Supporting Information for

Catalytic Asymmetric Synthesis of Tetrahydropyridazines via Inverse Electron-Demand aza-Diels-Alder Reaction of Enol Ethers with Azoalkenes

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I. General Remarks

¹H NMR spectra were recorded on a VARIAN Mercury 300 MHz spectrometer in CDCl₃. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data are reported as (s = single, d = double, t = triple, q = quartet, m = multiple or unresolved, and brs = broad single). ¹³C NMR spectra were recorded on a Bruker 100 MHz or 75 MHz spectrometer in CDCl₃. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Commercially available reagents were used without further purification. All reactions were monitored by TLC with silica gel-coated plates. Diastereomeric ratios were determined from crude ¹H NMR or HPLC analysis. Enantiomeric ratios were determined by HPLC, using a chiralpak IB-H column, a chiralpak AD-H column or a chiralcel AS-H column with hexane and *i*-PrOH as solvents and Azoalkenes¹ and chiral ligands L4-L7² were prepared according to the literature procedure. The absolute configuration of **3aa** were determined unequivocally according to the X-ray diffraction analysis, and those of other adducts were deduced on the basis of these results.

II. N-acyl Substituent Hydrazones Screening for Catalytic Asymmetric IEDDA of enol ethers with Azoalkenes



Table S-1. Optimization Results^a

Entry	Hydrazone	Time/h	Yield/% ^b	Ee/% ^c
1	5	12	78	0
2	6	12	67	0
3	7	12	11	n.d
4	8	12	trace	n.d

^{*a*} All reactions were carried out with 0.20 mmol of hydrazone and 0.50 mmol of **2a** in 2.0 mL of CH₂Cl₂. ^{*b*} Isolated yield. ^{*c*} Ee was determined by HPLC analysis.

III. General Procedure for Catalytic Asymmetric IEDDA of Enol Ethers with Azoalkenes Catalyzed by $Cu(II)/(S,S_p)$ -^tBu-Phosferrox

Under argon atmosphere, (S, S_p) -^{*t*}Bu-Phosferrox (11 mg, 0.022 mmol) and Cu(OTf)₂ (7.2 mg, 0.020 mmol) were dissolved in 2 mL of DCM, and stirred at room temperature for about 0.5 h. After the reaction temperature was dropped to -20 °C, α -halogeno-hydrozone **2** (0.2 mmol), Na₂CO₃ (0.4 mmol) were added sequentially. Then, the Enol Ether **1** (0.8 mmol) was added. Once starting material was consumed (monitored by TLC), the organic solvent was removed and the residue was purified by column chromatography to give the cycloaddition product, which was then directly analyzed by HPLC to determine the enantiomeric excess.

(R)-(6-(tert-butoxy)-3-phenyl-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanone (Table 2, entry 2): Yield (83%); white solid; $[\alpha]^{25}_{D} = -218.7$ (*c* 0.88, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.74 (d, *J* = 6.3 Hz, 2H), 7.63-7.60 (m, 2H), 7.47-7.39 (m, 3H), 7.33-7.30 (m, 3H), 6.39 (s, 1H), 2.99-2.85 (m, 1H), 2.72-2.64 (m, 1H), 2.19-2.12 (m, 1H), 1.90-1.79 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.3, 148.3, 137.1, 135.4, 130.0, 129.5, 129.0, 128.1, 127.1, 125.2, 74.5, 68.9, 28.4, 25.1, 18.5. HRMS: calcd. for C₂₁H₂₄N₂O₂ + H⁺: 337.1871, found: 337.1909. The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); tr = 5.31 and 7.19 min.



(R)-(6-(tert-butoxy)-3-(4-methoxyphenyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanone (Table 2, entry 3): Yield (83%); white solid; $[\alpha]^{25}_{D} = -211.6$ (*c* 0.50, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.75 (d, *J* = 6.9 Hz, 2H), 7.57 (d, *J* = 8.1 Hz 2H), 7.45-7.42 (m, 3H), 7.33-7.31 (m, 3H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.34 (s, 1H), 3.82 (s, 3H), 2.94-2.84 (m, 1H), 2.69-2.62 (m, 1H), 2.18-2.11 (m, 1H), 1.91-1.80 (m, 1H), 1.32 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 160.3, 148.3, 135.6, 135.2, 130.8, 129.9, 129.5, 127.2, 126.7, 113.5, 74.5, 68.9, 55.2, 28.5, 25.3, 18.5; HRMS Calcd. For C₂₂H₂₆N₂O₃ + H⁺: 367.1977, found: 367.2041. The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 6.99 and 9.41 min.



(R)-(6-(tert-butoxy)-3-(p-tolyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanon e (Table 2, entry 4): Yield (90%); white solid; $[\alpha]^{25}_{D} = -220.5$ (*c* 0.88, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.74 (d, *J* = 6.3 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.46-7.40 (m, 3H), 7.14-7.10 (m, 2H), 6.38 (s, 1H), 2.90-2.83 (m, 1H), 2.70-2.62 (m, 1H), 2.34 (s, 3H), 2.17-2.10 (m, 1H), 1.88-1.82 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.4, 148.6, 139.1, 135.5, 134.5, 130.0, 129.5, 128.9, 127.2, 125.3, 74.6, 69.0, 28.5, 25.3, 18.6; HRMS Calcd. For C₂₂H₂₆N₂O₂ + H⁺: 351.2028, found: 351.2065. The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda = 254$ nm); t_r = 6.63 and 10.56 min.



(R)-(6-(tert-butoxy)-3-(m-tolyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methano e (Table 2, entry 5): Yield (71%); white solid; $[\alpha]^{25}_{D} = -201.5$ (*c* 1.02, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.76 (d, *J* = 6.9 Hz, 2H), 7.45-7.41 (m, 5H), 7.24-7.12 (m, 2H), 6.38 (s, 1H), 3.00-2.84 (m, 1H), 2.72-2.63 (m, 1H), 2.32 (s, 3H), 2.18-2.13 (m, 1H), 1.87-1.78 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.5, 148.7, 137.8, 137.2, 135.5, 130.1, 129.8, 129.7, 128.2, 127.2, 126.1, 122.5, 74.7, 69.0, 28.6, 25.3, 21.5, 18.7; HRMS Calcd. For C₂₂H₂₆N₂O₂ + H⁺: 351.2028, found: 351.2066. The product was analyzed by HPLC to determine the enantiomeric excess: 87% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 5.04 and 6.80 min.



(R)-(6-(tert-butoxy)-3-(o-tolyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanon e (Table 2, entry 6): Yield (82%); white solid; $[\alpha]^{25}_{D} = -239.5$ (*c* 0.92, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.62 (d, *J* = 6.0 Hz, 2H), 7.36-7.24 (m, 4H), 7.19-7.10 (m, 3H), 6.40 (s, 1H), 3.01-2.87 (m, 1H), 2.45-2.37 (m, 1H), 2.13 (s, 3H), 2.10-2.06 (m, 1H), 1.94-1.87 (m, 1H), 1.33 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.7, 152.8, 138.1, 136.0, 135.7, 130.9, 129.7, 129.0, 128.1, 127.6, 127.3, 125.5, 74.6, 68.6, 28.5, 25.6, 22.6, 20.5; HRMS Calcd. For C₂₂H₂₆N₂O₂ + H⁺: 351.2028, found: 351.2065. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 5.22 and 5.98 min.



(R)-(3-(4-bromophenyl)-6-(tert-butoxy)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 7): Yield (92%); white solid; $[\alpha]^{25}_{D} = -214.1$ (*c* 0.54, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.71 (d, *J* = 6.6 Hz, 2H), 7.49-7.39 (m, 7H), 6.37 (s, 1H), 2.95-2.82 (m, 1H), 2.66-2.58 (m, 1H), 2.19-2.11 (m, 1H), 1.88-1.79 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.4, 147.4, 136.1, 135.3, 131.3, 130.1, 129.5, 127.3, 126.9, 123.3, 74.7, 68.9, 28.5, 25.1, 18.4; HRMS Calcd. For C₂₁H₂₃BrN₂O₂ + H⁺: 415.0976, found: 415.1011. The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda = 254$ nm); t_r = 7.60 and 11.58 min.



(R)-(6-(tert-butoxy)-3-(4-chlorophenyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 8): Yield (92%); white solid; $[\alpha]^{25}_{D} = -201.5$ (*c* 0.84, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.71 (d, *J* = 6.6 Hz, 2H), 7.49-7.39 (m, 7H), 6.37 (s, 1H), 2.95-2.82 (m, 1H), 2.66-2.58 (m, 1H), 2.19-2.11 (m, 1H), 1.88-1.79 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.4, 147.3, 135.6, 135.3, 134.9, 130.1, 129.5, 128.4, 127.3, 126.6, 74.7, 68.9, 28.5, 25.1, 18.5; HRMS Calcd. For C₂₁H₂₃ClN₂O₂ + H⁺: 371.1482, found: 371.1519. The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 7.19 and 10.80 min.



(R)-(6-(tert-butoxy)-3-(3-chlorophenyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 9): Yield (78%); white solid; $[\alpha]^{25}_{D} = -226$ (*c* 0.06, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.73 (d, *J* = 6.3 Hz, 2H), 7.60 (m, 1H), 7.49-7.41 (m, 4H), 7.30-7.20 (m, 2H), 6.38 (s, 1H), 2.95-2.82 (m, 1H), 2.67-2.58 (m, 1H), 2.18-2.12 (m, 1H), 1.88-1.77 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.4, 147.3, 135.6, 135.3, 134.9, 130.1, 129.5, 128.4, 127.3, 126.6, 74.7, 68.9, 28.5, 25.1, 18.5; HRMS Calcd. For C₂₁H₂₃ClN₂O₂ + H⁺: 371.1482, found: 371.1519. The product was analyzed by HPLC to determine the enantiomeric excess: 72% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 7.11 and 11.39 min.



(R)-(6-(tert-butoxy)-3-(2-chlorophenyl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 10): Yield (90%); white solid; $[\alpha]^{25}D = -208.1$ (*c* 0.97, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.74 (d, *J* = 6.3 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.46-7.40 (m, 3H), 7.14-7.10 (m, 2H), 6.38 (s, 1H), 2.90-2.83 (m, 1H), 2.70-2.62 (m, 1H), 2.34 (s, 3H), 2.17-2.10 (m, 1H), 1.88-1.82 (m, 1H), 1.31 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.5, 151.6, 137.9, 135.1, 132.2, 130.1, 129.9, 129.7, 129.5, 128.6, 127.2, 126.6, 74.7, 69.1, 28.6, 25.4, 22.7; HRMS Calcd. For C₂₁H₂₃ClN₂O₂ + H⁺: 371.1482, found: 371.1519. The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 6.37 and 7.71 min.



(R)-(6-(tert-butoxy)-3-(naphthalen-1-yl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 11): Yield (85%); white solid; $[\alpha]^{25}_{D} = -48.4$ (*c* 0.64, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 8.03 (s, 1H), 7.80-7.69 (m, 6H), 7.48-7.45 (m, 5H), 6.42 (s, 1H), 3.05-2.98 (m, 1H), 2.88-2.79 (m, 1H), 2.23-2.19 (m, 1H), 1.95-1.87 (m, 1H), 1.33 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 157.6, 148.4, 135.5, 134.8, 133.6, 132.9, 130.2, 129.7, 128.4, 127.9, 127.6, 127.3, 126.6, 126.2, 125.2, 122.9, 74.8, 69.1, 28.6, 25.3, 18.5; HRMS Calcd. For C₂₅H₂₆N₂O₂ + H⁺: 387.2028, found: 387.2064. The product was analyzed by HPLC to determine the enantiomeric excess: 86% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 6.83 and 9.33 min.



(R)-(6-(tert-butoxy)-3-(naphthalen-2-yl)-5,6-dihydropyridazin-1(4H)-yl)(phenyl) methanone (Table 2, entry 12): Yield (88%); white solid; $[\alpha]^{25}D = -200.5$ (*c* 0.44, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 8.03 (m, 1H), 7.80-7.69 (m, 6H), 7.48-7.45 (m, 5H), 6.42 (s, 1H), 3.82 (s, 3H), 3.05-2.98 (m, 1H), 2.88-2.79 (m, 1H), 2.23-2.18 (m, 1H), 1.93-1.88 (m, 1H), 1.33 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.5, 148.3, 135.5, 134.7, 133.5, 132.9, 130.1, 129.6, 128.3, 127.8, 127.5, 127.3, 126.5, 126.2, 125.2, 122.8, 74.7, 69.1, 28.6, 25.3, 18.5; HRMS Calcd. For C₂₅H₂₆N₂O₂ + H⁺: 387.2028, found: 387.2064. The product was analyzed by HPLC to determine the enantiomeric excess: 84% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 6.82 and 9.33 min



((4S,6R)-6-(tert-butoxy)-4-chloro-3-phenyl-5,6-dihydropyridazin-1(4H)-yl)(phen yl)methanone (Table 2, entry 16): Yield (62%); white solid; $[\alpha]^{25}_{D} = -230.5$ (*c* 0.80, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.77 -7.69 (m, 4H), 7.48-7.33 (m, 6H), 6.41 (s, 1H), 4.97 (d, J = 5.7 Hz, 1H), 2.78-2.73 (m, 1H), 2.37-2.32 (m, 1H), 2.19-2.11 (m, 1H), 1.88-1.79 (m, 1H), 1.35 (s, 9H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 169.8, 143.7, 134.5, 130.6, 129.7, 129.5, 128.3, 127.4, 126.2, 75.3, 68.1, 40.9, 34.2, 28.5; HRMS Calcd. For C₂₁H₂₃ClN₂O₂ + H⁺: 371.1482, found: 371.1520. The product was analyzed by HPLC to determine the enantiomeric excess: 83% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda = 254$ nm); t_r = 7.36 and 10.60 min



(R)-(6-ethoxy-3-phenyl-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanone

(Scheme 2): Yield (88%); white solid; $[\alpha]^{25}_{D} = -184.6$ (*c* 0.94, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.62-7.61 (m, 2H), 7.50-7.41 (m, 3H), 7.33-7.31(m, 3H), 6.19 (s, 1H), 3.81-3.71 (m, 2H), 2.84-2.65 (m, 2H), 2.35-2.30 (m, 1H), 1.91-1.85 (m, 1H), 1.20 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, TMS, 75 MHz) 170.8, 148.0, 136.9, 134.9, 130.1, 129.7, 129.0, 128.1, 127.1, 125.2, 74.1, 63.9, 23.1, 18.3, 15.1. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, $\lambda = 254$ nm); t_r = 5.42 and 7.01 min.



(R)-phenyl(3-phenyl-6-propoxy-5,6-dihydropyridazin-1(4H)-yl)methanone

(Scheme 3): Yield (94%); white solid; $[\alpha]^{25}_{D} = -130.5$ (*c* 0.88, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.77 (d, J = 7.8 Hz, 2H), 7.62-7.60 (m, 2H), 7.49-7.41 (m, 3H), 7.33-7.31 (m, 3H), 6.18 (s, 1H), 3.74-3.59 (m, 2H), 2.85-2.68 (m, 2H), 2.38-2.31 (m, 1H), 1.90-1.83 (m, 1H), 1.62-1.52 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 170.8, 148.1, 136.9, 134.9, 130.1, 129.7, 129.0, 128.1, 127.1, 125.3, 74.3, 70.0, 23.0, 22.8, 18.3, 10.4. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda = 254$ nm); tr = 6.19 and 7.53 min



(R)-(6-butoxy-3-phenyl-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methanone

(Scheme 2): Yield (95%); white solid; $[\alpha]^{25}_{D} = -124.7$ (*c* 0.66, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.77 (d, *J* = 7.8 Hz, 2H), 7.63-7.60 (m, 2H), 7.49-7.41 (m, 3H), 7.33-7.31 (m, 3H), 6.18 (s, 1H), 3.70 (q, *J*₁ = 6.9 Hz, *J*₂ = 19.2 Hz, 2H), 2.84-2.71 (m, 2H), 2.35-2.30 (m, 1H), 1.92-1.80 (m, 1H), 1.57-1.52 (m, 2H), 1.35-1.29 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 170.9, 148.2, 137.0, 135.0, 130.2, 129.7, 129.1, 128.2, 127.2, 125.3, 74.3, 68.3, 31.7, 23.2, 19.2, 18.4, 13.8. The product was analyzed by HPLC to determine the enantiomeric excess: 88% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda = 254$ nm); t_r = 5.96 and 7.25 min



(R)-(6-(2-chloroethoxy)-3-phenyl-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methan one (Scheme 2): Yield (93%); white solid, $[\alpha]^{25}_{D} = -94.5$ (*c* 0.60, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.77 (d, *J* = 6.6 Hz, 2H), 7.62-7.60 (m, 2H), 7.50-7.41 (m, 3H), 7.34-7.31 (m, 3H), 6.21 (s, 1H), 4.07-3.93 (m, 2H), 3.70-3.60 (m, 2H), 2.91-2.68 (m, 2H), 2.45-2.37 (m, 1H), 1.95-1.88 (m, 1H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 171.1, 148.5, 136.8, 134.6, 130.5, 129.9, 129.3, 128.3, 127.3, 125.3, 74.5, 68.5, 43.0, 23.0, 18.3; HRMS Calcd. For C₁₉H₁₉ClN₂O₂ + H⁺: 343.1169, found: 343.1205. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 10.61 and 14.02 min.



(R)-(3-(4-bromophenyl)-6-ethoxy-5,6-dihydropyridazin-1(4H)-yl)(phenyl)methan one (Scheme 2): Yield (95%); white solid, $[\alpha]^{25}_{D} = -184.5$ (*c* 0.71, CH₂Cl₂); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.73 (d, *J* = 6.6 Hz, 2H), 7.51-7.42 (m, 7H), 6.17 (s, 1H), 3.82-3.70 (m, 2H), 2.87-2.74 (m, 1H), 2.68-2.60 (m, 1H), 2.37-2.30 (m, 1H), 1.91-1.81 (m, 1H), 1.23 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 170.7, 147.1, 135.9, 134.9, 131.3, 130.3, 129.6, 127.3, 126.8, 123.3, 74.1, 64.1, 23.1, 18.2, 15.1; The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 7.73 and 10.02 min.

IV. Procedure for Transformation of 3ae



A suspension of Pd/C (10 mg) and **3ae** (0.3 mmol) in MeOH (5 mL) was stirred at 40 °C under 30 atm hydrogen atmosphere. After being stirred for 15 h, the mixture was filtrated through a pad of Celite and the filtration was concentrated in vacuo, the residue was purified by column chromatography on silica gel to afford the desired the product **4ae** in 95% yield (dr > 20:1), which was then directly analyzed by HPLC to determine the enantiomeric excess.



((3R,6R)-6-(2-chloroethoxy)-3-phenyltetrahydropyridazin-1(2H)-yl)(phenyl)meth anone (Scheme 3): Yield (95%); white solid; $[\alpha]^{25}_{D} = -195.5$ (*c* 0.80, CHCl₃); ¹H NMR (CDCl₃, TMS, 300 MHz) 7.69 (d, *J* = 6.9 Hz, 2H), 7.41-7.38 (m, 3H), 7.27-7.26 (m, 6H), 6.00 (s, 1H), 4.18-4.14 (m, 1H), 4.00-3.91 (m, 2H), 3.79-3.69 (m, 3H), 2.23-2.01 (m, 4H); ¹³C NMR (CDCl₃, TMS, 75 MHz) δ 167.6, 139.8, 130.1, 128.3, 128.4, 127.6, 127.4, 126.6, 76.1, 67.8, 60.1, 28.8, 24.3; HRMS Calcd. For C₁₉H₂₁ClN₂O₂ + H⁺: 345.1325, found: 345.1363. The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak IB-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); t_r = 10.12 and 12.02 min.

V. References

- 1 a) J.-R. Chen, W.-R. Dong, M. Candy, F.-F. Pan, M. Jörres, C. Bolm, *J. Am. Chem.* Soc. 2012, 134, 6924; b) M. S. South, T. L. Jakuboski, M. D. Westmeyer, D. R. Dukesherer, *J. Org. Chem.* 1996, 61, 8921.
- 3. C. J. Richards, A. W. Mulvaney, Tetrahedron: Asymmetry 1996, 7, 1419.

VI. ¹H NMR and ¹³C NMR spetra














































NOE spectrum of 3la





















S-46







COSY and ROESY Spectra of 4ae





VII. HPLC Chromatograms



Data File D:\LC\DATA\WL\WL-4-1\WL-4-1-2 2013-12-06 18-39-17\083-0101.D Sample Name: WL-4-1A-2

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Totals :	4950.73804	587.56738					

Instrument 1 4/29/2014 10:08:25 AM LJ





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Instrument 1 4/29/2014 11:07:01 AM LJ

Instrument 1 4/30/2014 2:55:36 PM WL



Instrument 1 4/29/2014 10:23:40 AM LJ



Instrument 1 4/29/2014 10:53:25 AM LJ



Instrument 1 4/29/2014 10:55:08 AM LJ



Instrument 1 4/29/2014 10:52:19 AM LJ



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Instrument 1 4/29/2014 3:12:25 PM WL


Instrument 1 4/29/2014 3:13:45 PM WL



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Instrument 1 3/12/2015 10:29:24 AM HR



Instrument 1 3/12/2015 10:25:07 AM HR



Instrument 1 4/29/2014 11:27:46 AM LJ



Instrument 1 4/29/2014 11:32:20 AM LJ



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Instrument 1 4/29/2014 11:09:26 AM LJ



Instrument 1 4/29/2014 11:08:45 AM LJ



Instrument 1 3/12/2015 10:41:39 AM HR



Instrument 1 3/12/2015 10:44:24 AM HR



Data File D:\LC\DATA\WL\WL-5-84\WL-5-84-HYDR0GENATION 2014-07-16 19-40-00\042-0201.D Sample Name: WL-5-84-RAC

Acq. Operator : LJ Seq. Line : 2 Acq. Instrument : Instrument 1 Location : Vial 42 Injection Date : 7/16/2014 7:52:26 PM Inj: 1 Inj Volume : 5 µl Acq. Method : D:\LC\DATA\WL\WL-5-84\WL-5-84-HYDR0GENATION 2014-07-16 19-40-00\ASH-10-90-1ML-254NM.M Last changed : 7/16/2014 7:38:20 PM by LJ Analysis Method : D:\LC\DATA\UL\UL-5-84\UL-5-84-HYDROGENATION 2014-07-16 19-40-00\042-0201. D\DA.M (ASH-10-90-1ML-254NM.M) Last changed : 3/24/2015 8:27:09 PM by HR (modified after loading) W/DIA, Wavelength=254 nm (D\LCUDATAW/LWL-584W/L5-84-HYDROGENATION 2014-07-16 19-40-00/042-0201.D) 2 mAU ā 25 20 12.012 15 10 -5 16 18 10 12 14 min _____ Area Percent Report Sorted By Sional Multiplier 1.0000 : 1.0000 Dilution : Use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=254 nm Peak RetTime Type Width Height Area Area # [min] [min] mAU *5 [mAU] % 1 10.170 VB 0.5242 872.56244 25.33277 50.4484 2 12.012 BB 0.7827 857.04962 15.62326 49.5516 1729.61206 40.95603 Totals :

Instrument 1 3/24/2015 8:27:14 PM HR



Instrument 1 3/24/2015 8:24:43 PM HR