Supporting Information

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Highly Enantioselective Construction of Quaternary Stereocenters on β -Ketoesters by Phase-Transfer Catalytic Asymmetric Alkylation and Michael Reaction

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Characterization of *N*-Spiro C_2 -Symmetric Chiral Quaternary Ammonium Salt (*S,S*)-1: $[\alpha]_D^{27} +43.2^\circ$ (*c* 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.33 (2H, s, Ar-H), 8.24 (2H, s, Ar-H), 8.15 (2H, d, $J = 8.4$ Hz, Ar-H), 7.83 (2H, d, $J = 8.0$ Hz, Ar-H), 7.68 (2H, t, $J = 8.0$ Hz, Ar-H), 7.51 (2H, t, $J = 8.0$ Hz, Ar-H), 7.40 (2H, t, $J = 8.0$ Hz, Ar-H), 7.26-7.17 (4H, m, Ar-H), 7.08 (2H, d, $J = 8.4$ Hz, Ar-H), 8.60-8.00 (2H, br, Ar-H), 8.00-6.80 (4H, br, Ar-H), 6.25 (2H, d, $J = 8.4$ Hz, Ar-H), 4.82 (2H, d, $J = 12.4$ Hz, ArCH_2), 4.64 (2H, d, $J = 13.2$ Hz, ArCH_2), 4.54 (2H, d, $J = 13.6$ Hz, ArCH_2), 3.67 (2H, d, $J = 12.8$ Hz, ArCH_2); IR (KBr) 3649, 3379, 3057, 1618, 1470, 1377, 1311, 1281, 1177, 1134, 1030, 897, 847, 752, 681 cm^{-1} . MS: m/z 998 (M^+) (100%), 381, 718, 786, 929. HRMS (FAB) calcd for $\text{C}_{60}\text{H}_{36}\text{F}_{12}\text{N}$ (M^+): 998.2656, Found: 998.2645.

General Procedure for Enantioselective Alkylation of β -Ketoesters under Solid-Liquid Phase-Transfer Conditions. To a mixture of β -ketoester (0.30 mmol) and (*S,S*)-1 (3.2 mg, 0.003 mmol, 1 mol%) in toluene (2 mL) was added alkyl halide (0.36 mmol) and $\text{CsOH}\cdot\text{H}_2\text{O}$ (255 mg, 1.5 mmol) at $-60\sim-30^\circ\text{C}$ under argon atmosphere and the mixture was stirred for several hours at the same temperature. The resulting mixture was diluted with water and extracted with Et_2O (3 times). The combined ethereal extracts were washed with water and brine, and then dried over Na_2SO_4 . Evaporation of solvent and purification of the residual crude products by column chromatography on silica gel (hexane/ Et_2O as eluent) gave the corresponding alkylation product.

Characterization of Alkylation Products.

2-Benzyl-2-(*tert*-butoxycarbonyl)-1-indanone (3a): $[\alpha]_D^{26} +134.3^\circ$ (*c* 1.2, CHCl_3) (95% *ee*); ^1H NMR (400 MHz, CDCl_3) δ 7.72 (1H, d, $J = 7.2$ Hz, Ar-H), 7.51 (1H, t, $J = 7.2$ Hz, Ar-H), 7.33 (1H, d, $J = 7.2$ Hz, Ar-H), 7.31 (1H, t, $J = 7.2$ Hz, Ar-H), 7.20-7.06 (5H, m, Ph), 3.56 (1H, d, $J = 17.2$ Hz, CH_2), 3.43 (1H, d, $J = 17.6$ Hz, CH_2), 3.26 (1H, d, $J = 17.6$ Hz, CH_2), 3.12 (1H, d, $J = 17.2$ Hz, CH_2), 1.38 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, CDCl_3) δ 202.4, 169.5, 153.2, 136.7, 135.3, 134.9, 129.8, 128.0, 127.3, 126.5, 126.0, 124.4, 82.0, 62.4, 39.4, 35.7, 27.8; IR (liquid film) 2978, 2930, 1740, 1709, 1607, 1456, 1369, 1254, 1215, 1151, 1026, 932, 847, 762, 739, 702 cm^{-1} . HRMS (ESI-TOF) calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3\text{Na}$ ($[\text{M}+\text{Na}]^+$): 345.1461, Found: 345.1470. HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 14.2 min (*R*), 17.1 min (*S*).

2-Methyl-2-(*tert*-butoxycarbonyl)-1-indanone: $[\alpha]_D^{27} +35.2^\circ$ (*c* 1.3, CHCl₃) (87% *ee*); ¹H NMR (400 MHz, CDCl₃) δ 7.78 (1H, d, *J* = 8.0 Hz, Ar-H), 7.61 (1H, t, *J* = 8.0 Hz, Ar-H), 7.46 (1H, d, *J* = 8.0 Hz, Ar-H), 7.40 (1H, t, *J* = 8.0 Hz, Ar-H), 3.64 (1H, d, *J* = 17.2 Hz, CH₂), 2.97 (1H, d, *J* = 17.2 Hz, CH₂), 1.46 (3H, s, CH₃), 1.38 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃) δ 203.6, 170.9, 152.5, 134.9, 134.9, 127.5, 126.2, 124.7, 81.5, 56.8, 40.3, 27.8, 20.8; IR (liquid film) 2978, 2932, 1740, 1717, 1609, 1456, 1394, 1369, 1285, 1211, 1151, 1097, 972, 847, 739 cm⁻¹. HRMS (ESI-TOF) calcd for C₁₅H₁₉O₃ ([M+H]⁺): 247.1329, Found: 247.1322. HPLC conditions: DAICEL Chiralpak-AS, hexane/*i*-PrOH = 400:1, flow rate = 0.5 mL/min, retention time; 16.7 min (*S*), 19.8 min (*R*).

2-Allyl-2-(*tert*-butoxycarbonyl)-1-indanone: $[\alpha]_D^{25} +104.2^\circ$ (*c* 1.0, CHCl₃) (91% *ee*); ¹H NMR (400 MHz, CDCl₃) δ 7.76 (1H, d, *J* = 7.6 Hz, Ar-H), 7.60 (1H, t, *J* = 7.6 Hz, Ar-H), 7.46 (1H, d, *J* = 7.6 Hz, Ar-H), 7.38 (1H, t, *J* = 7.6 Hz, Ar-H), 5.65 (1H, ddt, *J* = 17.2, 10.0, 7.2 Hz, C=CH), 5.12 (1H, dd, *J* = 17.2, 1.2 Hz, C=CH₂), 5.03 (1H, dd, *J* = 10.0, 1.2 Hz, C=CH₂), 3.58 (1H, d, *J* = 17.6 Hz, CH₂), 3.10 (1H, d, *J* = 17.6 Hz, CH₂), 2.84 (1H, dd, *J* = 14.0, 7.2 Hz, C=CCH₂), 2.56 (1H, dd, *J* = 14.0, 7.2 Hz, C=CCH₂), 1.39 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃) δ 202.4, 169.6, 153.1, 135.2, 135.0, 133.0, 127.4, 126.2, 124.5, 118.9, 81.8, 60.7, 38.9, 36.1, 27.8; IR (liquid film) 2980, 1740, 1713, 1609, 1474, 1369, 1256, 1211, 1151, 920, 847, 741 cm⁻¹. HRMS (ESI-TOF) calcd for C₁₇H₂₀O₃Na ([M+Na]⁺): 295.1305, Found: 295.1317. HPLC conditions: DAICEL Chiralpak-AD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 12.1 min (minor), 14.3 min (major).

2-Cinnamyl-2-(*tert*-butoxycarbonyl)-1-indanone: $[\alpha]_D^{26} +126.9^\circ$ (*c* 0.6, CHCl₃) (96% *ee*); ¹H NMR (400 MHz, CDCl₃) δ 7.77 (1H, d, *J* = 7.6 Hz, Ar-H), 7.59 (1H, dt, *J* = 1.2, 7.6 Hz, Ar-H), 7.44 (1H, d, *J* = 7.6 Hz, Ar-H), 7.37 (1H, t, *J* = 7.6 Hz, Ar-H), 7.27-7.15 (5H, m, Ph), 6.47 (1H, d, *J* = 16.0 Hz, PhCH=C), 6.06 (1H, dt, *J* = 16.0, 7.6 Hz, PhC=CH), 3.61 (1H, d, *J* = 17.6 Hz, CH₂), 3.15 (1H, d, *J* = 17.6 Hz, CH₂), 3.01 (1H, ddd, *J* = 14.0, 7.6, 1.2 Hz, C=CCH₂), 2.68 (1H, ddd, *J* = 14.0, 7.6, 1.2 Hz, C=CCH₂), 1.41 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃) δ 202.3, 169.5, 153.0, 136.9, 135.1, 135.1, 133.8, 128.3, 127.5, 127.2, 126.2, 126.0, 124.7, 124.5, 81.9, 61.1, 38.1, 36.1, 27.8; IR (liquid film) 2978, 2932, 1736, 1713, 1609, 1464, 1369, 1254, 1213, 1151, 968, 928, 845, 741, 694 cm⁻¹. HRMS (ESI-TOF) calcd for C₂₃H₂₄O₃Na ([M+Na]⁺): 371.1618, Found: 371.1617. HPLC conditions: DAICEL Chiralpak-AD, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 22.2 min (minor), 24.6 min (major).

2-(4-Benzoylphenyl)methyl-2-(*tert*-butoxycarbonyl)-1-indanone: $[\alpha]_D^{26} +119.3^\circ$ (*c* 1.0, CHCl₃) (97% *ee*); ¹H NMR (400 MHz, CDCl₃) δ 7.73 (1H, d, *J* = 7.6 Hz, Ar-H), 7.70 (2H, d, *J* = 7.6 Hz, Ar-H), 7.62 (2H, d, *J* = 8.4 Hz, Ar-H), 7.57 (1H, t, *J* = 7.6 Hz, Ar-H), 7.54 (1H, t, *J* = 7.6 Hz, Ar-H), 7.45 (2H, t, *J* = 7.6 Hz, Ar-H), 7.36 (1H, d, *J* = 7.6 Hz, Ar-H), 7.34 (1H, t, *J* = 7.6 Hz, Ar-H), 7.27 (2H, d, *J* = 8.4 Hz, Ar-H), 3.60 (1H, d, *J* = 17.6 Hz, CH₂), 3.51 (1H, d, *J* = 14.4 Hz, CH₂), 3.36 (1H, d, *J* = 14.4 Hz, CH₂), 3.11 (1H, d, *J* = 17.6 Hz, CH₂), 1.38 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃)

δ202.0, 196.0, 169.2, 152.9, 141.7, 137.4, 135.7, 135.1, 135.0, 132.1, 129.8, 129.7, 129.7, 128.0, 127.4, 126.0, 124.4, 82.2, 62.1, 39.2, 35.8, 27.8; IR (liquid film) 3057, 2978, 2932, 1730, 1705, 1653, 1607, 1447, 1369, 1317, 1250, 1150, 1026, 924, 847, 781, 741, 704 cm⁻¹. HRMS (ESI-TOF) calcd for C₂₈H₂₆O₄Na ([M+Na]⁺): 449.1723, Found: 449.1741. HPLC conditions: DAICEL Chiralpak-AD, hexane/EtOH = 4:1, flow rate = 0.5 mL/min, retention time; 15.3 min (major), 18.2 min (minor).

2-Cinnamyl-2-(tert-butoxycarbonyl)cyclopentanone: [α]_D²⁵ +53.7° (*c* 1.0, CHCl₃) (92% *ee*); ¹H NMR (400 MHz, CDCl₃) δ7.35-7.17 (5H, m, Ph), 6.43 (1H, d, *J* = 15.6 Hz, PhCH=C), 6.10 (1H, dt, *J* = 15.6, 7.6 Hz, PhC=CH), 2.75 (1H, dd, *J* = 14.0, 7.6 Hz, C=CCH₂), 2.51 (1H, dd, *J* = 14.0, 7.6 Hz, C=CCH₂), 2.47-2.36 (2H, m, CH₂), 2.26-2.15 (1H, m, CH₂), 2.05-1.86 (3H, m, CH₂), 1.44 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃) δ214.7, 170.0, 137.0, 133.7, 128.4, 127.2, 126.0, 124.8, 81.8, 60.8, 38.1, 37.0, 32.5, 28.0, 19.7; IR (KBr) 2974, 2934, 1744, 1720, 1493, 1369, 1321, 1296, 1250, 1177, 1150, 1101, 986, 851, 754, 698 cm⁻¹. HRMS (ESI-TOF) calcd for C₁₉H₂₄O₃Na ([M+Na]⁺): 323.1618, Found: 323.1619. HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 15.9 min (minor), 18.8 min (major).

2-Benzyl-2-(tert-butoxycarbonyl)cyclohexanone: [α]_D²⁷ -104.4° (*c* 1.0, EtOH) (92% *ee*); ¹H NMR (400 MHz, CDCl₃) δ7.25-7.14 (5H, m, Ph), 3.26 (1H, d, *J* = 14.0 Hz, PhCH₂), 2.87 (1H, d, *J* = 14.0 Hz, PhCH₂), 2.55-2.43 (2H, m, CH₂), 2.36 (1H, ddd, *J* = 14.0, 6.0, 3.2 Hz, CH₂), 2.06-1.96 (1H, m, CH₂), 1.76-1.50 (3H, m, CH₂), 1.45-1.38 (1H, m, CH₂), 1.37 (9H, s, *t*-Bu); IR (KBr) 2974, 2866, 1719, 1701, 1440, 1367, 1344, 1283, 1250, 1231, 1164, 1140, 845, 746, 704 cm⁻¹. HRMS (ESI-TOF) calcd for C₁₈H₂₄O₃Na ([M+Na]⁺): 311.1618, Found: 311.1629. HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 150:1, flow rate = 0.5 mL/min, retention time; 12.5 min (*R*), 13.7 min (*S*).

tert-Butyl 2-Benzoyl-2-methyl-3-phenylpropanoate: [α]_D²⁶ -5.5° (*c* 1.0, CHCl₃) (85% *ee*); ¹H NMR (400 MHz, CDCl₃) δ7.91 (2H, d, *J* = 7.6 Hz, Ph), 7.54 (1H, t, *J* = 7.6 Hz, Ph), 7.44 (2H, t, *J* = 7.6 Hz, Ph), 7.24-7.19 (3H, m, Ph), 7.06-7.00 (2H, m, Ph), 3.40 (1H, d, *J* = 13.6 Hz, PhCH₂), 3.35 (1H, d, *J* = 13.6 Hz, PhCH₂), 1.45 (3H, s, CH₃), 1.27 (9H, s, *t*-Bu); ¹³C NMR (100 MHz, CDCl₃) δ197.2, 172.5, 136.2, 135.9, 132.4, 130.4, 128.7, 128.2, 127.8, 126.6, 82.1, 58.8, 42.1, 27.7, 21.4; IR (liquid film) 2980, 2936, 1732, 1684, 1497, 1456, 1369, 1275, 1250, 1150, 1117, 974, 845, 700 cm⁻¹. HRMS (ESI-TOF) calcd for C₂₁H₂₄O₃Na ([M+Na]⁺): 347.1618, Found: 347.1606. HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 1000:1, flow rate = 0.8 mL/min, retention time; 25.8 min (major), 29.5 min (minor).

2-Benzyl-2-(methoxycarbonyl)-1-indanone:^[1] [α]_D²⁸ +113.4° (*c* 0.6, EtOH); ¹H NMR (400 MHz, CDCl₃) δ 7.74 (1H, d, *J* = 7.6 Hz, Ar-H), 7.53 (1H, t, *J* = 7.6 Hz, Ar-H), 7.34 (1H, d, *J* = 7.6 Hz, Ar-H), 7.33 (1H, t, *J* = 7.6 Hz, Ar-H), 7.20-7.10 (5H, m, Ph), 3.72 (3H, s, CH₃), 3.63 (1H, d, *J* = 17.6 Hz, CH₂), 3.49 (1H, d, *J* = 14.0 Hz, CH₂), 3.29 (1H, d, *J* = 14.0 Hz, CH₂), 3.17 (1H, d, *J* = 17.6 Hz, CH₂);

HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 32.3 min (*R*), 48.9 min (*S*).

2-Methyl-2-(methoxycarbonyl)-1-indanone:^[2] $[\alpha]_{\text{D}}^{28} +20.4^{\circ}$ (*c* 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.80 (1H, d, *J* = 7.6 Hz, Ar-H), 7.64 (1H, t, *J* = 7.6 Hz, Ar-H), 7.48 (1H, d, *J* = 7.6 Hz, Ar-H), 7.42 (1H, t, *J* = 7.6 Hz, Ar-H), 3.72 (1H, d, *J* = 17.2 Hz, CH₂), 3.69 (3H, s, CH₃), 2.91 (1H, d, *J* = 17.2 Hz, CH₂), 1.53 (3H, s, CH₃); HPLC conditions: DAICEL Chiralpak-AS, hexane/*i*-PrOH = 200:1, flow rate = 0.5 mL/min, retention time; 31.7 min (*S*), 36.2 min (*R*).

Reduction of 2-Benzyl-2-(*tert*-butoxycarbonyl)cyclopentanone (4). To a solution of **4** (27.0 mg, 0.0984 mmol) in THF (3 mL) was added a 1 M THF solution of L-Selectride (300 μ L, 0.30 mmol) at -78°C under argon atmosphere and the mixture was stirred for 3 h at the same temperature. The reaction was quenched with 1 N HCl and extracted with Et₂O (3 times). The combined ethereal extracts were washed with brine and then dried over Na₂SO₄. Evaporation of solvent and purification of the residual crude products by column chromatography on silica gel (hexane/Et₂O = 5:1 as eluent) gave the corresponding β -hydroxy ester **5** (24.5 mg, 0.889 mmol, 90%, dr = 86:14). Major isomer: ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.12 (5H, m, Ph), 3.97 (1H, q, *J* = 6.0 Hz, OCH), 3.23 (1H, d, *J* = 6.0 Hz, OH), 3.10 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.73 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.15-2.00 (2H, m, CH₂), 1.84-1.50 (4H, m, 2CH₂), 1.40 (9H, s, *t*-Bu); IR (liquid film) 3460, 2974, 2930, 1717, 1497, 1456, 1367, 1256, 1155, 1093, 1030, 849, 738, 702 cm⁻¹. HRMS (ESI-TOF) calcd for C₁₇H₂₄O₃Na ([M+Na]⁺): 299.1618, Found: 299.1620. HPLC conditions: DAICEL Chiralcel-OD, hexane/*i*-PrOH = 200:1, flow rate = 0.5 mL/min, retention time; 25.5 min (*S,S*), 28.2 min (*R,R*). Minor isomer: ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.14 (5H, m, Ph), 4.31-4.26 (1H, m, OCH), 3.20 (1H, d, *J* = 14.0 Hz, PhCH₂), 2.77 (1H, d, *J* = 14.0 Hz, PhCH₂), 2.10 (1H, d, *J* = 3.2 Hz, OH), 2.04-1.93 (2H, m, CH₂), 1.80-1.57 (4H, m, 2CH₂), 1.35 (9H, s, *t*-Bu). The stereochemistry of the major diastereomer was determined by comparison between ¹H NMR spectra of the (*R*)- and (*S*)-MTPA esters.

(*R*)-MTPA Ester of the Major Diastereomer: ¹H NMR (400 MHz, CDCl₃) δ 7.56-7.50 (2H, m, Ph), 7.41-7.35 (3H, m, Ph), 7.28-7.18 (3H, m, Ph), 7.14-7.08 (2H, m, Ph), 5.27 (1H, dd, *J* = 5.6, 2.0 Hz, OCH), 3.52 (3H, s, OCH₃), 3.05 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.59 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.34-2.23 (1H, m, CH₂), 2.17-2.05 (1H, m, CH₂), 1.96-1.85 (2H, m, CH₂), 1.84-1.71 (2H, m, CH₂), 1.16 (9H, s, *t*-Bu).

(*S*)-MTPA Ester of the Major Diastereomer: ¹H NMR (400 MHz, CDCl₃) δ 7.52-7.48 (2H, m, Ph), 7.41-7.36 (3H, m, Ph), 7.29-7.21 (3H, m, Ph), 7.16-7.11 (2H, m, Ph), 5.31 (1H, d, *J* = 4.0 Hz, OCH), 3.50 (3H, s, OCH₃), 3.08 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.61 (1H, d, *J* = 13.6 Hz, PhCH₂), 2.30-2.20 (1H, m, CH₂), 2.15-1.96 (1H, m, CH₂), 1.95-1.70 (4H, m, 2CH₂), 1.22 (9H, s, *t*-Bu).

Reductive Amination of 4. To a mixture of **4** (27.8 mg, 0.101 mmol) and molecular sieves 4A (1.5 g) in methanol (2 mL) was added benzylamine (66.0 μ L, 0.60 mmol) and acetic acid (20 μ L) at RT

under argon atmosphere and the mixture was refluxed for 12 h with stirring. After filtration, Et₂O was added to the filtrate and the solution was washed with 0.5 N NaOH and brine, and then dried over Na₂SO₄. Evaporation of solvent and purification of the residual crude products by column chromatography on silica gel (hexane/Et₂O = 5:1 as eluent) gave the corresponding *N*-protected β -amino ester **6** (36.3 mg, 0.993 mmol, 98%, dr = 84:16). Major isomer: ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.15 (10H, m, Ph), 3.93 (1H, d, *J* = 13.6 Hz, PhCH₂N), 3.73 (1H, d, *J* = 13.6 Hz, PhCH₂N), 3.37 (1H, d, *J* = 14.0 Hz, PhCH₂C), 3.17 (1H, t, *J* = 8 Hz, NCH), 2.68 (1H, d, *J* = 14.0 Hz, PhCH₂C), 2.10-1.90 (2H, m, CH₂), 1.75-1.55 (5H, m, 2CH₂, NH), 1.35 (9H, s, *t*-Bu); IR (liquid film) 3330, 2972, 2931, 1720, 1495, 1452, 1367, 1256, 1153, 849, 735, 700 cm⁻¹. HRMS (ESI-TOF) calcd for C₂₄H₃₂NO₂ ([M+H]⁺): 366.2428, Found: 366.2417. HPLC conditions: DAICEL Chiralcel-OD-H, hexane/*i*-PrOH = 100:1, flow rate = 0.5 mL/min, retention time; 12.1 min (*S,R*), 13.7 min (*R,S*). Minor isomer: ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.10 (10H, m, Ph), 3.91 (1H, d, *J* = 13.6 Hz, PhCH₂N), 3.75 (1H, d, *J* = 13.6 Hz, PhCH₂N), 3.25 (1H, d, *J* = 13.6 Hz, PhCH₂C), 2.90 (1H, t, *J* = 7.2 Hz, NCH), 2.66 (1H, d, *J* = 13.6 Hz, PhCH₂C), 2.10-1.92 (2H, m, CH₂), 1.83-1.48 (5H, m, 2CH₂, NH), 1.41 (9H, s, *t*-Bu). The stereochemistry of each diastereomer was determined by a NOE experiment (Figure 1).

Figure 1. The NOE contacts between methine proton and benzyl protons.

General Procedure for Catalytic Asymmetric Michael Reaction of β -Ketoester with Acrolein.

To a mixture of β -ketoester (0.30 mmol) and (*S,S*)-**1** (6.5 mg, 0.006 mmol, 2 mol%) in cumene (3 mL) was added K₂CO₃ (4.1 mg, 0.030 mmol) and freshly distilled acrolein (40.1 μ L, 0.60 mmol) at -78 °C under argon atmosphere. After being stirred for 5 min, the mixture was allowed to warm to -35~-40 °C and stirred for several hours. The resulting mixture was diluted with H₂O and extracted with Et₂O (3 times). The combined extracts were dried over Na₂SO₄ and concentrated. Then, the residual crude product was treated with 2-ethyl-2-methyl-1,3-dioxolane (1~2 mL) and a catalytic amount of *p*-toluenesulfonic acid monohydrate at RT for several hours. The resulting mixture was diluted with H₂O and extracted with Et₂O (3 times). The ethereal extracts were dried over Na₂SO₄. Evaporation of solvents and purification of the residue by column chromatography on silica gel (hexane/EtOAc as eluent) afforded the protected Michael adduct for HPLC analysis.

Characterization of β -Ketoester.

2-(9-Fluorenyloxycarbonyl)cyclopentanone (7b): ^1H NMR (400 MHz, CDCl_3) δ 7.66 (2H, d, $J = 7.6$ Hz, Ar-H), 7.59 (1H, d, $J = 7.6$ Hz, Ar-H), 7.54 (1H, d, $J = 7.6$ Hz, Ar-H), 7.43-7.38 (2H, m, Ar-H), 7.32 (1H, ddd, $J = 7.6, 7.6, 1.2$ Hz, Ar-H), 7.29 (1H, ddd, $J = 7.6, 7.6, 0.8$ Hz, Ar-H), 6.83 (1H, s, ArCHAr), 3.27 (1H, t, $J = 9.2$ Hz, COCHCO), 2.39-2.30 (4H, m, CH_2), 2.19-2.10 (1H, m, CH), 1.93-1.81 (1H, m, CH); ^{13}C NMR (100 MHz, CDCl_3) δ 211.6, 170.2, 141.7, 141.6, 141.0, 140.8, 129.5, 129.5, 127.9, 127.8, 125.8, 125.8, 119.9, 119.9, 75.9, 55.0, 38.0, 27.5, 21.0; IR (liquid film) 2968, 1747, 1726, 1454, 1352, 1325, 1294, 1252, 1186, 1111, 997, 972, 760, 746 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{19}\text{H}_{16}\text{O}_3\text{Na}$ ($[\text{M}+\text{Na}]^+$): 315.0992, Found: 315.0997.

Characterization of Michael Products.

2-tert-Butoxycarbonyl-2-(3,3-ethylenedioxypropyl)cyclopentanone (8a): $[\alpha]_{\text{D}}^{30} -1.17^\circ$ (c 1.0, CHCl_3) (79% *ee*); ^1H NMR (400 MHz, CDCl_3) δ 4.85 (1H, t, $J = 4.4$ Hz, $\text{CH}(-\text{OCH}_2\text{CH}_2\text{O}-)$), 3.97-3.94 (2H, m, OCH_2), 3.86-3.82 (2H, m, OCH_2), 2.48-2.37 (2H, m, CH_2), 2.27-2.18 (1H, m, CH), 2.03-1.76 (5H, m, CH_2), 1.68 (1H, ddd, $J = 13.6, 4.0, 1.2$ Hz, CH), 1.64-1.54 (1H, m, CH), 1.43 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, CDCl_3) δ 214.7, 170.0, 104.0, 81.7, 64.8, 60.2, 37.8, 33.1, 29.2, 28.0, 27.6, 19.5; IR (liquid film) 2974, 2887, 1749, 1724, 1454, 1408, 1394, 1369, 1319, 1252, 1144, 1034, 945, 918, 878, 847 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{24}\text{O}_5\text{Na}$ ($[\text{M}+\text{Na}]^+$): 307.1516, Found: 307.1536. Enantiomeric excess was determined to be 79% *ee* by HPLC analysis using chiral column [DAICEL Chiralcel-OD, hexane/EtOH = 8:1, flow rate = 1.0 mL/min, $\lambda = 220$ nm, retention time; 5.7 min (minor) and 6.5 min (major)].

2-(9-Fluorenyloxycarbonyl)-2-(3,3-ethylenedioxypropyl)cyclopentanone (8b): $[\alpha]_{\text{D}}^{30} +6.34^\circ$ (c 1.0, CHCl_3) (90% *ee*); ^1H NMR (400 MHz, CDCl_3) δ 7.65 (2H, dd, $J = 3.0, 7.6$ Hz, Ar-H), 7.49 (1H, d, $J = 7.6$ Hz, Ar-H), 7.46 (1H, d, $J = 7.6$ Hz, Ar-H), 7.40 (2H, ddd, $J = 7.6, 7.6, 3.6$ Hz, Ar-H), 7.28 (2H, ddd, $J = 7.6, 7.6, 3.0$ Hz, Ar-H), 6.77 (1H, s, ArCHAr), 4.86 (1H, t, $J = 3.6$ Hz, $\text{CH}(-\text{OCH}_2\text{CH}_2\text{O}-)$), 3.94-3.91 (2H, m, OCH_2), 3.84-3.81 (2H, m, OCH_2), 2.57-2.49 (1H, m, CH), 2.41-2.33 (1H, m, CH), 2.30-2.21 (1H, m, CH), 2.10 (1H, dt, $J = 3.6, 12.8$ Hz, CH), 2.01-1.83 (4H, m, CH_2), 1.79 (1H, dd, $J = 12.8, 3.6$ Hz, CH), 1.66 (1H, tt, $J = 12.8, 4.0$ Hz, CH); ^{13}C NMR (100 MHz, CDCl_3) δ 213.9, 171.8, 141.6, 141.5, 141.0, 140.8, 129.4, 129.4, 127.8, 127.8, 125.6, 125.6, 120.0, 119.9, 103.9, 75.8, 64.9, 59.8, 37.8, 33.0, 29.3, 27.6, 19.7; IR (liquid film) 2963, 2885, 1751, 1724, 1452, 1406, 1313, 1217, 1188, 1144, 1032, 978, 910, 762, 743 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{24}\text{H}_{24}\text{O}_5\text{Na}$ ($[\text{M}+\text{Na}]^+$): 415.1516, Found: 415.1517. HPLC conditions: DAICEL Chiralpak-OJ, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, retention time; 17.2 min (minor) and 24.7 min (major).

General Procedure for Catalytic Asymmetric Michael Reaction of β -Ketoester with Methyl Vinyl Ketone. The reaction was performed in a similar manner as described above. Without

protection, the crude product was purified by column chromatography on silica gel (hexane/EtOAc as eluent) to give the corresponding Michael adduct.

2-(9-Fluorenyloxycarbonyl)-2-(3-oxobutyl)cyclopentanone (9): $[\alpha]_D^{30} +1.92^\circ$ (c 1.0, CHCl_3) (97% *ee*); ^1H NMR (400 MHz, CDCl_3) δ 7.65 (2H, dd, $J = 7.6, 3.2$ Hz, Ar-H), 7.49 (1H, d, $J = 7.6$ Hz, Ar-H), 7.46 (1H, d, $J = 7.6$, Ar-H), 7.40 (2H, ddd, $J = 7.6, 7.6, 2.4$ Hz, Ar-H), 7.29 (2H, dd, $J = 7.6, 7.6$ Hz, Ar-H), 6.78 (1H, s, ArCHAr), 2.79 (1H, ddd, $J = 18.4, 9.6, 6.0$ Hz, CH), 2.59-2.45 (2H, m, CH_2), 2.33-2.28 (2H, m, CH_2), 2.19-2.12 (4H, m, CH and CH_3), 2.04-1.90 (4H, m, CH_2); ^{13}C NMR (100 MHz, CDCl_3) δ 214.2, 207.5, 172.2, 141.5, 141.4, 141.9, 140.7, 129.5, 129.4, 127.8, 127.8, 125.5, 125.5, 120.0, 119.9, 75.8, 59.1, 38.8, 37.9, 34.4, 29.9, 26.9, 19.6; IR (liquid film) 2964, 1749, 1720, 1611, 1452, 1369, 1356, 1258, 1227, 1161, 980, 916, 762, 743 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{23}\text{H}_{22}\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 385.1410, Found: 385.1414. HPLC conditions: DAICEL Chiralpak-AD-H, hexane/EtOH = 10:1, flow rate = 1.0 mL/min, retention time; 20.5 min (*R*), 23.8 min (*S*). The absolute configuration of **9** was determined to be *S* by the comparison of the optical rotation with the reported value after the conversion to the corresponding methyl ester as described below.

To the Michael product **9** was added TFA (0.5 mL) dropwise at 0°C . After stirring for 2 h, the reaction mixture was diluted with Et_2O and H_2O was added. The aqueous layer was extracted with Et_2O . The organic layer was dried over Na_2SO_4 and concentrated. The resulting crude mixture was treated with freshly prepared CH_2N_2 in Et_2O until the color of the reaction mixture became yellow. A small amount of acetic acid was added for quenching. The whole mixture was washed with H_2O and brine. Further purification was carried out by column chromatography on silica gel (hexane/acetone = 10:1 as eluent) to give the corresponding methyl ester in 48% yield.

$[\alpha]_D^{29} +14.7^\circ$ (c 1.0, CHCl_3) [Lit: $[\alpha]_D^{15} -12.4^\circ$ (c 0.44, CHCl_3) (92% *ee*, *R* enantiomer)]^[3]

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