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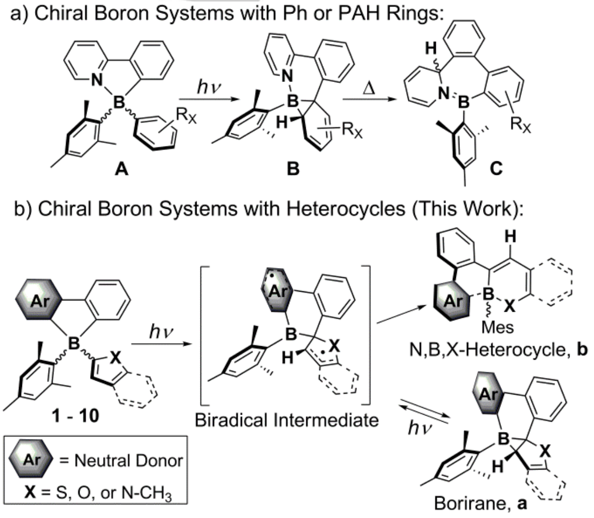
Photochemical Generation of Chiral *N,B,X*-Heterocycles *via* Heteroaromatic C–X Bond Scission (X = S, O) and Boron Insertion

Soren K. Mellerup,[a] Cally Li,[a] Julian Radtke,[b] Xiang Wang,[a] Quan-Song Li,[c]* and Suning Wang[a],[c]*

Abstract: Chiral organoboron compounds with a chelate backbone and mesityl/heterocycle substituents (thienyl, furyl and derivatives) undergo a quantitative phototransformation yielding rare, chiral *N,B,X*-embedded heterocycles (**b**) (*e.g.* base-stabilized 1,2-thiaborinines and 1,2-oxaborinines). Boriranes (**a**) were observed as intermediates in some of these transformations. The oxaborinines display further reactivity, generating 4a,12b-dihydro-benzo[*h*][1,2]-oxaborinino-[4,3-*f*]quinolones through a sequential conrotatory electrocyclization and [1,5]-H shift. Compounds **b** display strong blue-green to orange-red emission in the solid state. Combined DFT//CASP2T calculations suggest that a common biradical intermediate is responsible for the formation of **a** and **b**, as well as **a** to **b** conversion in the excited state.

The selective manipulation of specific chemical bonds within molecular frameworks has been of a longstanding interest to synthetic chemists both from a practical[1] and fundamental[2] perspective. Much like transition metal complexes, which were recognized to be highly effective in bond activation and catalysis decades ago,[3] recent advances in main-group chemistry have revealed great promise/potential for p-block element enabled chemical transformations.[4] Nevertheless, there still remain many substrates that are routinely handled by transition metals, *e.g.* C–X bonds (X = S, O, or N) in heteroaromatic systems,[5] most of which have yet to be established for main-group analogues.[6,7]

The key facet of main-group systems that allows them to activate various chemical bonds is their possession of "unquenched reactivity" imposed by specific electronic and steric constraints.[8] Aside from designing systems with the necessary features to yield these types of reactive systems, one promising alternative is the use of light to bring molecules into their excited state(s) such that bond activation can be performed *via* these higher energy species.[9] This methodology has several advantages, with the most prominent being access to reactive intermediates from easily prepared and often air stable starting materials. Using this approach, we have recently unveiled a number of photo-initiated transformations available to N,C-chelate boron compounds (*e.g.* **A**, Scheme 1), wherein readily accessible precursors are converted to novel B,N-embedded systems such as azaboratabisnorcaradienes (**B**),[10a,b] B,N-1,4,6-cyclooctatrienes,[10c] azaborabenzotropilidenes,[10d] and 4b*H*-azaborepins (**C**),[10e,f] each of which possesses interesting properties and would be very difficult to prepare by traditional synthetic protocols. In many of these examples, the photo-generated boriranes **B** act as reactive intermediates, enabling subsequent transformations to more stable isomers. Based on this idea of "storing" energy within boriranes to encourage new reactivity, we hypothesized that by pre-organizing appropriate functionalities near the three-membered boracycle, it may be possible to tune their reactivity towards specific, desirable transformations involving both borirane and installed functionality.



Scheme 1. Reactivity of chiral boron systems (a) and (b).

To this end, we designed a series of chiral, chelate boron systems bearing two different aryl groups at boron, consisting of the necessary mesityl anchor,[10e] various chelate units, and a range of 2-heterocycles (**1** – **10**, **1′** in Scheme 2). The anticipated regioselective borirane formation[10e] on the heterocycles would place their C2–X bonds in close proximity to the borirane ring (**a**) and potentially facilitate C–X bond activation through either photochemical borylene insertion[11] or heterocycle rearrangement.[12] In this way, a variety of base-stabilized X-borinines (X = O, S; **b**) could be conveniently prepared. It is known that replacing aromatic C=C bonds with B–N bonds leads to significant changes in molecular properties, lending such species to a variety of new applications including optoelectronic materials and medicines.[13] As a result, synthetic methodologies for accessing azaborinines are well developed. By comparison, oxa- and thiaborinines remain rare and underdeveloped,[14] which furthers the need for new methods to prepare such systems. Indeed, the new chiral boron compounds undergo the targeted phototransformation, yielding rare, chiral *N,B,X*-heterocycles (**b**) with interesting photophysical properties.

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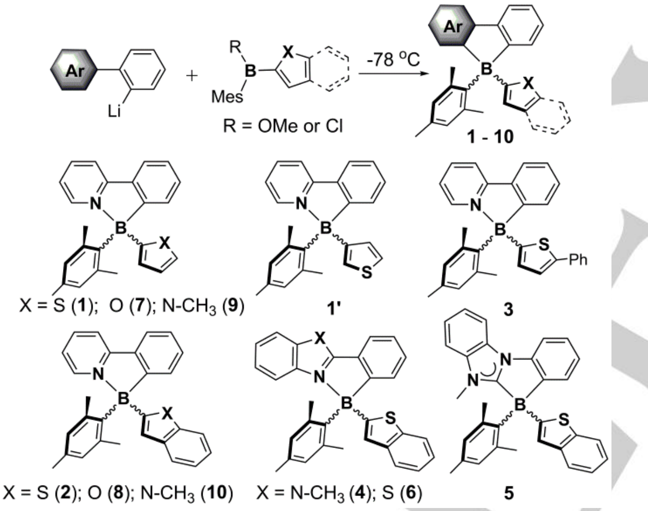
Labile B←N bonding in 1,2-(benzo)oxaborinines allows further photoisomerization, resulting in *N,B,O*-embedded 4a,12b-dihydrotriphenylene derivatives. CASPT2 calculations suggest that heterocycle ring-opening/migration is responsible for the formation of the *N,B,X*-heterocycles, as well as implicate a common biradical intermediate connecting the excited-state reaction pathways leading to **a** and **b**. The details of this rare phototransformation and mechanistic insight are presented herein.

The chiral boron compounds **1** – **10** were prepared in low to moderate yields (~5-50%) by a modified procedure,[10e] employing B(R)(Ar)Mes and lithiated chelating ligands (see Scheme 2 and Supporting Information). In addition, compound **1′**, an isomer of **1**, was also prepared. All compounds were fully characterized by ^{1}H, ^{13}C, and ^{11}B NMR and HRMS spectroscopic analyses. The crystal structures of **2**, **5**, **6**, and **1′** were determined by single crystal x-ray diffraction analysis and have bond lengths around the B atom similar to those of **A** (see SI).[10e,f] These compounds all have strong and broad absorption bands ranging from 300-405 nm (ε = 8000 – 20000 cm^{-1} L^{-1} mol), and fluoresce weakly in the visible region (λ_{em} = 400 – 570 nm, Φ_{fl} = ~ 0.05 – 0.30) due to their charge transfer (CT) S_1 transition from heterocycle (π, HOMO) to chelate backbone (π*, LUMO).[10]



Scheme 2. Synthesis of compounds **1** – **10** and **1’**.

Irradiation of **1** or **2** with 365 nm light initiates a two-step phototransformation as illustrated by the ^{1}H NMR tracking experiment of **2** shown in Figure 1. As **2** is consumed, two sets of new resonances appear. From the singlet at ~1.2 ppm, it is clear that one of the products is **2a**, where regioselective borirane formation has occurred on the 2-benzothienyl ring. Notably, **2a** is only detected as the minor product after each irradiation interval, with the major product being the base-stabilized 1,2-benzothiaborinine **2b**. Further irradiation converts all of the remaining **2** and **2a** to **2b** cleanly and quantitatively. The ^{11}B chemical shift (1.8 ppm) of **2b** is similar to that of **2** (2.6 ppm), indicating a tetrahedral environment around boron. **2b** is air-stable, with its structure first established by 2D NMR (see SI) and subsequently confirmed by x-ray crystallography (Figure 2).

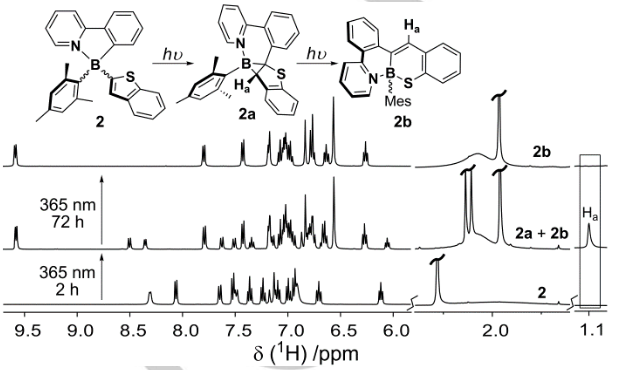


Figure 1. ^{1}H NMR spectra showing the conversion of **2** to **2b** (20 mg in 0.4 mL of C_6D_6) with irradiation at 365 nm.

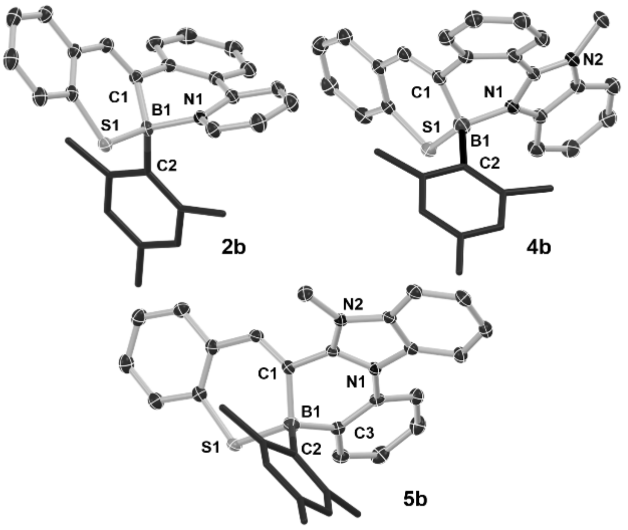
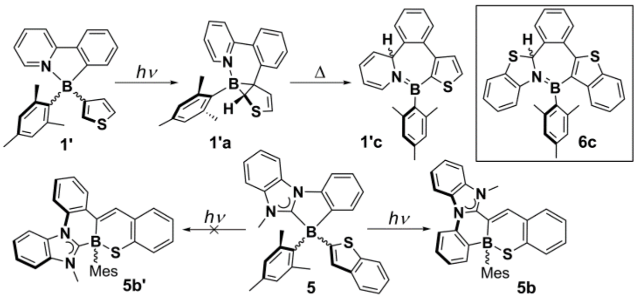


Figure 2. Crystal structures of **2b**, **4b**, and **5b** with 35% thermal ellipsoids.

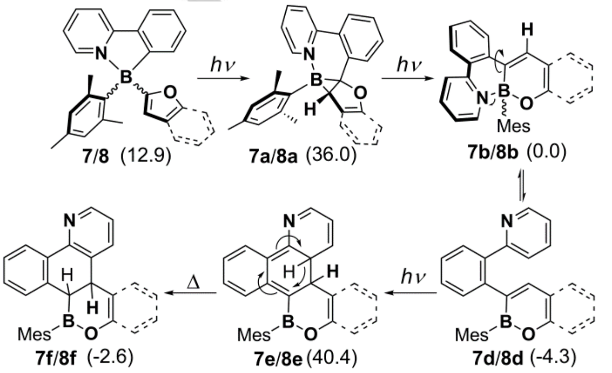
The crystal structure of **2b** confirms the chiral boron atom, which has formally inserted into the C–S bond of benzothiophene. Coordination of the py group decreases the B1–S1 and B1–C1 bonds of 1,2-benzothiaborinine (1.920(2) and 1.590(2) Å, respectively) relative to base-free 1,2-thiaborinines.[14c] To the best of our knowledge, **2b** represents the first example of heteroaromatic C–S bond activation by a main-group system, as well as a previously unknown 1,2-benzothiaborinine derivative. Compound **1** undergoes a similar structural change as does **2**, however, continued irradiation leads to the decomposition of **1b** (see Figure S3C). Control experiments established that the **1**/**2** to **1b**/**2b** transformation occurs *via* the excited state of **1**/**2**, and is not a thermal process (see SI). Due to concomitant formation of two photoproducts, quantum yields of isomerization could not be determined. The importance of boron and C2–S bond proximity in **1**/**1a** and **2**/**2a** was confirmed by the photoreaction of **1‘** (Scheme 3), which follows that of **A** → **C** in Scheme 1.[10e,f] Therefore, the C2–B connectivity in **1**/**1a** and **2**/**2a** plays a critical role in facilitating the photogeneration of **1b** and **2b**, which is elucidated in the computed reaction pathway for **1** to **1b**.



Scheme 3. Reactivity of **1’** and **5**, and the structure of **6c**.

To establish the scope of this new photoreaction, compounds **3** – **5** bearing a 2-(5-phenyl)thienyl or 2-benzothieyl substituent and different chelate backbones were studied. Similar to **1** and **2**, irradiation of **3** at 365 nm yields **3b** quantitatively (see Figures S3S –S3W), establishing that substituted 1,2-thiaborinine derivatives can be prepared by this approach. Unlike **1b**, compound **3b** is stable towards irradiation, allowing its quantitative isolation. The benzimidazole and NHC functionalized **4** and **5** convert to their respective products **4b** and **5b** quantitatively, which were both characterized by NMR and x-ray diffraction (see SI and Figure 2). While **4b** shares structural features with **2b**, the connectivity in **5b** is unusual in that the C2 atom of benzothienyl is bound to the carbon atom of the NHC with a C–C bond length of 1.449(4) Å. This implies that the initial C–C bond formation in the phototransformation occurs regioselectively at the NHC instead of phenyl, which leads to the product **5b′** shown in Scheme 3, and is contrary to our previous observations in related B(NHC-Ph)Mes$_2$ systems where C–C bond formation is selective for the phenyl ring.[11] Although the origin of this discrimination is not understood, the resulting bonding arrangement in **5b** is rather unique, as it contains a 1,4-azaborinine unit and has a more pronounced zwitterionic character compared to **2b** and **4b** (*e.g.* its B–C/B–S bonds are considerably longer). Attempts to decouple the internal donor from its 1,2-benzothiaborinine by utilizing a weaker donor (**6**) gave **6c** after irradiation (Scheme 3, see SI) due to the low aromaticity of the thiazolyl ring.[10c] Furthermore, reactions of **2b** with external Lewis or Brønsted acids (BF$_3$ or [(Et$_2$O)$_2$H][BAr$^F{}_4$]) were unsuccessful, perhaps due to strong B←N coordination (see Figure S3M for V.T. ^{11}B NMR).

The possibility of activating other aromatic C–X bonds (X = O or N) was also explored with 2-furyl (**7**), 2-benzofuryl (**8**), *N*-methyl-2-pyrrolyl (**9**), and *N*-methyl-2-indolyl (**10**) at boron. Compound **7** behaves similar to **1** and **2** when irradiated at 365 nm, initially forming its dark isomer **7a** and base-stabilized 1,2-oxaborinine **7b**. Addtionally, a third new species appears with time (**7f**, Scheme 4) and was isolated quantitatively. **7f** was determined to be 4a,12b-dihydro-benzo[*h*][1,2]-oxaborinino[4,3-*f*]quinoline by 2D NMR experiments (see SI), where the two inner H-atoms have a *trans*-configuration and large ^3J coupling constant (~18 Hz). Control experiments indicated that **7f** is generated *via* a photo- process (see Figure S3ZW), likely according to the sequence shown in Scheme 4. **7b** exhibits weak B←N coordination (^{11}B = ~20 ppm) due to O-atom lone pair delocalization with boron, causing the unbound form (**7d**) to be more stable (based on DFT calculated energies). **7d** structurally resembles *o*-terphenyl derivatives which are known to undergo conrotatory photocyclization.[15] The photocyclized product *trans*-4a,4b-dihydrotriphenylene **7e** is unstable[15] and undergoes an H-shift forming the more stable 4a,12b-dihydrotriphenylene isomer **7f**, clearly driven by the re-aromatization of py and ph. The retained *trans*-configuration of the inner H-atoms in **7f** is consistent with a suprafacial [1,5]-H shift as per the Woodward-Hoffman rules.



Scheme 4. Reactivity of **7/8** and the relative DFT computed energies (kcal/mol) of **7**–**7f** (B3LYP/6-31G*).

In contrast to **7f**, which was generated and isolated as a pure substance, compound **8** yields a mixture of **8a**, **8b**, **8c** (analogue of **1′c**), and **8f**, attributable to the slow photo-conversion of **8a** to **8b** and the relatively high internal reaction temperature caused by long UV exposure times.[10e] Attempts to obtain the fully aromatized *N,B,O*-triphenylene analogues *via* oxidative dehydrogenation using air or I$_2$ were unsuccessful,[15] resulting in a variety of unidentifiable decomposition products. *N*-heterocycle substituted **9** and **10** show the least photoreactivity of the entire series, with **9** being completely inert. **10** does show evidence for regioselective borirane formation on the indole substituent (see SI), however, prolonged irradiation results predominantly in decomposition. Photoproducts **2b** – **5b** all display strong emission in the solid state (blue-green to orange-red, see Table S5A) due to CT from HOMO (π-thiaborinine) to LUMO (π*-chelate), indicating the tunable photophysical properties of such systems.

To gain a better understanding of the dynamics following excitation at 365 nm, *ab initio* calculations combining the CASPT2//CASSCF method with DFT and TD-DFT were employed to study the phototransformation of **1** (see Figure 3 and SI). Excitation of **1** at 365 nm populates its S$_1$ state, which is of π-thienyl (HOMO) → π*-(ppy) (LUMO) CT character. Comparing S$_0$ and S$_1$ minimum structures at the CAM-B3LYP level of theory, the B–C$_{Ph}$ bond is weakened (1.62 *vs.* 1.66 Å; see SI).

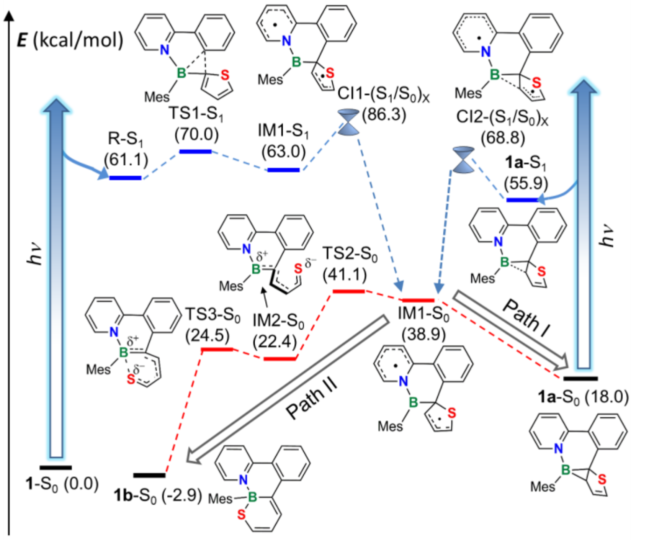


Figure 3. Computed reaction pathways of the **1** to **1b** transformation based on CASPT2 energies. IM = intermediate; CI = conical intersection.

At the CASSCF/6-31G* level of theory, structural relaxation following excitation leads to the S$_1$ state minimum (**1**-S$_1$) with a B–C$_{Ph}$ bond of 1.64 Å. Along the B–C$_{Ph}$ bond stretching direction, a transition state (TS1-S$_1$) on S$_1$ was located, residing 8.9 kcal/mol above **1**-S$_1$. At TS1-S$_1$, simultaneous B–C$_{Ph}$ bond (2.09 Å) cleavage and C$_{Ph}$–C$_{thienyl}$ bond (2.45 Å) formation is noted. The resulting intermediate IM1 exhibits biradical character in both its S$_1$ and S$_0$ states with the two singly occupied molecular orbitals (SOMOs) localized on thienyl and pyridyl (see Table S7C). The accessible conical intersection between excited and ground state, CI1-(S$_1$/S$_0$)$_X$, facilitates decay from IM1-S$_1$ to IM1-S$_0$. From IM1-S$_0$ there are two distinct reaction paths, leading to either the borirane isomer **1a**-S$_0$ (path I) or final product **1b**-S$_0$ *via* a thienyl ring opened intermediate IM2-S$_0$ (path II). Reaction path I from IM1-S$_0$ to **1a**-S$_0$ is barrierless, indicating that **1a**-S$_0$ is the kinetic product while **1b**-S$_0$ is the thermodynamic product (ΔE ~ 21 kcal/mol). Interestingly, excitation at 365 nm can also populate the S$_1$ state of **1a**, which is close to a second conical intersection, ultimately allowing access to IM1-S$_0$ from **1a**. Along with the small TS2-S$_0$ barrier (2.2 kcal/mol), this explains the quantitative formation of **1b**, as any **1a** formed during the reaction can be converted to **1b**-S$_0$ *via* the excited state.

In summary, we have demonstrated that appropriate functionalization of chiral chelate boron systems can lead to photoactive molecules capable of undergoing specific chemical bond activation. The resulting products represent the first examples of base-stabilized 1,2-(benzo)thiaborinines and 1,2-(benzo)oxaborinines, with the former displaying interesting solid state emission properties. The labile nature of B←N coordination in oxaborinines allows for the photogeneration of 4a,12b-dihydro-benzo[*h*][1,2]-oxaborinino[4,3-*f*]quinolines *via* electro-cyclization and [1,5]-H migration. Mechanistic excited-state calculations indicate that biradical species are key intermediates in the photogeneration of thiaborinines and boriranes. These results provide a promising strategy for the activation of chemical bonds *via* reactive excited state intermediates, and pave the way for new developments in organoboron photochemistry.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: Photochemistry • Photoisomerization • C–X Bond Cleavage • Boron Insertion • Boron chemistry

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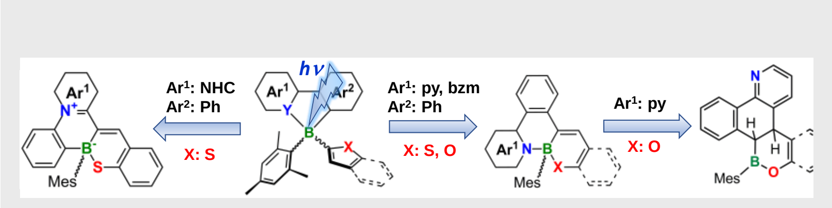

Photoisomerization of chiral chelate boron compounds generates rare chiral *N,B,X*-heterocycles quantitatively *via* boron insertion into a C-X bond.

S. K. Mellerup, C. Li, J. Radtke, X. Wang, Q.-S. Li, and S. Wang**

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Photochemical Generation of *N,B,X*-Heterocycles via Heteroaromatic C–X Bond Scission (X = S, O) and Boron Insertion