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An Efficient Procedure for the Synthesis of Electron Rich Bisphosphines Containing Homochiral Backbones.

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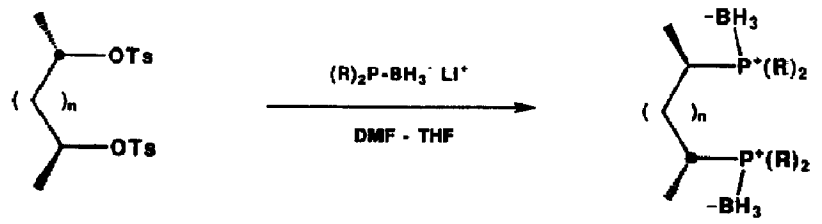
Abstract: **An eminently practical method for the synthesis of homochiral bisphosphines is described. This procedure entails the sequential reaction of homochiral ditosylate with the appropriate dialkylphosphine-borane anion followed by BH_3 decomplexation mediated by HBF_4·OMe_2.**

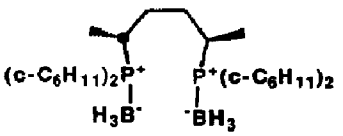
Bisphosphines containing homochiral backbone linkages constitute the largest family of ligands which have found utility for transition metal based asymmetric catalysis.[2] The most common procedure that has been utilized for the synthesis of these phosphines involves the alkylation of diaryl or dialkyl metallophosphides with the appropriate homochiral ditosylate (or dihalide).[3] For reactions involving the very basic lithium derivatives of sterically hindered dialkylphosphides, poor yields of the desired bisphosphine have typically been obtained as a consequence of competing side reactions (e.g., base mediated elimination, electron transfer processes, etc.).[4] In these instances, the desired mode of nucleophilic substitution could only be achieved by using a homochiral *difluoride* as the substrate.[5] As part of a seminal investigation, Imamoto has noted the mildly basic characteristics of diarylphosphine-borane anions.[6] It is therefore surprising that the use of the corresponding *dialkyl*phosphine-borane anions for the synthesis of electron rich homochiral bisphosphines has not been reported.[7a] In this communication we describe the use of a variety of phosphine-borane anions in a convenient procedure for the preparation of several new ligand types. The general synthetic protocol entails deprotonation of the requisite monophosphine-borane adduct[6b] (*n*-BuLi, THF, −78 °C) followed by the addition of a DMF solution of the homochiral ditosylate of interest (−50 °C) and subsequent stirring at ambient temperature until bis-alkylation has been achieved (Scheme 1).[8,9] A series of *new* bisphosphine-borane complexes that have been synthesized in this way appears in Table I. The preparative generality of the above procedure can be inferred from the high yields obtained for the α,α'-branched cyclohexyl bearing bisphosphine-boranes 2a and 2d as well as for the sterically congested bis(diarylphosphine-borane) analog 2c.



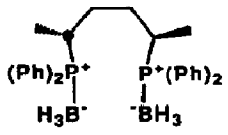
1 2

Scheme 1

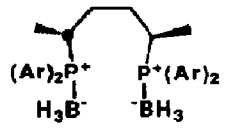
Table I. Synthesis of Representative Bisphosphine-boranes via Nucleophilic Displacement with Phosphine-borane Anions.



2a (86 %)

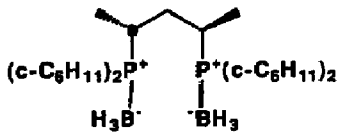


2b (88 %)

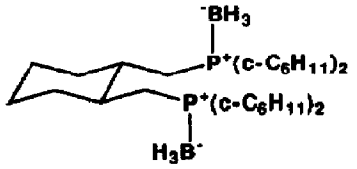


2c (82 %)

[Ar = 2-CH3-4-(CH3O)C6H3]



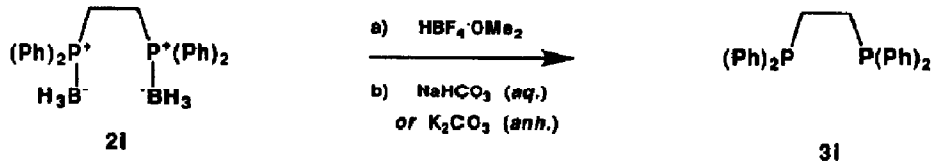
2d (91 %)



2e (89 %)

The reported procedures for converting phosphine-boranes to the corresponding free phosphines involve heating the parent complexes with a *large excess* of a secondary amine (e.g., morpholine or diethyl amine)[6b] or DABCO.[7b] Although **2b** could be converted to bisphosphine **3b** by either of the published procedures, the bisborane complexes **2a**, **2d** and **2e** proved remarkably resistant toward amine mediated BH_3 exchange. Even at elevated temperatures (e.g., 100 °C), these complexes were incompletely converted to the corresponding bisphosphines. Presumably, the enhanced strength of the P-B bond in borane complexes of *electron rich* phosphines is responsible for the observed lethargy of **2a**, **2d** and **2e** toward aminolysis. In light of this apparent limitation, we set out to develop an alternative and *complementary* method for phosphine-borane decomplexation. Imamoto has reported that representative sulfonic acids react with phosphine-boranes in aprotic media to provide the corresponding borane sulfonate derivatives.[6a] In a preliminary study to determine if this type of

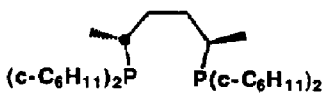
reaction could serve as a basis for phosphine deprotection, DPPE·$(BH_3)_2$ (2i) was treated with a variety of acids (i.e., CH_3SO_3H, CF_3SO_3H, etc., CH_2Cl_2, −5 °C → 25 °C) and subsequently hydrolyzed [$NaHCO_3$ *aq.*, 0 °C (10 min under Ar) *or* K_2CO_3 *anh.*, 25° C (6.5 h under Ar)]. A rough measure of the efficiency of decomplexation was obtained by TLC analyses of reaction aliquats. This procedure readily revealed the stepwise conversion of 2i to DPPE (3i) (Scheme 2).[10] Of the various acids that were examined, commercial HBF_4·OMe_2 proved the most efficacious in terms of rate as well as isolated yield of free phosphine. Although reaction conditions custom tailored to a given phosphine-borane could be readily derived, the *standard* conditions that were used for *all* of the examples described here involve treatment with HBF_4·OMe_2 [(5 equiv/P·BH_3 moiety), CH_2Cl_2, −5 °C → 25 °C, 12 h] followed by hydrolysis ($NaHCO_3$ *aq.*, 0 °C). The results obtained for the decomplexation of a range of phosphine-boranes are illustrated in Table II.



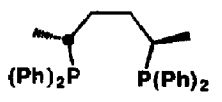
2i 3i

Scheme 2

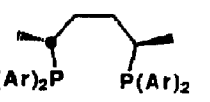
Table II. HBF_4·OMe_2 Mediated Decomplexation of Representative Bisphosphine-boranes.



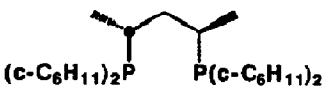
3a (91 %)



3b (99 %)

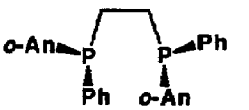


3c (96 %)
[Ar = 2-CH3-4-(CH3O)C6H3]

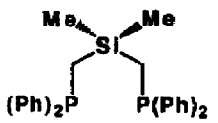


3d (91 %)

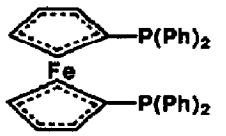
3e (97 %)



3f (98 %)



3g (89 %)



3h (94 %)

3i (92 %)

As is evident from the examples presented above, the $HBF_4 \cdot OMe_2$ decomplexation procedure can facilitate rapid access to certain *electron rich* homochiral bisphosphines that are otherwise very difficult to prepare. In addition, the conditions for decomplexation are sufficiently mild to permit the survival of the C-Si and ferrocenyl linkages of ligands **3g** and **3h**.[11] The efficient phosphine decomplexation procedure described here, in combination with the generalized protocol for the synthesis of homochiral bisphosphine-boranes, should facilitate access to a wide variety of new phosphines for catalyst development. The results of our continuing studies in this area will be described in upcoming accounts from these laboratories.

Acknowledgements. Generous support for this research by grants from the National Institutes of Health and the National Science Foundation is gratefully acknowledged.

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4. In selected instances, elimination has been minimized by the use of cyclic sulfates as substrates in displacement reactions which employ an *unhindered* lithium phosphide as a nucleophile: Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518.
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7. a) During the course of this work a single example was reported in which the lithium derivative of *diphenyl*phosphine-borane was used to synthesize DIOP.[7b] b) Brisset, H.; Gourdel, Y.; Pellon, P.; Le Corre, M. *Tetrahedron Lett.* **1993**, *34*, 4523.
8. Diastereomeric purity for **2a-e** was inferred by high field ^1H and ^{13}C NMR analysis which indicated the absence of *meso* isomers. In addition, **2a-e** were homogeneous by HPLC and GLC.
9. All new compounds were fully characterized by ^1H, ^{13}C and ^{31}P NMR , IR and possessed satisfactory combustion analyses or exact mass.
10. A transient compound [presumably the monoborane complex DPPE·(BH_3) (**4**)] was observed at intermediate stages of the reaction. An authentic sample of **4** was prepared (albeit with poor selectivity) by the exposure of **3i** (1.2 equiv) to $BH_3 \cdot SMe_2$ (1.0 equiv) followed by chromatographic purification.
11. In contrast, the 1,3-dioxolane linkage present within the bisborane derivative of DIOP was degraded under the prescribed set of reaction conditions.

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