365. *Di*iso*propyl Phosphorofluoridate.*

By A. H. Ford-Moore, L. J. Lermit, and C. Stratford.

Methods for preparing di*iso*propyl phosphorofluoridate from three different starting materials are described. Two are modifications of known methods and all give a product of high purity in yields of at least 60%. Some physical constants of material fractionated to constant refractive index are recorded.

Di*iso*propyl phosphorofluoridate, $(Pr^iO)_2POF$, has been studied by McCombie, Saunders, and Stacey, and their co-workers (*J.*, 1945, 381; 1948, 698; *Nature*, 1946, **157**, 287). Their method of preparation was based on the steps:

$$\text{(i)}\quad 3Pr^iOH + PCl_3 \longrightarrow \underset{\text{(I)}}{HPO(OPr^i)_2} + Pr^iCl + 2HCl$$

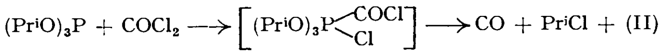
$$\text{(ii)}\quad \text{(I)} + Cl_2 \longrightarrow \underset{\text{(II)}}{(Pr^iO)_2POCl} + HCl$$

$$\text{(iii)}\quad \text{(II)} + NaF \longrightarrow \underset{\text{(III)}}{(Pr^iO)_2POF} + NaCl$$

The phosphorochloridate (II) could also be obtained by the action of chlorine on tri*iso*propyl phosphite (cf. McCombie, Saunders, and Stacey, *loc. cit.*, 1945; Ford-Moore and Howarth Williams, *J.*, 1947, 1465; Ford-Moore and Perry, *Org. Synth.*, 1951, **31**, 111).

Saunders and Stacey (*loc. cit.*, 1948) also described a one-stage synthesis of (III) from *iso*propanol and phosphorus trichloride, neither (I) nor (II) being isolated, but the present authors found difficulty in repeating this work. Certain modifications have therefore been introduced. Thus sulphuryl chloride (cf. Atherton, Howard, and Todd, *J.*, 1948, 1106) was found to react more smoothly than chlorine in stage (ii). In stage (iii), the use of ammonium fluoride (U.S.P. 2,409,039) was found more convenient than that of sodium fluoride.

When tri*iso*propyl phosphite was used as the starting material, carbonyl chloride was found to be a convenient reagent for its conversion into (II), apparently functioning as follows :



$$(\mathrm{Pr^iO})_3\mathrm{P} + \mathrm{COCl_2} \longrightarrow \left[(\mathrm{Pr^iO})_3\mathrm{P}\genfrac{}{}{0pt}{}{\mathrm{COCl}}{\mathrm{Cl}}\right] \longrightarrow \mathrm{CO} + \mathrm{Pr^iCl} + \mathrm{(II)}$$

This reaction proceeded equally well with primary alkyl phosphites such as triethyl phosphite. If desired, the pure phosphorochloridate could be isolated, by distillation, in about 90% yield. For conversion into (III), the crude (II), after removal of volatile matter under reduced pressure, was heated with dry ammonium fluoride in the absence of a diluent and the phosphorofluoridate isolated by vacuum distillation without filtration from the ammonium salts.

The simplest one-stage process is expressed by :

$$\mathrm{POCl_3} + 2\mathrm{Pr^iOH} + 5\mathrm{NaF} \longrightarrow \mathrm{(III)} + 3\mathrm{NaCl} + 2\mathrm{NaHF_2}$$

An attempt to realise this reaction showed that it was uncontrollable, probably owing to decomposition of the intermediate *iso*propyl phosphorodichloridate (IV). But if the preparation of (IV) (though not the actual isolation, since it begins to decompose about 55°) was carried out as a separate stage, a good yield of (III) could be obtained :

$$\mathrm{Pr^iOH} + \mathrm{POCl_3} \longrightarrow \mathrm{HCl} + \mathrm{Pr^iO{\cdot}POCl_2} \quad \mathrm{(IV)}$$

$$\mathrm{(IV)} + \mathrm{Pr^iOH} + 3\mathrm{NaF} \longrightarrow \mathrm{(III)} + 2\mathrm{NaCl} + \mathrm{NaHF_2}$$

Use of sodium fluoride in the final stage was quite satisfactory.

The phosphorofluoridate could also be obtained by treating (I) with sulphuryl chloride in the presence of sodium fluoride :

$$\mathrm{(I)} + \mathrm{SO_2Cl_2} + 3\mathrm{NaF} \longrightarrow \mathrm{(III)} + 2\mathrm{NaCl} + \mathrm{NaHF_2}$$

Very pure phosphorofluoridate was obtained by fractional distillation under reduced pressure of good-grade material prepared as described above.

EXPERIMENTAL

Di*iso*propyl hydrogen phosphite was made by the method of McCombie, Saunders, and Stacey (*loc. cit.*). For certain of the preparations described, it was isolated and purified by distillation under reduced pressure. In others, *e.g.*, treatment with sulphuryl chloride, it was sufficient to remove hydrogen chloride and diluent by distillation and use the crude material. Triethyl and tri*iso*propyl phosphite were made by Ford-Moore and Perry's method (*loc. cit.*).

Diïsopropyl Phosphorochloridate (II).—(*a*) Crude di*iso*propyl hydrogen phosphite, diluted with carbon tetrachloride, was treated with one equivalent of sulphuryl chloride (cf. Todd *et al.*, *loc. cit.*). The product, isolated by distillation under reduced pressure, had b. p. 68°/2 mm. (yield, 85—90%).

(*b*) Redistilled tri*iso*propyl phosphite (104 g.) was treated with a fairly rapid stream of carbonyl chloride, with stirring, the temperature being kept at 30—35°. Reaction was complete in about 1 hr., when rise of temperature and effervescence ceased. Next morning, the product was degassed at the water-pump and then distilled under reduced pressure, giving the phosphorochloridate (92 g., 92%), b. p. 63°/1 mm., n_{D}^{25} 1·4142 (Found : Cl, 17·9. Calc. for $\mathrm{C_6H_{14}O_3ClP}$: Cl, 17·7%).

Diethyl phosphorochloridate (81 g., 94%), prepared from triethyl phosphite by a similar procedure on a 0·5-molar scale, had b. p. 54°/1 mm., n_{D}^{25} 1·4147 (Found : Cl, 20·6%).

Diïsopropyl Phosphorofluoridate.—(*a*) Redistilled phosphorochloridate (100 g.) in dry acetone (200 c.c.) was treated with coarsely ground ammonium fluoride, previously dried by distillation with carbon tetrachloride. A mildly exothermic reaction set in; this was completed by 1 hr.' refluxing. After cooling, the mixture was filtered and the filter cake washed with dry acetone. Removal of the diluent from the filtrate and distillation under reduced pressure gave crude fluoridate (82 g., 89%), b. p. 53°/4 mm., n_D^{25} 1·3791. When crude phosphorochloridate (from di*iso*propyl hydrogen phosphite and sulphuryl chloride) was used, the initial reaction was much more vigorous and external cooling was necessary. The yield of distilled product in a 0·5-molar run was 75 g. (81%, calc. on the crude ester).

(*b*) Di*iso*propyl phosphorochloridate (44·7 g., 41 c.c.) and dried ammonium fluoride (12 g.) were heated under reflux in an oil-bath. A vigorous reaction set in at about 120° (bath-temp.). When it had ceased, the mixture was cooled and filtered, the filter cake being washed with a little methylene chloride. The product (27 g., 71%), isolated by distillation under reduced pressure, had b. p. 52—53°/4 mm., n_D^{25} 1·3790.

One-stage Methods.—(*a*) A mixture of undistilled di*iso*propyl hydrogen phosphite (83 g., 0·5 mole) and dry sodium fluoride (75 g., 1·75 mole) in dry benzene was stirred under reflux and warmed to 35°. Sulphuryl chloride (42 c.c., 0·52 mole) was added, with cooling, at such a rate that the temperature was kept at 45—50°. After the addition, the mixture was stirred and refluxed for 2 hr. After cooling, dry kieselguhr (15 g.) was added and the mixture filtered, the filter cake being washed with dry benzene. Removal of solvent from the filtrate and distillation under reduced pressure gave di*iso*propyl phosphorofluoridate (63 g., 68%), b. p. 48°/3 mm., n_D^{25} 1·3794. Addition of the phosphite to the other reactants resulted in a lower yield.

(*b*) Dry *iso*propanol (38 c.c., 0·5 mole) was added slowly to phosphorus oxychloride (46 c.c., 0·5 mole) and carbon tetrachloride (100 c.c.) at 30—35°. The reaction was only mildly exothermic and little cooling was necessary. Next morning the diluent and hydrogen chloride were removed under reduced pressure, at $\ngtr$50°. A mixture of *iso*propanol (42 c.c., 0·55 mole) and sodium fluoride (75 g., 1·75 mole) in dry benzene or carbon tetrachloride was stirred and warmed to 40° (the lowest temperature for reaction). The crude *iso*propyl phosphorodichloridate was added at such a rate that the temperature was 45—50°. The mixture was then refluxed with stirring for 0·5 hr. and the phosphorofluoridate isolated as above (yield, 55 g.; b. p. 49°/3 mm., n_D^{25} 1·3790).

(*c*) Tri*iso*propyl phosphite (104 g., 0·5 mole) was stirred and treated at 30—35° (cooling) with a fairly rapid stream of carbonyl chloride. Next morning the mixture was degassed at the water pump till the pressure fell below 20 mm. and treated under a reflux fractionating column with dry ammonium fluoride (30 g., 0·75 mole) and then heated rapidly to 120° (oil-bath). When the vigorous reaction had moderated, the material was kept at 120° for a further 0·5 hr. The product (59 g.), isolated by distillation under reduced pressure, without filtering, had b. p. 46—47°/2·5 mm., n_D^{25} 1·3792. It was slightly turbid owing to a small amount of ammonium salts which could be removed by decantation after 2 days.

Pure Di*iso*propyl Phosphorofluoridate.*—The various samples of high-grade material prepared as described above were combined and distilled under reduced pressure from about 5% (vol.) of diethylaniline, under a 15″ helix-packed column surmounted with a Whitmore–Lux total-reflux variable-take-off still-head, until the refractive index of the distillate, determined with an Abbé refractometer, was constant. It was collected at 41—42°/1·5 mm. (Found: C, 39·0; H, 7·8; F, 10·4. Calc. for $C_6H_{14}O_3FP$: C, 39·1; H, 7·7; F, 10·3%). The product had b. p. 42—43°/2 mm., d_4^{25} 1·0571, η 0·01323 poise, and n and v. p. as tabulated.

Temp.	10°	15°	20°	25°	30°
n_D	1·3854	1·3834	1·3814	1·3791	1·3773
V. p. (mm.)	—	0·48	0·72	1·08	1·61

This paper is published by permission of the Chief Scientist, Ministry of Supply, whom authors thank. Microanalyses were by F. E. Charlton and Miss B. A. Jones, vapour-pressure determinations by E. Neale, using an effusion manometer, and densities and viscosity by A. W. H. Wardrop.

Chemical Defence Experimental Establishment,
Porton, Wilts.

[*Received, September 4th,* 1952.]