Work-Up-Free Deprotection of Borane Complexes of Phosphines, Phosphites, and Phosphinites with Polymer-Supported Amines

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Abstract: Borane complexes of phosphorus compounds, a very common oxidation-free relay for catalytic ligands (phosphines, phosphites, and phosphinites), can be easily deprotected by treatment with polymer-supported piperazine or *N*-methylpiperazine. Deprotection conditions have been optimized for the different types of phosphorus compounds, and the resulting solutions can be used without any intermediate work-up or purification process.

Key words: deprotection, ligands, phosphorus, boron, supported reagents

The design and preparation of functionalized phosphines is an area of great interest mainly due to their application as ligands in transition-metal catalysis.[1] In most cases, however, the use of phosphines is laborious due to the special precautions required in order to avoid their oxidation. In this respect their preparation and manipulation requires strict oxygen exclusion or, alternatively, their protection against oxidation. Phosphine–borane complexes should solve these problems since they are very stable, not sensitive to the usual oxidizing reagents, and can be handled and stored without special requirements.[2] These borane adducts are easily accessible and represent versatile precursors for the synthesis of free phosphines for application in catalysis.[3]

Decomplexation of these adducts must therefore be effected as simply as possible. The first examples of such a process were reported by Imamoto[4] and involved the use of a large excess of diethylamine or morpholine as competitor Lewis bases. Nevertheless, after the results reported by Le Corre[5] the amine most frequently used for this purpose is DABCO, and toluene is commonly chosen as the solvent for this deboronation procedure. Also protic acids such as MsOH, TfOH, and HBF_4 have been efficiently used for deprotecting phosphine–borane complexes.[6]

In all these cases, once the decomplexation is complete either aqueous treatment involving phase-separation or purification by short-path column chromatography is required.[7] If the tendency of the free phosphines to undergo oxidation is considered, it becomes clear that this final treatment is not desirable.

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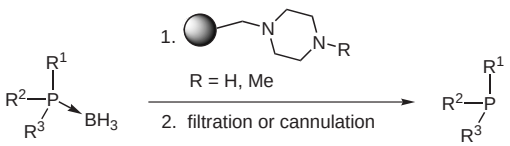
In this paper we report a very efficient and facile new method for the deprotection of organophosphorus–borane complexes using strongly nucleophilic amines anchored to polystyrene resins. From a practical perspective, attaching the amine onto a polymer support offers several advantages over its use in solution. These advantages include the separation of the phosphines from the resin-supported amine–borane complex by a simple filtration or cannulation and the easy recovery and recycling of the deboronation agent.



Scheme 1 Decomplexation of organophosphorus–borane complexes.

According to previously reported results on deboronation and polymer swelling properties, toluene or THF could be suitable solvents for our purposes.[3] Moreover, commercially available piperazinomethyl polystyrene resin **1** [0.80–1.50 mmol/g resin, styrene, 1% divinyl benzene (DVB)] and homemade *N*-methylpiperazine-functionalized polystyrene prepared from a Merrifield resin (final functionalization: 1.93 mmol/g resin; 1% DVB), seemed to be appropriate, as they readily form gels which swell in these solvents. Supporting *N*-methylpiperazine on a Merrifield resin was easily achieved in one step.[8] Determination of the level of functionalization of the final resin

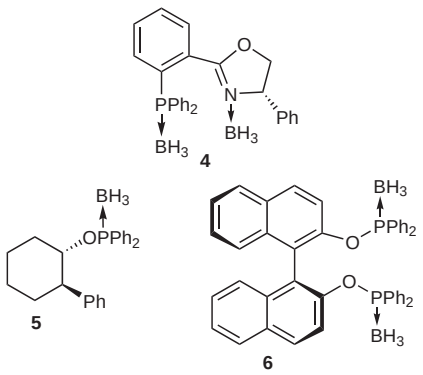


Figure 1 Phosphine–borane and phosphinite–borane complexes synthesized.

2[9] (mmol piperazine groups/g resin) was calculated by a previously reported procedure.[10]

Except for triphenylphosphine borane which was obtained from commercial sources, the phosphite–borane and phosphine–borane complexes were prepared by the reaction of readily available phosphines with BH_3·THF complex (1 M).[11] Thus, treating *S*-(+)-2-[(2-diphenylphosphino)phenyl]-4-phenyl-2-oxazoline with 2.2 equivalents of the borane solution in THF overnight provided, after solvent removal in vacuo, the diborane adduct **4**[12] (Figure 1). On the other hand, the phosphinite–borane complexes **5** and **6** (Figure 1) were prepared from the corresponding alcohols in two steps without isolation of the intermediate phosphinites. Reaction of (+)-(1*S*,2*R*)-2-phenylcyclohexanol in THF with two equivalents of chlorodiphenylphosphine for one hour in the presence of Et_3N and DMAP afforded the desired phosphinite, which was directly treated with BH_3·THF to obtain **5** in 67% total yield.[13] With regard to compound **6**,[14] (*S*)-2,2′-bis(diphenylphosphinooxy)-1,1′-binaphthyl was synthesized from (*S*)-BINOL according to the literature procedure,[15] and

Table 1 Deprotection of Phosphorus–Borane Complexes with Piperazine or *N*-Methylpiperazine Anchored to Polystyrene Resins

Entry	Substrate	δ ($^{31}P\{^1H\}$)[a] ppm	Resin (equiv)	Solvent	Temp (°C)	Time (h)	Conversion (%)[b]	δ ($^{31}P\{^1H\}$)[c] ppm
1	$Ph_3P{\rightarrow}BH_3$	23.9	**1** (4)	THF	reflux	4.5	99	–2.3
2	$Ph_3P{\rightarrow}BH_3$		**1** (2)	THF	60	4.5	95	
3	$Ph_3P{\rightarrow}BH_3$		**1** (2)	toluene	60	4.5	99	
4	$Ph_3P{\rightarrow}BH_3$		**1**[d] (2)	toluene	60	4.5	99	
5	$Ph_3P{\rightarrow}BH_3$		**2** (3)	THF	45	16	93	
6	$Ph_3P{\rightarrow}BH_3$		**2** (4)	THF	reflux	4.5	99	
7	$Ph_3P{\rightarrow}BH_3$		**2** (3)	toluene	60	4.5	88	
8	$Ph_3P{\rightarrow}BH_3$		**2**[d] (4)	toluene	60	4.5	99	
9	$PhMe_2P{\rightarrow}BH_3$	5.9	**1** (2)	toluene	60	17	4	–42.4
10	$PhMe_2P{\rightarrow}BH_3$		**1** (2)	toluene	115[e]	17	68	
11	$Ph_2PCH_2CH_2PPh_2$	21.2	**1** (4)	toluene	60	4	90	–9.5
12	$Ph_2PCH_2CH_2PPh_2$		**1** (5)	toluene	60	6	93	
13	$Ph_2PCH_2CH_2PPh_2$		**1** (5)	toluene	60	16	100	
14	$(PhO)_3P{\rightarrow}BH_3$	110.2	**1** (2)	toluene	60	1.5	100	131
15	$(PhO)_3P{\rightarrow}BH_3$		**1**[d] (2)	toluene	60	1.5	100	
16	(–)-DIOP$\rightarrow BH_3$	17.7	**1** (4)	toluene	60	22	100	–20.3
17	CamPHOS$\rightarrow BH_3$	28.3	**1** (2)	toluene	60	4	99	–6.2
18	PuPHOS$\rightarrow BH_3$	26.5	**1** (2)	toluene	60	2	95	–2.2
19	PuPHOS$\rightarrow BH_3$		**1** (2)	THF	60	4	93	
20	**4**	26.9	**1** (2.5)	THF	60	4.5	100	–2.3
21	**4**		**1** (2.5)	toluene	60	2	98	
22	**4**		**2** (4)	THF	reflux	4.5	100	
23	**4**		**2**[d] (4)	THF	reflux	4.5	100	
24	**5**	105.5	**1** (2)	toluene	reflux	16	99	112
25	**6**	111	**1** (4)	toluene	60	16	99	113.5

[a] $^{31}P\{^1H\}$ NMR spectra were recorded at 162 MHz ($CDCl_3$) for phosphorus–borane complexes.
[b] Determined by integration of the residual borane complex signals and the free phosphorus product signals in the ^1H NMR and ^{31}P NMR spectra of the reaction mixture after filtration and solvent removal.
[c] $^{31}P\{^1H\}$ NMR spectra were recorded at 162 MHz ($CDCl_3$) for free phosphorus compounds.
[d] Experiment performed with a recovered sample of resin.
[e] In a sealed tube.

protected as the diborane complex without further purification (70% total yield).

Triphenylphosphine–borane complex was used to determine the optimal conditions for the removal of the borane group[16] (Table 1, entries 1–8). In general, treatment of the complex with two equivalents of the piperazino resin **1** in THF or toluene for a few hours at 60 °C is sufficient for full deprotection (Table 1, entries 1–3). The lower nucleophilicity of the supported *N*-methylpiperazino moiety requires the use of a higher amount of resin **2**, but the removal of borane could be efficiently performed under the same mild conditions (Table 1, entries 5–7). In addition, it is worth mentioning that the resins could be simply recovered for reuse by treatment with Et_3N followed by washing with THF and drying; no decrease in its performance is observed after using the same sample three times (Table 1, entries 4 and 8).

In the deprotection of dimethylphenylphosphine (Table 1, entries 8 and 9) a longer reaction time and harsher reaction conditions were required. After heating resin **1** in toluene at 115 °C for 17 hours under an argon atmosphere in a sealed tube, the conversion was over 70%. Unfortunately, phosphines with higher basicity like tributylphosphine could not be fully deprotected under these conditions even in the presence of a large excess of amine.

Cleavage of the P–B bond in the dppe–bis(borane) complex was almost complete after stirring with five equivalents of resin **1** in toluene for four to six hours (Table 1, entries 11 and 12); heating for a longer time provided total conversion (Table 1, entry 13).

Functional groups like acetals or thioacetals were tolerated by this mild deprotection method. Thus, (–)-DIOP and chiral phosphines CamPHOS and PuPHOS were easily recovered from their borane complexes[17] (Table 1, entries 16–19). The bis(borane) complex **4** was also fully deprotected in a few hours using polymer-supported piperazine (2.2 equiv) or *N*-methylpiperazine (4 equiv) as the nucleophile under the same reaction conditions (Table 1, entries 20–22). Recovered resin **2** also provided total conversion (Table 1, entry 23).

This deprotection procedure is also suitable for phosphinite and phosphite–borane complexes. Triphenylphosphite was quantitatively obtained after heating with resin **1** in toluene for 1.5 hours (Table 1, entry 14). As expected, reusing the same resin sample for the deprotection leads to no decrease in its efficiency (Table 1, entry 15).

Longer reaction times were required to achieve complete deboronation in the decomplexation of the phosphinite–boranes **5** and **6** (Table 1, entries 24 and 25).

In summary, we have developed a straightforward procedure for the in situ deprotection of borane complexes of different types of phosphorus compounds by simple treatment with resin-supported piperazines. The phosphine solutions resulting from this protocol can be directly used in a catalytic application without any manipulation or, if desired, through simple cannulation to a different flask under an inert atmosphere. We think that this most practical method can greatly facilitate the manipulations required to convert pre-catalyst into active catalytic species in many different types of processes.

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(8) Anchoring *N*-Methylpiperazine onto a Merrifield Resin: The amine (1 mmol) was added to a mixture of (chloromethyl)polystyrene (10 mmol) and Cs_2CO_3 (2.5 mmol) in DMF (10 mL). The mixture was heated for 24 h at 50 °C. After cooling the suspension was filtered and the resin was washed with DMF (4 × 10 mL), H_2O (4 × 10 mL), H_2O–MeOH (1:1; 2 × 10 mL), MeOH (4 × 10 mL), toluene (4 × 10 mL), and CH_2Cl_2 (4 × 10 mL). The solid was dried in vacuo for 24 h at 40 °C to constant weight.

(9) Resin **2** (1% DVB, f_{max} = 2.15) from (chloromethyl)polystyrene (1% DVB, f_o = 2.0–2.5 mmol/g). ^{13}C gel-phase NMR (100 MHz, $CDCl_3$): δ = 40.6, 46.1, 52.9, 55.2, 62.8, 127.7. Anal. Found: N, 5.41; C, 84.82; H, 10.47; *f* = 1.93 mmol/g.

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(12) (*S*)-2-[2-(Diphenylphosphino)phenyl]-4-phenyl-4,5-dihydrooxazole Diborane Complex (**4**): White solid; yield: 98%; mp 95–96 °C; $[\alpha]_D^{27}$ +26.6 (*c* 1.00, $CHCl_3$). IR (ATR): 3064, 2966, 2864, 2385–2262, 1650, 1478, 1434, 1387, 1321, 1168, 1062, 928, 742, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.95–1.98 (br s, 6 H), 3.86 (dd, *J* = 10.5, 9.3 Hz, 1 H), 4.17 (dd, *J* = 9.2, 6.7 Hz, 1 H), 4.58 (dd, *J* = 11.0, 6.7 Hz, 1 H), 7.18–7.21 (m, 2 H), 7.32–7.68 (m, 12 H), 7.70–7.76 (m, 2 H), 7.78–7.86 (m, 2 H), 7.94–7.99 (m, 1 H). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 26.9 (br m). ^{11}B NMR (128 MHz, $CDCl_3$): δ = –36.5 (br m, PBH_3), –19.42

(br s, NBH_3). HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{28}B_2NOPNa$ (M + Na): 458.1992; found: 458.2012.

(13) Diphenyl[(1*S*,2*R*)-2-phenylcyclohexyloxy]phosphine–Borane Complex (**5**): $[\alpha]_D^{27}$ +87.9 (*c* 0.70, CH_2Cl_2). IR (ATR): 3057, 3027, 2931, 2856, 2378, 1739, 1600, 1492, 1437, 1361, 1114, 1063, 1014, 975, 737, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.55–1.65 (br m, 3 H), 1.20–1.71 (m, 4 H), 1.68–1.83 (m, 2 H), 1.88–1.97 (m, 1 H), 2.13–2.25 (m, 1 H), 2.74 (ddd, *J* = 12.4, 10.5, 3.8 Hz, 1 H), 4.57–4.66 (m, 1 H), 6.78–6.83 (m, 2 H), 7.04–7.09 (m, 2 H), 7.14–7.28 (m, 6 H), 7.38–7.51 (m, 3 H), 7.64–7.70 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.8, 25.7, 34.3, 34.9, 52.0 (d, *J* = 6.4 Hz), 82.2 (d, *J* = 2.5 Hz), 126.5, 127.9, 128.0, 128.3, 128.4, 130.7, 130.8, 131.3, 131.4, 131.5 (d, *J* = 2.9 Hz), 133.6, 143.5. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 105.5 (br m). ^{11}B NMR (128 MHz, $CDCl_3$): δ = –39.7 (m, BH_3). HRMS (ESI+): *m*/*z* calcd for $C_{24}H_{28}BOPNa$ (M + Na): 397.1869; found: 397.1886.

(14) (*S*)-2,2′-Bis(diphenylphosphinooxy)-1,1′-binaphthyl–Diborane Complex (**6**): White solid; mp 190–191 °C; $[\alpha]_D^{26}$ –2.5 (*c* 0.83, THF). IR (ATR): 3051, 2372, 2333, 1585, 1500, 1455, 1227, 1114, 975, 830, 730, 664 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.7–1.6 (br s, 3 H), 6.96–7.02 (m, 4 H), 7.05–7.15 (m, 6 H), 7.16–7.27 (m, 8 H), 7.30–7.41 (m, 4 H), 7.42–7.52 (m, 4 H), 7.55 (d, *J* = 8.9 Hz, 2 H), 7.81 (t, *J* = 9.6 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 120.3 (d, *J* = 4.0 Hz), 122.8 (d, *J* = 5.1 Hz), 125.2, 126.4, 127.0, 127.9, 128.2 (d, *J* = 10.5 Hz), 128.7 (d, *J* = 10.5 Hz), 129.6, 130.7, 131.0 (d, *J* = 4.4 Hz), 131.1 (d, *J* = 4.4 Hz), 131.7 (d, *J* = 2.0 Hz), 131.8 (d, *J* = 2.0 Hz), 131.9, 132.5, 133.7, 148.7 (d, *J* = 4.2 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 111 (br m). ^{11}B NMR (128 MHz, $CDCl_3$): δ = –39 (m, BH_3). HRMS (ESI+): *m*/*z* calcd for $C_{44}H_{38}B_2O_2P_2Na$ (M + Na): 705.2459; found: 705.2431.

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(16) P–B Bond Cleavage; General Procedure: A solution of the phosphorus–borane complex (0.025 mmol) in anhyd toluene (0.5 mL) was added to a smoothly stirred suspension of the resin (see Table 1, *f* = 1.93–0.86 mmol/g) in anhyd toluene (1 mL) placed in a schlenk tube under an argon atmosphere at 60 °C. The mixture was heated at 60–63 °C to complete deprotection (see Table 1) and then the solution was filtered under an argon atmosphere and the resin was washed with toluene (2 × 1 mL). Removal of the solvent in vacuo provided the pure phosphorus compound without further purification.

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