ORGANIC
LETTERS

2011
Vol. 13, No. 12
3008–3011

Synthesis of Pyridine-*N*-oxide–Borane Intramolecular Complexes by Palladium-Catalyzed Reaction of 2-Bromopyridine-*N*-oxides with Alkynyltriarylborates

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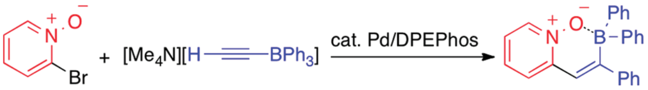
Received April 1, 2011

ABSTRACT



Pyridine-*N*-oxide–borane intramolecular complexes having an aza-stilbene π-framework were synthesized by the palladium-catalyzed reaction of 2-bromopyridine-*N*-oxides with alkynyltriarylborates.

Intramolecular boron complexes of nitrogen-containing π-conjugated compounds, in which the nitrogen atom coordinates to the boron atom suitably positioned within the molecule, have gained increasing attention from the viewpoint of development of new π-electron materials.[1] Various aza-π-conjugated compounds including thiazoles,[1e] azobenzenes,[1f] pyridines,[1g,i] and imines[1h] can form boron complexes, exhibiting unique properties such as strong fluorescence and high electron affinity. Such intramolecular complexes have been synthesized through lithiation of the parent aza-π-frameworks followed by a substitution reaction with organoborane derivatives. On the other hand, pyridine *N*-oxides can also form complexes with boranes through donation of the lone pair electrons of oxygen with their electron affinity being enhanced.[2] However, such complexes have been limited to *intermolecular* variants because *intramolecular* complexes are difficult to synthesize. A pyridine-*N*-oxide moiety is vulnerable to reagents for lithiation, and hence, the conventional lithiation methods are not applicable. We previously developed the palladium-catalyzed reactions of alkynyl(aryl)borates with aryl halides, which gave (1,2-diarylalkenyl)boranes stereoselectively.[3] The palladium-catalyzed reaction was extended to the rearrangement of alkynylborates bearing a pyridinium moiety, giving pyridine–borane complexes which exhibited intense fluorescence and high electron affinity.[4] During the course of our study on the development of new π-conjugated materials, we are then interested in the synthesis of pyridine-*N*-oxide–borane intramolecular complexes. Herein is described the palladium-catalyzed reaction of 2-bromopyridine-*N*-oxides

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(4) Ishida, N.; Narumi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 1279.

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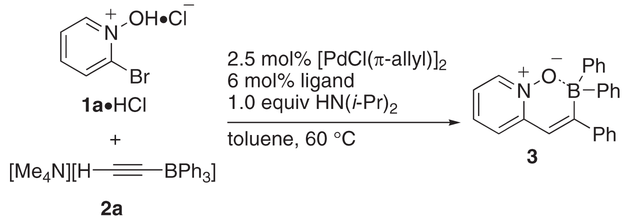
10.1021/ol2008439 © 2011 American Chemical Society
Published on Web 05/23/2011

with alkynyl(triaryl)borates to furnish pyridine-*N*-oxide–borane complexes having an aza-stilbene skeleton.[5]

We initially examined a reaction of 2-bromopyridine-*N*-oxide hydrochloride (**1a**·HCl), which was commercially available, with ethynyltriphenylborate **2a**[6] and diisopropylamine[7] in the presence of catalytic amounts of $[\mathrm{Pd}(\pi\text{-allyl})\mathrm{Cl}]_2$ and various additional ligands (Table 1). When $\mathrm{P}(o\text{-tol})_3$ was employed as the ligand,[3a] pyridine-*N*-oxide–borane complex **3** was produced in 25% yield (entry 1). The use of XANTPhos, which was the best ligand for the reaction of alkynyl(aryl)(9-BBN)s with aryl halides,[3b] gave complex **3** in 40% yield (entry 2). When 2,2′-bipyridine was used instead of phosphine ligands, the yield was improved to 70% (entry 3). We finally found DPEPhos gave the best result, affording **3** in 78% NMR yield (entry 4). The pyridine-*N*-oxide–borane complex **3** thus formed was considerably more stable toward air than ordinary triorganoboranes and was isolated in 69% yield after column chromatography on silica gel. The stability can be ascribed to the intramolecular coordination of oxygen to boron, which was supported by an upfield shift of the ^{11}B NMR signal (δ = 5.0 ppm).

Table 1. Screening of Ligands[a]

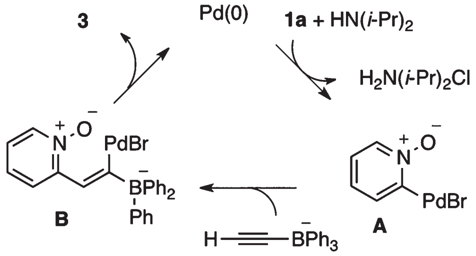


entry	ligand	yield of **3** /%[b]
1	$\mathrm{P}(o\text{-tol})_3$	25
2	XANTPhos	40
3	2,2′-Bipyridine	70
4	DPEPhos	78(69)

[a] Reaction conditions: 1.0 equiv of 2-bromopyridine-*N*-oxide hydrochloride (**1a**·HCl), 1.0 equiv of ethynyltriphenylborate **2a**, 1.0 equiv of $\mathrm{HN}(i\text{-Pr})_2$, 2.5 mol % $[\mathrm{Pd}(\pi\text{-allyl})\mathrm{Cl}]_2$, 6 mol % ligand, toluene, 60 °C, 1 h. [b] Determined by NMR analyses. Isolated yield in parentheses.

A number of mechanisms have been reported for the reactions of alkynylborates with electrophilic species which induce migration of a boron-substituent onto its α sp-carbon.[8,9] Although it is difficult to establish only one mechanism for the formation of **3**, one of the plausible reaction mechanisms is depicted in Scheme 1. Oxidative addition of 2-bromopyridine-*N*-oxide (**1a**) to palladium(0) gives arylpalladium bromide **A**. The resulting arylpalladium species **A** undergoes carbopalladation across the alkyne moiety of the alkynylborate **2a** in a *cis*-fashion to afford alkenylpalladium **B**, with which palladium is located on the carbon α to boron. Then, the phenyl group on boron migrates onto the α-carbon, leaving the boron p orbital empty.[3b] The migrating phenyl group attacks from the backside of the α-carbon–palladium bond, resulting in inversion of the stereochemistry of the α sp^2-carbon.[10,11] The palladium(0) species is released and the oxygen atom on the pyridine-*N*-oxide coordinates to boron to form the pyridine-*N*-oxide–borane complex **3**.

Scheme 1. Possible Reaction Mechanism



Next, we examined the substrate scope of the palladium-catalyzed reaction. Both the electron-donating methoxy group (**1b**) and electron-withdrawing trifluoro-methyl group (**1c**) on the 5-position of the pyridine moiety have little influence on the reactivity, resulting in the formation of the corresponding pyridine-*N*-oxide–borane complexes **4** and **5** in 79 and 80% yield, respectively (Table 2, entries 1 and 2). 2-Bromoquinoline-*N*-oxide (**1d**) could also participate in the reaction (entry 3). The unprotected hydroxyl group at the 6-position of the pyridine-*N*-oxide **1e** was tolerated under the reaction conditions (entry 4). Pyridine-*N*-oxide–borane complexes having a tetrasubstituted olefin moiety **8** and **9** could be synthesized by employing alkynyltriphenylborates **2b** (R′ = Me) and **2c** (R′ = Et) instead of **2a** (entries 5 and 6). Ethynyltri(*p*-methoxyphenyl)borate **2d** and ethynyltri(*p*-fluorophenyl)borate **2e** successfully provided the corresponding pyridine-*N*-oxide–borane complexes (entries 7 and 8).

Further derivatization of the pyridine-*N*-oxide–borane complex **3** was possible. When **3** was treated with 1.5 equiv

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(6) Alkynyltriarylborate **2a** was synthesized by simply treating a triphenylborane–pyridine complex with ethynylmagnesium bromide and subsequently with tetramethylammonium chloride. See Supporting Information for detail.

(7) Diisopropylamine gave a better yield than $\mathrm{HNEt_2}$, $\mathrm{Et_3N}$, pyridine, or $\mathrm{K_2CO_3}$.

(8) A review on the reaction of organoborates with electrophiles: Negishi, E. *J. Organomet. Chem.* **1976**, *108*, 281.

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(10) For substitutive 1,2-migration from boron to the α-carbon with inversion of stereochemistry, see: Köbrich, G.; Merkle, H. R. *Angew. Chem., Int. Ed.* **1967**, *6*, 74.

(11) For related $\mathrm{S_N2}$-type substitution reactions at sp^2 carbons with inversion of configuration, see: (a) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059. (b) Luccini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1993**, *115*, 4527. (b) Shiers, J. J.; Shipman, M.; Hayes, J.; Slawin, A. M. Z. *J. Am. Chem. Soc.* **2004**, *126*, 6868. (c) Ando, K.; Kitamura, M.; Miura, K.; Narasaka, K. *Org. Lett.* **2004**, *6*, 2461. (d) Bernasconi, C.; Rappoport, Z. *Acc. Chem. Res.* **2009**, *42*, 993 and references cited therein.

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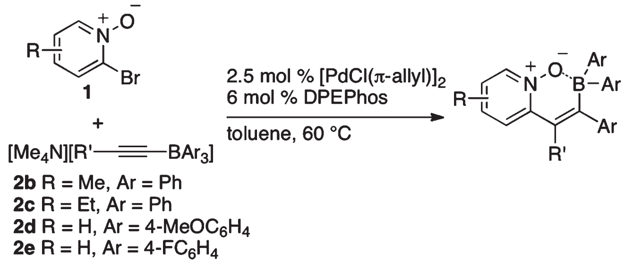
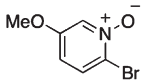
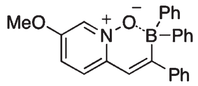
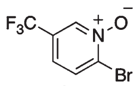
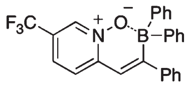
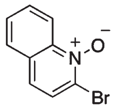
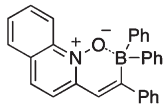
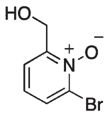
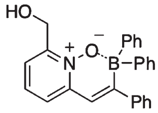
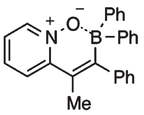
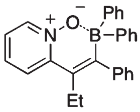
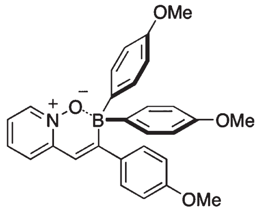
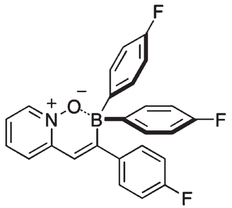
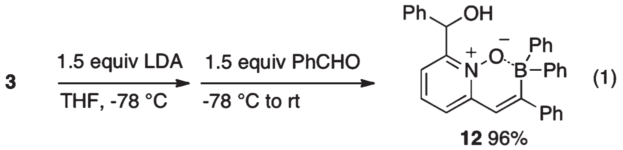
Table 2. Synthesis of Pyridine-*N*-oxide–Borane Complexes[a]



entry	pyridine-*N*-oxide **1**	**2**	products[b]
1	 **1b**	2a	 **4** 79%
2	 **1c**	2a	 **5** 80%
3	 **1d**	2a	 **6** 70%
4	 **1e**	2a	 **7** 76%
5[c]	**1a·HCl**	2b	 **8** 67%
6[c]	**1a·HCl**	2c	 **9** 71%
7[c]	**1a·HCl**	2d	 **10** 82%
8[c]	**1a·HCl**	2e	 **11** 67%

[a] Reaction conditions: 1.0 equiv of **1**, 1.0 equiv of alkynyltriarylborate **2**, 2.5 mol % [Pd(π-allyl)Cl]$_2$, 6 mol % DPEPhos, toluene, 60 °C, 1 h. [b] Isolated yield. [c] 1.0 equiv of HN(i-Pr)$_2$ was added.

of LDA in THF, the 6-position of the pyridine ring was selectively deprotonated.[12] Subsequent treatment with benzaldehyde gave alcohol **12** in 96% yield (eq 1).



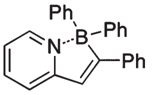
12 96%

The optical and electronic properties of pyridine-*N*-oxide–borane complexes were briefly compared with those of pyridine–borane complexes (Table 3). Pyridine-*N*-oxide–borane complex **3** exhibited no fluorescence unlike the pyridine–borane complex **13**.[4,13] Electrochemical data were determined by cyclic voltammetry, and both π-conjugated compounds showed reversible reduction waves. The *N*-oxide derivative **3** had a less negative reduction potential ($V_{1/2}$ = −2.0 V) than **13** ($V_{1/2}$ = −2.2 V), indicating the pyridine-*N*-oxide–borane moiety was acting as a stronger electron-accepting group than the corresponding pyridine–borane moiety. Notably, the reduction potential of **3** was less negative than the reduction peak potential of conventional electron-transporting material Alq$_3$ (V_{pc} = −2.14 V), which shows **3** has a lower LUMO level than Alq$_3$.

Table 3. Photophysical[a] and Electrochemical[b] Properties of **3** and **13**

compd	λ_{ab}	Log ε	λ_{em}	Φ	$V_{1/2}/V^c$
3	368	4.14	–	0	−2.0
13	359	4.17	422	0.44	−2.2

[a] Determined in CH$_2$Cl$_2$. [b] Determined in γ-butyrolactone with Bu$_4$NClO$_4$ at a scan rate of 100 mV s^{-1}. [c] Potentials vs ferrocene/ferrocenium.


13

In summary, we synthesized pyridine-*N*-oxide–borane intramolecular complexes having an aza-stilbene π-framework by the palladium-catalyzed reaction of 2-bromopyridine-*N*-oxides with alkynylborates. The pyridine-*N*-oxide–borane complexes exhibited higher electron affinities than the corresponding pyridine–borane complexes. Such π-conjugated compounds having a low-lying LUMO

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(13) The molar absorption coefficients of **3** and **13** are similar (log ε = 4.14 for **3**, 4.17 for **13**). This indicates that the radiative lifetimes should be similar for both compounds according to the Strickler–Berg relation. Internal conversion from the excited state of the pyridine-*N*-oxide–borane complex might be faster than that of the pyridine–borane complex.

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level are expected as air-stable semiconducting materials.[14] Further studies on the properties and application of the pyridine-*N*-oxide–borane complexes are ongoing.

Acknowledgment. This work was supported in part by MEXT (Grand-in-Aid for Young Scientist (B) No. 22750038), New Energy and Industrial Technology Development Organization (NEDO, 09C46603d), and the Asahi Glass Foundation.

Supporting Information Available. Experimental details, structural data for all new compounds, copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.