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

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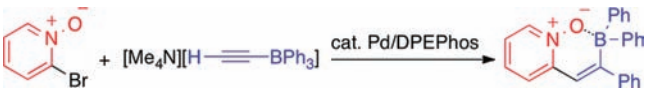
ABSTRACT



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.

(5) For palladium-catalyzed reactions of pyridine-*N*-oxide derivatives, see: (a) Campeau, L.-S.; Rousseaux, S.; Fagnou, K. *J. Am. Chem. Soc.* **2005**, *127*, 18020. (b) Cho, S. H.; Hwang, S. J.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 9254. (c) Campeau, L.-C.; Stuart, D. R.; Leclerc, J.-P.; Bertrand-Laperle, M.; Villemure, E.; Sun, H.-Y.; Lasserre, S.; Guimond, N.; Lecavallier, M.; Fagnou, K. *J. Am. Chem. Soc.* **2009**, *131*, 3291. (d) Xi, P; Yang, F.; Qin, S.; Zhao, D.; Lan, J.; Gao, G.; Hy, C.; You, J. *J. Am. Chem. Soc.* **2010**, *132*, 1822.

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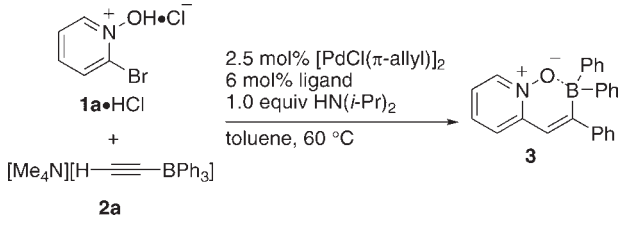
with alkynyl(triaryl)borates to furnish pyridine-*N*-oxide–borane complexes having an aza-stilbene skeleton.[5]

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 [Pd(π-allyl)Cl]$_2$ and various additional ligands (Table 1). When P(*o*-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

Table 1. Screening of Ligands[a]



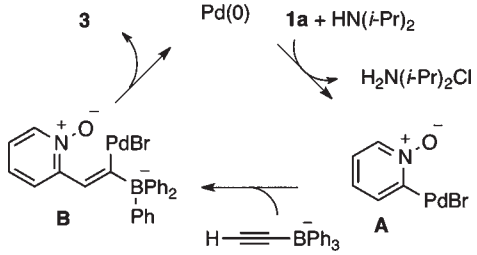
entry	ligand	yield of **3** /%[b]
1	P(*o*-tol)$_3$	25
2	XANTPhos	40
3	2,2′-Bipyridine	70
4	DPEPhos	78(69)

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

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).

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

(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 HNEt$_2$, Et$_3$N, pyridine, or K$_2$CO$_3$.

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

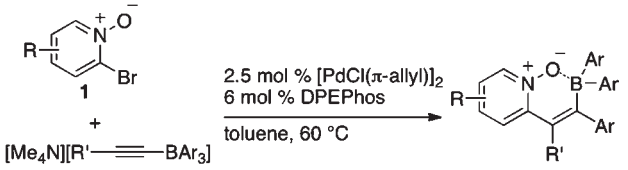
(9) (a) Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652. (b) Binger, P.; Köster, R. *Synthesis* **1974**, 350. (c) Miyaura, N.; Yoshinari, T.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1974**, *15*, 2961. (d) Pelter, A.; Bentley, T. W.; Harrison, C. R.; Subrahmanyam, C.; Laub, R. J. *J. Chem. Soc., Perkins 1* **1976**, 2419.

(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.

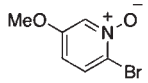
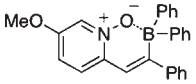
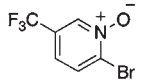
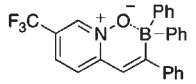
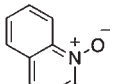
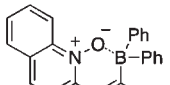
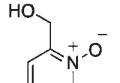
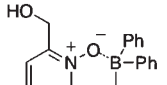
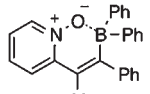
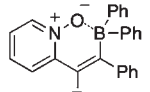
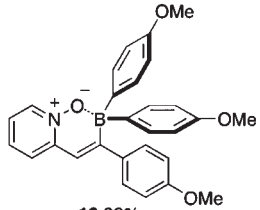
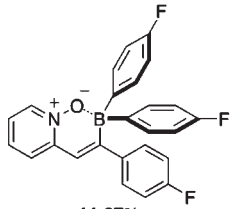
(11) For related S$_N$2-type substitution reactions at sp^2 carbons with inversion of configuration, see: (a) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059. (b) Luccini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1993**, *115*, 4527. (b) Shiers, J. J.; Shipman, 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.

(12) (a) Zoltewicz, J. A.; Kauffman, G. M. *J. Org. Chem.* **1969**, *34*, 1405. (b) Taylor, S. L.; Lee, D. Y.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156.

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

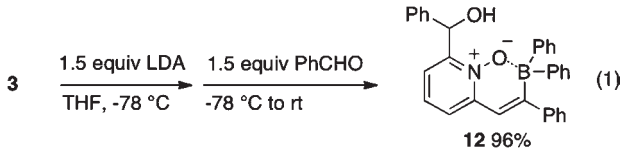


2b R = Me, Ar = Ph
2c R = Et, Ar = Ph
2d R = H, Ar = 4-MeOC$_6$H$_4$
2e R = H, Ar = 4-FC$_6$H$_4$

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).

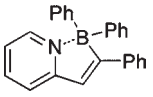


The optical and electronic properties of pyridine-*N*-oxide–borane complexes were briefly compared with those of pyridine–borane complexes (Table 3). Pyridine-*N*-oxide–borane complex **3** exhibited no fluorescence unlike the pyridine–borane complex **13**.[4,13] Electrochemical data were determined 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_2Cl_2. [b] Determined in γ-butyrolactone with Bu_4NClO_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

(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.

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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.