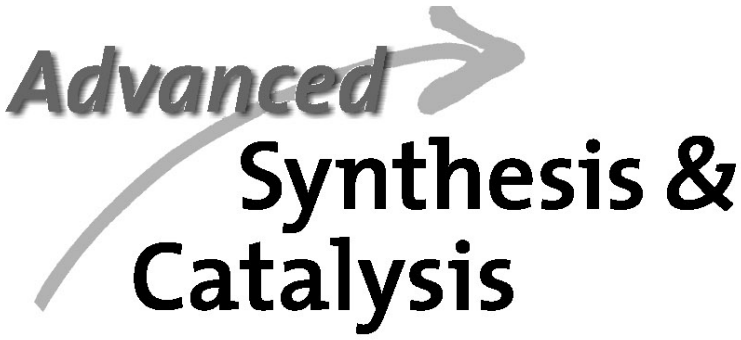


Supporting Information

Osmium Catalyzed Olefin Dihydroxylation and Aminohydroxylation in the Second Catalytic Cycle

Peng Wu, Robert Hilgraf, and Valery V. Fokin*

Department of Chemistry, The Scripps Research Institute,
10550 N. Torrey Pines Road, La Jolla, CA 92037, USA
Fax: +1-858-784-7562
E-mail: fokin@scripps.edu

Supporting Information

In general, reagents and solvents were used as purchased without further purification. Melting points are uncorrected. Analytical TLC was performed using silica gel 60 F_{254} glass plates (Merck). Flash column chromatography was performed on silica gel 60 Geduran (35–75 μm, EM Science). NMR (^{1}H, ^{13}C) spectra were recorded either on a Bruker AMX-400, AMX-500 or AMX-600 MHz spectrometer. Coupling constants (*J*) are reported in hertz, and chemical shifts are reported in parts per million (δ) relative to $CHCl_3$ (7.26 ppm for ^{1}H and 77.2 ppm for ^{13}C) or DMSO (2.50 ppm for ^{1}H and 39.5 ppm for ^{13}C) or CD_3OD (3.31 ppm for ^{1}H and 49.0 ppm for ^{13}C) as internal reference. 4-(trifluorometylsulfonyl)benzaldehyde was prepared according to the reported procedure by Oida, etc.[1]

Synthesis of Osmium Bis(azaglycolate) Complex V

A 5 mL Flask, equipped with a magnetic stir bar, was charged with 22.2 mg (0.06 mmol) of potassium osmate ($K_2OsO_2(OH)_4$), 1.5 mL of 1% aqueous potassium hydroxide. After potassium osmate totally dissolved into the solution, *cis*-*N*-(2-hydroxycyclohexyl)-tosylamide (97 mg, 0.36 mmol) in 2 mL of ethanol was added.[2] After the solution color changed (ca. 0.5 h), the reaction mixture was acidified by treatment with acetic acid. The resulting suspension was extracted by $CHCl_3$. Then, the organic phase was dried and concentrated for flash column chromatography using $CHCl_3$

as an eluent. ^{1}H-NMR (CD_3CN, 400MHz): *d* = 7.74 (d, J= 8.0Hz, 4H), 7.27 (d, J= 8.0Hz, 4H), 4.17-4.22 (m, 2H), 4.10-4.12 (m, 2H), 2.36 (s, 6H), 1.25-2.19 (m, 16H). MS (FAB^+) Calcd for ($C26H34N2O7S2Os+Cs^+$): 875. Found: 875.

X-ray Crystallographic Study

A dark brown, hexagonal prismatic shaped crystal was mounted along the largest dimension and data were collected with a Rigaku AFC6S diffractometer equipped with a molybdenum sealed tube and a graphite monochromator. A constant scan speed of 8°/min in *w* was used and the weak reflection[$I<5\sigma(I)$] were rescanned to a maximum of 4 times and the counts accumulated to assure good counting statistics. Unit cell dimensions and standard deviations were obtained by least squares fit to 25 reflections ($20<2\theta<40°$). Data were corrected for Lorentz and polarization effects and an absorption correction based on a psi-scan was applied. The structure was solved using SHELXS86 and Fourier techniques. Osmium, nitrogen and oxygen atoms were refined anisotropically and carbon atoms isotropically by the full matrix least-squares method. Hydrogen atoms were included in the ideal positions with a fixed isotropic U value of 0.08Å^2. The final difference map was devoid of significant features.

Table 3. Crystal data and structure refinement for osmium *bis*-azaglycolate **V**

Empirical formula	$C_{26}H_{34}N_2O_9OsS_2$
Formula weight	772.87
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Hexagonal
Space group	$P6_2$
Unit cell dimensions	a = 13.906(2) Å α = 90°
	b = 13.906(2) Å β = 90°
	c = 14.443(3) Å γ = 120°
Volume	2418.8(7) Å^3
Z	3

Density (calculated)	1.592 Mg/m^3
Absorption coefficient	4.132 mm^{-1}
F(000)	1152
Crystal size	0.12 mm x 0.22 mm x 0.26 mm
Theta range for data collection	2.20 to 24.99°.
Index ranges	0<=h<=14, 0<=k<=8, 0<=l<=17
Reflections collected	893
Independent reflections	893 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	888 / 0 / 101
Goodness-of-fit on F^2	1.204
Final R indices [I>2sigma(I)]	R1 = 0.0521, wR2 = 0.1355
R indices (all data)	R1 = 0.0982, wR2 = 0.2910
Absolute structure parameter	-0.04(4)
Extinction coefficient	0.0039(11)
Largest diff. peak and hole	0.868 and -0.569 $e.Å^{-3}$

$R1= (\sum|| ||F_o||- ||F_c|| ||/ \sum||F_o||)$, $wR2= \sum w(F_o^2- F_c^2)^2/\sum w[(F_o^2)^2]^{½}$, $S= [w(F_o^2- F_c^2)^2/(n-p)]^{½}$

Table 4. Selected bond distances (Å) and angles (°) for osmium *bis*-(*cis*-cyclohexanyl azaglycolate) V

Os(1)-O(1)	1.62(3)	Os(1)-O(2)	1.87(2)
Os(1)-O(2)#1	1.87(2)	Os(1)-N(1)#1	2.00(2)
Os(1)-N(1)	2.00(2)	S(1)-O(4)	1.40(20
S(1)-O(3)	1.40(3)	S(1)-N(1)	1.61(3)
S(1)-C(7)	1.78(2)	O(2)-C(1)	1.55(3)
N(1)-C(6)	1.49(4)		
O(1)-Os(1)-O(2)	121.3(6)	O(1)-Os(1)-O(2)#1	121.3(6)
O(2)-Os(1)-O(2)#1	117.4(12)	O(1)-Os(1)-N(1)#1	100.3(7)
O(2)-Os(1)-N(1)#1	87.7(10)	O(2)#1-Os(1)-N(1)#1	81.7(9)

O(1)-Os(1)-N(1)	100.3(7)	O(2)-Os(1)-N(1)#1	81.7(9)
O(2)#1-Os(1)-N(1)	87.7(10)	N(1)#1-Os(1)-N(1)	159.4(14)
C(6)-N(1)-Os(1)	113(2)	S(1)-N(1)-Os(1)	126.9(14)

Typical Dihydroxylation Procedure as Exemplified for Methyl 4-Nitrocinnamate. Methyl 4-nitrocinnamate (207 mg, 1 mmol) and *N*-(4-toluenesulfonyl)-(L)-threonine (13.6 mg, 5 mol%)[3] were dissolved in a *t*-BuOH/H_2O mixture (1:1, 2 mL). NMO (50 wt% in water, 228 μL, 1.1 mmol) and OsO_4 (0.1M in acetonitrile, 20 μL, 0.002 mmol) were added successively. The pH was adjusted to 5 by addition of 2N H_2SO_4 (150 μL), and the reaction mixture was stirred vigorously for 24 h, at which time the pH was adjusted to 5 again. After an additional 12 h (>95% conversion by liquid chromatography), methyl (2*R*, 3*S*)-(+)-2,3-dihydroxy-3-(p-nitrophenyl)-propionate[4] was obtained in 70% *ee* (HPLC: Chiralcel OG, 20% *i*-PrOH/hexane). The reaction time can be reduced to about 24 h by maintaining constant pH using a pH-stat. A 10 mmol scale reaction, performed under these conditions, afforded product as white solid. Yield: 1.8 g (75%, 70% *ee*). Recrystallization from ethanol produced needle shaped crystals in 57% yield and 81% *ee*.

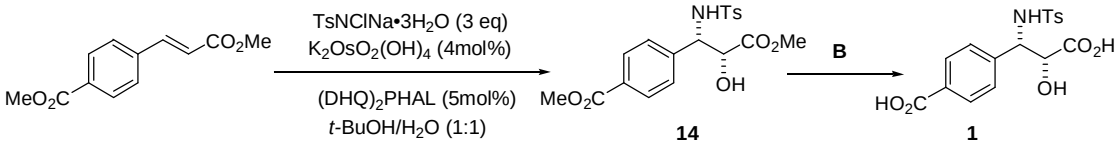
Typical Aminohydroxylation Procedure as Exemplified for Styrene. (2*R*, 3*S*)-*N*-(4-toluenesulfonyl)-2,4-dinitroisophenylserine, **4**, (212 mg, 0.5 mmol) and sodium bicarbonate (42 mg, 0.5 mmol) were dissolved in *t*-BuOH/H_2O (1:1, 20 mL). Styrene (1.040 g, 10 mmol), Chloramine-T trihydrate (2.870 g, 10 mmol), and $K_2OsO_2(OH)_4$ (36 mg, 0.1 mmol) were then added successively. The reaction mixture was stirred at room temperature for 20 h, at which point LC-MS analysis indicated 90% conversion. Sodium sulfite (100 mg) was added, and the mixture was stirred for an additional hour. It was then extracted (ethyl acetate, 3×25 mL), dried over anhydrous sodium sulfate, and concentrated to yield amorphous solid. Flash chromatography purification afforded a mixture of regioisomers 12:13 (32:68, determined by ^{1}H-NMR) as a white crystalline product. Yield: 2.5 g (86%). Regioisomers were separated by preparative HPLC (CH_3CN/H_2O, 30:70, 0.1% trifluoroacetic acid (TFA), YMCC18 column, 100 mg scale).

Enantiomeric excess was determined by chiral HPLC and the absolute configuration was established by comparing optical rotation with authentic samples. (*S*)-**12**, *ee* 43%, (Chiralcel-OG, *i*-PrOH/ hexane, 30:70, 1.5 mL/min) and (*R*)-**13**, *ee* 55% (Chiralcel-AS, *i*-PrOH/hexane, 30:70, 1.5 mL/min).

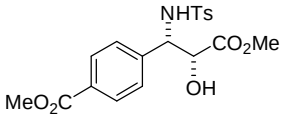
General Procedure for the Acidic Hydrolysis of *N*-Sulfonyl *a*, ß-Hydroxyaminoacid Methyl Esters (Method A). Methyl ester (1.20 mmol) was added to a HCl (5 mL, 4M in H_2O) solution and heated at 60°C overnight, at which point LC-MS analysis indicated complete consumption of the starting ester. 10 mL H_2O was added and the aqueous layer was extracted with EtOAc (2×20 mL), and the combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4 and evaporated to afford pure amino acid as white (yellow) powder.

General Procedure for Basic Hydrolysis of *N*- Sulfonyl *a*, ß-Hydroxyaminoacid Methyl Esters (Method B). To a methanol solution of Methyl ester (0.5 M, 1.20 mmol) was added $LiOH{\cdot}H_2O$ (10 mg, 2.40 mmol) and 0.1 ml H_2O. The resulting solution was stirred at room temp until LC analysis indicated complete consumption of the starting ester.10 mL H_2O was added and the *p*H of the solution was then adjusted to 4 and extracted with EtOAc (2×10 mL), and the combined organic extracts were washed with brine (10 mL), dried with Na_2SO_4 and evaporated to afford pure amino acid as white (or yellow) powder.

Synthesis of Ligand 1.



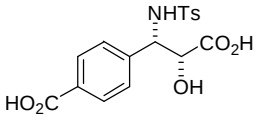
14 **1**



14

Methyl 4-(1S,2R)-2-hydroxy-3-methoxy-1- (4-methylphenylsulfonamido) -3-oxopropyl) benzoate, 14. $(DHQ)_2PHAL$ 93 mg (0.119 mmol) was dissolved in a mixture of 75 ml *t*-BuOH/H_2O (1:1). Chloramine T trihydate 4.09 g (14.52 mmol), (*E*)-methyl 4-(3-methoxy-3-oxoprop-1-enyl)benzoate 1.05 g (4.77 mmol) and potassium osmate dihydrate 36 mg (0.098 mmol) were added. The reaction mixture was stirred at rt for 40 hours. After cooling to 0 °C for one hour the solid was filtered off to give the product **14** as a white solid. Yield: 1.39 g (72 %). *ee* > 95 % (OD-H, hexane/*i*-PrOH 70/30, flowing rate 0.8 mL/min). ^{1}H-NMR (d_6-DMSO, 400MHz): *d* = 8.35 (d, J = 10.0Hz, 1H), 7.66 (d, J = 8.2Hz, 2H), 7.41 (d, J= 8.2Hz, 2H), 7.28 (d, J= 8.2Hz, 2H), 7.09 (d, J= 8.2Hz, 2H), 5.73 (d, J= 6.4Hz, 1H), 4.74 (dd, J= 10.0, 3.8Hz, 1H), 4.24 (dd, J= 6.4, 3.8Hz, 1H), 3.82 (s, 3H) 3.50 (s, 3H), 2.24 (s, 3H). ^{13}C{^{1}H}-NMR (d_6-DMSO, 100MHz): *d* =171.5, 166.0, 143.7, 142.2, 138.4, 129.0, 128.5, 128.1, 127.8, 126.4, 74.0, 59.9, 52.1, 51.7, 20.8. M. p. 168-170 °C.

The corresponding acid (**1)** was obtained using basic hydrolysis **B.**

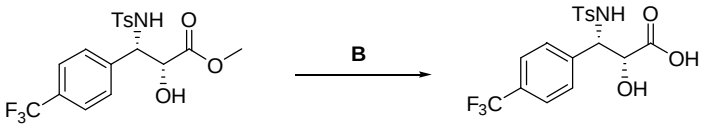


1

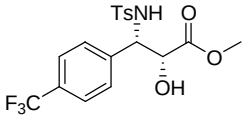
4-((1*S*,2*R*)-2-Carboxy-2-hydroxy-1-(4-methylphenylsulfonamido)ethyl)benzoic acid, **1.** ^{1}H-NMR (DMSO-d_6, 600MHz): *d* = 8.20 (d, J = 10.0Hz, 1H), 7.58 (d, J = 8.3Hz, 2H), 7.35 (d, J= 7.9Hz, 2H), 7.18 (d, J= 8.3Hz, 2H), 7.01 (d, J= 7.9Hz, 2H), 5.97 (br, 3H), 4.76

(dd, J= 10.0, 3.5Hz, 1H), 3.54 (d, J= 3.5Hz, 1H), 2.19 (s, 3H). $^{13}C\{^{1}H\}$-NMR (DMSO-d_6, 150MHz): d = 172.7, 167.2, 143.3, 142.1, 138.4, 129.2, 128.9, 128.9, 128.6, 127.8, 126.5, 74.1, 60.0, 20.9. HRMS calcd for $C_{17}H_{17}NO_7S$ (MH^+): 380.0798. Found: 380.0792. M. p. 197-199 °C (dec.).

Synthesis of Ligand 2.



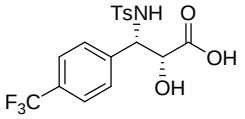
15 **2**



15

Methyl (2*R*, 3*S*)-*N*-(*p*-toluenesulfonyl)-3-amino-2-hydroxy-3-(4-trifluoromethyl) phenylpropanoate, **15**. The compound was synthesized by Sharpless asymmetric aminohydroxylation[5] and recrystallized from *t*-BuOH/H_2O 1:1 solution. Analysis of enantiomeric excess: Chiralcel OD, 10% *i*-PrOH/hexane, flowing rate: 0.8 mL/min. 16.6 min (2*S*, 3*R*), 36.4 min (2*R*, 3*S*). *ee* > 92%. ^{1}H NMR ($CDCl_3$, 400 MHz): d = 7.45(d, J = 8.4Hz, 2H), 7.37(d, J = 8.0Hz 2H), 7.22(d, J = 8.4Hz, 2H), 7.03(d, J = 8.4Hz 2H), 5.65(d, J = 10.0Hz, 1H), 4.89(dd, J = 10.0, 2.0Hz, 1H), 4.31(d, J = 2.4Hz 1H), 3.76(s, 1H), 2.29 (s, 1H). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 150 MHz): d = 171.0, 139.3, 138.2, 129.3, 128.9, 128.4, 126.4, 125.6, 124.3, 73.8, 59.8, 51.7, 20.7. M.p. 145-147 °C.

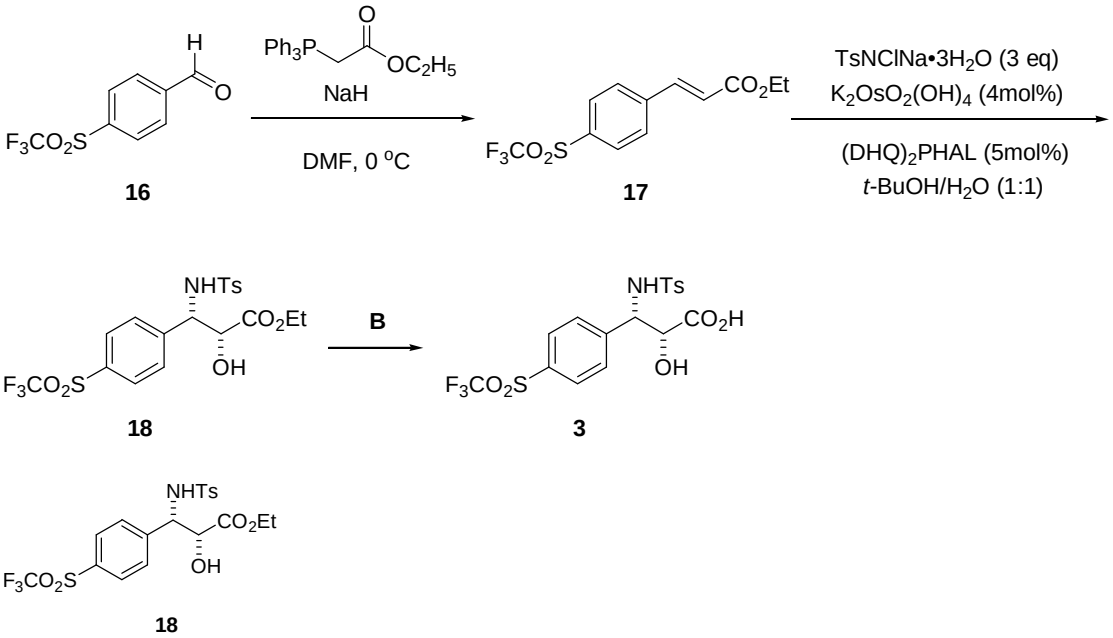
The corresponding acid (**2)** was obtained using basic hydrolysis **B**.



2

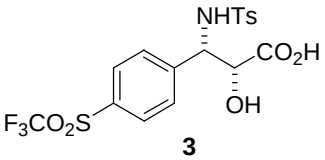
(2R,3S)-2-Hydroxy-3-(4-methylphenylsulfonamido)-3-(4-(trifluoromethyl)phenyl) propanoic acid, 2. ^{1}H NMR (d_6-DMSO, 400 MHz): *d* = 12.82(br, 1H), 8.27(d, J= 10.0Hz, 1H), 7.31(m, 6H), 6.97(d, J= 8.0Hz 2H), 5.42(d, J= 6.0Hz, 1H), 4.78(dd, J= 10.0, 3.6Hz, 1H), 4.09(d, J= 3.6Hz, 1H), 2.18(s, 3H). ^{13}C{^{1}H} NMR (d_6-DMSO, 100 MHz): *d* = 172.6, 142.6, 141.9, 138.2, 128.7, 128.4, 126.5, 124.2, 73.7, 59.8, 20.6. m.p. 210°C (dec.). HRMS calcd for $C_{17}H_{16}F_3NO_5S$ (MH^+): 404.0774. Found: 404.0769.

Synthesis of Ligand 3.



(2R,3S)-Ethyl 2-hydroxy-3-(4-methylphenylsulfonamido)-3-(4-(trifluoromethyl sulfonyl)phenyl)propanoate, 18. 69 mg (0.089 mmol) $(DHQ)_2PHAL$ was dissolved in a mixture of 50 mL *t*-BuOH/H_2O (1:1). 2.73 g (9.69 mmol) Chloramine T trihydate, 0.98 g (3.18 mmol) **17** and 30 mg (0.081 mmol) potassium osmate dihydrate were added and the reaction mixture was stirred at rt for 40 hours. After cooling to 0 °C for one hour the solid was filtered off to give the product **18** as a white solid. Yield: 0.884 g (56 %). *ee* > 95% (OD-H, hexane/*i*-PrOH 70/30, flowing rate: 0.4 mL/min). ^{1}H-NMR ($CDCl_3$, 500MHz): *d* = 7.97 (d, 2H), 7.79 (d, 2H), 7.42 (d, 2H), 7.35 (d, 2H), 5.18 (d, 1H), 4.24 (d, 1H), 4.14 (q, 2H), 2.35 (s, 3H), 1.93 (t, 3H).

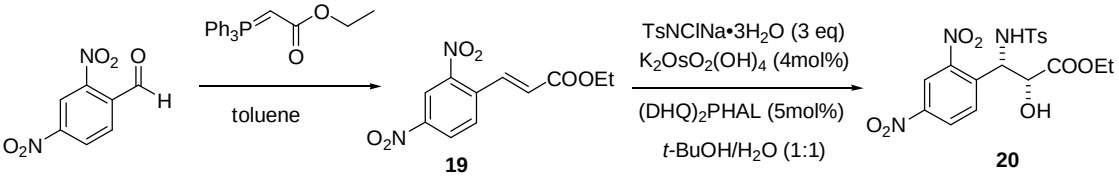
The corresponding acid (**3**) was obtained using basic hydrolysis **B**.



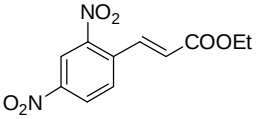
3

(2R,3S)-Ethyl 2-hydroxy-3-(4-methylphenylsulfonamido)-3-(4-(trifluoromethyl sulfonyl)phenyl)propanoate, 3. ^{1}H NMR (DMSO-d_6, 600 MHz): d = 8.48(d, J= 10.0Hz, 1H), 7.75(d, J= 8.3Hz, 2H), 7.55(d, J= 8.3Hz, 2H), 7.34(d, J= 7.9Hz, 2H), 6.99(d, J= 7.9Hz, 2H), 5.52(br, 1H), 4.93(dd, J= 10.1, 3.1Hz, 1H), 4.09(d, J= 3.5Hz, 1H), 2.19(s, 3H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): d = 172.3, 148.6, 142.2, 138.0, 129.8, 128.8, 127.7, 126.5, 73.4, 59.8, 20.7. HRMS calcd for $C_{17}H_{16}F_3NO_7S_2$ (MH^+): 468.0393. Found: 468.0390. M.p. 218-220 °C.

Synthesis of Ligand 4.



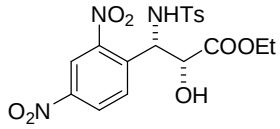
19 **20**



19

(E)-Ethyl 3-(2,4-dinitrophenyl)acrylate, 19. 2,4-dinitrobenzaldehyde 4.0 g (20.4 mmol) and (carbethoxymethylene) triphenylphosphorane 7.2 g (20.67 mmol) were dissolved in 140 mL dry toluene and heated at 90°C for 8 hours. The solvent was evaporated and the residue was purified by column (DCM) and recrystallization in EtOH to give the product **19** as a white solid. Yield: 4.15 g (76 %). ^{1}H-NMR ($CDCl_3$, 600MHz): d = 8.89 (d, J= 2.2Hz, 1H), 8.48 (dd, J= 8.3, 2.2Hz, 2H), 8.10 (d, J= 15.8Hz, 1H) 7.84 (d, J= 8.8Hz, 2H), 6.43 (d, J= 15.8Hz, 1H), 4.31 (q, J= 7.0Hz, 2H), 1.35 (t, J= 7.0Hz, 3H). ^{13}C{^{1}H}-NMR

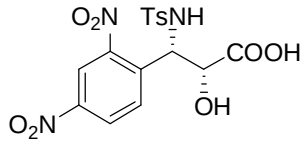
($CDCl_3$, 150MHz): *d* = 165.1, 148.3, 148.2, 137.8, 136.7, 130.8, 127.8, 126.8, 120.8, 61.6, 14.4. M.p. 94-96°C.



20

(2*R*,3*S*)-Ethyl 3-(2,4-dinitrophenyl)-2-hydroxy-3-(4-methylphenylsulfonamido) propanoate, 20. $(DHQ)_2PHAL$ 200 mg (0.257 mmol) was dissolved in a mixture of 175 mL *t*-BuOH/H_2O (1:1). Chloramine T trihydate 8.23 g (29.22 mmol), 2.5 g (9.61 mmol) **19** and 80 mg (0.217 mmol) potassium osmate dihydrate were added. The reaction mixture was stirred at rt for 16 hours. After cooling to 0°C for one hour the solid was filtered off to give **20** as a white solid. Yield: 3.73 g (86 %). *ee* > 95 % (OD-H, hexane/*i*-PrOH 70/30, flowing rate 0.8 mL/min). ^{1}H-NMR (DMSO-d_6, 500MHz): *d* = 8.75 (d, J= 10.3Hz, 1H), 8.57 (d, J= 2.2Hz, 1H), 8.16 (d, J= 8.8Hz, 1H), 7.73 (d, J= 8.8Hz, 1H), 7.30 (d, J= 8.4Hz, 2H), 7.07 (d, J= 8.1Hz, 2H), 5.99 (d, J= 5.9Hz, 1H), 5.32 (dd, J= 10.2, 3.0Hz, 1H), 4.37 (dd, J= 5.9, 3.0Hz, 1H), 4.08 (q, J= 7.4Hz, 2H), 1.19 (t, J= 7.4Hz, 3H). ^{13}C{^{1}H}-NMR (DMSO-d_6, 125MHz): *d* = 170.5, 147.9, 146.12, 142.7, 138.8, 137.5, 133.2, 129.2, 126.2, 125.9, 119.0, 72.0, 60.9, 54.9, 20.6, 14.0. M. p. 168-170 °C.

The corresponding acid **4** was obtained using acidic hydrolysis **A**.

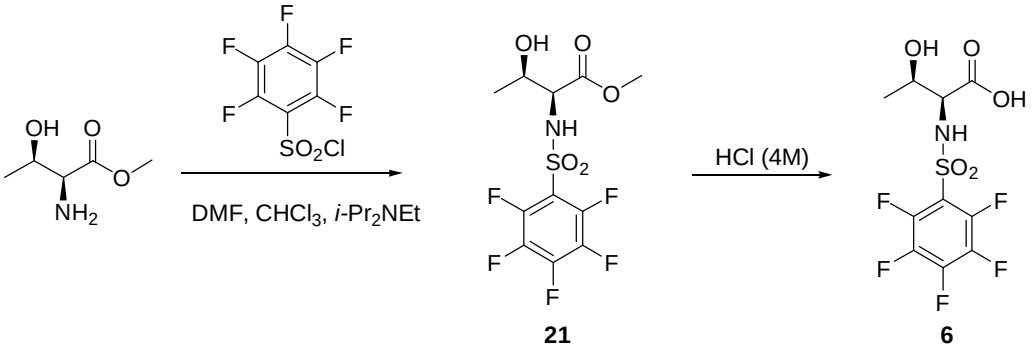


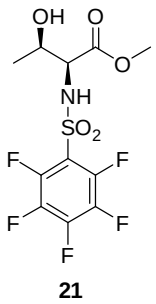
4

(2R,3S)-3-(2,4-Dinitrophenyl)-2-hydroxy-3-(4-methylphenylsulfonamido)propanoic acid, 4. ^{1}H-NMR (DMSO-d_6, 600MHz): *d* = 8.67 (d, J= 10.0Hz, 1H), 8.54 (d, J= 2.6Hz, 1H), 8.08 (d, J= 8.8Hz, 1H), 7.65 (d, J= 8.8Hz, 1H), 7.28 (d, J= 8.3Hz, 2H), 7.03 (d, J= 7.9Hz, 2H), 5.72 (br, 1H), 5.32 (dd, J= 10.0, 2.6Hz, 1H), 4.27 (s, 1H), 2.17 (s, 3H). ^{13}C{^{1}H}-NMR (DMSO-d_6, 150MHz): *d* = 172.1, 148.1, 146.1, 142.6, 138.7, 137.6, 133.1, 129.1, 126.2, 125.9, 118.9, 72.0, 54.8, 20.6. IR n_{max}: 3357, 3270, 3093, 1742,

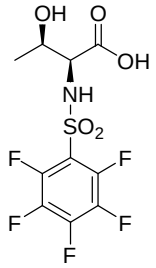
1539, 1339, 1275, 1158, 1103, 739 cm^{-1}. HRMS calcd for $C_{16}H_{15}N_3O_9S$ (MH^+): 426.0602. Found: 426.0600. M.p. 234 °C (dec.)

Synthesis of Ligand 6.





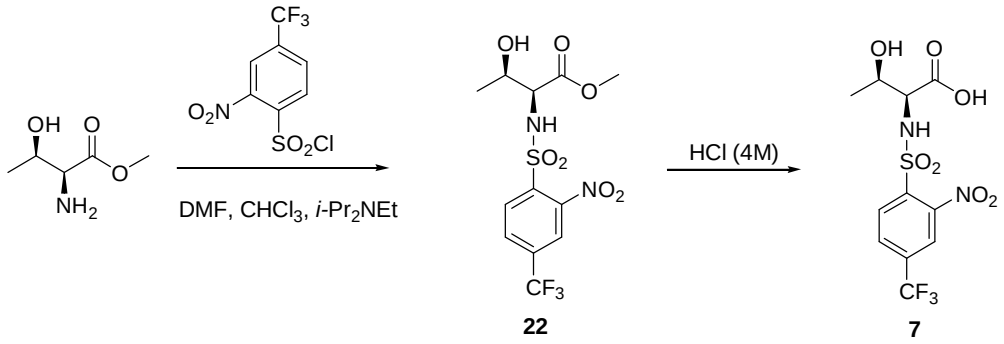
(2*S*,3*R*)-Methyl 3-hydroxy-2-(perfluorophenylsulfonamido)butanoate, 21. (L)-Threoline methyl ester 680 mg (4 mmol) was dissolved in DMF 0.7 mL and $CHCl_3$ 1 mL in a two necked flask under nitrogen. The mixture was cooled to –20°C, then $C_6F_5SO_2Cl$ 0.9 ml (6 mmol) was added dropwise, followed by the addition of *i*-Pr_2NEt 2.4 mL. The reaction was allowed to warm to room temperature and the progress of the reaction was followed by LC-MS. 4 hrs later, 25 mL of methylene chloride was added to the flask followed by 5 mL 10% H_2SO_4. The organic phase was separated, dried over Na_2SO_4. After evaporating of the solvent, the crude product was purified by column chromatography (silica gel, EtOAC: Hexane =1:1) to give **21**. Yield: 600 mg (41%). ^1H NMR ($CDCl_3$, 400 MHz): d =6.01(d, J= 9.6Hz, 1H), 4.41(dd, J= 6.0, 2.0Hz, 1H), 4.13 (dd, J= 9.6, 2.0Hz, 1H), 3.67(s, 3H), 1.35(d, J= 6.4Hz, 3H).



6

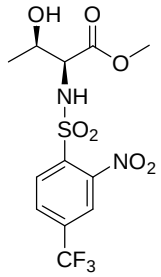
(2*S*,3*R*)-3-Hydroxy-2-(perfluorophenylsulfonamido)butanoic acid, 6. This compound was obtained using acidic hydrolysis **A**. ^{1}H NMR (d_6-DMSO, 600 MHz): d = 8.91(d, J= 9.2Hz, 1H), 4.79(br, 1H), 4.06(dd, J= 6.1, 4.4Hz, 1H),3.83(dd, J= 8.8, 4.0Hz, 1H),1.09 (d, J= 6.5Hz, 3H). ^{13}C{^{1}H}-NMR (DMSO-d_6, 150MHz): d = 170.9, 66.5, 62.3, 20.2 ppm. HRMS calcd for $C_{10}H_8F_5NO_5S$ (MNa^+): 371.9936. Found: 371.9930. M.p. 181-183°C.

Synthesis of Ligand 7.



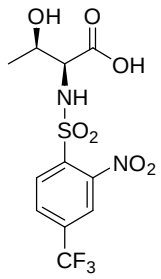
22 **7**

Compound **22** was prepared using the same procedure for **21**. The corresponding acid **7** was obtained using acidic hydrolysis **A**.



22

(2S,3R)-methyl 3-hydroxy-2-(2-nitro-4-(trifluoromethyl) phenylsulfonamido) butanoate, 22. ^{1}H NMR ($CDCl_3$, 400 MHz): *d* = 8.18 (m, 2H), 7.96(m, 1H), 6.35(d, J= 9.6Hz, 1H), 4.38(dq, J= 6.4, 2.4Hz, 1H), 4.11 (dd, J= 9.6, 2.4Hz, 1H), 3.54 (s, 3H), 1.35 (d, J= 6.4Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): *d* =170.1, 131.3, 129.6, 122.9(d), 68.1, 62.0, 52.8, 20.1.

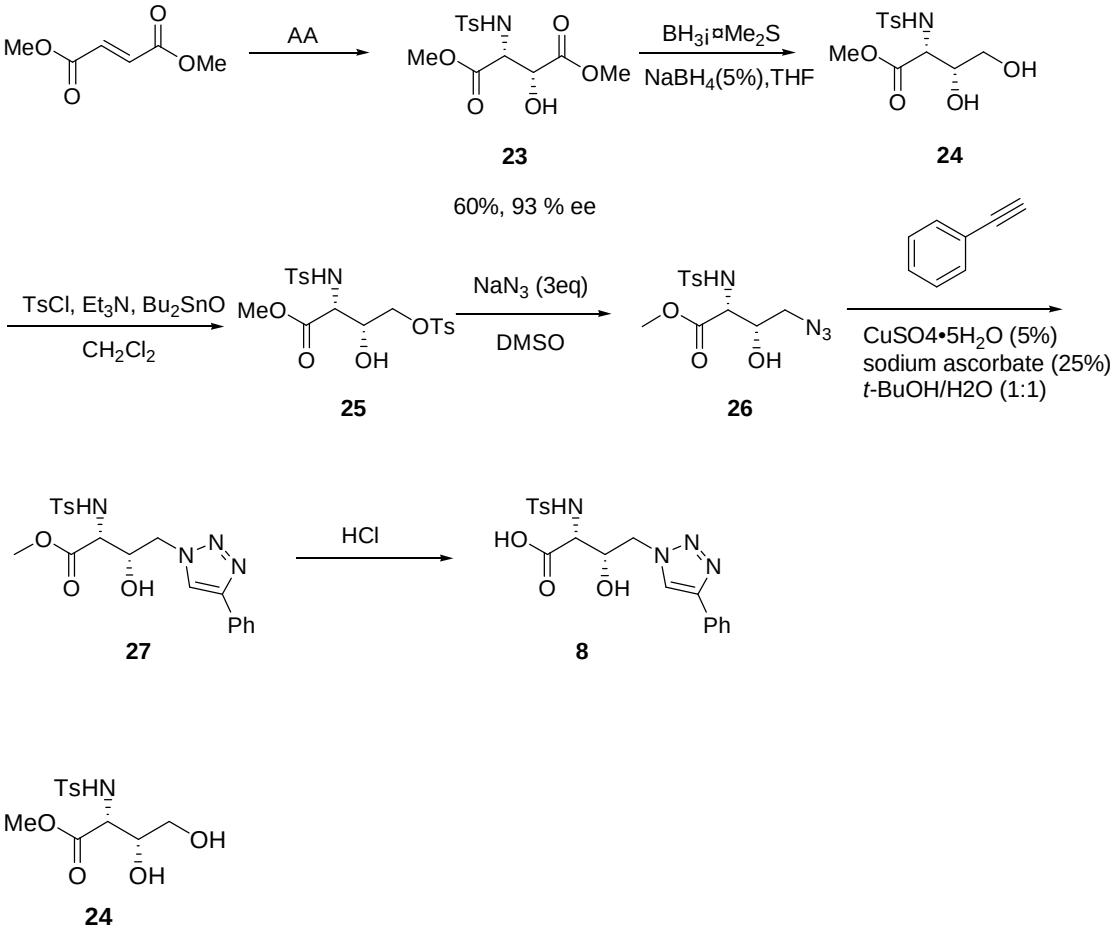


7

(2S,3R)-3-hydroxy-2-(2-nitro-4-(trifluoromethyl)phenylsulfonamido)butanoic acid, 7. ^{1}H NMR (DMSO-d_6, 600 MHz): *d* = 8.52 (s, 1H), 8.35(m, 2H), 8.27(d, J=7.9Hz, 1H), 5.01(br, 1H), 4.16(dq, J= 6.2, 2.6Hz, 1H), 3.83 (dd, J= 9.2, 2.6Hz, 1H), 3.34 (s, 1H), 1.09(d, J= 6.2Hz, 3H). ^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz): *d* =171.0, 147.3, 137.0, 131.8, 129.1, 123.3, 121.4, 66.6, 62.0, 20.4. IR ν_{max}: 3488, 3327, 3073, 1728, 1550, 1392, 1354, 1324, 1198,1170, 1143, 1084, 717, 605 cm^{-1}. HRMS calcd for $C_{11}H_{11}F_3N_2O_7S$ (MNa^+): 395.0131. Found: 395.0125. M.p. 145-146°C.

Synthesis of Ligand 8.

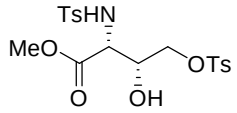
Dimethyl (2*R*, 3*R*)-*N*-(*p*-toluenesulfonyl)-3-amino-2-hydroxysuccinate (**23**) was synthesized using the Sharpless asymmetric aminohydroxylation.[4] Yield: 13.5 g (68 %). *ee* > 92%



Methyl (2*R*, 3*R*)-*N*-(*p*-toluenesulfonyl)-2-amino-3,4-dihydroxy butyrate, 24.[6]

Dimethyl (2*R*, 3*R*)-*N*-(*p*-toluenesulfonyl)-3-amino-2-hydroxysuccinate (1.84 g, 5.54 mmol) was dissolved in dry THF (9 mL) in a 25 mL two-necked flask. A solution of $BH_3 \cdot SMe_2$ in THF (2.9 mL, 2M, 5.8mmol) was added dropwise over 10 minutes against positive nitrogen flow. The resulting mixture was stirred for additional 30 minutes, and then $NaBH_4$ (14 mg, 5 mol%) was added. Stirring was continued overnight and quenched by MeOH (10 mL) and TsOH (10 mg). The resulting suspension was stirred for 30 minutes and concentrated to give a colorless gum. It was redissolved in 20 mL benzene-methanol (1:1) mixture and concentrated again. To the residue was added 15 mL benzene and concentrated to eliminate $B(OMe)_3$ as thoroughly as possible. The residue was purified by column chromatography (silica gel, EtOAC) to give **24** as a white solid. Yield: 1.34g (80%). ^{1}H NMR ($CDCl_3$, 400 MHz): *d* =7.70(d, J= 8.2Hz, 2H), 7.27(d, J=

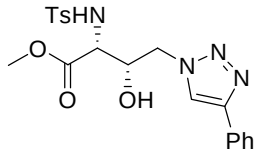
8.0Hz, 2H), 5.89(d, J= 9.2Hz, 1H), 4.10(dt, J= 6.4, 2.4Hz, 1H), 4.05(dd, J= 9.2, 2.4Hz, 1H), 3.71(d, J= 6.4Hz, 2H), 3.52(s, 3H), 2.40 (s, 3H). MS (ESI): 304.0 (MH^+).



25

(2R,3R)-Methyl 3-hydroxy-2-(4-methylphenylsulfonamido)-4-(tosyloxy)butanoate (25). Bu_2SnO (56mg, 0.2mmol) was added to a solution of **24** (1.38g, 4.55mmol) in dry CH_2Cl_2 (9 ml), followed by *p*-TsCl (0.87g, 4.55mmol) and Et_3N (0.64 ml, 4.55mmol). The reaction mixture was stirred until TLC indicated complete consumption of the starting alcohol. The mixture was filtered and the filtrate was concentrated in *vacuo*. The residue was chromatographed (silica gel, Hexane:EtOAC 1:1) to afford **25** as light yellow solid. Yield: 1.45g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77(d, J=8.4Hz, 2H), 7.66 (d, J=8.4Hz, 2H), 7.35 (d, J=8.4Hz, 2H), 7.26(d, J=8.4Hz, 2H), 5.40(d, J=9.2Hz, 1H), 4.29(m, 1H), 4.10 (m, 2H), 3.96(dd, J=9.2, 2.4Hz, 1H), 3.52 (s, 3H), 2.45 (s, 3H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 169.2, 145.4, 144.1, 136.0, 132.1, 130.1, 129.7, 128.0, 127.2, 70.6, 70.1, 56.8, 53.1, 21.7, 21.6. MS (ESI): m/z 458.0 (MH^+). M.p. 111-112 °C.

Methyl (1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-2-amino-3-hydroxy-4-azido butyrate, 26. NaN_3 (70 mg, 1.08 mmol) was added to a solution of **25** (0.20 g, 0.44 mmol) in DMSO (2 mL), the resulting solution was heated at 60°C for 4 hrs and then cooled to room temp. 20 mL H_2O was added and the aqueous layer was extracted with EtOAc (20 mL), dried with Na_2SO_4 and concentrated. The residue was chromatographed (silica gel, Hexane:EtOAC 1:1) to afford **26**, which was then used directly for the next step. Yield: 90 mg (63%).



27

(2R,3S)-Methyl 3-hydroxy-2-(4-methylphenylsulfonamido)-4-(4-phenyl-1H-1,2,3-triazol-1-yl)butanoate, **27**. Azide **26** (80 mg, 0.24 mmol) and phenyl acetylene (27 µL, 0.25mmol) were suspended in 0.5mL *tert*-butanol/water 1:1 mixture. Sodium ascorbate (0.256 mL, 0.285 M solution in water, 73 µmol) was added, followed by copper(II) sulfate pentahydrate(0.122 mL, 0.1 M in H_2O, 12 µmol). The heterogeneous mixture was stirred vigorously until LC analysis indicated complete consumption of **26**. The reaction miture was diluted with 5 mL H_2O, cooled in ice, and the white precipitate was collected by filtration. After washing with cold water, the precipitate was dried under vacuum to afford **27** as white powder.Yield: 95 mg (91%). ^{1}H NMR (DMSO-d_6, 500 MHz): d = 8.49(s, 1H), 8.24(d, J= 9.9Hz, 1H), 7.83(d, J= 7.3Hz, 2H), 7.70(d, J= 8.1Hz, 2H), 7.36(t, J= 7.4Hz, 2H), 7.32(m, 3H), 5.69(d, J= 5.9Hz, 1H), 4.49(d, J=12.1 Hz, 1H), 4.32(m, 2H), 4.16(d, J= 9.9Hz, 1H), 3.39(s, 3H), 2.27(s, 3H). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz): d = 169.4, 146.0, 142.7, 137.9, 130.8, 129.3, 128.9, 127.7, 126.7, 125.1, 122.3, 70.0, 58.6, 52.6, 52.0, 20.9. HRMS calcd for $C_{20}H_{22}N_4O_5S$ (MH^+): 431.1384. Found 431.1378. M. p. 180-182 °C.

The corresponding acid **8** was obtained by acidic hydrolysis **A**. HRMS calcd for $C_{19}H_{20}N_4O_5S$ (MH^+): 417.1227. Found 417.1228.

References

1. S.Oida, Y. Tajima, T. Konosu, Y.Nakamura, A. Somada, T. Tanaka, S. Habuki, T. Harasaki, Y. Kamai, T. Fukuoka, S. Ohya, H.Yasuda, *Chem. Pharm. Bull.* **2000**, *48*, 694.
2. More KOH solution or a higher temperature (35°) can be used to dissolve potassium osmate. Acetonitrile can be used as a substituent of ethanol.
3. M. Brenner, K. Rüfenacht, E. Sailer, *Helv. Chim. Acta*. **1951**, *36*, 2102.

4. J. A. Denis, A. Correa, A. E. Greene, *J. Org. Chem.* **1990**, *55*, 1957.

5. (a) G. Li, H.-T. Chang, K. B. Sharpless, *Angew. Chem.,Int. Ed. Engl*. **1996**, *35*, 451. (b) G. Li, H. H. Angert, K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2813.

6. E. Fernández-Megía, M.A. Montaos, F.J. Sardina, *J. Org. Chem.* **2000**, *65*, 6780.