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# **Supporting Information**

## Palladium-Catalyzed Asymmetric Hydrogenation of 3-Phthalimido Substituted Quinolines

Xian-Feng Cai, Wen-Xue Huang, Zhang-Pei Chen and Yong-Gui Zhou\* State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics Chinese Academy of Sciences, Dalian 116023, P. R. China

### **Table of Contents**

1.	General	S2
2.	Synthesis of 3-Nitroquinolines	S2
3.	Synthesis of 3-Phthalimido Substituted Quinolines	S3
4.	Asymmetric Hydrogenation of Substituted Quinolines	S4
5.	Copy of NMR and HPLC for Racemic and Chiral Compounds	S10

### 1. General:

Commercially available reagents were used without further purification. Solvents were treated prior to use according to the standard methods. <sup>1</sup>H NMR, <sup>13</sup>C NMR and <sup>19</sup>F NMR spectra were recorded at room temperature in CDCl<sub>3</sub> on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Enantiomeric excess was determined by HPLC analysis, using chiral column described below in detail. Optical rotations were measured by polarimeter. Flash column chromatography was performed on silica gel (200-300 mesh).

#### 2. Synthesis of 3-Nitroquinolines

3-Nitroquinoline derivatives can be conveniently synthesized according to the known literature procedure.<sup>[1,2,3]</sup> 2-butyl-3-nitroquinoline (**7a**), 2-methyl-3-nitroquinoline (**7b**), 2-ethyl-3-nitroquinoline (**7c**), 2-propyl-3-nitroquinoline (**7d**), 2-isobutyl-3-nitroquinoline (**7f**), 2-isopentyl - 3-nitroquinoline (**7g**), 2-hexyl-3-nitroquinoline (**7h**), 2-phenethyl-3-nitroquinoline (**7i**), 2-phenyl - 3-nitroquinoline (**7k**), (*E*)-2-styryl-3-nitroquinoline (**7l**), and (*E*)-2-(4-fluorostyryl)-3-nitroquinoline (**7l**) are known compounds.

#### 2.1. Synthesis of 3-Nitroquinoline 7e



Following a known literature report:<sup>2,3</sup> A mixture of 2-chloro-3-nitroquinoline (150 mg, 0.72 mmol), cyclopropylboronic acid (74 mg, 0.86 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (83 mg, 0.07 mmol) and K<sub>2</sub>CO<sub>3</sub> (297 mg, 2.15 mmol) in 1,4-dioxane (6 mL) was stirred at reflux for 18 h, then cooled to rt, diluted with water (15 mL), then extracted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL×3). The combined organic layers were dried with Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane/EtOAc 30:1) to yield the product **7e**.

**2-Cyclopropyl-3-nitroquinoline (7e):** 83% yield, white solid, mp 104-106 °C,  $R_f = 0.90$  (hexane/EtOAc 10:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 8.61$  (1 H, s), 7.97 (d, J = 8.5, 1 H), 7.85

NO<sub>2</sub> (d, J = 8.2, 1 H), 7.82-7.76 (1 H, m), 7.55 (t, J = 7.5, 1 H), 2.81-2.70 (1 H, m), 1.43-1.35 (2 H, m), 1.20-1.11 (2 H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 155.6$ , 148.7, 144.5, 132.5, 132.3, 128.9, 128.6, 127.2, 124.7, 14.0, 11.4; HRMS Calculated for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 215.0821, found 215.0822.

### 2.2. Synthesis of 3-Nitroquinoline 7j



Following a known literature report:<sup>4</sup> To a solution of 2-amino-5-fluorobenzaldehyde (790

<sup>1</sup> G. A. Molander and C.-S. Yun, Tetrahedron 2002, 58, 1465.

<sup>2</sup> X.-F. Cai, M.-W. Chen, Z.-S. Ye, R.-N. Guo, L. Shi, Y. Li and Y.-G. Zhou, Chem. Asian J. 2013, 8, 1381.

<sup>3</sup> X.-F. Cai, R.-N. Guo, M.-W. Chen, L. Shi and Y.-G. Zhou, *Chem. Eur. J.* **2014**, DOI:10.1002/chem.201402592. 4 M.-C. Yan, Z. Tu, C. Lin, S. Ko, J. Hsu and C.-F. Yao, *J. Org. Chem.* **2004**, *69*, 1565.

mg, 5.68 mmol) in toluene (25 mL) was added (*E*)-1-nitrohex-1-ene (880 mg, 6.81 mmol). The resulting mixture was placed in an oil bath and heated at 45 °C for 13.5 h, then 1,4-diaza-bicycle [2.2.2]octane (DABCO, 319 mg, 2.84 mmol) was added, the mixture was stirred for another 12 h. After cooled to room temperature, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 1.934 g, 8.52 mmol) was added and the solution was vigorously stirred for 0.5 h. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (hexane/EtOAc 20:1) to yield the product 7j.

**2-Butyl-6-fluoro-3-nitroquinoline (7j):** 22% yield, light brown oil,  $R_f = 0.70$  (hexane/EtOAc 10:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 8.63$  (s, 1H), 8.11 (dd, J = 9.3, 5.2, 1H), 7.66-7.58

Final (m, 1H), 7.52 (dd, J = 8.2, 2.8, 1H), 3.27-3.19 (m, 2H), 1.88-1.76 (m, 2H), 1.54-1.42 (m, 2H), 0.98 (t, J = 7.4, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 161.0$  (d, <sup>1</sup> $J_{FC} = 251.2$ ), 154.8 (d, <sup>4</sup> $J_{FC} = 2.9$ ), 145.8, 144.5, 132.1 (d, <sup>4</sup> $J_{FC} = 5.7$ ), 131.7 (d, <sup>3</sup> $J_{FC} = 9.2$ ), 126.1 (d, <sup>3</sup> $J_{FC} = 10.5$ ), 122.9 (d, <sup>2</sup> $J_{FC} = 25.9$ ), 111.5 (d, <sup>2</sup> $J_{FC} = 22.4$ ), 35.8, 30.9, 22.7, 13.8; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta = -111.0$ ; HRMS Calculated for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 249.1039, found 249.1036.

#### 3. Synthesis of 3-Phthalimido Substituted Quinolines

Quinolin-3-amines **2** can be conveniently synthesized according to the known literature procedure.<sup>[3]</sup> 2-(2-Butylquinolin-3-yl)isoindoline-1,3-dione (**2a**), 2-(2-methylquinolin-3-yl)isoindoline-1,3-dione (**2b**), 2-(2-ethylquinolin-3-yl)isoindoline-1,3-dione (**2c**), 2-(2-propylquinolin-3-yl)isoindoline-1,3-dione (**2d**), 2-(2-isobutylquinolin-3-yl) isoindoline-1,3-dione (**2f**), 2-(2-isopent-yl-quinolin-3-yl)isoindoline-1,3-dione (**2g**), 2-(2-hexyl-quinolin-3-yl)isoindoline-1,3-dione (**2h**), 2-(2-phenethylquinolin-3-yl)isoindoline-1,3-dione (**2h**), 2-(2-phenethylquinolin-3-yl)isoindoline-1,3-dione (**2h**), 2-(2-phenethylquinolin-3-yl)isoindoline-1,3-dione (**2h**), 2-(2-phenethylquinolin-3-yl)isoindoline-1,3-dione (**2h**), 2-(2-phenylquinolin-3-yl)isoindoline-1,3-dione (**2h**)



Following a known literature report:<sup>3</sup> To a solution of 7 (0.60 mmol) in a mixed solvent of ethanol and  $H_2O$  with a ratio of 4/1 (5.0 mL) was added iron powder (134 mg, 2.40 mmol) followed by HCl (0.1 M, 0.30 mL, 0.03 mmol), and the resulting mixture was vigorously stirred at 85 °C for 0.5-1.5 h. When the reduction reaction was complete (determined by TLC), saturated NaHCO<sub>3</sub> (5.0 mL) was added and the mixture was filtered through celite. The filtrate was extracted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL×3) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was removed under reduced pressure and the crude product was pure enough for further reaction.

In a 25 mL round-bottom flask, the crude product and phthalic anhydride (89 mg, 0.60 mmol) were combined in acetic acid (5.0 mL). The resulting mixture was vigorously stirred at 120 °C for 18 h. The solvent was removed under reduced pressure, the residue was resolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and washed with saturated NaHCO<sub>3</sub> (15 mL). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>). After filtration, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexane/EtOAc 5:1) to yield the product.

**2-(2-Cyclopropylquinolin-3-yl)isoindoline-1,3-dione (2e):** 73% yield, white solid, mp 199-201 °C,  $R_f = 0.35$  (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 8.05$ -7.96 (m, 4H), 7.82

(dd, J = 5.3, 3.1, 2H), 7.77 (d, J = 8.0, 1H), 7.74-7.67 (m, 1H), 7.48 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 2.06-1.97 (m, 1H), 7.148 (t, J = 7.4, 1H), 7.11H), 1.36-1.28 (m, 2H), 1.02-0.93 (m, 2H);  $^{13}$ C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = NPhth 167.6, 160.4, 148.2, 136.0, 134.8, 132.1, 130.5, 129.0, 127.8, 126.6, 126.2, 125.2, 124.2, 13.9, 10.2; HRMS Calculated for C<sub>20</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 315.1134,

found 315.1141.

2-(2-Butyl-6-fluoroquinolin-3-yl)isoindoline-1,3-dione (2j): 70% yield, white solid, mp 

1H), 8.00 (dt, J = 6.9, 3.5, 2H), 7.96 (s, 1H), 7.84 (dd, J = 5.2, 3.1, 2H), NPhth

7.52 (td, J = 8.9, 2.8, 1H), 7.41 (dd, J = 8.6, 2.6, 1H), 2.89-2.78 (m, 2H), 1.76 (dt, J = 15.4, 7.6, 2H), 1.40-1.26 (m, 2H), 0.84 (t, J = 7.4, 3H); <sup>13</sup>C

NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 167.3, 160.4 (d, <sup>1</sup>*J*<sub>FC</sub> = 248.3), 159.9 (d, <sup>4</sup>*J*<sub>FC</sub> = 2.9), 145.1, 135.9 (d,  ${}^{4}J_{\text{FC}}$  = 5.4), 134.7, 131.9, 131.5 (d,  ${}^{3}J_{\text{FC}}$  = 9.2), 127.4 (d,  ${}^{3}J_{\text{FC}}$  = 10.3), 125.7, 124.1, 120.6 (d,  ${}^{2}J_{\text{FC}}$ = 25.8), 110.6 (d,  ${}^{2}J_{FC}$  = 22.1), 34.3, 30.4, 22.6, 13.8;  ${}^{19}F$  NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  = -113.5; HRMS Calculated for C<sub>21</sub>H<sub>18</sub>FN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 349.1352, found 349.1371.

(E)-2-(2-(4-Fluorostyryl)quinolin-3-yl)isoindoline-1,3-dione (2m): 64% yield, light yellow solid, mp 269-271 °C,  $R_f = 0.50$  (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 8.17$  (d, J =



8.5, 1H), 8.10-7.99 (m, 4H), 7.87 (dd, J = 5.3, 3.1, 2H), 7.79 (dd, J = 17.1, 8.1, 2H), 7.54 (t, J = 7.5, 1H), 7.48 (dd, J = 8.4, 5.6, 2H), 6.99 (dd, J = 11.9, 6.5, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 167.5, 163.2$  $(d, {}^{1}J_{FC} = 248.8), 152.9, 148.3, 136.8, 135.7, 135.0, 133.0, 132.9,$ 

132.0, 131.0, 129.5, 129.5 (d,  ${}^{3}J_{FC} = 8.3$ ), 127.9, 127.4, 127.0, 124.3, 121.9 (d,  ${}^{4}J_{FC} = 2.1$ ), 115.8 (d,  ${}^{2}J_{FC} = 21.7$ );  ${}^{19}F$  NMR (376 MHz, CDCl<sub>3</sub>)  $\delta = -112.3$ ; HRMS Calculated for C<sub>25</sub>H<sub>16</sub>FN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 395.1196, found 395.1187.

#### 4. Asymmetric Hydrogenation of Substituted Quinolines



Pd(OCOCF<sub>3</sub>)<sub>2</sub> (1.7 mg, 0.005 mmol) and L3 (4.7 mg, 0.006 mmol) were placed in a dried Schlenk tube under nitrogen atmosphere, and degassed anhydrous acetone was added. The mixture was stirred at room temperature for 1 h, then, the solvent was removed under vacuum to give the catalyst. In a glovebox, quinolines (0.10 mmol) and TFA (6.8 mg, 4.4 µL, 0.06 mmol) were stirred in 1.0 mL CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 1 min. Subsequently, the above catalyst together with 3 mL CH<sub>2</sub>Cl<sub>2</sub> was added to the reaction mixture. The hydrogenation was performed at 70 °C (or 80 °C) under H<sub>2</sub> (1000 psi) in a stainless steel autoclave for 18 h. After carefully releasing the hydrogen, saturated aqueous NaHCO<sub>3</sub> (5 mL) was added to the resulting mixture. After stirring for 10 min, the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 5 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Purification was performed by flash chromatography on silica gel (hexane/EtOAc 10:1) to give the product.

2-((2S,3S)-2-Butylquinolin-3-yl)isoindoline-1,3-dione (3a): known compound,<sup>[3]</sup> 91% yield, 90% ee, light yellow oil,  $[\alpha]^{20}_{D} = -149.2$  (c 0.60, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = +181.6$  (c 0.64, CH<sub>2</sub>Cl<sub>2</sub>) for 93% ee (2R,3R)], R<sub>f</sub> = 0.60 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, NPhth  $CDCl_3$ )  $\delta = 7.87-7.79$  (m, 2H), 7.75-7.67 (m, 2H), 7.01 (dd, J = 15.1, 7.4, 7.42H), 6.68 (t, J = 7.4, 1H), 6.57 (d, J = 7.9, 1H), 4.87-4.78 (m, 1H), 4.04 (s,

1H), 3.93 (dd, J = 16.6, 9.6, 1H), 3.50-3.41 (m, 1H), 3.04 (dd, J = 16.6, 6.2, 1H), 1.60 (dt, J = 13.0, 6.8, 1H), 1.50-1.39 (m, 2H), 1.32-1.23 (m, 3H), 0.86 (dd, J = 13.5, 6.6, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 168.8, 143.3, 134.0, 131.8, 129.0, 127.0, 123.2, 120.0, 117.6, 114.5, 54.4, 50.4, 30.3, 28.6, 27.2, 22.7, 14.1; HPLC: Chiracel OD-H column, 254 nm, 30 °C,$ *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 12.2 min and 14.2 min (major).

**2-((2***S***,3***S***)-2-Methylquinolin-3-yl)isoindoline-1,3-dione (3b):** known compound,<sup>[3]</sup> 86% yield, 81% ee, light yellow solid, mp 165-167 °C,  $[\alpha]^{20}{}_{D}$  = -159.2 (*c* 0.60, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}{}_{D}$  =

 $\begin{array}{l} \begin{array}{l} \begin{array}{l} \text{(NPhth} & +170.2 \ (c \ 0.56, \ CH_2Cl_2) \ for \ 81\% \ ee \ (2R,3R)], \ R_f = 0.40 \ (hexane/EtOAc \ 5:1). \\ & ^{1}\text{H} \ \text{NMR} \ (400 \ \text{MHz}, \ CDCl_3) \ \delta = 7.86-7.78 \ (m, \ 2\text{H}), \ 7.74-7.67 \ (m, \ 2\text{H}), \ 7.02 \ (t, \ J = 8.6, \ 2\text{H}), \ 6.69 \ (td, \ J = 7.5, \ 0.9, \ 1\text{H}), \ 6.55 \ (d, \ J = 7.9, \ 1\text{H}), \ 4.83-4.76 \ (m, \ 1\text{H}), \ 3.91 \ (dd, \ J = 16.6, \ 9.2, \ 1\text{H}), \ 3.84 \ (s, \ 1\text{H}), \ 3.73-3.65 \ (m, \ 1\text{H}), \ 3.06 \ (dd, \ J = 16.6, \ 6.4, \ 1\text{H}), \ 1.22 \ (d, \ J = 6.6, \ 3\text{H}); \ ^{13}\text{C} \ \text{NMR} \ (100 \ \text{MHz}, \ \text{CDCl}_3) \ \delta = 168.8, \ 143.4, \ 134.0, \ 131.8, \ 128.9, \ 127.0, \ 123.2, \ 119.9, \ 117.8, \ 114.5, \ 50.4, \ 49.8, \ 26.8, \ 17.9; \ \text{HPLC}: \ \text{Chiracel OD-H \ column}, \ 254 \ \text{nm}, \ 30 \ ^{\circ}\text{C}, \ n-hexane/i-propanol = 70/30, \ flow = 0.7 \ \text{mL/min}, \ \text{retention \ time \ 21.7 \ min \ and \ 27.9 \ min \ (major).} \end{array}$ 

**2-((2S,3S)-2-Ethylquinolin-3-yl)isoindoline-1,3-dione (3c):** known compound,<sup>[3]</sup> 93% yield, 85% ee, light yellow solid, mp 162-164 °C,  $[\alpha]^{20}_{D} = -182.8$  (*c* 0.56, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = -182.8$ 

 $\begin{array}{l} \begin{array}{c} \text{(NPhth} \\ \text{H} \end{array} & \begin{array}{c} +197.7 \ (c \ 0.60, \ \text{CH}_2\text{Cl}_2) \ \text{for} \ 90\% \ \text{ee} \ (2R,3R)], \ \text{R}_{\text{f}} = 0.45 \ (\text{hexane/EtOAc} \ 5:1). \\ \text{IH} \ \text{NMR} \ (400 \ \text{MHz}, \ \text{CDCl}_3) \ \delta = 7.86\text{-}7.79 \ (\text{m}, \ 2\text{H}), \ 7.74\text{-}7.68 \ (\text{m}, \ 2\text{H}), \ 7.01 \\ (\text{dd}, \ J = 15.4, \ 7.5, \ 2\text{H}), \ 6.68 \ (\text{t}, \ J = 7.4, \ 1\text{H}), \ 6.57 \ (\text{d}, \ J = 7.9, \ 1\text{H}), \ 4.88\text{-}4.81 \ (\text{m}, \ 1\text{H}), \ 4.09 \ (\text{s}, \ 1\text{H}), \ 3.95 \ (\text{dd}, \ J = 16.5, \ 9.8, \ 1\text{H}), \ 3.36 \ (\text{dt}, \ J = 9.7, \ 3.7, \ 1\text{H}), \ 3.02 \ (\text{dd}, \ J = 16.5, \ 6.2, \ 1\text{H}), \ 1.67\text{-}1.47 \ (\text{m}, \ 2\text{H}), \ 0.97 \ (\text{t}, \ J = 7.4, \ 3\text{H}); \ ^{13}\text{C} \ \text{NMR} \ (100 \ \text{MHz}, \ \text{CDCl}_3) \ \delta = 168.8, \ 143.2, \ 134.0, \ 131.8, \ 129.0, \ 127.0, \ 123.2, \ 120.0, \ 117.6, \ 114.5, \ 56.0, \ 50.3, \ 27.1, \ 23.5, \ 10.7; \ \text{HPLC: Chiracel OD-H column, \ 254 \ nm}, \ 30 \ ^{\circ}\text{C}, \ n\text{-hexane/}i\text{-propanol} = 70/30, \ \text{flow} = 0.7 \ \text{mL/min, retention time} \ 13.8 \ \text{min and} \ 20.5 \ \text{min} \ (\text{major}). \end{array}$ 

**2-((2***S***,3***S***)-2-Propylquinolin-3-yl)isoindoline-1,3-dione (3d):** known compound,<sup>[3]</sup> 97% yield, 87% ee, light yellow solid, mp 154-156 °C,  $[\alpha]^{20}_{D} = -186.8$  (*c* 0.62, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = +204.3$  (*c* 0.60, CH<sub>2</sub>Cl<sub>2</sub>) for 92% ee (2*R*,3*R*)], R<sub>f</sub> = 0.45 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 7.88-7.79$  (m, 2H), 7.75-7.67 (m, 2H), 7.01 (dd, *J* = 14.3, 7.3, 2H), 6.69 (dd, *J* = 10.7, 4.0, 1H), 6.56 (d, *J* = 7.9, 1H), 4.86-4.79 (m, 1H), 4.03 (s, 1H), 3.94 (dd, *J* = 16.6, 9.7, 1H), 3.47 (dt, *J* = 10.0, 3.2, 1H), 3.04 (dd, *J* = 16.6, 6.2, 1H), 1.65-1.38 (m, 3H), 1.35-1.23 (m, 1H), 0.89 (t, *J* = 7.1, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 168.8$ , 143.2, 134.0, 131.8, 129.0, 127.0, 123.2, 120.0, 117.6, 114.5, 54.1, 50.4, 32.6, 27.2, 19.5, 14.0; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 12.6 min and 16.6 min (major).

**2-((2S,3S)-2-Cyclopropylquinolin-3-yl)isoindoline-1,3-dione (3e):** 72% yield, 80% ee, yellow solid, mp 152-154 °C,  $[\alpha]^{20}_{D} = -197.6$  (*c* 0.38, CH<sub>2</sub>Cl<sub>2</sub>),  $R_f = 0.45$  (hexane/EtOAc 5:1). <sup>1</sup>H

NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.88-7.80 (m, 2H), 7.76-7.67 (m, 2H), 7.07-6.96 (m, 2H), 6.67 (t, *J* = 7.3, 1H), 6.56 (d, *J* = 7.9, 1H), 4.93-4.85 (m, 1H), 4.17 (dd, *J* = 16.3, 10.5, 1H), 4.05 (s, 1H), 3.04 (dd, *J* = 16.3, 5.9, 1H), 2.72 (dd, *J* = 9.3, 4.1, 1H), 1.20-1.05 (m, 1H), 0.54-0.40 (m, 2H), 0.21-0.11 (m, 1H), 0.06 (dq, *J* = 9.8, 4.7, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 166.5, 141.0, 131.7, 129.5, 126.6, 124.8, 120.9, 117.5, 115.2, 111.8, 56.8, 47.9, 24.8, 10.9, 1.0, -0.0; HRMS Calculated for C<sub>20</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 319.1447, found 319.1453; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30,

flow = 0.7 mL/min, retention time 18.9 min and 28.8 min (major).

**2-((2***S***,3***S***)-2-Isobutylquinolin-3-yl)isoindoline-1,3-dione (3f):** known compound,<sup>[3]</sup> 94% yield, 90% ee, light yellow oil,  $[\alpha]^{20}_{D} = -178.7$  (*c* 0.62, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = +203.2$  (*c* 0.66, (NPhth) CH<sub>2</sub>Cl<sub>2</sub>) for 94% ee (2*R*,3*R*)], R<sub>f</sub> = 0.65 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.87-7.78 (m, 2H), 7.76-7.66 (m, 2H), 7.02 (dd, *J* = 14.1, 7.1, 2H), 6.69 (td, *J* = 7.4, 0.9, 1H), 6.57 (d, *J* = 7.8, 1H), 4.85-4.76 (m, 1H), 3.97 (s, 1H), 3.87 (dd, *J* = 16.7, 9.1, 1H), 3.58 (dt, *J* = 10.3, 3.3, 1H), 3.08 (dd, *J* = 16.7, 6.3, 1H), 1.79-1.67 (m, 1H), 1.63-1.54 (m, 1H), 1.25-1.18 (m, 1H), 0.91 (d, *J* = 6.6, 3H), 0.85 (d, *J* = 6.6, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 168.8, 143.4, 134.0, 131.8, 128.9, 127.0, 123.3, 120.1, 117.7, 114.5, 52.1, 50.5, 39.5, 27.4, 24.6, 23.9, 21.5; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 10.2 min and 17.4 min (major).

**2-((2***S***,3***S***)-2-Isopentylquinolin-3-yl)isoindoline-1,3-dione (3g):** known compound,<sup>[3]</sup> 91% yield, 90% ee, yellow oil,  $[\alpha]^{20}_{D} = -184.2$  (*c* 0.64, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = +176.8$  (*c* 0.68, CH<sub>2</sub>Cl<sub>2</sub>) for 88% ee (2*R*,3*R*)], R<sub>f</sub> = 0.65 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.86-7.79 (m, 2H), 7.74-7.68 (m, 2H), 7.01 (dd, *J* = 15.5, 7.5, 2H), 6.68 (t, *J* = 7.4, 1H), 6.57 (d, *J* = 7.9, 1H), 4.87-4.78 (m, 1H), 4.03 (s, 1H), 3.90 (dd, *J* = 16.6, 9.4, 1H), 3.42 (dt, *J* = 9.4, 3.6, 1H), 3.04 (dd, *J* = 16.6, 6.2, 1H), 1.63-1.43 (m, 3H), 1.39-1.28 (m, 1H), 1.23-1.12 (m, 1H), 0.82 (dd, *J* = 8.8, 6.7, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 168.8, 143.3, 134.0, 131.8, 128.9, 127.0, 123.2, 120.1, 117.6, 114.5, 54.8, 50.4, 35.7, 28.6, 28.1, 27.4, 22.8, 22.4; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.6 mL/min, retention time 13.2 min and 14.6 min (major).

**2-((2S,3S)-2-Hexylquinolin-3-yl)isoindoline-1,3-dione (3h):** known compound,<sup>[3]</sup> 86% yield, 90% ee, yellow oil,  $[\alpha]^{20}{}_{D} = -169.5$  (*c* 0.62, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}{}_{D} = +180.4$  (*c* 0.70, CH<sub>2</sub>Cl<sub>2</sub>)

for 92% ee (2R,3R)], R<sub>f</sub> = 0.70 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.82 (dt, *J* = 7.0, 3.5, 2H), 7.75-7.67 (m, 2H), 7.01 (dd, *J* = 15.0, 7.4, 2H), 6.68 (td, *J* = 7.4, 0.8, 1H), 6.57 (d, *J* = 7.9, 1H), 4.86-4.79 (m, 1H), 4.03 (s, 1H), 3.92 (dd, *J* = 16.6, 9.6, 1H), 3.50-3.41 (m, 1H), 3.04 (dd, *J* = 16.6, 6.2, 1H), 1.59 (dd, *J* = 18.7, 9.4, 1H), 1.51-1.39 (m, 2H), 1.25 (dd, *J* = 14.3, 9.4, 7H), 0.83 (t, *J* = 6.8, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 168.8, 143.3, 134.0, 131.8, 129.0, 127.0, 123.2, 120.0, 117.6, 114.5, 54.4, 50.4, 31.8, 30.6, 29.2, 27.2, 26.4, 22.6, 14.0; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 11.3 min and 12.5 min (major).

**2-((2***S***,3***S***)-2-Phenethylquinolin-3-yl)isoindoline-1,3-dione (3i):** known compound,<sup>[3]</sup> 95% yield, 90% ee, yellow oil,  $[\alpha]^{20}_{D} = -147.2$  (*c* 0.72, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = +156.0$  (*c* 0.76, CH<sub>2</sub>Cl<sub>2</sub>) for 93% ee (2*R*,3*R*)], R<sub>f</sub> = 0.50 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.85-7.76 (m, 2H), 7.74-7.65 (m, 2H), 7.20 (t, *J* = 7.2, 2H), 7.12 (dd, *J* = 8.9, 7.9, 3H), 7.00 (dd, *J* = 13.1, 7.1, 2H), 6.68 (t, *J* = 7.0, 1H), 6.48 (d, *J* = 16.6, 6.2, 1H), 2.84-2.74 (m, 1H), 2.72-2.58 (m, 1H), 2.00-1.79 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 168.8, 143.0, 141.4, 134.0, 131.8, 129.0, 128.5, 128.4, 127.1, 126.0, 123.3, 120.0, 117.8, 114.7, 54.1, 50.5, 32.9, 32.0, 27.2; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 20.7 min and 56.5 min (major).

**2-((2***S***,3***S***)-2-Butyl-6-fluoroquinolin-3-yl)isoindoline-1,3-dione (3j): 97% yield, 79% ee, yellow oil, [\alpha]^{20}\_{D} = -114.0 (***c* **0.52, CH<sub>2</sub>Cl<sub>2</sub>), R\_{f} = 0.45 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz,** 

CDCl<sub>3</sub>)  $\delta$  = 7.88-7.78 (m, 2H), 7.76-7.66 (m, 2H), 6.75 (dd, *J* = 15.0, 6.3, 2H), 6.51 (dd, *J* = 8.4, 4.8, 1H), 4.80 (td, *J* = 7.9, 3.5, 1H), 3.89 (s, 1H), 3.76 (dd, *J* = 17.1, 8.1, 1H), 3.45-3.36 (m, 1H), 3.09 (dd, *J* = 17.1, 6.7, 6.7, 6.7)

1H), 1.58-1.39 (m, 3H), 1.35-1.21 (m, 3H), 0.86 (t, J = 7.0, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 168.8, 156.0$  (d, <sup>1</sup> $J_{FC} = 235.5$ ), 139.8, 134.0, 131.8, 123.3, 121.8 (d, <sup>3</sup> $J_{FC} = 7.1$ ), 115.4 (d, <sup>3</sup> $J_{FC} = 7.7$ ), 115.0 (d, <sup>2</sup> $J_{FC} = 22.2$ ), 113.5 (d, <sup>2</sup> $J_{FC} = 22.5$ ), 54.8, 49.8, 30.3, 28.6, 28.0, 22.6, 14.0; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta = -127.3$ ; HRMS Calculated for C<sub>21</sub>H<sub>22</sub>FN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 353.1665, found 353.1656; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 9.9 min and 14.1 min (major).

**2-((2***S***,3***S***)-2-Phenylquinolin-3-yl)isoindoline-1,3-dione (3k):** known compound,<sup>[3]</sup> 83% yield, 14% ee, light yellow solid, mp 254-256 °C,  $[\alpha]^{20}_{D} = -39.3$  (*c* 0.60, CH<sub>2</sub>Cl<sub>2</sub>) [lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = -39.3$ 

 $\begin{array}{l} +135.4 \ (c \ 0.70, \ CH_2Cl_2) \ for \ 40\% \ ee \ (2R,3R)], \ R_f = 0.40 \ (hexane/EtOAc \ 5:1). \\ {}^{1}H \ NMR \ (400 \ MHz, \ CDCl_3) \ \delta = 7.75 \cdot 7.69 \ (m, \ 2H), \ 7.69 \cdot 7.63 \ (m, \ 2H), \ 7.26 \cdot 7.01 \ (m, \ 7H), \ 6.72 \ (t, \ J = 7.1, \ 1H), \ 6.62 \ (d, \ J = 7.9, \ 1H), \ 4.97 \ (dt, \ J = 10.4, \ 5.1, \ 1H), \ 4.75 \ (d, \ J = 4.6, \ 1H), \ 4.32 \ (s, \ 1H), \ 3.95 \ (dd, \ J = 16.3, \ 10.7, \ 1H), \ 3.03 \ (dd, \ J = 16.3, \ 10.7$ 

J = 16.3, 5.4, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 168.1, 143.5, 141.1, 133.9, 131.6, 129.0, 128.3, 127.9, 127.4, 127.3, 123.1, 119.4, 117.5, 113.4, 57.7, 51.1, 26.6; HPLC: Chiracel OD-H column, 254 nm, 30 °C,$ *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 18.7 min and 32.8 min (major).

2-((2S,3S)-2-Phenethylquinolin-3-yl)isoindoline-1,3-dione (3i, the hydrogenation product is the same as hydrogenation of (*E*)-2-(2-phenethylquinolin-3-yl)isoindoline-1,3-dione (2i) due to

hydrogenation of C=C double bond of side chain of substrate **21**): known compound,<sup>[3]</sup> 99% yield, 90% ee, yellow oil,  $R_f = 0.50$  (hexane/EtOAc 5:1). HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30,

flow = 0.7 mL/min, retention time 20.7 min and 55.9 min (major).

2-((2S,3S)-2-(4-fluorophenethyl)-1,2,3,4-tetrahydroquinolin-3-yl)isoindoline-1,3-dione

(3m): 86% yield, 88% ee, light yellow oil,  $[\alpha]^{20}_{D} = -132.2$  (*c* 0.64, CH<sub>2</sub>Cl<sub>2</sub>), R<sub>f</sub> = 0.60 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 7.81$  (dt, J = 7.0, 3.5, 2H), 7.76-7.65 (m, 2H), 7.12-6.96 (m, 4H), 6.87 (t, J = 8.7, 2H), 6.69 (t, J = 7.2, 1H), 6.51 (d, J = 7.9, 1H), 4.85-4.76 (m, 1H), 3.95 (dd, J = 16.5, 10.0, 2H), 3.48 (dt, J = 7.2, 3.3, 1H), 3.02 (dd, J = 16.6, 6.1,

1H), 2.84-2.71 (m, 1H), 2.69-2.55 (m, 1H), 2.00-1.72 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 168.8, 161.3 (d, <sup>1</sup>*J*<sub>FC</sub> = 243.8), 142.9, 137.0 (d, <sup>4</sup>*J*<sub>FC</sub> = 3.2), 134.1, 131.8, 129.7 (d, <sup>3</sup>*J*<sub>FC</sub> = 7.8), 129.0, 127.1, 123.3, 112.0, 117.9, 115.2 (d, <sup>2</sup>*J*<sub>FC</sub> = 21.1), 114.7, 54.0, 50.4, 32.2, 32.0, 27.1; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  = -117.4; HRMS Calculated for C<sub>25</sub>H<sub>22</sub>FN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 401.1665, found 401.1664; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 21.0 min (major) and 41.2 min

(*cis*)-Propyl 2-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (8a): 52% yield, 35% ee, known compound,<sup>[5]</sup> colorless oil,  $[\alpha]^{20}{}_{D} = -13.3$  (*c* 0.24, CH<sub>2</sub>Cl<sub>2</sub>),  $[lit.^{[5]}: [\alpha]^{20}{}_{D} = +23.4$  (*c* 1.0,

<sup>5</sup> Z.-P. Chen, Z.-S. Ye, M.-W. Chen, Y.-G. Zhou, Synthesis 2013, 45, 3239.

CHCl<sub>3</sub>) for 85% ee (2*R*,3*R*)],  $R_f = 0.50$  (hexane/EtOAc 10:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 0.90$  (dd, J = 14.6, 7.5, 2H), 6.64 (dd, J = 10.7, 4.1, 1H), 6.50 (d, J = 7.9, 1H), A = 14.4.02 (m, 2H), 3.98-3.82 (m, 2H), 3.12-3.00 (m, 1H), 3.00-2.87 (m, 2H), 1.72-1.60 (m, 2H), 1.14 (d, J = 6.5, 3H), 0.94 (t, J = 7.4, 3H); <sup>13</sup>C NMR (100

MHz, CDCl<sub>3</sub>)  $\delta$  = 173.0, 142.9, 129.5, 127.0, 119.1, 117.4, 114.6, 66.2, 47.4, 42.3, 25.5, 22.0, 17.9, 10.4; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 70/30, flow = 0.7 mL/min, retention time 7.6 min (major) and 8.2 min.

(*trans*)-Propyl 2-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (8b): 39% yield, 0% ee, colorless oil,  $R_f = 0.60$  (hexane/EtOAc 10:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta = 6.98$  (t, J = 7.4,  $CO_2^{n}Pr$  2H), 6.62 (dd, J = 10.7, 4.1, 1H), 6.49 (d, J = 7.7, 1H), 4.15-4.05 (m, 2H), 3.68 (s, 1H), 3.54 (dq, J = 9.3, 6.2, 1H), 3.05 (dd, J = 16.0, 11.4, 1H), 2.91 (dd, J = 16.0, 4.9, 1H), 2.53-2.43 (m, 1H), 1.75-1.62 (m, 2H), 1.24 (t, J = 5.8, 3H), 0.96 (t, J = 7.4, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 174.4$ , 143.6, 129.1, 127.1, 119.5, 117.3, 113.8, 66.2, 49.1, 45.8, 30.6, 22.0, 20.6, 10.4; HRMS Calculated for C<sub>14</sub>H<sub>20</sub>NO<sub>2</sub> [M+H]<sup>+</sup> 234.1494, found 234.1497.

*N*-((*cis*)-2-butyl-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide (9a): 11% yield, 51% ee, known compound,<sup>[3]</sup> white solid, mp 164-165 °C,  $[\alpha]^{20}_{D} = +11.3$  (*c* 0.08, CH<sub>2</sub>Cl<sub>2</sub>),

NHTs

[lit.<sup>[3]</sup>:  $[\alpha]^{20}_{D} = -46.5$  (*c* 0.20, CH<sub>2</sub>Cl<sub>2</sub>) for >99% ee (2*S*,3*S*)], R<sub>f</sub> = 0.55 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.72 (d, *J* = 8.2, 2H), 7.27 (d, *J* = 8.1, 2H), 6.98 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.77 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.71 (d, *J* = 7.4, 1H), 6.63 (t, *J* = 7.5, 1H), 6.71 (d, J = 7.5, 1H), 71 (d, J = 7.5, 1H), 71 (d, J = 7.5, 1H), 71 (d, J = 7.5, 1H),

7.3, 1H), 6.48 (d, J = 7.9, 1H), 4.87 (d, J = 9.2, 1H), 3.80-3.69 (m, 1H), 3.60 (s, 1H), 3.19 (t, J = 6.5, 1H), 2.87 (dd, J = 16.6, 3.9, 1H), 2.57 (dd, J = 16.6, 2.1, 1H), 2.42 (s, 3H), 1.46-1.26 (m, 2H), 1.23-1.05 (m, 4H), 0.84 (t, J=6.9, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 143.5$ , 143.2, 138.8, 130.5, 129.6, 127.3, 127.0, 118.5, 117.8, 114.2, 54.8, 48.4, 34.3, 31.7, 27.7, 22.6, 21.5, 13.9; HPLC: Chirapak AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 80/20, flow = 0.9 mL/min, retention time 11.6 min and 13.2 min (major).

*N*-((*trans*)-2-butyl-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide (9b): 22% yield, 9% ee, known compound,<sup>[3]</sup> colorless oil,  $R_f = 0.50$  (hexane/EtOAc 5:1). <sup>1</sup>H NMR

NHTs (400 MHz, CDCl<sub>3</sub>)  $\delta = 7.72$  (d, J = 8.3, 2H), 7.28 (d, J = 8.1, 2H), 6.98 (t, J = 7.3, 1H), 6.78 (d, J = 7.4, 1H), 6.61 (td, J = 7.4, 0.8, 1H), 6.47 (d, J = 8.0, 1H), 4.92 (d, J = 9.3, 1H), 3.98 (s, 1H), 3.62 (td, J = 8.0, 3.6, 1H), 3.06-2.95 (m, 1H), 2.82 (dd, J = 16.7, 4.5, 1H), 2.53-2.39 (m, 4H), 1.36-1.17 (m, 6H), 0.84 (t, J = 7.0, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta = 143.3, 142.0, 138.6, 130.3, 129.7, 127.5, 126.9, 117.7, 116.5, 114.3, 55.0, 49.0, 33.8, 29.7, 27.7, 22.4, 21.5, 13.9; HPLC: Chirapak AD-H column, 254 nm, 30 °C,$ *n*-hexane/*i*-propanol = 75/25, flow = 0.8 mL/min, retention time 10.5 min (major) and 12.3 min.

Methyl 2-methyl-1,2,3,4-tetrahydroquinoline-6-carboxylate (10): known compound (CAS: 1389882-44-3), 48% yield, 27% ee, white solid, mp 68-70 °C,  $[\alpha]^{20}{}_{\rm D}$  = -34.2 (*c* 0.12, CH<sub>2</sub>Cl<sub>2</sub>), R<sub>f</sub> MeO<sub>2</sub>C = 0.55 (hexane/EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ = 7.68-7.61 (m, 2H), 6.39 (d, *J* = 8.8, 1H), 4.14 (s, 1H), 3.83 (s, 3H), 3.53-3.43 (m, 1H), 2.87-2.70 (m, 2H), 1.99-1.90 (m, 1H), 1.63-1.51 (m, 1H), 1.23 (d, *J* = 6.3, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ = 167.5, 148.7, 131.1, 129.1, 119.7, 117.7, 112.6, 51.4, 47.2, 29.5, 26.3, 22.4; HPLC: Chiracel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 85/15, flow = 0.7 mL/min, retention time 12.3 min and 15.0 min (major).

# 5. Copy of NMR and HPLC for racemic and chiral compounds











1H NMR FC-6-36 in CDCl3 //Yzc/G/新 NMR 2013/1236/fid







10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 f1 (ppm)





1H NMR FC-4-99B in CDCI3







2.8527 2.8133 2.8133 2.8133 1.7804 1.7704 1.

1H NMR FC-6-40 in CDCl3 //Yzc/g/新 NMR 2013/1274/fid







10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 f1 (ppm)



1H NMR FC-5-46 in CDCl3 //Yzc/g/新 NMR 2013/1263/fid





13C NMR FC-5-46 in CDCl3





10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 f1 (ppm)





1H NMR FC-6-19B in CDCI3 G:/新 NMR 2013/956/fid







1H NMR FC-6-21A in CDCI3







1H NMR FC-6-21H in CDCI3







1H NMR FC-6-21G in CDCl3







1H NMR FC-6-25G in CDCl3







1H NMR FC-6-25F in CDCl3







1H NMR FC-6-25E in CDCI3






1H NMR FC-6-21C in CDCl3







1H NMR FC-6-21I in CDCI3







1H NMR FC-6-44A in CDCl3 G:/新 NMR 2014/1845/fid







10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 f1 (ppm)



1H NMR FC-6-21D in CDCI3







1H NMR FC-6-30A in CDCI3





13C NMR FC-6-30A in CDCI3





10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 f1 (ppm)



1H NMR FC-6-25D2 in CDCI3







1H NMR FC-6-25D1 in CDCI3







1H NMR FC-6-44C1 inCDCl3 G:/新 NMR 2014/2082/fid







1H NMR FC-6-44C2 in CDCl3 //Yzc/g/新 NMR 2013/1359/fid





13C NMR FC-6-44C2 in CDCl3 //Yzc/g/新 NMR 2013/1360/fid







Data File C:\FC-2\YZN002874.D Sample Name: FC-4-91D

Acq. Operator	:	WH				
Acq. Instrument	:	Instrument 1	Location	:	Vial 1	
Injection Date	:	5/25/2013 3:34:54 PM				
Acq. Method	:	C:\CHEM32\1\METHODS\DEF LC.M				
Last changed	:	5/25/2013 3:18:43 PM by WH				
		(modified after loading)				
Analysis Method	:	C:\CHEM32\1\METHODS\DEF LC.M				
Last changed	:	10/24/2013 8:18:08 PM by B				
		(modified after loading)				
Sample Info	:	OD-H, H/i-PrOH = 70/30, 0.7 mL/m	ain, 30 où	١,	254mm	



Area Percent Report Sorted By : Signal Multiplier: : 1.0000 Dilution: : 1.0000 Use Multiplier & Dilution Factor with ISTDs



*cis*-(±)-**3a** 

\*\*\* End of Report \*\*\*

3290.53223 152.07918

Instrument 1 10/24/2013 8:18:11 PM B

Totals :

Page 1 of 1

Instrument 1 3/19/2014 1:42:06 PM Z

Totals :

1 12.235 BB 0.3061 240.73900 12.19050 5.2448 2 14.222 BB 0.3585 4349.30615 188.11835 94.7552

4590.04515 200.30884

\*\*\* End of Report \*\*\*

\_\_\_\_\_

Page 1 of 1

Data File C:\FC-4 PD\YZ005160.D Sample Name: FC-6-19B Acq. Instrument : Instrument 1 Location : Vial 1 Instrument : Instrument 1 Location : Vial 1 Instrument : Il/3/2013 7:47:45 AM Acq. Method : C:\HPCHEN\\NETHODS\DEMOCAL2.M Last changed : Il/3/2013 5:56:48 Mb yz HOOU (modified after loading) Analysis Method : C:\(HEM32\)\NETHODS\DEF LC.M Last changed : 3/19/2014 1:42:02 PM by Z (modified after loading) Sample Info : 0 D-H, H/1-FCH = 70/30 0.7 mL/min, 30 oC, 254 nm







Acq. Operator :	: WH						
Acq. Instrument :	: Instrument 1	Location : Vial 1					
Injection Date	: 6/5/2013 1:31:59 AM						
Acq. Method	C:\HPCHEM\1\METHODS\DEF LC.M						
Last changed	: 6/5/2013 1:14:42 AM by WH						
	(modified after loading)						
Analysis Method :	C:\CHEM32\1\METHODS\DEF LC.M						
Last changed	: 10/9/2013 10:16:54 PM by B						
-	(modified after loading)						
Sample Info :	: OD-H, H/i-PrOH = 70/30, 0.7 ml	./min, 30 oC, 254 nm					



Area Percent Report

Signal

:

: 1.0000 : 1.0000 Multiplier: Dilution: Use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=254 nm Peak RetTime Type Width Area Height Area # [min] [min] mAU \*s [mAU ] ÷ 1 13.827 BB 0.3250 2529.78125 120.51426 50.0247 2 20.498 BB 0.4955 2527.28491 79.63683 49.9753 Totals : 5057.06616 200.15109 \_\_\_\_\_

\*\*\* End of Report \*\*\*



cis-(±)-**3c** 

Data File C:\FC-4 PD\YZ005277.D Sample Name: FC-6-21H Acg. Operator : 2HOU Acg. Instrument : Instrument 1 Location : Vial 1 Intection Date : 11/16/2013 12:43:13 FM Acg. Method : C:\FPCHEN\\NETHODS\DEFNCAL2.M Last changed : 11/16/2013 11:40:55 AM by ZHOU (modified after loading) Analysis Method : C:\FHEN32\1\METHODS\DEF LC.M Last changed : 3/19/2014 2:03:59 FM by Z (modified after loading) Sample Info : 0D-H, H/:-PTCH =70/30, 0.70 mL/min, 30 oC, 254nm



Area Percent Report NPhth Sorted By Signal . Multiplier: : 1.0000 Dilution: . 1.0000 Use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=254 nm Peak RetTime Type Width Height Area Area cis-(-)-3c # [min] [min] mAU \*s [mAU ] ÷ -- | ----- | 1 13.849 BB 0.3228 431.96985 20.75943 7.7395 2 20.480 BB 0.4888 5149.38428 163.28098 92.2605 Totals : 5581.35413 184.04040



Instrument 1 10/9/2013 10:17:57 PM B

Sorted By

Page 1 of 1

Instrument 1 3/19/2014 2:04:03 PM Z

Page 1 of 1





Acq. Operator	:	WH				
Acq. Instrument	:	Instrument 1 Location : Vial 1				
Injection Date	:	6/5/2013 2:18:54 AM				
Acq. Method	:	C:\HPCHEM\1\METHODS\DEF LC.M				
Last changed	:	6/5/2013 1:14:42 AM by WH				
		(modified after loading)				
Analysis Method	:	C:\CHEM32\1\METHODS\DEF LC.M				
Last changed	:	3/19/2014 2:24:22 PM by Z				
-		(modified after loading)				
Sample Info	:	OD-H, H/i-PrOH = 70/30, 0.7 mL/min, 30 oC, 254 nm				



Area Percent Report

Signal

:

Multiplier: Dilution:	:	1.0000		
Use Multiplier & Di	lution Factor with	h ISTDs		
Signal 1: VWD1 A, W	Javelength=254 nm			
Peak RetTime Type # [min]	Width Area [min] mAU *s	Height [mAU ]	Area %	V N H
1 18.751 BB 2 29.960 BB	0.4242 553.47186 0.8173 540.57367	20.21572 10.11172	50.5895 49.4105	cis-(±)- <b>3e</b>
Totals :	1094.04553	30.32744		

\*\*\* End of Report \*\*\*

Data File C: NFC-4 ED/YZ005280.D Sample Name: FC-6-25G Acq. Operator : ZHOU Acq. Instrument : Instrument 1 Location : Vial 1 Intection Date : 11/16/2013 2:13:53 PM Acq. Method : C: NFPCHENLYMETHOD SNDEMOCAL2. M Last changed : 11/16/2013 2:33:12 PM ho ZHOU (modified after loading) Analysis Method : C: (HEFM231/NEFTHOD SNDEF LC.M Last changed : 3/19/2014 2:25:16 PM by Z (modified after loading) Sample Info : Or-H, H/1-FPCH =70/30, 0.70 mL/min, 30 oC, 254mm







Instrument 1 3/19/2014 2:24:31 PM Z

Sorted By

Page 1 of 1

NPhth

Instrument 1 3/19/2014 2:25:31 PM Z

Page 1 of 1



Acq. Operator :	WH					
Acq. Instrument :	Instrument 1	Location : Vial l				
Injection Date :	6/14/2013 4:15:31 PM					
Acq. Method :	C:\CHEM32\1\METHODS\DEF LC.M					
Last changed :	6/14/2013 4:13:10 PM by WH					
	(modified after loading)					
Analysis Method :	C:\CHEM32\1\METHODS\DEF LC.M					
Last changed :	10/9/2013 10:19:15 PM by B					
	(modified after loading)					
Sample Info :	OD-H, H/i-PrOH = 70/30, 0.7 mL/m	in, 30 oC, 254 nm				



..... Area Percent Report -----

Signal

:



\*\*\* End of Report \*\*\*

NPhth

Data File C:\FC-4 PD\YZ005278.D Sample Name: FC-6-25F -----Acq. Operator : ZHOU Acq. Instrument 1 Injection Date : 11/16/2013 1:12:40 PM Acq. Method : C:\HPCHEM\1\METHODS\DEMOCAL2.M Location : Vial 1 Last changed : 11/16/2013 11:40:55 AM by ZHOU (modified after loading) Analysis Method: C:(CEEM32),1WE Floating Last changed : 3/19/2014 2:13:30 PM by Z (modified after loading) Sample Info : 0D-H, H/1-PrOH =70/30, 0.70 mL/min, 30 oC, 254mm





Dilution: Use Multiplier &	Dilution Factor wi	1.0000 th ISTDs		N N
Signal 1: VWD1 A	, Wavelength=254 nm			н
Peak RetTime Typ # [min]	e Width Area [min] mAU *s	Height A: [mAU ]	rea %	<i>cis</i> -(–)- <b>3f</b>
1 10.177 BB 2 17.365 BB	0.2342 279.0687 0.4575 5049.3325	9 18.50447 5 2 170.54918 94	.2374 7626	
Totals :	5328.4013	L 189.05365		

\_\_\_\_\_ \*\*\* End of Report \*\*\*

Instrument 1 10/9/2013 10:21:44 PM B

Sorted By

Page 1 of 1

Instrument 1 3/19/2014 2:13:42 PM Z

Page 1 of 1

∼\_..\NPhth







Instrument 1 10/9/2013 10:27:46 PM B

Page 1 of 1

Instrument 1 3/19/2014 2:11:59 PM Z

Page 1 of 1

NPhth

Ρh



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Data File C:\FC-2\YZN002989.D
Sample Name: FC-5-5F
```

						===
Acq. Operator	:	WH				
Acq. Instrument	:	Instrument 1	Location	1 :	Vial	1
Injection Date	:	6/13/2013 6:02:46 PM				
Acq. Method	:	C:\CHEM32\1\METHODS\DEF LC.M				
Last changed	:	6/13/2013 5:57:07 PM by WH				
		(modified after loading)				
Analysis Method	:	C:\CHEM32\1\METHODS\DEF LC.M				
Last changed	:	10/9/2013 10:30:44 PM by B				
		(modified after loading)				
Sample Info	:	OD-H, H/i-PrOH = 70/30, 0.7 mL/m	min, 30 d	bC.	254 n	m



Area Percent Report





```
Acq. Instrument : Instrument 1 Location : Vial 1
Intection Date : 11/26/2013 2:04:15 AM
Acq. Method : C:\HFCHEM1\NETHODS\DEMOCAL2.M
Last changed : 11/26/2013 1:01:57 AM by 2HOU
(modified after 1 loading)
Analysis Method : C:\CHEMS2\1\METHODS\DEF LC.M
Last changed : 3/19/2014 2:09:40 PM by Z
(modified after 1 loading)
Sample Info : 0D-H, H/i-FUGH = 70/30, 0.7 mL/min, 30 oC, 254 nm
```





\*\*\*\* End of Report \*\*\*

6076.82910 132.20589

Instrument 1 10/9/2013 10:31:17 PM B

Page 1 of 1

Instrument 1 3/19/2014 2:09:50 PM Z

Totals :

Page 1 of 1







S72




S74



Instrument 1 3/19/2014 3:00:36 PM Z

Page 1 of 1





Page 1 of 1