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Electrophilic C–H Borylation and Related Reactions of B–H Boron Cations

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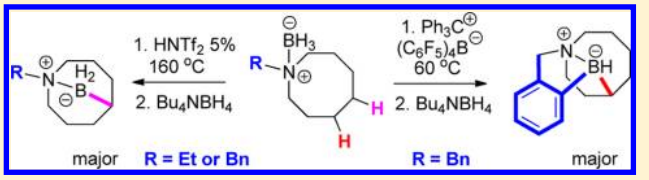
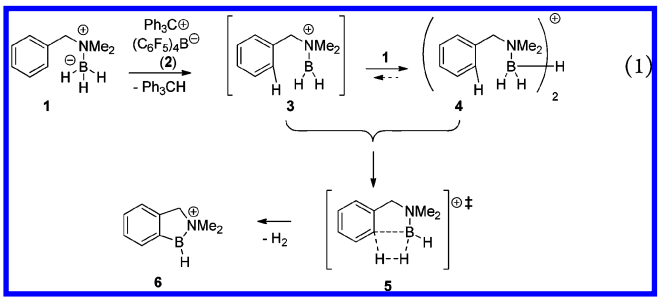
Supporting Information

ABSTRACT: Catalytic procedures are described for the amine-directed borylation of aliphatic and aromatic tertiary amine–boranes. Sequential double borylation is observed in cases where two or more C–H bonds are available that allow 5-center or 6-center intramolecular borylation. The $HNTf_2$-catalyzed borylation of benzylamine–boranes provides a practical means for the synthesis of ortho-substituted arylboronic acid derivatives, suitable for Suzuki–Miyaura cross-coupling applications.



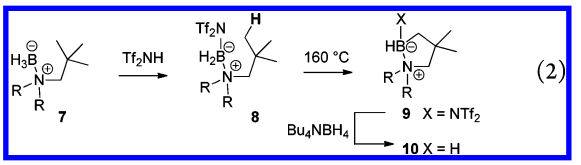
INTRODUCTION

Recent reports from our laboratory have described the intramolecular borylation of aromatic C–H bonds via hydride abstraction from amine–borane **1** with $Ph_3C^+B(C_6F_5)_4^-$ (**2**; eq 1).[1−4] Near-stoichiometric activation procedures gave the best



results using 90 mol % of the trityl salt **2** at room temperature, and borylation was attributed to transient borenium intermediates **3** or equivalent species, although the only observable borocations were the relatively stable hydride-bridged "dimers" **4** (at 50% loading of **2**) and the product borenium salts **6** (using 90% of **2**).[3] Although the mechanistic details remain uncertain, conversion to **6**[4] requires a dehydrogenation step that may correspond to the transition state **5**.

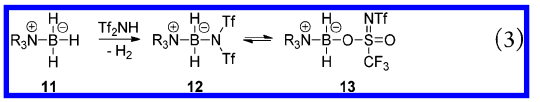
We have also disclosed related chemistry for the borylation of aliphatic C–H bonds in a preliminary account.[5,6] In this case, the stoichiometric process using trityl salt **2** also occurs at room temperature, but cleaner reactions are observed in several examples using the strong acid Tf_2NH as catalyst at 160 °C (eq 2), apparently via the initial conversion of the amine–borane **7**



to the intermediate **8** and hydrogen gas. Subsequent borylation affords a mixture of the hydrolytically labile **9** and the cyclic amine–borane **10** resulting from intermolecular hydride transfer from **7** to **9**, and reductive quenching with Bu_4NBH_4 completes the conversion to the stable product **10**. We now describe a more extensive investigation of catalytic and stoichiometric borylations involving aliphatic substrates and also show that a similar catalytic borylation gives much-improved yields with representative aromatic substrates. In some examples, the stoichiometric and catalytic methods give distinctly different product mixtures.

RESULTS AND DISCUSSION

The first stage of our investigation was designed to clarify the nature of activated intermediates derived from amine–boranes and Tf_2NH. Thus, treatment of a range of amine–borane complexes **11** with 1 equiv of Tf_2NH in CD_2Cl_2 or d_8-PhMe generally produced mixtures of two isomeric species (eq 3; Table



1). The reactions proceeded vigorously, and gas liberation ceased within seconds at room temperature, indicating complete consumption of Tf_2NH. The products were identified as N- and O-bound covalent boron bis(triflimides) **12** and **13** on the basis of multinuclear NMR spectroscopy. Thus, both species could be reliably assigned as tetracoordinate boron complexes on the basis of ^{11}B NMR data. From ^{19}F and ^{13}C NMR data it is also apparent that in one of the isomers both CF_3 groups are magnetically equivalent, as expected in the N-bound isomer **12**, but they are distinctly different in the O-bound isomer **13**.

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Table 1. ^{11}B and ^{19}F NMR Data for $R_3N{\cdot}BH_2NTf_2$ Complexes 12 and 13[a]

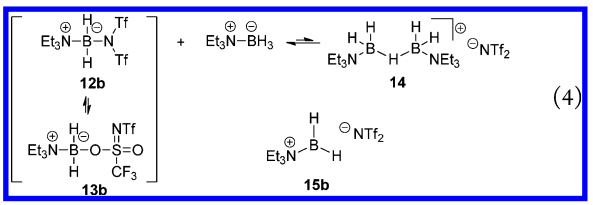
entry	R_3N		δ ^{11}B, ppm	δ ^{19}F, ppm	**12:13** ratio at equilibrium[b]
1	Me_3N	**12a**	−3.7	−69.2	7:1
		13a	4.0	−77.6, −79.1	
2	Et_3N	**12b**	−7.4	−68.9	1:4.7
		13b	0.7	−76.7, −79.1	
3	$(i\text{-Pr})_2NEt$	**12c**	ND	−68.4	<1:25
		13c	1.2	−77.0, −79.1	
4	*p*-MeBnNMe$_2$	**12d**	−3.2	−69.0	4.2:1
		13d	4.0	−76.6, −79.1	
5[c]	t-Bu, N	**12e**	−4.6	−69.2	1:2.6
		13e	−0.6	−76.7, −78.7	

[a]Conditions: 1:1 $R_3N{\cdot}BH_3$:Tf_2NH, CD_2Cl_2, room temperature. [b]Monitored up to 2−14 days at room temperature. [c]In d_8-PhMe.

Bis(triflimide) connectivity isomerism has not previously been observed in boron compounds (very few boron sulfonylimides have been reported so far),[7] although similar isomerism is a known phenomenon in Si bis(triflimides).[8]

In most cases the ratio of **12** to **13** measured immediately following mixing of **11** and Tf_2NH was different from that observed after a few hours at room temperature, suggesting a kinetic preference for the formation of one of the isomers. Such kinetic product mixtures initially contained larger amounts of the O-bound isomer **13**, which partially turned into **12** over time. Activation of $Me_3N{\cdot}BH_3$ with Tf_2NH in d_8-PhMe serves as a representative example where equilibration to the thermodynamic product ratio was observed to be particularly slow (hours at room temperature). To avoid discrepancies caused by slow kinetics, ratios of N- vs O-bound products (**12** vs **13**) summarized in Table 1 were confirmed to remain unchanged for days following the initial equilibration period. The product ratio (**12** vs **13**) measured at equilibrium correlates reasonably well with steric properties of the amine fragment. Thus, while **12** is the thermodynamically preferred isomer in the relatively unhindered Me_3N series (7:1 **12a**:**13a**), the O-bound isomer is clearly the dominant species in the far more hindered i-Pr_2NEt derivatives (<1:25 **12c**:**13c**). Similar observations in Si bis(triflimides) have been rationalized on the basis of lower steric demands of the bis(triflimide) fragment in the O-bound isomer,[8] and the same considerations apparently can be extended to boron compounds. The observed equilibration suggests facile interconversion of **12** and **13**, although the exact mechanism of this process is unclear.

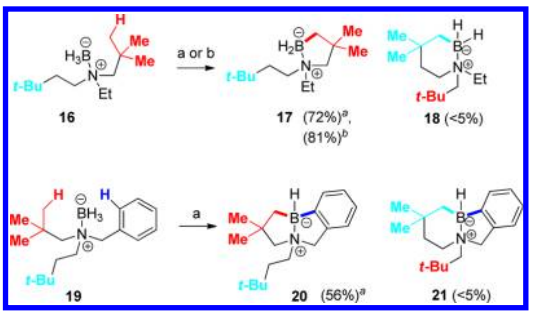
When activations of amine−boranes were performed using only a substoichiometric amount of Tf_2NH, formation of an additional product was observed by NMR spectroscopy. Thus, when $Et_3N{\cdot}BH_3$ was treated with 0.5 equiv of Tf_2NH in CD_2Cl_2, NMR assay after 30 min at room temperature indicated the presence of three new compounds aside from unreacted amine−borane (eq 4). While two of the products were found to be **12b** and **13b** in the same 1:4.7 ratio as in the stoichiometric Tf_2NH activation experiment (Table 1), the third product was assigned as the unusual H-bridged borocation **14** on the basis of the similarity of the multinuclear NMR spectra to data reported previously for the corresponding $[B(C_6F_5)_4]^-$ salt.[1] Structurally, the central 3c-2e B−H−B bond of borocation **14** can be viewed as being derived from the σ-basic B−H bond of $Et_3N{\cdot}BH_3$ and the formally empty p orbital of the hypothetical primary borenium cation **15b**. The observed equilibrium ratio among $Et_3N{\cdot}BH_3$, **12b**, **13b**, and **14** (ca. 7.2:1.1:5.0:1.0 mol) thus suggests that B−H σ bonds of $Et_3N{\cdot}BH_3$ are sufficiently nucleophilic to compete with Tf_2N^- for binding to **15b** in the thermodynamic sense.



Despite the structural description of cation **14** as a complex between $Et_3N{\cdot}BH_3$ and **15b**, the free primary borenium cation (**15b**) is not necessarily present at any stage of the reaction shown in eq 4, since both the forward and the reverse processes can also be envisioned as proceeding by S_N2-type displacements at boron for **12b** or **13b** (forward process) or **14** (reverse process). Presumably, such displacements would involve the weakly nucleophilic Tf_2N^- anion that is inevitably present as a contaminant in all Tf_2NH activations, as suggested by ^{19}F NMR data. On the other hand, reversible dissociation of **12b**/**13b** to **15b** and of **14** to $Et_3N{\cdot}BH_3$ and **15b** provides a sufficient explanation for our observations in the absence of evidence to the contrary. In terms of reactivity as well as structure, H-bridged cations analogous to **14b** occupy an intermediate position between tricoordinate borenium and tetracoordinate boronium species.[3] Furthermore, eq 4 represents the borderline case for the formation of covalent counterion adducts **12**/**13** in the presence of **14**. Any further decrease in the coordinating ability of the anion can be expected to favor conversion of **12**/**13** to hydride-bridged species such as **14** when excess borane complex is present, as observed when the anion is $B(C_6F_5)_4^-$.

Having developed a better understanding of the activation process, we turned our attention to broadening the substrate scope for the aliphatic borylations reported in the preliminary study.[5] Several amine−borane substrates were selected for evaluation under optimum stoichiometric and/or catalytic activation conditions (Scheme 1). In most cases the substrates were chosen such that multiple C−H bonds would be in proximity to the cationic boron center in activated intermediates so that issues of regioselectivity or multiple borylation could be addressed.

Scheme 1. [a]



[a]Legend: (a) catalytic borylation conditions, 5 mol % of Tf_2NH, PhMe, sealed tube, 160 °C, 14 h, quenched with ca. 10 mol % of n-Bu_4NBH_4; (b) stoichiometric borylation conditions, 0.9 equiv of $Ph_3C^+[B(C_6F_5)_4]^-$, PhF, room temperature, 4 h, quenched with ca. 1.1 equiv of n-Bu_4NBH_4.

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First, the substrate **16** was investigated to allow 6 assessment of the potential for competition between intramolecular borylation pathways leading to 5- vs six-membered rings. Under both catalytic and stoichiometric reaction conditions, borylation of the *N*-neopentyl group was preferred, resulting in **17** as the dominant product after reductive quenching to convert intermediate *B*-NTf_2 species to B−H. The isomeric six-membered borylation product **18** or doubly borylated products were not detected in either the catalytic or stoichiometric experiments. In the case of the catalytic reaction using 5 mol % of Tf_2NH in toluene at 160 °C (sealed tube), the material balance consisted of **17** (72% isolated) together with recovered starting material **16** due to incomplete reaction. The corresponding stoichiometric experiment using 0.90 mol % of $Ph_3C^+B(C_6F_5)_4^-$ (**2**) in fluorobenzene at room temperature gave an 81% yield of **17**, but isolation of the product was complicated by substantial amounts of the Ph_3CH byproduct.

The modified substrate **19** (Scheme 1) was designed to have two reactive C−H's within a 5-atom distance from the boron atom, and formation of the doubly borylated **20** was the result (catalytic conditions; structure of **20** confirmed by a single-crystal X-ray diffraction study, Figure 1). Similar to the experiment starting from **16**, no substantial amount of the isomeric product **21** resulting from a 6-center intramolecular borylation was observed. Although the timing of sequential borylation events was not established, formation of **20** indicates that both the aliphatic and aromatic C−H bonds have comparable reactivity in this example.

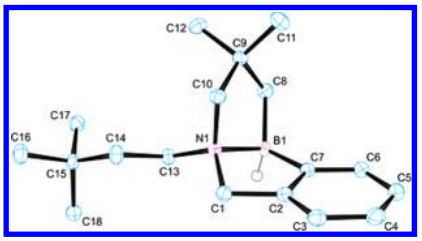
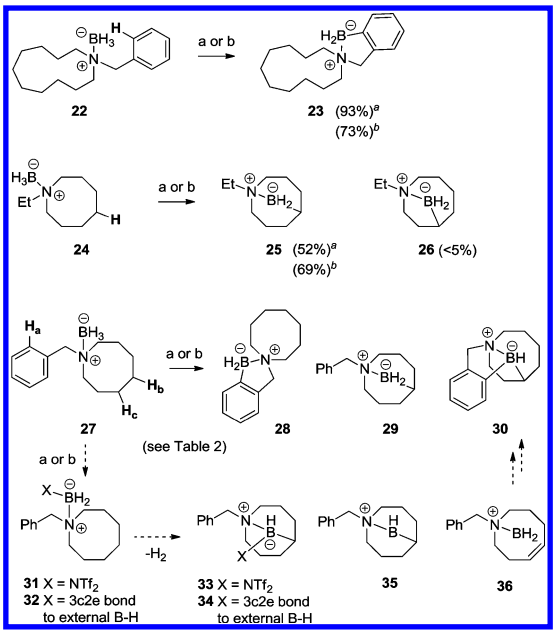


Figure 1. X-ray structure of amine−borane **20** (50% probability ellipsoids, H atoms omitted for clarity except at B). Selected bond lengths (Å) and angles (deg): B1−N1, 1.66; B1−C7, 1.61; B1−C8, 1.63; N1−B1−C7, 97; N1−B1−C8, 101.

The next step was to evaluate the reactivity of C−H bonds in a transannular position, accomplished using 11- and 8-membered-ring substrates **22**, **24**, and **27** (Scheme 2). No borylation of the aliphatic ring was observed in **22**, and the spirocyclic structure **23** was the only product isolated under standard catalytic or stoichiometric activation conditions. However, transannular borylation was observed in the 8-membered cyclic amine−borane **24** to give the symmetrical bicyclo[3.3.1] product **25**. In contrast to the other borylations discussed so far, **25** is the result of a 6-center borylation process. The modest isolated yield (52%) of **25** in the high-temperature catalytic protocol is largely the result of incomplete consumption of the starting material **24**, although traces of a second product were detected by NMR spectroscopy. This substance could not be purified, but the limited NMR data are consistent with the tentative assignment of structure **26**, having the isomeric bicyclo[4.2.1] skeleton.

We also explored the 8-membered amine borane **27**, an analogue of **24** having an *N*-benzyl subunit in place of *N*-ethyl. The modified substrate **27** showed remarkably rich behavior due to the presence of three reactive C−H bonds (Scheme 2; Table 2). When it was subjected to the standard catalytic conditions

Scheme 2. [a]



[a]Legend: (a) catalytic borylation conditions, 5 mol % of Tf_2NH, PhMe, sealed tube, 160 °C, 14 h, quenched with ca. 10 mol % of *n*-Bu_4NBH_4; (b) stoichiometric borylation conditions, 0.9 equiv of $Ph_3C^+[B(C_6F_5)_4]^-$, PhF, room temperature, 4 h, quenched with ca. 1.1 equiv of *n*-Bu_4NBH_4.

Table 2. Borylations of 27

		yield, %		
entry	conditions	28	29	30
1	5 mol % Tf_2NH, 160 °C, 14 h	30[a]	48[a]	0
2	0.9 equiv $Ph_3C^+[B(C_6F_5)_4]^-$, room temp, 4 h	29[b]	38[b]	25[b]
3	0.9 equiv $Ph_3C^+[B(C_6F_5)_4]^-$, 60 °C, 20 h	17[b]	4[b]	70[b]

[a]Isolated yields. [b]NMR yields vs internal reference.

with $HNTf_2$, **27** was converted exclusively to monoborylated products **28** and **29** in a 1:1.7 ratio after the usual reductive quench with *n*-Bu_4NBH_4 (^{1}H NMR assay of the crude reaction mixture). Products **28** and **29** were isolated in 30% and 48% yields, respectively. No products of a second borylation event were observed, not even with extended reaction times at 160 °C! A partial explanation for these observations is shown in Scheme 2 by considering a pathway from **27** to the activated intermediate **31** followed by the expected borylation to give **33**. Subsequent reductive quenching would then afford the major product **29**. On the other hand, *stoichiometric activation* of **27** with $Ph_3C^+B(C_6F_5)_4^-$ (**2**) at room temperature (4 h) followed by reductive quenching did afford a doubly borylated product (**30**) in addition to **28** and **29** (Table 2). As established by X-ray crystallography (Figure 2), structure **30** is noteworthy because it contains a bicyclo[4.2.1] subunit involving the borylated azacene ring. Surprisingly, **30** becomes the dominant product and accumulates at the expense of the symmetrical bicyclo[3.3.1] product **29**, as evidenced by the borylation outcome under more forcing stoichiometric conditions at 60 °C (Table 2, entry 3). A convincing explanation for these findings would require a more detailed knowledge of the timing of initial C−H insertion events under stoichiometric conditions, but analogy suggests that a hypothetical 3c-2e structure **32** is generated first and that it undergoes borylation to give **34** or, more likely, the

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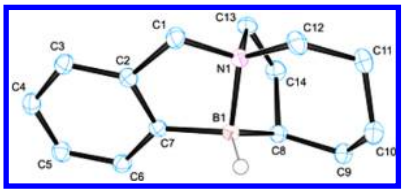


Figure 2. X-ray structure of amine−borane **30** (50% probability ellipsoids, H atoms omitted for clarity except at B). Selected bond lengths (Å) and angles (deg): B1−N1, 1.65; B1−C7, 1.61; B1−C8, 1.62; N1−B1−C7, 97; N1−B1−C8, 101.

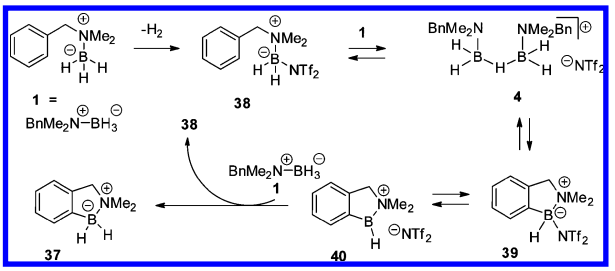
precedented[5,6] monoalkyl borenium cation **35**. Either **34** or **35** might serve as the precursor of **29** when the entire stoichiometric reaction sequence, including reductive quenching, is conducted at room temperature. However, if the borylation is conducted at 60 °C, then the activated intermediates apparently can undergo a competing retrohydroboration process. For the sake of simplicity, we assume that the borenium cation **35** undergoes retrohydroboration to generate **36**, which rapidly recloses to afford the bicyclo[4.2.1] skeleton followed by borylation of the aromatic ring (not shown). However, it is conceivable that **36** would borylate the aromatic ring faster than it hydroborates the alkene. In either case, reductive quenching would ultimately afford the doubly borylated product **30**. Precedents for facile retrohydroboration under similar thermal conditions are well-known,[9] including reported cases involving borenium equivalents generated from N-heterocyclic carbene−boranes with $HNTf_2$.[9e]

It is important to note that **30** was obtained when the borylation of **27** was performed under stoichiometric conditions at room temperature or at 60 °C *but was not detected* under catalytic conditions at 160 °C. This observation argues against the involvement of identical activated intermediates in both the catalytic and the stoichiometric experiments. Stated more explicitly, if the borenium cation **35** was responsible for the formation of **30**, then it either was not formed or was not viable in the catalytic process at 160 °C.

As discussed in the preceding sections, the catalytic activation method using $HNTf_2$ allows efficient borylation with optimal substrates such as **22**. In other, less hindered aliphatic examples, the catalytic process does not go to completion, suggesting some form of product inhibition of the catalytic cycle or a dead end decomposition pathway perhaps involving the product borenium cations. The reasons for this behavior remain unexplained in the aliphatic borylations, and the potential for retrohydroboration may be partially responsible for unknown decomposition or disproportionation events that interfere with catalyst turnover. On the other hand, aromatic borylations should be less prone to complications under catalytic conditions. The product borenium cations are somewhat more stabilized due to their "bora-benzylic" nature, involving delocalization between the aromatic π system and the planar tricoordinate boron. Furthermore, the aromatic borylation products are incapable of undergoing retrohydroboration. On the basis of these considerations, we tested the catalytic activation method with the simple *N,N*-dimethylbenzylamine−borane **1** (Scheme 3) and were pleased to find that >90% of the known borylation product **37** was formed after reductive quenching. Evidently, an efficient catalytic cycle is possible.

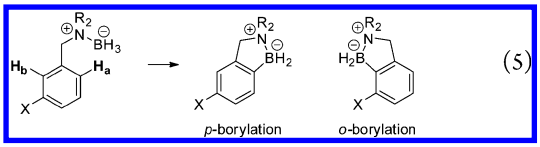
A hypothetical catalytic cycle is illustrated in Scheme 3 so that plausible intermediates can be mentioned. Although several important details are not addressed in this cycle, it does show

Scheme 3



that the key activated intermediate **38** can be regenerated from the initial borylation product **39** or its corresponding ion pair **40** as required for catalyst turnover. The cycle includes the hydride-bridged cation **4** because its presence is predicted from eq 4 and Table 1. While we have no direct evidence that **4** is the immediate precursor of **39** or **40**, our preliminary investigation of internal borylation using stoichiometric activation had found a correlation between effective electrophiles (Ph_3C^+ salts, Tf_2NH, $B(C_6F_5)_3$, or $AlCl_3$) and the generation of hydride-bridged "dimers" similar to **4**. Weaker electrophiles such as TfOH converted **1** to a tetracoordinate analogue of **38**, gave no **4**, and did not induce borylation. Intriguingly, while catalytic amounts of Tf_2NH efficiently promoted the borylation of **1** at >120 °C, essentially no cyclization was observed using a 1:1 ratio of Tf_2NH and **1**. This observation suggests that the crucial borylating agent can be formed from **4** but not by spontaneous $BNTf_2$ heterolysis from **38** ($BnMe_2N{\cdot}BH_2NTf_2$). So far, the observation remains unexplained and is particularly surprising in view of the comparable affinity of $[R_3N{-}BH_2]^+$ for $R_3N{\cdot}BH_3$ and Tf_2N^- (eq 4).

With a catalytic cycle established for the simple substrate **1** under $HNTf_2$ catalysis, the regioselectivity of aromatic borylations with several meta-substituted *N,N*-dimethylbenzylamine−boranes was investigated using similar catalytic conditions (eq 5; Table 3).[10]



(5)

Table 3. Aromatic C−H Borylation in Meta-Substituted Benzylamine−Boranes

entry	substrate	X	R	para:ortho borylation	combined yield,[a] %
1	**1**	H	Me	**37**	94
2	**41**	Cl	Me	**42**:**43**, 25:1[a] (1:1.2)[b]	93[c]
3	**44**	I	Me	**45**:**46**, 40:1[a] (1:2.4)[b]	91[c]
4	**47**	Cl	$(CH_2)_4$	**48**:**49**, 10:1[a]	95
5	**50**	F	Me	**51**:**52**, 13:1[a] (4:1)[b]	95[c]
6	**53**	PhO	Me	**54**:**55**, 10:1[a]	96

[a]Catalytic borylation conditions: 5 mol % of Tf_2NH, PhMe, sealed tube, 160 °C, 14 h, quenched with ca. 10 mol % of *n*-Bu_4NBH_4. [b]Stoichiometric borylation conditions: 0.9 equiv of $Ph_3C^+[B(C_6F_5)_4]^-$, PhBr, room temperature, 4 h, quenched with ca. 1.1 equiv of *n*-Bu_4NBH_4. [c]24 h.

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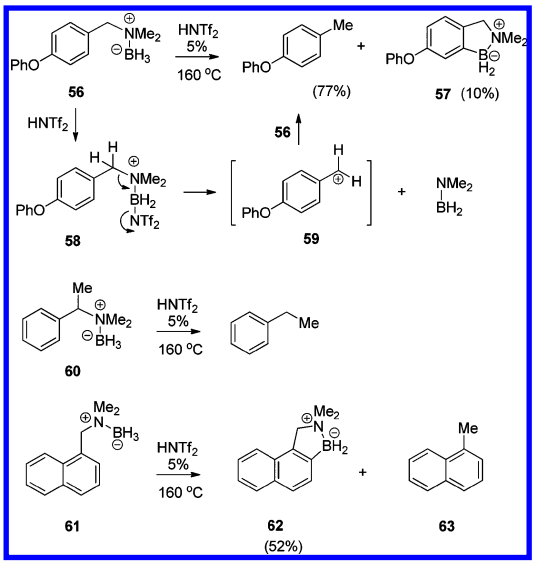
The most striking difference between the catalytic and stoichiometric borylation processes is in the opposite trends in regioselectivity for the halogenated amine−boranes **41**, **44**, and **50**. While in the catalytic process the para:ortho selectivity increases from F or Cl to I, the changes are not systematic in view of the two contrasting chlorine examples (entries 2 and 4). In the stoichiometric trityl-activated borylations at room temperature for the meta halides, the selectivity is much lower and decreases from fluoride (4:1, entry 5) to chloride (1:1.2, entry 2) but inverts for iodide (1:2.4, entry 3). It is tempting to assume that the differences in catalytic vs stoichiometric product ratios arise from thermodynamic equilibration under the high-temperature conditions, but so far all indications suggest that the catalytic borylations are kinetically controlled. Thus, the product regioisomer ratios do not change with percent conversion, and the isolated borylation products do not undergo equilibration under the reaction conditions. To support this assertion, each of the purified isomers **42** and **43** was activated with 5 mol % of Tf_2NH in d_8-PhMe, and the resulting solutions were heated at 120 °C.[11] No equilibration of pure **42** or **43** to the isomer mixture was observed, although the catalytic activation of **41** under the same conditions gave a ca. 25:1 mixture of **42**:**43**.

Since it can be argued that catalytic activation of the products **42** or **43** did not exactly mimic the borylation conditions because the starting amine−borane was not present, a modified set of experiments was also performed. Thus, mixtures of 0.1 equiv of either **42** or **43** with 1 equiv of **1** in toluene were activated with 5 mol % of Tf_2NH and then heated in sealed tubes at 160 °C. Under the reaction conditions, full conversion of **1** to **37** was observed after 10 mol % borohydride quench, but **42** and **43** were recovered unchanged. In a second control experiment under similar conditions, 0.1 equiv of **41** and 1 equiv of **1** were used along with 5% $HNTf_2$. This time, a mixture of the cyclized products **37**, **42**, and **43** was formed, and the ratio of **42** and **43** was found to be the same as in the cyclization of **41** with no **1** present (ca. 25:1 **42**:**43**). This suggests that the starting amine−borane **41** cyclizes to form a mixture of **42** and **43** under the indicated conditions, while the interconversion of the two isomers does not occur. In this series of experiments, the cyclization of **1** to **37** serves not only to mimic the actual cyclization conditions but also to act as a probe confirming that the catalytic cycle is viable.

The rates of the catalytic borylation are qualitatively insensitive to the electronic effects in the substrate. In an attempt to estimate the rate effect caused by a phenoxy group positioned para with respect to the C−H bond that undergoes borylation (i.e., the *m*-PhO-benzylamine substrate), a 1:1 mixture of **1** and **53** (Table 3) activated with 10% $HNTf_2$ in d_8-PhMe was heated at 120 °C. The relative rates of consumption of both amine−boranes were monitored in situ using NMR spectroscopy and were found to be similar (equal, within experimental uncertainty).

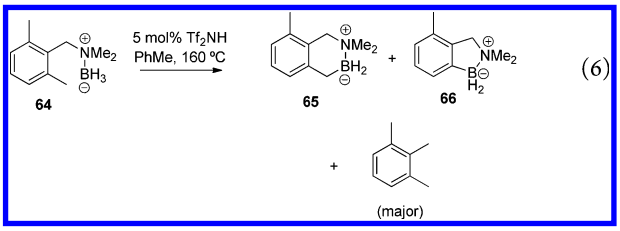
In sharp contrast to the high-yielding cyclization of the *m*-PhO substrate **53** (96% isolated yield of **54** + **55**), the cyclization of the corresponding para isomer **56** delivered only 10% of the expected **57**, while the major product was found to be *p*-phenoxytoluene (77% isolated; the only other product detected in the crude mixture was the dimer of Me_2NBH_2) (Scheme 4). To explain the net hydrodeamination from **56**, we suggest that activation produces **58** as usual, followed by fragmentation to the stabilized benzylic cation **59** that abstracts hydride from the starting **56**. Similar hydrodeamination was observed during attempted borylation of α-methylbenzylamine derivative **60** to

Scheme 4. Benzylic Amine−Borane Hydrodeamination



give ethyltoluene and, to a lesser extent, for 1-(dimethylaminomethyl)naphthalene−borane (**61**). In the latter case, the expected borylation product **62** was obtained in 52% yield, while 1-methylnaphthalene **63** and $(Me_2N{-}BH_2)_2$ constituted the rest of the crude reaction mixture according to NMR and GC-MS assay. Overall, it appears that C−N fragmentation predominates in those cases where a reasonably stable carbocation can be formed.

While a substantial degree of C−N cleavage (ca. 70%) was observed in the catalytic borylation of ortho,ortho′-disubstituted amine−borane **64**, this substrate also presented an unusual case of C−C bond reactivity (eq 6). Thus, aside from the 1,2,3-



trimethylbenzene and the expected aliphatic borylation product **65**, a small amount of the C-demethylation product **66** (ca. 6.3:1 **65**:**66**) was isolated and identified by comparison with an authentic sample.[2] The mechanism of this process was not investigated, but the observed demethylation can be understood as an insertion of electrophilic tricoordinate boron into a C−C bond, forming CH_4 as the byproduct.[12,13]

The success of small-scale catalytic aromatic borylations in the substituted benzylamine−borane series prompted experiments to develop a larger scale (3−4 g) reaction protocol featuring a more scalable isolation procedure. Performing the reaction with 5% $HNTf_2$ in dry tetralin at 180 °C obviated the need for sealed glass tubes, and removal of tetralin was accomplished by precipitating the crude product with hexane. Subsequent extraction of the crude solid with either toluene (**37**) or THF/Et_2O (**45**) separated the products from insoluble Tf_2N derivatives, affording pure products **37** (77% after crystallization) and **45** (95%).[14]

Having demonstrated gram-scale access to representative aromatic borylation products, we briefly tested their conversion to arylboronic acid derivatives that are potentially useful

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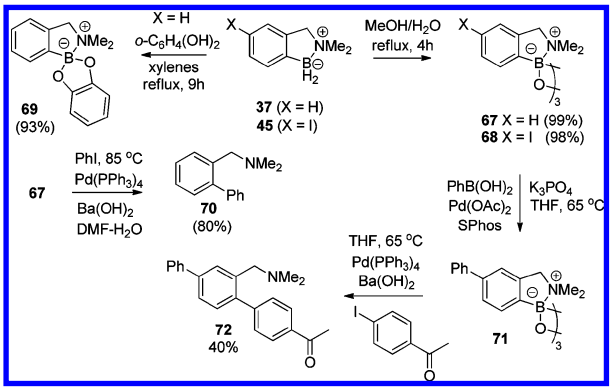
substrates for transition-metal-catalyzed cross-coupling reactions. Thus, refluxing amine−boranes **37** and **45** in aqueous MeOH for 4 h followed by concentration and azeotropic removal of water furnished cyclic boroxines **67** and **68**, respectively, in nearly quantitative yields (Scheme 5). Alternatively, refluxing **37** with catechol in xylenes afforded the catechol ester **69** in 93% yield after crystallization.

Scheme 5. Cross-Couplings of 67 and 68



Attempts to use boronic anhydride **67** in Suzuki−Miyaura cross coupling indicated that its reactivity is somewhat lower in comparison to that of arylboronic acids (Scheme 5). Thus, **67** could be efficiently coupled with $PhI/Pd(PPh_3)_4$ in DME/H_2O using $Ba(OH)_2{\cdot}8H_2O$ as base (82% of **70** isolated), but no coupling was observed using $K_3PO_4/Pd(OAc)_2$/SPhos in THF, conditions that are known to effect the cross-coupling of aryl iodides with $PhB(OH)_2$.[15] This suggested the possibility of using **68** in a sequence of two distinct Suzuki−Miyaura coupling events. The added base was identified as the crucial variable determining the reactivity of the C−B bond of **67**, and a protocol for a selective two-stage cross coupling of **68** with $PhB(OH)_2$ was developed. First, **68** was reacted with $PhB(OH)_2$ using $K_3PO_4/Pd(OAc)_2$/SPhos in THF, the same conditions that gave no coupling with **67**. Selective coupling was evident from the ^1H NMR spectrum of the crude reaction mixture, suggesting that only a single benzylamine derivative (**71**) was present. In the second stage, $Ba(OH)_2{\cdot}8H_2O$ was used to activate the boroxine moiety of **71**, and this enabled cross-coupling with added 4-iodoacetophenone. While the unoptimized isolated yield of **72** is modest (40%), the goal of this sequence was to illustrate the potential of the bifunctional coupling partner **68** for selective sequential attachment of two distinct aromatic substituents. The analogy between these results and selective coupling reactions of MIDA-protected boronates[16] suggests that the pendant (dimethylamino)methyl moiety is responsible for the decreased boroxine reactivity in **68**.

SUMMARY

Catalytic borylation conditions (5% $HNTf_2$, 160 °C) have been developed that allow intramolecular borylation starting from tertiary amine−boranes. The reactions of aliphatic amine−boranes are shown to have a preference for 5-membered-ring formation, although 6-membered rings can be formed with biased substrates. Retrohydroboration appears to be possible under the reaction conditions and is responsible for skeletal isomerization during the borylation step from **29** to **30**. Two sequential borylations are demonstrated starting from amine−boranes **19** and **27**.

The same catalytic conditions are especially effective for amine-directed aromatic borylation and generally give yields well above 90%. The catalytic method is more practical than an earlier variation using stoichiometric $Ph_3C^+B(C_6F_5)_4^-$ (**2**) for hydride abstraction from the amine−borane.[1,2] The catalytic reactions also give considerably higher regioselectivity with meta-substituted benzylamine−boranes. Conversion of the borylation products into arylboronic acid derivatives is possible and is illustrated in selective Suzuki−Miyaura cross-coupling reactions.

EXPERIMENTAL SECTION

General Remarks. All reactions were performed at room temperature (unless otherwise stated), under an atmosphere of dry nitrogen, either in a glovebox or using standard Schlenk techniques. Nuclear magnetic resonance experiments were performed on Varian Inova 700, Varian Inova 500, and Inova 400 spectrometers at the following frequencies: ^1H, 700, 500, or 400 MHz; ^{11}B and $^{11}B\{^1H\}$, 225, 160, or 128 MHz; $^{13}C\{^1H\}$, 176, 126, or 101 MHz; ^{19}F, 471 MHz. All spectra were recorded in $CDCl_3$, d_5-PhBr, or CD_2Cl_2 and referenced to the ^1H signal of internal Me_4Si according to IUPAC recommendations,[17] using a Ξ (referencing parameter) value of 32.083974 for $BF_3{\cdot}OEt_2$ (^{11}B), a Ξ value of 25.145020 for Me_4Si (^{13}C), and a Ξ value of 94.094011 for CCl_3F (^{19}F). When the internal Me_4Si reference could not be used, residual solvent peaks in ^1H NMR spectra were referenced instead. Hexanes, CH_2Cl_2, and THF were dried by passing through a column of activated alumina. Hexanes and CH_2Cl_2 were further dried by storing over activated 3 Å molecular sieves in the glovebox. Commercially available NMR grade deuterated solvents (Cambridge Isotope Laboratories) as well as benzene and fluorobenzene were not distilled; instead, they were simply dried over a large amount of activated 3 Å molecular sieves in the glovebox. All other reagents were used as received from commercial suppliers or prepared according to published procedures.

Amine−Borane Activations with Tf_2NH. In Situ NMR Study. Every possible effort was made to protect the reaction mixtures from exposure to air and moisture. The reactions were set up in dry J. Young NMR tubes under an N_2 atmosphere in a glovebox. The NMR tubes were dried in a heating oven at ca. 200 °C overnight, and the fitted Teflon valves were dried in a desiccator over Drierite. Commercial grade Tf_2NH and amine−boranes ($Me_3N{\cdot}BH_3$ (**11a**), $Et_3N{\cdot}BH_3$ (**11b**), and $(i\mathrm{Pr})_2EtN{\cdot}BH_3$ (**11c**)) were used without further purification. The benzylic amine−borane *p*-$MeC_6H_4CH_2NMe_2{\cdot}BH_3$ (**11d**)[2] and 1-neopentylpyrrolidine−borane (**11e**)[5] were prepared as reported previously. Commercial grade CD_2Cl_2 and d_8-PhMe (Cambridge Isotope Laboratories) were not distilled but simply dried with freshly activated molecular sieves in the glovebox.

When solid amine−boranes were used ($Me_3N{\cdot}BH_3$ (**11a**), *p*-$MeC_6H_4CH_2NMe_2{\cdot}BH_3$ (**11d**), 1-neopentylpyrrolidine−borane (**11e**)), the reaction tube was charged with a mixture of solid Tf_2NH and the corresponding amine−borane. The solid mixture was dissolved by adding the solvent (either 0.6 mL of CD_2Cl_2 or 0.8 mL of d_8-PhMe) to the tube in one portion at room temperature. Gas liberation was observed, although no substantial exotherm was noted, potentially due to the small scale of the reaction. The tube was sealed with a fitted Teflon valve and then shaken vigorously for ca. 1 min. The amounts of the reagents used in each particular case are listed below.

When liquid amine−boranes were used ($Et_3N{\cdot}BH_3$ (**11b**) and $(i\mathrm{Pr})_2EtN{\cdot}BH_3$ (**11c**)), the reaction tube was charged with a solution of Tf_2NH in 0.6 mL of CD_2Cl_2. Neat amine−borane was then added to the solution via a microsyringe at room temperature, causing intense gas liberation, although no substantial exotherm was noted, potentially due to the small scale of the reaction. The tube was sealed with a fitted Teflon valve and then shaken vigorously for ca. 1 min. The amounts of the reagents used in each particular case are listed below.

The ratios of N- to O-bound isomers of the products were measured by NMR after the initial equilibration had completed and were confirmed to remain stable for 2−14 days at room temperature.

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12a:**13a**, 7:1 ratio after equilibration. The following reagents were used: trimethylamine−borane (**11a**; 8.0 mg, 0.109 mmol), Tf_2NH (30.7 mg, 0.109 mmol), CD_2Cl_2 (0.6 mL). **12a**: ^1H NMR (500 MHz, CD_2Cl_2) δ 3.2−1.9 (br m, 2H), 2.65 ppm (s, 9H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ −3.7 ppm (t, J = 115 Hz); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 119.6 (q, J_{C-F} = 326 Hz), 51.8 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −69.2 ppm (s). **13a**: ^1H NMR (500 MHz, CD_2Cl_2) δ 3.2−1.9 (br m, 2H), 2.69 ppm (s, 9H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ 4.0 ppm (t, J = 120 Hz); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 119.1 (q, J_{C-F} = 320 Hz), 118.7 (q, J_{C-F} = 321 Hz), 49.7 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −76.6 (s), −79.1 ppm (s).

12b:**13b**, 1:4.7 ratio after equilibration. The following reagents were used: triethylamine−orane (**12b**; 13.3 μL, 90.7 μmol), Tf_2NH (25.5 mg, 90.7 μmol), CD_2Cl_2 (0.6 mL). **12b**: ^1H NMR (500 MHz, CD_2Cl_2) δ 3.4−1.9 (br m, 2H), 2.88 (q, J = 7.2 Hz, 6H), 1.21 ppm (t, J = 7.2 Hz, 9H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ −7.4 ppm (unres t); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 119.6 (q, J_{C-F} = 327 Hz), 49.8, 8.2 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −68.9 ppm (s). **13b**: ^1H NMR (500 MHz, CD_2Cl_2) δ 3.4−1.9 (br m, 2H), 2.90 (q, J = 7.2 Hz, 6H), 1.21 ppm (t, J = 7.2 Hz, 9H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ 0.7 ppm (unres t); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 119.2 (q, J_{C-F} = 320 Hz), 118.7 (q, J_{C-F} = 321 Hz), 49.2, 7.5 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −76.7 (s), −79.1 ppm (s).

12c:**13c**, <1:25 ratio after equilibration. The following reagents were used: $(i\text{Pr})_2\text{EtN}\cdot BH_3$ (**11c**; 26.7 μL, 0.153 mmol), Tf_2NH (43.0 mg, 0.153 mmol), CD_2Cl_2 (0.6 mL). Due to the low concentration of the N-bound isomer **12c** in solution, only ^{19}F signals were assigned. **12c**: ^{19}F NMR (471 MHz, CD_2Cl_2) δ −68.4 ppm (s). **13c**: ^1H NMR (500 MHz, CD_2Cl_2) δ 3.70−3.60 (m, 2H), 3.4−2.1 (br m, 2H), 3.01 (q, J = 7.3 Hz, 2H), 1.37−1.33 (m, 12H), 1.26 ppm (t, J = 7.3 Hz, 3H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ 1.2 ppm (unres t); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 119.2 (q, J_{C-F} = 321 Hz), 118.7 (q, J_{C-F} = 321 Hz), 56.7, 56.6, 45.3, 18.3 (overlapping s), 9.5 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −77.0 (s), −79.1 ppm (s).

12d:**13d**, 4.2:1 ratio after equilibration. The following reagents were used: $p\text{-MeC}_6H_4CH_2NMe_2\cdot BH_3$ (**11d**; 23.0 mg, 0.141 mmol), Tf_2NH (39.6 mg, 0.141 mmol), CD_2Cl_2 (0.6 mL). **12d**: ^1H NMR (500 MHz, CD_2Cl_2) δ 7.30−7.17 (m, 4H), 3.96 (s, 2H), 3.3−2.0 (br m, 2H), 2.48 (s, 6H), 2.39 ppm (s, 3H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ −3.2 ppm (unres t); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 140.0, 132.5, 129.4, 125.5, 119.7 (q, J_{C-F} = 326 Hz), 64.9, 46.8, 20.9 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −69.0 ppm (s). **13d**: ^1H NMR (500 MHz, CD_2Cl_2) δ 7.30−7.17 (m, 4H), 3.99−3.97 (m, 2H), 3.3−2.0 (br m, 2H), 2.54 (s, 3H), 2.53 (s, 3H), 2.39 ppm (s, 3H); ^{11}B NMR (160 MHz, CD_2Cl_2) δ 4.0 ppm (unres t); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 140.3, 132.3, 129.5, 125.1, 119.2 (q, J_{C-F} = 321 Hz), 118.8 (q, J_{C-F} = 321 Hz), 63.5, 45.5, 45.4, 20.9 ppm; ^{19}F NMR (471 MHz, CD_2Cl_2) δ −76.6 (s), −79.1 ppm (s).

12e:**13e**, 1:2.6 ratio after equilibration. The following reagents were used: 1-neopentylpyrrolidine−borane (**11e**; 10.9 mg, 70.3 μmol), Tf_2NH (19.8 mg, 70.3 μmol), d_8-PhMe (0.8 mL). **12e**: ^1H NMR (700 MHz, d_8-PhMe) δ 3.2−2.3 (br m, 2H), 3.01−2.94 (m, 2H), 2.60−2.55 (m, 2H), 2.44 (s, 2H), 1.57−1.42 (m, 2H), 1.22−1.11 (m, 2H), 0.73 ppm (s, 9H); ^{11}B NMR (225 MHz, d_8-PhMe) δ −4.6 ppm (unres t); ^{13}C NMR (176 MHz, d_8-PhMe) δ 120.5 (q, J_{C-F} = 327 Hz), 68.8, 57.8, 33.0, 30.3, 22.0 ppm; ^{19}F NMR (471 MHz, d_8-PhMe) δ −69.2 ppm (s). **13e**: ^1H NMR (700 MHz, d_8-PhMe) δ 3.2−2.3 (br m, 2H), 3.01−2.94 (m, 1H), 2.79−2.74 (m, 1H), 2.33 (d, J = 13.7 Hz, 1H), 2.08 (d, J = 13.7 Hz, 1H), 1.98−1.93 (m, 1H), 1.93−1.86 (m, 1H), 1.57−1.42 (m, 2H), 1.22−1.11 (m, 2H), 0.78 ppm (s, 9H); ^{11}B NMR (225 MHz, d_8-PhMe) δ 0.6 ppm (unres t); ^{13}C NMR (176 MHz, d_8-PhMe) δ 120.2 (q, J_{C-F} = 320 Hz), 119.6 (q, J_{C-F} = 320 Hz), 72.2, 60.4, 59.4, 33.1, 29.7, 22.6, 22.1 ppm; ^{19}F NMR (471 MHz, d_8-PhMe) δ −76.7 (s), −78.7 ppm (s).

Preparation of Borylation Substrates. *Preparation of **16**. N-(3,3-Dimethylbutyl)pivalamide.* Pivaloyl chloride (2.68 mL, 2.62 g, 21.7 mmol) in 20.0 mL of CH_2Cl_2 was slowly added to a stirred solution of 3,3-dimethylbutan-1-amine (2.00 g, 19.8 mmol) and Et_3N (3.0 mL, 2.20 g, 21.7 mmol) in 20.0 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for 6 h, following which it was acidified with 1 N HCl and extracted with CH_2Cl_2. The organic extracts were washed twice with saturated $NaHCO_3$ solution and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting amide (2.49 g, 68%) was used in subsequent transformations without further purification. The expected structure was confirmed by ^1H NMR spectroscopy. ^1H NMR (500 MHz, $CDCl_3$): δ 5.52 (s, 1H), 3.30−3.18 (m, 2H), 1.43−1.37 (m, 2H), 1.18 (s, 9H), 0.93 ppm (s, 9H).

*Amine−Borane **16**.* The commercially available KH suspension in mineral oil (30 wt %, 0.78 g, 5.82 mmol) was shaken vigorously, and the resulting slurry was quickly transferred to a flask with a pipet and weighed; the flask was then immediately sealed with a septum and purged with dry nitrogen. Anhydrous THF (10.0 mL) was added to the flask, and a solution of *N*-(3,3-dimethylbutyl)pivalamide (980 mg, 5.29 mmol) in 10.0 mL of THF was then added dropwise. The reaction mixture was stirred for 1 h at room temperature. Ethyl iodide (0.47 mL, 907 mg, 5.82 mmol) was added dropwise, and the reaction mixture was stirred for an additional 5 h at room temperature, following which it was carefully quenched with isopropyl alcohol and diluted with water. The reaction mixture was extracted three times with EtOAc, and the combined organic extracts were washed with brine and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow oil was dissolved in 10.0 mL of anhydrous THF and treated with $Me_2S\cdot BH_3$ (0.95 mL, 9.52 mmol). The addition of the borane complex resulted in an exothermic reaction after a short induction period. After the exothermic reaction had ceased, the reaction mixture was refluxed for 1 h, following which it was filtered through a short (2−3 cm) plug of silica, while eluting with CH_2Cl_2, to decompose the residual $Me_2S\cdot BH_3$. Crystallization from hexanes afforded 0.691 g (61%) of **16** as a white crystalline solid, mp 49 °C (hexanes). ^1H NMR (500 MHz, $CDCl_3$): δ 3.02−2.90 (m, 2H), 2.89−2.79 (m, 2H), 2.70 (AB q, J = 14.3 Hz, 2H), 1.9−1.1 (br m, 3H), 1.71−1.55 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H), 1.15 (s, 9H), 0.93 ppm (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 69.4, 57.0, 55.0, 36.2, 33.6, 31.0, 29.9, 29.4, 9.4 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −11.79 ppm (q, J = 90 Hz). HRMS (EI): m/z calcd for $C_{13}H_{30}N$ $[M - BH_3 + H]^+$ 200.2373, found 200.2376 (+1 ppm). IR ($CDCl_3$, NaCl): 3258, 2954, 2865, 1465, 1364, 1311, 1215, 1027 cm^{-1}.

*Preparation of **19**.* This compound was prepared following the procedure given above for the preparation of **16**, using BnBr (0.549 mL, 789 mg, 4.61 mmol) instead of EtI. Yield: 0.685 g (59%) of a white crystalline solid, mp 107 °C (hexanes). ^1H NMR (500 MHz, $CDCl_3$): δ 7.48−7.43 (m, 2H), 7.38−7.33 (m, 3H), 4.11 (d, J = 12.9 Hz, 1H), 3.96 (d, J = 12.9 Hz, 1H), 2.98−2.88 (m, 1H), 2.79 (d, J = 13.9 Hz, 1H), 2.73 (td, J = 12.1, 5.7 Hz, 1H), 2.61 (d, J = 13.9 Hz, 1H), 2.0−1.3 (br m, 3H), 1.84−1.72 (m, 2H), 1.19 (s, 9H), 0.90 ppm (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 132.8, 132.1, 128.7, 127.9, 70.6, 66.0, 56.4, 36.6, 33.7, 31.2, 30.1, 29.5 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −11.23 ppm (q, J = 70 Hz). HRMS (EI): m/z calcd for $C_{18}H_{32}N$ $[M - BH_3 + H]^+$ 262.2529, found 262.2534 (+2 ppm). IR ($CDCl_3$, NaCl): 2958, 2867, 2383, 2335, 2283, 2242, 1455, 1364, 1172 cm^{-1}.

*Preparation of **22**. 1-Benzylazacycloundecan-2-one.* The commercially available KH suspension in mineral oil (30 wt %, 1.54 g, 11.5 mmol) was shaken vigorously, and the resulting slurry was quickly transferred to a flask with a pipet and weighed and then immediately sealed with a septum and purged with dry nitrogen. Anhydrous THF (10.0 mL) was added to the flask, and a solution of undecan-2-one (1.77 g, 10.5 mmol) in 20.0 mL of THF was then added dropwise. The reaction mixture was stirred for 1 h at room temperature. Benzyl bromide (1.50 mL, 2.15 g, 12.6 mmol) was then added dropwise, and the reaction mixture was stirred for an additional 8 h at room temperature and then carefully quenched with isopropyl alcohol and diluted with water. The reaction mixture was extracted three times with EtOAc, and the combined organic extracts were washed with brine and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (10/1 hexanes/EtOAc) afforded 2.45 g (90%) of the amide as a white powder. The product was obtained as a mixture of *E*/*Z* amide isomers at room temperature, which prevented accurate assignment of the peaks and their integral values. ^1H NMR (500 MHz, $CDCl_3$): δ 7.36−7.22 (m), 7.16 (d, J = 7.3 Hz), 5.00 (d, J = 16.7 Hz), 4.63 (s), 4.46−4.39 (m), 4.36 (d, J = 16.7 Hz), 3.43 (s), 2.65−2.45 (m), 2.22−2.11 (m), 1.94−1.63

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(m), 1.64−1.19 ppm (m). ^{13}C NMR (126 MHz, $CDCl_3$): δ 175.5, 173.8, 137.8, 137.2, 128.8, 128.5, 128.3, 127.5, 127.2, 126.4, 51.7, 46.5, 46.3, 44.9, 34.0, 29.3, 27.3, 26.3, 25.7, 25.14, 25.07, 25.0, 24.9, 24.7, 24.3, 24.1, 23.8, 23.6, 22.6 ppm. HRMS (ES+): m/z calcd for $C_{17}H_{26}NO$ $[M + H]^+$ 260.2009, found 260.2011 (+1 ppm).

Amine−Borane ***22***. Dry 1-benzylazacycloundecan-2-one (2.41 g, 9.3 mmol) was dissolved in 9.3 mL of anhydrous THF and then treated with $Me_2S{\cdot}BH_3$ (1.7 mL, 17 mmol). The addition of the borane complex resulted in an exothermic reaction after a short induction period. After the exothermic reaction had ceased, the reaction mixture was refluxed for 1 h, following which it was filtered through a short (2−3 cm) plug of silica, while eluting with CH_2Cl_2, to decompose the residual $Me_2S{\cdot}BH_3$. Crystallization of the crude product from hexanes afforded 1.71 g (71%) of pure **22** as a white crystalline solid, mp 103 °C (hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.46 (m, 2H), 7.36−7.31 (m, 3H), 3.81 (s, 2H), 3.03−2.91 (m, 2H), 2.89−2.75 (m, 2H), 1.9−1.1 (br m, 3H), 1.79−1.66 (m, 4H), 1.56−1.33 ppm (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 133.0, 131.9, 128.7, 127.7, 65.8, 56.5, 25.3, 24.9, 24.5, 20.3 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −12.0 ppm (q, J = 75 Hz). HRMS (EI): m/z calcd for $C_{17}H_{28}N$ $[M - BH_3 + H]^+$ 246.2216, found 246.2221 (+2 ppm). IR ($CDCl_3$, NaCl): 2927, 2894, 2845, 2408, 2343, 2287, 1481, 1453, 1172, 742, 696 cm^{-1}.

N-Ethylheptamethyleneimine−Borane ***(24)***. Acetic anhydride (0.86 mL, 0.93 g, 9.14 mmol) was added dropwise to a solution of heptamethyleneimine (0.941 g, 8.31 mmol) in 5 mL of anhydrous CH_2Cl_2. Triethylamine (2 mL) was added to the mixture, and the resulting solution was stirred overnight at room temperature. Following concentration under reduced pressure the residue was partitioned between CH_2Cl_2 and 10% NaOH solution (10 mL), and the aqueous layer was additionally extracted with 2 × 10 mL of CH_2Cl_2. The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residual oil was dissolved in anhydrous THF (10 mL), and $Me_2S{\cdot}BH_3$ (1.4 mL, 14 mmol) was then added. The addition of the borane complex resulted in an exothermic reaction after a short induction period. After the exothermic reaction had ceased, the reaction mixture was refluxed for 1 h, following which it was quenched with water (*frothing!*) and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography (∼150 mL silica gel, PhMe) afforded 0.591 g (49%) of a colorless oil. ^{1}H NMR (700 MHz, $CDCl_3$): δ 3.14−3.09 (m, 2H), 2.82−2.78 (m, 2H), 2.78 (q, J = 7.2 Hz, 2H), 1.91−1.83 (m, 2H), 1.8−1.2(br m, 3H), 1.78−1.65 (m, 5H, integral intensity somewhat uncertain due to overlap with B−H signal), 1.59−1.45 (m, 3H, integral intensity uncertain due to overlap with B−H signal), 1.29 ppm (t, J = 7.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 56.0, 55.3, 27.4, 25.2, 22.9, 9.6 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −12.3 ppm (q, J = 100 Hz). IR ($CDCl_3$, NaCl): 2926, 2378, 2278, 1482, 1448, 1175, 1038 cm^{-1}.

N-Benzylheptamethyleneimine−Borane ***(27)***. Benzoyl chloride (1.44 mL, 1.73 g, 12.3 mmol) in 12.0 mL of CH_2Cl_2 was slowly added to a solution of heptamethyleneimine (1.27 g, 11.2 mmol) and Et_3N (2.35 mL, 1.70 g, 16.8 mmol) in 12.0 mL of CH_2Cl_2 at room temperature. After 18 h at room temperature the reaction mixture was acidified with 1 N HCl and extracted with CH_2Cl_2. The organic phase was washed with saturated $NaHCO_3$ solution and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting dark yellow oil was dissolved in 11 mL of anhydrous THF and then treated with $Me_2S{\cdot}BH_3$ (2.1 mL, 21 mmol). The addition of the borane complex resulted in an exothermic reaction after a short induction period. After the exothermic reaction had ceased, the reaction mixture was refluxed for 1 h, following which it was filtered through a short (2−3 cm) plug of silica, while eluting with CH_2Cl_2, to decompose the residual $Me_2S{\cdot}BH_3$. Crystallization of the crude product from hexanes afforded 2.20 g (90%) of the pure product as a white crystalline solid, mp 76 °C (hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51−7.42 (m, 2H), 7.40−7.31 (m, 3H), 3.87 (s, 2H), 3.10−2.92 (m, 4H), 2.01 (m, 2H), 1.9−1.2 (br m, 3H), 1.77−1.65 (m, 1H), 1.66−1.43 ppm (m, 7H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 132.8, 132.0, 128.7, 127.8, 67.0, 55.5, 27.2, 25.3, 23.5 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −11.7 ppm (q, J = 93 Hz). HRMS (EI): m/z calcd for $C_{14}H_{22}N$ $[M - BH_3 + H]^+$ 204.1747, found 204.1751 (+2 ppm). IR ($CDCl_3$, NaCl): 2993, 2952, 2916, 2871, 2860, 2398, 2334, 2275, 1482, 1454, 1177, 1168, 748, 695 cm^{-1}.

N,N-Dimethyl-3-iodobenzylamine−Borane ***(44)***. This compound was prepared according to the previously published procedure for substituted *N,N*-dimethylbenzylamine−borane complexes from *m*-iodobenzyl bromide.[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (dt, J = 8.0, 1.5 Hz, 1H), 7.69 (t, J = 1.5 Hz, 1H), 7.34−7.31 (m, 1H), 7.15 (t, J = 8.0 Hz, 1H), 3.91 (s, 2H), 2.52 (s, 6H), 2.2−1.4 ppm (br m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.9, 138.2, 133.5, 131.5, 130.1, 94.1, 66.8, 49.9 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −8.2 ppm (q, J = 90 Hz). HRMS (EI): m/z calcd for $[M - 3H]^+$ 272.0108, found 272.0108 (0 ppm).

N,N-Dimethyl-3-chlorobenzylamine−Borane ***(47)***. Neat pyrrolidine (20 mL, 17.4 g, 0.245 mol) was added slowly to a stirred solution of 3-chlorobenzyl bromide (1.96 g, 9.54 mmol) in MeOH (10 mL) at 0 °C. Upon full consumption of the bromide the reaction mixture was concentrated under vacuum, and the residue was dissolved in 10 mL of 6 M HCl. The solution was washed with 3 × 10 mL of Et_2O (washes discarded) and then carefully made strongly basic by adding NaOH. The reaction mixture was then extracted with Et_2O, and the combined extracts were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Treatment of the resulting oil with $Me_2S{\cdot}BH_3$ (0.96 mL, 9.5 mmol) in CH_2Cl_2 afforded a clear solution, which was concentrated under reduced pressure. Dissolution of the crude product in $CHCl_3$ followed by filtration through a fine frit afforded a white solid after concentration. Crystallization of the solid from cyclohexane/$CHCl_3$ produced 1.57 g (79%) of the desired amine−borane. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41−7.39 (m, 1H), 7.39−7.35 (m, 1H), 7.34−7.29 (m, 2H), 3.99 (s, 2H), 3.16−3.05 (m, 2H), 2.88−2.78 (m, 2H), 2.28−2.12 (m, 2H), 2.1−1.2 (br m, 3H), 1.89−1.74 ppm (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 134.1, 133.9, 132.4, 130.8, 129.4, 129.1, 64.9, 59.2, 22.5 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −11.1 ppm (q, J = 95 Hz). HRMS (ES+): m/z calcd for $[M + Na]^+$ 232.1040, found 232.1042 (+1 ppm).

N,N-Dimethyl-3-phenoxybenzylamine−Borane ***(53)***. A solution of 3-phenoxybenzoic acid (2.14 g, 10 mmol) in 20 mL of $SOCl_2$ was refluxed for 3.5 h. Unreacted $SOCl_2$ was distilled off, and the residual oil was dissolved in 20 mL of CH_2Cl_2. The acid chloride solution was then added dropwise to 40% aqueous Me_2NH (40 mL) at 0 °C, and the resulting mixture was stirred at room temperature for several hours. The reaction mixture was then carefully acidified with 10% aqueous HCl and extracted with 3 × 40 mL of CH_2Cl_2. The combined extracts were washed with 10% NaOH, dried with $MgSO_4$, concentrated, and dried under vacuum. The crude amide was dissolved in 25 mL of THF and then treated with $BH_3{\cdot}SMe_2$ (3.0 mL). After a brief induction period an exothermic reaction followed. The reaction mixture was then refluxed for 1 h, diluted with hexanes (∼20 mL), and left in the freezer overnight. The slurry was filtered through a glass frit, and the clear solution was then passed through a short plug of silica, while eluting with CH_2Cl_2. Concentration of the solution afforded a clear oil, which was crystallized from $CHCl_3$/hexanes, affording 1.90 g (79%) of a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.32 (m, 3H), 7.16−7.11 (t, J = 7.3 Hz, 1H), 7.08−6.99 (m, 4H), 6.97 (s, 1H), 3.94 (s, 2H), 2.51 (s, 6H), 2.2−1.2 ppm (br m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.4, 156.7, 133.1, 129.9, 129.7, 126.9, 123.8, 122.4, 119.2, 119.0, 67.2, 49.8 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −8.2 ppm (q, J = 80 Hz). HRMS (ES): m/z calcd for $C_{15}H_{20}BNONa$ $[M + Na]^+$ 264.1530, found 264.1532. Mp: 68 °C ($CHCl_3$/hexanes).

N,N-Dimethyl-4-phenoxybenzylamine−Borane ***(56)***. This compound was prepared following the procedure given above for the preparation of **53**, using 4-phenoxybenzoic acid (2.14 g, 10 mmol) instead of 3-phenoxybenzoic acid. It was crystallized by dissolving the crude product oil in cyclohexane and allowing the solution to stand at room temperature overnight. Yield: 1.36 g (56%) of **56**, mp 144 °C (hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40−7.33 (m, 2H), 7.27 (m, 2H), 7.18−7.13 (m, 1H), 7.06−7.02 (m, 2H), 7.02−6.97 (m, 2H), 3.95 (s, 2H), 2.51 (s, 6H), 2.1−1.5 ppm (br m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 158.4, 156.3, 133.7, 129.9, 125.7, 124.0, 119.5, 118.0, 66.9, 49.7 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −8.5 ppm (q, J = 70

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Hz). HRMS (EI): m/z calcd for $C_{15}H_{18}NO$ [M − BH_3 + H]$^+$ 228.1383, found 228.1382. IR ($CDCl_3$, NaCl): 3003, 2949, 2373, 2324, 2272, 2248, 1589, 1508, 1489, 1243, 1168, 1017 cm^{-1}.

*N,N-Dimethyl-1-naphthylmethylamine−Borane (**61**).* This compound was prepared according to the previously published procedure for substituted *N,N*-dimethylbenzylamine−borane complexes from 1-(chloromethyl)naphthalene.[2] ^{1}H NMR (500 MHz, $CDCl_3$): 8.31 (d, J = 8.5 Hz, 1H), 7.95−7.88 (m, 2H), 7.59 (ddd, J = 8.2, 6.8, 1.4 Hz, 1H), 7.55−7.48 (m, 3H), 4.55 (s, 2H), 2.53 (s, 6H), 2.6−1.6 ppm (br m, 3H). ^{11}B NMR (128 MHz, $CDCl_3$): δ −7.7 ppm (q, J = 95 Hz).

*N,N-Dimethyl-2,6-dimethylbenzylamine−Borane (**64**).* This compound was prepared according to the previously published procedure for substituted *N,N*-dimethylbenzylamine−borane complexes from 2,6-dimethylbenzyl chloride.[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (dd, J = 8.2, 6.9 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 4.26 (s, 2H), 2.52 (s, 6H), 2.44 (s, 6H), 2.3−1.5 ppm (br m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.8, 129.2, 128.9, 128.7, 59.4, 50.1, 21.6 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ −7.7 ppm (q, J = 95 Hz). HRMS (ES+): m/z calcd for $C_{11}H_{18}N$ [M − BH_3 + H]$^+$ 164.1434, found 164.1431 (−2 ppm).

Intramolecular C−H Borylation. General Procedures. *Small-Scale Activation.* Stoichiometric borylations using 0.9 equiv of $Ph_3C[B(C_6F_5)_4]$ were performed as described in the previously published procedure.[2] Catalytic activation used the previously published procedure as follows.[5] A dry 12 mL thick-walled Schlenk tube fitted with a Teflon stopper was charged with a mixture of solid amine−borane (1.32 mmol) and Tf_2NH (18.6 mg, 66.2 μmol). Solvent (3 mL) was then added, and some minor frothing due to gas formation was observed. The gas which formed during the initial activation stage was identified as H_2 in an in situ NMR study. After H_2 liberation ceased, and the gas was allowed to escape the reaction vessel, the tube was sealed and heated at 160 °C (bath) for the indicated time. When liquid amine−borane complexes were used, the substrate was first dissolved in 1 mL of the solvent, and then Tf_2NH and the additional solvent were added. The reaction mixture was quenched by adding solid n-Bu_4NBH_4 (~30 mg) under an N_2 atmosphere. The mixture was then diluted with CH_2Cl_2 and filtered through a short plug of silica, with CH_2Cl_2 or $CHCl_3$ as eluent. The products were isolated by concentration of the solution, followed by crystallization or chromatography to isolate pure isomers.

*Large-Scale Catalytic Borylation of **1**.* A dry 50 mL flask was charged with a mixture of solid $BnNMe_2{\cdot}BH_3$ (**1**; 4.00 g, 26.8 mmol) and Tf_2NH (0.377 g, 1.34 mmol). To the solid mixture was added 10 mL of dry tetralin, and the resulting suspension was heated to 180 °C for 17 h. When the reaction mixture was cooled to room temperature, 20 mL of hexanes was added, and the resulting suspension was left in the freezer overnight. The solid was filtered out and thoroughly washed with 2 × 10 mL of cold hexanes. The crude product was extracted on the filter with 20 mL + 2 × 10 mL of PhMe, and the combined toluene extracts were concentrated under vacuum. Recrystallization from 10 mL of cyclohexane, followed by washing the product with 2 × 4 mL of cyclohexane and drying under vacuum, afforded 3.05 g (77%) of **37** as a white solid, identical by NMR assay with material prepared on a small scale using the stoichiometric method.[5]

*Large-Scale Catalytic Borylation of **44**.* A dry 50 mL flask was charged with a mixture of solid **44** (4.00 g, 14.5 mmol) and Tf_2NH (204 mg, 0.727 mmol). To the solid mixture was added 10.0 mL of dry tetralin, and the resulting suspension was heated to 180 °C for 17 h. When the reaction mixture was cooled to room temperature, 20 mL of hexanes was added, and the resulting suspension was left in the freezer overnight. The solid was collected by filtration and thoroughly washed with 2 × 10 mL of cold hexanes. The crude product was extracted on the filter with 20 mL + 2 × 15 mL of a 2:1 mixture of THF and Et_2O, the organic extracts were combined, and solvents were evaporated under reduced pressure. The product **45** (3.77 g, 95%) was found to be sufficiently pure to be used further without recrystallization.

Intramolecular C−H Borylation Products. 17: clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99−2.67 (m, 4H), 2.64−2.51 (unres AB q, J = 12.6 Hz, 2H), 2.3−1.7 (br m, 2H), 1.58 (td, J = 12.6, 4.3 Hz, 1H), 1.30 (ddd, J = 12.9, 10.5, 4.1 Hz, 1H), 1.13 (m, 9H), 0.93 (s, 9H), 0.68 ppm (t, J = 5.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 73.0, 53.7, 52.1, 37.6, 36.6, 32.5, 32.4, 30.3, 29.7, 29.3, 9.2 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −4.4 ppm (t, J = 80 Hz); HRMS (ESI+) m/z calcd for $C_{13}H_{29}BN$ [M − H]$^+$ 210.2388, found 210.2388; IR ($CDCl_3$, NaCl) 2955, 2864, 2348, 1467, 1366, 1235, 1197, 1171, 1133 cm^{-1}.

20: white crystalline solid, mp 78 °C (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 7.2 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 4.21 (d, J = 14.6 Hz, 1H), 4.08 (d, J = 14.6 Hz, 1H), 3.57−2.60 (br m, 1H), 3.09 (ddt, J = 17.2, 13.5, 8.3 Hz, 2H), 2.88 (d, J = 12.4 Hz, 1H), 2.68 (d, J = 12.4 Hz, 1H), 1.56 (dd, J = 17.2, 9.1 Hz, 2H), 1.11 (d, J = 9.9 Hz, 3H), 1.05 (dd, J = 13.4, 7.1 Hz, 1H), 0.94 (s, 9H), 0.83−0.78 ppm (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0−155.7 (br m), 138.1, 128.9, 127.1, 124.8, 121.3, 72.1, 66.2, 58.1, 39.6, 37.5, 32.9, 31.3, 29.8, 29.3 ppm (the additional $^{13}C_{aliph}$−B signal is likely to be located between 33.6 and 32.0 ppm, as suggested by peak shape analysis, but precise assignment is complicated by the overlapping sharp signal at 32.9 ppm); ^{11}B NMR (128 MHz, $CDCl_3$) δ 6.0 ppm (unres d); HRMS (ESI+) m/z calcd for $C_{18}H_{29}BN$ [M − H]$^+$ 270.2388, found 270.2396 (+3 ppm); IR ($CDCl_3$, NaCl) 3056, 3000, 2956, 2898, 2863, 2833, 2351, 2330, 1456, 1446, 1365, 1172, 1070, 1018, 844 cm^{-1}.

23: white crystalline solid, mp 73 °C (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 7.1 Hz, 1H), 7.17 (td, J = 7.1, 1.8 Hz, 1H), 7.10 − 7.03 (m, 2H), 3.97 (s, 2H), 3.11 − 2.97 (m, 4H), 2.96 − 2.34 (br m, 2H), 1.91 − 1.78 (m, 2H), 1.78 − 1.66 (m, 2H), 1.53 (m, 4H), 1.49 − 1.35 ppm (m, 8H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0−152.2 (br m), 138.5, 129.6, 127.0, 124.7, 121.5, 65.0, 54.7, 25.7, 25.3, 24.8, 21.4 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −2.9 ppm (t, J = 90 Hz); HRMS (ESI+) m/z calcd for $C_{17}H_{27}BN$ [M − H]$^+$ 256.2231, found 256.2233 (+1 ppm); IR ($CDCl_3$, NaCl) 2999, 2960, 2915, 2859, 2386, 2343, 2299, 1480, 1448, 1173, 1072 cm^{-1}.

25: white crystalline solid, mp 56 °C (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94−2.87 (m, J = 11.7 Hz, 2H), 2.87−2.74 (m, 2H), 2.78 (q, J = 7.4 Hz, 2H), 2.22−2.07 (m, 2H), 2.07−1.36 (br m, 2H), 1.89 (ddd, J = 17.7, 12.1, 5.6 Hz, 2H), 1.76−1.64 (m, 4H), 1.18 (t, J = 7.4 Hz, 3H), 0.93 ppm (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 61.5, 57.4, 30.8, 24.8, 21.1−20.0 (br m), 7.1 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −4.8 ppm (t, J = 95 Hz); HRMS (ESI+) m/z calcd for $C_9H_{19}BN$ [M − H]$^+$ 152.1605, found 152.1604 (−1 ppm); IR ($CDCl_3$, NaCl) 2989, 2893, 2834, 2315, 1468, 1450, 1184, 1150, 794 cm^{-1}.

*Formation of Isomers **28**−**30** by Borylation of **27**.* The isomer mixture was separated by preparative TLC on silica gel (1:1 CH_2Cl_2:hexanes). **28**: white crystalline solid, mp 85 °C (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 7.2 Hz, 1H), 7.17 (td, J = 7.1, 1.9 Hz, 1H), 7.09−7.03 (m, 2H), 4.03 (s, 2H), 3.24 (tt, J = 30.6, 12.0 Hz, 2H), 3.08 (ddd, J = 14.0, 8.3, 2.0 Hz, 2H), 2.94−2.41 (br m, 2H), 1.97−1.87 (m, 2H), 1.86−1.75 (m, 2H), 1.74−1.59 ppm (m, 8H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 129. 6, 127.0, 124.7, 121.6, 66.1, 55.0, 27.4, 24.7, 23.5 ppm, aromatic ^{13}C−B signal not detected; ^{11}B NMR (128 MHz, $CDCl_3$) δ −2.3 ppm (t, J = 91 Hz); HRMS (ESI+) m/z calcd for $C_{14}H_{21}BN$ [M − H]$^+$ 214.1762, found 214.1764 (+1 ppm); IR ($CDCl_3$, NaCl) 2920, 2855, 2342, 2283, 1476, 1446, 1340, 1177, 1068, 1021 cm^{-1}. **29**: white crystalline solid, mp 105 °C (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.35 (m, 3H), 7.31 (dt, J = 7.8, 3.8 Hz, 2H), 3.89 (s, 2H), 3.04−2.90 (m, 2H), 2.85 (dd, J = 11.9, 6.3 Hz, 2H), 2.04 (dtd, J = 19.3, 13.0, 6.2 Hz, 2H), 1.97−1.86 (m, 2H), 1.84−1.59 (br m, 2H), 1.75−1.64 (m, 4H), 0.96 ppm (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.6, 130.4, 128.8, 128.2, 71.4, 57.7, 30.7, 25.0, 21.9−20.2 ppm (br m); ^{11}B NMR (128 MHz, $CDCl_3$) δ −3.3 ppm (t, J = 85 Hz); HRMS (ESI+) m/z calcd for $C_{14}H_{21}BN$ [M − H]$^+$ 214.1762, found 214.1763; IR ($CDCl_3$, NaCl) 2895, 2839, 2319, 1452, 1150, 1097, 1021 cm^{-1}. **30**: white crystalline solid, mp 94 °C (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 7.1 Hz, 1H), 7.19−7.15 (m, 1H), 7.10−7.04 (m, 2H), 4.26 (d, J = 13.2 Hz, 1H), 4.07 (d, J = 13.2 Hz, 1H), 3.46−2.79 (br m, 1H), 3.12 (dd, J = 9.3, 3.6 Hz, 2H), 2.99 (td, J = 12.4, 6.1 Hz, 1H), 2.87 (ddd, J = 12.4, 9.3, 5.5 Hz, 1H), 2.16−2.06 (m, 1H), 2.05−1.93 (m, 2H), 1.91−1.83 (m, 1H), 1.82−1.72 (m, 2H), 1.71−1.61 (m, 1H), 1.36 ppm (ddd, J = 14.3, 12.1, 5.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 128.6, 126.9, 124.7, 121.7, 68.4, 61.9, 59.2, 37.1, 35.8, 29.5−27.4 (br m), 26.3, 25.6 ppm, aromatic ^{13}C−B signal not detected; ^{11}B NMR (128 MHz, $CDCl_3$) δ 2.25 ppm (d, J = 95

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Hz); HRMS (ESI+) m/z calcd for $C_{14}H_{19}BN$ $[M - H]^+$ 212.1605, found 212.1610 (+2 ppm); IR ($CDCl_3$, NaCl) 3057, 2999, 2923, 2833, 2325, 1459, 1448, 1334, 1177, 1177, 1117, 1055, 990 cm^{-1}.

*Borylation of **47** To Give **48** and **49**.* The major product **48** was isolated by crystallizing the crude isomer mixture from hexanes. The minor product **49** was recovered from the concentrated mother liquor by preparative TLC on silica gel (4:1 hexanes:EtOAc). **48**: white crystalline solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 7.8 Hz, 1H), 7.14 (dd, J = 7.8, 1.9 Hz, 1H), 7.05 (d, J = 1.9 Hz, 1H), 4.07 (s, 2H), 3.36−3.25 (m, 2H), 3.1−2.3 (br m, 2H), 2.29−2.82 (m, 2H), 2.23−2.11 (m, 2H), 2.05−1.94 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0−150.3 (br m), 140.9, 130.7, 130.4, 127.0, 121.5, 66.3, 60.3, 22.6 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −3.3 ppm (t, J = 95 Hz); HRMS (EI) m/z calcd $[M - H]^+$ 206.0908, found 206.0916 (+4 ppm). **49**: colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, J = 7.9 Hz, 1H), 7.02 (t, J = 7.7, 1H), 6.95 (d, J = 7.5 Hz, 1H), 4.15 (s, 2H), 3.41−3.32 (m, 2H), 3.2−2.3 (br m, 2H), 2.94−2.83 (m, 2H), 2.27−2.15 (m, 2H), 2.06−1.95 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7−150.5 (br m), 140.7, 136.1, 127.3, 126.7, 119.5, 66.9, 60.7, 22.5 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −3.6 ppm (t, J = 95 Hz); HRMS (EI) m/z calcd $[M - H]^+$ 206.0908, found 206.0899 (−4 ppm).

*Borylation of **53** To Form **54** and **55**.* The major product **54** was isolated by crystallizing the crude isomer mixture from hexanes/$CHCl_3$. The minor product **55** was recovered from the concentrated mother liquor by preparative TLC on silica gel (eluted with 2:1 hexanes:EtOAc to collect the fraction with R_f = 0.38, which was then additionally purified by preparative TLC using PhMe eluent). **54**: white solid, mp 109 °C (hexanes); R_f = 0.53 (2:1 hexanes:EtOAc); ^1H NMR (700 MHz, $CDCl_3$) δ 7.37 (d, J = 7.8, 1H), 7.31−7.28 (m, 2H), 7.04 (tt, J = 7.4, 0.9 Hz, 1H), 6.99−6.96 (m, 2H), 6.89 (dd, J = 7.8, 2.2 Hz, 1H), 6.77 (d, J = 1.7 Hz, 1H), 4.00 (s, 2H), 3.1−2.4 (br m, 2H), 2.77 (s, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.3, 154.8, 148.4−147.3 (br m), 140.2, 130.7, 129.5, 122.4, 118.6, 118.1, 113.2, 69.4, 51.0 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −1.5 ppm (unres t); HRMS (EI) m/z calcd for $C_{15}H_{17}BNO$ $[M - H]^+$ 238.1403, found 238.1412 (+4 ppm). **55**: white solid; ^1H NMR (700 MHz, $CDCl_3$) δ 7.27−7.24 (m, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.99 (tt, J = 7.4, 1.1 Hz, 1H), 6.96−6.93 (m, 2H), 6.90 (d, J = 7.4 Hz, 1H), 6.85 (d, J = 7.9 Hz, 1H), 4.05 (s, 2H), 3.0−2.3 (br m, 2H), 2.73 (s, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.4, 157.3, 144.4−143.0 (br m), 141.4, 129.1, 127.0, 121.7, 118.7, 118.0, 117.8, 69.4, 50.9 ppm; ^{11}B NMR (225 MHz, $CDCl_3$) δ −2.6 ppm (unres t); HRMS (ES+) m/z calcd for $C_{15}H_{17}BNO$ $[M - H]^+$ 238.1398, found 238.1401 (+1 ppm). **57**: white colorless solid, mp 88 °C (hexanes); ^1H NMR (700 MHz, $CDCl_3$) δ 7.30 (dt, J = 8.3, 4.8 Hz, 2H), 7.07−6.99 (m, 5H), 6.74 (dd, J = 8.0, 2.3 Hz, 1H), 4.02 (s, 2H), 3.0−2.4 (br m, 2H), 2.76 (s, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 157.9, 156.6, 156.4−155.5 (br m), 133.6, 129.5, 122.7, 122.5, 120.1, 118.6, 115.7, 69.2, 50.9 ppm; ^{11}B NMR (225 MHz, $CDCl_3$) δ −1.5 ppm (unres t); HRMS (ESI+) m/z calcd for $C_{15}H_{17}BNO$ $[M - H]^+$ 238.1398, found 238.1400 (+1 ppm). **62**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 6.6 Hz, 1H), 7.45 (dd, J = 8.0, 6.8 Hz, 1H), 7.32 (dd, J = 8.2, 6.9 Hz, 1H), 7.12 (m, 1H), 4.22 (s, 2H), 3.3−2.4 (br m, 2H), 2.72 ppm (s, 6H); ^{11}B NMR (128 MHz, $CDCl_3$) δ −4.0 ppm (t, J = 95 Hz).

*Borylation of **64**: Isolation of **65**.* Isolation of **64** and **65** was accomplished by repeated preparative TLC on silica gel (4:1 hexanes:EtOAc). The identity of C−C bond insertion product **64** was established by ^1H and ^{13}C NMR analysis.[2] **65**: colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.3 Hz, 1H), 3.82 (s, 2H), 2.67 (s, 6H), 2.4−1.6 (br m, 2H), 2.19 (s, 3H), 1.97 ppm (unres t, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 134.4, 130.1, 129.6, 126.8, 126.3, 62.4, 51.2, 20.1−18.4 (br m), 19.5 ppm; ^{11}B NMR (128 MHz, $CDCl_3$) δ −6.0 ppm (t, J = 90 Hz); HRMS (EI) m/z calcd $[M]^+$ 175.1532, found 175.1525 (−4 ppm).

*Hydrolysis of **45** and Preparation of **72**.* A 250 mL round-bottom flask was charged with **45** (3.50 g, 12.8 mmol), 90 mL of MeOH, and 18 mL of H_2O, and the resulting mixture was refluxed for 4 h, following which the contents were concentrated under reduced pressure. The residue was then azeotropically dried by evaporating with toluene (five to seven times) under reduced pressure, affording 3.60 g (98%) of the boroxine **68** as a pale yellow powder after drying under vacuum, sufficiently pure for use in the next stage. Under an N_2 atmosphere, in a preheated 20 mL vial $Pd(OAc)_2$ (13 mg, 58 μmol) and SPhos (48 mg, 116 μmol) were dissolved in 10.0 mL of degassed, anhydrous THF, and the resulting solution was stirred at room temperature for 20 min. A preheated 100 mL round-bottom flask was charged with a portion of the boroxine **68** from above (0.50 g, 0.58 mmol), phenylboronic acid (425 mg, 3.49 mmol), dry K_3PO_4 (740 mg, 3.49 mmol), and 20.0 mL of degassed, anhydrous THF. Under an N_2 atmosphere, the catalyst solution was then added to this mixture, which was then stirred for 22 h at 65 °C. A solution of *p*-iodoacetophenone (1.14 g, 4.63 mmol) in 5.0 mL of degassed, anhydrous THF and solid $Ba(OH)_2{\cdot}8H_2O$ (1.10 g, 3.49 mmol) were then added under an N_2 atmosphere, and the reaction mixture was stirred for additional 20 h at 65 °C. The reaction was filtered through Celite, concentrated under reduced pressure, and purified by column chromatography (95/5/2 CH_2Cl_2/MeOH/NH_4OH). The purified compound still contained minor impurities; therefore, it was acidified with 1 N HCl and washed with Et_2O (×3). The aqueous layer was then made basic by adding 10% NaOH solution and extracted with Et_2O (×3). Organic layers were combined, dried over $MgSO_4$, and concentrated to afford 228 mg (40%) of **72** as a pale yellow powder. **72**: ^1H NMR (500 MHz, $CDCl_3$) δ 8.06−7.99 (m, 2H), 7.81 (t, J = 7.4 Hz, 1H), 7.69−7.63 (m, 2H), 7.58−7.52 (m, 3H), 7.45 (dd, J = 10.6, 4.7 Hz, 2H), 7.38 − 7.35 (m, 1H), 7.31 (t, J = 8.0 Hz, 1H), 3.38 (s, 2H), 2.68−2.60 (m, 3H), 2.18 ppm (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 146.3, 140.69, 140.63, 140.3, 136.8, 135.7, 130.3, 129.9, 128.82, 128.77, 128.1, 127.4, 127.2, 125.6, 61.2, 45.3, 26.7 ppm; HRMS (ES+): m/z calcd $[M + H]^+$ 330.1852, found 330.1854 (+1 ppm).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, and CIF files giving X-ray crystallography data and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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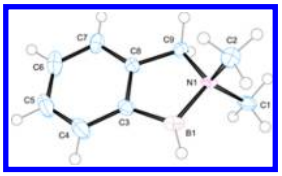
(6) To strengthen the structural assignment of the product cation **6** previously deduced on the basis of NMR data, X-ray-quality crystals of the $[HCB_{11}Cl_{11}]^-$ salt were obtained from CH_2Cl_2/hexanes. The structure is fully consistent with the proposed connectivity, but extraction of the exact structural parameters was prevented by disorder; the X-ray structure is shown for the borenium salt corresponding to **6** with anion = $[HCB_{11}Cl_{11}]^-$ (50% probability ellipsoids; the counterion is omitted for clarity).



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(10) Preliminary results on the catalytic borylations of **1** and **41** were reported in refs 2 and 5, respectively.
(11) The NMR study to probe **42**/**43** interconversion was performed at 120 °C for reasons of experimental convenience. The temperature decrease from 160 to 120 °C was confirmed to have no effect on the ratio of **42**/**43** (ca. 25:1) formed in the cyclization of **41**.
(12) Electrophilic borane insertions in C−C bonds are rare. For selected examples, see: (a) Xu, B.-H.; Kehr, G.; Fröhlich, R.; Erker, G. *Chem. Eur. J.* **2010**, *16*, 12538. (b) Xu, B.-H.; Kehr, G.; Fröhlich, R.; Grimme, S.; Erker, G. *J. Am. Chem. Soc.* **2011**, *133*, 3480.
(13) The reductive C−N bond cleavage is made possible by the combination of strongly electrophilic and reducing conditions and is somewhat reminiscent of the recently studied silylium ion promoted hydrodefluorination: Douvris, C.; Ozerov, O. *Science* **2008**, *321*, 1188 In view of this analogy, the reactivity of $PhCF_3$ with 1 equiv of $Me_3N{\cdot}BH_3$ activated by 5 mol % of Tf_2NH was briefly explored. Indeed, after 18 h at 120 °C ca. 30% conversion to $PhCH_3$ was observed, although neither Tf_2N^- nor *n*-$C_{12}F_{26}$ were affected..
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