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BN Isosteres of Indole

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Abstract

Indole is a heterocycle of great importance to biological systems and materials applications. Synthesis of indole and its derivatives has been a major focus of research for over a century. BN/CC isosterism is an emerging strategy for expanding the structural diversity of indole-based compounds. Two classes of BN indoles have been reported to date: the well-studied “external” BN indoles (or 1,3,2-benzodiazaborolines), and the recently reported “fused” BN indoles. This perspective presents the history of both classes of indole isosteres, with a general overview of their synthesis, functionalization, and properties.

1 Introduction

BN/CC isosterism is emerging as a means of altering the electronic structure of classic organic motifs with minimal disruption to the geometric shape of the structure being mimicked. The past half century has witnessed a slow but continuous development of isoelectronic BN substitutions of CC bonds found in sp^3 ,¹ sp^2 (olefin),² and sp^2 (aromatic) skeletons,³ with renewed attention in the past two decades. In particular, BN isosteres of aromatic molecules have captured the imagination of chemists seeking to expand the diversity of classic arene structures without drastically changing the shape of the resulting molecules.

BN arenes include 1,2-analogs in which a C=C bond has been replaced by an isoelectronic BN bond, as well as 1,3⁴ and 1,4 isomers.⁵ In 1,2-substituted BN arenes, such as 1,2-dihydro-1,2-azaborines, the nitrogen lone pair interacts directly with the empty p orbital of boron. In 1,3 and 1,4 analogs, the nitrogen and boron atoms communicate electronically through one or two sp^2 carbon atoms, respectively.

BN isosteres of many “classic” arenes have been studied and recently reviewed.⁶ An important class of aromatic compounds is the family of indoles. Indole **1** (i.e., benzopyrrole) consists of a pyrrole ring fused to a phenyl ring, resulting in a 10 π -aromatic system in which the nitrogen lone pair is part of the π electron system (Figure 1). Indole is one of the most ubiquitous heterocycles in biological systems. Indole-based molecules have been incorporated into dye-sensitized solar cells,⁷ OLED chromophores,⁸ and hydrogen storage materials.⁹ According to a recent review “the synthesis and functionalization of indoles has been the object of research for over 100 years.”¹⁰ Not surprisingly, chemists have pursued BN indoles as an avenue for expanding the chemical space of indole-based structures through “elemental isosterism”.

To date, two classes of BN-substituted indoles have been synthesized. The “external” BN indoles **2**, more commonly known as 1,3,2-benzodiazaborolines, are bicyclic aromatic heterocycles in which a BN pyrrole (better known as a 1,3,2-diazaboroline) is fused to a benzene ring (Fig. 1).¹¹ 1,3,2-benzodiazaborolines were first reported by Goubeau in 1957 and are the first example of a carbon(C)-boron(B)-nitrogen(N)-containing arene.¹² The second class of BN indoles is the “fused” BN indoles **3**, first reported in 2010 (Fig. 1).¹³

The early contributions to the chemistry of 1,3,2-benzodiazaborolines will first be reviewed, followed by sections devoted to 1) the exploration of the common methods of synthesis and functionalization of these heterocycles and to 2) potential applications. The applications can be divided into two categories: a) development of boryl ligands for organometallic chemistry and b) exploration of the optoelectronic properties of derivatives of **2**.

The scope of this review is not intended to be comprehensive, but rather a tutorial review devoted to survey both currently known classes of BN indoles, and provide a comparison to their carbonaceous counterparts. The body of work concerning CBN arenes other than BN indoles is beyond the scope of this review. Furthermore, polycyclic aromatic compounds containing a BN indole motif, as well as polymeric materials containing this structure will not be discussed.

2 “External” BN Indoles, or 1,3,2-Benzodiazaborolines

2.1 Early Explorations of 1,3,2-Benzodiazaboroline Chemistry

Almost every synthesis of 1,3,2-benzodiazaborolines proceeds by condensation of a 1,2-phenylenediamine **4** with a borane **5** (Scheme 1, eq 1), including the initial synthesis by Goubeau.¹² Reaction of phenylenediamine with trimethylborane provided the first 1,3,2-benzodiazaboroline **8**, the B-Me derivative in 60% yield (Scheme 1, eq 2).

A year later, Dewar reported the synthesis of the B-Ph derivative **10** by condensing 1,2-phenylenediamine **6** with phenylboron dichloride **9** (Scheme 1, eq 3). Dewar was one of the first to recognize the potential of elemental isosterism as a means to access new aromatic heterocycles. In the same report, BN isosteres of benzofuran and benzothiophene were synthesized in a similar manner.¹⁴

Soloway prepared a variety of derivatives by condensing aryl and a lkylboronic acid derivatives **5** with substituted 1,2-phenylenediamines **4** in refluxing xylenes (Scheme 1, eq 1; R = alkyl, aryl; X= OMe). The potential application of BN derivatives as surrogates of natural arenes in boron neutron capture therapy (BNCT) was recognized.¹⁵ Letsinger serendipitously prepared BPh 1,3,2-benzodiazaboroline **10** in an attempt to accelerate amide formation between the ethyl tartrate ester of benzenboronic acid **11** and phenylenediamine **6** (Scheme 2).¹⁶ Probing the reaction further, they noted that attempts to form BN bonds from phenylboronic acid **13** and either ethylenediamine or aniline did not yield the

corresponding BN compounds even at high temperatures. On the other hand, the reaction between phenylboronic acid **13** and phenylenediamine **6** proceeds readily even at room temperature. They conclude that the “unusual reactivity of phenylenediamine is related to its particular geometry and the stability of the ring system which is formed”. This is one of the earliest observations of potential aromatic stabilization in CBN arenes. Letsinger used this observation as a way to characterize boronic acids in further work, by preparing stable derivatives of sensitive boronic acids such as **14** (Scheme 2). This led to the first example of a conjugated polycyclic BN indole **15** connected by a phenylethynyl linkage.¹⁷

In 1960, Hawthorne demonstrated the synthesis of alkyl 1,3,2-benzodiazaborolines **17** from phenylenediamine **6** and trimethylaminealkylboranes **16** (Scheme 3) with concomitant release of H₂ and trimethylamine.¹⁸ The parent 1,3,2-benzodiazaboroline **18** was synthesized by Goubeau in 1964 by condensation of phenylenediamine hydrochloride **6**•HCl with sodium borohydride (Scheme 3).¹⁹ Many other examples of 1,3,2-benzodiazaborolines with various boron and nitrogen substituents were synthesized using the general strategy of condensing a phenylenediamine **4** with a substituted borane **5** (Scheme 1, eq 1).

A paucity of development of 1,3,2-benzodiazaboroline chemistry occurred from the late 1960's until the late 1980's, when interest was renewed in these compounds. With the early contributions outlined, we will now focus on general strategies of functionalization of 1,3,2-benzodiazaborolines.

2.2 Functionalization at Nitrogen

Two primary strategies for functionalization at nitrogen are utilized: 1) begin with an *N*-substituted *o*-phenylenediamine, such as the diethyl *o*-phenylenediamine **19** used in the synthesis of **20** (Scheme 4, top equation);²⁰ 2) functionalize at nitrogen after condensation with boron, such as the lithiation/silylation sequence employed in the synthesis of **23** (Scheme 4, bottom equation).²¹ Strategy 1 seems to be the preferred method, as it avoids the use of potentially harsh conditions associated with *N*-substitution in the presence of sensitive boron-containing functionalities. The second strategy is viable if the transformations are compatible with the BN motif, and is employed if the nitrogen substituent is not compatible with the Lewis acidic borane being used.

2.3 Functionalization at Boron

More attention has been given to boron functionalization, perhaps because this is where the unique properties of 1,3,2-benzodiazaborolines are derived from. The strategies available for boron functionalization are similar to those used for substitution at nitrogen: either functionalize before heterocycle formation, or after. A variety of boron precursors **5** can be condensed with phenylenediamines **4** (Scheme 1), provided they have compatible leaving groups, which include halides, amides, alkoxides, hydroxides and even methyl groups. The boron precursors can be substituted with aryl, alkyl, alkenyl, alkynyl, and metallo groups, or one of the aforementioned leaving groups. One interesting example is the condensation of the *N,N'*-dimethylphenylenediamine **24** with the boryl osmium complex **25** to afford the osmium-bound 1,3,2-benzodiazaboroline **26** (Scheme 5).²² A bis-substituted thiophene derivative **28** can be synthesized from the bis-dibromoborylthiophene **27** with *N,N'*-diethylphenylenediamine **19** in the presence of triethylamine.

Boron substitution after heterocycle formation is also a widely used strategy. With a labile group such as bromide on 1,3,2-benzodiazaboroline **29** and **20**, nucleophiles such as group 14²³ and carbon-based²⁴ lithiates and can be added to boron (Scheme 6). If the leaving group on boron is a halide, silver-based nucleophiles such as silver cyanide²⁰ are useful for

creating cyanide-substituted heterocycles **32**. Additionally, bromide substituted 1,3,2-benzodiazaborolines **20** can be reduced with alkali metals such as Na/K²⁰ to afford the diboryl species **33**. Attempts to further reduce **33** to the anion with Na/K were unsuccessful.

The first well-characterized boryllithiums were created from 1,3,2-diazaborolines and are capable of acting as boron nucleophiles.²⁵ The corresponding 1,3,2-benzodiazaborolines boryllithiums were prepared analogously via a reduction of B–Br bond in the presence of elemental lithium (Scheme 7).²⁶

Boryl anions are currently a subject of great interest, due to their unusual electronic structure. All other first row lithiates (i.e., LiF, LiOR, LiNR₂, LiCR₃) have a complete octet, whereas boryl lithiates only have six valence electrons, making them isoelectronic with carbenes. The diazaboryl lithiates were found to have a similar polarity to alkyl lithiates, making them strong nucleophiles. In addition to their theoretical novelty, stable boron nucleophiles have the potential to be extremely useful synthons for chemists. Boron moieties traditionally have electrophilic character, and rely on nucleophilic substitution for functionalization. Nucleophilic boron centers open the door to a much wider array of 1,3,2-benzodiazaboroline-containing structures.

The benzodiazaboryllithium complex **35**•(THF)₂ containing two THF solvent molecules was characterized by X-ray crystallography (Fig. 2). The structural characteristics of **35**•THF are very similar to an analogous carbene **37**, with almost identical bond angles at the nucleophilic center (NBN **35**•(THF)₂ = 100.0(3)° vs. NCN **37** = 103.8(2)°) and an elongated BN bond (~0.1 Å) resulting from boron's larger atomic radius. The CC and CN bonds of **35**•(THF)₂ range from 1.38–1.42 Å, and the ring system is highly planar, consistent with aromatic delocalization. The BN bonds are 1.474 Å long, slightly longer than in other 1,3,2-benzodiazaborolines.²⁶

2.4 Development of Boryl Ligands for Organometallic Chemistry

The interactions of 1,3,2-benzodiazaborolines with transition metals is a burgeoning field. Construction of 1,3,2-benzodiazaboroline-metal complexes follows the aforementioned strategies for boron functionalization: 1) form the B–M bond before heterocycle formation as in the synthesis of osmium complex **26** (Scheme 5), or more frequently, form the B–M bond from the 1,3,2-benzodiazaboroline with a labile group on boron, such as H, halide, or cyano ligands via oxidative addition. An example of the latter approach is the addition of 1,3,2-benzodiazaboroline **29** to platinum complex **38** (Scheme 8).²³

Organometallic transformations involving 1,3,2-benzodiazaboroline-metal intermediates have mostly been limited to borylation-type reactions. Examples include hydroboration (Scheme 9, eq 1),²⁷ cyanoboration (eq 2),²⁸ and carboboration (eq 3)²⁹ reactions. The 1,3,2-benzodiazaboroline substrate is a stoichiometric reagent, ultimately forming a B–C bond in the presence of a transition metal catalyst.

Boron-based ligands are strong σ -donors, with better electron-releasing character than the other first row elements (e.g. C, N, O, F). Nozaki recently reported the iridium complex **47** using a tridentate PBP ligand **46** containing a 1,3,2-benzodiazaboroline core (Scheme 10).³⁰ Complex **47** has a longer Ir–Cl bond than the corresponding PCP pincer complex, indicative of the stronger σ -donor ability of the boryl ligand compared to carbon. Such boryl complexes may soon begin to find broader application in organometallic chemistry due to their unique properties.

2.5 1,3,2-Benzodiazaborolines as Optoelectronic Materials

1,3,2-benzodiazaborolines have received much recent attention as new building blocks for optoelectronic materials. By incorporating 1,3,2-benzodiazaborolines into common conjugated structures using the previously discussed functionalization strategies, Weber et al. were able to make blue fluorescent chromophores such as **48**, in which 1,3,2-benzodiazaborolines are serving as end groups linked by different types of bridges (Scheme 11, top).³¹ Such chromophores have good emission quantum yields, high extinction coefficients, and were all analyzed structurally by XRD. The authors report shorter exocyclic B-C bond lengths for thiophene-substituted chromophores compared to phenylene spacers, resulting in better π -overlap, but the phenyl-based molecules had higher quantum yields. The same authors performed a similar study on arylethynyl systems containing 1,3,2-benzodiazaborolines (Scheme 11, bottom).³² These compounds were all highly fluorescent, with quantum yields ranging from 0.89–0.99 in the violet-blue region, with the SMe derivative being the least fluorescent. In contrast to other conjugated systems with sp^2 boron centers, such as $-\text{BAr}_2$, 1,3,2-benzodiazaborolines appear to act as π -electron donors. The HOMO in these compounds is largely benzodiazaborolyl based whereas the LUMO is localized in the bridging moiety. The absorption maxima of these materials are reproduced well by TD-DFT computations (B3LYP/6–31G*), and arise from strong, low energy HOMO–LUMO transitions. Gas-phase UV photoelectron spectra of the series of 2-arylethynyl-1,3,2-benzodiazaboroles **49** have been experimentally measured.³³ The determined first ionization energies of these benzodiazaboroles are in the order $-\text{NMe}_2 < -\text{OMe} < -\text{Me} < \text{H} \sim \text{SMe}$, consistent with the NMe_2 substituted derivative being the most electron rich of the series. In both studies, the 1,3,2-benzodiazaboroline rings were highly planar, with CC and CN bonds in the ranging from 1.39–1.41 Å, consistent with aromatic delocalization. BN bonds ranged from 1.43–1.44 Å, also consistent with aromatic delocalization.

Maruyama et al. reported similar compounds by condensing phenylenediboronic acids **51** with prefunctionalized phenylenediamines **50** to yield 1,3,2-benzodiazaborolines **52** linked by a phenylene spacer³⁴ (Scheme 12). The authors point out that 1,3,2-benzodiazaborolines are well suited to application in optoelectronic materials because in contrast to many other boron-containing molecules, 1,3,2-benzodiazaborolines are quite stable to air and water and are readily prepared. Like Weber's fluorophores, these compounds emit in the blue region and have high quantum yields ($\phi = 0.66$ –0.99).

One novel application of 1,3,2-benzodiazaborolines that takes advantage of their optical properties is the construction of resorcin[4]arene cavitands **54** with 1,3,2-benzodiazaboroline walls (Scheme 13).³⁵ Encapsulation of a quaternary ammonium cationic guest causes a dramatic blue shift in the fluorescence emission of the capsule (from 404 to 357 nm), imparting sensing abilities to this assembly that differ from the normal Lewis base-sensing abilities usually associated with boron-containing compounds. The authors report association constants as high as $K_a > 10^9 \text{ M}^{-1}$. Given the abundance of desirable optical properties as well as facile assembly and stability, 1,3,2-benzodiazaborolines may become a staple for chemists seeking to create new optoelectronic materials.

3 “Fused” BN Indoles

3.1 Synthesis of “Fused” BN Indoles

To date, three *N*-substituted “fused” BN indoles **3** have been synthesized ($\text{R} = t\text{-Bu}$, TBS, H), all following the same general strategy. First, an *in situ* generated allylboron dichloride is condensed with an *N*-protected *N'*-allylethylenediamine **55** in the presence of base to afford the five-membered heterocycle **56** (Scheme 14). Ring-closing metathesis forms the

bicyclic BN indole precursor **57**. High temperature oxidative dehydrogenation in the presence of Pd/C catalyst provides the fully aromatic *N*-protected “fused” BN indole **3**.

The first “fused” BN indole was the *N*-*t*-Bu BN indole **3b**, reported by Liu and co-workers in 2010.¹³ This synthesis proceeds via the aforementioned strategy, with condensation of *in situ* generated allylboron dichloride with *N*-*t*-Bu-*N'*-allylethylenediamine **58** to afford heterocycle **59** in 50% yield (Scheme 15). Ring-closing metathesis with either 6% Grubbs' generation 1 catalyst **a** or 4% Schrock's catalyst **b** affords the bicyclic product **60** in 51% or 79% yield, respectively. Oxidative dehydrogenation with 30 mol% Pd/C in refluxing decane affords the fully aromatic *N*-*t*-Bu BN indole **3b** in 32% yield.

In 2011, Liu and coworkers reported the *N*-*t*-butyldimethylsilyl (TBS) “fused” BN indole **3c**, which was deprotected to provide the parent BN indole **3a**.³⁶ Synthesis of **3c** follows the general strategy, beginning with protection of *N*-allylethylenediamine to provide *N*-TBS-*N'*-allylethylenediamine **61** in 87% yield (Scheme 16). Condensation of *in situ* generated allylboron dichloride with *N*-TBS-*N'*-allylethylenediamine **61** affords heterocycle **62** in 57% yield. Ring-closing metathesis with 4% Grubbs' generation 1 catalyst provides the bicyclic **63** in 55% yield. Oxidative dehydrogenation with 30 mol % Pd/C in perfluorodecalin at 185 °C affords the fully aromatic **3c** in 26% yield. Removal of the *N*-TBS group with tetrabutylammonium fluoride (TBAF) provides the parent **3a** in 55% yield. Interestingly, all non-aromatic BN indole precursors are highly air and water-sensitive, requiring purification by air-free distillation. Upon aromatization, the “fused” BN indoles **3a–3c** exhibit considerable air and water stability compared to their precursors, allowing purification via silica gel chromatography.

3.2 Reactivity of “Fused” BN Indoles

Indoles are known to exhibit high nucleophilicity at the 3-position in electrophilic aromatic substitution (EAS) reactions. The essential amino acid tryptophan is biosynthesized from L-serine and indole via an enzymatic EAS-type reaction.³⁷ Attempted removal of the *N*-*t*Bu group in BN indole **3b** under acidic conditions yielded a single crystal of trimer **64** (Fig. 3) indicating that “fused” BN indoles can undergo indole trimerization, also an EAS-type reaction. After this realization, other electrophiles were surveyed (Table 1), demonstrating that “fused” BN indole **3b** reacts with the same regioselectivity towards electrophiles as organic indoles. A Mannich reaction with dimethyliminium chloride provides the grammine analog in 53% yield (Table 1, entry 2). Friedel-Crafts acylation catalyzed by diethylaluminum chloride affords the acylated product **65** in 27% yield (Table 1, entry 5; Fig. 3).

A competition study between **3b** and its organic analog **66** in an EAS reaction indicates that **3b** is significantly more nucleophilic. One equivalent of **3b** and **66** were combined in an NMR tube, and 0.5 equivalents of dimethyliminium chloride was added. ¹H NMR indicated that the 3-substituted BN indole **67** was the exclusive EAS product, with **66** left intact (Scheme 17).

The acid/base chemistry of parent **3a** was also investigated. A series of ¹H NMR bracketing experiments indicated that the *pK_a* of **3a** is around 30, roughly nine orders of magnitude less acidic than natural indole. The *N*-H of indole is a critical component to the reactivity of indole-containing biomolecules,³⁸ and this study indicates significant differences between the *N*-H of natural indole and “fused” BN indole **3a**.

3.3 Structural Studies

XRD structures of two EAS products of **3b** were obtained: the previously mentioned trimerization product **64**, and the Friedel-Crafts acylation product **65**. Structures **64** and **65** both show a high degree of planarity and bond length homogenization consistent with aromatic delocalization. Comparison of **64** to a similar 3-alkyl indole revealed striking similarities between the two structures. The bond lengths are quite similar, and both structures have a short C2–C3 bond with significant double bond character, which is responsible for much of indole's unique chemistry. The major differences between the two structures is the longer C–B bonds compared to the corresponding C–C bond, which is likely a result of the larger covalent radius of boron.³⁹ The Friedel-Crafts acylation product **65** shows that the N(1)–C(2) (1.363(2) Å), C(2)–C(3) (1.372(2) Å), and the B(1)–N(2) bond distances in **65** are consistent with a significant contribution of structure **65'**.

In the studies of the parent **3a**, crystals suitable for X-ray diffraction were isolated, but were disordered, preventing structural determination. Crystals of natural parent indole **1a** were similarly disordered and had an identical unit cell to crystals of **3a**. XRD studies of π -complexes between electron deficient arenes and **3a** (**3a•Ar**; Ar = ethyl 4-chloro-3,5-dinitrobenzoate) and **3c** (**3c•Fnap**; Fnap = perfluoronaphthalene) allowed structural comparisons to be made between BN indole complexes and the indole picrate complex (**1a•Pic**) (Table 2). The structures of the BN indole complexes (**3a•Ar** and **3c•Fnap**) were extremely similar to the indole complex (**1a•Pic**). All three indoles were highly planar and readily formed nearly parallel π -complexes with their respective electron-deficient arenes. The bond lengths were quite similar, with the exception of a shorter bond 4 and longer bond 9 (Table 2). The shortened bond 4 is consistent with the smaller covalent radius of nitrogen. The longer bond 9 is consistent with a larger covalent radius of boron.

3.4 Electronic and Photophysical Studies

Indoles are known to undergo a single electron oxidation, a critical component to the charge carrying ability of tryptophan in electron transport in proteins.⁴⁰ The parent BN “fused” indole **3a** was characterized by cyclic voltammetry and compared to natural indole **1a**. Indole **1a** had a peak oxidation potential of 1.18 V, while the potential for BN indole **3a** was 1.04 V vs. SCE, consistent with a higher energy HOMO for **3a**.

The photophysical properties of the indole side chain of tryptophan make it one of the principle intrinsic fluorophores in protein fluorescence analysis.⁴¹ A comparison of the optical properties of indole **1a** with BN indole **3a** shows that the absorbance and emission spectra of **3a** are bathochromically shifted with respect to **1a**, consistent with a smaller HOMO-LUMO bandgap for **3a**. Indole's absorbance maximum was found at $\lambda_{\text{max}} = 268$ nm compared to BN indole **3a** at 293 nm in CH₃CN. Indole's emission λ_{em} was found at 315 nm, compared to **3a**'s emission at $\lambda_{\text{em}} = 360$ nm in CH₃CN. Thus, BN indole **3a** displays a larger Stoke's shift (6350 cm⁻¹) than natural indole **1a** (5570 cm⁻¹). The fluorescence quantum yield of **3a** ($\Phi = 0.08$) is lower than that exhibited for **1a** ($\Phi = 0.32$), as is the molar absorptivity ($\epsilon = 6400$ vs 8200 M⁻¹ cm⁻¹, respectively).

Conclusions

1,3,2-Benzodiazaborolines are a well-studied class of BN-substituted indole analogs with a rich history dating back to 1957. After roughly two decades of relative inactivity, these heterocycles are receiving renewed interest. 1,3,2-benzodiazaborolines have evolved from a chemical curiosity to a building block of optical materials and a ligand with unique properties that are just beginning to be unlocked. Despite their isoelectronic and isostructural relationship to indoles, 1,3,2-benzodiazaborolines bear only a cursory resemblance to indole.

The six-membered rings of indole **1** and 1,3,2-benzodiazaborolines **2** are almost identical, but the 5-membered rings are quite different. The CN bonds of **2** are about the same length as indole **1**, but the two BN bonds are about 0.1 Å longer than the corresponding CN and CC bonds of indole, an expected result of boron's larger covalent radius. Additionally, 1,3,2-benzodiazaborolines have an additional mirror plane compared to indole. These heterocycles behave more like a diamine-chelated boron that is stabilized by aromaticity, making them useful for the aforementioned applications. 1,3,2-Benzodiazaborolines lack a C=C bond on the five-membered ring, and therefore cannot participate in electrophilic aromatic substitution (EAS) reactions in the same manner as indole.

The exploration of “fused” BN indoles is just beginning, yet the greater similarity to “natural” indoles has quickly become apparent. “Fused” BN indoles have almost identical structures to indoles, with the expected bond length differences associated with the larger covalent radius of boron. Additionally, they are isosymmetric with indoles and have the same unit cell in the solid state. The EAS reactivity of BN “fused” indoles displays the same regioselectivity as natural indoles, but with greatly enhanced reactivities. Despite their similarities, indoles and “fused” BN indoles have important differences. The *N*-H of the parent “fused” BN indole is significantly less acidic than natural indole and the excitation and emission spectra are bathochromically shifted. Photophysical data as well as CV measurements are consistent with a higher energy HOMO and smaller bandgap for “fused” BN indoles. The similarities in structure and reactivity between “fused” BN indoles and indoles combined with their altered opto-electronic properties may provide new tools for biomedical and materials applications. With only two reports to date, the exploration of “fused” BN indoles is only beginning. More research is needed before the relationship between both classes of BN indoles and their carbonaceous counterpart can be well understood, yet the emerging details present a fascinating story of the nature of structural diversity born from BN/CC elemental isosterism.

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Fig. 1.
Organic indole vs. BN indoles.

35•(THF)₂

Dip = 2,6-diisopropylphenyl

37

Ad = adamantyl

Figure 2.
Structural parameters of benzodiazaboroyllithium complex.

Figure 3.
Structural analysis of EAS products **64** and **65**.

Scheme 1.

General strategy for 1,3,2-benzodiazaboroline construction, and the first examples.

Scheme 2.

Early studies of 1,3,2-benzodiazaborolines by Letsinger.

Scheme 3.
Early routes to 1,3,2-benzodiazaborolines.

Scheme 4.
Functionalization at nitrogen.

Scheme 5.

Boron functionalization before heterocycle formation.

Scheme 6.
Boron functionalization after heterocycle formation.

Scheme 7.
Synthesis of benzodiazaboryl lithium **35**.

Scheme 8. Oxidative addition of a BBr bond to platinum complex **38**.

Scheme 9.

Hydroboration (1), cyanoboration (2), and carboboration (3) using 1,3,2-benzodiazaborolines.

Scheme 10.
Synthesis of boryl iridium pincer complex **47**.

Scheme 11.
1,3,2-benzodiazaboroline-containing fluorophores prepared by Weber et al.

Scheme 12.
Synthesis of chromophores from phenylenediboronic acids.

Scheme 13.
Synthesis of 1,3,2-benzodiazaboroline cavitand **54**.

Scheme 14.
General synthetic strategy for "fused" BN indoles.

Scheme 15.
Synthesis of *N*-*t*-Bu BN indole **3b**.

Scheme 16.
Synthesis of Parent “Fused” BN indole **3a**.

Scheme 17.
Competition experiment probing EAS reactivity.

Table 1

EAS studies of **3b**.

entry	electrophile (E ⁺)	catalyst	3-substituent (E)	yield (%)
1	Br ₂	-		39
2		-		53
3		ZrCl ₄		57
4	CD ₃ OD/D ₂ O	-		39 ^a
5		Et ₂ AlCl		23

^a¹H NMR indicates ~80% deuterium enrichment.

Table 2

Structural analysis of **3a** and **3c** in comparison to **1a**.

Bond	Complex		
	3c•Fnap	3a•Ar	1a•Pic
1	1.444(8)	1.417(7)	1.401(7)
2	1.408(7)	1.369(8)	1.354(9)
3	1.304(9)	1.339(9)	1.304(9)
4	1.403(8)	1.402(7)	1.468(9)
5	1.349(8)	1.367(7)	1.36(1)
6	1.384(10)	1.357(10)	1.42(1)
7	1.392(11)	1.395(11)	1.37(1)
8	1.343(9)	1.361(10)	1.361(9)
9	1.525(9)	1.487(8)	1.378(7)
Bridgehead	1.442(8)	1.423(7)	1.392(7)

3c•Fnap
2:1

3a•Ar
1:1

1a•Pic
1:1