JOC*Note*

pubs.acs.org/joc

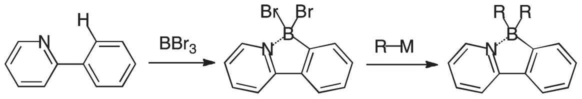
Synthesis of Pyridine−Borane Complexes via Electrophilic Aromatic Borylation

Naoki Ishida,[†] Taisaku Moriya,[†] Tsuyoshi Goya,[‡] and Masahiro Murakami*,[†]

[†]*Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Katsura, Kyoto 615-8510, Japan, and* [‡]*Advanced Materials Research Center, Nippon Shokubai Co., Ltd., 5-8, Nishi Otabi-cho, Suita, Osaka 564-0034, Japan*

murakami@sbchem.kyoto-u.ac.jp

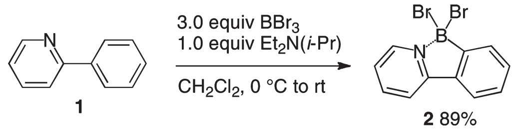
Received September 30, 2010



Pyridine−borane complexes were synthesized from 2-arylpyridines through an electrophilic aromatic borylation reaction with BBr_3. The intermediate 2-(2-dibromoborylaryl)pyridines were stable enough to be handled in air and served as the synthetic platform for variously substituted pyridine−borane complexes. This facile method would be useful for the synthesis of aza-π-conjugated materials having boron−nitrogen coordination.

Aza-π-conjugated frameworks containing an intramolecular boron−nitrogen coordination bond have attracted significant attention owing to their interesting photophysical and electronic properties.[1] For example, 2-(3-boryl-2-thienyl)-thiazole derivatives exhibit higher electron affinity than conventional electron-transporting materials like tris(8-hydroxyquinoline)aluminum (Alq_3) and 2-(4-biphenyl)-5-(4-*tert*-butylphenyl)-1,3,4-oxadiazole (PBD), which indicates their potential as n-type semiconducting materials.[1a] Such coordination compounds have been synthesized through lithiation of bromo-substituted *N*-heteroaromatics with *n*-butyllithium followed by a substitution reaction with haloborane derivatives. However, the highly nucleophilic and basic character of organolithium reagents may cause undesired side reactions, limiting the range of structural modifications. Thus, development of new synthetic methods for aza-π-conjugated frameworks which dispense with the use of organolithium intermediates are desired. Recently, we have developed the palladium-catalyzed rearrangement reaction of alkynylborates equipped with a tertiary pyridinium moiety.[2] The rearrangement reaction successfully afforded various aza-π-conjugated materials having a boron−nitrogen coordination bond, which exhibited interesting properties such as strong fluorescence. We then looked for a more straightforward synthetic access to an analogous structural motif. Herein is described a facile synthetic method of pyridine−borane complexes via an electrophilic aromatic borylation reaction of 2-phenylpyridine derivatives with BBr_3.

Boron trihalides are known to borylate aromatic hydrocarbons with assistance of nitrogen directing groups.[3] For instance, 2-phenylbenzimidazole reacts with BCl_3 at 300 °C to give 2-(2-borylphenyl)benzimidazole.[4] 1-Amino-2-phenylbenzene reacts with BCl_3 in the presence of $AlCl_3$ to provide 10-chloro-9,10-azaboraphenathrene.[5] We envisaged that the pyridine moiety of 2-arylpyridines would act as a directing group[6] to promote a regioselective C−H borylation reaction with boron trihalides. The resulting pyridine−dihaloborane complexes would work as precursory platforms for various pyridine−borane complexes, which are potent light-emitting materials possessing a low-lying LUMO level. Thus, a reaction of 2-phenylpyridine (**1**) with BCl_3 and BBr_3 was examined. When 2-phenylpyridine (**1**) was treated with 3.0 equiv of BBr_3 and 1.0 equiv of $Et_2N(i\text{-Pr})$ in dichloromethane at room temperature, pyridine−dibromoborane complex **2** was obtained in 89% yield. On the other hand, BCl_3 failed to afford the corresponding borylated product under the same reaction conditions. The product **2** was stable toward air and moisture, making it easy to handle for further transformations.

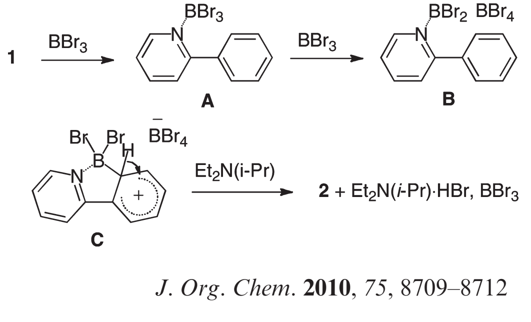


1 **2** 89% (1)

A plausible reaction mechanism for the formation of **2** is depicted in Scheme 1. The Lewis basic nitrogen atom of pyridine coordinates to the Lewis acidic boron center to provide the complex **A**. Another BBr_3 abstracts a bromide anion from the complex **A**, giving trivalent cationic boron species **B** (borenium ion).[7,8] Then, the cationic boron center of **B** electrophilically attacks the neighboring aromatic moiety,[9] and the following rearomatization furnishes pyridine−dibromoborane complex **2**.

Various aryl-*N*-heteroaromatics were successfully borylated by treatment with BBr_3 (Table 1). Bromo groups on the

SCHEME 1. Plausible Mechanism of Electrophilic Aromatic Borylation



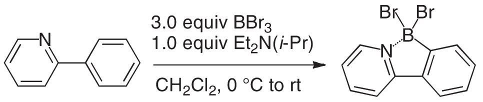
---

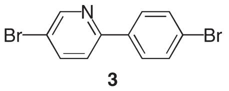
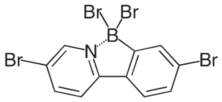
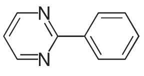
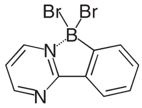
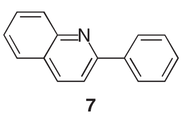
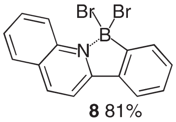
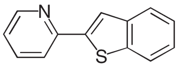
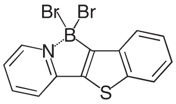
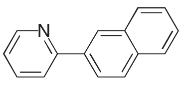
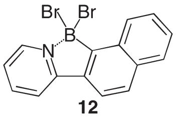
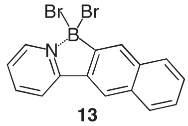
(1) (a) Wakamiya, A.; Taniguchi, T.; Yamaguchi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 3170. (b) Yoshino, J.; Kano, N.; Kawashima, T. *Chem. Commun.* **2007**, 559. (c) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891. (d) Baik, C; Hudson, Z. M.; Amarne, H.; Wang, S. *J. Am. Chem. Soc.* **2009**, *131*, 14549.

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

DOI: 10.1021/jo101920p

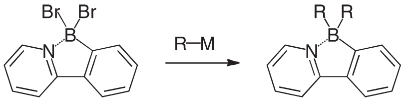
TABLE 1. Electrophilic Aromatic Borylation Reactions of 2-Arylpyridine Derivatives[a]

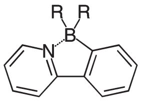
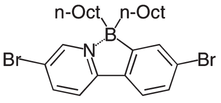
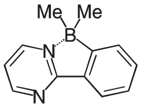
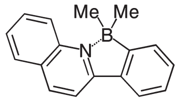
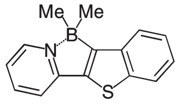
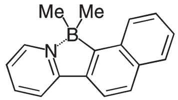
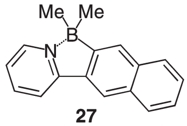


entry	substrates	products
1	 **3**	 **4** 82%
2	 **5**	 **6** 91%
3	 **7**	 **8** 81%
4	 **9**	 **10** 87%
5	 **11**	 **12**  **13** 89% (**12**:**13** = 3:1)

[a]Reaction conditions: 3.0 equiv of BBr$_3$, 1.0 equiv of Et$_2$N(i-Pr), CH$_2$Cl$_2$ (0.2 M), 0 °C to rt.

TABLE 2. Synthesis of Various Pyridine−Borane Complex Derivatives[a]



entry	substrates	R–M	products
1	**2**	LiAlH$_4$[a]	 R = H, **14**, 80%
2		Me$_3$Al[b]	R = Me, **15**, 91%
3		Et$_3$Al[b]	R = Et, **16**, 82%
4		(i-Pr)$_2$Zn[c]	R = i-Pr, **17**, 77%
5		Ph$_3$Al[b]	R = Ph, **18**, 90%
6		(4-MeOC$_6$H$_4$)$_2$Zn[c]	R = 4-MeOC$_6$H$_4$, **19**, 90%
7		(4-CF$_3$C$_6$H$_4$)$_2$Zn[c]	R = 4-CF$_3$C$_6$H$_4$,**20**, 98%
8		(C$_6$F$_5$)$_2$Zn[c]	R = C$_6$F$_5$, **21**, 89%
9	**4**	(n-Oct)$_3$Al[b,d]	 **22** 85%
10	**6**	Me$_3$Al[b]	 **23** 89%
11	**8**	Me$_3$Al[b]	 **24** 78%
12	**10**	Me$_3$Al[b]	 **25** 74%
13	**12** and **13** (**12**:**13** = 3:1)	Me$_3$Al[b]	 **26**  **27** 85% (**26**:**27** = 3:1)

[a]2.1 equiv of LiAlH$_4$, Et$_2$O, 0 °C to rt, 1 h. [b]2.1 equiv of R$_3$Al, toluene, rt. [c]2.1 equiv of R$_2$Zn, toluene, 70 °C. [d]A mixture of CH$_2$Cl$_2$ and toluene was used as solvent.

aryl group remained intact under the reaction conditions to give tetrabromo compound **4** in 82% yield (entry 1). The substrate **5** having a pyrimidine group, which was less basic than pyridine, successfully participated in the borylation reaction (entry 2). A sterically demanding quinoline group also worked as the directing group to afford the corresponding dibromoborane complex **8** in 81% yield (entry 3). 2-(2-Pyridyl)benzothiophene (**9**) was borylated at the thiophene moiety, resulting in the formation of complex **10** in 87% yield (entry 4). 2-(2-Naphthyl)pyridine (**11**) gave a regioisomeric mixture of **12** and **13** (3:1) in 89% combined yield (entry 5). The 1-position of the naphthyl group was preferentially borylated over the 3-position, as were the cases with conventional electrophilic aromatic substitution reactions of naphthalenes. This regiochemical outcome could be ascribed to the stability of the cationic species corresponding to the intermediate **C**. The cation formed by 1-borylation is more stable than the cation formed by 3-borylation.

Pyridine−dibromoborane complexes thus obtained were next treated with organometallic reagents to substitute the bromo groups on boron with hydrogens or carbon substituents

---

(3) Onak, T. In *Organoborane Chemistry, Organometallic Chemistry, A Series of Monographs*; Academic Press, Inc.: New York, 1975.

(4) Letsinger, R. L.; MacLean, D. B. *J. Am. Chem. Soc.* **1963**, *85*, 2230.

(5) Dewar, M. J. S.; Kubba, V. P.; Pettit, R. *J. Chem. Soc.* **1958**, 3073.

(6) Pyridine-directed direct C−H functionalization reactions: (a) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (c) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (d) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147.

(7) Reviews: (a) Kölle, P.; Nöth, H. *Chem. Rev.* **1985**, *85*, 399. (b) Piers, W. E.; Bourke, S. C.; Conroy, K. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 5016.

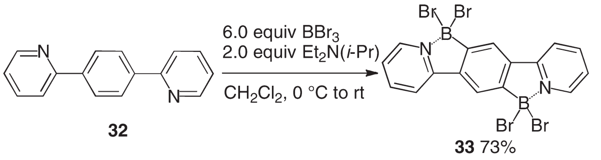
(8) (a) Ryschkewitsch, G. E.; Miller, V. R. *J. Am. Chem. Soc.* **1973**, *95*, 2836. (b) Cowley, A. H.; Lu, Z.; Jones, J. N.; Moore, J. A. *J. Organomet. Chem.* **2004**, *689*, 2562. (c) Uddin, M. K.; Nagano, Y.; Fujiyama, R.; Kiyooka, S.-i.; Fujio, M.; Tsuno, Y. *Tetrahedron Lett.* **2005**, *46*, 627. (d) Chiu, C.-W.; Gabbai, F. P. *Organometallics* **2008**, *27*, 1657.

(9) De Vries, T. S.; Prokofjevs, A.; Harvey, J. N.; Vedejs, E. *J. Am. Chem. Soc.* **2009**, *131*, 14679.

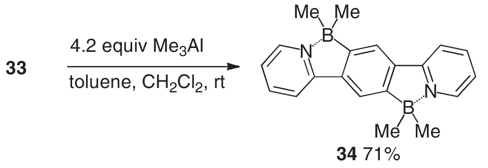
(Table 2). Treatment of $LiAlH_4$ in Et_2O gave borohydride **14** in 80% yield (entry 1). The reaction of pyridine−dibromoborane complexes with triorganylaluminum reagents such as Me_3Al, Et_3Al, Ph_3Al, and $(n\text{-Oct})_3Al$ rapidly proceeded at room temperature to complete within 5 min. The corresponding alkylated products were isolated in yields ranging from 74 to 91% (entries 2, 3, 5, and 9−13). Diorganylzincs were also effective, although the alkylation/arylation reaction was slower than that with triorganylaluminum reagents (entries 4 and 6−8). On the other hand, PhMgBr gave an inferior result (43% yield of **18**), and PhLi afforded a complex mixture. $PhSnBu_3$ and PhCu species failed to afford the desired product.

Next, functionalization and extension of the aromatic chain were examined using pyridine−borane complex **22** as the model substrate (Scheme 2). The palladium-catalyzed Suzuki−Miyaura coupling reaction of **22** with phenylboronic acid (2.0 equiv) successfully proceeded to give diarylated product **28** in 82% yield. The boryl group coordinated by the pyridine moiety remained intact under the reaction conditions. Amination of **22** with diphenylamine was catalyzed by $Pd_2dba_3 \cdot CHCl_3$ and $P(t\text{-Bu})_3$,[10] providing diaminated product **29** in 74% yield. When **22** was treated with 2.1 equiv of *n*-BuLi in THF, dilithiated pyridine−borane complex was generated by double bromine−lithium exchange. A subsequent reaction with *i*-PrOBpin (4.0 equiv) afforded diboronic ester **30** in 54% isolated yield. On the other hand, when 1.1 equiv of *n*-BuLi was used in Et_2O, selective monolithiation on the pyridine ring took place, and a subsequent reaction with *i*-PrOBpin (2.0 equiv) furnished monoboronic ester **31** in 64% yield.

Finally, bridged teraryl **34** was synthesized from 1,4-di-(2-pyridyl)benzene (**32**). Electrophilic aromatic borylation of **32** occurred at the two positions of the benzene ring which were para to each other to afford diborylated product **33** in 73% yield (eq 2). Then, **33** was treated with trimethylaluminum in toluene to provide tetramethylated product **34** in 71% yield (eq 3).



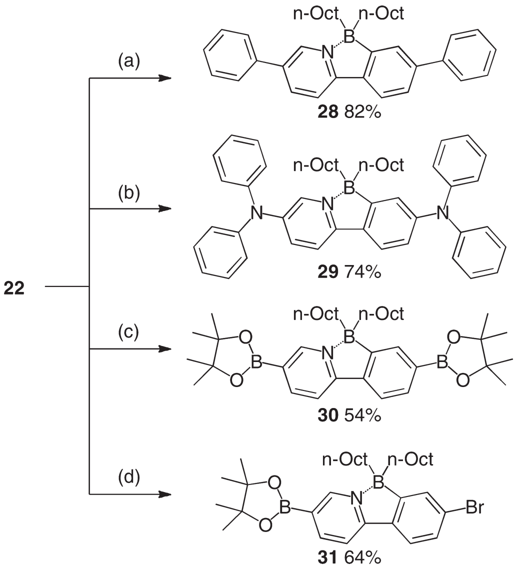
(2)



(3)

The synthesized pyridine−boranes exhibited high electron affinity, which indicates such π-materials have low-lying LUMO level. In addition, strong fluorescence in the solid state as well as in solution was observed.[11] Therefore, they are expected as air-stable light-emitting materials.[12] Studies on photophysical properties and application to optoelectronic devices are now underway and will be reported elsewhere.

SCHEME 2. Reactions of 22[a]



[a]Key: (a) 5 mol % of $Pd(PPh_3)_4$, 2.0 equiv of $PhB(OH)_2$, 2.0 equiv of Na_2CO_3, toluene, H_2O, 90 °C; (b) 5 mol % of $Pd_2dba_3 \cdot CHCl_3$, 40 mol % of $P(t\text{-Bu}_3)$, 3.0 equiv of Ph_2NH, 10 equiv of NaO-*t*-Bu, toluene, 100 °C; (c) 2.1 equiv of *n*-BuLi, THF, −78 °C; then 4.0 equiv of (*i*-PrO)Bpin, rt; (d) 1.1 equiv of *n*-BuLi, Et_2O, −78 °C; then 2.0 equiv of (*i*-PrO)Bpin, rt.

In conclusion, we have developed a synthetic method for pyridine−borane complexes via an electrophilic aromatic borylation reaction with BBr_3 followed by substitution reactions with organometallic reagents. This facile method would be useful for the synthesis of aza-π-conjugated materials having boron−nitrogen coordination.

Experimental Section

Electrophilic Aromatic Borylation of 2-Phenylpyridine (eq 1): A General Procedure. To a stirred solution of 2-phenylpyridine (77.6 mg, 0.5 mmol) and $i\text{-}Pr_2NEt$ (64.6 mg, 0.5 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C was added BBr_3 (1.0 M in CH_2Cl_2, 1.5 mL, 1.5 mmol). *Caution: BBr_3 is highly moisture sensitive and decomposes in air with an evolution of corrosive HBr. It should be handled in a well-ventilated hood.* After being stirred at room temperature for 24 h, saturated K_2CO_3 aqueous solution was added to the reaction mixture. The organic layer was separated and extracted with CH_2Cl_2 (twice), washed with water (once) and brine (once), dried over $MgSO_4$, and concentrated. The resulting solid was collected by filtration and washed with hexane to give pyridine−borane complex **2** (145 mg, 0.45 mmol, 89% yield): ^1H NMR δ 7.42 (t, J = 7.5 Hz, 1H), 7.55−7.60 (m, 2H), 7.75 (d, J = 7.8 Hz, 1H), 7,87 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 8.16 (t, J = 7.8 Hz, 1H), 8.95 (d, J = 5.4 Hz, 1H); ^{13}C NMR δ 118.5, 121.9, 123.6, 128.7, 130.7, 133.17, 133.24, 143.7, 144.4, 155.9; ^{11}B NMR δ −1.1; HRMS (EI) calcd for $C_{11}H_7BBr_2N$ $(M - H)^+$ 321.9039, found 321.9052. Anal. Calcd for $C_{11}H_8BBr_2N$: C, 40.68; H, 2.48; Br, 49.20; N, 4.31. Found: C, 40.61; H, 2.60; Br, 48.94; N 4.31.

Alkylation of Pyridine−Borane Complex 2 with Me_3Al (Table 2, Entry 2): A General Procedure. To a stirred solution of **2** (32.5 mg, 0.10 mmol) in toluene (1.0 mL) at room temperature was

---

(10) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617.

(11) Very recently, photophyical and electrochemical properties of some compounds were reported: Amarne, H.; Baik, C.; Murphy, S. K.; Wand, S. *Chem.—Eur. J.* **2010**, *16*, 4750.

(12) Anthopoulos, T. D.; Anyfantis, G. C.; Papavassiliou, G. C; de Leeuw, D. M. *Appl. Phys. Lett.* **2007**, *90*, 122105.

added Me_3Al (1.1 M in hexane, 0.2 mL, 0.22 mmol). After being stirred at this temperature for 5 min, the reaction was quenched by adding water. The organic layer was separated and extracted with AcOEt (twice), washed with water (once) and brine (once), dried over $MgSO_4$, and concentrated. The residue was purified by preparative thin-layer chromatography on silica gel (eluent: hexane/AcOEt = 2/1) to afford **15** (17.7 mg, 0.091 mmol, 91% yield): ^{1}H NMR δ 0.05 (s, 6H), 7.26−7.38 (m, 2H), 7.43 (td, J = 7.5, 0.9 Hz, 1H), 7.65 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.93−7.99 (m, 2H), 8.44 (dt, J = 5.7, 1.2 Hz, 1H); ^{13}C NMR δ 8.8, 117.7, 121.3, 121.5, 125.1, 129.1, 130.2, 135.0, 139.2, 142.1, 156.8; ^{11}B NMR δ 1.1; HRMS (EI) calcd for $C_{13}H_{13}BN$ $(M - H)^+$ 194.1141, found 194.1136.

Acknowledgment. This work was supported in part by New Energy and Industrial Technology Development Organization (NEDO, 09C46603d).

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