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1,1-Hydroboration of Fused Azole−Isoindole Analogues as an Approach for Construction of *B,N*-Heterocycles and Azole-Fused *B,N*-Naphthalenes

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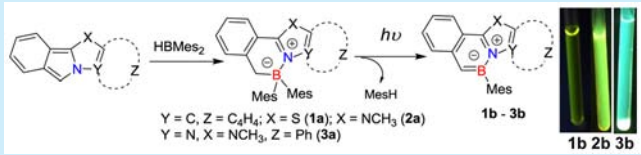
Supporting Information

ABSTRACT: Three isoelectronic analogues of pyrido[2,1-*a*]isoindole have been found to undergo a facile 1,1-hydroboration with $HBMes_2$ borane, which provides a new and convenient method for the synthesis of *B,N*-heterocycles **1a**−**3a** in high yields. Compounds **1a**−**3a** can undergo photoelimination upon irradiation at 300 nm, generating heterocycle-fused *B,N*-naphthalene molecules **1b**−**3b**, which display distinct yellow-green and blue fluorescent colors, respectively. Compound **1a** undergoes thermal elimination, producing **1b** at 280 °C, while compound **2a** only undergoes partial elimination, forming **2b** at 320 °C. Compound **3a** is thermally stable up to 320 °C.



Pyrido[2,1-*a*]isoindole (**isocarb**, Figure 1) and its isoelectronic analogues such as pyrrolo[1,2-*a*]pyridine are known

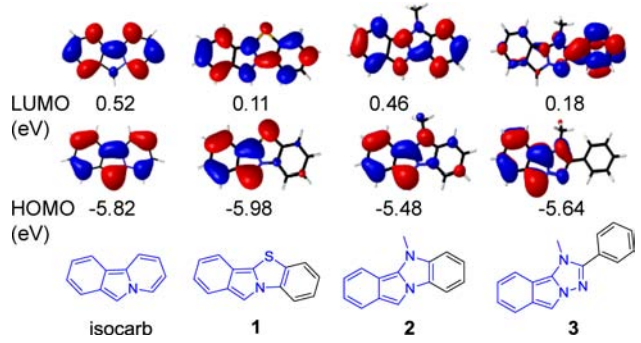


Figure 1. DFT calculated HOMO and LUMO energies and orbital diagrams of **isocarb** and its isoelectronic analogues.

to be reactive heterocycles that can readily undergo 1,3-dipolar cycloadditions with alkynes to generate a variety of interesting π-conjugated systems.[1] This is facilitated by the unique C6 atom of **isocarb** (and its familial equivalents), which is highly nucleophilic and easily reacts with electrophiles such as acyl groups to form C−C-coupled products.[2] Recently, we discovered that **isocarb** can undergo unprecedented and unusual 1,1-hydroboration reactions with a variety of HBR_2 boranes,[3] leading to the convenient synthesis of *B,N*-heterocyclic compounds that are known precursors to a class of rare and highly emissive *B,N*-phenanthrenes.[4] Given the potential applications of and tremendous current research interest in *B,N*-heterocycles[5] and azaborinines,[6−9] as well as the underdeveloped nature of 1,1-hydroboration chemistry,[3,10] we set out to expand the scope of our 1,1-hydroboration protocol by demonstrating its viability with various isoelectronic analogues of **isocarb**. Three fused azole−isoindole molecules, benzo[4,5]thiazolo[2,3-*a*]isoindole (**1**), 5-methyl-5*H*-benzo[4,5]imidazo[2,1-*a*]isoindole (**2**), and 1-methyl-2-phenyl-1*H*-[1,2,4]triazolo[5,1-*a*]isoindole (**3**), shown in Figure 1 were chosen as representative examples for our investigation.

The possibility that compounds **1**−**3** may undergo 1,1-hydroboration in the same manner as **isocarb** was first supported by the results of DFT computational study, which revealed that the electronic structures of **1**−**3** are in fact similar to those of **isocarb**. As can be seen in Figure 1, the unique carbon atom of each species has a significant contribution to the HOMO level much like **isocarb**, suggesting that they should all possess similar nucleophilic character. Additionally, the HOMO level is either similar in energy or destabilized relative to that of **isocarb**, which indicates that the basicity/nucleophilicity of compounds **1**−**3** should either be similar or greater than that of **isocarb**. Indeed, our experimental work has confirmed that compounds **1**−**3** are also capable of facile 1,1-hydroboration, which provides a new, simple, and highly efficient synthetic route to *B,N*-heterocycles based on heterocycle-fused isoindoles. The details are presented herein.

Compound **1** was prepared directly according to a modified literature procedure.[11] The precursor compounds 11*H*-benzo[4,5]imidazo[2,1-*a*]isoindole (**pre-2**) and 2-phenyl-5*H*-[1,2,4]-triazolo[5,1-*a*]isoindole (**pre-3**) for **2** and **3**, respectively, were prepared according to literature procedures (see the Supporting Information).[2,12] Compounds **pre-2** and **pre-3** were converted in good yields to their methylated salts, [**pre-2-Me**]**I** and [**pre-**

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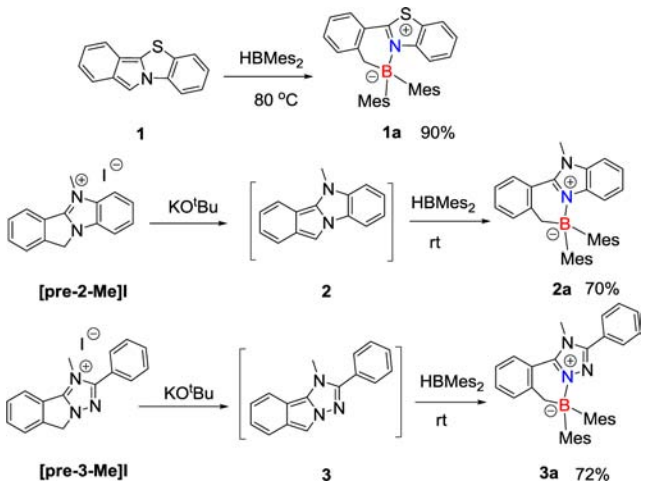
3-Me]I, respectively, by first reacting with dimethyl sulfate followed by the addition of 30% aqueous KI solution. Deprotonation [**pre-2-Me]I** and [**pre-3-Me]I** using bases such as NaOH or Na_2CO_3 were unsuccessful due to the formation of ring-opened products in the presence of hydroxide.[12] Use of a non-nucleophilic base such as KO^{t}Bu in toluene did give the desired products **2** and **3**; however, attempts to purify these heterocycles proved problematic due to their extremely high sensitivity to air, which always led to contamination by the decomposition products. Therefore, we designed a one-pot procedure for the generation of **2** and **3** and their borylated counterparts **2a** and **3a**. In this procedure (Scheme 1), [**pre-2-Me]I** and [**pre-3-Me]I** were reacted with

Scheme 1. 1,1-Hydroboration of 1 and Analogous One-Pot Procedure for 2 and 3



excess KO^{t}Bu in toluene at ambient temperature. After the removal of KI and excess KO^{t}Bu by filtration under nitrogen, the filtrates were used directly for the hydroboration reaction. Surprisingly, the addition of $HBMes_2$ (Mes = mesityl) to the solution of in situ generated **2** or **3** in benzene or toluene at ambient temperature resulted in the formation of the corresponding borylated products **2a** and **3a** in good yields (70% and 72%, respectively, after purification and isolation by column chromatography). Compound **1** reacted with $HBMes_2$ at 80 °C to produce the borylated product **1a** in high yield (90%). The successful synthesis of compounds **1a−3a** demonstrates that 1,1-hydroboration is a general reactivity of fused azole-isoindole derivatives and can be used to build heteroatom-doped polycyclic organoboron compounds.

This new, one-pot 1,1-hydroboration protocol of **isocarb** analogues is an extremely useful synthetic method, as it is the only viable approach of achieving borylated compounds such as **1a**, **2a**, and **3a** in high yield. Our previously established procedure for achieving the $BMes_2$-chelated 2-(*o*-tolyl)pyridine species involved the use of *n*-BuLi at −78 °C, which is prone to the generation of side products such as *ortho*-metalation at the sp^2-phenyl carbon rather than the desired sp^3-methyl.[4] These undesired deprotonations become even more likely upon the introduction of additional heteroatoms into the chelating framework, such as 1-methyl-2-(*o*-tolyl)-1*H*-benzo[*d*]imidazole and 4-methyl-3-phenyl-5-(*o*-tolyl)-4*H*-1,2,4-triazole, which would be the required substrates for the preparation of **2a** and **3a**, respectively, under such conditions. To compare these two methods, 1-methyl-2-(*o*-tolyl)-1*H*-benzo[*d*]imidazole was prepared[13] and reacted with *t*-BuLi/$BMes_2F$, resulting in a 16% isolated yield of **2a** (see the SI).

Compounds **1a**, **2a**, and **3a** were fully characterized by NMR and HRMS analyses. All three molecules display a ^{11}B chemical shift (3.70, 1.80, and 1.80 ppm, respectively) that is characteristic of four-coordinated boron.[3,4] In addition, the crystal structures of **1a** and **3a** were established by single-crystal X-ray diffraction analysis. The B−C bond lengths in both molecules are similar and comparable to those of 2-(*o*-tolyl)pyridine-$BMes_2$ and derivatives.[4] The B−N bond in **3a** (1.636(2) Å) is however significantly shorter than that in **1a** (1.669(2) Å) and 2-(*o*-tolyl)pyridine-$BMes_2$ (1.666(2) Å), which could be attributed to the reduced congestion around the boron center in **3a** (Figure 2). All three compounds are stable in solution and in the solid state under ambient conditions.

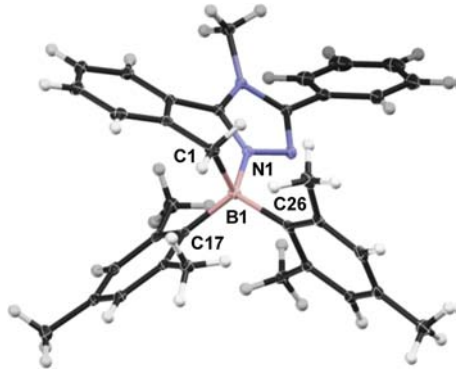


Figure 2. Crystal structure of **3a**. Important bond lengths (Å) and angles (deg): B(1)−N(1) 1.636(2), B(1)−C(1) 1.654(2), B(1)−C(17) 1.666(2), B(1)−C(26) 1.655(2); C(1)−B(1)−N(1) 97.04(11), C(1)−B(1)−C(17) 106.76(12), C(1)−B(1)−C(26) 119.37(13), N(1)−B(1)−C(17) 111.83(12), N(1)−B(1)−C(26) 107.93(11), C(17)−B(1)−C(26) 112.88(12).

To establish if compounds **1a−3a** can act as precursors for the generation of azaborinine derivatives, their photoreactivity was examined. Compounds **1a−3a** have low energy absorption bands with λ_{max} = ~ 295, 310, and 310 nm, respectively (see the SI) and are not fluorescent in solution. However, as the solutions of **1a−3a** are irradiated with 300 nm UV light, they become brightly fluorescent and display distinct fluorescent colors. For example, THF solutions (~10^{-5} M) of **1a** and **2a** changed from nonfluorescent to yellow-green and green fluorescent, respectively, following irradiation, with new absorption peaks appearing at λ_{max} = 450 nm (**1b**) and 445 nm (**2b**) in their UV−vis spectra (Figure 3). Accompanying this change in absorptions are new emission peaks with well-resolved vibrational features at λ_{max} = 520 nm (**1b**, Φ_{FL} = 0.022) and 495 nm (**2b**, Φ_{FL} = 0.47) in their fluorescence spectra. For **3a**, its solution produced intense sky-blue fluorescence after irradiation with a new absorption peak at λ_{max} = 405 nm and a broad, featureless emission peak at λ_{max} = 478 nm (Φ_{FL} = 0.13) in the UV−vis and the fluorescence spectra, respectively. NMR and HRMS analyses confirmed that the new fluorescent species are heterocycle-fused *B,N*-naphthalenes **1b**, **2b**, and **3b**, respectively (Scheme 2) and that the photochemical conversion of **1a−3a** to **1b−3b** is clean (see the SI). The ^{11}B chemical shifts of **1b−3b** (36.3, 34.1, and 33.6 ppm, respectively) are consistent with azaborinines.[3,4] Compound **1b** is similar to a $BMes_2$-chelate molecule we reported recently,[4] while compounds **2b** and **3b** are new

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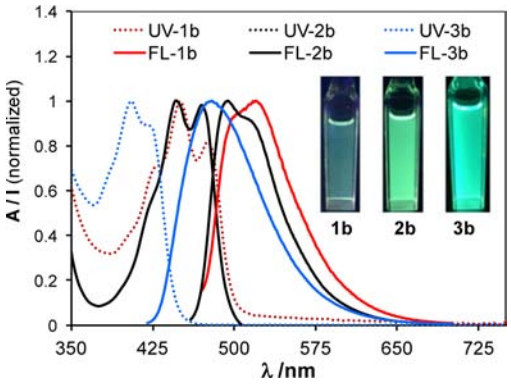
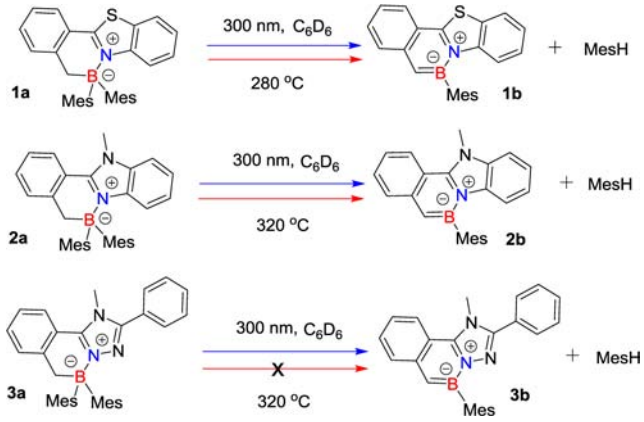


Figure 3. Absorption (dotted lines) and fluorescence spectra (solid line) of **1b**−**3b** in THF (~1×10^{-5} M). The fluorescence spectra were recorded at λ_{max} of absorption. Inset: photographs showing the emission colors of **1b**−**3b**.

Scheme 2. Photo- and Thermal Reactivity of 1a−3a



members of the *B,N*-arene family. Efforts to grow single crystals of **2b** and **3b** for X-ray diffraction analysis were unsuccessful. The successful synthesis of **1b**−**3b** via photoelimination of the chelate precursors **1a**−**3a** demonstrates that this transformation is a general reactivity for *B,N*-heterocycles possessing an azole-fused backbone. The distinct emission colors of **1b**−**3b** indicate that the fused benzazole ring of the *B,N*-naphthalenes has a significant influence on the photophysical properties of this class of compounds and may therefore be used as a convenient approach to tune the emission color of *B,N*-arenes.

To gain insight into the impact of the fused benzazole unit on compounds **1b**−**3b**, TD-DFT calculations were performed at the cam-B3LYP/6-31g(d) level of theory. The general trend of absorption and fluorescence spectra of **1b**−**3b** is corroborated by TD-DFT data as shown in Figure 4. For **1b** and **2b**, the transition to the first excited state primarily involves HOMO (H) → LUMO (L) (96%) with large oscillator strength. For **3b**, the transition to the first excited state is from H to L (57%) and LUMO+1 (L + 1, 38%), also with large oscillator strength. The H orbital for all three compounds is a π orbital concentrated primarily on the *B,N*-naphthalene portion of the molecule, while the L orbital for **1b** and **2b** is a π^* orbital involving the entire conjugated unit. For **3b**, L and L+1 orbitals have significant contributions from the phenyl substituent on the triazole ring. The nonrestricted rotation of this phenyl ring in **3b** is believed to be responsible for the broad and featureless emission band and the relatively large Stokes shift of **3b**. It is noteworthy that the fused azole−isoindole molecules **1**−**3** and

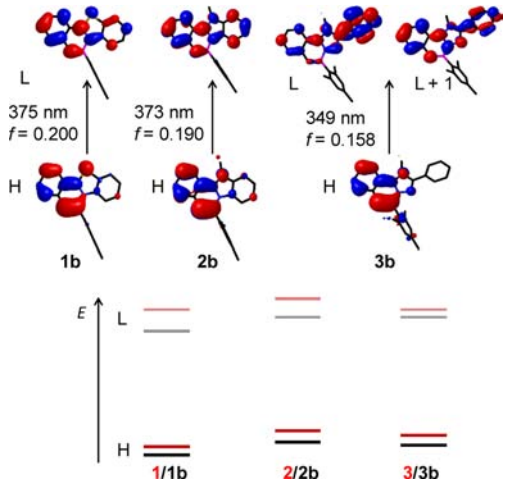


Figure 4. (Top) TD-DFT calculated $S_0 \rightarrow S_1$ transition energies, oscillator strength, and orbital diagrams for **1b**−**3b**. (Bottom) H and L energy level change from isoindole heterocycles to *B,N*-arenes.

corresponding *B,N*-arenes have the same number of π electrons in their respective conjugated units. However, the insertion of a *B*-Mes unit into the isoindole ring significantly stabilizes both H and L levels of the molecule (H is lowered by 0.23, 0.36, and 0.27 eV, respectively from **1**−**3** to **1b**−**3b**) as shown in Figure 4. The stabilization of the HOMO level leads to an enhanced stability of the *B,N*-arenes toward oxygen relative to the isoindole heterocycles and a narrowing of the H−L gap with respect to **1** and **2** (see the SI for details).

Previously, we have shown that $BMes_2$-chelated **isocarb** compounds can display either *retro*-1,1-hydroboration (deborylation) or mesitylene elimination upon heating.[3] To determine if $BMes_2$-chelate compounds based on **isocarb** analogues display similar reactivities, we examined the thermal reaction of compounds **1a**−**3a**. Compound **1a** was found to undergo a clean thermal elimination upon heating at 280 °C, producing **1b** nearly quantitatively. Compound **2a** is stable at 280 °C and undergoes partial conversion to **2b** along with the formation of unidentified products at 320 °C. In contrast, **3a** is thermally stable and shows no change at temperatures between 280 and 320 °C. On the basis of these findings, it is clear that the conjugated heterocyclic backbone has an impact not only on the electronic structure of the corresponding *B,N*-arenes but also on the stability/reactivity of the chelate compounds. The fact that no deborylation products were observed in any of the thermal reactions indicates that deborylation is likely a thermodynamically disfavored process.

In summary, we have established that the 1,1-hydroboration of isoindole derivatives is a general reactivity available to this class of molecules and can be used as a simple and effective method of preparing *B,N*-heterocycles. Further, we have shown that this new synthetic protocol can be implemented in tandem with our previously described photo- and thermal reactivity to afford a wide variety of unexplored *B,N*-arenes. Ongoing research efforts are focused on exploiting the generality of these transformations with the aim of creating larger and more complex *B,N*-doped nanographenes.

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■ ASSOCIATED CONTENT

Supporting Information

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Synthetic details, characterization data, TD-DFT data, photo- and thermal elimination experiments, UV−vis spectra, and X-ray diffraction analysis data (PDF)
Crystal data of **1a** and **2a** (CIF)

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Author Contributions

§Y.-g.S. and D.-T.Y. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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