# Enantioselective Conjugate Hydrosilylation of $\alpha,\beta$ -Unsaturated Ketones

Huan Yang,<sup>[a]#</sup> Guanglin Weng,<sup>[a]#</sup> Dongmei Fang, <sup>[b]</sup> Changjiang Peng, <sup>[a]</sup> Yuanyuan Zhang, <sup>[a]</sup> Xiaomei Zhang\* <sup>[a]</sup> and Zhouyu Wang\*<sup>[a]</sup>

<sup>a</sup> Department of Chemistry, Xihua University, Chengdu, 610039, China. E-mail: xmzhang@cioc.ac.cn. , <u>zhouyuwang77@163.com</u> , <sup>b</sup> Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, 610041, China. <sup>#</sup>These authors contributed equally to this work and should be considered co-first authors. Fax: +86-028-8772-3006; Tel: +86-028-8772-9463

#### 1. General remarks

Chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by TLC. Racemic products were obtained from corresponding substrates catalyzed by dry DMF at room temperature. Flash column chromatography was performed on silica gels (200-300 mesh). <sup>1</sup>H NMR and <sup>13</sup>C NMR (300 or 400 and 75 or 100 MHz, respectively) spectra were recorded on a Bruker 300 MHz or 400 MHz NMR spectrometer in CDCl<sub>3</sub> or DMSO. <sup>1</sup>H NMR chemical shifts are reported in ppm ( $\delta$ ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl<sub>3</sub>, § 7.26 ppm, DMSO-d<sub>6</sub> at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, td = triplet of doublets, q = quartet, m = multiplet), coupling constants (Hz) and integration. <sup>13</sup>C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl<sub>3</sub>,  $\delta$  77.0 ppm, DMSO-d<sub>6</sub> at 39.51 ppm). All enantiomeric ratios have been controlled by co-injections of the pure sample with the racemates. HRMS data were obtained on a Bruker Daltonics. Inc mass instrument (ESI). Chiralpak AD-H column, Chiralcel OD column and Chiralpak IC column were purchased from Daicel Chemical Industries (Hong Kong, China). Optical rotations were measured on a Perkin-Elmer 241 Polarimeter. Melting points were recorded on a Buchi Melting Point B-545.

## 2. Procedures and characterizations data of compounds.

2.1Synthesis of novel lewis base catalysts: catalysts 2a,<sup>[1]</sup> 2b, <sup>[2]</sup> 2c, <sup>[3]</sup> 2d-2i,<sup>[4]</sup> were synthesized according to the literature procedures and the analytical data were identical

to those of literatures. Catalysts 2j-2m were synthesized according to the literature procedure.<sup>[4]</sup>



 $J = 7.9 \text{ Hz}, 1\text{H}, 7.74-7.64 \text{ (m, 5H)}, 7.55 - 7.48 \text{ (m, 3H)}, 7.03 \text{ (d, } J = 8.3 \text{ Hz}, 2\text{H}), 4.62 - 4.53 \text{ (m, 1H)}, 4.14 - 4.04 \text{ (m, 1H)}, 2.21 \text{ (s, 3H)}, 2.16 - 2.13 \text{ (m, 2H)}, 1.83 - 1.67 \text{ (m, 3H)}, 1.48 - 1.32 \text{ (m, 3H)}. {}^{13}\text{C} \text{ NMR} (100 \text{ MHz}, \text{DMSO}) \delta 163.3, 150.8, 149.2, 148.9, 144.2, 137.1, 134.3, 131.3, 130.1, 129.9, 128.5, 127.4, 125.9, 124.0, 119.4, 84.5, 51.3, 33.1, 31.3, 24.3, 24.0, 21.4. [\alpha]^{20.0}\text{ D} = -27.6 \text{ (c } = 0.5, \text{ CH}_2\text{Cl}_2\text{)}; \text{ HRMS} \text{ (ESI)}: \text{ Calcd. for } [\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_4\text{S}+\text{H}] + 451.1613, \text{ found} 451.1686.$ 



(1R,2R)-2-(3-methylpicolinamido)cyclohexyl4-methylbenzene-sulfonate (2k): white solid, m.p: 75-76°C, 45% yield. <sup>1</sup>H NMR (300 MHz,CDCl3)  $\delta$  8.35-8.33 (m, 1H), 8.09 (d, J = 9.5 Hz, 1H), 7.66 (d, J = 8.3 Hz,

2H), 7.58 – 7.55 (m, 1H), 7.30 (dd, J = 4.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 4.57-4.49 (m, 1H), 4.07-3.96 (m, 1H), 2.66 (s, 3H), 2.26 (s, 3H), 2.19- 2.04 (m, 2H), 1.80-1.69 (m, 3H), 1.45-1.26 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  165.3, 146.8, 145.2, 144.0, 140.7, 135.5, 134.3, 129.4, 127.5, 125.6, 83.1, 51.6, 32.4, 31.7, 24.0, 24.0, 21.6, 20.6. [ $\alpha$ ]<sup>20.0</sup><sub>D</sub> = -53.6 (c= 0.5, CH<sub>2</sub>Cl<sub>2</sub>); HRMS (ESI): Calcd for [C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub>S+H]<sup>+</sup> 389.1457, found 389.1530.



# (1S,2R)-1-(picolinamido)-2,3-dihydro-1H-inden-2-yl 4-methyl-

benzenesulfonate (21): white solid, m.p: 123-124°C, 57% yield. <sup>1</sup>H NMR

(300 MHz, DMSO)  $\delta$  8.68 (d, J = 4.1 Hz, 1H), 8.38 (d, J = 9.6 Hz, 1H), 8.09-8.04 (m, 1H), 8.02-7.94 (m, 1H), 7.83-7.52 (m, 3H), 7.50-7.14 (m, 4H), 7.10 (d, J = 8.0 Hz, 2H), 5.72-5.67 (m, 1H), 5.33-5.30 (m, 1H), 3.40 (d, J = 4.6 Hz, 1H), 3.10 (d, J = 17.2 Hz, 1H), 2.22 (s, 3H).<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  164.2, 149.2, 148.2, 144.5, 139.5, 138.5, 137.2, 133.3, 129.5, 128.6, 127.9, 127.5, 126.4, 125.3, 123.6, 122.3, 83.6, 55.9, 38.5, 21.6.  $[\alpha]^{20.0}_{D} = -4.8 \text{ (c} = 0.5, \text{CH}_2\text{Cl}_2\text{); HRMS (ESI): Calcd. for } [C_{22}\text{H}_{20}\text{N}_2\text{O}_4\text{S}+\text{H}]^+ 409.1144\text{, found} 409.1217.$ 

(R)-1-(2-(picolinamido)naphthalen-1-yl)naphthalen-2-yl 4-methylbenzenesulfonate (2m): white solid, m.p: 211 - 212°C, 40% yield. <sup>1</sup>H NMR (300 MHz, *d*-DMSO)  $\delta$  9.64 (s, 1H), 8.61 (d, *J* = 9.1 Hz, 1H), 8.29 (d, *J* = 9.0 Hz, 1H), 8.17-8.11 (m, 3H), 8.07 - 7.93 (m, 3H), 7.66 (d, *J* = 9.1 Hz, 1H), 7.55 - 7.43 (m, 3H), 7.36 - 7.24 (m, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.01 (t, *J* = 9.8 Hz, 3H), 6.84 (d, *J* = 8.7 Hz, 1H), 2.21 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  161.9, 149.5, 147.8, 146.1, 144.6, 137.3, 134.8, 133.1, 132.7, 132.6, 132.4, 130.8, 130.6, 129.4, 129.2, 128.2, 127.8, 127.5, 127.4, 126.6, 126.5, 126.3, 126.1, 125.8, 124.7, 124.5, 12.0, 121.9, 120.1, 119.7, 21.6. [ $\alpha$ ]<sup>20.0</sup><sub>D</sub> = - 87.6 (c = 0.5, CH<sub>2</sub>Cl<sub>2</sub>); HRMS (ESI): Calcd for [C<sub>33</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub>S+H]<sup>+</sup> 545.1547, found 545.1530.

Synthesis of catalyst 2n:



To a solution of (1R,2R)-cyclohexane-1,2-diamine (10.0 mmol) in 35 mL of toluene was added tosyl acid (11.0 mmol) and phthalic anhydride (10.0 mmol). The mixture was heated under reflux for 8 hours. Then the mixture was cooled to room temperature and the precipitate was separated by filtration. To the solid was added 35 mL of  $CH_2Cl_2$  and 25 mL of water. Then  $K_2CO_3$  was added to the mixture until pH = 9. The mixture was stirred at room temperature overnight and the phases were separated. The aqueous phase was extrated with  $CH_2Cl_2$  (3×30 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvents were removed under reduced pressure. The crude product (4) was used in the next step without further purification. To a solution of pyridine-2-carboxylic acid (2.2 mmol) in 15 mL of CH<sub>2</sub>Cl<sub>2</sub> was added EDCI (2.4 mmol), HOBT (2.4 mmol) and DIEA (4.0 mmol) successively. The mixture was cooled with an ice-water bath and stirred for 20 minutes. Then compound 4 (2.0 mmol) was added in the solution. The solution was stirred overnight, during which time the reaction temperature naturally rose to room temperature. The solvent was removed under reduced pressure. Then saturated aqueous NaHCO<sub>3</sub> (20 mL) was added to the residue and the aqueous layer was extracted with EtOAc (3×15 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvents were removed under reduced pressure. The residue was purified by silica-gel chromatography with ethyl acetate/petroleum ether to give the pure product 5 (555.0 mg, 1.6 mmol). Then compound 5 (555.0 mg, 1.6 mmol) was dissolved in 4 mL of EtOH and hydrazine hydrate (80%, 300 µL, 3.0 eq.) was added in the solution. The mixture was heated under reflux for 0.5 hour. Then the mixture was cooled to room temperature and the precipitate was separated by filtration. The solid was dissolved in 10 mL of CH<sub>2</sub>Cl<sub>2</sub>. Then Et<sub>3</sub>N (4.8 mmol) and DMAP (0.16 mmol) were added in the solution. The mixture was stirred at 0 °C for 0.5 hour. Then tosyl chloride (1.6 mmol) was added in the solution and the solution was stirred overnight, during which time the reaction temperature naturally rose to room temperature. The solvents were removed under reduced pressure. The residue was purified by silica-gel chromatography with ethyl acetate/petroleum ether to give the pure product **2n**.

# N-((1R,2R)-2-(4-methylphenylsulfonamido)cyclohexyl)picolinamide

(2n): white solid, m.p:  $173-174^{\circ}$ C, 60 % yield. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):

 $\delta 8.41 \text{ (d, } J = 4.5 \text{ Hz, } 1\text{H}\text{), } 8.11 \text{ (d, } J = 7.8 \text{ Hz, } 1\text{H}\text{), } 7.91 - 7.85(\text{m, } 1\text{H}\text{), } 7.63$ (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.47 - 7.43(m, 1H), 6.75 (d, J = 9.0 Hz, 2H), 5.97(d,  $J = 5.3 \text{ Hz, } 1\text{H}\text{), } 3.85 - 3.74(\text{m, } 1\text{H}\text{), } 3.04 - 2.94(\text{m, } 1\text{H}\text{), } 2.25 \text{ (d, } J = 13.9 \text{ Hz, } 1\text{H}\text{), } 2.12(\text{s, } 3\text{H}\text{), } 1.99 - 1.95(\text{m, } 1\text{H}\text{), } 1.77 - 1.72(\text{m, } 2\text{H}\text{), } 1.52 - 1.39(\text{m, } 1\text{H}\text{), } 1.37 - 1.25(\text{m, } 3\text{H}\text{). } [\alpha]^{20.0}\text{_D} = - 8.6 \text{ (c } = 0.5, \text{ CH}_2\text{Cl}_2\text{); } \text{HRMS (ESI): Calcd for } [\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}_3\text{S} + \text{H}]^+ 374.1460\text{, found } 374.1533\text{.}$  Synthesis of catalyst 20:



To a solution of compound 4 (2.5 mmol) in 25 mL of  $CH_2Cl_2$  was added  $Et_3N$  (13.0 mmol) and tosyl chloride (2.5 mmol) were added in the solution and the solution was stirred overnight at room temperature. The solvents were removed under reduced pressure. The residue was purified by silica-gel chromatography with ethyl acetate/petroleum ether to give the pure product 7 (800 mg). Then compound 7 (800 mg) was dissolved in 4 mL of DMF and  $K_2CO_3$  (2.2 mmol) and  $CH_3I$  (2.2 mmol) were added to the solution. The mixture was stirred overnight at room temperature. Then water was added in the solution. The aqueous phase was extracted with EtOAc (3×15 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvents were removed under reduced pressure. The residue was purified by silica-gel chromatography with ethyl acetate/petroleum ether to give the solution and the solution and condensation with pyridine-2-carboxylic acid as above afforded the catalyst **20**.

# N-((1R,2R)-2-(N,4-dimethylphenylsulfonamido)cyclohexyl)picolinamide (20): white solid,

m.p: 108-109°C, 43 % yield. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  8.59 (d, J = 4.6Hz, 1H), 8.12 (t, J = 9.3 Hz, 2H), 7.86 - 7.80 (m, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.44-7.40 (m, 1H), 7.06 (d, J = 8.1 Hz, 2H), 4.13 - 3.99 (m, 1H), 3.89 -

3.80 (m, 1H), 2.77 (s, 3H), 2.30 (s, 3H), 2.22-2.18 (m, 1H), 1.86 - 1.69 (m, 2H), 1.53-1.50 (m, 1H), 1.46 - 1.23 (m, 4H).<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  164.0, 149.8, 148.2, 142.8, 137.4,

137.1, 129.4, 127.0, 126.0, 122.1, 60.0, 49.0, 33.4, 29.3, 28.6, 25.2, 24.7, 21.5.  $[\alpha]^{20.0}_{D} = -12.4$ (c = 0.5, CH<sub>2</sub>Cl<sub>2</sub>); HRMS (ESI): Calcd. for  $[C_{20}H_{25}N_3O_3S+H]^+$  388.1617, found 388.1689.

### 2.2 Enantioselective conjugate hydrosilylation of $\alpha,\beta$ -unsaturated ketones 1



A solution of trichlorosilane (21  $\mu$ L, 0.2 mmol, 2.0 equiv) in 0.5 mL of toluene was added to a stirred solution of the corresponding  $\alpha,\beta$ -unsaturated ketones (0.1 mmol) and the catalyst **2f** (0.02 mmol) in toluene (2.0 mL) at -10 °C. The mixture was stirred at the same temperature for 48 hours. The reaction mixture was then treated with saturated aqueous solution of NaHCO<sub>3</sub> at room temperature for 20 minutes. Then the mixture was extracted with EtOAc. The combined extracts were washed with brine and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvents were removed under reduced pressure. The residue was purified by silica-gel chromatography with ethyl acetate/petroleum ether to give the pure product. The *ee* values were determined using established HPLC techniques with chiral stationary phases.



(S)-1,3-diphenylbutan-1-one (3a): white solid, 97% yield, 65% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 6.43$  min,  $tr_{minor} = 6.82$  min; <sup>1</sup>H

NMR (300 MHz, CDCl<sub>3</sub>) δ 7.95-7.92 (m, 2H), 7.58 - 7.52 (m, 1H), 7.47 - 7.42 (m, 2H), 7.34 - 7.29 (m, 4H), 7.23 - 7.17 (m, 1H), 3.57 - 3.45 (m, 1H), 3.35 - 3.15 (m, 2H), 1.34 (d, *J* = 6.9 Hz, 3H).



(S)-3-(4-fluorophenyl)-1-phenylbutan-1-one (3b): colorless oil, 98% yield, 50% ee. HPLC conditions: AD-H column, hexane/iPrOH = 95/5, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 6.96$  min,  $tr_{major}$ 

= 8.26 min; <sup>1</sup>H NMR (300 MHz, d-DMSO) δ 7.93-7.90 (m, 2H), 7.58 - 7.53(m, 1H), 7.47 -

7.42 (m, 2H), 7.26 - 7.20 (m, 2H), 7.01 - 6.93 (m, 2H), 3.56 - 3.44 (m, 1H), 3.31 - 3.13 (m, 2H), 1.32 (d, *J* = 6.9 Hz, 3H).



(S)-3-(4-chlorophenyl)-1-phenylbutan-1-one (3c): colorless oil, 94% yield, 48% ee. HPLC conditions: AD-H column, hexane/iPrOH = 95/5, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 7.01$  min,

 $tr_{major} = 8.80 \text{ min; }^{1}H \text{ NMR} (300 \text{ MHz}, d-DMSO) \delta 7.93-7.90 (m, 2H), 7.58-7.53 (m, 1H), 7.47 -7.42 (m, 2H), 7.28-7.27 (m, 1H), 7.25-7.19 (m, 3H), 3.55-3.44 (m, 1H), 3.31-3.13 (m, 2H), 1.32 (d, <math>J = 6.9 \text{ Hz}, 3H$ ).



(S)-1-phenyl-3-(p-tolyl)butan-1-one (3d): white solid, 97% yield, 53% ee. HPLC conditions: AD-H column, hexane/iPrOH = 95/5, flow rate

1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 5.88$  min,  $tr_{major} = 7.24$  min; <sup>1</sup>H NMR (300 MHz, *d*-DMSO)  $\delta$  7.93 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.16-7.10 (m, 4H), 3.53 - 3.41 (m, 1H), 3.32 - 3.13 (m, 2H), 2.32 (s, 3H), 1.32 (d, *J* = 6.9 Hz, 3H).

(S)-3-(4-methoxyphenyl)-1-phenylbutan-1-one (3e): colorless oil, 91% yield, 62% ee. HPLC conditions: AD-H column, hexane/iPrOH = 95/5, flow rate 1.0 mL/min, UV detection at 254 nm, tr<sub>minor</sub> = 8.92 min, tr<sub>major</sub> = 11.47 min; <sup>1</sup>H NMR (300 MHz, *d*-DMSO)  $\delta$  7.94 - 7.91 (m, 2H),

7.58 - 7.52 (m, 1H), 7.47 - 7.42 (m, 2H), 7.21 - 7.17 (m, 2H), 6.87 - 6.82 (m, 2H), 3.78 (s, 3H), 3.54 - 3.41 (m, 1H), 3.31 - 3.11 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H).



min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.00 (d, J = 7.3 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.26 - 7.18 (m, 2H), 6.94 (t, J = 7.4 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 3.91 - 3.79 (m, 4H), 3.41 - 3.01 (m, 2H), 1.31 (d, J = 6.9 Hz, 3H).



nm, tr<sub>major</sub> = 7.54 min, tr<sub>minor</sub> = 9.19 min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 - 7.92 (m, 2H), 7.58 - 7.53 (m, 1H), 7.47 - 7.42 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.83 (t, *J* = 2.1 Hz, 1H), 6.77 - 6.73 (m, 1H), 3.80 (s, 3H), 3.56 - 3.43 (m, 1H), 3.34 - 3.14 (m, 2H), 1.33 (d, *J* = 6.9 Hz, 3H).



(S)-3-(naphthalen-2-yl)-1-phenylbutan-1-one (3i): white solid, 97% yield, 65% ee. HPLC conditions: AD-H column, hexane/iPrOH = 95/5, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 8.00$ 

min, tr<sub>major</sub> = 9.24 min; <sup>1</sup>H NMR (300 MHz, *d*-DMSO)  $\delta$  7.99 - 7.96 (m, 2H), 7.86 - 7.78 (m, 4H), 7.65 - 7.60 (m, 1H), 7.55 - 7.40 (m, 5H), 3.57 - 3.40 (m, 3H), 1.33 (d, *J* = 6.5 Hz, 3H).

(S)-3-(furan-2-yl)-1-phenylbutan-1-one (3k): white solid, 90% yield, 57%
ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm, tr<sub>minor</sub> = 6.97 min, tr<sub>major</sub> = 8.03 min; <sup>1</sup>H
NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 - 7.87 (m, 2H), 7.52 - 7.46 (m, 1H), 7.41 - 7.36 (m, 2H), 7.23 - 7.22 (m, 1H), 6.21 - 6.19 (m, 1H), 6.02 (d, J = 3.2 Hz, 1H), 3.65 - 3.5 (m, 1H), 3.39 - 2.97 (m, 2H), 1.26 (d, J = 6.9 Hz, 3H).



(S)-1-phenyl-3-(thiophen-2-yl)butan-1-one (3l): white solid, 96% yield, 59% ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 8.23$  min,  $tr_{maior} = 9.34$  min;

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 - 7.94 (m, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.14 - 7.12 (m, 1H), 6.94 - 6.87 (m, 2H), 3.92 - 3.80 (m, 1H), 3.42 - 3.17 (m, 2H), 1.43 (d, J = 6.9 Hz, 3H).



(S)-1-(4-chlorophenyl)-3-phenylbutan-1-one (3n): colorless oil, 95% yield, 64% ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm, tr<sub>minor</sub> = 9.05

min, tr<sub>major</sub> = 10.71 min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.88 - 7.84 (m, 2H), 7.43 - 7.39 (m, 2H), 7.34 - 7.27 (m, 3H), 7.25 - 7.17 (m, 1H), 3.55 - 3.43 (m, 1H), 3.31 - 3.11 (m, 2H), 1.34 (d, J = 6.9 Hz, 3H).



(S)-3-phenyl-1-(p-tolyl)butan-1-one (3o): white solid, 94% yield, 58% ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 10.13$  min,  $tr_{major} =$ 

13.40 min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.84 (d, J = 8.2 Hz, 2H), 7.33 - 7.28 (m, 4H), 7.25 - 7.17 (m, 3H), 3.56 - 3.44 (m, 1H), 3.31 - 3.12 (m, 2H), 2.40 (s, 3H), 1.33 (d, J = 6.9 Hz, 3H).



(S)-1-(4-methoxyphenyl)-3-phenylbutan-1-one (3p): white solid, 94% yield, 59% ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm, tr<sub>minor</sub> =

20.17 min,  $tr_{major} = 27.94$  min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.93 - 7.90 (m, 2H), 7.33 - 7.28 (m, 4H), 7.22 - 7.16 (m, 1H), 6.91 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H), 3.56 - 3.43 (m, 1H), 3.28 - 3.09(m, 2H), 1.33 (d, J = 6.9 Hz, 3H).



(8)-1-(3-fluorophenyl)-3-phenylbutan-1-one (3q): white solid, 91% yield, 54% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 6.18$  min,  $tr_{minor}$ 

= 6.56 min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.74 - 7.65 (m, 1H), 7.62 - 7.57 (m, 1H), 7.45 - 7.38 (m, 1H), 7.33 - 7.27 (m, 4H), 7.25 - 7.17 (m, 2H), 3.55 - 3.44 (m, 1H), 3.32 - 3.11 (m, 2H), 1.34 (d, *J* = 6.9 Hz, 3H).



(8)-3-phenyl-1-(m-tolyl)butan-1-one (3r): white solid, 95% yield, 52% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 7.23$  min,  $tr_{minor} = 7.89$ 

min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.72 (d, J = 6.8 Hz, 2H), 7.35 - 7.28 (m, 6H), 7.22 - 7.14 (m, 1H), 3.36 - 3.44 (m, 1H), 3.32 - 3.13 (m, 2H), 2.40 (s, 3H), 1.34 (d, J = 6.9 Hz, 3H).

(S)-3-phenyl-1-(o-tolyl)butan-1-one (3s): colorless oil, 90% yield, 28%
 ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm, tr<sub>minor</sub> = 6.15 min, tr<sub>major</sub> = 6.90 min; <sup>1</sup>H
 NMR (300 MHz, CDCl<sub>3</sub>) δ 7.46 (d, J = 7.8 Hz, 1H), 7.39 - 7.28 (m, 2H), 7.25 - 7.15 (m, 6H), 3.51 - 3.40 (m, 1H), 3.25 - 3.07 (m, 2H), 2.35 (s, 3H), 1.32 (d, J = 6.9 Hz, 3H).



(S)-1,3-diphenylpentan-1-one (3t): white solid, 94% yield, 65% ee. HPLC conditions: AD-H column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 7.95$  min,  $tr_{major} = 10.16$  min;

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.91 - 7.89 (m, 2H), 7.56 - 7.41 (m, 1H), 7.45 - 7.40 (m, 2H), 7.31 - 7.27 (m, 2H), 7.26 - 7.15 (m, 3H), 3.34 - 3.19 (m, 3H), 1.86 - 1.57 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H).



(S)-4-bromo-1,3-diphenylbutan-1-one (3u): colorless oil, 76% yield, 67% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 13.06$  min,  $tr_{minor} = 13.84$  min;

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.03 - 7.93 (m, 2H), 7.66 - 7.43 (m, 4H), 7.36 - 7.27 (m, 3H), 7.25 - 7.23 (m, 1H), 3.84 - 3.78 (m, 1H), 3.76 - 3.66 (m, 2H), 3.62 (d, *J* = 6.1 Hz, 1H), 3.47 - 3.39 (m, 1H).



(R)-4-methyl-1,3-diphenylpentan-1-one (3v): white solid, 88% yield, 65% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 8.68$  min,  $tr_{minor} = 10.42$ 

min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 - 7.87 (m, 2H), 7.56 - 7.50 (m, 1H), 7.45 - 7.39 (m, 2H), 7.28 - 7.27 (m, 2H), 7.25 - 7.12 (m, 3H), 3.37 (d, *J* = 7.0 Hz, 2H), 3.20 - 3.13 (m, 1H), 2.00 - 1.89 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H).



(S)-1,3,4-triphenylbutan-1-one (3x): white solid, 91% yield, 59% ee. HPLC conditions: IC column, hexane/iPrOH = 98/2, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{major} = 11.40$  min,  $tr_{minor} = 11.99$  min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 - 7.83 (m, 2H), 7.58 - 7.49 (m, 1H),

7.44 - 7.33 (m, 2H), 7.31 - 7.14 (m, 8H), 7.10 - 7.07 (m, 2H), 3.72 - 3.62 (m, 1H), 3.40 - 3.24 (m, 2H), 3.05 - 2.86 (m, 2H).



**3-(4-methoxyphenyl)-1,3-diphenylpropan-1-one (3y):** white solid, 70% yield, 11% ee. HPLC conditions: OD-H column, hexane/iPrOH = 90/10, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 7.17$  min,  $tr_{major} = 7.99$  min; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 - 7.93 (m, 2H), 7.59 - 7.531

(m, 1H), 7.47 - 7.42 (m, 2H), 7.32 - 7.25 (m, 4H), 7.21 - 7.15 (m, 3H), 6.83 - 6.81 (m, 2H), 4.79 (t, *J* = 7.3 Hz, 1H), 3.76 (s, 3H), 3.72 (d, *J* = 7.3 Hz, 2H).

**1-phenyl-2-(1,2,3,4-tetrahydronaphthalen-1-yl)ethan-1-one (3z):** white solid, 98% yield, 22% ee. HPLC conditions: OD-H column, hexane/iPrOH = 95/5, flow rate 1.0 mL/min, UV detection at 254 nm,  $tr_{minor} = 6.22 \text{ min}, tr_{major} = 6.61 \text{ min}; {}^{1}\text{H} \text{ NMR} (300 \text{ MHz}, \text{CDCl}_3) \delta 8.00 - 7.98 (m, 2\text{H}), 7.61 -$ 7.55 (m, 1H), 7.50 - 7.47 (m, 2H), 7.20 - 7.08 (m, 4H), 3.68 - 3.60 (m, 1H), 3.39 - 3.23 (m, 2H),2.86 - 2.71 (m, 2H), 1.99 - 1.90 (m, 1H), 1.86 - 1.66 (m, 3H).

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### 4. HPLC Charts of Products















