Nontoxic, Nonvolatile, and Highly Efficient Osmium Catalysts for Asymmetric Dihydroxylation of Alkenes and Application to One Mol-scale Synthesis of Anticancer Drug, Camptothecin Intermediate

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Electronic Supplementary Information

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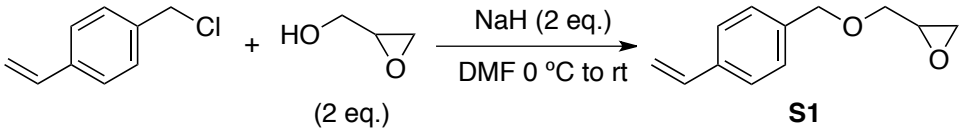
General Methods. Infrared (IR) spectrum was recorded on a JASCO FT/IR-4200 spectrometer, ν_{max} in cm^{-1}. Data are reported as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). ^{1}H NMR spectra were recorded on a JEOL ECA-500 (500 MHz) at ambient temperature. Chemical shifts are reported in ppm with the solvent references as the internal standard ($CHCl_3$: δ 7.24). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a JEOL ECA-500 (125 MHz) with complete proton decoupling. Chemical sift were recorded in ppm with the solvent references as the internal standard ($CDCl_3$: δ 77.0). Gel permeation chromatography (GPC) was performed on a SHIMAZU LC-10ADvp (flow rate = 1 mL/min, 40 ºC, eluant: THF) coupled with refraction index detector RID-10A, degasser DGU-12A, column oven CTO-10Avp and column of SHIMAZU Shim-pack 803 (ϕ8.0 x 300 mm), Shim-pack 804 (ϕ8.0 x 300 mm) and Shim-pack 8025 (ϕ8.0 x 300 mm) with standard curve of polystyrene. Quantitative analysis of osmium was performed on SHIMAZU Rayny EDX-720 or EDX-800 with standard curve. Enantiomeric excess (*ee*) was determined in comparison with authentic racemic material and analytical HPLC was performed on a SHIMAZU LC-20AB coupled with UV-VIS detector SPD-20AV, degasser DGU-20A3, column oven CTO-20AC and column of DAICEL CHIRALCEL OD-H (ϕ4.6 x 250 mm), DAICEL CHIRALCEL OJ-H (ϕ4.6 x 250 mm) or DAICEL CHIRALPACK AS-H (ϕ4.6 x 250 mm). Optical rotation was measured on a JASCO P-2100. High-resolution mass spectrometry was performed on a JEOL JMS-T100TD (AccuTOFTLC). For TLC analysis, Merk precoated TLC plates (silica gel 60 F_{254} 0.25 mm) were used. For preparative TLC, Wako TLC plates (silica gel 70 PF_{254} 0.75 mm) were used. For preparative column chromatography, Merk silica gel 60 (0.063–0.200 mm) was used.

All reactions were conducted under air atmosphere in round bottom flask. All commercially available reagents were used as received for the reactions without any purification. Liquid reagents were handled with a Gilson Pipetman. Chiral ligand, $(DHQD)_2PHAL$ and $(DHQD)_2PYR$ were synthesized according to reported procedures.[1,2] α-Bromomethylstyrene was synthesized from α-methylstyrene based on a reported procedure.[3] 4-Ethyl-8-methoxy-1*H*-pyrano[3,4-*c*]pyridine (**1i**) was synthesized according to a reported procedure.[4]

Synthesis of polymers.

Synthesis of 4-vinylbenzyl glycidyl ether (S1)[5].

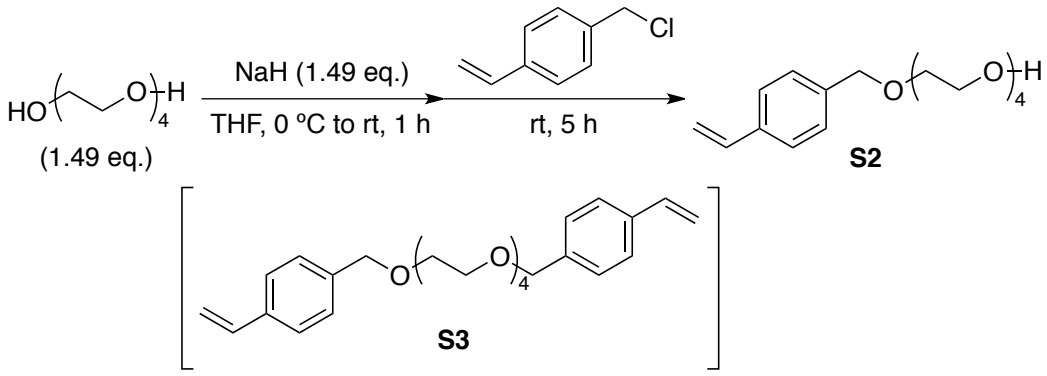


(2 eq.) **S1**

A 3 L round bottom flask containing sodium hydride (40.0 g, 60% in mineral oil, 1.00 mol) was charged with anhydrous DMF (563 mL) and cooled to 0 ºC. To this suspension, a mixture of 4-(chloromethyl)styrene (70.7 mL, 500 mmol) and glycidol (66.4 mL, 1.00 mol) was slowly added. After 3 h, tlc (hexane) indicated the complete conversion of the starting material. After the mixture was cooled to 0 °C and diluted with diethyl ether, saturated aqueous ammonium chloride was added to quench the reaction and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (hexane/EtOAc = 9/1) to afford 4-vinylbenzyl glycidyl ether (**S1**, 84.1 g, 442 mmol, 88% yield) as a yellow oil.

4-Vinylbenzyl glycidyl ether (S1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.60 (1H, dd, *J* = 2.3, 4.8 Hz), 2.78 (1H, dd, *J* = 4.8, 4.8 Hz), 3.17 (1H, m), 3.40 (1H, dd, *J* = 5.7, 11.3 Hz), 3.75 (1H, dd, *J* = 2.8, 11.3 Hz), 4.56 (1H, d, *J* = 12.5 Hz), 4.58 (1H, d, *J* = 12.5 Hz), 5.23 (1H, d, *J* = 10.8 Hz), 5.37 (1H, d, *J* = 17.6 Hz), 6.70 (1H, dd, *J* = 10.8, 17.6 Hz), 7.29 (2H, d, *J* = 7.9 Hz), 7.38 (2H, d, *J* = 7.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.2, 50.8, 70.7, 72.9, 113.8, 126.2, 127.9, 136.4, 137.0, 137.4.

Synthesis of tetraethylene glycol mono-4-vinylbenzyl ether (S2)[6].

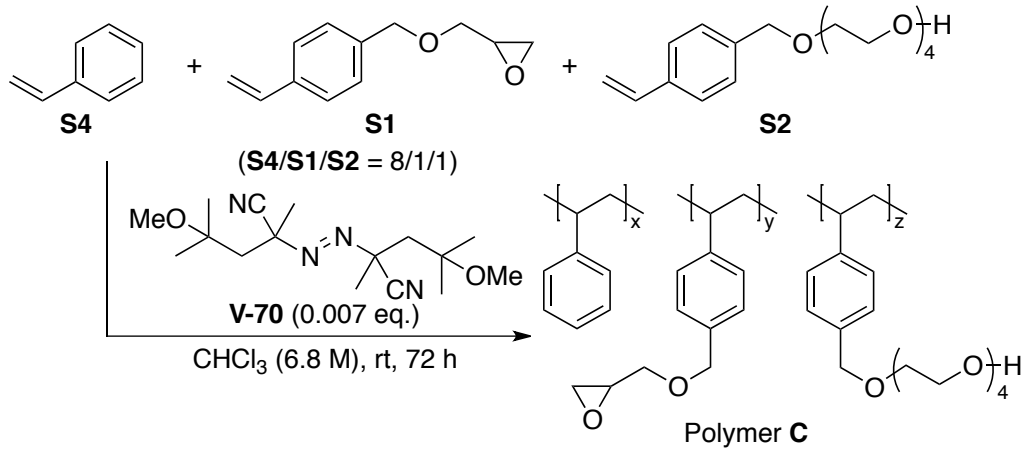


A 3 L round bottom flask containing sodium hydride (29.8 g, 60% in mineral oil, 745 mmol) was charged with anhydrous THF (855 mL) and cooled to 0 ºC. To this suspension, tetraethylene glycol (129 mL, 745 mmol) was slowly added at 0 °C. After the reaction mixture was stirred for 1 h at room temperature, 4-(chloromethyl)styrene (70.0 mL, 500 mmol) was added. After 5 h, tlc (hexane) indicated the complete conversion of the starting material. After the mixture was cooled to 0 °C and diluted with diethyl ether, saturated aqueous ammonium chloride was added to quench the reaction and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by silica gel column chromatography (hexane/EtOAc = 1/1, EtOAc only and EtOAc/MeOH = 9/1) to afford tetraethyleneglycol di-4-vinylbenzyl ether[7] (**S3**, 17.5 g, 41.0 mmol, 16% yield) and tetraethyleneglycol mono-4-vinylbenzyl ether (**S2**, 124 g, 399 mmol, 80% yield).

Tetraethyleneglycol mono-4-vinylbenzyl ether (S2): Orange oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87 (1H, s), 3.50–3.66 (16H, m), 4.47 (2H, s), 5.16 (1H, d, J = 11.3 Hz), 5.67 (1H, d, J = 17.7 Hz), 6.63 (1H, dd, J = 11.3, 17.7 Hz), 7.23 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 61.5, 69.2, 70.2, 70.4, 70.45, 70.47, 72.4, 72.8, 113.6, 126.1, 127.8, 136.4, 136.8, 137.7.

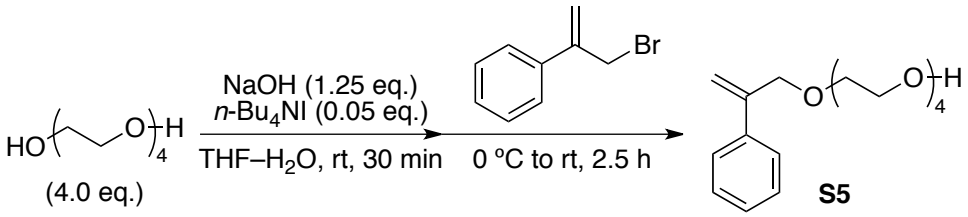
Tetraethyleneglycol di-4-vinylbenzyl ether (S3): Orange oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.55–3.65 (16H, m), 4.49 (4H, s), 5.18 (2H, d, J = 10.9 Hz), 5.69 (2H, d, J = 17.7 Hz), 6.65 (2H, dd, J = 10.9, 17.7 Hz), 7.25 (4H, d, J = 8.3 Hz), 7.33 (4H, d, J = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.2, 70.4, 70.5, 72.7, 113.6, 126.0, 127.7, 136.4, 136.7, 137.7.

Synthesis of polymer C.



Styrene (**S4**, 355 mL, 3.10 mol), 4-vinylbenzyl glycidyl ether (**S1**, 73.7 g, 388 mmol) and tetraethyleneglycol mono-4-vinylbenzyl ether (**S2**, 120 g, 388 mmol) were combined in anhydrous chloroform (570 mL) in a 3 L round bottom flask. The mixture was degassed under Ar for 30 min. 2,2'-Azobis(4-methoxy)-2,4-dimethylvaleronitrile (**V-70**, 8.37 g, 27.1 mmol) was added to the mixture and the whole mixture was stirred at 200 rpm for 72 h at room temperature. The resulting polymer solution was concentrated *in vacuo*. To the residue, MeOH (1 L) was slowly added with vigorously stirring. Polymer and solvents were separated by decantation. The precipitated polymer was dissolved in THF (300 mL) and to this solution, MeOH (1 L) was added. After repeating the same precipitation procedure, the resulting polymer was dried at 40 ºC under reduced pressure to afford desired polymer **C** (241 g, 47% yield). The molar ratio of the components was determined by ^{1}H NMR analysis (x/y/z = 80/9/11). Mw = 3 3400; Mn = 2 4500; Mw/Mn = 1.36 (GPC).

Synthesis of tetraethylene glycol mono-2-phenyl-2-propenyl ether (S5)[8].

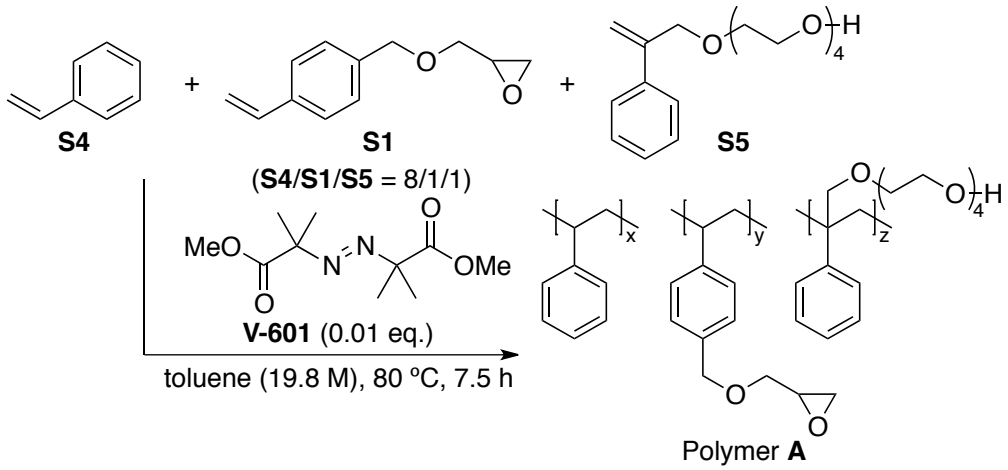


Sodium hydroxide (17.3 g, 431 mmol) was dissolved in water (26 mL) in a 1 L round bottom flask, and to this solution, tetraethylene glycol (238 mL, 1.38 mol), THF (173

mL) and tetrabutylammonium iodide (6.37 g, 17.3 mmol) were added. After the mixture was cooled to 0 °C, a THF solution (69 mL) of α-bromomethylstyrene (97.4 g, 70% purity, including β-bromo-α-methylstyrene, 345 mmol) was added over 5 min. The mixture was allowed to warm to room temperature. After 2.5 h, tlc (hexane) indicated the complete conversion of the starting material. The mixture was diluted with water and diethyl ether and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford tetraethylene glycol mono-2-phenyl-2-propenyl ether (**S5**, 130 g, 69% purity, including β-bromo-α-methylstyrene, 290 mmol, 84% yield) as a orange oil. To determine the yield and purity of the product, a part of the crude material (153 mg) was analyzed by ^{1}H NMR using durene as an internal standard. The product was used in subsequent reaction without further purification.

Tetraethylene glycol mono-2-phenyl-2-propenyl ether (S5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.91 (1H, s), 3.49–3.67 (16H, m), 4.35 (2H, s), 5.27 (1H, s), 5.46 (1H, s), 7.14–7.31 (3H, m), 7.37–7.44 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 61.5, 69.1, 70.1, 70.37, 70.42, 72.3, 72.9, 114.2, 125.9, 127.6, 128.1, 138.5, 143.9.

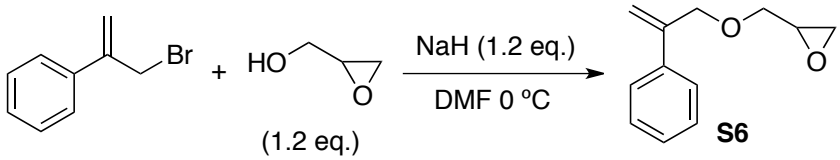
Synthesis of polymer A.



Styrene (**S4**, 273 mL, 2.38 mol), 4-vinylbenzyl glycidyl ether (**S1**, 50.2 g, 264 mmol) and tetraethylene glycol mono-2-phenyl-2-propenyl ether (**S5**, 92.4 g, 89% purity, including β-bromo-α-methylstyrene, 264 mmol) were combined in toluene (133 mL) in a 1 L round bottom flask. The mixture was degassed under Ar for 30 min and stirred at 75 °C for 30 min. Dimethyl 2,2'-azobis(2-methylpropionate) (**V-601**, 6.08 g, 26.4

mmol) was added to the mixture and the whole mixture was stirred at 80 ºC for 7.5 h. To the resulting polymer solution, MeOH (2.2 L) was slowly added with vigorously stirring. The polymer and solvents were separated by decantation. The precipitated polymer was dissolved in THF (220 mL) and to this solution, MeOH (2.2 L) was added. The resulting polymer was dried at 40 ºC under reduced pressure to afford the desired polymer **A** (248 g, 70% yield). The molar ratio of the components was determined by ^{1}H NMR analysis (x/y/z = 82/12/6). Mw = 60 800; Mn = 26 800; Mw/Mn = 2.27 (GPC).

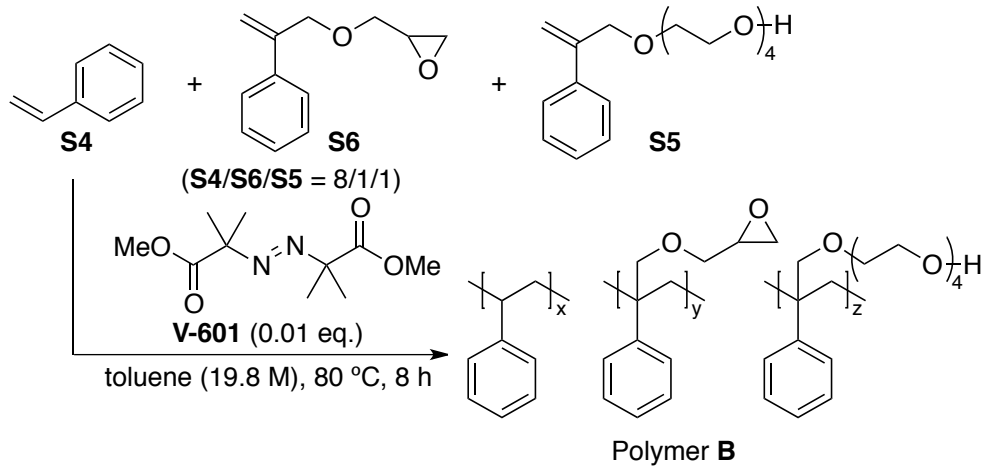
Synthesis of glycidyl 2-phenyl-2-propenyl ether (S6)[9].



A 1 L round bottom flask containing sodium hydride (9.19 g, 60% in mineral oil, 230 mmol) was charged with anhydrous DMF (250 mL) and cooled to 0 ºC. To this suspensuion, anhydrous DMF solution (50 mL) of α-bromomethylstyrene (40.7 g, 93% purity, including β-bromo-α-methylstyrene, 191 mmol) and glycidol (15.3 mL, 231 mol) was added over 30 min at 0 °C. After 40 min, tlc (hexane/EtOAc = 6/1) indicated the complete conversion of the starting material. After the mixture was cooled to 0 °C and diluted with diethyl ether, saturated aqueous ammonium chloride was added to quench the reaction and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by distillation (82~114 ºC/0.15 mmHg) to afford glycidyl 2-phenyl-2-propenyl ether (**S6**, 29.7 g, 93% purity, including β-bromo-α-methylstyrene, 146 mmol, 76% yield) as a yellow oil.

Glycidyl 2-phenyl-2-propenyl ether (S6): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55 (1H, dd, *J* = 2.6, 4.7 Hz), 2.74 (1H, dd, *J* = 4.7, 4.7 Hz), 3.12 (1H, m), 3.42 (1H, dd, *J* = 6.0, 11.6 Hz), 3.74 (1H, dd, *J* = 3.1, 11.6 Hz), 4.38 (1H, d, *J* = 13.2 Hz), 4.45 (1H, d, *J* = 13.2 Hz), 5.32 (1H, s), 5.51 (1H, s), 7.21–7.35 (3H, m), 7.42–7.47 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.2, 50.7, 70.5, 73.0, 114.5, 125.9, 127.7, 128.3, 138.5, 143.8.

Synthesis of polymer B.



Styrene (**S4**, 242 mL, 2.11 mol), glycidyl 2-phenyl-2-propenyl ether (**S6**, 97% purity, including β-bromo-α-methylstyrene, 60.7 g, 309 mmol) and tetraethylene glycol mono-2-phenyl-2-propenyl ether (**S5**, 69% purity, including β-bromo-α-methylstyrene, 128 g, 287 mmol) were combined in anhydrous toluene (150 mL) in a 1 L round bottom flask. The mixture was degassed under Ar for 30 min and stirred at 75 ºC for 30 min. Dimethyl 2,2'-azobis(2-methylpropionate) (**V-601**, 6.86 g, 29.8 mmol) was added to the mixture and the whole mixture was stirred for 8 h at 80 ºC. To the resulting polymer solution, MeOH (2.5 L) was slowly added with vigorously stirring. The polymer and solvents were separated by decantation. The precipitated polymer was dissolved in THF (250 mL) and to this solution, MeOH (2.5 L) was added. The resulting polymer was dried at 40 ºC under reduced pressure to afford desired polymer **B** (212 g, 54% yield). The molar ratio of the components was determined by ^{1}H NMR analysis (x/y/z = 85/9/6). Mw = 44 700; Mn = 10 200; Mw/Mn = 4.37 (GPC).

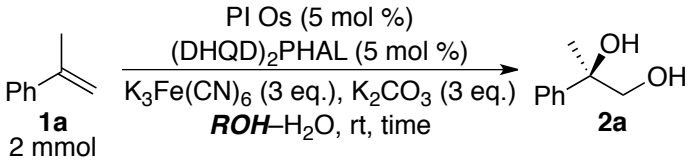
Preparation of polymer incarcerated osmium (PI Os) catalysts. Polymer **C** (100 g) was dissolved in THF–MeOH (4/1, 1.6 L) in a 5 L round bottom flask, and to this solution, osmium tetroxide (19.6 g, 77.2 mmol) was added and the mixture was stirred at room temperature. The color of the mixture turned from yellow to black gradually. After 72 h stirring, hexane (2.8 L) was added dropwise to form a black microencapsulated osmium (MC Os) catalyst and this suspension was stirred overnight. The solvents were then removed by decantation and the resulting MC Os **C** was washed with hexane several times and dried *in vacuo* to afford MC Os **C** (108 g). Next, MC

Os was heated at 150 ºC for 5.5 h by using oven, filtered and washed with THF to afford PI Os **C** (102 g), which was insoluble in almost all organic solvents. The loading of the catalyst was determined from the recovered osmium component in washing by fluorescence X-ray (XRF) analysis (Loading of PI Os **C**: 0.754 mmol/g, >99%).

PI Os **A** and **B** could be also prepared by using the same procedure as that of PI Os **C** and >99% of osmium component was immobilized onto polymers respectively (Loading of PI Os **A**: 1.212 mmol/g; PI Os **B**: 1.112 mmol/g).

Investigation of reaction conditions using α-methylstyrene (1a). We investigated reaction conditions using α-methylstyrene (**1a**) as a model substrate (Table S1). When PI Os **A** was used as a catalyst, although the reaction proceeded smoothly to afford 2-phenyl-1,2-propanediol (**2a**) in good yield with good enantiomeric excess, slightly higher leaching of osmium was observed by XRF analysis (Table S1, entries 1 and 2). On the other hand, PI Os **B** gave the same catalytic activity and selectivity as that of PI Os **A** with less amount of leaching of osmium (Table S1, entries 3 and 4). In the case of PI Os **C**, *t*-BuOH was not a suitable solvent for **1a** different from camptothecin intermediate **1i** (Table S1, entry 5). However, in *i*-PrOH, the same result as that of PI Os **A** was obtained after 5 h (Table S1, entry 6). We focused on PI Os **C** because of. availability of the polymer. Next, we examined the concentration of the substrate and the ratio of *i*-PrOH and H_2O. However, no improvement for leaching of osmium was obtained (Table S1, entries 7–9).

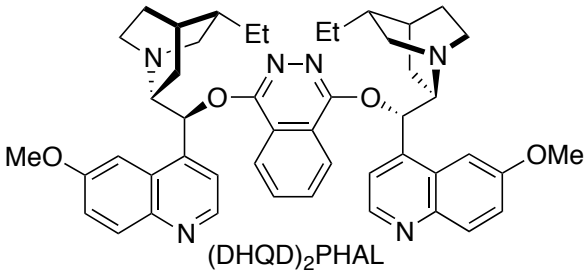
Table S1. Asymmetric dihydroxylation of α-methylstyrene (**1a**) using PI Os catalysts



Entry	PI Os	*ROH*	Solvent Ratio	Conc. (M)	Time (h)	Yield of **2a** (%)[a]	*ee* (%)[b]	Leaching (%)[c]
1	**A**	*t*-BuOH	1/1	0.1	2.5	95	92	3
2	**A**	*i*-PrOH	1/1	0.1	5	94	92	5

3	**B**	*t*-BuOH	1/1	0.1	2	90	92	2
4	**B**	*i*-PrOH	1/1	0.1	2	87	91	1
5	**C**	*t*-BuOH	1/1	0.1	16	89 (86, 96)[d]	92 (92, 92)[d]	12 (7, 5)[d]
6	**C**	*i*-PrOH	1/1	0.1	5	88 (92, 96)[d]	92 (92, 91)[d]	1 (3, 2)[d]
7	**C**	*i*-PrOH	1/1	0.2	17	90	90	2
8	**C**	*i*-PrOH	1/2	0.1	3	94	91	2
9	**C**	*i*-PrOH	2/1	0.1	24	93	90	4

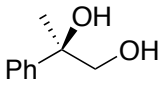
[a] Yield of isolated product after purification. [b] Ee was determined by HPLC analysis. [c] Leaching of osmium was determined by XRF analysis. [d] Results in 2nd run and 3rd run.



(DHQD)$_2$PHAL

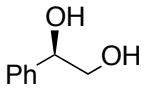
Representative procedure for the asymmetric dihydroxylation of olefins.

Asymmetric dihydroxylation of α-methylstyrene (Table 1, entry 3). PI Os **C** (133 mg, 0.1 mmol), (DHQD)$_2$PHAL (77.9 mg, 0.1 mmol), $K_3Fe(CN)_6$ (1.98 g, 6 mmol) and K_2CO_3 (829 mg, 6 mmol) were combined in *i*-PrOH–H_2O (1/1, 20 mL) in a 50 mL round bottom flask. After stirring for 10 min, α-methylstyrene (**1a**, 260 μL, 2 mmol) was added, and the mixture was further stirred at room temperature. After 5 h, tlc (hexane/EtOAc = 1/1) indicated the complete conversion of the starting material. $Na_2S_2O_3$ (633 mg, 4 mmol) and *i*-PrOH (20 mL) were added, and the mixture was stirred for 10 min. PI Os **C** was separated by filtration and washed with *i*-PrOH and H_2O subsequently. The organic and aqueous filtrates were analyzed by XRF analysis to determine the leaching of osmium from the catalyst. Next, the whole filtrates were combined and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by preparative TLC (hexane/EtOAc = 1/1) to afford (*R*)-2-phenyl-1,2-propanediol (**2a**) as a colorless oil (268 mg, 1.76 mmol, 88% yield).

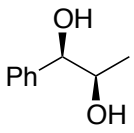


(*R*)-2-Phenyl-1,2-propanediol (2a)[10]**:** Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (3H, s), 3.36 (1H, d, *J* = 11.6 Hz), 3.50 (1H, d, *J* = 11.6 Hz), 3.59 (2H, br), 7.08–7.29 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.7, 70.4, 74.7, 124.9, 126.8, 128.1, 144.9; Enantiomeric excess was determined to be 92% by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, UV = 254 nm, 40 ºC); t_R(*S*)= 10.9 min, t_R(*R*) = **13.8 min**.

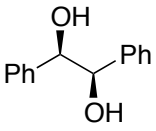
Other compounds:



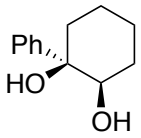
(*R*)-1-Phenyl-1,2-ethanediol (2b)[10] **(Table 1, entry 4):** White solid (224 mg, 1.62 mmol, 81% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.45 (1H, dd, *J* = 8.6, 11.6 Hz), 3.52 (1H, dd, *J* = 2.9, 11.6 Hz), 4.16 (2H, br), 4.60 (1H, dd, *J* = 2.9, 8.6 Hz), 7.11–7.21 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 67.8, 74.6, 126.0, 127.7, 128.3, 140.3; Enantiomeric excess was determined to be 95% by chiral HPLC analysis (DAICEL CHIRALPACK AS-H, hexane/*i*-PrOH = 95/5, flow rate = 0.5 mL/min, UV = 254 nm, 26 ºC); t_R(*S*)= 43.0 min, t_R(*R*) = **44.7 min**.



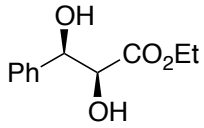
(1*R*,2*R*)-1-Phenyl-1,2-propanediol (2c)[10] **(Table 1, entry 5):** One equivalent of methanesulfonamide was added as an additive. Colorless oil (277 mg, 1.82 mmol, 91% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (3H, d, *J* = 6.3 Hz), 3.76 (1H, dq, *J* = 6.3, 7.7 Hz), 4.15 (1H, d, *J* = 7.7 Hz), 7.12–7.23 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.6, 72.0, 79.3, 126.8, 127.8, 128.2, 141.0; Enantiomeric excess was determined to be 97% by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/*i*-PrOH = 95/5, flow rate = 0.5 mL/min, UV = 254 nm, 40 ºC); t_R(1*S*,2*S*) = 32.0 min, t_R(1*R*,2*R*) = **33.2 min**.



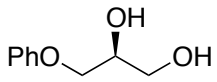
(1*R*,2*R*)-1,2-Diphenyl-1,2-ethanediol (2d)[10] **(Table 1, entry 6):** One equivalent of methanesulfonamide was added as an additive. White solid (410 mg, 1.91 mmol, 96% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.84 (2H, br), 4.71 (2H, s), 7.11–7.16 (4H, m), 7.21–7.27 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.1, 126.9, 127.9, 139.8; Enantiomeric excess was determined to be 99% by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, UV = 254 nm, 40 ºC); t_R(1*S*,2*S*) = 25.0 min, t_R(1*R*,2*R*) = **28.5 min**.



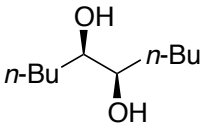
(1*R*,2*R*)-1-Phenyl-1,2-cyclohexanediol (2e)[10] **(Table 1, entry 7):** The reaction was carried out in *t*-BuOH–H_2O (1/1) and one equivalent of methanesulfonamide was added as an additive. White solid (336 mg, 1.75 mmol, 87% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32–1.44 (1H, m), 1.48–1.55 (1H, m), 1.58–1.73 (3H, m), 1.75–2.00 (4H, m), 2.71 (1H, br), 3.90 (1H, dd, *J* = 4.5, 10.8 Hz), 7.21–7.27 (1H, m), 7.32–7.38 (2H, m), 7.43–7.50 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 24.3, 29.1, 38.4, 74.4, 75.7, 125.1, 126.8, 128.3, 146.4; Enantiomeric excess was determined to be 97% by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, UV = 254 nm, 40 ºC); t_R(1*S*,2*S*) = 15.7 min, t_R(1*R*,2*R*) = **18.5 min**.



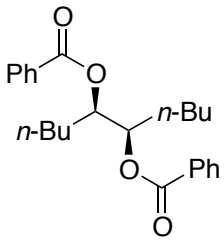
(2*S*,3*R*)-Ethyl 2,3-dihydroxy-3-phenyl-propionate (2f)[11] **(Table 1, entry 8):** The reaction was carried out in *t*-BuOH–H_2O (1/1) and one equivalent of methanesulfonamide was added as an additive. White solid (336 mg, 1.60 mmol, 80% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (3H, dt, *J* = 1.1, 7.3 Hz), 2.49–3.50 (2H, br), 4.17 (2H, q, *J* = 7.3 Hz), 4.26 (1H, dd, *J* = 1.1, 2.8 Hz), 4.91 (1H, d, *J* = 2.8 Hz), 7.20–7.36 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 62.1, 74.5, 74.7, 126.2, 128.0, 128.4, 139.9, 172.7; Enantiomeric excess was determined to be >99.5% by chiral HPLC analysis (DAICEL CHIRALCEL OJ-H, hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, UV = 254 nm, 40 ºC); t_R(1*S*,2*S*) = 25.3 min, t_R(1*R*,2*R*) = **33.1 min**.



(*S*)-3-Phenoxy-1,2-propanediol (2g)[10] **(Table 1, entry 9):** White solid (275 mg, 1.64 mmol, 82% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.23–3.48 (2H, br), 3.63 (1H, dd, *J* = 6.2, 11.3 Hz), 3.72 (1H, dd, *J* = 2.8, 11.3 Hz), 3.90 (1H, d, *J* = 5.1 Hz), 3.95–4.05 (1H, m), 6.75–6.90 (3H, m), 7.12–7.22 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 63.6, 68.8, 70.5, 114.4, 121.2, 129.5, 158.3; Enantiomeric excess was determined to be 82% by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, UV = 254 nm, 40 ºC); t_R(*R*) = 6.8 min, t_R(*S*) = **9.9 min**.



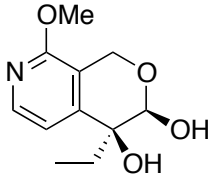
(5*R*,6*R*)-5,6-Decanediol (2h)[10] **(Table 1, entry 10):** One equivalent of methanesulfonamide was added as an additive. White solid (319 mg, 1.83 mmol, 92% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (3H, t, *J* = 7.1 Hz), 1.17–1.48 (12H, m), 3.21 (2H, br), 3.25–3,22 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 22.7, 27.8, 33.1, 74.4. Next, the obtained diol **2h** was dissolved in 5 mL of pyridine and cooled to 0 ºC. To this solution, benzoyl chloride (510 μL, 4.39 mmol) and 4-dimethylaminopyridine (22.4 mg, 18.3 μmol) were added and the reaction mixture was allowed to warm to room temperature. After 1 h, tlc (hexane/EtOAc = 6/1) indicated the complete conversion of the starting material. The mixture was diluted with CH_2Cl_2 and H_2O. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by chromatography on sillica gel (hexane/EtOAc = 9/1) to afford (5*R*,6*R*)-decane-5,6-diyl dibenzoate (**4**) as a white solid (670 mg, 1.75 mmol, 96% yield).



(5*R*,6*R*)-Decane-5,6-diyl dibenzoate (4)[12]**:** White solid; IR (KBr): 3419 (w), 3065 (w), 2959 (br), 2867 (s), 1978 (w), 1923 (w), 1832 (w), 1720(s), 1594 (m), 1458 (s), 1272 (br), 1173 (m), 1106 (s), 1070 (s), 1032 (s), 977 (s), 885 (m), 857 (m), 802 (w), 714 (s), 592 (w), 471 (m), ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.78 (3H, t, *J* = 7.1 Hz), 1.16–1.36 (8H, m), 1.58–1.72 (4H, m), 5.32 (2H, dt, *J* = 4.7, 9.6 Hz), 7.30–7.38 (4H, m), 7.42–7.48 (2H, m), 7.94–8.00 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 22.5, 27.3, 30.7, 74.6, 128.3, 129.6, 130.1, 132.9, 166.1; Enantiomeric excess was determined to be 97% by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/*i*-PrOH = 99.8/0.2, flow rate = 1.0 mL/min, UV = 254 nm, 26 ºC); t_R(5*S*,6*S*) = 8.9 min, t_R(5*R*,6*R*) = **12.3 min**; Optical Rotation: $[\alpha]^{20}_D$ = +54.0 (*c* 1.0, $CHCl_3$, 97% *ee*); DART-HRMS (*m*/*z*) calcd for $C_{24}H_{31}O_4$ ($M+H^+$) 383.2222, found 383.2221.

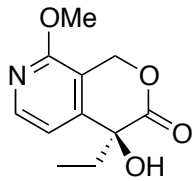
Asymmetric dihydroxylation of olefin 1i (Table 2, entry 3). PI Os **C** (133 mg, 0.1 mmol), $(DHQD)_2PYR$ (88.1 mg, 0.1 mmol), $K_3Fe(CN)_6$ (1.98 g, 6 mmol), K_2CO_3 (829 mg, 6 mmol), and methanesulfonamide (191 mg, 2 mmol) were combined in *t*-BuOH–H_2O (1/1, 20 mL). After stirring for 10 min, olefin **1i** (333 μL, 2 mmol) was added, and the mixture was further stirred at room temperature. After 16 h, tlc (hexane/EtOAc = 1/1) indicated the complete conversion of the starting material.

$Na_2S_2O_3$ (633 mg, 4 mmol) and *i*-PrOH (20 mL) was added, and the mixture was stirred for 10 min. PI Os **C** was separated by filtration and washed with *i*-PrOH and H_2O subsequently. The organic and aqueous filtrates were analyzed by XRF analysis to determine the leaching of osmium from the catalyst. Next, the whole filtrates were combined and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by chromatography on silica gel (hexane/EtOAc = 1/1) to afford (3*R*,4*S*)-4-ethyl-8-methoxy-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridin-3,4-diol (**2i**) as a white solid (405 mg, 1.80 mmol, 90% yield).



(3*R*,4*S*)-4-Ethyl-8-methoxy-3,4-dihydro-1*H*-pyrano[3,4-*c*]pyridin-3,4-diol (2i):[4] White solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (3H, t, *J* = 7.6 Hz), 1.75 (2H, q, *J* = 7.6 Hz), 3.89 (3H, s), 4.55 (1H, d, *J* = 16.4 Hz), 4.72 (1H, d, *J* = 16.4 Hz), 5.09 (2H, s), 7.07 (1H, d, *J* = 5.4 Hz), 8.00 (1H, d, *J* = 5.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.6, 31.6, 53.5, 58.1, 70.7, 93.4, 114.6, 116.1, 144.2, 148.7, 158.5.

Oxidation of diol 2i for determination of enantiomeric excess (Table 2, entry 3).[13] Next, the obtained diol **2i**, $NaHCO_3$ (26.0 mg, 0.31 mmol), KBr (28.6 mg, 0.24 mmol), and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 12.5 mg, 0.08 mmol) were combined in CH_2Cl_2–H_2O (12/1, 13 mL) in a 50 mL round bottom flask and cooled to 0 ºC. To the resulting suspension, NaOCl (4.6 mL, approximately 10wt%) was slowly added over 30 min. After stirring for 1 h, tlc (hexane/EtOAc = 1/1) indicated the complete conversion of the starting material. After adding $NaHSO_3$, the mixture was diluted with H_2O. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by chromatography on silica gel (hexane/EtOAc = 1/1) to afford (*S*)-4-ethyl-4-hydroxy-8-methoxy-1*H*-pyrano[3,4-*c*]pyridin-3(4*H*)-one (**3**) as a colorless oil (338 mg, 1.51 mmol, 84% yield).



(*S*)-4-Ethyl-4-hydroxy-8-methoxy-1*H*-pyrano[3,4-*c*]pyridin-3(4*H*)-one (3):[4] Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (3H, t, *J* = 7.4 Hz), 1.71 (2H, m), 3.89 (3H, s), 5.12 (1H, d, *J* = 15.9 Hz), 5.45 (1H, d, *J*

= 15.9 Hz), 7.06 (1H, d, *J* = 5.1 Hz), 8.09 (1H, d, *J* = 5.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.4, 31.5, 53.6, 65.4, 72.7, 111.2, 112.9, 146.9, 148.0, 158.5, 174.0; Enantiomeric excess was determined to be 85% by chiral HPLC analysis (DAICEL CHIRALCEL OD-H, hexane/EtOH = 98/2, flow rate = 0.5 mL/min, UV = 276 nm, 26 ºC); t_R(*S*)= **29.2 min**, t_R(*R*) = 30.4 min.

One mol Scale asymmetric dihydroxylation of olefin 1 (Fig. 4). PI Os **C** (66.3 g, 50 mmol), $(DHQD)_2PYR$ (44.1 g, 50 mmol), $K_3Fe(CN)_6$ (988 g, 3 mol), K_2CO_3 (415 g, 3 mol), and methanesulfonamide (95.1 g, 1 mol) were combined in *t*-BuOH–H_2O (1/1, 9.5 L) in a 10 L round bottom flask. After stirring at 600 rpm for 10 min, a *t*-BuOH–H_2O (1/1, 500 mL) solution of olefin **1i** (190 g, 1 mol) was added, and the mixture was further stirred at 600 rpm at ambient temperature (21~29 ºC). After 16 h, tlc (hexane/EtOAc = 1/1) indicated the complete conversion of the starting material. $Na_2S_2O_3$ (316 g, 2 mol) and *i*-PrOH (2 L) was added, and the mixture was stirred for 10 min. PI Os **C** was separated by filtration, washed with *i*-PrOH and H_2O subsequently and dried under reduced pressure. PI Os **C** was recovered (64.1 g, 97% recovery). The organic and aqueous filtrates were analyzed by XRF analysis to determine the leaching of osmium from the catalyst (Table S2). To determine the *ee* of the product, a part of the organic phase was treated with catalytic amounts of TEMPO and NaOCl according to the procedure described above, and 86% *ee* was obtained. Next, the whole filtrates were combined and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude material (276 g). The crude material was dissolved in a CH_2Cl_2–MeOH mixture, and to this solution, hexane was added for precipitation of diol **2i**. The resulting solid was collected by filtration and washed with a hexane–CH_2Cl_2 (4/1) mixture several times and dried under reduced pressure to afford the 1st crop as a white solid (171 g, 98% purity, 747 mmol, 75% yield). The filtrate was concentrated *in vacuo* and precipitation was conducted again to afford the 2nd crop as a light orange solid (36.6 g, 72% purity, 117 mmol, 12% yield). The filtrate was concentrated *in vacuo* again and the resulting residue was purified by chromatography on silica gel (400 g) with EtOAc (2 L) as a eluant to afford diol **2i** as a white solid (26.7 g, 91% purity, 107 mmol, 11% yield). The further elution with MeOH (3 L) afforded $(DHQD)_2PYR$ as a light orange solid (42.5 g, 48.2 mmol, 97% recovery). It was confirmed that the

impurity in the diol **2i** was methanesulfonamide and the chiral ligand was separated completely from **2i**.

Table S2. XRF analysis of filtrates

Sample	Volume (L)	Ammount of Os (ppm)	Leaching of Os (%)
Organic 1	5	6.07	0.32
Organic 2	3.5	4.94	0.18
Aqueous 1	5	10.4	0.55
Aqueous 2	1.25	8.93	0.12

Acute toxicity assay.

All experiments were conducted according to the Guide for Care and Use of Laboratory Animals of The University of Tokyo. Male ICR mice (8-14 weeks; SLC, Shizuoka, Japan) were bred and housed in group cages in the animal room of our laboratory. Mice were maintained on a 12:12 h inverted cycle with lights on from 7 a.m. to 7 p.m., and had access to food and water ad libitum. OsO_2 and PI Os **C** were suspended in saline including 0.5% Tween 80. To analyze the deposited osmium, the esophagus, stomach, ileum, liver, heart, lung and spleen were excised after OsO_4–induced death or euthanasia, which was induced by cervical dislocation following diethyl ether anesthesia. The organs were homogenized in phosphate buffered saline including 0.1% Triton X-100. Quantitative analysis of osmium was conducted by XRF analysis with standard curve. Results were shown in Table S3.

Table S3. XRF analysis of deposited osmium in organs

Organ	OsO_4 (300 mg/kg)	OsO_2 (300 mg/kg)	PI Os **C** (300 mg/kg)	PI Os **C** (3000 mg/kg)
Esophagus	33.7 ppm	N.D.[a]	N.D.	N.D.
Stomach	780.7 ppm	N.D.	N.D.	N.D.
Ileum	N.D.	N.D.	N.D.	N.D.
Liver	N.D.	N.D.	N.D.	N.D.
Hart	N.D.	N.D.	N.D.	N.D.

Lung	17.4 ppm	N.D.	N.D.	N.D.
Spleen	N.D.	N.D.	N.D.	N.D.

[a] N.D. = <2.3 ppm

Treatment of OsO_4 with MeOH. A 30 mL round bottom flask was charged with OsO_4 (1.04 g, 4.08 mmol) and MeOH (10 mL). After stirring at room temperature for 90 h, all volatile materials were removed under reduced pressure to afford a black powder (1.17 g).

Measurements and analyses of Os L_3-edge X-ray absorption fine structure.

X-ray absorption experiments were carried out on the beam line 9C at Photon Factory, Institute of Materials Structure Science, High Energy Accelerator Research Organization (KEK-PF), Tsukuba Japan, with a ring energy of 2.5 GeV and stored current of ca. 450 mA. X-ray absorption spectra were recorded in a transmission mode at room temperature with a Si (111) double crystal monochromator. The intensities of the incident and transmitted X-ray were measured with 17-cm ion chamber with a flowing gas mixture of N_2 (85%) and Ar (15%) and a 31-cm ion chamber with a Ar gas flow, respectively. Energy calibration was carried out using K-edge of a Cu foil. The sample was sealed with a polyethylene film. Normalization of XANES and data reduction on EXAFS was carried out as described elsewhere[14].

The non-linear curve-fitting analysis was performed for the Fourier-filtered EXAFS. For Fourier-filtering, a set of the peaks in a Fourier-transforms of the EXAFS spectra was isolated with a Hanning window in the region of ca. 0.8–2.2 Å (corresponding to the first shells around the target Os atom), and was inversely Fourier transformed. The curve-fitting analysis was carried out using the following equation (1).

$$k\chi(k) = \sum A_j(k) \times N_j/r_j^2 \times \exp(-2\Delta\sigma_j^2 k^2) \sin(2kr_j + \phi_j(k)) \qquad (1)$$

In this equation, N_j means the coordination number of scattering atoms at distance r_j, and $\Delta\sigma_j^2$ means the difference between the Debye-Waller factors of an interested sample and a reference sample. The backscattering amplitude $A_j(k)$ and the phase shift $\phi_j(k)$ for the Os–O shell were extracted from the EXAFS spectrum of an OsO_4 solid. These parameters were verified to be available for the EXAFS simulation through the analysis for a reference sample $K_2OsO_4 \cdot 2H_2O$ as shown in Table S4.

Table S4. Results of curve-fitting analyses and crystallographic data of $K_2OsO_4•2H_2O$

	Curve-fitting Results		Crystallographic Data	
Shell	Coordination Number	Interatomic Distance (Å)	Coordination Number	Interatomic Distance (Å)
Os-O	2.0	1.75	2.0	1.75
Os-O	4.0	2.00	4.0	1.99

Fig. S1 shows Os L_3-edge XANES spectra of OsO_4, OsO_2, PI Os **C**, a black precipitate from a methanol solution of OsO_4, and $K_2OsO_4•2H_2O$. Each spectrum was normalized by the height of the edge jump around 10.94 keV after removal of the contribution from the absorptions by other shells than the Os L_3-shell. All these samples show an intense peak (white line) around 10.873–10.877 keV. For the XANES spectrum of the Os catalyst (Fig. S1c), the peak position of white line is not close to those for OsO_4 nor K_2OsO_4, which stand for Os^{8+} and Os^{6+} (Fig. S1a and S1e), but identical to that for OsO_2, which stands for Os^{4+} (Fig. S1b). This means that the oxidation state was reduced from Os^{8+} in OsO_4 as the starting material to Os^{4+} in the catalyst sample during the catalyst preparation. It is noted that the black precipitate obtained from the methanol solution of OsO_4 (Fig. S1d) shows the same peak position as that of the Os catalyst, suggesting that the Os species in the precipitate sample would be reduced by methanol. Thus, the Os species in the Os catalyst would be also reduced by the methanol during the catalyst preparation.

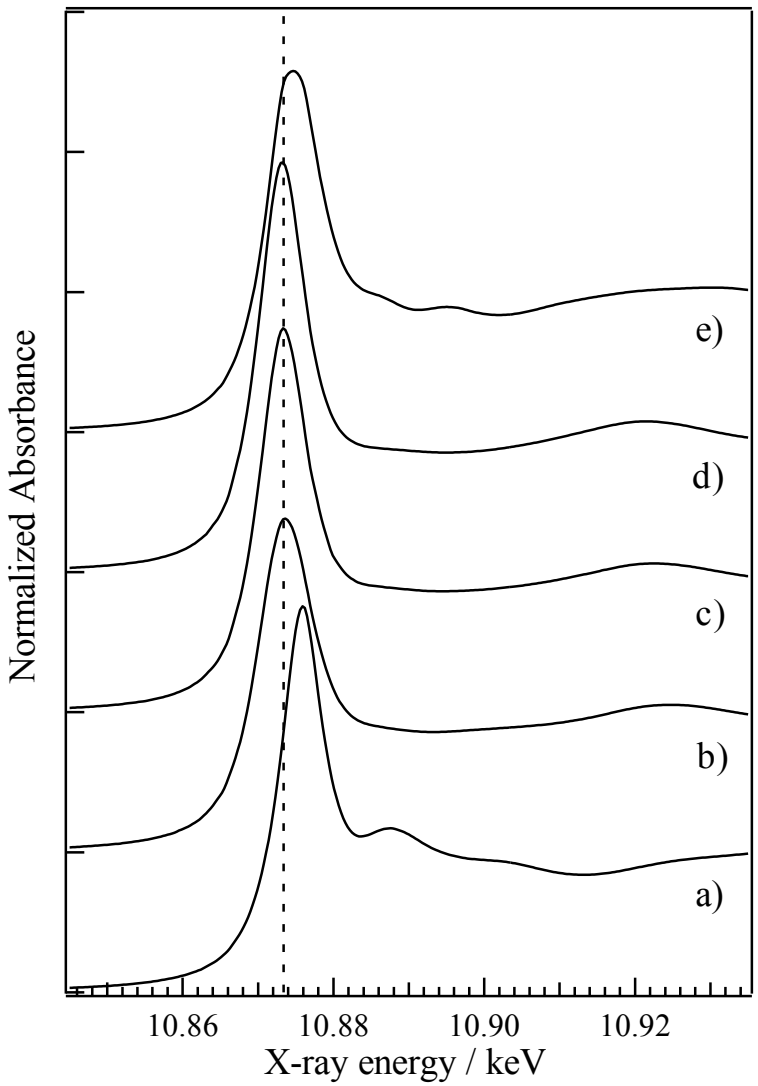


Fig. S1. Os L_3-edge XANES spectra of PI Os and reference compounds. (a) OsO_4, (b) OsO_2, (c) PI Os **C**, (d) a black precipitate from a methanol solution of OsO_4 and (e) $K_2OsO_4 \cdot 2H_2O$.

Fig. S2 shows k^3-weighted Os L_3-edge EXAFS spectra of OsO_4, OsO_2, PI Os **C** and the black precipitate mentioned above. The EXAFS spectrum of the Os catalyst has a characteristic pattern, that is, the amplitude around 4–6 $Å^{-1}$ in k space is intense, which is similar to the EXAFS spectrum of OsO_2 rather than that of OsO_4. The difference in the local structures around the Os atoms of these samples became visually clearer when a Fourier transform was performed on the EXAFS spectra in the 3–14.5 $Å^{-1}$ region as shown in Fig. S3. The intense and sharp peak was observed around 1–2 Å, which is attributed to the first neighboring oxygen atoms (Os–O shells). The

position and the amplitude of this peak in the catalyst, the black precipitate and OsO_2 were similar to each other, which strongly indicate the similarity of the local structure in these samples.

To clarify the local structure around the Os atoms in the Os catalyst, we performed nonlinear curve-fitting analyses of the Fourier-filtered EXAFS. The results are summarized in Table S5. The coordination numbers and interatomic distances for the Os–O bonds in the catalyst were estimated as 2.0 and 1.86 Å for the short Os–O bond, and 4.0 and 2.03 Å for the long Os–O bond, respectively, which consisted with the values for the OsO_2 reference sample (2.0 and 1.85 Å, and 4.0 and 2.02 Å), respectively. These results demonstrate that the Os species in the catalyst would have similar local structure to that in OsO_2. The curve-fitting analysis also indicates that the local structure of the black precipitate is fundamentally the same as that of the catalyst. Therefore, it can be proposed that the starting material OsO_4 was reduced to OsO_2 with methanol during the encapsulation in polymer backbone.

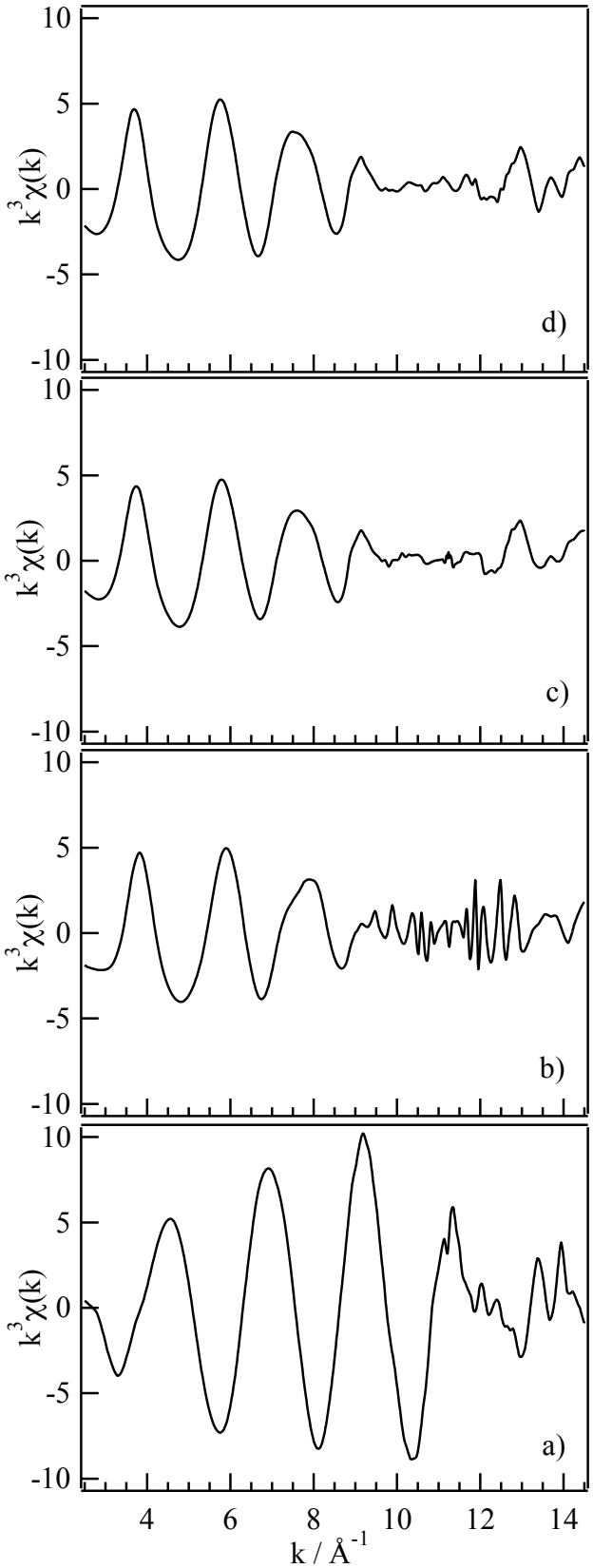


Fig. S2. k^3-weighted Os L_3-edge EXAFS spectra of PI Os catalyst and Os oxide samples, (a) OsO_4, (b) OsO_2, (c) PI Os **C**, and (d) a black precipitate from a methanol solution of OsO_4.

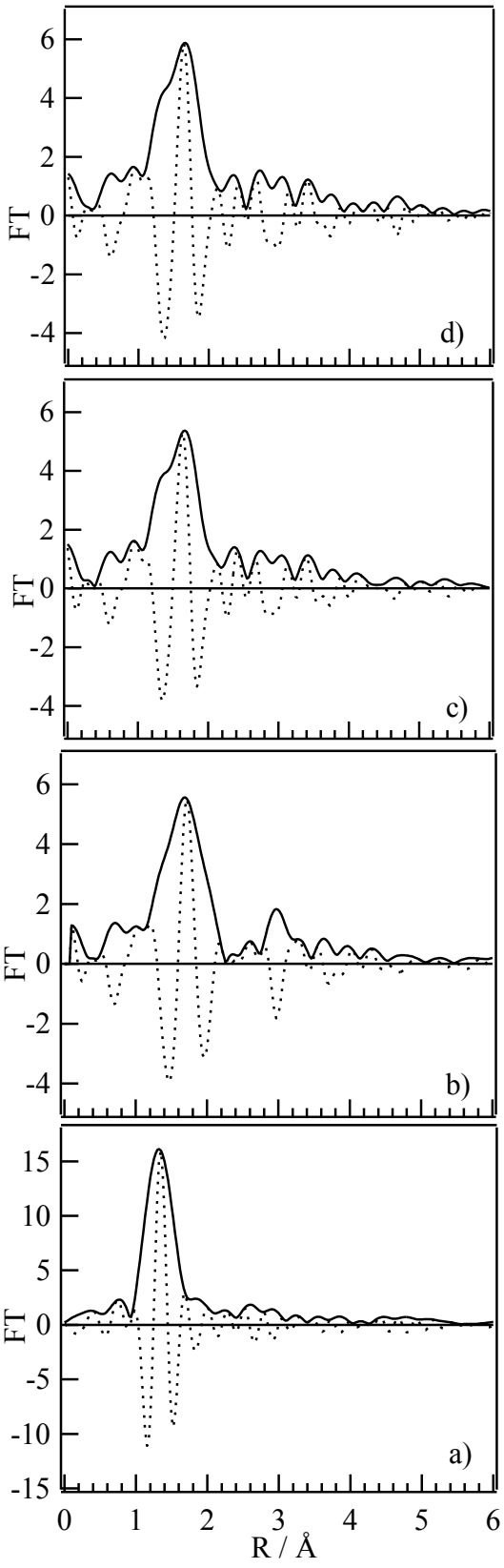


Fig. S3. Fourier-transforms of k^3-weighted Os L_3-edge EXAFS spectra of the Os catalyst and Os oxide samples. See the caption of Fig. S2 as for (a)–(d).

Table S5. Results of curve-fitting analyses

Sample	Shell	Coordination Number	Interatomic Distance (Å)	$\Delta\sigma^2$
OsO_4	Os-O (C)	4.0	1.70	0
OsO_2	Os-O (C)	2.0	1.85	0.00089
	Os-O (C)	4.0	2.02	0.00316
PI Os **C**	Os-O (C)	2.0	1.86	0.00021
	Os-O (C)	4.0	2.03	0.00205
Black Precipitate	Os-O (C)	2.0	1.87	–0.00134
	Os-O (C)	4.0	2.03	0.00069

$\Delta\sigma^2$: The difference of Debye-Waller factor from that for OsO_4. The errors in coordination number and interatomic distance are ±20% and ±0.01 Å.

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