Supporting Information

A Formal Synthesis of SCH 351448

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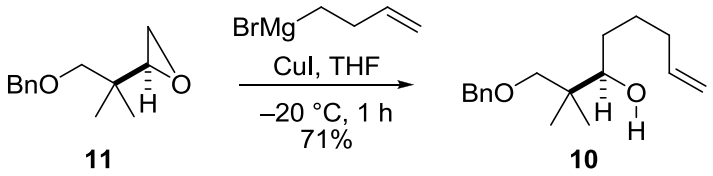
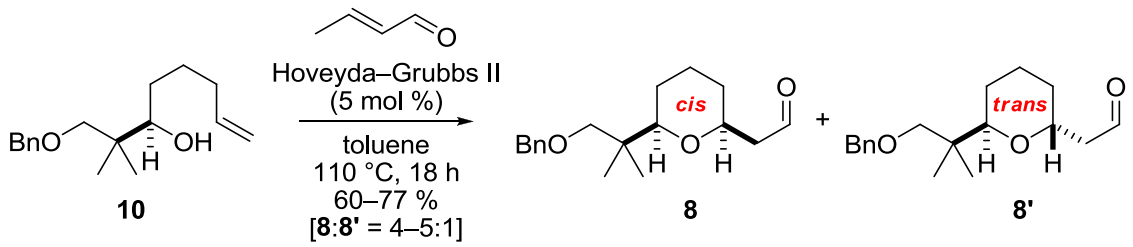


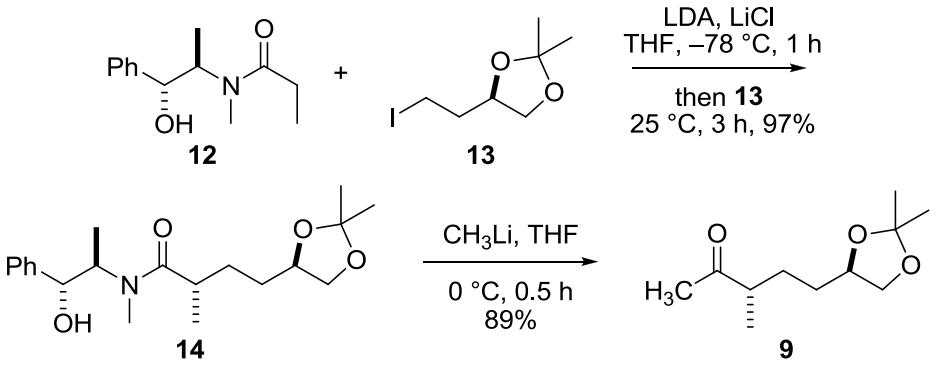
To a cooled (–78 °C) solution of 3-butenylmagnesium bromide (163 mg, 3.636 mmol) in THF (10 mL) were added CuI (93 mg, 0.485 mmol) and epoxide **11** (500 mg, 2.424 mmol) in THF (5 mL). After stirred for 1 h at –20 °C, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/20) to afford hydroxy alkene **10** (450 mg, 71%): $[\alpha]^{25}_{D}$= +29.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.37 (m, 5H), 5.83 (dddd, *J* = 17.0, 10.0, 6.5, 6.5 Hz, 1H), 5.02 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.95 (dd, *J* = 10.5, 1.0 Hz, 1H), 4.51 (d, *J* = 4.0 Hz, 2H), 3.42–3.45 (m, 1H), 3.40 (d, *J* = 8.5 Hz, 1H), 3.29 (d, *J* = 9.0 Hz, 1H), 3.20 (d, *J* = 4.0 Hz, 1H), 2.04–2.14 (m, 2H), 1.69–1.79 (m, 1H), 1.38–1.50 (m, 2H), 1.26–1.34 (m, 1H), 0.92 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 137.9, 128.5, 127.76, 127.56, 114.4, 80.0, 78.5, 73.6, 38.4, 33.9, 31.1, 26.0, 22.9, 19.8; IR (neat) 3500, 1098, 910, 738, 698 cm^{-1}; HRMS (ESI) *m/z* 263.2004 [$(M+H)^+$, $C_{17}H_{26}O_2$ requires 263.2006].

Preparation of 2,6-*cis*-Tetrahydropyran 8 by Tandem CM/Oxa-Michael Reaction



To a solution of hydroxy alkene **10** (50–200 mg, 0.191–0.762 mmol) in toluene (3–10 mL) were added (*E*)-crotonaldehyde (0.08–0.32 mL, 0.955–3.811 mmol) and Hoveyda–Grubbs II catalyst (5 mol %) at 25 °C. After refluxed for 18 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/40 to 1/20) to afford 2,6-*cis*-tetrahydropyran **8** (29–113 mg, 49–51%) and 2,6-*trans*-tetrahydropyran **8′** (6–29 mg, 10–13%): **[For 2,6-*cis*-tetrahydropyran 8]** $[\alpha]^{25}_{D}$= –9.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 (dd, *J* = 3.0, 2.0 Hz, 1H), 7.25–7.38 (m, 5H), 4.48 (s, 2H), 3.79–3.85 (m, 1H), 3.33 (dd, *J* = 11.0, 1.5 Hz, 1H), 3.32 (d, *J* = 8.5 Hz, 1H), 3.15 (d, *J* = 8.5 Hz, 1H), 2.46 (ddd, *J* = 16.0, 8.0, 3.0 Hz, 1H), 2.39 (ddd, *J* = 16.0, 4.5, 2.0 Hz, 1H), 1.85–1.91 (m, 1H), 1.48–1.60 (m, 3H), 1.17–1.31 (m, 2H), 0.89 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 139.1, 128.3, 127.41, 127.37, 81.4, 76.9, 73.5, 73.2, 50.0, 38.5, 31.5, 24.6, 23.8, 21.5, 20.3; IR (neat) 1725, 1090, 1048, 734 cm^{-1}; HRMS (ESI) *m/z* 291.1954 [$(M+H)^+$, $C_{18}H_{26}O_3$ requires 291.1955]. **[For 2,6-*trans*-tetrahydropyran 8′]** $[\alpha]^{25}_{D}$= –33.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (dd, *J* = 2.5, 2.0 Hz, 1H), 7.27–7.40 (m, 5H), 4.59–4.63 (m, 1H), 4.53 (d, *J* = 12.5 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 3.53 (dd, *J* = 11.5, 2.0 Hz, 1H), 3.29 (d, *J* = 8.5 Hz, 1H), 3.14 (d, *J* = 9.0 Hz, 1H), 3.06 (ddd, *J* = 16.0, 10.0, 3.0 Hz, 1H), 2.37 (ddd, *J* = 16.0, 10.5, 2.0 Hz, 1H), 1.78–1.86 (m, 1H), 1.70–1.76 (m, 1H), 1.55–1.66 (m, 2H), 1.42–1.46 (m, 1H), 1.34 (ddd, *J* = 24.5, 12.5, 4.0 Hz, 1H), 0.90 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 139.0, 128.2, 127.43, 127.34, 76.7, 73.1, 72.8, 68.5, 44.4, 38.3, 28.3, 24.9, 21.5, 20.1, 18.8.

Preparation of Methyl Ketone 9 by Myers' Asymmetric Alkylation

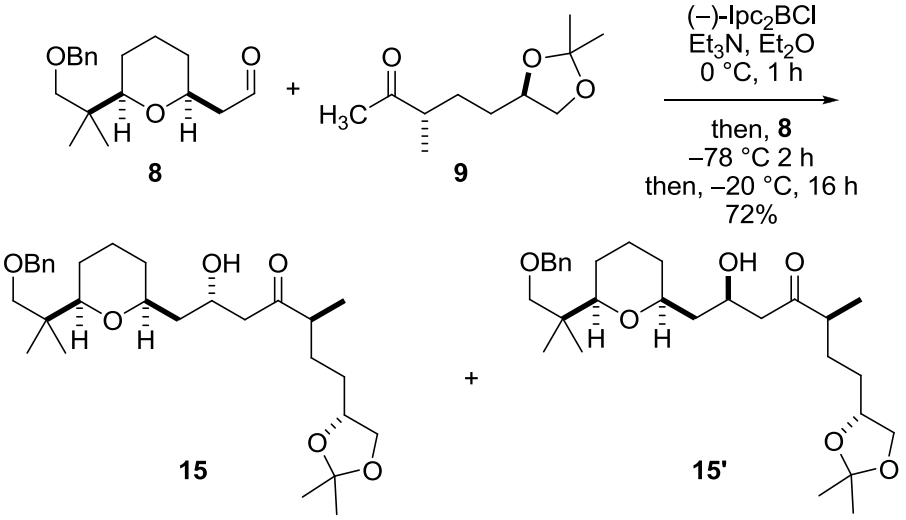


To a cooled (–78 °C) suspension of lithium chloride (153 mg, 3.616 mmol) in THF (2 mL) were added LDA (1.0 M, 1.4 mL, 1.4 mmol) and amide **12** (100 mg, 0.452 mmol) in THF (5 mL). The reaction mixture was stirred at –78 °C for 1 h, at 0 °C for 15 min, at 25 °C for 5 min and then, cooled to 0 °C, and iodide **13** (310 mg, 1.356 mmol) was added. After stirred for 3 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/1 to 2/1) to afford amide **14** (153 mg, 97 %): $[\alpha]^{25}_{D}$= –69.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (2:1 rotamer ratio, * denotes minor rotamer peaks, 500 MHz, C_6H_6) δ 7.05–7.35 (m, 5H), 5.12 (br, 1H), 4.56 (dd, *J* = 6.0 Hz, 1H), 4.38–4.45 (m, 1H), 4.34–4.40* (m, 1H), 4.27* (s, 1H), 4.07–4.13* (m, 1H), 3.90–3.96* (m, 1H), 3.87* (dd, *J* = 7.0 Hz, 1H), 3.78–3.83 (m, 1H), 3.76 (dd, *J* = 7.0 Hz, 1H), 3.42* (dd, *J* = 7.0 Hz, 1H), 3.32 (dd, *J* = 7.0 Hz, 1H), 2.82–2.89 (m, 1H), 2.84* (s, 3H), 2.35 (s, 3H), 2.23–2.28 (m, 1H), 2.04–2.11* (m, 1H), 1.62–1.85 (m, 1H), 1.02–1.53 (m, 2H), 1.42* (s, 3H), 1.39 (s, 3H), 1.34* (s, 3H), 1.29 (s, 3H), 0.99* (d, *J* = 6.5 Hz, 3H), 0.96* (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.71 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (2:1 rotamer ratio, * denotes minor rotamer peaks, 125 MHz, C_6H_6) δ 177.2, 176.5*, 143.3, 142.9*, 128.3*, 128.0, 127.0, 126.5, 108.4, 76.0*, 75.74, 75.65, 74.9*,

69.4*, 69.2, 57.8, 36.1, 35.3*, 31.14, 31.11*, 30.0*, 29.7, 26.97, 26.94, 25.77*, 25.60, 18.1*, 17.1, 15.3*, 14.0 ; IR (neat) 3389, 1615, 1214, 1050, 701 cm^{-1}; HRMS (ESI) *m/z* 350.2326 [$(M+H)^+$, $C_{20}H_{31}NO_4$ requires 350.2326].

To a cooled (–78 °C) solution of **14** (80 mg, 0.229 mmol) in THF (5 mL) was added methyllithium in diethyl ether (1.6 M, 0.72 mL, 1.145 mmol). The resulting mixture was warmed to 0 °C and stirred for 15 min at 0 °C. Excess methyllithium was scavenged by the addition of diisopropylamine (0.13 mL, 0.916 mmol) at 0 °C. The reaction mixture was quenched by addition of acetic acid in diethyl ether (10% v/v, 2 mL). After stirred for 15 min at 25 °C, the reaction mixture was neutralized with addition of saturated aqueous $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/10) to afford methyl ketone **9** (41 mg, 89 %): $[\alpha]^{25}_D$= –6.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90–3.97 (m, 2H), 3.39 (t, *J* = 7.0 Hz, 1H), 2.41–2.46 (m, 1H), 2.03 (s, 3H), 1.65–1.73 (m, 1H), 1.35–1.47 (m, 2H), 1.28 (s, 3H), 1.22–1.28 (m, 1H), 1.22 (s, 3H), 1.00 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.1, 108.7, 75.7, 69.2, 45.8, 31.1, 28.6, 27.9, 26.9, 25.6, 16.2; IR (neat) 1713, 1057, 668 cm^{-1}; HRMS (ESI) *m/z* 223.1305 [$(M+Na)^+$, $C_{11}H_{20}O_3$ requires 223.1305].

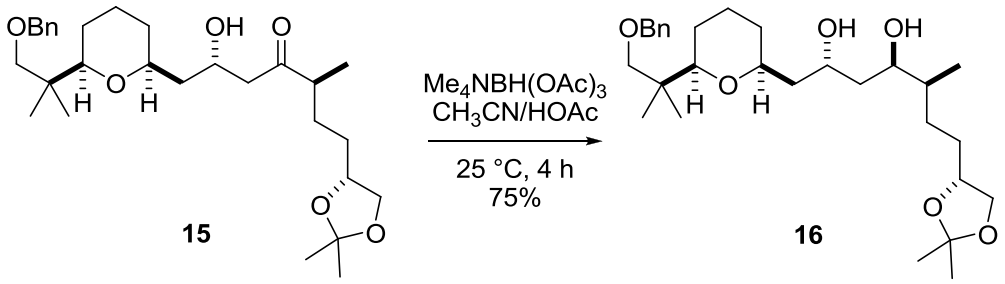
Preparation of *β*-Hydroxy Ketone 15



A flask charged with (–)-Ipc_2BCl (2.9 g, 9.09 mmol) was further dried under high vacuum for 2 h to remove traces of HCl. To a cooled (0 °C) solution of dried (–)-Ipc_2Cl in Et_2O (40 mL) were added methyl ketone **9** (910 mg, 4.54 mmol) in Et_2O (20 mL) and triethylamine (1.9 mL, 13.63 mmol), and the resulting white suspension was stirred for 1 h at 0 °C. The mixture was cooled to –78 °C, and aldehyde **8** (1.8 g, 6.19 mmol) in Et_2O (30 mL) was added slowly. The reaction mixture was stirred for 2 h at –78 °C and for additional 2 h at –20 °C. The reaction mixture was kept in –20°C refrigerator for 14 h. The resulting mixture was stirred at 0 °C and pH 7 Phosphate buffer solution (8 mL), MeOH (2 mL), and 50% H_2O_2 (5 mL) were added to the reaction mixture at 0 °C, and the resulting mixture was stirred for 1 h at 25 °C. The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to afford an inseparable 9:1 mixture of **15** and **15′** (1.6 g, 72%): **[For 15]** $[\alpha]^{25}_{D}$= –0.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.38 (m, 5H), 4.48 (AB, Δυ = 32.5 Hz, J_{AB} = 12.5 Hz, 2H), 4.26–4.31 (m, 1H), 3.98–4.07 (m, 3H), 3.57–3.62 (m, 1H), 3.50 (dd, *J* = 7.0, 6.5 Hz, 1H), 3.35 (d, *J* = 5.5 Hz, 1H), 3.25 (d, *J* = 9.0 Hz, 1H), 3.18 (d, *J* = 9.0 Hz,

1H), 2.71 (dd, J = 16.5, 6.5 Hz, 1H), 2.56 (dd, J = 7.0 Hz, 1H), 2.50 (dd, J = 16.5, 5.0 Hz, 1H), 1.76–1.86 (m, 2H), 1.44–1.65 (m, 7H), 1.40 (s, 3H), 1.34 (s, 3H), 1.19–1.33 (m, 3H), 1.09 (d, J = 7.0 Hz, 3H), 0.92 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.5, 138.9, 128.3, 127.42, 127.36, 108.8, 82.1, 78.8, 77.2, 75.8, 73.2, 69.3, 67.9, 48.1, 46.6, 42.7, 38.3, 32.1, 31.1, 28.4, 26.9, 25.7, 24.9, 23.6, 21.6, 21.0, 16.2; IR (neat) 3478, 1709, 1368, 1046, 735 cm^{-1}; HRMS (ESI) m/z 513.3189 [$(M+Na)^+$, $C_{29}H_{46}O_6$ requires 513.3187].

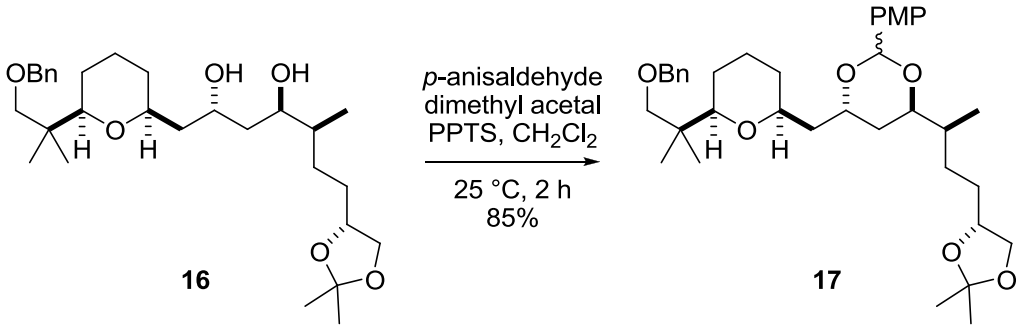
Preparation of 1,3-*anti*-Diol 16



To a cooled (–20 °C) solution of $Me_4NBH(OAc)_3$ (3.7 g, 14.265 mmol) in CH_3CN/HOAc (1:1, 70 mL) was added **15** (1.4 g, 2.853 mmol) in CH_3CN (5 mL). After stirred for 4 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/7 to 1/2) to afford 1,3-*anti*-diol **16** (1.05 g, 75%): $[\alpha]^{25}_D$= –4.3 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.38 (m, 5H), 4.48 (AB, Δυ = 31.0 Hz, J_{AB} = 12.5 Hz, 2H), 4.40 (s, 1H), 4.15–4.19 (m, 1H), 4.01–4.09 (m, 2H), 3.71–3.74 (m, 1H), 3.60 (dd, J = 10.5 Hz, 1H), 3.50 (dd, J = 7.0 Hz, 1H), 3.37–3.39 (m, 2H), 3.23 (d, J = 9.5 Hz, 1H), 3.17 (d, J = 9.0 Hz, 1H), 1.73–1.86 (m, 2H), 1.44–1.68 (m, 10H), 1.40 (s, 3H), 1.34 (s, 3H), 1.19–1.33 (m, 2H), 1.05–1.13 (m, 1H), 0.91 (s, 3H), 0.87 (d, J = 6.0 Hz, 3H), 0.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 128.3, 127.52, 127.48, 108.6, 82.3, 80.14, 77.3,

76.5, 73.2, 72.3, 70.8, 69.6, 42.4, 38.95, 38.81, 38.34, 32.4, 31.2, 28.3, 27.0, 25.8, 24.9, 23.6, 21.8, 21.1, 15.2; IR (neat) 3445, 1368, 1046, 735 cm^{-1}; HRMS (ESI) *m/z* 493.2523 [$(M+H)^+$, $C_{29}H_{48}O_6$ requires 493.2524].

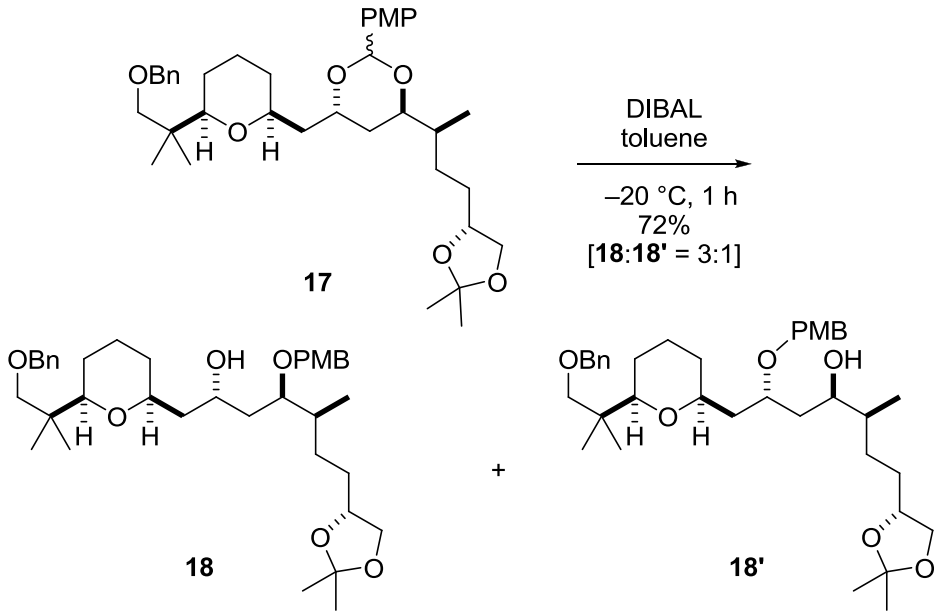
Preparation of Acetal 17



To a cooled (0 °C) solution of 1,3-*anti*-diol **16** (1.0 g, 2.029 mmol) in CH_2Cl_2 (100 mL) were added *p*-anisaldehyde dimethyl acetal (1.1 g, 6.089 mmol) and PPTS (102 mg, 0.406 mmol). After stirred for 2 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/ hexanes, 1/10) to afford 3:2 mixture of acetal **17** (1.05 g, 85%): $[\alpha]^{25}_D$= –4.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 3:2 mixture, * denotes minor peaks) δ 7.42* (d, *J* = 9.0 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.26–7.35 (m, 5H), 6.88* (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 5.72 (s, 1H), 5.67* (s, 1H), 4.45–4.53 (m, 2H), 4.16–4.42* (m, 1H), 4.01–4.09 (m, 2H), 3.79 (s, 3H), 3.72–3.76 (m, 1H), 3.45–3.52* (m, 1H), 3.33–3.40 (m, 1H), 3.36 (d, *J* = 9.0 Hz, 1H), 3.26–3.30* (m, 2H), 3.25 (d, *J* = 9.0 Hz, 1H), 3.20* (d, *J* = 11.5 Hz, 1H), 3.16 (d, *J* = 9.0 Hz, 1H), 2.30–2.38* (m, 1H), 2.10–2.16 (m, 1H), 1.77–1.98 (m, 4H), 1.45–1.71 (m, 7H), 1.42 (s, 3H), 1.41* (s, 3H), 1.37 (s,

3H), 1.36* (s, 3H), 1.10–1.30 (m, 3H), 0.96* (s, 3H), 0.90–0.91 (m, 9H); IR (neat) 1516, 1246, 1048, 669 cm^{-1}; HRMS (ESI) *m/z* 633.3754 [$(M+Na)^+$, $C_{37}H_{54}O_7$ requires 633.3762].

Preparation of Alcohol 18

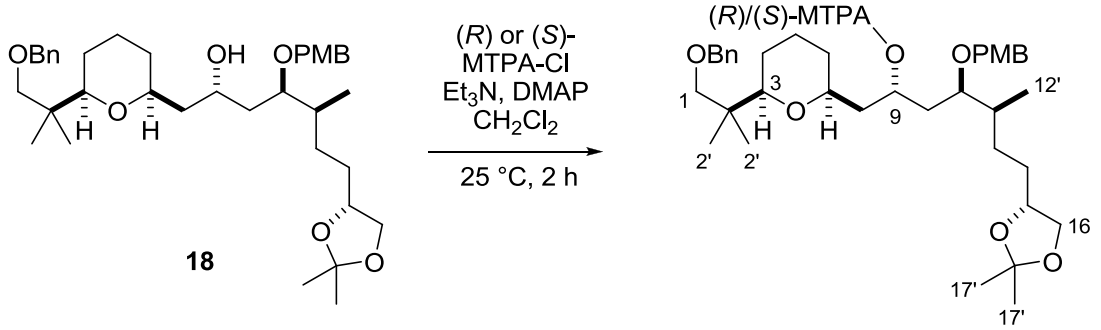


To a cooled (–20 °C) solution of acetal **17** (50 mg, 0.081 mmol) in toluene (2 mL) was added diisobutylaluminum hydride (1.0 M, 0.4 mL, 0.405 mmol). After stirred for 1 h at the same temperature, the reaction mixture was quenched with addition of saturated aqueous potassium sodium tartate solution and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/10) to afford **18** (27 mg, 54%) and **18′** (9 mg, 18%): **[For 18]** $[\alpha]^{25}_{D}$= +8.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.37 (m, 5H), 7.24 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.44 (d, *J* = 12.5 Hz, 1H), 4.00–4.11 (m, 4H), 3.77 (s, 3H), 3.64 (ddd, *J* = 5.5, 5.0, 5.0 Hz, 1H), 3.58 (dd, *J* = 10.5, 10.0 Hz, 1H), 3.49 (dd, *J* = 7.0 Hz, 1H), 3.39 (d, *J* = 11.0 Hz, 1H),

3.29 (d, J = 9.0 Hz, 1H), 3.21 (d, J = 8.5 Hz, 1H), 1.79–1.86 (m, 2H), 1.45–1.66 (m, 10H), 1.41 (s, 3H), 1.35 (s, 3H), 1.18–1.32 (m, 2H), 1.04–1.13 (m, 1H), 0.95 (s, 3H), 0.87 (d, J = 5.5 Hz, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 138.9, 131.3, 129.4, 128.3, 127.48, 127.42, 113.8, 108.6, 82.1, 79.8, 79.3, 77.3, 76.3, 73.3, 72.0, 69.5, 68.8, 55.3, 43.9, 38.45, 38.38, 35.8, 32.4, 31.7, 29.0, 27.0, 25.8, 24.9, 23.7, 21.6, 21.1, 14.3; IR (neat) 3501, 1516, 1250 cm^{-1}; HRMS (ESI) *m/z* 635.3910 [$(M+Na)^+$, $C_{37}H_{56}O_7$ requires 635.3918].

[For 18′] $[\alpha]^{25}_{D}$= +3.6 (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 5H), 7.25 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 4.50 (d, J = 11.5 Hz, 1H), 4.47 (d, J = 10.0 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 4.40 (d, J = 11.0 Hz, 1H), 4.01–4.07 (m, 2H), 3.88–3.94 (m, 1H), 3.78 (s, 3H), 3.61–3.66 (m, 1H), 3.48 (dd, J = 7.0, 6.0 Hz, 1H), 3.28 (d, J = 8.5 Hz, 1H), 3.24–3.30 (m, 1H), 3.18 (d, J = 11.5 Hz, 1H), 3.16 (d, J = 8.5 Hz, 1H), 3.05 (s, 1H), 1.92–1.99 (m, 1H), 1.81–1.87 (m, 1H), 1.68–1.74 (m, 1H), 1.45–1.64 (m, 9H), 1.40 (s, 3H), 1.35 (s, 3H), 1.15–1.32 (m, 2H), 1.02–1.09 (m, 1H), 0.90 (s, 3H), 0.88 (s, 3H) 0.82 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 139.2, 130.5, 129.6, 128.3, 127.42, 127.36, 113.9, 108.7, 81.6, 77.2, 76.6, 74.7, 73.9, 73.3, 72.2, 70.4, 69.6, 55.4, 39.6, 38.91, 38.68, 35.6, 32.3, 31.2, 28.3, 27.1, 25.9, 25.0, 24.0, 21.6, 20.7, 15.4.

Determination of Absolute Stereochemistry of C9



[(*R*)-MTPA ester of 18] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.56 (m, 2H), 7.34–7.39 (m, 3H), 7.22–7.33 (m, 7H), 6.86 (d, J = 9.0 Hz, 2H), 5.55–5.61 (m, 1H), 4.42 (d, J = 12.5 Hz, 1H), 4.37

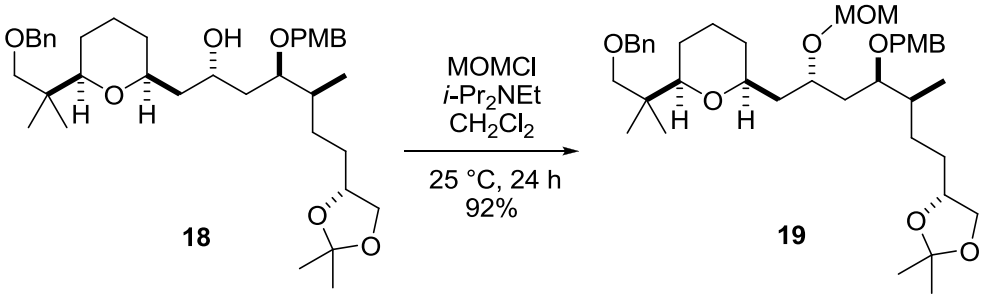
(d, J = 11.0 Hz, 1H), 4.32 (d, J = 12.5 Hz, 1H), 4.20 (d, J = 10.5 Hz, 1H), 3.92–3.99 (m, 2H), 3.78 (s, 3H), 3.55 (s, 3H), 3.40–3.45 (m, 1H), 3.26–3.33 (m, 1H), 3.24 (d, J = 9.0 Hz, 1H), 3.14 (d, J = 11.0 Hz, 1H), 3.11 (d, J = 8.5 Hz, 1H), 3.09–3.13 (m, 1H), 1.91–1.98 (m, 1H), 1.74–1.85 (m, 2H), 1.65–1.72 (m, 2H), 1.58–1.63 (m, 1H), 1.42–1.52 (m, 5H), 1.40 (s, 3H), 1.35 (s, 3H), 1.08–1.24 (m, 3H), 0.92–1.01 (m, 1H), 0.89 (s, 3H), 0.83 (s, 3H), 0.79 (d, J = 6.5 Hz, 3H).

[(*S*)-MTPA ester of 18] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.55 (m, 2H), 7.34–7.39 (m, 3H), 7.22–7.33 (m, 7H), 6.86 (d, J = 8.5 Hz, 2H), 5.50–5.58 (m, 1H), 4.43 (d, J = 13.0 Hz, 1H), 4.32 (d, J = 10.5 Hz, 1H), 4.35 (d, J = 12.5 Hz, 1H), 4.25 (d, J = 10.5 Hz, 1H), 3.97–4.01 (m, 2H), 3.78 (s, 3H), 3.49 (s, 3H), 3.42–3.47 (m, 1H), 3.17–3.27 (m, 2H), 3.24 (d, J = 9.0 Hz, 1H), 3.12 (d, J = 8.5 Hz, 1H), 3.09 (d, J = 11.5 Hz, 1H), 1.62–1.89 (m, 6H), 1.29–1.55 (m, 5H), 1.40 (s, 3H), 1.36 (s, 3H), 1.00–1.24 (m, 4H), 0.89 (s, 3H), 0.84 (d, J = 6.5 Hz, 3H), 0.83 (s, 3H).

Chemical shift of (*R*) and (*S*)-MTPA ester of 18

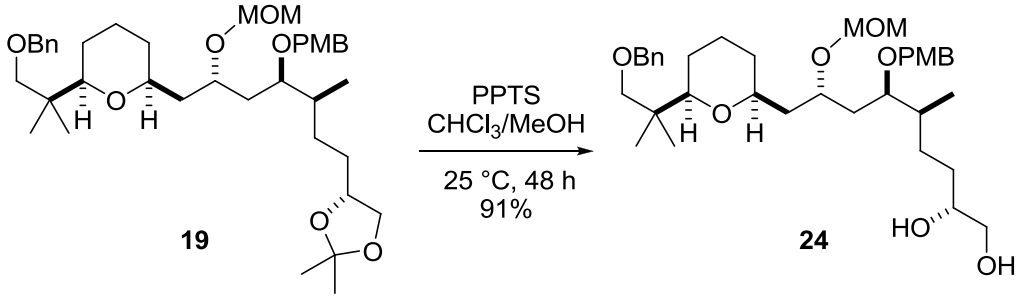
	H-1A	H-2′	H-2′	H-3	H-16A	H-16B	H-17′	H-17′	H-12′
(*S*)–MTPA ester	3.237	0.888	0.828	3.092	3.448	3.991	1.403	1.355	0.845
(*R*)–MTPA ester	3.244	0.892	0.829	3.140	3.429	3.965	1.401	1.353	0.795
δ_S–δ_R (ppm)	–0.007	–0.004	–0.001	–0.048	+0.019	+0.026	+0.002	+0.002	+0.050

Preparation of 19



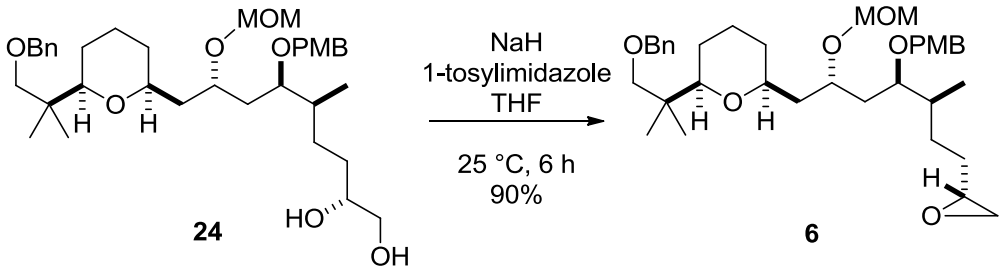
To a solution of alcohol **18** (300 mg, 0.489 mmol) in CH_2Cl_2 (15 mL) were added *N*,*N*-diisopropylethylamine (1.7 mL, 9.790 mmol) and chloromethyl methyl ether (0.37 mL, 4.895 mmol) at 25 °C. After stirred for 24 h at the same temperature, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to afford **19** (299 mg, 92%): $[\alpha]^{25}_{D}$= +11.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.36 (m, 7H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.67 (d, *J* = 7.0 Hz, 1H), 4.57 (d, *J* = 6.5 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 12.5 Hz, 1H), 4.38 (d, *J* = 11.0 Hz, 1H), 4.03–4.09 (m, 2H), 3.96–4.01 (m, 1H), 3.80 (s, 3H), 3.57–3.60 (m, 1H), 3.51 (dd, *J* = 5.5 Hz, 1H), 3.39 (s, 3H), 3.36–3.42 (m, 1H), 3.29 (d, *J* = 8.5 Hz, 1H), 3.21 (d, *J* = 9.0 Hz, 1H), 3.20 (d, *J* = 10.5 Hz, 1H), 1.82–1.96 (m, 3H), 1.45–1.69 (m, 8H), 1.44 (s, 3H), 1.38 (s, 3H), 1.08–1.30 (m, 4H), 0.95 (s, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 139.3, 131.4, 129.3, 128.2, 127.33, 127.26, 113.7, 108.7, 96.2, 81.7, 79.1, 77.2, 76.4, 74.5, 73.22, 73.18, 70.9, 69.6, 55.8, 55.3, 42.8, 38.6, 35.8, 34.9, 32.3, 31.9, 29.3, 27.1, 25.8, 25.0, 24.1, 21.45, 21.27, 13.9; IR (neat) 1514, 1246, 1034, 697 cm^{-1}; HRMS (ESI) *m/z* 679.4170 [$(M+Na)^+$, $C_{39}H_{60}O_8$ requires 679.4180].

Preparation of Diol 24



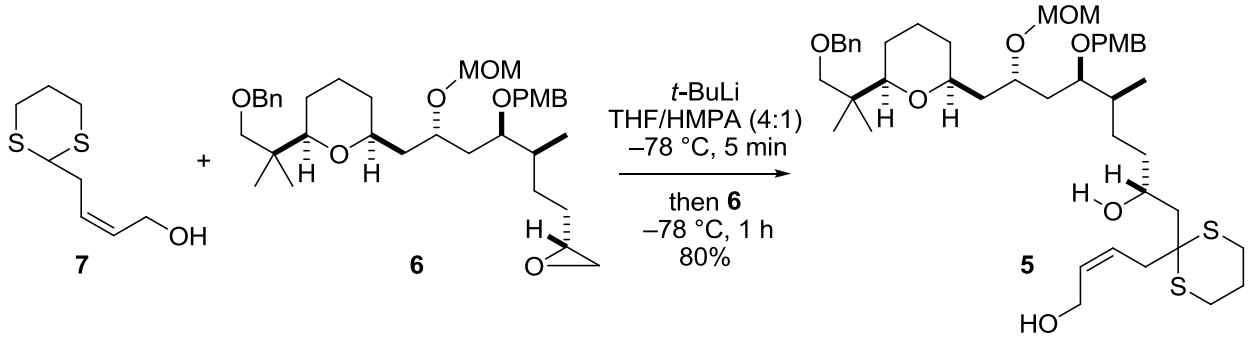
To a solution of **19** (295 mg, 0.449 mmol) in $CHCl_3$/MeOH (1:1, 14 mL) was added PPTS (113 mg, 0.449 mmol) at 25 °C. After stirred for 48 h at the same temperature, the reaction mixture was quenched with addition of saturated aqueous $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/3 to 2/1) to afford diol **24** (249 mg, 91%): $[\alpha]^{25}_{D}$= +15.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.36 (m, 7H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.66 (d, *J* = 6.5 Hz, 1H), 4.57 (d, *J* = 6.5 Hz, 1H), 4.52 (d, *J* = 10.5 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 12.5 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 3.95–4.05 (m, 1H), 3.80 (s, 3H), 3.63–3.68 (m, 2H), 3.57–3.61 (m, 1H), 3.35–3.45 (m, 2H), 3.39 (s, 3H), 3.29 (d, *J* = 9.0 Hz, 1H), 3.21 (d, *J* = 9.0 Hz, 1H), 3.20 (d, *J* = 10.5 Hz, 1H), 2.56 (br s, 1H), 2.41 (br s, 1H), 1.81–1.96 (m, 3H), 1.63–1.70 (m, 1H), 1.41–1.59 (m, 8H), 1.12–1.29 (m, 3H), 0.95 (s, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 139.3, 131.3, 129.3, 128.2, 127.34, 127.27, 113.7, 96.1, 81.7, 78.9, 77.2, 74.5, 73.31, 73.19, 72.6, 70.8, 66.8, 55.8, 55.3, 42.8, 38.6, 35.7, 34.9, 32.3, 31.4, 29.1, 25.0, 24.1, 21.43, 21.24, 14.1; IR (neat) 3418, 1456, 1250, 739 cm^{-1}; HRMS (ESI) *m/z* 639.3851 [$(M+Na)^+$, $C_{36}H_{56}O_8$ requires 639.3867].

Preparation of Epoxide 6



To a cooled (0 °C) solution of diol **24** (245 mg, 0.397 mmol) in THF (10 mL) was added NaH (60% dispersion in mineral oil, 48 mg, 1.192 mmol) and the resulting mixture was stirred for 20 min before 1-tosylimidazole (106.0 mg, 0.476 mmol) was added. After stirred for 6 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to afford epoxide **6** (214 mg, 90%): $[\alpha]^{25}_{D}$= +22.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.33 (m, 7H), 6.85 (d, *J* = 9.0 Hz, 2H), 4.65 (d, *J* = 6.5 Hz, 1H), 4.55 (d, *J* = 6.5 Hz, 1H), 4.51 (d, *J* = 11.0 Hz, 1H), 4.45 (d, *J* = 12.5 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 10.5 Hz, 1H), 3.93–3.99 (m, 1H), 3.78 (s, 3H), 3.54–3.59 (m, 1H), 3.33–3.40 (m, 1H), 3.37 (s, 3H), 3.27 (d, *J* = 8.5 Hz, 1H), 3.19 (d, *J* = 9.0 Hz, 1H), 3.18 (d, *J* = 13.0 Hz, 1H), 2.87–2.91 (m, 1H), 2.74 (dd, *J* = 4.5, 4.0 Hz, 1H), 2.46 (dd, *J* = 5.0, 3.0 Hz, 1H), 1.90–1.96 (m, 1H), 1.79–1.86 (m, 2H), 1.41–1.71 (m, 9H), 1.12–1.31 (m, 3H), 0.93 (s, 3H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 139.3, 131.4, 129.3, 128.2, 127.33, 127.25, 113.8, 96.2, 81.7, 79.1, 77.2, 74.5, 73.24, 73.17, 70.9, 55.8, 55.3, 52.6, 47.1, 42.8, 38.6, 35.8, 34.7, 32.3, 30.8, 29.4, 25.0, 24.1, 21.44, 21.25, 13.9; IR (neat) 1513, 1247, 1035, 668 cm^{-1}; HRMS (ESI) *m/z* 621.3753 [$(M+Na)^+$, $C_{36}H_{54}O_7$ requires 621.3762].

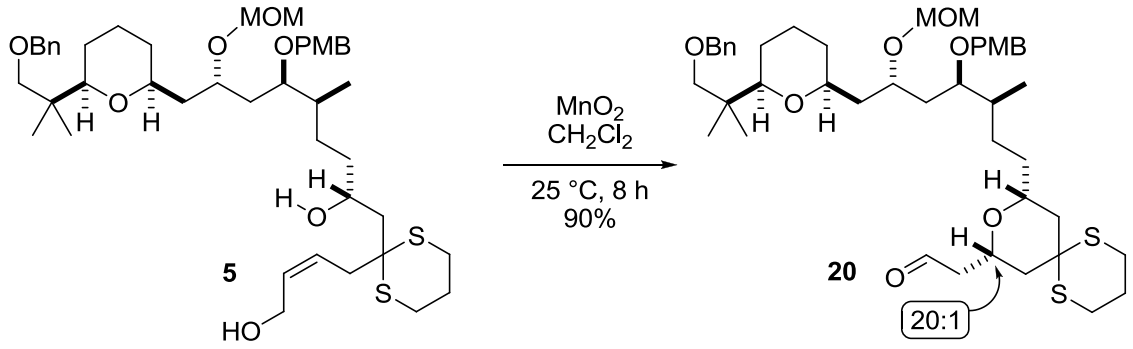
Preparation of Allyl Alcohol 5



To a cooled (–78 ºC) solution of **7** (405 mg, 2.138 mmol) in THF/HMPA (4:1, 12.5 mL) was added dropwise *t*-BuLi (2.5 mL, 1.7 M in pentane, 4.276 mmol) and the resulting mixture was stirred for 5 min before epoxide **6** (160 mg, 0.267 mmol) was added. After stirred for 1 h at –78 ºC, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/2) to afford allyl alcohol **5** (168 mg, 80%): $[\alpha]^{25}_{D}$= +7.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.35 (m, 7H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.81–5.86 (m, 1H), 5.69–5.74 (m, 1H), 4.66 (d, *J* = 7.0 Hz, 1H), 4.56 (d, *J* = 6.0 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.47 (d, *J* = 12.5 Hz, 1H), 4.39 (d, *J* = 10.0 Hz, 1H), 4.37 (d, *J* = 8.0 Hz, 1H), 4.24 (dd, *J* = 12.5, 6.5 Hz, 1H), 4.16 (dd, *J* = 12.5, 6.5 Hz, 1H), 3.94–4.05 (m, 2H), 3.79 (s, 3H), 3.56–3.60 (m, 1H), 3.38 (s, 3H), 3.34–3.42 (m, 1H), 3.28 (d, *J* = 8.5 Hz, 1H), 3.21 (d, *J* = 9.0 Hz, 1H), 3.19 (d, *J* = 9.0 Hz, 1H), 2.79–3.00 (m, 5H), 2.73 (dd, *J* = 15.0, 7.0 Hz, 1H), 2.19–2.26 (m, 2H), 1.80–2.09 (m, 7H), 1.62–1.70 (m, 1H), 1.42–1.59 (m, 8H), 1.12–1.29 (m, 3H), 0.95 (s, 3H), 0.91 (d, *J* = 6.0 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 139.3, 132.0, 131.4, 129.3, 128.2, 127.32, 127.22, 126.2, 113.7, 96.1, 81.7, 79.0, 77.2, 74.5, 73.25, 73.14, 70.7, 69.1, 58.4, 55.8,

55.3, 51.9, 44.7, 42.8, 38.6, 37.3, 36.2, 35.6, 34.7, 32.3, 29.0, 26.46, 26.25, 25.03, 24.89, 24.1, 21.41, 21.19, 13.9; IR (neat) 3445, 1516, 1249, 1039, 739 cm^{-1}; HRMS (ESI) *m/z* 811.4242 [$(M+Na)^+$, $C_{44}H_{68}O_8S_2$ requires 811.4248].

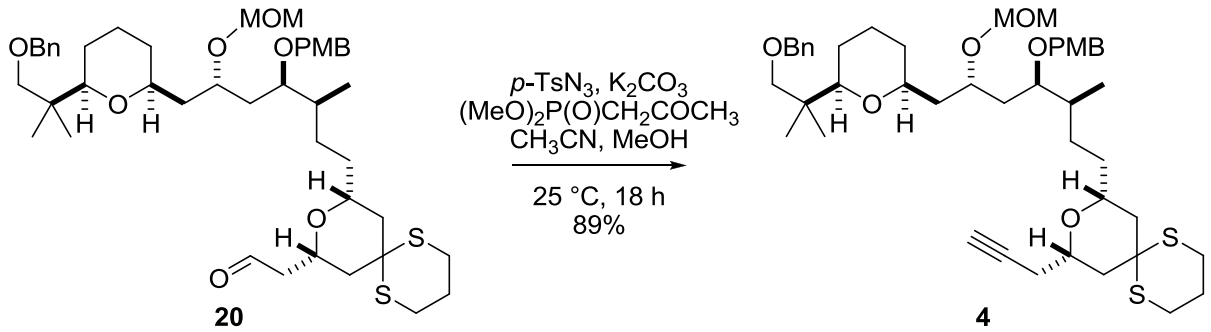
Preparation of 2,6-*cis*-Tetrahydropyran Aldehyde 20 by Tandem Oxidation/Oxa-Michael Reaction



To a stirred solution of allyl alcohol **5** (128 mg, 0.162 mmol) in CH_2Cl_2 (10 mL) was added MnO_2 (212 mg, 2.433 mmol) at 25 °C. After stirred for 8 h at the same temperature, the reaction mixture was filtered through celite with EtOAc and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5 to 1/3) to afford 2,6-*cis*-tetrahydropyran aldehyde **20** (115 mg, 90%): $[\alpha]^{25}_D$= +15.1 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.25–7.35 (m, 7H), 6.86 (d, *J* = 5.0 Hz, 2H), 4.67 (d, *J* = 7.0 Hz, 1H), 4.57 (d, *J* = 6.5 Hz, 1H), 4.52 (d, *J* = 10.5 Hz, 1H), 4.47 (d, *J* = 13.0 Hz, 1H), 4.39 (d, *J* = 9.0 Hz, 1H), 4.37 (d, *J* = 7.5 Hz, 1H), 4.30–4.35 (m, 1H), 3.94–4.05 (m, 1H), 3.79 (s, 3H), 3.73–3.82 (m, 1H), 3.54–3.58 (m, 1H), 3.39 (s, 3H), 3.34–3.42 (m, 1H), 3.28 (d, *J* = 8.5 Hz, 1H), 3.21 (d, *J* = 9.0 Hz, 1H), 3.19 (d, *J* = 10.5 Hz, 1H), 2.73–3.00 (m, 4H), 2.62 (ddd, *J* = 16.5, 8.0, 2.5 Hz, 1H), 2.47 (ddd, *J* = 16.5, 4.5, 2.5 Hz, 1H), 2.37 (d, *J* = 13.5 Hz, 1H), 2.20 (d, *J* = 13.5 Hz, 1H), 1.95–2.10 (m, 2H), 1.81–1.92 (m, 3H), 1.44–1.69 (m, 11H), 1.12–1.29 (m, 3H), 0.95 (s, 3H), 0.89 (d, *J*

= 8.0 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 159.0, 139.3, 131.4, 129.3, 128.2, 127.31, 127.21, 113.7, 96.2, 81.7, 79.2, 77.2, 74.5, 73.21, 73.14, 73.03, 70.8, 68.5, 55.8, 55.3, 49.1, 47.8, 43.20, 42.90, 42.78, 38.6, 35.8, 34.8, 33.9, 32.3, 28.8, 26.00, 25.93, 25.81, 25.0, 24.1, 21.4, 21.2, 13.9; IR (neat) 1725, 1512, 1035, 668 cm^{-1}; HRMS (ESI) *m/z* 809.4087 [$(M+Na)^+$, $C_{44}H_{66}O_8S_2$ requires 809.4081].

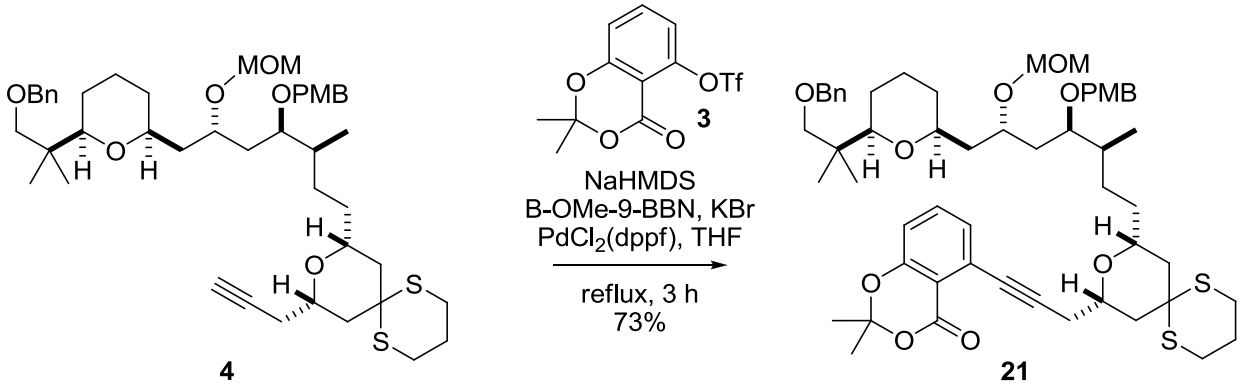
Preparation of Alkyne 4



To a suspension of K_2CO_3 (351 mg, 2.541 mmol) and *p*-toluenesulfonyl azide (1.0 M, 1.02 mL, 1.016 mmol) in CH_3CN (7 mL) was added dimethyl-2-oxopropylphosphonate (169 mg, 1.016 mmol) at 25 °C. The resulting suspension was stirred for 2 h at the same temperature and then the aldehyde **20** (160 mg, 0.203 mmol) in MeOH (5 mL) was added. After stirred for 18 h at the same temperature, the solvents were removed *in vacuo* and the residue was dissolved in EtOAc/H_2O (1:1, 30 mL). The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to afford alkyne **4** (141 mg, 89%): $[\alpha]^{25}_D$= +16.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.35 (m, 7H), 6.86 (d, *J* = 9.0 Hz, 2H), 4.67 (d, *J* = 7.0 Hz, 1H), 4.58 (d, *J* = 6.5 Hz, 1H), 4.52 (d, *J* = 10.5 Hz, 1H), 4.47 (d, *J* = 12.5 Hz, 1H), 4.39 (d, *J* = 12.5 Hz, 1H), 4.36 (d, *J* = 11.0 Hz, 1H), 3.95–4.05 (m, 1H), 3.89–3.95 (m, 1H), 3.80 (s, 3H), 3.74–3.81 (m, 1H), 3.55–3.59 (m,

1H), 3.39 (s, 3H), 3.35–3.42 (m, 1H), 3.29 (d, J = 9.0 Hz, 1H), 3.21 (d, J = 9.0 Hz, 1H), 3.20 (d, J = 9.5 Hz, 1H), 2.73–3.02 (m, 4H), 2.57 (d, J = 13.5 Hz, 1H), 2.52 (ddd, J = 16.5, 5.5, 3.0 Hz, 1H), 2.34 (ddd, J = 16.5, 7.5, 2.5 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.95–2.10 (m, 3H), 1.81–1.94 (m, 3H), 1.44–1.70 (m, 11H), 1.12–1.29 (m, 3H), 0.95 (s, 3H), 0.89 (d, J = 7.5 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 139.4, 131.5, 129.3, 128.2, 127.34, 127.23, 113.7, 96.2, 81.7, 80.5, 79.3, 77.2, 74.5, 73.22, 73.17, 73.15, 71.2, 70.8, 70.5, 55.8, 55.3, 48.0, 43.2, 42.9, 42.1, 38.6, 35.8, 34.8, 34.0, 32.3, 28.9, 26.03, 25.93 (2 carbons), 25.5, 25.0, 24.1, 21.4, 21.2, 13.8; IR (neat) 3304, 1514, 1248, 1038, 738 cm^{-1}; HRMS (ESI) *m/z* 805.4136 [$(M+Na)^+$, $C_{45}H_{66}O_7S_2$ requires 805.4142].

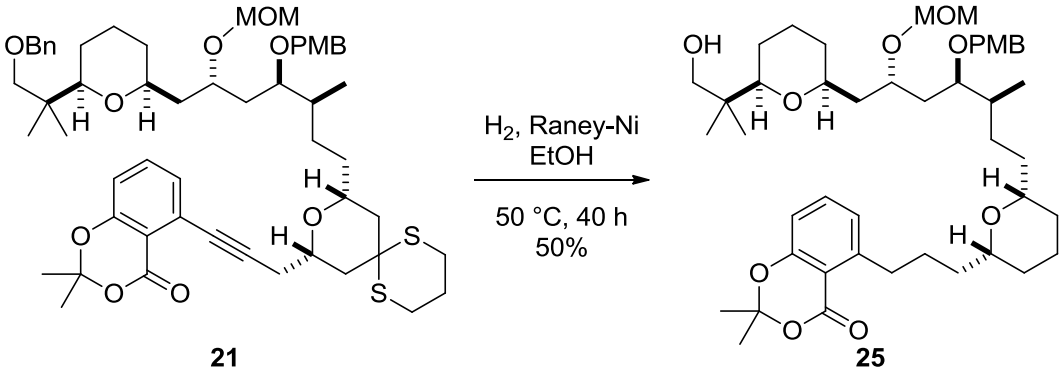
Preparation of 21



To a cooled (–78 ºC) solution of alkyne **4** (117 mg, 0.149 mmol) in THF (10 mL) was added NaHMDS (1.0 M, 0.30 mL, 0.299 mmol). After stirred for 30 min at the same temperature, B-OMe-9-BBN (1.0 M, 0.37 mL, 0.374 mmol) was added and the resulting mixture was then warmed to 25 ºC. After stirred for 30 min, KBr (36 mg, 0.299 mmol), $PdCl_2$(dppf) (22 mg, 0.030 mmol), and triflate **3** (98 mg, 0.299 mmol) were added. After refluxed for 3 h, the reaction mixture was cooled to 25 ºC and quenched with addition of saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined

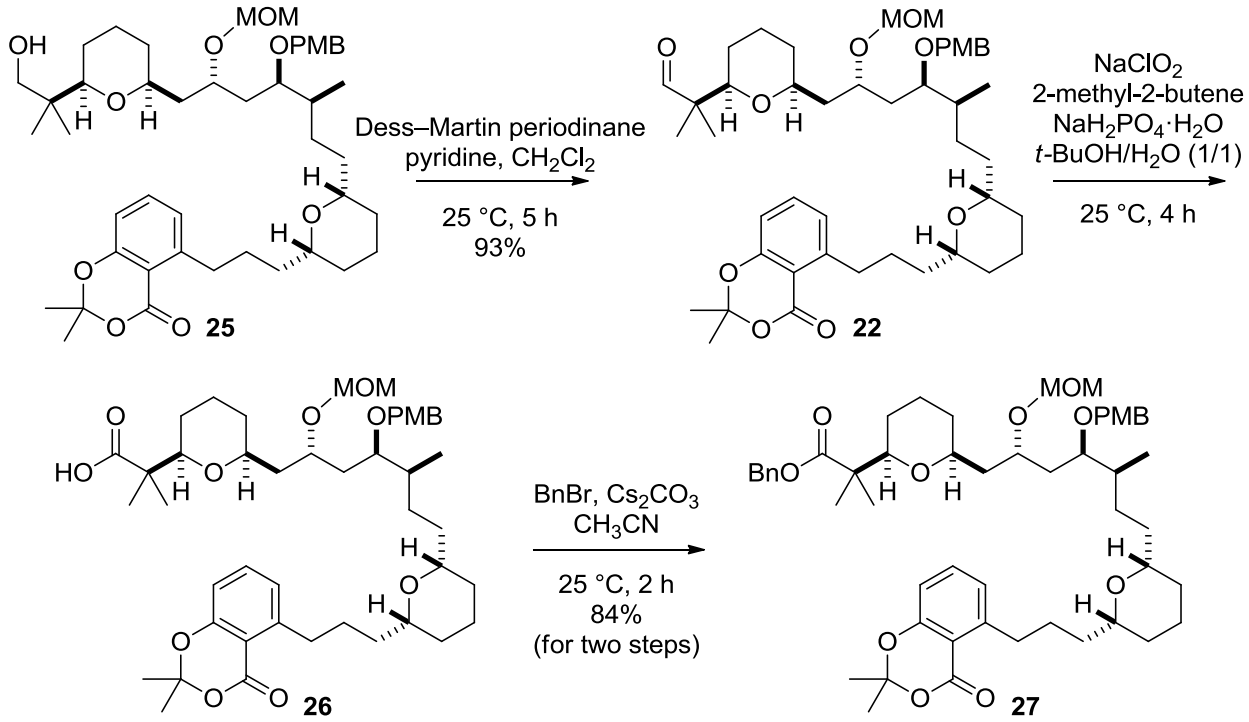
organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/10 to 1/5) to afford **21** (122 mg, 73%): $[\alpha]^{25}_{D}$= +1.6 (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.5, 7.5 Hz, 1H), 7.21–7.33 (m, 8H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.64 (d, *J* = 7.0 Hz, 1H), 4.55 (d, *J* = 6.0 Hz, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 13.0 Hz, 1H), 4.36 (d, *J* = 12.5 Hz, 1H), 4.34 (d, *J* = 10.5 Hz, 1H), 4.01–4.07 (m, 1H), 3.92–3.99 (m, 1H), 3.77 (s, 3H), 3.73–3.82 (m, 1H), 3.52–3.58 (m, 1H), 3.36 (s, 3H), 3.31–3.40 (m, 1H), 3.15–3.27 (m, 4H), 2.74–3.05 (m, 2H), 2.85 (dd, *J* = 17.0, 5.0 Hz, 1H), 2.73–2.79 (m, 1H), 2.63–2.68 (m, 1H), 2.63 (dd, *J* = 17.0, 9.0 Hz, 1H), 2.05–2.13 (m, 2H), 1.79–1.97 (m, 4H), 1.71 (s, 6H), 1.41–1.69 (m, 11H), 1.10–1.23 (m, 3H), 0.92 (s, 3H), 0.86 (d, *J* = 8.0 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 158.9, 156.6, 139.4, 134.9, 131.5, 129.4, 129.1, 128.2, 127.37, 127.25, 125.9, 116.9, 114.3, 113.8, 105.6, 96.2, 93.9, 81.8, 80.6, 79.2, 77.2, 74.6, 73.25, 73.20, 72.7, 71.9, 70.8, 55.8, 55.4, 48.2, 43.6, 42.9, 42.2, 38.6, 35.8, 34.8, 34.1, 32.3, 28.9, 26.9, 26.08, 26.02, 25.86, 25.85, 25.76, 25.1, 24.1, 21.5, 21.2, 13.8; IR (neat) 2232, 1738, 1271, 1036, 734cm^{-1}; HRMS (ESI) *m/z* 981.4615 [$(M+Na)^+$, $C_{55}H_{74}O_{10}S_2$ requires 981.4616].

Preparation of Alcohol 22



To a stirred solution of coupling product **21** (40 mg, 0.042 mmol) in EtOH (0.5 mL) was added Raney® 2400 nickel slurry in EtOH (2 pipets). After stirred under H_2 atmosphere for 40 h at 50 °C, the reaction mixture was then filtered through celite with EtOAc and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5 to 2/1) to afford alcohol **25** (16 mg, 50%): $[\alpha]^{25}_{D}$= +26.6 (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 7.5 Hz, 1H), 4.59 (d, *J* = 7.0 Hz, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.49 (d, *J* = 7.0 Hz, 1H), 4.31 (d, *J* = 11.0 Hz, 1H), 3.87–3.93 (m, 1H), 3.79 (s, 3H), 3.56 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.47 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.31 (s, 3H), 3.17–3.36 (m, 5H), 3.09 (dd, *J* = 7.0 Hz, 2H), 2.95 (dd, *J* = 10.0, 4.0 Hz, 1H), 1.75–1.95 (m, 5H), 1.68 (s, 6H), 1.54–1.67 (m, 6H), 1.36–1.52 (m, 10H), 1.24–1.30 (m, 1H), 1.08–1.20 (m, 3H), 0.86 (s, 3H), 0.86 (d, *J* = 8.0 Hz, 3H), 0.72 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 159.1, 157.1, 148.3, 135.1, 130.8, 129.8, 125.2, 115.1, 113.7, 112.0, 104.9, 96.3. 83.7, 78.9, 78.0, 77.7, 75.4, 73.2, 70.7, 70.2, 55.6, 55.3, 42.2, 38.0, 36.4, 34.81 (2 carbons), 34.27, 34.24, 32.0, 31.69 (2 carbons), 29.1, 27.1, 25.72, 25.62, 25.0, 23.9, 23.7, 22.7, 19.5, 13.4; IR (neat) 3520, 1738, 1038, 751 cm^{-1}; HRMS (ESI) *m/z* 791.4702 [$(M+Na)^+$, $C_{45}H_{68}O_{10}$ requires 791.4705].

Preparation of Benzyl Ester 27



[Dess−Martin Oxidation] To a stirred solution of alcohol **25** (16 mg, 0.021 mmol) in CH_2Cl_2 (1 mL) were added pyridine (3.4 μL, 0.042 mmol) and Dess−Martin periodinane (13 mg, 0.032 mmol) at 25 ºC. After stirred for 5 h, the reaction mixture was quenched with addition of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/ hexanes, 1/2) to afford aldehyde **22** (15 mg, 93%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.38 (dd, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 7.0 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 2H), 6.79 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.58 (d, *J* = 6.0 Hz, 1H), 4.50 (d, *J* = 10.5 Hz, 1H), 4.48 (d, *J* = 8.0 Hz, 1H), 4.30 (d, *J* = 11.5 Hz, 1H), 3.83–3.89 (m, 1H), 3.79 (s, 3H), 3.48–3.53 (m, 1H), 3.32 (s, 3H), 3.24–3.40 (m, 3H), 3.17–3.23 (m, 1H), 3.09 (dd, *J*

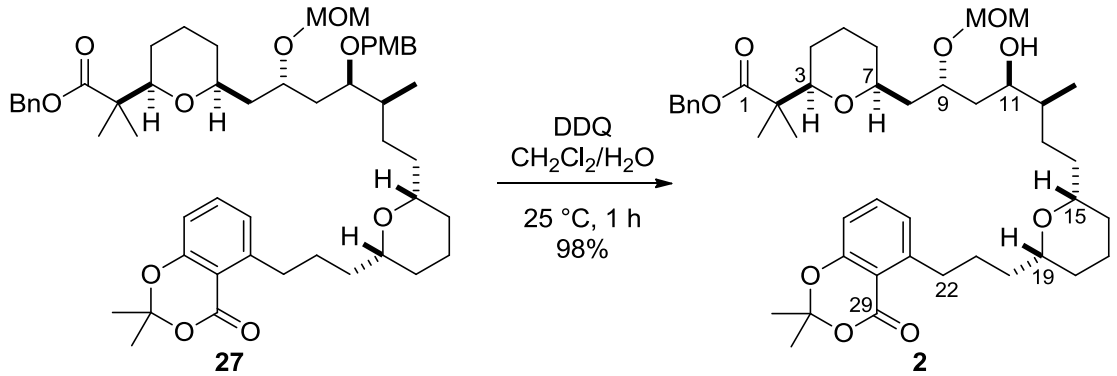
= 7.0 Hz, 2H), 1.71–1.94 (m, 5H), 1.69 (s, 3H), 1.68 (s, 3H), 1.54–1.67 (m, 4H), 1.36–1.52 (m, 11H), 1.08–1.23 (m, 5H), 1.00 (s, 3H), 0.99 (s, 3H), 0.87 (d, *J* = 7.0 Hz, 3H).

[Oxidation to Carboxylic Acid] To a solution of aldehyde **22** (15 mg, 0.019 mmol) in *t*-BuOH/ H_2O (1/1, 2 mL) were added 2-methyl-2-butene (83 μL, 0.782 mmol), sodium phosphate monobasic monohydrate (5.2 mg, 0.038 mmol), and sodium chlorite (3.5 mg, 0.038 mmol) at 25 °C. After stirred for 4 h at 25 °C, the reaction mixture was diluted with EtOAc and H_2O. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford the crude carboxylic acid **26**, which was employed in the next step without further purification.

[Esterification] To a solution of carboxylic acid **26** in CH_3CN (1 mL) were added Cs_2CO_3 (31 mg, 0.095 mmol) and benzyl bromide (23 μL, 0.190 mmol) at 25 °C. After stirred for 2 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to afford benzyl ester **27** (14 mg, 84% for two steps): $[\alpha]^{25}_{D}$= +14.1 (*c* 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 7.5 Hz, 1H), 7.28–7.35 (m, 5H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 7.5 Hz, 1H), 5.07 (s, 2H), 4.58 (d, *J* = 7.0 Hz, 1H), 4.50 (d, *J* = 6.5 Hz, 1H), 4.48 (d, *J* = 12.5 Hz, 1H), 4.30 (d, *J* = 11.5 Hz, 1H), 3.85–3.91 (m, 1H), 3.77 (s, 3H), 3.49–3.54 (m, 1H), 3.45 (dd, *J* = 11.0, 1.5 Hz, 1H), 3.35–3.41 (m, 1H), 3.32 (s, 3H), 3.24–3.29 (m, 1H), 3.17–3.22 (m, 1H), 3.09 (dd, *J* = 7.0 Hz, 2H), 1.85–1.92 (m, 1H), 1.74–1.82 (m, 3H), 1.69 (s, 6H), 1.32–1.64 (m, 16H), 1.08–1.24 (m, 5H), 1.19 (s, 3H), 1.11 (s, 3H), 0.86 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 160.4, 159.1, 157.3, 148.3, 136.7, 135.3, 131.5, 129.4, 128.6, 128.00, 127.91, 125.3, 115.3, 113.8, 112.2, 105.1, 96.3, 82.1, 79.3, 78.2,

77.9, 75.0, 73.2, 70.7, 66.1, 55.8, 55.4, 46.9, 42.9, 36.6, 35.9, 35.0, 34.7, 34.4, 32.01, 31.82 (2 carbons), 29.2, 27.3, 25.85, 25.76, 25.70, 23.90, 23.82, 22.2, 20.3, 13.8; IR (neat) 1737, 1513, 1389, 1039, 669 cm^{-1}; HRMS (ESI) *m/z* 895.4966 [$(M+Na)^+$, $C_{52}H_{72}O_{11}$ requires 895.4967].

Preparation of 2



To a cooled (0 °C) solution of benzyl ester **27** (14 mg, 0.016 mmol) in CH_2Cl_2/H_2O (10:1, 1.1 mL) was added DDQ (11 mg, 0.048 mmol). After stirred for 1 h at 25 °C, the reaction mixture was quenched with addition of saturated aqueous $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1/5) to **2** (12 mg, 98%): $[\alpha]^{25}_D$= +7.9 (*c* 0.07, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 8.0 Hz, 1H), 7.27–7.35 (m, 5H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 5.12 (s, 2H), 4.61 (d, *J* = 6.0 Hz, 1H), 4.58 (d, *J* = 6.5 Hz, 1H), 3.92–3.98 (m, 1H), 3.63–3.68 (m, 1H), 3.50 (d, *J* = 10.0 Hz, 1H), 3.17–3.37 (m, 3H), 3.35 (s, 3H), 3.06–3.13 (m, 2H), 2.94 (d, *J* = 4.0 Hz, 1H), 1.74–1.88 (m, 3H), 1.69 (s, 6H), 1.38–1.65 (m, 16H), 1.07–1.28 (m, 6H), 1.20 (s, 3H), 1.12 (s, 3H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 160.4, 157.3, 148.4, 136.6, 135.2, 128.6, 128.1, 127.9, 125.4, 115.3, 112.2, 105.1, 96.2, 82.4, 78.4, 77.8, 75.1, 73.6, 71.7, 66.3, 55.9, 46.9, 41.3, 39.1, 37.2, 36.6, 34.4,

34.3, 32.0, 31.9, 31.7, 28.3, 27.3, 25.9, 25.8, 25.3, 23.9, 23.8, 21.3, 20.7, 15.3; IR (neat) 3521, 1733, 1456, 1038, 734 cm^{-1}; HRMS (ESI) *m/z* 775.4390 [$(M+Na)^+$, $C_{44}H_{64}O_{10}$ requires 775.4392].

Table 1. Comparison of ^{1}H NMR data for **2** ($CDCl_3$)[1]

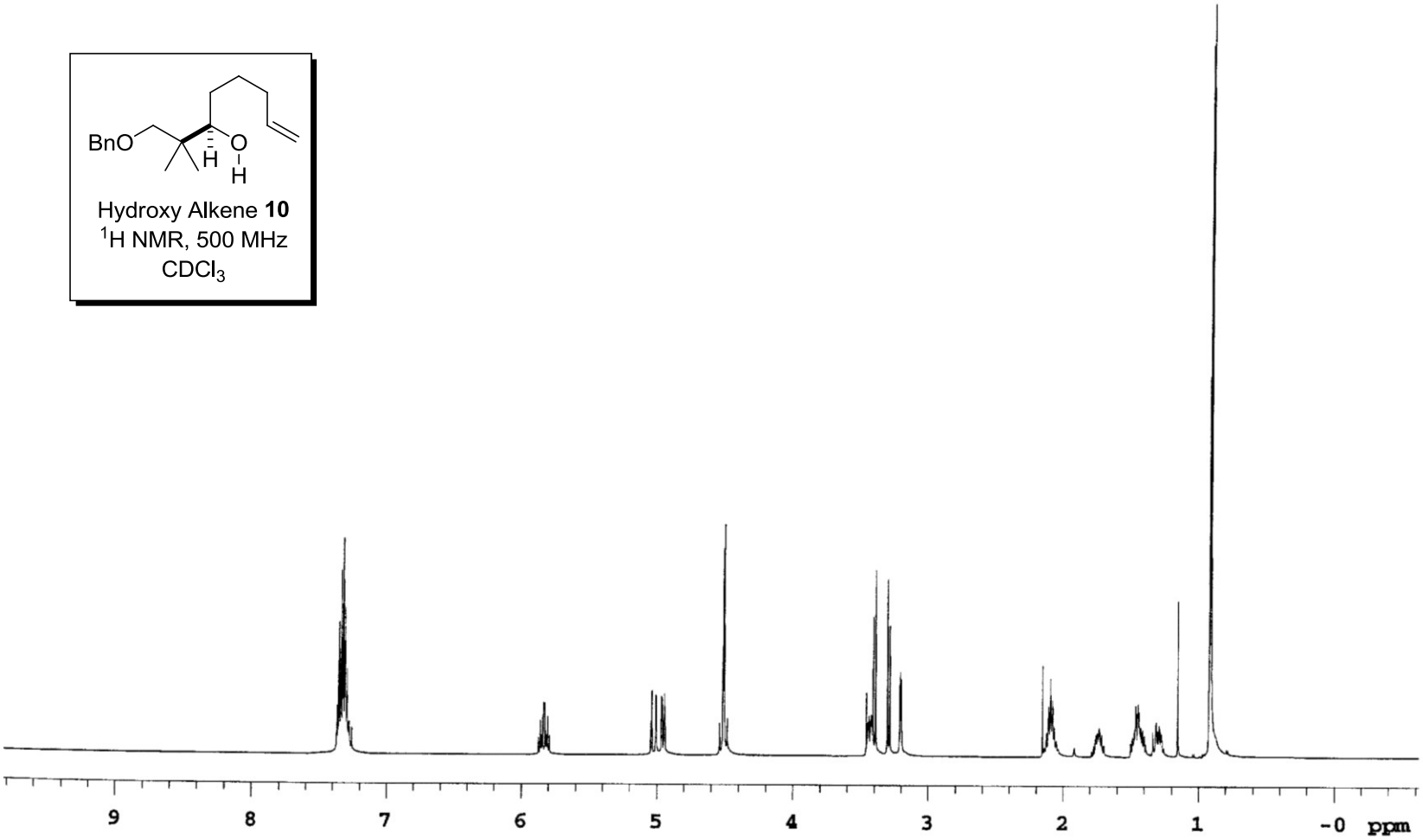
Carbon #	chemical shifts (δ)		**Carbon #**	chemical shifts (δ)	
	De Brabander (400 MHz)	Hong (500 MHz)		De Brabander (400 MHz)	Hong (500 MHz)
1	–	–	**20**	1.39–1.65 (m)	1.38–1.65 (m)
2	–	–	**21**	1.74–1.88 (m)	1.74–1.88 (m)
3	3.51 (d)	3.50 (d)		1.07–1.28 (m)	1.06–1.28 (m)
4	1.39–1.65 (m)	1.38–1.65 (m)	**22**	3.06-3.13 (m)	3.06-3.13 (m)
5	1.74–1.88 (m)	1.74–1.88 (m)	**23**	–	–
	1.39–1.65 (m)	1.38–1.65 (m)	**24**	6.78 (d)	6.78 (d)
6	1.39–1.65 (m)	1.38–1.65 (m)	**25**	7.28 (t)	7.38 (t)
	1.07–1.28 (m)	1.06–1.28 (m)	**26**	6.93 (d)	6.93 (d)
7	3.17–3.40 (m)	3.17–3.37 (m)	**27**	–	–
8	1.39–1.65 (m)	1.38–1.65 (m)	**28**	–	–
9	3.90–4.00 (m)	3.92–3.98 (m)	**29**	–	–
10	1.39–1.65 (m)	1.38–1.65 (m)	**30**	–	–
11	3.63–3.69 (m)	3.63–3.68 (m)	**1**-OCH_2**Ph**	7.27–7.40 (m)	7.27–7.35 (m)
12	1.39–1.65 (m)	1.38–1.65 (m)	**1**-O**CH_2**Ph	4.58 (d)	4.58 (d)
13	1.39–1.65 (m)	1.38–1.65 (m)	**1**-O**CH_2**Ph	4.61 (d)	4.61 (d)
	1.07–1.28 (m)	1.06–1.28 (m)	**2**-Me	1.12 (s)	1.12 (s)
14	1.07–1.28 (m)	1.06–1.28 (m)	**2**-Me	1.20 (s)	1.20 (s)
15	3.17–3.40 (m)	3.17–3.37 (m)	**9**-O**CH_2**OCH_3	5.12 (s)	5.12 (s)
16	1.39–1.65 (m)	1.38–1.65 (m)	**9**-OCH_2O**CH_3**	3.35 (s)	3.35 (s)
17	1.39–1.65 (m)	1.38–1.65 (m)	**11**-OH	2.95 (m)	2.94 (d)
	1.74–1.88 (m)	1.74–1.88 (m)	**12**-Me	0.86 (d)	0.86 (d)
18	1.39–1.65 (m)	1.38–1.65 (m)	**30**-Me	1.69 (s)	1.69 (s)
	1.07–1.28 (m)	1.06–1.28 (m)	**30**-Me	1.69 (s)	1.69 (s)
19	3.17–3.40 (m)	3.17–3.37 (m)			

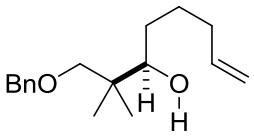
[1]Chemical shifts of methylenes in the upfield region may be interchangeable.

Table 2. Comparison of ^{13}C NMR data for **2** ($CDCl_3$)

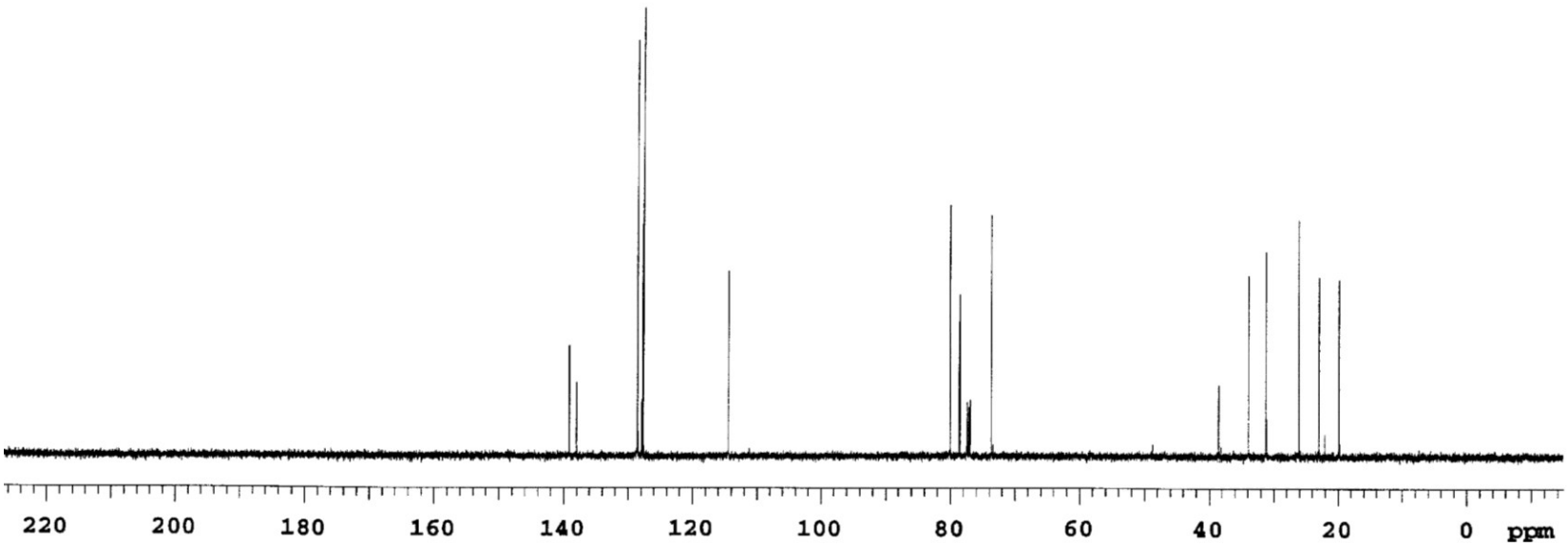
Carbon #	chemical shifts (δ)		**Carbon #**	chemical shifts (δ)	
	De Brabander (100 MHz)	Hong (125 MHz)		De Brabander (100 MHz)	Hong (125 MHz)
1	176.9	176.9	**22**	34.4	34.4
2	46.9	46.9	**23**	148.4	148.4
3	82.4	82.4	**24**	125.4	125.4
4	36.6	36.6	**25**	135.3	135.2
5	23.8	23.8	**26**	115.3	115.3
6	32.0	32.0	**27**	112.2	112.2
7[1]	75.2	75.1	**28**	160.4	160.4
8	41.4	41.3	**29**	157.3	157.3
9	73.6	73.6	**30**	105.1	105.1
10	39.1	39.1	**1**-OCH_2**Ph**	136.6	136.6
11	71.7	71.7		128.6	128.6
12	37.2	37.2		128.1	128.1
13	27.3	27.3		127.9	127.9
14	25.3	25.3	**1**-O$\mathbf{CH_2}$Ph	66.3	66.3
15[1]	77.8	77.8	**2**-Me	21.4	21.3
16	31.9	31.9	**2**-Me	20.7	20.7
17	23.9	23.9	**9**-O$\mathbf{CH_2}$$OCH_3$	96.2	96.2
18	31.7	31.7	**9**-OCH_2O$\mathbf{CH_3}$	56.0	55.9
19[1]	78.5	78.4	**12**-Me	15.3	15.3
20	34.3	34.3	**30**-Me	25.9	25.9
21	28.4	28.3	**30**-Me	25.8	25.8

[1]Chemical shifts may be interchangeable.

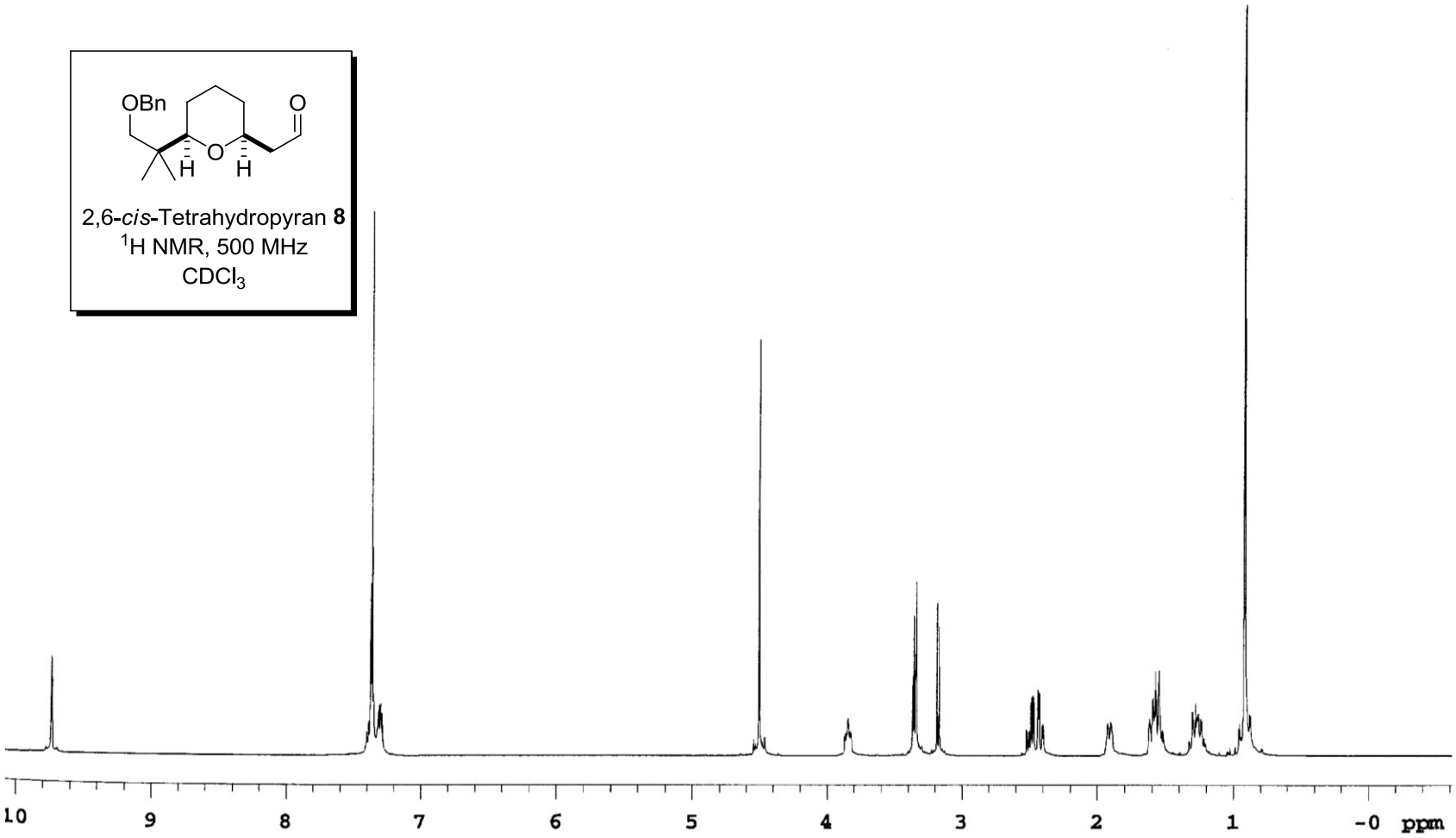

BnO
H
O
H
Hydroxy Alkene **10**
^{1}H NMR, 500 MHz
$CDCl_3$
9
8
7
6
5
4
3
2
1
-0
ppm

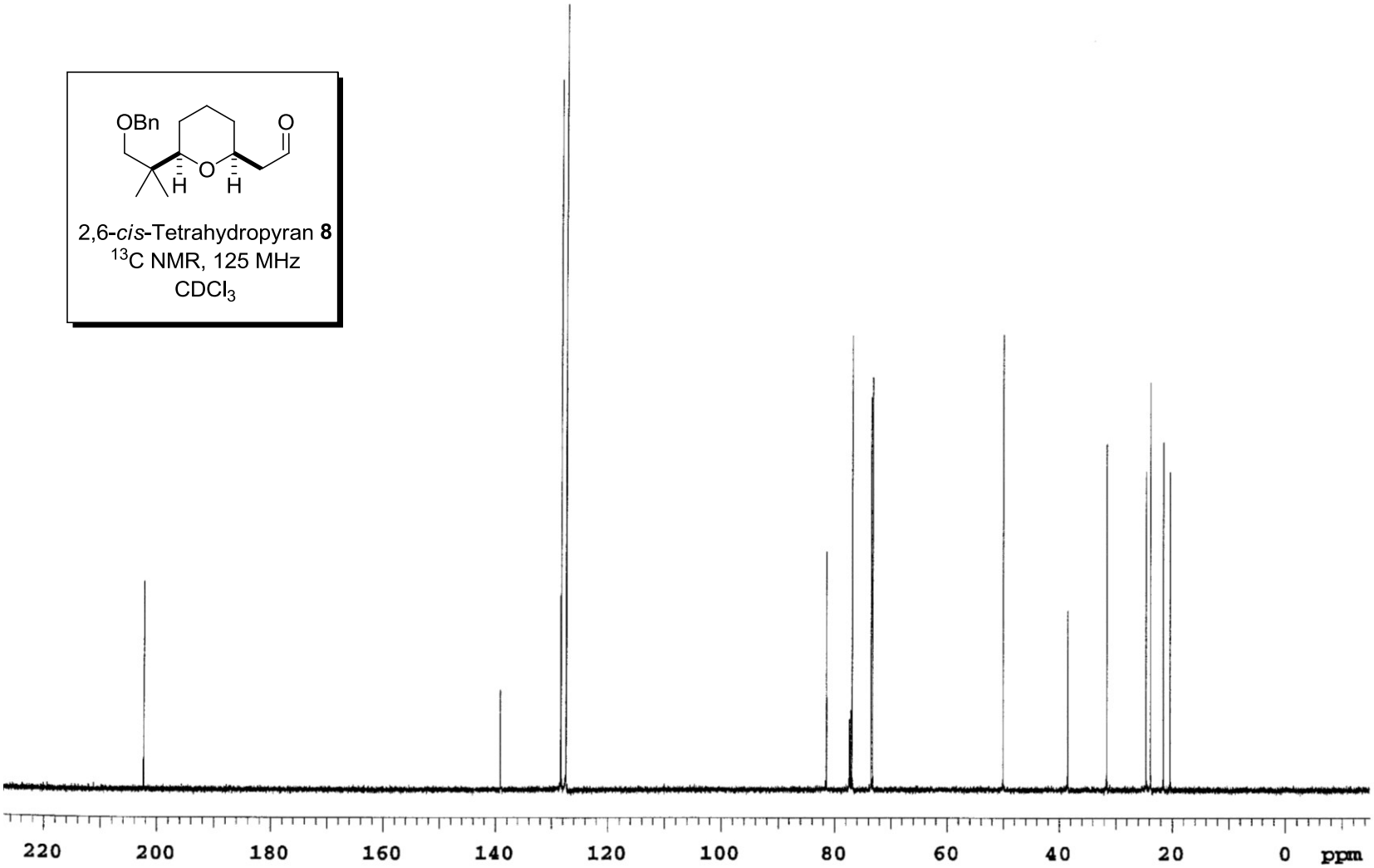


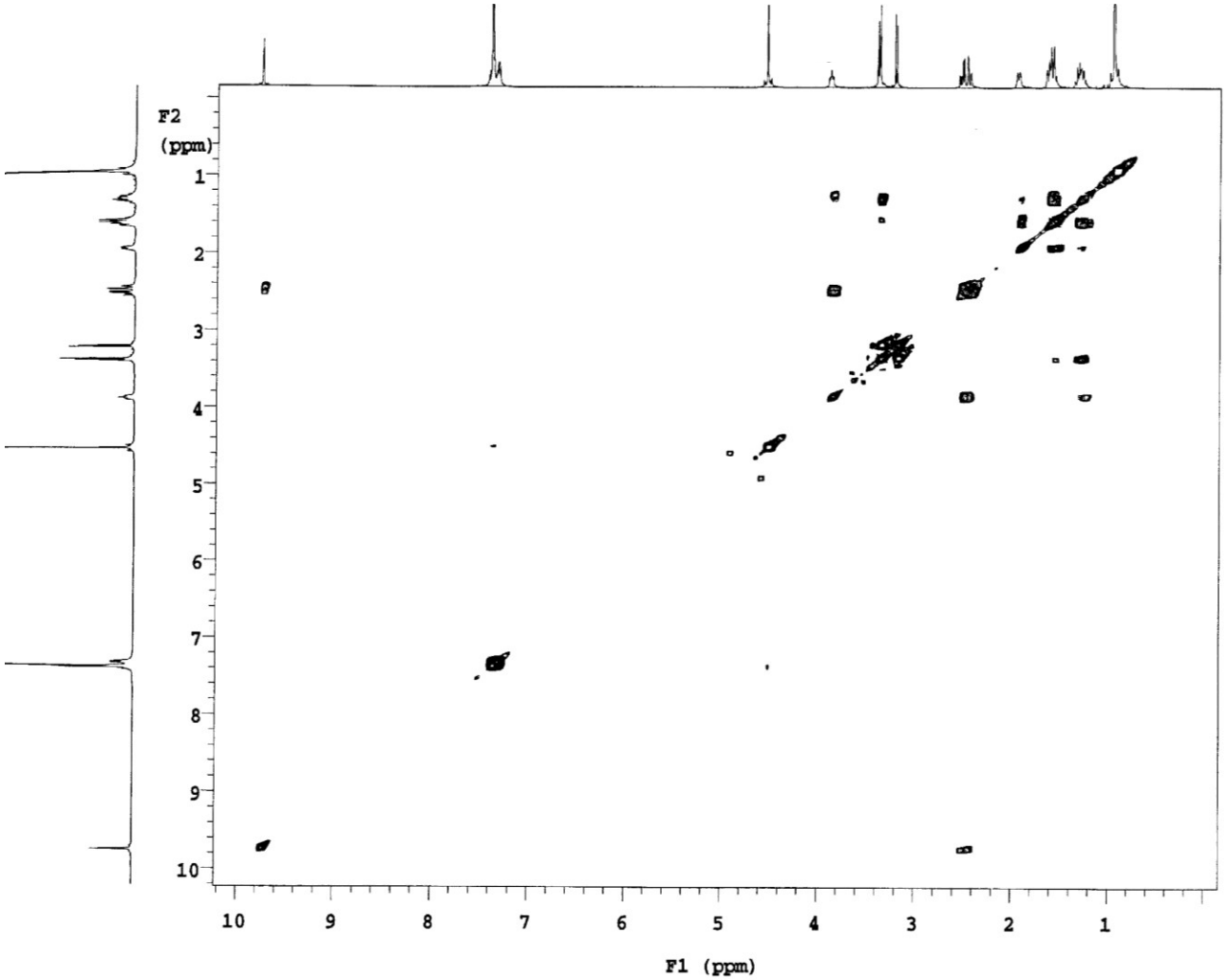
Hydroxy Alkene **10**
^{13}C NMR, 125 MHz
$CDCl_3$

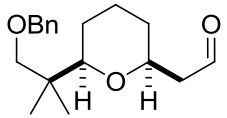


2,6-*cis*-Tetrahydropyran **8**
^{1}H NMR, 500 MHz
$CDCl_3$

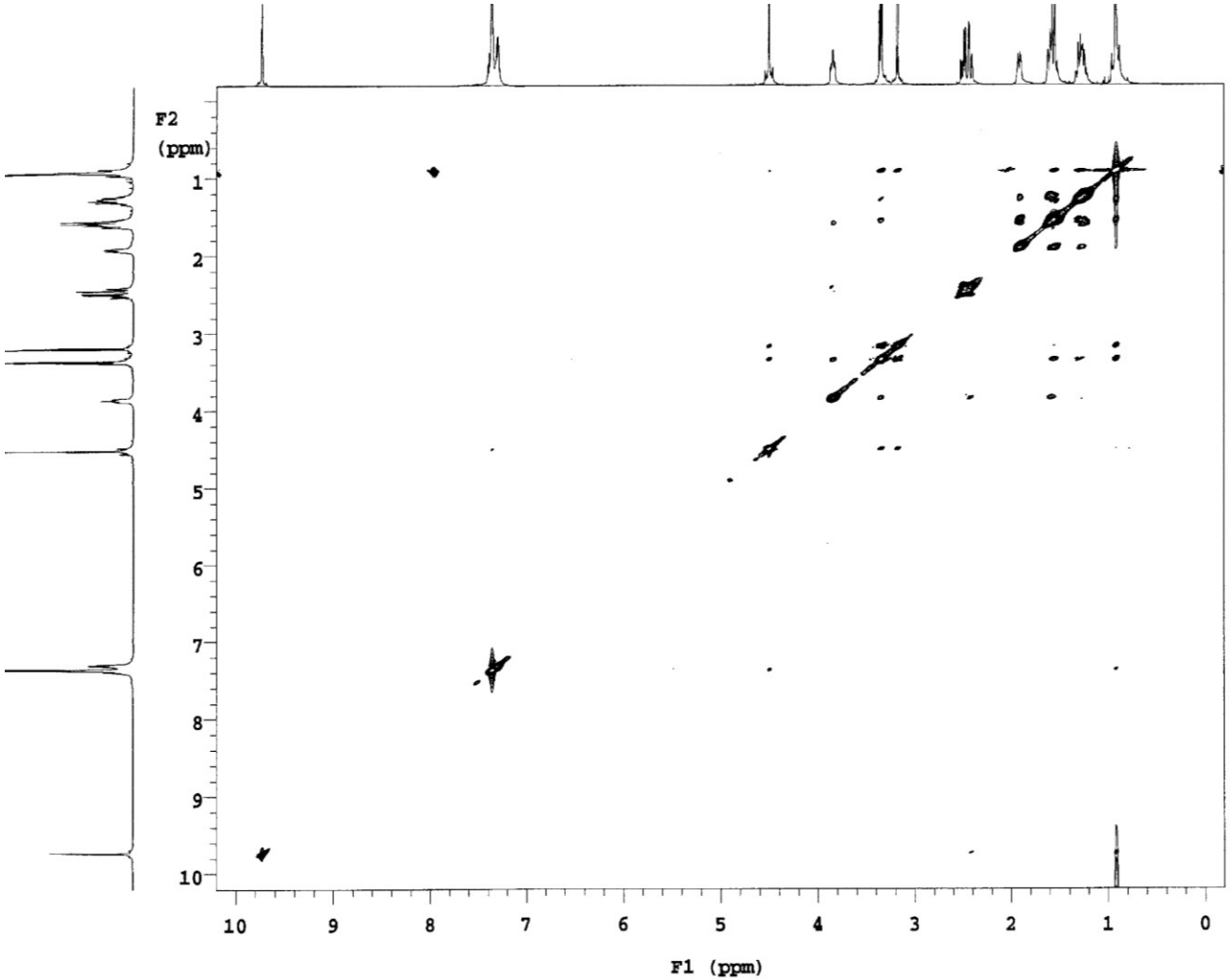


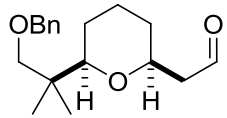

OBn
O
H
O
H
2,6-*cis*-Tetrahydropyran **8**
^{13}C NMR, 125 MHz
$CDCl_3$
220
200
180
160
140
120
100
80
60
40
20
0
ppm



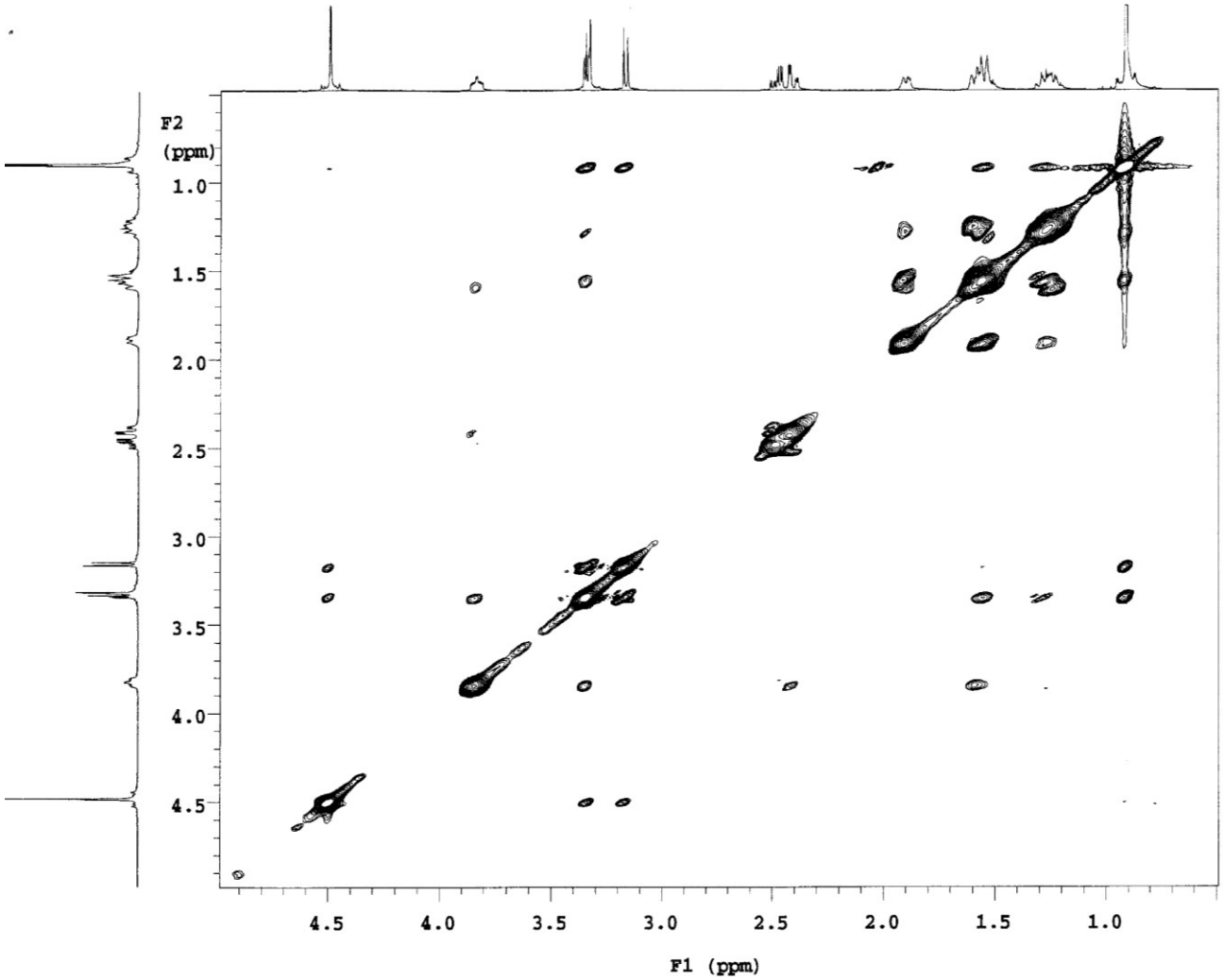


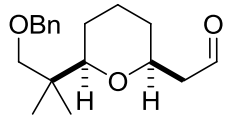
2,6-*cis*-Tetrahydropyran **8**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$



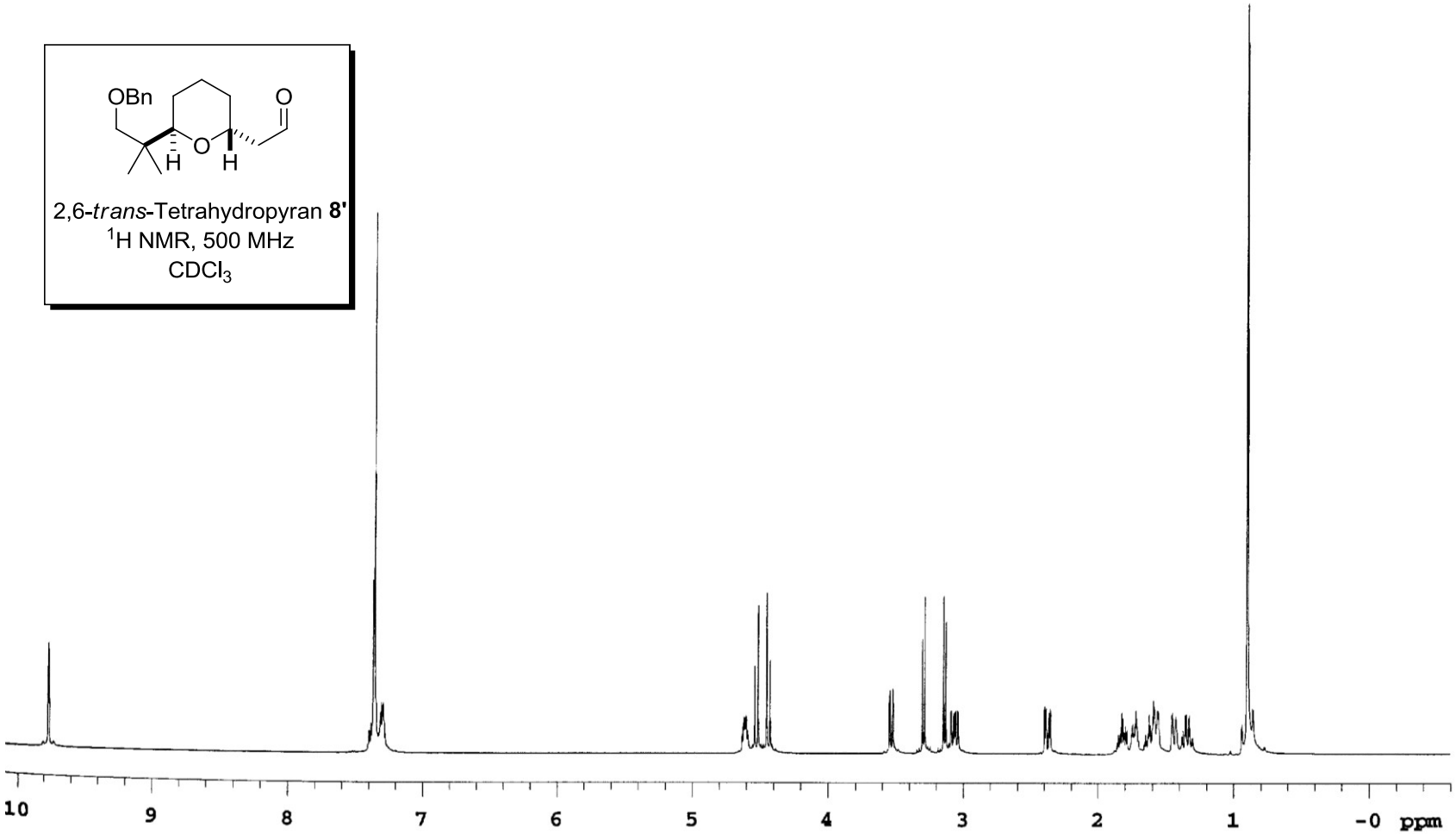


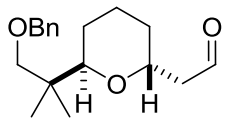
2,6-*cis*-Tetrahydropyran **8**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$



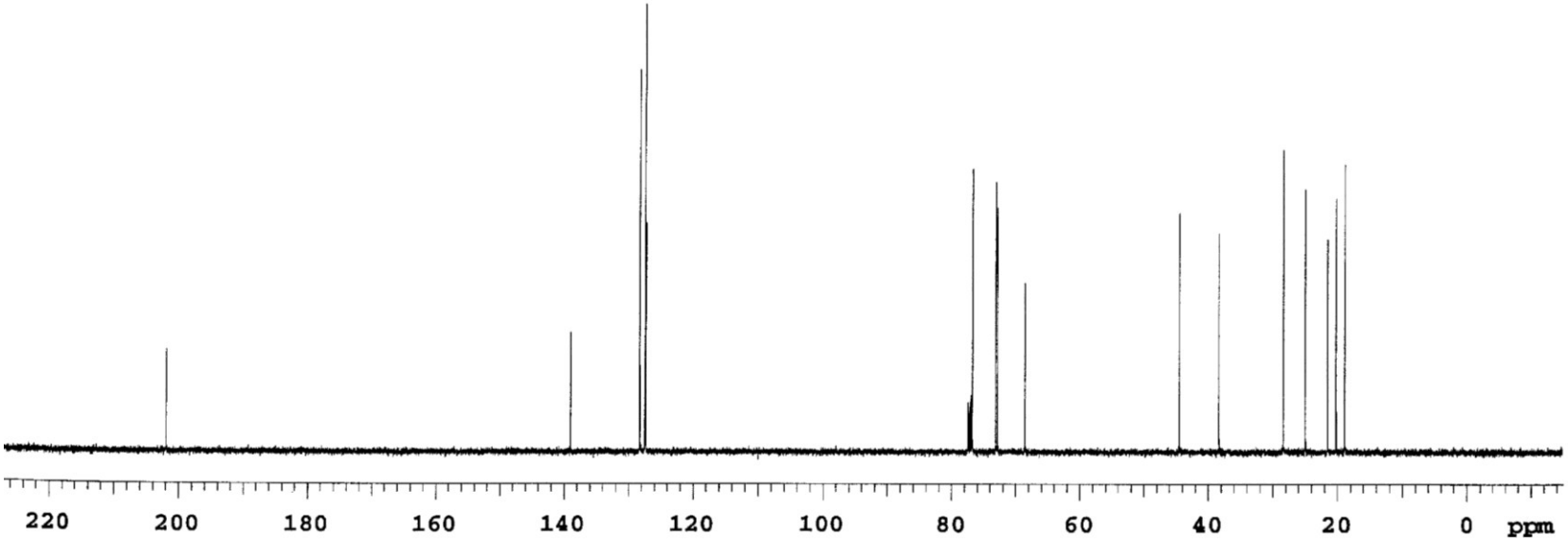


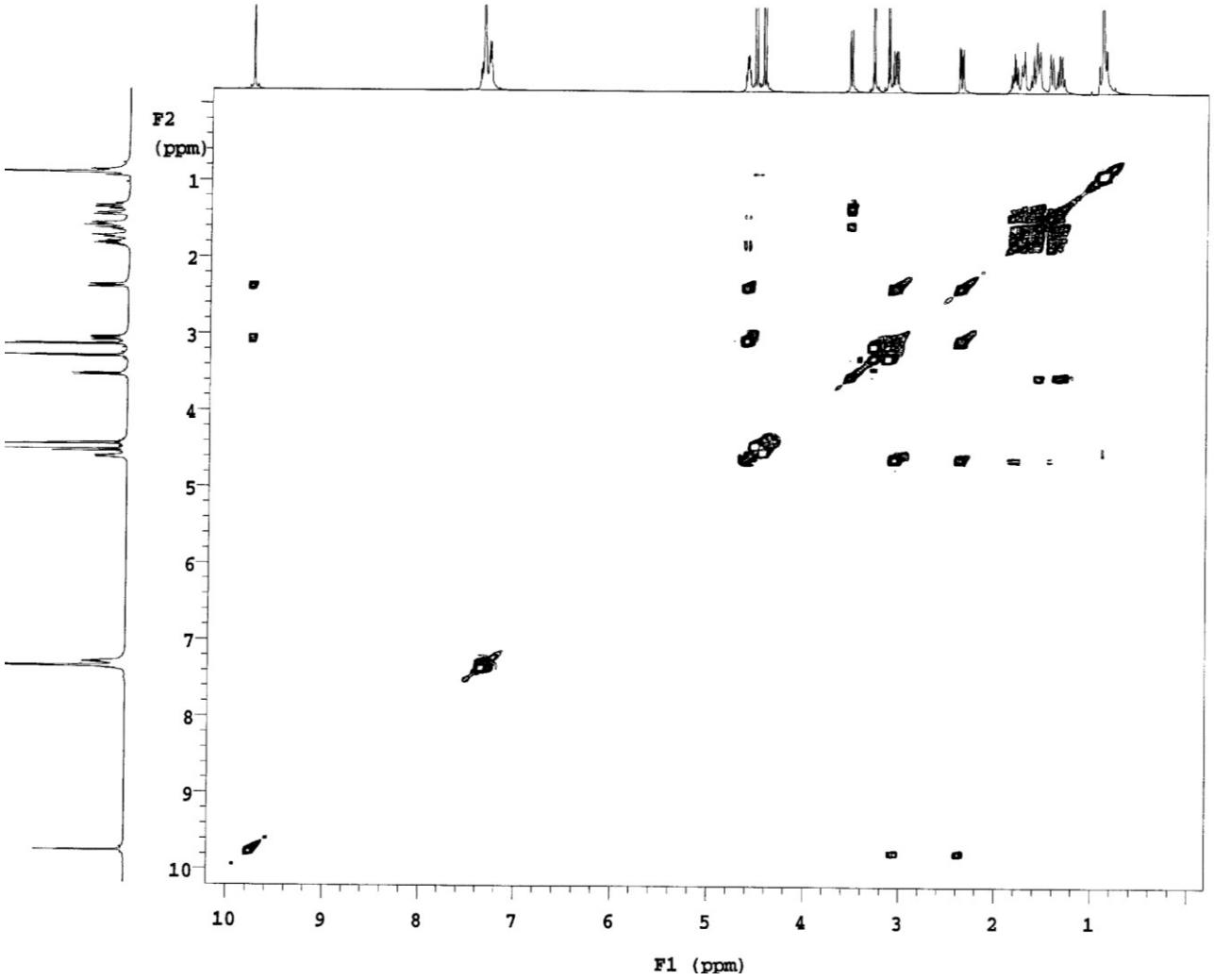
2,6-*cis*-Tetrahydropyran **8**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$

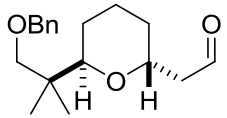

OBn
O
H
O
H
2,6-*trans*-Tetrahydropyran **8'**
^{1}H NMR, 500 MHz
$CDCl_3$
10
9
8
7
6
5
4
3
2
1
-0
ppm



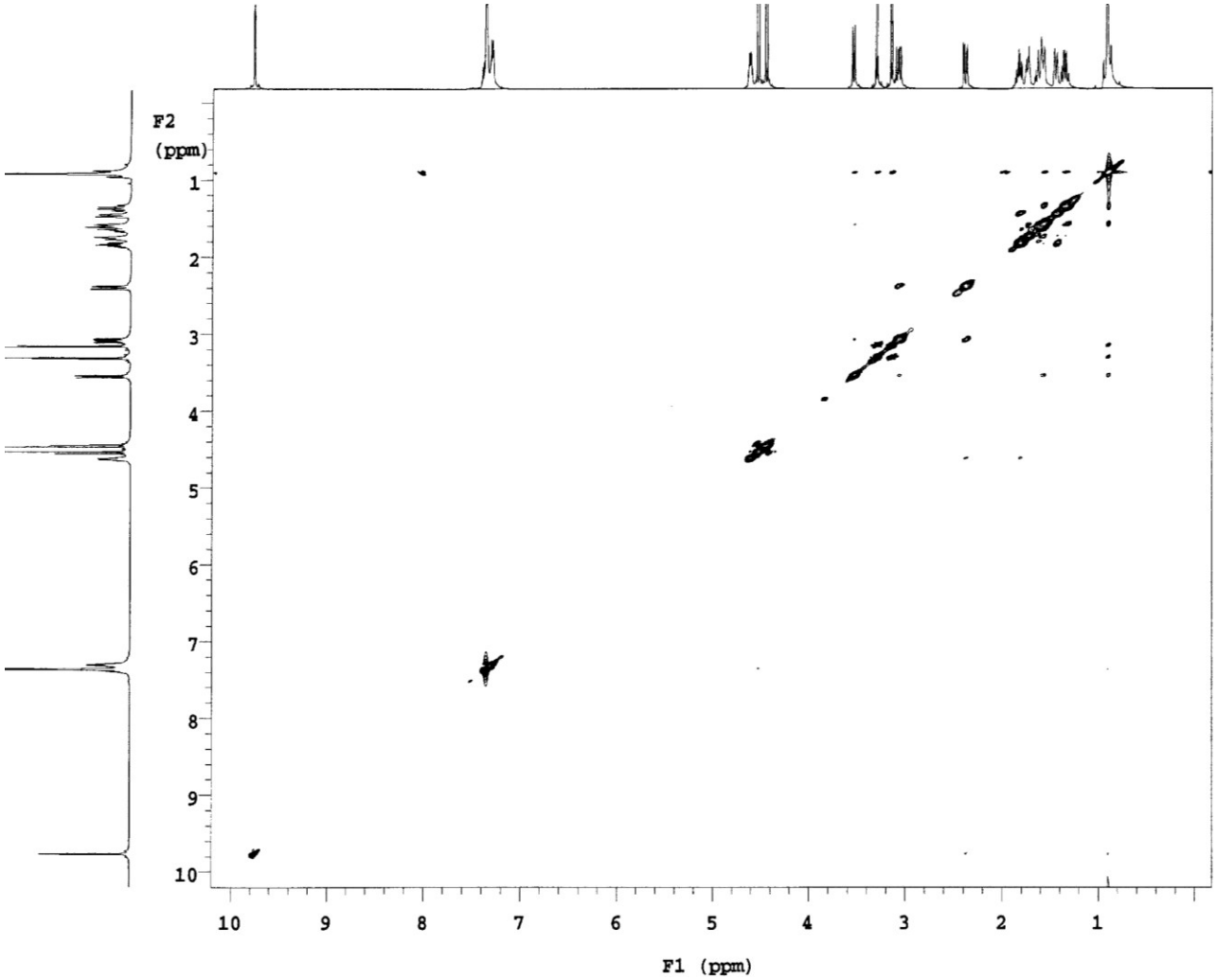
2,6-*trans*-Tetrahydropyran **8'**
^{13}C NMR, 125 MHz
$CDCl_3$

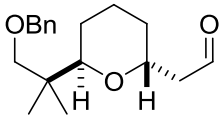




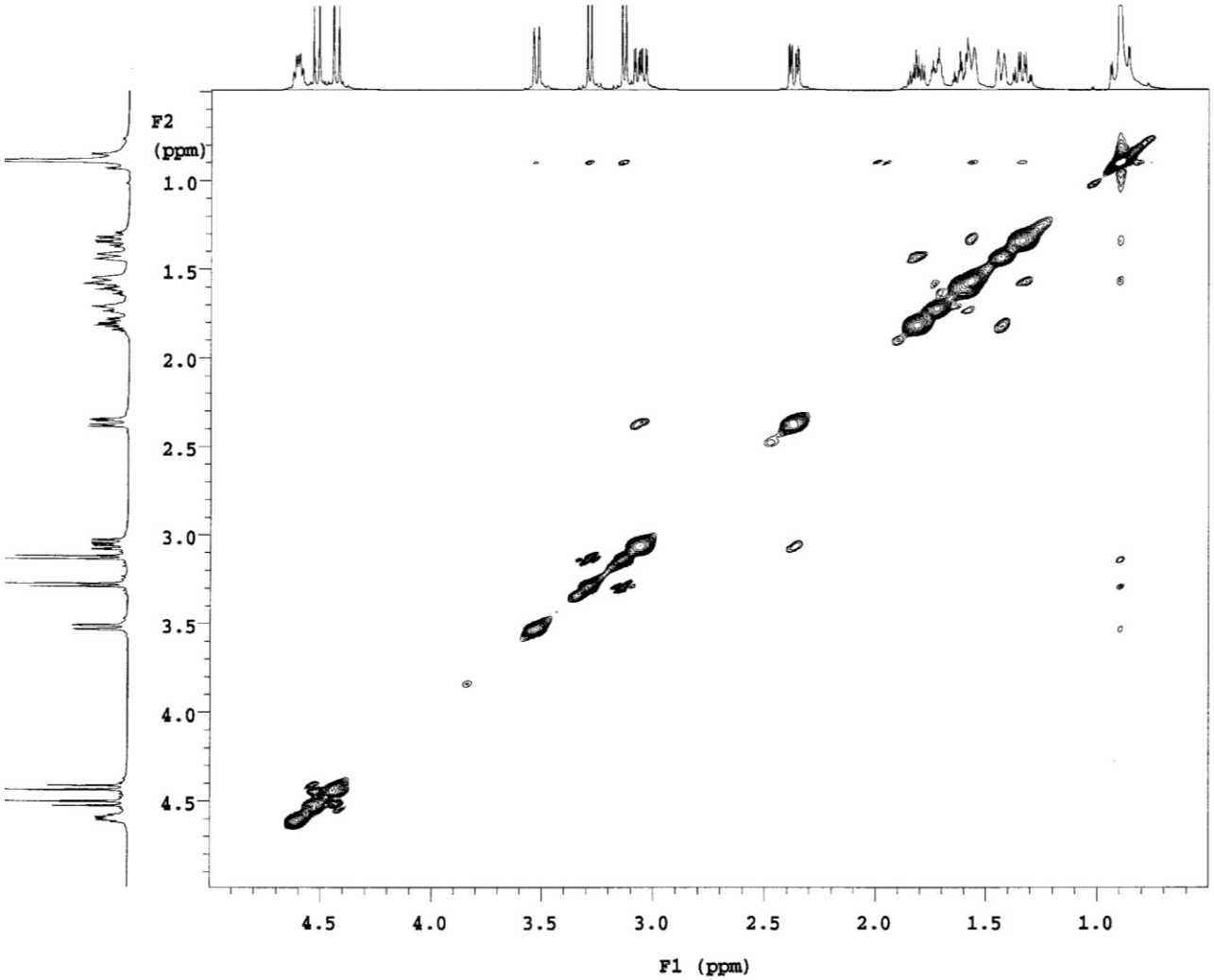


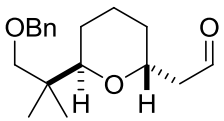
2,6-*trans*-Tetrahydropyran **8'**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$



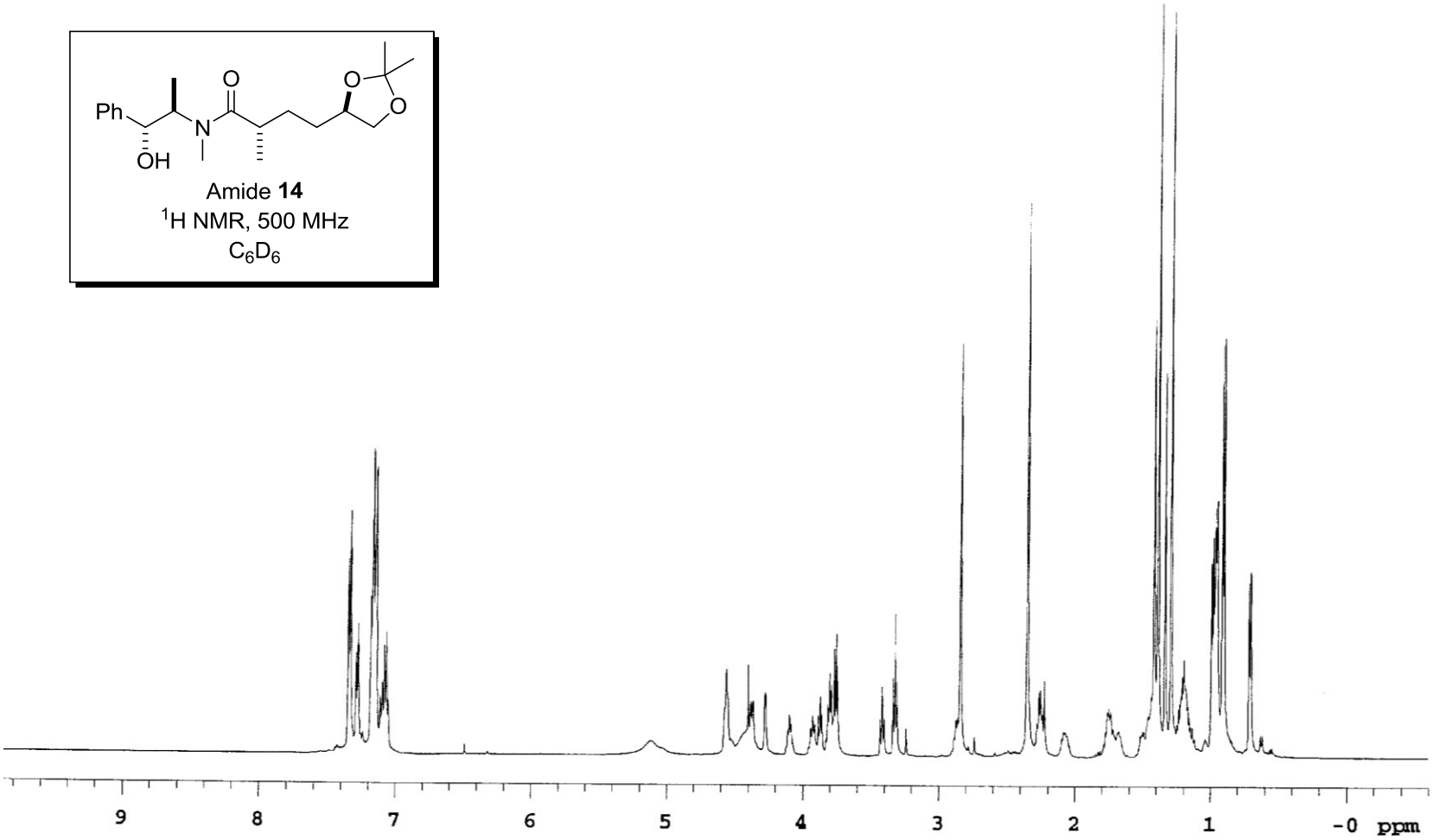


2,6-*trans*-Tetrahydropyran **8'**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$

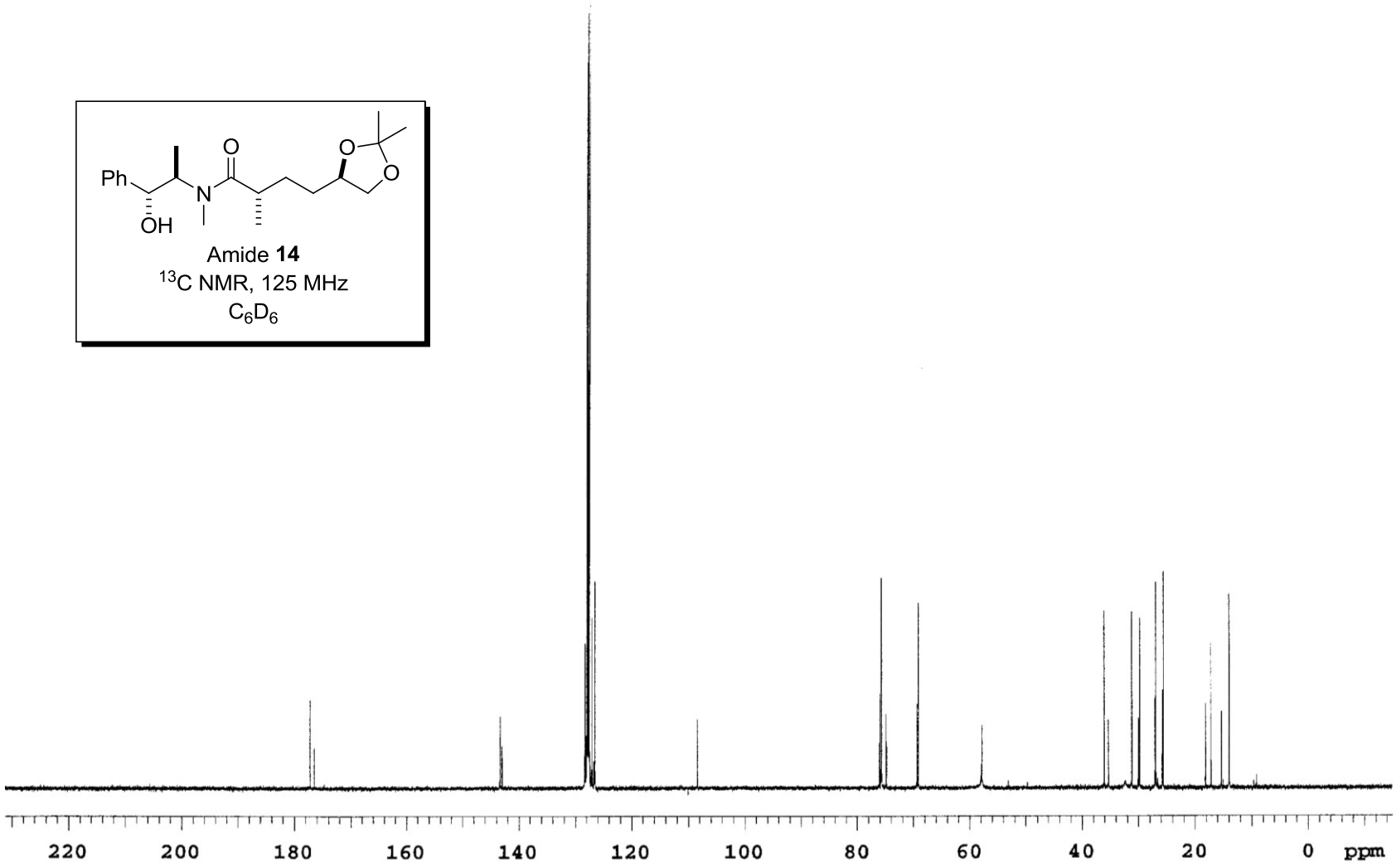


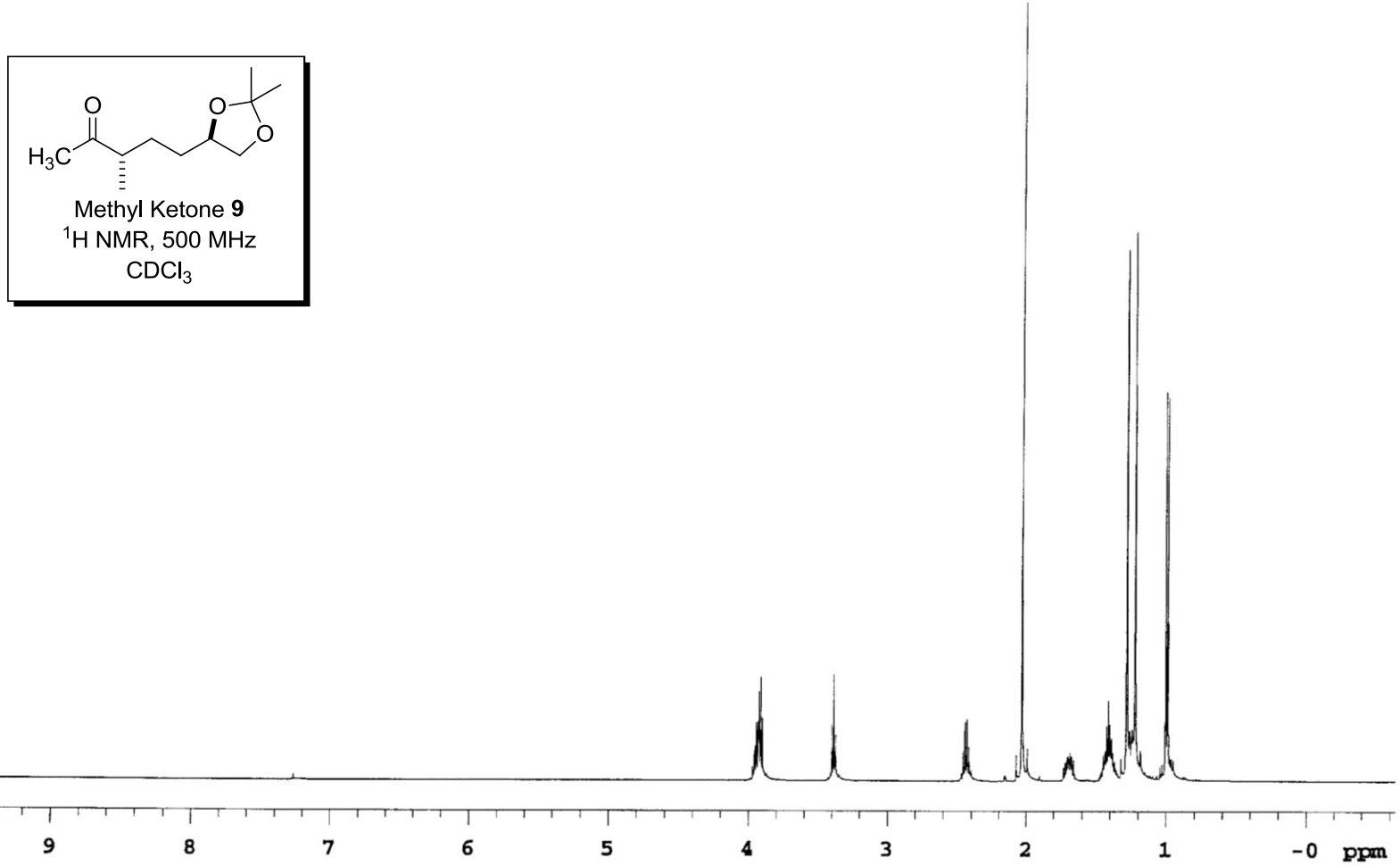


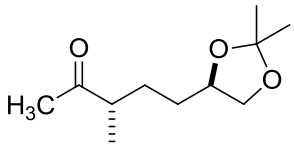
2,6-*trans*-Tetrahydropyran **8'**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$


Ph
OH
N
O
O
O
Amide 14
1H NMR, 500 MHz
C6D6
9
8
7
6
5
4
3
2
1
-0
ppm

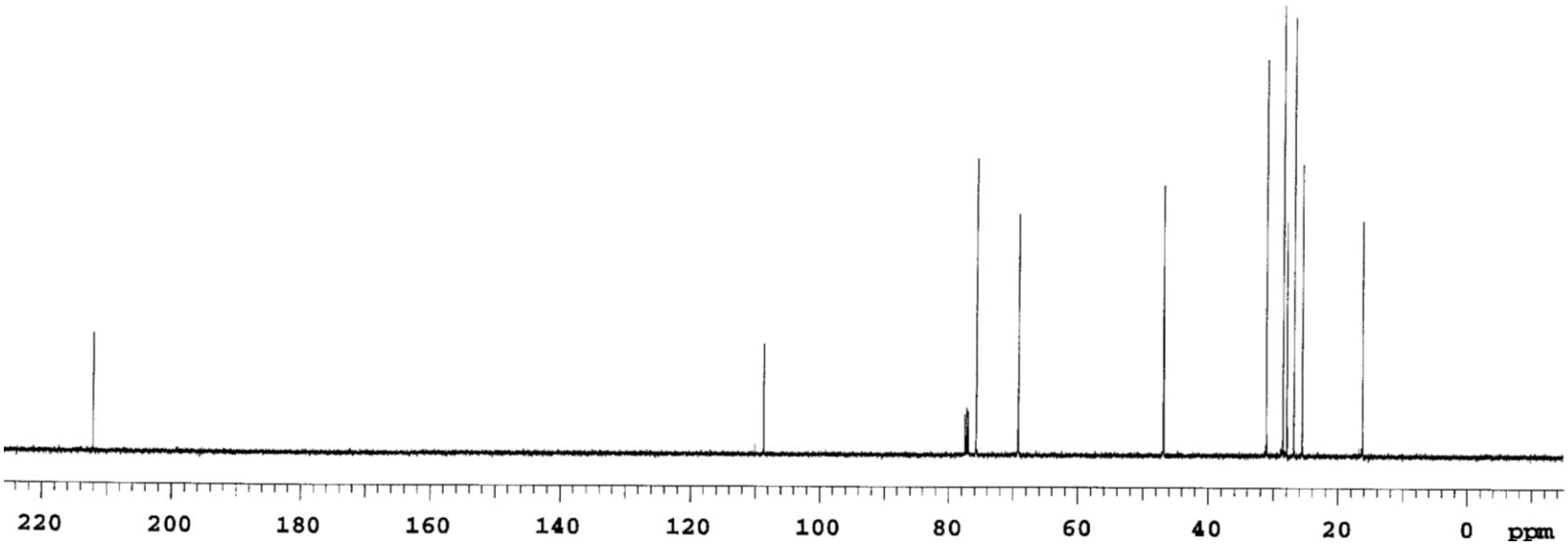
Amide **14**
^{13}C NMR, 125 MHz
C_6D_6

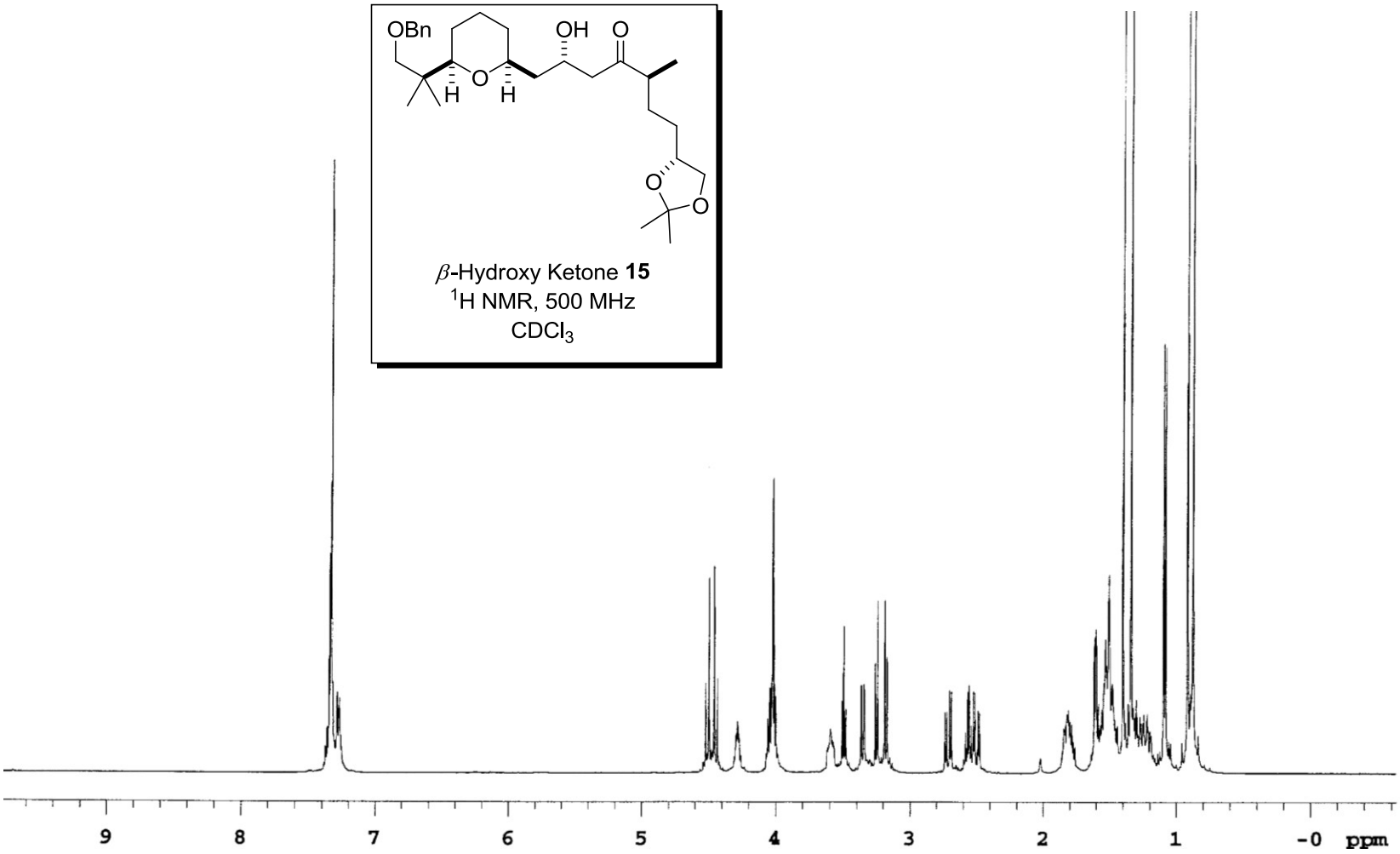


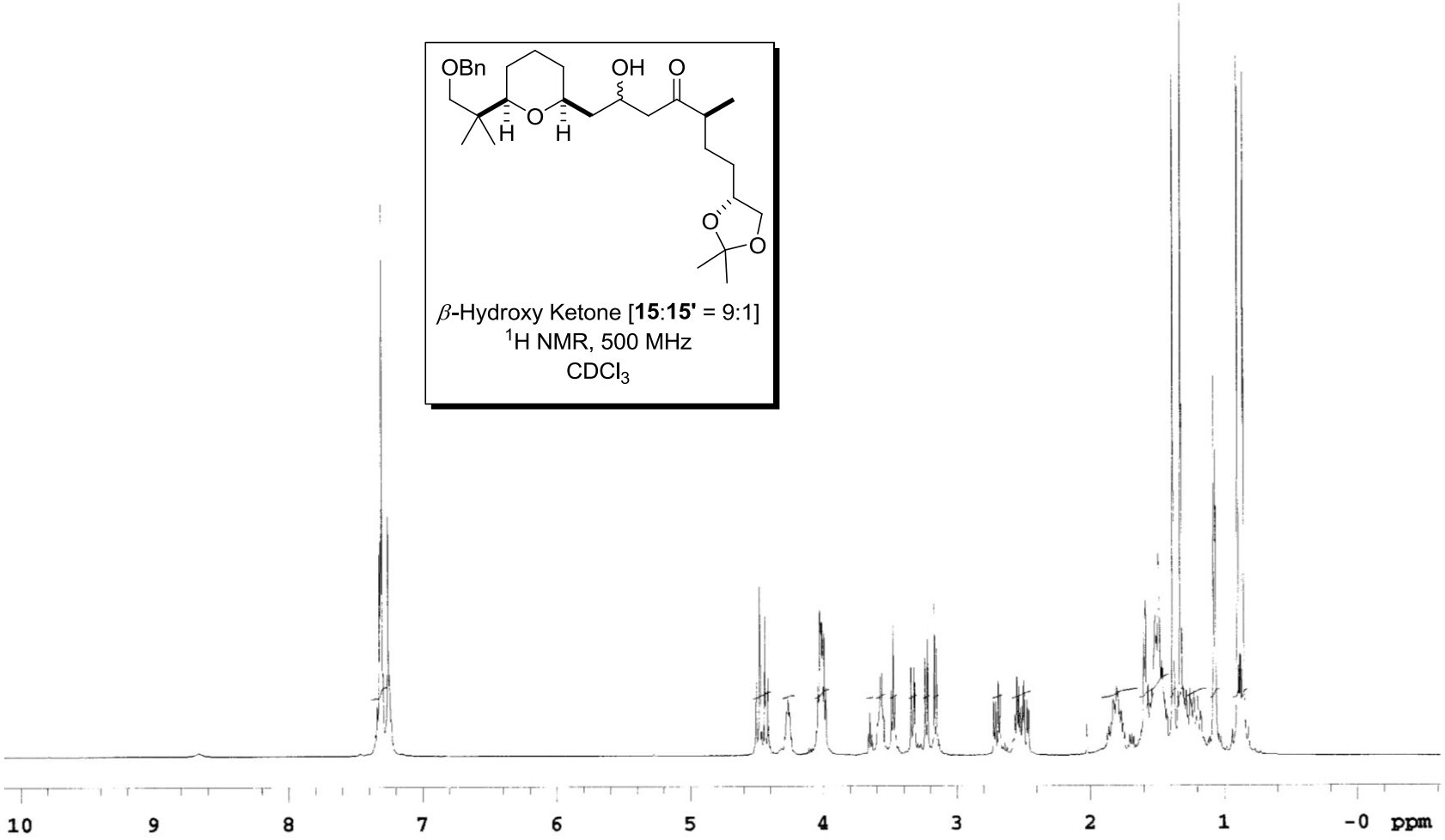

Methyl Ketone 9
1H NMR, 500 MHz
CDCl3
9
8
7
6
5
4
3
2
1
-0
ppm

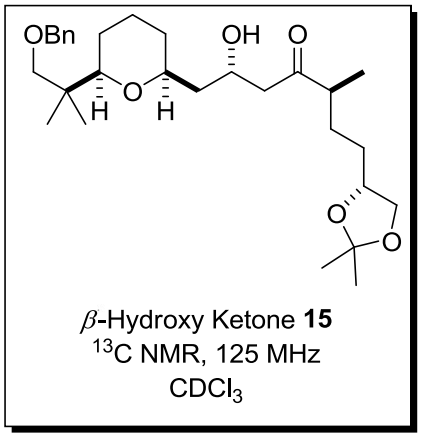


Methyl Ketone **9**
^{13}C NMR, 125 MHz
$CDCl_3$

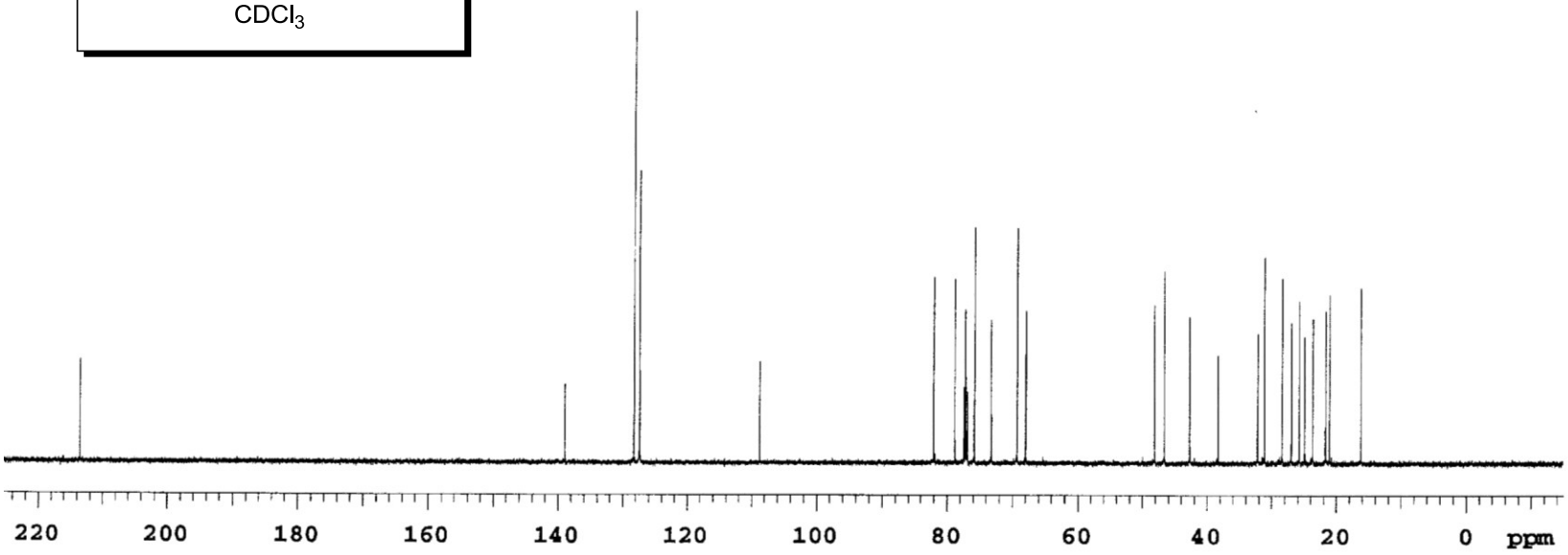


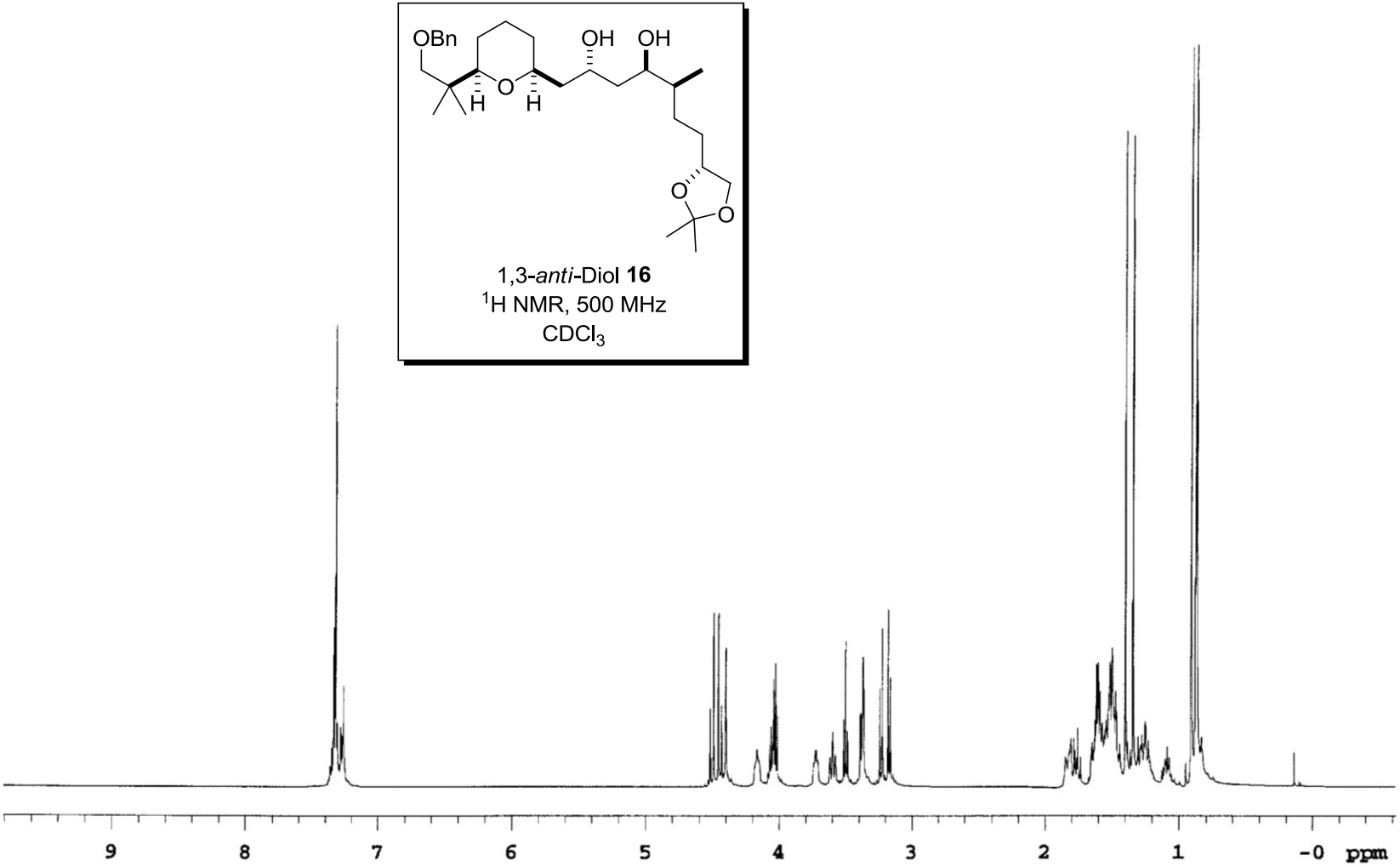

OBn
OH
O
H
O
H
O
O
β-Hydroxy Ketone 15
1H NMR, 500 MHz
CDCl3
9
8
7
6
5
4
3
2
1
-0
ppm

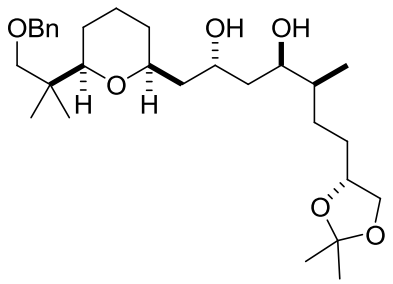

OBn
OH
O
O
H
H
O
O
β-Hydroxy Ketone [15:15' = 9:1]
1H NMR, 500 MHz
CDCl3
10
9
8
7
6
5
4
3
2
1
-0
ppm



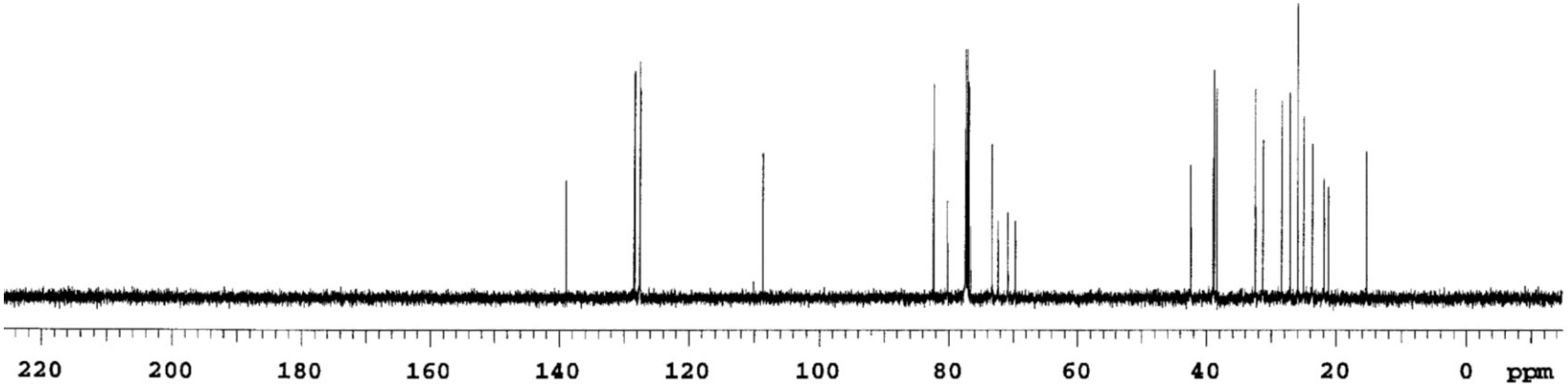
β-Hydroxy Ketone **15**
^{13}C NMR, 125 MHz
$CDCl_3$

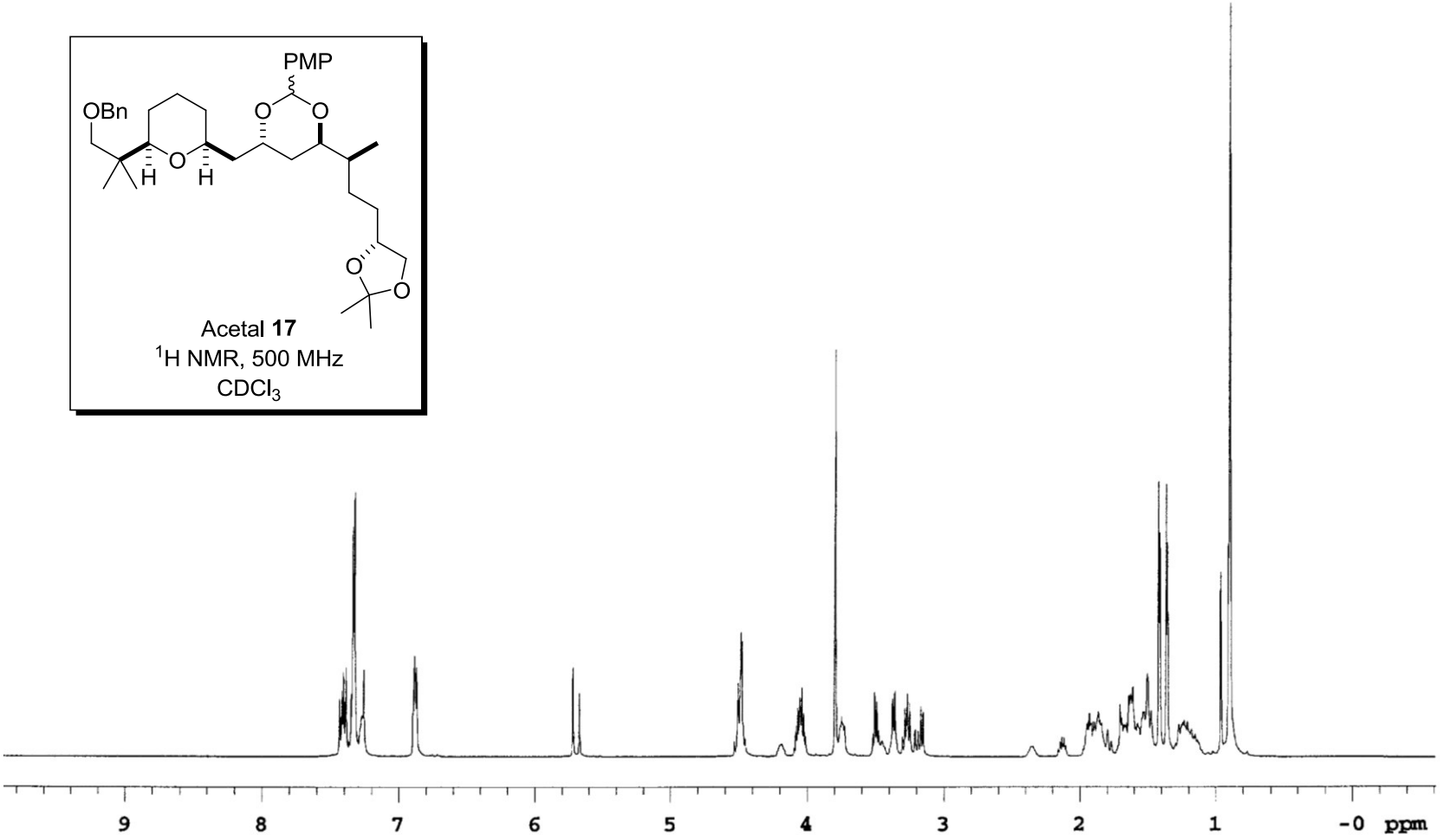


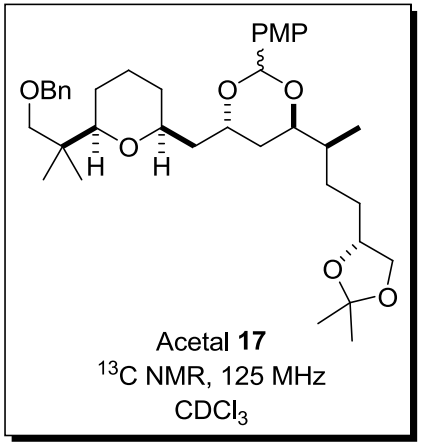

OBn
OH
OH
O
H
H
O
O
1,3-*anti*-Diol **16**
^{1}H NMR, 500 MHz
$CDCl_3$
9
8
7
6
5
4
3
2
1
-0
ppm



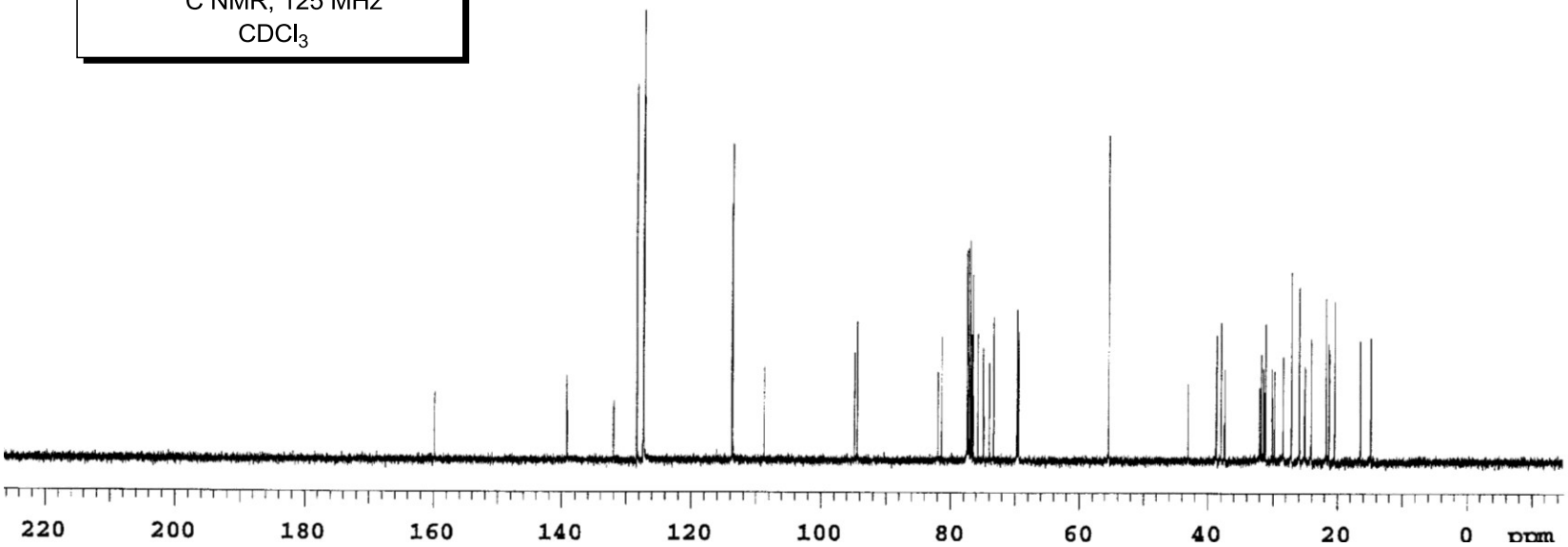
1,3-*anti*-Diol **16**
^{13}C NMR, 125 MHz
$CDCl_3$

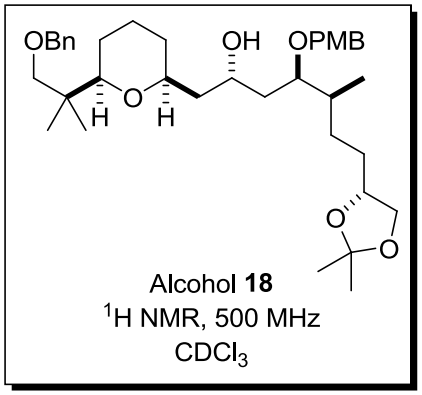



PMP
OBn
O
O
O
H
H
O
O
Acetal 17
1H NMR, 500 MHz
CDCl3
9
8
7
6
5
4
3
2
1
-0
ppm

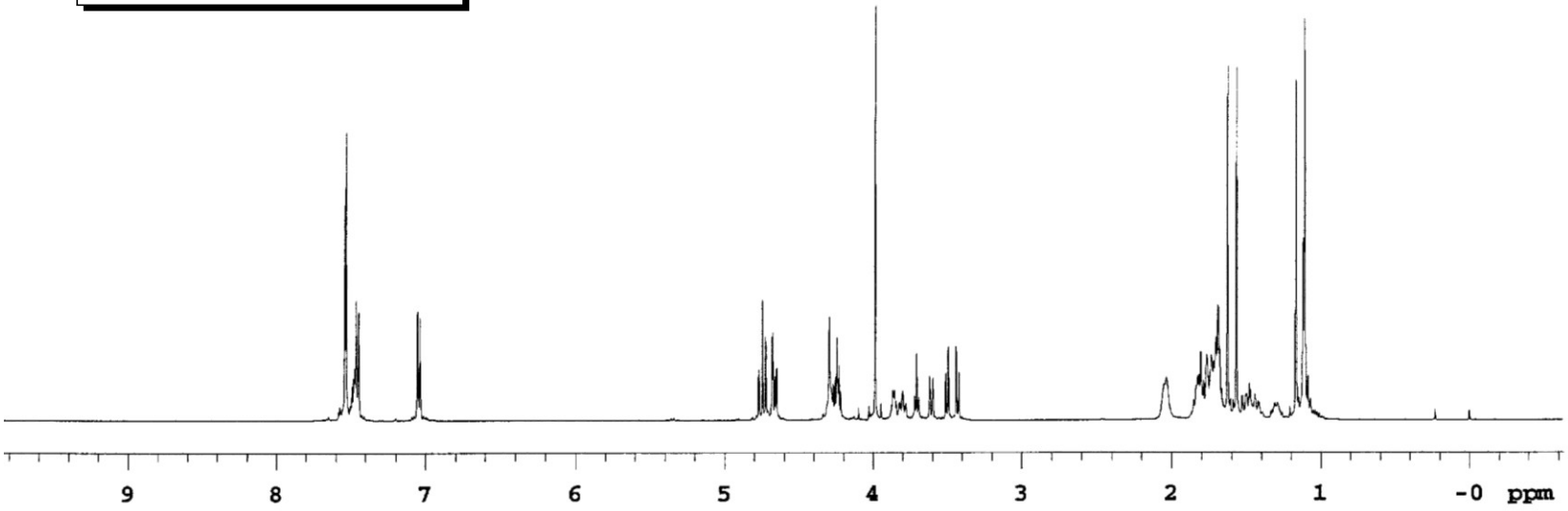


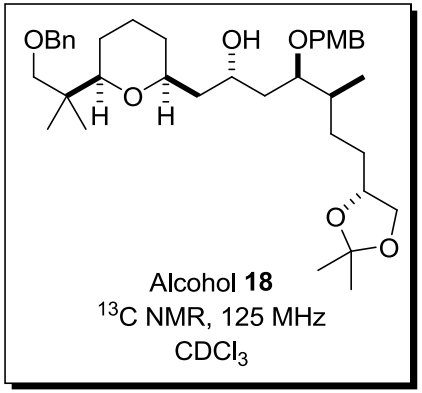
Acetal **17**
^{13}C NMR, 125 MHz
$CDCl_3$



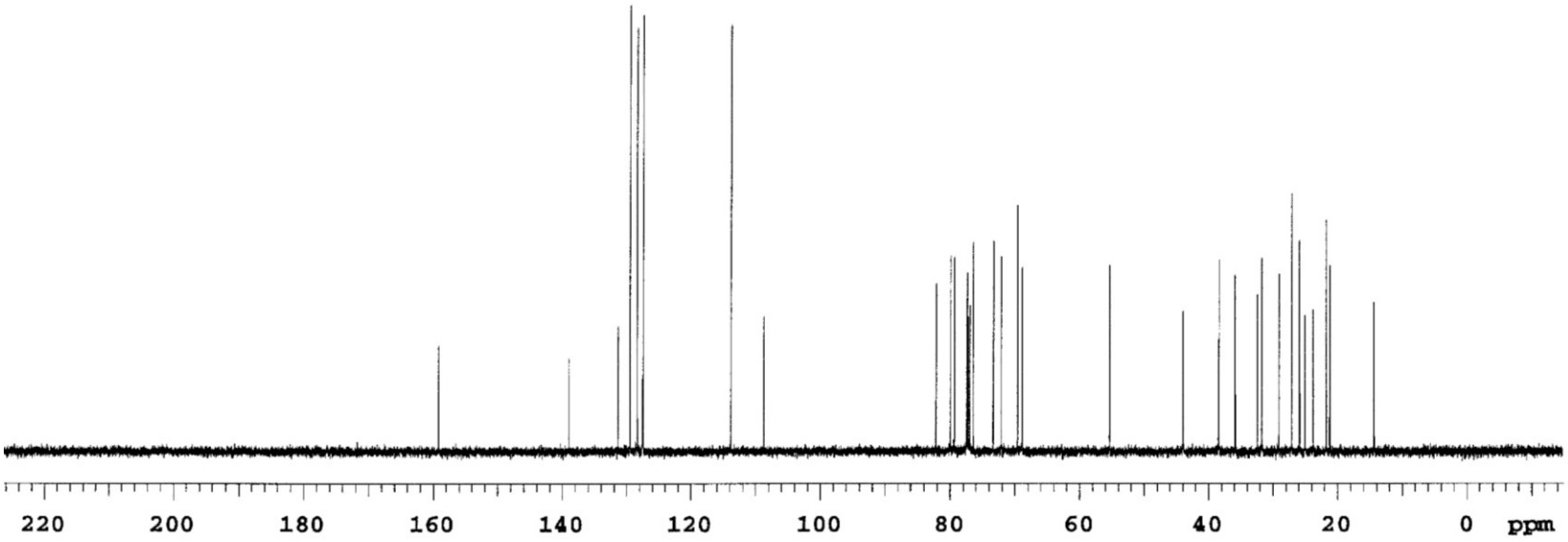


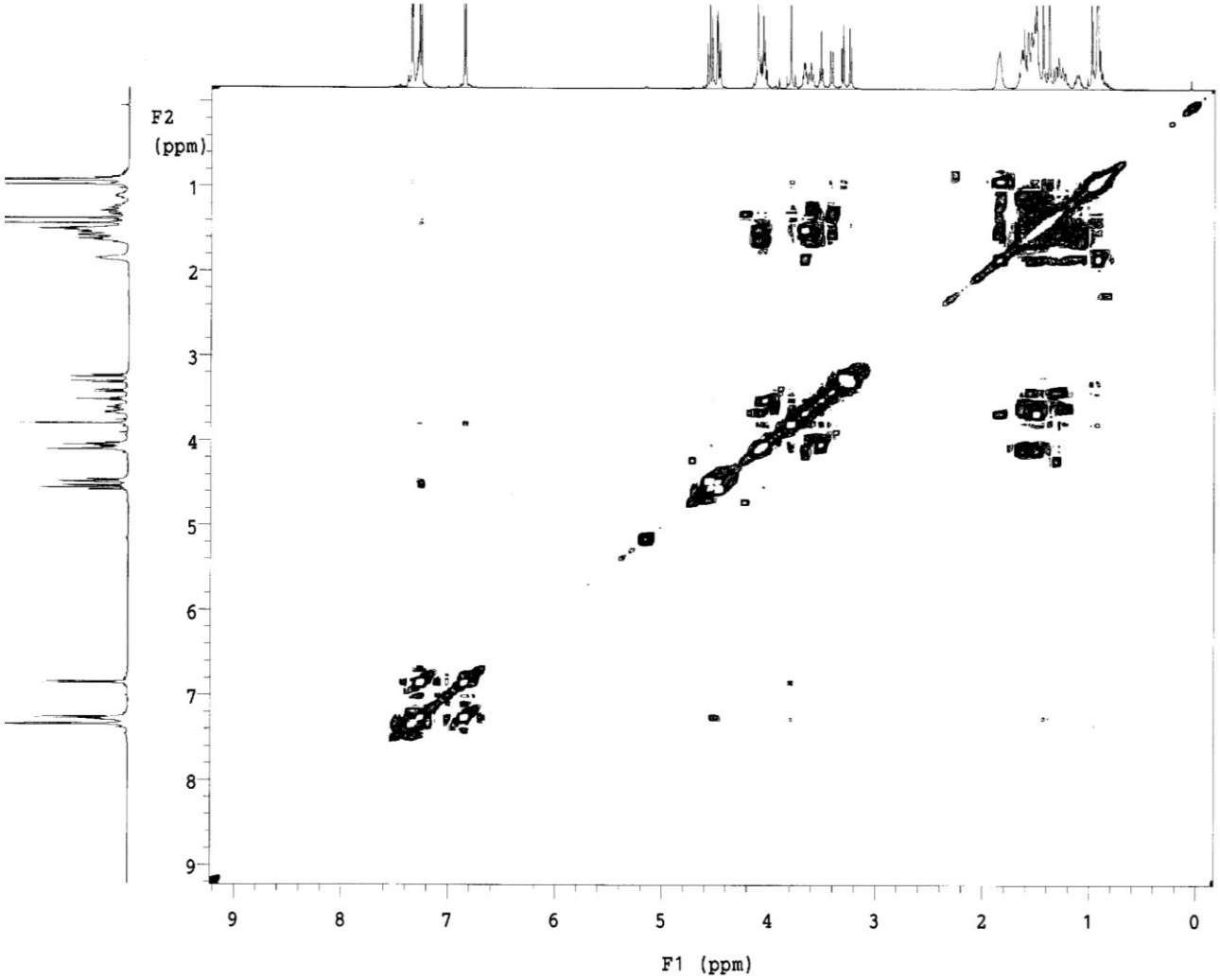
Alcohol **18**
^{1}H NMR, 500 MHz
$CDCl_3$

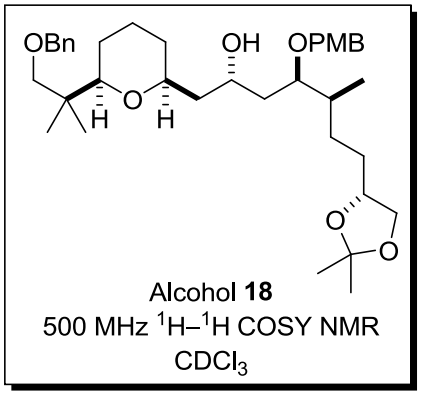




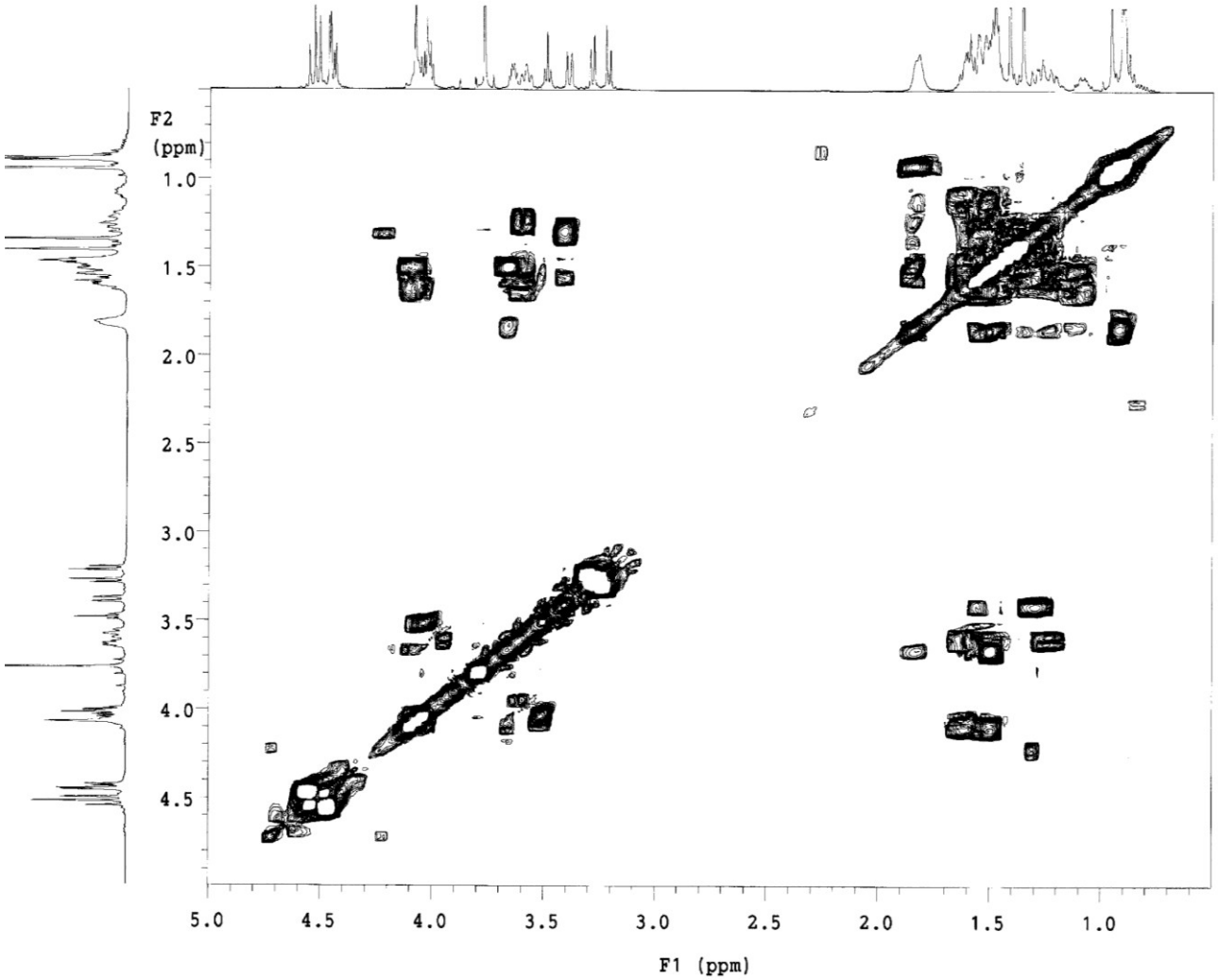
Alcohol **18**
^{13}C NMR, 125 MHz
$CDCl_3$

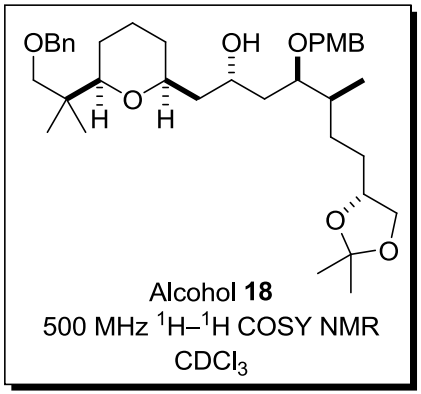




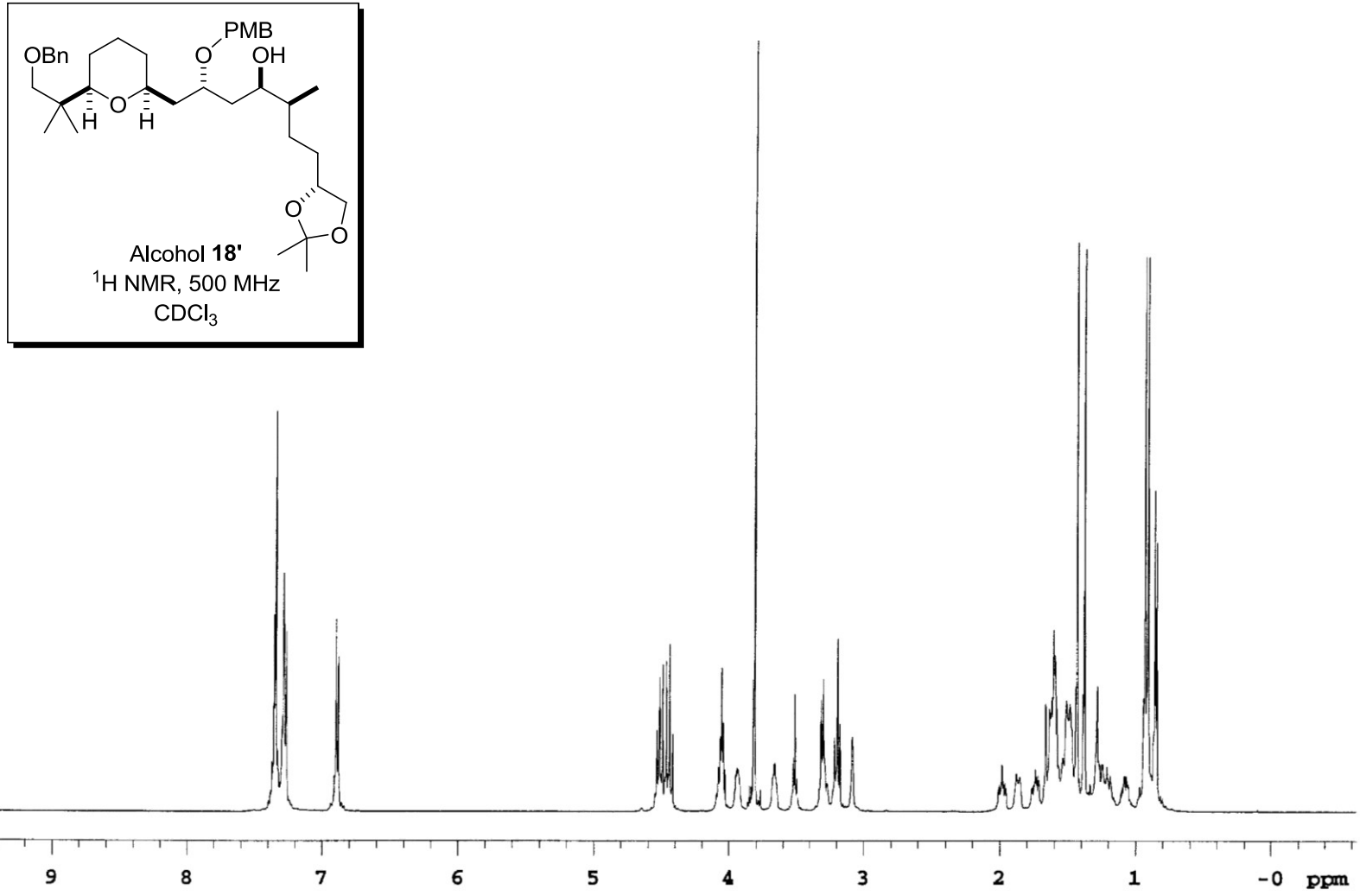


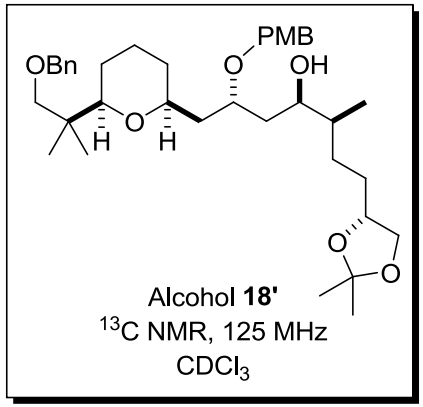
Alcohol **18**
500 MHz ^{1}H–^{1}H COSY NMR
$CDCl_3$

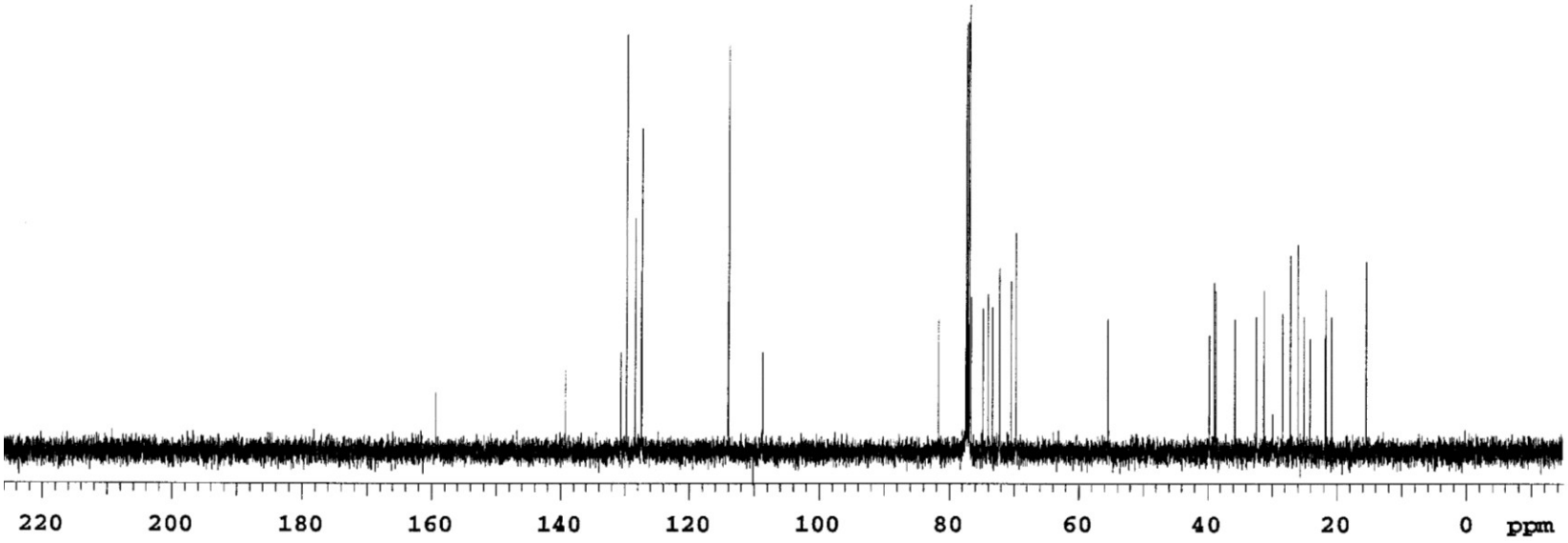


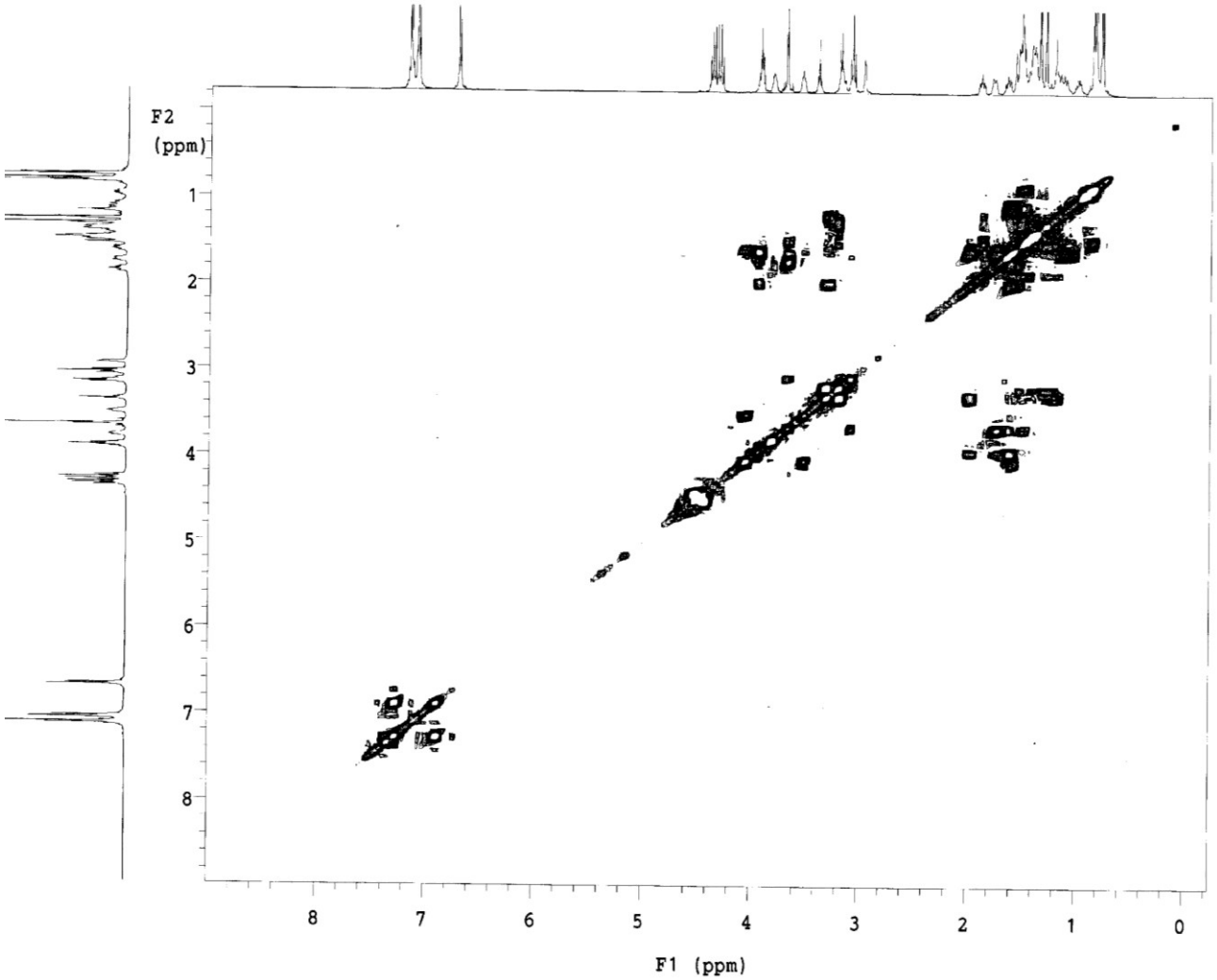


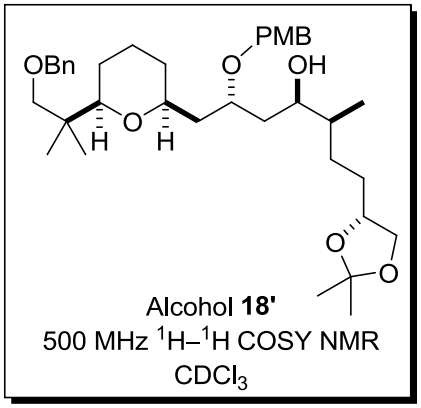
Alcohol **18**
500 MHz ^{1}H–^{1}H COSY NMR
$CDCl_3$


OBn
PMB
O
OH
O
H
H
O
O
Alcohol **18'**
^{1}H NMR, 500 MHz
$CDCl_3$
9
8
7
6
5
4
3
2
1
-0
ppm

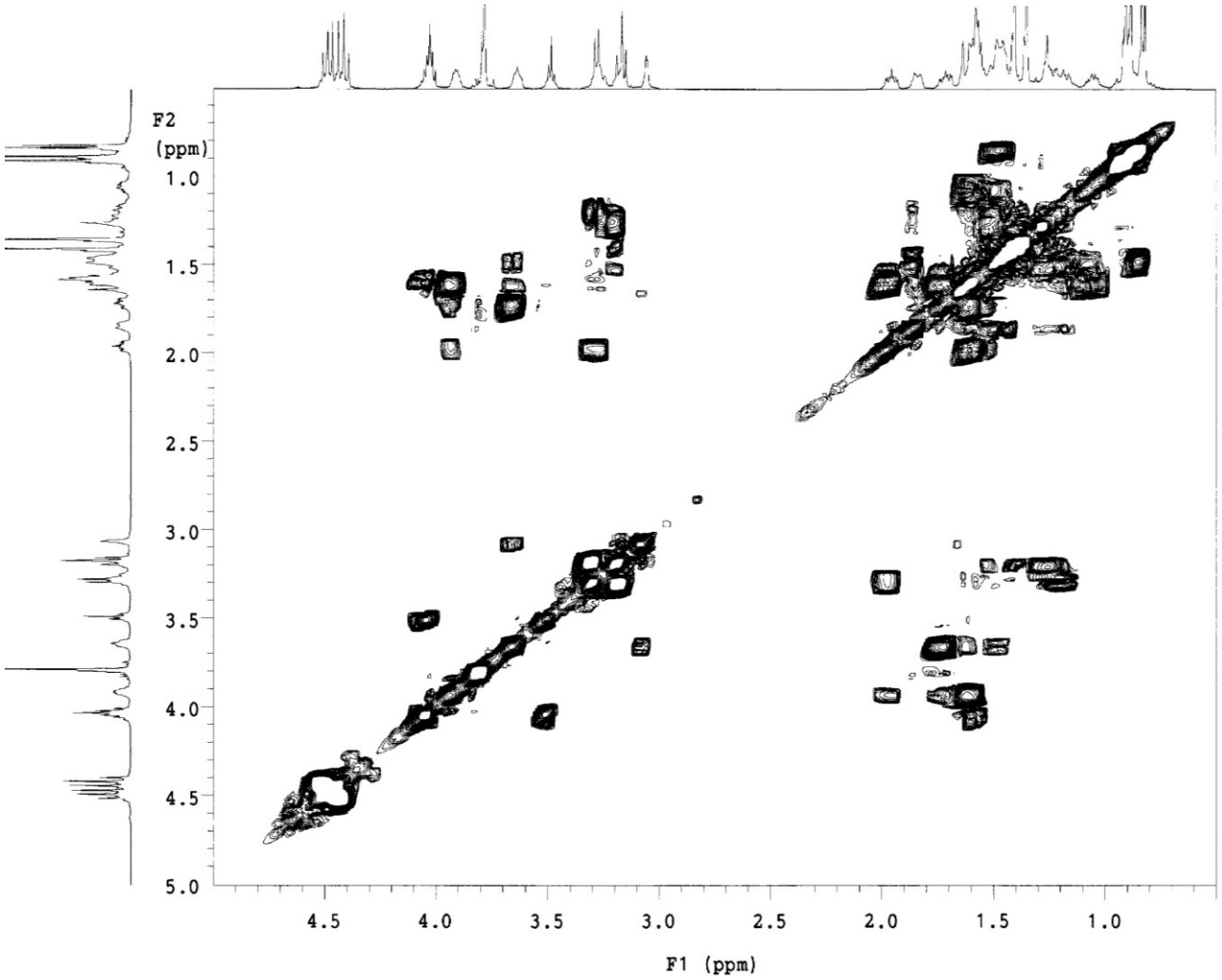

OBn
PMB
O
OH
O
H
H
O
O
Alcohol **18'**
^{13}C NMR, 125 MHz
$CDCl_3$

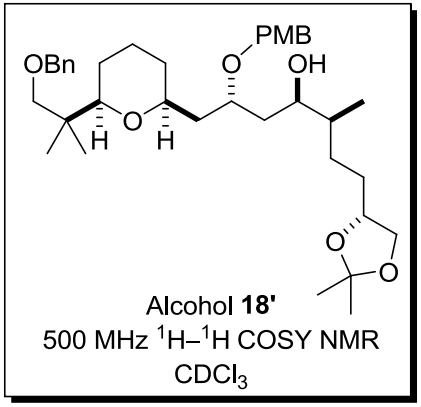

220
200
180
160
140
120
100
80
60
40
20
0
ppm



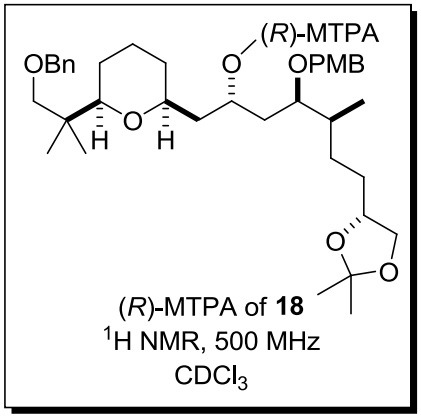


Alcohol **18'**
500 MHz ^{1}H–^{1}H COSY NMR
$CDCl_3$

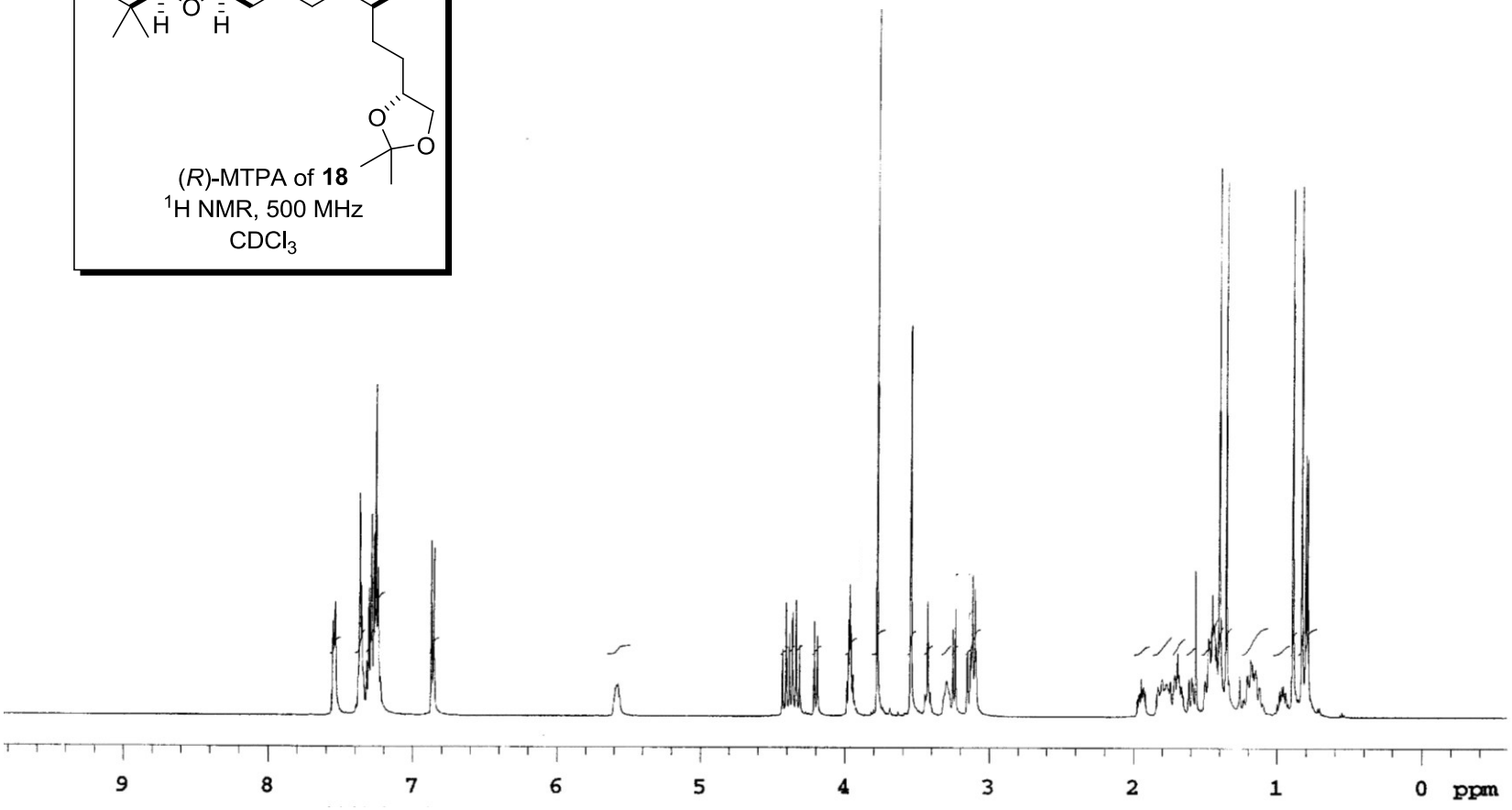


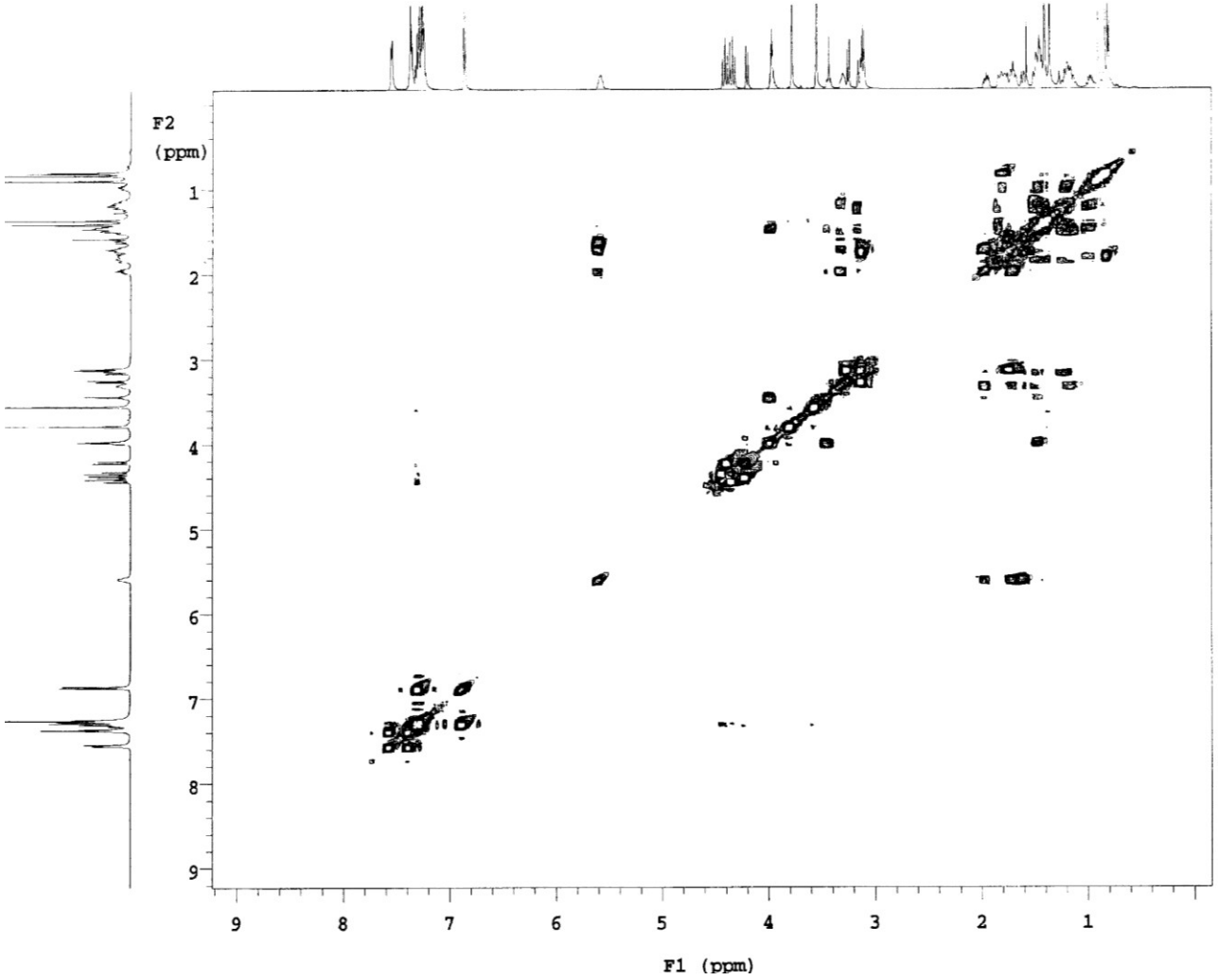


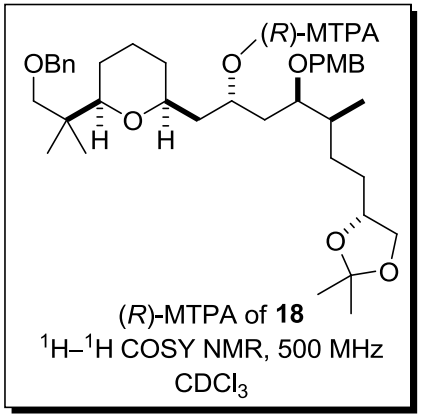
Alcohol **18'**
500 MHz ^{1}H–^{1}H COSY NMR
$CDCl_3$



(*R*)-MTPA of **18**
^{1}H NMR, 500 MHz
$CDCl_3$

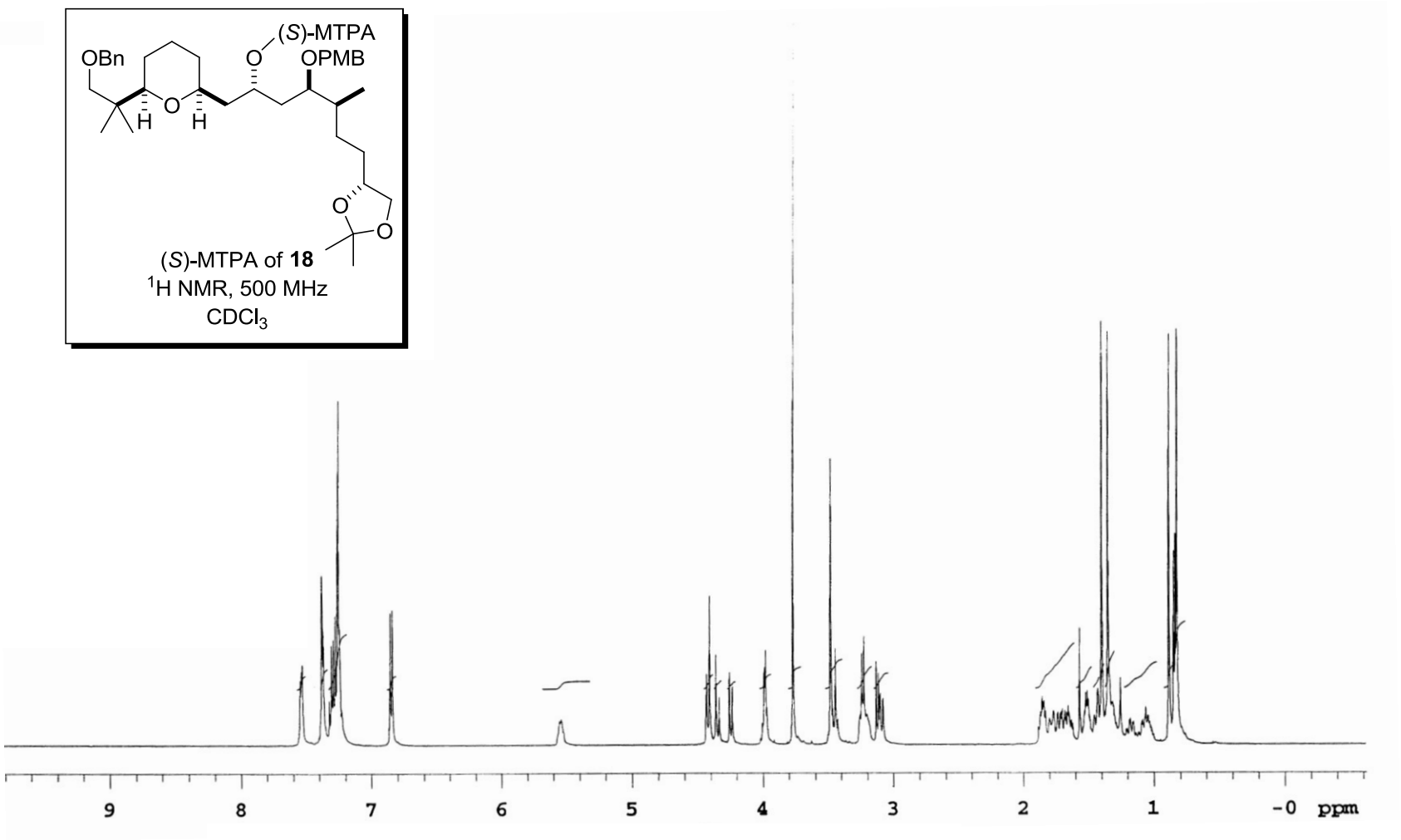


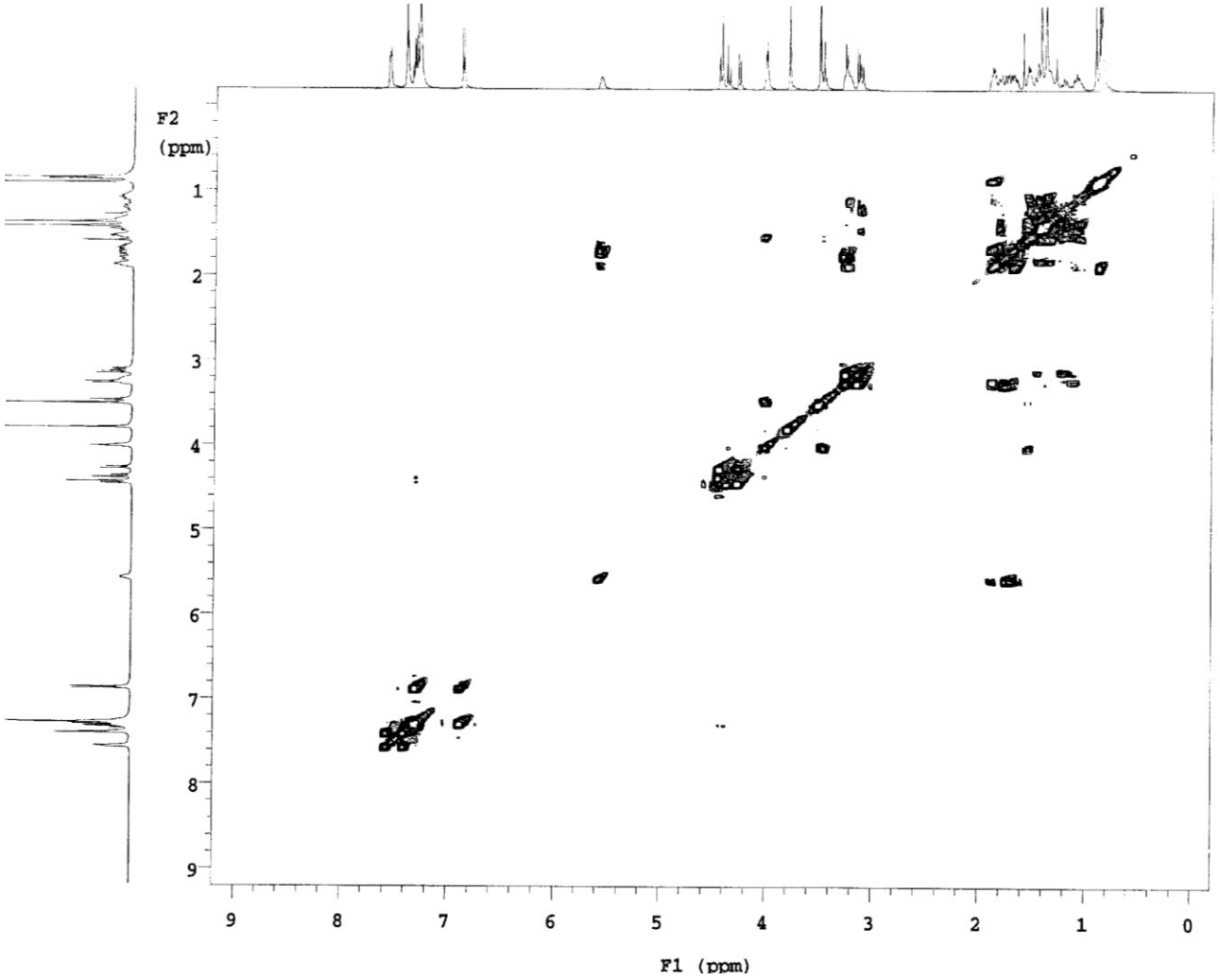


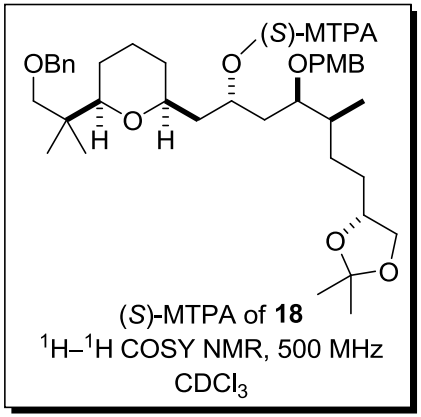


(*R*)-MTPA of **18**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$

(S)-MTPA
OBn
O
OPMB
H
O
H
O
O
(S)-MTPA of 18
1H NMR, 500 MHz
CDCl3


9
8
7
6
5
4
3
2
1
-0
ppm



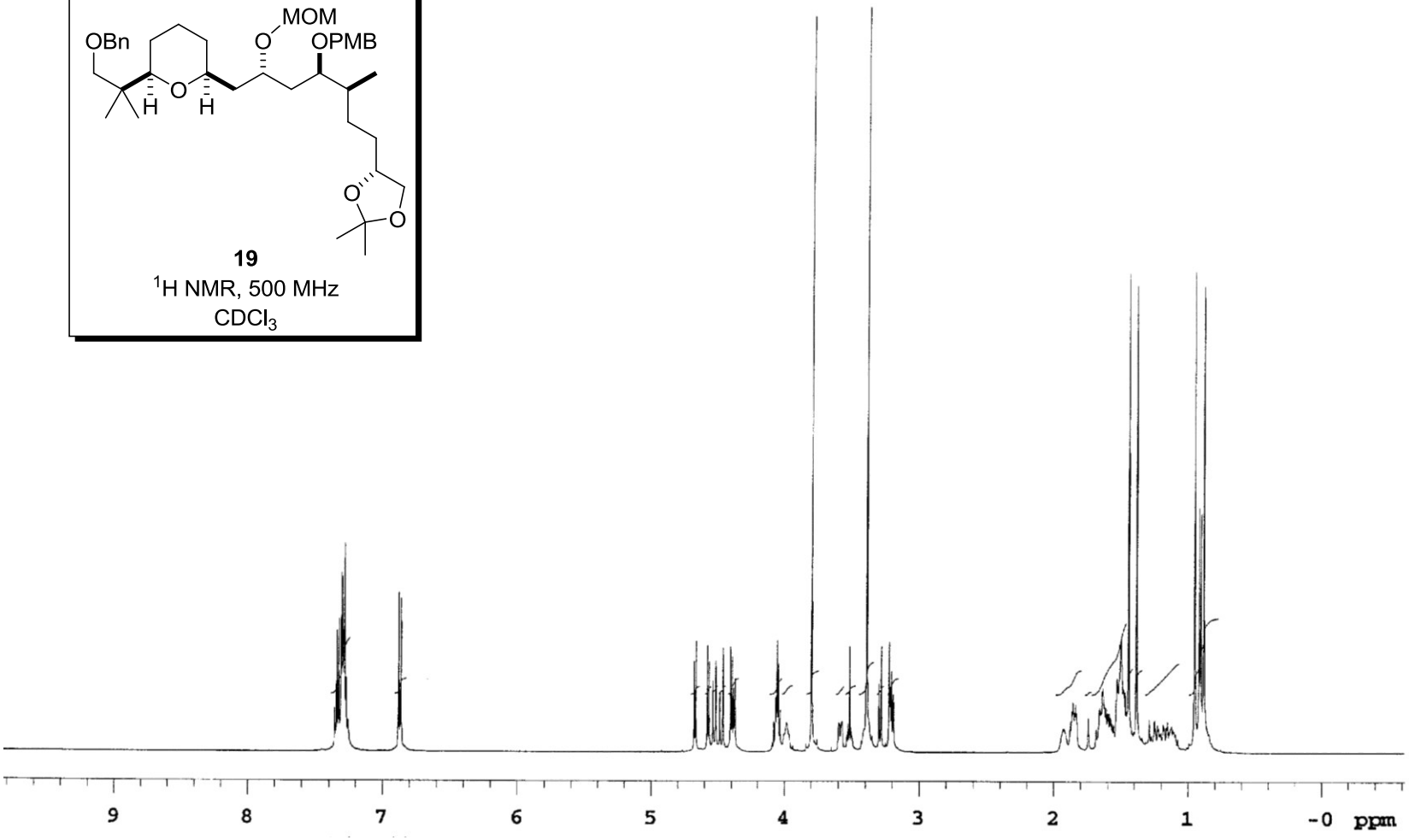


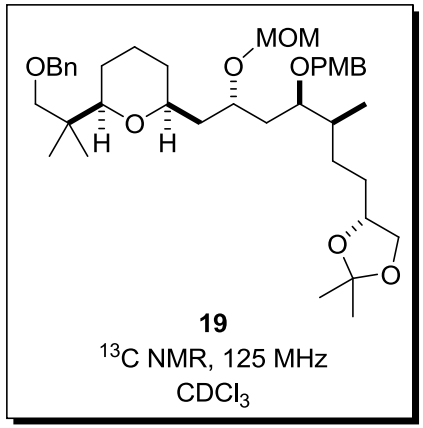
(*S*)-MTPA of **18**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$

19

^{1}H NMR, 500 MHz

$CDCl_3$

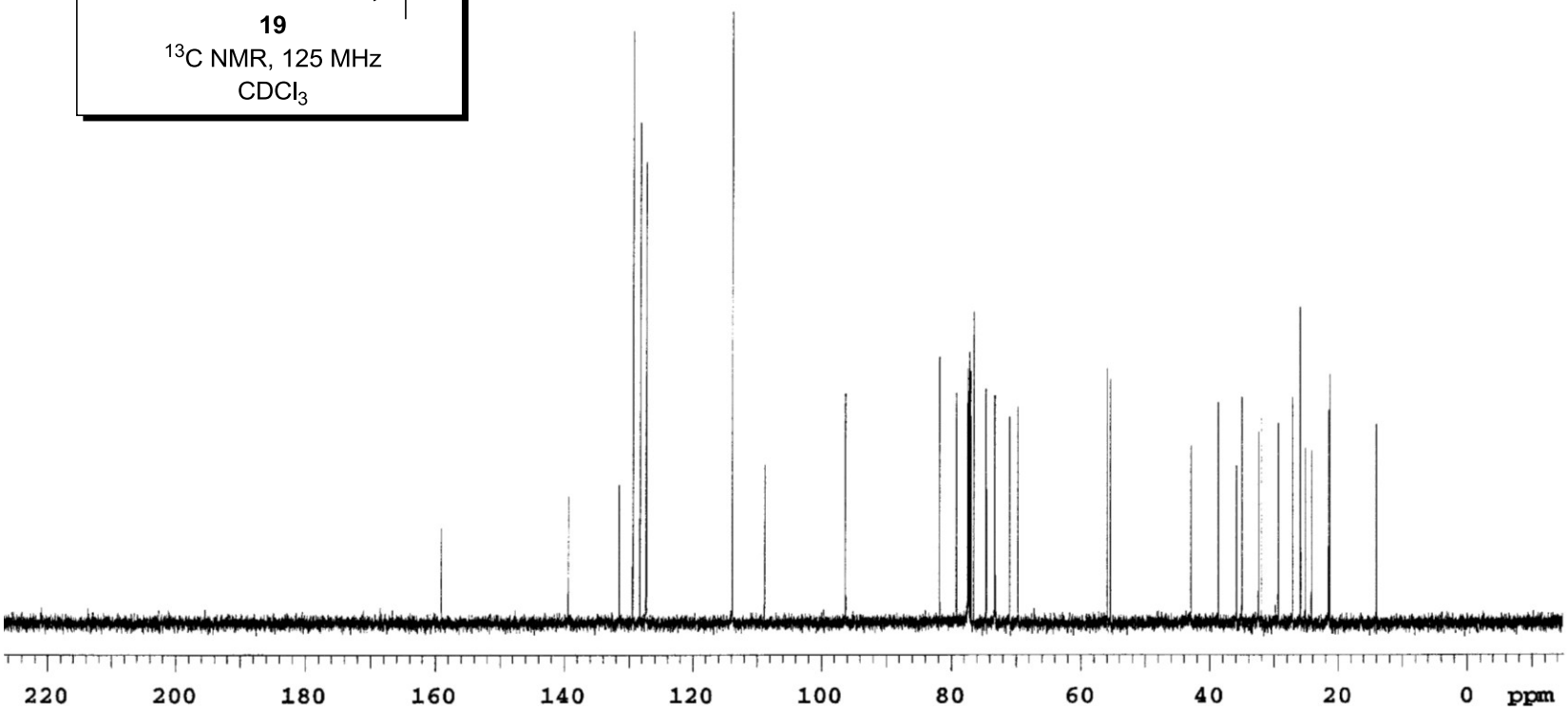




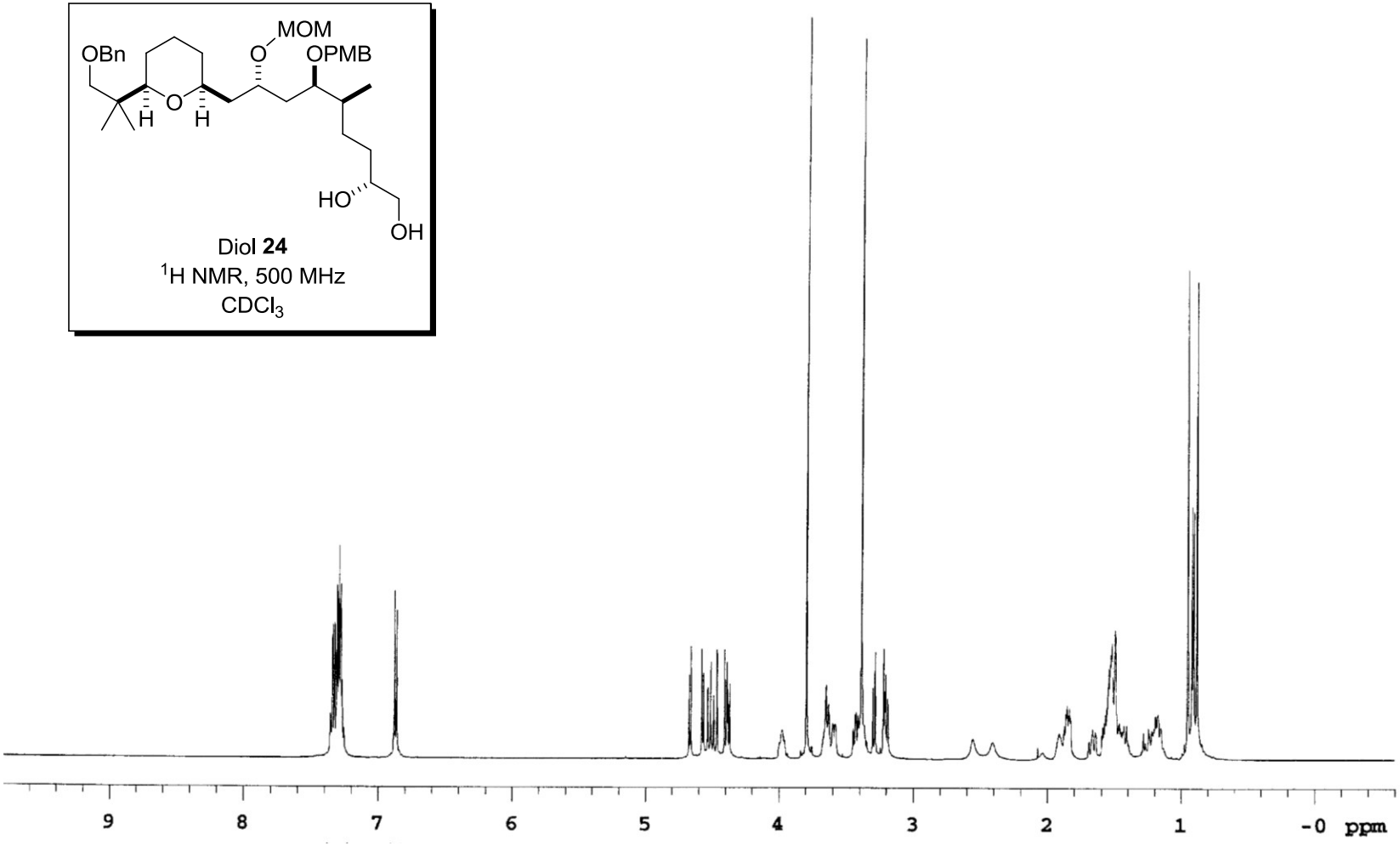
19

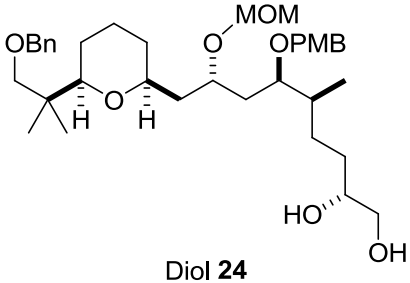
^{13}C NMR, 125 MHz

$CDCl_3$

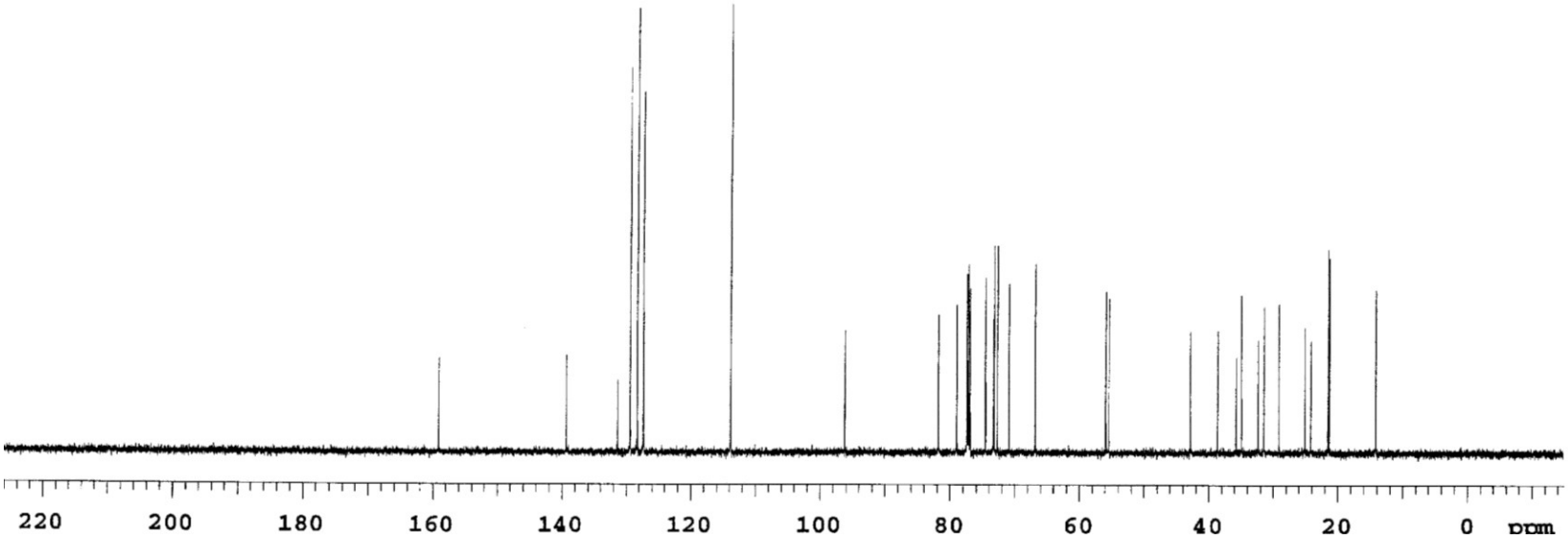


Diol **24**
^{1}H NMR, 500 MHz
$CDCl_3$

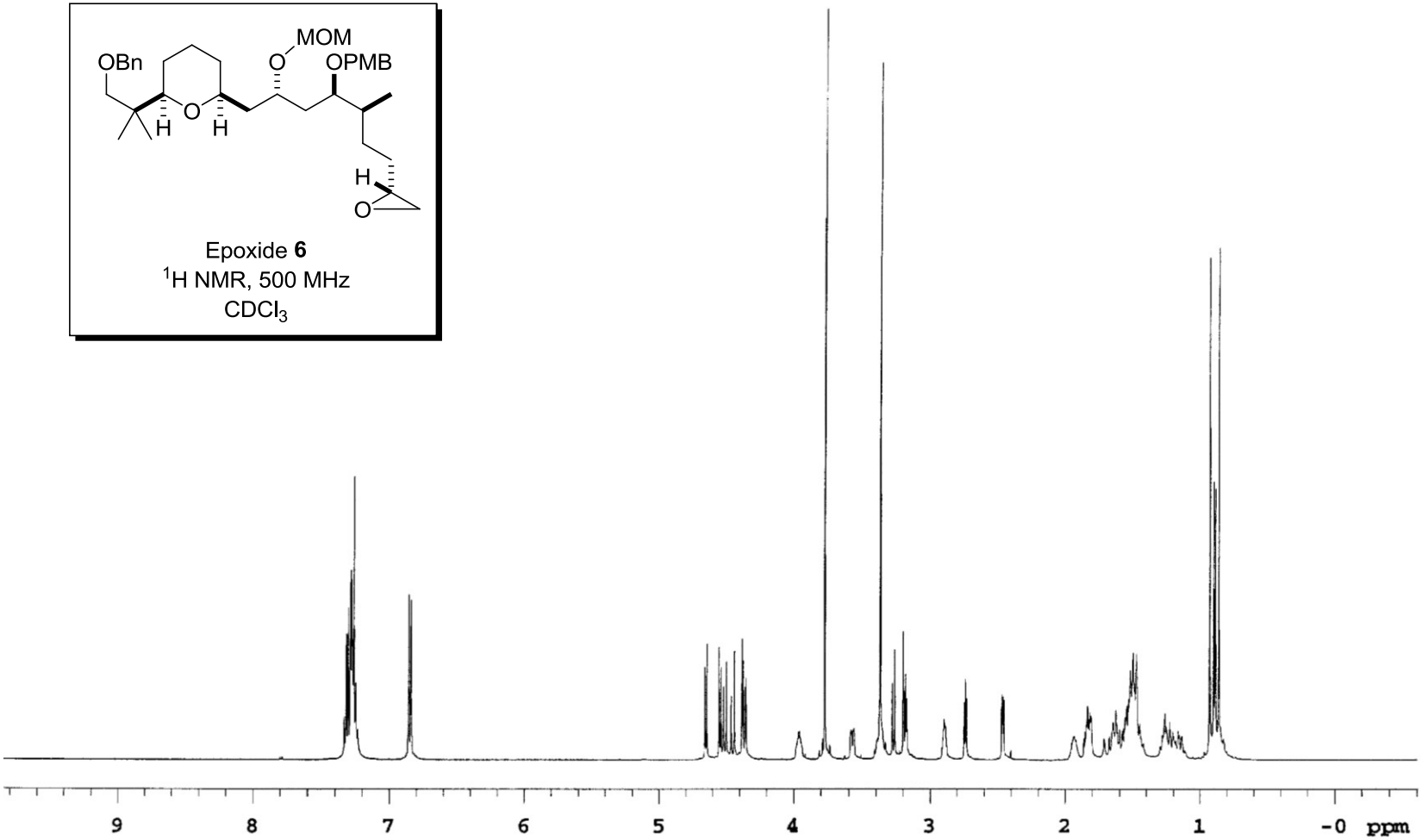


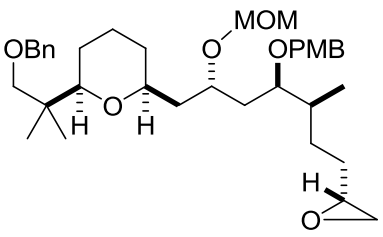


Diol **24**
^{13}C NMR, 125 MHz
$CDCl_3$

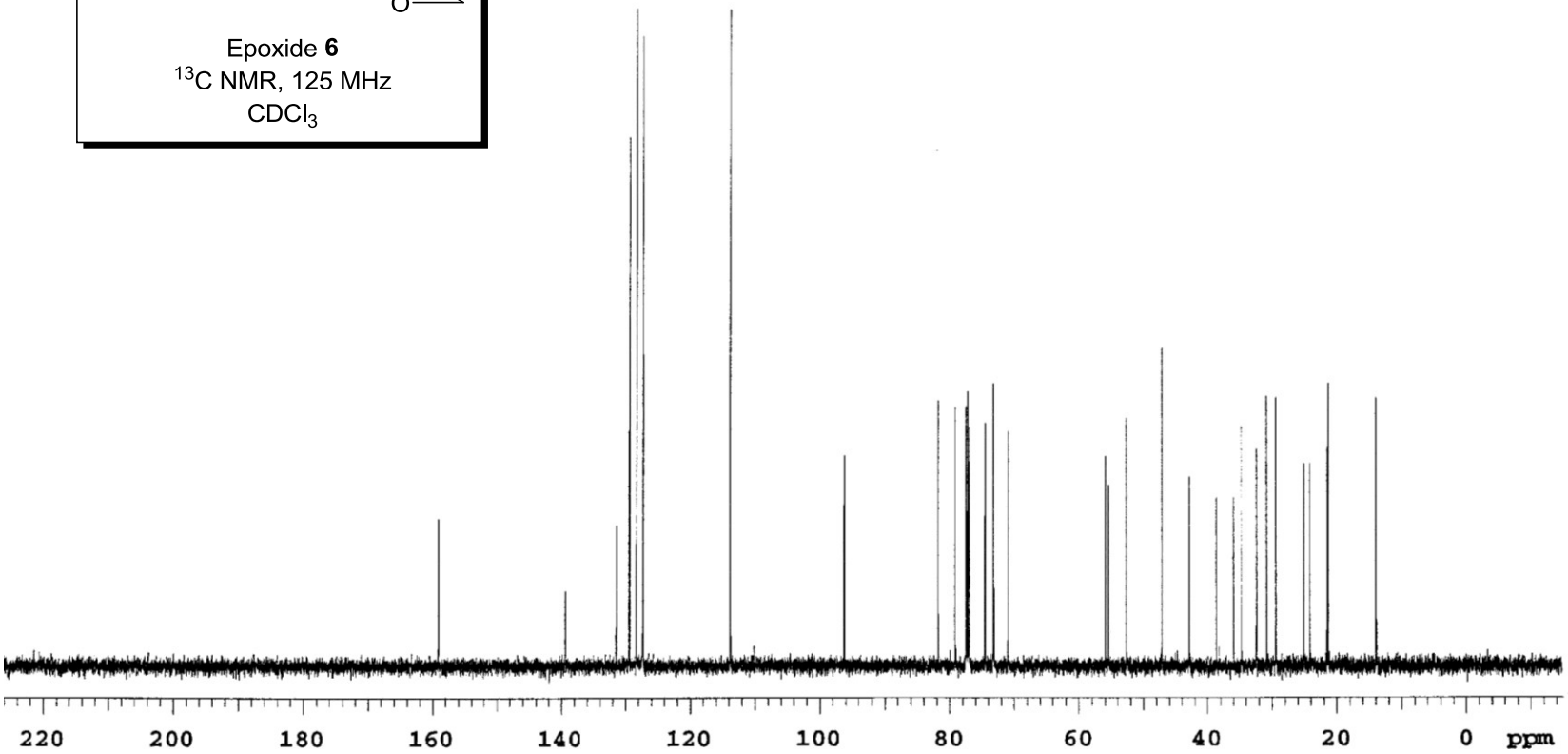


Epoxide **6**
^{1}H NMR, 500 MHz
$CDCl_3$

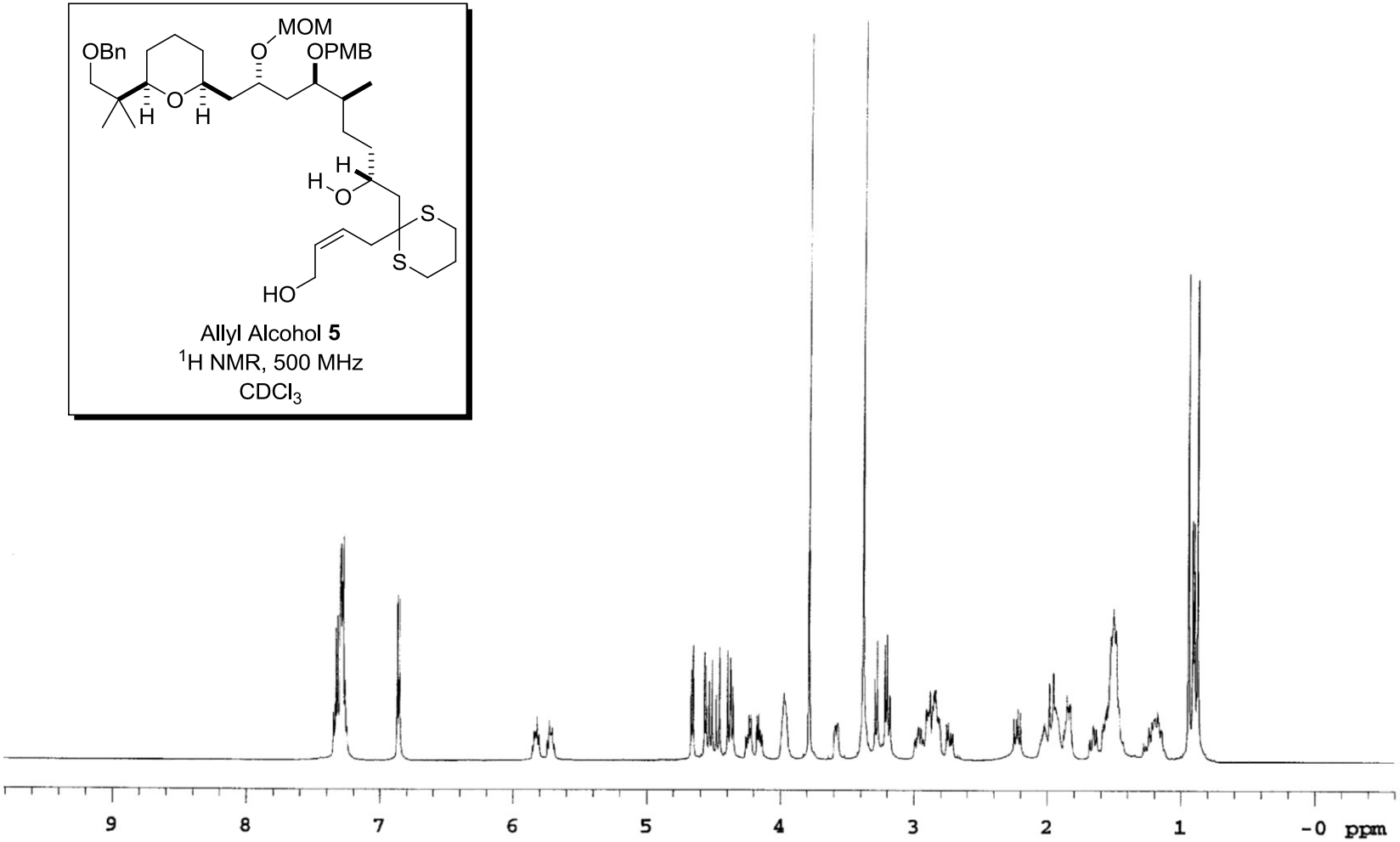


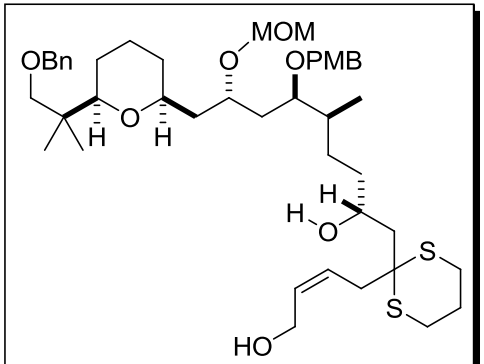


Epoxide **6**
^{13}C NMR, 125 MHz
$CDCl_3$

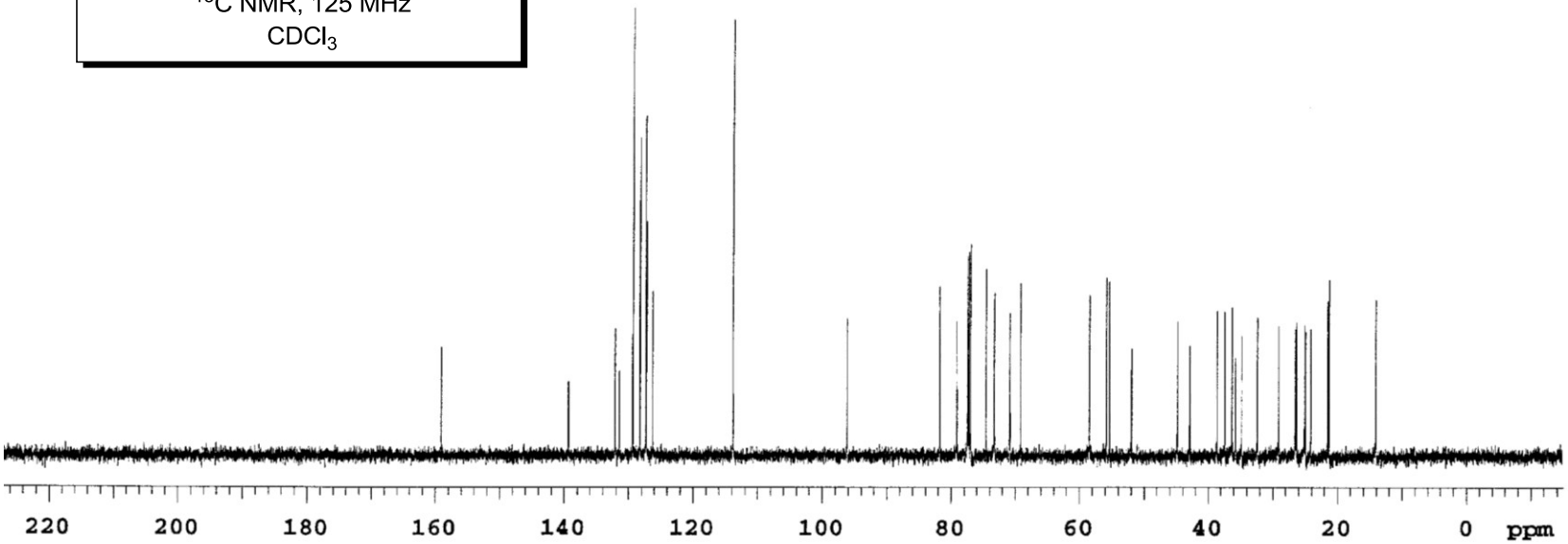


Allyl Alcohol **5**
^{1}H NMR, 500 MHz
$CDCl_3$

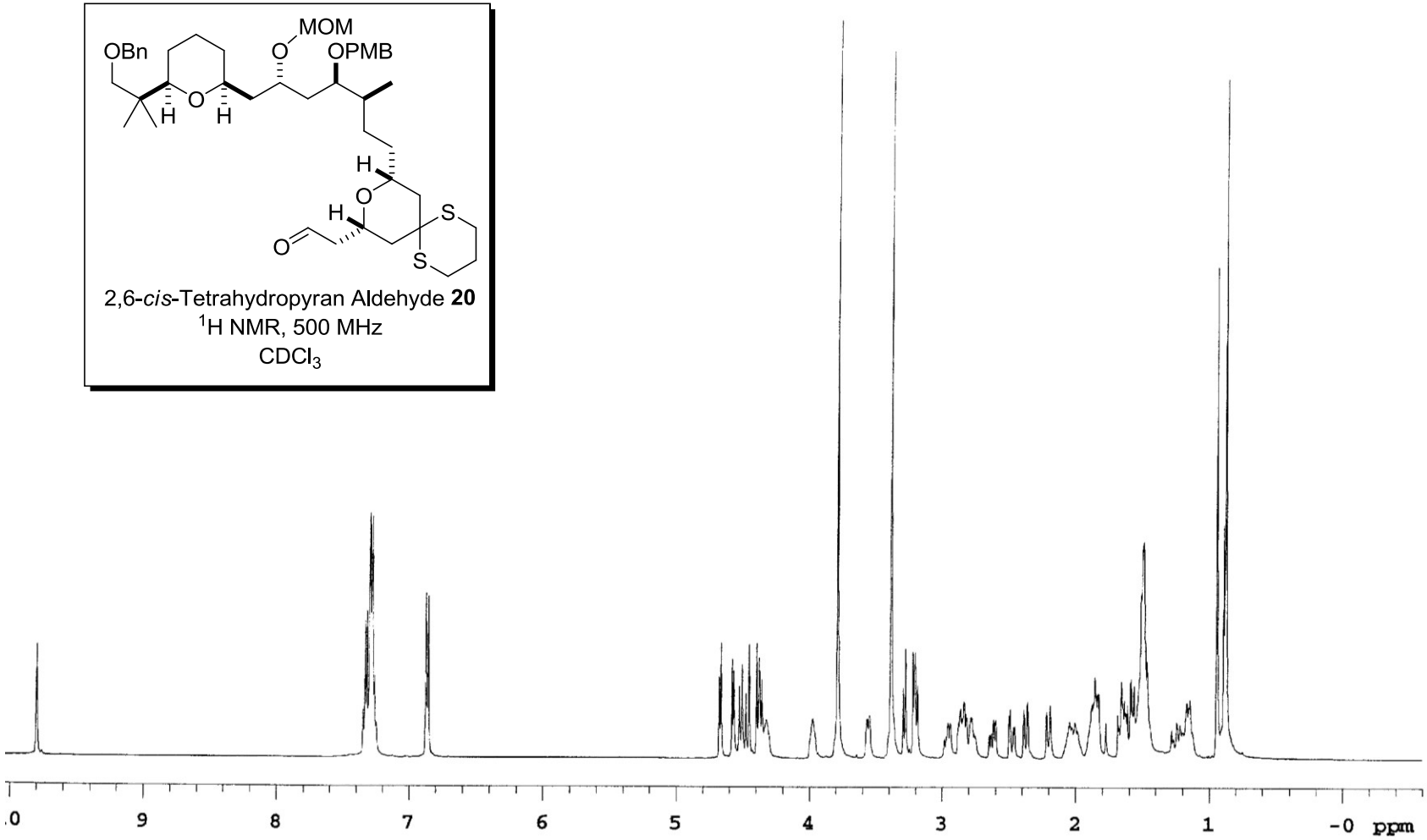


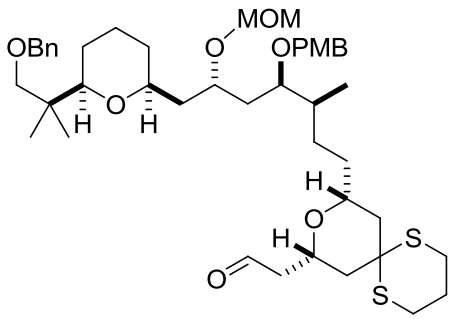


Allyl Alcohol **5**
^{13}C NMR, 125 MHz
$CDCl_3$

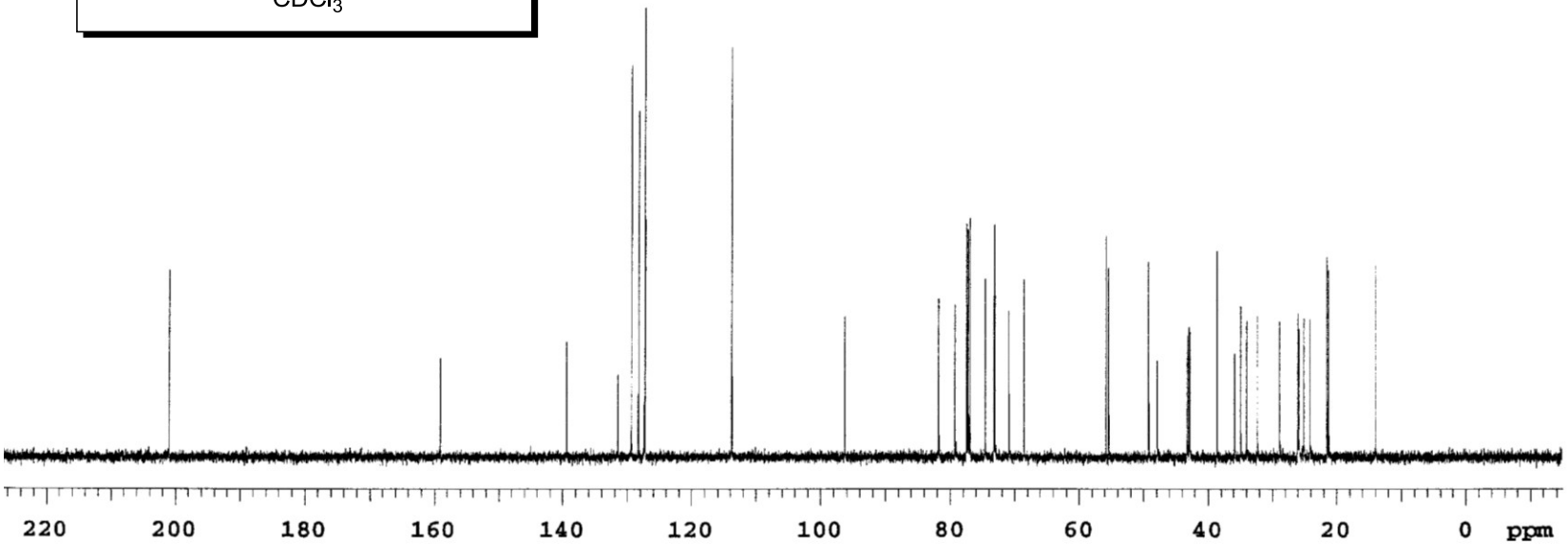


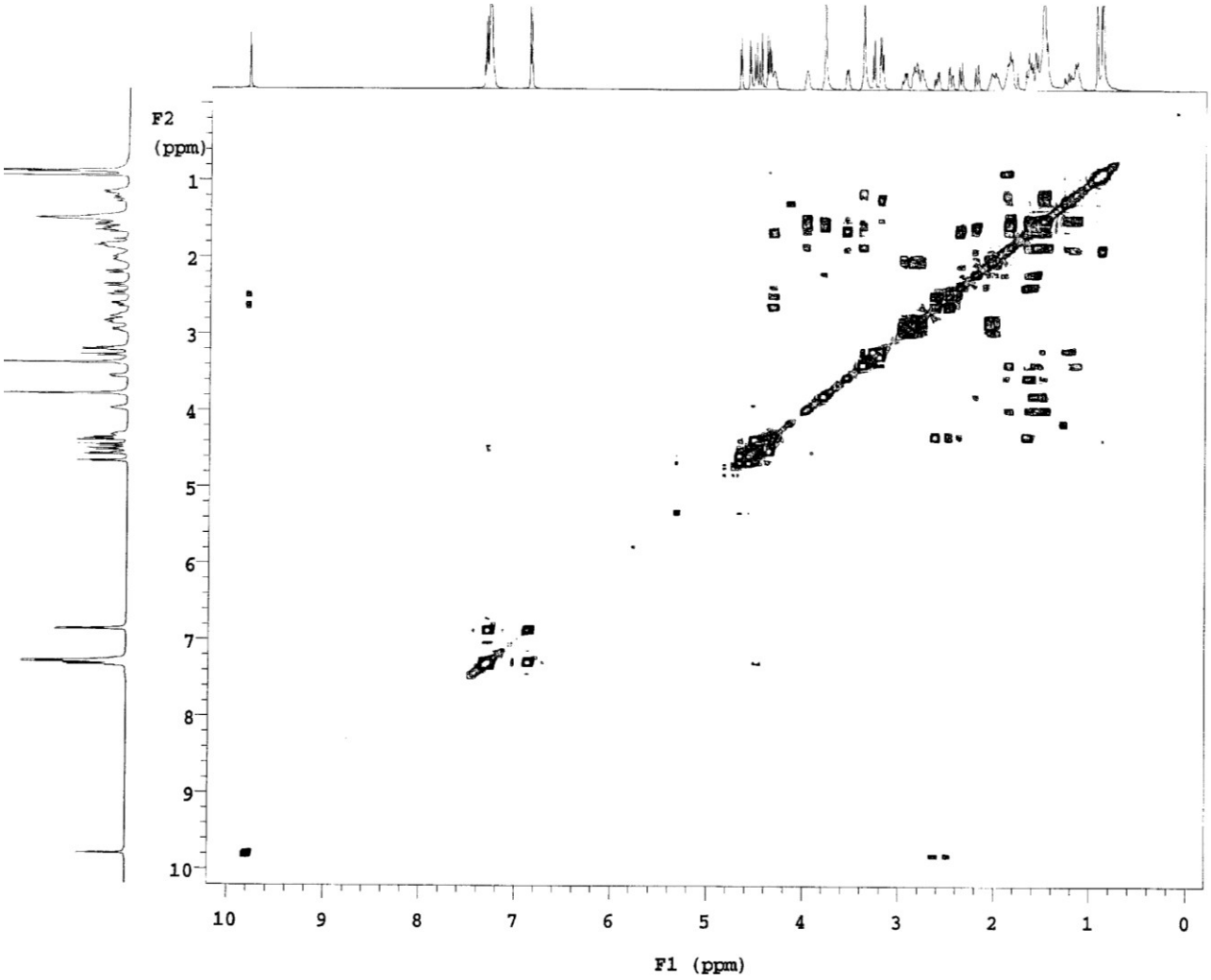
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{1}H NMR, 500 MHz
$CDCl_3$

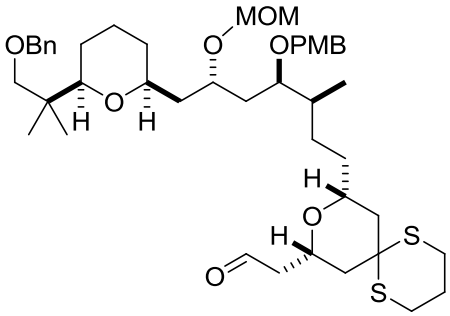




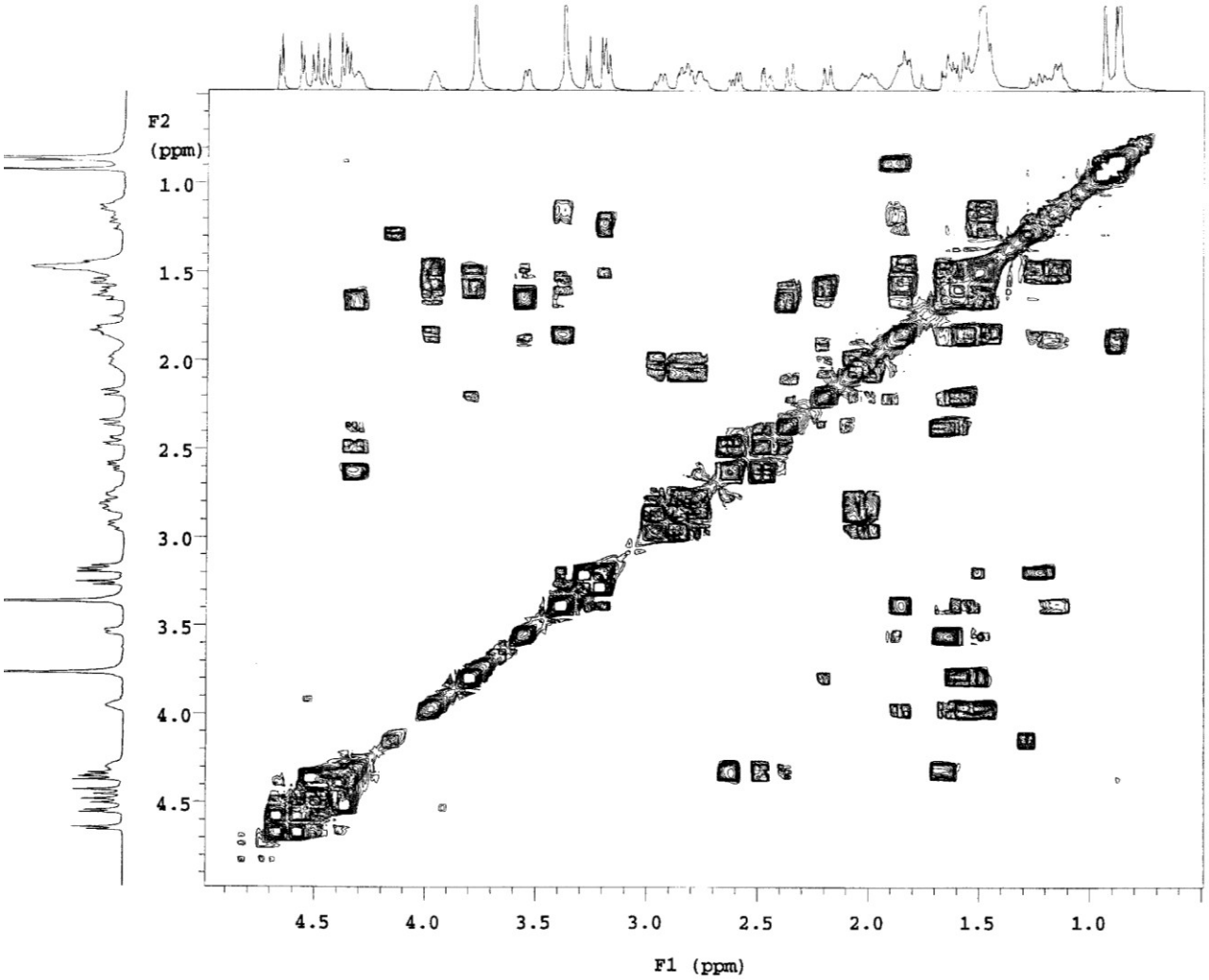
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{13}C NMR, 125 MHz
$CDCl_3$

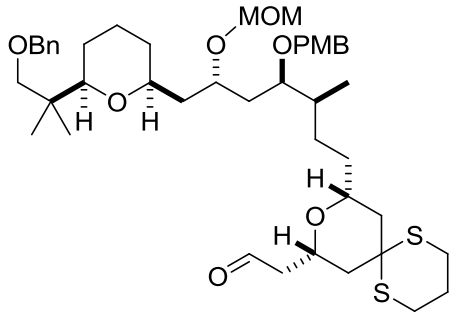




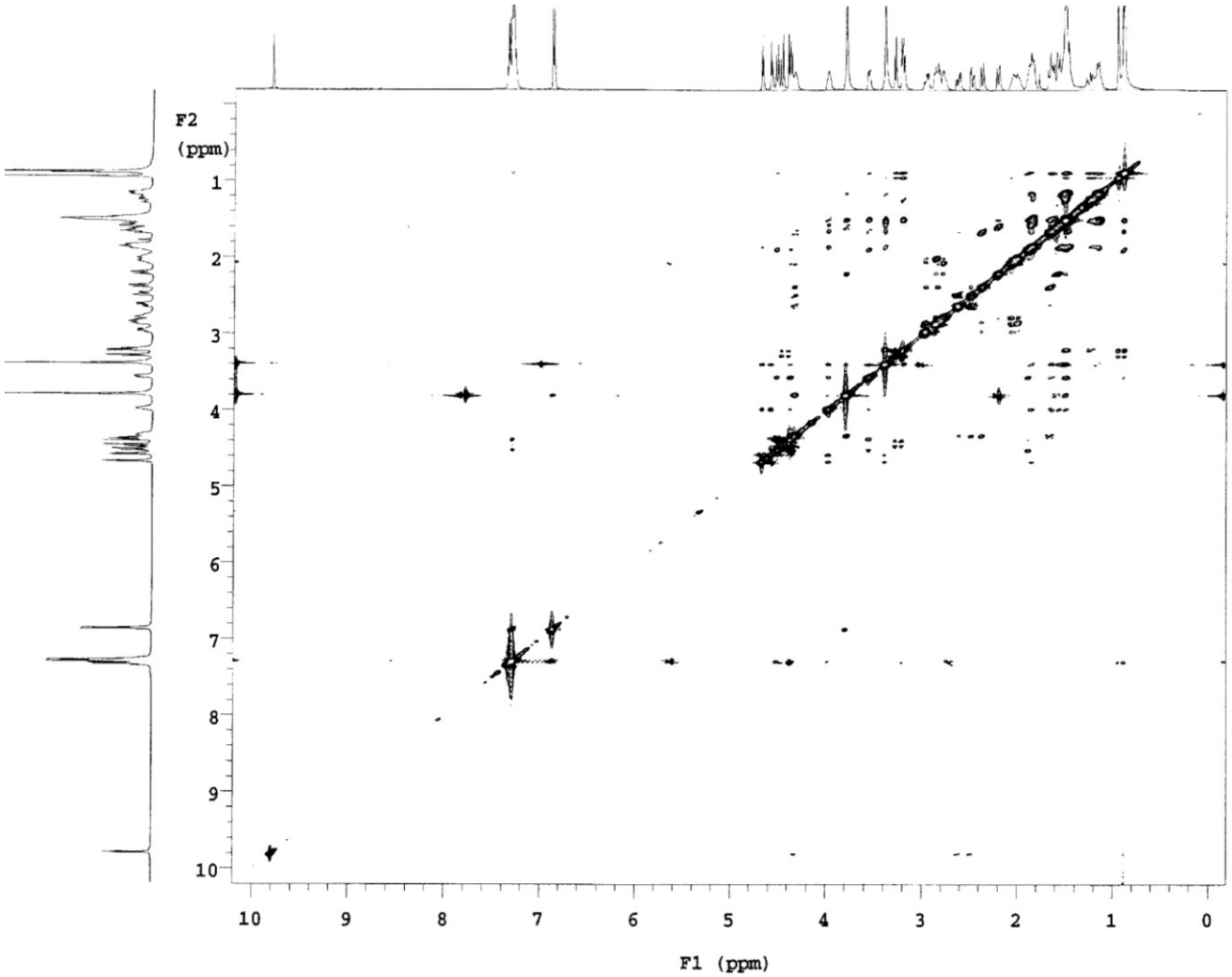


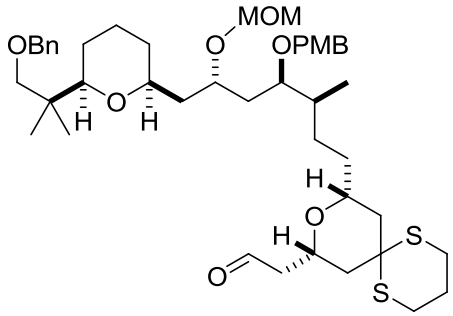
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$



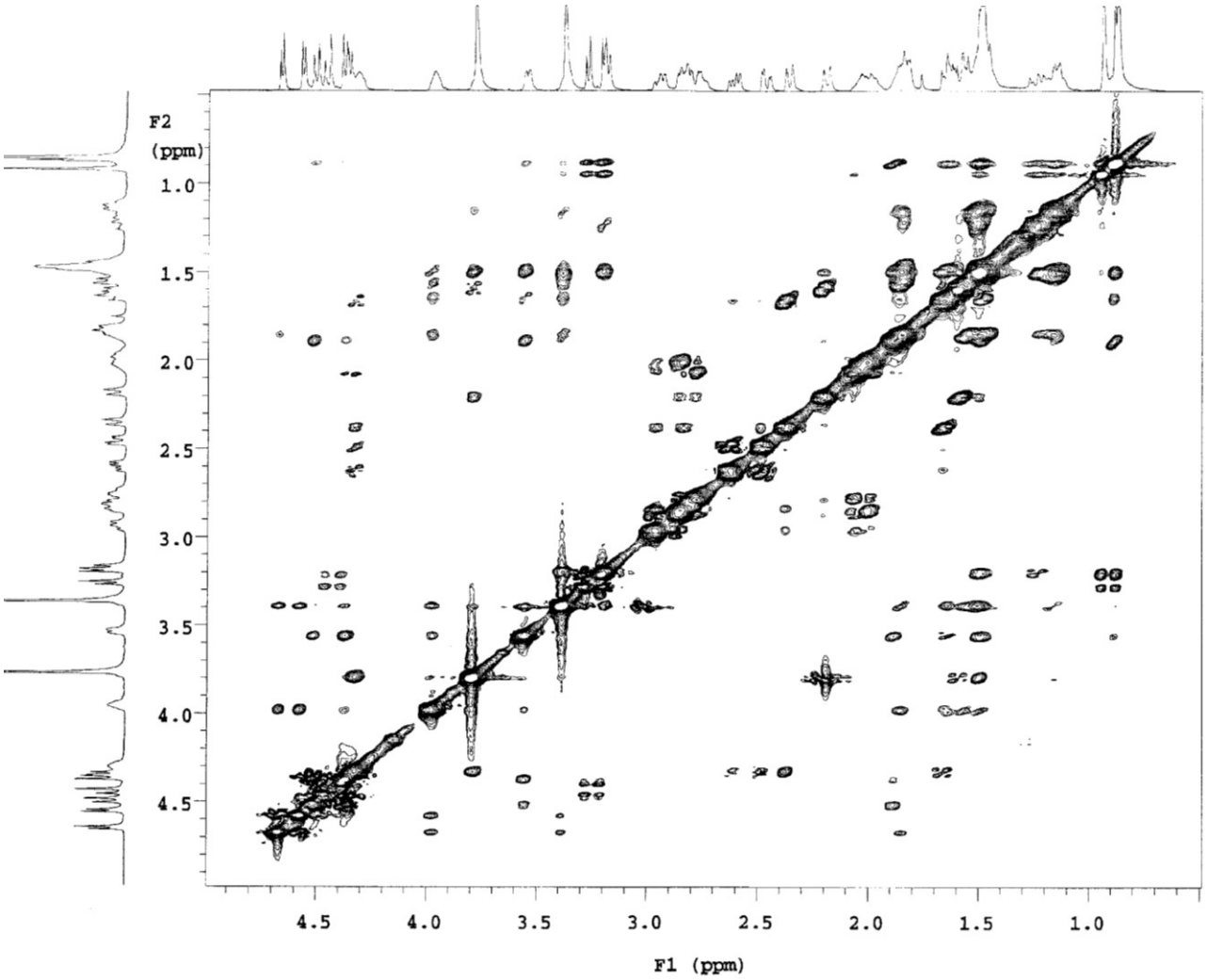


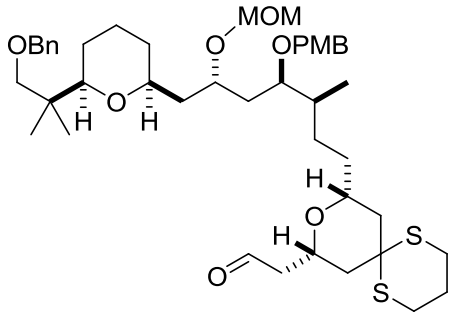
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{1}H–^{1}H COSY NMR, 500 MHz
$CDCl_3$



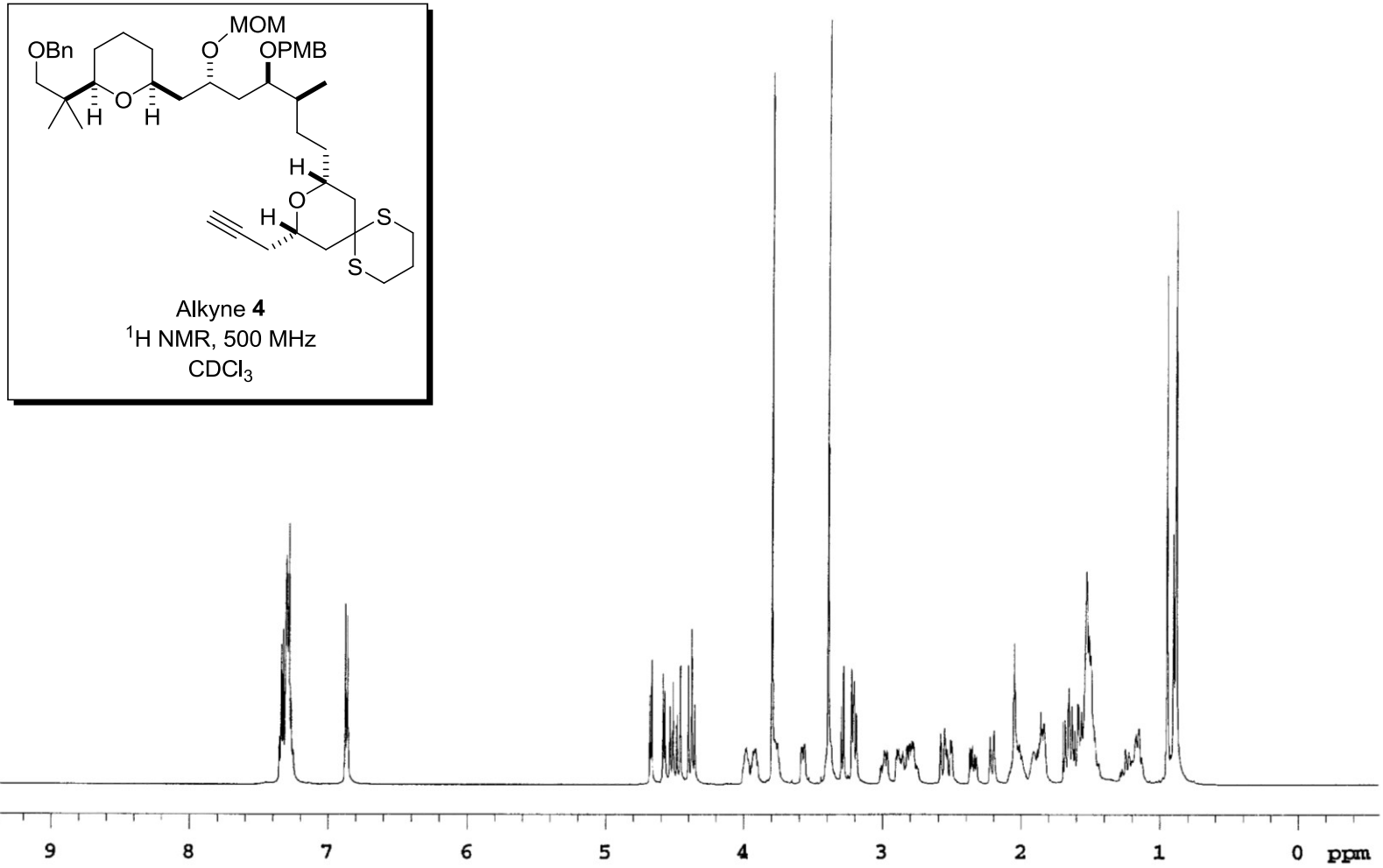


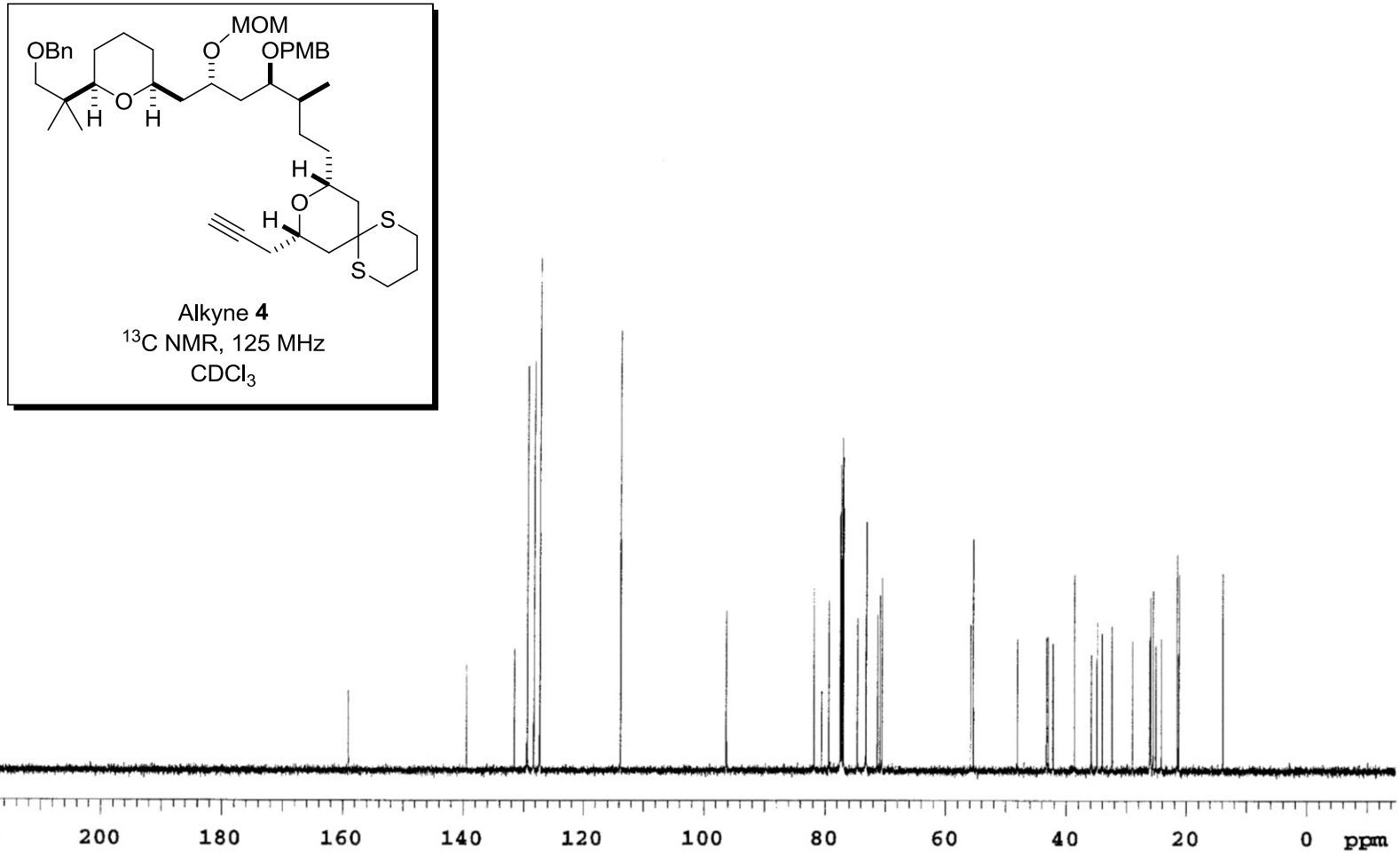
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$

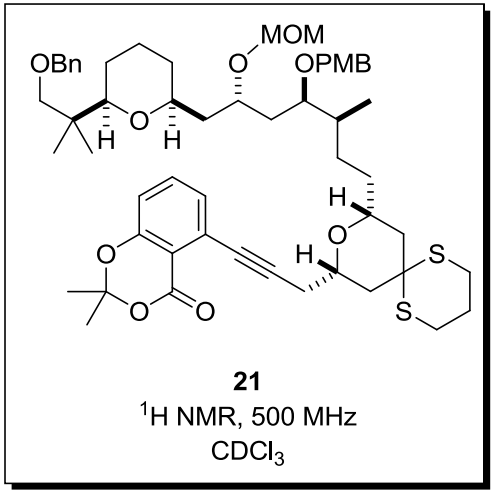




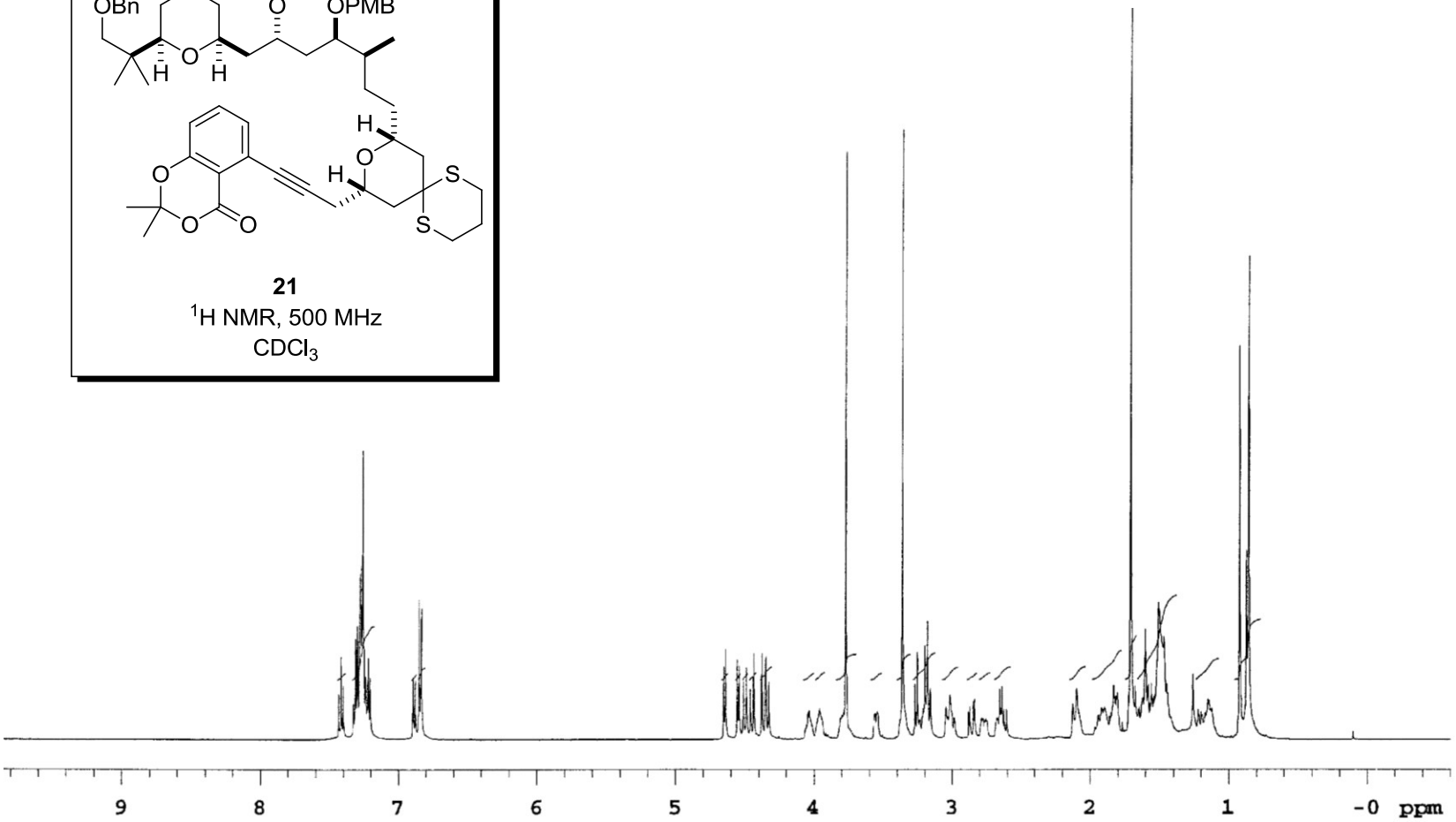
2,6-*cis*-Tetrahydropyran Aldehyde **20**
^{1}H–^{1}H NOESY NMR, 500 MHz
$CDCl_3$

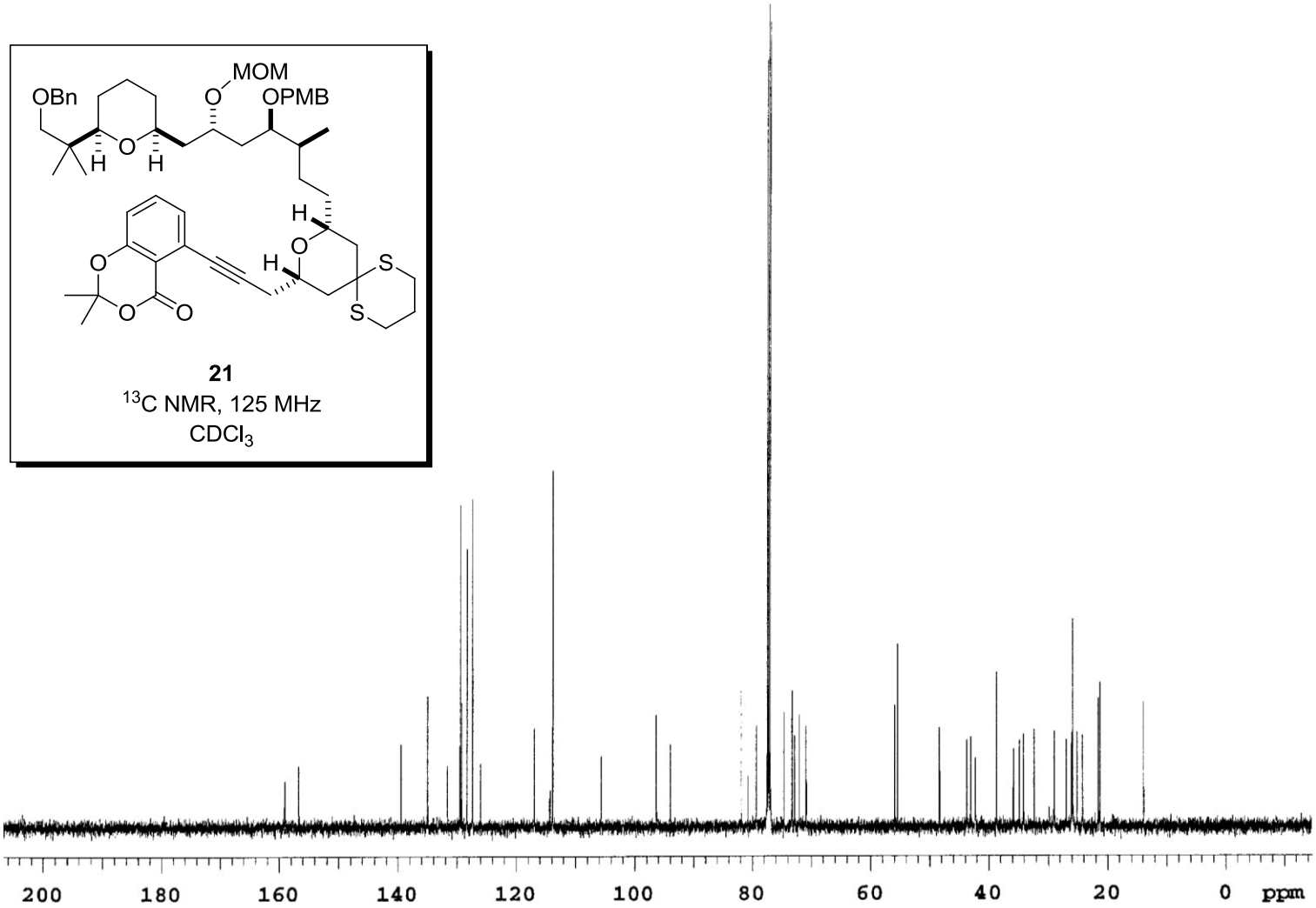

MOM
OBn
O
OPMB
H
O
H
H
O
H
S
S
Alkyne 4
1H NMR, 500 MHz
CDCl3
9
8
7
6
5
4
3
2
1
0
ppm

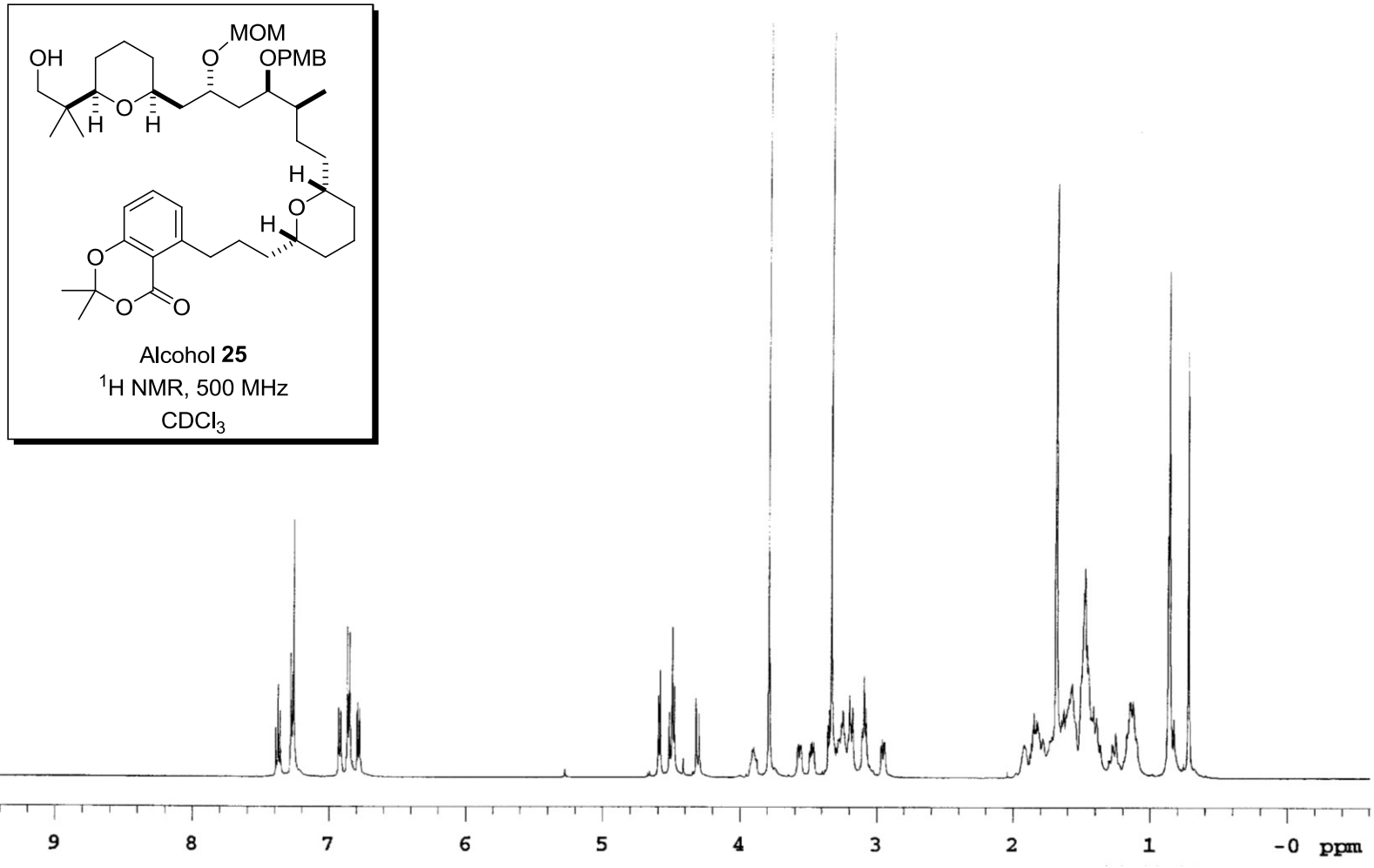

MOM
OBn
O
OPMB
H
O
H
H
O
H
S
S
Alkyne 4
13C NMR, 125 MHz
CDCl3
220
200
180
160
140
120
100
80
60
40
20
0
ppm

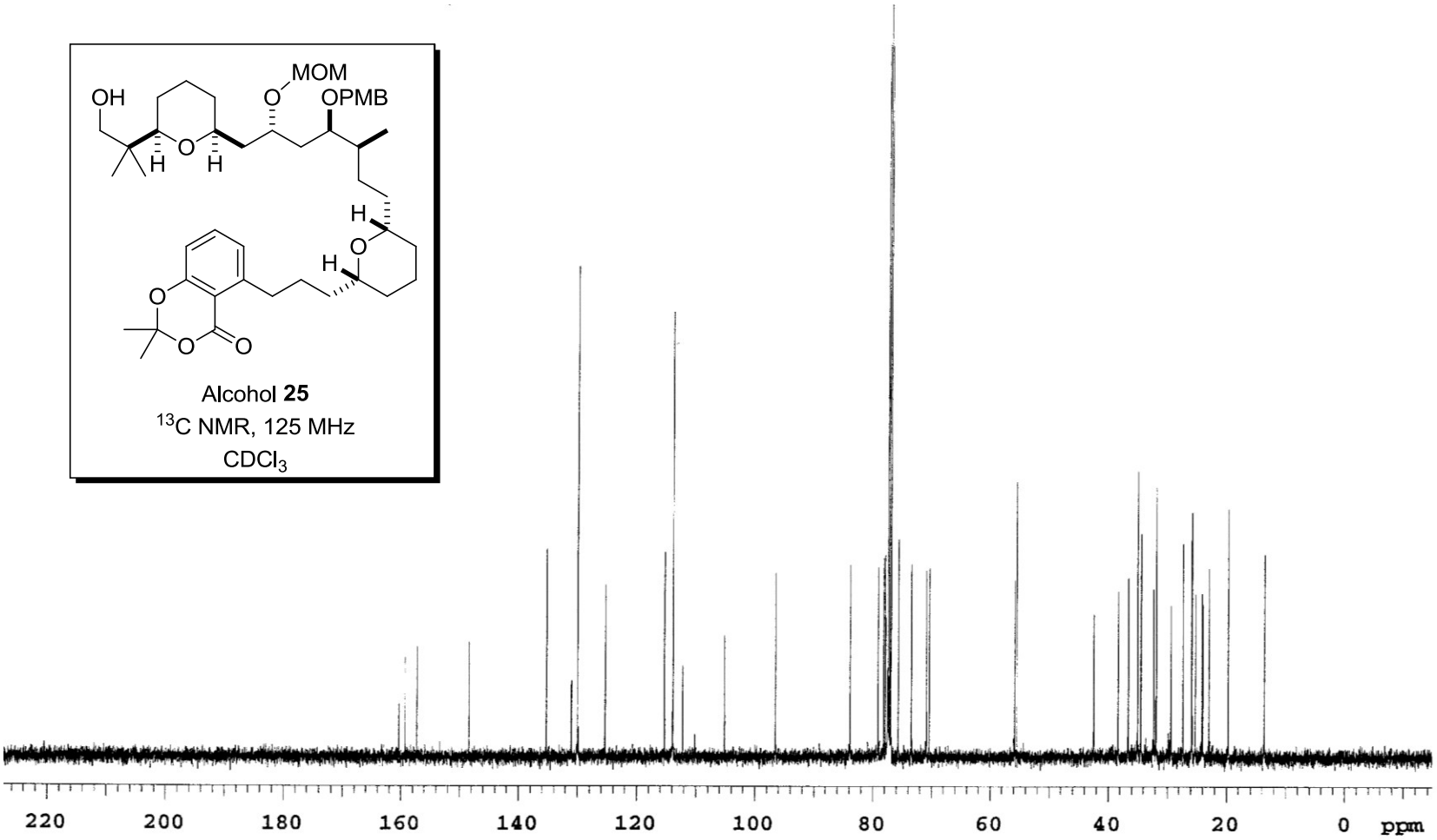


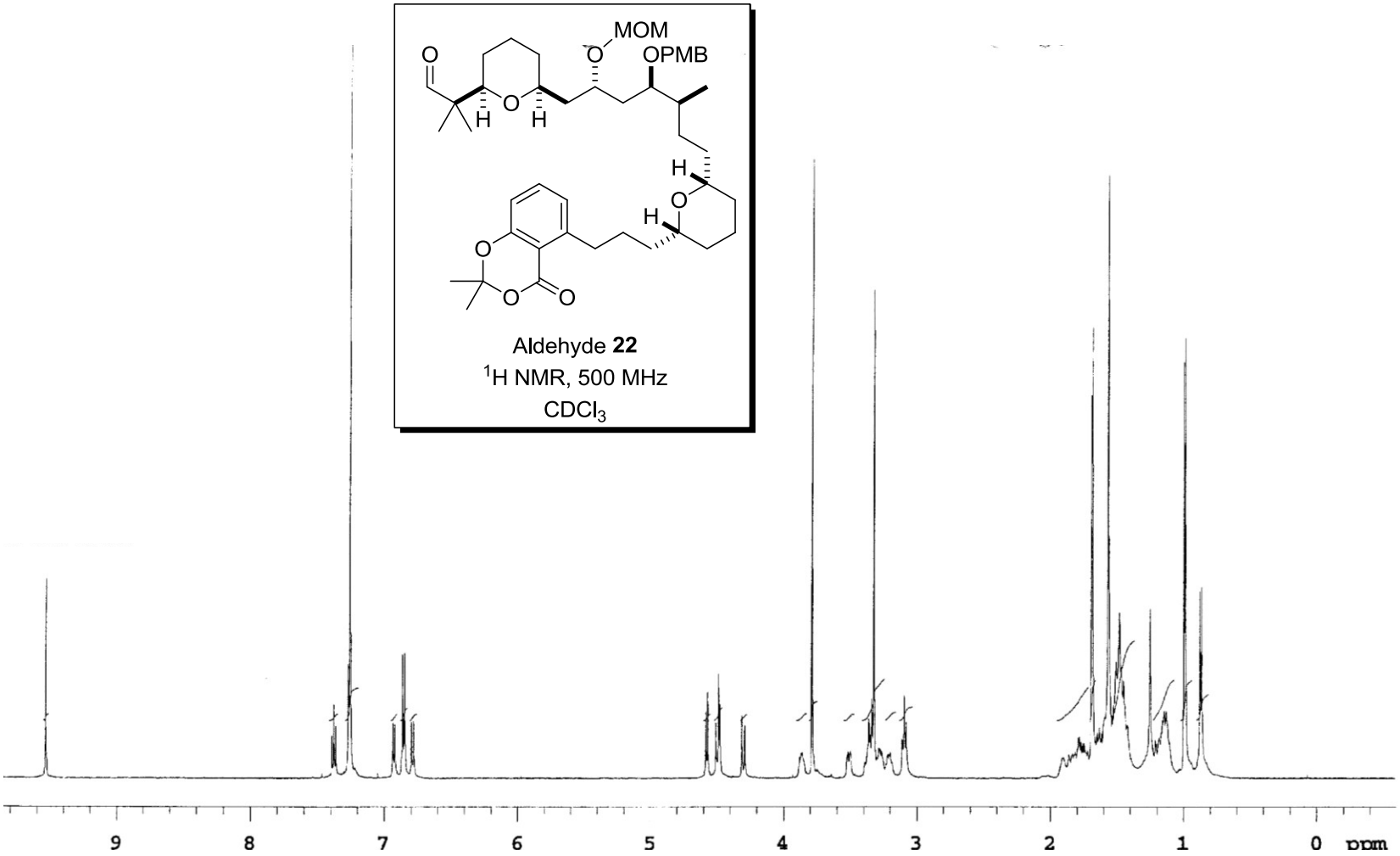
21
^{1}H NMR, 500 MHz
$CDCl_3$




MOM
OBn
O
OPMB
H
O
H
H
O
H
O
S
O
O
O
S
21
13C NMR, 125 MHz
CDCl3
200
180
160
140
120
100
80
60
40
20
0
ppm

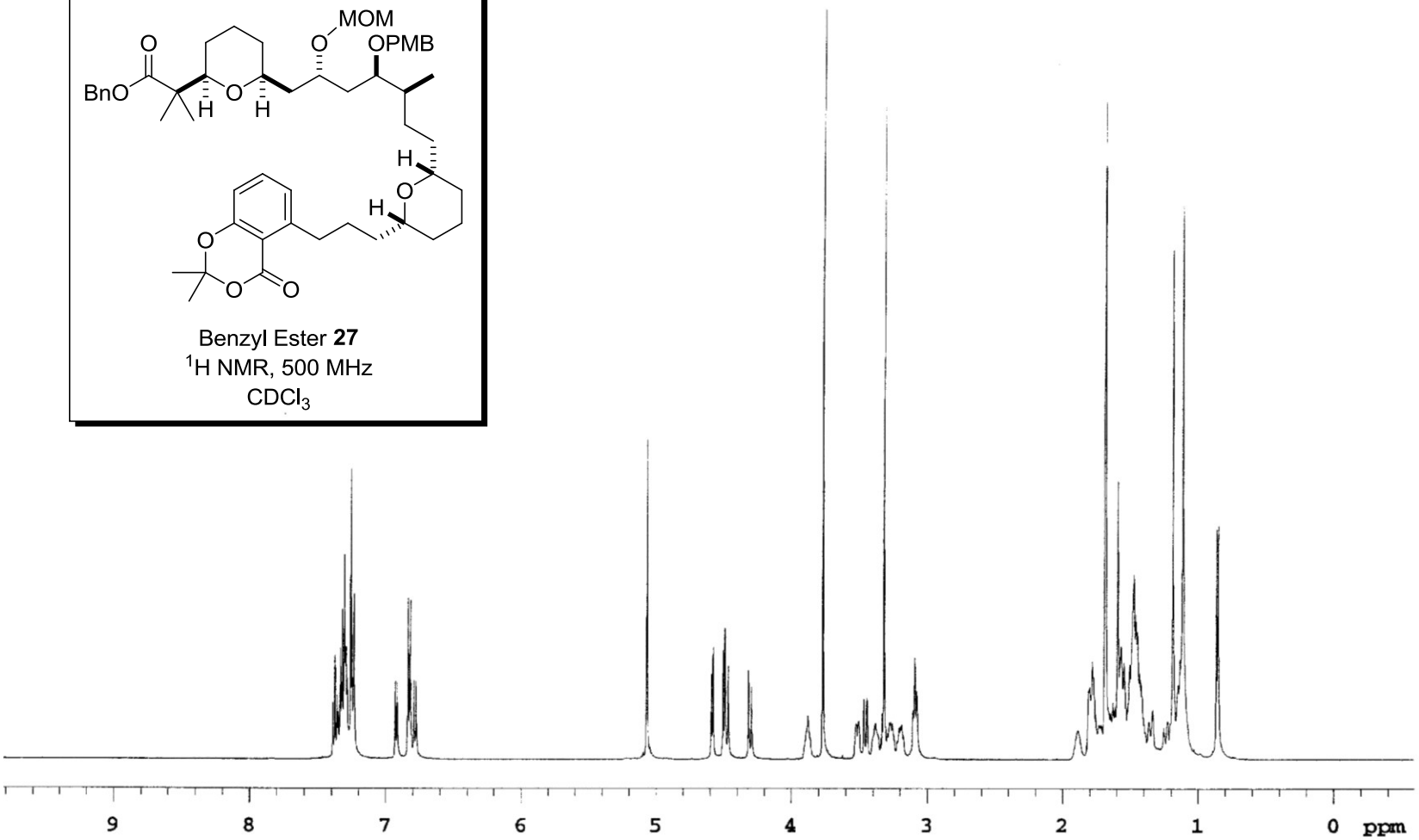

MOM
OH
O
OPMB
H
O
H
H
O
H
O
O
O
O
Alcohol 25
1H NMR, 500 MHz
CDCl3
9
8
7
6
5
4
3
2
1
-0 ppm


MOM
OH
O
OPMB
H
O
H
H
O
H
O
O
O
O
Alcohol 25
13C NMR, 125 MHz
CDCl3
220
200
180
160
140
120
100
80
60
40
20
0
ppm

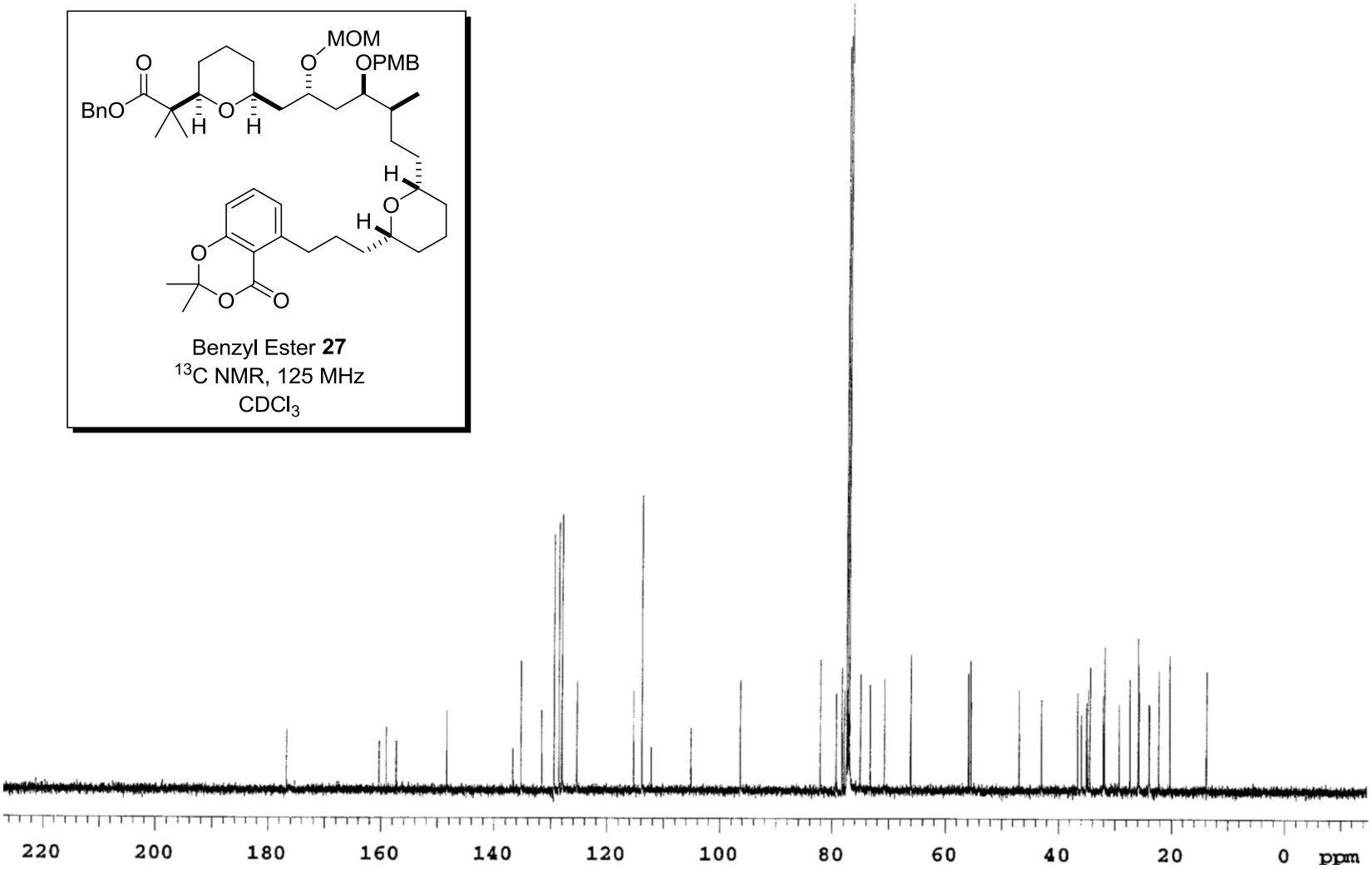


Aldehyde **22**
^{1}H NMR, 500 MHz
$CDCl_3$

Benzyl Ester **27**
^{1}H NMR, 500 MHz
$CDCl_3$



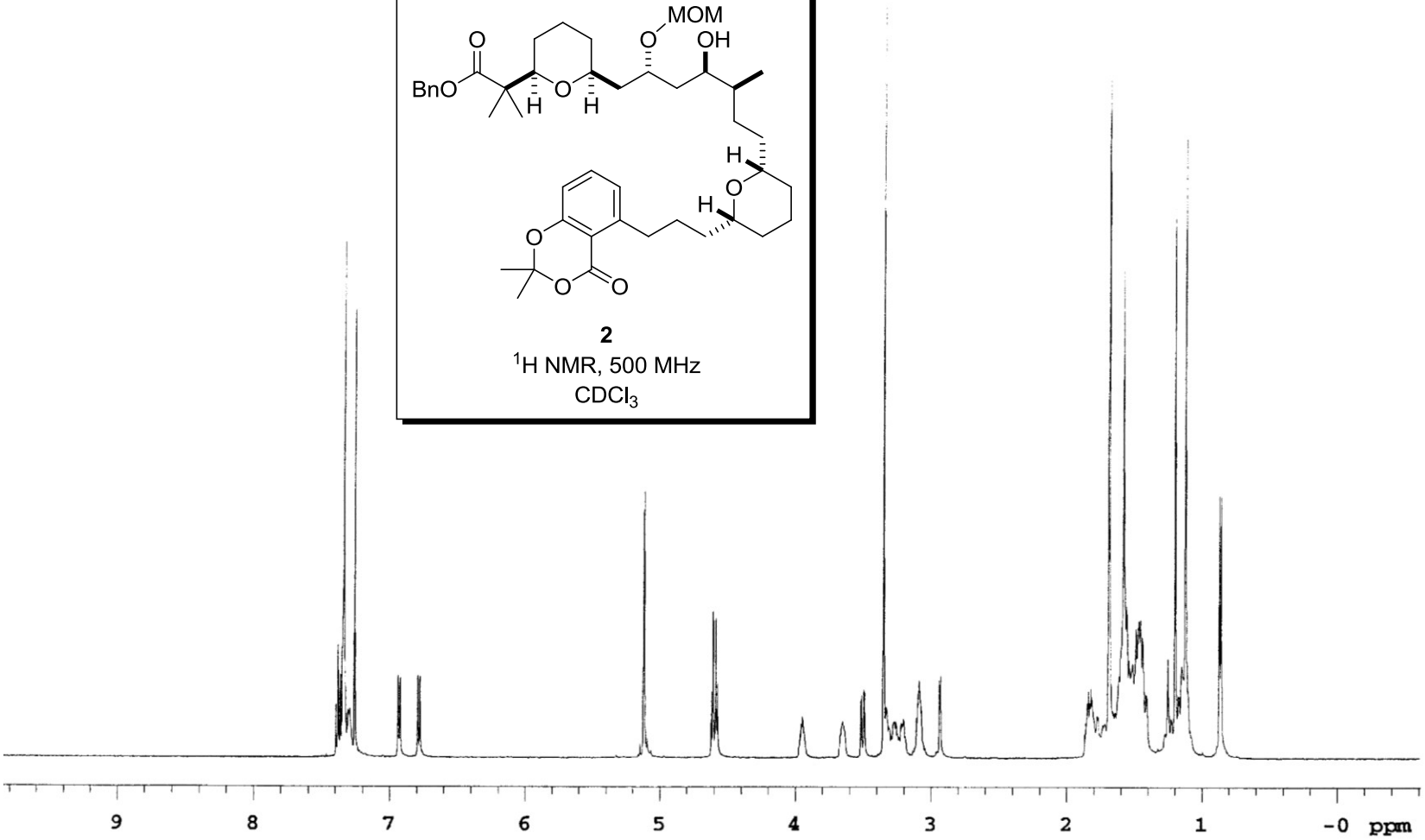
Benzyl Ester **27**
^{13}C NMR, 125 MHz
$CDCl_3$



2

^{1}H NMR, 500 MHz

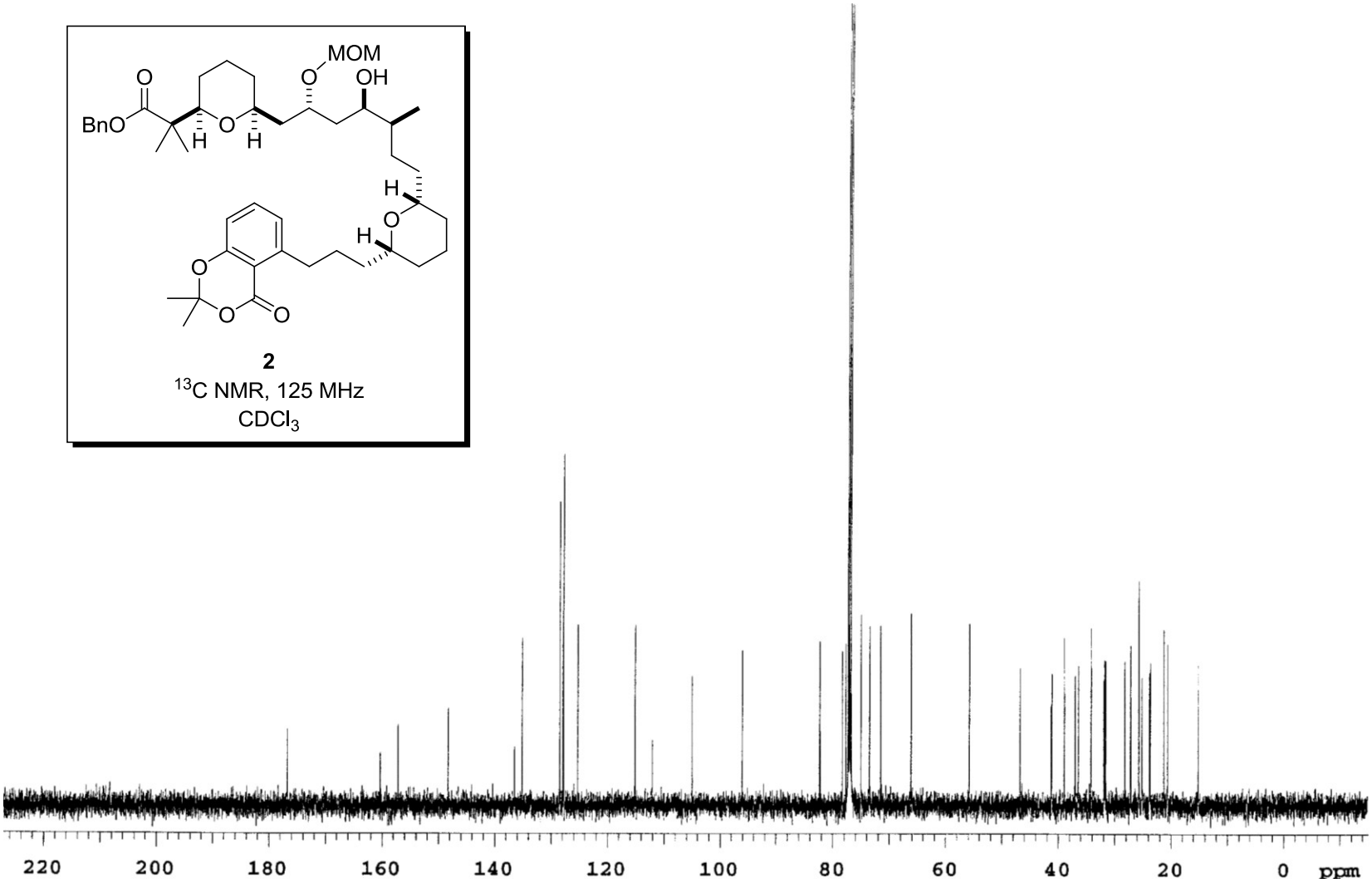
$CDCl_3$

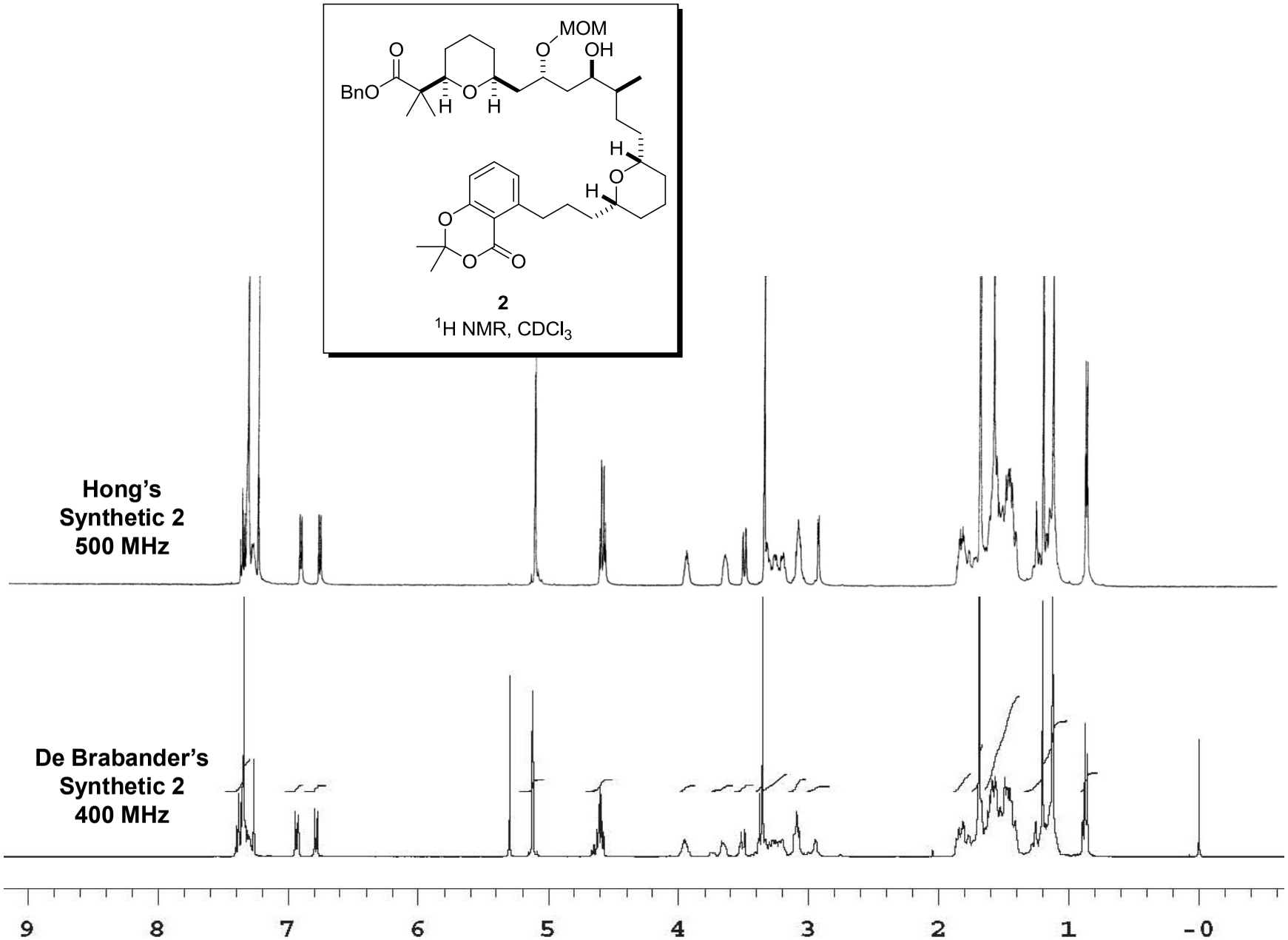


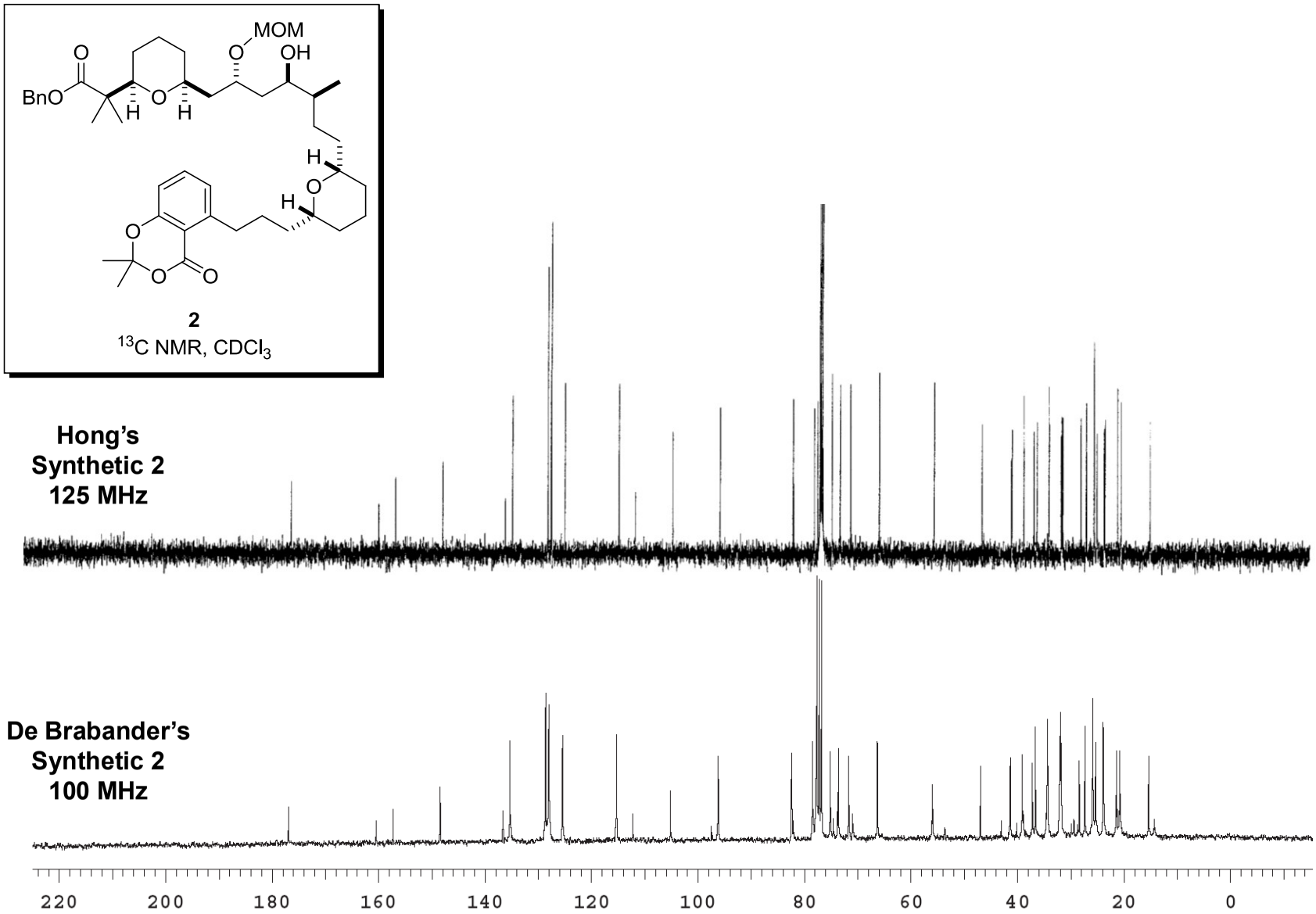
2

^{13}C NMR, 125 MHz

$CDCl_3$




MOM
O
OH
BnO
O
H
H
H
O
H
O
O
O
O
2
1H NMR, CDCl3
Hong's
Synthetic 2
500 MHz
De Brabander's
Synthetic 2
400 MHz
9
8
7
6
5
4
3
2
1
-0


MOM
O
OH
BnO
O
H
H
H
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H
O
O
O
O
2
13C NMR, CDCl3
Hong's
Synthetic 2
125 MHz
De Brabander's
Synthetic 2
100 MHz
220
200
180
160
140
120
100
80
60
40
20
0