

Supporting Information

**A Stereoselective Formal  
Synthesis of Leucascandrolide A**

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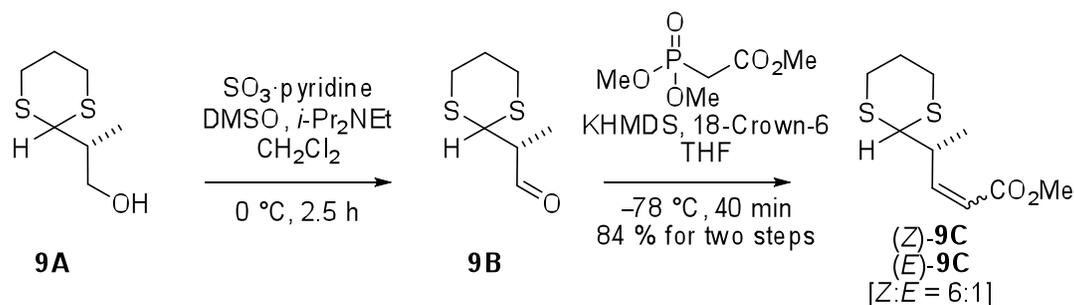
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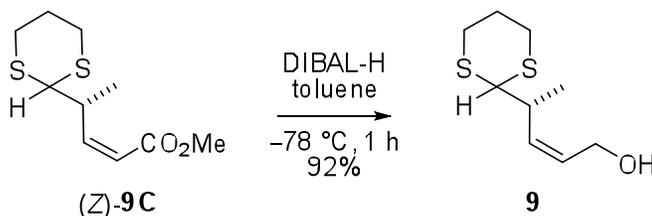
## Preparation of Enoates



**[Oxidation]** To a cooled ( $0\text{ }^\circ\text{C}$ ) solution of known alcohol **9A**<sup>1</sup> (1.750 g, 9.83 mmol) in  $\text{CH}_2\text{Cl}_2$  (110 mL, 0.089 M) were added DMSO (2.79 mL, 39.31 mmol),  $i\text{-Pr}_2\text{NEt}$  (3.42 mL, 19.66 mmol), and  $\text{SO}_3 \cdot \text{pyridine}$  (3.128 g, 19.66 mmol). After stirred at the same temperature for 2.5 h, the reaction mixture was quenched with saturated aqueous  $\text{Na}_2\text{S}_2\text{O}_3$  and saturated aqueous  $\text{NaHCO}_3$  and diluted with  $\text{Et}_2\text{O}$ . The layers were separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude aldehyde **9B** was employed in next step without further purification. **[Horner–Wadsworth–Emmons Olefination]** To a cooled ( $-78\text{ }^\circ\text{C}$ ) solution of trimethyl phosphonoacetate (2.83 mL, 19.66 mmol) and 18-Crown-6 (5.197 g, 19.66 mmol) in THF (400 mL, 0.024 M) was added dropwise KHMDS (31.45 mL, 0.5 M in toluene, 15.73 mmol) and the resulting mixture was stirred for 10 min before the above aldehyde **9B** was added. After stirred at  $-78\text{ }^\circ\text{C}$  for 40 min, the reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  and diluted with  $\text{EtOAc}$ . The layers were separated, and the aqueous layer was extracted with  $\text{EtOAc}$ . The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 20/1) to afford enoates **(Z)-9C** (1.660g, 73%) and **(E)-9C** (0.265 g, 12%) as colorless oils. **[For (Z)-9C]**  $[\alpha]_{\text{D}}^{25} = -35.6$  ( $c$  1.21,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.21–6.28 (m, 1H), 5.83 (dd,  $J = 8.5, 1.0$  Hz, 1H), 3.99–4.06 (m, 2H), 3.72 (s, 3H), 2.80–2.92 (m, 4H), 2.04–2.12 (m, 1H), 1.82–1.92 (m,

1H), 1.23 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 150.6, 118.9, 52.4, 50.6, 36.6, 29.4, 25.4, 17.4; IR (neat) 2361, 1715, 1641, 1434, 1197, 871  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  233.0671  $[(\text{M}+\text{H})^+]$ ,  $\text{C}_{10}\text{H}_{16}\text{O}_2\text{S}_2$  requires 233.0670]. [For (*E*)-**9C**]  $[\alpha]_{\text{D}}^{25} = +36.8$  ( $c$  0.63,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.96 (ddd,  $J = 15.6, 8.0, 1.0$  Hz, 1H), 5.88 (dd,  $J = 15.6, 1.2$  Hz, 1H), 4.11 (d,  $J = 6.0$  Hz, 1H), 3.73 (s, 3H), 2.78–2.92 (m, 4H), 2.73 (dddd,  $J = 13.2, 6.4, 6.4, 6.4$  Hz, 1H), 2.04–2.16 (m, 1H), 1.78–1.90 (m, 1H), 1.26 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4, 149.5, 121.4, 52.8, 51.4, 41.3, 30.48, 30.40, 25.6, 16.9; IR (neat) 2360, 1715, 1433, 1270, 1172, 978  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  233.0664  $[(\text{M}+\text{H})^+]$ ,  $\text{C}_{10}\text{H}_{16}\text{O}_2\text{S}_2$  requires 233.0664].

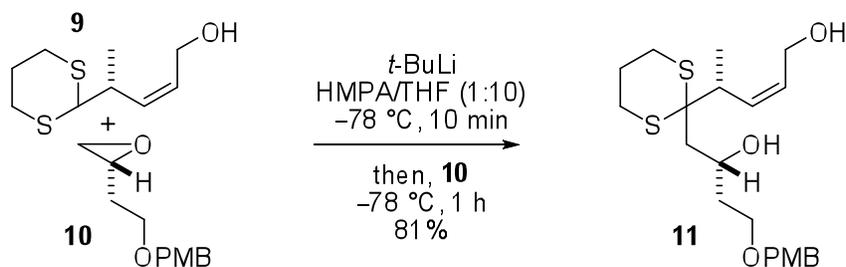
### Preparation of Allyl Alcohol **9**



To a cooled ( $-78\text{ }^\circ\text{C}$ ) solution of (*Z*)-**9C** (420 mg, 1.81 mmol) in toluene (20 mL, 0.09 M) was added DIBAL-H (4.52 mL, 1.0 M in toluene, 4.52 mmol). After stirred at the same temperature for 1 h, the reaction mixture was quenched with MeOH followed by aqueous Rochelle's salt solution and diluted with  $\text{Et}_2\text{O}$ . The resulting mixture was stirred for 5 h at  $25\text{ }^\circ\text{C}$ . The layers were separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 3/1 to 1/2) to afford the (*Z*)-allyl alcohol **9** (341 mg, 92%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = -10.4$  ( $c$  1.23,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.68 (ddd,  $J = 11.0, 7.0, 7.0$  Hz, 1H), 5.46 (dd,  $J = 11.0, 11.0$  Hz, 1H), 4.22 (dd,  $J = 12.5, 7.0$  Hz, 1H), 4.14 (dd,  $J = 12.5, 7.0$  Hz, 1H), 3.99 (d,  $J = 6.5$  Hz, 1H), 2.77–2.90 (m, 5H), 2.04–2.11

(m, 1H), 1.76–1.87 (m, 1H), 1.73 (br s, 1H), 1.15 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  133.2, 129.5, 58.0, 53.6, 36.7, 30.29, 30.16, 25.6, 18.5; IR (neat) 3349, 1421, 1275, 985, 907, 736  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  205.0717 [(M+H) $^+$ ,  $\text{C}_9\text{H}_{16}\text{OS}_2$  requires 205.0715].

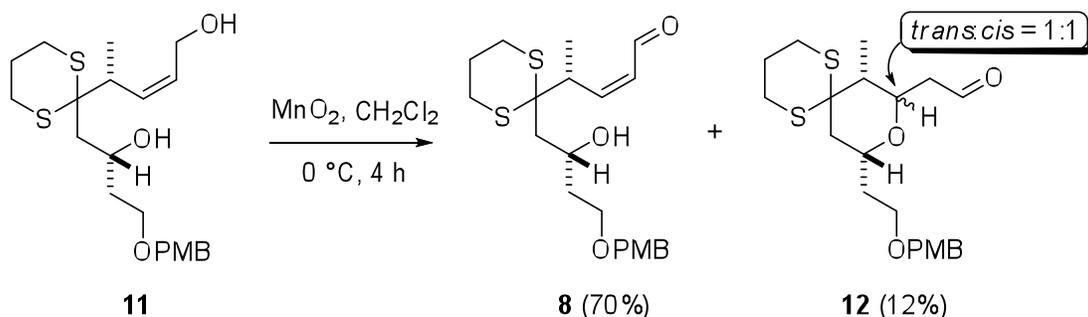
### Preparation of Diol 11



To a cooled ( $-78\text{ }^\circ\text{C}$ ) solution of dithiane **9** (1.126 g, 5.510 mmol) in HMPA/THF (1:10, 110 mL) was added dropwise  $t\text{-BuLi}$  (9.73 mL, 1.7 M in pentane, 16.530 mmol). The resulting mixture was stirred for 10 min before the known epoxide **10**<sup>2</sup> (1.357 g, 8.265 mmol) was added. After stirred at  $-78\text{ }^\circ\text{C}$  for 1 h, the reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$ , 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  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1 to 1/1) to afford diol **11** (1.841 g, 81%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +17.0$  ( $c$  0.73,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (d,  $J = 8.5$  Hz, 2H), 6.88 (d,  $J = 8.5$  Hz, 2H), 5.70–5.80 (m, 2H), 4.45 (s, 2H), 4.29 (dd,  $J = 13.0, 8.5$  Hz, 1H), 4.19–4.23 (m, 1H), 4.00–4.03 (m, 1H), 3.80 (s, 3H), 3.71 (br s, 1H), 3.59–3.68 (m, 2H), 3.25 (dddd,  $J = 9.5, 7.0, 7.0, 7.0$  Hz, 1H), 2.97 (ddd,  $J = 14.0, 11.0, 3.0$  Hz, 1H), 2.87 (ddd,  $J = 14.0, 10.5, 3.0$  Hz, 1H), 2.70–2.76 (m, 2H), 2.43 (br s, 1H), 2.31 (dd,  $J = 15.5, 8.5$  Hz, 1H), 2.19 (dd,  $J = 15.0, 2.5$  Hz, 1H), 1.98–2.05 (m, 1H), 1.80–1.91 (m, 2H), 1.71–1.79 (m, 1H), 1.18 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.0, 132.9, 129.9, 129.16, 129.02, 113.6, 72.6, 67.6, 67.3, 57.8, 56.6, 55.1, 42.4,

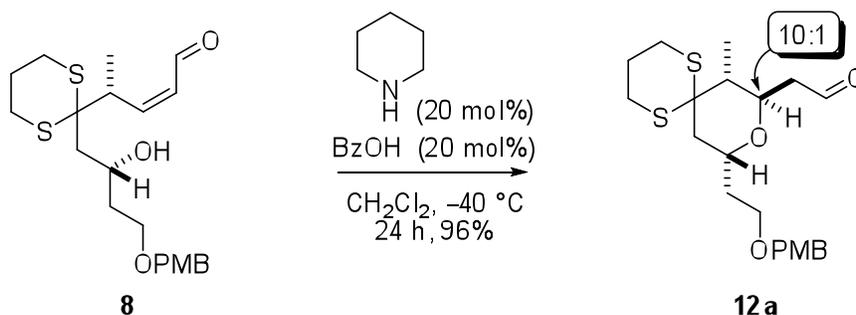
38.8, 37.6, 25.9, 24.7, 16.6; IR (neat) 3398, 1611, 1512, 1440, 1301, 1220, 1088, 1032, 820  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  411.1654  $[(M-H)^+]$ ,  $\text{C}_{21}\text{H}_{32}\text{O}_4\text{S}_2$  requires 411.1658].

### Preparation of $\alpha,\beta$ -Unsaturated Aldehyde **8**



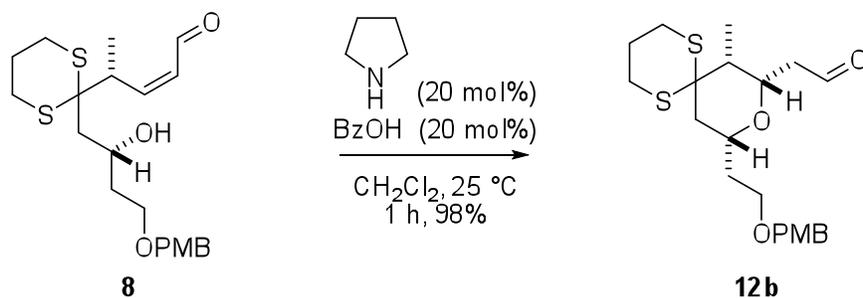
To a solution of diol **11** (1.460 g, 3.54 mmol) in  $\text{CH}_2\text{Cl}_2$  (50.0 mL, 0.071 M) was added  $\text{MnO}_2$  (1.539 g, 17.69 mmol), and the resulting mixture was stirred for 1 h at  $0\text{ }^\circ\text{C}$ . An addition of  $\text{MnO}_2$  (1.539 g, 17.69 mmol) was repeated two times every 30 min. When diol **11** was completely consumed, the reaction mixture was filtered through a pad of celite and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 3/1) to afford  $\alpha,\beta$ -unsaturated aldehyde **8** (1.014 g, 70%) along with a 1:1 mixture (0.169 g, 12%) of tetrahydropyrans **12** as colorless oils: [For Aldehyde **8**]  $[\alpha]_D^{25} = +24.3$  ( $c$  2.17,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  10.07 (d,  $J = 7.5$  Hz, 1H), 7.25 (d,  $J = 8.0$  Hz, 2H), 6.84–6.90 (m, 3H), 6.01 (ddd,  $J = 11.5, 7.5, 1.0$  Hz, 1H), 4.45 (s, 2H), 4.21–4.26 (m, 1H), 4.00 (dddd,  $J = 11.5, 7.0, 7.0, 7.0$  Hz, 1H), 3.80 (s, 3H), 3.60–3.68 (m, 2H), 3.56 (d,  $J = 2.0$  Hz, 1H), 2.96 (ddd,  $J = 14.0, 10.0, 3.0$  Hz, 1H), 2.87 (ddd,  $J = 14.0, 9.5, 3.0$  Hz, 1H), 2.77 (dddd,  $J = 21.5, 14.0, 6.5, 3.0$  Hz, 2H), 2.30 (dd,  $J = 15.5, 9.0$  Hz, 1H), 2.11 (dd,  $J = 15.5, 1.5$  Hz, 1H), 1.97–2.05 (m, 1H), 1.81–1.94 (m, 2H), 1.70–1.77 (m, 1H), 1.25 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  190.7, 159.0, 152.0, 130.0, 129.1, 113.6, 72.6, 67.3, 66.9, 55.4, 55.0, 42.2, 38.8, 37.5, 26.1, 25.5, 24.4, 16.3; IR (neat) 3433, 1671, 1512, 1245, 1086, 1031, 819  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  411.1653  $[(M+H)^+]$ ,  $\text{C}_{21}\text{H}_{30}\text{O}_4\text{S}_2$  requires 411.1658].

## Representative Procedure for the Secondary Amine-Catalyzed Oxa-Michael Reaction



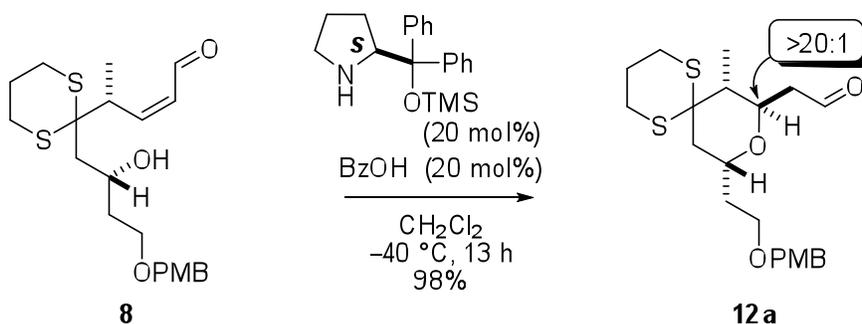
To a cooled ( $-40\text{ }^\circ\text{C}$ ) solution of aldehyde **8** (29.0 mg, 0.071 mmol) in  $\text{CH}_2\text{Cl}_2$  (3.0 mL, 0.024 M) was added dropwise a mixture of piperidine·BzOH (0.26 mL, 0.055 M in  $\text{CH}_2\text{Cl}_2$ ). After stirred at  $-40\text{ }^\circ\text{C}$  for 24 h, the reaction mixture was diluted with hexanes (30.0 mL), filtered through a short pad of silica gel (hexanes/EtOAc, 3/1), and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford a 10:1 mixture of 2,3-*trans*-2,6-*trans*-tetrahydropyran **12a** and 2,3-*cis*-2,6-*cis*-tetrahydropyran **12b** in 96% yield as colorless oils: [**For 2,3-*trans*-2,6-*trans*-Tetrahydropyran 12a**]:  $[\alpha]_{\text{D}}^{25} = +11.6$  ( $c$  0.67,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.72 (dd,  $J = 3.0, 1.5$  Hz, 1H), 7.26 (d,  $J = 8.5$  Hz, 2H), 6.87 (d,  $J = 8.5$  Hz, 2H), 4.41 (AB,  $\Delta\nu = 15.0$  Hz,  $J_{\text{AB}} = 11.5$  Hz, 2H), 4.25 (ddd,  $J = 10.5, 7.0, 4.0$  Hz, 1H), 4.11 (dddd,  $J = 9.5, 4.5, 4.5, 4.5$  Hz, 1H), 3.80 (s, 3H), 3.45–3.53 (m, 2H), 3.01 (ddd,  $J = 14.5, 11.0, 3.0$  Hz, 1H), 2.88 (ddd,  $J = 14.5, 11.0, 3.5$  Hz, 1H), 2.81 (ddd,  $J = 13.0, 9.0, 3.0$  Hz, 1H), 2.68–2.76 (m, 3H), 2.41 (dd,  $J = 14.5, 6.0$  Hz, 1H), 2.21–2.29 (m, 2H), 1.92–2.04 (m, 2H), 1.80–1.91 (m, 2H), 1.23 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  201.5, 159.1, 130.5, 129.4, 113.7, 72.8, 69.7, 67.8, 66.8, 55.3, 52.4, 47.6, 42.6, 39.5, 33.5, 26.2, 25.7, 25.2, 14.6; IR (neat) 1721, 1611, 1511, 1244, 1100, 1031, 818  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  411.1658  $[(\text{M}+\text{H})^+]$ ,  $\text{C}_{21}\text{H}_{30}\text{O}_4\text{S}_2$  requires 411.1658]. [**For 2,3-*cis*-2,6-*cis*-Tetrahydropyran 12b**]:  $[\alpha]_{\text{D}}^{25} = -15.7$  ( $c$  0.76,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.69 (dd,  $J = 2.0, 2.0$  Hz, 1H), 7.25 (d,  $J = 8.5$  Hz, 2H), 6.88 (d,  $J = 9.0$  Hz, 2H), 4.78 (ddd,  $J = 9.5, 3.5, 2.0$  Hz, 1H), 4.40 (AB,  $\Delta\nu = 20.0$

Hz,  $J_{AB} = 12.0$  Hz, 2H), 3.97–4.04 (m, 1H), 3.80 (s, 3H), 3.48–3.52 (m, 2H), 2.80–2.90 (m, 2H), 2.70–2.79 (m, 2H), 2.60 (ddd,  $J = 16.5, 9.5, 2.5$  Hz, 1H), 2.28 (ddd,  $J = 16.5, 4.0, 2.0$  Hz, 1H), 2.07 (ddd,  $J = 7.0, 7.0, 7.0$  Hz, 1H), 1.91–2.05 (m, 3H), 1.65–1.77 (m, 3H), 1.10 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  201.2, 159.1, 130.4, 129.3, 113.7, 72.7, 70.3, 70.1, 65.9, 55.2, 53.5, 47.4, 38.43, 38.22, 35.8, 26.0, 25.38, 25.21, 9.0; IR (neat) 1724, 1612, 1512, 1246, 1089, 1032, 819  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  433.1479 [(M+Na) $^+$ ,  $\text{C}_{21}\text{H}_{30}\text{O}_4\text{S}_2$  requires 433.1478].



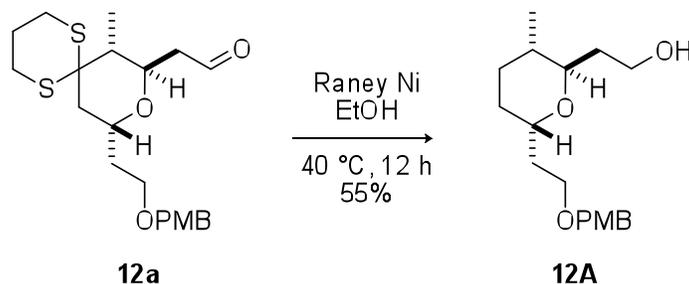
To a solution of aldehyde **8** (32.3 mg, 0.078 mmol) in  $\text{CH}_2\text{Cl}_2$  (3.0 mL, 0.026 M) was added dropwise a mixture of pyrrolidine·BzOH (0.28 mL, 0.054 M in  $\text{CH}_2\text{Cl}_2$ ) at 25 °C. After stirred at 25 °C for 1 h, the reaction mixture was diluted with hexanes (30.0 mL), filtered through a short pad of silica gel (hexanes/EtOAc, 3/1), and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford 2,3-*cis*-2,6-*cis*-tetrahydropyran **12b** (31.6 mg, 98%) as a colorless oil.

## Organocatalytic Oxa-Michael Reaction for the Synthesis of 2,3-*trans*-2,6-*trans*-Tetrahydropyran **12a**



To a cooled (-40 °C) solution of aldehyde **8** (965 mg, 2.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50.0 mL, 0.047 M) was added dropwise a mixture of (S)-(-)- $\alpha,\alpha$ -diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (**S-13**) (153 mg, 0.47 mmol) and BzOH (57 mg, 0.47 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL). After stirred at -40 °C for 13 h, the reaction mixture was diluted with hexanes (150.0 mL), and filtered through a short pad of silica gel (hexanes/EtOAc, 3/1) and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford 2,3-*trans*-2,6-*trans*-tetrahydropyran **12a** (946 mg, 98%) as a colorless oil.

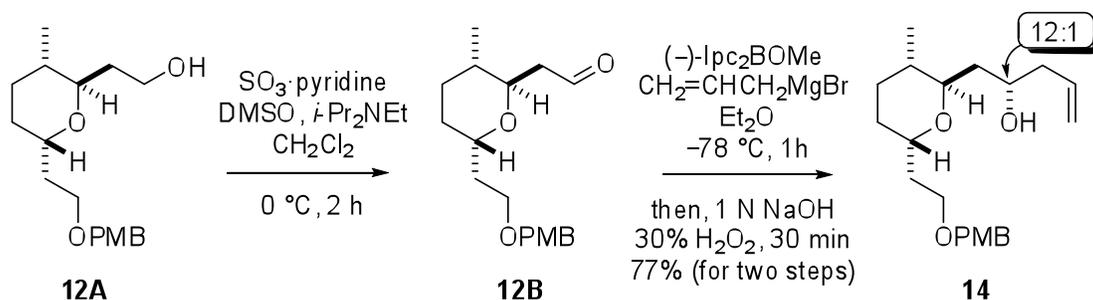
### Preparation of Alcohol **12A**



To a stirred solution of aldehyde **12a** (851.5 mg, 2.07 mmol) in EtOH (25.0 mL) was added freshly prepared Raney 2400 Ni (~13 g) in EtOH (5.0 mL) at 25 °C. After stirred at 40 °C for 12 h, the reaction mixture was filtered through a pad of celite and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford alcohol **12A** (354.3 mg, 55%) as a colorless oil:  $[\alpha]_D^{25} = +47.5$  (*c* 0.43, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500

MHz, CDCl<sub>3</sub>)  $\delta$  7.26 (d,  $J$  = 8.5 Hz, 2H), 6.88 (d,  $J$  = 8.5 Hz, 2H), 4.44 (AB,  $\Delta\nu$  = 17.5 Hz,  $J_{AB}$  = 11.5 Hz, 2H), 4.03–4.08 (m, 1H), 3.80 (s, 3H), 3.67–3.79 (m, 2H), 3.53 (dd,  $J$  = 7.0, 5.5 Hz, 2H), 3.44 (ddd,  $J$  = 9.0, 9.0, 2.5 Hz, 1H), 3.01 (dd,  $J$  = 8.0, 4.0 Hz, 1H), 2.16 (dddd,  $J$  = 14.0, 10.0, 5.5, 5.5 Hz, 1H), 1.76–1.84 (m, 2H), 1.66–1.72 (m, 1H), 1.56–1.66 (m, 2H), 1.40–1.50 (m, 2H), 1.29–1.37 (m, 1H), 0.86 (d,  $J$  = 6.5 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  159.0, 130.3, 129.3, 113.7, 76.0, 72.7, 69.4, 67.0, 61.3, 55.2, 34.79, 34.64, 30.8, 28.4, 26.9, 18.0; IR (neat) 3439, 1513, 1457, 1247, 1090, 1035, 820 cm<sup>-1</sup>; HRMS (FAB)  $m/z$  309.2059 [(M+H)<sup>+</sup>, C<sub>18</sub>H<sub>28</sub>O<sub>4</sub> requires 309.2060].

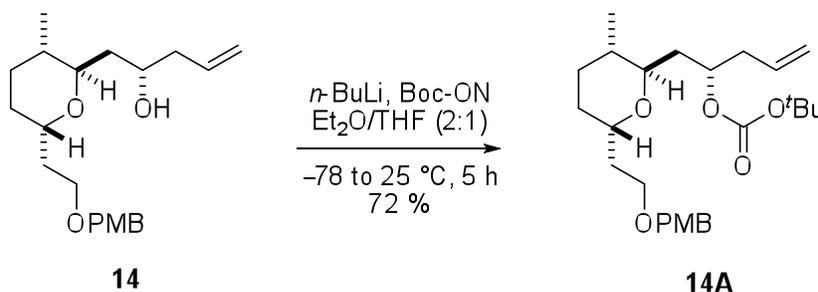
#### Preparation of Homoallyl Alcohol 14



**[Oxidation]** To a cooled (0 °C) solution of alcohol **12A** (480.0 mg, 1.56 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (25.0 mL, 0.062 M) were added DMSO (0.44 mL, 6.23 mmol), *i*-Pr<sub>2</sub>NEt (0.54 mL, 3.11 mmol), and SO<sub>3</sub>·pyridine (495.3 mg, 3.11 mmol). After stirred at 0 °C for 2 h, the reaction mixture was quenched with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and saturated aqueous NaHCO<sub>3</sub> and diluted with Et<sub>2</sub>O. The layers were separated, and the aqueous layer was extracted with Et<sub>2</sub>O. The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The crude aldehyde **12B** was employed in next step without further purification. **[Brown Allylation]** To a cooled (-78 °C) solution of (-)-Ipc<sub>2</sub>B(OMe) (984.5 mg, 3.11 mmol) in Et<sub>2</sub>O (40.0 mL, 0.08 M) was added dropwise allylmagnesium bromide (3.11 mL, 3.11 mmol, 1.0 M in Et<sub>2</sub>O). The reaction mixture was stirred for 15 min at -78 °C and for 1 h at 25 °C. The reaction mixture was recooled

to  $-78\text{ }^{\circ}\text{C}$ , and a solution of **12B** in  $\text{Et}_2\text{O}$  (2 mL) was added dropwise. After stirred at  $-78\text{ }^{\circ}\text{C}$  for 1 h, the resulting mixture was quenched with 1 N NaOH/30%  $\text{H}_2\text{O}_2$  (1:1, total 20 mL). The resulting mixture was stirred for 30 min at  $25\text{ }^{\circ}\text{C}$ , and diluted with  $\text{Et}_2\text{O}$ . The layers were separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 5/1 to 3/1) to afford homoallyl alcohol **14** (418.5 mg, 77%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +45.5$  ( $c$  1.37,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (d,  $J = 8.8$  Hz, 2H), 6.87 (d,  $J = 8.8$  Hz, 2H), 5.82 (dddd,  $J = 16.8, 10.4, 7.2, 7.2$  Hz, 1H), 5.05–5.12 (m, 2H), 4.44(AB,  $\Delta\nu = 14.8$  Hz,  $J_{\text{AB}} = 11.6$  Hz, 2H), 4.00–4.06 (m, 1H), 3.86–3.92 (m, 1H), 3.80 (s, 3H), 3.50–3.56 (m, 3H), 3.07 (d,  $J = 3.6$  Hz, 1H), 2.12–2.29 (m, 3H), 1.74–1.84 (m, 1H), 1.55–1.70 (m, 4H), 1.41–1.51 (m, 2H), 1.28–1.39 (m, 1H), 0.85 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.0, 135.1, 130.3, 129.2, 117.0, 113.6, 72.71, 72.63, 69.8, 67.23, 67.17, 55.1, 42.0, 38.3, 34.2, 30.7, 28.6, 27.0, 18.0; IR (neat) 3438, 1612, 1512, 1363, 1245, 1033, 819  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  349.2372  $[(\text{M}+\text{H})^+]$ ,  $\text{C}_{21}\text{H}_{32}\text{O}_4$  requires 349.2373].

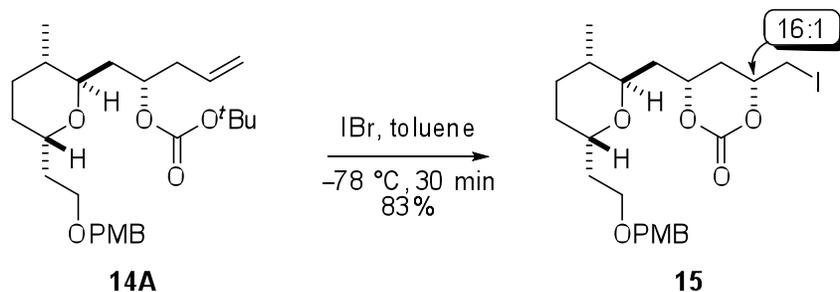
#### Preparation of *tert*-Butyl Carbonate 14A



To a cooled ( $-78\text{ }^{\circ}\text{C}$ ) solution of alcohol **14** (103.1 mg, 0.30 mmol) in  $\text{Et}_2\text{O}$  (6.0 mL, 0.05 M) was added dropwise *n*-BuLi (0.14 mL, 0.35 mmol, 2.5 M in hexanes). After stirred for 30 min at the same temperature, the cold reaction mixture was quickly transferred to a solution of Boc-ON

(145.3 mg, 0.59 mmol) in THF (3.0 mL) at 0 °C via cannular. After stirred at 25 °C for 5 h, the reaction mixture was quenched with saturated aqueous NH<sub>4</sub>Cl, and diluted with Et<sub>2</sub>O. The layers were separated, and the aqueous layer was extracted with Et<sub>2</sub>O. The combined organic layers were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 8/1) to afford carbonate **14A** (95.2 mg, 72%) as a colorless oil:  $[\alpha]_D^{25} = +67.9$  (*c* 2.45, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.27 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.77 (dddd, *J* = 17.0, 10.0, 7.5, 7.5 Hz, 1H), 5.03–5.11 (m, 2H), 4.91–4.97 (m, 1H), 4.45 (AB, Δ*v* = 31.0 Hz, *J*<sub>AB</sub> = 11.0 Hz, 2H), 3.96 (dddd, *J* = 9.0, 4.5, 4.5, 4.5 Hz, 1H), 3.79 (s, 3H), 3.48–3.57 (m, 2H), 3.36 (ddd, *J* = 10.0, 7.0, 2.0 Hz, 1H), 2.37 (dd, *J* = 9.0, 9.0 Hz, 2H), 2.00 (dddd, *J* = 16.5, 11.5, 6.5, 6.5 Hz, 1H), 1.79 (ddd, *J* = 18.5, 7.5, 3.0, 1H), 1.58–1.74 (m, 4H), 1.48 (s, 9H), 1.42–1.48 (m, 1H), 1.32–1.37 (m, 2H), 0.91 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 159.0, 153.1, 133.6, 130.8, 129.3, 117.8, 113.7, 81.5, 73.1, 72.7, 71.8, 68.5, 66.9, 55.2, 39.7, 36.9, 34.3, 32.0, 28.2, 27.8, 26.8, 18.2; IR (neat) 1734, 1514, 1367, 1276, 1169, 1094 cm<sup>-1</sup>; HRMS (FAB) *m/z* 466.3165 [(M+NH<sub>4</sub>)<sup>+</sup>, C<sub>26</sub>H<sub>40</sub>O<sub>6</sub> requires 466.3163].

### Preparation of Cyclic Carbonate **15**

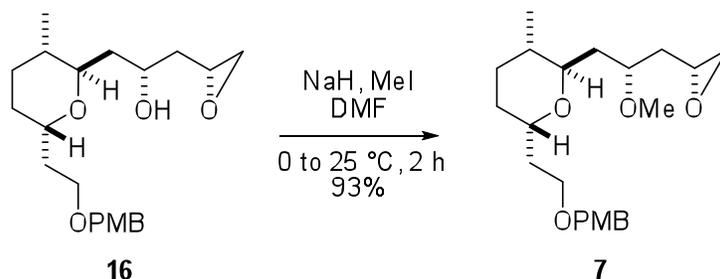


To a cooled (−78 °C) solution of *tert*-butyl carbonate **14A** (184.3 mg, 0.41 mmol) in toluene (10.0 mL, 0.041 M) was added dropwise IBr (0.62 mL, 0.62 mmol, 1.0 M in CH<sub>2</sub>Cl<sub>2</sub>) via syringe. After stirred for 30 min at the same temperature, the reaction mixture was quenched with



hexanes/EtOAc, 3/1) to afford epoxide **16** (114.2 mg, 71%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +42.9$  (*c* 0.58, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.41 (AB, Δ*v* = 14.0 Hz, *J*<sub>AB</sub> = 11.5 Hz, 2H), 4.01–4.10 (m, 2H), 3.79 (s, 3H), 3.50–3.55 (m, 3H), 3.40 (d, *J* = 3.5 Hz, 1H), 3.04–3.09 (m, 1H), 2.75 (dd, *J* = 4.5, 4.0 Hz, 1H), 2.48 (dd, *J* = 5.0, 2.0 Hz, 1H), 2.18 (dddd, *J* = 18.5, 12.0, 7.5, 7.5 Hz, 1H), 1.76–1.84 (m, 1H), 1.68–1.75 (m, 2H), 1.54–1.67 (m, 4H), 1.43–1.52 (m, 2H), 1.29–1.38 (m, 1H), 0.85 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.1, 130.3, 129.3, 113.7, 72.71, 72.62, 70.3, 67.4, 66.1, 55.2, 50.1, 46.7, 39.9, 39.1, 34.4, 30.6, 28.8, 27.2, 18.0; IR (neat) 3432, 1612, 1512, 1246, 1089, 1033, 820 cm<sup>-1</sup>; HRMS (FAB) *m/z* 365.2322 [(M+H)<sup>+</sup>, C<sub>21</sub>H<sub>32</sub>O<sub>5</sub> requires 365.2323].

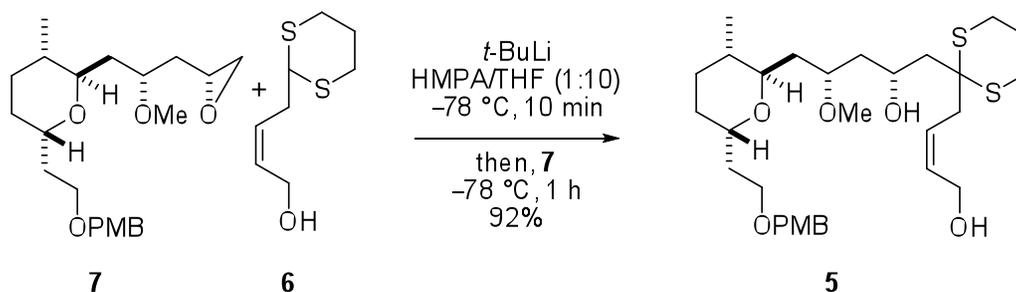
### Preparation of Methyl Ether **7**



To a stirred solution of alcohol **16** (142.5 mg, 0.39 mmol) in DMF (5.0 mL, 0.078 M) were added NaH (28 mg, 1.17 mmol) and MeI (0.05 mL, 0.78 mmol) at 0 °C. After stirred for 2 h at 25 °C, reaction mixture was quenched with saturated aqueous NH<sub>4</sub>Cl and H<sub>2</sub>O, and diluted with CH<sub>2</sub>Cl<sub>2</sub>. The layers were separated, and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford methyl ether **7** (137.4 mg, 93%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +63.5$  (*c* 1.53, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.26 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.45 (s, 2H), 3.96 (dddd, *J* = 9.2, 4.8, 4.8, 4.8 Hz, 1H), 3.80 (s, 3H), 3.47–3.62 (m, 4H), 3.31 (s, 3H), 2.95 (m, 1H), 2.76 (dd, *J* = 5.2, 5.2 Hz, 1H), 2.46 (dd, *J* = 5.2, 2.8 Hz, 1H), 2.06

(dddd,  $J = 14.4, 8.4, 6.0, 6.0$  Hz, 1H), 1.57–1.80 (m, 7H), 1.45–1.52 (m, 1H), 1.30–1.41 (m, 2H), 0.93 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.0, 130.5, 129.1, 113.7, 74.9, 72.7, 71.9, 68.3, 66.9, 56.7, 55.2, 49.0, 46.7, 38.3, 36.3, 34.3, 32.0, 28.2, 26.7, 18.3; IR (neat) 1612, 1512, 1365, 1245, 1087, 1034, 820  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  379.2477 [(M+H) $^+$ ,  $\text{C}_{21}\text{H}_{34}\text{O}_5$  requires 379.2479].

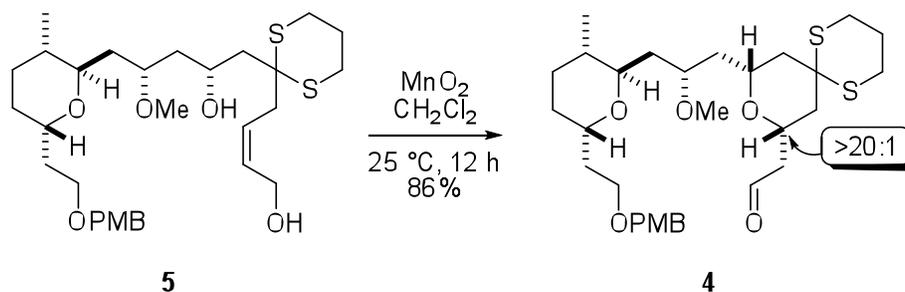
### Preparation of Diol 5



To a cooled ( $-78$  °C) solution of dithiane **6**<sup>3</sup> (113.6 mg, 0.60 mmol) in HMPA/THF (1:10, total 11.0 mL) was added dropwise  $t$ -BuLi (1.05 mL, 1.7 M in pentane, 1.79 mmol) and the resulting mixture was stirred for 10 min before epoxide **7** (147.0 mg, 0.39 mmol) was added. After stirred at  $-78$  °C for 1 h, the reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  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  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 1/1) to afford diol **5** (202.9 mg, 92%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +18.8$  ( $c$  3.20,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (d,  $J = 8.5$  Hz, 2H), 6.86 (d,  $J = 8.5$  Hz, 2H), 5.80 (ddd,  $J = 11.5, 7.0, 7.0$  Hz, 1H), 5.70 (ddd,  $J = 11.0, 7.0, 7.0$  Hz, 1H), 4.43 (AB,  $\Delta\nu = 16.0$  Hz,  $J_{\text{AB}} = 12.0$  Hz, 2H), 4.16–4.21 (m, 1H), 4.08–4.12 (m, 2H), 3.94 (dddd,  $J = 9.0, 4.5, 4.5, 4.5$  Hz, 1H), 3.87 (s, 1H), 3.78 (s, 3H), 3.47–3.57 (m, 3H), 3.41–3.44 (m, 1H), 3.29 (s, 3H), 2.83–2.92 (m, 2H), 2.72–2.83 (m, 5H), 2.17 (dd,  $J = 15.0, 8.5$  Hz, 1H), 1.88–2.04 (m, 4H), 1.78 (ddd,  $J =$

14.0, 9.0, 6.0 Hz, 1H), 1.58–1.73 (m, 5H), 1.44–1.54 (m, 2H), 1.30–1.41 (m, 2H), 0.92 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.1, 131.8, 130.4, 129.2, 126.3, 113.7, 76.6, 72.9, 72.5, 68.5, 66.85, 66.81, 58.1, 56.0, 55.2, 51.8, 45.0, 42.1, 37.7, 36.7, 34.3, 31.9, 28.1, 26.6, 26.2, 26.1, 24.9, 18.3; IR (neat) 3401, 1611, 1512, 1245, 1086, 1031, 818, 733  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  569.2961 [(M+H) $^+$ ],  $\text{C}_{30}\text{H}_{48}\text{O}_6\text{S}_2$  requires 569.2965].

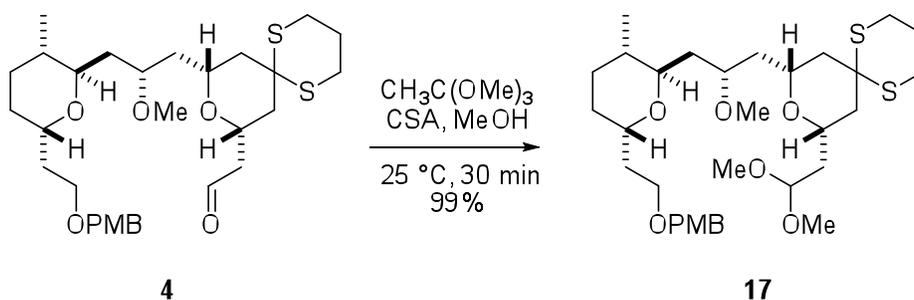
#### Preparation of 2,6-*cis*-Tetrahydropyran **4**



To a stirred solution of diol **5** (73.0 mg, 0.19 mmol) in  $\text{CH}_2\text{Cl}_2$  (5.5 mL, 0.023 M) was added  $\text{MnO}_2$  (55.8 mg, 0.64 mmol), and the resulting mixture was stirred for 1 h at 25 °C. An addition of  $\text{MnO}_2$  (55.8 mg, 0.64 mmol) was repeated three times every 1 h. After stirred for additional 8 h, the reaction mixture was filtered through a pad of celite and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford bis-tetrahydropyran **4** (62.5 mg, 86%) as a colorless oil:  $[\alpha]_{\text{D}}^{25} = +28.8$  ( $c$  1.28,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.75 (dd,  $J = 3.0, 2.0$  Hz, 1H), 7.26 (d,  $J = 8.5$  Hz, 2H), 6.86 (d,  $J = 8.5$  Hz, 2H), 4.41 (AB,  $\Delta\nu = 16.5$  Hz,  $J_{\text{AB}} = 11.5$  Hz, 2H), 4.31 (dddd,  $J = 10.5, 8.5, 4.5, 2.0$  Hz, 1H), 3.89–3.97 (m, 2H), 3.79 (s, 3H), 3.48–3.55 (m, 3H), 3.43–3.47 (m, 1H), 3.27 (s, 3H), 2.82–2.95 (m, 2H), 2.71–2.82 (m, 2H), 2.54 (ddd,  $J = 16.5, 11.0, 3.0$  Hz, 1H), 2.41 (ddd,  $J = 16.0, 4.0, 2.0$  Hz, 1H), 2.31 (d,  $J = 13.5$  Hz, 1H), 2.23 (d,  $J = 13.5$  Hz, 1H), 1.93–2.09 (m, 3H), 1.45–1.78 (m, 10H), 1.25–1.39 (m, 2H), 0.91 (d,  $J = 6.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  200.8, 159.0, 130.6, 129.1, 113.6, 74.1, 72.6, 72.0, 69.5, 68.3, 68.2, 67.1, 56.6, 55.1, 48.9, 47.6, 43.3, 42.5,

39.3, 38.4, 34.2, 32.0, 28.1, 26.7, 25.75, 25.67, 25.57, 18.2; IR (neat) 2361, 2337, 1700, 1512, 1436, 1245, 1092, 1033, 819  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  567.2808  $[(M+H)^+]$ ,  $\text{C}_{30}\text{H}_{46}\text{O}_6\text{S}_2$  requires 567.2809].

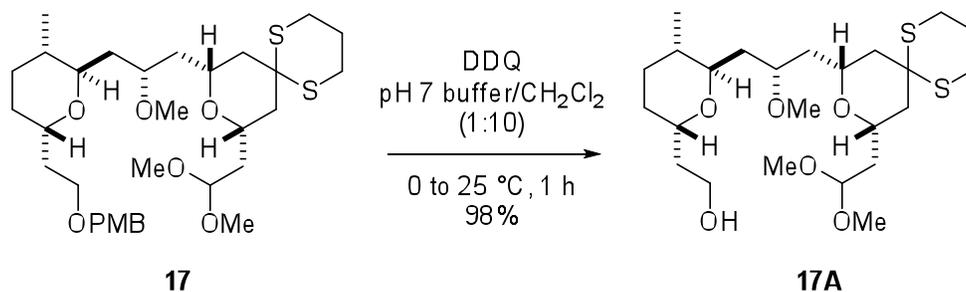
### Preparation of Dimethyl Acetal 17



To a stirred solution of aldehyde **4** (72.5 mg, 0.13 mmol) in MeOH (4.0 mL, 0.032 M) were added trimethyl orthoacetate (0.05 mL, 0.38 mmol) and (1*S*)-(+)-10-camphorsulfonic acid (3.0 mg, 0.013 mmol) at 25 °C. After stirred for 30 min at 25 °C, reaction mixture was quenched with saturated aqueous  $\text{NaHCO}_3$ , and diluted with EtOAc and  $\text{H}_2\text{O}$ . The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford acetal **17** (77.8 mg, 99%) as a colorless oil:  $[\alpha]_D^{25} = +23.6$  ( $c$  1.66,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (d,  $J = 8.5$  Hz, 2H), 6.86 (d,  $J = 8.5$  Hz, 2H), 4.59 (dd,  $J = 7.5$  Hz, 1H), 4.43 (AB,  $\Delta\nu = 13.5$  Hz,  $J_{\text{AB}} = 11.5$  Hz, 2H), 3.94 (dddd,  $J = 9.0, 4.5, 4.5, 4.5$  Hz, 1H), 3.81–3.87 (m, 2H), 3.79 (s, 3H), 3.50–3.59 (m, 1H), 3.53 (dd,  $J = 7.0, 6.5$  Hz, 2H), 3.43–3.47 (m, 1H), 3.37 (s, 3H), 3.29 (s, 3H), 3.28 (s, 3H), 2.83–2.93 (m, 2H), 2.70–2.80 (m, 2H), 2.24 (d,  $J = 12.5$  Hz, 1H), 2.21 (d,  $J = 12.5$  Hz, 1H), 2.02–2.11 (m, 1H), 1.94–2.01 (m, 2H), 1.80 (ddd,  $J = 14.5, 8.0, 4.5$  Hz, 1H), 1.51–1.77 (m, 11H), 1.44–1.50 (m, 2H), 1.31–1.38 (m, 2H), 0.90 (d,  $J = 6.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  159.1, 130.6, 129.2, 113.7, 102.1, 74.0, 72.7, 71.7, 69.31, 69.29, 68.6, 67.2, 56.6, 55.2, 54.2,

52.8, 47.9, 43.7, 43.2, 39.5, 39.4, 38.5, 34.7, 31.7, 28.4, 27.0, 25.87, 25.78, 25.76, 18.3; IR (neat) 1724, 1512, 1457, 1247, 1093, 1038, 820  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  630.3496  $[(M+NH_4)^+]$ ,  $C_{32}H_{52}O_7S_2$  requires 630.3493].

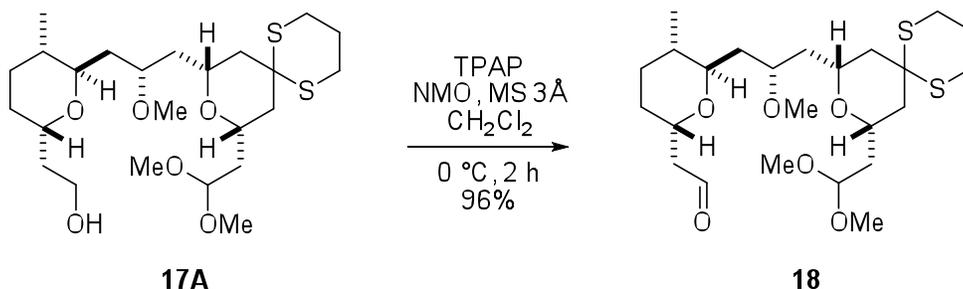
### Preparation of Alcohol 17A



To a stirred solution of PMB-ether **17** (73.3 mg, 0.12 mmol) in pH 7 buffer/ $\text{CH}_2\text{Cl}_2$  (1/10, total 5.5 mL) was added DDQ (40.5 mg, 0.18 mmol) at 0 °C. The reaction mixture was stirred at 25 °C for 1 h, quenched with saturated aqueous  $\text{NaHCO}_3$ , and diluted with  $\text{H}_2\text{O}$ . The resulting mixture was stirred vigorously for 1 h. The layers were separated, and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 1/2) to afford alcohol **17A** (57.4 mg, 98%) as a colorless oil:  $[\alpha]_D^{25} = +27.1$  ( $c$  1.08,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.62 (dd,  $J = 7.5, 3.5$  Hz, 1H), 3.94 (dddd,  $J = 10.0, 5.0, 5.0, 5.0$  Hz, 1H), 3.69–3.86 (m, 4H), 3.54–3.62 (m, 2H), 3.34 (s, 3H), 3.32 (s, 3H), 3.30 (s, 3H), 2.87–2.90 (m, 3H), 2.74–2.77 (m, 3H), 2.23 (d,  $J = 12.0$  Hz, 1H), 2.21 (d,  $J = 12.0$  Hz, 1H), 1.97–2.04 (m, 3H), 1.86 (ddd,  $J = 13.5, 9.0, 4.5$  Hz, 1H), 1.66–1.81 (m, 4H), 1.44–1.64 (m, 7H), 1.34–1.45 (m, 2H), 0.96 (d,  $J = 6.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  101.7, 74.2, 72.6, 69.7, 69.39, 69.30, 60.6, 56.4, 53.4, 52.4, 47.9, 43.6, 43.2, 39.23, 39.10, 37.4, 35.0, 33.7, 28.1, 26.4, 25.88, 25.80, 25.74, 18.4; IR (neat) 2360, 2338, 1733,

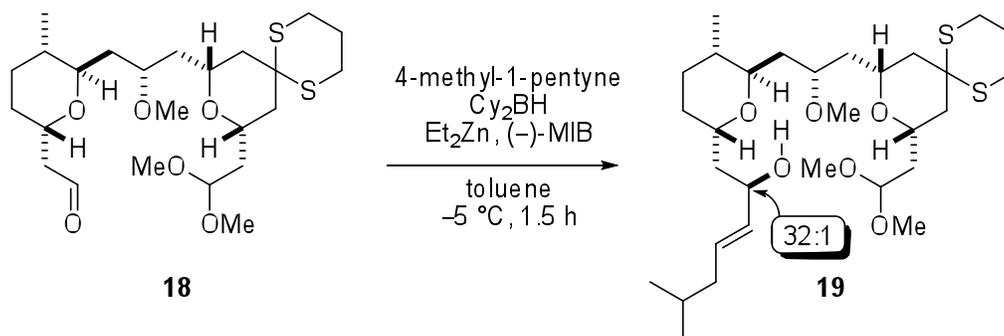
1558, 1456, 1243, 1122, 1052, 667  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  510.2918  $[(M+NH_4)^+]$ ,  $C_{24}H_{44}O_6S_2$  requires 510.2918].

### Preparation of Aldehyde **18**



To a stirred solution of alcohol **17A** (85.3 mg, 0.17 mmol) in  $\text{CH}_2\text{Cl}_2$  (5.0 mL, 0.035 M) were added MS 3Å (~170 mg), NMO (40.5 mg, 0.35 mmol), and TPAP (3 mg) at 0 °C. After stirred at 0 °C for 2 h, the reaction mixture was diluted with hexanes (4 mL). The resulting mixture was stirred for 30 min and filtered through a short pad of silica gel to afford aldehyde **18** (81.4 mg, 96%) as a colorless oil:  $[\alpha]_D^{25} = +25.3$  ( $c$  0.79,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.77 (dd,  $J = 3.0, 1.5$  Hz, 1H), 4.55 (dd,  $J = 8.0, 3.5$  Hz, 1H), 4.39 (dddd,  $J = 9.0, 4.0, 4.0, 4.0$  Hz, 1H), 3.76–3.84 (m, 2H), 3.45–3.51 (m, 2H), 3.34 (s, 3H), 3.28 (s, 3H), 3.27 (s, 3H), 2.84–2.91 (m, 3H), 2.72–2.76 (m, 2H), 2.40 (ddd,  $J = 16.0, 5.0, 2.0$  Hz, 1H), 2.22 (d,  $J = 13.5$  Hz, 1H), 2.18 (d,  $J = 13.5$  Hz, 1H), 1.94–2.02 (m, 2H), 1.79 (ddd,  $J = 14.0, 8.5, 4.5$  Hz, 1H), 1.62–1.76 (m, 4H), 1.53–1.61 (m, 4H), 1.46–1.52 (m, 1H), 1.38–1.45 (m, 1H), 1.28–1.38 (m, 2H), 0.91 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  201.3, 101.9, 73.8, 72.4, 69.31, 69.21, 66.9, 56.7, 53.9, 52.7, 47.9, 45.9, 43.5, 43.1, 39.6, 39.2, 38.2, 34.1, 28.0, 26.6, 25.8, 25.7, 18.1; IR (neat) 1724, 1457, 1387, 1099, 1052  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  508.2760  $[(M+NH_4)^+]$ ,  $C_{24}H_{42}O_6S_2$  requires 508.2761].

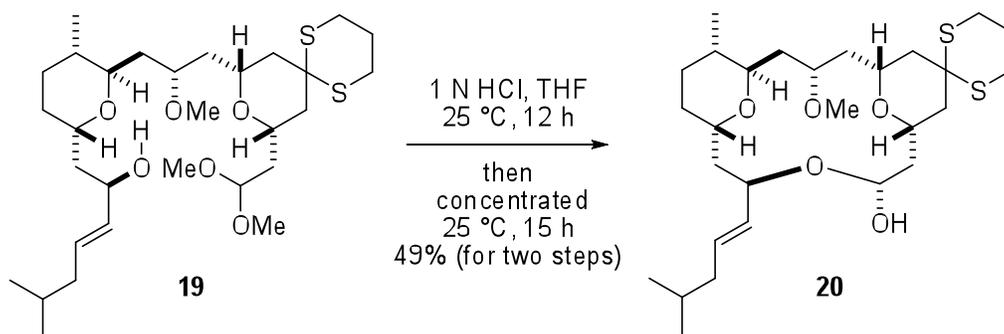
## Preparation of Allyl Alcohol 19



To a cooled ( $-5\text{ }^\circ\text{C}$ ) solution of (-)-MIB (1.0 mg, 0.004 mmol) and  $\text{Et}_2\text{Zn}$  (0.29 mL, 0.32 mmol, 1.1 M in toluene) in toluene (2.0 mL) was added aldehyde **18** (52.0 mg, 0.11 mmol) in toluene (0.5 mL). Vinylborane (0.22 mL, 0.22 mmol, 1.0 M in toluene, freshly prepared according to Oppolzer's report<sup>4</sup>) was slowly added by a syringe pump over 1 h. The reaction mixture was stirred for additional 30 min at  $-5\text{ }^\circ\text{C}$ , quenched with saturated aqueous  $\text{NH}_4\text{Cl}$ , and diluted with  $\text{Et}_2\text{O}$ . The resulting mixture was stirred for 1 h at  $25\text{ }^\circ\text{C}$ . The layers were separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was filtered through a short pad of silica gel (hexanes/ $\text{EtOAc}$ , 2/1) to afford crude allyl alcohol **19** (dr = 32:1) as a colorless oil:  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.67 (dddd,  $J = 15.0, 7.0, 7.0, 1.0$  Hz, 1H), 5.52 (dd,  $J = 15.5, 6.0$  Hz, 1H), 4.69 (dd,  $J = 7.5, 3.5$  Hz, 1H), 4.34 (br d, 3.5 Hz, 1H), 4.08 (dddd,  $J = 9.5, 5.0, 5.0, 5.0$  Hz, 1H), 3.81–3.89 (m, 2H), 3.61–3.67 (m, 1H), 3.56–3.60 (m, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 3.32 (s, 3H), 3.06 (d,  $J = 4.5$  Hz, 1H), 2.90–2.93 (m, 2H), 2.79 (dd,  $J = 6.5, 4.5$  Hz, 2H), 2.23 (d,  $J = 13.5$  Hz, 1H), 2.26 (d,  $J = 13.5$  Hz, 1H), 1.85–2.04 (m, 6H), 1.68–1.82 (m, 4H), 1.57–1.67 (m, 5H), 1.46–1.55 (m, 2H), 1.35–1.46 (m, 2H) 0.99 (d,  $J = 6.5$  Hz, 3H), 0.91 (d,  $J = 6.5$  Hz, 3H), 0.90 (d,  $J = 6.5$  Hz, 3H); IR (neat) 3459, 1717, 1386, 1095, 968, 667  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  592.3693 [ $(\text{M}+\text{NH}_4)^+$ ,  $\text{C}_{30}\text{H}_{54}\text{O}_6\text{S}_2$  requires 592.3700].

The diastereomeric ratio was determined by Shimadzu HPLC system through Phenomenex Luna C<sub>18</sub> (5 micron, 4.60 × 250 mm) column with a flow rate of 1 mL/min and isocratic 80% MeOH in H<sub>2</sub>O using SPD-20A UV/VIS detector (230 nm, 254 nm). The 1:1 mixture of (17*S*)- and (17*R*)-alcohols was prepared by Dess–Martin oxidation of the crude alcohol **19** and DIBAL-H reduction of the resulting ketone.

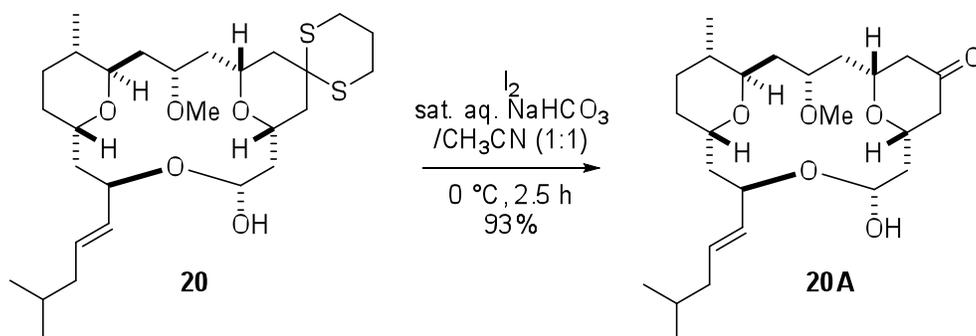
### Preparation of Macrolactol **20**



To a stirred solution of the above alcohol **19** in THF (2.0 mL) was added 1 N HCl (1.0 mL) at 25 °C. After stirred vigorously for 12 h at the same temperature, the reaction mixture was diluted with H<sub>2</sub>O, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The resulting crude oil was left for 15 h at 25 °C, and the residue was purified by column chromatography (silica gel, hexanes/EtOAc, 4/1) to afford macrolactol **20** (27.5 mg, 49% for two steps) as a colorless oil:  $[\alpha]_D^{25} = +59.8$  (*c* 0.22, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.73 (ddd, *J* = 14.5, 7.0, 7.0 Hz, 1H), 5.12 (dd, *J* = 15.0, 9.0 Hz, 1H), 4.71 (ddd, *J* = 9.5, 9.5, 4.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.34 (ddd, *J* = 11.0, 11.0, 3.0 Hz, 1H), 3.92 (d, *J* = 11.5 Hz, 1H), 3.74–3.81 (m, 2H), 3.63 (dd, *J* = 11.5, 11.5 Hz, 1H), 3.37 (s, 3H), 2.90 (ddd, *J* = 5.0, 4.5, 4.5 Hz, 2H), 2.78 (dd, *J* = 7.0, 4.5 Hz, 2H), 2.48 (dd, *J* = 14.0, 12.5 Hz, 1H), 2.22 (d, *J* = 14.5 Hz, 1H), 2.18 (d, *J* = 13.5 Hz, 1H), 1.85–2.04 (m, 5H), 1.69–1.83 (m, 4H), 1.45–1.65 (m, 5H), 1.42 (d, *J* = 12.0 Hz, 1H), 1.32

(d,  $J = 14.5$  Hz, 1H), 1.26 (dd,  $J = 13.0, 13.0$  Hz, 1H), 1.18 (d,  $J = 7.5$  Hz, 3H), 1.05 (ddd,  $J = 14.5, 11.0, 2.5$  Hz, 1H), 0.88 (dd,  $J = 6.5$  Hz, 3H), 0.86 (dd,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  134.2, 130.7, 90.9, 74.1, 73.7, 71.8, 71.0, 68.7, 63.2, 57.1, 47.6, 44.2, 43.5, 43.3, 41.7, 39.5, 38.4, 35.8, 31.1, 28.1, 27.2, 26.04, 25.96, 25.7, 24.4, 22.32, 22.27, 18.4; IR (neat) 3481, 1733, 1558, 1456, 1088, 973, 667  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  546.3276  $[(\text{M}+\text{NH}_4)^+]$ ,  $\text{C}_{28}\text{H}_{48}\text{O}_5\text{S}_2$  requires 546.3281].

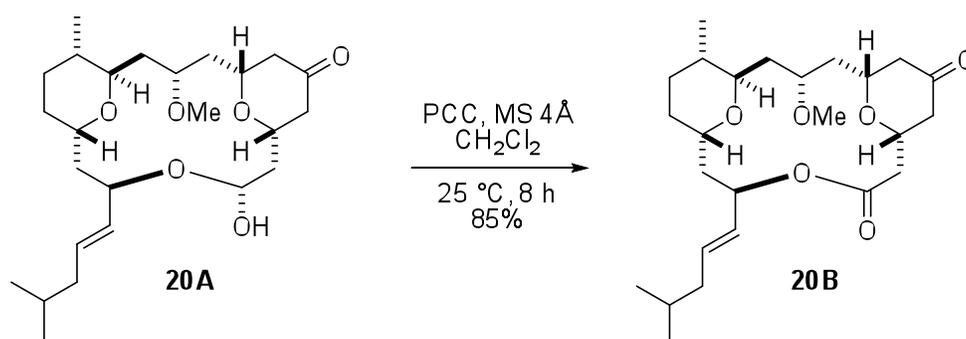
### Preparation of Ketone **20A**



To a stirred solution of dithiane **20** (12.3 mg, 0.023 mmol) in saturated aqueous  $\text{NaHCO}_3/\text{CH}_3\text{CN}$  (1:1, total 1.5 mL) was added  $\text{I}_2$  (11.8 mg, 0.046 mmol) at  $0^\circ\text{C}$ . An addition of  $\text{I}_2$  (11.8 mg, 0.046 mmol) was repeated two times every 20 min at the same temperature. The reaction mixture was quenched with saturated aqueous  $\text{Na}_2\text{S}_2\text{O}_3$  and saturated aqueous  $\text{NaHCO}_3$ , and diluted with  $\text{Et}_2\text{O}$ . The layers were separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/ $\text{EtOAc}$ , 4/1) to afford ketone **20A** (9.4 mg, 93%) as a colorless oil.  $[\alpha]_{\text{D}}^{25} = +70.8$  ( $c$  0.17,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.75 (ddd,  $J = 15.0, 7.0, 7.0$  Hz, 1H), 5.11 (dd,  $J = 15.5, 9.0$  Hz, 1H), 4.95 (dd,  $J = 12.0, 2.5$  Hz, 1H), 4.68–4.74 (m, 1H), 4.47 (d,  $J = 12.0$  Hz, 1H), 4.27 (dddd,  $J = 10.5, 10.5, 3.0, 3.0$  Hz, 1H), 3.93 (d,  $J = 11.5$  Hz, 1H), 3.68 (dd,  $J = 11.5, 11.5$  Hz, 2H), 3.60 (ddd,  $J = 10.5, 10.5, 4.5$  Hz,

1H), 3.41 (s, 3H), 2.30–2.44 (m, 5H), 2.11 (ddd,  $J = 11.5, 11.5, 2.0$  Hz, 1H), 1.84–1.97 (m, 5H), 1.38–1.66 (m, 4H), 1.36 (dd,  $J = 12.0, 12.0$  Hz, 1H), 1.25–1.29 (m, 2H), 1.17 (d,  $J = 7.5$  Hz, 3H), 1.80 (ddd,  $J = 14.5, 10.5, 2.0$  Hz, 1H), 0.88 (d,  $J = 6.5$  Hz, 3H), 0.86 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  205.6, 134.5, 130.4, 90.5, 75.31, 75.09, 73.81, 73.54, 69.0, 63.3, 57.2, 48.0, 47.7, 44.1, 41.7, 40.4, 39.1, 35.8, 30.9, 28.1, 27.1, 24.3, 22.31, 22.26, 18.3; IR (neat) 3499, 1718, 1436, 1365, 1241, 1089, 989  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  456.3317 [(M+NH $_4$ ) $^+$ , C $_{25}$ H $_{42}$ O $_6$  requires 456.3320].

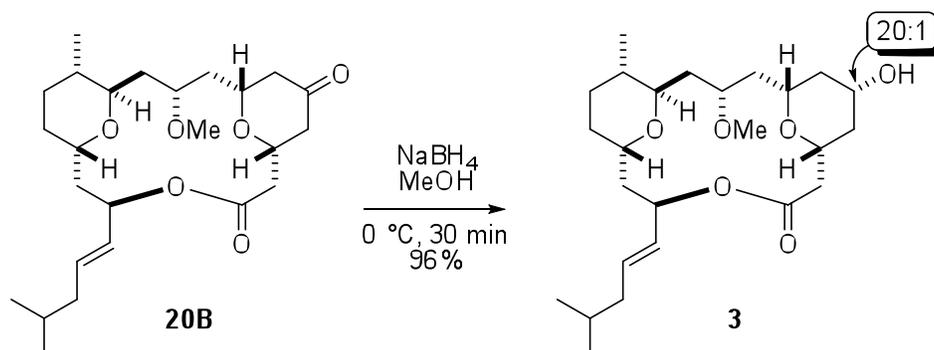
### Preparation of Macrolactone 20B



To a stirred solution of lactol **20A** (6.5 mg, 0.015 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL, 0.015 M) were added PCC (16.0 mg, 0.074 mmol) and MS 4Å (13 mg) at 25 °C. After stirred for 8 h at the same temperature, the reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and filtered through a short pad of silica gel. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford lactone **20B** (5.6 mg, 85%) as a white solid:  $[\alpha]_{\text{D}}^{25} = +69.2$  ( $c$  0.12,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.68–5.77 (m, 1H), 5.30–5.41 (m, 2H), 4.02 (dddd,  $J = 11.5, 11.5, 3.0, 3.0$  Hz, 1H), 3.89 (d,  $J = 11.5$  Hz, 1H), 3.45–3.56 (m, 3H), 3.38 (s, 3H), 2.64 (dd,  $J = 13.0, 3.5$  Hz, 1H), 2.44–2.50 (m, 2H), 2.25–2.38 (m, 3H), 2.11 (ddd,  $J = 13.5, 11.5, 2.0$  Hz, 1H), 1.82–1.94 (m, 3H), 1.58–1.75 (m, 3H), 1.41–1.58 (m, 3H), 1.29–1.34 (m, 2H), 1.16 (d,  $J = 7.0$  Hz, 3H), 1.05 (ddd,  $J = 14.5, 11.0, 2.5$  Hz, 1H), 0.86 (d,  $J = 6.5$  Hz, 3H), 0.84 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$

NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  205.6, 168.6, 132.8, 129.8, 74.4, 73.57, 73.55, 73.5, 71.3, 63.1, 57.4, 47.9, 47.4, 43.4, 42.7, 41.6, 39.6, 35.6, 30.9, 28.1, 27.1, 24.1, 22.2, 18.2; IR (neat) 1733, 1372, 1235, 1021, 734 cm<sup>-1</sup>; HRMS (ESI)  $m/z$  454.3164 [(M+NH<sub>4</sub>)<sup>+</sup>, C<sub>25</sub>H<sub>40</sub>O<sub>6</sub> requires 454.3163].

### Preparation of Leucascandrolide A Macrolactone (**3**)

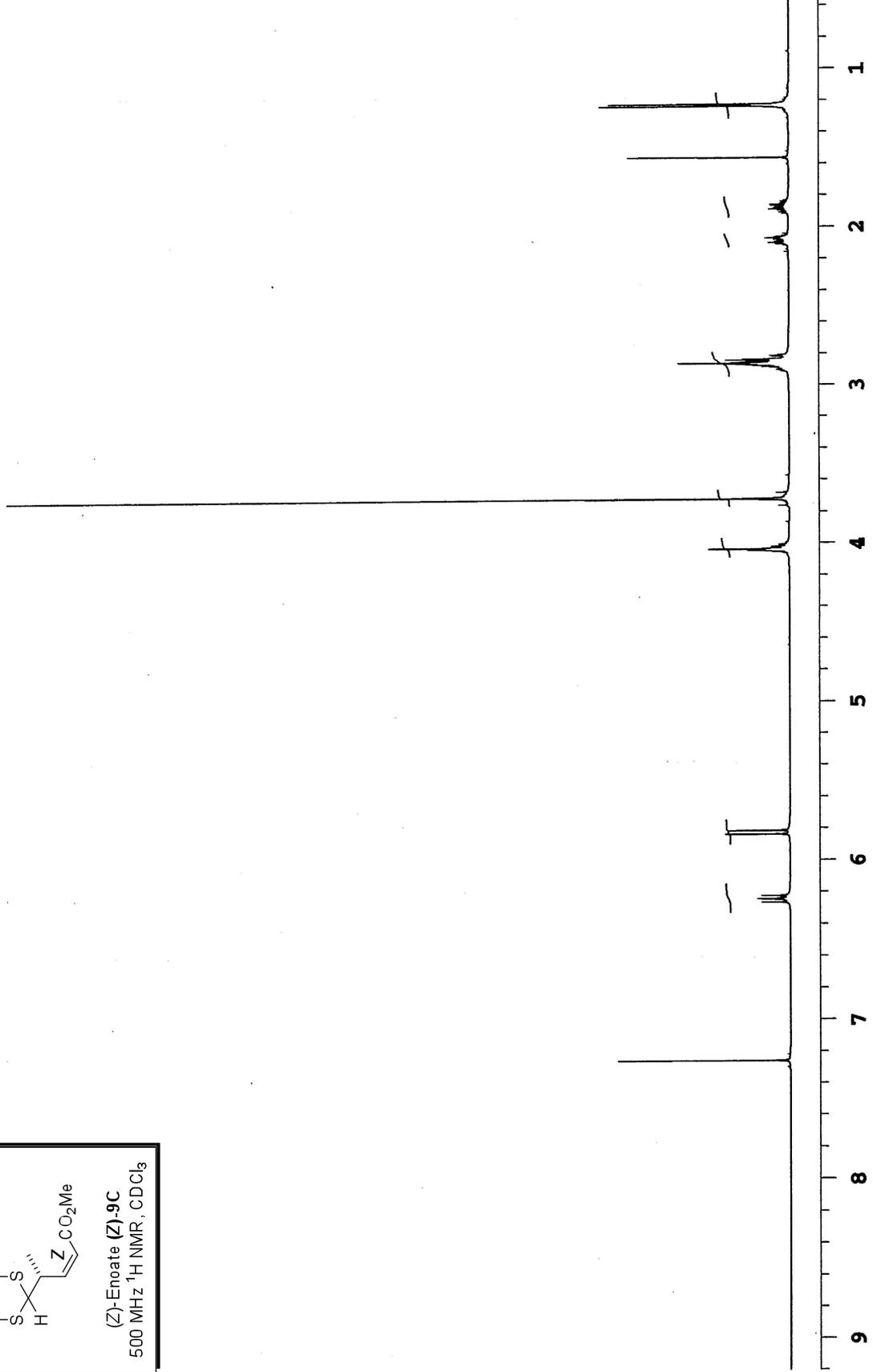
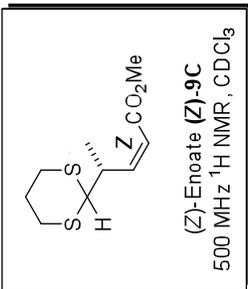


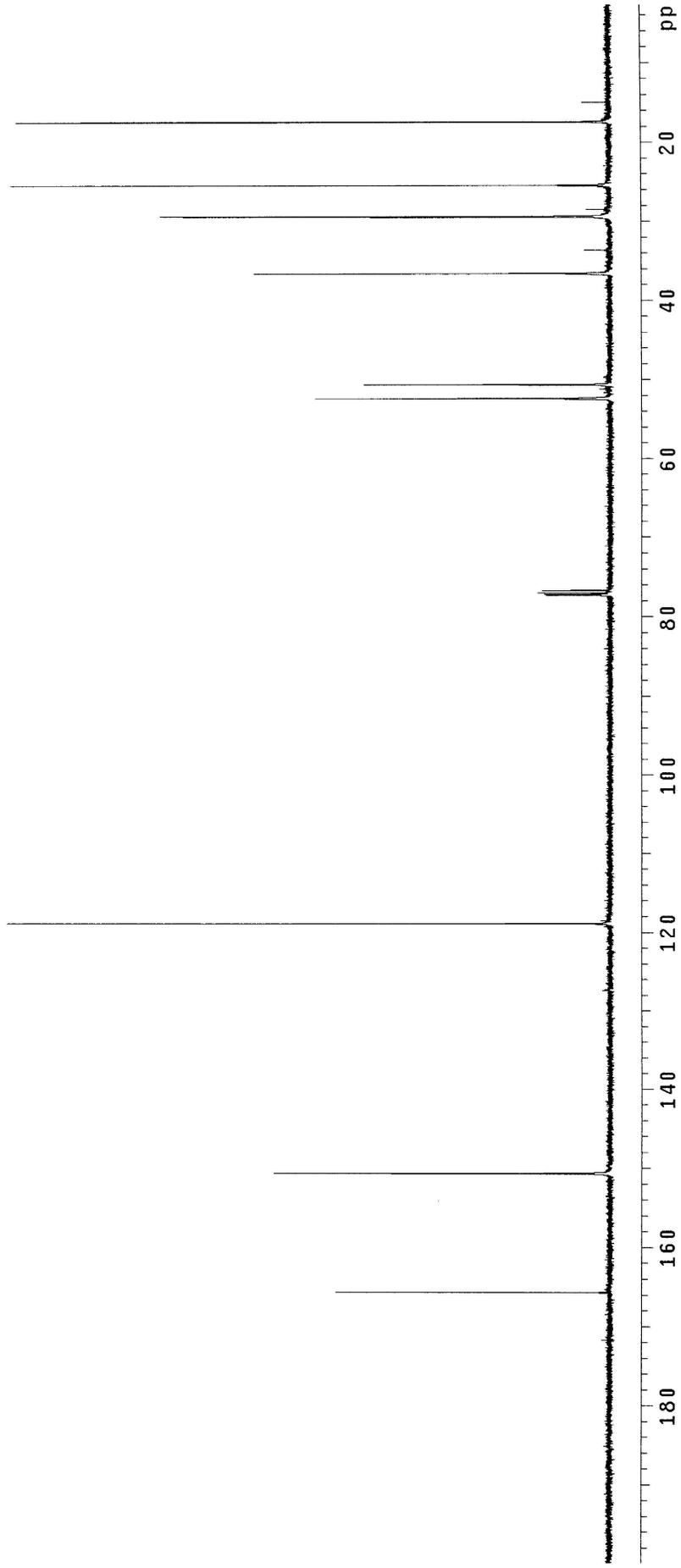
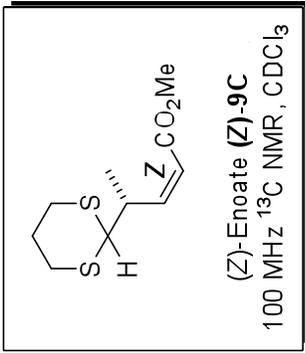
To a stirred solution of ketone **20B** (5.4 mg, 0.012 mmol) in MeOH (1 mL) was added NaBH<sub>4</sub> (1.8 mg, 0.048 mmol) at 0 °C. The reaction mixture was stirred for 30 min at the same temperature before AcOH (0.02 mL) was added. The resulting mixture was concentrated and the residue was purified by column chromatography (silica gel, hexanes/EtOAc, 1/1 to 1/2) to afford the known leucascandrolide A macrolactone **3** (5.2 mg, 96% as a 20:1 mixture of diastereomers) as a white solid whose spectral data were identical to those of the known synthetic **3**<sup>5a-c</sup>:  $[\alpha]_{\text{D}}^{25} = +54.1$  ( $c$  0.07, EtOH); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.70 (ddd,  $J = 14.0, 7.0, 7.0$  Hz, 1H), 5.31–5.38 (m, 2H), 3.89 (d,  $J = 9.0$  Hz, 2H), 3.72 (dddd,  $J = 7.5, 7.5, 2.0, 2.0, 2.0$  Hz, 1H), 3.51 (dd,  $J = 10.5, 10.5$  Hz, 2H), 3.35 (s, 3H), 3.21 (dd,  $J = 11.5, 11.5$  Hz, 1H), 2.56 (dd,  $J = 13.0, 3.5$  Hz, 1H), 2.30–2.42 (m, 2H), 2.00–2.05 (m, 2H), 1.81–1.92 (m, 4H), 1.56–1.74 (m, 3H), 1.47–1.56 (m, 3H), 1.40–1.46 (m, 1H), 1.20–1.33 (m, 4H), 1.16 (d,  $J = 7.0$  Hz, 3H), 1.00 (ddd,  $J = 14.0, 10.5, 2.0$  Hz, 1H), 0.85 (d,  $J = 6.0$  Hz, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  169.3, 132.4, 130.1, 73.61, 73.54, 73.0, 72.2, 70.8, 68.0, 63.0, 57.3, 43.1, 42.8, 41.6, 41.1, 40.8, 39.1, 35.5, 31.0, 28.1,

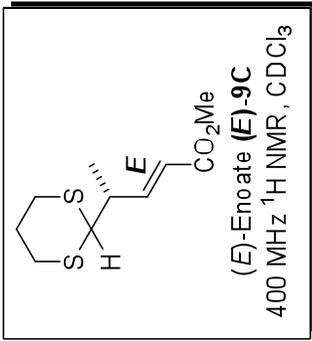
27.1, 24.1, 22.2, 18.2; IR (neat) 3438, 1739, 1457, 1261, 1085, 962  $\text{cm}^{-1}$ ; HRMS (FAB)  $m/z$  456.3321 [(M+NH<sub>4</sub>)<sup>+</sup>, C<sub>25</sub>H<sub>42</sub>O<sub>6</sub> requires 456.3320].

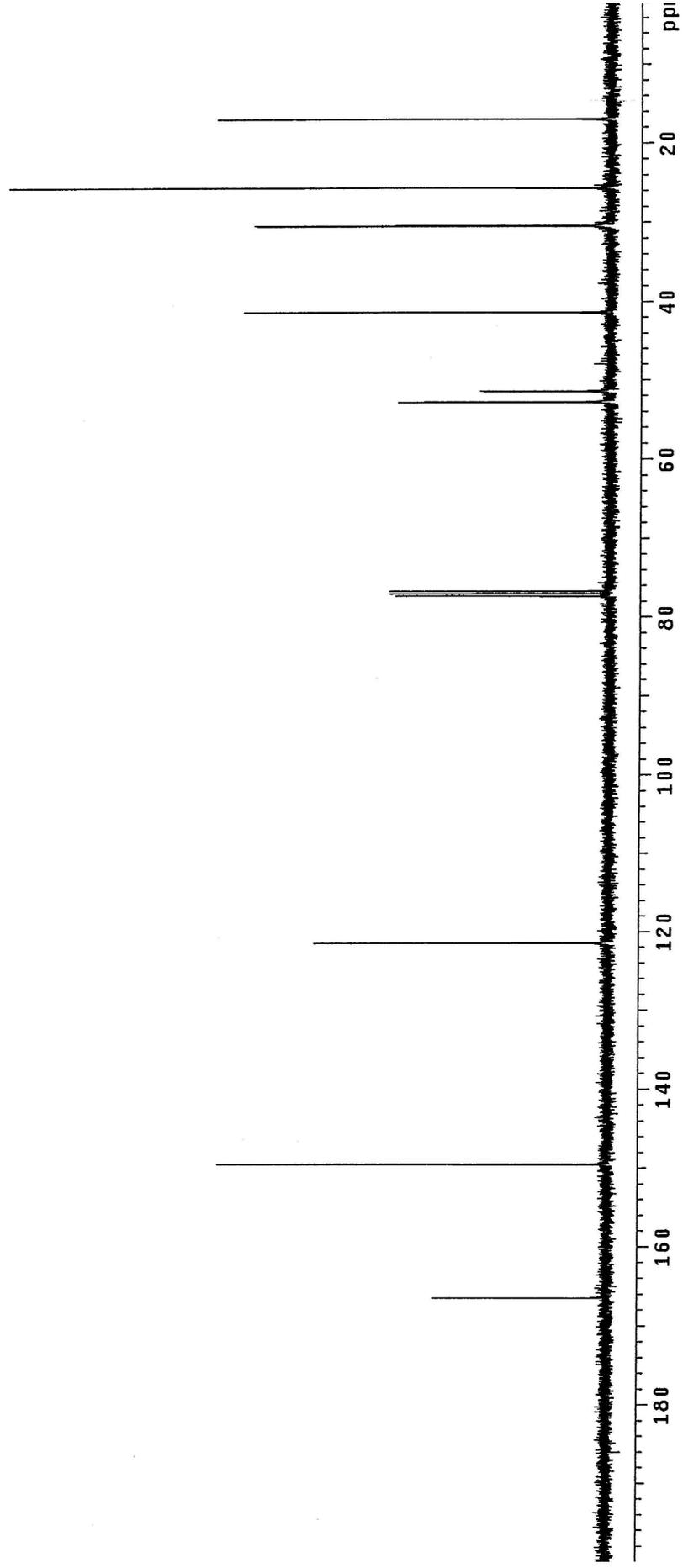
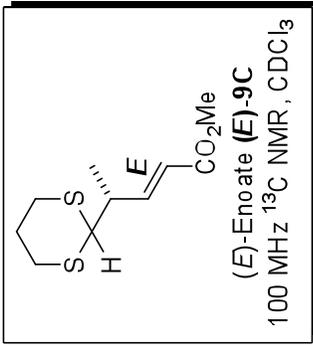
## References

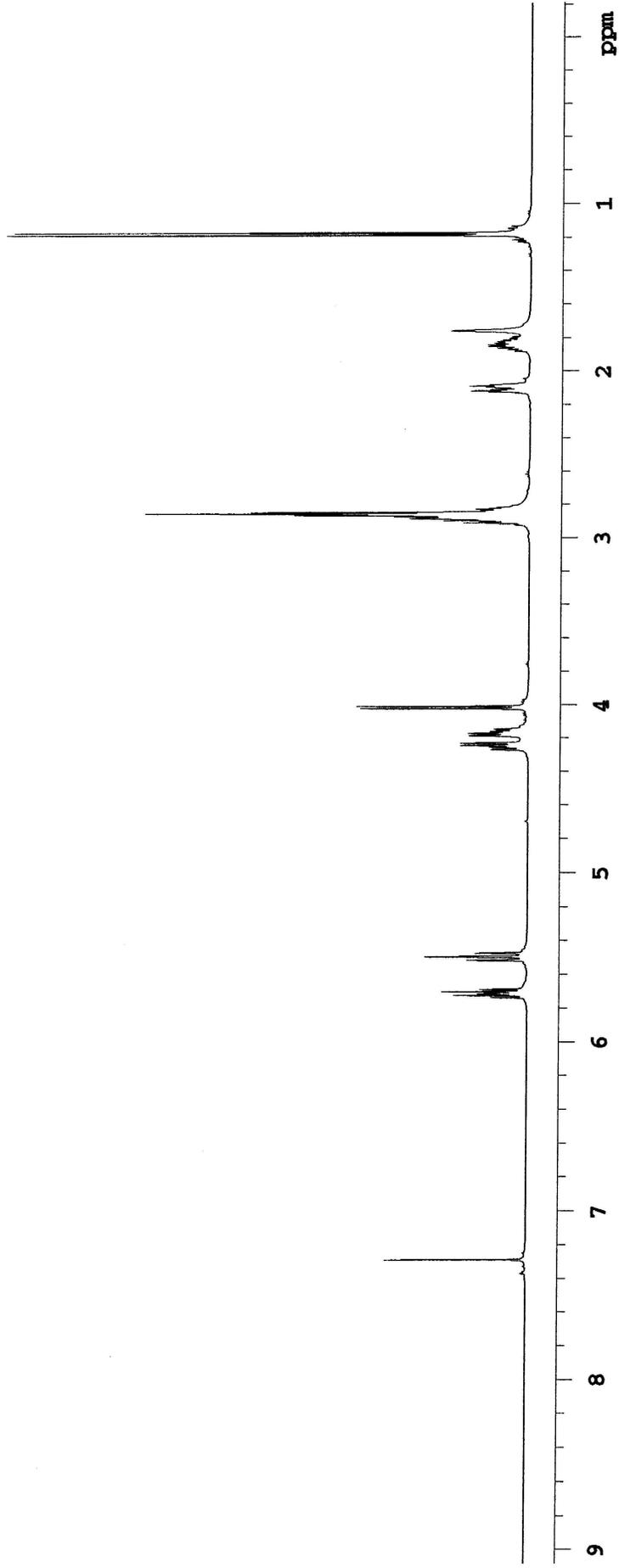
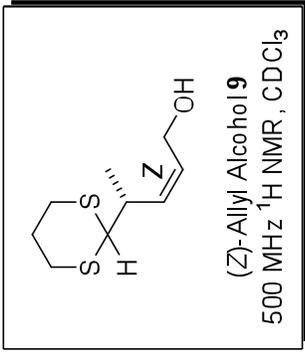
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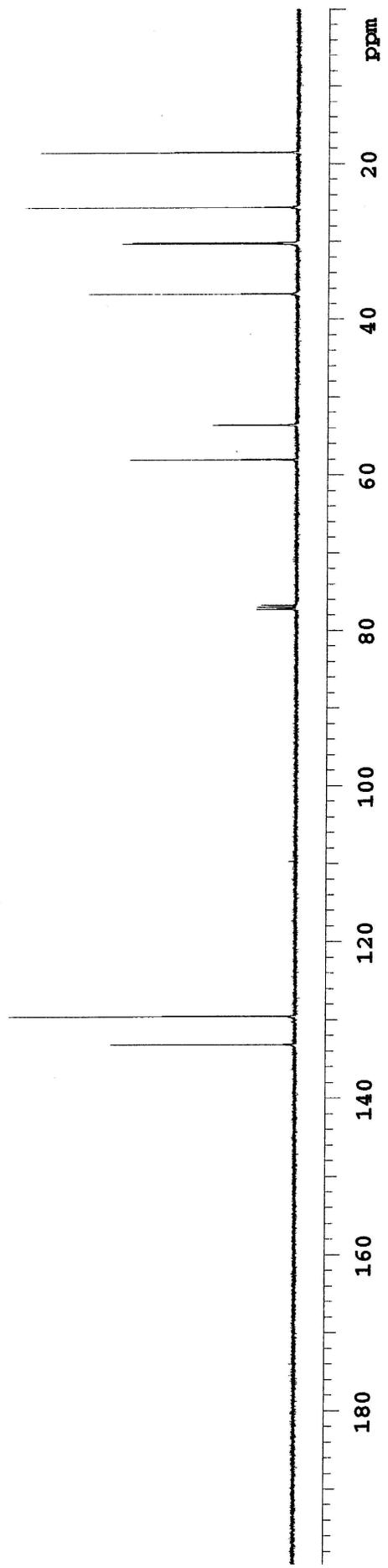
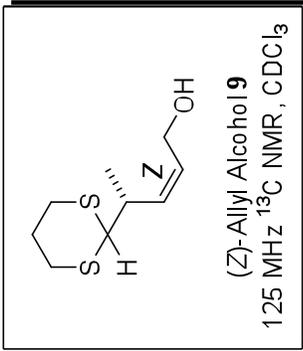


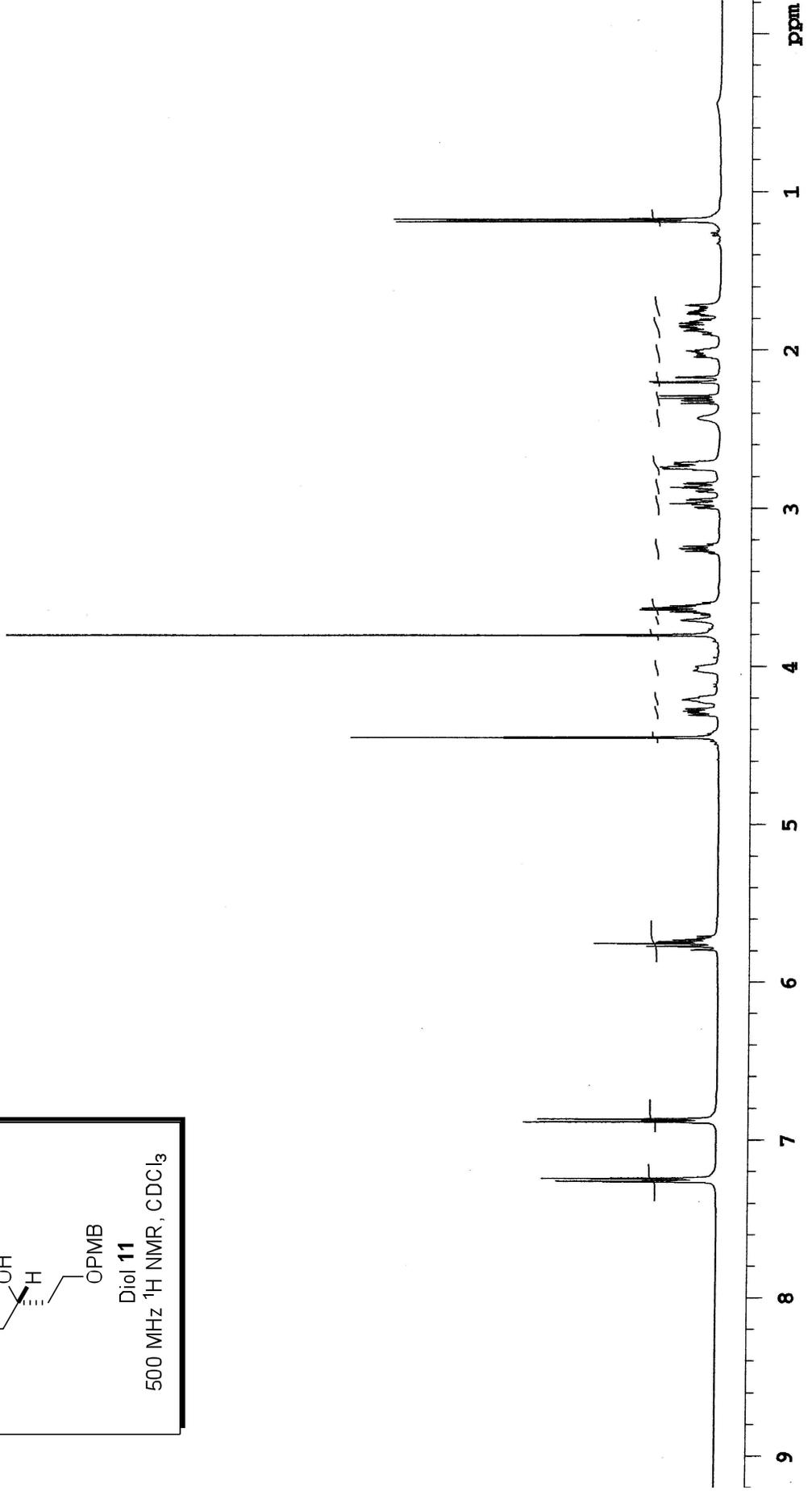
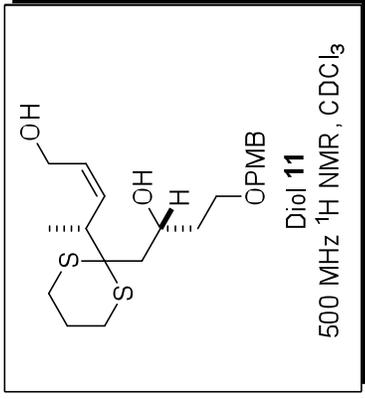


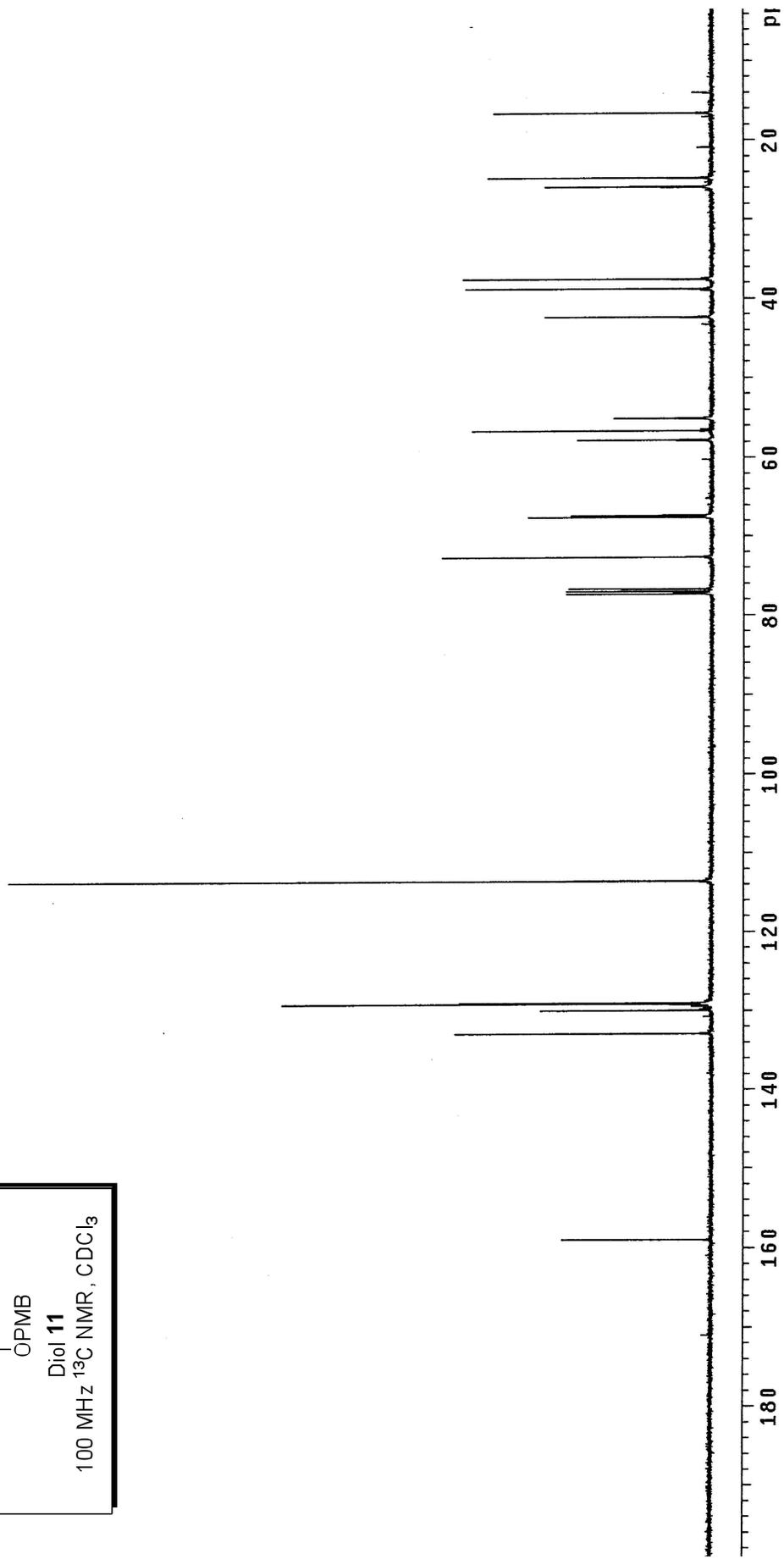
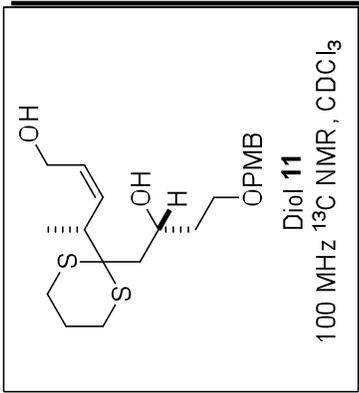


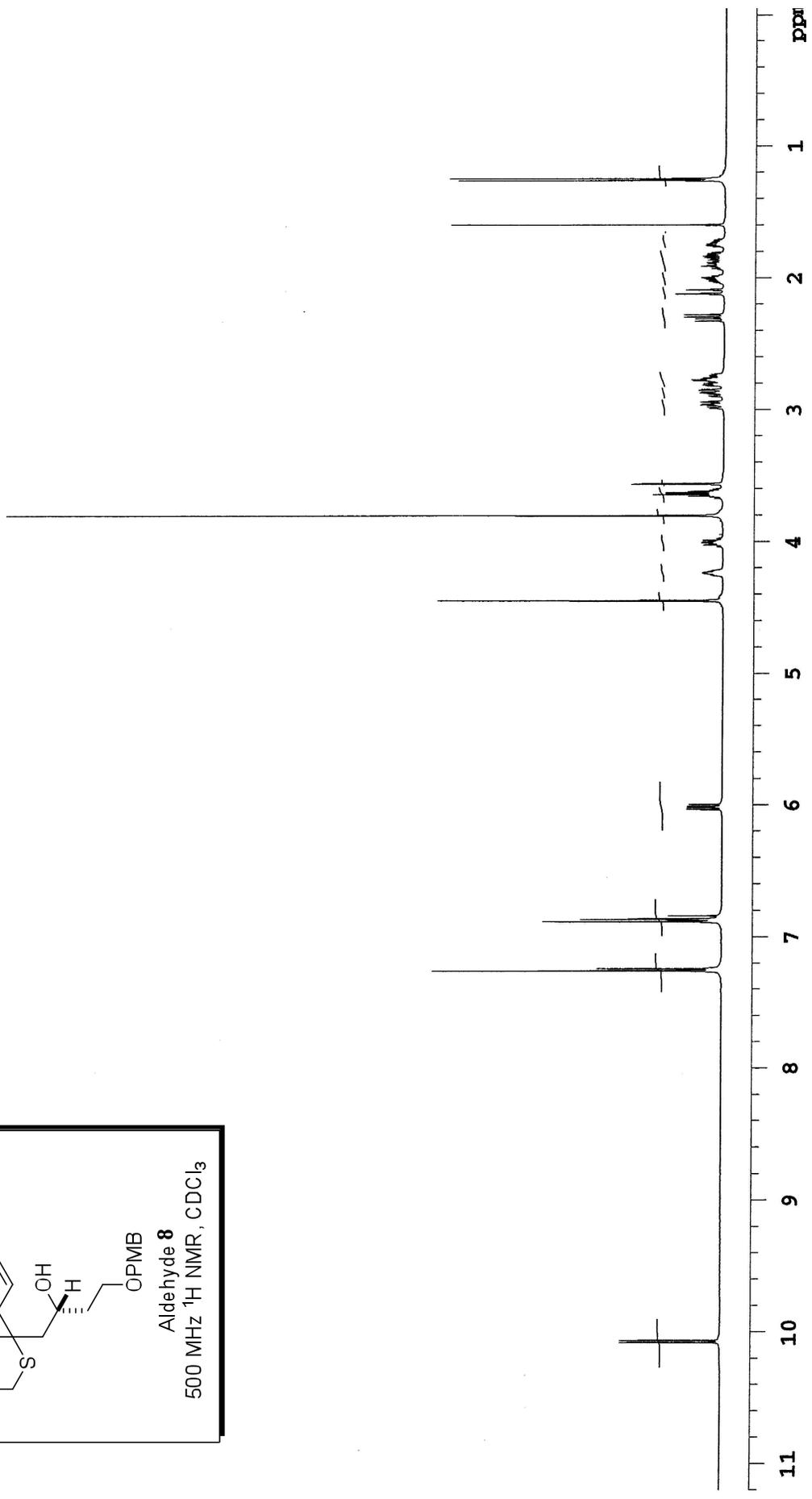
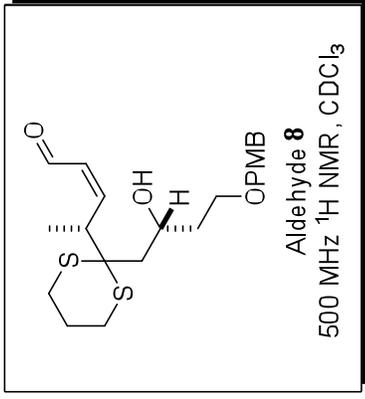


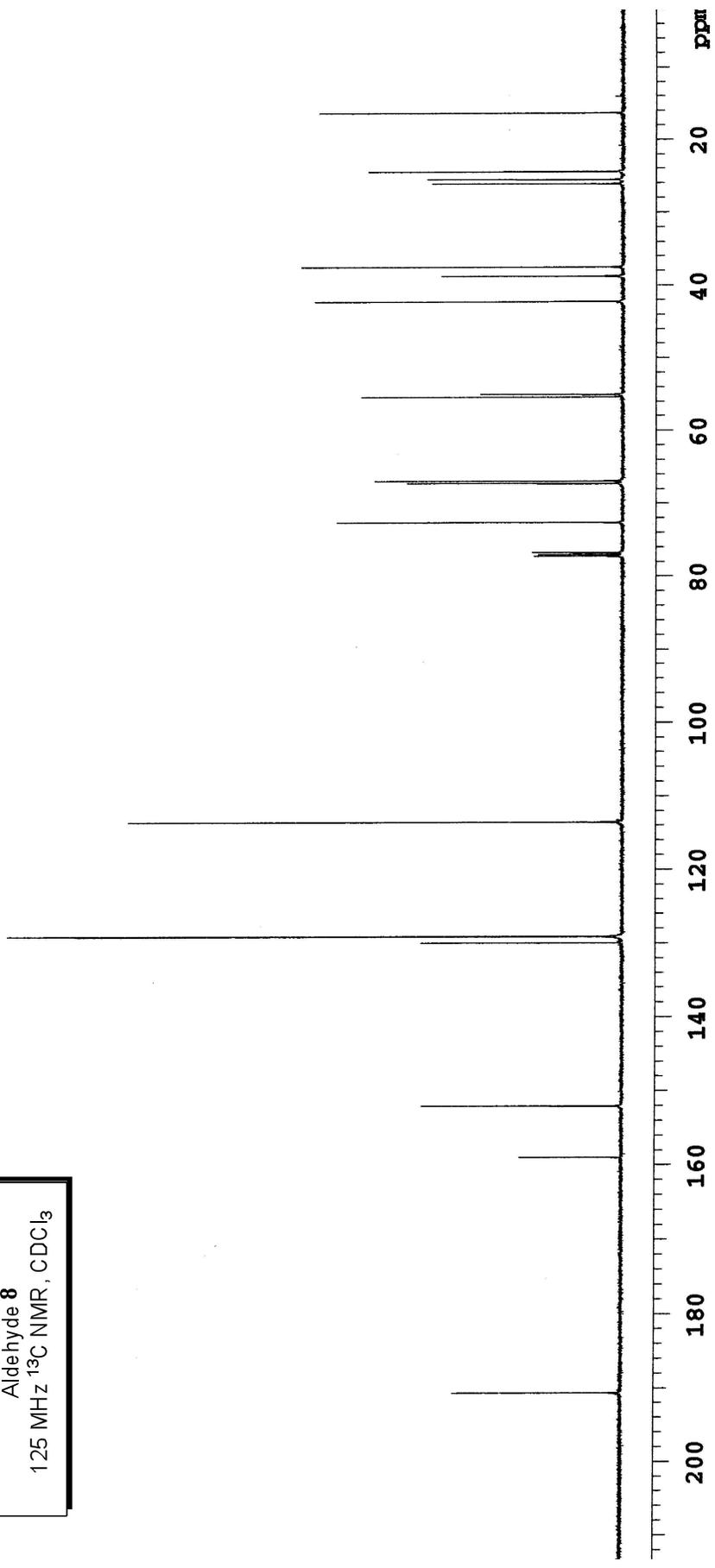
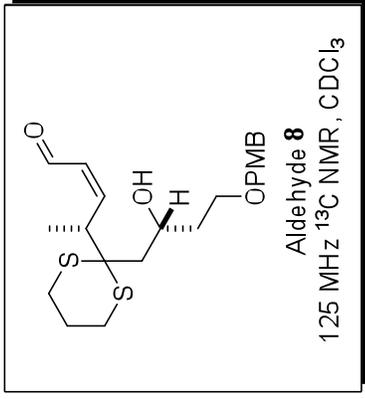


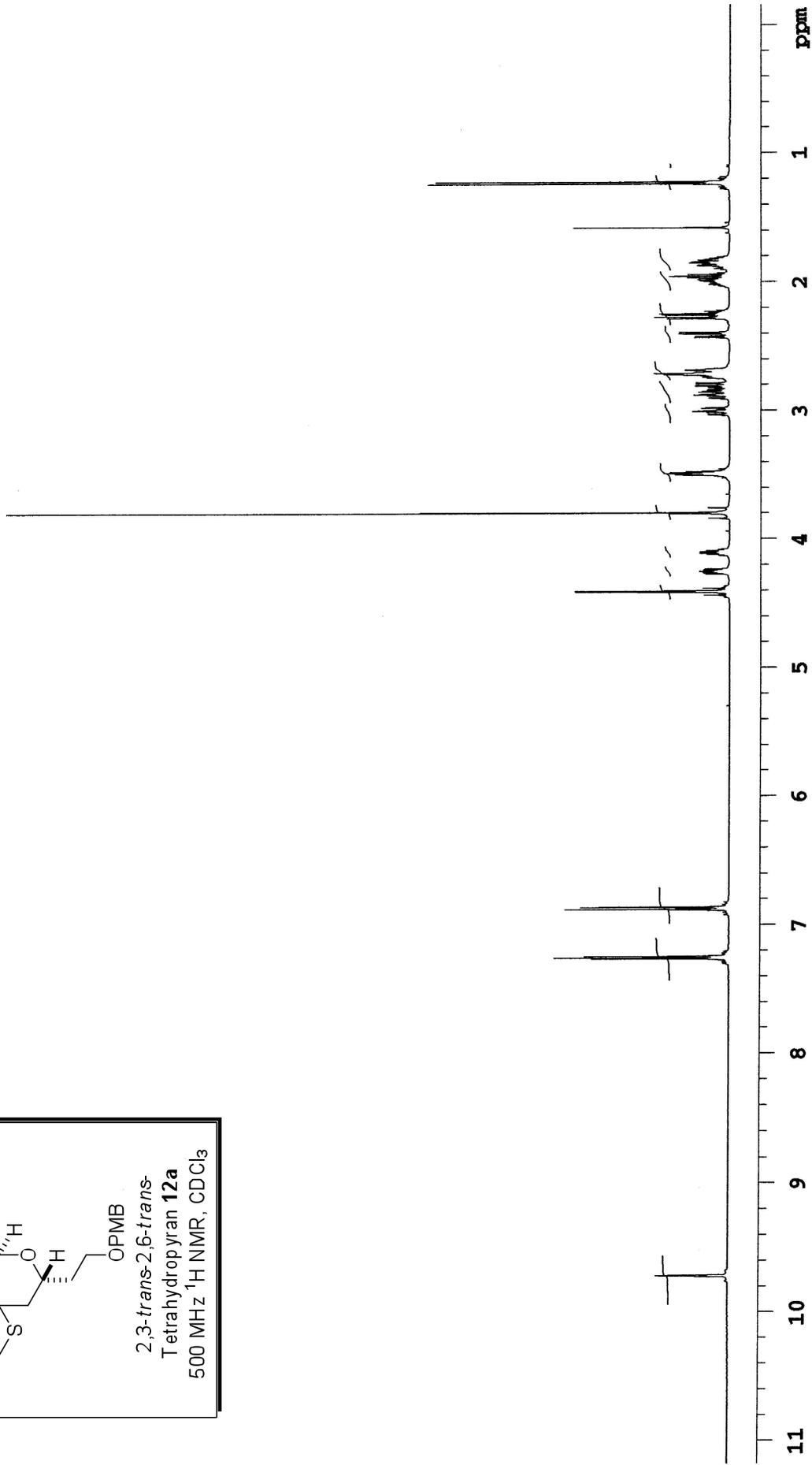
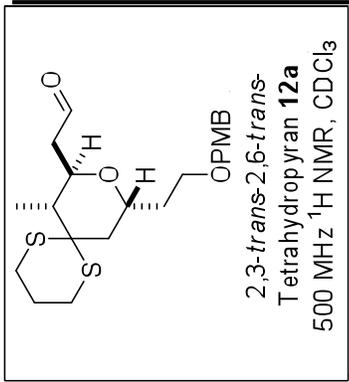


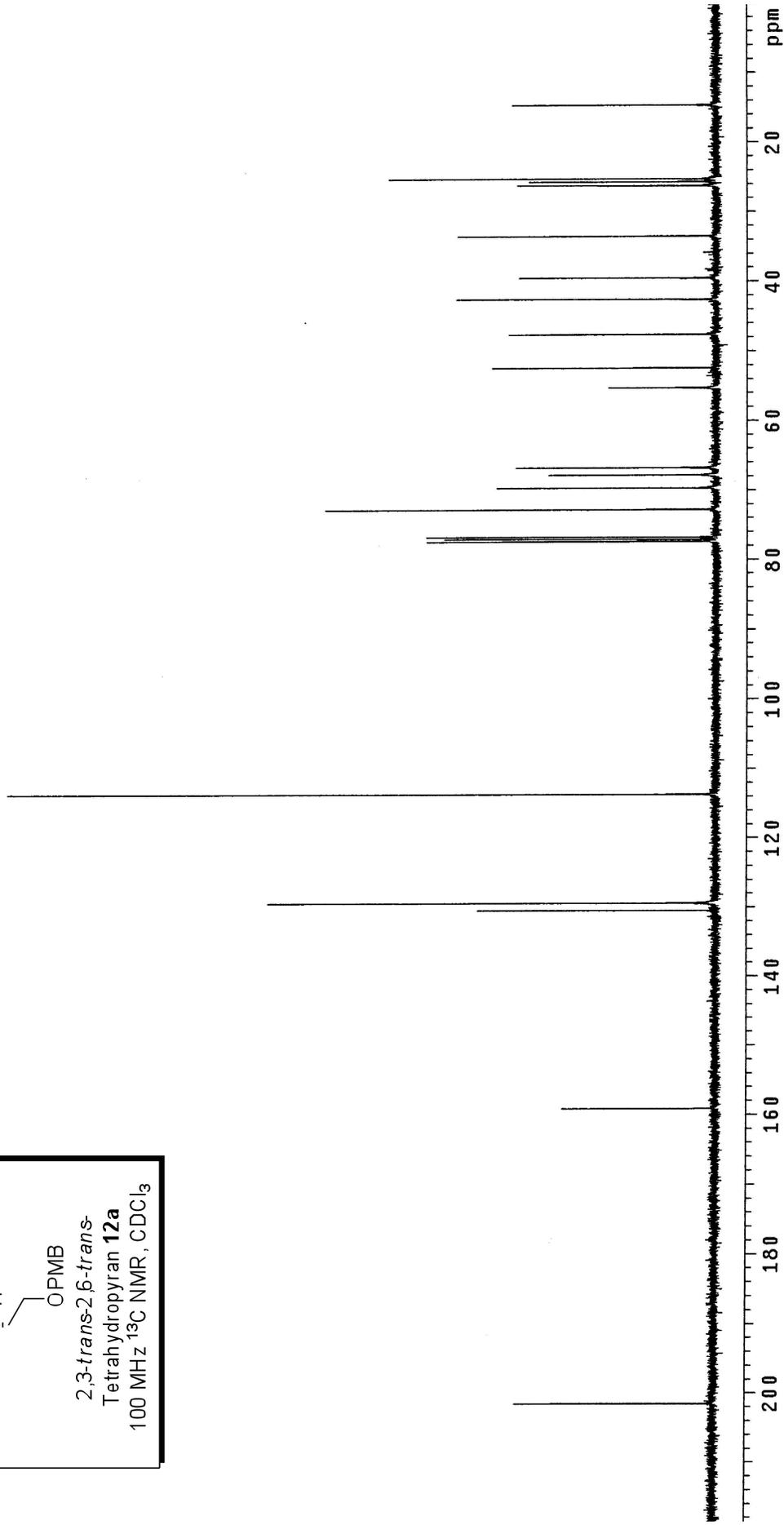
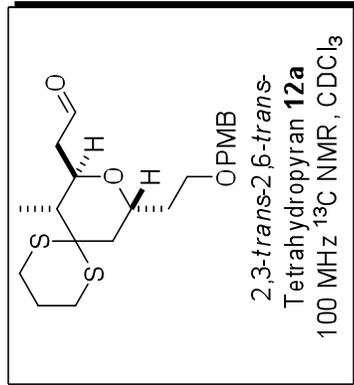


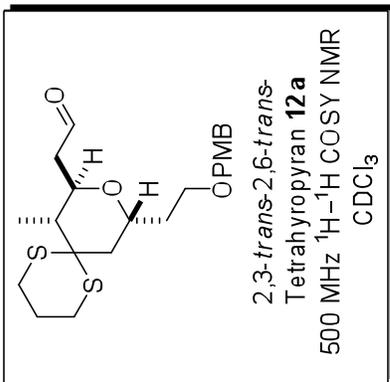
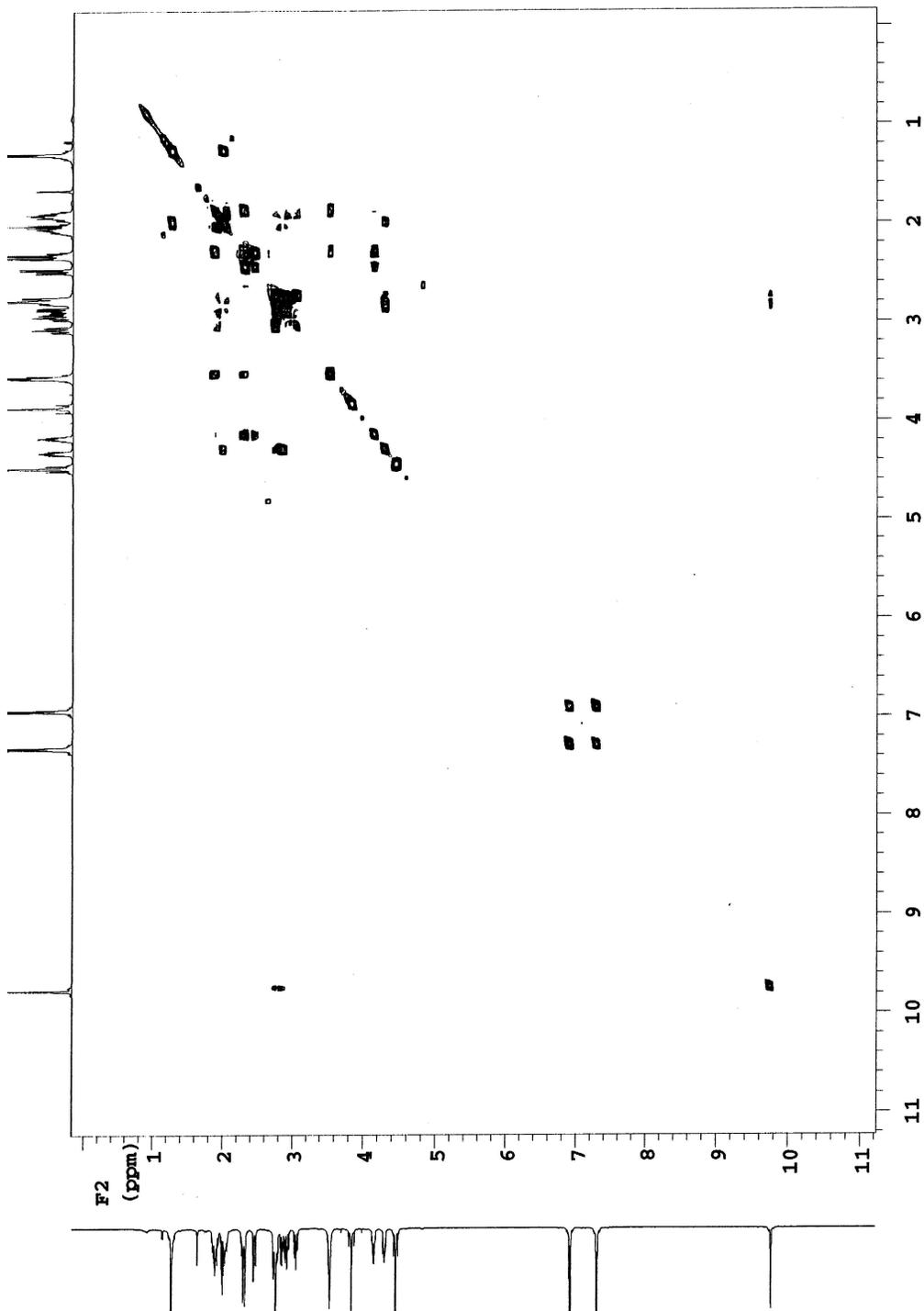




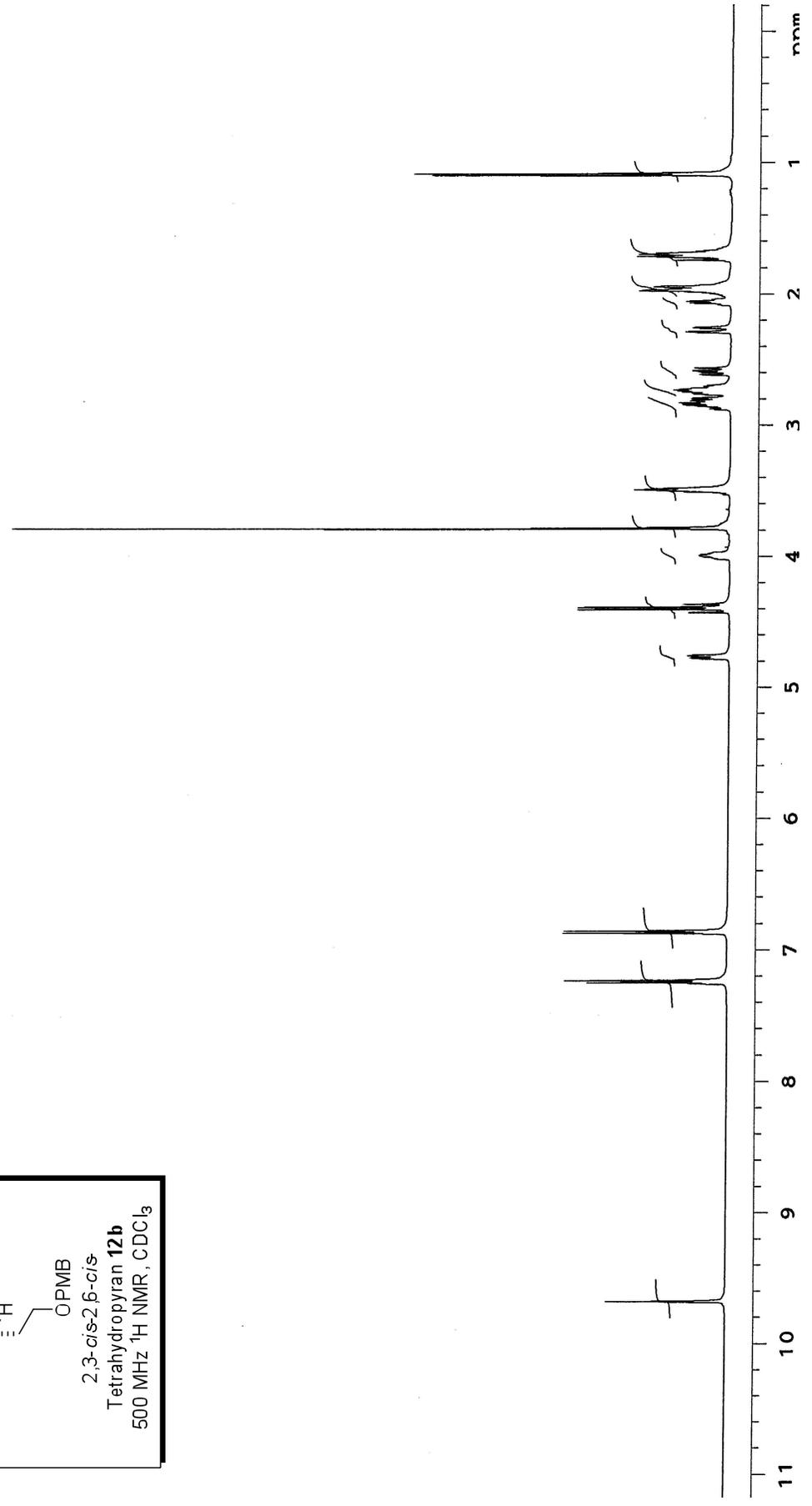
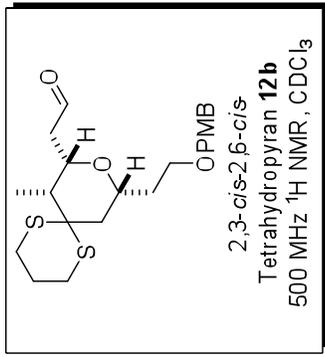


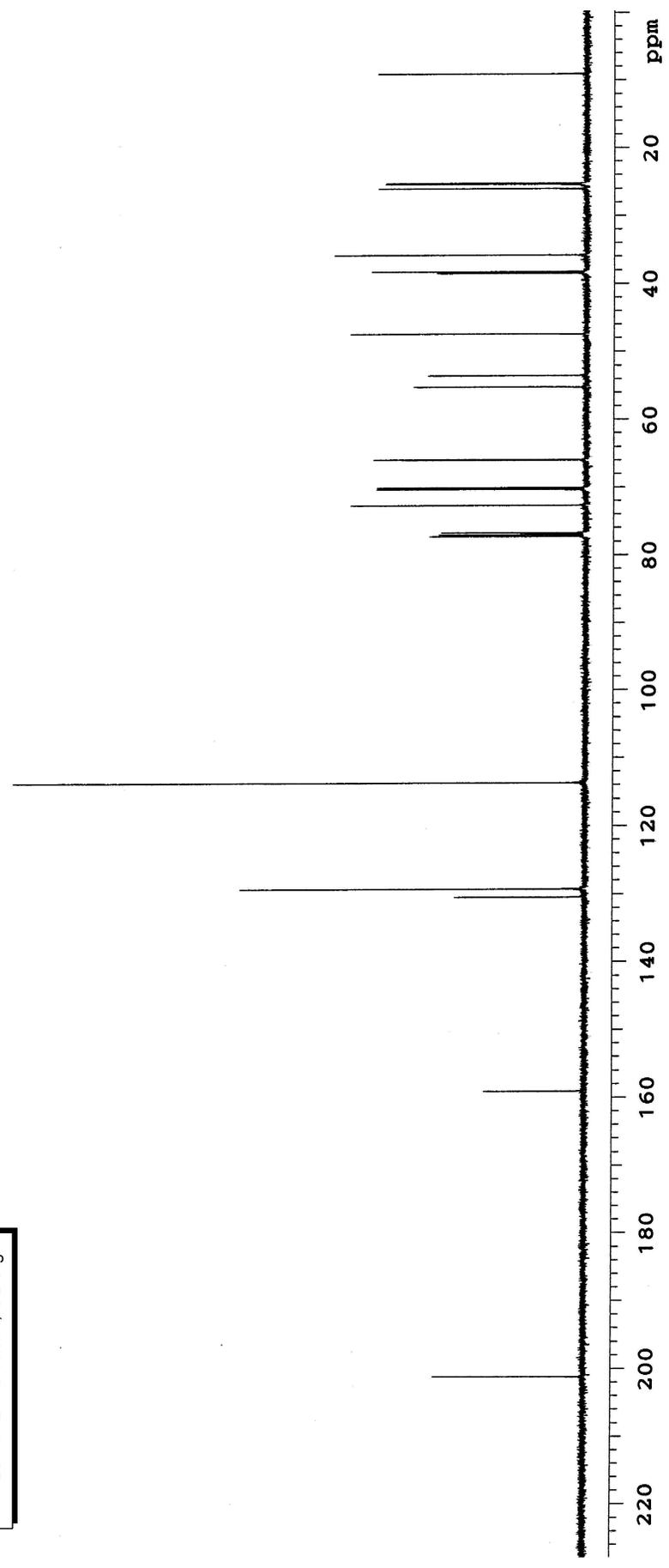
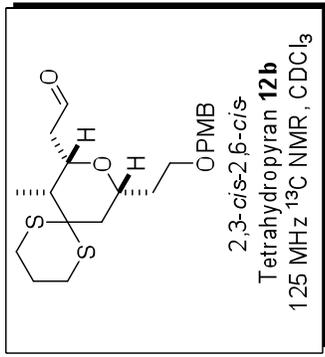


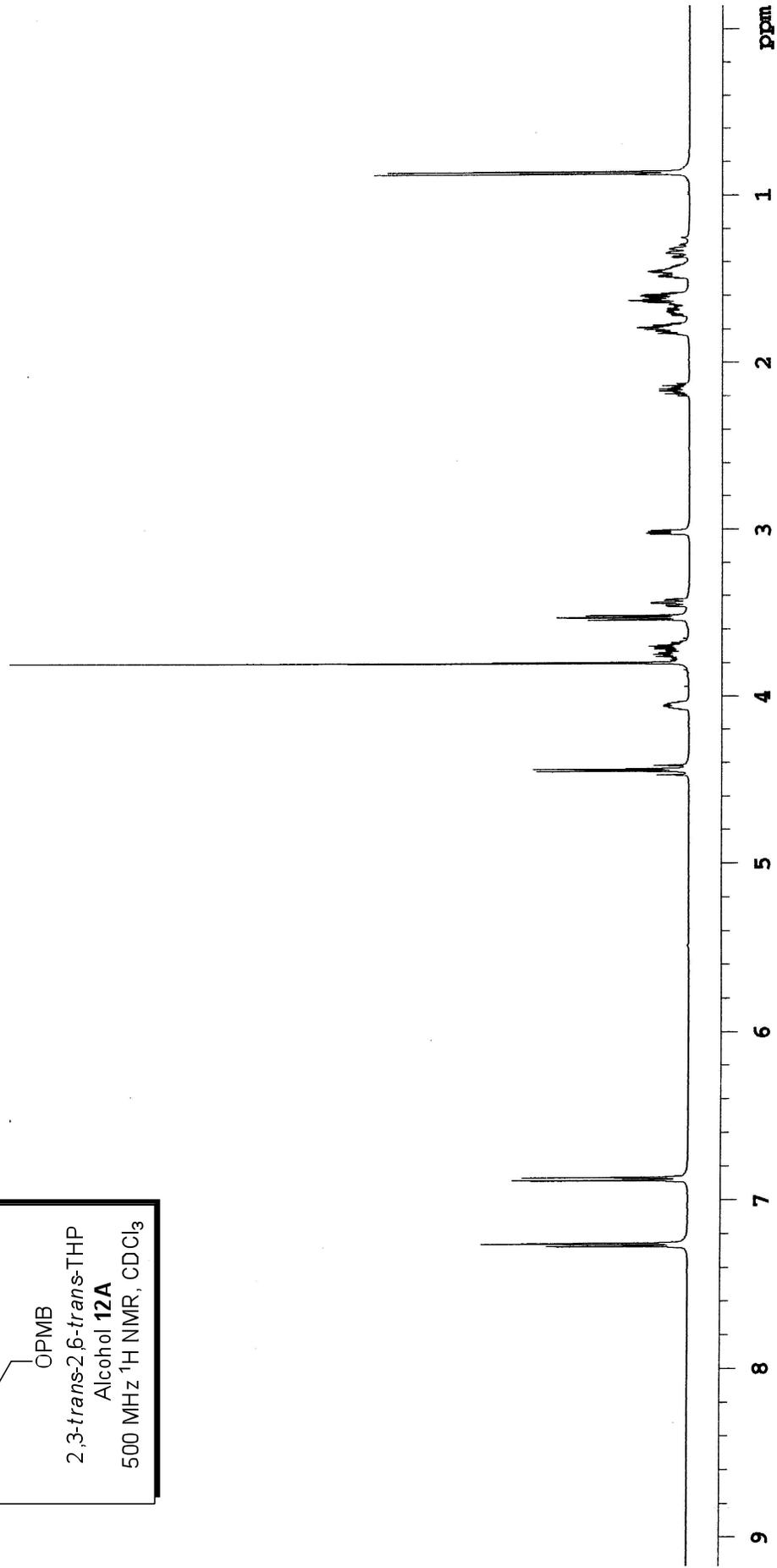
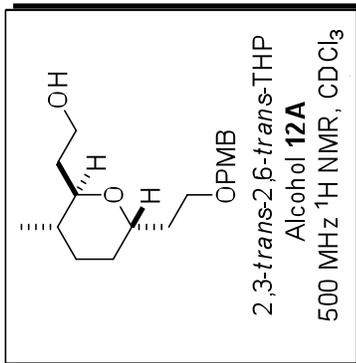


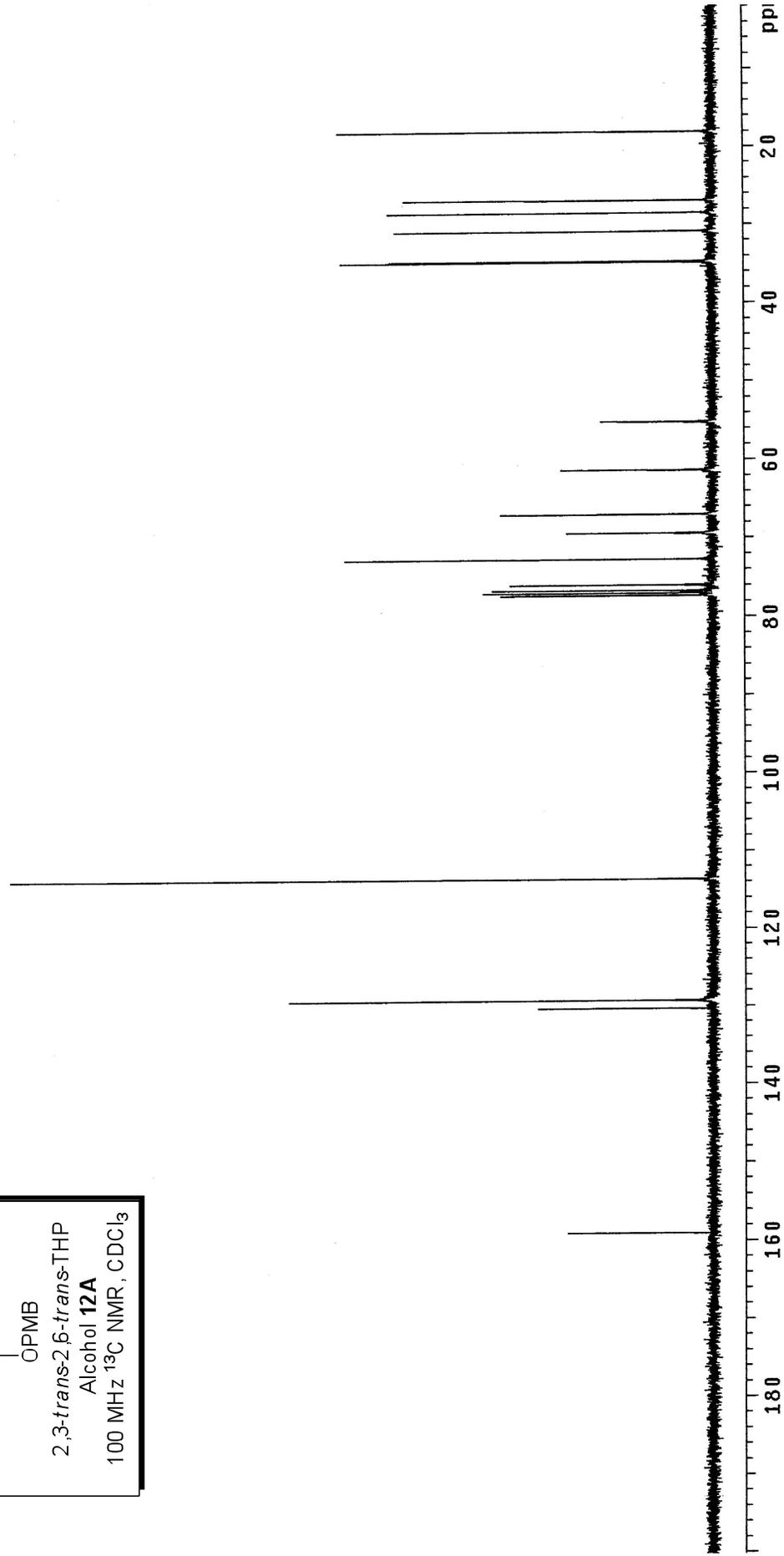
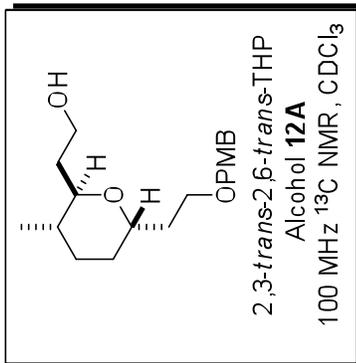


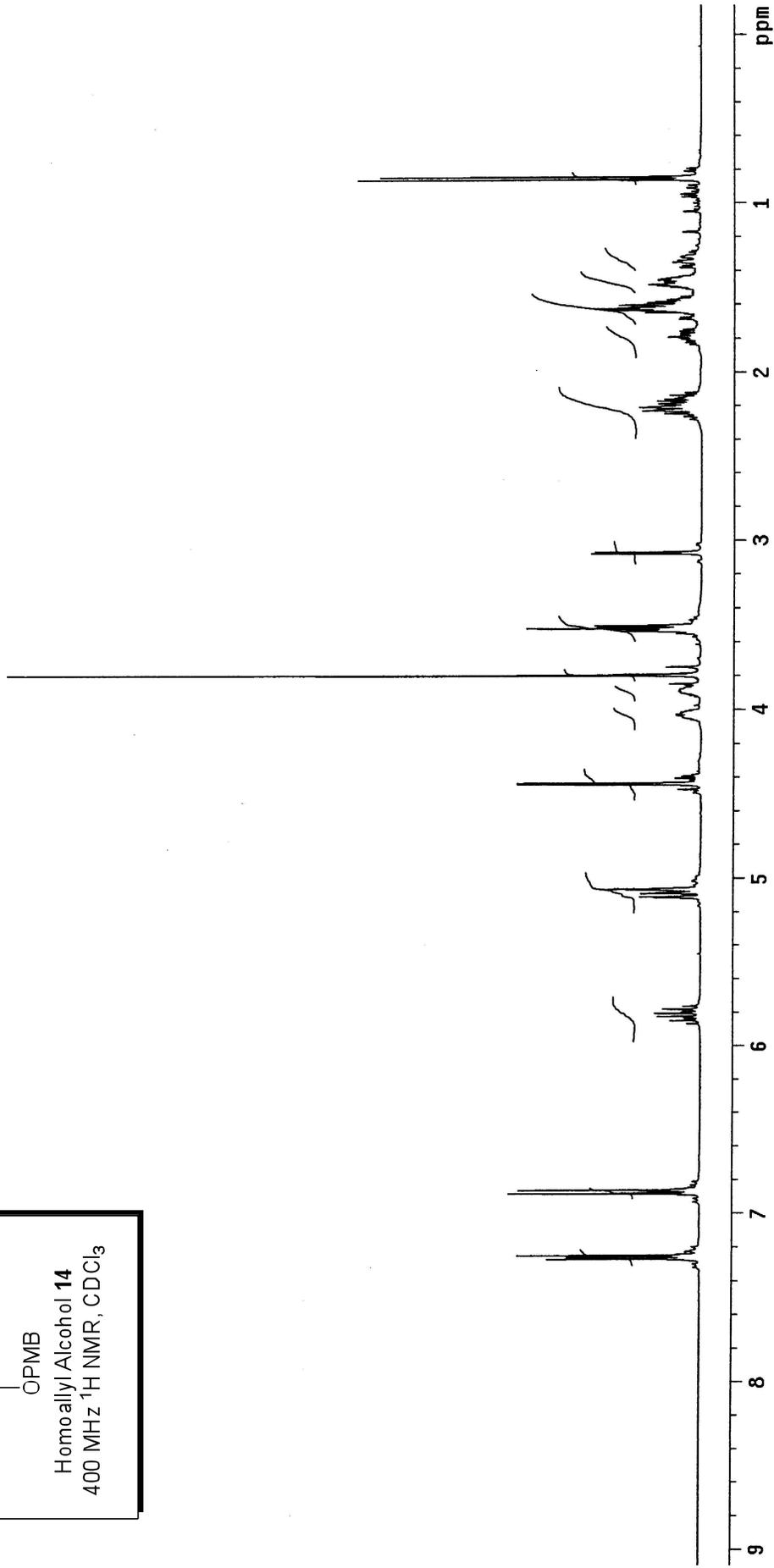
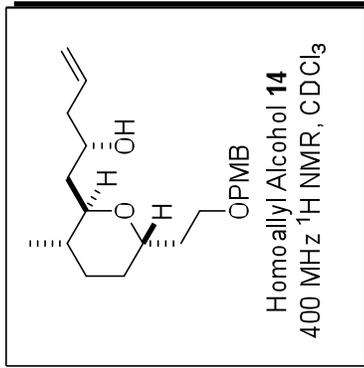


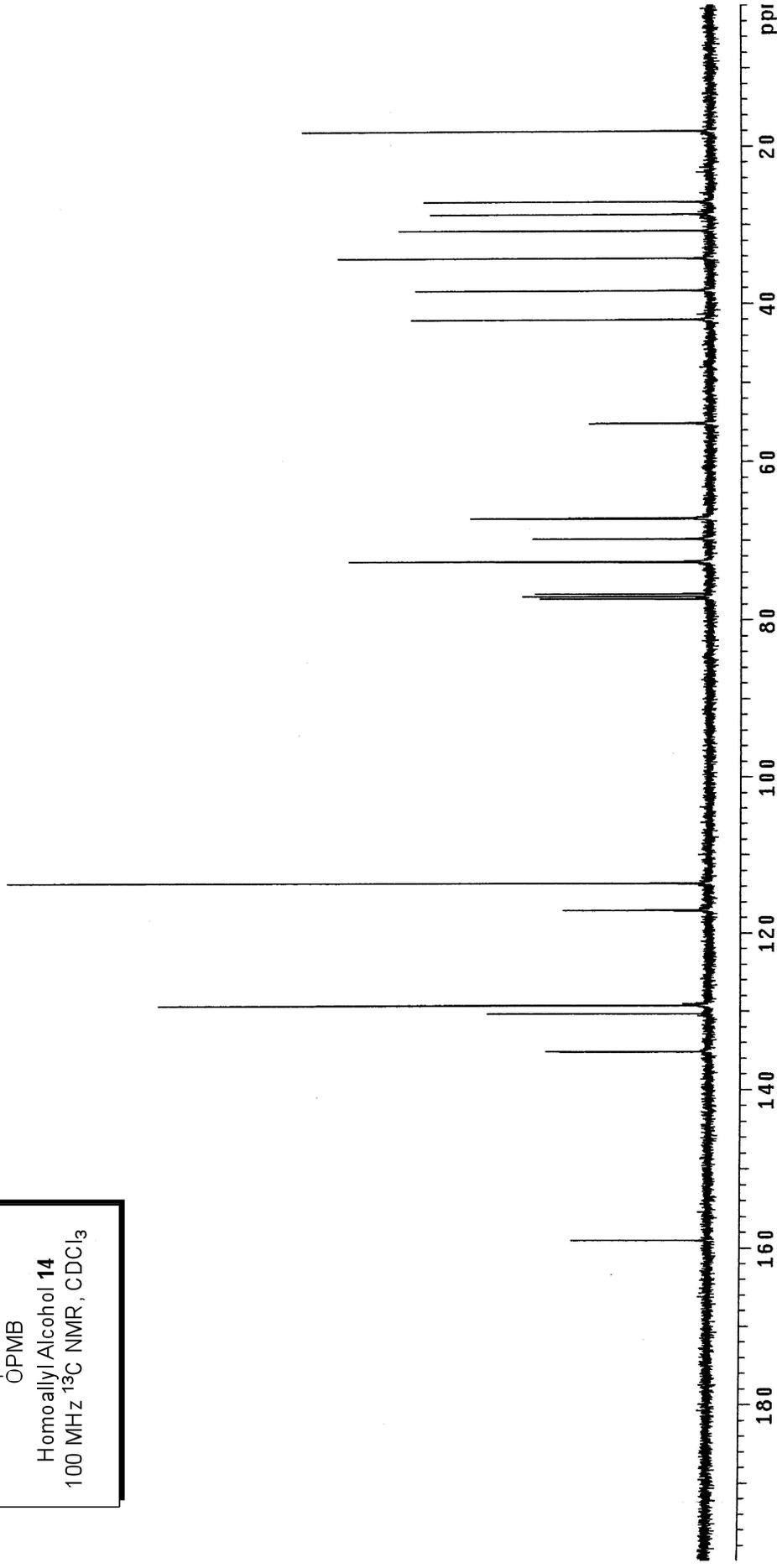
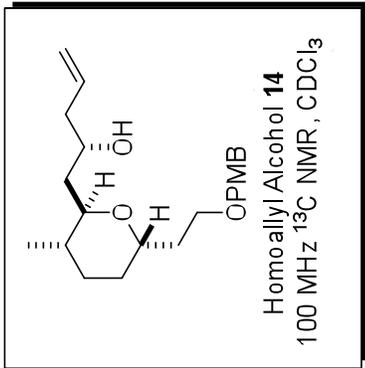


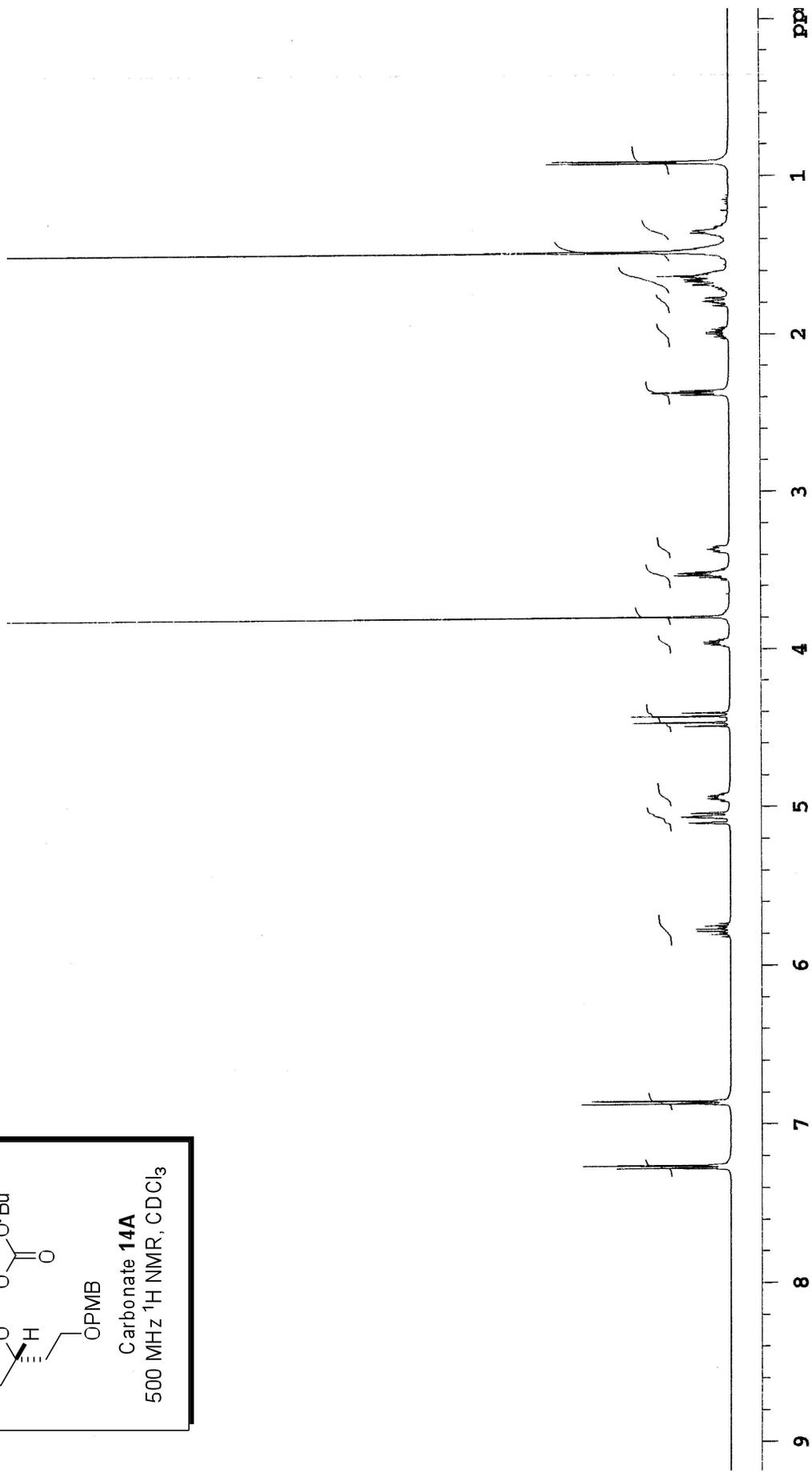
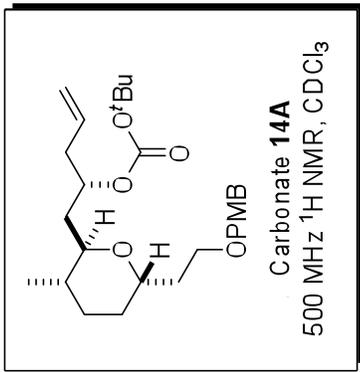


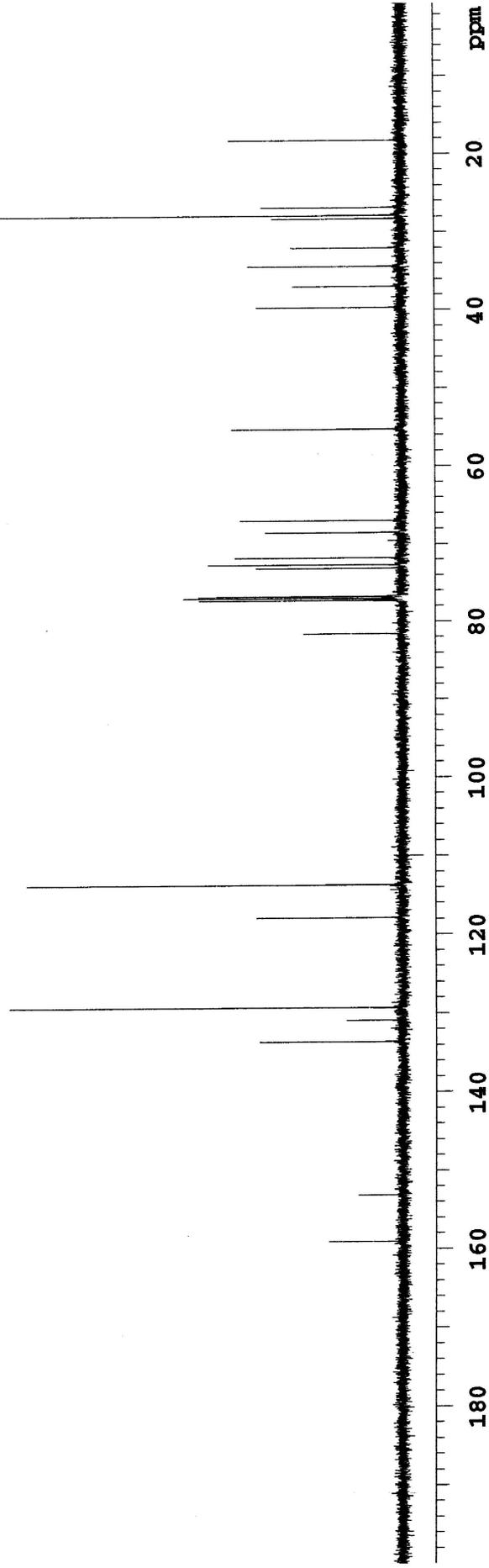
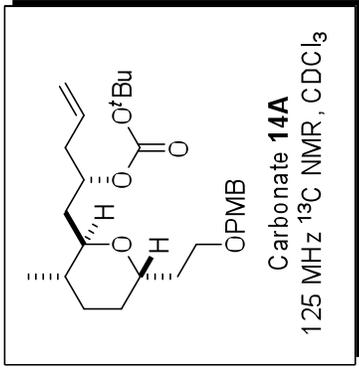


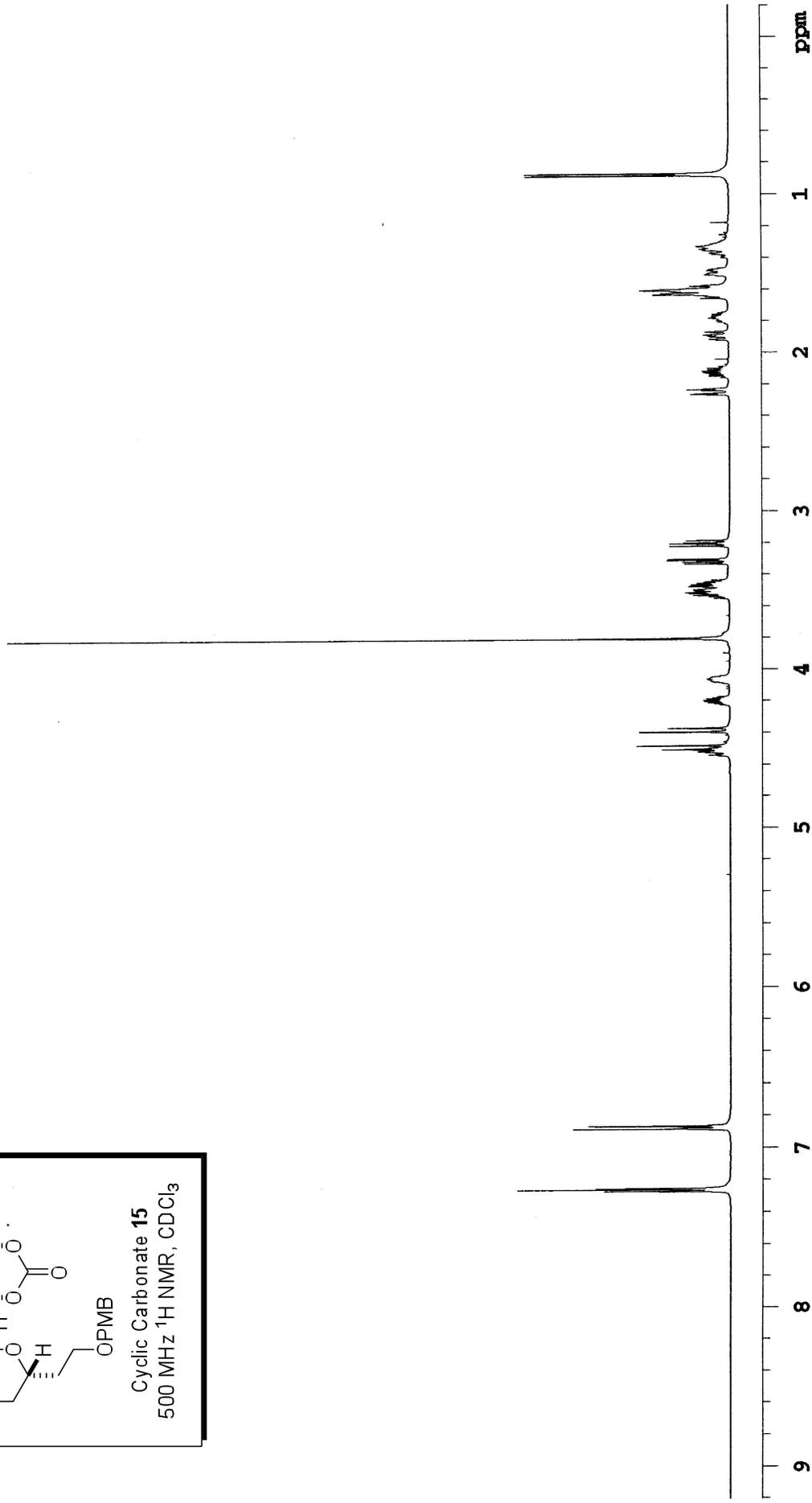
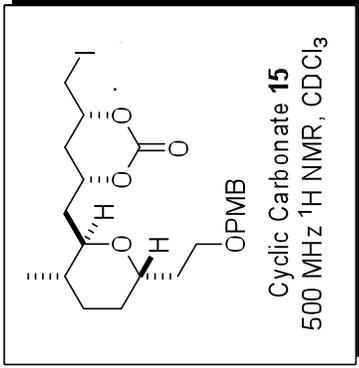


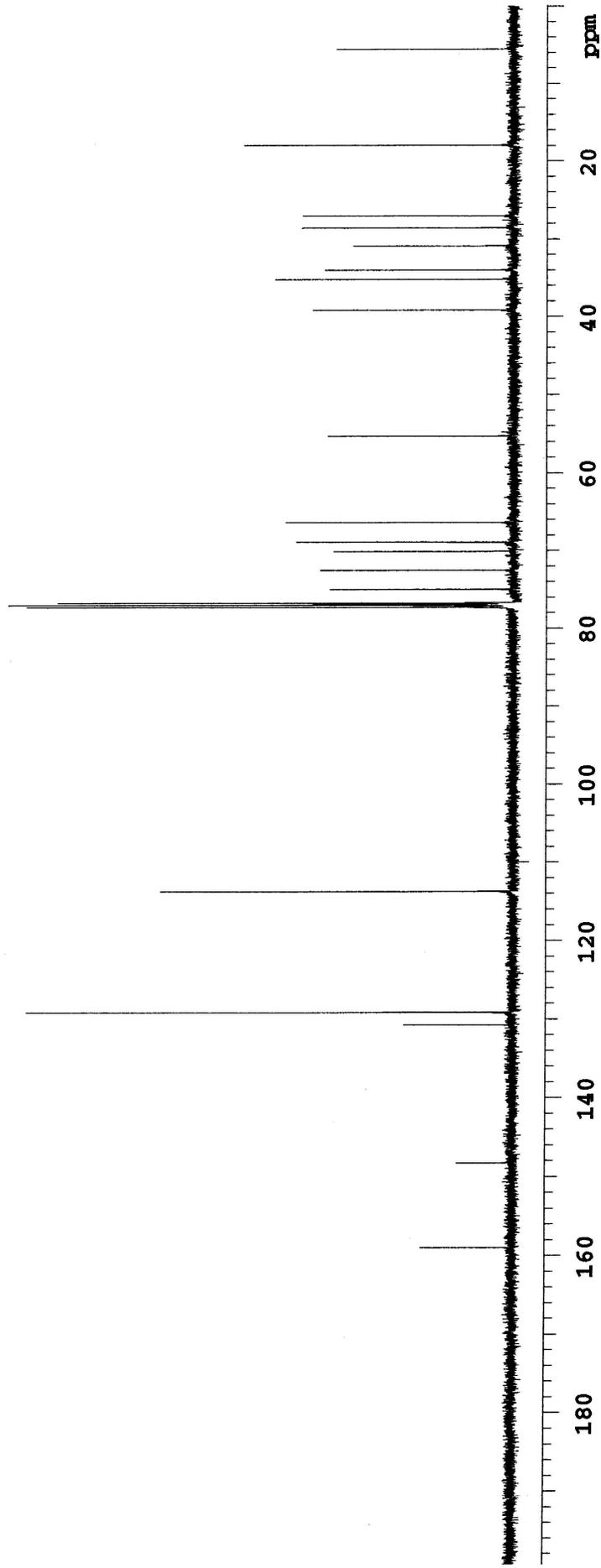
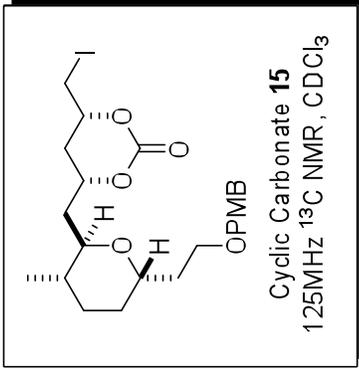


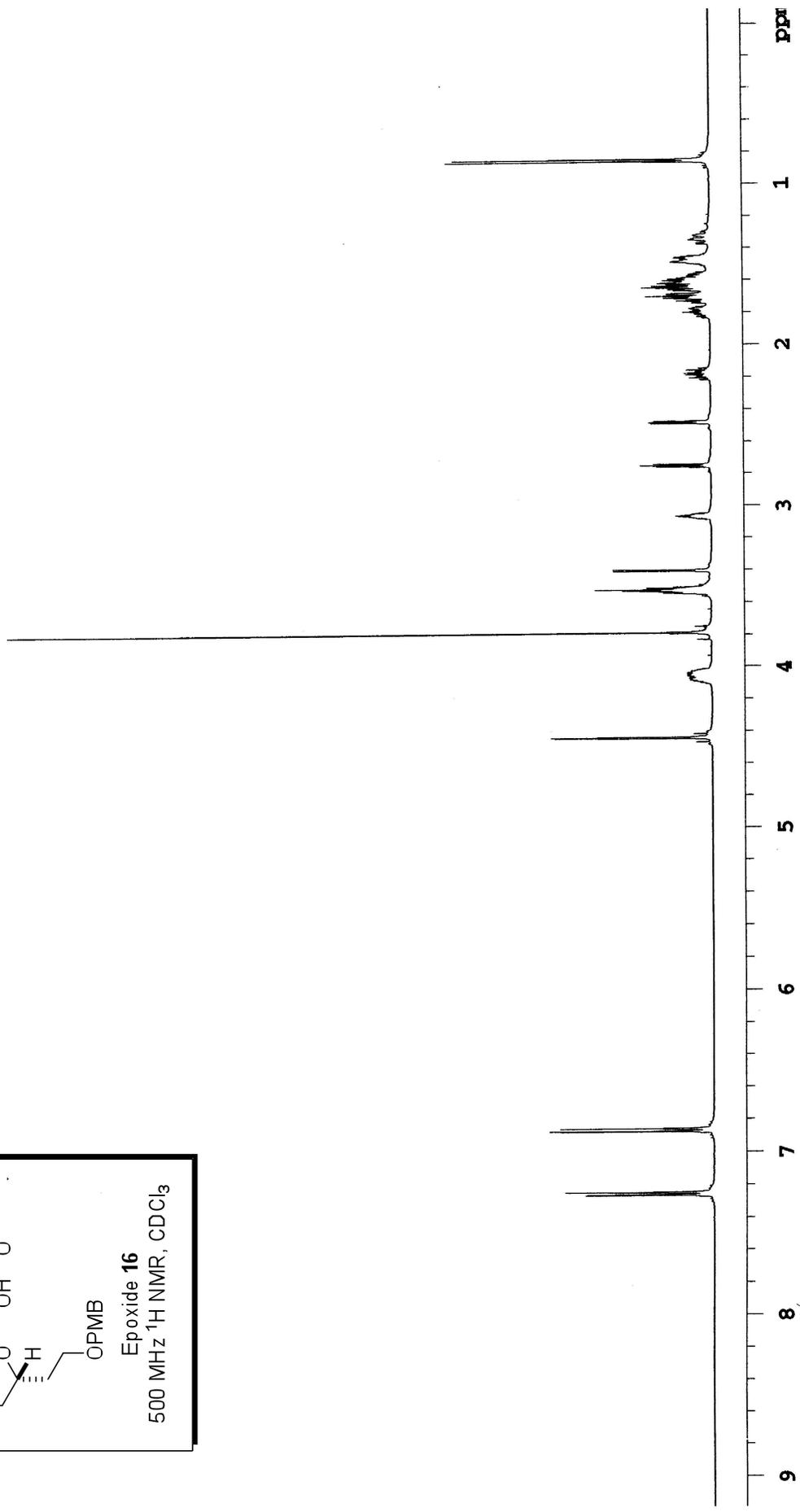
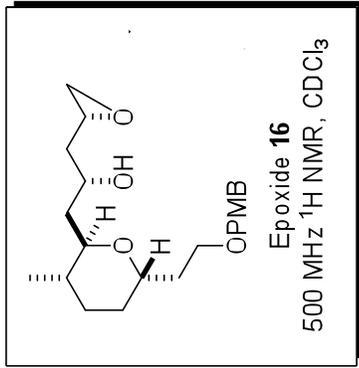


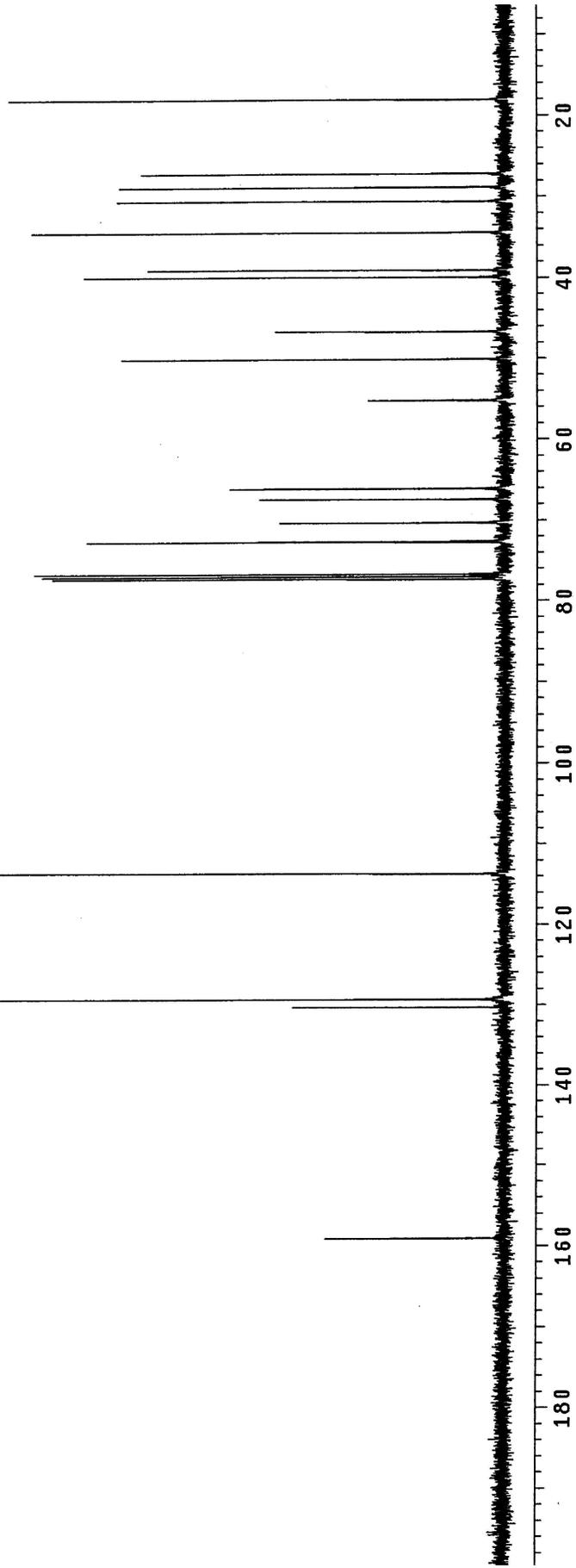
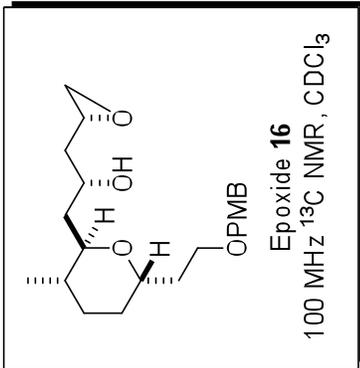


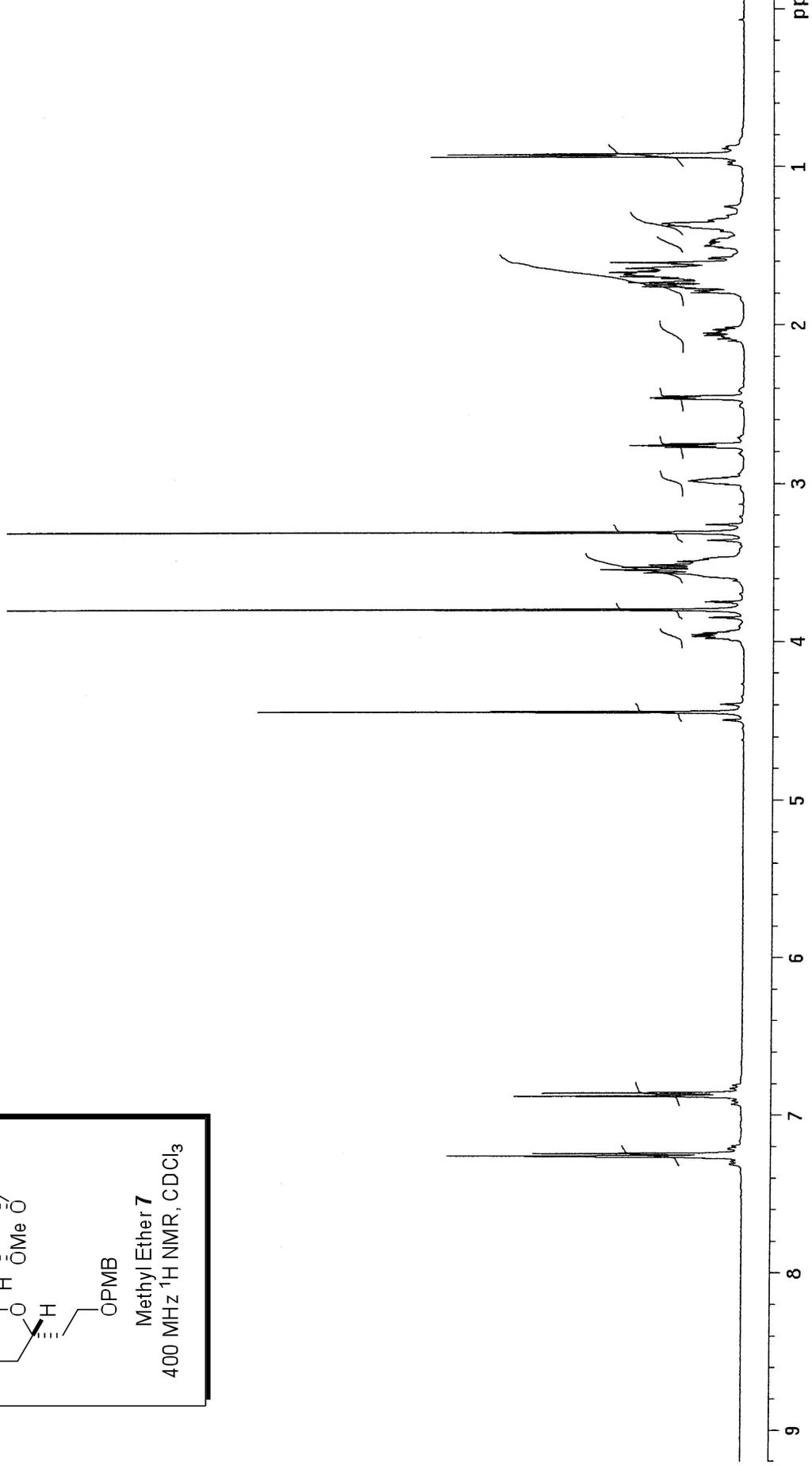
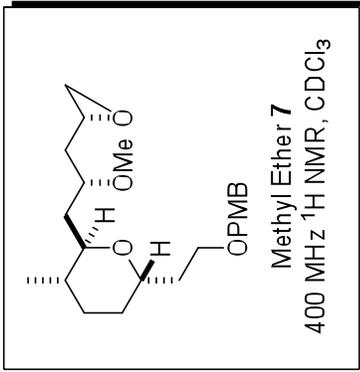


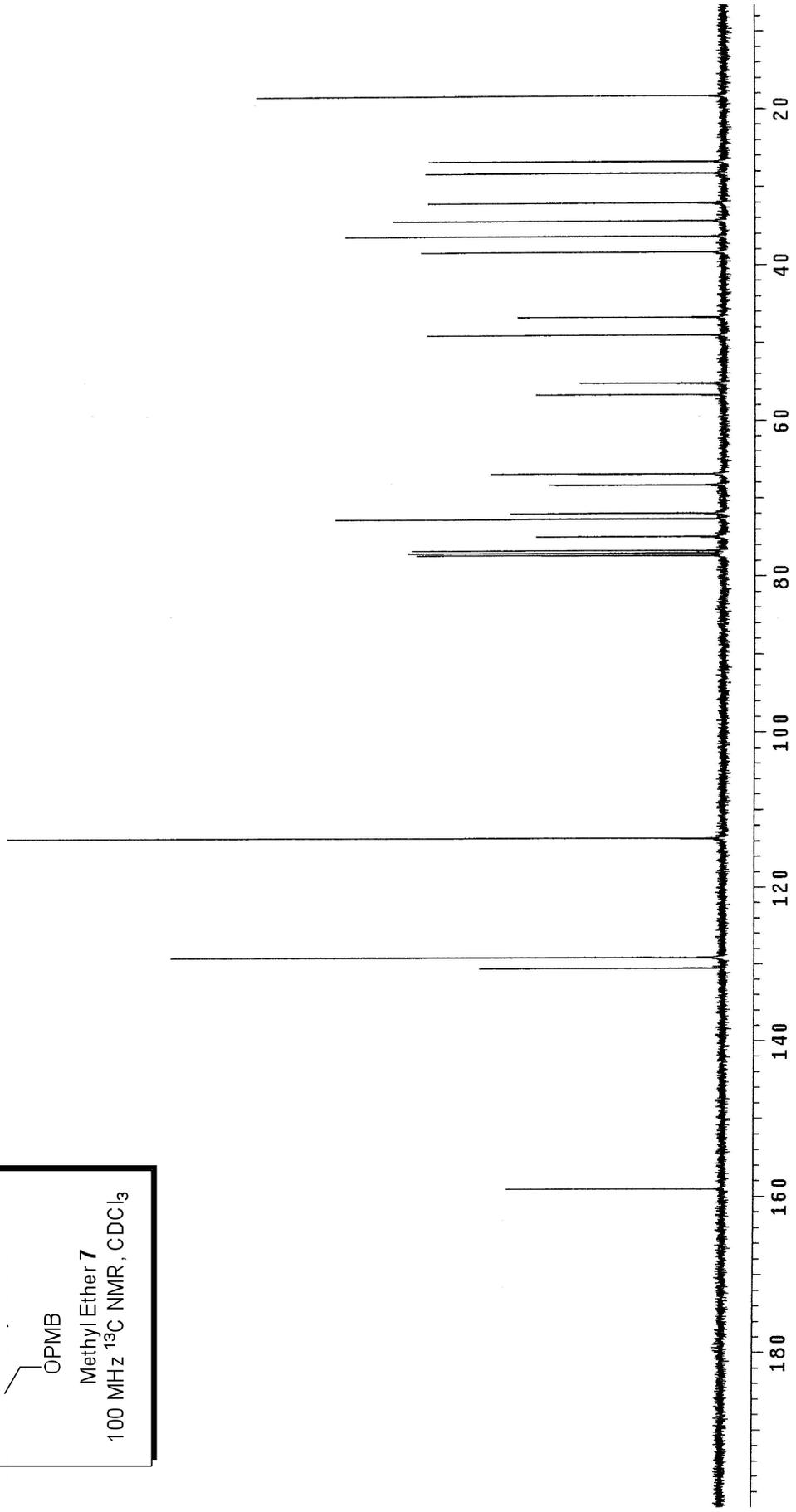
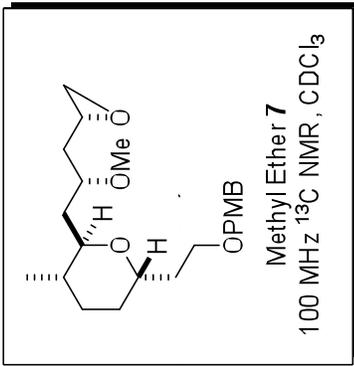


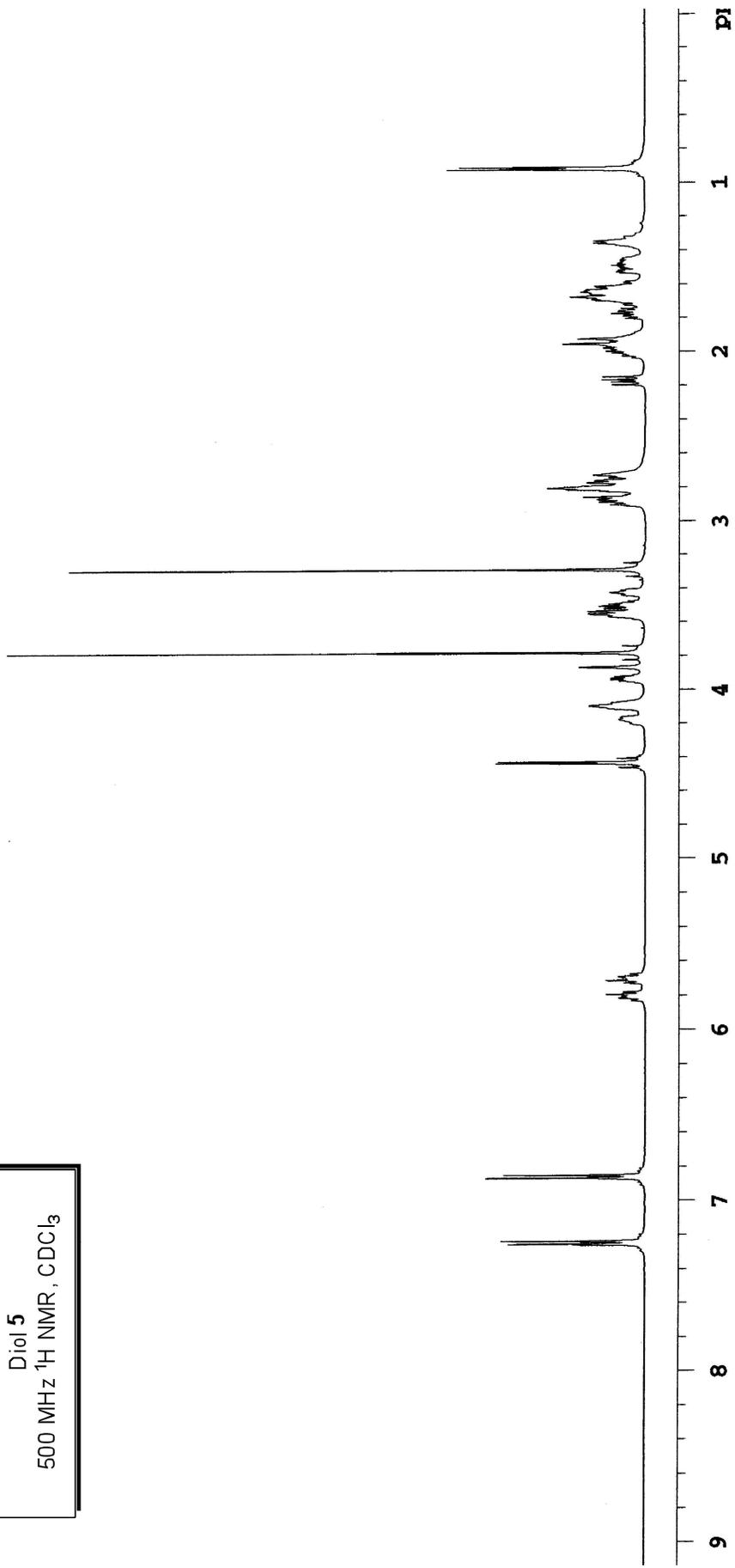
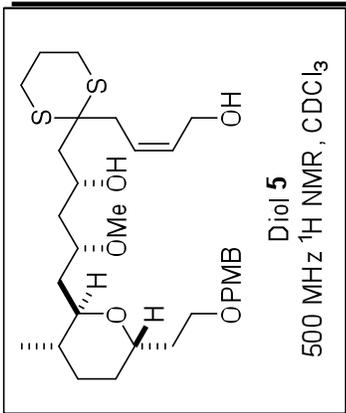


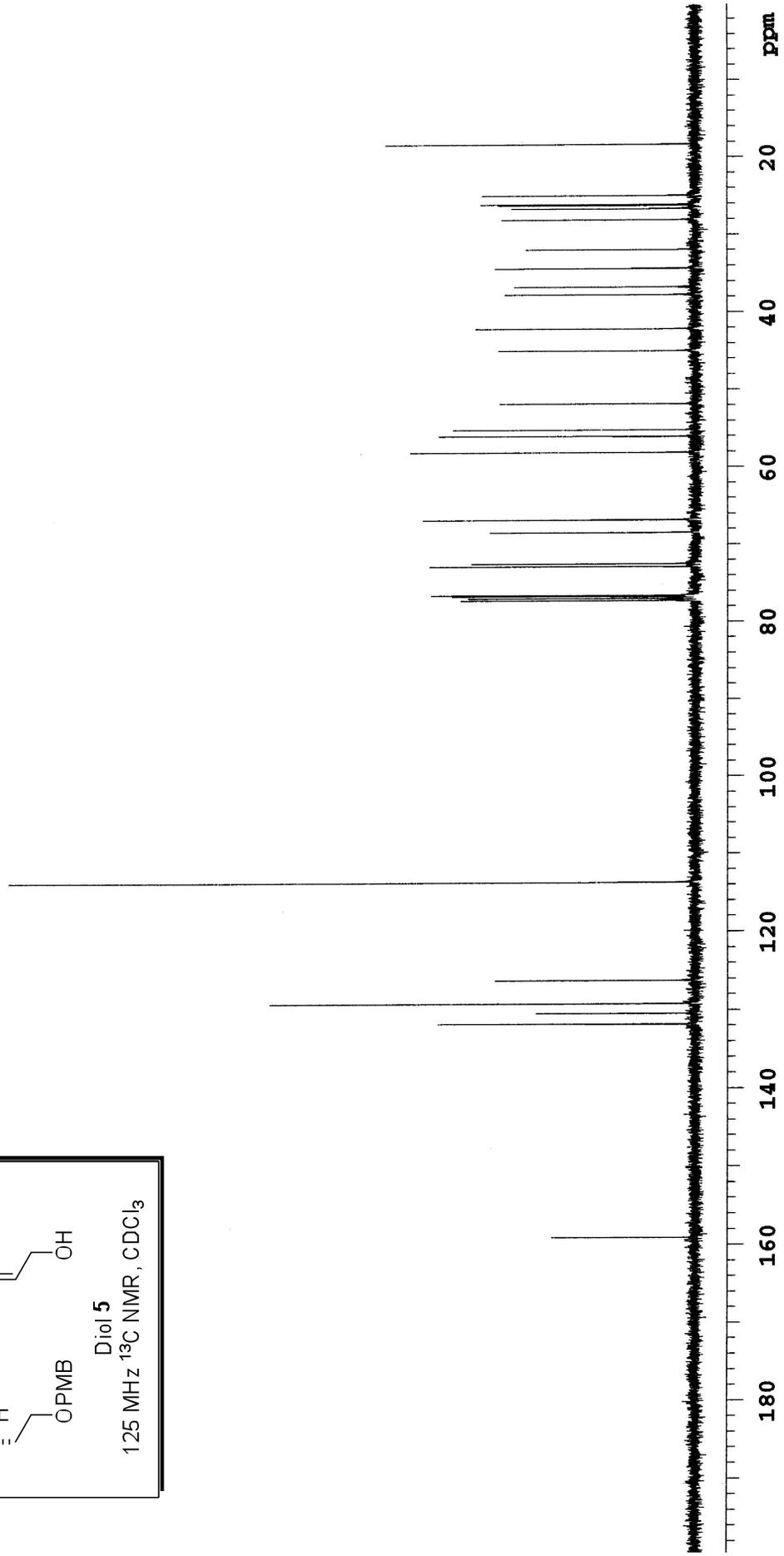
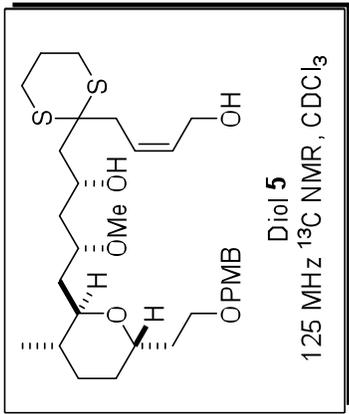


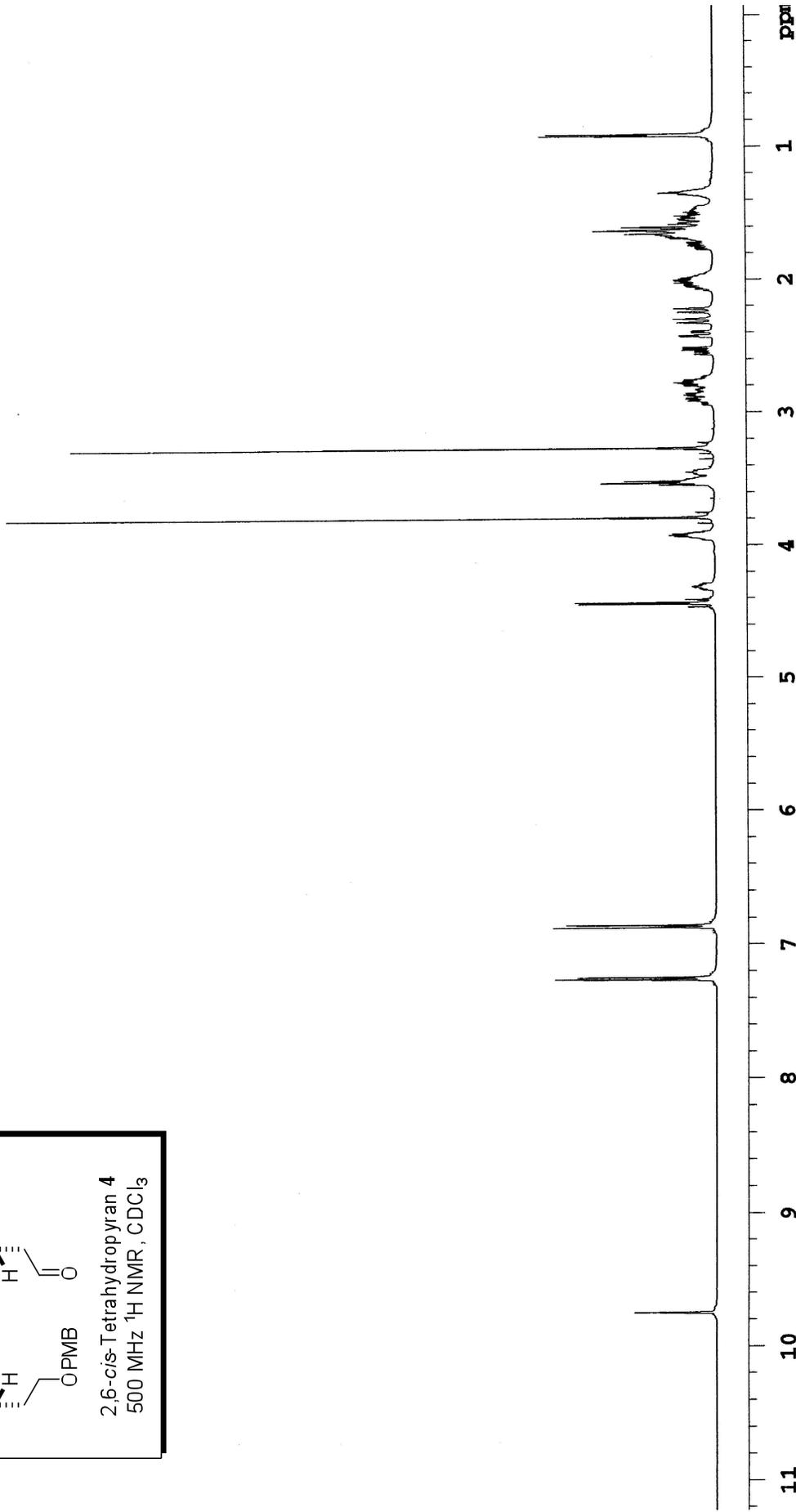
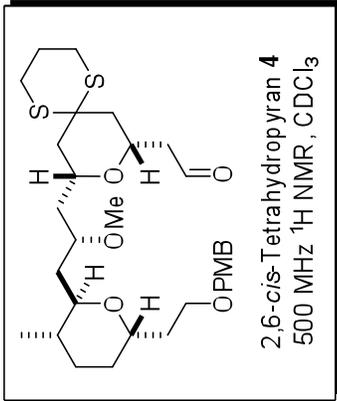




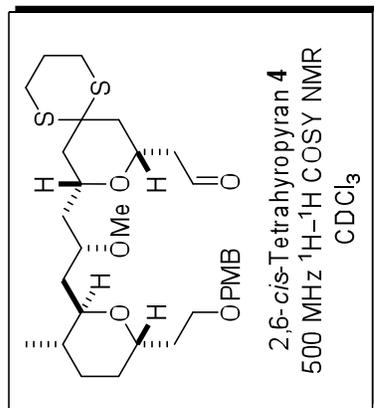
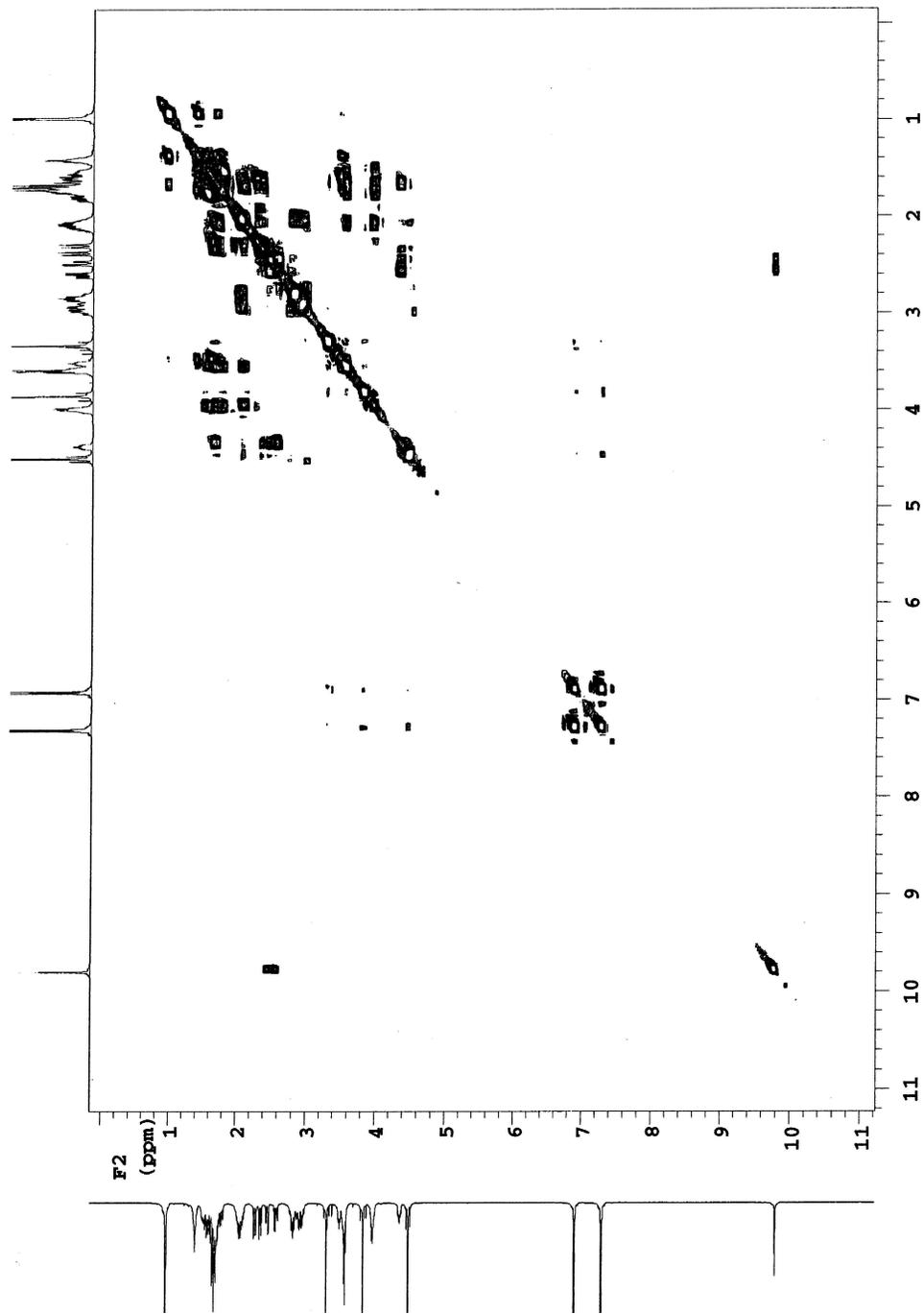


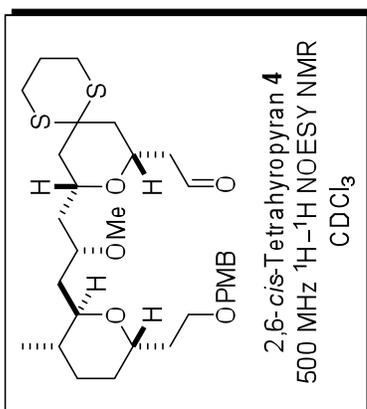
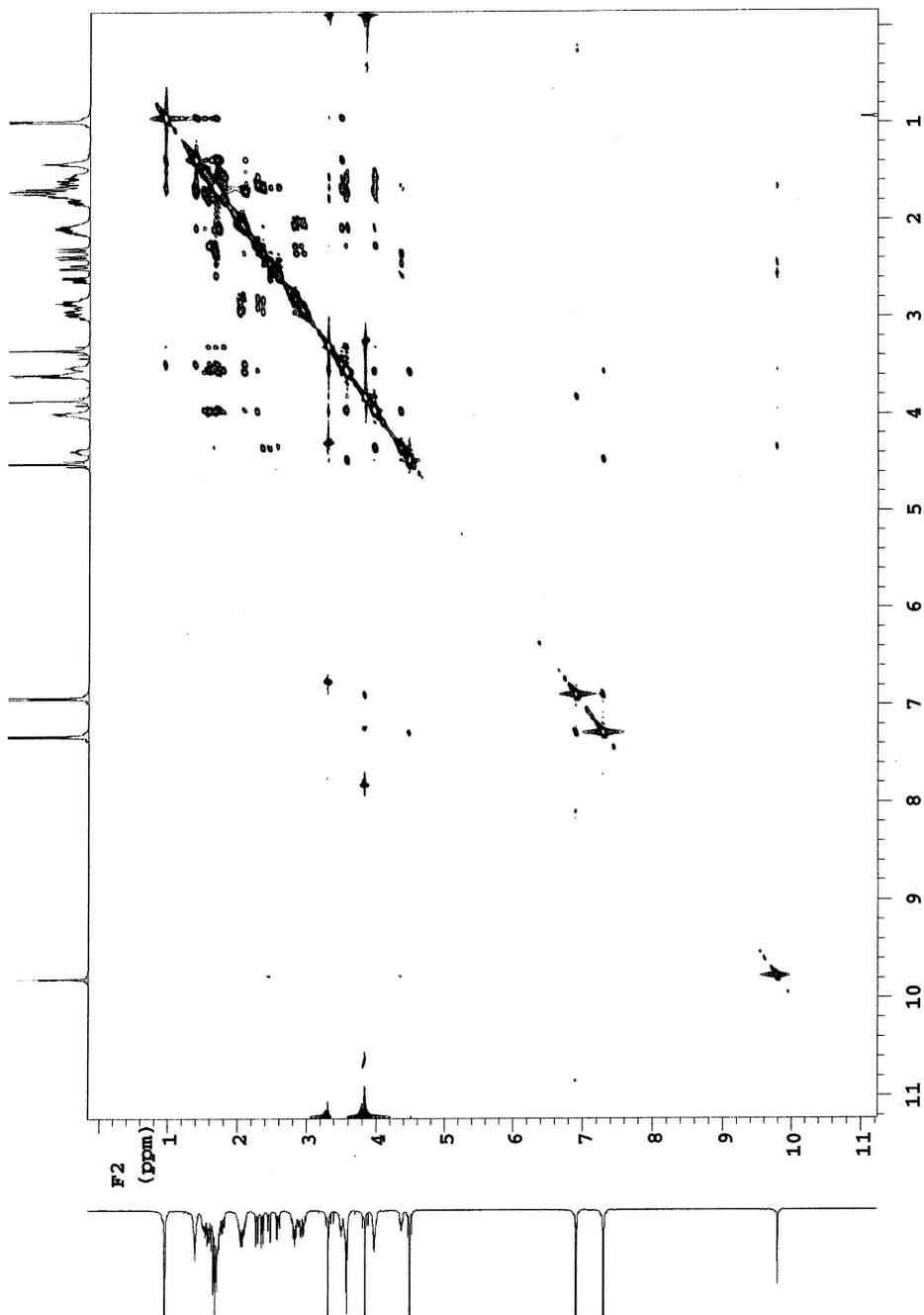


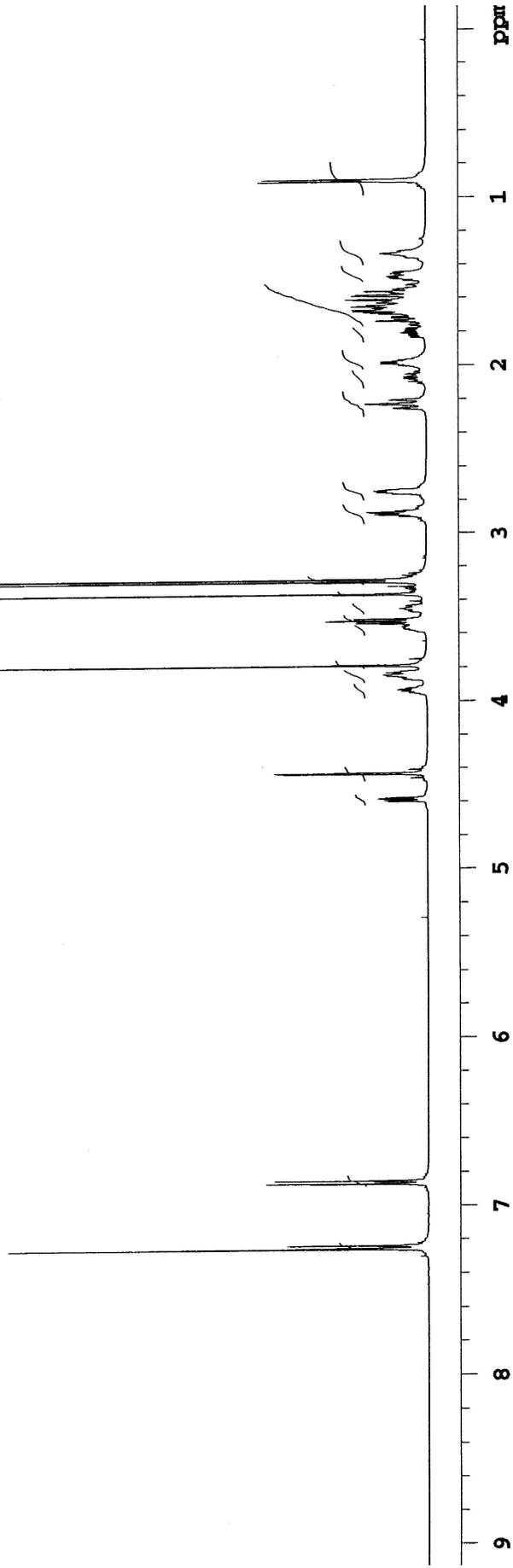
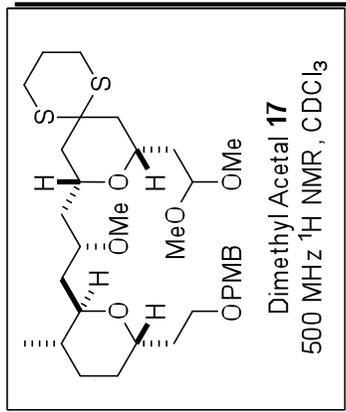


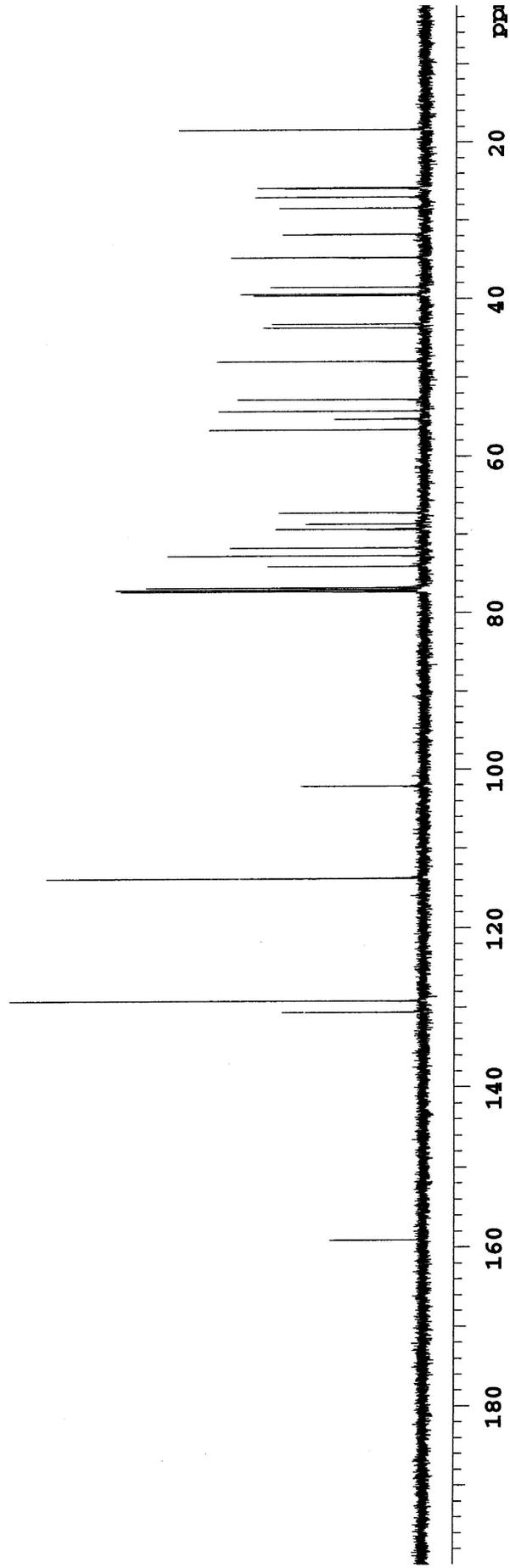
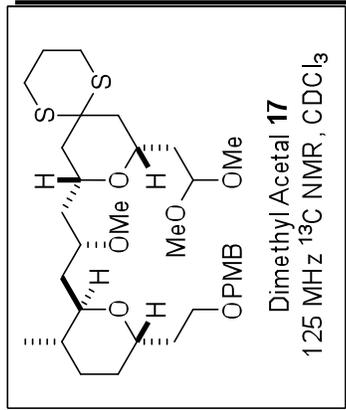


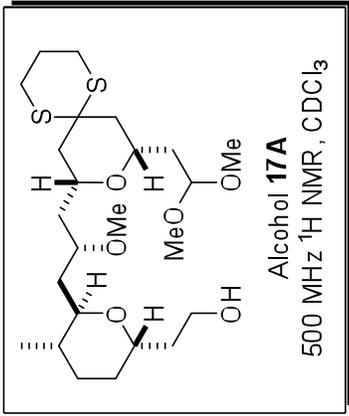






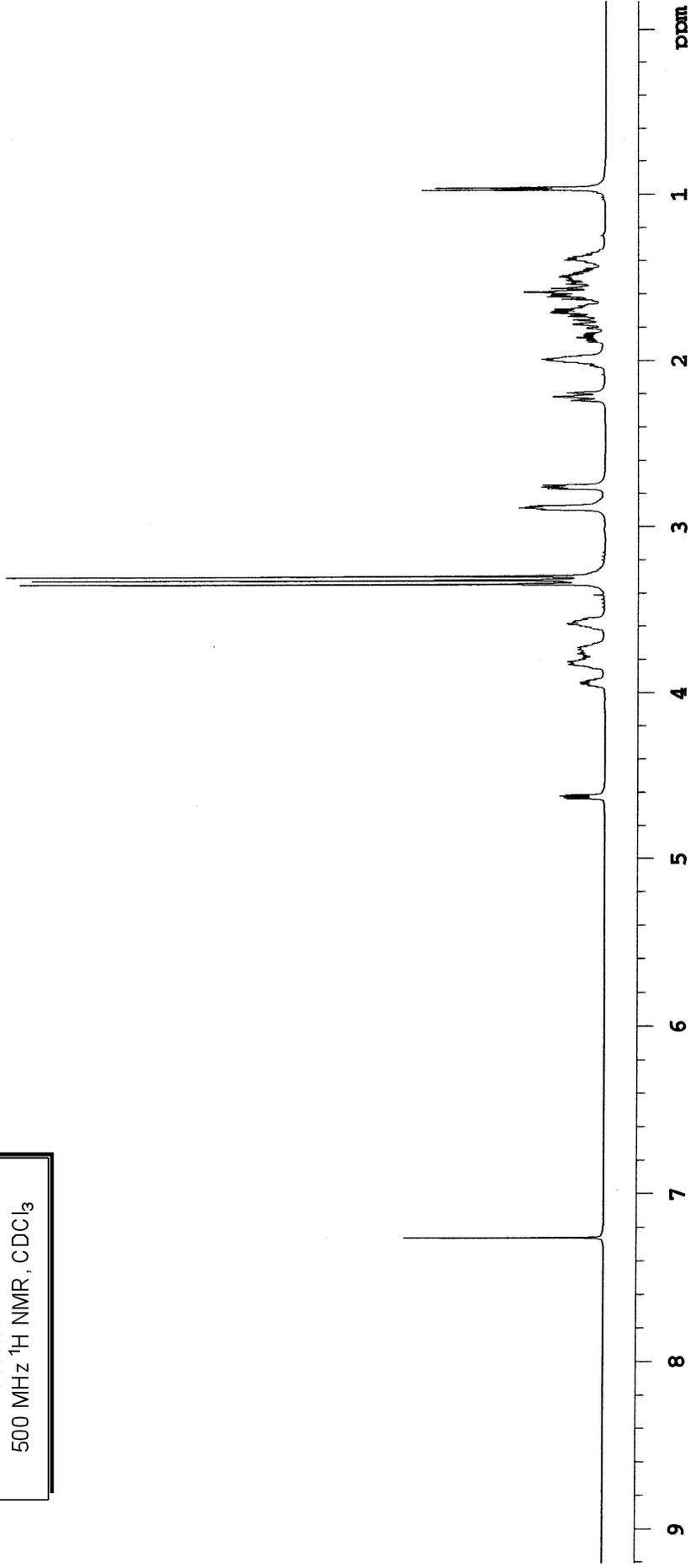


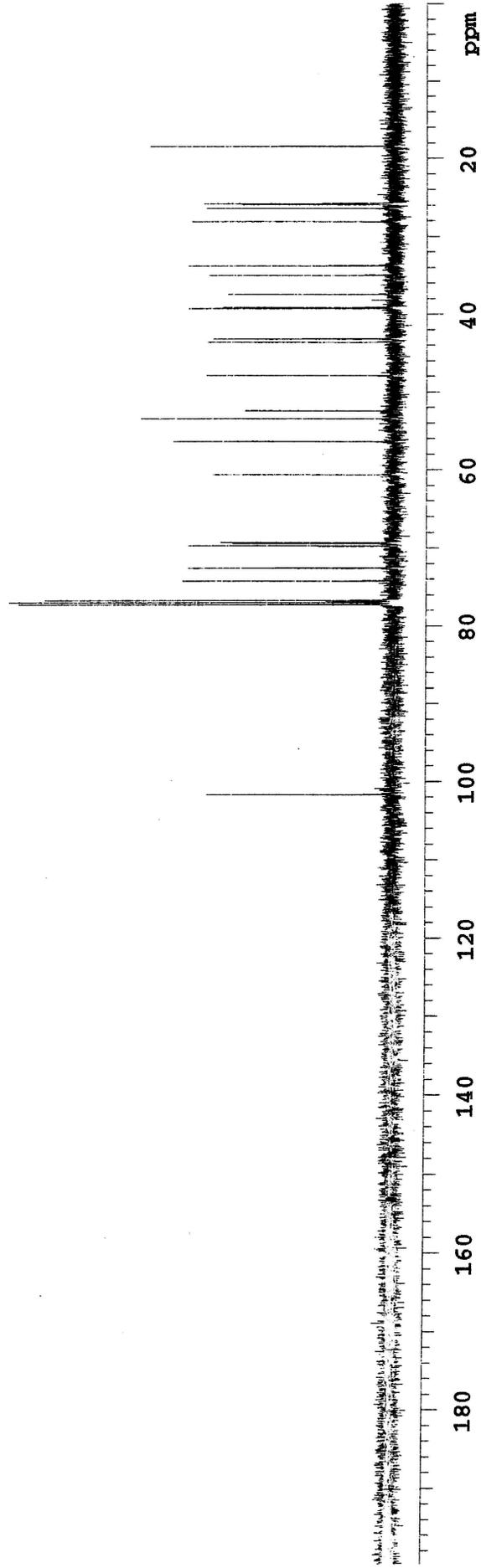
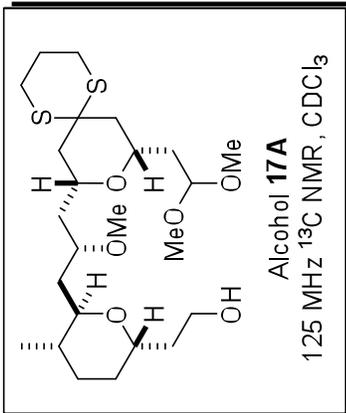


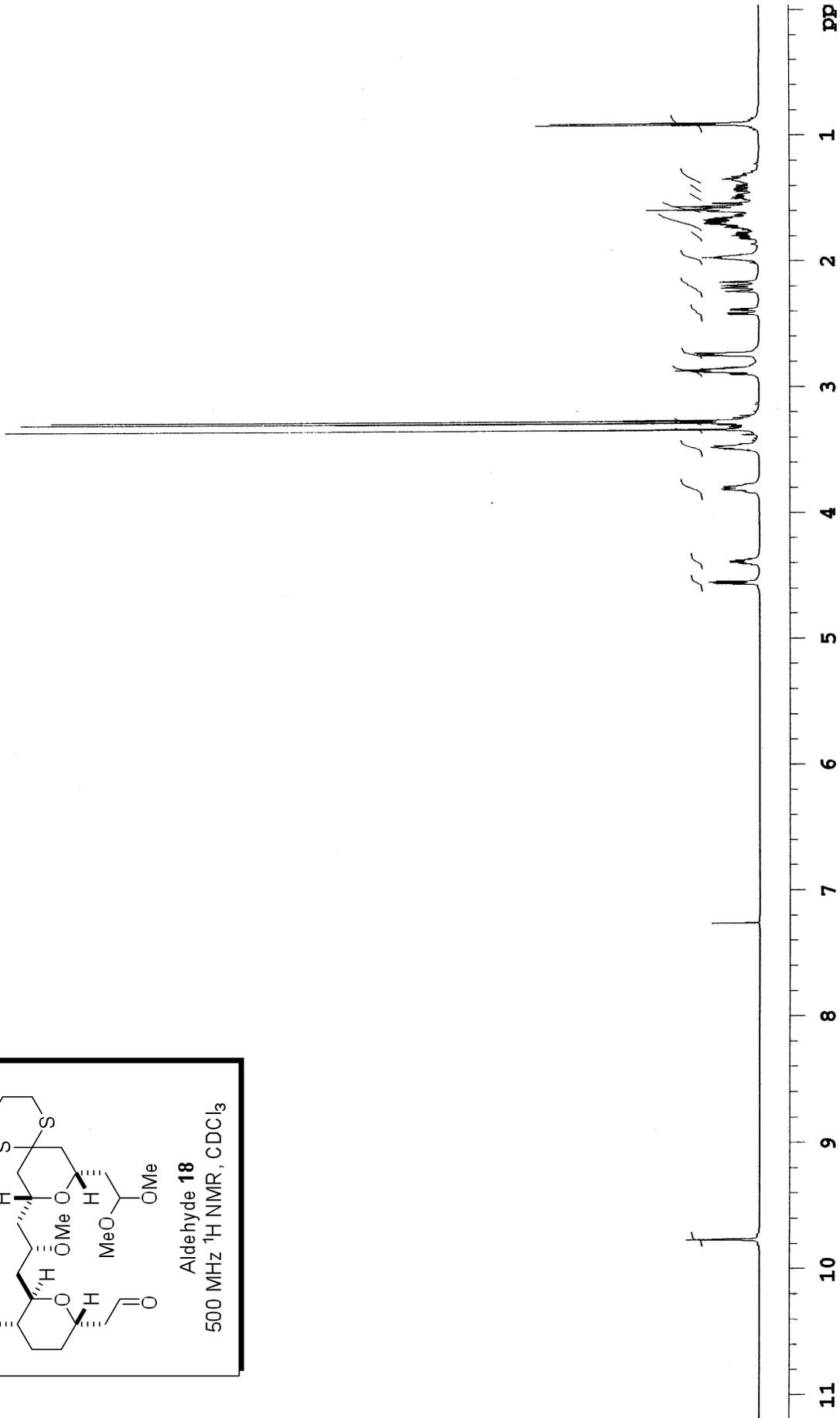
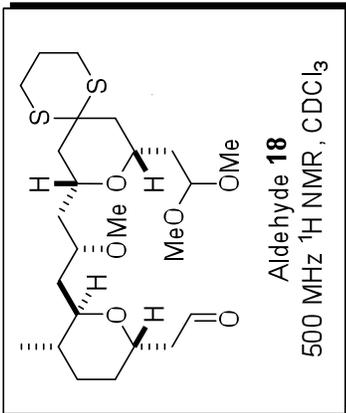


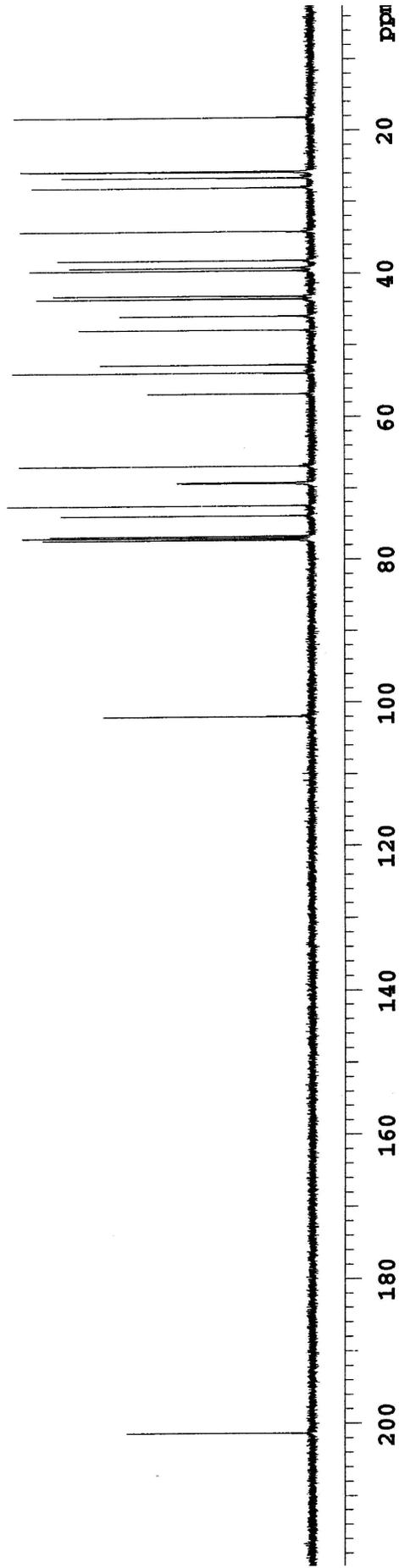
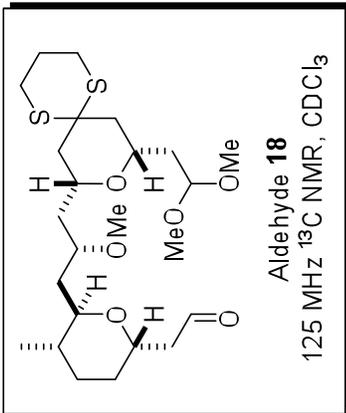
Alcohol 17A

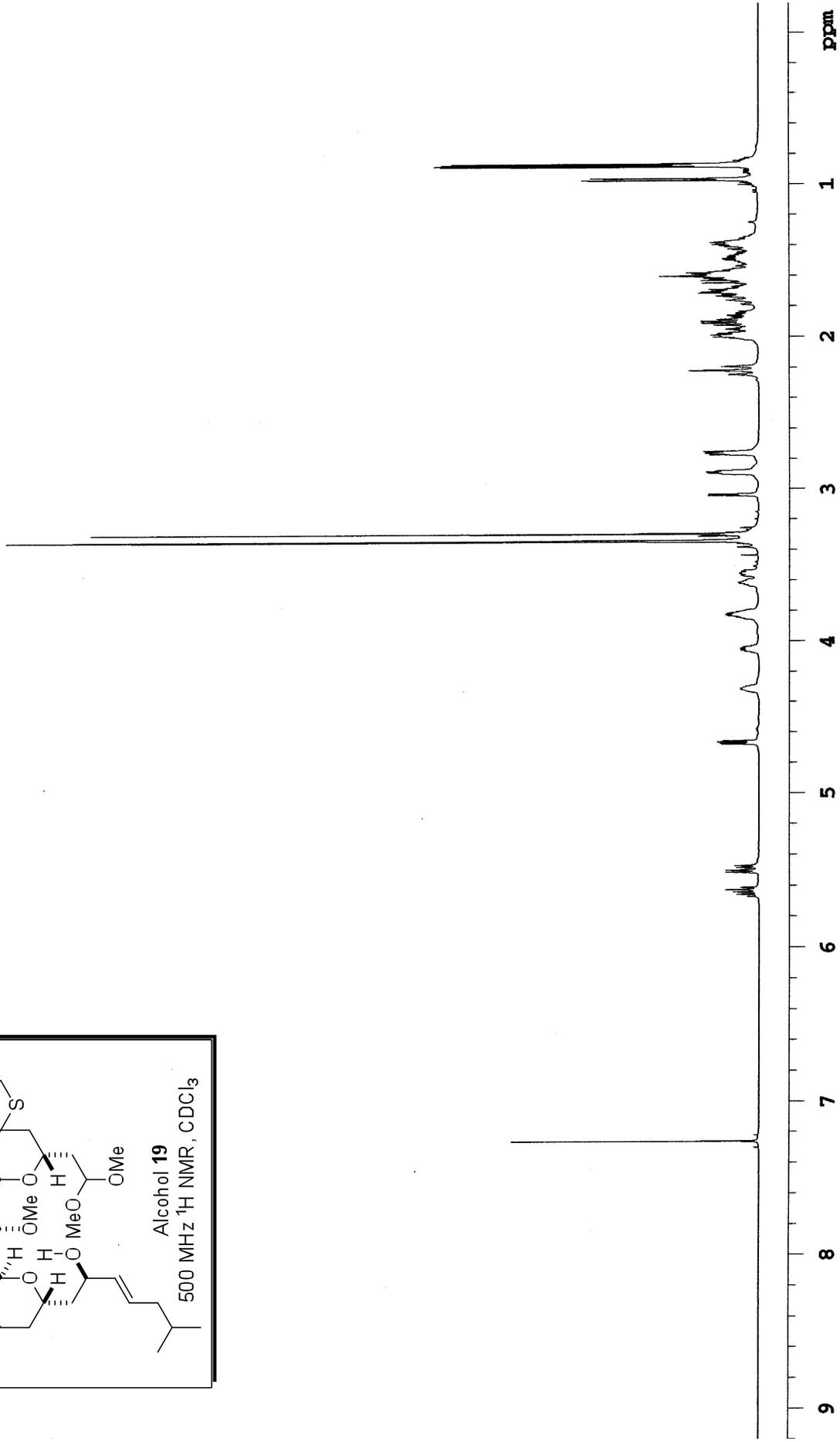
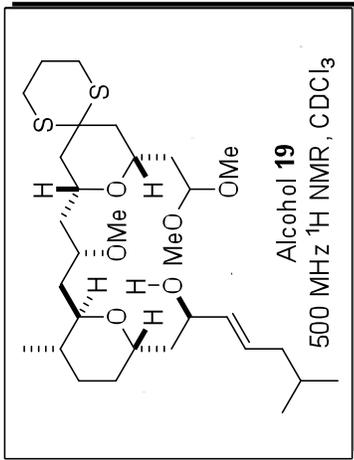
500 MHz  $^1\text{H}$  NMR,  $\text{CDCl}_3$

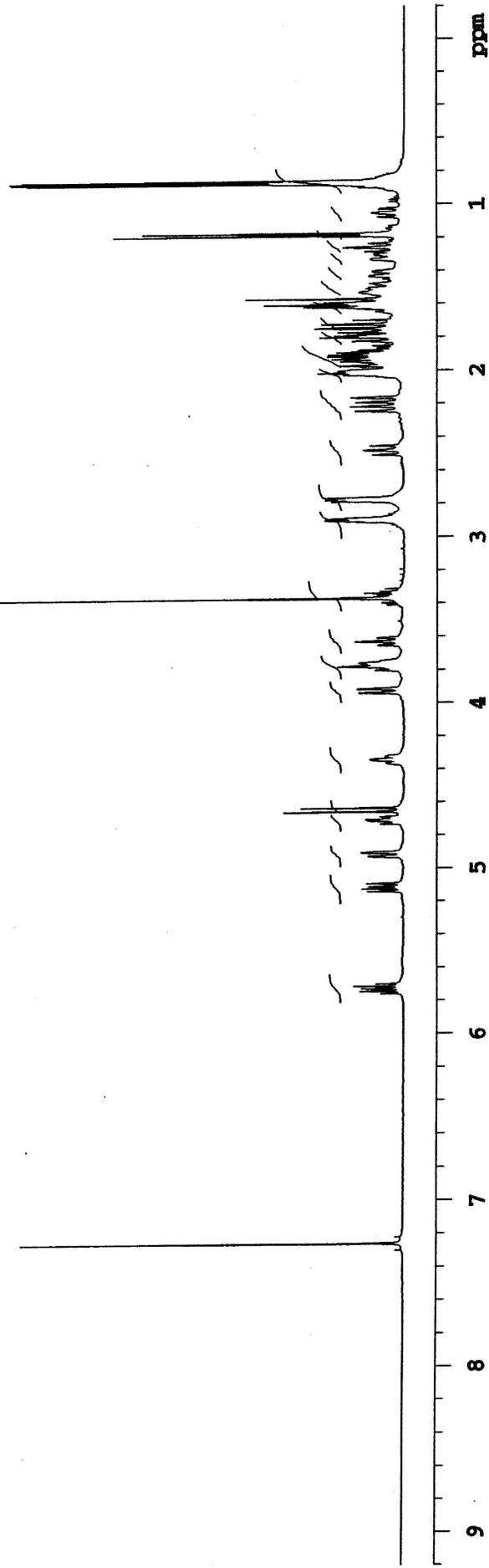
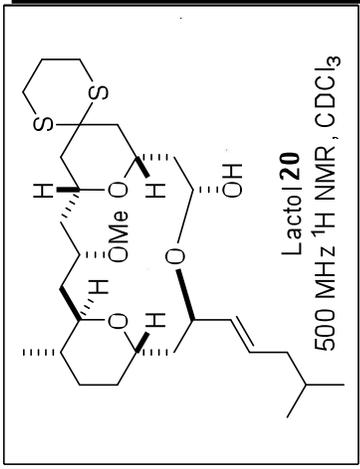


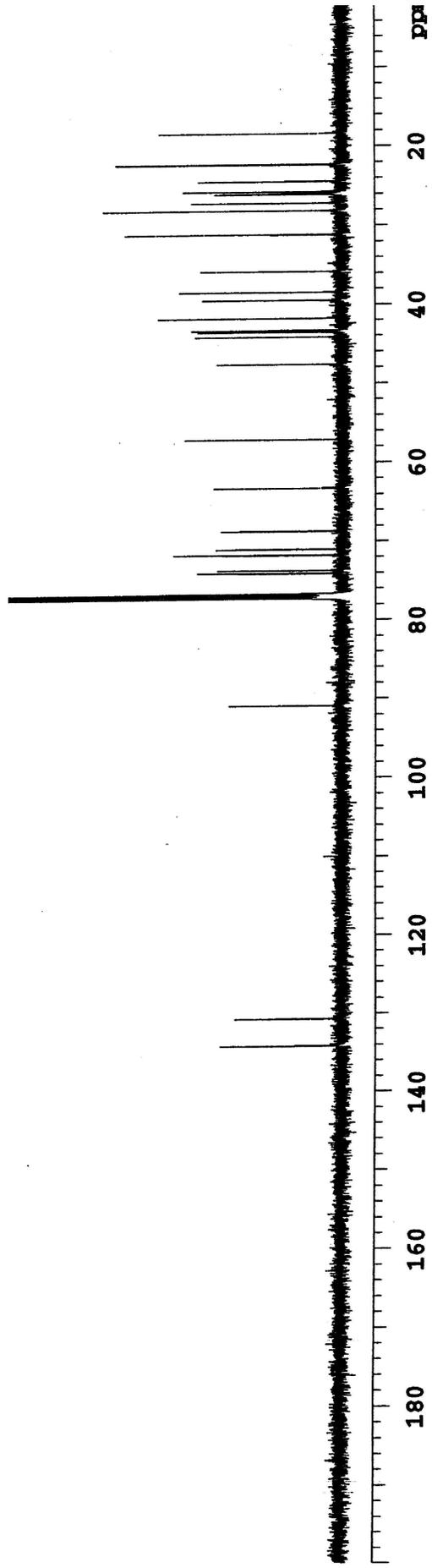
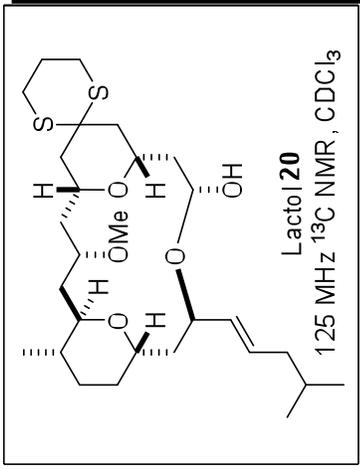


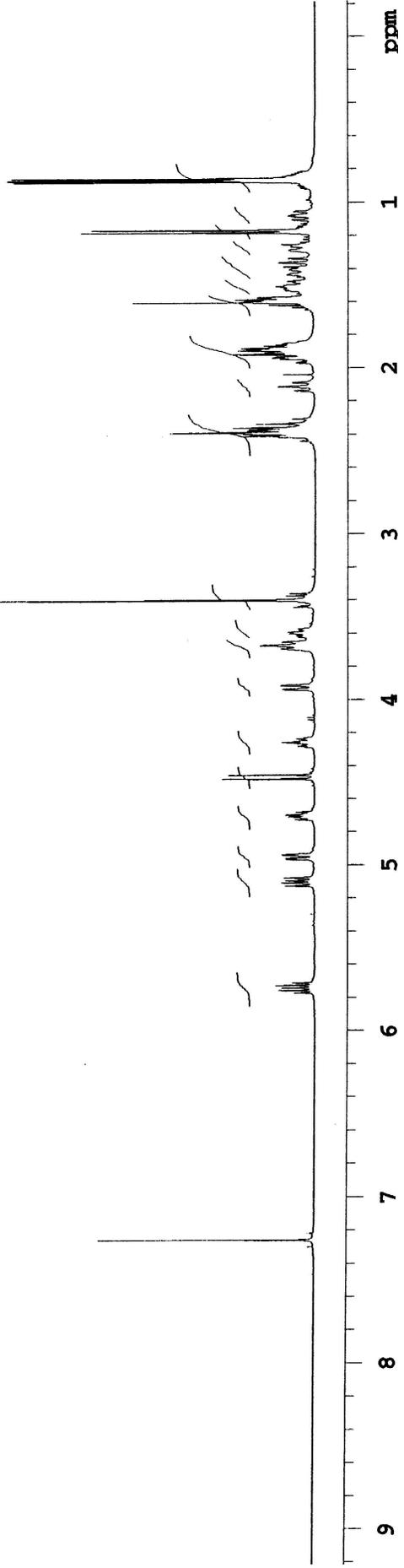
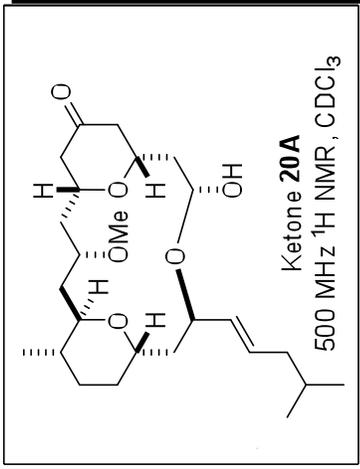


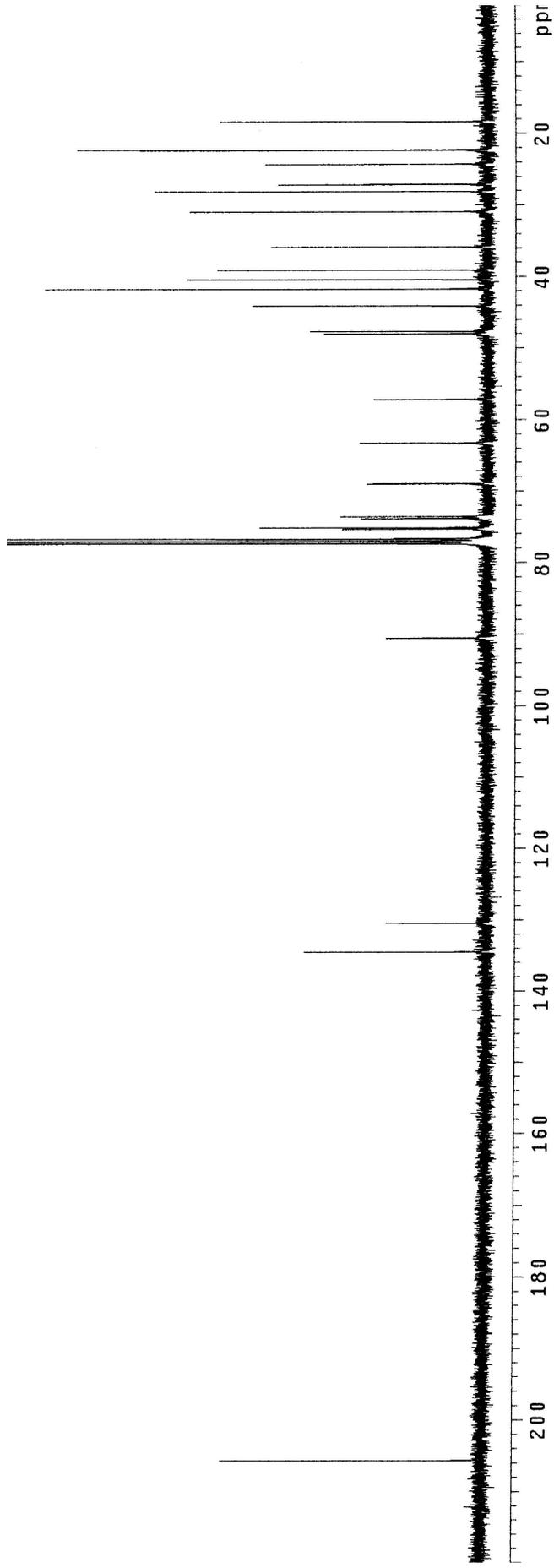
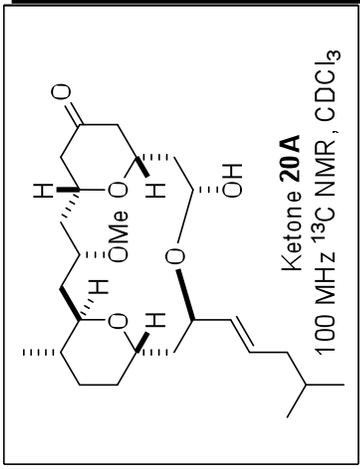


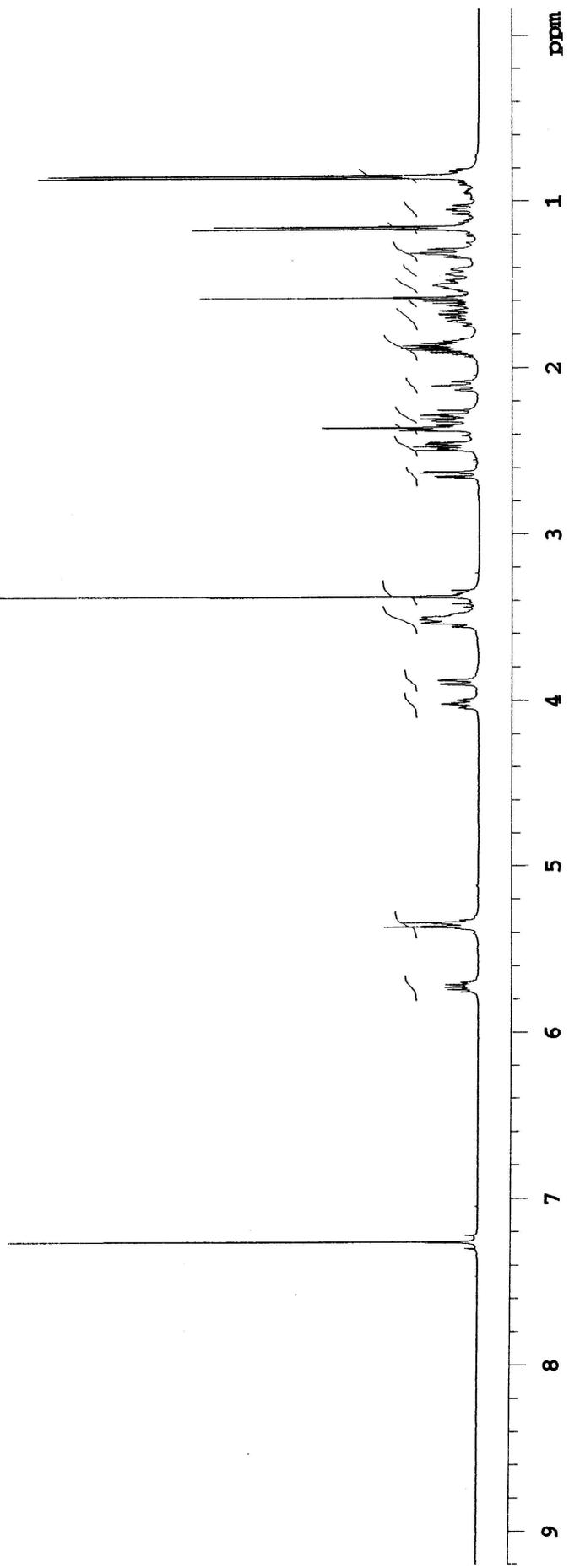
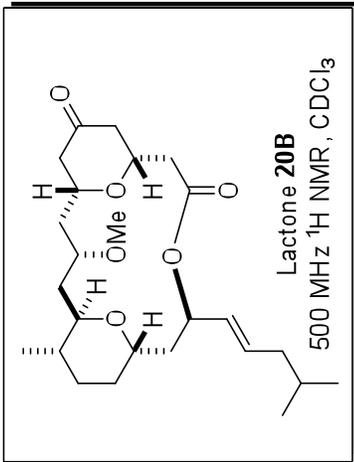


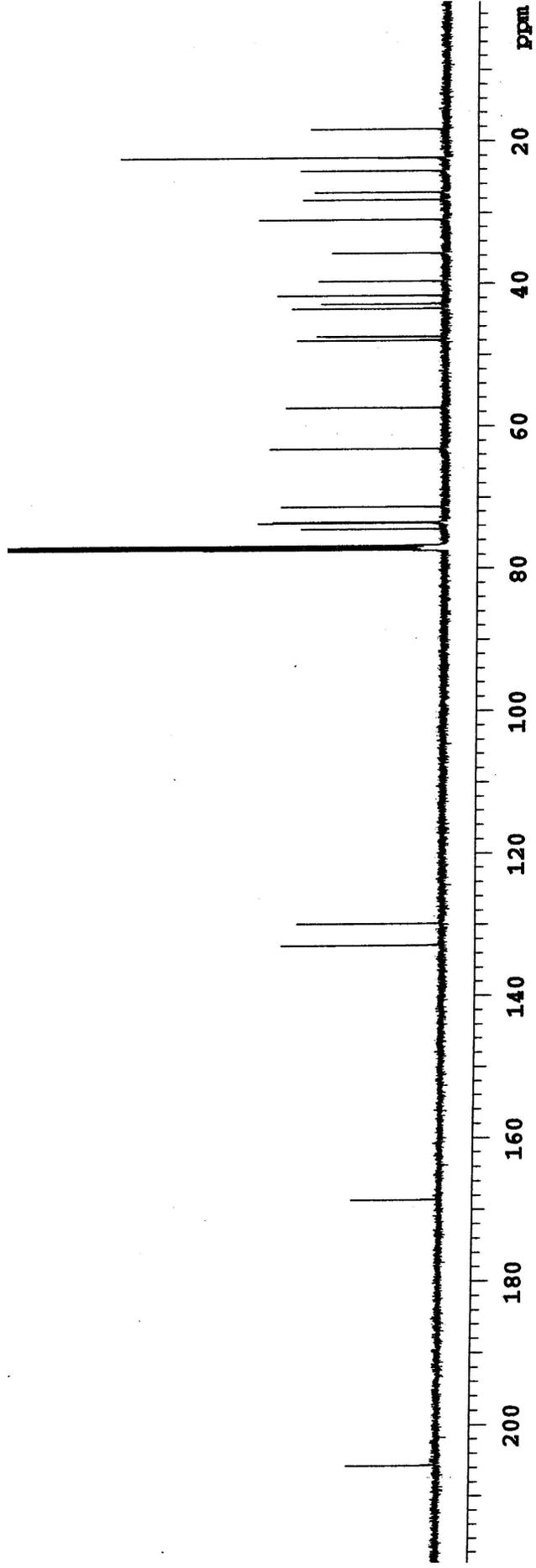
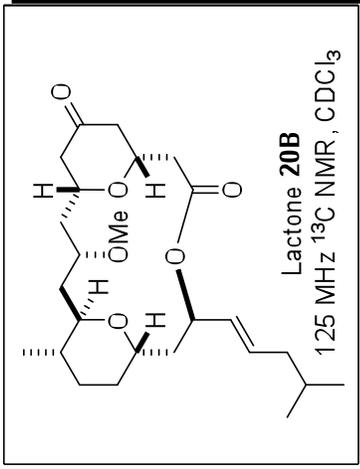


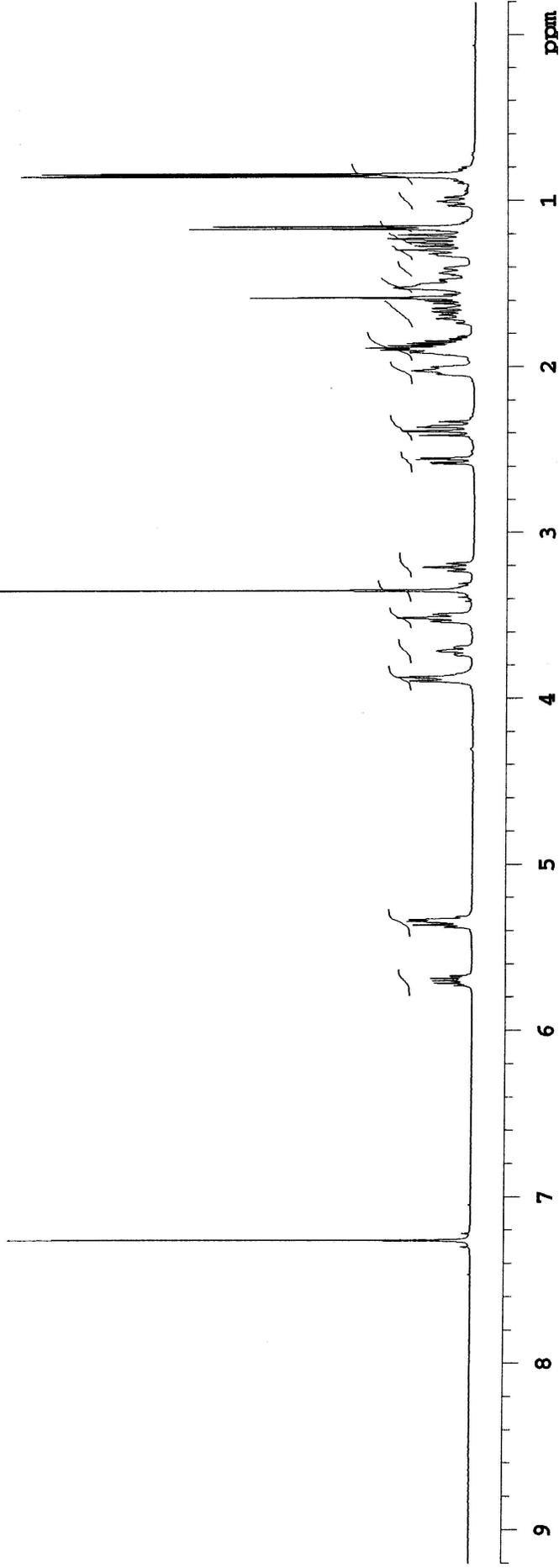
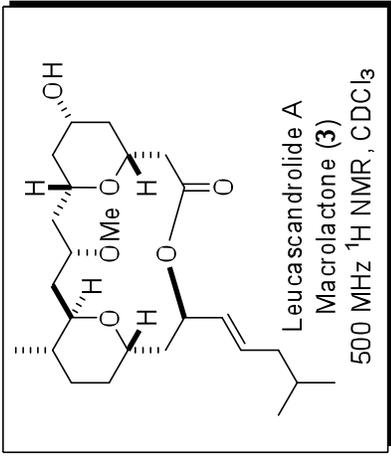


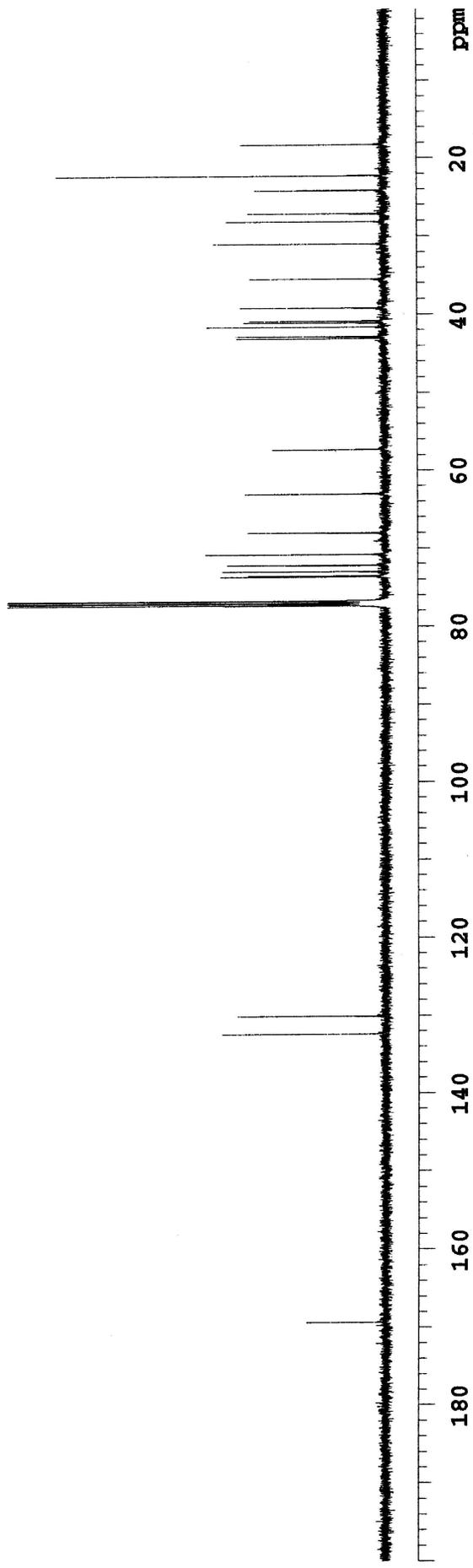
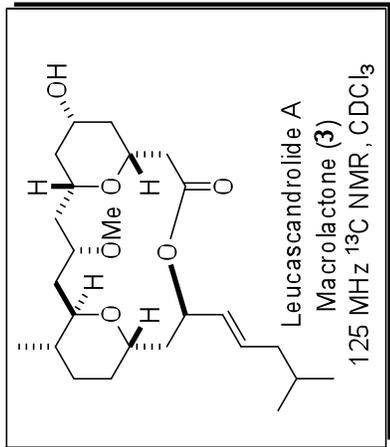


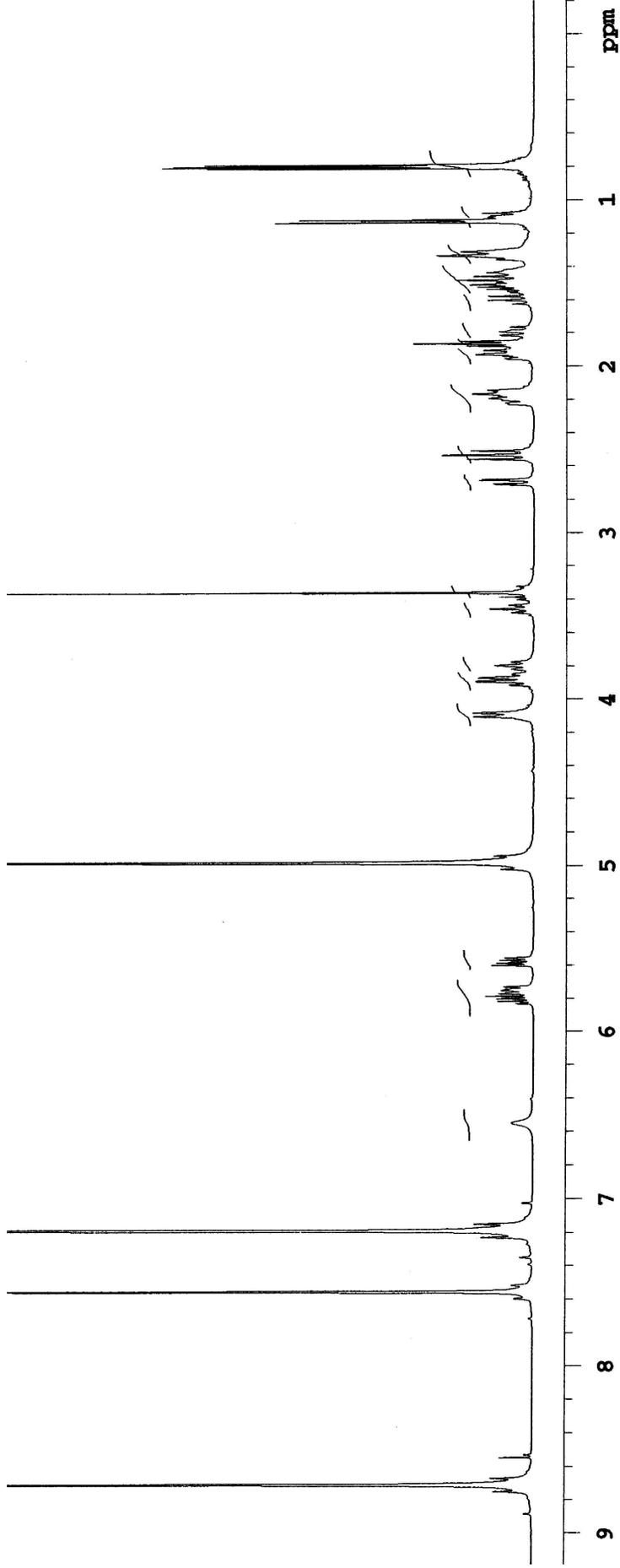
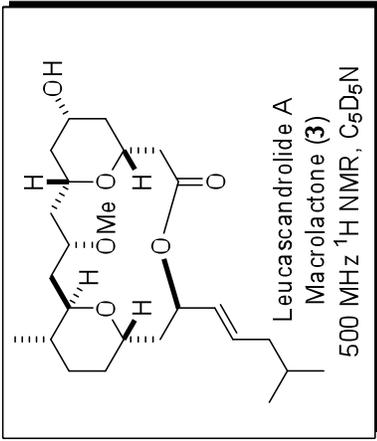


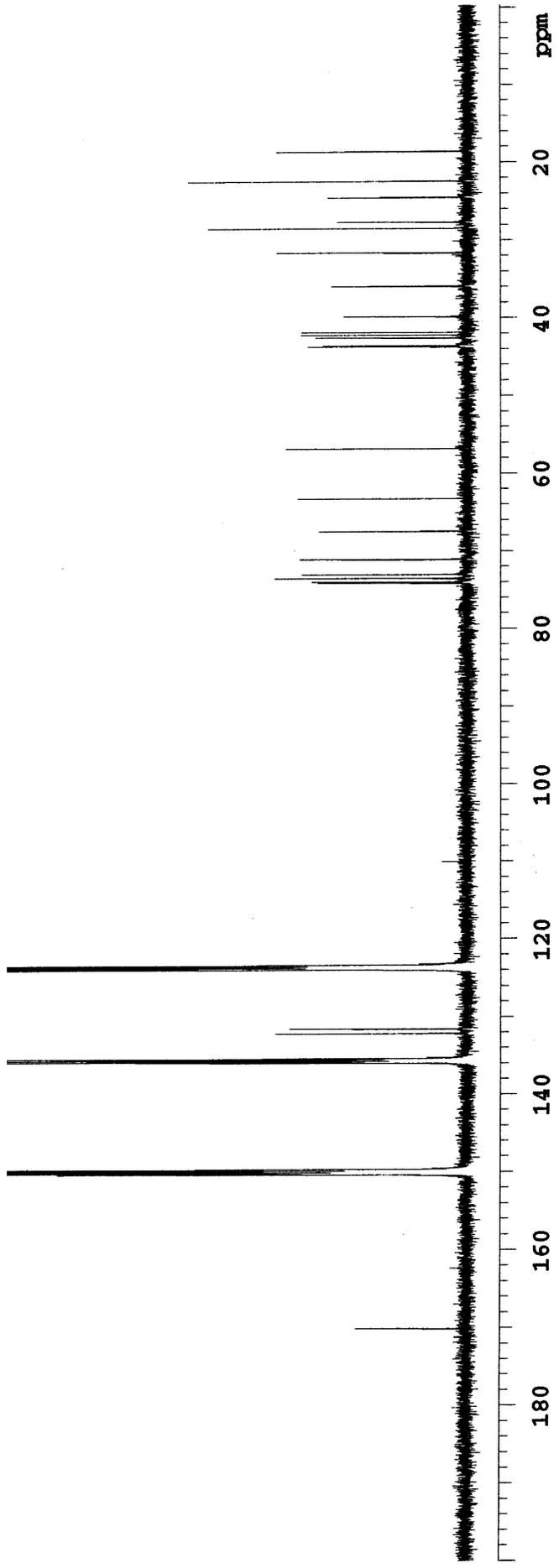
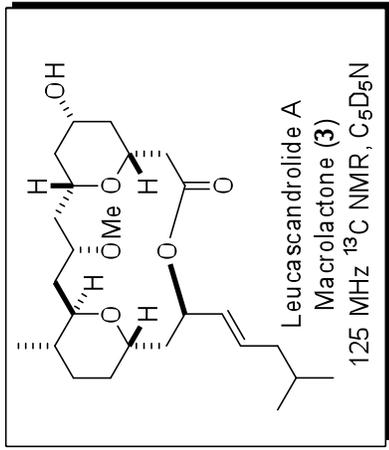


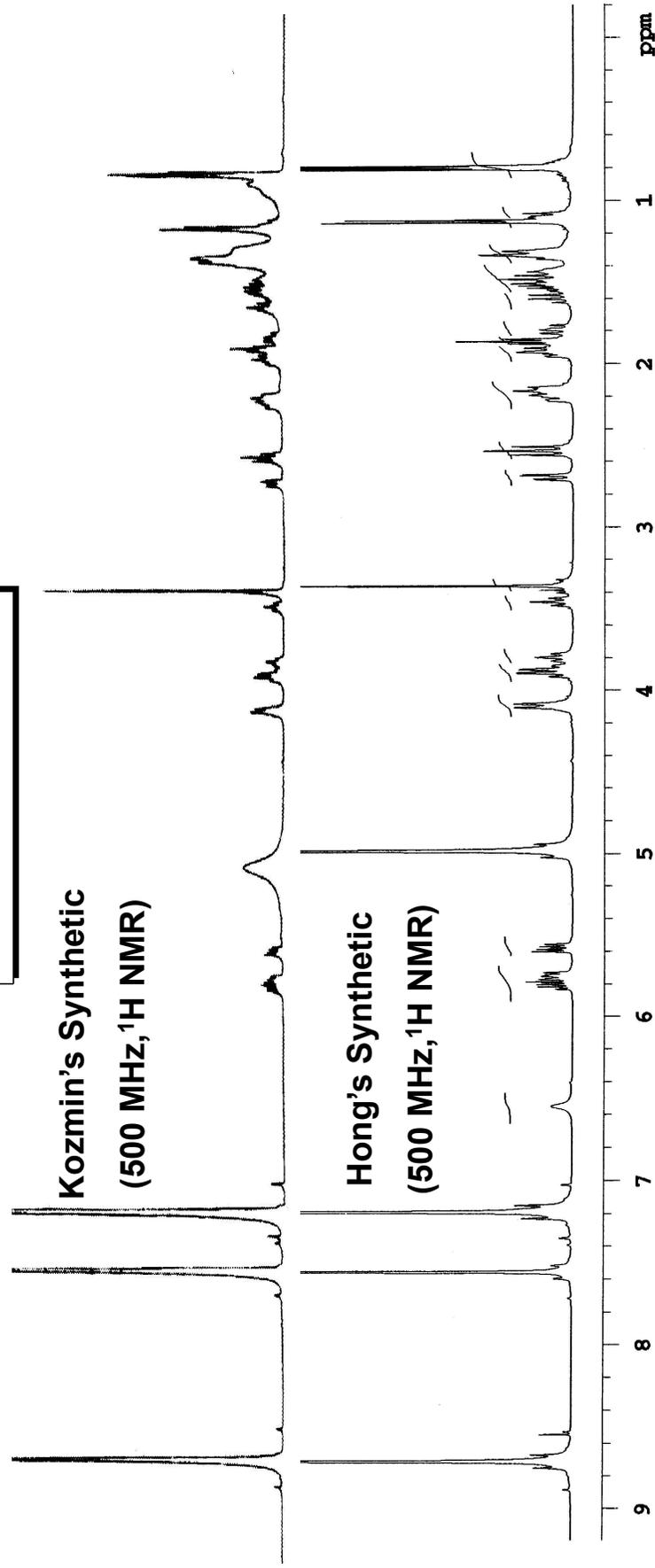
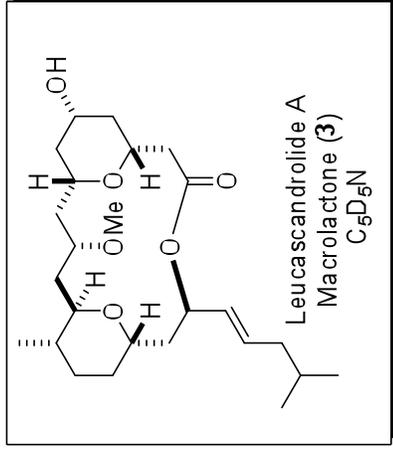


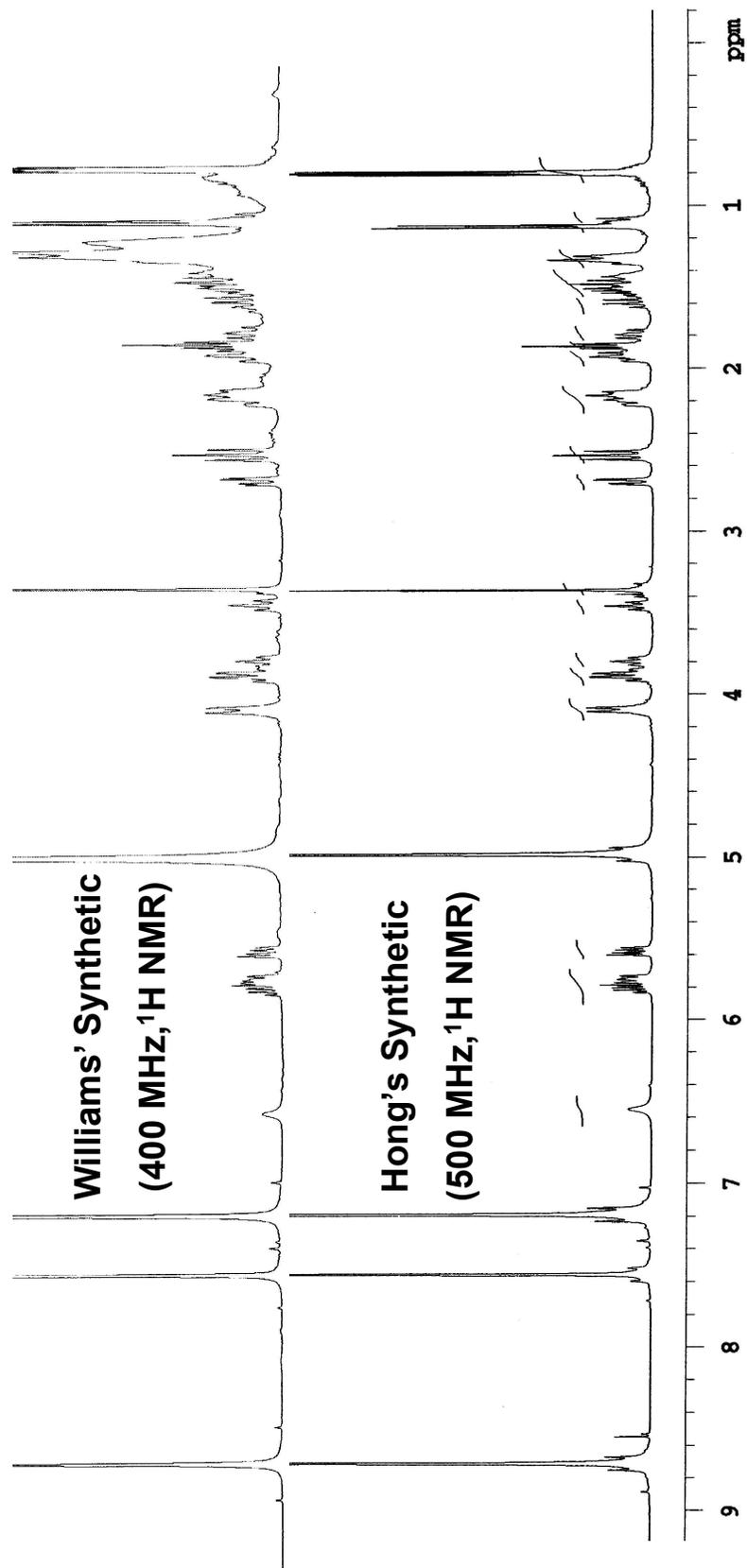
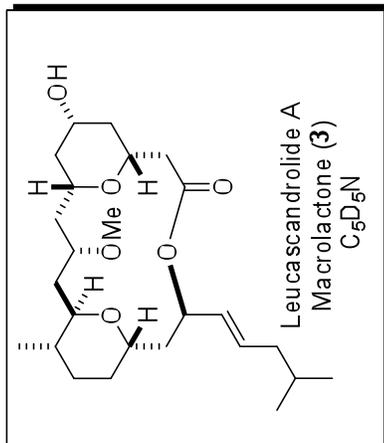


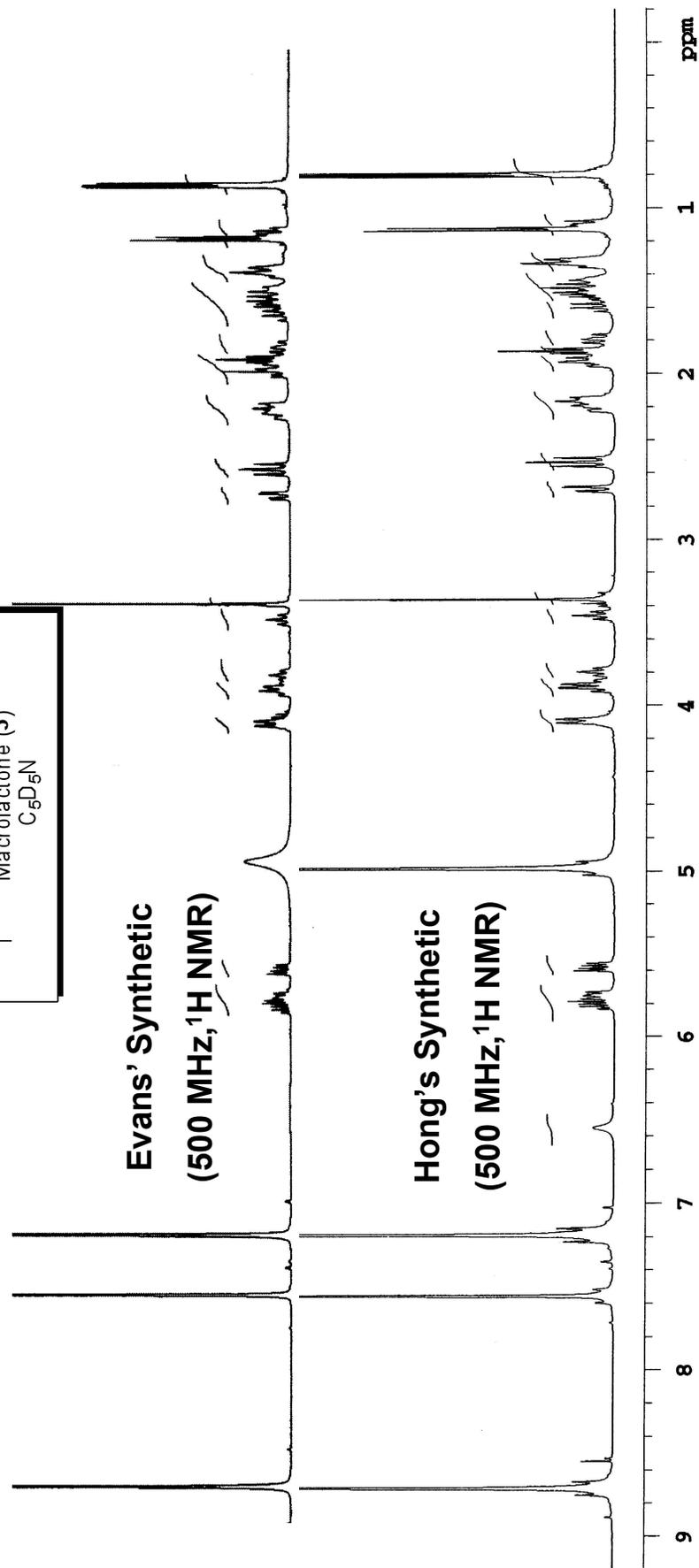
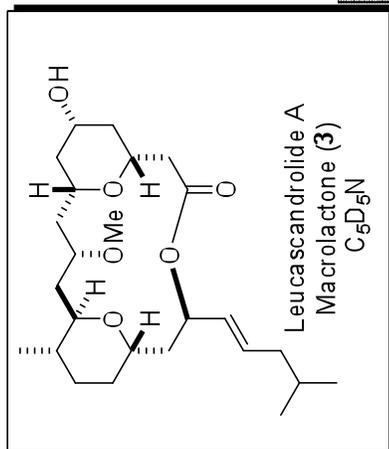


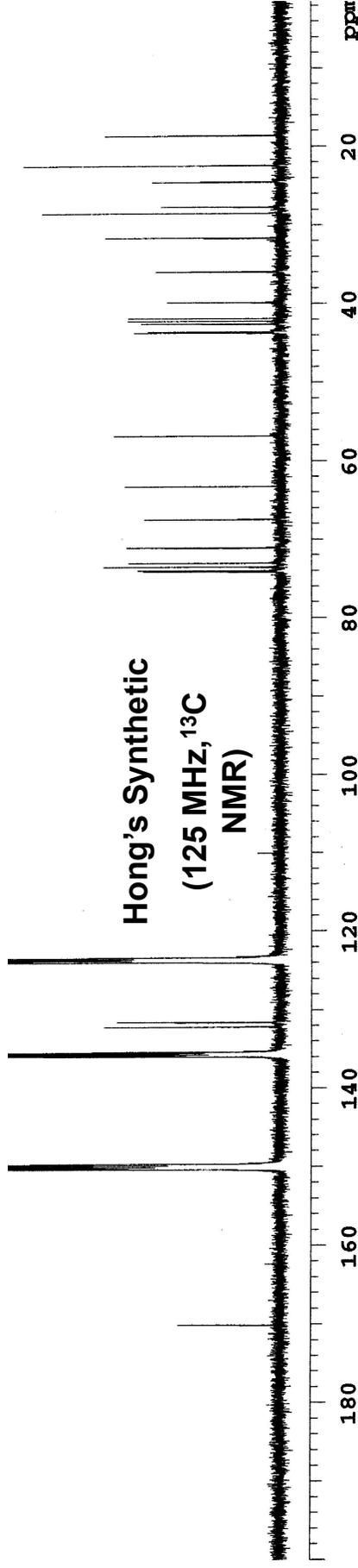
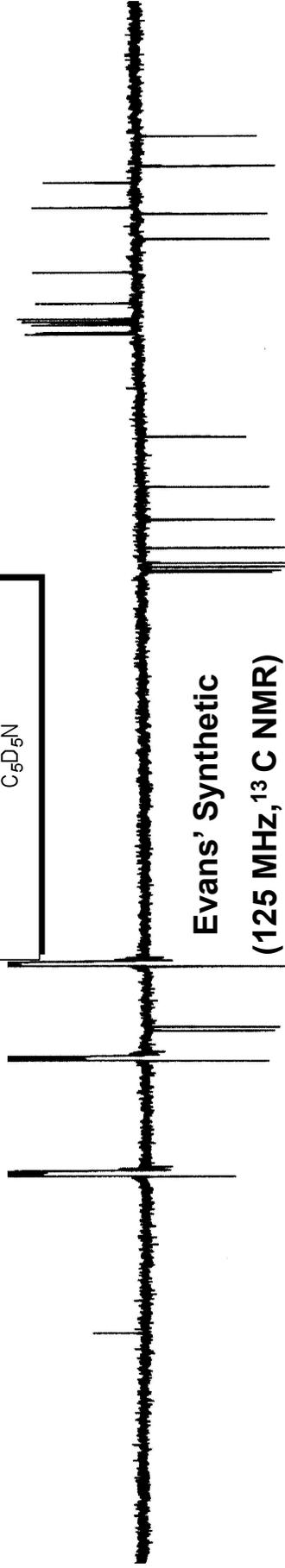
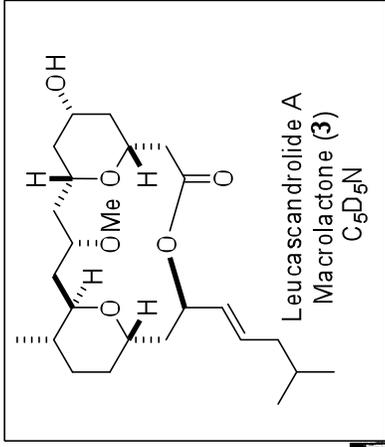








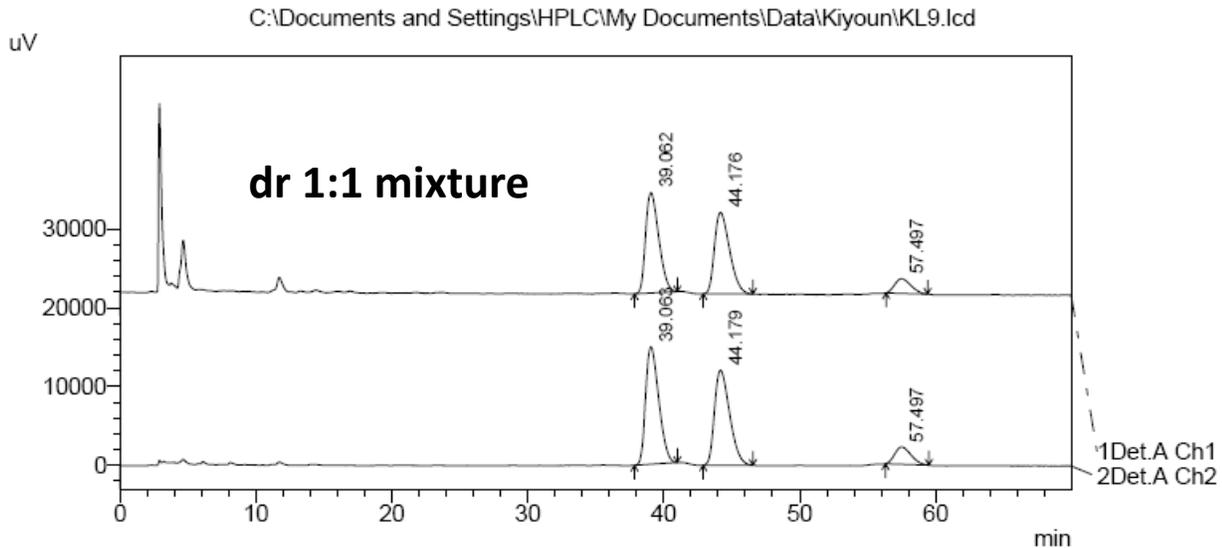




# ==== Shimadzu LCsolution Analysis Report ====

C:\Documents and Settings\HPLC\My Documents\Data\Kiyoun\KL9.lcd  
 Acquired by : Admin  
 Sample Name : KL-VI-vinylzinc-real  
 Sample Description : flow rate:1.0ml/min  
 Condition:75% meoh  
 Data File Name : KL9.lcd  
 Method File Name : KL.lcm  
 Batch File Name :  
 Report File Name : Default.lcr  
 Data Acquired : 5/4/2010 11:19:10 AM  
 Data Processed : 5/4/2010 2:45:06 PM

## <Chromatogram>



1 Det.A Ch1/230nm  
 2 Det.A Ch2/254nm

PeakTable

UV detector Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Name
1	39.062	858304	12718	47.423	
2	44.176	798093	10340	44.096	
3	57.497	153509	1859	8.482	
Total		1809905	24918	100.000	

PeakTable

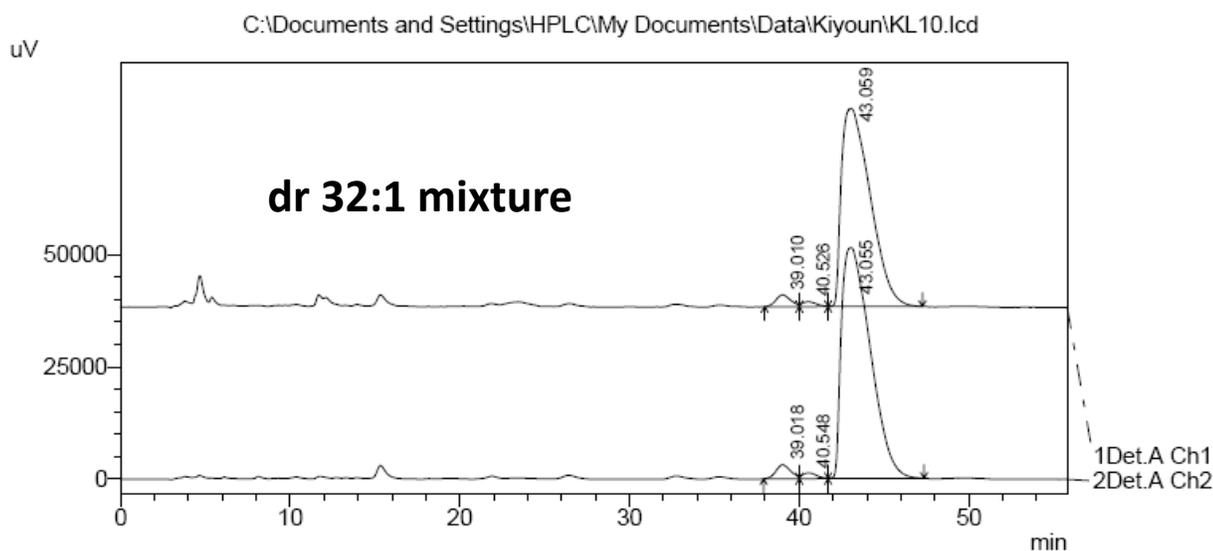
UV detector Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Name
1	39.063	1003131	14887	47.323	
2	44.179	932727	12067	44.001	
3	57.497	183916	2199	8.676	
Total		2119774	29153	100.000	

# ==== Shimadzu LCsolution Analysis Report ====

C:\Documents and Settings\HPLC\My Documents\Data\Kiyoun\KL10.lcd  
 Acquired by : Admin  
 Sample Name : KL-VI-vinylzinc-real  
 Sample Description : flow rate:1.0ml/min  
 Condition:75% meoh  
 Data File Name : KL10.lcd  
 Method File Name : KL.lcm  
 Batch File Name :  
 Report File Name : Default.lcr  
 Data Acquired : 5/4/2010 1:26:53 PM  
 Data Processed : 5/4/2010 2:38:04 PM

## <Chromatogram>



S81

PeakTable

UV detector Ch1 230nm

Peak#	Ret. Time	Area	Height	Area %	Name
1	39.010	157198	2616	2.902	
2	40.526	62564	1080	1.155	
3	43.059	5197118	44118	95.943	
Total		5416880	47814	100.000	

PeakTable

UV detector Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Name
1	39.018	188543	3103	2.979	
2	40.548	75228	1278	1.189	
3	43.055	6065866	51409	95.833	
Total		6329637	55790	100.000	