[Supporting Information]

Large Scale Synthesis of Eldecalcitol

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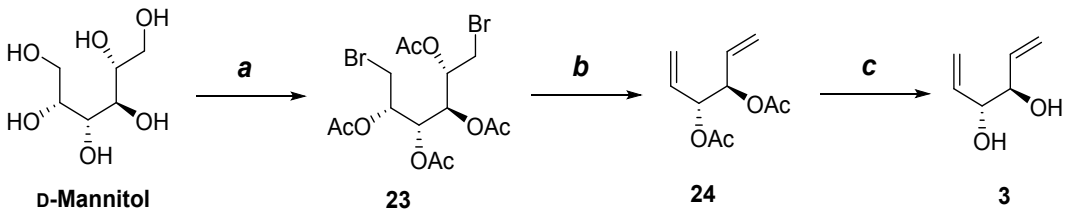
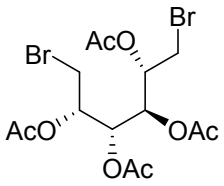


D-Mannitol 23 24 3

Scheme S1. Synthesis of **3**. *Reagents and conditions*: (a) i) AcBr, 1,4-dioxane, 3 d, rt; ii) Ac_2O, pyridine, 12 h, rt, 36%; (b) NaOAc, Zn, AcOH, 110 °C, 1 h, 100%; (c) K_2CO_3, MeOH, rt, 1 h, 100%.

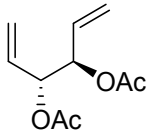
Experimental Procedures

(2*S*,3*S*,4*S*,5*S*)-1,6-Dibromohexane-2,3,4,5-tetrayl tetraacetate (**23**)



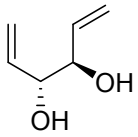
To a dispersion of D-mannitol (15.0 kg, 82.3 mol) in 1,4-dioxane (151 L) was added AcBr (14.8 L, 199.7 mol) at rt for 3 days and solvent was evaporated. To the resulting substance was added pyridine (34 L, 414.3 mol) and cooled to 10 °C. To the reaction mixture was added Ac_2O (36 L, 377.0 mol) at 10 °C. The reaction mixture was stirred at rt for 12 h and solvent was evaporated. To the resulting substance was added EtOH (23 L). The solution was stirred at rt for 1 h, filtered, washed with EtOH (12 L), and concentrated *in vacuo*. The product **23** (14.2 kg, 29.8 mol, 36%) was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (2H, d, J = 8.1 Hz), 5.13–5.08 (2H, m), 3.55 (2H, dd, J = 11.7, 3.6 Hz), 3.39 (1H, d, J = 6.0 Hz), 3.35 (1H, d, J = 6.0 Hz), 2.12 (6H, s), 2.11 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 169.8, 69.3, 69.0, 30.8, 20.9, 20.8.

(3*R*,4*R*)-Hexa-1,5-diene-3,4-diyl diacetate (**24**)



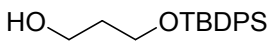
To a solution of compound **23** (14.2 kg, 29.8 mol) in AcOH (71 L) were added NaOAc (5.38 kg, 65.6 mol) and Zn (7.80 kg, 119.3 mol) at rt. The reaction mixture was stirred at 110 °C for 1 h, cooled to rt, filtered, and evaporated. To the crude compound were added water (71 L) and AcOEt (71 L). The reaction mixture was stirred for 30 min. The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo*. The product **24** (5.91 kg, 29.8 mol, 100%) was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82–5.71 (2H, m), 5.44–5.38 (2H, m), 5.33 (2H, d, J = 17.1 Hz), 5.28 (2H, d, J = 10.5 Hz), 2.09 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 132.8, 119.3, 74.4, 21.0.

(3*R*,4*R*)-Hexa-1,5-diene-3,4-diol (**3**)



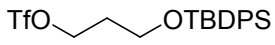
To solution of compound **24** (5.91 kg, 29.8 mol) in MeOH (30 L) was added K_2CO_3 (0.82 kg, 5.93 mol). The reaction mixture was stirred at rt for 1 h and concentrated *in vacuo*. The product **3** (3.41 kg, 29.8 mol, 100%) was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92–5.81 (2H, m), 5.36 (2H, d, J = 17.4 Hz), 5.25 (2H, d, J = 10.8 Hz), 4.00 (2H, dd, J = 9.7, 5.3 Hz), 2.94 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.7, 117.5, 75.8.

3-((*tert*-Butyldiphenylsilyl)oxy)propan-1-ol (**7**)



To a dispersion of 1,3-propanediol (1.35 kg, 17.7 mol) in CH_2Cl_2 (20.3 L) was added Et_3N (2.48 L, 17.7 mol) at rt. The reaction mixture was cooled to 0 °C. TBDPSCl (4.63 L, 17.7 mol) was added dropwise to the reaction mixture using dropping funnel. The reaction mixture was stirred at rt for 15 h, quenched with water (18 L), and stirred for 10 min. The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo*. Thin film distillation of the resulting substance at 155 °C under 0.2 torr gave the product **7** (5.04 kg, 16.0 mol, 90%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.66 (4H, m), 7.46–7.35 (6H, m), 3.86–3.81 (4H, m), 2.42 (1H, s), 1.84–1.76 (2H, m), 1.06–1.05 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7, 133.4, 129.9, 127.9, 63.3, 62.0, 34.4, 27.0, 19.2.

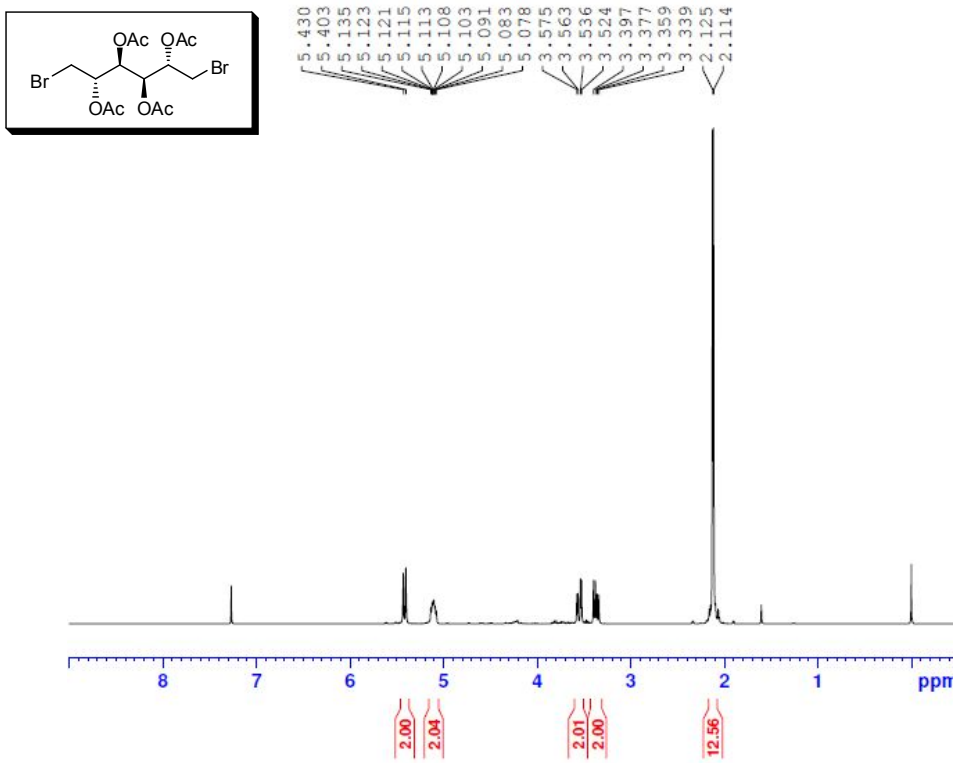
3-((*tert*-Butyldiphenylsilyl)oxy)propyl trifluoromethanesulfonate (**8**)



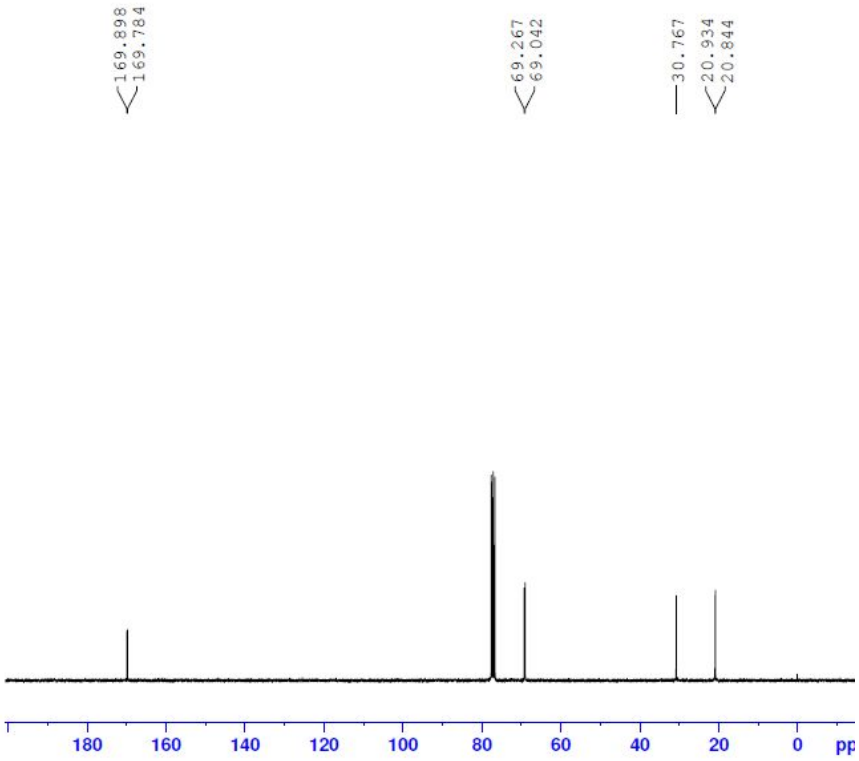
To a dispersion of compound **7** (5.04 kg, 16.0 mol) in *n*-heptane (30 L) was added DIPEA (2.93 L, 16.8 mol) at rt. The reaction mixture was cooled to 10 °C. $(TfO)_2O$ (2.69 L, 16.0 mol) was added dropwise to the reaction mixture using dropping funnel. The reaction mixture was stirred at 10 °C for 30 min, quenched with water (14 L), and stirred for 10 min. The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo*. The product **8** (6.79 kg, 15.2 mol, 95%) was immediately used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66–7.63 (4H, m), 7.47–7.35 (6H, m), 4.74 (2H, t, J = 6.2 Hz), 3.77 (2H, t, J = 5.7 Hz), 2.05–1.97 (2H, m), 1.07–1.04 (9H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 133.3, 130.0, 128.0, 74.6, 58.8, 32.3, 26.9, 19.3.

Compound **23**

^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



Compound **24**

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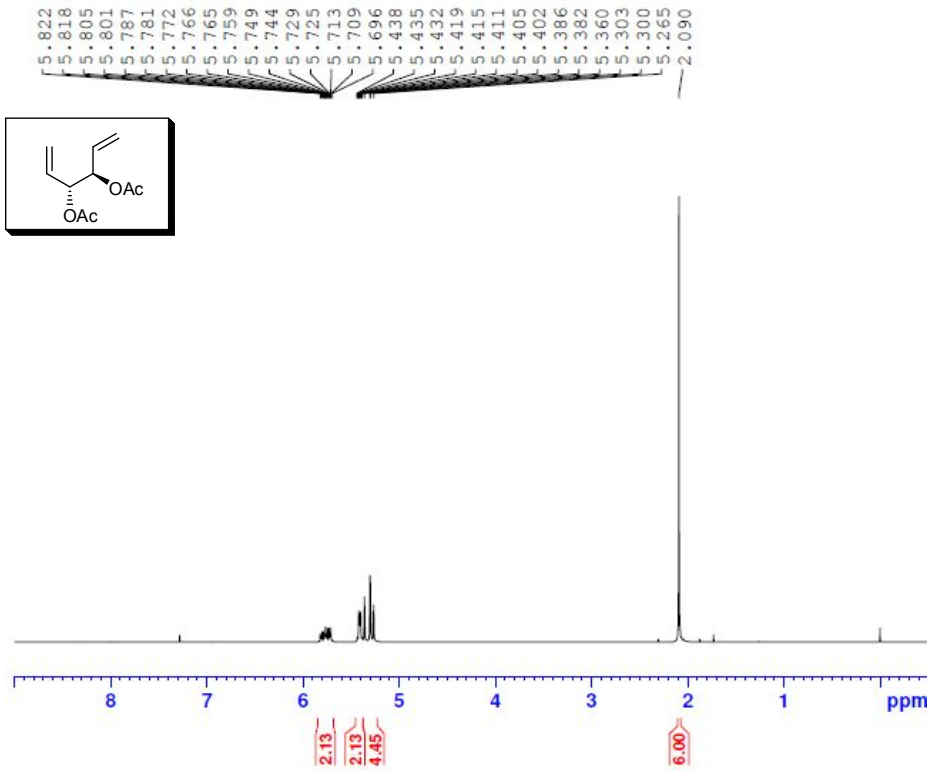

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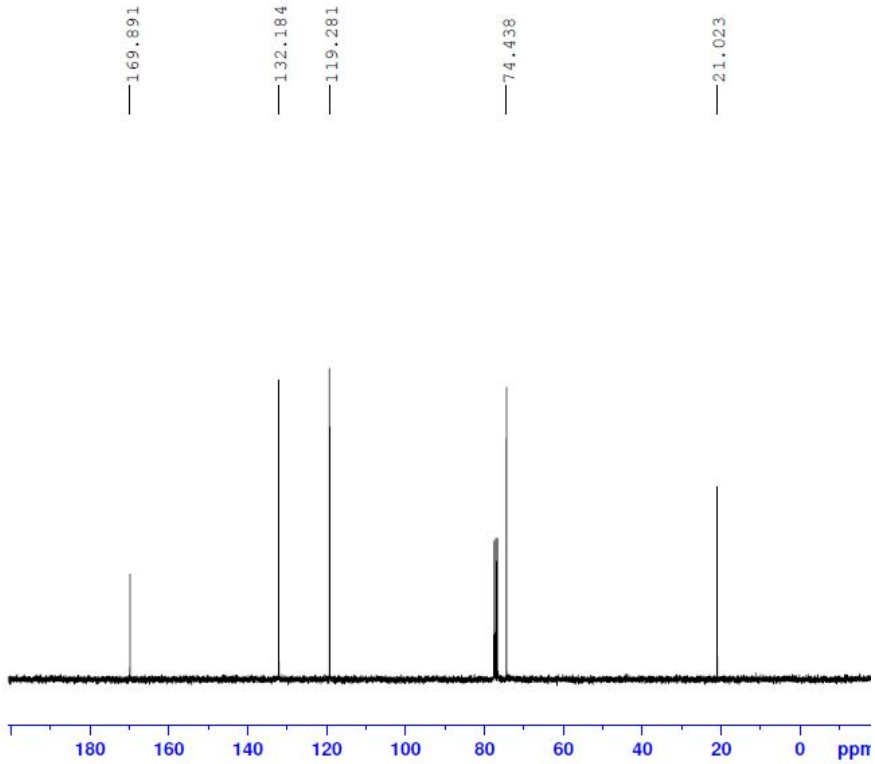
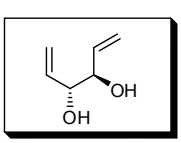
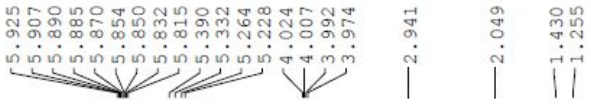
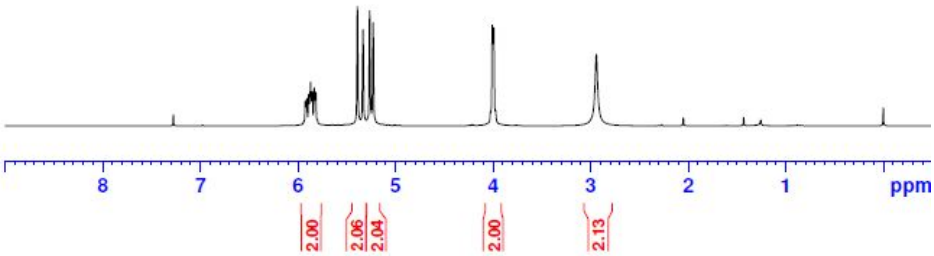


Compound **3**

^{1}H NMR ($CDCl_3$, 300 MHz)







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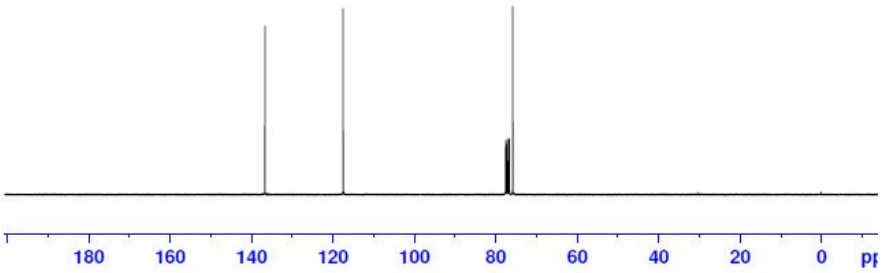

Compound **4**

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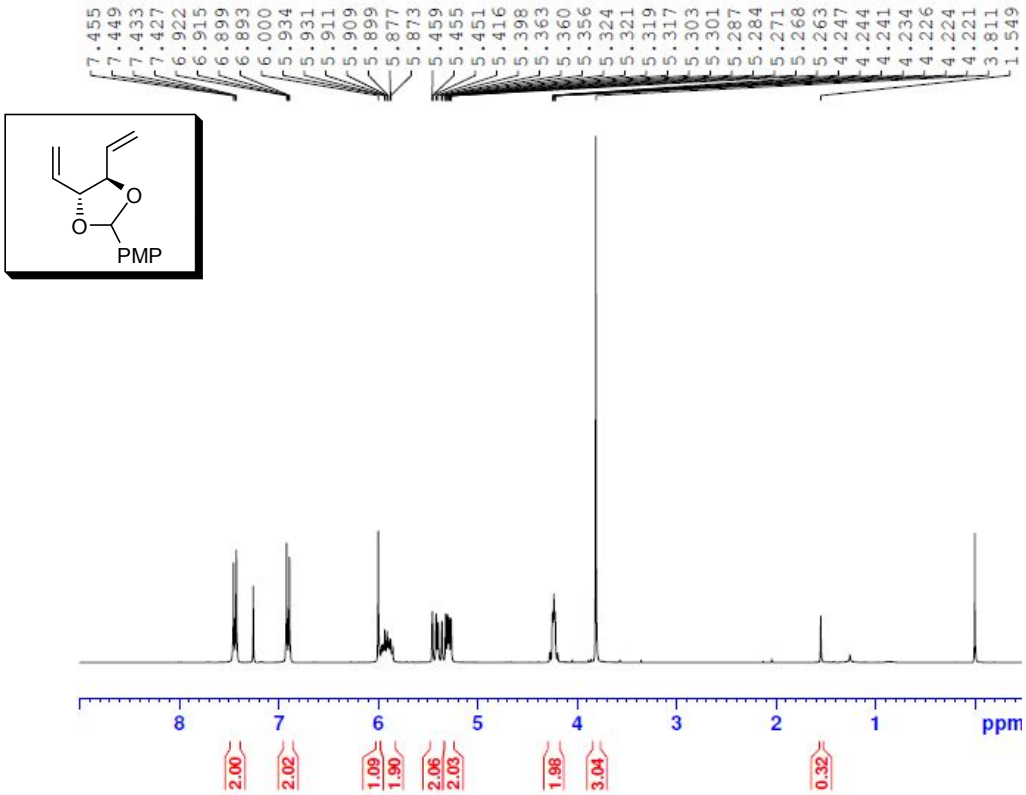

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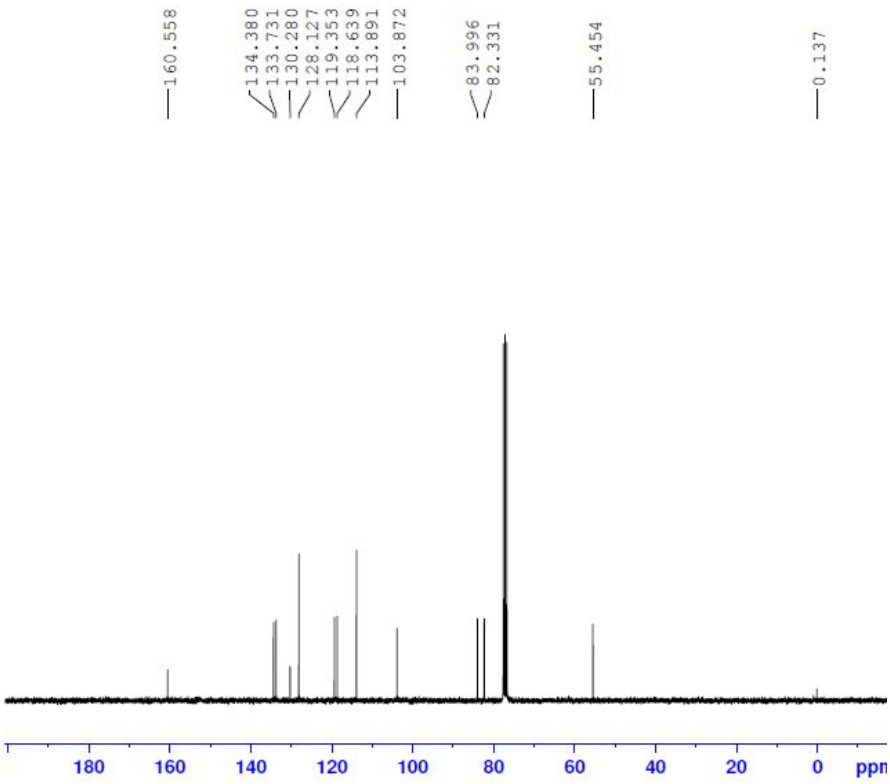

Compound **5**

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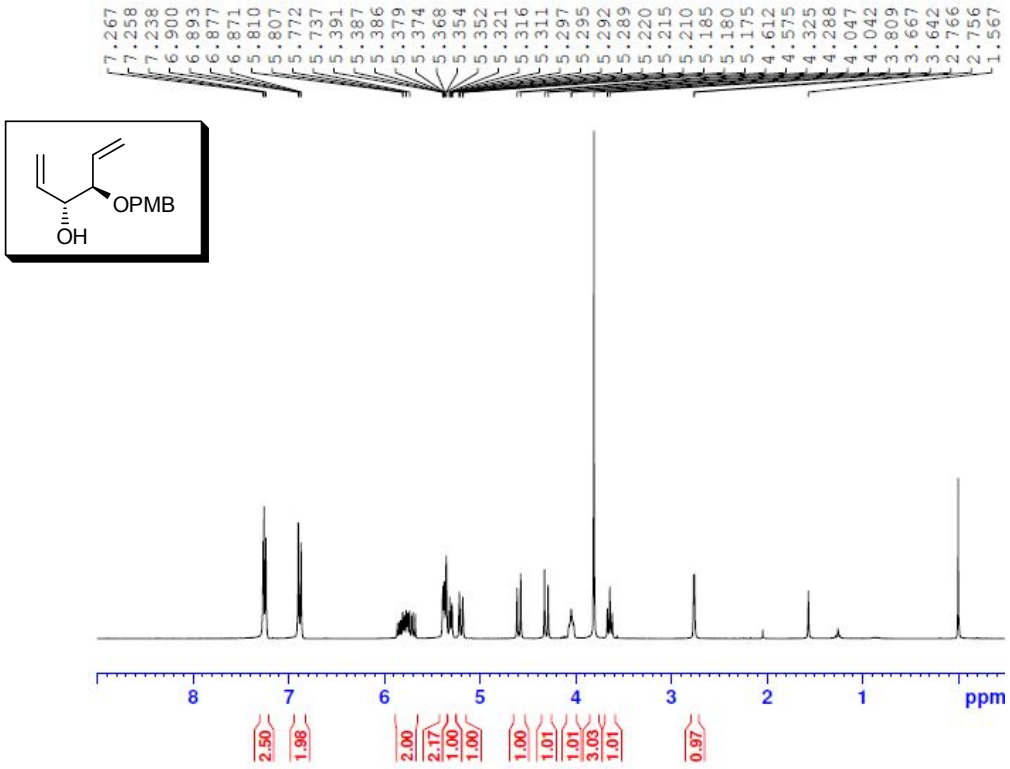

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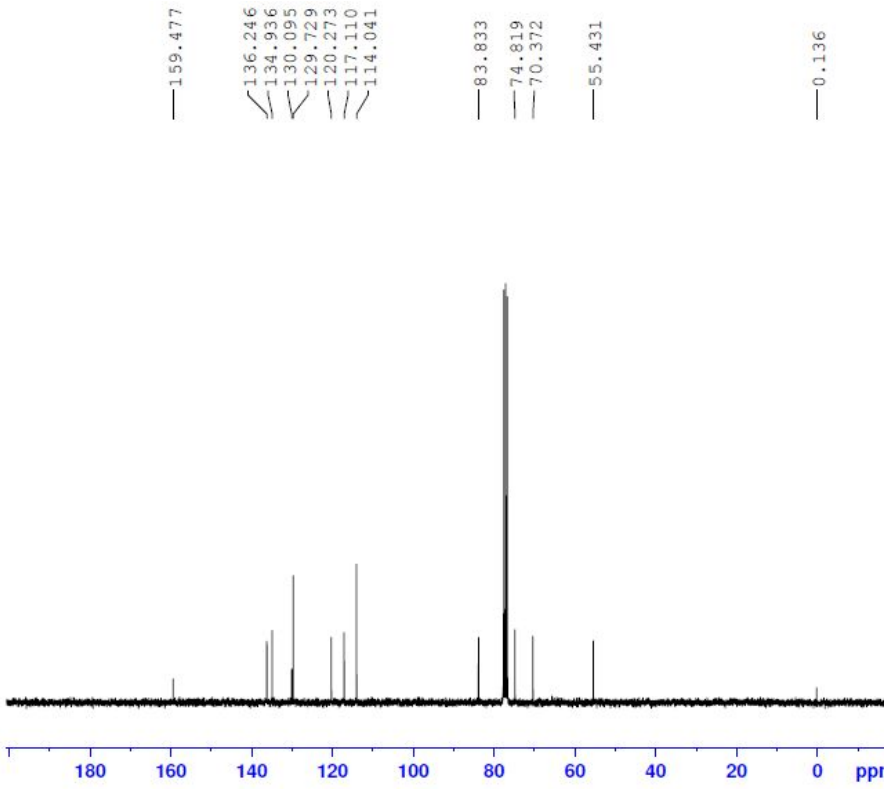

Compound **6**

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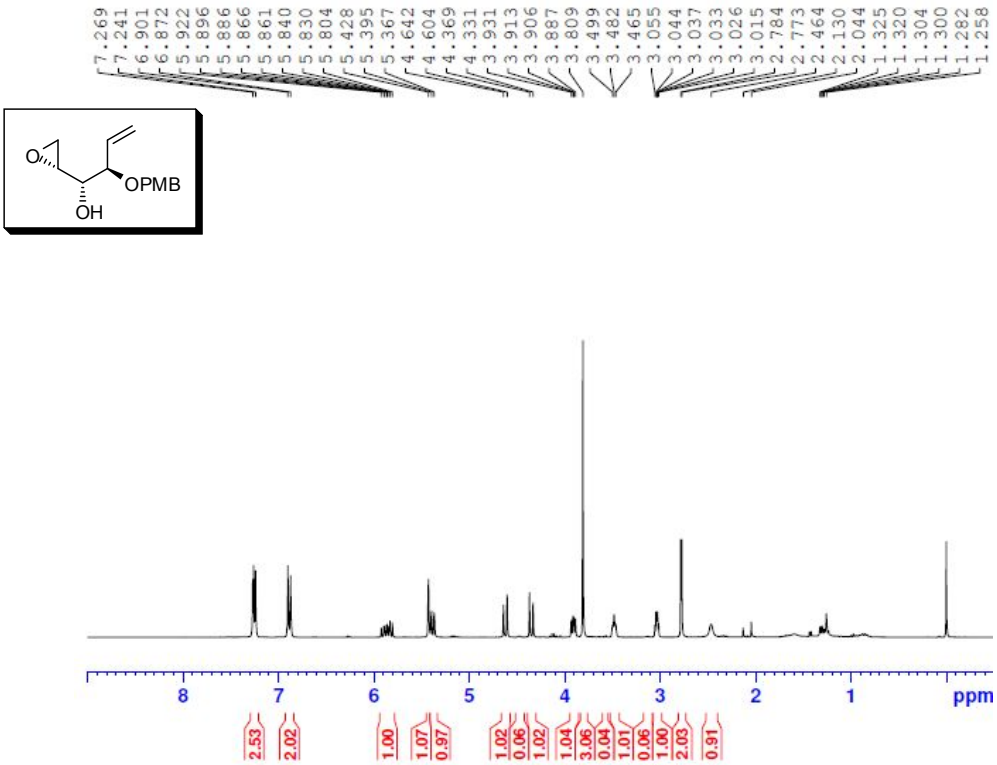

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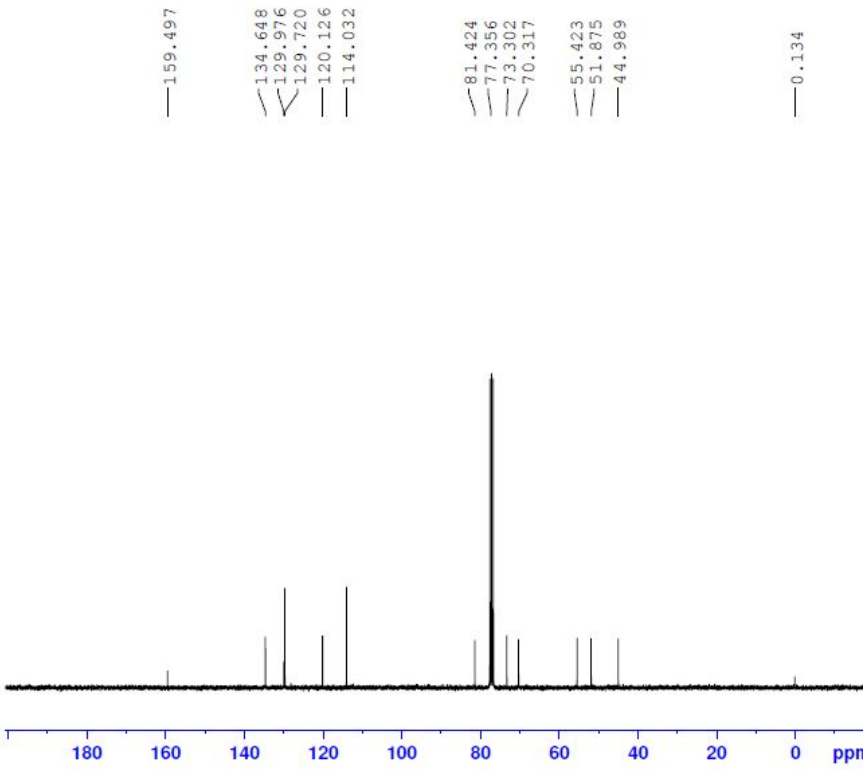
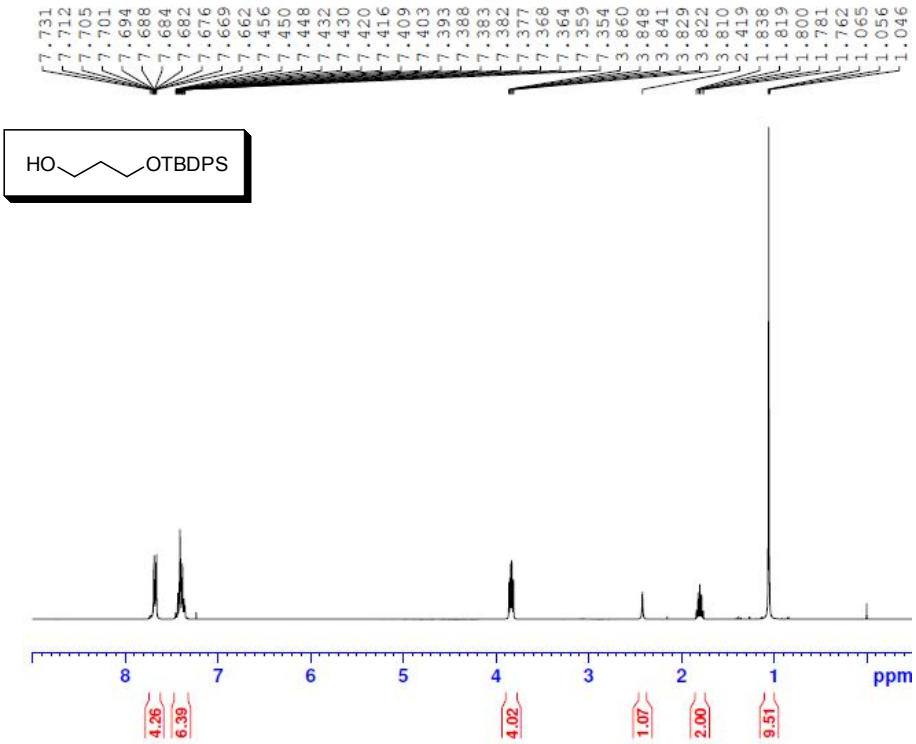
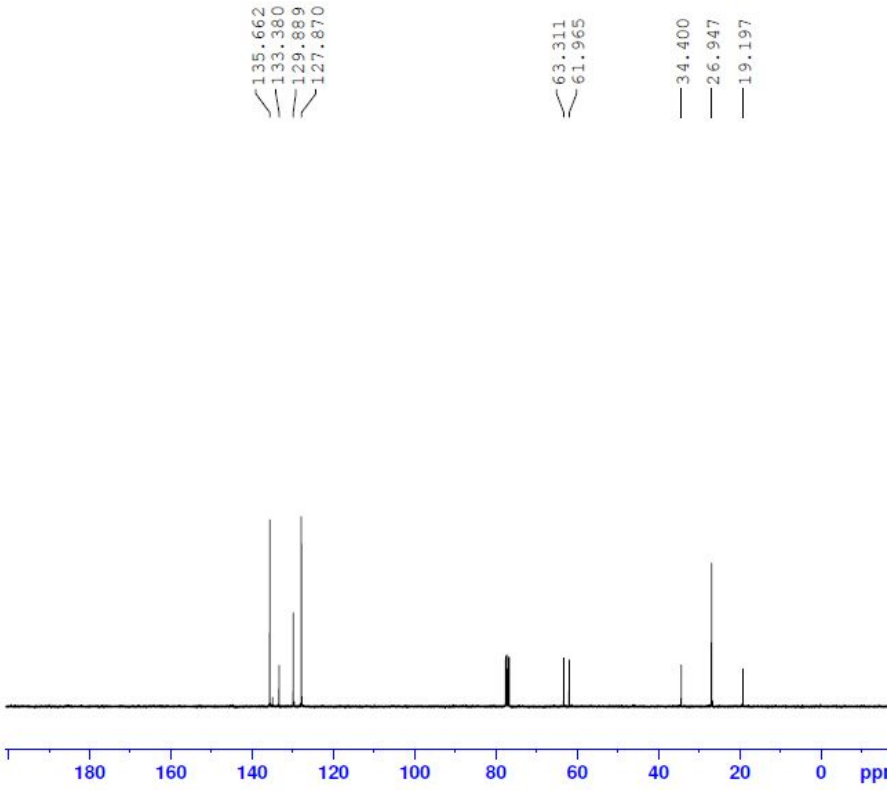


Compound **7**

^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



Compound **8**

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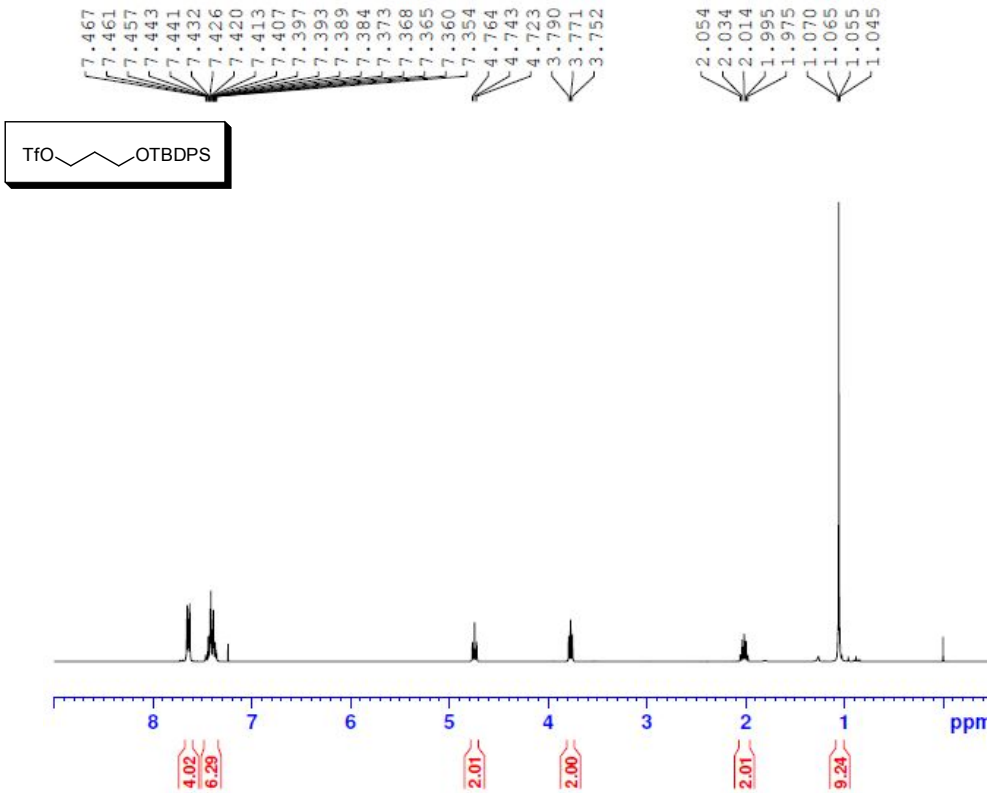

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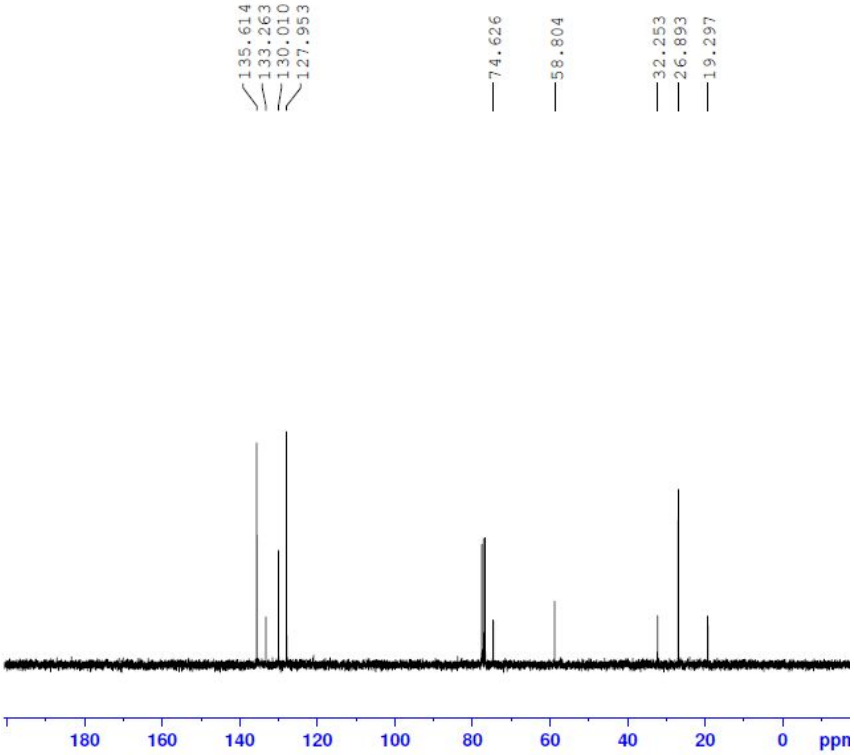

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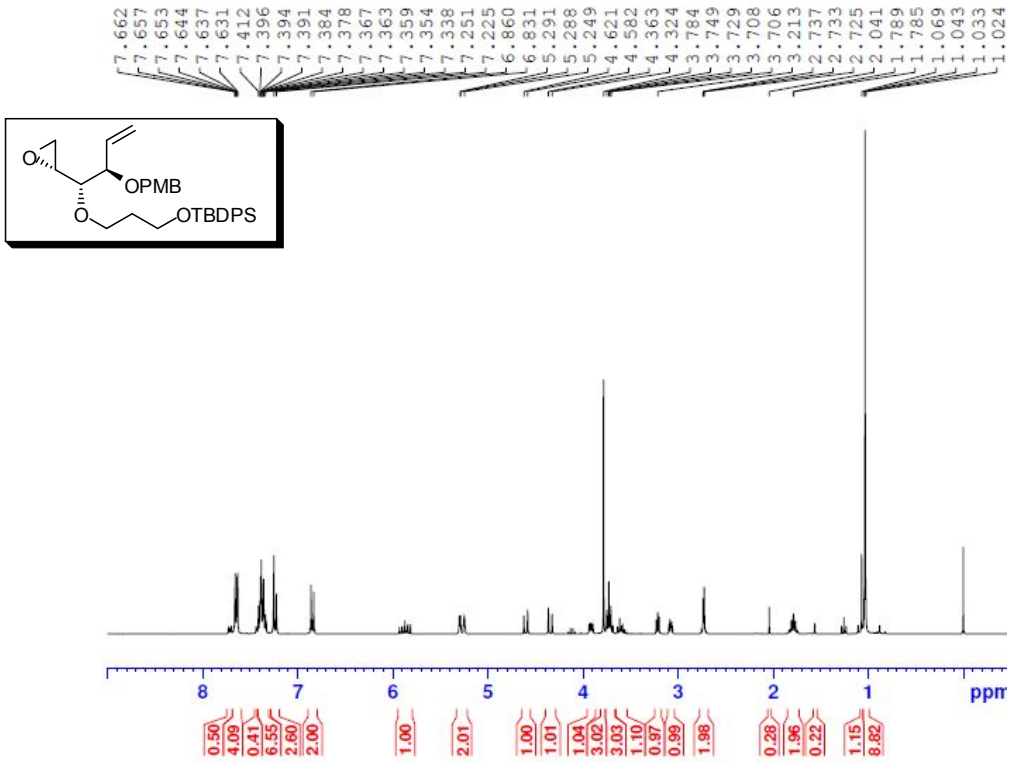

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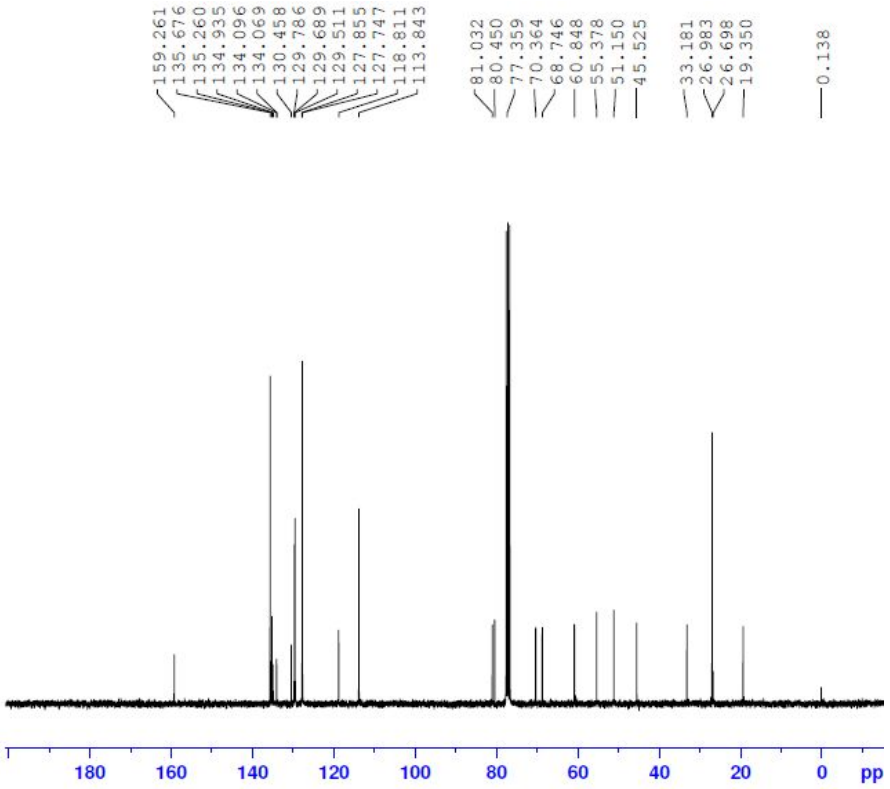

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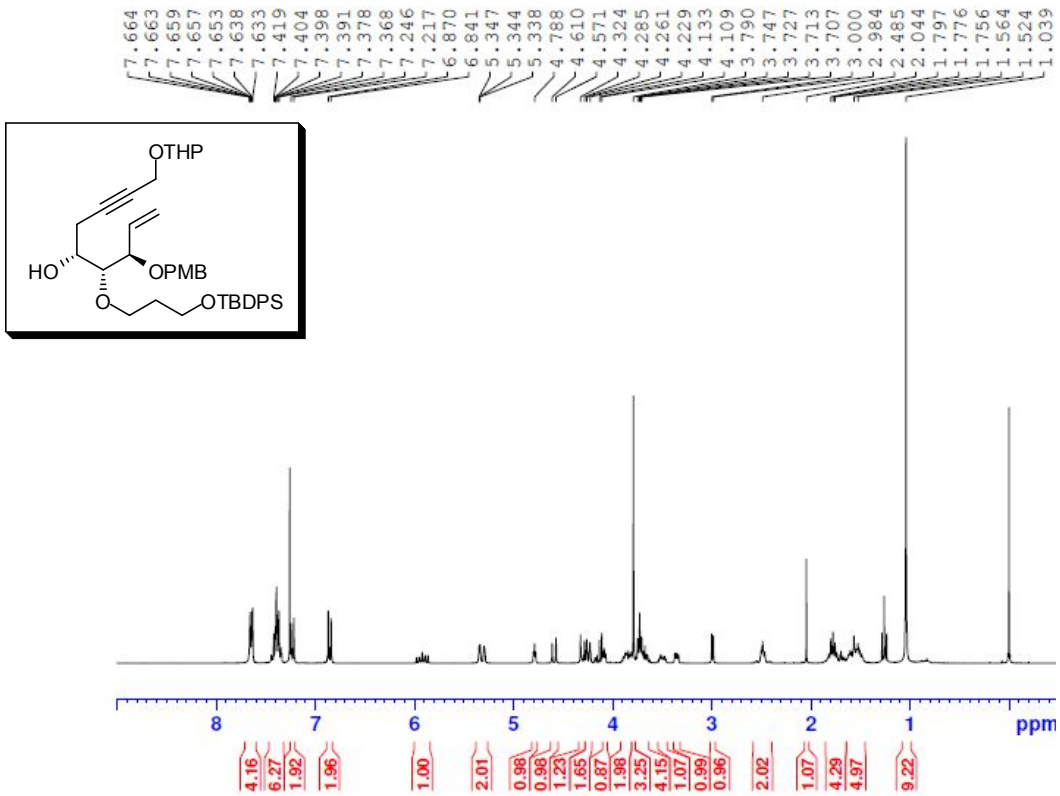

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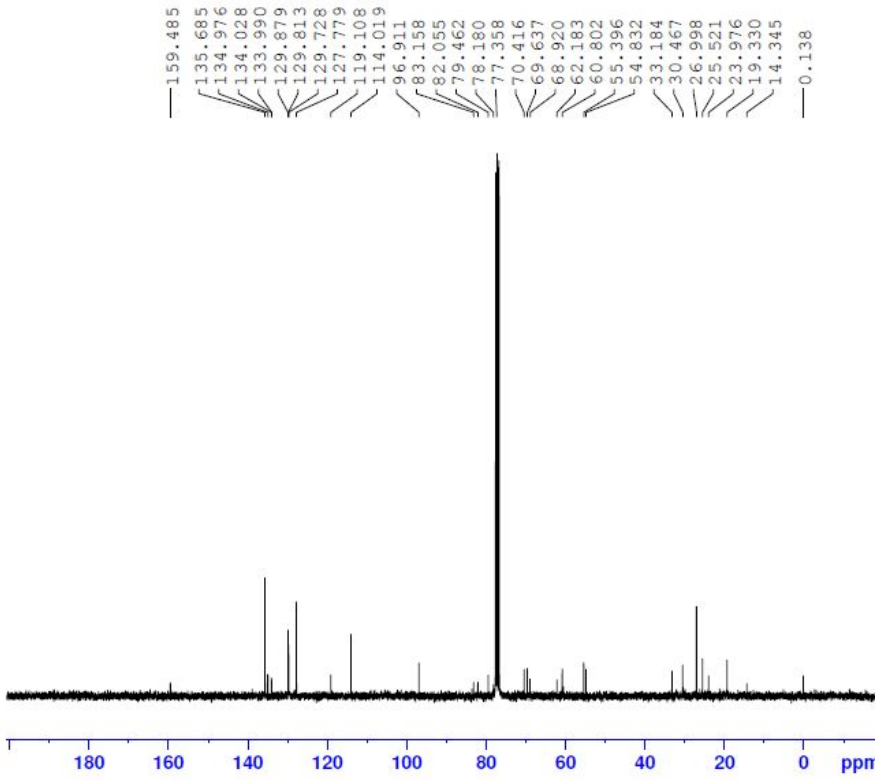

Compound **12**

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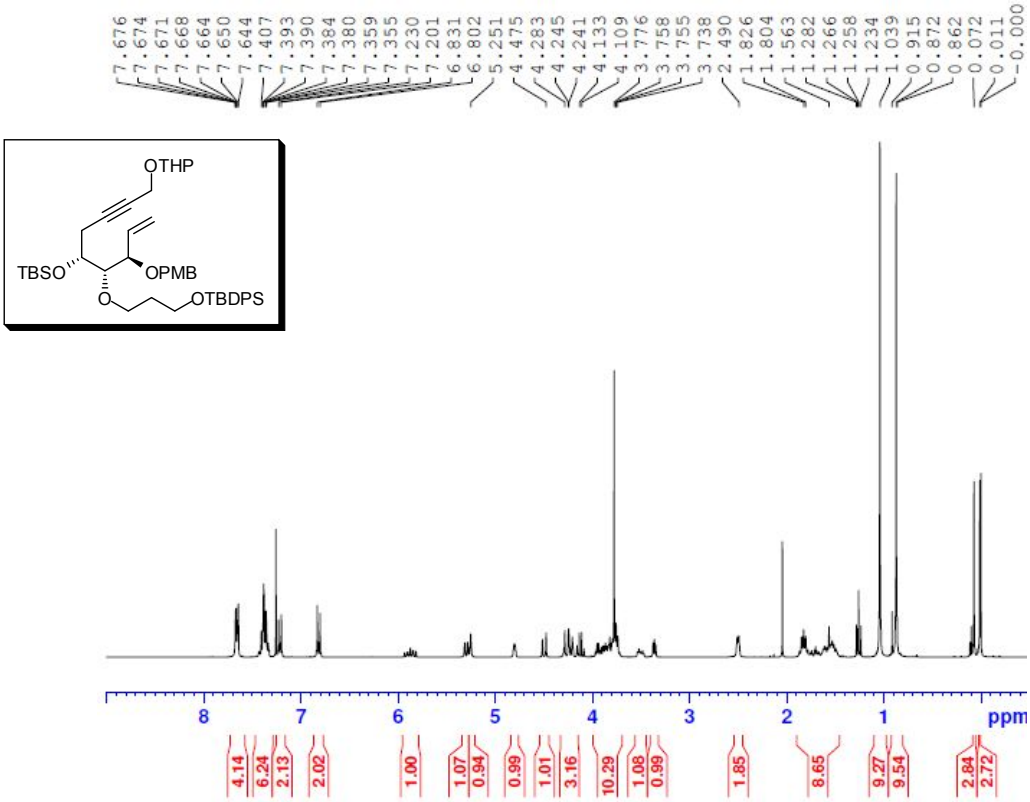

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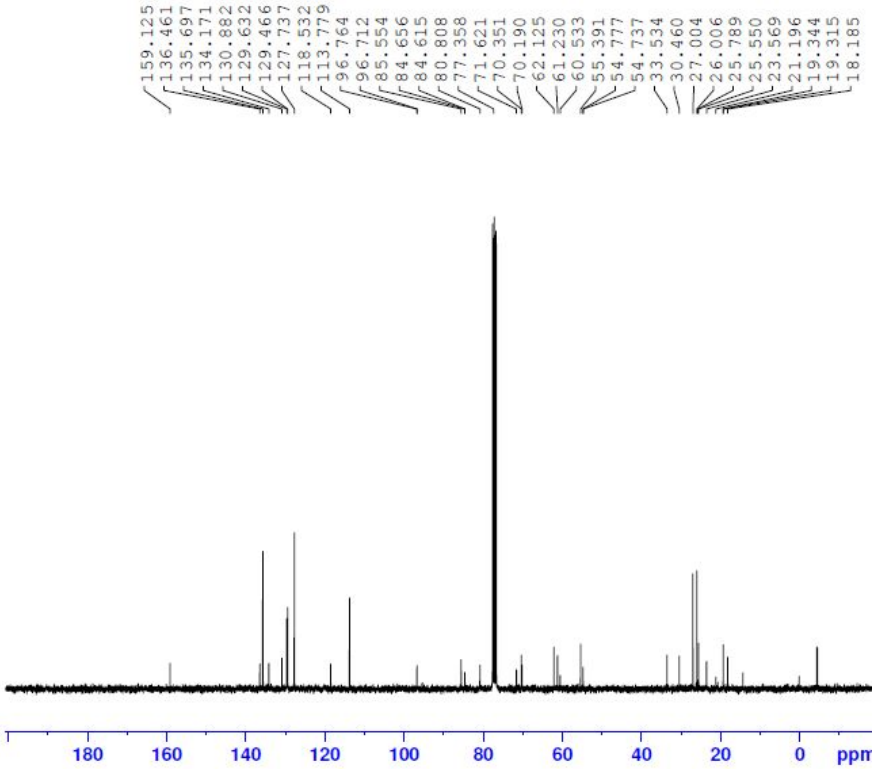
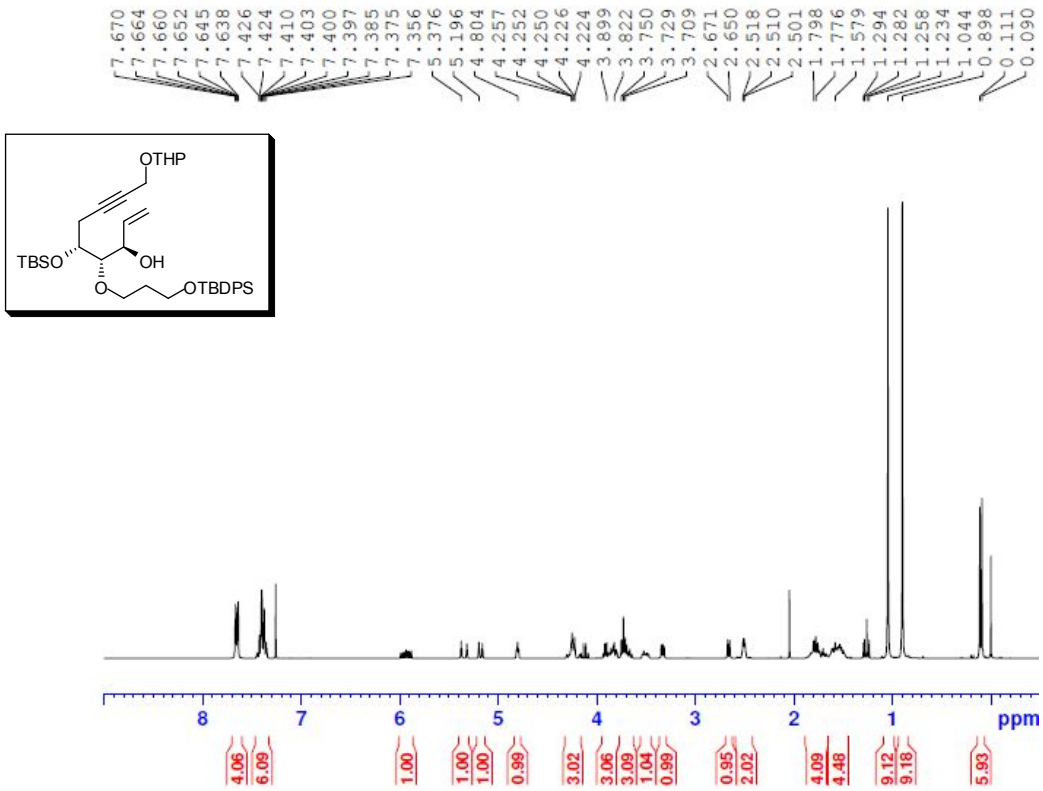


Compound **13**

^{1}H NMR ($CDCl_3$, 300 MHz)



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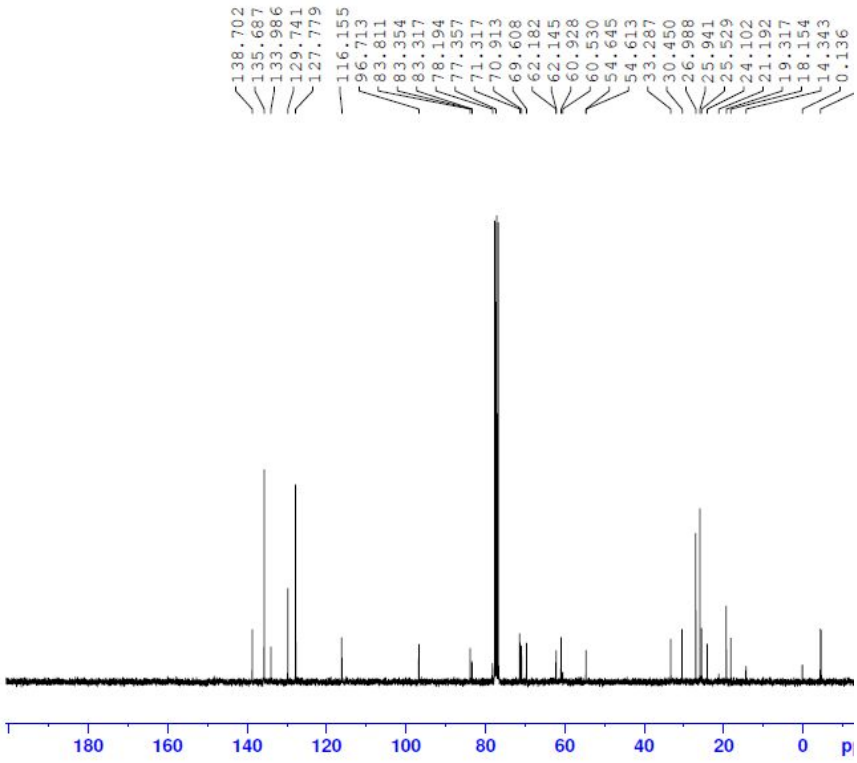
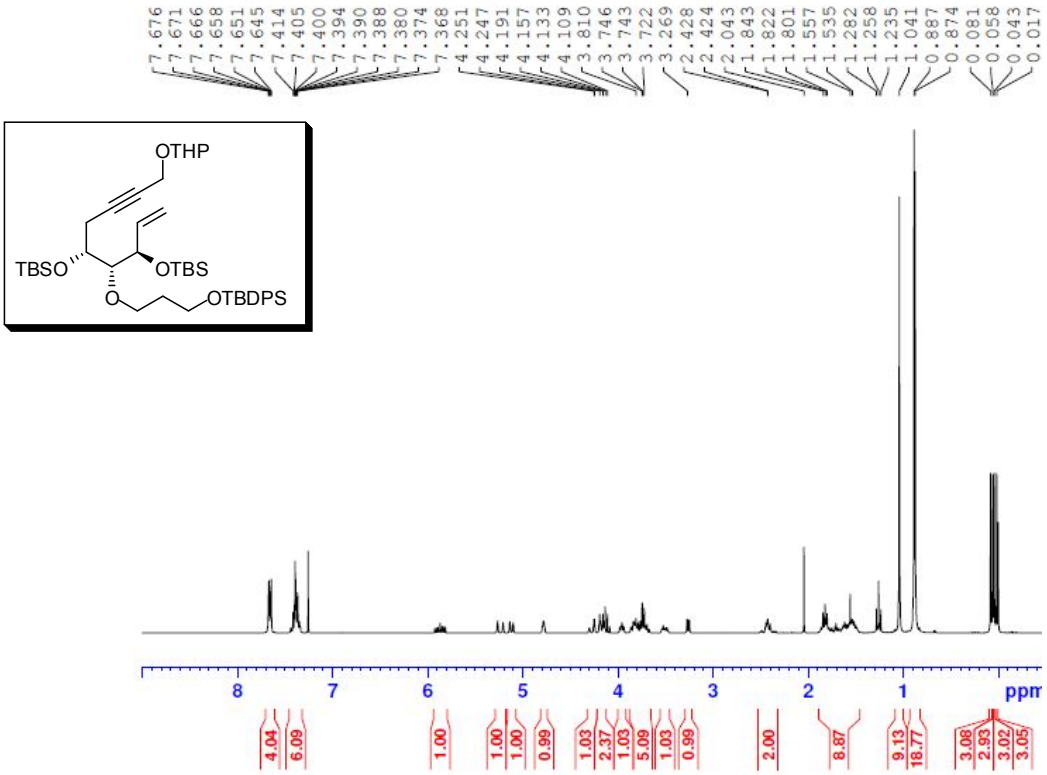


Compound **14**

^{1}H NMR ($CDCl_3$, 300 MHz)



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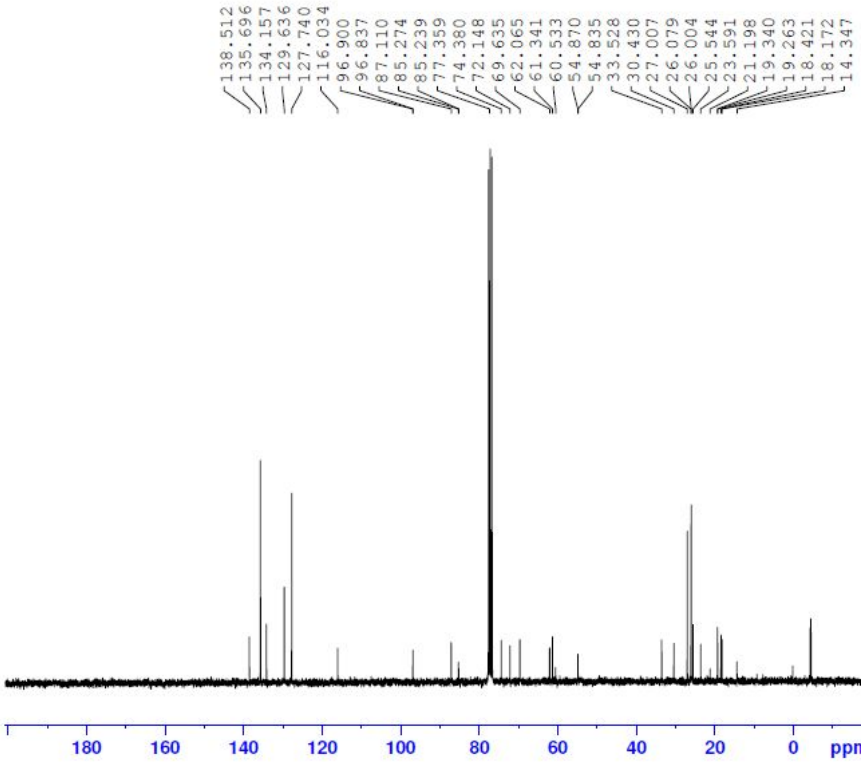

Compound **15**

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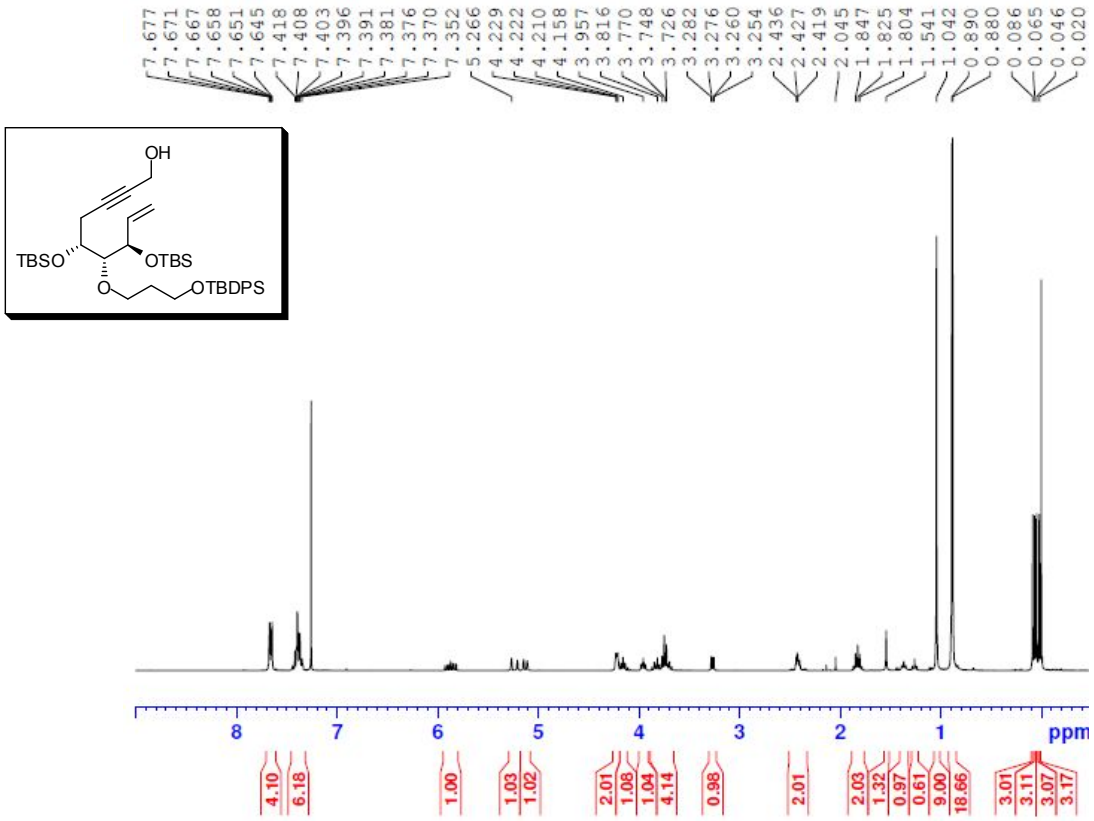

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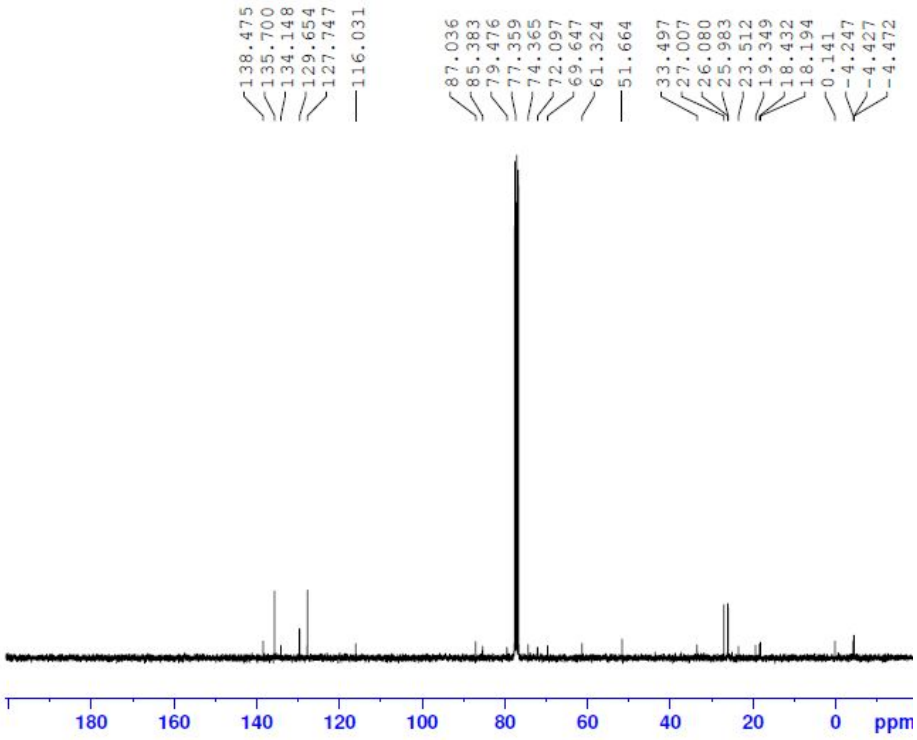

Compound **16**

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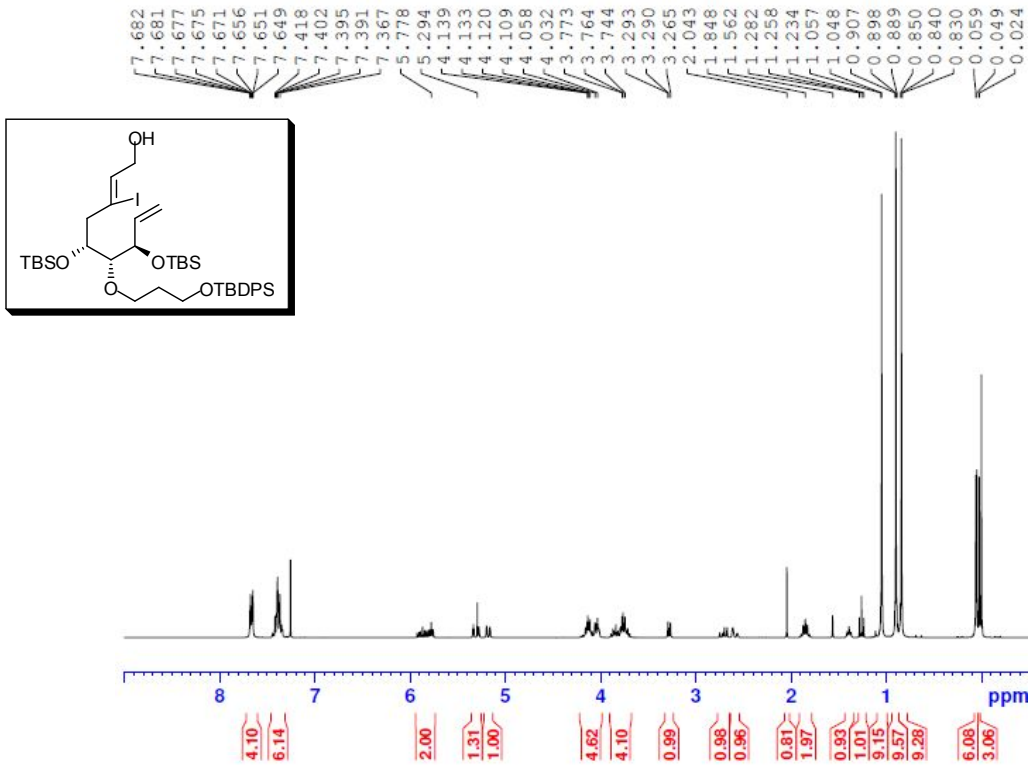
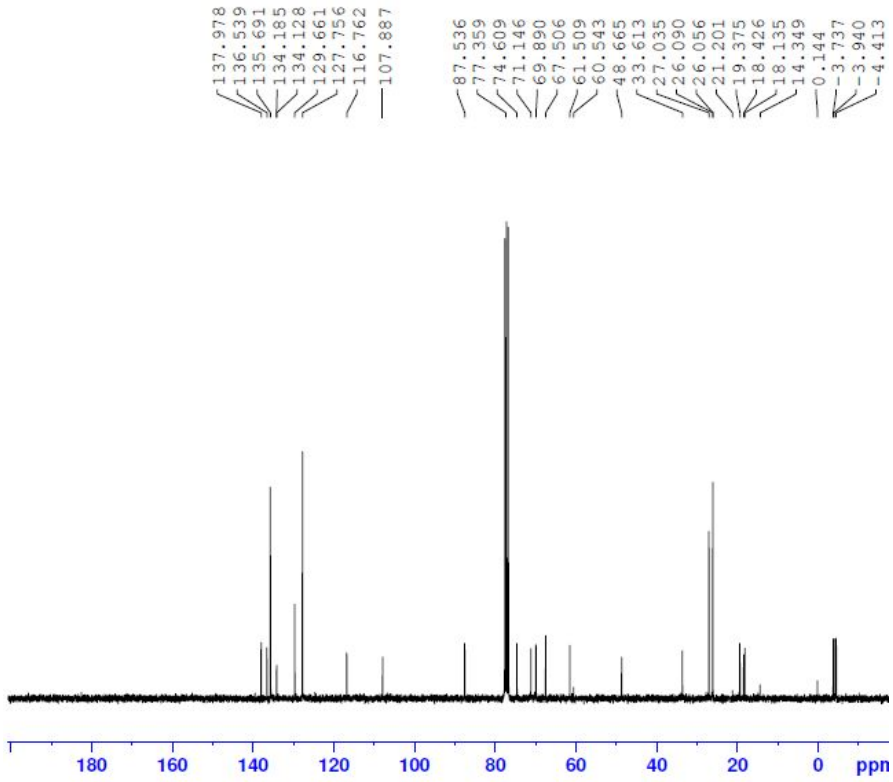


^{13}C NMR ($CDCl_3$, 75 MHz)



Compound **17**

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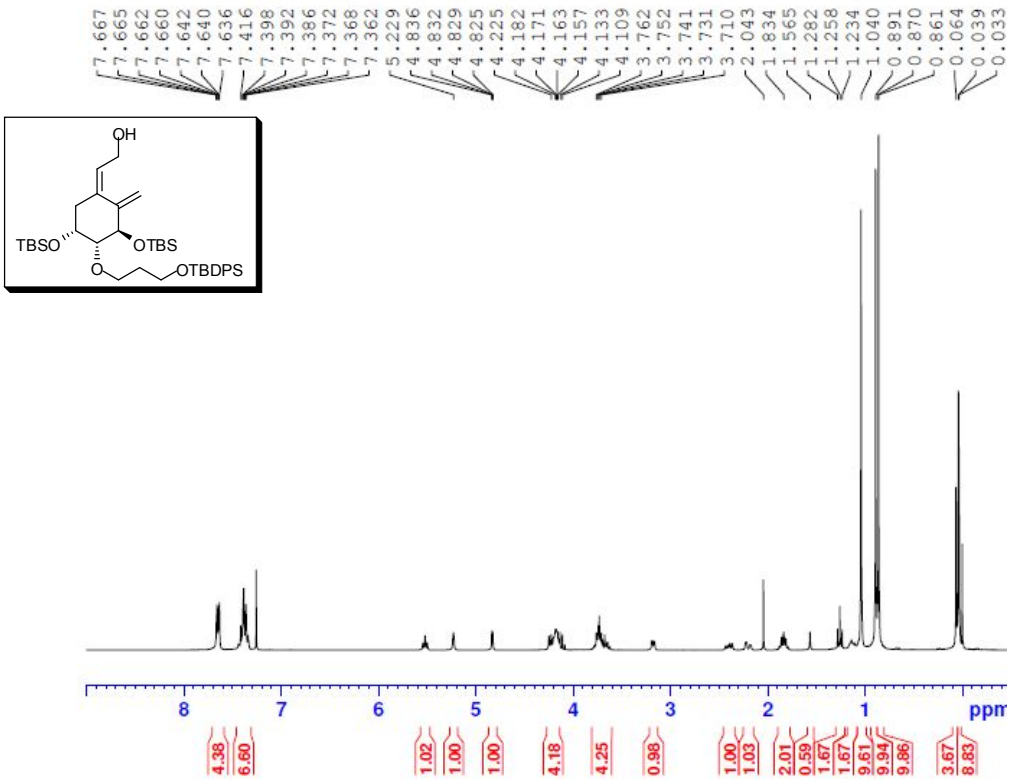

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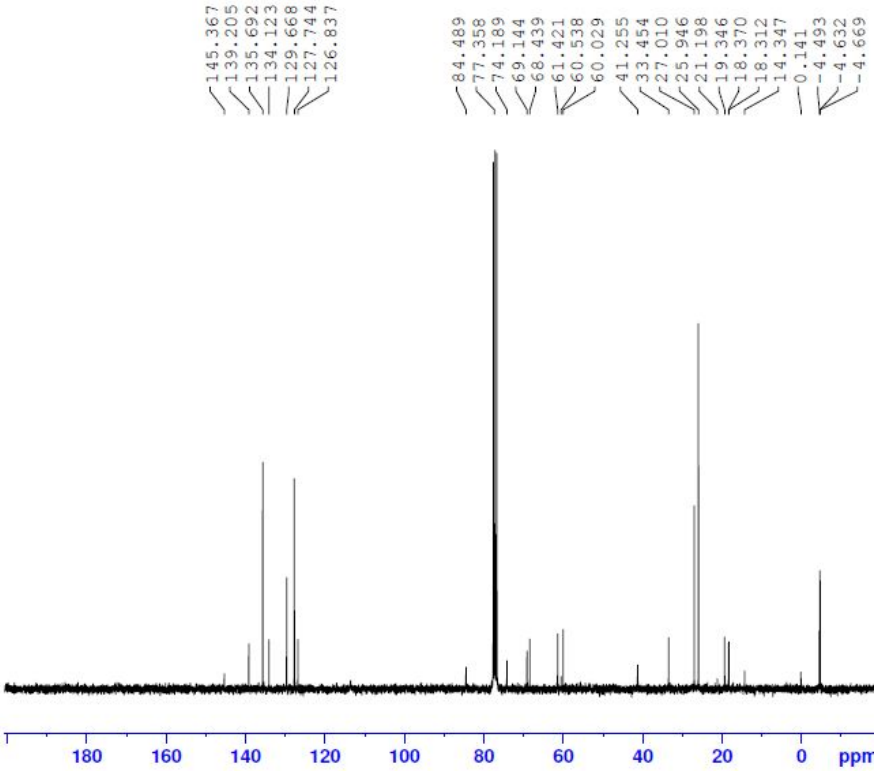

Compound **18**

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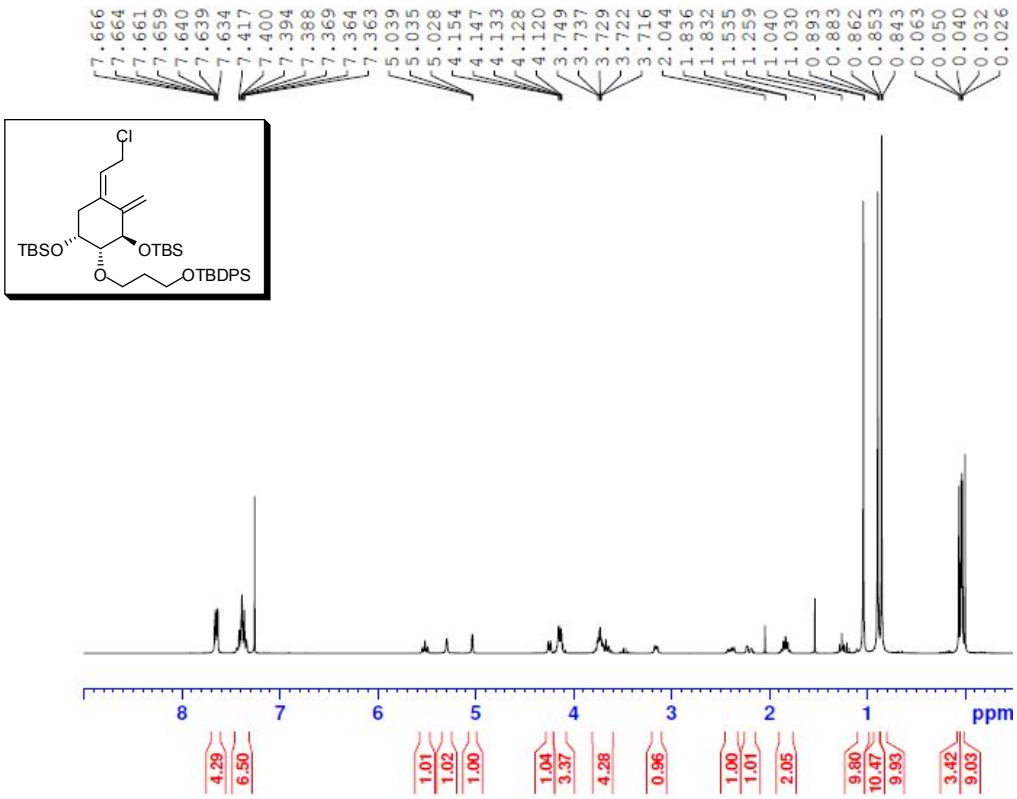
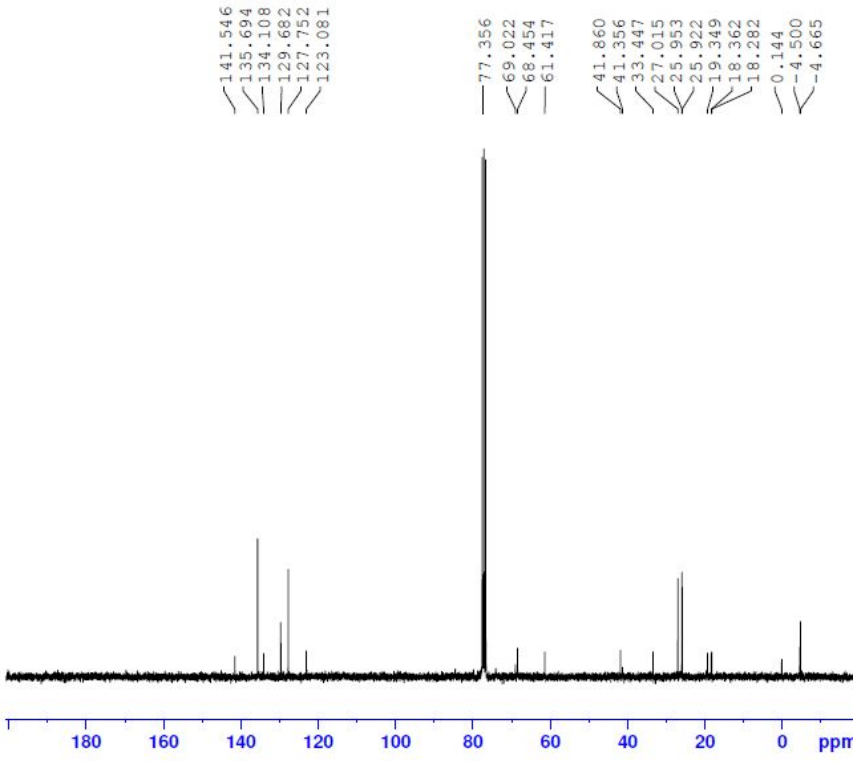
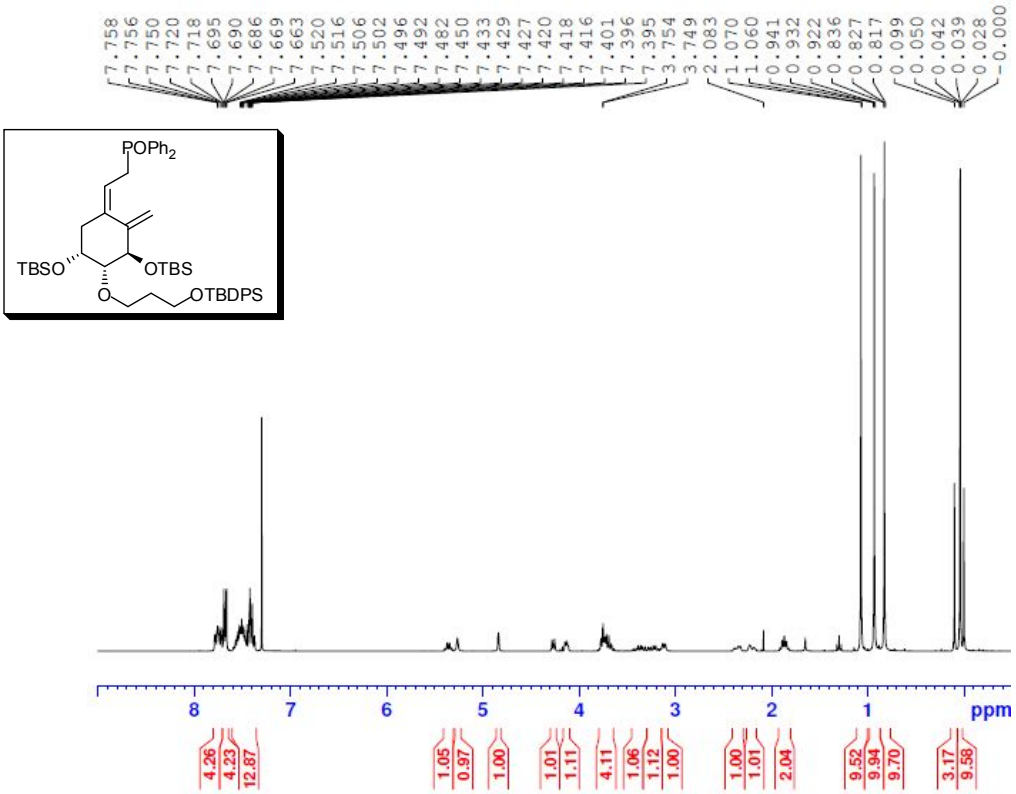


^{13}C NMR ($CDCl_3$, 75 MHz)

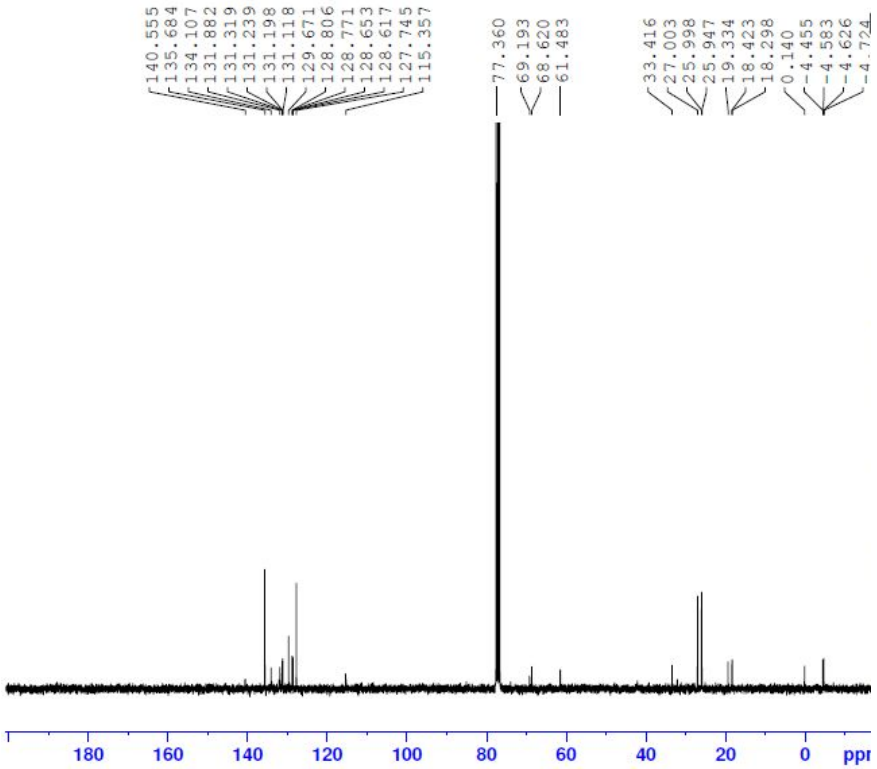


Compound **2**

^{1}H NMR ($CDCl_3$, 300 MHz)

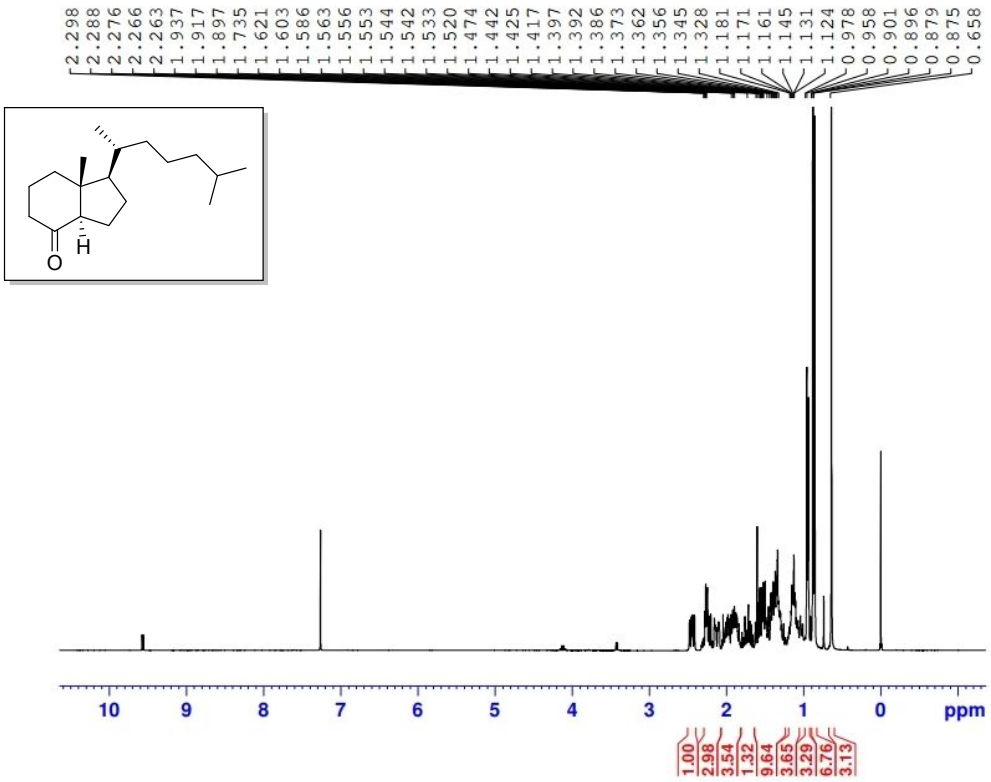


^{13}C NMR ($CDCl_3$, 75 MHz)

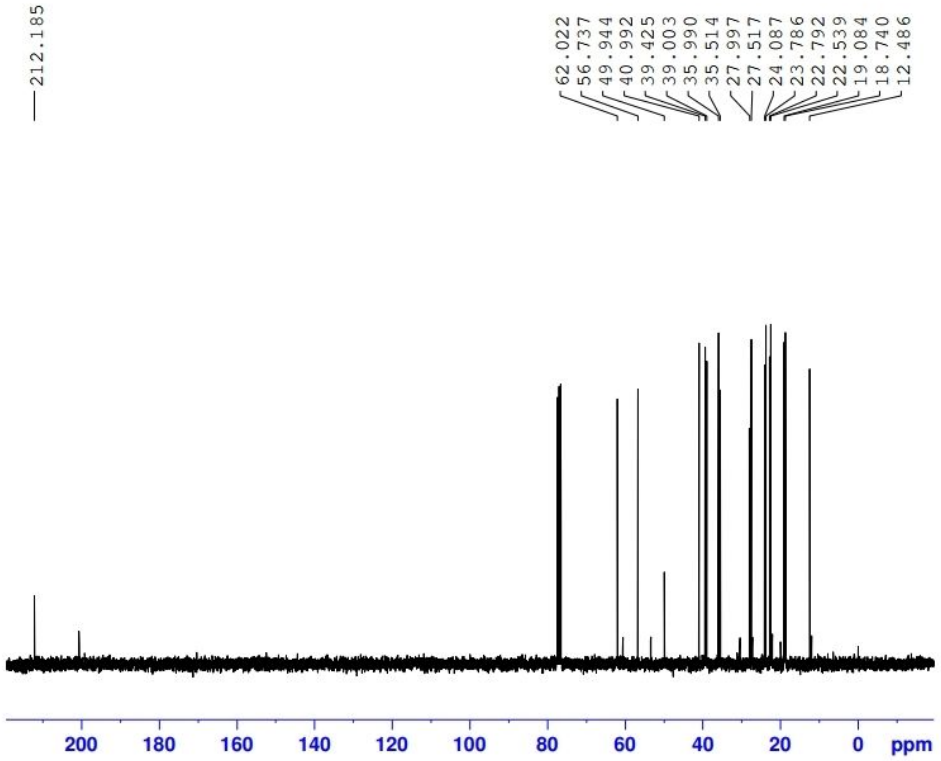


Compound **19**

^{1}H NMR ($CDCl_3$, 300 MHz)

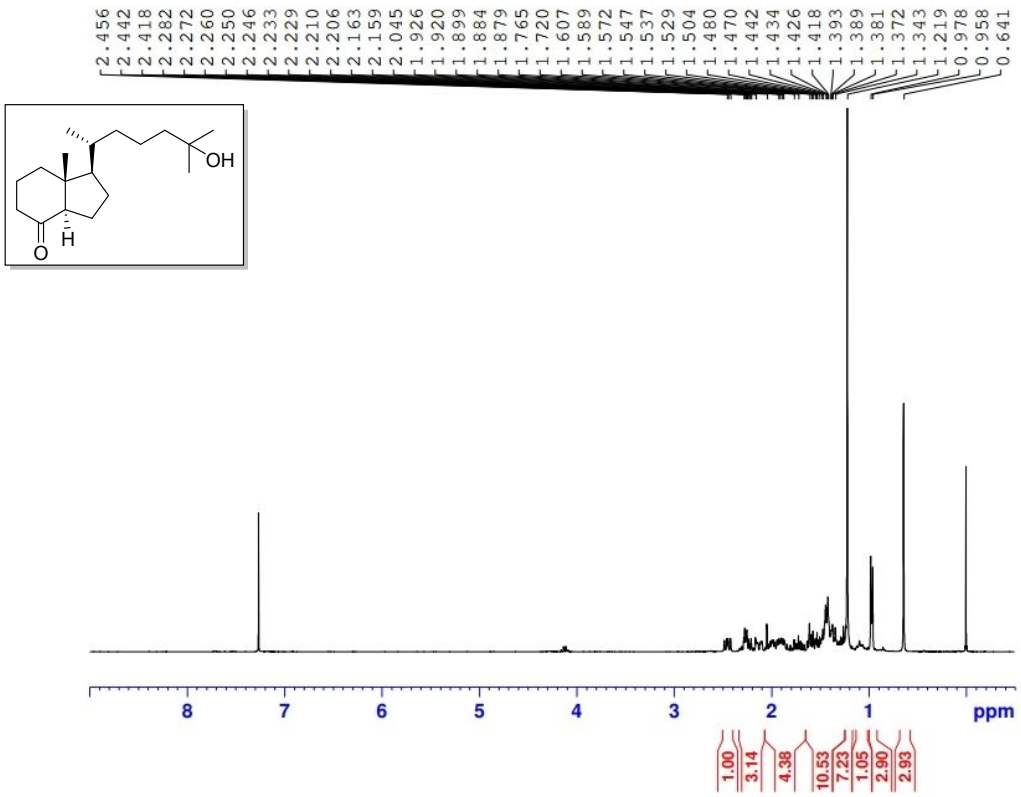


^{13}C NMR ($CDCl_3$, 75 MHz)

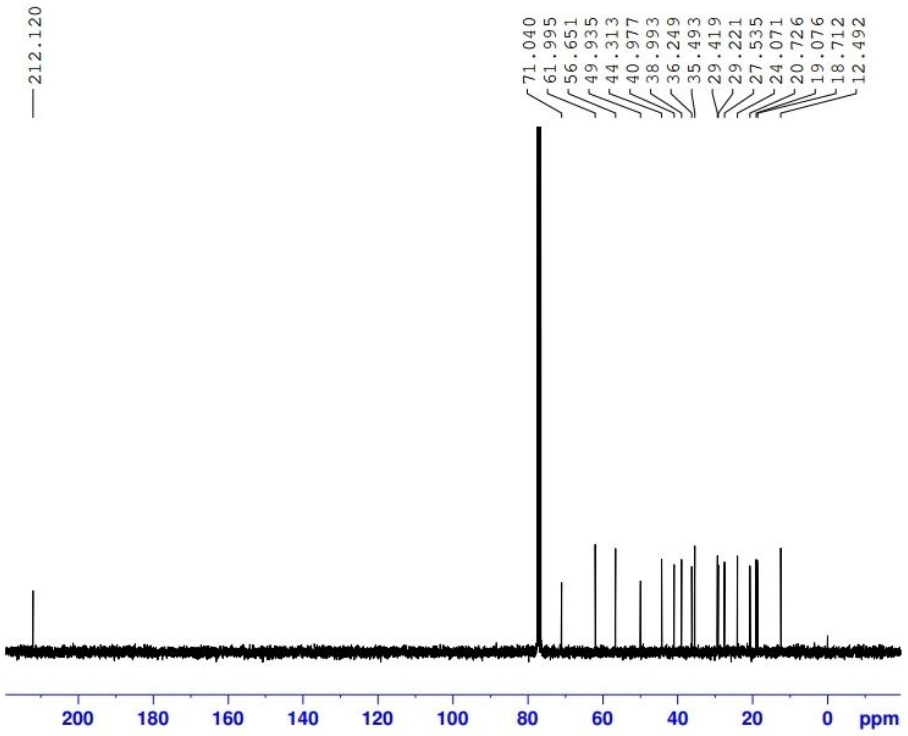


Compound **20**

^{1}H NMR ($CDCl_3$, 300 MHz)

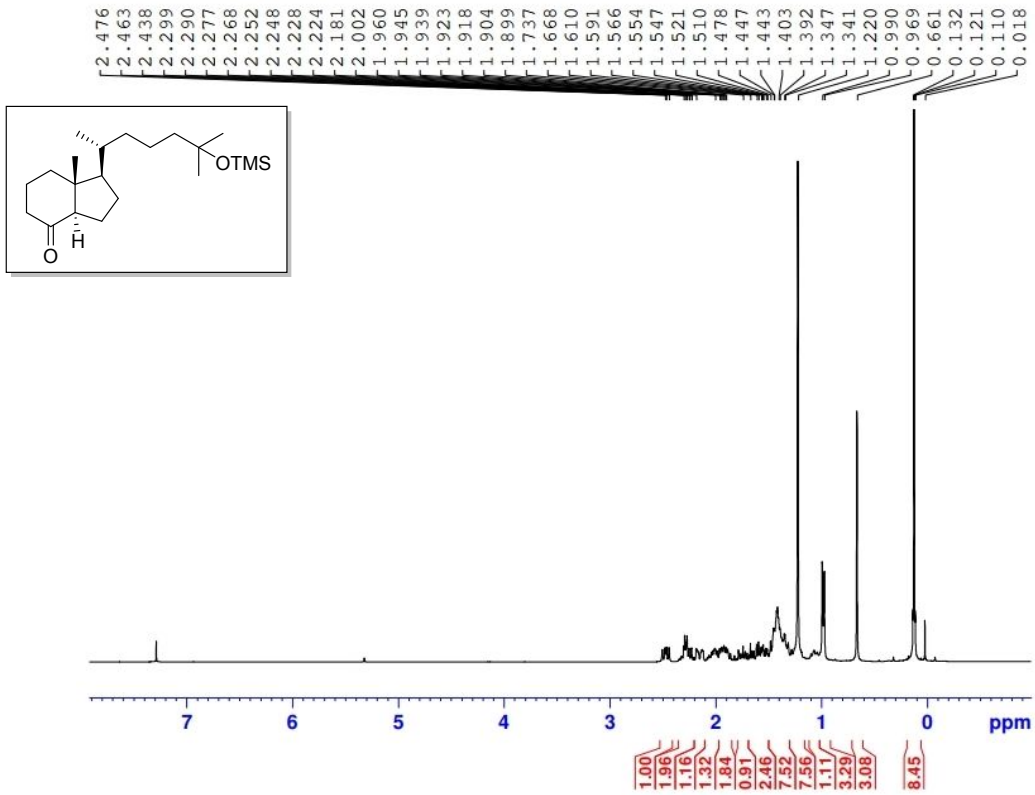


^{13}C NMR ($CDCl_3$, 75 MHz)

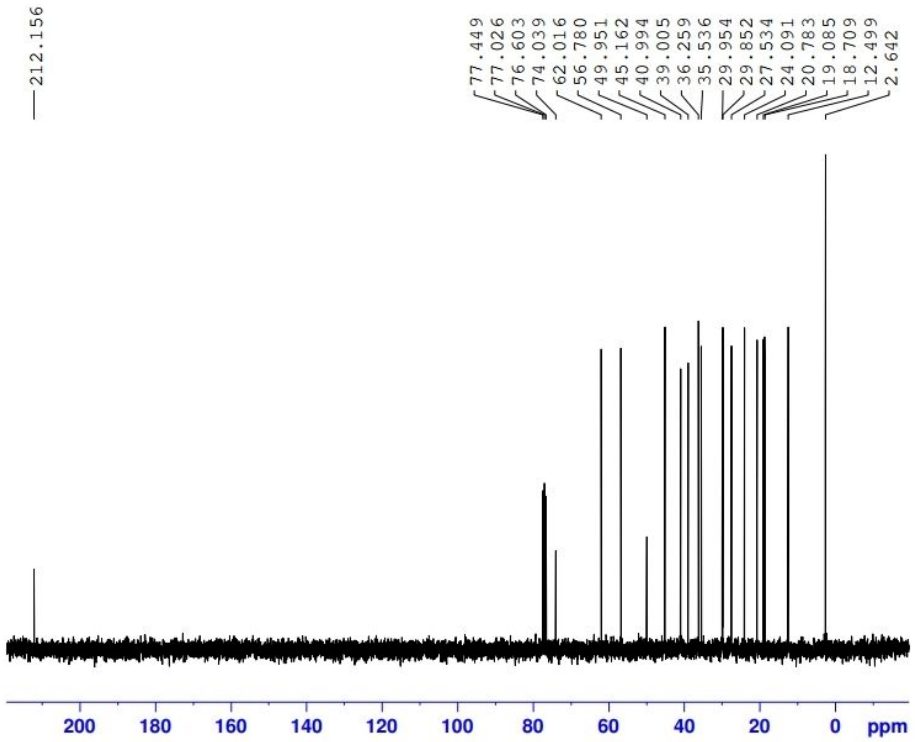


Compound **21**

^{1}H NMR ($CDCl_3$, 300 MHz)

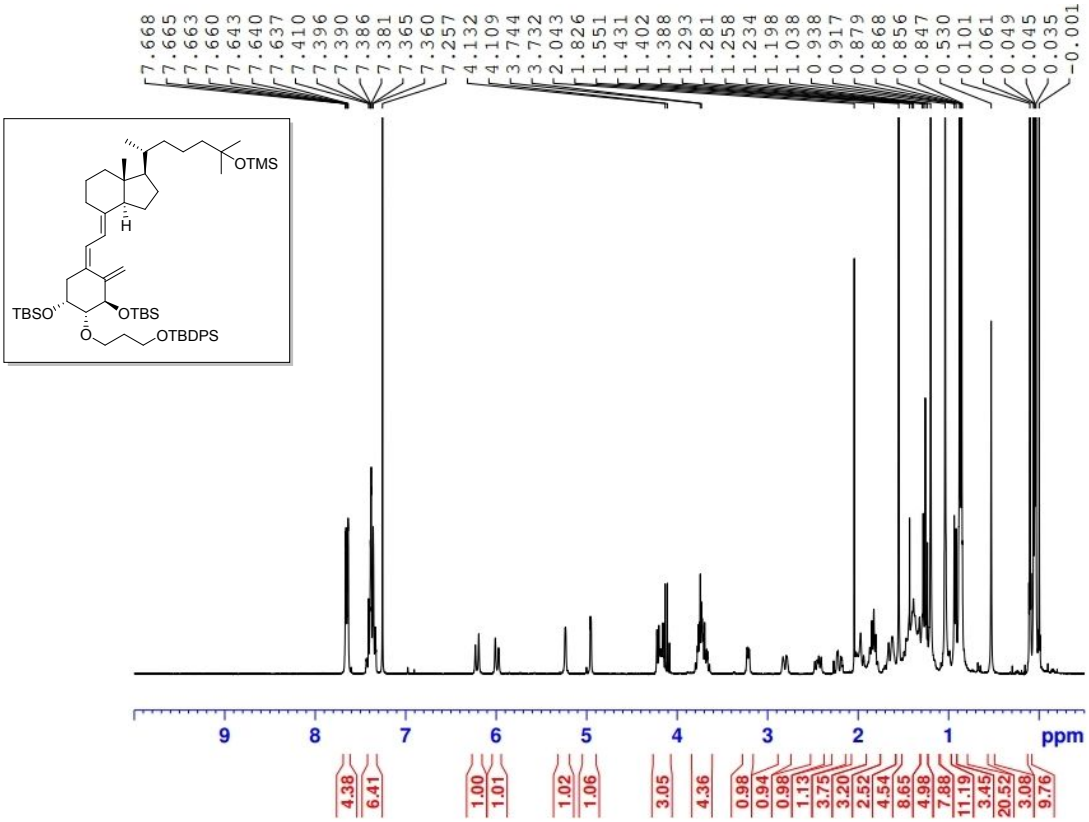


^{13}C NMR ($CDCl_3$, 75 MHz)

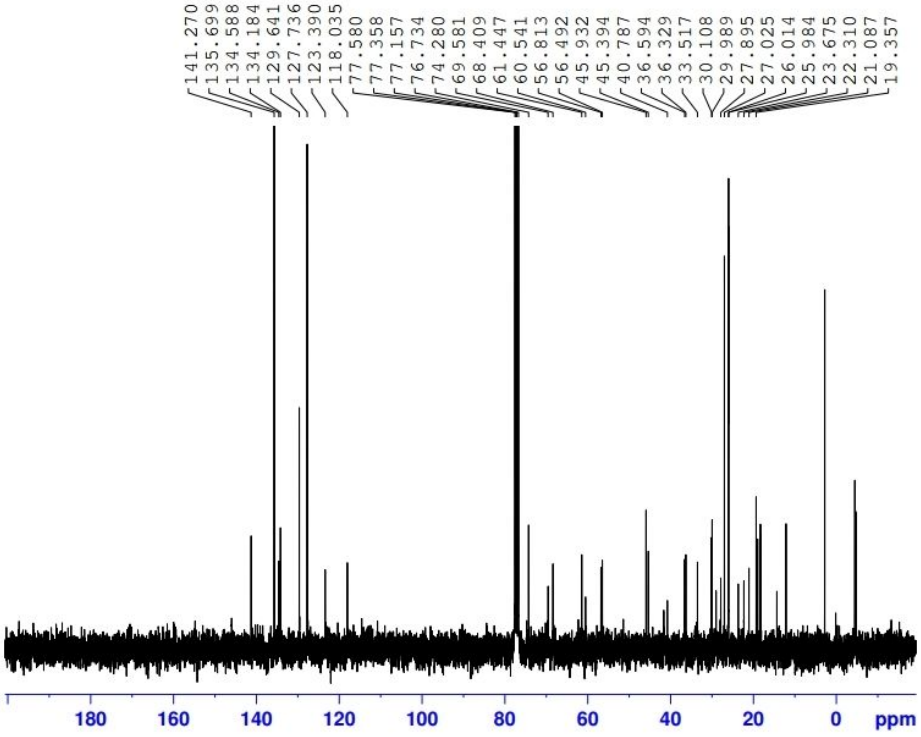


Compound **22**

^{1}H NMR ($CDCl_3$, 300 MHz)

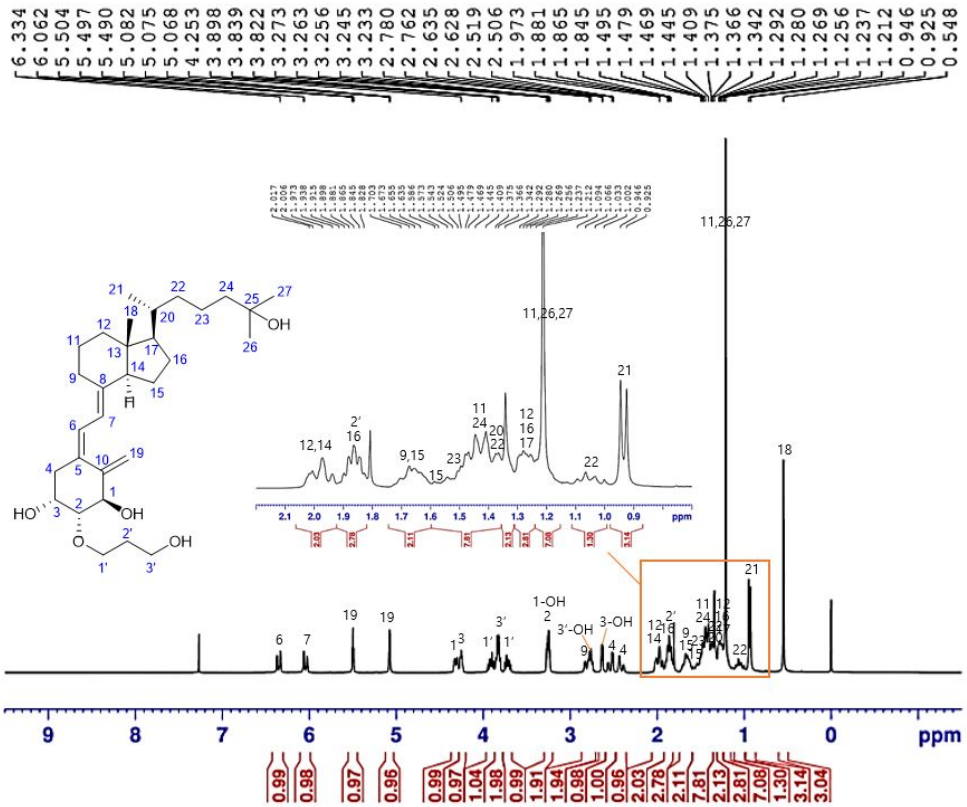


^{13}C NMR ($CDCl_3$, 75 MHz)

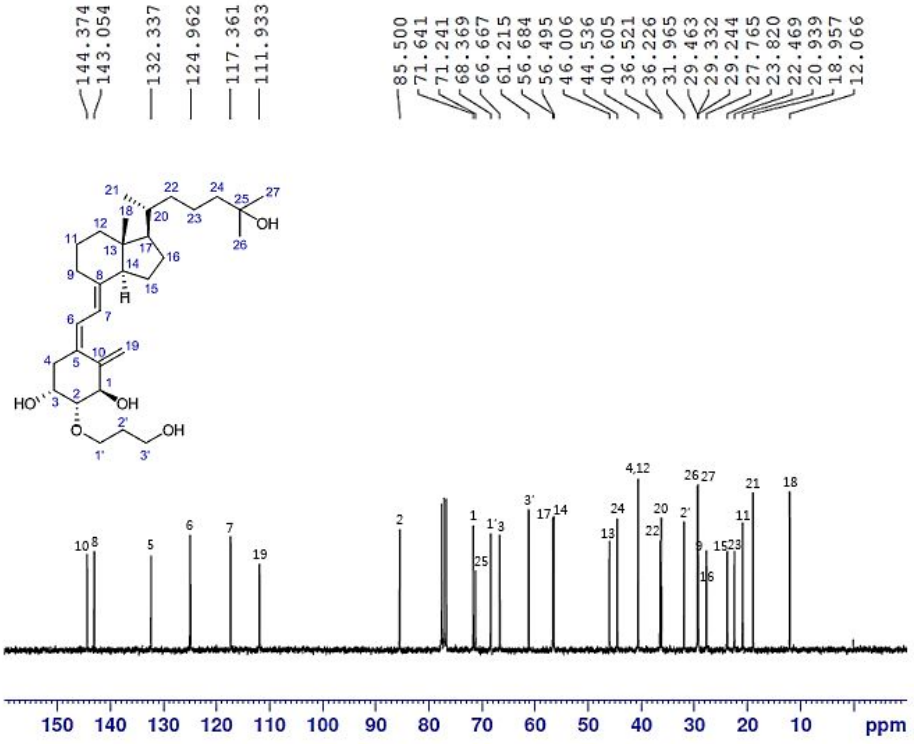


Compound **1** (eldecalcitol)

^{1}H NMR ($CDCl_3$, 300 MHz)

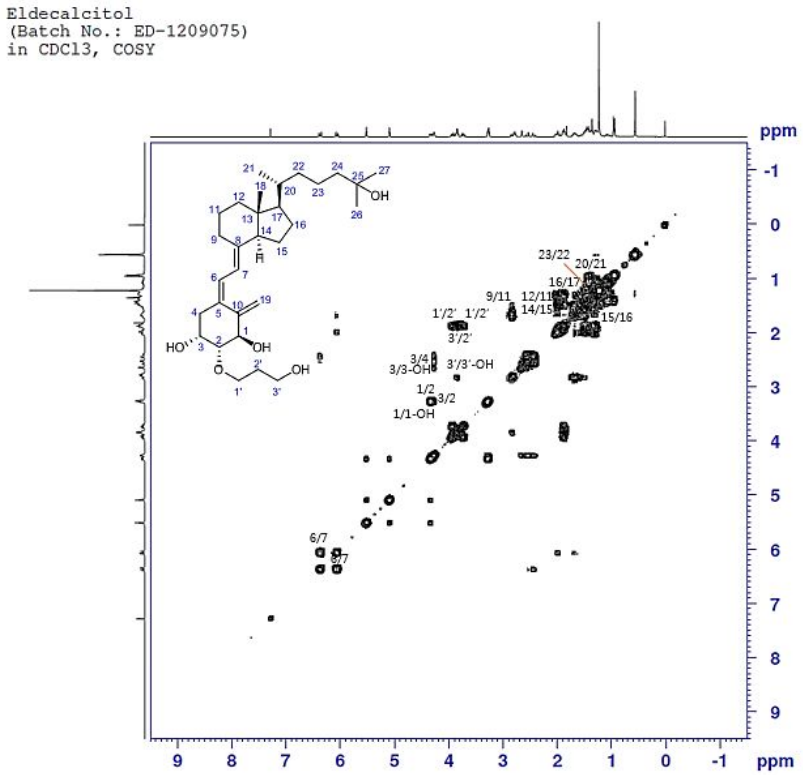


^{13}C NMR ($CDCl_3$, 75 MHz)



Compound **1** (eldecalcitol)

COSY ($CDCl_3$, 300 MHz)



HSQC ($CDCl_3$, 300 MHz)