Immobilization of Chiral Ligands on Polymer Fibers by Electron Beam Induced Grafting and Applications in Enantioselective Catalysis

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Supporting Information

General Considerations. All operations involving air-sensitive reagents and materials were carried out under nitrogen or argon atmosphere using standard Schlenk, vacuum, or drybox techniques. THF was distilled from sodium-benzophenone under argon prior to use. Toluene (anhydrous, Aldrich) was purified by passing through columns containing alumina. Dimethyl tartrate (Aldrich), Et_2Zn (1.1 M solution in toluene) (Fluka), 4-chlorostyrene, $BF_3{\cdot}Et_2O$ and $Ti(O\textit{i}Pr)_4$ (Acros Organics) were used as received. Benzaldehyde and acetophenone (Merck) were distilled prior to use. All other commercially available chemicals and solvents were of puriss. p.a. quality, or purified and dried according to standard methods. TLC: precoated silica gel 60 F_{254} (Merck); visualization by irradiation with UV light. Flash Chromatography (FC): silica gel 60 (0.04-0.063, Merck). Infrared (IR) spectra were recorded using a Perkin Elmer Spectrum 1000 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM A 500 NMR spectrometer operating at 500.13 MHz for ^{1}H and 125.78 MHz for ^{13}C, respectively. The chemical shifts are expressed in ppm downfield from internal TMS or referenced against the solvent signal. Polarimetric analyses were performed using a Perkin Elmer 241 polarimeter. Capillary gas chromatography (CGC) analysis were carried out on a HP-5 GC (Crosslinked 5% PH ME siloxane, column: 15 m × 0.53 mm × 1.5 μm Film Thickness). GC/MS analyses were performed on a HP-5890 Series II Gas Chromatograph equipped with a 5971 A Mass Selective Detector; column: 30 m × 0.25 mm × 0.25 μm HP-1MS. Melting points are uncorrected. Elemental analyses were obtained from the Microanalytical Service of Micro Kemi AB, Uppsala (Sweden), and the Microanalytical Department of the University of Groningen (the Netherlands).

Polymer Supported TADDOLs P1 and P1B. (4*R*,5*R*)-2-(4-Ethenylphenyl)-2-methyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethanol (**1**) was prepared according to the literature[1] and purified by flash chromatography on silica gel (diethyl ether/pentane 1:2). The fiber supported catalyst **P1** (graft copolymerization) was prepared by irradiation of cut polyethylene fibers (10 g, 0.7 Dtex) in an inert atmosphere to a total dose of 200 kGy using an electron accelerator operating at an acceleration voltage of 175 kV and beam current of 5 mA. In a typical experiment, the irradiated fibers were immediately immersed in a reaction mixture containing 15 g of styrene, 1.8 g of **1**, 40 mL of ethanol and 20 mL of water. To the reaction mixture was additionally added 0.03 g of divinyl

benzene and 0.155 g of a 25 wt-% solution of dibenzoyl peroxide The reaction mixture was purged with nitrogen before initiating the reaction and the grafting reaction was allowed to continue to completion, which usually took approximately 6 hours. The temperature was raised to 80 °C for 2 hours. The resulting fibers were filtered and washed subsequently with ethanol and dichloroethane. The weight gain of the recovered fibres were determined and the conversion of the monomers was calculated to 80 %. The loading of **P1** (0.15 mmol/g) was determined gravimetrically. FTIR analysis of the fibrous catalyst was consistent with successful grafting of the chiral ligand. IR (KBr, cm^{-1}): 3532, 3060, 3026, 2917, 2848, 1601, 1583, 1493, 1472, 1452, 1370, 1068, 906, 840, 757, 696. The reference catalyst **P1B** (loading 0.6 mmol/g) supported on polystyrene beads was prepared by suspension copolymerization of **1** with styrene using divinylbenzene as a cross-linking agent as described in the literature.[1] In a typical experiment, 2.4 g of **1**, 0.323 g of benzoylperoxide and 4.9 g of a 2 mol-% divinylbenzene/styrene mixture was dissolved at ambient temperature under nitrogen. The monomers were carefully added under stirring to 50 mL of a 2 wt-% gum arabic solution in water at 95 °C. Stirring was continued for 6 h at 95 °C under nitrogen. The beads were separated on a black ribbon filter paper in a Büchner funnel under vacuum, washed with ethanol and dried in vacuo. Materials: Styrene 99% inhibited with 10-15 ppm 4-*tert*-butylcatecol was obtained from Aldrich. Divinylbenzene (80% mixture of isomers in ethylvinylbenzene) was obtained from Aldrich. Gum arabic was obtained from Fluka. Benzoylperoxide (containing 25 wt-% water) was obtained from Interchim Austria.

(*S*)-(-)-α,α-Di(4-vinylphenyl)-2-[(*N*-ethoxycarbonyl)pyrrolidine]methanol (2). *N*-(ethoxycarbonyl)-*S*-proline methyl ester[2] (10g, 50 mmol) was dissolved in dry THF (100 mL). 4-Vinylphenylmagnesium chloride (200 mmol) prepared from magnesium turnings (9.72 g) and 4-chlorostyrene (27.72 g, 200 mmol) in THF (250 mL) was added via cannula at 0 °C. After completed addition, the reaction mixture was stirred for 3.5 hours and quenched with saturated ammonium chloride (50 mL). The organic phase was removed and the supernatant liquid was taken up in chloroform and stirred. The combined organic phases were washed with brine and dried over magnesium sulphate. The solvent was removed and the residue was purified by flash chromatography on silica gel (eluent: *n*-pentane/ethyl acetate 3:1, Rf = 0.46) yielding 12.8 g (69%) of **2** as a white foamy solid. Anal. Calcd for $C_{24}H_{27}NO_3$: C, 76.36; H, 7.21; N, 3.71. Found: C, 76.43; H, 7.18; N, 3.61. EIMS (calcd/found): 377.1990/377.1984. Mp. 34-37 °C. $[\alpha]_D$ = -52.0 (c = 0.1, $CHCl_3$, 20 °C). IR (KBr, cm^{-1}): 2917, 1670, 1601, 1493, 1472, 1451, 1028, 906, 756. ^{1}H NMR ($CDCl_3$, δ): 7.27-7.24 (m, 8H, CH); 6.61 (ddd, $2H_c$, $^3J_{ac}$ = 17.5 Hz, $^3J_{bc}$ = 10.8 Hz, ^4J = 2.8 Hz, =CH-); 5.65 (dd, $1H_a$, $^3J_{ac}$ = 17.5 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.64 (dd, $1H_a$, $^3J_{ac}$ = 17.5 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.14 (dd, $1H_b$, $^3J_{bc}$ = 10.8 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.13 (dd, $1H_b$, $^3J_{bc}$ = 10.8 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 4.81 (dd, 1H, ^3J = 8.9 Hz, 3.7 Hz, -CH-); 4.06-4.01 (m, 1H, $-O-CH_2-$); 3.97 (m, 1H, $-O-CH_2-$); 3.37-3.32 (m, 1H, CH_2); 2.89 (m, 1H, CH_2); 2.03-1.95 (m, 1H, $-CH_2-CH-$); 1.86-1.80 (m, 1H, $-CH_2-CH-$); 1.44-1.38 (m, 1H, CH_2); 1.12 (t, 3H, ^3J = 6.9 Hz, $-CH_3$); 0.83 (m, 1H, CH_2). ^{13}C NMR ($CDCl_3$, δ): 158.46, 145.99, 143.49, 136.66, 136.62, 136.58, 136.55, 128.44, 127.90, 125.86, 125.47, 114.02, 113.91, 81.56, 66.13, 62.05, 47.91, 29.75, 23.22, 14.75.

(*S*)-(-)-α,α-Di(4-vinylphenyl)-2-pyrrolidinemethanol (3).[3] To a solution of **2** (1.94 g, 5.15 mmol) in dry methanol (25 mL) under argon atmosphere was added KOH

(3.2 g). The mixture was refluxed for 2 hours, cooled to room temperature and evaporated to dryness. The light brown mixture was treated with distilled water (20 mL) and extracted with chloroform (2 × 40 mL). The organic extract was washed with water and dried over magnesium sulphate. The solvent was evaporated and the residue purified by flash chromatography on silica gel (*n*-hexane/ethyl acetate 2:1) to give 1.33 g (84%) of **3** as an oil which solidified upon standing at 4 °C. Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.90; H, 7.60; N, 4.57. Mp. 85 °C (Mp. litt.[3] = 82-83 °C). $[\alpha]_D$ = -51.4 (c = 0.1, $CHCl_3$, 20 °C) ($[\alpha]_D$ litt.[3] = -52.3 (c = 1.95, $CHCl_3$)). IR (KBr, cm^{-1}): 3372, 2917, 1601, 1493, 1472, 1451, 1028, 906, 756. ^{1}H NMR ($CDCl_3$, δ): 7.52-7.49 (m, 2H, CH); 7.45-7.42 (m, 2H, CH); 7.33-7.29 (m, 4H, CH); 6.65 (ddd, $2H_c$, $^3J_{ac}$ = 17.6 Hz, $^3J_{bc}$ = 10.9 Hz, ^4J = 1.4 Hz, =CH-); 5.68 (dd, $1H_a$, $^3J_{ac}$ = 17.6 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.67 (dd, $1H_a$, $^3J_{ac}$ = 17.6 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.18 (dd, $1H_b$, $^3J_{bc}$ = 10.9 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 5.17 (dd, $1H_b$, $^3J_{bc}$ = 10.9 Hz, $^2J_{ab}$ = 0.9 Hz, $=CH_2$); 4.22 (t, 1H, ^3J = 7.6 Hz, -CH-); 3.03-2.90 (m, 2H, $-CH_2$-N-); 1.78-1.52 (m, 4H, $-CH_2-CH_2$-). ^{13}C NMR (CD_2Cl_2, δ): 148.33, 145.64, 136.84, 136.71, 136.22, 136.07, 126.40, 126.38, 126.16, 125.97, 113.78, 113.58, 77.27 (overlapping with solvent when measured in $CDCl_3$), 64.50, 47.16, 26.60, 25.90.

Fiber Supported Proline Derived Catalysts P2 and P3. In a typical procedure, 10 g of cut polyethylene fibers (0.7 Dtex) were irradiated in an inert atmosphere to a total dose of 200 kGy using an electron accelerator operating at an acceleration voltage of 175 kV and beam current of 5 mA. The irradiated fibers were immediately immersed in a reaction mixture containing 15 g of styrene, 2 g of **2**, and 25 mL of ethanol. The reaction mixture was purged with nitrogen before initiating the reaction and the grafting reaction was allowed to continue to completion, which usually took approximately 6 hours. The temperature was raised to 80 °C for 1 hour. The resulting fibers were filtered and washed subsequently with ethanol and dichloroethane. The weight gain of the recovered fibers was determined and the conversion of the monomers was calculated to 93 %. Loading of **P2** was confirmed by nitrogen analysis (average of two runs: 0.29 wt % N, corresponding to a loading of 0.21 mmol ligand/g fiber). IR (KBr, cm^{-1}): 3060, 2918, 2849, 1670, 1601, 1583, 1493, 1472, 1452, 1379, 1097, 1028, 906, 830, 757. For removal of the ethoxycarbonyl group, a mixture of **P2** (5.0 g) and KOH (20 g) was refluxed in a 1:4 mixture of THF and *i*PrOH (100 mL) for 24 hours. The fibers were filtered on a glass frit and washed with water (500 mL), MeOH (500 mL), toluene (500 mL), MeOH (200 mL) and dried in vacuo. FTIR analysis was consistent with quantitative deprotection. Loading of **P3** was confirmed by nitrogen analysis (average of two runs: 0.275 wt% N, corresponding to a loading of 0.21 mmol ligand/g fiber). IR (KBr, cm^{-1}): 3372, 3060, 2917, 2849, 1601, 1583, 1493, 1472, 1452, 1370, 1097, 1028, 906, 830, 757.

Titanium TADDOLate Catalyzed Addition of Et_2Zn to PhCHO. The homogeneous titanium catalyzed addition of Et_2Zn to PhCHO in the presence of 0.2 equiv. of soluble TADDOL **4** was carried out as described in the literature.[4] Reactions employing the polymer supported TADDOLs **P1** and **P1B** were performed essentially according to the procedure described by Seebach.[1] In a typical experiment, the calculated amount of fiber-bound TADDOL **P1** (0.15 mmol, loading 0.15 mmol/g, 1g of polymer) was suspended in toluene (10 mL) and stirred for one hour at room temperature. The solvent was stripped off in vacuo to remove traces of moisture. The polymer was suspended again in toluene (10 mL), $Ti(O$*i*$Pr)_4$ (0.15 mmol, 44.65 µL) was added and the

solution was stirred for 16 hours at room temperature. The solvent and volatiles were removed and the polymer was dried in vacuo for several hours. The obtained polymer-bound titanium TADDOLate was suspended in toluene (12 mL) and cooled to -30 °C. Benzaldehyde (76 µL, 0.75 mmol), Ti(O*i*Pr)$_4$ (268 µL, 1 mmol) and Et_2Zn (1.2 mL of a 1.1 M solution in toluene, 1.32 mmol) were added subsequently. The yellow solution was stirred for 19 hours at -30 °C, quenched by addition of 2M HCl (5 mL) and stirred for 90 minutes at room temperature. The polymer was filtered on a glass filter and washed with water (20 mL), THF (10 mL) and Et_2O (50 mL). The phases were separated and the aqueous layer extracted with additional portions of Et_2O (2 × 50 mL). The combined organic extracts were dried over magnesium sulphate and evaporated to give the product. The polymer was regenerated for subsequent runs by washing with water (3 × 100 mL), MeOH (3 × 100 mL) and acetone (3 × 200 mL) and drying in vacuo. Reactions employing the beads supported TADDOL **P1B** and the proline derived fibrous ethyl carbamate **P2** were carried out in a similar fashion. All reactions were followed by CGC and the enantioselectivities determined by chiral CGC.

Prolinol Catalyzed Addition of Et_2Zn to PhCHO. Additions of Et_2Zn to PhCHO in the presence of the soluble prolinols **3** and **5** were carried out according to standard procedures. In a typical experiment, a solution of ligand **3** (230 mg, 0.753 mmol) in dry toluene (30 mL) under argon atmosphere was cooled to 0 °C and Et_2Zn (34.2 mL of a 1.1 M solution in toluene, 37.7 mmol) was added. The yellow solution was stirred for 30 minutes and benzaldehyde (1.60 g, 1.53 mL) was added during a period of 10 minutes. After completed addition, the solution was stirred at 0 °C for 24 hours. The reaction was quenched by addition of 10% HCl (10 mL) and extracted with Et_2O (3 × 30 mL). The combined extracts were washed with saturated $NaHCO_3$ solution (2 × 20 mL) and dried with Na_2CO_3. The solvent was removed in vacuo to leave 1.44 g of a colorless oil. Purification of the residue on short silica gel using *n*-hexane/ethyl acetate 4:1 as eluent gave pure 1-phenylpropan-1-ol in 70% isolated yield. The optical purity was determined by chiral CGC. Experiments with fibrous ligand were carried out accordingly. In a typical experiment, the calculated amount of fiber-bound prolinol **P3** (0.21 mmol, loading 0.21 mmol/g, 1g of polymer) was suspended in toluene (8 mL) and stirred for 30 minutes. The solvent was stripped off in vacuo to remove traces of moisture. The polymer was suspended again in toluene (8 mL), cooled to 0 °C and Et_2Zn (9.6 mL of a 1.1 M solution in toluene, 10.5 mmol) was added during a period of 10 minutes. The resulting solution was stirred for 30 minutes at room temperature, cooled to 0 °C and benzaldehyde (0.45 g, 4.21 mmol) was added during a period of 15 minutes. The reaction mixture was stirred for 24 hours, quenched by addition of 2 M HCl (10 mL) and stirred for additional 30 minutes at room temperature. The polymer was filtered on a glass filter and washed with water (20 mL), THF (10 mL) and Et_2O (50 mL). The phases were separated and the aqueous layer was extracted with additional portions of Et_2O (2 × 50 mL). The combined organic extracts were dried over magnesium sulphate and evaporated to dryness. The conversion and enantioselectivity were determined by CGC and chiral CGC. The polymer was regenerated for subsequent runs by washing with water (3 × 100 mL), MeOH (3 × 100 mL) and acetone (3 × 200 mL) and drying in vacuo.

Prolinol Catalyzed Reduction of PhCOMe with $NaBH_4$/TMSCl. Reductions of PhCOMe in the presence of the soluble prolinols **3** and **5** were carried out essentially according to published procedures.[5] In a typical experiment, freshly distilled trimethylsilyl chloride (130 mg, 1.2 mmol) was added to a suspension of $NaBH_4$ (45 mg, 1.2 mmol) in dry THF (5 mL). The reaction mixture was brought to reflux and a solution of **3** (30 mg, 0.1 mmol) in THF (2 mL) was added. After the gas evolution had stopped, a solution of acetophenone (120 mg, 1 mmol) in THF (2 mL) was slowly added during a period of two hours. After completed addition, the mixture was hydrolyzed with 2 M HCl (5 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine, and dried over sodium sulphate. The solvent was removed in vacuo and the oily residue was analyzed by GC. The GC and GC/MS analyses revealed a trace of acetophenone. Purification of the residue by flash chromatography on silica gel (*n*-hexane/ethyl acetate 4:1 as eluent) afforded 1-phenylethanol (125 mg) in > 98% yield. Enantioselectivities of the individual runs were determined by chiral CGC. Experiments with the fibrous catalyst **P3** were carried out accordingly. In a typical experiment, freshly distilled trimethylsilyl chloride (151.34 µl, 1.2 mmol) was added to a suspension of $NaBH_4$ (45 mg, 1.2 mmol) in dry THF (5 mL). The mixture was refluxed for one hour and a suspension of the fibrous catalyst **P3** (0.105 mmol, loading 0.21 mmol/g, 0.5 g of polymer) in THF (2 mL) was added. After the gas evolution had stopped, a solution of acetophenone (120 mg, 1 mmol) in THF (2 mL) was slowly added during a period of three hours. After completed addition, the mixture was hydrolyzed with 2 M HCl (10 mL), the fibers were filtered off and washed successively with water (20 mL), THF (20 mL) and Et_2O (3 × 10 mL). The combined organic layers were washed with brine and dried over sodium sulphate. The solvent was removed in vacuo and the oily residue was analyzed by GC. The GC and GC/MS analyses revealed a trace of acetophenone. The yield (99%) and enantioselectivity were determined by CGC and chiral CGC.

References and Notes

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