B,N Heteroarenes

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Recent Advances in Azaborine Chemistry

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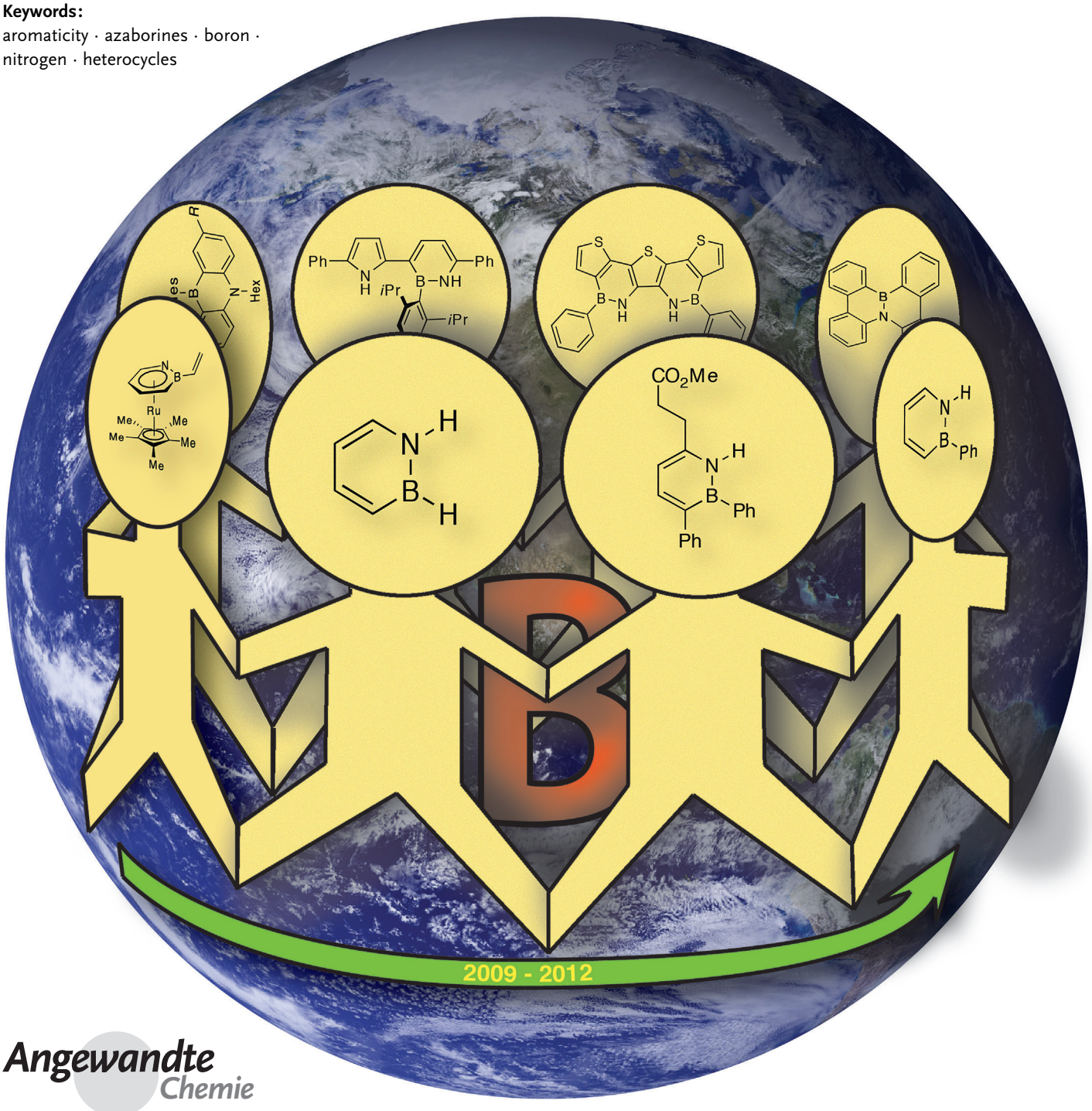
aromaticity · azaborines · boron · nitrogen · heterocycles



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The chemistry of organoboron compounds has been primarily dominated by their use as powerful reagents in synthetic organic chemistry. Recently, the incorporation of boron as part of a functional target structure has emerged as a useful way to generate diversity in organic compounds. A commonly applied strategy is the replacement of a CC unit with its isoelectronic BN unit. In particular, the BN/CC isosterism of the ubiquitous arene motif has undergone a renaissance in the past decade. The parent molecule of the 1,2-dihydro-1,2-azaborine family has now been isolated. New mono- and polycyclic B,N heterocycles have been synthesized for potential use in biomedical and materials science applications. This review is a tribute to Dewar's first synthesis of a monocyclic 1,2-dihydro-1,2-azaborine 50 years ago and discusses recent advances in the synthesis and characterization of heterocycles that contain carbon, boron, and nitrogen.

From the Contents

1. Introduction

Boron plays a crucial role in the field of chemistry. William Lipscomb (1976),[1] Herbert C. Brown (1979),[2] and more recently, Akira Suzuki (2010)[3] have each been recognized with the Nobel Prize for their contributions in boron chemistry. Today, boron-containing compounds act as powerful tools for synthetic chemists.[4–7] In most targeted synthetic applications, however, the element boron typically is not part of the final functional structure. Because of boron's unique electronic structure and its ability to form covalent bonds with carbon, the inclusion of boron in organic structures has recently received significant attention in biomedical research[8] and in optoelectronic materials applications.[9]

An emerging strategy of incorporation of boron in organic structures is the substitution of a C=C bond with an isoelectronic and isosteric B–N unit (BN/CC isosterism). The isoelectronic nature between the B–N and C=C bonding arises from the fact that boron has three valence electrons and nitrogen has five valence electrons, and consequently, a BN unit has the same valence electron count (that is, eight valence electrons) as a corresponding CC unit in which each carbon contributes four valence electrons (Figure 1).

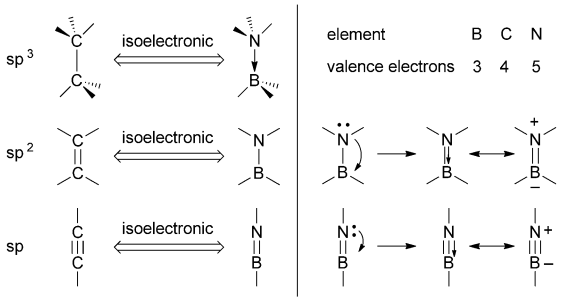

Figure 1. Isoelectronic relationship between CC and BN. The notation illustrated on the left column is used throughout this review.

Despite the same total valence electron count, differences in molecular properties can be expected when replacing an organic CC unit with the corresponding BN unit. The comparison between ethane versus ammonia–borane (AB) and ethene versus aminoborane nicely illustrates this point (Figure 2). Ethane is a volatile gas under standard conditions (bp −89 °C), it has no effective dipole moment,[10] and the C–C bond dissociation energy (BDE) is 90.1 kcal mol^{-1}.[11] In contrast, ammonia–borane is a solid under standard conditions (mp 104 °C); it has a strong dipole moment of 5.2 D;[12] its bond dissociation energy (27.2 kcal mol^{-1}) is significantly smaller than that of ethane.[13] Similar to ethane, the unsaturated ethene is an isolable volatile gas under standard conditions (bp −104 °C); owing to symmetry of the molecule, its dipole moment is also zero;[10] the BDE is 174.1 kcal mol^{-1} of which 109.1 kcal mol^{-1} is due to σ bond contribution and 65 kcal mol^{-1} is due to π contribution.[11,14] On the other hand, the BN analogue of ethene, aminoborane, is a reactive molecule with a strong tendency to polymerize/oligomerize under standard conditions. The parent aminoborane monomer has been characterized in the gas phase by microwave spectroscopy, which indicated an ethene-like planar structure.[15] The BN BDE in aminoborane is 139.7 kcal mol^{-1} of

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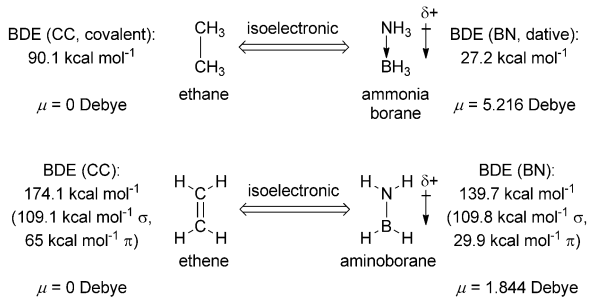

Figure 2. Molecular consequences of BN/CC isosterism.

which 109.8 kcal mol^{-1} is attributed to the σ bond and only 29.9 kcal mol^{-1} to the π contribution.[13] Aminoborane has a dipole moment of 1.84 D,[15] which is significantly lower than that of ammonia–borane.

It has been postulated that the reduced dipole moment in aminoborane (vs. AB) is a result of opposing forces present in the two resonance structures representing aminoborane.[16] Figure 3 illustrates that the dipole that is due to the higher electronegativity of nitrogen (vs. boron) in the left resonance structure opposes the dipole that is due to the formal charges in the right resonance structure as a result of π bonding.

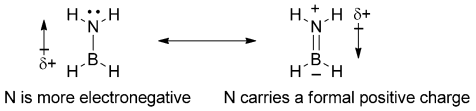

Figure 3. An intuitive explanation for reduced dipole moment in aminoborane versus ammonia–borane.

Among the three possible variants to replace a CC unit with BN (Figure 1), the sp^2-type BN/CC isosterism associated with conjugated aromatic systems has received the most attention. This is because of the ubiquity and wide utility of arene-containing compounds and the increased stability of the corresponding BN-containing isosteres compared to sp^3-type BN isosteres. The potential to dramatically increase the diversity of aromatic structures and tune their electronic properties through BN/CC isosterism have led to a burgeoning interest in this area. The first example of BN/CC isosterism of an arene was reported by Alfred Stock in 1926[17] with the synthesis of borazine (*c*-$B_3N_3H_6$), the inorganic counterpart to the quintessential aromatic compound benzene (*c*-C_6H_6). Similar to benzene, borazine continues to receive significant attention in pure and applied chemistry.[18–23] Although commonly referred to as the "inorganic benzene", the aromatic character of borazine remains controversial to date.[24–27]

Since the pioneering contribution by Stock, the isoelectronic relationship between B–N and C=C has led to the development of aromatic systems partially substituted with boron and nitrogen (carbon–boron–nitrogen (CBN) heterocycles). Though somewhat limited in scope, the first major achievements in the synthesis of CBN heterocycles took place in the 1960s. After several decades of diminished activity in the field, modern synthetic procedures have prompted a resurgence in the study of CBN heterocycles since the turn of the millennium.

This review is a summary of the advances made since the last comprehensive review on the subject by Piers and coworkers in early 2009,[28] and is not an exhaustive history of CBN heterocycle chemistry. For the sake of brevity, and in recognition of the 50th Anniversary of Dewar's first synthesis of a monocyclic 1,2-dihydro-1,2-azaborine, we will focus on aromatic six-membered heterocycles that are isoelectronic with benzene and which contain only one BN substitution. This particular substitution pattern results in three possible isomers, referred to throughout this text as 1,2-azaborine **A**, 1,3-azaborine **B**, and 1,4-azaborine **C** (Figure 4). Examples of each isomer have now been synthesized and will be discussed herein, along with polycyclic compounds containing either the 1,2- or 1,4-azaborine core (1,3-azaborine-containing polycyclic compounds are as yet unknown). Important early work that has been covered in prior reviews will be discussed briefly to provide context for recent developments. The chemistry of boron dipyrrole (BODIPY)[29] and phthalocyanine dyes[30] as

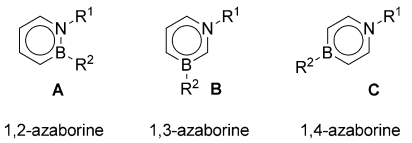

Figure 4. Isomeric forms of singly substituted aromatic CBN heterocycles.

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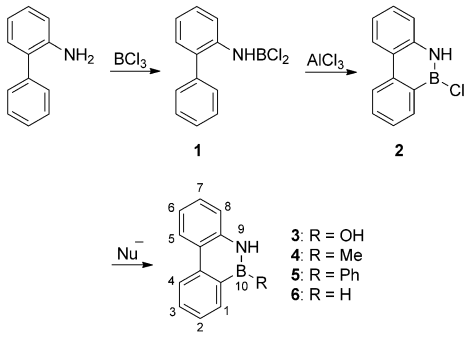
Dr. Adam J. V. Marwitz was born in Laramie, WY, in 1981 and received his B.S. degree in Chemical Engineering from the Colorado School of Mines in 2004. In 2010, he completed his Ph.D. at the University of Oregon under the direction of Professor Shih-Yuan Liu, investigating the chemistry of the 1,2-dihydro-1,2-azaborine heterocycle. He is currently a postdoctoral fellow at the University of Calgary under the supervision of Professor Warren Piers.

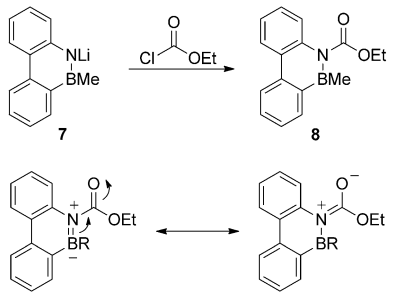
well as substitution with BN units in cluster compounds and graphitic materials,[28] are beyond the scope of this work. This review is organized by research group and will explore how the targeted applications of the products, along with the unique methodologies employed in their synthesis, have contributed to the present wealth and diversity of BN-containing compounds.

2. Pioneering Work

In 1958, Dewar reported the synthesis of the first singly BN-substituted aromatic compounds, 9,10-azaboraphenanthrenes.[31] The reaction of 2-phenylaniline with BCl_3 and $AlCl_3$ gave 9,10-azaboraphenanthrene **2** (Scheme 1), presumably through the Friedel–Crafts cyclization of intermediate **1**. The substitution of various nucleophiles at the reactive B–Cl unit of **2** allowed for the synthesis of several BN-phenanthrene derivatives **3**–**6**. The isoelectronic relationship between BN-phenanthrene **6** and its carbon analogue was explored by UV/Vis spectroscopy. The spectrum of **6** resembles very closely that of phenanthrene in the position of the main absorption bands. However, an increase in the intensity of the α band was observed, an effect that was attributed to removing the molecular orbital degeneracy in the BN-substituted heterocycle. The reactivity of BN-phenanthrene was explored in depth. It was found to undergo electrophilic aromatic substitution regioselectively at the 6 and 8 positions, depending on the electrophile.[32–35] Deprotonation/substitution was possible at the nitrogen position, and tuning the electronics of the nitrogen substituent was found to have an effect on the electronics of the heterocycle as a whole. For example, the N-acyl substituted compound **8** rapidly oxidized when exposed to air, in sharp contrast to other derivatives, which were quite air-stable (Scheme 2).[36]

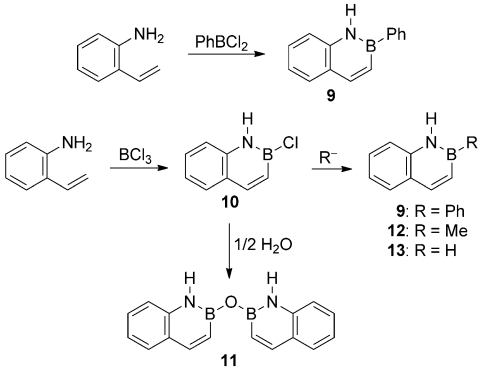


Scheme 1. Preparation of boron-substituted 9,10-azaboraphenanthrene derivatives.



Scheme 2. Installation of a π-accepting group at the nitrogen atom of BN-phenanthrene.

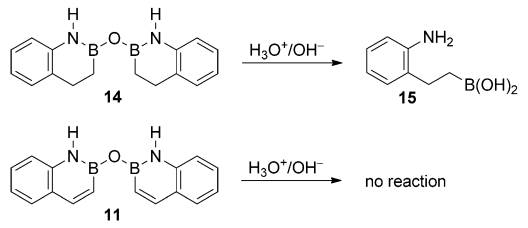
The first BN-naphthalene was synthesized by Dewar and co-workers in 1959.[37] The reaction of 2-aminostyrene with phenylboron dichloride led to the direct formation of 2-phenyl-1,2-azaboranaphthalene **9** (Scheme 3). BN-naphthalenes **9, 11**–**13** were reported to be unreactive toward strong base and $KMnO_4$, signifying a high degree of resonance stabilization.[38] Further evidence of resonance stabilization in BN-naphthalene was provided by the comparative reactivity of partially reduced heterocycle **14**, which reacted immediately with acid or base to give ring-opened **15** (Scheme 4).[39] In contrast, BN-naphthalene **11** was completely stable to hydrolysis, even upon heating.



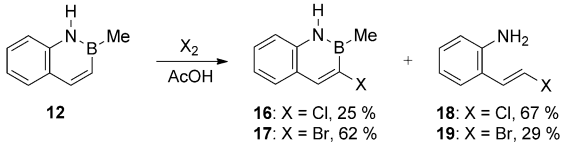
Scheme 3. Synthesis of B-substituted 1,2-azaboranaphthalenes.

Dewar and co-workers also reported the first electrophilic aromatic substitution reactions of BN-naphthalene (Scheme 5).[40] The halogenation of 1,2-azaboranaphthalene **12** with Cl_2 and Br_2 produced a mixture of C3-substituted products **16** and **17** and ring-opened side-products **18** and **19.** The structural assignments of **16** and **17** were confirmed by an independent synthesis of these compounds.

Prof. Shih-Yuan Liu was born in Hsinchu, Taiwan in 1975. His family moved to Austria when he was ten. He began his undergraduate studies in Chemistry at Vienna University of Technology in 1994. In 1998 he received his first diploma (B.S. equivalent) from Vienna University of Technology. He did his doctoral work at MIT with Prof. Gregory C. Fu and received his Ph.D. degree in organic chemistry in 2003. He then pursued his postdoctoral studies in inorganic chemistry with Prof. Daniel G. Nocera, also at MIT. Prof. Shih-Yuan Liu began his independent career at the University of Oregon in 2006, where he is currently an Assistant Professor of Chemistry.

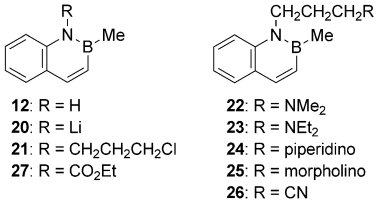


Scheme 4. Comparison of hydrolytic stability of BN-naphthalene **11** versus reduced anhydride **14**.



Scheme 5. EAS reactivity of BN-naphthalene **12**.

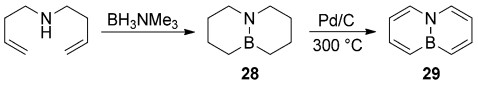
The aqueous stability of 1,2-azaboranaphthalenes made them attractive targets for the biological incorporation of boron (for example, cancer treatment using boron neutron-capture therapy).[41] However, 1,2-azaboranaphthalene was found to be water-insoluble, thus limiting its use in biological systems. Dewar and co-workers were however able to improve the solubility of 1,2-azaboranaphthalenes by functionalizing **12** at the nitrogen position (Scheme 6).[41]



Scheme 6. Synthesis of water-soluble BN-naphthalenes.

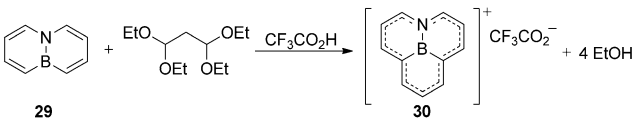
Dewar and co-workers also synthesized the 9,10 isomer of BN-naphthalene (Scheme 7).[42] Treatment of di-3-butenylamine with trimethylamine–borane formed bicycle **28**. Subsequent oxidation with Pd/C at high temperature afforded **29**, which was characterized by ^{1}H and ^{11}B NMR spectroscopy as well as mass spectrometry. Notably, the bridgehead-substituted BN-naphthalene **29** was found to have the same odor as naphthalene, which is a qualitative yet astounding testament to the chemical similarity between BN heterocycles and their carbon analogues.

The EAS reactivity of **29** was demonstrated, by H/D exchange, to occur at the carbon atoms α to boron.[37] Dewar and co-workers therefore sought to synthesize the 10,11-azaboraphenalenium ion **30** by substitution at the α-carbon



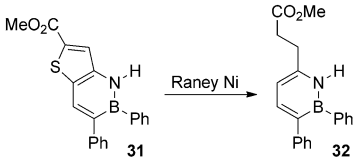
Scheme 7. Synthesis of bridgehead BN-naphthalene **29**.

atoms of **29**.[43] The reaction of **29** with malonaldehyde bis(diethylacetal) and CF_3CO_2H led to the formation of an intense purple solution, which was attributed to the formation of **30** (characterized by ^{1}H NMR spectroscopy and mass spectrometry); this compound was stable at −78 °C but decomposed at higher temperatures (Scheme 8). The ^{1}H NMR spectrum of the BN-phenalenium ion was similar to that of its carbon analogue.

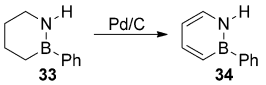


Scheme 8. Formation of BN-phenalenium ion **30** from BN-naphthalene **29**.

Dewar and White pioneered the first syntheses of monocyclic 1,2-azaborine derivatives independently in the early 1960s. In 1962, Dewar and co-workers used a desulfurization strategy from BN-benzothiophene **31** to generate highly-substituted 1,2-azaborine **32** (Scheme 9).[44] Compound **32** was resistant to degradation under prolonged exposure to both acid and base in ethanol. Acid/base stability and the inertness of the 1,2-azaborine double bonds toward Raney nickel are indications of the aromatic stability of the 1,2-azaborine core. In 1963, White reported the synthesis of 1-H-2-phenyl-1,2-azaborine **34** by palladium-catalyzed dehydrogenation from saturated heterocycle **33** (Scheme 10).[45]



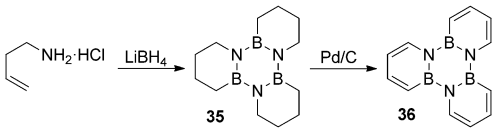
Scheme 9. Synthesis of 1,2-azaborine derivative **32** by desulfurization with Raney nickel (Dewar, 1962).



Scheme 10. Dehydrogenation route to 1,2-azaborine **34** (White, 1963).

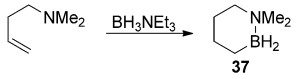
In 1967, Dewar and co-workers attempted the first synthesis of the parent 1,2-dihydro-1,2-azaborine using a hydroboration–oxidation method, but were unsuccessful (Scheme 11).[46] They concluded that "borazarene [1,2-dihydro-1,2-azaborine] therefore seems to be a very reactive and chemically unstable system, prone to polymerization and other reactions…" In fact, multiple attempts to isolate the parent 1,2-dihydro-1,2-azaborine from BN-triphenylene **36** were unsuccessful.

Other pioneers of BN-heterocycle chemistry include Polivka and co-workers who followed a similar route to Dewar's BN-naphthalene synthesis to generate 1,2-azabor-



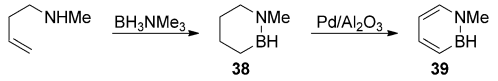
Scheme 11. Hydroboration–oxidation procedure leading to undesired trimerization to BN-triphenylene **36**.

acyclohexane **37** from dimethylaminobut-3-ene (Scheme 12); however, no attempts were made to aromatize this compound.[47,48]



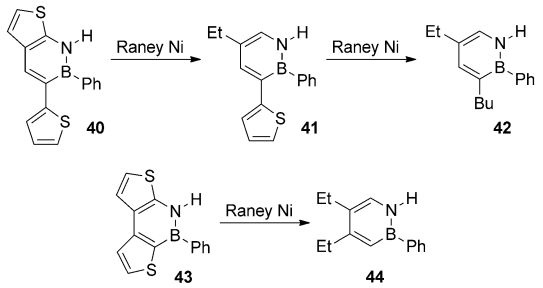
Scheme 12. Hydroboration to stable 1,2-azaboracyclohexane **37**.

Goubeau and co-workers used a secondary butenyl amine (as in White's earlier work) to form the cyclohexene analogue **38** by hydroboration (Scheme 13).[49] Dehydrogenation with Pd/Al_2O_3 provided the first B–H-substituted 1,2-azaborine **39**, which was characterized by mass spectrometry.[50]



Scheme 13. Hydroboration–oxidation to generate 1,2-azaborine **39** containing a B–H group.

Gronowitz and co-workers synthesized a series of BN-benzothiophenes, which upon desulfurization yielded the first examples of monocyclic 1,2-azaborines substituted at C4 and/or C5 (Scheme 14).[51–53]

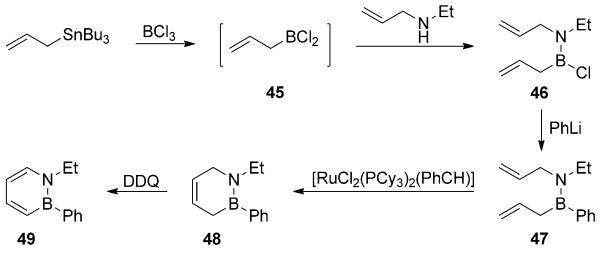


Scheme 14. Desulfurization of BN-benzothiophenes with Raney nickel to generate 4- and 5-substituted 1,2-azaborines.

The pioneering efforts of these groups hinted at the potential of azaborine-containing compounds as arene mimics in a diverse variety of structural motifs. However, early development was hampered by the limited material characterization capabilities of the times and harsh synthetic conditions incompatible with many functional groups. Modern synthetic methods and instrumentation have enabled a new generation of chemists to pick up where Dewar, White, and others left off, and take azaborine chemistry into uncharted and exciting territory.

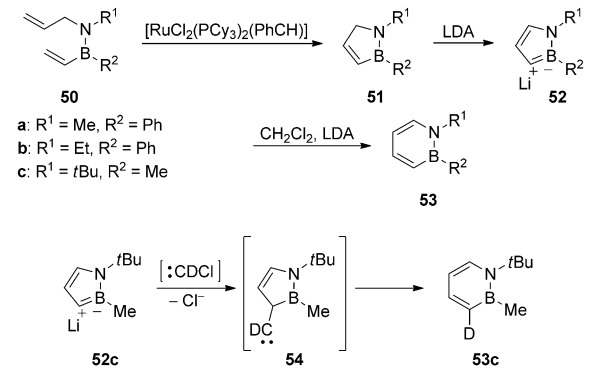
3. The Ashe Group, University of Michigan

The Ashe group achieved a breakthrough in the mild synthesis of monocyclic 1,2-azaborines in 2000 and sparked renewed interest in the field of aromatic BN-heterocycles. Previous syntheses relied on desulfurization or dehydrogenation at extreme temperatures as discussed above, but Ashe and co-workers developed a ring-closing metathesis/oxidation procedure that enabled mild and efficient formation of 1,2-azaborines (Scheme 15).[54] Transmetalation of allyltributyltin with BCl_3 generated allylboron dichloride **45** in situ. Condensation with allylethylamine produced bis(allyl) aminoborane **46**. The addition of PhLi led to the displacement of chloride from the labile B–Cl bond to give B–Ph aminoborane **47** in good yield. Ring-closing metathesis with Grubbs' first generation catalyst formed 1,2-azaborine precursor **48** featuring an olefin at the 4-position. The oxidation to 1,2-azaborine **49** was accomplished in good yield using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) at 35 °C.



Scheme 15. Mild synthesis of 1,2-azaborine **49** by ring-closing metathesis.

A year later, Ashe and co-workers explored a ring-expansion route to 1,2-azaborines from the 1,2-azaborolide heterocycle, which is formally isoelectronic with the ubiquitous cyclopentadienide (Cp) ion (Scheme 16).[55] Ring-closing metathesis from *B*-vinyl aminoboranes **50** provided heterocycles **51**, which were deprotonated to give 1,2-azaborolides **52**. The reaction of **52** with CH_2Cl_2 and lithium diisopropylamide (LDA) (the Katz reaction) gave 1,2-azaborines **53a–c**. A deuterium labeling study suggested that the initial attack of chlorocarbene occurs at the C3 position of **52c**. Carbene



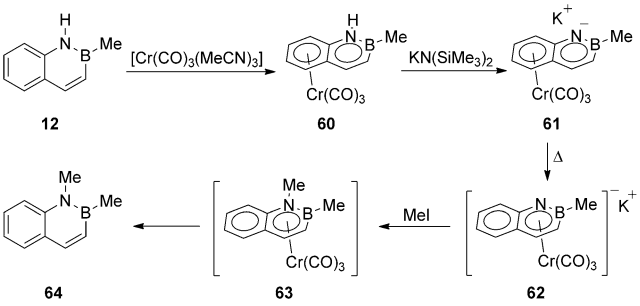
Scheme 16. Ring-expansion route to 1,2-azaborines **53a–c** and deuterium labeling.

insertion into the B–C bond leads to a 3-deuterio isomer of **53c** via carbene **54**. Deuterium incorporation at this position rules out initial substitution at C5.

The Ashe group has explored the reactivity of 1,2-azaborines extensively, especially with regard to their transition-metal chemistry. They have synthesized η^6 piano-stool chromium and molybdenum complexes,[55] ruthenium sandwich compounds,[56] as well as η^1 zirconium complexes bound at the deprotonated azaborine nitrogen.[57] They developed a new route to 5- and 6-membered ring-fused bicyclic 1,2-azaborines.[58] They also demonstrated the first electrophilic aromatic substitution reactions of a moncyclic 1,2-azaborine.[59] The majority of the work the Ashe group has carried out in this field was described in detail in Piers' 2009 review[28] and we will not repeat it here. However, since then, two new reports have emerged from Ashe and co-workers regarding BN-aromatic compounds.

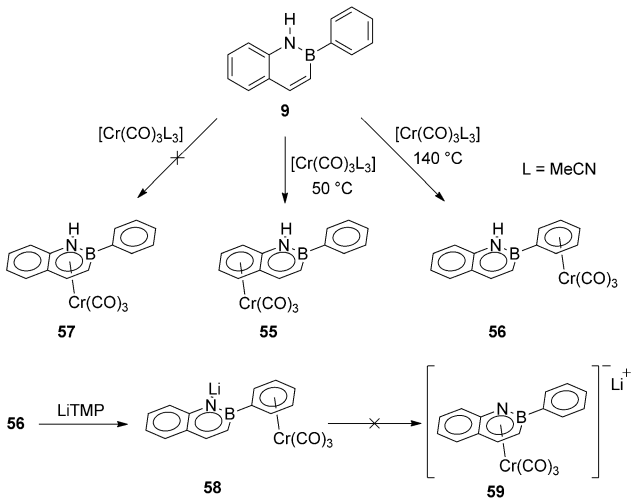
In one report, Ashe and co-workers investigated the haptotropic migration of *B*-phenyl 1,2-azaboranaphthalene (**9**) in $Cr(CO)_3$ piano-stool complexes (Scheme 17).[60] The complexation of **9** with $Cr(CO)_3$ was envisioned to occur at the benzenoid, 1,2-azaborine, or even the boron-substituted phenyl ring. In fact, η^6 binding of the benzenoid ring was observed under mild heating to form complex **55**. At higher temperatures, however, a shift of chromium complexation to the boron-substituted phenyl ring occurred, forming complex **56**, with no evidence for the formation of complex **57**. In fact, even when **56** was deprotonated with LiTMP to generate complex **58**, no haptotropic migration to **59** was observed; instead complex **58** was prone to thermal degradation. These data indicate that the heterocyclic ring of BN-naphthalene is a poor ligand for transition metals relative to monocyclic 1,2-azaborines.

Ashe and co-workers strategized that removal of the competitive *B*-phenyl binding site would allow for the binding of transition metals to the heterocyclic fragment of BN-naphthalene. To that end, *B*-methyl 1,2-azaboranaphthalene (**12**) was treated with $[Cr(CO)_3(MeCN)_3]$ to give complex **60** (Scheme 18). Though no complexation to the heterocyclic fragment was observed, deprotonation of **60** with potassium hexamethyldisilazide provided **61**, which increased the electron-richness of the 1,2-azaborine heterocycle. Upon heating, complex **61** underwent a haptotropic migration to afford the desired anionic complex **62** in which chromium is η^6-bound to the heterocyclic ring. Methylation of **62** presumably led to complex **63**; however, the coordination of the neutral heterocyclic fragment was so tenuous that decomplexation to free BN-naphthalene **64** occurred at room temperature.

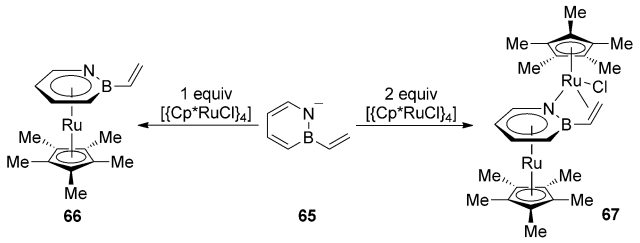


Scheme 18. Haptotropic migration of chromium complexes of *B*-methyl-1,2-azaboranaphthalene **12**.

In their most recent report in this field, the Ashe group explored the ligand properties of deprotonated BN-styrene **65**, which was synthesized by the ring expansion route shown in Scheme 16.[61] The reaction of **65** with one equivalent of $[\{Cp^*RuCl\}_4]$ gave complex **66** in which BN-styrene is η^6-bound to ruthenium (Scheme 19). However, when two equivalents of $[\{Cp^*RuCl\}_4]$ were added, diruthenium complex **67** was formed, in which η^6-binding occurs between one ruthenium atom and the 1,2-azaborine ring, while the second ruthenium binds η^1 to the 1,2-azaborine nitrogen and η^2 to the B-vinyl group.



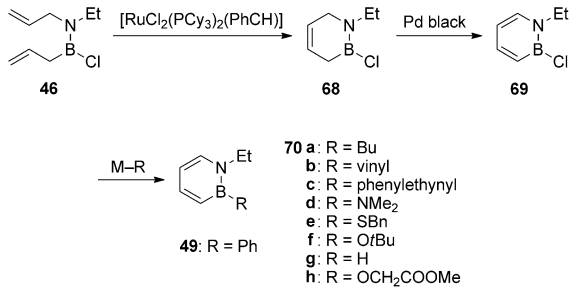
Scheme 17. Haptotropic migration of chromium complexes of *B*-phenyl-1,2-azaboranaphthalene **9**.



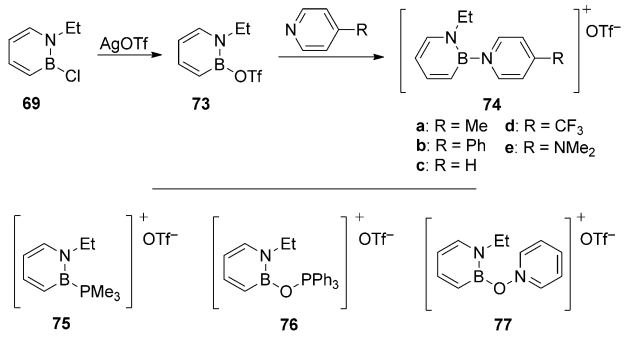
Scheme 19. Synthesis of complexes **66** and **67** from BN-styrene **65**.

4. The Liu Group, University of Oregon

Liu and co-workers have extended the synthetic methods developed by Ashe to create 1,2-azaborines with various heteroatom substituents at boron. Catalytic ring-closing metathesis in the presence of the reactive B–Cl bond of bis(allyl) aminoborane **46** readily furnished cyclized aminoborane **68** (Scheme 20).[62] Oxidation conditions were screened, and it was determined that Pd black efficiently



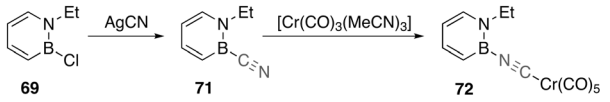
Scheme 20. Nucleophilic substitution of **69** to generate *B*-substituted 1,2-azaborines.



Scheme 22. Synthesis of 1,2-azaborine cations **74**–**77**.

dehydrogenates **68** to give 1,2-azaborine **69**. Treatment with various carbon-based and heteroatomic nucleophiles provided the known 1,2-azaborine **49** as well as new 1,2-azaborine derivatives **70a**–**h** in good yield. Several of these derivatives are of particular interest as they relate to their phenyl analogues, including glycolate-substituted **70h**, which is isoelectronic with a known hypolipidemic agent.[63] The stability of 1,2-azaborines to H_2O and O_2 was demonstrated for a series of boron- and C3-substituted derivatives, and it was determined using kinetics experiments that substitution at these positions had a substantial effect on compound stability.[64]

In a subsequent report, Liu and co-workers demonstrated that the 1,2-azaborine analogue of benzonitrile **71** was readily available by treating **69** with AgCN (Scheme 21).[65] The

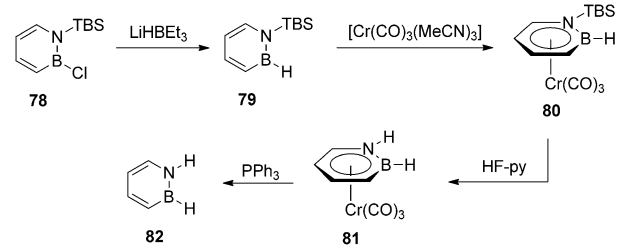


Scheme 21. Synthesis of BN-benzonitrile **71** and unexpected isomerization to complex **72**.

formation of the B–CN bond rather than the alternative B–NC bond was supported by calculations and was unambiguously confirmed by an isotopic labeling experiment using $Ag^{13}C^{15}N$. Complexation of **71** with chromium(0) led to isomerization of the CN group to form complex **72**, which was characterized by X-ray crystallography. Complex **72** was also readily available by the direct reaction of **69** with $Na^+[Cr(CO)_5CN]^-$.

Although the B–Cl bond in compound **69** is susceptible to nuleophilic aromatic substitution with a variety of anionic nucleophiles, less reactive neutral nucleophiles do not displace chloride from the boron atom. Liu and co-workers found that treatment of **69** with AgOTf smoothly forms species **73**, which contains the much more labile B–OTf bond. Compound **73** was shown to react with both electron-rich and electron-poor *para*-substituted pyridines to generate the first examples of 1,2-azaborine cations, **74a**–**e** (Scheme 22, top).[66] The solid-state fluorescence was measured for **74a**–**e** and compared to their carbon analogues. It was found that 1,2-azaborine substitution causes a red-shift of the emission maxima relative to the carbon species, and that the nature of the *para* substituent has a substantial effect on the emissive properties. Protonated pyridinium analogues of **74** (that is, without the 1,2-azaborine group) were not fluorescent under identical conditions, confirming the critical role the 1,2-azaborine moiety plays in the observed emissions. In a later paper, the synthetic method was expanded to include substitution of **73** with trimethylphosphine, triphenylphosphine oxide, and pyridine-*N*-oxide to generate the cationic 1,2-azaborines **75**–**77** (Scheme 22, bottom).[67]

The first successful synthesis of the parent 1,2-dihydro-1,2-azaborine **82** was reported by Liu and co-workers in 2009 (Scheme 23).[68] The incorporation of the *tert*-butyldimethylsilyl (TBS) nitrogen protecting group permitted the formation



Scheme 23. Synthesis of 1,2-dihydro-1,2-azaborine **82**.

of a versatile 1,2-azaborine **78** by the same ring-closing/oxidation procedure presented above. Substitution at boron with superhydride provided *N*-TBS-1,2-azaborine **79** with a B–H bond. Direct deprotection to the parent compound was unsuccessful, however treatment with $[Cr(CO)_3(MeCN)_3]$ to form complex **80** activated the N-TBS group toward cleavage by HF–pyridine and afforded complex **81** in which 1,2-dihydro-1,2-azaborine is η^6-bound to the $Cr(CO)_3$ fragment. X-ray quality crystals of **81** were obtained, which showed that chromium is centered about the planar 1,2-dihydro-1,2-azaborine ring in analogy to the corresponding benzene–$Cr(CO)_3$ complex. Bond lengths, carbonyl stretching frequencies, along with computationally predicted parameters are presented in Figure 5. Decomplexation of the 1,2-dihydro-1,2-azaborine ligand by exchange with PPh_3 provided **82** in good yield, as shown by ^{1}H NMR spectroscopy; however, the volatility of **82** resulted in a low yield of isolated product. Compound **82** was characterized by ^{1}H, ^{11}B, and ^{13}C NMR spectroscopy, as well as IR spectroscopy and

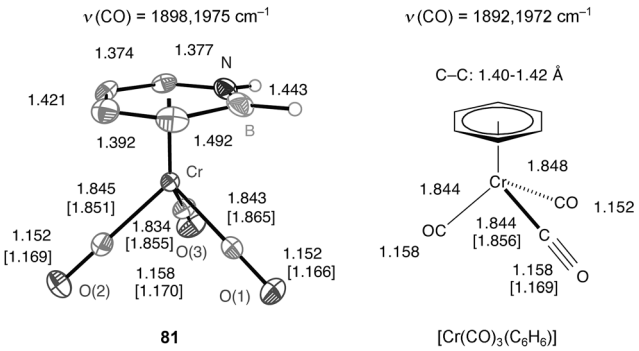
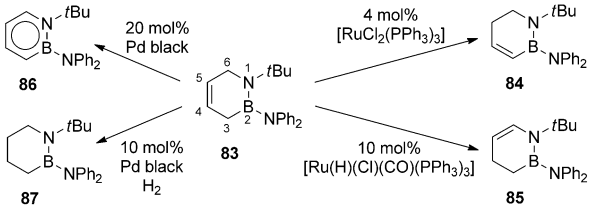


Figure 5. Bond lengths (in Å) and carbonyl stretching frequencies for **81** and benzene-Cr(CO)$_3$. Computed values are in parentheses.



Scheme 24. Catalytic formation of 1,2-azaborine isomers **84**–**87** from common intermediate **83**.

HRMS, which supported the assigned structure. The UV/Vis spectrum of **82** is consistent with an aromatic heterocycle; the lowest-energy absorption at 269 nm ($\varepsilon = 15\,632\ \mathrm{L\,mol^{-1}\,cm^{-1}}$) is close in energy to the α band of benzene (255 nm, $\varepsilon = 977\ \mathrm{L\,mol^{-1}\,cm^{-1}}$); however, this absorption was much stronger in **82**. The corresponding band in borazine is virtually nonexistent. The electronic spectra indicate that **82** possesses significant aromatic character and more closely resembles benzene than borazine. 1,2-Dihydro-1,2-azaborine was found to be quite thermally and hydrolytically stable. Deuterium exchange at the N–H position occurred over approximately 24 h in a CD_3OD solution of **82**, demonstrating the unique reactivity of **82** relative to benzene.

The aromaticity of azaborine systems is of considerable interest not only from a fundamental point of view, but also as it relates to potential applications of BN/CC isosterism. Reactivity, structure, energy, and magnetic criteria are the four metrics most used to characterize the aromaticity of a compound. Dewar, Ashe, and others have demonstrated reactivity consistent with aromatic systems (for example, electrophilic aromatic substitution, π complexation), and the reported structures of azaborine compounds have indicated planarity and bond lengths typical of aromatic systems. In a series of reports, the Liu group has endeavored to systematically characterize the aromaticity of 1,2-azaborine systems with regard to bond delocalization, resonance stabilization energy, reactivity, and magnetic properties. The results are summarized below.

Though the solid-state structural analysis of **82** (m.p. −45 °C) has not been reported, microwave spectroscopy has provided a means of elucidating the structural features. Kukolich, Liu, and co-workers recently collected microwave spectroscopic data for several isotopomers of **82**.[69] The results indicate that the 1,2-dihydro-1,2-azaborine ring is planar with a B–N bond length of 1.45(3) Å. The B–C and N–C bond lengths were found to be 1.51(1) Å and 1.37(3) Å, respectively. These bond lengths are somewhat longer than the values reported for substituted derivatives in the solid state (see Table 1).

Liu and co-workers obtained evidence of bond delocalization in 1,2-azaborine by crystallographic analysis.[70] 1,2-azaborine precursor **83** was a versatile intermediate in the formation of a family of aminoboranes in various oxidation states with respect to the intra-ring carbon atoms (**84**–**87** in Scheme 24). Transition-metal catalysis was used in all cases to generate the desired heterocycle. The isomerization of **83** to *B*-vinyl **84** was achieved in good yield using $[RuCl_2(PPh_3)_3]$. Alternatively, $[Ru(H)(Cl)(CO)(PPh_3)_3]$ isomerized the double bond in **83** to *N*-vinyl **85**. Pd black catalyzed the oxidation to 1,2-azaborine **86**. The same catalyst in the presence of H_2 reduced **83** to **87**. Structural data for compounds **83**–**87** were obtained by single-crystal X-ray diffraction and are presented in Table 1. Upon oxidation to 1,2-azaborine **86**, the B–N bond lengthens relative to that in

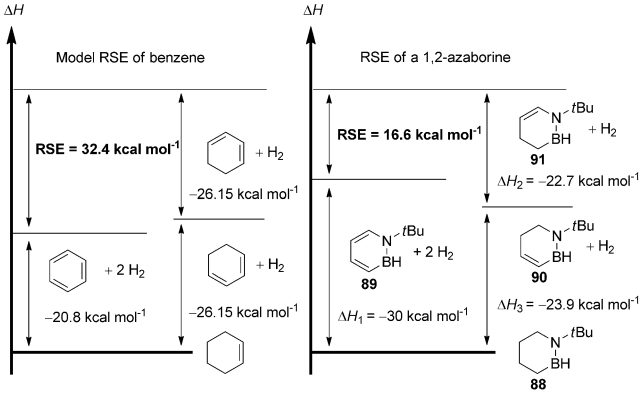
Table 1: Selected bond distances and deviations from planarity (in Å) for heterocycles **83**–**87**.[a]

	87	**83**	**84**	**85**	**86**
B–N_{ring}	1.403(2)	1.405(2)	1.407(2)	1.417(3)	1.446(2)
B–C3	1.584(3)	1.590(2)	1.559(2)	1.579(4)	1.518(2)
C3–C4	1.511(3)	1.493(2)	1.338(2)	1.504(4)	1.363(2)
C4–C5	1.511(3)	1.319(2)	1.479(2)	1.494(4)	1.412(2)
C5–C6	1.508(3)	1.493(2)	1.503(2)	1.319(3)	1.356(2)
C6–N_{ring}	1.479(2)	1.477(2)	1.479(2)	1.432(3)	1.383(2)
B–N_{exo}	1.488(2)	1.487(2)	1.483(2)	1.480(3)	1.486(2)
planarity[b]	0.226	0.164	0.199	0.183	0.048

[a] See structure **83** in Scheme 24 for atom numbering. [b] Root mean square deviation of intraring atoms from least-squares plane.

the other heterocycles. Similarly, the C=C bonds in **84** and **85** are shorter than the corresponding bonds in **86**. The lengthening of these formal double bonds in the structure of **86** is an indication of bond delocalization. Conversely, the C4–C5 single bond in **86** is shorter than the corresponding bonds in **84** and **85** by over 0.07 Å. A similar shortening of the B–C3 and C6–N bonds in 1,2-azaborine **86** versus all other derivatives is consistent with bond delocalization.

In 2010, Liu and co-workers reported the experimental determination of the resonance stabilization energy (RSE) of 1,2-azaborine, a quantitative measure of aromaticity.[71] By comparing the heat of hydrogenation (measured using reaction calorimetry) of the aromatic compound **89** against the sum of the heats of hydrogenation of the compounds **90** and **91** (that is, $\mathrm{RSE} = \Delta H_1 - (\Delta H_2 + \Delta H_3)$), the RSE of 1,2-azaborine was found to be $(16.6 \pm 1.3)\ \mathrm{kcal\,mol^{-1}}$, which is consistent with significant aromatic character (Scheme 25). This result is in good agreement with computationally

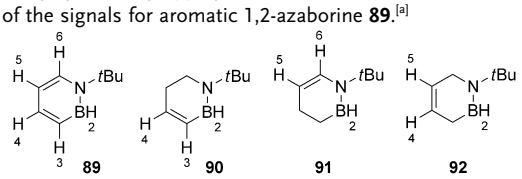


Scheme 25. Experimentally determined resonance stabilization energy (RSE) of a 1,2-azaborine.

predicted values for 1,2-azaborines, and significantly less than the RSE of benzene (32.4 kcal mol^{-1}).

Protons attached to aromatic systems typically display downfield NMR chemical shifts owing to the shielding effects of the ring current. Liu and co-workers have performed ^{1}H NMR experiments that confirm that azaborine protons are indeed shifted downfield as the molecules become aromatic. The NMR chemical shifts of the non-aromatic compounds **90**–**92** along with the aromatic compound **89** are presented in Table 2. All protons were assigned using the 2D HETCOR technique. There is a clear down field shift ranging from $\Delta\delta =$ 0.76 to 1.83 ppm as isolated olefinic protons become aromatic.

Table 2: δ(^{1}H) values (in ppm) for **89**–**92** and downfield shifts $\Delta\delta$ (in ppm) of the signals for aromatic 1,2-azaborine **89**.[a]

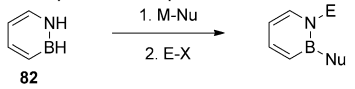


	89	**90**	**91**	**92**
H_{B2}	5.23	4.45 (0.78)	4.91 (0.32)	4.75 (0.48)
H_{C3}	6.84	5.91 (0.93)	–	–
H_{C4}	7.54	6.55 (0.99)	–	5.71 (1.83)
H_{C5}	6.38	–	5.02 (1.36)	5.62 (0.76)
H_{C6}	7.63	–	6.21 (1.42)	–

[a] Values in brackets are downfield shifts $\Delta\delta$ given as the difference of the δ values for comparable protons in **89** and its non-aromatic congeners.

Complementing Ashe's pioneering work on electrophillic aromatic substitution of 1,2-azaborines, Liu and co-workers studied nucleophillic aromatic substitution of the parent 1,2-dihydro-1,2-azaborine **82**.[72] Treatment of **82** with two equivalents of nucleophile led to deprotonation at the nitrogen position and substitution at boron; reactions with only one equivalent of nucleophile had dramatically lower yields. Quenching with an appropriate electrophile (including H^+) led to a diverse array of products (Table 3). Thorough experimental and computational mechanistic analysis

Table 3: Substrate scope of nucleophilic aromatic substitution of **82**.



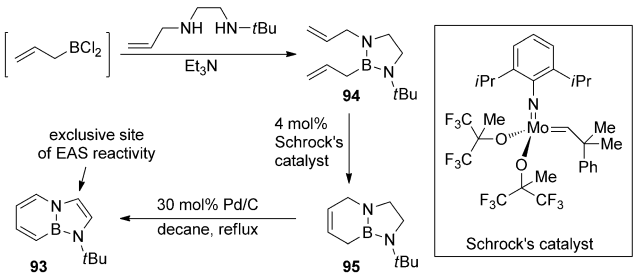
Entry	M-Nu	E-X	Yield [%][a]
1	Na-O*t*Bu	H-Cl	63
2	K-Oallyl	H-Cl	79
3	Li-*t*Bu	H-Cl	81
4	Li-*n*Bu	H-Cl	80
5	Li-Ph	H-Cl	98
6	BrMg-vinyl	H-Cl	59
7	BrMg—≡—Ph	H-Cl	71
8	Li-*n*Bu	TMS-Cl	89
9	Li-*n*Bu	Me-I	67
10	Li-*n*Bu	Bn-Br	60

[a] Yield of isolated product.

revealed that the reaction most likely proceeds by two distinct pathways depending on the nature of the nucleophile.

Apart from exploring the fundamental properties of 1,2-azaborines, the Liu group is interested in utilizing these compounds in biological and materials science applications. A proof-of-concept demonstration of the biomimetic potential of 1,2-azaborine was reported in 2009 by Matthews, Liu, and co-workers.[73] The L99A mutant of T4 lysozyme is known to possess an internalized hydrophobic pocket that selectively binds aromatic hydrocarbons such as benzene. Using X-ray crystallography, neat 1,2-dihydro-1,2-azaborine **82** and *N*-ethyl 1,2-azaborine **70g** were found to diffuse into the hydrophobic pocket of crystalline L99A lysozyme in an identical manner to benzene and ethylbenzene, respectively. The selective binding of **82** within this hydrophobic pocket is quite interesting given the potential for the N–H group of **82** to undergo non-specific hydrogen bonding with the protein. Thus, 1,2-dihydro-1,2-azaborine effectively acts as a boron-containing hydrophobic benzene mimic in this specific pocket, and may provide access to the study of 1,2-azaborine in a biological context.

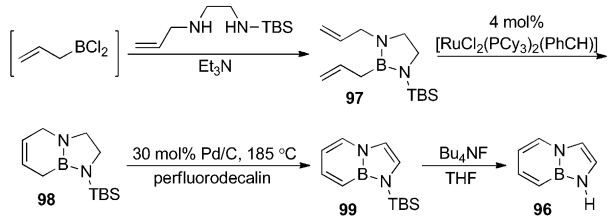
Indole is a ubiquitious heterocyclic motif in nature. It is found free in cells, as part of the amino acid tryptophan, and the indole moiety is present in myriad natural products and biologically active compounds. Externally substituted, phenylenediamine-type BN-indole analogues were reported as early as 1957.[74] In 2010, Liu and co-workers reported the syntheses and reactivity of the first internally substituted ("fused") BN-indole derivatives.[75] The synthesis of N-*t*Bu-protected BN-indole **93** is analogous to the route previously describe for monocyclic 1,2-azaborine derivatives (Scheme 26). It begins with the condensation of *N*-*t*Bu-*N*′-allylethylenediamine with allyl boron dichloride generated in situ to generate bis(allyl) species **94**. Ring-closing metathesis was found to proceed in high yield using Schrock's molybdenum RCM catalyst to give bicycle **95**. Both rings were dehydrogenated using Pd/C to give the desired product **93**. Electrophilic aromatic substitution (EAS) reactivity, which is a crucial reaction in the biochemistry of indoles (and one which has not been shown for externally BN substituted indole analogues), was demonstrated for **93**, and as with



Scheme 26. Synthesis of *N*-*t*Bu-BN-indole **93**.

natural indole, EAS reactions of **93** were regioselective for the 3-position exclusively. EAS competition experiments between **93** and natural indole using dimethylimminum chloride revealed that **93** is significantly more nucleophilic.

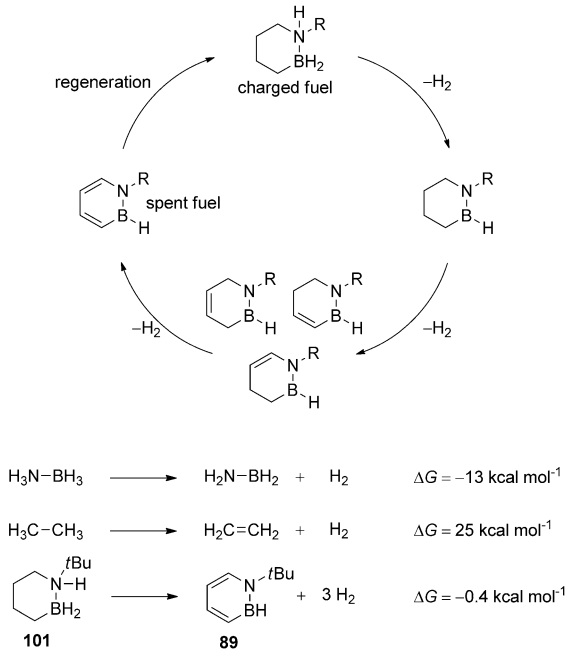
In 2011, Liu and co-workers reported the synthesis of the parent "fused" BN-indole **96**.[76] This molecule contains the free N–H fragment that is an important feature in the biochemistry of indole and its derivatives. Synthesis was similar to the route described above, with a number of key distinctions (Scheme 27). First, the use of TBS rather than *t*Bu as a nitrogen protecting group allowed for its facile removal



Scheme 27. Synthesis of the parent "fused" BN-indole **96**.

later in the synthesis. Second, the use of Grubbs' first-generation catalyst was found to be more effective for the RCM generation of **98** than Schrock's catalyst. Third, the use of perfluorodecalin as the solvent for the oxidation step allowed the aromatic product **99** to be recovered with simple THF extraction rather than distillation. The TBS group could be removed in the last step using nBu$_4$NF to afford the product **96** in moderate yield. A non-disordered single crystal X-ray structure was obtained by co-crystallization of **96** with ethyl-4-chloro-3,5-nitrobenzoate and revealed **96** to be a planar molecule with bond lengths consistent with aromatic delocalization. The optical and electronic properties of **96** were probed and compared to natural indole. The absorption maximum of BN-indole is red-shifted from that of natural indole ($\lambda = 293$ nm vs. 268 nm in CH_3CN). The emission maximum is likewise red-shifted for **96** compared to natural indole ($\lambda_{em} = 360$ nm vs. 315 nm, in CH_3CN) and displays a greater Stokes shift and lower quantum yield ($\Phi = 0.08$ vs. 0.32 for indole). The red-shifted absorbance and emission maxima are consistent with a smaller HOMO–LUMO gap for **96**. Using ^{1}H NMR bracketing experiments, the pK_a of the N–H proton was estimated to be about 30, which is roughly nine orders of magnitude less acidic than natural indole ($pK_a = 20.95$).

Boron–nitrogen-containing compounds have received considerable attention as potential hydrogen storage materials owing to their high hydrogen content and favorable kinetics of H_2 release. Moreover, calculations suggest that H_2 uptake and release by a combined CC/BN system should be essentially free-energy-neutral (that is, $\Delta G \approx 0$), potentially allowing efficient H_2 absorption/desorption with minimal energy input. Liu and co-workers have described a system by which 1,2-azaborines can potentially store and release three equivalents of H_2 per molecule (Scheme 28). As a proof of concept, they reported the mild regeneration of the "spent

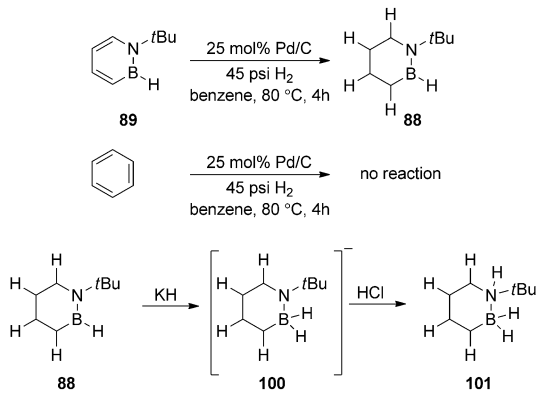


Scheme 28. Hydrogen storage by CBN heterocycles. ΔG values from CCSD(T) calculations for 298 K.

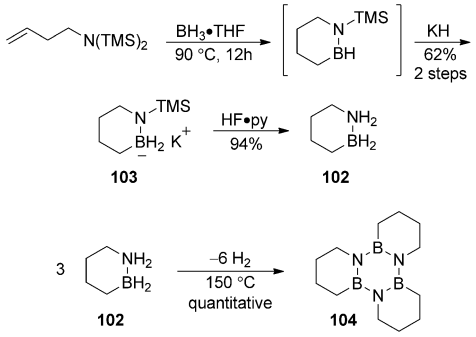
fuel" (that is, aromatic, unsaturated) 1,2-azaborine to the "charged fuel" (that is, fully H_2-saturated) amine–borane fuel by the formal addition of three equivalents of H_2.[77]

The first two equivalents of H_2 were added across the formal C=C bonds of **89** using catalytic hydrogenation with Pd/C and H_2 gas to give heterocycle **88** (Scheme 29). Under identical conditions, the reduction of benzene was not observed. The third equivalent of "H_2" was added across the B–N bond in a sequential manner. The reaction of KH with **88** installed H^- at the boron atom to give anionic intermediate **100**, which was then treated with HCl to give the fully charged fuel **101**.

As part of their effort to develop a BN-heterocycle based hydrogen storage platform, Liu and co-workers published an alternative route to fully saturated six-membered BN-heterocycles such as **101**, including the parent 1,2-azaboracyclohexane **102** (Scheme 30).[78] Treatment of a bis(trimethylsilyl)-protected homoallylamine with BH_3·THF and subsequent addition of KH gave a mono(trimethysilyl)-protected BN-



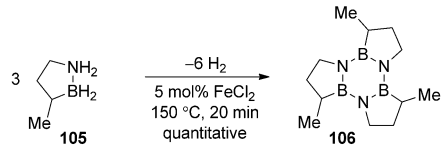
Scheme 29. Regeneration of 1,2-azaborine spent fuel **89** by catalytic hydrogenation of C=C bonds and sequential addition of H^-/H^+ across the B–N bond.



Scheme 30. Synthetic route to 1,2-azaboracyclohexane **102** and dehydrogenation/trimerization to form **104**.

cyclohexane potassium salt **103** in moderate yield. Deprotection/protonation with HF·pyridine generated 1,2-azaboracyclohexane **102**. X-ray structural analysis confirmed the assigned structure, which, like cyclohexane, assumes a chair conformation. The free energy of activation for the chair flip was found to be significantly lower for **102** than for the carbon version (8.8 vs. 10.5 kcal mol^{-1}, under identical conditions), attributed to the longer B–N bond (1.614(1) Å) versus the C–C bond in cyclohexane (1.51–1.53(1) Å) and to the shallow potential curve for the B–N stretch. Upon thermal activation (150 °C), compound **102** underwent a trimerization reaction to form **104** with concomitant release of six equivalents of H_2. The conversion was clean and quantitative, in marked contrast to dehydrogenation reactions of ammonia–borane (H_3N–BH_3), which can produce various mixtures of oligomeric products depending on the dehydrogenation conditions used. Clean dehydrogenation to a well-defined single product using mild conditions make **102** a promising material for hydrogen storage. Furthermore, the moderate hydrogen capacity of 4.7 wt % can potentially be increased to 9.4 wt % if the H_2 release from BN can be coupled with dehydrogenation from the carbon positions as well.

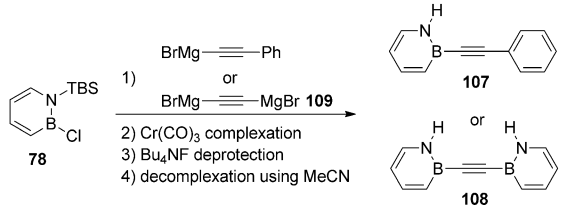
In a further refinement of the intramolecular hydroboration/cyclization method described in Scheme 30, Liu and co-workers recently disclosed the synthesis of the BN-methycyclopentane **105** (Scheme 31).[79] This material is liquid at room



Scheme 31. Liquid hydrogen storage material based on BN-methylcyclopentane **105**. Charged fuel **105** and spent fuel **106** are both liquids at 20 °C.

temperature and can release hydrogen using cheap metal halide catalysts (for example, $FeCl_2$) at 80 °C, which are both very desirable properties for potential hydrogen storage materials.

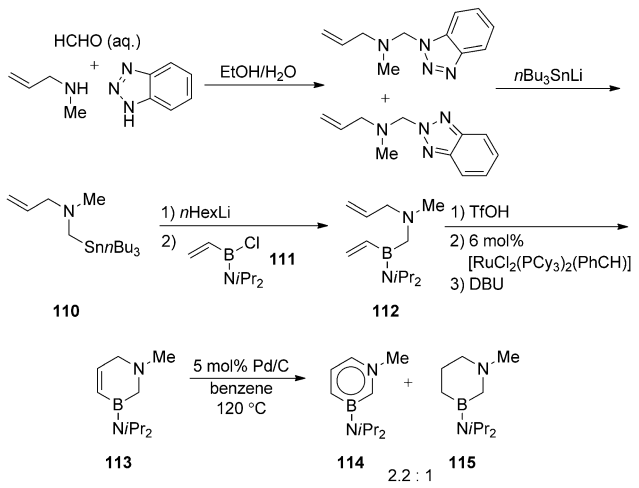
As part of their efforts to develop π-conjugated azaborine optical materials, Liu and co-workers reported the synthesis and characterization of the BN analogue of diphenylacetylene (tolan; Scheme 32).[80] Synthesis of BN-tolan **107** and



Scheme 32. Synthesis of BN-tolan analogues **107** and **108**.

bis(BN)-tolan **108** was achieved by reaction of the known TBS-protected precursor **78** with either phenylethynylmagnesium bromide or the Grignard reagent **109**. The resulting compounds were deprotected using a chromium complexation route analogous to that used in the parent 1,2-dihydro-1,2-azaborine synthesis (see Scheme 23). Single-crystal X-ray analysis revealed both compounds **107** and **108** to be linear with respect to the B–C≡C–X axis with a coplanar orientation of the aromatic rings, which is indicative of significant π overlap throughout the bicycle. The other noteworthy feature of the crystal structure was the observation of dimers formed through a rarely seen N–H–π(C≡C) hydrogen bonding interaction. UV/Vis absorbance maxima for **107** and **108** are centered at 299 nm and are broadened relative to tolan. Emission maxima in THF for **107** and **108** are 350 nm ($\Phi = 0.012$) and 388 nm ($\Phi = 0.020$), respectively, which are significantly red-shifted from tolan (317 nm, $\Phi = 0.007$); the emissions display minimal solvatochromism.

One of the most exciting recent developments to emerge from the Liu group is the disclosure of the first example of a 1,3-azaborine.[81] This significant synthetic achievement was accomplished by harnessing the power of ring-closing metathesis and tin chemistry previously developed in the Liu group, with several substantial modifications (Scheme 33). The stannane reagent **110** was produced in two steps from allylmethylamine, formaldehyde, and benzotriazole. Direct transmetalation between **110** and the vinylboron chloride **111** was unsuccessful; however, lithium–tin exchange followed by addition of the electrophile **111** afforded the RCM precursor



Scheme 33. Synthesis of the first 1,3-azaborine **114**.

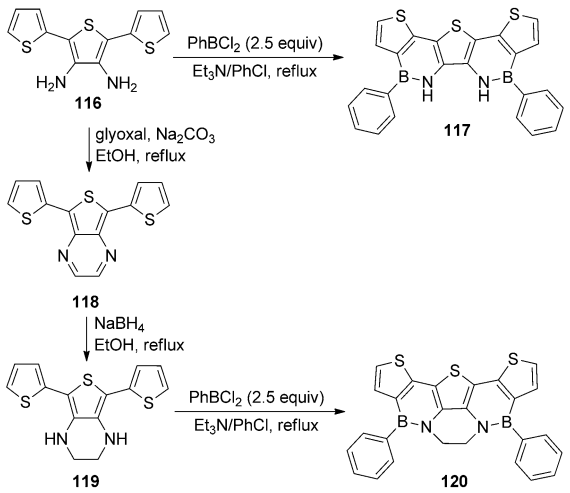
112 in modest yield. Both Grubbs' first generation and Schrock's catalysts failed to cyclize **112**, which is presumably due to degradation of the catalyst caused by the relatively nucliophilic amine. This was overcome by first forming the ammonium salt of **112** with triflic acid, closing the ring using Grubbs' first generation catalyst, and finally deprotonating the ring-closed ammonium salt with DBU to furnish **113**.

Dehydrogenation of **113** to generate the aromatic final product also proved to be a challenge, with significant formation of fully reduced species **115** (2.2:1 **114**/**115**) observed even under optimized conditions. The desired product was isolated by distillation and fully characterized. Single-crystal X-ray analysis revealed that the 1,3-azaborine ring is completely planar, with intraring bond lengths consistent with electron delocalization. To further probe the aromatic nature of the 1,3-azaborine ring, **114** was treated with $[(MeCN)_3Cr(CO)_3]$ to generate the pianostool complex. A close inspection of the crystal structure of the complex showed that it is best characterized as an η^5 π complex in which the boron atom does not participate, as it lies 0.21 Å above the root-mean-square of the plane containing the other five atoms. Compound **114** was found to be inert to a variety of nucleophiles, but reacts with acetic acid to form a B–OAc adduct. Electrophilic aromatic substitution reactivity was also probed, and **114** was found to undergo EAS regioselectively in the presence of dimethyl(methylene)ammonium chloride.

5. The Perepichka Group, McGill University

In 2010, Perepichka and co-workers investigated the incorporation of 1,2-azaborines into oligothiophene organic electronic materials.[82] Structurally related thienoazaborine and dithienoazaborines have been reported, but their optoelectonic properties were not explored in depth. The addition of boron into conjugated systems has been shown to increase luminescence efficiency and improve light-emitting properties of a material.[83] The Lewis acidic boron centers have typically been stabilized through steric screening using bulky aryl substituents, but in the solid state these groups can suppress π stacking critical to intermolecular charge transfer. In 1,2-azaborines, the boron center is stabilized through orbital interactions with a lone pair of electrons from the adjacent nitrogen atom, and the resulting planar molecules should not interfere with π stacking.

Treatment of known diaminothiophene **116** with excess $PhBCl_2$ (a synthetic strategy reminiscent of Dewar's early work) afforded bis(azaborine) **117** (Scheme 34). It was



Scheme 34. Synthesis of 1,2,-azaborine-fused oligothiophene materials **117** and **120**.

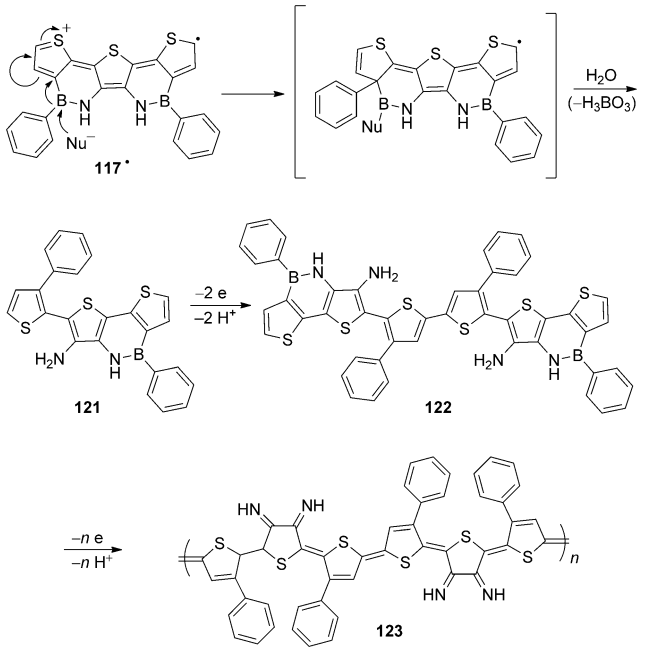
anticipated that the strong acidity of the N–H protons could be problematic for the intended applications or further functionalization, so the ethylene-linked species **120** was synthesized by borylation of the ethylenediaminothiophene compound **119**. The ethylene linker does not distort the planarity of the ring system. X-ray crystallographic analysis of **117** and **120** revealed B–N bond lengths of 1.405–1.460 Å, similar to other reported azaborines and consistent with electron delocalization in the azaborine ring. The structures were almost planar with regard to thiophene rings; however, the phenyl rings lie out of the plane, limiting their conjugation with the polycyclic moiety. Both compounds formed slipped π stacks with alternating head-to-tail orientation and interplanar distances between the parallel thiophene ring systems of 3.47–3.83 Å.

Analysis of UV/Vis absorption spectra for **117** and **120** revealed that the ethylene bridge does not significantly affect the electronic structure; both compounds display almost identical absorption spectra ($\lambda_{abs} = 395$ and 397 for **117** and **120**, respectively). λ_{max} for **117** and **120** is red-shifted compared to non-fused terthiophene (354 nm) and S-bridged pentathienoacene (357 nm). Compounds **117** and **120** exhibit deep-blue photoluminescence at $\lambda_{max} = 407$–410 nm, with $\Phi_{PL} = 25$–34 %. Redox properties for the two compounds were studied by cyclic voltammetry. Both compounds undergo irreversible electrochemical oxidation with anodic peak potential E_{pa} at 0.48 V vs. $[Cp_2Fe]/[Cp_2Fe]^+$, ca. 0.2 V more positive than diaminoterthiophene and consistent with the electron-withdrawing effects of boron.

The stabilizing effect of the intramolecular Lewis acid–base interaction between nitrogen and boron was probed by introducing weak to moderate Lewis bases to solutions of **117** and **120**. No complexation was detected with H_2O, THF, amines, Cl^-, Br^-, I^-, OH^-, or OCH_3^-. However, addition of Bu_4NF to solutions of **120** led to the formation of a mono-(fluoride) adduct, even in the presence of a very large excess of F^-. The binding constant ($\log K_a = 3.3 \pm 0.1$ in CH_2Cl_2) is lower than that of triarylboranes without electronic stabilization of the empty p orbital (for example, $\log K_a = 6.3$ for dithienylmesitylborane in CH_2Cl_2). The emission band of the fluoride adduct is red-shifted to 540 nm with a corresponding color change from blue to green observable by the naked eye. While fluoride sensing by conjugated boron derivatives is well known, most systems are characterized by a blue-shift of the absorbance and quenching of the fluorescence. The authors propose that systems based on **120** could be used as an "off–on" sensor for F^-.

In a subsequent report, Perepichka and co-workers subjected the compounds **117** and **120** to higher oxidation potentials and discovered interesting electropolymerization reactivity that ultimately led to the expulsion of boron and the formation of a low-band-gap polymer.[84] Through careful isolation of partially deborylated donor–acceptor oligomer intermediates **121** and **122** and comprehensive spectroscopic characterization, they were able to elucidate the composition of the insoluble polymer **123**. The proposed mechanism for the formation of electrochemical products is illustrated in Scheme 35.

Controlled potential electrolysis of solutions of **117** was performed at a potential 100 mV more positive than the first oxidation wave. During the first oxidation process, boron elimination and the formation of a new C–C bond between the thiophene and phenyl ring occurs to give species **121**. The first oxidation process of **121** does not lead to boron elimination but instead to a radical coupling process to form the dimer **122** (as in usual thiophene polymerzation). Exposing **122** to high potential (1.07 V vs. $[Cp_2Fe]/[Cp_2Fe]^+$) led to the formation of polymer films analogous to those grown directly from **117**.

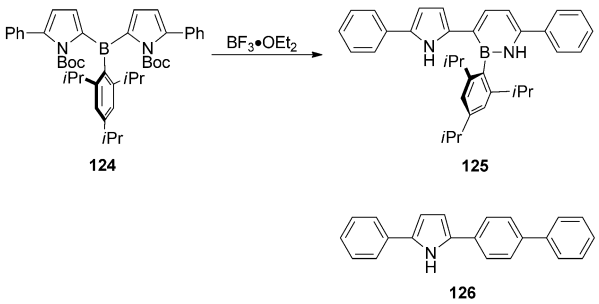


Scheme 35. Proposed formation of deborylated polymer **123** from **117** via intermediates **121** and **122**.

The optical properties of **121** and **122** were probed by UV/Vis and fluorescence spectroscopy. **121** displays blue-shifted absorption ($\lambda_{max} = 352$ nm, $\log \varepsilon = 4.1$) compared to the starting material **117** ($\lambda_{max} = 391$ nm), attributed to an out-of-plane shift of the deborylated thiophene ring. Compound **122** has a red-shifted absorption compared to both **117** and **121** ($\lambda_{max} = 420$ nm, $\log \varepsilon = 4.0$) owing to extended π conjugation. The fluorescence spectra of **121** and **122** exhibit large Stokes shifts of 0.9 and 0.6 eV (6950 and 5013 cm^{-1}), respectively, which points to large structural rearrangements in the excited state. The emission color shifts from deep-blue for **117** to sky-blue for **121** to bright-green-yellow for the dimer **122**.

6. The Yamaguchi Group, Nagoya University

Yamaguchi and co-workers recently reported the synthesis of 1,2-azaborine in an extended π-conjugated system that was unexpectedly obtained in the course of their studies of triarylborane-based functional materials.[85] Attempts to remove the Boc protecting group from triarylborane species **124** by treatment with $BF_3{\cdot}OEt_2$ in refluxing THF led to a complex mixture of products (Scheme 36). Careful separation using preparative gel permeation chromatography enabled the isolation of migratory ring expanded product **125** in 13% yield along with products (totaling 60% yield) resulting from the cleavage of the pyrrole–boron bond. Seizing the opportunity to investigate the potential utility of 1,2-azaborine as a building block in π-conjugated materials, various structural, photophysical, and electrochemical studies of **125** were undertaken and the results were compared with the carbon analogue **126**.



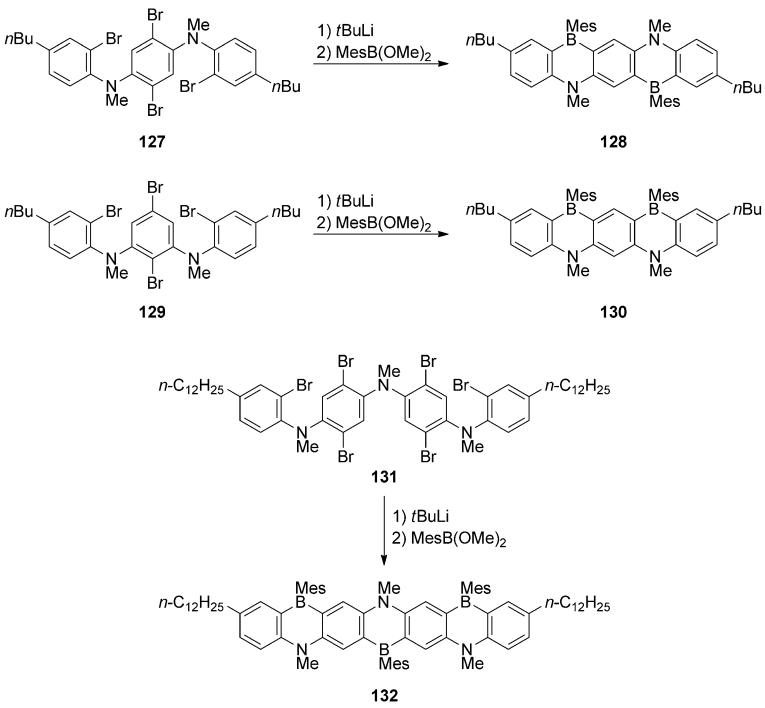
Scheme 36. Synthesis of π-congugated 1,2-azaborine material **125**. Compound **126** was synthesized for comparison.

Two crystallographically independent molecules of **125** exist in a unit cell, with reasonably coplanar π-conjugated skeletons. Dihedral angles between the pyrrole and the azaborine and between the azaborine and the phenyl group

are in the range of 7–14° and 30–34°, respectively. The bulky 2,4,6-triisopropylphenyl (Tip) group does not impede π-conjugation over the framework, but prevents intermolecular π–π interactions. Analysis of bond lengths in the azaborine portion of **125** revealed that the B–N moiety has less double bond character than an isolated B–N bond due to π conjugation in the azaborine ring; however, the extension of the π conjugation at the 3- and 6-positions may decrease the aromatic character of the azaborine ring compared to non-π-extended 1,2-azaborines.

In CH_2Cl_2, UV/Vis absorbance and fluorescence maxima for **125** are red-shifted from the carbon analogue **126** by 57 and 70 nm, respectively. Both compounds show only subtle solvatochromism in both the absorbance and emission spectra. Compound **125** has very high quantum yields, which are close to unity even in polar solvents such as MeOH and significantly higher than **126**.

Cyclic voltammetry experiments performed on **125** and **126** indicate a higher HOMO level and a narrower HOMO–LUMO gap for **125**, consistent with the red-shifted absorption maximum. The authors reasoned that the differences in the redox potential and photophysical properties between **125** and **126** are due to the nonaromatic character of the azaborine ring. In this context, the azaborine ring can be considered a cyclic butadiene analogue and, in fact, DFT calculations at the B3LYP/6-31G(d) level revealed that the frontier orbital energy levels of **125** are more similar to a cyclohexa-1,3-diene model than the benzene-containing **126**. NICS(0) calculations performed on the 1,2-azaborine ring in **125** were slightly more positive ($\delta = -4.73$ ppm) than the parent 1,2-azaborine ($\delta = -5.10$ ppm), which is indicative of decreased aromaticity.



Scheme 37. Synthesis of BN-pentacene isomers **128** and **130** and BN-heptacene **132**.

Table 4: Photophysical properties of BN-acenes.

	λ_{max} [nm]/log (ε)	λ_{em} [nm]	Φ
128	523/4.23	534	0.69
130	415/3.94	428	0.21
132	608/4.28	625	0.55

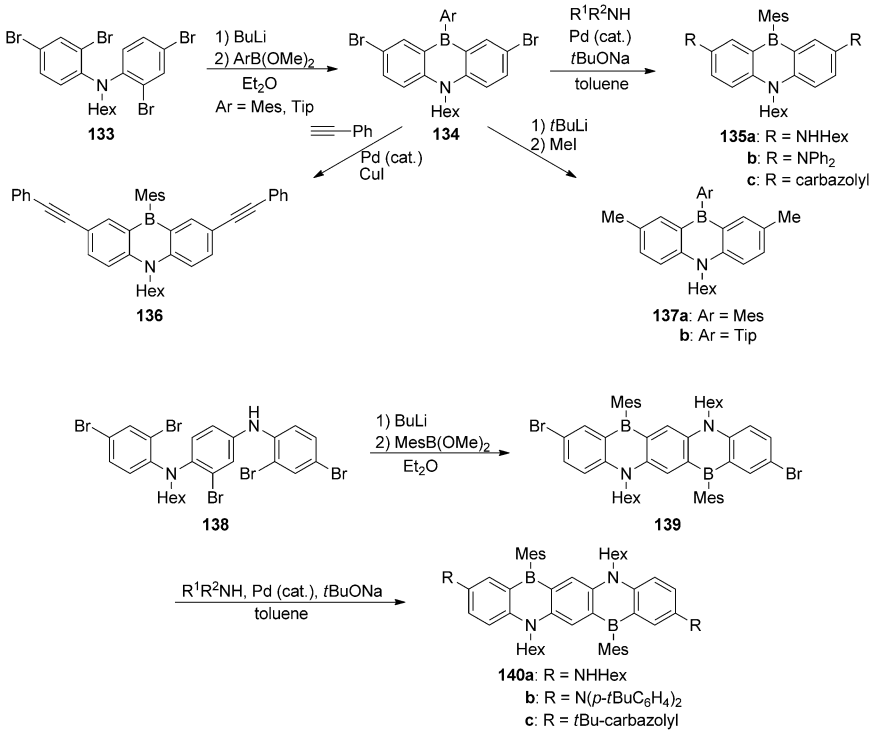
7. The Kawashima Group, University of Tokyo

Kawashima and co-workers have explored the incorporation of the 1,4-azaborine motif into anthracene and ladder-type pentacene and heptacene analogues, with the goal of utilizing these compounds in OLED devices.[86] The synthesis of BN-pentacene **128** was achieved by treatment of the *para*-diamino arene **127** with $MesB(OMe)_2$ (Scheme 37). Similar transformations from *meta*-diamino arene **129** and triaminoarene **131** generated **130** and **132**, respectively. All three compounds were air- and moisture-stable, which was ascribed in part to the sterically demanding mesityl substituents at boron.

The X-ray crystal structure of **128** revealed that the BN-pentacene framework is virtually coplanar, indicating an extended π-conjugated system. No evidence of intermolecular π stacking was observed owing to the bulky mesityl groups, which interfere with close packing. The absorption and emission properties of **128**, **130**, and **132** were examined and are summarized in Table 4. The absorption and emission maxima observed for **128** and **132** are red-shifted relative to BN-anthracene, which is consistent with extended conjugation. On the other hand, BN-pentacene **130**, in which the 1,4-azaborine rings are oriented parallel to each other, displayed optoelectronic properties that were very similar to BN-anthracene.

After their initial report on BN-pentacene and heptacene analogues, Kawashima and co-workers developed a more general route to substituted 1,4-azaborine containing anthracene as well as previously described anti-parallel pentacene derivatives (Scheme 38).[87] An *ortho*-selective dilithiation of **133** and subsequent treatment with arylbroronic esters generated dibromo-substituted products **134**, which could be further elaborated by Buchwald-Hartwig amination, Sonogashira cross-coupling, or lithium–halogen exchange/electrophile addition (MeI) to give products **135**–**137**. The same procedure could be expanded to the synthesis of ladder-type azaborines by tetralithiation of **138**. The bromonated product of this reaction, compound **139**, could not be isolated owing to poor solubility; however, solublizing groups could be added to the crude mixture and the substituted BN-pentacene compounds **140a–c** could be isolated in moderate yield.

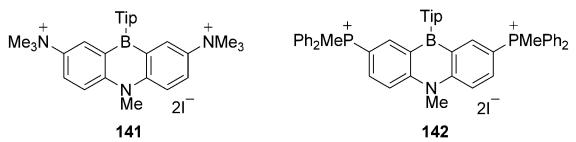
UV/Vis spectra for compounds bearing electron-donating amino groups (that is, HexNH in **135a** and Ph_2N in **135b**)



Scheme 38. General route to BN-anthracenes **135**–**137** and BN-pentacenes **140a**–**c**.

showed red-shifted absorptions relative to the reference compound, methyl-substituted **137a**, owing to elevation of the HOMO level. The carbazolyl-substituted BN-anthracene **135c** had an absorption wavelength close to that of the reference compound **137a** and had a fluorescence quantum yield of unity, attributed to molecular rigidity. The ladder-type azaborines **140a–c** displayed similar absorbance properties, with red-shifted absorption maxima corresponding to increasing electron-donating ability of the pendant amine groups. The carbazolyl substituted derivative **140c** also showed the highest fluorescence quantum yield.

In a subsequent report, Kawashima and co-workers utilized the same general reaction sequence to develop dicationic ammonium- and phosphonium-functionalized BN-acenes **141** and **142**, which are capable of acting as fluorescent sensors for biologically relevant anions such as fluoride and cyanide (Scheme 39).[88] These compounds retain the optical properties of the azaborine motif and do not aggregate in aqueous media. The complexation ability of ammonium-functionalized species **141** with all of the anions screened was too weak to observe by UV/Vis or fluorescence spectroscopy; however, the phosphonium species **142** displayed a very high affinity for the cyanide ion and was almost inactive against other environmentally common anions under

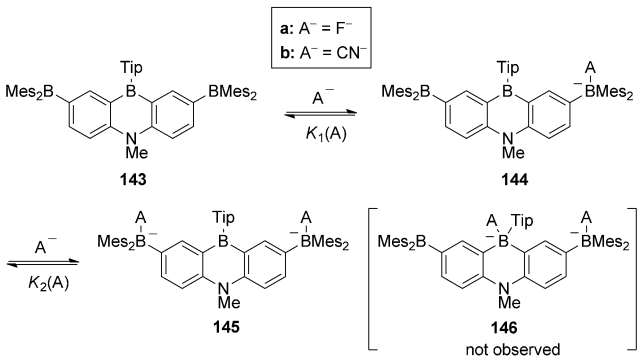


Scheme 39. Dicationic BN-anthracenes **141** and **142**.

the testing conditions. Titration experiments were used to find the complex formation constant between **142** and the cyanide ion ($(1.2(4)\times10^5\,L\,mol^{-1}$ in DMSO/H_2O (4:6 v/v) and $5.2(5)\times10^4\,L\,mol^{-1}$ in 100% H_2O). Fluorescence quenching experiments with various anions revealed that only CN^- quenched the emission of **142** to a degree that was clearly observable with the naked eye.

Around the same time, Kawashima and co-workers reported the synthesis and fluoride sensing ability of a bis(dimesitylboryl)azaborine **143**, again taking advantage of the general synthetic methodol they had previously developed (Scheme 40, series **a**).[89] Their rationale for the introduction of strong π acceptors (that is, Mes_2B) into the 1,4-azaborine framework was twofold: First, the Mes_2B group decreases the LUMO energy level, thus increasing the Lewis acidity of the azaborine unit. Second, coordination of multiple Lewis bases to the peripheral boron atoms (in addition to the azaborine boron center) can alter the donor–acceptor interactions within the molecule and thus vary the absorption and emission color based on the amount of guest ion. The introduction of dimesitylboryl groups resulted in a hypsochromic shift in the absorbance maximum (377 nm vs. 405 nm for the *N*-Me derivative of **137a**) and an about tenfold increase in the extinction coefficient. To investigate the Lewis base detection ability, **143** was treated with excess nBu_4NF and monitored by FAB mass spectrometry and ^{11}B NMR spectroscopy. Signals consistent with the formation of **144a** and **145a**, rather than **146a**, were observed (that is, shifting of the peak corresponding to Mes_2B groups but not the azaborine peak). This conclusion was supported by molecular orbital calculations, which show that the LUMO is distributed over the two Mes_2B groups, kinetically favoring Lewis base coordination at those sites. UV/Vis-monitored titration of **143** with nBu_4NF showed the stepwise formation of **144a** and **145a** and the values of K_1 and K_2 were determined to be $>10^8\,L\,mol^{-1}$ and $7\times10^5\,L\,mol^{-1}$, respectively. Fluorescence spectrometry could also be used to monitor complex formation, and it was possible to detect the fluoride ion at sub-micromolar concentrations. However, because of the much smaller value of K_2 than K_1, the blue-shifted emission band corresponding to species **145a** was only visible upon addition of a large excess of fluoride ion.

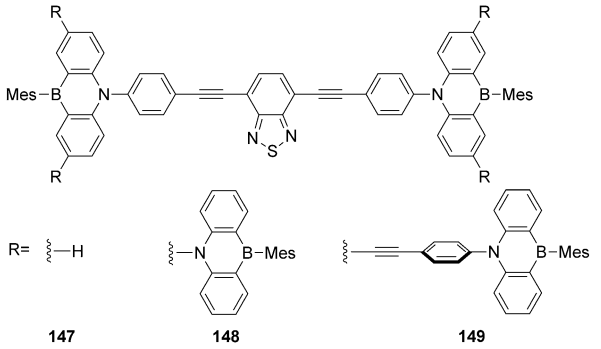
In another report published in 2009, Kawashima and co-workers used the bis(dimesitylboryl)azaborine **143** for multistep detection of the cyanide ion (Scheme 40, series **b**).[90] In the case of CN^-, the values of both K_1 and K_2 exceed the limit of precise estimation ($>10^8\,L\,mol^{-1}$ in THF), thus the cyanide ion seems to form a much stronger complex with **143** than the fluoride ion does, despite the affinity of boron for fluoride. The fluorescent color shift from violet ($\lambda = 420$ nm) corre-



Scheme 40. Multistep F^- and CN^- anion sensing with bis(dimesitylboryl)azaborine **143**.

sponding to the mono(cyanoborate) species **144b** to blue ($\lambda =$ 433 nm) corresponding to dicyanoborate **145b** was visible with the naked eye upon addition of just 2.6 equiv of CN^-.

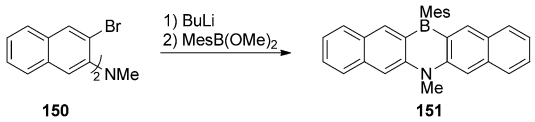
The Kawashima group has also reported the construction of π-conjugated dendrimeric structures based on a 1,4-BN-anthracene branching unit that features additional pendant BN-acene groups (Scheme 41).[91] Conjugated dendrimers bearing both electron donors and acceptors are expected to



Scheme 41. π-Conjugated dendrimers based on BN-anthracene.

show n-type or ambipolar charge transfer ability, both of which are important in organic field-effect transistors. Both the branching and terminal BN-acene moieties were synthesized in a similar manner to the compounds described above, and the dendron arms were synthesized by palladium-catalyzed coupling reactions between branching and terminal units. The optical properties of the dendrons are similar to those of the parent azaborines, indicating that the azaborine units are aligned perpendicularly to each other. Dendrimers **147**–**149** were constructed from TMS-protected dendrons using standard Sonogashira conditions. Emission from the dendrimers stems from an intramolecular charge transfer (ICT) between the dendrons and the core. DFT calculations suggest that electron transfer from the dendrons to the core is thermodynamically favorable process, but experimental results indicate that the fate of the ICT excited states strongly depends on the generation of the dendron.

In 2010 Kawashima and co-workers reported the synthesis of a dinaphthoazaborine based on a modification of their general synthetic method (Scheme 42).[92] Dilithiation of the dibromoamino species **150** with subsequent addition of $MesB(OMe)_2$ at −78 °C afforded dinaphthoazaborine **151**. Analysis of the single-crystal X-ray structure of **151** showed

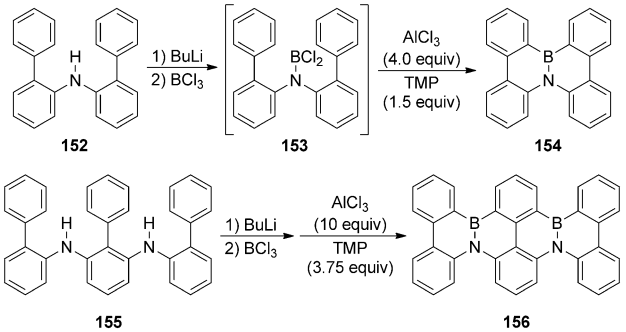


Scheme 42. Synthesis of dinapthoazaborine **151**.

that the dinaphthoazaborine skeleton is butterfly-like and the angle between the two naphthalene rings is 15°, compared to the 9° (average) bent angle between the two benzene rings of the *N*-Me derivative of **137a**. In contrast to **137a**, there are clear intermolecular π–π and CH–π interactions between molecules of **151** in the solid state, which affect its solid-state fluorescence properties. In hexanes, the UV/Vis absorbance maximum for **151** ($\lambda = 519$ nm) is red-shifted by 114 nm from that of **137a**, indicating elongation of the π-system and a decreased HOMO–LUMO energy gap. The emission maximum of **151** is red-shifted by 103 nm; however, the quantum yield is lower than that of **137a**. Also, unlike **137a**, **151** does not show detectable solid-state fluorescence. Electrochemical analyses revealed that **151** forms a stable radical anion at relatively low potential (−2.1 V vs. $[Cp_2Fe]/[Cp_2Fe]^+$), which could lead to possible applications as an electron acceptor and anion sensor.

8. The Nakamura Group, Kyoto University

Hatakeyama, Nakamura, and co-workers very recently reported an efficient route to BN-fused analogues of polycyclic aromatic hydrocarbons (PAHs) based on a tandem intramolecular electrophilic arene borylation procedure (Scheme 43).[93] Facile access to this structural motif allowed them to characterize these materials with an eye toward potential applications in organic electronic functional materials. The arene borylation precursor, dichloroboraneamine **153**, was generated in situ from bis(biphenyl-2-yl)amine **152**. After screening a variety of Lewis acids and Brønsted bases, it was found that treatment of **153** with 4 equivalents of $AlCl_3$



Scheme 43. Synthesis of BN-fused polyaromatics **154** and **156**.

and 1.5 equivalents of 2,2,6,6-tetramethylpiperidene (TMP) afforded the BN-PAH **154** in 67% yield. It was also determined that the $AlCl_3$/TMP stoichiometry is critical to achieving a high yield. The same optimized conditions could be used to generate the bis(BN)-fused PAH **156** from starting amine **155**.

The X-ray crystal structure of **154** revealed that the B–N bond length (1.426(3) Å) is shorter than typical in BN-aromatics (1.45–1.47 Å) and more consistent with a B=N double bond. B–C and N–C bond lengths are consistent with single-bond character. The low apparent aromaticity of the azaborine ring is in agreement with the calculated NICS(1) value of −2.9. In the solid state, **154** adopts a twisted configuration at the heteroatom bridge and an alternating enantiomeric (that is, left- or right-handed) helical packing structure. The carbon analogue of **154**, dibenzo[*g*,*p*]chrysene, was also analyzed by X-ray crystallography and displayed remarkably similar solid-state parameters (for example, a twisted structure with significant double-bond character of the bridging C–C bond) and similar physical properties, including melting point (229 °C vs. 227 °C for **154**). However, the solubility of **154** was much higher than dibenzo-[*g*,*p*]chrysene in common organic solvents, which is presumably due to its dipole moment. Surprisingly, despite its extended polycyclic aromatic structure, **156** was found to be moderately soluble in organic solvents such as chloro- and 1,2-dichlorobenzene.

Using time-resolved microwave conductivity measurements, **154** was found to have high intrinsic hole mobility ($0.07\ cm^2V^{-1}s^{-1}$), which is ten times higher than dibenzo-[*g*,*p*]chrysene, and rivals rubrene ($0.05\ cm^2V^{-1}s^{-1}$), one of the most popular organic semiconductors. The superior hole mobility of **154** was attributed to partial localization of the frontier orbitals induced by BN substitution, which strengthens the electronic coupling between neighboring atoms in the solid state. The favorable electronic properties, straightforward synthesis, and surprising solubility make **154** and **156** suitable for use in organic electronics.

9. Emerging Applications and Future Directions

From the breadth of synthetic approaches and novel reactivity presented herein it is clear that the ubiquity of the arene motif coupled with the unique properties stemming from BN/CC isosterism present no shortage of potential applications for this chemistry. BN incorporation into aromatic scaffolds can lend favorable properties to organic optoelectronic materials and create highly selective molecular ion sensing platforms. The dual hydridic/protic nature of B–H/N–H bonds can be harnessed for chemical hydrogen storage. BN/CC isosterism can also be used as a way to "disguise" boron for potential biological applications. The study of BN aromatic compounds can also enrich our fundamental understanding of aromaticity itself. Emerging synthetic techniques stemming from this research may further expand the toolkit available to curious chemists in other fields as well.

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