*Supplementary Information***The Role of Non-Covalent Interactions in the Enantioselective Reduction of Aromatic Ketimines with Trichlorosilane**

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Scheme S1. Catalyst Synthesis

Experimental Section

General Methods. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were recorded in CHCl_3 at 25 °C unless otherwise indicated, with an error of $\leq \pm 0.1$. The $[\alpha]_D$ values are given in $10^{-1} \text{ deg cm}^3 \text{ g}^{-1}$. The NMR spectra were recorded in CDCl_3 , ^1H at 400 MHz and ^{13}C at 100.6 MHz with chloroform- d_1 (δ 7.26, ^1H ; δ 77.0, ^{13}C) as internal standard unless otherwise indicated. Various 2D-techniques and DEPT experiments were used to establish the structures and to assign the signals. The IR spectra were recorded for CHCl_3 solutions unless otherwise indicated. The mass spectra (EI and/or CI) were measured on a dual sector mass spectrometer using direct inlet and the lowest temperature enabling evaporation. All reactions were performed under an atmosphere of dry, oxygen-free nitrogen in oven-dried glassware, twice evacuated and filled with inert gas. Solvents and solutions were transferred by syringe-septum and cannula techniques. All solvents for the reactions were of reagent grade and were dried and distilled immediately before use (dichloromethane from calcium hydride). Petroleum ether refers to the fraction boiling in the range of 60-80 °C. Yields are given for isolated products showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. The identity of the products prepared by different methods was checked by comparison of their NMR, IR, and MS data and by the TLC behavior. The chiral GC and HPLC methods were calibrated with the corresponding racemic mixtures. The imines **1a**,^{S1,S2} **1b**,^{S1} **1d**,^{S3} **1e**,^{S1} **1f**,^{S1,S4} **1g**,^{S5} **1h**,^{S5} **1i**,^{S6} **1j**,^{S7} **1k**,^{S1} and **1l**^{S4} are known compounds and were prepared according to the procedure shown for **1c**, the only new member of this series. Amines **2a**,^{S8} **2b**,^{S1} **2c**,^{S9} **2d**,^{S10} **2e**,^{S8} **2f**,^{S4} **2g**,^{S5} **2h**,^{S11} **2i**,^{S12} **2j**,^{S2} **2k**,^{S1,S2} and **2l**^{S4,S10} are all known compounds and their absolute configuration was established in reference to the literature data.

Imine 1c. A mixture of NaHCO_3 (2.2 g, 26 mmol), aniline (0.48 mL, 5.3 mmol), *p*-trifluoromethylacetophenone (1.0 g, 5.3 mmol), and activated molecular sieves (4 g, 4 Å) in anhydrous toluene (5 mL) was heated at 80 °C for 12 h under an argon atmosphere.

The mixture was filtered through celite and the celite was washed with CH₂Cl₂. The filtrate was evaporated in vacuo and the product was crystallized from petroleum ether at 5 °C to give pure **1c** (0.67 g, 48%): mp 74-77 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.17 (s, 3H), 6.71 (d, *J* = 8.0 Hz, 2H), 7.03 (t, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 8.0, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.99 (d *J* = 8.2, 2H); ¹³C NMR δ 17.80 (CH₃), 119.57 (CH), 124.04 (CH), 125.72 (CH), 127.92 (CH), 129.44 (CH), 132.31 (CF₃), 143 (C), 151.51 (C), 164.69 (C); IR (NaCl) ν 1643 cm⁻¹; MS *m/z* (%) 263 (M⁺, 61%) 248 (100), 244 (7), 152 (4), 181 (16), 77 (71); HRMS (EI): 263.0922 (C₁₅H₁₂N₂F₃ requires 263.0921).

General Procedure for the Catalytic Hydrosilylation of Imines **1a-k**.

Trichlorosilane (77 μL, 0.77 mmol) was added dropwise to a stirred solution of the imine **1a-k** (0.51 mmol) and the catalyst (0.051 mmol) and in anhydrous CH₂Cl₂ (or CHCl₃ or MeCN; see Tables 1-2) at 0 °C (or at -20 °C), and the mixture was allowed to stir overnight at room temperature (or at -20 °C) under an argon atmosphere. The reaction was quenched with a saturated solution of NaHCO₃ (10 mL) and the product was extracted with ethyl acetate (100 mL). The extract was washed with brine and dried over anhydrous MgSO₄ and the solvent was evaporated. Purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (24:1) afforded the product as an oil. The yields and ee are given in Table 1 and 2.

(S)-(+)-2a. [α]_D +16.8 (*c* 0.5, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 1.41 (d, *J* = 7.1 Hz, 3H), 3.94 (br s, 1H), 4.41 (q, *J* = 6.7 Hz, 1H), 6.44 (d, *J* = 8.6 Hz, 2H), 6.57 (t, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 2H), 7.13 (t, *J* = 6.8 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 2H) in agreement with the literature data;^{S8} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 15:1 + 0.1% NEt₃, 0.5 mL/min) showed 92% ee (*t*_R = 15.1 min, *t*_S = 17.7 min).

(S)-(+)-2b. [α]_D +4.45 (*c* 0.5, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 1.38 (d, *J* = 7.2 Hz, 3H), 3.68 (s, 3H), 3.90 (br s, 1H), 4.35 (q, *J* = 6.6 Hz, 1H), 6.41 (d, *J* = 8.5 Hz, 2H), 6.55 (t, *J* = 7.31 Hz, 1H), 6.77 (d, *J* = 7.2 Hz, 2H), 6.97 (t, *J* = 6.5 Hz, 2H), 7.14 (d, *J* = 7.2 Hz, 2H) in agreement with the literature data;^{S1} chiral HPLC (Chiralcel OD-H,

hexane/2-propanol 15:1 + 0.1% NEt₃ 0.5 mL/min) showed 80% ee (t_R = 19.3 min, t_S = 22.7 min).

(S)-(+)-2c. $[\alpha]_D +20.0$ (c 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.46 (d, J = 7.1 Hz, 3H), 3.97 (br s, 1H), 4.46 (q, J = 6.7 Hz, 1H), 6.38 (d, J = 7.6 Hz, 2H), 6.59 (t, J = 7.4 Hz, 1H), 7.02 (t, J = 7.3 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.2 Hz, 2H) in agreement with the literature data;^{S9} chiral GC (Supelco β -DEX 120 column, oven: 125 °C for 2 min, then 1 °C/min to 200 °C, 10 min at that temperature) showed ee of 89% (t_S = 42.8 min, t_R = 43.2 min).

(S)-(+)-2d. $[\alpha]_D +20.0$ (c 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.47 (d, J = 7.1 Hz, 3H), 4.0 (br s, 1H), 4.49 (m, 1H), 6.38 (d, J = 8.6 Hz, 2H), 6.61 (t, J = 7.3 Hz, 1H), 7.0 (t, J = 7.3 Hz, 2H), 7.46 (d, J = 7.6 Hz, 2H), 8.11 (d, J = 7.4 Hz, 2H) in agreement with the literature data;^{S10} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 95:5, 1.00 mL/min) showed 86% ee (t_R = 24.6 min, t_S = 26.9 min).

(S)-(+)-2e. $[\alpha]_D +16.2$ (c 1.0, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 1.49 (d, J = 7.1 Hz, 3H), 4.03 (broad singlet, 1H), 4.54 (q, J = 6.7 Hz, 1H), 6.45 (d, J = 8.0 Hz, 2H), 6.56 (t, J = 7.5 Hz, 1H), 6.98 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.8 Hz, 2H), 7.36 (d, J = 7.2 Hz, 2H), 7.70 (s, 2H) in agreement with the literature data;^{S8} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 15:1 + 0.1% NEt₃, 0.5 mL/min) showed 88% ee (t_R = 18.7 min, t_S = 21.2 min).

(S)-(+)-2f. $[\alpha]_D +6.1$ (c 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.91-1.80 (m, 11H), 1.05 (d, J = 6.7 Hz, 3H), 3.2 (q, J = 8.0 Hz, 1H), 3.38 (br s, 1H), 6.49 (d, J = 8.0 Hz, 2H), 6.55 (t, J = 8.0 Hz, 1H), 7.07 (t, J = 10.0 Hz, 2H) in agreement with the literature data;^{S4} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 99:1, 0.75 mL/min) showed 37% ee (t_R = 8.2 min, t_S = 8.7 min).

(S)-(+)-2g. $[\alpha]_D +2.5$ (c 1.0, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 1.40 (d, J = 7.0 Hz, 3H), 3.60 (s, 3H), 4.32 (q, J = 6.4 Hz), 6.37 (d, J = 8.1 Hz, 2H), 6.61 (d, J = 7.6 Hz, 2H), 7.15 (t, J = 7.4 Hz, 1H), 7.22 (t, J = 7.4 Hz, 2H), 7.28 (d, J = 7.6 Hz, 2H) in agreement with the literature data;^{S5} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 99:1, 0.75 mL/min) showed 85% ee (t_R = 15.5 min, t_S = 18.6 min).

(S)-(+)-2h. $[\alpha]_D +9.2$ (c 0.5, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 1.44 (d, J = 7.1 Hz, 3H), 3.80 (s, 3H), 4.38 (q, J = 6.8 Hz, 1H), 4.54 (br s, 1H), 6.25 (d, J = 8.0 Hz, 1H), 6.52 (t, J = 6.9 Hz, 1H), 6.61 (t, J = 7.2 Hz, 1H), 6.69 (d, J = 7.1 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.24 (t, J = 7.2 Hz, 2H), 7.33 (d, J = 7.2 Hz, 2H) in agreement with the literature data;^{S11} chiral HPLC (Chiralcel OD-H, hexane/2-propanol 99:1, 0.75 mL/min) showed 22% ee (t_R = 7.1 min, t_S = 8.1 min).

(±)-2i. ^1H NMR (400 MHz, CDCl_3) δ 0.91-2.29 (m, 11H), 1.34 (d, J = 6.8 Hz, 3H), 3.93 (q, J = 6.8 Hz, 1H), 7.16-7.29 (m, 5H) in agreement with the literature data.^{S12} The racemic nature was confirmed by running the NMR spectrum in the presence of mandelic acid (2 equiv).

(±)-2j. ^1H NMR (400 MHz, CDCl_3) δ 0.79 (t, J = 7.3 Hz, 3H), 1.19 (m, 2H), 1.32 (d, J = 7.2 Hz, 3H), 1.36 (m, 2H), 2.40 (m, 2H), 3.73 (q, J = 6.6 Hz, 1H), 7.1-7.3 (arom, 5H) in agreement with the literature data.^{S2} The racemic nature was confirmed by running the NMR spectrum in the presence of mandelic acid (2 equiv).

2k. ^1H NMR (400 MHz, CDCl_3) δ 1.30 (d, J = 7.1 Hz, 3H), 2.13 (br s, 1H), 3.53 (m, 2H), 3.73 (q, J = 5.5 Hz, 1H), 7.1-7.3 (arom, 10H) in agreement with the literature data.^{S1,S2} The almost racemic nature was confirmed by running the NMR spectrum in the presence of mandelic acid (2 equiv).

(S)-2l. ^1H NMR (400 MHz, CDCl_3) δ 1.41 (d, J = 6.6 Hz, 3H), 2.36 (s, 3H), 3.93 (bs, 1H), 4.60 (q, J = 6.6 Hz, 1H), 6.36 (d, J = 8.6 Hz, 2H), 6.50 (t, J = 7.3 Hz, 1H), 6.94-7.46 (m, 6H).^{S4} For ee determination, the amine **2l** was converted to the acetyl derivative by heating at reflux with 3 eq. of acetyl chloride, 3 eq. of triethylamine and cat. DMAP in CHCl_3 for 30 min. Aqueous work up followed by purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (2:1) afforded the product as an oil. ^1H NMR (400 MHz, CDCl_3) δ 1.43 (d, J = 6.7 Hz, 3H), 1.69 (s, 3H), 2.48 (s, 3H), 6.27 (q, J = 6.8 Hz, 1H), 6.57 (d, J = 8.00 Hz, 1H), 6.82 (t, J = 7.6 Hz, 1H), 6.84-7.23 (m, 7H); chiral HPLC (Whelk-O1, hexane/2-propanol 91:9, 1.0 mL/min) showed 92% ee (t_S = 12.7 min, t_R = 14.5 min).

(S)-2-(tert-Butoxycarbonyl-methyl-amino)-3-methyl-butyric Acid (S)-(8).

Sodium hydride (60% dispersion in mineral oil; 3.0 g, 138 mmol) was added in small portions to a stirred solution of (S)-2-tert-butoxycarbonylamino-3-methyl-butyric acid (S)-6 (3.0 g, 13.8 mmol) and iodomethane (19.6 g, 138 mmol) in anhydrous THF (60 mL) to 0 °C. The mixture was allowed to stir at room temperature for 24 h under an argon atmosphere. The reaction was then quenched with water (15 mL), ethyl acetate (10 mL) and evaporated in vacuo. The concentrate was diluted in water (300 mL) and washed with ethyl acetate (150 mL). The aqueous solution was acidified to pH 3.5 with a solution of 5% citric acid and extracted with ethyl acetate (200 mL). The extract was washed with brine, dried over anhydrous MgSO₄, and evaporated *in vacuo* to give the (S)-8 as an oil (3.15 g, 13.6 mmol, 98%), which was used in the following step without further purification: ¹H NMR (400 MHz, CDCl₃) δ 0.93 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 1.49 (s, 9H), 2.39 (m, 1H), 2.90 (s, 3H), 4.01 (d, *J* = 10.4 Hz, 1H), in agreement with the literature.^{S13}

General Procedure for the Synthesis of Amides (S)-7a-d and 7f-h.

Methylchloroformate (0.55 mL, 7.15 mmol) was added dropwise to a stirred solution of (S)-8 (1.40 g, 6.05 mmol) and triethylamine (1.0 mL, 7.15 mmol) in anhydrous THF (30 mL) at 0 °C under an argon atmosphere and the mixture was stirred at that temperature for 2 h. The precipitate was removed by filtration in vacuo and the filtrate was added drop-wise to a solution of the corresponding amine (8.5 mmol) and triethylamine (1.0 mL, 7.15 mmol) in anhydrous THF (30 mL) at 0 °C. The mixture was allowed to stir at room temperature overnight under an argon atmosphere and the solvent was then removed under reduced pressure. The residue was purified using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (4:1) to afford (S)-7; the yields are given below.

(S)-7a (oil, 803 mg, 43%): ¹H NMR (400 MHz, CDCl₃) δ 0.85 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 1.43 (s, 9H), 2.32 (m, 1H), 2.75 (s, 3H), 4.03 (d, *J* = 10.2 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 8.19 (br s, 1H); ¹³C NMR δ 18.99 (CH₃), 20.30 (CH₃), 26.24 (CH₃), 28.76 (CH₃), 30.94 (CH₃), 66.70 (C), 81.10 (C), 120.06 (CH), 124.48 (CH), 129.37 (CH), 138.45 (C), 169.18

(CO); IR (Golden Gate) ν 3311 (NH), 1658 (CO); MS m/z (%) 306 (M^+ , 6%) 214 (7), 186 (14), 130 (71), 83 (100), 57 (39), 47 (17); HRMS (EI): 306.1943 ($C_{17}H_{26}O_3N_2$ requires 306.1943).

(S)-7b (oil, 188 mg, 59%): 1H NMR (400 MHz, $CDCl_3$) δ 0.81 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H), 1.37 (s, 9H), 2.27 (m, 1H), 2.77 (s, 3H), 3.66 (s, 3H), 4.07 (d, J = 10.9 Hz, 1H), 6.72 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H), 8.33 (br s, 1H); ^{13}C NMR δ 17.65 (CH_3), 18.79 (CH_3), 25.17 (CH), 27.33 (CH_3), 29.44 (CH_3), 64.76 (CH), 79.46 (CH), 113.02 (CH), 120.47 (CH), 130.27 (CH_3), 155.21 (C), 156.31 (C), 167.70 (C).

(S)-7c. Purification of the crude product using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (1:1) afforded **7c** as an oil (451 mg, 29%); 1H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H), 1.39 (s, 9H), 2.95 (m, 1H), 2.75 (s, 3H), 3.70 (s, 6H), 4.00 (m, 1H), 6.15 (s, 1H), 6.68 (s, 2H), 8.18 (br s, 1H).

(S)-7d. Purification of the crude product using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (24:1) afforded the product **7c** as an oil (240 mg, 70%); 1H NMR (400 MHz, $CDCl_3$) δ 0.77 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.5 Hz, 3H), 1.38 (s, 9H), 2.17 (s, 6H), 2.25 (m, 1H), 2.76 (s, 3H), 4.08 (d, J = 10.8 Hz, 1H), 6.62 (s, 1H), 7.07 (s, 2H), 8.24 (br s, 1H).

(S)-7f. Purification of the crude product using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (6:1) afforded **7c** as an oil (105 mg, 28%); 1H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H), 1.41 (s, 9H), 2.30 (m, 1H), 2.76 (s, 3H), 3.95 (d, J = 10.8 Hz, 1H), 7.00 (s, 1H), 7.41 (s, 2H), 8.51 (brs, 1H).

(S)-7g. Purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (3:1) afforded the product as an oil (928 mg, 61%): 1H NMR (400 MHz, $CDCl_3$) δ 0.80 (m, 9H), 1.29 (m, 2H), 1.39 (s, 9H), 2.20 (m, 1H), 2.73 (s, 3H), 3.17 (m, 2H), 3.90 (d, J = 10.9 Hz, 1H), 6.04 (br s, 1H).

(S)-7h. Purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (3:1) afforded **7g** as an oil (72 mg, 22%); 1H NMR (400 MHz, $CDCl_3$) δ 0.74 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H), 1.13 (s, 9H), 2.34 (m, 1H),

2.79 (s, 3H), 3.25 (s, 3H), 4.23 (d, $J = 10.8$ Hz, 1H), 7.11 (t, $J = 7.5$ Hz, 1H), 7.33 (t, $J = 7.7$ Hz, 2H), 7.41 (d, $J = 7.5$ Hz, 2H).

Amide (S)-7e. Following a literature protocol,^{S14} a solution of pivaloyl chloride (1.1 mL, 8.6 mmol) in anhydrous THF (8 mL) at -15 °C was added dropwise to a stirred solution of (S)-**8** (2.0 g, 8.6 mmol) and triethylamine (1.2 mL, 8.6 mmol) in anhydrous THF (16 mL). The solution was then warmed to 0 °C and allowed to stir at this temperature for 5 min. The solution was then again cooled to -15 °C and a solution of 3,5-bis(trifluoromethyl)-aniline (1.34 mL) in anhydrous THF (8 mL) was added dropwise and the mixture was allowed to stir at 0 °C for 1 h. The mixture was then warmed to room temperature and stirring was continued for 27 h under an argon atmosphere. The solvent was then removed under reduced pressure, the residue was diluted with water (20 mL) and then extracted with ethyl acetate (20 mL). The extracts were then washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. Purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (1:1) afforded deprotected (S)-**7e** as an oil (185 mg, 7%): ^1H NMR (400 MHz, CDCl_3) δ 0.87 (d, $J = 6.9$ Hz, 3H), 0.99 (d, $J = 7.0$ Hz, 3H), 2.15 (m, 1H), 2.42 (s, 3H), 2.87 (d, $J = 4.24$ Hz, 1H), 7.50 (s, 1H), 8.05 (s, 2H), 9.69 (br s, 1H).

General Procedure for the Synthesis of Formamides (S)-4a-g: The BOC derivative (S)-**7a-h** (330 mg, 1.03 mmol) was dissolved in trifluoroacetic acid (2.0 mL) at room temperature. After 1 hour the reaction mixture was evaporated in vacuo, the residue was dissolved in formic acid (1.5 mL) and the resulting solution was cooled to 0 °C. Acetic anhydride (0.68 mL, 7.21 mmol) was added dropwise and the mixture was allowed to stir at room temperature overnight. The solvent was then removed by reduced pressure. Purification using column chromatography on silica gel with a petroleum ether-ethyl acetate mixture (1:1) afforded the (S)-**4a-f** and (S)-**5a,b**; the yields are give below.

(S)-(-)-**4a** (oil, 180 mg, 75%): $[\alpha]_D -187.0$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.85 (d, $J = 6.6$ Hz, 3H), 0.99 (d, $J = 6.7$ Hz, 3H), 2.40 (m, 1H), 2.92 (s, 3H), 4.41 (d, $J = 10.3$ Hz, 1H), 7.0 (t, $J = 7.4$ Hz, 1H), 7.22 (t, $J = 7.8$ Hz, 2H), 7.46 (d, $J = 7.7$ Hz, 2H), 8.09 (s, 1H), 8.50 (br s, 1H); ^{13}C NMR δ 17.59 (CH_3), 17.78 (CH_3), 18.49

(CH₃), 24.47 (CH), 30.60 (CH₃), 67.99 (CH), 118.95 (CH), 123.39 (CH), 127.92 (CH) 136.80 (C), 162.94 (CO), 166.31 (CO); IR (Golden Gate) ν 3274 (NH), 1650 (CO); MS m/z (%) 234 (M⁺, 8), 142 (20), 114 (35), 84 (65), 47 (15); HRMS (EI) 234.1368 (C₁₃H₁₈O₂N₂ requires 234.1367).

(S)-(-)-4b (oil, 84 mg, 57%): [α]_D -201.6 (*c* 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.83 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 2.40 (m, 1H), 2.90 (s, 3H), 3.7 (s, 3H), 4.3 (d, *J* = 11.2 Hz, 1H), 6.70 (d, *J* = 6.8 Hz, 2H), 7.30 (d, *J* = 9.0 Hz, 2H), 7.90 (br s, 1H), 8.10 (s, 1H); ¹³C NMR δ 183.94 (CH₃), 19.96 (CH₃), 25.65 (CH), 31.99 (CH₃), 55.88 (CH₃), 63.44 (CH), 114.51 (CH), 121.97 (CH), 131.16 (C), 156.87 (C), 164.3 (CO), 167.3 (CO); IR (Golden Gate) ν 3274 (NH), 2834 (OMe), 1648 (CO); MS m/z (%) 264 (M⁺, 6), 249 (1), 192 (3), 162 (5), 142 (41), 114 (100), 83 (68), 47 (11); HRMS (EI) 264.1474, (C₁₄H₂₀O₃N₂ requires 264.1474).

(S)-(-)-4c (oil, 131 mg, 26%): [α]_D -137.5 (*c* 1.0, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 0.94 (d, *J* = 6.7 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 2.49 (m, 1H), 3.02 (s, 3H), 3.79 (s, 6H), 4.38 (d, *J* = 11.2 Hz, 1H), 6.25 (s, 1H), 6.78 (s, 2H), 8.04 (br s, 1H), 8.17 (s, 1H); ¹³C NMR δ 18.89 (CH₃), 19.95 (CH₃), 25.57 (CH₃), 32.04 (CH), 55.79 (CH₃), 63.76 (CH), 97.5 (CH), 98.37 (CH), 139.73 (CH), 161.42 (C), 164.50 (CO), 167.52 (CO); IR (NaCl) ν 3293 (NH), 1655 (CO); MS m/z (%) 294 (M⁺, 4), 280 (41), 220 (3), 192 (11), 153 (100), 100 (40), 55 (19); HRMS (EI) 294.1580 (C₁₅H₂₂O₄N₂ requires 294.1582).

(S)-(-)-4d (oil, 142 mg, 82%): [α]_D -19.2 (*c* 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.84 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H), 2.20 (s, 6H), 2.39 (m, 1H), 2.95 (s, 3H), 4.35 (d, *J* = 11.2 Hz, 1H), 6.67 (s, 1H), 7.09 (d, *J* = 8.3 Hz, 2H), 8.07 (s, 1H), 8.18 (br s, 1H); ¹³C NMR δ 18.97 (CH₃), 19.92 (CH₃), 21.71 (CH₃), 25.74 (CH), 31.96 (CH), 63.47 (CH), 118.21 (CH), 126.56 (CH), 137.92 (C), 139.13 (C), 164.35 (CO), 167.61 (CO); IR (Golden Gate) ν 3284 (NH), 1650 (CO); MS m/z (%) 262 (M⁺, 29), 160 (7), 142 (43), 114 (100), 86 (21), 83 (19), 42 (7); HRMS (EI) 262.1681 (C₁₅H₂₂O₂N₂ requires 262.1680).

(S)-(-)-4e (NOTE: no need for *t*-BOC deprotection step) (solid, 189 mg, 95%): mp 152-154°C; [α]_D -81.5 (*c* 1.5, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 0.89 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 2.45 (m, 1H), 2.96 (s, 3H), 4.34 (d, *J* = 11.3 Hz, 1H), 7.52 (s, 1H), 7.95 (s, 2H), 8.10 (s, 1H), 8.90 (br s, 1H); ¹³C NMR δ 19.06 (CH₃), 19.85

(CH₃), 26.02 (CH₃), 32.29 (CH), 63.67 (CH), 69.41 (CH), 117.80 (CH), 119.94 (CH), 139.84 (C), 164.51 (CO), 168.35 (CO); IR (NaCl) ν 3233 (NH), 1648 (CO); MS m/z (%) 370 (M^{+} , 24), 351 (65), 299 (16), 256 (15), 228 (26), 188 (8); HRMS 370.1118 (C₁₅H₁₆O₂N₂F₆ requires 370.1116).

(S)-(-)-4f (oil, 35 mg 41%): $[\alpha]_D$ -99.4 (c 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.82 (d, J = 6.7 Hz, 3H), 0.97 (d, J = 6.5 Hz, 3H), 2.39 (m, 1H), 2.96 (s, 3H), 4.37 (d, J = 11.2 Hz, 1H), 7.05 (s, 1H), 7.48 (s, 2H), 8.10 (s, 1H), 8.84 (br s, 1H); ¹³C NMR δ 19.01 (CH₃), 19.85 (CH₃), 25.87 (CH), 32.25 (CH₃), 63.74 (CH), 118.55 (CH), 118.66 (CH), 124.64 (CH), 135.53 (C), 140.06 (C), 164.52 (CO), 168.01 (CO); MS m/z (%) 303 (M^{+} , 100), 269 (9), 216 (5), 142 (39), 114 (25), 81 (52); HRMS (EI): 303.0067 (C₁₃H₁₇O₂N₂Cl₂ requires 303.0673).

(S)-(-)-5a Purification using column chromatography on silica gel with an ethyl acetate-methanol mixture (9:1) afforded the product as oil (357 mg, 51%): $[\alpha]_D$ -8.10 (c 1.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.91 (m, 9H), 1.32 (m, 2H), 1.49 (m, 2H), 2.41 (m, 1H), 3.00 (s, 3H), 3.21 (m, 2H), 4.24 (d, J = 11.2 Hz, 1H), 6.14 (br s, 1H), 8.15 (s, 1H); ¹³C NMR δ 14.00 (CH₃), 18.87 (CH₃), 19.86 (CH₃), 20.2 (CH₂), 25.6 (CH), 27.8 (CH₃), 31.6 (CH₂), 39.5 (CH₂), 62.5 (CH), 164.4 (CO), 169.3 (CO); IR (NaCl) ν 3318 (NH), 1653 (CO), 1558; MS m/z (%) 215 (M^{+} , 100), 201 (5), 132 (8), 114 (6), 79 (4); HRMS (EI): 215.1760 (C₁₁H₂₃O₂N₂ requires 215.1760).

(S)-(-)-5b (oil, 20 mg, 37%): $[\alpha]_D$ -104.0 (c 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.61 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.5, 3H), 2.37 (m, 1H), 2.76 (s, 3H), 3.20 (s, 3H), 4.54 (d, J = 10.9 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.33 (d, J = 7.7 Hz, 2H), 7.84 (s, 1H); ¹³C NMR δ 18.50 (CH₃), 18.77 (CH₃), 27.29 (CH), 31.39 (CH₃), 38.01 (CH₃), 64.21 (CH), 128.11 (CH), 129.16 (CH), 130.65 (CH), 142.98 (C), 168.66 (CO), 169.77 (CO); IR (Golden Gate) ν 1658 (CO); MS m/z (%) 248 (M^{+} , 3), 142 (21), 114 (53), 83 (100), 77.0 (5), 47.0 (16); HRMS 248.1526 (C₁₄H₂₀O₂N₂ requires 248.1525).

(S)-(+)-5c Prepared from **(S)-6** following the general scheme but skipping the formation of **8** step. Purification using column chromatography on silica gel with an ethyl acetate-methanol mixture (2:1) afforded the product (solid, 191 mg, 60%): mp 151-153 °C; $[\alpha]_D$ +1.2 (c 1.0, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 0.96 (d, J = 6.8 Hz, 3H),

0.98 (d, $J = 6.7$ Hz, 3H), 2.12 (m, 1H), 3.69 (s, 6H), 6.50 (t, $J = 7.8$ Hz, 1H), 6.16 (s, 1H), 6.48 (d, $J = 8.6$ Hz, 1H), 6.70 (s, 2H), 8.21 (s, 1H), 8.37 (br s, 1H); ^{13}C NMR δ 18.76 (CH₃), 19.67 (CH₃), 31.83 (CH), 55.72 (CH₃), 58.44 (CH), 97.4 (CH), 98.58 (CH), 139.73 (CH), 161.36 (C), 161.74 (CO), 169.79 (CO); IR (NaCl) ν 3272 (NH), 1645 (CO); MS (CI) m/z (%) 281 ([MH⁺], 100), 263 (2), 192 (3); HRMS (CI) 281.1501 (C₁₄H₂₁O₄N₂ requires 281.1501).

References and Notes

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