Supporting Information For:
Thiourea-Catalyzed Asymmetric Michael Addition of Activated
Methylene Compounds to α,β -Unsaturated Imides; Dual Activation
of Imide by Intra- and Intermolecular Hydrogen-bondings

Tsubasa Inokuma, Yasutaka Hoashi, and Yoshiji Takemoto

*Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 6068501,
Japan*

General. Nominal (LR-MS) and exact mass (HR-MS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. ^1H NMR and ^{13}C NMR spectra were registered on JEOL JNM-LA500 using TMS as an internal standard. (s = singlet, d = doublet, dd = double doublet, ddd = doublet of double doublets, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad). Optical rotations were measured in CHCl_3 unless otherwise noted with a JASCO DIP-360 digital polarimeter. For column chromatography, Kanto Silica gel 60 (spherical, 63-210 mm) was employed and preparative thin-layer chromatography (PTLC) was carried out using Silica gel 60 (Merck). Enantiomer ratios were determined by chiral HPLC using a Shimadzu SPD-10A with Daicel Chemical Industries, LTD. Chiralpak AD-H (0.46cm x 25 cm), Chiralpak OJ-H (0.46cm x 25 cm) or Chiralpak OD-H (0.46cm x 25 cm), Chiralpak AS-H (0.46cm x 25 cm).

Materials. Unless otherwise noted, materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used without purification. **3A**, **3B**, **3D**, **3E**, **5A** were prepared according to literatures¹.

3C

1-Methyl-3-[(E)-3-phenylacryloyl]imidazolidin-2-one (3C): To a stirred solution of 1-methyl-2-imidazolidinone² (500 mg, 5 mmol), cinnamoyl chloride (916 mg, 5.5 mmol), and CuCl (49.5 mg, 0.5 mmol) in dry CH_2Cl_2 (5 mL) was added diisopropyl ethyl amine (948 μL , 5.5 mmol). After 1 h, water was added and the mixture extracted three times with CHCl_3 . The combined organic layers were dried over Na_2SO_4 and solvent evaporated at reduced pressure. Purification over silica gel with AcOEt afforded **3C** (1.10 g, 96%). Colorless solid; M.p. 146-148 $^\circ\text{C}$ (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 8.11 (d, J = 15.7 Hz, 1H), 7.80 (d, J = 15.7 Hz, 1H), 7.65-7.58 (m, 2H), 7.40-7.33 (m, 3H), 4.00-3.93 (m, 2H), 3.51-3.43 (m, 2H), 2.93 (s, 3H) ppm; ^{13}C NMR (126 MHz,

CD₃OD) δ 167.5, 156.7, 144.8, 136.5, 131.4, 130.1, 129.3, 119.7, 44.1, 41.0, 30.8 ppm; IR (CHCl₃) ν 3014, 1725, 1661, 1617 cm⁻¹; MS (EI⁺) 230 (M⁺, 41), 131 (100); *Anal.* Calcd. for C₁₃H₁₄N₂O₂: C, 67.81; H, 6.13; N, 12.17; Found: C, 67.79; H, 6.12; N, 12.14.

3G

(*E*)-*N*-Acetyl-*N*-methylcinnamamide (3G): A procedure similar to that described for the preparation of **3D** afforded **3G** (475 mg, 47%). Colorless solid; M.p. 75-76 °C (Hexane/AcOEt); ¹H NMR (500 MHz, CDCl₃) δ 7.73 (d, *J* = 15.6 Hz, 1H), 7.58-7.50 (m, 2H), 7.41-7.33 (m, 3H), 7.07 (d, *J* = 15.6 Hz, 1H), 3.30 (s, 3H), 2.44 (s, 3H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.5, 169.3, 145.1, 134.7, 130.5, 129.0, 128.3, 120.2, 32.0, 26.1 ppm; IR (CHCl₃) ν 3031, 1684, 1619 cm⁻¹; MS (EI⁺) 203 (M⁺, 39), 131 (100); *Anal.* Calcd. for C₁₂H₁₃NO₂: C, 70.92; H, 6.45; N, 6.89; Found: C, 70.92; H, 6.16; N, 6.88.

Typical procedure for enantioselective Michael addition of malononitrile to α,β -unsaturated imides catalyzed by thiourea. A mixture of **7A** (171 mg, 0.61 mmol), malononitrile **2a** (2.0 equiv., 80 mg), and thiourea **1a** (0.1 equiv., 25 mg) in dry toluene (6.1 ml) was stirred at room temperature for 14 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (2/1) to afford desired Michael adduct **8A** (201 mg, 95%).

4B

(3*R*)-3-(4,4-Dicyano-3-phenylbutanoyl)oxazolidin-2-one (4B): Yellow amorphous; [α]_D²⁸ +10.9 (*c* 0.95, CHCl₃, 83% ee); ¹H NMR (500 MHz, CDCl₃) δ 7.47-7.35 (m, 5H), 4.51 (d, *J* = 6.1 Hz, 1H), 4.49-4.37 (m, 2H), 4.06-3.93 (m, 2H), 3.86 (ddd, *J* = 8.4, 6.0, 5.8 Hz, 1H), 3.70 (dd, *J* = 18.4, 5.8 Hz, 1H), 3.60 (dd, *J* = 18.4, 8.4 Hz, 1H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 170.0, 153.4, 136.0, 129.4, 129.3, 128.0, 111.7, 111.5, 62.3, 42.3, 41.6, 37.3, 28.8 ppm; IR (CHCl₃) ν 3030, 1786, 1698 cm⁻¹; MS (EI⁺) 283 (M⁺, 6), 131 (100); HRMS (EI⁺) Calcd for [C₁₅H₁₃N₃O₃]⁺: 283.0957; Found: 283.0960; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 210 nm, retention times: (major) 60.4 min, (minor) 75.6 min].

(3R)-1-(4,4-Dicyano-3-phenylbutanoyl)-3-methylimidazolidin-2-one (4C): Colorless solid; $[\alpha]_D^{26} +6.25$ (*c* 0.96, CHCl₃, 81% ee); M.p. 139-141 °C (Hexane/ AcOEt); ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.30 (m, 5H), 4.63 (d, *J* = 5.8 Hz, 1H), 3.90-3.75 (m, 3H), 3.70 (dd, *J* = 18.0, 5.2 Hz, 1H), 3.62 (dd, *J* = 18.0, 8.9 Hz, 1H), 3.47-3.37 (m, 2H), 2.88 (s, 3H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 170.0, 154.5, 136.5, 129.1, 128.9, 128.1, 112.0, 111.7, 43.0, 41.8, 39.2, 37.1, 30.5, 28.8 ppm; IR (CHCl₃) ν 3030, 1736, 1672 cm⁻¹; MS (EI⁺) 296 (M⁺, 20), 131 (100); *Anal.* Calcd. for C₁₆H₁₆N₄O₂: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.72; H, 5.42; N, 18.86; HPLC [Chiralcel AD-H, hexane/2-propanol = 80/20, 0.5 mL/min, λ = 210 nm, retention times: (major) 48.1 min, (minor) 55.5 min].

(3R)-1-(4,4-Dicyano-3-phenylbutanoyl)pyrrolidin-2-one (4D): Colorless solid; $[\alpha]_D^{26} +8.64$ (*c* 1.00, CHCl₃, 93% ee); M.p. 103-105 °C (Hexane/ AcOEt); ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.35 (m, 5H), 4.57 (d, *J* = 5.8 Hz, 1H), 3.86-3.74 (m, 3H), 3.63-3.58 (m, 2H), 2.68-2.55 (m, 2H), 2.13-2.00 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 175.7, 170.9, 136.3, 129.3, 129.1, 128.1, 111.9, 111.6, 45.3, 41.6, 38.8, 33.3, 28.8, 17.1 ppm; IR (CHCl₃) ν 3030, 1742, 1688 cm⁻¹; MS (EI⁺) 281 (M⁺, 12), 131 (100); *Anal.* Calcd. for C₁₆H₁₅N₃O₂: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.37; H, 5.66; N, 15.02; HPLC [Chiralcel AS-H, hexane/ethanol = 80/20, 0.5 mL/min, λ = 210 nm, retention times: (major) 50.8 min, (minor) 47.0 min].

(3R)-1-[4,4-Dicyano-3-phenylbutanoyl]piperidin-2-one (4E): Colorless oil; $[\alpha]_D^{28} +6.17$ (*c* 0.67, CHCl₃, 59% ee); ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.33 (m, 5H), 4.54 (d, *J* = 5.5 Hz, 1H), 3.83 (dt, *J* = 8.5, 5.5 Hz, 1H), 3.76-3.56 (m, 4H), 2.64-2.50 (m, 2H), 1.92-1.75 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.7, 173.6, 136.6, 129.2, 129.0, 128.1, 112.0, 111.7, 44.3, 42.2, 41.7, 34.7, 28.8, 22.2, 20.0 ppm; IR (CHCl₃) ν 3027, 2957, 1737, 1692 cm⁻¹; MS (EI⁺) 295 (M⁺, 8), 131 (100);

HRMS (EI^+) Calcd for $[\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_2]^+$: 295.1321; Found: 295.1314; HPLC [Chiralcel AS-H, hexane/EtOH = 80/20, 0.5 mL/min, λ = 210 nm, retention times: (major) 41.7 min, (minor) 36.4 min].

(3R)-N-Acetyl-4,4-dicyano-N-methyl-3-phenylbutanamide (4G): Colorless oil; $[\alpha]_{\text{D}}^{26} +8.98$ (c 0.72, CHCl_3 , 56% ee); ^1H NMR (500 MHz, CDCl_3) δ 7.51-7.31 (m, 5H), 4.56 (d, J = 5.5 Hz, 1H), 3.88-3.77 (m, 1H), 3.54 (dd, J = 18.5, 8.5 Hz, 1H), 3.47 (dd, J = 18.5, 5.3 Hz, 1H), 3.24 (s, 3H), 2.37 (s, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.2, 173.1, 136.5, 129.3, 129.1, 128.0, 111.9, 111.6, 42.1, 40.7, 31.9, 28.7, 26.1 ppm; IR (CHCl_3) ν 3030, 1737, 1700 cm^{-1} ; MS (EI^+) 269 (M^+ , 14), 131 (100); HRMS (EI^+) Calcd for $[\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_2]^+$: 269.1164; Found: 269.1155; HPLC [Chiralcel OJ-H, hexane/2-propanol = 50/50, 0.5 mL/min, λ = 210 nm, retention times: (major) 56.4 min, (minor) 79.0 min].

(E)-N-3-Phenylacryloyl-3,5-bis-trifluoromethylbenzamide (5B): A procedure similar to that described for the preparation of **3D** afforded **5B** (395 mg, 41%). White solid; M.p. 234-235 $^{\circ}\text{C}$ (AcOEt); ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 11.53 (s, 1H), 8.56 (s, 2H), 8.41 (s, 1H), 7.77 (d, J = 15.9 Hz, 1H), 7.71-7.67 (m, 2H), 7.50-7.45 (m, 3H), 7.30 (d, 1H, J = 15.9 Hz) ppm; ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 165.9, 164.5, 144.0, 136.2, 134.3, 130.7, 130.3, 129.3, 129.2, 128.3, 125.9, 122.0, 120.8 ppm; IR (CHCl_3) ν 3450, 2996, 1662, 1432 cm^{-1} ; *Anal.* Calcd. for $\text{C}_{18}\text{H}_{11}\text{F}_6\text{NO}_2$: C, 55.82; H, 2.86; N, 3.62; F, 29.44; Found: C, 55.75; H, 3.02; N, 3.65; F, 29.42.

(E)-2-Methoxy-N-3-phenylacryloylbenzamide (7A): A procedure similar to that described for the

preparation of **3D** afforded **7A** (327 mg, 64%). White solid; M.p. 112-114 °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.28 (s, 1H), 8.22 (dd, $J = 8.0, 1.8$ Hz, 1H), 7.90 (d, $J = 15.8$ Hz, 1H), 7.86 (d, $J = 15.6$ Hz, 1H), 7.68-7.64 (m, 2H), 7.56 (td, $J = 8.0, 1.9$ Hz, 1H), 7.44-7.38 (m, 3H), 7.14 (t, $J = 7.7$ Hz, 1H), 7.04 (d, $J = 8.2$ Hz, 1H), 4.06 (s, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 167.7, 164.1, 157.8, 145.8, 134.9, 134.7, 132.9, 130.5, 128.9, 121.8, 120.6, 111.8, 56.2 ppm; IR (CHCl_3) ν 3230, 3021, 1671, 1619, 1479, 1341 cm^{-1} ; *Anal.* Calcd. for $\text{C}_{17}\text{H}_{15}\text{NO}_3$: C, 72.58; H, 5.37; N, 4.98; Found: C, 72.58; H, 5.51; N, 4.99.

(E)-2,6-Dimethoxy-N-3-phenylacryloylbenzamide (5C): A procedure similar to that described for the preparation of **3D** afforded **5C** (123 mg, 72%). White solid; M.p. 159-160 °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 8.28 (s, 1H), 7.87 (d, $J = 15.6$ Hz, 1H), 7.74 (d, $J = 15.9$ Hz, 1H), 7.66-7.61 (m, 2H), 7.40 (t, $J = 3.0$ Hz, 3H), 7.35 (t, $J = 8.5$ Hz, 1H), 6.60 (d, $J = 8.2$ Hz, 2H), 3.85 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 166.8, 164.9, 157.6, 146.3, 134.7, 132.0, 130.6, 128.9, 128.7, 119.9, 114.3, 104.0, 56.0 ppm; IR (CHCl_3) ν 3393, 3021, 2942, 2841, 2360, 1717, 1678, 1619, 1597, 1475, 1340, 1257 cm^{-1} ; *Anal.* Calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_4$: C, 69.44; H, 5.50; N, 4.50; Found: C, 69.26; H, 5.58; N, 4.50.

(E)-2-Methyl-N-3-phenylacryloylbenzamide (5D): A procedure similar to that described for the preparation of **3D** afforded **5D** (766 mg, 78%). White solid; M.p. 124-125 °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 8.46 (s, 1H), 7.91 (d, $J = 15.9$ Hz, 1H), 7.74 (d, $J = 15.9$ Hz, 1H), 7.66-7.63 (m, 2H), 7.51 (d, $J = 7.6$ Hz, 1H), 7.44-7.40 (m, 4H), 7.31-7.25 (m, 2H), 2.52 (s, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 168.3, 167.2, 146.8, 137.5, 134.5, 134.3, 131.7, 131.5, 130.8, 128.9, 128.7, 127.0, 126.1, 119.2, 20.0 ppm; IR (CHCl_3) ν 3691, 3391, 2398, 1712, 1681, 1619, 1337 cm^{-1} ; *Anal.* Calcd. for $\text{C}_{17}\text{H}_{15}\text{NO}_2$: C, 76.95; H, 5.70; N, 5.28; Found: C, 77.00; H, 5.77; N, 5.16.

(3R)-N-(4,4-Dicyano-3-phenylbutanoyl)benzamide (6A): Colorless solid; $[\alpha]_D^{26} -16.5$ (*c* 1.25, CHCl₃, 84% ee); M.p. 150-155 °C (Hexane/AcOEt); ¹H NMR (500 MHz, CDCl₃) δ 8.58 (br s, 1H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.48-7.37 (m, 5H), 4.59 (d, *J* = 5.5 Hz, 1H), 3.93-3.86 (m, 1H), 3.79-3.71 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.0, 165.6, 136.1, 133.8, 132.0, 129.3, 129.24, 129.19, 128.1, 127.7, 111.8, 111.5, 41.4, 39.6, 28.9 ppm; IR (CHCl₃) ν 3396, 3018, 1701 cm⁻¹; MS (EI⁺) 317 (M⁺, 4), 105 (100); HRMS (EI⁺) Calcd for [C₁₉H₁₅N₃O₂]⁺: 317.1164; Found: 317.1160; HPLC [Chiralcel AD-H, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 210 nm, retention times: (major) 62.8 min, (minor) 33.9 min].

(3R)-N-(4,4-Dicyano-3-phenylbutyryl)-3,5-bis-trifluoromethylbenzamide (6B): Colorless amorphous; $[\alpha]_D^{21}$ 0.00 (*c* 2.52, CHCl₃, 89% ee); ¹H NMR (500 MHz, CDCl₃) δ 8.83 (s, 1H), 8.29 (s, 2H), 8.14 (s, 1H), 7.46-7.34 (m, 5H), 4.49 (d, *J* = 5.8 Hz, 1H), 3.95-3.87 (m, 1H), 3.76-3.68 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.2, 163.4, 135.8, 134.2, 133.3, 133.0, 132.8, 132.5, 129.5, 128.3, 127.9, 127.1, 123.7, 121.5, 111.5, 111.4, 41.3, 39.9, 29.0 ppm; IR (CHCl₃) ν 3692, 3031, 2360, 1701, 1376, 1280 cm⁻¹; MS (FAB⁺) 454 (MH⁺, 100); HRMS (FAB⁺) Calcd for [C₂₁H₁₄F₆N₃O₂]⁺: 454.099; Found: 454.0991; HPLC [Chiralcel OD-H, hexane/2-propanol = 80/20, 0.3 mL/min, λ = 254 nm, retention times: (major) 57.7 min, (minor) 52.7 min].

(3R)-N-(4,4-Dicyano-3-phenylbutyryl)-2-methoxybenzamide (8A): Colorless amorphous; $[\alpha]_D^{21} +9.69$ (*c* 1.32, CHCl₃, 91% ee); ¹H NMR (500 MHz, CDCl₃) δ 10.39 (s, 1H), 8.14 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.55 (td, *J* = 8.1, 1.6 Hz, 1H), 7.48-7.35 (m, 5H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 4.64 (d, *J* = 5.5 Hz, 1H), 3.99 (s, 3H), 3.93-3.88 (m, 1H), 3.71 (d, *J* = 6.4 Hz, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 172.9, 164.0, 157.7, 136.3, 135.2, 132.8, 129.2, 129.0, 128.1, 121.8,

119.4, 112.0, 111.8, 111.6, 56.2, 41.3, 40.1, 28.7 ppm; IR (CHCl₃) ν 3314, 2360, 1714, 1683, 1602, 1477 cm⁻¹; MS (FAB⁺) 348 (MH⁺, 42), 135 (100); HRMS (FAB⁺) Calcd for [C₂₀H₁₈N₃O₃]⁺: 348.1348; Found: 348.1352; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 254 nm, retention times: (major) 86.7 min, (minor) 43.9 min].

(3R)-N-(4,4-Dicyano-3-phenylbutyryl)-2,6-dimethoxybenzamide (6C): Colorless amorphous; $[\alpha]_D^{21}$ +0.39 (*c* 1.10, CHCl₃, 62% ee); ¹H NMR (500 MHz, CDCl₃) δ 8.41 (s, 1H), 7.47-7.36 (m, 6H), 6.59 (d, *J* = 8.5 Hz, 2H), 4.61 (dd, *J* = 4.6, 1.2 Hz, 1H) 3.84 (s, 7H), 3.72-3.68 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 172.5, 164.4, 157.8, 136.2, 132.7, 129.2, 129.2, 128.2, 111.9, 111.5, 104.3, 104.1, 56.1, 41.5, 39.5, 28.8 ppm; IR (CHCl₃) ν 3029, 2360, 1699, 1597, 1476, 1259 cm⁻¹; MS (FAB⁺) 378 (MH⁺, 35), 165 (100); HRMS (FAB⁺) Calcd for [C₂₁H₂₀N₃O₄]⁺: 378.1454; Found: 378.1449; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 254 nm, retention times: (major) 102.7 min, (minor) 60.6 min].

(3R)-N-(4,4-Dicyano-3-phenylbutyryl)-2-methylbenzamide (6D): Colorless amorphous; $[\alpha]_D^{25}$ +0.35 (*c* 1.12, CHCl₃, 89% ee); ¹H NMR (500 MHz, CDCl₃) δ 8.77 (s, 1H), 7.46-7.39 (m, 7H), 7.32-7.25 (m, 2H), 4.51 (d, *J* = 5.2 Hz, 1H), 3.85-3.80 (m, 1H), 3.71-3.68 (m, 2H), 2.47 (s, 3H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.1, 167.9, 137.9, 136.1, 133.0, 132.1, 131.9, 129.3, 129.2, 128.0, 127.0, 126.1, 111.8, 111.5, 41.4, 39.4, 28.7, 20.0 ppm; IR (CHCl₃) ν 1729, 1701, 1457, 1386 cm⁻¹; MS (FAB⁺) 332 (MH⁺, 46), 119 (100); HRMS (FAB⁺) Calcd for [C₂₀H₁₈N₃O₂]⁺: 332.1399; Found: 332.1404; HPLC [Chiralcel OD, hexane/2-propanol = 80/20, 0.5 mL/min, λ = 254 nm, retention times: (major) 62.5 min, (minor) 54.0 min].

General procedure for the preparation of imides 7B, C, D, E³.

***N*-2-Chloroacetyl-2-methoxybenzamide:** A mixture of *o*-methoxybenzamide (2.17 g, 14.4 mmol) and chloroacetylchloride (1.93 mL, 24.4 mmol) was stirred at 110 °C for 2 h. After the reaction mixture was evaporated, the obtained residue was purified over silica gel with Hexane/AcOEt (3/2) to afford *N*-2-chloroacetyl-2-methoxybenzamide. Colorless solid; M.p. 115-117 °C (Hexane/AcOEt); ¹H NMR (500 MHz, CDCl₃) δ 10.76 (s, 1H), 8.18 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.58 (td, *J* = 7.9, 1.8 Hz, 1H), 7.14 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 8.3 Hz, 1H), 4.67 (s, 2H), 4.05 (s, 3H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 168.0, 163.7, 157.8, 135.3, 133.1, 121.9, 119.4, 111.8, 56.2, 45.4 ppm; IR (CHCl₃) ν 3540, 3313, 3026, 2956, 1750, 1726, 1687, 1600, 1479, 1292 cm⁻¹; *Anal.* Calcd. for C₁₀H₁₀ClNO₃: C, 52.76; H, 4.43; N, 6.15; Cl, 15.57; Found: C, 52.56; H, 4.44; N, 6.16; 15.85.

2-(2-Methoxybenzoylamino)-2-oxoethylphosphonic acid diethyl ester: Triethylphosphite (2.7 mL, 15.7 mmol) was added to *N*-2-chloroacetyl-2-methoxybenzamide and the reaction mixture was stirred at 80 °C for 53 h. Purification over silica gel with AcOEt afforded 2-(2-methoxybenzoylamino)-2-oxoethylphosphonic acid diethyl ester. Yellow oil; ¹H NMR (500MHz, CDCl₃) δ 10.53 (s, 1H), 8.17 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.56 (td, *J* = 7.7, 1.9 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 4.25-4.15 (m, 4H), 4.03 (s, 3H), 3.73 (d, *J* = 22 Hz, 2H), 1.33 (t, *J*

= 7.0 Hz, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 166.5, 163.5, 157.6, 134.8, 132.7, 121.5, 119.7, 111.6, 62.4, 62.4, 56.0, 37.5, 36.5, 16.0, 16.0 ppm; IR (CHCl_3) ν 3320, 3001, 1750, 1710, 1684, 1601, 1479, 1215 cm^{-1} ; MS (FAB^+) 330 (MH^+ , 87), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{14}\text{H}_{21}\text{NO}_6\text{P}]^+$: 330.1106; Found: 330.1103.

(E)-N-3-(4-Fluorophenyl)acryloyl-2-methoxybenzamide (7B): A 1.54 M solution of *n*-buthyl lithium in *n*-hexane (2.0 mL, 3.0 mmol) was added dropwise to a solution of 2-(2-methoxybenzoylamino)-2-oxoethylphosphonic acid diethyl ester (500 mg, 1.5 mmol) in THF (6.0 mL) at -78°C . The resulting bright yellow solution was stirred at this temperature for 15 min. A solution of *p*-fluorobenzaldehyde (0.16 mL, 1.5 mmol) in THF (0.5 mL) was added and the mixture was stirred at room temperature for 3 h. After the reaction mixture was diluted with H_2O and then acidified by 1N HCl, the resulting mixture was extracted with CHCl_3 . The extract was dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was purified over silica gel with Hexane/AcOEt (1/1) to afford desired imide **7B** (382 mg, 84%). White solid; M.p. $131\text{--}132^\circ\text{C}$ (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.29 (s, 1H), 8.21 (dd, $J = 7.9, 1.8$ Hz, 1H), 7.86 (d, $J = 15.9$ Hz, 1H), 7.80 (d, $J = 15.8$ Hz, 1H), 7.67–7.63 (m, 2H), 7.57 (td, $J = 7.7, 1.9$ Hz, 1H), 7.15 (t, $J = 7.9$ Hz, 1H), 7.12–7.08 (m, 2H), 7.05 (d, $J = 8.3$ Hz, 1H), 4.06 (s, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 167.6, 165.0, 164.1, 163.0, 157.8, 144.5, 134.8, 132.9, 131.1, 130.5, 130.4, 121.7, 120.3, 116.1, 115.9, 111.7, 56.2 ppm; IR (CHCl_3) ν 3329, 3022, 1696, 1670, 1599, 1508, 1480, 1223 cm^{-1} ; Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{FNO}_3$: C, 68.22; H, 4.71; N, 4.68; F, 6.35; Found: C, 68.22; H, 4.91; N, 4.64; F, 6.34.

(E)-2-Methoxy-N-3-(4-fluorophenyl)acryloylbenzamide (7C): A procedure similar to that described for the preparation of **7B** afforded **7C** (184 mg, 84%). White solid; M.p. $107\text{--}108^\circ\text{C}$ (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.24 (s, 1H), 8.19 (d, $J = 7.9$ Hz, 1H), 7.85 (d, $J = 15.8$ Hz, 1H), 7.71 (d, $J = 15.6$ Hz, 1H), 7.59 (d, $J = 8.1$ Hz, 2H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.11 (t, J

= 7.9 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 6.91 (d, J = 8.5 Hz, 2H), 4.01 (s, 3H), 3.82 (s, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 167.6, 163.9, 161.5, 157.6, 145.5, 134.5, 132.7, 130.2, 127.5, 121.5, 120.4, 117.9, 114.2, 111.6, 56.1, 55.2 ppm; IR (CHCl_3) ν 3331, 3009, 2360, 1694, 1668, 1599, 1510, 1479, 1216 cm^{-1} ; Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_4$: C, 69.44; H, 5.50; N, 4.50; Found: C, 69.53; H, 5.64; N, 4.42.

(E)-N-(But-2-enoyl)-2-methoxybenzamide (7D): A procedure similar to that described for the preparation of **7B** afforded **7D** (296 mg, 71%). Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ 10.16 (s, 1H), 8.17 (dd, J = 8.0, 1.8 Hz, 1H), 7.54 (td, J = 7.3, 1.8 Hz, 1H), 7.21-7.08 (m, 3H), 7.02 (d, J = 8.3 Hz, 1H), 4.02 (s, 3H), 1.98 (d, J = 6.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 167.2, 163.9, 157.7, 145.9, 134.6, 132.8, 125.2, 121.6, 120.5, 111.7, 56.1, 18.3 ppm; IR (CHCl_3) ν 3330, 3017, 1739, 1670, 1479 cm^{-1} ; MS (FAB^+) 220 (MH^+ , 100); HRMS (FAB^+) Calcd for $[\text{C}_{12}\text{H}_{14}\text{NO}_3]^+$: 220.0974; Found: 290.0967.

(E)-N-[(tert-Butyldimethylsilyloxy)-oct-2-enoyl]-2-methoxybenzamide (7E): A procedure similar to that described for the preparation of **7B** afforded **7E** (5.45 g, 70%). Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ 10.12 (s, 1H), 8.11 (dd, J = 7.8, 1.6 Hz, 1H), 7.48 (td, J = 7.8, 1.6 Hz, 1H), 7.15-7.01 (m, 3H), 6.97 (d, J = 8.6 Hz, 1H), 3.96 (s, 3H), 3.56 (t, J = 6.4 Hz, 2H), 2.30-2.20 (m, 2H), 1.53-1.46 (m, 4H), 1.39-1.30 (m, 2H), 0.84 (s, 9H), 0.01 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 163.8, 157.6, 150.6, 134.5, 132.7, 123.7, 121.5, 120.4, 111.6, 62.9, 56.0, 32.5, 32.4, 27.8, 25.8, 25.3, 18.1, -5.5 ppm; IR (CHCl_3) ν 3331, 2933, 1699, 1673, 1600, 1479, 1347 cm^{-1} ; MS (FAB^+) 406 (MH^+ , 54), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{22}\text{H}_{36}\text{NO}_4\text{Si}]^+$: 406.2414; Found: 406.2421.

(3R)-N-[4,4-Dicyano-3-(4-fluorophenyl)butyryl]-2-methoxybenzamide (8B): Colorless amorphous; $[\alpha]_D^{28} +10.2$ (*c* 1.00, CHCl₃, 92% ee); ¹H NMR (500 MHz, CDCl₃) δ 10.42 (s, 1H), 8.15 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.58 (td, *J* = 7.9, 1.6 Hz, 1H), 7.48-7.42 (m, 2H), 7.16-7.09 (m, 3H), 7.03 (d, *J* = 8.5 Hz, 1H), 4.63 (d, *J* = 5.2 Hz, 1H), 4.02 (s, 3H), 3.93-3.87 (m, 1H), 3.70 (d, *J* = 7.0 Hz, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 172.8, 164.1, 162.0, 157.8, 135.4, 132.9, 132.1, 132.1, 130.0, 129.9, 121.9, 119.4, 116.3, 116.1, 111.9, 111.8, 111.4, 56.2, 40.7, 40.2, 28.8 ppm; IR (CHCl₃) ν 3314, 2360, 1710, 1683, 1604, 1514, 1478, 1243 cm⁻¹; MS (FAB⁺) 366 (MH⁺, 92), 135 (100); HRMS (FAB⁺) Calcd for [C₂₀H₁₉FN₃O₃]⁺: 366.1254; Found: 336.1248; HPLC [Chiralcel OD, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 254 nm, retention times: (major) 101.6 min, (minor) 44.0 min].

(3R)-N-[4,4-Dicyano-3-(4-methoxyphenyl)butyryl]-2-methoxybenzamide (8C): Colorless amorphous; $[\alpha]_D^{24} +11.0$ (*c* 1.21, CHCl₃, 90% ee); ¹H NMR (500 MHz, CDCl₃) δ 10.38 (s, 1H), 8.15 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.57 (td, *J* = 8.0, 1.9 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.13 (t, *J* = 8.6 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 2H), 4.59 (d, *J* = 5.5 Hz, 1H), 4.01 (s, 3H), 3.89-3.83 (m, 1H), 3.81 (s, 3H), 3.69 (d, *J* = 7.1 Hz, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.0, 164.0, 160.0, 157.8, 135.3, 132.9, 129.3, 128.2, 121.9, 119.5, 114.5, 112.1, 111.8, 111.7, 56.2, 55.2, 40.8, 40.3, 29.1 ppm; IR (CHCl₃) ν 3316, 3024, 1709, 1683, 1514, 1479, 1217 cm⁻¹; MS (FAB⁺) 378 (MH⁺, 87), 135 (100); HRMS (FAB⁺) Calcd for [C₂₁H₂₀N₃O₄]⁺: 378.1454; Found: 378.1447; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, λ = 254 nm, retention times: (major) 85.4 min, (minor) 48.8 min].

(3R)-N-[4,4-Dicyano-3-methylbutyryl]-2-methoxybenzamide (8D): Yellow oil; $[\alpha]_D^{20} -23.3$ (*c* 1.61, CHCl₃, 90% ee); ¹H NMR (500 MHz, CDCl₃) δ 10.36 (s, 1H), 8.15 (dd, *J* = 7.9, 1.8 Hz, 1H),

7.58 (td, $J = 7.7, 1.9$ Hz, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 7.04 (d, $J = 8.2$ Hz, 1H), 4.46 (d, $J = 4.6$ Hz, 1H), 4.04 (s, 3H), 3.28 (dd, $J = 18.7, 4.8$ Hz, 1H), 3.20 (dd, $J = 18.6, 8.6$ Hz, 1H), 2.84-2.75 (m, 1H), 1.40 (d, $J = 6.7$ Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.3, 164.0, 157.8, 135.3, 132.9, 121.9, 119.5, 112.5, 111.8, 111.2, 56.3, 41.1, 31.7, 27.8, 17.0 ppm; IR (CHCl_3) ν 3316, 3026, 1707, 1685, 1600, 1479, 1383 cm^{-1} ; MS (FAB^+) 286 (MH^+ , 64), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{15}\text{H}_{16}\text{N}_3\text{O}_3]^+$: 286.1192; Found: 286.1187; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, $\lambda = 254$ nm, retention times: (major) 36.1 min, (minor) 27.9 min].

(3R)-N-[(8-tert-Butyldimethylsilyloxy)-3,3-dicyanomethyloctanoyl]-2-methoxybenzamide

(8E): Yellow oil; $[\alpha]_{\text{D}}^{28} -25.9$ (c 2.28, CHCl_3 , 93% ee); ^1H NMR (500 MHz, CDCl_3) δ 10.35 (s, 1H), 8.14 (dd, $J = 8.0, 1.8$ Hz, 1H), 7.57 (td, $J = 8.0, 1.8$ Hz, 1H), 7.13 (t, $J = 7.9$ Hz, 1H), 7.03 (d, $J = 8.2$ Hz, 1H), 4.47 (d, $J = 4.5$ Hz, 1H), 4.03 (s, 3H), 3.60 (t, $J = 6.4$ Hz, 2H), 3.39 (dd, $J = 18.8, 4.0$ Hz, 1H), 3.11 (dd, $J = 18.8, 9.1$ Hz, 1H), 2.65-2.58 (m, 1H), 1.84-1.76 (m, 1H), 1.70-1.62 (m, 1H), 1.58-1.48 (m, 3H), 1.44-1.36 (m, 3H), 0.88 (s, 9H), 0.03 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.7, 164.0, 157.8, 135.3, 133.0, 121.9, 119.6, 112.5, 111.8, 111.7, 62.9, 56.3, 38.7, 36.1, 32.4, 31.2, 26.9, 26.5, 25.9, 25.6, 18.3, -5.4 ppm; IR (CHCl_3) ν 3316, 3021, 1711, 1477, 1417, 1362, 1221 cm^{-1} ; MS (FAB^+) 472 (MH^+ , 56), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{25}\text{H}_{38}\text{N}_3\text{O}_4\text{Si}]^+$: 472.2632; Found: 472.2636; HPLC [Chiralcel OD-H, hexane/2-propanol = 70/30, 0.5 mL/min, $\lambda = 254$ nm, retention times: (major) 21.6 min, (minor) 18.2 min].

Typical procedure for enantioselective Michael addition of methylcyanoacetate to α,β -unsaturated imides catalyzed by thiourea. A solution of **7A** (100 mg, 0.36 mmol), methylcyanoacetate **2b** (2.0 equiv., 63 μL), and thiourea **1a** (0.1 equiv., 15 mg) in dry toluene (0.72 mL) was stirred at 80 $^\circ\text{C}$ for 52 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (3/2) to afford desired Michael adduct **9A** (127 mg, 94%). To determine the ee value of the Michael adduct, methanolysis and decarboxylation reaction were employed⁴.

(3S)-2-Cyano-5-(2-methoxybenzoylamino)-5-oxo-3-phenylpentanoic acid methyl ester (9A):

Colorless oil; $[\alpha]_D^{22}$ -3.18 (c 1.99, CHCl_3); ^1H NMR (500 MHz, CDCl_3) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 10.33 (s, 1H), 8.16 (td, $J = 7.3$, 1.8 Hz, 1H), 7.59-7.52 (m, 1H), 7.42-7.28 (m, 5H), 7.12 (t, $J = 7.3$ Hz, 1H), 7.01 (t, $J = 8.5$ Hz, 1H), 4.37 (d, $J = 5.8$ Hz, 1H), 4.12-4.04 (m, 1H), 4.01 (s, 3H), 3.65 (s, 3H), 3.78-3.58 (m, 2H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.3, 173.0, 165.6, 163.9, 157.7, 139.0, 138.1, 135.0, 135.0, 132.9, 128.9, 128.8, 128.2, 128.1, 127.8, 121.8, 121.7, 119.8, 119.8, 115.5, 115.3, 111.7, 56.2, 56.1, 53.3, 53.2, 43.7, 43.3, 41.3, 41.0, 40.6, 40.4 ppm; IR (CHCl_3) ν 3316, 2360, 1753, 1710, 1680, 1476 cm^{-1} ; MS (FAB^+) 381 (MH^+ , 50), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{21}\text{H}_{21}\text{N}_2\text{O}_5]^+$: 381.145; Found: 381.1448.

(3S)-2-Cyano-3-phenylpentanedioic acid dimethyl ester (9A'): To a stirred solution of **9A** (27 mg, 0.071 mmol) in MeOH (0.30 mL) was added $\text{Er}(\text{OTf})_3$ (0.05 equiv., 2.2 mg) at 0 °C. After 4 h, the reaction mixture was concentrated *in vacuo* and the residue was purified by column chromatography (Hexane/AcOEt = 2/1) to afford desired methylester **9A'** (17mg, 92%). Yellow oil; $[\alpha]_D^{20}$ $+7.80$ (c 1.44, CHCl_3); ^1H NMR (500 MHz, CDCl_3) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 7.37-7.26 (m, 5H), 4.24 (d, $J = 5.5$ Hz, 1H), 3.94-3.90 (m, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 3.06-2.85 (m, 2H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 171.2, 171.0, 165.3, 165.2, 138.2, 137.3, 128.9, 128.8, 128.3, 128.2, 127.7, 127.3, 115.1, 114.9, 53.4, 53.1, 51.9, 51.8, 43.6, 43.1, 41.4, 40.9, 36.9, 36.3 ppm; IR (CHCl_3) ν 3028, 2956, 2252, 1747, 1454, 1439, 1266 cm^{-1} ; MS (FAB^+) 262 (MH^+ , 67), 154 (100); HRMS (FAB^+) Calcd for $[\text{C}_{14}\text{H}_{16}\text{NO}_4]^+$: 262.1079; Found: 262.1082.

(3S)-4-Cyano-3-phenylbutanoic acid methyl ester (12A): A mixture of **9A'** (16 mg, 0.061 mmol) and NaCl (1.0 equiv., 3.6 mg) in DMSO/ H_2O (0.6mL/0.1mL) was stirred at 130 °C. After 24 h, the reaction mixture was purified by column chromatography (Hexane/AcOEt = 3/2) to afford desired product **12A** (11 mg, 92%). Colorless oil; $[\alpha]_D^{21}$ $+16.3$ (c 1.00, CHCl_3 , 82% ee); ^1H NMR (500 MHz, CDCl_3) δ 7.38-7.34 (m, 2H), 7.33-7.24 (m, 3H), 3.66 (s, 3H), 3.52 (qn, $J = 7.1$ Hz, 1H), 2.86 (dd, $J = 16.4$, 8.0 Hz, 1H), 2.79 (dd, $J = 16.5$, 9.8 Hz, 1H), 2.75 (d, $J = 6.7$ Hz, 2H) ppm; ^{13}C NMR (126

MHz, CDCl₃) δ 171.5, 140.4, 129.0, 127.9, 127.0, 117.9, 51.9, 38.7, 37.9, 24.2 ppm; IR (CHCl₃) ν 3026, 2360, 1733, 1438, 1216 cm⁻¹; MS (FAB⁺) 204 (MH⁺, 94), 154 (100); HRMS (FAB⁺) Calcd for [C₁₂H₁₄NO₂]⁺: 204.1025; Found: 204.1027. HPLC [Chiralcel OD-H, hexane/2-propanol = 90/10, 0.3 mL/min, λ = 254 nm, retention times: (major) 63.4 min, (minor) 52.8 min]

(3S)-2-Cyano-3-(4-fluorophenyl)-5-(2-methoxybenzoylamino)-5-oxo-pentanoic acid methyl ester (9B): Colorless amorphous; $[\alpha]_D^{22}$ -5.86 (*c* 2.97, CHCl₃); ¹H NMR (500 MHz, CDCl₃) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 10.34 (s, 1H), 8.16 (td, *J* = 7.4, 1.9 Hz, 1H), 7.52-7.50 (m, 1H), 7.48-7.46 (m, 2H), 7.13 (t, *J* = 7.9 Hz, 1H), 7.01-6.98 (m, 3H), 4.34 (d, *J* = 5.5 Hz, 1H), 4.11-4.05 (m, 1H), 4.02 (s, 3H), 3.68 (s, 3H), 3.72-3.55 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 173.2, 165.5, 163.9, 157.8, 149.4, 146.1, 135.1, 135.1, 133.8, 132.9, 129.8, 129.6, 129.5, 121.8, 121.8, 119.7, 115.9, 115.8, 115.7, 115.7, 115.4, 115.2, 111.8, 56.2, 56.2, 53.4, 53.3, 43.6, 43.3, 41.4, 40.7, 40.4, 39.6 ppm; IR (CHCl₃) ν 3319, 3026, 2252, 1750, 1709, 1684, 1602, 1511, 1479, 1385, 1244, 1228 cm⁻¹; MS (FAB⁺) 399 (MH⁺, 73), 135 (100); HRMS (FAB⁺) Calcd for [C₂₁H₂₀FN₂O₅]⁺: 399.1356; Found: 399.1358.

(3S)-4-Cyano-3-(4-fluorophenyl)butanoic acid methyl ester (12): $[\alpha]_D^{25}$ +6.68 (*c* 1.12, CH₃CN, 85% ee); HPLC [Chiralcel OJ-H, hexane/ethanol = 85/15, 0.5 mL/min, λ = 254 nm, retention times: (major) 89.1 min, (minor) 37.3 min].

(3S)-2-Cyano-5-(2-methoxybenzoylamino)-3-methyl-5-oxo-pentanoic acid methyl ester (9D): Colorless oil; $[\alpha]_D^{27}$ -3.90 (*c* 1.11, CHCl₃); ¹H NMR (500 MHz, CDCl₃) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 10.22 (s, 1H), 8.06 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.51-7.44 (m, 1H), 7.06-7.01 (m, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 4.03 (d, *J* = 4.3 Hz, 1H),

3.95 (s, 3H), 3.76 (s, 3H), 3.07 (d, $J = 6.1$ Hz, 2H), 2.88-2.78 (m, 1H), 1.11 (d, $J = 6.7$ Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.6, 173.5, 166.2, 165.9, 163.8, 163.7, 157.7, 135.0, 134.9, 132.8, 121.7, 119.8, 119.8, 115.6, 115.0, 111.7, 56.1, 53.3, 53.2, 42.5, 42.2, 41.5, 30.7, 30.0, 18.0, 16.7 ppm; IR (CHCl_3) ν 3323, 3023, 2360, 2252, 1749, 1709, 1684, 1480 cm^{-1} ; MS (FAB^+) 319 (MH^+ , 100); HRMS (FAB^+) Calcd for $[\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_5]^+$: 319.1294; Found: 319.1295.

(3S)-2-Cyano-3-methylpentanedioic acid dimethyl ester (9D'): Colorless oil; $[\alpha]_{\text{D}}^{23} -16.98$ (c 1.17, CHCl_3); ^1H NMR (500 MHz, CDCl_3) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 3.93 (d, $J = 6.3$ Hz, 1H), 3.78 (s, 3H), 3.66 (s, 3H), 2.76-2.68 (m, 1H), 2.58-2.34 (m, 2H), 1.07 (d, $J = 7.0$ Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 171.7, 171.6, 165.9, 165.7, 115.2, 114.8, 53.4, 53.4, 51.8, 42.7, 42.5, 38.0, 37.3, 31.3, 30.7, 18.0, 16.6 ppm; IR (CHCl_3) ν 3028, 2955, 1747, 1439 cm^{-1} ; MS (FAB^+) 200 (MH^+ , 12), 154 (100); HRMS (FAB^+) Calcd for $[\text{C}_9\text{H}_{14}\text{NO}_4]^+$: 200.0923; Found: 200.0926.

(3S)-4-Cyano-3-methylbutanoic acid methyl ester (12D): Colorless oil; $[\alpha]_{\text{D}}^{26} -20.39$ (c 2.28, CHCl_3 , 92% ee); ^1H NMR (500 MHz, CDCl_3) δ 3.70 (s, 3H), 2.49-2.35 (m, 5H), 1.16 (d, $J = 5.8$ Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 172.1, 118.2, 51.8, 39.4, 27.4, 23.8, 19.4 ppm; IR (CHCl_3) ν 3025, 2251, 1734 cm^{-1} ; MS (CI^+) 142 (MH^+ , 100); HPLC [Chiralcel AS-H, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda = 210$ nm, retention times: (major) 27.0 min, (minor) 25.8 min].

(3S)-8-tert-Buthyldimethylsilanyloxy-2-cyano-3-[2-(2-methoxybenzoylamino)-2-oxoethyl]octanoic acid methyl ester (9E): Colorless oil; $[\alpha]_{\text{D}}^{25} -9.82$ (c 1.67, CHCl_3); ^1H NMR (500 MHz, CDCl_3) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 10.27 (s, 1H), 8.09 (dd, $J = 8.0$ Hz, 1H), 7.52 (t, $J = 7.3$ Hz, 1H), 7.08 (t, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 8.2$ Hz, 1H), 4.12 (d, $J = 3.9$ Hz, 1H), 3.98 (s, 3H), 3.77 (s, 3H), 3.55 (t, $J = 4.8$ Hz, 2H), 3.28-2.98 (m,

2H), 2.78-2.69 (m, 1H), 1.58-1.51 (m, 2H), 1.49-1.42 (m, 2H), 1.37-1.25 (m, 4H), 0.84 (s, 9H), 0.01 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 174.0, 173.6, 166.3, 166.2, 163.8, 163.6, 163.4, 157.6, 134.9, 134.9, 132.7, 121.6, 119.8, 119.7, 115.4, 115.3, 113.0, 111.7, 111.7, 62.9, 62.8, 56.1, 53.4, 53.2, 41.7, 40.9, 39.7, 39.5, 35.2, 34.5, 32.4, 32.3, 31.2, 26.6, 25.8, 25.5, 25.4, 24.3, 18.1, -5.5 ppm; IR (CHCl_3) ν 3323, 2933, 1753, 1709, 1684, 1479 cm^{-1} ; MS (FAB^+) 505 (MH^+ , 28); HRMS (FAB^+) Calcd for $[\text{C}_{26}\text{H}_{41}\text{N}_2\text{O}_6\text{Si}]^+$: 505.2734; Found: 505.2748.

(3S)-2-Cyano-3-(5-hydroxypentyl)pentanedioic acid dimethyl ester (9E'): Colorless oil; $[\alpha]_{\text{D}}^{22}$ -12.40 (c 1.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3) (3:2 mixture of diastereomers, with signals corresponding to the major indicated by) δ 4.06 (d, J = 7.0 Hz, 1H), 3.78 (s, 3H), 3.66 (s, 3H), 3.59-3.54 (m, 2H), 2.64-2.59 (m, 1H), 2.54-2.35 (m, 2H), 1.74 (s, 1H), 1.55-1.46 (m, 4H), 1.40-1.30 (m, 4H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 172.1, 171.9, 166.1, 115.0, 62.5, 60.3, 53.4, 51.9, 51.8, 41.6, 41.0, 35.8, 35.7, 35.3, 35.3, 32.2, 231.1, 26.4, 26.2, 25.4, 25.3, 20.9, 14.0 ppm; IR (CHCl_3) ν 3021, 1747, 1711, 1362 cm^{-1} ; MS (FAB^+) 272 (MH^+ , 100); HRMS (FAB^+) Calcd for $[\text{C}_{13}\text{H}_{22}\text{NO}_5]^+$: 272.1498; Found: 272.1492.

(3S)-3-Cyanomethyl-8-hydroxyoctanoic acid methyl ester (12E): Colorless oil; $[\alpha]_{\text{D}}^{28}$ -10.41 (c 3.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 3.63 (s, 3H), 3.56 (t, J = 6.4 Hz, 2H), 2.44 (d, J = 5.8 Hz, 2H), 2.40 (dd, J = 11.3, 5.5 Hz, 1H), 2.33 (dd, J = 13.1, 8.2 Hz, 1H), 2.19-2.13 (m, 1H), 1.75 (s, 1H), 1.55-1.48 (m, 2H), 1.44-1.38 (m, 2H), 1.35-1.27 (m, 4H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 172.3, 118.1, 62.5, 51.7, 37.4, 33.2, 32.3, 31.8, 26.2, 25.4, 21.5 ppm; IR (CHCl_3) ν 3021, 2360, 1732, 1439 cm^{-1} ; MS (FAB^+) 214 (MH^+ , 98), 154 (100); HRMS (FAB^+) Calcd for $[\text{C}_{11}\text{H}_{20}\text{NO}_3]^+$: 214.1443; Found: 214.1442.

(3S)-Benzoic acid 7-cyano-6-methoxycarbonylmethylheptylester (12E'): To a solution of **12E** (29.5 mg, 0.138 mmol) in CH_2Cl_2 (0.28 mL) at 0 $^\circ\text{C}$ were added pyridine (1.5 equiv., 0.017 mL) and BzCl (1.5 equiv., 0.024 mL) and the solution was stirred at room temperature for 4 h. Then the

reaction mixture was extracted with CHCl_3 , dried over MgSO_4 and purified by column chromatography (Hexane/AcOEt = 4/1) to afford desired product **12E'** (39.5 mg, 90%). Colorless oil; $[\alpha]_{\text{D}}^{22} -4.92$ (*c* 2.21, CHCl_3 , 92% ee); ^1H NMR (500 MHz, CDCl_3) δ 8.05 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 4.32 (t, *J* = 6.7 Hz, 2H), 3.69 (s, 3H), 2.51 (dd, *J* = 5.7, 2.1 Hz, 2H), 2.48 (dd, *J* = 12.1, 5.5 Hz, 1H), 2.40 (dd, *J* = 16.5, 7.9 Hz, 1H), 2.26-2.19 (m, 1H), 1.83-1.75 (m, 2H), 1.55-1.45 (m, 4H), 1.44-1.37 (m, 2H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 172.2, 166.6, 132.9, 130.3, 129.5, 128.3, 118.0, 64.7, 51.7, 37.4, 33.1, 31.8, 28.4, 26.2, 25.8, 21.6 ppm; IR (CHCl_3) ν 3021, 1711, 1436, 1419 cm^{-1} ; MS (FAB^+) 318 (MH^+ , 40), 105 (100); HRMS (FAB^+) Calcd for $[\text{C}_{18}\text{H}_{24}\text{NO}_4]^+$: 318.1705; Found: 318.1707. HPLC [Chiralcel AS-H, hexane/2-propanol = 80/20, 0.5 mL/min, λ = 254 nm, retention times: (major) 54.9 min, (minor) 31.0 min].

Typical procedure for enantioselective Michael addition of nitromethane to α,β -unsaturated imides catalyzed by thiourea. A solution of **7A** (120 mg, 0.43 mmol), nitromethane **2c** (40 equiv., 1.0 mL), and thiourea **1a** (0.1 equiv., 18 mg) in dry toluene (0.86 ml) was stirred at 60 °C for 168 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (3/1) to afford desired Michael adduct **10A** (102 mg, 56%).

(3S)-2-Methoxy-N-(4-nitro-3-phenylbutyryl)benzamide (10A): White solid; $[\alpha]_{\text{D}}^{29} -46.0$ (*c* 1.14, CHCl_3 , 87% ee) M.p. 115-117 °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.29 (s, 1H), 8.15 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.56 (td, *J* = 7.9, 1.8 Hz, 1H), 7.37-7.31 (m, 4H), 7.29-7.24 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 4.81 (dd, *J* = 12.5, 6.4 Hz, 1H), 4.69 (dd, *J* = 12.5, 8.5 Hz, 1H), 4.23-4.15 (m, 1H), 4.00 (s, 3H), 3.56 (dd, *J* = 17.9, 6.8 Hz, 1H), 3.43 (dd, *J* = 17.6, 7.4 Hz, 1H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.1, 164.0, 157.8, 139.1, 135.1, 132.9, 129.0, 127.8, 127.6, 121.8, 119.8, 111.8, 79.6, 56.2, 41.5, 39.4 ppm; IR (CHCl_3) ν 3320, 3024, 1710, 1684, 1555, 1479, 1379 cm^{-1} ; Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_5$: C, 63.15; H, 5.30; N, 8.18; Found: C, 63.34; H, 5.37; N, 8.13; HPLC [Chiralcel OD-H, hexane/2-propanol = 80/20, 0.5 mL/min, λ = 254 nm, retention times: (major) 92.4 min, (minor) 63.4 min].

10B

(3S)-2-Methoxy-N-[3-(4-fluorophenyl)-4-nitrobutyryl]benzamide (10B): White solid; $[\alpha]_D^{23}$ -30.2 (c 1.03, CHCl_3 , 86% ee) M.p. $132\text{--}134$ °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.31 (s, 1H), 8.14 (dd, $J = 7.8, 1.9$ Hz, 1H), 7.56 (td, $J = 7.7, 1.8$ Hz, 1H), 7.35–7.26 (m, 2H), 7.13 (t, $J = 8.0$ Hz, 1H), 7.05–6.98 (m, 2H), 4.80 (dd, $J = 12.5, 6.1$ Hz, 1H), 4.65 (dd, $J = 12.7, 8.5$ Hz, 1H), 4.23–4.15 (m, 1H), 4.00 (s, 3H), 3.52 (dd, $J = 17.7, 7.0$ Hz, 1H), 3.40 (dd, $J = 17.9, 7.3$ Hz, 1H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.0, 164.1, 157.8, 135.2, 134.7, 132.9, 129.3, 121.8, 119.6, 116.0, 115.8, 111.8, 79.6, 56.2, 41.5, 38.7 ppm; IR (CHCl_3) ν 3319, 3026, 1710, 1684, 1555, 1511, 1479, 1290 cm^{-1} ; Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{FN}_2\text{O}_3$: C, 60.00; H, 4.76; N, 7.77; F, 5.27; Found: C, 59.87; H, 4.69; N, 7.77; F, 5.25; HPLC [Chiralcel OD-H, hexane/2-propanol = 80/20, 0.5 mL/min, $\lambda = 254$ nm, retention times: (major) 72.4 min, (minor) 84.7 min].

10D

(3S)-2-Methoxy-N-(3-methyl-4-nitro-butyl)benzamide (10D): White solid; $[\alpha]_D^{26}$ $+2.88$ (c 1.09, CHCl_3 , 83% ee) M.p. $82\text{--}83$ °C (Hexane/AcOEt); ^1H NMR (500 MHz, CDCl_3) δ 10.32 (s, 1H), 8.16 (d, $J = 8.0$, 1H), 7.57 (t, $J = 8.2$ Hz, 1H), 7.13 (t, $J = 7.3$ Hz, 1H), 7.04 (d, $J = 8.3$ Hz, 1H), 4.57 (dd, $J = 15.3, 5.5$ Hz, 1H), 4.39 (dd, $J = 11.9, 7.6$ Hz, 1H), 4.04 (s, 3H), 3.17–3.09 (m, 2H), 3.01–2.94 (m, 1H), 1.17 (d, $J = 7.0$ Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 173.7, 163.9, 157.7, 135.0, 132.9, 121.8, 119.9, 111.7, 80.4, 56.2, 41.7, 28.7, 17.5 ppm; IR (CHCl_3) ν 3324, 3025, 1709, 1685, 1552, 1480 cm^{-1} ; MS (FAB^+) 281 (MH^+ , 71), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_5]^+$: 281.1137; Found: 281.1135. HPLC [Chiralcel AS-H, hexane/2-propanol = 50/50, 1.0 mL/min, $\lambda = 254$ nm, retention times: (major) 19.9 min, (minor) 13.4 min].

10E

(3S)-N-[8-(tert-Butyldimethylsilyloxy)-3-nitromethyloctanoyl]-2-methoxybenzamide (10E): Colorless oil; $[\alpha]_D^{22}$ -6.89 (c 3.90, CHCl_3 , 80% ee); ^1H NMR (500 MHz, CDCl_3) δ 10.26 (s,

1H), 8.12 (dd, $J = 7.9, 1.8$ Hz, 1H), 7.52 (td, $J = 7.9, 1.8$ Hz, 1H), 7.09 (t, $J = 8.2$ Hz, 1H), 6.99 (d, $J = 8.3$ Hz, 1H), 4.52 (dd, $J = 12.1, 6.1$ Hz, 1H), 4.46 (dd, $J = 12.1, 6.1$ Hz, 1H), 3.99 (s, 3H), 3.55 (t, $J = 6.4$ Hz, 2H), 3.14-3.02 (m, 2H), 2.80-2.73 (m, 1H), 1.52-1.43 (m, 4H), 1.40-1.29 (m, 4H), 0.84 (s, 9H), 0.01 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3) δ 174.0, 163.9, 157.8, 135.0, 132.9, 121.8, 120.0, 111.7, 78.6, 65.8, 63.0, 56.2, 39.7, 33.4, 32.5, 31.6, 25.9, 18.3, 15.2, -5.4 ppm; IR (CHCl_3) ν 3324, 2933, 1709, 1684, 1600, 1551, 1479 cm^{-1} ; MS (FAB^+) 467 (MH^+ , 10), 135 (100); HRMS (FAB^+) Calcd for $[\text{C}_{23}\text{H}_{39}\text{N}_2\text{O}_6\text{Si}]^+$: 467.2577; Found: 467.2575. HPLC [Chiralcel AD-H, hexane/ethanol = 95/5, 0.5 mL/min, $\lambda = 254$ nm, retention times: (major) 25.7 min, (minor) 27.8 min].

11

(3S)-4,4-Dicyano-3-(4-fluorophenyl)butanoic acid methyl ester (11)⁴: To a stirred solution of **8B** (35 mg, 0.096 mmol) in MeOH (0.35 mL) was added $\text{Er}(\text{OTf})_3$ (0.10 equiv., 6.0 mg) at room temperature. After 3 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (Hexane/AcOEt = 2/1) to afford desired product **11** (23mg, 96%). Colorless oil; $[\alpha]_{\text{D}}^{24} +17.3$ (c 1.24, CHCl_3)

13

(3S)-4-Nitro-3-phenylbutanoic acid methyl ester (13)⁵: To a stirred solution of **10B** (5.0 mg, 0.015 mmol) in MeOH (0.10 mL) was added $\text{Er}(\text{OTf})_3$ (0.10 equiv., 1.0 mg) at room temperature. After 90 min, the reaction mixture was concentrated *in vacuo* and the residue was purified by column chromatography (Hexane/AcOEt = 3/2) to afford desired product **13** (2.1mg, 64%). Colorless oil; $[\alpha]_{\text{D}}^{29} -13.3$ (c 0.21, CHCl_3).

14A

(3R)-4,4-Dicyano-3-phenylbutyric acid methyl ester (14A): A solution of **8A** (33 mg, 0.086 mmol) and thiourea **1a** (0.1 equiv., 4.0 mg) in dry methanol (0.17 mL) was stirred at room

temperature for 24 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (3/2) to afford desired product **14A** (17.4 mg, 87%). Colorless oil; $[\alpha]_D^{20} +20.1$ (*c* 1.51, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.39 (m, 3H), 7.38-7.34 (m, 2H), 4.50 (d, *J* = 5.5 Hz, 1H), 3.78-3.68 (m, 1H), 3.71 (s, 3H), 3.07 (dd, *J* = 17.1, 8.6 Hz, 1H), 2.96 (dd, *J* = 17.1, 6.1 Hz, 1H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 170.8, 135.7, 129.3, 129.3, 127.7, 111.6, 111.3, 52.4, 42.1, 35.9, 28.8 ppm; IR (CHCl₃) ν 3027, 2360, 1733, 1440, 1216 cm⁻¹; MS (FAB⁺) 229 (MH⁺, 55), 154 (100); HRMS (FAB⁺) Calcd for [C₁₃H₁₃N₂O₂]⁺: 229.0977; Found: 229.0975.

(3R)-4,4-Dicyano-3-phenylbutyric acid benzyl ester (14B): A solution of **8A** (64 mg, 0.184 mmol) and thiourea **1a** (0.1 equiv., 8.0 mg) in benzylalcohol (0.37 ml) was stirred at room temperature for 88 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (5/2) to afford desired product **14B** (49.7 mg, 89%). Yellow oil; $[\alpha]_D^{20} +14.9$ (*c* 1.33, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.43-7.38 (m, 3H), 7.36-7.33 (m, 5H), 7.28-7.25 (m, 2H), 5.11 (s, 2H), 4.45 (d, *J* = 5.5 Hz, 1H), 3.73 (q, *J* = 6.4 Hz, 1H), 3.11 (dd, *J* = 16.9, 8.5 Hz, 1H), 3.00 (dd, *J* = 16.9, 6.5 Hz, 1H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 170.3, 135.6, 135.0, 129.4, 129.4, 128.7, 128.6, 128.4, 127.8, 111.5, 111.3, 67.3, 42.2, 36.1, 28.8 ppm; IR (CHCl₃) ν 3031, 2913, 1730, 1498, 1455, 1389, 1172 cm⁻¹; MS (FAB⁻) 303 (MH⁻, 100); HRMS (FAB⁻) Calcd for [C₁₉H₁₅N₂O₂]⁻: 303.1134; Found: 303.1135.

(3R)-N-Benzyl-4,4-dicyano-3-phenylbutyramide (14C): A solution of **8A** (33 mg, 0.086 mmol), benzylamine (2.0 equiv., 21L), and thiourea **1a** (0.1 equiv., 4.0 mg) in dry toluene (0.17 ml) was stirred at room temperature for 3 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (5/2) to afford desired amide **14C** (20.0 mg, 77%). Colorless amorphous; $[\alpha]_D^{20} -2.45$ (*c* 2.12, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.44-7.25 (m, 8H), 7.12 (dd, *J* = 7.2, 1.5 Hz, 2H), 5.98 (s, 1H), 4.75 (d, *J* = 5.5 Hz, 1H), 4.40 (dd, *J* = 14.8, 6.1 Hz, 1H), 4.33 (dd, *J* = 14.7, 5.5 Hz, 1H), 3.82-3.75 (m, 1H), 2.90 (dd, *J* = 15.7, 8.5 Hz, 1H), 2.75 (dd, *J* = 15.7, 5.8 Hz, 1H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 168.9, 137.3, 136.1, 129.3, 129.2, 128.8, 127.8, 127.8, 127.6, 111.9, 111.8, 43.7, 42.4, 37.7, 28.5 ppm; IR (CHCl₃) ν 3439, 3028, 2360, 1671, 1518 cm⁻¹; MS (FAB⁺) 304 (MH⁺, 100); HRMS (FAB⁺) Calcd for [C₁₉H₁₈N₃O]⁺: 304.145; Found:

304.1453;

(3R)-4,4-Dicyano-N-methoxy-N-methyl-3-phenylbutyramide (14D): A solution of **8A** (214 mg, 0.288 mmol), 3.8 M solution of *N,O*-dimethylhydroxylamine in toluene⁶ (3.0 equiv., 0.5 mL), and thiourea **1a** (0.1 equiv., 26 mg) in dry toluene (0.4 mL) was stirred at 60 °C for 20 h. After concentrated *in vacuo*, the reaction mixture was purified by silica gel column chromatography with Hexane/AcOEt (3/2) to afford desired Weinreb amide **14D** (119 mg, 75%). Yellow oil; $[\alpha]_D^{24} +8.93$ (*c* 1.08, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.37 (m, 5H), 4.81 (d, *J* = 5.2 Hz, 1H), 3.76 (qn, *J* = 4.8 Hz, 1H), 3.68 (s, 3H), 3.19 (s, 3H), 3.16-3.00 (m, 2H) ppm; ¹³C NMR (126 MHz, CDCl₃) δ 170.4, 136.5, 129.2, 129.0, 128.0, 112.0, 111.8, 61.3, 41.5, 33.6, 32.0, 28.4 ppm; IR (CHCl₃) ν 3028, 1654, 1457, 1218 cm⁻¹; MS (FAB⁺) 258 (MH⁺, 100); HRMS (FAB⁺) Calcd for [C₁₄H₁₆N₃O₂]⁺: 258.1243; Found: 258.1249.

- (1) (a) Sibi, M. P.; Chen, J. *J. Am. Chem. Soc.* 2001, *123*, 9472-9473. (b) Soloshonok, V. A.; Cai, C.; Hruby, V. J.; Meervelt, L. V.; Yamazaki, T. *J. Org. Chem.* 2000, *65*, 6688-6696. (c) Ishihara, H.; Hori, K.; Sugihara, H.; Ito, Y. N.; Katsuki, T. *Helvetica Chimica Acta* 2002, *85*, 4272-4286
- (2) Powers, T. S.; Wulff, W. D.; Quinn, J.; Shi, Y.; Jiang, W.; Hsung, R.; Parisi M.; Rahm, A.; Jiang, X. W.; Yap, G. P. A.; Rheingold, A. L. *Journal of Organometallic chemistry*. 2001, *617-618*, 182-208.
- (3) Wenzel, A. G.; Jacobsen, E. N. *Adv. Synth. Catal.* 2002, *344*, 9, 953-956.
- (4) Taylor, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* 2003, *125*, 11204-11205.
- (5) Felluga, F.; Gombac, V.; Pitacco, G.; Valentin, E. *Tetrahedron Asymmetry*. 2005, *16*, 1341-1345.
- (6) Yamaguchi, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* 2003, *125*, 16178-16179.