Supporting Information

Direct Catalytic Asymmetric Mannich-type Reaction of Hydroxyketone Using a Et₂Zn/linked-BINOL Complex: Synthesis of either *anti*- or *syn*-β-Amino Alcohols

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Experimental Section

General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ¹H NMR and 125.65 MHz for ¹³C NMR. Chemical shifts in CDCl₃ were reported downfield from TMS (= 0) or in the scale relative to CHCl₃ (7.24 ppm) for ¹H NMR. For ¹³C NMR, chemical shifts were reported in the scale relative to CHCl₃ (77.0 ppm for ¹³C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI mass spectra were measured on Waters-ZQ4000. Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-2080 or PU-980; detector, UV-2075 or UV-970, measured at 254 nm; column, DAICEL CHIRALCEL OD, OD-H, CHIRALPAK AS-H; mobile phase, hexane–2-propanol; Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Et₂Zn (1.0 M, in hexanes) was purchased from Aldrich. Dpp-imines **3** were prepared as described in lit. Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561. Di(*o*-tolyl)phosphinoyl imine **3m** was prepared by reported the method; lit. Miyazaki, D.; Nomura, K.; Yamashita, T.; Iwakura I.; Ikeno, T.; Yamada, T. *Org. Lett.* **2003**, *5*, 3555. Boc-imines **4** were prepared as described in lit. Kanazawa, A. M.; Denis, J.; Greene, A. E. *J. Org. Chem.* **1994**, *59*, 1238. Other reagents were purified by the usual methods.

Linked-BINOL is commercially available from Wako Pure Chemical Industries, Ltd. Cat. No. 152-02431 for (*S,S*)-ligand, No. 155-02421 for (*R,R*)-ligand. Fax +1-804-271-7791 (USA), +81-6-6201-5964 (Japan), +81-3-5201-6590 (Japan).

Procedure for Catalytic Asymmetric *anti*-Selective Mannich-type Reaction Promoted by Et₂Zn/(*S,S*)-linked-BINOL **1** Complex (1 mol % catalyst loading):

MS 3A (100 mg) in a test tube was activated prior to use under reduced pressure (ca.

0.7 kPa) at 160 °C for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S,S*)-linked-BINOL (3.39 mg, 9.44w/w% diethyl ether and hexane included, 0.005 mmol) in THF (167 μ L) was charged. To this suspension was added Et₂Zn (20 μ L, 0.02 mmol, 1.0 M in hexanes). After stirring for 10 min at –20 °C, a solution of **2** (166.17 mg, 1.0 mmol) in THF (1.11 mL) and **3a** (159.67 mg, 0.5 mmol) in THF (2.0 mL) was added successively, and stirred at the same temperature. The stirring was continued for 9 h at this temperature and quenched by addition of saturated aqueous NH₄Cl. The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Evaporation of solvent gave a crude mixture of the Mannich products. The diastereomeric ratio was determined by ¹H NMR analysis of the crude product. The crude mixture was purified by flash silica gel column chromatography (AcOEt 100%) to afford **5a** (237.6 mg, 98% yield, *anti/syn* = 96/4, 98% ee (*anti* isomer)).

Procedure for Catalytic Asymmetric *anti*-Selective Mannich-type Reaction Promoted by Et₂Zn/(*S,S*)-linked-BINOL 1 Complex (0.02 mol % catalyst loading):

MS 3A (2.5 g) in a flask was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 °C for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S,S*)-linked-BINOL (3.33 mg, 7.6w/w% diethyl ether and hexane included, 0.005 mmol) in THF (10 mL) was charged. To this suspension was added Et₂Zn (20 μ L, 0.02 mmol, 1.0 M in hexanes). After stirring for 10 min at 0 °C, a solution of **2a** (831 mg, 5.0 mmol) in THF (2.5 mL) was added, and the mixture was stirred for 10 min at 0 °C. Then, a mixture solution of **2a** (5.401 g, 32.5 mmol) and **3b** (7.984 g, 25 mmol) in THF/CH₂Cl₂ (5 mL/5 mL) was added, and stirred at 0 °C. The stirring was continued for 24 h at 0 °C and quenched by addition of saturated aqueous NH₄Cl. The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Evaporation of solvent gave a crude mixture of the Mannich products. The diastereomeric ratio was determined by ¹H NMR analysis of the crude product. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 1/1 to 0/1, then AcOEt/methanol = 9/1) to afford **5b** (11.95 g, 24.6 mmol, 98.4% yield, *anti/syn* = 98/2, 97% ee (*anti* isomer)).

Synthesis of the *anti*-Mannich Products:

(*2R, 3R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(4-methylphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5a**):**

3a (0.5 mmol) was added as THF (2 mL) solution.

colorless foam; IR (KBr) ν 3357, 1662, 1598, 1486 cm⁻¹; ¹H NMR (CDCl₃) δ 2.19 (s, 3H), 3.87 (s, 3H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.41 (dd, *J* = 7.3, 11.3 Hz, 1H), 4.63 (ddd, *J* = 2.4, 11.3, 11.3 Hz, 1H), 5.62 (brd, *J* = 2.4, 7.0 Hz, 1H), 6.61 (d, *J* = 7.6

Hz, 2H), 6.82-6.87 (m, 4H), 7.15-7.19 (m, 2H), 7.28-7.45 (m, 6H), 7.62 (dd, $J = 8.2$, 12.2 Hz, 2H), 7.84 (dd, $J = 8.2$, 11.9 Hz, 2H); ^{13}C NMR (CDCl_3) δ 21.0, 55.8, 56.2, 81.3, 111.6, 120.7, 123.7, 127.1, 128.1, 128.2, 128.4, 128.4, 128.5, 131.4, 131.6, 131.7, 131.8, 131.8, 132.4, 132.5, 132.8, 133.8, 135.2, 135.3, 135.3, 137.0, 159.1, 198.3; ESI-MS m/z 508 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{25} +14.9$ (c 2.0, CHCl_3) (98% ee); HRMS (FAB): m/z calcd for $\text{C}_{29}\text{H}_{29}\text{O}_4\text{NP}$ $[\text{M}+\text{H}]^+$: 486.1834; found: 486.1835; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_{R} 9.3 min (major) and 12.9 min (minor). The relative stereochemistry of major diastereomer was determined to be *anti* after conversion to the corresponding cyclic carbamate by NOE.

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(2-methylphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5b):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3b** (0.5 mmol) was added as $\text{CH}_2\text{Cl}_2/\text{THF} = 2/1$ (1.5 mL) solution.

colorless crystal; IR (KBr) ν 3349, 1660, 1598, 1486 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.09 (s, 3H), 3.96 (s, 3H), 4.31 (brs, 1H), 4.45 (dd, $J = 7.6$, 11.0 Hz, 1H), 4.72 (ddd, $J = 3.3$, 11.0, 11.0 Hz, 1H), 5.69 (brd, $J = 3.3$ Hz, 1H), 6.76 (d, $J = 7.4$ Hz, 1H), 6.83-6.92 (m, 2H), 7.04 (dd, $J = 7.3$, 7.3 Hz, 1H), 7.13 (dd, $J = 7.3$, 7.3 Hz, 1H), 7.20-7.26 (m, 2H), 7.34-7.54 (m, 7H), 7.67 (dd, $J = 7.6$, 12.2 Hz, 2H), 7.90 (dd, $J = 7.6$, 11.8 Hz, 2H); ^{13}C NMR (CDCl_3) δ 17.8, 50.8, 55.9, 80.6, 111.5, 120.9, 124.0, 126.0, 127.3, 127.4, 128.2, 128.3, 128.5, 128.6, 129.9, 131.3, 131.6, 131.7, 131.8, 131.9, 131.9, 132.6, 132.7, 134.7, 135.2, 159.5, 198.6; ESI-MS m/z 508 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{24} +56.5$ (c 0.49, CHCl_3) (99% ee); HRMS (FAB): m/z calcd for $\text{C}_{29}\text{H}_{29}\text{O}_4\text{NP}$ $[\text{M}+\text{H}]^+$: 486.1834; found: 486.1835; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_{R} 15.0 min (major) and 20.4 min (minor). Relative configuration was determined by X-ray crystallographic analysis (see main text). CIF file is available as Supporting Information. The absolute stereochemistry was determined by Mosher's method.

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-phenyl-3-(*N*-diphenylphosphinoylamino)-1-propanone (5c):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3c** (0.5 mmol) was added as $\text{CH}_2\text{Cl}_2/\text{THF} = 2/1$ (1.5 mL) solution.

colorless foam; IR (KBr) ν 3337, 1663, 1598, 1486 cm^{-1} ; ^1H NMR (CDCl_3) δ 3.95 (s, 3H), 4.08 (brs, 1H), 4.47 (dd, $J = 7.0$, 11.3 Hz, 1H), 4.74 (ddd, $J = 3.2$, 11.3, 11.3 Hz, 1H), 5.68 (brs, 1H), 6.78 (d, $J = 7.0$ Hz, 2H), 6.89-6.92 (m, 2H), 7.08-7.24 (m, 5H), 7.33-7.50 (m, 6H), 7.66 (dd, $J = 7.0$, 12.2 Hz, 2H), 7.91 (dd, $J = 7.0$, 11.9 Hz, 2H); ^{13}C NMR (CDCl_3) δ 55.9, 56.5, 81.2, 111.6, 120.8, 123.8, 127.3, 127.6, 127.8, 128.2, 128.3, 128.5, 128.6, 131.4, 131.7, 131.8, 131.9, 132.4, 132.5, 132.6, 132.8, 133.8, 135.3, 138.3, 138.4, 159.1, 198.3; ESI-MS m/z 494 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{22} +9.0$ (c 0.31, CHCl_3) (99% ee);

HRMS (FAB): m/z calcd for $C_{28}H_{27}O_4NP$ $[M+H]^+$: 472.1678; found: 472.1671; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_R 9.1 min (major) and 12.5 min (minor).

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(4-methoxyphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5d):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3d** (0.5 mmol) was added as $CH_2Cl_2/THF = 2/1$ (1.5 mL) solution.

colorless foam; IR (KBr) ν 3346, 1662, 1598, 1464 cm^{-1} ; 1H NMR ($CDCl_3$) δ 3.73 (s, 3H), 3.93 (s, 3H), 4.06 (brs, 1H), 4.41 (dd, $J = 7.3, 11.3$ Hz, 1H), 4.68 (ddd, $J = 2.7, 11.3, 11.3$ Hz, 1H), 5.66 (brd, $J = 2.7$ Hz, 1H), 6.63 (d, $J = 8.5$ Hz, 2H), 6.70 (d, $J = 8.5$ Hz, 2H), 6.88-6.92 (m, 2H), 7.21-7.26 (m, 2H), 7.36 (dd, $J = 7.0, 7.0$ Hz, 1H), 7.40-7.51 (m, 6H), 7.67 (dd, $J = 7.3, 12.2$ Hz, 2H), 7.90 (dd, $J = 7.0, 11.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.1, 55.8, 55.9, 81.3, 111.6, 113.1, 120.8, 123.7, 128.1, 128.2, 128.4, 128.5, 131.6, 131.7, 131.8, 131.9, 131.9, 132.5, 132.6, 135.2, 158.8, 159.1, 198.4; ESI-MS m/z 524 $[M+Na]^+$; $[\alpha]_D^{25} +21.6$ (c 0.7, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{29}H_{29}O_5NP$ $[M+H]^+$: 502.1783; found: 502.1788; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 16.5 min (major) and 24.6 min (minor).

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(4-nitrophenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5e):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3e** (0.5 mmol) was added as $THF/CH_2Cl_2 = 5/3$ (2.0 mL) solution.

colorless foam; IR (KBr) ν 3331, 1664, 1598, 1486 cm^{-1} ; 1H NMR ($CDCl_3$) δ 3.94 (s, 3H), 4.20 (brd, $J = 5.5$ Hz, 1H), 4.57 (dd, $J = 7.3, 11.0$ Hz, 1H), 4.86 (ddd, $J = 2.7, 11.0, 11.0$ Hz, 1H), 5.68 (brs, 1H), 6.89-6.98 (m, 4H), 7.20-7.25 (m, 2H), 7.36 (dd, $J = 7.3, 7.3$ Hz, 1H), 7.42-7.53 (m, 5H), 7.66 (dd, $J = 7.6, 11.9$ Hz, 2H), 7.90 (dd, $J = 7.3, 11.9$ Hz, 2H), 7.95 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.8, 55.9, 80.7, 111.8, 121.0, 122.9, 123.1, 128.7, 128.4, 128.6, 128.7, x, 131.6, 131.8, 131.8, 131.9, 132.1, 132.2, 133.0, 135.9, 145.9, 147.2, 197.5; ESI-MS m/z 539 $[M+Na]^+$; $[\alpha]_D^{26} +64.7$ (c 1.48, $CHCl_3$) (98% ee); HRMS (FAB): m/z calcd for $C_{28}H_{26}O_6N_2P$ $[M+H]^+$: 517.1529; found: 517.1530; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 20.4 min (major) and 27.4 min (minor).

(2*R*, 3*R*)-3-(4-Chlorophenyl)-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5f):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3f** (0.5 mmol) was added as $CH_2Cl_2/THF = 2/1$ (1.5 mL) solution.

colorless foam; IR (KBr) ν 3335, 1663, 1597, 1487 cm^{-1} ; 1H

NMR (CDCl₃) δ 3.92 (s, 3H), 4.16 (brd, J = 5.2 Hz, 1H), 4.49 (dd, J = 7.0, 11.0 Hz, 1H), 4.70 (ddd, J = 2.7, 11.0, 11.0 Hz, 1H), 5.65 (brs, 1H), 6.71 (d, J = 8.6 Hz, 2H), 6.87-6.92 (m, 2H), 7.06 (d, J = 8.6 Hz, 2H), 7.19-7.26 (m, 2H), 7.33-7.49 (m, 6H), 7.63 (dd, J = 7.3, 11.8 Hz, 2H), 7.88 (dd, J = 7.3, 11.9 Hz, 2H); ¹³C NMR (CDCl₃) δ 55.8, 55.8, 81.0, 111.6, 120.8, 123.4, 127.9, 128.1, 128.2, 128.4, 128.5, 128.7, 131.2, 131.6, 131.7, 131.8, 131.9, 131.9, 132.2, 132.3, 132.4, 133.3, 134.4, 137.0, 137.0, 159.0, 197.9; ESI-MS m/z 528 [M+Na]⁺; [α]_D²⁶ +49.4 (*c* 0.81, CHCl₃) (98% ee); HRMS (FAB): m/z calcd for C₂₈H₂₆O₄NCIP [M+H]⁺: 506.1288; found: 506.1292; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 15.8 min (major) and 22.9 min (minor).

(2*R*, 3*R*)-3-(4-Bromophenyl)-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5g)

To a mixture of Et₂Zn, **1**, and **2a** in THF, **3g** (0.5 mmol) was added as CH₂Cl₂/THF = 2/1 (1.5 mL) solution.

colorless foam; IR (KBr) ν 3335, 1734, 1662, 1597, 1486 cm⁻¹;

¹H NMR (CDCl₃) δ 3.96 (s, 3H), 4.17 (brd, J = 5.5 Hz, 1H), 4.50 (dd, J = 7.0, 11.3 Hz, 1H), 4.72 (ddd, J = 2.5, 11.3, 11.3 Hz, 1H), 5.68 (brs, 1H), 6.68 (d, J = 8.3 Hz, 2H), 6.92-6.96 (m, 2H), 7.23-7.29 (m, 4H), 7.39 (dd, J = 7.3, 7.3 Hz, 1H), 7.44-7.47 (m, 2H), 7.49-7.54 (m, 3H), 7.66 (dd, J = 7.3, 11.8 Hz, 2H), 7.92 (dd, J = 7.3, 11.6 Hz, 2H); ¹³C NMR (CDCl₃) δ 55.8, 55.8, 80.9, 111.7, 120.9, 121.5, 123.4, 128.2, 128.3, 128.5, 128.6, 129.1, 130.8, 131.7, 131.7, 131.8, 131.9, 131.9, 131.9, 132.3, 132.4, 133.4, 135.5, 137.5, 137.5, 159.1, 197.9; ESI-MS m/z 573, 574 [M+Na]⁺; [α]_D²² +46.1 (*c* 2.17, CHCl₃) (98% ee); HRMS (FAB): m/z calcd for C₂₈H₂₆O₄NBrP [M+H]⁺: 550.0783; found: 550.0798; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 16.1 min (major) and 24.0 min (minor).

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(1-naphthyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5h):

To a mixture of Et₂Zn, **1**, and **2a** in THF, **3h** (0.5 mmol) was added as CH₂Cl₂/THF = 2/1 (1.5 mL) solution.

colorless foam; IR (KBr) ν 3353, 1664, 1596, 1438 cm⁻¹; ¹H NMR

(CDCl₃) δ 3.64 (s, 3H), 4.51 (dd, J = 6.4, 11.3 Hz, 1H), 4.68 (dd, J = 7.5 Hz, 1H), 5.63 (ddd, J = 3.0, 11.3, 11.3 Hz, 1H), 5.84 (dd, J = 3.0, 7.5 Hz, 1H), 6.62 (dd, J = 7.5, 7.5 Hz, 1H), 6.73 (d, J = 8.2 Hz, 1H), 6.84 (dd, J = 7.0, 7.0 Hz, 1H), 6.99 (brd, J = 8.3 Hz, 1H), 7.05 (dd, J = 1.6, 8.0 Hz, 1H), 7.10 (ddd, J = 3.3, 7.6, 7.6 Hz, 2H), 7.19-7.34 (m, 4H), 7.40-7.51 (m, 3H), 7.57 (brd, J = 7.0 Hz, 1H), 7.64-7.70 (m, 4H), 7.92 (dd, J = 7.0, 11.9 Hz, 2H); ¹³C NMR (CDCl₃) δ 51.8, 55.4, 79.8, 111.2, 120.6, 122.0, 124.8, 125.0, 125.3, 128.0, 128.2, 128.3, 128.5, 128.6, 130.1, 130.8, 131.7,

131.7, 131.8, 131.9, 132.0, 132.0, 132.4, 132.5, 132.6, 133.2, 133.4, 134.7, 134.7, 158.8, 199.3; ESI-MS m/z 544 $[M+Na]^+$; $[\alpha]_D^{25}$ +40.2 (c 0.47, $CHCl_3$) (>99% ee); HRMS (FAB): m/z calcd for $C_{32}H_{29}O_4NP$ $[M+H]^+$: 522.1834; found: 522.1835; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_R 10.6 min (major) and 14.6 min (minor).

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(2-naphthyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5i):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3i** (0.5 mmol) was added as THF/ CH_2Cl_2 = 5/3 (2.0 mL) solution.

colorless foam; IR (KBr) ν 3344, 1662, 1597, 1486 cm^{-1} ; 1H NMR ($CDCl_3$) δ 3.94 (s, 3H), 4.19 (brd, J = 6.1 Hz, 1H), 4.63 (dd, J = 7.0, 11.2 Hz, 1H), 4.91 (ddd, J = 3.0, 11.2, 11.2 Hz, 1H), 5.77 (brd, J = 3.0 Hz, 1H), 6.88 (dd, J = 7.2, 7.2 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 7.06-7.08 (m, 2H), 7.17 (ddd, J = 3.0, 7.3, 7.3 Hz, 2H), 7.31 (dd, J = 7.6, 7.6 Hz, 1H), 7.36-7.54 (m, 8H), 7.62 (d, J = 8.8 Hz, 1H), 7.67 (dd, J = 7.0, 11.2 Hz, 2H), 7.74 (d, J = 7.6 Hz, 1H), 7.93 (dd, J = 7.0, 10.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.8, 56.6, 81.3, 111.6, 120.7, 123.8, 125.3, 125.8, 125.8, 126.3, 127.4, 127.5, 127.8, 128.1, 128.2, 128.4, 128.5, 131.3, 131.7, 131.8, 131.8, 132.4, 132.5, 132.6, 132.7, 133.7, 135.2, 135.9, 135.9, 159.0, 198.2; ESI-MS m/z 544 $[M+Na]^+$; $[\alpha]_D^{26}$ +69.4 (c 0.23, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{32}H_{29}O_4NP$ $[M+H]^+$: 522.1834; found: 522.1835; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 17.7 min (major) and 23.8 min (minor).

(2*R*, 3*S*)-3-Furyl-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone (5j):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3j** (0.5 mmol) was added as THF/ CH_2Cl_2 = 5/3 (2.0 mL) solution.

colorless foam; IR (KBr) ν 3347, 1664, 1598, 1486 cm^{-1} ; 1H NMR ($CDCl_3$) δ 3.84 (s, 3H), 4.14 (brs, 1H), 4.30 (dd, J = 8.2, 11.2 Hz, 1H), 4.87 (ddd, J = 7.0, 11.2, 11.2 Hz, 1H), 5.58 (brs, 1H), 5.89 (d, J = 3.1 Hz, 1H), 6.15 (dd, J = 1.8, 3.1 Hz, 1H), 6.87 (d, J = 7.7 Hz, 1H), 6.93 (dd, J = 8.0, 8.0 Hz, 1H), 7.16 (d, J = 1.8 Hz, 1H), 7.30-7.34 (m, 2H), 7.39-7.50 (m, 5H), 7.64 (dd, J = 1.8, 7.9 Hz, 1H), 7.79 (dd, J = 6.7, 11.9 Hz, 2H), 7.91 (dd, J = 6.7, 11.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 51.3, 55.7, 80.4, 107.4, 109.9, 111.6, 120.8, 123.8, 128.3, 128.4, 128.5, 128.6, 131.4, 131.5, 131.8, 131.8, 131.9, 132.0, 132.3, 132.4, 135.1, 141.7, 152.2, 158.9, 198.5; ESI-MS m/z 484 $[M+Na]^+$; $[\alpha]_D^{25}$ -1.3 (c 1.3, $CHCl_3$) (>99% ee); HRMS (FAB): m/z calcd for $C_{26}H_{25}O_5NP$ $[M+H]^+$: 462.1470; found: 462.1463; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_R 10.0 min (major) and 13.6 min (minor). The relative stereochemistry of major diastereomer was determined to be *anti* after conversion to the

corresponding cyclic carbamate by NOE as shown below (7.0%).

4E-(2R, 3R)-2-Hydroxy-1-(2-methoxyphenyl)-5-phenyl-3-(N-diphenylphosphinoylamino)-4-penten-1-one (5k):

To a mixture of Et₂Zn, **1**, and **2a** in THF, **3k** (0.5 mmol) was added as THF (2.0 mL) solution.

colorless foam; IR (KBr) ν 3335, 1672, 1597, 1486 cm⁻¹; ¹H NMR (CDCl₃) δ 3.85 (s, 3H), 4.03 (dd, J = 7.6, 11.0 Hz, 1H), 4.28-4.35 (m, 2H), 5.56 (brs, 1H), 5.91-6.04 (m, 2H), 6.90 (d, J = 8.5 Hz, 1H), 6.95 (dd, J = 7.0, 7.0 Hz, 1H), 7.13-7.29 (m, 5H), 7.35-7.53 (m, 7H), 7.67 (dd, J = 1.5, 7.6 Hz, 1H), 7.91 (dd, J = 7.0, 12.2 Hz, 2H), 7.96 (dd, J = 6.7, 11.9 Hz, 2H); ¹³C NMR (CDCl₃) δ 55.4, 55.7, 80.1, 111.7, 120.8, 123.9, 125.8, 125.8, 126.4, 127.6, 128.3, x, 128.4, 128.5, 131.4, 131.7, 131.8, 131.8, 132.4, 132.4, 132.5, 132.7, 133.7, 135.1, 136.3, 158.9, 199.4; ESI-MS m/z 520 [M+Na]⁺; [α]_D²⁵ +62.4 (c 0.76, CHCl₃) (>99% ee); HRMS (FAB): m/z calcd for C₃₀H₂₉O₄NP [M+H]⁺: 498.1834; found: 498.1843; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 17.5 min (major) and 23.3 min (minor). The relative stereochemistry of major diastereomer was determined to be *anti* after conversion to the corresponding cyclic carbamate by NOE (8.0%) as shown below.

(2R, 3R)-3-cyclopropyl-2-hydroxy-1-(2-methoxyphenyl)-3-(N-diphenylphosphinoylamino)-1-propanone (5l):

To a mixture of Et₂Zn, **1**, and **2a** in THF, **3l** (0.5 mmol) was added as CH₂Cl₂/THF = 1/1 (1.0 mL) solution.

colorless foam; IR (KBr) ν 3349, 1663, 1598, 1486 cm⁻¹; ¹H NMR (CDCl₃) δ -0.40—0.34 (m, 1H), 0.14-0.18 (m, 2H), 0.28-0.34 (m, 1H), 0.85-0.93 (m, 1H), 2.95-3.02 (m, 1H), 3.59 (s, 3H), 3.83 (dd, J = 10.4, 10.4 Hz, 1H), 4.46 (d, J = 6.1 Hz, 1H), 5.39 (dd, J = 2.4, 6.1 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.82 (dd, J = 7.5, 7.5

Hz, 1H), 7.36-7.46 (m, 7H), 7.76 (dd, $J = 1.5, 7.5$ Hz, 1H), 7.82 (dd, $J = 7.0, 11.1$ Hz, 2H), 7.92 (dd, $J = 7.0, 10.7$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 3.1, 5.2, 12.9, 12.9, 55.4, 57.4, 80.8, 111.7, 120.7, 124.1, 128.2, 128.4, 128.5, 131.3, 131.6, 131.7, 131.9, 132.0, 132.1, 132.7, 133.0, 133.7, 134.0, 134.9, 158.9, 199.5; ESI-MS m/z 458 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{25} -23.3$ (c 1.3, CHCl_3) (97% ee); HRMS (FAB): m/z calcd for $\text{C}_{25}\text{H}_{27}\text{O}_4\text{NP}$ $[\text{M}+\text{H}]^+$: 436.1678; found: 436.1679; HPLC (DAICEL CHIRALPAK AS-H, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_{R} 10.5 min (minor) and 27.9 min (major). The relative stereochemistry of major diastereomer was determined to be *anti* by NOE observation (9.0%) as shown below, after conversion to the corresponding cyclic carbamate. The absolute stereochemistry was determined by Mosher's method.

(2R, 3R)-3-cyclopropyl-2-hydroxy-1-(2-methoxyphenyl)-3-[N-di-(2-methyl-phenyl)-phosphinoylamino]-1-propanone (5m):

To a mixture of Et_2Zn , **1**, and **2a** in THF, **3m** (0.5 mmol) was added as $\text{CH}_2\text{Cl}_2/\text{THF} = 1/1$ (1.0 mL) solution.

colorless foam; IR (KBr) ν 3399, 1656, 1597 cm^{-1} ; ^1H NMR (CDCl_3) δ -0.50 - -0.25 (m, 1H), 0.10-0.50 (m, 3H), 0.95-1.10 (m, 1H), 2.64 (s, 6H), 3.23-3.30 (m, 1H), 3.54 (s, 3H), 3.67 (dd, $J = 11, 15$ Hz, 1H), 4.50 (d, $J = 5.8$ Hz, 1H), 5.47 (dd, $J = 2.5, 5.8$ Hz, 1H), 6.89 (d, $J = 8.3$ Hz, 1H), 7.00 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.10-7.60 (m, 8H), 7.76 (dd, $J = 7.6, 14.4$ Hz, 2H), 7.87 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 3.8, 5.8, 13.2, 21.7, 55.2, 57.3, 80.9, 111.8, 120.8, 123.9, 125.1, 125.4, 131.6, 131.7, 132.6, 133.2, 135.1, 142.6, 159.0, 199.4; ESI-MS m/z 486 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{24} -20.1$ (c 1.4, CHCl_3) (97% ee); HRMS (FAB): m/z calcd for $\text{C}_{27}\text{H}_{31}\text{O}_4\text{NP}$ $[\text{M}+\text{H}]^+$: 464.1991; found: 464.1993; HPLC (DAICEL CHIRALPAK AS-H, 2-propanol/hexane 50/50, flow 0.5 mL/min, detection at 254 nm) t_{R} 9.9 min (minor) and 17.9 min (major).

2-Hydroxy-1-(4-methoxyphenyl)-3-(2-methylphenyl)-3-(N-diphenylphosphinoylamino)-1-propanone:

colorless foam; IR (KBr) ν 3329, 1681, 1438 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.25 (s, 3H), 3.83 (s, 3H), 4.26 (d, $J = 8.0$ Hz, 1H), 4.55 (dd, $J = 6.8, 11.3$ Hz, 1H), 4.88 (ddd, $J = 2.8, 11.3, 11.3$ Hz, 1H), 5.57 (dd, $J = 2.8, 8.0$ Hz, 1H), 6.83-6.88 (m, 3H), 7.07 (dd, $J = 7.0, 7.0$ Hz, 1H), 7.15 (dd, $J = 7.0, 7.0$ Hz, 1H), 7.26-7.30 (m, 2H), 7.38-7.52 (m, 5H), 7.72-7.77 (m, 2H), 7.86 (d, $J = 8.9$ Hz, 2H), 7.87-7.93 (m, 2H), 7.71-7.78 (m, 24H), 7.88-7.93 (m, 2H); ^{13}C NMR (CDCl_3)

δ 18.5, 53.5, 55.5, 76.4, 114.2, 126.0, 127.0, 127.5, 127.8, 128.4, 128.5, 128.6, 128.7, 130.2, 131.1, 131.7, 131.7, 131.9, 132.1, 132.6, 132.7, 133.0, 134.6, 136.1, 136.1, 164.3, 196.6; ESI-MS m/z 508 $[M+Na]^+$; $[\alpha]_D^{25} +48$ (c 1.5, $CHCl_3$) (92% ee); HRMS (FAB): m/z calcd for $C_{29}H_{29}O_4NP$ $[M+H]^+$: 486.1834; found: 486.1842; HPLC (DAICEL CHIRALCEL AD-H, 2-propanol/hexane 50/50, flow 0.50 mL/min, detection at 254 nm) t_R 23.4 min (major) and 26.4 min (minor).

2-Hydroxy-3-(2-methylphenyl)-1-phenyl-3-(*N*-diphenylphosphinoylamino)-1-propanone:

colorless foam; IR (KBr) ν 3317, 1670, 1599, 1261 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.22 (s, 3H), 4.37 (d, J = 8.0 Hz, 1H), 4.53 (dd, J = 6.7, 11.3 Hz, 1H), 4.89 (ddd, J = 2.8, 11.3, 11.3 Hz, 1H), 5.60 (dd, J = 2.8, 8.0 Hz, 1H), 6.85 (d, J = 7.4 Hz, 1H), 7.06-7.15 (m, 2H), 7.28-7.32 (m, 2H), 7.37-7.54 (m, 8H), 7.73-7.78 (m, 2H), 7.82 (d, J = 7.4 Hz, 2H), 7.89-7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.3, 53.4, 76.5, 126.1, 127.6, 128.4, 128.5, 128.6, 128.7, 128.7, 128.9, 130.2, 130.9, 131.7, 131.8, 131.9, 132.6, 132.7, 132.9, 134.1, 134.6, 136.0, 136.0, 198.5; ESI-MS m/z 478 $[M+Na]^+$; $[\alpha]_D^{25} +0.7$ (c 0.9, $CHCl_3$) (58% ee); HRMS (FAB): m/z calcd for $C_{28}H_{27}O_3NP$ $[M+H]^+$: 456.1729; found: 456.1735; HPLC (DAICEL CHIRALCEL AD-H, 2-propanol/hexane 50/50, flow 0.50 mL/min, detection at 254 nm) t_R 15.7 min (major) and 17.9 min (minor).

2-Hydroxy-1-(4-methylphenyl)-3-(2-methylphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone:

colorless foam; IR (KBr) ν 3322, 1676, 1605, 1438 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.23 (s, 3H), 2.36 (s, 3H), 4.32 (d, J = 7.6 Hz, 1H), 4.56 (dd, J = 6.5, 11.0 Hz, 1H), 4.89 (ddd, J = 2.7, 11.0, 11.0 Hz, 1H), 5.58 (dd, J = 2.7, 7.6 Hz, 1H), 6.84 (d, J = 7.3 Hz, 1H), 7.07 (ddd, J = 8.5 Hz, 1H), 7.06-7.08 (m, 2H), 7.17 (ddd, J = 3.0, 7.3, 7.3 Hz, 2H), 7.31 (dd, J = 0.9, 7.3, 7.3 Hz, 1H), 7.12-7.19 (m, 3H), 7.25-7.31 (m, 2H), 7.37-7.52 (m, 5H), 7.71-7.78 (m, 24H), 7.88-7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.4, 21.8, 53.4, 76.5, 126.0, 127.5, 127.7, 128.4, 128.5, 128.6, 128.7, 128.7, 129.6, 130.2, 131.0, 131.5, 131.7, 131.7, 131.7, 131.9, 132.0, 132.1, 132.6, 132.7, 132.9, 134.6, 136.1, 136.1, 145.2, 197.9; ESI-MS m/z 492 $[M+Na]^+$; $[\alpha]_D^{25} +17.1$ (c 2.6, $CHCl_3$) (65% ee); HRMS (FAB): m/z calcd for $C_{29}H_{29}O_3NP$ $[M+H]^+$: 470.1886; found: 470.1884; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.15 mL/min, detection at 254 nm) t_R 28.0 min (minor) and 31.5min (major).

2-Hydroxy-1-(2-furyl)-3-(2-methylphenyl)-3-(*N*-diphenylphosphinoylamino)-1-propanone:

colorless foam; IR (KBr) ν 3279, 1671, 1567, 1465 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.60 (s, 3H), 4.53 (dd, J = 5.8, 11.3 Hz, 1H), 4.78 (d, J = 8.9 Hz, 1H), 4.91 (ddd, J = 3.0, 11.3, 11.3 Hz, 1H), 5.21 (dd, J = 3.0, 8.9 Hz, 1H),

6.43 (dd, $J = 1.8, 3.6$ Hz, 1H), 6.93 (brd, $J = 7.3$ Hz, 1H), 7.05-7.13 (m, 2H), 7.23-7.25 (m, 1H), 7.31 (ddd, $J = 3.4, 7.6, 7.6$ Hz, 2H), 7.37 (brd, $J = 7.3$ Hz, 1H), 7.40-7.52 (m, 5H), 7.70-7.77 (m, 2H), 7.85-7.91 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.5, 54.6, 60.4, 75.8, 112.6, 119.9, 126.1, 127.1, 127.6, 128.4, 128.5, 128.6, 128.7, 130.3, 130.5, 131.6, 131.7, 131.7, 132.0, 132.2, 132.6, 132.7, 134.5, 134.5, 136.1, 136.2, 147.4, 150.8, 187.2; ESI-MS m/z 468 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{25} -0.6$ (c 1.7, CHCl_3) (36% ee); HRMS (FAB): m/z calcd for $\text{C}_{26}\text{H}_{25}\text{O}_4\text{NP}$ $[\text{M}+\text{H}]^+$: 446.1521; found: 446.1517; HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.1 mL/min, detection at 254 nm) t_{R} 44.4 min (minor) and 48.0 min (major).

Procedure for Catalytic Asymmetric *syn*-Selective Mannich-type Reaction Promoted by $\text{Et}_2\text{Zn}/(S,S)$ -linked-BINOL **1 Complex (1 or 5 mol % catalyst loading):**

MS 3A (103 mg) in a test tube was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 °C for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S,S*)-linked-BINOL (16.9 mg, 9.44w/w% diethyl ether and hexane included, 0.025 mmol) in THF (0.8 mL) was charged. To this suspension was added Et_2Zn (100 μL , 0.10 mmol, 1.0 M in hexanes). After stirring for 10 min at -40 °C, a solution of **2** (166 mg, 1.0 mmol) in THF (1.0 mL) and **4a** (103 mg, 0.5 mmol) in THF (1.5 mL) was added successively, and stirred at -40 °C. The stirring was continued for 19 h at -40 °C and quenched by addition of saturated aqueous NH_4Cl . The mixture was extracted with ethyl acetate (x3) and the combined organic layers were washed with brine and dried over Na_2SO_4 . Evaporation of solvent gave a crude mixture of the Mannich products. The diastereomeric ratio was determined by ^1H NMR analysis of the crude product. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1) to afford **6a** (174.8 mg, 94% yield, *anti/syn* = 12/88, 99% ee (*syn* isomer)).

Procedure for Catalytic Asymmetric *syn*-Selective Mannich-type Reaction Promoted by $\text{Et}_2\text{Zn}/(S,S)$ -linked-BINOL **1 Complex (0.05 mol % catalyst loading):**

MS 3A (2.06 g) in a test tube was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 °C for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S,S*)-linked-BINOL (3.07 mg, 0.005 mmol) in THF (3.8 mL) was charged. To this suspension was added Et_2Zn (20 μL , 0.02 mmol, 1.0 M in hexanes). After stirring for 10 min at -20 °C, a solution of **2a** (3.32 g, 20 mmol) in THF (20 mL) and **4a** (2.05 g, 10 mmol) in THF (2 mL) was added successively, and stirred at -20 °C. The stirring was continued for 48 h at -20 °C and quenched by addition of saturated aqueous NH_4Cl . The mixture was extracted with ethyl acetate (x3) and the combined organic layers were washed with brine and dried over Na_2SO_4 . Evaporation of solvent gave a crude

mixture of the Mannich products. The diastereomeric ratio was determined by ^1H NMR analysis of the crude product. The crude mixture was purified by flash silica gel column chromatography (hexane/acetone = 10/1) to afford **6a** (3.28 g, 88% yield, *anti/syn* = 15/85, 98% ee (*syn* isomer)).

(2R, 3S)-2-Hydroxy-1-(2-methoxyphenyl)-3-(N-tert-butoxycarbonylamino)-3-phenyl-1-propanone (6a):

colorless oil; IR (neat) ν 3435, 1717, 1676, 1243, 1164 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.31 (s, 9H), 3.95 (s, 3H), 4.25 (d, J = 3.7 Hz, 1H), 5.22 (brd, J = 9.7 Hz, 1H), 5.31 (brd, J = 9.7 Hz, 1H), 5.43 (d, J = 2.8 Hz, 1H), 7.02-7.08 (m, 2H), 7.25-7.45 (m, 5H), 7.56 (dd, J = 7.6, 7.6 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H); ^{13}C NMR (CDCl_3) δ 28.1, 55.0, 55.5, 79.4, 79.6, 111.7, 121.3, 123.5, 126.5, 127.2, 128.5, 131.6, 135.3, 140.9, 154.7, 158.7, 200.6; ESI-MS m/z 394 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{25}$ +53.9 (c 0.798, CHCl_3) (99% ee); HRMS (FAB): m/z calcd for $\text{C}_{21}\text{H}_{26}\text{O}_5\text{N}$ $[\text{M}+\text{H}]^+$: 372.1811; found: 372.1807; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 18.4 min (major) and 9.7 min (minor). The absolute and relative stereochemistry of major diastereomer was determined after conversion to the side chain of Taxotere **10**.

(2R, 3S)-2-Hydroxy-1-(2-methoxyphenyl)-3-(4-methoxyphenyl)-3-(N-tert-butoxycarbonylamino)-1-propanone (6b):

colorless oil; IR (neat) ν 3435, 1715, 1512, 1245, 1164 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.30 (s, 9H), 3.80 (s, 3H), 3.94 (s, 3H), 4.24 (d, J = 3.4 Hz, 1H), 5.16 (brd, J = 9.8 Hz, 1H), 5.25 (brd, J = 9.8 Hz, 1H), 5.39 (brs, 1H), 6.90 (d, J = 8.6 Hz, 2H), 7.02-7.08 (m, 2H), 7.35 (d, J = 8.6 Hz, 2H), 7.56 (dd, J = 7.5, 7.5 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H); ^{13}C NMR (CDCl_3) δ 28.2, 54.5, 55.2, 55.5, 79.3, 79.7, 111.7, 113.9, 121.3, 123.5, 127.7, 131.6, 133.2, 135.3, 154.7, 158.7, 200.6; ESI-MS m/z 424 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{26}$ +38.3 (c 1.38, CHCl_3) (96% ee); HRMS (FAB): m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_6\text{N}$ $[\text{M}+\text{H}]^+$: 402.1916; found: 402.1913; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 21.4 min (major) and 13.5 min (minor). The absolute and relative stereochemistry of major diastereomer was determined after conversion to *epi*-cytoxazone **12**.

(2R, 3S)-2-Hydroxy-1-(2-methoxyphenyl)-3-(4-methylphenyl)-3-(N-tert-butoxycarbonylamino)-1-propanone (6c):

colorless oil; IR (neat) ν 3447, 1716, 1670, 1486, 1243, 1163 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.23 (s, 9H), 2.26 (s, 3H), 3.87 (s, 3H), 4.14 (d, J = 3.7 Hz, 1H), 5.11 (brd, J = 9.8 Hz, 1H), 5.20 (brd, J = 9.8 Hz, 1H), 5.33 (d, J = 2.5 Hz, 1H), 6.92-7.00 (m, 2H), 7.10 (d, J = 7.9 Hz, 2H),

7.23 (d, $J = 7.9$ Hz, 2H), 7.78 (dd, $J = 7.3, 7.3$ Hz, 1H), 7.76 (d, $J = 7.3$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 20.0, 27.1, 53.7, 54.5, 78.2, 78.6, 110.6, 120.2, 122.5, 125.4, 128.1, 130.5, 134.2, 135.8, 136.9, 153.7, 157.7, 199.6; ESI-MS m/z 408 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{26} +39.1$ (c 1.6, CHCl_3) (99% ee); HRMS (FAB): m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_5\text{N}$ $[\text{M}+\text{H}]^+$: 386.1967; found: 386.1968; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 15.2 min (major) and 7.4 min (minor).

(2R, 3S)-2-Hydroxy-1-(2-methoxyphenyl)-3-(3-methylphenyl)-3-(*N*-tert-butoxycarbonylamino)-1-propanone (6d): colorless oil; IR (neat) ν 3447, 1716, 1676,

1486, 1243, 1163 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.31 (s, 9H), 2.37 (s, 3H), 3.96 (s, 3H), 4.23 (d, $J = 3.6$ Hz, 1H), 5.18 (brd, $J = 9.8$ Hz, 1H), 5.29 (brd, $J = 9.8$ Hz, 1H), 5.41 (brs, 1H), 7.02-7.27 (m, 6H), 7.56 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.84 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 21.6, 28.1, 54.9, 55.5, 79.3, 79.7, 111.6, 121.3, 123.5, 123.5, 127.2, 128.0, 128.4, 131.6, 135.3, 138.0, 140.8, 154.7, 158.7, 200.6; ESI-MS m/z 408 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{26} +44.8$ (c 1.6, CHCl_3) (99% ee); HRMS (FAB): m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_5\text{N}$ $[\text{M}+\text{H}]^+$: 386.1967; found: 386.1968; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 12.0 min (major) and 7.0 min (minor).

(2R, 3S)-2-Hydroxy-1-(2-methoxyphenyl)-3-(2-methylphenyl)-3-(*N*-tert-butoxycarbonylamino)-1-propanone (6e): colorless oil; IR (neat) ν 3448, 1710, 1244,

1164 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.33 (s, 9H), 2.33 (s, 3H), 3.77 (s, 3H), 4.21 (brs, 1H), 5.21 (brd, $J = 9.2$ Hz, 1H), 5.32 (brd, $J = 9.2$ Hz, 1H), 5.37 (brs, 1H), 6.97-7.24 (m, 5H), 7.53 (brs, 2H), 7.73 (d, $J = 7.3$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.1, 28.2, 51.5, 55.4, 78.2, 79.4, 111.3, 121.3, 124.4, 126.1, 127.2, 127.4, 130.3, 131.3, 134.7, 135.2, 138.9, 154.6, 158.2, 201.7; ESI-MS m/z 408 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{26} +98.2$ (c 1.1, CHCl_3) (99% ee); HRMS (FAB): m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_5\text{N}$ $[\text{M}+\text{H}]^+$: 386.1967; found: 386.1967; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 16.3 min (major) and 8.5 min (minor).

(2R, 3S)-3-(4-Chlorophenyl)-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-tert-butoxycarbonylamino)-1-propanone (6f): colorless foam; IR (KBr) ν 3430, 1715, 1487,

1243, 1164 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.29 (s, 9H), 3.94 (s, 3H), 4.26 (d, $J = 4.0$ Hz, 1H), 5.16 (brd, $J = 9.5$ Hz, 1H), 5.27 (brd, $J = 9.5$ Hz, 1H), 5.37 (d, $J = 2.8$ Hz, 1H), 7.03-7.11 (m, 2H), 7.32-7.38 (m, 4H), 7.57 (dd, $J = 7.7, 7.7$ Hz, 1H), 7.84 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 28.1, 54.5, 55.6, 79.4, 79.6, 111.8, 121.4, 123.3, 128.0, 128.6, 131.6, 133.1, 135.5, 139.6, 154.7, 158.7, 200.2; ESI-MS

m/z 428 $[M+Na]^+$; $[\alpha]_D^{24} +37.8$ (c 0.818, $CHCl_3$) (98% ee); HRMS (FAB): m/z calcd for $C_{21}H_{25}O_5NCl$ $[M+H]^+$: 406.1421; found: 406.1431; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 21.1 min (major) and 8.1 min (minor).

(2*R*, 3*S*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(1-naphthyl)-3-(*N*-*tert*-butoxycarbonylamino)-1-propanone (6g):

colorless solid; IR (KBr) ν 3451, 1704, 1656, 1487, 1235 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.42 (s, 9H), 3.64 (s, 3H), 4.33 (brs, 1H), 5.32 (brd, $J = 10.0$ Hz, 1H), 5.59 (brs, 1H), 5.97 (brd, $J = 10.0$ Hz, 1H), 7.01 (d, $J = 7.8$ Hz, 1H), 7.10 (dd, $J = 7.8, 7.8$ Hz, 1H), 7.46-7.52 (m, 3H), 7.57 (dd, $J = 7.8, 7.8$ Hz, 1H), 7.80-7.86 (m, 4H), 8.12 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.2, 51.0, 55.5, 78.4, 79.5, 111.5, 121.4, 123.2, 124.1, 124.8, 125.4, 125.5, 126.1, 128.2, 128.9, 130.4, 131.6, 133.9, 135.0, 136.6, 154.7, 158.5, 201.2; ESI-MS m/z 444 $[M+Na]^+$; $[\alpha]_D^{24} +56.1$ (c 1.04, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{25}H_{28}O_5N$ $[M+H]^+$: 422.1967; found: 422.1970; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 15.1 min (major) and 12.6 min (minor).

(2*R*, 3*S*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(2-naphthyl)-3-(*N*-*tert*-butoxycarbonylamino)-1-propanone (6h):

colorless solid; IR (KBr) ν 3424, 1712, 1668, 1167 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.32 (s, 9H), 3.95 (s, 3H), 4.31 (d, $J = 4.0$ Hz, 1H), 5.37 (brd, $J = 9.8$ Hz, 1H), 5.40 (brd, $J = 9.8$ Hz, 1H), 5.53 (d, $J = 3.4$ Hz, 1H), 7.03-7.09 (m, 2H), 7.43-7.48 (m, 2H), 7.55-7.60 (m, 2H), 7.80-7.93 (m, 5H); ^{13}C NMR ($CDCl_3$ - CD_3OD mixture) δ 28.6, 56.3, 56.9, 80.4, 80.8, 112.9, 122.0, 125.5, 125.8, 126.2, 126.6, 127.0, 128.4, 128.7, 128.9, 132.0, 133.9, 134.5, 135.9, 139.2, 157.0, 159.8, 201.7; ESI-MS m/z 444 $[M+Na]^+$; $[\alpha]_D^{26} +27.0$ (c 1.08, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{25}H_{28}O_5N$ $[M+H]^+$: 422.1967; found: 422.1972; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 20.1 min (major) and 13.2 min (minor).

(2*R*, 3*R*)-3-(2-Furyl)-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-*tert*-butoxycarbonylamino)-1-propanone (6i):

pale yellow oil; IR (neat) ν 3440, 1715, 1665, 1244, 1165 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.33 (s, 9H), 3.97 (s, 3H), 4.28 (d, $J = 4.6$ Hz, 1H), 5.16 (brd, $J = 9.9$ Hz, 1H), 5.33 (brd, $J = 9.9$ Hz, 1H), 5.56 (d, $J = 4.0$ Hz, 1H), 6.27 (brs, 1H), 6.35 (brs, 1H), 7.01-7.08 (m, 2H), 7.41 (brs, 1H), 7.56 (dd, $J = 7.6, 7.6$ Hz, 1H), 7.89 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.1, 50.5, 55.5, 77.7, 79.6, 106.3, 110.4, 111.8, 121.2, 123.0, 131.6, 135.6, 141.9, 153.7, 154.8,

159.2, 199.4; ESI-MS m/z 384 $[M+Na]^+$; $[\alpha]_D^{24} +35.2$ (c 1.30, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{19}H_{24}O_6N$ $[M+H]^+$: 362.1603; found: 362.1609; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 10.7 min (major) and 6.9 min (minor).

(2*R*, 3*R*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(*N*-*tert*-butoxycarbonylamino)-3-(2-thiophenyl)-1-propanone

(6j): pale yellow oil; IR (neat) ν 3488, 1675, 1662, 1240, 1161 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.32 (s, 9H), 3.96 (s, 3H), 4.35 (d, J = 4.3 Hz, 1H), 5.24 (brd, J = 9.8 Hz, 1H), 5.47 (d, J = 3.4 Hz, 1H),

5.51 (brd, J = 9.8 Hz, 1H), 6.96-7.09 (m, 5H), 7.24 (d, J = 4.9 Hz, 1H), 7.57 (dd, J = 7.6, 7.6 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.1, 51.7, 55.6, 79.6, 79.8, 111.8, 121.3, 123.1, 124.5, 124.6, 126.7, 131.7, 135.6, 144.5, 154.6, 159.0, 199.2; ESI-MS m/z 400 $[M+Na]^+$; $[\alpha]_D^{24} +63.6$ (c 0.96, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{19}H_{24}O_5NS$ $[M+H]^+$: 378.1375; found: 378.1377; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 14.3 min (major) and 8.8 min (minor).

(2*R*, 3*S*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(*N*-*tert*-butoxycarbonylamino)-3-(3-pyridyl)-1-propanone

(6k): colorless foam; IR (KBr) ν 3480, 1713, 1687, 1291, 1245 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.30 (s, 9H), 3.97 (s, 3H), 4.36 (brs, 1H),

5.25 (brd, J = 9.5 Hz, 1H), 5.36 (brd, J = 9.5 Hz, 1H), 5.38 (brs, 1H), 7.05-7.10 (m, 2H), 7.31 (dd, J = 4.0, 7.6 Hz, 1H), 7.59 (dd, J = 7.6, 7.6 Hz, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.0 Hz, 1H), 8.70 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 28.1, 53.3, 55.7, 79.2, 79.8, 111.8, 121.5, 123.2, 123.4, 131.7, 134.4, 135.6, 136.6, 148.5, 148.7, 154.7, 158.7, 199.8; ESI-MS m/z 373 $[M+H]^+$; $[\alpha]_D^{24} +65.3$ (c 0.77, $CHCl_3$) (99% ee); HRMS (FAB): m/z calcd for $C_{20}H_{25}O_5N_2$ $[M+H]^+$: 373.1763; found: 373.1762; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 20.2 min (major) and 15.7 min (minor).

4*E*-(2*R*, 3*S*)-2-Hydroxy-1-(2-methoxyphenyl)-3-(*N*-*tert*-butoxycarbonylamino)-5-phenyl-4-penten-1-one

(6l): colorless solid; IR (KBr) ν 3437, 1708, 1673, 1507, 1165 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.32 (s, 9H), 3.96 (s, 3H), 4.22 (d, J = 4.6 Hz, 1H), 4.81 (brd, J = 9.5 Hz, 1H), 4.96 (brd, J = 9.5 Hz, 1H), 5.27 (brs, 1H), 6.35 (dd, J = 6.1, 15.9 Hz, 1H), 6.59 (d, J = 15.9 Hz, 1H), 7.01-7.05 (m, 2H), 7.23-7.42 (m, 5H), 7.56 (dd, J = 7.4, 7.4 Hz, 1H), 7.84 (d, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.2, 54.0, 55.6, 78.9, 79.4, 111.7, 121.3, 123.5, 126.5, 127.6, 128.3, 128.5, 131.0, 131.5, 135.3, 136.7, 154.7, 158.9, 200.2; ESI-MS m/z 420 $[M+Na]^+$;

$[\alpha]_D^{24} +22.7$ (*c* 0.93, CHCl₃) (99% ee); HRMS (FAB): *m/z* calcd for C₂₃H₂₈O₅N [M+H]⁺: 398.1967; found: 398.1975; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) *t_R* 14.8 min (major) and 11.4 min (minor).

4*E*-(2*R*, 3*S*)-2-Hydroxy-1-(2-methoxyphenyl)-4-methyl-3-(*N*-*tert*-butoxycarbonylamino)-5-phenyl-4-penten-1-one (6m): colorless foam; IR (KBr) ν 3439, 1716,

1488, 1245, 1165 cm⁻¹; ¹H NMR (CDCl₃) δ 1.33 (s, 9H), 2.01 (s, 3H), 3.94 (s, 3H), 4.20 (d, *J* = 3.6Hz, 1H), 4.62 (brd, *J* = 10.0 Hz, 1H), 5.08 (brd, *J* = 10.0 Hz, 1H), 5.44 (d, *J* = 2.5Hz, 1H), 6.49 (s, 1H), 7.00-7.07 (m, 2H), 7.18-7.34 (m, 5H), 7.55 (dd, *J* = 7.3, 7.3Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H); ¹³C NMR (CDCl₃) δ 15.7, 28.2, 55.4, 57.8, 77.7, 79.3, 111.4, 121.2, 123.5, 125.7, 126.3, 128.0, 129.1, 131.5, 135.2, 136.3, 137.7, 154.7, 158.5, 201.3; ESI-MS *m/z* 434 [M+Na]⁺; $[\alpha]_D^{24} +57.4$ (*c* 1.78, CHCl₃) (99% ee); HRMS (FAB): *m/z* calcd for C₂₄H₃₀O₅N [M+H]⁺: 412.2124; found: 412.2134; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 0.5 mL/min, detection at 254 nm) *t_R* 39.1 min (major) and 18.2 min (minor).

4*E*-(2*R*, 3*S*)-5-(2-Furyl)-2-hydroxy-1-(2-methoxyphenyl)-3-(*N*-*tert*-butoxycarbonylamino)-4-penten-1-one (6n): colorless foam; IR (KBr) ν 3430, 2975,

1714, 1487, 1244, 1165 cm⁻¹; ¹H NMR (CDCl₃) δ 1.32 (s, 9H), 3.97 (s, 3H), 4.19 (d, *J* = 3.6Hz, 1H), 4.81 (dd, *J* = 3.6, 9.8 Hz, 1H), 4.93 (brd, *J* = 9.8 Hz, 1H), 5.26 (brs, 1H), 6.24-6.43 (m, 4H), 6.98-7.10 (m, 2H), 7.35 (brs, 1H), 7.56 (brs, 1H), 7.56 (dd, *J* = 7.7, 7.7Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H); ¹³C NMR (CDCl₃) δ 28.1, 53.5, 55.6, 78.7, 79.4, 108.1, 111.2, 111.7, 119.2, 121.2, 123.3, 127.0, 131.5, 135.4, 141.9, 152.2, 154.7, 158.9, 200.0; ESI-MS *m/z* 410 [M+Na]⁺; $[\alpha]_D^{23} +23.4$ (*c* 0.847, CHCl₃) (99% ee); HRMS (FAB): *m/z* calcd for C₂₁H₂₆O₆N [M+H]⁺: 388.1760; found: 388.1761; HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 90/10, flow 1.0 mL/min, detection at 254 nm) *t_R* 12.9 min (major) and 8.1 min (minor).

Determination of absolute and relative configurations.

Absolute configurations of **5b**, **6h**, **6j**, and **6l** were determined by Mosher's method. Relative configurations of **5b** and **6g** were determined by X-ray crystallographic analysis. CIF files are available as Supporting Information. Relative configurations of **5a**, **5b**, **5j**, **5k**, **5l**, **6e**, **6g**, and **6i** were determined by NOE experiments of corresponding cyclic carbamates. Absolute and relative configuration of **6a** was determined by comparison of α_D value and NMR after conversion into a side chain of Taxotere **10**. Absolute and relative configuration of **6b** was determined by comparison of α_D value and NMR after conversion

into *epi*-cytoxazone **12**. Absolute and relative configurations of other Mannich-adducts were speculated by analogy.

Initial rate kinetic studies:

General Procedure for kinetic study:

To a stirred solution of (*S,S*)-linked-BINOL **1** (x mmol) in THF at –20 °C, was added Et₂Zn (4x mmol, 1.0 M in hexanes). After stirring for 30 min at the same temperature, a solution of **2a** (y mmol) in THF and imine **3** or **4** (z mmol) was added. The reaction mixture was stirred at –20 °C. Samples were taken at recorded times according to the following procedure: 0.1 mL of the reaction mixture was taken with a syringe filled with 0.3 mL of saturated aqueous NH₄Cl solution and was immediately poured onto saturated aqueous NH₄Cl (2.0 mL). The resulting mixture was extracted with ethyl acetate. After evaporating solvents, the crude residue was analyzed by ¹H NMR to determine yield. x, y, z-Values, total amount of solvent used, and initial concentration are shown in the following Figures.

anti-Mannich-type reaction:

<Initial rate kinetics of Et₂Zn/linked-BINOL complex>

<Initial rate kinetics of imine 3b>

<Initial rate kinetics of ketone 2>

syn-Mannich-type reaction:

<Initial rate kinetics of Et₂Zn/linked-BINOL complex>

<Initial rate kinetics of imine 4a>

<Initial rate kinetics of ketone 2>

<Relationship between Ee of Mannich-adduct and Ligand>

There was linear relationship between ee of Mannich-adduct **5b** from Dpp-imine **3b** and ee of linked-BINOL, as summarized in the Figure below. Reaction rate was almost same in all cases using ligand of >99% ee, 75% ee, 50% ee, 25% ee, and 0% ee.

(C) Transformations of Mannich Adducts:

(4*R*, 5*R*)-5-(*o*-Anisoyl)-4-(2-methylphenyl)-2-oxazolidinone (**7**)

To a stirred solution of **5b** (296.2 mg, 0.610 mmol) in THF (3.05 ml) was added concd. HCl (3.05 mL, 0.702 mmol) at 0°C . After stirring at room temperature for 1 h, the reaction mixture was basified with K_2CO_3 (pH 10) and extracted with CH_2Cl_2 . The combined organic extracts were washed with brine and dried over Na_2SO_4 . The CH_2Cl_2 solvent was evaporated under reduced pressure (to ~6 mL, due to the instability of the intermediate under highly concentrated conditions). After cooling to -78°C , pyridine (79.6 μL , 0.976 mmol) and triphosgene (488 μL , 1.0 M in CH_2Cl_2 , 0.488 mmol) was added slowly and stirred for 30 min at this temperature. The resulting solution was quenched with saturated aqueous NaHCO_3 and extracted with ether. The combined

organic extracts were washed successively with 1N HCl, saturated aqueous NaHCO₃ and brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to give **7** (159.6 mg, 0.512 mmol, yield 84 %) as a white solid: IR (neat) ν 1782, 1695, 1598, 1487 cm⁻¹; ¹H NMR (CDCl₃) δ 1.95 (s, 3H), 3.87 (s, 3H), 5.72 (brs, 1H), 6.43 (d, J = 9.5 Hz, 1H), 6.60-6.66 (m, 2H), 6.70 (d, J = 7.6 Hz, 1H), 6.78 (d, J = 8.5 Hz, 1H), 6.99 (dd, J = 7.6, 7.6 Hz, 1H), 7.10 (dd, J = 7.6, 7.6 Hz, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.29 (ddd, J = 2.4, 8.5, 8.5 Hz, 1H); ¹³C NMR (CDCl₃) δ 18.5, 54.9, 55.7, 82.0, 110.7, 120.9, 125.7, 126.6, 126.6, 128.4, 130.0, 130.5, 133.4, 133.9, 135.6, 157.5, 159.0, 194.8; ESI-MS m/z 334 [M+Na]⁺; [α]_D²⁵ +33.8 (c 0.34, CHCl₃). The relative stereochemistry was confirmed by NOESY experiment.

2'-Methoxyphenyl (4R,5R)-4-(2-methylphenyl)-2-oxo-oxazolidin-5-carboxylate (8):

To a stirred solution of **7** (24.2 mg, 0.0777 mmol) in dichloroethane (0.77 mL) at room temperature were added NaH₂PO₄·2H₂O (48.5 mg, 0.312 mmol) and *m*-chloroperbenzoic acid (40.2 mg, 0.233 mmol). After being stirred for 3 h at 60 °C, the reaction mixture was quenched with saturated aqueous Na₂S₂O₃. The resulting mixture was extracted with diethyl ether. The combined organic extracts were washed with ice-cooled saturated aqueous NaHCO₃ and brine, and then dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 2/1) to give **8** (22.3 mg, 0.0681 mmol, yield 88%) as a colorless solid: IR (KBr) ν 1782, 1501 cm⁻¹; ¹H NMR (CDCl₃) δ 2.40 (s, 3H), 3.71 (s, 3H), 5.57-5.65 (m, 3H), 5.91 (brs, 1H), 6.64 (dd, J = 7.6, 8.0 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 7.07 (dd, J = 7.6, 8.2 Hz, 1H), 7.20 (d, J = 7.3 Hz, 1H), 7.26-7.33 (m, 2H), 7.48 (d, J = 7.3 Hz, 1H); ¹³C NMR (CDCl₃) δ 19.3, 55.1, 55.7, 77.0, 112.2, 120.4, 121.8, 126.1, 126.9, 127.3, 129.1, 130.7, 133.3, 136.5, 138.2, 150.7, 158.1, 164.3; ESI-MS m/z 350 [M+Na]⁺; [α]_D²⁴ -169.1 (c 0.48, CHCl₃) HRMS (EI): m/z calcd for C₁₈H₁₇O₅N [M⁺]: 327.1107; found: 327.1110. The relative stereochemistry was confirmed by NOE observation.

(2R,3S)-2-Acetoxy-1-(2-methoxyphenyl)-3-(N-tert-butoxycarbonylamino)-3-phenyl-1-propanone:

To a solution of **6b** (230 mg, 0.619 mmol) in pyridine (4 mL) at 0 °C were added DMAP (15.1 mg, 0.124 mmol) and Ac₂O (105 μ L, 1.12 mmol). The mixture was stirred at 25 °C for 12 h, then H₂O was added. The mixture was extracted with diethyl ether (x 3). The combined organic layers were washed with 1 M *aq.* HCl, sat. *aq.* NaHCO₃, brine, and dried over Na₂SO₄. After evaporation under reduced pressure, the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 1/2) to give Ac-adduct (241.6 mg, yield 94 %) as colorless foam; IR (KBr) ν 1749, 1716,

1232 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.33 (s, 9H), 2.10 (s, 3H), 3.95 (s, 3H), 5.44 (brs, 2H), 6.38 (brs, 1H), 7.01-7.06 (m, 2H), 7.25-7.37 (m, 5H), 7.54 (dd, $J = 7.0, 7.0\text{ Hz}$, 1H), 7.83 (d, $J = 7.0\text{ Hz}$, 1H); ^{13}C NMR (CDCl_3) δ 20.5, 28.1, 53.3, 55.7, 79.7, 81.2, 111.7, 121.2, 124.4, 126.2, 127.4, 128.5, 131.6, 135.0, 139.5, 154.7, 158.5, 169.8, 193.9; ESI-MS m/z 436 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{24}$ -45.3 (c 1.1, CHCl_3); HRMS (FAB): m/z calcd for $\text{C}_{23}\text{H}_{28}\text{O}_6\text{N}$ $[\text{M}+\text{H}]^+$: 414.1916; found: 414.1913.

2-Methoxyphenyl (2R,3S)-2-Acetoxy-3-(N-tert-butoxycarbonylamino)-3-phenyl-propanoate (9):

A mixture of Ac-adduct (24.8 mg, 0.06 mmol), *m*CPBA (51.8 mg, 0.3 mmol), Na_2HPO_4 (85.2 mg, 0.6 mmol), and 4,4'-thiobis(6-tert-butyl-*m*-cresol) (1.0 mg) was stirred at 60 $^\circ\text{C}$ for 10 h. After cooling down to rt, sat. *aq.* $\text{Na}_2\text{S}_2\text{O}_3$ was added. The mixture was extracted with ethyl acetate (x 3), organic layers were washed with cold sat. *aq.* NaHCO_3 , brine, and dried over Na_2SO_4 . After evaporation under reduced pressure, the resulting residue was purified by silica gel column chromatography (hexane/diethyl ether = 1/1) to give **9** (25.1 mg, yield 97 %) as colorless oil; IR (KBr) ν 1784, 1755, 1717, 1501, 1170 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.45 (s, 9H), 2.10 (s, 3H), 3.83 (s, 3H), 5.60 (brs, 2H), 5.73 (d, $J = 8.6\text{ Hz}$, 1H), 6.93 (dd, $J = 7.6, 8.0\text{ Hz}$, 1H), 6.97 (d, $J = 8.0$, 1H), 7.09 (d, $J = 7.3$, 1H), 7.22 (dd, $J = 7.3, 7.6$, 1H), 7.25-7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ 20.4, 28.3, 54.6, 55.9, 74.6, 80.0, 112.4, 120.6, 122.7, 126.4, 127.3, 127.8, 128.6, 138.2, 139.0, 150.8, 154.8, 165.8, 169.5; ESI-MS m/z 452 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{25}$ -1.34 (c 1.6, CHCl_3); HRMS (FAB): m/z calcd for $\text{C}_{23}\text{H}_{28}\text{O}_7\text{N}$ $[\text{M}+\text{H}]^+$: 430.1866; found: 430.1869.

Taxotere® side chain (10):

A mixture of **9** (10.8 mg, 0.025 mmol) and K_2CO_3 (10.4 mg, 0.075 mmol) in MeOH (1 mL) was stirred at 25 $^\circ\text{C}$ for 1 h. Then, H_2O was added and the mixture was extracted with ethyl acetate (x3). The organic layers were washed with H_2O , sat. *aq.* NH_4Cl , brine, and dried over Na_2SO_4 . After evaporation under reduced pressure, the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 2/1) to give **10** (7.5 mg, yield quant) as colorless solid; IR (KBr) ν 3510, 3380, 1734, 1689, 1518, 1249 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.42 (s, 9H), 3.24 (d, $J = 4.0\text{ Hz}$, 1H), 3.83 (s, 3H), 4.47 (brs, 1H), 5.22 (brd, $J = 9.2\text{ Hz}$, 1H), 5.44 (brd, $J = 9.2\text{ Hz}$, 1H), 7.26-7.38 (m, 5H); ^{13}C NMR (CDCl_3) δ 28.2, 53.0, 56.0, 73.5, 79.9, 126.7, 127.7, 128.6, 139.0, 155.1, 173.4; ESI-MS m/z 318 $[\text{M}+\text{Na}]^+$; $[\alpha]_{\text{D}}^{24}$ -6.1 (c 1.4, CHCl_3); Spectra data matched well with reported data. Lit. $[\alpha]_{\text{D}}^{20}$ -6.81 (c 1.0, CHCl_3), *Tetrahedron Asymmetry* **2000**, 11, 4485.

(4S,5R)-5-(*o*-Anisoyl)-4-(4-methoxyphenyl)-2-oxazolidinone: To a mixture of anisole (189.2 mg, 1.75

mmol) and TFA (1.0 mL) at 0 °C, was added **6b** (70.3 mg, 0.175 mmol). After stirring at room temperature for 5 min, the reaction mixture was basified with K₂CO₃ (2 g in 20 mL H₂O) and extracted with CH₂Cl₂ (x 3). The combined organic extracts were washed with H₂O, brine and dried over Na₂SO₄. The CH₂Cl₂ solvent was evaporated under reduced pressure (to ~5 mL, due to the instability of the intermediate under highly concentrated conditions). After cooling to -78 °C, pyridine (45.3 µL, 0.56 mmol) and triphosgene (83.1 mg, 0.28 mmol) in CH₂Cl₂ (0.40 mL) was added slowly and stirred for 30 min at -78 °C. The resulting solution was quenched with saturated aqueous NaHCO₃ and extracted with ether. The combined organic extracts were washed successively with 1M HCl, saturated aqueous NaHCO₃ and brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to give oxazolidinone adduct (52.6 mg, yield 92 %) as colorless oil; IR (KBr) ν 1759, 1678, 1247 cm⁻¹; ¹H NMR (CDCl₃) δ 3.47 (s, 3H), 3.82 (s, 3H), 4.81 (d, *J* = 4.3 Hz, 1H), 5.65 (d, *J* = 4.3 Hz, 1H), 6.35 (brs, 1H), 6.89-6.93 (m, 3H), 7.05 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.24-7.28 (m, 2H), 7.52 (ddd, *J* = 1.7, 7.6, 7.6 Hz, 1H), 7.82 (dd, *J* = 1.7, 7.6 Hz, 1H); ¹³C NMR (CDCl₃) δ 55.2, 55.3, 58.0, 85.5, 111.4, 114.3, 121.1, 124.0, 127.7, 131.4, 132.6, 135.2, 158.7, 158.8, 159.7, 194.8; ESI-MS *m/z* 350 [M+Na]⁺; [α]_D²⁴ -56.4 (*c* 1.14, CHCl₃); HRMS (FAB): *m/z* calcd for C₁₈H₁₈O₅N [M+H]⁺: 328.1185; found: 328.1175.

2'-Methoxyphenyl (4S,5R)-4-(4-methoxyphenyl)-2-oxo-oxazolidin-5-carboxylate (11):

A mixture of oxazolidinone adduct (44.6 mg, 0.136 mmol), *m*CPBA (70.5 mg, 0.409 mmol), and NaH₂PO₄·2H₂O (85.0 mg, 0.545 mmol) was stirred at 60 °C for 3 h. After cooling down to rt, sat. *aq.* Na₂S₂O₃ was added. The mixture was extracted with diethyl ether (x 3), organic layers were washed with cold sat. *aq.* NaHCO₃, brine, and dried over Na₂SO₄. After evaporation under reduced pressure, the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to give **11** (29.3 mg, yield 63 %) as colorless solid; IR (KBr) ν 1783, 1760, 1743 cm⁻¹; ¹H NMR (CDCl₃) δ 3.82 (s, 3H), 3.87 (s, 3H), 4.98 (d, *J* = 5.5 Hz, 1H), 5.18 (d, *J* = 5.5 Hz, 1H), 6.23 (brs, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.95-7.01 (m, 2H), 7.08 (dd, *J* = 1.5, 7.9 Hz, 1H), 7.23-7.31 (m, 1H), 7.37 (dd, *J* = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 55.4, 55.9, 58.9, 80.3, 112.4, 114.6, 120.9, 122.4, 127.3, 127.6, 130.8, 138.8, 150.6, 157.8, 160.2, 166.3; ESI-MS *m/z* 366 [M+Na]⁺; [α]_D²⁵ -130.3 (*c* 1.52, CHCl₃); HRMS (FAB): *m/z* calcd for C₁₈H₁₈O₆N [M+H]⁺: 344.1134; found: 344.1135.

epi-Cytoxazone (12): To a mixture of NaBH₄ (11.3 mg, 0.299 mmol) in THF (1 mL) at 0 °C was added **11** (51.3 mg, 0.149 mmol) in THF (2 mL), and then acetic acid (8.5 µL, 0.149 mmol). The mixture was stirred at 25 °C for 2 h, then sat. *aq.* NH₄Cl was added. The

mixture was extracted with diethyl ether (x 3), organic layers were washed with sat. *aq.* NaHCO₃, H₂O, brine, and dried over Na₂SO₄. After evaporation under reduced pressure, the resulting residue was purified by silica gel column chromatography (CHCl₃/methanol = 10/1) to give **12** (29.3 mg, yield 88 %) as colorless oil; IR (KBr) ν 3253, 3148, 1751, 1740, 1725 cm⁻¹; ¹H NMR (acetone-d₆) δ 3.66-3.71 (m, 1H), 3.80 (s, 3H), 3.78-3.85 (m, 1H), 4.23-4.26 (m, 1H), 4.35 (brs, 1H), 4.78 (d, *J* = 6.6 Hz, 1H), 6.94-6.97 (m, 3H), 7.31-7.35 (m, 2H); ¹³C NMR (acetone-d₆) δ 55.5, 57.6, 62.4, 85.6, 115.0, 128.4, 133.8, 159.0, 160.6; ESI-MS *m/z* 246 [M+Na]⁺; [α]_D²⁵ -27.2 (*c* 1.1, MeOH); Spectra data matched well with reported data. Lit. [α]_D²⁸ -30.4 (*c* 1.0, MeOH), Sakamoto, Y.; Shiraishi, A.; Seonhee, J.; Nakata, T. *Tetrahedron Lett.* **1999**, *40*, 4203.