Supporting Information:

Highly Enantioselective Hydrogenation of Quinolines under Solvent-Free or Highly Concentrated Conditions

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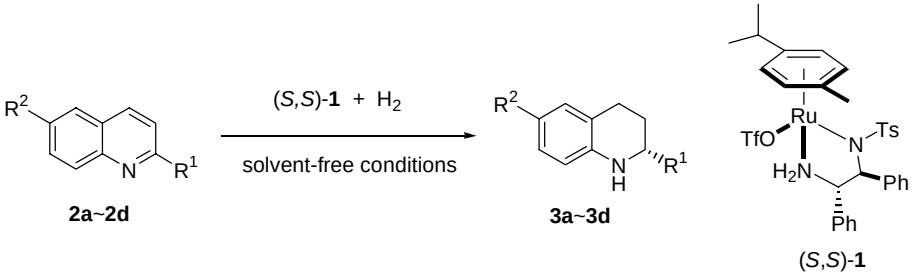
1. General Information

Unless otherwise noted, all experiments were carried out under nitrogen atmosphere. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Model Avance DMX 300 Spectrometer (^{1}H 300 MHz and ^{13}C 75 MHz respectively). Chemical shifts (δ) are given in ppm and are referenced to residual solvent peaks (^{1}H and ^{13}C NMR). All solvents were dried using standard, published methods and were distilled before use. All other chemicals were used as received from commercial source without further purification. The catalyst Ru(OTf)(TsDPEN)(η^{6}-cemene) (*S*,*S*)-**1** was prepared according to Noyori's method.[1]

2. General procedure for the asymmetric hydrogenation of quinolines under solvent-free conditions with (*S*,*S*)-1[2]



2a~2d **3a~3d** (*S*,*S*)-**1**

In a 50 mL glass-lined stainless steel reactor with a magnetic stirring bar was charged with liquid 2-substituted quinolines (2 mmol) and (*S*,*S*)-**1** (1.5 mg, 0.002 mmol). The autoclave was closed, and hydrogen was initially introduced into the autoclave at a pressure of 50 atm, before being reduced to 1 atm. This procedure was repeated three times. Then, the autoclave was pressurized with H_2 to 50-80 atm, and the reaction mixture was stirred vigorously under the H_2 pressure at 25 ^{o}C for 24-60 h. After careful venting of hydrogen, conversion and enantioselectivity of the hydrogenated products were determined by ^{1}H NMR and chiral HPLC analysis, respectively. Pure

tetrahydroquinolines were obtained by silica gel chromatography (eluting with petroleum ether / dichloromethane).

(*S*)-2-Methyl-1,2,3,4-tetrahydroquinoline (3a). 293 mg, 99% yield. 97% ee, $[\alpha]^{20}_{D}$ = -82.8 (*c* 0.103, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (t, *J* = 6.60 Hz, 2H), 6.64 (t, *J* = 6.78 Hz, 1H), 6.50 (d, *J* = 8.49 Hz, 1H), 3.46-3.40 (m, 1H), 2.86-2.75 (m, 2H), 1.96-1.93 (m, 1H), 1.66-1.57 (m, 1H), 1.19 (d, *J* = 6.54 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 129.3, 126.7, 121.1, 117.0, 114.0, 47.2, 30.2, 26.6, 22.6. EI-MS for $C_{10}H_{14}N$ $[M+1]^+$ calcd: 148.2; found 148.1. HPLC (Chiralcel-OJ-H, elute: hexanes / *i*-PrOH = 90 /10, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 23.65 min, minor isomer: t_R = 26.09 min.

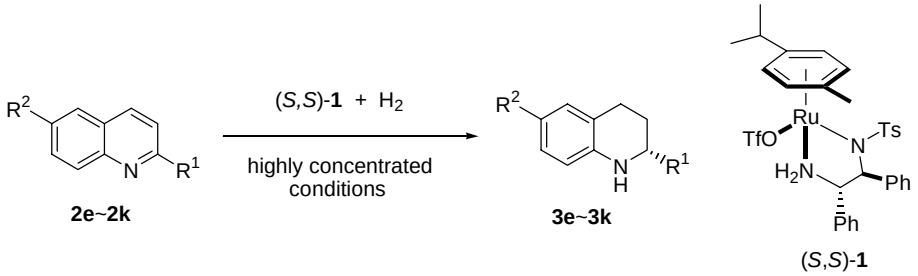
(*S*)-2-Ethyl-1,2,3,4-tetrahydroquinoline (3b). 314 mg, 98% yield. 95% ee, $[\alpha]^{20}_{D}$ = -75.7 (*c* 0.101, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.02 (t, *J* = 7.05 Hz, 2H), 6.66 (t, *J* = 7.35 Hz, 1H), 6.52 (d, *J* = 8.37 Hz, 1H), 3.23-3.21 (m, 1H), 2.88-2.80 (m, 2H), 2.05-2.00 (m, 1H), 1.66-1.55 (m, 3H), 1.05 (t, *J* = 7.53 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 129.3, 126.8, 121.4, 116.9, 114.1, 53.1, 29.5, 27.7, 26.5, 10.1. EI-MS for $C_{11}H_{16}N$ $[M+1]^+$ calcd: 162.2; found 162.1. HPLC (Chiralcel-OJ-H, elute: hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 21.07 min, minor isomer: t_R = 23.68 min.

(*S*)-2-Propyl-1,2,3,4-tetrahydroquinoline (3c). 341 mg, 97% yield. 94% ee, $[\alpha]^{20}_{D}$ = -79.4 (*c* 0.102, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (t, *J* = 7.17 Hz, 2H), 6.64 (t, *J* = 7.36 Hz, 1H), 6.51 (d, *J* = 8.21 Hz, 1H), 3.33-3.26 (m, 1H), 2.88-2.73 (m, 2H), 2.02-1.95 (m, 1H), 1.65-1.46 (m, 5H), 1.01 (t, *J* = 7.11 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 129.3, 126.7, 121.4, 116.9, 114.1, 51.4, 38.9, 28.2, 26.5, 18.9, 14.2.

EI-MS for $C_{12}H_{18}N$ $[M+1]^+$ calcd: 176.3; found 176.2. HPLC (Chiralcel-OJ-H, elute: hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 19.64 min, minor isomer: t_R = 25.41 min.

(*S*)-2-Pentyl-1,2,3,4-tetrahydroquinoline (3d). 404 mg, 99% yield. 94% ee, $[\alpha]^{20}_D$ = -81.7 (*c* 0.101, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97-6.93 (m, 2H), 6.59 (t, *J* = 7.4 Hz, 1H), 6.45 (d, *J* = 8.3 Hz, 1H), 3.24-3.22 (m, 1H), 2.81-2.73 (m, 2H), 1.95-1.94 (m, 1H), 1.47-1.45 (m, 1H), 1.42-1.26 (m 8H), 0.91 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.7, 129.2, 126.7, 121.4, 116.9, 114.0, 51.6, 36.7, 32.0, 28.1, 26.4, 25.4, 22.6, 14.0. EI-MS for $C_{14}H_{22}N$ $[M+1]^+$ calcd: 204.2; found 204.1. HPLC (Chiralcel-OJ-H, elute: hexanes / *i*-PrOH = 90 / 10, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 15.25 min, minor isomer: t_R = 16.96 min.

3. General procedure for the asymmetric hydrogenation of quinolines under highly concentrated conditions with (*S*,*S*)-1[2]



In a 50 mL glass-lined stainless steel reactor with a magnetic stirring bar was charged with solid 2-substituted quinolines (1 mmol), (*S*,*S*)-**1** (1.5 mg, 0.002 mmol) and 0.1 mL ^{i}PrOH (containing 0.001 mmol TfOH). The autoclave was closed, and hydrogen was initially introduced into the autoclave at a pressure of 80 atm, before being reduced to 1 atm. This procedure was repeated three times. Then, the autoclave was pressurized

with H_2 to 50-80 atm, and the reaction mixture was stirred vigorously with magnetic under the H_2 pressure at 80 ^oC for 48 h. After careful releasing of hydrogen, conversion and enantioselectivity of the hydrogenated products were determined by ^1H NMR and chiral HPLC analysis, respectively. Pure tetrahydroquinoline was obtained by silica gel chromatography (eluting with petroleum ether / dichloromethane).

(*S*)-2-Phenethyl-1,2,3,4-tetrahydroquinoline (3e). 224 mg, 95% yield. 92% ee, $[\alpha]^{20}_D$ = -71.5 (*c* 0.106, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.31-7.16 (m, 5H), 6.95 (t, *J* = 7.32 Hz, 2H), 6.59 (t, *J* = 7.55 Hz, 1H), 6.43 (d, *J* = 8.16 Hz, 1H), 3.32-3.24 (m, 1H), 2.80-2.69 (m, 4H), 1.98-1.94 (m, 1H), 1.85-1.78 (m, 2H), 1.70-1.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 141.9, 129.3, 128.6, 128.4, 126.8, 126.0, 121.3, 117.1, 114.2, 51.2, 38.3, 32.2, 28.0, 26.3. EI-MS for $C_{17}H_{20}N$ $[M+1]^+$ calcd: 238.4; found 238.3. HPLC (Chiralcel-AS-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1 mL / min, 15 ^oC), major isomer: t_R = 6.06 min, minor isomer: t_R = 6.75 min.

(*S*)-2-(3',4'-Methylenedioxyphenethyl)-1,2,3,4-tetrahydroquinoline (3f). 279 mg, 99% yield. 87% ee, $[\alpha]^{20}_D$ = -53 (c 0.101, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): 6.90-6.86 (m, 2H), 6.67-6.52 (m, 4H), 6.37 (t, *J* = 8.1 Hz, 1H), 5.84 (m, 2H), 3.20 (s, 1H), 2.75 (m, 1H), 2.73-2.55 (m, 4H), 1.88 (m, 1H), 1.74-1.67 (m, 2H), 1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7, 145.8, 144.5, 135.7, 129.3, 126.8, 121.3, 121.0, 117.1, 114.2, 108.8, 108.2, 100.8, 51.0, 38.5, 31.9, 28.0, 26.2. EI-MS for $C_{18}H_{20}NO_2$ $[M+1]^+$ calcd: 282.4.; found 282.1. HPLC (Chiralcel-AS-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 30.75 min, minor isomer: t_R = 40.12 min.

(*S*)-2-(3',4'-Dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (3g). 290 mg, 98% yield. 85% ee, $[\alpha]^{20}_D$ = -56.3 (*c* 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): 6.99 (t, *J* =

7.26 Hz, 2H), 6.79 (m, 3H), 6.59 (t, *J* = 7.55 Hz, 1H), 6.43 (d, *J* = 8.16 Hz, 1H), 3.27 (m, 1H), 2.75 (m, 4H), 1.96 (m, 1H), 1.83 (m, 2H), 1.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 141.9, 129.3, 128.6, 128.4, 126.8, 126.0, 121.3, 117.1, 114.2, 51.2, 38.3, 32.2, 28.0, 26.3. EI-MS for $C_{19}H_{24}NO_2$ $[M+1]^+$ calcd: 298.4; found 298.2. HPLC (Chiralcel OD-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1 mL / min), minor isomer: t_R = 29.08 min, major isomer: t_R = 30.73 min.

(*R*)-2-Methyl-1-(1,2,3,4-tetrahydroquinolin-2-yl)-propan-2-ol (3h). 188 mg, 92% yield. 97% ee, $[\alpha]^{20}_D$ = -48.8 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): 6.98-6.93 (m, 2H), 6.59 (t, *J* = 7.39 Hz, 1H), 6.49 (d, *J* = 7.86 Hz, 1H), 3.62-3.53 (m, 1H), 2.94-2.69 (m, 2H), 1.88-1.57 (m, 4H), 1.33 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 129.2, 126.7, 120.9, 116.7, 114.4, 72.0, 48.8, 48.5, 32.8, 29.8, 27.9, 26.6. EI-MS for $C_{13}H_{20}NO$ $[M+1]^+$ calcd: 206.3; found 206.2. HPLC (Chiralcel-OD-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1 mL / min), minor isomer: t_R = 10.59 min, major isomer: t_R = 13.23 min.

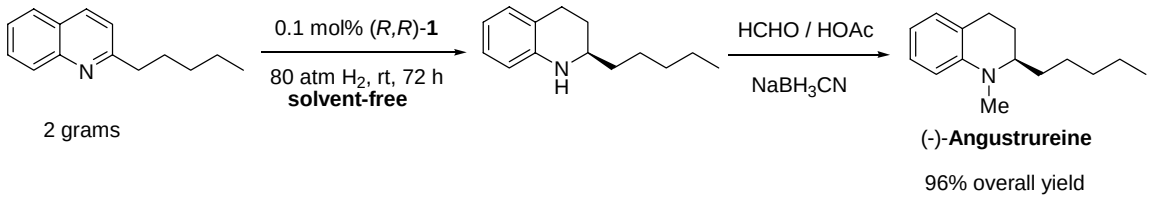
(*R*)-1-(1,2,3,4-tetrahydroquinolin-2-ylmethyl)-cyclohexanol (3i). 242 mg, 98% yield. 97% ee, $[\alpha]^{20}_D$ = -41.2 (*c* 0.102, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): 6.98-6.93 (m, 2H), 6.59 (t, *J* = 7.12 Hz, 1H), 6.49 (d, *J* = 7.67 Hz, 1H), 3.62-3.55 (m, 1H), 2.92-2.69 (m, 2H), 1.88-1.28 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 129.2, 126.7, 121.0, 116.7, 114.5, 72.6, 47.8, 47.3, 40.6, 35.8, 30.0, 26.6, 25.8, 22.2, 22.2. EI-MS for $C_{16}H_{24}NO$ $[M+1]^+$ calcd: 246.4; found 246.3. HPLC (Chiralcel-OD-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1 mL / min), minor isomer: t_R = 11.48 min, major isomer: t_R = 12.16 min.

(*S*)-6-Methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (3j). 176 mg, 99% yield. 93% ee,

$[\alpha]^{20}_D$ = -69.8 (*c* 0.105, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): 6.54 (m, 2H), 6.38 (d, *J* = 8.12 Hz, 1H), 3.65 (s, 3H), 3.29-3.23 (m, 1H), 2.78-2.60 (m, 2H), 1.88-1.80 (m, 1H), 1.53-1.48 (m, 1H), 1.13 (d, *J* = 6.23 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.9, 138.9, 122.5, 115.3, 114.7, 112.9, 55.8, 47.5, 30.3, 26.9, 22.6. EI-MS for $C_{11}H_{16}NO$ $[M+1]^+$ calcd: 178.2; found 178.2. HPLC (Chiralcel-OD-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 0.5 mL / min), major isomer: t_R = 42.67 min, minor isomer: t_R = 52.07 min.

(*S*)-6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (3k). 159 mg, 96% yield. 90% ee, $[\alpha]^{20}_D$ = -76.6 (*c* 0.099, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 6.71-6.66 (m, 2H), 6.43-6.38 (m, 1H), 3.37-3.32 (m, 1H), 2.83-2.72 (m, 2H), 1.95-1.89 (m, 1H), 1.60-1.54 (m, 1H), 1.21 (d, *J* = 6.26 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.1, 154.0, 141.0, 122.5, 122.4, 115.4, 115.2, 114.8, 114.7, 113.3, 113.0, 47.3, 29.9, 26.7, 22.5. EI-MS for $C_{10}H_{13}FN$ $[M+1]^+$ calcd: 166.2; found 166.1. HPLC (Chiralcel-OD-H, elute: hexanes / *i*-PrOH = 95 / 5, detector: 254 nm, flow rate: 1 mL / min), minor isomer: t_R = 6.03 min, major isomer: t_R = 7.36 min.

4. Enantioselective synthesis of naturally occurring tetrahydroquinoline alkaloid (-)-Angustureine[2]

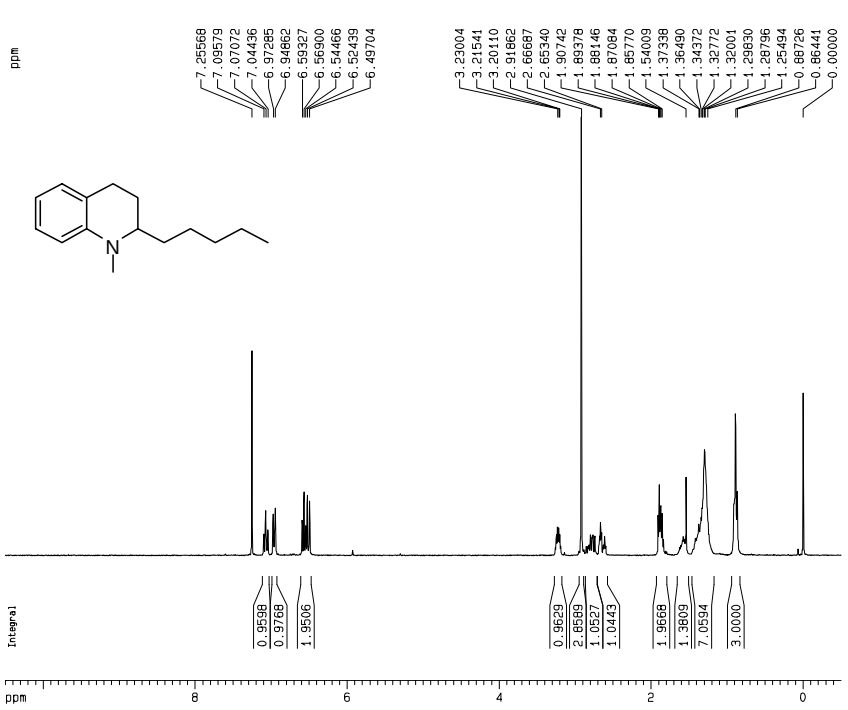


2-Pentyl quinoline (2 g, 10 mmol) and catalyst (*R*,*R*)-**1** (7.5 mg, 0.01 mmol) was combined and transferred to a glass-linked stainless steel autoclave in a glovebox. The

hydrogenation was performed at 25 ^{o}C under 80 atm H_2 for 72 h. The ^{1}H NMR and HPLC analysis indicated that 2-pentyl-1,2,3,4-tetrahydroquinoline (*R*)-**2d** with 94% ee was obtained in quantitative conversion {$[\alpha]^{20}_{D}$ = + 74.2 (*c* 0.1, $CHCl_3$)} .

To a stirred solution of the above crude (*R*)-**2d** and 11.2 mL (150.6 mmol) of 37% aqueous formaldehyde in 50 mL acetonitrile was added 2.733 g of sodium cyanoborohydride. Glacial acetic acid (2 mL) was added, and the reaction was stirred at room temperature for 30 min. The reaction mixture was poured into 50 mL of ether and then washed with three portions of 50 mL 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. Further purification was performed by silica gel chromatography eluted with petroleum ether / dichloromethane to give pure 2-pentyl-1,2,3,4-tetrahydro-1-methylquinoline (2.08 g, 96% overall yield). $[\alpha]^{20}_{D}$ = -7.33 (*c* 1.0, $CHCl_3$) ^{1}H NMR (300 MHz, CDCl3): δ 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.59 – 6.50 (m, 2H), 3.23-3.20 (m, 1H), 2.92 (S, 3H), 2.90- 2.65 (m, 2H), 1.91-1.86 (m, 2H), 1.54-1.25 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 145.5, 128.8, 127.2, 121.9, 115.4, 110.5, 59.1, 38.1, 32.2, 31.3, 25.9, 24.6, 23.7, 22.9, 14.3. According to the sign of optical rotation, the product is in the *R*-configuration as the naturally occurring alkaloid (-)-Angustureine.

5. ^{1}H and ^{13}C NMR spectra of (-)-Angustureine

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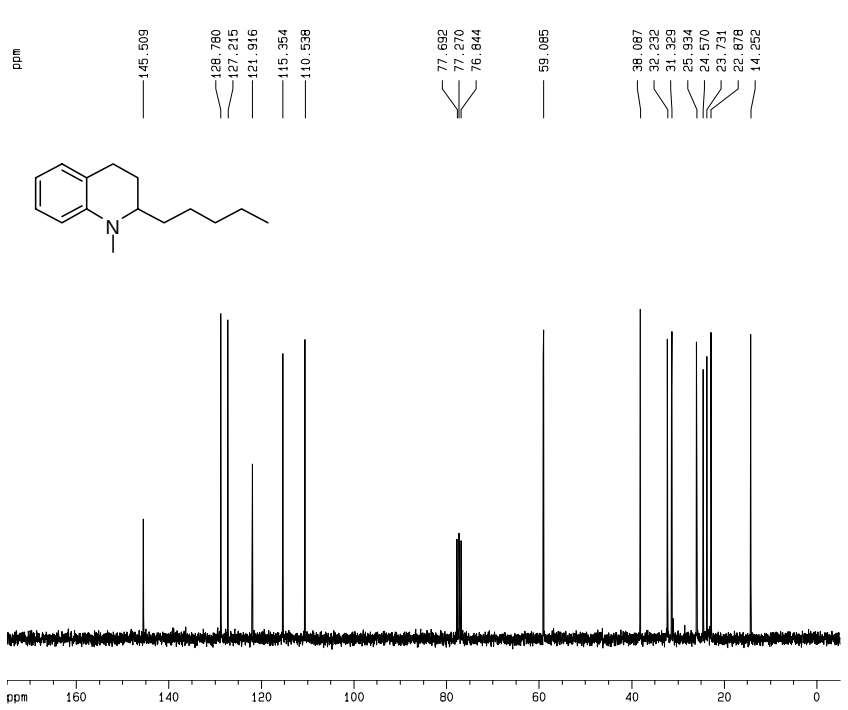


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Reference

1. T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandoval, R. Noyori, *J. Am. Chem. Soc*. **2006**, *128*, 8724.
2. W. B. Wang, S. M. Lu, P. Y. Yang, X. W. Han, Y. G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536.