Supplementary Materials for

Enantioselective Fluorescent Recognition of a Soluble “Supported” Chiral Acid: Toward a New Method for Chiral Catalyst Screening

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Experimental

Preparation and Characterization of 2c: At 0 °C, sodium hydride (0.46g, 19.1mmol) was added to a solution of 4-hydroxybenzaldehyde (2.14 g, 17.5 mmol) in THF (150 mL). After the mixture was stirred at 0 °C for 2 h, the solvent was removed and the residue was dried under vacuum. A solution of C_{22}H_{45}Br (8.1 g, 20.8 mmol) in DMF (150 mL) was added. The mixture was stirred at 70 °C for ~12 h and then cooled down to 0 °C. Water was added to quench the reaction and diethyl ether was used for extraction. The crude mixture was further purified by column chromatograph on silica gel eluted with 5% ethyl acetate in petroleum ether to give 2c as a white solid in 76% yield (5.2 g). ¹H NMR (CDCl₃, 300 MHz) δ 9.87 (s, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 4.03 (t, J = 6.6 Hz, 2H), 3.75 (s, 3H), 1.81 (quintet, J = 6.6 Hz, 2H), 1.52-1.14 (m, 38H), 0.88 (t, J = 6.6Hz, 3H). ¹³C NMR (CDCl₃,
75 MHz) δ 191.0, 164.5, 132.2, 130.0, 114.9, 68.6, 32.2, 29.9, 29.6, 29.3, 26.2, 22.9, 14.4. 

MS Calcd for C\textsubscript{29}H\textsubscript{50}O\textsubscript{4}: 430.4. Found: 430.2.

**A General Procedure for the Conversion of 2c to 3c and Characterization of 3c.** Two methods were used to prepare the chiral ligand-Ti(IV) catalysts: (1) For DIPT. To a methylene chloride solution of (+)- or (-)-DIPT, Ti(O\textsubscript{iPr})\textsubscript{4} was added and the resulting mixture was stirred at room temperature for 2 h. The solvent was then removed and toluene was added and evaporated (3 times) in order to dry the residue. The resulting solid was dissolved in methylene chloride and 1 equiv (versus Ti) of isopropanol was added. The mixture was stirred for 10 min and TMSCN and 2c were added sequentially. (2) For ligand 6. Compound 6 was dissolved in an organic solvent and then combined with Ti(O\textsubscript{iPr})\textsubscript{4}. The resulting mixture was stirred for 20 min and TMSCN and 2c were added sequentially.

After the addition of 2c to the above catalyst solution, the reaction was monitored by TLC analysis until it reached completion. Water was added to quench the reaction and methylene chloride was used for extraction. The resulting mixture was passed through a short silica gel column eluted with 15% ethyl acetate in hexane to remove the Ti compounds. After removal of the solvents, HCl (g) in diethyl ether and methanol (3:1) was added to the residue and stirred for 6 h. The solvent was then removed and the residue was dissolved in a mixture of KOH (1 M aq., 2 mL) and dioxane (8 mL). The resulting solution was heated at 60 °C for 18 h and then cooled down to 0 °C. The pH was adjusted to 4 with 0.5 N HCl solution. After centrifugation, the liquid phase was removed and the white precipitate was washed with 95% methanol until pH ~ 7. The white precipitate was dissolved in THF and the insoluble material was removed after centrifugation. After evaporation of THF, 3c was
obtained as a white solid. $^1$H NMR (THF-$d_8$; 300 MHz) δ 7.34 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 4.98 (d, J = 5.4 Hz, 1H), 4.64 (d, J = 5.4 Hz, 1H), 3.93 (t, J = 6.3 Hz, 2H), 1.73 (m, 2H), 1.52-1.21 (m, 38H), 0.88 (t, J = 6.3 Hz, 3H). $^{13}$C NMR (THF-$d_8$, 75 MHz) δ 174.3, 159.1, 132.4, 127.7, 113.9, 72.4, 67.7, 32.1, 31.0, 29.9, 29.6, 29.5, 26.3, 22.8, 13.7. MS Calcd for C$_{30}$H$_{52}$O$_4$: 476.4. Found: 476.0.

**The Modified Procedure for Reference 7.** (+)- or (-)-DIPT (0.81 mmol) and Ti(OiPr)$_4$ (0.81 mmol) were added to methylene chloride (10 mL) and the resulting mixture was stirred at room temperature for 2 h. After the solvent was removed, toluene (3 x 3 mL) was added and evaporated to dryness. The resulting solid was dissolved in methylene chloride (20 mL) and combined with isopropanol (1 equiv. verse Ti). The mixture was stirred for 10 min and TMSCN (4.6 mmol) and 2c (1.2 mmol) were added sequentially. The stirring continued for two days and then the reaction was quenched with water.

**General Procedure to Convert 4 to Compounds 3a-c:** Compound 4 was dissolved in hot 90% ethanol (10%H$_2$O) and 3eq of KOH was added and stirred for 30 min. An alkyl bromide (1.2 equiv) was added and the mixture was maintained at reflux for 20 h. A HCl (0.5 M) solution was added to quench the reaction. For 3a the water layer was extracted with diethyl ether to obtain the product; for 3b the water layer was extracted with methylene chloride; and for 3c the precipitate was washed by water and a 1:1 mixture of EtOH:H$_2$O to remove the impurities. The final products were all obtained as white solids.

**Preparation and Characterization of 5.** From the asymmetric reaction of 2c with TMSCN in the presence of the chiral titanium complexes, the optically active cyanohydrin
trimethylsilyl ether was first obtained. After removal of the solvent, HCl (g)† in diethyl ether and methanol (3:1) was added to the residue. After stirred at room temperature for 6 h and removal of the solvent, the crude product was passed through a flash column on silica gel eluted with 10 to 15% ethyl acetate in hexane to give 5 as a white solid in 62 - 78% yield. †H NMR (CDCl₃, 300 MHz): δ 7.32 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 5.12 (s, 1H), 3.94 (t, J = 6.6 Hz, 2H), 3.75 (s, 3H), 1.76 (quintet, J = 6.6 Hz, 2H), 1.45-1.18 (m, 38H), 0.88 (t, J = 6.6 Hz, 3H). 13C NMR (CDCl₃, 75 MHz): δ 159.7, 130.4, 128.1, 114.8, 72.8, 68.3, 53.2, 32.1, 30.0, 29.7, 29.5, 26.3, 23.0, 14.4. MS Calcd for C₃₁H₅₄O₄: 490.4. Found: 490.6.


**Conditions for the HPLC Analysis of 5:** HPLC analyses were carried out on the Waters 600 instrument observed at 254 nm with the Waters 486 by using the Diacel Chiralcel OD column and the hexane/2% i-PrOH eluent at a flow rate of 1.0 mL/min. The retention times for the two enantiomers were 14.2 min and 18.3 min respectively.

**Configuration Assignment for 3c.** The optically active (S)-4 (86% ee) was obtained by optical resolution following a literature procedure.¹² (S)-4 was converted to (S)-3c according to Scheme 2 and the specific optical rotation of (S)-3c was [α]D = +37.2 (c = 0.5, THF). The product 3c obtained from the reaction of 2c with TMSCN catalyzed by 70% (+)-DIPT and Ti(OiPr)₄ gave the specific optical rotation. [α]D = +34.1 (c = 1.0, THF), indicating a S configuration. By comparing the HPLC plots of the compounds 5 generated from the catalyst screening experiments, the absolute configurations were assigned.

Sample Preparation for Fluorescence Measurements. All of the solvents were HPLC grade from Aldrich Company. The benzene stock solutions of the sensors were freshly prepared for the measurements. For the fluorescence study, the R or S sensor solutions were mixed with the solution of 3c at room temperature in a 5 mL volumetric flask and then diluted to the desired concentration for fluorescence measurement.

Conditions for the Fluorescence Measurements: Fluorescence spectra were recorded on a Perkin-Elmer LS-50B luminescence. The scan speed was set at 100 nm/min. The excitation wavelength was 332 nm and the emission wavelength was 418 nm with the slit widths at 3.5nm/6.5nm (excitation/emission). For the final measurement, the sensor’s concentration was 2.0 x 10^{-5} M and that of the acid was 2.0 x 10^{-4} M in a ternary solvent of THF (4%), benzene (22%) and hexane (74%).

Fluorescence Spectra of (R)- and (S)-1 in the Presence of Mandelic Acid. The fluorescence spectra of (R)- or (S)-1 (2.0 x 10^{-5} M) in the presence of (R)- and (S)-3c (2.0 x 10^{-4} M) (\lambda_{exc} = 332 nm, slit = 3.5; 6.5 nm) in 4%THF, 22%benzene and 74% hexane are given below: