Complex Boron-Containing Molecules through a 1,2-Metalate Rearrangement/anti-SN2’ Elimination/Cycloaddition Reaction Sequence

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Supplementary Material

Table of Contents

1 General Experimental S2
2 Synthesis of Benzylamines S4
3 Synthesis of Boronic Esters S6
4 General Procedure S9
5 Product Characterization S12
6 Assignment of Diastereoisomers S41
7 Crystallography S42
8 Investigation of Other Dienophiles S46
9 NMR Spectra S47
10 References S75


1 General Experimental

Solvents and Reagents. Reactions with air- or moisture-sensitive materials were carried out under a nitrogen atmosphere using Schlenk techniques. Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. All solvents were commercially supplied or provided by the communal stills of the School of Chemistry, University of Bristol. (+)-Sparteine and (−)-sparteine were obtained from the commercially available sulfate pentahydrate salt (99%, Acros) and isolated according to literature procedure. The sparteine free base readily absorbs atmospheric carbon dioxide (CO$_2$) and should be stored under nitrogen at −20 °C in a Schlenk tube. $n$-BuLi, sec-BuLi, and tert-BuLi were purchased from Acros. The molarity of organolithium solutions was determined by titration using N-benzyl benzamide as an indicator. Copper(I) chloride was purified from aq. HCl (37%) and water prior to use according to a literature procedure. All other reagents were purchased from commercial sources and used as received.

Chromatography. Flash column chromatography (FCC) was carried out using Sigma-Aldrich silica gel (60 Å, 230 – 400 mesh, 40 – 63 μm). All reactions were followed by thin-layer chromatography (TLC) when practical, using Merck Kieselgel 60 F$_{254}$ fluorescent treated silica gel, which was visualized under UV light or by staining with aqueous basic potassium permanganate.

Spectroscopy. $^1$H and $^{13}$C{$_^1$H} NMR spectra were recorded using Jeol ECP(Eclipse) 300 MHz, Jeol ECS 400 MHz, Varian CNMR 400 MHz and Bruker Avance DPX 400 MHz spectrometers. $^1$H and $^{13}$C positive chemical shifts (δ) are downfield from tetramethylsilane and are given in parts per million (ppm). Coupling constants (J) are given in Hertz (Hz). The $^1$H NMR spectra are reported as follows: ppm (multiplicity, coupling constants, assignment). NMR assignments are made according to spin systems, using two-dimensional (COSY, HSQC, HMBC) NMR spectroscopy to assist the assignment. High resolution mass spectra (HRMS) were recorded on a VG Analytical Autospec by Electron Ionisation (EI) or Chemical Ionisation (CI) or on a Bruker Daltonics Apex IV by Electrospray Ionisation (ESI). IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR as a thin film. Only selected absorption maxima ($\nu_{\text{max}}$) are reported in wavenumbers (cm$^{-1}$). Melting points were recorded in degrees Celsius (°C), using a Kofler hot-stage microscope apparatus and are reported uncorrected. Optical rotations ([α]$_D^T$) were measured on a Bellingham and Stanley Ltd. ADP220 polarimeter and are quoted in (° mL)(g dm)$^{-1}$. Chiral HPLC was performed on a HP agilent 1100 with a Chiralpak IA, IB or IC column and monitored by DAD.
(Diode Array Detector). Chiral SFC was performed on a Waters TharSFC system using a Diacel Chiralpak IB column (4.6 m × 250 mm × 5 μm) and monitored by DAD (Diode Array Detector). GC-MS was performed on an Agilent 7820A using a HP-5MS UI column (30 m × 0.25 mm × 0.25 μm).

*Naming of Compounds.* Compound names are those generated by ChemBioDraw 13.0 software (PerkinElmer), following IUPAC nomenclature.
2 Synthesis of Benzylamines

1-(2-Bromophenyl)-N,N-dimethylmethanamine (1a)

\[
\begin{align*}
\text{PhBr} + \text{Me}_{2} \text{NH} \rightarrow \text{PhN} \text{Me}_{2} \\
\text{CH}_{2} \text{Cl}_{2}, \text{reflux, 6 h} \rightarrow \text{PhNMe}_{2} \text{Br} \\
\text{89%}
\end{align*}
\]

Prepared according to a literature procedure in 89% on a 25 mmol scale.\(^{S4}\)

1-(2-Bromo-6-methylphenyl)-N,N-dimethylmethanamine (1b)

\[
\begin{align*}
\text{PhB(OH)Cl} + \text{CuBr}_{2} \rightarrow \text{PhN} \text{Me}_{2} \\
\text{MeOH/H}_{2} \text{O, reflux, 5 h} \rightarrow \text{PhNMe}_{2} \text{Br} \\
\text{75%}
\end{align*}
\]

Prepared according to a literature procedure in 75% on a 7.5 mmol scale.\(^{S5}\)

\(N,N\)-Dimethyl-1-(p-tolyl)methanamine (1c)

\[
\begin{align*}
\text{PhCHO} + \text{Me}_{2} \text{NH} \rightarrow \text{PhN} \text{Me}_{2} \\
\text{NaBH(OAc)}_{3}, \text{AcOH} \rightarrow \text{PhNMe}_{2} \\
1,2\text{-DCE, rt, 16 h} \rightarrow \text{PhNMe}_{2} \text{Br} \\
\text{57%}
\end{align*}
\]

Prepared according to a literature procedure in 57% on a 16 mmol scale.\(^{S5}\)

1-(2-Bromo-6-fluorophenyl)-N,N-dimethylmethanamine (1d)

\[
\begin{align*}
\text{PhFBr} + \text{NaBH(OAc)}_{3}, \text{NEt}_{3} \rightarrow \text{PhN} \text{Me}_{2} \\
1,2\text{-DCE, rt, 16 h} \rightarrow \text{PhNMe}_{2} \text{Br} \\
\text{74%}
\end{align*}
\]

Prepared according to a literature procedure in 74% on a 12 mmol scale.\(^{S5}\)

1-(2-Bromo-5-fluorophenyl)-N,N-dimethylmethanamine (1e)

\[
\begin{align*}
\text{PhFBr} + \text{NaBH(OAc)}_{3} \rightarrow \text{PhN} \text{Me}_{2} \\
1,2\text{-DCE, rt, 16 h} \rightarrow \text{PhNMe}_{2} \text{Br} \\
\text{44%}
\end{align*}
\]

Prepared according to a literature procedure in 44% on a 12 mmol scale.\(^{S5}\)
(S)-1-(2-Bromophenyl)-N,N-dimethylethan-1-amine (1f)

Prepared according to a literature procedure in 72% on a 34 mmol scale. The enantiomeric excess was determined after debromination. HPLC: Chiralpak OD-H (hexane:2-propanol:HNEt$_2$ = 99.9:0.1:0.01, flow rate 0.5 mL/min, $\lambda$ = 230 nm), retention times $t_R$(minor) = 11.0 min, $t_R$(major) = 12.4 min; 94.4% ee.

(R)-1-(2-Bromophenyl)-N,N-dimethylethan-1-amine (1g)

Prepared according to a literature procedure in 75% on a 34 mmol scale. The enantiomeric excess was determined after debromination. HPLC: Chiralpak OD-H (hexane:2-propanol:HNEt$_2$ = 99.9:0.1:0.01, flow rate 0.5 mL/min, $\lambda$ = 230 nm), retention times $t_R$(major) = 11.0 min, $t_R$(minor) = 12.4 min; 98.0% ee.
3 Synthesis of Boronic Esters

Boronic acid pinacol esters 2a, 2b, 2c, 2d, 2e, and 2f were obtained from commercial sources and used as received.

4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (2g)

![Reaction Scheme]

Prepared according to a literature procedure in 57% on a 27 mmol scale.\textsuperscript{S6}

tert-Butyldimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy)silane (2h)

In analogy to a literature procedure,\textsuperscript{S7} (3-bromopropoxy)(tert-butyl)dimethylsilane (2.50 g, 9.87 mmol) was added to CuCl (29.3 mg, 296 μmol, 3.00 mol%), Xantphos (171 mg, 296 μmol, 3.00 mol%), B₂pin₂ (3.02 g, 11.8 mmol, 1.20 equiv) and KO'Bu (9.87 mL, 1.0 M in THF, 9.87 mmol, 1.00 equiv) in THF (20 mL) and stirred overnight at rt. The solution was filtered with EtOAc:hexane (20:80) through a pad of Celite and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (Et₂O:pentane = 2:98) afforded the product as a colorless liquid. Yield: 2.78 g (88%). \textit{R}t (Et₂O:pentane = 5:95): 0.56. \textit{¹H NMR} (400 MHz, CDCl₃): δ 3.56 (t, \(J_{HH'} = 6.8\) Hz, 2H, CH₂OTBS), 1.65 – 1.57 (m, 2H, CH₂), 1.23 (s, 12H, CH₃(pin)), 0.88 (s, 9H, C(CH₃)₃), 0.79 – 0.73 (m, 2H, CH₂Bpin), 0.03 (s, 6H, Si(CH₃)₂). \textit{¹³C\{¹H\} NMR} (101 MHz, CDCl₃): δ 83.0 (2C, OC(CH₃)₂), 65.3 (CH₂OTBS), 27.4 (CH₂), 26.2 (3C, C(CH₃)₃), 25.0 (4C, CH₃(pin)), 18.5 (C(CH₃)₃), 7.2 (CH₂Bpin), –5.1 (2C, Si(CH₃)₂). \textit{¹¹B\{¹H\} NMR} (128 MHz, CDCl₃): δ 34.1 (br s). Analytical data is in agreement with the literature.\textsuperscript{S8}
2-(3-Azidopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2i)

![Chemical structure](image)

Prepared according to a literature procedure in 82% on a 20 mmol scale.\textsuperscript{S5}

2-(2-(1,3-Dioxolan-2-yl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2j)

![Chemical structure](image)

Prepared according to a literature procedure in 88% on a 14 mmol scale.\textsuperscript{S6}

2-(4-(4-Methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (±-2k)

![Chemical structure](image)

Prepared according to a literature procedure in 87% on a 25 mmol scale.\textsuperscript{S7}

(R)-2-(4-(4-Methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2k)

![Chemical structure](image)

Prepared according to a literature procedure in 76% on a 7.0 mmol scale.\textsuperscript{S9} Enantiomeric excess was determined after oxidation to the corresponding alcohol. **HPLC**: Chiralpak IB (hexane:2-propanol = 97:3, flow rate 0.7 mL/min, \(\lambda = 230\) nm), retention times \(t_R\)(major) = 18.1 min, \(t_R\)(minor) = 21.2 min; 90.0% ee.
2-((1R,2R,5R)-2-Isopropyl-5-methylcyclohexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2l)

Prepared according to a literature procedure in 37% and with dr >95:5 on a 11 mmol scale.\textsuperscript{S7}
4 General Procedure

The boronic ester 2x (500 μmol) was added to the ortho-lithiated benzyl amine Li-1x (525 μmol, 1.05 equiv, prepared from 1x) in THF (2 mL) at −78 °C and the solution was stirred at −78 °C for 15 min, after which the cooling bath was removed and the reaction was allowed to stir for a further 15 min. 2,2,2-Trichloro-1,1-dimethylethyl chloroformate (132 mg, 550 μmol, 1.10 equiv) was added at −78 °C and the solution was stirred at −78 °C for 15 min, after which the cooling bath was removed and the reaction was allowed to stir for a further 5 min. 4-Phenyl-1,2,4-triazoline-3,5-dione (96.3 mg, 550 μmol, 1.10 equiv) was added and the solution was stirred for 1 h at rt. CHCl₃ (50 mL) was added and the solution was washed with water (25 mL) and saturated aqueous NaCl solution (25 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel afforded the pure product.

Lithiation Conditions

\( n\text{-BuLi} \) (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1a (112 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred at −78 °C for 45 min to give a yellow solution.

\( n\text{-BuLi} \) (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1b (120 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 1 h at −78 °C to give a yellow solution.
TBME (90.0 μL, 750 μmol, 1.50 equiv) and n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) were added to 1c (78.4 mg, 525 μmol, 1.05 equiv) in hexane (2 mL) at rt and the solution was heated to 60 °C and stirred for 6 h to give a dark yellow solution. THF (2 mL) was added prior to borylation.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1d (122 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 45 min at −78 °C to give a yellow solution.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1e (122 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 45 min at −78 °C to give a yellow solution.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1f (148 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 45 min at −78 °C to give a yellow solution.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1g (128 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 45 min at −78 °C to give a yellow solution.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1h (136 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred for 45 min at −78 °C to give a yellow solution.

n-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1i (120 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred at −78 °C for 60 min to give a yellow solution.
$n$-BuLi (328 μL, 1.6 M in hexanes, 525 μmol, 1.05 equiv) was added to 1j (120 mg, 525 μmol, 1.05 equiv) in THF (2 mL) at −78 °C and the solution was stirred at −78 °C for 60 min to give a yellow solution.
5   Product Characterization

(±)-(5S,8R,11S)-11-Cyclohexyl-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3aa)

Prepared following the general procedure on a 500 μmol (105 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as a white solid. Yield: 121 mg (51%), dr = 17:1. **MP:** 86 °C. **Rf** (EtOAc:pentane = 15:85): 0.47. **IR** (neat, cm⁻¹): 2927, 1771, 1710, 1397, 1138, 908, 727, 644. **¹H NMR** (400 MHz, CDCl₃): δ 7.48 – 7.36 (m, 4H, Ar-H), 7.34 – 7.28 (m, 1H, Ar-H), 6.50 (ddd, 3JH,H' = 7.7, 5.5 Hz, 4JH,H' = 1.8 Hz, 1H, =CH), 6.43 (ddd, 3JH,H' = 7.7, 5.4 Hz, 4JH,H' = 1.7 Hz, 1H, =CH), 5.39 (s, 1H, =CHH), 5.26 – 5.21 (m, 2H, =CHH (1H) + CHN (1H)), 5.11 (dd, 3JH,H' = 5.5 Hz, 4JH,H' = 1.7 Hz, 1H, CHN), 2.08 – 2.00 (m, 1H, CHH), 1.79 – 1.61 (m, 4H, CHH), 1.26 (s, 6H, CH₃ (pin)), 1.24 (s, 6H, CH₃ (pin)), 1.23 – 1.02 (m, 6H, CH (1H) + CHH (5H)). **¹³C{¹H} NMR** (101 MHz, CDCl₃): δ 155.8 (CO), 155.3 (CO), 142.9 (=C), 131.8 (arom.), 129.9 (=CH), 129.0 (2C, arom.), 128.6 (=CH), 128.0 (arom.), 125.4 (2C, arom.), 113.9 (=CH₂), 84.2 (2C, OC(CH₃)₂), 59.0 (CHN), 57.0 (CHN), 44.4 (CH), 31.0 (CH₂), 29.8 (CH₂), 27.3 (CH₂), 27.1 (CH₂), 26.4 (CH₂), 25.1 (2C, CH₃ (pin)), 24.4 (2C, CH₃ (pin)), carbon attached to boron not observed due to quadrupolar relaxation. **¹¹B{¹H} NMR** (128 MHz, CDCl₃): δ 33.5 (br s). **HRMS** (ESI): Calcd. for C₂₇H₃₄BN₃NaO₄ m/z 498.2535, found m/z 498.2554 [M+Na]⁺.
Prepared following the general procedure on a 500 μmol (156 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 30:70) afforded the product as a colorless oil. Yield: 193 mg (67%), dr >20:1. $R_f$ (EtOAc:pentane = 40:60): 0.39. IR (neat, cm$^{-1}$): 2978, 1771, 1712, 1683, 1399, 1137, 908, 726, 644. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.38 – 7.31 (m, 4H, Ar-H), 7.27 – 7.21 (m, 1H, Ar-H), 6.49 (m, 1H, =CH), 6.36 (ddd, $^3$J$_{H,H'}$ = 7.8, 5.5 Hz, $^4$J$_{H,H'}$ = 1.6 Hz, 1H, =CH), 5.36 (s, 1H, =CHH), 5.16 – 5.12 (m, 2H, =CHH (1H) + CHN (1H)), 5.05 (dd, $^3$J$_{H,H'}$ = 5.5 Hz, $^4$J$_{H,H'}$ = 1.6 Hz, 1H, CHN), 4.06 (br s, 2H, CHHNN), 2.43 (br s, 2H, CHHNN), 1.92 – 1.85 (m, 1H, CHH), 1.59 – 1.48 (m, 1H, CHH), 1.44 – 1.34 (m, 1H, CHH), 1.38 (s, 9H, C(CH$_3$)$_3$), 1.25 – 1.20 (m, 2H, CH (1H) + CHH (1H)), 1.18 (s, 6H, CH$_3$ (pin)), 1.16 (s, 6H, CH$_3$ (pin)). $^{13}$C$\{^1$H$\}$ NMR (101 MHz, CDCl$_3$): $\delta$ 155.8 (CO), 155.2 (CO), 154.6 (CO), 142.0 (=C), 131.6 (arom.), 129.3 (=CH), 129.1 (=CH), 129.0 (2C, arom.), 128.0 (arom.), 125.3 (2C, arom.), 114.4 (=CH$_2$), 84.3 (2C, OC(CH$_3$)$_2$), 79.3 (OC(CH$_3$)$_3$), 58.7 (CHN), 56.8 (CHN), 44.5 (2C, CH$_2$N), 42.6 (CH), 41.2 (CBpin), 29.9 (CH$_2$), 28.7 (CH$_2$), 28.4 (3C, C(CH$_3$)$_3$), 25.0 (2C, CH$_3$ (pin)), 24.3 (2C, CH$_3$ (pin)). $^{11}$B$\{^1$H$\}$ NMR (128 MHz, CDCl$_3$): $\delta$ 33.1 (br s). HRMS (ESI): Calcd. for C$_{31}$H$_{41}$BN$_4$NaO$_6$ $m/z$ 599.3017, found $m/z$ 599.3017 [M+Na]$^+$. 
(±)-(5S,8R,11S)-11-((3S,5S,7S)-Adamantan-1-yl)-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ac)

Prepared following the general procedure on a 500 μmol (132 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as a white solid. Yield: 112 mg (43%), dr >20:1. **MP**: 195 °C. **Rf** (EtOAc:pentane = 10:90): 0.59. **IR** (neat, cm⁻¹): 2905, 2849, 1772, 1720, 1502, 1397, 1322, 1260, 1143, 1062, 1017. **1H NMR** (400 MHz, CDCl₃): δ 7.44 – 7.38 (m, 4H, Ar-H), 7.35 – 7.29 (m, 1H, Ar-H), 6.53 – 6.45 (m, 2H, =CH), 5.50 (s, 1H, =CHH), 5.33 (dd, 3J_H,H' = 4.8 Hz, 4J_H,H' = 2.4 Hz, 1H, CHN), 5.29 (s, 1H, =CHH), 5.11 (dd, 3J_H,H' = 5.0 Hz, 4J_H,H' = 2.3 Hz, 1H, CHN), 1.98 – 1.90 (m, 6H, CH (3H) + CHH (3H)), 1.69 – 1.55 (m, 9H, CHH), 1.27 (s, 6H, CH₃ (pin)), 1.26 (s, 6H, CH₃ (pin)). **13C{1H} NMR** (101 MHz, CDCl₃): δ 155.9 (CO), 155.6 (CO), 142.0 (=C), 131.8 (arom.), 131.1 (=CH), 129.2 (=CH), 129.1 (2C, arom.), 128.1 (arom.), 125.4 (2C, arom.), 114.6 (=CH₂), 84.2 (2C, OC(CH₃)₂), 60.4 (CHN), 57.1 (CHN), 47.0 (CBpin), 40.0 (3C, CH₂), 37.7 (C), 36.8 (3C, CH₂), 29.1 (3C, CH), 25.1 (2C, CH₃ (pin)), 24.7 (2C, CH₃ (pin)). **11B{1H} NMR** (128 MHz, CDCl₃): δ 32.0 (br s). **HRMS** (ESI): Calcd. for C₃₁H₃₀BN₃O₄ m/z 528.3034, found m/z 528.3009 [M+H]+.
(±)-(5S,8R,11S)-10-Methylene-2,11-diphenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ad)

Prepared following the general procedure on a 500 μmol (102 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 25:75) afforded the product as separable diastereoisomers as a white solids. Yield: 71 mg (30%) and 47 mg (20%), dr = 1.5:1. **Major diastereoisomer (syn-3ad):** **MP:** >200 °C. **Rf** (EtOAc:pentane = 35:65): 0.50. **IR** (neat, cm⁻¹): 2978, 1772, 1709, 1396, 1328, 1139, 909, 727, 644. **1H NMR** (400 MHz, CDCl₃): δ 7.49 – 7.41 (m, 6H, Ar-H), 7.36 – 7.32 (m, 1H, Ar-H), 7.30 – 7.26 (m, 2H, Ar-H), 7.22 – 7.18 (m, 1H, Ar-H), 6.55 (ddd, 3J_H,H' = 7.7, 5.7 Hz, 4J_H,H' = 1.7 Hz, 1H, =CH), 6.10 (ddd, 3J_H,H' = 7.0, 5.5 Hz, 4J_H,H' = 1.5 Hz, 1H, =CH), 5.77 (s, 1H, =CHH), 5.39 (dd, 3J_H,H' = 5.5 Hz, 4J_H,H' = 1.5 Hz, 1H, CHN), 5.30 (dd, 3J_H,H' = 5.5 Hz, 4J_H,H' = 1.5 Hz, 1H, CHN), 5.27 (s, 1H, =CHH), 1.28 (s, 6H, CH₃ (pin)), 1.23 (s, 6H, CH₃ (pin)). **13C{¹H} NMR** (101 MHz, CDCl₃): δ 155.6 (CO), 155.3 (CO), 140.5 (arom.), 140.4 (=C), 131.7 (arom.), 130.6 (=CH), 129.2 (2C, arom.), 128.9 (=CH), 128.5 (2C, arom.), 128.2 (arom.), 127.9 (2C, arom.), 126.8 (arom.), 125.5 (2C, arom.), 117.4 (=CH₂), 84.7 (2C, OCH(CH₃)₂), 59.6 (CHN), 58.6 (CHN), 43.2 (CBpin), 24.8 (2C, CH₃ (pin)), 24.3 (2C, CH₃ (pin)). **11B{¹H} NMR** (128 MHz, CDCl₃): δ 32.6 (br s). **HRMS** (ESI): Calcd. for C₂₇H₂₈BN₃NaO₄ m/z 492.2074, found m/z 492.2074 [M+Na]+. **Minor diastereoisomer (anti-3ad):** **MP:** >200 °C. **Rf** (EtOAc:pentane = 35:65): 0.41. **IR** (neat, cm⁻¹): 2978, 1770, 1710, 1399, 1331, 1140, 910, 852, 727. **1H NMR** (400 MHz, CDCl₃): δ 7.55 – 7.52 (m, 2H, Ar-H), 7.41 – 7.22 (m, 8H, Ar-H), 6.70 (app. t, 3J_H,H' = 7.0 Hz, 1H, =CH), 6.56 (app. t, 3J_H,H' = 7.0 Hz, 1H, =CH), 5.63 (s, 1H, =CHH), 5.32 (d, 3J_H,H' = 5.8 Hz, 1H, CHN), 5.32 (s, 1H, =CHH), 5.21 (d, 3J_H,H' = 5.6 Hz, 1H, CHN), 1.23 (s, 6H, CH₃ (pin)), 1.18 (s, 6H, CH₃ (pin)). **13C{¹H} NMR** (101 MHz, CDCl₃): δ 155.7 (CO), 155.6 (CO), 140.7 (arom.), 140.5 (=C), 133.4 (=CH), 131.7 (arom.), 129.2 (=CH), 129.1 (2C, arom.), 128.8 (2C, arom.), 128.1 (3C, arom.), 127.0 (arom.), 125.6 (2C, arom.), 116.0 (=CH₂), 84.7 (2C, OCH(CH₃)₂), 60.3 (CHN), 58.6 (CHN), 24.6 (2C, CH₃ (pin)), 24.5 (2C, CH₃ (pin)), carbon attached to boron not
observed due to quadrupolar relaxation. \(^{11}\text{B}\{^1\text{H}\} \text{ NMR}\) (128 MHz, CDCl\(_3\)): \(\delta\) 31.5 (br s). \text{HRMS}\) (ESI): Calcd. for C\(_{27}\)H\(_{29}\)BN\(_3\)O\(_4\) \(m/z\) 470.2250, found \(m/z\) 470.2238 [M+H]+.
(±)-(5S,8R,11R)-11-Cyclopropyl-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ae)

Prepared following the general procedure on a 500 μmol (84 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as separable diastereoisomers as white solids. Yield: 81 mg (37%) and 49 mg (23%), dr = 1:1.6. **Major diastereoisomer (anti-3ae):** MP: >200 °C. *R* (EtOAc:pentane = 25:75): 0.31. IR (neat, cm⁻¹): 2979, 1772, 1712, 1655, 1600, 1502, 1458, 1396, 1371, 1327, 1270, 1213, 1166, 1139, 1074, 1024. **¹H NMR** (400 MHz, CDCl₃): δ 7.48 – 7.39 (m, 4H, Ar-H), 7.35 – 7.30 (m, 1H, Ar-H), 6.58 (dd, 3J_H,H' = 7.9, 5.6 Hz, 4J_H,H' = 1.6 Hz, 1H, =CH), 6.47 (dd, 3J_H,H' = 8.0, 5.6 Hz, 4J_H,H' = 1.4 Hz, 1H, =CH), 5.29 (s, 1H, =CHH), 5.25 (s, 1H, =CHH), 5.12 (dd, 3J_H,H' = 5.6 Hz, 4J_H,H' = 1.6 Hz, 1H, CHN), 5.07 (dd, 3J_H,H' = 5.6 Hz, 4J_H,H' = 1.4 Hz, 1H, CHN), 1.23 – 1.19 (m, 1H, CH), 1.17 (s, 6H, CH₃ (pin)), 1.16 (s, 6H, CH₃ (pin)), 0.68 – 0.47 (m, 3H, CHH), 0.46 – 0.38 (m, 1H, CHH). **¹³C[¹H] NMR** (101 MHz, CDCl₃): δ 156.3 (CO), 155.3 (CO), 143.4 (=C), 133.2 (=CH), 131.8 (arom.), 129.4 (=CH), 129.1 (2C, arom.), 128.1 (arom.), 125.6 (2C, arom.), 112.8 (=CH₂), 84.4 (2C, OC(CH₃)₂), 58.7 (CHN), 58.3 (CHN), 38.7 (CBpin), 24.9 (2C, CH₃ (pin)), 24.4 (2C, CH₃ (pin)), 17.4 (CH), 3.5 (CH₂), 2.0 (CH₂). **¹¹B[¹H] NMR** (128 MHz, CDCl₃): δ 31.5 (br s). HRMS (ESI): Calcd. for C₂₆H₂₆BN₃NaO₄ m/z 456.2065, found m/z 456.2078 [M+Na]+. **Minor diastereoisomer (syn-3ae):** MP: >200 °C. *R* (EtOAc:pentane = 25:75): 0.40. IR (neat, cm⁻¹): 2979, 1771, 1709, 1654, 1600, 1502, 1458, 1397, 1380, 1372, 1259, 1213, 1167, 1138, 1109, 1069. **¹H NMR** (400 MHz, CDCl₃): δ 7.47 – 7.38 (m, 4H, Ar-H), 7.35 – 7.29 (m, 1H, Ar-H), 6.56 – 6.48 (m, 2H, =CH), 5.35 (s, 1H, =CHH), 5.25 (s, 1H, =CHH), 5.17 (dd, 3J_H,H' = 5.2 Hz, 4J_H,H' = 1.9 Hz, 1H, CHN), 5.10 (dd, 3J_H,H' = 5.0 Hz, 4J_H,H' = 1.9 Hz, 1H, CHN), 1.23 (s, 6H, CH₃ (pin)), 1.22 (s, 6H, CH₃ (pin)), 0.74 – 0.67 (m, 1H, CHH), 0.59 – 0.47 (m, 2H, CH (1H) + CHH (1H)), 0.41 – 0.26 (m, 2H, CHH). **¹³C[¹H] NMR** (101 MHz, CDCl₃): δ 155.6 (CO), 155.5 (CO), 144.2 (=C), 131.7 (arom.), 129.9 (=CH), 129.1 (3C, arom. (2C) + =CH (1C)), 128.1 (arom.), 125.5 (2C, arom.), 112.7 (=CH₂), 84.5 (2C, OC(CH₃)₂), 58.5 (CHN), 58.4 (CHN), 38.6 (CBpin), 25.0 (2C, CH₃ (pin)).
(2C, CH3 (pin)), 18.5 (CH), 4.6 (CH2), 1.3 (CH2). \(^{11}\text{B}^1\text{H} \) NMR (128 MHz, CDCl3): \( \delta \) 32.2 (br s).

HRMS (ESI): Calcd. for C\(_{24}\)H\(_{28}\)BN\(_3\)NaO\(_4\) m/z 456.2065, found m/z 456.2075 [M+Na]⁺.

X-ray structure of \textit{anti-3ae}: Clear crystals of \textit{anti-3ae} were obtained from hot EtOAc. X-ray structure of \textit{syn-3ae}: Clear crystals were obtained by layering a saturated EtOAc solution of \textit{syn-3ae} with hexane. See Section 7 for Crystallography.

\((\pm)\)-(5\(S\),8\(R\),11\(R\))-11-Hexyl-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1\(H\)-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2\(H\))-dione (3af)
Prepared following the general procedure on a 500 μmol (106 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil that solidified upon standing. Yield: 141 mg (59%), \( \text{dr} = 1.2.7 \). **MP:** 143 °C. **Rt** (EtOAc:pentane = 25:75): 0.74. **IR** (neat, cm\(^{-1}\)): 2928, 2857, 1771, 1710, 1214, 1167, 1138, 1063, 1025. **\(^1\)H NMR** (400 MHz, CDCl\(_3\)): major diastereoisomer: \( \delta 7.48 - 7.38 \) (m, 4H, Ar-H), 7.35 - 7.28 (m, 1H, Ar-H), 6.60 (ddd, \( ^3J_{HH} = 7.5, 5.8 \text{ Hz} \), \( ^4J_{HH} = 1.5 \text{ Hz} \), 1H, =CH), 6.45 - 6.38 (m, 1H, =CH), 5.22 (s, 1H, =CHH), 5.14 - 5.07 (m, 2H, =CHH(1H) + CHN(1H)), 5.06 - 5.03 (m, 1H, CHN), 1.92 - 1.75 (m, 2H, CHH), 1.59 - 1.41 (m, 1H, CHH), 1.40 - 1.26 (m, 7H, CHH), 1.18 (s, 6H, CH\(_3\) (pin)), 1.17 (s, 6H, CH\(_3\) (pin)), 0.88 (dd, \( ^3J_{HH} = 6.6 \text{ Hz} \), 3H, CH\(_3\)); minor diastereoisomer: \( \delta 7.48 - 7.38 \) (m, 4H, Ar-H), 7.35 - 7.28 (m, 1H, Ar-H), 6.50 (ddd, \( ^3J_{HH} = 7.4, 5.6 \text{ Hz} \), \( ^4J_{HH} = 1.7 \text{ Hz} \), 1H, =CH), 6.45 - 6.38 (m, 1H, =CH), 5.32 (s, 1H, =CHH), 5.14 - 5.07 (m, 3H, =CHH(1H) + CHN(2H)), 1.59 - 1.41 (m, 3H, CHH), 1.40 - 1.26 (m, 7H, CHH), 1.25 (s, 6H, CH\(_3\) (pin)), 1.23 (s, 6H, CH\(_3\) (pin)). **\(^{13}\)C\{\(^1\)H\} NMR** (101 MHz, CDCl\(_3\)): major diastereoisomer: \( \delta 156.5 \) (CO), 155.8 (CO), 145.3 (=C), 133.6 (=CH), 131.7 (arom.), 129.0 (2C, arom.), 128.3 (=CH), 128.1 (arom.), 125.5 (2C, arom.), 111.5 (=CH\(_2\)), 84.1 (2C, OC(CH\(_3\))\(_2\)), 58.5 (CHN), 55.2 (CHN), 37.3 (CH\(_2\)), 31.6 (CH\(_2\)), 29.8 (CH\(_2\)), 26.5 (CH\(_2\)), 24.7 (2C, CH\(_3\) (pin)), 24.5 (2C, CH\(_3\) (pin)), 22.6 (CH\(_2\)), 14.1 (CH\(_3\)), carbon attached to boron not observed due to quadrupolar relaxation; minor diastereoisomer: \( \delta 156.5 \) (CO), 155.2 (CO), 144.4 (=C), 131.8 (arom.), 129.4 (=CH), 129.0 (2C, arom.), 128.9 (=CH), 128.0 (arom.), 125.4 (2C, arom.), 112.3 (=CH\(_2\)), 84.1 (2C, OC(CH\(_3\))\(_2\)), 58.2 (CHN), 56.9 (CHN), 38.3 (CH\(_2\)), 31.6 (CH\(_2\)), 29.9 (CH\(_2\)), 26.7 (CH\(_2\)), 24.9 (2C, CH\(_3\) (pin)), 24.3 (2C, CH\(_3\) (pin)), 22.6 (CH\(_2\)), 14.1 (CH\(_3\)), carbon attached to boron not observed due to quadrupolar relaxation. **\(^{11}\)B\{\(^1\)H\} NMR** (128 MHz, CDCl\(_3\)): \( \delta 32.7 \) (br s). **HRMS** (ESI): Calcd for C\(_{27}\)H\(_{36}\)BN\(_3\)NaO\(_4\) \( m/z \) 500.2691, found \( m/z \) 500.2685 [M+Na]\(^+\).
(±)-(5S,8R,11R)-10-Methylene-11-phenethyl-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ag)

Prepared following the general procedure on a 500 μmol (116 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil that solidified upon standing. Yield: 139 mg (56%), dr = 1:3.0. **MP**: 137 ºC. **Rf** (EtOAc:pentane = 25:75): 0.62. **IR** (neat, cm⁻¹): 2978, 2929, 2094, 1772, 1710, 1653, 1599, 1502, 1457, 1397, 1372, 1353, 1327, 1259, 1214, 1141, 1111, 1060, 1025. **¹H NMR** (400 MHz, CDCl₃): major diastereoisomer: δ 7.50 – 7.37 (m, 4H, Ar-H), 7.34 – 7.10 (m, 6H, Ar-H), 6.68 – 6.59 (m, 1H, =CH), 6.48 – 6.43 (m, 1H, =CH), 5.23 (s, 1H, =CHH), 5.20 – 5.09 (m, 3H, =CHH (1H) + CHN (2H)) 2.91 – 2.73 (m, 1H, CHH), 2.66 – 2.53 (m, 1H, PhCHH), 2.21 – 2.06 (m, 2H, CHH), 1.21 (s, 12H, CH₃ (pin)); minor diastereoisomer: δ 7.50 – 7.37 (m, 4H, Ar-H), 7.34 – 7.10 (m, 6H, Ar-H), 6.51 (ddd, 3JHH′ = 7.6, 5.6 Hz, 4JHH′ = 1.7 Hz, 1H, =CH), 6.43 – 6.38 (m, 1H, =CH), 5.36 (s, 1H, =CHH), 5.20 – 5.09 (m, 3H, =CHH (1H) + CHN (2H)) 2.91 – 2.73 (m, 1H, PhCHH), 2.66 – 2.53 (m, 1H, PhCHH), 1.87 – 1.77 (m, 1H, CHH), 1.62 – 1.52 (m, 1H, CHH), 1.28 (s, 6H, CH₃ (pin)), 1.27 (s, 6H, CH₃ (pin)). **¹³C{¹H} NMR** (101 MHz, CDCl₃): major diastereoisomer: δ 156.6 (CO), 155.8 (CO), 144.8 (=C), 142.0 (arom.), 133.3 (=CH), 131.7 (arom.), 129.1 (2C, arom.), 128.5 (=CH), 128.44 (2C, arom.), 128.40 (2C, arom.), 128.1 (arom.), 126.0 (arom.), 125.4 (2C, arom.), 111.9 (=CH₂), 84.4 (2C, OC(CH₃)₂), 58.4 (CHN), 55.2 (CHN), 39.4 (CH₂), 36.9 (CBpin), 33.1 (CH₂Ph), 24.8 (2C, CH₃ (pin)), 24.6 (2C, CH₃ (pin)); minor diastereoisomer: δ 155.6 (CO), 155.3 (CO), 144.0 (=C), 141.9 (arom.), 131.7 (arom.), 129.20 (=CH), 129.17 (=CH), 129.0 (2C, arom.), 128.5 (2C, arom.), 128.2 (2C, arom.), 128.1 (arom.), 126.1 (arom.), 125.4 (2C, arom.), 112.7 (=CH₂), 84.4 (2C, OC(CH₃)₂), 58.1 (CHN), 56.9 (CHN), 40.1 (CH₂), 37.1 (CBpin), 33.2 (CH₂Ph), 25.0 (2C, CH₃ (pin)), 24.4 (2C, CH₃ (pin)). **¹¹B{¹H} NMR** (128 MHz, CDCl₃): δ 31.9 (br s). **HRMS** (ESI): Calcd. for C₂₀H₃₂BN₃NaO₄ m/z 520.2378, found m/z 500.2377 [M+Na]⁺.
(±)-(5S,8R,11R)-11-(3-((tert-Butyldimethylsilyl)oxy)propyl)-10-methylene-2-phenyl-11-(4,4, 5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-α]pyridazine-1,3(2H)-dione (3ah)

Prepared following the general procedure on a 500 μmol (150 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil. Yield: 122 mg (43%), dr = 1:2.4. \( R_t \) (EtOAc:pentane = 25:75): 0.71. IR (neat, cm\(^{-1}\)): 2957, 2929, 1774, 1720, 1391, 1257, 1144. \(^1\)H NMR (400 MHz, CDCl\(_3\)): major diastereoisomer: \( \delta \) 7.47 – 7.38 (m, 4H, Ar-H), 7.35 – 7.29 (m, 1H, Ar-H), 6.63 – 6.58 (m, 1H, =CH), 6.46 – 6.38 (m, 1H, =CH), 5.24 (s, 1H, =CHH), 5.13 (s, 1H, =CHH), 5.13 – 5.08 (m, 1H, CHN), 5.05 – 5.02 (m, 1H, CHN), 3.69 – 3.51 (m, 2H, CHHOTBS), 1.99 – 1.92 (m, 1H, CHH), 1.85 – 1.65 (m, 2H, CHH), 1.60 – 1.53 (m, 1H, CHH), 1.19 (s, 6H CH\(_3\) (pin)), 1.18 (s, 6H CH\(_3\) (pin)), 0.88 (s, 9H, C(CH\(_3\))\(_3\)), 0.04 (s, 6H, SiCH\(_3\)); minor diastereoisomer: \( \delta \) 7.47 – 7.38 (m, 4H, Ar-H), 7.35 – 7.29 (m, 1H, Ar-H), 6.53 – 6.49 (m, 1H, =CH), 6.46 – 6.38 (m, 1H, =CH), 5.34 (s, 1H, =CHH), 5.14 – 5.08 (m, 3H, CHN (2H) + =CHH (1H)), 3.69 – 3.51 (m, 2H, CHHOTBS), 1.85 – 1.65 (m, 1H, CHH), 1.60 – 1.53 (m, 1H, CHH), 1.36 – 1.27 (m, 2H, CHH), 1.25 (s, 6H CH\(_3\) (pin)), 1.23 (s, 6H CH\(_3\) (pin)), 0.88 (s, 9H, C(CH\(_3\))\(_3\)), 0.03 (s, 6H, SiCH\(_3\)). \(^{13}\)C\(^{1}\)H NMR (101 MHz, CDCl\(_3\)): major diastereoisomer: \( \delta \) 156.6 (CO), 155.9 (CO), 145.2 (=C), 133.5 (=CH), 131.76 (arom.), 129.2 (2C, arom.), 128.6 (=CH), 128.2 (arom.), 125.7 (2C, arom.), 111.9 (=CH\(_2\)), 84.2 (2C, OC(CH\(_3\))\(_2\)), 63.3 (CH\(_2\)OTBS), 58.5 (CHN), 55.4 (CHN), 36.5 (CBpin), 33.5 (CH\(_2\)), 29.9 (CH\(_2\)), 26.0 (3C, C(CH\(_3\))\(_3\)), 24.8 (2C, CH\(_3\) (pin)), 24.6 (2C, CH\(_3\) (pin)), 18.4 (C(CH\(_3\))\(_3\)), –5.2 (2C, SiCH\(_3\)); minor diastereoisomer: \( \delta \) 155.7 (CO), 155.4 (CO), 144.3 (=C), 131.78 (arom.), 129.4 (=CH), 129.1 (2C, arom.), 129.0 (=CH), 128.1 (arom.), 125.5 (2C, arom.), 112.6 (=CH\(_2\)), 84.2 (2C, OC(CH\(_3\))\(_2\)), 63.2 (CH\(_2\)OTBS), 58.3 (CHN), 57.0 (CHN), 36.5 (CBpin), 34.4 (CH\(_2\)), 30.1 (CH\(_2\)), 26.0 (3C, C(CH\(_3\))\(_3\)), 25.0 (2C, CH\(_3\) (pin)), 24.4 (2C, CH\(_3\) (pin)), 18.4 (C(CH\(_3\))\(_3\)), –5.1 (2C, SiCH\(_3\)). \(^{11}\)B\(^{1}\)H NMR (128 MHz, CDCl\(_3\)): \( \delta \) 32.1 (br s). HRMS (ESI): Calcd. for C\(_{30}\)H\(_{45}\)BN\(_3\)O\(_5\)Si \( m/z \) 566.3222, found \( m/z \) 566.3210 [M+H]\(^+\).
(±)-(5S,8R,11R)-11-(3-Azidopropyl)-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-di-
oxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione
(1ai)

Prepared following the general procedure on a 500 μmol (106 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as separable diastereoisomers as a white solid and a colorless oil, respectively. Yield: 61 mg (26%) and 22 mg (9%), dr = 1:2.8. **Major diastereoisomer (anti-3ai):** MP: 186 °C. **Rt** (EtOAc:pentane = 25:75): 0.48. **IR** (neat, cm⁻¹): 2978, 2931, 2095, 1772, 1710, 1651, 1600, 1502, 1457, 1398, 1372, 1355, 1327, 1258, 1168, 1140, 1087, 1057, 1025. **¹H NMR** (400 MHz, CDCl₃): δ 7.48 – 7.40 (m, 4H, Ar-H), 7.38 – 7.31 (m, 1H, Ar-H), 6.60 (ddd, 3J_H,H' = 7.7 Hz, 5.8 Hz, 4J_H,H' = 1.5 Hz, 1H, =CH), 6.46 (ddd, 3J_H,H' = 7.7 Hz, 5.6 Hz, 4J_H,H' = 1.4 Hz, 1H, =CH), 5.26 (s, 1H, =CHH), 5.14 (s, 1H, =CHH), 5.11 (dd, 3J_H,H' = 5.6 Hz, 4J_H,H' = 1.5 Hz, 1H, CHN), 5.02 (dd, 3J_H,H' = 5.8 Hz, 4J_H,H' = 1.4 Hz, 1H, CHN), 3.40 – 3.33 (m, 1H, CHHN₃), 3.30 – 3.22 (m, 1H, CHHN₃), 2.02 – 1.79 (m, 3H, CHH), 1.67 – 1.56 (m, 1H, CHH), 1.20 (s, 6H, CH₃ (pin)), 1.20 (s, 6H, CH₃ (pin)). **¹³C{¹H} NMR** (101 MHz, CDCl₃): δ 156.7 (CO), 155.9 (CO), 144.7 (=C), 133.2 (=C), 131.6 (arom.), 129.2 (2C, arom.), 128.7 (CH), 128.3 (arom.), 125.6 (2C, arom.), 112.1 (CH₂), 84.5 (2C, OC(CH₃)₂), 58.4 (CHN), 55.2 (CHN), 51.7 (CH₂N₃), 36.3 (CBpin), 34.2 (CH₂), 26.0 (CH₂), 24.7 (2C, CH₃ (pin)), 24.6 (2C, CH₃ (pin)). **¹¹B{¹H} NMR** (128 MHz, CDCl₃): δ 32.4 (br s). **HRMS** (ESI): Calcd. for C₂₄H₂₉BN₅NaO₄ m/z 499.2236, found m/z 499.2240 [M+Na]⁺. **Minor diastereoisomer (syn-3ai):**

**Rt** (EtOAc:pentane = 25:75): 0.37. **IR** (neat, cm⁻¹): 2978, 2929, 2095, 1772, 1713, 1653, 1599, 1502, 1457, 1398, 1372, 1353, 1327, 1259, 1214, 1142, 1111, 1069, 1025. **¹H NMR** (400 MHz, CDCl₃): δ 7.47 – 7.40 (m, 4H, Ar-H), 7.36 – 7.30 (m, 1H, Ar-H), 6.55 (ddd, 3J_H,H' = 7.7 Hz, 5.6 Hz, 4J_H,H' = 1.7 Hz, 1H, =CH), 6.43 (ddd, 3J_H,H' = 7.7 Hz, 5.5 Hz, 4J_H,H' = 1.5 Hz, 1H, =CH), 5.37 (s, 1H, =CHH), 5.15 (dd, 3J_H,H' = 5.6 Hz, 4J_H,H' = 1.5 Hz, CHN), 5.11 – 5.07 (m, 2H, =CHH (1H) + CHN (1H)), 3.26 – 3.21 (m, 2H, CHHN₃), 1.86 – 1.75 (m, 1H, CHH), 1.66 – 1.52 (m, 2H, CHH), 1.41 – 1.30 (m, 1H, CHH), 1.26 (s, 6H, CH₃ (pin)), 1.25 (s, 6H, CH₃ (pin)). **¹³C{¹H} NMR** (101
MHz, CDCl₃): δ 155.7 (CO), 155.4 (CO), 143.9 (=C), 131.7 (arom.), 129.5 (=CH), 129.2 (2C, arom.), 129.1 (=CH), 128.2 (arom.), 125.5 (2C, arom.), 112.9 (=CH₂), 84.5 (2C, OC(CH₃)₂), 58.2 (CHN), 56.9 (CHN), 51.8 (CH₂N₃), 35.0 (CBpin), 35.0 (CH₂), 26.2 (CH₂), 25.0 (2C, CH₃ (pin)), 24.4 (2C, CH₃ (pin)). ¹¹B{¹H} NMR (128 MHz, CDCl₃): δ 33.0 (br s). HRMS (ESI): Calcd. for C₂₄H₂₉BN₆NaO₄ m/z 499.2236, found m/z 499.2230 [M+Na]+.
Prepared following the general procedure on a 500 μmol (114 mg) scale. Flash column chromatography on silica gel (Et₂O:pentane = 60:40) afforded the product as separable diastereoisomers as clear oils. Yield: 93 mg (38%) and 41 mg (17%), dr = 1:2.3. **Major diastereoisomer (anti-3aj):** R<sub>f</sub> (Et₂O:pentane = 75:25): 0.58. IR (neat, cm⁻¹): 2977, 2927, 2885, 1771, 1716, 1502, 1400, 1260, 1142, 1026. **<sup>1</sup>H NMR** (400 MHz, CDCl₃): δ 7.47 – 7.30 (m, 4H, Ar-H), 7.34 – 7.29 (m, 1H, Ar-H), 6.59 (dd, <sup>3</sup>J<sub>HH</sub> = 7.7, 5.8 Hz, <sup>4</sup>J<sub>HH</sub> = 1.6 Hz, 1H, =CH), 6.44 (dd, <sup>3</sup>J<sub>HH</sub> = 7.7, 5.6 Hz, <sup>4</sup>J<sub>HH</sub> = 1.3 Hz, 1H, =CH), 5.25 (s, 1H, =CHH), 5.14 (s, 1H, =CHH), 5.09 (dd, <sup>3</sup>J<sub>HH</sub> = 5.6 Hz, <sup>4</sup>J<sub>HH</sub> = 1.6 Hz, 1H, CH<sub>N</sub>), 5.01 (dd, <sup>3</sup>J<sub>HH</sub> = 5.8 Hz, <sup>4</sup>J<sub>HH</sub> = 1.3 Hz, 1H, CHN), 4.90 – 4.87 (m, 1H, CH(OCH<sub>2</sub>)₂), 3.99 – 3.90 (m, 2H, CHHO), 3.88 – 3.79 (m, 2H, CHHO), 2.04 – 1.88 (m, 3H, CHH), 1.74 – 1.64 (m, 1H, CHH), 1.18 (s, 6H, CH<sub>3</sub> (pin)), 1.18 (s, 6H, CH<sub>3</sub> (pin)). **<sup>13</sup>C<sup>1</sup>H NMR** (101 MHz, CDCl₃): δ 156.6 (CO), 155.9 (CO), 144.7 (=C), 133.3 (=CH), 131.7 (arom.), 129.1 (2C, arom.), 128.6 (=CH), 128.1 (arom.), 125.6 (2C, arom.), 112.1 (=CH₂), 104.4 (CH(OCH<sub>2</sub>)₂), 84.3 (2C, OC(CH<sub>3</sub>)₂), 65.0 (CH₂O), 64.9 (CH₂O), 58.4 (CHN), 55.4 (CHN), 36.2 (CBpin), 31.0 (CH₂), 30.8 (CH₂), 24.8 (2C, CH₃ (pin)), 24.5 (2C, CH₃ (pin)). **<sup>11</sup>B<sup>1</sup>H NMR** (128 MHz, CDCl₃): δ 32.2 (br s). HRMS (ESI): Calcd. for C₂₅H₂₈BN₃NaO₆ m/z 516.2281, found m/z 516.2283 [M+Na]<sup>+</sup>. **Minor diastereoisomer (syn-3aj):** R<sub>f</sub> (Et₂O:pentane = 75:25): 0.40. IR (neat, cm⁻¹): 2976, 2930 2886, 1773, 1713, 1501, 1397, 1259, 1141. **<sup>1</sup>H NMR** (400 MHz, CDCl₃): δ 7.47 – 7.38 (m, 4H, Ar-H), 7.35 – 7.29 (m, 1H, Ar-H), 6.52 (dd, <sup>3</sup>J<sub>HH</sub> = 7.7, 5.6 Hz, <sup>4</sup>J<sub>HH</sub> = 1.7 Hz, 1H, =CH), 6.43 (dd, <sup>3</sup>J<sub>HH</sub> = 7.7, 5.5 Hz, <sup>4</sup>J<sub>HH</sub> = 1.5 Hz, 1H, =CH), 5.36 (s, 1H, =CHH), 5.14 (dd, <sup>3</sup>J<sub>HH</sub> = 5.6 Hz, <sup>4</sup>J<sub>HH</sub> = 1.5 Hz, 1H, CHN), 5.11 – 5.08 (m, 2H, =CHH (1H) + CHN (1H)), 4.81 – 4.78 (m, 1H, CH(OCH<sub>2</sub>)₂), 3.98 – 3.89 (m, 2H, CHHO), 3.87 – 3.78 (m, 2H, CHHO), 1.96 – 1.79 (m, 1H, CHH), 1.72 – 1.60 (m, 2H, CHH), 1.47 – 1.35 (m, 1H, CHH), 1.25 (s, 6H, CH₃ (pin)), 1.24 (s, 6H, CH₃ (pin)). **<sup>13</sup>C<sup>1</sup>H NMR** (101 MHz, CDCl₃): δ 155.7 (CO), 155.4 (CO), 144.0
(=C), 131.8 (arom.), 129.3 (=CH), 129.2 (=CH), 129.1 (2C, arom.), 128.1 (arom.), 125.5 (2C, arom.), 112.8 (=CH\(_2\)), 104.3 (CH(OCH\(_2\))\(_2\)), 84.4 (2C, OC(CH\(_3\))\(_2\)), 65.04 (CH\(_2\)O), 65.01 (CH\(_2\)O), 58.3 (CHN), 57.0 (CHN), 36.5 (CBpin), 31.6 (CH\(_2\)), 30.9 (CH\(_2\)), 25.0 (2C, CH\(_3\) (pin)), 24.4 (2C, CH\(_3\) (pin)). \(^{11}\)B\(^{1}\)H NMR (128 MHz, CDCl\(_3\)): \(\delta\) 33.2 (br s). \textbf{HRMS} (ESI): Calcd. for C\(_{26}\)H\(_{32}\)BN\(_3\)NaO\(_6\) \(m/z\) 516.2281, found \(m/z\) 516.2286 [M+Na]\(^+\).
(±)-(5S,8R,11S)-11-Cyclohexyl-8-methyl-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ba)

Prepared following the general procedure on a 500 μmol (105 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as a clear oil. Yield: 202 mg mg (83%), dr = 15:1. \( R_f \) (EtOAc:pentane = 15:85): 0.82. \( \text{IR (neat, cm}^{-1}) \): 2977, 2928, 2852, 1767, 1714, 1503, 1450, 1398, 1321, 1267, 1140, 1096, 1026. \( ^1H \text{NMR (400 MHz, CDCl}_3 \): \( \delta \) 7.41 – 7.29 (m, 4H, Ar-H), 7.25 – 7.18 (m, 1H, Ar-H), 6.36 (dd, \( 3J_{H,H'} = 7.7, 5.6 \) Hz, 1H, =CH), 6.14 (d, \( 3J_{H,H'} = 7.7 \) Hz, 1H, =CH), 5.33 (s, 1H, =CHH), 5.22 (s, 1H, =CHH), 5.17 (d, \( 3J_{H,H'} = 5.6 \) Hz, 1H, CHN), 2.02 – 1.91 (m, 1H, 1H, CHH), 1.98 (s, 3H, CH₃), 1.74 – 1.51 (m, 4H, CHH), 1.16 (s, 6H, CH₃ (pin)), 1.14 (s, 6H, CH₃ (pin)), 1.12 – 0.95 (m, 6H, CH (1H) + CHH (5H)). \( ^{13}C\{^1H\} \text{NMR (101 MHz, CDCl}_3 \): \( \delta \) 153.5 (C=O), 152.7 (C=O), 146.6 (=C), 133.6 (=CH), 131.9 (arom.), 129.6 (=CH), 128.9 (2C, arom.), 127.8 (arom.), 125.6 (2C, arom.), 111.5 (=CH₂), 84.0 (2C, OC(CH₃)₂), 62.5 (CN), 55.0 (CHN), 44.3 (CH), 31.0 (CH₂), 29.7 (CH₂), 27.3 (CH₂), 27.1 (CH₂), 26.4 (CH₂), 25.0 (2C, CH₃ (pin)), 24.3 (2C, CH₃ (pin)), 18.3 (CH₃), carbon attached to boron not observed due to quadrupolar relaxation. \( ^{11}B\{^1H\} \text{NMR (128 MHz, CDCl}_3 \): \( \delta \) 33.8 (br s). \( \text{HRMS (ESI): Calcd. for C}_{28}H_{36}BN_3NaO_4 \text{ m/z 512.2696, found m/z 512.2689 [M}+\text{Na}^+].\)
(±)-(5R,8R,11S)-11-Cyclohexyl-6-methyl-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborol-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ca)

![Chemical structure of 3ca]

Prepared following the general procedure on a 500 μmol (105 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as a white solid. Yield: 180 mg (74%), dr >20:1. **MP:** 77 °C. **Rf** (EtOAc:pentane = 15:85): 0.56. **IR** (neat, cm⁻¹): 2925, 2851, 1774, 1718, 1502, 1445, 1397, 1323, 1268, 1139, 1026. **¹H NMR** (400 MHz, CDCl₃): δ 7.47 – 7.37 (m, 4H, Ar-H), 7.33 – 7.27 (m, 1H, Ar-H), 6.07 (ddd, J_H,H' = 5.6 Hz, J_H,H' = 1.7, 1.5 Hz, 1H, =CH), 5.40 (s, 1H, =CHH), 5.14 (s, 1H, =CHH), 5.10 (d, J_H,H' = 1.7 Hz, 1H, CHN), 5.04 (d, J_H,H' = 5.8 Hz, 1H, CHN), 2.05 – 1.61 (m, 5H, CHH), 1.94 (d, J_H,H' = 1.5 Hz, 3H, CH₃), 1.25 (s, 6H, CH₃ (pin)), 1.23 (s, 6H, CH₃ (pin)), 1.20 – 1.02 (m, 6H, CH (1H) + CHH (5H)). **¹³C{¹H} NMR** (101 MHz, CDCl₃): δ 156.0 (CO), 155.6 (CO), 142.1 (=C), 139.9 (=C), 131.8 (arom.), 129.0 (2C, arom.), 127.9 (arom.), 125.2 (2C, arom.), 121.1 (=CH), 113.8 (=CH₂), 84.0 (2C, OC(CH₃)₂), 61.1 (CHN), 60.0 (CHN), 43.7 (CH), 41.7 (CBpin), 30.5 (CH₂), 29.9 (CH₂), 27.1 (CH₂), 27.0 (CH₂), 26.4 (CH₂), 25.1 (2C, CH₃ (pin)), 24.2 (2C, CH₃ (pin)), 20.7 (CH₃). **¹¹B{¹H} NMR** (128 MHz, CDCl₃): δ 32.6 (br s). **HRMS** (ESI): Calcd. for C₂₈H₃₆BN₃NaO₄ m/z 512.2696, found m/z 512.2693 [M+Na]⁺.
(±)-(5S,8S,11S)-11-Cyclohexyl-8-fluoro-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3da)

Prepared following the general procedure on a 500 μmol (105 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as a white solid. Yield: 85 mg (34%), dr >20:1. **MP**: 181 °C. **Rf** (EtOAc:pentane = 20:80): 0.76. **IR** (neat, cm⁻¹): 2980, 2979, 2858, 1788, 1730, 1396, 1233, 1140, 1055. **¹H NMR** (400 MHz, CDCl₃): δ 7.45 – 7.39 (m, 4H, Ar-H), 7.37 – 7.31 (m, 1H, Ar-H), 6.60 (ddd, 3JH,H' = 8.7 Hz, 3JF,H = 7.3 Hz, 4JH,H' = 1.4 Hz, 1H, =CH), 6.42 (ddd, 3JH,H' = 8.7 Hz, 4JF,H = 5.6 Hz, 3JH,H' = 5.5 Hz, 1H, =CHH), 5.73 (d, 4JF,H = 1.3 Hz, 1H, =CHH), 5.45 (d, 4JF,H = 5.6 Hz, 1H, =CHH), 5.26 (dd, 3JH,H' = 5.5 Hz, 4JH,H' = 1.4 Hz, 1H, CHN), 2.07 – 1.98 (m, 1H, CHH), 1.81 – 1.69 (m, 3H, CHH), 1.67 – 1.60 (m, 1H, CHH), 1.27 (s, 6H, CH₃ (pin)), 1.26 (s, 6H, CH₃ (pin)), 1.23 – 1.01 (m, 6H, CH (1H)CHH (5H)). **¹³C{¹H} NMR** (101 MHz, CDCl₃): δ 156.8 (CO), 155.1 (d, 3JF,C = 3.3 Hz, CO), 141.4 (d, 2JF,C = 12.1 Hz, =C), 131.3 (arom.), 129.2 (d, 2JF,C = 31.8 Hz, =CH), 129.1 (2C, arom.), 129.0 (d, 3JF,C = 9.8 Hz, =CH), 128.4 (arom.), 125.6 (2C, arom.), 111.9 (d, 3JF,C = 12.9 Hz, =CH₂), 101.4 (d, 1JF,C = 228.8 Hz, CF), 84.4 (2C, OC(CH₃)₂), 58.1 (CHN), 44.3 (CH), 42.3 (CBpin), 30.8 (CH₂), 29.6 (CH₂), 27.1 (CH₂), 26.9 (CH₂), 26.3 (CH₂), 25.2 (2C, CH₃ (pin)), 24.5 (2C, CH₃ (pin)). **¹⁹F NMR** (377 MHz, CDCl₃): δ –163.3 (dddd, 3JF,H = 7.3 Hz, 4JF,H = 5.6, 5.6, 1.3 Hz). **HRMS** (ESI): Calcd. for C₂₇H₃₄BFN₃O₄ m/z 494.2625, found m/z 494.2626 [M+H]⁺.
(±)-(5S,8S,11S)-11-Cyclohexyl-7-fluoro-10-methylene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3ea)

Prepared following the general procedure on a 500 μmol (105.1 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 10:90) afforded the product as a white solid. Yield: 141.3 mg (57%), dr >20:1, \( \text{MP} \): 166 °C. \( R_f \) (EtOAc:pentane = 10:90): 0.62. IR (neat, cm\(^{-1}\)): 2982, 2927, 2851, 1782, 1714, 1664, 1395, 1327, 1141. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.50–7.40 (m, 4H, Ar-\( H \)), 7.39–7.30 (m, 1H, Ar-\( H \)), 5.64 (\( \text{ddd} \), \( ^3J_{\text{H,H'}} = 6.5 \) Hz, \( ^3J_{\text{F,H}} = 5.3 \) Hz, \( ^4J_{\text{H,H'}} = 2.7 \) Hz, 1H, =CH), 5.49 (s, 1H, =CHH), 5.36 – 5.31 (m, 2H, =CHH (1H) + CHN (1H)), 5.14 (dd, \( ^3J_{\text{H,H'}} = 7.7 \) Hz, \( ^4J_{\text{F,H}} = 2.7 \) Hz, 1H, CHN), 2.10 – 2.01 (m, 1H, CHH), 1.84 – 1.60 (m, 4H, CHH), 1.26 (s, 6H, CH\(_3\) (pin)), 1.25 (s, 6H, CH\(_3\) (pin)), 1.22 – 1.01 (m, 6H, CH (1H) + CHH (5H)). \(^{13}\)C{\(^1\)H} NMR (101 MHz, CDCl\(_3\)): \( \delta \) 159.4 (CO), 156.4 (CO), 155.73 (\( d, ^1J_{\text{F,C}} = 56.9 \) Hz, =CF), 141.7 (\( d, ^3J_{\text{F,C}} = 1.4 \) Hz, =C), 131.4 (arom.), 129.1 (2C, arom.), 128.2 (arom.), 125.3 (2C, arom.), 115.6 (=CH\(_2\)), 101.3 (=CH), 84.3 (2C, OC(CH\(_3\))\(_2\)), 60.2 (\( d, ^2J_{\text{F,C}} = 24.9 \) Hz, CHN), 57.9 (\( d, ^3J_{\text{F,C}} = 6.2 \) Hz, CHN), 44.2 (CH), 42.5 (CBpin), 30.8 (CH\(_2\)), 29.4 (CH\(_2\)), 27.1 (CH\(_2\)), 26.9 (CH\(_2\)), 26.2 (CH\(_2\)), 25.1 (2C, CH\(_3\) (pin)), 24.3 (2C, CH\(_3\) (pin)). \(^{11}\)B{\(^1\)H} NMR (128 MHz, CDCl\(_3\)): \( \delta \) 31.4 (br s). \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): \( \delta \) –107.8 (\( dd, ^3J_{\text{F,H}} = 7.6, 5.6 \) Hz). HRMS (ESI): Calcd. for C\(_{27}\)H\(_{34}\)BF\(_3\)NaO\(_4\) \( m/z \) 516.2447, found \( m/z \) 516.2445 [M+Na]\(^{+}\).
\((-\)-(5R,8S,11R,Z)-11-Cyclohexyl-10-ethylidene-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3fa)

Prepared following the general procedure on a 500 μmol (105 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as a colorless oil that solidified upon standing. Yield: 169 mg (69%), dr >20:1. \([\alpha]_D^{23} = -3.9 \text{ (c 1.03, CHCl}_3\text{). MP: } >200 ^\circ\text{C.} \) 

\[ \text{IR (neat, cm}^{-1} \text{): 2976, 2926, 2855, 1772, 1717, 1502, 1397, 1264, 1140.} \] 

\[ \text{1H NMR (400 MHz, CDCl}_3\text{):} \delta 7.47 – 7.39 \text{ (m, 4H, Ar-H), 7.34 – 7.29 \text{ (m, 1H, Ar-H)}, 6.48 – 6.41 \text{ (m, 2H, =CH), 5.72 (q, J}_{H,H'} = 7.0 \text{ Hz, 1H, =CH), 5.61 (dd, J}_{H,H'} = 4.9 \text{ Hz, J}_{H,H'} = 2.4 \text{ Hz, 1H, CHN), 5.22 (dd, J}_{H,H'} = 4.8 \text{ Hz, J}_{H,H'} = 2.5 \text{ Hz, 1H, CHN), 2.05 – 1.98 \text{ (m, 1H, CHH), 1.88 (d, J}_{H,H'} = 7.0 \text{ Hz, 3H, CH}_3\text{), 1.78 – 1.60 \text{ (m, 4H, CHH), 1.25 (s, 6H, CH}_3\text{ (pin)), 1.22 (s, 6H, CH}_3\text{ (pin)), 1.20 – 1.02 \text{ (m, 6H, CH (1H) + CHH (5H))}.} \]

\[ \text{13C\{1H} \text{ NMR (101 MHz, CDCl}_3\text{):} \delta 155.7 \text{ (CO), 155.2 (CO), 133.3 (=C), 132.0 (arom.), 130.4 (=CH), 129.1 (2C, arom.), 128.5 (=CH), 128.0 (arom.), 125.5 (2C, arom.), 122.9 (=CH), 84.0 (2C, OC(CH}_3\text{)_2), 56.9 (CHN), 51.2 (CHN), 44.5 (CH), 31.2 (CH}_2\text{), 30.0 (CH}_2\text{), 27.50 (CH}_2\text{), 27.3 (CH}_2\text{), 26.5 (CH}_2\text{), 25.2 (2C, CH}_3\text{ (pin)), 24.4 (2C, CH}_3\text{ (pin)), 14.2 (CH}_3\text{), carbon attached to boron not observed due to quadrupolar relaxation.} \]

\[ \text{11B\{1H} \text{ NMR (128 MHz, CDCl}_3\text{):} \delta 33.3 \text{ (br s). HRMS (ESI): Calcd. for C}_{28}\text{H}_{36}\text{BN}_3\text{NaO}_4 \text{ m/z 512.2696, found m/z 512.2693 [M+Na]^+.} \]
The enantiomeric excess of 3fa was determined after oxidation to the corresponding alcohol 4fa. Sodium perborate tetrahydrate (36 mg, 0.23 mmol, 1.3 equiv) and water (1 mL) were added to 3fa (88 mg, 0.18 mmol) in THF (1 mL) and the solution was stirred at rt for 16 h. The solution was diluted with EtOAc (50 mL), washed with water (25 mL) and saturated aqueous NaCl solution (25 mL), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (EtOAc:pentane = 40:60) afforded the product 4fa as a white solid. Yield: 30 mg (44%), dr >20:1. $R_f$ (EtOAc:pentane = 40:60): 0.35. IR (neat, cm$^{-1}$): 3460, 2948, 2924, 2851, 1779, 1714, 1400, 788. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.45 – 7.41 (m, 4H, Ar-H), 7.38 – 7.32 (m, 1H, Ar-H), 6.51 – 6.42 (m, 2H, =C-H), 5.83 ($q$, $^3$J$_{H,H'}$ = 7.0 Hz, 1H, =C-H), 5.63 ($dd$, $^3$J$_{H,H'}$ = 5.5 Hz, $^4$J$_{H,H'}$ = 1.8 Hz, 1H, CHN), 4.92 ($dd$, $^3$J$_{H,H'}$ = 5.6 Hz, $^4$J$_{H,H'}$ = 2.0 Hz, 1H, CHN), 2.65 (s, 1H, OH), 2.18 – 2.12 (m, 1H, CHH), 1.88 – 1.82 (m, 1H, CHH), 1.85 ($d$, $^3$J$_{H,H'}$ = 7.0 Hz, 3H, CH$_3$), 1.77 – 1.57 (m, 3H, CH (1H) + CHH (2H)), 1.47 – 1.40 (m, 1H, CHH), 1.30 – 0.91 (m, 5H, CHH). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$): $\delta$ 157.4 (CO), 155.5 (CO), 135.0 (=C), 131.5 (arom.), 130.1 (=CH), 129.3 (CH), 129.2 (2C, arom.), 128.4 (arom.), 125.6 (2C, arom.), 124.0 (=CH), 76.9 (COH), 60.6 (CHN), 51.3 (CHN), 45.6 (CH), 29.9 (CH$_2$), 27.44 (CH$_2$), 27.42 (CH$_2$), 26.8 (CH$_2$), 26.5 (CH$_2$), 13.7 (CH$_3$). HRMS (ESI): Calcd. for C$_{22}$H$_{35}$N$_3$O$_3$ m/z 380.1969, found m/z 380.1971 [M+H]$^+$. HPLC: Chiralpak IA (hexane:2-propanol = 85:15, flow rate 1.0 mL/min, $\lambda$ = 230 nm), retention times $t_R$(major) = 16.6 min, $t_R$(minor) = 22.2 min; 89.2% ee.
Figure S1: HPLC traces of 4fa: racemic (top) and enantioenriched (bottom)
Scale-up procedure for the synthesis of (±)-3fa:

\[ \text{boronic ester} + \text{amine} \rightarrow \text{product} \]

1) n-BuLi, THF, –78 °C, 60 min
2) THF, –78 °C to rt, 45 mins
3) PTAD, THF, rt, 60 mins

\( \text{2a} \) (1.05 g, 5.00 mmol) was added and the solution was stirred at –78 °C for 15 min, after which the cooling bath was removed and the reaction was allowed to stir for a further 10 min. 4-Phenyl-1,2,4-triazoline-3,5-dione (963 mg, 5.50 mmol, 1.10 equiv) was added and the solution was stirred for 60 min at rt. CHCl₃ (150 mL) was added and the solution was washed with water (75 mL) and saturated aqueous NaCl solution (75 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (gradient EtOAc:pentane = 5:95 to 20:80) afforded the product as a white solid. Yield: 1.81 g (74%), dr = 15:1.

\( n\)-BuLi (3.28 mL, 1.6 M in hexanes, 5.25 mmol, 1.05 equiv) was added to (±)-1f (1.20 g, 5.25 mmol, 1.05 equiv) in THF (20 mL) at –78 °C and the solution was stirred at –78 °C for 60 min. 2a (1.05 g, 5.00 mmol) was added and the solution was stirred at –78 °C for 15 min, after which the cooling bath was removed and the reaction was allowed to stir for a further 30 min. 2,2,2-Trichloro-1,1-dimethylethyl chloroformate (1.32 g, 5.50 mmol, 1.10 equiv) was added at –78 °C and the solution was stirred for 15 min at –78 °C, after which the cooling bath was removed and the reaction was allowed to stir for a further 10 min. 4-Phenyl-1,2,4-triazoline-3,5-dione (963 mg, 5.50 mmol, 1.10 equiv) was added and the solution was stirred for 60 min at rt. CHCl₃ (150 mL) was added and the solution was washed with water (75 mL) and saturated aqueous NaCl solution (75 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (gradient EtOAc:pentane = 5:95 to 20:80) afforded the product as a white solid. Yield: 1.81 g (74%), dr = 15:1.
(-)-(5R,8S,11S,Z)-10-Ethylidene-11-phenethyl-2-phenyl-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (3fg)

Prepared following the general procedure on a 500 μmol (116 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil. Yield: 77 mg (30%), dr = 1:2.2. [α]D 23 = -10 (c 1.00, CHCl₃). Rf (EtOAc:pentane = 20:80): 0.46. IR (neat, cm⁻¹): 2977, 2925, 1770, 1716, 1502, 1399, 1324, 1262, 1142. ¹H NMR (400 MHz, CDCl₃): major diastereoisomer: δ 7.52 – 7.42 (m, 4H, Ar-H), 7.38 – 7.12 (m, 6H, Ar-H), 6.66 (ddd, 3J_H,H' = 7.4 Hz, 5.8 Hz, 4J_H,H' = 1.5 Hz, 1H, =CH), 6.48 – 6.43 (m, 1H, =CH), 5.69 – 5.60 (m, 1H, =CH), 5.58 (ddd, 3J_H,H' = 5.7 Hz, 4J_H,H' = 1.3 Hz, 1H, CHN), 5.17 (dd, 3J_H,H' = 5.8 Hz, 4J_H,H' = 1.5 Hz, 1H, CHN), 2.92 – 2.75 (m, 1H, PhCHH), 2.65 – 2.53 (m, 1H, PhCHH), 2.19 – 2.05 (m, 2H, CHH), 1.80 (d, 3J_H,H' = 7.0 Hz, 3H, CH₃), 1.24 (s, 12H, CH₃ (pin)); minor diastereoisomer: δ 7.52 – 7.42 (m, 4H, Ar-H), 7.38 – 7.12 (m, 6H, Ar-H), 6.53 (ddd, 3J_H,H' = 7.6 Hz, 5.7 Hz, 4J_H,H' = 1.8 Hz, 1H, =CH), 6.48 – 6.43 (m, 1H, =CH), 5.69 – 5.60 (m, 2H, =CH (1H) + CHN (1H)), 5.21 (dd, 3J_H,H' = 5.5 Hz, 4J_H,H' = 1.8 Hz, 1H, CHN), 2.92 – 2.75 (m, 2H, PhCHH), 2.65 – 2.53 (m, 1H, CHH), 1.86 (d, 3J_H,H' = 7.0 Hz, 3H, CH₃), 1.58 – 1.49 (m, 1H, CHH), 1.30 (s, 6H, CH₃ (pin)), 1.29 (s, 6H, CH₃ (pin)). ¹³C [¹H] NMR (101 MHz, CDCl₃): major diastereoisomer: δ 156.6 (CO), 155.9 (CO), 142.3 (arom.), 135.6 (=C), 133.5 (=CH), 131.8 (arom.), 129.1 (2C, arom.), 128.6 (arom.), 128.5 (4C, =CH (1C) + arom. (3C)), 128.1 (arom.), 125.9 (arom.), 125.6 (2C, arom.), 121.1 (=CH), 84.2 (2C, OC(CH₃)₂), 55.3 (CHN), 51.6 (CHN), 39.9 (PhCH₂), 36.5 (CBpin), 33.1 (CH₂), 24.9 (2C, CH₃ (pin)), 24.7 (2C, CH₃ (pin)), 13.9 (CH₃); minor diastereoisomer: δ 155.5 (CO), 155.2 (CO), 142.2 (arom.), 134.8 (=C), 131.9 (arom.), 129.4 (=CH), 129.2 (=CH), 129.1 (2C, arom.), 128.6 (2C, arom.), 128.5 (2C, arom.), 128.1 (arom.), 126.1 (arom.), 125.5 (2C, arom.), 122.1 (=CH), 84.2 (2C, OC(CH₃)₂), 58.6 (CHN), 51.1 (CHN), 40.6 (PhCH₂), 36.5 (CBpin), 33.4 (CH₂), 25.1 (2C, CH₃ (pin)), 24.4 (2C, CH₃ (pin)), 14.1 (CH₃).
$^{11}$B{$^1$H} NMR (128 MHz, CDCl$_3$): $\delta$ 32.9 (br s). HRMS (ESI): Calcd. for C$_{30}$H$_{35}$BN$_3$O$_4$ m/z 512.2720, found m/z 512.2696 [M+Na]$^+$. 

$(5S,8R,11S,E)$-10-Ethylidene-11-hydroxy-11-phenethyl-2-phenyl-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (4fg)

The enantiomeric excess of 3fg was determined after oxidation to the corresponding alcohol 4fg. Sodium perborate tetrahydrate (17 mg, 0.11 mmol, 2.2 equiv) and water (1 mL) were added to 3fg (25 mg, 49 μmol) in THF (1 mL) and the solution was stirred at rt for 16 h. The solution was diluted with EtOAc (50 mL), washed with water (25 mL) and saturated aqueous NaCl solution (25 mL), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (EtOAc:pentane = 50:50) afforded the product 4fg as a white solid. Yield: 11.4 mg (58%), dr>20:1. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.49 – 7.43 (m, 4H, Ar-H), 7.41 – 7.35 (m, 1H, Ar-H), 7.32 – 7.25 (m, 4H, Ar-H), 7.22 – 7.17 (m, 1H, Ar-H), 6.73 ($^{3}$J$_{H,H'}$ = 7.7, 5.7 Hz, $^4$J$_{H,H'}$ = 1.7 Hz, 1H, =CH), 5.88 (q, $^3$J$_{H,H'}$ = 7.0 Hz, 1H, =CH), 5.62 ($^{3}$J$_{H,H'}$ = 5.7 Hz, $^4$J$_{H,H'}$ = 1.7 Hz, 1H, CHN), 5.11 ($^{3}$J$_{H,H'}$ = 5.6 Hz, $^4$J$_{H,H'}$ = 1.7 Hz, 1H, CHN), 3.01 – 2.89 (m, 2H, PhCH$_2$H), 2.30 – 2.13 (m, 2H, CHH), 1.84 ($^{3}$J$_{H,H'}$ = 7.0 Hz, 3H, CH$_3$), 1.75 (s, 1H, OH). $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$): $\delta$ 155.9 (CO), 155.8 (CO), 141.9 (arom.), 140.2 (=C), 132.3 (=CH), 131.5 (arom.), 130.3 (=CH), 129.3 (2C, arom.), 128.63 (2C, arom.), 128.61 (2C, arom.), 128.5 (arom.), 126.1 (arom.), 125.6 (2C, arom.), 123.2 (=CH), 73.7 (COH), 57.2 (CHN), 51.5 (CHN), 40.8 (CH$_2$), 29.9 (PhCH$_2$), 13.7 (CH$_3$). HPLC: Chiralpak IB (hexane:2-propanol = 85:15, flow rate 1.0 mL/min, $\lambda$ = 210 nm), retention times $t_R$(major) = 9.9 min, $t_R$(minor) = 13.9 min; 82.8%ee.
Figure S2: HPLC traces of 4fg: racemic (top) and enantioenriched (bottom)
\((-\)(5R,8S,11R,Z)-10-Ethylidene-11-\((R)\)-4-(4-methoxyphenyl)butan-2-yl)-2-phenyl-11-(4,4, 5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo[1,2-\(\alpha\)]py-ridazine-1,3(2H)-dione (3fk)

Prepared following the general procedure on a 500 μmol (145 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil. Yield: 217 mg (76%), dr = 9:1. [\(\alpha\)]\(_D\)^23 = –4.7 (c 1.06, CHCl\(_3\)). \(R\)_\(f\) (EtOAc:pentane = 20:80): 0.36. IR (neat, cm\(^{-1}\)): 2976, 2930, 1771, 1716, 1611, 1512, 1457, 1399, 1319, 1247, 1143, 1036. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.48 – 7.39 (m, 4H, Ar-H), 7.34 – 7.29 (m, 1H, Ar-H), 7.05 – 7.01 (m, 2H, Ar-H), 6.85 – 6.81 (m, 2H, Ar-H), 6.35 (ddd, \(^3\)\(J\)\(_{H,H'}\) = 7.7, 5.8 Hz, \(^4\)\(J\)\(_{H,H'}\) = 1.7 Hz, 1H, =CH), 6.28 – 6.22 (m, 1H, =CH), 5.61 (dd, \(^3\)\(J\)\(_{H,H'}\) = 5.8 Hz, \(^4\)\(J\)\(_{H,H'}\) = 1.4 Hz, 1H, CHN), 5.54 (q, \(^3\)\(J\)\(_{H,H'}\) = 7.0 Hz, 1H, =CH), 5.19 (dd, \(^3\)\(J\)\(_{H,H'}\) = 5.5 Hz, \(^4\)\(J\)\(_{H,H'}\) = 1.8 Hz, 1H, CHN), 3.78 (s, 3H, OCH\(_3\)), 2.73 – 2.64 (m, 1H, ArCHH), 2.33 – 2.24 (m, 1H, ArCHH), 1.85 (d, \(^3\)\(J\)\(_{H,H'}\) = 7.0 Hz, 3H, CH\(_3\)), 1.77 – 1.67 (m, 1H, CHH), 1.58 – 1.48 (m, 1H, CH), 1.28 – 1.23 (m, 1H, CHH), 1.25 (s, 6H, CH\(_3\) (pin)), 1.22 (s, 6H, CH\(_3\) (pin)), 1.12 (d, \(^3\)\(J\)\(_{H,H'}\) = 6.8 Hz, 3H, CH\(_3\)). \(^{13}\)C\({^1}\)H NMR (101 MHz, CDCl\(_3\)): \(\delta\) 157.8 (arom.), 155.3 (CO), 155.1 (CO), 134.1 (=C), 132.9 (arom.), 131.8 (arom.), 130.3 (=CH), 129.3 (2C, arom.), 128.9 (2C, arom.), 127.9 (arom.), 127.8 (=CH), 125.4 (2C, arom.), 122.4 (=CH), 113.7 (2C, arom.), 83.8 (2C, OC(CH\(_3\))\(_2\)), 56.1 (CHN), 55.2 (OCH\(_3\)), 51.3 (CHN), 41.3 (CBpin), 37.2 (CH), 35.7 (CH\(_2\)), 33.9 (ArCH\(_2\)), 25.0 (2C, CH\(_3\) (pin)), 24.2 (2C, CH\(_3\) (pin)), 17.0 (CH\(_3\)), 14.0 (CH\(_3\)). \(^{11}\)B\({^1}\)H NMR (128 MHz, CDCl\(_3\)): \(\delta\) 35.0 (br s). HRMS (ESI): Calcd. for C\(_{33}\)H\(_{40}\)BN\(_3\)NaO\(_5\) \(m/z\) 592.2959, found \(m/z\) 592.2966 [M+Na]\(^+\).
Prepared following the general procedure on a 500 μmol (145 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 15:85) afforded the product as an inseparable mixture of diastereoisomers as a colorless oil. Yield: 191 mg (67%), dr = 10:1. [α]D23 = +39.6 (c 1.01, CHCl3). Rf (EtOAc:pentane = 20:80): 0.42. IR (neat, cm⁻¹): 2976, 2925, 1772, 1718, 1512, 1400, 1247, 1142. 1H NMR (400 MHz, CDCl3): δ 7.48 – 7.39 (m, 4H, Ar-H), 7.34 – 7.29 (m, 1H, Ar-H), 7.09 – 7.05 (m, 2H, Ar-H), 6.86 – 6.80 (m, 2H, Ar-H), 6.47 – 6.40 (m, 2H, =C-H), 5.68 (q, 3J_H,H' = 7.0 Hz, 1H, =C-H), 5.63 (dd, 3J_H,H' = 4.6 Hz, 4J_H,H' = 2.7 Hz, 1H, CHN), 5.19 (dd, 3J_H,H' = 4.5 Hz, 4J_H,H' = 2.7 Hz, 1H, CHN), 3.79 (s, 3H, OCH3), 2.75 – 2.67 (m, 1H, ArCHH), 2.44 – 2.35 (m, 1H, ArCHH), 2.17 – 2.08 (m, 1H, CHH), 1.86 (d, 3J_H,H' = 7.0 Hz, 3H, CH3), 1.59 – 1.50 (m, 1H, CH), 1.47 – 1.35 (m, 1H, CHH), 1.23 (s, 6H, CH3 (pin)), 1.20 (s, 6H, CH3 (pin)), 0.96 (d, 3J_H,H' = 6.8 Hz, 3H, CH3). 13C{1H} NMR (101 MHz, CDCl3): δ 157.8 (arom.), 155.4 (CO), 155.1 (CO), 134.3 (arom.), 133.8 (==C), 131.8 (arom.), 130.4 (==C), 129.2 (2C, arom.), 129.0 (2C, arom.), 128.4 (==C), 127.9 (arom.), 125.4 (2C, arom.), 122.4 (==C), 113.8 (2C, arom.), 83.9 (2C, OC(CH3)2), 56.5 (CHN), 55.3 (OCH3), 51.2 (CHN), 41.0 (CBpin), 38.5 (CH), 36.8 (CH2), 33.7 (ArCH2), 25.0 (2C, CH3 (pin)), 24.3 (2C, CH3 (pin)), 16.5 (CH3), 14.1 (CH3). 11B{1H} NMR (128 MHz, CDCl3): δ 31.2 (br s). HRMS (ESI): Calcd. for C33H40BN3NaO5 m/z 592.2959, found m/z 592.2963 [M+Na]+.
(−)-(5R,8S,11R,Z)-10-Ethylidene-11-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-2-phenyl-11-(4,4,5,5-tetramethyl-1,3-dioxaborolan-2-yl)-5,8-dihydro-1H-5,8-ethano[1,2,4]triazolo-[1,2-a]pyridazine-1,3(2H)-dione (3f)

Prepared following the general procedure on a 500 μmol (133 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 7:93) afforded the product as an inseparable mixture of diastereoisomers as a white solid. Yield: 231 mg (85%), dr 17:1. [α]D23 = −37.6 (c 1.01, CHCl3). MP: 77 °C. Rt (EtOAc:pentane = 10:90): 0.34. IR (neat, cm⁻¹): 2925, 2868, 1769, 1714, 1601, 1503, 1456, 1398, 1310, 1266, 1142, 1073, 1025. ¹H NMR (400 MHz, CDCl3): δ 7.51 – 7.46 (m, 2H, Ar-H), 7.42 – 7.37 (m, 2H, Ar-H), 7.32 – 7.25 (m, 1H, Ar-H), 6.59 (ddd, 3J_HH' = 7.5, 5.7 Hz, 4J_HH' = 1.3 Hz, 1H, =CH), 6.34 (ddd, 3J_HH' = 7.5, 5.9 Hz, 4J_HH' = 1.5 Hz, 1H, =CH), 5.81 (q, 3J_HH' = 7.0 Hz, 1H, =CH), 5.62 (dd, 3J_HH' = 5.9 Hz, 4J_HH' = 1.3 Hz, 1H, CHN), 5.13 (dd, 3J_HH' = 5.7 Hz, 4J_HH' = 1.5 Hz, 1H, CHN), 1.85 – 1.73 (m, 2H, CH), 1.79 (d, 3J_HH' = 7.0 Hz, 3H, CH3), 1.67 – 1.52 (m, 3H, CHH), 1.36 – 1.27 (m, 1H, CH), 1.18 (s, 6H, CH3 (pin)), 1.15 (s, 6H, CH3 (pin)), 1.02 – 0.87 (CH (1H) + CHH (2H), 0.85 (d, 3J_HH' = 6.5 Hz, 3H, CH3), 0.82 – 0.74 (m, 1H, CHH), 0.71 (d, 3J_HH' = 6.9 Hz, 3H, CH3), 0.61 (d, 3J_HH' = 6.7 Hz, 3H, CH3). ¹³C{¹H} NMR (101 MHz, CDCl3): δ 154.0 (CO), 153.6 (CO), 133.1 (=C), 132.1 (arom.), 131.0 (=CH), 128.9 (2C, arom.), 127.6 (arom.), 126.8 (=CH), 125.2 (2C, arom.), 122.0 (=CH), 83.3 (2C, OC(CH3)2), 53.9 (CHN), 50.8 (CHN), 46.8 (CH), 43.5 (CH), 42.7 (CBpin), 42.4 (CH2), 34.7 (CH2), 33.6 (CH), 26.4 (CH), 25.5 (CH2), 24.6 (2C, CH3 (pin)), 24.4 (2C, CH3 (pin)), 22.7 (CH3), 21.3 (CH3), 15.7 (CH3), 13.7 (CH3). ¹¹B{¹H} NMR (128 MHz, CDCl3): δ 32.4 (br s). HRMS (ESI): Calcd. for C₃₂H₄₄BN₃NaO₄ m/z 568.3323, found m/z 568.3314 [M+Na]^+. 

S39
Prepared following the general procedure on a 500 μmol (133 mg) scale. Flash column chromatography on silica gel (EtOAc:pentane = 7:93) afforded the product as a white solid. Yield: 204 mg (75%), dr > 20:1. [α]D23 = –68.9 (c 1.03, CHCl3). MP: 128 °C. IR (neat, cm−1): 2952, 2927, 1771, 1716, 1502, 1397, 1315, 1263, 1139, 1071. 1H NMR (400 MHz, CDCl3): δ 7.53–7.48 (m, 2H, Ar-H), 7.45–7.38 (m, 2H, Ar-H), 7.34–7.28 (m, 1H, Ar-H), 6.61 (ddd, 3JH,H′ = 7.7, 5.9 Hz, 4JH,H′ = 1.3 Hz, 1H, =CH), 6.24 (ddd, 3JH,H′ = 7.7, 5.7 Hz, 4JH,H′ = 1.3 Hz, 1H, =CH), 5.57 (dd, 3JH,H′ = 5.7 Hz, 4JH,H′ = 1.4 Hz, 1H, CHN), 5.51 (q, 3JH,H′ = 7.1 Hz, 1H, =CH), 4.92 (dd, 3JH,H′ = 5.9 Hz, 4JH,H′ = 1.3 Hz, 1H, CHN), 2.08–1.96 (m, 2H, CH (1H) + CHH (2H)), 1.82 (d, 3JH,H′ = 7.1 Hz, 3H, CH3), 1.75–1.58 (m, 3H, CH (1H) + CHH (2H)), 1.48 (ddd, 3JH,H′ = 11.3, 11.3, 2.7 Hz, 1H, CH), 1.20–1.12 (m, 1H, CH), 1.17 (s, 6H, CH3 (pin)), 1.11–0.95 (m, 10H, CHH (2H) + CH3 (3H) + CH3 (6H, pin)), 0.87 (d, 3JH,H′ = 6.6 Hz, 3H, CH3), 0.83 (d, 3JH,H′ = 6.5Hz, 3H, CH3), 0.82–0.76 (m, 1H, CHH). 13C{1H} NMR (101 MHz, CDCl3): δ 156.4 (CO), 155.7 (CO), 134.9 (=CH), 132.6 (=C), 131.9 (arom.), 128.9 (2C, arom.), 127.9 (arom.), 125.3 (2C, arom.), 125.2 (=CH), 122.9 (=CH), 83.7 (2C, OC(CH3)2), 54.5 (CHN), 52.0 (CHN), 44.0 (CH), 43.4 (CH), 37.9 (CBpin), 36.8 (CH2), 34.9 (CH2), 33.9 (CH), 27.7 (CH), 26.1 (CH2), 25.4 (2C, CH3 (pin)), 23.9 (2C, CH3 (pin)), 23.1 (CH3), 22.6 (CH3), 17.4 (CH3), 13.7 (CH3). 11B{1H} NMR (128 MHz, CDCl3): δ 33.0 (br s). HRMS (ESI): Calcd. for C32H44BN3NaO4 m/z 568.3323, found m/z 568.3328 [M+Na]+.
6 Assignment of Diastereoisomers

The relative configuration of compounds syn-3ae and anti-3ae were determined by X-ray diffraction. The relative configuration of the other compounds was assigned by comparison of $^{13}$C NMR shifts:

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<th>anti-1</th>
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<td>25.0, 24.3</td>
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<tr>
<td>3aa (Cy)</td>
<td>129.9, 128.6</td>
<td>25.1, 24.4</td>
</tr>
<tr>
<td>3ad (Ph)</td>
<td>130.6, 128.8</td>
<td>24.8, 24.3</td>
</tr>
<tr>
<td>3ae (CH(CH$_2$)$_2$)</td>
<td>129.9, 129.1</td>
<td>25.0, 24.3</td>
</tr>
<tr>
<td>3aj ((CH)$_2$CH(OCH$_2$)$_2$)</td>
<td>129.3, 129.2</td>
<td>25.0, 24.4</td>
</tr>
<tr>
<td>3ah ((CH)$_2$)$_3$OTBS)</td>
<td>129.4, 129.0</td>
<td>25.0, 24.3</td>
</tr>
<tr>
<td>3af (Hex)</td>
<td>129.4, 128.9</td>
<td>24.9, 24.3</td>
</tr>
<tr>
<td>3ai ((CH)$_2$)$_3$N$_3$)</td>
<td>129.5, 129.1</td>
<td>25.0, 24.4</td>
</tr>
<tr>
<td>3ag ((CH)$_2$)$_2$Ph)</td>
<td>129.2, 129.2</td>
<td>25.0, 24.4</td>
</tr>
</tbody>
</table>

Most indicative is the chemical shift for $=\text{CH}$, which is shifted to 133.2 – 133.6 ppm in anti-3xx, where it lies below the Bpin moiety.
7 Crystallography

X-ray diffraction experiments on **anti-3ae** and **syn-3ae** were carried out at 200(2) and 100(2) K respectively on a Bruker APEX II diffractometer using Mo-K\(\alpha\) radiation ($\lambda = 0.71073$ Å). Intensities were integrated in SAINT\(^1\) and absorption corrections based on equivalent reflections were applied using SADABS.\(^\text{11}\) Both of the structures were solved using ShelXT\(^\text{12}\) and refined by full matrix least squares against \(F^2\) in ShelXL\(^\text{13,14}\) using Olex2\(^\text{15}\). All the non-hydrogen atoms were refined anisotropically. While all the hydrogen atoms were located geometrically and refined using a riding model. In the case of **anti-3ae** the crystal was twinned and refined against a ShelXL hklf5 file with a twin scale fraction of ~18%. Crystal structure and refinement data are given in Table 1. Crystallographic data for compounds **anti-3ae** and **syn-3ae** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 1867794-1867795. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax(+44) 1223 336033, e-mail: deposit@ccdc.cam.ac.uk].
Table 1 Crystal data and structure refinement for anti-3ae and syn-3ae.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>anti-3ae</th>
<th>syn-3ae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{24}H_{28}BN_{3}O_{4}</td>
<td>C_{24}H_{28}BN_{3}O_{4}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>433.30</td>
<td>433.30</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>200(2)</td>
<td>100(2)</td>
</tr>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
<td>P2₁/c</td>
</tr>
<tr>
<td>a/Å</td>
<td>12.3790(5)</td>
<td>7.1504(3)</td>
</tr>
<tr>
<td>b/Å</td>
<td>13.7312(5)</td>
<td>25.7621(9)</td>
</tr>
<tr>
<td>c/Å</td>
<td>15.5643(6)</td>
<td>12.2985(5)</td>
</tr>
<tr>
<td>α/°</td>
<td>100.082(2)</td>
<td>90</td>
</tr>
<tr>
<td>β/°</td>
<td>108.612(2)</td>
<td>93.516(3)</td>
</tr>
<tr>
<td>γ/°</td>
<td>110.859(2)</td>
<td>90</td>
</tr>
<tr>
<td>Volume/Å³</td>
<td>2214.91(15)</td>
<td>2261.23(15)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>ρ_{calc}/g/cm³</td>
<td>1.299</td>
<td>1.273</td>
</tr>
<tr>
<td>μ/mm⁻¹</td>
<td>0.088</td>
<td>0.086</td>
</tr>
<tr>
<td>F(000)</td>
<td>920.0</td>
<td>920.0</td>
</tr>
<tr>
<td>Crystal size/mm³</td>
<td>0.53 × 0.36 × 0.23</td>
<td>0.42 × 0.25 × 0.11</td>
</tr>
<tr>
<td>Radiation</td>
<td>MoKα (λ = 0.71073)</td>
<td>MoKα (λ = 0.71073)</td>
</tr>
<tr>
<td>2θ range for data collection/°</td>
<td>3.358 to 52.744</td>
<td>3.162 to 55.848</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-15 ≤ h ≤ 14, -17 ≤ k ≤ 16, 0 ≤ l ≤ 19</td>
<td>-9 ≤ h ≤ 9, -33 ≤ k ≤ 32, -16 ≤ l ≤ 16</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>9080</td>
<td>20468</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>9080/0/586</td>
<td>5403/0/293</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.023</td>
<td>1.041</td>
</tr>
<tr>
<td>Final R indexes [I≥2σ (I)]</td>
<td>R₁ = 0.0481, wR₂ = 0.1119</td>
<td>R₁ = 0.0531, wR₂ = 0.1013</td>
</tr>
</tbody>
</table>
Final R indexes [all data]  
\[ R_1 = 0.0702, \quad R_1 = 0.0978, \]
\[ wR_2 = 0.1253, \quad wR_2 = 0.1159 \]

Largest diff. peak/hole / e Å\(^{-3}\)  
\[ 0.29/-0.31, \quad 0.41/-0.25 \]

**Figure S3** – The structure of **anti-3ae** with atomic numbering scheme shown, anisotropic displacement parameters are depicted at the 50% probability level. Only one of the two independent molecules in the asymmetric unit are shown and hydrogen atoms are omitted for clarity.
**Figure S4** – The structure of syn-3ae with atomic numbering scheme shown. Anisotropic displacement parameters depicted at the 50% probability level. Hydrogen atoms omitted for clarity.
8 Investigation of Other Dienophiles

Several other highly activated dienophiles were also examined during initial investigations into the cycloaddition reaction. These were performed using the dearomatized intermediate generated upon the reaction of lithiated benzylic amine (+/-)-Li-1f with boronic ester 2a.

![Reaction Scheme]

The results of the reaction of the various dienophiles are given in the table below.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Dienophile</th>
<th>$T$ (°C)</th>
<th>Cycloaddition product yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>diethyl acetylenedicarboxylate</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>maleic anhydride</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>diethyl fumarate</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>diethyl fumarate</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>diethyl maleate</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>diethyl maleate</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>nitrosobenzene</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>PTAD</td>
<td>25</td>
<td>42$^b$</td>
</tr>
</tbody>
</table>

$^a$ Determined by $^1$H NMR analysis using an internal standard. $^b$ Isolated yield after purification by flash column chromatography

In the cases were no cycloaddition was observed, $^1$H NMR analysis of the crude reaction showed 1-cyclohexyl-2-ethylbenzene (formed by protodeboronation) as the major product.
9 NMR spectra

Figure S5: $^1$H NMR of 3aa (400 MHz, CDCl$_3$)

![NMR spectrum of 3aa](image)

Figure S6: $^{13}$C{$^1$H} NMR of 3aa (101 MHz, CDCl$_3$)

![NMR spectrum of 3aa](image)
Figure S7: $^1$H NMR of 3ab (400 MHz, CDCl$_3$)

Figure S8: $^{13}$C{$^1$H} NMR of 3ab (101 MHz, CDCl$_3$)
Figure S9: $^1$H NMR of 3ac (400 MHz, CDCl$_3$)

![NMR Spectrum](image)

syn-3ac

Figure S10: $^{13}$C($^1$H) NMR of 3ac (101 MHz, CDCl$_3$)

![NMR Spectrum](image)

syn-3ac
Figure S11: $^1$H NMR of syn-3ad (400 MHz, CDCl$_3$)

Figure S12: $^{13}$C($^1$H) NMR of syn-3ad (101 MHz, CDCl$_3$)
Figure S13: $^1$H NMR of anti-3ad (400 MHz, CDCl$_3$)

Figure S14: $^{13}$C{$^1$H} NMR of anti-3ad (101 MHz, CDCl$_3$)
Figure S15: $^1$H NMR of anti-3ae (400 MHz, CDCl$_3$)

Figure S16: $^{13}$C{$_1^1$H} NMR of anti-3ae (101 MHz, CDCl$_3$)
Figure S17: $^1$H NMR of *syn-3ae* (400 MHz, CDCl$_3$)

![Image of syn-3ae 1H NMR spectrum]

Figure S18: $^{13}$C($^1$H) NMR of *syn-3ae* (101 MHz, CDCl$_3$)

![Image of syn-3ae 13C{1H} NMR spectrum]
Figure S19: $^1$H NMR of anti-3af + syn-3af (400 MHz, CDCl$_3$)

Figure S20: $^{13}$C{$^1$H} NMR of anti-3af + syn-3af (101 MHz, CDCl$_3$)
Figure S21: $^1$H NMR of anti-3ag + syn-3ag (400 MHz, CDCl$_3$)

Figure S22: $^{13}$C($^1$H) NMR of anti-3ag + syn-3ag (101 MHz, CDCl$_3$)
Figure S23: $^1$H NMR of *anti*-3ah + *syn*-3ah (400 MHz, CDCl$_3$)

Figure S24: $^{13}$C{$_^1$H} NMR of *anti*-3ah + *syn*-3ah (101 MHz, CDCl$_3$)
Figure S25: $^1$H NMR of anti-3ai (400 MHz, CDCl$_3$)

Figure S26: $^{13}$C($^1$H) NMR of anti-3ai (101 MHz, CDCl$_3$)
Figure S27: $^1$H NMR of syn-3ai (400 MHz, CDCl$_3$)

Figure S28: $^{13}$C($^1$H) NMR of syn-3ai (101 MHz, CDCl$_3$)
Figure S29: $^1$H NMR of *anti-3aj* (400 MHz, CDCl$_3$)

![Figure S29: $^1$H NMR of *anti-3aj* (400 MHz, CDCl$_3$)](image)

Figure S30: $^{13}$C($^1$H) NMR of *anti-3aj* (101 MHz, CDCl$_3$)

![Figure S30: $^{13}$C($^1$H) NMR of *anti-3aj* (101 MHz, CDCl$_3$)](image)
Figure S31: $^1$H NMR of syn-3aj (400 MHz, CDCl$_3$)

Figure S32: $^{13}$C{$^1$H} NMR of syn-3aj (101 MHz, CDCl$_3$)
Figure S33: $^1$H NMR of 3ba (400 MHz, CDCl$_3$)

Figure S34: $^{13}$C{$^1$H} NMR of 3ba (101 MHz, CDCl$_3$)
Figure S35: $^1$H NMR of 3ca (400 MHz, CDCl$_3$)

Figure S36: $^{13}$C($^1$H) NMR of 3ca (101 MHz, CDCl$_3$)
Figure S37: $^1$H NMR of 3da (400 MHz, CDCl$_3$)

Figure S38: $^{13}$C($^1$H) NMR of 3da (101 MHz, CDCl$_3$)
Figure S39: $^{19}$F NMR of 3da (377 MHz, CDCl$_3$)
Figure S40: $^1$H NMR of 3ea (400 MHz, CDCl$_3$)

Figure S41: $^{13}$C{$_^1$H} NMR of 3ea (101 MHz, CDCl$_3$)
Figure S42: $^{19}$F NMR of 3ea (377 MHz, CDCl$_3$)
Figure S43: $^1$H NMR of 3fa (400 MHz, CDCl$_3$)

Figure S44: $^{13}$C($^1$H) NMR of 3fa (101 MHz, CDCl$_3$)
Figure S45: $^1$H NMR of 4fa (400 MHz, CDCl$_3$)

Figure S46: $^{13}$C{$^1$H} NMR of 4fa (101 MHz, CDCl$_3$)
Figure S47: $^1$H NMR of 3fg (400 MHz, CDCl$_3$)

Figure S48: $^{13}$C{${^1}$H} NMR of 3fg (101 MHz, CDCl$_3$)
Figure S49: $^1$H NMR of 4fg (400 MHz, CDCl$_3$)

![H NMR spectrum of 4fg](image)

Figure S50: $^{13}$C{H} NMR of 4fg (101 MHz, CDCl$_3$)

![C{H} NMR spectrum of 4fg](image)
**Figure S51:** $^1$H NMR of 3fk (400 MHz, CDCl$_3$)

**Figure S52:** $^{13}$C($^1$H) NMR of 3fk (101 MHz, CDCl$_3$)
Figure S53: $^1$H NMR of 3gk (400 MHz, CDCl$_3$)

Figure S54: $^{13}$C{$^1$H} NMR of 3gk (101 MHz, CDCl$_3$)
Figure S55: $^1$H NMR of $3fi$ (400 MHz, CDCl$_3$)

Figure S56: $^{13}$C($^1$H) NMR of $3fi$ (101 MHz, CDCl$_3$)
Figure S57: $^1$H NMR of 3gl (400 MHz, CDCl$_3$)

Figure S58: $^{13}$C($^1$H) NMR of 3gl (101 MHz, CDCl$_3$)
References


