963. *Anhydrides of Organophosphorus Acids. Part II.* The Synthesis of Tri- and Tetra-alkyl Esters of Phosphorous Phosphoric Anhydride.*

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A convenient method of preparing tri- and tetra-alkyl esters of phosphorous phosphoric anhydride is described.

THE esters of phosphorous phosphoric anhydride are of considerable interest but, since they have been difficult to prepare, little is known about them. As yet, synthesis of an anhydride of type (I) has been reported only by Corby, Kenner, and Todd [1] who have shown that *O*-benzylphosphorous *OO*-diphenylphosphoric anhydride is formed by condensation of diphenyl phosphorochloridate and benzyl hydrogen phosphite in the presence of pyridine. They were unable to obtain this compound in pure state, but they applied it successfully *in situ* as a convenient phosphorylating agent.

$$\text{(I)}\ (RO)_2PO{\cdot}O{\cdot}PHO{\cdot}OR' \qquad (RO)_2PO{\cdot}O{\cdot}P(OR')_2\ \text{(II)}$$

The first attempts [2] to synthesize an ester (II) were based on the action of alkyl halides on the silver salt of hypophosphoric acid, and failed. Miłobędzki and Walczyńska [3] were also unsuccessful in their efforts to prepare anhydrides (II) by treating sodium dialkyl phosphates and phosphites with dialkyl phosphorochloridites and phosphorochloridates, respectively, probably owing to difficulties in purifying the products.

Authentic tetraethyl and tetrapropyl esters of phosphorous phosphoric anhydride were first reported by A. E. and B. A. Arbuzov.[4] Produced in minute yield together with many other products of the reaction between bromine and sodium dialkyl phosphites, the substances were isolated by tedious fractional distillation. There are reports [5] that small amounts of the esters (II) are formed as a by-product in other reactions, but there is no general method for their synthesis.

We find that pure tri- and tetra-alkyl esters of phosphorous phosphoric anhydride are relatively easy to prepare. We obtained a number of them of type (I) by condensing diethyl phosphorochloridate with alkyl hydrogen phosphites in the presence of 2,6-lutidine in benzene at 35°: $(RO)_2POCl + R'O{\cdot}PHO{\cdot}OH \longrightarrow \text{(I)} + HCl$. Tetra-alkyl esters of type (II) were prepared similarly from dialkyl phosphorochloridites and dialkyl hydrogen phosphates in the presence of pyridine in benzene at 0—5°.

The reactions were smooth, but for good yields pure starting materials were needed.

Properties of our products are tabulated. At $>100°$, particularly in the presence of impurities, compounds of type (I) tend to decompose. Their structures seem evident from the mode of formation and infrared spectra (also from their behaviour with water, alcohols, amines, and acids which will be reported later). *O*-Ethylphosphorous *OO*-diethylphosphoric anhydride has absorption maxima (as liquid film) at 2329 (P–H), 1270 (P=O), 937, 965 (P–O–P), and 1012 cm.$^{-1}$ (P–O–Et).

From these investigations emerged the need for a more efficient method for the preparation of dialkyl phosphorochloridites. These are usually obtained by the method of Cook *et al.*,[6] in which a mixture of alcohol and tertiary amine (2 mol. of each) is added to ethereal

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* Part I, *Roczniki Chem.*, 1961, **35**, 619.

[1] Corby, Kenner, and Todd, *J.*, 1952, 3669.

[2] Sänger, *Annalen*, 1886, **232**, 1; Rosenheim, Stadler, and Jacobsohn, *Ber.*, 1906, **39**, 2837; Rosenheim and Pritze, *Ber.*, 1908, **41**, 2708.

[3] Miłobędzki and Walczyńska, *Roczniki Chem.*, 1928, **8**, 486.

[4] A. E. Arbuzov and B. A. Arbuzov, *Zhur. obshchei Khim.*, 1932, **2**, 345; B. A. Arbuzov and Razumov, *ibid.*, 1937, **7**, 1762.

[5] Steinberg, *J. Org. Chem.*, 1950, **15**, 637; Kosolapoff, U.S.P. 2,503,204; Arbuzov and Balitova, *Doklady Akad. Nauk S.S.S.R.*, 1952, **83**, 577.

[6] Cook, Ilett, Saunders, Stacey, Watson, Wilding, and Woodcock, *J.*, 1949, 2921.

TABLE 1.

Trialkyl esters (I) of phosphorous phosphoric anhydride.

R	R′	Yield (%)	B. p./0·005 mm.	n_D^{20}	Found (%) C	Found (%) H	Found (%) P	Formula	Required (%) C	Required (%) H	Required (%) P
Et	Et	51	85—86°	1·4225	29·4	6·5	25·1	$C_6H_{16}O_6P_2$	29·3	6·5	25·2
Et	Pr^n	51	88—89	1·4235	32·5	6·8	23·8	$C_7H_{18}O_6P_2$	32·3	6·9	23·8
Et	Pr^i	59	81—82	1·4240	32·4	7·1	23·6	$C_7H_{18}O_6P_2$	32·3	6·9	23·8
Et	Bu^n	52	88—89	1·4230	35·0	7·2	22·7	$C_8H_{20}O_6P_2$	35·0	7·3	22·6
Et	CH_2Ph	45	91—92	1·4574	43·3	6·3	19·9	$C_{11}H_{18}O_6P_2$	42·9	5·8	20·1
Et	Allyl	52	86—87	1·4248	32·6	6·3	23·7	$C_7H_{15}O_6P_2$	32·6	6·2	24·0

TABLE 2.

Tetra-alkyl esters (II) of phosphorous phosphoric anhydride.

R	R′	Yield (%)	B. p./mm.	n_D^{25}	Found (%) C	Found (%) H	Found (%) P	Formula	Required (%) C	Required (%) H	Required (%) P
Et	Et	70	74°/0·01	1·4254	35·0	7·2	22·6	$C_8H_{20}O_6P_2$	35·0	7·35	22·6
Pr^n	Et	77	84—85°/0·001	1·4277	39·65	7·9	20·6	$C_{10}H_{24}O_6P_2$	39·7	8·0	20·5
Pr^n	Bu^n	78	114—115°/0·001	1·4342	47·6	9·0	17·2	$C_{14}H_{32}O_6P_2$	46·9	9·0	17·3
Pr^i	Pr^i	53	106—108°/0·15	1·4186	42·8	8·95	17·9	$C_{12}H_{28}O_6P_2$	43·6	8·5	18·75
Bu^n	Bu^n	70	106—107°/0·005	1·4341	49·7	9·4	15·3	$C_{16}H_{36}O_6P_2$	49·7	9·4	16·0
CH_2Ph	Et	88 *	—	1·5206	52·9	5·75	15·1	$C_{18}H_{24}O_6P_2$	54·3	6·1	15·55

* Crude product.

phosphorus trichloride. We have found that by adding successively pyridine (1 mol.), a mixture of alcohol and diethylaniline (1 mol. of each), and finally alcohol (1 mol.) to a benzene solution of phosphorus trichloride (1 mol.), dialkyl phosphorochloridites can be obtained in 60—70% yields, *i.e.*, double those in the method used hitherto. The products are pure and virtually free from trialkyl phosphites. The order in which amines and alcohol have to be added suggests that formation of an intermediate pyridine–phosphorus trichloride complex is an important step in this reaction.

EXPERIMENTAL

Preparation of Dialkyl Phosphorochloridites.—To phosphorus trichloride (1·0 mole) in benzene (750 ml.) pyridine (1·0 mole) was added in about 20 min. at −5° to 0° with cooling and stirring. The solution was stirred at 0° for 15 min., then a mixture of diethylaniline (1·0 mole) and the required alcohol (1·0 mole) was added during 15 min. at 0—5°. After 15 min. the second mole of alcohol was added at 0—10°. The resulting mixture was stirred for 1·5 hr. at 10—15°, then filtered, and the precipitate was washed with benzene (300 ml.). Benzene was removed at 30—40° under reduced pressure and the products were purified by distillation *in vacuo*.

The following dialkyl phosphorochloridites were prepared: diethyl (59%), b. p. 53·5—54·5°/25 mm., n_D^{20} 1·4370 (lit.,[7] 63—65°/30 mm., 1·4350); dipropyl (60%), b. p. 80°/17 mm., n_D^{20} 1·4426 (lit.,[8] 65·5—66·5°/8 mm., 1·4420); dibutyl (73%), b. p. 115—117°/25 mm., n_D^{20} 1·4454 (lit.,[9] 100—103°/12—14 mm., 1·4455); *di-isopropyl* (49%), b. p. 62—64°/12 mm., n_D^{20} 1·4242 (Found: C, 39·0; H, 7·6; P, 16·85. $C_6H_{14}ClO_2P$ requires C, 39·0; H, 7·6; P, 16·8%).

Preparation of Alkyl Hydrogen Phosphites.—Sodium ethyl, propyl, isopropyl, and butyl hydrogen phosphites were prepared as described by Nylen,[10] by the action of 1 mol. of sodium hydroxide on 1 mol. of the corresponding dialkyl phosphite in water–ethanol (1 : 1). This method was also used for preparing the sodium allyl hydrogen phosphite; the crude product (91·5%) had m. p. 180—185° (Found: P, 22·0. Calc. for $C_3H_6NaO_3P$: P, 21·5%). Ammonium benzyl hydrogen phosphite was prepared as described by Christie *et al.*[11] (71·5%; m. p. 153—154°).

The alkyl dihydrogen phosphites were prepared as follows: Dry hydrogen chloride was

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[7] A. E. Arbuzov and B. A. Arbuzov, *Ber.*, 1932, **65**, 195.

[8] B. A. Arbuzov and Razumov, *Zhur. obshchei Khim.*, 1937, **7**, 1762.

[9] Gerrard, Isaacs, Machell, Smith, and Wyvill, *J.*, 1953, 1920.

[10] Nylen, *Svensk kem. Tidskr.*, 1936, **48**, 2.

[11] Christie, Elmore, Kenner, Todd, and Weymouth, *J.*, 1953, 2947.

passed through the suspension of sodium alkyl hydrogen phosphite (0·4 mole) in benzene (250 ml.) for 30 min. at 10—20° with cooling and stirring. The excess of hydrogen chloride was removed under reduced pressure, and sodium chloride was separated by means of a centrifuge and washed with benzene (*ca.* 200 ml.). The solvent was evaporated under reduced pressure and the crude alkyl dihydrogen phosphites were used for the condensations. The following alkyl dihydrogen phosphites were prepared: ethyl (91%), n_D^{20} 1·4230; propyl (67%), n_D^{20} 1·4257; isopropyl (95%), n_D^{20} 1·4211; butyl (95%), n_D^{20} 1·4292; allyl (98%), n_D^{20} 1·4390; benzyl (94%), n_D^{25} 1·5278.

Dialkyl hydrogen phosphates were prepared by Toy's method.[12] Diethyl phosphorochloridate was prepared as described by Fiszer and Michalski.[13]

O-*Alkylphosphorous* OO-*Diethylphosphoric Anhydrides.*—To diethyl phosphorochloridate (0·15 mole) and the alkyl dihydrogen phosphite (0·15 mole) in benzene (100 ml.) 2,6-lutidine (0·15 mole) in benzene (10 ml.) was added dropwise in 15 min. at 30—35° with cooling and stirring. The mixture was stirred at room temperature for 15 min. and left overnight in a refrigerator. 2,6-Lutidine hydrochloride (80—90%) was then filtered off and washed with benzene (100 ml.). After removal of benzene under reduced pressure the *anhydrides* were purified by distillation *in vacuo*. They are described in Table 1.

Preparation of Tetra-alkyl Phosphorous Phosphoric Anhydrides.—To the solution of dialkyl hydrogen phosphate (0·2 mole) and pyridine (0·2 mole) in benzene (200 ml.) the dialkyl phosphorochloridite (0·2 mole) was added dropwise in 30 min. at 0—5° with cooling and stirring. The mixture was stirred at room temperature for 1 hr., then pyridine hydrochloride (90—95%) was filtered off and washed with benzene (100 ml.). Benzene was removed under reduced pressure and the *anhydrides* were purified by distillation *in vacuo*. They are described in Table 2.

OO-Diethylphosphorous *OO*-dibenzylphosphoric anhydride could not be distilled; when it was heated above 150° violent decomposition was observed.

OO-Diethylphosphorous *OO*-diethylphosphoric anhydride was also prepared as follows. To a suspension of sodium diethyl phosphate (20·3 g.) in benzene (140 ml.) diethyl phosphorochloridite (18·0 g.) was added at 3—5° with cooling and stirring. The mixture was then stirred at 20° for 2 hr. and sodium chloride was removed by use of a centrifuge. After removal of benzene under reduced pressure distillation gave the tetraethyl ester of phosphorous phosphoric anhydride (18·0 g., 57%), b. p. 78—80°/0·05 mm., n_D^{20} 1·4269.

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[12] Toy, *J. Amer. Chem. Soc.*, 1948, **70**, 3882.
[13] Fiszer and Michalski, *Roczniki Chem.*, 1952, **26**, 688.