

278. *The Reaction between Trialkyl Phosphites and Alkyl Halides.*

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The rearrangement of trialkyl phosphites (Arbusov) has been extended so as to afford a simple method for preparing the dialkyl esters of alkyl- and halo-alkyl-phosphonic acids. When the halogen (bromine) atom in diethyl halogeno-alkylphosphonates is in the β -position to the phosphorus, hydrogen bromide is readily lost, giving dialkyl alkylenephosphonates.

THE ARBUSOV rearrangement in its simplest form (*Chem. Zentr.*, 1906, II, 1640) consists of the isomerisation of a trialkyl phosphite to a dialkyl alkylphosphonate (in 95% yield) by warming it with the corresponding alkyl iodide. Arbusov and Kushkova (*J. Gen. Chem. Russia*, 1936, 6, 283) extended the reaction to methylene iodide and found that when this compound was heated with triethyl phosphite (I), diethyl iodomethylphosphonate could be isolated from the reaction mixture.

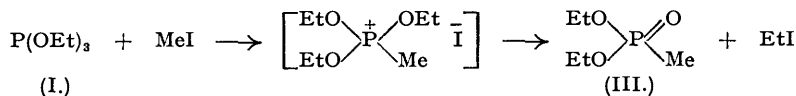
Later, Kosolapoff (*J. Amer. Chem. Soc.*, 1944, 66, 1511) reinvestigated the reaction between (I) and butyl bromide, hexyl bromide, ethylene bromide, and trimethylene bromide. He found that when the first three bromides were heated with (I), ethyl bromide was eliminated and some diethyl ethylphosphonate (II) formed. He was unable to isolate any other product of the reaction. With trimethylene bromide, he obtained some tetraethyl trimethylenediphosphonate and diethyl 3-bromopropylphosphonate, the latter as the free acid after hydrolysis.

In our hands, the Arbusov rearrangement was found to be of much wider application and can be used for preparing several series of compounds. In all cases except one (in which triisopropyl phosphite was used), the reaction was carried out with (I).

When (I) is warmed with an equimolar quantity of methyl iodide for a short time, a vigorous reaction sets in, and, on fractionation of the product, almost quantitative yields of ethyl iodide and diethyl methylphosphonate (III) are obtained. The reaction between methyl iodide and triisopropyl phosphite proceeds even more easily, the products being isopropyl iodide and diisopropyl methylphosphonate.

The interaction of (I) and ethylene bromide was next examined. If the reaction is carried out under reflux, the mixture on fractionation gives ethyl bromide, a considerable amount of (II), and a high boiling residue.

The reaction between (I) and methyl iodide gives strong support to the suggestion that the rearrangement takes place through the formation of an unstable phosphonium halide. In this particular case, the larger radical is eliminated as halide:



It seemed probable, therefore, that, in the reaction between (I) and ethylene bromide, if the ethyl bromide were allowed to escape, the amount of high-boiling residue formed would increase at the expense of the (II). This was found to be so. When the reaction was carried out under a column so that the ethyl bromide distilled out as fast as it was formed, the residue of high-boiling material was considerably greater. This, on further distillation at 1–2 mm., was found to be a mixture of diethyl 2-bromoethylphosphonate (IV) and tetraethyl ethylene-

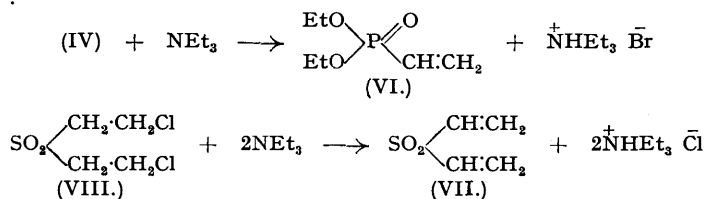


1 : 2-diphosphonate (V). Contrary to the observation of Kosolapoff (*loc. cit.*), they both appear to distil at this pressure without decomposition.

This reaction can be extended to primary alkyl bromides. With *n*-hexyl bromide or higher homologues, the reaction proceeds very smoothly giving ethyl bromide and a small amount of (II), most of the product consisting of the diethyl alkylphosphonate, isolated by distillation in a vacuum. The reaction of (I) with *n*-amyl bromide goes less easily; with *n*-butyl bromide and *iso*amyl bromide, it takes place very sluggishly; ethyl bromide is slowly evolved, a considerable amount of (II) is formed, and the yield of alkylphosphonate is poor. No reaction between secondary bromides, such as *cyclohexyl* bromide and 2-bromo-octane, and (I) takes place.

When methylene bromide is used, the reaction goes slowly and a poor yield of tetraethyl methylenediphosphonate results, the bromomethylphosphonic ester being almost entirely absent. No difficulty is experienced in obtaining the methylenediphosphonate when methylene iodide is used in place of the bromide, the iodomethylphosphonic ester being formed simultaneously (cf. Arbusov and Kushkova, *loc. cit.*). With trimethylene bromide, we had no difficulty in obtaining tetraethyl trimethylenediphosphonate, but we were unable to prepare the bromopropylphosphonate either pure or in any quantity.

(IV) undergoes an interesting reaction on treatment with triethylamine in dry benzene. Triethylamine hydrobromide is formed, and diethyl vinylphosphonate (VI) can be isolated from the residue by distillation under reduced pressure. This reaction recalls the preparation of divinyl sulphone (VII) from 2 : 2'-dichlorodithiethyl sulphone (VIII) (Alexander and McCombie, *J.*, 1931, 1913) :



Unlike (VII), which reacts with thiophenol with evolution of heat [to give 2 : 2'-bis(phenylthioethyl) sulphone], no reaction takes place between thiophenol and (VI).

Since secondary bromides do not enter into this reaction, we hoped to prepare diethyl 2-bromopropylphosphonate (IX) by the interaction of propylene bromide and (I); (IX) should lose HBr on treatment with triethylamine to give diethyl propenylphosphonate (X) :



When (I) and propylene bromide are heated, ethyl bromide distils but no trace of (IX) can be isolated, the product consisting of (II) together with a rather poor yield of (X).

The (I) used in these reactions was prepared by the method of McCombie, Saunders, and Stacey (*J.*, 1945, 380) who obtained it by the action of phosphorus trichloride on ethanol in ether in the presence of dimethylaniline. We found that the dimethylaniline could be replaced with advantage by diethylaniline and the ether by light petroleum (b. p. 40—60°). The diethylaniline hydrochloride formed is non-hygroscopic, a 95% recovery of the base is obtained without difficulty, and the yield of (I) is at least 85%.

EXPERIMENTAL.

Triethyl Phosphite (I).—This, prepared in 87—92% yield by the method of McCombie, Saunders, and Stacey (*loc. cit.*) but with light petroleum (b. p. 40—60°) and diethylaniline in place of ether and dimethylaniline, had the following constants: b. p. 52°/14 mm., 57·5°/19 mm. (McCombie, Saunders, and Stacey give b. p. 48°/12·5 mm.), d_{15}^{15} 0·963, $n_D^{17.5}$ 1·4140.

Triisopropyl phosphite was prepared similarly, but owing to the closeness of its b. p. to that of diethylaniline, an equivalent amount of pyridine, or, better, triethylamine was used in place of the former.

Diethyl Methylphosphonate (III).—(I) (55 g.) and methyl iodide (50 g.) were refluxed gently for 2 hours on a steam-bath. On distillation at ordinary pressure, ethyl iodide (50 g.) was recovered. The residue distilled in a vacuum gave *diethyl methylphosphonate* (52·5 g.; 95%), b. p. 64—65°/2 mm., n_D^{15} 1·4120 (Found: C, 39·18; H, 8·83. $\text{C}_6\text{H}_{13}\text{O}_3\text{P}$ requires C, 39·47; H, 8·55%).

Diisopropyl methylphosphonate was obtained similarly from triisopropyl phosphite and methyl iodide in 95% yield. The reaction is vigorous and the conversion complete within a few minutes; b. p. 66°/3 mm., $n_D^{15.5}$ 1·4120 (Found: C, 45·95; H, 9·53. $\text{C}_7\text{H}_{17}\text{O}_3\text{P}$ requires C, 46·66; H, 9·44%).

The Diethyl Alkylphosphonates.—Diethyl ethylphosphonate (II) was prepared in 95% yield by the method of Arbusov (*loc. cit.*) from (I) and ethyl iodide; b. p. 62°/2 mm., d_{15}^{15} 1·032, n_D^{15} 1·4172.

Diethyl n-dodecylphosphonate. (I) (62·5 g.) and n-dodecyl bromide (94 g.) were heated under a column attached to a condenser set for distillation. At about 160°, ethyl bromide started to distil. After about 1·5 hours, ethyl bromide (31·5 g.) stopped distilling and the mixture was fractionated under reduced pressure to give: (II) (7 g.), b. p. 60—70°/3 mm.; dodecyl bromide (8 g.), b. p. 124°/1 mm.; *diethyl n-dodecylphosphonate* (73 g.), b. p. 160°/1 mm., $n_D^{15.5}$ 1·4419 (Found: C, 62·86; H, 11·60. $\text{C}_{16}\text{H}_{33}\text{O}_3\text{P}$ requires C, 62·74; H, 11·51%).

The following esters were obtained similarly. *Diethyl n-butylphosphonate*, b. p. 74°/1 mm., n_D^{17} 1·4244 (Found: C, 47·40; H, 10·21. $\text{C}_8\text{H}_{19}\text{O}_3\text{P}$ requires C, 49·49; H, 9·86%). *Diethyl n-amylphosphonate*, b. p. 86°/1·5 mm., $n_D^{15.5}$ 1·4282 (Found: C, 51·12; H, 10·36. $\text{C}_9\text{H}_{21}\text{O}_3\text{P}$ requires C, 51·90; H, 10·17%). *Diethyl n-hexylphosphonate*, b. p. 103°/2 mm., n_D^{17} 1·4311 (Found: C, 53·34; H, 10·58. $\text{C}_{10}\text{H}_{23}\text{O}_3\text{P}$ requires C, 54·08; H, 10·43%). *Diethyl n-heptylphosphonate*, b. p. 113°/1·9 mm., $n_D^{16.5}$

1.4325 (Found: C, 54.90; H, 10.87. $C_{11}H_{25}O_3P$ requires C, 55.90; H, 10.66%). *Diethyl n-octylphosphonate*, b. p. $119^\circ/1.2$ mm., n_D^{15} 1.4360 (Found: C, 57.54; H, 10.88. $C_{13}H_{27}O_3P$ requires C, 57.59; H, 10.88%). *Diethyl 3-methyl-n-butyl-1-phosphonate*, b. p. $75^\circ/0.8$ mm., $n_D^{15.5}$ 1.4266 (Found: C, 51.54; H, 10.26. $C_9H_{21}O_3P$ requires C, 51.90; H, 10.17%).

Diethyl 2-bromoethylphosphonate (IV). (I) (83 g. = 0.5 mol.) and ethylene bromide (141 g. = 0.75 mol.) were heated as in the preparation of the dodecylphosphonic ester described above. The reaction was complete in about two hours, 48 g. of ethyl bromide having distilled. The residue on fractionation under reduced pressure gave the following products: recovered ethylene bromide, 77 g.; (II) b. p. $60-70^\circ/3$ mm., 15 g.; *diethyl bromoethylphosphonate*, b. p. $101^\circ/0.8$ mm., $n_D^{15.5}$ 1.4600, 48.5 g. (Found: C, 29.71; H, 5.96. $C_6H_{14}O_3BrP$ requires C, 29.40; H, 5.76%); tetraethyl ethylenediphosphonate, (*q.v.*), b. p. $167^\circ/1$ mm.

Diethyl iodomethylphosphonate, b. p. $101^\circ/0.7$ mm., n_D^{17} 1.4975 (Found: C, 21.94; H, 4.58. Calc. for $C_6H_{12}O_3IP$: C, 21.60; H, 4.36%) and tetraethyl methylenediphosphonate, b. p. $143^\circ/1.5$ mm., $n_D^{19.5}$ 1.4312 (Found: C, 35.68; H, 7.67. $C_8H_{22}O_6P_2$ requires C, 37.51; H, 7.70%) were obtained similarly by substituting methylene iodide for ethylene bromide. Tetraethyl methylenediphosphonate was also obtained by using methylene bromide in place of methylene iodide, but in poor yield; the expected diethyl bromomethylphosphonate was almost entirely absent.

Diethyl vinylphosphonate (VI). (IV) (48.5 g.), triethylamine (22 g. = 30 c.c.), and benzene (70 c.c.) were refluxed for 1 hour. After standing overnight, the triethylamine hydrobromide was filtered off, the benzene distilled from the filtrate, and the residue fractionated under reduced pressure. *Diethyl vinylphosphonate* (26 g.), n_D^{15} 1.4320, distilled at $63^\circ/2.5$ mm. (Found: C, 43.54; H, 8.37. $C_8H_{12}O_3P$ requires C, 43.88; H, 7.98%).

Tetraethyl ethylenediphosphonate (V). (I) (157 g.) and ethylene bromide (100 g. = 47 c.c.) were allowed to react as in the preparation of (IV) and the product was worked up similarly. Ethyl bromide (75 g.) distilled during the reaction, and the residue gave the following fractions: (II), b. p. $55-60^\circ/2$ mm., 55 g.; (IV), b. p. $99-115^\circ/1$ mm., 18 g.; *tetraethyl ethylenediphosphonate*, b. p. $167^\circ/1$ mm. ($180^\circ/2.5$ mm.), 71 g., $n_D^{15.5}$ 1.4425 (Found: C, 39.26; H, 7.96. $C_{10}H_{24}O_6P_2$ requires C, 39.73; H, 8.00%).

Tetraethyl trimethylenediphosphonate. This was made similarly from (I) and trimethylene bromide; it had b. p. $175^\circ/0.8$ mm., $n_D^{15.5}$ 1.4508 (Found: C, 40.34; H, 8.18. Calc. for $C_{11}H_{28}O_6P_2$: C, 39.73; H, 8.29%).

When (I) and 1:2-dibromopropane were similarly treated, no diethyl 2-bromopropylphosphonate could be isolated. After repeated fractionation under reduced pressure, the product was *diethyl propenylphosphonate* (X), b. p. $78-81^\circ/2$ mm., n_D^{21} 1.4320 (Found: C, 46.60; H, 8.79. $C_7H_{14}O_3P$ requires C, 47.19; H, 8.49%).

The microanalyses were carried out by Mr. W. Brown. The consistently low values found for carbon are probably due to the difficulty in effecting the complete combustion of these substances.

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