitrogen before sealing, utilizing freshly dis-

(1) This work was done on a subcontract with the University of Chicago in fulfillment of a contract with the Chemical Corps.

(2) Member of the Armed Forces assigned to the Army Chemical Corps.

(3) F. W. Hoffmann, R. J. Ess, and R. P. Usinger, Jr., *J. Am. Chem. Soc.*, **78**, 5817 (1956).

(4) R. Reuter, U.S. Patent 2,175,509 (1939); S. R. Laudaner and H. N. Rydon, *J. Chem. Soc.*, 2224 (1953).

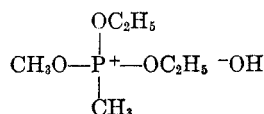
(5) T. Milobenzki and K. Szulgin, *Chemik Polski*, **15**, 66 (1917); *Chem. Abstr.*, **13**, 2867 (1919).

(6) For comparison purposes in the present investigation, infrared spectra were recorded for appropriate known compounds; however, extensive use was made of the valuable source material in L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, Methuen and Co. Ltd., London, 1954, Chap. 18.

(7) When the reaction mixture was heated in a steel bomb, no volatile liquid products were obtained.

tilled triethyl phosphite and methanol dried over magnesium, there was no significant effect on the composition of the phosphonate fraction. Further, the reaction appears not to be catalyzed by traces of acid, for it proceeded about as well in a run in which 0.015 mole equivalent of magnesium metal had been allowed to react with the methanol before the phosphite was added. When the phosphite was heated similarly without addition of methanol, even for periods of 15 hr., 93% of it was recovered, and there was only 4% of the phosphonate fraction. Mixed methyl ethyl phosphites were also essentially unaltered (as determined by infrared analysis) by heating alone or in presence of 5% by weight of ethanol. When the heating period in presence of methanol was extended to 15 hr., the yield of phosphonate fraction was reduced to about 50%, but the composition of the fraction was the same as that observed after the 5 hr. heating period. After the longer heating period, a quantity of diethyl ether was recovered, and there was about 22% yield of a nonvolatile residue; so conversion of the initial products to compounds of the pyrophosphate type is indicated. Further, if only one molar equivalent of methanol is heated with triethyl phosphite, conversion to phosphonate is much slower, and the product contains less diethyl phosphonate and more triethyl phosphate.

Although we are unable to suggest a mechanism which will correlate the observations concerning all the products detected in the phosphonate fraction, it is possible that the major product, diethyl methylphosphonate, is formed *via* an intermediate of the type shown in the formula, analogous to the presumed intermediate in the widely investigated Ar-



buzov⁸ reaction for preparation of alkylphosphonates from phosphites and alkyl halides. Although the Arbuzov reaction has been utilized with a great variety of halides (including acid chlorides) and is usually regarded as applying specifically to halides, numerous similar reactions have been reported with other types of compounds. These methods include substitution of gramine for a halide,⁹ synthesis of a monothiophosphate (phosphorothioate) by use of ethyl thiocyanate¹⁰ or diethyl disulfide,¹¹ and

preparation of carbethoxyalkylphosphonates from α,β -unsaturated acids¹² or from β - or γ -lactones.¹³ It has also been claimed¹⁴ that a trialkyl phosphite may be converted to a dialkyl alkylphosphonate by heating at 150° with catalytic amounts of sodium iodide. An intermediate such as proposed would be expected to form more readily with methanol than with higher alcohols, as is observed; and if this type of intermediate is involved, it must also be the case that methyl is abstracted from oxygen considerably more readily than is ethyl. If this were not the case, mixed esters such as methyl ethyl methylphosphonate would be formed, and these would have shorter retention times in gas phase chromatography than diethyl methylphosphonate. One or two minor bands of shorter retention times were frequently observed in the chromatograms, but the sum of these never exceeded 3% of the total. In addition, there was observed no absorption in the infrared at 8.4 μ , the region of P—O—CH₃ absorption.⁶ Presence of significant amounts of ethylphosphonate is also contraindicated by the infrared spectrum of the acid obtained on hydrolysis of the phosphonate fraction; there was no significant absorption at 7.2 μ , the region of CH₃—C absorption.

The facility of methyl groups in this reaction was also demonstrated by heating at 210–215° for 5 hr. a mixed methyl ethyl phosphite with about 0.1 mole equivalent of methanol. As judged by infrared analysis for the P → O bond, there was about 55% conversion to phosphonate. Further, when trimethyl phosphite was heated similarly with 0.08 mole equivalent of methanol, there was realized a 92% yield of dimethyl methylphosphonate, in which no other compounds could be detected by either infrared spectroscopy or gas phase chromatography. These observations, as well as certain of those previously mentioned, strongly suggest that the first reaction between triethyl phosphite and methanol is transesterification; and indeed this reaction occurs readily when the mixture is simply heated under reflux, with the equilibrium highly favorable to methyl ester.

During the course of the present work, it was noted that in pentavalent phosphorus compounds the CH₃—P structure gives absorption at 7.65 ± 0.02 μ . Absorption in this region was noted not only for diethyl methylphosphonate and dimethyl methylphosphonate, but also in other compounds including methylphosphonic dichloride [CH₃—P(O)Cl₂] and bistetrahydrofurfuryl methylphosphonate. The tentative assignment by Bellamy⁶ for absorption by the CH₃—P structure at about 7.75 μ has been observed by us only in trivalent phospho-

(8) The Arbuzov reaction is discussed by G. M. Kosolapoff, *Organophosphorus Compounds*, John Wiley & Sons, Inc., New York, 1950, pp. 121–3. Numerous applications of the reaction have been reported since 1950; one critical examination is by A. E. Arbuzov and L. V. Nesterov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 361 (1954); *Chem. Abstr.*, **49**, 9541 (1955).

(9) A. F. Torralba and T. C. Myers, *J. Org. Chem.*, **22**, 972 (1957).

(10) J. Michalski and J. Wiczorkowski, *Bull. acad. polon. sci., Classe 3*, 4279 (1956); *Chem. Abstr.*, **51**, 4266 (1957).

(11) H. I. Jacobson, R. G. Harvey, and E. V. Jensen, *J. Am. Chem. Soc.*, **77**, 6064 (1955).

(12) G. Kamai and V. A. Kukhtin, *Doklady Akad. Nauk S.S.S.R.*, **109**, 91 (1956); *Chem. Abstr.*, **51**, 1827 (1957).

(13) R. L. McConnell and H. W. Coover, *J. Am. Chem. Soc.*, **78**, 4553 (1956).

(14) H. Coates and P. C. Crofts, British Patent 713,669, Aug. 18, 1954.

rus compounds such as trimethylphosphine and methyl dichlorophosphine.

EXPERIMENTAL¹⁵

Materials. Triethyl phosphate and triethyl phosphite were redistilled commercial grades. Triethyl phosphite must be distilled just before use or else protected from air, for it slowly oxidizes to triethyl phosphate. *Trimethyl phosphite*, b.p. 113°, was prepared from phosphorus trichloride and methanol in presence of dimethylaniline. According to a published procedure,¹⁶ *diethyl methylphosphonate* was prepared by heating under reflux for 15 hr. a mixture of 20 g. (0.12 mole) of triethyl phosphite and 100 g. (0.70 mole) of methyl iodide; yield 13.5 g. (62.5%), b.p. 83°/13 mm., n_D^{25} 1.4118 (lit.,¹⁷ b.p. 56.5°/3.5 mm., n_D^{20} 1.4140).

Anal. Calcd. for $C_6H_{15}O_3P$: C, 39.47; H, 8.61. Found: C, 39.86; H, 8.62.

Diethyl phosphonate was prepared by a published procedure¹⁸ from phosphorus trichloride and anhydrous ethanol; yield 62%, b.p. 72–73°/11 mm., n_D^{25} 1.4061 (lit.,^{17,19} b.p. 75°/15 mm., n_D^{20} 1.4080).

Anal. Calcd. for $C_4H_{11}O_3P$: C, 34.78; H, 8.03. Found: C, 34.94; H, 8.05.

Transesterification of triethyl phosphite with methanol. A mixture of 11.06 g. (0.067 mole) of triethyl phosphite and 4.28 g. (0.134 mole) of anhydrous methanol was heated under reflux for 16 hr., then distilled to yield 5.27 g. of ethanol containing a little methanol, b.p. 69–80°; 4.89 g. of mixed phosphite of b.p. 128–145°; and 3.60 g. of mixed phosphite of b.p. 145–154°. Boiling points of the mixed phosphites have not been reported, but trimethyl phosphite has b.p. 111–112°, and triethyl phosphite has b.p. of 154.5–155.5°.

In a similar run, except that there was used 0.062 mole of methanol, distillation yielded 2.81 g. (theory, 2.85 g.) of ethanol, b.p. 75–80°; 0.05 g. of intermediate fraction; 4.69 g. of mixed phosphite, b.p. 142–148°; and 3.34 g. of mixed phosphite of b.p. 148–155°.

Heat stability of phosphites. A sample of mixed phosphite, b.p. 128–154°, also a sample of pure triethyl phosphite, were heated for 5 hr. at 210–215° in sealed glass tubes. This treatment caused no significant change in the infrared spectra, in particular there was no evidence of $P \rightarrow O$ absorption at about 8μ . A 10-g. sample of triethyl phosphite heated similarly for 15 hr. yielded on distillation 9.3 g. of triethyl phosphite, b.p. 57–58°/18 mm., and 0.4 g. of material distilling principally at 45°/0.5 mm. and giving infrared absorption characteristic of the $P \rightarrow O$ bond.

High temperature reaction of phosphites with methanol.

(15) Boiling points are uncorrected; distillations were through a half-meter simple Podbielniak column of the type which has been described in detail (J. Cason and H. Rapoport, *Laboratory Text in Organic Chemistry*, Prentice-Hall, Inc., New York, 1950, pp. 237–43). Microanalyses were by the Microanalytical Division, Department of Chemistry, University of California, Berkeley. Infrared spectra were taken in carbon disulfide or carbon tetrachloride solution and recorded on a Baird double-beam recording spectrophotometer. Gas phase chromatography was in a 2 m. \times 9 mm. tube, packed with $-30 + 60$ mesh Celite firebrick impregnated with Dow-Corning High-Vacuum Silicone grease (10 parts firebrick: 4 parts grease). All sealed glass tubes were heated in steel pressure bombs.

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

(17) C. I. Meyrick and H. W. Thompson, *J. Chem. Soc.*, 225 (1950). The values for index of refraction given by Kosolapoff (cf. ref. 8, p. 149), which includes that given in ref. 16, appear to be in error.

(18) H. McCombie, B. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, 380 (1945).

(19) B. A. Arbuzov and V. S. Vinogradova, *Doklady Akad. Nauk S.S.S.R.*, 55, 31 (1947).

Results of the more significant runs are described in this section, and criteria for identification of the components of the phosphonate fractions are described in the next section.

A. Trimethyl phosphite. A mixture of 5.0 g. (0.040 mole) of freshly distilled trimethyl phosphite and 0.10 g. (0.003 mole) of anhydrous methanol was heated in a sealed tube at 210–215° for 5 hr. Distillation of the reaction product yielded two drops of methanol and a single fraction of b.p. 87.5–88.0°/28 mm., n_D^{25} 1.4111, weight 4.6 g. (92%); lit.,²⁰ for dimethyl methylphosphonate, b.p. 67°/12 mm., n_D^{25} 1.4105. Only one component was observed in gas phase chromatography. The infrared spectrum showed no absorption at 4.15μ ($P-H$ bond), but showed strong bands at 7.65μ (CH_3-P), 8.0μ ($P \rightarrow O$), and 8.4μ (CH_3-O-P).

B. Mixed phosphite. A 500-mg. sample of phosphite of b.p. 128–145° was heated with 10 mg. of anhydrous methanol as described in (A). Infrared absorption at 8μ indicated 50–60% conversion to products containing the $P \rightarrow O$ grouping.

C. Triethyl phosphite. In the procedure giving most satisfactory conversion to phosphonates, a mixture of 11.06 g. (0.067 mole) of freshly distilled triethyl phosphite and 2.50 g. (0.077 mole) of anhydrous methanol was heated in a sealed glass tube (flushed with nitrogen before filling) at 210–215° for 5 hr. When the cooled tube was opened a small amount of gas (not investigated) escaped; distillation of the contents of the tube yielded three principal fractions: (1) 2.5 g., b.p. 64–80°, ethanol containing a trace of methanol; (2) 1.1 g., b.p. 74–80°/48 mm., mixed phosphites, as judged by the characteristic infrared spectrum⁶ and its rapid exothermic reaction with sulfur; (3) 9.3 g. (84%), b.p. 102–108°/48 mm., phosphonate fraction determined as described below to consist of about 15% triethyl phosphate, 25% diethyl phosphonate, and 60% diethyl methylphosphonate.

Results of certain of the variations of this procedure are described below.

(a) When the heating period was extended to 15 hr., considerably more gas was evolved on opening the cooled reaction tube. Distillation yielded three principal fractions: (1) 1.6 g., b.p. 27–35°, diethyl ether; (2) 5.3 g. (48%), b.p. 67–69°/9 mm., phosphonate fraction consisting of 10% triethyl phosphate, 26% diethyl phosphonate, 61% diethyl methylphosphonate, and 3% minor components more volatile than diethyl methylphosphonate; (3) 2.4 g. of non-volatile residue.

(b) When the heating period was reduced to 4 hr., fractions obtained on distillation were: (1) 0.65 g., b.p. 61–77°; (2) 1.75 g., b.p. 77–79°; (3) 3.80 g., b.p. 64–80°/50 mm., phosphite fraction; (4) 6.00 g., b.p. 70–80°/8 mm., phosphonate fraction.

(c) When the heating period was 5 hr. and the methanol was reduced to 0.067 mole (equimolar with phosphite), distillation yielded: (1) 1.9 g., b.p. 74–80°; (2) 9.1 g. (82% recovery), b.p. 64–80°/48 mm., phosphite fraction; (3) 1.6 g. (14%), b.p. 105–108°/48 mm., phosphonate fraction consisting of 24% triethyl phosphate, 15% diethyl phosphonate, and 61% diethyl methylphosphonate.

(d) When heating was in a steel bomb, rather than a glass tube, the only products were considerable gas and an amorphous nonfusible solid.

(e) In a run made as first described except that 1.0 g. of alumina was added, products (in addition to considerable gas) were 4.3 g. of diethyl ether, b.p. 27–35°, and 3.6 g. of a nonvolatile liquid.

(f) In a run as first described except that 25 mg. of magnesium metal was allowed to react with the methanol before addition of phosphite to the tube, no significant phosphite fraction was recovered; principal products obtained on distillation were: (1) 0.5 g., b.p. 27–37°; (2) 0.4 g., b.p. 37–77°; (3) 1.0 g., b.p. 77–79°; (4) 8.4 g., b.p. 102–105°/41 mm., phosphonate fraction.

(20) B. A. Arbuzov and V. S. Vinogradova, *Izvest. Akad. Nauk S.S.S.R. Otdel. Khim. Nauk*, 459 (1947).

Identification of components of phosphonate fractions. Gas phase chromatography¹⁵ in the 2-m. tube at 143° resolved the peaks for the three major components, and the retention times were the same as those of authentic samples. With a pressure of 4 cm. of mercury applied to the tube, retention times were 4' 05" (min., sec.) for diethyl phosphonate, 4' 30" for diethyl methylphosphonate, and 6' 00" for diethyl phosphate. Triethyl phosphite has essentially the same retention time as diethyl phosphonate; however, this component is readily separated from the mixture by distillation, as indicated in the results described in the preceding section. The two phosphonates lie too close together for determination of areas under the peaks. Although a 4-m. column would probably supply sufficient resolution, it was deemed expedient to determine total phosphonate from area under the combined peaks, then determine diethyl phosphonate from the intensity of the 4.15- μ band in the infrared (the spectra of the methylphosphonate and phosphate are entirely clear in this region). In runs on pure components, areas under the peaks were found to be approximately proportional to weights of components. In runs on known mixtures, values within 5% of the true values were obtained.

In some runs, such as variation (a) under section C above, two small peaks were observed with lower retention times than diethyl phosphonate; these were usually barely detectable, never more than 3% of the total area of all bands. No other peaks were observed.

Although excellent coincidence with known compounds was obtained in gas phase chromatography of the reaction products, and the infrared spectra showed absorption at all expected places,⁶ additional verification of the identity of the components was obtained. A solution of 10 g. of phosphonate fraction in 50 ml. of benzene was allowed to stand overnight with 5 g. of sodium cut in small pieces; hydrogen was evolved. Filtration of the resultant mixture and recovery of material from the benzene solution yielded 3.9 g. of product distilling chiefly at 94–95°/21 mm. Gas phase chromatography of this product showed the peaks characteristic of triethyl phosphate and diethyl methylphosphonate, and absence of that attributed to diethyl phosphonate.

One sample of phosphonate fraction was carefully distilled in the half-meter column and separated into 8 fractions. Of these, the second, b.p. 103–104°/58 mm., showed the 4.15- μ infrared absorption characteristic of diethyl phosphonate; however, fraction 7, b.p. 114°/58 mm., showed no absorption at 4.15 μ . Gas phase chromatography of the latter fraction showed no diethyl phosphonate, and indicated about two parts of diethyl phosphate to one of diethyl methylphosphonate. Analysis was in agreement with the composition of these compounds.

Anal. Calcd. for C₆H₁₃O₂P (methylphosphonate): C, 39.47; H, 8.61. Calcd. for C₆H₁₅O₄P (phosphate): C, 39.56; H, 8.30. Found: C, 39.97; H, 8.47.

Analysis of fraction 3 from this distillation, b.p. 104–106°/58 mm., gave values of C, 37.64; H, 8.27. Similar values to these latter ones were obtained on analysis of several of the total phosphonate fractions.

Reaction of phosphites with ethanol. When a 500 mg. sample of mixed phosphite, b.p. 128–145°, was heated with 50 mg. of anhydrous ethanol at 210–215° for 5 hr., there was no significant change in the infrared spectrum of the phosphite, in particular no absorption in the 8- μ region.

When a mixture of 11.06 g. (0.067 mole) of triethyl phosphite and 3.06 g. (0.067 mole) of anhydrous ethanol was heated in a sealed glass tube at 210–215° for 15 hr., there was recovered by distillation 2.35 g. of ethanol, 6.45 g. (58%) of triethyl phosphite, and 3.85 g. (35%) of phosphonate fraction (infrared absorption at 8 μ).

Reaction of triethyl phosphite with n-butyl alcohol. A mixture of 11.06 g. (0.067 mole) of triethyl phosphite and 4.93 g. (0.067 mole) of n-butyl alcohol was heated at 210–215° in a sealed glass tube for 15 hr. Distillation of the product yielded: (1) 2.8 g., b.p. 78–79°, n_D^{25} 1.3610, infrared spectrum that of ethyl alcohol; (2) 13 g. in a series of fractions of b.p. in the range from 64°/23 mm. to 70°/1 mm.; all fractions gave the phosphite infrared spectrum, reacted rapidly and exothermally with sulfur, and showed no significant absorption at 8 μ .

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