Use of Polymeric Phosphine-Halogen Complexes in the Conversion of Epoxides to Halohydrins

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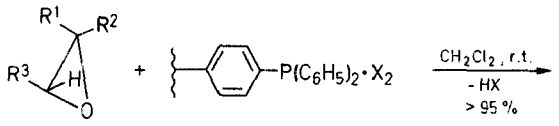
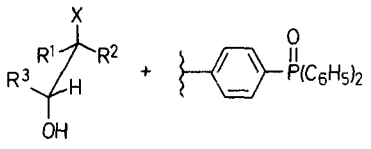
Polystyryldiphenylphosphine-halogen complexes are convenient reagents for converting epoxides to halohydrins under mild and non-acidic conditions. The method requires only a filtration and evaporation process for product isolation.

The reaction of epoxides **1** with triphenylphosphine-halogen complexes in anhydrous dichloromethane at room temperature[1] represents one of the most convenient synthetic methods for clean, fast and quantitative halohydrin **2** formation, under mild and non-acidic conditions. However, considering its utilization in small-scale reactions as well as the synthesis of non-volatile or unstable halohydrins (e.g., those bearing iodine on a tertiary carbon atom[2]), the necessary chromatographic separation of triphenylphosphine oxide, which is formed in the reaction, represents, in fact, a flaw and sometimes a limitation of the method itself[3].

Therefore, we thought to modify our procedure by replacing triphenylphosphine with a polymer-supported triarylphosphine[4] (namely, polystyryldiphenylphosphine[5]) in order to have, at the end of the reaction, a polymer-supported triarylphosphine oxide which could be simply filtered off, thus rendering any chromatographic separations unnecessary for the halohydrin **2** isolation.



1



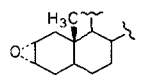
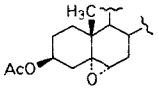
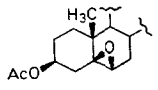
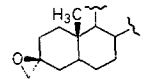
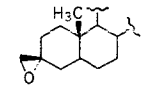
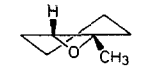
2

X = Cl, Br, J

The preparation of polystyryldiphenylphosphine-halogen complexes is reported in the experimental section together with a general procedure for the halohydrin formation. The results obtained are listed in the Table. Their comparison with the results we had reported previously[1] shows that the oxirane-ring opening remains *regio*- and *stereo*-selective, the yields are still high, unaffected by the cumbersome reagent, somewhat higher in the case of iodohydrins, most probably due to the simplified work-up procedure.

Polystyryldiphenylphosphine-halogen complexes[6] are handy, semi-crystalline solids, which are quite stable at room temperature and are rapidly decomposed by the moisture giving the corresponding phosphine oxide and hydrogen halides. We found that, when dried and kept properly, they can be stored (at least) for weeks at room temperature under an argon atmosphere. Under more critical storage conditions, the observed stability of the complexes was in the order chlorine $\gg$ bromine $>$ iodine complex.

Table. Conversion of Epoxides **1** to Halohydrins **2** using Polystyryldiphenylphosphine-Halogen Complexes

Substrate	X in Complex	Product **2**	Yield [%][a]	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit. data	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
1a 	J	2β-J; 3α-OH; 5α-H	97 (93)	135–136°	132–133°[7]	4.32 (1H, *m*, C3-H); 4.43 (1H, *m*, C2-H)
	Br	2β-Br; 3α-OH; 5α-H	95 (95)	114–116°	115–118°[8]	4.19 (1H, *m*, C3-H); 4.26 (1H, *m*, C2-H)
	Cl	2β-Cl; 3α-OH; 5α-H	96 (94)	122–124°	118–120°[8]	4.05 (1H, *m*, C3-H); 4.11 (1H, *m*, C2-H)
1b 	J	3β-OAc; 5α-OH; 6β-J	95 (90)	145–147°	$C_{29}H_{49}JO_3$ (572.6)	5.05 (1H, *m*, C3-H); 4.16 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
	Br	3β-OAc; 5α-OH; 6β-Br	96 (94)	140–142°	188°[9]	4.00 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
	Cl	3β-OAc; 5α-OH; 6β-Cl	98	180–182°	186–187°[9]	3.75 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
1c 	J	3β-OAc; 5α-J; 6β-OH	95 (93)	–	unstable[2]	4.27 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
	Br	3β-OAc; 5α-Br; 6β-OH	96 (95)	159–161°	177–179°[10]	4.18 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
	Cl	3β-OAc; 5α-Cl; 6β-OH	97	195–197°	198–200°[11]	4.05 (1H, *m*, C6-H, $w\frac{1}{2}$ = 8 Hz)
1d 	J	3β-OH; 3α-CH_2J	95 (90)	82–85°	$C_{28}H_{49}JO$ (528.6)	3.56 (2H, *s*, CH_2J)
	Cl	3β-OH; 3α-CH_2Cl	97 (92)	119–120°	$C_{28}H_{49}ClO$ (437.2)	3.70 (2H, *s*, CH_2Cl)
1e 	J	3α-OH; 3β-CH_2J	94 (88)	108–112°	$C_{28}H_{49}JO$ (528.6)	3.30 (2H, *s*, CH_2J)
1f 	J	1-CH_3; *trans*-1-OH, 2-J	84 (82)	43–44°	44–45°[12]	1.39 (3H, *s*, CH_3); 4.34 (1H, *dd*, C2-H)
		1-CH_3; *trans*-1-J, 2-OH	14 (13)	–	oily acetate[12]	2.00 (3H, *s*, Ac); 1.94 (3H, *s*, CH_3) 5.13 (1H, *dd*, C2-H, $w\frac{1}{2}$ = 11 Hz)
	Br	1-CH_3; *trans*-1-OH, 2-Br	70 (68)	105–108°/12	96–98°/8.5[13]	1.30 (3H, *s*, CH_3); 4.08 (1H, *m*, C2-H)
		1-CH_3; *trans*-1-Br, 2-OH	26 (22)	–	$C_7H_{13}BrO$ (193.1)	
	Cl	1-CH_3; *trans*-1-OH, 2-Cl	53 (50)	70–72°/12	73–75°/15[14]	1.70 (3H, *s*, CH_3); 3.77 (1H, *m*, C2-H)
		1-CH_3; *trans*-1-Cl, 2-OH	45 (42)	–	$C_7H_{13}ClO$ (148.6)	1.24 (3H, *s*, CH_3); 3.80 (1H, *m*, C2-H) 1.50 (3H, *s*, CH_3); 3.75 (1H, *m*, C2-H)

[a] Yield of **2** (purity ≥95%) based on **1**; figure in parenthesis indicates yield reported for reaction of **1** with triphenylphosphine-halogen complex.
[b] Satisfactory microanalyses obtained: C ± 0.57, H ± 0.57.

The advantage of having a reaction which requires only a filtration and evaporation process for product isolation is not diminished by the higher cost of polystyryldiphenylphosphine in comparison with triphenylphosphine, particularly if one considers that the polymeric phosphine oxides can be readily reduced to the phosphine form with trichlorosilane[5].

Further studies in progress in our laboratory are aimed at the investigation of other synthetic applications of polymer-supported triarylphosphine-halogen complexes.

Unless stated otherwise, all reagents were obtained commercially and were used without further purification. Polystyryldiphenyl phosphine was purchased from Fluka AG (Switzerland). Dichloromethane (reagent grade, Carlo Erba) was dried by passage through a short column of alumina.

Polystyryldiphenylphosphine-Halogen Complexes:
To a magnetically stirred suspension of polystyryldiphenylphosphine beads (1.0 g; 3 mmol phosphine units/g) in anhydrous dichloromethane (15 ml) in a 50-ml round bottomed flask equipped with a no-air stopper, at room temperature and under dry argon atmosphere, a 1 molar solution (3 ml) of bromine (or iodine) in the same solvent is added via forced siphon through a stainless steel cannula under a slight argon pressure. (In the case of chlorine, it is expedient to bubble gently the dry, gaseous halogen through the suspension of polymer beads in dichloromethane until the solvent becomes pale yellow.) The halogen is consumed almost immediately and, at the end of the addition, the complex is already formed. It is either used as such in the subsequent epoxide cleavage (see below) or rapidly filtered, washed with dichloromethane, and dried under vacuum at room temperature. Elemental analyses indicated that more than 90% of the calculated phosphine units were halogenated. The three complexes, after three weeks storage under argon at room temperature, gave a neutral reaction when suspended in anhydrous dichloromethane.

Halohydrins 2; General Procedure:
To a magnetically stirred suspension of the appropriate complex (1.4 mmol phosphine-Hal_2 units; prepared *in situ* or stored, as reported above) in anhydrous dichloromethane (15 ml) in a 50-ml round bottomed flask equipped with a no-air stopper, at room temperature and under a dry argon atmosphere, a solution of the epoxide **1** (1.2 mmol) in few ml of the same solvent is added via syringe in one portion. The reaction, monitored by T.L.C. is complete within 10 min. The suspension is then filtered and the resin is washed with moist dichloromethane (3 × 10 ml). The combined filtrate is concentrated by rotary evaporation leaving a residue consisting of the practically pure (T.L.C., ^{1}H-N.M.R.) halohydrin **2**. (Table).

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[1] Palumbo, G., Ferreri, C., Caputo, R. *Tetrahedron Lett.* **1983**, *24*, 1307.
Caputo, R., Chianese, M., Ferreri, C., Palumbo, G. *Tetrahedron Lett.* **1985**, *26*, 2011.
[2] Lack, R.E., Nemorin, J., Ridley, A.B. *J. Chem. Soc. Perkin Trans. 2* **1971**, 629.
[3] Dawe, R.D., Molinski, T.F., Turner, J.V. *Tetrahedron Lett.* **1984**, *25*, 2061.
[4] Heitz, W., Michels, R. *Angew. Chem.* **1972**, *84*, 296; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 298.
Mc Kinley, S.V., Rakshys, Jr., J.V. *J. Chem. Soc. Chem. Commun.* **1972**, 134.
Camps, F., Castells, J., Font, J., Vela, F. *Tetrahedron Lett.* **1971**, 1715.
[5] Regen, S.L., Lee, D.P. *J. Org. Chem.* **1975**, *40*, 1669.
[6] Michels, R., Heitz, W. *Makromol. Chem.* **1975**, *176*, 245.
Relles, H.M., Schluenz, R.W. *J. Am. Chem. Soc.* **1974**, *96*, 6469.
[7] Barton, D.H.R., King, J.F. *J. Chem. Soc.* **1958**, 4398.
[8] Alt, G.H., Barton, D.H.R. *J. Chem. Soc.* **1954**, 4284.
[9] Ueno, Y. *J. Pharm. Soc. (Japan)* **1952**, *72*, 1620.
[10] James, D.R., Shoppee, C.W. *J. Chem. Soc.* **1954**, 4224.
[11] Hattori, Z. *J. Pharm. Soc. (Japan)* **1940**, *60*, 334.
[12] Parrilli, M., Barone, G., Adinolfi, M., Mangoni, L. *Gazz. Chim. Ital.* **1974**, *104*, 835.
[13] Filler, R., Camara, B.R., Naqvi, S.M. *J. Am. Chem. Soc.* **1959**, *81*, 658.
[14] Bartlett, P.D., Rosenwald, R.H. *J. Am. Chem. Soc.* **1934**, *56*, 1990.