

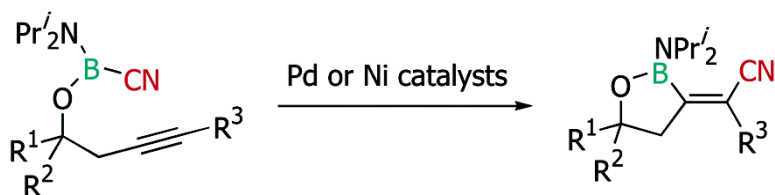
Communication

**Palladium- and Nickel-Catalyzed Intramolecular Cyanoboration of Alkynes**

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*J. Am. Chem. Soc.*, **2003**, 125 (21), 6358-6359 • DOI: 10.1021/ja0349195 • Publication Date (Web): 30 April 2003

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## Palladium- and Nickel-Catalyzed Intramolecular Cyanoboration of Alkynes

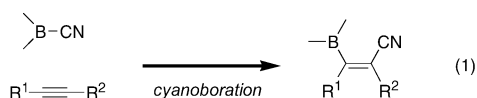
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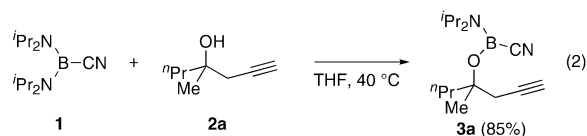
Transition metal-catalyzed  $\sigma$ -bond additions across carbon-carbon multiple bonds have attracted much attention in synthetic organic chemistry, because such reactions can provide efficient routes for the synthesis of highly functionalized molecules from simple starting materials.<sup>1,2</sup> In particular, additions of silicon- and boron-containing  $\sigma$ -bonds have been investigated extensively in recent years, following the growing recognition of the utility of isolable organometallic products as synthetic intermediates.<sup>3,4</sup> Further development of new addition reactions following this line of inquiry is, therefore, highly desirable.

Recently, we reported on an efficient Strecker-type aminative cyanation of carbonyl compounds using bis(dialkylamino)cyanoboranes.<sup>5</sup> This study showed for the first time the synthetic utility of cyanoboranes as a nucleophilic cyanation reagent. In the course of our research program, we became interested in the application of cyanoboranes to the transition-metal-catalyzed cyanoboration of carbon-carbon multiple bonds.<sup>6</sup> Although some related addition reactions of the cyano-containing  $\sigma$ -bond are known,<sup>7-10</sup> cyanoboration is highly attractive in that two synthetically valuable functionalities, that is, boryl and cyano groups, can be introduced in a regio- and stereoselective fashion and thus produce useful synthetic intermediates (eq 1). In this Communication, we report



on the first cyanoboration reaction, which is catalyzed by palladium and nickel complexes.

Our initial attempt at carrying out the intermolecular reaction of bis(dialkylamino)cyanoboranes with phenylacetylene in the presence of a palladium catalyst failed. We then turned our attention to an intramolecular variant by using homopropargylic cyanoboryl ethers. The requisite cyanoboryl ether **3a** was readily prepared by the reaction of homopropargylic tertiary alcohol **2a** with diaminocyanoborane **1** in a high yield (eq 2).<sup>11</sup> It is interesting to note that



the selective substitution of one of the two amino groups by the alcohol took place without any loss of the cyano group from the boron atom.

With the cyanoboryl ether **3a** in hand, intramolecular cyanoboration was examined in the presence of a palladium or nickel catalyst. As shown in Table 1, several palladium complexes and salts successfully catalyze the intramolecular cyclization of **3a**. The cyclization proceeded via the *cis*-addition of the B-CN bond in a regioselective 5-exo fashion. We assume that the oxidative addition

**Table 1.** Catalyst Screening for Intramolecular Cyanoboration of **3a**<sup>a</sup>

catalyst	% yield (reaction time) <sup>b</sup>		
	at 50 °C	at 80 °C	at 110 °C
Pd(acac) <sub>2</sub>	nr	nr	86 (8 h)
PdCl <sub>2</sub>	nr	nr	83 (8 h)
PdCl <sub>2</sub> (MeCN) <sub>2</sub>	nr	94 (5 h)	—
PdCl <sub>2</sub> -pyridine	nr	71 (3 h)	—
Pd(PPh <sub>3</sub> ) <sub>4</sub>	38 (96 h)	70 (14 h)	74 (1 h)
Pd <sub>2</sub> (dba) <sub>3</sub>	94 (18 h)	98 (2 h)	—
Ni(COD) <sub>2</sub>	13 (96 h)	80 (96 h)	93 (2 h)

<sup>a</sup> Cyanoborane **3a** (0.30 mmol) in toluene-*d*<sub>8</sub> (0.5 mL) was heated in the presence of the palladium or nickel complexes (5 mol % Pd or Ni). <sup>b</sup> NMR yield (1,3-dimethoxybenzene as an internal standard). Abbreviations: nr = no reaction in 3 h; — = reactions not carried out.

of the B-CN bond to a palladium(0) species is involved to constitute a Pd(0)-Pd(II) catalytic cycle. Among the palladium catalysts tested, Pd<sub>2</sub>(dba)<sub>3</sub> exhibited the highest activity, completing the cyanoboration at 50 °C in 18 h. Although higher temperatures were required, other palladium catalysts also gave **4a** in good yields. The cyanoboration product thus obtained was readily isolable by distillation, although the hydrolytic lability of the B-N bond hampered its isolation using chromatography on a silica gel. It is noteworthy that a nickel catalyst was also effective for cyanoboration. The reaction of **3a** at 110 °C in the presence of Ni(COD)<sub>2</sub> afforded **4a** in high yield.

A series of cyanoboryl ethers **3** were subjected to intramolecular cyanoborations (Table 2). The cyanoboryl ether **3b** afforded the corresponding product **4b** in high yield (entry 1). Reactions of the tertiary internal homopropargylic ethers **3c** and **3d** proceeded at reaction rates similar to those of **3a** and **3b**, affording cyclization products **4c** and **4d** (entries 2 and 3). Intramolecular cyanoboration was also possible for the *primary* and *secondary* propargylic ethers (entries 4-7).<sup>12</sup> It was noteworthy that the use of a Ni(COD)<sub>2</sub> catalyst was essential to attain a high yield in the intramolecular cyanoboration of the *sec*-propargylic ether **3f** bearing a terminal alkyne group (entry 5). The use of palladium catalysts in this reaction resulted in the partial decomposition of the starting material, yielding the cyclization product only in moderate yields (40-50%). In the cyclization of the corresponding internal alkynes, Pd(PPh<sub>3</sub>)<sub>4</sub> served as the most effective catalyst in terms of product yield (entries 4, 6, and 7). The enyne **3h** underwent a cyanoboration reaction only at the carbon-carbon triple bond to form the conjugated diene **4h** in good yield (entry 7).

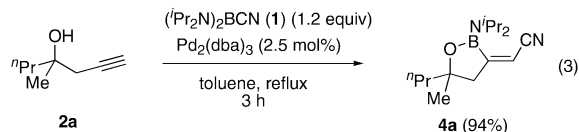
Cyanoboryl ether formation and subsequent intramolecular cyanoboration were carried out in one pot to improve the accessibility of the new cyclization reaction. Thus, homopropargylic

**Table 2.** Intramolecular Cyanoboration of Homopropargylic Ethers<sup>a</sup>

entry	substrate	conditions, <sup>b</sup> time/h	product	% yield <sup>c</sup>
1		A, 2		88 (99)
2		A, 2		84 (97)
3		A, 7		92 (98)
4		B, 5		88 (99)
5		C, 10		63 (83)
6		B, 43		94
7		B, 20		86 <sup>d</sup> (99)

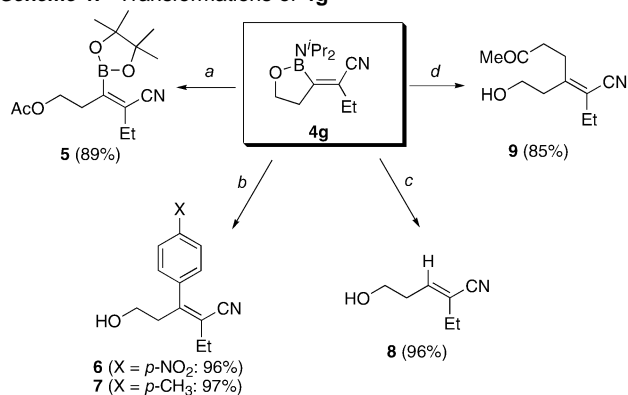
<sup>a</sup> Cyanoborane **3** in toluene was heated in the presence of the catalyst (5 mol % Pd or Ni). <sup>b</sup> Condition A: Pd<sub>2</sub>(dba)<sub>3</sub>, 80 °C. B: Pd(PPh<sub>3</sub>)<sub>4</sub>, 110 °C. C: Ni(COD)<sub>2</sub>, 110 °C. <sup>c</sup> NMR yield in parentheses (1,3-dimethoxybenzene as an internal standard). <sup>d</sup> E:Z = 93:7.

alcohol **2a** was added dropwise to a toluene solution of cyanoborane **1** (1.2 equiv) in the presence of Pd<sub>2</sub>(dba)<sub>3</sub> at 110 °C (eq 3). After



3 h, cyanoboration product **4a** was formed in 94% yield. This one-pot protocol enables the efficient synthesis of cyclic organoboron compounds directly from propargylic alcohols.

The synthetic utilities of the cyanoboration products were demonstrated by transformations of the representative product **4g** (Scheme 1). Treatment of **4g** with pinacol and Ac<sub>2</sub>O gave **5** in high yield.<sup>13</sup> The pinacolborane derivative **5** was stable enough to be isolated by silica gel chromatography, thus being regarded as a handy synthetic equivalent of **4g**. Iodobenzene derivatives underwent the Suzuki–Miyaura coupling<sup>14</sup> with **4g** to give  $\alpha,\beta$ -unsaturated nitriles **6** and **7** possessing a highly substituted, stereodefined C=C bond. Protodeboration giving **8** was achieved in high yield in the presence of a rhodium catalyst.<sup>15</sup> Moreover, we found that the cyanoboration product reacted with methyl vinyl ketone in the presence of a rhodium catalyst to provide a 1,4-addition product **9**.<sup>15</sup>

**Scheme 1.** Transformations of **4g**<sup>a</sup>

<sup>a</sup> (a) Pinacol (1.2 equiv), Ac<sub>2</sub>O (1.2 equiv), THF, 40 °C; (b) *p*-XC<sub>6</sub>H<sub>4</sub>-I, Pd<sub>2</sub>(dba)<sub>3</sub>, *t*-Bu<sub>3</sub>P, KF, H<sub>2</sub>O, dioxane, 80 °C; (c) Rh(acac)(COD), dppp, H<sub>2</sub>O, dioxane, 50 °C; (d) methyl vinyl ketone, Rh(acac)(COD), dppp, MeOH, dioxane, 50 °C.

In summary, we developed the transition metal-catalyzed intramolecular cyanoboration of alkynes. Investigations into the mechanism, expansion of the reaction scope, and further synthetic utilization of the reaction products are now being undertaken in this laboratory.

**Acknowledgment.** This work was supported in part by a Grant-in-Aid from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (21st Century COE on Kyoto University Alliance for Chemistry).

**Supporting Information Available:** Detailed experimental procedures and spectral data for the new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- Caution!** Handling of cyanoboranes needs special caution to avoid inhalation of hydrogen cyanide, which may be generated by hydrolysis of the cyanoboranes. Although the cyanoboranes can be handled in air for a short period, for example, to be weighed, all operations should be carried out in a fume hood.
- The *prim*- and *sec*-propargylic ethers were prepared by procedures different from that of the *tert*-propargylic ethers shown in eq 2. See Supporting Information.
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JA0349195