

# Platinum-Catalyzed Intramolecular Asymmetric Hydroarylation of Unactivated Alkenes with Indoles

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## Supporting Information

Experimental procedures, analytical and spectroscopic data, and copies of NMR spectra for products of  
catalytic hydroarylation (51 pages).

## Experimental Section

**General Methods.** Catalytic reactions were performed in a thick-walled pressure tube (Ace Glass) under an air atmosphere. NMR spectra were obtained on a Varian spectrometer operating at 400 MHz for  $^1\text{H}$  NMR and 100 MHz for  $^{13}\text{C}$  NMR in  $\text{CDCl}_3$  unless otherwise noted. IR spectra were obtained on a Bomen MB-100 FT IR spectrometer. Gas chromatography was performed on a Hewlett-Parkard 5890 gas chromatography equipped with a 25 m polydimethylsiloxane capillary column. Flash column chromatography was performed employing 200-400 mesh silica gel (EM). Thin layer chromatography (TLC) was performed on silica gel 60 F<sub>254</sub> eluting with a 2:1 mixture of hexanes and ethyl acetate unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). 1,4-Dioxane (Acros, anhydrous), HCl solution (4.0 M, 1,4-dioxane, Aldrich), and anhydrous MeOH (Aldrich) were stored in an inert atmosphere glovebox.  $\text{PtCl}_2$ ,  $[\text{Pt}(\text{CH}_2=\text{CH}_2)\text{Cl}_2]_2$ , (*S*)-Tol-BINAP, (*R*)-3,5-Xylyl-BINAP,  $\text{Pt}(\text{COD})\text{Cl}_2$  (Strem), ethyl 5-methoxy indole-2-carboxylate, 5-fluoro indole-2-carboxylate (Alfa Aesar), and ethyl indole-2-carboxylate (Aldrich) were used as received. (*R*)-3,5-*i*-Pr-MeOBIPHEP, and (*S*)-3,5-*t*-Bu-4-MeO-MeOBIPHEP [(*S*)-4] were provided by Dr. Rudolph Schmid (Hoffmann-LaRoche). Alkenyl indoles **3**, 2-(1,1-dimethyl-4-pentenyl)-1-methylindole, 2-(1,1-dimethyl-4-pentenyl)indole, and 2-(2-carbomethoxy-4-pentenyl)-1-methylindole (**7**),<sup>S1</sup>  $[(S)\text{-BINAP}]\text{PtCl}_2$ ,<sup>S2</sup> and ethyl 3,3-dimethyl-5-hexenate were synthesized employing literature procedures.<sup>S3</sup>

## Platinum Complexes

**[(*S*)-Tol-BINAP] $\text{PtCl}_2$ .** [(*S*)-Tol-BINAP] $\text{PtCl}_2$  was isolated in 91% yield as a white solid from reaction of (*S*)-Tol-BINAP and  $\text{Pt}(\text{COD})\text{Cl}_2$  employing a procedure similar to that reported for the synthesis of  $[(S)\text{-BINAP}]\text{PtCl}_2$ .<sup>S2</sup>  $^1\text{H}$  NMR:  $\delta$  7.72-7.09 (m, 22 H), 6.74 (d,  $J = 8.8$  Hz, 2 H), 6.43 (br s,

4 H), 2.39 (s, 6 H), 1.98 (s, 6 H).  $^{31}\text{P}\{^1\text{H}\}$  NMR:  $\delta$  9.6 (s,  $^1J_{\text{Pt}} = 3664$  Hz). Anal. Calcd. (found) for  $\text{C}_{48}\text{H}_{40}\text{Cl}_2\text{P}_2\text{Pt}$ : C, 61.02 (60.87); H, 4.27 (4.36).

**[(*R*)-Xylyl-BINAP]PtCl<sub>2</sub>.** [(*R*)-Xylyl-BINAP]PtCl<sub>2</sub> was isolated in 73% yield as a white solid employing a procedure similar to that reported for [(*S*)-BINAP]PtCl<sub>2</sub><sup>S2</sup> from reaction of (*R*)-Xylyl-BINAP and Pt(COD)Cl<sub>2</sub>.  $^1\text{H}$  NMR:  $\delta$  7.60-7.01 (m, 20 H), 6.50 (d,  $J = 8.4$  Hz, 2 H), 6.33 (s, 2 H), 2.31 (s, 12 H), 1.85 (s, 12 H).  $^{31}\text{P}\{^1\text{H}\}$  NMR:  $\delta$  10.4 (s,  $^1J_{\text{Pt}} = 3673$  Hz). Anal. Calcd. (found) for  $\text{C}_{52}\text{H}_{48}\text{Cl}_2\text{P}_2\text{Pt}$ : C, 62.40 (62.21); H, 4.83 (5.02).

**[(*R*)-3,5-*i*-Pr-MeOBIPHEP]PtCl<sub>2</sub>.** [(*R*)-3,5-*i*-Pr-MeOBIPHEP]PtCl<sub>2</sub> was isolated in 82% yield as a pale yellow solid employing a procedure similar to that reported for [(*S*)-BINAP]PtCl<sub>2</sub><sup>S2</sup> from reaction of (*R*)-3,5-*i*-Pr-MeOBIPHEP and Pt(COD)Cl<sub>2</sub>.  $^1\text{H}$  NMR:  $\delta$  7.60-6.40 (m, 18 H), 3.50 (s, 6 H), 2.90-2.78 (m, 8 H), [1.24 (d,  $J = 7.2$  Hz), 1.21 (d,  $J = 6.8$  Hz), 1.18 (d,  $J = 7.2$  Hz), 1.17 (d,  $J = 6.8$  Hz), 48 H].  $^{31}\text{P}\{^1\text{H}\}$  NMR:  $\delta$  11.5 (s,  $^1J_{\text{Pt}} = 3654$  Hz). Anal. Calcd. (found) for  $\text{C}_{62}\text{H}_{80}\text{Cl}_2\text{O}_2\text{P}_2\text{Pt}$ : C, 62.83 (62.76); H, 6.80 (7.13).

**[(*S*)-3,5-*t*-Bu-4-MeO-MeOBIPHEP]PtCl<sub>2</sub> {(*S*)-4]PtCl<sub>2</sub>}.** [(*S*)-4]PtCl<sub>2</sub> was isolated in 89% yield as a pale yellow solid employing a procedure similar to that reported for [(*R*)-BINAP]PtCl<sub>2</sub><sup>S2</sup> from reaction of (*S*)-4 and Pt(COD)Cl<sub>2</sub>.  $^1\text{H}$  NMR:  $\delta$  8.60-6.50 (m, 14 H), 3.68 (s, 6 H), 3.61 (s, 12 H), 1.37 (s, 72 H).  $^{31}\text{P}\{^1\text{H}\}$  NMR:  $\delta$  11.4 (s,  $^1J_{\text{Pt}} = 3664$  Hz). Anal. Calcd. (found) for  $\text{C}_{74}\text{H}_{104}\text{Cl}_2\text{O}_6\text{P}_2\text{Pt}$ : C, 62.70 (62.56); H, 7.39 (7.52).

## 2-Alkenyl Indoles

**2-(2,2-dicarbomethoxy-4-pentenyl)-1-benzylindole (S1; Table 2, entry 1).** Ethyl 1-benzylindole-2-carboxylate (**S2**)<sup>S4</sup> was synthesized employing a literature procedure from reaction of ethyl indole-2-carboxylate and benzyl chloride.<sup>S4</sup> A solution of **S2** (1.40 g, 5.02 mmol) in THF (15 mL)

was added slowly to a suspension of LiAlH<sub>4</sub> (286 mg, 7.53 mmol) in THF (20 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight, quenched with 1 N HCl (30 mL), and extracted with ether (2 × 50 mL). The combined ether extracts were washed with water (50 mL), dried (MgSO<sub>4</sub>), and concentrated under vacuum to give crude 2-hydroxymethyl-1-methylindole (**S3**), which was used for next step without further purification.

*n*-BuLi (2.5 M solution in hexanes, 1.96 mL, 4.89 mmol) was added to a solution of crude product of **S3** in THF (35 mL) at −78 °C. After stirring for 2 min, methanesulfonyl chloride (0.58 g, 5.1 mmol) and LiBr (1.22 g, 14.0 mmol) were added sequentially. The resulting mixture was warmed to 0 °C, stirred for 30 min, and transferred via cannula to a solution of sodium dimethyl allylmalonate [generated from dimethyl allylmalonate (0.88 g, 5.1 mmol) and NaH (0.123 g, 5.13 mmol) in THF (25 mL)]. The reaction mixture was stirred at room temperature for 4 h, quenched with water, and extracted with ether (2 × 50 mL). The combined organic extracts were washed (brine), dried (MgSO<sub>4</sub>), and concentrated under vacuum. Column chromatography of the residue (hexanes–EtOAc = 5:1) gave **S1** (1.04 g, 53% from **S2**) as a white solid.

**For S1:** mp 116–118 °C. TLC: *R*<sub>f</sub> = 0.68. <sup>1</sup>H NMR: δ 7.55 (d, *J* = 8.0 Hz, 1 H), 7.25–7.18 (m, 4 H), 7.12–7.05 (m, 2 H), 6.89 (d, *J* = 8.0 Hz, 2 H), 6.33 (s, 1 H), 5.61–5.50 (m, 1 H), 5.34 (s, 2 H), 5.02–4.97 (m, 2 H), 3.69 (s, 6 H), 3.35 (s, 2 H), 2.82 (d, *J* = 7.2 Hz, 2 H). <sup>13</sup>C{<sup>1</sup>H} NMR: δ 171.4, 138.0, 137.3, 135.0, 132.6, 129.1, 128.3, 127.6, 126.2, 121.7, 120.5, 120.1, 119.8, 109.9, 101.5, 57.9, 53.0, 46.6, 37.3, 29.5. IR (neat, cm<sup>−1</sup>): 2954, 1735, 1461, 1224, 925. Anal. Calcd (found) for C<sub>24</sub>H<sub>25</sub>NO<sub>4</sub>: C, 73.64 (73.50); H, 6.44 (6.69); N, 3.58 (3.63).

**2-(2,2-dicarbomethoxy-4-pentenyl)-1-allylindole (S4; Table 2, entry 2):** Ethyl 1-allylindole-2-carboxylate (**S5**)<sup>S4</sup> was synthesized employing a literature procedure from ethyl indole-2-carboxylate and allyl bromide.<sup>S4</sup> **S4** was isolated in 27% yield as a white solid from reaction of **S5** and dimethyl

allylmalonate employing a procedure similar to that used to synthesize **S1**. mp 61-63 °C. TLC:  $R_f$  = 0.63.  $^1\text{H}$  NMR:  $\delta$  7.54 (d,  $J$  = 8.0 Hz, 1 H), 7.24 (d,  $J$  = 8.0 Hz, 1 H), 7.16 (t,  $J$  = 7.6 Hz, 1 H), 7.08 (t,  $J$  = 7.2 Hz, 1 H), 6.29 (s, 1 H), 5.95-5.86 (m, 1 H), 5.75-5.64 (m, 1 H), 5.12-5.05 (m, 3 H), 4.77-4.73 (m, 3 H), 3.74 (s, 6 H), 3.39 (s, 2 H), 2.88 (d,  $J$  = 7.2 Hz, 2 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  171.5, 136.9, 134.8, 133.5, 132.6, 128.2, 121.5, 120.5, 119.93, 119.88, 116.6, 109.7, 101.2, 57.9, 53.0, 45.4, 37.3, 29.3. IR (neat,  $\text{cm}^{-1}$ ): 2951, 1736, 1462, 1435, 1290, 924. Anal. Calcd (found) for  $\text{C}_{20}\text{H}_{23}\text{NO}_4$ : C, 70.36 (70.51); H, 6.79 (6.97); N, 4.10 (4.23).

**2-(2,2-dicarbomethoxy-4-pentenyl)-1-methyl-5-methoxyindole (S6; Table 2, entry 3).** Ethyl 5-methoxy-1-methylindole-2-carboxylate<sup>S5</sup> was synthesized employing a literature procedure from ethyl 5-methoxy indole-2-carboxylate and MeI.<sup>S4</sup> **S6** was isolated in 26% yield as a yellow solid from reaction of ethyl 5-methoxy-1-methyl-indole-2-carboxylate and dimethyl allylmalonate employing a procedure similar to that used to synthesize **S1**. Yellow solid. mp 89-91 °C. TLC:  $R_f$  = 0.56.  $^1\text{H}$  NMR:  $\delta$  7.15 (d,  $J$  = 8.4 Hz, 1 H), 7.00 (s, 1 H), 6.85-6.82 (m, 1 H), 6.18 (br s, 1 H), 5.78-5.67 (m, 1 H), 5.14-5.07 (m, 2 H), 3.84 (s, 3 H), 3.73 (s, 6 H), 3.63 (s, 3 H), 3.41 (s, 2 H), 2.79 (d,  $J$  = 7.2 Hz, 2 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  171.5, 154.4, 135.5, 132.9, 132.7, 128.3, 119.8, 111.6, 110.1, 102.3, 101.0, 58.3, 56.2, 53.0, 37.3, 30.1, 29.6. IR (neat,  $\text{cm}^{-1}$ ): 2949, 1734, 1483, 1433, 1213. Anal. Calcd (found) for  $\text{C}_{19}\text{H}_{23}\text{NO}_5$ : C, 66.07 (65.86); H, 6.71 (6.85); N, 4.06 (3.88).

**2-(2,2-dicarbomethoxy-4-pentenyl)-1-methyl-5-fluoroindole (S7; Table 2, entry 4).** Ethyl 5-fluoro-1-methyl-1*H*-indole-2-carboxylate<sup>S4</sup> was synthesized employing a literature procedure from ethyl 5-fluoro indole-2-carboxylate and MeI.<sup>S4</sup> **S7** was isolated in 62% yield as a pale yellow solid from reaction of ethyl 5-fluoro-1-methylindole-2-carboxylate and dimethyl allylmalonate employing a procedure similar to that used to synthesize **S1**. TLC:  $R_f$  = 0.64.  $^1\text{H}$  NMR:  $\delta$  7.18-7.14 (m, 2 H), 6.94-6.88 (m, 1H), 6.23 (s, 1 H), 5.78-5.68 (m, 1 H), 5.16-5.08 (m, 2 H), 3.74 (s, 6 H), 3.65 (s, 3 H), 3.42 (s, 2

H), 2.79 (d,  $J = 7.6$  Hz, 2 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  171.3, 158.2 (d,  $J = 232.5$  Hz), 136.7, 134.2, 132.5, 128.2 (d,  $J = 10.2$  Hz), 119.9, 109.9 (d,  $J = 9.8$  Hz), 109.6 (d,  $J = 26.1$  Hz), 105.1 (d,  $J = 23.1$  Hz), 101.3 (d,  $J = 4.6$  Hz), 58.2, 53.0, 37.3, 30.2, 29.6. IR (neat,  $\text{cm}^{-1}$ ): 2952, 1735, 1483, 1435, 1214, 1136. Anal. Calcd (found) for  $\text{C}_{18}\text{H}_{20}\text{FNO}_4$ : C, 64.85 (64.85); H, 6.05 (6.29); N, 4.20 (4.19).

**2-(2,2-dihydroxymethyl-4-pentenyl)-1-methylindole (S8; Table 2, entry 5).** A solution of **3**<sup>S1</sup> (1.30 g, 4.13 mmol) in THF (15 mL) was added slowly to a suspension of  $\text{LiAlH}_4$  (471 mg, 12.4 mmol) in THF (20 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight, quenched with 1 N HCl (50 mL), and extracted with ether ( $2 \times 50$  mL). The combined ether extracts were washed with water (50 mL), dried ( $\text{MgSO}_4$ ), and concentrated under vacuum to give an oil that solidified upon addition of hexanes/EtOAc (3:1, 3 mL). The solid was washed with hexanes (3 mL) to give **S8** (0.54 g, 50% yield) as a white solid. mp 96-97.5 °C. TLC:  $R_f = 0.14$ .  $^1\text{H}$  NMR:  $\delta$  7.55 (d,  $J = 7.6$  Hz, 1 H), 7.30 (d,  $J = 8.0$  Hz, 1 H), 7.19 (t,  $J = 7.2$  Hz, 1 H), 7.11 (t,  $J = 6.8$  Hz, 1 H), 6.37 (br s, 1 H), 5.96-5.85 (m, 1 H), 5.18-5.14 (m, 2 H), 3.74 (s, 3 H), 3.63 (ABq,  $J = 10.8$  Hz, 4 H), 2.88 (s, 2 H), 2.27 (br s, 2 H), 2.18 (d,  $J = 7.6$  Hz, 2 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  137.7, 137.3, 134.2, 128.2, 121.2, 120.1, 119.9, 118.9, 109.6, 102.0, 67.8, 43.9, 37.5, 30.4, 28.8. IR (neat,  $\text{cm}^{-1}$ ): 3384, 2929, 1466, 1317, 1024, 918. Anal. Calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{NO}_2$ : C, 74.10 (74.24); H, 8.16 (8.09); N, 5.40 (5.65).

**2-[2,2-di-(2,2-Dimethyl-propionyloxymethyl)-4-pentenyl]-1-methylindole (S9; Table 2, entry 6).** Pivaloyl chloride (0.37 mL, 3.00 mmol) was added slowly to a solution of **S8** (312 mg, 1.20 mmol),  $\text{Et}_3\text{N}$  (0.50 mL, 3.6 mmol), and DMAP (73 mg, 0.6 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight, quenched with brine (20 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (30 mL). The organic layer was dried ( $\text{MgSO}_4$ ) and concentrated under vacuum. Column chromatography of the residue (hexanes–EtOAc = 5:1) gave **S9** (0.47 g, 90 % yield) as a viscous colorless oil. TLC:  $R_f = 0.85$ .  $^1\text{H}$  NMR:  $\delta$  7.56 (d,  $J = 7.6$  Hz, 1 H), 7.28 (d,  $J = 8.0$  Hz, 1 H), 7.20 (t,  $J$

= 7.2 Hz, 1 H), 7.11 (t,  $J$  = 7.6 Hz, 1 H), 6.32 (s, 2 H), 5.87-5.77 (m, 1 H), 5.18-5.10 (m, 2 H), 4.03 (s, 4 H), 3.70 (s, 3 H), 2.94 (s, 2 H), 2.26 (d,  $J$  = 7.2 Hz, 2 H), 1.24 (s, 9 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  178.3, 137.7, 135.4, 132.7, 128.1, 121.4, 120.2, 120.0, 119.8, 109.6, 102.8, 65.9, 42.2, 39.3, 37.4, 30.2, 29.2, 27.5. IR (neat,  $\text{cm}^{-1}$ ): 2972, 1730, 1479, 1282, 1150. Anal. Calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{NO}_2$ : C, 73.03 (72.97); H, 8.72 (8.78); N, 3.28 (3.52).

**2-(2,2-dicarbo-*t*-butoxy-4-pentenyl)-1-methylindole (Table 2, entry 7).** 2-(2,2-Dicarbo-*t*-butoxy-4-pentenyl)-1-methylindole was isolated in 50% yield as a white solid from reaction of 2-hydroxymethyl-1-methylindol<sup>S1</sup> and di-*t*-butyl allylmalonate employing a procedure similar to that used to synthesize **S1**. mp 45-47 °C. TLC:  $R_f$  = 0.63.  $^1\text{H}$  NMR:  $\delta$  7.51 (d,  $J$  = 8.0 Hz, 1 H), 7.24 (d,  $J$  = 8.4 Hz, 1 H), 7.14 (t,  $J$  = 7.2 Hz, 1 H), 7.04 (t,  $J$  = 7.2 Hz, 1 H), 6.32 (br s, 1 H), 5.74-5.63 (m, 1 H), 5.09-5.00 (m, 2 H), 3.66 (s, 3 H), 3.31 (s, 2 H), 2.75 (d,  $J$  = 7.2 Hz, 2 H), 1.42 (s, 18 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  170.3, 137.3, 135.6, 133.0, 128.2, 121.1, 120.3, 119.6, 119.4, 109.2, 101.0, 82.1, 58.4, 37.1, 30.1, 28.9, 28.2. IR (neat,  $\text{cm}^{-1}$ ): 2977, 2939, 1727, 1468, 1368, 1224, 1149, 920. Anal. Calcd (found) for  $\text{C}_{23}\text{H}_{33}\text{NO}_4$ : C, 72.15 (72.25); H, 8.33 (8.41); N, 3.51 (3.67).

**2-(2,2-dimethyl-4-pentenyl)-1-methylindole (S10; Table 2, entry 8).** *n*-BuLi (2.5 M solution in hexanes, 8.92 mL, 22.3 mmol) was added dropwise to a solution of *N*-trimethylsilyl-*o*-toluidine<sup>S6</sup> (1.81 g, 10.13 mmol) in hexanes (50 mL) at 0 °C. The resulting orange solution was refluxed for 5 h, cooled to -78 °C, and treated with a solution of ethyl 3,3-dimethyl-5-hexenate<sup>S3</sup> (2.07 g, 12.16 mmol) in THF (10 mL). The resulting mixture was warmed to room temperature, stirred for 0.5 h, and quenched with brine. The aqueous layer was extracted with ether (2  $\times$  50 mL). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and concentrated under vacuum. Column chromatography of the residue (hexanes- $\text{CH}_2\text{Cl}_2$  = 10:1) gave an oil that was chromatographed a second time (hexanes-EtOAc = 20:1) to give 2-(2,2-dimethyl-4-pentenyl)indole (**S11**, 0.79 g, 37%) as a pale yellow oil.

A solution of **S11** (0.74 g, 3.5 mmol) in DMF (9 mL) was added slowly to a suspension of NaH (88 mg, 3.65 mmol) in DMF (5 mL) at 0 °C. The mixture was stirred at 0 °C for 20 min and MeI (0.518 g, 3.65 mmol) was added. The reaction mixture was stirred at room temperature for 1 hour, quenched with brine (50 mL), extracted with ether (2 × 40 mL). The combined ether extracts were washed with water (50 mL), dried (MgSO<sub>4</sub>), and concentrated under vacuum. Column chromatography of the residue (hexanes–EtOAc = 25:1) gave **S10** (0.74 g, 94 %) as a pale yellow oil.

**For S11:** TLC (hexanes–EtOAc = 5:1):  $R_f$  = 0.50. <sup>1</sup>H NMR:  $\delta$  7.85 (br s, 1 H), 7.59 (d,  $J$  = 7.6 Hz, 1 H), 7.33 (d,  $J$  = 7.6 Hz, 1 H), 7.17 (t,  $J$  = 7.2 Hz, 1 H), 7.12 (t,  $J$  = 7.2 Hz, 1 H), 6.28 (s, 1 H), 6.00–5.89 (m, 1 H), 5.18–5.10 (m, 2 H), 2.64 (s, 2 H), 2.08 (d,  $J$  = 7.2 Hz, 2 H), 1.00 (s, 6 H). <sup>13</sup>C{<sup>1</sup>H} NMR:  $\delta$  137.2, 136.0, 135.9, 129.1, 121.3, 120.1, 119.9, 117.8, 110.6, 102.5, 46.7, 41.2, 34.9, 27.4. IR (neat, cm<sup>-1</sup>): 3409, 2958, 2926, 1455, 1287, 913. HRMS Calcd (found) for C<sub>15</sub>H<sub>19</sub>N (M<sup>+</sup>): 213.1517 (213.1519).

**For S10:** TLC (hexanes–EtOAc = 5:1):  $R_f$  = 0.67. <sup>1</sup>H NMR:  $\delta$  7.55 (d,  $J$  = 7.6 Hz, 1 H), 7.27 (d,  $J$  = 8.0 Hz, 1 H), 7.16 (t,  $J$  = 7.2 Hz, 1 H), 7.08 (t,  $J$  = 7.6 Hz, 1 H), 6.29 (s, 1 H), 5.95–5.84 (m, 1 H), 5.11–5.04 (m, 2 H), 3.67 (s, 3 H), 2.68 (s, 2 H), 2.10 (d,  $J$  = 7.6 Hz, 2 H), 0.94 (s, 6 H). <sup>13</sup>C{<sup>1</sup>H} NMR:  $\delta$  138.7, 137.6, 135.6, 128.2, 120.8, 120.0, 119.7, 117.9, 109.4, 102.1, 47.2, 38.4, 35.6, 30.5, 27.0. IR (neat, cm<sup>-1</sup>): 3056, 2957, 1467, 1340, 1317, 913. Anal. Calcd (found) for C<sub>16</sub>H<sub>21</sub>N: C, 84.53 (84.63); H, 9.31 (9.35); N, 6.16 (6.34).

**2-(2,2-dicarbomethoxy-5-hexenyl)-1-methylindole (Table 2, entry 11).** 2-(2,2-Dicarbomethoxy-5-hexenyl)-1-methylindole was isolated in 35% yield as a viscous pale yellow oil from reaction of 2-hydroxymethyl-1-methylindole<sup>S1</sup> and dimethyl 3-butenylmalonate employing a procedure similar to that used to synthesize **S1**. TLC:  $R_f$  = 0.47. <sup>1</sup>H NMR:  $\delta$  7.52 (d,  $J$  = 8.0 Hz, 1 H), 7.27 (d,  $J$  = 8.0 Hz, 1 H), 7.18 (dt,  $J$  = 1.2, 7.6 Hz, 1 H), 7.07 (dt,  $J$  = 1.2, 7.6 Hz, 1 H), 6.24 (s, 1 H), 5.81–5.71 (m,



1 H), 5.06-4.96 (m, 2 H), 3.74 (s, 6 H), 3.67 (s, 3 H), 3.46 (s, 2 H), 2.15-2.10 (m, 2 H), 2.07-2.01 (m, 2 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR:  $\delta$  171.7, 137.5, 137.4, 134.9, 128.0, 121.4, 120.3, 119.8, 115.6, 109.4, 101.4, 57.9, 52.9, 31.8, 29.9, 29.7, 29.0. IR (neat,  $\text{cm}^{-1}$ ): 2952, 1732, 1464, 1437, 1204, 917. HRMS Calcd (found) for  $\text{C}_{19}\text{H}_{23}\text{NO}_4$  ( $\text{M}^+$ ): 329.1627 (329.1624).

## Polycyclic Indoles

Complete optimization for the conversion of **3** to **5** is depicted in Tables S1 and S2.

**2,2-Dicarbomethoxy-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (5).**<sup>S1</sup> A suspension of **3** (67 mg, 0.21 mmol), [(*S*)-**4**]PtCl<sub>2</sub> (30 mg,  $2.1 \times 10^{-2}$  mmol), and AgOTf (5 mg,  $2.1 \times 10^{-2}$  mmol) in MeOH (0.82 mL) was stirred at 60 °C for 20 hours, cooled to room temperature, and filtered through a plug of silica gel. The silica gel was eluted with ether, the filtrate and eluant were combined, and concentrated under vacuum. Chromatography of the residue (hexanes–EtOAc = 10:1) gave **5** (62 mg, 93%, 90% ee) as a white solid. The enantiomeric excess of **5** was determined by HPLC analysis using a Chiralpak AD-H column (Figure S1).

All remaining polycyclic indole derivatives were isolated from the corresponding 2-alkenylindoles employing a similar procedure to that for the synthesis of **5** unless noted otherwise. 1,1,4,9-Tetramethyl-2,3,4,9-tetrahydrocarbazole (Table 2, entry 9), 1,1,4-trimethyl-2,3,4,9-tetrahydrocarbazole (Table 2, entry 10), and **8** have been previously characterized.<sup>S1</sup> The enantiomeric excess of polycyclic indole derivatives were determined by HPLC analysis using a Chiralpak AD-H column (250 mm) (See Figures S2-S13).

**2,2-Dicarbomethoxy-4-methyl-9-benzyl-1,3,4,9-tetrahydrocarbazole (S12; Table 2, entry 1).** White solid. mp 44-48 °C. TLC:  $R_f$  = 0.62.  $^1\text{H}$  NMR (Figure S14):  $\delta$  7.63 (d,  $J$  = 8.0 Hz, 1 H), 7.29-7.18 (m, 4 H), 7.12-7.02 (m, 4 H), 5.28 (s, 2 H), 3.76 (s, 3 H), 3.60 (s, 3 H), 3.45 (d,  $J$  = 16.4 Hz, 1

H), 3.27-3.21 (m, 1 H), 3.04 (d,  $J = 16.0$  Hz, 1 H), 2.73 (dd,  $J = 6.0, 13.6$  Hz, 1 H), 1.88 (dd,  $J = 10.4, 13.2$  Hz, 1 H), 1.49 (d,  $J = 6.8, 3$  H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S15):  $\delta$  172.5, 171.0, 138.0, 137.5, 132.3, 129.0, 127.6, 126.8, 126.4, 121.3, 119.8, 119.3, 113.5, 109.7, 54.8, 53.2, 53.0, 46.7, 38.7, 28.5, 26.4, 21.6. IR (neat,  $\text{cm}^{-1}$ ): 2952, 1735, 1465, 1250, 1028. Anal. Calcd (found) for  $\text{C}_{24}\text{H}_{25}\text{NO}_4$ : C, 73.64 (73.76); H, 6.44 (6.83); N, 3.58 (3.66).

**2,2-Dicarbomethoxy-4-methyl-9-allyl-1,3,4,9-tetrahydrocarbazole (S13; Table 2, entry 2).**

Colorless oil. TLC:  $R_f = 0.52$ .  $^1\text{H}$  NMR (Figure S16):  $\delta$  7.60 (d,  $J = 8.0$  Hz, 1 H), 7.23 (d,  $J = 8.0$  Hz, 1 H), 7.14 (t,  $J = 8.4$  Hz, 1 H), 7.06 (t,  $J = 8.0$  Hz, 1 H), 5.97-5.88 (m, 1 H), 5.13 (dd,  $J = 1.2, 10.8$  Hz, 1 H), 4.86 (dd,  $J = 1.2, 16.8$  Hz, 1 H), 4.66 (t,  $J = 2.4$  Hz, 2 H), 3.78 (s, 3 H), 3.63 (s, 3 H), 3.45 (d,  $J = 16.0$  Hz, 1 H), 3.22-3.12 (m, 1 H), 3.06 (dd,  $J = 2.0, 16.0$  Hz, 1 H), 2.71 (ddd,  $J = 2.0, 5.6, 13.4$  Hz, 1 H), 1.87 (dd,  $J = 10.0, 13.4$  Hz, 1 H), 1.45 (d,  $J = 6.8$  Hz, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S17):  $\delta$  172.5, 171.0, 137.2, 133.5, 132.2, 126.7, 121.1, 119.8, 119.2, 116.6, 113.2, 109.4, 54.8, 53.2, 53.0, 45.4, 38.7, 28.4, 26.3, 21.6. IR (neat,  $\text{cm}^{-1}$ ): 2953, 1735, 1464, 1250, 1199, 922. Anal. Calcd (found) for  $\text{C}_{20}\text{H}_{23}\text{NO}_4$ : C, 70.36 (70.30); H, 6.79 (6.57); N, 4.10 (4.05).

**2,2-Dicarbomethoxy-4,9-dimethyl-6-methoxy-1,3,4,9-tetrahydrocarbazole (S14; Table 2, entry 3).**

White solid. mp 108-109 °C. TLC:  $R_f = 0.45$ .  $^1\text{H}$  NMR (Figure S18):  $\delta$  7.16 (d,  $J = 8.8$  Hz, 1 H), 7.07 (d,  $J = 2.4$  Hz, 1 H), 6.84 (dd,  $J = 8.8$  Hz, 1 H), 3.86 (s, 3 H), 3.81 (s, 3 H), 3.68 (s, 3 H), 3.63 (s, 3 H), 3.49 (d,  $J = 16.0$  Hz, 1 H), [3.15-3.07 (m), 3.09 (dd,  $J = 2.0, 16.0$  Hz), 2 H], 2.71 (dd,  $J = 4.4, 13.4$  Hz, 1 H), 1.87 (dd,  $J = 10.4, 13.2$  Hz, 1 H), 1.45 (d,  $J = 6.8$  Hz, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S19):  $\delta$  172.5, 171.1, 153.8, 133.3, 126.7, 112.4, 110.4, 109.6, 102.7, 56.4, 54.7, 53.2, 53.1, 38.7, 29.6, 28.6, 26.3, 21.4. IR (neat,  $\text{cm}^{-1}$ ): 2954, 1737, 1485, 1248, 1222, 1039. Anal. Calcd (found) for  $\text{C}_{19}\text{H}_{23}\text{NO}_5$ : C, 66.07 (66.21); H, 6.71 (6.80); N, 4.06 (4.14).

**2,2-Dicarbomethoxy-4,9-dimethyl-6-fluoro-1,3,4,9-tetrahydrocarbazole (S15; Table 2, entry 4).** White solid. mp 137-138 °C. TLC:  $R_f$  = 0.55.  $^1\text{H}$  NMR (Figure S20):  $\delta$  7.24-7.21 (m, 1 H), 7.17-7.14 (m, 1 H), 6.92-6.86 (m, 1 H), 3.81 (s, 3 H), 3.68 (s, 3 H), 3.64 (s, 3 H), 3.50 (d,  $J$  = 16.0 Hz, 1 H), [3.19-3.05 (m), 3.08 (d,  $J$  = 8.0 Hz), 2 H], 2.70 (dd,  $J$  = 5.2, 13.4 Hz, 1 H), 1.86 (dd,  $J$  = 10.4, 13.4 Hz, 1 H), 1.42 (d,  $J$  = 6.8 Hz, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S21):  $\delta$  172.4, 171.1, 157.7 (d,  $J$  = 231.7 Hz), 134.5, 134.4, 126.6 (d,  $J$  = 9.5 Hz), 112.9 (d,  $J$  = 4.5 Hz), 109.5 (d,  $J$  = 9.9 Hz), 108.9 (d,  $J$  = 26.2 Hz), 104.8 (d, d,  $J$  = 23.5 Hz), 54.7, 53.3, 53.2, 38.6, 29.7, 28.6, 26.2, 21.3. IR (neat,  $\text{cm}^{-1}$ ): 2954, 1736, 1484, 1246, 1199. Anal. Calcd (found) for  $\text{C}_{18}\text{H}_{20}\text{FNO}_4$ : C, 64.85 (64.95); H, 6.05 (6.16); N, 4.20 (4.27).

**2,2-Dihydroxymethyl-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (S16; Table 2, entry 5).** Pale yellow solid. mp 145-147 °C. TLC:  $R_f$  = 0.07.  $^1\text{H}$  NMR (Figure S22):  $\delta$  7.60 (d,  $J$  = 7.6 Hz, 1 H), 7.24 (d,  $J$  = 8.4 Hz, 1 H), 7.13 (t,  $J$  = 7.2 Hz, 1 H), 7.04 (t,  $J$  = 7.6 Hz, 1 H), [3.70-3.59 (m), 3.59 (s), 7 H], 3.01-2.77 (m, 1 H), 2.77 (d,  $J$  = 16.8 Hz, 1 H), 2.44 (dd,  $J$  = 2.0, 16.4 Hz, 1 H), 2.26 (br s, 2 H), 1.94 (dd,  $J$  = 5.2, 13.6 Hz, 1 H), 1.42 (d,  $J$  = 6.8 Hz, 3 H), 1.22 (dd,  $J$  = 10.8, 13.0 Hz, 1 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S23):  $\delta$  137.8, 134.0, 126.7, 120.8, 119.8, 119.0, 113.0, 109.1, 72.6, 67.1, 40.3, 38.4, 29.4, 26.8, 25.7, 21.9. IR (neat,  $\text{cm}^{-1}$ ): 3294, 2929, 1467, 1420, 1322, 1026. Anal. Calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{NO}_2$ : C, 74.10 (73.89); H, 8.16 (8.01); N, 5.40 (5.37).

**2,2-di-(2,2-Dimethyl-propionyloxymethyl)-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (S17; Table 2, entry 6).** White solid. mp 141-145 °C. TLC:  $R_f$  = 0.81.  $^1\text{H}$  NMR (Figure S24):  $\delta$  7.65 (d,  $J$  = 7.6 Hz, 1 H), 7.65 (d,  $J$  = 8.4 Hz, 1 H), 7.18 (dt,  $J$  = 1.2, 7.6 Hz, 1 H), 7.09 (td,  $J$  = 1.2, 7.6 Hz, 1 H), [4.13 (Abq,  $J$  = 10.8 Hz), 4.06 (Abq,  $J$  = 11.2 Hz), 4 H], 3.62 (s, 3 H), 3.11-3.04 (m, 1 H), 2.67 (Abq,  $J$  = 16.8 Hz, 2 H), 2.06 (dd,  $J$  = 5.2, 13.2 Hz), [1.48 (d,  $J$  = 6.8 Hz), 1.46 (dd,  $J$  = 10.8, 13.2 Hz), 4 H], 1.27 (s, 9 H), 1.21 (s, 9 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S25):  $\delta$  178.5, 178.2, 137.8, 132.8, 126.6, 121.0,

119.8, 119.1, 112.9, 109.1, 68.9, 64.7, 39.3, 39.2, 38.8, 38.3, 29.4, 27.6, 27.5, 25.5, 21.8. IR (neat,  $\text{cm}^{-1}$ ): 2971, 1731, 1470, 1284, 1167, 1034. Anal. Calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{NO}_2$ : C, 73.03 (73.19); H, 8.72 (8.81); N, 3.28 (3.43).

**2,2-Dicarbo-*t*-butoxy-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (S18; Table 2, entry 7).**

White solid. mp 140-143 °C. TLC:  $R_f$  = 0.48.  $^1\text{H}$  NMR (Figure S26):  $\delta$  7.62 (d,  $J$  = 8.0 Hz, 1 H), 7.28 (d,  $J$  = 8.4 Hz, 1 H), 7.17 (t,  $J$  = 8.0 Hz, 1 H), 7.07 (t,  $J$  = 7.6 Hz, 1 H), 3.68 (s, 3 H), 3.41 (d,  $J$  = 16.0 Hz, 1 H), 3.20-3.18 (m, 1 H), 2.94 (d,  $J$  = 16.0 Hz, 1 H), 2.61 (dd,  $J$  = 5.6, 13.4 Hz, 1 H), 1.82 (dd,  $J$  = 10.8, 13.0 Hz, 1 H), 1.53 (s, 9 H), 1.49 (d,  $J$  = 6.8 Hz, 3 H), 1.39 (s, 9 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S27):  $\delta$  171.5, 169.8, 137.8, 133.2, 126.7, 120.7, 119.7, 118.8, 112.9, 109.0, 82.1, 81.5, 55.8, 38.8, 29.5, 28.3, 28.2, 28.1, 26.4, 21.7. IR (neat,  $\text{cm}^{-1}$ ): 2975, 1728, 1470, 1368, 1255, 1167. Anal. Calcd (found) for  $\text{C}_{23}\text{H}_{33}\text{NO}_4$ : C, 72.15 (71.97); H, 8.33 (8.45); N, 3.51 (3.67).

**2,2,4,9-tetramethyl-1,3,4,9-tetrahydrocarbazole (S19; Table 2, entry 8).** Colorless oil. TLC

(hexanes–EtOAc = 5:1):  $R_f$  = 0.64.  $^1\text{H}$  NMR (Figure S28):  $\delta$  7.73 (d,  $J$  = 7.6 Hz, 1 H), 7.32 (d,  $J$  = 7.6 Hz, 1 H), 7.21 (dt,  $J$  = 0.8, 7.2 Hz, 1 H), 7.13 (dt,  $J$  = 1.2, 7.2 Hz, 1 H), 3.65 (s, 3 H), 3.16-3.06 (m, 1H), 2.53 (ABq,  $J$  = 16.0 Hz, 2 H), 1.76 (dd,  $J$  = 5.6, 13.0 Hz, 1 H), 1.51 (d,  $J$  = 6.8 Hz, 3 H), 1.36 (t,  $J$  = 7.6 Hz, 1 H), 1.36 (dd,  $J$  = 11.2, 12.8 Hz, 1 H), 1.23 (s, 3 H), 1.02 (s, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S29):  $\delta$  137.7, 135.7, 127.0, 120.4, 119.8, 118.8, 112.7, 109.0, 47.6, 36.5, 32.2, 31.4, 29.3, 26.6, 25.8, 21.7. IR (neat,  $\text{cm}^{-1}$ ): 2950, 2899, 1469, 1371, 1182. Anal. Calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{N}$ : C, 84.53 (84.45); H, 9.31 (9.09); N, 6.16 (6.13).

**7,7-Dicarbomethoxy-5,10-dimethyl-5,6,7,8,9,10-hexahydro-cyclohepta[*b*]**

**indole (S20; Table 2, entry 11).** Pale yellow solid. mp 74-76 °C. TLC:  $R_f$  = 0.47.  $^1\text{H}$  NMR (Figure S30):  $\delta$  7.51 (d,  $J$  = 7.6 Hz, 1 H), 7.26 (d,  $J$  = 8.0 Hz, 1 H), 7.16 (dt,  $J$  = 1.2, 7.2 Hz, 1 H), 7.07 (dt,  $J$  = 0.8, 7.6 Hz, 1 H), 3.79 (s, 3 H), 3.76 (s, 3 H), 3.61 (s, 3 H), 3.57 (d,  $J$  = 15.6 Hz, 1 H), 3.38-3.32 (m,

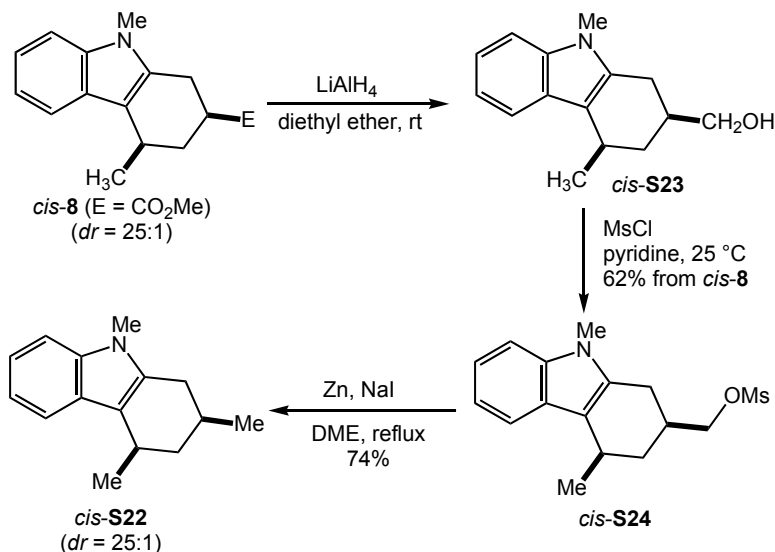
with a doublet  $\delta$  3.35  $J$  = 15.6 Hz, 2 H), 2.50 (ddd,  $J$  = 2.0, 10.8, 12.0 Hz, 1 H), 2.31-2.25 (m, 1 H), 2.06-1.98 (m, 1 H), 1.92-1.84 (m, 1 H), 1.33 (d,  $J$  = 6.8 Hz, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (Figure S31):  $\delta$  172.9, 171.4, 136.7, 132.0, 127.2, 121.0, 118.9, 118.2, 117.5, 109.5, 57.2, 53.2, 52.8, 31.0, 30.2, 29.9, 29.6, 29.5, 20.3. Anal. Calcd (found) for  $\text{C}_{19}\text{H}_{23}\text{NO}_4$ : C, 69.28 (69.17); H, 7.04 (6.92); N, 4.25 (4.24).

**Cyclization of 7 Catalyzed by [(S)-4]PtCl<sub>2</sub>/AgOTf.** A suspension of 7 (63 mg, 0.23 mmol), [(S)-4]PtCl<sub>2</sub> (33mg, 0.023 mmol), and AgOTf (6 mg, 0.023) in 0.90 ml of MeOH was stirred at 60 °C for 64 hours, cooled to room temperature, and filtered through a plug of silica gel, eluting with ether. The filtrate was concentrated under vacuum and the residue was chromatographed (hexanes–EtOAc = 10:1) to give a 9:1 mixture of *cis*-8 and *trans*-8 (59 mg 94%) that contained ~5% of an unidentified impurity. The enantiomeric excess of *cis*-8 and *trans*-8 were determined by HPLC analysis of the corresponding alcohols *cis*- and *trans*-2-methylhydroxy-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (S21), generated via LiAlH<sub>4</sub> reduction of *cis*-8 and *trans*-8 (Figure S13).

**Cyclization of 7 Catalyzed by [(±)-BINAP]PtCl<sub>2</sub>.** A suspension of 7 (69 mg, 0.25 mmol), [(±)-BINAP]PtCl<sub>2</sub>, (22 mg, 0.025 mmol), and AgOTf (6 mg, 0.025 mmol) in MeOH (1 mL) was stirred at 60 °C for 38 hours, cooled to room temperature, and filtered through a plug of silica gel, eluting with ether. The filtrate was concentrated under vacuum and the residue was chromatographed (hexanes–EtOAc = 10:1) to give a 25:1 mixture of *cis*-8 and *trans*-8 (64 mg, 93%).

**For *cis*-8:**  $^1\text{H}$  NMR (500 MHz, Figure S32):  $\delta$  7.66 (d,  $J$  = 8.0 Hz, 1 H), 7.30 (d,  $J$  = 8.0 Hz, 1 H), 7.20 (t,  $J$  = 7.6 Hz, 1 H), 7.10 (t,  $J$  = 8.0 Hz, 1 H), 4.34 (dd,  $J$  = 5.6, 9.6 Hz, 1 H), 4.27 (dd,  $J$  = 7.2, 9.6 Hz, 1 H), 3.80 (s, 3 H), 3.65 (s, 3 H), 3.24-3.14 (m 1 H), 3.02 (tdd,  $J$  = 1.5, 5.5, 16.0 Hz, 1 H), 2.95 (ddd,  $J$  = 2.5, 10.5, 16.0 Hz, 1 H), 2.90-2.83 (m, 1 H), 2.44-2.39 (m, 1 H), 1.57 (dt  $J$  = 11.0, 13.0 Hz, 1 H), 1.50 (d,  $J$  = 6.5 Hz, 3 H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Figure S33):  $\delta$  137.6, 134.0, 126.6, 120.9, 119.8, 119.1, 109.1, 74.1, 37.7, 36.8, 35.2, 29.4, 29.0, 25.8, 21.8.

**Stereochemistry of *cis*-8.** The stereochemistry of *cis*-8 was determined by conversion of *cis*-8 to *cis*-2,4,9-trimethyl-1,3,4,9-tetrahydrocarbazole (*cis*-S22) in 46% yield over three steps (Scheme S1), followed by X-ray crystallographic analysis of *cis*-S22 (Figure S34, Tables S3-S7). The crystal of *cis*-S22 used for X-ray analysis was recovered and subjected to GC analysis, which confirmed its identity as the major diastereomer.



**Scheme S1**

***cis*-2,4,9-trimethyl-1,3,4,9-tetrahydrocarbazole (*cis*-S22).** A solution of (8, *cis*:*trans* = 25:1, 64 mg, 0.24 mmol) in diethyl ether (3 mL) was added slowly to a suspension of LiAlH<sub>4</sub> (18 mg, 0.48 mmol) in diethyl ether (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 40 minutes and quenched via slow addition of water. The resulting mixture was filtered through a short plug of silica gel and eluted with ether (5 mL). The filtrate and eluant were combined and concentrated under vacuum to give crude 2-hydroxymethyl-4,9-dimethyl-1,3,4,9-tetrahydrocarbazole (S23) that was used in the next step without further purification. Methane sulfonylchloride (0.3 mL, 3.9 mmol) was added dropwise to a solution of crude S23 in pyridine (2.0

mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 hours, quenched with ice-water (10 mL), and extracted with ether (50 mL). The combined ether extracts were washed with 0.5 HCl (2 × 20 mL), saturated aqueous NaHCO<sub>3</sub> (20 mL), and brine (20 mL), dried (MgSO<sub>4</sub>), and concentrated under vacuum. The residue was chromatographed (hexanes–EtOAc = 3:1) to give **S24** (46 mg, 62% from **8**) as a pale yellow oil.

A mixture of **S24** (44 mg, 0.14 mmol), NaI (63 mg, 0.42 mmol), and Zn power (55 mg, 0.84 mmol) in DME (2.5 mL) and water (0.05 mL) was refluxed for 3 hours. The resulting mixture was cooled to room temperature, filtered through a short plug of silica gel and eluted with ether (5 mL). The filtrate and eluant were combined and concentrated under vacuum. The residue was chromatographed (hexanes–diethyl ether = 20:1) to give a 25:1 mixture of *cis*-**S22** and *trans*-**S22** (23 mg, 74% yield) as a white solid. Crystals of pure *cis*-**S22** suitable for X-ray analysis were obtained by slow evaporation of a hexanes/ether solution.

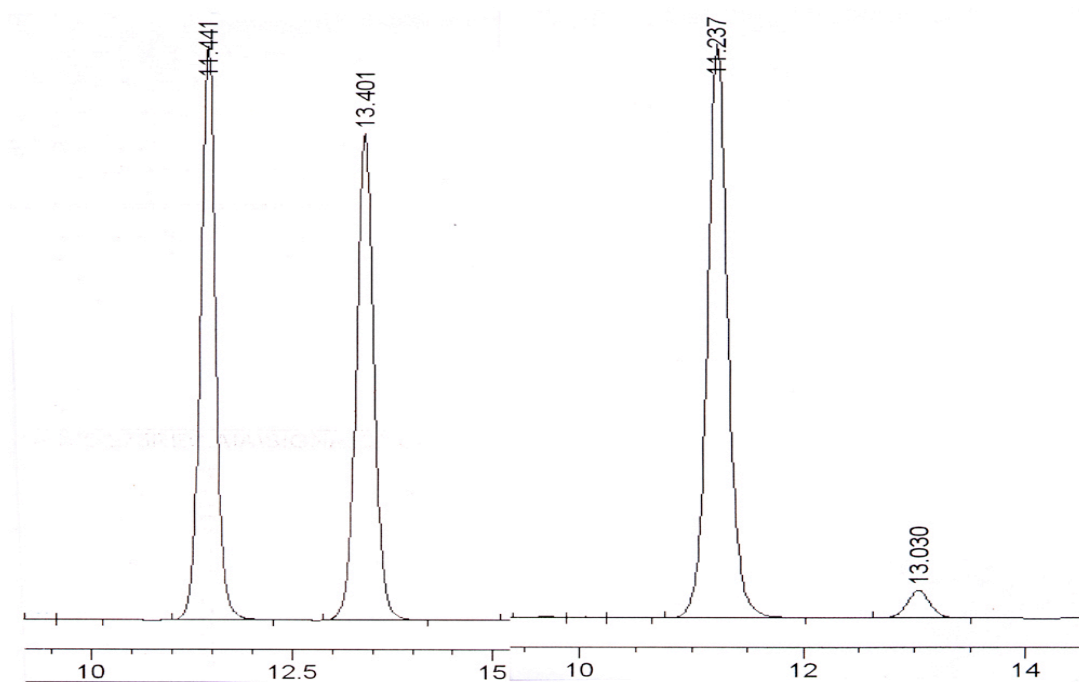
**For *cis*-S22:** TLC:  $R_f$  = 0.68. <sup>1</sup>H NMR:  $\delta$  7.67 (d,  $J$  = 8.0 Hz, 1 H), 7.28 (d,  $J$  = 8.0 Hz, 1 H), 7.16 (t,  $J$  = 7.6 Hz, 1 H), 7.07 (t,  $J$  = 7.6 Hz, 1 H), 3.63 (s, 3 H), 3.16-3.04 (m, 1 H), 2.78 (d,  $J$  = 3.6 Hz, 16.0, 1 H), 2.29 (ddd,  $J$  = 2.4, 10.8, 15.2 Hz, 1 H), 2.40-1.90 (m, 2 H), 1.46 (d,  $J$  = 6.8 Hz, 3 H), 1.20-1.11 (m, 4 H with a doublet at  $\delta$  6.4,  $J$  = 7.6 Hz). <sup>13</sup>C{<sup>1</sup>H} NMR:  $\delta$  137.5, 136.2, 126.9, 120.5, 119.8, 118.8, 114.1, 109.0, 43.4, 31.2, 29.6, 29.3, 22.7, 22.0. IR (neat, cm<sup>-1</sup>): 2950, 1470, 1413, 1376, 1241. Anal. Calcd (found) for C<sub>14</sub>H<sub>17</sub>N: C 84.46 (84.34); H 8.98 (9.09); N 6.57 (6.60).

**For *cis*-S24:** TLC:  $R_f$  = 0.28. <sup>1</sup>H NMR:  $\delta$  7.66 (d,  $J$  = 8.0 Hz, 1 H), 7.29 (d,  $J$  = 8.4 Hz, 1 H), 7.19 (dt,  $J$  = 0.8, 8.0 Hz, 1 H), 7.09 (dt,  $J$  = 0.8, 8.0 Hz, 1 H), 4.34 (dd,  $J$  = 5.6, 9.6 Hz, 1 H), 4.27 (dd,  $J$  = 7.2, 9.6 Hz, 1 H), 3.64 (s, 3 H), 3.20-3.10 (m 1 H), 3.08 (s, 3 H), 2.92 (dd,  $J$  = 5.2, 15.8 Hz, 1 H), 2.50 (ddd,  $J$  = 2.4, 11.2, 15.8 Hz, 1 H), 2.40-2.28 (m, 1 H), 2.12-2.07 (m, 1 H), 1.48 (d,  $J$  = 6.8 Hz, 3 H), 1.26 (q,  $J$  = 12.4 Hz, 1 H). <sup>13</sup>C{<sup>1</sup>H} NMR:  $\delta$  137.6, 134.0, 126.6, 120.9, 119.8, 119.1, 109.1, 74.1, 37.7,

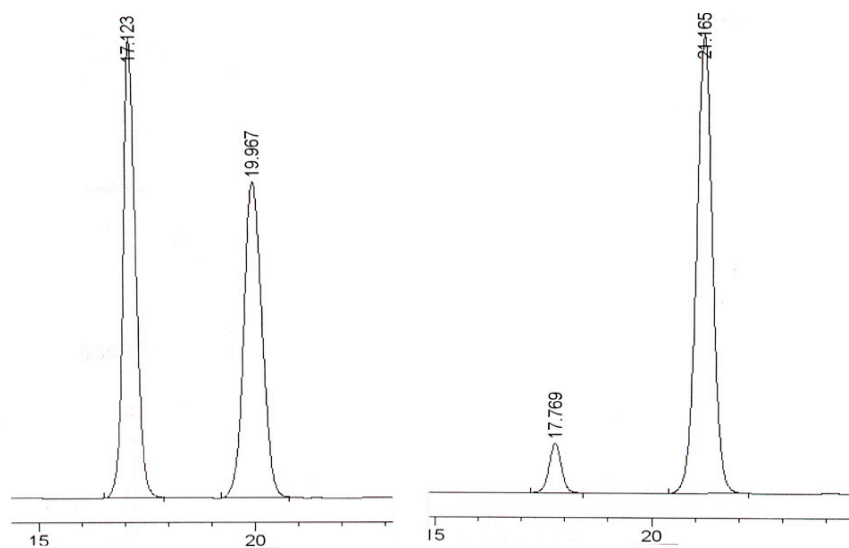
36.8, 35.2, 29.4, 29.0, 25.8, 21.8. IR (neat,  $\text{cm}^{-1}$ ): 2920, 1470, 1353, 1174, 955, 832. HRMS calcd (found) for  $\text{C}_{16}\text{H}_{21}\text{NO}_3\text{S}$ : 307.1242 (307.1241).



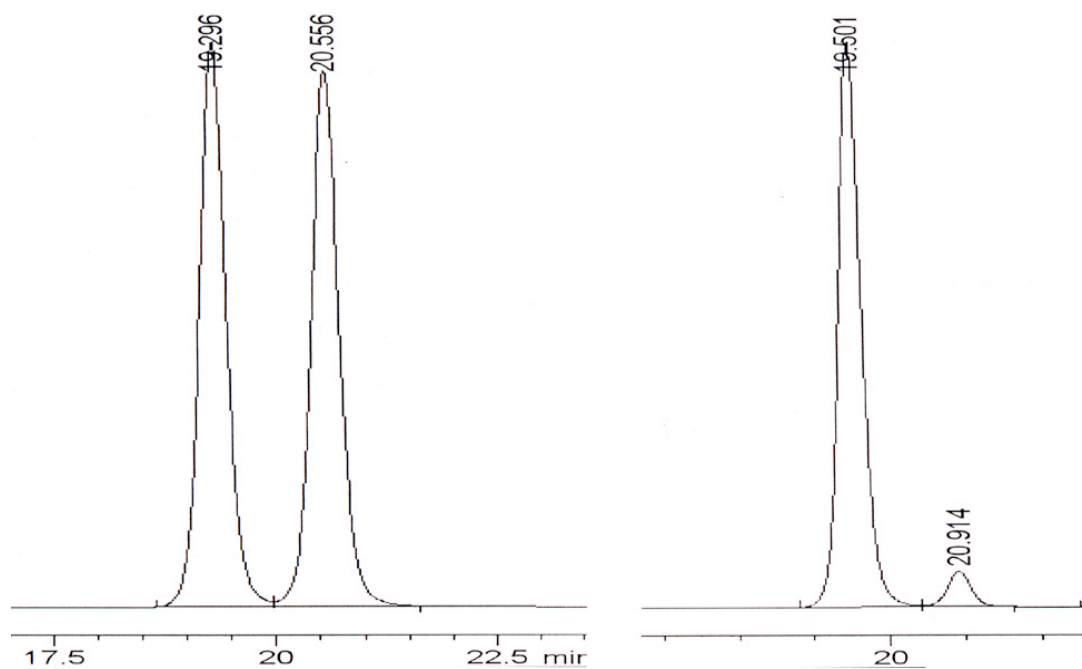
**Figure S1.** Chiral HPLC trace for racemic **5** (left trace) and enantiomerically enriched **5** (right trace) (hexanes/isopropanol = 90/10, 0.6 mL/min).



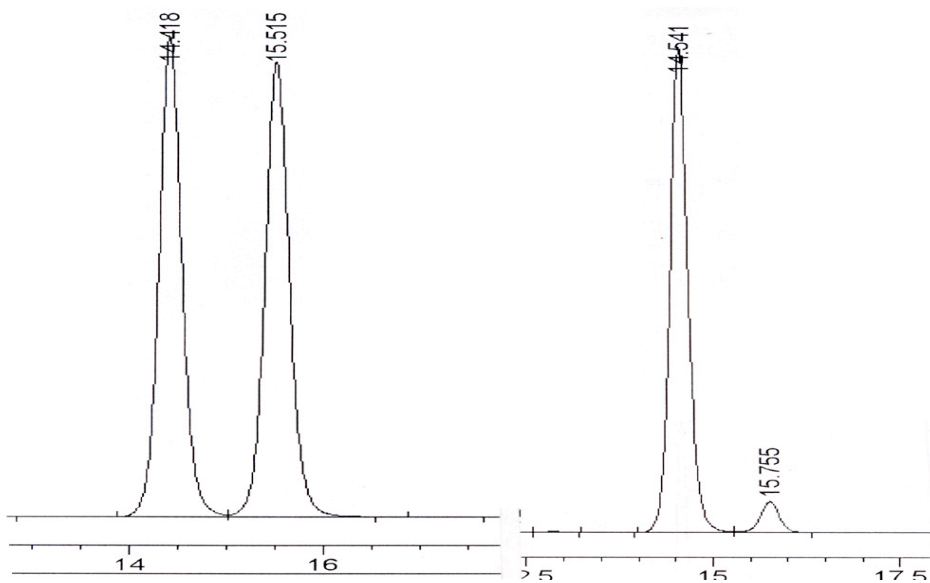
**Figure S2.** Chiral HPLC trace for racemic **S12** (left trace) and enantiomerically enriched **S12** (right trace) (hexanes/isopropanol = 90/10, 0.5 mL/min).



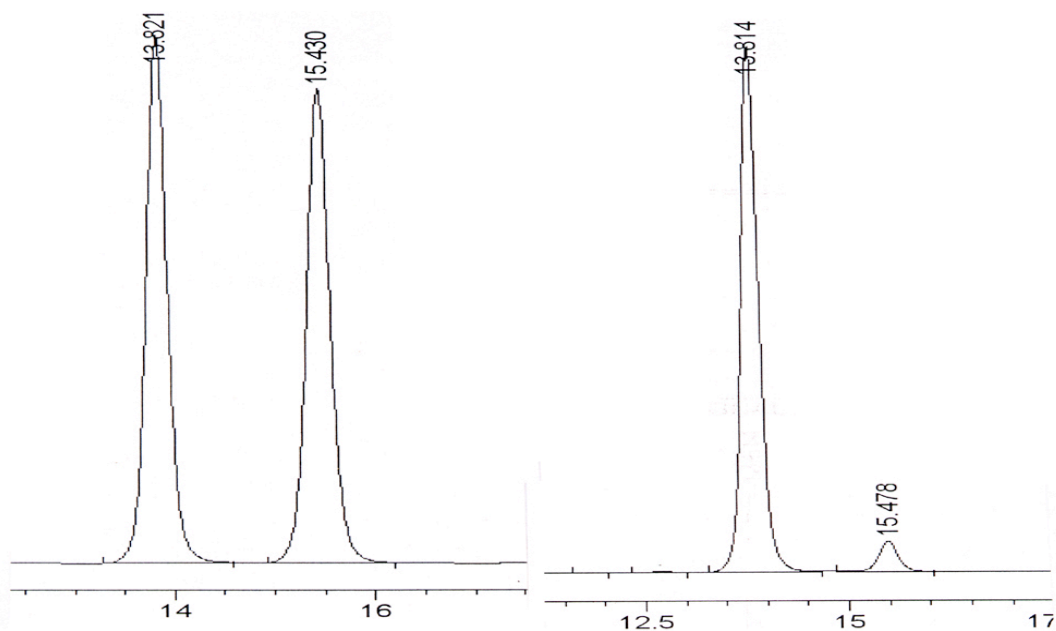
**Figure S3.** Chiral HPLC trace for racemic **S13** (left trace) and enantiomerically enriched **S13** (right trace) (hexanes/isopropanol = 90/10, 0.35 mL/min).



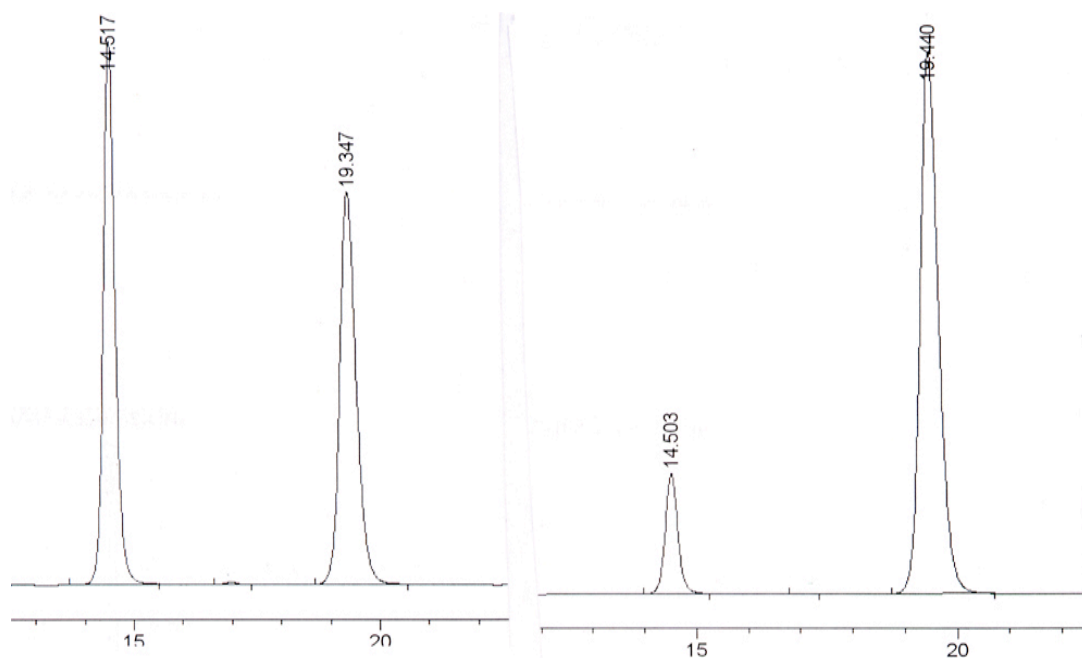
**Figure S4.** Chiral HPLC trace for racemic **S14** (left trace) and enantiomerically enriched **S14** (right trace) (hexanes/isopropanol = 80/20, 0.5 mL/min).



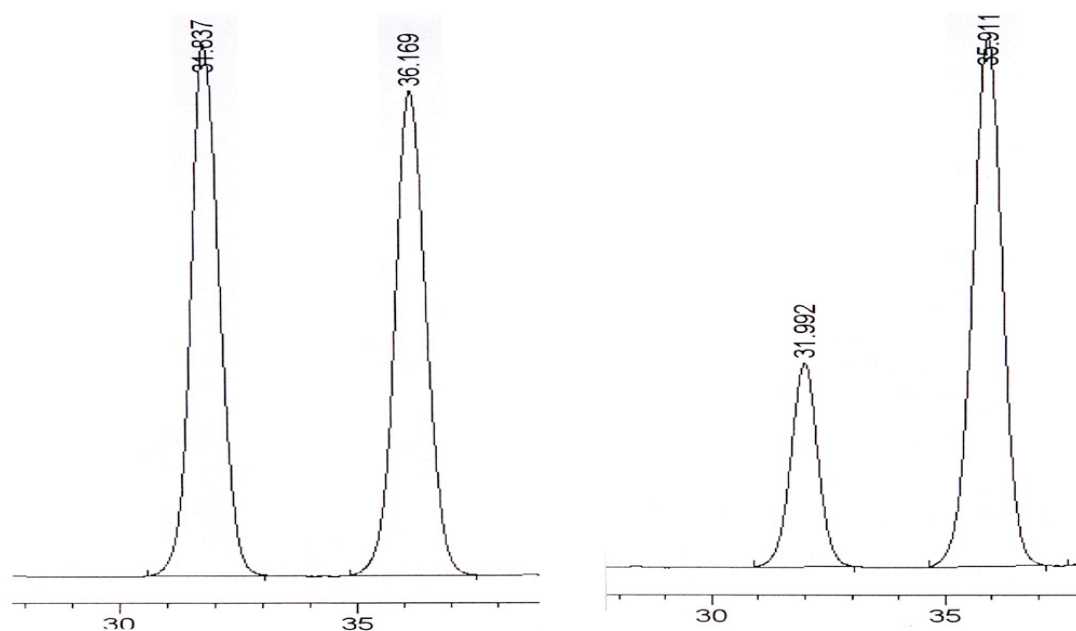
**Figure S5.** Chiral HPLC trace for racemic **S15** (left trace) and enantiomerically enriched **S15** (right trace) (hexanes/isopropanol = 80/20, 0.5 mL/min).



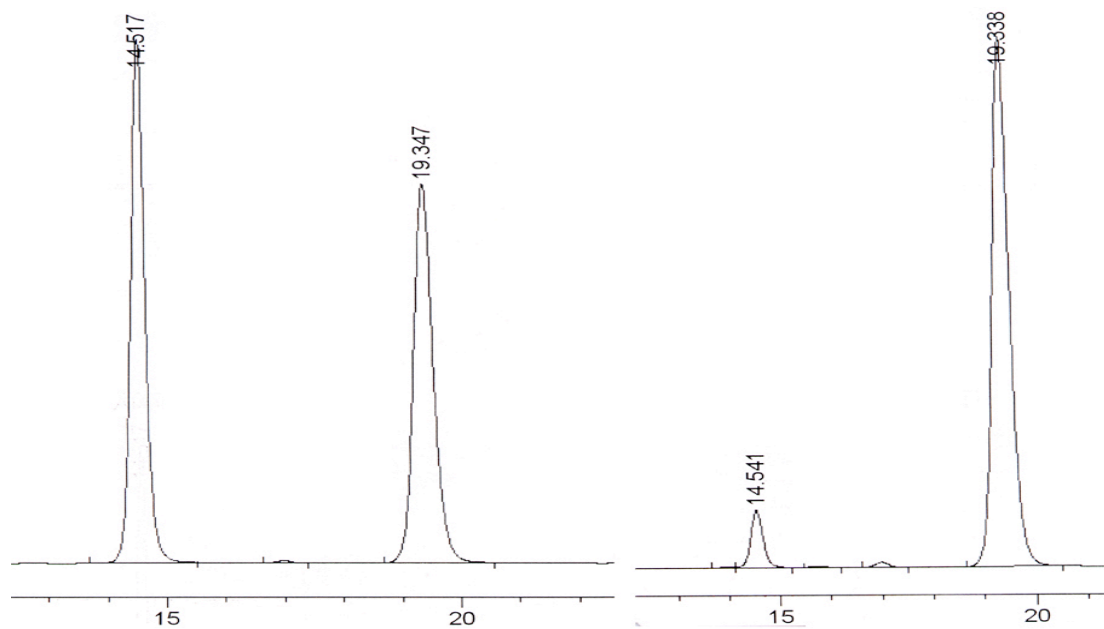
**Figure S6.** Chiral HPLC trace for racemic **S16** (left trace) and enantiomerically enriched **S16** (right trace) (hexanes/isopropanol = 85/15, 0.5 mL/min).



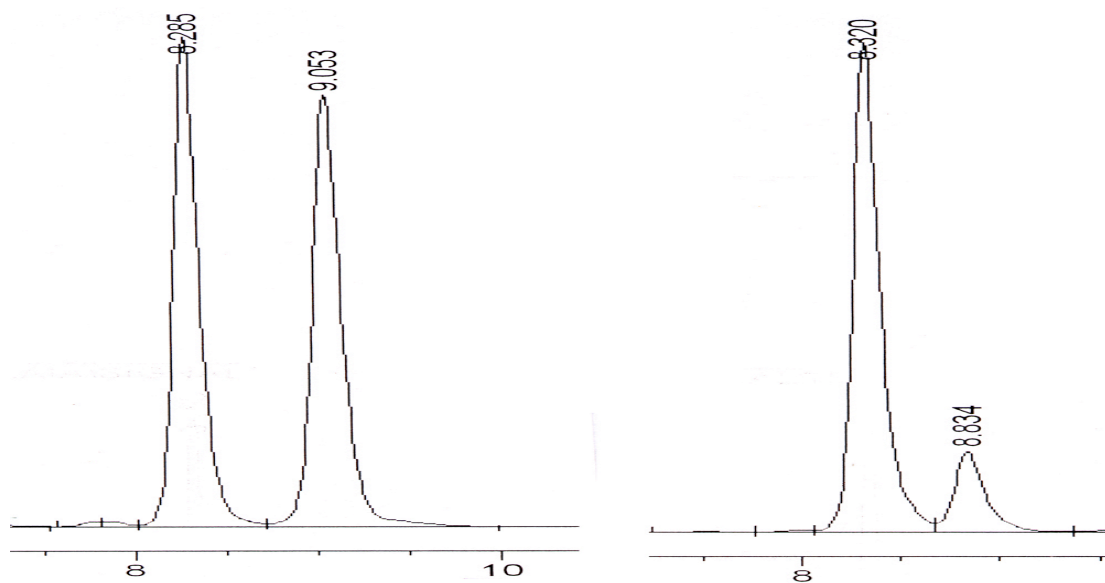
**Figure S7.** Chiral HPLC trace for racemic **S17** (left trace) and enantiomerically enriched **S17** (right trace) (hexanes/isopropanol = 99.5/0.5, 0.5 mL/min).



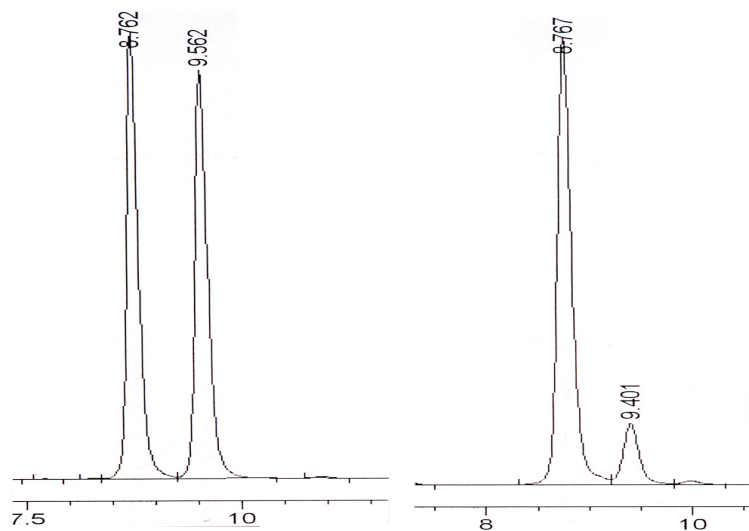
**Figure S8.** Chiral HPLC trace for racemic **S16** (left trace) and **S16** synthesized via  $\text{LiAlH}_4$  reduction of enantiomerically enriched **S18** (right trace, hexanes/isopropanol = 85/15, 0.5 mL/min).



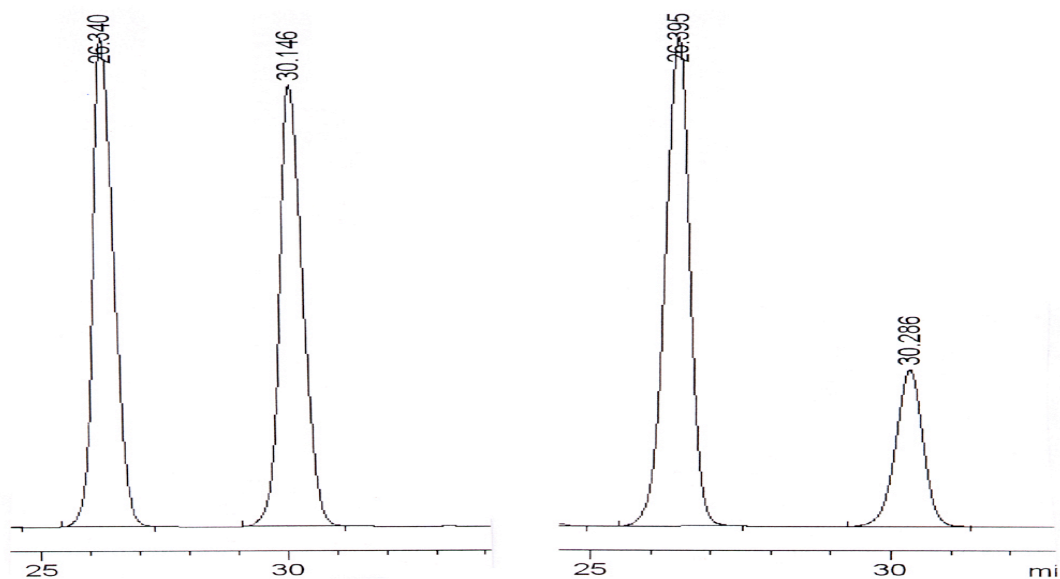
**Figure S9.** Chiral HPLC trace for racemic **S19** (left trace) and enantiomerically enriched **S19** (right trace) (hexanes/isopropanol = 99.5/0.5, 0.5 mL/min).



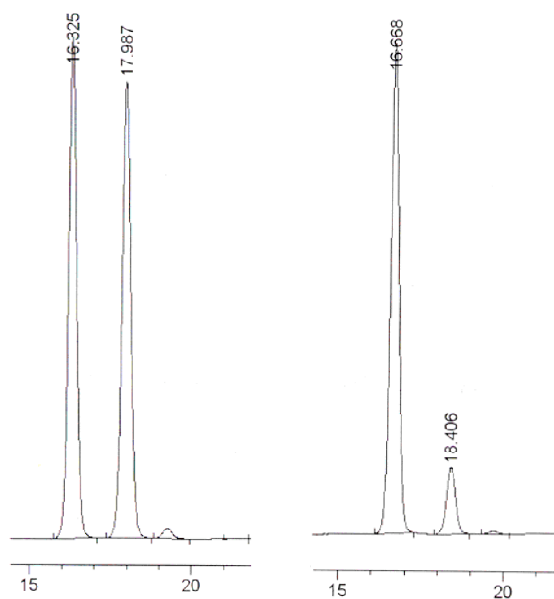
**Figure S10.** Chiral HPLC trace for racemic 1,1,4,9-tetramethyl-2,3,4,9-tetrahydrocarbazole (left trace) and enantiomerically enriched 1,1,4,9-tetramethyl-2,3,4,9-tetrahydrocarbazole (right trace) (hexanes/isopropanol = 99.7/0.3, 0.5 mL/min).



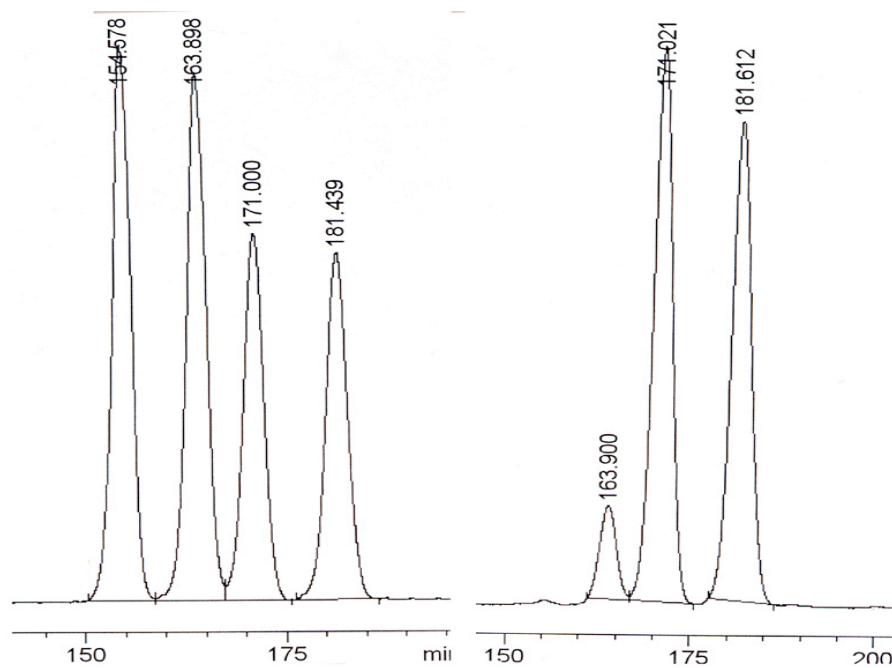
**Figure S11.** Chiral HPLC trace for racemic 1,1,4-trimethyl-2,3,4,9-tetrahydrocarbazole (left trace) and enantiomerically enriched 1,1,4-trimethyl-2,3,4,9-tetrahydrocarbazole (right trace) (hexanes/isopropanol = 99/1, 0.5 mL/min).



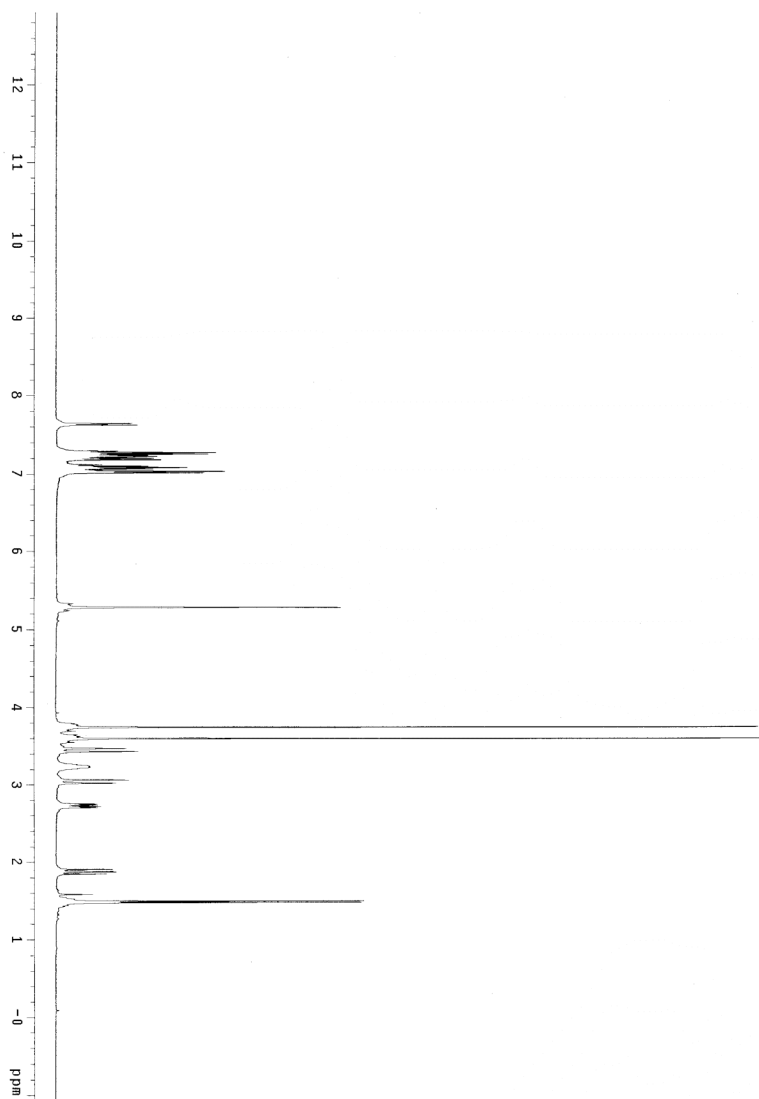
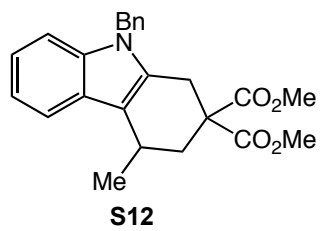
**Figure S12.** Chiral HPLC trace for racemic mixture of **S20** (left trace) and enantiomerically enriched **S20** (right trace) (hexanes/isopropanol = 98/2, 0.5 mL/min).



**Figure S13.** Chiral HPLC trace for racemic mixture of **S21** (cis:trans = 1:2) (left trace) and enantiomerically enriched **S21** (cis:trans = 9:1) (right trace) (hexanes/isopropanol = 98.5/1.5, 0.3 mL/min).

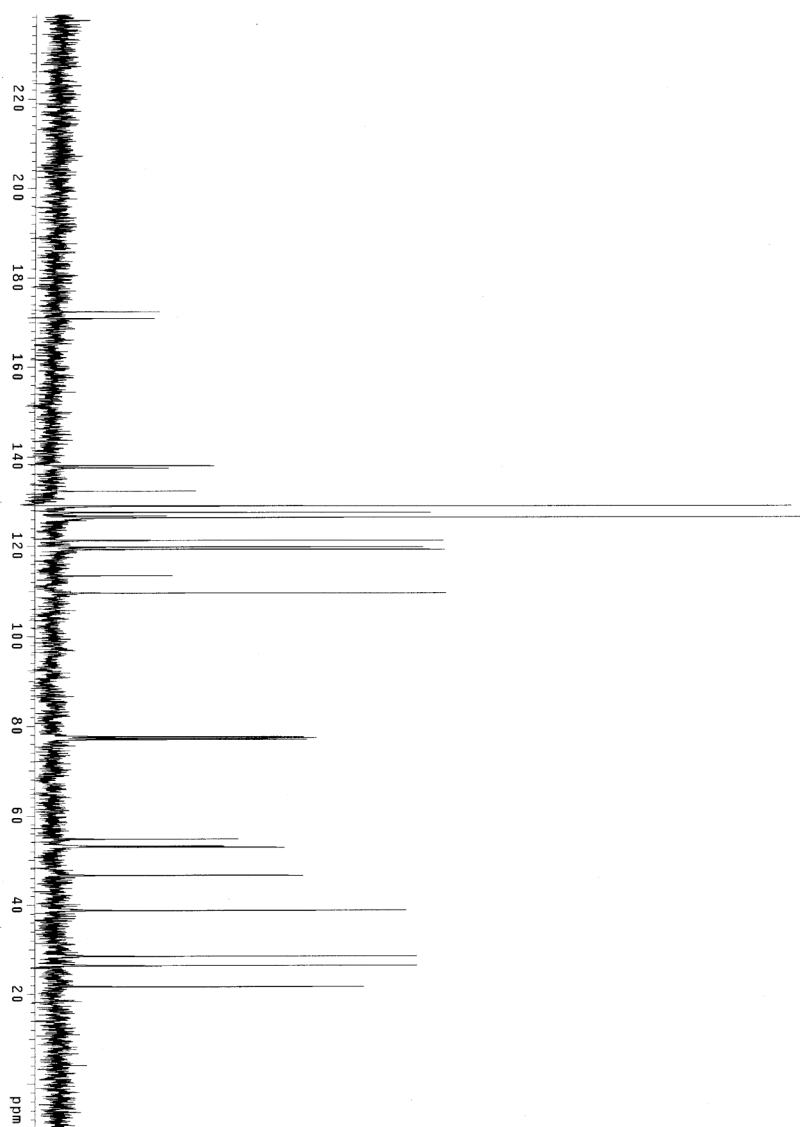
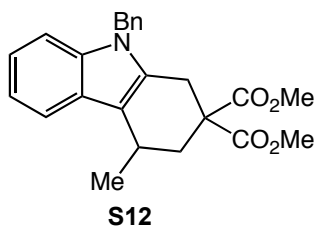


**Figure S14.**  $^1\text{H}$  NMR spectrum of **S12** in  $\text{CDCl}_3$ .

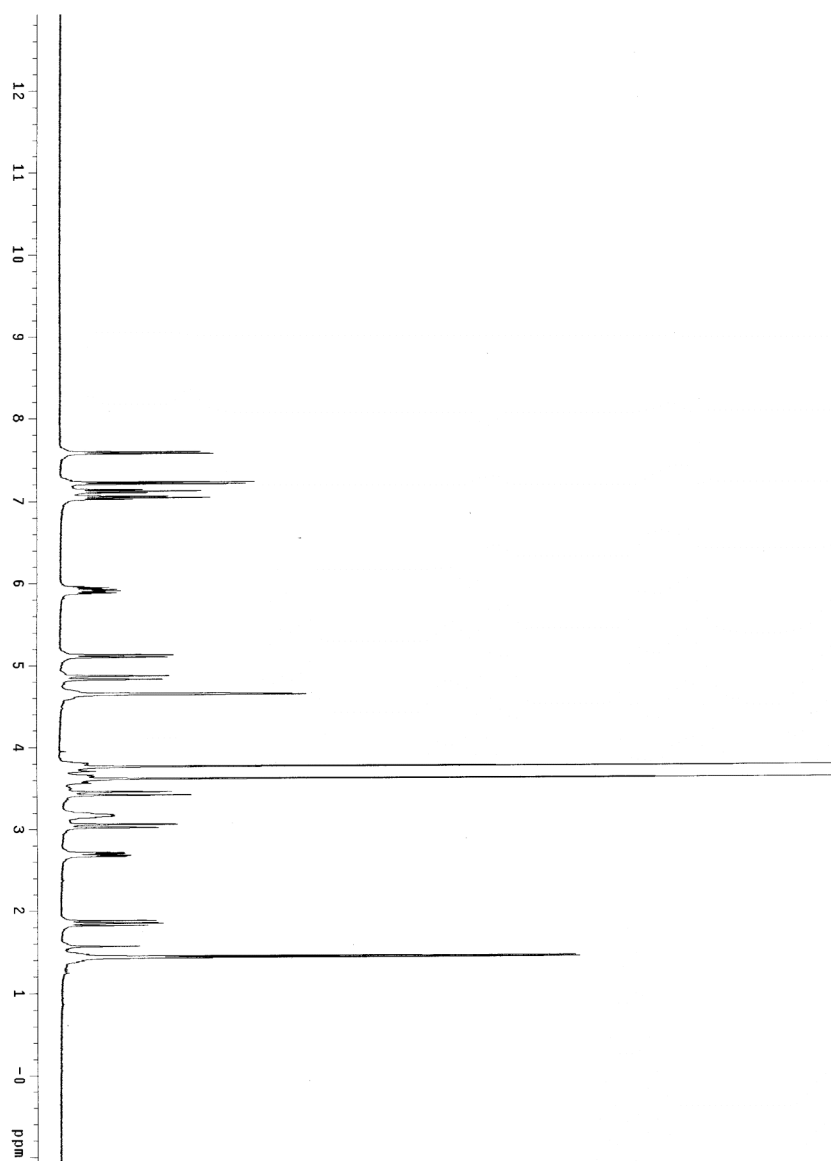
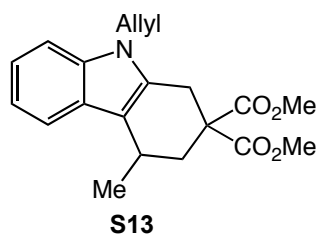




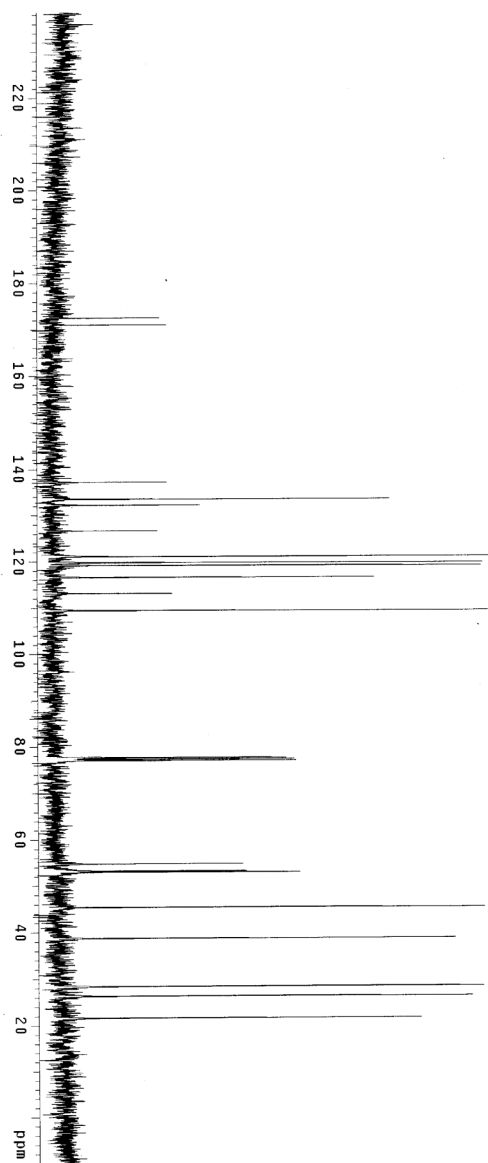
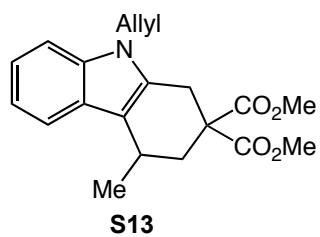
**Figure S15.**  $^{13}\text{C}$   $\{^1\text{H}\}$  spectrum of **S12** in  $\text{CDCl}_3$ .



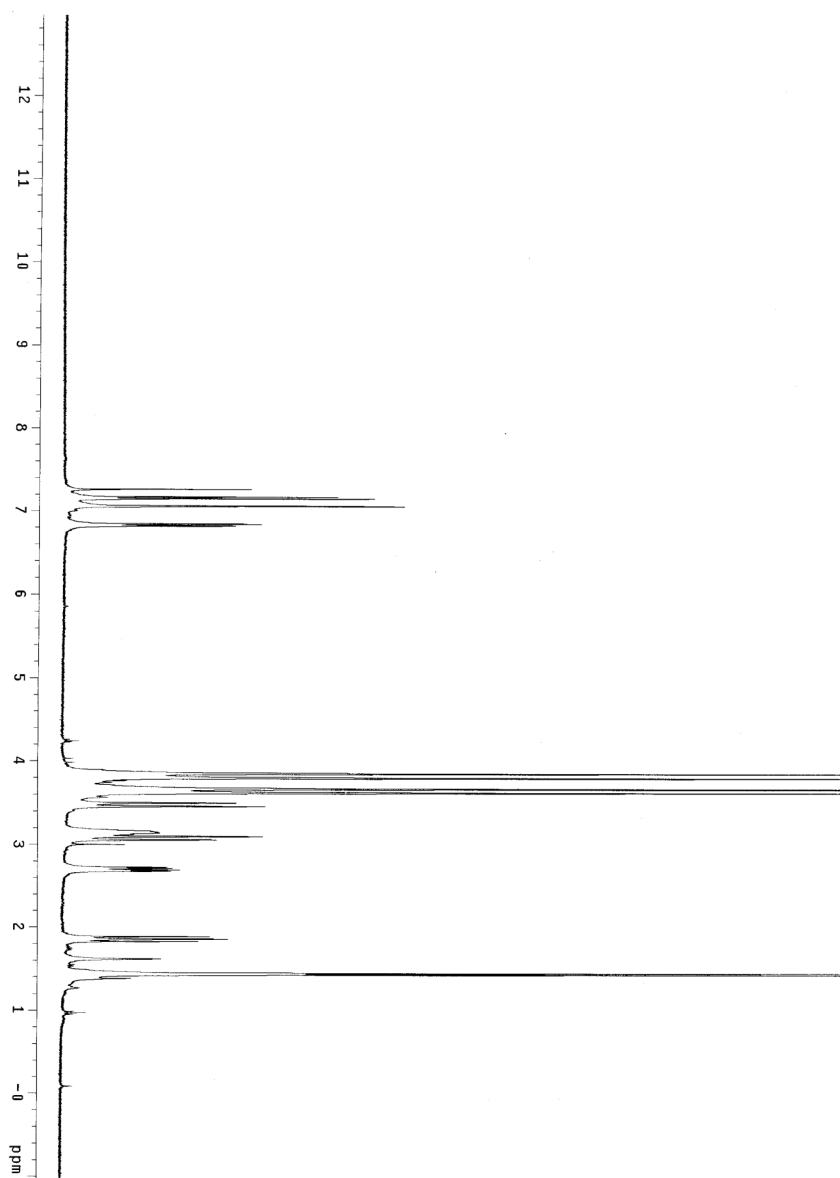
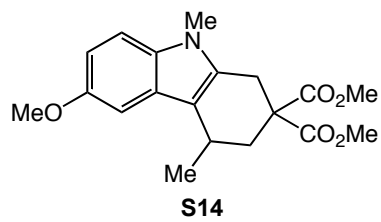
**Figure S16.**  $^1\text{H}$  NMR spectrum of **S13** in  $\text{CDCl}_3$ .



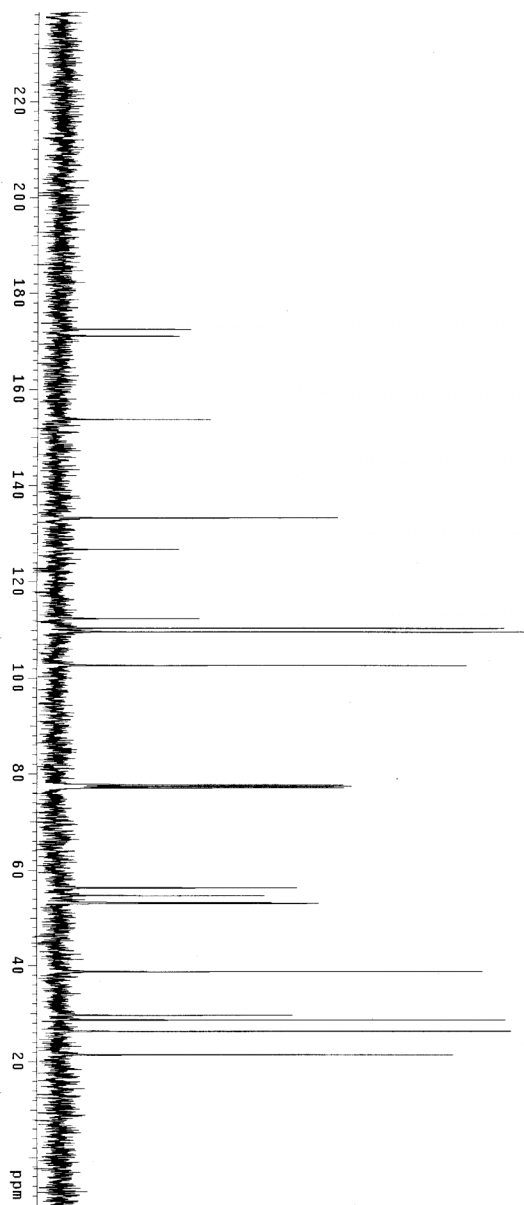
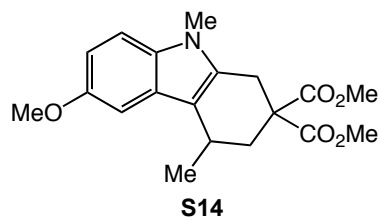
**Figure S17.**  $^{13}\text{C}\{^1\text{H}\}$  spectrum of **S13** in  $\text{CDCl}_3$ .



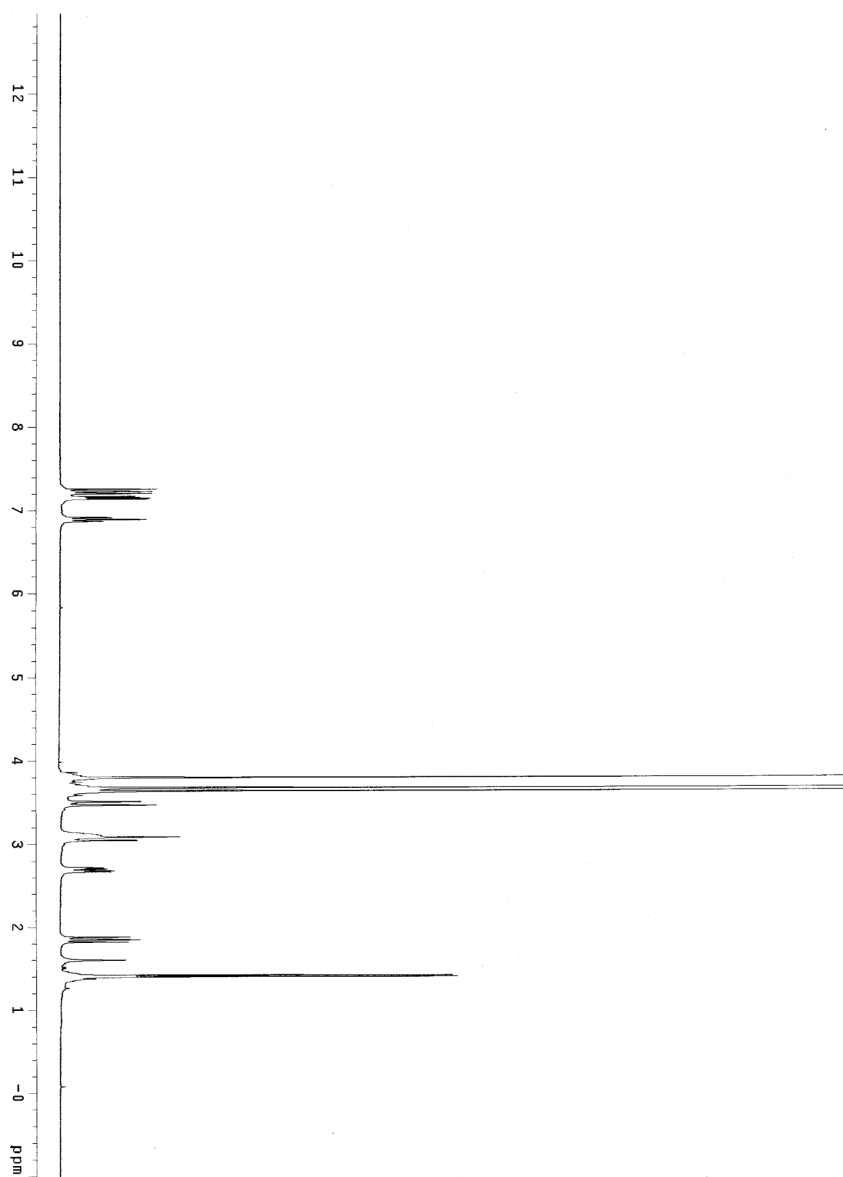
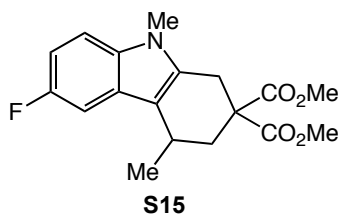
**Figure S18.**  $^1\text{H}$  spectrum of **S14** in  $\text{CDCl}_3$



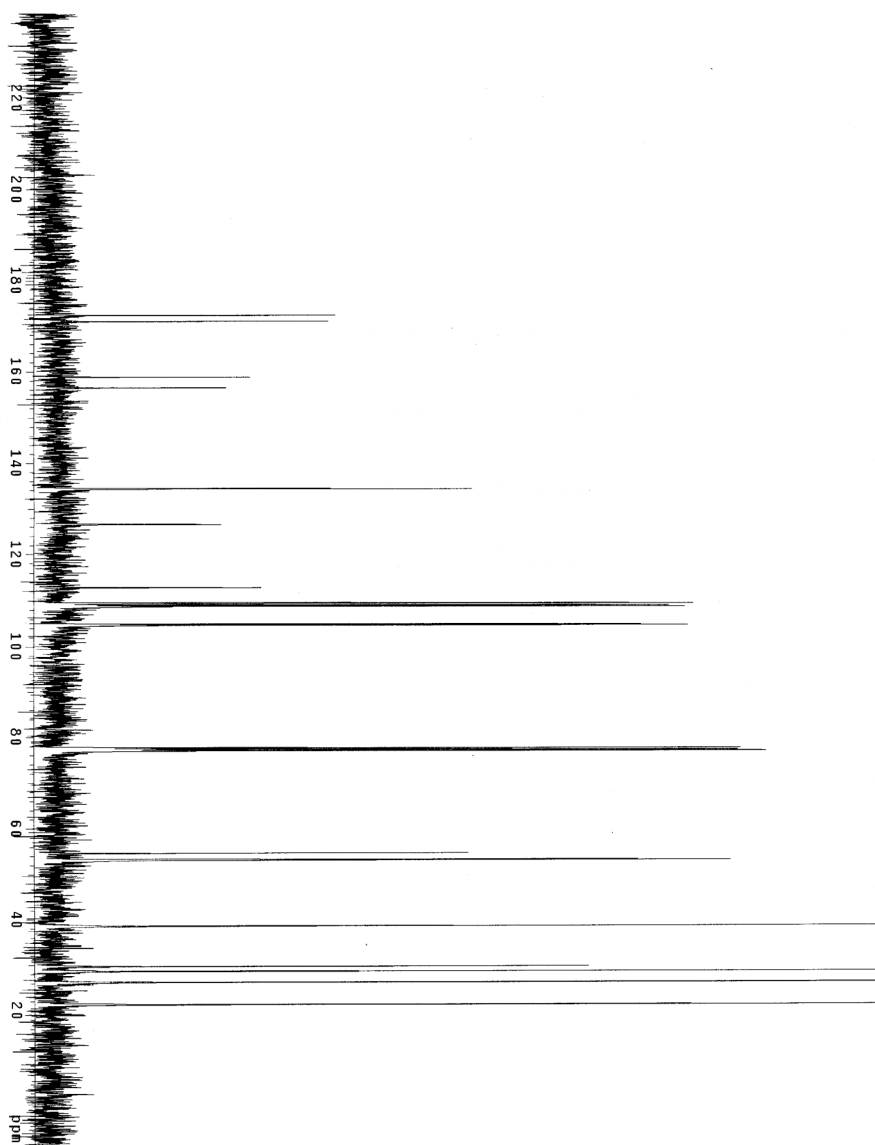
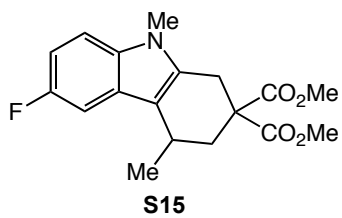
**Figure S19.**  $^{13}\text{C}\{^1\text{H}\}$  spectrum of **S14** in  $\text{CDCl}_3$ .



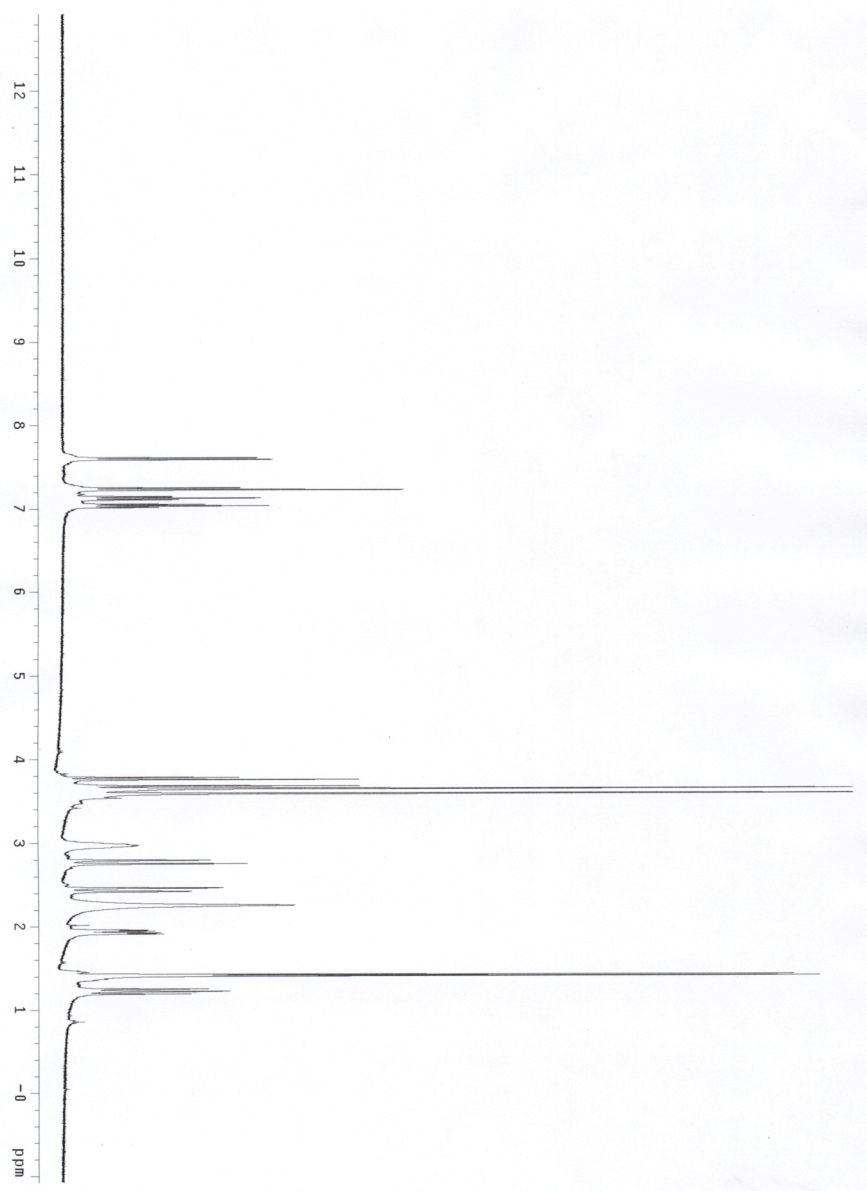
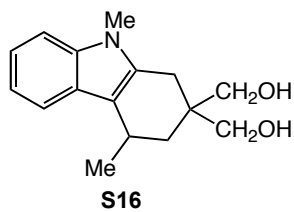
**Figure S20.**  $^1\text{H}$  NMR spectrum of **S15** in  $\text{CDCl}_3$ .



**Figure S21.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S15** in  $\text{CDCl}_3$ .

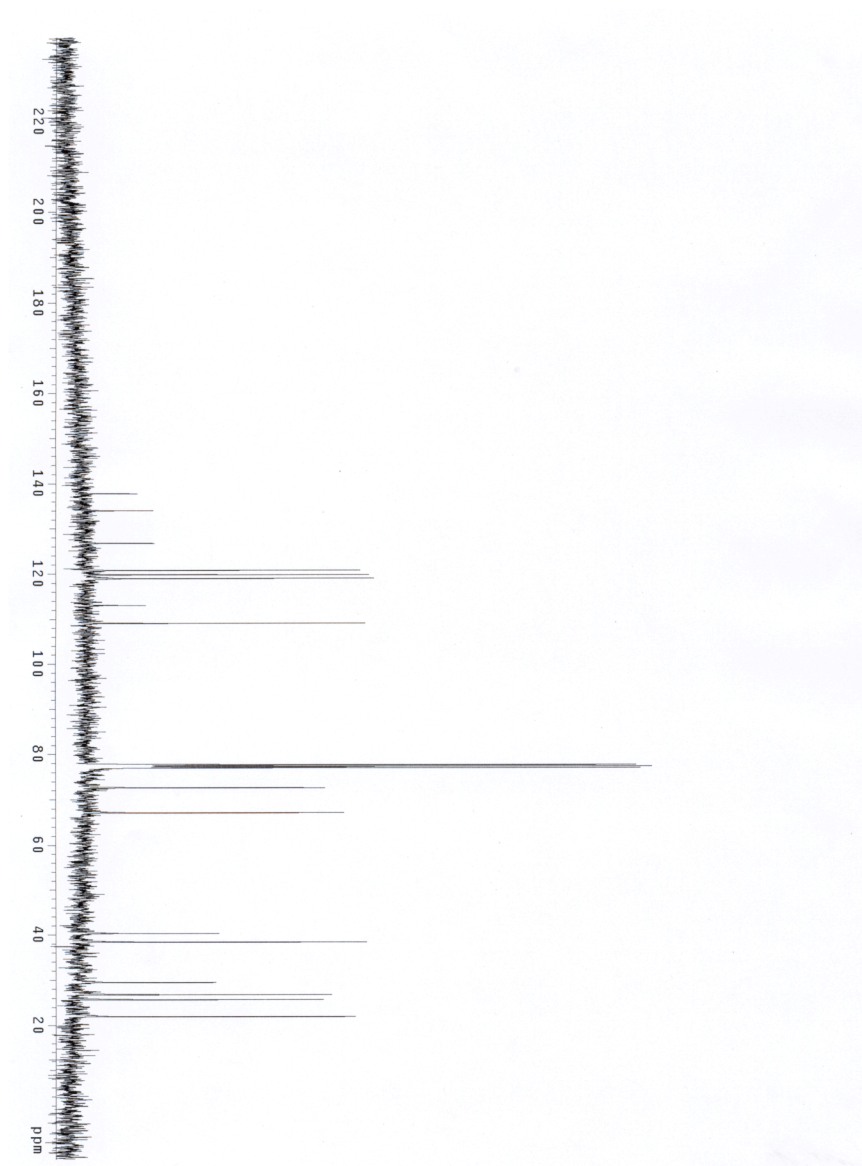
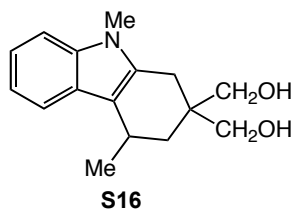


**Figure S22.**  $^1\text{H}$  NMR spectrum of **S16** in  $\text{CDCl}_3$ .

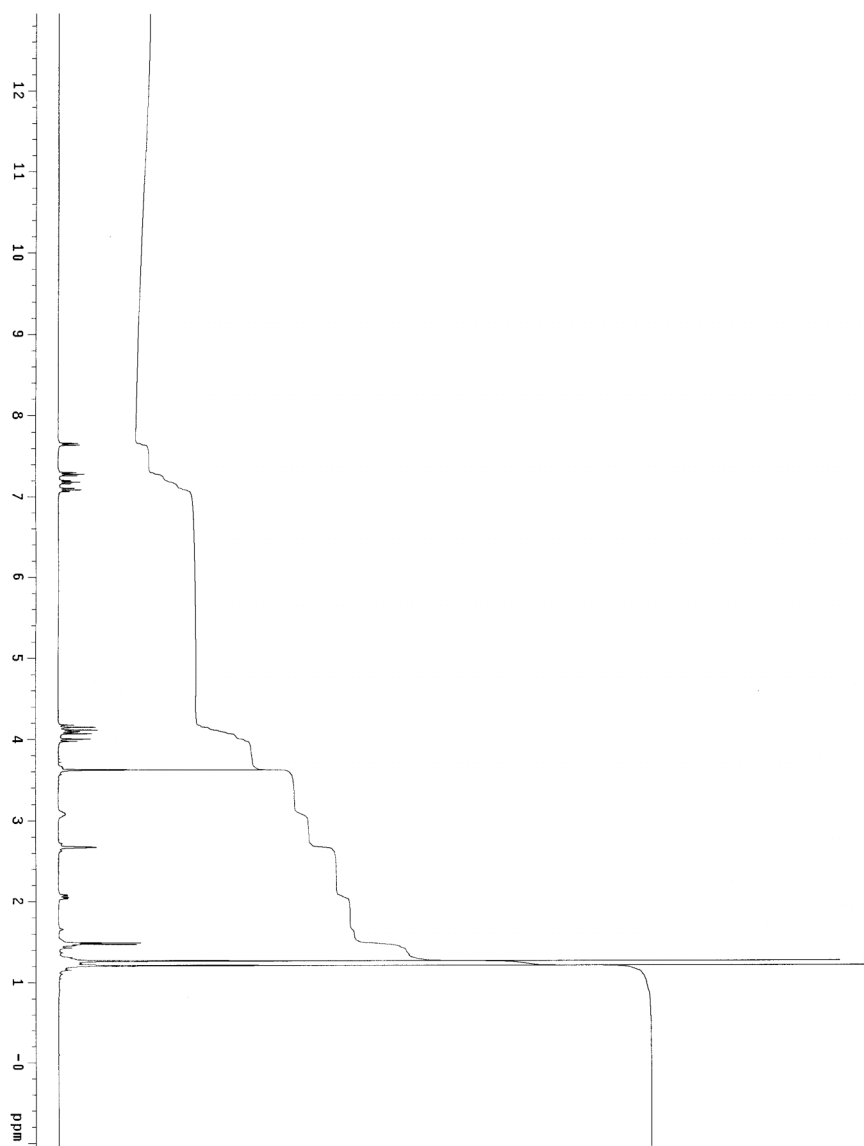
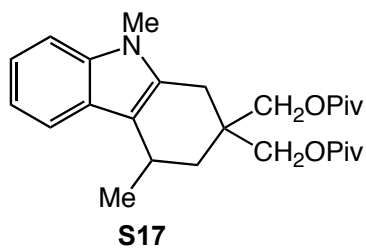




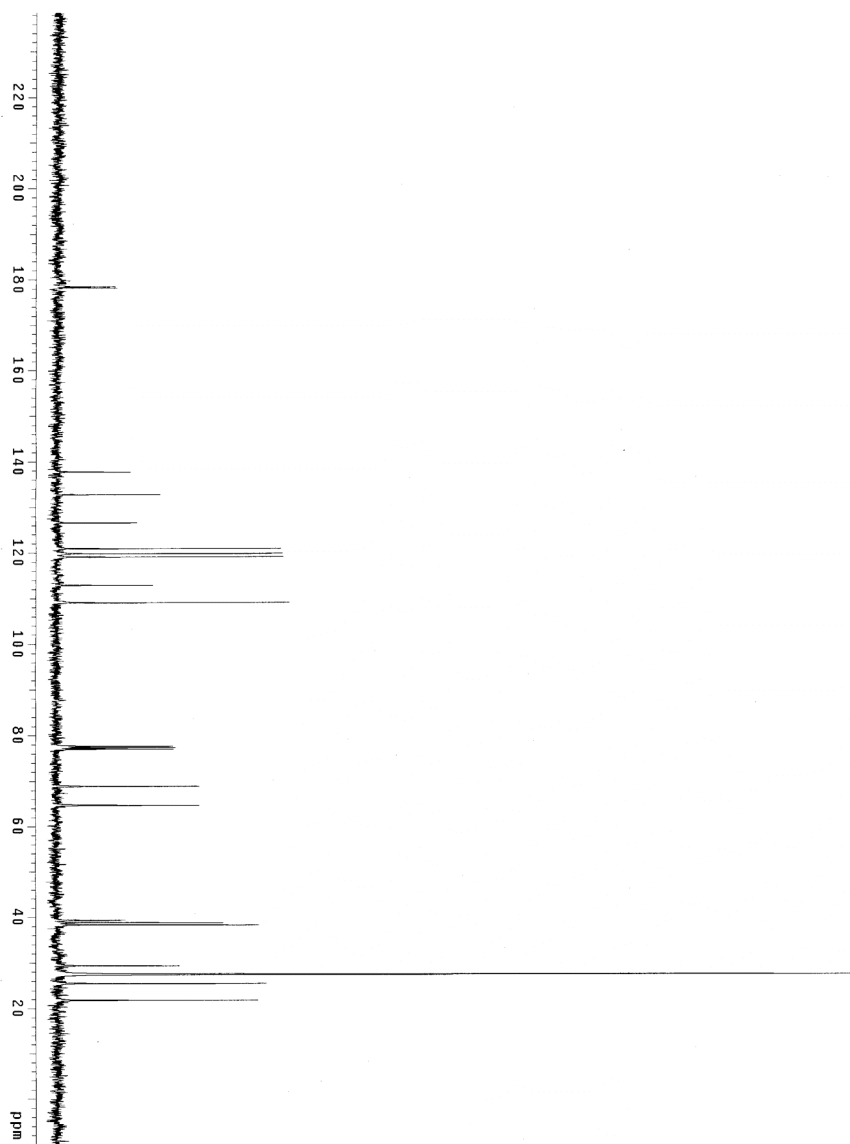
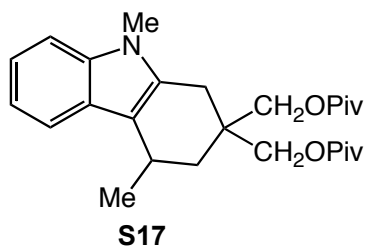
**Figure S23.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S16** in  $\text{CDCl}_3$ .



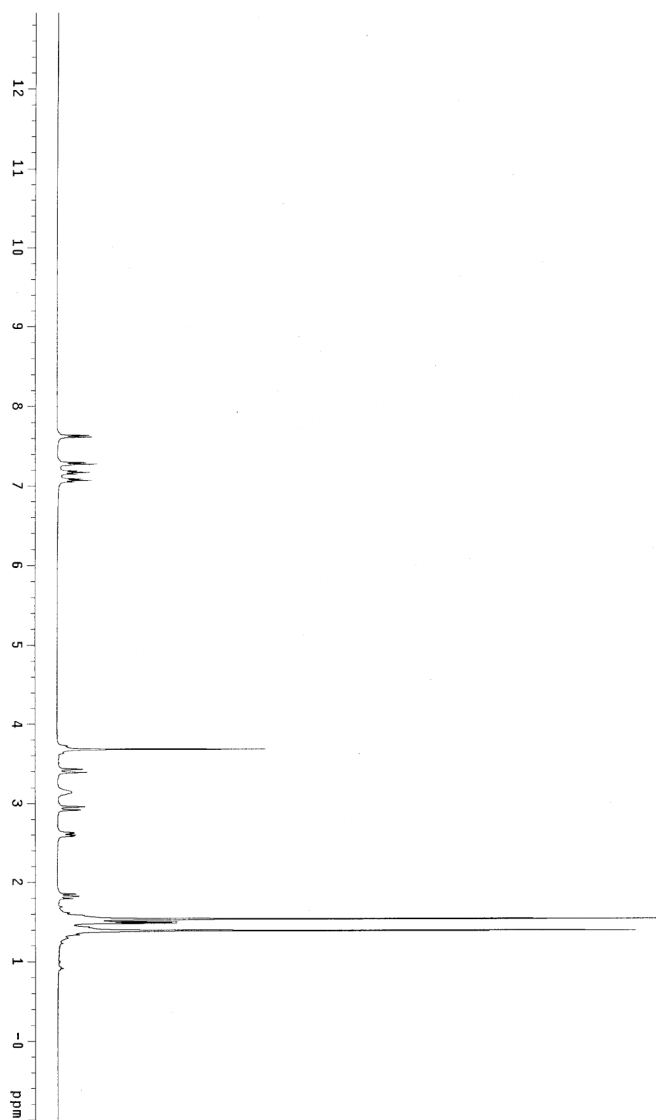
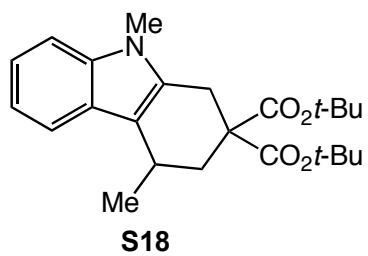
**Figure S24.**  $^1\text{H}$  NMR spectrum of **S17** in  $\text{CDCl}_3$ .



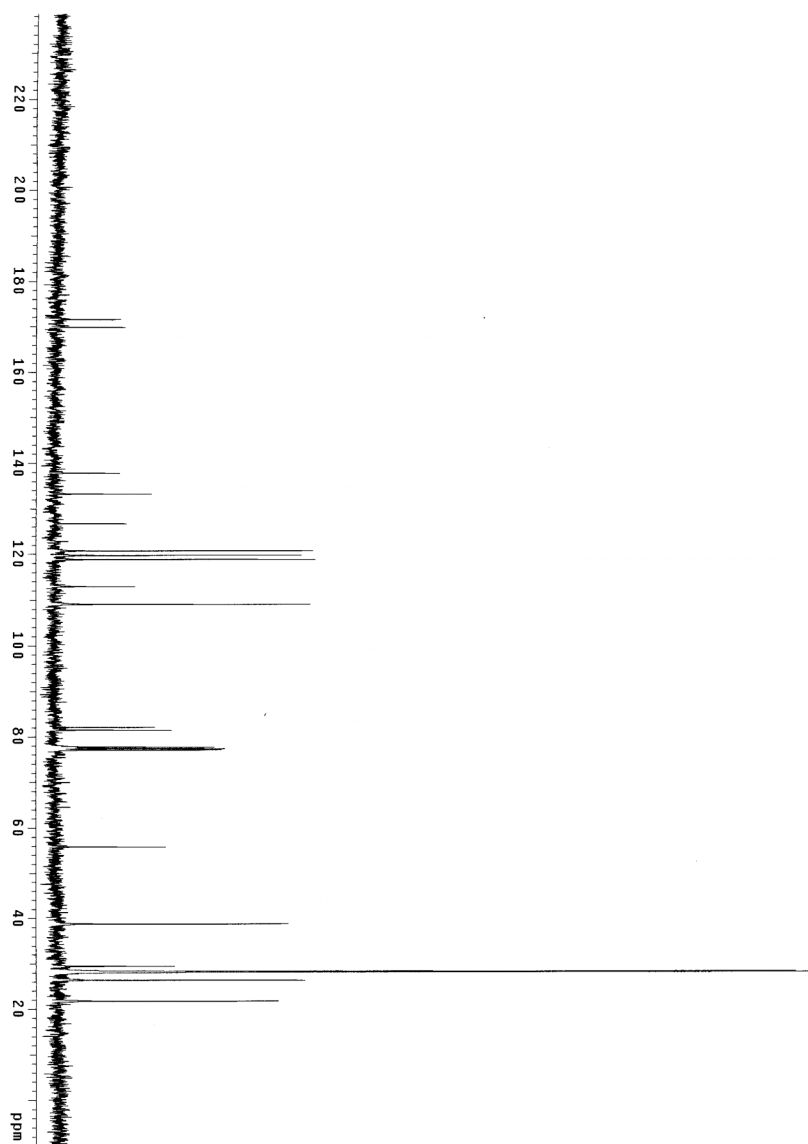
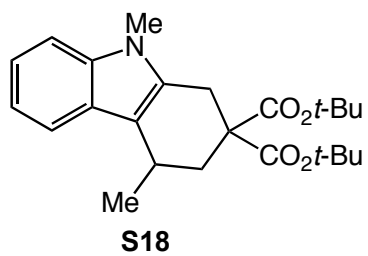
**Figure S25.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S17** in  $\text{CDCl}_3$ .



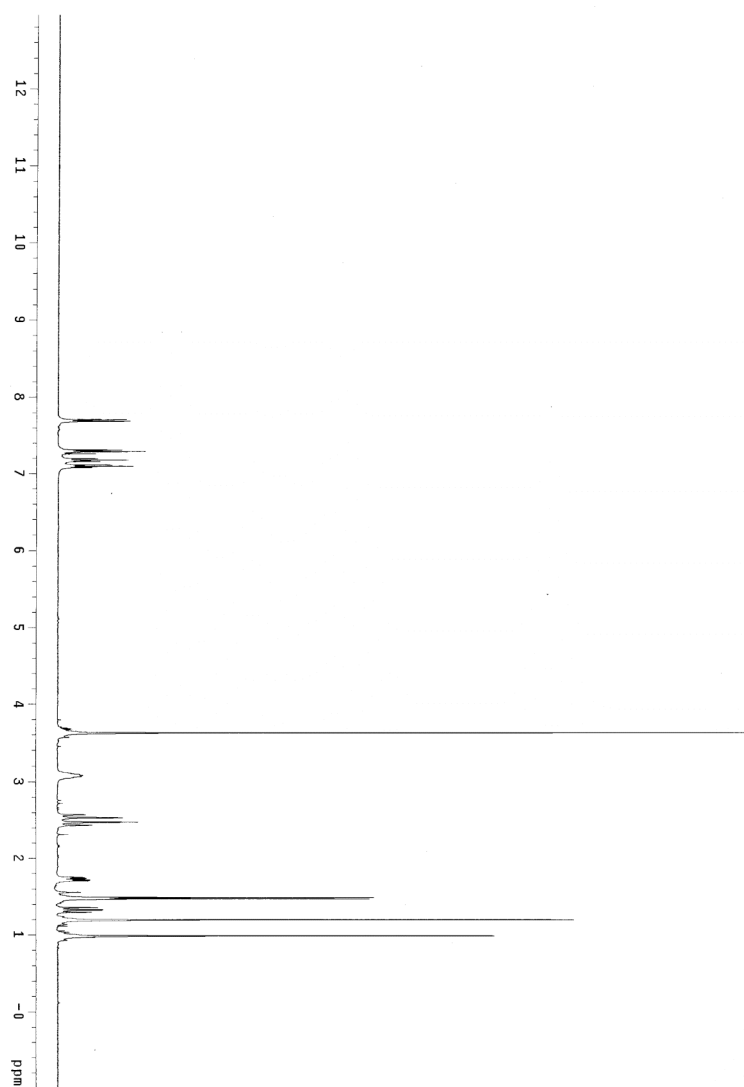
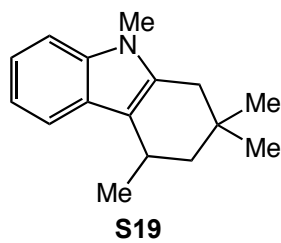
**Figure S26.**  $^1\text{H}$  NMR spectrum of **S18** in  $\text{CDCl}_3$ .



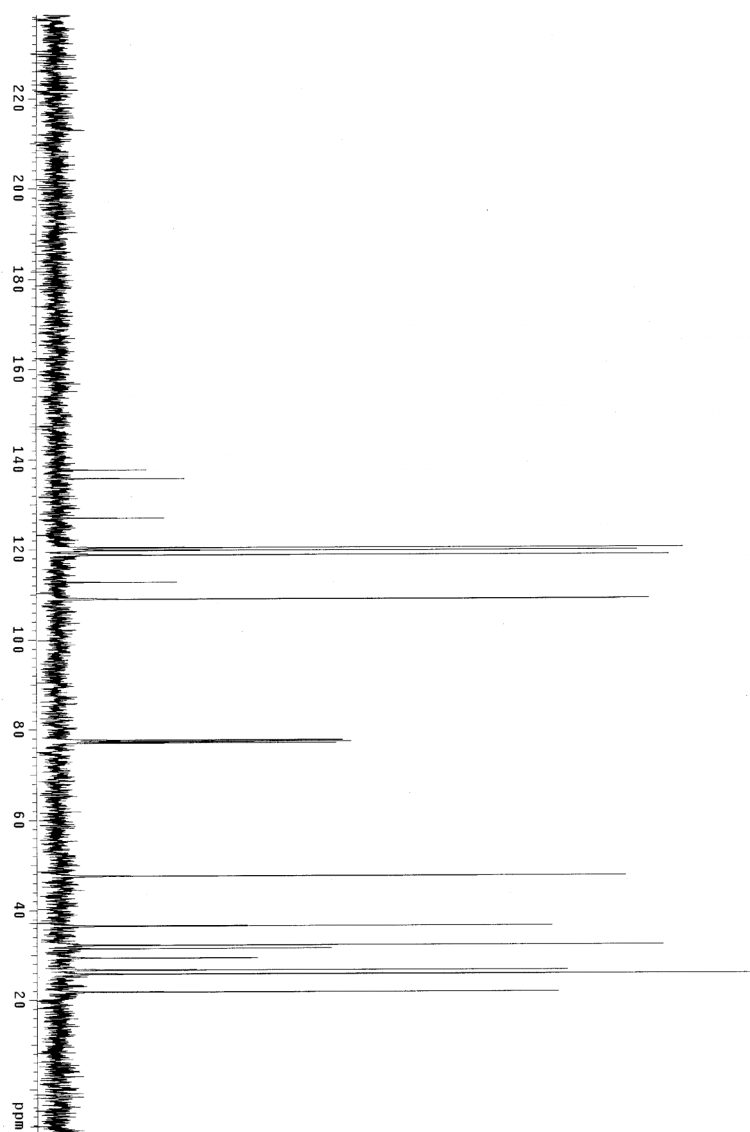
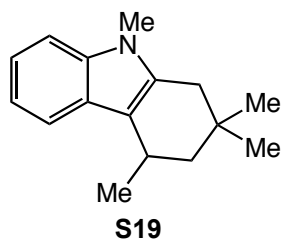
**Figure S27.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S18** in  $\text{CDCl}_3$ .



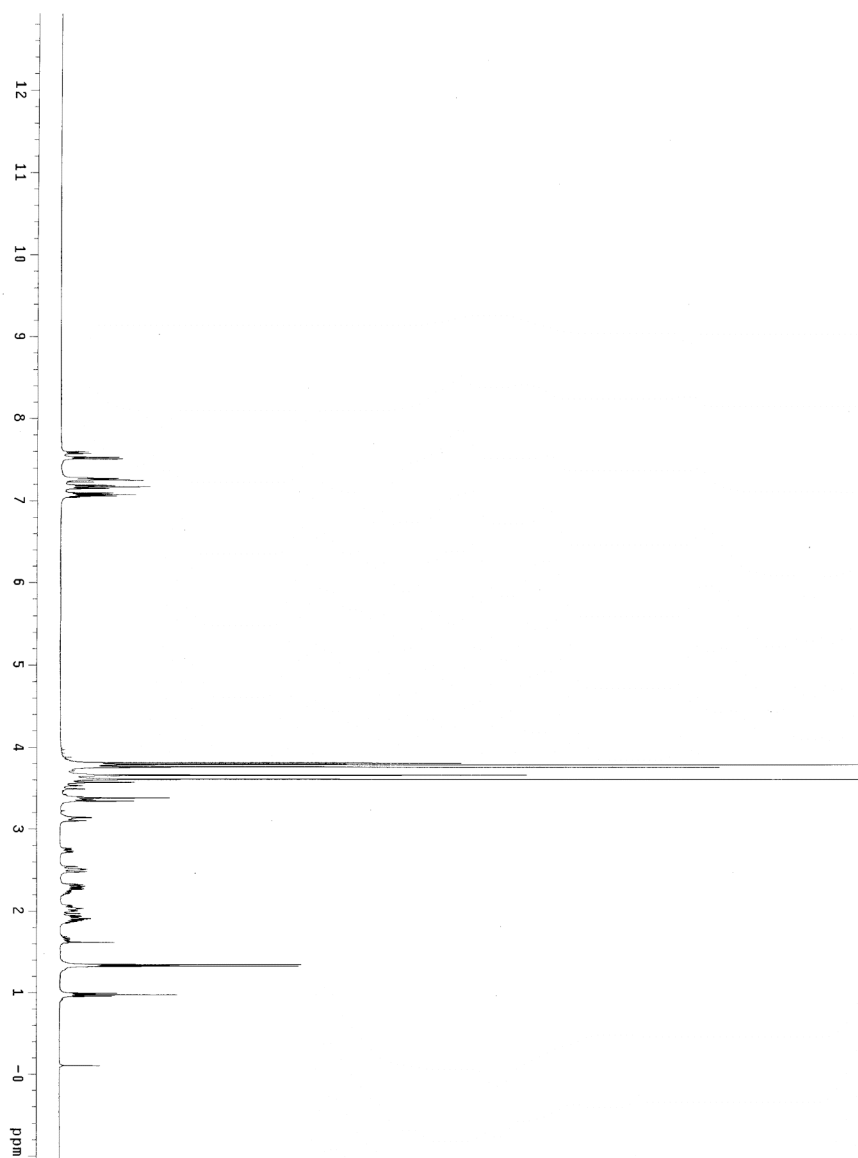
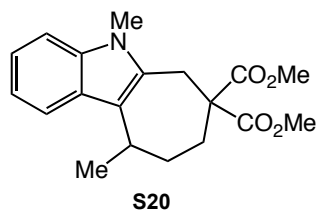
**Figure S28.**  $^1\text{H}$  NMR spectrum of **S19** in  $\text{CDCl}_3$ .



**Figure S29.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S19** in  $\text{CDCl}_3$ .

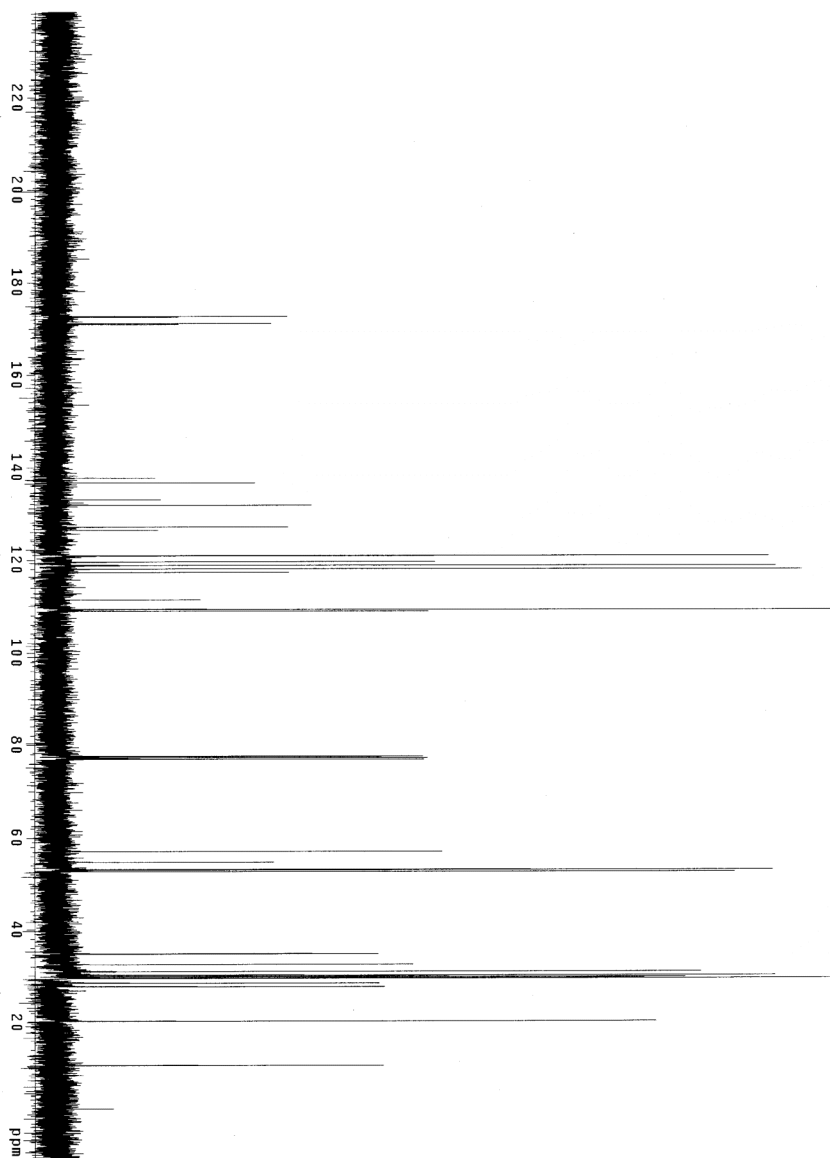
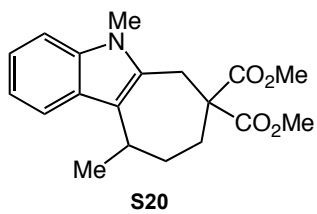


**Figure S30.**  $^1\text{H}$  NMR spectrum of **S20** in  $\text{CDCl}_3$ .

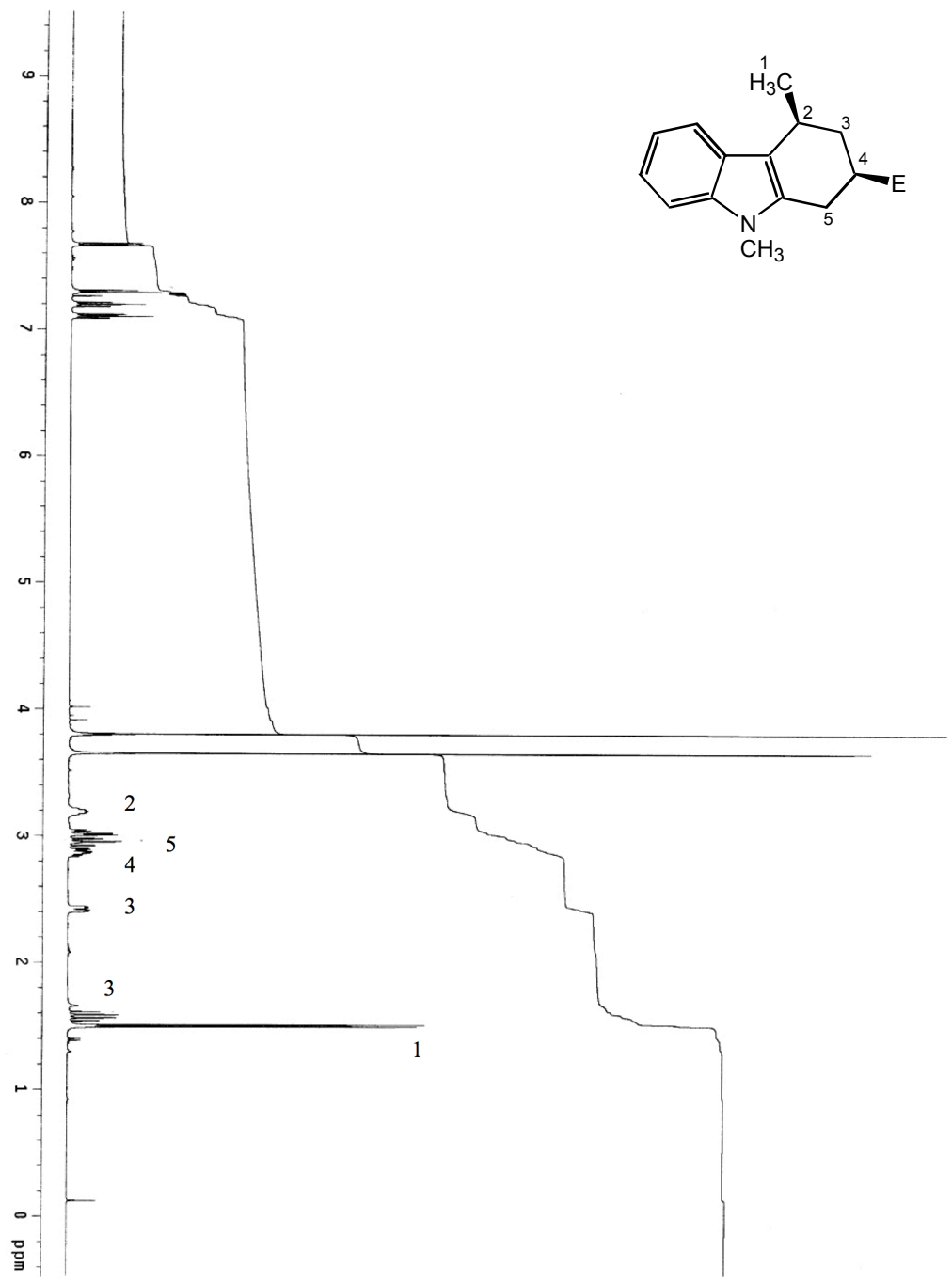




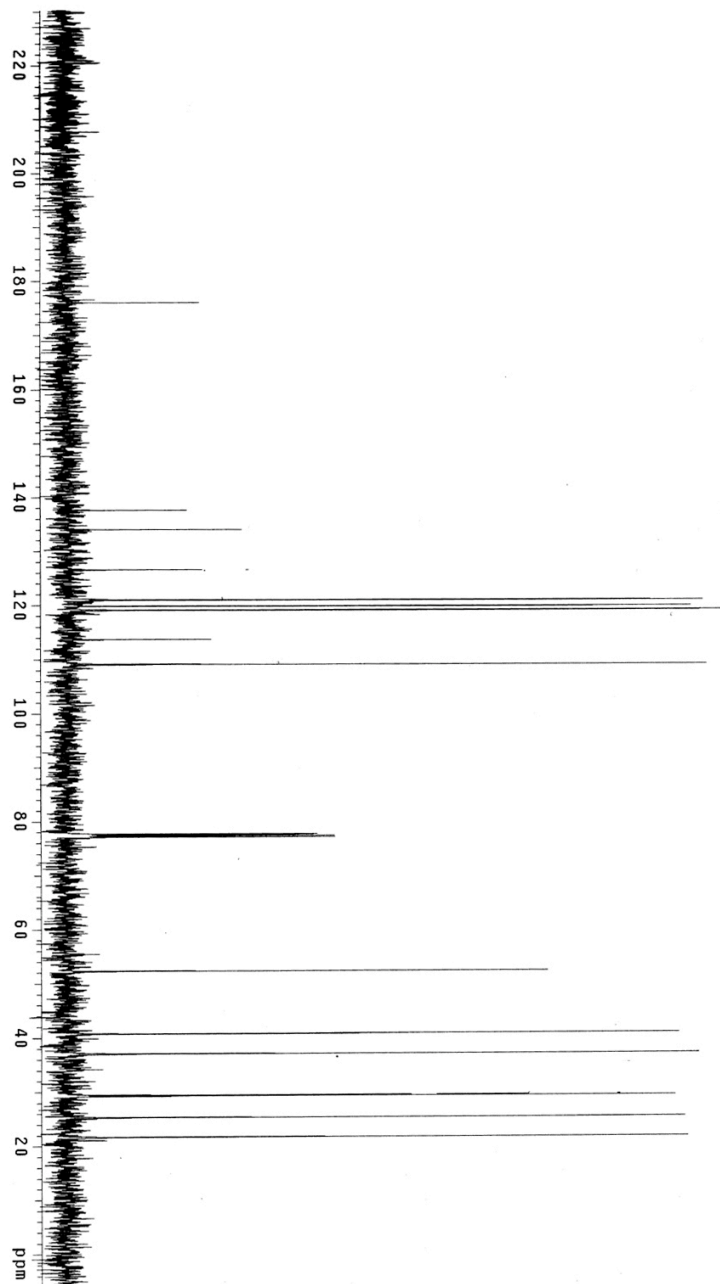
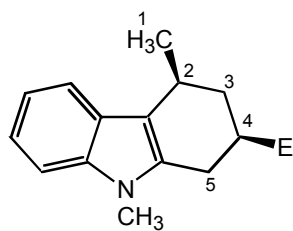
**Figure S31.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **S20** in  $\text{CDCl}_3$ .



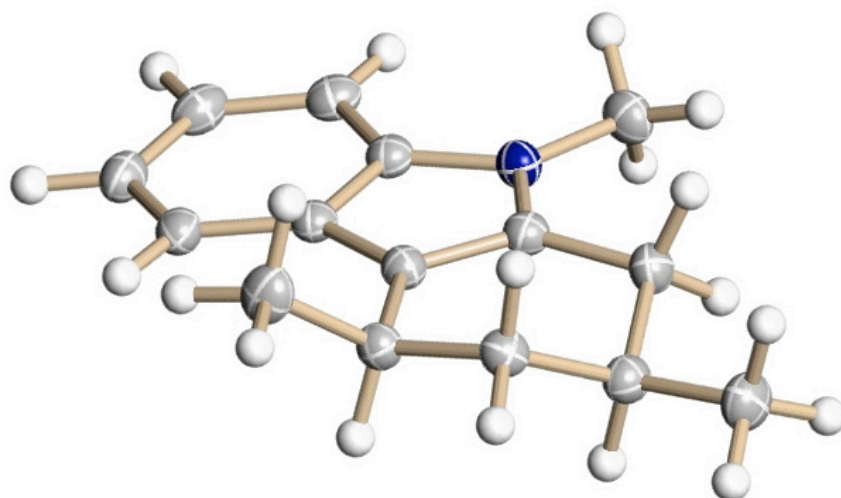
**Figure S32.**  $^1\text{H}$  NMR spectrum for *cis*-**8** in  $\text{CDCl}_3$ .



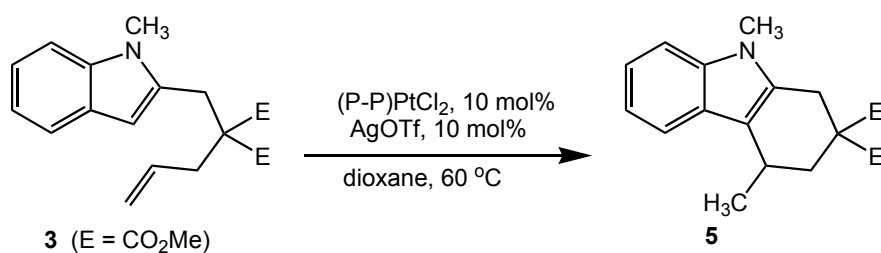
**Figure S33.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum for *cis*-**8** in  $\text{CDCl}_3$ .



**Figure S34.** X-ray crystal structure of *cis*-**S22**.



**Table S1.** Effect of BINAP and MeOBIPHEP ligands on platinum-catalyzed cyclization of **3** to **5** in dioxane at 60 °C.



entry	P-P	R'	R''	time (h)	yield (%) <sup>a</sup>	ee (%) <sup>b</sup>
1	( <i>S</i> )-Binap	H	H	22	82	≤5
2	( <i>S</i> )-Tol-Binap	H	Me	24	83	21
3	( <i>R</i> )-3,5-Xylyl-Binap	Me	H	24	81	41
4	( <i>R</i> )-3,5-Xylyl-Binap	Me	H	24	66	21 <sup>c</sup>
5	( <i>R</i> )-3,5- <i>i</i> -Pr-MeOBiphep	<i>i</i> -Pr	H	24	86	63
6	( <i>S</i> )- <b>4</b>	<i>t</i> -Bu	MeO	23	88	87

<sup>a</sup> Isolated product ≥ 95 % purity. <sup>b</sup> ee was determined by HPLC using Chiral Pak AD-H column. <sup>c</sup> 20 mol % of AgOTf was used.

**Table S2.** Effect of silver salt and solvent on cyclization of **3** to **5** catalyzed by [(*S*)-**4**]PtCl<sub>2</sub> (10 mol %) at 60 °C.

**3** (E = CO<sub>2</sub>Me) **5**

entry	solvent	AgX	time (h)	yield (%) <sup>a</sup>	ee (%) <sup>b</sup>
1	1,4-dioxane	AgOTf	23	88	87
2	1,4-dioxane	AgAsF <sub>6</sub>	46	20	87
3	acetone	AgOTf	21	83	90
4	acetone	AgSbF <sub>6</sub>	18	84	88
5	MeOH	AgOTf	20	93	90
6	MeOH	AgBF <sub>4</sub>	20	95	89
7	<i>t</i> -BuOH	AgOTf	43	94	90
8	toluene	AgOTf	24	20 <sup>c</sup>	~ <sup>d</sup>
9	CH <sub>3</sub> CN	AgOTf	24	7 <sup>c</sup>	~ <sup>d</sup>
10	Cl <sub>2</sub> CHCHCl <sub>2</sub>	AgOTf	19	47	< 5
11	DCE	AgOTf	45	79	81
12	THF	AgOTf	23	92	89
13	CH <sub>2</sub> Cl <sub>2</sub>	AgOTf	43	82	83
14	DMF	AgBF <sub>4</sub>	24	< 1 <sup>c</sup>	~ <sup>d</sup>

<sup>a</sup>Isolated product ≥ 95 % purity. <sup>b</sup>ee was determined by HPLC using Chiral Pak AD-H column. <sup>c</sup>As determined by GC analysis of the crude reaction mixture. <sup>d</sup>ee was not determined.

**Table S3.** X-ray crystal data and refinement for *cis*-S22.

empirical formula	C <sub>15</sub> H <sub>19</sub> N
fw	213.31
Temp (K)	98(2)
Wavelength	0.71073 Å
crystal size, mm	0.40 x 0.17 x 0.14
crystal system	monoclinic
color and habit	colorless needle
space group	<i>P</i> 2 <sub>1</sub> /n
<i>a</i> , Å	13.6855(5)
<i>b</i> , Å	28.583(1)
<i>c</i> , Å	14.6784(5)
<i>V</i> , Å <sup>3</sup>	1174.9(5)
<i>Z</i>	4
scan mode	$\omega$
2 $\theta$ limits (deg)	3.62 $\leq$ 2 $\theta$ $\leq$ 31.81
<i>D</i> <sub>c</sub> (g cm <sup>-3</sup> )	1.206
abs. coeff. (mm <sup>-1</sup> )	0.069
reflections	12477
unique reflections	3730
data with <i>I</i> > 2.5 $\sigma$ ( <i>I</i> )	2818
<i>F</i> (000)	464
<i>R</i> ( <i>F</i> )	0.0623
<i>R</i> <sub>w</sub> ( <i>F</i> )	0.1279
GoF	0.979
no. param	221
max $\Delta/\sigma$	0.18
largest res. density (e/Å <sup>3</sup> )	0.457

**Table S4.** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for *cis*-**S22**.  $U_{(\text{eq})}$  is defined as one third of the trace of the orthogonalized  $U^{\text{ij}}$  tensor.

	x	y	z	U(eq)
N(1)	2494(1)	5261(1)	-60(1)	20(1)
C(12)	881(1)	7809(1)	796(1)	20(1)
C(6)	2264(1)	5682(1)	-1113(1)	19(1)
C(5)	1634(1)	6701(1)	-996(1)	18(1)
C(7)	2018(1)	5987(1)	715(1)	19(1)
C(13)	3013(2)	4208(1)	178(1)	25(1)
C(9)	1993(1)	5788(1)	1942(1)	21(1)
C(11)	1282(1)	7678(1)	2056(1)	21(1)
C(1)	2547(1)	5249(1)	-2158(1)	23(1)
C(10)	861(1)	6610(1)	2487(1)	22(1)
C(8)	1520(1)	6881(1)	183(1)	18(1)
C(3)	1448(1)	6829(1)	-3006(1)	25(1)
C(4)	1215(1)	7268(1)	-1971(1)	22(1)
C(15)	1663(2)	8819(1)	401(1)	28(1)
C(14)	1065(2)	6548(1)	3759(1)	28(1)
C(2)	2121(1)	5834(1)	-3099(1)	25(1)

**Table S5.** Bond lengths [Å] and angles [°] for *cis*-**S22**.

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N(1)-C(6)	1.3743(12)		
N(1)-C(7)	1.3829(12)		
N(1)-C(13)	1.4489(13)		
C(12)-C(8)	1.5041(13)		
C(12)-C(15)	1.5252(15)		
C(12)-C(11)	1.5288(15)		
C(6)-C(1)	1.3956(14)		
C(6)-C(5)	1.4176(14)		
C(5)-C(4)	1.4008(14)		
C(5)-C(8)	1.4341(14)		
C(7)-C(8)	1.3687(14)		
C(7)-C(9)	1.4887(14)		
C(9)-C(10)	1.5361(15)		
C(11)-C(10)	1.5210(15)		
C(1)-C(2)	1.3821(15)		
C(10)-C(14)	1.5215(15)		
C(3)-C(4)	1.3811(15)		
C(3)-C(2)	1.3966(16)		
<hr/>			
C(6)-N(1)-C(7)	108.40(8)	C(6)-N(1)-C(13)	125.20(9)
C(7)-N(1)-C(13)	126.23(9)	C(8)-C(12)-C(15)	113.60(9)
C(8)-C(12)-C(11)	109.70(8)	C(15)-C(12)-C(11)	109.87(8)
N(1)-C(6)-C(1)	129.72(10)	N(1)-C(6)-C(5)	108.01(8)
C(1)-C(6)-C(5)	122.27(9)	C(4)-C(5)-C(6)	118.18(9)
C(4)-C(5)-C(8)	135.06(9)	C(6)-C(5)-C(8)	106.71(8)
C(8)-C(7)-N(1)	110.13(9)	C(8)-C(7)-C(9)	125.93(9)
N(1)-C(7)-C(9)	123.89(9)	C(7)-C(9)-C(10)	109.42(8)
C(10)-C(11)-C(12)	113.60(8)	C(2)-C(1)-C(6)	117.67(10)
C(11)-C(10)-C(9)	111.97(9)	C(11)-C(10)-C(9)	111.12(8)
C(14)-C(10)-C(9)	110.90(9)	C(7)-C(8)-C(5)	106.72(8)
C(7)-C(8)-C(12)	122.93(9)	C(5)-C(8)-C(12)	130.23(9)
C(4)-C(3)-C(2)	121.17(10)	C(3)-C(4)-C(5)	119.55(10)
C(1)-C(2)-C(3)	121.09(10)		

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**Table S6.** Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for *cis*-**S22**. The anisotropic displacement factor exponent takes the form:  $-2\pi^2 [h^2 a^{*2} U^{11} + 2hk a^* b^* U^{12}]$ .

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{23}$	$U^{13}$	$U^{12}$
N(1)	22(1)	17(1)	20(1)	0(1)	1(1)	1(1)
C(12)	21(1)	19(1)	20(1)	-1(1)	1(1)	1(1)
C(6)	16(1)	19(1)	21(1)	0(1)	1(1)	-3(1)
C(5)	15(1)	19(1)	20(1)	0(1)	1(1)	-2(1)
C(7)	17(1)	19(1)	19(1)	-1(1)	0(1)	-1(1)
C(13)	27(1)	18(1)	29(1)	1(1)	-1(1)	2(1)
C(9)	23(1)	21(1)	20(1)	2(1)	-1(1)	0(1)
C(11)	22(1)	22(1)	20(1)	-3(1)	0(1)	0(1)
C(1)	20(1)	22(1)	26(1)	-4(1)	4(1)	-4(1)
C(10)	22(1)	25(1)	19(1)	0(1)	1(1)	-1(1)
C(8)	17(1)	18(1)	19(1)	0(1)	1(1)	-1(1)
C(3)	24(1)	30(1)	20(1)	3(1)	1(1)	-5(1)
C(4)	20(1)	23(1)	22(1)	3(1)	1(1)	-2(1)
C(15)	37(1)	18(1)	30(1)	-1(1)	5(1)	0(1)
C(14)	34(1)	33(1)	19(1)	1(1)	1(1)	-1(1)
C(2)	25(1)	30(1)	21(1)	-5(1)	4(1)	-7(1)

**Table S7.** Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters for *cis*-**S22**.

	x	y	z	U(eq)
H(1)	3005(17)	4565(11)	-2215(10)	28(3)
H(4)	765(16)	7988(10)	-1929(10)	26(3)
H(9B)	1523(18)	5093(11)	2117(11)	35(4)
H(2)	2292(17)	5545(11)	-3829(11)	35(4)
H(11A)	2547(17)	7818(9)	2222(10)	23(3)
H(3)	1147(16)	7227(10)	-3676(10)	26(3)
H(9A)	3226(17)	5805(10)	2304(10)	26(3)
H(12)	-437(16)	7844(9)	646(10)	21(3)
H(15B)	2980(20)	8826(11)	542(13)	44(4)
H(15C)	1224(18)	9405(11)	823(11)	32(3)
H(14A)	822(18)	5841(11)	4041(11)	31(3)
H(11B)	562(17)	8192(10)	2469(10)	24(3)
H(15A)	1360(20)	8978(11)	-410(13)	44(4)
H(10)	-431(16)	6472(9)	2226(10)	22(3)
H(14B)	2290(20)	6709(11)	4050(11)	37(4)
H(13B)	2150(20)	3732(13)	-81(14)	60(5)
H(14C)	207(19)	7056(12)	4108(12)	40(4)
H(13C)	3410(30)	4133(15)	939(17)	76(6)
H(13A)	3930(30)	3979(13)	-340(15)	68(5)

## References

- S1) Liu, C.; Han, X.; Wang, X.; Widenhoefer, R. A., *J. Am. Chem. Soc.* 2004, 126, 3700.
- S2) Strukul, G.; Varagnolo, A.; Pinna, F., *J Mol. Catal. A-Chem.* **1997**, 117, 413.
- S3) Beckwith, A. L.J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, 53, 1632.
- S4) Hlasta, K. J.; Luttinger, D.; Perrone, M. H.; Silibernagle, M. J.; Ward, S. J.; Saubricht, D. R. *J. Med. Chem.* **1987**, 30, 1555.
- S5) Fernandez-Garcia, C.; Marco, J. L.; Fernandez-Alvarez, E. *Eur. J. Med. Chem.* **1992**, 27, 909.
- S6) Smith, A. B. L.; Visnick, M.; Hasletine, J. N.; Sprengeler, P. A. *Tetrahedron* **1986**, 42, 2957.