ORGANIC LETTERS

2003
Vol. 5, No. 13
2347−2349

Alkylation of Phosphine Boranes by Phase-Transfer Catalysis

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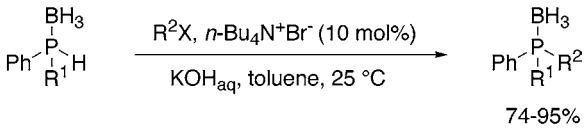
Received April 29, 2003

ABSTRACT



The alkylation of phosphine boranes with various electrophiles proceeds with good to excellent yields in a biphasic solution in the presence of tetrabutylammonium bromide as a phase-transfer catalyst.

The preeminence of phosphines as ligands in transition-metal chemistry[1] and as chiral controllers in asymmetric processes[2] is now well-recognized. Recently, phosphine synthesis has been extremely simplified by their protection as phosphine borane complexes, which are inert toward moisture and air.[3] A variety of diversified phosphines have been synthesized through the alkylation of phosphine−borane complexes.[4] The preparation of enantiomerically enriched *P*-chiral phosphines by using such a strategy has also been reported.[5−7] Although very effective, these methods necessitate stoichiometric amounts of a strong base, such as the butyllithium−sparteine complex to deprotonate the phosphine borane complex. The development of a catalytic enantioselective synthesis of *P*-chiral phosphines that involve mild bases is still a highly challenging task. In this paper, we present the alkylation of phosphine boranes by phase-transfer catalysis that proceeds under mild conditions with aqueous potassium hydroxide as a base. This method constitutes a powerful means to access various disubstituted and trisubstituted phosphines in high yields. The use of a chiral phase-transfer catalyst allows the preparation of enantioenriched *P*-chiral phosphines, albeit with low enantiomeric excess.

Many advantages are associated with phase-transfer catalysis methods, including mild reaction conditions, the simplicity of the reaction procedure, as well as the use of inexpensive and environmentally friendly reagents.[8] Although the alkylation of phosphine boranes with potassium hydroxide in methanol was previously known,[4] their reactivity and stability under phase-transfer reaction conditions were never tested before. The synthesis of achiral and racemic trisubstituted phosphine borane complexes was first investigated (Table 1).

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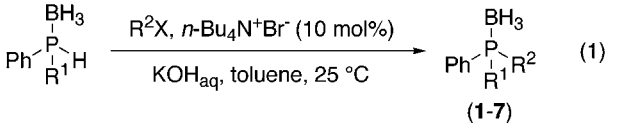
10.1021/ol0347139 CCC: $25.00
Published on Web 06/03/2003

Table 1. Alkylation of Disubstituted Phosphine Boranes under Phase-Transfer Catalysis (eq 1)[a]

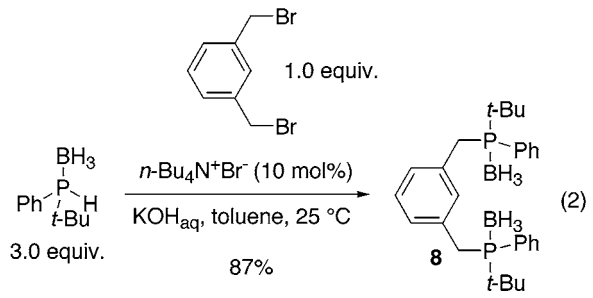


entry	R^1	R^2X	yield[b] (%)
1	Ph	MeI	88 (**1**)
2	Ph	BnBr	85 (**2**)
3	Ph	*i*-PrBr	82 (**3**)
4	*t*-Bu	MeI	88 (**4**)
5	*t*-Bu	allylBr	81 (**5**)
6	*t*-Bu	BnBr	95 (**6**)
7	*t*-Bu	1-naphthylCH_2Br	85 (**7**)
8	*t*-Bu	*i*-PrBr	NR

[a] Conditions: R^2X (1.1 equiv), *n*-Bu_4NBr (0.1 equiv). [b] Isolated yield.

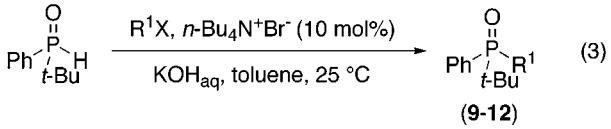
When a solution of *tert*-butylphenylphosphine borane in toluene was treated with 30% aqueous potassium hydroxide and benzyl bromide, no conversion was observed. Conversely, the desired phosphine borane complex **6** was isolated in 95% yield after 1 h, when 10 mol % of tetrabutylammonium bromide was added to the reaction mixture (entry 6). Other primary alkyl bromides were also reacted to produce a variety of trisubstituted phosphine borane complexes with excellent yields using the same catalyst (entries 1−7). The alkylation of diphenylphosphine borane with secondary alkyl bromides, such as 2-propyl bromide, proceeds equally well, although a longer reaction time is required (24 h) (entry 3). However, no reaction was observed with the more sterically encumbered *tert*-butylphenylphosphine borane and 2-propyl bromide (entry 8).

Polydentate phosphines are successful phosphine ligands for many organometallic complexes.[9] Among them, phosphorus−carbon−phosphorus (PCP) tridentate ligands have attracted considerable attention.[10] Double alkylation of the 2,6-bis(bromomethyl)benzene with a slight excess of *tert*-butylphenylphosphine borane in toluene and 30% aqueous potassium hydroxide in the presence of 10 mol % of tetrabutylammonium bromide produced the desired PCP phosphine **8** in 87% yield (eq 2). In comparison, the same alkylation under standard conditions using *n*-butyllithium produced the desired bisphosphine **8** in only 35% yield.[11]



We were delighted to find that the alkylation of phosphine oxides proceeds as well under similar phase-transfer reaction conditions (Table 2). High yields of trisubstituted phosphine

Table 2. Alkylation of Disubstituted Phosphine Oxides under Phase-Transfer Catalysis (eq 3)[a]



entry	R^1X	yield[b] (%)
1	MeI	84 (**9**)
2	allylBr	77 (**10**)
3	BnBr	92 (**11**)
4	1-naphthylCH_2Br	70 (**12**)

[a] Conditions: R^2X (1.1 equiv), *n*-Bu_4NBr (0.1 equiv). [b] Isolated yield.

oxides could be achieved using various electrophiles. Here again, the *tert*-butylphenylphosphine oxide is too hindered to be alkylated with secondary alkyl bromides, such as 2-propyl bromide.

A more challenging reaction is the monoalkylation of monosubstituted phosphine borane complexes. It is now required to control the stoichiometry of the base as only 1 equiv is necessary, instead of using an excess of base as in the previous cases. Indeed, the alkylation of phenylphosphine borane with 1 equiv of potassium hydroxide, 10 mol % of tetrabutylammonium bromide, and various alkyl halides in a mixture of toluene and water led to the exclusive formation of the corresponding disubstituted phosphine borane in good to excellent yields (Table 3). Up to 90% isolated yield could be obtained with primary alkyl halides (entries 1−4), whereas the alkylation of 2-propyl bromide, a secondary alkyl bromide, proceeds in 75% yield (entry 5). This approach allows the synthesis of a variety of chiral racemic disubstituted phosphine boranes that are not easily prepared using other strategies.[12]

Several chiral phase-transfer catalysts have been described and were found to be particularly useful in the enantioselective synthesis of α-amino acids.[13,14] *Cinchona* alkaloid ammonium salts were shown to be quite impressive at catalyzing various reactions with high enantioselectivities. The alkylation of *tert*-butylphenylphosphine borane with several electrophiles in the presence of a variety of chiral

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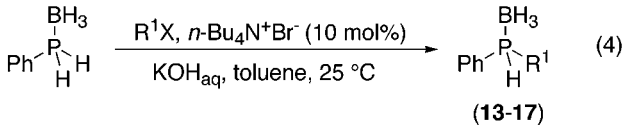
Table 3. Monoalkylation of Substituted Phosphine Boranes under Phase-Transfer Catalysis (eq 4)[a]



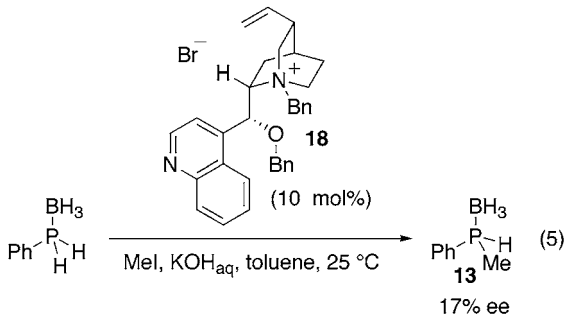
(4)

(**13**-**17**)

entry	R^1X	yield[b] (%)
1	MeI	90 (**13**)
2	EtI	85 (**14**)
3	BnBr	81 (**15**)
4	allylBr	79 (**16**)
5	*i*-Pr	75 (**17**)

[a] Conditions: R^2X (1.0 equiv), *n*-Bu_4NBr (0.1 equiv), KOH (1.0 equiv). [b] Isolated yield.

phase-transfer catalysts leads to the formation of a racemic mixture of the corresponding chiral trisubstituted phosphine borane. On the other hand, low enantioselectivities were observed in the monoalkylation of phenylphosphine borane with methyl iodide in the presence of *Cinchona* alkaloid-derived catalyst **18** (eq 5).



(5)

Surprisingly, in both cases, the reaction was accelerated by the presence of the chiral catalyst as the reaction proceeded in 15 min compared to more than 1 h with the achiral version. The catalysts might be dissociated or not involved in the alkylation step accounting for the lack of enantioselectivity.[15]

In summary, we have described a versatile synthesis of some useful substituted phosphine boranes using phase-transfer catalysts. We have shown that phosphine boranes were alkylated very efficiently in the presence of tetrabutylammonium bromide. In addition, a selective monoalkylation was observed in the case of the alkylation of monosubstituted phosphine boranes. As a result, this method provides a new strategy for the preparation of chiral, racemic phosphine borane complexes. Furthermore, low enantioselectivity could be achieved when using a chiral phase-transfer catalyst and the development of a more efficient asymmetric version is still under investigation.

Acknowledgment. This research was supported by NSERC (Canada), F.C.A.R (Québec), the Canadian Foundation for Innovation, and the Université de Montréal.

Supporting Information Available: Experimental procedures, compound characterization data, and ^1H and ^{13}C spectra of all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) We do not think that the racemization of the product under the reaction conditions could explain the low enantiomeric excess, as the same enantioselectivities were observed when the reaction was run in the presence of 0.5 equiv of the base for less than 5 min.