Engineering Polymeric Chiral Catalyst Using Hydrogen Bonding and Coordination Interactions

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Methods

$^1$H-NMR and $^{13}$C-NMR spectroscopies were taken in deuteriochloroform on a Varian Mercury 300 ($^1$H: 300 MHz; $^{13}$C: 75 MHz) spectrometer. Chemical shifts are reported in ppm relative to an internal standard: tetramethylsilane (0 ppm) for $^1$H-NMR and deuteriochloroform (77.0 ppm) for $^{13}$C NMR. Coupling constants, $J$, are listed in hertz. $^{31}$P-NMR spectra were referenced with an external 85% H$_3$PO$_4$ sample. $^{31}$P NMR CP/MAS spectra were measured with a Bruker dsx300 NMR spectrometer (125 MHz) and the chemical shift of spectra were determined by taking the $^{31}$P of 70% H$_3$PO$_4$ (0.0 ppm) as an external reference standard. EI (70 ev) and ESI mass spectra were obtained on HP5989A and Mariner LC-TOF spectrometers respectively. HRMS spectra were determined on a Q-Tof micro instrument or APEXIII 7.0 TESLA FTMS. Elemental analysis was preformed with an Elemental VARIO EL apparatus. Optical rotations were measured on a Perkin-Elmer 341 automatic polarimeter. Infrared spectra were obtained on a BIO-RAD FTS-185 Fourier transform spectrometer in KBr pellelt. Scanning electron micrographs were taken on a Hitachi S-570 Scanning electron microscope. Powder X-ray diffraction (XRD) spectra were carried out on a Bruker-AXS D8Advance. ICP analysis of Rh and P leaching was performed with Varian spectra AA. Liquid chromatographic analyses were conducted on a JASCO 1580 system. GC analyses were measured on Agilent 6890N network system. All the experiments sensitive to moisture or air were carried out under argon atmosphere using standard Schlenk techniques. Commercial reagents were used as received without further purification unless otherwise noted. Dichloromethane, chloroform were freshly distilled from calcium hydride and THF, diethyl ether and toluene from sodium benzophenone ketyl. Compound 1a was prepared following a literature method.$^1$
Scheme S1. Preparation of ligands 1b and 1c. Conditions and reagents: 1) K$_2$[Fe(CN)$_6$] (0.25 equiv.), Pd(OAc)$_2$ (0.5 mol%), dppf (1.0 mol%), Na$_2$CO$_3$ (1.0 eq.), NMP, 120°C, 5 h, 84%; 2) LiAlH$_4$, dry THF, 60°C, 10 h, 99%; 3) CHCl$_3$, 60°C, 5 h, 95%; 4) CHCl$_3$, MeOH, HCl (12M), 40°C, 92%; 5) Toluene, HMPT, 80°C, 4 h, 65%

Synthesis of 6-cyano-2,2'-bismethoxymethoxy-1,1'-binaphthalene (S2): To a solution of S1 (4.5 g, 10.0 mmol) and K$_2$[Fe(CN)$_6$] (920.0 mg, 2.5 mmol) in NMP (10 ml) were added Pd(OAc)$_2$ (11.2 mg, 0.05 mmol), dppf (55.4 mg, 0.1 mmol) and Na$_2$CO$_3$ (1.06 g, 10.0 mmol) successively. The resulting mixture was heated at 120 °C for 5 h under argon atmosphere until the starting material was almost consumed as monitored by TLC (hexane: ethyl acetate = 5:1). After being cooled
to room temperature, the reaction mixture was passed through a pad of Celite and the filtrate was then evaporated under reduced pressure. The residue was added water (40 ml) and dichloromethane (50 ml). The organic phase was separated and the water phase was extracted with dichloromethane (40 ml \times 3). The combined organic phase was washed with saturated aqueous NaHCO₃ (60 ml), water (80 ml), and brine (50 ml), respectively. The organic phase was dried over Na₂SO₄ and then concentrated. The residue was purified by column chromatography on silica gel with hexane-ethyl acetate (10:1) as eluent to afford S₂ in 84% yield as a white solid. M.p. 76 – 77°C. \([\alpha]_D^{20} = +27.9\ (c = 0.50\ \text{in CHCl}_3)\

\(^1\text{H NMR}\ (300\ \text{MHz, CDCl}_3): \delta = 8.26\ (s, 1\text{H}), 8.02-7.96\ (m, 2\text{H}), 7.89\ (d, 1\text{H}, J = 6), 7.72\ (d, J = 9, 1\text{H}), 7.65\ (d, J = 30, 1\text{H}), 7.37-7.32\ (m, 2\text{H}), 7.27-7.07\ (m, 2\text{H}), 7.06\ (d, 1\text{H}, J = 6), 5.16 – 4.98\ (m, 4\text{H}), 3.18\ (s, 3\text{H}), 3.14\ (s, 3\text{H}); \(^{13}\text{C NMR}\ (75\text{MHz, CDCl}_3): \delta = 154.9, 152.4, 135.4, 134.0, 133.4, 129.8, 129.8, 129.6, 128.2, 127.9, 126.5, 126.4, 124.7, 124.0, 121.0, 119.4, 119.3, 117.9, 116.6, 107.0, 94.7, 94.3, 55.8, 55.6 ; FTIR (KBr pellet): \nu = 3050, 2991, 2962, 2905, 2831, 2233, 1619, 1591, 1479, 1351, 1200, 1151, 1092, 1073, 1024, 918, 884, 808, 759, 692, 681\ \text{cm}^{-1}; \ ESI-MS\ (m/z): [M'] = 399.1; \ HRMS\ (MALDI - DHB) calcd. for C_{25}H_{21}NO_{4}Na^{+1} [M' + Na]: 422.1376; Found: 422.1362.

**Synthesis of 6-aminomethyl-2,2'-bismethoxymethoxy-1,1'-binaphthalene (S₃):** In a 25-ml round-bottomed flask, S₂ (400 mg, 1 mmol) was dissolved in THF (8 ml) under argon atmosphere. LiAlH₄ (114 mg, 3 mmol ) was then added to the solution portion wise. The mixture was heated to 60°C and stirred for 10 h. After cooling to room temperature, methanol (1 ml) was added slowly and stirred for 10 min to quench the reaction. The reaction mixture was then passed through a pad of Celite and the filtrate was evaporated under reduced pressure to yield a compound S₃ in 99% yield. The compound is pure enough for the next reaction without further purification. \([\alpha]_D^{20} = -26.3\ (c = 0.50\ \text{in CHCl}_3)\n
\(^1\text{H NMR}\ (300\ \text{MHz, CDCl}_3): \delta = 7.93-7.85\ (m, 3\text{H}), 7.78\ (s, 1\text{H}), 7.58-7.54\ (m, 2\text{H}), 7.36-7.31\ (m, 2\text{H}), 7.24-7.10\ (m, 4\text{H}), 5.06\ (d, 2\text{H}, J = 9), 4.98-4.94\ (m, 2\text{H}), 3.97\ (s, 1\text{H}), 3.15-3.12\ (m, 6\text{H}). \ FTIR (KBr pellet): \nu = 3404, 2924, 1594, 1506, 1481, 1358, 1243, 1198,
Synthesis of 1c: The CDI-activated 6-(1-ethylpentyl)isocytosine S4 (260 mg, 1.2 mmol) was mixed with S3 (403 mg, 1 mmol) in chloroform (10 ml) and the mixture was heated at 60°C for 5 h. After cooling to room temperature, the solution was filtrated to remove the unreacted S4, and the filtrate was evaporated in vacuo. Finally, the residue was recrystallized from dichloromethane / hexane to yield 1c in 95% yield as a white solid. M.p. 164 – 166°C. \([\alpha]_D^{20} = -34.4\) (c = 0.60 in CHCl₃); $^1$H NMR (300 MHz, CDCl₃): δ = 12.99 (s, 1H), 12.02 (s, 1H), 10.88 (s, 1H), 7.94-7.80 (m, 4H); 7.57-7.52 (m, 2H), 7.35-7.18 (m, 3H), 7.12-7.08 (m, 2H), 5.78 (s, 1H), 5.05 (q, 2H, J = 3.5), 4.95 (q, 2H, J = 3.2), 4.55 (d, 2H, J = 5.4), 3.15-3.12 (m, 6H), 2.18 (s, 3H); $^{13}$C NMR (75MHz, CDCl₃): δ = 172.9, 156.7, 154.5, 152.5, 152.4, 148.2, 134.3, 133.9, 133.1, 129.7, 129.2, 127.7, 126.1, 125.9, 125.5, 123.9, 121.2, 121.1, 117.3, 117.2, 106.6, 95.1, 55.79, 55.72, 43.3, 18.8; FTIR (KBr pellet): ν = 3200, 3050, 1699, 1663, 1586, 1506, 1245, 1198, 1149, 1070, 1015, 921, 811, 751 cm$^{-1}$; ESI-MS (m/z): [M$^+$], 555; HRMS (MALDI - DHB) calcd. for C$_{31}$H$_{31}$N$_4$O$_6$ +1 [M$^+$]: 555.2242; Found: 555.2238.

Synthesis of S5: To a solution of 1c (403 g, 1.0 mmol) in mixed solvent of chloroform (30 ml) and methanol (10 ml) was added aqueous HCl (12 M, 0.5 ml, ~ 6 mmol). The resulting solution was stirred for 10 h at room temperature until the complete conversion of 1c (monitored by TLC, dichloromethane: methanol = 15 : 1). The saturated aqueous NaHCO$_3$ solution was added to neutralize the reaction mixture and the precipitation was filtered off. The resulting precipitation was washed with water and dried under reduced pressure to give the product S5 in 92 % yield as a white powder. M.p. 216 – 218°C. \([\alpha]_D^{20} = -82.7\) (c = 0.507 in DMSO); $^1$H NMR (300 MHz, DMSO-d$_6$): δ = 8.29 (s, 1H), 7.84-7.79 (m, 3H), 7.71 (s, 1H), 7.30-7.26 (m, 2H) 7.21-7.09 (m, 3H), 6.90-6.86 (m, 2H), 5.67 (s, 1H), 4.41 (s, 2H), 2.06 (d, 3H, J = 2.7); $^{13}$C NMR (75MHz, DMSO-d$_6$): δ = 155.2, 153.0, 152.9, 151.9, 134.1, 133.3, 132.7, 128.6, 128.1, 127.9, 127.8, 125.85, 125.80, 124.8, 124.3, 122.2, 118.8, 118.5, 115.4, 104.5, 79.1, 42.8, 30.6; FTIR (KBr
pellet): $\nu = 3510, 3208, 3054, 1697, 1508, 1435, 1382, 1340, 1248, 1215, 1144, 817, 751, 607 \text{ cm}^{-1}$; ESI-MS ($m/z$): $[M^+]$, 467; HRMS (MALDI - DHB) calcd. for $C_{27}H_{23}N_4O_4^{+1}$ $[M^+]$: 467.1716; Found: 467.1713.

**Synthesis of 1b:** A solution of $S5$ (370 mg, 0.8 mmol) and hexamethyolphosphorustriamide (0.2 ml, 1mmol) in dry toluene (2 ml) was heated at 80°C under Argon for 5h until the complete conversion of substrate $S5$ (monitored by TLC, dichloromethane : methanol = 15 : 1). After cooling to room temperature, the mixture was concentrated under vacuum and the residue was purified by a flash column chromatography on silica gel with dichloromethane / acetone (20 / 1) as eluent to give the product 1b in 65% yield as white powder. M.p. 190 – 191°C. $[\alpha]_D^{20} = +348.6$ (c = 0.50 in CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 12.98$ (s, 1H), 12.06 (s, 1H), 10.94 (s, 1H), 7.95-7.83 (m, 4H), 7.49-7.44 (m, 1H), 7.42-7.32 (m, 4H), 7.28-7.23 (m, 2H), 5.79, (s, 1H), 4.60-4.56 (m, 2H), 2.55-2.51 (m, 6H), 2.19 (s, 1H); $^{31}$P NMR (121 MHz, CDCl$_3$) $\delta$ 149.69, 149.56 ppm; FTIR (KBr pellet): $\nu = 3051, 1700, 1662, 1588, 1507, 1468, 1333, 1251, 1068, 982, 945, 821, 751, 691 \text{ cm}^{-1}$; ESI-MS ($m/z$): $[M^+]$, 540.45; HRMS (MALDI - DHB) calcd. for $C_{29}H_{27}N_5O_4P^2 \cdot [M^+]$: 540.1819; Found: 540.1795.

**Synthesis of 2.** To a dichloromethane (1.0 mL) solution of 1b (11.3 mg, 0.021 mmol) was added [Rh(COD)$_2$]BF$_4$ (4.1 mg, 0.01 mmol) in dichloromethane (0.5 mL). The resulting mixture was stirred at room temperature for 1 h to afford the yellow precipitate. After removal of the solvent at 50 °C under reduced pressure, the resulting yellow powder was washed with toluene to remove the trace amount of soluble low molecular weight species. The isolated yellow solids (2) were dried in vacuo for 2 h at RT. IR (KBr): 3510, 3208, 3054, 2933, 1699, 1662, 1507, 1469, 1326, 1226, 1071, 988, 947, 828, 753 cm$^{-1}$; Anal. calcd (%) for $[C_{58}H_{52}N_{10}O_8P_2 \cdot Rh(COD)BF_4 \cdot CH_2Cl_2]$$_n$: C, 55.05; H, 4.55; N, 9.58; P, 4.24. Found: C, 55.36; H, 4.96; N, 8.99; P, 4.16. $^{31}$P CPMAS (125 MHz): 135.7 ppm.

**Hydrogenation.** (a) Standard. For example, polymeric solid 2 (0.01 mmol, 10 mM), 3b (1 mmol, 1.0 M) in anhydrous toluene (1.0 mL) were placed in a test
tube under argon atmosphere. The test tube was placed in a stainless steel autoclave, and then sealed. After purging with hydrogen for 3 times, final H₂ pressure was adjusted to 40 atm and stirring commenced. Following a period of 20 h, H₂ was released and the catalyst recovered by cannula filtration under an argon atmosphere. The product was analyzed following removal of toluene under the reduced pressure. Conversion and enantiomeric excess were determined by ¹H NMR and chiral GC (Supelco BETA-DEX225 column), respectively.

¹H NMR of products 4a-e.

Product 4a: ¹H NMR (300 MHz, CDCl₃): δ = 6.57 (s, 1H), 4.63-4.54 (m, 1H), 3.76 (s, 3H), 2.02 (s, 3H), 1.40 (d, 3H) ppm.

Product 4b: ¹H NMR (300 MHz, CDCl₃): δ = 6.35 (s, 1H), 4.62-4.56 (m, 1H), 3.72 (s, 3H), 2.01 (s, 3H), 2.03-1.67 (m, 2H), 0.88 (t, 3H) ppm.

Product 4c: ¹H NMR (300 MHz, CDCl₃): δ = 6.08 (s, 1H), 4.61-4.53 (m, 1H), 3.72 (s, 3H), 2.01 (s, 3H), 1.88-1.72 (m, 2H), 1.76-1.62 (m, 2H), 1.47-1.32 (m, 3H) ppm.

Product 4d: ¹H NMR (300 MHz, CDCl₃): δ = 5.88 (s, 1H), 4.76-4.61 (m, 1H), 3.73 (s, 3H), 2.01 (s, 3H), 1.78-1.62 (m, 2H), 1.65-1.54 (m, 1H), 0.94-0.93 (m, 6H) ppm.

Product 4e: ¹H NMR (300 MHz, CDCl₃): δ = 7.28-7.17 (m, 5H), 6.32 (s, 1H), 5.04-4.99 (q, 1H), 1.87 (s, 3H), 1.40-1.37 (d, 3H) ppm.

(b) Reaction Profile. Procedure as (a) above. An autoclave equipped with a sampling needle allowed for aliquots to be analyzed during hydrogenation under an atmosphere of H₂.³ Conditions: [2] = 2 mM, [3b]= 0.2 M, P (H₂) = 15 atm. Conversion and ee% determined by GC (Supelco BETA-DEX225 column). Note, ¹H NMR and chiral GC analysis gave the same conversion results.
(c) Turn over frequency (TOF) determination. Procedure as (a) above. Reaction was stopped at ca. >50% conversion estimated from reaction profile above and the product mixture analyzed by $^1$H NMR and chiral GC (Supelco BETA-DEX225 column). Following catalyst recovery by filtration under argon atmosphere the next hydrogenation was conducted. TOF = TON/reaction time (TON = mol of product/mol of catalyst).

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References


Figure S1. XRD pattern of solid-state catalyst 2

Figure S2. DSC-TG Curve of catalyst 2.
Figure S3. a) Polymeric supramolecular catalyst 2 (yellow solids at the bottom of the reactor) in toluene prior to hydrogenation. b) The colorless toluene filtrate obtained by simple filtration of solid catalyst 2 following the hydrogenation.
Figure S4. Chiral GC analysis of products 4a-4e

product 4a

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Dilution  : 1.0000

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2 10.485 BB  0.0998  355.72717  45.18896 50.02653
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12
product 4c

NHAc

CO₂Me

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Product 4e

NHAc
Ph

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Curr. Date: 27-Sep-2005 11:29:30
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Group: DATA
Control Method: BENJI-XIAN

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File name: sl-3-90002.CH2

Info:

AD, i-PrOH:HEX=50:50, 250 nm,

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Control Method: BENJI-XIAN

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