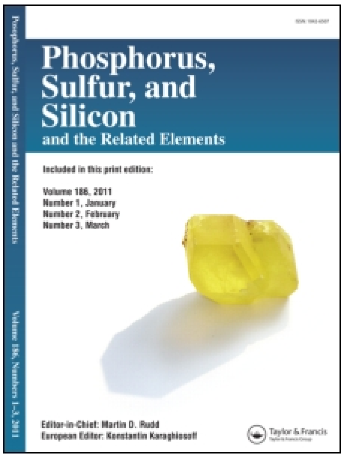

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# DEPROTECTION TECHNIQUES FOR PHOSPHINE-BORANE COMPLEXES: METHODS AND EXTRACTION COEFFICIENTS

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*Triarylphosphine-, diarylalkylphosphine-, and trialkylphosphine-borane complexes were deprotected using various amines and acids. After deprotection, the resulting borane species were extracted from the free phosphines using various solvent systems. The aqueous layers were analyzed for borane making use of inductively coupled plasma optical emission spectroscopy; and extraction coefficients were then calculated from the analytical data.*

*Keywords:* Deprotection; extraction coefficients; phosphine-borane

## INTRODUCTION

The design and preparation of functionalized phosphines is an area of great importance in chemistry. One of the major applications of functionalized phosphines is their use as ligands for transition metal catalysts. The fine tuning of phosphine ligands is often crucial to the selectivity and success of catalyzed reactions.[1] Phosphines also play an important role in radiopharmaceuticals[2] and in membrane chemistry.[3]

Functionalized phosphines are often oxygen sensitive and the borane moiety can be used as an effective protecting group during their syntheses.[4] The stability of the phosphine-borane complexes towards a variety of reaction conditions, (including harsh acidic/oxidizing conditions),[5] makes the borane a very versatile protecting reagent. Borane is used not only as a protecting group but also can be used to

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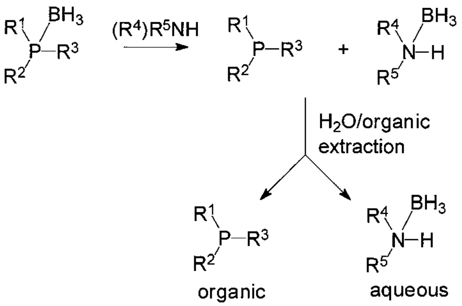
activate the phosphorus towards certain reagents, and has thus played a definitive role in the preparation of a variety of chiral phosphines.[6–9] The synthesis of phosphine-borane complexes has been well described and they can either be prepared by reacting the free phosphine with $BH_3$-THF or from the phosphine oxide using $LiAlH_4/NaBH_4/CeCl_3$.[4] Various reagents have been employed for the subsequent deprotection step, most frequently secondary amines such as diethylamine,[4] morpholine,[4] pyrolidine,[10] and DABCO.[11] Acids such as $CH_3SO_3H$ or $CF_3SO_3H$ also have been used for deprotecting phosphine-borane complexes.[12]

In line with our interest in the preparation of highly functionalized phosphines as ligands for transition metal catalyst systems, we have prepared a range of novel functionalized phosphines.* The intermediates were protected against oxidation early on in the synthetic sequences, as their corresponding borane complexes. The phosphines were to be used as ligands for transition metal catalyzed reactions, for instance in the palladium catalyzed Heck reaction. In order to achieve palladium-ligand complexation, the P—B—bond was cleaved using diethylamine,[4] after which various Pd(II) salts were added respectively. The amine-borane complex, however, acted as a reducing agent in all cases, and caused the Pd(II) compound to be reduced to Pd(0) metal which precipitated from the reaction mixture. It was therefore necessary to rid the phosphines altogether of the borane before the introduction of the metal catalyst. This was very effectively accomplished by a phase extraction (Scheme 1). In this report, we wish to describe the deprotection of phosphines using a small variety of amines and acids. The borane species were extracted from the organic layer with water, after which the aqueous layers were analysed using inductively coupled plasma optical emission spectroscopy (ICP-OES), and the extraction coefficients (D) were determined by calculation.



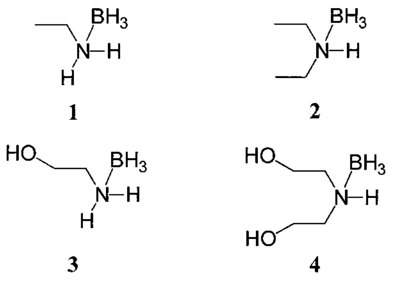
SCHEME 1

## RESULTS AND DISCUSSION

Three representative phosphine-borane complexes were used for the current study: triphenylphosphine-borane, butyldiphenylphosphine-borane, and tributylphosphine-borane, with their basicity increasing along the series. Some nucleophilic amines were used to test the efficiency of the deprotection step and the efficiency of the subsequent extraction of the corresponding borane complexes into water from a variety of organic solvents. For these reactions, ethylamine, diethylamine, monoethanolamine, diethanolamine, and tetrabutylammonium cyanide were used respectively.

In general, triphenylphosphine (lowest basicity) readily was deprotected using only two equivalents of the mentioned amines in THF under reflux. In the deprotection of butyldiphenylphosphine, longer reaction times and 4–5 equivalents of the amine were required. Tributylphosphine (highest basicity) could not be fully deprotected, even in the presence of a large excess of amine, emphasizing one of the limitations of using a THF-amine system: Very basic phosphines cannot be fully deprotected in a mixture of THF and amine. This type of phosphine-borane complex can, however, be deprotected using the neat amine as solvent. For example, the use of neat morpholine,[7] and diethylamine[4] has been reported for such deprotection reactions. We found that these borane complexes could be deprotected under acidic conditions in dichloromethane, using $CH_3SO_3H$ or $CF_3SO_3H$.[12]

The borane species **1–5**, resulting from the deprotection reactions (Figure 1), were extracted into the aqueous layers, which were analyzed for boron via ICP-OES. The extraction coefficients were then calculated from the analytical data and are given in Table I. In all



$Bu_4N[BH_3(CN)]$

**5**

**FIGURE 1** Amine-Borane complexes.

**TABLE I** Extraction Coefficients D

| | Organic phases employed | | |
|---|---|---|---|
| Amine-borane | DCM | EtOAc | EtOAc/Hexane 1:1 |
| 1 | 1.63 | 1.48 | 2.15 |
| 2 | 0.02 | 0.03 | 0.05 |
| 3 | 2.97 | 1.34 | 8.93 |
| 4 | 4.16 | 0.88 | 7.37 |
| 5 | 5.62 | 1.40 | 38.86 |

instances, recovery of the phosphine was greater than 90% (auto oxidation of electron rich phosphines was sometimes a problem, necessitating manipulations under argon).

From Table I it can be seen that extractions from EtOAc/hexane as the organic phase gave the best D-values, followed by DCM. Tetrabutylammonium cyanide was the deprotecting agent that offered the best extraction coefficient. However, this reagent required longer reaction times than most of the amines to effect complete deprotection. Diethylamine-borane dissolved the best in the organic phases, leading to concomitantly low D-values.

## CONCLUSION

To our knowledge, this was the first time that monoethanolamine, diethanolamine, and tetrabutylammonium cyanide were successfully used as deprotecting reagents for a variety of phosphine-borane species. Due to the low $pK_a$ value of tributylphosphine, harsher acidic conditions or neat amine were required to effect complete deprotection. By the judicious selection of amine and solvent system, the borane species effectively can be removed from the free phosphine with phase extractions, allowing the use of higher oxidation state metals (e.g., $Pd^{2+}$) in complexation reactions.

## EXPERIMENTAL

Deprotection reactions were carried out by dissolving the phosphine-borane complex in dry THF (0.035 mmol/mL) and adding the amine (2–6 equivalents) to the solution. The reaction mixture was heated under reflux until full conversion was observed (TLC-monitoring). The THF was then removed under reduced pressure after which the crude reaction mixture was extracted using the appropriate organic solvent

**TABLE II** Optimized ICP-OES Conditions

| | |
|---|---|
| Analytical wavelength | 208.959 nm |
| Viewing height | 6 mm |
| Search window | 0.027 nm |
| Filter | 1 |
| Order | 3 |
| Photomultiplier voltage | 650 kV |
| Power | 1.3 kW |
| Plasma gas flow rate | 15 L/min |
| Auxiliary gas flow rate | 1.5 L/min |
| Peristaltic pump speed | 15 rpm |
| Nebulizer pressure | 150 kPa |

and water (see Table I). The aqueous layers were then analysed for boron using ICP-OES, as described below.

A Varian Liberty 110 ICP-OES spectrometer with an inert V-groove nebulizer was used for boron determinations in the aqueous phase after extraction. The relatively high organic content of the aqueous phase in some instances necessitated a modification of standard plasma conditions to prevent plasma quenching. The optimized ICP-OES conditions for boron determinations in these matrices are listed in Table II. Increasing the plasma power and reducing the rate of nebulization afforded the desired stabilisation of the plasma. Boron standards (1, 20, and 50 $\mu$g/mL) were prepared from a 1000 $\mu$g/mL disodium tetraborate stock solution by appropriate dilution.

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[*] Syntheses to be reported elsewhere.