Supplementary Material (ESI) for Green Chemistry

Functionalized Chiral Ionic Liquid as Efficient Organocatalyst for Asymmetric Michael Addition to Nitroalkenes

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Experimental section:

(1) Synthesis of compound 1

To a solution of N-Boc-(S)-2-aminomethylpyrrolidine (1.00g, 5.0 mmol) in CH_2Cl_2 (20 mL) was added Et_3N (0.7 mL, 5.5 mmol), the solution was coolied to 0^oC and 3-Chloropropanesulfonyl chloride (0.89 g, 5.0 mmol) was added. After addition, the reaction mixture was warmed up to stir at room temperature for 17 h, diluted with CH_2Cl_2 (60 mL) and washed with 0.5 M HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), and brine (15 mL). The organic phase was dried with Na_2SO_4 and purified by flash chromatography on silica gel (hexane : ethyl acetate = 2 : 1) to afford the product **1** (1.22 g, 72%). $[\alpha]_D^{20}$ = -24.4^o (c = 0. 55, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.33-6.18 (br, 1H), 4.02-3.85 (br, 1H), 3.66 (t, *J* = 6.0 Hz, 2H), 3.50-3.05 (m, 6H), 2.35-2.20 (m, 2H), 2.08-1.97 (m, 1H), 1.92-1.76 (m, 2H), 1.74-1.62 (m, 1H), 1.44 (s, 9H); ^{13}C NMR (75

MHz, $CDCl_3$) δ 156.5, 80.4, 57.0, 49.1, 48.5, 47.3, 42.9, 29.5, 28.4, 26.9, 23.8; IR (neat) υ = 2976, 1670, 1397, 1148, 1111 cm^{-1}; HRMS (ESI) m/z (%) Calcd for $C_{13}H_{26}ClN_2O_4S$ (MH^+): 341.1296, Found: 341.1286.

(2) Synthesis of compound 2

To a solution of compound **1** (1.22g, 3.58 mmol) in acetone (15 mL) was added NaI (5.3 g, 35.3 mmol) under N_2. The reaction mixture was stirred at reflux for 24 h, removed the solvent, diluted with CH_2Cl_2 (60 mL), washed with water and brine. The organic phase was dried over Na_2SO_4, filtrated and concentrated to give the crude iodine product (1.45 g, 96%), which was used for the next step directly without further characterization.

The above iodine compound (1.45 g, 3.36 mmol) and 1-methylimidazole (0.30 g, 3.69 mmol) were dissolved in CH_3CN (2 mL) and the solution was stirred for 14 h at 65°C, at which time the solvent was evaporated under reduced pressure. The residue was washed with Et_2O (2 x 5 mL) and dried to give the compound **2** (1.55 g, 90%). ^1H NMR (300 MHz, CD_3OD) δ 9.01 (s, 1H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.59 (d, *J* = 1.6 Hz, 1H), 4.43 (t, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 3.87-3.79 (m, 1H); 3.37-3.23 (m, 3H), 3.15 (t, *J* = 7.2 Hz, 2H), 3.11-3.02 (m, 1H), 2.36 (dt, *J* = 14.4 and 7.2 Hz, 2H), 2.00-1.77 (m, 4H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ 156.7, 156.3, 138.0, 125.2, 123.6, 81.2, 80.9, 58.8, 58.5, 45.9, 36.9, 29.6, 29.2, 28.8, 25.9, 24.4, 23.6. This compound was used for the next step without further characterization.

(3) Synthesis of compound 3

The compound **2** (1.55 g, 3.02 mmol) was dissolved in a 1 : 1 mixture of trifluoroacetic acid and dichloromethane (10 mL) and the solution was stirred for 2 h at rt, at which time the solvent was evaporated under reduced pressure. The pH was adjusted to 8 with

aqueous $NaHCO_3$ and $LiNTf_2$ (0.87 g, 3.02 mmol) was added and the mixture was stirred for 1 h at rt, extracted with CH_2Cl_2 (3 x 20 mL) and the organic phase was dried over $NaSO_4$ and purified by flash chromatography on silica gel (CH_2Cl_2 : MeOH = 10 : 1) to afford the product **3** (1.51 g, 88% for 2 steps). $[\alpha]_D^{20}$ = +0.42° (c = 0.71, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 8.85 (s, 1H), 7.62 (t, *J* = 1.6 Hz, 1H), 7.57 (t, *J* = 1.6 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.72-3.65 (m, 1H); 3.45 (dd, *J* = 15.2 and 4.4 Hz, 1H), 3.40-3.25 (m, 3H), 3.21 (t, *J* = 7.2 Hz, 2H), 2.38 (dt, *J* = 14.4 and 7.2 Hz, 2H), 2.23-2.00 (m, 3H), 1.80-1.70 (m, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 138.1, 125.3, 123.6, 121.2 (*q*, J = 319.2 Hz, 2C), 62.0, 46.6, 44.6, 44.3, 36.6, 28.1, 25.6, 23.9; IR (neat) υ = 1568, 1347, 1187, 1133, 1056 cm^{-1}; HRMS (ESI +) m/z (%) Calcd for $[C_{12}H_{23}N_4OS]^+$: 287.1542, Found: 287.1536; HRMS (ESI -) m/z (%) Calcd for $[N(SO_2CF_3)_2]^-$: 279.9173, Found: 279.9202.

(4) (R)-2-[(S)-2-Nitro-1-phenylethyl]hexanal 4b:[1] $[\alpha]_D^{20}$ = -5.5° (c = 0.22 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (d, *J* = 2.8 Hz, 1H), 7.38-7.15 (m, 5H), 4.73-4.62 (m, 2H), 3.78 (dt, *J* = 9.6 and 5.2 Hz, 1H), 2.73-2.67 (m, 1H), 1.53-1.11 (m, 6H), 0.78 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.2, 136.8, 129.1, 128.1, 128.0, 78.4, 53.9, 43.1, 28.5, 27.0, 22.4, 13.6; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 15/85, flow rate 1 mL/min, λ = 254 nm): t_{minor} = 12.8 min, t_{major} = 16.0 min; ee = 68%.

(5) (R)-2-[(S)-1-(4-Methylphenyl)-2-Nitroethyl]hexanal 4c: $[\alpha]_D^{20}$ = +53.9° (c = 0.18 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.70 (d, *J* = 2.8 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 4.72-4.58 (m, 2H), 3.73 (dt, *J* = 9.6 and 5.2 Hz, 1H), 2.71-2.63 (m, 1H), 2.32 (s, 3H), 1.53-1.08 (m, 6), 0.79 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 137.8, 133.6, 129.7, 127.8, 78.5, 53.9, 42.8, 28.5, 27.0, 22.5, 21.0,

13.6; IR (neat) υ = 2932, 1723, 1554, 1379, 1117 cm^{-1}; HRMS (ESI) m/z (%) Calcd for $C_{15}H_{22}NO_3$ (MH^+): 264.1594, Found: 264.1584; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 20/80, flow rate 1 mL/min, λ = 254 nm): t_{minor} = 9.7 min, t_{major} = 11.3 min; ee = 67%.

(6) (R)-2-[(S)-1-(4-Methoxylphenyl)-2-Nitroethyl]pentanal 4d:[1] $[\alpha]_D^{20}$ = +29.2° (c = 0.12 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.70 (d, *J* = 2.8 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 4.70-4.55 (m, 2H), 3.80-3.69 (m, 1H), 2.70-2.60 (m, 1H), 1.60-1.10 (m, 4H), 0.81 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 159.3, 129.0, 128.5, 114.5, 78.6, 55.2, 54.0, 42.5, 29.4, 19.8, 13.9; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 10/90, flow rate 1 mL/min, λ = 254 nm): t_{minor} = 20.5 min, t_{major} = 22.4 min; ee = 67%.

(7) (2*R*, 3*S*)-2-(methylethyl)-4-nitro-3-phenylbutanal 4e:[2] $[\alpha]_D^{20}$ = +32.7° (c = 0.15 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.93 (d, *J* = 2.4 Hz, 1H), 7.40-7.13 (m, 5H), 4.70-4.53 (m, 2H), 3.90 (dt, *J* = 10.4 and 4.4 Hz, 1H), 2.80-2.73 (m, 1H), 1.75-1.67 (m, 1H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 137.1, 129.1, 128.1, 127.9, 79.0, 58.8, 41.9, 27.9, 21.6, 17.0; HPLC (Chiralpak AS-H, i-Propanol/Hexane = 5/95, flow rate 0.5 mL/min, λ = 254 nm): t_{minor} = 30.3 min, t_{major} = 31.8 min; ee = 66%.

(8) (2*R*, 3*S*)-2-(methylethyl)-4-nitro-3-(4-mthylphenyl)butanal 4f: $[\alpha]_D^{20}$ = +39.2° (c = 0.25 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.92 (d, *J* = 2.4 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 2H); 4.64 (dd, *J* = 12.8 and 4.0 Hz, 1H), 4.54 (d, *J* = 12.0 and 9.6 Hz, 1H), 3.86 (dt, *J* = 10.0 and 4.4 Hz, 1H), 2.73 (ddd, *J* = 10.8, 4.4, and 2.8 Hz, 1H), 1.78-1.68 (m, 1H), 1.09 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75

MHz, $CDCl_3$) δ 204.5, 137.8, 133.9, 129.8, 127.8, 79.1, 58.8, 41.6, 27.8, 21.6, 21.0, 16.9; IR (neat) υ = 2915, 1730, 1718, 1552, 1179 cm^{-1}; HRMS (ESI) m/z (%) Calcd for $C_{14}H_{20}NO_3$ (MH^+): 250.1438, Found: 250.1443; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 5/95, flow rate 0.5 mL/min, λ = 254 nm): t_{minor} = 30.5 min, t_{major} = 32.2 min; ee = 73%.

(9) (R)-2-[(S)-2-Nitro-1-phenylethyl]pentanal 4g:[1] $[\alpha]_D^{20}$ = -13.3° (c = 0.15 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.70 (d, *J* = 2.8 Hz, 1H), 7.38-7.15 (m, 5H), 4.75-4.61 (m, 2H), 3.77 (dt, *J* = 9.6 and 4.2 Hz, 1H), 2.75-2.67 (m, 1H), 1.53-1.10 (m, 4H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.2, 137.8, 129.1, 128.2, 128.1, 128.0, 78.4, 53.8, 43.2, 29.5, 19.8, 13.9; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 20/80, flow rate 1 mL/min, λ = 254 nm): t_{minor} = 11.9 min, t_{major} = 15.5 min; ee = 64%.

(10) (R)-2-[(S)-1-(4-Methylphenyl)-2-Nitroethyl]pentanal 4h: $[\alpha]_D^{20}$ = +41.8° (c = 0.11 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (d, *J* = 2.8 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H); 4.68 (dd, *J* = 12.8 and 5.6 Hz, 1H), 4.61 (d, *J* = 12.8 and 9.6 Hz, 1H), 3.73 (dt, *J* = 9.6 and 5.2 Hz, 1H), 2.70-2.64 (m, 1H), 2.33 (s, 3H), 1.60-1.10 (m, 4H), 0.81 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 137.9, 133.6, 129.8, 127.8, 78.5, 53.9, 42.9, 29.4, 21.1, 19.8, 13.9; IR (neat) υ = 1722, 1553, 1515, 1379, 817 cm^{-1}; HRMS (ESI) m/z (%) Calcd for $C_{14}H_{20}NO_3$ (MH^+): 250.1438, Found: 250.1426; HPLC (Chiralcel OD-H, i-Propanol/Hexane = 20/80, flow rate 1 mL/min, λ = 254 nm): t_{minor} = 10.4 min, t_{major} = 12.6 min; ee = 68%.

(11) (S)-2-((R)-2-nitro-1-phenylethyl)cyclohexanone 4i:[3] $[\alpha]_D^{20}$ = -28° (c = 0.05 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.23 (m, 3H), 7.17 (d, J = 6.8 Hz, 2H), 4.94

(dd, *J* = 12.4 and 4.4 Hz, 1H), 4.63 (dd, J = 12.4 and 10.0 Hz, 1H), 3.76 (dt, J = 10.0 and 4.8 Hz, 1H), 2.72-2.65 (m, 1H), 2.52-2.34 (m, 2H), 2.13-2.04 (m, 1H), 1.83-1.50 (m, 4H), 1.30-1.18 (m, 1H); HPLC (Chiralpak AS-H, i-Propanol/Hexane = 10/90, flow rate 0.7 mL/min, λ = 238 nm): t_{minor} = 22.8 min, t_{major} = 34.5 min; ee = 88%.

References:

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