Reactions of Dialkyl Phosphorobromidates relating to the Reaction of Phosphoryl Bromide with Alcohols and with Trialkyl Phosphates.

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Tributyl phosphite and bromine quickly gave the alkyl bromide and dibutyl phosphorobromidate, which gave alkyl bromide slowly at 15°, quickly at 95°, and by hydrogen bromide was quickly dealkylated to alkyl bromide. Because of the last reaction the bromidate cannot be isolated when the hydrogen phosphite is used with bromine. With (+)-2-octyl compounds, (−)-2-bromo-octane was formed. Neither the dibromidate nor the bromidate (*n*-butyl) could be isolated by the reaction between phosphoryl bromide and the alcohol or trialkyl phosphate.

COMPARED with phosphoryl chloride–alcohol systems (Walczynska, *Roczn. Chem.* 1926, **6**, 110; Gerrard, *J.*, 1940, 1464; 1945, 106; Gerrard, Green, and Nutkins, *J.*, 1952, 4076), phosphoryl bromide systems differ markedly in the lower stability of the dialkyl phosphorobromidate, the quicker dealkylation of the esters by hydrogen bromide, and the greater ease of replacement of the third atom of halogen by alkoxyl in the presence of a tertiary base.

Dibutyl phosphorobromidate, prepared by the reaction (1), gave an almost quantitative yield of 1-bromobutane at 15° (several days) and at 95° (15 min.). The phosphite from

$$\text{(1)} \qquad P(OR)_3 + Br_2 \longrightarrow RBr + (RO)_2P(\!:\!O)Br$$

(+)-octan-2-ol gave (—)-2-bromo-octane by the primary reaction with bromine, and the accompanying bromidate gave also the (—)-halide when heated, there being an inversion of configuration, with little loss in optical activity, in both reactions. Addition of bromine to the phosphite, resulting in the compound $(RO)_3PBr_2$, followed by an intramolecular elimination of alkyl bromide would lead to retention of configuration. The mechanism suggested is therefore (2) (cf. Gerrard and Philip, *Research*, 1948, **1**, 477):

$$\mathrm{(RO)_3P\!:\!\dashrightarrow Br\overset{\curvearrowright}{-}Br} \longrightarrow \mathrm{\bar{B}r\dashrightarrow RO(RO)_2\overset{+}{P}Br} \longrightarrow \mathrm{RBr + (RO)_2P(\colon O)Br} \tag{2}$$

Decomposition of the bromidate could hardly have been intramolecular either, and probably involved a bromide ion formed by a mechanism not yet clear.

From the bromidate, hydrogen bromide readily removed both alkyl groups as alkyl bromide, and because of this the bromidate cannot be isolated by the interaction of bromine and butyl hydrogen phosphite (3); reaction (4) occurs, followed by (5):

$$\mathrm{(RO)_2PH(\colon O) + Br_2} \longrightarrow \mathrm{(RO_2)P(\colon O)Br + HBr} \tag{3}$$

$$\mathrm{(RO)_2P(\colon O)Br + HBr} \longrightarrow \mathrm{RO(OH)P(\colon O)Br + RBr} \tag{4}$$

$$\mathrm{RO(OH)P(\colon O)Br} \longrightarrow \mathrm{RBr} + \text{(a phosphorus compound)} \tag{5}$$

By reactions (3) and (4) di-2-octyl (di-1-methyl-*n*-heptyl) hydrogen phosphite [from (+)-octan-2-ol] gave (−)-2-bromo-octane probably without loss in rotatory power, but there was some loss by reaction (5).

McCombie, Saunders, and Stacey (*J.*, 1945, 380) recommended the hydrogen phosphite instead of the trialkyl phosphite for the preparation of a phosphorochloridate. There is no choice with bromine—the triester must be used. Neither is there a choice with iodine, as McCombie, Saunders, and Stacey (*J.*, 1945, 921) found; and although they attributed lack of success with the hydrogen phosphite to the reduction of diethyl phosphoroiodidate by hydrogen iodide they were aware that the reaction was more complicated than is represented by equation (6). It appears that the dominating process here is dealkylation to ethyl iodide (cf. Gerrard and Whitbread, *J.*, 1952, 914).

$$\mathrm{(EtO)_2P(\colon O)I + HI} \rightleftharpoons \mathrm{(EtO)_2PH(\colon O) + I_2} \tag{6}$$

Attempts to prepare butyl phosphoro-dibromidate and -bromidate by the interaction of tributyl phosphate and phosphoryl bromide were fruitless. Little definite except alkyl bromide could be obtained by the reaction between butan-1-ol (3 mols.) and phosphoryl bromide (1 mol.); but with the latter in equimolecular proportion, the residue, after removal (below 20°) of volatile matter including any unchanged oxybromide, appeared to contain dibromidate as judged from the bromine content. We were unable to study the dealkylation of the dibromidate by hydrogen bromide, but there is evidence (Gerrard and Nutkins, unpublished work) that the dealkylation of pure butyl phosphorodichloridate by hydrogen bromide is much faster than by hydrogen chloride.

In the preparation of a trialkyl phosphate by the reaction of phosphoryl chloride (1 mol.) with an alcohol (3 mols.) in the presence of pyridine (3 mols.) in ether or pentane, base hydrochloride equivalent to 2 atoms of chlorine is quickly formed (cf. Gerrard and Shepherd, *J.*, 1953, 2069), but the third equivalent is only slowly precipitated at 15°, as is clearly shown by using the chloridate (7). On a steam-bath precipitation is complete in 5 hr. With phosphoryl bromide, however, complete precipitation of hydrobromide was quickly achieved at 15°, and so this reagent is useful for the preparation of trialkyl phosphates at room temperature.

$$\mathrm{(RO)_2P(\colon O)Cl + ROH + C_5H_5N} \longrightarrow \mathrm{(RO)_3PO + C_5H_5N,HCl} \tag{7}$$

EXPERIMENTAL

Formation of Dibutyl Phosphorobromidate.—Into tributyl phosphite (41 g.), bromine, in carbon dioxide as carrier gas, was passed until the liquid became red, 26·3 g. being absorbed. At 15°/15 mm. 1-bromobutane (22·4 g.) was removed and trapped at −80°. The yield corresponds with the equation: $\mathrm{(RO)_3P + Br_2 \longrightarrow O\colon PBr(OR)_2 + RBr}$. The residue (44·8 g.) appeared to be a good specimen of *dibutyl phosphorobromidate* (Found: Br, 29·25; P, 11·4. $\mathrm{C_8H_{18}O_3BrP}$ requires Br, 29·3; P, 11·35%). Hydrolysis was conducted in aqueous sodium hydroxide to determine halogen. The bromidate (15·1 g.) decomposed when an attempt was made to distil it at 0·001 mm., and 1-bromobutane (8·1 g.), b. p. 100—101°, was collected in the cold trap; this weight corresponds to the complete removal of all the bromine and one alkyl group. From the bromidate (8·5 g.), after it had been heated on a steam-bath for 15 min., 1-bromobutane (4·0 g.), b. p. 101°, d_4^{25} 1·2684, containing all the bromine originally present, was obtained.

When air was used instead of carbon dioxide as carrier gas, some of the phosphite was oxidised to phosphate.

The bromidate (3·41 g.) was allowed to remain at room temperature for several days, and then 1-bromobutane (1·68 g., 98%), b. p. 101°, d^{25} 1·2684 (Found: Br, 58·3. Calc. for C_4H_9Br: Br, 58·4%), was isolated at 15°/15 mm.

Dealkylation of Dibutyl Phosphorobromidate.—Dry hydrogen bromide was passed into the bromidate (17·1 g.) at −5° for 1 hr., by which time 10·2 g. of the gas had been absorbed. At 15°/15 mm. 1-bromobutane (16·8 g., 98% for 2 alkyl groups), b. p. 101°, d_4^{25} 1·2684, was isolated. Some alkyl bromide was formed when the bromidate was poured on ice or into water, and we ascribe this to dealkylation by hydrogen bromide before it can be dispersed in the water. For this reason it is necessary to hydrolyse the bromidate with aqueous alkali.

Interaction of Bromine and Dibutyl Hydrogen Phosphite.—Bromine vapour in a stream of carbon dioxide was passed into the hydrogen phosphite (6·1 g.) at −5°, but colour appeared immediately, and it was only when the flask was removed from the cooling bath that decoloration quickly occurred. More bromine was admitted at −5°, with the same result. By repeating the operation permanent coloration showing excess of bromine was obtained. Increase in weight was 5·0 g., equiv. to 1 mol. of bromine per mol. of hydrogen phosphite. At 15°/15 mm. 1-bromobutane (4·3 g.), b. p. 101° (Found: Br, 58·2%), was isolated from a residue (6·8 g.) which by hydrolysis with cold alkali was shown to be equivalent to $O{:}PBr(OH)OR$ (Found: Br, 36·8%; equiv., 72·0. $C_4H_{10}O_3BrP$ requires Br, 36·9%; equiv., 72·3). This *butyl hydrogen phosphorobromidate* (6·1 g.), after being at −30° for 40 hr., gave at 15°/15 mm. 1-bromobutane (3·7 g.) which accounts for 96% of the bromine present.

*Interaction of Di-*n*-butyl Phosphorobromidate and Phosphoryl Bromide.*—Phosphoryl bromide (10·8 g., 1 mol.) was mixed with bromidate (9·1 g., 1 mol.). After 4 weeks at 15° only 0·20 mol. of phosphoryl bromide had reacted; but 1·18 mols. of 1-bromobutane had been formed. After 7 weeks the numbers were 0·22 and 1·31, and after 19 weeks 0·23 and 1·44. It therefore appeared that alkyl bromide was formed partly, at least, independently of reaction concerning the oxybromide.

Interaction of Tributyl Phosphate and Phosphoryl Bromide.—Preliminary experiments showed that interaction was slow, and that 1-bromobutane was formed, and an additional amount was formed when the reaction mixture was poured on ice with the purpose of isolating the acid esters. Hydrolysis with sodium hydroxide solution avoided this source of alkyl bromide, and it was shown that in these conditions the already formed alkyl bromide was not affected. Two examples are given of the results when hydrolysis was by ice.

The phosphate (25·7 g., 2 mol.) and phosphoryl bromide (13·55 g., 1 mol.) were mixed, and 3 aliquot portions of the mixture were kept at 15° for respectively 9, 18, and 29 days. The yields of 1-bromobutane (in mols.) were: 2·25, 2·32, and 2·84. The corresponding yields for a different proportion of reagents (phosphate, 12·8 g., 1 mol.; phosphoryl bromide, 27·5 g., 2 mol.) were 1·63, 1·66, and 1·74.

In the following procedure, treatment with water was avoided. After the stated interval, alkyl bromide was isolated at 20°/15 mm. (trap at −80°), and then unchanged phosphoryl bromide was obtained at 20°/0·1 mm. (trap at −80°).

Mol. ratio $(RO)_3PO$: $POBr_3$	2 : 1		1 : 1		0·5 : 1	
RBr and $POBr_3$ (mols.) reacting at 20° in x days:	RBr	$POBr_3$	RBr	$POBr_3$	RBr	$POBr_3$
$x = 3$	0·32	0·32	0·28	0·48	0·25	0·48
6	—	—	—	—	0·48	0·92
9	1·05	0·86	0·89	0·92	0·79	0·96
14	1·52	0·87	1·20	0·96	0·89	0·98
19	1·96	0·88	1·40	0·99	—	—

The specimens of 1-bromobutane were obtained in good purity, *e.g.*, b. p. 100—101°, n_D^{13} 1·443, d_4^{25} 1·2680 (Found: Br, 58·2. Calc. for C_4H_9Br: Br, 58·4%).

Interaction of Phosphoryl Halides and Alcohols in the Presence of Pyridine.—Gerrard and Stranz (unpublished work) found that, when butan-1-ol, pyridine, and phosphoryl chloride are mixed in ethereal solution the replacement of the first chlorine atom by alkoxyl is quick at 15°, replacement of the second is slower, and of the third is very much slower. Thus with the reagents in the ratio $POCl_3 : ROH : C_5H_5N = 1 : 1 : 1$ at a concentration of 0·5 mole/l. with respect to oxychloride, base hydrochloride was almost quantitatively (98%) formed in 6 min., whereas with the ratio 1 : 2 : 2 50% of the total chlorine was replaced in 6 min., and 55% in 1 hr., and with the ratio 1 : 3 : 3 70% of the total was replaced in 6 min., 84% in 12 hr., and 92% in 24 hr. Similarly with the dichloridate (1 mol.), alcohol (2 mol.), and base (2 mol.), 36% of the chlorine was replaced in 6 min., 63% in 2 hr., and 80% in 12 hr.; and with the chloridate (1 mol.), alcohol (1 mol.), and base (1 mol.) 3% of the chlorine was replaced in 6 min., 16% in 1 hr., and 90% in 24 hr.

We now show that for the ratio $ROH : POCl_3 : C_5H_5N = 3 : 1 : 3$, at the same concentration in pentane the chlorine replaced was as follows: at −30°, 0·1 hr. (55%); at 35°, 2·5 hr. (86%); and at 35°, 5 hr. (99%). For *iso*butyl alcohol at 35°, the value after 5 hr. was 98%. When the oxybromide was used in place of the oxychloride with both these alcohols 98% of the bromine was replaced in 0·3 hr. at −30°.

The precipitates were good specimens of the hydrohalide (*e.g.*, Found: Cl, 30·7; C_5H_5N, 68·3. Calc. for C_5H_6NCl: Cl, 30·75; C_5H_5N, 68·4. Found: Br, 49·5; C_5H_5N, 50·1. Calc. for C_5H_6NBr: Br, 50·0; C_5H_5N, 49·4%). From reaction with the oxybromide at −30°, and from reaction with the oxychloride at 35° (5 hr.), tributyl phosphate, b. p. 116—118°/0·1 mm. (Found: P, 11·6. Calc. for $C_{12}H_{27}O_4P$: P, 11·65%), and tri*iso*butyl phosphate, b. p. 116—118°/0·1 mm. (Found: P, 11·6%), were obtained.

Iodine and Triethyl Phosphite or Hydrogen Phosphite.—Iodine (2·54 g., 0·01 mole) and triethyl phosphite (1·67 g., 0·01 mole) were mixed in pentane (McCombie *et al.*, *J.*, 1945, 921, used ether) at 0°. Removal of the solvent at low pressure (trap at −78°) gave two layers, and from the upper one, together with trap contents, ethyl iodide (2·36 g., 50% based on *three* ethyl groups), b. p. 71·8° (Found: I, 81·8. Calc. for C_2H_5I; I, 81·4%), was obtained. When hydrogen iodide was passed into the reaction mixture before distillation, ethyl iodide (8·99 g., 96% based on three alkyl groups in the phosphite, 3·3 g.), b. p. 71·6° (Found: I, 81·3%), was obtained.

Iodine (2·54 g., 0·01 mole) in dry pentane (10 c.c.) was added slowly to diethyl hydrogen phosphite (1·36 g., 0·01 mole) at 0°. The iodine was slowly decolorised, more quickly at 15°, and when half of the iodine had been added a brown oil began to separate. After 12 hr. there was a brown lower layer and a colourless upper solution from which ethyl iodide (1·55 g., 50% based on 2 alkyl groups), b. p. 72° (Found: I, 81·5%), was obtained.

Reaction of Phosphoryl Bromide with Butan-1-*ol*.—The oxybromide (6·5 g., 1·04 mol.) and butan-1-ol (1·6 g., 1 mol.) were mixed in ether (12 c.c.) at 20°. After 2 hr., volatile matter was withdrawn at 20°/14 mm., leaving a residue (6·3 g.) which at 20°/0·1 mm. afforded 1-bromobutane (0·6 g.), b. p. 99—100°, n_D^{20} 1·4400, and a further residue (5·52 g.). At 100°/0·1 mm., the residue gave 1-bromobutane (1·45 g.), b. p. 100°, n_D^{20} 1·4400, and a residue (1·5 g.) (Found: Br, 25·0%). Phosphoryl bromide (1·65 g.) condensed as a white solid in the trap tubes. Therefore the amount which had reacted gave 2·05 g. of alkyl bromide (Calc.: 2·29 g.). With the oxybromide (2·1 g., 0·33 mol.) and alcohol (1 mol.), 1-bromobutane (1·0 g.), and a residue (1·8 g.) (Found: Br, easily hydrolysed, 10·2%) were obtained at 20°/0·1 mm. The residue decomposed on attempted distillation.

Experiments with Optically Active Substances.—The (+)-octan-2-ol (Kenyon, *J.*, 1922, **121**, 2540) used had α_D^{20} +8·0° ($l = 1$). (All rotatory powers are for $l = 1$.) In ether, the alcohol (3 mol.), pyridine (3 mol.), and oxybromide (1 mol.) behaved as did butan-1-ol, quickly affording base hydrobromide (98%) (Found: Br, 49·9; C_5H_5N, 48·6%) and, from the washed and dried solution, a residue (no distillate up to 110°/15 mm.), α_D^{16} +6·9° (Found: P, 6·9. Calc. for $C_{24}H_{51}O_4P$: P, 7·1%). The aqueous washings contained no phosphate ions, and merely a trace of bromide ions. Octan-1-ol (6·5 g. 1 mol.) behaved precisely similarly; the residue weighed 6·35 g. (after being at 140°/15 mm.) (Found: P, 6·9%).

Tri-2-octyl (tri-1-methylheptyl) phosphite (Gerrard, *J.*, 1944, 85) (8·3 g., 1 mol.) was treated with bromine as described. The mixture was added to dilute aqueous sodium hydroxide, and from the dried ethereal extract 2-bromo-octane (3·8 g.), b. p. 67°/9 mm., n_D^{17} 1·4517, α_D^{17} −41·0° (Found: Br, 40·8. Calc. for $C_8H_{17}Br$: Br, 41·4%), was obtained. When the primary mixture was heated on a steam-bath for 0·5 hr. before treatment with alkali, 2-bromo-octane (5·9 g.), b. p. 67°/9 mm., n_D^{17} 1·4520, α_D^{17} −41·2° (Found: Br, 41·0%), was obtained.

Similarly from the hydrogen phosphite (10·0 g.) (Gerrard, *J.*, 1944, 85) and bromine, there was very little hydrogen bromide evolved, and after dry air had been passed for 30 min. the residue (15·95 g.) was divided into two parts, A (7·35 g.) and B (8·60 g.). Part A was added to aqueous sodium carbonate, and from the dried ethereal extract 2-bromo-octane (2·0 g.), b. p. 72°/13 mm., n_D^{17} 1·4510, d_4^{20} 1·0982, α_D^{20} $-40·1°$ (Found: Br, 41·4%), and octene (0·55 g.), trapped at $-80°$ and giving dibromo-octane (0·8 g.), b. p. 109°/13 mm., n_D^{20} 1·4960, were obtained. On acidification, the carbonate solution gave an oil (2·2 g.) (Found: P, 11·65%). Part B was set aside for 96 hr. at 20°, and then treated as for part A. The distillate had a long boiling range, 66—90°/14 mm., α_D^{20} $-33·4°$, d_4^{15} 1·1198, n_D^{20} 1·4535, and after several fractionations 2-bromo-octane (3·17 g.), b. p. 77—80°/18 mm., α_D^{20} $-38·00°$, n_D^{20} 1·4518, was separated. When bromine (5·34 g.) was added dropwise to the hydrogen phosphite (10·0 g.) at 0°, no hydrogen bromide was evolved. Portion A gave similar results, and portion B (7·8 g.) was heated at 100° for 12 min. A solution of sodium carbonate gave with the product an oil (5·95 g.) comprising mainly 2-bromo-octane (4·47 g.), b. p. 74°/14 mm., α_D^{20} $-36·6°$, and dibromo-octane (1·25 g.), b. p. 109—114°/12 mm.

Materials.—Tributyl phosphite and dibutyl phosphite were prepared as described by Gerrard (*J.*, 1940, 1464). Phosphoryl bromide was obtained as a white crystalline substance by interaction of phosphorus pentabromide and *iso*propanol (Gerrard, Nechvatal, and Wyvill, *Chem. and Ind.*, 1947, 437).

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