β -Isocupreidine-Catalyzed Asymmetric Baylis-Hillman Reaction of Imines

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General. Where appropriate, reactions were performed in flame-dried glassware under an argon atmosphere. All extracts were dried over MgSO_4 and concentrated by rotary evaporation below 30 °C at ca. 25 Torr. Analytical and preparative thin layer chromatography was performed with Merck F-254 TLC plates. Column chromatography was performed employing silica gel 60 (230-400 mesh ASTM, Merk). β -Isocupreidine (β -ICD) was dried by azeotropic removal of water with THF. Commercial 1,1,1,3,3,3-hexafluoroisopropyl acrylate (HFIPA) was used without further purification. *N,N*-dimethylformamide (DMF) was distilled from calcium hydride. Melting points were obtained with a Yanagimoto micro point apparatus and are uncorrected. Infrared spectra were measured on a JASCO FT/IR-230 spectrometer. Optical rotations were recorded on a JASCO DIP-370 polarimeter at ambient temperature. ^1H and ^{13}C NMR spectra were measured on a Varian Gemini 300 or a Varian Unity plus 500 spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) in d units and coupling constants are given in hertz. TMS was defined as 0 ppm for ^1H NMR spectra and the center line of the triplet of CDCl_3 was also defined as 77.10 ppm for ^{13}C NMR spectra. EI and FAB Mass spectra were measured on a JEOL JMS-DX303.

General procedures for β -ICD-catalyzed Baylis-Hillman reaction of imines with HFIPA and transformation of 1,1,1,3,3,3-hexafluoroisopropyl acrylates to the corresponding methyl acrylates. To a stirred solution of the imine¹ (1.0 mmol) and β -ICD (31.0 mg, 0.10 mmol) in DMF (1.0 ml) at –55 °C was added HFIPA (0.22 ml, 1.3 mmol). After the reaction time indicated in the table, the reaction mixture was diluted with AcOEt and washed with 0.1M HCl, saturated NaHCO_3 , and saturated NaCl. The organic layer was dried, evaporated, and chromatographed to give the 1,1,1,3,3,3-hexafluoroisopropyl acrylate.

To a stirred solution of the 1,1,1,3,3,3-hexafluoroisopropyl acrylate (1.0 mmol) in MeOH (10 ml) at room temperature was added Et_3N (1.0 ml, 7.2 mmol) and the mixture was stirred for 30 min. The reaction mixture was acidified with DOWEX[®] 50WX8-200, stirred for 10 min, filtered, evaporated. Purification of the residue by column chromatography on silicagel gave the methyl acrylate, the enantiomeric excess of which was determined by HPLC analysis using a chiral column.

1,1,1,3,3,3-Hexafluoroisopropyl (*S*)-2-(Benzoylaminophenylmethyl)acrylate (2d). Compound **2d** (51.5 mg, 13% ee) was obtained as a colorless solid from **1d** (100 mg, 0.48 mmol) in 73% yield.

mp 131-134 °C; $[\alpha]_D^{19} +4.5^\circ$ (*c* 1.38, CHCl₃); FT-IR (film) 3290, 1757, 1643, 1529, 1385, 1292, 1122 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (d, *J* = 7.5 Hz, 2H), 7.53-7.50 (m, 1H), 7.46-7.41 (m, 2H), 7.38-7.25 (m, 5H), 7.06 (br d, *J* = 8.4 Hz, 1H), 6.63 (s, 1H), 6.26 (d, *J* = 8.4 Hz, 1H), 6.20 (s, 1H), 5.75 (hept, *J* = 6.0 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃) δ 166.4, 162.4, 138.3, 136.9, 133.6, 131.9, 131.0, 128.9, 128.6, 128.1, 127.0, 126.5, 120.2 (q, ¹*J*_{C,F} = 283.5 Hz), 66.6 (hept, ²*J*_{C,F} = 34.7 Hz), 54.7; HRMS (EI) calcd for C₂₀H₁₅F₆NO₃ (M⁺): 431.0956, found: 431.0957.

Methyl (S)-2-(Benzoylamino phenylmethyl)acrylate. The methyl ester (98 mg) was prepared as a colorless oil from **2d** in 94% yield. The enantiomeric purity was determined to be 13% ee by HPLC (CHIRALCEL OJ, 1:5 *i*-PrOH-hexane, 1.0 ml/min; *t*_R = 14.9 min (*R*), 24.4 min (*S*)). mp 93-95 °C; $[\alpha]_D^{18} -2.5^\circ$ (*c* 1.95, CHCl₃); FT-IR (film) 3307, 1718, 1643, 1525, 1444, 1298, 1147 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.84 (dd, *J* = 1.2, 8.1 Hz, 2H), 7.53-7.41 (m, 4H), 7.34-7.25 (m, 5H), 6.41 (s, 1H), 6.23 (d, *J* = 9.0 Hz, 1H), 6.02 (s, 1H), 3.71 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 166.3, 139.5, 138.8, 134.1, 131.7, 128.6, 128.6, 127.9, 127.6, 127.0, 126.3, 55.3, 52.0; HRMS (EI) calcd for C₁₈H₁₇NO₃ (M⁺): 295.1208, found: 295.1203.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-(Methanesufonylamino phenylmethyl)acrylate (2e).

Compound **2e** (222 mg, 66% ee) was obtained as a colorless oil from **1e** (100 mg, 0.55 mmol) in 100% yield. $[\alpha]_D^{19} +20.9^\circ$ (*c* 4.44, CHCl₃); FT-IR (film) 3282, 2972, 1761, 1631, 1346 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.30 (m, 5H), 6.65 (s, 1H), 6.27 (s, 1H), 5.72 (hept, *J* = 6.0 Hz, 1H), 5.55 (d, *J* = 8.7 Hz, 1H), 5.42 (d, *J* = 8.7 Hz, 1H), 2.87 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 162.1, 137.8, 131.2, 129.2, 128.7, 126.7, 120.2 (q, ¹*J*_{C,F} = 281.2 Hz), 66.9 (hept, ²*J*_{C,F} = 34.7 Hz), 58.4, 41.9; HRMS (EI) calcd for C₁₄H₁₃F₆NO₄S (M⁺): 405.0469, found: 405.0507.

Methyl (S)-2-(Methanesufonylamino phenylmethyl)acrylate. The methyl ester (147 mg) was prepared as a colorless oil from **2e** in 100% yield. The enantiomeric purity was determined to be 66% ee by HPLC (CHIRALCEL OJ, 1:5 *i*-PrOH-hexane, 1.0 ml/min; *t*_R = 38.3 min (*R*), 41.4 min (*S*)). $[\alpha]_D^{23} +9.63^\circ$ (*c* 2.9, CHCl₃); FT-IR (film) 3288, 1718, 1444, 1327, 1153, 1068 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.29 (m, 5H), 6.43 (s, 1H), 5.99 (s, 1H), 5.59 (d, *J* = 9.0 Hz, 1H), 5.48 (d, *J* = 9.0 Hz, 1H), 3.71 (s, 3H), 2.89 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 165.7, 139.5, 138.7, 128.6, 128.2, 127.8, 127.6, 126.6, 58.5, 52.1, 41.6; HRMS (EI) calcd for C₁₂H₁₅NO₄S (M⁺): 269.0722, found: 269.0723.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-(*p*-Toluenesufonylamino phenylmethyl)acrylate (2f).

Compound **2f** (137.4 mg, 46% ee) was obtained as a colorless solid from **1f** (100 mg, 0.39 mmol) in 74% yield. mp 87-89 °C; $[\alpha]_D^{18} +18.3^\circ$ (*c* 2.38, CHCl₃); FT-IR (film) 3278, 1753, 1236, 1163, 1122 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.68 (d, *J* = 8.7 Hz, 2H), 7.28-7.23 (m, 5H), 7.07-7.04 (m, 2H), 6.49 (s, 1H), 6.20 (s, 1H), 5.63 (hept, *J* = 6.0 Hz, 1H), 5.34 (d, *J* = 8.1 Hz, 1H), 5.22 (d, *J* = 8.1 Hz, 1H), 2.43 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 161.8, 143.7, 137.5, 137.0, 136.6, 131.1, 129.6, 128.7, 128.2, 127.1, 126.4, 120.1 (q, ¹*J*_{C,F} = 281.2 Hz), 66.6 (hept, ²*J*_{C,F} = 34.7 Hz), 58.1, 21.4; HRMS (EI) calcd for C₂₀H₁₇F₆NO₄S (M⁺): 481.0782, found: 481.0787.

Methyl (S)-2-(*p*-Toluenesufonylamino phenylmethyl)acrylate . The methyl ester (88 mg) was

prepared as a colorless oil from **2f** in 90% yield. The enantiomeric purity was determined to be 46% ee by HPLC (CHIRALCEL OJ, 1:5 *i*-PrOH-hexane, 1.0 ml/min; t_R = 20.7 min (*R*), 31.7 min (*S*)). $[\alpha]_D^{17} +11.7^\circ$ (*c* 1.8, CHCl₃) {lit.² +19.5° (83% ee), lit.³ +16.8° (68% ee)}; FT-IR (film) 3290, 3026, 2954, 1720, 1631, 1444, 1063 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.68 (d, *J* = 8.1 Hz, 2H), 7.25-7.22 (m, 5H), 7.16-7.13 (m, 2H), 6.22 (s, 1H), 5.83 (s, 1H), 5.67 (d, *J* = 9.0 Hz, 1H), 5.31 (d, *J* = 9.0 Hz, 1H), 3.60 (s, 3H), 2.41 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 165.8, 143.4, 138.6, 137.6, 129.5, 128.6, 127.9, 127.8, 127.3, 126.5, 59.0, 52.1, 21.6; HRMS (EI) calcd for C₁₇H₁₆NO₃S [(M-OMe)⁺]: 314.0851, found: 314.0848.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-(Diphenylphosphinoylamino)phenylmethyl)acrylate (2g).

Compound **2g** (1.67 g, 67% ee) was obtained as a colorless solid from **1g** (1.07 g, 3.50 mmol) in 90% yield. Recrystallization of this solid from 1:3 CH₂Cl₂-hexane gave **2g** of 95% ee in 66%. mp 192-193°C; $[\alpha]_D^{23} = +31.3^\circ$ (*c* 1.40, CHCl₃) (67% ee), $[\alpha]_D^{23} = +46.9^\circ$ (*c* 0.71, CHCl₃) (95% ee); FT-IR (film) 3207, 1749, 1444, 1385, 1282, 1126 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.90-7.80 (m, 4H), 7.54-7.39 (m, 6H), 7.32-7.24 (m, 5H), 6.57 (s, 1H), 6.23 (s, 1H), 5.65 (hept, *J* = 6.0 Hz, 1H), 5.18 (t, *J* = 10.8 Hz, 1H), 3.93 (dd, *J* = 10.8, 8.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 162.2, 140.1, 140.0, 138.9, 138.9, 132.9, 132.5, 132.2, 132.1, 132.0, 131.9, 131.2, 130.8, 130.7, 128.7, 128.7, 128.5, 128.5, 128.4, 127.7, 126.4, 122.1 (q, ¹*J*_{C,F} = 283.4 Hz), 66.5 (hept, ²*J*_{C,F} = 34.7 Hz), 56.4, 30.8 ppm; HRMS (EI) calcd for C₂₅H₂₀F₆NO₃P (M⁺): 527.1085, found: 527.1104.

Methyl (S)-2-(Diphenylphosphinoylamino)phenylmethyl)acrylate . The methyl ester (42 mg) was prepared as a pale yellow solid from **2g** in 87% yield. The enantiomeric purity was determined to be 67% ee by HPLC (CHIRALCEL OJ, 1:5 *i*-PrOH-hexane, 0.5 ml/min; t_R = 15.7 min (*R*), 23.5 min (*S*)). mp 153-155 °C; $[\alpha]_D^{23} +17.8^\circ$ (*c* 0.84, CHCl₃); FT-IR (film) 3168, 1718, 1522, 1344, 1190 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.93-7.84 (m, 4H), 7.50-7.22 (m, 11H), 6.34 (s, 1H), 5.89 (s, 1H), 5.09 (t, *J* = 11.1 Hz, 1H), 4.31 (dd, *J* = 11.1, 8.4 Hz, 1H), 3.62 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.2, 141.2, 141.0, 133.0, 132.4, 132.2, 132.1, 132.0, 128.7, 128.6, 128.5, 128.4, 127.4, 127.1, 126.5, 57.2, 51.9; HRMS (EI) calcd for C₂₃H₂₂NO₃P (M⁺): 391.1337, found: 391.1347.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-[(Diphenylphosphinoylamino)(*p*-methoxyphenyl)methyl]acrylate (2h). Compound **2h** (70.0 mg, 73% ee) was obtained as a colorless solid from **1h** (101 mg, 0.30 mmol) in 42% yield. Recrystallization of this solid from 1:5 AcOEt-hexane gave **2h** of 96% ee in 76%. mp 158-160°C; $[\alpha]_D^{21} +37.7^\circ$ (*c* 1.40, CHCl₃) (73% ee), $[\alpha]_D^{23} +51.2^\circ$ (*c* 0.83, CHCl₃) (96% ee); FT-IR (film) 3178, 1751, 1240, 1190, 1115 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.90-7.81 (m, 4H), 7.56-7.40 (m, 6H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.55 (s, 1H), 6.23 (s, 1H), 5.66 (hept, *J* = 6.0 Hz, 1H), 5.14 (t, *J* = 10.5 Hz, 1H), 3.78 (s, 3H), 3.75 (dd, *J* = 10.5, 8.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 162.3, 159.1, 139.1, 133.0, 132.6, 132.2, 132.1, 131.9, 131.2, 130.8, 130.3, 128.7, 128.6, 128.5, 128.4, 127.6, 120.2 (q, ¹*J*_{C,F} = 278.0 Hz), 114.1, 66.5 (hept, ²*J*_{C,F} = 34.7 Hz), 55.9, 55.3 ppm; HRMS (EI) calcd for C₂₆H₂₂F₆NO₄P (M⁺): 557.1190, found: 557.1177.

Methyl (S)-2-[(Diphenylphosphinoylamino)(*p*-methoxyphenyl)methyl]acrylate. The methyl

ester (22 mg) was prepared as a colorless solid from **2h** in 86% yield. The enantiomeric purity was determined to be 73% ee by HPLC (CHIRALCEL OJ, 1:5 *i*-PrOH-hexane, 0.5 ml/min; t_R = 17.1 min (*R*), 20.9 min (*S*)). mp 133-135°C; $[\alpha]_D^{23}$ = +37.7° (*c* 0.43, CHCl₃); FT-IR (film) 3182, 1718, 1512, 1442, 1255, 1190, 1117, 1074 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.87 (br t, *J* = 8.4 Hz, 4H), 7.48-7.28 (m, 6H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.32 (s, 1H), 5.90 (s, 1H), 5.10 (t, *J* = 11.1 Hz, 1H), 4.34 (d, *J* = 11.1 Hz, 1H), 3.74 (s, 3H), 3.60 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.0, 158.5, 141.1, 141.0, 133.2, 133.1, 132.8, 132.1, 132.0, 131.9, 131.8, 131.7, 131.5, 131.1, 128.4, 128.3, 128.2, 128.1, 127.5, 126.4, 113.6, 56.3, 55.0, 51.6; HRMS (EI) calcd for C₂₄H₂₄NO₄P (M⁺): 421.1443, found: 421.1445.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-[(Diphenylphosphinoylamino)(*p*-nitrophenyl)methyl]acrylate (2i). Compound **2i** (790 mg, 54% ee) was obtained as a colorless solid from **1i** (500 mg, 1.43 mmol) in 97% yield. Recrystallization of this solid from 1:2 AcOEt-hexane followed by concentration of the mother liquor gave **2i** of 93% ee in 59%. mp 206-208 °C; $[\alpha]_D^{25}$ +28.3° (*c* 1.17, CHCl₃) (54% ee), $[\alpha]_D^{24}$ +53.2° (*c* 1.02, CHCl₃) (93% ee); FT-IR (film) 3143, 1751, 1523, 1352, 1194, 1120 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.13 (d, *J* = 8.4 Hz, 2H), 7.85-7.78 (m, 4H), 7.53 (d, *J* = 9.0 Hz, 4H), 7.47-7.41 (m, 4H), 6.63 (s, 1H), 6.25 (s, 1H), 5.67 (hept, *J* = 6.0 Hz, 1H), 5.25 (t, *J* = 11.1 Hz, 1H), 4.39 (dd, *J* = 11.1, 8.7 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 161.9, 147.4, 147.3, 137.8, 132.4, 132.2, 132.1, 132.0, 131.9, 131.7, 130.4, 130.2, 128.8, 128.7, 128.6, 128.5, 127.5, 123.8, 120.0 (q, ¹*J*_{C,F} = 282.3 Hz), 66.6 (hept, ²*J*_{C,F} = 34.7 Hz), 56.0; HRMS (EI) calcd for C₂₅H₁₉F₆N₂O₅P (M⁺): 572.0935, found: 572.0940.

Methyl (S)-2-[(Diphenylphosphinoylamino)(*p*-nitrophenyl)methyl]acrylate. The methyl ester (190 mg) was prepared as a colorless solid from **2i** in 77% yield. The enantiomeric purity was determined to be 54% ee by HPLC (CHIRALCEL OD-H, 1:5 *i*-PrOH-hexane, 0.5 ml/min; t_R = 23.6 min (*R*), 31.9 min (*S*)). mp 179-181°C; $[\alpha]_D^{23}$ = +29.1° (*c* 1.264, CHCl₃); FT-IR (neat) ν 3174, 1720, 1522, 1444, 1346, 1078 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 8.16 (d, *J* = 9.0 Hz, 2H), 7.91-7.82 (m, 4H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.53-7.41 (m, 6H), 6.39 (s, 1H), 5.89 (s, 1H), 5.14 (t, *J* = 11.1 Hz, 1H), 4.51 (dd, *J* = 11.1, 9.0 Hz, 1H), 3.66 (s, 3H) ppm; ¹³C-NMR (75 MHz, CDCl₃) δ 165.8, 148.5, 148.5, 147.1, 139.8, 139.7, 132.7, 132.6, 132.2, 132.2, 132.1, 132.0, 131.8, 131.0, 130.9, 128.8, 128.7, 128.6, 128.5, 128.3, 127.4, 123.6, 57.1, 52.1 ppm; HRMS (EI) calcd for C₂₃H₂₁N₂O₅P (M⁺): 436.1188, found: 436.1184.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-[(Diphenylphosphinoylamino)(1-naphthyl)methyl]acrylate (2j). Compound **2j** (45.5 mg, 72% ee) was obtained as a colorless solid from **1j** (35.5 mg, 0.10 mmol) in 79 % yield. Recrystallization of this solid from 3:4 AcOEt-hexane followed by concentration of the mother liquor gave **2j** of 100% ee in 50%. mp 180-182 °C; $[\alpha]_D^{24}$ +3.6° (*c* 0.73, CHCl₃) (72% ee), $[\alpha]_D^{24}$ +6.4° (*c* 1.08, CHCl₃) (100% ee); FT-IR (film) 3161, 1753, 1441, 1387, 1194, 1119 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.86-7.75 (m, 7H), 7.53-7.35 (m, 10H), 6.70 (s, 1H), 6.57 (s, 1H), 6.01 (t, *J* = 9.6 Hz, 1H), 5.58 (hept, *J* = 6.1 Hz, 1H), 3.58 (br t, *J* = 9.6 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 162.4, 139.8, 136.5, 134.0, 132.8, 132.4, 132.3, 132.2, 132.1, 131.9,

131.8, 131.1, 130.5, 130.2, 129.0, 128.7, 128.6, 128.4, 126.5, 126.0, 125.1, 124.2, 123.1, 120.1 (q, $^1J_{\text{C,F}} = 278.9$ Hz), 66.5 (hept, $^2J_{\text{C,F}} = 33.8$ Hz), 51.6; HRMS (EI) calcd for $\text{C}_{29}\text{H}_{22}\text{F}_6\text{NO}_3\text{P}$ (M^+): 577.1241, found: 577.1264.

Methyl (S)-2-[(Diphenylphosphinoylamino)(1-naphthyl)methyl]acrylate. The methyl ester (30.5 mg) was prepared as a colorless solid from **2j** in 88% yield. The enantiomeric purity was determined to be 72% ee by HPLC (CHIRALCEL OD-H, 1:5 *i*-PrOH-hexane, 0.5 ml/min; $t_{\text{R}} = 14.0$ min (*R*), 16.6 min (*S*)). mp 145-147°C; $[\alpha]_{\text{D}}^{23} = +2.28^\circ$ (*c* 0.614, CHCl_3); FT-IR (film) 3178, 2962, 1718, 1441, 1261, 1192, 1119 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.87-7.75 (m, 7H), 7.60 (d, $J = 6.9$ Hz, 1H), 7.51-7.30 (m, 9H), 6.40 (s, 1H), 6.09 (s, 1H), 6.02 (t, $J = 9.9$ Hz, 1H), 3.86 (dd, $J = 9.9$, 8.4 Hz, 1H), 3.56 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.4, 142.0, 137.2, 137.1, 133.9, 133.4, 132.3, 132.0, 131.9, 131.7, 130.7, 130.3, 128.7, 128.5, 128.3, 126.8, 126.2, 125.7, 125.2, 124.4, 123.4, 52.1, 51.9; HRMS (EI) calcd for $\text{C}_{27}\text{H}_{24}\text{NO}_3\text{P}$ (M^+): 441.1494, found: 441.1492.

1,1,1,3,3,3-Hexafluoroisopropyl (S)-2-[(Diphenylphosphinoylamino)(2-naphthyl)methyl]acrylate (2k). Compound **2k** (9.0 mg) was prepared as a colorless solid from **1k** (35.5 mg, 0.10 mmol) in 16% yield. mp 198-200 °C; FT-IR 3199, 1747, 1236, 1192, 1101 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.93-7.76 (m, 7H), 7.69 (s, 1H), 7.55-7.42 (m, 9H), 6.64 (s, 1H), 6.31 (s, 1H), 5.63 (hept, $J = 6.0$ Hz, 1H), 5.36 (t, $J = 10.5$ Hz, 1H), 3.91 (dd, $J = 10.5$, 8.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 162.4, 139.0, 138.9, 137.7, 137.6, 133.3, 133.0, 132.9, 132.6, 132.4, 132.3, 132.2, 132.1, 131.3, 131.0, 128.9, 128.8, 128.7, 128.6, 128.1, 127.7, 126.5, 126.4, 125.3, 124.7, 120.2 (q, $^1J_{\text{C,F}} = 282.3$ Hz), 66.7 (hept, $^2J_{\text{C,F}} = 34.7$ Hz), 56.6 ppm; HRMS (EI) calcd for $\text{C}_{29}\text{H}_{22}\text{F}_6\text{NO}_3\text{P}$ (M^+): 577.1241, found: 577.1253.

Transformation of acrylates 2d-g to the corresponding α -amino acid methyl esters. To a solution of the 1,1,1,3,3,3-hexafluoroisopropyl acrylate (0.16 mmol) in THF (0.55 ml) was added 1M KOH (0.38 ml) and the mixture was stirred at room temperature overnight. The reaction mixture was acidified with 1M HCl, extracted with Et_2O , dried, and evaporated. The residue was dissolved in 1:1 MeCN/ H_2O (1.3 ml) and NaClO_2 (0.80 mmol) and $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (0.02 mmol) were added. After stirring for 15 min at room temperature, the reaction mixture was diluted with CH_2Cl_2 , washed with H_2O , dried, and evaporated. The residue was dissolved in Et_2O (1 ml) and ethereal CH_2N_2 was added at 0 °C until the solution became yellow. The mixture was evaporated and purified by preparative TLC (1:1 AcOEt-hexane) gave the α -amino acid methyl ester.

Methyl (S)-2-Benzoylamino-2-phenylacetate. This compound (49.6 mg) was prepared as a colorless solid from **2d** in 56% yield. mp 86-87°C; $[\alpha]_{\text{D}}^{20} = +12.9^\circ$ (*c* 0.99, CHCl_3); FT-IR (film) 3319, 3062, 2952, 1751, 1668, 1348, 1097, 1001 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.03 (d, $J = 8.1$ Hz, 2H), 7.74-7.51 (m, 8H), 7.44 (br s, 1H), 5.99 (d, $J = 7.2$ Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.5, 166.5, 136.5, 133.5, 131.8, 129.0, 128.5, 127.3, 127.1, 56.7, 52.9; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_3$ (M^+): 269.1052, found: 269.1049. The spectral data were identical with those of authentic methyl (*R*)-2-benzoylamino-2-phenylacetate, $[\alpha]_{\text{D}}^{20} = -112.5^\circ$ (*c* 0.70, CHCl_3),

prepared from (*R*)-(-)-phenylglycine.

Methyl (*S*)-2-Methanesulfonylamino-2-phenylacetate. This compound (8.1 mg) was prepared as a colorless solid from **2e** in 21% yield. $[\alpha]_D^{23} = +90.9^\circ$ (*c* 0.41, CHCl₃); FT-IR (film) 3280, 1741, 1444, 1333, 1217, 1109 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.38 (m, 5H), 5.54 (d, *J* = 6.3 Hz, 1H), 5.23 (d, *J* = 6.3 Hz, 1H), 3.75 (s, 3H), 2.73 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.7, 135.6, 129.1, 129.0, 127.3, 59.4, 53.1, 42.0; HRMS (EI) calcd for C₁₀H₁₃NO₄S (M⁺): 243.0565, found: 243.0588. The spectral data were identical with those of authentic methyl (*R*)-2-methanesulfonylamino-2-phenylacetate, $[\alpha]_D^{20} = -146.7^\circ$ (*c* 0.74, CHCl₃), prepared from (*R*)-(-)-phenylglycine.

Methyl (*S*)-2-(*p*-Toluenesulfonyl)amino-2-phenylacetate. This compound (7.0 mg) was prepared as a colorless solid from **2f** in 22% yield. mp 131-133°C; $[\alpha]_D^{19} = +57.4^\circ$ (*c* 0.505, CHCl₃); FT-IR (film) 3267, 1736, 1442, 1338, 1163, 1084 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.27-7.19 (m, 7H), 5.66 (d, *J* = 7.8 Hz, 1H), 5.06 (d, *J* = 7.8 Hz, 1H), 3.57 (s, 3H), 2.39 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.5, 143.3, 136.8, 135.1, 129.4, 128.7, 128.5, 127.1, 127.0, 59.2, 52.9, 21.4; HRMS (EI) calcd for C₁₆H₁₇NO₄S (M⁺): 319.0878, found: 319.0874. The spectral data were identical with those of authentic methyl (*R*)-2-(*p*-toluenesulfonyl)amino-2-phenylacetate, $[\alpha]_D^{20} = -97.2^\circ$ (*c* 1.71, CHCl₃) {lit.⁴ $[\alpha]_D^{25} = -113.6^\circ$ (*c* 2.33, CHCl₃)}, prepared from (*R*)-(-)-phenylglycine.

Methyl (*S*)-2-Diphenylphosphinoylamino-2-phenylacetate. This compound (10.1 mg) was prepared as a colorless solid from **2g** in 19% yield. mp 135-137 °C; $[\alpha]_D^{21} = +43.4^\circ$ (*c* 0.350, CHCl₃); FT-IR (film) 3176, 1741, 1442, 1300, 1200, 1117 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.88 (d, *J* = 12.3 Hz, 1H), 7.85 (dd, *J* = 12.3, 1.5 Hz, 1H), 7.75 (d, *J* = 12.3 Hz, 1H), 7.73 (dd, *J* = 12.3, 1.5 Hz, 1H), 7.53-7.40 (m, 4H), 7.34-7.24 (m, 7H), 4.95 (t, *J* = 10.2 Hz, 1H), 4.32 (dd, *J* = 10.2, 6.3 Hz, 1H), 3.67 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 172.5, 172.4, 138.2, 138.1, 132.9, 132.3, 132.1, 132.0, 131.9, 131.8, 131.6, 131.2, 130.6, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.3, 126.8, 56.6, 52.7; HRMS (EI) calcd for C₂₁H₂₀NO₃P (M⁺): 365.1181, found: 365.1195. The spectral data were identical with those of authentic methyl (*R*)-2-diphenylphosphinoylamino-2-phenylacetate, $[\alpha]_D^{20} = -77.1^\circ$ (*c* 0.75, CHCl₃), prepared from (*R*)-(-)-phenylglycine.

Conversion of **2g to (*S*)-3-methylene-4-phenyl-azetidin-2-one (**5**).** A mixture of **2g** (97.8 mg, 0.185 mmol, 65% ee) in 20% HCl (1.8 ml) was refluxed for 2 h. The reaction mixture was washed with Et₂O and AcOEt and evaporated. The residue was lyophilized to dryness to give amino acid hydrochloride **4** (25.5 mg, 65%) as a colorless solid, which was used without further purification. ¹H NMR (300 MHz, D₂O) δ 7.40-7.20 (m, 5H), 6.50 (s, 1H), 5.87 (s, 1H), 5.27 (s, 1H); HRMS (EI) calcd for C₁₀H₁₁NO₂ [(M-HCl)⁺]: 177.07896, found: 177.07888.

To a stirred solution of **4** (23.0 mg, 0.108 mmol) in THF (29 ml) at room temperature were added Et₃N (60 μ l, 0.431 mmol) and bis(2-oxo-3-oxazolidinyl)phosphinic chloride (BOPCl) (41.0 mg,

0.161 mmol). After 3days, most of the THF was removed in vacuo and the residue was extracted with AcOEt. The extract was washed with water, saturated NaHCO₃, and saturated NaCl, dried, and evaporated. Purification of the residue by preparative TLC (1:1 AcOEt-hexane) gave β -lactam **5** (12.1 mg, 70%) as a colorless solid. The enantiomeric purity was determined to be 62% ee by HPLC (CHIRALCEL AD, 1:10 *i*-PrOH-hexane, 0.5 ml/min; *t_R* = 21.1 min (*R*), 24.6 min (*S*)). mp 133-139 °C (lit.⁵ mp 106-107 °C); [α]_D²⁶ = +7.8° (*c* 0.18, CHCl₃); FT-IR (film) 3242, 1749, 1454, 1354, 1254, 1159 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.38 (br s, 5H), 6.56 (br s, 1H), 5.78 (s, 1H), 5.14 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 164.3, 151.8, 138.4, 128.8, 128.6, 126.4, 111.1, 59.4; HRMS (EI) calcd for C₁₀H₉NO (*M*)⁺: 159.06840, found: 159.06876.

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^1H NMR (300 MHz, CDCl_3)

^{13}C NMR (75 MHz, CDCl_3)

^1H NMR (300 MHz, CDCl_3)

¹³C NMR (75 MHz, CDCl₃)

^1H NMR (300 MHz, CDCl_3)

^{13}C NMR (75 MHz, CDCl_3)

^1H NMR (300 MHz, CDCl_3)

^{13}C NMR (75 MHz, CDCl_3)

¹H NMR (300 MHz, CDCl₃)

^1H NMR (300 MHz, CDCl_3)

^{13}C NMR (75 MHz, CDCl_3)

^1H NMR (300 MHz, CDCl_3)

^1H NMR (300 MHz, CDCl_3)

^{13}C NMR (75 MHz, CDCl_3)