**Catalytic, Enantioselective α -Additions of Isocyanides:
Lewis-Base-Catalyzed Passerini-Type Reactions**

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SUPPORTING INFORMATION

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General Experimental

All reactions were performed in oven (140 °C) or flame-dried glassware under an inert atmosphere of dry N₂. All reaction temperatures correspond to internal temperatures measured with Teflon-coated thermocouples unless otherwise noted. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents: hexane (CaCl₂); methylene chloride (CaCl₂); ethyl acetate (K₂CO₃). Reaction solvents were distilled from the indicated drying agents: methylene chloride (P₂O₅); methanol (Mg). Diisopropylethylamine was freshly distilled from CaH₂. Flash column chromatography was performed using 230-400 mesh silica gel. SiCl₄ was continuously distilled under nitrogen. Benzaldehyde, 4-tolualdehyde, 4-anisaldehyde, 4-trifluoromethyl-benzaldehyde, 2-naphthaldehyde, 1-naphthaldehyde, 2-furaldehyde, (*E*)-cinnamaldehyde, (*E*)-2-methylcinnamaldehyde, hydrocinnamaldehyde, cyclohexanecarboxaldehyde were freshly distilled before use. Phenylpropargylaldehyde was prepared according to the literature

procedure.¹ *tert*-Butyl isocyanide, tosylmethyl isocyanide and 1,1,3,3-tetramethylbutyl isocyanide were used as received. Ethyl isocyanoacetate was distilled before use. Phenyl isocyanide was prepared according to the literature procedure.² The bisphosphoramides **1a**-**1c**^{10a}, **1d**^{10b}, **1f**^{10c}, (*P*)-(*R,R*)-**1g**^{10d} were prepared as described in the literature.

NMR spectra were recorded at 400 MHz (¹H); 100 MHz (¹³C) and 376 (¹⁹F) MHz or 500 MHz and 126 MHz (¹³C). ¹H NMR and ¹³C NMR spectra are referenced to residual chloroform (δ 7.26 ppm, ¹H; δ 77.0 ppm, ¹³C). ¹⁹F NMR spectra are referenced externally to C₆F₆. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), *d* (doublet), t (triplet), q (quartet), m (multiplet) or br (broadened). Coupling constants, *J*, are reported in Hertz. All ¹H and ¹³C NMR assignments are corroborated by 2D experiments (HETCOR and COSY). Spectra available on request from denmark@scs.uiuc.edu.

Low-resolution electron impact (EI) mass spectra were obtained with a typical ionization voltage of 70 eV. Data are reported in the form *m/z* (intensity relative to base = 100). Infrared spectra (IR) are reported in cm⁻¹ with the following relative intensities: s (strong, 67-100%), m (medium, 34-66%), w (weak, 0-33%). Bulb-to-bulb distillations were done on a Kugelrohr apparatus; boiling points (bp) refer to air bath temperatures (ABT) and are uncorrected. Analytical TLC was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with potassium permanganate. Chiral stationary phase, supercritical fluid chromatography (CSP-SFC) was performed using Daicel Chiralpak columns with built-in photometric detector (λ = 220 nm or 258 nm) ns. Analytical capillary gas chromatography (GC) was performed with a flame ionization detection (H₂ carrier gas, 16 mL/min) using the following column : Astec (Chiraldex) BPH 30m x 0.25mm x 0.125 μ m. The injector temperature was 225 °C, the detector temperature was 300 °C. Analytical high pressure liquid chromatography (HPLC) was performed using a photometric detector (λ = 220 nm or 258 nm) using a Rexchrom (*S,S*) β -Gem 1 column. Solvents for HPLC use were of spectroscopic grade and filtered before use. All separation methods for chiral samples were calibrated with racemic samples. Melting points (mp) were determined on a capillary melting point apparatus and are uncorrected. Optical rotations were obtained on a digital polarimeter and are reported as follows: $[\alpha]_D^T$, concentration (*c* = g/100 mL), and solvent.

General Procedure I. Pyridine *N*-Oxide Catalyzed Additions of *tert*-Butyl isocyanide

A solution of *tert*-butyl isocyanide (1.2 equiv, 1.0 M in CH₂Cl₂) was added to a solution of an aldehyde (1.0 M in CH₂Cl₂ based on aldehyde), pyridine *N*-oxide (0.1 equiv), and SiCl₄ (1.1 equiv) at –74 °C over 30 min via a syringe pump. After being stirred for the indicated time, the reaction mixture was warmed to rt and transferred dropwise to a vigorously stirred, ice-cold, saturated aqueous solution of NaHCO₃ (20 mL). The mixture was further stirred for 2 h at rt. The white precipitate was filtered off through Celite and the filtrate was extracted with CH₂Cl₂ (4 x 20 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. Pyridine *N*-oxide was separated from the product by silica gel chromatography (hexane/EtOAc). Analytically pure product was obtained after recrystallization (heptane/benzene).

General Procedure II. Catalytic Asymmetric Additions of *tert*-Butyl isocyanide

A solution of *tert*-butyl isocyanide (1.2 equiv, 1.0 M in CH₂Cl₂) was added to a solution of an aldehyde (1.0 M in CH₂Cl₂ based on aldehyde), chiral catalyst (0.05 equiv or 0.1 equiv), SiCl₄ (1.1 equiv), and diisopropylethylamine (0.1 equiv) at –74 °C over the indicated time via a syringe pump. After being stirred for the indicated time, the reaction mixture was transferred dropwise to a vigorously stirred, ice-cold, saturated aqueous solution of NaHCO₃ (20 mL). The mixture was stirred for 2 h at rt. The white precipitate was filtered off through Celite and the

filtrate was extracted with CH₂Cl₂ (4 x 20 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. The catalyst was separated from the product by silica gel chromatography (hexane/EtOAc). Analytically pure product was obtained after sublimation or recrystallization (heptane/benzene).

***N*-tert-Butyl-2-hydroxy-2-phenylacetamide ((±)-5a)**

Following General Procedure I, a mixture of benzaldehyde (104 μL , $d = 1.044$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl₄ (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.22, hexane/EtOAc, 3/1), 195 mg (94%) of (±)-**5a** was obtained as a white solid.

Data for (±)-**5a**:

mp: 120–122 $^\circ\text{C}$ (benzene)

SFC: (*R*)-**5a**, t_R 4.68 min (49.9%); (*S*)-**5a**, t_R 5.15 min (50.1%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 $^\circ\text{C}$, 2.5 mL min⁻¹)

HMPA-Catalyzed Addition of *tert*-Butyl isocyanide to Benzaldehyde

Following General Procedure I, a mixture of benzaldehyde (104 μL , $d = 1.044$, 1.0 mmol), HMPA (18 μL , $d = 1.030$, 0.1 mmol, 0.1 equiv), SiCl₄ (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.22, hexane/EtOAc, 3/1), 187 mg (90%) of (±)-**5a** was obtained as a white solid.

Optimization of Asymmetric Addition of *tert*-Butyl isocyanide Catalyzed by (*R,R*)-1b****

A. One-portion addition of *t*-BuNC. A solution of *tert*-butyl isocyanide (63 μ L, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added in one portion to the cold solution of benzaldehyde (52 μ L, $d = 1.044$, 0.5 mmol), catalyst (*R,R*)-**1b** (22 mg, 0.025 mmol, 0.05 equiv), and SiCl_4 (63 μ L, $d = 1.483$, 0.55 mmol, 1.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C . The mixture was stirred for 4 h at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 85 mg (83%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 9.8/90.2, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.60 min (9.8%); (*S*)-**5a**, t_R 4.94 min (90.2%) (Chiracel AD, 4.5% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

B. Two-hour addition of *t*-BuNC. A solution of *tert*-butyl isocyanide (63 μ L, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added via a syringe pump to the cold solution of benzaldehyde (52 μ L, $d = 1.044$, 0.5 mmol), catalyst (*R,R*)-**1b** (22 mg, 0.025 mmol, 0.05 equiv), and SiCl_4 (63 μ L, $d = 1.483$, 0.55 mmol, 1.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 2 h. The mixture was stirred further for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 97 mg (94%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 5.7/94.3, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.64 min (5.7%); (*S*)-**5a**, t_R 4.97 min (94.3%) (Chiracel AD, 4.5% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

C. With 30 mol % *i*-Pr₂NEt. A solution of *tert*-butyl isocyanide (63 μ L, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added via a syringe pump to the cold solution of benzaldehyde (52 μ L, $d = 1.044$, 0.5 mmol), catalyst (*R,R*)-**1b** (22 mg, 0.025 mmol, 0.05 equiv), SiCl_4 (63 μ L, $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (27 μ L, $d = 0.742$, 0.15 mmol, 0.3 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 3 h. The mixture was stirred further for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 92 mg (89%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 1.9/98.1, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.67 min (1.9%); (*S*)-**5a**, t_R 5.03 min (98.1%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

D. Optimized conditions. A solution of *tert*-butyl isocyanide (125 μ L, d = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to the cold solution of benzaldehyde (104 μ L, d = 1.044, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.5 equiv), SiCl₄ (125 μ L, d = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, d = 0.742, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred for 90 min at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.22, hexane/EtOAc, 3/1), 199 mg (96%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 0.1/99.9, (*R*)-**5a**/(*S*)-**5a**. From the sign of optical rotation of the product ($[\alpha]_D^{24}$ +28.8, MeOH), the absolute configuration of **5a** was deduced to be *S* (lit.⁵, (*S*) enantiomer, $[\alpha]_D^{24}$ +28.3, MeOH).

Data for (*S*)-(+)-**5a**:

mp: 83-84 °C (benzene)

¹H NMR: (400 MHz, CDCl₃)

7.32-7.38 (m, 5 H, aryl); 5.80 (bs, 1 H, NH); 4.89 (s, 1 H, HC(2)); 4.89 (bs, 1 H, OH); 1.32 (s, 9 H, 3 X H₃C(2"))

SFC: (*R*)-**5a**, t_R 4.64 min (0.1%); (*S*)-**5a**, t_R 4.93 min (99.9%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ +28.8 (c = 0.54, MeOH)

Analysis: C₁₂H₁₇NO₂ (207.27)

Calcd: C, 69.54; H, 8.27; N, 6.76%

Found: C, 69.47; H, 8.35; N, 6.97%

Catalyst Survey for the Asymmetric Addition of *tert*-Butyl isocyanide to Benzaldehyde

Following General Procedure II, a solution of *tert*-butyl isocyanide (63 μL , $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added to the cold solution of benzaldehyde (52 μL , $d = 1.044$, 0.5 mmol), catalyst (*R,R*)-**1a** (21 mg, 0.025 mmol, 0.05 equiv), SiCl_4 (63 μL , $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 μL , $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 4 h. The mixture was further stirred for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 97 mg (93%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 3.6/96.4, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.56 min (3.6%); (*S*)-**5a**, t_R 4.86 min (96.4%) (Chiracel AD, 4.5% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

Following General Procedure II, a solution of *tert*-butyl isocyanide (63 μL , $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added to the cold solution of benzaldehyde (52 μL , $d = 1.044$, 0.5 mmol), catalyst (*R,R*)-**1c** (22 mg, 0.025 mmol, 0.05 equiv), SiCl_4 (63 μL , $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 μL , $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 4 h. The mixture was further stirred for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 89 mg (86%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 4.4/95.6, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.63 min (4.4%); (*S*)-**5a**, t_R 4.94 min (95.6%) (Chiracel AD, 4.5% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

Following General Procedure II, a solution of *tert*-butyl isocyanide (63 μL , $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added to the cold solution of benzaldehyde (52 μL , $d = 1.044$, 0.5 mmol), catalyst **1d** (25 mg, 0.05 mmol, 0.1 equiv), SiCl_4 (63 μL , $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 μL , $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 4 h. The mixture was further stirred for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 85

mg (82%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 65.3/34.7, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.50 min (65.3%); (*S*)-**5a**, t_R 4.87 min (34.7%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

Following General Procedure II, a solution of *tert*-butyl isocyanide (63 µL, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH₂Cl₂ (0.5 mL) was added to the cold solution of benzaldehyde (52 µL, $d = 1.044$, 0.5 mmol), catalyst **1e** (35 mg, 0.05 mmol, 0.1 equiv), SiCl₄ (63 µL, $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 µL, $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH₂Cl₂ (0.5 mL) at -74 °C over 4 h. The mixture was further stirred for 90 min at -74 °C. After work-up and silica gel chromatography (10 mm column, 15 g SiO₂, R_f 0.22, hexane/EtOAc, 3/1), 95 mg (92%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 48.6/51.4, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.59 min (48.6%); (*S*)-**5a**, t_R 4.97 min (51.4%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

Following General Procedure II, *tert*-butyl isocyanide (63 µL, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH₂Cl₂ (0.5 mL) was added to the cold solution of benzaldehyde (52 µL, $d = 1.044$, 0.5 mmol), catalyst **1f** (25 mg, 0.05 mmol, 0.1 equiv), SiCl₄ (63 µL, $d = 1.463$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 µL, $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH₂Cl₂ (0.5 mL) at -74 °C over 3 h. The mixture was further stirred for 90 min at -74 °C. After work-up and silica gel chromatography (10 mm column, 15 g SiO₂, R_f 0.22, hexane/EtOAc, 3/1), 90 mg (87%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 33.7/66.3, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.65 min (33.7%); (*S*)-**5a**, t_R 5.00 min (66.3%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

Following General Procedure II, a solution of *tert*-butyl isocyanide (63 μL , $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added to the cold solution of benzaldehyde (52 μL , $d = 1.044$, 0.5 mmol), catalyst (*P*)-(*R,R*)-**1g** (25 mg, 0.05 mmol, 0.1 equiv), SiCl_4 (63 μL , $d = 1.483$, 0.55 mmol, 1.1 equiv), and diisopropylethylamine (9 μL , $d = 0.742$, 0.05 mmol, 0.1 equiv) in CH_2Cl_2 (0.5 mL) at -74°C over 4 h. The mixture was further stirred for 90 min at -74°C . After work-up and silica gel chromatography (10 mm column, 15 g SiO_2 , R_f 0.22, hexane/EtOAc, 3/1), 90 mg (87%) of **5a** was obtained as a white solid. The enantiomeric ratio was determined to be 51.5/48.5, (*R*)-**5a**/(*S*)-**5a**.

SFC: (*R*)-**5a**, t_R 4.62 min (51.5%); (*S*)-**5a**, t_R 5.03 min (48.5%) (Chiracel AD, 4.5% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

***N*-*tert*-Butyl-2-hydroxy-2-(4-methylphenyl)acetamide (($\pm$)-**5b**)**

Following General Procedure I, a mixture of 4-tolualdehyde **3b** (118 μL , $d = 1.019$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.20, hexane/EtOAc, 3/1), 188 mg (87%) of ($\pm$)-**5b** was obtained as a white solid. White needle-like crystals of ($\pm$)-**5b** (150 mg, 69%) were obtained after recrystallization from a 3/1 mixture of heptane/benzene.

Data for ($\pm$)-**5b**:

mp: $119.5\text{--}120^\circ\text{C}$ (heptane/benzene, 3/1)

$^1\text{H NMR}$: (400 MHz, CDCl_3)

7.16-7.24 (m, 4 H, aryl); 5.50 (bs, 1 H, NH); 4.86 (d, $J = 3.4$, 1 H, HC(2)); 3.60 (d, $J = 3.4$, 1 H, OH); 2.35 (s, 3 H, H₃C(5')); 1.32 (s, 9 H, 3 X H₃C(2'))

¹³C NMR: (100 MHz, CDCl₃)

171.4 (C(1)), 138.4 (C(1')), 136.9 (C(4')), 129.6 (C(3')), 126.8 (C(2')), 74.0 (C(2)), 54.5 (C(1'')), 28.6 (C(2'')), 21.2 (C(5'))

IR: (CHCl₃)

3612 (m), 3413 (s), 3008 (s), 2977 (s), 2929 (m), 2873 (w), 1675 (s), 1614 (s), 1523 (s), 1481 (m), 1392 (m), 1367 (m), 2929 (m), 1265 (s), 1232 (w), 1076 (w)

TLC: R_f 0.20 (hexane/EtOAc, 3/1)

SFC: (*R*)-**5b**, t_R 5.28 min (49.3%); (*S*)-**5b**, t_R 5.89 min (50.7%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

MS: (FI, 70 eV)

221 (100), 222 (15)

Analysis: C₁₃H₁₉NO₂ (221.30)

Calcd: C, 70.56; H, 8.65; N, 6.33%

Found: C, 70.58; H, 8.78; N, 6.44%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μL, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of 4-tolualdehyde **3b** (118 μL, $d = 1.019$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μL, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μL, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred further for 4 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.20, hexane/EtOAc, 3/1), 210 mg (91%) of **5b** was obtained as a white solid. An analytically pure sample was obtained after sublimation (75 °C/0.5 mm Hg).

Data for (*S*)-(+)-**5b**:

mp: 77-79 °C (sublimation)

SFC: (*R*)-**5b**, t_R 5.28 min (0%); (*S*)-**5b**, t_R 5.89 min (100%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_{\text{D}}^{24} +28.5$ ($c = 0.735$, MeOH)

Analysis: C₁₃H₁₉NO₂ (221.30)

Calcd: C, 70.56; H, 8.65; N, 6.33%

Found: C, 70.58; H, 8.78; N, 6.44%

***N*-tert-Butyl-2-hydroxy-2-(4-methoxyphenyl)acetamide ((±)-5c)**

Following General Procedure I, a mixture of 4-methoxybenzaldehyde **3c** (136 mg, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.22, hexane/EtOAc, 65/35), 218 mg (92%) of (±)-**5c** was obtained as a white solid. White plate-like crystals of (±)-**5c** (171mg, 70%) were obtained after recrystallization from a 7/3 mixture of heptane and benzene.

Data for (±)-**5c**:

mp: 96-97°C (heptane/benzene, 7/3)

¹H NMR: (400 MHz, CDCl₃)

6.89-7.23 (m, 4 H, Ar); 5.75 (bs, 1 H, NH); 4.85 (d, $J = 3.4$, 1 H, HC(2)); 3.81 (s, 3 H, H₃C (5')); 3.59 (d, $J = 3.7$, 1 H, OH); 1.32 (s, 9 H, 3 X H₃C (2''))

¹³C NMR: (100 MHz, CDCl₃)

171.5 (C(1)), 159.7 (C(4')), 132.1 (C(1')), 128.2 (C(2')), 114.2 (C(3')), 73.7 (C(2)), 55.3 (C(1'')), 51.4 (C(5')), 28.6 (C(2''))

IR: (CHCl₃)

3606 (m), 3411 (s), 3008 (s), 2969 (s), 2937 (s), 2910 (s), 2873 (m), 2838 (m),

1672 (s), 1612 (s), 1587 (w), 1511 (s), 1457 (s), 1394 (s), 1367 (s), 1303 (m),
1249 (s), 1197 (s), 1035 (s), 948 (s), 906 (w), 862 (w)

TLC: R_f 0.22 (hexane/EtOAc, 65/35)

SFC: (*R*)-**5c**, t_R 2.99 min (49.9%); (*S*)-**5c**, t_R 3.43 min (50.1%) (Chiracel AD, 8.0%
MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

MS: (FI, 70 eV)
237 (100), 238 (15)

Analysis: C₁₃H₁₉NO₃ (237.29)

Calcd:	C, 65.80;	H, 8.07;	N, 5.90%
Found:	C, 65.61;	H, 8.12;	N, 6.03%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, d = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of 4-methoxybenzaldehyde **3c** (136 mg, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, d = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred further for 4 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.22, hexane/EtOAc, 65/35), 211 mg (89%) of **5c** was obtained as a white solid. An analytically pure sample was obtained after sublimation (100 °C/0.5 mm Hg).

Data for (*S*)-(+)-**5c**:

mp: 103-104 °C (sublimed)

SFC: (*R*)-**5c**, t_R 3.00 min (1.7%); (*S*)-**5c**, t_R 3.44 min (98.3%) (Chiracel AD, 8.0%
MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ +30.9 (c = 0.755, MeOH)

Analysis: C₁₃H₁₉NO₃ (237.29)

Calcd:	C, 65.80;	H, 8.07;	N, 5.90%
Found:	C, 65.47;	H, 8.14;	N, 6.09%

***N*-tert-Butyl-2-hydroxy-2-(4-trifluoromethylphenyl)acetamide ((±)-5d)**

Following General Procedure I, a mixture of 4-(trifluoromethyl)benzaldehyde **3d** (137 μL , $d = 1.275$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.11, hexane/EtOAc, 3/1), 235 mg (87%) of (±)-**5d** was obtained as a white solid. White crystals of (±)-**5d** (180mg, 65%) were obtained after recrystallization from a 4/1 mixture of heptane and benzene.

Data for (±)-5d:

mp: $135\text{--}136^\circ\text{C}$ (heptane/benzene, 4/1)

^1H NMR: (400 MHz, CDCl_3)

7.58 (AB quartet, $J = 8.6$, 4 H, Ar); 5.93 (bs, 1 H, NH); 4.97 (d, $J = 3.9$, 1 H, HC(2)); 3.59 (d, $J = 3.9$, 1 H, OH); 1.32 (s, 9 H, 3 $\times$ $\text{H}_3\text{C}(2'')$)

^{19}F NMR: (376 MHz, CDCl_3)

-62.77

^{13}C NMR: (100 MHz, CDCl_3)

170.3 (C(1)), 143.7 (C(1')), 130.5 (q, $J = 32.8$, C(4')), 127.0 (C(2')), 125.7 (q, $J = 3.8$, C(3')), 124.0 (q, $J = 271.6$, C(5')), 73.6 (C(2)), 51.6 (C(1'')), 28.6 (C(2''))

IR: (CHCl_3)

3612 (m), 3411 (s), 2998 (m), 2971 (m), 2935 (m), 2908 (m), 2873 (m), 1679 (s), 1672 (s), 1619 (m), 1523 (s), 1456 (m), 1419 (m), 1394 (m), 1367 (s), 1326 (s), 1276 (m), 1213 (m), 1168 (s), 1132 (s), 1068 (s), 1018 (m), 842 (w)

TLC: R_f 0.11 (hexane/EtOAc, 3/1)

SFC: (*R*)-**5d**, t_R 2.54 min (50.0%); (*S*)-**5d**, t_R 3.52 min (50.0%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

MS: (FI, 70 eV)
277 (2), 276 (14), 275 (47), 176 (3), 175 (46), 101 (6), 100 (100)

Analysis: C₁₃H₁₆F₃NO₂ (275.27)
Calcd: C, 56.72; H, 5.86; N, 5.09%
Found: C, 56.86; H, 6.11; N, 5.19%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 µL, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to the cold solution of 4-(trifluoromethyl)benzaldehyde **3d** (137 µL, $d = 1.275$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 µL, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 µL, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred further for 4 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.11, hexane/EtOAc, 3/1), 245 mg (89%) of (*S*)-**5d** was obtained as a white solid. An analytically pure sample was obtained after sublimation (80 °C/0.5 mm Hg).

Data for (*S*)-(+)-5d**:**

mp: 87-88 °C (sublimed)

SFC: (*R*)-**5d**, t_R 2.12 min (3.5%); (*S*)-**5d**, t_R 3.02 min (96.5%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24} +18.5$ ($c = 0.625$, MeOH)

Analysis: C₁₃H₁₆F₃NO₂ (275.27)
Calcd: C, 56.72; H, 5.86; N, 5.09%
Found: C, 56.62; H, 5.78; N, 5.13%

***N*-tert-Butyl-2-hydroxy-2-(2-naphthyl)acetamide ((±)-5e)**

Following General Procedure I, a mixture of 2-naphthaldehyde **3e** (156 mg, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.17, hexane/EtOAc, 3/1), 230 mg (90%) of ((±)-**5e** was obtained as a white solid. White crystals of ((±)-**5e** (204 mg, 80%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for ((±)-5e:

mp: 118-119°C (heptane/benzene, 3/1)

¹H NMR: (400 MHz, CDCl_3)

7.45-7.87 (m, 7 H, aryl); 5.72 (bs, 1 H, NH); 5.06 (d, $J = 3.7$, 1 H, HC(2)); 3.88 (d, $J = 3.4$, 1 H, OH); 1.31 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

¹³C NMR: (100 MHz, CDCl_3)

171.2 (C(1)), 137.2 (C(2')), 133.4 (C(9') or C(10')), 133.2 (C(9') or C(10')), 129.0 (C(8')), 128.0 (C(3')), 127.8 (C(4')), 126.5 (C(5')), 126.4 ((C(1') or C(6')), 126.3 (C(6') or C(1')), 124.0 (C(7')), 74.2 (C(2)), 51.6 (C(1'')), 28.6 (C(2''))

IR: (CHCl_3)

3612 (m), 3413 (m), 3010 (m), 2973 (m), 1677 (s), 1602 (s), 1523 (s), 1425 (w), 1394 (w), 1367 (m), 1278 (w), 1267 (m), 1234 (w), 1170 (w), 1124 (w), 1079 (m), 877 (w)

TLC: R_f 0.17 (hexane/EtOAc, 3/1)

SFC: (*R*)-**5e**, t_R 3.71 min (50.3%); (*S*)-**5e**, t_R 4.58 min (49.7%) (Chiracel AD, 10.0% MeOH in CO_2 , 125 bar, 40°C , 3.0 mL min^{-1})

MS: (FI, 70 eV)

258 (19), 257 (100)

Analysis: C₁₆H₁₉NO₂ (257.33)

Calcd: C, 74.68; H, 7.44; N, 5.44%

Found: C, 74.65; H, 7.70; N, 5.61%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to the cold solution of 2-naphthaldehyde **3e** (156 mg, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at $-74\text{ }^{\circ}\text{C}$ over 4 h. The mixture was stirred further for 4 h at $-74\text{ }^{\circ}\text{C}$. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.17, hexane/EtOAc, 3/1), 242 mg (93%) of (+)-**5e** was obtained as a white solid. An analytically pure sample was obtained after sublimation ($90\text{ }^{\circ}\text{C}/0.5\text{ mm Hg}$).

Data for (*S*)-(+)-**5e**:

mp: 94-96 $^{\circ}\text{C}$ (sublimed)

SFC: (*R*)-**5e**, t_R 3.73 min (0.3%); (*S*)-**5e**, t_R 4.58 min (99.7%) (Chiracel AD, 10% MeOH in CO₂, 125 bar, $40\text{ }^{\circ}\text{C}$, 3.0 mL min^{-1})

Opt. Rot.: $[\alpha]_D^{24} +44.9$ ($c = 0.96$, MeOH)

Analysis: C₁₆H₁₉NO₂ (257.33)

Calcd: C, 74.68; H, 7.44; N, 5.44%

Found: C, 74.60; H, 7.54; N, 5.66%

***N*-tert-Butyl-2-hydroxy-2-(1-naphthyl)acetamide ((±)-5f)**

Following General Procedure I, a mixture of 1-naphthaldehyde **3f** (136 μL , $d = 1.150$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 8 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.26, hexane/EtOAc, 70/30), 223 mg (87%) of (±)-**5f** was obtained as a white solid. White crystals of (±)-**5f** (183 mg, 71%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for (±)-5f:

mp: 133-133.5°C (heptane/benzene, 3/1)

¹H NMR: (400 MHz, CDCl_3)

8.09-8.12 (m, 1 H, H(C(4'))); 7.84-7.89 (m, 2 H, H(C(2')) and H(C(3'))); 7.44-7.53 (m, 4 H, Ar); 5.72 (bs, 1 H, NH); 5.46 (d, $J = 3.7$, 1 H, HC(2)); 3.96 (d, $J = 3.4$, 1 H, OH); 1.27 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

¹³C NMR: (100 MHz, CDCl_3)

171.8 (C(1)), 135.0 (C(1')), 134.2 (C(10')), 131.1 (C(9')), 129.6 (C(5')), 128.8 (C(4')), 127.0 (C(7')), 126.6 (C(6')), 126.0 (C(3')), 125.2 (C(2')), 123.9 (C(8')), 73.1 (C(2)), 51.6 (C(1'')), 28.5 (C(2''))

IR: (CHCl_3)

3602 (w), 3413 (s), 3052 (w), 3010 (s), 2971 (s), 2935 (m), 1675 (s), 1598 (s), 1521 (s), 1456 (m), 1394 (m), 1367 (m), 1265 (m), 1234 (w), 1169 (w), 1101 (m), 1064 (m), 1020 (w), 944 (w)

TLC: R_f 0.26 (hexane/EtOAc, 70/30)

HPLC: (S)-**5f**, t_R 6.57 min (49.6%); (R)-**5f**, t_R 13.82 min (50.4%) (Rexchrom (S,S)

BETA-GEM 1, hexane / isopropanol, 70 / 30, 1.0 mL min⁻¹)

MS: (FI, 70 eV)

258 (18), 257 (100)

Analysis: C₁₆H₁₉NO₂ (257.33)

Calcd: C, 74.68; H, 7.44; N, 5.44%

Found: C, 74.52; H, 7.35; N, 5.61%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, d = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of 1-naphthaldehyde **3f** (136 μ L, d = 1.150, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, d = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred further for 8 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.26, hexane/EtOAc, 70/30), 236 mg (92%) of (S)-**5f** was obtained as a white solid. An analytically pure sample was obtained after sublimation (110°C/0.5 mm Hg).

Data for (S)-(+)-5f**:**

mp: 113-116°C

HPLC: (S)-**5f**, t_R 6.64 min (92.2%); (R)-**5f**, t_R 14.05 min (7.8%) (Rexchrom (S,S) BETA-

GEM 1, hexane / isopropanol, 70 / 30, 1.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ +40.8 (c = 0.66, MeOH)

Analysis: C₁₆H₁₉NO₂ (257.33)

Calcd: C, 74.68; H, 7.44; N, 5.44%

Found: C, 74.60; H, 7.54; N, 5.66%

***N*-tert-Butyl-2-hydroxy-4-phenyl-3-ene-butenamide ((±)-**5g**)**

Following General Procedure I, a mixture of *trans*-cinnamaldehyde **3g** (126 μL , $d = 1.048$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.26, hexane/EtOAc, 2/1), 170 mg (73%) of (±)-**5g** was obtained as an off-white solid. White crystals of (±)-**5g** (132 mg, 57%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for (±)-**5g**:

mp: $93\text{--}94^\circ\text{C}$ (heptane/benzene, 3/1)

^1H NMR: (400 MHz, CDCl_3)

7.27–7.42 (m, 5 H, aryl); 6.74 (d, $J = 15.9$, 1 H, HC(4)); 6.25 (dd, $J = 15.8$, 3.0, 1 H, HC(3)); 5.95 (bs, 1 H, NH); 4.58 (d, $J = 6.8$, 1 H, HC(2)); 3.41 (bs, 1 H, OH); 1.37 (s, 9 H, 3 $\times$ $\text{H}_3\text{C}(2'')$)

^{13}C NMR: (100 MHz, CDCl_3)

170.9 (C(1)), 136.0 (C(1')), 133.3 (C(4)), 128.6 (C(3')), 128.1 (C(3)), 127.2 (C(4')), 126.7 (C(2')), 73.0 (C(2)), 51.5 (C(1'')), 28.7 (C(2''))

IR: (CHCl_3)

3614 (m), 3413 (m), 3006 (m), 2973 (m), 2935 (m), 1678 (s), 1521 (s), 1456 (m), 1394 (w), 1367 (m), 1276 (w), 1236 (w), 1216 (w), 1108 (m), 1072 (w), 968 (m)

TLC: R_f 0.26 (hexane/EtOAc, 2/1)

SFC: (*S*)-**5g**, t_R 2.35 min (50.2%); (*R*)-**5g**, t_R 2.77 min (49.8%) (Chiracel AD, 10.0% MeOH in CO_2 , 125 bar, 40°C , 3.0 mL min $^{-1}$)

MS: (FI, 70 eV)

234 (16), 233 (100), 232 (3), 231 (16), 207 (3), 148 (2)

Analysis: C₁₄H₁₉NO₂ (233.31)

Calcd: C, 72.07; H, 8.21; N, 6.00%

Found: C, 71.91; H, 8.23; N, 6.06%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, d = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of *trans*-cinnamaldehyde **3g** (126 μ L, d = 1.048, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, d = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, d = 0.742, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.26, hexane/EtOAc, 2/1), 188 mg (81%) of (*S*)-**5g** was obtained as a white solid. An analytically pure sample was obtained after sublimation (70 °C/0.5 mm Hg).

Data for (*S*)-(-)-5g:

mp: 71-74 °C (sublimation)

SFC: (*R*)-**5g**, t_R 2.35 min (2.2%); (*S*)-**5g**, t_R 2.77 min (97.8%) (Chiracel AD, 10.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ -7.2 (c = 1.06, MeOH)

Analysis: C₁₄H₁₉NO₂ (233.31)

Calcd: C, 72.07; H, 8.21; N, 6.00%

Found: C, 71.75; H, 8.13; N, 6.04%

***N*-tert-Butyl-2-hydroxy-3-methyl-4-phenyl-3-butenamide ((±)-5h)**

Following General Procedure I, a mixture of (*E*)-2-methyl-cinnamaldehyde **3h** (140 μL , $d = 1.047$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.28, hexane/EtOAc, 3/1), 211 mg (86%) of (±)-**5h** was obtained as a white solid. White crystals of (±)-**5h** (185 mg, 75%) were obtained after recrystallization from a 4/1 mixture of heptane and benzene.

Data for (±)-5h:

mp: 125.5-126.0°C (heptane/benzene, 4/1)

^1H NMR: (400 MHz, CDCl_3)

7.25-7.41 (m, 5 H, aryl); 6.62 (s, 1 H, HC(4)); 5.78 (bs, 1 H, NH); 4.48 (d, $J = 3.4$, 1 H, HC(2)); 3.89 (d, $J = 3.2$, 1 H, OH); 1.83 (s, 3 H, $\text{H}_3\text{C}(5')$); 1.39 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

^{13}C NMR: (100 MHz, CDCl_3)

170.9 (C(1)), 137.2 (C(1') or C(3)), 136.6 (C(1') or C(3)), 130.6 (C(4)), 128.9 (C(3')), 129.0 (C(2')), 127.1 (C(4')), 77.8 (C(2)), 51.6 (C(1'')), 28.7 (C(2'')), 12.2 (C(5''))

IR: (CHCl_3)

3411 (s), 3010 (s), 2971 (s), 2935 (m), 2912 (m), 2873 (m), 1678 (s), 1523 (s), 1492 (m), 1456 (s), 1393 (s), 1367 (s), 1274 (s), 1232 (s), 1178 (m), 1083 (s), 1016 (s), 950 (m), 919 (m)

TLC: R_f 0.28 (hexane/EtOAc, 3/1)

SFC: (S)-**5h**, t_R 7.24 min (49.8%); (R)-**5h**, t_R 7.95 min (50.2%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹)

MS: (FI, 70 eV)
248 (15), 247 (100)

Analysis: C₁₅H₂₁NO₂ (247.33)

Calcd: C, 72.84; H, 8.56; N, 5.66%

Found: C, 72.83; H, 8.67; N, 5.88%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 µL, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to the cold solution of (*E*)-2-methyl -cinnamaldehyde **3h** (140 µL, $d = 1.047$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 µL, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 µL, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 4 h. The mixture was stirred further for 4 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.28, hexane/EtOAc, 3/1), 212 mg (86%) of **53h** was obtained as a white solid. The enantiomeric ratio was determined to be 67.4/32.6, (S)-**5h**/(R)-**5h**. Analytically pure sample (165 mg, 67%), which has an enantiomeric ratio of 59.4/40.6, (S)-**5h**/(R)-**5h**, was obtained after recrystallization from a 4/1 mixture of heptane and benzene.

Data for (S)-5h**:**

mp: 112-113 °C (heptane/benzene, 4/1)

SFC: (S)-**5h**, t_R 7.27 min (67.4%); (R)-**5h**, t_R 7.97 min (32.6%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹) (before recrystallization)

SFC: (S)-**5h**, t_R 7.22 min (59.4%); (R)-**5h**, t_R 7.93 min (40.6%) (Chiracel AD, 4.5% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹) (after recrystallization)

Analysis: C₁₅H₂₁NO₂ (247.33)

Calcd: C, 72.84; H, 8.56; N, 5.66%

Found: C, 72.80; H, 8.61; N, 5.80%

***N*-tert-Butyl-2-hydroxy-4-phenyl-3-butynamide ((±)-**5i**)**

Following General Procedure I, a mixture of phenylpropargyl aldehyde **3i** (125 μ L, $d = 1.047$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (2.0 mL) was stirred for 4 h at -74°C . The mixture was poured into an ice-cold, saturated aqueous solution of KF (20 mL) with vigorous stirring. The mixture was stirred at rt for 1 h and then was extracted with CH₂Cl₂ (4 X 10 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. The product (±)-**5i** (197 mg, 85%) was obtained as a pale yellow solid after silica gel column chromatography (20 mm column, 60 g SiO₂, R_f 0.26, hexane/EtOAc, 3/1). White crystals of (±)-**5i** (153 mg, 66%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for (±)-**5i**:

mp: 127-128°C (heptane/benzene, 3/1)

SFC: (*S*)-**5i**, t_R 4.96 min (50.0%); (*S*)-**5i**, t_R 5.58 min (50.0%) (Chiracel AD, 5.0% MeOH in CO₂, 125 bar, 40 $^\circ\text{C}$, 3.0 mL min⁻¹)

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of phenylpropargyl aldehyde **3i** (125 μ L, $d = 1.047$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), and SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) at -74°C over 4 h. The mixture was stirred further for 4 h at -74°C and then poured into an ice cold, saturated aqueous solution of KF (20 mL) with vigorous stirring. The mixture was stirred at rt for 1 h and then was extracted by CH₂Cl₂ (4 X 10 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. After silica gel chromatography (20

mm column, 60 g SiO₂, *R_f* 0.26, hexane/EtOAc, 3/1), 177 mg (76%) of (*S*)-**5i** was obtained as a pale yellow solid. An analytically pure sample was obtained after sublimation (90°C/0.5 mm Hg).

Data for (*S*)-**5i**:

mp: 94-96°C (sublimation)

¹H NMR: (400 MHz, CDCl₃)

7.32-7.47 (m, 5 H, aryl); 6.12 (bs, 1 H, NH); 4.89 (d, *J* = 2.9, 1 H, HC(2)); 3.60 (bs, 1 H, OH); 1.41 (s, 9 H, 3 X H₃C(2''))

¹³C NMR: (100 MHz, CDCl₃)

168.0 (C(1)), 131.9 (C(2')), 128.8 (C(4')), 128.3 (C(3')), 121.8 (C(1')), 85.9 (C(3) or C(4)), 85.5 (C(3) or C(4)), 62.9 (C(2)), 51.8 (C(1'')), 28.6 (C(2''))

IR: (CHCl₃)

3602 (m), 3411 (s), 2973 (m), 2225 (w), 1689 (s), 1523 (s), 1490 (s), 1456 (s), 1394 (s), 1367 (s), 1278 (s), 1232 (m), 1085 (m), 815 (m)

TLC: *R_f* 0.26 (hexane/EtOAc, 3/1)

SFC: (*S*)-**5i**, *t_R* 4.99 min (77.0%); (*R*)-**5i**, *t_R* 5.61 min (23.0%) (Chiracel AD, 5.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

MS: (EI, 70 eV)

233 (1), 232 (6), 231 (8), 175 (14), 174 (12), 132 (36), 131 (100), 103 (19)

Opt. Rot.: [α]_D²⁴ +9.96 (*c* = 1.77, EtOH with 5% aq. HCl)

Analysis: C₁₄H₁₇NO₂ (231.29)

Calcd: C, 72.70; H, 7.41; N, 6.06%

Found: C, 72.63; H, 7.42; N, 5.92%

***N*-tert-Butyl-2-hydroxy-4-phenylbutamide ((±)-**5j**)**

Following General Procedure I, a solution of *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added via a syringe pump to a cold solution of hydrocinnamaldehyde **3j** (132 μL , $d = 1.019$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), and SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH_2Cl_2 (1.0 mL) at -74°C over 8 h. The mixture was stirred for 8 h further at -74°C . After silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.21, hexane/EtOAc, 3/1), 209 mg (89%) of ($\pm$)-**5j** was obtained as a white solid. White crystals of ($\pm$)-**5j** (168 mg, 71%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for ($\pm$)-**5j**:

mp: $86\text{--}87^\circ\text{C}$ (heptane/benzene, 3/1)

^1H NMR: (400 MHz, CDCl_3)

7.20–7.29 (m, 5 H, aryl); 6.20 (bs, 1 H, NH); 3.97–4.02 (m, 1 H, HC(2)); 3.00 (bs, 1 H, OH); 2.75 (t, $J = 7.2$, 2 H, $\text{H}_2\text{C}(4)$); 1.89–2.13 (m, 2 H, $\text{H}_2\text{C}(3)$); 1.37 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

^{13}C NMR: (100 MHz, CDCl_3)

173.0 (C(1)), 141.4 (C(1')), 128.5 (C(3') and C(4')), 126.0 (C(2')), 71.5 (C(2)), 51.0 (C(1'')), 36.6 (C(4)), 31.2 (C(3)), 28.7 (C(2''))

IR: (CHCl_3)

3619 (m), 3407 (s), 3008 (s), 2969 (s), 2932 (m), 1670 (s), 1525 (s), 1496 (s), 1456 (m), 1367 (s), 1282 (s), 1232 (m), 1174 (m), 1095 (m), 1074 (m), 825 (m)

TLC: R_f 0.21 (hexane/EtOAc, 3/1)

SFC: (*R*)-**5j**, t_R 4.05 min (50.3%); (*S*)-**5j**, t_R 5.28 min (49.7%) (Chiracel AD, 5.0% MeOH in CO_2 , 125 bar, 40°C , 3.0 mL min^{-1})

MS: (FI, 70 eV)

236 (19), 235 (100)

Analysis: C₁₄H₁₉NO₂ (235.32)

Calcd: C, 71.46; H, 8.99; N, 5.95%

Found: C, 71.53; H, 8.96; N, 6.14%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of hydrocinnamaldehyde **3j** (132 μ L, $d = 1.019$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv) and SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 8 h. The mixture was stirred further for 8 h at -74 °C. After work-up and silica gel column chromatography (20 mm column, 60 g SiO₂, R_f 0.21, hexane/EtOAc, 3/1), 217 mg (92%) of (*S*)-**5j** was obtained as a white solid. An analytically pure sample (199 mg, 84%) was obtained after sublimation (70 °C/0.5 mmHg).

Data for (*S*)-(-)-5j:

mp: 74-78 °C

SFC: (*R*)-**5j**, t_R 4.09 min (18.1%); (*S*)-**5j**, t_R 5.86 min (81.9%) (Chiracel AD, 5.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ -22.7 ($c = 1.07$, MeOH)

Analysis: C₁₄H₂₁NO₂ (235.32)

Calcd: C, 71.46; H, 8.99; N, 5.95%

Found: C, 71.45; H, 9.05; N, 6.10%

***N*-tert-butyl-2-hydroxy-2-cyclohexylacetamide ((±)-**5k**)**

Following General Procedure I, a mixture of cyclohexanecarboxaldehyde **3k** (121 μL , $d = 0.926$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was stirred for 24 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.35, hexane/EtOAc, 3/1), 152 mg (72%) of ($\pm$)-**5k** was obtained as a white solid. White crystals of ($\pm$)-**5k** (120 mg, 50%) were obtained after recrystallization from a 3/1 mixture of heptane and benzene.

Data for ($\pm$)-**5k**:

mp: $122\text{--}123^\circ\text{C}$ (heptane/benzene, 3/1)

^1H NMR: (400 MHz, CDCl_3)

6.24 (bs, 1 H, NH); 3.78 (m, 1 H, HC(2)); 2.95 (bs, 1 H, OH); 1.08–1.78 (m, 11 H, cyclohexyl); 1.36 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

^{13}C NMR: (100 MHz, CDCl_3)

172.4 (C(1)), 76.1 (C(2)), 51.1 (C(1'')), 41.8 (C(1')), 29.6, 28.8 (C(2'')), 26.3, 26.1, 26.0, 25.7

IR: (CHCl_3)

3627 (m), 3405 (s), 3002 (s), 2969 (s), 2931 (s), 2856 (s), 1660 (s), 1527 (s), 1479 (m), 1452 (s), 1394 (m), 1365 (m), 1280 (m), 1232 (m), 1189 (w), 1112 (m), 993 (w)

TLC: R_f 0.35 (hexane/EtOAc, 3/1)

GC: (*S*)-**5k**, t_R 17.80 min (49.4%); (*R*)-**5k**, t_R 18.46 min (50.6%) (Chiraldex BPH, 150°C , 20 psi)

MS: (FI, 70 eV)

215 (4), 214 (23), 213 (3), 213 (100), 212 (2), 81 (3)

Analysis: C₁₂H₂₃NO₂ (213.32)

Calcd: C, 67.57; H, 10.86; N, 6.57%

Found: C, 67.53; H, 11.05; N, 6.76%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to the cold solution of cyclohexanecarboxaldehyde **3k** (121 μ L, $d = 0.926$, 1.0 mmol), catalyst (*R,R*)-**1b** (85 mg, 0.10 mmol, 0.1 equiv) and SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 12 h. The mixture was stirred for 12 h further at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.35, hexane/EtOAc, 3/1), 113 mg (53%) of (*S*)-**5k** was obtained as a white solid. An analytically pure sample was obtained after sublimation (100 °C/0.5 mm Hg).

Data for (*S*)-(-)-**5k**:

mp: 118-120 °C (sublimed)

GC: (*S*)-**5k**, t_R 17.81 min (87.1%); (*R*)-**5k**, t_R 18.49 min (12.89%) (Chiraldex BPH, 150 °C, 20 psi)

Opt. Rot.: $[\alpha]_D^{24} -39.2$ ($c = 0.91$, MeOH)

Analysis: C₁₂H₂₃NO₂ (213.32)

Calcd: C, 67.57; H, 10.86; N, 6.57%

Found: C, 67.52; H, 10.86; N, 6.65%

***N*-tert-Butyl-2-hydroxy-2-(2-furyl)acetamide ((±)-**5I**)**

Following General Procedure I, a mixture of 2-furaldehyde **3I** (83 μL , $d = 1.160$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.29, hexane/EtOAc, 2/1), 147 mg (76%) of (±)-**5I** was obtained as a white solid. White crystals of (±)-**5I** (124 mg, 63%) were obtained after recrystallization from a 4/1 mixture of heptane and benzene.

Data for (±)-5I**:**

mp: 83-84 $^\circ\text{C}$ (heptane/benzene, 4/1)

^1H NMR: (400 MHz, CDCl_3)

7.41 (m, 1 H, HC(5')); 6.39 (t, $J = 3.4$, 1 H, HC(4')); 6.37 (dd, $J = 3.4$, 1.7, 1 H HC(3')); 5.88 (bs, 1 H, NH); 4.99 (bs, 1 H, HC(2)); 3.68 (d, $J = 3.7$, 1 H, OH); 1.36 (s, 9 H, 3 X $\text{H}_3\text{C}(2'')$)

^{13}C NMR: (100 MHz, CDCl_3)

168.6 (C(1)), 152.1 (C(2')), 142.9 (C(5')), 110.6 (C(4')), 108.3 (C(3')), 67.6 (C(2)), 51.8 (C(1'')), 28.6 (C(2''))

IR: (CHCl_3)

3683 (m), 3604 (w), 3415 (m), 3020 (s), 2979 (m), 2935 (w), 2873 (w), 1681 (s), 1581 (w), 1525 (s), 1477 (m), 1456 (m), 1423 (m), 1367 (m), 1216 (s), 1149 (m), 1068 (w), 1012 (m), 929 (m)

TLC: R_f 0.29 (hexane/EtOAc, 2/1)

GC: (*S*)-**5I**, t_R 42.17 min (49.5%); (*R*)-**5I** t_R 42.82 min (50.5%) (Chiraldex BPH, 114 $^\circ\text{C}$, 20 psi)

MS: (FI, 70 eV)

198 (15), 197 (100)

Analysis: C₁₀H₁₅NO₃ (197.23)

Calcd: C, 60.90; H, 7.67; N, 7.10%

Found: C, 60.70; H, 7.72; N, 7.10%

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of 2-furaldehyde **3l** (83 μ L, $d = 1.160$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74°C over 4 h. The mixture was stirred further for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.29, hexane/EtOAc, 2/1), 163 mg (83%) of (*S*)-**5l** was obtained as a white solid. An analytically pure sample was obtained after sublimation (100 $^\circ\text{C}$ /0.5 mm Hg).

Data for (*S*)-(+)-**5l**:

mp: 103-104.5 $^\circ\text{C}$ (sublimed)

GC: (*S*)-**5l**, t_R 42.69 min (95.9%); (*R*)-**5l**, t_R 43.28 min (4.1%) (Chiraldex BPH, 114 $^\circ\text{C}$, 20 psi)

Opt. Rot.: $[\alpha]_D^{24} +15.5$ ($c = 0.53$, MeOH)

Analysis: C₁₀H₁₅NO₃ (197.23)

Calcd: C, 60.90; H, 7.67; N, 7.10%

Found: C, 60.77; H, 7.64; N, 7.12%

***N*-tert-Butyl-2-hydroxy-2-(2-thiophene)acetamide ((±)-**5m**)**

Following General Procedure I, a mixture of 2-furaldehyde **3m** (94 μL , $d = 1.200$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 was stirred for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.42, hexane/EtOAc, 2/1), 189 mg (89%) of ((±)-**5m** was obtained as a white solid. White crystals of ((±)-**5m** (144 mg, 67%) were obtained after recrystallization from a 4/1 mixture of heptane and benzene.

Data for ((±)-**5m**:

mp: $89\text{--}90^\circ\text{C}$ (heptane/benzene, 4/1)

GC: (*R*)-**5m**, t_R 6.30 min (49.5%); (*S*)-**5m** t_R 6.61 min (50.5%) (Chiraldex GTA, 150°C , 20 psi)

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added via a syringe pump to a cold solution of 2-furaldehyde **3m** (94 μL , $d = 1.200$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μL , $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH_2Cl_2 (1.0 mL) at -74°C over 4 h. The mixture was stirred further for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.42, hexane/EtOAc, 2/1), 194 mg (91%) of (*S*)-**5m** was obtained as a white solid. An analytically pure sample was obtained after sublimation ($100^\circ\text{C}/0.5\text{ mm Hg}$).

Data for (*S*)-(+)-**5m**:

mp: $113\text{--}114^\circ\text{C}$ (sublimed)

¹H NMR: (400 MHz, CDCl₃)

7.30 (dd, $J = 4.9, 1.0$, 1 H, HC(5')); 7.06 (t, $J = 4.2, 0.9$, 1 H, HC(4')); 6.98 (dd, $J = 4.9, 3.4$, 1 H HC(3')); 5.91 (bs, 1 H, NH); 5.18 (s, 1 H, HC(2)); 3.78 (bs, 1 H, OH); 1.35 (s, 9 H, 3 X H₃C(2''))

¹³C NMR: (100 MHz, CDCl₃)

170.1 (C(1)), 143.0 (C(2')), 126.8, 126.1, 125.9, 70.0 (C(2)), 51.6 (C(1'')), 28.5 (C(2''))

IR: (CHCl₃)

3683 (m), 3604 (w), 3415 (m), 3020 (s), 2979 (m), 2935 (w), 2873 (w), 1681 (s), 1581 (w), 1525 (s), 1477 (m), 1456 (m), 1423 (m), 1367 (m), 1216 (s), 1149 (m), 1068 (w), 1012 (m), 929 (m)

TLC: R_f 0.20 (hexane/EtOAc, 3/1)

GC: (*S*)-**5m**, t_R 6.21 min (97.9%); (*R*)-**5m**, t_R 6.57 min (2.1%) (Chiraldex BPH, 114 °C, 20 psi)

Opt. Rot.: $[\alpha]_D^{24} +13.9$ ($c = 0.59$, EtOH)

MS: (FI, 70 eV)

214 (100), 213 (15)

Analysis: C₁₀H₁₅NO₃ (197.23)

Calcd: C, 60.90; H, 7.67; N, 7.10%

Found: C, 60.77; H, 7.64; N, 7.12%

***N*-tert-Butyl-2-hydroxy-2-(1-(4-methylphenyl)sulfonyl-1H-pyrrole)acetamide ((±)-**5n**)**

Following General Procedure I, a mixture of pyrrole-2-carboxaldehyde **3n** (250 mg, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl₄ (125 µL, *d* = 1.483, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 µL, *d* = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ was stirred for 4 h at −74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, *R_f* 0.42, hexane/EtOAc, 2/1), 333 mg (95%) of (±)-**5n** was obtained as a white solid. White crystals of (±)-**5m** (256 mg, 73%) were obtained after recrystallization from a 1/1 mixture of heptane and benzene.

Data for (±)-5n**:**

mp: 135–136 °C (heptane/benzene, 1/1)

SFC: (*R*)-**5n**, *t_R* 4.59 min (50.3%); (*S*)-**5n**, *t_R* 5.37 min (49.7%) (Chiracel AD, 6.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min^{−1})

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 µL, *d* = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of pyrrole-2-carboxaldehyde **3n** (250 mg, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 µL, *d* = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 µL, *d* = 0.742, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at −74 °C over 4 h. The mixture was stirred further for 4 h at −74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, *R_f* 0.29, hexane/EtOAc, 2/1), 312 mg (89%) of (*S*)-**5n** was obtained as a white solid. An analytically pure sample was obtained after sublimation (130 °C/0.5 mm Hg).

Data for (S)-(-)-5n:

mp: 135-137°C (sublimed)

¹H NMR: (400 MHz, CDCl₃)

7.70 (d, *J* = 8.6, 1 H, HC(2''')); 7.30 (d, *J* = 8.5, 1 H, HC(3''')); 7.27 (dd, *J* = 3.7, 1.7, 1 H, HC(5')); 6.57 (bs, 1 H, NH); 6.31 (dd, *J* = 3.4, 1.7, 1 H, HC(3'')); 6.26 (t, *J* = 3.4, 1 H, HC(4')), 5.27 (s, 1 H, HC(2)); 4.20 (bs, 1 H, OH); 2.40 (s, 3 H, H₃C(5''')); 1.37 (s, 9 H, 3 X H₃C(2''))

¹³C NMR: (100 MHz, CDCl₃)

169.0 (C(1)), 145.5 (C(2')), 135.5 (C(1''')), 134.2 (C(4''')), 130.2 (C(3''')), 126.6 (C(2''')), 123.6 (C(5')), 114.3 (C(4')), 112.3 (C(3')), 66.2 (C(2)), 51.6 (C(1'')), 28.5 (C(5''')), 21.6 (C(2''))

IR: (CHCl₃)

3683 (m), 3604 (w), 3415 (m), 3020 (s), 2979 (m), 2935 (w), 2873 (w), 1681 (s), 1581 (w), 1525 (s), 1477 (m), 1456 (m), 1423 (m), 1367 (m), 1216 (s), 1149 (m), 1068 (w), 1012 (m), 929 (m)

TLC: *R_f* 0.25 (hexane/EtOAc, 3/1)

SFC: (*R*)-5n, *t_R* 4.47 min (4.8%); (*S*)-5n, *t_R* 5.22 min (95.2%) (Chiracel AD, 6.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: [α]_D²⁴ -25.2 (*c* = 1.40, EtOH)

MS: (EI, 70 eV)

250 (100), 195 (5), 155 (45)

Analysis: C₁₀H₁₅NO₃ (197.23)

Calcd: C, 60.90; H, 7.67; N, 7.10%

Found: C, 60.77; H, 7.64; N, 7.12%

***N*-tert-Butyl-2-hydroxy-3-(1-(4-methylphenyl)sulfonyl-1H-indole)acetamide ((±)-**5o**)**

Following General Procedure I, a mixture of indole-3-carboxaldehyde **3o** (300 mg, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), SiCl₄ (125 μL, *d* = 1.483, 1.1 mmol, 1.1 equiv), and *tert*-butyl isocyanide (125 μL, *d* = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ was stirred for 4 h at −74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, *R_f* 0.25, hexane/EtOAc, 2/1), 320 mg (80%) of (±)-**5o** was obtained as a white solid. White crystals of (±)-**5o** (260 mg, 65%) were obtained after recrystallization from a 1/1 mixture of heptane and benzene.

Data for (±)-**5o**:

mp: 191–192 °C (heptane/benzene, 1/1)

SFC: (*R*)-**5o**, *t_R* 5.12 min (50.3%); (*S*)-**5o**, *t_R* 6.05 min (49.7%) (Chiracel AD, 6.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min^{−1})

Following General Procedure II, a solution of *tert*-butyl isocyanide (125 μL, *d* = 0.735, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of indole-3-carboxaldehyde **3o** (300 mg, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μL, *d* = 1.483, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μL, *d* = 0.742, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at −74 °C over 4 h. The mixture was stirred further for 4 h at −74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, *R_f* 0.29, hexane/EtOAc, 2/1), 323 mg (81%) of (*S*)-**5o** was obtained as a white solid. An analytically pure sample was obtained after sublimation (200 °C/0.5 mm Hg).

Data for (S)-(-)-5o:

mp: 191-193°C (sublimed)

¹H NMR: (400 MHz, CDCl₃)

7.97 (d, $J = 8.5$, 1 H, HC(4')); 7.79 (d, $J = 8.6$, 1 H, HC(3''')); 7.64 (s, 1 H, HC(2')); 7.56 (d, $J = 8.6$, 1 H, HC(7')); 7.33 (dd, $J = 8.2, 1.0$, 1 H, HC(6')); 7.22 (d, $J = 8.0$, 1 H, HC(5')); 7.21 (dd, $J = 8.0, 1.0$, 1 H, HC(5')); 5.69 (bs, 1 H, NH); 5.12 (d, $J = 3.2$, 1 H, HC(2)); 3.85 (d, $J = 3.4$, 1 H, OH); 2.36 (s, 3 H, H₃C(5''')); 1.29 (s, 9 H, 3 X H₃C(2''))

¹³C NMR: (100 MHz, CDCl₃)

170.3 (C(1)), 145.2 (C(8')), 135.5 (C(3') or C(1''')), 134.9 (C(3') or C(1''')), 130.0, 128.1, 126.9, 125.4, 125.2, 123.6, 120.6, 120.4, 113.6, 67.2 (C(2)), 51.8 (C(1')), 28.5 (C(5''')), 21.6 (C(2''))

IR: (CHCl₃)

3683 (m), 3604 (w), 3415 (m), 3020 (s), 2979 (m), 2935 (w), 2873 (w), 1681 (s), 1581 (w), 1525 (s), 1477 (m), 1456 (m), 1423 (m), 1367 (m), 1216 (s), 1149 (m), 1068 (w), 1012 (m), 929 (m)

TLC: R_f 0.25 (hexane/EtOAc, 2/1)

SFC: (R)-5o, t_R 4.92 min (3.1%); (S)-5o, t_R 5.79 min (96.9%) (Chiracel AD, 5.5% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24} -17.3$ ($c = 0.59$, EtOH)

MS: (FI, 70 eV)

400 (100), 300 (15)

Analysis: C₂₁H₂₄N₂O₄S (400.49)

Calcd: C, 62.98; H, 6.04; N, 6.99%

Found: C, 63.03; H, 5.90; N, 6.97%

***N*-(1,1,3,3,-Tetramethylbutyl)-2-hydroxy-4-phenylbutamide ((±)-6)**

Following General Procedure I, 1,1,3,3-tetramethylbutyl isocyanide (210 μ L, $d = 0.799$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of hydrocinnamaldehyde **3j** (132 μ L, $d = 1.019$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), and SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 8 h. The mixture was stirred further for 8 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.27, hexane/EtOAc, 4/1), 244 mg (84%) of (±)-**6** was obtained as colorless oil. Bulb-to-bulb distillation provided 240 mg (82%) of analytically pure (±)-**6**.

Data for (±)-6:

bp: 200°C ABT (0.5 mm Hg)

¹H NMR: (400 MHz, CDCl₃)

7.20-7.31 (m, 5 H, aryl); 6.22 (bs, 1 H, NH); 3.96-4.00 (m, 1 H, HC(2)); 2.60-2.79 (m, 2 H, H₂C(4)); 2.61 (dd, $J = 5.1$, 1 H, OH); 1.86-2.19 (m, 2 H, H₂C(3)); 1.73 (s, 2 H, H₂C(2'')); 1.42 (s, 6 H, 2 X H₃C(5'')); 1.00 (s, 9 H, 3 X H₃C(4''))

¹³C NMR: (100 MHz, CDCl₃)

172.3 (C(1)), 141.3 (C(1')), 128.5 (C(3') and C(4')), 126.0 (C(2')), 71.7 (C(2)), 55.0 (C(1'')), 52.1 (C(3'')), 36.5 (C(4)), 31.6 (C(3)), 31.5 (C(2'')), 31.4 (C(5'')), 29.0 (C(5'')), 28.9 (C(4''))

IR: (CHCl₃)

3622 (m), 3397 (s), 2992 (s), 2958 (s), 2871 (s), 1658 (s), 1602 (s), 1529 (s), 1496 (s), 1479 (s), 1454 (s), 1388 (m), 1367 (s), 1155 (m), 1095 (m), 827 (m)

TLC: R_f 0.27 (hexane/EtOAc, 4/1)

SFC: (*R*)-**6**, t_R 1.52 min (50.0%); (*R*)-**6**, t_R 1.84 min (50.0%) (Chiracel AD, 15.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

MS: (EI, 70 eV)
292 (2), 291 (6), 220 (34), 187 (40), 180 (16), 114 (11), 58 (100)

Analysis: C₁₈H₂₉NO₂ (291.43)

Calcd: C, 74.18; H, 10.03; N, 4.81%

Found: C, 74.44; H, 10.12; N, 5.01%

Following General Procedure II, a solution of 1,1,3,3-tetramethylbutyl isocyanide (210 μ L, $d = 0.799$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of hydrocinnamaldehyde **3m** (132 μ L, $d = 1.019$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv) and SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 8 h. The mixture was stirred for 8 h further at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.27, hexane/EtOAc, 4/1), 252 mg (87%) of (*S*)-**6** was obtained as colorless oil. Bulb-to-bulb distillation provided 244 mg (84%) of analytically pure (*S*)-**6** (200 °C/ 0.5 mm Hg).

Data for (S)-(-)-6:

SFC: (R)-**6**, t_R 1.56 min (30.0%); (S)-**6**, t_R 1.87 min (70.0%) (Chiracel AD, 15.0% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Opt. Rot.: $[\alpha]_D^{24}$ -12.5 (c = 3.1, MeOH)

Analysis: C₁₈H₂₉NO₂ (291.43)

Calcd: C, 74.18; H, 10.03; N, 4.81%

Found: C, 74.00; H, 10.21; N, 4.97%

N-Phenyl-2-hydroxy-2-phenylacetamide ((±)-7)

Following General Procedure I, a mixture of phenyl isocyanide **2c** (122 mg, 1.2 mmol), benzaldehyde (104 μ L, d = 1.044, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), and SiCl₄ (125 μ L, d = 1.483, 1.1 mmol, 1.1 equiv) was stirred for 4 h at -74 °C. After work-up and silica gel chromatography (20 mm column, 60 g SiO₂, R_f 0.37, hexane/EtOAc, 1/1), 173 mg (76%) of (±)-**7** was obtained as a white solid. An analytically pure sample was obtained after recrystallization from benzene.

Data for (±)-7:

mp: 148-149 °C (benzene)

SFC: (S)-**7**, t_R 5.35 min (49.9%); (R)-**7**, t_R 6.49 min (50.7%) (Chiracel AD, 10% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹)

Following General Procedure II, phenyl isocyanide **2c** (122 mg, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of benzaldehyde (104 μ L, d = 1.044, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, d = 1.483,

1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH_2Cl_2 (1.0 mL) at -74°C over 4 h. The mixture was stirred further for 4 h at -74°C . After work-up and silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.37, hexane/EtOAc, 1/1), 186 mg (82%) of (*S*)-**7** was obtained as a white solid. An analytically pure sample was obtained after sublimation ($140^\circ\text{C}/0.5$ mm Hg).

Data for (*S*)-**7**:

mp: $147\text{--}149^\circ\text{C}$ (sublimed)

^1H NMR: (400 MHz, CDCl_3)

8.12 (bs, 1 H, NH); 7.10–7.53 (m, 10 H, aryl); 5.18 (d, $J = 3.4$, 1 H, HC(2)); 3.41 (d, $J = 3.4$, 1 H, OH)

TLC: R_f 0.37 (hexane/EtOAc, 1/1)

SFC: (*S*)-**7**, t_R 5.28 min (73.2%); (*R*)-**7**, t_R 6.43 min (26.9%) (Chiracel AD, 10% MeOH in CO_2 , 125 bar, 40°C , 3.0 mL min^{-1})

Opt. Rot.: $[\alpha]_D^{24} +2.4$ ($c = 2.43$, EtOH with 5% aq. HCl)

Analysis: $\text{C}_{14}\text{H}_{13}\text{NO}_2$ (227.26)

Calcd: C, 73.99; H, 5.77; N, 6.16%

Found: C, 73.86; H, 5.76; N, 6.20%

(2-Hydroxy-2-phenyl-acetyl-amino)acetic Acid Ethyl Ester (($\pm$)-8**)**

Ethyl isocyanoacetate **2d** (135 μ L, $d = 1.150$, 1.2 mmol, 1.2 equiv) was added in one portion to a solution of benzaldehyde (104 μ L, $d = 1.044$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), and SiCl_4 (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH_2Cl_2 (5.0 mL) at -74°C . The mixture was stirred at -74°C for 24 h and then was quenched by pouring into an

ice-cold, saturated aqueous solution of NaHCO_3 (20 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted with CH_2Cl_2 (4 X 20 mL). The combined organic layers were dried (MgSO_4) and concentrated under reduced pressure. After silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.32, hexane/EtOAc, 1/2), 171 mg (72%) of ($\pm$)-**8** was obtained as a white solid. White crystals of ($\pm$)-**8** (104 mg, 44%) were obtained after recrystallization from a 1/1 mixture of heptane and benzene.

Data for ($\pm$)-**8**:

mp: 97-99°C (heptane/benzene, 1/1)

^1H NMR: (400 MHz, CDCl_3)

7.33-7.49 (m, 5 H, aryl); 6.73 (bs, 1 H, NH); 5.11 (s, 1 H, HC(2)); 4.19 (q, J = 8.1, 2 H, $\text{H}_2\text{C}(2')$); 4.03 (qd, J = 18.4, 5.7, 2 H, $\text{H}_2\text{C}(1')$); 3.51 (bs, 1 H, OH); 1.26 (t, J = 7.1, 3 H, $\text{H}_3\text{C}(3')$)

TLC: R_f 0.32 (hexane/EtOAc, 1/2)

SFC: (*R*)-**8**, t_R 3.87 min (49.9%); (*R*)-**8**, t_R 4.95 min (50.1%) (Chiracel AD, 15% MeOH in CO_2 , 125 bar, 40 °C, 3.0 mL min $^{-1}$)

Ethyl isocyanoacetate **2c** (135 μL , d = 1.15, 1.2 mmol, 1.2 equiv) was added in one portion to a solution of benzaldehyde (104 μL , d = 1.044, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), and SiCl_4 (125 μL , d = 1.483, 1.1 mmol, 1.1 equiv) in CH_2Cl_2 (5.0 mL) at -74 °C. The mixture was stirred at -74 °C for 24 h and then was quenched by pouring into an ice-cold, saturated aqueous solution of NaHCO_3 (20 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted by CH_2Cl_2 (4 X 20 mL). The combined organic layers were dried (MgSO_4) and concentrated under reduced pressure. The product **8** (197 mg, 83%) was obtained as an off-white solid after silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.32, hexane/EtOAc, 1/2). White crystals of **8** (154 mg, 65%) were obtained after re-crystallization from a 1/1 mixture of benzene and heptane.

Data for (+)-**8**:

mp: 80-82°C (heptane/benzene, 1/1)

SFC: (*R*)-**8**, t_R 3.87 min (16.7%); (*S*)-**8**, t_R 4.95 min (83.3%) (Chiracel AD, 15% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹) (before recrystallization)

SFC: (*R*)-**8**, t_R 3.77 min (19.2%); (*S*)-**8**, t_R 4.85 min (80.8%) (Chiracel AD, 15% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min⁻¹) (after recrystallization)

Opt. Rot.: $[\alpha]_D^{24} +18.6$ ($c = 1.07$, MeOH)

Analysis: C₁₄H₁₃NO₂ (237.25)

Calcd: C, 60.75; H, 6.37; N, 5.90%

Found: C, 60.38; H, 6.33; N, 5.90%

Ethyl (2-Hydroxy-2-phenyl-acetyl-amino)-3-hydroxy-3-phenyl)propionate (**13**)

Ethyl isocyanoacetate **2d** (1.35 mL, $d = 1.15$, 12.0 mmol, 1.2 equiv) was added in one portion to a solution of benzaldehyde (1.04 mL, $d = 1.044$, 10.0 mmol), pyridine *N*-oxide (94 mg, 1.0 mmol, 0.1 equiv), diisopropylethylamine (180 μ L, $d = 0.742$, 1.0 mmol, 0.1 equiv) and SiCl₄ (1.25 mL, $d = 1.483$, 11.0 mmol, 1.1 equiv) in CH₂Cl₂ (50.0 mL) at -74 °C. The mixture was stirred at -74 °C for 24 h and then was quenched by pouring into an ice-cold, saturated aqueous solution of NaHCO₃ (200 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted with CH₂Cl₂ (3 X 100 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. The brownish oily residue (2.72 g) was dissolved in CH₂Cl₂ (20 mL) and was loaded onto a column (40 mm) packed with silica gel (250 g). The products were eluted by solvent gradient mixtures as follows: hexane/EtOAc, 5/1, 600 mL; hexane/EtOAc, 1/1, 800 mL; hexane/EtOAc, 1/2, 600 mL; EtOAc, 600 mL. Eighty-five fractions (85 X 30mL) were collected. Fractions 44-53 were combined and concentrated to provide a brown-colored oily

residue (447 mg), which was a mixture of ($\pm$)-**8** and **13**. The by-product **13** (178 mg, 10%) was obtained as a light yellow, wax-like solid after purification by column chromatography (30 mm, 120 g SiO₂, hexane/EtOAc, 1/1), along with an additional 250 mg of the product ($\pm$)-**8**. Fractions 54-64 were combined and concentrated to provide a light-brown-colored, foam-like product ($\pm$)-**8** (1.03 g). Fractions 68-74 were combined and concentrated to provide a brownish residue (244 mg), which contained mixture of unidentified by-products.

Data for **13**:

¹H NMR: (300 MHz, CDCl₃)

7.22-7.38 (m, 9 H, aryl); 7.07-7.18 (m, 2 H, aryl and NH(exchangable)); 5.22 (dd, $J = 4.7, 4.3$, 1 H, HC(3)); 5.06 (d, $J = 3.0$, 1 H, C(2')); 4.90 (dd, $J = 3.8, 3.7$, 1 H, HC(2)); 4.33 (d, $J = 4.9$, 1 H, HOC(3) (exchangable)); 4.15 (q, $J = 7.0$, 2 H, H₂C(1'')); 3.46 (d, $J = 3.6$, 1 H, HOC(2') (exchangable)); 1.19 (t, $J = 7.0$, 3 H, H₃C(2''))

¹³C NMR: (75 MHz, CDCl₃)

173.6 (C(1)), 169.3 (C(1')), 138.7, 128.9, 128.4, 128.1, 127.8, 126.6, 125.8, 125.2, 74.4 (C(2')), 74.0 C(3)), 61.8 (C(1'')), 58.6 (C(2)), 13.7 (C(2''))

IR: (KBr)

3406 (s), 2890 (m), 1752 (s), 1665 (s), 1531 (s), 1460 (m), 1378 (m), 1219 (s), 1071 (m)

TLC: R_f 0.28 (hexane/EtOAc, 1/1)

HRMS: C₁₉H₂₂NO₅

Calcd: 344.1498 (M + H⁺)

Found: 344.1497

***N*-(Tosylmethyl)-2-hydroxy-4-phenylbutamide ((±)-9)**

Tosylmethyl isocyanide **2e** (235 mg, 1.2 mmol, 1.2 equiv) was added in one portion to a solution of benzaldehyde (104 μL , $d = 1.044$, 1.0 mmol), pyridine *N*-oxide (9.5 mg, 0.1 mmol, 0.1 equiv), and SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH_2Cl_2 (5.0 mL) at -74°C . The mixture was stirred at -74°C for 24 h and then was quenched by pouring into an ice-cold, saturated aqueous solution of NaHCO_3 (20 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted with CH_2Cl_2 (4 X 20 mL). The combined organic layers were dried (MgSO_4) and concentrated under reduced pressure. The product ($\pm$)-**9** (220 mg, 69%) was obtained as a fluffy white solid after silica gel chromatography (20 mm column, 60 g SiO_2 , R_f 0.36, hexane/EtOAc, 1/2). White crystals of ($\pm$)-**9** (190 mg, 60%) were obtained after recrystallization from a 1/1 mixture of heptane and benzene.

Data for ($\pm$)-**9**:

mp: $118\text{--}119^\circ\text{C}$ (heptane/benzene, 1/1)

SFC: (*R*)-**17**, t_R 4.87 min (49.9%); (*S*)-**17**, t_R 6.10 min (50.1%) (Chiracel AD, 15% MeOH in CO_2 , 125 bar, 40°C , 3.0 mL min^{-1})

Tosylmethyl isocyanide **2e** (235 mg, 1.2 mmol, 1.2 equiv) was added in one portion to a solution of benzaldehyde (104 μL , $d = 1.044$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), and SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv) in CH_2Cl_2 (5.0 mL) at -74°C . The mixture was stirred at -74°C for 24 h and then was quenched by pouring into an ice-cold, saturated aqueous solution of NaHCO_3 (20 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted with CH_2Cl_2 (4 X 20 mL). The combined organic layers were dried (MgSO_4) and concentrated under

reduced pressure. The product **9** (255 mg, 80%) was obtained as a white solid after silica gel chromatography (20 mm column, 60 g SiO₂, *R_f* 0.36, hexane/EtOAc, 1/2). White crystals of **9** (211 mg, 66%) were obtained after recrystallization from a 1/1 mixture of benzene and heptane.

Data for (–)-**9**:

mp: 117–119 °C (heptane/benzene, 1/1)

¹H NMR: (400 MHz, CDCl₃)

7.60 (d, *J* = 8.1, 2 H, HC(2'')); 7.15–7.38 (m, 5 H, aryl); 7.18 (d, *J* = 8.1, 2 H, HC(3'')); 7.15 (bs, 1 H, NH); 5.01 (d, t, *J* = 3.4, 1 H, HC(2)); 4.56–4.77 (m, 2 H, H₂C(1'')); 3.03 (bs, 1 H, OH); 2.39 (s, 3 H, H_cC(5''))

¹³C NMR: (100 MHz, CDCl₃)

171.8 (C(1)), 145.6 (C(1')), 138.5, 138.6, 130.1, 129.1, 129.1, 128.9, 126.8, 74.4 (C(2)), 60.1 (CH₂Tos), 22.0 (Me(C(4''))

IR: (CHCl₃)

3622 (m), 3397 (s), 2992 (s), 2958 (s), 2871 (s), 1658 (s), 1602 (s), 1529 (s), 1496 (s), 1479 (s), 1454 (s), 1388 (m), 1367 (s), 1155 (m), 1095 (m), 827 (m)

TLC: *R_f* 0.36 (hexane/EtOAc, 1/2)

SFC: (*R*)-**9**, *t_R* 4.87 min (11.5%); (*S*)-**9**, *t_R* 6.10 min (88.5%) (Chiracel AD, 15% MeOH in CO₂, 125 bar, 40 °C, 3.0 mL min^{–1})

MS: (FI, 70 eV)

320 (50), 319 (100)

Opt. Rot.: [α]_D²⁴ –2.21 (*c* = 0.73, MeOH)

Analysis: C₁₆H₁₇NO₄S (319.38)

Calcd: C, 60.17; H, 5.37; N, 4.39%

Found: C, 59.90; H, 5.27; N, 4.38%

2-Hydroxy-1,2-diphenylethanone (14a)⁸ and *N*-(*p*-toluenesulfonylmethyl)formamide 14b^{9a,b}

Tosylmethyl isocyanide **2e** (1.95 g, 10.0 mmol, 1.0 equiv) was added in one portion to a solution of benzaldehyde (1.04 mL, $d = 1.044$, 10.0 mmol), pyridine *N*-oxide (95 mg, 1.0 mmol, 0.1 equiv), diisopropylethylamine (180 μ L, $d = 0.742$, 1.0 mmol, 0.1 equiv) and SiCl_4 (1.25 mL, $d = 1.483$, 11.0 mmol, 1.1 equiv) in CH_2Cl_2 (50.0 mL) at -74°C . The resulting milky mixture was stirred at -74°C for 24 h and then was poured into an ice-cold, saturated aqueous solution of NaHCO_3 (200 mL) with vigorous stirring. After being stirred for 2 h at rt, the white precipitate was filtered off through Celite and the filtrate was extracted with CH_2Cl_2 (3 X 100 mL) and the extracts were concentrated in vacuo. The brownish solid residue (3.22 g) was dissolved in CH_2Cl_2 (20 mL) and was loaded onto a column (40 mm) packed with silica gel (250 g). The products were eluted by solvent gradient mixtures as follows: hexane/EtOAc, 5/1, 600 mL; hexanes/EtOAc, 1/1, 800 mL; hexane/EtOAc, 1/2, 600 mL; EtOAc, 600 mL. Eighty-five fractions (85 X 30mL) were collected. Fractions 19-25 were combined and concentrated to provide a light-brown-colored solid (137 mg), which was repurified by a second chromatography (20 mm, 60 g SiO_2 , hexane/EtOAc, 5/1) to afford the product **14a** (116 mg, 9%) as a light-yellow solid. Recrystallization of **14a** from toluene afforded colorless crystals (mp $133\text{--}134^\circ\text{C}$; lit.⁸, mp 137°C).

Fractions 58-71 were combined and concentrated to provide product ($\pm$)-**9** (2.04 g, 64%, hexane/EtOAc, 1/2) as a light-brown oil, which solidified upon standing at rt. Fractions 72-77 were combined and concentrated to provide *N*-(*p*-toluenesulfonylmethyl)formamide **14b** (135 mg, 7%) as a light-brown solid. Recrystallization of **14b** from isopropyl alcohol afforded white crystals (mp. $108\text{--}110^\circ\text{C}$; lit.^{9a}, mp $104\text{--}107^\circ\text{C}$; lit.^{9b}, mp $106\text{--}110^\circ\text{C}$).

Data for 14a:

mp: 133-134°C (toluene)

¹H NMR: (300 MHz, CD₃CN)

7.88-8.01 (m, 2 H, aryl and HC(3)); 7.49-7.63 (m, 1 H, aryl); 7.39-7.49 (m, 2 H, aryl); 6.06 (d, *J* = 5.9, 1 H, HC(1')); 4.47 (d, *J* = 6.2, 1 H, HOC(1')) (exchangeable))

¹³C NMR: (75 MHz, CDCl₃)

198.9 (C(2)), 138.9, 133.9, 133.4, 129.11, 129.0, 128.7, 128.6, 128.2, 127.7, 125.3, 76.2 (C(1'))

¹³C NMR: (75 MHz, CDCl₃, DEPT90)

133.9, 129.1, 129.0, 128.7, 128.6, 128.2, 127.7, 76.2 (C(1'))

IR: (KBr)

3416 (m), 3375 (s), 2934 (s), 1685 (s), 1598 (s), 1460 (s), 1271 (s), 1210 (s), 978 (s), 763(s)

TLC: *R_f* 0.31 (hexane/EtOAc, 5/1)

HRMS: C₁₄H₁₂O₂

Calcd: 212.0837 (M⁺)

Found: 212.0831

Data for 14b:

mp: 108-110°C (isopropyl alcohol)

¹H NMR: (300 MHz, CDCl₃)

8.09 (s, 1 H, CHO); 7.80 (d, *J* = 8.5, 2 H, aryl); 7.36 (d, *J* = 8.1, 2 H, aryl); 6.69 (bs, 1 H, NH); 4.72 (d, *J* = 6.0, 2 H, H₂C(1)); 2.45 (s, 3 H, H₃C)

TLC: *R_f* 0.27 (hexane/EtOAc, 1/2)

General Procedure III. Conversion of Imidoyl Chlorides to Methyl Esters

A. A solution of *tert*-butyl isocyanide (1.2 equiv, 1.0 M in CH₂Cl₂) was added to a solution of an aldehyde (1.0 M in CH₂Cl₂ based on aldehyde), catalyst (*R,R*)-**1b** (0.05 equiv), SiCl₄ (1.1 equiv), diisopropylethylamine (0.1 equiv) at -74°C over the indicated time by syringe pump. After being stirred further for the indicated time, dry MeOH (2.5 mL) was added dropwise to the reaction mixture at -74°C . After being stirred for 40 min at -74°C , the mixture was transferred dropwise to a vigorously stirred, ice-cold, saturated aqueous solution of NaHCO₃ (20 mL) and stirred for 2 h further at rt. The white precipitate was filtered off through Celite and the filtrate was extracted with CH₂Cl₂ (4 x 20 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. The catalyst was separated from the product by silica gel column chromatography (hexane/EtOAc).

B. A solution of *tert*-butyl isocyanide (1.2 equiv, 1.0 M in CH₂Cl₂) was added to a solution of an aldehyde (1.0 M in CH₂Cl₂ based on aldehyde), pyridine-*N*-oxide (0.1 equiv), SiCl₄ (1.1 equiv) at -74°C over 30 min via a syringe pump. After being stirred further for the indicated time, dry MeOH (2.5 mL) was added dropwise to the reaction mixture at -74°C . After being stirred for 40 min at -74°C , the mixture was transferred dropwise to a Vigorously stirred, ice-cold, saturated aqueous solution of NaHCO₃ (20 mL) and stirred for 2 h further at rt. The white precipitate was filtered off through Celite and the filtrate was extracted with CH₂Cl₂ (4 x 20 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. Pyridine-*N*-oxide was separated from the product by silica gel column chromatography (hexane/EtOAc).

(S)-(+)-Methyl-2-Hydroxy-2-phenylacetate ((S)-10)

Following General Procedure III A, a solution of *tert*-butyl isocyanide (125 μL , $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added via a syringe pump to the cold solution of benzaldehyde (104 μL , $d = 1.044$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl_4 (125 μL , $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μL , $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH_2Cl_2 (1.0 mL) at -74°C over 4 h. The mixture was stirred for 4 h at -74°C . Work-up with the methanol quench provided 160 mg (97%) of (*S*)-**10** after silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.31, hexane/EtOAc, 3/1), Bulb-to-bulb distillation provided 158 mg (95%) of (*S*)-**10** as colorless oil, which solidified upon standing. From the sign of optical rotation of the product ($[\alpha]_{\text{D}}^{24} +143.2$, MeOH), the absolute configuration was deduced to be *S* (lit.⁶, (*S*) enantiomer, $[\alpha]_{\text{D}}^{24} +144.0$, MeOH).

Data for (*S*)-(+)-**10**:mp: 56-58 $^\circ\text{C}$ bp: 120 $^\circ\text{C}$ (0.5 mm Hg) ^1H NMR: (400 MHz, CDCl_3)7.33-7.44 (m, 5 H, aryl); 5.18 (d, $J = 5.3$, 1 H, HC(2)); 3.77 (s, 3 H, OCH_3); 3.42 (d, $J = 4.7$, 1 H, OH)TLC: R_f 0.31 (hexane/EtOAc, 3/1)SFC: (*S*)-**10**, t_{R} 3.97 min (99.9%); (*R*)-**10**, t_{R} 4.31 min (0.1%) (Chiracel AS, 1.4% MeOH in CO_2 , 125 bar, 40 $^\circ\text{C}$, 2.5 mL min^{-1})Opt. Rot.: $[\alpha]_{\text{D}}^{24} +143.2$ ($c = 0.57$, MeOH)

Following General Procedure III B, a solution of *tert*-butyl isocyanide (63 μ L, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added via a syringe pump to the cold solution of benzaldehyde (52 μ L, $d = 1.044$, 0.5 mmol), pyridine-*N*-oxide (4.7 mg, 0.05 mmol, 0.1 equiv), SiCl_4 (63 μ L, $d = 1.483$, 0.55 mmol, 1.1 equiv) at -74°C over 30 min. The mixture was stirred for 4 h at -74°C . Work-up with the methanol quench provided 69 mg (83%) of ($\pm$)-**10** after silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.31, hexane/EtOAc, 3/1).

Data for ($\pm$)-**10**:

SFC: (*S*)-**10**, t_R 3.93 min (49.9%); (*R*)-**10**, t_R 4.31 min (50.1%) (Chiracel AS, 1.4% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min^{-1})

(2*S*,3*E*)-(+)-Methyl 2-Hydroxy-2-phenyl-3-butenolate ((*S*)-11**)**

Following General Procedure III A, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added via a syringe pump to the cold solution of *trans*-cinnamaldehyde **3g** (126 μ L, $d = 1.048$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl_4 (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH_2Cl_2 (1.0 mL) at -74°C over 4 h. The mixture was stirred for 4 h at -74°C . Work-up with the methanol quench provided 136 mg (71%) of **11** after silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.25, hexane/EtOAc, 3/1). Bulb-to-bulb distillation provided 132 mg (69%) of (*S*)-**11** as colorless oil. From the sign of optical rotation of the product ($[\alpha]_D^{24} +112.3$, MeOH), the absolute configuration was deduced to be *S* (lit.⁶, (*R*)/(*S*), 99.1/0.9, $[\alpha]_D^{24} -115.0$, MeOH).

Data for (*S*)-(+)-**11**:

bp: 140°C ABT (0.5 mm Hg)

$^1\text{H NMR}$: (400 MHz, CDCl_3)

7.23-7.37 (m, 5 H, aryl); 6.81 (d, $J = 15.9$, 1 H, HC(4)); 6.25 (dd, $J = 15.8$, 5.7, 1 H, HC(3)); 4.85 (d, $J = 5.6$, 1 H, HC(2)); 3.83 (s, 3 H, OCH₃); 3.35 (bs, 1 H, OH)

GC: (S)-**11**, t_R 37.92 min (97.9%); (R)-**11**, t_R 38.61 min (2.1%) (Chiraldex BPH, 93 °C, 20 psi)

Opt. Rot.: $[\alpha]_D^{24} +112.3$ ($c = 0.52$, MeOH)

Following General Procedure III B, a solution of *tert*-butyl isocyanide (63 μ L, $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH₂Cl₂ (0.5 mL) was added via a syringe pump to the cold solution of *trans*-cinnamaldehyde **3g** (63 μ L, $d = 1.048$, 0.5 mmol), pyridine-*N*-oxide (4.8 mg, 0.05 mmol, 0.1 equiv), SiCl₄ (63 μ L, $d = 1.483$, 0.55 mmol, 1.1 equiv) at -74 °C over 30 min. The mixture was stirred for 4 h at -74 °C. Work-up with the methanol quench provided 71mg (74%) of ($\pm$)-**11** after silica gel column chromatography (20 mm column, 60 g SiO₂, R_f 0.25, hexane/EtOAc, 3/1).

Data for ($\pm$)-**11**:

GC: (S)-**11**, t_R 37.80 min (49.4%); (R)-**11**, t_R 38.54 min (50.6%) (Chiraldex BPH, 93 °C, 20 psi)

(S)-(+)-Methyl 2-Hydroxy-4-phenylbutanoate (**12**)

Following General Procedure III A, a solution of *tert*-butyl isocyanide (125 μ L, $d = 0.735$, 1.2 mmol, 1.2 equiv) in CH₂Cl₂ (1.0 mL) was added via a syringe pump to a cold solution of hydrocinnamaldehyde (132 μ L, $d = 1.019$, 1.0 mmol), catalyst (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv), SiCl₄ (125 μ L, $d = 1.483$, 1.1 mmol, 1.1 equiv), and diisopropylethylamine (18 μ L, $d = 0.742$, 0.1 mmol, 0.1 equiv) in CH₂Cl₂ (1.0 mL) at -74 °C over 8 h. The mixture was stirred

for 8 h at $-74\text{ }^{\circ}\text{C}$. Work-up with a methanol quench provided 171 mg (88%) of **12** after silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.25, hexane/EtOAc, 3/1). Bulb-to-bulb distillation provided 170 mg (88%) of (*S*)-**12** as colorless oil. From the sign of optical rotation of the product ($[\alpha]_{\text{D}}^{24} +21.1$, CHCl_3), the absolute configuration was deduced to be *S* (lit.^{7a}, (*S*) enantiomer, $[\alpha]_{\text{D}}^{24} +32.4$, CHCl_3 ; lit.^{7b}, (*R*) enantiomer, $[\alpha]_{\text{D}}^{24} -32.5$, CHCl_3).

Data for (*S*)-(+)-**12**:

bp: $140\text{ }^{\circ}\text{C}$ ABT (0.5 mm Hg)

^1H NMR: (400 MHz, CDCl_3)

7.18-7.31 (m, 5 H, aryl); 4.19-4.21 (m, 1 H, $\text{H}(\text{C}(2))$); 3.76 (s, 3 H, OCH_3); 2.72-2.80 (m, 2 H, $\text{H}_2(\text{C}(4))$); 2.75 (s, 1 H, OH); 1.91-2.17 (m, 2 H, $\text{H}_2(\text{C}(3))$)

SFC: (*S*)-**12**, t_{R} 3.37 min (81.8%); (*R*)-**12**, t_{R} 3.69 min (18.2%) (Chiracel AS, 2.5% MeOH in CO_2 , 125 bar, $40\text{ }^{\circ}\text{C}$, 2.5 mL min^{-1})

Opt. Rot.: $[\alpha]_{\text{D}}^{24} +21.1$ ($c = 0.52$, CHCl_3)

Following General Procedure III B, a solution of *tert*-butyl isocyanide (63 μL , $d = 0.735$, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added via a syringe pump to the cold solution of hydrocinnamaldehyde (66 μL , $d = 1.019$, 0.5 mmol), pyridine-*N*-oxide (4.7 mg, 0.05 mmol, 0.1 equiv), SiCl_4 (63 μL , $d = 1.483$, 0.55 mmol, 1.1 equiv) at $-74\text{ }^{\circ}\text{C}$ over 8 h. The mixture was stirred for 8 h further at $-74\text{ }^{\circ}\text{C}$. Work-up with the methanol quench provided 81 mg (83%) of ($\pm$)-**12** after silica gel column chromatography (20 mm column, 60 g SiO_2 , R_f 0.28, hexane/EtOAc, 3/1).

Data for ($\pm$)-**12**:

SFC: (*S*)-**12**, t_{R} 3.39 min (50.5%); (*R*)-**12**, t_{R} 3.71 min (49.5%) (Chiracel AS, 2.5% MeOH in CO_2 , 125 bar, $40\text{ }^{\circ}\text{C}$, 2.5 mL min^{-1})

(S)-N-[(S)-1-Phenylethyl]mandelamide ((S,S)-15)

A solution of (*S*)-1-phenylethyl isocyanide (145 μ L, d = 0.909, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added via syringe to a solution of the mixture of benzaldehyde (105 μ L, d = 1.02, 1.0 mmol), SiCl_4 (125 μ L, d = 1.483, 1.2 mmol, 1.2 equiv), (*R,R*)-**1b** (43 mg, 0.05 mmol, 0.05 equiv) and diisopropylethylamine (18 μ L, d = 0.742, 0.1 mmol, 0.1 equiv) in CH_2Cl_2 (1.0 mL) over 4 h at -74°C . The mixture was further stirred for 4 h at -74°C before it was poured into a sat. aq. NaHCO_3 solution (20 mL). The mixture was further stirred for 2 h at rt and the white precipitate was filtered off through Celite. The filtrate was extracted with CH_2Cl_2 (4 X 20 mL). The combined organic layers were dried (MgSO_4) and concentrated under reduced pressure. A small amount of the residue was used to determine the ratio of (*S*)-*N*-[(*S*)-1-phenylethyl]mandelamide and (*R*)-*N*-[(*S*)-1-phenylethyl]mandelamide. The major portion of the residue was purified by silica gel chromatography (10 mm column, 60 g SiO_2) to provide the products (*1S,2S*)-**15** (195 mg, 77%, R_f 0.17, hexane/EtOAc 3/1) and (*1S,2R*)-**15** (11.2 mg, 5%, R_f 0.10, hexane/EtOAc 3/1) as white solid. According to the sign of optical rotation ($[\alpha]_{\text{D}}^{24}$ -3.3 , CHCl_3), the absolute configuration of the newly generated stereocenter in the major product was deduced to be (*S*) (lit.⁴, (*1R,2R*)-**15**, $[\alpha]_{\text{D}}^{24}$ $+3.5$, CHCl_3). The ^1H NMR spectrum of the minor product matches with that of (*1R,2S*)-**15** reported in the literature⁴ and accordingly it was assigned as (*1S,2R*)-**15**.

Data for 15:

SFC: (*1S,2S*)-**15**, t_{R} 4.18 min (Chiracel AD, 15.0% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min⁻¹)

SFC: (*1S,2R*)-**15**, t_{R} 2.86 min (Chiracel AD, 15.0% MeOH in CO_2 , 125 bar, 40°C , 2.5 mL min⁻¹)

SFC: (1*S*,2*R*)-**15**, t_R 2.91 min (9.3%); (1*S*,2*S*)-**15**, t_R 4.24 min (90.7%) (Chiracel AD, 15.0% MeOH in CO₂, 125 bar, 40 °C, 2.5 mL min⁻¹) (the reaction mixture before column chromatography)

Opt. Rot.: $[\alpha]_D^{24}$ -3.3 (c = 0.72, CHCl₃) ((1*S*,2*S*)-**15**)

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