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Development of Enantiospecific Coupling of Secondary and Tertiary Boronic Esters with Aromatic Compounds

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Supporting Material I

Experimental procedures, React-IR experiments and plots, DFT calculations

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1. General Information
All required fine chemicals were used directly without purification unless otherwise noted. All air- and water-sensitive reactions were carried out in flame-dried glassware under nitrogen atmosphere by using standard Schlenk manifold techniques. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were acquired at various field strengths as indicated, and were referenced to CHCl$_3$ (7.27 and 77.0 ppm for $^1$H and $^{13}$C, respectively) or DMSO (2.54 and 40.45 ppm for $^1$H and $^{13}$C, respectively). $^1$H NMR coupling constants are reported in Hertz. Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, dd = doublet of doublets) and integration. $^{11}$B NMR spectra were recorded with
complete proton decoupling by using BF$_3$·Et$_2$O (0.0 ppm) as an external standard. High resolution mass spectra were recorded using electronic ionization (EI), electron spray ionization (ESI) or chemical ionization (CI). For CI, methane or NH$_4$OAc/MeOH were used as reagent gases. All IR data was obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Optical rotations were obtained on a Perkin-Elmer 241MC polarimeter. Analytical TLC: aluminium-backed plates precoated (0.25 mm) with Merck Silica Gel 60 F254. Compounds were visualized by exposure to UV light or by dipping the plates in permanganate (KMnO$_4$) stain followed by heating. Flash column chromatography was performed using Merck Silica Gel 60 (40–63 μm). All mixed solvent eluents are reported as v/v solutions. Chiral HPLC was performed using Diacel Chiralpak IA, IB and IC columns (4.6 × 250 mm × 5 μm) fitted with the respective guards (4 × 10 mm) and monitored by DAD (diode array detector). Chiral GC was performed on an Agilent Technologies 6890N Network GC system by using a Supelco DM column (30 m × 2.5 mm). Solvents were purified by standard methods. TMEDA was distilled over CaH$_2$. (−)-Sparteine was obtained from the commercially available sulfate pentahydrate salt (99%, Acros) and isolated according to literature procedure.¹ The (−)-sparteine free base readily absorbs atmospheric carbon dioxide (CO$_2$) and should be stored under argon/nitrogen at −20 °C in a Schlenk flask. sec-BuLi (1.3 M sol. in cyclohexane/hexane (92/8)) was purchased from Acros. n-BuLi (1.6 M sol. in hexanes) and t-BuLi (1.7 M sol. in pentane) were purchased from Sigma-Aldrich. Abbreviations: PMP = para-methoxyphenyl; DDQ = 2,3-dichloro-4,5-dicyano-1,4-benzoquinone; NBS = N-bromosuccinimide; NIBS = N-iodosuccinimide; DBDMH = 1,3d-dibromo-5,5-dimethylhydantoin.

2. General Procedures

Hydroborations with HBB₂•SMe₂ and BBr₃ – General Procedure 1
A solution of the alkene (1.1 eq.) in CH₂Cl₂ (0.5 M) was cooled to 0 °C and dibromoborane dimethylsulfide complex (1.0 eq., 1 M in CH₂Cl₂) and boron tribromide (1.0 eq.) were added dropwise. The cooling bath was removed and the mixture was stirred for 2 h at room temperature. ¹¹B NMR spectroscopy revealed the complete formation of the hydroborated product [¹¹B NMR (96 MHz, CH₂Cl₂) δ₈ ~ 63 ppm]. In a second flask, pinacol (3.0 eq.) was dissolved in CH₂Cl₂ (0.5 M), Et₃N (8.0 eq.) was added and the resulting solution was cooled to 0 °C. The crude hydroborated product was slowly added dropwise. The mixture was allowed to warm to room temperature and stirred for 2 h. ¹¹B NMR spectroscopy revealed complete formation of the pinacol boronic ester [¹¹B NMR (96 MHz, CH₂Cl₂) δ₈ ~ 32 ppm]. The mixture was diluted with CH₂Cl₂ (50 mL) and washed with water (50 mL). The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were concentrated under vacuum. The crude material was dissolved in MeOH and water was added until the mixture turned turbid. The solvents were evaporated to dryness under vacuum. The cycle of dissolution/concentration was repeated (x 6) until TLC analysis showed almost complete removal of pinacol. The crude product was dissolved in CH₂Cl₂, dried over MgSO₄, filtered and concentrated. Purification by column chromatography on silica gel, gave the desired boronic ester.

C(sp³)-C(sp²) coupling of boronic esters with furan by using NBS–General Procedure 2
A solution of furan (1.2 eq.) in THF (0.3 M) was cooled to −78 °C and treated with n-BuLi (1.2 eq., 1.6 M in hexanes). The cooling bath was removed and the mixture was stirred at room temperature for 1 h. The mixture was cooled to −78 °C and the boronic ester (1.0 eq.) was added dropwise as a solution in THF (0.5 M). The mixture was stirred at −78 °C for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [¹¹B NMR (96 MHz, THF) δ₈ ~ 8 ppm]. A solution of N-bromosuccinimide (NBS, 1.2 eq.) in THF (0.3 M) was added dropwise. After 1 h at −78 °C, a saturated aqueous solution of Na₂S₂O₃ was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et₂O and water. The layers were separated and the aqueous layer was extracted with Et₂O. The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by column chromatography on silica gel, gave
the desired product. **NOTE:** NBS must be dissolved and added to the ‘ate’ complex solution before it turns orange. This applies particularly to examples where NBS (or other electrophile) is added in MeOH.

**C(sp³)-C(sp²) coupling of boronic esters with furan by using DDQ—General Procedure 3**

A solution of furan (1.2 eq.) in THF (0.3 M) was cooled to −78 °C and treated with n-BuLi (1.2 eq., 1.6 M in hexanes). The cooling bath was removed and the mixture was stirred at room temperature for 1 h. The mixture was cooled to −78 °C and the boronic ester (1.0 eq.) was added dropwise as a solution in THF (0.5 M). The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^{11}$B NMR (96 MHz, THF) $\delta_B \sim 8$ ppm]. A solution of DDQ (1.5 eq.) in THF (0.3 M) was added dropwise. After 1 h at −78 °C, a saturated aqueous solution of Na$_2$S$_2$O$_3$ was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et$_2$O and water. The layers were separated and the aqueous layer was extracted with Et$_2$O. The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by column chromatography on silica gel, gave the desired product. **NOTE:** NBS must be dissolved and added to the ‘ate’ complex solution before it turns orange. This applies particularly to examples where NBS (or other electrophile) is added in MeOH.
3. Synthesis of the starting materials

(R)-4,4,5,5-Tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane [(R)-1a]

\[ \text{OCb} \quad \xrightarrow{1. \text{sec-BuLi, (-)-sparteine, Et}_2\text{O, -78 °C, 5 h}} \quad \xrightarrow{2. \text{Ph(CH}_2)_2\text{Bpin, -78 °C, 1h}} \quad \xrightarrow{3. \text{MgBr}_2\cdot\text{Et}_2\text{O, reflux, 16 h}} \quad \text{B(pin)} \]

Prepared according to a literature known procedure.\(^2\)

(S)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-1b]

\[ \text{OTIB} \quad \xrightarrow{1. \text{sec-BuLi, (+)-sparteine, Et}_2\text{O, -78 °C, 4 h}} \quad \xrightarrow{2. \text{PMP(CH}_2)_2\text{Bpin, -78 °C, 1h}} \quad \text{B(pin)} \]

Prepared according to a literature known procedure.\(^3\)

(S)-4,4,5,5-Tetramethyl-2-(4-methyl-1-phenylpentan-3-yl)-1,3,2-dioxaborolane [(S)-1c]

\[ \text{OCb} \quad \xrightarrow{1. \text{sec-BuLi, (-)-sparteine, Et}_2\text{O, -78 °C, 5 h}} \quad \xrightarrow{2. \text{Ph(CH}_2)_2\text{Bpin, -78 °C, 1h}} \quad \xrightarrow{3. \text{MgBr}_2\cdot\text{Et}_2\text{O, reflux, 16 h}} \quad \text{B(pin)} \]

Prepared using the same procedure as reported for [(R)-1a]. Data in accordance with the literature.\(^4\)

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A solution of the (3-(4-methoxyphenyl)propyl 2,4,6-triisopropylbenzoate (345 mg, 0.87 mmol, 1.0 eq.) and (+)-sparteine (245 mg, 1.04 mmol, 1.2 eq.) in Et₂O (4.5 ml) was cooled to –78 °C. The solution was treated with sec-BuLi (0.82 mL, 1.042 mmol, 1.15 eq., 1.4 M in cyclohexane). The mixture was stirred for 4h at –78 °C and then a solution of 2-(3-methylbut-2-en-1-yl)-B(pin) (219 mg, 1.04 mmol, 1.2 eq.) in Et₂O (5.0 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 1 h and at refluxing conditions for 16h. Water (10 mL) was added and the layers were separated. The aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were washed with brine (30 ml), dried over MgSO₄ and concentrated under vacuum. The crude material was purified by column chromatography on silica gel, eluting with petrol:Et₂O (99:1) to give (R)-1d (196 mg, 63%), which was obtained as an oil; er (R:S) 96:4; Rₙ 0.51 (pentane:Et₂O 95:5); [α]D²⁴ –2 (c 1.0, CHCl₃); IR (film): ν (cm⁻¹) 2977, 2923, 2855, 1511, 1379, 1314, 1244, 1143; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.14–7.09 (m, 2H), 6.86–6.80 (m, 2H), 5.14 (br t, J = 7.1 Hz, 1H), 3.79 (s, 3H), 2.64–2.49 (m, 2H), 2.09–1.91 (m, 2H), 1.80–1.60 (m, 2H), 1.71 (s, 3H), 1.61 (s, 3H), 1.52 (m, 1H), 1.42 (m, 1H), 1.28 (s, 12H), 1.08 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.6, 135.2, 131.1, 129.2, 124.9, 113.6, 82.9, 55.2, 34.6, 33.6, 31.4, 27.7, 25.7, 24.8, 17.6; ¹¹B NMR (96 MHz, NONE) δ ppm 34.1; HRMS (ESI) calcd. for C₂₂H₃₅BNaO₃ [M+Na⁺]⁺ 381.2571, found 381.2586.

1d was converted into the corresponding alcohol through oxidation to achieve resolution of the enantiomers in chiral HPLC analysis (see below):

Boronic ester 1d was treated with a solution of 2 N NaOH/30% H₂O₂ (2:1 v/v) in THF/ET₂O (1:1 v/v) to give, after purification by column chromatography (SiO₂, 85:15 petrol/EtOAc), the desired secondary alcohol (20 mg, 95%) as an oil. R₂ₙ 0.42 (petrol: ET₂O 85:15); [α]D²⁴ –20 (c 0.6, CHCl₃); IR (film): ν (cm⁻¹) 3371, 2924, 2855, 1612, 1511, 1243, 1037, 820; ¹H
NMR (400 MHz, CDCl₃) δ ppm 7.16–7.10 (m, 2H), 6.87–6.81 (m, 2H), 5.14 (br t, J = 7.1 Hz, 1H), 3.80 (s, 3H), 3.64 (m, 1H), 2.75 (m, 1H), 2.63 (m, 1H), 2.20–2.00 (m, 2H), 1.82–1.71 (m, 2H), 1.70 (s, 3H), 1.63 (s, 3H), 1.52–1.45 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.8, 134.2, 132.2, 129.3, 124.0, 113.8, 71.2, 55.2, 37.4, 31.1, 25.7, 24.4, 17.7; HRMS (ESI) calcd. for C₁₆H₂₄NaO₂ [M+Na]⁺ 271.1669, found 271.1668.

Resolution of the enantiomers of the alcohol was achieved by using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO₂:[n-hexane:i-PrOH (9:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P= 125 bar). Injection volume: 20 µL of a 2 g L⁻¹ solution of the compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) eluted at 11.5 and 13.4 min., respectively, with a total analysis time of 18 min.

(R)-tert-Butyl 6-Phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate [(R)-1e]

\[
\text{Ph} \quad \text{OTIB} \quad \text{B(pin)} \quad \text{Ph} \quad \text{CO₂f-Bu}
\]

1. sec-BuLi, (-)-sparteine, Et₂O, -78 °C, 4 h
2. t-BuO₂C-B(pin), -78 °C, 1 h

![Conversion diagram]

81 %
er 96:4

Prepared according to a literature known procedure.³

(R)-2-(7-azido-1-(4-methoxyphenyl)heptan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(R)-1f]

\[
\text{PMP} \quad \text{OTIB} \quad \text{B(pin)} \quad \text{PMP} \quad \text{N₃}
\]

1. sec-BuLi, (+)-sparteine, Et₂O, -78 °C, 4h
2. N₃(CH₂)₂Bpin, -78 °C, 1h
3. reflux, 16h

51 %
er 96:4

Prepared according to a literature known procedure.³
(S)-4,4,5,5-Tetramethyl-2-(3-methyl-1-phenylpentan-3-yl)-1,3,2-dioxaborolane [(S)-1g]

\[
\begin{align*}
\text{Ph} & \quad \text{OTIB} \\
\text{Ph} & \quad \text{B(pin)}
\end{align*}
\]

1. sec-BuLi, TMEDA, CPME, -60 °C, 2 h
2. EtB(neop), -60 °C, 1 h
3. 50 °C, 16 h
4. pinacol, H₂O

71%  
er >99:1

Prepared according to a literature known procedure.⁵

(R)-4,4,5,5-Tetramethyl-2-(2-phenylbutan-2-yl)-1,3,2-dioxaborolane [(R)-1h]

\[
\begin{align*}
\text{Ph} & \quad \text{OCb} \\
\text{Ph} & \quad \text{B(pin)}
\end{align*}
\]

1. sec-BuLi, Et₂O, -78 °C, 30 min
2. EtB(pin), -78 °C, 1 h
3. rt, 2 h

97%  
er 99:1

Prepared according to a literature known procedure.⁶

(R)-4,4,5,5-Tetramethyl-2-(4-methyl-2-phenylpentan-2-yl)-1,3,2-dioxaborolane [(R)-1i]

\[
\begin{align*}
\text{Ph} & \quad \text{OCb} \\
\text{Ph} & \quad \text{B(pin)}
\end{align*}
\]

1. sec-BuLi, Et₂O, -78 °C, 30 min
2. i-BuB(pin), -78 °C, 1 h
3. rt, 2 h

61%  
er 99:1

Prepared according to a literature known procedure.⁷

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A solution of the (S)-1-phenylethyl diisopropylcarbamate (1.5 g, 6.02 mmol, 1.15 eq.) in Et₂O (15.0 ml) was cooled to –78 °C and treated with sec-BuLi (4.3 mL, 6.02 mmol, 1.15 eq., 1.4 M in cyclohexane). The mixture was stirred for 30 min –78 °C and then a solution of cyclopropyl–B(pin) (955 μL, 5.24 mmol, 1.0 eq.) in Et₂O (5.0 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 1 h and then at room temperature for 2 h. Water (15 mL) was added and the layers were separated. The aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO₄ and concentrated under vacuum. Purification by column chromatography on silica gel, eluting with petrol:Et₂O (99:1) gave 1j (1.2 g, 81%), which was obtained as an oil; er (S:R) 99:1; Rf 0.33 (pentane:Et₂O 95:5); [α]D²⁵ 25 (c 1.0, CHCl₃); IR (film): ν (cm⁻¹) 3058, 2977, 1380, 1371, 1306, 849, 698; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.45–7.41 (m, 2H), 7.32–7.27 (m, 2H), 7.15 (m, 1H), 1.23 (s, 3H), 1.22 (s, 6H), 1.21 (s, 6H), 1.13 (m, 1H), 0.52–0.47 (m, 3H), 0.33 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 148.4, 128.0, 127.2, 125.2, 83.3, 24.7, 24.6, 21.8, 18.6, 2.1, 1.6; ¹¹B NMR (96 MHz, NONE) δ ppm 32.9; HRMS (EI) calcd. for C₁₇H₂₅BO₂ [M]+ 272.1948, found 272.1954.

Ij was oxidised to the corresponding alcohol to determine enantiopurity:

Resolution of the enantiomers of the alcohol was achieved by using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO₂:[n-hexane:i-PrOH (9:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P= 125 bar). Injection volume: 20μL of a 2 g L⁻¹ solution of the compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 5.3 and 5.9 min., respectively, with a total analysis time of 15 min. [α]D²⁴ 28 (c 0.5, CHCl₃) in accordance with literature precedent ([α]D²⁴ 28.5 (c 0.49, CHCl₃)⁸).

Data in accordance with literature precedent.\(^8\)

\((R)-2-(1-(4-Bromophenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane \quad [(R)-1k]\)

A solution of the (S)-1-phenylethyl diisopropylcarbamate (300 mg, 1.20 mmol, 1.2 eq.) in Et\(_2\)O (5.0 ml) was cooled to \(-78 \, ^\circ\)C and treated with sec-BuLi (1.0 mL, 1.25 mmol, 1.25 eq., 1.4 M in cyclohexane). The mixture was stirred for 20 min at \(-78 \, ^\circ\)C and then a solution of \(p\)-Br-Ph–B(pin) (283 mg, 1.00 mmol, 1 eq.) in Et\(_2\)O (1.0 mL) was added dropwise. The reaction mixture was stirred at \(-78 \, ^\circ\)C for 30 min and at room temperature for 2 h. Water (5 mL) was added and the layers were separated. The aqueous layer was extracted with Et\(_2\)O (3 x 10 ml). The combined organic layers were washed with brine (30 ml), dried over MgSO\(_4\) and concentrated under vacuum. Purification by column chromatography on silica gel, eluting with petrol:Et\(_2\)O (99:1→95:5), gave (\(R\))-1k (265 mg, 69%) as an amorphous solid; er \((R:S)\) 99:1; \(R_f\) 0.43 (petrol:Et\(_2\)O 20:1); \([\alpha]_D^{22} +8.6 \,(c \,0.5, \,CHCl_3)\); IR (film): \(\nu\) (cm\(^{-1}\)) 2929, 2854, 1464, 1378, 1318, 1252, 1142, 1078, 1063, 836, 770; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.39–7.33 (m, 2H), 7.29–7.22 (m, 2H), 7.21–7.13 (m, 3H), 7.12–7.06 (m, 2H), 1.65 (s, 3H), 1.20 (s, 6H), 1.19 (s, 6H); \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 147.1, 146.8, 131.0, 130.4, 128.4, 128.1, 125.6, 119.3, 83.9, 25.7, 24.5; \(^1^B\) NMR (96 MHz, CDCl\(_3\)) \(\delta\) 32.9 ppm; HRMS (EI) calcd. for C\(_{20}\)H\(_{24}\)BBrO\(_2\) \([M]^+\) 386.1053, found 386.1048.

\(1s\) was oxidised to the corresponding alcohol to aid in determining enantiopurity (see below):

Resolution of the enantiomers of the alcohol was achieved by using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO\(_2\):[\(n\)-hexane:i-ProH (1:1 v:v)] (95:5 v:v) as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) (\(P= 125\) bar). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of the compound in the eluent. Under these conditions,
the faster running component (R) and the slower running component (S) were eluted at 11.5 and 12.2 min., respectively, with a total analysis time of 15 min.

(R)-4,4,5,5-Tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane [(R)-II]

Prepared according to a literature known procedure.\(^9\)

4,4,5,5-Tetramethyl-2-((1S,2R,3S,6R)-3,7,7-trimethylbicyclo[4.1.0]heptan-2-yl)-1,3,2-dioxaborolane (1m)

Following GP1 (3.35 mmol scale), 1m (448 mg, 51%) was obtained as an oil; Rf 0.27 (petrol: Et₂O 98:2); [α]\(_D\)\(^{20}\) −3.0 (c 1.0, CHCl₃); IR (film): ν (cm\(^{-1}\)) 2978, 2921, 2864, 1368, 1314, 1142; \(^1\)H NMR (400 MHz, CDCl₃) δ ppm 1.86–1.76 (m, 1H), 1.71 (dd, \(J = 14.4, 6.7\) Hz, 1H), 1.35 (dddd, \(J = 13.0, 7.7, 3.2, 1.8\) Hz, 1H), 1.27 (s, 6H), 1.26 (s, 6H), 1.22 (m, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.80 (d, \(J = 6.6\) Hz, 3H), 0.65 (m, 1H), 0.57 (dd, \(J = 9.1, 5.0\) Hz, 1H), 0.42 (t, \(J = 9.1\) Hz, 1H), 0.35 (dd, \(J = 11.8, 5.0\) Hz, 1H); \(^1\)C NMR (100 MHz, CDCl₃, CH–B not observed) δ ppm 82.8, 31.7, 29.6, 24.7, 24.6, 22.5, 22.2, 19.6, 18.5, 17.9, 15.5; \(^{11}\)B NMR (96 MHz, CDCl₃) δ ppm 32.0; LRMS 264 (GC-MS); HRMS (EI) calcd. for C\(_{16}\)H\(_{29}\)BO\(_2\) \([M]^+\) 264.2261, found 264.2266.

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4,4,5,5-Tetramethyl-2-((1R,2S,3R,5R)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)-1,3,2-dioxaborolane (1n)

Following GP1 (3.35 mmol scale). 1n (490 mg, 56%) was obtained as an oil; Rf 0.51 (petrol:Et2O 95:5); [α]D²⁰ –10.0 (c 1.0, CHCl₃); IR (film): ν (cm⁻¹) 2978, 2897, 2870, 1369, 1346, 1311, 1144; ¹H NMR (400 MHz, CDCl₃) δ ppm 2.29 (ddd, J = 9.3, 6.3, 2.0 Hz, 1H), 2.14 (dqd, J = 8.3, 7.4, 2.0 Hz, 1H), 2.04 (ddd, J = 12.0, 3.1, 2.0 Hz, 1H), 1.92–1.81 (m, 2H), 1.76 (td, J = 5.5, 2.0 Hz, 1H), 1.25 (s, 12H), 1.17 (s, 3H), 1.04 (s, 3H), 1.02 (s, 3H), 0.87–0.80 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, CH–B not observed) δ ppm 82.7, 47.9, 41.2, 38.5, 38.2, 34.1, 28.6, 28.4, 24.7, 24.6, 23.1, 22.7; ¹¹B NMR (96 MHz, CDCl₃) δ ppm 33.0; LRMS 264 (GC-MS); HRMS (ESI) calcd. for C₁₆H₃₀BO₂ [M+H]⁺ 265.2339, found 265.2336.

(3S,5R,6S,8R,10S,13R,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (1o)

Freshly distilled catecholborane (1.4 mL, 13.36 mmol, 6.0 eq.) was added to a Schlenk flask containing cholesterol (2.2 g, 5.69 mmol, 1.0 eq.). The resulting mixture was heated to 100 °C at which point a solution formed. After 16 h at the same temperature, the mixture was cooled to room temperature and TLC analysis (petrol:EtOAc 7:3) revealed complete consumption of cholesterol. Excess catecholborane was removed under high vacuum (0.2 mbar, 2 h, r.t.). The crude material was diluted with CH₂Cl₂ (15 mL) and Et₃N (2.5 mL, 17.82 mmol, 8.0 eq.) and pinacol (788 mg, 6.68 mmol, 3.0 eq.) were added. After 1 h the mixture
was diluted with CH$_2$Cl$_2$ (20 mL) and water (20 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organics layers were dried over MgSO$_4$, filtered, and concentrated under vacuum. Purification by column chromatography on silica gel, eluting with n-hexane:EtOAc (95:5→75:25) gave 1o (592 mg, 52%) as an amorphous solid; $R_f$ 0.41 (petrol:EtOAc 7:3; mp 196–199 °C; $[\alpha]_D^{23} +32.4$ (c 1.0, CHCl$_3$); IR (film): ν (cm$^{-1}$) 3229, 2929, 2865, 1371, 1315, 1143, 1043, 850; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm. 3.62 (tt, $J = 10.5, 4.4$ Hz, 1H), 1.95 (br d, $J = 12.5$ Hz, 1H), 1.85–1.75 (m, 2H), 1.71 (m, 1H), 1.64–1.44 (m, 5H), 1.32–1.29 (m, 5H), 1.24 (s, 16H), 1.15–0.95 (m, 10H), 0.94–0.84 (m, 11H) 0.80 (s, 3H), 0.68 (m, 1H), 0.61 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 82.9, 71.2, 56.2, 53.9, 45.3, 42.6, 40.0, 39.5, 37.7, 36.7, 36.2, 35.8, 35.6, 35.2, 33.5, 31.5, 28.2, 28.0, 24.8, 24.7, 24.2, 23.8, 22.8, 22.5, 21.2, 18.6, 12.4, 12.0; $^{11}$B NMR (96 MHz, CDCl$_3$) δ ppm 32.1; LRMS 514 (GC-MS); HRMS (ESI) calcd. for C$_{33}$H$_{59}$BNaO$_3$ [M+Na]$^+$ 537.4455, found 537.4451.

tert-Butyl(((3S,5R,6S,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)dimethylsilane (1p)

A solution of 1o (150 mg, 0.29 mmol, 1.0 eq.) in CH$_2$Cl$_2$ (3 mL) was cooled to 0 °C and imidazole (60 mg, 0.87 mmol, 3.0 eq.) and tert-butyldimethylsilyl chloride (132 mg, 0.87 mmol, 3.0 eq.) were added. The reaction mixture was allowed to warm to room temperature overnight and was quenched with water (3 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 10 mL). The combined organics layers were dried over MgSO$_4$, filtered, and concentrated under vacuum. Purification by column chromatography on silica gel, eluting with n-hexane:EtOAc (99:1→97:3) gave 1p (161 mg, 88%) as an amorphous solid; $R_f$ 0.55 (petrol:EtOAc 95:5; mp 180–182 °C; $[\alpha]_D^{22} +8.6$ (c 0.5, CHCl$_3$); IR (film): ν (cm$^{-1}$) 2929, 2854, 1464, 1378, 1318, 1252, 1142, 1078, 1063, 836, 770; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 3.57 (tt, $J = 10.8, 4.5$ Hz, 1H), 1.95 (dt, $J = 12.5, 3.3$ Hz, SI-I-13
1H), 1.79 (m, 1H), 1.70–1.60 (m, 3H), 1.60–1.40 (m, 5H), 1.40–1.27 (m, 5H), 1.24 (m, 14H), 1.06 (m, 11H), 0.91–0.78 (m, 19H), 0.78 (s, 3H), 0.72–0.61 (m, 1H), 0.56 (s, 3H), 0.04 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 82.6, 71.9, 56.1, 56.0, 53.8, 45.3, 42.4, 39.9, 39.4, 37.9, 36.7, 36.0, 35.6, 35.4, 35.1, 33.4, 31.7, 28.1, 27.8, 25.8, 24.7, 24.6, 24.0, 23.7, 22.7, 22.4, 21.0, 18.5, 18.2, 12.3, 11.9, −4.7, −4.8; 11B NMR (96 MHz, CDCl3) δ ppm 32.0; HRMS (ESI) calcd. for C39H73BNaO3Si [M+Na]+ 651.5320, found 651.5321.

2-((1R,2R,5R)-2-isopropyl-5-methylcyclohexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1q)

Prepared according to literature known procedure.10

4,4,5,5-tetramethyl-2-(oxetan-3-yl)-1,3,2-dioxaborolane (1r)

In air, CuI (9.5 mg, 0.05 mmol, 0.01 eq.), PPh3 (183 mg, 0.07 mmol, 0.14 eq.), LiOMe (418 mg, 10.9 mmol, 2.0 eq.), and bis(pinacolato)diboron (2.1 g, 8.3 mmol, 1.5 eq.) were added to a Schlenk tube equipped with a stir bar. The vessel was evacuated and filled with nitrogen (three cycles). DMF (10.5 mL), 3-iodooxetane (920 mg, 0.5 mmol, 1.0 eq.) were added in turn by syringe under a nitrogen atmosphere. The resulting reaction mixture was stirred at 60 °C for 24 h. The reaction mixture was then diluted with Et2O (30 mL), filtered through silica gel with copious amount of Et2O. Evaporation of solvent under vacuum and purification by column chromatography eluting with n-hexane:EtOAc (75:25) gave 1r (186 mg, 21%) as a solid; Rf 0.12 (pentane:Et2O 85:15); mp. 24–26 °C; IR (film): ν (cm−1) 2977, 2871, 1385,

1320, 1216, 1141, 857; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 4.70–4.55 (m, 4H), 2.59 (m, 1H), 1.13 (s, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$, CH–B not observed) δ ppm 83.2, 73.0, 24.3; HRMS (CI) calcd. for C$_9$H$_{18}$BO$_3$ [M+H]$^+$ 185.1349, found 185.1342.

Prepared using a modification of a literature known procedure.$^{11}$

(R)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanenitrile [(R)-1s]

![Chemical Reaction Image]

Prepared according to a literature known procedure.$^{12}$

(S)-tert-Butyl 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolidine-1-carboxylate [(S)-1t]

![Chemical Reaction Image]

Prepared according to a literature known procedure.$^{13}$

(S)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) [(S)-1u]

![Chemical Reaction Image]

Prepared according to a literature known procedure.$^{14}$


4. Oxidant/Electrophile Screening

**General Procedure for the Screening:**

A solution of furan (44 µL, 0.6 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.37 mL, 0.6 mmol, 1.2 eq., 1.6 M in hexanes). The cooling bath was removed and the mixture was stirred at room temperature for 1 h. The mixture was cooled to −78 °C and (R)-1a (66 mg, 0.5 mmol, 1.0 eq.) was added dropwise as a solution in THF (1.0 mL). The mixture was stirred at −78 °C for 1 h at which point $^1^1$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^1^1$B NMR (96 MHz, THF) $\delta_B \sim 8$ ppm]. A solution of an oxidant/electrophile (0.6 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h at −78 °C, a saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et$_2$O (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with Et$_2$O. The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-2a.

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<th>Yield (%)</th>
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5. Reaction Products – Coupling to heterocycles

(R)-2-(4-Phenylbutan-2-yl)furan [(R)-2a]

Following GP2 (0.50 mmol scale), (R)-2a (91 mg, 91%) was obtained as an oil; er (R:S) 98:2; $R_t$ 0.82 (petrol:Et$_2$O 95:5); $[\alpha]_D^{23}$ 28.3 (c 0.5, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 3114, 3085, 3063, 3027, 2966, 2927, 2858, 1454, 1008, 727, 697; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.38 (br s, 1H), 7.36–7.31 (m, 2H), 7.26–7.21 (m, 3H), 6.35 (dd, $J = 3.1$, 1.9 Hz, 1H), 6.07 (d, $J = 3.1$ Hz, 1H), 2.92 (sx, $J = 6.9$ Hz, 1H), 2.66 (t, $J = 8.1$ Hz, 2H), 2.08 (m, 1H), 1.89 (m, 1H), 1.33 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 160.3, 142.4, 128.4, 128.3, 125.8, 109.9, 103.8, 37.6, 33.5, 32.8, 19.3; HRMS (CI) calcd. for C$_{14}$H$_{16}$O $[M]^{+}$ 200.1201, found 200.1210.

Resolution of the enantiomers of 2a was achieved by using a chiral HPLC system fitted with a Chiralpak AD-H column with guard as the stationary phase with n-hexanes the mobile phase at a flow rate of 0.2 mL min$^{-1}$ ($T = 0$ °C). Injection volume: 20μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 51.1 and 56.1 min., respectively, with a total analysis time of 75 min.

Coupling in the presence of DDQ was performed following GP3 and resulted in 82% yield and 100% e.s.

(S)-2-(4-Methyl-1-phenylpentan-3-yl)furan [(S)-2c]

Following GP2 (0.50 mmol scale), (S)-2c (105 mg, 92%) was obtained as an oil; er (S:R) 97:3; $R_t$ 0.90 (petrol:Et$_2$O 95:5); $[\alpha]_D^{25}$ 9.0 (c 1.0, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 3112, 3085, 3063, 3027, 2957, 2929, 2870, 1454, 1009, 727, 697; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.40 (br s, 1H), 7.35–7.27 (m, 2H), 7.25–7.16 (m, 3H), 6.35 (dd, $J = 3.0$, 1.9 Hz, 1H), 6.07 (d, $J = 3.0$ Hz, 1H), 2.63–2.53 (m, 2H), 2.47 (m, 1H), 2.08–1.96 (m, 2H), 1.92 (app. oct, $J = 6.8$ Hz, 1H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.85 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 157.7, 142.6, 140.7, 128.4, 128.3, 125.7, 109.8, 106.2, 45.4, 34.1, 33.1, 32.2, 20.8, 19.8; HRMS (EI) calcd. for C$_{16}$H$_{20}$O $[M+H]^+$ 228.1514, found 228.1516.

Resolution of the enantiomers of 2c was achieved using a chiral GC system fitted with a Supelco DM column. Injector $T = 250$ °C, detector $T = 300$ °C. Oven conditions: $T = 70$ °C for 3 min then ramp (1 °C min$^{-1}$) until 180 °C, H$_2$ carrier gas at 14 psi. Under these
conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 64.6 and 64.7 min respectively with a total analysis time of 75 min.

Coupling in the presence of DDQ was performed following GP3 and resulted in 67% yield and 100% e.s.

\((R)-2-(1-(4-methoxyphenyl)-7-methyloct-6-en-3-yl)furan [(R)-2d]\)

Following GP2 (0.28 mmol scale), \((R)-2d\) (78 mg, 94\%) was obtained as an oil; er \((R:S)\) 92:8; \(R_t\) 0.63 (petrol:Et\(_2\)O 95:5); \([\alpha]_D^{22}= -8.7 \text{ (c 1.3, CHCl}_3); IR (film): \nu (\text{cm}^{-1}) 2928, 2857, 1511, 1244, 1176, 1037, 728; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.35 (br s, 1H), 7.11–7.04 (m, 2H), 6.86–6.80 (m, 2H), 6.32 (dd, \(J = 3.1, 1.9\) Hz, 1H), 6.03 (br d, \(J = 3.1\) Hz, 1H), 5.08 (m, 1H), 3.80 (s, 3H), 2.72 (m, 1H), 2.55–2.39 (m, 2H), 1.99–1.81 (m, 4H), 1.78–1.56 (m, 2H), 1.68 (s, 3H), 1.54 (s, 3H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 158.6, 157.7, 140.7, 134.5, 131.6, 129.2, 124.2, 113.7, 109.8, 105.2, 55.2, 38.1, 36.2, 34.3, 32.6, 25.7, 25.7, 17.6; HRMS (EI) calcd. for C\(_{20}\)H\(_{26}\)O\(_2\) [\(M^+\)] 298.1933, found 298.1935.

Resolution of the enantiomers of 2d was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with 99:1 \([\text{n-hexanes:}(10 \% \text{i-PrOH in n-hexanes}]\) the mobile phase at a flow rate of 0.5 mL min\(^{-1}\) (\(T = 0^\circ\)C). Injection volume: 5 \(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 16.4 and 17.5 min., respectively, with a total analysis time of 35 min.

\((R)-\text{tert-Butyl 4-}(\text{furan-2-yl)-6-phenylhexanoate [(R)-2e]}\)

Following GP2 (0.50 mmol scale), \((R)-2e\) (142 mg, 90\%) was obtained as an oil; er \((R:S)\) 96:4; \(R_t\) 0.72 (petrol:Et\(_2\)O 95:5); \([\alpha]_D^{21}=+8.0 \text{ (c 1.0, CHCl}_3); IR (film): \nu (\text{cm}^{-1}) 3063, 3027, 2977, 2931, 2862, 1726, 1366, 1146, 729, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.37 (dd, \(J = 1.8, 0.7\) Hz, 1H), 7.31–7.26 (m, 2H), 7.22–7.14 (m, 3H), 6.33 (dd, \(J = 3.2, 1.8\) Hz, 1H), 6.07 (d, \(J = 3.2\) Hz, 1H), 2.80–2.72 (m, 1H), 2.62–2.48 (m, 2H), 2.22–2.10 (m, 2H), 2.08–1.86 (m, 4H), 1.44 (s, 9H); \(^1\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 172.8, 157.4, 142.1, 141.1, 128.4, 128.3, 125.8, 109.9, 105.9, 80.1, 38.0, 35.9, 33.5, 33.3, 29.5, 28.1; HRMS (EI) calcd. for C\(_{20}\)H\(_{26}\)O\(_3\) [\(M^+\)] 314.1882, found 314.1870.

Resolution of the enantiomers of 2e was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with \(n\)-hexane:\textit{i}-PrOH (99:1 v:v) as
the mobile phase at a flow rate of 0.5 mL min\(^{-1}\) \((T = 20 \, ^\circ\text{C})\). Injection volume: 20\(\mu\text{L}\) of a 2 g L\(^{-1}\) solution of the compound in the eluent. Under these conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 9.5 and 10.3 min., respectively, with a total analysis time of 30 min.

Coupling in the presence of DDQ was performed following GP3 and resulted in 71% yield and 100% e.s.

\((R)-2-(7\text{-azido-1-(4-methoxyphenyl)heptan-3-yl)furan}\) ([\(R\)-2f]

Following GP2 (0.23 mmol scale), \((R)-2f\) (52 mg, 71%) was obtained as an oil; er \((R:S)\) 96:4; \(R\)\(_t\) 0.32 (petrol:Et\(_2\)O 95:5); \([\alpha]^D\)\(_{24}^\circ\) = 11 \((c, 0.6, \text{CHCl}_3)\); IR (film): \(\nu\) (cm\(^{-1}\)) 2935, 2860, 2091, 1510, 1052, 730; \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.36 (dd, \(J = 1.9, 0.8\) Hz, 1H), 7.10–7.05 (m, 2H), 6.86–6.81 (m, 2H), 6.33 (dd, \(J = 3.1, 1.9\) Hz, 1H), 6.05 (br d, \(J = 3.1\) Hz, 1H), 3.60 (s, 3H), 3.26–3.18 (m, 2H), 2.70 (m, 1H), 2.56–2.39 (m, 2H), 2.01–1.80 (m, 2H), 1.73–1.47 (m, 4H), 1.36–1.22 (m, 2H); \(^{13}\text{C}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 158.2, 157.7, 140.8, 134.2, 129.2, 113.7, 109.8, 105.4, 55.2, 51.3, 38.4, 36.2, 33.8, 32.6, 28.8, 24.4; HRMS (EI) calcd. for C\(_{18}\)H\(_{23}\)N\(_3\)O \([M]^+\) 313.1790, found 313.1786.

Resolution of the enantiomers of 2f was achieved using a chiral SFC system fitted with a Chiralcel IB column as the stationary phase with CO\(_2\):n-hexane as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) \((P = 125\) bar). Injection volume: 10\(\mu\text{L}\) of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 8.8 and 10.0 min., respectively, with a total analysis time of 15 min.

\((R)-2-(1\text{-Phenylethyl)furan}\) ([\(R\)-2l]

Following GP2 (0.5 mmol scale), \((R)-2l\) (80 mg, 93%) was obtained as an oil; er \((R:S)\) 93:7; \(R\)\(_t\) 0.90 (petrol:Et\(_2\)O 95:5); \([\alpha]^D\)\(_{23}^\circ\) = 24.3 \((c, 1, \text{CHCl}_3)\) [Lit. for \((R)-2l\) \([\alpha]^D\)\(_{20}^\circ\) = 40.9 \((c, 0.88, \text{CHCl}_3)\), er \((R:S)\) 98:2\(^\text{13}\); \(^1\text{H}\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) ppm 7.36–7.16 (m, 6H), 6.29 (dd, \(J = 3.2, 1.8\) Hz, 1H), 6.05 (dt, \(J = 3.2, 0.9\) Hz, 1H), 4.12 (q, \(J = 7.2, 1\)H), 1.60 (d, \(J = 7.2\) Hz, 3H); \(^{13}\text{C}\) NMR (CDCl\(_3\), 100 MHz) \(\delta\) ppm 159.0, 144.1, 141.3, 128.5, 127.3, 126.5, 109.9, 104.9, 39.2, 20.5.

Resolution of the enantiomers of 2l was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with n-hexane as the mobile phase at a flow rate of 0.3 mL min\(^{-1}\) \((T = 5 \, ^\circ\text{C})\). Injection volume: 20 \(\mu\text{L}\) of a 2 g L\(^{-1}\) solution of the
compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 39.6 and 41.7 min, respectively, with a total analysis time of 60 min.

Data in accordance with the literature.\textsuperscript{15}

The stereospecificity of the process has been determined to be retentive by comparing the chiral HPLC traces and the optical rotation of this compound with the literature.\textsuperscript{15}

\textbf{2-((1R,2R,3S,6R)-3,7,7-Trimethylbicyclo[4.1.0]heptan-2-yl)furan (2m)}

Following GP\textsubscript{2} (0.5 mmol scale), 2m (69 mg, 68\%) was obtained as an oil; \(R_f\) 0.77 (petrol: Et\(_2\)O 95:5); \([\alpha]_D^{22}\) \(\approx\) –34.0 (c 1.0, CHCl\(_3\); IR (film): \(\nu\) (cm\(^{-1}\)) 2922, 2864, 1458, 1375, 1148, 1009, 792, 724; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.35 (dd, \(J = 1.8, 0.8\) Hz, 1H), 6.32 (dd, \(J = 3.1, 1.9\) Hz, 1H), 6.04 (dd, \(J = 3.1, 0.6\) Hz, 1H), 2.08 (dd, \(J = 11.5, 4.7\) Hz, 1H), 1.90 (ddt, \(J = 14.5, 11.5, 7.9\) Hz, 1H), 1.76 (ddt, \(J = 14.0, 6.8, 1.3\) Hz, 1H), 1.55 (dddtt, \(J = 14.0, 7.9, 3.6, 1.8\) Hz, 1H), 1.47 (m, 1H), 1.05 (s, 3H), 1.00 (s, 3H), 0.92–0.81 (m, 2H), 0.71 (d, \(J = 6.5\) Hz, 3H), 0.65 (td, \(J = 8.0, 1.3\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 160.5, 140.5, 109.8, 104.6, 39.2, 33.2, 31.6, 29.4, 26.7, 20.2, 19.6, 19.3, 17.6, 15.6; HRMS (EI) calcd. for C\(_{14}\)H\(_{20}\)O \([M]^+\) 204.1516, found 204.1514.

Coupling in the presence of DDQ was performed following GP\textsubscript{3} and resulted in 58\% yield and 100\% e.s.

\textbf{2-((1R,2R,3R,5S)-2,6,6-Trimethylbicyclo[3.1.1]heptan-3-yl)furan (2n)}

Following GP\textsubscript{2} (0.50 mmol scale), 2n (84 mg, 82\%) was obtained as an oil; \(R_f\) 0.84 (petrol: Et\(_2\)O 95:5); \([\alpha]_D^{21}\) \(\approx\) –34.0 (c 0.5, CHCl\(_3\); IR (film): \(\nu\) (cm\(^{-1}\)) 2924, 2902, 2870, 1507, 1454, 1150, 1008, 796, 784, 691; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.35 (dd, \(J = 1.9, 0.9\) Hz, 1H), 6.32 (dd, \(J = 3.0, 1.9\) Hz, 1H), 6.04 (dd, \(J = 3.1, 0.8\) Hz, 1H), 3.07 (dt, \(J = 10.5, 7.3\) Hz, 1H), 2.44–2.30 (m, 2H), 2.21 (pd, \(J = 7.3, 2.0\) Hz, 1H), 2.06–1.98 (m, 2H), 1.88 (td, \(J = 6.2, 2.0\) Hz, 1H), 1.26 (s, 3H), 1.13–1.05 (m, 7H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 161.4, 141.0, 109.8, 103.4, 47.6, 42.3, 41.4, 38.6, 36.5, 34.1, 33.5, 28.3, 23.0, 21.6; HRMS (Cl) calcd. for C\(_{14}\)H\(_{22}\)O \([M+H]^+\) 205.1592, found 205.1607.

Coupling in the presence of DDQ was performed following GP3 and resulted in 62% yield and 100% e.s.

\[
(3S,5R,6S,8S,10R,13R,17R)-6-(\text{Furan}-2-\text{yl})-10,13-\text{dimethyl}-17-((R)-6-\text{methylheptan}-2-\text{yl})\text{hexadecahydro-1H-cyclopenta}[\alpha]\text{phenanthren-3-ol (2o)}
\]

A solution of furan (31 μL, 0.43 mmol, 2.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.3 mL, 0.43 mmol, 2.2 eq., 1.6 M in hexanes). The mixture was stirred at −78 °C for 30 min. at r.t. for 30 min. The mixture was cooled to −78 °C and a solution of \(\text{1o}\) (100 mg, 0.19 mmol, 1.0 eq.) in THF (2.0 mL) was added dropwise. The mixture was stirred at −78 °C for 1 h at which point \(^{11}\text{B NMR}\) spectroscopy showed complete formation of the boron-ate complex \(\text{[}^{11}\text{B NMR (96 MHz, THF)} \delta_B \sim 8 \text{ ppm]}\). A solution of NBS (62 mg, 0.23 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. The mixture was stirred at −78 °C for 16 h at which point saturated aqueous solution of \(\text{Na}_2\text{S}_2\text{O}_3\) (1 mL) was added. The reaction mixture was diluted with \(\text{Et}_2\text{O}\) (10 mL) and washed with water (15 mL). The aqueous layer was extracted with \(\text{Et}_2\text{O}\) (2 x 15 mL). The combined organic layers were dried over \(\text{MgSO}_4\), filtered and concentrated under vacuum. Purification by flash column chromatography on silica gel, eluting with petrol:EtOAc (95:55→85:15) gave 2o (69 mg, 78 %) as a solid; \(R_f\) 0.77 (petrol:EtOAc 7:3); mp. 126-130 °C; \([\alpha]_D^{22} + 21.9 \text{ (c 0.73, CHCl}_3\text{)}\); IR (film): \(\nu \text{ (cm}^{-1}\text{)} 3256, 2931, 2855, 1467, 1381, 1073, 1049, 1009, 796, 724; \(^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta \text{ ppm 7.28 (dd, } J = 1.8, 0.6 \text{ Hz, 1H), 6.26 (dd, } J = 3.1, 1.8 \text{ Hz, 1H), 5.95 (dd, } J = 3.1, 0.6 \text{ Hz, 1H), 3.49 (tt, } J = 11.0, 4.8 \text{ Hz, 1H), 2.60 (td, } J = 12.0, 3.6 \text{ Hz, 1H), 1.83-1.73 (m, 4H), 1.58-1.45 (m, 5H), 1.39-1.22 (m, 7H), 1.20-0.97 (m, 12H), 0.92-0.84 (m, 13H), 0.77 (m, 1H) 0.67 (s, 3H); \(^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta \text{ ppm 159.1, 140.5, 109.8, 104.6 , 71.3, 56.2, 56.2, 53.9, 48.6, 42.6, 40.0, 39.5, 38.1, 38.0, 37.0, 36.1, 35.9, 35.8, 35.1, 34.9, 31.1, 28.2, 28.0, 24.1, 23.8, 22.8, 22.5, 21.3, 18.7, 12.9, 12.1, 1.0; HRMS (ESI) calcd. for C\text{31H}_5\text{1O}_2 [M+H]^+ 455.3884, found 455.3865.}

\[\text{2-}((1R,2S,5R)-2-\text{isopropyl-5-methylcyclohexyl)furan (2q)}\]

Following GP2 (0.45 mmol scale), 2q (63 mg, 80%) was obtained as an oil; \(R_f\) 0.91 (pentane:EtO 99:1); \([\alpha]_D^{23} - 45 \text{ (c 1, CHCl}_3\text{)}\); IR (film): \(\nu \text{ (cm}^{-1}\text{)} 3675, 2954, 2918, 1594, 1505, 1455, 1385, 1368, 1347, 1321, 1238, 1222,
1171, 1148, 1073, 1056, 977, 949, 914, 885, 874, 794, 725, 691, 599, 526; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.28 (dd, J = 1.8, 0.8 Hz, 1H), 6.27 (dd, J = 3.1, 1.8 Hz, 1H), 5.95 (dd, J = 3.1, 0.8 Hz, 1H), 2.57 (td, J = 11.8, 3.4 Hz, 1H), 1.86–1.75 (m, 2H), 1.71 (dq, J = 12.8, 3.1 Hz, 1H), 1.52–1.37 (m, 3H), 1.71 (dq, J = 12.8, 3.1 Hz, 1H), 1.52–1.37 (m, 3H), 1.27 (m, 1H), 1.10 (m, 1H), 0.99 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.72 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 159.7, 140.2, 109.8, 104.1, 46.8, 42.0, 40.9, 35.0, 32.9, 28.3, 24.8, 22.4, 21.2, 15.7; HRMS (EI) calcd. for C₁₄H₂₂O [M]+ 206.1671, found 206.1673.

2-(oxetan-3-yl)furan (2r)

Following GP2 (0.22 mmol scale), 2r (10 mg, 38%) was obtained as an oil; Rf 0.41 (pentane:Et₂O 85:15); IR (film): ν (cm⁻¹) 2958, 2881, 1148, 979, 931, 734; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.40 (br s, 1H), 6.35 (m, 1H), 6.20 (d, J = 3.2 Hz, 1H), 4.94 (dd, J = 8.3, 5.8 Hz, 2H), 4.90–4.84 (m, 2H), 4.32 (qi, J = 8.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 154.1, 141.9, 110.4, 105.7, 76.5, 33.9; HRMS (EI) calcd. for C₇H₈O₂ [M]+ 124.0524, found 124.0529.

(R)-3-(furan-2-yl)-3-phenylpropenitrile [(R)-2s]

A solution of furan (36 µL, 0.48 mmol) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.2 mL, 0.32 mmol, 1.6 M in hexanes). The mixture was stirred at room temperature for 1 h. The mixture was cooled to −98 °C (MeOH/liquid N₂) and a solution of boronic ester (R)-1s (84.8 mg, 0.33 mmol, 1.0 eq.) in THF (1.0 mL) was added dropwise. The reaction was stirred at −98°C during 1 h at which time possible excess of organolithium was quench adding 200 µL of EtOH to the reaction mixture. ¹¹B NMR spectroscopy showed complete formation of the boron-ate complex [¹¹B NMR (96 MHz, THF) δB ~ 8 ppm]. The mixture was kept at −98 °C and a solution of NBS (69 mg, 0.38 mmol, 1.15 eq.) in THF (2.0 mL) was added dropwise and allowed to warm to r.t. for 1h. At this point saturated aqueous solution of Na₂S₂O₃ (1 mL) was added. The reaction mixture was diluted with Et₂O (10 mL) and washed with water (15 mL). The aqueous layer was extracted with Et₂O (2 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by column chromatography on silica gel, eluting with petrol:Et₂O (95:5→7:3) gave (R)-2s (mg, 90 %) as an oil; er (R:S) 98:2; Rf 0.25 (petrol:Et₂O 8:2) [α]D²² 33; ¹H NMR (400 MHz, CDCl₃) δ ppm; 7.41–7.35 (m, 3H), 7.34–7.26 (m, 3H) 6.34 (dd, J = 3.2, 1.9 Hz, 1H), 6.17 (d, 1H, J = 3.2 Hz, 1H), 4.39 (t, J =
7.3 Hz, 1H), 3.09 (dd, J = 16.7, 7.3 Hz, 1H), 2.96 (dd, J = 16.7, 7.3 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 153.6, 142.4, 139.0, 129.0, 127.9, 127.5, 117.8, 110.4, 107.1, 41.7, 23.5.

Data in accordance with literature.$^{16}$

Resolution of the enantiomers of 2s was achieved using a chiral SFC system fitted with a Chiralcel Whelk-01 column as the stationary phase with CO$_2$: [n-hexane:i-PrOH (1:1 v:v)] as the mobile phase at a flow rate of 2.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 10μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component ($R$) and the slower running component ($S$) were eluted at 11.6 and 12.5 min., respectively, with a total analysis time of 20 min.

$(R)$-tert-butyl 2-(furan-2-yl)pyrrolidine-1-carboxylate [(R)-2t]

Following GP2, (0.25 mmol scale), $(R)$-2t (56 mg, 74%) was obtained as an oil; er ($R$:S) 93:7; $R$: 0.24 (petrol:EtOAc 95:5); [$a]_{D}^{22}$ –90.6 (c 1.0, CHCl$_3$); IR (film): ν (cm$^{-1}$) 2974, 2929, 2879, 1693, 1387, 1365, 1159, 1111, 1007, 729; $^1$H NMR (400 MHz, CDCl$_3$, broad signals due to rotamers) δ 7.29 (dd, J = 1.8, 0.9 Hz, 1H), 6.28 (dd, J = 3.2, 1.8 Hz, 1H), 6.17-5.99 (br m, 1H), 4.97 & 4.84 (br s, 1H), 3.54 (br s, 1H), 3.45 (br s, 1H), 2.13 (br s, 1H), 2.08–1.97 (m, 2H), 1.89 (m, 1H), 1.45 & 1.35 (br s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$, broad signals due to rotamers) δ 154.4, 141.0, 110.0, 105.2, 79.3, 54.7 & 54.5, 46.3 & 46.0, 32.2 & 31.9, 28.3, 24.2 & 23.6; HRMS (CI) calcd. for C$_{13}$H$_{20}$NO$_3$ [M+H]$^+$ 238.1443, found 238.1443.

Resolution of the enantiomers of 2t was achieved using a chiral SFC system fitted with a Chiralcel Whelk-01 column as the stationary phase with CO$_2$: [n-hexane:i-PrOH (1:1 v:v)] (9:1 v:v) as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component ($S$) and the slower running component ($R$) were eluted at 4.7 and 6.7 min., respectively, with a total analysis time of 15 min.

(R)-2,2’-(4-phenylbutane-1,2-diyl)difuran [(R)-2u]

(R)-2u was synthesised through a modification of the GP2 procedure. A solution of furan (21 µL, 0.28 mmol, 2.2 eq.) in THF (0.3 M) was cooled to 0 °C and treated with n-BuLi (0.2 mL, 0.28 mmol, 2.2 eq., 1.6 M in hexanes). The mixture was stirred at this temperature for 1 h and the boronic ester (R)-1u (50 mg, 0.13 mmol, 1.0 eq.) was added dropwise as a solution in THF (0.5 M). The mixture was stirred at 0 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [11B NMR (96 MHz, THF) δB ~ 8 ppm]. A solution of N-bromosuccinimide (NBS, 57.4 mg, 0.32 mmol, 2.5 eq.) in anhydrous MeOH (0.2 M) was added dropwise. A suspension of NaOMe (17 mg, 0.32 mmol, 2.65 eq.) in anhydrous MeOH (0.2 M) was added 1 min. after NBS addition. After 1 h at 0 °C, a saturated aqueous solution of Na2S2O3 was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et2O (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with Et2O (2 x 15 mL). The combined organic layers were dried over MgSO4, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-pentane to give (R)-2u (20 mg, 58%) as an oil; er (R:S) 97.3; Rf 0.89 (pentane:Et2O: 95:5); [α]D23 +13.0 (c 0.6, CHCl3); IR (film): ν (cm–1) 3027, 2926, 1506, 1147, 1008, 725. 1H NMR (400 MHz, CDCl3) δ ppm; 7.36 (dd, J = 1.8, 0.8 Hz, 1H), 7.28–7.24 (m, 2H), 7.18 (m, 1H), 7.15–7.11 (m, 2H), 6.30 (dd, J = 3.2, 1.8 Hz, 1H), 6.24 (dd, J = 3.1, 1.8 Hz, 1H), 6.02 (br d, J = 3.2 Hz, 1H), 5.88 (dd, J = 3.1, 0.8 Hz, 1H), 3.13 (m, 1H), 3.02 (dd, J = 14.9, 7.2 Hz, 1H), 2.93 (dd, J = 14.9, 7.2 Hz, 1H), 2.59 (dq, J = 9.4, 5.9 Hz, 1H), 2.51 (dq, J = 9.4, 5.9 Hz, 1H), 2.07–1.89 (m, 2H); 13C NMR (100 MHz, CDCl3) δ ppm 157.4, 153.8, 142.0, 141.0, 140.9, 128.4, 128.3, 125.7, 110.1, 109.9, 106.2, 105.5, 37.9, 35.0, 33.3, 32.8; HRMS (EI) calcd. for C18H18O2 [M]+ 266.1307, found 266.1303.

Resolution of the enantiomers of 2u was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO2:[n-hexane] as the mobile phase at a flow rate of 4.0 mL min–1 (P = 125 bar). Injection volume: 20 µL of a 2 g L–1 solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 2.6 and 3.0 min., respectively, with a total analysis time of 15 min.
(R)-tert-Butyl 4-(furan-3-yl)-6-phenylhexanoate [(R)-3e]

A solution of 3-bromofuran (29 μL, 0.32 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to –78 °C and treated with n-BuLi (0.2 mL, 0.32 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at –78 °C for 1 h. (R)-1e (90 mg, 0.25 mmol, 1.0 eq.) was added as a solution in THF (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the boron-ate complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. A solution of NBS (53 mg, 0.32 mmol, 1.2 eq.) in THF (1.0 mL) was added dropwise. After 1 h at –78 °C, saturated aqueous solution of NaN$_2$S$_2$O$_3$ (2 mL) was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with Et$_2$O (5 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with Et$_2$O (2 x 5 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-3e (65 mg, 85%) as an oil; er (R:S) 96:4; $R_f$ 0.44 (n-hexane:Et$_2$O 95:5); $[\alpha]_D^{24}$ +0.1 (c 0.5, CHCl$_3$); IR (film): ν (cm$^{-1}$) 2923, 2855, 1728, 1454, 1367, 1146, 1028, 874, 699; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 7.41 (t, $J = 1.7$ Hz, 1H), 7.30–7.23 (m, 3H), 7.21–7.10 (m, 3H), 6.29 (s, 1H), 2.66–2.42 (m, 3H), 2.22–2.02 (m, 2H), 1.98–1.63 (m, 4H), 1.41 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 173.0, 143.12, 142.2, 139.4, 128.4, 128.3, 128.3, 127.4, 125.7, 108.9, 80, 37.6, 34.8, 33.5, 33.4, 31.2, 29.6, 28.0; HRMS (EI) C$_{20}$H$_{26}$O$_3$ [M$^+$] calcd. 314.1882, found 314.1875

Resolution of the enantiomers of 3e was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO$_2$:n-hexane (4:1, v:v) as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20μL of 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 3.9 and 4.6 min., respectively, with a total analysis time of 15 min.

(R)-tert-Butyl 4-(Benzofuran-2-yl)-6-phenylhexanoate [(R)-4e]

A solution of benzofuran (35 μL, 0.32 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to –78 °C and treated with n-BuLi (0.2 mL, 0.32 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was warmed to r.t. and stirred for 1 h. The mixture was cooled to –78 °C and (R)-1e (90 mg,
A solution of 1-methylpyrrole (23 μL, 0.26 mmol, 1.5 eq.) in THF (2.0 mL) was cooled to –78 °C and treated with s-BuLi (0.2 mL, 0.26 mmol, 1.5 eq., 1.3 M in cyclohexane/hexane (92/8). The mixture was stirred at –78 °C for 5 min. and then it was allowed to warm to r.t. After 40 min. a solution of (R)-1b (50 mg, 0.17 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. A solution of NIS (46 mg, 0.21 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h at –78 °C, saturated aqueous solution of Na2S2O3 (2 mL) was added and the reaction mixture was allowed to warm to room temperature. The

0.25 mmol, 1.0 eq.) was added as a solution in THF (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. A solution of NBS (53 mg, 0.32 mmol, 1.2 eq.) in THF (1.0 mL) was added dropwise. After 1 h at –78 °C, saturated aqueous solution of Na2S2O3 (2 mL) was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with Et2O (5 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with Et2O (2 x 5 mL). The combined organic layers were dried over MgSO4, filtered and concentrated under vacuum.

The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-4e (65 mg, 66%) as an oil; er (R):S 96:4; Rf 0.29 (n-hexane:Et2O 95:5); [α]D23 13.4 (c 1.0, CHCl3); IR (film): ν (cm–1) 2979, 2952, 2933, 1727, 1452, 1248, 1142, 849, 745; 1H NMR (400 MHz, CDCl3) δ ppm 7.52 (br d, J = 7.3 Hz, 1H), 7.45 (dt, J = 3.3 Hz, 1H), 7.31–7.12 (m, 7H), 6.45 (m, 1H), 2.87 (m, 1H), 2.69–2.49 (m, 2H), 2.25–1.90 (m, 6H), 1.40 (s, 9H); 13C NMR (100 MHz, CDCl3) δ ppm 172.7, 160.4, 154.7, 141.8, 128.4, 128.3, 125.8, 123.2, 122.4, 120.3, 110.9, 103.2, 80.2, 38.4, 35.5, 33.5, 33.2, 29.2, 28.0; HRMS (EI) C24H28O3 [M]+ calcd. 364.2038, found 364.2040.

Resolution of the enantiomers of 4e was achieved using a chiral SFC system fitted with a Chiralcel IB column as the stationary phase with CO2:n-hexane:i-PrOH (1:1 v:v) (4:1 v:v) as the mobile phase at a flow rate of 4.0 mL min–1 (P = 125 bar). Injection volume: 20μL of a 2 g L–1 solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 4.5 and 5.3 min., respectively, with a total analysis time of 15 min.

(R)-2-(4-(4-methoxyphenyl)butan-2-yl)-1-methyl-1H-pyrrole [(R)-5b]
reaction mixture was diluted with EtOAc (10 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give \((R)-5b\) (20 mg, 47%) as an oil; \(\text{er (R:S)} \ 95:5\); \(R_f\) 0.25 (petrol:Et₂O 95:5); \([\alpha]_D^{2\text{°}}\) 2.7 (\(c\) 0.37, CHCl₃); IR (film): \(\nu\) (cm\(^{-1}\)) 2957, 2930, 1698, 1511, 1298, 1242, 1034, 700; \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) ppm 7.11–7.05 (m, 2H), 6.85–6.81 (m, 2H), 6.52 (m, 1H), 6.10 (m, 1H), 5.93 (dd, \(J = 3.5, 1.8\) Hz, 1H), 3.80 (s, 3H), 3.48 (s, 3H), 2.75 (sx, \(J = 6.9\) Hz, 1H), 2.67–2.53 (m, 2H), 1.95 (qid, \(J = 8.8, 6.9\) Hz, 1H), 1.81 (qid, \(J = 8.8, 6.9\) Hz, 1H), 1.26 (d, \(J = 6.9\) Hz, 3H); \(^13\)C NMR (100 MHz, CDCl₃) \(\delta\) ppm 157.7, 138.5, 134.4, 129.2, 120.8, 113.7, 106.5, 103.5, 55.2, 39.0, 33.5, 32.6, 30.0, 21.0; HRMS (EI) calcd. for \(\text{C}_{16}\text{H}_{21}\text{NO}\) \([M]^{+}\) 243.1623, found 243.1619.

Resolution of the enantiomers of \(5b\) was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with n-hexane as the mobile phase at a flow rate of 0.5 mL min\(^{-1}\) (\(T = 0^\circ\)C). Injection volume: 5 µL of the sample prepared in a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 41.5 and 48.5 min., respectively, with a total analysis time of 60 min.

\((R)-1\)-Methyl-2-(4-phenylbutan-2-yl)-1H-indole [(\(R\))-\(6a\)]

A solution of \(N\)-methylindole (50 µL, 0.40 mmol, 1.6 eq.) in THF (1.0 mL) was treated with BuLi (0.3 mL, 0.40 mmol, 1.6 eq., 1.6 M in hexanes) at r.t. The mixture was heated under refluxing conditions for 3 h. The mixture was gradually cooled to \(-78^\circ\)C and \((R)-1a\) (65 mg, 0.25 mmol, 1.0 eq.) was added dropwise as a solution in THF (1.0 mL). The mixture was stirred at \(-78^\circ\)C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex [\((^{11}\text{B NMR, 96 MHz, THF)}\) \(\delta_{^{11}\text{B}}\ ~8\) ppm]. A solution of NIS (68 mg, 0.30 mmol, 1.2 eq.) in THF (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of \(\text{Na}_2\text{S}_2\text{O}_3\) (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with \(n\)-hexane:Et₂O (99:1) gave \((R)-6a\) (57 mg, 86%) as an oil; \(\text{er (R:S)} \ 98:2\); \(R_f\) 0.82 (petrol:EtOAc 95:5); \([\alpha]_D^{2\text{°}}\) 54.3 (\(c\) 1.0, CHCl₃); IR (film): \(\nu\) (cm\(^{-1}\)) 3056, 3025, 2962,
 Resolution of the enantiomers of 6a was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO₂:[n-hexane:i-PrOH (1:1 v:v)] (9:1 v:v) as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P = 125 bar). Injection volume: 20μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 6.9 and 7.5 min., respectively, with a total analysis time of 15 min.

2-((3S,5R,6S,8S,9S,10R,13R,14S,17R)-3-((tert-Butyldimethylsilyloxy)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[α]phenanthren-6-yl)-1-methyl-1H-indole (6p)
solid; \( R_f \) 0.30 (petrol:Et\(_2\)O 99:1); mp 194–196 °C; \([\alpha]_D^{22} + 30.4 \) (c 0.9, CHCl\(_3\)); IR (film): \( \nu \) (cm\(^{-1}\)) 2927, 2851, 1447, 1444, 1248, 1099, 1084, 867, 834, 768, 749, 728; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm 7.53 (br d, \( J = 7.8 \) Hz, 1H), 7.27 (m, 1H), 7.14 (m, 1H), 7.04 (m, 1H), 6.20 (s, 1H), 3.67 (s, 3H), 3.44 (m, 1H), 2.74 (td, \( J = 11.6, 3.6 \) Hz, 1H), 2.06–1.99 (dt, \( J = 12.6, 3.2 \) Hz, 1H), 1.93–1.86 (dt, \( J = 13.2, 3.9 \) Hz, 1H), 1.84–1.74 (m, 2H), 1.72–1.67 (m, 1H), 1.60–1.54 (m, 2H), 1.54–1.50 (m, 2H), 1.49–1.47 (m, 1H), 1.46–1.43 (m, 1H), 1.39–1.32 (m, 4H), 1.27 (s, 3H), 1.19–1.16 (m, 1H), 1.15–1.09 (m, 4H), 1.07–1.02 (m, 3H), 1.0–0.99 (m, 4H), 0.92 (d, \( J = 6.5 \) Hz, 3H), 0.87 (dd, \( J = 6.6, 1.8 \) Hz, 8H), 0.74 (s, 9H), 0.70 (s, 3H), –0.09 (s, 3H), –0.13 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm 145.7, 136.6, 128.2, 120.2, 119.6, 119.1, 108.8, 96.8, 72.3, 56.2, 54.2, 50.9, 42.6, 40.7, 40.0, 39.5, 37.3, 36.2, 36.2, 35.8, 35.4, 35.1, 34.8, 31.8, 29.7, 29.5, 28.2, 28.0, 25.8, 24.1, 23.8, 22.8, 22.6, 21.3, 18.7, 18.2, 13.2, 12.1, –4.7; HRMS (ESI) calcd. for C\(_{42}\)H\(_{70}\)NOSi \([M+H]^+\) 632.5221, found 632.5227.

2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-1-methyl-1H-indole (6q)

A solution of N-methylindole (75 \( \mu \)L, 0.60 mmol, 1.6 eq.) in THF (1.0 mL) was treated with \( n \)-BuLi (0.4 mL, 0.60 mmol, 1.6 eq., 1.6 M in hexanes) at r.t. The mixture was heated under refluxing conditions for 3 h. The mixture was cooled to –78 °C and 1q (100 mg, 0.38 mmol, 1.0 eq.) was added dropwise as a solution in THF (2.0 mL). The mixture was stirred at –78 °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex [\(^{11}\)B NMR, 96 MHz, THF] \( \delta_B \sim 8 \) ppm]. A solution of NIS (135 mg, 0.60 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na\(_2\)S\(_2\)O\(_3\) (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with \( n \)-hexane:Et\(_2\)O (99:1) gave 6q (66 mg, 65%) as an oil; \( R_f \) 0.40 (pentane:Et\(_2\)O 99:1); \([\alpha]_D^{23} – 105 \) (c 1, CHCl\(_3\)); IR (film): \( \nu \) (cm\(^{-1}\)) 3677, 3056, 2951, 2918, 2867, 1543, 1466, 1409, 1384, 1367, 1342, 1308, 1265, 1226, 1170, 1143, 1129, 1114, 1097, 1081, 1054, 1013, 977, 939, 916, 904, 870, 833, 775, 746, 729, 688, 672, 589, 569, 535, 525; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm 7.61 (d, \( J = 7.7 \) Hz, 1H), 7.53 (d, \( J = 8.0 \) Hz, 1H), 7.22 (t, \( J = 7.7 \) Hz, 1H), 7.14 (t, \( J = 7.7 \) Hz, 1H), 6.30 (s, 1H), 3.77 (s, 3H), 2.75 (br t, \( J = 11.5 \) Hz,
1H), 1.99–1.83 (m, 4H), 1.68 (d, J = 11.9 Hz, 1H), 1.56 (m, 1H), 1.32–1.04 (m, 3H) 0.95 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 0.72 (d, J = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 146.0, 136.6, 128.2, 120.1, 119.6, 119.2, 108.8, 96.8, 47.3, 45.0, 38.4, 35.0, 33.1, 29.3, 27.3, 24.6, 22.4, 21.7, 15.8; HRMS (ESI) calcd. for C$_{19}$H$_{28}$N [M+H]$^+$ 270.2216, found 270.2215.

(R)-2-(4-Phenylbutan-2-yl)thiophene [(R)-7a]

A solution of thiophene (48 μL, 0.60 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to –78 °C and treated with n-BuLi (0.4 mL, 0.60 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was warmed to 0 °C and stirred for 30 min. The mixture was cooled to –78 °C and the (R)-1a (130 mg, 0.50 mmol, 1.0 eq.) was added dropwise as a solution in THF (1.0 mL). The mixture was stirred at –78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^{11}$B NMR (96 MHz, THF) δ$_B$ ~ 8 ppm]. A solution of NBS (107 mg, 0.60 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with EtOAc (10 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-7a (100 mg, 92 %) as an oil; er (R:S) 98:2; R$_f$ 0.47 (n-hexane); [$\alpha$]$_D^{24}$ = 25.0 (c 1.0, CHCl$_3$); IR (film): ν (cm$^{-1}$) 3062, 3026, 2958, 2923, 2856, 1603, 1496, 1453, 1030, 849, 746; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 7.38–7.32 (m, 2H), 7.29–7.23 (m, 3H), 7.22 (dd, J = 5.1, 1.2 Hz, 1H), 7.02 (dd, J = 5.1, 3.5 Hz, 1H), 6.92–6.89 (br d, J = 3.5 Hz, 1H), 3.15 (app. sx, J = 6.9 Hz, 1H), 2.68 (t, J = 8.3 Hz, 2H), 2.12–1.96 (m, 2H), 1.44 (d, J = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 151.6, 142.3, 128.5, 128.4, 126.5, 125.8, 122.8, 122.5, 41.0, 34.9, 33.7, 23.5; HRMS (EI) calcd. for C$_{14}$H$_{16}$S $[M]^+$ 216.0973, found 216.0972.

Resolution of the enantiomers of 7a was achieved using a chiral HPLC system fitted with a Chiralcel OD column with guard as the stationary phase with n-hexane as the mobile phase at a flow rate of 0.3 mL min$^{-1}$ ($T = 0$ °C). Injection volume: 20μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 76.8 and 85.8 min., respectively, with a total analysis time of 100 min.
2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)thiophene (7q)

A solution of thiophene (36 μL, 0.45 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.3 mL, 0.45 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was warmed to 0 °C and stirred for 30 min. The mixture was cooled to −78 °C and the 1q (100 mg, 0.38 mmol, 1.0 eq.) was added dropwise as a solution in THF (1.0 mL). The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^{11}$B NMR (96 MHz, THF) δ$_B$ ~ 8 ppm]. A solution of NBS (81 mg, 0.45 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h at −78 °C, saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give 7q (54 mg, 65%) as an oil; $R_t$ 0.87 (pentane:Et$_2$O 99:1); [$\alpha$]$_D^{23}$ – 38 ($c$ 1, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 3677, 3069, 2953, 2917, 2869, 2846, 1455, 1444, 1385, 1368, 1347, 1312, 1277, 1266, 1239, 1224, 1187, 1131, 1075, 1054, 1038, 997, 975, 929, 861, 845, 819, 772, 750, 688, 607, 586, 532; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 7.12 (br d, $J$ = 5.1 Hz, 1H), 6.91 (dd, $J$ = 5.1, 3.4 Hz, 1H), 6.77 (br d, $J$ = 3.4 Hz, 1H), 2.80 (td, $J$ = 11.6, 3.6 Hz, 1H), 1.95 (dq, $J$ = 12.8, 2.8 Hz, 1H), 1.82 (m, 1H), 1.74 (dq, $J$ = 12.8, 3.2 Hz, 1H), 1.59 (qid, $J$ = 6.9, 2.8 Hz, 1H), 1.48 (m, 1H), 1.34 (tt, $J$ = 11.6, 2.8 Hz, 1H), 1.23 (m, 1H), 1.13 (m, 1H), 1.02 (m, 1H), 0.91 (d, $J$ = 6.6 Hz, 3H), 0.83 (d, $J$ = 6.9 Hz, 3H), 0.72 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 150.8, 126.2, 123.0, 122.2, 49.6, 46.5, 43.0, 35.0, 33.9, 27.4, 24.6, 22.4, 21.5, 15.3; HRMS (EI) calcd. for C$_{14}$H$_{22}$S [$M]^+$ 222.1443, found 222.1441.

(R)-2-(4-(4-methoxyphenyl)butan-2-yl)benzo[b]thiophene [(R)-8b]

A solution of benzothiophene (35 μL, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.2 mL, 0.30 mmol, 1.2 eq., 1.6 M in hexane). The mixture was stirred at −78 °C for 1 h and then a solution of (R)-1b (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δ$_B$ ~ 8 ppm]. A solution of NBS (53 mg, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was added dropwise. After 1 h
at –78 °C, saturated aqueous solution of Na₂S₂O₃ (2 mL) was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-8b (58 mg, 78%) as an oil; er (R:S) 96.4; Rf 0.36 (pentane:Et₂O: 95:5); [α]D²³ 38 (c 1.0, CHCl₃); mp. 56-58 °C; IR (film): ν (cm⁻¹) 2971, 2927, 1610, 1511, 1431, 1241, 1175, 1035, 819, 743, 726. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.81 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 7.27 (t, J = 7.7 Hz, 1H), 7.09 (d, J = 7.7 Hz, 2H), 7.05 (s, 1H), 6.83 (d, J = 7.8 Hz, 2H), 3.80 (s, 3H), 3.12 (sx, J = 6.8 Hz, 1H), 2.59 (m, 2H), 2.00 (m, 2H), 1.42 (d, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.7, 152.5, 140.0, 138.9, 134.1, 129.3, 124.0, 123.4, 122.8, 122.3, 119.4, 113.8, 55.3, 40.7, 35.6, 32.6, 23.1; HRMS (EI) calcd. for C₁₉H₂₀OS [M]⁺ 296.1235, found 296.1238.

Resolution of the enantiomers of 8b was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO₂:[n-hexane:i-PrOH (9:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P = 125 bar). Injection volume: 20μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 15.0 and 17.0 min., respectively, with a total analysis time of 15 min.
6. Reaction Products – Coupling of secondary boronic esters to 6-membered aromatics

(R)-1,3-Dimethoxy-5-(4-phenylbutan-2-yl)benzene [(R)-9a]

A solution of 3,5-(dimethoxy)bromobenze (50 mg, 0.23 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to −78 °C and treated with t-BuLi (0.27 mL, 0.46 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min. and then a solution of (R)-1a (50 mg, 0.19 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^1$B NMR, 96 MHz, THF] $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −78 °C. A solution of NBS (41 mg, 0.23 mmol, 1.2 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm up to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (98:2) gave (R)-9a (43 mg, 83%) as an oil, er (R:S) 98:2; $\rho$ 0.49 (n-hexane:Et$_2$O 95:5); [α]$_D$ $^{22}$ −19.7 (c 1.0, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2926, 2837, 1593, 1454, 1427, 1203, 1150, 1056, 831, 696; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.31–7.25 (m, 2H), 7.22–7.14 (m, 3H), 6.38 (d, $J = 2.3$ Hz, 2H), 6.32 (t, $J = 2.3$ Hz, 1H), 3.80 (s, 6H), 2.66 (app. sx, $J = 6.9$ Hz, 1H), 2.53 (t, $J = 8.0$, 2H), 2.00–1.84 (m, 2H), 1.26 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 160.8, 149.9, 142.5, 128.4, 128.3, 125.6, 105.3, 97.6, 55.2, 39.9, 39.8, 33.9, 22.4; HRMS (EI) calcd. for C$_{18}$H$_{22}$O$_2$ [$M$]$^+$ 270.1620, found 270.1625.

Resolution of the enantiomers of 9a was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO$_2$:n-hexane (95:5, v:v) as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 7.3 and 8.0 min., respectively, with a total analysis time of 15 min.
A solution of 3,5-(dimethoxy)bromobenzene (70.5 mg, 0.325 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to −78 °C and treated with t-BuLi (0.38 mL, 0.65 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min. and then a solution of (S)-1I (58 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −78 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO4, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et2O (98:2) gave (S)-9l (39 mg, 64%) as an oil; er (S:R) 97:3; Rf 0.26 (petrol:Et2O 95:5); [α]D 21 = 0.3 (c 0.7, CHCl3) (lit. [α]D 20 = −2.5 (c 0.4, CHCl3) for (R)-enantiomer); 1H NMR (400 MHz, CDCl3) δ ppm; 7.32–7.20 (m, 4H), 7.18 (tt, J = 7.0, 1.5 Hz, 1H), 6.39 (d, J = 2.3 Hz, 2H), 6.30 (t, J = 2.3 Hz, 1H), 4.08 (q, J = 7.2 Hz, 1H), 3.75 (s, 6H), 1.61 (d, J = 7.2 Hz, 3H) 13C NMR (100 MHz, CDCl3) δ ppm 160.7, 148.8, 146.0, 128.3, 127.5, 126.1, 106.0, 97.6, 55.2, 55.2, 45.0, 21.7.

Data in accordance with literature. Resolution of the enantiomers of 9l was achieved using a chiral HPLC system fitted with a Chiralpak IA column with guard as the stationary phase with n-hexanes as the mobile phase at a flow rate of 1.0 mL min−1. Injection volume: 2 µL of a 2 g L−1 solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 18.5 and 20.3 min., respectively, with a total analysis time of 40 min.

A solution of 3,5-(dimethoxy)bromobenze (126 mg, 0.58 mmol, 3.0 eq.) in THF (4.0 mL) was cooled to −78 °C and treated with t-BuLi (0.5 mL, 0.71 mmol, 2.6 eq., 1.4 M in pentane). The mixture was stirred at −78 °C for 30 min and then a solution of 1o (100 mg, 0.19 mmol, 1.0 eq.) in THF (2.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the boron-ate complex [11B NMR, 96 MHz] δB ~ 8 ppm. A solution of NBS (104 mg, 0.58 mmol, 3.0 eq.) in MeOH (3.0 mL) was added dropwise. The mixture was allowed to warm to room temperature overnight and saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min, the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO4, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:EtOAc 9:1→7:3) gave 9o (93 mg, 91%) as an amorphous solid; Rf 0.50 (n-hexane:EtOAc 7:3); mp. 96–98 °C; [α]D22 + 66.9 (c 3.0, CHCl3); IR (film): ν (cm⁻¹) 3364, 2929, 2866, 1594, 1460, 1428, 1204, 1152, 1061, 756, 698. 1H NMR (400 MHz, CDCl3) δ ppm 6.29 (br s, 3H), 3.78 (s, 6H), 3.44 (tt, J = 11.0, 4.8 Hz, 1H), 2.38 (td, J = 12.0, 3.1 Hz, 1H), 2.01 (br d, J = 12.5 Hz, 1H), 1.86–1.72 (m, 4H), 1.61–1.47 (m, 4H), 1.40–1.29 (m, 6H), 1.28–1.23 (m, 3H), 1.18–1.10 (m, 6H), 1.06–0.99 (m, 5H), 0.94–0.90 (m, 6H), 0.89–0.85 (m, 6H), 0.68 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 148.5, 97.6, 71.5, 56.3, 56.2, 55.2, 54.2, 49.4, 45.1, 42.6, 41.0, 40.0, 39.5, 37.1, 36.2, 36.0, 35.8, 35.3, 34.5, 31.0, 29.7, 28.2, 28.0, 24.1, 23.8, 22.8, 22.6, 21.3, 20.8, 18.7, 17.5, 17.3, 14.6, 13.2, 12.1, 7.9; HRMS (ESI) calcd. for C35H56NaO3 [M+Na]⁺ 547.4127, found 547.4122.

1-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-3,5-dimethoxybenzene (9q)

A solution of 3,5-(dimethoxy)bromobenze (70.5 mg, 0.325 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to −78 °C and treated with t-BuLi (0.38 mL, 0.65 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min. and then a solution of 1q (67mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’
complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −78 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm up to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (98:2) gave 9q (58 mg, 84%) as an oil; $R$; 0.27 (pentane:Et$_2$O 99:1); $[\alpha]_D^{23} = 40$ (c 1, CHCl$_3$); IR (film): ν (cm$^{-1}$) 3675, 2951, 2914, 2869, 2843, 1593, 1457, 1427, 1384, 1367, 1342, 1311, 1292, 1248, 1220, 1203, 1149, 1060, 993, 981, 954, 940, 930, 913, 877, 828, 698, 604, 570, 539; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm; 6.34 (d, $J = 2.3$ Hz, 2H), 6.29 (t, $J = 2.3$ Hz, 1H), 3.80 (s, 6H), 2.38 (td, $J = 11.6$, 3.2 Hz, 1H), 1.85–1.70 (m, 3H), 1.58–1.38 (m, 3H), 1.18–1.07 (dq, $J = 11.6$, 2.5 Hz, 2H), 1.12 (m, 1H), 0.90 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.9$ Hz, 3H), 0.70 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 160.7, 149.3, 105.6, 97.3, 55.2, 48.4, 47.3, 45.1, 35.3, 33.2, 27.4, 24.5, 22.5, 21.6, 15.5.; HRMS (ESI) calcd. for C$_{18}$H$_{29}$O$_2$ [M+H]$^+$ 277.2168, found 277.2164.

($R$)-$N,N$-Dimethyl-3-(4-phenylbutan-2-yl)aniline [(R)-10a]

A solution of 3-$N,N$-dimethylaminobromobenze (43 µL, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.2 mL, 0.30 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of ($R$)-1a (65 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NIS (68 mg, 0.30 mmol, 1.2 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (99:1) gave ($R$)-10a
(41 mg, 65 %) as an oil; er (R:S) 98:2; Rf 0.60 (petrol:Et2O 95:5); [α]D20 + 2.0 (c 1.0, CHCl3); IR (film): ν (cm⁻¹) 3025, 2954, 2922, 2854, 2801, 1601, 1495, 1348, 1348, 994, 773, 746, 696; ¹H NMR (400 MHz, CDCl3) δ ppm 7.31–7.14 (m, 6H), 6.66–6.61 (m, 3H), 2.97 (s, 6H), 2.70 (app. sx, J = 6.9 Hz, 1H), 2.56 (t, J = 8.0 Hz, 2H), 2.02–1.85 (m, 2H), 1.26 (d, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl3) δ ppm 150.6, 148.3, 142.7, 129.1, 128.4, 128.2, 125.6, 115.7, 111.9, 110.6, 40.9, 40.0, 39.9, 34.0, 22.6; HRMS (EI) calcd. for C₁₈H₂₃N [M]+ 253.1830, found 253.1825.

Resolution of the enantiomers of 10a was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO₂:n-hexane (9:1 v:v) as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P = 125 bar). Injection volume: 20 μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 6.5 and 7.2 min., respectively, with a total analysis time of 15 min.


A solution of 3-N,N-dimethylaminobromobenze (27 μL, 0.19 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to –78 ºC and treated with n-BuLi (0.1 mL, 0.19 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at –78 ºC for 1 h and then a solution of 1p (100 mg, 0.16 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 ºC for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [¹¹B NMR, 96 MHz, THF] δB ~ 8 ppm. A solution of NIS (43 mg, 0.19 mmol, 1.2 eq.) in MeOH (1.0 mL) was added dropwise. The mixture was allowed to warm to room temperature overnight and saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. The reaction mixture was extracted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et₂O (98:2) gave 10p (67 mg, 68%) as an amorphous solid; Rf 0.26 (petrol:Et₂O 99:1); mp 53–56 ºC; [α]D22 + 54.3 (c 2.0, CHCl₃); IR (film): ν (cm⁻¹) 2929,
2852, 1601, 1467, 1440, 1250, 1096, 872, 834, 772, 700; 1H NMR (400 MHz, CDCl₃) δ ppm 7.16 (br s, 1H), 6.60 (br d, J = 7.7 Hz, 1H), 6.52 (br s, 2H), 3.42 (m, 1H, H), 2.94 (s, 6H), 2.38 (br t, J = 11.0 Hz, 1H), 2.02 (br d, J = 12.4 Hz, 1H), 1.87–1.73 (m, 3H), 1.72–1.65 (m, 1H), 1.61–1.46 (m, 4H), 1.42–1.25 (m, 8H), 1.24–1.08 (m, 6H), 1.08–0.98 (m, 6H), 0.98–0.92 (m, 6H), 0.88 (dd, J = 6.6, 1.6 Hz, 7H), 0.79 (s, 9H), 0.70 (s, 3H), –0.08 (s, 3H), –0.10 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ ppm 147.0, 128.9, 114.1, 110.2, 72.7, 54.4, 49.5, 45.2, 42.6, 41.6, 41.0, 40.1, 39.5, 37.6, 36.2, 36.0, 35.8, 34.8, 31.8, 29.7, 28.3, 28.0, 26.0, 24.2, 23.8, 22.8, 22.6, 21.3, 18.7, 18.3, 13.3, 12.1, –4.6, –4.8; HRMS (ESI) calcd. for C₄₁H₇₂NOSi [M+H]+ 622.5305, found 622.5386.

3-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-N,N-dimethylaniline (10q)

A solution of 3-N,N-dimethylaminobromobenzene (43 µL, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to –78 °C and treated with n-BuLi (0.2 mL, 0.30 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at –78 °C for 1 h and then a solution of 1q (67 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [11B NMR, 96 MHz, THF] δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to –78 °C. A solution of NIS (68 mg, 0.30 mmol, 1.2 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et₂O (99:1) gave 10q (54 mg, 70%) as an oil; Rf 0.18 (pentane:Et₂O 99:1); [α]D²³ – 45 (c 1, CHCl₃); IR (film): ν (cm⁻¹) 2951, 2914, 2869, 2845, 2801, 1684, 1600, 1579, 1500, 1454, 1437, 1383, 1347, 1230, 1177, 1150, 1135, 1098, 1060, 995, 972, 934, 847, 835, 772, 733, 723, 699, 640, 589, 535, 525; 1H NMR (400 MHz, CDCl₃) δ ppm 7.17 (t, J = 8.0 Hz, 1H), 6.63–6.55 (m, 3H), 2.96 (s, 6H), 2.40 (td, J = 11.6, 3.4 Hz, 1H), 1.86–1.78 (m, 2H), 1.78-1.71 (m, 1H), 1.58–1.42 (m, 3H), 1.23–1.09 (m, 2H), 1.02 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.81 (d, J = 6.9 Hz, 3H), 0.71 (d, J = 6.9 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ ppm 150.7, 147.6, 128.8, 110.2, 48.6,
A solution of 3-methoxybromobenzene (29 \( \mu \)L, 0.23 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to \(-78 \, ^\circ\)C and treated with \( n \)-BuLi (0.15 mL, 0.23 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at \(-78 \, ^\circ\)C for 1 h and then a solution of (\( R \))-1a (50 mg, 0.19 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at \(-78 \, ^\circ\)C for 1 h at which point \( ^{11}B \) NMR spectroscopy showed complete formation of the ‘ate’ complex [(\( ^{11}B \) NMR, 96 MHz, THF) \( \delta_B \sim 8 \, ppm \)]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to \(-78 \, ^\circ\)C. A solution of NBS (62 mg, 0.35 mmol, 1.8 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of \( Na_2S_2O_3 \) (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over \( MgSO_4 \), filtered and concentrated under vacuum. Purification by flash column chromatography (\( n \)-hexane:Et\(_2\)O 98:2) gave (\( R \))-11a (33 mg, 72 %) as an oil; er (\( R:S \)) 98:2; \( R_f \) 0.56 (petrol:Et\(_2\)O 95:5); \([\alpha]_{D}^{20} \sim -11.2 \) (c 0.67, CHCl\(_3\)); IR (film): \( \nu \) \( (\text{cm}^{-1}) \) 3026, 2956, 2926, 2834, 1600, 1583, 1485, 1453, 1259, 1157, 1045, 871, 777, 747; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm 7.31–7.23 (m, 3H), 7.21–7.13 (m, 3H), 6.83 (br d, \( J = 7.5 \) Hz, 1H), 6.79–6.74 (m, 2H), 3.83 (s, 3H), 2.72 (sx, \( J = 6.9 \) Hz, 1H), 2.60–2.49 (m, 2H), 2.01–1.85 (m, 2H), 1.29 (d, \( J = 7.5 \) Hz, 3H); \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm 159.7, 149.0, 142.5, 129.3, 128.4, 128.2, 125.6, 119.5, 113.1, 110.9, 55.1, 39.9, 39.6, 33.9, 22.5; HRMS (CI) calcd. For C\(_{17}\)H\(_{21}\)O \([M+H]^+\) 241.1592, found 241.1590.

Resolution of the enantiomers of 11a was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO\(_2\):[\( n \)-hexane:1-ProOH (9:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) (\( P = 125 \) bar). Injection volume: 20\( \mu \)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (\( S \)) and the slower running component (\( R \)) were eluted at 3.8 and 4.2 min., respectively, with a total analysis time of 15 min.
(R)-1-methoxy-3-(1-phenylethyl)benzene [(R)-11]

A solution of 3-methoxybromobenzene (40 μL, 0.32 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with n-BuLi (0.2 mL, 0.32 mmol, 1.2 eq., 1.6 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of (R)-11 (58 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (62 mg, 0.35 mmol, 1.8 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO4, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:Et2O 98:2) gave (R)-11 (25 mg, 43%) as an oil; er (R:S) 97:3; Rf 0.49 (petrol:Et2O 95:5); [α]D23 2 (c 1, CHCl3); 1H NMR (400 MHz, CDCl3) δ ppm 7.31–7.15 (m, 6H), 6.83 (br d, J = 7.5 Hz, 1H), 6.78 (m, 1H), 6.73 (ddd, J = 8.2, 2.6, 0.8 Hz, 1H), 4.12 (q, J = 7.2 Hz, 1H), 3.77 (s, 3H), 1.63 (d, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 159.6, 148.0, 146.2, 129.3, 128.3, 127.6, 126.0, 120.1, 113.8, 110.9, 55.1, 44.8, 21.8.

Data in accordance with literature.18

Resolution of the enantiomers of 11 was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO2:n-hexane as the mobile phase at a flow rate of 4.0 mL min−1 (P = 125 bar). Injection volume: 20μL of a 2 g L−1 solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 10.5 and 13.2 min., respectively, with a total analysis time of 20 min.

**{(R)-1,2-dimethoxy-3-(4-(4-methoxyphenyl)butan-2-yl)benzene [(R)-12b]}**

A solution of 3,4-dimethoxybromobenze (29 μL, 0.19 mmol, 1.1 eq.) in THF (1.0 mL) was cooled to –78 °C and treated with t-BuLi (0.2 mL, 0.38 mmol, 2.2 eq., 1.7 M in hexanes). The mixture was stirred at –78 °C for 1 h and then a solution of (R)-1b (50 mg, 0.17 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B$ ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of NBS (46 mg, 0.26 mmol, 1.5 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:Et$_2$O 98:2) gave (R)-12b (24 mg, 46%) as an oil; er (R:S) 95:5; $R_f$ 0.23 (pentane:Et$_2$O 85:15); [$\alpha$]$_D^{22}$ 33 (c 0.48, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2956, 2931, 2833, 1611, 1582, 1510, 1475, 1243, 1036, 1008, 745; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.11–7.03 (m, 3H), 6.88–6.76 (m, 4H), 3.88 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.26 (app. sx, $J$ = 7.0 Hz, 1H), 2.55 (m, 1H), 2.45 (m, 1H), 1.96–1.79 (m, 2H), 1.27 (d, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 157.6, 152.7, 146.7, 141.1, 134.8, 129.2, 124.0, 118.7, 113.6, 109.6, 60.8, 55.6, 55.2, 39.6, 33.2, 31.7, 22.0; HRMS (EI) calcd. for C$_{19}$H$_{24}$O$_3$ [$M$$^+$] 300.1725, found 300.1717.

Resolution of the enantiomers of 12b was achieved using a chiral HPLC system fitted with a Chiracel IB column as the stationary phase with hexane:MTBE (95:5) as the mobile phase at a flow rate of 0.7 mL min$^{-1}$. Injection volume: 2 μL of a 2 g L$^{-1}$ solution of the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 34.3 and 38.7 min., respectively, with an analysis time of 40 min.

**{(R)-1,2-dimethoxy-4-(4-(4-methoxyphenyl)butan-2-yl)benzene [(R)-13b]}**

A solution of 3,4-dimethoxybromobenze (29 μL, 0.19 mmol, 1.1 eq.) in THF (1.0 mL) was cooled to –78 °C and treated with t-BuLi (0.2 mL, 0.38 mmol, 2.2 eq., 1.7 M in hexanes). The mixture was stirred at –78 °C for 1 h and then a solution of (R)-1b (50 mg, 0.17 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B$ ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of NBS (46 mg, 0.26 mmol, 1.5 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:Et$_2$O 98:2) gave (R)-13b (24 mg, 46%) as an oil; er (R:S) 95:5; $R_f$ 0.23 (pentane:Et$_2$O 85:15); [$\alpha$]$_D^{22}$ 33 (c 0.48, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2956, 2931, 2833, 1611, 1582, 1510, 1475, 1243, 1036, 1008, 745; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.11–7.03 (m, 3H), 6.88–6.76 (m, 4H), 3.88 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.26 (app. sx, $J$ = 7.0 Hz, 1H), 2.55 (m, 1H), 2.45 (m, 1H), 1.96–1.79 (m, 2H), 1.27 (d, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 157.6, 152.7, 146.7, 141.1, 134.8, 129.2, 124.0, 118.7, 113.6, 109.6, 60.8, 55.6, 55.2, 39.6, 33.2, 31.7, 22.0; HRMS (EI) calcd. for C$_{19}$H$_{24}$O$_3$ [$M$$^+$] 300.1725, found 300.1717.

Resolution of the enantiomers of 13b was achieved using a chiral HPLC system fitted with a Chiracel IB column as the stationary phase with hexane:MTBE (95:5) as the mobile phase at a flow rate of 0.7 mL min$^{-1}$. Injection volume: 2 μL of a 2 g L$^{-1}$ solution of the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 34.3 and 38.7 min., respectively, with an analysis time of 40 min.
eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (46 mg, 0.26 mmol, 1.5 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:EtO 98:2) gave (R)-13b (26 mg, 51%) as an oil; er (R:S) 95:5; R$_f$ 0.16 (pentane:EtO 85:15); [$\alpha$]$_D^{22}$ – 20 (c 0.73, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2954, 2931, 2833, 1591, 1511, 1441, 1243, 1030, 830; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.08–7.04 (m, 2H), 6.85–6.81 (m, 3H), 6.76 (dd, $J = 8.0, 1.9$ Hz, 1H), 6.72 (d, $J = 1.9$ Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.80 (s, 3H), 2.67 (app. sx, $J = 7.0$ Hz, 1H), 2.51–2.44 (m, 2H), 1.91–1.83 (m, 2H), 1.27 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 157.6, 148.8, 147.1, 140.0, 134.6, 129.2, 118.8, 113.7, 111.2, 110.3, 55.9, 55.8, 55.2, 40.3, 39.0, 33.0, 22.7; HRMS (EI) calcd. for C$_{19}$H$_{24}$O$_3$ [M]$^{+}$ 300.1725, found 300.1721.

Resolution of the enantiomers of 13b was achieved using a chiral HPLC system fitted with a Chiracel IC column as the stationary phase with hexane:i-PrOH as the mobile phase at a flow rate of 0.7 mL min$^{-1}$. Injection volume: 2 μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 24.3 and 26.3 min., respectively, with a total analysis time of 40 min.

*(S)-1-bromo-3-methoxy-5-(4-(4-methoxyphenyl)butan-2-yl)benzene [(S)-14b]*

A solution of 3,5-dibromoanisole (85 mg, 0.32 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to −78 °C and treated with $t$-BuLi (0.4 mL, 0.64 mmol, 2.4 eq., 1.7 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of (S)-1b (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A
solution of NBS (108 mg, 0.61 mmol, 2.4 eq.) in MeOH (5.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:Et₂O 98:2) gave (S)-14b (70 mg, 81%) as an oil; [α]D²² = –1 (c 1, CHCl₃); IR (film): ν (cm⁻¹) 2957, 2926, 2848, 2350, 1595, 1567, 1512, 1457, 1267, 1244, 1037, 820, 693. 

 Resolution of the enantiomers of 14b was achieved using a chiral HPLC system fitted with a Chiralpak IA column with guard as the stationary phase with n-hexanes as the mobile phase at a flow rate of 0.8 mL min⁻¹ (T = 0 °C). Injection volume: 5 μL of a 2 g L⁻¹ solution of the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 44.2 and 56.3 min., respectively, with a total analysis time of 70 min.

(R)-1-(4-Phenylbutan-2-yl)naphthalene [(R)-15a]

A solution of 1-bromonaphthalene (28 μL, 0.16 mmol, 1.2 eq.) in Et₂O (1.0 mL) was cooled to 0 °C and n-BuLi (0.1 mL, 0.16 mmol, 1.2 eq., 1.6 M in hexanes) was added dropwise. The mixture was stirred at 0 °C for 1 h. (R)-1a (36 mg, 0.125 mmol, 1.0 eq.) was added as a solution in Et₂O (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the boron-ate complex [(¹¹B NMR, 96 MHz) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −78 °C. A solution of NBS (53 mg, 0.32 mmol, 2.4 eq.) in MeOH (3.0 mL) was added dropwise and the reaction mixture was warmed to r.t. After 1 h saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers

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were dried over MgSO₄, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (R)-15a (23 mg, 89%) as an oil; er (R:S) 98:2; \( R_I \) 0.47 (petrol); \( [\alpha]_D^{22} \) 40 (c 1.0, CHCl₃); IR (film): \( \nu \) (cm⁻¹) 3026, 2959, 2926, 2858, 1596, 1509, 1496, 1453, 1395, 1375, 1256, 1168, 797, 777, 747; \(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) ppm 8.00 (m, 1H), 7.88 (m, 1H), 7.73 (dd, \( J \) = 7.4, 1.7 Hz, 1H), 7.50–7.43 (m, 3H), 7.30–7.25 (m, 3H), 7.21–7.13 (m, 3H), 3.64 (app. sx, \( J \) = 6.9 Hz, 1H); \(^1^3\)C NMR (100 MHz, CDCl₃) \( \delta \) ppm 143.3, 142.4, 133.9, 131.6, 128.9, 128.4, 128.3, 126.3, 125.7, 125.6, 125.2, 123.1, 122.5, 39.5, 33.9, 31.5, 21.77; HRMS (EI) calcd. for C₂₀H₂₀ [M] 260.1565, found 260.1570.

Resolution of the enantiomers of 15a was achieved using chiral HPLC system fitted with a Chiracel OJ-H column with guard as the stationary phase and n-hexane:i-PrOH (99:1) as the mobile phase at a flow rate of 0.5 mL min⁻¹ \((T \text{ = 5 °C})\). Injection volume: 20μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) major were eluted at 50.7 min and 60.7 min., respectively, with an analysis time of 85 min.

(S)-2-(4-(4-methoxyphenyl)butan-2-yl)naphthalene [(S)-16b]

A solution of 2-bromonaphthalene (43 mg, 0.21 mmol, 1.2 eq.) in Et₂O (1.0 mL) was cooled to −15 °C and treated with \( n \)-BuLi (0.13 mL, 0.21 mmol, 1.2 eq., 1.7 M in hexanes). The mixture was stirred at −15 °C for 30 min. and then a solution of (S)-1b (50 mg, 0.17 mmol, 1.0 eq.) in Et₂O (1.0 mL) was added. The mixture was stirred at −15 °C for 30 min. at which point \(^{11}\)B NMR spectroscopy showed complete formation of the `ate` complex \([^{11}\text{B NMR, 96 MHz, THF} \delta_B \sim 8 \text{ ppm}]\). The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −15 °C. A solution of NBS (74 mg, 0.41 mmol, 2.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na₂S₂O₅ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography \((n\text{-hexane:Et}_2\text{O 98:2})\) gave (S)-16b (31 mg, 62%) as an oil; er (S:R) 96:4; \( R_I \) 0.72 (petrol:Et₂O 95:5); IR (film): \( \nu \) (cm⁻¹) 2955, 2924,
1510, 1243, 1037, 817, 745; 1H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.87–7.80 (m, 3H), 7.65 (s, 1H), 7.52–7.42 (m, 2H), 7.38 (dd, $J = 8.5$, 1.3 Hz, 1H), 7.11–7.05 (m, 2H), 6.89–6.83 (m, 2H), 3.80 (s, 3H), 2.90 (app. sx, $J = 6.9$ Hz, 1H), 2.58–2.44 (m, 2H), 2.10–1.91 (m, 2H), 1.39 (d, $J = 6.9$ Hz, 3H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 157.6, 144.8, 134.5, 133.6, 132.2, 129.2, 128.0, 127.6, 127.5, 125.8, 125.3, 125.1, 115.1, 40.0, 39.5, 33.0, 22.5; HRMS (EI) calcd. for C$_{21}$H$_{22}$O$_2$ [M]$^+$ 290.1671, found 290.1668.

(S)-4-(3-(naphthalen-2-yl)butyl)phenol ((S)-16b[OH])

The enantioenriched material 16b could not be purified on several attempts. The impure product was therefore derivatised by subjecting it to demethylation conditions.$^{19}$ A round bottom flask was charged with 16b (71 mg, 0.26 mmol). Anhydrous CH$_2$Cl$_2$ ([0.025]) was added and the solution cooled to 0 °C. BBr$_3$ (1 M in CH$_2$Cl$_2$, 0.2 mL, 0.2 mmol, 2.0 eq.) was added. After 1 h at 0 °C, H$_2$O was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et$_2$O (10 mL) and water (10 mL). The layers were separated and the aqueous layer was extracted with Et$_2$O. The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane: EtOAc (95:5) to give ((S)-16b-[OH]) (22 mg, 30%) as a solid; er (S:R) 96:4; $R_1$ 0.29 (petrol:EtOAC 9:1); [$\alpha$]$_{D}^{24}$ 18 (c 0.6, CHCl$_3$); mp. 111–114°C; IR (film): $\nu$ (cm$^{-1}$) 3490, 2920, 2857, 1509, 1227, 816, 718; 1H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.85–7.79 (m, 3H), 7.63 (s, 1H), 7.50–7.41 (m, 2H), 7.38 (dd, $J = 8.5$, 1.7 Hz, 1H), 7.07–7.01 (m, 2H), 6.78–6.72 (m, 2H), 4.55 (s, 1H), 2.90 (app. sx, $J = 6.9$ Hz, 1H), 2.56–2.42 (m, 2H), 2.07–1.90 (m, 2H), 1.37 (d, $J = 6.9$ Hz, 3H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 153.4, 144.7, 134.7, 133.6, 132.2, 129.4, 128.0, 127.6, 127.5, 125.8, 125.7, 125.3, 125.1, 115.1, 40.0, 39.5, 33.0, 22.4; HRMS (EI) calcd. for C$_{20}$H$_{20}$O$_2$ [M]$^+$ 276.1514, found 276.1526.

Resolution of the enantiomers of 16b-[OH] was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO$_2$: [n-hexane:i-PrOH (1:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20µL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running

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component (S) and the slower running component (R) were eluted at 26.1 and 29.3 min., respectively, with an analysis time of 40 min.

(S)-9-(4-(4-methoxyphenyl)butan-2-yl)phenanthrene [(S)-17b]

A solution of 9-bromoanthracene (53 mg, 0.21 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to −78 °C and treated with t-BuLi (0.26 mL, 0.41 mmol, 2.4 eq., 1.7 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of (S)-1b (50 mg, 0.17 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (74 mg, 0.41 mmol, 2.4 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO4, filtered and concentrated under vacuum.

Purification by flash column chromatography (n-hexane:EtO 98:2) gave (S)-17b (27 mg, 47%) as an oil; er (S:R) 96:4; Rf 0.55 (pentane:EtO 95:5); [α]D20 −12.1 (c 0.4, CHCl3); IR (film): ν (cm⁻¹) 2958, 2930, 1610, 1510, 1450, 1243, 1035, 745, 724; 1H NMR (400 MHz, CDCl3) δ ppm 8.78 (d, J = 8.2 Hz, 1H), 8.68 (d, J = 7.2 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 6.8 Hz, 1H), 7.70–7.56 (m, 5H), 7.12–7.07 (m, 2H), 6.86–6.81 (m, 2H), 3.80 (s, 3H), 3.63 (app. sx, J = 6.8 Hz, 1H), 2.76–2.63 (m, 2H), 2.26 (m, 1H), 2.04 (m, 1H), 1.53 (d, J = 6.8 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 157.7, 141.4, 134.5, 131.9, 131.1, 130.8, 129.4, 129.4, 128.3, 126.6, 126.4, 126.0, 125.9, 123.8, 123.3, 122.4, 113.7, 55.3, 39.4, 33.0, 29.7, 21.4; HRMS (EI) calcd. for C25H24O [M]+ 340.1827, found 340.1823.

(S)-4-(3-(phenanthren-9-yl)butyl)phenol {(S)-17b[OH]}

The enantioenriched material (S)-17b could not be purified on several attempts. The impure product was therefore derivatised by subjecting it to demethylation conditions. A round bottom flask was charged with (S)-17b (31 mg, 0.09 mmol). Anhydrous CH2Cl2 [0.025] was added and the solution cooled to 0 °C. BBr3 (1M in CH2Cl2, 0.2 mL, 0.2 mmol, 2.0 eq)
was added. After 1 h at 0 °C, water (1 mL) was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with Et₂O (10 mL) and water (10 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum.

The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane: EtOAc (95:5) to give (S)-17b-[OH] (19 mg, 66%) as an oil; er (S:R) 96:4; Rf 0.30 (petrol:EtOAC 90:10); [α]D²⁴ 13 (c 0.63, CHCl₃) IR (film): ν (cm⁻¹) 3330, 3021, 2960, 2925, 2856, 1512, 1449, 1224, 746, 725; ¹H NMR (400 MHz, CDCl₃) δ ppm 8.78 (d, J = 8.0 Hz, 1H), 8.69 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 7.1 Hz, 1H), 7.71–7.58 (m, 5H), 7.07–7.01 (m, 2H), 6.79–6.72 (m, 2H), 4.74 (s, 1H), 3.63 (app. sx, J = 6.8 Hz, 1H), 2.68 (m, 2H), 2.25 (m, 1H), 1.51 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 153.5, 141.4, 134.6, 131.9, 131.0, 130.7, 129.5, 129.3, 128.2, 126.5, 126.4, 126.0, 125.9, 123.7, 123.3, 123.0, 122.4, 115.1, 39.4, 33.0, 21.4; HRMS (EI) calcd. for C₂₄H₂₂O [M]+ 326.1671, found 326.1674.

Resolution of the enantiomers of 17b-[OH] was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with n-hexane:i-PrOH (97:3) as the mobile phase at a flow rate of 0.3 mL min⁻¹. Injection volume: 5 μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 94.0 and 104.5 min., respectively, with a total analysis time of 130 min.

(S)-1-(4-(4-methoxyphenyl)butan-2-yl)-3,5-dimethylbenzene [(S)-18b]

A solution of 3,5-dimethylbromobenzene (70 μL, 0.52 mmol, 1.5 eq.) in THF (3.0 mL) was cooled to −78 °C and treated with t-BuLi (0.5 mL, 1.03 mmol, 3.0 eq., 1.9 M in pentane). The mixture was stirred at −78 °C for 1 h and then a solution of (S)-1b (100 mg, 0.34 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [(¹¹B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum.

The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (122 mg, 0.69 mmol, 2.0 eq.) in MeOH (5.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers
were dried over MgSO₄, filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (5.0 mL) and p-toluenesulfonic acid (327 mg, 1.72 mmol, 5.0 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (15 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography on silica gel eluting with pentane:Et₂O (95:5), gave (S)-18b (78 mg, 83%) as an oil; er (S:R) 96:4; Rf 0.70 (pentane:Et₂O 95:5); [α]D²³ 23 (c 2.6, CHCl₃); IR (film): ν (cm⁻¹) 2954, 2920, 2855, 1607, 1511, 1242, 1176, 1037, 826, 705; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.10–7.05 (m, 2H), 6.88–6.81 (m, 5H), 3.80 (s, 3H), 2.65 (app. sx, J = 7.0 Hz, 1H), 2.52–2.45 (m, 2H), 2.32 (s, 6H), 1.96–1.79 (m, 2H), 1.75 (d, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.7, 147.5, 137.8, 134.8, 129.3, 127.7, 124.9, 113.7, 55.3, 40.2, 39.4, 33.2, 22.6, 21.5.; HRMS (EI) calcd. for C₁₉H₂₄O [M⁺] 268.1827, found 268.1827.

Resolution of the enantiomers of 18b was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO₂:n-hexane as the mobile phase at a flow rate of 2.0 mL min⁻¹ (P = 125 bar). Injection volume: 20µL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 14.3 and 15.3 min., respectively, with a total analysis time of 20 min.

1,3-dimethyl-5-(1-phenylethyl)benzene (18l)

A solution of 3,5-dimethylbromobenzene (64 µL, 0.47 mmol, 1.1 eq.) in THF (3.0 mL) was cooled to −78 °C and treated with t-BuLi (0.61 mL, 1.04 mmol, 2.2 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 1 h and then a solution of 11 (100 mg, 0.43 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [(¹¹B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (153 mg, 0.86 mmol, 2.0 eq.) in MeOH (5.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were
dried over MgSO₄, filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (5.0 mL) and p-toluenesulfonic acid (327 mg, 1.72 mmol, 5.0 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of NaHCO₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (15 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography on silica gel eluting with pentane:Et₂O (95:5), gave 18l (19 mg, 21%) as an oil; \( R_f \) 0.47 (pentane:Et₂O 97.5:2.5); \(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) ppm 7.09–6.89 (m, 5H), 6.62–6.57 (m, 3H), 3.83 (q, \( J = 7.2 \) Hz, 1H), 2.03 (s, 6H), 1.38 (d, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (76 MHz, CDCl₃) \( \delta \) ppm 146.6, 146.3, 137.7, 128.3, 127.6, 127.7, 125.9, 125.4, 44.7, 21.9, 21.4.

Data in accordance with literature precedent.\(^20\)

1-(4-(4-methoxyphenyl)butan-2-yl)-3-methylbenzene (19b)

A solution of 3-bromotoluene (40 µL, 0.33 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to –78 °C and treated with t-BuLi (0.42 mL, 0.66 mmol, 2.4 eq., 1.6 M in pentane). The mixture was stirred at –78 °C for 1 h and then a solution of 1b (80 mg, 0.28 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex [(\(^{11}\)B NMR, 96 MHz, THF) \( \delta_B \sim 8 \) ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was redissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of NBS (118 mg, 0.66 mmol, 2.4 eq.) in MeOH (4.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were dried (MgSO₄), filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (4.0 mL) and p-toluenesulfonic acid (238 mg, 0.69 mmol, 5.0 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and NaHCO₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (15 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum.

Purification by flash column chromatography on silica gel eluting with pentane:Et₂O (95:5), gave a mixture of 19b and 1-(3-bromobutyl)-4-methoxybenzene in a ¹H NMR ratio of 28:72 in favour of 1-(3-bromobutyl)-4-methoxybenzene. Compound 19b was isolated in 17% yield (12 mg). 19b: Rf 0.77 (pentane:Et₂O 95:5); diagnostic peaks from ¹H NMR analysis (400 MHz, CDCl₃) δ ppm 3.79 (s, 3H), 2.36 (s, 3H), 1.27 (d, J = 7.0 Hz, 3H); GC-MS: Rf 7.37 min., m/z: 254, 161, 147, 135, 121, 105, 91, 77. 1-(3-bromobutyl)-4-methoxybenzene: Rf 0.80 (pentane:Et₂O 95:5); diagnostic peaks from ¹H NMR analysis (400 MHz, CDCl₃) δ ppm 4.08 (m, 1H), 3.80 (s, 3H), 1.72 (d, J = 6.7 Hz, 3H); GC-MS: Rf 5.39 min., m/z: 242/244, 162, 147, 121, 105, 121, 105, 91, 77.

(S)-2-methoxy-6-(4-(4-methoxyphenyl)butan-2-yl)pyridine [(S)-20b]

A solution of 2-bromo-6-methoxypyridine (36 µL, 0.29 mmol, 1.7 eq.) in THF:Et₂O:pentane (4:1:1, 0.3 M) was cooled to −78 °C and treated with n-BuLi (0.2 mL, 0.29 mmol, 1.7 eq., 1.6 M in hexanes) and the mixture was stirred at this temperature for 30 min. (S)-1b (50 mg, 0.17 mmol, 1.0 eq.) was added dropwise as a solution in THF (0.5 mL). The mixture was stirred at −78 °C for 30 min. at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [¹¹B NMR (96 MHz, THF) δ_B ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. A solution of DBDMH (1,3-dibromo-5,5-dimethylydantoin) (197 mg, 0.69 mmol, 2.0 eq.) in MeOH (5.0 mL) was added dropwise. After 1 h at 0 °C saturated aqueous solution of Na₂S₂O₅ was added and the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (S)-20b (27 mg, 58%) was obtained as an oil; er (S:R) 95:5; Rf 0.40 (petrol:Et₂O 95:5); [α]D₂⁰ 23 27 (c 0.15, CHCl₃); IR (film): ν (cm⁻¹) 2935, 2855, 1577, 1510, 1463, 1413, 1288, 1242, 1175, 1029, 801, 743; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.49 (t, J = 7.3 Hz, 1H), 7.10–7.02 (d, J = 8.5 Hz, 2H), 6.89–6.81 (m, 2H), 6.70 (d, J = 7.3 Hz, 1H), 6.55 (d, J = 7.3 Hz, 1H), 3.94 (s, 3H), 3.79 (s, 3H), 2.80 (app. sx, J = 6.8 Hz, 1H), 2.54–2.42 (m, 2H), 2.13 (m, 1H), 1.85 (m, 1H), 1.29 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.0, 163.6, 157.6, 138.6, 134.8, 129.2, 114.3, 113.6, 107.4, 55.2, 53.1, 40.9, 38.6, 32.9, 20.9; HRMS (El) calcd. for C₁₇H₂₁NO₂ [M]⁺ 271.1572, found 271.1570.
Resolution of the enantiomers of 20b was achieved using a chiral HPLC system fitted with a Chiralpak AD-H column with guard as the stationary phase with \([n\text{-hexane}:10\%\text{ i-PrOH in } n\text{-hexanes} (99:1, v:v)]\) as the mobile phase at a flow rate of 0.5 mL min\(^{-1}\) \((T = 0 \degree C)\). Injection volume: 5 \(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (\(S\)) and the slower running component (\(R\)) were eluted at 24.6 and 26.6 min., respectively, with a total analysis time of 35 min.

7. Reaction Products – Coupling of tertiary boronic esters to 6-membered aromatics

\((S)-2-(3\text{-Methyl-1-phenylpentan-3-yl})\text{furan} [(S)-2g]\)

Following GP2 (0.25 mmol scale), \((S)-2g\) (51 mg, 89%) was obtained as an oil; er \((S):R > 99:1; R\); 0.30 \((n\text{-hexane})\); \([\alpha]_D^{24} = 22.0\) \((c 1, \text{ CHCl}_3)\); IR (film): \(\nu\) \((\text{cm}^{-1})\) 2966, 2929, 2877, 1506, 1497, 1455, 1156, 1011, 729, 680; \(^1\text{H NMR (400 MHz, CDCl}_3\)) \(\delta\) ppm 7.36 \((m, 1H)\), 7.28 – 7.13 \((m, 5H)\), 6.29 \((m, 1H)\), 6.04 \((m, 1H)\), 2.48 \((td, J = 13.0, 5.1 Hz, 1H)\), 2.32 \((td, J = 13.1, 4.6 Hz, 1H)\), 1.98 \((td, J = 13.0, 4.5 Hz, 1H)\), 1.85 – 1.7 \((m, 2H)\), 1.67 – 1.55 \((m, 1H)\), 1.29 \((s, 3H)\), 0.77 \((t, J = 7.5 Hz, 3H)\); \(^{13}\text{C NMR (100 MHz, CDCl}_3\)) \(\delta\) ppm 161.4, 143.1, 140.7, 128.3, 128.2, 109.6, 104.9, 42.3, 39.5, 32.9, 31.0, 22.3, 8.6; HRMS (EI) calcd. for C\(_{16}\)H\(_{20}\)O \([M]^+\) 228.1514, found 228.1508.

Resolution of the enantiomers of 2g was achieved using a chiral HPLC system fitted with a Chiralpak OD column with guard as the stationary phase with \(n\text{-hexanes}\) as the mobile phase at a flow rate of 0.5 mL min\(^{-1}\) \((T = 0 \degree C)\). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (\(S\)) and the slower running component (\(R\)) were eluted at 29.9 and 34.3 min., respectively, with a total analysis time of 60 min.

\((S)-2-(2\text{-Phenylbutan-2-yl})\text{furan} [(S)-2h]\)

Following GP2 (0.25 mmol scale), \((S)-2h\) (82 mg, 83%) was obtained as an oil; er \((S):R > 99:1; R\); 0.5 \((n\text{-hexane})\); \([\alpha]_D^{23} = -2.3\) \((c 0.5, \text{ CHCl}_3)\); IR (film): \(\nu\) \((\text{cm}^{-1})\) 2970, 2929, 2879, 1599, 1504, 1494, 1456, 1380, 1159, 1014, 923, 730, 699, 598; \(^1\text{H NMR (400 MHz, CDCl}_3\)) \(\delta\) ppm 7.32 \((dd, J = 1.8, 0.9 Hz, 1H)\), 7.30 – 7.26 \((m, 2H)\), 7.22 – 7.15 \((m, 3H)\), 6.31 \((dd, J = 3.1, 1.9 Hz, 1H)\), 6.16 – 6.13 \((m, 1H)\), 2.14 \((dq, J = 13.3, 7.4 Hz, 1H)\), 2.09 – 1.98 \((m, 1H)\), 1.6 \((s, 3H)\), 0.78 \((t, J = 7.4 Hz, 3H)\); \(^{13}\text{C NMR (MHz, CDCl}_3\)) \(\delta\)
Resolution of the enantiomers of 2h was achieved using a chiral HPLC system fitted with a Chiracel OJ-RH column with guard as the stationary phase with MeCN:water (4:1, v:v) as the mobile phase at a flow rate of 1.0 mL min\(^{-1}\) \((T = 20 \, ^\circ C)\). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 21.0 and 27.3 min., respectively, with a total analysis time of 60 min.

**((S)-2-(4-Methyl-2-phenylpentan-2-yl)furan [(S)-2i])**

Following GP2 (0.5 mmol scale), (S)-2i (82 mg, 76%) was obtained as an oil; er \((S):R\) 99:1; \(R_t\) 0.29 \((n\)-hexane\); \([\alpha]_D^{23}\) \(-15.4 \,(c\,1.0,\,CHCl_3)\); IR (film): \(\nu\) (cm\(^{-1}\)) 2954, 2927, 1495, 1445, 1158, 1011, 729, 697, 598; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.34–7.30 \((m, 1H)\), 7.30–7.25 \((m, 2H)\), 7.23–7.15 \((m, 3H)\), 6.32 \((dd, J = 3.1, 1.9 \, Hz, 1H)\), 6.16–6.12 \((m, 1H)\), 2.08 \((dd, J = 13.8, 5.8 \, Hz, 1H)\), 1.94 \((dd, J = 13.8, 5.1 \, Hz, 1H)\), 1.66 \((s, 3H)\), 1.65–1.60 \((m, 1H)\), 0.79 \((br \, d, J = 6.7 \, Hz, 3H)\), 0.72 \((br \, d, J = 6.6 \, Hz, 3H)\); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 161.5, 147.7, 140.8, 128.0, 126.3, 125.9, 109.8, 105.4, 49.0, 43.8, 25.6, 25.0, 24.7, 24.0; HRMS (EI) calcd. for C\(_{16}\)H\(_{20}\)O \([M]^+\) 228.1514, found 228.1522.

Resolution of the enantiomers of 2i was achieved using a chiral GC system fitted with a Supelco \(\beta\)-DM column. Injector \(T = 250 \, ^\circ C\), detector \(T = 300 \, ^\circ C\). Oven conditions: \(T = 70 \, ^\circ C\) for 3 min., then ramp \((0.5 \, ^\circ C \, \text{min}^{-1})\) until 180 \, ^\circ C, H\(_2\) carrier gas at 14 psi. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 64.6 and 64.7 min., respectively, with a total analysis time of 75 min.

**((R)-2-(1-cyclopropyl-1-phenylethyl)furan [(R)-2j])**

Following GP2 (0.29 mmol scale), (R)-2j (58 mg, 94%) was obtained as an oil; er \((R):S\) 98:2; \(R_t\) 0.83 \((\text{pentane:Et}_2\text{O} \, 95:5)\); \([\alpha]_D^{22}\) 22.7 \((c\,1.5,\,CHCl_3)\); IR (film): \(\nu\) (cm\(^{-1}\)) 3059, 2981, 1502, 1494, 1010, 730, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.30 \((br \, s, 1H)\), 7.29–7.24 \((m, 4H)\), 7.20 \((m, 1H)\), 6.31 \((dd, J = 3.1, 1.8 \, Hz, 1H)\), 6.20 \((d, J = 3.1 \, Hz, 1H)\), 1.53 \((s, 3H)\), 1.43 \((m, 1H)\), 0.58–0.44 \((m, 2H)\), 0.30–0.18 \((m, 2H)\); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 161.0, 146.4, 141.3, 127.9, 127.1, 126.2, 109.5, 106.0, 43.8, 24.4, 20.5, 1.8, 1.5; HRMS (EI) calcd. for C\(_{15}\)H\(_{16}\)O \([M]^+\) 212.1201, found 212.1200.
Resolution of the enantiomers of 2j was achieved using a chiral HPLC system fitted with a Chiralpak OJ-RH column with guard as the stationary phase with MeCN:water (85:15, v:v) as the mobile phase at a flow rate of 1.0 mL min\(^{-1}\). Injection volume: 2 \(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 3.3 and 3.9 min., respectively, with a total analysis time of 15 min.

\((S)-2-(1-(4\text{-Bromophenyl})-1\text{-phenylethyl})\text{furan}\) \([\text{(S)}-2k]\)

Following GP2 (0.25 mmol scale), \((S)-2k\) (43 mg, 53%) was obtained as an amorphous solid; er (S:\(R\)) 98:2; \(R_t \) 0.37 (n-hexane); \([\alpha]_D^{21} \) -7.6 (c 0.5, CHCl\(_3\)); IR (film): \(\nu\) (cm\(^{-1}\)) 3058, 2980, 1589, 1489, 1395, 1373, 1359, 1260, 1209, 1148, 1075, 1026, 1008, 923, 884, 829, 803, 789, 750, 734; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.42–7.36 (m, 3H), 7.31–7.19 (m, 3H), 7.08 (dt, \(J = 6.4, 1.9\) Hz, 2H), 6.99 (dt, \(J = 9.0, 2.1\) Hz, 2H), 6.30 (dd, \(J = 3.1, 1.9\) Hz, 1H), 5.93 (d, \(J = 3.3\) Hz, 1H), 2.04 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 159.7, 146.6, 146.3, 141.9, 131.0, 129.8, 128.0, 127.8, 126.5, 120.4, 109.9, 107.8, 49.2, 27.7; HRMS (EI) calcd. for C\(_{18}\)H\(_{15}\)BrO \([M]^+\) 326.0306, found 326.0304.

The enantiomers of 2k could not be separated by chiral GC, HPLC or SFC. In order to evaluate the enantiomeric ratio of the reaction product it was further functionalized using Suzuki cross-coupling.

\[
\text{PhMe}:\text{H}_2\text{O (5:1), reflux, 16h}
\]

A flask was charged with Pd(PPh\(_3\))\(_4\) (12 mg, 0.01 mmol, 10 mol%), Cs\(_2\)CO\(_3\) (4 mg, 0.01 mmol, 10 mol%) and \(m\)-methoxyphenyl boronic acid (31 mg, 0.20 mmol, 2.0 eq.). The flask was evacuated and refilled with nitrogen (x 3). Degassed toluene (1.0 mL) and water (0.2 mL) were added. A solution of \((S)-2s\) (33 mg, 0.10 mmol, 1.0 eq.) in degassed toluene (1.0 mL) was added and the mixture was heated under refluxing conditions for 16 h. The reaction was cooled to room temperature and water (5 mL) was added. The layers were separated and the aqueous layer was extracted with Et\(_2\)O (3 x 5 mL). The combined organic layers were
dried over MgSO₄, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting n-hexane:Et₂O (99:1→99:5) to give the desired product (24 mg, 70%) as an oil; er (S:R) 98:2; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.65–6.80 (m, 13H), 6.33 (dd, J = 3.4, 1.8 Hz, 1H), 5.98 (dd, J = 9.0, 3.5 Hz, 1H), 3.80 (s, 3H), 2.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 160.3, 159.9, 147.1, 146.4, 142.3, 141.8, 139.0, 129.7, 128.7, 128.4, 128.0, 126.7, 126.4, 119.6, 112.7, 112.6, 109.9, 107.7, 55.3, 49.3, 27.8; HRMS (EI) calcd. for C₂₅H₂₂O₂ [M]+ 354.1620, found 354.1627.

Resolution of the enantiomers of the cross-coupling product was achieved using a chiral HPLC system fitted with a Chiralcel OD + OD-H column as the stationary phase with n-hexane:i-Pr (99.8:0.2, v:v) as the mobile phase at a flow rate of 0.7 mL min⁻¹ (T = 0 °C). Injection volume: 20μL of 2 g L⁻¹ solution of compound in the eluent. Under these conditions the faster running component (R) and the slower running component (S) were eluted at 96.0 and 102.3 min., respectively, with a total analysis time of 120 min.

(S)-2-(3-methyl-1-phenylpentan-3-yl)benzofuran [(S)-4g]

A solution of benzofuran (14 μL, 0.12 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to 0 °C and treated with n-BuLi (0.1 mL, 0.12 mmol, 1.2 eq., 1.6 M in hexane). The mixture was stirred at 0 °C for 1 h and then a solution of (R)-1g (30 mg, 0.10 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at 0 °C for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [(¹¹B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to 0 °C. A solution of NBS (22 mg, 0.12 mmol, 1.2 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et₂O (98:2) gave (S)-4g (20 mg, 69%) was obtained as an oil; er (S:R) 99:1; Rf 0.75 (pentane:Et₂O 95:5); [α]D²³ –25 (c 0.6, CHCl₃); R (film): ν (cm⁻¹) 2966, 2933, 1453, 1252, 1167, 884, 750, 738; ¹H NMR (400 MHz, CDCl₃) δ ppm 7.53(m, 1H), 7.47 (m, 1H), 7.30–7.25 (m, 3H), 7.20–7.14 (m, 1H), 7.10–7.07 (m, 3H), 6.96–6.88 (m, 2H), 6.80–6.70 (m, 1H), 6.30–6.23 (m, 1H), 3.70 (s, 3H), 2.10 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 160.3, 159.9, 147.1, 146.4, 142.3, 141.8, 139.0, 129.7, 128.7, 128.4, 128.0, 126.7, 126.4, 119.6, 112.7, 112.6, 109.9, 107.7, 55.3, 49.3, 27.8; HRMS (EI) calcd. for C₂₅H₂₂O₂ [M]+ 354.1620, found 354.1627.
(m, 3H), 6.47 (d, J = 1 Hz, 1H), 2.56 (dt, J = 13.1, 4.8 Hz, 1H), 2.41 (dt, J = 13.1, 4.8 Hz, 1H), 2.14 (dt, J = 13.1, 4.8 Hz, 1H), 1.98–1.87 (m, 2H), 1.72 (dq, J = 13.1, 7.5, 1H), 1.41 (s, 3H), 0.84 (t, J = 7.5 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 164.6, 154.7, 142.8, 128.7, 128.3, 125.6, 123.1, 122.3, 120.3, 110.8, 102.2, 42.0, 40.0, 32.7, 30.9, 22.2, 8.6; HRMS (EI) calcd. for C20H22O [M]+ 278.1671 found 278.1675.

Resolution of the enantiomers of 4g was achieved using a chiral HPLC system fitted with a Chiralpak OJ-RH column as the stationary phase with MeCN:water (7:3, v:v) as the mobile phase at a flow rate of 0.5 mL min⁻¹ (T= 20 °C). Injection volume: 5 μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 23.3 and 30.2 min., respectively, with a total analysis time of 35 min.

(R)-2-(2-phenylbutan-2-yl)benzofuran [(R)-4h]

A solution of benzofuran (14 μL, 0.12 mmol, 1.2 eq.) in THF (1.0 mL) was cooled to 0 °C and treated with n-BuLi (0.1 mL, 0.12 mmol, 1.2 eq., 1.6 M in hexane). The mixture was stirred at 0 °C for 1 h and then a solution of (R)-1h (26 mg, 0.10 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at 0 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to 0 °C. A solution of NBS (22 mg, 0.12 mmol, 1.2 eq.) in MeOH (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO4, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et2O (98:2) gave (R)-4h (16 mg, 64%) as an oil; [α]D 23 12 (c 0.5, CHCl3); IR (film): ν (cm⁻¹) 2970, 2950, 1578, 1498, 1453, 1301, 1250, 1168, 1028, 1006, 937, 798, 750, 738; 1H NMR (400 MHz, CDCl3) δ ppm 7.54 (m, 1H), 7.40 (m, 1H), 7.34–7.26 (m, 4H), 7.25–7.18 (m, 3H), 6.57 (d, J = 0.9 Hz, 1H), 2.29 (dq, J = 13.7, 7.4 Hz, 1H), 2.17 (dq, J = 13.7, 7.4 Hz, 1H), 1.72 (s, 3H), 0.85 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 164.6, 154.7, 146.2, 128.5, 128.2, 126.6, 126.2, 123.3,
Resolution of the enantiomers of 4h was achieved using a chiral HPLC system fitted with a Chiracel OD-H column as the stationary phase with heptane:MTBE (95:5, v:v) as the mobile phase at a flow rate of 0.5 mL min$^{-1}$. Injection volume: 2 μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 16.7 and 20.8 min., respectively, with a total analysis time of 30 min.

(S)-1,3-dimethoxy-5-(3-methyl-1-phenylpentan-3-yl)benzene [(S)-9g]

A solution of 3,5-(dimethoxy)bromobenze (35 mg, 0.16 mmol, 1.3 eq.) in THF (2.5 mL) was cooled to −78 °C and treated with t-BuLi (0.17 mL, 0.32 mmol, 2.6 eq., 1.4 M in pentane). The mixture was stirred at −78 °C for 30 min. and then a solution of (R)-1g (36 mg, 0.125 mmol, 1.0 eq.) in THF (0.5 mL) was added. The mixture was stirred at −78 °C for 1 h and then warm to r.t. at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The reaction mixture was stirred at −78 °C and a solution of NBS (27 mg, 0.15 mmol, 1.2 eq.) in MeOH (3.0 mL) was added dropwise and the mixture was warmed to r.t. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-pentane:Et$_2$O (98:2) gave (S)-9g (28 mg, 78%) as an oil, er (S:R) 99:1; $R_f$ 0.38 (n-pentane:Et$_2$O 95:5); $[\alpha]_D^{20} -14$ (c 0.5, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2962, 2933, 1593, 1454, 1421, 1298, 1260, 1203, 1153, 1124, 1060, 925, 801, 746, 699; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.28–7.21 (m, 2H), 7.15 (tt, $J = 7.4,$ 2.3 Hz, 1H), 7.12–7.08 (m, 2H), 6.51 (d, $J = 2.2$ Hz, 2H), 6.33 (t, $J = 2.2$ Hz, 1H), 3.81 (s, 6H), 2.46 (td, $J = 13.1,$ 5.1 Hz, 1H), 2.27 (td, $J = 13.0,$ 4.4 Hz, 1H), 1.97 (td, $J = 13.1,$ 4.4 Hz, 1H), 1.87–1.68 (m, 2H), 1.67–1.55 (m, 1H), 1.33 (s, 3H), 0.72 (t, $J = 7.4$ Hz, 3H), $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 160.5, 150.1, 143.2, 128.2, 125.5, 105.3, 96.7, 55.2, 45.2, 41.6, 35.7, 30.8, 23.2, 8.65.

Resolution of the enantiomers of 9g was achieved using a chiral HPLC system fitted with a Chiracel IB column with guard as the stationary phase, n-hexane:i-PrOH (99.9:0.1 v:v) as the
mobile phase at a flow rate of 0.6 mL min\(^{-1}\). Injection volume: 2\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((R)\) and the slower running component \((S)\) were eluted at 22.3 and 25.0 min., respectively, with a total analysis time of 30 min.

\(\text{(R)-1,3-dimethoxy-5-(2-phenylbutan-2-yl)benzene \[(R)-9h]\}}\)

A solution of 3,5-(dimethoxy)bromobenze (117 mg, 0.54 mmol, 1.3 eq.) in THF (5.0 mL) was cooled to –78 °C and treated with \(t\)-BuLi (0.5 mL, 1.08 mmol, 2.6 eq., 1.9 M in pentane). The mixture was stirred at –78 °C for 30 min. and then a solution of \((S)-1\text{h}\) (70 mg, 0.27 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex \([\text{\(^{11}\)B NMR, 96 MHz, THF} \delta_B \sim 8 \text{ ppm}]\). The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of DBDMH (1,3-dibromo-5,5-dimethylhydantoin) (176 mg, 0.61 mmol, 2.0 eq.) in MeOH (5.0 mL) was added dropwise. After 1 h reaction mixture was warmed to 70 °C and heated at this temperature for 3 h. The reaction mixture was cooled to r.t. and saturated aqueous solution of Na\(_2\)S\(_2\)O\(_3\) (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with \(n\)-hexane:Et\(_2\)O (98:2) gave \(\text{(R)-9h}\) (73 mg, 63%) as an oil, er \((R:S) \approx 99:1\); \(\text{[\(\alpha\)]\(\text{D}\)\(\text{20}\) \(= -22.0 \text{ (c 1.0, CHCl\(_3\)})\}}\); IR (film): \(\nu \text{ (cm}^{-1}\)) 2959, 2933, 2836, 1592, 1454, 1203, 1057, 831; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \text{ ppm 7.27–7.13 (m, 5H), 6.35 (d, } J = 2.2 \text{ Hz, 2H), 6.28 (t, } J = 2.2 \text{ Hz, 1H), 3.72 (s, 6H), 2.10 (q, } J = 7.4 \text{ Hz, 1H), 1.56 (s, 3H) 0.72 (t, } J = 7.4 \text{ Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta \text{ ppm 160.2, 152.2, 149.3, 127.8, 127.2, 125.5, 106.3, 96.8, 55.1, 46.7, 33.9, 26.8, 9.1; \)}}\; HRMS (ESI) calcd. for C\(_{18}\)H\(_{23}\)O\(_2\) \([\text{M+H]}^+\) 271.1694, found 271.1693.

Resolution of the enantiomers of \(9\text{h}\) was achieved using a chiral HPLC system fitted with a Chiracel OD-H column as the stationary phase with \(n\)-hexane:\(i\)-Pr (99.5:0.5 v:v) as the mobile phase at a flow rate of 0.5 mL min\(^{-1}\). Injection volume: 20 \(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((R)\) and the
slower running component (S) were eluted at 9.4 and 10.9 min., respectively, with a total analysis time of 30 min.

(R)-1-methoxy-3-(2-phenylbutan-2-yl)benzene [(R)-11h]

![Chemical Structure](image)

A solution of 3-methoxybromobenzene (43 μL, 0.34 mmol, 1.1 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.42 mL, 0.68 mmol, 2.2 eq., 1.7 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of (S)-1h (80 mg, 0.31 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [11B NMR, 96 MHz, THF] \( \delta_B \approx 8 \) ppm. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to −78 °C. A solution of DBDMH (176 mg, 0.61 mmol, 2.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h saturated aqueous solution of \( \text{Na}_2\text{S}_2\text{O}_3 \) (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography (n-hexane:Et\(_2\)O 98:2) gave (R)-11h (34 mg, 47%) as an oil; er (R:S) 99:1; \( R_f \) 0.50 (pentane:Et\(_2\)O 95:5); \([\alpha]_D^{21} \) 43 (c 0.1, CHCl\(_3\)); IR (film): \( \nu \) (cm\(^{-1}\)) 2968, 2936, 1598, 1580, 1253, 774, 762, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm 7.30–7.24 (m, 2H), 7.22–7.14 (m, 4H), 6.80–6.76 (m, 2H), 6.73 (ddd, \( J = 8.1, 2.4, 0.9 \) Hz, 1H), 3.77 (s, 3H), 2.13 (q, \( J = 7.4 \) Hz, 2H), 1.61 (s, 3H), 0.75 (t, \( J = 7.4 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm 159.2, 151.4, 149.5, 128.7, 127.8, 127.3, 125.5, 120.2, 114.1, 110.0, 55.1, 46.5, 34.0, 26.8, 9.2; HRMS (EI) calcd. for C\(_{17}\)H\(_{20}\)O \([M]^+\) 240.1514, found 240.1516.

Resolution of the enantiomers of 11h was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO\(_2\):n-hexane as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) (\( P = 125 \) bar). Injection volume: 10μL of a 2 g L\(^{-1}\) solution of the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 3.7 and 4.3 min., respectively, with a total analysis time of 10 min.
(S)-1-(3-Methyl-1-phenylpentan-3-yl)naphthalene [(S)-15g]

A solution of 1-bromonaphthalene (28 μL, 0.16 mmol, 1.2 eq.) in Et₂O (1.0 mL) was cooled to 0 °C and n-BuLi (0.1 mL, 0.16 mmol, 1.2 eq., 1.6 M in hexanes) was added dropwise. The mixture was stirred at 0 °C for 1 h. (R)-1g (36 mg, 0.125 mmol, 1.0 eq.) was added as a solution in Et₂O (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the boron-ate complex [($^{11}$B NMR, 96 MHz) $\delta_B$ ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to $-78 \, ^\circ\mathrm{C}$. A solution of NBS (53 mg, 0.32 mmol, 2.4 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (3.0 mL) and p-toluenesulfonic acid (49 mg, 0.26 mmol, 2.5 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of NaHCO₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with pentane gave (S)-15g (27 mg, 75%) as an oil; er (S:R) 99:1; Rf 0.17 (pentane); [$\alpha$]$_D^{21}$ +1 (c 0.5, CHCl₃); IR (film): ν (cm$^{-1}$): 3048, 3025, 2966, 2932, 2876, 1601, 1510, 1496, 1454, 1397, 1380, 1279, 1030, 800, 777, 748, 698, 573, 497; $^1$H NMR (400 MHz, CDCl₃) $\delta$ ppm 8.50 (m, 1H), 7.89 (m, 1H), 7.75 (d, J = 7.7 Hz, 1H), 7.54–7.34 (m, 4H), 7.19 (tt, J = 7.5, 1.5 Hz, 2H), 7.11 (tt, J = 7.3, 2.1, 1H), 7.02–6.92 (m, 2H), 2.75–2.62 (m, 1H), 2.49–2.34 (m, 2H), 2.10–1.96 (m, 2H), 1.88 (dq, J = 13.8, 7.4 Hz, 1H), 1.63 (s, 3H), 0.65 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ ppm 143.2, 142.0, 134.9, 132.2, 129.7, 128.2, 128.1, 127.6, 126.5, 125.8, 125.5, 125.0, 124.9, 44.4, 43.7, 34.5, 31.4, 27.1, 9.0.

Resolution of the enantiomers of 15g was achieved using chiral HPLC system fitted with a Chiracel IB column with guard as the stationary phase with n-hexane:i-PrOH (99.9:0.1, v:v) as the mobile phase at a flow rate of 0.5 mL min$^{-1}$ ($T = 0 \, ^\circ\mathrm{C}$). Injection volume: 2μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) major were eluted at 16.1 min and 17.0 min., respectively, with a total analysis time of 30 min.
A solution of 1-bromonaphthalene (32 mg, 0.16 mmol, 1.5 eq.) in Et₂O (1.0 mL) was cooled to −15 °C and n-BuLi (0.1 mL, 0.16 mmol, 1.5 eq., 1.6 M in hexanes) was added dropwise. The mixture was stirred at −15 °C for 30 min. (R)-1g (30 mg, 0.1 mmol, 1.0 eq.) was added as a solution in Et₂O (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the boron-ate complex ($^{11}$B NMR, 96 MHz) $\delta_B$ ~ 8 ppm. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −15 °C. A solution of NBS (37 mg, 0.21 mmol, 2.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (3.0 mL) and p-toluenesulfonic acid (49 mg, 0.26 mmol, 2.5 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with pentane gave (S)-16g (14 mg, 49%) as an oil; $\text{er (S:R)}$ 95:5; $R_f$ 0.87 (petrol:Et₂O 95:5); $\alpha$D $^23$ 2 (c 0.4, CHCl₃) IR (film): $\nu$ (cm$^{-1}$) 2963, 2925, 1454, 1380, 816, 744, 699; $^1$H NMR (400 MHz, CDCl₃) $\delta$ ppm 7.87–7.80 (m, 3H), 7.73 (br d, $J = 2.0$ Hz, 1H), 7.53 (dd, $J = 8.7$, 2.0 Hz, 1H), 7.50–7.41 (m, 2H), 7.26–7.20 (m, 2H), 7.14 (m, 1H), 7.10–7.05 (m, 2H), 2.47 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.22 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.12 (dt, $J = 13.0$, 4.5 Hz, 1H), 1.98–1.84 (m, 2H), 1.71 (dq, $J = 13.0$, 7.4 Hz, 1H), 1.47 (s, 3H), 0.72 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ ppm 144.8, 143.2, 133.4, 131.7, 128.2, 128.2, 127.9, 127.7, 127.3, 125.7, 125.5, 125.3, 125.2, 125.0, 45.1, 41.5, 35.5, 31.0, 23.2, 8.7; HRMS (EI) calcd. for C₂₂H₂₄ [M] 288.1878, found 288.1883.

A solution of 1-bromonaphthalene (32 mg, 0.16 mmol, 1.5 eq.) in Et₂O (1.0 mL) was cooled to −15 °C and n-BuLi (0.1 mL, 0.16 mmol, 1.5 eq., 1.6 M in hexanes) was added dropwise. The mixture was stirred at −15 °C for 30 min. (R)-1g (30 mg, 0.1 mmol, 1.0 eq.) was added as a solution in Et₂O (0.5 mL) and the reaction was stirred at the same temperature for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the boron-ate complex ($^{11}$B NMR, 96 MHz) $\delta_B$ ~ 8 ppm. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to −15 °C. A solution of NBS (37 mg, 0.21 mmol, 2.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (3.0 mL) and p-toluenesulfonic acid (49 mg, 0.26 mmol, 2.5 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with pentane gave (S)-16g (14 mg, 49%) as an oil; er (S:R) 95:5; $R_f$ 0.87 (petrol:Et₂O 95:5); $\alpha$D $^23$ 2 (c 0.4, CHCl₃) IR (film): $\nu$ (cm$^{-1}$) 2963, 2925, 1454, 1380, 816, 744, 699; $^1$H NMR (400 MHz, CDCl₃) $\delta$ ppm 7.87–7.80 (m, 3H), 7.73 (br d, $J = 2.0$ Hz, 1H), 7.53 (dd, $J = 8.7$, 2.0 Hz, 1H), 7.50–7.41 (m, 2H), 7.26–7.20 (m, 2H), 7.14 (m, 1H), 7.10–7.05 (m, 2H), 2.47 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.22 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.12 (dt, $J = 13.0$, 4.5 Hz, 1H), 1.98–1.84 (m, 2H), 1.71 (dq, $J = 13.0$, 7.4 Hz, 1H), 1.47 (s, 3H), 0.72 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ ppm 144.8, 143.2, 133.4, 131.7, 128.2, 128.2, 127.9, 127.7, 127.3, 125.7, 125.5, 125.3, 125.2, 125.0, 45.1, 41.5, 35.5, 31.0, 23.2, 8.7; HRMS (EI) calcd. for C₂₂H₂₄ [M] 288.1878, found 288.1883.
a solution of (R)-1g (36 mg, 0.125 mmol, 1.0 eq.) in THF (0.5 mL) was added. The mixture was stirred at –78 °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex \([^{11}\text{B NMR, 96 MHz, THF]} \delta_{\text{B}} \approx 8 \text{ ppm}\). The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of NBS (53 mg, 0.32 mmol, 2.4 eq.) in MeOH (3.0 mL) was added dropwise and the reaction mixture was warmed to r.t. After 1 h Na\(_2\)S\(_2\)O\(_3\) sat (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried (MgSO\(_4\)), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with pentane gave (S)-18g (22 mg, 66%) as an oil; er (S:R) 99:1; \(R_{\text{f}}\) 0.32 (pentane); \([\alpha]_{\text{D}}^{21}\) –11 (c 0.65, CHCl\(_3\)) IR (film): \(\nu\ (\text{cm}^{-1})\) 3026, 2965, 2920, 2877, 1603, 1496, 1454, 1377, 1031, 847, 707, 698, 502; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta_{\text{ppm}}\) 7.30–7.22 (m, 2H), 7.21–7.08 (m, 3H), 6.97–6.92 (m, 2H), 6.84 (m, 1H), 2.52–2.22 (m, 2H), 2.32 (s, 6H), 1.99 (td, \(J = 13.1, 4.4 \text{ Hz}, 1\)H), 1.88–1.70 (m, 2H), 1.61 (m, 1H), 1.33 (s, 3H), 0.72 (t, \(J = 7.4 \text{ Hz}, 3\)H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta_{\text{ppm}}\) 147.4, 143.4, 137.2, 128.4, 128.2, 127.0, 125.5, 124.3, 44.9, 40.9, 35.5, 30.9, 23.5, 21.6; HRMS (ESI) calcd. for C\(_{20}\)H\(_{26}\) [M]+ 266.2035, found 266.2027.

Resolution of the enantiomers of 18g could not be separated by either chiral GC, HPLC and SFC. In order to evaluate the enantiomeric ratio of the reaction product we separated the enantiomers of the B(pin)-incorporated reaction by-product 18ga (< 10%). This compound is formed due to preferential B(pin) migration over elimination after the key 1,2-metalate rearrangement. Thus its enantiomeric enrichment reflects the one of 18g.

\[(\text{S})-18\text{ga}: \begin{align*} R_{\text{f}} & 0.3 \text{ (pentane:Et}_2\text{O 95:5)}; \text{ IR (film): } \nu \ (\text{cm}^{-1})\ & 2975, 2927, 1607, 1453, 1372, 1324, 1295, 1141, 1059, 855, 699, 684, 745; \text{ } ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \ \delta \ (\text{ppm})\ & 7.24–7.14 \text{ (m, 4H), } 7.11 \text{ (tt, } J = 7.1, 1.6, 1\)H), 6.97–6.91 \text{ (m, } 1\)H), 6.80 \text{ (dt, } J = 1.4, 0.7 \text{ Hz, } 1\)H), 2.45–2.08 \text{ (m, } 3\)H), 2.39 \text{ (s, } 3\)H), 2.28 \text{ (s, } 3\)H), 1.91 \text{ (dq, } J = 14.6, 7.4 \text{ Hz, } 1\)H), 1.83–1.70 \text{ (m, } 1\)H), 1.63 \text{ (dq, } J = 13.5, 7.3 \text{ Hz, } 1\)H), 1.41 \text{ (s, } 3\)H), 1.38 \text{ (s, } 6\)H), 1.36 \text{ (s, } 6\)H), 0.70 \text{ (t, } J = 7.3 \text{ Hz, } 3\)H); \text{ } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \ \delta \ (\text{ppm})\ & 147.4, 143.4, 137.2, 128.4, 128.2, 127.0, 125.5, 124.3, 44.9, 40.9, 35.5, 30.9, 23.5, 21.6; \text{ } ^{11}\text{B NMR (96 MHz, CDCl}_3\text{)} \ \delta \ 31.2 \text{ ppm; } \text{ HRMS (ESI) calcd. for } \text{C}_{28}\text{H}_{37}\text{BO}_2 \ [M+H]^+\ & 393.2964, \text{ found 393.2949, } [\text{M+Na}^+]\ & 415.2783, \text{ found 415.2766.}\end{align*}\]

Resolution of the enantiomers of 18ga was achieved using a chiral SFC system fitted with a Chiracel Whelk-01 column as the stationary phase with CO\(_2\):n-hexane as the mobile phase at
a flow rate of 2.0 mL min\(^{-1}\) \((P = 125\) bar\). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component \((S)\) and the slower running component \((R)\) were eluted at 18.0 and 19.0 min., respectively, with an analysis time of 25 min.

**1,3-dimethyl-5-(2-phenylbutan-2-yl)benzene (18h)**

A solution of 3,5-dimethylbromobenze (115 \(\mu\)L, 0.85 mmol, 1.1 eq.) in THF (3.0 mL) was cooled to −78 °C and treated with \(t\)-BuLi (1.0 mL, 1.69 mmol, 2.2 eq., 1.7 M in hexanes). The mixture was stirred at −78 °C for 1 h and then a solution of 1h (200 mg, 1.54 mmol, 1.0 eq.) in THF (2.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex \([\text{\(^{11}\)B NMR, 96 MHz, THF}] \delta_{B} \sim 8 \text{ ppm}\]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (5.0 mL) and the mixture was cooled to −78 °C. A solution of NBS (274 mg, 1.92 mmol, 2.0 eq.) in MeOH (5.0 mL) was added dropwise and the reaction mixture was warmed to r.t. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 \times 15 mL) and the combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (5.0 mL) and \(p\)-toluenesulfonic acid (366 mg, 1.92 mmol, 2.5 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of NaHCO\(_3\) (2 mL) was added. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (5 mL). The aqueous layer was extracted with EtOAc (2 \times 15 mL), the combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with pentane gave 18h (43 mg, 24%) as an oil; \(R_f\) 0.17 (pentane); IR (film): \(\nu\) (cm\(^{-1}\)) 2967, 2922, 2877, 1599, 1494, 1445, 765, 698; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) ppm 7.34–7.13 (m, 5H), 6.83 (s, 3H), 2.28 (s, 6H), 2.14 (q, \(J = 7.3\) Hz, 2H), 1.60 (s, 3H), 0.75 (d, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (76 MHz, CDCl\(_3\)) \(\delta\) ppm 149.8, 149.6, 137.0, 127.8, 127.4, 127.2, 125.3, 125.3, 46.3, 34.0, 26.9, 21.5, 9.2; HRMS (EI) calcd. for C\(_{18}\)H\(_{22}\) [\(M\)\(^+\)] 238.1722, found 238.1714.
A solution of 3-bromotoluene (14 µL, 0.12 mmol, 1.1 eq.) in THF (0.5 mL) was cooled to –78 °C and treated with t-BuLi (0.13 mL, 0.23 mmol, 2.2 eq., 1.7 M in pentane). The mixture was stirred at –78 °C for 1 h and then a solution of (R)-Ig (30 mg, 0.1 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [(${}^{11}$B NMR, 96 MHz, THF) $\delta_B$ ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was redissolved in MeOH (2.0 mL) and the mixture was cooled to –78 °C. A solution of NBS (44 mg, 0.25 mmol, 2.4 eq.) in MeOH (2.0 mL) was added dropwise. After 1 h the reaction mixture was diluted with pentane (15 mL) and washed with water (15 mL). The aqueous layer was extracted with pentane (2 x 15 mL) and the combined organic layers were dried (MgSO$_4$), filtered and concentrated under vacuum. The residue was dissolved in 2,2,2-trifluoroethanol (3.0 mL) and p-toluenesulfonic acid (49 mg, 0.26 mmol, 2.5 eq.) was added. The reaction mixture was heated under reflux for 3 h. The reaction was cooled to r.t. and saturated aqueous solution of NaHCO$_3$ (2 mL) was added. The reaction mixture was diluted with EtOAc (15 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography on silica gel eluting with pentane:Et$_2$O (95:5), gave (0.10 mmol scale), (S)-19g (12 mg, 46%) as an oil; er (S:R) 99:1; $R_f$ 0.86 (petrol:Et$_2$O 97.5:2.5); $[\alpha]_{D}^{23}$ – 1 (c 0.3, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 3026, 2964, 2926, 1604, 1496, 1454, 705, 699; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.27–7.19 (m, 3H), 7.18–7.07 (m, 5H), 7.01 (d, $J = 7.3$ Hz, 1H), 2.44 (dt, $J = 13.1$, 4.3 Hz, 1H), 2.37 (s, 3H), 2.26 (dt, $J = 12.9$, 4.3 Hz, 1H), 2.01 (dt, $J = 13.1$, 4.3 Hz, 1H), 1.83 (dt, $J = 12.9$, 5.0 Hz, 1H), 1.77 (dq, $J = 14.7$, 7.3 Hz, 1H), 1.61 (dq, $J = 14.7$, 7.3 Hz, 1H), 1.35 (s, 3H), 0.71 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 147.3, 143.3, 137.4, 128.2, 127.9, 127.2, 126.1, 125.5, 123.5, 45.1, 41.1, 35.6, 30.9, 23.4, 21.8, 8.7; HRMS (EI) calcd. for C$_{19}$H$_{24}$ [M]$^+$ 252.1878, found 252.1876.

Resolution of the enantiomers of 19g was achieved using a chiral HPLC system fitted with a Chirapak IB column as the stationary phase with n-heptane as the mobile phase at a flow rate of 0.5 mL min$^{-1}$. Injection volume: 2 µL of a 2 g L$^{-1}$ solution of the eluent. Under these
conditions, the faster running component (S) and the slower running component (R) were eluted at 12.4 and 12.8 min., respectively, with a total analysis time of 20 min.

(S)-2-methoxy-6-(3-methyl-1-phenylpentan-3-yl)pyridine [(S)-20g]

A solution of 2-bromo-6-methoxypyridine (0.17 μL, 0.14 mmol, 1.3 eq.) in THF:EtO:pentane (4:1:1, 0.3 M) was cooled to −78 °C and treated with n-BuLi (0.2 mL, 0.14 mmol, 1.3 eq., 1.6 M in hexanes) and the mixture was stirred at this temperature for 30 min. (R)-1g (30 mg, 0.1 mmol, 1.0 eq.) was added dropwise as a solution in THF (0.5 mL). The mixture was stirred at −78 °C for 30 min at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex $^{11}$B NMR (96 MHz, THF) δB ~ 8 ppm. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeOH (2 mL) and the mixture was cooled to 0 °C. A solution of DBDMH (74 mg, 0.26 mmol, 2.0 eq.) in MeOH (3.0 mL) was added dropwise. After 1 h at 0 °C saturated aqueous solution of Na$_2$S$_2$O$_3$ was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with EtOAc (15 mL) and water (15 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. The crude material was adsorbed on silica and purified by flash column chromatography on silica gel eluting with n-hexane to give (0.10 mmol scale), (S)-20g (17 mg, 60%) as an oil; er (S:R) 99:1; $R_t$ 0.59 (pentane:EtO 97:5:2.5); $[\alpha]_D^{23}$ -1 (c 1.5, CHCl$_3$); IR (film): ν (cm$^{-1}$) 2964, 2926, 1580, 1461, 1408, 1256, 1029, 801, 742, 698; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 7.52 (t, J = 7.7 Hz, 1H), 7.28–7.22 (m, 2H), 7.19–7.10 (m, 3H), 6.86 (d, J = 7.7 Hz, 1H), 6.56 (d, J = 7.7 Hz, 1H), 3.94 (s, 3H), 2.47 (dt, J = 12.8, 3.8 Hz, 1H), 2.30–2.18 (m, 2H), 1.92 (m, 1H), 1.85 (dt, J = 12.8, 3.8 Hz, 1H), 1.65 (m, 1H), 1.37 (s, 3H) 0.73 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 164.6, 162.9, 143.5, 138.3, 128.2, 128.2, 125.4, 113.5, 107.1, 53.0, 43.8, 43.6, 34.4, 31.0, 22.4, 8.7; HRMS (ESI) calcd. for C$_{18}$H$_{24}$NO [M+H]$^+$ 270.1852, found 270.1842.

Resolution of the enantiomers of 20g was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with [$n$-heptane:MTBE (98:2, v:v)] as the mobile phase at a flow rate of 0.5 mL min$^{-1}$ ($T = 0$ °C). Injection volume: 2 μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component
(S) and the slower running component (R) were eluted at 11.3 and 11.8 min., respectively, with a total analysis time of 30 min.

8. Reaction products – B(pin) incorporation

(S)-2-(2,4-dimethoxy-6-(4-(4-methoxyphenyl)butan-2-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-9ba]

A solution of 3,5-(dimethoxy)bromobenze (65 mg, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min and then a solution of (S)-1b (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 11B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeCN (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na2S2O3 (2 mL) was added. After 2 min. the reaction mixture was allowed to warm up to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried MgSO4, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:EtOAc (95:5) gave (S)-9ba (41 mg, 38%) as an oil; er (S:R) 95:5; Rf 0.22 (petrol:Et2O 90:10); [α]D25 = 25 (c 0.8, CHCl3); IR (film): ν (cm−1) 2961, 2928, 2852, 1601, 1511, 1330, 1243, 1199, 1142, 1034, 857, 829, 698; 1H NMR (400 MHz, CDCl3) δ ppm; 7.10–7.05 (m, 2H), 6.83-6.78 (m, 2H), 6.39 (d, J = 2.0 Hz, 1H), 6.25 (d, J = 2.0 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 2.76 (sx, J = 6.9 Hz, 1H), 2.60-2.40 (m, 2H), 1.96 (m, 1H), 1.87 (m, 1H), 1.35 (s, 6H), 1.34 (s, 6H), 1.26 (d, J = 6.9 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ ppm 163.9, 162.1, 157.5, 153.6, 134.9, 129.2, 113.6, 102.2, 95.0, 83.53, 55.4, 55.2, 55.1, 39.8, 39.7, 33.1, 29.7, 24.8, 24.6, 22.6; 11B NMR (96 MHz, NONE) δ ppm 31.7; HRMS (EI) calcd. for C25H33BO5 [M]+ 426.2578, found 426.2563.

Resolution of the enantiomers of 9ba was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO2:[n-hexane:i-PrOH (9:1, v:v)] as the
mobile phase at a flow rate of 4.0 mL min\(^{-1}\) \((P = 125\) bar\). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of the eluent. Under these conditions, the faster running component \((S)\) and the slower running component \((R)\) were eluted at 5.2 and 7.8 min., respectively, with a total analysis time of 15 min.

\((S)-2-(4\text{-methoxy}-2-(4\text{-methoxyphenyl})\text{butan}-2\text{-yl})\text{phenyl})-4,4,5,5\text{-tetramethyl-1,3,2-dioxaborolane} [\((S)-11\text{ba-major}\)]

A solution of 3-bromoanisole (56 mg, 0.30 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to \(-78\) °C and treated with \(t\)-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at \(-78\) °C for 1 h and then a solution of \((S)-1\text{b} \) (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at \(-78\) °C for 1 h at which point \(^{11}\text{B}\) NMR spectroscopy showed complete formation of the ‘ate’ complex \([\text{\(^{11}\text{B}\) NMR, 96 MHz, THF} \delta_{B} \approx 8 \text{ ppm}]\). The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeCN (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na\(_2\)S\(_2\)O\(_3\) (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with \(n\)-hexane:EtOAc (95:5) gave \((S)-11\text{ba-major} \) (40 mg, 40%) as an oil; er \((S:R)\) 96:4; \(R_f\) 0.21 (petrol:Et\(_2\)O 95:5); \([\alpha])_{D}^{23} = -20\) (c 1, CHCl\(_3\)); IR (film): \(\nu\) (cm\(^{-1}\)) 2974, 2931, 2837, 1600, 1511, 1347, 1243, 1144, 1029, 859, 817, 659; \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.75 (d, \(J = 8.3\) Hz, 1H), 7.08–7.03 (m, 2H), 6.87 (d, \(J = 2.4\) Hz, 1H), 6.83–6.77 (m, 2H), 6.73 (dd, \(J = 8.3, 2.4\) Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.65 (sx, \(J = 7.0\) Hz, 1H), 2.56 (m, 1H), 2.47 (m, 1H), 1.91 (m, 1H), 1.81 (m, 1H), 1.32 (s, 6H), 1.31 (s, 6H), 1.27 (d, \(J = 7.0\) Hz, 3H); \(^{13}\text{C NMR} \) (100 MHz, CDCl\(_3\)) \(\delta\) ppm 162.0, 157.5, 156.7, 137.8, 135.2, 129.1, 113.6, 111.4, 109.8, 83.1, 55.2, 55.0, 40.8, 36.4, 33.2, 30.9, 24.9, 24.8, 22.4; \(^{11}\text{B}\) NMR (96 MHz, NONE) \(\delta\) ppm 30.4; HRMS (ESI) calcd. for C\(_{24}\)H\(_{34}\)BO\(_4\) \([M+H]^+\) 397.2549, found 397.2537.

Resolution between the enantiomers of \(11\text{ba-major}\) was achieved using a chiral SFC system fitted with a Chiracel Whelk-01 column as the stationary phase with CO\(_2\):\(n\)-hexane:i-PrOH
(9:1 v:v)] as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) (\(P = 125\) bar). Injection volume: 10\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running component (\(R\)) and the slower running component (\(S\)) were eluted at 33.5 and 35.0 min., respectively, with a total analysis time of 45 min.

(S)-2-(2-methoxy-6-(4-(4-methoxyphenyl)butan-2-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-11ba-minor]

A solution of 3-bromoanisole (56 mg, 0.30 mmol, 1.2 eq.) in THF (2.5 mL) was cooled to \(-78\) °C and treated with \(t\)-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at \(-78\) °C for 1 h and then a solution of (\(S\))-1b (50 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at \(-78\) °C for 1 h at which point \(^{11}\)B NMR spectroscopy showed complete formation of the ‘ate’ complex [(\(^{11}\)B NMR, 96 MHz, THF) \(\delta_B \sim 8\) ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:\(i\)-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeCN (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na\(_2\)S\(_2\)O\(_3\) (2 mL) was added. After 2 min the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO\(_4\), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:EtOAc (95:5) gave (\(S\))-11ba-minor (15 mg, 15%) was obtained as an oil; er (\(S:\(R\)) 96:4; \(R_f\) 0.15 (petrol:Et\(_2\)O 9:1); \([\alpha]_D^{23} = -58\) (c 0.5, CHCl\(_3\)); IR (film): \(\nu\) (cm\(^{-1}\)) 2987, 2972, 2901, 1511, 1372, 1248, 1074, 855; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.28 (t, \(J = 7.9\) Hz, 1H), 7.10–7.03 (m, 2H), 6.86 (d, \(J = 7.9\) Hz, 1H), 6.83–6.87 (m, 2H), 6.66 (d, \(J = 7.9\) Hz, 1H), 3.78 (s, 6H), 2.72 (sx, \(J = 7.0\) Hz, 1H), 2.59–2.40 (m, 2H), 1.98 (m, 1H), 1.83 (m, 1H), 1.37 (s, 6H), 1.36 (s, 6H), 1.27 (d, \(J = 7.0\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 162.4, 157.5, 152.2, 134.9, 130.5, 129.2, 117.5, 113.6, 107.1, 83.8, 55.4, 55.2, 39.8, 39.7, 33.1, 24.8, 24.7, 22.7; \(^{11}\)B NMR (96 MHz, NONE) \(\delta\) ppm 32.8; HRMS (ESI) calcd. for C\(_{24}\)H\(_{34}\)BO\(_4\) [\(M+H\)]\(^+\) 397.2549, found 397.2541.

Resolution of the enantiomers of 11ba-minor was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO\(_2\)\([\eta\text{-hexane:}\(i\)-PrOH (1:1, v:v)] as the mobile phase at a flow rate of 4.0 mL min\(^{-1}\) (\(P = 125\) bar). Injection volume: 20\(\mu\)L of a 2 g L\(^{-1}\) solution of compound in the eluent. Under these conditions, the faster running
component (S) and the slower running component (R) were eluted at 5.7 and 7.3 min., respectively, with a total analysis time of 15 min.

(S)-2-(1-(4-(4-methoxyphenyl)butan-2-yl)naphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-15ba]

A solution of 1-bromonaphthalene (42 μL, 0.30 mmol, 1.2 eq.) in Et₂O (1.0 mL) was cooled to 0 °C and n-BuLi (0.19 mL, 0.30 mmol, 1.2 eq., 1.6 M in hexanes) was added dropwise. The mixture was stirred at 0 °C for 1 h. (S)-1b (72 mg, 0.25 mmol, 1.0 eq.) was added and the mixture was stirred at 0 °C for 1 h at which point ¹¹B NMR spectroscopy showed complete formation of the ‘ate’ complex [(¹¹B NMR, 96 MHz, THF) δB ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude residue was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (128 mg, 0.72 mmol, 2.4 eq.) in MeCN (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na₂S₂O₃ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et₂O (95:5) gave (S)-15ba (75 mg, 72%) as an oil; er (S:R) 95:5; Rf 0.23 (petrol:Et₂O 95:5); [α]D²⁴ – 25 (c 0.3, CHCl₃) IR (film): ν (cm⁻¹) 2987, 2972, 2901, 1393, 1249, 1075, 1066, 878; ¹H NMR (500 MHz, DMSO, 90 °C) δ ppm 8.28 (m, 1H), 7.92 (m, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.56–7.50 (m, 2H), 7.07-7.02 (m, 2H), 6.85–6.80 (m, 2H), 3.95 (sX., J = 7.2 Hz, 1H), 3.75 (s, 3H), 2.63 (dt, J = 13.9, 7.8 Hz, 1H), 2.40 (dt, J = 13.9, 7.8 Hz, 1H), 2.26 (q, J = 7.8 Hz, 2H), 1.57 (d, J = 7.2 Hz, 3H), 1.40 (s, 6H), 1.39 (s, 6H); ¹³C NMR (126 MHz, DMSO, 90 °C) δ ppm 158.0, 149.8, 135.4, 134.6, 131.5, 130.7, 129.4, 129.3, 126.3, 125.9, 125.7, 114.4, 84.2, 55.6, 55.6, 39.6, 34.0, 25.1, 21.6; ¹¹B NMR (96 MHz, NONE) δ ppm 30.7; HRMS (ESI) calcd. for C₂₇H₃₃BNaO₃ [M+Na]⁺ 439.2415, found 439.2406.

Resolution of the enantiomers of 15ba was achieved using a chiral SFC system fitted with a Chiracel IA column as the stationary phase with CO₂:[n-hexane:i-PrOH (1:1, v:v)] as the mobile phase at a flow rate of 4.0 mL min⁻¹ (P = 125 bar). Injection volume: 20μL of a 2 g L⁻¹ solution of compound in the eluent. Under these conditions, the faster running component
(R) and the slower running component (S) were eluted at 10.3 and 11.5 min., respectively, with a total analysis time of 15 min.

(S)-2-(2,4-dimethyl-6-(4-phenylbutan-2-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-18aa]

A solution of 3,5-(dimethyl)bromobenzene (41 mg, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min and then a solution of (S)-1a (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point 

$^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [(11B NMR, 96 MHz, THF) $\delta_B \approx 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (107 mg, 0.6 mmol, 2.4 eq.) in MeCN (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (9:1) gave (S)-18aa (82 mg, 90%) as an oil; er (R:S) 95:5; $R_f$ 0.38 (petrol:Et$_2$O 9:1); [$\alpha$]$_D^{21}$ $\approx$ −36 (c 1, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2981, 2931, 2850, 1327, 1296, 1141, 1060, 855, 697, 685.; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.29–7.22 (m, 2H), 7.20–7.12 (m, 3H), 6.89 (s, 1H), 6.81 (s, 1H) 2.88 (sx, $J = 7.1$ Hz, 1H), 2.63 (m, 1H), 2.51(m, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 2.08–1.95 (m, 1H), 1.92–1.79 (m, 1H), 1.36 (s, 12H), 1.28 (d, $J = 7.1$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm; 151.3, 142.9, 141.1, 138.9, 128.3, 128.2, 127.8, 125.5, 122.5, 83.6, 39.8, 39.3, 34.2, 25.1, 25.0, 22.9, 22.1, 21.5; $^{11}$B NMR (96 MHz, NONE) $\delta$ ppm 31.6; HRMS (ESI) calcd. for C$_{24}$H$_{33}$BO$_2$ [M+H]$^+$ 365.2651, found 365.2642.

Resolution of the enantiomers of 18aa was achieved using a chiral HPLC system fitted with a Chiralpak IB column with guard as the stationary phase with n-hexanes the mobile phase at a flow rate of 1.0 mL min$^{-1}$ ($T = 0$ °C). Injection volume: 2 µL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 38.4 and 48.8 min., respectively, with a total analysis time of 70 min.
(S)-2-(2,4-dimethoxy-6-(3-methyl-1-phenylpentan-3-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(S)-9ga]

A solution of 3,5-(dimethoxy)bromobenze (65 mg, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 30 min. and then a solution of (R)-1g (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) $\delta_B \sim 8$ ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (45 mg, 0.25 mmol, 1.0 eq.) in MeCN (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:EtOAc (95:5) gave (S)-9ga (48 mg, 46%) as an oil; er (S:R) 99:1; $R_f$ 0.32 (petrol:Et$_2$O 65:35); [$\alpha$]$^D_{23}$ – 3 (c 0.1, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2973, 2931, 1599, 1569, 1453, 1325, 1293, 1141, 1041, 856, 698 $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm; 7.25–7.18 (m, 4H), 7.16–7.10 (m, 1H), 6.52 (d, $J = 2.0$ Hz, 1H), 6.30 (d, $J = 2.06$ Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 2.42 (dt, $J = 13.1$, 4.6 Hz, 1H), 2.29 (dt, $J = 13.1$, 4.6 Hz, 1H), 2.16 (dt, $J = 13.1$, 4.6 Hz, 1H), 1.90 (m, 1H), 1.74 (dt, $J = 13.1$, 4.6 Hz, 1H), 1.59 (m, 1H), 1.40 (s, 3H), 1.37 (s, 6H), 1.36 (s, 6H), 0.71 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 164.5, 161.0, 153.3, 143.5, 128.6, 128.0, 125.3, 106.1, 94.2, 83.6, 55.4, 55.1, 45.6, 43.2, 36.0, 31.1, 25.1, 24.9, 24.2, 8.7; $^{11}$B NMR (96 MHz, NONE) $\delta$ ppm 30.4; HRMS (EI) calcd. for C$_{26}$H$_{37}$BO$_4$ [M$^+$] 424.2421, found 424.2427.

Resolution of the enantiomers of 9ga was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO$_2$:n-hexane:i-PrOH (9:1 v:v) as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20µL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 5.8 and 6.8 min., respectively, with a total analysis time of 15 min.
A solution of 3,5-(dimethyl)bromobenzene (41 mg, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to −78 °C and treated with t-BuLi (0.35 mL, 0.60 mmol, 2.4 eq., 1.7 M in pentane). The mixture was stirred at −78 °C for 1 h and then a solution of (R)-1g (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at −78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [$^{11}$B NMR, 96 MHz, THF] $\delta_B \sim 8$ ppm. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (107 mg, 0.6 mmol, 2.4 eq.) in MeCN (2.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried over MgSO$_4$, filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (9:1) gave (S)-18ga (81 mg, 83%) as an oil $R_f$ 0.3 (pentane:Et$_2$O 95:5); IR (film): $\nu$ (cm$^{-1}$) 2975, 2927, 1607, 1453, 1372, 1324, 1295, 1180, 1159, 1059, 855, 699, 684, 745; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.25–7.21 (m, 2H), 7.20–7.17 (m, 2H), 7.13 (m, 1H) 7.11 (tt, $J = 7.2$, 1.5 Hz, 1H), 6.96 (m, 1H), 6.82 (br s, 1H), 2.41 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.26 (dt, $J = 13.0$, 4.5 Hz, 1H), 2.20 (dt, $J = 13.0$, 4.5 Hz, 1H ), 1.93 (dq, $J = 14.4$, 7.4 Hz, 1H), 1.78 (dt, $J = 13.5$, 4.5 Hz, 1H), 1.65 (dq, $J = 14.4$, 7.4 Hz, 1H), 1.43 (s, 3H), 1.40 (s, 6H), 1.38 (s, 6H), 0.72 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 150.5, 143.7, 140.8, 137.4, 128.6, 128.0, 127.5, 125.3, 125.2, 83.7, 45.4, 42.9, 35.8, 31.2, 25.8, 25.6, 24.8, 22.50 21.6, 8.8.; $^{11}$B NMR (96 MHz, CDCl$_3$) $\delta$ ppm 31.2; HRMS (ESI) calcd. for C$_{26}$H$_{37}$BO$_2$ [M+H]$^+$ 393.2964, found 393.2949. Resolution of the enantiomers of 18ga was achieved using a chiral SFC system fitted with a Chiracel Whelk-01 column as the stationary phase with CO$_2$:n-hexane as the mobile phase at a flow rate of 2.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 20μL of a 2 g L$^{-1}$ solution of compound in the eluent. Under these conditions, the faster running component (S) and the slower running component (R) were eluted at 18.0 and 19.0 min., respectively, with a total analysis time of 25 min.
A solution of benzothiophene (35 μL, 0.30 mmol, 1.2 eq.) in THF (2.0 mL) was cooled to –78 °C and treated with t-BuLi (0.2 mL, 0.30 mmol, 1.2 eq., 1.6 M in hexane). The mixture was stirred at –78 °C for 1 h and then a solution of (R)-1b (72 mg, 0.25 mmol, 1.0 eq.) in THF (1.0 mL) was added. The mixture was stirred at –78 °C for 1 h at which point $^{11}$B NMR spectroscopy showed complete formation of the ‘ate’ complex [($^{11}$B NMR, 96 MHz, THF) δ$_B$ ~ 8 ppm]. The mixture was warmed to r.t. and the solvents were removed under high vacuum. The crude was re-dissolved in MeCN:i-PrOH (1:1, 2 mL) and the mixture was cooled to 0 °C. A solution of NBS (53 mg, 0.3 mmol, 1.2 eq.) in MeCN (1.0 mL) was added dropwise. After 1 h saturated aqueous solution of Na$_2$S$_2$O$_3$ (2 mL) was added. After 2 min. the reaction mixture was allowed to warm to r.t. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (15 mL). The aqueous layer was extracted with EtOAc (2 x 15 mL), the combined organic layers were dried (MgSO$_4$), filtered and concentrated under vacuum. Purification by flash column chromatography eluting with n-hexane:Et$_2$O (9:1) gave (R)-8ba (48 mg, 46%) as an oil; er (R:S) 96:4; $R_f$ 0.21 (petrol:Et$_2$O 95:5); [$a]_D^{23}$ – 39 (c 1, CHCl$_3$); IR (film): $\nu$ (cm$^{-1}$) 2973, 2921, 1511, 1456, 1370, 1234, 1142, 762; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm; 8.33 (br d, $J = 8.0$ Hz, 1H), 7.77 (br d, $J = 8.0$ Hz, 1H), 7.34 (m, 1H), 7.27 (m, 1H), 7.10–7.04 (m, 2H), 6.83–6.76 (m, 2H), 4.01 (sx, $J = 7.0$ Hz, 1H), 3.77 (s, 3H), 2.66–2.45 (m, 2H), 2.01–1.90 (m, 2H), 1.39 (d, $J = 7.0$ Hz, 3H), 1.37 (s, 6 H), 1.36 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 167.51, 157.73, 144.27, 139.10, 134.72, 129.32, 125.12, 124.16, 123.43, 121.78, 113.78, 83.17, 55.33, 41.96, 35.50, 33.23, 25.08, 24.99, 24.17; HRMS (ESI) calcd. for C$_{25}$H$_{32}$BO$_3$S [M+H]$^+$ 423.2165, found 423.2186.

Resolution of the enantiomers of 8ba was achieved using a chiral SFC system fitted with a Chiracel IB column as the stationary phase with CO$_2$:[$n$-hexane:i-PrOH (9:1, v:v)] as the mobile phase at a flow rate of 4.0 mL min$^{-1}$ ($P = 125$ bar). Injection volume: 10μL of a 2 g L$^{-1}$ solution of the eluent. Under these conditions, the faster running component (R) and the slower running component (S) were eluted at 14.3 and 19.0 min., respectively, with a total analysis time of 25 min.
9. React-IR studies

The following reaction was studied with use of React-IR:

![Reaction diagram]

Experimental procedure:

A three-neck round bottom flask equipped with a stirring bar was connected to the React-IR probe, evacuated and refilled with N₂ (x 3). The flask was charged with 3,5-(dimethoxy)bromobenzene (50 mg, 0.23 mmol, 1.2 eq.) and evacuation/refilling procedure was repeated (x3). THF (2.0 mL) was added and the solution was cooled to −78 °C. The background spectrum was acquired. t-BuLi (0.27 mL, 0.46 mmol, 2.4 eq., 1.7M in pentane) was added dropwise and the reaction mixture was stirred for 30 min. The peak at 1379 cm⁻¹ was selected to follow organolithium species. The solution of boronic ester 1a (50 mg, 0.19 mmol, 1.0 eq.) in THF (1.0 mL) was added (slow addition is necessary to avoid signal fluctuation) and the reaction mixture was stirred for 30 min. At this point, the development of new species was observed immediately. The new peak at 1512 cm⁻¹ was attributed to the 'ate' complex xx and its presence was confirmed by ¹¹B-NMR analysis of a reaction aliquot (δB ~ 8 ppm). React-IR instrument was switched off. The reaction mixture was allowed to warm to r.t and the solvent was removed under high vacuum. The crude was re-dissolved in MeOH (2.0 mL) and the resulting solution was cooled to −78 °C. The React-IR instrument was switched on and the spectrum of 'ate' complex in MeOH −78 °C recorded. The peak at 1583 cm⁻¹ was selected to follow the 'ate' complex ate-9a. The solution of NBS (34 mg, 0.19 mmol, 1.0 eq.) in MeOH (3.0 mL) was added slowly. Two peaks: 1712 cm⁻¹ and 1570 cm⁻¹ appeared rapidly and were attributed to succinimide and the product 9a, respectively. The diagnostic peak for 9a was confirmed by preparing the compound separately and recording a React-IR spectrum in MeOH. Et₂O and water were added to the reaction mixture at −78°C and warmed to ambient temperature. The layers were separated and the aqueous phase was extracted with Et₂O (x 2). The combined organic layers were dried over MgSO₄ and the solvent was removed under vacuum. ¹H NMR spectroscopy analysis of the crude revealed complete formation of 9a.
Figure 1. Formation of 3,5-dimethoxyaryllithium.
Figure 2. Formation of ‘ate’ complex 26.
Figure 3. Product formation upon addition of N-Bromosuccinimide.

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10. DFT calculations

**General.** Calculations were performed with the GAUSSIAN 09 suite of programs.\(^{21}\) Density Functional Theory (DFT) was applied by the means of the B3LYP hybrid functional\(^{22}\) corrected for dispersion as proposed by Grimme (D2 correction).\(^{23}\) The 6-31+G(d) basis set was used for all atoms. Geometry optimizations were performed without any symmetry constraints. The stationary points were characterized by full vibration frequencies calculations. Gibbs free energies at 195 K were obtained from the standard enthalpies and entropies computed at 298 K in Gaussian based on the rigid rotor harmonic oscillator approach to statistical mechanics. Also, Gibbs energies were corrected to take into account a standard state corresponding to species in solution at a concentration of 1 M. To do this, we used the correction: 

\[G^{1M} = G^{1atm} + RT \ln(C^{1M}/C^{1atm})\]

where \(G^{1atm}\) is the Gibbs free energy at 195 K, \(C^{1M}\) is the assumed concentration in solution and \(C^{1atm}\) is the gas phase concentration (\(C^{1atm} = 1/V_m = P/RT = 0.0409 \text{ mol.L}^{-1}\) for an ideal gas at 195.15 K and 1 atm). Solvent effects (thf or MeOH) were included by means of SMD single point calculations on the gas-phase optimized structures.\(^{24}\) Gibbs free energies in solution were estimated as: 

\[G^{thf} = G^{1M} + E^{thf} - E^{gas\ phase}\]

The counter-cation was not explicitly included in the calculations as it is not expected to actively participate in the reaction.

**Results.** We chose to focus our computational work on the reactivity of furan-, thiophene- and phenyl-substituted boronate complexes. In order to avoid unnecessary conformational issues, we considered model complexes (Scheme 1).

---


Scheme 1. Complexes under study.

Reaction with NBS

\[
\text{Scheme 2. Proposed mechanistic scheme based on DFT calculations.}
\]

\[
\text{Reaction with DDQ. The calculated potential energy surface for Path C (Scheme 3) involves initial formation of a strongly bound encounter complex - or “charge-transfer” complex. It then involves nucleophilic addition of the boronate to DDQ followed by migration of the alkyl group from boron to carbon. The resulting species can undergo facile elimination of the DDQ and boronate moieties. The migration step is computed to be highly exothermic (} \Delta G_{\text{mig}}^0 \text{ ranges from -39.0 to -40.6 kcal.mol}^{-1} \text{ depending on the position of the attack), so that the backward reaction is not expected to compete with the subsequent elimination step. Mayr recently showed that addition of a } \pi \text{-nucleophile to DDQ can occur either through C or O}
\]

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attack. Based on our calculations, we predict that both of these processes should be very fast at -78 °C (ΔG^‡_{add} = 3.7 kcal.mol⁻¹ for C attack and ΔG^‡_{add} = 6.8 kcal.mol⁻¹ for O attack). C attack appears to be kinetically favored but thermodynamically disfavored, in agreement with Mayr’s experimental observations. The apparent second-order rate constant for aromatic electrophilic substitution (k_C) is given by

\[
\frac{1}{k_C} = \frac{1}{k_{diff}} + \frac{1}{K_{CT}k_{add}}
\]

where \(k_{diff}\) is the rate constant for diffusion under the experimental conditions (\(k_{diff} \approx (BRT)/(3\eta) = 2 \times 10^9\) M⁻¹.s⁻¹ in THF at -78 °C), \(K_{CT}\) is the equilibrium constant for formation of the encounter complex and \(k_{add}\) is the first-order rate constant for electrophilic addition within the charge-transfer complex.

Scheme 3. Computed free energy surfaces for Path C (B3LYP-D2) for 24.

Computed first- and second-order rate constants for nucleophilic addition of selected boronate complexes to DDQ are summarized below.


26 http://ddbonline.ddbst.de/VogelCalculation/VogelCalculationCGI.exe (accessed the 24/06/2016).
In both cases, the second order rate constant for C attack is found to be equal to $k_{diff}$, owing to the exothermicity of the formation of the encounter complex ($K_{CT} = 10^5-10^7$ M$^{-1}$). On another hand, the first-order rate constant is computed to be significantly slower in the case of the less nucleophilic thiophene-substituted boronate complex.

The calculated potential energy surface for Path D first involves the formation of the encounter complex. This initial step is followed by single electron transfer from the boronate moiety to the DDQ moiety of the complex, which occurs with a rate constant $k_{ET}$. DFT calculations have revealed that single-electron oxidation of 24 occurs by removing an electron from the $\sigma$ C–B bond. The SOMO of the resulting neutral radical complex (single point calculation at the optimized geometry of 24) is indeed predominantly localized on the boronate moiety, with only very small coefficients on the furan ring (below, left). As one might expect, this molecular orbital corresponds to the HOMO of 24 (below, right). Geometry optimization of the neutral radical complex accordingly led to C–B bond breaking and generated a carbon-centred radical intermediate and the corresponding boronic ester. A relaxed scan along the C-B distance showed that this process is barrierless.

<table>
<thead>
<tr>
<th></th>
<th>$K_{CT}$ (M$^{-1}$)</th>
<th>$\Delta G_{add}^\ddagger$ (kcal.mol$^{-1}$)</th>
<th>$k_{add}$ (s$^{-1}$)</th>
<th>$k_C$ (M$^{-1}$.s$^{-1}$)</th>
<th>$\Delta G_{C}^\ddagger$ (kcal.mol$^{-1}$)</th>
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<td>Ia</td>
<td>C attack</td>
<td>3.4 10$^7$</td>
<td>3.7 10$^8$</td>
<td>2 10$^9$</td>
<td>2.9</td>
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<tr>
<td></td>
<td>O attack</td>
<td>6.8 10$^5$</td>
<td>1 10$^5$</td>
<td>2 10$^9$</td>
<td>2.9</td>
</tr>
<tr>
<td>Ic</td>
<td>C attack</td>
<td>6.4 10$^5$</td>
<td>6.9 10$^4$</td>
<td>2 10$^9$</td>
<td>2.9</td>
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<td></td>
<td>O attack</td>
<td>11.8 2 10$^{-1}$</td>
<td>2 10$^5$</td>
<td>6.6</td>
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</tbody>
</table>

It is possible to connect path D to path C, by locating a transition state associated with addition of the radical formed upon single electron transfer to the boronic ester, as shown in Scheme 4. This transition state lies 12.6 kcal.mol$^{-1}$ above the separated radical and boronic
ester in solvated free energy. This suggests that addition of the radical would be relatively slow, so that this intermediate would be long-lived enough to racemize. Hence this mechanism is inconsistent with (i) the observed stereospecific coupling and (ii) the retention of the cyclopropane unit in some cases.

Scheme 4. Computed free energy surface for Path D (B3LYP-D2) for 24.

The rate constant $k_{ET}$ was calculated using Marcus-Savéant theory. In this theory, the free energy of activation ($\Delta G^*$) for a concerted dissociative electron transfer is given by

$$\Delta G^* = \frac{\lambda_0 + BDE}{4} \left(1 + \frac{\Delta G^0}{\lambda_0 + BDE}\right)^2$$

where $\lambda_0$ is the solvent reorganization energy, $BDE$ is the dissociation energy of the C-B bond and $\Delta G^0$ is the standard free energy of the reaction. The solvent reorganization energy was estimated using Marcus’ equation

$$\lambda_0 = \Delta e^2 \left(\frac{1}{\epsilon_{opt}} - \frac{1}{\epsilon_s}\right) \left(\frac{1}{2a_1} + \frac{1}{2a_2} - \frac{1}{R}\right)$$

where $\epsilon_{opt}$ and $\epsilon_s$ are the optical and static dielectric constants of the solvent ($\epsilon_{opt} = 1.97$ and $\epsilon_s = 7.52$ for THF). $\Delta e$ is the amount of charge transferred (here, 1 atomic unit of charge), $a_1$ is the radius of the donor (boronate complex) $a_2$ is the radius of the acceptor (DDQ) and $R$ is the radius of the charge transfer complex. The radii were obtained based on single-point B3LYP calculations as implemented in Gaussian (using the keyword “volume”, which requests that the molecular volume, i.e. the volume enclosed by an electron isodensity surface with the value 0.001 electrons/Bohr$^3$, be computed, derives the corresponding radius assuming that the species is a sphere and adds 0.5 Å). The bond dissociation energy was calculated as the difference, in solvated energy, between the boronate complex and the two fragments resulting from the homolytic cleavage of the C-B bond in their relaxed geometries ([furane-B(pin)]$^-$ and [R]$^-$).

$$BDE = E^{thf}([B]^-) + E^{thf}([R]^+) - E^{thf}([B-R]^-)$$

Finally, the standard free energy of the reaction was calculated as the difference, in solvated free energy, between the initial diabatic state (boronate complex + DDQ) and the final diabatic state ([furane-B(pin)] + [R]$^+$ + [DDQ]$^-$).

<table>
<thead>
<tr>
<th>$a_1$ (Å)</th>
<th>$a_2$ (Å)</th>
<th>$R$ (Å)</th>
<th>$\lambda_0$</th>
<th>$BDE$</th>
<th>$\Delta G^0$</th>
<th>$\Delta G^*$</th>
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<td>4.7</td>
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<td>6.2</td>
<td>5.3</td>
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<td>4.7</td>
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<td>5.9</td>
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<td>-42.5</td>
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</table>

In the adiabatic limit, the first-order (intra-complex) rate constant for the electron transfer is given by

$$k_{ET} = \kappa_{el} \nu_n \exp \left( \frac{-\Delta G^*}{RT} \right)$$

where $\kappa_{el}$ is the electronic transmission coefficient and $\nu_n$ is the nuclear vibration frequency related to electron transfer ($\kappa_{el} \nu_n$ was approximated to $10^{12}$ M$^{-1}.s^{-1}$). The apparent second-order rate constant for electron transfer ($k_D$) is given by

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The table below summarizes the results as far as the reactivity towards DDQ is concerned.

\[
\frac{1}{k_D} = \frac{1}{k_{diff}} + \frac{1}{K_{CT} k_{ET}}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>$K_{CT}$ (M$^{-1}$)</th>
<th>$k_{add}$ (s$^{-1}$)</th>
<th>$k_C$ (M$^{-1}$s$^{-1}$)</th>
<th>$k_{ET}$ (s$^{-1}$)</th>
<th>$k_D$ (M$^{-1}$s$^{-1}$)</th>
<th>Favored Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Compound 1]</td>
<td>$3 \times 10^7$</td>
<td>$3 \times 10^8$</td>
<td>$k_{diff}$</td>
<td>$3 \times 10^6$</td>
<td>$k_{diff}$</td>
<td>C $&gt;$ D</td>
</tr>
<tr>
<td>![Compound 2]</td>
<td>$1 \times 10^7$</td>
<td>$8 \times 10^7$</td>
<td>$k_{diff}$</td>
<td>$2 \times 10^9$</td>
<td>$k_{diff}$</td>
<td>D $&gt;$ C</td>
</tr>
<tr>
<td>![Compound 3]</td>
<td>$6 \times 10^5$</td>
<td>$5 \times 10^6$</td>
<td>$k_{diff}$</td>
<td>$2 \times 10^8$</td>
<td>$k_{diff}$</td>
<td>D $&gt;$ C</td>
</tr>
</tbody>
</table>
Cartesian Coordinates.

\[
\begin{align*}
E &= -1485.112755 \text{ Hartree} \\
C &\begin{pmatrix} -0.309151 & 0.089515 & -0.012886 \\ 1.050908 & 0.089592 & 0.012753 \\ 1.830628 & 1.377696 & 0.027006 \\ 1.050015 & 2.656965 & 0.011899 \\ -0.308520 & 2.656988 & -0.013711 \\ -1.089001 & 1.377530 & -0.028029 \\ -2.303501 & 1.357221 & -0.050898 \\ 3.045128 & 1.357525 & 0.049977 \\ -1.248087 & 4.095242 & -0.031876 \\ 1.989436 & 4.095427 & 0.029157 \\ -1.073560 & -1.116519 & -0.026889 \\ 1.815439 & -1.116355 & 0.027574 \\ -1.691113 & -2.101590 & -0.038198 \\ 2.433092 & -2.101355 & 0.039551 
\end{pmatrix}
\end{align*}
\]

\[
E = -1485.255263 \text{ Hartree}
\]

\[
\begin{align*}
C &\begin{pmatrix} -0.330629 & 0.128508 & -0.013367 \\ 1.072385 & 0.128588 & 0.013084 \\ 1.851727 & 1.361148 & 0.027219 \\ 1.054942 & 2.607522 & 0.012061 \\ -0.313443 & 2.607444 & -0.013738 \\ -1.110092 & 1.360979 & -0.028620 \\ -2.356044 & 1.370436 & -0.052435 \\ 3.097691 & 1.370747 & 0.050403 \\ -1.237423 & 4.087511 & -0.031291 \\ 1.978758 & 4.087694 & 0.029346 \\ -1.064352 & -1.095229 & -0.026609 \\ 1.806224 & -1.095065 & 0.027511 \\ -1.653333 & -2.101366 & -0.037233 \\ 2.395302 & -2.101135 & 0.039098 
\end{pmatrix}
\end{align*}
\]

\[
E = -1485.859260 \text{ Hartree}
\]

\[
\begin{align*}
C &\begin{pmatrix} 1.357354 & -0.749170 & -0.001199 \\ 1.337865 & 0.674816 & -0.004273 \\ 0.132601 & 1.381263 & 0.005960 \\ -1.071357 & 0.642225 & -0.004764 \\ -1.084535 & -0.745438 & -0.001918 \\ 0.143784 & -1.551681 & 0.000164 \\ 0.130010 & -2.801140 & 0.002840 \\ 0.172238 & 2.755317 & -0.008525 \\ -2.588406 & -1.629949 & -0.000686 \\ -2.576497 & 1.582442 & -0.007288 \\ 2.600051 & -1.441624 & 0.000636 \\ 2.557228 & 1.424520 & -0.005800 \\ 3.626518 & -1.998145 & 0.002542 \\ 3.544113 & 2.043699 & -0.007217 \\ -0.738833 & 3.092492 & -0.010754 \\
\end{pmatrix}
\end{align*}
\]

\[
E = -759.353569 \text{ Hartree}
\]
Cl 0.071310 -0.408336 0.002255
O 0.765658 -0.487553 -1.180360
O 0.874613 -0.163701 1.093879

\[
\begin{align*}
\text{C} & \quad 3.261186 \quad 0.361359 \quad -1.406204 \\
\text{C} & \quad 4.156899 \quad -0.701465 \quad 0.675927 \\
\text{C} & \quad 2.250001 \quad -0.304112 \quad -2.353042 \\
\text{H} & \quad 1.517409 \quad 0.443701 \quad -2.674452 \\
\text{H} & \quad 2.749431 \quad -0.718947 \quad -3.239969 \\
\text{H} & \quad 1.707153 \quad -1.102132 \quad -3.841478 \\
\text{C} & \quad 4.048744 \quad 1.424708 \quad -2.175273 \\
\text{C} & \quad 4.682420 \quad 0.956586 \quad -2.942424 \\
\text{C} & \quad 3.349148 \quad 2.108741 \quad -2.673404 \\
\text{H} & \quad 4.680500 \quad 2.008736 \quad -1.498283 \\
\text{C} & \quad 5.448237 \quad -0.075013 \quad -0.114614 \\
\text{H} & \quad 5.912666 \quad -0.791211 \quad 0.574809 \\
\text{H} & \quad 6.162100 \quad 0.161373 \quad 0.916446 \\
\text{H} & \quad 5.219876 \quad 0.843577 \quad 0.434978 \\
\text{C} & \quad 4.526144 \quad -1.912952 \quad -1.536160 \\
\text{C} & \quad 5.069422 \quad -1.596852 \quad -2.438359 \\
\text{H} & \quad 5.171574 \quad -2.589112 \quad -0.959676 \\
\text{C} & \quad 3.628926 \quad -2.462716 \quad -1.837115 \\
\text{C} & \quad 0.936726 \quad -0.682800 \quad 0.929268 \\
\text{C} & \quad 0.560337 \quad -2.031082 \quad 1.020665 \\
\text{O} & \quad -0.123363 \quad 0.062295 \quad 1.392247 \\
\text{H} & \quad -0.740886 \quad -2.095721 \quad 1.549078 \\
\text{H} & \quad 1.206618 \quad -2.847099 \quad 0.729670 \\
\text{C} & \quad -1.140068 \quad -0.783442 \quad 1.722218 \\
\text{H} & \quad -1.346400 \quad -2.973303 \quad 1.732421 \\
\text{H} & \quad -2.033392 \quad -0.326163 \quad 2.122361 \\
\text{C} & \quad 2.804869 \quad 0.678822 \quad 2.220122 \\
\text{C} & \quad 3.881643 \quad 0.880303 \quad 2.106743 \\
\text{C} & \quad 2.631081 \quad -0.268119 \quad 3.415220 \\
\text{H} & \quad 1.565614 \quad -0.473338 \quad 3.609061 \\
\text{H} & \quad 3.128903 \quad -1.228961 \quad 3.226290 \\
\text{H} & \quad 3.047211 \quad 0.163680 \quad 4.341675 \\
\text{C} & \quad 2.095220 \quad 2.015860 \quad 2.467844 \\
\text{H} & \quad 2.489420 \quad 2.516323 \quad 3.370245 \\
\text{H} & \quad 2.226513 \quad 2.687514 \quad 1.610054 \\
\text{B} & \quad 1.017369 \quad 1.868626 \quad 2.617571 \\
\text{B} & \quad 2.415503 \quad -0.010707 \quad 0.748082 \\
\text{O} & \quad 2.575059 \quad 0.987071 \quad -0.327530 \\
\text{O} & \quad 3.334473 \quad 1.126355 \quad 0.404322 \\
\text{O} & \quad -0.750241 \quad -0.973019 \quad -1.384373 \\
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\text{C} & \quad -2.939176 \quad -1.323837 \quad -0.544481 \\
\text{C} & \quad -1.958139 \quad 0.988593 \quad -0.761597 \\
\text{C} & \quad -4.150208 \quad -0.780438 \quad -0.177496 \\
\text{C} & \quad -3.149605 \quad 1.523390 \quad -0.368483 \\
\text{O} & \quad -3.433194 \quad 0.685135 \quad 0.047306 \\
\text{O} & \quad -5.406727 \quad 1.165762 \quad 0.309053 \\
\text{Cl} & \quad -0.582903 \quad 1.937510 \quad -1.156181
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & \quad -3.386744 \quad 3.235931 \quad -0.210279 \\
\text{O} & \quad -5.279555 \quad -1.597812 \quad 0.129768 \\
\text{C} & \quad -2.786775 \quad -2.741290 \quad -0.707508 \\
\text{C} & \quad -2.692657 \quad -3.892768 \quad -0.843051 \\
\text{N} & \quad -6.195099 \quad -2.272236 \quad 0.380606
\end{align*}
\]

E = -2244.514690 Hartree

E = -2244.498072 Hartree

SI-I-86
Cl 3.134464 -2.924120 -1.284154
Cl 5.314233 -1.991356 0.901109
C 3.267004 2.764415 0.807587
C 1.388441 1.958724 -1.238469
N 0.871467 2.774462 -1.881031
N 3.198235 3.859445 1.219213

\[
E = -2244.574206 \text{ Hartree}
\]

C -3.788417 -0.534186 -1.479253
C -4.281962 0.804786 -0.809777
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H -0.604192 -0.934876 4.198547
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O -3.018339 -1.153299 -0.407663
O -3.283434 1.034607 0.222895
O 0.613910 -0.708434 -2.123160
C 1.461886 -0.310167 -1.344815
C 1.223122 0.894540 -0.414229
C 2.761025 -0.991140 -1.148874
C 2.473064 1.720717 -0.140548
C 3.808939 -0.326187 -0.596676
C 3.761220 1.135206 -0.141759
O 4.831480 1.684924 0.180425

\[
E = -2244.574206 \text{ Hartree}
\]

SI-I-90
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