Copper-Catalysed Enantioselective Michael Addition of Malonic Esters to β-Trifluoromethyl-α,β-Unsaturated Imines

Miguel Espinosa, a Jorge Herrera, Gonzalo Blay,*, a Luz Cardona, M. Carmen Muñoz, b and José R. Pedro*a

a Departament de Química Orgànica, Facultat de Química, Universitat de València, C/Dr. Moliner, 50, E-46100 Burjassot (València), Spain
b Departament de Física Aplicada, Universitat Politècnica de València, Camí de Vera s/n, E-46022-València, Spain

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General Experimental Methods

Reactions were carried out under nitrogen in round bottom flasks oven-dried overnight at 120 °C. Commercial reagents were used as purchased. Dichloromethane was distilled from CaH2. 4 Å molecular sieves (8-12 mesh, beads Aldrich 208604) were dried at the flame under vacuum (oil pump) and stored in a closed flask and used before a week. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for 1H and at 75 MHz for 13C NMR using residual nondeuterated solvent (CHCl3) as internal standard (δ 7.26 and 77.0 ppm, respectively), and at 282 MHz for 19F NMR using CFCl3 as internal standard. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a Q-TOF spectrometer equipped with an electrospray source with a capillary voltage of 3.3 kV (ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary phase columns from Daicel or from Phenomenex. N-Tosyl unsaturated imines 2 were prepared according to the procedure described by A. D. Smith.1

General procedure for the enantioselective conjugate addition of methyl malonate to β-trifluoromethyl α,β-unsaturated N-sulfonylimines 2

Cu(OTf)2 (4.5 mg, 0.0125 mmol) was dried in a Schlenk tube under vacuum. BOX7 (4.4 mg, 0.0125 mmol) was added and the tube was filled with nitrogen. CH2Cl2 (0.55 mL) was added via syringe and the mixture was stirred for 30 min. A solution of imine 2 (0.125 mmol) dissolved in dry CH2Cl2 (0.5 mL), was added via syringe, followed by 4 Å MS (110 mg) and dimethyl malonate (34 μL, 0.3 mmol). The mixture was stirred at room temperature for the indicated time and chromatographed on silica gel eluting with hexane/EtOAc mixtures to give compounds 3.

Racemic compounds for comparative purpose were prepared by following the same procedure, using La(OTf)3-pyBOX (rac) at 40 °C.

Dimethyl (S,E)-2-(1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-4-phenylbut-3-en-2-yl)malonate (3a)

Chiral HPLC analysis: Chiralpak AD-H, hexane-iPrOH 80:20, 1 mL/min, E-diastereomer: major enantiomer (S) tr = 8.4 min, minor enantiomer (R) tr = 14.0 min; Z-diastereomer: major enantiomer tr = 12.4 min, minor enantiomer tr = 9.4 min.

Major E-diastereomer: White solid, m.p. 159-161 °C (hexane-EtOAc); [α]20D -54.0 (c 1.0, CHCl3) for the mixture of diastereomers; white solid, M.p. 153.4-160.2 °C (hexane-
EtOAc); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.76 (2H, d, \(J = 8.4\) Hz, Ar), 7.40-7.27 (5H, m, Ar), 7.10 (2H, m, Ar), 6.21 (1H, s, NH), 5.57 (1H, d, \(J = 10.8\) Hz, =CH), 3.73 (3H, s, MeO), 3.68 (1H, d, \(J = 8.4\) Hz, CHCO\(_2\)Me), 3.64 (1H, s, Me-Ar), 2.45 (3H, s, Me-Ar); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.7 (C), 166.4 (C), 144.2 (C), 141.3 (C), 135.9 (C), 134.0 (C), 129.6 (CH), 129.5 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 125.4 (C, q, \(J_{C-F} = 264.8\) Hz), 102.9 (CH, q, \(J_{C-F} = 2.4\) Hz), 52.93 (CH\(_3\)), 52.90 (CH\(_3\)), 51.0 (CH), 42.7 (CH, q, \(J_{C-F} = 27.9\) Hz), 21.5 (CH\(_3\)); \(^1\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) = -70.1 (s, CF\(_3\)) ppm; HRMS (ESI) \(m/z\) 486.1197, C\(_{22}\)H\(_{23}\)F\(_3\)NO\(_6\)S requires 486.1193.

Minor Z-diastereomer: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.95 (s, 1H), 7.59 (2H, d, \(J = 8.4\) Hz, Ar), 7.41 (2H, d, \(J = 8.1, 1.5\) Hz, Ar), 7.36-7.26 (3H, m, Ar), 7.22 (2H, d, \(J = 8.4\) Hz, Ar), 5.22 (1H, d, \(J = 11.1\) Hz, =CH), 3.81 (3H, s, MeO), 3.76-3.48 (2H, m, CH-CF\(_3\), CHCO\(_2\)Me), 3.76 (3H, s, MeO), 2.39 (3H, s, 3H); \(^1\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) = -69.8 (s, CF\(_3\)) ppm.

Dimethyl \((S,E)-2-(1,1,1\text{-trifluoro-4-((4-methylphenyl)sulfonamido)-4-\(p\)-tolyl)but-3-en-2-yl)malonate (3b)

Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH 85:15, 1 mL/min, E-diastereomer: major enantiomer \((S)\) \(t_r = 13.4\) min, minor enantiomer \((R)\) \(t_r = 16.1\) min; Z-diastereomer: major enantiomer \(t_r = 14.5\) min, minor enantiomer \(t_r = 11.9\) min.

Major E-diastereomer: White solid, m.p. 138-146 °C (hexane-EtOAc); [\(\alpha\)]\(^{20}\) -38.6 (c 0.95, CHCl\(_3\)) for the mixture of diastereomers; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.75 (2H, d, \(J = 8.4\) Hz, Ar), 7.32 (2H, d, \(J = 8.4\) Hz, Ar), 7.13 (2H, d, \(J = 8.1\) Hz, Ar), 6.97 (2H, d, \(J = 8.1\) Hz, Ar), 6.18 (1H, s, NH), 5.52 (1H, d, \(J = 10.8\) Hz, =CH), 3.72 (3H, s, MeO), 3.67 (1H, d, \(J = 8.1\) Hz, CHCO\(_2\)Me), 3.64 (1H, s, CHCF\(_3\)), 3.63 (3H, s, MeO), 2.45 (3H, s, Me-Ar), 2.33 (3H, s, Me-Ar); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.8 (C), 166.5 (C), 144.2 (C), 141.3 (C), 139.5 (C), 135.9 (C), 131.2 (C), 129.6 (CH), 129.5 (CH), 128.4 (CH), 127.7 (CH), 125.4 (C, q, \(J_{C-F} = 249.7\) Hz), 102.6 (CH, q, \(J_{C-F} = 2.0\) Hz), 52.94 (CH\(_3\)), 52.91 (CH\(_3\)), 51.0 (CH), 42.7 (CH, q, \(J_{C-F} = 27.9\) Hz), 21.5 (CH\(_3\)), 21.3 (CH\(_3\)); \(^1\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) = -70.2 (s, CF\(_3\)) ppm; HRMS (ESI) \(m/z\) 500.1356 \((M+H)^+\) C\(_{23}\)H\(_{25}\)F\(_3\)NO\(_6\)S requires 500.1349.

Minor Z-diastereomer: \(^1\)H NMR (300 MHz, CDCl\(_3\)), representative signals taken from the \(^1\)H NMR of the diastereomer mixtures, \(\delta\) 7.91 (1H, s, NH), 7.86 (2H, d, \(J = 8.1\) Hz, Ar), 7.60 (2H, d, \(J = 8.1\) Hz, Ar), 7.25 (2H, d, \(J = 8.1\) Hz, Ar), 7.22 (2H, d, \(J = 8.1\) Hz, Ar), 5.16 (1H, d, \(J = 10.8\) Hz, =CH), 3.82-3.60 (2H, m, CH-CF\(_3\), CHCO\(_2\)Me), 3.76 (3H, s, MeO), 3.67 (3H, s, MeO), 2.43 (3H, s, Me-Ar), 2.39 (3H, s, Me-Ar); \(^1\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) = -69.9 (s, CF\(_3\)) ppm.
**Dimethyl (S,E)-2-(4-(4-chlorophenyl)-1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-but-3-en-2-yl)malonate (3c)**

Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH 95:05, 1 mL/min. **E-diastereomer:** major enantiomer (S) tr = 38.4 min, minor enantiomer (R) tr = 47.9 min; **Z-diastereomer:** major enantiomer tr = 48.4 min, minor enantiomer tr = 33.9 min.

**Major E-diastereomer:** White solid, m.p. 142-150 °C (hexane-EtOAc); [α]D²⁰ = -21.3 (c 0.95, CHCl₃) for the mixture of diastereomers; ¹H NMR (300 MHz, CDCl₃) δ 7.70 (2H, d, J = 8.4 Hz, Ar), 7.34-7.24 (4H, m, Ar), 7.04 (2H, d, J = 8.7 Hz, Ar), 6.42 (1H, s, NH), 5.52 (1H, d, J = 10.8 Hz, =CH), 3.72 (3H, s, MeO), 3.67 (1H, d, J = 8.4 Hz, CHCO₂Me), 3.64 (3H, s, MeO), 3.55 (1H, m, CHCF₃), 2.44 (3H, s, Me-Ar); ¹³C NMR (75 MHz, CDCl₃) δ 166.6 (C), 166.5 (C), 144.3 (C), 140.4 (C), 135.9 (C), 135.6 (C), 132.3 (C), 130.2 (CH), 129.7 (CH), 129.0 (CH), 127.6 (CH), 125.4 (C, q, J_C-F = 278 Hz), 104.23 (CH, q, J_C-F = 2.5 Hz), 53.04 (CH₃), 52.99 (CH₃), 50.9 (CH), 42.6 (CH, q, J_C-F = 28.0 Hz), 21.6 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ = -70.1 (s, CF₃) ppm; HRMS (ESI) m/z 520.0795 (M+H)+, C₂₂H₂₂ClF₃NO₆S requires 520.0803.

**Minor Z-diastereomer:** ¹H NMR (300 MHz, CDCl₃), representative signals taken from the ¹H NMR of the diastereomer mixtures, δ 8.01 (1H, s, NH), 7.57 (2H, d, J = 8.4 Hz, Ar), 7.40-7.19 (6H, m, Ar), 5.19 (1H, d, J = 11.4 Hz, =CH), 3.80 (3H, s, MeO), 3.76 (1H, d, J = 7.2 Hz, CHCO₂Me), 3.68 (3H, s, MeO), 3.51 (1H, m, CHCF₃), 2.39 (3H, s, Me-Ar); ¹⁹F NMR (282 MHz, CDCl₃) δ = -69.8 (s, CF₃) ppm.

**Dimethyl (S,E)-2-(4-(4-bromophenyl)-1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-but-3-en-2-yl)malonate (3d)**

Chiral HPLC analysis: Chiralpak IC, hexane-iPrOH 95:05, 1 mL/min. **E-diastereomer:** major enantiomer (S) tr = 47.9 min, minor enantiomer (R) tr = 57.1 min; **Z-diastereomer:** major enantiomer tr = 31.9 min, minor enantiomer tr = 40.2 min.

**Major E-diastereomer:** Yellow solid, m.p. 130-133 °C (hexane-EtOAc); [α]D²⁰ = -12.8 (c 1.02, CHCl₃) for the mixture of diastereomers; ¹H NMR (300 MHz, CDCl₃) δ 7.71 (2H, d, J = 8.4 Hz, Ar), 7.45 (2H, d, J = 8.4 Hz, Ar), 7.31 (2H, d, J = 8.4 Hz, Ar), 7.04 (2H, d, J = 6.2 Hz, Ar), 6.29 (1H, s, NH), 5.53 (1H, d, J = 10.8 Hz, =CH), 3.73 (3H, s, MeO), 3.68 (1H, d, J = 8.4 Hz, CHCO₂Me), 3.65 (3H, s, MeO), 3.55 (1H, m, CHCF₃), 2.45 (3H, s, Me-Ar); ¹³C NMR (75 MHz, CDCl₃) δ 166.6 (C), 166.5 (C), 144.4 (C), 140.4 (C), 135.9 (C), 132.8 (C), 132.0 (CH), 130.4 (CH), 129.7 (CH), 127.6 (CH), 125.4 (C, q, J_C-F = 278 Hz), 124.0 (C), 104.3 (CH, q, J_C-F = 2.3 Hz), 53.07 (CH₃), 53.01
(CH3), 50.9 (CH), 42.6 (CH, q, J_{CF} = 28.0 Hz), 21.6 (CH3); \textsuperscript{19}F NMR (282 MHz, CDCl3) \(\delta = -70.0\) (s, CF3) ppm; HRMS (ESI) \textit{m/z} 564.0295 (M+H\textsuperscript{+}), \(C_{22}H_{22}BrF_{3}NO_{6}S\) requires 564.0298.

Minor Z-diastereomer: \(^1\)H NMR (300 MHz, CDCl3), representative signals taken from the \(^1\)H NMR of the diastereomer mixtures, \(\delta\) 8.01 (1H, s, NH), 7.58 (2H, d, J = 8.4 Hz, Ar), 7.41 (2H, d, J = 8.4 Hz, Ar), 7.31 (2H, d, J = 8.4 Hz, Ar), 7.25 (2H, d, J = 8.4 Hz, Ar), 5.21 (1H, d, J = 11.4 Hz, =CH), 3.80 (3H, s, MeO), 3.77 (1H, d, J = 7.2 Hz, CHCO\textsubscript{2}Me), 3.68 (3H, s, MeO), 3.52 (1H, m, CHCF\textsubscript{3}), 2.40 (3H, s, Me-Ar); \(^{19}\)F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta = -69.8\) (s, CF3) ppm.

Dimethyl (S,E)-2-(1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-4-(4-nitrophenyl)but-3-en-2-yl)malonate (3e)

Chiral HPLC analysis: Chiralpak IC, hexane-iPrOH 90:10, 1 mL/min, \textit{E}-diastereomer: major enantiomer (S) \(tr = 60.4\) min, minor enantiomer (R) \(tr = 69.2\) min; \textit{Z}-diastereomer: major enantiomer \(tr = 50.2\) min, minor enantiomer \(tr = 94.8\) min.

Major E-diastereomer: Orange oil; \([\alpha]_D^{20}\) 1.1 (c 1.0, CHCl\textsubscript{3}) for the mixture of diastereomers; \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 8.14 (2H, d, J = 9.0 Hz, Ar), 7.68 (2H, d, J = 8.1 Hz, Ar), 7.37-3.28 (4H, m, Ar), 6.80 (1H, s, NH), 5.58 (1H, d, J = 11.1 Hz, =CH), 3.73 (3H, s, MeO), 3.68 (1H, d, J = 8.4 Hz, CHCO\textsubscript{2}Me), 3.65 (3H, s, MeO), 3.49 (1H, m, CHCF\textsubscript{3}), 2.45 (3H, s, Me-Ar); \(^{13}\)C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta\) 166.5 (C), 166.4 (C), 148.2 (C), 144.6 (C), 140.1 (C), 139.6 (C), 135.7 (C), 130.2 (C), 129.7 (C), 127.6 (CH), 125.2 (C, q, J_{CF} = 279 Hz), 123.8 (C), 106.5 (CH, q, J_{CF} = 2.1 Hz), 53.2 (CH\textsubscript{3}), 53.1 (CH\textsubscript{3}), 50.7 (CH), 42.6 (CH, q, J_{CF} = 28.2 Hz), 21.6 (CH\textsubscript{3}); \(^{19}\)F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta = -69.9\) (s, CF3) ppm; HRMS (ESI) \textit{m/z} 531.1034 (M+H\textsuperscript{+}), \(C_{22}H_{22}ClF_{3}N_{2}O_{8}S\) requires 531.1043.

Minor Z-diastereomer: \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}), representative signals taken from the \(^1\)H NMR of the diastereomer mixture, \(\delta\) 8.19 (1H, s, NH), 8.14 (2H, d, J = 9.0 Hz, Ar), 7.60 (4H, m, Ar), 7.25 (2H, d, J = 8.0 Hz, Ar), 5.40 (1H, d, J = 10.8 Hz, =CH), 3.83 (3H, s, MeO), 3.80 (1H, d, J = 5.7 Hz, CHCO\textsubscript{2}Me), 3.69 (3H, s, MeO), 3.49 (1H, m, CHCF\textsubscript{3}), 2.40 (3H, s, Me-Ar); \(^{13}\)C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta\) 168.2 (C), 166.9 (C), 148.2 (C), 144.4 (C), 143.2 (C), 140.0 (C), 136.5 (C), 129.7 (CH), 128.7 (CH), 126.9 (CH), 125.2 (C, q, J_{CF} = 279 Hz), 123.3 (C), 114.8 (CH, q, J_{CF} = 2.1 Hz), 54.0 (CH\textsubscript{3}), 53.4 (CH\textsubscript{3}), 50.7 (CH), 41.8 (CH, q, J_{CF} = 29.0 Hz), 21.4 (CH\textsubscript{3}); \(^{19}\)F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta = -69.6\) (s, CF3) ppm; \(^{19}\)F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta = -69.6\) (s, CF3) ppm.
Dimethyl (S,E)-2-(1,1,1-trifluoro-4-((4-methoxyphenyl)sulfonamido)-4-((4-methylphenyl)but-3-en-2-yl)malonate (3f)

Chiral HPLC analysis: Chiralpak IC, hexane-iPrOH 90:10, 1 mL/min, E-diastereomer: major enantiomer (S) tr = 44.2 min, minor enantiomer (R) tr = 63.8 min; Z-diastereomer: major enantiomer tr = 38.0 min, minor enantiomer tr = 50.9 min.

**Major E-diastereomer:** Yellow oil; [α]D20 -16.3 (c 1.0, CHCl3) for the mixture of diastereomers; 1H NMR (300 MHz, CDCl3) δ 7.75 (2H, d, J = 8.1 Hz, Ar), 7.32 (2H, d, J = 8.7 Hz, Ar), 6.84 (2H, d, J = 8.7 Hz, Ar), 6.16 (1H, s, NH), 5.48 (1H, d, J = 10.8 Hz, =CH), 3.79-3.66 (2H, m, CH-CF3, CHCO2Me), 3.80 (3H, s, MeO), 3.73 (3H, s, MeO), 3.64 (3H, s, MeO), 2.45 (3H, s, Me-Ar); 13C NMR (75 MHz, CDCl3) δ 166.8 (C), 166.5 (C), 160.3 (C), 144.1 (C), 141.2 (C), 136.0 (C), 130.0 (CH), 129.6 (CH), 125.6 (C, q, JC-F = 279 Hz, CF3), 114.1 (CH), 102.7 (C, q, JC-F = 2.0 Hz, CF3), 55.2 (CH3), 52.96 (CH3), 52.91 (CH3), 51.1 (CH), 42.6 (CH, q, JC-F = 27.8 Hz, CF3), 21.6 (CH3); 19F NMR (282 MHz, CDCl3) δ = -70.2 (s, CF3) ppm; HRMS (ESI) m/z 516.1294 (M+H)+, C23H25F3NO7S requires 516.1298.

**Minor Z-diastereomer:** 1H NMR (300 MHz, CDCl3), representative signals taken from the 1H NMR of the diastereomer mixture, δ 7.60 (2H, d, J = 8.1 Hz, Ar), 7.23 (2H, d, J = 8.1 Hz, Ar), 6.93 (2H, d, J = 9.0 Hz, Ar), 6.79 (2H, d, J = 9.0 Hz, Ar), 5.09 (1H, d, J = 11.4 Hz, =CH), 2.43 (3H, s, Me-Ar); 19F NMR (282 MHz, CDCl3) δ = -69.9 (s, CF3) ppm.

Dimethyl (S,E)-2-(1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-4-((m-tolyl)but-3-en-2-yl)malonate (3g)

Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH 80:20, 1 mL/min, E-diastereomer: major enantiomer (S) tr = 7.0 min, minor enantiomer (R) tr = 10.7 min; Z-diastereomer: major enantiomer tr = 9.5 min, minor enantiomer tr = 7.8 min.

**Major E-diastereomer:** White solid, m.p. 117-120 °C (hexane-EtOAc); [α]D20 -40.7 (c 1.0, CHCl3) for the mixture of diastereomers; 1H NMR(300 MHz, CDCl3) δ 7.75 (2H, d, J = 8.1 Hz, Ar), 7.32 (2H, d, J = 8.1 Hz, Ar), 7.21-7.13 (2H, m, Ar), 6.89 (1H, d, J = 7.5 Hz, Ar), 6.81 (1H, s, Ar), 6.18 (1H, s, NH), 5.55 (1H, d, J = 10.8 Hz, =CH), 3.76-3.67 (2H, m, CH-CF3, CHCO2Me), 3.73 (3H, s, MeO), 3.63 (3H, s, MeO), 2.45 (3H, s, Me-Ar), 2.28 (3H, s, Me-Ar); 13C NMR (75 MHz, CDCl3) δ 166.8 (C), 166.5 (C), 144.2 (C), 141.4 (C), 138.5 (C), 136.0 (C), 134.0 (C), 130.2 (CH), 129.6 (CH), 129.1 (CH), 128.7 (CH), 127.7 (CH), 125.6 (CH), 125.4 (C, q, JC-F = 255 Hz), 102.9 (CH, q, JC-F = 2.0 Hz), 52.93 (CH3), 52.91 (CH3), 51.1 (CH), 42.6 (CH, q, JC-F = 27.9 Hz), 21.5 (CH3), 21.3 (CH3); 19F NMR (282 MHz, CDCl3) δ = -70.2 (s, CF3) ppm; HRMS (ESI) m/z 500.1354 (M+H)+, C23H23F3NO6S requires 500.1349.
Minor Z-diastereomer: $^1$H NMR (300 MHz, CDCl$_3$), representative signals taken from the $^1$H NMR of the diastereomer mixture, $\delta$ 7.90 (1H, s, NH), 7.58 (2H, d, $J$ = 8.4 Hz, Ar), 7.35-6.75 (6H, m, Ar), 5.22 (1H, d, $J$ = 11.4 Hz, =CH), 3.82-3.60 (2H, m, CH-CF$_3$, CHCO$_2$Me), 3.80 (3H, s, MeO), 3.68 (3H, s, MeO), 2.43 (3H, s, Me-Ar), 2.26 (3H, s, Me-Ar); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -69.8 (s, CF$_3$) ppm.

Dimethyl ($S,E$)-2-(4-(3-chlorophenyl)-1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)but-3-en-2-yl)malonate (3h)

Chiral HPLC analysis: Lux Amylose-1, hexane-PrOH 80:20, 1 mL/min, $E$-diastereomer: major enantiomer ($S$) $t_r$ = 7.2 min, minor enantiomer ($R$) $t_r$ = 11.1 min; $Z$-diastereomer: major enantiomer $t_r$ = 9.5 min, minor enantiomer $t_r$ = 8.2 min.

Major E-diastereomer: yellow solid, m.p. 100-107 °C (hexane-EtOAc); $[\alpha]^{20}_D$ -20.8 (c 0.96, CHCl$_3$) for the mixture of diastereomers; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.71 (2H, d, $J$ = 8.4 Hz, Ar), 7.32 (2H, d, $J$ = 8.4 Hz, Ar), 7.31-7.17 (2H, m, Ar), 7.05 (1H, dt, $J$ = 7.2, 1.5 Hz, Ar), 6.93 (1H, t, $J$ = 1.5 Hz, Ar), 6.34 (1H, s, NH), 5.58 (1H, d, $J$ = 10.8 Hz, =CH), 3.74 (3H, s, MeO), 3.68 (1H, d, $J$ = 8.1 Hz, CHCO$_2$Me), 3.64 (3H, s, MeO), 3.56 (1H, m, CHCF$_3$), 2.45 (3H, s, Me-Ar); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 166.6 (C), 166.4 (C), 144.4 (C), 135.8 (C), 135.5 (C), 134.5 (C), 130.0 (C), 129.7 (CH), 129.6 (CH), 128.8 (CH), 127.6 (CH), 127.0 (CH), 125.4 (C, $J_{CF} = 280$ Hz), 104.9 (CH, $J_{CF} = 2.0$ Hz), 53.03 (CH$_3$), 52.98 (CH$_3$), 50.9 (CH), 42.6 (CH, q, $J_{CF} = 28.0$ Hz), 21.5 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -70.0 (s, CF$_3$) ppm; HRMS (ESI) $m/z$ 520.0801 (M+H)$^+$, C$_{22}$H$_{22}$ClF$_3$NO$_6$S requires 520.0803.

Minor Z-diastereomer: $^1$H NMR (300 MHz, CDCl$_3$), representative signals taken from the $^1$H NMR of the diastereomer mixture, $\delta$ 8.00 (1H, s, NH), 7.57 (2H, d, $J$ = 8.4 Hz, Ar), 7.33-7.20 (6H, m, Ar), 5.26 (1H, dd, $J$ = 10.8, 0.6 Hz, =CH), 3.81 (3H, s, MeO), 3.78 (1H, d, $J$ = 6.3 Hz, CHCO$_2$Me), 3.69 (3H, s, MeO), 3.56 (1H, m, CHCF$_3$), 2.39 (3H, s, Me-Ar); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -69.7 (s, CF$_3$) ppm.

Dimethyl ($S,E$)-2-(1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-4-(3-nitrophenyl)but-3-en-2-yl)malonate (3i)

Chiral HPLC analysis: Lux Amylose-1, hexane-PrOH 95:05, 2 mL/min, $E$-diastereomer: major enantiomer ($S$) $t_r$ = 42.9 min, minor enantiomer ($R$) $t_r$ = 78.2 min; $Z$-diastereomer: major enantiomer $t_r$ = 50.6 min, minor enantiomer $t_r$ = 30.9 min.

Major E-diastereomer: Yellow oil; $[\alpha]^{20}_D$ -9.5 (c 0.97, CHCl$_3$) for the mixture of diastereomers; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.18 (1H, m, Ar), 7.82 (1H, dd, $J$ = 7.8, 1.8, 1.2 Hz, Ar), 7.76 (1H, t, $J$ = 1.8 Hz, Ar), 7.65 (2H, d, $J$ = 8.0 Hz, Ar), 7.54 (1H, t, $J$ = 8.0 Hz, Ar), 7.30 (2H, d, $J$ = 8.0 Hz, Ar), 6.62 (1H, s, NH), 5.63 (1H, d, $J$ = 11.1 Hz, =CH), 3.76 (3H, s, MeO), 3.67 (1H, d, $J$ = 7.4 Hz, CHCO$_2$Me), 3.65 (3H, s, MeO), 3.48 (1H, m, CHCF$_3$), 2.44 (3H, s, Me-Ar); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 166.5 (C), 166.4
(C), 148.1 (C), 144.7 (C), 139.5 (C), 135.7 (C), 135.2 (CH), 135.1 (C), 129.8 (CH,
overlapped signals), 127.5 (CH), 125.3 (C, q, J_C-F = 279 Hz), 124.2 (CH), 124.1 (CH),
106.9 (CH, q, J_C-F = 2.0 Hz), 53.17 (CH3), 53.12 (CH3), 50.7 (CH), 42.6 (CH, q, J_C-F =
28.2 Hz), 21.5 (CH3); 19F NMR (282 MHz, CDCl3) δ = -69.9 (s, CF3) ppm; HRMS (ESI)
m/z 531.1036 (M+H)^+ requires 531.1043.

Minor Z-diastereomer: 1H NMR (300 MHz, CDCl3), representative signals taken from
the 1H NMR of the diastereomer mixture, δ 8.19 (1H, s, NH), 8.16 (1H, m, Ar), 8.11
(1H, t, J = 1.9 Hz, Ar), 7.63-7.53 (3H, m, Ar), 7.50 (1H, t, J = 8.1 Hz, Ar), 7.23 (2H, d,
J = 8.0 Hz, Ar), 5.38 (1H, dd, J = 10.8, 0.6 Hz, =CH), 3.83 (3H, s, MeO), 3.81 (1H, d,
J = 6.3 Hz, CHCO2Me), 3.71 (3H, s, MeO), 3.58 (1H, m, CH-CF3), 2.39 (3H, s, Me-Ar);
13C NMR (75 MHz, CDCl3) δ 168.2 (C), 167.0 (C), 148.0 (C), 144.4 (C), 139.8 (C),
138.5 (C), 136.6 (C), 134.1 (CH), 129.7 (CH), 129.2 (CH), 126.9 (CH), 125.3 (C, q, J_C-F
= 279 Hz), 123.9 (CH), 122.7 (CH), 113.8 (CH, q, J_C-F = 2.4 Hz), 54.0 (CH3), 53.4
(CH3), 50.7 (CH), 41.9 (CH, q, J_C-F = 28.29 Hz), 21.4 (CH3); 19F NMR (282 MHz,
CDCl3) δ = -69.6 (s, CF3) ppm.

Dimethyl (S,E)-2-(1,1,1-trifluoro-4-(3-methoxyphenyl)-4-((4-methylphenyl)
sulfonamido)but-3-en-2-yl)malonate (3j)

[Diagram of the molecule]

Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH
90:10, 1 mL/min, E-diastereomer: major enantiomer (S) tr =
19.4 min, minor enantiomer (R) tr = 30.7 min; Z-
diastereomer: major enantiomer tr = 26.5 min, minor
enantiomer tr = 21.8 min.

Major E-diastereomer: Yellow solid, m.p. 102-105 °C (hexane-EtOAc); [α]_D^20 -40.3 (c
0.95, CHCl3) for the mixture of diastereomers; 1H NMR (300 MHz, CDCl3) δ 7.82
(2H, d, J = 8.4 Hz, Ar), 7.38 (2H, d, J = 8.4 Hz, Ar), 7.28-7.25 (1H, m, Ar), 6.93 (1H,
J = 8.4, 2.4, 1.2 Hz, Ar), 6.71-6.69 (2H, m, Ar), 6.31 (1H, s, NH), 5.65 (1H, d, J =
10.8 Hz, =CH), 3.88 (1H, d, J = 8.7 Hz, CHCO2Me), 3.80 (3H, s, MeO), 3.79 (3H, s,
MeO), 3.76-3.75 (1H, m, CH-CF3), 3.70 (3H, s, MeO), 2.50 (3H, s, Me-Ar); 13C NMR(75 MHz, CDCl3) δ 166.8 (C), 166.6 (C), 159.6 (C), 144.2 (C), 141.1 (C), 135.9
(C), 135.3 (C), 129.9 (CH), 129.6 (CH), 127.7 (CH), 125.4 (C, q, J_C-F = 257.3 Hz),
120.6 (CH), 115.7 (CH), 113.6 (CH), 102.9 (CH, q, J_C-F = 2.0 Hz), 55.2 (CH3), 52.95
(CH3), 52.94 (CH3), 51.0 (CH), 42.6 (CH, q, J_C-F = 27.9 Hz), 21.5 (CH3); 19F NMR (282
MHz, CDCl3) δ = -70.2 (s, CF3) ppm; HRMS (ESI) m/z 516.1294 (M+H)^+,
C_{23}H_{25}F_{3}NO_{7}S requires 516.1298.

Minor Z-diastereomer: 1H NMR (300 MHz, CDCl3), representative signals taken from
the 1H NMR of the diastereomer mixture, δ 7.99 (1H, s, NH), 7.65 (2H, d, J = 8.4 Hz,
Ar), 7.37-7.32 (1H, m, Ar), 7.06 (dt, J = 7.8, 1.2 Hz, Ar), 6.75-6.65 (2H, m, Ar), 5.31
(1H, d, J = 11.4 Hz, =CH), 3.89-3.67 (2H, m, CH-CF3, CHCO2Me), 3.86 (3H, s, MeO),
3.80 (3H, s, MeO), 3.75 (3H, s, MeO), 2.45 (3H, s, Me-Ar); 19F NMR (282 MHz,
CDCl3) δ = - 69.8 (s, CF3) ppm.
Dimethyl \((S,E)-2-(1,1,1\text{-}trifluoro\text{-}4\text{-}((4\text{-}methylphenyl)sulfonamido)but\text{-}3\text{-}en\text{-}2\text{-}yl)malonate\) (3k)

Chiral HPLC analysis: Chiralpak AD-H, hexane-\(\text{-iPrOH}\) 90:10, 1 mL/min, \(E\)-diastereomer: major enantiomer (S) \(t_r = 21.6\) min, minor enantiomer (R) \(t_r = 47.2\) min; \(Z\)-diastereomer: major enantiomer \(t_r = 38.3\) min, minor enantiomer \(t_r = 32.7\) min.

**Major \(E\)-diastereomer:** Yellow solid, m.p. 129-133 °C (hexane-EtOAc); \(\left[\alpha\right]_D^{20}\) -32.2 (c 0.92, CHCl3) for the mixture of diastereomers; \(^1\)H NMR(300 MHz, CDCl3) δ 7.72 (2H, d, \(J = 8.4\) Hz, Ar), 7.28-7.25 (2H, m, Ar), 6.89 (1H, dt, \(J = 7.5, 1.2\) Hz, Ar), 6.82 (1H, dd, \(J = 8.4, 1.2\) Hz, Ar), 6.18 (1H, s, NH), 5.69 (1H, d, \(J = 10.8\) Hz, =CH), 3.75 (3H, s, MeO), 3.69-3.55 (2H, m, CH-CF3, CHCO2Me), 3.65 (3H, s, MeO), 3.60 (3H, s, MeO), 2.42 (3H, s, Me-Ar); \(^{13}\)C NMR (75 MHz, CDCl3) δ 166.8 (C), 166.6 (C), 156.7 (C), 143.8 (C), 138.8 (C), 136.1 (C), 131.2 (C), 131.0 (C), 129.3 (CH), 128.9 (CH), 127.9 (CH), 127.1 (CH), 125.0 (C, q, \(J_{C-F} = 258.8\) Hz), 120.6 (CH), 111.0 (CH), 113.6 (CH), 105.6 (CH, q, \(J_{C-F} = 2.0\) Hz), 55.1 (CH3), 52.9 (CH3), 51.1 (CH), 42.8 (CH, q, \(J_{C-F} = 27.8\) Hz), 21.5 (CH3); \(^{19}\)F NMR (282 MHz, CDCl3) δ = -70.2 (s, CF3) ppm; HRMS (ESI) \(m/z\) 516.1302 (M+H)+, C23H25F3NO7S requires 516.1298.

**Minor \(Z\)-diastereomer:** \(^1\)H NMR (300 MHz, CDCl3), representative signals taken from the \(^1\)H NMR of the diastereomer mixture, \(\delta\) 7.81 (2H, d, \(J = 8.1\) Hz, Ar), 7.38-6.49 (7H, m, Ar, NH), 5.44 (1H, d, \(J = 10.8\) Hz, =CH), 3.82-3.60 (2H, m, CH-CF3, CHCO2Me), 3.83 (3H, s, MeO), 3.73 (3H, s, MeO), 3.55 (3H, s, MeO), 2.31 (3H, s, Me-Ar); \(^{19}\)F NMR (282 MHz, CDCl3) δ = -69.5 (s, CF3) ppm.

Dimethyl \((S,E)-2-(1,1,1\text{-}trifluoro\text{-}4\text{-}((4\text{-}methylphenyl)sulfonamido)\text{-}4\text{-}(\text{naphthalen}-\text{-}2\text{-}yl)but\text{-}3\text{-}en\text{-}2\text{-}yl)malonate\) (3l)

Chiral HPLC analysis: Lux Amylose-1, hexane-\(\text{-iPrOH}\) 80:20, 1 mL/min, \(E\)-diastereomer: major enantiomer (S) \(t_r = 11.3\) min, minor enantiomer (R) \(t_r = 13.8\) min; \(Z\)-diastereomer: major enantiomer \(t_r = 12.3\) min, minor enantiomer \(t_r = 9.4\) min.

**Major \(E\)-diastereomer:** Yellow solid, m.p. 98-103 °C (hexane-EtOAc); \(\left[\alpha\right]_D^{20}\) 1.0 (c 0.96, CHCl3) for the mixture of diastereomers; \(^1\)H NMR (300 MHz, CDCl3) δ 7.80-7.74 (5H, m, Ar), 7.59-7.58 (1H, m, Ar), 7.53-7.49 (2H, m, Ar), 7.30 (2H, d, \(J = 8.1\) Hz Ar), 7.14 (1H, dd, \(J = 8.1, 1.8\) Hz, Ar), 6.38 (1H, s, NH), 5.65 (1H, d, \(J = 10.8\) Hz, =CH), 3.82-3.69 (2H, m, CH-CF3, CHCO2Me), 3.76 (3H, s, MeO), 3.60 (3H, s, MeO), 2.44 (3H, s, Me-Ar); \(^{13}\)C NMR (75 MHz, CDCl3) δ 166.7 (C), 166.5 (C), 144.2 (C), 141.4 (C), 136.0 (C), 133.3 (C), 132.8 (C), 131.2 (C), 129.6 (CH), 128.64 (CH), 128.57 (CH), 128.3 (CH), 127.7 (CH), 127.1 (CH), 126.6 (CH), 125.5 (CH), 125.4 (C, q, \(J_{C-F} = 264.8\) Hz), 123.7 (CH), 104.0 (CH, q, \(J_{C-F} = 2.0\) Hz), 53.0 (CH3), 52.9 (CH3), 51.1 (CH), 42.7
(CH, q, $J_{CF} = 28.5$ Hz), 21.5 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta = -70.0$ (s, CF$_3$) ppm; HRMS (ESI) $m/z$ 536.1346 (M+H)$^+$, C$_{26}$H$_{25}$F$_3$NO$_6$S requires 536.1349.

**Minor Z-diastereomer:** $^1$H NMR (300 MHz, CDCl$_3$), representative signals taken from the $^1$H NMR of the diastereomer mixture, $\delta$ 8.05 (1H, s, NH), 7.87-6.94 (11H, m, Ar), 5.37 (1H, d, $J = 11.1$ Hz, =CH), 3.82 (3H, s, MeO), 3.80-3.60 (2H, m, CH-CF$_3$, CHCO$_2$Me), 3.68 (3H, s, MeO), 2.34 (3H, s, Me-Ar); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta = -69.6$ (s, CF$_3$) ppm.
Synthetic transformations of compound 3a

**Dimethyl 2-((2S,4R)-1,1,1-trifluoro-4-((4-methylphenyl)sulfonamido)-4-phenylbutan-2-yl)malonate (4a)**

To a sample of compound (S,E)-3a (52.0 mg, 0.11 mmol, E/Z 96:4, ee = 89%/69%), dissolved in dry CH₂Cl₂ (3.3 mL) under nitrogen atmosphere was added triethylsilane (50 μL, 0.428 mmol) followed by BF₃·Et₂O (67 μL, 0.471 mmol). After stirring for 48 h at room temperature, the mixture was chromatographed on silica gel eluting with hexane:EtOAc (80:20) to give 48.1 mg (92%) of compound 4a, as a ca. 88:12 of two diastereomers. Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH 90:10, 1 mL/min, (2S,4R) major diastereomer (ee = 87%), major enantiomer tr = 16.4 min, minor enantiomer tr = 15.0 min; (2S,4S) minor diastereomer unresolved tr = 8.3 min. Chiralpak IC, hexane-iPrOH 95:05, 2 mL/min, (2S,4R) major diastereomer, tr > 120 min; (2S,4S) minor diastereomer (ee = 89%) major enantiomer tr = 37.6 min, minor enantiomer tr = 35.8 min;

(2S,4R)-4a (major): colorless oil; [α]D20 7.8 (c 0.97, CHCl₃) for the diastereomer mixture; ¹H NMR (300 MHz, CDCl₃) δ 7.52 (2H, d, J = 8.1 Hz, Ar), 7.20-7.13 (3H, m, Ar), 7.10 (2H, d, J = 8.1 Hz, Ar), 7.02-7.6.90 (2H, m, Ar), 4.47 (1H, q, J = 7.8 Hz, CHPh), 3.73 (3H, s, MeO), 3.69 (1H, d, J = 5.4 Hz, CHCO₂Me), 2.83 (1H, m, CHCF₃), 2.34 (3H, s, Me-Ar), 2.32-2.10 (2H, m, CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 167.1 (C), 167.0 (C), 143.1 (C), 138.8 (C), 137.2 (C), 129.3 (CH), 128.6 (CH), 128.5 (C), 127.9 (CH), 127.0 (CH), 126.8 (CH), 126.6 (C, q, JCF = 278 Hz), 56.4 (CH), 53.1 (CH₃), 52.8 (CH₃), 49.9 (CH), 40.0 (CH, q, JCF = 26.8 Hz), 33.4 (CH₂), 21.4 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ = -68.5 (s, CF₃) ppm; HRMS (ESI) m/z 488.1357 (M+H)+, C₂₂H₂₅F₃NO₆S requires 488.1349.

(2S,4S)-4a (minor): ¹H NMR (300 MHz, CDCl₃), representative signals taken from the diastereomer mixture δ 7.58 (2H, d, J = 8.4 Hz, Ar), 7.40-6.90 (7H, m, Ar), 5.95 (1H, d, J = 6.9 Hz, NH), 4.45 (1H, m, CHPh), 3.81 (3H, s, MeO), 3.72 (3H, s, MeO), 2.83 (1H, m, CHCF₃), 2.34 (3H, s, Me-Ar), 2.32-2.10 (2H, m, CH₂); ¹⁹F NMR (282 MHz, CDCl₃) δ = -70.1 (s, CF₃) ppm.

**Methyl (3R,4S,6R)-2-oxo-6-phenyl-1-tosyl-4-(trifluoromethyl)piperidine-3-carboxylate.**

A 25% solution of tetraethylammonium hydroxide in MeOH (24 μL, 0.14 mmol) was added to a solution of compound 4a (28.0 mg, 0.037 mmol, ee = 87%) in dimethylsulfoxide (1.6 mL) under nitrogen, and the reaction flask was introduced in a bath at 80 °C. After 14 h, the reaction mixture was diluted with EtOAc (75 mL), washed with water (5 × 5 mL), brine (5 mL), and dried over MgSO₄. Purification by column chromatography eluting with hexane:EtOAc (80:20) gave 13.2 mg (78%) of compound 5a. Chiral HPLC analysis: Lux Amylose-1, hexane-iPrOH 90:10, 1 mL/min,
major enantiomer $t_r = 24.0$ min, minor enantiomer $t_r = 22.1$ min. White solid, m.p. 177-179 °C (hexane-EtOAc); $[\alpha]_D^{20} -4.5$ (c 1.0, CHCl$_3$, ee = 87% ); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.56 (2H, d, $J = 8.5$ Hz, Ar), 7.40-7.32 (3H, m, Ar), 7.20-7.14 (4H, m, Ar), 5.93 (1H, t, $J = 3.8$ Hz, CH-Ph), 3.78 (3H, s, OMe), 3.65 (1H, d, $J = 11.4$ Hz, CHCO$_2$Me), 3.11 (1H, m, CHCF$_3$), 2.40 (3H, s, Me-Ar), 2.35-2.28 (2H, m, CH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.3 (C), 164.3 (C), 145.4 (C), 138.1 (C), 134.5 (C), 129.7 (CH), 129.0 (CH), 128.5 (C), 126.5 (CH), 125.6 (C, q, $J_{C-F} = 278$ Hz), 58.3 (CH), 53.4 (CH$_3$), 52.8 (CH$_3$), 50.2 (CH), 37.1 (CH, q, $J_{C-F} = 28.5$ Hz), 29.9 (CH$_2$), 21.7 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -73.1 (s, CF$_3$) ppm; HRMS (ESI) $m/z$ 456.1087 (M+H)$^+$, C$_{21}$H$_{21}$F$_3$NO$_5$S requires 456.1077.

**Determination of the relative stereochemistry of compounds 4a and 5a**

The relative stereochemistry of compound 5a, and hence, of its precursor, the major diastereomer of compound 4a, was established considering the coupling constants of the ring-attached protons (see figure):

![Coupling constants in compound 5a](image)

**Figure S1.** Coupling constants in compound 5a

$^1$H NMR, CDCl$_3$, 300 MHz

$^{13}$C NMR, CDCl$_3$, 75 MHz
$^1$H NMR
CDCl$_3$, 300 MHz

$^{13}$C NMR
CDCl$_3$, 75 MHz
### 3: 240 nm, 4 nm Results

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\[ \text{NMR Spectra} \]

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$^{1}H$ NMR
CDCl$_3$, 300 MHz

$^{13}C$ NMR
CDCl$_3$, 75 MHz
Lux-Amylose 1
Chiralpak IC

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</tr>
<tr>
<td>37.59</td>
<td>21738335</td>
<td>96.896</td>
</tr>
</tbody>
</table>
Chemical structure of compound 5a is shown with its retention time and area measurements in two different wavelengths (250 nm, 4 nm and 220 nm, 4 nm). The results indicate that the retention time for the major peak is around 21.48 minutes with an area of 8879396 and an area percent of 49.76%. The minor peak is at 22.12 minutes with an area of 7086461 and an area percent of 6.584%.
Figure 2S. Ortep plot for the X-ray structure of compound 2a. The thermal ellipsoids are drawn at the 50% probability level.

Figure 3S. Ortep plot for the X-ray structure of compound 3a. The thermal ellipsoids are drawn at the 50% probability level.
Table S-1. Enantioselective conjugate addition of dimethyl malonate 1 to imine 2a catalyzed by trivalent metal complexes.\textsuperscript{a}

![Diagram of the reaction](image)

\begin{tabular}{cccccc}
Entry & La(OTf)\textsubscript{3} & pyBOX & t (h) & Yield (%)\textsuperscript{b} & dr (E:Z) & ee (%) (E/Z)\textsuperscript{c} \\
1 & La(OTf)\textsubscript{3} & pyBOX1 & 16h & >99 & 72:28 & 75/34 \\
2 & La(OTf)\textsubscript{3} & pyBOX2 & 43h & >99 & 78:23 & 45:3 \textsuperscript{c} \\
3 & La(OTf)\textsubscript{3} & pyBOX3 & 48h & >99 & 72:28 & -15/\textsuperscript{2}2 \\
4 & La(OTf)\textsubscript{3} & pyBOX4 & 40h & >99 & 78:23 & -18/\textsuperscript{2}9 \\
5 & La(OTf)\textsubscript{3} & pyBOX5 & 40h & >99 & 78:23 & -28/\textsuperscript{2}11 \\
6 & La(OTf)\textsubscript{3} & pyBOX6 & 37h & 79 & 82:18 & -16/\textsuperscript{2}5 \\
7 & La(OTf)\textsubscript{3} & pyBOX7 & 44h & 86 & 89:11 & -76/\textsuperscript{2}39 \\
8 & Sc(OTf)\textsubscript{3} & pyBOX1 & 96 & \textsuperscript{-d} & \textsuperscript{-d} & \textsuperscript{-d} \\
9 & Yb(OTf)\textsubscript{3} & pyBOX1 & 96 & 19 & 43:57 & 69:42 \\
10 & In(OTf)\textsubscript{3} & pyBOX1 & 96 & \textsuperscript{-d} & \textsuperscript{-d} & \textsuperscript{-d} \\
\end{tabular}

\textsuperscript{a} Reaction conditions: 2 (0.3 mmol), 11 (0.12 mmol), ligand (0.012 mmol), M(OTf)\textsubscript{3} (0.012 mmol), 4Å MS (110 mg), CH\textsubscript{2}Cl\textsubscript{2} (1.1 mL). \textsuperscript{b} Yield of isolated product. \textsuperscript{c} Determined by HPLC with chiral stationary phases. \textsuperscript{d} Little advance of the reaction was observed after the indicated time.