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3-Boryl-2,1-borazonaphthalene: Umpolung Reagents for Diversifying Naphthalene Isosteres

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Abstract

A Pd-catalyzed Miyaura borylation of 3-bromo-2,1-borazonaphthalenes is reported. This method allows the formation of umpolung reagents for subsequent Pd-mediated cross-coupling. Coupling of this nucleophilic partner with a variety of commercially available aryl- and heteroaryl halides allows facile and rapid diversification of these cores.

Abstract

Introduction

The substitution of a B-N bond for a C=C bond in polyunsaturated ring systems provides access to a class of molecules known as “1,2-azaborines”. These motifs are isoelectronic and isosteric to their all-carbon counterparts. They retain a majority of the properties of aromatic structures but are uniquely polarized, allowing access to complex molecular architectures not available to their all-carbon analogs. Of particular interest among azaborine systems is the 2,1-borazonaphthalene core. In the last several years, robust methods to access and elaborate this core have been developed.¹ These processes have enabled biological studies to be conducted, revealing that these species show promise for medicinal applications. Indeed, a propranolol analog containing the 2,1-borazonaphthalene fragment has shown potency as a β -blocker with high bioavailability and low toxicity.² Likewise, a borazonaphthalene-based inhibitor of the phosphodiesterase enzyme PDE10A, which has drawn attention owing to potential therapeutic ability in a variety of diseases and disorders, was also reported as a biologically stable compound and a viable candidate for further investigation.³ Beyond their medicinal uses, polymers and small molecules containing 1,2-azaborines are of interest as

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Associated content

Supporting Information

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semiconductor materials and, in some instances, have been incorporated into organic field transistors and organic LEDs.⁴⁻⁶ Polymerization of a vinyl 2,1-borazonaphthalene monomer was recently accomplished, allowing access to materials with interesting physical properties.⁷

Our group previously reported the site-selective bromination of an array of 2,1-borazonaphthalenes that provided a functional handle for diversification at the 3-position.⁸ Although successful as an electrophile in cross-coupling processes, the potential for diversification at this position is limited by the diversity and commercial availability of aryl- and heteroaryl boronates. In comparison, an umpolung approach, wherein the 2,1-borazonaphthalene serves as the nucleophilic component, would allow the expansive commercial availability and sheer diversity of aromatic halides to be tapped for enhanced breadth of chemical space. In addition to increased diversity, other types of functionalization wholly unavailable^{9,10} from its brominated precursor would be possible (Scheme 1). Thus, we reasoned that a strategy for constructing 3-boryl-2,1-borazonaphthalenes would dramatically enrich the potential for accessing diverse libraries of 2,1-borazonaphthalenes.

Results and Discussion

2,1-Borazonaphthalene cores were synthesized and subsequently brominated using a previously published protocol.^{8,11} 3-Bromo-2-phenyl-2,1-borazonaphthalene was selected as a model substrate for the desired borylation. A microscale high throughput experimentation (HTE) approach¹² was applied to assess variables in the borylation such as palladium catalyst, base, solvent, and catalyst loading (See Supporting Information). In the first round of screening, palladium sources were evaluated in tandem with a number of bases historically successful in Miyaura borylation reactions. The bases tested were all oxygen-based, as the known oxophilicity of boron is a crucial driving force of the transmetalation step. The initial results from this analysis revealed that potassium phenoxide was a suitable base, and Pd(dppf)Cl₂ {[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride} could serve as a fitting palladium catalyst. This is consistent with Miyaura's reports that phenoxide is sufficiently strong to promote the desired transmetalation. Additionally, the base is effective in suppressing the formation of byproducts because of its inability to generate a tetrahedral, activated product that can further react to generate unwanted byproducts.¹³ In addition, this base had the added benefit of being selective toward strictly B₂Pin₂ activation, and no 5-dearylation of the 2,1-borazonaphthalene core was observed. However, given that potassium phenoxide is not commercially available and is highly hygroscopic, an attempt was made to form the active base species *in situ* by using 2 equiv of phenol and 4 equiv of K₂CO₃. Although yields were initially inferior to those with KOPh, it was determined that a pre-stirring period prior to the addition of the other reaction components provided yields comparable to those when using KOPh. As an added benefit, the amount of the proto-deborylated by-product was reduced when employing this modification. A second round of screening was used to optimize catalyst loading and more thoroughly assess solvent effects with the benchtop modifications in place. Results of this screen indicated that, when using the *in situ* generated base, toluene was the ideal solvent, and a 5 mol % catalyst loading resulted in the highest product formation. During the optimization studies, the reactions were heated to ~80 °C. Upon scale-up, it was found that

full conversion was achieved in ~30 min. As such, it was posited that the reaction could be run at a lower temperature. Indeed, when the reaction was conducted at room temperature, full conversion was reached in just four hours. At this lower temperature, decreasing the palladium loading to below 5 mol % resulted in incomplete conversion. With conditions for the borylation established, the scope of the method was assessed by subjecting a representative selection of 3-bromo-2,1-borazaronaphthalenes to the reaction conditions (Table 1). A number of substrates substituted at boron with electron-rich and electron-poor aryl- and heteroaryl groups were well-tolerated and afforded moderate to good yields. In addition, substitution on the adjacent aromatic ring to the boryl ring was permissible as well.

Next, these bis-boryl compounds were assessed as nucleophiles in cross-coupling. Success here would validate the umpolung strategy for diversification. Using slightly modified conditions optimized for coupling of 8-borylated-2,1-borazaronaphthalenes, coupled products were obtained in good yield (Table 2). Cross-coupling could be achieved with electron-rich, electron-poor, and electron-neutral arenes as well as a representative basic heterocycle.

Owing to the unique, long-term stability and crystallinity of organotrifluoroborate salts, we attempted to convert some of the synthesized, borylated products into their corresponding organotrifluoroborates. Treatment of the borylated material with aqueous KHF_2 enabled the facile conversion of these species into the desired organotrifluoroborates without any detectable degradation of the B-aryl linkage. Yields for the syntheses of these salts were excellent, and isolation was accomplished without issue (Table 3).¹⁴

To confirm that these partners retained amenability toward cross-coupling, we attempted to apply the conditions from our report on the coupling of 3-bromo-2,1-borazaronaphthalenes with alkenyl BF_3K s to the current system.¹⁵ Using these conditions, no product was observed. Using HTE screening, a modified set of conditions was established. Using $\text{Pd}(\text{PPh}_3)_4$ as the palladium source and Et_3N as a base, these azaboryl BF_3K s proved to be competent nucleophiles in Suzuki-type cross coupling, affording fair to moderate yields of the desired coupling products (Table 4). These couplings displayed the same trends observed with the corresponding Bpin derivatives.

As a means of further capitalizing on the unique reactivity of these umpolung reagents, we exposed **3a** to conditions we had previously reported for the electrophilic chlorination of organotrifluoroborates (Scheme 2).¹⁶ Indeed, this enabled access to a chlorinated core, which is not accessible via electrophilic chlorination of the parent 2,1-borazaronaphthene, to be prepared in 89% yield in a mere 30 minutes. Although one example, this reaction illustrates the potential of these reagents as nucleophilic partners and may proffer a new means of achieving other previously unattainable substitution patterns.

Conclusions

A general method for accessing 3-boryl-2,1-borazaronaphthalenes has been reported. Both the boronic acid pinacol esters and the corresponding potassium organotrifluoroborate salts are accessible. These species are competent nucleophiles in Suzuki coupling with aryl- and

heteroaryl bromides. This umpolung approach enables the commercial availability and diversity of bromide partners to be tapped in a highly effective manner. Ultimately, this strategy will facilitate the rapid derivatization of these scaffolds from bench-stable reagents.

Experimental Section

General considerations:

All reactions were carried out under an inert atmosphere of argon in oven-dried glassware using standard techniques for handling air-sensitive reagents. Toluene and cyclopentyl methyl ether (CPME) were dried using a solvent delivery system. All reagents were purchased and used as received from a supplier unless otherwise noted, including palladium sources. An automated system was used for all flash chromatography (monitoring at 254 and 280 nm) with silica cartridges (60 Å porosity, 20–40 nm). Melting points (°C) are uncorrected. Accurate mass measurement analyses were conducted on either a time-of-flight GCMS with electron ionization (EI), or a time-of-flight LCMS with electrospray ionization (ESI). Samples were taken up in a suitable solvent for analysis. The signals were mass measured against an internal lock mass reference of perfluorotributylamine (PFTBA) for EI-GCMS, and leucine enkephalin for ESI-LCMS. Commercial software calibrated the instruments and reported measurements by use of neutral atomic masses. The mass of the electron is not included. IR spectra were recorded using either the neat oil or solid products. NMR spectra (^1H , ^{13}C { ^1H }, ^{11}B , ^{19}F { ^1H }) were obtained at 298 K. ^1H (500.4 MHz) NMR chemical shifts are referenced to residual, non-deuterated CHCl_3 (δ 7.26) in CDCl_3 , residual $\text{DMSO}-d_5$ (δ 2.50) in $\text{DMSO}-d_6$ and acetone- d_5 (δ 2.09) in acetone- d_6 . ^{13}C { ^1H } (125.8 MHz) NMR chemical shifts are reported relative to CDCl_3 (δ 77.3) and the carbonyl carbon of acetone (δ 205.9). ^{11}B (128.4 MHz) chemical shifts are uncorrected. ^{19}F NMR spectra with C-F/C-H decoupling were referenced to internal standard hexafluorobenzene (δ -164.9). ¹⁷ Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant J (Hz) and integration.

Synthesis of 2,1 Borazaronaphthalenes.

2,1-Borazaronaphthalenes were synthesized according to the literature procedure¹¹ using organotrifluoroborate salts and 2-vinylaniline prepared according to previous publications.¹⁸

7-Fluoro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine

(0.971 g, 73%) was prepared according to general azaborine synthesis procedure from 5-fluoro-2-vinylaniline (0.494 g, 3.6 mmol) and PhBF_3K (0.552 g, 3 mmol). The desired azaborine was obtained as a crystalline white solid (mp = 144–147 °C). ^1H NMR (CDCl_3 , 500 MHz) δ 8.10 (d, J = 11.4 Hz, 2 H), 7.88 – 7.95 (m, 2 H), 7.62 (dd, J = 8.2, 6.6 Hz, 1 H), 7.45 – 7.54 (m, 3 H), 7.23 (d, J = 11.6 Hz, 1 H), 7.03 (dd, J = 9.9, 1.5 Hz, 1 H), 6.95 (td, J = 8.5, 2.1 Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 1215 MHz) δ 162.9 (d, $J_{\text{C-F}}$ = 246.5 Hz), 145.3, 141.6 (d, $J_{\text{C-C-C-F}}$ = 11.0 Hz), 133.0, 131.4 (d, $J_{\text{C-C-C-F}}$ = 10.1 Hz), 130.1, 128.6, 122.7, 109.8 (d, $J_{\text{C-C-F}}$ = 22.9 Hz), 104.4 (d, $J_{\text{C-C-F}}$ = 24.7 Hz) ppm. ^{11}B NMR (CDCl_3 , 128.4 MHz) δ 33.8. ^{19}F NMR (CDCl_3 , 471 MHz) δ -115.17 (s, 1 F). FT-IR (cm^{-1} , neat, ATR) 3383 (vw), 2923 (vw), 1595 (m), 1213 (m), 835 (m), 700.92 (vs). HRMS (EI) calcd for $\text{C}_{14}\text{H}_{11}\text{BFN}$ $[\text{M}]^+$: 223.0969, found: 223.0962.

Bromination of 2,1-Borazonaphthalenes.

3-Bromo 2,1-borazonaphthalenes were synthesized according to a literature procedure with a modified workup.⁸ To a flame-dried 100 mL round bottom flask equipped with a stir bar was added the corresponding 2,1-borazonaphthalene (2.0 mmol). The flask was sealed with a rubber septum, evacuated under vacuum, and purged with argon three times. A stock solution of Br₂ (0.23 M) in anhyd CH₂Cl₂ was prepared in a separate, purged round bottom flask by adding 43 mL of CH₂Cl₂ to 0.5 mL of Br₂. Anhyd CH₂Cl₂ (10 mL) was added to the flask, and the reaction was cooled to 0 °C in an ice/water bath. Br₂ (0.352 g, 2.2 mmol, 1.1 equiv) in CH₂Cl₂ (10 mL) was added *via* syringe pump using a Teflon needle at a rate of 1.1 mmol/h. When the starting material was consumed as determined by ¹H NMR, the reaction mixture was carefully transferred to a separatory funnel containing 20 mL of a 10 % aq Na₂S₂O₃ solution. The mixture was shaken vigorously, the layers were separated, and the aqueous layer was further extracted with CH₂Cl₂ (2 × 20 mL). The combined organic layers were dried (anhyd N₂SO₄) and concentrated *in vacuo*. The crude, brominated product was purified by flash chromatography, eluting with a gradient of 0 to 30% EtOAc/hexane to afford the desired 3-bromo-2,1-borazonaphthalene.

3-Bromo-2-(4-methoxyphenyl)-1,2-dihydrobenzo[e][1,2]azaborinine,

(0.363 g, 58%) was prepared according to *the general bromination procedure with the following modification*: the combined column fractions containing the product were washed with 2 M HCl (2 × 30 mL), dried, and concentrated. The desired 3-bromo-borazonaphthalene was obtained as a powdery tan solid (mp = 85–86 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.43 (s, 1H), 7.98 (br s, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 3H). ¹³C NMR (CDCl₃, 125 MHz) δ 161.0, 146.9, 139.6, 135.2, 129.0, 128.9, 125.1, 122.0, 118.3, 113.8, 55.4. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 32.7. FT-IR (cm⁻¹, neat, ATR) 3363 (w), 2926 (w), 1598 (m), 1426 (m), 1179 (m), 824 (m), 760 (vs). HRMS (EI) calcd for C₁₅H₁₃BBrNO [M]⁺: 313.0274, found: 313.0276.

3-Bromo-7-fluoro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine,

(0.212 g, 70%) was prepared according to *the general bromination procedure* from 7-fluoro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine (0.223 g, 1 mmol). The desired 3-bromo-borazonaphthalene was obtained as a powdery white solid (mp = 107–109 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.42 (s, 1H), 8.00 (br s, 1H), 7.89 (d, *J* = 3.5 Hz, 2H), 7.58 (dd, *J* = 8.3, 6.2 Hz, 1H), 7.43–7.51 (m, 3H), 6.95–7.04 (m, 2H). ¹³C NMR (CDCl₃, 125 MHz) δ 163.0 (d, *J*_{C-F} = 249.8 Hz), 146.6, 140.6 (d, *J*_{C-C-C-F} = 10.9 Hz), 133.5, 130.8 (d, *J*_{C-C-C-F} = 10.0 Hz), 129.9, 128.2, 122.1 (d, *J*_{C-C-C-C-F} = 1.8 Hz), 110.9 (d, *J*_{C-C-F} = 22.7 Hz), 104.4 (d, *J*_{C-C-F} = 24.5 Hz). ¹¹B NMR (CDCl₃, 128.4 MHz) δ 33.6. ¹⁹F NMR (CDCl₃, 471 MHz) δ -113.67 (s, 1F). FT-IR (cm⁻¹, neat, ATR) 3381 (w), 3017 (vw), 1207 (m), 849.71 (s), 717 (vs), 700 (vs), 520 (s). HRMS (EI) calcd for C₁₄H₁₀BBrFN [M]⁺: 301.0074, found: 301.0089.

Borylation of 3-Bromo-2,1 Borazaronaphthalenes

To an 8 mL screw top vial equipped with a stir bar (vial A) was added PhOH (0.094 g, 2.0 equiv) and K₂CO₃ (0.234 g, 4 equiv). To a second vial (vial B) equipped with a stir bar was added the corresponding 3-bromo-2,1-borazaronaphthalene (1 equiv), B₂Pin₂ (0.140 g, 1.1 equiv), and Pd(dppf)Cl₂ (0.018 g, 5 mol %). The reaction vessels were sealed with caps containing TFE-lined silicone septa, evacuated under vacuum, and purged with argon three times. Anhyd toluene (2.5 mL) was added to each vial, and both mixtures were stirred vigorously at rt for 15 min. The contents of vial B was transferred *via* syringe to vial A, and the reaction mixture was stirred at rt for 4 h. The reaction was monitored by HPLC. For select substrates, if the starting material was not consumed after this period, the reaction mixture was heated to 60 °C for an additional 2 h. The crude reaction mixture was concentrated *in vacuo* and purified by flash chromatography, eluting with a gradient of 0 to 15% EtOAc/hexane to afford the desired borylated 2,1 borazaronaphthalenes.

2-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, **1a**

(0.073 g, 63%) was prepared according to the general borylation procedure from 3-bromo-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine (0.099 g, 0.35 mmol). On large scale, **1a** (1.391 g, 70%) was prepared according to the scale up borylation procedure from 3-bromo-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine (1.704 g, 6 mmol). The desired borylated borazaronaphthalene **1a** was obtained as a powdery white solid (mp = 113–114 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.61 (s, 1H), 7.98 (br s, 1H), 7.82 – 7.87 (m, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.46 (td, *J* = 7.8, 1.2 Hz, 1H), 7.37 – 7.43 (m, 3H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 1.34 (s, 12H). ¹³C NMR (CDCl₃, 125 MHz) δ 155.0, 141.3, 133.9, 130.4, 129.8, 128.9, 127.7, 125.5, 121.4, 118.3, 83.6, 25.1. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 35.5, 32.4. FT-IR (cm⁻¹, neat, ATR) 3381 (vw), 2977 (w), 1614 (w), 1557 (m), 1335 (m), 1140 (m), 757 (m), 699 (vs), 475 (m). HRMS (EI) calcd for C₂₀H₂₃B₂NO₂ [M]⁺: 331.1915, found: 331.1916

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(*p*-tolyl)-1,2-dihydrobenzo[e][1,2]azaborinine, **1b**

(0.138 g, 80%) was prepared according to the general borylation procedure from 3-bromo-2-(*p*-tolyl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.149 g, 0.5 mmol). The desired borylated borazaronaphthalene **1b** was obtained as a powdery white solid (mp = 145–146 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.59 (s, 1H), 7.94 (br s, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.45 (m, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.17 (td, *J* = 7.5, 0.9 Hz, 1H), 2.41 (s, 3H), 1.35 (s, 12H). ¹³C NMR (CDCl₃, 125 MHz) δ 154.9, 141.4, 138.7, 134.0, 130.4, 129.7, 128.6, 125.5, 121.2, 118.2, 83.6, 25.2, 21.8. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 35.2, 32.6. FT-IR (cm⁻¹, neat, ATR) 3334 (w), 2975 (w), 1555 (s), 1337 (vs), 1138 (vs), 797 (m). HRMS (EI) calcd for C₂₁H₂₅B₂NO₂ [M]⁺: 345.2071, found: 345.2065.

2-(4-Methoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1c

(0.132 g, 73%) was prepared according to the general borylation procedure from 3-bromo-2-(4-methoxyphenyl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.157 g, 0.5 mmol) *with the following modification*: the crude reaction mixture was washed with 4 M NaOH (4 × 10 mL) and dried (N₂SO₄) prior to concentration *in vacuo*. The desired borylated borazaronaphthalene **1c** was obtained as a powdery yellow solid (mp = 155–156 °C). **¹H NMR** (CDCl₃, 500 MHz) δ 8.57 (s, 1H), 7.90 (br s, 1H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H), 7.26 (d, *J* = 5.2 Hz, 1H), 7.16 (td, *J* = 7.3, 0.8 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H), 1.35 (s, 12H). **¹³C NMR** (CDCl₃, 125 MHz) δ 160.7, 154.9, 141.5, 135.5, 130.4, 129.7, 125.4, 121.2, 118.2, 113.5, 83.6, 55.4, 25.2. **¹¹B NMR** (CDCl₃, 128.4 MHz) δ 34.92, 32.41. **FT-IR** (cm⁻¹, neat, ATR) 3380 (vw), 2973 (w), 1557 (s), 1335 (s), 1140 (s), 777 (vs), 699 (m). **HRMS** (EI) calcd for C₂₁H₂₅B₂NO₃ [M]⁺: 361.2021, found: 361.2013.

2-(4-Fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1d

(0.131 g, 75%) was prepared according to the general borylation procedure from 3-bromo-2-(4-fluorophenyl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.151 g, 0.5 mmol). The desired borylated borazaronaphthalene **1d** was obtained as a white solid (mp = 124–126 °C). **¹H NMR** (CDCl₃, 500 MHz) δ 8.62 (s, 1H), 7.90 (br s, 1H), 7.82 (dd, *J* = 8.3, 6.3 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.19 (td, *J* = 7.6, 0.9 Hz, 1H), 7.10 (t, *J* = 8.9 Hz, 2H), 1.33 (s, 12H). **¹³C NMR** (CDCl₃, 125 MHz) δ 164.0 (d, *J*_{C-F} = 247.0 Hz), 155.3, 141.3, 135.8 (d, *J*_{C-C-F} = 7.3 Hz), 130.5, 129.9, 125.5, 121.5, 118.3, 114.7 (d, *J*_{C-C-F} = 20.0 Hz), 83.7, 25.1. **¹¹B NMR** (CDCl₃, 128.4 MHz) δ -34.7, 32.4. **¹⁹F NMR** (CDCl₃, 471 MHz) δ -116.51 (s, 1F). **FT-IR** (cm⁻¹, neat, ATR) 3380 (vw), 2976 (w), 2925 (w), 1560 (m), 1338 (vs), 1139 (vs), 767 (s). **HRMS** (EI) calcd for C₂₀H₂₂B₂FNO₂ [M]⁺: 349.1821, found: 349.1844.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(4-(trifluoromethyl)phenyl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1e

(0.141 g, 70%) was prepared according to the general borylation procedure from 3-bromo-2-(4-(trifluoromethyl)phenyl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.176 g, 0.5 mmol). The desired borylated borazaronaphthalene **1e** was obtained as a powdery off-white solid (mp = 160–161 °C). **¹H NMR** (CDCl₃, 500 MHz) δ 8.68 (s, 1H), 7.98 (br s, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.49 (td, *J* = 7.6, 1.1 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.23 (td, *J* = 7.5, 0.8 Hz, 1H), 1.32 (s, 12H). **¹³C NMR** (CDCl₃, 125 MHz) δ 155.8, 141.1, 134.0, 130.6, 130.6 (q, *J*_{C-C-F} = 32.6 Hz), 130.1, 125.7, 124.2 (q, *J*_{C-C-C-F} = 3.6 Hz), 121.8, 124.9 (q, *J*_{C-F} = 272.5 Hz), 118.4, 83.7, 25.1. **¹¹B NMR** (CDCl₃, 128.4 MHz) δ 35.0, 32.7. **¹⁹F NMR** (CDCl₃, 471 MHz) δ -65.74 (s, 3F). **FT-IR** (cm⁻¹, neat, ATR) 3373 (vw), 2975 (w), 2924 (w), 2854 (w), 1559 (m), 1323 (vs), 1116 (vs), 767 (m). **HRMS** (EI) calcd for C₂₁H₂₂B₂F₃NO₂ [M]⁺: 399.1789, found: 399.1801.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(thiophen-3-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1f

(0.110 g, 65%) was prepared according to the general borylation procedure from 3-bromo-2-(thiophen-3-yl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.145 g, 0.5 mmol). The desired borylated borazaronaphthalene **1f** was obtained as a powdery white solid (mp = 125–126 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.63 (s, 1H), 8.19 (dd, *J* = 2.6, 0.9 Hz, 1H), 7.94 – 8.05 (m, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.63 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.45 (td, *J* = 7.6, 1.4 Hz, 1H), 7.41 (dd, *J* = 4.8, 2.7 Hz, 1H), 7.27 (d, 1H), 7.17 (td, *J* = 7.5, 0.8 Hz, 1H), 1.38 (s, 12H). ¹³C NMR (CDCl₃, 125 MHz) δ 155.7, 141.4, 133.3, 132.0, 130.5, 129.9, 125.4, 124.9, 121.3, 118.1, 83.7, 25.2. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 32.20. FT-IR (cm⁻¹, neat, ATR) 3373 (vw), 2978 (w), 1557 (s), 1334 (s), 1137 (s), 767 (vs). HRMS (EI) calcd for C₁₈H₂₁B₂NO₂S [M]⁺: 337.1479, found: 337.1471.

7-Fluoro-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1g

(0.118 g, 68%) was prepared according to the general borylation procedure from 3-bromo-7-fluoro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine (0.151 g, 0.5 mmol). The desired borylated borazaronaphthalene **1g** was obtained as a powdery white solid (mp = 153–155 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.56 (s, 1H), 7.93 (br s, 1H), 7.83 (dd, *J* = 6.7, 2.7 Hz, 2H), 7.67 (dd, *J* = 8.4, Hz, 1H), 7.38 – 7.44 (m, 3H), 6.90 – 6.99 (m, 2H), 1.33 (s, 12H). ¹³C NMR (CDCl₃, 125 MHz) δ 163.7 (d, *J*_{C-F} = 248.0 Hz), 154.5, 142.6 (d, *J*_{C-C-F} = 11.8 Hz), 133.8, 132.3 (d, *J*_{C-C-F} = 10.0 Hz), 129.1, 127.8, 122.4, 110.0 (d, *J*_{C-C-F} = 22.7 Hz), 104.1 (d, *J*_{C-C-F} = 23.6 Hz), 83.7, 25.1. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 35.4, 32.4. ¹⁹F NMR (CDCl₃, 471 MHz) δ -113.27 (s, 1F). FT-IR (cm⁻¹, neat, ATR) 3323 (w), 2980 (w), 1267 (m), 1141 (vs), 850 (m), 689 (m). HRMS (EI) calcd for C₂₀H₂₂B₂FNO₂ [M]⁺: 349.1821, found: 349.1828.

2-(Dibenzo[b,d]furan-4-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 1h

(0.175 g, 83%) was prepared according to the general borylation procedure from 3-bromo-2-(dibenzo[b,d]furan-4-yl)-1,2-dihydrobenzo[e][1,2]azaborinine (0.187 g, 0.5 mol). The desired borylated borazaronaphthalene **1h** was obtained as a colorless oil. ¹H NMR (CDCl₃, 500 MHz) δ 9.02 (br s, 1H), 8.70 (s, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 8.01 (t, *J* = 7.8 Hz, 2H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.39 – 7.44 (m, 2H), 7.32 – 7.38 (m, 1H), 7.20 – 7.25 (m, 1H), 1.31 (s, 12H). ¹³C NMR (CDCl₃, 125 MHz) δ 159.6, 155.7, 154.8, 140.9, 134.5, 130.1, 129.5, 126.6, 125.2, 124.4, 122.9, 122.5, 122.2, 121.3, 121.1, 120.5, 118.3, 83.3, 24.8. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 33.0. FT-IR (cm⁻¹, neat, ATR) 3396 (vw), 2978 (w), 1556 (m), 1337 (m), 1142 (m), 907 (m), 728 (vs). HRMS (EI) calcd for C₂₆H₂₅B₂NO₃ [M]⁺: 421.2021, found: 421.2045.

Representative Scale up Procedure- Borylation of 3-Bromo-2-phenyl-1,2-dihydrobenzo[e] [1,2]azaborinine

To a 250 mL round bottom flask equipped with a stir bar (flask A) was added PhOH (1.13 g, 12.0 mmol, 2.0 equiv) and K₂CO₃ (3.32 g, 24.0 mmol, 4 equiv). To a 50 mL round bottom flask (flask B) equipped with a stir bar was added 3-bromo-2-phenyl-1,2-dihydrobenzo[e] [1,2]azaborinine (1.70 g, 6.0 mmol 1 equiv), B₂Pin₂ (1.68 g, 6.6 mmol, 1.1 equiv), and Pd(dppf)Ch•CH₂Ch (0.246 g, 0.3 mmol, 5 mol %). The reaction vessels were sealed with rubber septa, evacuated under vacuum, and purged with argon three times. Anhyd toluene (30 mL) was added to each flask, and both mixtures were stirred vigorously at rt for 15 min. The contents of flask B was transferred *via* syringe to the flask A and the reaction mixture was stirred at rt for 6 h. The reaction was monitored by HPLC. The crude reaction mixture was concentrated *in vacuo* by rotary evaporation, adhered to silica, and purified by flash chromatography, eluting with a gradient of 0 to 15% EtOAc/hexane to afford **1a** (1.39 g, 70%)

Suzuki cross-coupling of Bpin Derivatives of 2,1 Borazaronaphthalenes

Coupled 2,1-borazaronaphthalenes were synthesized according to a literature procedure.¹⁹ To a microwave vial equipped with a stir bar was added **1a** (1.0 equiv), aryl bromide (if solid, 1.1 equiv), K₂CO₃ (3.0 equiv), and XPhos-Pd-G2 catalyst (2 mol %). The reaction vessel was sealed with a cap containing a TFE-lined silicone septa, evacuated under vacuum, and purged with argon three times. A solvent mixture of degassed *t*-BuOH/H₂O (1:1 v.v.; 2 mL/mmol) was added. At this point, any liquid aryl bromides (1.1 equiv) were also added. The reaction was heated to 40 °C for 18 h. Upon completion, the reaction was cooled to rt, transferred to a separatory funnel, and washed with H₂O (20 mL). The layers were separated, and the aqueous layer was further extracted with CH₂Cl₂ (2 × 20 mL). The combined organic layers were further washed with saturated NH₄Cl (20 mL), dried (anhyd Na₂SO₄) and concentrated *in vacuo*. The crude product was purified by flash chromatography, eluting with a gradient of 0 to 30% EtOAc/hexane to afford the desired coupled 2,1-borazaronaphthalene.

2-Phenyl-3-(p-tolyl)-1,2-dihydrobenzo[e][1,2]azaborinine, **2a**

(0.089 g, 61%) was prepared according to the general cross-coupling procedure from **1a** (0.166 g, 0.5 mmol) and 4-bromotoluene (0.094 g, 0.55 mmol). The desired borazaronaphthalene **2a** was obtained as a tan oil ¹H NMR (CDCl₃, 500 MHz) δ 8.06 (br s, 1H), 8.04 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 6.6 Hz, 2H), 7.46 (td, *J* = 7.6, 1.0 Hz, 1H), 7.30 – 7.39 (m, 4H), 7.20 – 7.26 (m, 3H), 7.11 (d, *J* = 7.8 Hz, 2H), 2.38 (s, 3H). ¹³C NMR (CDCl₃, 125 MHz) δ 143.4, 141.5, 139.7, 135.9, 133.5, 129.8, 129.0, 128.9, 128.8, 128.5, 128.0, 125.7, 121.7, 118.0, 21.4. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 34.5. FT-IR (cm⁻¹, neat, ATR) 3376 (w), 3048 (w), 1615 (m), 1561 (m), 1423 (s), 820 (m), 753 (vs), 703 (s). HRMS (EI) calcd for C₂₁H₁₈BN [M]⁺: 295.1532, found: 295.1536.

3-(4-Methoxyphenyl)-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine, 2b

(0.070 g, 45%) was prepared according to the general cross-coupling procedure from **1a** (0.166 g, 0.5 mmol) and 4-bromoanisole (0.103 g, 0.55 mmol). The desired borazaronaphthalene **2b** was obtained as a powdery off-white solid (mp = 56–58 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.04 (br s, 1H), 8.02 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.44 (td, *J* = 7.6, 1.4 Hz, 1H), 7.30 – 7.39 (m, 4H), 7.20 – 7.26 (m, 3H), 6.85 (s, 2H), 3.82 (s, 3H). ¹³C NMR (CDCl₃, 125 MHz) δ 158.6, 143.0, 139.7, 136.9, 133.5, 130.1, 129.8, 128.8, 128.4, 128.1, 125.7, 121.8, 118.0, 113.8, 55.5. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 36.6. FT-IR (cm⁻¹, neat, ATR) 3368 (vw), 3008 (vw), 1509 (m), 1240 (vs), 1174 (m), 829 (m), 750 (vs), 701 (vs), 617 (m). HRMS (EI) calcd for C₂₁H₁₈BNO [M]⁺: 311.1481, found: 311.1479.

4-(2-Phenyl-1,2-dihydrobenzo[e][1,2]azaborinin-3-yl)benzonitrile, 2c

(0.087, 57%) was prepared according to the general cross-coupling procedure from **1a** (0.166 g, 0.5 mmol) and 4-bromobenzonitrile (0.100 g, 0.55 mmol). The desired borazaronaphthalene **2c** was obtained as a powdery white solid (mp = 157–159 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.12 (br s, 1H), 8.06 (s, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.51 (td, *J* = 7.7, 1.2 Hz, 1H), 7.30 – 7.42 (m, 8H), 7.27 (t, *J* = 7.8 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ 149.5, 144.9, 140.2, 133.4, 132.2, 130.2, 129.7, 129.6, 129.2, 128.3, 125.2, 122.2, 119.6, 118.3, 109.9. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 34.3. FT-IR (cm⁻¹, neat, ATR) 3342 (w), 3052 (w), 2225 (m), 1600 (vs), 1562 (vs), 839 (m), 755 (s), 703 (m). HRMS (EI) calcd for C₂₁H₁₅BN₂ [M]⁺: 306.1328, found: 306.1322.

2-Phenyl-3-(pyrimidin-5-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, 2d

(0.090 g, 64%) was prepared according to the general cross-coupling procedure from **1a** (0.166 g, 0.5 mmol) and 5-bromopyrimidine (0.088 g, 0.55 mmol). The desired borazaronaphthalene **2d** was obtained as a powdery off-white solid (mp = 180–181 °C). ¹H NMR (CDCl₃, 500 MHz) δ 9.10 (s, 1H), 8.65 (s, 2H), 8.19 (br s, 1H), 8.10 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.53 (td, *J* = 7.6, 1.2 Hz, 1H), 7.32 – 7.43 (m, 6H), 7.29 (t, *J* = 7.5 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ 156.7, 156.3, 145.4, 140.3, 137.6, 133.2, 130.3, 129.9, 129.4, 128.6, 125.1, 122.3, 118.4. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 34.3. FT-IR (cm⁻¹, neat, ATR) 3339 (w), 3018 (vw), 1614 (m), 1563 (m), 1409 (m), 703 (vs). HRMS (EI) calcd for CuHuBN [M]⁺: 283.1281, found: 283.1284.

Synthesis of Potassium Organotrifluoroborates from Pinacolboronates

To a 10 mL round bottom flask equipped with a stir bar was added the corresponding borylated 2,1-borazaroaphthalene (1 equiv). MeOH (1 mL) was added to the flask, and the mixture was cooled to 0 °C in an ice/water bath. The solution was stirred, and aq KHF₂ (4 equiv, 4.5 M) was added dropwise *via* an addition funnel. The reaction was allowed to warm to rt while stirring for an additional 45 min. The reaction mixture was then concentrated *in vacuo*. Portions of toluene were added to azeotrope excess pinacol. The crude material was taken up in boiling acetone to solubilize the organotrifluoroborate, and the mixture was filtered through a coarse fritted glass funnel to remove inorganic byproducts. The product was concentrated *in vacuo* to afford the desired 2,1-borazaronaphthyltrifluoroborates.

2-Phenyl-3-(trifluoro-*l*-4-boraneyl)-1,2-dihydrobenzo[*e*][1,2]azaborinine, Potassium Salt, 3a

(0.139 g, 89%) was prepared according to the general organotrifluoroborate synthesis procedure from **1a** (0.158 g, 0.5 mmol). The desired trifluoroborate **3a** was obtained as a powdery white solid (mp > 200 °C). ¹H NMR (acetone-*d*₆, 500 MHz) δ 8.88 (br s, 1H), 8.32 (s, 1H), 8.10 (d, *J* = 6.6 Hz, 2H), 7.53 (dd, *J* = 14.8, 7.9 Hz, 2H), 7.20 – 7.34 (m, 4H), 7.05 (td, *J* = 7.5, 0.8 Hz, 1H). ¹³C NMR (acetone-*d*₆, 125 MHz) δ 146.8 (q, *J*_{C-C-F} = 5.4 Hz), 141.3, 134.7, 129.1, 127.9, 127.4, 126.8, 120.3, 118.3. ¹¹B NMR (acetone-*d*₆, 128.4 MHz) δ 36.0, 4.2. ¹⁹F NMR (acetone-*d*₆, 471 MHz) δ 137.27 (s, 3F). FT-IR (cm⁻¹, neat, ATR) 3366 (w), 3052 (vw), 1556 (m), 1114 (m), 1005 (m), 945 (m), 906 (s), 751 (vs), 709 (m). HRMS (ESI-) calcd for C₁₄H₁₁B₂F₃N [M]⁻: 272.1030, found: 272.1019.

2-(4-Methoxyphenyl)-3-(trifluoro-*l*-4-boraneyl)-1,2-dihydrobenzo[*e*][1,2]azaborinine, Potassium Salt, 3b

(0.152 g, 89%) was prepared according to the general organotrifluoroborate synthesis procedure from **1c** (0.181 g, 0.5 mmol). The desired trifluoroborate **3b** was obtained as a powdery off-white solid (mp > 200 °C). ¹H NMR (acetone-*d*₆, 500 MHz) δ 8.80 (br s, 1H), 8.30 (s, 1H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.51 (dd, *J* = 16.6, 7.9 Hz, 2H), 7.25 (td, *J* = 7.5, 1.2 Hz, 1H), 7.03 (td, *J* = 7.5, 0.9 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 3.78 (s, 3H). ¹³C NMR (acetone-*d*₆, 125 MHz) δ 160.4, 146.7 (q, *J* = 5.4 Hz), 141.3, 136.1, 129.1, 127.0 (br), 126.8, 120.1, 118.1, 118.0, 113.1, 54.8. ¹¹B NMR (acetone-*d*₆, 128.4 MHz) δ 36.1, 4.4. ¹⁹F NMR (acetone-*d*₆, 471 MHz) δ 137.22 (s, 3F). FT-IR (cm⁻¹, neat, ATR) 3374 (w), 3356 (w), 2925 (vw), 1596 (m), 1554 (m), 1228 (m), 1178 (m), 995 (vs), 543 (m). HRMS (ESI-) calcd for C₁₅H₁₃B₂F₃NO [M]⁻: 302.1135, found: 302.1119.

2-(4-Fluorophenyl)-3-(trifluoro-*l*-4-boraneyl)-1,2-dihydrobenzo[*e*][1,2]azaborinine, Potassium Salt, 3c

(0.157 g, 96%) was prepared according to the general organotrifluoroborate synthesis procedure from **1d** (0.175 g, 0.5 mmol). The desired trifluoroborate **3c** was obtained as a powdery white solid (mp > 200 °C). ¹H NMR (acetone-*d*₆, 500 MHz) δ 8.90 (br s, 1H), 8.32 (s, 1H), 8.20 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 6.96 – 7.08 (m, 3H). ¹³C NMR (acetone-*d*₆, 125 MHz) δ 163.7 (d, *J*_{C-F} = 243.8 Hz), 146.8 (q, *J*_{C-C-B-F} = 4.7 Hz), 141.1, 136.8 (br), 129.1, 127.2, 126.8, 120.3, 118.3, 113.9 (d, *J*_{C-C-F} = 19.2 Hz). ¹¹B NMR (acetone-*d*₆, 128.4 MHz) δ 36.0, 4.3. ¹⁹F NMR (acetone-*d*₆, 471 MHz) δ -117.22 (s, 1 F), -137.35 (br s, 3 F). FT-IR (cm⁻¹, neat, ATR) 3399 (vw), 1560 (m), 14131 (m), 998 (vs), 906 (vs), 754 (vs), 543 (m). HRMS (ESI-) calcd for C₁₄H₁₀B₂F₄N [M]⁻: 290.0935, found: 290.0927.

3-(Trifluoro-*l*-4-boraneyl)-2-(4-(trifluoromethyl)phenyl)-1,2-dihydrobenzo[*e*][1,2]azaborinine, Potassium Salt, 3d

(0.114 g, 60%) was prepared according to the general organotrifluoroborate synthesis procedure from **1e** (0.200 g, 0.5 mmol). The desired trifluoroborate **3d** was obtained as a powdery off-white solid (mp > 200 °C). ¹H NMR (acetone-*d*₆, 500 MHz) δ 9.10 (br s, 1H), 8.35 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 3H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.30 (td, *J* = 7.6, 1.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.1 Hz, 1H). ¹³C NMR (acetone-*d*₆, 125 MHz) δ

147.1 (q, $J_{\text{C-C-B-F}} = 5.5$ Hz), 140.9, 135.0 (q, $J_{\text{C-C-C-C-F}} = 1.8$ Hz), 129.1, 127.3, 126.9, 123.6 (q, $J_{\text{C-C-C-F}} = 3.7$ Hz), 125.7 (q, $J_{\text{C-F}} = 271.3$ Hz), 120.6, 118.4. ^{11}B NMR (acetone- d_6 , 128.4 MHz) δ 35.7, 4.3. ^{19}F NMR (acetone- d_6 , 471 MHz) δ -63.09 (s, 3 F), -137.28 (br s, 3 F). FT-IR (cm^{-1} , neat, ATR) 3419 (vw), 2927 (vw), 1556 (m), 1327 (vs), 845 (vs), 749 (m). HRMS (ESI-) calcd for $\text{C}_{15}\text{H}_{10}\text{B}_2\text{F}_6\text{N}$ $[\text{M}]^-$: 340.0904, found: 340.0914.

Suzuki Cross-Coupling of 2,1-Borazaronaphthyltrifluoroborates

To an 8 mL screw top vial equipped with a stir bar was added **3c** (0.189 g, 0.55 mmol, 1.1 equiv) and the appropriate aryl bromide (0.5 mmol, 1 equiv). The vial was taken into the glovebox where $\text{Pd}(\text{PPh}_3)_4$ (0.289 g, 0.05 equiv) was added. The reaction vessel was sealed with caps containing a TFE-lined silicone septa and taken out of the glove box. Et_3N (0.210 mL, 3 equiv) and a 1:1 mixture of degassed toluene and H_2O were added to the vial (0.5 M), and the reaction was stirred vigorously at 80 °C for 18 h. The reaction mixture was carefully transferred to a separatory funnel and extracted with EtOAc (3×10 mL). The combined organic layers were concentrated *in vacuo* by rotary evaporation, and the crude material was purified by flash chromatography, eluting with a gradient of 0 to 30% EtOAc /hexane to afford the desired 3-aryl-2,1-borazaronaphthalene.

2-(4-Fluorophenyl)-3-(p-tolyl)-1,2-dihydrobenzo[e][1,2]azaborinine, **4a**

(0.102 g, 65%) was prepared according to the general cross-coupling procedure from **3c** (0.181 g, 0.55 mmol) and 4-bromotoluene (0.086 g, 0.5 mmol). The desired borazaronaphthalene **4a** was obtained as a viscous tan oil. ^1H NMR (CDCl_3 , 500 MHz) δ 8.06 (s, 1H), 8.04 (br s, 1H), 7.75 (d, $J = 7.6$ Hz, 1H), 7.46 – 7.52 (m, 3H), 7.36 (d, $J = 8.1$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.23 (d, $J = 8.0$, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 7.06 (t, $J = 8.9$ Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (CDCl_3 , 125 MHz) δ 163.7 (d, $J_{\text{C-F}} = 249.3$ Hz), 143.6, 141.4, 139.7, 136.0, 135.4 (d, $J_{\text{C-C-C-F}} = 8.2$ Hz), 129.8, 129.1, 128.9, 128.6, 125.7, 121.8, 118.0, 115.1 (d, $J_{\text{C-C-F}} = 19.2$ Hz), 21.4. ^{11}B NMR (CDCl_3 , 128.4 MHz) δ 34.3. ^{19}F NMR (CDCl_3 , 471 MHz) δ -115.93 (s, 3F). FT-IR (cm^{-1} , neat, ATR) 3380 (vw), 3022 (vw), 1594 (m), 1422 (m), 1217 (m), 818 (m), 761 (vs), 516 (m). HRMS (EI) calcd for $\text{C}_{21}\text{H}_{17}\text{BFN}$ $[\text{M}]^+$: 313.1438, found: 313.1431.

2-(4-Fluorophenyl)-3-(4-methoxyphenyl)-1,2-dihydrobenzo[e][1,2]azaborinine, **4b**

(0.070 g, 45%) was prepared according to the general cross-coupling procedure from **3c** (0.181 g, 0.55 mmol) and 4-bromoanisole (0.094 g, 0.5 mmol). The desired borazaronaphthalene **4b** was obtained as a powdery white solid (mp = 95–96 °C). ^1H NMR (CDCl_3 , 500 MHz) δ 8.00 (s, 1H), 8.00 (br s, 1H), 7.70 (d, $J = 7.8$ Hz, 1H), 7.40 – 7.48 (m, 3H), 7.33 (d, $J = 7.9$ Hz, 1H), 7.19 – 7.25 (m, 3H), 7.02 (t, $J = 8.9$ Hz, 2H), 6.85 (d, $J = 8.7$ Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (CDCl_3 , 125 MHz) δ 163.8 (d, $J_{\text{C-F}} = 248.9$ Hz), 158.6, 143.2, 139.6, 136.8, 135.4 (d, $J_{\text{C-C-C-F}} = 7.3$ Hz), 130.1, 129.8, 128.5, 125.7, 121.9, 118.0, 115.2 (d, $J_{\text{C-C-F}} = 20.0$ Hz), 113.9, 55.5. ^{11}B NMR (CDCl_3 , 128.4 MHz) δ 34.4. ^{19}F NMR (CDCl_3 , 471 MHz) δ -115.92 (s, 3F). FT-IR (cm^{-1} , neat, ATR) 3372 (br, vw), 2927 (w), 1594 (m), 1507 (s), 1240 (s), 827 (s), 761 (vs). HRMS (EI) calcd for $\text{C}_{21}\text{H}_{17}\text{BFNO}$ $[\text{M}]^+$: 329.1387, found: 329.1373.

4-(2-(4-Fluorophenyl)-1,2-dihydrobenzo[e][1,2]azaborinin-3-yl)benzonitrile, **4c**

(0.087 g, 53%) was prepared according to the general cross-coupling procedure from **3c** (0.181 g, 0.55 mmol) and 4-bromobenzonitrile (0.091 g, 0.5 mmol). The desired borazaronaphthalene **4c** was obtained as a powdery white solid (mp = 160–161 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.08 (br s, 1H), 8.05 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.51 (td, *J* = 7.8, 0.9 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 5H), 7.27–7.30 (m, 1H), 7.03 (t, *J* = 8.9 Hz, 2H). ¹³C NMR (CDCl₃, 125 MHz) δ 163.9 (d, *J*_{C-F} = 248.0 Hz), 149.5, 145.0, 140.1, 135.3 (d, *J*_{C-C-F} = 7.3 Hz), 132.2, 130.2, 129.7, 125.2, 122.3, 119.5, 118.3, 115.5 (d, *J*_{C-C-F} = 20.0 Hz), 110.1. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 34.8. ¹⁹F NMR (CDCl₃, 471 MHz) δ –115.10 (s, 3F). FT-IR (cm^{–1}, neat, ATR) 3391 (w), 2978 (vw), 2219 (m), 1591 (m), 1206 (m), 831 (s), 764 (vs), 572 (m). HRMS (EI) calcd for C₂₁H₁₄BFN₂ [M]⁺: 324.1234, found: 324.1224.

2-(4-Fluorophenyl)-3-(pyrimidin-5-yl)-1,2-dihydrobenzo[e][1,2]azaborinine, **4d**

(0.097 g, 64%) was prepared according to the general cross-coupling procedure from **3c** (0.181 g, 0.55 mmol) and 5-bromopyrimidine (0.080 g, 0.5 mmol). The desired borazaronaphthalene **4d** was obtained as a powdery off-white solid mp = 159–160 °C). ¹H NMR (CDCl₃, 500 MHz) δ 9.11 (s, 1H), 8.64 (s, 2H), 8.15 (br s, 1H), 8.10 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 (td, *J* = 7.6, 1.1 Hz, 1H), 7.39 (dd, *J* = 7.9, 5.8 Hz, 3H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 8.9 Hz, 2H). ¹³C NMR (CDCl₃, 125 MHz) δ 163.9 (d, *J*_{C-F} = 251.0 Hz), 156.8, 156.3, 145.6, 140.2, 137.5, 135.2, 135.2, 130.2 (d, *J*_{C-C-F} = 33.6 Hz), 125.1, 122.4, 118.4, 115.8 (d C-C-C-F, *J* = 20.0 Hz). ¹¹B NMR (CDCl₃, 128.4 MHz) δ 34.1. ¹⁹F NMR (CDCl₃, 471 MHz) δ –114.85 (s, 3F). FT-IR (cm^{–1}, neat, ATR) 3235 (br, w), 3025 (w), 2975 (w), 1568 (m), 1219 (vs), 834 (s), 724 (vs), 553 (m). HRMS (EI) calcd for C₈H₁₃BFN₃ [M]⁺: 301.1187, found: 301.1181.

Chlorination of a 2,1-Borazaronaphthyltrifluoroborate

3-Chloro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine was synthesized according to a literature procedure.¹⁶ To an 8 mL screw top vial equipped with a stir bar was added 2,1-borazaronaphthyltrifluoroborate in a 1:1 mixture of EtOAc/H₂O (0.1 M). Trichloroisocyanuric acid (0.038 g, 0.33 equiv) was added in one portion, and the biphasic mixture was stirred vigorously for 15 min. The reaction was quenched with 10% Na₂SO₃ (w/v), transferred to a separatory funnel containing H₂O (5 mL) and Et₂O (5 mL). The layers were separated, and the aqueous layer was further extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were further washed with 1 M NaOH (3 × 10 mL), dried (anhyd N₂SO₄) and concentrated *in vacuo*.

3-Chloro-2-phenyl-1,2-dihydrobenzo[e][1,2]azaborinine, **5**

(0.107 g, 89%) was prepared according to the chlorination procedure from **3a** (0.155 g, 1.0 equiv). The desired borazaronaphthalene **5** was obtained as a powdery beige solid mp = 99–100 °C). ¹H NMR (CDCl₃, 500 MHz) δ 8.17 (s, 1H), 8.08 (br s, 1H), 7.90–7.96 (m, 2H), 7.61 (d, *J* = 7.78 Hz, 1H), 7.44–7.50 (m, 4H), 7.33 (d, *J* = 8.09 Hz, 1H), 7.24 (td, *J* = 7.50, 1.10 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ 143.6, 139.2, 133.6, 129.8, 129.0, 129.0, 128.3, 124.6, 122.3, 118.3. ¹¹B NMR (CDCl₃, 128.4 MHz) δ 32.9. FT-IR (cm^{–1}, neat,

ATR) 3378 (br, w), 1557 (m), 1421 (m), 748 (vs), 699 (vs), 605 (m). **HRMS** (EI) calcd for $C_{14}H_{11}BCIN$ $[M]^+$: 239.0673, found: 239.0668.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 1:

Approaches to the Diversification of 2,1-Borazonaphthalene Scaffolds

Scheme 2:

Chlorination of a 2,1-Borazonaphthyltrifluoroborate

Table 1:

Scope of the Pd-Catalyzed Borylation of Various Brominated 2,1-Borazonaphthalenes^a

^a General reaction conditions: 8-bromo-2,1-borazonaphthalene (0.5 mmol, 1.0 equiv), B_2Pin_2 (1.1 equiv), $Pd(dppf)Cl_2$ (5 mol %), K_2CO_3 (4 equiv), $PhOH$ (2 equiv), toluene (0.1 M), rt, 4–6 h; All yields are isolated yields after purification.

^b Reaction performed on a 6 mmol scale.

Table 2:Scope of the Direct Cross-Coupling with *B*-Phenyl 2,1-Borazaronaphthalene^c

^cGeneral reaction conditions: 8-borylated-2,1-borazaronaphthalene (0.5 mmol, 1.0 equiv), ArBr (1 equiv), XPhos Pd G2 (2nd Generation XPhos Precatalyst: chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II), (3 mol %), K₂CO₃ (3 equiv), *t*-BuOH/H₂O (1:1, 0.5 M), 40 °C, 18 h; All yields are isolated yields after purification.

Table 3:Scope of BF_3K Synthesis with Various Borylated 2,1-Borazaronaphthalenes^d

^d General reaction conditions: 8-borylated-2,1-borazaronaphthalene (0.5 mmol, 1.0 equiv), aqueous KHF_2 (4.5 M, 4 equiv) MeOH (1 M), 0 °C to rt, 18 h. All yields are isolated yields after purification.

Table 4:

Scope of BF_3K Coupling with *B*-(4-Fluorophenyl)-2,1-borazonaphthalene^e

^eGeneral reaction conditions: Trifluoroborato-2,1-borazonaphthalene (1.1 equiv), ArBr (0.5 mmol, 1 equiv), $\text{Pd}(\text{PPh}_3)_4$ (5 mol %), Et_3N (3 equiv), toluene/ H_2O (1:1, 0.5 M), 80 °C, 18 h; All yields are isolated yields after purification.