Monobromination of Activated Aromatic Compounds with Polyvinylbenzyltriphenylphosphonium Supported Tribromide

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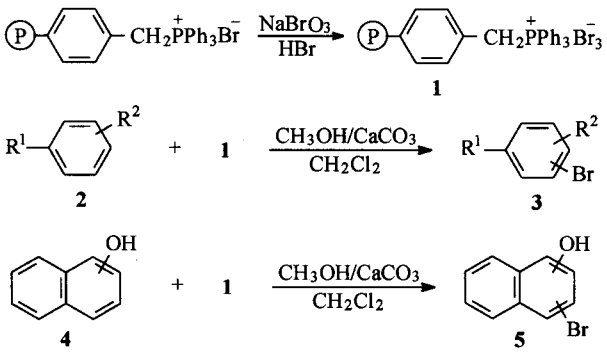
Chloromethylated crosslinked co-polyvinylbenzene-divinylbenzene (2% DVB) was treated with triphenylphosphine and then with sodium bromate and hydrobromic acid to afford red colored insoluble polyvinylbenzyltriphenylphosphonium supported tribromide. This reagent could be used as a mild and efficient monobrominating reagent for activated aromatic compounds such as phenols, aromatic ethers, aromatic amines and acetylanilines with good yields and high *para*-selectivity.

Keywords Polymeric reagent, brominating reagent, polyvinylbenzyltriphenylphosphonium supported tribromide, aromatic compound

Introduction

Electrophilic substitution reactions represent a very important class of reactions for the fuctionalization of aromatic compounds. Among them bromination is frequently involved in modern organic synthesis. The most frequently used brominating reagents are limited to bromine and *N*-bromo compounds.[1] However, it is, in general, difficult to carry out a step-by-step bromination of activated aromatic compounds with them since the reaction proceeds very rapidly and leads to the polybromo-substituted products. To overcome this disadvantage, some quaternary ammonium bromide reagents have been investigated,[2-5] among which the polymer-supported reagents[6,7] are attractive in the application to organic synthesis and received more and more attention, because of their known advantages over monomeric molecules in some cases. Though several polymer-supported reagents have been developed,[8-10] most of them suffered from at least one of the following disadvantages: expensive preparation, instability, long reaction time and large excess amount of reagents being used. Moreover, no bromination of activated aromatic compounds with less reactive polymer-supported reagent has been reported. In connection with our interest in the preparation and applications of polymeric reagents for organic synthesis,[11] we now report the preparation of polyvinylbenzyltriphenylphosphonium supported tribromide (**1**) and its application to the monobromination of aromatic compounds as shown in Scheme 1.

Scheme 1



Results and discussion

Polyvinylbenzyltriphenylphosphonium supported tribromide was prepared by treating chloromethylated co-polyvinylbenzene-divinylbenzene (2% DVB) with sodium bromide and hydrobromic acid in water in place of bromine in carbon tetrachloride. The bromine contents of

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the resin obtained in the two methods, respectively, were almost the same. However, this method proceeded in water, and avoided bromine being directly used. It is more facile and easier to manipulate. This polymeric reagent is in the form of red, remarkable stable and odorless beads, which can be stored at room temperature for long periods without appreciable loss of its activity, and insoluble in almost all solvents.

Bromination of activated aromatic compounds was carried out in mixed solvent methanol-dichloromethane due to two reasons. One is that the presence of methanolmarkedly facilitates the bromination, which can be presumed that active species which generates bromocation was probably methyl hypobromite produced from the reaction of the resin with methanol. The other is that the swelling of the resin in dichloromethane was moderate. Calcium carbonate powder was added to the system of bromination in order to neutralize hydrogen bromide produced.

Bromination of phenols. aromatic ethers, aromatic amines and acetylanilines with polyvinylbenayltriphenyulphosphonium supported tribromide afforded *para*-bromo substituted products with good yield and high regioselectivity (the results were listed in Tables 1,2 and 3, respectively), for steric interactions between substrates and polymer - supported reagents are usually very

Table 1 Monobromination of aromatic ethers with polyvinylbenzyltriphenyl phosphonium supported tribromide

Substrate	R^1	R^2	Product	Time (h)	Yield (%)[a]	^{1}H NMR (δ)
2a	CH_3O	H	*p*-Br	1.5	84	3.58 (s, 3H), 6.91—7.26 (m, 4H)
2b	CH_3O	*o*-CH_3	*p*-Br	1.5	86	2.47(s, 3H), 3.37 (s, 3H), 6.82—7.08 (m, 3H)
2c	C_2H_5O	H	*p*-Br	1.5	82	1.28(t, J=6.7 Hz, 3H), 3.39(q, J=6.7 Hz, 2H), 6.74—7.27 (m, 4H)
2d	C_4H_9O	H	*p*-Br	1.5	81	0.91—1.13 (m, 5H), 1.63—1.74 (m, 2H), 3.38 (q, J=7.2 Hz, 2H), 6.82—7.01 (m, 4H)

[a] Recrystallized with methanol-water: 3/1(V/V).

Table 2 Monobromination of phenols with polyvinylbenzyltriphenylphosphonium supported tribromide

Substrate	R^1 or OH	R^2 or H	Product	Time (h)	Yield (%)[a]	^{1}H NMR (δ)
2e	OH	H	*p*-Br	1.0	75	5.23 (s, 1H) 6.74—7.35 (m, 4H)
2f	OH	*p*-CH_3	*o*-Br	1.0	81	2.16 (s, 3H), 5.15 (s, 1H), 6.82—7.18 (m, 3H)
2g	OH	*o*-CH_3	*p*-Br	1.0	83	2.33 (s, 3H), 6.45—6.78 (m, 3H)
2h[b]	OH	*p*-NO_2	*o*-Br	1.5	72	5.02 (s, 1H), 6.41—8.03 (m, 3H)
2i[b]	OH	*m*-NO_2	*p*-Br	1.5	74	5.44 (s, 1H), 6.92—7.57 (m, 3H)
2j[b]	OH	*o*-NO_2	*p*-Br	1.5	70	5.61 (s, 1H), 6.54—8.35 (m, 3H)
4a	1-OH		4-Br	1.0	84	5.87 (s, 1H), 7.24—7.88 (m, 6H)
4b	2-OH		1-Br	1.0	80	5.04 (s, 1H), 6.62—8.25 (m, 6H)

[a] Recrystallized with methanol-water: 3/1(V/V). [b] Using sodium hydrogen carbonate in place of calcium carbonate in the bromination of nitrophenols.

Table 3 Monobromination of aromatic amines and acetylanilines with polyvinyl-benzyltriphenylphosphonium supported tribromide

Starting Material	R^1	R^2	Product	Time (h)	Yield (%)[a]	^{1}H NMR (δ)
2k	NH_2	H	*p*-Br	1.0	74	4.21 (s, 2H), 6.62—7.25 (m, 4H)
2l	NH_2	*p*-Br	*o*-Br	1.0	81	4.02 (s, 2H), 6.65—7.48 (m, 3H)
2m	NH_2	*p*-Cl	*o*-Br	1.0	80	3.85 (s, 2H), 6.26—7.29 (m, 3H)
2n	NH_2	*p*-NO_2	*o*-Br	1.5	77	3.92 (s, 2H), 6.24—7.81 (m, 3H)
2o	NH_2	*m*-NO_2	*p*-Br	1.5	79	3.85 (s, 2H), 6.66—7.27 (m, 3H)
2p	NH_2	*o*-NO_2	*p*-Br	1.5	81	4.12(s, 2H), 6.25—8.06 (m, 3H)
2q	$(CH_3)_2N$	H	*p*-Br	1.0	83	2.90 (s, 6H), 6.55—7.24 (m, 4H)
2r	PhNH	H	*p*-Br	1.0	82	3.60 (s, 1H), 6.42—6.94 (8H)
2s	N-CH_3-PhN	H	*p*-Br	1.0	85	2.81 (s, 3H), 6.25—6.85 (m, 8H)
2t	CH_3CONH	H	*p*-Br	1.0	78	1.90 (s, 3H), 2.77 (s, 1H), 7.21—7.36 (m, 4H)
2u	CH_3CONH	*o*-CH_3	*p*-Br	1.0	83	2.02 (s, 3H), 2.35 (s, 3H), 2.76 (s, 1H), 7.18—7.52 (m, 3H)

[a] Recrystallized with methanol-water; 3/1(*V*/*V*). [b] A weight of 4 g of polymeric reagent was used.

important factors. When the polymeric reagent was applied to bromination of less activated aromatic molecules such as nitrophenols, sodium hydrogen carbonate was added in the reaction to yield phenoxy anion promoting the bromination. In contrast to the already reported monomeric reagent, polyvinylbenzyltriphosphonium supported tribromide is non-acidic and can be used for bromination of acid sensitive compounds, and also no wetting of dry reagent is needed prior to the reactions.

The polymeric reagent was easily regenerated by simple washing with hydrochloric acid and then aqueous sodium hydroxide followed by reaction with aqueous sodium bromate and hydrobromic acid. It had the same color and physical appearance as the original, and could be used repeatedly five times with the same activity as the original.

Experimental

Melting points were determined on electrothermal melting point apparatus and uncorrected. Elemental analysis was carried out in the PE-2400 elemental analyzer. Bromine content was measured using iodimetry, and chlorine content and phosphorus using oxygen-flask method. All yields refer to isolated products. IR spectra were run on an IR-440 infrared spectrometer. ^{1}H NMR spectra were recorded on an AC-80 spectrometer using TMS as internal standard and $CDCl_3$ as a solvent.

Preparation of chloromethylated co-polyvinylbenzene-divinylbenzene

The procedure[12] for the preparation of this resin was that described previously using zinc chloride as catalyst, chloromethylated co-polyvinylbenzene-divinylbenzene (2% DVB) for chloromethylation at 35—37℃. And the resulting chloromethylated resin was washed with methanol and water, and dried *in vacuo*. 16.3%—17.0% of chlorine were determined.

Preparation of polyvinylbenzyltriphenylphosphonium chloride

It was prepared in literature procedure.[10] 5.2—

5.9% of phosphorus was determined.

Preparation of polyvinylbenzyltriphenylphosphonium supported tribromide

Hydrobromic acid (40%, 30 mL) was added dropwise to polyvinylbenzyltriphenylphosphonium chloride (45 g) and sodium bromate (60 g) in water (60 mL) with stirring at room temperature. The mixture was stirred for additional 6 h. The resulting resin was collected by filtration and washed with water, acetone and dichloromethane, respectively. After drying *in vacuo* at 40℃, red polyvinylbenzyltriphenylphosphonium supported tribromide with 22.1—22.9% of bromine was obtained in 51.3%.

General procedure for bromination of aromatic compounds with polyvinylbenzyl triphenylphosphonium supported tribromide

To a stirring suspension of polyvinylbenzyltriphenylphosphonium supported tribromide (2 g, ca. 5.5 mmol) and calcium carbonate powder or sodium hydrogen carbonate (0.5 g) (as shown in Table 2) in dichloromethane-methanol (*V*/*V*; 3/2, 50 mL) was added substrate (5 mmol) at room temperature until the red color of the resin disappear. The mixture was filtered and then washed with dichloromethane-methanol. Evaporation of the filtration *in vacuo* to remove the solvent gave a residue, which was washed with 5% sodium hydrogen sulfite and extracted with ether. The purification of the product was carried out by column chromatography on silica gel or recrystallization. The reaction conditions and the yields of the monobromination products are summarized in Tables 1—3.

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