Supporting Information for
Catalytic Enantioselective Epoxidation of Homoallylic Alcohols
by Chiral Zirconium Complexes

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General Experimental:

Optical rotations were recorded on a Jasco P-1030 digital polarimeter. Infrared (IR) spectra were recorded on a JASCO FT/IR-550 Fourier transform infrared spectrometer. ¹H NMR spectra were recorded on a JNM-GSX 270 (270 MHz). ¹³C NMR spectra were recorded on a JNM-GSX 270 (68 MHz). High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700V GCmate. Matrix-assisted laser desorption/ionization time-of-flight mass spectra (MALDI TOF MS) were recorded on a Voyager DE STR. Analytical TLC was performed on Merck DC-Platten Kieselgel 60 F254 plates. Silica gel column chromatography was carried out with Merck Kieselgel (60-mesh). MS 4A was purchased in powder form from Aldrich, and activated at 400°C under vacuum for 4 hr. Chlorobenzene was dried over MS 4A. Homoallylic alcohol **1e** was prepared according to the literature.¹ All reactions were carried out under a nitrogen atmosphere.

Typical experimental procedure for asymmetric epoxidation using Zr(*Ot*-Bu)₄ and dibenzyl L-tartramide (DBTA) in a 1:1 ratio:

To a mixture of (L)-DBTA (0.22 mmol) and molecular sieves 4A (100 mg) in chlorobenzene (8 ml) was added Zr(*Ot*-Bu)₄ (0.2 mmol) at 20°C. The mixture was stirred at 20°C for 1 h, and cooled to -40°C. A chlorobenzene solution of cumen hydroperoxide (2 mmol) and a homoallylic alcohol (1 mmol) were successively added. The mixture was stirred at -40°C for 1 day. Saturated aq. Na₂SO₄ (0.5 ml) and ether (5 ml) were added to quench the reaction. After the mixture was stirred at 10°C for 15 min, Celite (200 mg) and anhydrous Na₂SO₄ (2 g) were added. The mixture was stirred for 15 min, filtrated through a Celite pad. The filtrate was evaporated under reduced pressure. The crude products were chromatographed on silica gel to give the desired epoxides.

Triphenylmethyl chloride (1.1 mmol) was added to the epoxide and Et₃N (2 mmol) in CH₂Cl₂ (5 ml) at room temperature under nitrogen. After stirring for 4 - 6 h, the reaction was quenched with water. The

mixture was extracted with CH_2Cl_2 . Then the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 . The solvents were evaporated, and the crude product was purified by preparative TLC on silica gel to give triphenylmethyl ethers. The optical purity of the triphenylmethyl ethers was determined by HPLC analysis using a chiral column (see below).

Typical experimental procedure for asymmetric epoxidation using $\text{Zr}(\text{Ot-Bu})_4$ and diisopropyl L-tartrate (DIPT) in a 1:2 ratio:

To a mixture of (L)-DIPT (0.41 mmol) and molecular sieves 4A (100 mg) in chlorobenzene (8 ml) was added $\text{Zr}(\text{Ot-Bu})_4$ (0.2 mmol) at 20°C . The mixture was stirred at 20°C for 1 h, and cooled to 0°C . A chlorobenzene solution of cumen hydroperoxide (2 mmol) and a homoallylic alcohol (1 mmol) were successively added. The mixture was stirred at 0°C for 3 - 5 days. Saturated aq. Na_2SO_4 (0.5 ml) and ether (5 ml) were added to quench the reaction. After the mixture was stirred at 10°C for 15 min, Celite (200 mg) and anhydrous Na_2SO_4 (2 g) were added. The mixture was stirred for 15 min and filtrated through a Celite pad. The filtrate was evaporated under reduced pressure. The crude products were chromatographed on silica gel to give the desired epoxides.

Triphenylmethyl chloride (1.1 mmol) was added to the epoxide and Et_3N (2 mmol) in CH_2Cl_2 (5 ml) at room temperature under nitrogen. After stirring for 4 - 6 h, the reaction was quenched with water. The mixture was extracted with CH_2Cl_2 . Then the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 . The solvents were evaporated, and the crude product was purified by preparative TLC on silica gel to give triphenylmethyl ethers. The optical purity of the triphenylmethyl ethers was determined by HPLC analysis using a chiral column (see below).

(3S, 4S)-3, 4-Epoxyhexan-1-ol (2a): colorless oil. $[\alpha]_{\text{D}}^{27} - 43.77^\circ$ (*c* 1.72, EtOH). IR (CHCl_3) 3626, 3524, 2974, 2937, 2879, 1459, 1243, 1055, 884 cm^{-1} . ^1H NMR (CDCl_3): δ 1.00 (t, *J* = 7.6 Hz, 3H), 1.53 – 1.76 (m, 3H), 1.92 – 2.05 (m, 1H), 2.08 (brs, 1H), 2.79 (dt, *J* = 2.4 and 5.4 Hz, 1H), 2.86 – 2.91 (m, 1H), 3.76 – 3.82 (m, 2H). ^{13}C NMR (CDCl_3): δ 9.9, 25.1, 34.2, 56.6, 59.3, 60.1. HRMS: Calcd for $\text{C}_6\text{H}_{11}\text{O}_2$ ($[\text{M-H}]^+$) 115.0759. found 115.0758.

(3S, 4S)-3, 4-Epoxyhexanyl triphenylmethyl ether: 87%ee. HPLC Daicel Chiralpak AD-H, hexane/*i*PrOH = 100/2, flow rate = 0.5 ml/min, column oven temp. = 20°C : t_{R} = 10 min (3S, 4S), t_{R} = 13 min (3R, 4R).

(3S, 4R)-3, 4-Epoxyhexan-1-ol (2b): colorless oil. $[\alpha]_{\text{D}}^{27} - 16.67^\circ$ (*c* 1.69, EtOH). IR (CHCl_3) 3625, 3535, 2974, 2938, 2880, 1467, 1390, 1243, 1053, 905 cm^{-1} . ^1H NMR (CDCl_3): δ 1.05 (t, *J* = 7.6 Hz, 3H), 1.50 – 1.63 (m, 2H), 1.66 – 1.76 (m, 1H), 1.83 – 1.94 (m, 1H), 2.05 (brs, 1H), 2.92 (dt, *J* = 4.3 and 6.5 Hz, 1H),

3.11 (dt, $J = 4.3$ and 7.8 Hz, 1H), 3.78 – 3.93 (m, 2H). ^{13}C NMR (CDCl_3): δ 10.5, 21.3, 30.5, 55.2, 57.9, 60.7. HRMS: Calcd for $\text{C}_6\text{H}_{11}\text{O}_2$ ($[\text{M}-\text{H}]^+$) 115.0759. found 115.0758.

(3*S*, 4*R*)-3, 4-Epoxyhexanyl triphenylmethyl ether: 72%ee. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 95/5, flow rate = 0.5 ml/min, column oven temp. = 40°C: $t_{\text{R}} = 10$ min (3*S*, 4*R*), $t_{\text{R}} = 12$ min (3*R*, 4*S*).

(3*S*)-4-Methyl-3, 4-epoxypentan-1-ol (2c): colorless oil. $[\alpha]_{\text{D}}^{29} - 16.32^\circ$ (c 2.14, CHCl_3). IR (CHCl_3) 3625, 3511, 2966, 2930, 2886, 1457, 1380, 1249, 1120, 1053, 836 cm^{-1} . ^1H NMR (CDCl_3): δ 1.30 (s, 3H), 1.34 (s, 3H), 1.65 – 1.77 (m, 1H), 1.84 – 1.97 (m, 1H), 2.03 (brs, 1H), 2.91 (dd, $J = 4.6$ and 7.8 Hz, 1H), 3.83 – 3.92 (br, 2H). ^{13}C NMR (CDCl_3): δ 19.0, 24.8, 31.6, 58.1, 60.7, 62.3. HRMS: Calcd for $\text{C}_6\text{H}_{13}\text{O}_2$ ($[\text{M}+\text{H}]^+$) 117.0916. found 117.0912.

(3*S*)-4-Methyl-3, 4-epoxypentanyl triphenylmethyl ether: 47%ee. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 100/2, flow rate = 0.5 ml/min, column oven temp. = 40°C: $t_{\text{R}} = 14$ min (3*R*), $t_{\text{R}} = 18$ min (3*S*).

(3*S*)-3, 4-Epoxybutan-1-ol (2d): colorless oil. $[\alpha]_{\text{D}}^{28} - 21.76^\circ$ (c 1.11, CH_2Cl_2). IR (CHCl_3) 3625, 3524, 2946, 2929, 2888, 1731, 1602, 1484, 1412, 1244, 1049, 855 cm^{-1} . ^1H NMR (CDCl_3): δ 1.64 – 1.76 (m, 1H), 1.92 – 2.04 (m, 1H), 2.36 (brs, 1H), 2.59 (dd, $J = 2.7$ and 4.6 Hz, 1H), 2.82 (t, $J = 4.6$ Hz, 1H), 3.07 – 3.14 (m, 1H), 3.80 (t, $J = 5.9$ Hz, 2H). ^{13}C NMR (CDCl_3): δ 34.8, 46.6, 50.5, 59.7. HRMS: Calcd for $\text{C}_4\text{H}_7\text{O}_2$ ($[\text{M}-\text{H}]^+$) 87.0446. found 87.0449.

(3*S*)-3, 4-Epoxybutanyl triphenylmethyl ether: 78%ee. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 90/10, flow rate = 0.5 ml/min, column oven temp. = 40°C: $t_{\text{R}} = 17$ min (3*S*), $t_{\text{R}} = 21$ min (3*R*).

(3*S*)-3-(3, 4-Dichlorophenyl)-3, 4-epoxybutan-1-ol (2e): colorless oil. $[\alpha]_{\text{D}}^{27} + 17.29^\circ$ (c 1.00, EtOH). IR (CHCl_3) 3622, 3565, 2956, 2889, 1601, 1559, 1473, 1382, 1061, 1031, 822 cm^{-1} . ^1H NMR (CDCl_3): δ 1.90 (t, $J = 5.4$ Hz, 1H), 2.09 (dt, $J = 5.4$ and 14.9 Hz, 1H), 2.45 (dt, $J = 5.4$ and 14.9 Hz, 1H), 2.73 (d, $J = 5.1$ Hz, 1H), 3.13 (d, $J = 5.1$ Hz, 1H), 3.68 – 3.76 (m, 2H), 7.20 – 7.48 (m, 3H). ^{13}C NMR (CDCl_3): δ 36.6, 55.0, 58.3, 58.8, 125.1, 127.7, 130.3, 131.7, 132.6, 140.0.

(3*S*)-3-(3, 4-Dichlorophenyl)-3, 4-epoxybutanyl triphenylmethyl ether: 89%ee. HRMS: Calcd for $\text{C}_{10}\text{H}_9\text{O}_2\text{Cl}_2$ ($[\text{M}-\text{H}]^+$) 230.9980. found 230.9983. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 80/20, flow rate = 0.5 ml/min, column oven temp. = 40°C: $t_{\text{R}} = 12$ min (3*S*), $t_{\text{R}} = 16$ min (3*R*).

(3S)-3-Methyl-3, 4-epoxybutan-1-ol (2f): colorless oil. $[\alpha]_D^{27} + 14.32^\circ$ (*c* 1.00, EtOH). IR (CHCl₃) 3623, 3514, 2967, 2933, 2888, 1602, 1488, 1390, 1243, 1070, 843 cm⁻¹. ¹H NMR (CDCl₃): δ 1.38 (s, 3H), 1.81 – 2.02 (m, 2H), 2.65 (dd, *J* = 3.0 and 4.6 Hz, 1H), 2.82 (t, *J* = 4.1 Hz, 1H), 3.69 – 3.74 (m, 2H). ¹³C NMR (CDCl₃): δ 22.0, 37.7, 53.0, 56.5, 59.2. HRMS: Calcd for C₅H₉O₂ ([M-H]⁺) 101.0603. found 101.0603.

(3S)-3-Methyl-3, 4-epoxybutanyl triphenylmethyl ether: 74%ee. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 95/5, flow rate = 0.5 ml/min, column oven temp. = 40°C: *t*_R = 19 min (3*S*), *t*_R = 22 min (3*R*).

MALDI TOF MS analysis of a 1:1 Zr(*Or*-Bu)₄/DIPT complex:

To a mixture of (L)-DIPT (0.22 mmol) and molecular sieves 4A (100 mg) in chlorobenzene (8 ml) was added Zr(*Or*-Bu)₄ (0.2 mmol) at 20°C, and the mixture was stirred at 20°C for 1 h. The sample for MALDI TOF MS was prepared using dithranol as a matrix. MALDI TOF MS data are shown in Supporting Information. MALDI TOF MS (*m/z*) (matrix:dithranol) mass calc. for trimer C₅₄H₁₀₃O₂₄Zr₃, ([M + H]⁺) 1405, found 1405.

MALDI TOF MS analysis of a 1:2 Zr(*Or*-Bu)₄/DIPT complex:

To a mixture of (L)-DIPT (0.41 mmol) and molecular sieves 4A (100 mg) in chlorobenzene (8 ml) was added Zr(*Or*-Bu)₄ (0.2 mmol) at 20°C, and the mixture was stirred at 20°C for 1 h. The sample for the MALDI TOF MS was prepared using dithranol as a matrix. MALDI TOF MS data are shown in Supporting Information. MALDI TOF MS (*m/z*) (matrix:dithranol) mass calc. for monomer C₂₈H₅₃O₁₄Zr, ([M + H]⁺) 703, found 703.

Synthesis of intermediate 3 for tachykinin receptor antagonist 4.

(3*R*)-3-(3, 4-Dichlorophenyl)-3, 4-epoxybutyl triphenylmethyl ether:

Triphenylmethyl chloride (2.35 mmol) was added to (*R*)-**2e** (89%ee, 2.14 mmol) and Et₃N (4.28 mmol) in CH₂Cl₂ (5 ml) at room temperature under nitrogen. After stirring for 4 - 6 h, the reaction was quenched with water. The mixture was extracted with CH₂Cl₂, and the combined organic layers were washed with brine and dried over anhydrous Na₂SO₄. The solvents were evaporated, and the crude product was crystallized with ethyl acetate / MeOH to afford triphenylmethyl ether (81% yield, 94%ee): white powder. $[\alpha]_D^{29} - 6.49^\circ$ (*c* 0.98, CH₂Cl₂). IR (CHCl₃) 3059, 1959, 1597, 1559, 1449, 1087, 761, 706 cm⁻¹. ¹H NMR (CDCl₃): δ 1.98 - 2.08 (m, 1H), 2.31 - 2.41 (m, 1H), 2.71 (d, *J* = 5.4 Hz, 1H), 3.01 (d, *J* = 5.4 Hz, 1H), 3.12 - 3.22 (m, 2H), 7.10 – 7.42 (m, 18H). ¹³C NMR (CDCl₃): δ 35.8, 55.7, 58.0, 59.6, 86.8, 125.4, 126.9,

127.6, 128.1, 130.1, 131.3, 132.3, 140.2, 143.8. HRMS: Calcd for $C_{29}H_{24}Cl_2O_2$ (M^+)474.1153. found 474.1150. HPLC Daicel Chiralcel OJ-H, hexane/*i*PrOH = 80/20, flow rate = 0.5 ml/min, column oven temp. = 40°C: t_R = 12 min (3*S*), t_R = 16 min (3*R*).

(2*R*)-2-(3, 4-Dichlorophenyl)-1-(2-hydroxy-ethylamino)-4-triphenylmethoxybutan-2-ol (3):

To the triphenylmethyl ether (0.42 mmol) in CH_3CN (2 ml) were successively added aminoethanol (2.1 mmol) and $LiClO_4 \cdot H_2O$ (1.26 mmol) at room temperature. After stirring at 90°C for 6 h, water was added, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4 . The solvent was evaporated, and the crude product was purified by preparative TLC on silica gel to give compound **3** (95% yield, 94%ee): white powder. $[\alpha]_D^{29} + 14.46^\circ$ (c 2.22, DMSO). IR ($CHCl_3$) 3460, 2947, 1597, 1559, 1449, 1071 cm^{-1} . 1H NMR ($CDCl_3$): δ 1.96 (ddd, J = 1.9, 2.4 and 7.8 Hz, 1H), 2.37 (ddd, J = 2.4, 5.1 and 7.8 Hz, 1H), 2.71 - 2.77 (m, 2H), 2.85 (s, 2H), 2.96 (dt, J = 1.9 and 5.1 Hz, 1H), 3.26 (dt, J = 2.7 and 5.1 Hz, 1H), 3.59 (t, J = 2.7 Hz, 1H), 7.03 – 7.43 (m, 18H). ^{13}C NMR ($CDCl_3$): δ 5.6, 18.2, 26.6, 27.4, 27.6, 43.0, 54.8, 91.9, 94.2, 94.3, 94.9, 95.4, 97.1, 97.7, 99.4, 110.3, 112.3. HRMS: Calcd for $C_{31}H_{31}Cl_2NO_3$ (M^+)535.1681. found 535.1683. HPLC Daicel Chiralcel OD-H, hexane/*i*PrOH = 90/10, flow rate = 1.0 ml/min, column oven temp. = 40°C: t_R = 15 min (3*R*), t_R = 19 min (3*S*).

Reference

(1) Okachi, T.; Fujimoto, K.; Onaka, M. *Org. Lett.* **2002**, *4*, 1667.

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1H amino form

DATUM
MENIF
OBNIC
OFR
OBSET
OBFN
PW1
DEADT
PREDL
MT
POINT
SPO
TIMES
DUMINY
FREOU
FLT
DELAY
ACQTM
PD
ADBIT
RGAIN
BF
T1
T2
T3
T4
EXMOD
EXPOM
IRNUC
IFR
IRSET
IRFN
IRPW
IRATN
DFILE
SF
LKSET
LKFN
LKLEV
LGAIN
LKPHS
LKSIG
CSPED
FLDC
FLDF

1H
500.00 MHz
160.00 KHz
1800.0 Hz
5.6 us
10.0 us
0.2000 ms
0.0 sec
32768
32768
8
1
7501.9 Hz
4500 Hz
63.1 us
4.368 sec
4.300 sec
16.00
21
0.12 Hz
0.00
0.00
90.00
100.00
SINGL-NON LQ
PW1,ACQTM,PD,s
1H
500.00 MHz
160.00 KHz
2410.0 Hz
47 us
511
C:\ALICE\DATA\K
TH5
70.00 KHz
334.0 Hz
200
24
17460
1602
12 Hz

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13C amino form

DATIM	13C
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OBNUC	120.00 KHz
OFR	7958.0 Hz
OBSET	4.7 us
OBFIN	10.0 us
PW1	0.2000 ms
DEADT	0.0 sec
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INT	32768
POINT	256
SPO	1
TIMES	33893.3 Hz
DUMMY	16950 Hz
FRECU	11.8 us
FLT	0.967 sec
DELAY	1.033 sec
ACQTM	16.00
PD	23
ADBIT	0.12 Hz
RGAIN	0.00
BF	0.00
T1	0.00
T2	90.00
T3	100.00
T4	SINGL-BCM LQ
EXMOD	PW1, ACQTM, PD, s'
EXPOM	1H
IRNUC	500.00 MHz
IFR	160.00 KHz
IRSET	2160.0 Hz
IRPIN	47 us
IRRPW	511
IRATN	TH5
DFLE	70.00 KHz
SF	334.0 Hz
LKSET	200
LKFN	24
LKLEV	17460
LGAIN	1600
LKPHS	11 Hz
LKSIG	
CSPED	
FILDC	
FILDF	

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Comment:Zr:DPT=1:1

Method: 02052802
Mode: Reflector
Accelerating Voltage: 20000
Grid Voltage: 70.000 %
Guide Wire Voltage: 0.005 %
Delay: 150 ON
Sample: 46

Laser: 2410
Scans Averaged: 256
Pressure: 2.79e-07
Low Mass Gate: 300.0
Timed Ion Selector: 382.2 OFF
Negative Ions: OFF
Collected: 6/20/02 2:19 PM

PerSeptive Biosystems

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 Guide Wire Voltage: 0.005 %
 Delay: 150 ON
 Sample: 46
 Laser: 2410
 Scans Averaged: 256
 Pressure: 2.79e-07
 Low Mass Gate: 300.0
 Timed Ion Selector: 382.2 OFF
 Negative Ions: OFF
 Collected: 6/20/02 2:19 PM

PerSeptive Biosystems

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Grid Voltage: 70.000 %	Low Mass Gate: 300.0
Guide Wire Voltage: 0.005 %	Timed Ion Selector: 382.2 OFF
Delay: 150 ON	Negative Ions: OFF
Sample: 44	Collected: 6/20/02 3:53 PM

PerSeptive Biosystems

Original Filename: c:\voyager\data\test\luka7_10.ms
 This File # 3 = C:\VOYAGER\DATA\TEST\luka7_10.MS
 Comment: Zr:DPT=1:2

Method: 02052802 Laser: 2814
 Mode: Reflect Scans Averaged: 256
 Accelerating Voltage: 20000 Pressure: 5.82e-07
 Grid Voltage: 70.000 % Low Mass Gate: 300.0
 Guide Wire Voltage: 0.005 % Timed Ion Selector: 382.2 OFF
 Delay: 150 ON Negative Ions: OFF
 Sample: 44 Collected: 6/20/02 3:53 PM