Supporting Information For:

Highly Enantioselective Iridium-Catalyzed Hydrogenation of Heteroaromatic Compounds, Quinolines

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1. General procedure for Ir-catalyzed asymmetric hydrogenation of quinoline derivatives.

A mixture of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.4 mg, 0.005 mmol) and (R)-MeO-Biphep (6.4 mg, 0.011 mmol) in toluene (5 mL) was stirred at room temperature for 30 min in a glovebox, the mixture was transferred by a syringe to stainless steel autoclave, in which I_2 (12.7 mg, 0.05 mmol) and substrate (1.0 mmol) were placed beforehand. The hydrogenation was performed at room temperature under H_2 (650 psi) for 12-15 h. After carefully releasing the hydrogen, the reaction mixture was diluted with dichloromethane (20 mL), saturated sodium carbonate aqueous solution (5 mL) was added, then stirred for 15 min, the aqueous layer was extracted with dichloromethane (3 x 15 mL), the combined organic layer was dried over sodium sulfate and concentrated to afford the crude product. Purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure product. The enantiomeric excesses were determined by chiral HPLC with chiral columns (OJ-H, OD-H, or AS-H).

2-Methyl-1,2,3,4-tetrahydroquinoline (2a). (Known compound, see: Grignon-Dubois, M.; Fialeix, M.; Leguerre, M.; Leger, J. M.; Gauffre, J. C. *J. Org. Chem.* **1993**, 58, 1926; Pope, W. J.; Peachey, S. J. *J. Chem. Soc.* **1899**, 75, 1066). 94% ee, $[\alpha]_{\text{D}}^{25} = +79.9$ (*c* 1.01, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.24 (t, *J* = 6.5 Hz, 3H), 1.62 (m, 1H), 1.96 (m, 1H), 2.81 (m, 2H), 3.42 (m, 1H), 3.50 (br, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 6.63 (m, 1H), 6.98 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 22.8, 26.8, 30.3, 47.4, 114.2, 117.2, 121.3, 126.9, 129.5, 144.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 0.5 mL / min), (S) t_1 = 27.2 min, (R) t_2 = 30.4 min.

2-Ethyl-1,2,3,4-tetrahydroquinoline (2b). (Known compound, see: Wee, A. G. H.; Liu, B.; Zhang, L. *J. Org. Chem.* **1992**, 57, 4404). 96% ee, $[\alpha]_{\text{D}}^{25} = +75.9$ (*c* 1.76, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 0.95 (t, *J* = 7.6 Hz, 3H), 1.52 (m, 3H), 1.92 (m, 1H), 2.73 (m, 2H), 3.12 (m, 1H), 3.68 (br, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 6.56 (t, *J* = 8.3 Hz, 1H), 6.92 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 10.2, 26.6, 27.7, 29.5, 53.2, 114.1, 116.9, 121.5, 126.8, 129.4, 144.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 0.5 mL / min), (S) t_1 = 23.1 min, (R) t_2 = 26.1 min.

2-Propyl-1,2,3,4-tetrahydroquinoline (2c). (Known compound, see: Pitts, M. R.; Harrison, J. R.; Moody, C. J. *J. Chem. Soc., Perkin Trans. I* **2001**, 955). 93% ee, $[\alpha]_{\text{D}}^{25} = +72.7$ (*c* 1.58, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 0.98 (t, *J* = 7.0 Hz, 3H), 1.43 (m,

3H), 1.50 (m, 1H), 1.95 (m, 1H), 2.76 (m, 2H), 3.26 (m, 1H), 3.75 (br, 1H), 6.48 (d, $J = 8.2$ Hz, 1H), 6.62 (m, 1H), 6.98 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 14.3, 19.0, 26.6, 28.2, 39.0, 51.4, 114.16, 116.9, 121.5, 126.8, 129.4, 144.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 0.5 mL / min), (S) $t_1 = 19.3$ min, (R) $t_2 = 24.7$ min.

2-Butyl-1,2,3,4-tetrahydroquinoline (2d). (Known compound, see; Goldstein, S. W.; Dambek, D. J. *Synthesis* **1989**, 221). 92% ee, $[\alpha]_D^{25} = +79.9$ (c 1.0, CHCl_3); ^1H -NMR (400 MHz, CDCl_3) 0.96 (t, $J = 7.0$ Hz, 3H), 1.49 (m, 7H), 1.95 (m, 1H), 2.75 (m, 2H), 3.21 (m, 2H), 3.71 (br, 1H), 6.45 (d, $J = 8.2$ Hz, 1H), 6.59 (m, 1H), 6.97 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 14.3, 23.2, 26.6, 28.1, 28.3, 36.6, 51.8, 114.2, 117.1, 121.6, 126.9, 129.4, 144.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate 0.5 mL / min), (S) $t_1 = 18.8$ min, (R) $t_2 = 22.5$ min.

2-Pentyl-1,2,3,4-tetrahydroquinoline (2f). (Known compound, see: Jacquemond-Collet, I.; Bessiere, J. M.; Hannedouche, S.; Bertrand, C.; Fouraste, I.; Moulis, C. *Phytochemical Analysis*, **2001**, 12, 312). 94% ee, $[\alpha]_D^{25} = +74.4$ (c 1.03, CHCl_3); ^1H -NMR (400 MHz, CDCl_3) 0.96 (t, $J = 7.0$ Hz, 3H), 1.42 (m, 8H), 1.51 (m, 1H), 1.99 (m, 1H), 2.79 (m, 2H), 3.27 (m, 1H), 3.76 (br, 1H), 6.49 (d, $J = 8.4$ Hz, 1H), 6.63 (t, $J = 8.4$ Hz, 1H), 6.99 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 14.2, 22.8, 25.6, 26.6, 28.3, 32.1, 36.8, 51.7, 114.1, 117.0, 121.5, 126.8, 129.4, 144.9; HRMS Calcd for $\text{C}_{14}\text{H}_{22}\text{N}$ ($M+1$) 204.1752, found 204.1753; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate 0.5 mL / min), (S) $t_1 = 16.7$ min, (R) $t_2 = 18.6$ min.

2-Phenethyl-1,2,3,4-tetrahydroquinoline (2g). (Known compound, see: Avromoff, M.; Sprinzak, Y. *J. Am. Chem. Soc.* **1956**, 78, 4090). 93% ee, $[\alpha]_D^{25} = +73.1$ (c 1.02, CHCl_3); ^1H -NMR (400 MHz, CDCl_3) 1.96 (m, 1H), 2.12 (m, 2H), 2.28 (m, 1H), 3.02 (m, 4H), 3.56 (m, 1H), 4.01 (br, 1H), 6.72 (d, $J = 8.2$ Hz, 1H), 6.91 (t, $J = 7.3$ Hz, 1H), 7.25 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 26.4, 28.1, 32.3, 38.4, 51.3, 114.3, 117.2, 121.4, 126.1, 126.9, 128.5, 128.6, 129.4, 142.0, 144.7; HPLC (AS-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate 1.0 mL / min), (S) $t_1 = 5.7$ min, (R) $t_2 = 6.5$ min.

2-(3',4'-Dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (2h). (Known compound, see: Jacquemond-Collet, I.; Bessiere, J. M.; Hannedouche, S.; Bertrand, C.; Fouraste, I.; Moulis, C. *Phytochemical Analysis*, **2001**, 12, 312). 96% ee, $[\alpha]_D^{25} = +61.7$ (c 0.80, CHCl_3); ^1H -NMR (400 MHz, CDCl_3) 1.65 (m, 1H), 1.81 (m, 2H), 1.98 (m, 1H), 2.67 (m, 4H), 2.77 (m, 1H), 3.28 (m, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 6.44 (d, $J = 8.0$ Hz, 1H), 6.59 (m, 1H), 6.74 (m, 3H), 6.94 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 26.6, 28.5, 32.3, 38.8, 51.7, 56.3, 56.4, 111.8, 112.1, 114.6, 117.5, 120.6, 121.7, 127.2, 129.7, 134.9, 144.9, 147.8, 149.4; HPLC (AS-H, elute: Hexanes / *i*-PrOH = 97 / 3, detector: 254 nm, flow rate 0.5 mL / min), (S) $t_1 = 38.5$ min, (R) $t_2 = 41.0$ min.

2-(3',4'-Methylenedioxyphenethyl)-1,2,3,4-tetrahydroquinoline (2i). (Known compound, see: Jacquemond-Collet, I.; Bessiere, J. M.; Hannedouche, S.; Bertrand, C.; Fouraste, I.; Moulis, C. *Phytochemical Analysis*, **2001**, 12, 312). 93% ee, $[\alpha]_D^{25} = +63.0$ (c 1.06, CHCl_3); ^1H -NMR (400 MHz, CDCl_3) 1.66 (m, 1H), 1.78 (m, 2H), 1.97 (m, 1H), 2.65 (m, 4H), 2.75 (m, 1H), 3.27 (m, 1H), 3.66 (br, 1H), 5.90 (s, 2H), 6.45 (d, $J = 8.0$ Hz, 1H), 6.65 (m, 4H), 6.95 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) 26.3, 28.0, 31.9, 38.5, 51.1, 100.8, 108.3, 108.9, 114.2, 117.1, 121.1, 121.3, 126.8, 129.3, 135.8, 144.6, 145.8, 147.8; HRMS Calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_2$ ($M+1$) 282.1494, found 282.1507; HPLC (AS-H,

elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1.0 mL / min), (S) t_1 = 14.6 min, (R) t_2 = 19.1 min.

6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (2j). (Known compound, see: Balint, J.; Egri, G.; Kiss, V.; Gajary, A.; Juvancz, Z.; Fogassy, E. *Tetrahedron: Asymmetry* **2001**, 12, 3435). 96% ee, $[\alpha]_D^{25} = +67.4$ (*c* 0.98, CH₃CH₂OH); ¹H-NMR (400 MHz, CDCl₃) 1.13 (d, *J* = 6.0 Hz, 3H), 1.53 (m, 1H), 1.85 (m, 1H), 2.64 (m, 1H), 2.74 (m, 1H), 3.28 (m, 1H), 3.70 (br, 1H), 6.34 (m, 1H), 6.61 (m, 2H); HPLC (OD-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate: 1.0 mL / min), (S) t_1 = 5.6 min, (R) t_2 = 6.7 min.

2,6-Dimethyl-1,2,3,4-tetrahydroquinoline (2k). (Known compound, see: Reinhardt, C.; Harms, K.; Kinzel, M.; Scharfer, G.; Stein, J.; Wocadlo, S. *Liebigs Ann.* **1995**, 317; Pope, W. J.; Rich, E. M. *J. Chem. Soc.* **1899**, 75, 1093). 91% ee, $[\alpha]_D^{25} = +73.5$ (*c* 0.98, benzene); ¹H-NMR (400 MHz, CDCl₃) 1.22 (d, *J* = 6.5 Hz, 3H), 1.60 (m, 2H), 1.93 (m, 1H), 2.22 (s, 2H), 2.73 (m, 2H), 3.38 (m, 1H), 6.36 (d, *J* = 8.2 Hz, 1H), 6.72 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) 20.4, 22.6, 26.6, 30.4, 47.3, 114.2, 121.2, 126.2, 127.2, 129.8, 142.5; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 0.5 mL / min), (S) t_1 = 26.8 min, (R) t_2 = 33.7 min.

6-Methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (2l). (Known compound, See: Kawase, M.; Kikugawa, Y. *Chem. Pharm. Bull.* **1981**, 29, 1615). 84% ee, $[\alpha]_D^{25} = +62.3$ (*c* 0.98, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 1.39 (t, *J* = 7.0 Hz, 3H), 1.79 (m, 1H), 2.11 (m, 1H), 2.93 (m, 2H), 3.51 (m, 1H), 3.67 (br, 1H), 3.92 (s, 3H), 6.63 (d, *J* = 8.2 Hz, 1H), 6.80 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) 22.6, 27.0, 30.5, 47.6, 55.9, 112.9, 114.8, 115.4, 122.6, 139.1, 151.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 0.5 mL / min), (S) t_1 = 28.9 min, (R) t_2 = 34.9 min.

2-Phenyl-1,2,3,4-tetrahydroquinoline (2m). (Known compound, see; Pitts, M. R.; Harrison, J. R.; Moody, C. J. *J. Chem. Soc., Perkin Trans. I* **2001**, 955). 72% ee, $[\alpha]_D^{25} = +69.9$ (*c* 1.0, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 2.02 (m, 1H), 2.12 (m, 1H), 2.76 (m, 1H), 2.90 (m, 1H), 4.04 (br, 1H), 4.45 (m, 1H), 6.55 (d, *J* = 8.2 Hz, 1H), 6.67 (m, 1H), 7.01 (m, 2H), 7.35 (m, 5H); ¹³C-NMR (100 MHz, CDCl₃) 26.9, 31.5, 56.8, 114.5, 117.7, 121.4, 127.1, 127.4, 127.9, 128.8, 129.1, 129.8, 145.3; HPLC (AS-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate 1.0 mL / min), (S) t_1 = 5.9 min, (R) t_2 = 20.4 min.

2-Methyl-1-(1,2,3,4-tetrahydroquinolin-2-yl)-propan-2-ol (2n). 91% ee, $[\alpha]_D^{25} = +52.8$ (*c* 0.98, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 1.24 (s, 3H), 1.26 (s, 3H), 1.60 (m, 3H), 1.75 (m, 1H), 2.66 (m, 1H), 2.78 (m, 1H), 3.48 (m, 1H), 6.39 (m, 1H), 6.50 (m, 1H), 6.93 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) 26.5, 27.7, 29.3, 32.7, 48.7, 49.0, 71.9, 114.3, 116.6, 120.9, 126.6, 128.4, 144.5; HRMS Calcd for C₁₃H₂₀NO (M+1) 206.1539, found 206.1551; HPLC (OD-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate: 1.0 mL / min), (S) t_1 = 8.8 min, (R) t_2 = 10.8 min

1-(1,2,3,4-tetrahydroquinolin-2-ylmethyl)-cyclohexanol (2p). 92% ee, $[\alpha]_D^{25} = +47.9$ (*c* 0.98, CHCl₃); ¹H-NMR (400 MHz, CDCl₃) 1.24 (m, 2H), 1.53 (m, 14H), 1.74 (m, 1H), 2.67 (m, 1H), 2.78 (m, 1H), 3.50 (m, 1H), 6.39 (m, 1H), 6.49 (m, 1H), 6.87 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) 22.1, 22.2, 25.7, 26.6, 29.9, 35.7, 40.6, 47.3, 47.7, 72.6, 114.4, 116.6, 120.9, 126.7, 129.2, 144.6; HRMS Calcd for C₁₆H₂₄NO (M+1) 246.1852, found 246.1868; HPLC (OD-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate: 1.0 mL / min), (S) t_1 = 8.2 min, (R) t_2 = 8.9 min

1,1-Diphenyl-2-(1,2,3,4-tetrahydroquinolin-2-yl)-ethanol (2r). 94% ee, $[\alpha]_D^{25} = +100.6$ (c 0.98, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.12 (d, $J = 6.1$ Hz, 1H), 1.21 (br, 1H), 1.68 (m, 2H), 2.39 (m, 2H), 2.63 (m, 2H), 3.24 (m, 1H), 6.33 (m, 1H), 6.53 (m, 1H), 6.83 (m, 2H), 7.18 (m, 2H), 7.25 (m, 4H), 7.35 (m, 4H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 25.9, 29.5, 47.2, 48.4, 79.1, 115.6, 117.7, 121.7, 126.1, 126.3, 126.8, 127.1, 127.4, 128.5, 129.4, 144.1, 146.3, 147.9; HRMS Calcd for $\text{C}_{23}\text{H}_{24}\text{NO}$ ($\text{M}+1$) 330.1852, found 330.1836; HPLC (OD-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate: 1.0 mL / min), (S) $t_1 = 12.3$ min, (R) $t_2 = 14.6$ min.

(1,2,3,4-tetrahydroquinolin-2-yl)-methanol (2s). *i*-PrOH is used as solvent (Known compound, see: Katayama, S.; Ae, N.; Nagata, R. *Tetrahedron: Asymmetry* **1998**, 9, 4295-4299), 75% ee, $[\alpha]_D^{25} = +40.9$ (c 0.64, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.68 (m, 1H), 1.89 (m, 1H), 2.78 (m, 2H), 3.10 (br, 2H), 3.44 (m, 1H), 3.54 (m, 1H), 3.73 (m, 1H), 6.55 (m, 1H), 6.65 (m, 1H); HPLC (OD-H, elute: Hexanes / *i*-PrOH = 80 / 20, detector: 254 nm, flow rate: 0.5 mL / min), (S) $t_1 = 13.2$ min, (R) $t_2 = 14.3$ min.

2-Isopropyl-1,2,3,4-tetrahydroquinoline (2t). (Known compound, see: Bertini, F.; Caronna, T.; Citterio, A.; Gross, L.; Minisci, F. *Chim. Ind.* **1974**, 56, 272-273), 94% ee, $[\alpha]_D^{25} = +21.1$ (c 0.32, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.01 (d, $J = 6.8$ Hz, 3H), 1.03 (d, $J = 6.8$ Hz, 3H), 1.74 (m, 2H), 1.93 (m, 1H), 2.79 (m, 2H), 3.06 (m, 1H), 3.79 (br, 1H), 6.51 (m, 1H), 6.62 (m, 1H), 6.99 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 18.2, 18.5, 23.7, 26.6, 32.5, 57.2, 113.9, 116.6, 121.4, 126.6, 129.1, 144.9; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 98 / 2, detector: 254 nm, flow rate: 0.5 mL / min), (S) $t_1 = 20.5$ min, (R) $t_2 = 21.6$ min.

Acetic acid 1,2,3,4-tetrahydroquinolin-2-ylmethyl ester (2u). 87% ee, $[\alpha]_D^{25} = +85.9$ (c 1.44, CHCl_3); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.70 (m, 1H), 1.96 (m, 1H), 2.11 (s, 3H), 2.80 (m, 2H), 3.58 (m, 1H), 3.94 (m, 1H), 4.26 (m, 1H), 6.53 (d, $J = 8.0$, 1H), 6.65 (m, 1H), 6.98 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 21.2, 24.7, 25.8, 50.3, 68.2, 114.5, 117.6, 121.1, 127.0, 129.3, 143.7, 170.9; HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{NO}_2$ ($\text{M}+1$) 206.1176, found 206.1184; HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 1.0 mL / min), (R) $t_1 = 24.6$ min, (S) $t_2 = 27.9$ min.

2. Enantioselective synthesis of three naturally occurring tetrahydroquinoline alkaloids Angustureine, Cuspareine and Galipinine.

2.1 Enantioselective synthesis of (-)-Angustureine.

A mixture of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.4 mg, 0.005 mmol) and (R)-MeO-Biphep (6.4 mg, 0.011 mmol) in toluene (5 mL) was stirred at room temperature for 30 min in a glovebox, the mixture was transferred by a syringe to stainless steel autoclave, in which I_2 (12.7 mg, 0.05 mmol) and 2-*n*-pentylquinoline (199 mg, 1.0 mmol) were placed beforehand. The hydrogenation was performed at room temperature under H_2 (650 psi) for 12-15 h. After carefully releasing the hydrogen, the reaction mixture was diluted with dichloromethane (20 mL), saturated sodium carbonate aqueous solution (5 mL) was added, then stirred for 15 min, the aqueous layer was extracted with dichloromethane (3 x 15 mL), the combined organic layer was dried over sodium sulfate and concentrated to afford the crude product. Purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-*n*-pentyl-1,2,3,4-tetrahydroquinoline 185 mg with 92% yield. E_e : 94%, $[\alpha]_D^{25} = +74.4$ (c 1.03, CHCl_3), HPLC (OJ-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate 0.5 mL / min), (R) $t_1 = 16.7$ min, (S) $t_2 = 18.6$ min. The absolute configuration is assigned as R by analogue.

To a stirred solution of 2-*n*-pentyl-1,2,3,4-tetrahydroquinoline (68 mg, 0.33 mmol) and 0.4 mL (5 mmol) of 37% aqueous formaldehyde in 3 mL of acetonitrile was added 95 mg of sodium cyanoborohydride. Glacial acetic acid (100 μL) was added, and the reaction was stirred at room temperature for 30 min, an additional 100 μL of glacial acid was added, and stirring was continued for 30 min more. The reaction mixture was poured into 30 mL of ether and then washed with three 10 mL portions of 1N KOH and one portion of brine. The ether solution was dried over potassium carbonate and evaporated *in vacuo* to give crude product as yellow oil, purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-*n*-pentyl-2,3,4-tetrahydro-1-methylquinoline 67 mg with 94% yield. $[\alpha]_D^{15} = -6.70$ (c 1.00, CHCl_3); ((-)-Angustureine, known compounds, $[\alpha]_D^{25} = -7.16$ (c 1.00, CHCl_3); which was isolated from *Galipea officinalis* Hancock, see: Jacquemond-Collet, I.; Hannedouche, S.; Fabre, N.; Fouraste, I.; Moulis, C. *Phytochemistry* **1999**, 51, 1167-1169). $^1\text{H-NMR}$ (400 MHz, CDCl_3) 0.94 (t, $J = 7.0$ Hz, 3H), 1.21 (m, 7H), 1.64 (m, 1H), 1.94 (m, 2H), 2.70 (m, 1H), 2.83 (m, 1H), 2.98 (s, 3H), 3.29 (m, 1H), 6.57 (d, $J = 8.2$ Hz, 1H), 6.63 (td, $J = 7.3, 1.0$ Hz, 1H), 7.02 (d, $J = 7.2$ Hz, 1H), 7.13 (t, $J = 8.2$ Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 14.4, 22.9, 23.8, 24.6, 26.0, 31.4, 32.3, 38.1, 59.1, 110.6, 115.4, 122.0, 127.2, 128.8, 145.6. According to sign of optical rotation, absolute configuration of naturally occurring alkaloid (-)-Angustureine is assigned as R.

2.2 Enantioselective synthesis of (-)-Cuspareine.

A mixture of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.4 mg, 0.005 mmol) and (S)-MeO-Biphep (6.4 mg, 0.011 mmol) in toluene (5 mL) was stirred at room temperature for 30 min in a glovebox, the mixture was transferred by a syringe to stainless steel autoclave, in which I_2 (12.7 mg, 0.05 mmol) and 2-(3,4-dimethoxyphenylethyl)quinoline (295 mg, 1.0 mmol) were placed beforehand. The hydrogenation was performed at room temperature under H_2 (650 psi) for 12-15 h. After carefully releasing the hydrogen, the reaction mixture was diluted with dichloromethane (20 mL), saturated sodium carbonate aqueous solution (5 mL) was added, then stirred for 15 min, the aqueous layer was extracted with dichloromethane (3 X 15 mL), the combined organic layer was dried over sodium sulfate and concentrated to afford the crude product. Purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-(3',4'-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline 261 mg with 86% yield. Ee: 96%, $[\alpha]_D^{25} = -61.7$ (c 0.80, CHCl_3), HPLC (AS-H, elute: Hexanes / *i*-PrOH = 97 / 3, detector: 254 nm, flow rate 0.5 mL / min), (R) $t_1 = 38.5$ min, (S) $t_2 = 41.0$ min. The absolute configuration is assigned as S by analogue.

To a stirred solution of 2-(3',4'-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (48 mg, 0.16 mmol) and 0.4 mL (5 mmol) of 37% aqueous formaldehyde in 3 mL of acetonitrile was added 95 mg of sodium cyanoborohydride. Glacial acetic acid (100 μL) was added, and the reaction was stirred at room temperature for 30 min, an additional 100 μL of glacial acid was added, and stirring was continued for 30 min more. The reaction mixture was poured into 30 mL of ether and then washed with three 10 mL portions of 1N KOH and one portion of brine. The ether solution was dried over potassium carbonate and evaporated *in vacuo* to give crude product as yellow oil, purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-(3',4'-dimethoxyphenethyl)-2,3,4-tetrahydro-1-methylquinoline 46 mg with 91% yield. $[\alpha]_D^{15} = -28.0$ (c 1.00, CHCl_3); ((-)-Cuspareine, $[\alpha]_D^{25} = -22.8$ (c 1.00, CHCl_3), known compound, which was isolated from *Galipea officinalis* Hancock, see: Rakotoson, J. H.; Fabre, N.; Jacquemond-Collet, I.; Hannedouche, S.; Fouraste, I.; Moulis, C. *Planta Medica*, **1998**, 64, 762). $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.78 (m, 1H), 1.98 (m, 3H), 2.57 (m, 1H), 2.69 (m, 2H), 2.83 (m, 1H), 2.94 (s, 3H), 3.31 (m, 1H), 3.88 (s, 3H), 3.90 (s, 3H), 6.58 (d, $J = 8.2$ Hz, 1H), 6.65 (t, $J = 7.3$ Hz, 1H), 6.78 (m, 2H), 6.84 (d, $J = 7.2$ Hz, 2H), 7.01 (d, $J = 7.2$ Hz, 1H), 7.11 (t, $J = 8.0$, 1H); $^{13}\text{C-NMR}$ (CDCl_3) 23.8, 24.6, 32.1, 33.3, 38.3, 56.1, 56.2, 58.6, 110.8, 11.5, 111.8, 115.6, 120.3, 121.9, 127.3, 128.9, 134.9, 145.5, 147.4, 149.1.

2.3 Enantioselective synthesis of (-)-Galipinine.

A mixture of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.4 mg, 0.005 mmol) and (S)-MeO-Biphep (6.4 mg, 0.011 mmol) in toluene (5 mL) was stirred at room temperature for 30 min in a glovebox, the mixture was transferred by a syringe to stainless steel autoclave, in which I_2 (12.7 mg, 0.05 mmol) and 2-(3',4'-dimethoxyphenylethyl)quinoline (279 mg, 1.0 mmol) were placed beforehand. The hydrogenation was performed at room temperature under H_2 (650 psi) for 12-15 h. After carefully releasing the hydrogen, the reaction mixture was diluted with dichloromethane (20 mL), saturated sodium carbonate aqueous solution (5 mL) was added, then stirred for 15 min, the aqueous layer was extracted with dichloromethane (3 X 15 mL), the combined organic layer was dried over sodium sulfate and concentrated to afford the crude product. Purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-(3',4'-methylenephenylethyl)-1,2,3,4-tetrahydroquinoline 242 mg with 88% yield. Ee: 93%, $[\alpha]_D^{25} = -63.0$ (c 1.06, CHCl_3), HPLC (AS-H, elute: Hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1.0 mL / min), (R) $t_1 = 14.6$ min, (S) $t_2 = 19.1$ min. The absolute configuration is assigned as S by analogue.

To a stirred solution of 2-(3',4'-methylenephenylethyl)-1,2,3,4-tetrahydroquinoline (64 mg, 0.23 mmol) and 0.4 mL (5 mmol) of 37% aqueous formaldehyde in 3 mL of acetonitrile was added 95 mg of sodium cyanoborohydride. Glacial acetic acid (100 μL) was added, and the reaction was stirred at room temperature for 30 min, an additional 100 μL of glacial acid was added, and stirring was continued for 30 min more. The reaction mixture was poured into 30 mL of ether and then washed with three 10 mL portions of 1N KOH and one portion of brine. The ether solution was dried over potassium carbonate and evaporated *in vacuo* to give crude product as yellow oil, purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure 2-(3',4'-methylenedioxyphenylethyl)-2,3,4-tetrahydro-1-methylquinoline $[\alpha]_D^{15} = -29.8$ (c 1.00, CHCl_3); ((-)-Galipinine, $[\alpha]_D^{20} = -33.4$ (c 1.00, CHCl_3), known compounds, which was isolated from *Galipea officinalis* Hancock, see: Rakotoson, J. H.; Fabre, N.; Jacquemond-Collet, I.; Hannedouche, S.; Fouraste, I.; Moulis, C. *Planta Medica*, **1998**, 64, 762) 63 mg with 94% yield. ^1H -NMR (400 MHz, CDCl_3) 1.72 (m, 1H), 1.95 (m, 3H), 2.51 (m, 1H), 2.65 (m, 2H), 2.73 (m, 1H), 2.94 (s, 3H), 3.31 (m, 1H), 5.95 (s, 3H), 6.55-6.77 (m, 5H), 7.02 (d, $J = 7.2$ Hz, 1H), 7.12 (t, $J = 7.9$ Hz, 1H); ^{13}C -NMR (100 MHz, CDCl_3) 23.7, 24.5, 32.2, 33.3, 38.2, 58.4, 100.9, 108.3, 108.9, 110.8, 115.6, 121.1, 121.9, 127.3, 128.9, 136.0, 145.5, 145.8, 147.8. According to sign of optical rotation, absolute configuration of naturally occurring alkaloid (-)-Galipinine is assigned as R.

3. Formal synthesis of antibacterial agent (S)-Flumequine

A mixture of $[\text{Ir}(\text{COD})\text{Cl}]_2$ (3.4 mg, 0.005 mmol) and (S)-MeO-Biphep (6.4 mg, 0.011 mmol) in toluene (5 mL) was stirred at room temperature for 30 min in a glovebox, the mixture was transferred by a syringe to stainless steel autoclave, in which I_2 (12.7 mg, 0.05 mmol) and substrate (161 mg, 1.0 mmol) were placed beforehand. The hydrogenation was performed at room temperature under H_2 (650 psi) for 12-15 h. After carefully releasing the hydrogen, the reaction mixture was diluted with dichloromethane (20 mL), saturated sodium carbonate aqueous solution (5 mL) was added, then stirred for 15 min, the aqueous layer was extracted with dichloromethane (3 X 15 mL), the combined organic layer was dried over sodium sulfate and concentrated to afford the crude product. Purification was performed by a silica gel column eluted with hexanes / EtOAc to give pure product 6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline 142 mg with 88% yield. 96% ee, $[\alpha]_D^{25} = -67.4$ (*c* 0.98, $\text{CH}_3\text{CH}_2\text{OH}$); $^1\text{H-NMR}$ (400 MHz, CDCl_3) 1.13 (d, *J* = 6.0 Hz, 3H), 1.53 (m, 1H), 1.85 (m, 1H), 2.64 (m, 1H), 2.74 (m, 1H), 3.28 (m, 1H), 3.70 (br, 1H), 6.34 (m, 1H), 6.61 (m, 2H); HPLC (OD-H, elute: Hexanes / *i*-PrOH = 94 / 6, detector: 254 nm, flow rate: 1.0 mL / min), (R) $t_1 = 5.6$ min, (S) $t_2 = 6.7$ min. 6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline is a known compound (see: Balint, J.; Egri, G.; Kiss, V.; Gajary, A.; Juvancz, Z.; Fogassy, E. *Tetrahedron: Asymmetry* **2001**, *12*, 3435), Egri and co-workers synthesized this antibacterial agent using chiral 6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline as key intermediate, which was resolved with 3-bromocamphor-8-sulfonic acid, for detailed procedure, see: Balint, J.; Egri, G.; Fogassy, E., Bocskei, Z.; Simon, K.; Gajary, A.; Friesz, A. *Tetrahedron: Asymmetry* **1999**, *10*, 1079.

¹H NMR (1# in CDCl₃)

¹³C NMR (1# in CDCl₃)

Applied Biosystems Mariner System 5303

Mariner Spec 1:19 (T 0.00:0.92) ASC=>MC=>MC=>MC=>MC=>MC[BP = 246.2, 18343]

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Calibration Constant B 68.020555
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SCIEX Heater         0.00
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Quadrupole DC Potential 6.01
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Mariner Mass Spectrum
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Printed: 10:53, March 18, 2003

¹H NMR (7# in CDCl₃)

¹³C NMR (7# in CDCl₃)

Applied Biosystems Mariner System 5303

Mariner Spec (2:93 (T (0.05:4.69) ASC))MC[BP = 145.0, 8109]

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Calibration Constant B 68.020555
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Standby at End of Acquisition OFF

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Acquired: Mar 18 14:37:00 2003
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Printed: 15:09, March 18, 2003

1H NMR (400 MHz, CDCl3)

¹³C NMR (5# in CDCl₃)

Applied Biosystems Mariner System 5303

Mariner Spec 2:62 (T 0.05:3.11) ASC=>MC=>MC=>MC=>MC[BP = 330.2, 6751]

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Nebulizer Gas        ON
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Calibration Constant B 68.020555
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Spray Tip Potential   4006.05
SCIEX Heater          0.00
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Skimmer 1 Potential   10.01
Quadrupole DC Potential 6.01
Deflection Voltage     0.29
Einzel Lens Potential -25.00
Quadrupole RF Voltage  999.76
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Nozzle Temperature     140.01
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Pull Bias Potential    10.00
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Reflector Potential    1549.99
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Standby at End of Acquisition OFF
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Acquired: Mar 18 10:11:00 2003
Mariner Mass Spectrum
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Printed: 10:37, March 18, 2003

¹H NMR (B in CDCl₃)

¹³C NMR (B in CDCl₃)

¹H NMR (A in CDCl₃)

¹³C NMR (A in CDCl₃)

N-Methyl-2-(piperonyl)-1, 2, 3, 4-Tetrahydroquinoline

N-Methyl-2-Piperonyl-1,2,3,4-Tetrahydroquinoline

Current Data Parameters
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 EXPNO 71
 PROCNO 1

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 SOLVENT CDCl3
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 RG 32768
 DW 22.000 usec
 DE 51.43 usec
 TE 300.0 K
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 D1 2.06000000 sec
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 D11 0.03000000 sec
 S2 30 dB
 P1 7.90 usec
 SF01 50.5658959 MHz
 NUCLEUS 13C

F2 - Processing parameters
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 WM EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters
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 F2P 0.000 ppm
 F2 0.00 Hz
 PPKCM 10.00000 ppm/cm
 HZCM 905.55750 Hz/cm