Supporting Information

A Recyclable Fluorous (S)-Pyrrolidine Sulfonamide Promoted Direct, Highly Enantioselective Michael Addition of Ketones and Aldehydes to Nitroolefins in Water

*Liansuo Zu, Jian Wang, Hao Li, and Wei Wang**

Department of Chemistry, University of New Mexico, Albuquerque, NM 87131-0001

General Information: Commercial reagents were used as received, unless otherwise stated. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F₂₅₄ were used for thin-layer chromatography (TLC) analysis. ¹H and ¹³C NMR spectra were recorded on the Bruker Avance 500, and tetramethylsilane (TMS) was used as a reference. Data for ¹H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Data for ¹³C NMR are reported as ppm. Mass Spectra were obtained from University of New Mexico mass spectral facility.

The compounds synthesized (shown in Table 3) in the manuscript are known compounds.¹⁻⁵ Their relative and absolute configurations of the products were determined by comparison with the known ¹H and ¹³C NMR, chiral HPLC analysis, and optical rotation values.

Procedures for the preparation of organocatalyst II and III.

Reagent and conditions: (a) R_fSO₂F, TEA, CH₂Cl₂, 12 h; (b) 10% Pd/C, H₂, MeOH, 3 h.

(S)-2-(Perfluoro-1-butane-sulfonylamino methyl)-1-N-Cbz-pyrrolidine (**b**₂).

To a solution of (*S*)-2-aminomethyl-1-*N*-Cbz-pyrrolidine **a** (2.0g, 8.55 mmol) and TEA (1.43 mL, 10.3 mmol) in 40 mL of dry CH₂Cl₂ was added perfluoro-1-butane-sulfonyl fluoride (3.1g, 10.3 mmol) dropwisely at 0 °C under N₂. The resulting solution was stirred for 12 h at rt, then diluted with 80 mL of CH₂Cl₂ and washed with 50 mL of 1N HCl aqueous solution. The organic layer was dried over MgSO₄ and concentrated *in vacuo*. Flash chromatography (Ethyl Acetate/Hexane = 1/3) afforded a colorless oil in 74% yield. ¹H NMR (500 MHz, CDCl₃): 8.01 (d, 1H, *J* = 4.5 Hz), 7.32-7.37 (m, 5H), 5.14 (s, 2H), 4.06 (m, 1H), 3.53 (m, 1H), 3.44 (m, 2H), 3.35 (m, 1H), 2.10 (m, 1H), 1.93 (m, 2H), 1.86 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 156.9, 136.0, 128.5, 128.1, 127.8, 67.6, 57.8, 48.6, 47.0, 29.0, 23.5; [α]_D²² = -7.0 (*c* = 2.0 in CHCl₃).

(S)-2-(Perfluoro-1-octane-sulfonylamino methyl)-1-N-Cbz-pyrrolidine (**b**₃).

The title compound was prepared by the similar procedure of compound (**b**₃) in 58% yield. ¹H NMR (500 MHz, CDCl₃): 8.00 (d, 1H, *J* = 4.0 Hz), 7.31-7.36 (m, 5H), 5.28 (s, 2H), 4.04 (m, 1H), 3.35-3.53 (m, 4H), 2.08 (m, 1H), 1.92 (m, 2H), 1.86 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 157.1, 136.0, 128.5, 128.2, 128.0, 67.7, 57.8, 49.1, 47.2, 29.2, 23.7; [α]_D²² = -4.7 (*c* = 1.0 in CHCl₃).

(S)-2-(Perfluoro-1-butane-sulfonylamino methyl)-pyrrolidine (**II**).

A solution of compound **b₂** (560 mg, 1.09 mmol) in 10 mL of MeOH was hydrogenated in the presence of 10% Pd/C (77.4 mg) with a H₂ balloon at rt for 3 h. The catalyst was filtered through a pad of celite and washed with 20 mL of MeOH. The combined filtrates were concentrated *in vacuo* to give a white solid in 96% yield. ¹H NMR (500 MHz, CDCl₃): 3.82 (m, 1H), 3.65 (m, 1H), 3.27-3.44 (m, 3H), 2.19 (m, 1H), 2.08 (m, 2H), 1.66 (m, 1H); ¹³C NMR (125 MHz, MeOH): δ 63.1, 47.2, 46.5, 28.3, 24.2; [α]_D²⁵ = -5.5 (*c* = 1.0 in CHCl₃).

(S)-2-(Perfluoro-1-octane-sulfonylamino methyl)-pyrrolidine (III).

The title compound was prepared by the similar procedure of **II** in 81% yield. ¹H NMR (500 MHz, MeOH): 3.48 (m, 1H), 3.32 (m, 1H), 3.13 (m, 3H), 1.99 (m, 3H), 1.70 (m, 1H); ¹³C NMR (125 MHz, DMSO): δ 62.1, 47.2, 44.9, 27.0, 23.2; [α]_D²² = -3.9 (*c* = 2.0 in benzotrifluoride).

General procedures for Michael Addition reaction and catalyst **II recovery.**

Cyclohexanone (196 mg, 2 mmol) and catalyst **II** (7.62 mg, 0.02 mmol) in 0.4 mL of H₂O was stirred at rt for 20 min. Then *trans*-β-nitrostyrene (29.8 mg, 0.2 mmol) was added and the resulting mixture was continued stirring at rt for 9 h. The reaction solution was directly loaded on fluorous silica gel (FluorousFlashTM SPE cartridge 2 grams, 8 cc tube) and then was first washed with 8 mL of CH₂Cl₂ to elute all the non-fluorous products. The combined filtrates were extracted with CH₂Cl₂ and the combined extracts were washed with water. The organic phase was dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel, eluted by hexane/EtOAc = 10:1 then 5:1 to give 47 mg (95%) of the desired product as a white solid. The fluorous catalyst **II** was recovered in a second passed elution of the fluorous silica gel eluting with 5 mL of THF. The evaporation of the THF filtrates *in vacuo* afforded **II**, which was used for the next cycle.

Reference:

- (1) Wang, W.; Wang, J.; Li, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 1369.
- (2) Saraswathy; V. G.; Sankararaman, S. *J. Org. Chem.* **1995**, *60*, 5024.
- (3) Ishii, T.; Fujioka, S.; Sekiguchi, Y.; Kotsuki, H. *J. Am. Chem. Soc.* **2004**, *126*, 9558.
- (4) Betancort, J. M.; Sakthivel, K.; Thayumanavan, R.; Tanaka, F. Barbas, C. F., III, *Synthesis*. **2004**, 1509.
- (5) Andrey, O.; Alexakis, A.; Tomassini, A.; Bernardinelli, G. *Adv. Synth. Catal.* **2004**, *346*, 1147.

9.701
9.696
9.473
9.467

7.357
7.343
7.327
7.306
7.292
7.277
7.262
7.179
7.165

4.830
4.817
4.804
4.792
4.773
4.755
4.747
4.723
4.713
4.698
4.688
4.660
4.641
4.635
4.615

3.799
3.789
3.779
3.769
3.750
3.750
2.714
2.696
2.677
2.618

1.486
1.477
1.468
1.458
1.440
1.408
1.387
1.274
1.153
0.887
0.880

203.212

136.797
136.259
129.066
128.198
128.102
127.975

78.419
77.863
77.259
77.005
76.751
53.875
53.457
44.415
43.103
31.820
31.639
31.530
29.515
29.432
29.288
28.930
28.766
27.483
27.290
27.019
26.325
22.622
22.494
14.061
13.979