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Sequential Wittig-Catalytic Asymmetric Epoxidation Reaction Reusing Waste $Ph_3P(O)$: Application of *N*-Acylpyrrole as Ester Surrogate

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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 ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (= 0) or in the scale relative to $CHCl_3$ (7.24 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CHCl_3$ (77.0 ppm for ^{13}C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI mass spectra were measured on Waters-ZQ4000. EI mass spectra were measured on JMS-BU20 GCmate. 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, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm; column, DAICEL CHIRALCEL OD, OJ, CHIRALPAK AD, AS, AD-H, AS-H; mobile phase, hexane–2-propanol; flow rate, 1.0 mL/min. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Sm(O-*i*-Pr)$_3$ was purchased from Kojundo Chemical Laboratory Co., Ltd. (Fax: +81-492-84-1351, sales@kojundo.co.jp). Other reagents were purified by the usual methods. MS 4A (powder) was purchased from Fluka and used without any prior activation.

Synthesis of Pyrrolylmethylenetriphenylphosphorane (ylide: 3)

To a suspension of methyl triphenylphosphonium bromide (12.9 g, 36 mmol) in THF (14 mL) at 0 °C was added PhLi (Et_2O solution, 28.1 mL, 36 mmol). The mixture was stirred at 25 °C for 60 min to afford methylenetriphenylphosphorane. Then, the mixture was cooled down to –78 °C, and the solution of 1,1'-carbonyl-dipyrrole (1.92 g, 12 mmol) in THF (18 mL) was added. The cooling bath was removed and the reaction mixture was stirred overnight at 25 °C. H_2O was added and the mixture was extracted with ethyl acetate/CH_2Cl_2 = 5/1 (x3). The organic layers were washed with brine and dried over

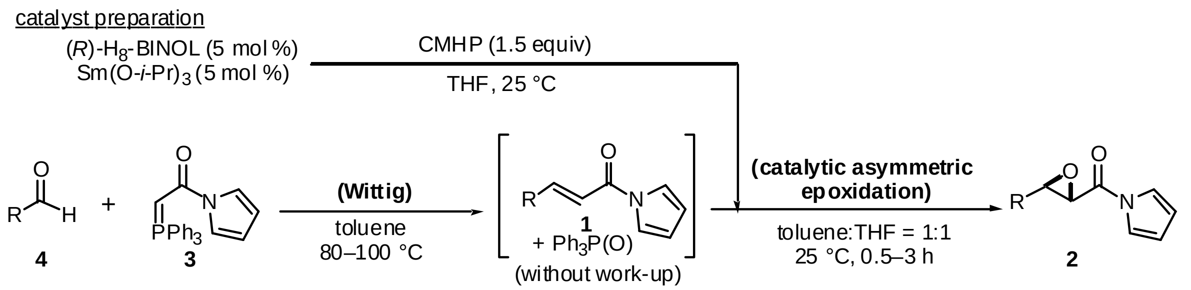
$MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography to afford ylide **3** (4.33 g, 11.7 mmol, y. 98%).

IR (KBr) ν 3434, 3048, 1601, 1438 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68. (ddd, *J* = 12.5, 7.4, 1.3 Hz, 6H), 7.56 (td, *J* = 7.4, 1.3 Hz, 3H), 7.47 (ddd, *J* = 7.4, 7.4, 2.8 Hz, 6H), 7.33-7.35 (m, 2H), 6.15-6.18 (m, 2H), 3.71 (d, *J* = 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.0 (d, *J* = 125 Hz), 109.3, 118.3, 126.4 (d, *J* = 91.5Hz), 128.8 (d, *J* = 12.4 Hz), 132.1 (d, *J* = 2.1 Hz), 132.9 (d, *J* = 10.3 Hz); ESI-MS *m/z* 370 [M+H]$^+$.

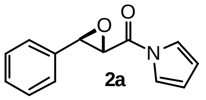
Preparation of Sm-(*R*)-H_8-BINOL Catalyst in THF: To a stirred suspension of MS4A (500 mg) and (*R*)-H_8-BINOL (7.4 mg, 0.025 mmol) in THF (2.14 mL), Sm(O-*i*-Pr)$_3$ (125 μL, 0.025 mmol, 0.2 M in THF) was added at 25 °C. After stirring for 20 min at this temperature, cumene hydroperoxide (CMHP) (231 μL, 0.75 mmol, 3.25M in toluene) was added. The stirring was continued for another 20 min at 25 °C to afford Sm-(*R*)-H_8-BINOL catalyst in THF. The resulting suspension was used for the second catalytic asymmetric epoxidation immediately.

General Procedure for Sequential Wittig-Catalytic Asymmetric Epoxidation Reaction : To a stirred suspension of ylide **3** (139.1 mg, 0.65 mmol) in toluene (1.25 mL) at 25 °C was added benzaldehyde (**4a**) (50.8 μL, 0.5 mmol). The stirring was continued for 36 h at 100 °C and cooled to 25 °C. To the reaction solution at 25 °C was added toluene (1.25 mL) and catalyst suspension prepared from Sm(O-*i*-Pr)$_3$ (125 μL, 0.025 mmol, 0.2 M in THF), (*R*)-H_8-BINOL (7.4 mg, 0.025 mmol), cumene hydroperoxide (CMHP) (231 μL, 0.75 mmol, 3.25M in toluene) and MS 4A (2.5 mL) by the above-mentioned procedure. The stirring was continued for 30 min and quenched with 2.5% aqueous citric acid. The mixture was filtered through Celite and the filtrate was extracted with ethyl acetate. Then combined organic layers were washed successively with sat. aq. $NaHCO_3$ and brine, and was dried over $MgSO_4$. The solvent was evaporated and the resulting crude residue was purified by flash silica gel column chromatography (ethyl acetate/hexane = 1/20) to afford **2a** (102.4 mg, 96% yield, >99.5% ee).

Scheme S1. Procedure for a sequential Wittig-catalytic asymmetric epoxidation reaction

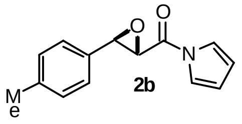


Synthesis of Pyrrolyl Epoxides via Sequential Processes.



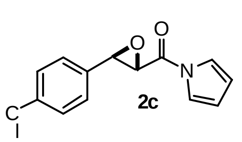
2a

(2*S*,3*R*)-*trans*-2,3-Epoxy-3-phenyl-1-pyrrol-1-yl-propan-1-one (2a): IR (KBr) ν 3149, 1714, 1287, 904 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.32-7.42 (m, 7H), 6.33-6.36 (m, 2H), 4.20 (d, *J* = 1.9 Hz, 1H), 4.01 (d, *J* = 1.9 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 57.3, 58.8, 114.1, 119.0, 125.7, 128.8, 129.2, 134.4, 164.3; ESI-MS *m/z* 236 [M+Na]$^+$; [α]$_D^{24}$ +150 (*c* 1.07, CHCl$_3$) (>99.5% ee); HRMS calcd. for $C_{13}H_{11}NO_2$ [M+H]$^+$: 213.0868, found 213.0870; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t$_R$ 28.0 min (minor) and 36.0 min (major).



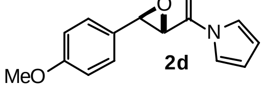
2b

(2*S*,3*R*)-*trans*-2,3-Epoxy-3-(4-methylphenyl)-1-pyrrol-1-yl-propan-1-one (2b): IR (KBr) ν 3152, 1713, 1284, 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.20-7.26 (m, 2H), 6.35-6.37 (m, 2H), 4.18 (d, *J* = 1.7 Hz, 1H), 4.02 (d, *J* = 1.7 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 21.2, 57.3, 58.9, 114.1, 119.0, 125.7, 129.5, 131.4, 139.3, 164.5; ESI-MS *m/z* 250 [M+Na]$^+$; [α]$_D^{25}$ +153 (*c* 1.22, CHCl$_3$) (99% ee); HRMS calcd. for $C_{14}H_{13}NO_2$ [M+H]$^+$: 228.1024, found 228.1026; HPLC (DAICEL CHIRALCEL OJ, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t$_R$ 33.1 min (major) and 50.2 min (minor).



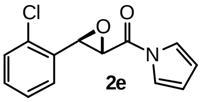
2c

(2*S*,3*R*)-3-(4-Chlorophenyl)-*trans*-2,3-epoxy-1-pyrrol-1-yl-propan-1-one (2c): IR (KBr) ν 1740, 1288, 798 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.35-7.39 (m, 4H), 7.26-7.28 (m, 2H), 6.34-6.36 (m, 2H), 4.18 (d, *J* = 1.7 Hz, 1H), 3.96 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 56.5, 57.4, 113.5, 118.2, 126.3, 128.3, 132.2, 134.5, 163.2; ESI-MS *m/z* 270 (for ^{35}Cl), 272 (for ^{37}Cl) [M+Na]$^+$; [α]$_D^{25}$ +153 (*c* 1.11, CHCl$_3$) (99% ee); HRMS calcd. for $C_{13}H_{10}ClNO_2$ [M+H]$^+$: 248.0478, found 248.0474; HPLC (DAICEL CHIRALPAK AD-H, 2-propanol/hexane 5/95, flow 1.0 mL/min, detection at 254 nm) t$_R$ 15.9 min (major) and 18.3 min (minor).



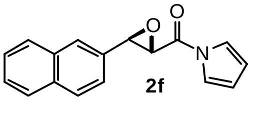
2d

(2*S*,3*R*)-*trans*-2,3-Epoxy-3-(4-methoxyphenyl)-1-pyrrol-1-yl-propan-1-one (2d): IR (KBr) ν 1715, 1288, 910, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39 (br, 2H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.33-6.35 (m, 2H), 4.14 (d, *J* = 1.9 Hz, 1H), 4.00 (d, *J* = 1.9 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 55.4, 57.3, 58.8, 114.1, 114.3, 119.0, 126.3, 127.2, 160.5, 164.5; ESI-MS *m/z* 266 [M+Na]$^+$; $[\alpha]_D^{25}$ +163 (*c* 0.93, $CHCl_3$) (98% ee); HRMS calcd. for $C_{14}H_{13}NO_3$ $[M+H]^+$: 244.0973, found 244.0968; HPLC (DAICEL CHIRALPAK AS-H, 2-propanol/hexane 20/80, flow 1.0 mL/min, detection at 254 nm) t_R 20.2 min (minor) and 37.1 min (major).



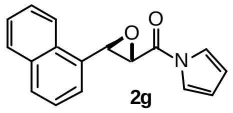
2e

(2*S*,3*R*)-3-(2-Chlorophenyl)-*trans*-2,3-epoxy-1-pyrrol-1-yl-propan-1-one (2e): IR (KBr) ν 1713, 1294, 903 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.37-7.43 (m, 3H), 7.29-7.36 (m, 3H), 6.35-6.37 (m, 2H), 4.52 (d, *J* = 1.8 Hz, 1H), 3.90 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 56.4, 56.6, 114.2, 119.1, 126.1, 127.3, 129.4, 130.0, 132.9, 133.3, 164.1; ESI-MS *m/z* 270 (for ^{35}Cl), 272 (for ^{37}Cl) [M+Na]$^+$; $[\alpha]_D^{25}$ –74.3 (*c* 1.15, $CHCl_3$) (97% ee); HRMS calcd. for $C_{13}H_{10}ClNO_2$ $[M+H]^+$: 248.0478, found 248.0476; HPLC (DAICEL CHIRALPAK AS, 2-propanol/hexane 10/90, flow 1.0 mL/min, detection at 254 nm) t_R 10.8 min (major) and 16.9 min (minor).



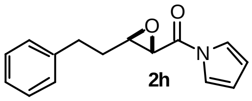
2f

(2*S*,3*R*)-*trans*-2,3-Epoxy-3-(2-naphthyl)-1-pyrrol-1-yl-propan-1-one (2f): IR (KBr) ν 1716, 1288, 910, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82-7.89 (m, 4H), 7.50-7.53 (m, 2H), 7.41 (br, 1H), 7.37 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.33-6.36 (m, 2H), 4.37 (br, 1H), 4.11 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 57.5, 59.1, 114.2, 119.1, 122.2, 125.9, 126.8, 126.8, 127.9, 127.9, 128.9, 131.8, 133.0, 133.7, 164.3; ESI-MS *m/z* 286 [M+Na]$^+$; $[\alpha]_D^{24}$ +169 (*c* 1.01, $CHCl_3$) (99% ee); HRMS calcd. for $C_{17}H_{13}NO_2$ $[M+H]^+$: 264.1024, found 264.1023; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 31.4 min (minor) and 40.0 min (major).

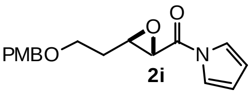


2g

(2*S*,3*R*)-*trans*-2,3-Epoxy-3-(1-naphthyl)-1-pyrrol-1-yl-propan-1-one (2g): IR (KBr) ν 1711, 1292, 901, 801 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.99-8.02 (m, 1H), 7.89-7.92 (m, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.47-7.58 (m, 4H), 7.44 (br, 2H), 6.35-6.38 (m, 2H), 4.84 (d, *J* = 1.7 Hz, 1H), 4.02 (d, *J* = 1.7 Hz, 1H) ; ^{13}C NMR ($CDCl_3$) δ 56.6, 57.3, 114.2, 119.1, 122.4, 122.6, 125.4, 126.3, 126.9, 128.9, 129.2, 130.7, 131.0, 133.2, 164.6; ESI-MS *m/z* 286 [M+Na]$^+$; $[\alpha]_D^{24}$ –157 (*c* 1.12, $CHCl_3$) (99% ee); HRMS calcd. for $C_{17}H_{13}NO_2$ $[M+H]^+$: 264.1024, found 264.1024; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 16.6 min (minor) and 24.6 min (major).

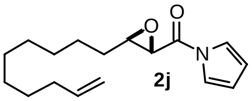

2h

(2*S*,3*R*)-*trans*-2,3-Epoxy-5-phenyl-1-pyrrol-1-yl-pentan-1-one (2h): IR (neat) ν 1723, 1288 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.25-7.30 (m, 2H), 7.16-7.23 (m, 5H), 6.28-6.31 (m, 2H), 3.69 (d, *J* = 1.9 Hz, 1H), 3.30 (dd, *J* = 5.8, 1.9 Hz, 1H), 2.85-2.91 (m, 1H), 2.75-2.82 (m, 1H), 2.00-2.11 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 31.7, 33.0, 53.7, 58.8, 113.9, 118.9, 126.4, 128.3, 128.7, 140.2, 165.4; ESI-MS *m/z* 264 [M+Na]$^+$; $[\alpha]_D^{24}$ +3.74 (*c* 0.98, CHCl$_3$) (97% ee); HRMS calcd. for $C_{15}H_{15}NO_2$ [M+H]$^+$: 242.1181, found 242.1178; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 22.3 min (minor) and 29.6 min (major).

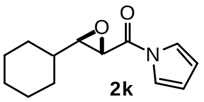


2i

(2*S*,3*R*)-*trans*-2,3-Epoxy-5-(4-methoxybenzyloxy)-1-pyrrol-1-yl-pentan-1-one (2i): IR (neat) ν 3145, 1727, 925, 820 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.36-7.38 (m, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.23-6.25 (m, 2H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 3.89 (d, *J* = 2.0 Hz, 1H), 3.79 (s, 3H), 3.56-3.62 (m, 2H), 3.32 (ddd, *J* = 4.6, 4.6, 2.0 Hz, 1H), 2.09-2.16 (m, 1H), 1.87-1.97 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 31.9, 53.9, 55.3, 57.3, 65.4, 73.0, 113.7, 113.8, 119.1, 129.5, 129.8, 159.3, 165.6; ESI-MS *m/z* 324 [M+Na]$^+$; $[\alpha]_D^{25}$ +163 (*c* 0.93, CHCl$_3$) (97% ee); HRMS calcd. for $C_{17}H_{19}NO_4$ [M+H]$^+$: 302.1392, found 302.1388; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 35.3 min (minor) and 43.1 min (major).

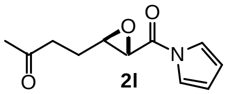

2j

(2*S*,3*R*)-*trans*-2,3-Epoxy-1-pyrrol-1-yl-tridec-12-en-1-one (2j): IR (KBr) ν 2918, 1719, 1296, 922 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.39-7.41 (m, 2H), 6.33-6.35 (m, 2H), 5.74-5.83 (m, 1H), 4.94-5.00 (m, 1H), 4.89-4.93 (m, 1H), 3.75 (d, *J* = 1.8 Hz, 1H), 3.25 (ddd, *J* = 4.9, 3.1, 1.8 Hz, 1H), 1.99-2.04 (m, 2H), 1.63-1.78 (m, 2H), 1.42-1.53 (m, 2H), 1.22-1.39 (m, 10H),; ^{13}C NMR (CDCl$_3$) δ 25.7, 28.9, 29.0, 29.2, 29.3, 29.3, 31.6, 33.8, 53.8, 59.5, 113.9, 114.2, 119.0, 139.1, 165.7; ESI-MS *m/z* 298 [M+Na]$^+$; $[\alpha]_D^{25}$ +0.84 (*c* 1.05, CHCl$_3$) (96% ee); HRMS calcd. for $C_{17}H_{25}NO_2$ [M+H]$^+$: 276.1963, found 276.1960; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 15.8 min (minor) and 18.6 min (major).

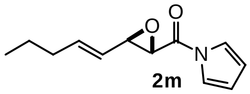

2k

(2*S*,3*R*)-3-Cyclohexyl-*trans*-2,3-epoxy-1-pyrrol-1-yl-propan-1-one (2k): IR (KBr) ν 3147, 2926, 1718, 1290, 901 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.38-7.41 (m, 2H), 6.32-6.35 (m, 2H), 3.82 (d, *J* = 2.2 Hz, 1H), 3.07 (dd, *J* = 2.2, 6.7 Hz, 1H), 1.86-1.91 (m, 1H), 1.73-1.80 (m, 3H), 1.65-

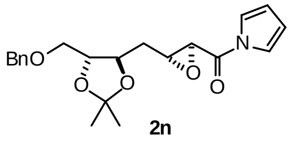
1.70 (m, 1H), 1.38-1.47 (m, 1H), 1.11-1.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.3, 25.4, 25.9, 28.7, 29.3, 39.6, 52.7, 63.5, 113.8, 118.9, 165.8; ESI-MS *m/z* 242 $[M+Na]^+$; $[\alpha]_D^{24}$ –26.1 (*c* 1.02, $CHCl_3$) (98% ee); HRMS calcd. for $C_{13}H_{17}NO_2$ $[M+H]^+$: 220.1337, found 220.1336; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 11.9 min (minor) and 15.9 min (major).


2l

(2*S*,3*R*)-*trans*-2,3-epoxy-1-pyrrol-1-yl-heptan-1,6-dione (2l): IR (KBr) ν 1732, 1704, 1295, 909 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39-7.41 (m, 2H), 6.32-6.34 (m, 2H), 3.82 (d, *J* = 1.9 Hz, 1H), 3.25 (dt, *J* = 1.9, 5.8 Hz, 1H), 2.65 (t, *J* = 6.1 Hz, 2H), 2.16 (s, 3H), 2.06-2.14 (m, 1H), 1.85-1.92 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 25.1, 30.0, 38.6, 54.0, 58.4, 114.0, 119.0, 165.3, 206.9; ESI-MS *m/z* 230 $[M+Na]^+$; $[\alpha]_D^{25}$ –9.81 (*c* 1.09, $CHCl_3$) (96% ee); HRMS calcd. for $C_{11}H_{13}NO_3$ $[M+Cs]^+$: 339.9949, found 339.9952; HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 20/80, flow 1.0 mL/min, detection at 254 nm) t_R 8.6 min (minor) and 14.2 min (major).


2m

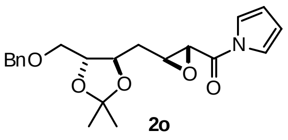
(2*S*,3*R*)-*trans*-2,3-epoxy-1-pyrrol-1-yl-4-octen-1-one (2m): IR (KBr) ν 2950, 1722, 1290, 903 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.37-7.40 (m, 2H), 6.32-6.34 (m, 2H), 6.06 (dt, *J* = 15.6, 7.2 Hz, 1H), 5.24 (ddt, *J* = 15.6, 8.2, 1.1 Hz, 1H), 3.89 (d, *J* = 1.8 Hz, 1H), 3.64 (dd, *J* = 8.2, 1.8 Hz, 1H), 2.07 (ddd, *J* = 7.3, 7.2, 1.1 Hz, 2H), 1.42 (dt, *J* = 7.3, 7.3 Hz, 2H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 13.6, 21.8, 34.4, 55.4, 59.2, 113.9, 119.0, 124.6, 140.2, 165.1; ESI-MS *m/z* 228 $[M+Na]^+$; $[\alpha]_D^{25}$ +4.59 (*c* 1.02, $CHCl_3$) (96% ee); HRMS calcd. for $C_{12}H_{15}NO_2$ $[M+H]^+$: 206.1181, found 206.1181; HPLC (DAICEL CHIRALPAK AS, 2-propanol/hexane 2/98, flow 1.0 mL/min, detection at 254 nm) t_R 13.4 min (major) and 21.3 min (minor).



2n

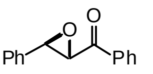
(2*S*,3*R*,5*R*,6*R*)-7-Benzyloxy-*trans*-2,3-epoxy-5,6-dihydroxy-5,6-*O*-isopropylidene-1-pyrrol-1-yl-1-heptanone (2n): Ylide **2** (1.176 g, 3.183 mmol) and chiral aldehyde **4n** (755 mg, 2.856 mmol) in toluene (11.3 mL) was stirred at 65 °C for 36 h, and then the mixture was cooled to 25 °C. MS4A (2.32 g) and toluene (7.3 mL) was added to the reaction mixture. To this mixture at 25 °C was added a catalyst suspension mixture prepared from Sm(O-*i*-Pr)$_3$ (0.2 M in THF, 0.727 ml, 0.1454 mmol), (*R*)-H$_8$-BINOL (42.9 mg, 0.1454 mmol), MS 4A (580 mg), THF (5.8 ml), and CMHP (2.5 M in toluene, 1.63 ml, 4.07 mmol). After stirring for 40 min at 25 °C, the mixture was cooled to 0 °C, 5% citric acid (12.5 mL) was added, then diluted with ethyl acetate (30 mL). MS4A was filtered off, organic layer was washed with sat. aq. $NaHCO_3$ (5 mL x 2), brine (5mL x 2), and was dried over Na_2SO_4 After evaporation, the residue oil was purified by silica gel column chromatography (hexane/diethyl ether = 4/1) to give **2n** (853 mg, 2.30 mmol, 80% yield) as pale yellow oil: IR (neat) 3144, 2985, 2867, 1731, 1599, 1545, 1472, 1361, 1289, 1094, 916 cm^{-1}; ^{1}H

NMR($CDCl_3$) δ 7.51 (t, *J* = 2.5 Hz, 2H), 7.25-7.40 (m, 5H), 6.34 (t, *J* = 2.5 Hz, 2H), 4.57 (s, 2H), 4.03 (m, 1H), 3.89 (d, *J* = 1.9 Hz, ,1H), 3.85 (m, 1H), 3.66 (dd, *J* = 10.1, 4.9 Hz, 1H), 3.57 (dd, *J* =10.1, 5.2 Hz, 1H), 3.37 (m, 1H), 2.25 (ddd, *J* = 14.1, 5.2, 2.5 Hz, 1H), 1.69 (ddd, *J* = 14.1, 10.0, 7.0 Hz, 1H), 1.45 (s, 3H), 1.41 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.2, 137.6, 128.4, 127.8, 127.6, 119.1, 113.7, 109.3, 79.4, 75.4, 73.6, 69.8, 56.7, 54.1, 35.9, 27.3, 26.8; $[\alpha]_D^{22}$ –17.4 (c 1.01, $CHCl_3$); HRMS calcd. for $C_{21}H_{26}NO_{55}$ $[M+H]^+$ 372.1811, found 372.1808.



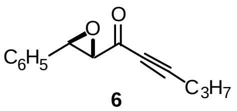
2o

(2*R*,3*S*,5*R*,6*R*)-7-Benzyloxy-*trans*-2,3-epoxy-5,6-dihydroxy-5,6-*O*-isopropylidene-1-pyrrol-1-yl-1-heptanone (2o): Ylide **3** (235 mg, 0.636 mmol) and chiral aldehyde **4n** (138 mg, 0.522 mmol) in toluene(2.0 mL) was stirred at 65 °C for 36 h, and then the mixture was cooled to 25 °C. MS4A (418 mg) and toluene (1.7 mL) was added to the reaction mixture. To this mixture at 25 °C was added a catalyst suspension mixture prepared from Sm(O-*i*-Pr)$_3$ (0.2 M in THF, 0.13 ml, 0.026 mmol), (*S*)-H_8-BINOL(7.7 mg, 0.026 mmol), MS4A(104 mg), THF(1.0 mL), and TBHP (5 M in decane, 0.235 ml, 1.17 mmol). After stirring for 40 min at 25 °C, the mixture was cooled to 0 °C, 5% citric acid (2.4 mL) was added, then diluted with ethyl acetate (30 mL). MS4A was filtered off, organic layer was washed with sat. aq. $NaHCO_3$ (3 mL x 2), brine (3 mL x 2), and was dried over Na_2SO_4 After evaporation, the residue oil was purified by silica gel column chromatography (hexane/diethyl ether = 4/1) to give **2o** (153.1 mg, 0.412 mmol, 78% yield) as pale yellow oil: IR (neat) 3147, 2985, 2865, 1729, 1599, 1546, 1471, 1406, 1363, 1289, 1076, 919 cm^{-1}; ^1H NMR($CDCl_3$) δ 7.44 (brs, 2H), 7.20-7.39(m, 5H), 6.36 (dd, *J* = 2.5, 2.5 Hz, 2H), 4.57 (s, 2H), 4.00 (d, *J* = 1.9 Hz, 1H), 3.95 (m, 2H), 3.64 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.55 (dd, *J* = 10.1, 4.9 Hz, 1H), 3.45 (dt, *J* = 1.8, 4.3 Hz, 1H), 2.15-2.21 (m, 1H), 2.04-2.11 (m, 1H), 1.41 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 165.4, 137.7, 128.4, 127.8, 127.7, 119.0, 113.9, 109.4, 78.8, 74.7, 73.6, 70.0, 56.1, 53.4, 33.6, 27.1, 27.0; $[\alpha]_D^{22}$ –4.19 (c 1.04, $CHCl_3$); HRMS calcd. for $C_{21}H_{26}NO_5$ $[M+H]^+$: 372.1811, found 372.1813.



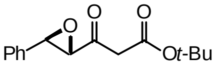
5

(2*S*,3*R*)-*trans*-2,3-epoxy-1,3-diphenylpentan-1-one (5): To a solution of bromobenzene (116 mg, 0.738 mmol) in THF (1.2 mL) at –78 °C was added BuLi (1.58 M in hexane, 0.47 mL,0.695 mmol). The mixture was stirred for 10 min at the same temperature. A solution of **2a** (96 mg, 0.45 mmol) in THF (1.2 mL) was added at –78 °C. After stirring for 10 min at -78 °C, sat. aq. NH_4Cl (1.5 ml) was added. The mixture was extracted with ethyl acetate. The organic layer was washed with aq. NaH_2PO_4, sat. aq. $NaHCO_3$, brine, and was dried over Na_2SO_4. After evaporation, the residue was dissolved in CH_2Cl_2, DBU (50 μL) was added, and the mixture was stirred for 20 min at 25 °C. The mixture was diluted with $CHCl_3$, washed with 1 M HCl, sat. aq. $NaHCO_3$, brine, and was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel column chromatography (hexane/diethyl ether = 10/1) to give **5** (89 mg, 0.3968 mmol, y. 88%) as colorless oil: IR (neat) 1687, 1597, 1449, 1231, 1008 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01 (d, *J* = 7.0 Hz, 2H), 7.30-7.68 (m, 8H), 4.30 (d, *J* = 1.8 Hz, 1H), 4.08 (d, *J* = 1.8 Hz,1H); ^{13}C NMR ($CDCl_3$) δ 193.0, 135.4, 134.0, 129.0, 128.8, 128.7, 128.3, 125.7, 70.0, 59.3,; ESI-MS *m/z* 247 $[M+Na]^+$; $[\alpha]_D^{24}$ –209 (c 1.0, CH_2Cl_2).



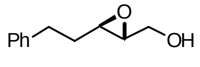
6

(1*S*,2*R*)-*trans*-1,2-epoxy-3-oxo-1-phenyl-4-octyne (6): To a solution of 1-pentyne (0.167 mL, 1.7 mmol) in THF (1.4 mL) at -78 °C was added BuLi (1.56 M in hexane, 0.96 ml, 1.5 mmol). The mixture was stirred for 30 min at the same temperature. A solution of **2a** (105 mg, 0.492 mmol) in THF (1.4 mL) was added at -78 °C. After stirring for 10 min at -78 °C, sat. aq. NH_4Cl (2 mL) was added. The mixture was extracted with ethyl acetate. The organic layer was washed with 1 M HCl, sat. aq. $NaHCO_3$, brine, and was dried over Na_2SO_4. After evaporation, obtained residue was dissolved in CH_2Cl_2 (15 mL), DBU (0.184 M in CH_2Cl_2, 0.1 mL, 0.0184 mmol) was added, stirred for 10 min at 0 °C. The mixture was diluted with $CHCl_3$, washed with 1 M HCl, sat. aq. $NaHCO_3$, brine, and was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel column chromatography (hexane/diethyl ether = 15/1 to 10/1) to give **6** (88.7 mg, 0.414 mmol, 84% yield) as yellow oil: IR (neat) 2965, 2935, 2875, 2210, 1667, 1457, 1405, 1257, 1179 cm^{-1}; ^1H NMR($CDCl_3$) δ 7.27-7.50 (m, 5H), 4.17 (d, *J* = 1.5 Hz, 1H), 3.61 (d, *J* = 1.8 Hz, 1H), 2.41 (t, *J* = 7.3 Hz, 2H), 1.65 (dq, *J* = 7.3, 7.3 Hz, 2H), 1.04 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 182.6, 134.8, 129.0, 128.7, 125.7, 98.8, 78.3, 63.6, 58.6, 21.1, 13.4; ESI-MS *m/z* 237 $[M+Na]^+$; $[\alpha]_D^{24}$+166 (c 0.95, $CHCl_3$).



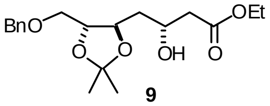
7

***tert*-Butyl (4*R*,5*S*)-*trans*-4,5-epoxy-3-oxo-5-phenylpentanoate (7)**: To a solution of 0.75 M LDA in THF-hexane(1.0 mL, 0.75 mmol) at –78 °C was added *t*-butyl acetate (0.10 mL, 0.742 mmol) slowly over 4 min. The mixture was stirred for 20 min at –78 °C. A solution of **2a** (56 mg, 0.262 mmol) in THF (0.8 mL) was added at –78 °C. After stirring for 10 min at –78 °C, sat. aq. NH_4Cl (1 mL) was added. The mixture was extracted with ethyl acetate. Organic layer was washed with 1M HCl, pH 7 phosphate buffer, brine, and was dried over Na_2SO_4. After evaporation, the residue oil was dissolved in CH_2Cl_2 (5 mL), DBU (90 mg, in CH_2Cl_2 1 mL) was added and stirred for 20 min at 25°C. To the reaction mixture was added $CHCl_3$, and then 1M HCl. The organic layer was washed with pH 7 phosphate buffer, brine, and was dried over Na_2SO_4, filtered and concentrated. After evaporation, the residue was purified by silica gel column chromatography (hexane/diethyl ether = 15/1 to 10/1) to give **7** (51.5 mg, 0.196 mmol, 74% yield) as pale yellow oil: IR (neat) 3437, 2979, 2932, 1733, 1713, 1652, 1457, 1369, 1325, 1253, 1154 cm^{-1}; ^1H NMR($CDCl_3$) δ 7.24-7.43(m, 5H), 4.06 (d, J= 1.7 Hz, 1H), 3.60 (d, J= 1.7 Hz, 1H), 3.43 (d, J= 3.1 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR ($CDCl_3$) major peaks δ 198.8, 165.6, 134.7, 129.1, 128.7, 128.6, 125.6, 91.7, 82.5, 63.0, 58.0, 45.3, 28.2, 28.1, 27.9, minor peaks 172.0, 170.2, 135.7, 81.6, 59.3, 59.1, 31.1; ESI-MS *m/z* 285 $[M+Na]^+$; $[\alpha]_D^{24}$–40.5 (c 0.7, $CHCl_3$).



8

(2*R*,3*R*)-*trans*-2,3-epoxy-5-phenyl-1-pentanol (8): To a suspension of $LiBH_4$ (15.6 mg, 0.72 mmol) in THF(0.8 mL) at 0 °C, was added a solution of **2a** (50.5 mg, 0.209 mmol) in THF(0.8 mL). The mixture was stirred for 20 min at 0 °C, then at 25 °C for 40 min. The reaction mixture was poured to ethyl acetate-sat. aq. NH_4Cl mixture at 0 °C. The organic layer was separated, washed with pH 7 phosphate buffer, brine, and was dried over Na_2SO_4. After evaporation, the residue oil was dissolved in THF (1 mL), and the solution was added to the suspension of $NaBH_4$ (27 mg, 0.71 mmol) in THF (1.5 mL) at 25 °C. After stirring for 4 h, the reaction mixture was poured to ethyl acetate-sat.aq.NH_4Cl mixture at 0 °C. Organic layer was separated, washed with pH 7 phosphate buffer, brine, and was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3/1) to give **8** (0.151 mmol, 72% yield) as colorless oil: IR (neat) 3409, 2926, 1603, 1496, 1454, 1231, 1087, 878 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18-7.32(m, 5H), 3.81-3.88 (m, 1H), 3.54-3.60 (m, 1H), 2.98-3.02 (m,1H), 2.80-2.88 (m, 2H), 2.70-2.78 (m, 1H), 1.84-1.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 141.0, 128.4, 128.3, 126.0, 61.6, 58.7, 55.3, 33.2, 32.1; ESI-MS m/z 201 $[M+Na]^+$; $[\alpha]_D^{25}$–42.6 (c 2.41, $CHCl_3$).



9

Ethyl (3*R*,5*R*,6*R*)-7-Benzyloxy-3,5,6-trihydroxy-5,6-*O*-isopropylidene-heptanoate (9): To a suspension of $NaBH_4$ (295 mg, 7.79 mmol) in EtOH at 0 °C was added diphenyl diselenide (1.21 g, 3.89 mmol). The mixture was stirred for 40 min at 25 °C. To the obtained pale yellow solution, acetic acid (0.075mL, 1.3 mmol) in EtOH (1 mL) was added. After 10 min, a solution of **2n** (853 mg, 2.29 mmol) in EtOH(12 ml) was added in one portion at 25 °C. The mixture was stirred for 15 min, cooled to 0 °C, diluted with ethyl acetate (160 mL), and poured to brine (30 ml). The organic layer was separated, washed with brine (30 mL x 2), and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4/1 to 1/1) to give corresponding alcohol intermediate (809 mg, 2.166 mmol, 94% yield).

Alcohol intermediate (809 mg, 2.166 mmol) was dissolved in EtOH (8.8 mL). To the mixture was added a solution of 0.5 M EtSLi in EtOH (4.3 mL) at 25 °C. The mixture was stirred for 40 min at 25 °C. Reaction mixture was diluted with EtOAc (100 mL). Organic layer was washed with a mixture of [0.5 M pH 7 phosphate buffer (10 mL) and 10% aq. NaCl (10 mL)], [1 M aq. KH_2PO_4 (10 mL) and 10% aq. NaCl (10 mL)], [10 % aq. $CuSO_4$ (5mL) and brine (5 mL)] x 3, [sat.$NaHCO_3$(5 mL) and brine (5 mL)] x 2, and was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel column chromatography (hexane/diethyl ether = 2/1 to 0/1) to give **9** (708.2 mg, 2.009 mmol, 92% yield) pale yellow oil: IR (neat) 3842, 2984, 2934, 1733, 1455, 1371, 1254, 1215, 1164, 1089, 835 cm^{-1}; ^1H NMR($CDCl_3$) δ 7.20-7.40(m, 5H), 4.58 (ABq, *J* = 12.2 Hz, 2H), 4.25 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 1H), 4.06 (dt, *J* = 8.6, 3.1 Hz, 1H), 3.89 (ddd, *J* = 8.3, 5.8, 4.3 Hz, 1H), 3.61 (dd, *J* = 10.1, 5.5 Hz, 1H), 3.56 (dt, *J* = 10.1 4.6Hz, 1H), 3.28 (d, *J* = 4.3 Hz, 1H), 2.54 (dd, *J* = 16.5, 3.7 Hz, 1H), 2.47 (dd, *J* = 16.5, 8.9 Hz, 1H), 1.81 (ddd, *J* = 14.4, 9.2, 3.4 Hz, 1H), 1.68 (ddd, *J* = 14.1, 8.6, 3.4 Hz, 1H), 1.41 (s, 3H), 1.40 (s, 3H), 1.27 (t, *J* = 7.4 Hz, 1H),; ^{13}C NMR ($CDCl_3$) δ 172.5, 137.8, 128.4, 127.7, 109.0, 79.8, 75.6, 73.5, 70.3, 65.6, 60.6, 41.6, 39.5, 27.2, 26.9, 14.1; $[\alpha]_D^{24}$ +6.09 (c 2.55, $CHCl_3$); HRMS calcd. for $C_{19}H_{29}O_6$ $[M+H]^+$: 353.1964, found 353.1963.