A Novel Mild Deprotection Method for Phosphine–Boranes

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Treatment of phosphine–boranes with molecular sieves 4Å in a mixture of an ethereal solvent and an alcohol provided deprotected free phosphines in quantitative yields. The phosphines can be obtained by a simple filtration/crystallization procedure in most cases. It should be noted that the current method is successfully applied to the deprotection of a phosphite–borane for the first time.

Phosphines are now widely used as ligands for transition metal catalysts. They are often air-sensitive and get oxidized easily, with a few exceptions such as triarylphosphines. The complex formation of phosphines with borane,[1] keeping the lone pair of the phosphorus atom from further reactions such as oxidation, is a powerful method for the protection of phosphines. The air-stability of phosphine–boranes facilitates the purification process and makes them storable for a long time. In addition, phosphine–boranes are easily accessible from phosphine oxides or substituted chlorophosphines by the reaction with borane, without isolating the intermediate phosphines. Thus, phosphine–boranes are known as one of the key intermediates for the preparation of new phosphines for catalysis.[2,3]

For the deprotection of phosphine–boranes to generate the desired free phosphines, several methods have been developed. The use of an excess amount of either secondary amines, such as diethylamine or morpholine,[3] or tertiary amines, such as DABCO or triethylamine[4] is one of the most common procedures for this purpose. Generally, treatment for a few hours at 40 °C in toluene completes the reaction. The P–B bond of phosphinite–boranes was also quantitatively cleaved.[5] Deprotection using strong protic acids, such as CH_3SO_3H, CF_3SO_3H, and HBF_4, is an alternative choice, especially in the case of electron-rich phosphines.[6]

Here we report a novel and mild deprotection process of phosphine–boranes; that is, the reaction of phosphine–boranes with molecular sieves 4Å (MS4A) in a mixture of an ethereal solvent and an alcohol. The phosphines can be obtained by a simple filtration/crystallization procedure in most cases. It should be noted that the current method is successfully applied to the deprotection of a phosphite–borane for the first time.

The deprotection of phosphine–boranes **1** was carried out as follows. The starting materials, phosphine–boranes **1**, were prepared by the reaction of readily available phosphines with $BH_3(SMe_2)$. A solution of phosphine–borane **1** in a protic solvent was allowed to react with activated MS4A at 25–115 °C (depending on the substituents at phosphorus) for over 22 h. After removal of MS4A by filtration, evaporation of solvents in vacuo afforded the deprotected phosphine in its pure form. The optimized conditions and results are summarized in Table 1. The characteristic features are; (1) The existence of molecular sieves was essential for the reaction. In its absence a highly unselective product formation was observed. For example, when entry 2 was run without molecular sieves, no phosphine **2b** but 3% of the corresponding phosphine oxide and 75% of unidentified products were detected by $^{31}P\{^1H\}$ NMR spectroscopy. (2) The existence of a protic solvent was also essential for the reaction. For example, the use of only THF instead of THF/MeOH for the experiment of entry 1 resulted in 1.5% conversion of **1a** to give the corresponding phosphine and phosphine oxide in 1% and 0.5% yields, respectively. (3) The deprotection proceeded without inversion of the chirogenic phosphorus atom (entry 8),[3] if the reaction temperature did not exceed 70 °C. (4) Functional groups like acetals (entry 7) and hydroxy groups (entry 8) were tolerated by this mild deprotection method. (5) By lowering the reaction temperature to 25 °C, deprotection of a phosphite–borane was successfully achieved for the first time (entry 9). No substituent scrambling was observed in this case, when the bulky *t*-BuOH was used instead of methanol.

Because addition of alcohol is essential for the deprotection, it seems that the reaction involves the formation of boron alkoxide accompanied by the molecular hydrogen production. Either or both of the Lewis acidic and basic sites of the aluminum/silicon oxide of molecular sieves likely catalyzed the process.

Experimental

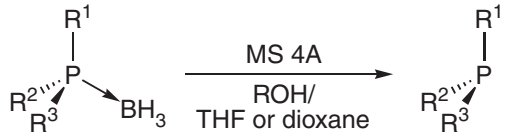
Preparation of Phosphine–Boranes. The phosphine–boranes **1** except for **1h** were prepared from commercially available phosphines according to the literature.[7] Chiral phosphine **1h** was prepared from $PhMe_2P(BH_3)$ according to a literature method.[8]

Activation of Molecular Sieves 4Å. Molecular sieves (MS) with a cavity of 4 Å were heated up to 250 °C under vacuum for several minutes and then purged with argon. Subsequently, the MS were ground up to homogeneously pulverize the catalyst. Finally the powder was then heated again to 250 °C under vacuum for several minutes, flushed with argon and this procedure was repeated several times.

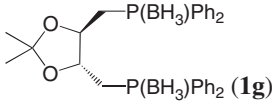
Deprotection of Phosphine–Boranes. Method A: In a common Schlenk tube was added to the activated molecular sieves 4Å (500 mg) a mixture of the ethereal solvent (THF or dioxane) (7 mL) and MeOH (3 mL). To this suspension was added the phosphine–boranes (0.3 mmol), and the mixture was stirred under argon at atmospheric pressure. Filtration through a pad of Celite under argon, rinsing with THF and removal of the solvents in vacuo provided pure phosphines, without further purification (phosphines **2a**, **2c–f**, **2i**). Recrystallization was necessary to further purify the products: **2a** and **2g** from MeOH/AcOEt (5:95); **2i** from

Published on the web October 9, 2004; DOI 10.1246/bcsj.77.1931

Table 1. Deprotection of Phosphine–Boranes into Free Phosphines



1 **2**

Entry	Substrate **1**	Method[a)]	Solvent	Temp./°C	Time/h	Yield/%
1	$Ph_3P\rightarrow BH_3$ (**1a**)	A	THF/MeOH	reflux	106	100
2	$(c\text{-}C_6H_{11})_3P\rightarrow BH_3$ (**1b**)	B	Dioxane/MeOH	115	42	92
3	$(n\text{-}C_4H_9)_3P\rightarrow BH_3$ (**1c**)	B	Dioxane/MeOH	115	28	100
4	$PhMe_2P\rightarrow BH_3$ (**1d**)	B	THF/MeOH	100	22	100
5	$Ph_2P(=O)CH_2P(BH_3)Ph_2$ (**1e**)	A	THF/MeOH	reflux	22	99
6	$(o\text{-MeO–}C_6H_4)P(BH_3)Ph_2$ (**1f**)	B	THF/MeOH	68	70	96
7	 (**1g**)	A	THF/MeOH	75	22	86[b)]
8	$(S)\text{-}Ph_2C(OH)CH_2PMePh(BH_3)$ (**1h**)	B	THF/MeOH	70	30	94[b)]
9	$(PhO)_3P\rightarrow BH_3$ (**1i**)	A	THF/*t*-BuOH	25	72	100

a) Method A: The reaction was carried out under an atmosphere of argon. Method B: Further care to avoid air oxidation was executed and the reaction was carried out in a closed system under argon pressure. b) No loss of chirality was confirmed by chiral HPLC analysis (Daicel Chiracel OD).

MeOH/AcOEt (20:80).

Method B: In order to avoid the phosphine oxidation by trace amounts of oxygen, the same procedure as method A was employed except that the filled reaction flask was purged with 2 atm of argon, then tightly closed by a stopcock and heated under pressure at the desired reaction temperature.

We thank the Ministry of Education, Culture, Sports, Science and Technology, for the Grant-in-Aid for COE Research on Elements Science, No. 12CE2005.

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