

Conversion of Alcohols into Alkyl Bromides using Polymer-supported Triphenylphosphine Dibromide and Polymer-supported Triphenylphosphine and Carbon Tetrabromide

Philip Hodge* and Ezzatollah Khoshdel

Department of Chemistry, University of Lancaster, Lancaster LA1 4YA

Alcohols were converted into alkyl bromides by reaction with polymer-supported triphenylphosphine dibromide and with polymer-supported triphenylphosphine and carbon tetrabromide. With both reagents excellent yields of bromides were obtained, but the reactions with the latter reagent were faster and cleaner and in favourable cases high yields of bromide were obtained within 15 min at 20 °C. An advantage of the polymer-supported reagents is that product isolation is facilitated by the ready separation of the supported from the non-supported species.

Triphenylphosphine dibromide (dibromotriphenylphosphorane) is a useful reagent for effecting various transformations.¹ We report the use of the polymer-supported phosphine dibromide (1) and the combination of supported phosphine (2) and carbon tetrabromide to convert alcohols into alkyl bromides. The latter reagent effects this transformation more quickly and cleanly than the former. The supported phosphine dibromide (1) has been used before to cleave ethers,² and to prepare carbodi-imides, ketenimines, and imidoyl bromides,³ but the use of the supported phosphine (2)-carbon tetrabromide reagent is new. Indeed, the combination of phosphine and carbon tetrabromide in general has only been used occasionally.^{4,5} An attractive feature of the polymer-supported reagents is that product isolation is facilitated by the ready separation of the supported from the non-supported species.⁶

The required polymer-supported phosphines (2) were prepared by brominating 1% crosslinked polystyrene beads⁷ then treating the products with lithium and either chlorodiphenylphosphine⁸ or triphenylphosphine⁹ in tetrahydrofuran. Triphenylphosphine is cheaper and more readily handled than chlorodiphenylphosphine but it has not previously been used in the preparation of the phosphine (2). The final products contained 1.25–3.2 mmol of phosphine per g.

The supported phosphine dibromide (1), prepared *in situ* by treating the phosphine (2) with bromine in chloroform, was treated with various alcohols. In most cases (see Table 1) the corresponding bromides were obtained in good yields, but to obtain conveniently short reaction times it was necessary to carry out the reactions at reflux temperature. The product from trinorbornan-*endo*-2-ol is assumed to be the *exo*-isomer, since this substrate reacts with triphenylphosphine dibromide to give trinorbornan-*exo*-2-yl bromide.¹⁰ The reaction of (–)-bornan-2-ol also proceeds with inversion^{5,11} and gives bornan-*exo*-2-yl bromide. The product contained some camphene formed by elimination. The reaction with cinnamyl alcohol produced a complex mixture.

A range of alcohols were then treated with the supported phosphine (2) (2.2 equiv.) and carbon tetrabromide (1.1 equiv.) in chloroform. These reactions (see Table 2) were faster and cleaner than those using reagent (1). Thus, the primary alcohols, including cinnamyl alcohol, generally gave high yields of the bromides within 15 min at 20 °C. This was even the case with the relatively bulky 4,4,4-triphenylbutan-1-ol, despite the fact that substrates need to diffuse into polymer-supported reagents to react.⁶ Trinorbornan-*endo*-2-ol, (–)-bornan-2-ol, and adamantanol required more vigorous conditions but still gave good yields of bromide. As before, the first two of these compounds gave trinorbornan-*exo*-2-yl

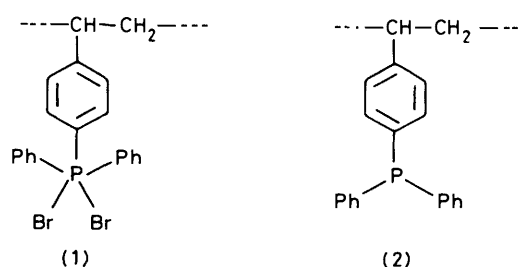


Table 1. Conversion of alcohols into bromides by reaction with polymer-supported triphenylphosphine dibromide in chloroform^a

Substrate	Reaction conditions temp. (°C), time (h)	% Yield of bromide	
		By g.l.c. or ¹ H n.m.r.	Isolated ^b
Octan-1-ol	20, 168	42	—
	61, 3	95	—
3-Phenylpropan-1-ol	61, 1	75	—
	61, 3	—	100
4,4,4-Triphenylbutan-1-ol	61, 2	—	95
Cinnamyl alcohol	61, 3	—	^c
Octan-2-ol	61, 3	—	84
Trinorbornan- <i>endo</i> -2-ol	61, 2	20 ^d	—
(–)-Bornan-2-ol	61, 2	—	59 ^e

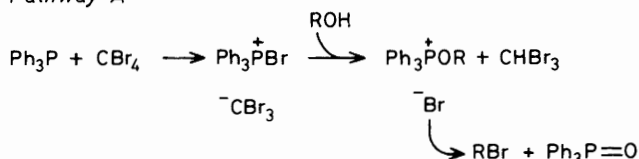
^a See Experimental section for details of a typical reaction procedure.

^b Product with b.p./m.p. in good agreement with literature value and satisfactory i.r. and ¹H n.m.r. spectra. ^c The bromine and phosphine were allowed to react prior to the addition of the substrate, but even so a complex mixture was produced. ^d Norbornan-*exo*-2-yl bromide. ^e Bornan-*exo*-2-yl bromide, plus 7% camphene.

bromide and bornan-*exo*-2-yl bromide, respectively. In view of the mild reaction conditions, the simple isolation procedure, and the excellent yields this is potentially an attractive method for converting small quantities of valuable alcohols into bromides.

Analogy with the phosphine-carbon tetrachloride reagent^{12,13} suggests that the reactions using carbon tetrabromide produce alkyl bromide by the two pathways outlined in the Scheme (for simplicity the reactions shown are also taken to represent the polymer-supported analogues). Pathway A consumes 1 mol of phosphine and produces 1 mol of

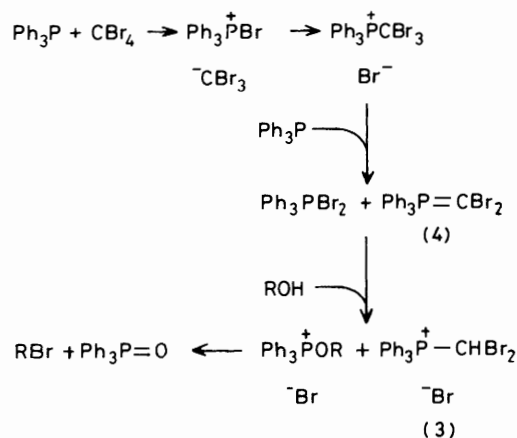
Pathway A



Overall equation:

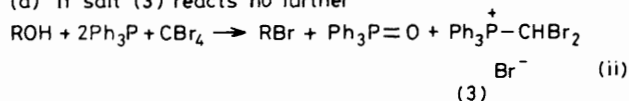


Pathway B

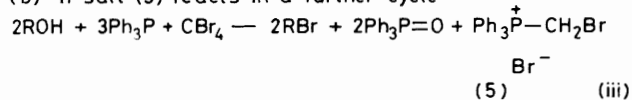


Overall equations:

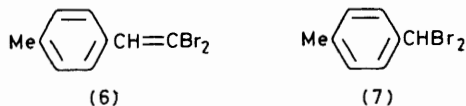
(a) If salt (3) reacts no further



(b) If salt (3) reacts in a further cycle



Scheme.



bromoform for each mol of alkyl bromide produced [see equation (i) in Scheme], whereas pathway B produces no bromoform and consumes between 1.5 and 2.0 mol of phosphine for each mol of alkyl bromide produced, depending on whether the phosphonium salt (3) is the end product or reacts further [see equations (ii) and (iii)].

The results obtained with the supported phosphine-carbon tetrabromide reagent are consistent with such a scheme and with pathway B being the major route. Thus, (a) the reactions produced bromoform (see Table 2) but in amounts ($\leq 30\%$ yields) which suggest pathway A is only a minor route, and (b) reactions using an excess of octan-1-ol consumed 1.4 mol of phosphine for each mol of 1-bromo-octane produced. Further support for pathway B was obtained by using *p*-

tolualdehyde as the substrate.^{14,15} This reacted with the dibromo ylide residues (4) to give the dibromo-olefin (6) (43% yield based on the aldehyde) and with the phosphine dibromide residues (1) to give the *gem*-dibromide (7) (26%).

The effective brominating reagent in pathway B is the supported phosphine dibromide (1). It is not clear why the reactions using the phosphine-carbon tetrabromide reagent are faster than those using reagent (1) alone, but we suggest the polymer-supported analogue of the dibromo ylide (5) assists reaction with the phosphine dibromide by removing the proton from the alcohol. The reactions using the phosphine dibromide (1) are probably less clean because hydrogen bromide is formed.

The spent polymer-supported phosphine dibromide (2) reagent can be regenerated by treatment with trichlorosilane and triethylamine,^{2,3} a reagent that reduces phosphine oxides to phosphines. However, it is expected that the polymer used in the phosphine-carbon tetrabromide reagent could only be regenerated usefully a few times with this reagent because on each cycle a portion of the phosphine residues (1) is converted into the supported analogues of the phosphonium salts (3) and (5).

Experimental

The 1% crosslinked polystyrene was Biobeads SX1 (Biorad, California) in the form of 200–400 mesh beads. Polymers were filtered off using no. 4 grade sintered glass filters and were dried in a vacuum oven (0.1 mmHg) at 50 °C to constant weight. G.l.c. was carried out with a Pye 104 machine (flame ionisation detector) and a 5 ft column containing PEGA, SE30, or Silicone FSI as the stationary phase. Peak areas were determined by triangulation and authentic samples were used to identify peaks and determine response ratios. M.p.s were determined with a Kofler hot-stage apparatus. Unless indicated otherwise ¹H n.m.r. spectra were recorded at 60 MHz for *ca.* 10% solutions in deuteriochloroform containing tetramethylsilane as internal reference.

Crosslinked Polymers with Phosphine Residues (2).—The 1% crosslinked polystyrene beads were brominated using bromine and thallium(III) acetate hydrate in carbon tetrachloride.⁷ In general the products were then treated with lithium and chlorodiphenylphosphine as described by Relles and Schlunz.⁸ By elemental analyses the products contained 2.7 and 3.2 mmol of phosphorus per g.

The phosphination using triphenylphosphine was carried out as follows. A mixture of brominated polystyrene beads (15.0 g; 81 mmol of bromo residues) and triphenylphosphine (42.5 g, 162 mmol) in dry tetrahydrofuran (500 ml) was stirred for 2 h at 20 °C under nitrogen. Lithium (2.5 g in small pieces, 357 mmol) was added and stirring continued for 3 days. The resin was then filtered off and washed successively with methylene chloride-methanol mixtures (2:3, 3:1, then 9:1 v/v) and finally methylene chloride. By elemental analyses the dried product (12.2 g) had P 3.87, Br 0.83%, corresponding to 1.25 mmol of phosphine residues and 0.10 mmol of bromo residues per g.

Preparation of Alkyl Bromides.—All the substrates except 4,4,4-triphenylbutan-1-ol¹⁶ were commercial samples. The reactions were carried out under nitrogen using the quantities of reactants and the reaction conditions indicated in the Tables. The following procedures are typical.

2-Bromo-octane. Bromine in chloroform (4.4 ml; 1M) was added to a vigorously stirred mixture of octan-2-ol (520 mg, 4.0 mmol) and supported phosphine (2) (2.75 g, 8.8 mmol of phosphine) in chloroform (25 ml) at 20 °C under nitrogen.

Table 2. Conversion of alcohols into bromides by reaction with supported phosphine and carbon tetrabromide in chloroform ^a

Substrate	Reaction conditions temp (°C), time	% Yield of bromide		Yield of CHBr ₃ ^c (%)
		By g.l.c. or ¹ H n.m.r.	Isolated ^b	
Octan-1-ol ^d	{ 20, 5 min 20, 20 min	98		10
Benzyl alcohol	20, 5 min	98	80	20
3-Phenylpropan-1-ol	20, 10 min		81	
4-Phenylbutan-1-ol	20, 15 min	98	82	20
4,4,4-Triphenylbutan-1-ol	20, 10 min	95	73	
Undec-10-en-1-ol	20, 5 h		89	
Cinnamyl alcohol	20, 10 min		89	30
Octan-2-ol	{ 20, 10 min 20, 40 min	65		20
Trinorbornan- <i>endo</i> -2-ol	61, 3 h		89 ^e	31
(-)-Bornan-2-ol	{ 20, 16 h 61, 6 h		82 ^{f,g} 71 ^{f,h}	8
Adamantanol	{ 20, 16 h 61, 16 h	50		0
			97	0

^a Reactions used substrate, phosphine, and carbon tetrabromide in the molar ratios 1.0 : 2.2 : 1.1; see Experimental section for full details of a typical reaction. ^b Product with b.p./m.p. in good agreement with literature values and satisfactory i.r. and ¹H n.m.r. spectra. ^c Percentage of the carbon tetrabromide converted into bromoform as determined by g.l.c. ^d A reaction using octan-1-ol, phosphine, and carbon tetrabromide in the molar ratio 1.4 : 1 : 1 carried out at 61 °C for 2 h gave a 52% yield of 1-bromo-octane, indicating that 1.4 mol of phosphine were required for each mol of bromide produced. ^e Trinorbornan-*exo*-2-yl bromide. ^f Bornan-*exo*-2-yl bromide. ^g Plus *ca.* 2% camphene. ^h Plus 17% camphene.

The mixture was heated under reflux for 3 h, then cooled, and the resin was filtered off and washed several times with chloroform. The combined filtrate and washings were concentrated under vacuum and the residue subjected to short-path distillation. This gave 2-bromo-octane (649 mg, 84%), b.p. 86 °C at 20 mmHg (lit.,¹⁷ 83–84 °C at 18 mmHg), with i.r. and ¹H n.m.r. spectra identical with those of an authentic sample.

1-Bromo-4,4,4-triphenylbutane. A mixture of 4,4,4-triphenylbutan-1-ol (302 mg, 1.0 mmol), carbon tetrabromide (365 mg, 1.1 mmol), and supported phosphine (2) (700 mg, 2.2 mmol of phosphine) in chloroform (8 ml) was vigorously stirred at 20 °C under nitrogen for 10 min. The polymer was then filtered off and the product recovered as in the preceding experiment. Recrystallisation of the crude product (355 mg) from hexane gave 1-bromo-4,4,4-triphenylbutane (267 mg, 73%), m.p. 135–136 °C (lit.,¹⁶ 136–137 °C), with i.r. and ¹H n.m.r. spectra identical with those of an authentic sample.

Some reaction products were analysed by g.l.c. or ¹H n.m.r. At the end of the reaction periods the polymers were filtered off and washed several times with chloroform. The filtrate and washings were combined and, when g.l.c. analysis was used, a known weight of β -methyl-naphthalene was added as an internal standard. The yields of alkyl bromide and bromoform were then determined by g.l.c. analysis (PEGA at 160 °C or SE30 at 200 °C).

When ¹H n.m.r. analysis was used the combined filtrate and washings were evaporated to constant weight under vacuum. The ¹H n.m.r. spectrum of the residue was measured and the proportions of bromide and alcohol were determined from the areas of the signals due to the protons on the carbon atom carrying the heteroatom. Where the resolution of these signals was inadequate, Eu(fod)₃ (10 mg, in 0.5 ml of deuteriochloroform) was added to the sample (100 mg in 0.5 ml). This shifted the alcohol signals downfield by *ca.* 0.7 p.p.m. Trinorbornan-*exo*-2-yl bromide had δ 3.88 (1 H, m, CHBr), and 1.0–2.5 (10 H, complex). Bornan-*exo*-2-yl bromide had δ (100 MHz) 0.85, 1.03, and 1.14 (singlets due to three CH₃), 1.0–2.6 (7 H, complex), and 4.12 (1 H, dd, *J* 8.0 and 4.5 Hz, CHBr),

different from that reported for the *endo*-isomer.¹⁸ The spectra of our product and the *endo*-isomer are very similar to those of the corresponding chloro compounds.¹⁹

Reaction of *p*-Tolualdehyde.—A mixture of *p*-tolualdehyde (120 mg, 1.0 mmol), carbon tetrabromide (366 mg, 1.1 mmol), and supported phosphine (2) (700 mg, 2.2 mmol) in chloroform (8 ml) was vigorously stirred at 50 °C under nitrogen for 1 h. The products were isolated in the usual way and the yields of dibromo-olefin (6) (43% yield based on the aldehyde) and *gem*-dibromide (7) (26%) were determined by g.l.c. analysis (Silicone FS1; 140 °C) in comparison with authentic samples.^{15,20}

Acknowledgements

We thank the S.E.R.C. for financial support.

References

- L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967, vol. 1, p. 1247.
- R. Michels and W. Heitz, *Makromol. Chem.*, 1975, **176**, 245.
- A. Akelah and M. El-Borai, *Polymer*, 1980, **21**, 255.
- J. Hooz and S. S. H. Giliani, *Can. J. Chem.*, 1968, **46**, 86.
- R. G. Weiss and E. I. Snyder, *J. Org. Chem.*, 1971, **36**, 403.
- P. Hodge and D. C. Sherrington (eds.), 'Polymer-supported Reactions in Organic Synthesis,' Wiley, London, 1980; A. Akelah and D. C. Sherrington, *Chem. Rev.*, 1981, **81**, 557.
- M. J. Farrall and J. M. J. Fréchet, *J. Org. Chem.*, 1976, **41**, 3877.
- H. M. Relles and R. W. Schluez, *J. Am. Chem. Soc.*, 1974, **96**, 6469.
- R. E. Ireland and D. M. Walba, *Org. Synth.*, 1977, **56**, 44.
- J. P. Schaefer and D. S. Weinberg, *J. Org. Chem.*, 1965, **30**, 2635.
- R. G. Weiss and E. I. Snyder, *Chem. Commun.*, 1968, 1358; *J. Org. Chem.*, 1970, **35**, 1627.
- R. Appel, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 801.
- C. R. Harrison and P. Hodge, *J. Chem. Soc., Chem. Commun.*, 1978, 813; C. R. Harrison, P. Hodge, B. J. Hunt, E. Khoshdel, and G. Richardson, *J. Org. Chem.*, 1983, in the press.

- 14 F. Ramirez, N. B. Desai, and N. McKelvie, *J. Am. Chem. Soc.*, 1962, **84**, 1745.
- 15 H. J. Bestmann and H. Frey, *Justus Liebigs Ann. Chem.*, 1980, 2061.
- 16 W. H. Starnes, *J. Org. Chem.*, 1968, **33**, 2767.
- 17 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965.
- 18 H. Heikman, P. Bäckström, and K. Torssell, *Acta Chem. Scand.*, 1968, **22**, 2034.
- 19 T. J. Flautt and W. F. Erman, *J. Am. Chem. Soc.*, 1963, **85**, 3212.
- 20 G. L. Closs and R. A. Moss, *J. Am. Chem. Soc.*, 1964, **86**, 4042.

Received 9th June 1983; Paper 3/960