Supporting Information

Asymmetric Reformatsky reaction of aldehydes catalyzed by novel β -amino alcohols and zinc complexes

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Experimental Section

General Methods. ^1H - and ^{13}C -NMR were recorded at 400 and 100 MHz, respectively, using CDCl_3 as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl_3 : 7.26 for ^1H , 77.0 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. Enantiomeric excesses were determined by chiral GC analysis on Chirasil DEX CB column or by chiral HPLC analysis on Chiralcel OD or AS column in comparison with the authentic racemates. All aldehydes and substituted salicylaldehydes were purchased and used directly without further purification. ZnMe_2 2M in toluene (Aldrich) was used for all the reactions. Solvents were purified by usual method. CH_2Cl_2 was distilled over CaH_2 . Other solvents were dried over Na.

Data of Ligands

1a: ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.37 (m, 6H), 7.18-7.24 (m, 4H), 7.13 (m, 1H), 6.80 (m, 2H), 6.70 (m, 1H), 4.90 (d, J = 6.4 Hz, 1H), 3.89 (d, J = 6.4 Hz, 1H), 3.81 (d, J = 13.6 Hz, 1H), 3.56 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.8, 140.3, 137.6, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 126.8, 122.5, 119.1, 116.4, 68.2, 50.2. [1]

1b: ^1H NMR (400 MHz, CDCl_3) δ 7.20-7.38 (m, 10H), 6.70 (m, 1H), 6.60-6.66 (m, 2H), 4.92 (d, J = 6.0 Hz, 1H), 4.89 (d, J = 6.4 Hz, 1H), 3.80 (d, J = 13.6 Hz, 1H), 3.54 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.9, 140.3, 137.7, 129.9, 128.7, 128.5, 128.4, 128.4, 128.2, 126.8, 126.0, 125.2, 121.9, 118.6, 68.4, 50.3, 15.7. [1]

1c: ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.36 (m, 6H), 7.18-7.22 (m, 5H), 6.67 (m, 2H), 6.60-6.66 (m, 2H), 4.94 (d, J = 6.0 Hz, 1H), 3.89 (d, J = 5.6 Hz, 1H), 3.83 (d, J = 13.2 Hz, 1H), 3.57 (d, J = 13.6 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.9, 140.4, 137.5, 136.8, 128.6, 128.4, 128.4, 128.2, 128.1, 126.7, 126.6, 126.0, 122.8, 118.3, 109.7, 67.9, 50.5, 34.7, 29.5. [1]

1e: ^1H NMR (400 MHz, CDCl_3) δ 7.11-7.36 (m, 11H), 6.65 (s, 1H), 4.92 (d, J = 6.4 Hz, 1H), 3.87 (d, J = 6.0 Hz, 1H), 3.76 (d, J = 13.2 Hz, 1H), 3.54 (d, J = 13.2 Hz, 1H), 2.14 (m, 15H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 154.5, 140.6, 137.8, 136.3, 128.6, 128.5, 128.4, 128.2, 128.1, 126.8, 123.2, 122.8, 122.0, 68.2, 51.1, 40.4, 37.2, 37.0, 34.1, 31.6, 29.2. [1]

Data of Products

3a: 68% Yield, ee = 63%. HPLC (OD, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 13.1 (S), 17.3 (R). 1H NMR (CDCl₃, 400 MHz): 7.31-7.18 (m, 5H), 5.07-5.02 (m, 1H), 4.09 (q, J = 8.1 Hz, 2H), 3.25 (d, J = 3.6 Hz, 1H), 2.72-2.57 (m, 2H), 1.18 (t, J = 6.9 Hz, 3H). 13C NMR (CDCl₃, 100 MHz): 172.31, 142.51, 128.47, 127.71, 125.62, 70.26, 60.79, 43.32, 14.08. [2]

3b: 63% Yield, ee = 61%. HPLC (AS, 5 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 17.8 (S), 20.1 (R). 1H NMR (400 MHz, CDCl₃) δ 7.42-7.33 (m, 4H), 7.32-7.26 (m, 1H), 5.19-5.09 (m, 1H), 4.19 (q, J = 7.1 Hz, 3H), 3.30-3.21 (m, 1H), 2.84-2.64 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 172.4, 142.5, 128.6, 127.8, 125.7, 70.3, 60.9, 43.3, 14.1. [2]

3c: 60% Yield, ee = 60%. HPLC (AS, 5 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 12.0 (S), 14.3 (R). 1H NMR (400 MHz, CDCl₃) δ 7.32 (s, 1H), 5.15-5.05 (m, 1H), 4.18 (q, J = 7.1 Hz, 1H), 3.36 (d, J = 3.5 Hz, 1H), 2.80-2.60 (m, 1H), 1.27 (t, J = 7.1 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 172.3, 141.0, 133.5, 128.7, 127.1, 69.6, 61.0, 43.2, 14.1. [3]

3d: 60% Yield, ee = 60%. HPLC (AS, 5 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 18.0 (S), 20.3 (R). 1H NMR (400 MHz, CDCl₃) δ 7.51-7.45 (m, 2H), 7.30-7.22 (m, 2H), 5.14-5.04 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.37 (d, J = 3.5 Hz, 1H), 2.78-2.63 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 172.3, 141.5, 131.6, 127.4, 121.6, 69.7, 61.0, 43.1, 14.1. [4]

3e: 60% Yield, ee = 60% %. HPLC (AS, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 39.1 (S), 31.3 (R). 1H NMR (400 MHz, CDCl₃) δ 7.35-7.28 (m, 2H), 6.94-6.84 (m, 2H), 5.09 (dt, J = 9.1, 3.6 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.80 (s, 2H), 3.15 (d, J = 3.4 Hz, 1H), 2.76 (dd, J = 16.3, 9.1 Hz, 1H), 2.68 (dd, J = 16.3, 3.8 Hz, 1H), 1.27 (t, J = 7.2 Hz, 2H); 13C NMR (100 MHz, CDCl₃) δ 172.5, 159.2, 134.7, 127.0, 113.9, 70.0, 60.8, 55.3, 43.3, 14.2. [2]

3f: 65% Yield, ee = 81%. HPLC (OD, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 16.1 (major), 21.3 (minor). 1H NMR (400 MHz, CDCl₃) δ 8.05 (d, J=8.2 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.78 (d, J=8.2 Hz, 1H), 7.69 (d, J = 7.1 Hz, 1H), 7.45-7.53 (m, 3H), 5.91 (m, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.44 (s, 1H), 2.79-2.92 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ 172.7, 138.0, 133.7, 130.0, 129.0, 128.2, 126.2, 125.6, 125.5, 122.9, 122.8, 67.3, 61.0, 42.7, 14.2. [4]

3g: 68% Yield, ee = 80%. HPLC (AS, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 29.1 (major), 33.3 (minor). 1H NMR (400 MHz, CDCl₃) δ 7.90-7.77 (m, 1H), 7.58-7.42 (m, 1H), 5.31 (dt, J = 8.1, 4.0 Hz, 1H), 4.20 (q, J = 7.1 Hz, 1H), 3.39 (d, J = 3.5 Hz, 1H), 2.97-2.71 (m, 1H), 1.27 (t, J = 7.1 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 172.4, 139.9, 133.3, 133.0, 128.4, 128.0, 127.7, 126.2, 126.0, 124.5, 123.7, 70.4, 60.9, 43.3, 14.2. [4]

3h: 45% Yield, ee = 53%. HPLC (AS, 5 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 15.9 (S), 16.9 (R). 1H NMR (400 MHz, CDCl₃) δ 7.38 (dd, J = 1.8, 0.8 Hz, 1H), 6.34 (dd, J = 3.2, 1.8 Hz, 1H), 6.30-6.27 (m, J = 3.3 Hz, 1H), 5.14 (dt, J = 8.8, 4.5 Hz, 1H), 4.20 (q, J = 7.2 Hz, 3H), 3.21 (dd, J = 5.0,

3.3 Hz, 1H), 2.91 (dd, J = 16.5, 8.5 Hz, 1H), 2.83 (dd, J = 16.5, 4.1 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.0, 154.7, 142.2, 110.2, 106.3, 64.2, 61.0, 39.8, 14.1. [2]

3i: 58% Yield, ee = 63%. HPLC (OD, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 10.9 (major), 23.9 (minor). ¹H NMR (400 MHz, CDCl₃) δ 7.25 (m, 1H), 6.95-6.98 (m, 2H), 5.37 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.47 (d, J = 4.2 Hz, 1H), 2.82-2.91 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 171.9, 146.2, 126.7, 124.8, 123.6, 69.1, 66.5, 43.1, 14.1. [4]

3j: 62% Yield, ee = 33%. HPLC (OD, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 22.1 (major), 24.9 (minor). ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.42 (5H, m), 6.68 (1H, d, J = 16.0), 6.23 (1H, dd, J = 16.0, 6.1), 4.75 (1H, m), 4.21 (2H, q, J = 7.1), 3.10 (1H, d, J = 4.2), 2.69 (1H, dd, J = 16.3, 4.1), 2.61 (1H, dd, J = 16.3, 5.9), 1.30 (3H, t, J = 7.1), ¹³C NMR (100 MHz, CDCl₃) δ 172.2, 136.6, 130.7, 130.2, 128.7, 127.9, 126.6, 69.0, 60.9, 41.8, 14.3. [5]

3k: 52% Yield, ee = 25%. HPLC (OD, 10 % i-PrOH, 1.0 mL/min, 30 °C, 254 nm): tr/min = 12.9 (major), 14.9 (minor). ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.30 (m, 2H), 7.16-7.20 (m, 3H), 4.16 (q, J = 7.2 Hz, 2H), 4.02 (m, 1H), 3.09 (bs, 1H), 2.83 (m, 1H), 2.70 (m, 1H), 2.50 (dd, J = 3.5 Hz, 16.5 Hz, 1H), 2.44 (dd, J = 8.6 Hz, 16.6 Hz, 1H), 1.85 (m, 1H), 1.74 (m, 1H), 1.26 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 173.0, 141.7, 128.4, 128.3, 125.9, 67.1, 60.7, 41.3, 38.1, 31.7, 14.1. [4]

3l: 56% Yield, ee = 45%. GC (initial temperature 50 °C for 60 min, then 10 °C/min until 70 °C, then 70 °C for 20 min): tr/min = 70.9 (major), 71.9 (minor). ¹H NMR (400 MHz, CDCl₃) δ 4.18 (q, J = 7.2 Hz, 2H), 3.78 (m, 1H), 2.89 (d, J = 3.2 Hz, 1H), 2.50 (dd, J = 2.8 Hz, 16.3 Hz, 1H), 2.40 (dd, J = 9.5 Hz, 16.3 Hz, 1H), 1.71 (m, 1H), 1.27 (t, J = 7.2 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 72.6, 60.6, 38.4, 33.1, 18.3, 17.7, 14.1. [4]

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