

**Supporting information for the manuscript entitled****Total Synthesis of (-)-Bitungolide F and Determination of Its Absolute Stereochemistry**

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**General Experimental Procedures.** All reactions were carried out in oven or flame-dried glassware with magnetic stirring under nitrogen atmosphere using dry, freshly distilled solvents, unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light,  $I_2$ , 7% ethanolic phosphomolybdic acid-heat and 2.5% ethanolic anisaldehyde (with 1% AcOH and 3.3% conc.  $H_2SO_4$ )-heat as developing agents. Silica gel finer than 200 mesh was used for flash column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. Melting points are uncorrected. IR spectra were recorded as neat liquids or KBr pellets. Mass spectra were obtained under electron impact ionisation (EI), liquid secondary ion mass spectrometric (LSIMS) technique, electron spray ionisation (ESI) and MALDI techniques. Optical rotations were measured with a digital polarimeter. NMR spectra were recorded on 500, 300 and 200 MHz spectrometers at 30 °C with 2-10 mM solutions in appropriate solvents using TMS as internal standard or the solvent signals as secondary standards and the chemical shifts are shown in  $\delta$  scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved lines), etc.  $^{13}C$  NMR spectra were recorded on 150, 100, 75 and 50 MHz spectrometers with complete proton decoupling.

**(4S)-4-Benzyl-3-((2S,3R,4R)-5-[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-2-ethyl- 3-hydroxy-4-methylpentanoyl)-1,3-oxazolan-2-one (17):**

To the compound **16** (5.07g, 20.3 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (50 mL) at 0 °C was added TiCl<sub>4</sub> (2.3 mL, 21.2 mmol) and after 5 min, (-)-sparteine (11.1 mL, 48.19 mmol) was added. After stirring at the same temperature for 20 min, aldehyde **14** (6.1 g, 18.6 mmol) was added as a solution of dry CH<sub>2</sub>Cl<sub>2</sub> under nitrogen atmosphere. The reaction mixture was quenched after 10 min with half saturated aqueous NH<sub>4</sub>Cl solution (30 mL) and extracted with EtOAc (2 x 300 mL). The combined organic layers were washed with water (100 mL), 0.5 N HCl (30 mL), brine (50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification of the crude residue by column chromatography (18- 22% EtOAc in petroleum ether) provided compound **17** (11.3 g, 95% yield) as a white solid. Optical rotation  $[\alpha]_D^{22} = +7.1$  (*c* 1, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  3492(br), 2961, 1781, 1694, 1386, 1208, 820, 746 and 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  7.69-7.65 (m, 4H), 7.43-7.37 (m, 6H), 7.34-7.21 (m, 5H) 4.76-4.67 (m, 1H), 4.15 (d, *J* = 4.9 Hz, 2H), 4.01 (td, *J* = 3.7, 9.8 Hz, 1H), 3.91 (dd, *J* = 3.7, 7.5 Hz, 1H), 3.82 (dd, *J* = 4.1, 10.2 Hz, 1H), 3.77 (brs, 1H), 3.68 (dd, *J* = 6.4, 10.2 Hz, 1H), 3.37 (dd, *J* = 3.0, 13.2 Hz, 1H), 2.74 (dd, *J* = 9.8, 13.2 Hz, 1H), 2.15-2.02 (m, 1H), 1.92-1.83 (m, 1H), 1.78-1.65 (m, 1H), 1.05 (s, 9H), 1.01 (t, *J* = 7.5 Hz, 3H) and 0.95 (d, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  175.3, 153.1, 135.6, 135.5, 132.9, 129.8, 129.3, 128.9, 127.7, 127.3, 75.7, 68.5, 65.9, 55.7, 47.6, 37.9, 26.8, 26.7, 19.1, 18.4, 13.6 and 11.9; HRMS (ESIMS): calcd for C<sub>34</sub>H<sub>43</sub>NO<sub>5</sub>NaSi [M + Na]<sup>+</sup>: 596.2802, found: 596.2834.

**(2*R*,3*R*,4*R*)-5-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-2-ethyl-4-methylpentane-1,3-diol (18):**

To a solution of compound **17** (11.3 g, 19.8 mmol) in dry ether at 0 °C were added one drop of distilled water followed by LiBH<sub>4</sub> (860 mg, 39.6 mmol) in portion wise and stirred at the same temperature for 10 min. The reaction was then quenched with careful addition of distilled water and extracted with EtOAc (2 x 100 mL), the combined organic layers were washed with water (50 mL), brine (50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification of the crude residue by column chromatography (25% EtOAc in petroleum ether) provided compound **18** (6.67g, 84% yield) as white solid. Optical rotation  $[\alpha]_D^{22} = -21.51$  (c 3.1, CHCl<sub>3</sub>); IR (KBr):  $\nu_{\text{max}}$  3427(br), 2959, 2864, 1465, 1109, 741 and 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  7.68-7.63 (m, 4H), 7.45-7.35 (m, 6H), 4.38-4.36 (m, 1H), 3.90-3.80 (m, 3H), 3.73 (dd, *J* = 4.4, 10.2 Hz, 1H), 3.0 (brs, 1H), 2.02-1.89 (m, 1H), 1.79-1.62 (m, 1H), 1.46-1.34 (m, 1H), 1.06 (s, 9H), 0.99 (t, *J* = 7.3 Hz, 3H) and 0.66 (d, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz):  $\delta$  135.5, 132.2, 129.9, 127.8, 81.4, 70.4, 64.7, 42.9, 37.1, 26.7, 18.9, 15.4, 12.8 and 12.1; HRMS (ESIMS): calcd for C<sub>24</sub>H<sub>36</sub>O<sub>3</sub>NaSi [M + Na]<sup>+</sup>: 423.2331, found: 423.2352.

**tert-Butyl((2*R*)-2-[(4*R*,5*R*)-5-ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]propyloxy)diphenylsilane (19):**

To the compound **18** (6.28 g, 15.7 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (35 mL) at 0 °C was added freshly prepared PMP acetal (4.1 mL, 6.35 mmol), CSA (360 mg, 1.57 mmol) and stirred the resulting reaction mixture at the ambient temperature for 6 h. The reaction mixture was quenched with saturated aqueous NaHCO<sub>3</sub> solution (60 mL) and extracted with EtOAc (2 x 175 mL). Combined organic layers were washed with water (90 mL), brine (90 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification of the crude residue by column chromatography (10-12% EtOAc in petroleum ether) provided

compound **19** (6.4 g, 94% yield) as colorless oil. Optical rotation  $[\alpha]_D^{22} = +7.88$  (*c* 2.45, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  2960, 2857, 1463, 1248, 1110, 824 and 703 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  7.68-7.59 (m, 4H, Ar-H), 7.39-7.30 (m, 6H), 7.19 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 9.1 Hz, 2H), 5.44 (s, 1H), 4.3 (d, *J* = 11.3 Hz, 1H), 3.97-3.90 (m, 3H), 3.80 (s, 3H), 3.65 (dd, *J* = 2.3, 9.8 Hz, 1H), 1.97-1.73 (m, 2H), 1.55-1.42 (m, 1H), 1.37-1.28 (m, 1H), 1.05 (s, 9H), 1.03 (d, *J* = 6.8 Hz, 3H) and 1.0 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  159.7, 135.6, 135.5, 133.9, 131.7, 129.5, 127.6, 127.3, 113.5, 101.6, 80.3, 69.5, 64.7, 55.3, 36.6, 26.9, 19.4, 16.3, 12.5 and 12.0; HRMS (ESIMS): calcd for C<sub>32</sub>H<sub>42</sub>O<sub>4</sub>NaSi [M + Na]<sup>+</sup>: 541.2750, found: 541.2771.

**(2*R*)-2-[(4*R*,5*R*)-5-Ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]propan-1-ol (20):**

To a stirred solution of compound **19** (6.38 g, 11.6 mmol) in dry THF (25 mL), TBAF (1M solution in THF 12.0 mL, 11.6 mmol) was added at 0 °C. Reaction mixture was warmed to room temperature and stirred for 4 h. It was quenched with saturated aqueous NH<sub>4</sub>Cl solution (25 mL), extracted with EtOAc (2 x 100 mL), washed with brine (40 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification by column chromatography (SiO<sub>2</sub>, 25% EtOAc in petroleum ether) afforded pure compound **20** (3.26 g, 92%) as colorless oil. Optical rotation  $[\alpha]_D^{22} = +17.25$  (*c* 0.8, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  3403(br), 2917, 2850, 1246, 1093, and 1034 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  7.47-7.40 (m, 2H), 6.97-6.90 (m, 2H), 5.56 (s, 1H), 4.35 (dd, *J* = 1.4, 11.5 Hz, 1H), 4.01-3.89 (m, 2H), 3.85 (s, 3H), 3.76 (dd, *J* = 7.2, 10.8 Hz, 1H), 3.65 (dd, *J* = 2.2, 9.4 Hz, 1H), 2.81 (brs, 1H), 2.21-2.04 (m, 1H), 2.01-1.81 (m, 1H), 1.72-1.50 (m, 1H), 1.44-1.33 (m, 1H), 1.08 (t, *J* = 7.2 Hz, 3H) and 0.88 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$

16.0, 131.0, 127.2, 113.7, 101.9, 85.9, 69.4, 68.1, 55.3, 36.8, 36.2, 16.5, 12.0 and 11.9; HRMS (ESIMS): calcd for  $C_{16}H_{24}O_4Na$   $[M + Na]^+$ : 303.1572, found: 303.1560.

**Dimethyl-(4S)-5-[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy-2-oxo-4-[(1,1,1-triethylsilyl)oxy]pentylphosphonate (12):**

To the freshly distilled dimethyl methylphosphonate (12.3 mL, 115.3 mmol) in dry THF was added  $^7\text{BuLi}$  (1.6 M solution in *n*-Hexane 70 mL, 111.9 mmol) drop wise at  $-78^\circ\text{C}$  over 15 min and stirred at the same temperature for 1 h. compound **24** (13.79 g, 28.8 mmol) was introduced into the reaction mixture slowly over a period of 10 min under nitrogen atmosphere as a solution of THF (50 mL). The resulting mixture was stirred for 1 h at the same temperature and then warmed to ambient temperature before quenching with saturated aqueous  $\text{NH}_4\text{Cl}$  solution (50 mL) at  $0^\circ\text{C}$ . The product was extracted with EtOAc (2 x 250 mL), washed with water (100 mL), brine (100 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $\text{SiO}_2$ , 50-60% EtOAc in petroleum ether) afforded pure compound **12** (13.2 g, 81%) as colorless oil. Optical rotation  $[\alpha]_D^{22} = -19.59$  (*c* 2.2,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  2954, 2877, 2360, 1717, 1260, 1110, 1033, 740 and 704  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.68-7.63 (m, 4H), 7.43-7.34 (m, 6H), 4.20 (tt, *J* = 4.5, 7.5 Hz, 1H), 3.79 (s, 3H), 3.75, (s, 3H), 3.60 (dd, *J* = 4.5, 9.8 Hz, 1H), 3.46 (dd, *J* = 6.8, 9.8 Hz, 1H), 3.19 (d, *J* = 22.6 Hz, 2H), 3.01 (dd, *J* = 4.5, 15.9 Hz, 1H), 2.78 (dd, *J* = 6.8, 15.8 Hz, 1H), 1.04 (s, 9H), 0.85 (t, *J* = 7.5 Hz, 9H) and 0.48 (q, *J* = 7.5 Hz, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  200.5, 135.5, 133.3, 129.7, 127.7, 69.2, 67.33, 52.9, 48.8, 43.3, 41.7, 26.8, 19.1, 6.7 and 4.7; HRMS (ESIMS): calcd for  $C_{29}H_{47}O_6NaSi_2P$   $[M + Na]^+$ : 601.2570, found: 601.2577.

**(2*S*,7*R*)-1-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-7-[(4*R*,5*R*)-5-ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-2-[(1,1,1-triethylsilyl)oxy]octan-4-one (26) :**

Compound **25** (1.74 g, 2.36 mmol) was dissolved in EtOAc (10 mL), Pd-C (10%) (70 mg) was added followed by NH<sub>4</sub>OAc (*ca.* 3 mg) and subjected to hydrogenation under atmospheric pressure using H<sub>2</sub>-filled balloon. After 2 h, the reaction mixture was filtered through a short pad of Celite and the filter cake was washed with EtOAc. The filtrate and washings were combined and concentrated in *vacuo*. Purification by column chromatography (SiO<sub>2</sub>, 10% EtOAc in petroleum ether eluant) afforded pure compound **26** (1.66 g, 95%) as a colorless syrup. Optical rotation  $[\alpha]_D^{27} = +0.93$  (*c* 3.35, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  2956, 2877, 1712, 1247, 1112, 740 and 704 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  7.66-7.54 (m, 4H), 7.41-7.30 (m, 8H), 6.85-6.78 (m, 2H), 5.40 (s, 1H), 4.29-4.12 (m, 2H), 3.89-3.79 (m, 2H), 3.76 (s, 3H), 3.59-3.50 (m, 1H), 3.40 (dd, *J* = 7.3, 10.2 Hz, 1H), 2.72 (dd, *J* = 4.4, 15.4 Hz, 1H), 2.56-2.40 (m, 3H), 2.09-1.90 (m, 2H), 1.86-1.63 (m, 2H), 1.48-1.18 (m, 2H), 1.02 (s, 9H), 0.99-0.94 (m, 3H), 0.87-0.77 (m, 12H) and 0.44 (q, *J* = 7.3 Hz, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  209.9, 159.7, 135.5, 133.4, 131.2, 129.6, 127.6, 127.2, 113.5, 101.7, 84.9, 69.3, 67.6, 55.2, 47.5, 42.2, 37.1, 33.4, 27.0, 26.79, 19.1, 16.2, 14.3, 11.9, 6.7, 6.5 and 4.7; HRMS (ESIMS): calcd for C<sub>43</sub>H<sub>64</sub>O<sub>6</sub>NaSi<sub>2</sub> [M + Na]<sup>+</sup>: 755.4139, found: 755.4171.

**(2*S*,7*R*)-1-[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy-7-[(4*R*,5*R*)-5-ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-2-hydroxy-octan-4-one (11):**

A solution of compound **26** (1.1 g, 1.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub>:MeOH (4:1, 6 mL) was treated with CSA (35 mg, 0.1 mmol) at 0 °C. After being stirred for 10 min, the reaction mixture was quenched with saturated aqueous NaHCO<sub>3</sub>. Solvent was removed in the

rotary evaporator and the residue was extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with water (10 mL), brine (20 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Column chromatography ( $\text{SiO}_2$ , 18-20% EtOAc in petroleum ether eluant) gave pure compound **11** (813 mg, 87%) as colorless syrup. Optical rotation  $[\alpha]_D^{27} = +11.10$  (*c* 5.5,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  3335(br), 2930, 1728, 1462, 1111, 741 and 703  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.65-7.58 (m, 4H), 7.42-7.31 (m, 8H), 6.85-6.78 (m, 2H), 5.39 (s, 1H), 4.31-4.04 (m, 2H), 3.90-3.78 (m, 2H), 3.75 (s, 3H), 3.56 (dd, *J* = 1.6, 3.9 Hz, 1H), 3.47 (dd, *J* = 1.6, 7.8 Hz, 1H), 2.83 (d, *J* = 3.9 Hz, 1H), 2.52-2.40 (m, 4H), 2.07-1.87 (m, 2H), 1.86-1.63 (m, 2H), 1.41-1.21 (m, 2H), 1.05 (s, 9H), 0.96 (t, *J* = 7.8 Hz, 3H) and 0.82 (d, *J* = 7.0 Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  190.8, 159.5, 135.6, 133.6, 131.9, 129.5, 127.6, 114.3, 113.5, 96.8, 68.4, 67.7, 64.3, 55.5, 44.8, 39.2, 30.2, 26.8, 26.3, 26.0, 20.9, 20.8, 19.2 and 11.2; HRMS (ESIMS): calcd for  $\text{C}_{37}\text{H}_{50}\text{O}_6\text{NaSi} [\text{M} + \text{Na}]^+$ : 641.3274, found: 641.3292.

**(2*S*,4*R*,7*R*)-7-[(4*R*,5*R*)-5-Ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]octane-1,2,4-triol (28):**

To a stirred solution of **27** (502 mg, 0.80 mmol) in dry THF (2 mL), TBAF (1M solution in THF, 0.9 mL, 0.92 mmol) was added at 0 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. It was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution, extracted with EtOAc, washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $\text{SiO}_2$ , 80 to 100% EtOAc in petroleum ether eluant) afforded pure **28** (304 mg, 95%) as colorless oil. Optical rotation  $[\alpha]_D^{27} = +16.44$  (*c* 1.8,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  3361(br), 2933, 1516, 1461, 1247, 1117 and 828  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.40-7.36 (m, 2H), 6.89-6.84 (m, 2H),

5.43 (s, 1H), 4.27 (m, 1H), 3.92-3.80 (m, 3H), 3.78 (s, 3H), 3.53-3.46 (m, 2H), 3.40 (dd,  $J$  = 6.8, 11.3 Hz, 1H), 1.84-1.68 (m, 3H), 1.62-1.49 (m, 3H), 1.49-1.37 (m, 4H), 0.99 (t,  $J$  = 7.6 Hz, 3H) and 0.82 (d,  $J$  = 6.8 Hz, 3H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  159.9, 131.4, 127.4, 113.6, 101.9, 85.1, 69.6, 69.4, 68.7, 66.8, 55.3, 39.1, 37.0, 34.5, 33.4, 28.9, 16.2, 14.5 and 11.9; HRMS (ESIMS): calcd for C<sub>21</sub>H<sub>34</sub>O<sub>6</sub>Na [M + Na]<sup>+</sup>: 405.2253, found: 405.2247.

**(2*S*,4*R*,7*R*)-1-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-7-[(4*R*,5*R*)-5-ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]octane-2,4-diol (29):**

To a stirred solution of **28** (304 mg, 0.79 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL), Et<sub>3</sub>N (0.22 mL, 1.59 mmol) and TBSCl (143 mg, 0.95 mmol) were added sequentially at 0 °C under nitrogen atmosphere followed by the addition of DMAP (9.7 mg, 0.08 mmol). The reaction mixture was warmed to room temperature and stirred for 3 h. It was quenched with saturated aqueous NH<sub>4</sub>Cl solution and extracted with EtOAc (40 mL), washed with brine (20 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification by column chromatography (SiO<sub>2</sub>, 25 to 30% EtOAc in petroleum ether eluant) gave pure compound **29** (0.3 g, 76%) as clear oil. Optical rotation  $[\alpha]_D^{22} = +6.08$  (*c* 1.2, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  3450, 2930, 2857, 2338, 1615, 1462, 1249, 1119 and 834 cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  7.39 (d,  $J$  = 8.7 Hz, 2H), 6.87 (d,  $J$  = 8.7 Hz, 2H), 5.43 (s, 1H), 4.27 (m, 1H), 3.98-3.82 (m, 4H), 3.79 (s, 3H), 3.58 (dd,  $J$  = 4.4, 10.2 Hz, 1H), 3.45 (dd,  $J$  = 7.3, 10.2 Hz, 1H), 1.87-1.66 (m, 3H), 1.63-1.47 (m, 4H), 1.45-1.27 (m, 3H), 0.99 (t,  $J$  = 7.3 Hz, 3H), 0.89 (s, 9H), 0.83 (d,  $J$  = 6.5 Hz, 3H) and 0.06 (s, 6H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  159.8, 131.5, 127.3, 113.5, 101.8, 85.0, 69.5, 68.9, 67.1, 55.2, 38.9, 37.0, 34.6, 33.6, 29.0, 25.8, 18.3, 16.2, 14.3, 12.0 and -5.4.

HRMS (ESIMS): calcd for  $C_{27}H_{48}O_6NaSi$   $[M + Na]^+$ : 519.3117, found: 519.3136.

**tert-Butyl((2S,4R,7R)-7-[(4R,5R)-5-ethyl-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-2,4-di[(1,1,1-triisopropylsilyl)oxy]octyloxy)dimethylsilane (10):**

To a stirred solution of compound **29** (300 mg, 0.6 mmol) in  $CH_2Cl_2$  (2 mL) at 0 °C, 2,6-lutidine (0.43 mL, 2.42 mmol) and TIPSOTf (0.36 mL, 1.33 mmol) were added sequentially. After 15 min, reaction was quenched with saturated  $NH_4Cl$  solution (10 mL), the reaction mixture was extracted with EtOAc (2 x 30 mL), washed with saturated aqueous  $CuSO_4$  solution (10 mL), brine (10 mL), dried ( $Na_2SO_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $SiO_2$ , 2-5% EtOAc in petroleum ether eluant) afforded pure compound **10** (460 mg, 95%) as colorless liquid. Optical rotation  $[\alpha]_D^{22} = +10.66$  (*c* 2.25,  $CHCl_3$ ); IR (neat):  $\nu_{max}$  2946, 2864, 2359, 1464, 1215, 759 and 671  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 400 MHz):  $\delta$  7.39 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 5.43 (s, 1H), 4.28 (m, 1H), 4.00 (dd, *J* = 4.0, 6.9 Hz, 1H) 3.91-3.82 (m, 2H), 3.79 (s, 3H), 3.58 (dd, *J* = 4.0, 9.4 Hz, 1H), 3.50-3.44 (m, 2H), 1.94-1.76 (m, 2H), 1.74-1.64 (m, 2H), 1.61-1.54 (m, 1H), 1.53-1.43 (m, 2H), 1.36-1.31 (m, 2H), 1.20 (m, 1H), 1.08-1.01 (m, 42H), 0.99 (t, *J* = 7.9 Hz, 3H), 0.86 (s, 9H), 0.81 (d, *J* = 6.5 Hz, 3H) and 0.02 (s, 6H);  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz):  $\delta$  159.6, 131.8, 127.3, 113.4, 101.7, 84.9, 71.4, 70.3, 69.4, 68.3, 55.2, 43.8, 37.1, 34.5, 34.1, 27.8, 25.9, 18.3, 18.2, 18.0, 17.7, 16.3, 14.1, 12.8, 12.7, 12.3, 12.0 and -5.5; HRMS (ESIMS): calcd for  $C_{45}H_{88}O_6NaSi_3$   $[M + Na]^+$ : 831.5786, found: 831.5756.

**(2R,3R,4R,7R,9S)-10-[1-(tert-Butyl)-1,1-dimethylsilyl]oxy-2-ethyl-3-[(4-methoxybenzyl)oxy]-4-methyl-7,9-di[(1,1,1-triisopropylsilyl)oxy]-decan-1-ol (30):**

To a solution of compound **10** (460 mg, 0.57 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (4 mL) at -40°C, DIBAL-H (1.4 M solution in toluene, 1.6 mL, 2.28 mmol) was added portion wise with stirring under nitrogen atmosphere. After stirring for 0.5 h at the same temperature, the reaction mixture was slowly brought to 0 °C and stirred for 2 h and then quenched with dry MeOH (3 mL) at -78 °C, stirred for 0.5 h at the same temperature, then added potassium sodium tartarate, stirred at room temperature for 1 h and extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with brine (20 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification of the residue by column chromatography (SiO<sub>2</sub>, 7% EtOAc in petroleum ether) provided compound **30** (422 mg, 92%) as colorless oil. Optical rotation  $[\alpha]_D^{27} = -0.33$  (*c* 1.82, CHCl<sub>3</sub>); IR (neat):  $\nu_{\text{max}}$  2927(br), 2866, 1215, 759, and 670 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  7.28-7.19 (m, 2H), 6.86-6.79 (m, 2H), 4.47 (ABq, *J* = 10.7 Hz, 2H), 4.01 (brm, 1H), 3.81 (m, 1H), 3.76 (s, 3H), 3.64 (d, *J* = 4.5 Hz, 2H), 3.57 (dd, *J* = 4.0, 9.4 Hz, 1H), 3.47 (m, 1H), 3.35 (m, 1H), 1.87-1.53 (m, 7H), 1.52-1.37 (m, 2H), 1.29 (m, 1H), 1.10-0.99 (m, 45H), 0.93-0.82 (m, 12H) and 0.01 (s, 6H); HRMS (ESIMS): calcd for C<sub>45</sub>H<sub>90</sub>O<sub>6</sub>NaSi<sub>3</sub> [M + Na]<sup>+</sup>: 833.5942, found: 833.5925.

**tert-Butyl((2S,4R,7R,8R,9R)-9-ethyl-8-[(4-methoxybenzyl)oxy]-7-methyl-2,4-di[(1,1,1-triisopropylsilyl)oxy]-10-undecenyl)dimethylsilane (31):**

To a stirred solution of **30** (422 mg, 0.52 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL), NaHCO<sub>3</sub> (148 mg, 1.04 mmol) was added at 0 °C, followed by Dess-Martin periodinane (DMP) (332 mg, 0.78 mmol) under nitrogen atmosphere. The reaction mixture was allowed to come to room temperature and stirred for 30 min. Saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (10 mL) and NaHCO<sub>3</sub> (2 mL) were added, and the biphasic mixture was stirred for 15 min and extracted with

hexane. The organic phase was washed with water (20 mL), brine (20 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. The aldehyde ( $R_f = 0.5$ , 3% EtOAc in petroleum ether), thus obtained, was directly used, after flash chromatography, for the next reaction without any further characterization.

Sodamide (244 mg, 6.26 mmol) was added to a suspension of methyltriphenylphosphonium iodide (844 mg, 2.08 mmol) in dry ether (10 mL) at 0 °C. The mixture was allowed to come to room temperature and stirred for 6 h. The methylenetriphenylphosphorane, thus obtained, was added to a solution of aldehyde in ether (4 mL) at 0 °C. After 10 min, the reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution. Crude reaction mixture was extracted with ether (50 mL), washed with water (20 mL), brine (15 mL) dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $\text{SiO}_2$ , 2 to 4% EtOAc in petroleum ether eluant) gave pure compound **31** (402 mg, 96%) as clear oil. Optical rotation  $[\alpha]_D^{23} = +0.7$  (*c* 2.0,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  2944, 2865, 2362, 2339, 1651, 1513, 1462, 1379 and 1249  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.21 (d,  $J = 8.6$  Hz, 2H), 6.80 (d,  $J = 8.6$  Hz, 2H), 5.54 (m, 1H), 5.00-4.91 (m, 2H), 4.43 (ABq,  $J = 10.1, 10.9$  Hz, 2H), 3.94 (m, 1H), 3.80 (m, 1H), 3.75 (s, 3H), 3.53 (dd,  $J = 5.4, 9.3$  Hz, 2H), 3.44 (dd,  $J = 5.4, 10.1$  Hz, 1H), 3.02 (m, 1H), 2.12 (m, 1H), 1.79-1.70 (m, 3H), 1.67-1.52 (m, 3H), 1.36 (m, 1H), 1.17 (m, 1H), 1.06-0.97 (m, 42H), 0.90 (d,  $J = 7.0$  Hz, 3H), 0.83 (m, 12H), 0.77 (t,  $J = 7.9$  Hz, 3H) and 0.02 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  140.6, 131.4, 128.9, 115.6, 113.6, 87.5, 74.3, 71.4, 70.3, 68.3, 55.2, 49.3, 43.7, 36.6, 35.8, 26.4, 25.9, 22.5, 18.3, 18.2, 16.9, 12.8, 12.7, 11.8 and -5.4; HRMS (ESIMS): calcd for  $\text{C}_{46}\text{H}_{90}\text{O}_5\text{NaSi}_3$   $[\text{M} + \text{Na}]^+$ : 829.5993, found: 829.5963.

**(3*R*,4*R*,5*R*,8*R*,10*S*)-11-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-3-ethyl-5-methyl-8,10-di[(1,1,1-triisopropylsilyl)oxy]-1-undecen-4-ol (32):**

To a stirred solution of **31** (400 mg, 0.49 mmol) in CHCl<sub>3</sub>:pH 7 Phosphate Buffer (20:1, 5 mL), DDQ (225 mg, 0.993 mmol) was added at 0 °C. The reaction mixture was then allowed to come to room temperature and stirred for 30 min. The reaction mixture was quenched with saturated NaHCO<sub>3</sub> (10 mL) and extracted with ether (60 mL), washed with water (30 mL), brine (30 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in *vacuo*. Purification by column chromatography (SiO<sub>2</sub>, 7 to 9% EtOAc in petroleum ether eluant) gave pure compound **32** (310 mg, 91%) as clear oil. Optical rotation [α]<sub>D</sub><sup>27</sup> = +6.37 (c 2.12, CHCl<sub>3</sub>); IR (neat): ν<sub>max</sub> 3020 (br), 2867, 1731, 1249, 1217, 1046, 759, and 671 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 5.57 (m, 1H), 5.11-4.98 (m, 2H), 4.01 (m, 1H), 3.84 (m, 1H), 3.59 (dd, *J* = 4.7, 10.1 Hz, 1H), 3.49 (dd, *J* = 6.2, 10.1 Hz, 1H), 3.26 (m, 1H), 2.07 (m, 1H), 1.86-1.76 (m, 2H), 1.74-1.66 (m, 3H), 1.64-1.55 (m, 3H), 1.40 (m, 1H), 1.09-1.03 (m, 42H), 0.91 (d, *J* = 6.2 Hz, 3H), 0.88 (s, 9H), 0.84 (t, *J* = 7.8 Hz, 3H) and 0.04 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 139.8, 116.1, 79.1, 71.4, 70.1, 68.3, 49.5, 43.6, 36.1, 35.2, 25.9, 24.5, 22.0, 18.3, 18.2, 18.0, 16.9, 12.8, 12.7, 11.7 and -5.5; HRMS (ESIMS): calcd for C<sub>38</sub>H<sub>82</sub>O<sub>4</sub>NaSi<sub>3</sub> [M + Na]<sup>+</sup>: 709.5412, found: 709.5405.

**(3*R*,4*R*,5*R*,8*R*,10*S*)-11-(*tert*-Butyl-dimethyl-silyloxy)-3-ethyl-5-methyl-8,10-di-triisopropylsilanyloxy-undec-1-en-4-ol acrylate (9):**

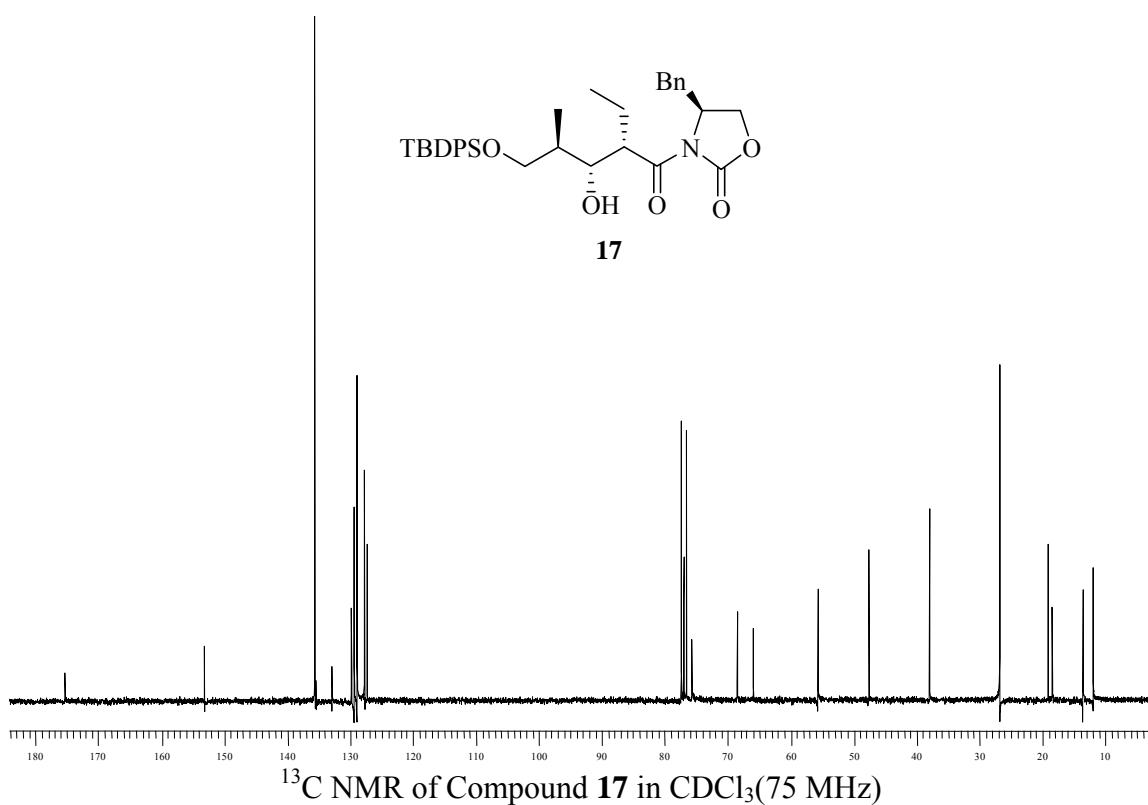
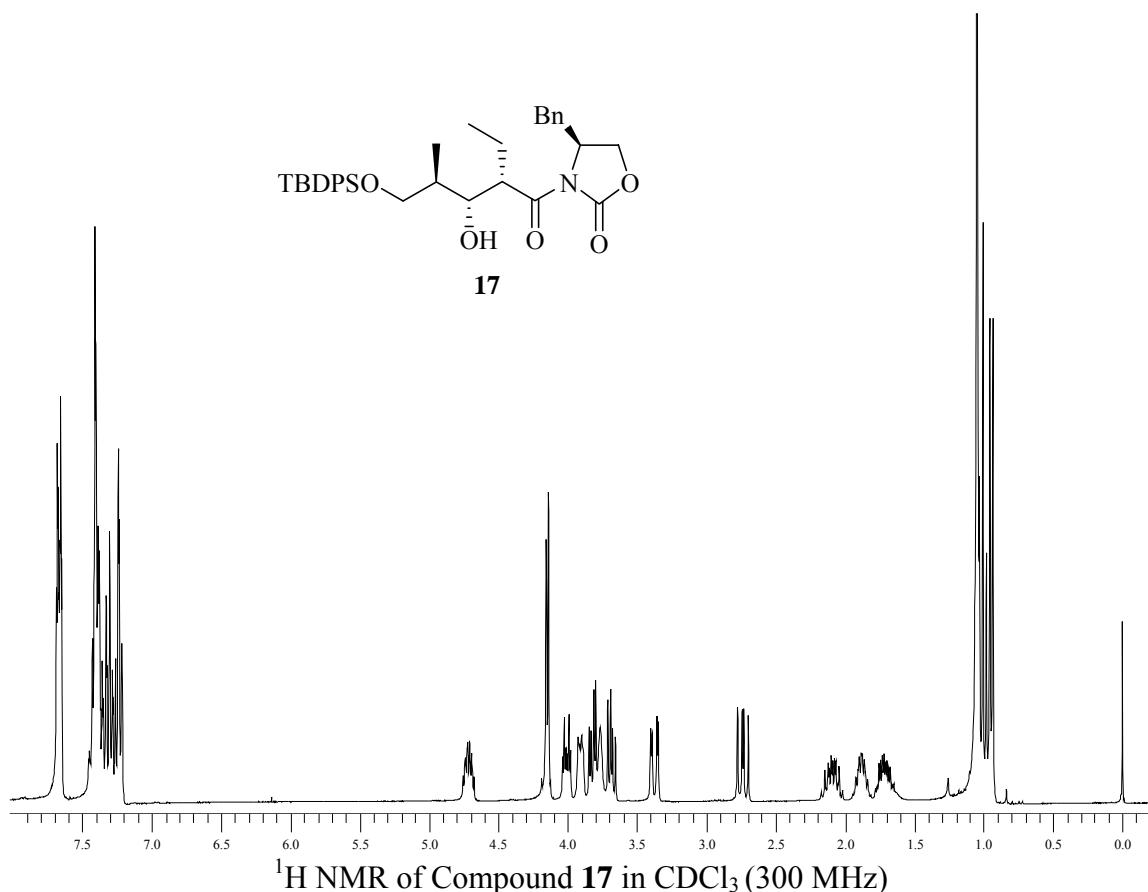
To a stirred solution of **32** (250 mg, 0.36 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL), Et<sub>3</sub>N (0.25 mL, 1.82 mmol) and acryloyl chloride (0.06 mL, 0.73 mmol) were added sequentially at 0 °C under nitrogen atmosphere. The reaction mixture was warmed to room temperature and stirred for 0.5 h. It was quenched with water and extracted with EtOAc, washed with

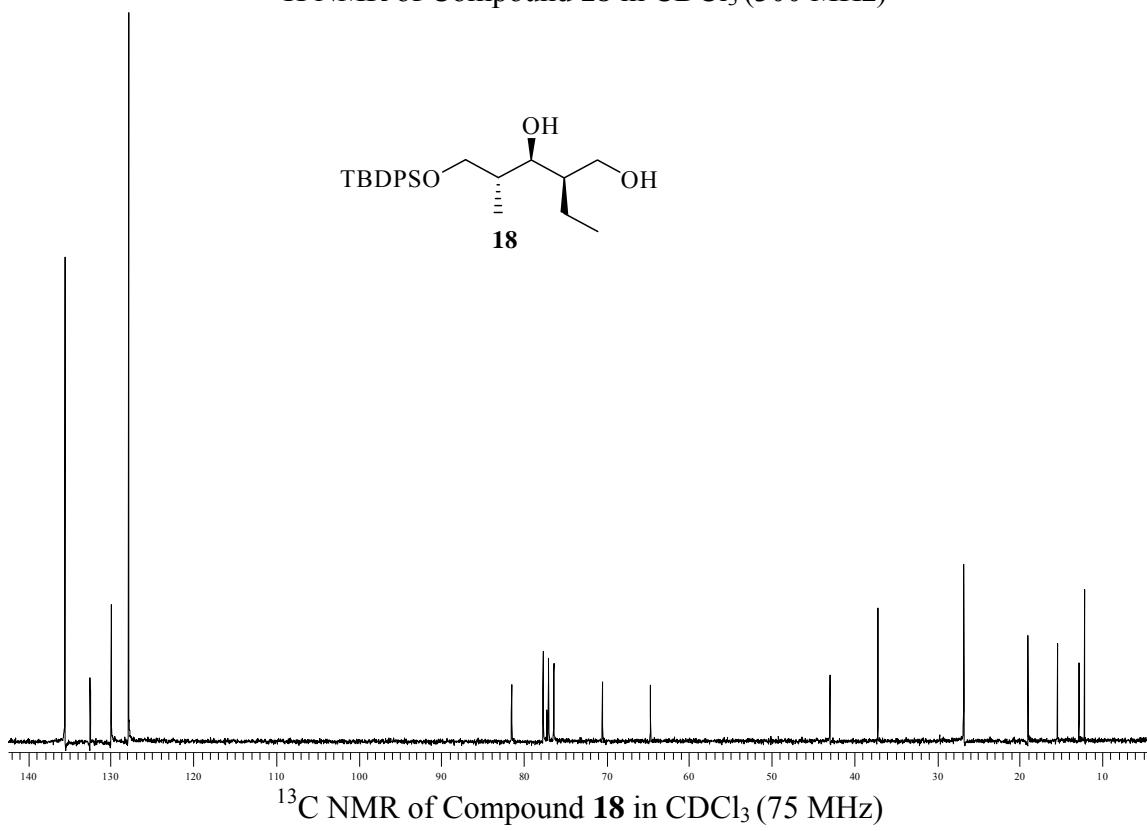
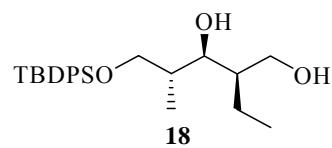
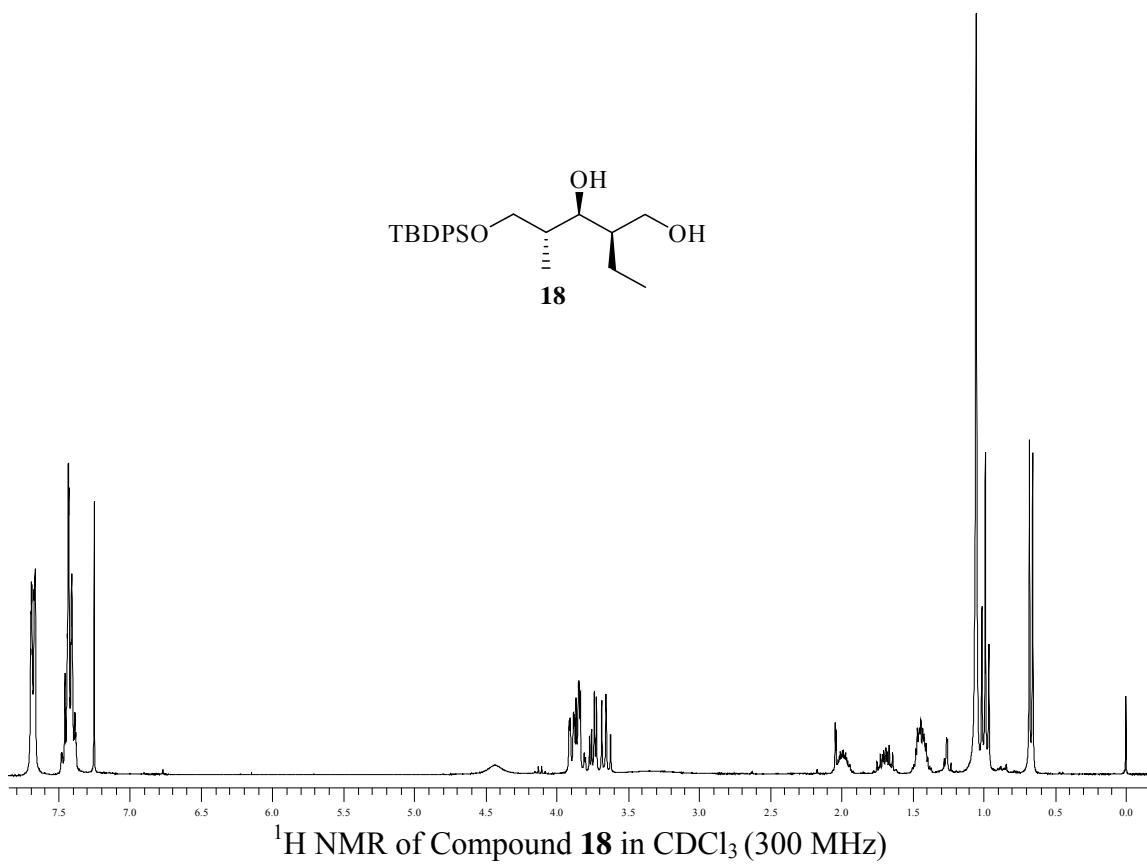
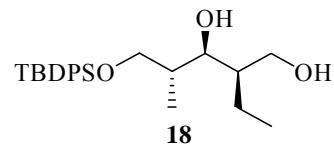
saturated aqueous  $\text{NaHCO}_3$  solution (5 mL), brine (5 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $\text{SiO}_2$ , 2 to 3% EtOAc in petroleum ether eluant) gave pure compound **9** (172 mg, 65%) as clear oil. Optical rotation  $[\alpha]_D^{24} = +0.99$  ( $c$  4.45,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  2924, 2864, 1721, 1216, 759 and 671  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  6.37 (dd,  $J$  = 1.5, 17.2 Hz, 1H), 6.10 (dd,  $J$  = 10.3, 17.2 Hz, 1H), 5.81 (dd,  $J$  = 1.5, 10.3 Hz), 5.47 (m, 1H), 5.40 (dd,  $J$  = 3.7, 10.1 Hz, 1H), 5.02 (dd,  $J$  = 1.6, 11.2 Hz), 4.88 (dd,  $J$  = 3.1, 8.7 Hz, 1H), 4.01 (m, 1H), 3.81 (m, 1H), 3.60 (dd,  $J$  = 4.4, 9.8 Hz, 1H), 3.48 (dd,  $J$  = 5.8, 9.8 Hz, 1H), 2.25 (m, 1H), 1.86-0.99 (m, 45H), 0.90-0.80 (m, 12H) and 0.03 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  166.2, 138.3, 130.4, 128.7, 117.0, 80.1, 71.4, 70.0, 68.3, 47.9, 43.7, 35.1, 25.9, 24.2, 22.8, 18.3, 18.2, 17.9, 16.9, 12.7, 12.7, 11.4 and -5.5; HRMS (ESIMS): calcd for  $\text{C}_{41}\text{H}_{84}\text{O}_5\text{NaSi}_3$   $[\text{M} + \text{Na}]^+$ : 763.5524, found: 763.5527.

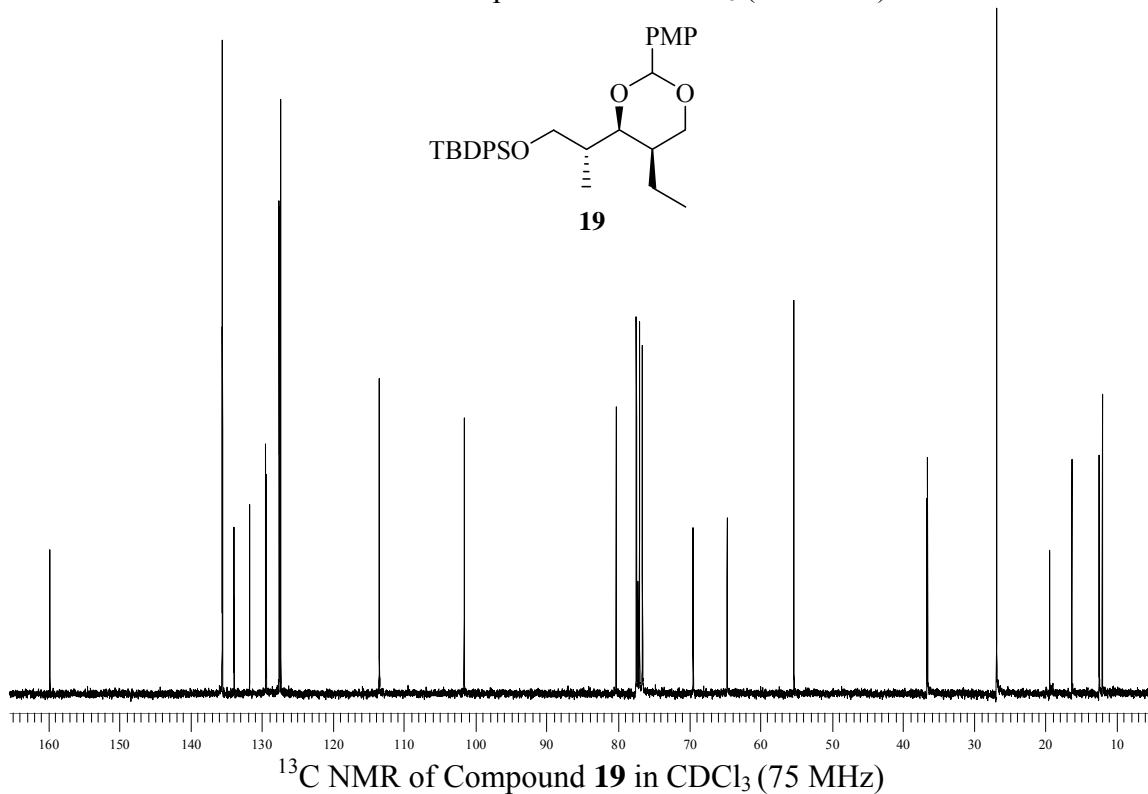
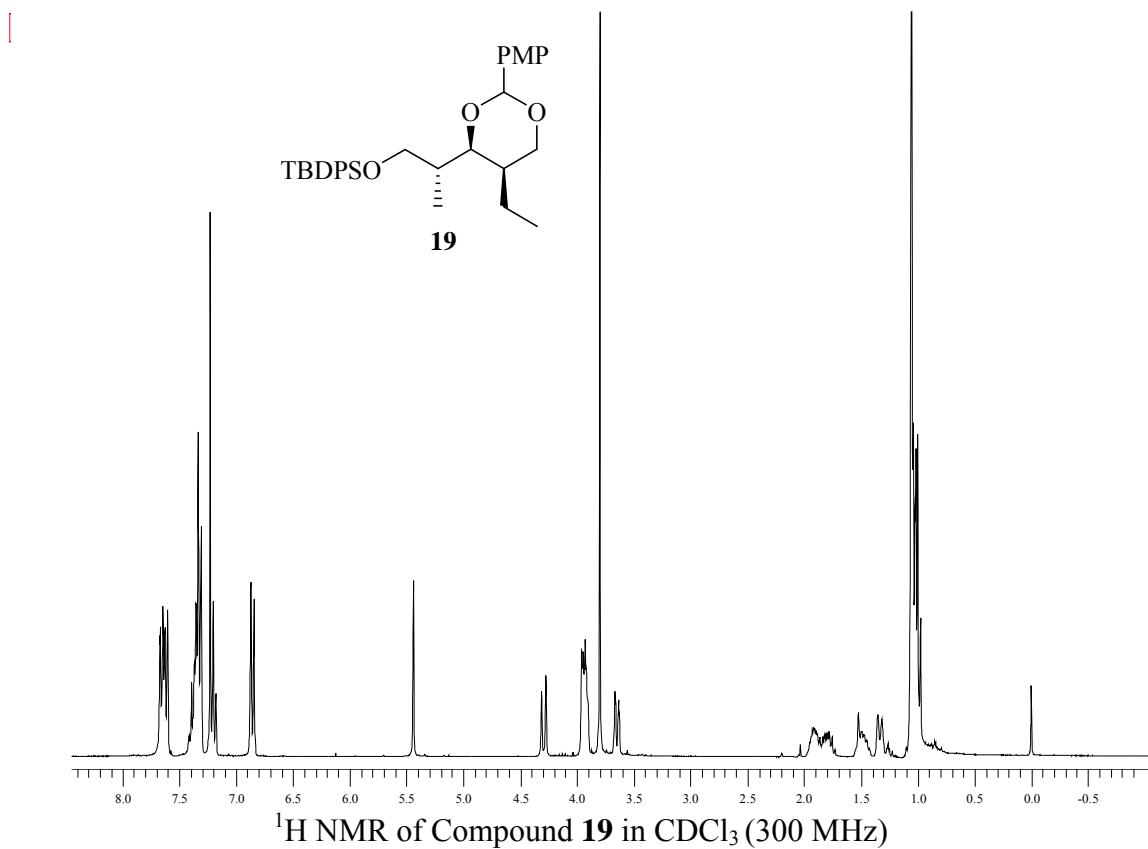
**(5*R*,6*R*)-5-Ethyl-6-((1*R*,4*R*,6*S*)-7-hydroxy-1-methyl-4,6-di-1,1,1-triisopropylsilyloxy-heptyl)-5,6-dihydro-2*H*-2-pyranone (34):**

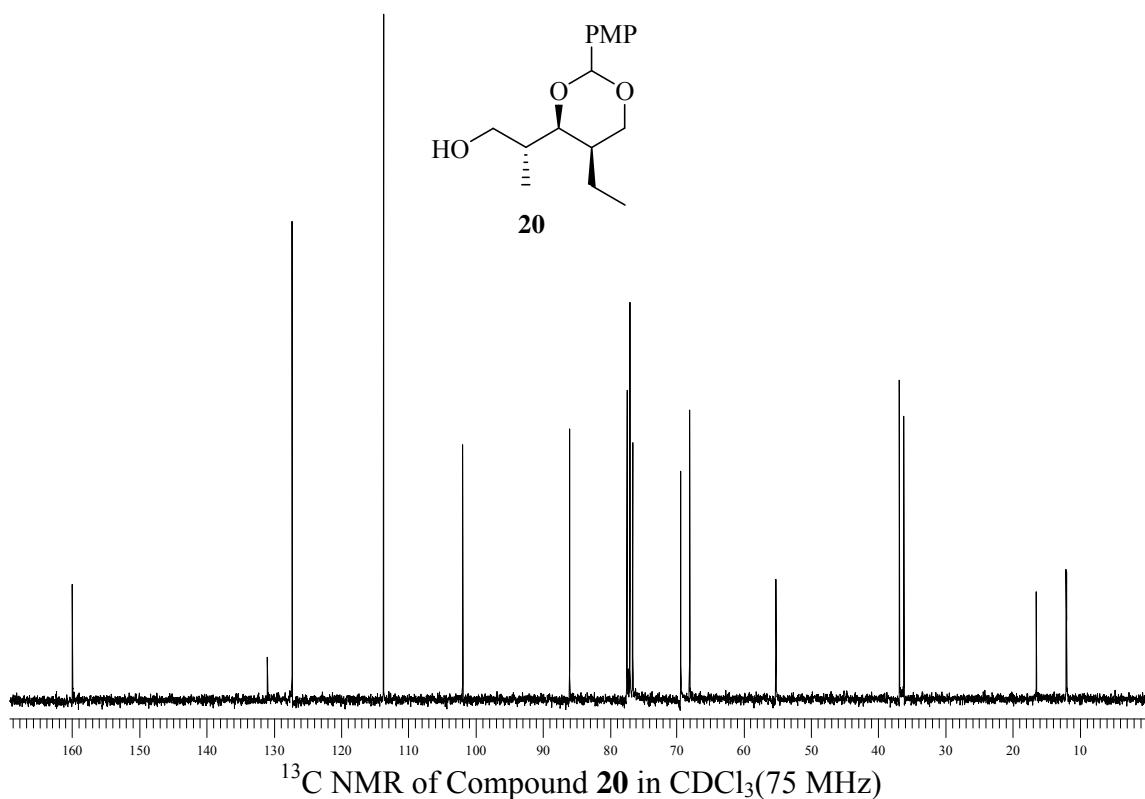
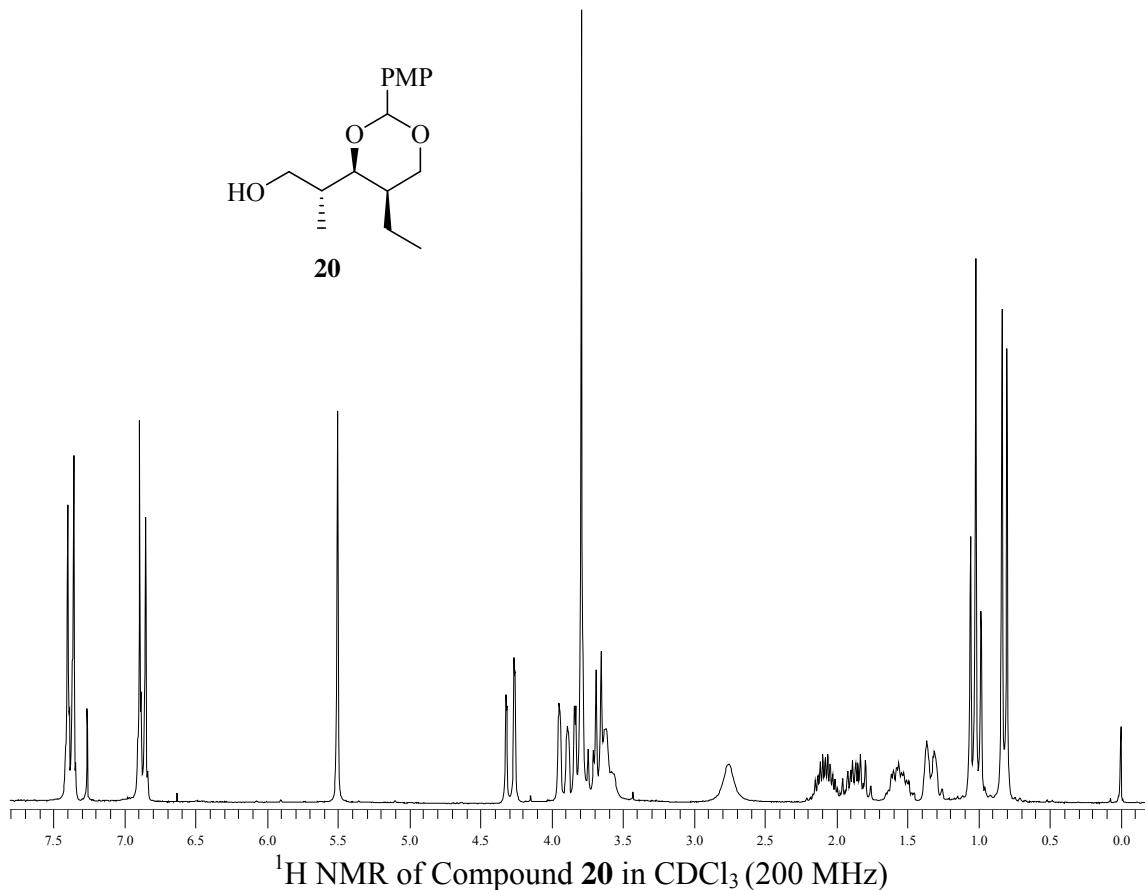
To a stirred solution of compound **33** (35 mg, 0.049 mmol) in dry  $\text{CH}_2\text{Cl}_2$ :MeOH (4:1, 1 mL), CSA (1.1 mg, 0.005 mmol) was added at 0 °C under nitrogen atmosphere and stirred for 24 h at the same temperature. Then, it was quenched with saturated aqueous  $\text{NaHCO}_3$  solution, extracted with EtOAc (15 mL), washed with brine (10 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated in *vacuo*. Purification by column chromatography ( $\text{SiO}_2$ , 20 to 25% EtOAc in petroleum ether eluant) eluted compound **34** (20 mg, 80% based on recovered starting material) as colorless liquid. Optical rotation  $[\alpha]_D^{27} = -52.5$  ( $c$  1.50,  $\text{CHCl}_3$ ); IR (neat):  $\nu_{\text{max}}$  3476, 2911, 1721, 1520 and 925  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.05 (dd,  $J$  = 6.2, 9.4 Hz, 1H), 6.03 (d,  $J$  = 9.4 Hz, 1H), 3.97 (dd,  $J$  = 3.1, 10.9

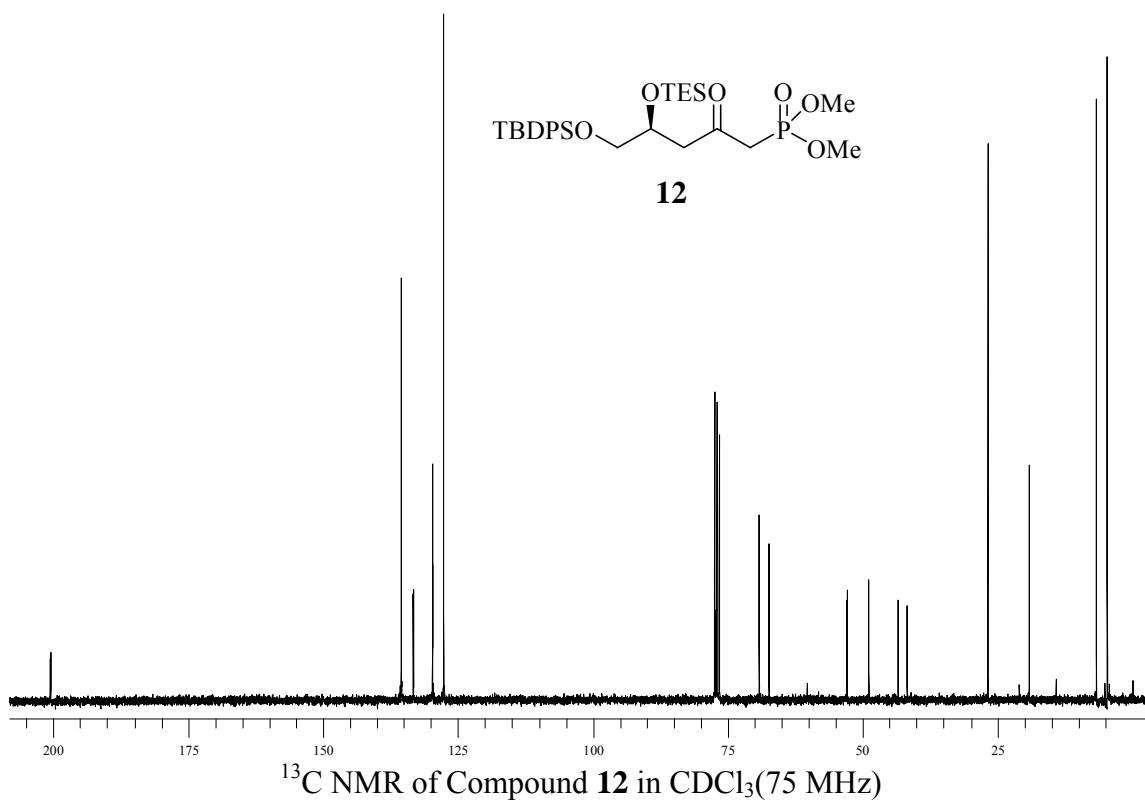
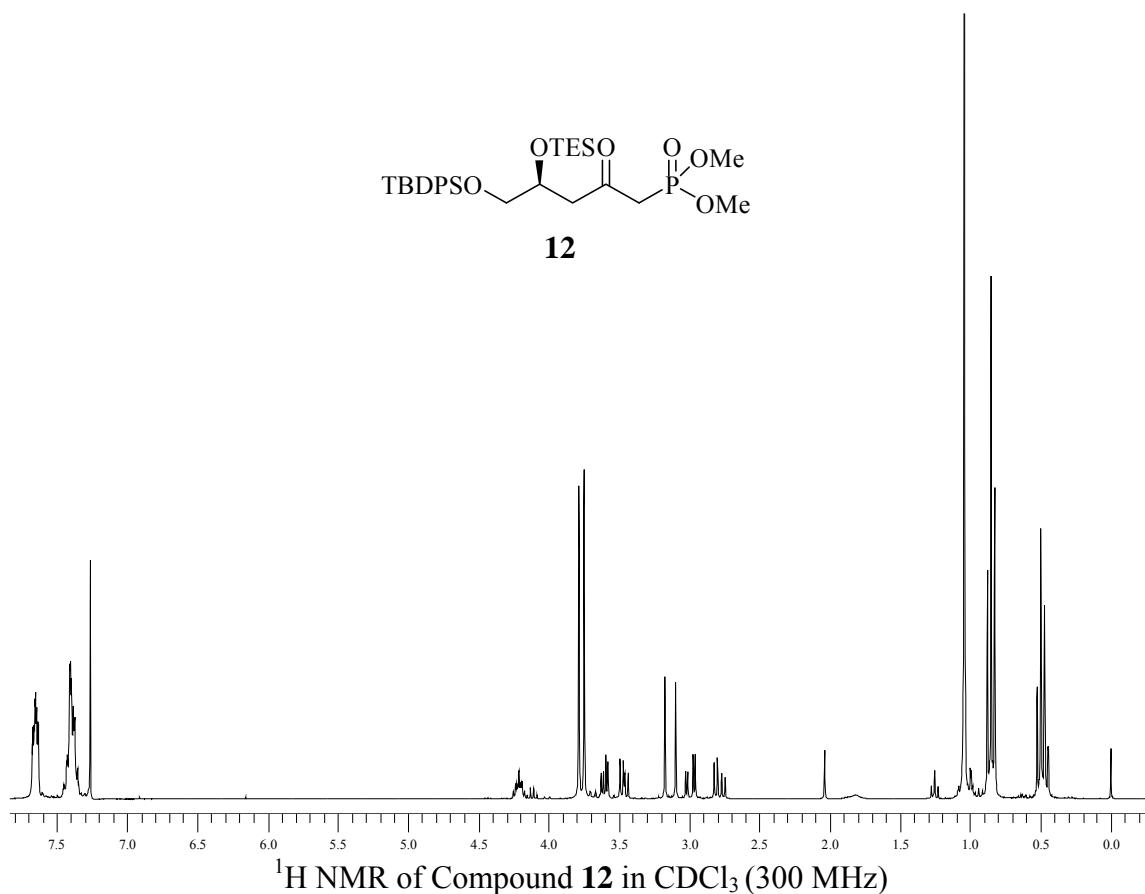
Hz), 3.93 (m, 1H), 3.85 (m, 1H), 3.65 (dd,  $J$  = 3.1, 10.9 Hz), 3.48 (dd,  $J$  = 3.1, 10.1 Hz, 1H), 2.31 (m, 1H), 1.97-1.85 (m, 2H), 1.83-1.75 (m, 2H), 1.72-1.61 (m, 2H), 1.56-1.42 (m, 3H), 1.08-1.03 (m, 42H), 0.95 (t,  $J$  = 7.8 Hz, 3H) and 0.88 (d,  $J$  = 6.2 Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  164.4, 150.9, 121.0, 84.2, 70.9, 70.3, 66.1, 41.8, 36.6, 34.1, 33.7, 27.9, 20.1, 18.2, 18.1, 14.8, 12.8, 12.4 and 11.0; HRMS (ESIMS): calcd for  $\text{C}_{33}\text{H}_{66}\text{O}_5\text{NaSi}_2$   $[\text{M} + \text{Na}]^+$ : 621.4346, found: 621.4346.

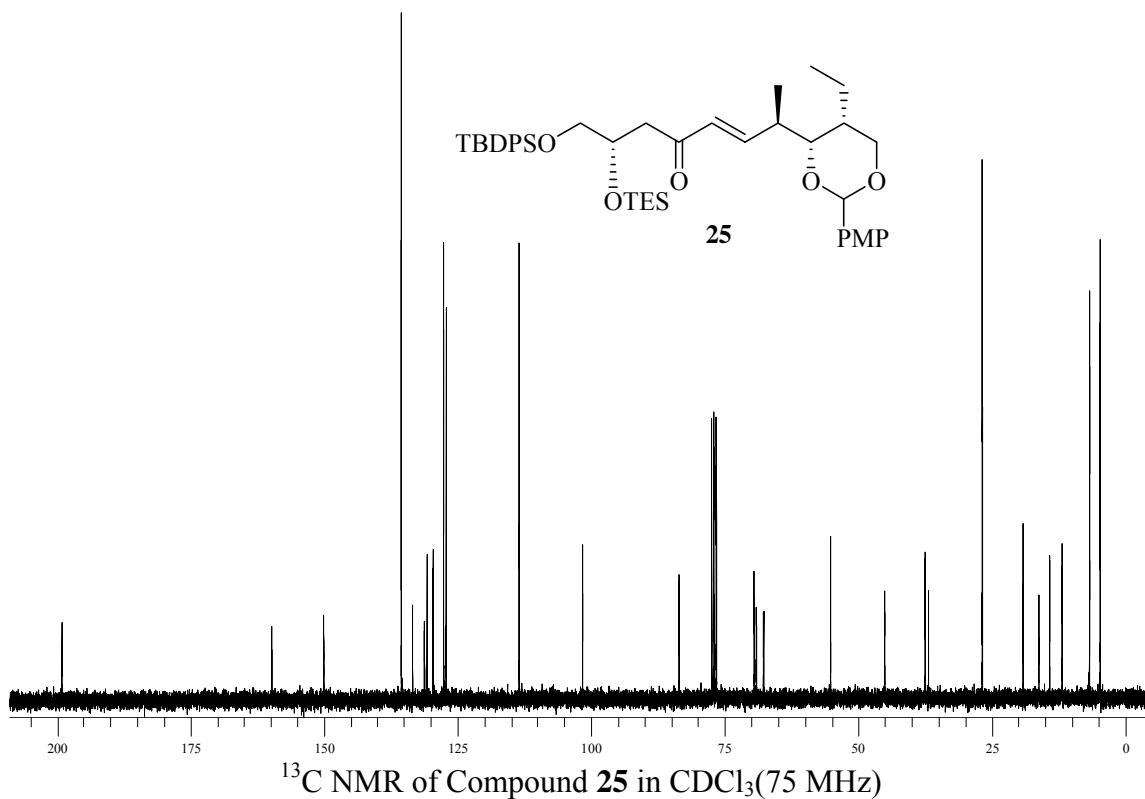
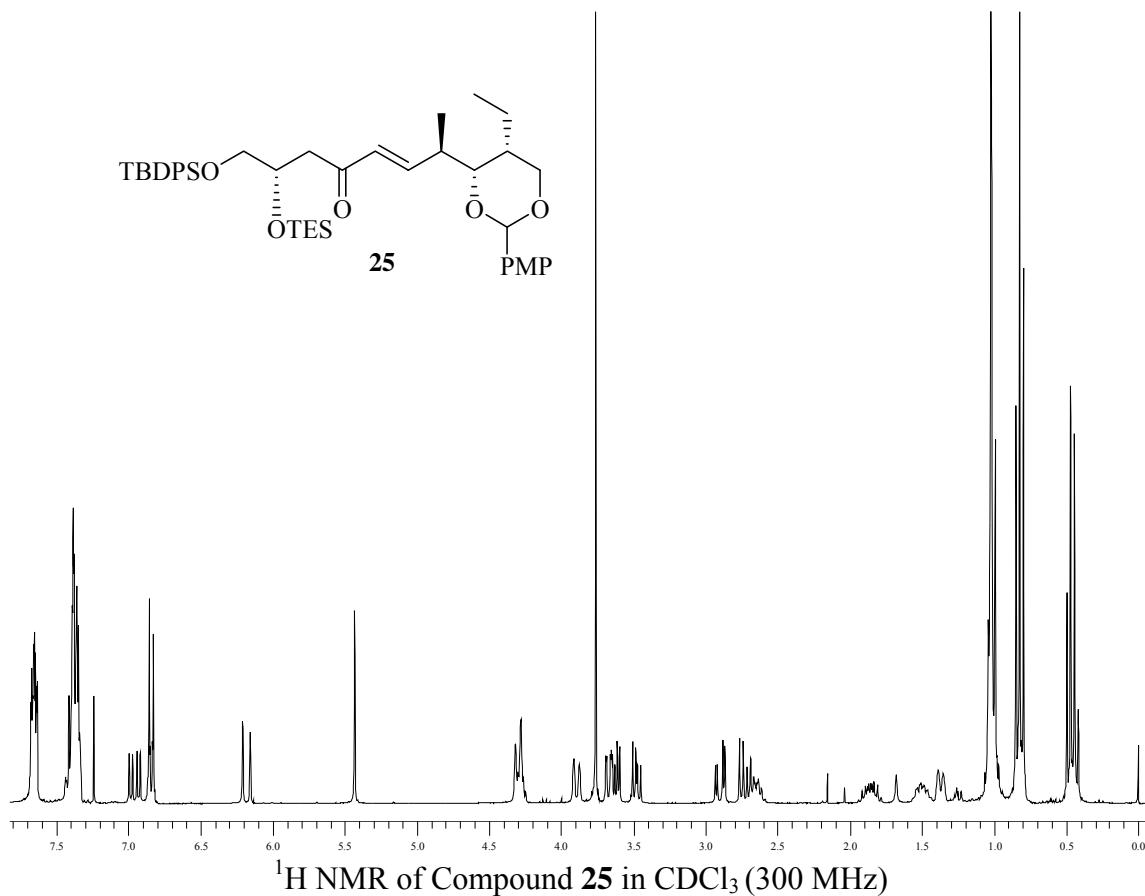


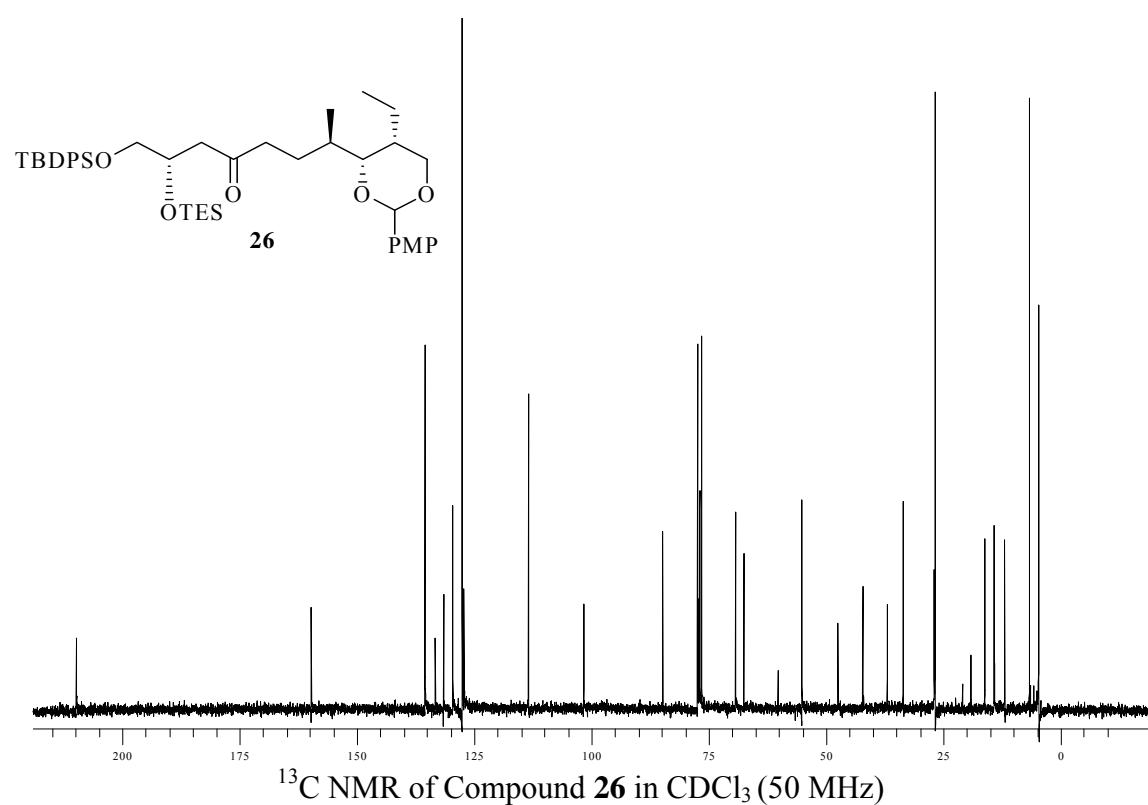
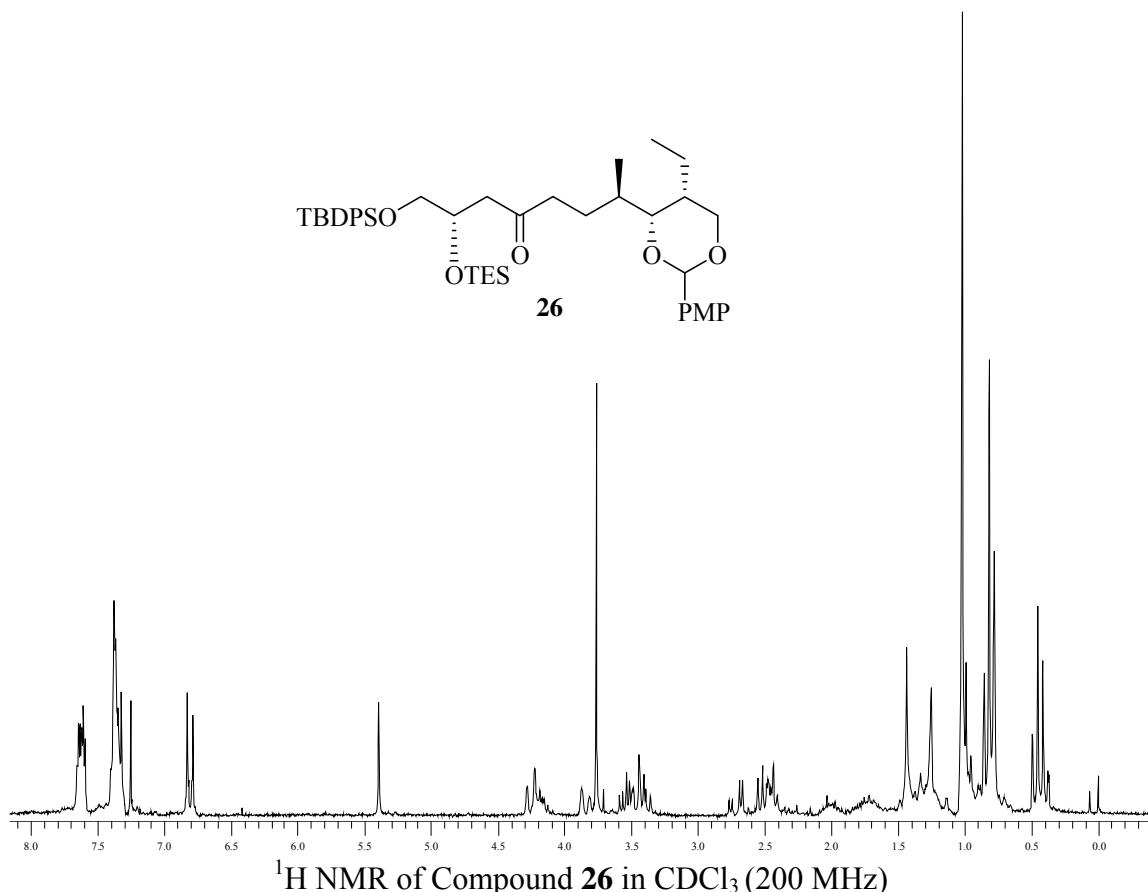


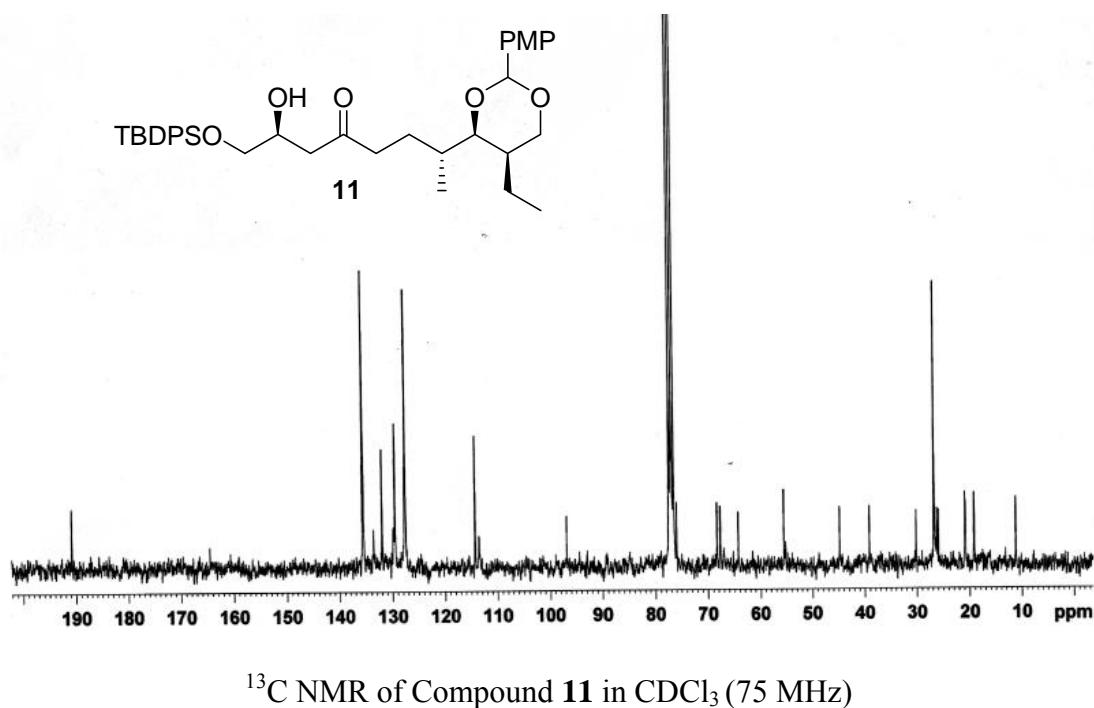
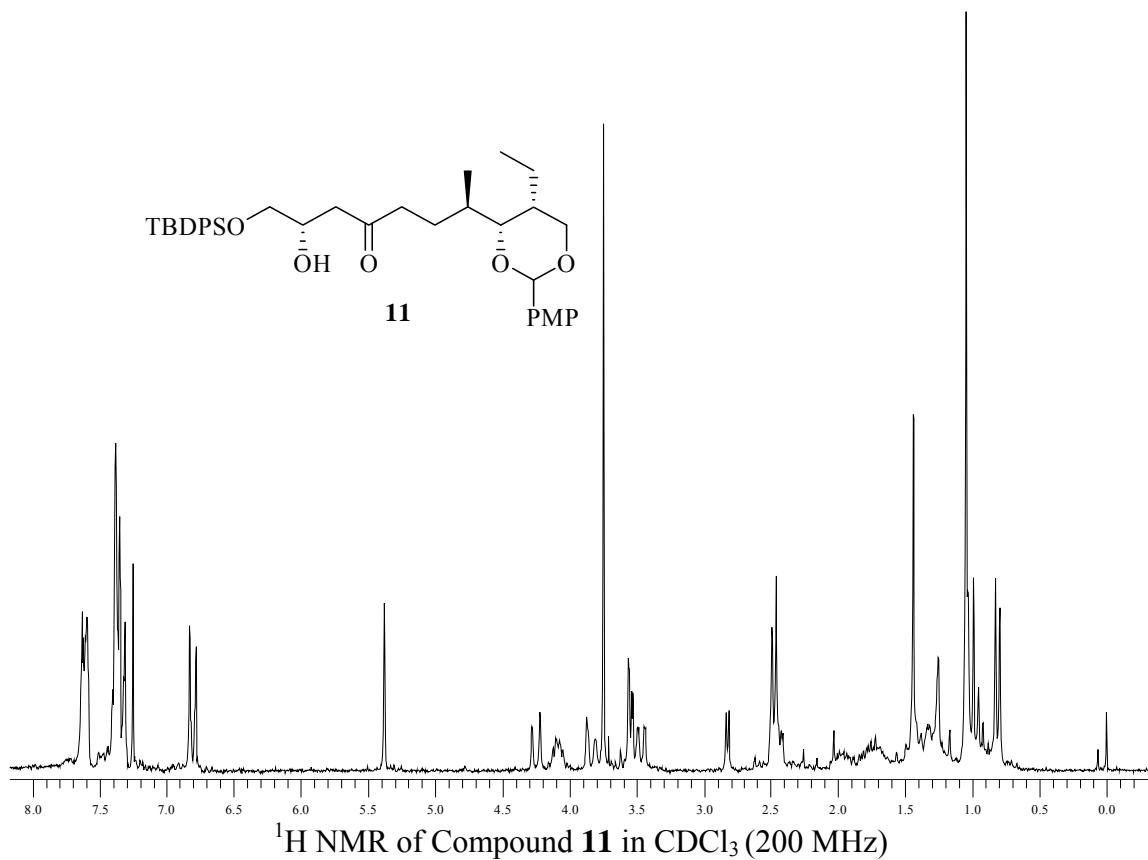


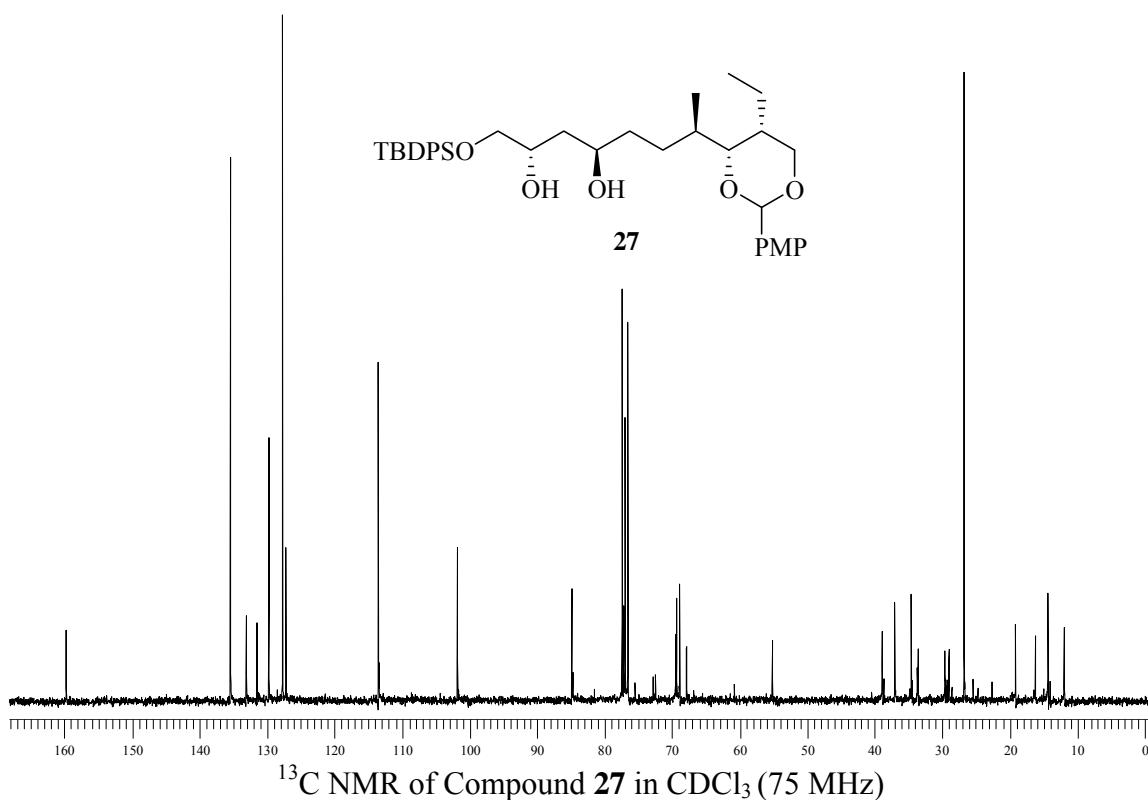
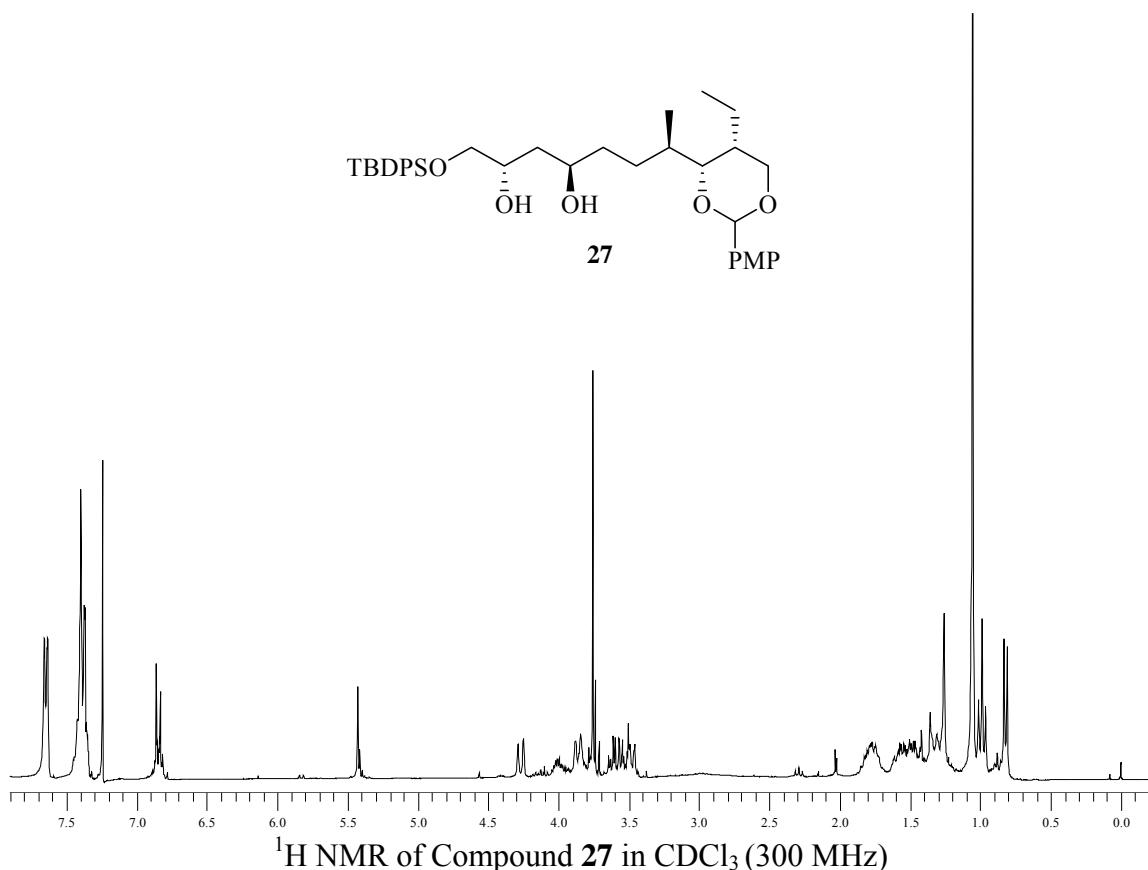


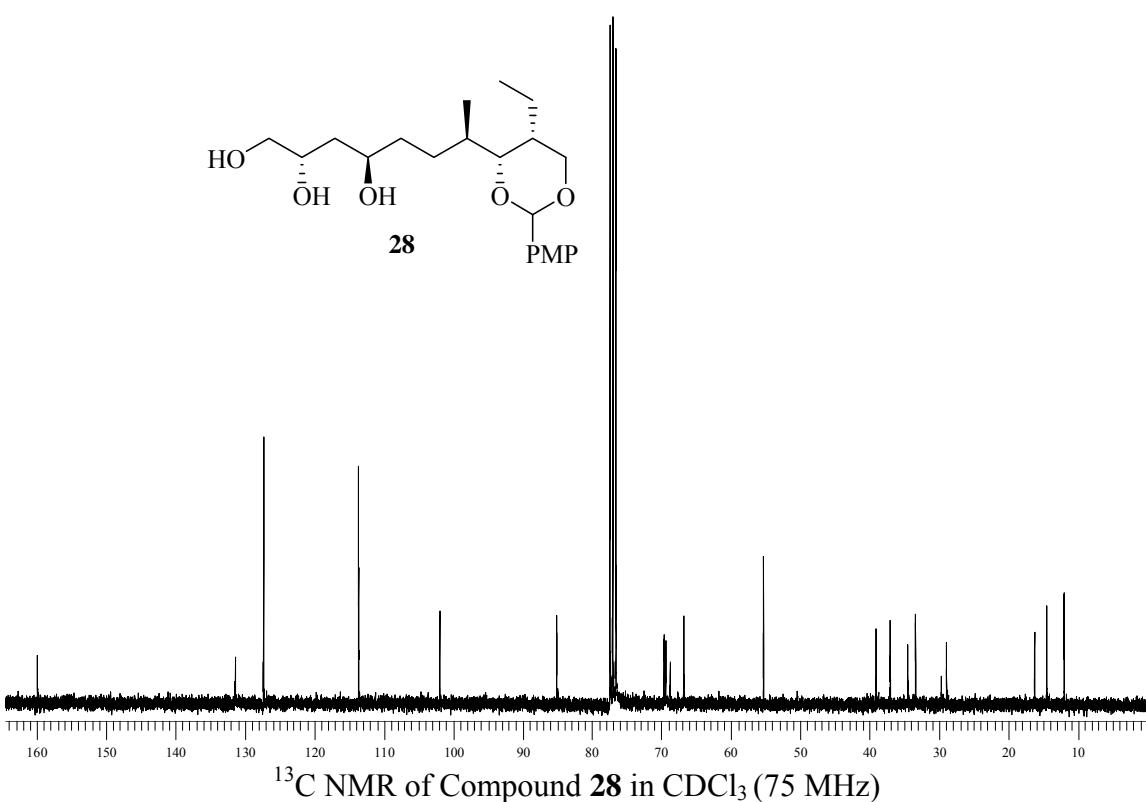
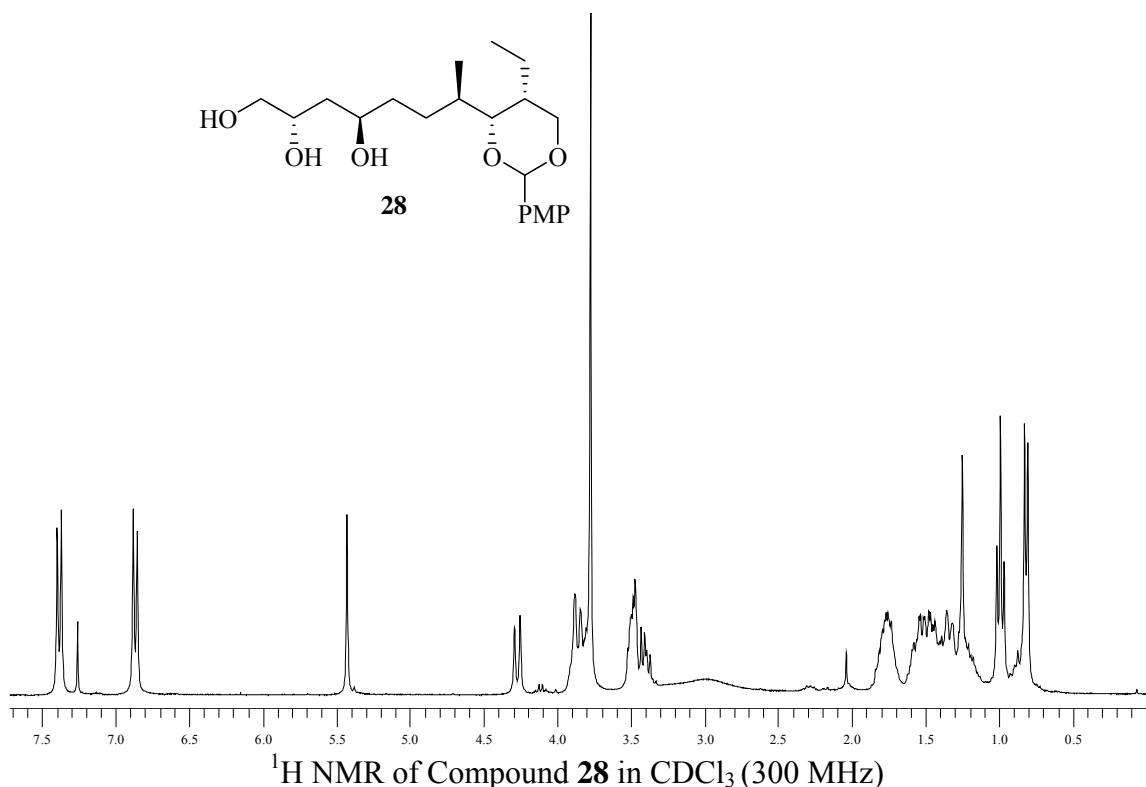


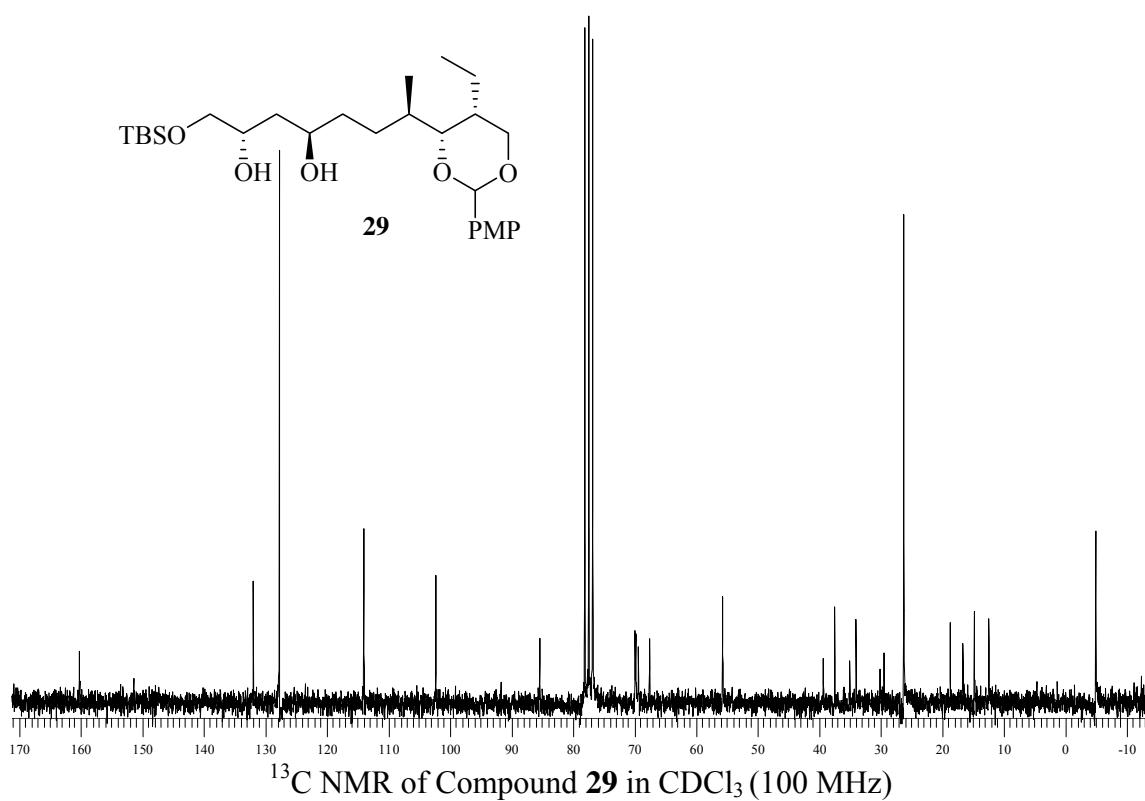
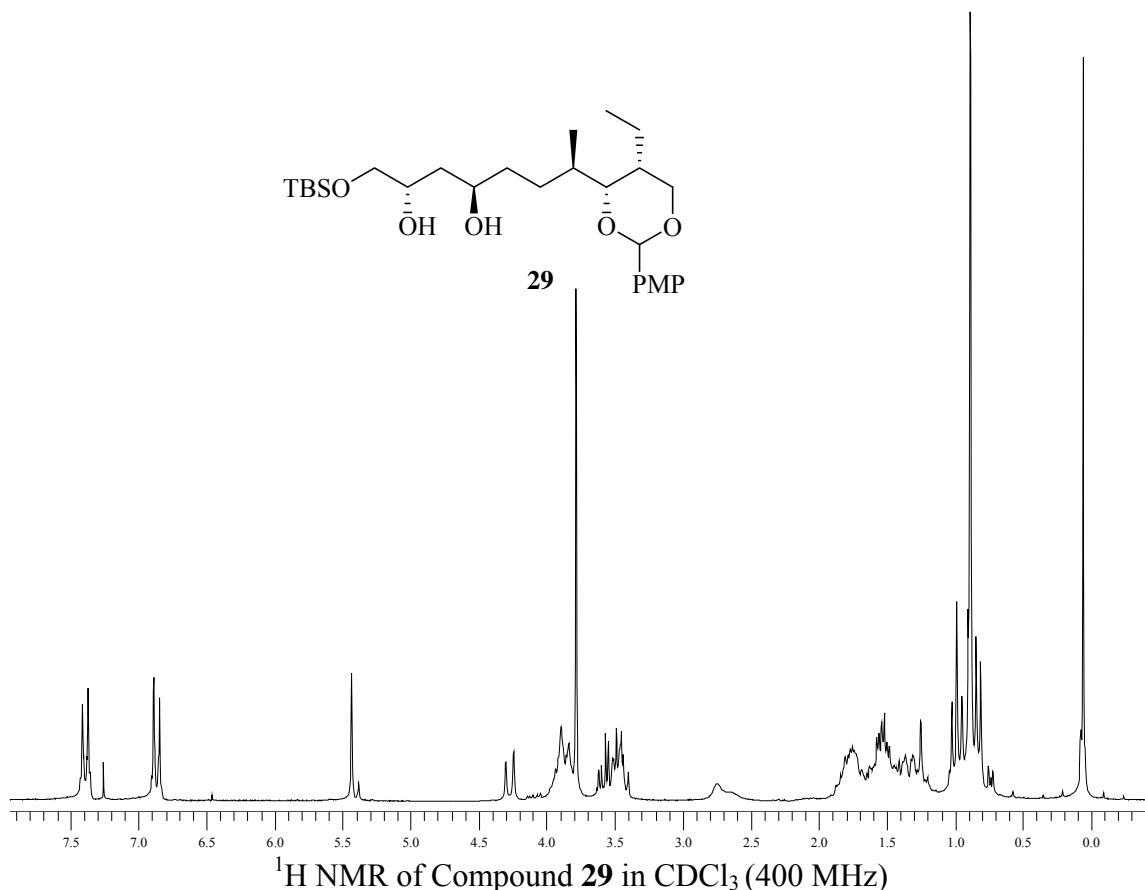


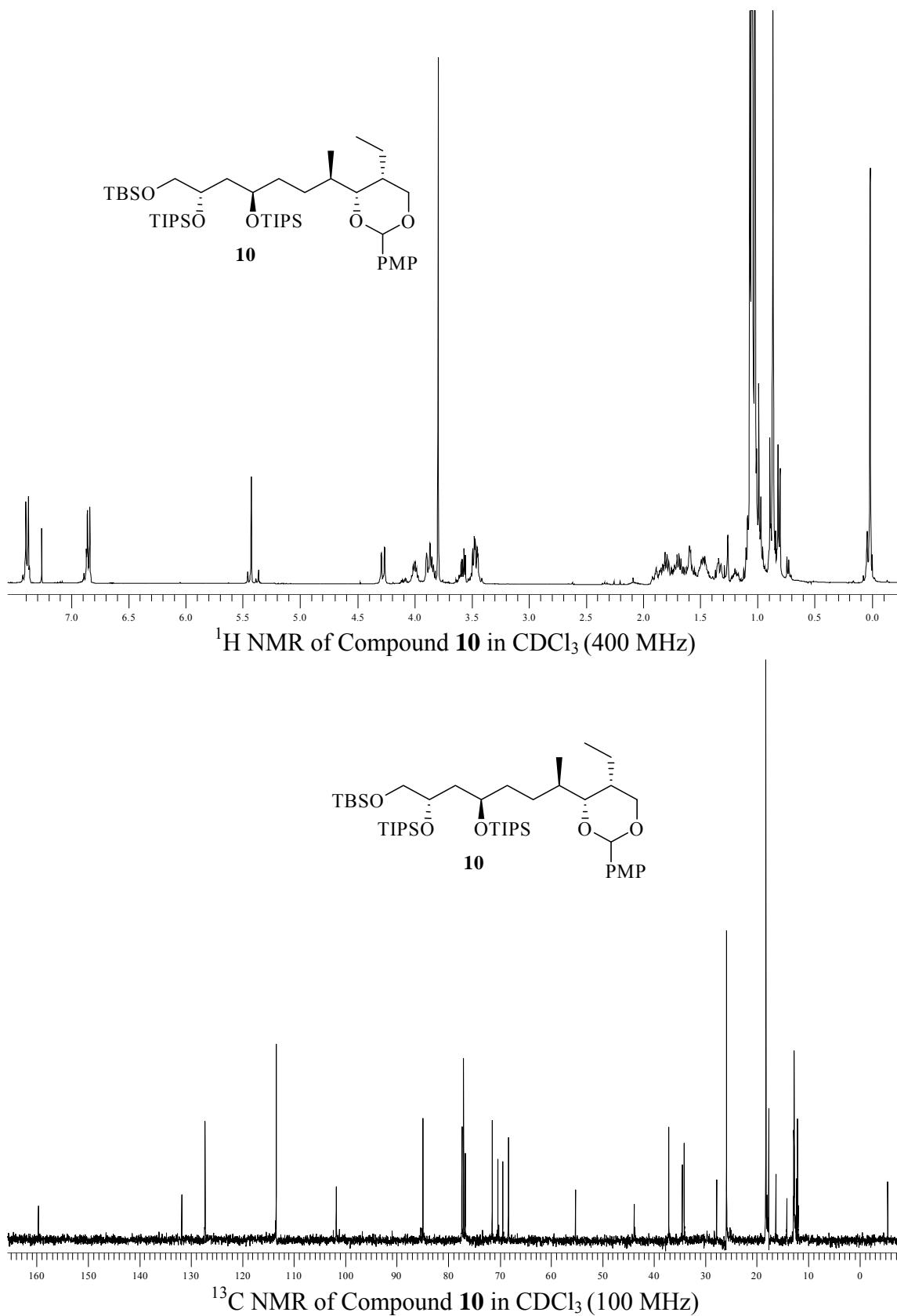


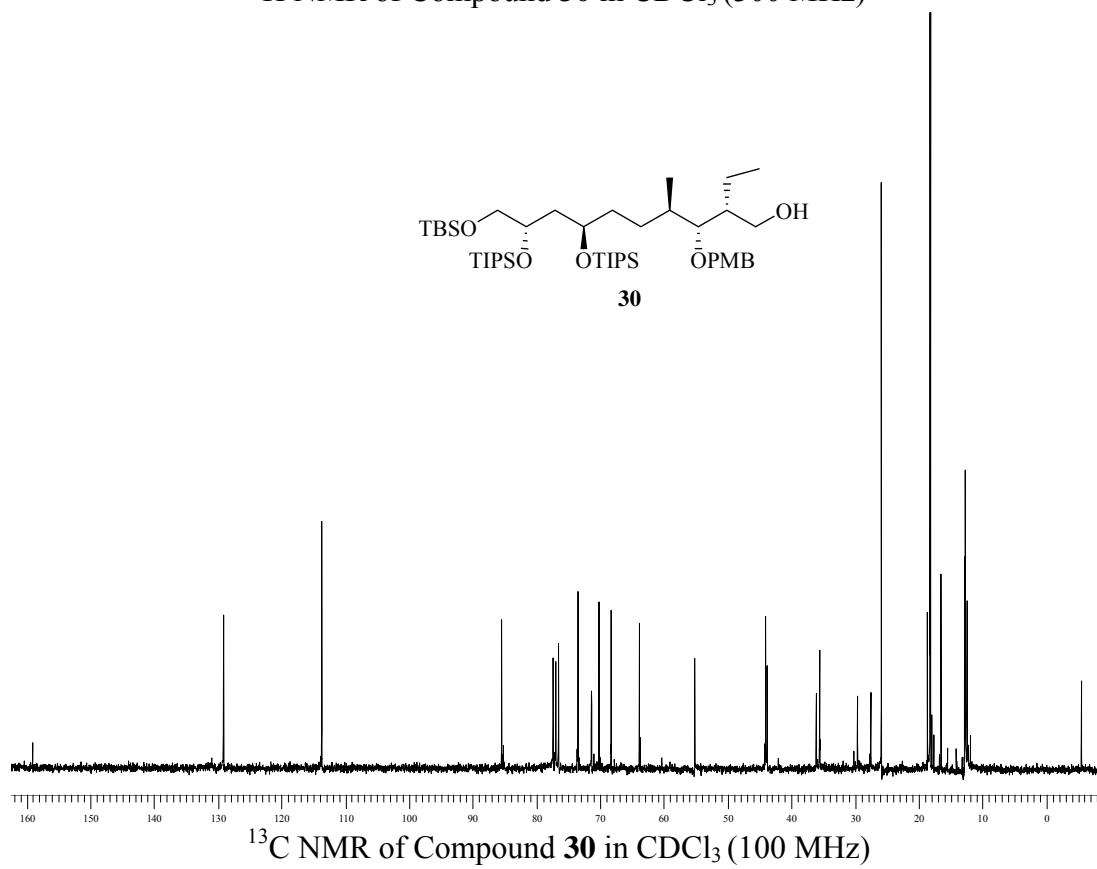
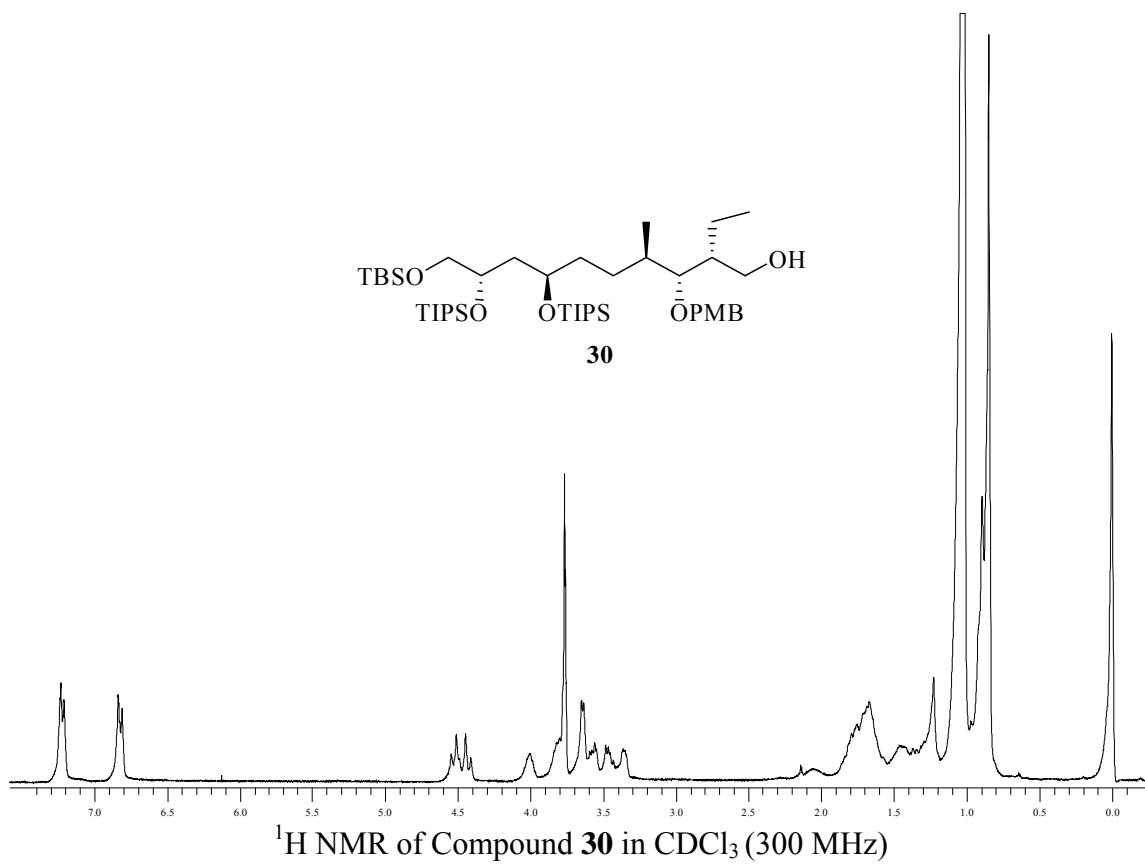


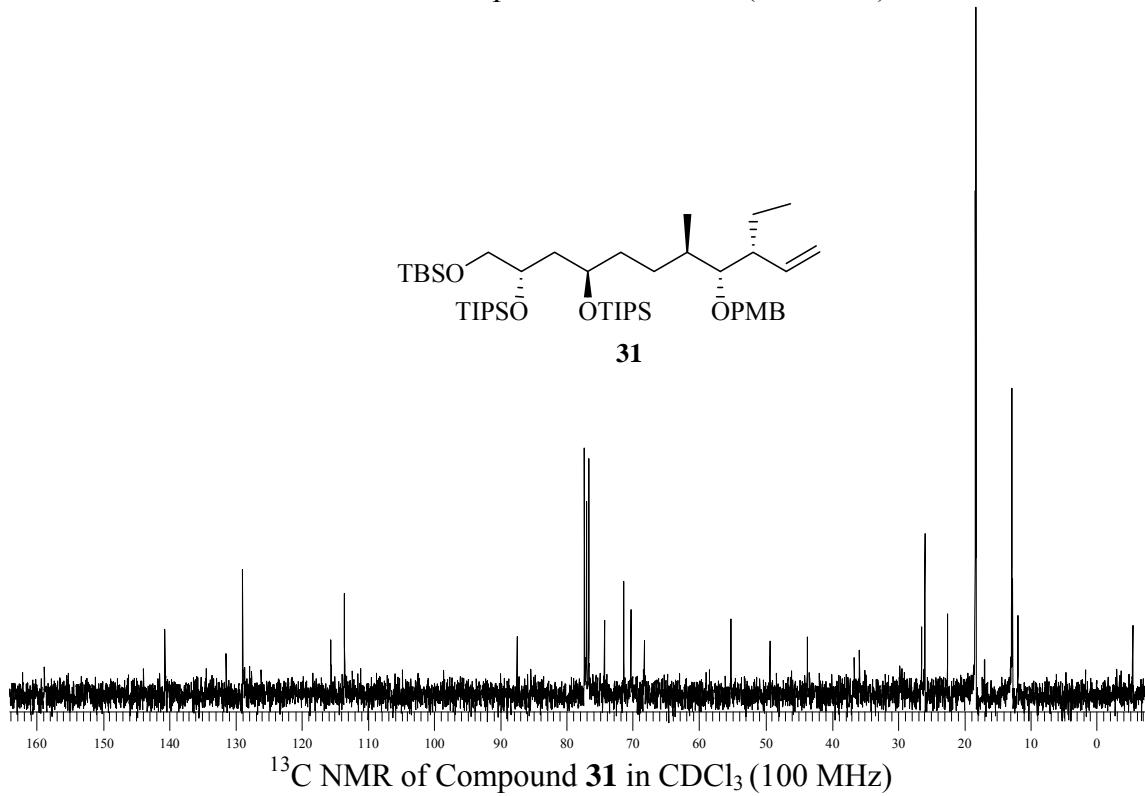
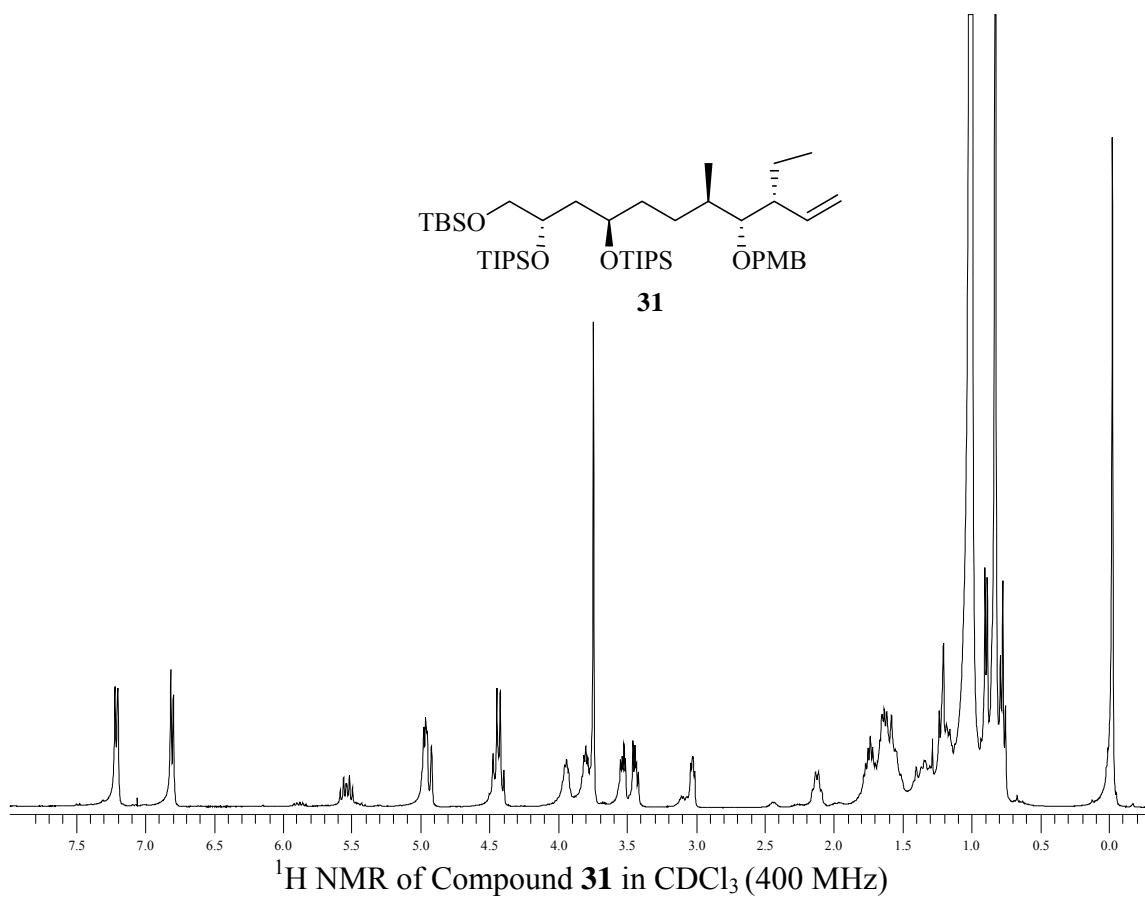


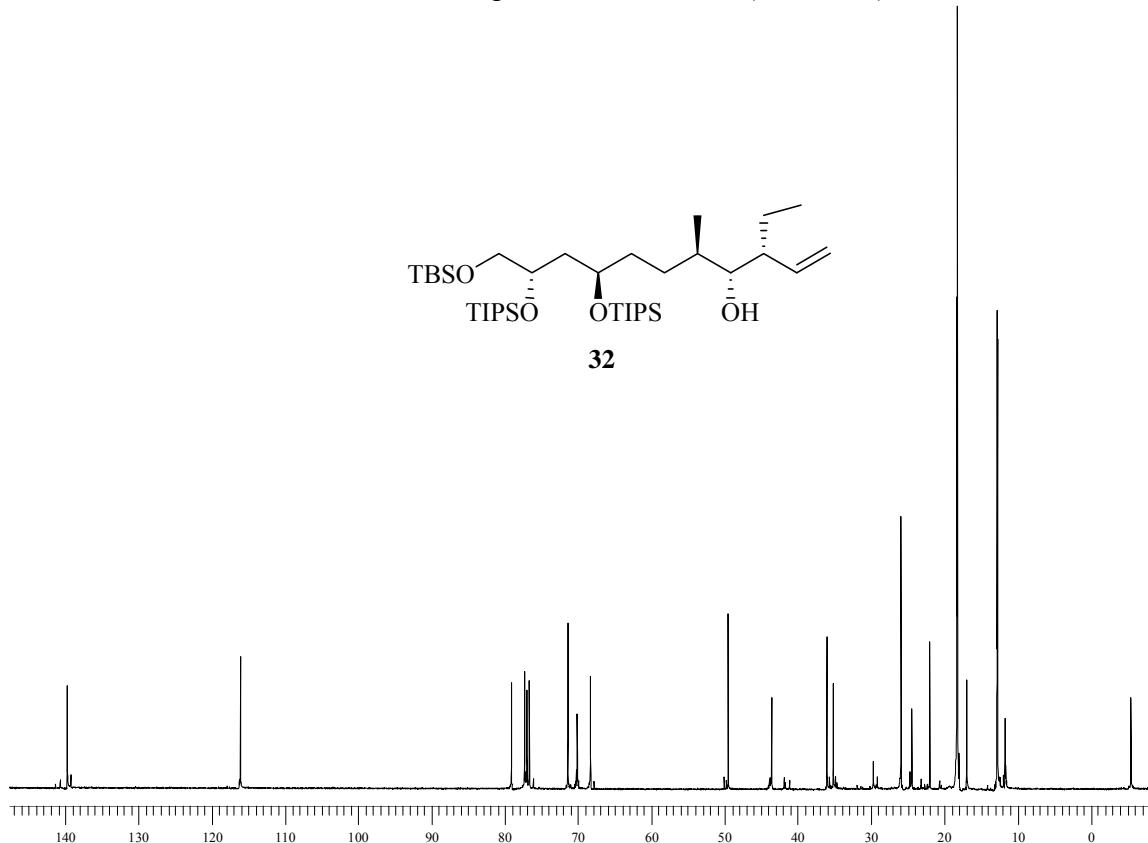
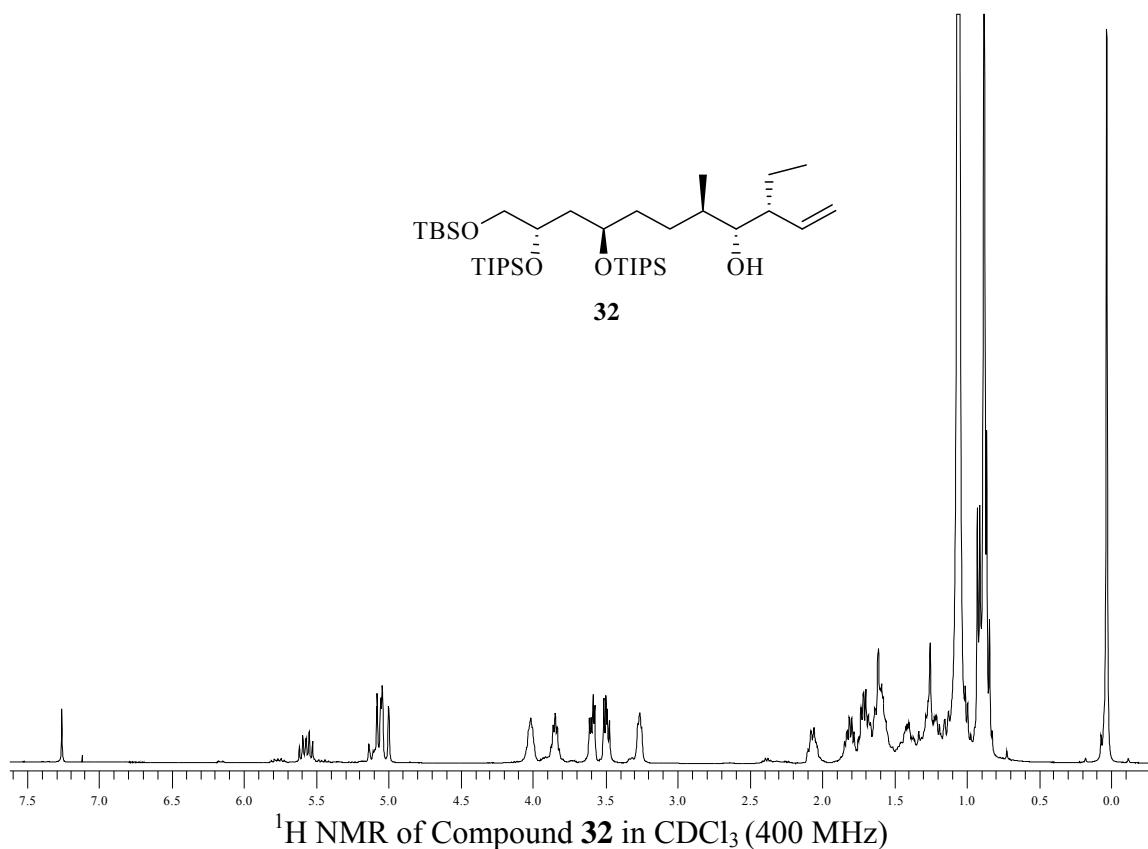


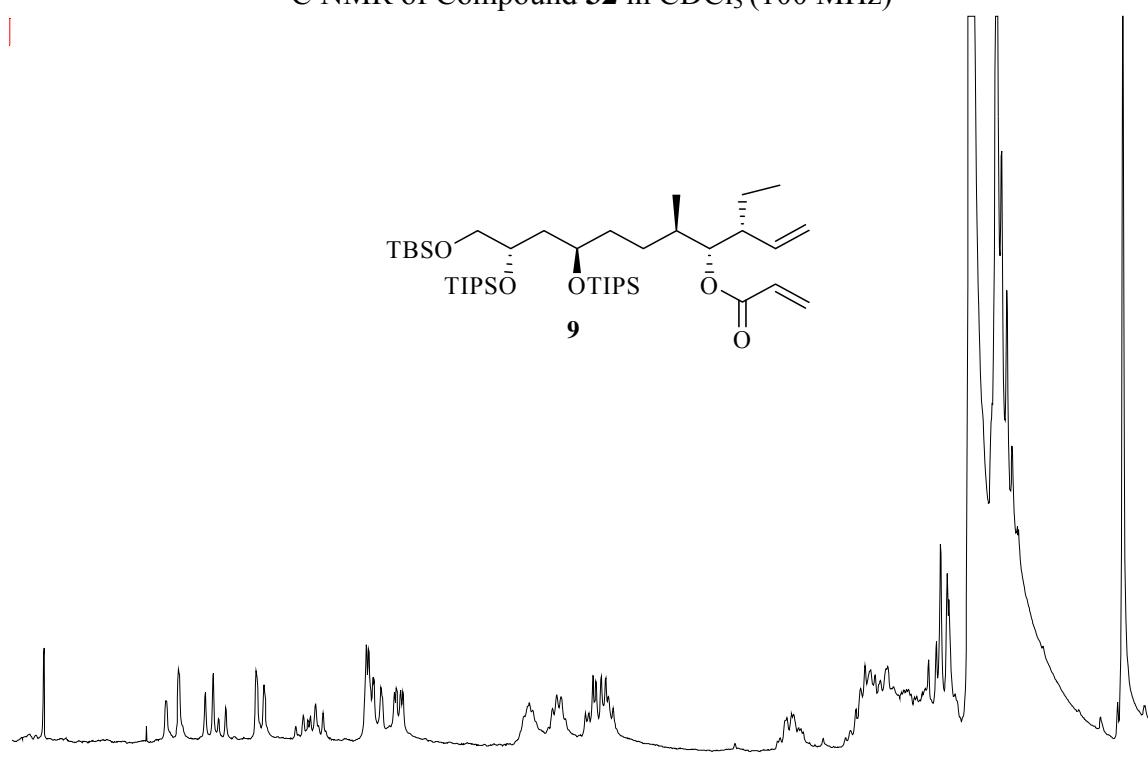
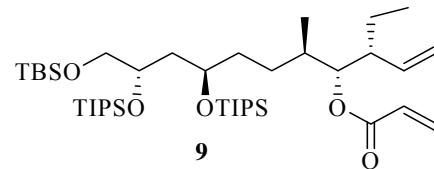
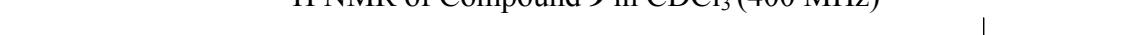
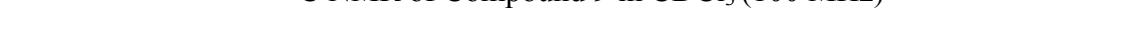


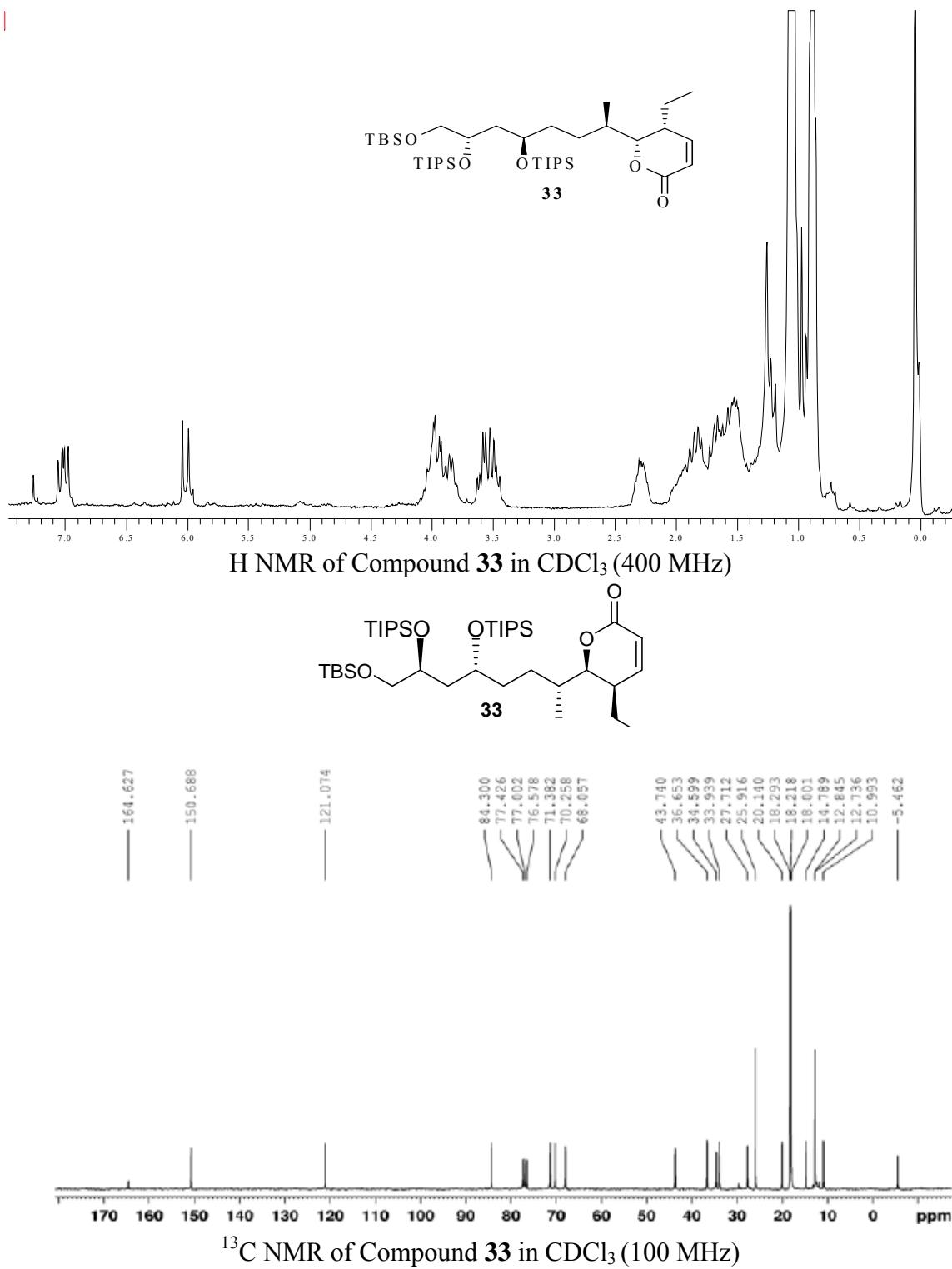


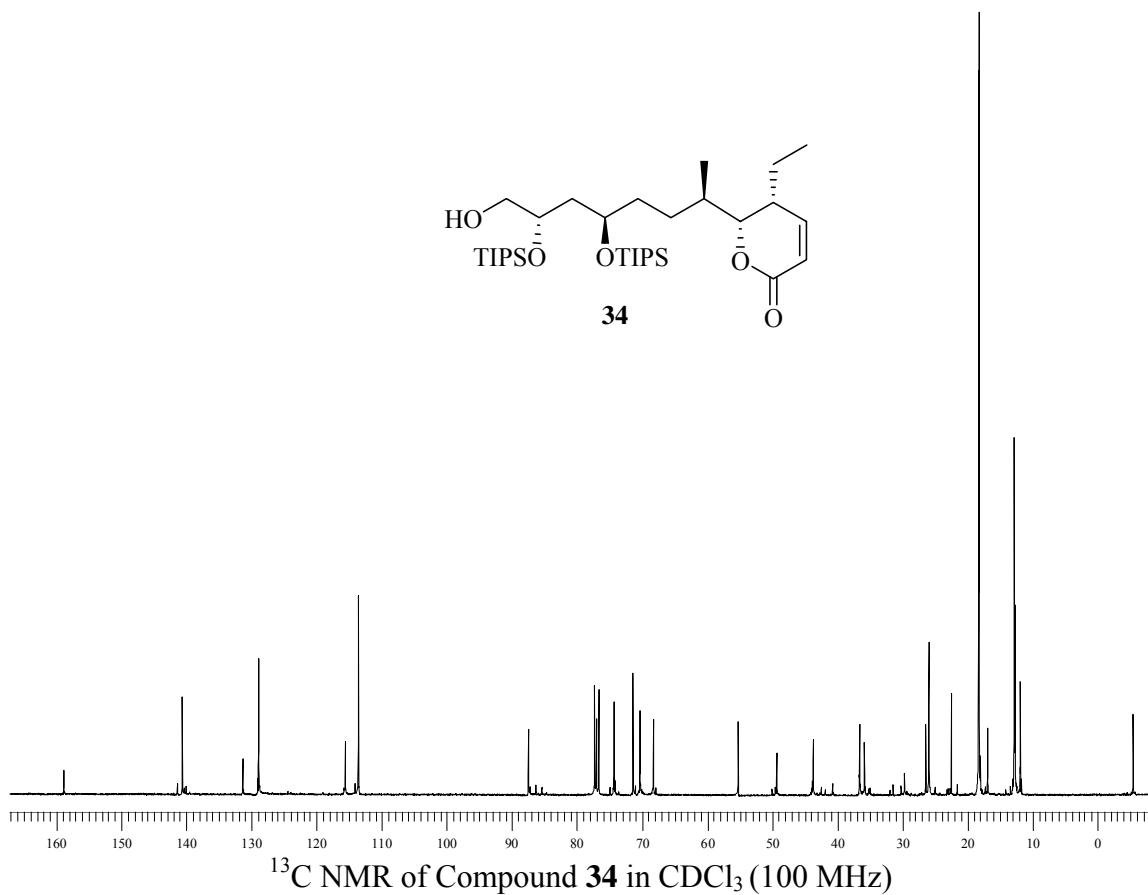
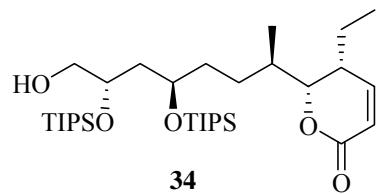
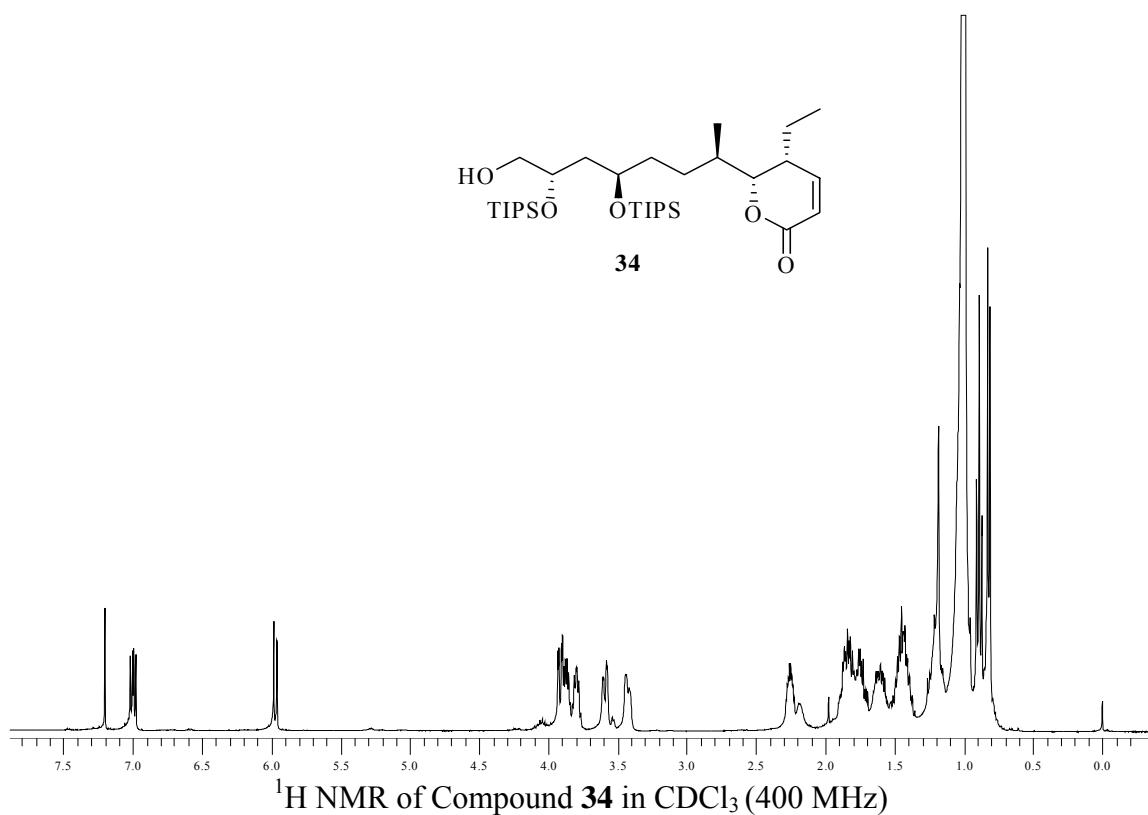
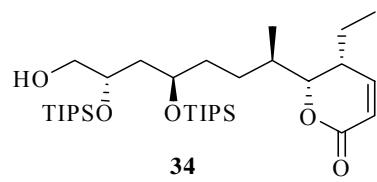


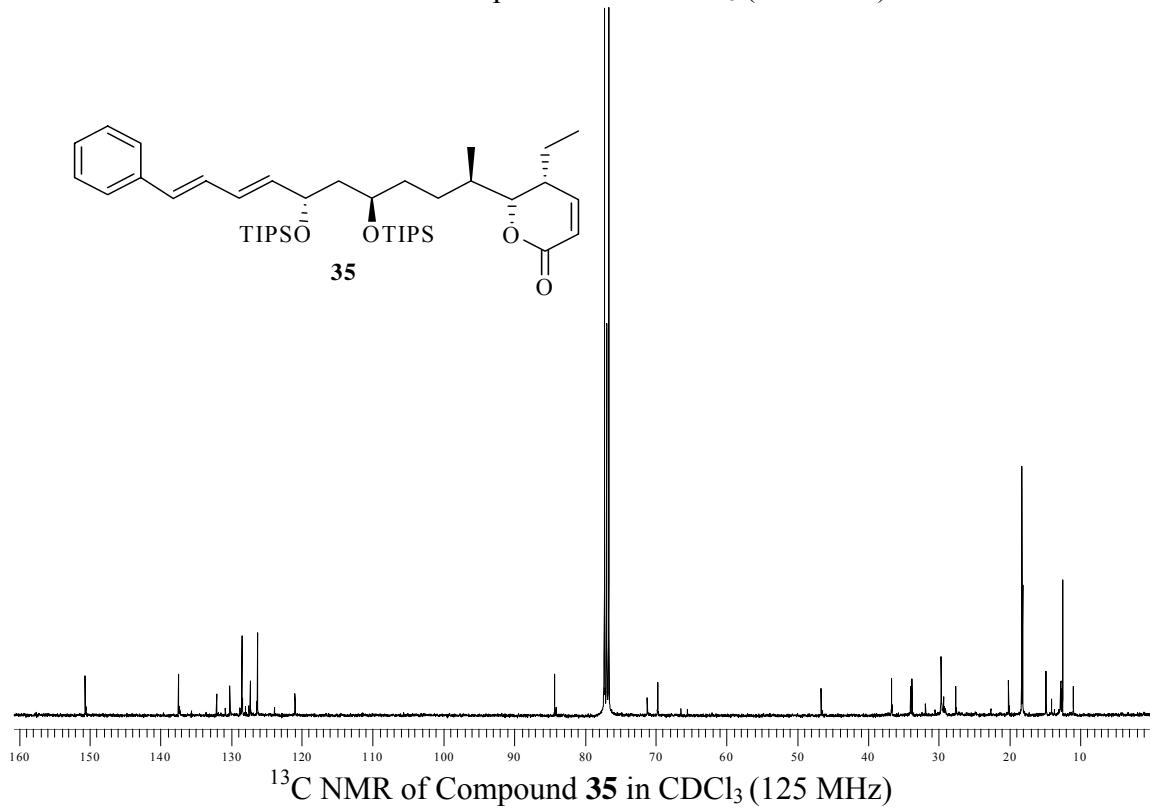
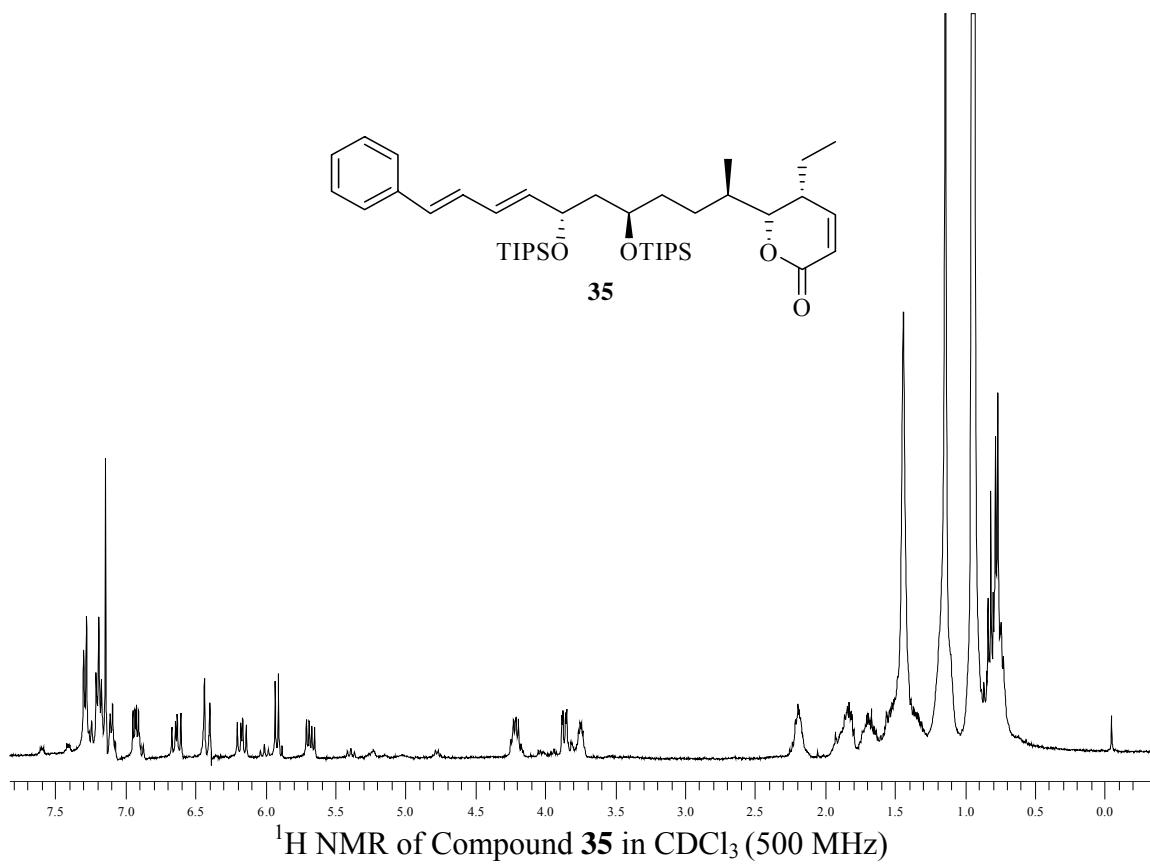


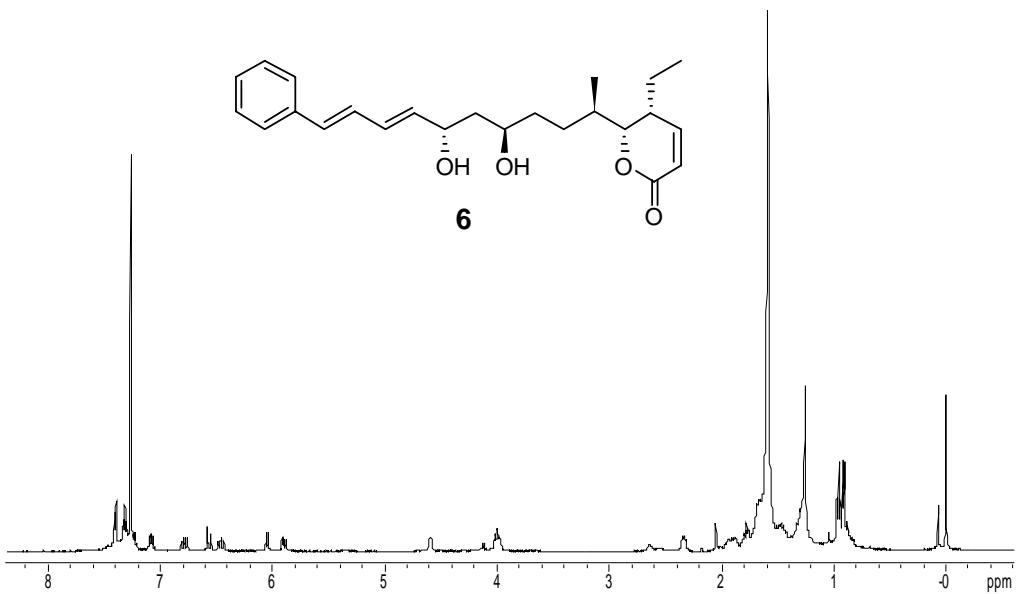


<sup>13</sup>C NMR of Compound **32** in CDCl<sub>3</sub> (100 MHz)<sup>1</sup>H NMR of Compound **9** in CDCl<sub>3</sub> (400 MHz)<sup>13</sup>C NMR of Compound **9** in CDCl<sub>3</sub> (100 MHz)









$^1\text{H}$  NMR of Compound 6 in  $\text{CDCl}_3$  (500 MHz)

