Supplementary Material:

Immobilization of Prolinol Precatalyst in Fluorous Phase for CBS Reduction

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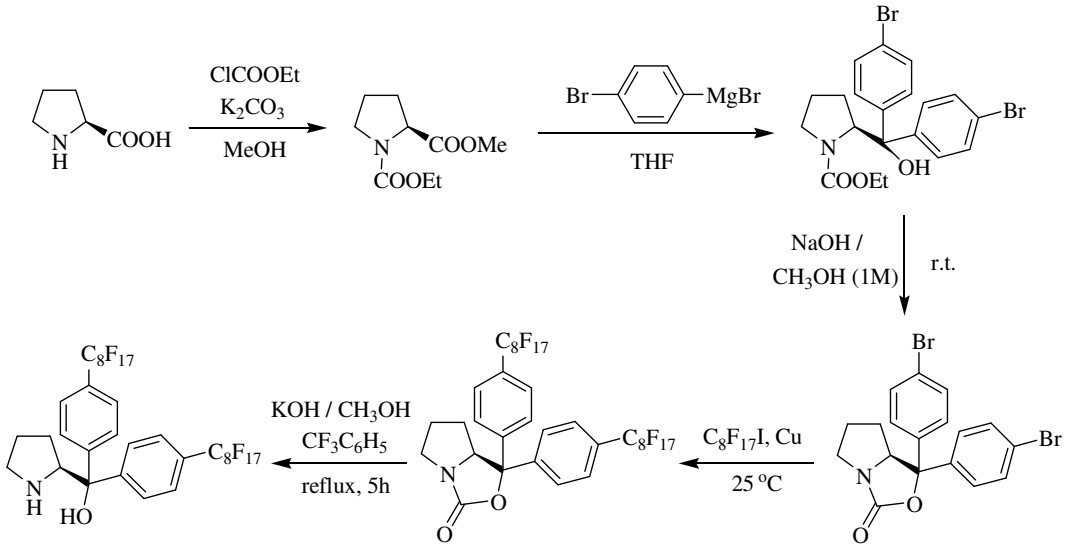
I. Materials and Methods

All starting materials, reagents and solvents were commercially available at Aldrich, 3M or Fluorous Technologies and used without further purification. GC analyses were performed on a Hewlett-Packard 5890 instrument with split mode (column: 30 m x 0.32 mm x 0.25 mm HP-1 methyl siloxane). HPLC analyses were performed on a Chiracel OD column (hexane:*i*-propanol, 98:2; flow, 1 mL/min; λ = 210 nm). NMR spectra were obtained on a Bruker AC-270 spectrometer (270 MHz).

II. Synthesis of Fluorous Prolinol Precatalyst

The fluorous prolinol precatalyst was synthesized from L-proline according to a reported route.[1,2] The overall yield of the five-step synthesis was 35% (Scheme 1).



Scheme 1. Synthesis of Fluorous Prolinol Precatalyst

III. Procedure A: CBS reduction in THF and corresponding partition experiment.

In a 10 mL flask equipped with magnetic stirrer and argon gas inlet, 54.5 mg fluorous prolinol (0.05 mmol, 0.1 equiv) was dissolved in 1 mL THF (anhydrous). 0.5 mL 1M BH_3·THF (0.5 mmol, 1 equiv BH_3) was added by a syringe. The mixture was stirred for one hour at room temperature. Then, a solution of acetophenone (0.06 mL, 0.5 mmol) in 1 mL THF (anhydrous) was added slowly over a period of one hour. The reaction mixture was strirred vigorously for an additionalone hour. The mixture was cooled to 0 ^oC and quenched with 0.1 mL MeOH. Two 1 μL samples were taken from the mixture for GC and HPLC analyses. The conversion of the reaction was determined by GC. Enantioselectivity of the product was determined by chiral HPLC. Rention time of the major product (R)-(+)-1-phenylethanol is 15.8 min, rention time for minor product (S)-(-)-1-phenylethanol is 17.5 min,

After removing the solvents by a rotary evaporator, the residue was dissolved in a biphasic system of 2 mL CH_3CN and 2 mL HFE-7500. The mixture was shaken by a shaker for 10 mins at a speed of 1200 rpm. After the two phase separated, 1 μL sample was taken from each layer and injected into GC for analysis. The ratio of two absolute peak areas of the product as well as the precatalyst in the two samples was utilized as an indicator of its distribution in the two phases. While the precatalyst was only found in the fluorous phase (HFE-7500), only 2 % of the product was in HFE-7500 layer and 98 % was in the organic layer (CH_3CN). The precatalyst (54 mg) was obtained by removing the HFE-7500 by rotary evaporation. The product (60 mg, 96 % yield, 97 % puirty) was obtained from the organic layer by removing CH_3CN with a rotavapor. The purity was assessed by GC and ^1H NMR analyses.

IV. Procedure B: CBS reduction in HFE-7500 with BH_3·THF and CH_3CN extractions.

In a 10 mL flask equipped with magnetic stirrer and argon gas inlet, 54.5 mg fluorous prolinol (0.05 mmol, 0.1 equiv) was dissolved in 2 mL HFE-7500 (dried over 4 Å molecular sieves). 0.3 mL 1M BH_3·THF (0.3 mmol, 0.6 equiv BH_3) was added by syringe at room temperature. The mixture was stirred for one hour followed by slow addition fo 0.06 mL acetophenone (0.5 mmol). The reaction mixture was strirred vigorously for two hours. The mixture was then cooled to 0 ^oC and quenched with 0.1 mL MeOH. Two 1 μL samples were taken from the mixture for GC and HPLC analyses. The conversion of the reaction was determined by GC. Enantioselectivity of the product was determined by chiral HPLC. The reaction mixture was extracted with CH_3CN (2 mL x 3), and then washed with H_2O (2 mL x 3). The fluorous layer was dried over 4Å molecular sieves. The molecular sieves was then filterated and washed with dry HFE-7500 to make volume of the the fluorous layer 2 mL for reuse in the next run. All the procedures in the next run were as same as those in the first run.

After six runs, the fluorous layer was concetrated by removing HFE-7500 with by rotary evaporation. The precatalyst (46 %, 25 mg) was recovered with a purity of 90 % (determined by ^1H NMR). The CH_3CN layers from all six runs were combined and concentrated. The product 1-phenylethanol was obtained with a overall yield of 93 % (349 mg) and purity of 96 % (determined by ^1H NMR).

V. Procedure C: CBS reduction in HFE-7500 with BH_3·DMS and DMSO extractions.

In a 10 mL flask equipped with magnetic stirrer and argon gas inlet, 54.5 mg fluorous prolinol (0.05 mmol, 0.1 equiv) was dissolved in 2 mL HFE-7500 (anhydrous). 0.06 mL 10M BH_3·DMS (0.6 mmol, 1.2 equiv BH_3) was added by a syringe. The mixture was stirred for one hour at room temperaturefollowed by slow addition of 0.06 mL acetophenone (0.5 mmol). The reaction mixture was strirred vigorously for two hours. It was cooled to 0 ^{o}C and quenched with 0.15 mL MeOH. Two 1 μL samples were taken from the mixture for GC and HPLC analyses. The conversion of the reaction was determined by GC. Enantioselectivity of the product was determined by chiral HPLC. The reaction mixture was extracted with DMSO (2 mL x 3). In cases where an emulsion formed a centrifuge was used to speed up the phase separation. The fluorous layer was then directly reused in the next run. All the procedures in the next run were as same as those in the first run.

After nine runs, the fluorous layer was concetrated by removing HFE-7500 with a rotavapor. The precatalyst (54 %, 29 mg) was recovered with a purity of 90 % (determined by ^{1}H NMR). All of the DMSO layers were combined. Brine (150 mL) was added. The mixture was extracted with ethyl ether (100 mL x 3). The ether layers were combined, washed with brine (50 mL x 3), dried over anhydrous $MgSO_4$, then filtered and concetrated to give the crude product. The final product 1-phenylethanol was obtained with an overall yield of 84 % (474 mg) and a purity of 99 % (determined by GC) after a flash chromatography (hexane:ethyl acetate, 10:1).

1. Kanth, J. V. B. Periasamy, M. *Tetahedron* **1993**, *49*, 5127.

2. Dalicsek, Z.; Pollreisz, F.; Gömöry, Á.; and Soós, T. *Org. Lett.* **2005**, *7*, 3243.