Published in final edited form as:
Chem Rev. 2012 July 11; 112(7): 4246–4282. doi:10.1021/cr200133c.

Cationic Tricoordinate Boron Intermediates: Borenium Chemistry from the Organic Perspective

Timothy S. De Vries, **Aleksandrs Prokofjevs**, and **Edwin Vedejs***
Department of Chemistry, University of Michigan, 930 N. University Ave., Ann Arbor MI 48109

1. Introduction

The focus of this review is on the reactivity of cationic, tricoordinated boron electrophiles, and on recent applications that rely on intermediates having sextet boron and net positive charge. Older reviews have appeared that address early studies involving a variety of boron cations,[1] or that emphasize the structural, bonding, and theoretical aspects of di-, tri-, and tetracoordinate boron cations (borinium, borenium, and boronium, respectively; Fig. 1).[2] The latter review by Kölle and Nöth is a milestone in the field of boron cation chemistry. It systematizes a number of earlier observations, and defines the currently accepted nomenclature for boron-containing cations. A more recent (2005) review by Piers *et al.* updates the structural and bonding aspects in depth,[3] discusses reactions of boron cations in the gas phase as well as in solution, and explores several other topics of special interest to the organoelement community. We will take a somewhat different approach to follow developments from the organic chemistry perspective, including selected historical aspects of reactivity, some of which have not appeared in prior reviews. Several topics will necessarily overlap with the excellent overview by Piers *et al.*, but detailed coverage will be limited to the solution chemistry of tricoordinate boron cations, the reactive intermediates known as borenium ions according to Nöth's classification.[2] This terminology depends on the number of ligands at boron and avoids distinctions based on bond order or resonance contributions. Nöth's treatment also recognizes the iso-electronic relationship between borenium and carbenium ions, both of which feature a formally vacant *p*-orbital at the central atom (boron and carbon, respectively) and the same overall positive charge. Consistent with the carbenium analogy, borenium ions have long been suspected as intermediates in classical nucleophilic substitution chemistry involving B–X bonds in tetracoordinate boron structures, although we will find that these suspicions were often unfounded. On the other hand, recent studies have revealed fascinating new roles for borenium intermediates, ranging from enantioselective catalysis and memory of chirality applications to hints of C–F activation and C–H insertion chemistry. It would be fair to say that these recent developments were slow to unfold, given the long history of borenium chemistry.

2. History of borenium ions: often considered, seldom confirmed

2.1 Suspected intermediates in B-N protonation

The first reports to our knowledge where cationic sextet boron was implicated are the two 1933 papers by Wiberg and Schuster that describe the reaction of dichloro(dimethylamino)borane **1** with hydrogen chloride.[4] The experiment was said to produce the hydrochloride (*chlorhydrat*) of **1**, drawn using the notation shown as **2a** (eq.1). This representation does not specify connectivity, and nothing in the 1933 papers indicates

edved@umich.edu.

whether **2a** is the same or different compared to the borenium salt **2b**. Whether the authors intended to distinguish **2a** from representations such as **3a** or **3b** is also uncertain. On the other hand, a 1947 paper by Wiberg and Hertwig shows a similar reaction ($R_2BNHR + HCl$, eq. 2) and provides two generalized drawings of a single ionic structure (**5a** and **5b**) that is clearly identified as the *unstable intermediate* leading to an isolable covalent adduct, drawn by Wiberg and Hertwig in two unambiguous representations **6a** and **6b**.[5] These drawings and appended comments leave no question about the structure of **5** and the greater stability of **6**. However, they may have escaped the notice of subsequent authors, some of whom accepted the borenium structure **2b** as a more stable alternative compared to **3b** and attributed this conjecture to Wiberg.

2.2 Hypothetical isomers of $Cl_3B{\cdot}NHMe_2$

In 1952, Brown and Osthoff argued that **2b** is "probably correct", and constitutes a better representation than **3b**. As partial support for this assignment, they noted that the substance reacts rapidly with aqueous silver ion to precipitate AgCl under conditions where $Cl_3B{\cdot}NMe_3$ is inert.[6] Two years later, a study by Goubeau *et al.* reached the opposite conclusion in favor of **3b** as the stable structure because a solution in chloroform does not conduct electric current, in contrast to diethylamine hydrochloride.[7] Nevertheless, **2b** appeared again in a subsequent report suggesting that the preferred structure may depend on the conditions used for the generation of **2**/**3**.[8] Such issues were not easily resolved using the instrumental methods available to most workers by 1960 (primarily, IR spectroscopy), and relevant ^{11}B NMR data were not reported until much later. In 1975, Ryschkewitsch and Myers observed a ^{11}B chemical shift of $\delta = 8.7$ ppm (downfield vs. $BF_3{\cdot}OEt_2$ at 0.0 ppm),[9] a value that is consistent with tetracoordinate boron as in **3b** and is well upfield of the range expected for **2b** according to more recent studies of non-stabilized borenium species (δ >50 ppm).[2,3] The former authors did not mention that there had been any disagreement regarding the structure (**2b** vs. **3b**), nor did they make strong claims regarding their own NMR-based assignment of structure **3b**.[9] However, Ryschkewitsch and Meyer did raise the possibility that an equilibrium between **3b** and the borenium salt **7** may explain the formation of a cationic byproduct **8** containing tetracoordinate boron (a boronium salt) when dimethylamine is reacted with BCl_3 (eq. 3).

2.3 The first observable borenium salt

By 1970, Ryschkewitsch *et al.* had already encountered related chemistry starting from the adduct **9** of 4-picoline and BCl_3 (eq. 4). Treatment of **9** with 2 equiv of aluminum chloride in dichloromethane gave an equilibrium mixture containing mostly (K_{eq} = ca. 20) the tri-coordinated cation **10** according to the concentration-dependent ^{11}B chemical shift (δ 47.3 = ppm).[10] The solution of **10** reacted spontaneously with trimethylamine to form the boronium salt **11**. In contrast to **10**, the starting **9** did not react with trimethylamine under similar room temperature conditions in the absence of aluminum chloride. Thus, **9** does not equilibrate with the borenium chloride **12** spontaneously, and the role of aluminum chloride is to force the equilibrium to **10** by abstraction and binding of chloride. Finally, addition of Me_4NCl to the solution of **10** resulted in reversion to **9**, thereby confirming the lower stability of the borenium ion **12** compared to **9**. This behavior is consistent with the presence of a mostly unoccupied orbital at boron in **10**, an issue that will be revisited in a later section of this review. Structure **10** has stood the test of time,[10b] and has become a reference point for the spectroscopic characterization of labile borenium structures. It has also established a definitive precedent for generating transient borenium intermediates by B–X heterolysis in the presence of halophilic Lewis acids (BCl_3, Al_2Cl_6, etc.).

2.4 Nucleophilic substitution of $X_3B{\cdot}NR_3$ and $Py{\cdot}BF_2X$

Facile leaving group displacements are known with many amine-trihaloborane adducts,[11–21] and rationales involving the S_N1-like generation of borenium ions have been considered repeatedly.[12–16] However, detailed investigations have found that bimolecular mechanisms are generally preferred. Persuasive evidence for S_N1-like leaving group heterolysis has been reported in only one system, the reaction of the trimethylamine triiodoborane complex **13** with anionic nucleophiles (eq. 5).[15] This process occurs in dichloromethane at 50 °C in the absence of added halophiles, and the qualitative observations implicate a borenium ion **14** as the intermediate in halide exchange leading to **15**. On the other hand, halide exchange from the analogous adducts **16** (X= F, Br) with BCl_3 occurs by a bimolecular process to afford **18** (eq. 6), among other products.[15] The reaction is believed to take place via a bimolecular transition state such as **17**, and not by S_N1 heterolysis to a borenium ion. No exchange of halides occurs between various pairs of reactants **13** and **16** at 50 °C, and **16** does not undergo exchange with Et_4NCl in the absence of BCl_3, in contrast to the behavior of **13**. Furthermore, isotopic label experiments using ^{10}B-containing substrates **13** and **16** rule out competing B–N dissociation pathways under the reaction conditions. This evidence is consistent with the borenium pathway for halide exchange from **13**, but not from **16**.

In a more recent investigation, the conversion of the difluorohaloborane complex **19** to the boronium salt **21** was shown to occur by a bimolecular mechanism according to the classical test that rate depends on the reactivity of the nucleophile (eq. 7).[16,17] Several qualitative reactivity comparisons were made, and the pyridine example (**19**, R= H) was found to procceed to **21** within minutes at room temperature, too fast for NMR monitoring. In contrast, the 2-picoline case (**19**, R= *o*-methyl) required 1–2 hours to achieve similar conversion to **22**. The fluorine substituents in **19** were essential for good reactivity, and are believed to help stabilize a penta-coordinated transition state **20**. The analogous BBr_3 adduct did not react at room temperature.

By the same test of nucleophile-dependent reactivity, the trimethylamine iodoborane complex **23** also reacts by an S_N2-like mechanism to form boronium salts **24** with various amines (eq. 8; R= H, 5 h at room temperature; R= CN, 5 h, 70 °C, both in benzene).[22,23] The relative ease of this bimolecular reaction for R= H is interesting because **23** is isosteric with neopentyl iodide. Evidently, the differences in bond lengths (dative B–N > C–C) and electronegativity (B < C) result in a looser S_N2 transition state that better tolerates the steric demands of the nucleophile. It is harder to say how the differences in electronegativity in **23** compared to neopentyl iodide would affect an S_N1 heterolysis process, but there is no evidence that a primary borenium ion **25** would be energetically accessible. Certainly, the isoelectronic and isostructural neopentyl carbenium ion would not be regarded as a plausible intermediate in benzene at room temperature, and generation of **25** under these conditions seems unlikely. Several related nucleophilic substitution reactions of **23** under comparably mild conditions have also been reported. [24–27]

Based on the evidence presented so far, simple borenium intermediates that lack stabilization from an adjacent electron donor such as the **π** system in **10** (eq. 4) should be invoked only after a careful evaluation of alternative mechanisms. There is some evidence that the combination of a weak B–I bond and increased substitution at boron may be sufficient to allow B–I heterolysis, as in the equilibrium between **13** and **14** (eq. 5), but this is an unusual environment. On the other hand, the presence of second row substituents (B–N, B–O) that can donate unshared electron pair density to boron is quite common, and promotes stabilization of borenium intermediates by lone pair (*n*) delocalization involving the boron *2p*-orbital, as discussed below.

2.5 Aminoborenium ions; stabilization by n-delocalization

Nöth and Fritz considered the possible role of *n*-stabilized aminoborenium ions in the protonation of bis(dialkylamino)boranes during the 1960's,[28] but convincing evidence was not obtained until well-behaved substrates were encountered in the 1,3-diazaborolidine series (Scheme 1). [29] Thus, protonation of **26** with triflic acid generated the amine-stabilized cation **27** in solution (^{11}B δ = 25.8 ppm). The same cation was obtained in crystalline form using an alternative method via nucleophilic displacement and internal proton transfer from **29**, and the structure was confirmed by X-ray crystallography. These experiments indicate that **27** is more stable than the covalent adduct **28**, although they do not exclude the possibility that **28** is present in equilibrium with the borenium ion **27**. Chemical shift comparisons among a number of related (diamino)borenium salts show δ ^{11}B values in the range of 24–31 ppm with counterions including bromide, triflate, and tetrachloroaluminate. The minimal anion dependence of chemical shifts is easily understood if tetracoordinated adducts such as **28** are minor components in equilibrium due to *n*-delocalization by the two amino groups. The *n*-delocalization effect is also responsible for the relatively high field ^{11}B chemical shift values for **27** and related salts compared to tricoordinate boron cations lacking *n*-delocalization (δ > ca. 45 ppm). [2] On the other hand, neutral tetracoordinate boron species similar to **28** are observed at δ ^{11}B values of ca. 0 ± 15 ppm.[2,29]

The nucleophilic displacement method can also be used with hindered amines, as illustrated by the reaction of triflate **29** with 2,6-lutidine to afford the borenium salt **30** (Scheme 1). A similar borenium salt can be obtained starting from the 2-chloro-1,3-diazaborolidine **31**, but the chloride is not sufficiently reactive unless it is converted into the isolable Lewis acid adduct **32** using $AlCl_3$. Although **32** has no net charge, it does contain a borenium subunit that apparently facilitates nucleophilic attack below room temperature via the presumed intermediate **33** to give **34** (>90% isolated). An alternative mechanism has not been ruled out where **32** is converted into the transient borinium cation **35** prior to attack by the nucleophile. Related acyclic borinium cations are known, but they are stabilized by allenic delocalization. In a cyclic environment, similar delocalization would require a larger ring (as in the observable **36** with n = 4) to accommodate sp-hybridized dicoordinate boron,[2] but this would not be feasible in the diazaborolidine environment (**36** with n = 0). Many other examples of relevant aminoborinium and aminoborenium ions are discussed by Kölle and Nöth in their 1985 review[2] that will not be repeated here. Nöth also addressed several methods for the generation of various other boron cations,[30] including borenium ions that lack *n*-delocalization. The following paragraphs will focus on newer developments in methodology. Most of these studies were conducted to explore the limits for isolation of minimally stabilized, highly electrophilic borenium species (Sections 3, 4), but some of the work was stimulated by intended applications in organic synthesis that are discussed later (Sections 5–7).

3. Recent developments in the generation of observable borenium intermediates

3.1 Electrophilic activation by protonation or by Lewis acid catalysis

Protonation of aminoboranes is the oldest method for generating transient as well as stable borenium salts. It has not been used extensively in recent efforts to detect minimally stabilized borenium species, but interesting synthetic applications have appeared that exploit chiral borenium ions and analogues as enantioselective catalysts (see Section 6 for details). A specific example is shown in eq. 9 where the oxazaborolidine **37** is treated with TfOH to generate a mixture of equilibrating species including **38** and **39** according to ^{1}H NMR considerations.[31] Although no ^{11}B NMR data were reported, the presence of the borenium ion **38** in the equilibrium mixture was supported by observing that the mixture functions as a

potent chiral Lewis acid catalyst for the Diels-Alder reaction of 1,3-butadiene at −78 °C. If **38** is one of the two major species observed by ^{1}H NMR, then substantial borenium cation stabilization by the oxygen electron pairs can be inferred.

Borenium salt **38** is structurally related to key intermediates in the enantioselective CBS reduction using the Corey-Itsuno catalysts **40** in combination with THF·BH_3 (eq. 10).[32] In the first stage of this fascinating process, borane is proposed to function as a Lewis acid that converts **40** into the activated intermediate **41**. Although **41** has no net charge, it does contain a borenium subunit and can therefore function as a Lewis acid that binds the carbonyl oxygen of a ketone substrate to accelerate nucleophilic attack by internal hydride in a 6-center process. The proposed role of **41** is supported by extensive enantioselectivity data and analogies to be discussed further in Section 6.

The conversion from **40** to **41** resembles the activation of **31** by aluminum chloride that was discussed in connection with Scheme 1. Lewis acid activation should also be possible with borane derivatives having B–O, B–F, or B–Cl bonds instead of B–N bonds. In the broader sense, any Lewis acid that is capable of interacting with the electron pair of a boron–heteroatom bond can produce transient species having partial borenium ion character.

3.2 Halide abstraction by a halophile

The first method shown to generate an observable borenium ion **10** was discussed in Section 2 (eq. 4) and involved chloride abstraction from the boron trichloride complex **9** by aluminum trichloride. Improved versions of this general approach are featured in several recent studies involving the generation of minimally stabilized borenium ions (Scheme 2). Thus, the pyridine complex **42** of diphenylchloroborane was treated with the chlorophile $SbCl_5$ in dichloromethane at rt to generate a dark yellow solution of the air-sensitive borenium salt **43** (^{11}B δ = 58.2 ppm).[33] This substance is of interest because it is isoelectronic with trityl cation, and because its properties help to clarify a long-standing mystery regarding the apparent generation of hypothetical dicoordinated diphenylborinium salts Ph_2B^+ ClO_4^- or Ph_2B^+ $SbCl_6^-$. Thus, treatment of **43** with 1 equiv of pyridine afforded the boronium salt **44** (^{11}B δ = 8.6 ppm). The same salt had been obtained earlier by the reaction of Ph_2BCl with $SbCl_5$ in deuterated nitromethane, followed by the addition of pyridine. However, the initially formed cation generated from Ph_2BCl and $SbCl_5$ in nitromethane was found to have a ^{11}B signal at δ = 19.8 ppm, far upfield of the 85.5 ppm value calculated for diphenylborinium cation, but consistent with the solvated (boronium) structure **45**. Presumably, **45** then reacts with sequentially added pyridine via dissociation to the borenium intermediate **46**. These findings suggest that earlier encounters with "Ph_2B^+ " species in polar solvents more plausibly involved the corresponding solvated (tetracoordinate) boron cations (boronium salts). Furthermore, chemical shift calculations indicate that the perchlorate derivative depicted earlier as the ionic borinium salt Ph_2B^+ ClO_4^- prefers the covalent structure Ph_2BOClO_3 based on a ^{11}B signal at δ = 46.0 ppm in nitromethane (calcd 47.0 ppm).[34] If the computational level [B3LYP/6–31+G(d)] in the hypothetical gas phase environment reflects the situation in nitromethane as suggested by the chemical shift match, then the perchlorate is bound to boron in a monodentate arrangement, and the tricoordinated Ph_2BOClO_3 is not complexed to the moderately nucleophilic nitromethane.

Many of the recent advances in the generation and isolation of highly electrophilic borenium salts have been made by using variations of the halide abstraction method (Scheme 2). Thus, Gabbai et al. employed an approach where the tetracoordinated substrates are formed in situ from hindered diarylfluoroboranes **47** and DMAP in the presence of trimethylsilyl triflate (TMSOTf) as the fluorophile.[35] This approach gave sterically protected, crystalline

borenium salts **48** or **49** that were sufficiently stable for X-ray structure determination. A similar approach allowed isolation of the *N*-heterocyclic carbene adduct **50** by using an in situ source of the nucleophilic carbene, 1,3-dimethylimidazolidene, in place of DMAP.[36] A related activation mechanism via a borenium intermediate has been suggested for the conversion of 9-chloro-9-bora-9,10-dihydroanthracene into boronium salts upon treatment with silver tetrafluoroborate in the presence of bipyridines.[37]

Scheme 2 also illustrates two halide abstraction examples involving extensively conjugated heterocyclic substrates. Both examples generate borenium cations (**52** from **51**[38] and **55** from **54**[39]) using triethylsilyl cation equivalents as exceptionally potent halophiles. In addition to their high reactivity, the triethylsilyl reagents serve as convenient sources of minimally interactive anions such as tetrakis(pentafluorophenyl)borate, $(C_6F_5)_4B^-$, and the brominated carborane $CbBr_6^-$ that are required for isolation and X-ray characterization of the highly electrophilic, air-sensitive borenium ions **52** and **55**.[38,39a,b] Another advantage of the triethylsilyl cation reagents is that the only byproduct of borenium ion generation is the volatile and easily removed triethylhalosilane. That key advantage was especially useful for the isolation of **55**, a cation that has been implicated as an intermediate in the substitution chemistry of the subphthalocyanine **54**, and also in the controlled ring expansion of **54** into phthalocyanines.[39c] In connection with the related preparation of **52**, it is also worth noting that the $(C_6F_5)_4B^-$ anion was sufficiently stable to survive under the conditions for reduction of **52** to **53** with di-isobutylaluminum hydride.[38] Like its precursor, **53** was characterized by X-ray methods, and the substance constitutes a rare example of an observable borenium ion that contains a B–H bond.

A somewhat different example of halide abstraction form a heterocyclic substrate is shown in eq. 11.[40] In contrast to the examples of Scheme 2, the tetracoordinate **56** is converted to a borenium ion **57** by the moderately fluorophilic borontrifluoride etherate, evidence that **57** has lower fluoride affinity. One might question whether it is correct to regard **57** as a borenium ion since the heterocyclic cation is part of a conjugated 6**π**-aromatic system, but the borenium terminology is based only on the coordination number and net positive molecular charge, and not on bond order at boron.[2] Nevertheless, it is clear that **57** and related aromatic cations of the general structure **58** belong in a very different stability category. In some cases, related cations survive if the counterion X^- is triflate, or even the relatively nucleophilic chloride anion.[40,41] Clearly, aromaticity is an important factor in this environment, and cations such as **57** and **58** constitute a special case. For that reason we will not comment more on their chemistry, although we will briefly revisit their electrophilicity in Section 4.

A special case at the lower end of the stability range is shown in eq. 12. Treatment of **59** with the strongly chlorophilic carborane salt $Ag^+ CbBr_6^-$ in the presence of 0.9 equiv of triethylphosphine oxide results in the formation of an isolable, crystalline borenium salt **60** that was characterized by X-ray crystallography.[42] Formation of **60** may involve a typical chloride abstraction from the phosphine oxide adduct **61** that should be formed reversibly. However, chloride abstraction also occurs in the absence of the phosphine oxide in experiments where **59** is treated with the $Et_3Si^+ CbBr_6^-$ reagent in aromatic solvents. These observations raise the intriguing possibility that a species equivalent to the borinium ion **62** may be accessible. No electrophilic boron species could be detected by spectroscopy in these experiments, but their generation is supported by the formation of electrophilic borylation products derived from the aromatic solvent as discussed further in Section 8. Although the prospects for generating dicoordinate boron cations such as **62** need to be evaluated with care in view of the "Ph_2B^+ " problem discussed earlier (Scheme 2), **62** does have the potential added benefit of *π*-delocalization from oxygen. On the other hand, **62** should be more electrophilic compared to the hypothetical borinium intermediate **35** in the

1,3-diazaborolidine series where *π*-delocalization from nitrogen should provide greater stabilization (Scheme 1).

3.3 The borinium-borenium interface; gas phase oxyborenium ions

Oxygen-stabilized dicoordinate boron cations related to **62** have not been detected in solution, although there are gas phase precedents under flowing afterglow conditions (eq. 13). For example, the borinium ion **63** was generated from trimethyl borate, and the derived oxygen-stabilized borenium adduct **64** with trimethyl borate was identified by mass spectroscopy.[43] This observation indicates that **63** is exceptionally electrophilic and interactive, and raises questions regarding the survival of "free" oxygen-substituted borinium species in solution. Other examples of gas phase generation of borenium ions from borinium species have been reviewed by Piers et al.[3] while the generation of borenium species from nitrogen-stabilized borinium ions in solution was covered in depth by Kölle and Nöth.[2] The latter review also discusses the role of ring size in *π*-delocalization. In brief summary, access to observable borinium ions requires delocalization by two sets of adjacent heteroatom lone pairs and results in an sp-hybridized, linear environment at boron. This may be feasible in an acyclic structure or in medium-sized rings, but is not expected in a 5-membered ring such as **62**.

3.4 Borenium salt generation by hydride abstraction

3.4.1 Hydride abstraction by tris(pentafluorophenyl)borane—Oxygen-stabilized tricoordinate boron cations (borenium ions) have also been generated in solution using the method of hydride abstraction (Scheme 3). This approach resembles halide abstraction in the sense that survival of the resulting borenium salt depends on controlling the nucleophilicity of the counterion. In one intriguing recent approach, this was done by generating both the anion and the cation from non-ionic reactants.[44] Thus, catechol borane **65** was treated with the electrophilic borane $B(C_6F_5)_3$ in the presence of tri-*tert*-butylphosphine as the nucleophile. Due to steric hindrance, the phosphine does not bind irreversibly to $B(C_6F_5)_3$ according to the frustrated lone pair concept of Stephan et al., thereby allowing the formation of the less hindered catechol borane adduct **66** in equilibrium. Subsequent hydride transfer to $B(C_6F_5)_3$ occurs to afford the isolable borenium salt **67** (^{11}B δ = 29.9 ppm for the cation; −25.4 ppm for the anion), structure confirmed by X-ray crystallography. Each step in this sequence is reversible, so the isolation of **67** in 96% yield indicates a clear thermodynamic advantage for the borenium salt **67** compared to the tetracoordinate **66**. Because the B3H bonds in **66** and **67** probably have similar energies, the energy advantage for **67** reflects destabilization of **66** by steric congestion, and more important, stabilization of borenium salt **67** by *π*-delocalization. The $B(C_6F_5)_3$ activation method has also been applied to pinacol borane **68** in combination with less hindered nucleophiles, although evidence for the formation of borenium salts is limited to ^{11}B chemical shifts of minor solution species suggesting partial conversion to structures assigned as **69a** (^{11}B δ 22.2 = ppm) and **69b** (^{11}B δ = 26.4 ppm).[45]

3.4.2 Hydride abstracton by trityl salts—An older method for hydride abstraction using trityl cation as the "hydridophile" was explored and updated in our laboratory. The original procedure had reported the conversion of pyridine borane into the boronium salt by reaction with trityl tetrafluoroborate in the presence of pyridine.[46] No intermediates in this process were mentioned, but the boronium salt $[Py_2BH_2]^+ BF_4^-$ was isolated and characterized. First attempts in our laboratory to perform an analogous reaction starting from a cyclic amine borane complex **70** (Scheme 3) utilized trityl tetrakis[(3,5-bistrifluoromethyl)phenyl]borate **71a** in an attempt to generate the borenium salt **72a**.[47a] No borenium species were detected, and the main product proved to be the unexpected

fluoroborane complex **73**, suggesting self-destruction by the highly reactive salt **72a**. When a similar experiment was performed using the more robust trityl tetrakis(pentafluorophenyl)borate **71b** as the electrophile, some evidence for the generation of borenium ions was indeed observed in the form of a transient NMR signal at ^{11}B δ = 39 ppm, but the reaction was difficult to control and the evidence was not conclusive.[47a] A subsequent re-investigation using rigorously anhydrous conditions observed a more strongly deshielded borenium signal at ^{11}B δ = 59 ppm, and demonstrated that this intermediate is the desired **72b** by hydride quenching to re-generate **70**.[47b] The more recent study also confirmed the conversion from **72b** into a second borenium species having the previously observed signal at ^{11}B δ = 39 ppm upon addition of one equivalent of water. Thus, initial experiments had detected **74** instead of **72b** due to contamination by water. High reactivity for **72b** is no surprise because the borenium subunit is stabilized only by the π-electrons of an appended benzene ring. As expected, **72b** reacts readily with good nucleophiles including Bu_4NBH_4 (to form **70)** or pyridine (to form the pyridine adduct boronium salt), but **72b** also reacts with the usually robust tetrakis(pentafluorophenyl)borate anion in a self-destruct mode. The latter process is very slow at room temperature, but affords the *B*-pentafluorophenyl adduct **75** in 46% yield after 24 h in refluxing benzene, followed by quenching with Bu_4NBH_4.

3.4.3 Hydride bridged borenium salt dimers—Attempts to extend the hydride abstraction method to simple borane compexes **76** (L= amine or phosphine) have encountered a more complex situation (Scheme 4).[48,49] In all cases explored to date using the trityl salt **71b**, the hydride abstraction process is quite fast at low temperatures, and triphenylmethane is formed as expected.[48] However, the reaction stops after consumption of 50 mol% of **71b** due to the formation of an observable intermediate **78** (^{11}B δ 0 to −3 ppm if L= tertiary amine or pyridine; ca. −27 ppm if L= tertiary phosphine) consisting of two borenium subunits linked by a hydride. This cationic structure features a symmetrical three-center two-electron (3c2e) B—H—B bond, and is formed by the interaction of **76** as an electron donor with the formally empty *p*-orbital of the hypothetical borenium ion **79** as the acceptor. Although mechanistic details of the hydride abstraction step have not been studied, initial interaction between **76** and **71b** may involve a 3c2e intermediate or transition state **77**. Nucleophilic attack by the starting borane complex (**76**) may then be feasible to displace triphenylmethane as the leaving group, resulting in a direct pathway to the symmetrical hydride-bridged “dimer” **78**, but dissociation of **77** to borenium ion **79** is an alternative that has not been ruled out. Mechanistic ambiguities are also reflected in the reactivity of **78** with weak nucleophiles. For example, solutions of **78** (L = triethylamine) generated in dichloromethane decompose at rt over several hours to form a complex mixture of products after quenching with borohydride. The volatile products include toluene and diphenylmethane among several fragments derived from the triphenylmethane that is generated in the hydride abstraction step. Apparently, these products are the result of a Friedel-Crafts alkylation of triphenylmethane at the *ipso*-carbon by the boronium salt **80** to form benzyl chloride and diphenylmethyl cation **81**, followed by hydride transfer. Thus, dichloromethane may be sufficiently nucleophilic to interact with **78**, thereby generating an equilibrium concentration of **80**. However, prior dissociation of **78** to the borenium ion **79** is not ruled out, and neither **79** nor **80** has been detected by spectroscopy. Similar questions arise in the conversion of **78** into observable tetracoordinated adducts **82** (complete conversion with X= OTf; partial conversion with X= NTf_2). In the absence of decisive evidence, species such as **77**, **78**, or **80** were regarded as equivalents (and potential sources) of the presumably higher energy borenium ion **79**,[47b] but direct involvement by **79** as a solution intermediate remains an open question. On the other hand, there can be no doubt regarding the relatively greater stability and structure of the hydride-bridged “dimers”, one of which (**78** with L = NMe_3) has been characterized by X-ray crystallography.[50] Thus, the

trityl cation method for hydride abstraction appears not to be suited for generating observable non-stabilized primary borenium ions.

In an independent study,[49a] a variation of the hydride abstraction method was developed with similar substrates using a strong acid as the activating electrophile. Thus, treatment of ammonia borane (**76** with L = NH_3) with $HOEt_2^+$ $B[C_6H_3(CF_3)_2]_4^-$ in ether resulted in hydrogen evolution and the formation of an isolable boronium salt **83**. This substance was presumably formed by nucleophilic attack by the ether solvent on the intermediate borenium ion, analogous to the conversion from **79** to **80**, and was characterized by the characteristic ^{11}B chemical shift (δ = 0.21 ppm) as well as analytical data. Further conversion from **83** to hydrogen gas and oligomeric aminoboranes was rationalized via the formation of the hydride-bridged structures **84** and **85** as hypothetical intermediates, and DFT calculations were used to support the proposal that **84** corresponds to an energy minimum in this sequence.[49a]

3.5 Borenium ion generation by nucleophilic addition-heterolysis

One additional method for generation of borenium salts is considered in Scheme 5, involving a nucleophilic addition-heterolysis pathway from the reaction of a nucleophile and a trivalent boron substrate that contains a potent leaving group.[1] Nöth has used the shorter descriptor “nucleophilic addition” for the same method, but we prefer the longer label because the process involves two stages, (1) reversible formation of a tetracoordinate boron intermediate, and (2) partial or total dissociation to release the borenium salt. Well-established examples of this approach involving amine-stabilized borenium ions were already discussed in connection with Scheme 1. However, examples where the borenium ion is not stabilized by *n*-electron donors may also have been encountered.[51] Thus, the triflate derivative of 9-BBN (**86**) was treated with 2,6-lutidine in dichloromethane to afford a solution having two ^{11}B signals at δ = 59 and 37 ppm (1:8 ratio). In contrast, pyridine reacted with **86** to afford the isolable tetracoordinate adduct **88a** in 65% yield (^{11}B δ = 13.4 ppm). This result implicates steric hindrance as the reason why **88b** does not accumulate in solution. If the 59 ppm signal observed from **86** + 2,6-lutidine is due to a contaminant,[51b] then the 37 ppm signal may represent a time-averaged mixture containing the borenium salt **90**, the adduct **88b**, and the reactants in equilibrium.[51a] A similar reaction of Bu_2BOTf with 2,6-lutidine gave a time averaged signal at ^{11}B δ = 55 ppm, and ligand exchange with excess lutidine was demonstrated at room temperature. This indirect evidence was not discussed in depth, but more definitive data were obtained using the method of halide abstraction starting from the pyridine adduct **89** obtained from 9-BBN-Cl (**87**). Addition of the potent chlorophile gallium trichloride to **89** resulted in a solution having three signals in the ^{11}B NMR spectrum at δ = 69.7, 58.5, and 6.1 ppm. The latter signal was attributed to unreacted **89**, while the 69.7 ppm signal was assigned to the borenium tetrachlorogallate **91**.[51a] Assuming a similar chemical shift for **90**, the latter may be a minor component of the equilibrium reaction mixture from **86** and 2,6-lutidine. Borenium salts **90** and **91** are presumably stabilized to some extent by the pyridine π-system, and **90** should also benefit from the steric shielding effect of a 2,6-lutidine substituent. Nevertheless, these structures would rank among the least stabilized borenium salts to be detected by NMR methods.

Recent experiments in our laboratory have extended the nucleophilic addition-heterolysis method to *p*-dimethylaminopyridine (DMAP) as the nucleophile.[52] In contrast to the reaction of pyridine with 9-BBN triflate (**86**), the analogous reaction of DMAP with 9-BBN bistriflimide **92** afforded a solution having two ^{11}B signals that do not interconvert on the NMR timescale, corresponding to the borenium salt **93** (^{11}B δ = 66.5 ppm; minor) and the isolable boronium salt **94** (^{11}B δ = 3.0 ppm; major). Support for structure **93** was obtained by generating the same δ = 66.5 ppm signal by an independent method via hydride

abstraction from **95** with $HNTf_2$, a process that gave **93** as the dominant solution species (>85% of ^{11}B signal intensity). The chemical shift of **93** is consistent with the value reported for **91** (^{11}B δ = 69.7 ppm),[51a] and provides additional support for the original interpretation of Narula and Nöth.

In view of the complications encountered in the pyridine series, it was surprising to find that the reaction of **92** with triethylamine is relatively simple (Scheme 5).[52] A single dominant product, the borenium salt **97**, was observed in solution according to chemical shift data (^{11}B δ = 85.1 ppm) while the initially formed nucleophilic addition product **96** was not detected. Evidently, the heterolysis step from **96** is strongly favored by the resulting decrease in non-bonded interactions, and also by the stability of the bis-triflimide leaving group. Structure **97** is unique among all of the borenium salts that have been observed in solution to date because it contains neither *n*-electron nor π-electron donors capable of stabilizing boron. Its relatively facile generation undoubtedly is due to steric protection by the 9-BBN ring system, a factor that not only favors the heterolysis step from **96**, but also prevents boronium adduct formation with unreacted triethylamine. On the other hand, the steric effect is not so large that boronium adduct formation with tertiary amines can be disregarded. Thus, **92** reacts readily with 1,8-bis(dimethylamino)naphthalene to give the isolable boronium adduct **99** (^{11}B δ = 16.2 ppm). As discussed later (Section 7), **99** is unusually reactive compared to more typical boronium salts, suggesting facile equilibrium with the borenium salt **98** or with other potentially electrophilic species. However, the chemical shift and X-ray data support the tetracoordinate boron structure.

4. Borenium Lewis acidity vs. structure

4.1 Experimental evaluation of Lewis acidity

Borenium ions are stronger Lewis acids compared to typical boranes due the combined effect of the net positive charge and a formally vacant *p*-orbital at tricoordinate boron, but how much stronger are they? There is no simple way to answer this question. Judging from the experimental data presented in Sections 2 and 3, the degree of Lewis acidity of borenium ions spans a rather wide range, depending on the nature of substituents attached to boron. Thus, if the ability to form covalent bonds to counterions is used as a rough measure of Lewis acidity, then the two representative limiting cases would be (1) the aromatic cation **58** which resists complexation with the relatively nucleophilic chloride anion,[40,41] and (2) the powerful electrophile $H_2BNMe_3^+$ (**25**) that covalently binds even to the weakly coordinating bistriflimidate anion to form the neutral adduct **82** (X = NTf_2; Scheme 4).[50] However, the Lewis acidity of borenium ions depends on the steric as well as the electronic availability of the vacant *p*-orbital on boron. Thus, the borenium cation **97** (Scheme 5) does not bind the bistriflimidate counterion even though it lacks stabilizing π or *n* electron donors, nor does it bind excess added triethylamine.[52] The more highly substituted **97** would have additional stabilizing hyperconjugative interactions with proximal σ-bonds compared to **25**, but severe steric crowding is a major factor that makes **97** a weaker Lewis acid than **25**. In contrast, the relatively unhindered borenium cation **58** (eq. 11) is unlikely to interfere sterically with an incoming nucleophile such as chloride ion, but **58** does not undergo conversion to the tetracoordinate boron adduct because the boron *p*-orbital is strongly populated by involvement in the aromatic π-system. In this case, electronic factors are dominant.

While most reports on borenium ion chemistry contain qualitative descriptors of Lewis acidity (such as the ability to coordinate counterions or other Lewis bases), comparisons of thermodynamic data that would help to rank the Lewis acidities for a broad range of borenium species have been rare. Such comparisons would be informative if performed using the same reference Lewis base to probe the equilibrium between tricoordinate and tetracoordinate boron species, but the literature data are very limited, while data obtained

using spectroscopic evaluation of tetracoordinate boron adducts are also limited and rather difficult to compare. Estimates of Lewis acidity for borenium ions based on NMR methods have been reported in some cases. Thus, Piers *et al.* investigated the effect of complexation by borenium species **52** and **53** (Scheme 2) on the ^{1}H chemical shift for the β-proton of crotonaldehyde (Child's test), and concluded that the Lewis acidities of **52** and **53** are mutually close and comparable to those of Et_2AlCl and BF_3.[38] In a somewhat different test involving non-equilibrium conditions, Ingleson *et al.* assessed the Lewis acidity of the hypothetical cation **62** (eq. 12) by measuring the ^{31}P chemical shift of the Et_3PO adduct **60** (δ = 106.9 ppm) and comparing this chemical shift with the corresponding values for the Et_3PO adducts of several reference Lewis acids including $(C_6F_5)_3B$ (δ = 76.6 ppm), $AlCl_3$ (δ = 80.3 ppm), and BBr_3 (δ = 91.2 ppm).[42] The chemical shifts for the three reference Lewis acids increased in the same order as their Lewis acidity determined from earlier studies using Child's test. This correlation suggests that the non-equilibrium ^{31}P chemical shifts may also be used to estimate relative Lewis acidities. Unfortunately, the standard Child's test (complex formation with crotonaldehyde in CD_2Cl_2) could not be performed with **62** due to its incompatibility with the solvent. This problem was avoided in C_6D_6 solution, but the crotonaldehyde chemical shift data obtained for **62** in C_6D_6 did not show a simple correlation with the reference data in CD_2Cl_2, and correlation data for the same solvent were not reported.

The simpler test based on the ^{31}P chemical shift of **60** is consistent with the notion that **62** is a very powerful Lewis acid that is probably more potent than the neutral boron Lewis acids $B(C_6F_5)_3$ and BBr_3. On the other hand, Lewis acidity estimates based on the ^{31}P chemical shift criterion would be influenced by other factors resulting from structural changes near the boron subunit. Thus, the ^{31}P chemical shifts for the Et_3PO adducts corresponding to the hypothetical, non-stabilized borenium cation $H_2BNMe_3^+$ (**25**) and the observable π-stabilized "borabenzylic" cation **72b** (Scheme 3) happen to be identical (δ = 85.7 ppm in CD_2Cl_2) despite the apparent difference in stabilization.[50] In view of these findings, more definitive experimental methods to probe the Lewis acidity of borenium species are needed, and remain to be developed.

4.2 Computational evaluation of Borenium Lewis acidity

In an early computational attempt to gain insight regarding the factors that influence the bonding, stability, and Lewis acidity of boron cations, Nöth, Bursten *et al.* studied a series of cations R_2BL^+ (R = H, NH_2; L = H_2O, pyridine, NH_3, etc.) using *ab initio* methods.[53] Two different geometries were compared for the L = pyridine case, and the fully planar structure was found to be favored by 12.6 kcal/mol compared to the geometry having the pyridine ring turned perpendicular to the plane of the boron σ-bonds. This energy difference was associated with a π-delocalization effect, the same stabilizing interaction involving delocalization between the pyridine ring with the boron *p*-orbital that had been deduced in earlier studies.[2] The *ab initio* investigation also explored the dissociation of the borenium cation $H_2BNH_3^+$ (**100**) into the simple components (the borinium ion H_2B^+ and ammonia).[53] This conversion was discussed in the context of heterolytic bond dissociation, a process that reflects the enthalpic component for B–N bond formation in the reverse reaction (ammonia + H_2B^+ as the Lewis acid), corresponding to the ammonia affinity of H_2B^+. Subject to the usual caveats regarding the evaluation of condensed phase phenomena using computed gas phase energies, this general approach offers a potential way to estimate NH_3 affinities of other boron cations, including labile borenium ions that are difficult to compare under standardized solution conditions.

An extrapolation from the above precedent has been performed with the goal of ranking a series of borenium ions according to their gas phase NH_3 affinities.[50] The range of borenium

ions studied (Table 1) includes several structures of synthetic interest (Lewis acid catalysts; electrophilic borylating agents). It also represents various bonding environments for boron, and includes most borenium examples characterized by X-ray crystallography during the past decade to allow the comparison of computed and experimental geometries. The sterically congested structures of observable borenium ions often pose obstacles for computational modeling due to the presence of significant non-bonding interactions that can be problematic for the most familiar DFT methods. On the other hand, Truhlar's parametrized M06-2X functional[54] has been found to perform well for very hindered boronium salts[52] and various amine borane complexes,[55a] and thus was chosen for the NH_3 affinity calculations. While the calculations disregard additional factors such as solvation, ion pairing, and conformational effects, a qualitative comparison of borenium Lewis acidities should still be possible. The data presented in Table 1 show that in the cases where reliable X-ray crystallographic data are available, the calculated bond lengths are in reasonable agreement with the experiment. Only qualitative enthalpies can be obtained from these computational results, but some trends deserve attention. Thus, Piers' borenium ions **52** and **53** are predicted to have comparable Lewis acidities (entries 7,8), well in accord with the reported data.[38] Moreover, the NH_3 affinities of **52** and **53** are close to the NH_3 affinity of BF_3 calculated using the same method ($\Delta H = -20.4$ kcal/mol), consistent with the Lewis acidities determined by Piers using Child's test.[38] As expected, borenium ions **25** or **100** having the highest NH_3 affinity are sterically unhindered, and experience relatively little electronic stabilization by the ligands due to the absence of *n*- or π-donors (entries 13,14). The 9-BBN-derived cation **97** also lacks *n*- or π-donors, but the calculated NH_3 affinity is rather modest (entry 4). The explanation for this contrast lies partly in the greater degree of boron substitution in **97** and the resulting hyperconjugative stabilization compared to **25**, but steric hindrance may be even more important. One consequence of the highly hindered environment is apparent in the substantially longer B–NEt_3 bond compared to the B–NH_3 bond in the ammonia adduct, evidence that the larger ligand encounters severe steric strain. More generally, the above example reflects the elongation of bonds to the boron atom that occurs upon complexation with the Lewis base, and the pronounced moderating effect of steric hindrance on borenium NH_3 affinity.

Nitrogen *n*-donor substituents at boron substantially decrease the NH_3 affinity of borenium ions, as exemplified by structure **27** (entry 1). Related borenium cations possessing oxygen *n*-donors such as cation **67** (entry 6) or Corey's Diels-Alder catalyst **38** (entry 10) are somewhat more Lewis acidic, apparently due to the increased electronegativity of oxygen compared to nitrogen. The substantial difference between **67** and **38** in terms of NH_3 affinity remains unexplained, although a reviewer has suggested a plausible rationale that **67** should be a weaker Lewis acid because it is part of a delocalized 10 π (aromatic) electron system. In any case, **38** clearly is a potent Lewis acid, as also expected from its catalytic reactivity. Similar oxygen electronegativity effects on NH_3 binding energies were noted for dicoordinate boron cations (borinium ions) by Nöth, Bursten *et al.* in their computational study,[53] and the general trends were recognized in earlier experimental work.[2]

Increased NH_3 affinity also correlates with the presence of a larger number of electronegative atoms in the conjugated π-systems attached to boron (entries 7, 8, 11), but other factors are difficult to evaluate in these more complex examples. Thus, cations **52** and **53** (entries 7,8) are formally antiaromatic 12π electron systems, a factor that should also enhance NH_3 affinity. However, Piers *et al.* found no evidence for substantial antiaromaticity using the nucleus-independent chemical shift criterion NICS(1),[38] precluding the unambiguous assessment of antiaromaticity and electronegativity vs. simple *n*-delocalization from the nitrogen substituent attached to boron in cations **52** and **53**.

The calculated NH_3 affinities are generally consistent with the empirical comparisons of borenium Lewis acidities as discussed in Sections 1–3. To a first approximation, the ordering of calculated NH_3 affinities may reflect the Lewis acidities of borenium ions toward other nucleophiles, provided that they are relatively unhindered. However, the structure of the test nucleophile is certainly important. One telling observation is the fact that **97** (Table 1, entry 4) does not form an adduct with triethylamine. If triethylamine had been selected as the test nucleophile for Table 1, then **97** would have to be classified as a weak Lewis acid, a ranking that would be somewhat at odds with reactivity trends to be discussed in Section 8.

The most striking feature of Table 1 is the broad range of ΔH values, differing by >50 kcal/mol from the weakest to the strongest Lewis acid (from entry 1 to entry 14). By comparison, the NH_3 affinities for simple borane derivatives (tricoordinate boron lacking any formally positive substituent) span a much narrower range. Thus, the same computational approach gave the following NH_3 affinities for several boranes: BMe_3 (ΔH = −14.3 kcal/mol), BF_3 (ΔH = −20.4 kcal/mol), BCl_3 (ΔH = −25.3 kcal/mol), BH_3 (ΔH = −27.9 kcal/mol), values that are in good agreement with earlier computational and experimental studies.[55] Because the inherent NH_3 affinities are much larger for borenium ions compared to boranes, the moderating effect of stabilizing substituents is also larger, and this trend is evident in Table 1.

5. Borenium ions and stereogenic boron

5.1 Racemization by heterolysis

The preceding sections establish correlations between empirical, computational, and spectroscopic data pertaining to the relative stabilities of borenium salts and the isomeric (tetra-coordinated) amine boranes. With very few exceptions, the amine borane isomers have proved to be more stable. The computational evidence provides a qualitative basis to answer the question “How much more stable?”, and there are also some answers to this question from experimental evidence. Thus, a classical study by Ryschkewitsch and Garrett succeeded in the first resolution of a tetra-coordinated, stereogenic boron cation using crystallization methods starting from **102**, the halogenation product of the boronium salt **101** (Scheme 6).[56] Challenging aspects of this work included controlling the homogeneity and solubility of the intermediate boronium salts involving the manipulation of up to three different anions after halogenation, depending on the halogen source (Z = I^-, ICl_2^-, PF_6^-, Br_3^-, Br^-). Solubility is especially important in the key anion metathesis from racemic **102** (Z = Br) and the chiral tris(catecholato)arsenate anion $As(C_6H_4O_2)_3^-$, leading eventually to the single enantiomer of the boronium hexafluorophosphate **103** (arbitrary absolute configuration shown). Survival of **103a** or **103b** in the solid state and in solution without racemization rules out the heterolysis events leading to achiral borenium cations **104** (by trimethylamine departure), **105** (by pyridine departure), or the increasingly improbable dication **106** (by bromide departure). In the most extreme test of configurational stability, the non-racemic *B*-chloro analog **103a** was recovered unchanged from boiling HCl, but racemization did occur upon warming with pyridine. The mechanistic aspects of racemization by pyridine were not discussed, but plausible rationales might include reversible nucleophilic attack by pyridine at tetra-coordinate boron.

A systematic investigation of potentially relevant mechanistic issues was reported many years later for a different chiral substrate.[57] Toyota *et al.* were able to separate boronium salt enantiomers **107** and *ent*-**107** using hplc methods (Scheme 6). Racemization did not occur at room temperature, but warming in heptane resulted in enantiomer interconversion. In the temperature range from 73–93 °C, the process was characterized by activation parameters $\Delta H^{\neq}$ = 146 kj/mol and $\Delta S^{\neq}$ = 84 J/mol-deg. The authors argued that a positive entropy of

activation is in good accord with a mechanism involving reversible B–N dissociation to form the less constrained intermediate **108**. The alternative formation of a borenium ion **109** would result in increased ionic character and (presumably) would lead to entropically unfavorable solvent ordering, resulting in a negative activation entropy. In a related system (**107** with fluoride in place of fluoropropionate), they also found no significant rate difference when the racemization was studied in tetrachloroethane or in the more polar solvent nitrobenzene. These observations are consistent with the B–N dissociation pathway for racemization and suggest that the borenium ion **109** is not involved.

5.2 Asymmetric memory at stereogenic boron

Beginning in the 1990's, reports from our laboratory described asymmetric memory applications for stereogenic boron that encounter similar questions about the relative ease of B–N dissociation vs. generation of borenium intermediates.[58] Thus, reaction of the amidine carboxylate **110** with KBF_3/TMSCl afforded a mixture of diastereomeric oxazaborolidinones **111** and **112** (Scheme 7). The initial isomer ratio varied with the experiment, but slow removal of solvent consistently gave a crystalline mass that was highly enriched in the *trans* diastereomer **112**. Subsequent enolization of recrystallized **112** with potassium *tert*-butoxide followed by alkylation afforded products with high enantiomeric purity, and in some cases, with excellent diastereoselectivity as illustrated by the conversion to **114**. This result requires that boron configuration is retained throughout the sequence from the reactant **112** to the intermediate enolate **113** and the final product **114**.

The conversion from the diastereomer mixture **111** + **112** into nearly pure **112** is an example of crystallization-induced asymmetric transformation (also known as "second order" asymmetric transformation), a phenomenon that can result in a near-total preference for that diastereomer having the higher crystal lattice stability. While the crystallization process is fascinating, the current discussion is concerned more with the mechanism for interconversion of **111** and **112** in solution. Reversible B–N bond dissociation provides a simple explanation, although the increased electronegativity of substituents at boron in **111**/**112** compared to the cyclic amine borane **107** (Scheme 6) should work against this pathway by increasing the B–N bond energy. The alternative involvement of borenium intermediates such as **115** was therefore considered, but decisive evidence for or against this possibility was not obtained due to the limited solubility of **111**/**112** and the potential involvement of subtle racemization pathways.

Added mechanistic insight required a more robust and more soluble oxazaborolidinone substrate that would resist epimerization at room temperature, and that would also be easier to assay (Scheme 8). Increased stability for tetra-coordinated boron species was demonstrated by R. W. Chapman upon incorporation of an electronegative fluorine substituent into the aryl group Ar*, a modification that allowed chromatographic separation of both diastereomeric oxazaborolidinones **117** and **118**.[59] To facilitate the assay of equilibrium events, the structures were further modified by incorporating a chiral reporter group into the aryl substituent, remote from the stereogenic boron. This feature allows monitoring changes of configuration at oxazaborolidinone carbon as well as at boron because all of the resulting stereoisomers are diastereomers that can be distinguished by simple NMR methods. Thus, it was shown that the initially formed 4:1 ratio of cis:trans diastereomers **117** and **118** is converted into an 8:1 trans:cis ratio by epimerization at boron in refluxing toluene. The same equilibrium ratio (8:1 trans:cis, or **118:117**) was obtained at room temperature upon treatment with TMSCl as catalyst, again via exclusive epimerization at boron. The catalyzed epimerization at room temperature probably involves reversible formation of borenium intermediates (**119** when TMSCl acts as a fluorophile; **120** when TMSCl acts as an oxophile), while the thermal equilibration is more likely to result from

reversible B–N dissociation. Both **119** and **120** would be stabilized by *n*-electron donation from adjacent heteroatoms (O and F, respectively), so their involvement as transient species is consistent with the stability comparisons discussed in Section 4.

The base-induced equilibration of **117** using DBU in $CDCl_3$ was also studied (Scheme 8), and gave a new trans diastereomer **121** (8:1 trans:cis = **121:117**; Scheme 8).[59] Separation of **121** followed by hydrolytic cleavage of the heterocycle and the amidine **123** gave phenylglycine **124** with >99.5% ee and overall inversion of carbon configuration compared to the starting materials **116** and **117**. This sequence proves that the base-catalyzed equilibration starting from **117** does not affect boron configuration, and therefore does not involve borenium intermediates. Simple base-induced enolization via the chiral enolate **122** is the pathway that equilibrates the diastereomers **117** and **121**.

5.3 Chiral salicylaldimine boronate complexes

The examples of Scheme 8 show that the configurational stability of stereogenic, tetra-coordinated boron is increased by an electron-withdrawing substituent (fluorine) attached to the Ar* group. This factor decreases the rate of all heterolysis events at boron, and protects against borenium ion pair formation as well as dissociation of the dative B–N bond to form neutral fragments (tri-coordinated borane and amine). Another way to stabilize tetra-coordinated boron structures is by incorporating additional fused rings that include boron and one or more of the boron ligands. This structural variation has been explored in salicylaldimine-derived boron complexes, some of which are discussed in connection with Scheme 9, below.

Activation of $KPhBF_3$ with TMSCl as fluorophile in the presence of the salicylaldimine **125** was found to produce diastereomeric salicylaldimine complexes **126** (*trans* methyl and phenyl) and **127** (*cis* methyl and phenyl).[60] Conventional room temperature crystallization afforded **126** in 73% yield, but crystallization-induced asymmetric transformation did not occur upon slow solvent removal at room temperature, as expected if epimerization at boron is negligibly slow. On the other hand, treatment of purified **126** with 10 mol % of TMSCl in dichloromethane produced an equilibrium ratio of 5.8: 1 **126: 127** after three days at room temperature. When this experiment was repeated under conditions of slow solvent evaporation, the resulting crystalline solid was found to have a ratio of 26: 1 **126: 127** (96% yield from the 5.8: 1 mixture of diastereomers). This result indicates that interconversion of boron epimers is catalyzed by TMSCl, and promotes asymmetric transformation during the crystallization. Although the mechanism of epimerization at boron is not firmly established, a role for the borenium intermediate **128** is implicated in view of the observed catalysis by the oxophilic Lewis acid TMSCl. The alternative of silicon-assisted heterolysis at the phenolic B–O bond is not ruled out, but access to the relevant oxygen electron pairs adjacent to the quaternary boron would encounter steric repulsions. On the other hand, B–O heterolysis to **129** might play some role in the thermal equilibration of diastereomers observed when **126** was heated in refluxing toluene. In this case, the high energy of a borenium-like species **129** may be partially offset by delocalization involving the neutral quinoid resonance form **130**. However, the alternative possibility for uncatalyzed (thermal) epimerization at boron involving B–N heterolysis must also be considered, as discussed below in a related context.

Several examples discussed in Schemes 8 and 9 demonstrate asymmetric memory (retention of configuration) at stereogenic boron in structures where no other stereogenic atom is present, as in the enolates **113** and **122**. A somewhat different example of the asymmetric memory phenomenon was encountered in a related context by Hutton *et al.*[61] Thus, warming the amino phenol **131** with phenylboronic acid and glyoxylic acid in DMF afforded a single

dominant enantiomer and diastereomer of the imine complex **133** (Scheme 10; 97% isolated; > 99% ee). Because **133** no longer contains a stereogenic carbon atom, the boron configuration must already be set at the stage of an intermediate **132**. Furthermore, the proton shift that converts **132** into **133** must occur much faster than potentially competing heterolysis events involving the B–O or B–N bonds. Once formed, **133** is very stable and survives heating in refluxing toluene (24h) without appreciable (<0.5%) racemization, in contrast to the analogous salicylaldimine complex **126** (Scheme 9) which does undergo thermal equilibration with the diastereomer **127** under the same conditions.

The above results are easy to explain if thermal epimerization at boron in **126** occurs by B–N dissociation. Hutton *et al.* have noted that the corresponding process in **133** is more difficult because it would require not only the B–N dissociation, but also the conformational changes needed to re-orient the B–Ph and C–Ph subunits in a sterically demanding medium ring environment **134** (Scheme 10). The medium ring intermediate may also have been encountered in the somewhat more labile complex **135** studied earlier by Braun *et al.*[62] Individual enantiomers of **135** were separated by hplc methods, and were shown to undergo thermal racemization at 65 °C in decane ($\Delta G^{\neq}$ 109 kJ/mol). The authors did not explicitly invoke the medium ring **136** as the intermediate responsible for racemization, but did note that racemization is somewhat slower in an analogoue having a shorter, and therefore stronger, B–N bond (replace Cl in **135** by NO_2; $\Delta G^{\neq}$ 115 kJ/mol). Braun *et al.* also provide references to a number of simpler examples of chiral amine boranes that contain stereogenic boron. So far, there is general agreement that loss of configuration at tetra-coordinated boron in the chiral amine boranes under uncatalyzed (thermal) conditions occurs by B–N dissociation.[63] On the other hand, heterolysis to generate borenium intermediates is implicated in reactions conducted in the presence of Lewis acid catalysts (Schemes 8, 9).

6. Enantioselective catalysis and chiral borenium ions

The preceding section considered chiral amine boranes containing stereogenic tetracoordinate boron. Configurational stability at boron was demonstrated in a number of examples under ambient conditions, and was optimized by adjusting electronic factors or steric constraints to a level sufficient to prevent the spontaneous generation of borenium ions. This allowed the stoichiometric use of chiral amine boranes in asymmetric synthesis applications that require memory of chirality. In a somewhat different approach to asymmetric synthesis, chiral amine boranes can also be used in a catalytic mode. This scenario typically involves the reversible generation of Lewis acidic borenium ions by leaving group departure from tetracoordinate boron in the starting amine complex. In contrast to the stoichiometric examples of Section 5, the catalytic applications require that borenium ions are generated spontaneously. Because the borenium catalyst must bind reversibly to all potential nucleophiles in the system, the substituents must be optimized to provide the desired level of stabilization. As briefly discussed in Section 3.1 and Section 4, this can be done by incorporating one or more π-electron donors as ligands at boron to moderate electrophilicity. A more detailed look at the structural requirements as well as some applications of this concept are presented in the context of enantioselective catalysis by chiral borenium sources in the following sections.

6.1 The Dual Function of Oxazaborolidines in the CBS Reduction

The first encounters with a chiral catalyst containing a borenium subunit were reported in 1983, well before the nature of the key catalytic event was understood (Scheme 11). In the course of studies directed toward enantioselective ketone reduction, Itsuno et al. reported that a reagent derived from diphenylvalinol (**137**) and BH_3·THF gave highly enantioselective reduction of aryl ketones (≥ 94% ee).[64] The 2:1 stoichiometry of BH_3·THF

to **137** was noted as an important variable, but the role of the second equivalent of borane was not known at the time of the initial report. During the subsequent optimization as reported in 1987, Itsuno et al. found that pretreatment of **137** with one equiv of BH_3·THF at 0 °C allowed isolation of a chiral complex, but the structure of the complex was not reported.[64b] This complex could be used catalytically with BH_3·THF for the enantioselective reduction of ketones and *O*-methyloximes, but the authors did not comment on the mechanism of borane activation or the nature of the hydride donor.

By 1987, Corey et al. had observed similar catalysis using preformed borane catalysts with BH_3·THF for ketone reduction.[65a] The previously unidentified complex was assigned as the oxazaborolidine **138** (Scheme 11), based in part on the ^{11}B NMR shift at δ = 28.1 ppm, in the range expected for trivalent boron containing nitrogen and oxygen substituents. The role of the borane adduct **139** in ketone reduction was recognized, and the related oxazaborolidine **141** (generated from **140** and BH_3·THF) was shown to be a superior catalyst. This complex was effective at catalyst loadings as low as 5 mol%, and reduced ketones within 1 min at rt using BH_3·THF at a reagent loading of 60 mol% relative to the substrate.

The structure of **141** as the major species in solution was supported by the ^{11}B NMR signal at δ = 28.3 ppm, while a small signal at 7.6 ppm was assigned to a dimeric structure. When a solution of **141** in THF was treated with excess BH_3·THF, two new upfield ^{11}B signals were observed at δ = 3.2 and −19.4 ppm, values that are consistent with the presence of tetracoordinate boron. A subsequent communication from Corey et al. described **142** (^{11}B δ = 33.5 ppm), the B-methyl analogue of **141**.[65b] In contrast to **141**, oxazaborolidine **142** reacted with BH_3·THF to gene rate a new *downfield* signal (δ ^{11}B = 36.5 ppm), consistent with the presence of an endocyclic tricoordinated boron nucleus as in **144**. An upfield-shifted signal for the exocyclic N–BH_3 resonance was also observed (δ^{11}B = −15.4 ppm), similar to one of the signals from the borane adduct of **141**. Apparently, the combination of oxygen *π*-delocalization as well as the steric and electronic effects of the *B*-methyl substituent in **144** is sufficient to favor tricoordinate boron, while the B–H analogue **143** is more electrophilic and exists mostly as the tetracoordinated THF adduct in the equilibrium mixture. Although **143** is net neutral and is not technically a borenium salt, the endocyclic boron is part of a borenium subunit that is strongly electrophilic compared to **141**.

Corey et al. proposed that oxazaborolidine catalysts related to **141** play a dual activation role in the ketone reductions. Borane complexation enhances the Lewis acidity of **141** by generating **143**, and promotes ketone activation via the Lewis acid-Lewis base adduct **145**. However, the formation of the tetracoordinate boron species **143** and **145** simultaneously activates the borane as a hydride donor, resulting in the facile intramolecular (6-center) hydride transfer from **145** (Scheme 11). This process is feasible only if the ketone coordinates from the less hindered, convex face of the bicyclic borenium core, *cis* to the complexed BH_3 subunit as shown in **145**, and leads to **146** as the initial product of hydride transfer. Like **143**, structure **146** contains a borenium subunit (the exocyclic tricoordinate BH_2 next to formally positive nitrogen), but in contrast to **143**, **146** has no stabilizing interaction between the ring boron with the oxygen *n*-electron donor ligands. On the other hand, **146** may gain some benefit from complexation between the exocyclic tricoordinate BH_2 boron with alkoxide oxygen *n*-electrons in a 4-center arrangement. Further interaction with the BH_3·THF reagent is then believed to occur via a 6-center process that eventually leads to expulsion of the reduced alkoxyborane fragment as shown. The latter incorporates a new B–O bond at the expense of the exocyclic B–O bond in **146**, while transfer of hydrogen from BH_3·THF to the tricoordinate boron results in regeneration of the catalyst **143**.

The favored configuration of the ketone in **145** places the larger substituent (R_L) *exo* with respect to the bicyclic core to minize steric interactions with the oxazaborolidine, and accounts for exceptional enantioselectivity over a broad range of substituents. Subsequent work has extended this methodology to allow facial discrimination even for ketones with sterically similar substituents, and a number of applications in total synthesis are also reported.[32,65b] These findings have been reviewed in depth[32] and will not be discussed here, except to note that the CBS reduction (Corey, Bakshi and Shibata[65]) has become one of the most powerful methods for enantioselective ketone reduction.[66] An interesting mechanistic analogy for the dual activation process has also been encountered in the oxazaborolidine-catalyzed enantioselective ethynylation of aldehydes by alkynyldimethylboranes.[67] The overall events are similar, including borane complexation to oxazaborolidine nitrogen, carbonyl binding at the Lewis acidic borenium subunit, and 6-center transfer of the *B*-ethynyl group to the activated aldehyde carbonyl.

6.2 The role of borenium species in Diels-Alder catalysis

Chiral boranes activated conventionally by electronegative substituents have been used as catalysts for the Diels-Alder reaction, but applications are largely limited to relatively reactive cyclic dienes.[68a] To improve reactivity, Corey et al. explored a family of catalysts that generate borenium salts *in situ.*[68b] Thus, a bicyclic oxazaborinane **148** was formed in solution from the protected chiral amino alcohol **147** by treatment with 0.9–1.0 equiv of BBr_3 at −78 °C (eq. 14).[69] Indirect evidence for an equilibrium between **148** and the borenium salt **149** was provided by the observation that this mixture ("reagent A") is a potent Diels-Alder catalyst for the reaction of acrolein derivatives with cyclopentadiene at −94 °C. However, reagent A did not catalyze the Diels-Alder reaction with less reactive acyclic dienes at −94 °C, and could not be used at temperatures above −60 °C due to decomposition. For access to more potent borenium catalysts, **148** was treated with BBr_3 or $AgBAr_4$ at low temperatures according to the method of halogen abstraction (Ar = $C_6H_3(CF_3)_2$; see Section 3.2 for analogies). In the BBr_3 experiment, direct evidence for a shift in equilibrium toward the presumed borenium salt **150** was obtained by observing the ^{11}B NMR signal of BBr_4^- anion, but no mention was made of the ^{11}B signals for the borenium subunit of either **150** or the analogous **151** generated using the $AgBAr_4$ procedure. The lack of direct ^{11}B NMR evidence for tricoordinate boron is also a recurring issue with most of the oxazaborolidine-derived borenium catalysts to be discussed in the next section. This problem may well be a consequence of the low-temperature enhancement of quadrupolar relaxation that effectively quenches the ^{11}B NMR signals of unsymmetrical boron species, a complication that should be less severe for the highly symmetrical (observable) BBr_4^- anion in the case of **150**.[70,71] The *in situ* generation of the borenium salt **151** (reagent B) allowed catalysis of representative Diels-Alder reactions within 1 h at temperatures as low as −94 °C, and expanded substrate scope to include the moderately reactive dienes 1,3-butadiene and 1,3-cyclohexadiene. Using α-bromoacrolein as the dienophile and **151** generated *in situ*, the corresponding cycloadducts **152** and **153** were obtained in high yields and with 93–94 % ee. However, the temperature requirement for experimentation at −60 °C or below somewhat limits potential applications for catalysts **150** or **151**.

Eventually, the problems of borenium catalyst stability and scope were overcome by developing optimal activation procedures in the readily accessible proline-derived oxazaborolidine environment.[31,72–77] The potential for Lewis acidity and carbonyl complexation had already been recognized in the context of CBS reduction using catalysts **141** or **142** (Scheme 11), but the method of activation had to be modified to avoid interference by the B–H bonds present in reagents and intermediates. At an early stage of catalyst development, Corey et al. reported that activation of **37** with the strong Brønsted

acid CF_3SO_3H (triflic acid, TfOH) generates a powerful catalyst for the Diels-Alder reaction.[31] As briefly mentioned in Section 3.1 in the context of electrophilic activation of B–N bonds by protonation, the catalytically active borenium cation **38** is present in equilibrium with the tetracoordinate boron complex **39** (Scheme 12). To gain more insight regarding the key equilibrium, attempts were made to perform a similar activation with methansulfonic acid (MsOH), but this did not afford a catalytically active source of borenium intermediates (Scheme 12). Corey et al. interpreted the outcome based on the lower acidity of MsOH compared to TfOH, and on the relatively low basicity of oxazaborolidine nitrogen resulting from the donation of *n*-electrons from N to B. Even if protonation had occurred, there is the added concern that increased nucleophilicity of MsO^- compared to TfO^- would decrease the equilibrium concentration of the catalytically active borenium salt (**38** adjusted for X = OMs) relative to the covalent, tetracoordinated amine borane adduct **39** (X = OMs). Similar equilibrium considerations apply to all methods for catalytic generation of chiral, formally cationic borenium intermediates as shown in Scheme 12, including oxazaborolidine B–N protonation of **37** (to **38**/**39** using TfOH;[31] to **155**/**156** using Tf_2NH72) or **154** (to **157**/**158** using TfOH[31]), and protonolysis of the borohydride B–H bond of **160** using Tf_2NH to give **161**/**162**.74 However, attempts to generate **161** directly from **37** by methylation were not successful due to the low nucleophilicity at nitrogen that results from *n*-electron donation to boron.

It is of considerable interest to characterize the reactive intermediates in Scheme 12 and to assay the relevant equilibria, but this has proven to be a challenging task. Among the borenium intermediates proposed, only **161** has been characterized by ^{11}B NMR (δ = 34 ppm),[74] a value that falls within the expected range given the presence of oxygen as an *n*-electron donor, and is shifted significantly downfield compared to the precursor **160** (δ ^{11}B = 7.7 ppm). No NMR signals were reported for the corresponding tetravalent triflimide adduct **162**, suggesting that the equilibrium strongly favors the borenium salt **161** as the only species observed. In contrast to **161**/**162**, the nature of the other intermediates shown in Scheme 12 has been deduced almost entirely from proton NMR chemical shift evidence (Table 2), and from relative reactivity comparisons. To help interpret the NMR data, Scheme 12 and Table 2 also include the somewhat distinctive case of electrophilic B–N activation from **37** by $AlBr_3$ as the Lewis acid.[75] The resulting adduct **163** has no net charge, but contains a borenium subunit and is a highly effective Diels-Alder catalyst.

Most of the chemical shift data in Table 2 were obtained from equilibrating mixtures containing activated tetracoordinate boron species (Scheme 12) that serve as borenium precursors according to the test of exceptional catalytic reactivity in the Diels-Alder reaction. Data are presented in three categories, starting with the parent oxazaborolidines (entries 1, 2), followed by the presumed tricoordinated borenium species (entries 3–6), two of the corresponding tetracoordinated structures (entries 7–8), and two related tetracoordinated complexes for comparison (entries 9, 10; amine borane **160** and the DMF adduct **157**·DMF). Because ^{11}B NMR data were not available for most of these structures, the borenium assignments (entries 3–5) were proposed by comparing chemical shifts for H_a from the observable species in equilibrium. Assuming that the higher field shift for H_a indicates tetracoordinate boron (for example, **158**, entry 8), the lower field shift would then be assigned to the corresponding borenium structure (**157**, entry 4).[31] For the specific pair of equilibrating tricoordinate and tetracoordinate boron structures **157** vs. **158**, the chemical shifts of H_b and H_c also follow the same pattern (entries 4 and 8, respectively), suggesting that the combination of formally positive nitrogen and tricoordinate boron is responsible for deshielding protons at adjacent carbons. However, in one case (entry 7; equilibrium of **155** with **156**), a total of three H_a signals were observed, including two that were assigned to a tetracoordinated structure **156** and attributed to the formation of two diastereomers.[72] By

analogy, two diastereomers of **158** might also be present in the equilibrium with borenium salt **157**. Given the similarity of chemical shifts for signals assigned to **157** and the signals of **158** ($\Delta\delta \leq 0.2$ ppm; entries 4 and 8),[31] the possibility remains that both sets of signals for H_a given in entry 8 were due to diastereomers of **158**. If this conjecture is correct, then the concentration of **157** may have been too low to detect. Nevertheless, **157** would still be present in equilibrium, and its intrinsic catalytic reactivity could be sufficiently large to catalyze the Diels-Alder reaction as observed.

Entries 9 and 10 are included in Table 2 to allow a broader range of ^{1}H NMR chemical shift comparisons for tetracoordinate with tricoordinate boron in the oxazaborolidine environment. Inspection of the ^{1}H data for all of the entries suggests that the absolute chemical shift values for H_a reflect the presence of electronegative groups at boron as much as they reflect coordination number, and there is some overlap in the range of values assigned to tricoordinate vs. tetracoordinate boron. Entry 3 (δ = 5.44 ppm) stands out as the most likely case of an observable borenium salt (**155**, tricoordinate B) because the chemical shift difference vs. entry 7 (**156**, tetracoordinate B) is relatively large (0.4–5 ppm). Also interesting is the H_a chemical shift (δ = 5.26 ppm) for the $AlBr_3$-complexed catalyst **163**. This value is close to the H_a chemical shift of **155** even though **163** has no net charge and might plausibly be involved in equilibrium with a hypothetical structure **164** (Scheme 12) where bromine is shared between boron and aluminum. According to the absolute values of chemical shifts for H_a, the assignment of a borenium structure **161** for entry 5 might be questioned because the observed H_a chemical shift of δ = 4.95 ppm is so similar to the H_a chemical shifts in entries 7 and 10. However, it is important to note that **161** has an *N*-methyl substituent, and that H_a in the best available comparison structure having the same substitution pattern (**160**, entry 9) appears well upfield (δ = 4.38 ppm).

6.3 Reactivity and scope of oxazaborolidine-derived Diels-Alder catalysts

The NMR evidence considered above supports the assignment of borenium structures for **155**, **161**, **163** in solution, but another important criterion is catalytic reactivity. Initial comparisons had shown that the triflate-activated catalyst **38**/**39** promotes the Diels-Alder reaction with modestly reactive dienes such as 1,3-butadiene, isoprene, or 1,3-cyclohexadiene, but this required the relatively potent dienophiles 2-bromoacrolein or 2-methacrolein (eq. 15, 16). Furthermore, full conversion in the cyclohexadiene/methacrolein example required 24h at −78 °C.[31] According to these observations, the reactivity of the equilibrium pair **38**/**39** as catalyst ranks between that of **148**/**149** (no reaction with either 1,3-butadiene and 1,3-cyclohexadiene) and that of the tetraarylborate salt **151** (both reactions complete within 2h at −94 °C).

Comparisons of oxazaborolidine catalysts reported by Corey et al. are summarized in Table 3 for the catalyzed reactions of cyclopentadiene with several representative dienophiles (methacrolein; diethyl fumarate; cyclopentenone; 2,5-dimethylquinone), arranged in approximate order of Diels-Alder reactivity for each catalyst with the more demanding fumarate or cyclopentenone dienophiles (compare entries 3, 5, 7, 12 for fumarate; or entries 4, 8, 11 for cyclopentenone). Given the differences in diene stoichiometry, dienophile concentration, and catalyst loading, the temperature/time data provide at best a very qualitative picture of reactivity. However, it is clear that the bistriflimide-activated catalysts **170**/**171** or **161**/**162** are more reactive than the triflate catalysts **38**/**39** or **168**/**169**. Overall, the fastest reactions are observed using the bistriflimide-activated **161**/**162**, or the $AlBr_3$-activated **163** (*N*-methyloxazaborolidine substrate). The latter catalyst was highly effective for promoting Diels-Alder cycloaddition with the less reactive substrates using catalyst loadings as low as 4 mol%,[75] while 10–20 mol% loading was needed for similar applications using other oxazaborolidine catalysts. The improved turnover for **163** was

attributed to the greater bulk of the $AlBr_3$ Lewis acid, a factor that may prevent product inhibition of the catalyst.[75] The reactivity trends are also reflected in Table 4 where a broader range of dienes and dienophiles is summarized. From the combined data of Tables 3 and 4, it is clear that the chiral oxazaborolidine catalysts provide excellent yields and enantioselectivities in many Diels-Alder reactions, and that the best catalysts offer remarkably broad scope for synthetic applications. These practical advantages for catalysts **38**/**39**, **155**/**156**, and **163** are reflected by the commercial availability of the precursor **37**.[76]

The oxazaborolidine-derived borenium source **168**/**169** (bis(3,5-dimethylphenyl) series; triflate anion) is an effective catalysts for modest dienophiles including α,β-unsaturated esters and ketones (Table 4, entries 4–6). However, the improved dienophile scope of catalyst **168**/**169** was demonstrated only for the highly reactive cyclopentadiene because catalyst decomposition was already problematic at 0 °C. On the other hand, the corresponding $HNTf_2$ activated catalyst **170**/**171** was stable even at rt, allowing Diels-Alder reaction of unsaturated lactones, cyclic enones, and quinones with the less reactive acyclic dienes (Table 4, entries 8–9; see also Scheme 13).[72] These findings have largely solved the problem of catalyst scope and reactivity.

The oxazaborolidine catalysts also have considerable potential for the control of regiochemistry (Scheme 13). Thus, the Diels-Alder reaction of trifluoroethyl acrylate with isoprene afforded the para isomer **172** with excellent regiocontrol using **170**/**171** as catalyst. However, the more challenging reaction of 2,5-dimethyl-1,4-benzoquinone **173** with isoprene produced a ca. 2:1 mixture of **174:175** as a consequence of poor discrimination by the activated dienophile complex.[72] Fortunately, the corresponding iodoquinone **176** reacted selectively to give a 13:1 ratio of **177:178**. This regioselectivity was attributed to preferential activation of the carbonyl group remote from iodine by the chiral Lewis acid **170** and subsequent cycloaddition at the less hindered double bond. If desired, adduct **177** can be converted to **174** by reductive deiodination, and **178** can also be used as a convenient partner in palladium-catalyzed coupling chemistry.

Excellent regiocontrol as well as useful enantioselectivity was observed in the oxazaborolidine-catalyzed 2+4 cycloadditions of diene **179** (Scheme 13). Thus, reaction with 2-methylcyclopentenone in the presence of *ent*-**161**/**162** afforded **180** as the exclusive product with 82% ee.[74] Adduct **180** was upgraded to 99% ee by simple crystallization, and was coverted into estrone methyl ether in several steps. In an alternative approach, the modified oxazaborolidine **180** was used to catalyze the Diels-Alder reaction of **179** with the enal ester **181** as the dienophile. In this case, the product **182** was obtained in 92% yield (94% ee), and was converted to estrone in seven steps.[77] Coverage of other important total synthesis applications of oxazaborolidine-catalyzed Diels-Alder reactions appears in a recent review, along with models to explain catalyst enantioselectivity.[68b]

One last topic in the Diels-Alder area will be mentioned in the context of catalyst reactivity. Thus, Yamamoto et al. studied the activation of a monocyclic oxazaborolidine **183** by protonation with several acids, including MsOH, TfOH, Tf_2NH, and the exceptionally strong carbon-based acid $HC(C_6F_5)Tf_2$ (**186**, Eq. 17).[78] No spectroscopic data were reported for the activated intermediates **184** or **185**, but catalytic reactivity was observed in the Diels-Alder reaction of cyclopentadiene with ethyl acrylate for all acids except MsOH (Table 5, entries 1–4). The reactivity pattern was interpreted based on the generation of borenium cations **184**, presumably in equilibrium with the tetracoordinate boron structures **185** as usual. In all cases where Diels-Alder reaction occurred with these catalysts, high enantioselectivity was observed, and the best ee as well as the highest yield were obtained using the highly hindered carbon acid **186** for activation.

The yields of Diels-Alder products obtained under standardized conditions (Table 5, entries 1–4) were found to increase as the coordinating ability of anion X^- derived from the HX used in the activation step decreases. This order of catalyst reactivity follows the same general trend as deduced by Corey et al. from a combination of NMR evidence and optimization data. Assuming that Tf_2NH is already strong enough to mostly protonate the oxazaborolidine substrates as indicated by the NMR data for Corey's bicyclic oxazaborolidine **161**, then greater Diels-Alder reactivity using Yamamoto's carbon acid $HC(C_6F_5)Tf_2$ (**186**) for activation can be taken as evidence that the hindered anion of **184d** ($^-C(C_6F_5)Tf_2$) is less coordinating compared to bis-triflimidate[79] (Tf_2N^-) and more resistant to formation of the covalent adduct **185d**. In any event, the excellent reactivity of Yamamoto's catalyst can be exploited for demanding Diels-Alder applications, including the regioselective cycloaddition of 2-alkylcyclopentadienes starting with mixtures that contain the 1-alkylcyclopentadiene isomer,[78] and also the catalyzed cycloaddition of sensitive α,β-acetylenic ketones with acyclic 1,3-dienes.[80]

Yamamoto et al. have also explored the electrophilic activation of **183** using $SnCl_4$ (Table 5 entries 5–7; eq. 18).[81] In the best experiments, the presumed Lewis acid-Lewis base adduct **187** was an effective catalyst at a loading of 1% relative to the dienophile. Catalysis was also observed using a deficiency of $SnCl_4$ relative to **183**, even at ratios as low as 1:4 $SnCl_4$:**183**. This finding prompted a study of the effect of Lewis basic impurities on the catalytic efficiency of **187**. Little change in yield or ee was observed upon addition of 5 mol% of water, iPrOH, EtOAc or even DMF to the reaction mixture, and practical results were obtained by performing the reaction in unpurified DCM at −78 °C. The high reactivity of **187** is reminiscent of the behavior of **163** in the bicyclic oxazaborolidine series. Several other Lewis acids such as $AlCl_3$ or $TiCl_4$ could also be used, but the choice of Lewis acid is important. Thus, the $BF_3{\cdot}OEt_2$ adduct was not an effective catalyst starting from oxazaborolidine **183**, and a similar observation was reported in the bicyclic series (**188**) in the prior study.[75]

6.4 Miscellaneous uses of chiral borenium Lewis acid catalysts

The Diels-Alder applications considered in Sections 6.2–6.3 rely on Lewis acid (borenium) complexation at dienophile carbonyl oxygen. The same phenomenon has been exploited in several other Lewis acid catalyzed reactions where the borenium cation serves as an oxophilic activating agent. This topic will be considered only briefly because most of these synthetic applications have not raised new structural or characterization issues that directly reflect on the properties of borenium catalysts. Nevertheless, some of the examples reveal interesting subtleties about the details of Lewis acid catalysis. For example, the Tf_2NH-activated catalyst **155**/**156** has been used to catalyze the Mukaiyama-Michael reaction of a ketene trimethylsilyl acetal **189** (eq. 19),[82] resulting in the expected 1,4-addition product **191** with good enantioselectivity. On the other hand, ketone-derived enol silanes **192** were shown to react with trifluoroethyl acrylate in the presence of catalyst **163** to give the cyclobutane product **193** (98 % ee; eq. 20).[83] This latter reaction has been described as an asynchronous 2+2 cycloaddition, while the related process of eq. 19 is believed to involve an ionic intermediate **190** resulting from Lewis acid-catalyzed 1,4-addition, followed by silyl transfer. However, catalyst **155**/**156** could not be used in the 2+2 cycloaddition (eq. 20) due to decomposition involving the silyl enol ether.

A mechanistically related synthesis of α-iodo-α,β-unsaturated esters **196** from benzaldehyde and acetylenic ester **194** has been reported using catalyst **170**/**171** in combination with TMSI (eq. 21). The process involves formation of a nucleophilic silyl ketene acetal **195** *in situ,* followed by Mukaiyama aldol reaction with the catalyst-benzaldehyde complex.[84]

Oxazaborolidinium triflimidate catalyst **170**/**171** has also been used for the enantioselective cyanosilylation of aliphatic as well as aromatic aldehydes, while the analogous triflate catalyst **168**/**169** gave better results for the cyanosilylation of ketones (eq. 22).[85] This application relies on an unusual nucleophilic cyanide equivalent, the isonitrile **197**, generated *in situ* from Me_3SiCN and methyldiphenylphosphine oxide. Because **197** is thought to be in equilibrium with its precursors, it is remarkable that the borenium catalyst **168**/**169** is an effective Lewis acid for carbonyl activation despite the presence of nucleophilic phosphine oxide as well as the isontrile **197**. The cyanosilylation of ketones was quite slow, and required many days at temperatures in the range of 25–45 °C. Nevertheless, useful enantioselectivity was observed for the product **198a** obtained from acetophenone, and especially for the triflate analogue **198b** (95% ee). Details of the enantioselective transition state geometry are beyond the scope of this review, but can be found in the full paper along with a number of related cyanosilylation examples.[85b] The triflate substituent of **198b** is uniquely suited for palladium catalyzed coupling applications, so the sequence of Eq. 22 potentially provides access to a range of non-racemic *p*-substituted benzene derivatives containing a quaternary carbon.

Some years earlier, Corey and Cimprich had reported a procedure for the enantioselective ethynylation of aldehydes using a monocyclic oxazaborolidine catalyst **199** (eq. 23).[67] Although the conversion implies some similarity to the cyanosilylation of eq. 22 because both reactions involve an *sp*-hybridized nucleophile and an oxazaborolidine Lewis acid for carbonyl activation, the proposed mechanism for eq. 23 is quite different and proceeds by a fascinating dual activation sequence reminiscent of the CBS reductions (Section 6.1). Thus, a Lewis acid-Lewis base interaction between the alkynylborane and the oxazaborolidine **199** generates the exocyclic B–N bond and borenium subunit, followed by aldehyde complexation to form the crucial intermediate **200**. The activated, exocyclic tetracoordinate boron then delivers nucleophilic alkyne for attack at the activated, boron-complexed carbonyl group to afford the propargylic alcohol after aqueous workup.

7. Miscellaneous applications of borenium Lewis acids

7.1 B–O activation

Apart from the enantioselective applications using the powerful oxazaborolidine-derived catalysts presented in the previous sections, there have been relatively few studies addressing boron cations as Lewis acid catalysts. In one informative example, protonation of the neutral, salicylaldimine-derived complex **201** with TfOH/THF resulted in an isolable product (Scheme 14).[86] The ^{11}B NMR signal at $\delta = 3.9$ ppm was consistent with tetracoordinate boron, and narrowed the choice of plausible solution species to **203** or **204**. However, ^{1}H NMR data revealed the presence of bound THF, confirmed by elemental analysis, thus ruling out the simpler structure **204**. Presumably, the tricoordinate (borenium) salt **202** is formed from **201** by protonation and heterolysis of the B–OCH_3 group, followed by solvation to give the THF adduct **203**. Formally, **203** is a boronium salt because it contains tetracoordinate boron in the cationic subunit, but facile heterolysis of the exocyclic B–O bond would be expected to release the weakly bound THF in solution, resulting in facile equilibrium with the higher energy borenium salt **202**. Therefore, **203** functions as an *in situ* source of **202**, and can be used as a Lewis acid catalyst. One example has been reported using **203** as pre-catalyst to induce the polymerization of propylene oxide. The authors proposed initiation via **205**, the Lewis acid-Lewis base adduct of **202** and propylene oxide. The subsequent propagation steps were not investigated in detail, but the authors considered possible explanations involving ligand B–O or B–N cleavage. Another rationale to consider for the propagation steps is a conventional sequence of S_N2 attack by monomer

(propylene oxide) at the less substituted oxiranium C(3) carbon in **205**, followed by repetitive S_N2 attack by propylene oxide on the oxiranium terminus C(3) in a growing chain.

Other Lewis acid catalyzed reactions have been rationalized by invoking intermediates that contain a borenium subunit in a neutral structure.[87–90] Thus, Evans *et al.* observed that samarium (III) iodide catalyzes the hydroboration of 3-pentenol (**206**) with catecholborane (**65**), resulting in an 11:1 ratio of the diols **207:208** after oxidative workup (eq. 24). Among other mechanisms considered for the activation of **65**, Evans *et al.* noted that formation of the borenium-like Lewis acid-Lewis base complex **209** should increase reactivity at the boron center. However, the alternative possibility of net hydroboration via intervention of metal hydride species was not ruled out.

In a somewhat different application of Lewis acid B–O activation, Hall et al. evaluated $Sc(OTf)_3$ as a catalyst for the crotylboration of aldehydes with the (*Z*)- or (*E*)-crotylboronates **210** (Scheme 15).[88] Formation of the rearranged products **212** was strongly accelerated compared to the uncatalyzed reactions and proceeded with high diastereospecificity (98:2 *syn:anti* from *Z*-**210**; 2:98 *syn:anti* from *E*-**210**), the classical test for crotylboration via a cyclic (closed) transition state such as **211**.[88b] To support the proposal that $Sc(OTf)_3$ accelerates the reaction by bonding to boronate and not carbonyl oxygen, comparisons were made between the prenyl derivative **213** and the 9-BBN analogue **214** in the reaction with hydrocinnamaldehyde. The boronate **213** reacted >100 times faster under identical catalyzed conditions (dichloromethane, −78 °C), while the 9-BBN-derived **214** reacted with no appreciable rate increase over the background (uncatalyzed) process. This evidence argues against carbonyl activation by the Lewis acidic $Sc(OTf)_3$, and is consistent with an important role for the borenium-like transition state **211**. Other oxophilic Lewis acids such as $AlCl_3$[89] or BF_3[90] have been used to catalyze similar aldehyde allylations or crotylations with boronate reagents.

Attempts to react the ester-containing allylic boronate **215** (Scheme 15) with benzaldehyde in toluene via the $Sc(OTf)_3$ activated intermediate **216** encountered a slow reaction at 0 °C (<5% conversion, 16 h). On the other hand, the analogous experiment with Brønsted acid catalysts resulted in a large rate enhancement.[91] The initially formed product **218** undergoes lactonization to **219** under the acid-catalyzed conditions. Although the mechanistic details remain uncertain, the borenium intermediate **217** was proposed as the species responsible for accelerating the reaction. Hall *et al.* have also developed effective catalysts for enantioselective crotylboration that may function via a related mechanism, although the use of a chiral diol additive as well as a Lewis acid raises additional mechanistic possibilities.[92]

7.2 Lewis acidity and π-conjugated borenium analogues

The Lewis formal charge representation of borenium cations (Section 1, Fig. 1) places no specific restrictions on the distance between boron and the formal plus charge. On the other hand, the dative bond representation of Fig. 1 ($L\rightarrow BR_2^+$) is more explicit and treats the ligand L as a typical Lewis base, presumably one that is capable of independent existence. No distinction between the more inclusive Lewis formal charge representation and the dative representation has been needed so far because nearly all of the borenium salts discussed in prior sections easily fit both representations. However, structure **50**[36] (Scheme 2) does raise some questions. In this example, the ligand in the $L\rightarrow BR_2^+$ representation corresponds to 1,3-dimethylimidazolidene as the Lewis base. There is no problem with terminology if L can be a transient nucleophilic carbene as well as a Lewis base, as in the preparation of **50**, resulting in a formal charge that is placed farther from boron. On the other hand, the boronopyridinium salt **220b** (Scheme 16) is a case where the dative bond representation **220a** is technically correct for the “nucleophilic carbene ligand” of a

borenium salt, but appears somewhat artificial. We prefer to classify **220** as a π-conjugated borenium analogue based on the simple criterion that its reactivity suggests enhanced electrophilicity at tricoordinate boron in the cationic environment. Several other examples are included in Schemes 16 and 17 where a positively charged substituent is present in a conjugated π-system connected to tricoordinate boron, and where borenium-like Lewis acidity is the only other criterion for regarding these structures as π-conjugated borenium analogues.

The Lewis acidity of **220** has not been evaluated directly, but enhanced electron demand at boron is implicit in the use of **220** and related substances as catalysts for the thermal condensation of amines and carboxylic acids to form amides.[93] These reactions are believed to involve the generation of an acyloxyborane **221** as the key intermediate,[93a] presumably formed by nucleophilic attack of carboxylate at boron in **220.** Catalysis by the cationic *N*-methylpyridinium salt was considerably more effective than by the parent pyridine, suggesting that attack by the nucleophile is accelerated by the remote positive charge.

Added insight regarding the effect of a cationic substituent on Lewis acidity at boron was provided in a study of the conjugated phosphonium borane **222** by Kawashima et al. (Scheme 16).[94] Surprisingly, the spectroscopic properties of this substance were found to have a pronounced temperature dependence. Thus, ^{11}B NMR spectroscopy above 273 K revealed a broad signal at δ = 56 ppm, consistent with trivalent boron in an aromatic environment. However, cooling the sample resulted in signal broadening, and eventually (< 230 K) gave a new broad maximum near δ = 0 ppm, a value that indicates conversion to a tetracoordinate boron structure **223** where the boron *p*-orbital is no longer part of a conjugated π-system. The UV spectrum was also temperature dependent, and decreased absorbance was observed for the 300 nm π-π* band upon cooling the sample. Treatment of the equilibrium mixture of **222**/**223** with ionic fluoride or chloride resulted in conversion to the corresponding product of halide exchange (**224**).

In another definitive study, Stephan *et al.* were able to generate several isolable conjugated borenium salts **226** using the method of hydride abstraction from the borohydrides **225** (Scheme 16).[95] The tricoordinate boron could not be detected using ^{11}B NMR methods, presumably due to quadrupolar relaxation,[70,71] but enhanced Lewis acidity was confirmed by other methods, including the Gutmann-Beckett test. This procedure (comparison of ^{31}P chemical shifts for the triethylphos-phine oxide adducts **227** with reference structures), resulted in Gutmann acceptor numbers of 78.1 for $(C_6F_5)_3B$ and 80.2–85.6 for **226** (R,R′ = alkyl or H), evidence for increased electron demand resulting from replacement of the C(4) fluoride by formally positive phosphorus.

7.3 π-Conjugated borenium analogues as selective anion sensors

A variety of conjugated borenium salts containing cationic aryl or heteroaryl boranes have been studied by Gabbaï *et al.* in connection with efforts to develop selective anion sensors. This topic has been reviewed in depth,[96] so only a few highlights will be mentioned. Most of the work has focused on the relatively simple, but very hindered (and therefore, isolable) borenium structures **228**–**233** (Scheme 17). All of these salts react with nucleophilic anions to form tetracoordinate boron species in organic solvents, but the challenge has been to develop anion sensors that might respond selectively in the presence of water. Fluoride or cyanide detection using boron-based reagents is a logical choice due to their relatively strong bonds and compact nature, but there are a number of hurdles to overcome, mostly related to the aqueous environment. The reagent needs sufficient anion affinity to overcome hydration enthalpy, especially in the fluoride case where the anion is stabilized by strong hydrogen bonds with water. High sensitivity also requires Lewis acid selectivity for the

anion over water or other Lewis bases, while practical applications require reagents that are stable under relevant assay conditions. Anion binding was expected to benefit from Coulombic attractions with the cationic substituent Z, while the LUMO energy-lowering effect of the cation would promote bonding with all nucleophiles. Indeed, the cationic phosphonium borane **228** (X = I) was shown to bind fluoride in water (10% methanol added for solubility).[97] The *ortho*-isomer **229** was found to have a higher fluoride binding constant in methanol by orders of magnitude ($K > 10^6\ M^{-1}$ for **229** vs $K \sim 400\ M^{-1}$ for **228**),[97b] but its limited stability in water was problematic.

The ammonium boranes **230** and **231** (X = OTf) proved to be sufficiently stable in aqueous media for detailed study, and both isomers formed cyanide as well as fluoride adducts in organic solvents.[98] According to assay by UV spectroscopy (suppression of the maximum at 320 nm), the *ortho*-isomer **231** retained fluoride affinity in 95:5 water:DMSO ($K = 910\ M^{-1}$) to give **235**, but did not bind cyanide ion under aqueous conditions, presumably due to increased steric interactions involving cyanide and the bulky $BMes_2$ and NMe_3 groups. In contrast, the *para*-isomer **230** displayed negligible fluoride affinity in the presence of water because of the lower activating effect of the *para* vs. *ortho* trimethylammonium groups, but **230** bound cyanide quite strongly ($K = 3.9\times10^8\ M^{-1}$ at pH 7, 3:2 water:DMSO) to form **234**. Neither isomer (**230** nor **231**) interacted with aqueous chloride, bromide, acetate, or nitrate. Thus, selective assay for fluoride (with **231**) or cyanide (with **230**) is possible using these reagents and their analogues. Overall, the fluoride binding affinities of **228**–**231** in aqueous systems may be too low for some applications, but substantially higher fluoride binding constants were observed in the phosphonium borane series for analogs of **228** having increasingly hydrophobic phosphorus substituents.[97c]

In yet another contrast in selectivity, Gabbaï *et al.* have reported that the *ortho*-dimethylsulfonium borane **232** (Scheme 17) does bind cyanide ion, and does so with high affinity.[99a] The 1,8-disubstituted naphthalene analog **233** was ca. 100-fold less effective. Binding constants were not reported, but a fluorescence quenching technique was used to detect the binding of **232** with aqueous cyanide at levels as low as 50 ppb. With 0.1 ppm of cyanide, the fluorescence quenching effect was large enough for simple visual evaluation. The origin of strong cyanide binding with **232** to give **236** was probed by DFT methods and NBO (Natural Bond Orbital) analysis. Stabilization was found not only by a donor-acceptor $\pi(CN)\rightarrow\sigma^*$ (S–C) interaction, but also by a back-bonding effect, $lp(S)\rightarrow\pi^*(CN)$. These energy contributions were estimated to total 4.1 kcal/mol for **236**, and may explain why **232** is a much better binding agent for cyanide compared to the ammonium analogue **231**.

One remaining problem with the anion sensors is that the reagents discussed so far report anion binding by decreased absorption or decreased fluorescence. This is the predicted outcome of anion binding to sp^2 boron in a conjugated π-system to form the less conjugating (tetracoordinate) sp^3 boron adduct, a factor that compromises sensitivity. Gabbaï *et al.* have reported a potential solution to this problem using reagent **240a** (eq. 25), a boronium salt, an example of a BODIPY dye (see also structures **52**, **53**, Section 3.2), and a sensor having a “turn-on” response under specialized conditions.[99b]

Access to **240a** was achieved using the method of halide abstraction from **237** with TMSOTf to generate a tetracoordinate boron complex **239** (eq. 25). By analogy to Scheme 2, this conversion may involve a borenium intermediate **238**, although no mechanistic proposal was invoked by the authors.[99b] Subsequent addition of DMAP afforded the air-stable tetracoordinate boronium triflate **240a** (^{11}B NMR, δ = 0.91 ppm). Both **237** and **240a** were strongly fluorescent in solution, but addition of 10 equiv of tetrabutylammonium iodide to **240a** suppressed most of the fluorescence, apparently due to a heavy element effect resulting from anion exchange to form the boronium iodide ion pair **240b**. However,

addition of an equivalent of fluoride ion to the solution containing **240b** gave a five-fold increase in fluorescent emission intensity, amounting to a "turn-on" response by **240b** as a fluoride sensor. The basis for restoration of fluorescence upon addition of fluoride was proposed to be the reaction of **240b** with fluoride to form the highly fluorescent **237**, and similar conversion to **237** was also observed from **240a**. The mechanism for these conversions is not known, although generation of borenium salts similar to **238** via S_N1-like DMAP dissociation followed by fluoride trapping might be considered. On the other hand, the boronium triflate **240a** does not react with chloride, bromide, or iodide ion. This observation raises questions about an S_N1-like heterolysis. A reviewer has suggested that a pentacoordinate boron transition state **241** may be involved in the nucleophilic displacement from **240** to **237**, by analogy to the pyridine-initiated bromide displacement discussed in connection with eq. 7 (Section 2.4), but this interesting alternative remains to be evaluated.

7.4 Tricoordinate boron in structures containing metal cations

Cyanide and fluoride affinity has also been probed using other cationic borane reagents,[100–102] some of which incorporate cationic transition metal substituents placed at a considerable distance from the boron center.[102] The latter structures can be included within the broadest representations of borenium salts suggested in Fig. 1 (Section 1), although there is no compelling reason to do so. In general, Lewis acidity at boron increases with proximity to the cationic site. Qualitatively, the activating effect increases as the number of conjugated cationic substituents increases.[101] Cationic structures are also known where a transition metal is directly connected to tricoordinate boron.[103] Although some of these structures can be potent Lewis acids and resemble more typical borenium salts in their ability to bind Lewis bases, the transition metal containing structures are beyond the scope of this review and will not be discussed beyond the inclusion of leading recent references.[100–103]

8. Borenium reagents for C-B bond formation

8.1 Borenium ion equivalents

The preceding sections describe methods that generate transient borenium intermediates or, rarely, that produce directly observable borenium salts in solution. Many of these techniques differ in the details of boron activation, but share the common feature that a tetracoordinate boron intermediate is in equilibrium with the borenium salt (tricoordinate boron). This rather simple statement deserves closer scrutiny when some of the relevant structures already discussed are considered side by side (Fig. 2), a comparison that raises questions about the importance of the coordination number at boron and the relevance of the borinium/borenium/boronium terminology. For example, the observable tetracoordinate boron cations **45**, **83**, and **203** should be classified as boronium salts, but all three can also be regarded as solvated borenium salts that may (or may not) dissociate in solution, while **45** could also be classified as a bis-nitromethane solvated borinium ion. If these complex cations do undergo dissociation, there is the added subtlety that solvated tight ion pairs or solvent-separated ion pairs may be formed. Such nuances were often discussed during the classical era of carbenium ion chemistry, but related questions have not been studied systematically for the analogous borenium ions.

Another issue is that borenium cations at the higher end of the NH_3 affinity range (Table 1) are likely to share electrons with solvent whether or not the complexes are observable. In the case of dichloromethane, this interaction can lead to solvent (and reagent) decomposition via *n*-electron sharing (see **80**, Fig. 2), while in aromatic solvents, the interaction can generate π-complexes that may or may not undergo further reactions depending on circumstances (see Section 8.3). Electron sharing can also involve unreacted precursor molecules, as in the hydride-bridged "dimers" **78** or **84** where the B–H bond of the starting amine borane serves

as a σ-donor leading to the 3c2e bond. It would be no surprise to encounter similar examples where *n*-electrons are shared loosely between a borenium ion and its precursor B–X: bond (X = Cl, O, N) in solution, similar to the gas phase adduct **64** (formally, a borenium ion that corresponds to a dimethoxyborinium ion bound to the precursor trimethyl borate as *n*-electron donor). In many cases where these issues arise, the only experimental evidence regarding boron coordination number is likely to be the ^{11}B chemical shift for the dominant observable species with no guarantee regarding its relevance to the reactive species. Added insight may be gained from DFT calculations that address the transient intermediates, but at the current level of development, we will not know with certainty whether free borenium ions, ion pairs, bridged dimers, or solvates are responsible for a given transformation.

In some cases, the species in solution may be characterized rather well (eq. 26), but their classification is still not entirely straightforward. Thus, structure **242** (from **241** + $SbCl_5$) has a tetracoordinate boron (formally, boronium) environment due to internal oxygen complexation according to its ^{11}B chemical shift of δ = 8.7 ppm in CD_2Cl_2, but in nitromethane, the observed chemical shift is δ = 16.2 ppm.[104] This latter value was interpreted as evidence for an equilibrium involving a borenium salt **243** as well as a boronium salt **244**, either or both of which might also be regarded as solvated borinium species, depending on the (unknown) B–O bond lengths. By the same logic, **242** could be regarded as an internally complexed borinium ion. Similar issues were considered in Scheme 5, in connection with the boronium salt **99** (Fig. 2), obtained form 9-BBN-NTf_2 and 1,8-dimethylaminonaphthalene, where unusually long B–N bonds could be taken as reason to classify **99** as a diamine complex of the corresponding borinium ion.

For all of the above reasons, it is simpler to think in terms of borenium ion equivalents in the reactions of high energy boron cations. This deliberately vague terminology includes all permutations of tetracoordinate (or partly tetracoordinate) boron structures that are potentially capable of dissociating in solution to give tricoordinate boron cations, and it also includes various activated structures such as the Lewis acid adducts discussed in Sections 6 and 7 where a borenium subunit is present in a neutral molecule. The following sections describe the reactivity of the higher energy borenium equivalents as reagents for the formation of C–B bonds. It is fair to say that the underlying mechanisms are not well known in these examples and that relevant studies are at an early stage, but substantial preparative potential is already clear.

8.2 Do borenium ions participate in hydroboration chemistry?

Studies in our laboratory have encountered olefin hydroboration using activated amine boranes that might be regarded as borenium equivalents. For example, pyridine iodoborane **245** converted β-methylstyrene into the iodoborane adduct **248** and treatment with pinacol in the presence of base afforded the pinacolboronate **249** in excellent yield (eq. 27).[105] According to most indications, related hydroborations do not typically involve a leaving group heterolysis event prior to the step that generates the alkene π-complex **246**, and are best regarded as nucleophilic displacements where the alkene attacks the iodoborane reagent to give **246** directly, followed by bond reorganization via the ion pair transition state **247**. The evidence in favor of the S_N2-like mechanism is mostly circumstantial, but it is reasonably satisfying. Thus, the rate of reaction is sensitive to the nature of the alkene as well as the pyridine ligand, suggesting that both reactants are involved in the rate-determining step. Furthermore, the reagent **245** belongs to the same family of activated pyridines studied many years ago and shown to resist spontaneous generation of borenium ions via leaving group heterolysis at room temperature (Section 2.4). Moreover, the hydroboration process works in toluene solution, a solvent where initial generation of a borenium intermediate would be suspect. Intramolecular versions of the hydroboration

process using tethered, unsaturated amine iodoborane complexes work especially well, but these reactions are also believed to take place without dissociation to borenium species.[106]

Hydroborations also take place using the high energy activation procedures. Little of this chemistry has been investigated so far, and only isolated examples can be mentioned. In one case, the C_3-symmetric chiral phosphine borane **250** (eq. 28) was treated with the trityl cation reagent $Tr^+B[C_6F_5]_4^-$ (**71b**) under conditions that should generate a hydride-bridged "dimer" from the phosphine borane.[48] When the activation was performed using a 3:1 ratio of **250:71b** in the presence of α-methylstyrene (toluene, rt) followed by conventional oxidative workup, the chiral alcohol **251** was obtained with 25% ee (190% yield relative to **71b** as limiting reagent).[107] We did not fail to notice that reagent **250** had been prepared starting from 3 equiv of commercial **251** (>95% ee) while the hydroboration produced 1.9 equiv of **251** with 25% ee.

Another attempt to access enantioselective hydroborating agents was made starting from the chiral pyridine borane **252** (eq. 29).[107,108] Activation of **252** with 50 mol% of the trityl salt **71b** at −78 °C followed by warming to −15 °C gave characteristic NMR signals indicating that **254** had been formed. In a similar experiment conducted in the presence of β-methylstyrene, subsequent quenching and oxidative workup gave only 20% of the desired alcohol **255** (14 % ee) while activation at room temperature produced racemic **255**. Activation at rt was also evaluated in the absence of the alkene, and a ^{11}B NMR signal was observed indicating that diborane had been formed, apparently via some process equivalent to pyridine transfer from **252** to the trityl cation in competition with the desired hydride transfer. This observation indicates that part (or all) of the racemic product product is formed without the direct involvement of **253** or **254**, but the 14% ee at lower temperatures supports at least some participation by a chiral B–H source with the B–N bond intact.

In a simpler context, activation of triethylamine borane was investigated using the trityl salt **71b** in the presence af an allylic silane (eq. 30).[50] This experiment was designed to test whether an electrophilic borylation/de-silylation sequence would compete with the hydroboration process, but oxidative workup gave the primary alcohol **258** in 87% yield based on triethylamine borane. Evidently, the simple hydroboration mechanism is dominant, and the hydride-bridged borenium source **256** is an effective hydroborating agent. Related reagents hold promise for specialized applications in work that is ongoing.

8.3 Borenium equivalents in electrophilic aromatic borylation

8.3.1 Intramolecular borylation—Electrophilic borylation of benzene derivatives has long been known. Nearly all of the early reports relied on drastic Friedel Crafts conditions in the temperature range from 100–200 °C, including several intramolecular borylations that produced boron-containing heterocycles.[109] However, in the striking example of **259** in the presence of Al_2Cl_6, the borylation to give **260** occurred within 30 min at 0 °C (Eq. 31).[110] A similar experiment using the more soluble Al_2Br_6 was monitored by ^1H NMR spectroscopy at −90 °C, and produced an intermediate assigned as the borenium ion **261** based on the presence of a doublet for the *N*-methyl group and an ABX pattern for the benzylic CH_2-N protons. When this solution was allowed to warm to 0 °C, conversion to a product assigned as **262** occurred. The presumed *N*-protonation was attributed to protic acid contaminants in the non-purified aluminum halide reagents. The structures of **261** and **262** were not confirmed by ^{11}B NMR spectroscopy, leaving open the possibility that the observable low temperature intermediate may contain tetracoordinate boron. Nevertheless, the facile cyclization at 0 °C does suggest the involvement of an unusually reactive electrophile such as the presumed borenium ion **261** or a related borenium equivalent.

Some years later, an analogous cyclization approach was investigated in our laboratory using amine borane activation under conditions that had been developed to access borenium equivalents in simpler systems (Scheme 18).[47a] Thus, *N,N*-dimethylbenzylamine borane **263** was treated with 50 mol% of the trityl salt **71b** to generate the H-bridged dimer **264** in bromobenzene solution. No cyclization was observed at 20 °C (or after > 24h heating at 50 °C in benzene), but further addition of 40 mol% of **71b** (or the use of 90 mol% **71b** from the outset) resulted in the formation of cyclic products within four hours at 20 °C. These findings suggest that **264** requires further activation, but it is also possible that **71b** scavenges unknown nucleophilic species that inhibit the cyclization. The main cyclization product was the previously described labile borenium salt **72b**,[47b] but quenching with Bu_4NBH_4 afforded the stable amine borane **70** (72% overall). A catalytic procedure for the conversion from **263** to **70** was also demonstrated using 5 mol% **71b**. This required considerably higher temperatures (160 °C in toluene, sealed tube) to overcome the activation barrier and to maintain a catalytic cycle at a convenient rate, but the procedure was efficient and gave **70** in 90% isolated yield. The stoichiometric activation method at 20 °C has been extended to prepare several other cyclic amine boranes including **265–268**.[47b]

In the course of studies aimed at clarifying the mechanism of the nitrogen-directed borylation of Scheme 18, the *ortho*-deuterated benzylamine borane **269** was explored (Eq. 32).[47b] Two isotopomeric products **270** and **271** were formed, corresponding to a deuterium isotope effect $k_H/k_D = 2.8$ for the product-determining step. This KIE result argues against rate-determining cyclization from the borenium equivalents **264** or **272** to a Wheland intermediate **273** (Fig. 3) followed by rapid deprotonation. However, it would be consistent with slow (product-determining) proton removal from **273**, or with mechanisms where C–H cleavage occurs in the transition state leading to cyclic products. One such possibility is suggested in Fig 3 starting from the hydride-bridged dimer **264**. According to DFT calculations, the borenium π-complex **272** and the Wheland intermediate **273** have nearly identical energies and very similar geometries. The lowest barrier found from these intermediates to cyclized products involves the transition structure **274**, corresponding to a C–H insertion mechanism that leads directly to the observed **72b** and hydrogen.

The available experimental evidence does not prove whether **72b** is the initial cyclization product from **272**/**273**, or whether **72b** forms via **273** and deprotonation to give **70**, followed by the known hydride abstraction (Scheme 18).[47b] The need for >50 mol% of the trityl salt **71b** to promote cyclization from **264** at room temperature is also not clear. A number of rationales remain to be evaluated, the simplest of which assumes that **71b** converts **264** to the borenium ion **272** by abstracting hydride from **263** to drive the unfavorable dissociation equilibrium from **264**. Alternative explanations might invoke a bonding 3c2e interaction between **71b** with a B–H bond in **264** to provide additional electron demand. Although this would require the interaction of two cationic species (**71b** + **264**), it may facilitate the dissociation of **264** to **272**, or the conversion of **264** into a new (currently unidentified) intermediate that is capable of borylation.

Several carbon- or heteroatom-tethered phosphorus analogies (**277** to **278**) for the cyclization from **263** to **70** have also been investigated briefly using the activating procedure with $TrB(C_6F_5)_4$ (**71b**), 90 mol% in bromobenzene at room temperature (Eq. 33).[107] After reductive workup with Bu_4NBH_4, the cyclized products **278** were obtained in somewhat lower yield compared to the amine borane examples. In the case of **278c**, the 30 % yield also reflects partial hydrolysis during chromatography. The same cyclization was demonstrated using activation with 1.1 equiv of the strong acid $HN(SO_2CF_3)_2$ in place of **71b**, and gave 67% conversion from **277c** to **278c** after 24 h at 100 °C according to NMR assay.

Presumably, all of these cyclizations involve the generation of borenium equivalents, but the intermediates were not investigated in depth.

8.3.2 Intermolecular borylation—Some of the borenium equivalents discussed in earlier sections are of interest as electrophilic reagents for intermolecular borylation. One unusual example has already been discussed briefly in a different context, involving the thermal decomposition of borenium salt **72b** to give **75** at 80 °C (Scheme 3).[47b] Although the mechanism of this reaction is not known, one possibility involves electrophilic *ipso* attack by the borenium cation on the tetraarylborate counterion, followed by fragmentation. Similar decomposition of borenium tetrakis(pentafluorophenyl)-borate salts has been noted by Ingleson *et al.*[42] These are not typical intermolecular borylations because they involve bond formation between the two components of an ion pair, but the bonding events are mechanistically similar.

Recently, electrophilic borylation has been demonstrated using catechol borane-derived reagents. Relevant structures were already mentioned in Section 3 in the context of the hydride or halide abstraction methods for preparation of observable borenium cations (Scheme 3), and indirect evidence was discussed regarding the possible generation of a transient borinium cation **62** from **59** using $AgCbBr_6$ (eq. 12). In a similar experiment, Ingleson *et al.* treated **59** or **279** with the triethylsilyl cation source **280** as the halophile in benzene solution (Scheme 19), and observed rapid conversion to the *B*-phenyl catecholboronate **283** under stoichiometric conditions at room temperature.[42] The reactive (transient) electrophilic intermediate was represented by the formula **281** and abbreviated as $CatB^+$. Despite considerable effort, cationic boron species were not detected and the specific structure of **281** was not established definitively. However, the borinium salt **62** was shown as one possibility, and the authors favored an electrophilic borylation mechanism via **282** that fits most simply if **281** is either the same as, or acts as a source of, the borinium salt **62**. In short, **281** can be taken to represent a borinium equivalent. Borenium salts **284** were also considered as potential intermediates (L = nucleophilic halide from the Et_3SiCl byproduct, or oxygen from catechol-containing species) and were discussed in connection with an alternative mechanism involving C-H insertion that was not favored by the authors. A third possibility that **284** may be capable of participating in a typical stepwise electrophilic aromatic substitution process was implied by noting that a tetracoordinate borylation transition state $[CatB(arene)L]^+$ may be viable (L = a weak nucleophile).[42]

An interesting catalytic version of the borylation was also developed using CatBH (**65**) as the stoichiometric boron source (Scheme 19b), with the reagents CatBBr (**279**) + $Et_3SiCbBr_6$ (**280**) serving in the role of pre-catalyst (arene solution, 80–100 °C).[42] The catalytic cycle depends on regeneration of **281** from CatBH (**65**) and "H^+" during or after aromatization of the Wheland intermediate **282**. As the most potent known electrophile, "H^+" exists in solution as **285**, where ligand L = the best available electron pair donor. Therefore, the ligand is also involved in the proton removal step from **282**, and could be part of the product-determining transition state leading from **282** to **283** + **285**. The aromatic substrate is one of the possible choices for L, in which case **285** could be identical to the π-complex (not drawn) or to the corresponding Wheland intermediate **282**.

The catalytic process worked well with benzene as the substrate at 80 °C and gave **283** in high yield. The catalytic borylation was also demonstrated with toluene (15 h at 100 °C; 93% isolated yield of a 1.2:1 *meta:para* mixture of borylation products),[42,111] and with *o*-dichlorobenzene (10 h at 100 °C, exclusive borylation at C_4, 99%). In the case of ethylbenzene, the product mixtures were considerably more complex due to alkyl migration under the superacidic conditions, including intermolecular ethyl transfer among the reactants

and products, resulting in ca. 1.7 ethyls per product boronate. Multiple products were also obtained using *meta* or *para* xylenes.

More recent studies of intermolecular borylation have explored reagents that are better defined structurally, but questions remain regarding the key mechanistic aspects.[52,112] Thus, Ingleson *et al.* described borylating agents prepared by the method of halide abstraction from CatB-Cl (**59**) or Cl_4CatB-Cl (**286**) in combination with Et_3N and $AlCl_3$ (Scheme 20).[112] Formation of the triethylamine adducts **287** was followed by $AlCl_3$-induced heterolysis to give the borenium tetrachloroaluminates **288** and **289**. The Cl_4CatB reagent **289** was characterized in the solid state by X-ray crystallography, and the solution structures of **288** and **289** were supported by ^{11}B NMR spectroscopy (δ = 27.9 and 28.1 ppm, respectively). These values are in good accord with those of the closely related and previously characterized borenium salts **67**and **69a** (Scheme 3).[44,45] The new reagents were shown to react with electron-rich aromatic and heteroaromatic substrates Ar-H at room temperature to afford the corresponding borylation products **290** with high efficiency. However, the electron rich environment facilitated protodeboronation in a number of cases, so the initially formed catecholboronates were converted into the more stable pinacolboronates by trans-esterification with pinacol in the presence of triethylamine. The resulting **291** were obtained in good to excellent yield and with high regioselectivity, as shown for selected examples in Scheme 20 to illustrate the trends. In examples **291a** and **291b**, the regioselectivities were shown to complement the sterically controlled, *meta*-selective iridium-catalyzed borylations.[112,113] In general, the more electrophilic reagent **289** (Cl_4CatB environment) was considerably more reactive compared to **288**, as seen in the shorter reaction time leading to product **291c**. Attempts were also made to prepare **291** directly using the known borenium salt **69a** as well as the 2,6-lutidine analogue **292**, but these reagents were not sufficiently reactive to borylate the most reactive substrates dimethylaniline or *N*-methylpyrrole. The lower reactivity was attributed to better delocalization between boron and the oxygen *n*-electrons in **292** compared to the catechol analogues **288** or **289**. Ingleson *et al.* did not comment further on the mechanism of the highly effective borylations using borenium salts **288** and **289** beyond noting the analogies with potential borylating agents considered in Scheme 19.

On a similar timescale, the intermolecular borylation of electron-rich aromatic substrates was reported from our laboratory using reagents containing the 9-BBN core (structures **92**, **97**, and **99**) that were mentioned in Scheme 5, and are discussed in the borylation context in Scheme 21.[52] Both of the cationic reagents **97** and **99** were found to borylate *N*-methylindole to afford **293a** at convenient rates in dichloromethane at 50 °C (thick-walled Schlenk tube). Surprisingly, the reagent **99** having formally tetracoordinate boron proved to have comparable reactivity compared to the borenium salt **97**. Because **99** is also more convenient to handle as the crystalline solid, it was used to prepare several other borylated products **293b–d** as shown in Scheme 21 under similar conditions with reaction times on the order of hours. The neutral borane reagent **92** did not convert the aromatic substrates into products **293** using the same procedure at 50 °C. However, when **92** was used in combination with the hindered pyridine base **294**, the borylation of *N*-methylindole proceeded within seconds at room temperature. Even though **92** + **294** is the most reactive reagent in the 9-BBN-derived series, it is far more difficult to handle compared to **99**, and was therefore not evaluated for the borylation of other aromatic substrates.

The intermolecular borylation studies from our laboratory[52] and from the independent work of Ingleson *et al.*[112] were reported in adjacent papers, and described the borylations of very similar electron-rich substrates. Although the featured reagents in Schemes 20 and 21 were markedly different, there was one other similarity worth noting. Thus, both studies described isolable, well-characterized reagents having structures established by X-ray crystallography.

However, this additional information has not helped to narrow the mechanistic choices. For purposes of illustrating the mechanistic dilemmas, several (speculative) alternatives are considered briefly in the context of Scheme 21. The first dilemma is that all of the reagents **92**, **97**, and **99** are potential sources of one and the same borinium ion **295** by variants of B–N bond heterolysis. Therefore, each reagent is also a potential source of various borinium equivalents **296** (L = weak nucleophile) that may produce analogues of the borenium ion **97** by dissociation of a single ligand. Any one of these dicoordinate or tricoordinate boron cations, or the neutral borane **92**, may serve in the role of the key electrophile responsible for borylation. Even the isolable **99** may already qualify as a reactive borinium equivalent due to its unusually long B–N bonds.

A second complication is that the role of base (external base with **92**; internal base with **97b** or **99**) has not been defined. It is not known whether the base serves only to scavenge the $HNTf_2$ byproduct after borylation, thereby preventing the reverse reaction (reversible protodeboronation of **293**), or whether the presence of base results in a lower activation barrier for borylation. In the special case of **99**, a transient borenium intermediate **297** is especially appealing because it contains strongly electrophilic boron as well as an internal base that might participate in the transition state if proton transfer is rate-determining. The final dilemma is that each of the potential electrophiles may be capable of reacting via at least three mechanisms, (1) electrophilic aromatic substitution (EAS) with rate-determining formation of the Wheland intermediate, (2) EAS with rate-determining deprotonation, or (3) an intermolecular variant of the C-H insertion mechanism discussed in Section 8.3.1 (Fig. 3) for intermolecular borylation. Such mechanistic nuances are notoriously difficult to distinguish.

Another example of aromatic ring borylation is presented to underscore the subtle interplay of structure and mechanism in these reactions using an activated form of triethylamine borane. As mention in Section 8.2, activation of Et_3N3BH_3 with the trityl cation source **71b** (50 mol %) generated the hydride-bridged "dimer" **256** (Eq. 30), but further hydride abstraction did not occur using excess **71b**. Activation with a deficiency of Tf_2NH also gave the corresponding "dimer" **299** according to NMR evidence (Scheme 22). However, addition of a full equivalent of the strong acid afforded the amine borane complex **298** exclusively, judging from the ^{11}B NMR chemical shift (two maxima, $\delta = 0.6$ and -7.4 ppm in CD_2Cl_2, assigned to *O*-bound and *N*-bound covalent bistriflimidate).[50] This evidence is consistent with reversible formation of **298** and the starting $Et_3N{\cdot}BH_3$ from **299**, followed by protonation of the $Et_3N{\cdot}BH_3$ and eventual conversion to the borenium salt **298**. Alternatively, direct protonation of the hydride-bridged dimer **299** may be feasible as a way to force the conversion to **298**.

The activated reagent **298** was not explored in depth, but proved sufficiently reactive to borylate *N*-methylindole over hours at room temperature to give an initial product tentatively assigned as **301**, along with $HNEt_3^+\ Tf_2N^-$ (Scheme 22). Definitive evidence for **301** was not obtained, but treatment with disodium iminodiacetate in methanol gave the isolable complex **302** (72%). The initial conversion from **298** to **301** was attributed to electrophilic borylation, followed by internal (4-center) proton transfer via transition state **300**, a pathway that forms the ammonium salt $HNEt_3^+\ Tf_2N^-$ directly, without releasing the strongly acidic Tf_2NH. This pathway contrasts with the intramolecular borylation of Fig. 3, where the products consist of molecular hydrogen and a borenium cation (**72b**) resulting from an alternative 4-center process in the final step.

8.3.3 Recent developments in Muetterties borylation (BX_3 plus proton scavenger)—Mechanisms based on borenium intermediates may be involved in typical aromatic borylations using BCl_3/Al, a classical procedure that allows the preparation of

arylboron dichlorides from benzene or other simple arenes using readily available reagents.[114–117] The aluminum additive is important in two roles: (1) it scavenges the HCl byproduct of borylation, thereby preventing reversible protodeborylation of the product, and (2) it forms $AlCl_3$ *in situ* as a chlorophilic Lewis acid that accelerates the borylation. In the first mechanism proposed for this reaction, Muetterties suggested initial formation of "active species BCl_2^+ or $ArH{\cdot}BCl_2^+$ $AlCl_4^-$", and eventually described the latter structure as the arene **π**-complex according to UV evidence.[114] The simpler cation (BCl_2^+) is a dichloroborinium ion according to current terminology, while the cationic **π**-complex can be regarded either as a borinium equivalent, or as a borenium ion Cl_2B^- L^+ where the ligand L is the arene substrate. Also interesting is a subsequent paper by Muetterties where footnote 10 mentions that "solvation of BCl_2^+ is a necessity", a statement that might constitute the first, albeit indirect, suggestion of a borenium mechanism if the author intended to invoke $Cl_2B–L^+$ (L = solvent) as the electrophile for aromatic borylation.[116] Another relevant structure $Cl_2B–(Cl^+)–AlCl_3^-$ for the activated electrophilic intermediate has been considered by Olah.[118] This potential intermediate contains a borenium subunit within a neutral structure. The identity of the key electrophile in these borylations remains uncertain, even though a borenium connection is plausible. Cautious interpretation is warranted, given that Muetterties borylations were often performed at elevated temperatures and that even diborane is a sufficiently strong electrophile for the borylation of benzene at ca. 100 °C.[119]

A more explicit connection with borenium intermediates was suggested in a recent modification of the Muetterties approach for use in the intramolecular borylation of 2-arylpyridines (Scheme 23).[120] Thus, treatment of 2-phenylpyridine **303** with 3 equiv of BBr_3 and Et_2NiPr as HBr scavenger in dichloromethane gave the cyclic product **307** (89%) at room temperature. The proposed sequence involves formation of a complex **304** and subsequent halide abstraction by the excess BBr_3 to give a transient borenium salt **305**, followed by electrophilic borylation via a Wheland intermediate **306**. The same procedure was effective for the *N*-directed borylation of several substituted or annulated derivatives of **303**, and also for the corresponding conversion from the benzothiophenyl analogue **308** to **309** (87%). The borenium intermediates were not observed directly in this study.

A modified Muetterties procedure has also been developed for the intermolecular borylation of electron-rich aromatic substrates by Ingelson et al. (Scheme 24).[10b] The ingredients include BCl_3 and $AlCl_3$, the same species that are present under the original Muetterties conditions (BCl_3/Al), along with a basic amine additive such as 2,6-lutidine or 4-dimethylaminotoluene (Me_2NTol). Not only does the amine function as an acid scavenger, but it also serves as the key ligand L that forms the BCl_3 complex **310**, the immediate precursor of a borenium salt **311** *in situ*. Using 2,6-lutidine as the base, it was possible to isolate the corresponding salt **311a** as a crystalline solid that was fully characterized by X-ray and spectroscopic methods (^{11}B δ = 46.9 ppm). A closely related 4-picoline analogue **10** was mentioned in Section 2.4 as the first observable borenium salt to be characterized by ^{11}B NMR spectroscopy.[10a]

Upon reaction with electron rich heteroarenes Ar-H at 25 °C, **311a** afforded the corresponding borylation products Ar-BCl_2 (**312**) on a timescale of hours (Scheme 24). Further treatment with pinacol in the presence of excess amine base produced the corresponding pinacol boronate esters **313a–c** in high yield. On the other hand, **311a** was not sufficiently reactive for the preparation of **313d–f**. For these borylations, the reagent generated *in situ* from BCl_3/$AlCl_3$ and Me_2NTol proved superior, and was used to prepare **313d–f** under similar room temperature conditions. The overall sequence worked well on multigram scale. However, a borenium intermediate **311b** could not be isolated and characteristic ^{11}B signals for tricoordinate boron were not detected, apparantly due to a dynamic equilibrium process involving other Me_2NTol complexes. If **311b** is the reactive

borylating agent present in equilibrium, then its reactivity appears to be considerably improved relative to that of **311a**, but not sufficiently improved for the borylation of less activated substrates such as toluene. The authors did observe borylation of *m*-xylene at 140 °C using **311b**, but the product mixture reflected competing isomerization of the xylene substrate. Overall, the Ingelson procedure has considerable potential for the borylation of electron rich arenes. The authors noted that borenium intermediates **311a** or **311b** may be the electrophiles that attack an aromatic ring carbon to form a C–B bond, but did not rule out other possibilities.

9. Extension of borenium chemistry to neighboring fields and unusual environments

9.1 N-Heterocyclic carbenes as stabilizing ligands for borenium salts

The recent focus on nucleophilic carbenes as stabilizing ligands for reactive species in both main group element and transition metal chemistry has stimulated logical extensions to borenium ion chemistry. To our knowledge, the first example of an *N*-heterocyclic carbene (NHC) ligand in a borenium environment appears in a 1997 report by Weber *et al.*[121] Following a typical B-X bond heterolysis approach, 2-bromo-2,3-dihydro-1*H*-1,3,2-diazaborole **314** was reacted with the corresponding free carbenes **315a** or **315b** in benzene at RT to prepare the NHC-stabilized borenium salts **316** (Scheme 25). The cationic products were characterized by multinuclear NMR spectroscopy (**316a** δ ^{11}B = 15.3 ppm; **316b** δ ^{11}B = 15.0 ppm) and X-ray crystallography in the case of **316a**. The ^{11}B chemical shifts are observed at unusually high field for tricoordinate boron species, but the same can be said for the neutral bromoborane **314** (δ ^{11}B = 16.2 ppm). The unusual heteroaromatic environment appears to be primarily responsible for these boron chemical shift values. According to the ^{11}B criterion, the tricoordinate borenium cations **316** resist formation of tetracoordinate species by addition of the bromide anion to boron. This degree of borenium stabilization probably reflects a cumulative effect of heteroaromatic delocalization as well as the substantial steric hindrance near the boron atom.

A more typical NHC-derived borenium salt **50** was mentioned in Section 3.2, Scheme 2 (Gabbaï et al.) to illustrate methods of borenium salt generation. The tricoordinate boron structure of **50** was established by X-ray crystallography,[36] and was further supported by the ^{11}B NMR chemical shift (δ = 66 ppm). In a related case (Lindsay et al.), the 9-BBN-derived borenium salt **318** was prepared using two independent pathways, (1) B-H hydride abstraction from **317** by TfOH, and (2) nucleophilic addition; heterolysis from 9-BBN-OTf (**319**) and carbene **320**, and the structure **318** was established by X-ray crystallography and by δ ^{11}B = 81.4 ppm.[122] The chemical shifts of **50** and **318** are similar to values reported for analogous amine-ligated borenium salts such as **48** (δ ^{11}B = 66 ppm, Section 3.2, Scheme 2) or the 9-BBN-containing **93** and **97** (δ ^{11}B = 66.5 and 85.1 ppm, respectively, Section 3.5, Scheme 5), suggesting that replacement of the amine ligands in **48**, **93** or **97** by the NHC ligand does not cause major electronic changes at boron. Importantly, the degree of ion pairing for **318** in CD_2Cl_2 was studied by diffusion ordered NMR spectroscopy (DOSY), a method that confirms the ion pair character of **318** and provides a welcome complement to the ^{11}B chemical shift as evidence for the presence of tricoordinate boron in solution.

While exploring the applicability of NHCs to stabilization of a wide range of highly reactive main group molecules, Robinson *et al.* prepared borenium salt **322** by nucleophilic addition; heterolysis from reaction of $(i\text{-Pr})_2NBCl_2$ with the carbene **321** (Scheme 25).[123] The tricoordinate borenium chloride structure **322** was established by X-ray crystallography and by δ ^{11}B = 32.2 ppm in solution. Apparently, the chloride anion resists coordination at the boron center of **322** due to the extreme steric congestion as well as some degree of cation

stabilization by nitrogen lone pair delocalization involving the diisopropylamido substituent. Robinson et al. also reported an unusual reaction involving the reduction of **322** with KC_8. This afforded a C-H insertion product **323**, presumably formed via a divalent borylene intermediate.

Other classes of *N*-heterocyclic carbenes have begun to attract attention. So far, one example has been described in a non-aromatic heterocyclic environment as shown for the conversion from **324** to **325** (δ ^{11}B = 51.4 ppm) by halide abstraction.[124] The analogous pyridine derivative **326** (δ ^{11}B = 42 ppm) as well as a related catechol boronate ester (δ ^{11}B = 28 ppm) were also prepared, and X-ray data as well as computational evaluations suggested a stabilizing electrostatic interaction between tricoordinate boron and the π-system of the flanking aryl groups.

All of the NHC-containing borenium salts mentioned so far contain two substituents at boron in addition to the carbene ligand. In an attempt to generate an unsubstituted NHC-BH_2^+ salt, Alcarazo et al. treated the hindered NHC borane **327** with $B(C_6F_5)_3$ as the electrophile for hydride abstraction (Scheme 25).[125] However, the only product observed was the hydride-bridged dimer **328** according to X-ray and ^{11}B NMR evidence. The authors concluded that δ-donation from the NHC substituent was not sufficient to prevent a 3c2e interaction between the incipient borenium cation with a B–H bond in the starting **327**. On the other hand, when the carbodiphosphorane-derived borane **329** was reacted with $B(C_6F_5)_3$, the primary borenium salt **330** was indeed formed and could be isolated as the crystalline solid. The structure of **330** is firmly established by X-ray evidence, by the ^{11}B NMR signal at δ = 56.6 ppm (triplet, J_{BH} = 29 Hz), and by the formation of a tetracoordinate boronium salt upon treatment with *p*-dimethylaminopyridine. The improved stability of **330** was attributed to π- as well as σ-donation from the carbodiphosphorane ligand to boron, and to steric protection by the flanking triphenylphosphonium substituents. By the criterion of borenium stability, the carbodiphosphorane subunit ($Ph_3P{=}C{=}PPh_3$) in **330** is a better electron donor than the NHC subunit in **327** or **328**. Structure **330** is the only primary borenium salt known to date.

9.2 Miscellaneous related topics involving BH species

Borenium equivalents could be relevant to several areas beyond the mainstream organic chemistry context of this review. In addition to the definitive gas phase studies at the borinium-borenium interface mention in Section 3.3,[3,43] other areas have emerged where a role for borenium equivalents is not assured, but may deserve consideration. These topics will be mentioned briefly in this paragraph to provide leading references. For example, hydrodefluorination has received some attention, and has been demonstrated using cationic alane- or silane-derived reagents, generated by the familiar trityl salt activation method.[126] By analogy, hydrodefluorination might have some potential using activated cationic boranes. Indeed, one unusual example has already been encountered involving a borenium salt intermediate, although this was not by design (see partial dehydrofluorination of **71a**, Scheme 3).[47a] A more extensively studied area is the activation of B–H bonds in amine or phosphine boranes using transition metal reagents or catalysts as well as Lewis acids. Possible applications of this chemistry include C–H insertion methodology, dehydrocoupling and dehydropolymerization, and reversible hydrogen storage.[127,128] The key event in the latter examples is the conversion of a borane complex $RR'ZH{\cdot}BH_3$ (Z = N or P) to $(RR'ZBH_2)_n$ and hydrogen. If the first step in this process is B–H activation, then a transient borenium equivalent may be involved.

Unusual pathways leading to observable or transient borenium salts have been reported in specialized systems. Thus, Piers *et al.* have developed an interesting variation of the hydride

abstraction method where the substrate reacts with trityl cation at the allylic C–H bond of a B–C=C–CH segment to generate borenium salt **53** in the BODIPY series (Scheme 3).[38b] A more typical halide abstraction approach to the related cation **52** was described in Section 3.2.[38a] In a different application, Piers *et al.* have also reported an unusual variation of electrophilic activation by protonation of neutral borabenzene pyridine complexes. In this case, a transient borenium ion is generated by the protonation of the borabenzene ring.[129] Protonation at carbon has also been used to form borenium salts from dienamines.[41c]

In two other recent examples, there is some evidence suggesting the generation of borenium salts[130] or borenium equivalents[131] by pathways that may not fit into the typical categories considered earlier. In the former example, the substrate can be represented by the formula $i\mathrm{Pr}_2\mathrm{NB(F)N(Ar)SiMe}_3$ while the crystalline borenium byproduct isolated after treatment with AlCl_3 contains the cation $i\mathrm{Pr}_2\mathrm{NB(C}_4\mathrm{H}_9\mathrm{)NH(Ar)}^+$.[130] The source of the butyl group in this structure, established by X-ray crystallography, is not known. The second example (Scheme 26)[131] involves the conversion from **331** to the cyclic boronium salt **334** using excess diborane. The authors favored a pathway via **332** and **333**, and discounted a role for other hydride-bridged 3c2e intermediates because treatment of the model substrate **335** with diborane gave no evidence for generation of an observable borenium salt **336** nor related boronium species. However, the high electrophilicity of an NHC-derived primary borenium ion as indicated by the conversion of **327** into **328** (Scheme 25) suggests that the role of potential 3c2e borenium equivalents in the cyclization of **332** may need to be re-evaluated. Furthermore, the known reductive quenching of other borenium equivalents by borohydride (Scheme 3) provides some evidence that **336** or derived hydride-bridged 3c2e cationic structures having borohydride counterions would not be observable because the equilibrium would strongly favor **335**. Finally, an unusual triborane-derived borenium intermediate has been suggested to explain conversion from a B–Cl subunit to the corresponding B–OH using $\mathrm{AgB[C}_6\mathrm{F}_5\mathrm{]}_4$ in ether.[132] The authors reported the GC detection of ethylene as supporting evidence, presumably resulting from the elimination of a hypothetical transient $\mathrm{B–OEt}_2^+$ intermediate.

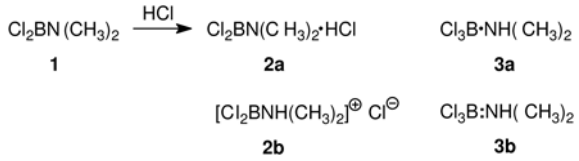
10. Summary

According to the discussion presented above, borenium ions are strongly electrophilic and Lewis acidic, and they resemble the isoelectronic carbenium ions in their reactions with nucleophiles. Even some of the weakest nucleophiles are sufficient to interact with non-stabilized cationic, tricoordinate boron species if the reaction conditions are carefully chosen to avoid solvent interference and the presence of potentially nucleophilic contaminants. Much of the borenium reactivity profile follows simple organic intuition based on the carbenium analogy, but some features stand in striking contrast and deserve a deeper analysis. For example, not a single example of a skeletal rearrangement involving borenium equivalents has been found in the literature, not even for potential sources of the non-stabilized, branched borenium cation **25** (Table 1) where the neopentyl analogy might imply that leaving group displacement would be very difficult. In fact, $\mathrm{S_N2}$ substitution of the corresponding primary iodide is quite easy (Section 2.4, eq. 8).[22,23] Partly, this is due to the relatively long B–N bond, a factor that decreases steric crowding for $\mathrm{S_N2}$ attack. Another important factor is the formally positive heteroatom adjacent to boron, the same factor that so strongly enhances electrophilicity at boron. Skeletal rearrangement by one of the adjacent N–C bonds in **25** would have to form sextet cationic nitrogen that is even higher in energy than the borenium salt due to the greater electronegativity of nitrogen vs. boron. With no realistic option for skeletal rearrangement, the borenium precursors and borenium equivalents can often be used at elevated temperatures with surprising ease, provided that other undesired intramolecular events such as nucleophilic attack or fragmentation have higher activation energies.

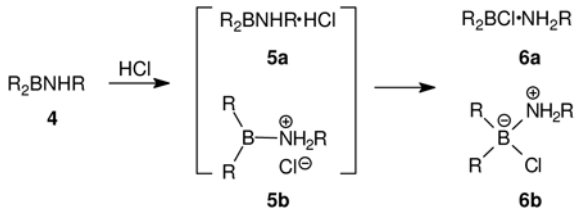
Another contrast with carbenium chemistry results from the highly interactive nature of activated amine, phosphine, or NHC boranes. Their tendency to form relatively stable hydride-bridged dimers such as **78** and **84** (Scheme 4), **256** (eq. 30), **264** (Scheme 18), **299** (Scheme 22), or **328** (Scheme 25) raises an interesting question: what would be the reactivity of a non-stabilized borenium cation that is incapable of hydride bridging? Similar questions arise in connection with heteroatom-substituted borenium species that may form stabilized heteroatom-bridged "dimers" or various solvent adducts; how reactive would they be if such covalent stabilization is prevented or minimized by careful choice of substituents? Possible answers to such questions are only now beginning to emerge (Schemes 20, 21).

Given the huge range of borenium electrophilicities (Table 1), and the almost unlimited potential for fine-tuning structure and reactivity, it is safe to predict that the exploration of synthetic uses of borenium equivalents has barely begun, despite the multi-decades long history of borenium chemistry presented in this review. Fascinating applications that exploit chiral borenium equivalents in stoichiometric or catalytic applications are already well-established. Further developments in enantioselective catalysis can be anticipated from the potential of borenium electrophiles to interact with a broad range of nucleophiles, even including C–H σ-bonds.

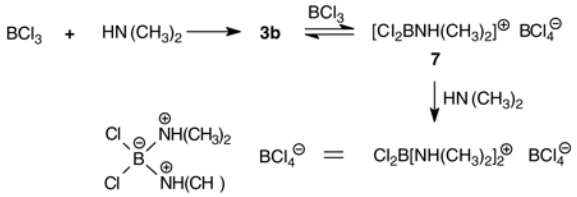
The first indications of C–H insertion chemistry have recently been communicated.[133] The example summarized in Scheme 27 proceeds at room temperature using stoichiometric trityl cation as the hydride abstracting agent, but the reaction can also be carried out catalytically with activation by 5% Tf_2NH at 160 °C. The key activation event from **336** + $Tr[B(C_6F_5)_4]$ to the H-bridged dimer **337** and the borylation step to give a cyclic, nonstabilized borenium salt **339** followed by reductive quenching to give the amine borane **340** resemble the nitrogen-directed aromatic borylations of Scheme 18, but they do raise questions. In particular, the role of the "extra 40%" of $Tr[B(C_6F_5)_4]$ remains unclear. Is the black box intermediate simply the primary borenium salt **338**? If so, does the extra activation step require hydride transfer from a cation (**337**) to another cation (Tr^+) to effect the conversion to **338**? These are typical of the many mechanistic questions that remain to be answered as we begin the ninth decade of research in borenium salt chemistry.



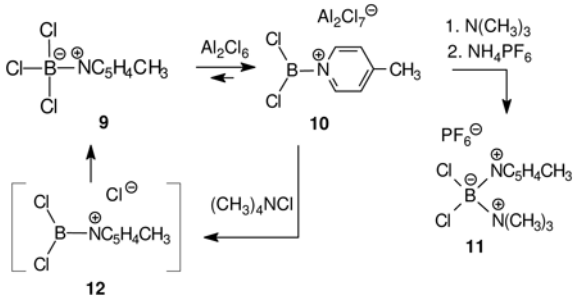
(1)



(2)

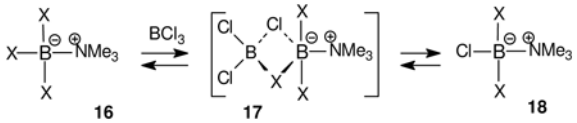


(3)

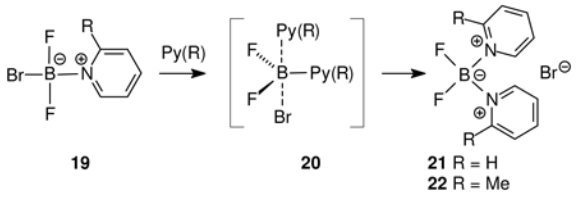


(4)

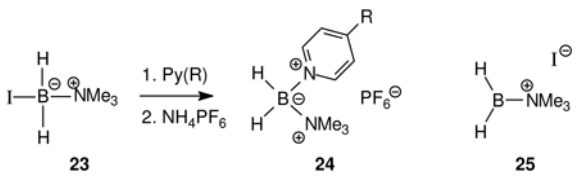
(5)



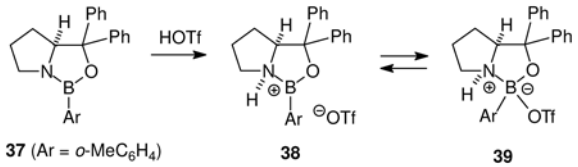
(6)



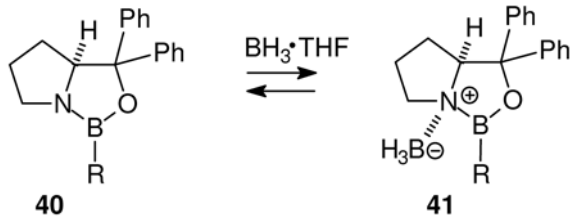
(7)



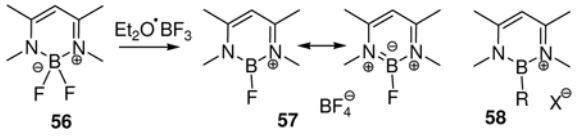
(8)



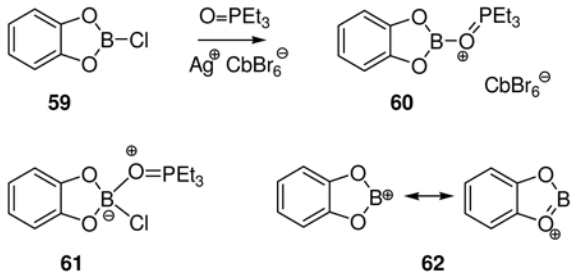
(9)



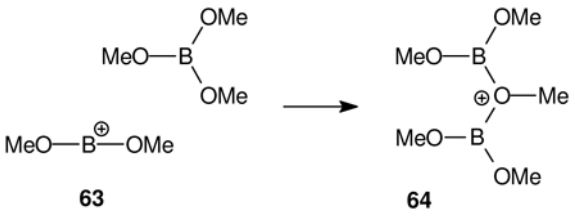
(10)



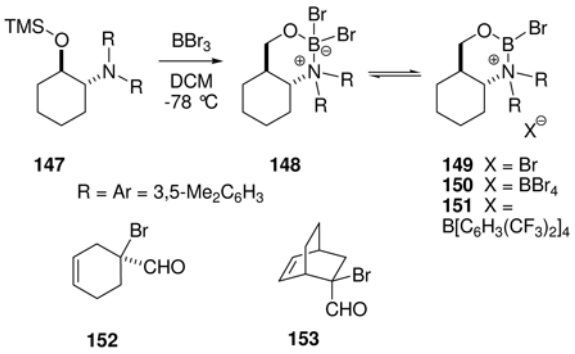
(11)



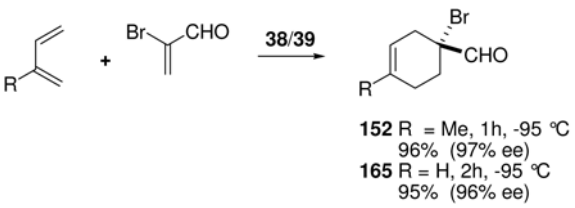
(12)



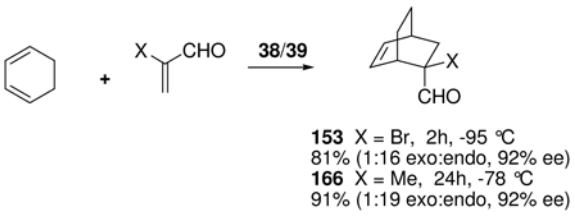
(13)



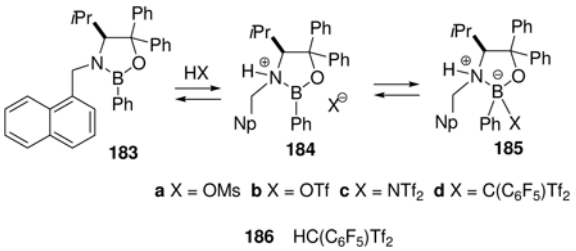
(14)



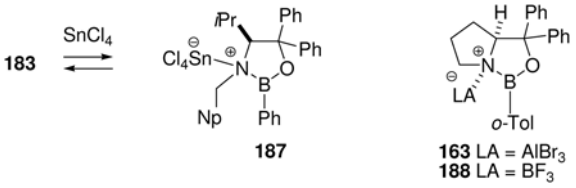
(15)



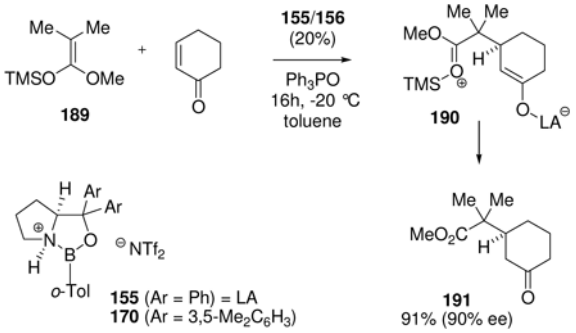
(16)



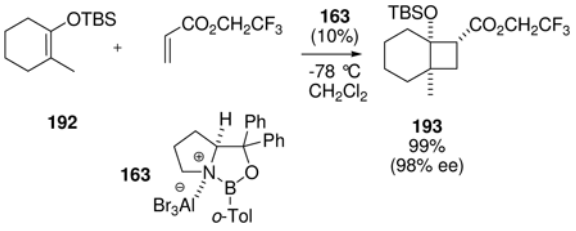
(17)



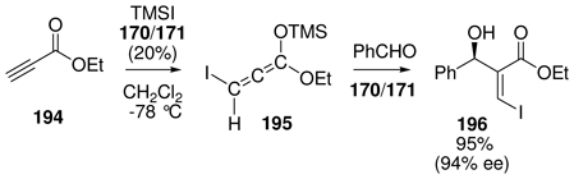
(18)



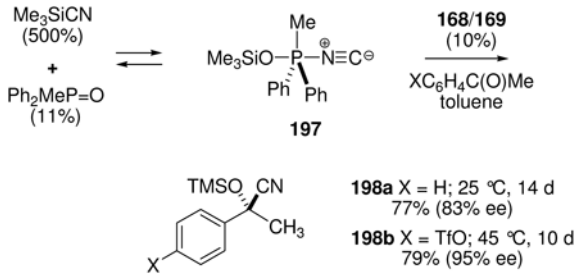
(19)



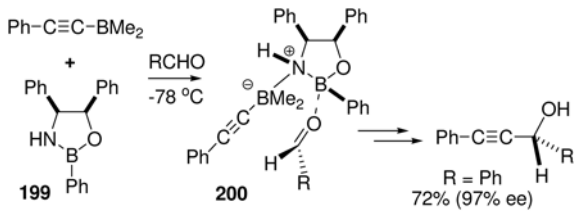
(20)



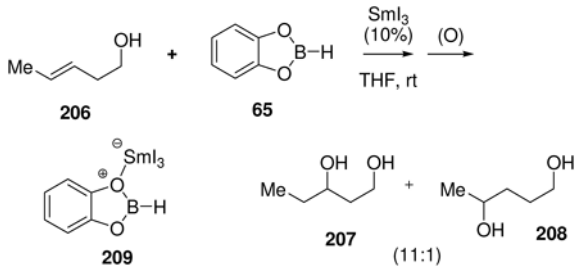
(21)



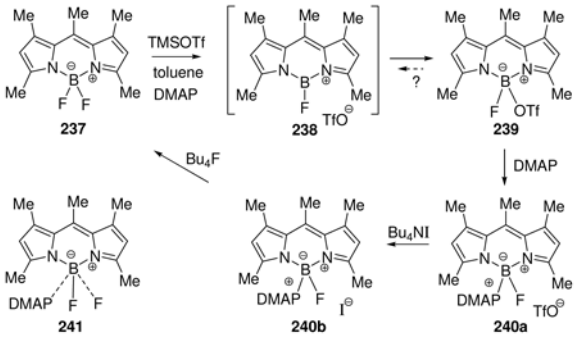
(22)



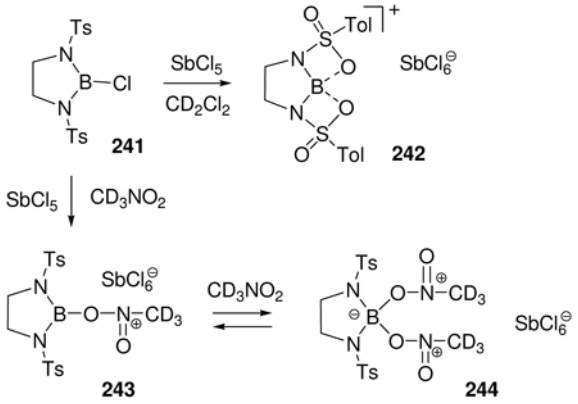
(23)



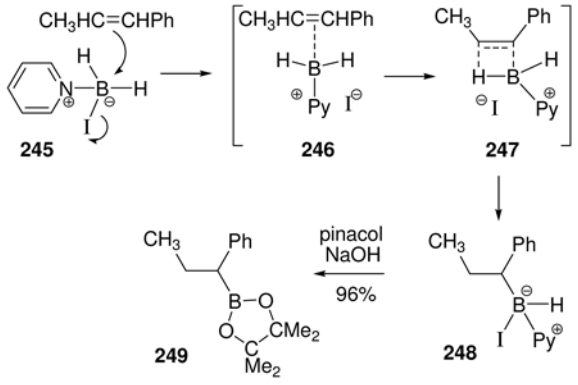
(24)



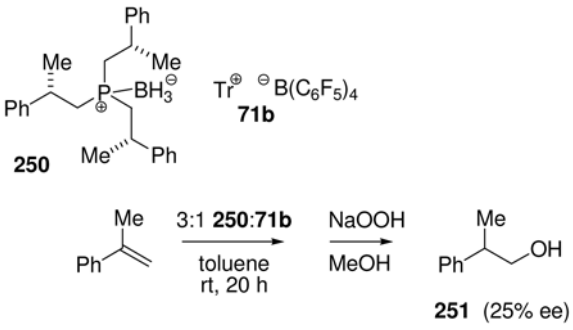
(25)



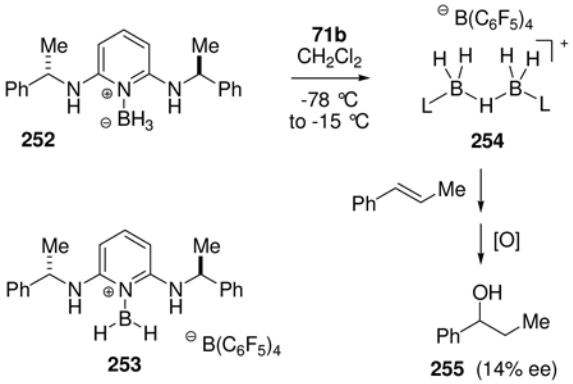
(26)



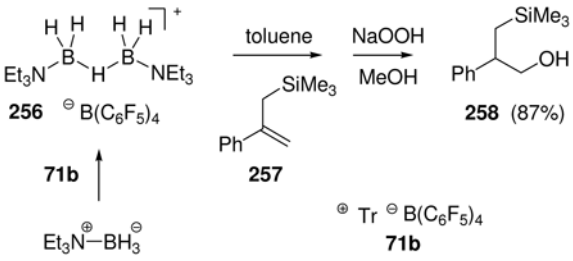
(27)



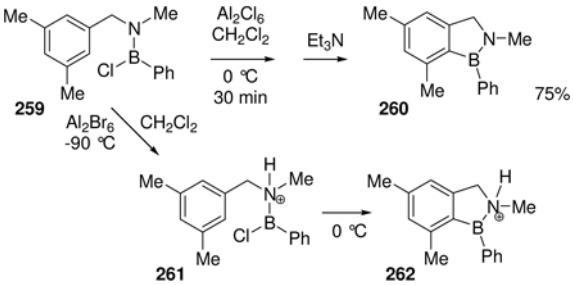
(28)



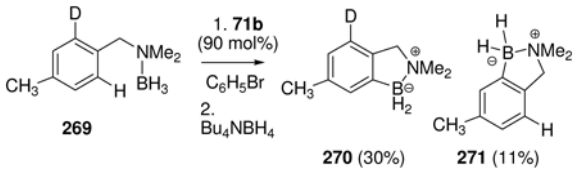
(29)



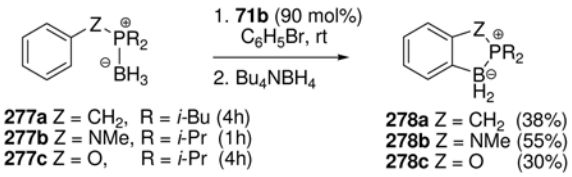
(30)



(31)



(32)



(33)

Acknowledgments

The authors are grateful to Prof. J. Harvey and Prof. F. Weinhold for stimulating conversations and many useful suggestions regarding boron electrophiles and related matters of a fundamental nature. Special thanks are also due to Drs. S. F. Fields, M. R. Schrimpf, R. W. Chapman, S. R. Hitchcock, S. Lin, M. Scheideman, G. Wang, R-A. Rarig, and C. Cazorla as well as to my co-authors, whose combined experimental efforts kept this chemistry alive over many years. Financial support for the senior author's current investigation of organoboron chemistry was generously supported by the taxpayers via the Institute of General Medical Sciences, NIH (GM067146)

References

1. Shitov OP, Ioffe SL, Tartakovskii VA, Novikov SS. Russ Chem Rev. 1970; 39:905.
2. Kölle P, Nöth H. Chem Rev. 1985; 85:399.
3. Piers WE, Bourke SC, Conroy KD. Angew Chem Int Ed. 2005; 44:5016.
4. (a) Wiberg E, Schuster K. Z Anorg Allg Chem. 1933; 213:77.(b) Wiberg E, Schuster K. Z Anorg Allg Chem. 1933; 213:89.
5. Wiberg E, Hertwig K. Z Anorg Chem. 1947; 255:141.
6. Brown CA, Osthoff RC. J Am Chem Soc. 1952; 74:2340.
7. Goubeau J, Rahtz M, Becher HJ. Z Anorg Allg Chem. 1954; 275:161.
8. Gerrard W, Hudson HR, Mooney EF. J Chem Soc. 1960:5168.
9. Ryschkewitsch GE, Myers WH. Synth React Inorg Metalorg Chem. 1975; 5:123.
10. Ryschkewitsch GE, Wiggins JW. J Am Chem Soc. 1970; 92:1790.Although **10** was not isolated, the closely related 2,6-lutidine derivative was recently prepared and was fully characterized, including the nearly identical ^{11}B chemical shift (δ = 46.9 ppm) and an X-ray structure determination as the tetrachloroaluminate salt: Del Grosso A, Helm MD, Solomon SA, Caras-Quintero D, Ingleson MJ. Chem Commun. 2011; 47:12459.
11. Nöth H, Schweizer P, Ziegelgänsberger F. Chem Ber. 1966; 99:1089.
12. Heaton GS, Riley PNK. J Chem Soc A. 1966:952.
13. Lowe JR, Uppal SS, Weidig C, Kelly HC. Inorg Chem. 1970; 9:1423.
14. Krishnamurthy SS, Lappert MF. Inorg Nucl Chem Lett. 1971; 7:919.
15. Benton BW, Miller JM. Can J Chem. 1974; 52:2866.
16. Farquharson MJ, Hartman JS. Can J Chem. 1989; 67:1711.
17. Farquharson MJ, Hartman JS. Can J Chem. 1996; 74:1309.
18. Hartman JS, Yuan Z, Fox A, Nguyen A. Can J Chem. 1996; 74:2131.

19. Hartman JS, Ilnicki EI, Shoemaker JAW, Szerminski WR, Yuan Z. Can J Chem. 1998; 76:1317.
20. Shoemaker JAW, Hartman JS. Can J Chem. 1999; 77:1856.
21. Hartman JS, Shoemaker JAW. Can J Chem. 2001; 79:426.
22. Nainan KC, Ryschkewitsch GE. J Am Chem Soc. 1969; 91:330.
23. Mathur MA, Ryschkewitsch GE. Inorg Chem. 1980; 19:887.
24. Bratt PJ, Brown MP, Seddon KR. J Chem Soc, Dalton Trans. 1974:2161.
25. Bratt PJ, Brown MP, Seddon KR. J Chem Soc, Dalton Trans. 1976:353.
26. Denniston ML, Chuisano M, Brown J, Martin DR. J Inorg Nucl Chem. 1976; 38:379.
27. Ref. 25 describes a puzzling solvolysis from **23** to a product said to be $BH_2(NH_3)_2I$ (fits elemental analysis; no NMR data) after reaction in liquid ammonia (44 h), followed by evaporation and heating to 120 °C under vacuum to remove unreacted **23**. Conversion from **23** is said to be accelerated by addition of NaBr due to a special salt effect, and the authors use this evidence to argue that a species drawn as $[Me_3N{\cdot}BH_2]I$ is an intermediate. Presumably, an ion pair corresponding to **25** was intended. No follow-up work has appeared to confirm this suggestion as far as we are aware, and the earlier studies described in references 23,24 were not cited.
28. Nöth H, Fritz P. Z Anorg Allg Chem. 1963; 322:297.
29. Narula CK, Nöth H. Inorg Chem. 1984; 23:4147.
30. Both the Nöth and the Piers reviews classify several methods for boron cation formation, and Piers lists Methods 1–6 in the same order as Nöth's text headings IIA–IIF. However, Nöth's text headings A–D are not the same as Methods A–D defined below his Table I. Our discussion presents methods specific to borenium ions according to mechanistic categories and makes comparisons with the Nöth/Piers text headings in the simpler cases.
31. Corey EJ, Shibata T, Lee TW. J Am Chem Soc. 2002; 124:3808. [PubMed: 11942799]
32. For a review, see: Corey EJ, Helal CJ. Angew Chem Int Ed. 1998; 37:1986.
33. Uddin MK, Nagano Y, Fujiyama R, Kiyooka S, Fujio M, Tsuno Y. Tetrahedron Lett. 2005; 46:627.
34. Kiyooka S, Fujiyama R, Kawai T, Fujimoto H, Goh K. Tetrahedron Lett. 2001; 42:4151.
35. Chiu CW, Gabbaï FP. Organometallics. 2008; 27:1657.
36. Matsumoto T, Gabbaï FP. Organometallics. 2009; 28:4252.
37. Wood TK, Piers WE, Keay BA, Parvez M. Chem Commun. 2009:5147.
38. (a) Bonnier C, Piers WE, Parvez M, Sorensen TS. Chem Commun. 2008:4593.(b) Bonnier C, Piers WE, Parvez M. Organometallics. 2011; 30:1067.
39. Kato T, Tham FS, Boyd PDW, Reed CA. Heteroatom Chem. 2006; 17:209.Similar subporphyrin borenium salts have also been prepared by abstraction of a methoxy group in place of chloride: Tsurumaki E, Hayashi S, Tham FS, Reed CA, Osuka A. J Am Chem Soc. 2011; 133:11956. [PubMed: 21766779] For a review on the chemistry of subphthalocyanines, see: Claessens CG, González-Rodríguez D, Torres T. Chem Rev. 2002; 102:835. [PubMed: 11890759]
40. Kuhn N, Kuhn A, Lewandowski J, Speis M. Chem Ber. 1991; 124:2197.
41. Qian B, Baek SW, Smith MR III. Polyhedron. 1999; 18:2405.Cowley AH, Lu Z, Jones JN, Moore JA. J Organomet Chem. 2004; 689:2562.Similar heteroaromatic borenium cations have been prepared by the protonation of a conjugated cyclic dienamine with TfOH: Someya CI, Inoue S, Präsang C, Irran E, Driess M. Chem Commun. 2011; 47:6599.Heteroaromatic borenium salts can be generated by the reaction of 1-ethyl-2-trifluorosulfonyloxy-1,2-azaborine with nucleophiles following an addition-heterolysis sequence (see Scheme 5 for mechanistic analogies): Marwitz AJV, Jenkins JT, Zakharov LN, Liu S-Y. Angew Chem Int Ed. 2010; 49:7444.Marwitz AJV, Jenkins JT, Zakharov LN, Liu S-Y. Organometallics. 2011; 30:52. [PubMed: 21278846]
42. Del Grosso A, Pritchard RG, Muryn CA, Ingleson MJ. Organometallics. 2010; 29:241.
43. Hettich RL, Cole T, Freiser BS. Int J Mass Spectrom. 1987; 81:203.For other gas phase studies of the borinium/borenium interface, see: Forte L, Lien MH, Hopkinson AC, Bohme DK. Can J Chem. 1989; 67:1576.Ranatunga TD, Kenttämaa HI. J Am Chem Soc. 1992; 114:8600.DePuy CH, Gareyev R, Hankin J, Davico GE, Damrauer R. J Am Chem Soc. 1997; 119:427.DePuy CH, Gareyev R, Hankin J, Davico GE, Krempp M, Damrauer R. J Am Chem Soc. 1998; 120:5086.
44. Dureen MA, Lough A, Gilbert TM, Stephan DW. Chem Commun. 2008:4303.

45. Lata CJ, Crudden CM. J Am Chem Soc. 2010; 132:131. [PubMed: 19968306]
46. Benjamin LE, Carvalho DA, Stafiej SF, Takacs EA. Inorg Chem. 1970; 9:1844.
47. (a) Vedejs E, Nguyen T, Powell DR, Schrimpf MR. Chem Commun. 1996:2721.(b) De Vries TS, Prokofjevs A, Harvey JN, Vedejs E. J Am Chem Soc. 2009; 131:14679. [PubMed: 19824728]
48. De Vries TS, Vedejs E. Organometallics. 2007; 26:3079. [PubMed: 18806887]
49. Stephens FH, Baker RT, Matus MH, Grant DJ, Dixon DA. Angew Chem Int Ed. 2007; 46:746.Hydride bridged cationic phosphine boranes were considered as potential reaction intermediates, but spectroscopic data were not reported: Kameda M, Kodama G. Inorg Chem. 1997; 36:4369. [PubMed: 11670094]
50. Prokofjevs, A. Ph D Dissertation. University of Michigan; 2012.
51. Narula CK, Nöth H. Inorg Chem. 1985; 24:2532.(b) The minor ^{11}B chemical shift (δ = 59 ppm) is consistent with contamination by $(9\text{-BBN})_2O$.
52. Prokofjevs A, Kampf JW, Vedejs E. Angew Chem Int Ed. 2011; 50:2098.
53. Schneider WF, Narula CK, Nöth H, Bursten BE. Inorg Chem. 1991; 30:3919.
54. Zhao Y, Truhlar DG. Theor Chem Acc. 2008; 120:215.
55. (a) Plumley JA, Evanseck JD. J Chem Theory Comput. 2008; 4:1249.Plumley JA, Evanseck JD. J Phys Chem A. 2009; 113:5985. [PubMed: 19388700] Janesko BG. J Chem Theory Comput. 2010; 6:1825.(b) Brown HC, Bartholomay H, Taylor MD. J Am Chem Soc. 1944; 66:435.
56. Ryschkewitsch GE, Garrett JM. J Am Chem Soc. 1968; 90:7234.
57. Toyota S, Ito F, Nitta N, Hakamata T. Bull Chem Soc Jpn. 2004; 77:2081.
58. (a) Vedejs E, Fields SC, Hayashi R, Hitchcock SR, Powell DR, Schrimpf MR. J Am Chem Soc. 1999; 121:2460.(b) Vedejs E, Fields SC, Lin S, Schrimpf MR. J Org Chem. 1995; 60:3028.
59. Chapman, RW. Ph D Dissertation. University of Wisconsin; 1994.
60. Vedejs E, Chapman RW, Lin S, Müller M, Powell DR. J Am Chem Soc. 2000; 122:3047.
61. Kaiser PF, White JM, Hutton CA. J Am Chem Soc. 2008; 130:16450. [PubMed: 19049441]
62. Braun M, Schlecht S, Engelmann M, Frank W, Grimme S. Eur J Org Chem. 2008; 2008:5221.
63. Heard PJ. Chem Soc Rev. 2007; 36:551. [PubMed: 17325791]
64. (a) Itsuno S, Ito K, Hirao A, Nakahama S. Chem Commun. 1983:469.(b) Itsuno S, Sakurai Y, Ito K, Hirao A, Nakahama S. Bull Chem Soc Jpn. 1987; 60:395.
65. (a) Corey EJ, Bakshi RK, Shibata S. J Am Chem Soc. 1987; 109:5551.(b) Corey EJ, Bakshi RK, Shibata S, Chen C-P, Singh VK. J Am Chem Soc. 1987; 109:7925.
66. Oxazaborolidines have also been demonstrated to catalyze the enantioselective reduction of oximes in ref 64b and in the following related reports: Sakito Y, Yoneyoshi Y, Suzukamo G. Tetrahedron Lett. 1988; 29:223.Itsuno S, Sakurai Y, Shimizu K, Ito K. J Chem Soc, Perkin Trans. 1990; 1:1859.
67. Corey EJ, Cimprich KA. J Am Chem Soc. 1994; 116:3151.
68. For chiral borane catalysts, see Corey EJ. Angew Chem, Int Ed. 2002; 41:1650.For chiral borenium catalysts, see Corey EJ. Angew Chem, Int Ed. 2009; 48:2100.
69. Hayashi Y, Rohde JJ, Corey EJ. J Am Chem Soc. 1996; 118:5502.
70. (a) Beall H, Bushweller CH, Dewkett WJ, Grace M. J Am Chem Soc. 1970; 92:3484.(b) Bacon J, Gillespie RJ, Hartman JS, Rao URK. Mol Phys. 1970; 18:561.
71. Moniz WB, Gutowsky HS. J Chem Phys. 1963; 38:1155.
72. Ryu DH, Corey EJ. J Am Chem Soc. 2003; 125:6388. [PubMed: 12785777]
73. Ryu DH, Lee TW, Corey EJ. J Am Chem Soc. 2002; 124:9992. [PubMed: 12188655]
74. Canales E, Corey EJ. Org Lett. 2008; 10:3271. [PubMed: 18582066]
75. Liu D, Canales E, Corey EJ. J Am Chem Soc. 2007; 129:1498. [PubMed: 17283985]
76. [accessed 2/15/11] Oxazaborolidine **37** is available from the Aldrich Chemical company: http://www.sigmaaldrich.com/catalog/ProductDetail.do?lang=en&N4=654302|ALDRICH&N5=SEARCH_CONCAT_PNO
77. Hu QY, Rege PD, Corey EJ. J Am Chem Soc. 2004; 126:5984. [PubMed: 15137761]
78. Payette JN, Yamamoto H. J Am Chem Soc. 2007; 129:9536. [PubMed: 17630749]

79. For comparisons of $HC(C_6F_5)Tf_2$, TfOH, and Tf_2NH, see Hasegawa A, Ishihara K, Yamamoto H. Angew Chem, Int Ed. 2003; 42:5731.

80. Payette JN, Yamamoto H. Angew Chem, Int Ed. 2009; 48:8060.

81. Futatsugi K, Yamamoto H. Angew Chem, Int Ed. 2005; 44:1484.

82. Liu D, Hong S, Corey EJ. J Am Chem Soc. 2006; 128:8160. [PubMed: 16787080]

83. Canales E, Corey EJ. J Am Chem Soc. 2007; 129:12686. [PubMed: 17900126]

84. Senapati BK, Hwang GS, Lee S, Ryu DH. Angew Chem, Int Ed. 2009; 48:4398.

85. (a) Ryu DH, Corey EJ. J Am Chem Soc. 2004; 126:8106. [PubMed: 15225038] (b) Ryu DH, Corey EJ. J Am Chem Soc. 2005; 127:5384. [PubMed: 15826176] (c) Corey EJ, Cimprich KA. J Am Chem Soc. 1994; 116:3151.

86. Wei P, Atwood DA. Inorg Chem. 1998; 37:4934. [PubMed: 11670659]

87. Evans DA, Muci AR, Stuermer R. J Org Chem. 1993; 58:5307.

88. (a) Kennedy JWJ, Hall DG. J Am Chem Soc. 2002; 124:11586. [PubMed: 12296710] (b) Rauniyar V, Hall DG. J Am Chem Soc. 2004; 126:4518. [PubMed: 15070360]

89. Ishiyama T, Ahiko T, Miyaura N. J Am Chem Soc. 2002; 124:12414. [PubMed: 12381174] For a computational evaluation of $AlCl_3$ activation supporting coordination to a B–O substituent see Sakata K, Fujimoto H. J Am Chem Soc. 2008; 130:12519. [PubMed: 18712868]

90. Chen M, Roush WR. Org Lett. 2010; 12:2706. [PubMed: 20476769]

91. (a) Yu SH, Ferguson MJ, McDonald R, Hall DG. J Am Chem Soc. 2005; 127:12808. [PubMed: 16159268] (b) Elford TG, Arimura Y, Yu SH, Hall DG. J Org Chem. 2007; 72:1276. [PubMed: 17288375]

92. Rauniyar V, Hall DG. J Org Chem. 2009; 74:4236. and references therein. [PubMed: 19422213]

93. Ishihara K, Ohara S, Yamamoto H. J Org Chem. 1996; 61:4196. [PubMed: 11667313] Latta R, Springsteen G, Wang B. Synthesis. 2001:1611.Maki T, Ishihara K, Yamamoto H. Org Lett. 2005; 7:5047–5050. [PubMed: 16235954] For the related esterification of α-hydroxycarboxylic acids see Maki T, Ishihara K, Yamamoto H. Org Lett. 2005; 7:5043. [PubMed: 16235953]

94. Agou T, Kobayashi J, Kawashima T. Inorg Chem. 2006; 45:9137. [PubMed: 17054375]

95. Welch GC, Cabrera L, Chase PA, Hollink E, Masuda JD, Wei P, Stephan DW. Dalton Trans. 2007:3407. [PubMed: 17664977]

96. Hudnall TW, Chiu C-W, Gabbaï FP. Acc Chem Res. 2009; 42:388. [PubMed: 19140747]

97. (a) Lee MH, Agou T, Kobayashi J, Kawashima T, Gabbaï FP. Chem Commun. 2007:1133.(b) Hudnall TW, Kim Y-M, Bebbington MWP, Bourissou D, Gabbaï FP. J Am Chem Soc. 2008; 130:10890. [PubMed: 18652460] (c) Kim Y, Gabbaï FP. J Am Chem Soc. 2009; 131:3363. [PubMed: 19256571]

98. Hudnall TW, Gabbaï FP. J Am Chem Soc. 2007; 129:11978. [PubMed: 17845043]

99. (a) Kim Y, Zhao H, Gabbaï FP. Angew Chem, Int Ed. 2009; 48:4957.(b) Hudnall TW, Gabbaï FP. Chem Commun. 2008:4596.

100. (a) Chiu C-W, Gabbaï FP. Dalton Trans. 2008:814. [PubMed: 18239838] (b) Xu Z, Kim SK, Han SJ, Lee C, Kociok-Kohn G, James TD, Yoon J. Eur J Org Chem. 2009:3058.

101. Review: Wade CR, Broomsgrove AEJ, Aldridge S, Gabbaï F. Chem Rev. 2010; 110:3958. [PubMed: 20540560] Chiu C-W, Kim Y, Gabbaï FP. J Am Chem Soc. 2009; 131:60. [PubMed: 19093849]

102. Fe cations: Dusemund C, Samankumara Sandanayake KRA, Shinkai S. J Chem Soc, Chem Commun. 1995:333.Venkatasubbaiah K, Nowik I, Herber RH, Jäkle F. Chem Commun. 2007:2154.Day JK, Bresner C, Coombs ND, Fallis IA, Ooi L-L, Aldridge S. Inorg Chem. 2008; 47:793. [PubMed: 17929916] Ir cations: Zhao Q, Li F, Liu S, Yu M, Liu Z, Yi T, Huang C. Inorg Chem. 2008; 47:9256. [PubMed: 18811148] Broomsgrove AEJ, Addy DA, Di Paolo A, Morgan IR, Bresner C, Chislett V, Fallis IA, Thompson AL, Vidovic D, Aldridge S. Inorg Chem. 2010; 49:157. [PubMed: 19957927] Pyridinium cations: Wade CR, Gabbaï FP. Dalton Trans. 2009:9169. [PubMed: 20449193] Ru cations: Wade CR, Gabbaï FP. Inorg Chem. 2010; 49:714. [PubMed: 20000628]

103. Reviews: Vidovic D, Pierce GA, Aldridge S. Chem Commun. 2009:1157.Braunschweig H, Dewhurst RD, Schneider A. Chem Rev. 2010; 110:3924. [PubMed: 20235583] Braunschweig H,

Chiu C-W, Radacki K, Brenner P. Chem Commun. 2010:916.Addy DA, Pierce GA, Vidovic D, Mallick D, Jemmis ED, Goicoechea JM, Aldridge S. J Am Chem Soc. 2010; 132:4586. [PubMed: 20232864] Saleh LMA, Birjkumar KH, Protchenko AV, Scwartz AD, Aldridge S, Jones C, Kaltsoyannis N, Mountford P. J Am Chem Soc. 2011; 133:3836. [PubMed: 21344905]

104. Kiyooka S, Fujiyama R, Uddin MK, Goh K, Nagano Y, Fujio M, Tsuno Y. Tetrahedron Lett. 2005; 46:209.
105. Karatjas AG, Vedejs E. J Org Chem. 2008; 73:9508. [PubMed: 19007135]
106. Scheideman M, Wang G, Vedejs E. J Am Chem Soc. 2008; 130:8669. [PubMed: 18549217]
107. De Vries, TS. Ph D Dissertation. University of Michigan; 2007.
108. Clay, JM. Ph D Dissertation. University of Michigan; 2007.
109. See ref. 52, footnote 39.
110. Genaev AM, Nagy SM, Salnikov GE, Shubin VG. Chem Commun. 2000:1587.
111. The originally reported toluene *ortho*-borylation product has been reassigned as the *meta*-regioisomer (personal communication from Prof. M. J. Ingleson).
112. Del Grosso A, Singleton PJ, Muryn CA, Ingleson MJ. Angew Chem, Int Ed. 2011; 50:2102.
113. Cho J-Y, Iverson CN, Smith MR III. J Am Chem Soc. 2000; 122:12868.Paul S, Chotana GA, Holmes D, Reichle RC, Maleczka RE Jr, Smith MR III. J Am Chem Soc. 2006; 128:15552. [PubMed: 17147340] Murphy JM, Tzschucke CC, Hartwig JF. Orglett. 2007; 9:757.Review: Mkhalid IAI, Barnard JH, Marder TB, Murphy JM, Hartwig JF. Chem Rev. 2010; 110:890. [PubMed: 20028025]
114. Muetterties EL. J Am Chem Soc. 1959; 81:2597.
115. Bujwid ZJ, Gerrard W, Lappert MF. Chem & Ind. 1959:1091.
116. Muetterties EL. J Am Chem Soc. 1960; 82:4163.
117. Muetterties EL, Tebbe FN. Inorg Chem. 1968; 7:2663.
118. Olah GA. Angew Chem, Int Ed. 1993; 32:767.
119. Hurd DT. J Am Chem Soc. 1948; 70:2053.
120. Ishida N, Moriya T, Goya T, Murakami M. J Org Chem. 2010; 75:8709. [PubMed: 21090764]
121. Weber L, Dobbert E, Stammler H-G, Neumann B, Boese R, Bläser D. Chem Ber. 1997; 130:705.
122. McArthur D, Butts CP, Lindsay DM. Chem Commun. 2011; 47:6650.
123. Wang Y, Robinson GH. Inorg Chem. 2011; 50:12326. [PubMed: 21634365]
124. Mansaray HB, Rowe ADL, Phillips N, Niemeyer J, Kelly M, Addy DA, Bates JI, Aldridge S. Chem Commun. 2011; 47:12295.
125. Inés B, Patil M, Carreras J, Goddard R, Thiel W, Alcarazo M. Angew Chem Int Ed. 2011; 50:8400.
126. Meier G, Braun T. Angew Chem, Int Ed. 2009; 48:1546.
127. Piers WE. Angew Chem, Int Ed. 2000; 39:1923.
128. Short review: Staubitz A, Robertson APM, Sloan ME, Manners I. Chem Rev. 2010; 110:4023. [PubMed: 20672859]
129. Ghesner I, Piers WE, Parvez M, McDonald R. Chem Commun. 2005:2480.
130. Ott H, Matthes C, Ringe A, Magull J, Stalke D, Klingbeil U. Chem Eur J. 2009; 15:4602. [PubMed: 19308982]
131. Tsai J-H, Lin S-T, Yang RB-G, Yap GPA, Ong T-G. Organometallics. 2010; 29:4004.
132. Hayashi Y, Segawa Y, Yamashita M, Nozaki K. Chem Commun. 2011; 47:5888.
133. Prokofjevs A, Kampf JW, Vedejs E. J Am Chem Soc. 2011; 133:20056. [PubMed: 22082151]

Biographies

Timothy De Vries was born in Highland, IN. He received his B.S. degree in Chemistry at Calvin College in Grand Rapids, MI, conducting research under Professor Ronald Blankespoor. He then moved to the University of Michigan, where he studied Lewis base complexes of borane as hydride sources, and C–B bond forming reactions of cationic, electrophilic boron intermediates under the direction of Professor Edwin Vedejs. He completed his Ph.D. in Organic Chemistry in 2007. After postdoctoral research investigating organolithium structures and kinetics under the supervision of Professor David Collum at Cornell University, Tim joined the Core R&D group within The Dow Chemical Company in 2010.

Aleksandrs Prokofjevs was born in 1985 and obtained his Bachelor’s degree from the University of Latvia, Riga, in 2006. While still in high school,. Aleksandrs began research work at the Latvian Institute of Organic Synthesis, Riga, under the supervision of Dr. Chem. Peteris Trapencieris, and continued this project throughout his undergraduate years. In 2006 he moved to the University of Michigan, Ann Arbor, where he is currently completing his Ph.D. degree with Prof. Edwin Vedejs. His current research is centered on the experimental and computational investigations of highly electrophilic boron cations and their use for synthetically valuable transformations, including borylations, C-H bond functionalizations, and hydroborations.

Edwin Vedejs was born in 1941 in Riga, Latvia. His family left in 1944 because of the impending Soviet takeover and emigrated to the United States in 1950. After completion of his BS (University of Michigan, 1962) and PhD (University of Wisconsin, 1966), he spent a postdoctoral year with E. J. Corey at Harvard. Prof. Vedejs then joined the chemistry faculty at the University of Wisconsin (1967). In 1999, he moved to the University of Michigan as

the Moses Gomberg Professor of Chemistry. He served as Associate Editor for Synthesis and Natural Products Chemistry, *J. Am. Chem. Soc.*, 1994–1999, and as Chair of the Organic Division of ACS, 2003. His recent awards include the H. C. Brown Award for Creative Research in Synthetic Methods, 2004, and the Order of Three Stars, Latvia, 2006.

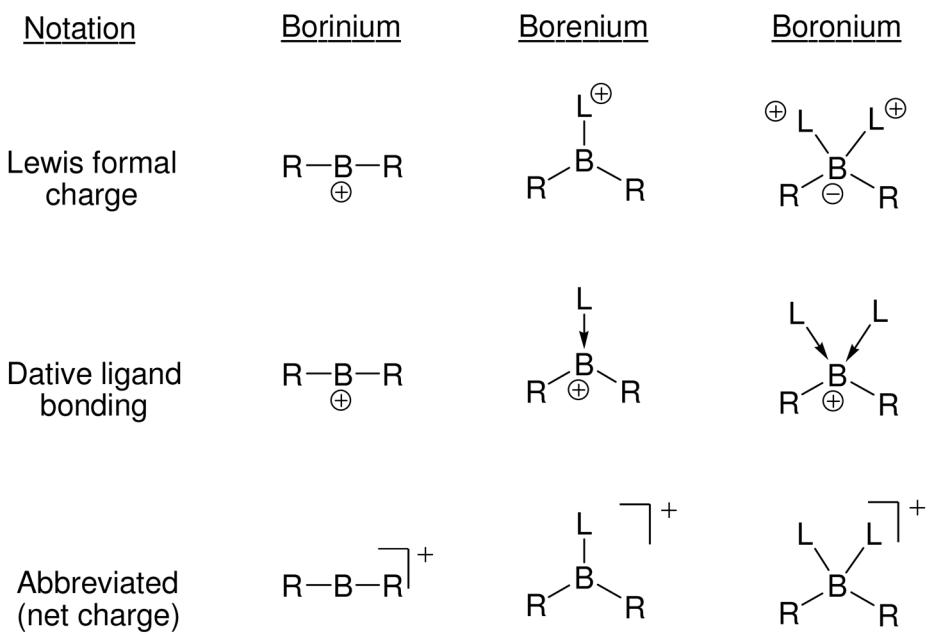


Fig. 1.
Boron cation nomenclature and structural representations in current use.

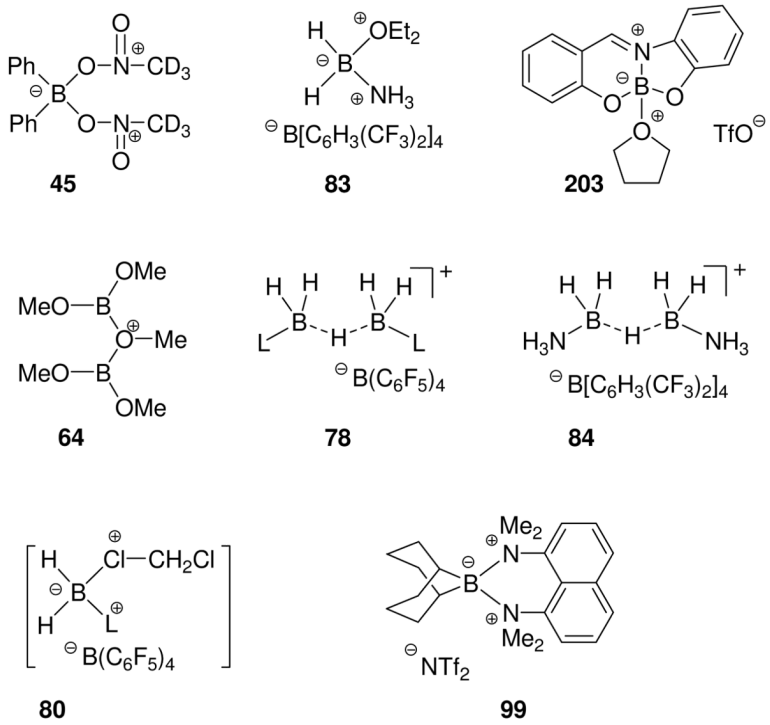


Fig. 2.
Borenium equivalents

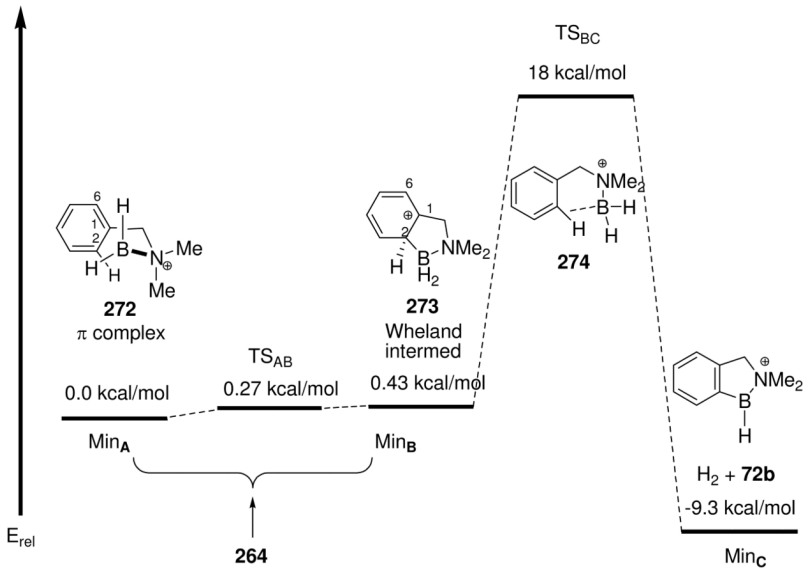
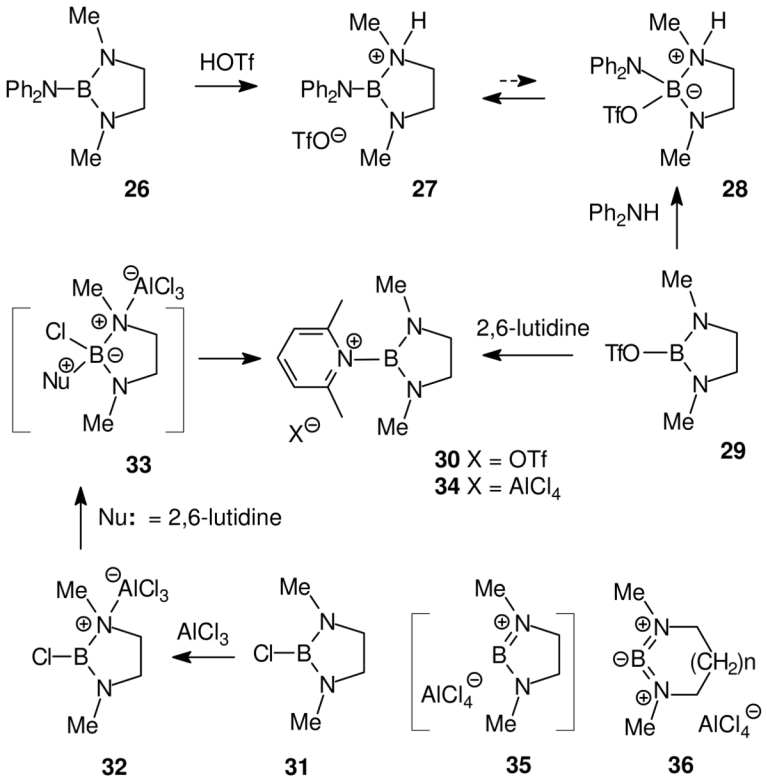
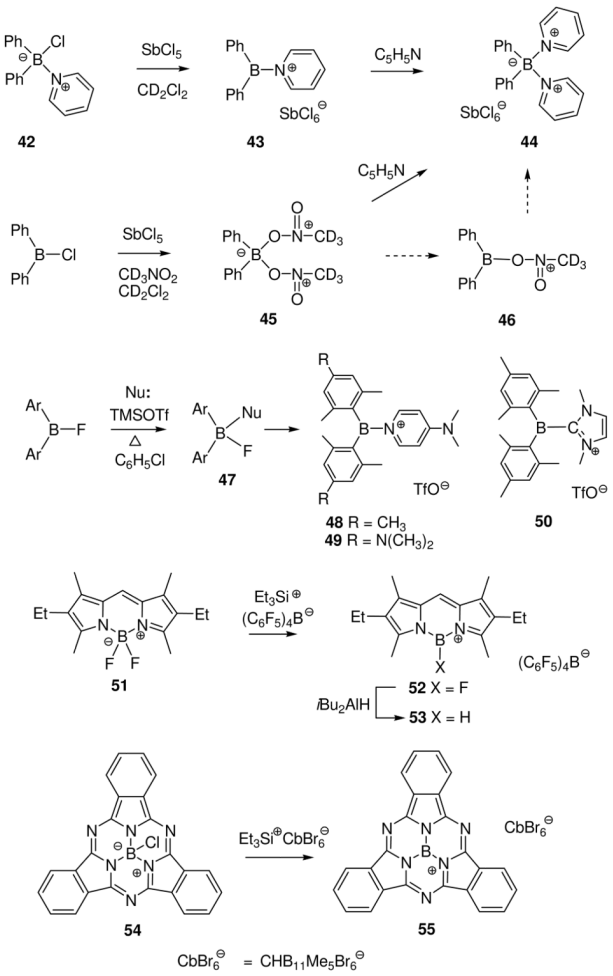


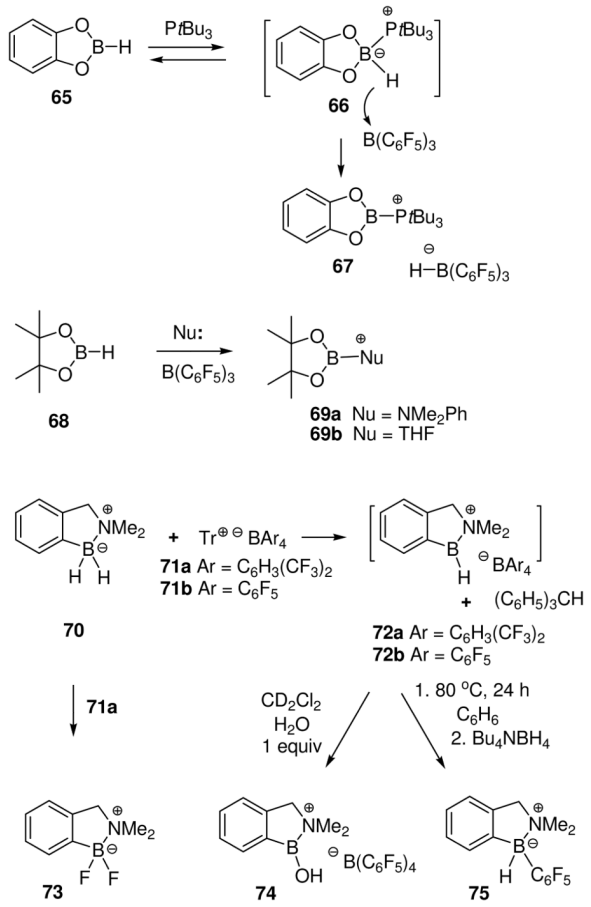
Fig. 3.
B3LYP/6-31G* energies for cationic structures from **264** to **72b**



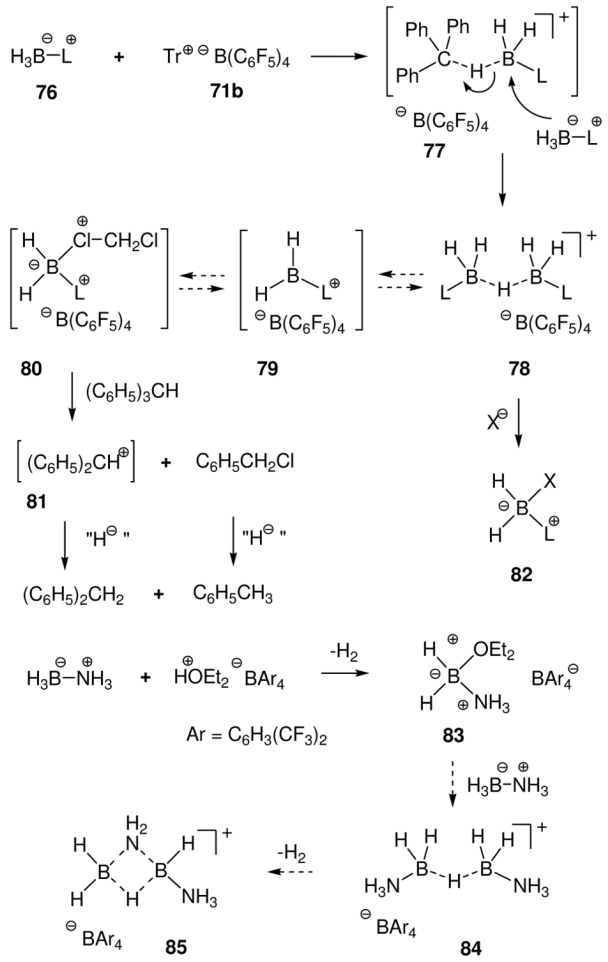
Scheme 1.
Electrophilic activation of 1,3-diazaborolidines by protonation or by Lewis acid catalysts[29]



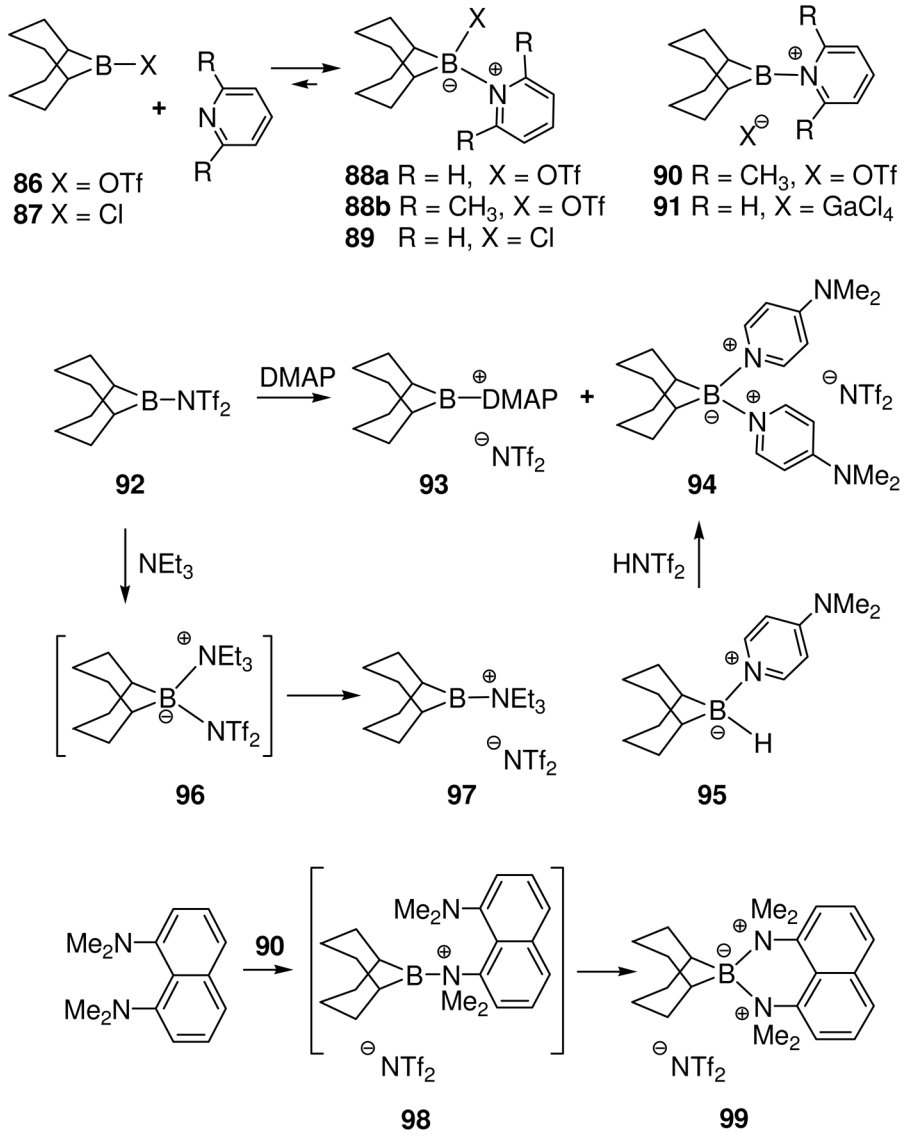
Scheme 2.
Generation of borenium ions by halide abstraction[33–39]



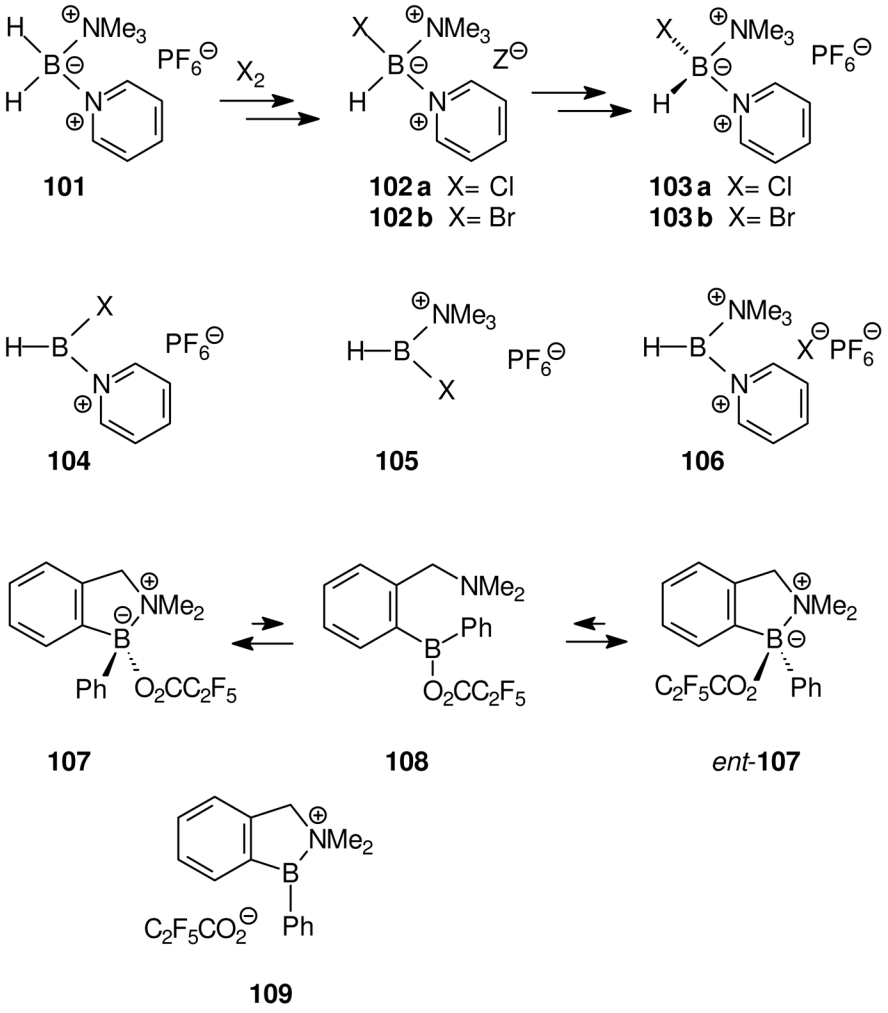
Scheme 3.
Borenium ion generation by hydride abstraction[44–47]



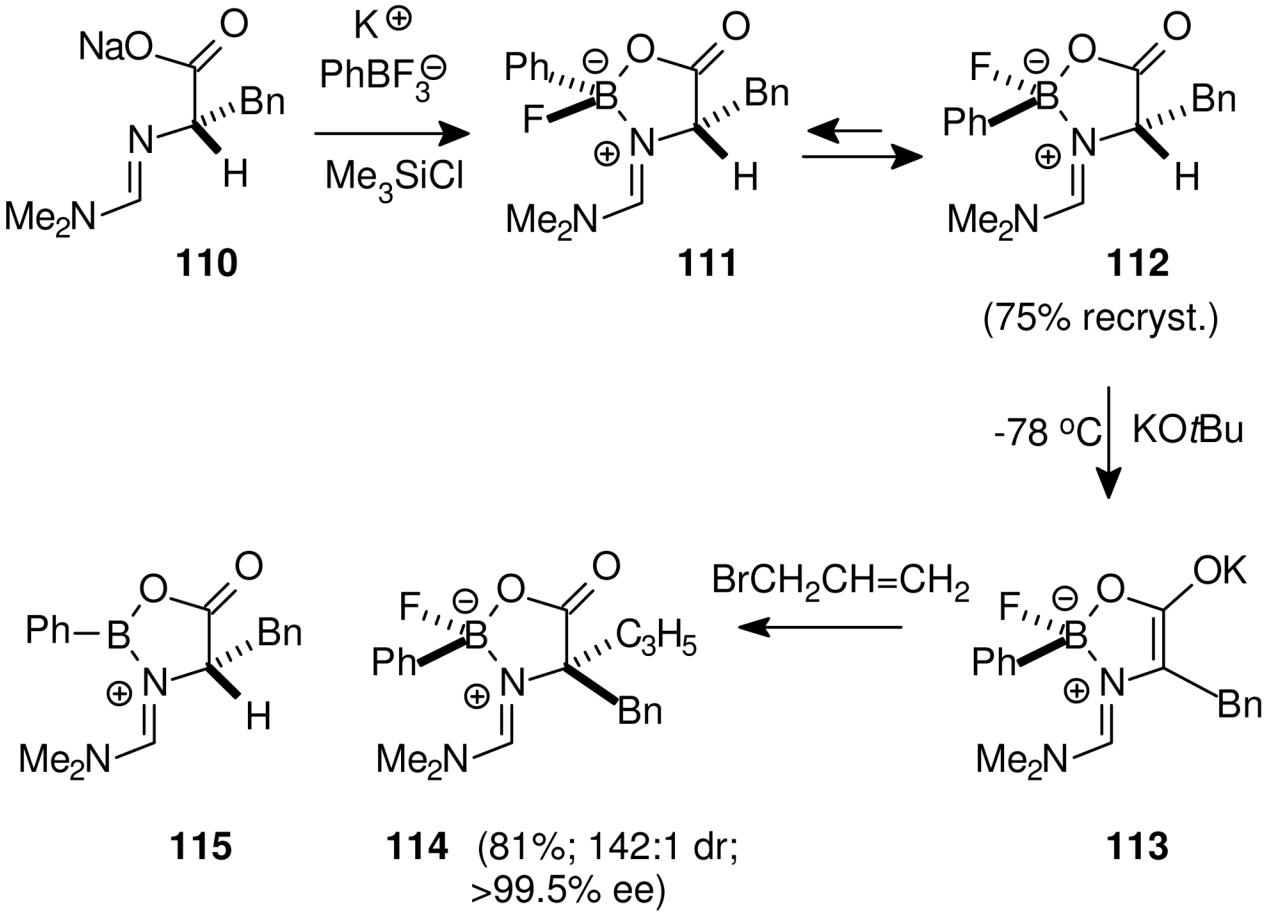
Scheme 4.
Generation of borenium ion equivalents by hydride abstraction[48–50]



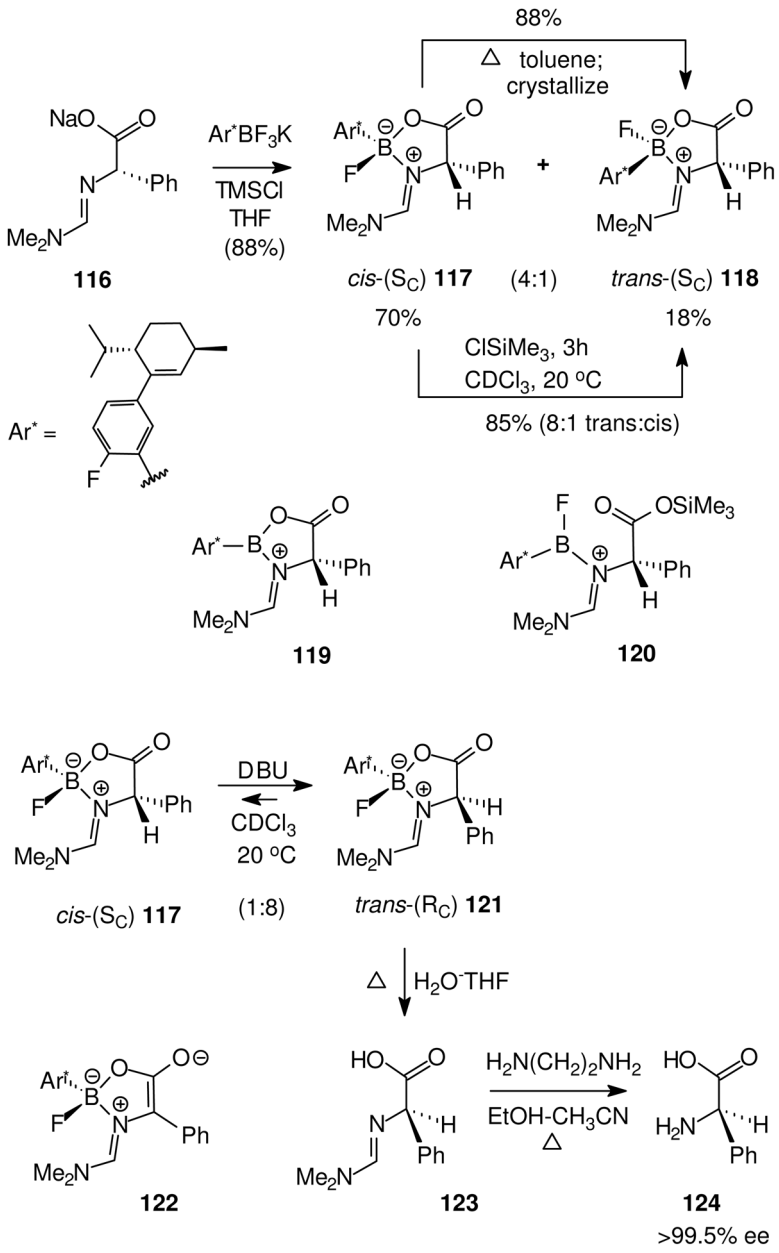
Scheme 5.
Minimally stabilized borenium ions by nucleophilic addition-heterolysis[51,52]



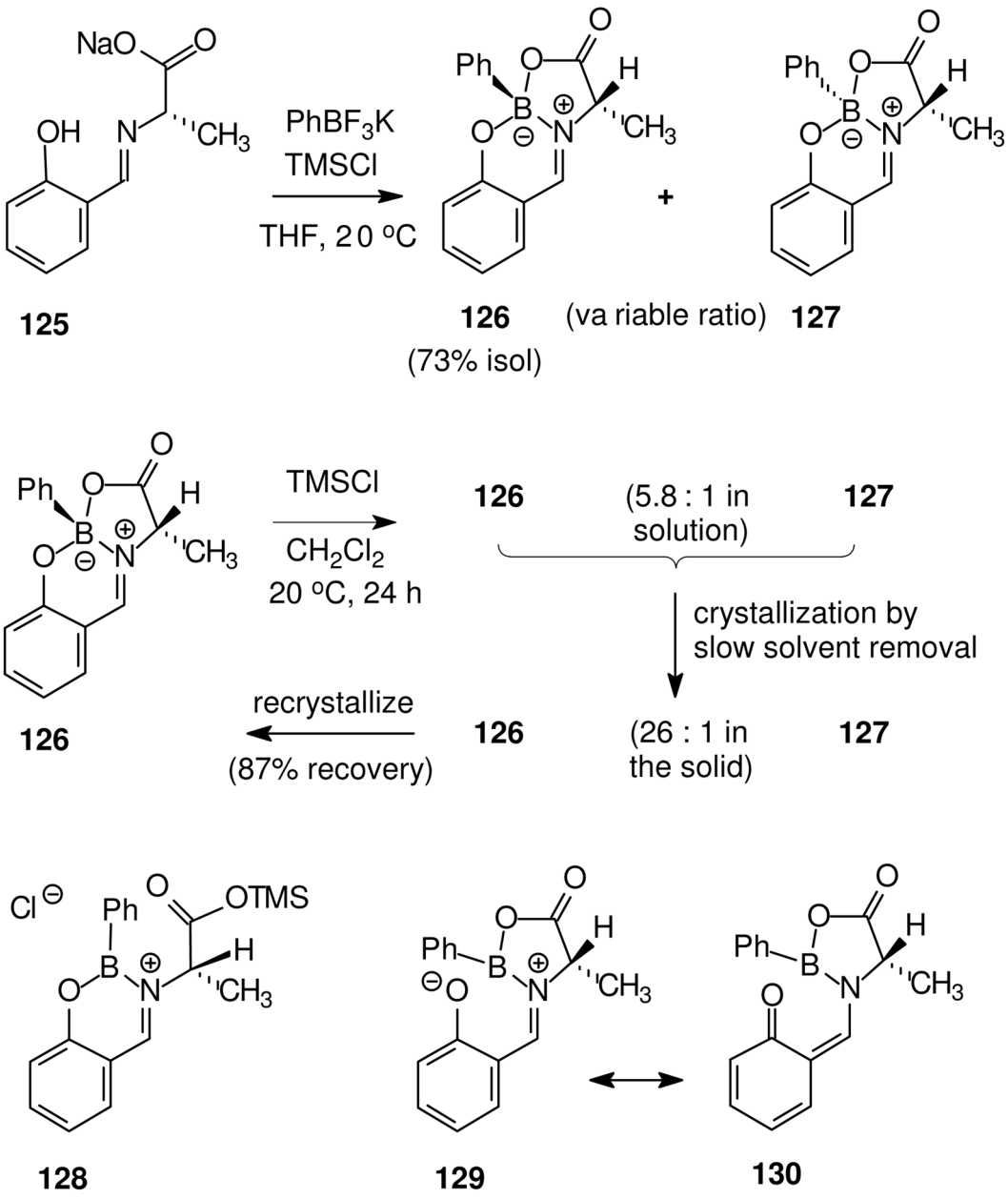
Scheme 6.
Stereogenic boron structures containing potential leaving groups[56,57]



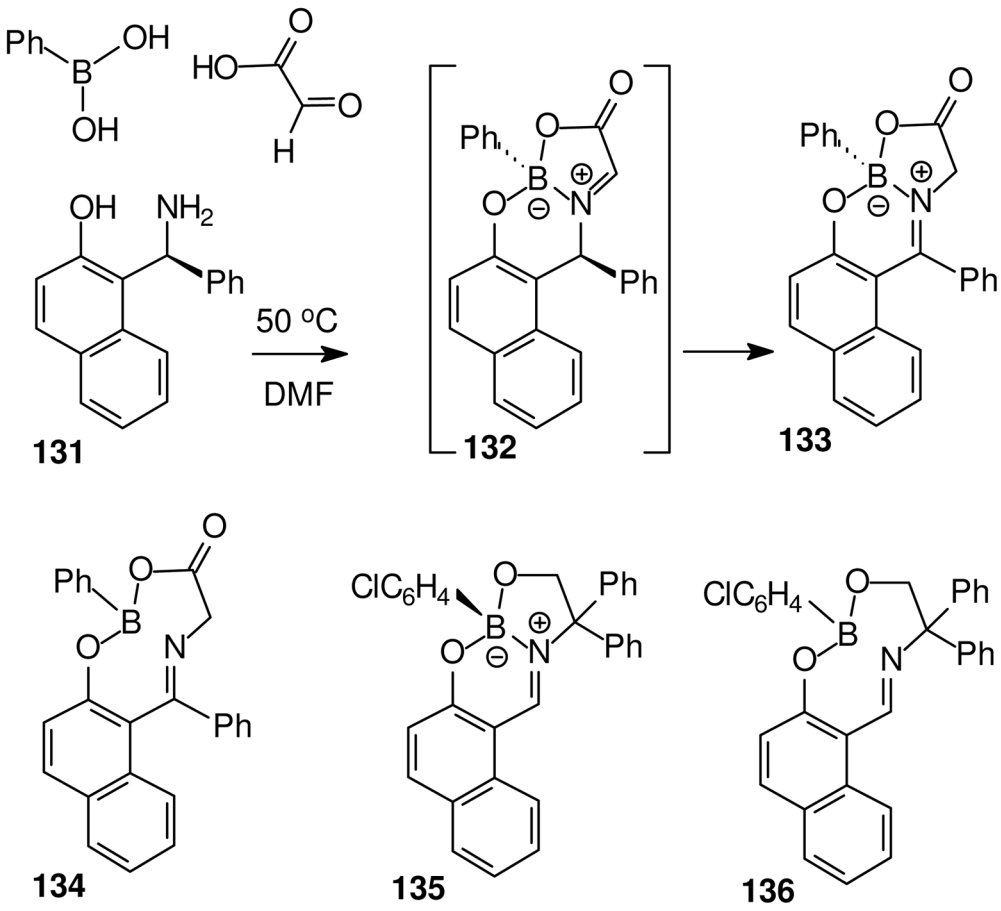
Scheme 7.
Asymmetric memory at stereogenic boron[58]



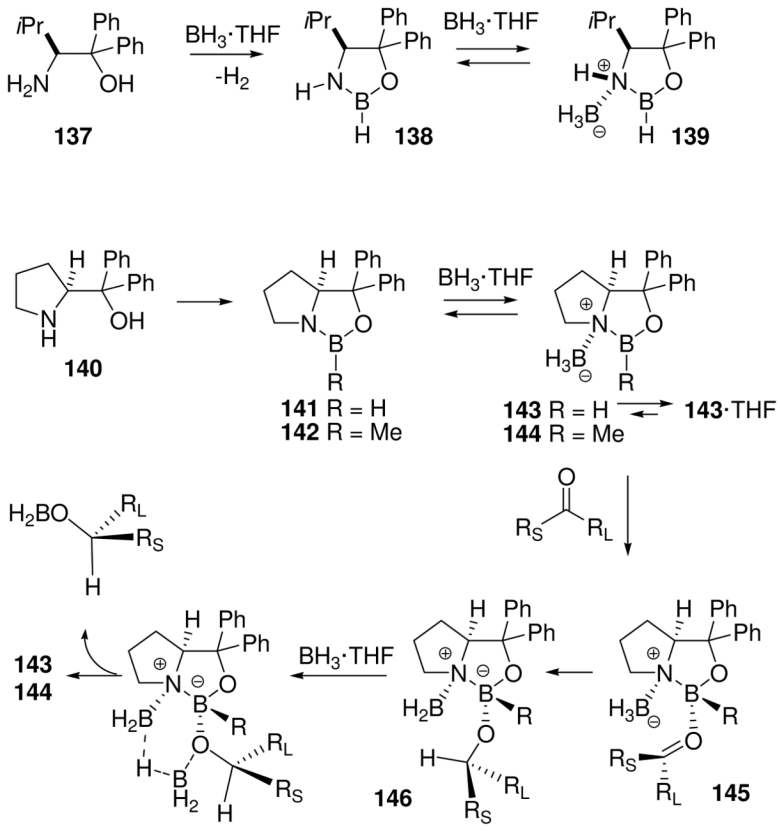
Scheme 8.
Epimerization at boron and asymmetric transformation[59]



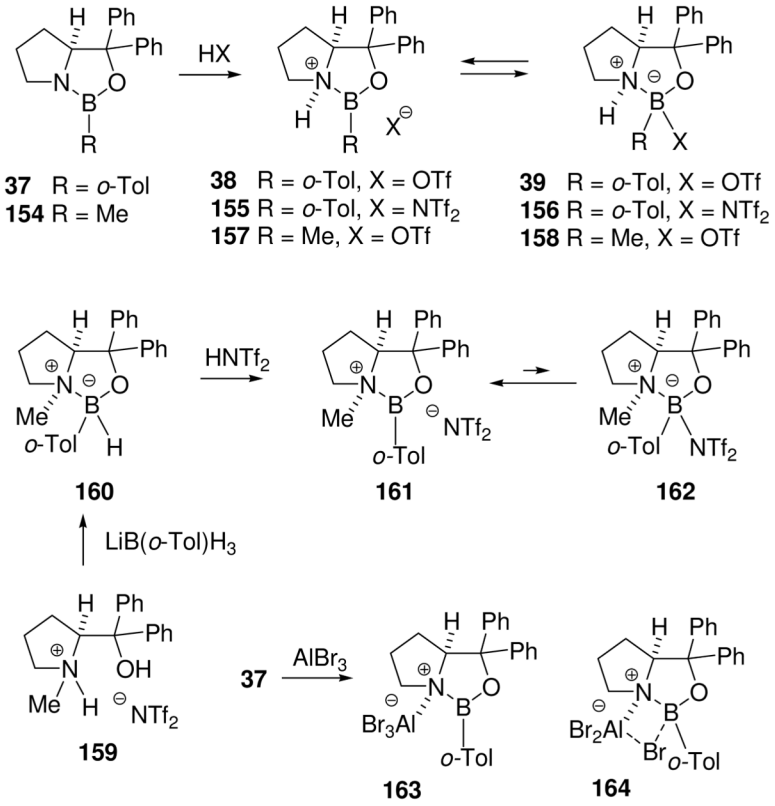
Scheme 9.
Epimerization in chiral salicylaldimine complexes[60]



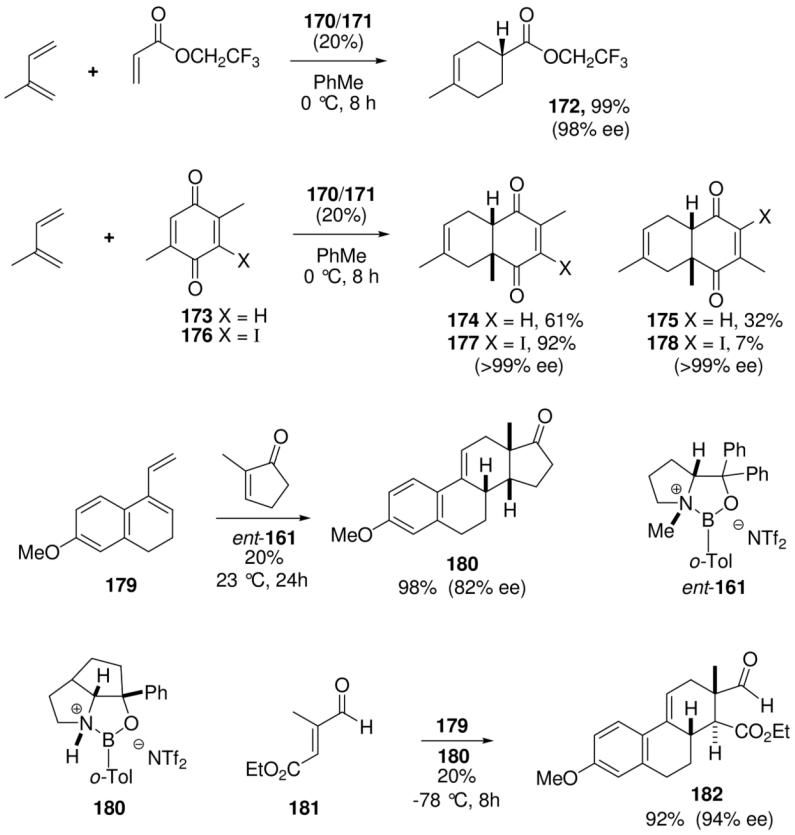
Scheme 10.
Configurational stability, conformational stability, and stereogenic boron[61,62]



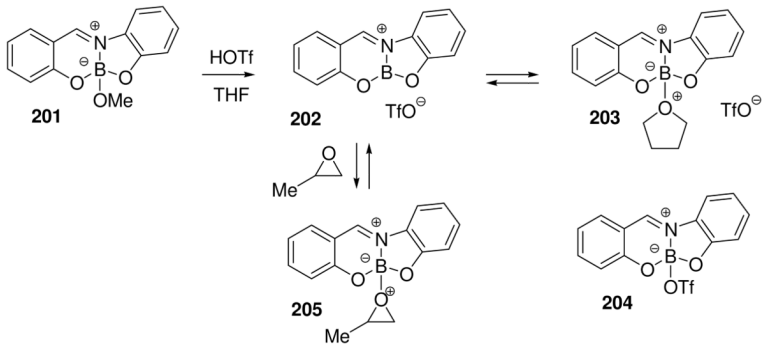
Scheme 11.
Oxazaborolidine catalysis in ketone reduction[64,65]



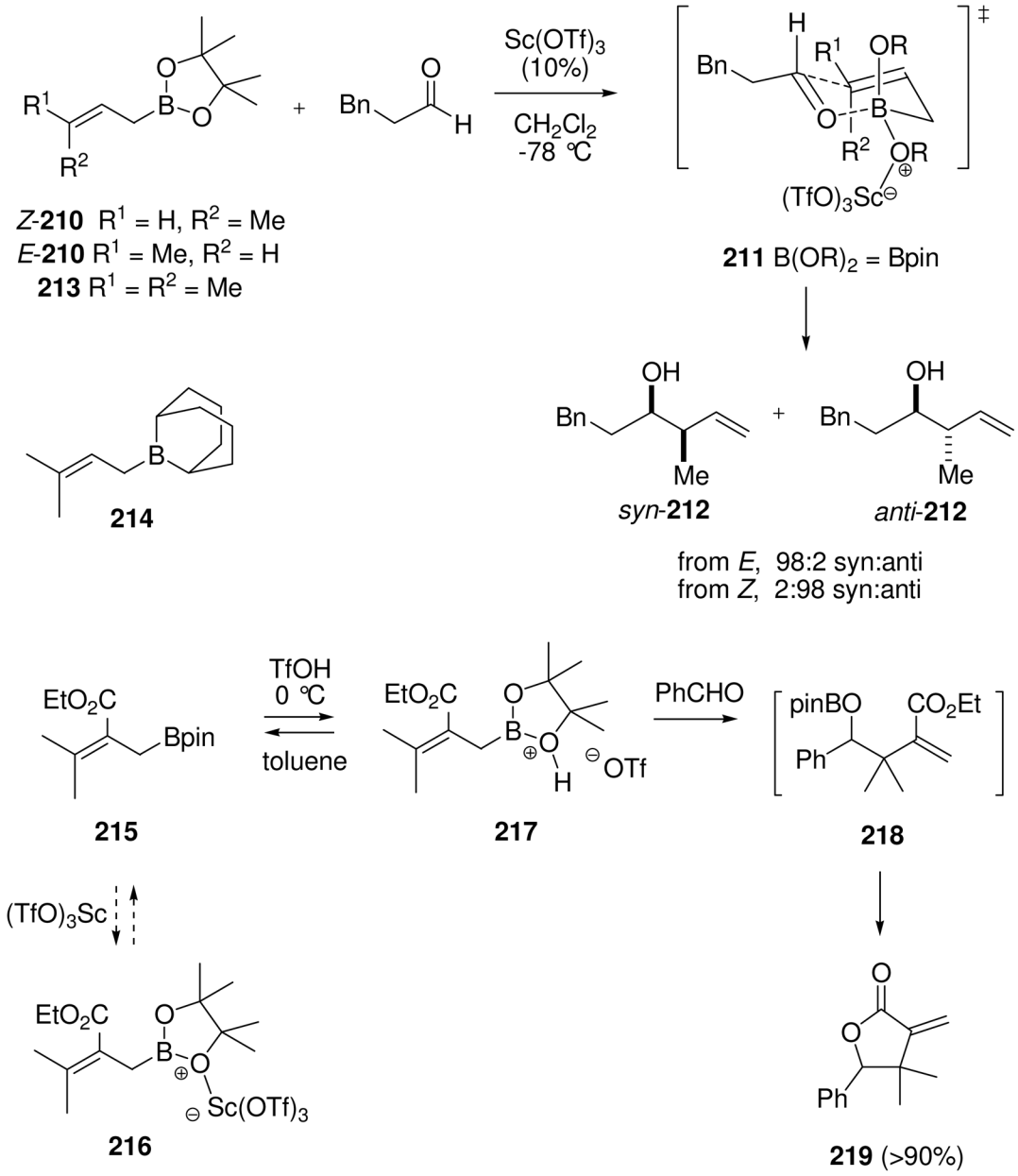
Scheme 12.
Chiral oxazaborolidines as sources of borenium salts[31,72,74,77]



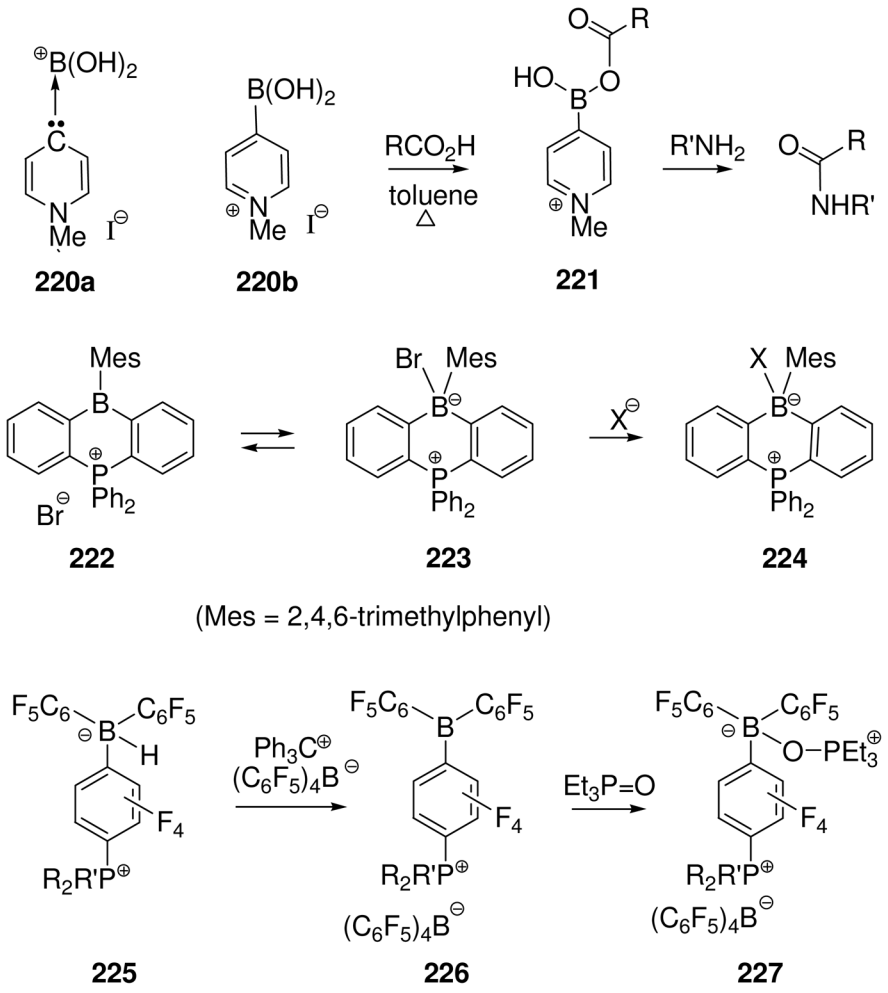
Scheme 13.
Enantioselective Diels-Alder reactions catalyzed by oxazaborolidines[72,74,77]



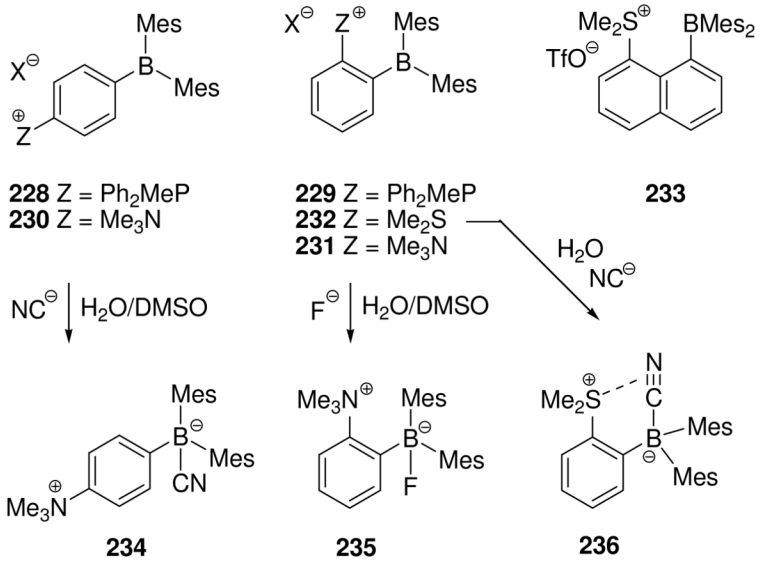
Scheme 14.
Generation of borenium salt **201** and polymerization catalysis[86]



Scheme 15.
Synthetic applications involving alkoxyborenium intermediates[88]

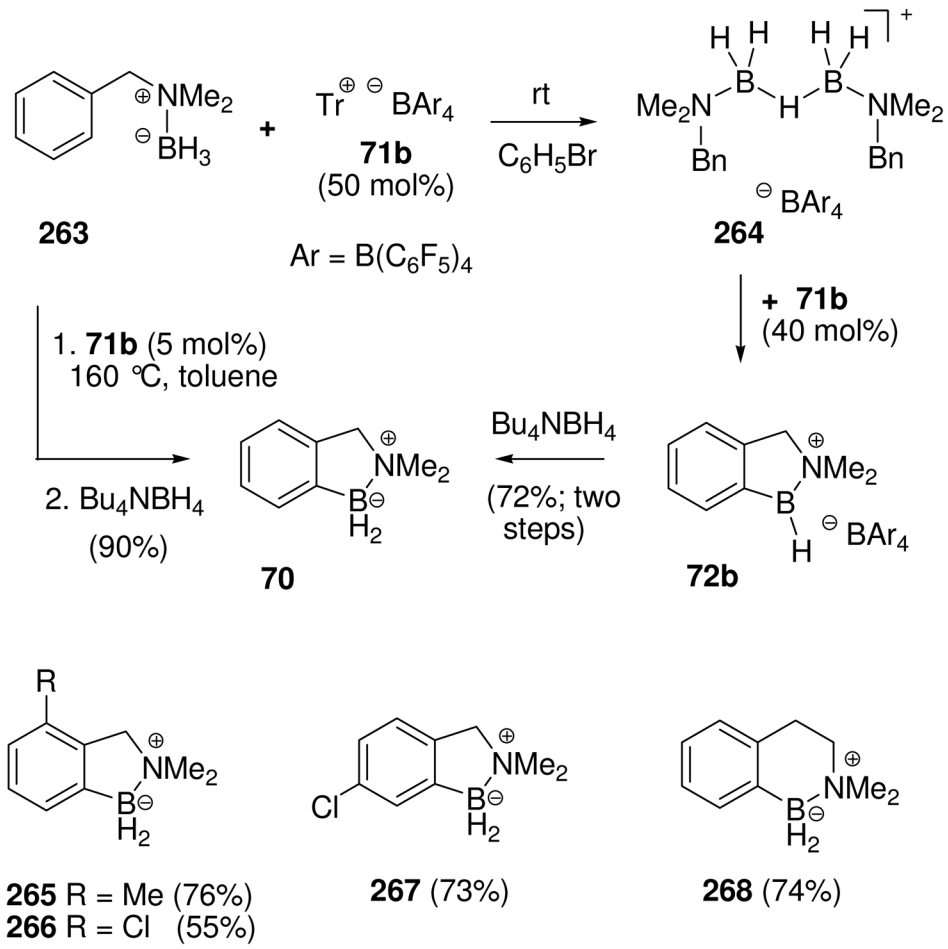


Scheme 16.
π-Conjugated borenium analogues[93–95]

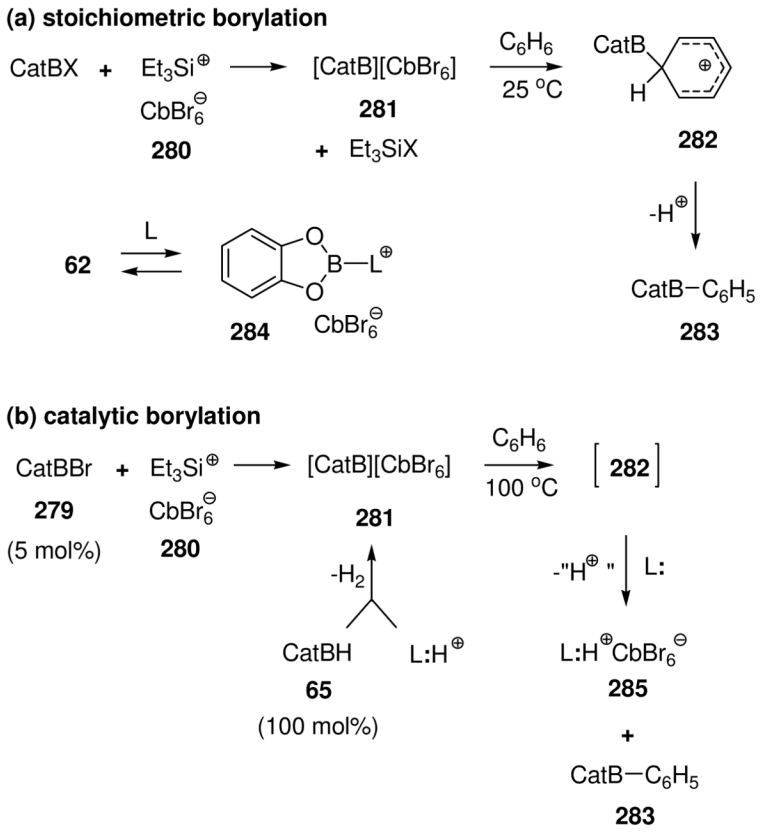


Scheme 17.

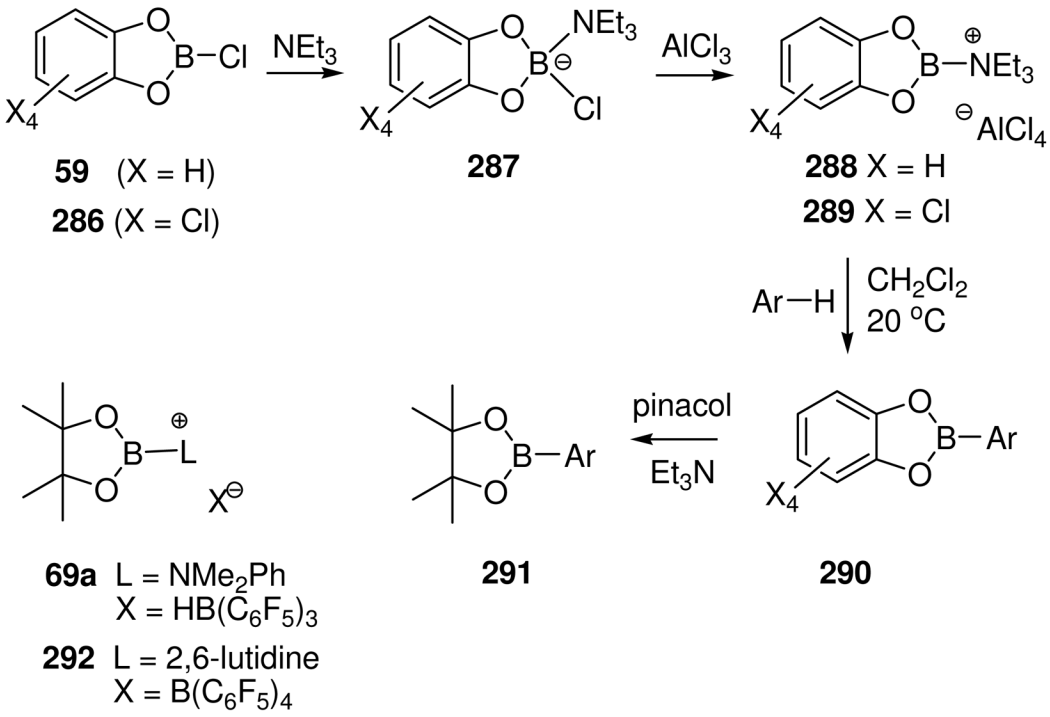
π-Conjugated borenium analogues as anion sensors[96–99]



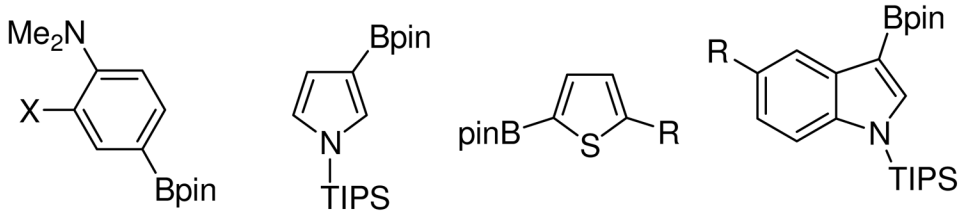
Scheme 18.
Intramolecular nitrogen-directed aromatic borylation[47]



Scheme 19.
Intermolecular aromatic borylation using catechol-derived borenium salts[42]

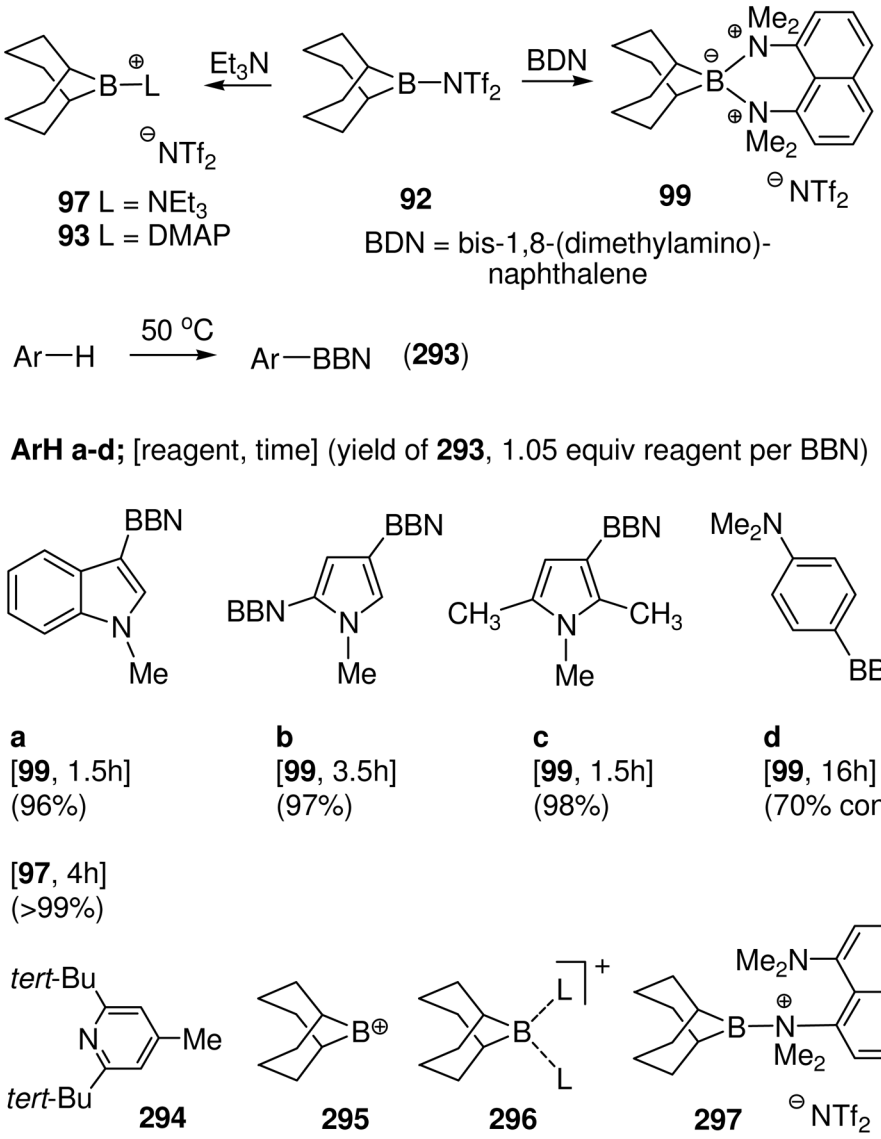


ArH a-g [reagent; time to prepare **290**] (product, overal yield of **291**)

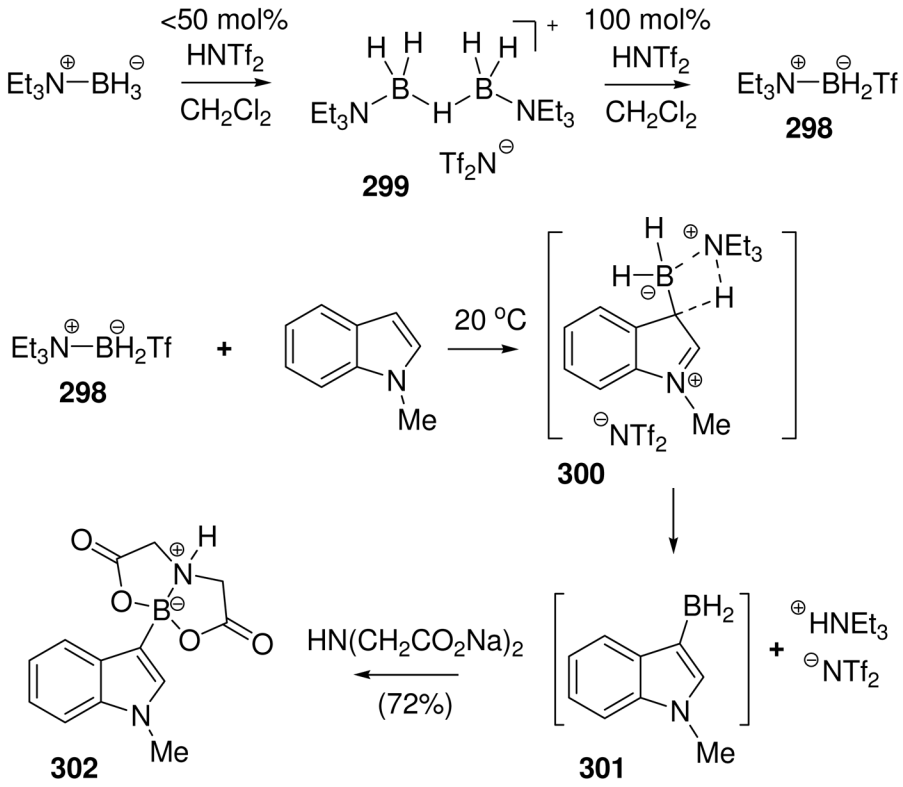


a X = H [**288**, 1h] (85%)	**c** [**288**, 72h] (89%)	**d** R = $N(CH_2)_5$ [**288**, 0.5h] (62%)	**f** R = MeO [**288**, 30h] (88%)
b X = Br [**289**, 32h] (93%)	**c** [**289**, 3h] (>95%)	**e** R = Me [**289**, 72h] (69%)	**g** R = Cl [**289**, 4h] (84%)

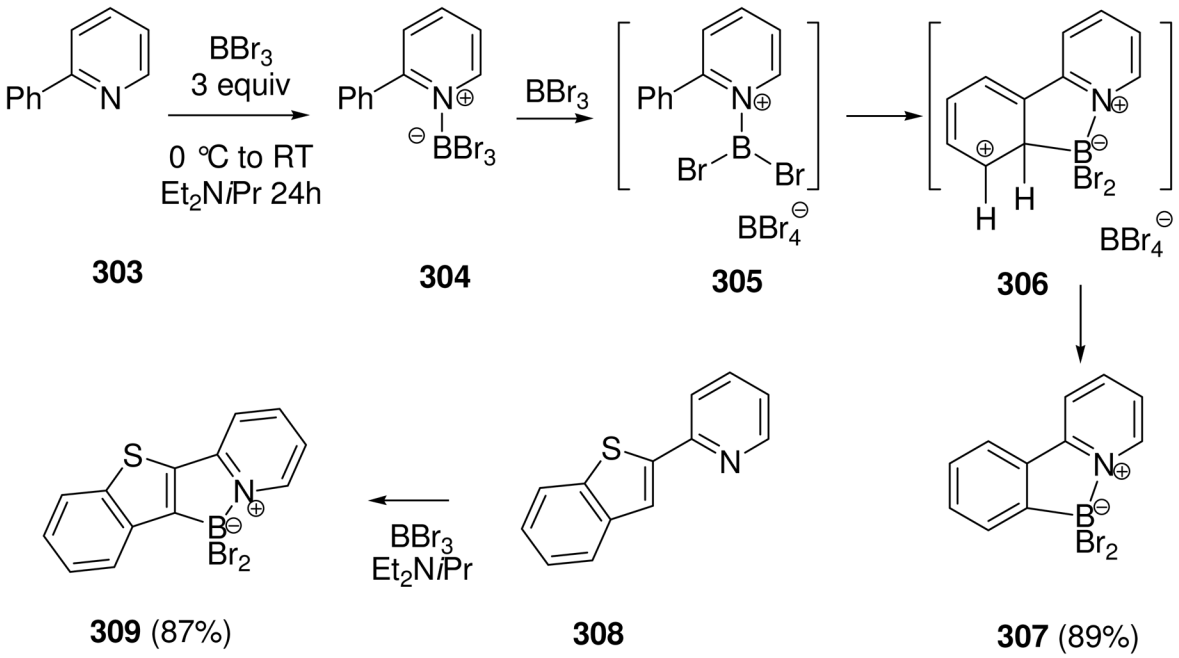
Scheme 20.
Electrophilic borylation of electron-rich aromatic and heteroaromatic substrates[112]



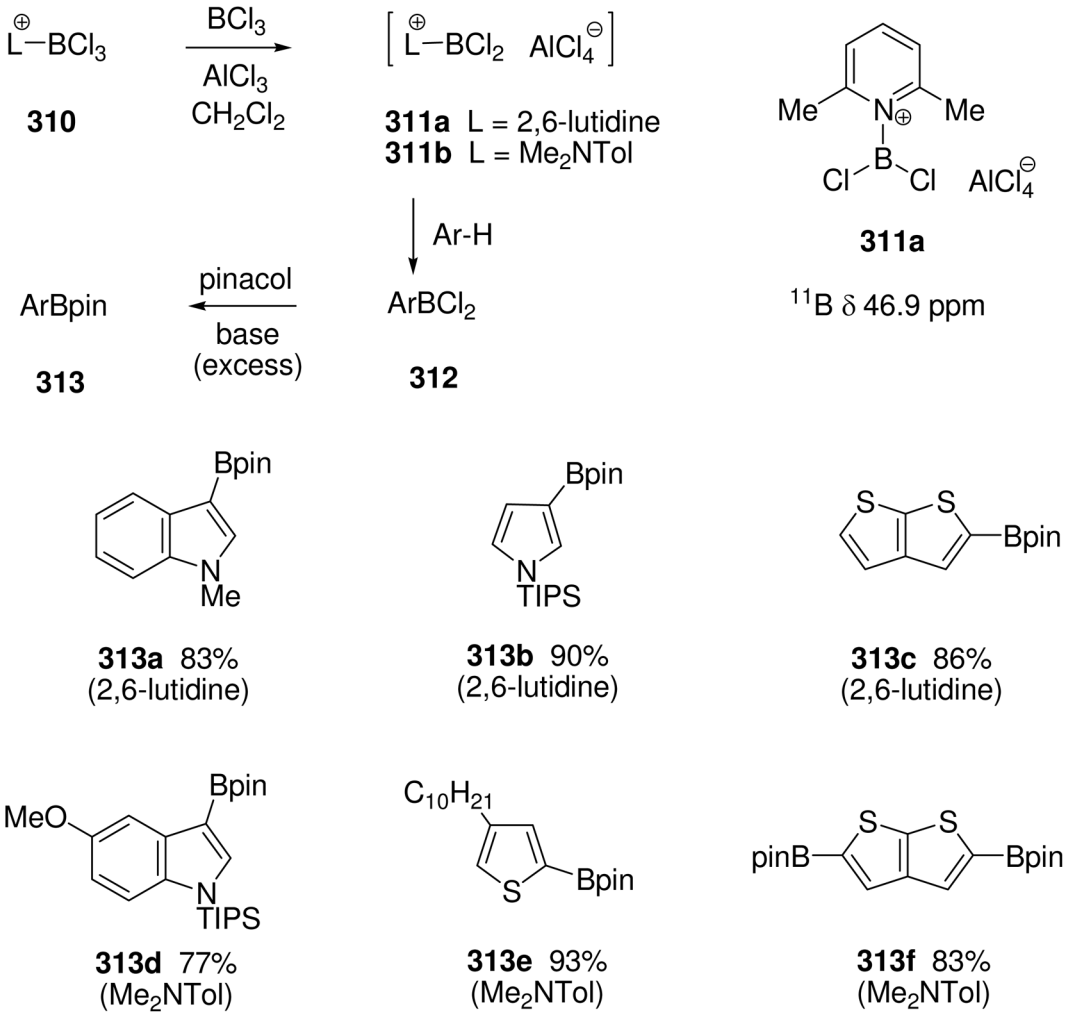
Scheme 21.
Intermolecular borylation using 9-BBN-derived borenium equivalents[52]



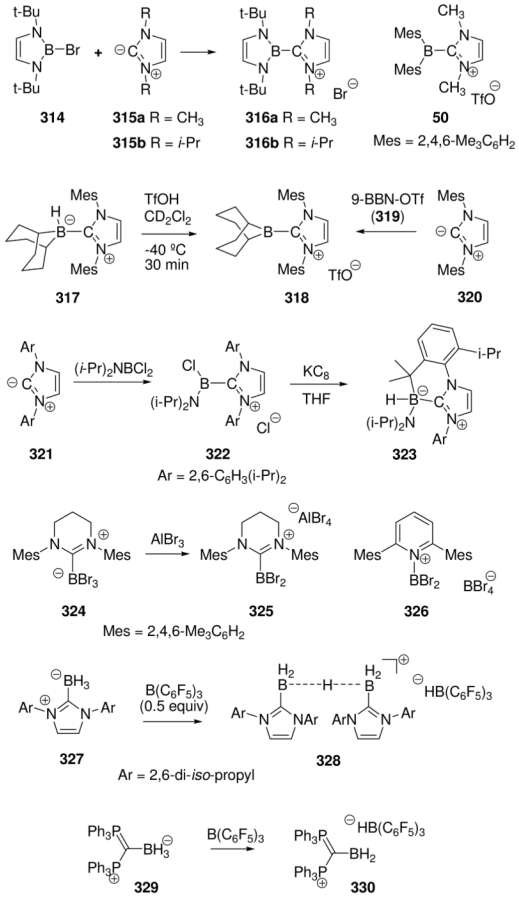
Scheme 22.
Activation of triethylamine borane for intermolecular borylation[50]



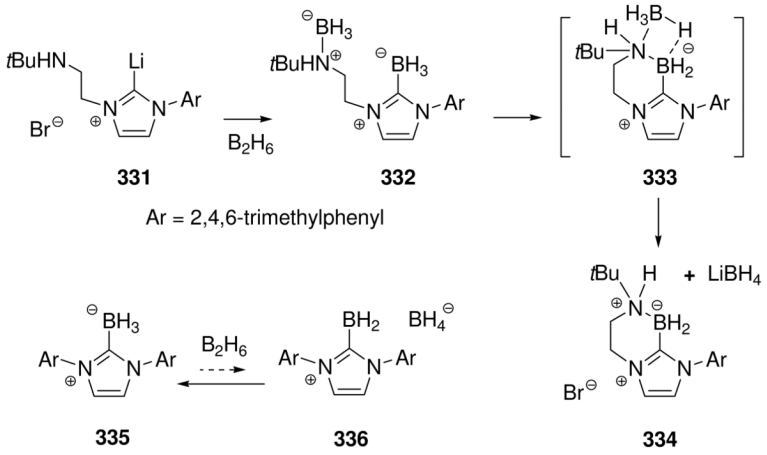
Scheme 23.
Intramolecular borylation using BBr_3/Et_2NiPr[120]



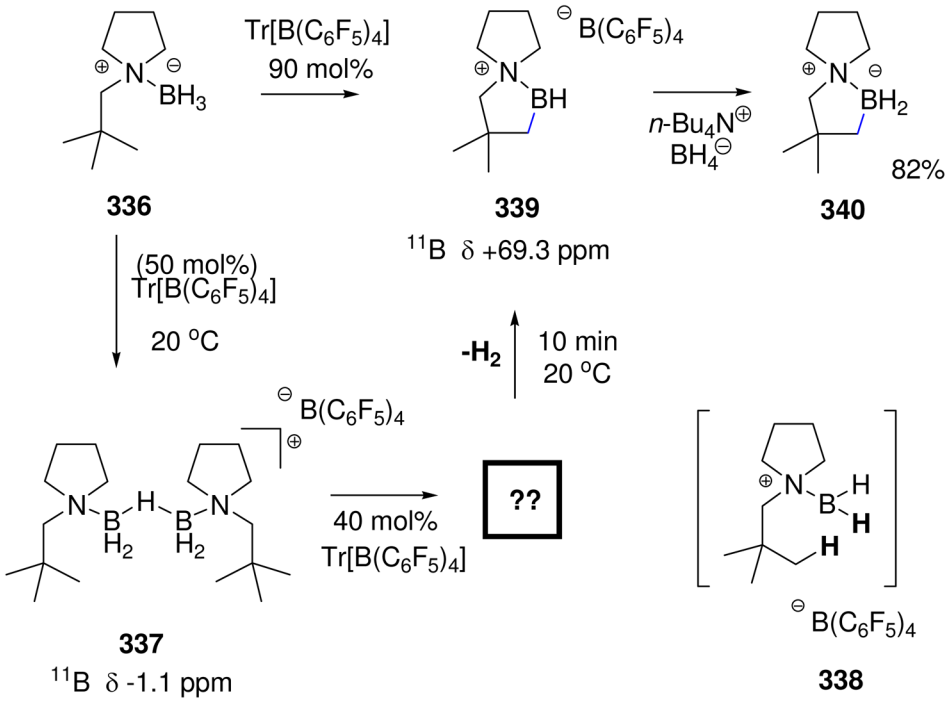
Scheme 24.
Intermolecular borylation using $BCl_3/AlCl_3$ and 2,6-lutidine or Me_2NTol[10b]



Scheme 25.
NHC-stabilized borenium salts[121–125]



Scheme 26.
NHC borane-amine cyclization[131]

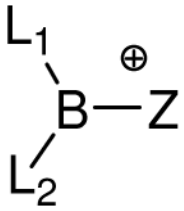
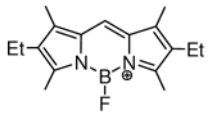
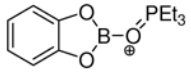
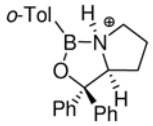
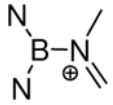
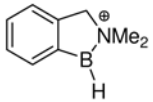
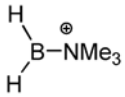
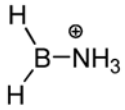


Scheme 27.
Aliphatic C-H insertion

Table 1

Calculated borenium geometries and NH_3 affinities[a,b]

entry	structure	borenium cation			NH_3 adduct $L_1L_2B(Z)NH_3$ (99)				ΔH^c
		B-L_1, Å	B-L_2, Å	B-Z, Å	B-L_1, Å	B-L_2, Å	B-Z, Å	B-NH_3, Å	
1	**27**[29]	1.408 **1.412**	1.395 **1.386**	1.576 **1.547**	1.489	1.469	1.659	1.706	−2.3
2	**49**[35]	1.541 **1.550**	1.541 **1.532**	1.533 **1.501**	1.616	1.620	1.619	1.689	−9.2
3	**48**[35]	1.553 **1.560**	1.553 **1.570**	1.517 **1.480**	1.626	1.623	1.610	1.682	−13.3
4	**97**[50]	1.559	1.555	1.571	1.618	1.621	1.712	1.660	−13.6
5	**50**[36]	1.551 **1.562**	1.551 **1.560**	1.602 **1.579**	1.636	1.631	1.648	1.688	−15.1
6	**67**[44]	1.368 **1.369**	1.369 **1.373**	1.945 **1.933**	1.438	1.440	2.015	1.665	−17.4
7	**53**[38]	1.438 1.**404**[d]	1.181 -	1.438 **1.402**[d]	1.522	1.196	1.520	1.664	−18.8

entry	structure		borenium cation			NH_3 adduct $L_1L_2B(Z)NH_3$ (99)				ΔH^c
			B-L_1, Å	B-L_2, Å	B-Z, Å	B-L_1, Å	B-L_2, Å	B-Z, Å	B-NH_3, Å	
8	**52**[38]		1.439 **1.429**[d]	1.323 **1.414**[d]	1.439 **1.430**[d]	1.520	1.379	1.520	1.659	−18.9
9	**60**[42]		1.377 **1.381**	1.360 **1.372**	1.386 **1.374**	1.443	1.438	1.474	1.631	−23.6
10	**38**[31]		1.534	1.340	1.576	1.592	1.423	1.664	1.659	−25.5
11	**55**[39]		1.385 **1.380**	1.385 **1.380**	1.385 **1.380**	1.466	1.466	1.466	1.650	−27.6
12	**72**[46]		1.504	1.183	1.559	1.587	1.199	1.627	1.633	−34.8
13	**25**[48]		1.181	1.181	1.528	1.198	1.198	1.604	1.620	−48.8
14	**100**[50]		1.178	1.178	1.554	1.194	1.194	1.615	1.615	−55.6

[a] Counterpoise-corrected heterolytic association enthalpies (298.15 K) determined using the M06-2X/6-311++G(3df,2p)//M06-2X/6-31+G(d,p) level of theory;[50, 54] solvents and counterions were not considered in the computation.

[b] Bold numbers indicate bond lengths taken from X-ray crystal structure determination as cited.

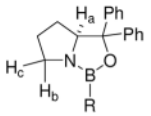
Chem Rev. Author manuscript; available in PMC 2013 July 11.

[c] ΔH corresponds to the enthalpy for [(cation + NH_3)−(ammonia adduct)] in kcal/mol

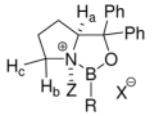
[d] X-ray data for **52** and **53** may be imprecise due to disorder as reported by Piers *et al.*[38]

Table 2

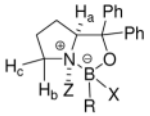
^{1}H NMR characterization of oxazaborolidine borenium equilibria



37, **154**
(entries 1-2)



155, **157**, **161**, **163**
(entries 3-6)



156, **158**, **160**
(entries 7-10)

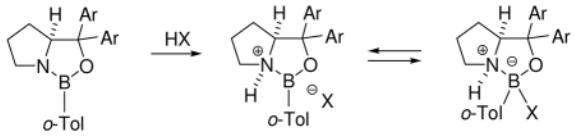
entry	Structure	B-coord	R	Z	X	H_a	H_b	H_c	Ref
1	**37**	3	*o*-Tol	Lp	--	4.54	3.40	3.24	31
2	**154**	3	Me	Lp	--	4.35	3.40	3.05	31
3	**155**	3	*o*-Tol	H	NTf_2	5.44	NA	NA	72
4	**157**	3	Me	H	OTf	4.85	3.40	3.20	31
5	**161**	3	*o*-Tol	Me	NTf_2	4.95	NA	NA	74
6	**163**	3	*o*-Tol	Br_3Al^-	--	5.26	3.95	3.51	75
7	**156**	4	*o*-Tol	H	NTf_2	5.01,4.90[b]	NA	NA	72
8	**158**	4	Me	H	OTf	4.75	3.15	3.00	31
9	**160**	4	*o*-Tol	Me	H	4.38	3.46	3.02	74
10	157·DMF	4	Me	H	DMF^+	5.00	3.50	3.00	31

[a] ^{1}H NMR data in ppm, CD_2Cl_2

[b] H_a values assigned to two diastereomers

Table 3

Reactivity of catalytic borenium sources with cyclopentadiene and selected dienophiles



167 Ar = 3,5-$Me_2C_6H_3$ **168** X = OTf, **170** X = NTf_2 **169** X = OTf, **171** X = NTf_2

entry	Catalyst	mol%	Dienophile	conc	T	time	Yield	ee[a]	Ref
1	**38**/**39**	6	methacrolein	0.2M[b]	−95 °C	1h	99%	91%	31
2	**168**/**169**	6	methacrolein	0.2M[b]	−95 °C	1h	97%	96%	31
3	**168**/**169**	20	di-Et fumarate	0.2M[c]	−35 °C	1.5h	99%	98%	73
4	**168**/**169**	20	cyclopentenone	0.2M[c]	−20 °C	14h	99%	92%	73
5	**155**/**156**	20	di-Et Fumarate	0.2M[d]	−60 °C	2h	99%	99%	72
6	**155**/**156**	20	di-Me-quinone	0.2M[d]	−95 °C	2h	99%	>99%	72
7	**161**/**162**	10	di-Et fumarate	0.25M[c]	−60 °C	8h	99%	96%	74
8	**161**/**162**	10	cyclopentenone	0.25M[c]	−50 °C	8h	99%	92%	74
9	**161**/**162**	10	di-Me-quinone	0.2M[c]	−78 °C	1h	97%	98%	74
10	**163**	4	methacrolein	0.5M[c]	−78 °C	2h	99%	93%	75
11	**163**	4	cyclopentenone	2.0M[c]	−40 °C	1h	95%	92%	75
12	**163**	4	di-Et fumarate	2.0M[c]	−78 °C	6h	95%	98%	75
13	**163**	4	di-Me-quinone	0.2M[c]	−78 °C	0.5h	99%	98%	75

[a] ee's refer to major cycloadduct

[b] 10:1 diene:dienophile

[c] 5:1 diene:dienophile

[d] diene:dienophile not given; a ratio of 1.1:1 is given for a related reaction.

Table 4

Simple Diels-Alder reactions catalyzed by oxazaborolidine-derived borenium sources[a]

entry	Catalyst	mol%	diene	Dienophile	T °C	time	yield	ee[a]	Ref
1	**168/169**	20	butadiene[b]	Methacrolein	−78 °C	24h	85%	94%	31
2	**168/169**	6	isoprene[b]	Methacrolein	−78 °C	13h	96%	97%	31
3	**168/169**	20	*c*-hexadiene[b]	Methacrolein	−78 °C	24h	58%	92%	31
4	**168/169**	20	*c*-pentadiene[c]	Et Acrylate	−20 °C	16h	96%	>99%	73
5	**168/169**	13	*c*-pentadiene[c]	Et Crotonate	4 °C	72h	46%	>98%	73
6	**168/169**	20	*c*-pentadiene[c]	Butenolide	−20 °C	64h	94%	90%	73
7	**170/171**	20	*c*-pentadiene[c]	Et Crotonate	20 °C	16h	94%	97%	72
8	**170/171**	20	butadiene[c]	di-Et Fumarate	20 °C	16h	92%	93%	72
9	**170/171**	20	butadiene[c]	di-Et Fumarate	20 °C	16h	92%	93%	72
10	**155/156**	20	*c*-pentadiene[c]	TFE Acrylate	−60 °C	2h	97%	>99%	72
11	**163**	4	*c*-pentadiene[c]	TFE Acrylate[d]	−78 °C	8h	98%	99%	75
12	**163**	4	isoprene[c]	Methacrolein[e]	−78 °C	16h	99%	97%	75
13	**161/162**	10	*c*-pentadiene[c]	TFE Acrylate[f]	−78 °C	1.5h	98%	97%	74

[a] reactions conducted in toluene or dichloromethane at a concentration of 0.2M unless noted; ee's refer to the major isomer

[b] 10:1 diene:dienophile

[c] 5:1 diene:dienophile

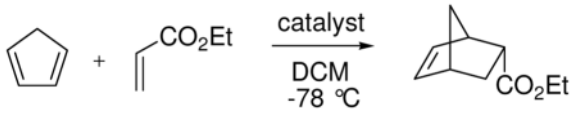
[d] concentration 2M

[e] concentration 0.5M

[f] concentration 0.25M

Table 5

Activation of oxazaborolidine **183** for Diels-Alder reaction with cyclopentadiene



entry	activator	mol%	dienophile	time	yield	ee	ref
1	MsOH	5%	Et acrylate[b]	1h	0%	--	78
2	TfOH	5%	Et acrylate[b]	1h	30%	97%	78
3	Tf_2NH	5%	Et acrylate[b]	1h	43%	97%	78
4	**186**	5%	Et acrylate[b]	1h	73%	>99%	78
5	$SnCl_4$	1%	methacrolein[c]	2h	>99%	95%	81
6	$SnCl_4$	10%	Et acrylate[c]	16h	96%	95%	81
7	$SnCl_4$	10%	di-Me-quinone[c]	1.5h	94%	99%	81

[a] experiments were conducted in DCM, [0.2M] in dienophile at −78 °C

[b] 5:1 diene to dienophile

[c] 3:1 diene:dienophile