Supporting Information

Syn-Selective Catalytic Asymmetric Nitro-Mannich Reactions Using a Heterobimetallic Cu-Sm-Schiff Base Complex

Shinya Handa, Vijay Gnanadesikan, Shigeki Matsunaga* and Masakatsu Shibasaki*

Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113-0033, Japan, phone: +81-3-5841-4830, fax: +81-3-5684-5206, E-mail: mshibasa@mol.f.u-tokyo.ac.jp; smatsuna@mol.f.u-tokyo.ac.jp

Experimental Section

General:

Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on 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 in the scale relative to CHCl_3 (7.26 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to CHCl_3 (77.0 ppm) as an internal reference. Column chromatography was performed with silica gel Merck 60 (230-400 mesh ASTM). Optical rotations were measured on a JASCO P-1010 polarimeter. FAB mass spectra were measured on JMS-MS 700V. ESI mass spectra were measured on Waters micromass ZQ. The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-2080 plus; detector, UV-2075 plus, measured at 254 nm; column, DAICEL CHIRALPAK AD-H; mobile phase, hexane-2-propanol. Reactions were carried out in dry solvents under argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. $\text{Sm}(\text{O}-i\text{Pr})_3$ was purchased from KOJUNDO CHEMICAL LAB CO., LTD (Fax: +81-492-84-1351, sales@kojundo.co.jp), which was dissolved into THF (0.2 M solution) before use. Aromatic imines **4a** to **4g** were prepared following the literature procedure (Lit. (a) Kanazawa, A. M.; Denis, J.; Greene, A. E. *J. Org. Chem.* **1994**, 59, 1238. See, also (b) Love, B. E.; Raje, P. S.; Williams, T. C., II. *Synlett* **1994**, 493.) and aliphatic imine **4h** was freshly prepared following the literature procedure (Lit. Song, J.; Wang, Y.; Deng, L. *J. Am. Chem. Soc.* **2006**, 128, 2778). Other reagents were purified by the usual methods.

Preparation of a Cu/Schiff Base **3** Pre-catalyst:

To a solution of (*R,R*)-Schiff base ligand **3** (709 mg, 2.0 mmol) in EtOH (20 mL), Cu(OAc)₂ (399 mg, 2.0 mmol) in water (5 mL) was added and stirred for 1 h under reflux. After cooling down to room temperature, a Cu/Schiff base **3** complex was collected by filtration of the reaction mixture suspension. Then, the solid was washed with EtOH (x 3), and dried under reduced pressure to afford the Cu/Schiff base **3** pre-catalyst (752 mg, 90%) as a purple solid. The complex was used for the asymmetric reaction without further purification, and can be stored under air at room temperature.

General Procedure for Catalytic Asymmetric Nitro-Mannich Reaction Using a Cu/Sm/Schiff base **3** = 1:1:1 with 4-*tert*-Butylphenol System:

To a suspension of Cu/Schiff base **3** pre-catalyst (8.3 mg, 0.02 mmol) in THF (300 μ L) was added Sm(O-*i*Pr)₃ (100 μ L, 0.02 mmol, 0.2 M in THF), and the mixture was stirred at 80 $^{\circ}$ C for 1 h to give a Cu/Sm/**3** complex. After cooling down the mixture to room temperature, 4-*tert*-butylphenol (100 μ L, 0.02 mmol, 0.2 M in THF) was added, and the mixture was stirred for 15 min at room temperature. The catalyst mixture was cooled down to -40 $^{\circ}$ C (or at -50 $^{\circ}$ C), and nitroethane **5a** (140 μ L, 2.0 mmol) was added. After stirring for 1 h at -40 $^{\circ}$ C (or at -50 $^{\circ}$ C), imine **4** (0.2 mmol in 400 μ L THF) was added. The stirring was continued for indicated time at indicated temperature (at -40 or 50 $^{\circ}$ C) in Table 2, and the reaction mixture was diluted with diethyl ether (3 mL). The resulting mixture suspension was filtered through a pad of Celite to remove the catalyst, and the filtrate solution was evaporated under reduced pressure. The resulting residue was analyzed by ¹H NMR to determine diastereomeric ratio, and was purified by silica gel flash column chromatography (hexane/diethyl ether = 5/1) to afford *syn*-**2**. In the crude ¹H NMR analysis, minor *anti*-isomer was not detected (*syn/anti* = >20/1).

General Procedure with Reduced Catalyst Loading (2.5 mol %):

To a suspension of Cu/Schiff base **3** pre-catalyst (8.3 mg, 0.02 mmol) in THF (300 μ L) was added Sm(O-*i*Pr)₃ (100 μ L, 0.02 mmol, 0.2 M in THF), and the mixture was stirred at 80 $^{\circ}$ C for 1 h to give a Cu/Sm/**3** complex. After cooling down the mixture to room temperature, 4-*tert*-butylphenol (200 μ L, 0.04 mmol, 0.2 M in THF) was added, and the mixture was stirred for 15 min at room temperature. After addition of THF (2.4 mL) at room temperature, the catalyst

mixture was cooled down to $-40\text{ }^{\circ}\text{C}$, and nitroethane **5a** (560 μL , 8.0 mmol) was added. After stirring for 1 h at $-40\text{ }^{\circ}\text{C}$, imine **4a** (0.8 mmol) and THF (400 μL) were added slowly. The stirring was continued for 72 h at $-40\text{ }^{\circ}\text{C}$, and the reaction mixture was diluted with diethyl ether (6 mL). The resulting mixture suspension was filtered through a pad of Celite to remove the catalyst, and the filtrate solution was evaporated under reduced pressure. The resulting residue was analyzed by ^1H NMR to determine diastereomeric ratio, and was purified by silica gel flash column chromatography (hexane/diethyl ether = 5/1) to afford *syn*-**2aa** (222 mg, 0.791 mmol, 99% and 97% ee). In the crude ^1H NMR analysis, minor *anti*-isomer was not detected (*syn/anti* = >20/1).

Determination of Relative and Absolute Configurations:

Relative configurations of β -nitroamines **2aa**, **2ba**, **2ca**, **2da**, **2ea**, **2fa**, **2ga**, and **2ab** from aryl and heteroaryl Boc-imines were determined as follows. *anti*-Adducts **1** from nitroethane **5a** and imines **4a**, **4b**, **4c**, **4d**, **4e**, **4f**, and **4g**, and nitropropane **5b** and imine **4a** are known compounds [Lit. (a) Nugent, B. M.; Yoder, R. A.; Johnston, J. N. *J. Am. Chem. Soc.* **2004**, *126*, 3418 (b) Yoon, T. P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 466. (c) Xu, X.; Furukawa, T.; Okino, T.; Miyabe, H.; Takemoto, Y. *Chem. Eur. J.* **2006**, *12*, 466.]. The authentic samples of both *syn*- and *anti*-diastereomers (racemates) were prepared with TBAF as a base (See, scheme below). The conditions below afforded mixtures of *syn*-**2** and *anti*-**1** with low diastereoselectivity. By comparing ^1H NMR charts of both diastereomers with those obtained in the present asymmetric reactions and with those of reported *anti*-**1** in the literature, the relative configurations of products (**2aa**, **2ba**, **2ca**, **2da**, **2ea**, **2fa**, **2ga**, and **2ab**) obtained with the Cu/Sm/**3** complex were determined to be *syn*.

[synthesis of authentic *syn*- and *anti*-isomers]

Absolute configurations of **2aa**, **2ca**, **2fa**, **2ga**, and **2ha**, were determined by reduction of nitro group, followed by condensation of 1,2-diamine with either (+)- or (–)-*O*-methyl-mandelic acid (See, scheme below). By ^1H NMR analysis, absolute configurations of **2aa**, **2ca**, **2fa**, **2ga**, and **2ha** were determined to be 2*R* [Lit. Trost, B. M.; Bunt, R. C.; Pulley, S. R. *J. Org. Chem.* **1994**, *59*, 4202.]. Absolute configurations of **2ba** and **2ea** were tentatively assigned by analogy.

Relative configuration of nitro-Mannich adduct **2ha** from aliphatic imine **4h** was determined to be *syn* by determining absolute configurations of **2ha** to be (*1R,2R*) as shown in the scheme below. Absolute configurations of both stereocenters were determined by Trost's method using (+)- or (-)-*O*-methyl-mandelic acid. [Lit. Trost, B. M.; Bunt, R. C.; Pulley, S. R. *J. Org. Chem.* **1994**, *59*, 4202.].

Spectra Data of New Compounds:

tert-Butyl (*1R,2R*)-2-nitro-1-phenylpropylcarbamate (**2aa**)

Colorless powder; IR (KBr) ν 3375, 2979, 1687, 1546, 1510, 1171 cm⁻¹; ¹H NMR (CDCl₃) δ 1.42 (s, 9H), 1.54 (brs, 3H), 4.95 (brs, 1H), 5.12 (brs, 1H), 5.63 (brs, 1H), 7.24-7.37 (m, 5H); ¹³C NMR (CDCl₃) δ 17.0, 28.2, 57.1, 80.3, 86.7, 126.4, 128.4, 129.0, 137.4, 155.1; ESI-MS m/z 303 [M+Na]⁺; HRMS calcd. for C₁₄H₂₀N₂O₄Na [M+Na]⁺:413.0472, found 413.0476; [α]_D²¹ -29.6 (*c* 0.81, CHCl₃); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_R 14.6 min (major) and 18.0 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(2-naphthyl)propylcarbamate (2ba)**

Colorless powder; IR (KBr) ν 3377, 2981, 1692, 1547, 1509, 1169 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.43 (s, 9H), 1.58 (brs, 3H), 5.06 (brs, 1H), 5.29 (brs, 1H), 5.73 (brs, 1H), 7.35 (dd, $J = 8.6, 1.9$ Hz, 1H), 7.49-7.51 (m, 2H), 7.73 (s, 1H), 7.82-7.85 (m, 3H); ^{13}C NMR (CDCl_3) δ 17.1, 28.2, 57.4, 80.5,

86.6, 123.8, 125.9, 126.5, 126.6, 127.7, 128.0, 129.0, 133.1, 133.2, 134.7, 155.1; ESI-MS m/z 353 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_4$ $[\text{M}+\text{Cs}]^+$:463.0628, found 463.0627; $[\alpha]_{\text{D}}^{27} -40.8$ (c 1.19, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 19.5 min (major) and 22.8 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(4-methylphenyl)propylcarbamate (2ca)**

Colorless powder; IR (KBr) ν 3371, 2989, 1684, 1547, 1524, 1168 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.41 (s, 9H), 1.52 (brs, 3H), 2.32 (s, 3H), 4.93 (brs, 1H), 5.08 (brs, 1H), 5.58 (brs, 1H), 7.13 (d, $J = 8.2$ Hz, 2H), 7.16 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 16.9, 21.0, 28.2, 56.9, 80.3, 86.8, 126.3, 129.6, 134.4, 138.2, 155.1; ESI-MS m/z 317 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_4$ $[\text{M}+\text{Cs}]^+$:427.0628, found 427.0630; $[\alpha]_{\text{D}}^{21} -42.6$ (c 1.36, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 12.1 min (major) and 14.4 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(3-methylphenyl)propylcarbamate (2da)**

Colorless solid; IR (neat) ν 3335, 2979, 1699, 1555, 1496, 1365, 1166 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.46 (s, 9H), 1.53 (brs, 3H), 2.34 (s, 3H), 4.93 (brs, 1H), 5.07 (brs, 1H), 5.57 (brs, 1H), 7.03 (d, $J = 7.6$ Hz, 1H), 7.04 (s, 1H), 7.11 (d, $J = 7.6$ Hz, 1H), 7.24 (dd, $J = 7.6, 7.6$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 17.0, 21.9, 56.9, 80.4, 86.8, 123.4, 127.2, 128.9, 129.2, 137.3, 138.8, 155.0;

ESI-MS m/z 317 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_4$ $[\text{M}+\text{Cs}]^+$:427.0628, found 427.0629; $[\alpha]_{\text{D}}^{22} -47.7$ (c 0.64, CHCl_3), (96% ee); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol=90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 13.2 min (major) and 17.6 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(4-methoxyphenyl)propylcarbamate (2ea)**

Colorless powder; IR (KBr) ν 3367, 2980, 1686, 1551, 1515, 1255, 1173 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.41 (s, 9H), 1.51 (brs, 3H), 3.78 (s, 3H), 4.90 (brs, 1H), 5.05 (brs, 1H), 5.53 (brs, 1H), 6.87 (d, $J = 8.7$ Hz, 2H), 7.16 (d,

$J = 8.7$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 16.9, 28.2, 55.2, 56.7, 80.3, 86.8, 114.3, 127.6, 129.4, 155.0, 159.5; ESI-MS m/z 333 $[\text{M}+\text{Na}]^+$; HRMS calcd. For $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_5\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 443.0578, found 443.0577; $[\alpha]_{\text{D}}^{21} -44.2$ (c 0.88, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 18.1 min (major) and 22.9 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(4-chlorophenyl)propylcarbamate (2fa)**

Colorless powder; IR (KBr) ν 3429, 2972, 1704, 1554, 1507, 1172 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.42 (s, 9H), 1.56 (brs, 3H), 4.93 (brs, 1H), 5.08 (brs, 1H), 5.64 (brd, $J = 8.0$ Hz, 1H), 7.19 (d, $J = 8.6$ Hz, 2H), 7.33 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 17.0, 28.2, 56.5, 80.6, 86.4, 127.8, 129.2,

134.3, 136.0, 155.1; ESI-MS m/z 337 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_4\text{ClCs}$ $[\text{M}+\text{Cs}]^+$: 447.0082, found 447.0081; $[\alpha]_{\text{D}}^{21} -28.4$ (c 1.08, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 14.6 min (minor) and 15.6 min (major).

***tert*-Butyl (1*S*,2*R*)-2-nitro-1-(2-furyl)propylcarbamate (2ga)**

Colorless powder; IR (KBr) ν 3356, 2984, 1685, 1552, 1510, 1161 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.45 (s, 9H), 1.55 (brd, $J = 6.5$ Hz, 3H), 5.05 (brs, 1H), 5.25 (brs, 1H), 5.41 (brs, 1H), 6.27 (d, $J = 3.2$ Hz, 1H), 7.33 (dd, $J = 1.4, 3.2$ Hz, 1H), 7.36 (d, $J = 1.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 16.2, 28.2, 51.5, 80.6, 84.3, 108.0, 110.6,

142.7, 149.9, 155.0; ESI-MS m/z 293 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_5\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 403.0265, found 403.0271; $[\alpha]_{\text{D}}^{17} -40.3$ (c 0.89, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 9.9 min (major) and 12.5 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(2-phenylethyl)propylcarbamate (2ha)**

Colorless powder; IR (KBr) ν 3364, 2980, 1687, 1550, 1528, 1173 cm^{-1} ;

^1H NMR (CDCl_3) δ 1.48 (s, 9H), 1.56 (d, $J = 6.7$ Hz, 3H), 1.74-1.87 (m, 2H), 2.64-2.77 (m, 2H), 3.95 (m, 1H), 4.73 (td, $J = 2.2, 6.7$ Hz, 1H), 4.98 (d, $J = 10.1$ Hz, 1H), 7.16-7.30 (m, 5H); ^{13}C NMR (CDCl_3) δ 16.4, 28.3, 32.3, 34.1, 52.3, 80.0,

85.7, 126.2, 128.4, 128.5, 140.6, 155.7; ESI-MS m/z 331 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_4\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 441.0785, found 441.0787; $[\alpha]_{\text{D}}^{26} +17.9$ (c 1.10, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 8.6 min (major) and 10.5 min (minor).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-phenylbutylcarbamate (2ab)**

Colorless powder; IR (KBr) ν 3336, 2975, 1674, 1553, 1528, 1176 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.98 (dd, $J = 7.3, 7.3$ Hz, 3H), 1.44 (s, 9H), 1.78 (brs, 1H), 2.08 (brs, 1H), 4.74 (m, 1H), 5.16 (brs, 1H), 5.71 (brs, 1H), 7.23-7.36 (m, 5H); ^{13}C NMR (CDCl_3) δ 10.3, 24.8, 28.2, 55.8, 80.3, 93.7, 126.3, 128.3, 129.0, 137.6, 155.0; ESI-MS m/z 317 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_4\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 427.0628, found 427.0630; $[\alpha]_{\text{D}}^{26} -20.7$ (c 1.27, CHCl_3); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol = 90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 13.6 min (minor) and 16.4 min (major).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(4-methylphenyl)butylcarbamate (2cb)**

Colorless powder; IR (KBr) ν 3377, 3009, 1681, 1550, 1512, 1369, 1292, 1171 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.98 (dd, $J = 7.3, 7.3$ Hz, 3H), 1.42 (s, 9H), 1.78 (brs, 1H), 2.07 (brs, 1H), 2.32 (s, 3H), 4.71 (brs, 1H), 5.11 (brs, 1H), 5.63 (brs, 1H), 7.12 (d, $J = 8.0$ Hz, 2H), 7.16 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 10.3, 21.1, 24.8, 28.2, 55.6, 80.2, 93.9, 126.1, 129.7, 134.6, 138.1, 155.0; ESI-MS m/z 331 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_4\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 441.0785, found 441.0794; $[\alpha]_{\text{D}}^{22} -43.3$ (c 0.73, CHCl_3), (95% ee); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol=90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 11.2 min (minor) and 14.3 min (major).

***tert*-Butyl (1*R*,2*R*)-2-nitro-1-(4-chlorophenyl)propylcarbamate (2eb)**

Colorless powder; IR (KBr) ν 3372, 2979, 1689, 1549, 1515, 1253, 1171 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.97 (dd, $J = 7.4, 7.4$ Hz, 3H), 1.41 (s, 9H), 1.76 (brs, 1H), 2.06 (brs, 1H), 3.79 (s, 3H), 4.69 (brs, 1H), 5.29 (brs, 1H), 5.60 (brs, 1H), 6.87 (d, $J = 8.7$ Hz, 2H), 7.15 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 10.3, 24.8, 28.2, 55.3, 80.2, 93.9, 114.4, 127.4, 129.7, 155.0, 159.5; ESI-MS m/z 347 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_5\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 457.0734, found 457.0735; $[\alpha]_{\text{D}}^{22} -38.6$ (c 1.14, CHCl_3), (91% ee); HPLC (DAICEL CHIRALPAK AD-H, hexane/2-propanol=90/10, flow 1.0 mL/min, detection at 254 nm) t_{R} 18.2 min (minor) and 22.4 min (major).

Transformation of Nitro-Mannich Product **2aa** to *syn*-1,2-Diamine **7**:

To a solution of the β -nitroamine **2aa** (112 mg, 0.40 mmol) in MeOH (3.0 mL), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (95 mg, 0.40 mmol) and NaBH_4 (75.7 mg, 2.0 mmol) was added at 0 °C. After stirring for 15 min at 0 °C, the reaction mixture was quenched with *sat. aq.* NH_4Cl and extracted with CH_2Cl_2 (x 3). The combined organic layers were washed with brine, dried over MgSO_4 . After evaporation under reduced pressure, the residue was purified by silica gel flash column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 5/1$) to give 1,2-diamine **6** as colorless solid (100 mg, 99%).

A part of 1,2-diamine **6** was further converted into differently protected *syn*-1,2-diamines **7**. To a solution of 1,2-diamine **6** (38.0 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL), Ac_2O (28 μL , 0.30 mmol) and Et_3N (42 μL , 0.30 mmol) were added at room temperature. After stirring for 30 min at room temperature, the reaction mixture was quenched with *sat. aq.* NH_4Cl and extracted with AcOEt (x 3). The combined organic layers were washed with brine and dried over MgSO_4 . After evaporation under reduced pressure, the residue was purified by silica gel flash column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 20/1$) to give acetylated product **7** as colorless powder (43.5 mg, 98% yield). Epimerized product was not detected by ^1H NMR analysis during the transformations from **2aa** to **7**; IR (KBr) ν 3361, 2980, 1687, 1651, 1524, 1173 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.95 (d, $J = 6.4$ Hz, 3H), 1.40 (s, 9H), 1.98 (s, 3H), 4.28 (m, 1H), 4.42 (dd, $J = 7.8, 10.0$ Hz, 1H), 5.31 (brd, $J = 7.8$ Hz, 1H), 6.32 (brd, $J = 7.8$ Hz, 1H), 7.27-7.35 (m, 5H); ^{13}C NMR (CDCl_3) δ 18.6, 23.4, 28.3, 50.8, 60.7, 79.7, 127.3, 128.0, 128.9, 139.6, 156.5, 170.4; ESI-MS m/z 315 $[\text{M}+\text{Na}]^+$; HRMS calcd. for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_3\text{Cs}$ $[\text{M}+\text{Cs}]^+$: 425.0836, found 425.0833; $[\alpha]_{\text{D}}^{21} -54.1$ (c 1.08, CHCl_3).

Optimizations of Nitro-Mannich Reaction:

1. Rare earth metal effects:

The results of rare earth metal screening are summarized in Table S1. The results indicated that ionic radius is important. The reaction proceeded with all rare earth metals examined; however rare earth metal affected both *syn*-selectivity and enantioselectivity. Sm(O-*i*Pr)₃ gave the best results (entry 3).

Table S1 Rare Earth Metal Effects

3

entry	Metal sources M ¹ M ²		yield (%)	dr (<i>syn</i> / <i>anti</i>)	% ee (<i>syn</i>)
1	Cu(OAc) ₂	La(O- <i>i</i> Pr) ₃	73	3/1	5
2	Cu(OAc) ₂	Pr(O- <i>i</i> Pr) ₃	82	1/1	9
3	Cu(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	96	>20/1	80
4	Cu(OAc) ₂	Eu(O- <i>i</i> Pr) ₃	93	>20/1	64
5	Cu(OAc) ₂	Dy(O- <i>i</i> Pr) ₃	89	7/1	48

2. Inner metal effects:

Effects of inner metals are summarized in Table S2. Neither Zn(OAc)₂, Mg(OAc)₂, nor Ni(OAc)₂ complex promoted the reaction. Rh(OAc)₂ promoted the reaction, but the *anti*-diastereomer was obtained in major and enantioselectivity of the product was poor.

Table S2 Inner Metal Effects

3

entry	Metal sources M ¹ M ²		yield (%)	dr (<i>syn</i> / <i>anti</i>)	% ee (<i>syn</i>)
1	Cu(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	96	>20/1	80
2	Zn(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	0	—	—
3	Mg(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	0	—	—
4	Ni(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	0	—	—
5	Rh(OAc) ₂	Sm(O- <i>i</i> Pr) ₃	90	1/3	1 (<i>anti</i>)

3. Cu/Sm/Schiff base 3 ratio effects:

Effects of Cu/Sm/Schiff base **3** ratio are summarized in Table S3. Neither Cu/Sm/Schiff base **3** = 1:0:1 nor Cu/Sm/Schiff base **3** = 0:1:1 was suitable for the present reaction (entries 2 and 3). Both

Cu and Sm were essential for good selectivity and reactivity (entry 1 vs entries 2-3). Cu/Sm/Schiff base **3** = 1:1:1 ratio was also crucial to obtain good enantio- and diastereoselectivity. When mixing Cu/Sm/Schiff base **3** in a different ratio (entry 4: 1:0.5:1, entry 5: 1:2:1), both *syn*-selectivity and enantioselectivity decreased significantly.

Table S3 Cu/Sm/Schiff Base **3** Ratio Effects

3

entry	ratio Cu/Sm/ 3	yield (%)	dr (<i>syn/anti</i>)	% ee (<i>syn</i>)
1	1:1:1	96	>20/1	80
2	1:0:1	0	—	—
3	0:1:1	14	2/1	29
4	1:0.5:1	14	16/1	3
5	1:2:1	90	7/1	3

4. Additive effects:

Additive effects of phenol derivatives are summarized in Table S4. 4-*tert*-Bu-phenol gave the best results (entry 5).

Table S4 Additive Effects

3

entry	additive	yield (%)	dr (<i>syn/anti</i>)	% ee (<i>syn</i>)
1	none	96	>20/1	80
2	phenol	81	>20/1	85
3	4-MeO-phenol	85	>20/1	82
4	4-NO ₂ -phenol	0	—	—
5	4- <i>t</i> -Bu-phenol	96	>20/1	94
6	2,6-di-Me-phenol	90	>20/1	89
7	2,6-di- <i>t</i> -Bu-phenol	91	>20/1	76

5. Effects of nitroalkane amount:

The amount of nitroalkane did not affect reactivity and enantioselectivity. As shown in Table S5, comparable results were obtained with 3, 5, 10, and 15 equiv of nitroethane **5a**.

Table S5 Effects of Nitroethane **5a** Amount

entry	EtNO ₂ (x equiv.)	yield (%)	dr (<i>syn/anti</i>)	% ee (<i>syn</i>)
1	3	90	>20/1	93
2	5	94	>20/1	91
3	10	96	>20/1	94
4	15	94	>20/1	93

6. Effects of 4-*t*-Bu-phenol additive amount:

The amount of 4-*t*-Bu-phenol additive affected enantioselectivity. As shown in Table S6, the best results were obtained when using 10 mol % of 4-*t*-Bu-phenol together with 10 mol % of Cu/Sm/ligand **3** or 5 mol % of Cu/Sm/ligand **3** (entries 3 and 7). 15 or 20 mol % of additive had negative effects on enantioselectivity (entries 4 and 5). 5 mol % of additive was also less effective (entries 2 and 6).

Table S6 Effects of 4-*t*-Bu-phenol Additive Amount

entry	Cu/Sm/ 3 (x mol %)	4- <i>t</i> -Bu-phenol (y mol %)	time (h)	yield (%)	dr (<i>syn/anti</i>)	% ee (<i>syn</i>)
1	10	0	23	96	>20/1	80
2	10	5	23	88	>20/1	86
3	10	10	23	96	>20/1	94
4	10	15	23	94	>20/1	92
5	10	20	23	87	>20/1	92
6	5	5	46	85	>20/1	92
7	5	10	44	92	>20/1	96

ESI-MS Analysis of Cu/Sm/Schiff base **3** = 1:1:1 Mixture:

To gain insight into the positive effects of 4-*tert*-Bu-phenol additive, we analyzed Cu/Sm/Schiff base **3** complex in the absence and in the presence of 4-*tert*-Bu-phenol additive by ESI-MS (Waters-ZQ4000). ESI-MS charts are summarized in Figures S1 and S2.

A: Cu/Sm/Schiff base **3** = 1:1:1 mixture without 4-*tert*-Bu-phenol additive:

sample preparation: To a suspension of Cu/Schiff base **3** pre-catalyst (8.3 mg, 0.02 mmol) in THF (300 μ L) was added Sm(O-*i*Pr)₃ (100 μ L, 0.02 mmol, 0.2 M in THF), and the mixture was stirred at 80 $^{\circ}$ C for 1 h to give a Cu/Sm/**3** complex. After cooling down the mixture to room temperature, the mixture was diluted with *i*PrOH (600 μ L) and CH₃CN (1.7 mL). The resulting solution was injected for analysis. ESI-MS chart is shown in Figure S1.

conditions: capillary 3.80 kV, cone 150 V, source temp 80 $^{\circ}$ C, desolvation temp 150 $^{\circ}$ C

Figure S1. ESI-MS of Cu/Sm/Schiff base **3** = 1:1:1 mixture without 4-*tert*-Bu-phenol additive.
S-12

B: Cu/Sm/Schiff base **3 = 1:1:1 mixture with 4-*tert*-Bu-phenol additive:**

sample preparation: To a suspension of Cu/Schiff base **3** pre-catalyst (8.3 mg, 0.02 mmol) in THF (300 μ L) was added Sm(O-*i*Pr)₃ (100 μ L, 0.02 mmol, 0.2 M in THF), and the mixture was stirred at 80 °C for 1 h to give a Cu/Sm/**3** complex. After cooling down the mixture to room temperature, 4-*tert*-butylphenol (500 μ L, 0.1 mmol, 0.2 M in THF) was added, and the mixture was stirred for 15 min at room temperature. The mixture was diluted with *i*PrOH (600 μ L) and CH₃CN (1.7 mL), and the resulting solution was injected for analysis. ESI-MS chart is shown in Figure S2.

conditions: capillary 3.80 kV, cone 150 V, source temp 80 °C, desolvation temp 150 °C

Figure S2. ESI-MS of Cu/Sm/Schiff base **3** = 1:1:1 mixture with 4-*tert*-Bu-phenol additive.

Discussion and speculative reaction mechanism:

In the present reaction, both $\text{Cu}(\text{OAc})_2$ and $\text{Sm}(\text{O-}i\text{Pr})_3$ were essential for good reactivity and selectivity. The 1:1 ratio of Cu(II) and Sm was also crucial (Table 1, maintext), and the addition of 4-*t*Bu-phenol had beneficial effects on enantioselectivity. Sterically hindered 2,6-(*t*-Bu)₂-phenol was not effective as an additive (Table 1, entry 17), suggesting that 4-*t*-Bu-phenol would work not as a simple proton source but as an achiral ligand.

In ESI-MS chart of Cu/Sm/Schiff base **3** = 1:1:1 mixture without 4-*tert*-Bu-phenol additive (Figure S1), peaks corresponding to a μ -oxo + OR Cu/Sm/Schiff base **3** trimer complex (OR = O-*i*Pr or OH) (m/z = 1710, $[\text{M-OR}]^+$) and other oligomers were observed. In Figure S1, a peak corresponding to a monomeric Cu/Sm/Schiff base **3** = 1:1:1 complex was not observed. On the other hand, in Figure S2 with 4-*tert*-Bu-phenol additive, a new peak corresponding to a monomeric Cu/Sm/Schiff base **3** = 1:1:1 complex (m/z = 565) was observed as a base peak, together with a peak of the trimer complex. Peaks of oligomers were negligible in Figure S2. The peak of m/z = 565 can be assigned to $[\text{M-OAr}]^+$ (M = Cu/Sm/Schiff base **3**/OAr = 1:1:1:1, Ar = 4-*tert*-Bu-C₆H₄). The peak of m/z = 1710 in Figure S2 can be assigned to a μ -oxo + OR Cu/Sm/Schiff base **3** trimer complex (OR = OAr, O-*i*Pr or OH). For each complex, several peaks were observed depending on Sm natural isotopes distribution pattern (¹⁴⁴Sm: 3.1%, ¹⁴⁷Sm: 15.0%, ¹⁴⁸Sm: 11.3%, ¹⁴⁹Sm: 13.8%, ¹⁵⁰Sm: 7.4%, ¹⁵²Sm: 26.7%, ¹⁵⁴Sm: 22.7%). On the basis of these ESI-MS analysis, as well as previous reports of related monomeric heterobimetallic Cu/rare earth metal/Schiff base complexes [Lit. Koner, R.; Lee, G.-H.; Wang, Y.; Wei, H.-H.; Mohanta, S. *Eur. J. Inorg. Chem.* **2005**, 1500], we assumed that a monomeric Cu/Sm/Schiff base **3**/4-*t*-Bu-phenol = 1:1:1:1 complex would be the active species. At the moment, we believe that the bimetallic Cu-Sm system, aligned suitably in dinucleating ligand **3**, would play a key role for high stereoselectivity. However, the possibility that the μ -oxo + OR Cu/Sm/Schiff base **3** trimer complex (OR = OAr, O-*i*Pr or OH) is the active species cannot be excluded at the current stage of studies. Further mechanistic studies are ongoing.

The postulated catalytic cycle and transition state model are shown in Figure S3. We speculate that the Cu/Sm/**3** complex works as a Lewis acid-Brønsted base bifunctional catalyst. The Brønsted basic Sm-phenoxide moiety would deprotonate the α -proton of nitroalkane **5** to generate a Sm-nitronate. Imine would interact with Cu(II). Addition of the nitronate to imine followed by protonation affords the product and regenerates the catalyst. TS1 is favorable to TS2 to avoid steric repulsion, thereby affording *syn*-**2** predominantly. Further mechanistic studies to clarify the precise role of each metal are ongoing.

Figure S3. Postulated catalytic cycle and transition state models.

DDR1121

Date : Wed Oct 25 17:40:53 2006

FileName : .LoadingFID.nmdata
 Comment : DDR1121
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMP0 32768 points
 FREQ0 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEAD0 10.0 usec
 INTVL 29.5 usec
 TIMES 256 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec
 13C
 OBNUC 125.65 MHz
 OBFRQ 127958.00 Hz
 OBSET 31
 RGAIN 1H
 IRNUC 500.00 MHz
 IRFRQ 162160.00 Hz
 IRSET 50.0 usec
 IRRPW 0
 IRRNS

SCANS 200 times

SLVNT CDCL3
 SPINNING 13 Hz
 TEMP 28.0 C

DDR1261

Date : Tue Nov 28 18:20:42 2006

FileName : LoadingFID.nmdata
 Comment : DDR1261
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMP0 32768 points
 FREQU 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEAD1 10.0 usec
 INTVL 29.5 usec
 TIMES 512 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec
 13C
 OBNUC 125.65 MHz
 OBFRQ 127958.00 Hz
 OBSET 31
 RGAIN 1H
 IRNUC 500.00 MHz
 IRFRQ 162150.00 Hz
 IPSET 50.0 usec
 IRRPW 0
 IRRNS 0
 SCANS 200 times
 SLVNT CDCl3
 SPINNING 10 Hz
 TEMP 28.4 C

DDR1206

Date : Thu Mar 8 02:11:42 2007

FileName : LoadingFID.nmdata
 Comment : DDR1398
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPO 32768 points
 FREQU 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEADT 15.1 usec
 INTVL 29.5 usec
 TIMES 512 times
 DUMMY 1 times
 PD 3.0000 sec
 ACGTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 5.25 usec
 13C 125.40 MHz
 OBFRQ 143041.00 Hz
 OBSET 29
 RGAIN 1H
 IRNUC 499.10 MHz
 IRFRQ 128250.00 Hz
 IRSET 65.0 usec
 IRRPW 0
 IRRNS
 SCANS 512 times
 SLVNT : CDCL3
 SPINNING 13 Hz
 TEMP 22.5 C

DDR1208

S-20

Date : Mon Oct 30 11:38:58 2006

FileName : LoadingFID.mdata
 Comment : DDR1208
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPO 32768 points
 FREQ 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 UADT 10.0 usec
 INVL 29.5 usec
 TIMES 512 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INWI 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec

13C 125.65 MHz
 127958.00 Hz
 30
 1H 500.00 MHz
 152150.00 Hz
 50.0 usec
 0

SCANS 330 times

SLVNT : CDCL3
 SPINNING 13.47
 TEMP 25.30

Date : Thu Nov 23 16:26:05 2006

FileName : LoadingFID.nmdata
Comment : DDR1253
SliceHistory :
EXMODE : bcmPOINT 32768 points
SAMP0 32768 points
FREQ0 33898.3 Hz
FILTR 16950 Hz
DELAY 11.8 usec
DEADT 10.0 usec
INTVL 29.5 usec
TIMES 256 times
DUMMY 1 times
PD 3.0000 sec
ACQTM 955.5560 msec
PREDL 0.01000 msec
IN1WT 1000.0000 msec
RESOL 1.03 Hz
PW1 6.25 usec
OBNUC 13C
OBFRQ 125.65 MHz
OBSET 127958.00 Hz
RGAIN 31
IRNUC 1H
IRFRQ 500.00 MHz
IRSET 162150.00 Hz
IRPWP 50.0 usec
IRPNS 0
SCANS 235 times
SLVNT CDCL3
SPINNING 10 Hz
TEMP 28.8 C

DDR1285

22-S

Date : Sat Dec 9 07:24:47 2006

FileName : LoadingFID.nmdata
 Comment : DDR1285
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPD 32768 points
 FREQU 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEAT 10.0 usec
 INTVL 29.5 usec
 TIMES 1500 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec
 OBNUC ¹³C
 OBFRQ 125.65 MHz
 OBSET 127958.00 Hz
 RGAIN 30
 LGNUC ¹H
 LRFRQ 500.00 MHz
 IRSET 162160.00 Hz
 IRRPW 50.0 usec
 IRNS 0

SCANS : 1300 times

SLVNT : CDCL₃
 SPINNING : 12 Hz
 TEMP : 27.7 C

DDR1263

S-23

Date : Tue Nov 28 20:27:35 2006

FileName : .LoadingFID.nmdata
 Comment : DDR1263
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPO 32768 points
 FREQ 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEAT 10.0 usec
 INTVL 29.5 usec
 TIMES 1000 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec
 13C
 OBNUC 125.65 MHz
 OBFRQ 127958.00 Hz
 OBSET 30
 RGAIN 1H
 IRNUC 500.00 MHz
 IRFRQ 162150.00 Hz
 IRSET 50.0 usec
 IRRPW 0
 IRRNS

SCANS : 1000 times
 SLVNT : CDCL3
 SPINNING : 11 Hz
 TEMP : 28.6 C

DDR1218

Date : Wed Nov 1 11:04:56 2006
 FileName : .LoadingFID.nmdata
 Comment : DDR1218
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPO 32768 points
 FREQU 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEATH 10.0 usec
 INTVL 29.5 usec
 TIMES 512 times
 DUMMY 1 times
 PD 3.0000 sec
 ACQIM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 6.25 usec

13C 125.65 MHz
 OBFRQ 127958.00 Hz
 OBSET 30
 RGAIN
 IRNUC 500.00 MHz
 IRFRQ 162160.00 Hz
 IRSET 50.0 usec
 IRRPW 0
 IRRNS

SCANS 330 times
 SLVNT CDCL3
 SPINNING 10 Hz
 TEMP 26.1 C

DDR1400

Date : Thu Mar 8 08:30:47 2007

FileName : LoadingFID nmdata
 Comment : DDR1400
 SliceHistory :
 EXMODE : bcm

POINT 32768 points
 SAMPO 32768 points
 FREQU 33898.3 Hz
 FILTR 16950 Hz
 DELAY 11.8 usec
 DEADT 15.1 usec
 INTVL 29.5 usec
 TIMES 1000 times
 DUMMY 1 times
 PD 3 0000 sec
 ACQTM 966.6560 msec
 PREDL 0.01000 msec
 INIWT 1000.0000 msec
 RESOL 1.03 Hz
 PW1 5.25 usec
 13C
 OBNUC 125.40 MHz
 OBFRQ 143041.00 Hz
 OBSET 30
 RGAIN 1H
 IRNUC 499.10 MHz
 IRFRQ 128250.00 Hz
 IRSET 65.0 usec
 IRRPW 0
 IRRNS
 SCANS 1000 times
 SLVNT CDCL3
 SPINNING 15 Hz
 TEMP 22.1 C

Date: Fri Dec 21 13:43:56 2006

File Name	Loading Comments
comment	comment
comment	comment

[illegible]

SWR	1.75	dB
RF SWR	1.55	dB
FLTR	15950	Hz
DELAY	11.8	usec
DEATH	10.0	usec
INTVL	29.5	usec
TIMES	512	times
CUMY	1	times
PU	3.0000	sec
ASSTW	450.0000	MHz
BDW	0.0000	Hz
FW	1000.0000	Hz
RIS	1.00	Hz
PW	0.00	usec
ORNUC	130	
ORFRQ	126.65	MHz
ORST	127958.00	Hz
ROAIN	31	
ORNUC	14	
ORFRQ	150.00	MHz
ORST	127958.00	Hz
ORPW	50.0	usec
ORNG	1000	times

SCANS	TIME	TEMP
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