Cascade CuH-Catalyzed Conversion of Alkynes to Enantioenriched 1,1-Disubstituted Products

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1. Supplementary methods

1.1 General Methods

Unless stated otherwise, all solvents were purified and dried according to standard methods prior to use. NMR spectra were recorded on Bruker AV-400, DRX-500 and AV-600 instruments. $^1$H NMR spectra were referenced relative to tetramethylsilane signals or residual protio solvent signals. Data for $^1$H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sex = sextet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for $^{13}$C NMR are reported in terms of chemical shift (δ, ppm). High-resolution mass spectra (HRMS) for new compounds were recorded on an Agilent LC/MSD TOF mass spectrometer.

1.2 General Procedure for the Synthesis of Substrates

Substrates 1a–j, 1n–o and ligands L1–L7 are commercially available and were used directly without further purification. Substrates 1k–m were synthesized according to known procedures.$^1,2$ Amination electrophiles 2$^{3-5}$, alkenyl–Bdan intermediate A$^3$ and HBdan (3)$^6$ were also synthesized according to known procedures (Supplementary Figure 1).
Supplementary Figure 1. Alkynes and hydroxylamine electrophiles used in this reaction.

1.3 Cascade Hydrofunctionalization of Alkynes

1.3.1 General Procedure A: Cascade Hydrofunctionalization of Alkynes

To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar were added CuBr (1.4 mg, 0.01 mmol, 0.05 equiv), \((R_\theta)-DTBM\)-Segphos (14.2 mg, 0.012 mmol, 0.06 equiv), and LiO\(^t\)Bu (50.0 mg, 0.625 mmol, 3.125 equiv) under N\(_2\) atmosphere, and the reaction vessel was evacuated under high vacuum for 10 min then back-filled with N\(_2\). Anhydrous THF (1.0 mL) was added, and the mixture was stirred at room temperature for 10 min. Next, polymethylhydrosiloxane (PMHS, 111.3 mg, 0.5 mmol, 2.5 equiv) and HBdan (40.3 mg, 0.24 mmol, 1.2 equiv) were added successively, and the resultant mixture was stirred at room temperature for an additional 10 min. Finally, alkyne 1 (0.2 mmol, 1.0 equiv) and BzONR\(^{1}\)R\(^2\) (0.24 mmol, 1.2 equiv) were added in succession. The reaction solution was allowed to stir at room temperature for 16 h, at which point it was filtered through a pad of celite and concentrated \textit{in vacuo}. After removal of volatiles under reduced pressure, the resulting residue was purified by silica gel flash column chromatography to afford the desired product 4.
Supplementary Figure 2. Photographic depiction of reaction setup following general procedure. (a) CuBr, \((R_a)-\text{DTBM-Segphos}\), LiO\textsubscript{Bu}, alkyne, and PMHS from commercial suppliers. (b) Model amine electrophile \(2a\) and HBdan. (c) Addition of CuBr, \((R_a)-\text{DTBM-Segphos}\), and LiO\textsubscript{Bu} under N\textsubscript{2} atmosphere. (d) Injection of anhydrous THF. (e) Injection of PMHS. (f) Addition of HBdan. (g) Injection of alkyne \(1a\). (h) Addition of amination reagent \(2a\). (i) Reaction stirring at room temperature until full conversion is reached.
1.3.2 Experimental details and analytical data for products

**(R)**-**N**,**N**-dibenzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentan-1-amine (4a): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/50, v/v/v) gave the product as a colorless oil (81.1 mg, 80% yield, 96% ee). [α]D²² = –76.0 (c = 0.5 Chloroform, 96% ee). **¹H NMR** (600 MHz, CDCl₃) δ 7.37–7.26 (m, 9H), 7.25–7.20 (m, 3H), 7.20–7.15 (m, 3H), 7.08 (t, J = 7.8 Hz, 2H), 6.99 (d, J = 8.2 Hz, 2H), 6.26 (d, J = 7.3 Hz, 2H), 5.77 (s, 2H), 3.70 (A₂B₂, JAB = 13.7 Hz, 2H), 3.61 (B₂A₂, JB₂A₂ = 13.7 Hz, 2H), 2.64 (t, J = 7.7 Hz, 2H), 2.37–2.30 (m, 1H), 1.91–1.79 (m, 1H), 1.73–1.61 (m, 2H), 1.56–1.48 (m, 1H), 1.46–1.29 (m, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 142.4, 140.9, 140.1, 136.3, 128.7, 128.4, 128.3, 127.5, 126.9, 125.7, 119.7, 117.5, 105.7, 56.1, 35.7, 31.7, 28.2, 24.9. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. **HRMS** (ESI-TOF) calcd for C₃₅H₃₇BN₃ [M+H]+: 510.3075, Found: 510.3077. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak AD-H column (3µm, 0.46×25 cm), CO₂/IPA = 85/15, 2.0 mL/min, λ = 210 nm, t (minor) = 21.613 min, t (major) = 23.773 min.

**(R)**-**N**,**N**-dibenzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-4-phenylbutan-1-amine (4b): The title compound was prepared from 1b (26.0 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/50, v/v/v) gave the product as a colorless oil (76.7 mg, 77% yield, 97% ee). [α]D²² = –74.4 (c = 0.5 Chloroform, 97% ee). **¹H NMR** (600 MHz, CDCl₃) δ 7.36–7.28 (m, 10H), 7.26–7.21 (m, 3H), 7.21–7.18 (m, 2H), 7.09–7.04 (m, 2H), 6.97 (dd, J = 8.3, 0.9 Hz, 2H), 6.20 (dd, J = 7.3, 0.9 Hz, 2H), 5.66 (s, 2H), 3.69 (AB, JAB = 13.6 Hz, 2H), 3.58 (d, JB₂A₂ = 13.7 Hz, 2H), 2.73–2.66 (m, 1H), 2.65–2.59 (m, 1H), 2.34 (dd, J = 9.3, 4.2 Hz, 1H), 1.90–1.80 (m, 1H), 1.72–1.60 (m, 2H), 1.54–1.47 (m, 1H). **¹³C NMR** (150 MHz, CDCl₃) δ 142.2, 140.9, 140.1, 136.3, 128.7, 128.6, 128.5, 128.3, 127.5, 126.9, 126.0, 119.7, 117.5, 105.6, 56.1, 36.0, 30.4, 23.7. Note: The carbon signal bound to the boron atom was not observed,
likely due to quadrupolar relaxation. **HRMS** (ESI-TOF) calcd for C_{32}H_{39}BN_{3} [M+H]^+: 476.3232, Found: 476.3235. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH_{3}) / CO_{2} = 40:60, 4.0 mL/min, λ = 331 nm, t (major) = 4.313 min, t (minor) = 6.488 min.

![Chemical structure](attachment:image.png)

(R)-N,N-dibenzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)octan-1-amine (4c): The title compound was prepared from 1c (22.0 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn_{2} (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO^tBu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (56.6 mg, 60% yield, 95% ee). [α]_{D}^{25} = –35.786 (c = 0.5 Chloroform, 95% ee).

**1H NMR** (600 MHz, CDCl_{3}) δ 7.38–7.34 (m, 4H), 7.34–7.29 (m, 4H), 7.25–7.20 (m, 2H), 7.11–7.07 (m, 2H), 6.99 (dd, J = 8.3, 1.0 Hz, 2H), 6.29 (dd, J = 7.3, 1.0 Hz, 2H), 5.82 (s, 2H), 3.72 (AB, J_{AB} = 13.7 Hz, 2H), 3.62 (BA, J_{BA} = 13.7 Hz, 2H), 2.35 (dd, J = 9.4, 4.4 Hz, 1H), 1.90–1.78 (m, 1H), 1.53–1.46 (m, 1H), 1.39–1.23 (m, 10H), 0.90 (t, J = 7.1 Hz, 3H). **13C NMR** (150 MHz, CDCl_{3}) δ 140.6, 139.8, 135.9, 128.3, 127.9, 127.1, 126.5, 119.3, 117.0, 105.2, 55.6, 31.4, 29.7, 28.8, 28.4, 24.4, 22.2, 13.7. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. **HRMS** (ESI-TOF) calcd for C_{34}H_{35}BN_{3} [M+H]^+: 496.2919, Found: 496.2921. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak OD-H column (3μm, 0.46×25 cm), CO_{2} / IPA = 80 / 20, 2.0 mL/min, λ = 210 nm, t (major) = 12.722 min, t (minor) = 15.056 min.

![Chemical structure](attachment:image.png)

(R)-N,N-dibenzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)pentan-1-amine (4d): The title compound was prepared from 1d (13.6 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn_{2} (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO^tBu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (51.6 mg, 60% yield, 95% ee). [α]_{D}^{25} = –105.1 (c = 0.5 Chloroform, 95% ee). **1H NMR** (600 MHz, CDCl_{3}) δ 7.35 (d, J = 7.1 Hz, 4H), 7.31 (t, J = 7.6 Hz, 4H), 7.25–7.19 (m, 2H), 7.08 (t, J = 7.8 Hz, 2H), 6.99 (d, J = 8.2 Hz, 2H), 6.28 (d, J = 7.3 Hz, 2H), 5.82 (s, 2H), 3.71 (AB, J_{AB} = 13.7 Hz, 2H), 3.62 (BA, J_{BA} = 13.7 Hz, 2H), 2.34 (dd, J = 9.4, 4.4 Hz, 1H), 1.89–1.81 (m, 1H), 1.53–1.46 (m, 1H), 1.39–1.23 (m, 10H), 0.90 (t, J = 7.1 Hz, 3H). **13C NMR** (150 MHz, CDCl_{3}) δ 140.6, 139.8, 135.9, 128.3, 127.9, 127.1, 126.5, 119.3, 117.0, 105.2, 55.6, 31.4, 29.7, 28.8, 28.4, 24.4, 22.2, 13.7. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation.
1H), 1.55–1.46 (m, 1H), 1.39–1.34 (m, 2H), 1.33–1.29 (m, 2H), 0.94 (t, J = 7.0 Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) δ 141.0, 140.3, 136.4, 128.8, 128.4, 127.6, 126.9, 119.8, 117.5, 105.7, 56.1, 31.1, 24.7, 23.3, 14.2. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C\(_{29}\)H\(_{33}\)BN\(_3\) [M+H]\(^+\): 434.2762, Found: 434.2765. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH\(_3\)) / CO\(_2\) = 20 / 80, 4.0 mL/min, λ = 331 nm, t (major) = 6.282 min, t (minor) = 6.707 min.

\[\text{(R)-N,N-dibenzyl-3-methyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)butan-1-amine} \ (4e): \text{The title compound was prepared from 1e} \ (13.6 \text{mg}, 0.2 \text{mmol, 1.0 equiv}), \text{HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn}_2 \ (76.1 \text{mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (52.9 mg, 61% yield, 95% ee).} \]

\[\text{[α]}_D^{22} = -114.3 \ (c = 0.5 \text{ Chloroform, 95% ee).} \]

\(^{1}H\) NMR (600 MHz, CDCl\(_3\)) δ 7.36 (d, J = 7.0 Hz, 4H), 7.31 (t, J = 7.5 Hz, 4H), 7.24–7.19 (m, 2H), 7.09 (t, J = 7.8 Hz, 2H), 6.99 (d, J = 8.3 Hz, 2H), 6.29 (d, J = 7.4 Hz, 2H), 5.81 (s, 2H), 3.70 (AB, J\(_{AB}\) = 13.7 Hz, 2H), 3.59 (BA, J\(_{BA}\) = 13.7 Hz, 2H), 2.47–2.39 (m, 1H), 1.73–1.64 (m, 1H), 1.62–1.54 (m, 1H), 1.46–1.38 (m, 1H), 0.96 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) δ 141.0, 140.3, 136.3, 128.7, 128.3, 127.5, 126.9, 119.8, 117.5, 105.6, 55.9, 34.0, 26.9, 23.8, 22.6. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C\(_{29}\)H\(_{33}\)BN\(_3\) [M+H]\(^+\): 434.2762, Found: 434.2765. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak OD-H column (3μm, 0.46×25 cm), CO\(_2\) / IPA = 80 / 20, 2.0 mL/min, λ = 210 nm, t (major) = 7.893 min, t (minor) = 9.800 min.

\[\text{(R)-N,N-dibenzyl-5-methyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)hexan-1-amine} \ (4f): \text{The title compound was prepared from 1f} \ (19.2 \text{mg}, 0.2 \text{mmol, 1.0 equiv}), \text{HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv) and BzONBn}_2 \ (76.1 \text{mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (54.4 mg, 59% yield, 98% ee).} \]

\[\text{[α]}_D^{25} = -32.294 \ (c = 0.5 \text{ Chloroform, 98% ee).} \]
$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.36 (d, $J = 7.2$ Hz, 4H), 7.32 (t, $J = 7.6$ Hz, 4H), 7.24–7.20 (m, 2H), 7.12–7.06 (m, 2H), 6.99 (d, $J = 7.9$ Hz, 2H), 6.29 (d, $J = 7.3$ Hz, 2H), 5.82 (s, 2H), 3.72 (AB, $J_{AB} = 13.7$ Hz, 2H), 3.62 (BA, $J_{BA} = 13.7$ Hz, 2H), 2.38–2.32 (m, 1H), 1.87–1.78 (m, 1H), 1.60–1.53 (m, 1H), 1.52–1.44 (m, 1H), 1.39–1.20 (m, 4H), 0.89 (dd, $J = 6.6$, 4.6 Hz, 6H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 141.0, 140.2, 136.3, 128.7, 128.3, 127.5, 126.9, 119.8, 117.5, 105.6, 56.0, 39.5, 27.8, 26.5, 25.1, 22.7, 22.6. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation.

HRMS (ESI-TOF) calcd for C$_{31}$H$_{37}$BN$_3$ [M+H]$^+$/: 462.3075, Found: 462.3076.

SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak AD-H column (3μm, 0.46×25 cm), CO$_2$ / IPA = 90 / 10, 2.0 mL/min, $\lambda = 210$ nm, t (major) = 13.39 min, t (minor) = 16.95 min.

(R)-N,N-dibenzyl-3-cyclohexyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)propan-1-amine (4g): The title compound was prepared from 1g (24.4 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn$_2$ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'tBu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (66.9 mg, 71% yield, 96% ee). $[\alpha]_D^{22} = -71.0$ (c = 0.5 Chloroform, 96% ee).

SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak IG column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ =15:85, 4.0 mL/min, $\lambda = 331$ nm, t (major) = 6.23 min, t (minor) = 6.78 min.

(R)-N,N-dibenzyl-1-cyclopropyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)methanamine (4h): The title compound was prepared from 1h (13.2 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5
mmol, 2.5 equiv), BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (53.5 mg, 62% yield, 98% ee). [α]D²² = –67.3 (c = 0.5 Chloroform, 98% ee).

**¹H NMR** (600 MHz, CDCl₃) δ 7.36 (d, J = 7.2 Hz, 4H), 7.32 (t, J = 7.6 Hz, 4H), 7.25–7.20 (m, 2H), 7.08 (t, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.28 (dd, J = 7.3, 1.0 Hz, 2H), 6.03 (s, 2H), 3.74 (AB, JAB = 13.8 Hz, 2H), 3.60 (BA, JBA = 13.8 Hz, 2H), 2.55 (dd, J = 9.6, 4.7 Hz, 1H), 1.77–1.67 (m, 1H), 1.57–1.46 (m, 1H), 0.72–0.63 (m, 1H), 0.59–0.49 (m, 2H), 0.23–0.16 (m, 1H), 0.15–0.07 (m, 1H).

**¹³C NMR** (150 MHz, CDCl₃) δ 141.1, 140.2, 136.3, 128.6, 128.4, 127.5, 126.9, 119.8, 117.4, 105.6, 55.9, 49.0 (The carbon signal bound to the boron atom was very week), 29.9, 10.3, 6.5, 5.9. HRMS (ESI-TOF) calcd for C₂₉H₃₁BN₃ [M+H]⁺: 432.2606, Found: 432.2607.

**SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak AD-H column (3μm, 0.46×25 cm), CO₂/IPA = 80/20, 2.0 mL/min, λ = 210 nm, t (minor) = 9.17 min, t (major) = 10.80 min.

(R)-N,N-dibenzyl-2-cyclohexyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)ethan-1-amine (4i): The title compound was prepared from **1i** (21.6 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv) and BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (60.8 mg, 64% yield, 97% ee). [α]D²² = –77.2 (c = 0.5 Chloroform, 97% ee).

**¹H NMR** (600 MHz, CDCl₃) δ 7.36 (d, J = 7.0 Hz, 4H), 7.31 (t, J = 7.7 Hz, 4H), 7.24–7.20 (m, 2H), 7.08 (t, 2H), 6.13–7.06 (m, 2H), 7.00 (dd, J = 8.4, 1.0 Hz, 2H), 6.30 (dd, J = 7.3, 1.0 Hz, 2H), 5.80 (s, 2H), 3.69 (AB, JAB = 13.7 Hz, 2H), 3.59 (BA, JBA = 13.7 Hz, 2H), 2.51–2.38 (m, 1H), 1.79–1.59 (m, 6H), 1.44–1.32 (m, 1H), 1.28–1.10 (m, 4H), 1.03–0.93 (m, 1H), 0.92–0.81 (m, 1H). **¹³C NMR** (150 MHz, CDCl₃) δ 141.0, 140.4, 136.3, 128.7, 128.3, 127.5, 126.9, 119.8, 117.5, 105.6, 55.9, 36.4, 34.6, 33.4, 32.4, 26.6, 26.4, 26.3. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C₃₂H₃₇BN₃ [M+H]⁺: 474.3075, Found: 474.3076. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH₃) / CO₂ = 40 / 60, 4.0 mL/min, λ = 331 nm, t (major) = 2.728 min, t (minor) = 2.962 min.
**tert-butyl (R)-4-(2-(dibenzyalamino)-2H-naphtho[1,8-de]-1,3,2-diazaborinin-2(3H)-yl)ethyl)piperidine-1-carboxylate (4j):** The title compound was prepared from 1j (41.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (60.3 mg, 52% yield, 97% ee). $[\alpha]_D^{22} = -75.1$ (c = 0.5 Chloroform, 97% ee).

**1H NMR** (600 MHz, CDCl₃) $\delta$ 7.35 (d, $J = 7.5$ Hz, 4H), 7.32 (t, $J = 7.5$ Hz, 4H), 7.24–7.21 (m, 2H), 7.10 (t, $J = 7.8$ Hz, 2H), 7.01 (d, $J = 7.3$ Hz, 2H), 6.31 (d, $J = 7.3$ Hz, 2H), 5.75 (s, 2H), 4.05 (s, 2H), 3.68 (AB, $J_{AB} = 13.7$ Hz, 2H), 3.62 (BA, $J_{BA} = 13.6$ Hz, 2H), 2.63 (s, 2H), 2.49–2.40 (m, 1H), 1.79–1.69 (m, 1H), 1.59–1.50 (m, 2H), 1.49–1.33 (m, 11H), 1.16–0.99 (m, 2H).

**13C NMR** (150 MHz, CDCl₃) $\delta$ 154.8, 140.8, 140.1, 136.3, 128.7, 128.4, 127.5, 127.0, 119.8, 117.7, 105.8, 79.3, 56.1, 34.5, 33.0, 32.3, 32.2, 28.5. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. **HRMS** (ESI-TOF) calced for C₃₆H₄₄BN₄O₂ [M+H]+: 575.3552, Found: 575.3555.

**SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH₃) / CO₂ = 40 / 60, 4.0 mL/min, $\lambda$ = 331 nm, t (major) = 2.715 min, t (minor) = 4.746 min.

**R-5-(dibenzyalamino)-5-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)pentyl benzoate (4k):** The title compound was prepared from 1k (37.6 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONBn₂ (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/60, v/v/v) gave the product as a colorless oil (80.0 mg, 72% yield, 96% ee). $[\alpha]_D^{22} = -17.5$ (c = 0.5 Chloroform, 96% ee).

**1H NMR** (600 MHz, CDCl₃) $\delta$ 8.07–8.00 (m, 2H), 7.57–7.52 (m, 1H), 7.40 (t, $J = 7.8$ Hz, 2H), 7.35 (d, $J = 7.2$ Hz, 4H), 7.30 (t, $J = 7.5$ Hz, 4H), 7.23–7.19 (m, 2H), 7.10–7.04 (m, 2H), 6.99 (d, $J = 8.2$ Hz, 2H), 6.27 (d, $J = 7.3$ Hz, 2H), 5.83 (s, 2H), 4.43–4.38 (m, 1H), 4.37–4.33 (m, 1H), 3.72 (AB, $J_{AB} = 13.7$ Hz, 2H), 3.63 (BA, $J_{BA} = 13.7$ Hz, 2H), 2.42–2.33 (m, 1H), 1.96–1.86 (m, 1H), 1.86–1.74 (m, 2H), 1.65–1.56 (m, 1H), 1.56–1.42 (m, 2H). **13C NMR** (150 MHz, CDCl₃) $\delta$ 166.7, 140.9, 140.1, 136.3, 132.9, 130.3, 129.5, 128.7, 128.4, 128.3, 127.5, 127.0, 119.8, 117.5, 105.7, 64.5,
56.1, 43.4, 29.2, 25.1, 24.8, 18.7. **HRMS** (ESI-TOF) calcd for C_{36}H_{37}BN_{3}O_{2} [M+H]^+: 554.2973, Found: 554.2975. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Daicel IB column (3μm, 4.6×250 mm), CO_{2} / MeOH = 65 / 35, 4.0 mL/min, λ = 229 nm, t (major) = 4.500 min, t (minor) = 10.309 min.

**AcO-**NBN_{2} _{\text{\textregistered} \text{dan}}

**(R)-5-(dibenzylamino)-5-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)pentyl acetate** (4l): The title compound was prepared from 1l (30.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv), BzONBn_{2} (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO{\text{Bu}} (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/15, v/v/v) gave the product as a colorless oil (60.9 mg, 59% yield, 96% ee). [α]_{D}^{22} = −10.4 (c = 0.5 Chloroform, 96% ee). **1H NMR** (600 MHz, CDCl_{3}) δ 7.40−7.37 (m, 4H), 7.35 (t, J = 7.6 Hz, 4H), 7.28−7.24 (m, 2H), 7.16−7.09 (m, 2H), 7.03 (dd, J = 8.3, 0.9 Hz, 2H), 6.33 (dd, J = 7.3, 1.0 Hz, 2H), 5.84 (s, 2H), 4.10 (t, J = 6.7 Hz, 2H), 3.75 (AB, J_{AB} = 13.7 Hz, 2H), 3.66 (BA, J_{BA} = 13.7 Hz, 2H), 2.41−2.36 (m, 1H), 2.09 (s, 3H), 1.92−1.83 (m, 1H), 1.70−1.63 (m, 2H), 1.58−1.50 (m, 1H), 1.45−1.35 (m, 6H). **13C NMR** (150 MHz, CDCl_{3}) δ 171.3, 141.0, 140.2, 136.3, 128.7, 128.3, 127.5, 127.0, 119.8, 117.5, 105.7, 64.5, 56.1, 29.8, 28.6, 25.9, 25.1, 21.1. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. **HRMS** (ESI-TOF) calcd for C_{31}H_{35}BN_{3}O_{2} [M+H]^+: 492.2817, Found: 492.2818. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak AD-H column (3μm, 0.46×25 cm), CO_{2} / IPA = 85 / 15, 2.0 mL/min, λ = 210 nm, t (minor) = 10.237 min, t (major) = 12.634 min.

**PhMeNOC-**NBN_{2} _{\text{\textregistered} \text{dan}}

**(R)-5-(dibenzylamino)-N-methyl-5-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-N-phenylpentanamide** (4m): The title compound was prepared from 1m (37.4 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv), BzONBn_{2} (76.1 mg, 0.24 mmol, 1.2 equiv), and LiO{\text{Bu}} (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/2, v/v/v) gave the product as a colorless oil (67.8 mg, 61% yield, 89% ee). [α]_{D}^{22} = −93.0 (c = 0.5 Chloroform, 89% ee). **1H NMR** (600 MHz, CDCl_{3}) δ 7.43 (t, J = 7.7 Hz, 2H), 7.37−7.26 (m, 9H), 7.22−7.16 (m, 4H), 7.13−7.07 (m, 4H), 6.96 (d, J = 8.2 Hz, 2H), 6.48 (d, J = 7.3 Hz, 2H), 3.74 (d,
$J = 13.5 \text{ Hz}, 2\text{H})$, $3.41 \text{ (d, } J = 13.5 \text{ Hz, } 2\text{H})$, $3.36 \text{ (s, } 3\text{H})$, $2.30–2.17 \text{ (m, } 2\text{H})$, $2.17–2.07 \text{ (m, } 1\text{H})$, $1.77–1.68 \text{ (m, } 1\text{H})$, $1.65 \text{ (q, } J = 12.2 \text{ Hz, } 1\text{H})$, $1.53 \text{ (q, } J = 11.4 \text{ Hz, } 1\text{H})$, $1.33–1.24 \text{ (m, } 1\text{H})$. $^{13}\text{C NMR}$ (150 MHz, CDCl$_3$) δ 173.2, 143.9, 141.9, 140.3, 136.4, 129.9, 128.7, 128.3, 127.9, 127.6, 127.4, 126.8, 120.1, 116.8, 105.5, 55.8, 48.1 (C–B, weak signal), 37.4, 33.9, 23.6, 21.9. $\text{HRMS (ESI-TOF) calcd for C}_{36}\text{H}_{38}\text{BN}_4\text{O}[\text{M+H}]^+:}$ 553.3133, Found: 553.3136. $\text{SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH}_3 / \text{ CO}_2 = 40 / 60, 4.0 \text{ mL/min, } \lambda = 331 \text{ nm, t (major) = 3.154 min, t (minor) = 3.499 min.}$

(R)-N,N-dibenzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-2-phenylethan-1-amine (4n): The title compound was prepared from 1n (20.4 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONEt$_2$ (46.3 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/hexane/ethyl acetate = 0.1%/50/1, v/v/v) gave the product as a colorless oil (55.6 mg, 60% yield, 97% ee). $^1\text{H NMR}$ (600 MHz, CDCl$_3$) δ 7.44–7.40 (m, 4H), 7.37 (t, $J = 7.7 \text{ Hz, } 4\text{H})$, 7.31 (t, $J = 7.5 \text{ Hz, } 2\text{H})$, 7.29–7.26 (m, 2H), 7.26–7.20 (m, 1H), 7.20–7.11 (m, 2H), 7.01 (dd, $J = 8.2, 7.3 \text{ Hz, } 2\text{H})$, 6.92 (dd, $J = 8.3, 1.0 \text{ Hz, } 2\text{H})$, 6.06 (dd, $J = 7.3, 1.0 \text{ Hz, } 2\text{H})$, 5.77 (s, 2H), 3.93 (d, $J = 13.8 \text{ Hz, } 2\text{H})$, 3.67 (d, $J = 13.8 \text{ Hz, } 2\text{H})$, 3.38 (dd, $J = 13.2, 4.4 \text{ Hz, } 1\text{H})$, 2.89 (dd, $J = 11.4, 4.4 \text{ Hz, } 1\text{H})$, 2.77 (dd, $J = 13.2, 11.4 \text{ Hz, } 1\text{H})$. $^{13}\text{C NMR}$ (150 MHz, CDCl$_3$) δ 141.1, 140.9, 139.97, 136.2, 128.9, 128.9, 128.6, 128.4, 127.4, 127.1, 126.4, 119.6, 117.3, 105.5, 55.9, 49.2, 29.5. $\text{HRMS (ESI-TOF) calcd for C}_{32}\text{H}_{30}\text{BN}_3[\text{M+H}]^+:}$ 467.2647, Found: 467.2647. $\text{SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), 40% MeOH containing 0.5 vol% 7M methanolic NH}_3 / \text{ CO}_2, 1600 \text{ psi backpressure, } 30 \text{ °C, } 4.0 \text{ mL/min, } \lambda = 231 \text{ nm, t (major) = 4.677 min, t (minor) = 4.309 min.}$

(R)-N,N-diethyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentan-1-amine (4o): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONEt$_2$ (46.3 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/methanol = 0.1%/20/1, v/v/v) gave the product as a colorless oil (64.2 mg, 83% yield, 97% ee). $[\alpha]_D^{22} = +47.4 \text{ (c = 0.5 Chloroform, 97% ee).}$ $^1\text{H NMR}$
(600 MHz, CDCl$_3$) $\delta$ 7.23 (t, $J = 7.6$ Hz, 2H), 7.18–7.12 (m, 3H), 7.09 (t, $J = 7.8$ Hz, 2H), 7.00 (d, $J = 8.2$ Hz, 2H), 6.29 (d, $J = 7.3$ Hz, 2H), 5.88 (s, 2H), 2.69–2.47 (m, 6H), 2.23 (dd, $J = 9.8$, 4.4 Hz, 1H), 1.78–1.57 (m, 3H), 1.52–1.37 (m, 2H), 1.35–1.25 (m, 1H), 0.99 (t, $J = 7.1$ Hz, 6H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.5, 141.1, 136.3, 128.3, 128.3, 127.5, 125.7, 119.8, 117.4, 105.6, 50.9 (C–B, weak signal), 44.9, 35.7, 32.0, 27.8, 27.5, 11.9.

HRMS (ESI-TOF) calcd for C$_{25}$H$_{33}$BN$_3$[M+H]$^+$: 386.2762, Found: 386.2765.

SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 20 / 80, 4.0 mL/min, $\lambda$ = 329 nm, t (major) = 6.530 min, t (minor) = 7.321 min.

(R)-N-benzyl-N-methyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentan-1-amine (4p): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONMeBn (57.9 mg, 0.24 mmol, 1.2 equiv), and LiO$_{t}$Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/3, v/v/v) gave the product as a colorless oil (74.1 mg, 85% yield, 97% ee). [$\alpha$]$_D^{22}$ = +14.0 (c = 0.5 Chloroform, 97% ee).

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.32–7.28 (m, 4H), 7.26–7.21 (m, 3H), 7.15 (d, $J = 6.2$ Hz, 3H), 7.09 (t, $J = 7.8$ Hz, 2H), 7.01 (d, $J = 8.2$ Hz, 2H), 6.31 (d, $J = 7.3$ Hz, 2H), 5.92 (s, 2H), 3.57 (AB, $J_{AB} = 13.1$ Hz, 1H), 3.51 (BA, $J_{BA} = 13.1$ Hz, 1H), 2.67–2.53 (m, 2H), 2.17 (s, 3H), 2.01 (dd, $J = 9.6$, 4.6 Hz, 1H), 1.87–1.75 (m, 1H), 1.70–1.53 (m, 3H), 1.52–1.42 (m, 1H), 1.39–1.30 (m, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.6, 141.0, 139.3, 136.4, 129.1, 128.4, 128.3, 127.6, 127.1, 125.7, 120.0, 117.6, 111.6, 105.8, 61.5, 55.8 (C–B, weak signal), 40.9, 35.8, 31.2, 28.4, 27.4. HRMS (ESI-TOF) calcd for C$_{29}$H$_{33}$BN$_3$[M+H]$^+$: 434.2762, Found: 434.2765. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 30:70, 4.0 mL/min, $\lambda$ = 331 nm, t (major) = 2.980 min, t (major) = 3.500 min.

(R)-N-(1-(1H-naphtho[1,8-de][1,3,2]diaza-borinin-2(3H)-yl)-5-phenylpentyl)-N-cyclohexylcyclohexanamine (4q): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzONCy$_2$ (72.2 mg, 0.24 mmol, 1.2 equiv), and LiO$_{t}$Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash
column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/10, v/v/v) gave the product as a colorless oil (87.8 mg, 89% yield, 96% ee). $[\alpha]_D^{22} = +8.7$ (c = 0.5 Chloroform, 96% ee). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.28 (t, $J = 7.5$ Hz, 2H), 7.21–7.15 (m, 3H), 7.08 (t, $J = 7.8$ Hz, 2H), 6.98 (d, $J = 8.3$ Hz, 2H), 6.25 (d, $J = 7.3$ Hz, 2H), 5.79 (s, 2H), 2.71–2.59 (m, 2H), 2.52 (t, 2H), 2.40 (t, $J = 6.9$ Hz, 1H), 1.81–1.66 (m, 8H), 1.65–1.52 (m, 6H), 1.42–1.16 (m, 10H), 1.02 (q, $J = 12.8$ Hz, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 142.5, 141.5, 136.4, 128.4, 128.4, 127.6, 125.8, 119.7, 117.1, 105.5, 57.7, 35.8, 34.7, 34.0, 32.3, 32.1, 28.4, 26.8, 26.7, 26.1. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C$_{31}$H$_{35}$BN$_3$[M+H]$^+$: 494.3696, Found: 494.3699.

SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IBN column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 20 / 80, 4.0 mL/min, $\lambda$ = 331 nm, $t$ (major) = 4.024 min, $t$ (minor) = 4.511 min.

(R)-N-allyl-N-benzyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentan-1-amine (4r): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv), BzONBnAllyl (64.1 mg, 0.24 mmol, 1.2 equiv), and LiOtBu (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/10, v/v/v) gave the product as a colorless oil (57.6 mg, 63% yield, 94% ee). $[\alpha]_D^{22} = -22.0$ (c = 0.5 Chloroform, 94% ee). $^1$H NMR (600 MHz, CDCl$_3$) δ 7.45–7.26 (m, 7H), 7.24 (d, $J = 7.4$ Hz, 3H), 7.15 (t, $J = 7.8$ Hz, 2H), 7.06 (d, $J = 8.3$ Hz, 2H), 6.34 (d, $J = 7.3$ Hz, 2H), 6.01–5.83 (m, 3H), 5.22 (dd, $J = 27.9$, 13.7 Hz, 2H), 3.79 (AB, $J_{AB} = 13.8$ Hz, 1H), 3.65 (BA, $J_{BA} = 13.8$ Hz, 1H), 3.22 (d, $J = 6.3$ Hz, 2H), 2.70 (t, $J = 7.7$ Hz, 2H), 2.44 (dd, $J = 9.3$, 4.5 Hz, 1H), 1.91–1.80 (m, 1H), 1.79–1.67 (m, $J = 6.7$ Hz, 2H), 1.62–1.53 (m, 1H), 1.52–1.45 (m, 1H), 1.44–1.36 (m, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 142.4, 141.0, 140.1, 136.4, 136.3, 128.7, 128.4, 128.3, 128.3, 127.5, 126.8, 125.7, 119.8, 117.5, 117.1, 105.7, 56.3, 54.5, 49.9 (C–B, weak signal), 35.7, 31.8, 28.0, 26.0. HRMS (ESI-TOF) calcd for C$_{31}$H$_{35}$BN$_3$[M+H]$^+$: 460.2919, Found: 460.2919. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IBN column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 40 / 60, 4.0 mL/min, $\lambda$ = 331 nm, $t$ (major) = 2.339 min, $t$ (minor) = 2.675 min.
**(R)-N,N-diallyl-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentan-1-amine (4s):** The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), BzON(CH2=CH2)2 (52.1 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/3 to 0.1%/1/2, v/v/v) gave the product as a colorless oil (44.2 mg, 54% yield, 95% ee). $[α]_D^{22} = +9.7$ (c = 0.5 Chloroform, 95% ee). $^1$H NMR (600 MHz, CDCl3) δ 7.29–7.22 (m, 2H), 7.20–7.14 (m, 3H), 7.09 (dd, $J$ = 8.3, 7.3 Hz, 2H), 7.00 (dd, $J$ = 8.3, 1.0 Hz, 2H), 6.28 (dd, $J$ = 7.3, 1.0 Hz, 2H), 5.97–5.77 (m, 4H), 5.28–5.06 (m, 4H), 3.21 (dd, $J$ = 14.4, 6.0 Hz, 2H), 3.14 (dd, $J$ = 14.4, 6.7 Hz, 2H), 2.61 (td, $J$ = 7.8, 2.7 Hz, 2H), 2.35 (dd, $J$ = 9.5, 4.4 Hz, 1H), 1.81–1.58 (m, 3H), 1.54–1.37 (m, 2H), 1.37–1.27 (m, 1H). $^{13}$C NMR (150 MHz, CDCl3) δ 142.4, 141.0, 136.3, 136.1, 128.4, 128.3, 127.5, 125.7, 119.8, 117.5, 117.1, 105.7, 54.9, 35.7, 31.9, 27.8, 26.8. HRMS (ESI-TOF) calcd for C27H33BN3[M+H]$: 410.2762$, Found: $410.2765$. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), 20% (MeOH containing 0.5 vol% 7M methanolic NH3) / CO2 = 20 / 80, 4.0 mL/min, λ = 329 nm, t (major) = 4.765 min, t (minor) = 5.377 min.

**(R)-2-(5-phenyl-(1-pyrrolidin-1-yl)pentyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine (4t):** The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), pyrrolidin-1-yl benzoate (45.9 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using flash silica gel column chromatography (triethylamine/ethyl acetate/methanol = 0.1%/10/1, v/v/v) gave the product as a colorless oil (45.2 mg, 59% yield, 94% ee). $[α]_D^{22} = +33.4$ (c = 0.5 Chloroform, 94% ee). $^1$H NMR (600 MHz, CDCl3) δ 7.22 (t, $J$ = 7.4 Hz, 2H), 7.17–7.12 (m, 1H), 7.12–7.08 (m, 4H), 7.05 (d, $J$ = 8.2 Hz, 2H), 7.02–6.85 (m, 2H), 6.48 (d, $J$ = 7.2 Hz, 2H), 3.05 (s, 4H), 2.63–2.56 (m, 1H), 2.56–2.48 (m, 1H), 2.33–2.21 (m, 1H), 2.13–2.03 (m, 1H), 2.01–1.87 (m, 4H), 1.86–1.76 (m, 1H), 1.69–1.57 (m, 2H), 1.55–1.45 (m, 1H), 1.39–1.30 (m, 1H). $^{13}$C NMR (150 MHz, CDCl3) δ 142.1, 140.4, 136.2, 128.3, 128.3, 127.6, 125.7, 120.2, 118.1, 106.5, 54.11, 35.5, 31.5, 30.3, 26.5, 23.1. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C25H31BN3[M+H]$: 407.2589$, Found: $407.2585$.
SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH₃) / CO₂ = 30 / 70, 4.0 mL/min, λ = 329 nm, t (major) = 4.092 min, t (minor) = 4.738 min.

(R)-2-(1-(azocan-1-yl)-5-phenylpentyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine (4u): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), azocan-1-yl benzoate (56.0 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using flash silica gel column chromatography (triethylamine/ethyl acetate/hexane = 0.1%/1/1, v/v/v) gave the product as a colorless oil (60.3 mg, 71% yield, 95% ee). [α]D²² = +19.7 (c = 0.5 Chloroform, 95% ee). ¹H NMR (600 MHz, CDCl₃) δ 7.24 (t, J = 7.6 Hz, 2H), 7.18–7.13 (m, 3H), 7.09 (t, 2H), 7.00 (d, J = 8.2 Hz, 2H), 6.29 (d, J = 7.3 Hz, 2H), 5.87 (s, 2H), 2.73–2.49 (m, 6H), 2.12 (dd, J = 9.4, 5.1 Hz, 1H), 1.77–1.46 (m, 14H), 1.36–1.27 (m, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 142.5, 141.1, 136.3, 128.4, 128.3, 127.6, 125.6, 119.8, 117.4, 105.6, 56.7, 53.4 (C–B, weak signal), 35.8, 31.9, 28.5, 27.8, 26.1. HRMS (ESI-TOF) calcd for C²₈H₃₇BN₃[M+H]+: 426.3075, Found: 426.3077. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IBN column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH₃) / CO₂ = 30 / 70, 4.0 mL/min, λ = 329 nm, t (major) = 2.980 min, t (minor) = 3.500 min.

(R)-2-(1-(3,4-dihydroisoquinolin-2(1H)-yl)-5-phenylpentyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine (4v): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (155.8 mg, 0.7 mmol, 3.5 equiv), 3,4-dihydroisoquinolin-2(1H)-yl benzoate (60.7 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (70.0 mg, 0.875 mmol, 4.375 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexane = 0.1%/1/1, v/v/v) gave the product as a colorless oil (38.1 mg, 43% yield, 94% ee). [α]D²² = +122.8 (c = 0.5 Chloroform, 94% ee). ¹H NMR (600 MHz, CDCl₃) δ 7.25–7.19 (m, 2H), 7.18–7.05 (m, 8H), 7.05–6.98 (m, 3H), 6.29 (d, J = 7.3 Hz, 2H), 5.94 (s, 2H), 3.84 (AB, JAB = 14.7 Hz, 1H), 3.58 (BA, JBA = 14.7 Hz, 1H), 3.04–2.88 (m, 1H), 2.87–2.72 (m, 3H), 2.68–2.52 (m, 2H), 1.98 (dd, J = 9.8, 4.5 Hz, 1H), 1.92–1.81 (m, 1H), 1.71–1.58 (m, 3H), 1.55–1.44 (m, 1H), 1.42–1.30 (m, 1H). ¹³C NMR (150 MHz, CDCl₃) δ
142.5, 140.9, 136.3, 135.0, 134.4, 128.6, 128.3, 128.3, 127.6, 126.8, 126.2, 125.6, 120.0, 117.6, 105.8, 56.6 (C–B, weak signal), 55.8, 50.9, 35.7, 32.1, 29.3, 29.1, 27.1.

**HRMS (ESI-TOF)** calcd for C$_{30}$H$_{33}$BN$_{3}$[M+H]$^+$: 446.2762, Found: 446.2762. **SFC (chiral column)** The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 40 / 60, 4.0 mL/min, λ = 329 nm, t (minor) = 3.530 min, t (major) = 4.024 min.

(R)-4-(1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentyl)morpholine (4w): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), morpholino benzoate (49.7 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a colorless oil (56.8 mg, 71% yield, 95% ee). $[\alpha]_D^{25}$ = +27.5 (c = 0.5 Chloroform, 95% ee).

**1H NMR** (600 MHz, CDCl$_3$) δ 7.24–7.18 (m, 2H), 7.15–7.06 (m, 5H), 7.02 (dd, $J$ = 8.3, 1.0 Hz, 2H), 6.31 (dd, $J$ = 7.3, 1.0 Hz, 2H), 5.86 (s, 2H), 3.78–3.70 (m, 2H), 3.70–3.63 (m, 2H), 2.65–2.50 (m, 4H), 2.40 (s, 2H), 1.79–1.70 (m, 2H), 1.67–1.56 (m, 2H), 1.55–1.38 (m, 2H), 1.35–1.26 (m, 1H).

(R)-4-(1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentyl)thiomorpholine (4x): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (133.5 mg, 0.6 mmol, 3.0 equiv), thiomorpholino benzoate (53.5 mg, 0.24 mmol, 1.2 equiv), and LiO’Bu (60.0 mg, 0.75 mmol, 3.75 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/2, v/v/v) gave the product as a colorless oil (61.1 mg, 73% yield, 95% ee). $[\alpha]_D^{22}$ = +24.7 (c = 0.5 Chloroform, 95% ee). **1H NMR** (600 MHz, CDCl$_3$) δ 7.23 (t, 2H), 7.15 (t, $J$ = 8.0 Hz, 3H), 7.10 (t, 2H), 7.02 (d, $J$ = 8.0 Hz, 2H), 6.31 (d, $J$ = 7.3 Hz, 2H), 5.82 (s, 2H), 2.88 (t, $J$ = 9.8 Hz).
Hz, 2H), 2.76–2.53 (m, 8H), 1.97 (dd, $J = 9.3, 4.6$ Hz, 1H), 1.82–1.70 (m, 1H), 1.69–1.58 (m, 2H), 1.54–1.37 (m, 2H), 1.37–1.28 (m, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.4, 140.8, 136.3, 128.3, 128.3, 127.5, 119.8, 117.7, 105.8, 57.4 (C–B, weak signal), 54.6, 35.7, 31.9, 28.4, 27.5, 27.5. HRMS (ESI-TOF) calcd for C$_{28}$H$_{31}$BN$_3$S[M+H]$^+$: 452.2326, Found: 452.2328. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IBN column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 35 / 65, 4.0 mL/min, $\lambda$ = 329 nm, t (minor) = 3.873 min, t (major) = 4.377 min.

(R)-5-(1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentyl)-4.5,6,7-tetrahydrothieno[3,2-c]pyridine (4y): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), 6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl benzoate (62.2 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/2, v/v/v) gave the product as a colorless oil (56.2 mg, 62% yield, 95% ee). $[^1]$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.30–7.24 (m, 2H), 7.22–7.10 (m, 6H), 7.08 (dd, $J = 8.3, 1.0$ Hz, 2H), 6.76 (d, $J = 5.1$ Hz, 1H), 6.36 (dd, $J = 7.3, 1.0$ Hz, 2H), 6.01 (s, 2H), 3.85 (d, $J = 14.3$ Hz, 1H), 3.56 (d, $J = 14.3$ Hz, 1H), 3.03–2.94 (m, 1H), 2.94–2.83 (m, 3H), 2.72–2.57 (m, 2H), 2.10 (dd, $J = 10.4, 4.5$ Hz, 1H), 1.95–1.85 (m, 1H), 1.78–1.64 (m, 3H), 1.60–1.47 (m, 1H), 1.44–1.35 (m, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.0, 140.4, 135.9, 133.0, 127.9, 127.8, 127.1, 125.2, 125.0, 122.5, 119.5, 117.3, 105.5, 55.8 (C–B, weak signal), 52.3, 50.6, 35.3, 31.6, 28.8, 26.6, 25.2. HRMS (ESI-TOF) calcd for C$_{28}$H$_{31}$BN$_3$S[M+H]$^+$: 452.2326, Found: 452.2329. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel Chiralpak IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH$_3$) / CO$_2$ = 40:60, 4.0 mL/min, $\lambda$ = 329 nm, t (minor) = 3.706 min, t (major) = 4.179 min.

$t$-butyl (R)-4-(1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentyl)piperazine-1-carboxylate (4z): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), tert-butyl 4-(benzoyloxy)piperazine-1-carboxylate (73.5 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash
column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a colorless oil (81.5 mg, 82% yield, 95% ee). \([\alpha]_D^{22} = +7.4\) (c = 0.5 Chloroform, 95% ee). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.28–7.23 (m, 2H), 7.21–7.12 (m, 5H), 7.06 (dd, \(J = 19.3\) Hz, 4H), 2.71–2.50 (m, 4H), 2.40 (s, 2H), 1.91–1.72 (m, 2H), 1.72–1.59 (m, 2H), 1.59–1.40 (m, 11H), 1.41–1.30 (m, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 154.8, 142.4, 140.8, 136.3, 128.4, 128.3, 127.6, 125.7, 119.9, 117.8, 105.9, 79.7, 57.2 (C–B, weak signal), 52.8, 35.7, 32.0, 28.7, 28.5, 27.0. HRMS (ESI-TOF) calcd for C\(_{30}\)H\(_{40}\)BN\(_4\)O\(_2\) [M+H]+: 499.3239, Found: 499.3239. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH\(_3\)) / CO\(_2\) = 40 / 60, 4.0 mL/min, \(\lambda = 329\) nm, t (major) = 2.572 min, t (minor) = 2.936 min.

**benzyl (R)-4-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-5-phenylpentyl)piperazine-1-carboxylate (4za):** The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), benzyl 4-(benzoyloxy)piperazine-1-carboxylate (81.6 mg, 0.24 mmol, 1.2 equiv), and LiO\(_t\)Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a colorless oil (90.0 mg, 85% yield, 94% ee). \([\alpha]_D^{22} = +9.3\) (c = 0.5 Chloroform, 95% ee). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.34 (d, \(J = 4.5\) Hz, 4H), 7.30 (h, \(J = 4.1\) Hz, 1H), 7.24–7.18 (m, 2H), 7.16–7.07 (m, 5H), 7.02 (d, \(J = 8.2\) Hz, 2H), 6.30 (d, \(J = 7.3\) Hz, 2H), 5.82 (s, 2H), 5.13 (s, 2H), 3.50 (t, \(J = 22.8\) Hz, 4H), 2.67–2.43 (m, 4H), 2.36 (s, 2H), 1.79 (dd, \(J = 9.8, 4.4\) Hz, 1H), 1.76–1.68 (m, 1H), 1.67–1.57 (m, 2H), 1.51 (s, 1H), 1.46–1.37 (m, 1H), 1.35–1.26 (m, 1H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 155.2, 142.4, 140.7, 136.8, 136.4, 128.5, 128.4, 128.3, 128.0, 127.9, 127.6, 125.7, 119.9, 117.8, 105.9, 67.1, 57.0 (C–B, weak signal), 52.7, 44.1, 35.7, 32.0, 28.7, 27.0. HRMS (ESI-TOF) calcd for C\(_{33}\)H\(_{38}\)BN\(_4\)O\(_2\) [M+H]+: 533.3082, Found: 533.3083. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IB column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH\(_3\)) / CO\(_2\) = 40 / 60, 4.0 mL/min, \(\lambda = 210\) nm, t (major) = 3.957 min, t (minor) = 4.527 min.
(R)-2-(5-phenyl-1-(4-(pyrimidin-2-yl)piperazin-1-yl)pentyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diaza-borinine (4zb): The title compound was prepared from 1a (28.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (68.2 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a colorless oil (51.4 mg, 54% yield, 94% ee). \([\alpha]D_{22}^2 = -5.8\) (c = 0.5 Chloroform, 94% ee).

\(1^H\) NMR (600 MHz, CDCl\(_3\)) \(\delta 8.29\) (d, \(J = 4.7\) Hz, 2H), 7.22 (dd, \(J = 8.1, 7.0\) Hz, 2H), 7.16–7.08 (m, 5H), 7.03 (dd, \(J = 8.3, 1.0\) Hz, 2H), 6.46 (t, \(J = 4.7\) Hz, 1H), 6.33 (dd, \(J = 7.3, 1.0\) Hz, 2H), 5.90 (s, 2H), 3.81 (d, \(J = 19.4\) Hz, 4H), 2.70–2.52 (m, 4H), 2.47 (s, 2H), 1.87–1.71 (m, 2H), 1.69–1.60 (m, 2H), 1.59–1.51 (m, 1H), 1.50–1.41 (m, 1H), 1.38–1.27 (m, 1H).

\(13^C\) NMR (150 MHz, CDCl\(_3\)) \(\delta 161.6, 157.7, 142.4, 140.8, 136.3, 128.3, 128.2, 127.6, 125.7, 119.9, 117.7, 109.8, 105.9, 57.3\) (C–B, weak signal), 52.9, 44.0, 35.7, 32.0, 28.8, 27.0. HRMS (ESI-TOF) calcd for C\(_{29}\)H\(_{34}\)BN\(_6\)[M+H]+: 477.2933, Found: 477.2933.

SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IH column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH\(_3\)) / CO\(_2\) = 35 / 65, 4.0 mL/min, \(\lambda = 329\) nm, t (major) = 2.145 min, t (minor) = 2.484 min.

(R)-4-(1H-naphtho[1,8-de][1,3,2]diazaborin-2(3H)-yl)-2-phenyl-ethylmorpholine (4zc): The title compound was prepared from 1n (20.4 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), morpholino benzoate (49.7 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a colorless oil (38.5 mg, 54% yield, 96% ee). \(1^H\) NMR (600 MHz, C\(_6\)D\(_6\)) \(\delta 7.08–6.97\) (m, 9H), 5.94 (dd, \(J = 6.8, 1.6\) Hz, 2H), 5.42 (s, 2H), 3.69–3.54 (m, 4H), 2.89 (dd, \(J = 12.9, 5.3\) Hz, 1H), 2.42 (ddd, \(J = 21.9, 11.5, 8.4\) Hz, 3H), 2.21 (ddd, \(J = 10.5, 6.1, 3.0\) Hz, 2H), 1.90 (dd, \(J = 10.8, 5.3\) Hz, 1H). \(13^C\) NMR (150 MHz, C\(_6\)D\(_6\)) \(\delta 141.2, 140.4, 134.0, 137.1, 129.5, 128.7, 128.0, 126.5, 120.5, 118.2, 106.1, 67.4, 59.3\) (C–B, weak signal), 53.5, 34.4. HRMS (ESI-TOF) calcd for C\(_{22}\)H\(_{34}\)BN\(_3\)O[M+H]+: 357.2127, Found: 357.2120. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IH column (3μm, 0.46×25 cm), 40% MeOH containing...
0.5 vol% 7M methanolic NH₃ / CO₂, 1600 psi backpressure, 30 °C, 4.0 mL/min, λ = 231 nm, t (major) = 2.382 min, t (minor) = 2.664 min.

(R)-4-(6-chloro-1-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)hexyl)morpholine (4zd): The title compound was prepared from 1o (27.3 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), morpholino benzoate (49.7 mg, 0.24 mmol, 1.2 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure A. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/1/1, v/v/v) gave the product as a white solid (38.2 mg, 50% yield, 94% ee). ¹H NMR (600 MHz, C₆D₆) δ 7.09 – 6.93 (m, 4H), 6.04 (dd, J = 6.5, 1.9 Hz, 2H), 5.55 (s, 2H), 3.74 – 3.48 (m, 4H), 3.07 (t, J = 6.5 Hz, 2H), 2.33 (s, 2H), 2.18 (d, J = 9.5 Hz, 2H), 1.42 (dq, J = 8.1, 5.0 Hz, 2H), 1.36 – 1.22 (m, 3H), 1.20 – 1.07 (m, 3H), 1.04 – 0.96 (m, 1H). ¹³C NMR (150 MHz, C₆D₆) δ 141.1, 137.1, 127.9, 120.6, 118.4, 106.3, 67.4, 57.7 (C–B, weak signal), 54.2, 45.0, 32.6, 29.1, 27.7, 26.6. HRMS (ESI-TOF) calcd for C₂₀H₂₈BClN₃O[M+H]⁺: 371.2050, Found: 371.2055. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IH column (3μm, 0.46×25 cm), 40% MeOH containing 0.5 vol% 7M methanolic NH₃ / CO₂, 1600 psi backpressure, 30 °C, 4.0 mL/min, λ = 231 nm, t (major) = 1.990 min, t (minor) = 2.617 min.

1.3.3 General Procedure B: Cascade Ring-Closing Hydrofunctionalization

To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar were added CuBr (1.4 mg, 0.01 mmol, 0.05 equiv), (R₃)-DTBM-Segphos (14.2 mg, 0.012 mmol, 0.06 equiv), and LiO'Bu (50.0 mg, 0.625 mmol, 3.125 equiv) under N₂ atmosphere, and the reaction vessel was evacuated under high vacuum for 10 min, then back-filled with N₂. Anhydrous THF (1.0 mL) was added, and the mixture was stirred at room temperature for 10 min. Next, PMHS (111.3 mg, 0.5 mmol, 2.5 equiv) and HBdan (40.3 mg, 0.24 mmol, 1.2 equiv) were added successively, and the solution was stirred at room temperature for another 10 min. Finally, alkyne 1 (0.2 mmol, 1.0
equiv) was added. The reaction mixture was allowed to stir at room temperature for 16 h, at which point it was filtered through a pad of celite and concentrated in vacuo. After the volatiles were removed under reduced pressure, the resulting residue was purified by silica gel flash column chromatography to afford the desired product 4.

\((R)-2-(1\text{-benzylazetidin-2-yl})-2,3\text{-dihydro-1H-naphtho[1,8-de][1,3,2]\text{diazaborinine}} (4\text{ze})\): The title compound was prepared from 0-benzoyl-N-benzyl-N-(prop-2-yn-1-yl)hydroxylamine (53.0 mg, 0.2 mmol, 1 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), and LiO\text{Bu} (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure B. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/2/1, v/v/v) gave the product as a colorless oil (39.3 mg, 63% yield, 89% ee). [\(\alpha\)D]22 = –67.4 (c = 0.5 Chloroform, 89% ee). 1H NMR (600 MHz, CDCl3) \(\delta\) 7.48–7.17 (m, 5H), 7.13–6.79 (m, 4H), 6.15 (s, 2H), 5.49 (s, 2H), 3.70–3.36 (m, 3H), 3.23–2.89 (m, 2H), 2.27–1.89 (m, 2H). 13C NMR (150 MHz, CDCl3) \(\delta\) 140.6, 137.9, 135.8, 128.7, 128.1, 127.1, 127.0, 119.4, 116.9, 105.2, 64.6, 56.2 (C–B, weak signal), 55.8, 20.4. HRMS (ESI-TOF) calcd for C20\text{H}21\text{BN3}[M+H]+: 314.1823, Found: 314.1825. SFC (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IBN column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH3) / CO2 = 40/60, 4.0 mL/min, \(\lambda\) = 329 nm, t (major) = 1.927 min, t (minor) = 2.296 min.

\((R)-2-(1\text{-benzylpyrrolidin-2-yl})-2,3\text{-dihydro-1H-naphtho[1,8-de][1,3,2]\text{Diazaborinine}} (4zf)\): The title compound was prepared from O-benzoyl-N-benzyl-N-(but-3-yn-1-yl)hydroxylamine (55.8 mg, 0.2 mmol, 1.0 equiv), HBdan (40.3 mg, 0.24 mmol, 1.2 equiv), PMHS (111.3 mg, 0.5 mmol, 2.5 equiv), and LiO\text{Bu} (50.0 mg, 0.625 mmol, 3.125 equiv) according to General Procedure B. Purification using silica gel flash column chromatography (triethylamine/ethyl acetate/hexanes = 0.1%/2/1, v/v/v) gave the product as a colorless oil (50.4 mg, 77% yield, 95% ee). [\(\alpha\)D]22 = –46.1 (c = 0.5 Chloroform, 95% ee). 1H NMR (600 MHz, CDCl3) \(\delta\) 7.32 (s, 4H), 7.21 (s, 1H), 7.09 (s, 2H), 7.00 (s, 2H), 6.31 (s, 2H), 5.97 (s, 2H), 3.94 (d, \(J = 12.9\) Hz, 1H), 3.24 (s, 1H), 3.01 (s, 1H), 2.13–1.87 (m, 3H), 1.78 (s, 3H). 13C NMR (150 MHz, CDCl3) \(\delta\) 141.2, 136.4, 129.0, 128.3, 127.6, 127.2, 120.0, 117.5, 105.8, 60.83, 54.97, 28.70, 24.48. Note: The carbon signal bound to the boron atom was not observed, likely due to quadrupolar relaxation. HRMS (ESI-TOF) calcd for C21\text{H}23\text{BN3}[M+H]+: 328.1980, Found:
The enantiomeric excess was determined by chiral SFC on a Diacel IG column (3μm, 0.46×25 cm), (MeOH containing 0.5 vol% 7M methanolic NH₃ / CO₂ = 35 / 65, 4.0 mL/min, λ = 331 nm, t (major) = 2.467 min, t (minor) = 2.763 min.

1.4 Deprotection of α-aminoboronate products and application in synthesis

Procedure C: To a reaction tube containing a Teflon-coated magnetic stir bar were added 4a (152.8 mg, 0.3 mmol, 1.0 equiv), 5 N aqueous HCl (0.6 mL, 10 equiv), and THF (1.5 mL) under N₂ atmosphere. The reaction mixture was stirred overnight at room temperature and then filtered through a pad of celite (washed with 40 mL Et₂O) and concentrated under reduced pressure. The mixture was concentrated to < 1 mL, and Et₂O (3 mL) was added. The mixture was sonicated for ~2 min, and the suspension was placed in the freezer (0 °C) overnight. The resulting white solid (129.6 mg, 77% yield) was collected via vacuum filtration, and further purified by repeated washing with Et₂O, giving the product 5 as a white solid (102.2 mg, 80% yield). [α]D²² = −23.1 (c = 0.5 Chloroform). ¹H NMR (600 MHz, CD₃OD) δ 7.57–6.80 (m, 15H), 4.88 (s, 2H), 4.68–4.08 (m, 3H), 2.72–2.43 (m, 2H), 1.96–1.67 (m, 2H), 1.55 (p, J = 7.7 Hz, 2H), 1.30–1.07 (m, 2H). ¹³C NMR (150 MHz, CD₃OD) δ 141.4, 130.4, 129.6, 129.1, 128.4, 127.6, 127.5, 124.9, 55.8, 34.4, 30.5, 25.4, 24.6.

Supplementary Figure 3. Deprotection of α-aminoboronate products and application in synthesis.
**Procedure D**: To an oven-dried flask containing a Teflon-coated magnetic stir bar were added 4a (519.9 mg, 1.2 mmol, 1 equiv), pinacol (558.7 mg, 4.728 mmol, 3.94 equiv), 5 N aqueous HCl (0.95 mL, 4.728 mmol, 3.94 equiv), and THF (6 mL) under N\textsubscript{2} atmosphere. The reaction mixture was stirred at room temperature for 7 h, filtered through a pad of celite, and concentrated under reduced pressure. Pinacol and water were azeotropically removed with toluene. The crude material was used directly in the next step without further purification.

To a reaction tube containing a Teflon-coated magnetic stir bar and the above residue were added methanol (6 mL), Pd/C (128.0 mg), and 1 N HCl (1.2 mL, in Et\textsubscript{2}O). The resulting mixture was stirred at room temperature under 1 atm H\textsubscript{2} atmosphere overnight, filtered through a pad of celite, and concentrated under reduced pressure. The crude material was used directly in the next step without further purification.

To a reaction tube containing a Teflon-coated magnetic stir bar were added the crude residue from the preceding step, DMAP (14.6 mg, 0.12 mmol, 10 mol%), PhCOCl (202.4 mg, 1.44 mmol, 1.2 equiv), and DCM (6 mL) under N\textsubscript{2} atmosphere. The reaction mixture was cooled to 0 °C, and triethylamine (303.6 mg, 3.0 mmol, 2.5 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature and stir for 4 h. Saturated aqueous NaHCO\textsubscript{3} (10 mL) was added to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification using silica gel column chromatography (ethyl acetate/hexanes = 1/2, v/v) gave the product 6 as a colorless oil (375.0 mg, 65% overall yield over three steps, 96% ee). \([\alpha]_{D}^{22} = -29.9 \) (c = 0.5 Chloroform, 96% ee).

**1H NMR** (600 MHz, CDCl\textsubscript{3}) \(\delta 7.6 \) (d, \(J = 7.7\) Hz, 2H), 7.51 (t, \(J = 7.6\) Hz, 1H), 7.42 (t, \(J = 7.6\) Hz, 2H), 7.35–7.20 (m, 5H), 7.20–7.05 (m, 5H), 4.83 (AB, \(J_{AB} = 15.8\) Hz, 1H), 4.42 (BA, \(J_{BA} = 15.8\) Hz, 1H), 2.69–2.48 (m, 3H), 1.85–1.70 (m, 1H), 1.70–1.56 (m, 3H), 1.54–1.40 (m, 2H), 1.20 (s, 12H).

**13C NMR** (150 MHz, CDCl\textsubscript{3}) \(\delta 173.4, 142.3, 133.8, 131.4, 128.5, 128.3, 128.0, 128.0, 127.8, 127.8, 127.7, 127.0, 125.1, 79.46, 49.1, 35.3, 31.3, 27.4, 25.5, 25.2, 25.0.**

**HRMS** (ESI-TOF) calcd for C\textsubscript{31}H\textsubscript{39}BNO\textsubscript{3}[M+H]\textsuperscript{+}: 484.3018, Found: 484.3019. **SFC** (chiral column) The enantiomeric excess was determined by chiral SFC on a Diacel IG column (3μm, 0.46×25 cm), MeOH / CO\textsubscript{2} = 15 / 85, 4.0 mL/min, \(\lambda = 230\) nm, t (major) = 2.000 min, t (minor) = 2.210 min.
**Procedure E:** To an oven-dried flask containing a Teflon-coated magnetic stir bar were added 4e (433.3 mg, 1.0 mmol, 1 equiv), pinacol (465.6 mg, 3.94 mmol, 3.94 equiv), 5 N aqueous HCl (0.79 mL, 3.94 mmol, 3.94 equiv), and THF (5 mL) under N₂ atmosphere. The reaction mixture was stirred at room temperature for 7 h and was filtered and concentrated under reduced pressure. Pinacol and water were azeotropically removed with toluene. The crude material was used directly in the next step without further purification.

To a reaction tube containing a Teflon-coated magnetic stir bar and the crude residue from the preceding step were added methanol (5 mL), Pd/C (150.0 mg), and HOAc (180.1 mg). The resulting mixture was stirred at room temperature under 1 atm H₂ atmosphere until the reaction had full conversion (as monitored by ¹H NMR analysis). The reaction mixture was filtered through a pad of celite, and concentrated under reduced pressure. The crude residue was used directly in the next step without further purification.

A scintillation vial containing a Teflon-coated magnetic stir bar and the crude residue from the preceding step (1 equiv) was charged with CH₂Cl₂ (5.0 mL) and cooled to 0 °C. Diisopropylethylamine (512 μL, 3.1 mmol, 3.1 equiv) was added dropwise to the flask. Boc-L-phenylalanine (424.5 g, 1.6 mmol, 1.6 equiv) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethylaminiumtetrafluoroborate (TBTU) (449.5 mg, 1.4 mmol, 1.4 equiv) were then added to the reaction mixture in succession. The reaction mixture was stirred at 0 °C for 7 h, at which point it was concentrated under reduced pressure while maintaining an external water bath temperature below 30 °C. After concentration, EtOAc (17 mL) was added. The organic layer was washed with H₂O (2 × 17 mL), 1% phosphoric acid (2 × 17 mL), 2% K₂CO₃ (2 × 17 mL), and brine (2 × 17 mL). Each aqueous layer was back-extracted with EtOAc (2 × 17 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure maintaining an external bath temperature below 30 °C. Purification using flash silica gel column chromatography (ethyl acetate/hexanes = 1/3, v/v/v) gave the product 7 as a white foam (230.1 mg, 50% yield over three steps, dr > 17:1). [α]D²² = −25.7 (c = 0.5 Chloroform). ¹H NMR (600 MHz, CDCl₃) δ 7.29 (s, 2H), 7.24 (s, 3H), 6.47 (s, 1H), 5.16 (s, 1H), 4.41 (s, 1H), 3.08 (s, 2H), 2.96 (s, 1H), 1.57–1.32 (m, 12H), 1.25 (s, 12H), 0.87 (s, 6H).
CH₂Cl₂ (2.0 mL) was charged to a vial containing pinacol N-Boc-L-phenylalanine-L-leucine boronate (0.5 mmol, 1 equiv). The mixture was cooled to 0 °C. 4.0 M HCl (1.75 mmol, 3.5 equiv, a solution in 1,4-dioxane) was added dropwise over 10 min. The resulting solution was stirred at 0 °C for 1 h, and then the bath was removed and the reaction mixture was stirred for an additional 5 h. The reaction mixture was concentrated to dryness and the resulting solid was washed with hexanes. The desired product 8 was used directly without purification.

CH₂Cl₂ (1.2 mL, 0.5 M) was added to a vial containing pinacol N-Boc-L-phenylalanine S-L-leucine boronate hydrochloride salt obtained from the previous step. The mixture was cooled to 0 °C. Diisopropylethylamine (174.5 mg, 1.35 mmol, 2.7 equiv) was added dropwise to the flask, and the reaction mixture was stirred for 5 min. 2-Pyrazine carboxylic acid (86.8 mg, 0.7 mmol, 1.4 equiv) was then added to the solution in one portion. 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate, TBTU (160.5 g, 0.5 mmol, 1.0 equiv) was then added to the reaction mixture. The reaction mixture was stirred at 0 °C for 2 h. Then it was allowed to warm to rt for an additional 12 h. The reaction mixture was then concentrated under reduced pressure maintaining an external bath temperature below 30 °C and then 8.5 mL of EtOAc was added. The organic layer was washed with H₂O (2 × 8.5 mL), 1% phosphoric acid (2 × 8.5 mL), 2% K₂CO₃ (2 × 8.5 mL), and brine (2 × 8.5 mL). Each aqueous layer was back-extracted with EtOAc (2 × 8.5 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure maintaining an external bath temperature below 30 °C. The resulting pale yellow foam was used directly in the next step without purification.

Distilled pentane (1.6 mL, 0.2M) and methanol (1.6 mL, 0.2M) were added to a vial containing pinacol boronate obtained from the previous step. 2-Methylpropaneboronic acid (185.5 mg, 1.82 mmol, 3.63 equiv) was then added to the solution in one portion. 1 N HCl (aq) (0.91 mL) was added to the reaction mixture, and the resulting biphasic solution was stirred vigorously for 20 h. Stirring was then stopped and the biphasic mixture was allowed to separate. The pentane layer was removed, and the aqueous layer was transferred to a separatory funnel and was extracted with pentane (2 x 10 mL). The aqueous methanol layer was then concentrated under reduced pressure maintaining an external bath temperature of 34 °C. The resulting film was diluted with CH₂Cl₂, transferred to a separatory funnel, and 2 N NaOH(aq) (1.2 mL) was added. The aqueous layer was extracted with the CH₂Cl₂ (3 x 10 mL). 1 N HCl(aq) was added to the aqueous layer until the pH of the solution was 6. CH₂Cl₂ was then added to the separatory funnel and the desired N-(2-
Pyrazinecarbonyl-L-phenylalanine-L-leucine boronic anhydride was extracted into the organic layer (3 x 10 mL of CH₂Cl₂). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The crude material was purified by reverse phase HPFC (30:70:0.1 CH₃CN:H₂O:formic acid-80:20:0.1), and the desired fractions were concentrated to remove the acetonitrile and water to give bortezomib as a white solid (103.7 mg, 54% over three steps, dr > 20:1). [α]D²² = −23.32 (c = 0.3, CD₃CN:D₂O = 5:1) ¹H NMR (600 MHz, CD₃CN:D₂O = 5:1) δ 9.14 (d, J = 1.3 Hz, 1H), 8.77 (dd, J = 2.4, 0.9 Hz, 1H), 8.68–8.62 (m, 1H), 7.30–7.24 (m, 3H), 7.24–7.19 (m, 1H), 4.80 (dd, J = 8.2, 5.9 Hz, 1H), 3.22 (dd, J = 13.9, 5.8 Hz, 1H), 3.10 (dd, J = 13.9, 8.2 Hz, 1H), 2.96 (dd, J = 9.9, 5.4 Hz, 1H), 1.47–1.35 (m, 2H), 1.30–1.23 (m, 1H), 0.83 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H). ¹³C NMR (150 MHz, CD₃CN:D₂O = 5:1) δ 170.9, 163.1, 147.3, 143.6, 143.2, 143.0, 136.3, 128.9, 128.0, 126.4, 53.4, 38.8, 37.1, 24.5, 22.1, 20.5.

1.5 Determination of the Absolute Configuration of 4v

The reaction depicted in Eq 1 was run according to a literature procedure by Hirano and Miura.³ In this previous report, one representative product prepared from (Rₐ)-DTBM-SEGPHOS was assigned as having the R configuration based on X-ray crystallography, and other products in the series were assigned by analogy. In the present manuscript, the series is assigned by comparison of optical rotation values. Specifically, Miura and Hirano’s method was used to prepare compound 4v (presumed to have the R configuration) in 94% ee, and the optical rotation of this sample was measured as [α]D²² = +26.3 (c = 0.5 Chloroform). Using our method, a sample of 4v was prepared in 95% ee and the optical rotation was measured as [α]D²² = +27.5 (c = 0.5 Chloroform). Based on

Supplementary Figure 4. Determination of the Absolute Configuration of 4v

The reaction depicted in Eq 1 was run according to a literature procedure by Hirano and Miura.³ In this previous report, one representative product prepared from (Rₐ)-DTBM-SEGPHOS was assigned as having the R configuration based on X-ray crystallography, and other products in the series were assigned by analogy. In the present manuscript, the series is assigned by comparison of optical rotation values. Specifically, Miura and Hirano’s method was used to prepare compound 4v (presumed to have the R configuration) in 94% ee, and the optical rotation of this sample was measured as [α]D²² = +26.3 (c = 0.5 Chloroform). Using our method, a sample of 4v was prepared in 95% ee and the optical rotation was measured as [α]D²² = +27.5 (c = 0.5 Chloroform). Based on

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the similarity in optical rotation values, we assigned 4v as having the R configuration. Other examples in this manuscript were assigned by analogy.

Cu(OAc)$_2$ (4.5 mg, 0.025 mmol, 10 mol%), (R$_a$)-DTBM-SEGPHOS (29.5 mg, 0.025 mmol, 10 mol%), and LiO'Bu (80.1 mg, 1.0 mmol, 4 equiv) were placed in a 10-mL oven-dried reaction flask containing a Teflon-coated magnetic stir bar under N$_2$ atmosphere. THF (0.50 mL) was then added to the flask, and the suspension was stirred for 15 min at ambient temperature. Polymethylhydrosiloxane (PMHS, 166.9 mg, 0.75 mmol, 3.0 equiv) and a solution of A (93.7 mg, 0.30 mmol, 1.20 equiv) and morpholino benzoate 2v (51.8 mg, 0.25 mmol, 1.0 equiv) in THF (1.0 mL) were sequentially added in a dropwise fashion. The solution was stirred at ambient temperature for 12 h, at which point it was filtered through a pad of celite and concentrated. After the solvent was removed under reduced pressure, the residue was purified by silica gel flash column chromatography to afford the desired product 4v (52.8 mg, 53%, 94% ee).

1.6 Control Experiments to Probe the Mechanism
A

\[
\begin{align*}
\text{Path A} & \quad \text{CuBr} \quad \text{LiO}^+\text{Bu, PMHS} \\
\text{L}^*\text{Cu}^{+}\text{-OBz} & \quad \text{R} \\
\text{R} & \quad \text{BzONBn}_2 \\
\text{NBN}_2 & \quad \text{BDan} \\
\text{H}_2 & \quad \text{CuL}^- \\
\text{L}^*\text{Cu}^{+}\text{-OBz} & \quad \text{R} \\
\text{R} & \quad \text{BzONBn}_2 \\
\text{NBN}_2 & \quad \text{BDan} \\
\text{H}_2 & \quad \text{CuL}^- \\
\end{align*}
\]

\[
\begin{align*}
\text{hydroamination cycle} & \quad \text{hydroboration cycle} \\
\end{align*}
\]

B

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \quad \text{Ph} \\
\text{1a} & \quad \text{1a} \\
\text{BzONBn}_2 & \quad \text{BzONBn}_2 \\
0.6 & \quad 1.2 \text{ equiv} \\
\text{CuBr (5 mol\%)} & \quad \text{CuBr (5 mol\%)} \\
\text{(R)\text{-DTBM-Segphos (6 mol\%)} & \quad \text{(R)\text{-DTBM-Segphos (6 mol\%)} \\
\text{PMHS (2.5 equiv) & \quad \text{PMHS (2.5 equiv) \\
\text{LiO}^+\text{Bu (3.125 equiv) & \quad \text{LiO}^+\text{Bu (3.125 equiv) \\
\text{THF, rt, 16 h & \quad \text{THF, rt, 16 h \\
\text{did not observe this product & \quad 18\% yield \\
\text{(< 2\% yield in the absence of PMHS) & \quad (< 2\% yield in the absence of PMHS) \\
\end{align*}
\]

C

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \quad \text{Ph} \\
\text{1a} & \quad \text{1a} \\
\text{BzONBn}_2 & \quad \text{BzONBn}_2 \\
0.6 & \quad 1.2 \text{ equiv} \\
\text{CuBr (5 mol\%)} & \quad \text{CuBr (5 mol\%)} \\
\text{(R)\text{-DTBM-Segphos (6 mol\%)} & \quad \text{(R)\text{-DTBM-Segphos (6 mol\%)} \\
\text{PMHS (2.5 equiv) & \quad \text{PMHS (2.5 equiv) \\
\text{LiO}^+\text{Bu (3.125 equiv) & \quad \text{LiO}^+\text{Bu (3.125 equiv) \\
\text{THF, rt, 3 h & \quad \text{THF, rt, 16 h \\
\text{40\% yield & \quad < 5\% yield \\
\end{align*}
\]
**Supplementary Figure 5.** (A) Proposed catalytic cycles for the cascade reaction. (B) Control experiments to test the reaction sequence. (C) The cascade reaction with delayed addition of BzONBn2 and the hydroamination reaction in the absence of PMHS.

1.7 Comparing the Catalytic Efficiency with Miura and Hirano’s Method

**Supplementary Figure 6.** Comparing the catalytic efficiency with Miura’s methodology.
1.8 Kinetic Studies

General procedure F for kinetic studies of concentration dependencies on individual components: To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar were added CuBr (3.5 mg, 0.025 mmol, 0.05 equiv), (Rₐ)-DTBM-Segphos (35.4 mg, 0.03 mmol, 0.06 equiv), LiO'Bu (125.1 mg, 1.5625 mmol, 3.125 equiv) and 1,3,5-trimethoxybenzene (84.0 mg, 0.5 mmol, 1 equiv, internal standard) under N₂ atmosphere. The reaction vessel was evacuated under high vacuum for 10 min and was then backfilled with N₂. Anhydrous THF (2.5 mL) was added, and the mixture was stirred at room temperature for 10 min. Next, polymethylhydrosiloxane (PMHS, 278.1 mg, 1.25 mmol, 2.5 equiv) and HBdan (100.9 mg, 0.6 mmol, 1.2 equiv) were added successively, and the reaction mixture stirred at room temperature for an additional 10 min. Finally, alkyne 1a (72.1 mg, 0.5 mmol, 1.0 equiv) and 2a (190.3 mg, 0.6 mmol, 1.2 equiv) were added in succession. Aliquots (~20 μL) were removed from the reaction at the indicated times and directly injected into a filter vial containing MeCN (1.0 mL) without the need for further quenching. The resulting sample was subjected to LC analysis.
Supplementary Figure 7. Reaction progress monitored by LC-MS analysis

General procedure G for initial rate experiments on the reactions with different [A]₀: To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar, were added CuBr (3.5 mg, 0.025 mmol, 0.05 equiv), (Rₐ)-DTBM-Segphos (35.4 mg, 0.03 mmol, 0.06 equiv), LiO'Bu (40.0 mg, 0.5 mmol, 1.0 equiv) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 0.5 equiv, internal standard) in an argon-filled glovebox. Anhydrous THF-d₈ (2.5 mL) was added, and the mixture was stirred at room temperature for 10 min. Next, polymethylhydrosiloxane (PMHS, 278.1 mg, 1.25 mmol, 2.5 equiv) and HBdan (100.9 mg, 0.6 mmol, 1.2 equiv) were added successively, and the reaction mixture stirred at room temperature for an additional 10 min. The pre-mixed solution of 550 μL was added to a J-Young NMR tube with 1a, 2a (38.1 mg, 0.12 mmol) and A.
Supplementary Figure 8. The copper-catalyzed cascade reactions monitored by $^1$H NMR analysis. (a) $[A]_0 = 0$ mM. $[1a] = 230$ mM (b) $[A]_0 = 0$ mM. $[1a] = 230$ mM (c) $[A]_0 = 100$ mM. $[1a] = 230$ mM (d) $[A]_0 = 230$ mM. $[1a] = 230$ mM (e) $[A]_0 = 200$ mM, $[1a] = 0$ mM.
Supplementary Figure 9. The copper-catalyzed hydroamination reaction of A monitored by $^1$H NMR analysis. (a) $[A]_0 = 300$ mM, $[1a] = 0$. (b) $[A]_0 = 200$ mM, $[1a] = 0$. (c) $[A]_0 = 120$ mM, $[1a] = 0$. (d) plot of initial rates vs. $[A]_0$.

1.9 $^{31}$P NMR Studies

Monitoring of the CuH-catalyzed cascade reaction by $^{31}$P NMR

To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar, were added CuBr (1.4 mg, 0.010 mmol, 0.05 equiv), ($R_a$)-DTBM-Segphos (14.2 mg, 0.012 mmol, 0.06 equiv), LiO'Bu (32.0 mg, 0.4 mmol, 2.0 equiv) and 1,3,5-trimethoxybenzene (16.8 mg, 0.10 mmol, 0.2 equiv, internal standard) in an argon-filled glovebox. Anhydrous THF-$d_8$ (1.0 mL) was added, and the mixture was stirred at room temperature for 10 min. An aliquot of the solution (0.5 mL) was transferred to a J-Young NMR tube and a $^{31}$P NMR spectrum was acquired (see Supplementary Figure 10 (b)). Next, polymethylhydrosiloxane (PMHS, 15.0 mg, 0.25 mmol, 2.5 equiv) was added to the same J-Young tube, the solution was mixed thoroughly and a $^{31}$P NMR spectrum was acquired (see Supplementary Figure 10 (c)). HBdan (20.2 mg, 0.12 mmol, 1.2 equiv), 1a (14.4 mg, 0.10 mmol, 1.0 equiv), 2a (38.1 mg, 0.12 mmol, 1.2 equiv) were added to the J-Young tube successively, and the reaction was monitored in situ over time by $^{31}$P NMR (see Supplementary Figure 10 (d) – (f)).
Supplementary Figure 10. $^{31}$P NMR spectra of CuH-catalyzed cascade reaction process.

Evidence for possible intermediate generated from LCuH species and alkenylBdan A

To a flame-dried reaction tube equipped with a Teflon-coated magnetic stir bar, were added CuBr (1.4 mg, 0.010 mmol, 0.05 equiv), (R$_a$)-DTBM-Segphos (14.2 mg, 0.012 mmol, 0.06 equiv), LiO'Bu (32.0 mg, 0.4 mmol, 2.0 equiv) and 1,3,5-trimethoxybenzene (16.8 mg, 0.10 mmol, 0.2 equiv, internal standard) in an argon-filled glovebox. Anhydrous THF-$d_8$ (1.0 mL) was added, and the mixture was stirred at room temperature for 10 min. Next, polymethylhydrosiloxane (PMHS, 30.0 mg, 0.50 mmol, 2.5 equiv) and HBdan (40.4 mg, 0.24 mmol, 1.2 equiv) were added successively, and the reaction mixture stirred at room temperature for an additional 10 min. Two aliquots of the solution (0.5 mL) were transferred to two J-Young NMR tubes and analyzed by $^{31}$P NMR. (see Supplementary Figure 11 (a))

1a (14.4 mg, 0.10 mmol, 1.0 equiv) was added to the first J-Young tube, the solution was mixed thoroughly, and a $^{31}$P NMR spectrum was acquired (see Supplementary Figure 11 (b), (d)). Two
new species RS1 and RS2 were initially observed at –7.1 ppm and –8.4 ppm. After 1.5 h, RS2 became the major resting state, which was converted the species at –4.6 ppm (the same resting state observed in the cascade reaction) upon addition of 2a (38.1 mg, 0.12 mmol, 1.2 equiv) to the reaction solution (see Supplementary Figure 11 (f)). The product 4a was also detected by ¹H NMR.

To the other J-Young tube, was added A (31.2 mg, 0.10 mmol, 1.0 equiv) and the solution was mixed thoroughly. At this stage, the ³¹P NMR spectra show the same major peaks as those observed in the first experiment during the “hydroboration only” phase (see Supplementary Figure 11 (c), (e)). Amine electrophile 2a (38.1 mg, 0.12 mmol, 1.2 equiv) was added to the reaction solution after 1.5 h and the new resting state was a species with a peak at –4.9 ppm (see Supplementary Figure 11 (g)). Although we could not isolate the species RS2, it does have a similar ³¹P NMR shift attributed to DTBM-SEGPHOS-ligated Cu(alkyl) complexes reported in the literature⁸. Based on these data, together with the result from DFT calculations, we propose that intermediate A reacts with the active LCuH catalyst to form a stable off-cycle complex, presumably the α-boryl-alkyl-Cu species depicted in Fig. 4, thereby inhibiting the hydroboration only cycle in the absence of 2a.
Supplementary Figure 11. Comparison of stepwise hydroboration-hydroamination of 1a and hydroamination of A by $^{31}$P NMR.

1.10 Computational Details:

Computational Methods: All geometry optimizations were performed using the dispersion corrected B3LYP functional\textsuperscript{9} with Grimme’s D3 dispersion correction\textsuperscript{10}, with a mixed basis set of
SDD\textsuperscript{11} for Cu and 6-31G(d) for other atoms. Single point energies were calculated with the SMD solvation model in THF (\(\epsilon = 7.6\)) with the M06\textsuperscript{12} functional and a mixed basis set of SDD for Cu and 6-311+G(d,p) for other atoms\textsuperscript{13,14}. All calculations were performed with Gaussian 16\textsuperscript{15}.

Reaction energy profiles presented in this study were obtained by optimizing molecular geometries and calculating energies of the reaction intermediates (local minima) and transition states (1st order saddle point) along plausible reaction pathways. Vibrational frequencies were computed at the same level of theory in geometry optimization to confirm whether the structures are intermediates (no imaginary frequency) or transition states (only one imaginary frequency). The reported Gibbs free energies and enthalpies include zero-point vibrational energies and thermal corrections at 298 K calculated using a harmonic-oscillator model. Since the harmonic-oscillator approximation may lead to spurious results for the computed entropies in molecules with low-frequency vibrational modes, the quasiharmonic approximation from Cramer and Truhlar was applied to compute the thermal corrections for a few key transition state structures\textsuperscript{16,17}. In the quasiharmonic approximation, vibrational frequencies lower than 100 cm\textsuperscript{-1} were raised to 100 cm\textsuperscript{-1} as a way to avoid spurious results associated with the harmonic-oscillator model for very low-frequency vibrations. The reported energies in the text were corrected using the quasiharmonic approximation. The Gibbs free energies in solution were calculated at 1 mol/L. The coordinates of optimized structures can be found in Supplementary Note 1.

**Additional Computational Results:** The computed full reaction energy profile of the hydroboration cycle is presented in Supplementary Figure 1\textsuperscript{2}. Propyne 9 was used as a model alkyne substrate in the calculations. Initiating from Cu-H active catalyst 8, the alkyne substrate (9) coordination is endergonic by 13.2 kcal/mol to generate four-coordinated \(\pi\)-alkyne complex 10. The subsequent hydrocupration has a reaction barrier of 11.4 kcal/mol with respect to 10, which then forms the thermodynamically stable alkenyl Cu intermediate 11. The nucleophilic attack of alkenyl-Cu complex to HBdan (TS3) has a relatively low barrier of 10.3 kcal/mol with respect to 11 to form intermediate 15, which then undergoes fast hydride transfer (TS4) with a barrier of 3.2 kcal/mol to form the alkenylBdan (12) bonded intermediate 13. Subsequent dissociation of 12 from 13 to regenerate the LCuH catalyst 8 is exergonic by 5.0 kcal/mol. Taken together, the computed
catalytic cycle of the CuH-catalyzed alkyne hydroboration indicated the rate-limiting step is the hydrocupration of the alkyne (TS1).

Supplementary Figure 12. Computed energy profile of Cu-H catalyzed hydroboration of propyne.

The computed reaction energy profile of the hydroamination cycle is presented in Supplementary Figure 13. BzONMe$_2$ was used as a model electrophile instead of the experimentally used BzONPh$_2$ in the calculations. Initiating from the Cu-H active catalyst 8, the alkenyl Bdan substrate 9 coordination is endergonic by 5.0 kcal/mol to generate four-coordinated π-alkene complex 13. The subsequent hydrocupration has a reaction barrier of 12.9 kcal/mol with respect to 13, which then forms the thermodynamically stable alkyl Cu intermediate 14. Subsequent C-N bond formation between 14 and BzONMe$_2$ forms the Cu(I)-OBz complex (16) and the hydroamination product. Our calculations indicated this step is highly exergonic by 34.3 kcal/mol. Previous computational studies suggest this C-N bond formation is likely to occur via an oxidative addition/reductive elimination mechanism involving a Cu(III) intermediate 17$^{18}$. However, attempts to locate the transition states (TS5, TS16) in this C-N bond formation step were not successful. Based on previous mechanistic studies from the Buchwald group on the CuH-catalyzed
hydroamination of styrenes and aliphatic olefins\textsuperscript{19,20}, this C-N bond formation step is unlikely to be rate-limiting in the hydroamination cycle.

**Supplementary Figure 13.** Computed energy profile of CuH-catalyzed hydroamination of alkenyl Bdan.
1.11 NMR Spectra and SFC Chromatograms
NMR Spectra and SFC Chromatograms of 4a
Signal 2: DAD1 B, Sig=210,4 Ref=360,100

| # | RetTime [min] | Type | Width [min] | Area [mAU*sec] | Height [mAU] | Area [%] |
|---|--------------|------|-------------|----------------|--------------|----------|
| 1 | 21.613       | BB   | 0.6464      | 441.31833      | 8.29904      | 1.8820   |
| 2 | 23.773       | BB   | 1.1379      | 2.30086e4      | 288.68143    | 98.1180  |
NMR Spectra and SFC Chromatograms of 4b

S43
| SampleName | ent1  | ent2  | ee   | Ent1  | Ent2  |
|------------|-------|-------|------|-------|-------|
| gdw-8-265-2| 98.70 | 1.30  | 97.39| 702282| 9269  |
NMR Spectra and SFC Chromatograms of 4c
Peak RetTime Type Width Area Height Area %

| #  | RetTime | Type | Width | Area     | Height | Area     | %    |
|----|---------|------|-------|----------|--------|----------|------|
| 1  | 12.722  | BV R | 0.5133| 333.10434| 97.3760|          |      |
| 2  | 15.065  | VB E | 0.4990| 327.21939| 7.83880| 2.6240   |      |

Totals: 1.24705e4 340.94314
NMR Spectra and SFC Chromatograms of 4d
NMR Spectra and SFC Chromatograms of 4e
| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 7.893   | BV R | 0.2512| 1.14677e4 | 664.97791 | 97.7869 |
| 2    | 9.800   | VB E | 0.3427| 259.53622 | 11.44048  | 2.2131  |
NMR Spectra and SFC Chromatograms of 4f
Signal 2: DAD1 B, Sig=210,4 Ref=360,100

| Peak | RetTime | Type | Width | Area  | Height | Area % |
|------|---------|------|-------|-------|--------|--------|
| 1    | 13.399  | BB   | 0.6734| 1.32386x10^4 | 285.25531 | 98.8715 |
| 2    | 16.958  | BB   | 0.6071| 151.10442 | 3.01274  | 1.1285  |
NMR Spectra and SFC Chromatograms of 4g
| SampleName | ent1 | ent2 | ee  | Ent1 | Ent2 |
|------------|------|------|-----|------|------|
| 1 gw-9-23-1| 50.11| 49.89| 0.22| 455020| 453027|
| 2 gw-9-23  | 98.02| 1.98 | 96.03| 1583546| 32055|
NMR Spectra and SFC Chromatograms of 4h
### Signal 2: DAD1 B, Sig=210.4 Ref=360.100

| #  | RetTime | Type | Width  | Area   | Height  | Area %  |
|----|---------|------|--------|--------|---------|---------|
| 1  | 9.189   | BB   | 0.4000 | 228.33351 | 7.74439 | 1.0575  |
| 2  | 10.808  | BB   | 0.5698 | 2.13642e4 | 579.88812 | 98.9425 |
NMR Spectra and SFC Chromatograms of 4i
NMR Spectra and SFC Chromatograms of 4j
| SampleName | ent1 | ent2 | ee   | Ent1  | Ent2  |
|------------|------|------|------|-------|-------|
| gw-8-271-1 | 98.72| 1.28 | 97.43| 348261| 4527  |
NMR Spectra and SFC Chromatograms of 4k
Area Summarized by Name

| SampleName | ent1 | ent2 | ee  | Ent1  | Ent2  |
|------------|------|------|-----|-------|-------|
| gcw-8-274-1| 98.12| 1.88 | 96.25| 498854| 9535  |
NMR Spectra and SFC Chromatograms of 4l
**Signal 2: DAD1 B, Sig=210,4 Ref=360,100**

| Peak | RetTime | Type | Width | Area      | Height     | Area %  |
|------|---------|------|-------|-----------|------------|---------|
| #    | [min]   | [min] | [mAU*s] | [mAU]     | %          |
| 1    | 10.237  | BB   | 0.5202 | 311.08194 | 7.75175    | 1.8039  |
| 2    | 12.634  | BB   | 0.9004 | 1.69334e4 | 270.47699  | 98.1961 |
NMR Spectra and SFC Chromatograms of 4m
NMR Spectra and SFC Chromatograms of 4n
NMR Spectra and SFC Chromatograms of 4o
NMR Spectra and SFC Chromatograms of 4p
| SampleName | ent1 | ent2 | ee  | Ent1  | Ent2  |
|------------|------|------|-----|-------|-------|
| gw-8-277-1| 97.62| 2.38 | 95.23| 561816| 13721 |
NMR Spectra and SFC Chromatograms of 4q
| SampleName | ent1  | ent2  | ee    | Ent1  | Ent2  |
|------------|-------|-------|-------|-------|-------|
| 1 yg-B-007 | 49.83 | 50.17 | -0.35 | 130124| 131031|
| 2 yg-B-007-B| 97.86 | 2.14  | 95.72 | 1091195| 23852 |
NMR Spectra and SFC Chromatograms of 4r

S75
| SampleName | ent1  | ent2  | ee    | Ent1  | Ent2  |
|------------|-------|-------|-------|-------|-------|
| 1          | 49.95 | 50.05 | -0.09 | 341733| 342376|
| 2          | 97.16 | 2.84  | 94.33 | 2577044| 75204 |
NMR Spectra and SFC Chromatograms of 4s
NMR Spectra and SFC Chromatograms of 4t
NMR Spectra and SFC Chromatograms of 4u
| SampleName | ent1 | ent2 | ee  | Ent1  | Ent2   |
|------------|------|------|-----|-------|--------|
| 1          | gdw-8-295-3 | 50.34 | 49.66 | 0.68 | 245177 | 241866 |
| 2          | gdw-8-277-1 | 97.62 | 2.38  | 95.23 | 561816 | 13721  |
NMR Spectra and SFC Chromatograms of 4v
NMR Spectra and SFC Chromatograms of 4w
| SampleName | ent1 | ent2 | ee  | Ent1   | Ent2   |
|------------|------|------|-----|--------|--------|
| gdw-8-282-1-1 | 97.35 | 2.65 | 94.69 | 582611 | 15876  |
NMR Spectra and SFC Chromatograms of 4x
| SampleName | ent1  | ent2  | ee   | Ent1 | Ent2 |
|------------|-------|-------|------|------|------|
| 2  gw-8-295-1 | 97.57 | 2.43  | 95.14 | 1201109 | 29942 |
NMR Spectra and SFC Chromatograms of 4y
| SampleName | ent1 | ent2 | ee  | Ent1 | Ent2 |
|------------|------|------|-----|------|------|
| gdw-8-275-3-1 | 2.14 | 97.86 | -95.73 | 4676 | 214154 |
NMR Spectra and SFC Chromatograms of 4z
| Sample Name | ent1 | ent2 | ee | Ent1 | Ent2 |
|-------------|------|------|----|------|------|
| 1 gw-8-296-2 | 50.29 | 49.71 | 0.59 | 429352 | 424337 |
| 2 gw-8-296-1 | 97.42 | 2.58 | 94.84 | 652871 | 17287 |
NMR Spectra and SFC Chromatograms of 4za
| SampleName | ent1 | ent2  | ee  | Ent1 | Ent2 |
|------------|------|-------|-----|------|------|
| 1 gw-9-11-2 | 50.59 | 49.41 | 1.19 | 423830 | 413873 |
| 2 gw-9-11-1 | 97.16 | 2.84  | 94.32 | 1280394 | 37427 |
NMR Spectra and SFC Chromatograms of 4zb
| SampleName | ent1 | ent2 | ee  | Ent1    | Ent2    |
|------------|------|------|-----|---------|---------|
| 1          | 50.05| 49.95| 0.11| 402896  | 401830  |
| 2          | 97.15| 2.85 | 94.30| 223902  | 6570    |
NMR Spectra and SFC Chromatograms of 4zc
| SampleName | ent1 | ent2 | ee  | Ent1  | Ent2  |
|------------|------|------|-----|-------|-------|
| YG-B72-2  | 97.69| 2.11 | 95.78| 742098| 16006 |
NMR Spectra and SFC Chromatograms of \textbf{4zd}
Area Summarized by Name

|   | SampleName | ent1  | ent2  | ee   | Ent1   | Ent2   |
|---|------------|-------|-------|------|--------|--------|
| 1 | YG-B91-2R  | 97.06 | 2.94  | 94.12| 2902843| 87891  |
NMR Spectra and SFC Chromatograms of 4ze
| SampleName | ent1 | ent2 | ee  | Ent1   | Ent2   |
|------------|------|------|-----|--------|--------|
| 1 gdw-9-65 | 49.92| 50.06| -0.16| 1186411| 1190306|
| 2 gdw-9-63 | 94.48| 5.52 | 88.96| 1355070| 79134  |
NMR Spectra and SFC Chromatograms of 4zf
NMR Spectra of 5
NMR Spectra and SFC Chromatograms of 8
$^1$H NMR Spectra of 7
NMR Spectra of Bortezomib
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