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Lithiated *Bis*(diethylamino)phosphine Borane Complex as Useful Nucleophilic Phosphorus Reagent

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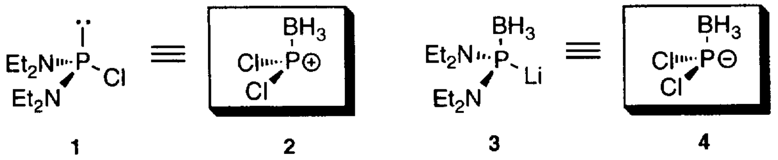
Abstract: *The reaction of bis(diethylamino)chlorophosphine borane complex with lithium naphthalenide affords the lithiated derivative 3 which undergoes nucleophilic substitution with primary and secondary alkyl halides, allylic and benzylic bromides and aryl iodides or bromides in good yields. The substitution of the diethylamino group via intermediate dichloroorganophosphine derivatives furnishes polyfunctional phosphines.*

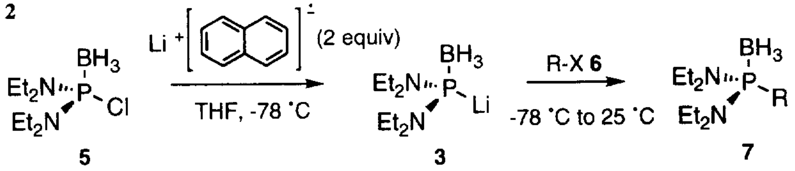
Catalysis of reactions by metal complexes has become a major field of research in the last decades.[1] Since many transition metal catalysts contain phosphine ligands, general methods for the preparation of structurally diverse phosphines are especially important.[2] Recently, we have reported that aminochlorophosphines like Et_2NPCl_2 or $(Et_2N)_2PCl$ (**1**) are excellent electrophilic phosphorus reagents toward zinc organometallics allowing the preparation of a range of polyfunctional chlorophosphines. The chlorophosphine **1** is a versatile synthetic equivalent of the phosphorus synthon **2** since the amino groups can be readily replaced by chlorides.[3]

Scheme 1



Herein, we wish to report the preparation and reactivity of the lithiated diaminophosphine borane complex **3** and show that this reagent is a versatile synthetic equivalent of the nucleophilic[4] phosphorus synthon **4** (Scheme 1). Thus the treatment of the *bis*(diethylamino)chlorophosphine borane complex **5** with lithium naphthalenide[4] (2 equiv) in THF (-78 °C, 10 min) furnishes an orange solution of the lithiated diaminophosphine borane complex **3**.

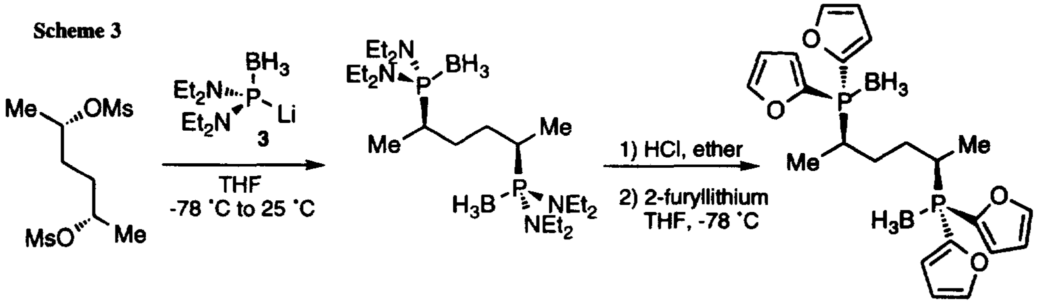
Scheme 2



R = prim, sec alkyl, allyl, benzyl, aryl

The treatment of **3** with various organic halides **6** furnishes *bis*(diethylamino)organophosphine borane complexes **7** in good yields (Scheme 2 and Table 1). The reactions are usually complete after warming up to 0 °C or 25 °C (2 h). The substitution proceeds well with primary alkyl iodides like octyl iodide **6a** or 1,4-diiodobutane **6b** (entries 1 and 2 of Table 1). By using the *trans*-1,2-diiodomethylcyclohexane **6c**,[5] the substitution reaction with **3** provides the C_2-symmetrical diphosphine borane complex **7c**. Other functional groups like an ester or a bromide are well tolerated in these nucleophilic substitution reactions (entries 4, 6 and 9). Benzylic and allylic bromides react smoothly with **3**, furnishing the expected benzylic and allylic phosphines **7e**, **7f** and **7i** (entries 5, 6 and 9). In the case of ethyl (α-bromomethyl)acrylate **6j** a double substitution occurs leading to the 1,3-diphosphine **7i** in 61 % isolated yield (entry 9). Substitution reaction at secondary sp^3-centers proceeds well with iodides and mesylates. Thus the (*S,S*)-dimesylate **8** prepared from commercially available (*S,S*)-2,5-hexanediol reacts readily with **3** providing the 1,4-diphosphine derivative **9** in 60 % yield. The treatment of **9** with HCl in ether[6] furnishes an intermediate tetrachlorophosphine which was directly treated with 2-furyllithium (-78 °C to 25°C, 4 h) giving the new C_2-symmetrical diphosphine **10** in 49 % yield[7] (Scheme 3). This reaction demonstrates that the aminophosphines of type **7** can be converted into triorganophosphines showing the broad synthetic scope of this reaction.

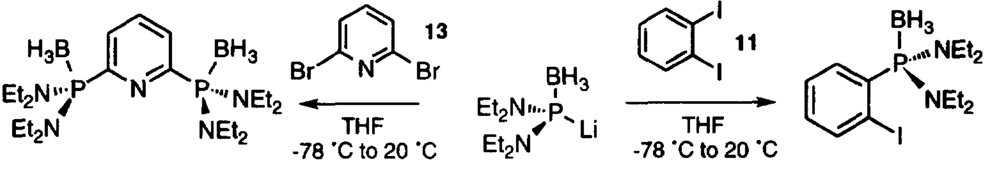
Scheme 3



8 **9**: 60 % **10**: 49 %

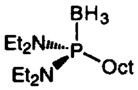
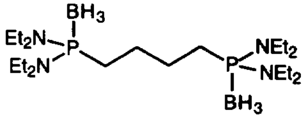
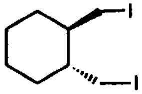
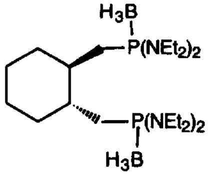
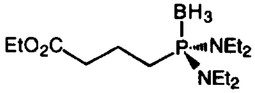
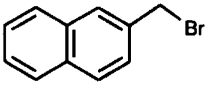
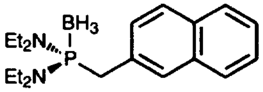
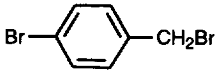
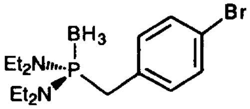
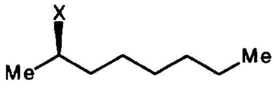
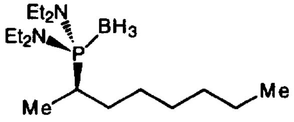
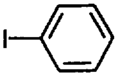
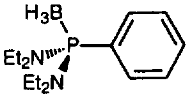
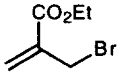
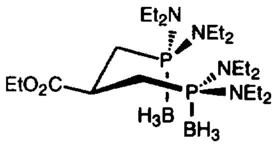
Interestingly, the substitution reaction with **3** is also possible with aryl iodides and bromides *in the absence of any palladium and nickel catalyst.*[8] Thus the cross-coupling of iodobenzene with **3** furnishes the diaminophenylphosphine borane complex **7h** in 63 % yield (entry 8). Under these conditions, 1,2-diiodobenzene **11** reacts selectively with **3** leading to the monosubstituted iodoarylphosphine **12** in 66 % yield. An heteroaryl dibromide like **13** reacts also well with the lithiated phosphine derivative **3** leading to the N,P,P-mixed chelating ligand **14** in 54 % yield (Scheme 4). The excellent reactivity of **3** toward aryl iodides and bromides supports an electron-transfer mechanism[9] for this cross-coupling reaction.

Scheme 4



14: 54 % **3** **12**: 66 %

Table 1. Polyfunctional phosphine borane complexes **7a-i** obtained by the nucleophilic substitution of organic halides or mesylates **6a-j** with the lithiated aminophosphine borane complex **3**.

Entry	Electrophile RX	Product of type **7**	Yield (%)[a]
1	Oct-I **6a**	 **7a**	80
2	I-(CH$_2$)$_4$-I **6b**	 **7b**	80
3	 **6c**	 **7c**	70
4	 **6d**	 **7d**	62[b]
5	 **6e**	 **7e**	63
6	 **6f**	 **7f**	58
7	 **6g**: X = I **6h**: X = OMs	 **7g**	76(82)[c]
8	 **6i**	 **7h**	63
9	 **6j**	 **7i**	61[b]

[a] Isolated yields of analytically pure products. [b] The reaction mixture was only warmed up to -30 °C. [c] The yield in parenthesis is obtained using the mesylate **6h**.

In summary, we have reported the preparation of a new versatile phosphorus reagent **3** and have shown its high nucleophilicity allowing the performance of substitution with primary and secondary alkyl iodides, benzylic and allylic bromides and aryl iodides or bromides.[10] The amino groups of the substitution products **7** can be subsequently replaced via the corresponding dichlorophosphine with organic groups leading potentially to a broad range of phosphines. Extensions of this methodology and applications to the preparation of chiral phosphines are currently underway in our laboratory.

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7. Treatment of a *meso-d,l* mixture of **8** with **3** furnishes a diastereomeric mixture of products. Comparison of the ^{13}C NMR spectra of this product mixture with the spectrum of *(R,R)*-**9** shows that the stereochemical purity of **9** is greater than 99 %. See also: Brunner, H.; Terfort, A. *Tetrahedron: Asymmetry* **1995**, *6*, 919.
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10. *Typical procedure:* Preparation of 1,4-*bis*(diethylaminophosphino)butane (**7b**). *Bis*(diethylamino)chlorophosphine **1** (1.68 g, 8 mmol) in THF (4 mL) was cooled to 0 °C and borane methyl sulfide (8 mL, 1M solution in CH_2Cl_2) was added. The reaction mixture was stirred 4 h at rt and the solvent was removed by vacuum affording the pure *bis*(diethylamino)chlorophosphine borane complex **5**. This crude material was diluted in THF (8 mL) and was added slowly to lithium naphthalenide prepared from naphthalene (2.04 g, 16 mol), cut lithium wire (110 mg, 16 mmol) at -78 °C. After 10 min of stirring, 1,4-diiodobutane (620 mg, 2.0 mmol) was added. The reaction mixture was stirred for 2 h at 78 °C. After usual workup and purification by flash chromatography (hexanes, then hexanes:ether 50:1), the desired diphosphine borane complex **7b** was obtained as white crystals (690 mg, 1.60 mmol, 80 % yield; mp 80 °C).

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