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Palladium-Catalyzed Cross-Coupling Reactions of 4*a*,8*a*-Azaboranaphthalene

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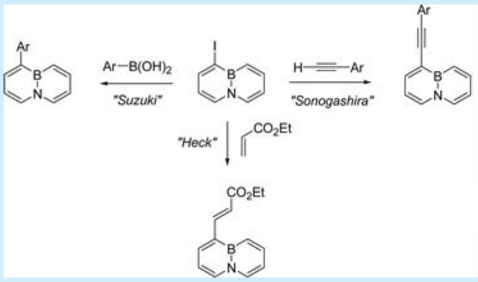
Supporting Information

ABSTRACT: A concise and effective three-step synthesis of 4*a*,8*a*-azaboranaphthalene (ABN) has been developed in gram scale. Electrophilic aromatic substitution reactions of ABN provide excellent functional-group-tolerant cross-coupling partners in various Pd-catalyzed cross-coupling reactions (e.g., Sonogashira, Suzuki−Miyaura, or Heck reaction). Photophysical, electrochemical, and DFT calculations all suggest a narrowed HOMO−LUMO gap with extended π-conjugation characters in the cross-coupled molecules. The ABN moiety as a new fluorophore has a distinct and selective fluorescence response toward Zn(II) and Cd(II) ions, demonstrating great potential for the ABN structural motif in fluorescent chemosensors.



Polycyclic aromatic hydrocarbons (PAHs) possess many intriguing and fascinating properties that have attracted extensive research efforts in areas such as asymmetric catalysis,[1] organic sensors,[2] organic semiconductors,[3] organic optoelectronics,[4] and organic superconductors,[5] owing to their well-defined yet sophisticated π-conjugation molecular architectures. In view of their contiguous applications, prodigious consumption of PAHs in the foreseeable future may be anticipated. However, PAHs are generally known as one of the most widespread organic pollutants, and exposure to PAHs can be detrimental to environmental safety and public health,[6] which creates an obligation to seek more ecologically benign alternatives.

In this context, one important strategy is to blend in a B−N unit that is isoelectronic and isostructural to the C═C bond of the aromatic systems.[7] The B−N incorporation inserts local dipole moments into the molecule and provides different optoelectronic properties with polarized delocalization.[8,9] Nonetheless, boron with a vacant p orbital is susceptible to nucleophilic attack, which often leads to vulnerable system stability. To circumvent this challenge, many ingenious approaches with the help of kinetic stabilization of boron have been utilized to enhance the long-term stability of the designed materials.[10,11] In contrast, thermodynamic stabilization of boron as useful approaches in molecular design has unfortunately often been neglected.[8e]

On the other hand, despite the fact that transition-metal-catalyzed cross-coupling reactions are emerging as powerful tools in the synthesis of PAHs,[12] their applications in the synthesis of BN-fused polycyclic aromatic compounds remain largely unexplored.[7−9] In fact, conventional syntheses of certain BN-fused PAHs with few molecular scaffolds relied solely on the electrophilic borylation reactions under harsh reaction conditions.[8,9] Only recently, Liu et al. reported a Stille-like Rh-catalyzed boron cross-coupling reaction of 1,2-azaborines and Molander et al. demonstrated a Ni-catalyzed cross-coupling reaction of 3-bromo-2,1-borazaronaphthalene with alkyl iodides.[13] Herein we present unprecedented Pd-catalyzed cross-coupling reactions of 4*a*,8*a*-azaboranaphthalene (ABN) as part of our inaugurated program toward "bottom-up" synthetic study and property investigation of BN-fused PAHs.

Our interest has been focused on the BN-fused naphthalene **3**, as naphthalene is the simplest PAH molecule (Figure 1). Unlike 1,2-azaborines,[14] the corresponding boron atom in **3** is less likely to be attacked by other nucleophiles due to additional aromatic π-electron delocalization. This thermodynamically stable boron is of significance in designing promising BN-substituted polycyclic aromatic materials suitable for stringent device performance requirements.[3,4] The synthesis of **3** was pioneered by Dewar, albeit the recorded yield was unfathomably as low as 0.2%.[15] Ashe reported an improved multistep synthesis of **3** involving ring-closing metathesis (RCM) and carbene ring expansion, though an overall yield of **3** was still too low to make it

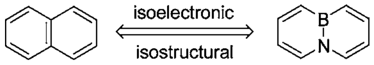


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Figure 1. Isosteric 4*a*,8*a*-azaboranaphthalene.

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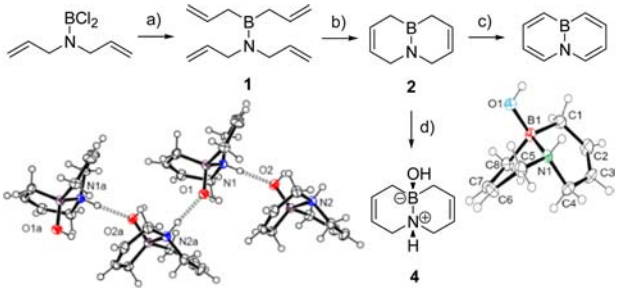
practical for further scrutiny.[16] Even most recently, the **3**-oriented synthesis reported from the Ashe group, utilizing B/Sn transmetalation and RCM, still led to unresolved **3**-containing mixtures after Pd/C oxidation.[17] The synthetic predicament prompted us to develop a more efficient synthesis of **3**.

Scheme 1. Synthesis of 3/4 and ORTEP Drawings of 4[a]



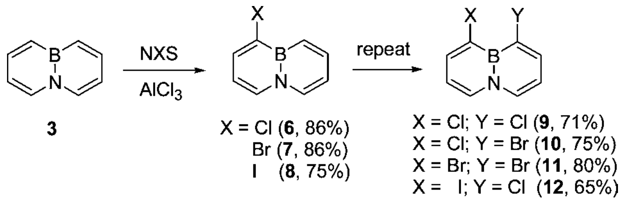
[a](a) C_3H_5MgBr (2 equiv), 70%; (b) $(Cy_3P)_2Cl_2Ru{=}CHPh$ (0.8 mol %), CH_2Cl_2, 92%; (c) DDQ (2 equiv), hexane, 60 °C, 17%; (d) H_2O, ca. 100%. Thermal ellipsoids are shown at 30% probability with hydrogen bonding in dash lines (1.953(5) Å).

Our synthesis of **3** (Scheme 1) is optimized in only three steps and starts from diallylaminoboron dichloride, which can be easily prepared by the reaction of inexpensive and commercially available BCl_3 and diallylamine. Subsequent allylation and RCM mediated by the Grubbs' catalyst afford **2**. In contrast to rather air- and moisture-sensitive compound **1**, **2** demonstrates impressive stability toward O_2 and only reacts slowly with a trace of water in solution to give the H_2O-adduct **4**, suggesting that the presence of the B−N unit maintains their respective Lewis acidity and basicity, yet at a relatively decreased level. Dehydrogenation of **2** has been tested at elevated temperatures with Pd-Black in cyclohexene or DDQ in hexane. It is interesting to note that the Pd-Black condition always generates a mixture of **3** and *H*-scrambled 1,2-azaborine compound **5** (see the Supporting Information (SI)) posing problems in separation and purification,[17] while the DDQ dehydrogenation surprisingly delivers only **3** as the final product, even though the reaction yield is 17%. Thus, **3** can be attained in gram scale with ease, which paves the way for our next study.

Catalyzed by Lewis acids such as $AlCl_3$, $AlBr_3$, or $BF_3{\cdot}Et_2O$, **3** can be halogenated by electrophilic NXS (X= Cl/Br/I) reagents. In this manner, mono- and dihalogenated ABN compounds **6**−**12** can be prepared respectively in good yields after sublimation (Scheme 2).

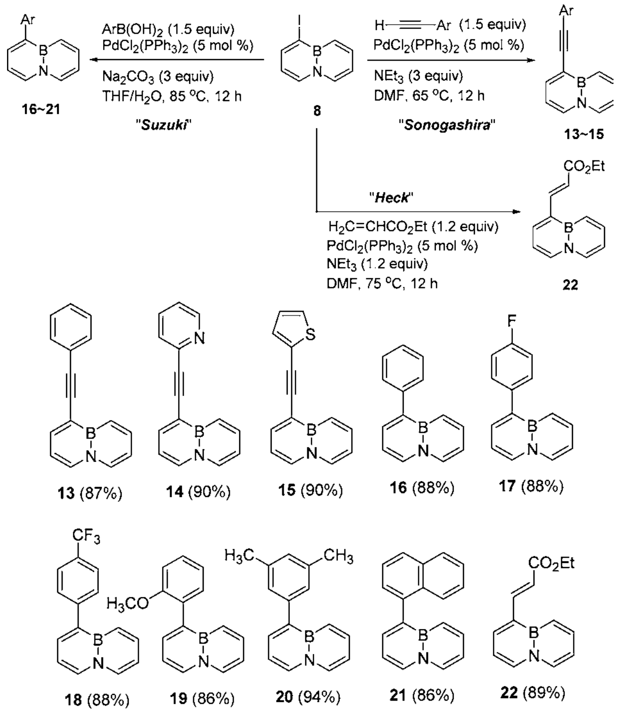
Interestingly, the second halogenation reaction occurs at the other ring without a halogen being attached, which may be due to the fact that the electron-richness of the halogenated ring becomes much retarded because of the electron-withdrawing character of halogen substituents. The halogenation of **6**−**12** takes place exclusively at the *α*-carbon positions next to boron. In the absence of bulky protecting groups, all ABN derivatives mentioned above can be handled indefinitely in air and water without any trace of decomposition,[18] indicating that the ABN system is indeed thermodynamically stable.

Scheme 2. Electrophilic Aromatic Substitution of 3



Pd-catalyzed cross-coupling reactions have been successfully honed to construct the C−C bonds of aromatic compounds.[19] Thus, 4-iodo-4*a*,8*a*-azanaphthalene **8** is initially chosen as the substrate, as the $C(sp^2)$−I bond in aromatic rings generally exhibits superior reactivity in oxidative addition reactions (Scheme 3). However, the chemistry of **8** seems to be divergent from other aromatic counterparts, because we have noted that **8** could not even be activated in some metal-assisted reactions (e.g., Grignard reaction and Cu-catalyzed borylation reactions[20]). To our delight, the iodide **8** could participate in the Sonogashira-type reactions and afford the cross-coupled alkyne products **13**−**15** in excellent yields up to 90%. It is worth noting that the coupling reactions are not hampered by the presence of heterocycles such as pyridine and thiophene, leaving plenty of synthetic opportunities for further applications.

Scheme 3. Pd-Catalyzed Cross-Couplings of 8[a]



[a]Isolated yields, average of at least two independent runs.

Encouraged by our initial success, we have turned our focus to the Suzuki-type coupling reactions, one of the most important preparative strategies to extend the *π* systems. In this case, we set out to examine the reactivity profile of **8** with different phenylboronic acid derivatives, because of the ready accessibility of diverse substituents of the phenyl ring possessing distinctive electronic and steric characters. Interestingly, various substituted phenyl motifs could be cross-coupled to the ABN ring via the Suzuki-type reactions and products **16**−**21** were obtained in excellent yields with unprotected boron in ABN rings. In the Heck-type reaction, $PdCl_2(PPh_3)_2$ is utilized to catalyze the reaction of **8** and ethyl acrylate in DMF, and compound **22** has been identified as the exclusive product of the reaction. The ABN ring is selectively coupled *trans* to the ester group across the C=

C bond, as evidenced by ${}^3J_{HH}$ = 16 Hz in the ^{1}H NMR spectrum of **22**.

Single crystals suitable for X-ray structural analysis were obtained by slow evaporation of **4**, **8**, **9**, **11**, **12**, and **21** in ether or hexane at rt, respectively. The corresponding Lewis pair property of the B−N unit in **2** is well-exemplified by the molecular structure of **4**, in which boron captures the OH group and the proton attaches to nitrogen, resulting in a *cis* arrangement (Scheme 1).

It is of particular interest to compare the X-ray crystal structures of homologous **8**, **9**, **11**, and **21** (Figure 2 and the SI).

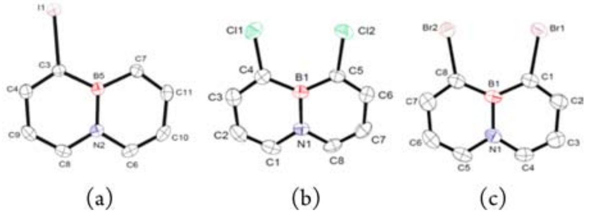


Figure 2. ORTEP drawings of **8**, **9**, and **11**. Thermal ellipsoids are shown at 30% probability; H-atoms are omitted for clarity: (a) **8**; (b) **9**; (c) **11**.

All BN-naphthalene rings in **8**, **9**, **11**, and **21** are completely planar, and the halogen substituents are accommodated within the plane. In all cases, the B−N bonds show double bond character, as their bond lengths (1.453(4)−1.467(7) Å) are consistent with those reported in BN aromatics.[8,9,21] The sums of bond angles around B and N atoms are all exactly 360°, indicating sp^2 hybridization of the boron and nitrogen centers. The B−C and N−C bond lengths (B−C: 1.514(4)−1.547(10) Å; N−C: 1.376(8)−1.399(8) Å) of **8**, **9**, and **11** are noticeably shorter than those of typical B−C and N−C single bonds (B−C: ca. 1.58 Å; N−C: ca. 1.47 Å) respectively,[21] suggesting that both boron and nitrogen participate actively in the delocalized π-system. In the presence of only one C−X bond (as in the case of **8**), the B−C−X bond angle (120.08(19)°) is exceedingly close to the ideal sp^2-hybridized bond angle (120°), whereas the corresponding angles become enlarged (122.2(2)°−125.3(5)°) with two neighboring C−X bonds tilted away from each other (as in the cases of **9** and **11**). This scenario may be attributed to severe electronic repulsion between two parallel C−X bonding orbitals, and the ideal sp^2 bond angle will be observed when a C−X bond is replaced with a less electron demanding C−H bond. In line with the above analysis, the ^{11}B NMR chemical shift values (δ in ppm) of monohalogenated **6** (28.1), **7** (28.1), and **8** (29.0) are close to that of **3** (28.5), but move to a lower magnetic field relative to those of **9** (25.9), **10** (25.8), **11** (25.9), and **12** (25.8). In fact, the electronegativity of halogen atoms contributes much less to the localized electron density at boron, because the δ (^{11}B) values shift prominently to the same extent toward a higher magnetic field only in the dihalogenated counterparts such as **9**−**12**. Compound **21** represents a rare example of an unsymmetrical isostere of the 1,1′-binaphthyl system. The molecular structure of **21** possesses two different ring moieties: one naphthyl group and one BN-fused naphthyl group, with a dihedral angle of 110.8(5)° between the mean planes of two naphthalene rings.

The direct comparison of the absorption and emission spectra of cross-coupled products **13**−**16** is shown in Figure 3. The absorption spectrum of **16** displays a λ_{max} at 258 nm along with a weak side peak at λ = 300 nm, whereas the absorbance maximums of **13** are clearly bathochromically shifted to 270 and 330 nm respectively with vibronic structures and an intensity increase. This bathochromic bimodal peak shift is also observable in the corresponding spectra of **13**−**15**. In this respect, the absorbance bands of **15** are red-shifted relative to those in **13** and **14**, which are found to be coincidentally overlapped. The emission properties of **13**−**16** resemble their absorption counterparts, and the 2-thienyl-extended derivative **15** exhibits the farthest bathochromic shift at λ_{em} = 390 nm with a moderate fluorescence quantum yield of $\mathbf{\Phi}_{PL}$ = 0.46(2), consistent with the DFT calculations indicating a contracted HOMO−LUMO gap (3.59 eV) of **15** in comparison to **13** (3.79 eV) and **14** (3.81 eV) at the B3LYP/6-311++G(d,p) level (see the SI). This demonstrates that the installation of a 2-thienyl group extends the effective length of the π-conjugation system.

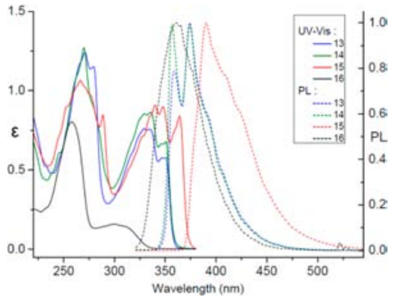


Figure 3. Photophysical data of **13**−**16** (in hexane; UV−vis: ε in 10^4 M^{-1} cm^{-1}; PL: normalized).

In cyclic voltammetry experiments, the reversible oxidation wave of thienyl derivative **15** has an earlier electrochemical oxidation onset relative to **13**, in qualitative agreement with a higher HOMO level of **15** by DFT calculations (see the SI). In contrast, the comparable reduction onsets of both compounds conform to a similar LUMO level also predicted by DFT calculations, which can be ascribed to less contribution of the electron-deficient character of boron to the π-conjugation system in both cases.

Driven by intense research interest in metal-ion sensing in biomedical and environmental analyses,[22] we decided to assess the potentials of ABN as a new fluorophore in fluorescent chemosensors. Thus, **14** was chosen as the sensor molecule with a pyridyl receptor. A variety of metal ions were screened in THF solution, and the emission intensities of probe **14** were found to be selectively enhanced in the presence of Zn^{2+} and Cd^{2+}. The addition of other metal ions showed no occurrence of detectable “turn-on” fluorescence enhancement. The representative fluorescence spectra of titration of **14** with $ZnCl_2$ are shown in Figure 4. Interestingly, the emission spectra of **14** (10 μM) show no alteration in the presence of excess CH_3CO_2H or TFA (*ca.* 10^3-fold), and the competition experiments reveal that the emission

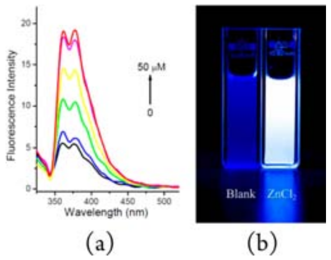


Figure 4. (a) Emission spectra and (b) fluorescence photo of titration of **14** with $ZnCl_2$: blank sample (left) vs [$ZnCl_2$] = 10 μM in THF (right).

intensity of putative Zn(II)-coordinated **14** is not further affected by the addition of strong Brønsted acids such as TFA. This metal-dependent fluorescence signaling of **14** is also supported by no measurable emission change in response to $[NHBu_3]^+[BPh_4]^-$, suggesting that the signal enhancement originates from the metal coordination to the lone pair of the pyridyl nitrogen via a photoinduced electron transfer (PET) mechanism.[2b]

In conclusion, we developed a concise and efficient three-step synthesis of ABN in gram scale and studied its electrophilic aromatic substitution reactions by structural characterization of the corresponding halogenated products. We have for the first time established Pd-catalyzed cross-coupling reactions of ABN, which provides different synthetic approaches toward BN-fused PAHs. Further studies directed toward carbon−heteroatom bond formation in ABN cross-coupling reactions are underway.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, characterization data (mp, ^1H, ^{13}C, ^{11}B, ^{19}F NMR, IR, HRMS, EA, CV, X-ray), and DFT calculation results. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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