

*Supporting Information*

*for*

## **A Novel Synthetic Approach to the Bicyclo[5.3.1]undecan-11-one Framework of Vinigrol**

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## 1. General Information

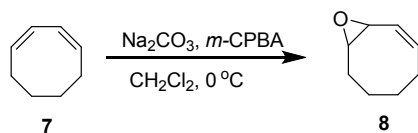
All non-aqueous reactions were run under a positive pressure of nitrogen. Anhydrous solvents were obtained using standard drying techniques. Commercial grade reagents were used without further purification unless stated otherwise. Flash chromatography was performed on 300-400 mesh silica gel with the indicated solvent systems.  $^1\text{H}$  NMR spectra were recorded on a Bruker 400 (400 MHz) spectrometer and chemical shifts are reported in ppm down field from TMS, using TMS (0.00 ppm) or residual chloroform (7.26 ppm) as an internal standard. Data are reported as: (s = singlet, br = broad, d = doublet, t = triplet, q = quartet, hept = heptalet, m = multiplet;  $J$  = coupling constant in Hz, integration.).  $^{13}\text{C}$  NMR spectra were recorded on a Bruker 400 (100 MHz) spectrometer, using proton decoupling unless otherwise noted. Chemical shifts are reported in ppm down field from TMS, using the central resonance of  $\text{CDCl}_3$  (77.00 ppm) as the internal standard. HRMS were recorded by using either FTMS-7 or IonSpec 4.7 spectrometers.

## 2. Experimental Procedures and Spectral Data

1,3-cyclooctadiene was purchased from Aldrich.

3-bromo-2-(bromomethyl)prop-1-ene<sup>[1]</sup> and IBX<sup>[2]</sup> was prepared as described in literature.

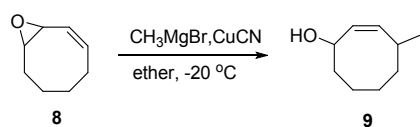
### (Z)-9-oxabicyclo[6.1.0]non-2-ene (2)<sup>[3]</sup>



A 250 mL flask charged with compound 7 (2.1 g, 19.5 mmol), anhydrous  $\text{Na}_2\text{CO}_3$  (5.0 g, 46.8 mmol) and  $\text{CH}_2\text{Cl}_2$  (100 mL) was cooled to  $0\text{ }^\circ\text{C}$ . Then  $m\text{-CPBA}$  (5.3 g, 25.9 mmol, 80% purity) was added portionwise within 20 min. The mixture was stirred at the temperature for 3 h. A mixed solution of saturated  $\text{Na}_2\text{CO}_3$  (30 mL) and saturated  $\text{Na}_2\text{S}_2\text{O}_3$  (30 mL) was added to the mixture until it became clear. The

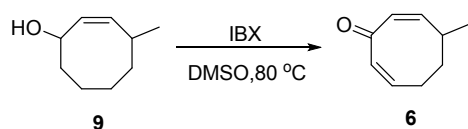
mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> for three times. The combined organic layers were washed with brine (50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated to provide the crude product **8** (2.2 g, crude yield 92%) as yellowish oil. It could be used directly in the next step without further purification. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.83-5.72 (m, 1H), 5.59 (d, *J* = 11.2 Hz, 1H), 3.45 (dd, *J*<sub>1</sub> = 2.8 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 3.11 (dt, *J*<sub>1</sub> = 4.0 Hz, *J*<sub>2</sub> = 8.4 Hz, 1H), 2.31 (m, 1H), 2.14-1.96 (m, 2H), 1.83-1.72 (m, 1H), 1.69-1.59 (m, 2H), 1.53-1.37 (m, 2H).

**(Z)-4-methylcyclooct-2-enol (9)**<sup>[4]</sup>



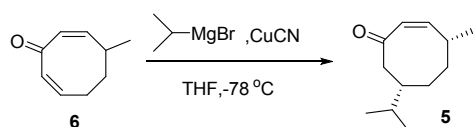
Anhydrous ether (80 mL) was added to a 250 mL flask charged with CuCN (4 g, 45.0 mmol) under N<sub>2</sub>. Then methylmagnesiumbromide (12.5 mL, 37.5 mmol, 3.0 M in THF) was added dropwise at -20 °C. After stirring for 20 min, compound **8** (1.6 g, 12.5 mmol) was added and the mixture was stirred at the temperature for 3 h. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl (50 mL). Insoluble substance was filtered through a pad of celite and the resulting clear solution was extracted with ether for three times. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to provide the crude product **9** (1.5 g, crude yield 86 %) as yellowish oil. It could be used directly in the next step without further purification. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.46 (ddd, *J*<sub>1</sub> = 12.0 Hz, *J*<sub>2</sub> = 5.3 Hz, *J*<sub>3</sub> = 1.3 Hz, 1H), 5.34 (dd, *J*<sub>1</sub> = 12.0 Hz, *J*<sub>2</sub> = 6.2 Hz, 1H), 4.72 (q, *J* = 6.7 Hz, 1H), 2.71 (m, 1H), 1.83-1.76 (m, 2H), 1.68-1.49 (m, 7H), 1.00 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 136.27, 131.05, 69.51, 36.41, 35.31, 32.95, 25.88, 22.84, 22.65; IR (thin film): ν 3334, 3003, 2956, 2926, 2867, 1651, 1454, 1373, 1300, 1057, 1028, 970, 829, 789, 726 cm<sup>-1</sup>; LRMS (EI): 122 (M-H<sub>2</sub>O)<sup>+</sup>; HRMS (EI): calcd. for C<sub>9</sub>H<sub>16</sub>O M<sup>+</sup>: 140.1201, found: 140.1198.

**(2Z,7Z)-4-methylcycloocta-2,7-dienone (6)**



To a 250 mL flask equipped with a stir bar was added compound **9** (2.30 g, 16.4 mmol), DMSO (70 mL) and IBX (13.8 g, 49.2 mmol). After stirring for 7 h at 80 °C the mixture was quenched with a solution of NaHCO<sub>3</sub>. The resulting clear solution was extracted with hexane for several times. The combined organic layers were washed with aqueous NaHCO<sub>3</sub>, then brine and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removing the solvent *in vacuo*, compound **6** (1.96 g, crude yield 88%) was obtained as yellowish oil. It could be used directly in the next step without further purification. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.41 (m, 1 H), 6.27 (d, *J* = 12 Hz, 1H), 6.24 (d, *J* = 11.6 Hz, 1H), 6.03 (dd, *J*<sub>1</sub> = 12 Hz, *J*<sub>2</sub> = 8.5 Hz, 1H), 2.96-2.82 (m, 1H), 2.68-2.55 (m, 1H), 2.19-2.10 (m, 1H), 1.84-1.72 (m, 1H), 1.53-1.42 (m, 1H), 1.11 (d, *J* = 6.5 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): δ 193.82, 148.36, 142.60, 135.58, 133.74, 36.29, 30.99, 25.89, 19.98; **IR** (thin film): ν 2933, 2873, 1639, 1612, 1456, 1403, 1285, 1200, 1115, 1038, 947, 859, 808, 759, 669 cm<sup>-1</sup>; **LRMS** (ESI): 159.1 (M+Na)<sup>+</sup>; **HRMS** (ESI): calcd. for C<sub>9</sub>H<sub>12</sub>NaO (M+Na)<sup>+</sup>: 159.07804, found: 159.07835.

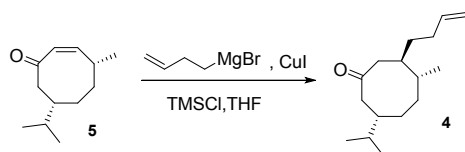
#### **rac-(4R,7S,Z)-7-isopropyl-4-methylcyclooct-2-enone (5)**



A 250mL flask charged with CuCN (4.64 g, 51.8 mmol) was added anhydrous THF(90 mL) under N<sub>2</sub>. Then isopropylmagnesiumbromide (12.5 mL, 12.5 mmol, 1.0 M in THF) was added dropwise at -20 °C. After stirring for 20 min, compound **6** (1.6 g, 12.5 mmol) was added at -78 °C and the mixture was stirred at the temperature for 1 h. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl (30 mL). Insoluble substance was filtered through a pad of celite and the resulting clear solution was extracted with ether. The combined organic layers were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 50/1) to give compound **5** (2.27 g, 88%) as yellowish oil. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 6.00 (dd, *J*<sub>1</sub> = 12.5 Hz, *J*<sub>2</sub> = 5.4 Hz, 1H), 5.87 (dd, *J*<sub>1</sub> = 12.5 Hz, *J*<sub>2</sub> = 2.0 Hz, 1H), 2.70 (dd, *J*<sub>1</sub> = 15.5 Hz, *J*<sub>2</sub> = 5.5 Hz,

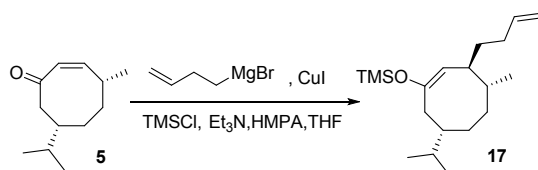
1H), 2.70 (m, 1H), 2.43 (dd,  $J_1 = 15.5$  Hz,  $J_2 = 6.9$  Hz, 1H), 1.83 (m, 1H), 1.68-1.54 (m, 3H), 1.45-1.35 (m, 2H), 1.10 (d,  $J = 6.7$  Hz, 3H), 0.88 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  206.69, 146.69, 130.16, 46.32, 39.69, 34.58, 33.83, 32.47, 29.28, 23.32, 19.70, 19.61; IR (thin film):  $\nu$  3013, 2959, 2904, 2873, 1712, 1656, 1463, 1370, 1271, 1191, 1105, 814, 747, 685  $\text{cm}^{-1}$ ; LRMS (ESI): 203.1 ( $\text{M}+\text{Na}$ ) $^+$ ; HRMS (ESI): calcd. for  $\text{C}_{12}\text{H}_{20}\text{NaO}$  ( $\text{M}+\text{Na}$ ) $^+$ : 203.14064, found: 203.14053.

**rac-(3R,4R,7S)-3-(but-3-enyl)-7-isopropyl-4-methylcyclooctanone (4)**



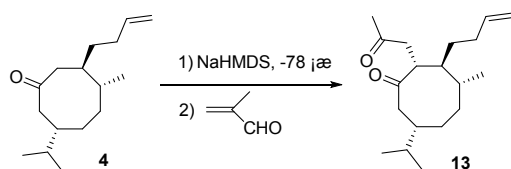
A 25 mL flask charged with CuI (1.6 g, 8.40 mmol) was added anhydrous THF (3 mL) under  $\text{N}_2$ . Then 3-Butenylmagnesium bromide (14 mL, 0.5 M in THF, 0.700 mmol) was added dropwise at  $-20$   $^\circ\text{C}$ . After stirring at the temperature for 20 min, a solution of compound **5** (422 mg, 2.34 mmol) and TMSCl (1.5 mL, 11.7 mmol) in THF (3.5 mL) was added at  $-20$   $^\circ\text{C}$ . The mixture was warmed to room temperature naturally and stirred for 6 h. The reaction was quenched with a saturated solution of  $\text{NH}_4\text{Cl}$  (10 mL). Insoluble substance was filtered through a pad of celite and the resulting clear solution was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layer was washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 100/1) to give compound **4** (486 mg, 88 %) as colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.81 (m, 1H), 5.00 (m, 2H), 2.46-2.29 (m, 3H), 2.20-2.09 (m, 2H), 2.06-1.95 (m, 1H), 1.90-1.83 (m, 1H), 1.81-1.72 (m, 1H), 1.71-1.60 (m, 2H), 1.56-1.40 (m, 3H), 1.32-1.23 (m, 3H), 0.97 (d,  $J = 6.6$  Hz, 3H), 0.91 (d,  $J = 6.4$  Hz, 3H), 0.88 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  217.18, 138.51, 114.50, 48.92, 45.09, 44.06, 39.97, 36.77, 33.40, 32.62, 32.28, 30.53, 26.29, 19.76, 19.70, 19.09; IR (thin film):  $\nu$  3077, 2959, 2876, 1698, 1641, 1466, 1387, 1369, 1262, 1097, 1020, 910, 802  $\text{cm}^{-1}$ ; LRMS (ESI): 259.2 ( $\text{M}+\text{Na}$ ) $^+$ ; HRMS (ESI): calcd. for  $\text{C}_{16}\text{H}_{28}\text{NaO}$  ( $\text{M}+\text{Na}$ ) $^+$ : 259.20324, found: 259.20328.

**rac-((3S,4R,7S,E)-3-(but-3-enyl)-7-isopropyl-4-methylcyclooct-1-enyloxy)trimethylsilane (17)**



A 5 mL flask charged with CuI (6.0 mg, 0.032 mmol) was added 3-butenylmagnesium bromide (0.9 mL, 0.5 M in THF, 0.045 mmol) dropwise under N<sub>2</sub> at -20 °C. After stirring at the temperature for 15 min, HMPA (0.11 mL, 0.63 mmol) was added and the mixture was stirred for another 10 min. Then a solution of compound **5** (28 mg, 0.16 mmol) and TMSCl (80 μL, 0.64 mmol) in THF (0.4 mL) was added. The mixture was stirred at -20 °C for 6 h. Et<sub>3</sub>N (90 μL, 0.64 mmol) was added and the mixture was concentrated *in vacuo* directly. The residue was purified via flash chromatography on alumina (Hexane) to give compound **17** (42 mg, 89 %) as colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.81 (m, 1H), 4.95 (m, 2H), 4.33 (d, *J* = 9.3 Hz, 1H), 2.23-2.10 (m, 2H), 1.99-1.89 (m, 1H), 1.86-1.66 (m, 4H), 1.62-1.55 (m, 1H), 1.49-1.32 (m, 4H), 1.29-1.21 (m, 1H), 1.15-1.05 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 6.9 Hz, 6H), 0.20 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 151.93, 139.39, 114.01, 111.78, 45.05, 41.08, 38.69, 36.72, 34.46, 33.23, 32.85, 32.44, 25.82, 19.42, 18.89, 18.21; IR (thin film): ν 3077, 2956, 2872, 1664, 1640, 1465, 1368, 1261, 1251, 1187, 1150, 1107, 974, 907, 845, 752 cm<sup>-1</sup>; LRMS (ESI): 331.3 (M+Na)<sup>+</sup>.

**rac-(2R,3S,4R,7S)-3-(but-3-en-1-yl)-7-isopropyl-4-methyl-2-(2-oxopropyl)cyclooctanone (13)**

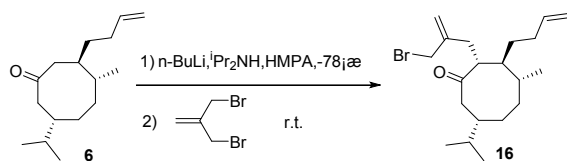


A solution of compound **4** (38 mg, 0.16 mmol) in THF (1 mL) was added a solution of NaHMDS (0.12 mL, 2.0 M in THF, 0.24 mmol) at -78 °C. After stirring for 20 min, 2-methylpropanal (27 μL, 0.32 mmol) was added and the mixture continued to be stirred at this temperature for 11 h. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl and extracted with hexane. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was

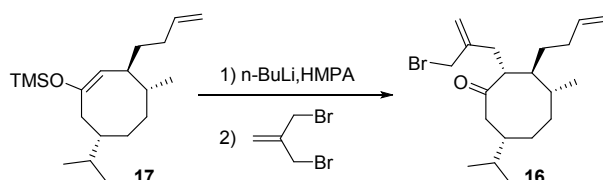
purified via flash chromatography on silica gel (Hexane/EtOAc = 60/1) to give compound **13** (8 mg, 13% or 28% b.r.s.m.) with recovered compound **4** (15 mg). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.79 (m, 1H), 4.98 (m, 2H), 3.21 (td,  $J_1 = 10.9$  Hz,  $J_2 = 2.8$  Hz, 1H), 3.06 (dd,  $J_1 = 17.7$  Hz,  $J_2 = 11.1$  Hz, 1H), 2.75 (d,  $J = 14.3$  Hz, 1H), 2.57 (dd,  $J_1 = 17.8$  Hz,  $J_2 = 3.4$  Hz, 1H), 2.25-1.82 (m, 3H), 2.10 (s, 3H), 1.95-1.82 (m, 1H), 1.67-1.44 (m, 4H), 1.35-1.21 (m, 5H), 0.95 (m, 9H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): δ 220.33, 208.17, 138.44, 114.50, 48.25, 47.87, 47.03, 45.77, 38.41, 34.51, 33.50, 32.66, 31.23, 30.05, 29.16, 27.59, 23.17, 19.89, 19.54; **IR** (thin film): ν 3076, 2943, 2924, 2851, 1718, 1695, 1641, 1464, 1369, 1261, 1166, 1104, 1027, 911, 804., 754 cm<sup>-1</sup>; **LRMS** (ESI): 315.1 (M+Na)<sup>+</sup>; **HRMS** (ESI): calcd. for C<sub>19</sub>H<sub>32</sub>NaO<sub>2</sub> (M+Na)<sup>+</sup>: 315.22945, found: 315.22960.

**rac-(2R,3S,4R,7S)-2-(2-(bromomethyl)allyl)-3-(but-3-en-1-yl)-7-isopropyl-4-methylcyclooctanone (16)**

**Procedure 1:**



**Procedure 2:**



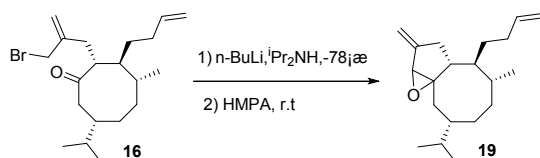
**Procedure 1:** A solution of diisopropylamine (38 μL, 0.27 mmol) in THF (0.4 mL) was added n-butyllithium (0.10 mL, 2.4 M in hexane, 0.24 mmol) dropwise at 0 °C and the mixture was stirred at the temperature for 15 min. After cooling down to -78 °C, a solution of compound **6** (45 mg, 0.19 mmol) and HMPA (0.1 mL, 0.57 mmol) in THF (0.4 mL) was added and the mixture was stirred for 50 min. Then a solution of 3-bromo-2-(bromomethyl)prop-1-ene (82 mg, 0.38 mmol) in THF (0.3 mL) was added after the temperature was warmed up to -30 °C. The mixture continued to be stirred overnight with warming to room temperature naturally. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The

combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 200/1) to give **16** (18 mg, 26% or b.r.s.m 59%, regioisomeric ratio 9/1 as determined by NMR) with recovered compound **6** (25 mg).

**Procedure 2:** A solution of compound **17** (190 mg, 0.63 mmol) in THF (3 mL) was added n-butyllithium (0.33 mL, 2.5 M in hexane, 0.83 mmol) dropwise at -25 °C. The mixture was stirred at the temperature for 30 min until the substrate disappeared. HMPA (0.22 mL, 1.26 mmol) was added and the mixture was stirred for another 10 min. Then a solution of 3-bromo-2-(bromomethyl)prop-1-ene (300 mg, 1.39 mmol) in THF (0.8 mL) was added. The mixture was warmed to room temperature naturally and stirred for 3 h. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 200/1) to give compound **16** (101 mg, 44 %).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.83 (m, 1H), 5.14 (br s, 1H), 5.02 (m, 2H), 4.86 (br s, 1H), 4.11 (d, *J* = 10.0 Hz, 1H), 3.89 (d, *J* = 10.0 Hz, 1H), 2.83-2.71 (m, 2H), 2.34 (t, *J* = 12.3 Hz, 1H), 2.17 (t, *J* = 13.0 Hz, 1H), 2.10-1.98 (m, 2H), 1.93 (m, 1H), 1.85 (m, 1H), 1.71-1.34 (m, 8H), 1.27-1.18(m, 1H), 0.97 (d, *J* = 6.0 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): δ 218.44, 143.14, 138.65, 117.52, 114.60, 53.11, 43.98, 43.81, 43.75, 35.95, 35.22, 34.59, 33.10, 32.29, 28.24, 27.80, 27.41, 21.31, 19.96, 19.24; **IR** (thin film): ν 3077, 2958, 2927, 1698, 1640, 1466, 1439, 1369, 1322, 1210, 1081, 992, 911, 632 cm<sup>-1</sup>; **LRMS** (ESI): 391.0, 393.2 (M+Na)<sup>+</sup>; **HRMS** (ESI): calcd. for C<sub>20</sub>H<sub>33</sub>BrNaO (M+Na)<sup>+</sup>: 391.16070, found: 391.16112.

**rac-(3aR,4S,5R,8S)-4-(but-3-en-1-yl)-8-isopropyl-5-methyl-2-methylenedecahydrocycloocta[1,5]cyclopenta[1,2-b]oxirene (19)**

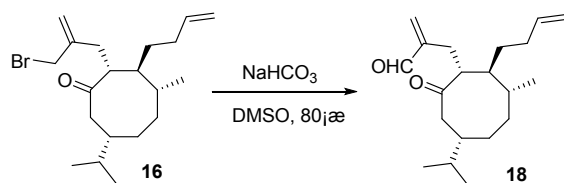


A solution of diisopropylamine (45 μL, 0.322 mmol) in THF (0.4 mL) was added n-



butyllithium (0.12 mL, 2.4 M in hexane, 0.293 mmol) dropwise at 0 °C and the mixture was stirred at the temperature for 15 min. After cooling down to -78 °C, a solution of compound **16** (54 mg, 0.146 mmol) and HMPA (51  $\mu$ L, 0.293 mmol) in THF (0.35 mL) was added. After 40 min the mixture was gradually warmed up to room temperature and stirred overnight. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 200/1) to give compound **19** (20 mg, 45 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  5.80 (m, 1 H), 5.17 (br s, 1H), 4.97 (br s, 1H), 4.95 (m, 2H), 3.34 (s, 1H), 2.63 (dd,  $J_1 = 16.3$  Hz,  $J_2 = 8.2$  Hz, 1H), 2.26-2.12 (m, 2H), 2.05-1.90 (m, 4H), 1.65-1.21 (m, 10H), 0.99 (d,  $J = 7.0$  Hz, 3H), 0.84 (d,  $J = 6.8$  Hz, 3H), 0.84 (d,  $J = 6.5$  Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  147.47, 139.35, 114.05, 109.68, 70.57, 70.34, 48.13, 42.49, 38.62, 38.46, 36.49, 33.46, 32.46, 30.61, 29.99, 28.48, 23.05, 19.48, 19.34; IR (thin film):  $\nu$  3076, 2956, 2926, 1661, 1640, 1598, 1466, 1386, 1369, 993., 908, 890, 863 cm<sup>-1</sup>; LRMS (ESI): 311.1 (M+Na)<sup>+</sup>; HRMS (ESI): calcd. for C<sub>20</sub>H<sub>32</sub>NaO (M+Na)<sup>+</sup>: 311.23454, found: 311.23499.

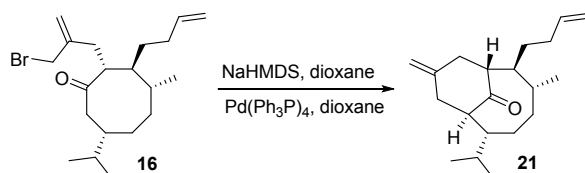
**rac-2-(((1R,2S,3R,6S)-2-(but-3-en-1-yl)-6-isopropyl-3-methyl-8-oxocyclooctyl)methyl)acrylaldehyde (18)**



A 25 mL flask charged with DMSO (0.6 mL) was added compound **16** (21 mg, 0.0570 mmol) and NaHCO<sub>3</sub> (14 mg, 0.167 mmol). The mixture was warmed to 80 °C and stirred at the temperature for 6 h under Ar. After completing the reaction water was added and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 100/1) to give compound **18** (14 mg, 81 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.47 (s, 1H), 6.17 (br s, 1H), 5.98 (br s, 1H), 5.85 (m, 1H), 5.01 (m, 2H), 2.93 (m, 1H), 2.69 (dd,  $J_1 = 12.9$  Hz,

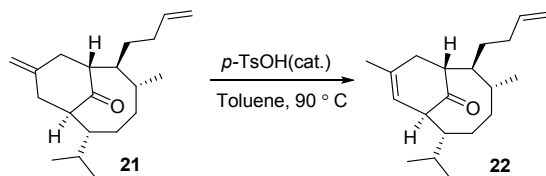
$J_2 = 3.2$  Hz, 1H), 2.25 (q,  $J = 11.9$  Hz, 2H), 2.20 (m, 1H), 2.04 (m, 1H), 1.91 (m, 1H), 1.80 (m, 1H), 1.76-1.60 (m, 2H), 1.59-1.47 (m, 4H), 1.40-1.32 (m, 2H), 1.29-1.81 (m, 1H), 0.96 (d,  $J = 5.5$  Hz, 3H), 0.87 (d,  $J = 6.8$  Hz, 3H), 0.84 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  218.71, 194.21, 147.58, 138.84, 136.62, 114.35, 51.91, 46.51, 46.06, 41.45, 34.57, 32.84, 32.79, 30.38, 28.91, 28.47, 27.60, 22.03, 19.83, 19.29 ; IR (thin film):  $\nu$  3076, 2958, 2828, 1695, 1640, 1465, 1387, 1370, 1261, 1178, 1102, 993, 911, 760  $\text{cm}^{-1}$ ; LRMS (ESI): 305.3 ( $[\text{M}+\text{H}]^+$ ), 327.3 ( $[\text{M}+\text{Na}]^+$ ); HRMS (ESI): calcd. for  $\text{C}_{20}\text{H}_{32}\text{NaO}_2$  ( $\text{M}+\text{Na}$ ) $^+$ : 327.22945, found: 327.22852.

**rac-(1R,2S,3R,6R,7R)-2-(but-3-en-1-yl)-6-isopropyl-3-methyl-9-methylenebicyclo[5.3.1]undecan-11-one (21)**



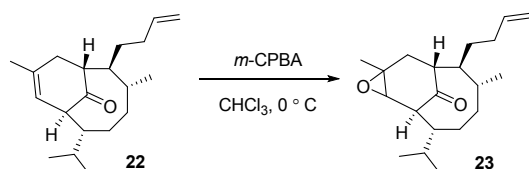
A solution of NaHMDS (0.86 mL, 2.0 M in THF, 1.72 mmol) was added to a solution of compound **16** (487 mg, 1.32 mmol) in toluene (4 mL) at  $-78$  °C under  $\text{N}_2$ . After stirring for 25 min at the temperature, the mixture was warmed to room temperature. And a solution of  $\text{Pd}(\text{PPh}_3)_4$  (305 mg, 0.264 mmol) in toluene (1 mL) was added. The mixture was stirred for 6 h. The reaction was quenched with a saturated solution of  $\text{NH}_4\text{Cl}$  and extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layer was washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 150/1) to give compound **21** (239 mg, 63 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.81 (m, 1H), 4.97 (m, 2H), 4.84 (br s, 1H), 4.77 (br s, 1H), 3.23 (td,  $J_1 = 12.6$  Hz,  $J_2 = 6.1$  Hz, 1H), 2.74-2.63 (m, 3H), 2.31 (q,  $J = 6.4$  Hz, 1H), 2.15 (t,  $J = 13.6$  Hz, 1H), 2.09-2.02 (m, 1H), 1.84 (m, 1H), 1.78-1.64 (m, 3H), 1.63-1.50 (m, 4H), 1.50-1.41 (m, 2H), 1.39-1.35 (m, 1H), 1.27-1.24 (m, 1H), 0.96 (d,  $J = 7.6$  Hz, 3H), 0.93 (d,  $J = 6.4$  Hz, 3H), 0.82 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  219.04, 143.02, 138.94, 114.42, 112.74, 52.44, 51.93, 49.74, 41.72, 39.36, 38.07, 37.80, 32.65, 31.22, 31.13, 30.93, 23.82, 21.49, 20.65, 19.17; IR (thin film): 3074, 2956, 2926, 2872, 1728, 1700, 1641, 1466, 1415, 1387, 1369, 1109, 995, 908, 612  $\text{cm}^{-1}$ ; LRMS (ESI): 311.1 ( $\text{M}+\text{Na}$ ) $^+$ ; HRMS (ESI): calcd. for  $\text{C}_{20}\text{H}_{32}\text{NaO}$  ( $\text{M}+\text{Na}$ ) $^+$ : 311.23454, found: 311.23488.

**rac-(1R,2S,3R,6R,7S)-2-(but-3-en-1-yl)-6-isopropyl-3,9-dimethylbicyclo[5.3.1]undec-8-en-11-one (22)**



A 5 mL flask charged with toluene (2 mL) was added compound **21** (58 mg, 0.2 mmol) and TsOH·H<sub>2</sub>O (2 mg, 0.01 mmol). The mixture was warmed to 90 °C and stirred at the temperature for 6 h. The reaction was quenched with a saturated solution of NaHCO<sub>3</sub> and extracted with ether. The combined organic layer was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 100/1) to give compound **22** (53 mg, 92 %). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.82 (m, 1H), 5.56 (m, 1H), 4.99 (m, 2H), 3.24 (td, *J*<sub>1</sub> = 12.4 Hz, *J*<sub>2</sub> = 4.8 Hz, 1H), 2.46-2.36 (m, 2H), 2.21-2.06 (m, 2H), 2.06-1.94 (m, 1H), 1.92-1.71 (m, 4H), 1.70(s, 3H), 1.63-1.51 (m, 2H), 1.47-1.36 (m, 2H), 1.20-1.07 (m, 2H), 1.01 (d, *J* = 7.5 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): δ 217.78, 138.98, 137.01, 127.22, 114.42, 55.84, 53.85, 50.36, 39.54, 38.19, 36.43, 33.92, 33.04, 31.75, 30.90, 23.24, 22.76, 21.57, 19.86, 19.08; **IR** (thin film): ν 3076, 2958, 2928, 2875, 1733, 1698, 1641, 1466, 1386, 1391, 1260, 1096, 1034, 901, 844, 804 cm<sup>-1</sup>; **LRMS** (ESI): 311.3 ([M+Na]<sup>+</sup>); **HRMS** (ESI): calcd. for C<sub>20</sub>H<sub>32</sub>NaO (M+Na)<sup>+</sup>: 311.23454, found: 311.23544.

**rac-(1R,2S,3R,6R,7S)-2-(but-3-en-1-yl)-6-isopropyl-3,10-dimethyl-9-oxatricyclo[5.4.1.08,10]dodecan-12-one (23)**



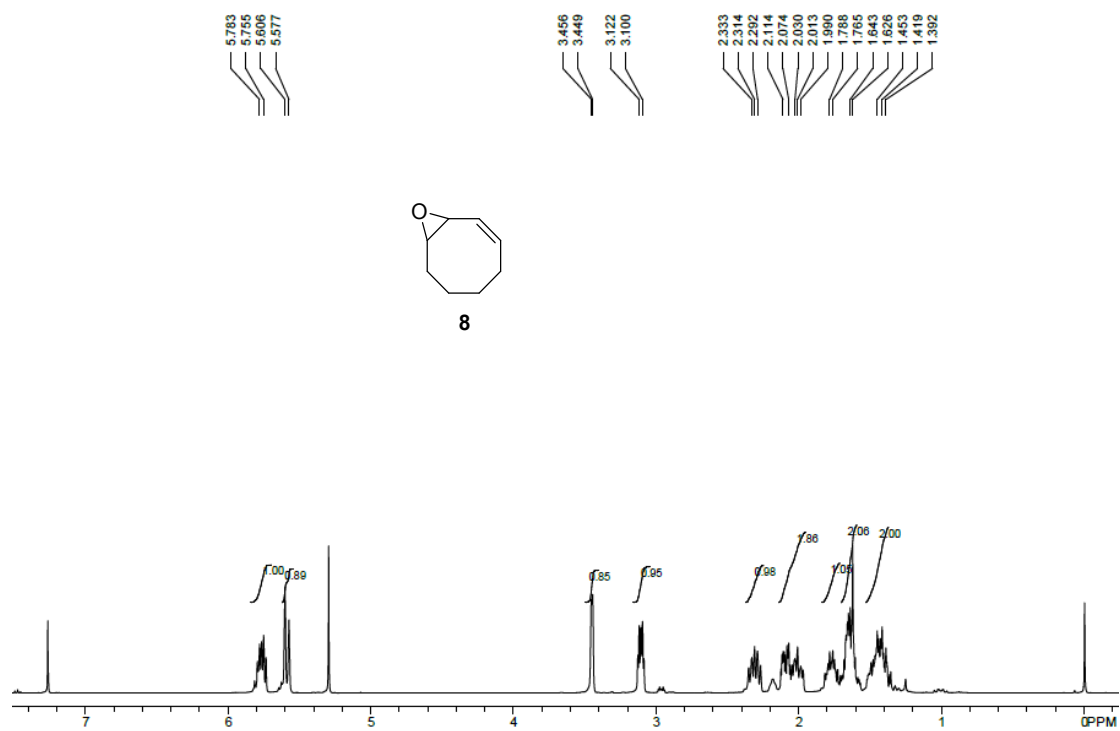
A 25 mL flask charged with CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was added compound **22** (10 mg, 0.036 mmol) and *m*-CPBA (2 mg, 0.036 mmol, 80% purity) at 0 °C. The mixture was stirred at the temperature for 1 h. The reaction was quenched with a saturated solution of

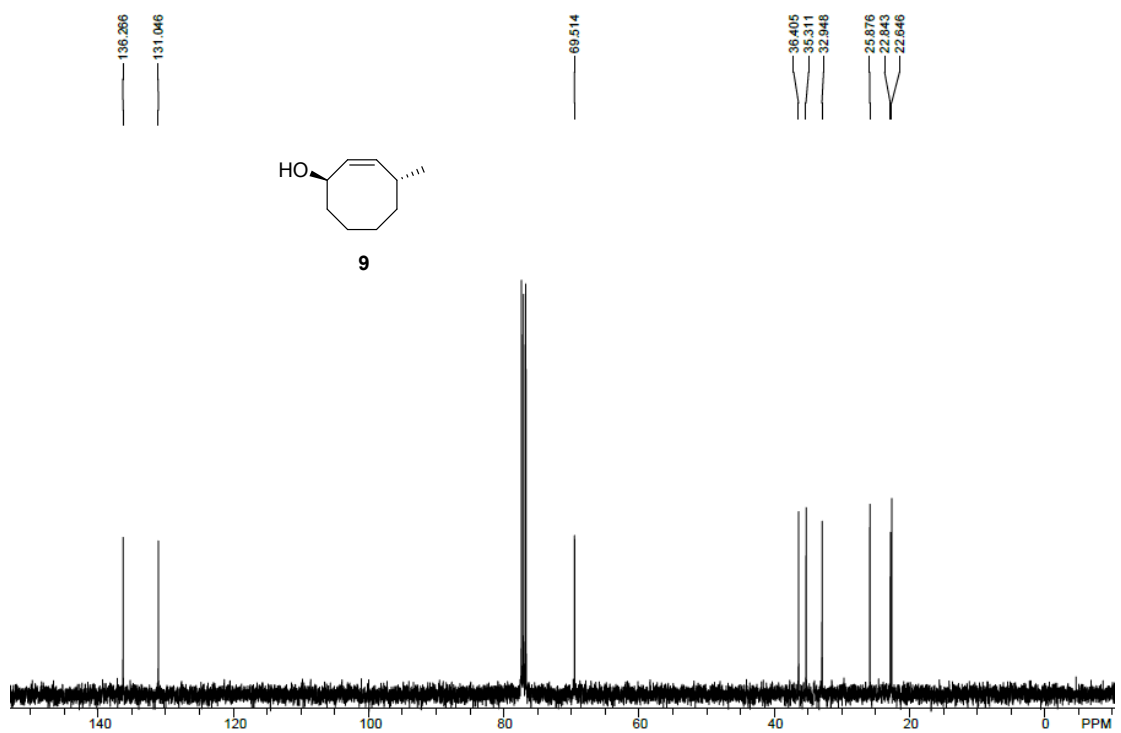
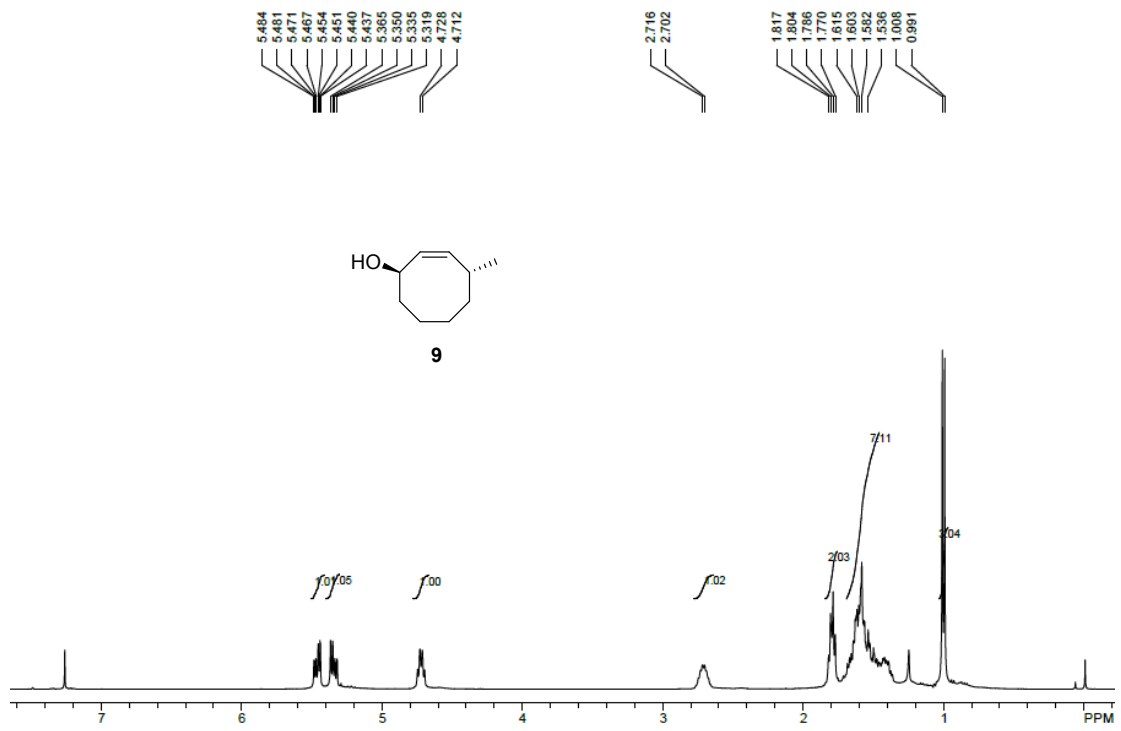
Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and filtered through a pad of celite. The filtrate was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layer was washed with saturated solution of Na<sub>2</sub>CO<sub>3</sub> and brine successively, then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified via flash chromatography on silica gel (Hexane/EtOAc = 100/1) to give compound **23** (9.1 mg, 82 %) as yellowish oil. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.79 (m, 1H), 4.97 (m, 2H), 3.12 (dd, *J*<sub>1</sub> = 5.6 Hz, *J*<sub>2</sub> = 1.3 Hz, 1H), 2.80 (td, *J*<sub>1</sub> = 12.5 Hz, *J*<sub>2</sub> = 4.3 Hz, 1H), 2.39-2.31 (m, 2H), 2.19-2.06 (m, 2H), 2.03-1.91 (m, 1H), 1.83-1.65 (m, 4H), 1.62-1.49 (m, 2H), 1.43-1.32 (m, 2H), 1.31 (s, 3H), 0.97-0.89 (m, 9H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): δ 216.08, 138.84, 114.47, 63.67, 59.85, 49.93, 47.37, 44.19, 37.69, 36.78, 35.81, 33.72, 33.42, 31.31, 30.60, 22.94, 22.67, 21.35, 19.90, 18.93; **IR** (thin film): ν 3076, 2959, 2928, 2873, 1732, 1641, 1455, 1379, 1260, 1093, 1034, 909, 868, 804 cm<sup>-1</sup>; **LRMS** (ESI): 327.2 ([M+Na]<sup>+</sup>); **HRMS** (ESI): calcd. for C<sub>20</sub>H<sub>32</sub>NaO<sub>2</sub> (M+Na)<sup>+</sup>: 327.22945, found: 327.23087.

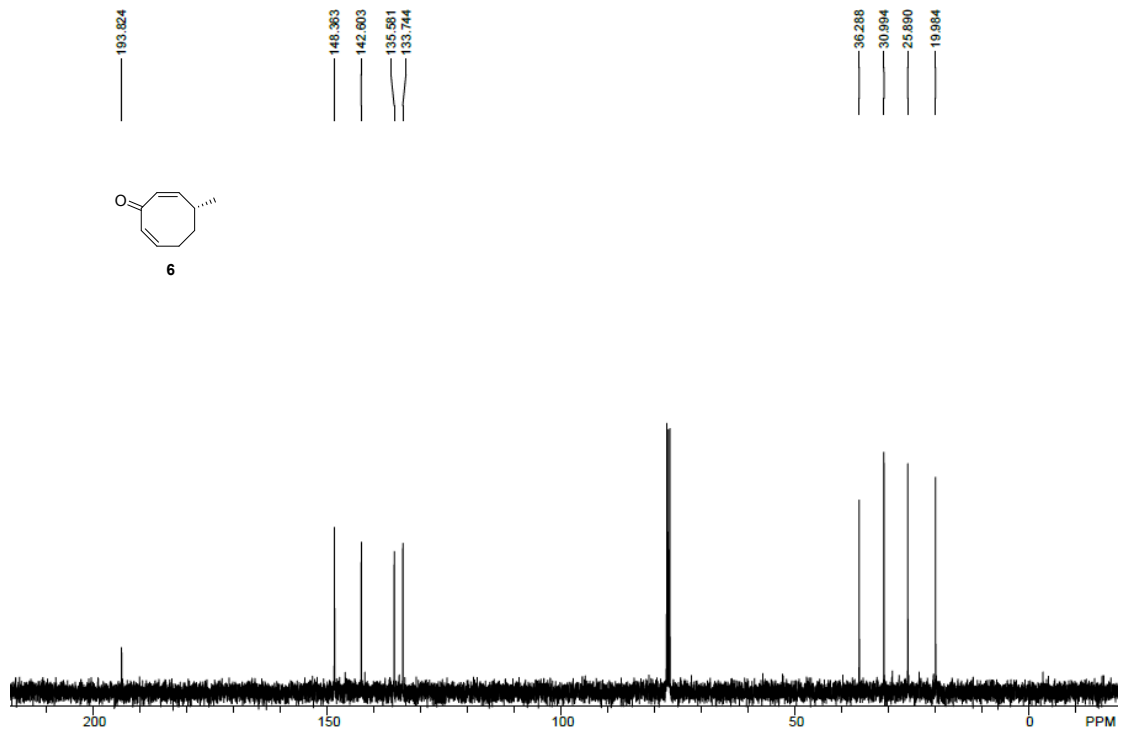
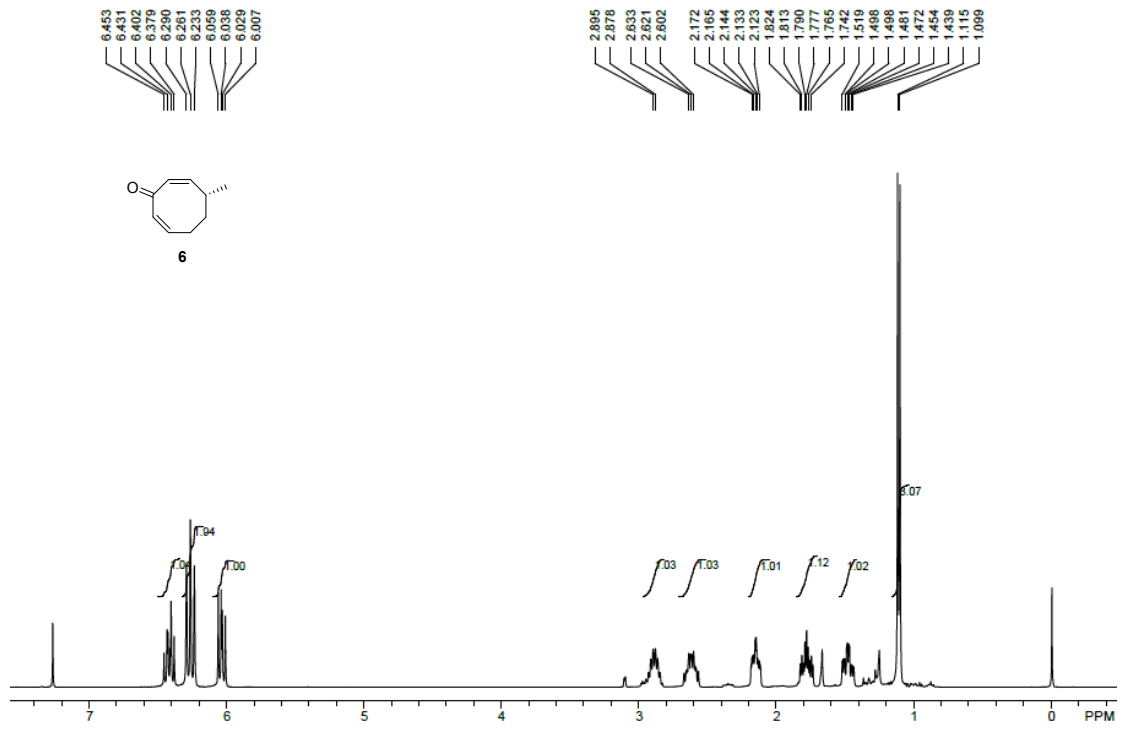
### 3. References

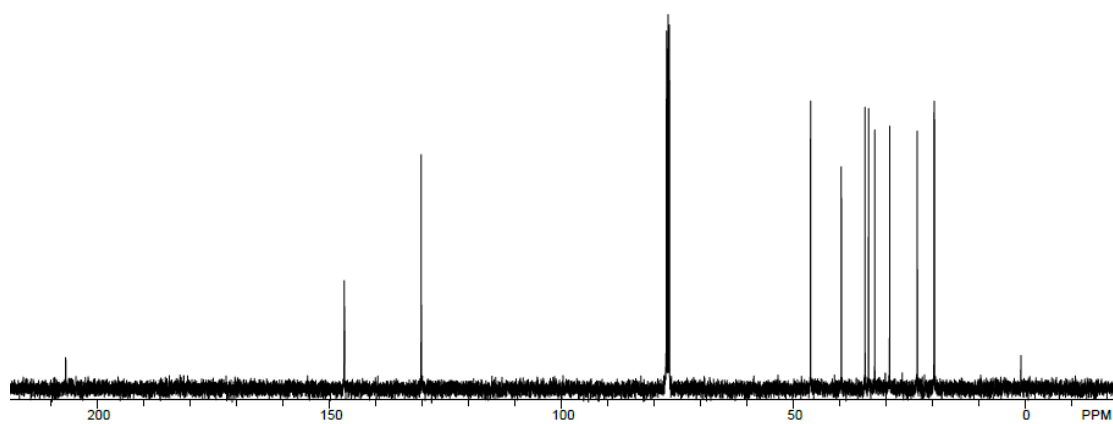
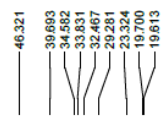
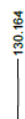
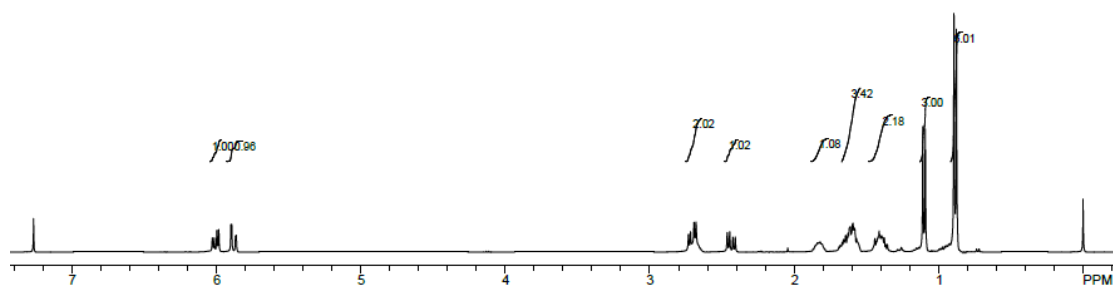
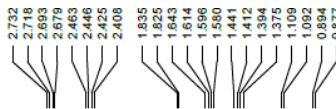
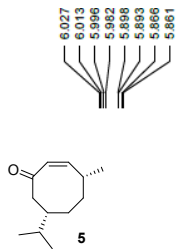
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## 4. NMR Spectra

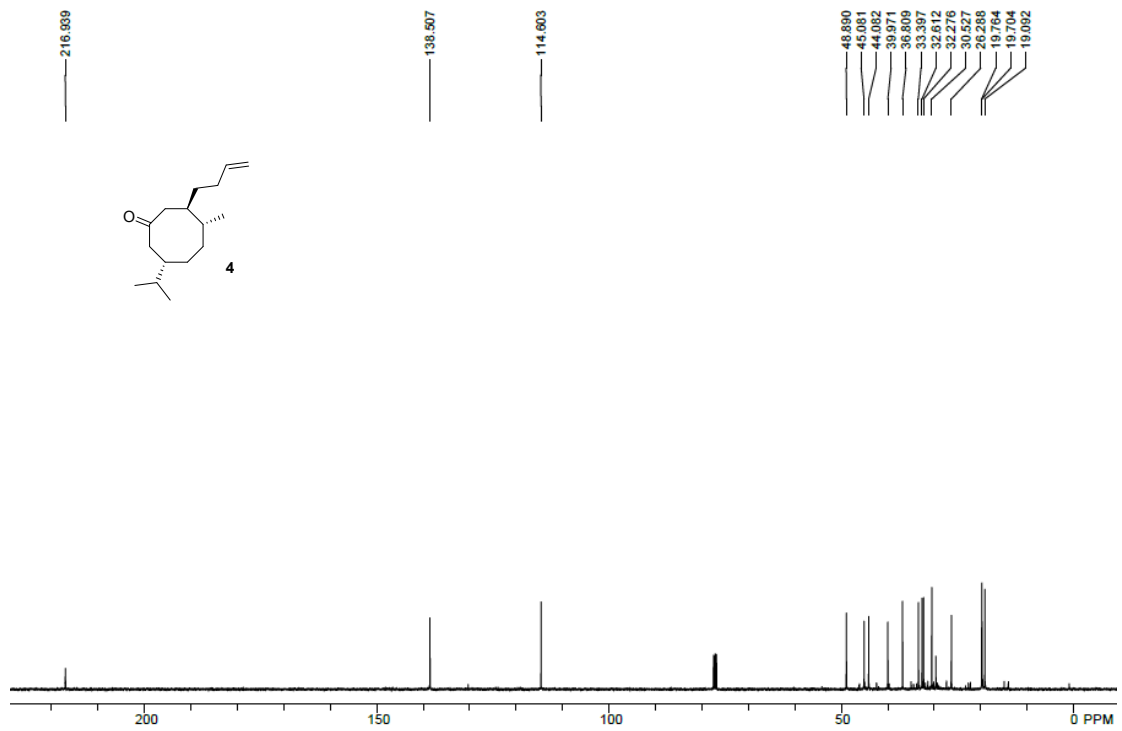
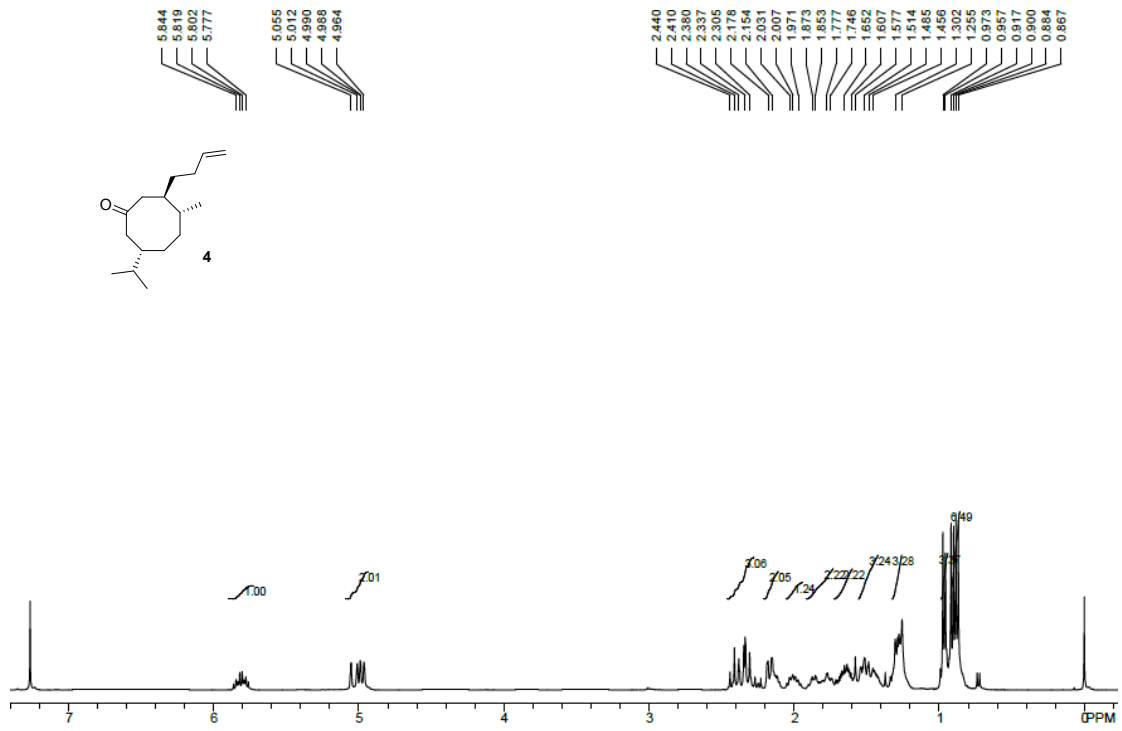


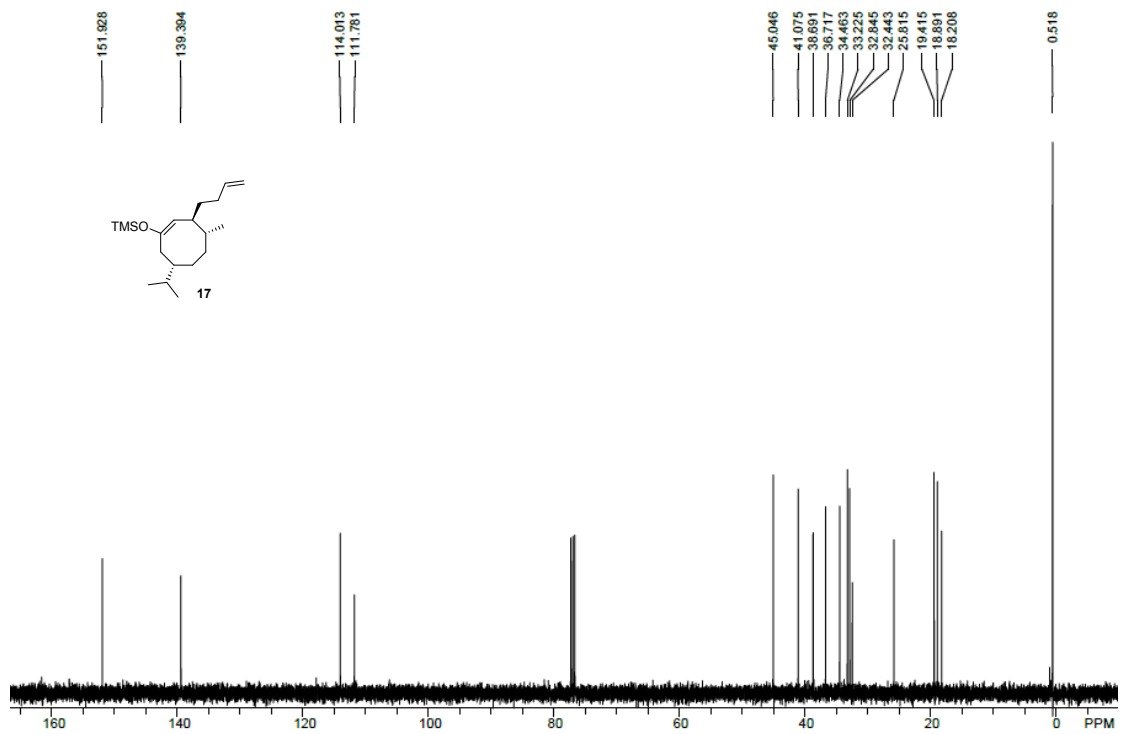
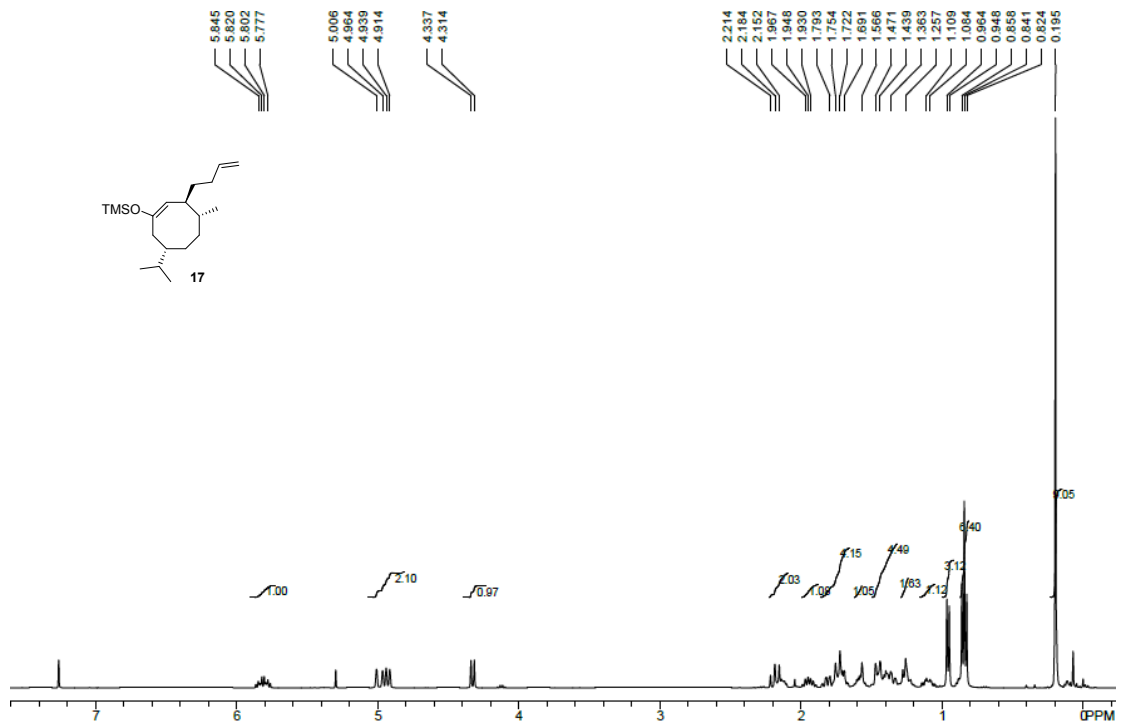


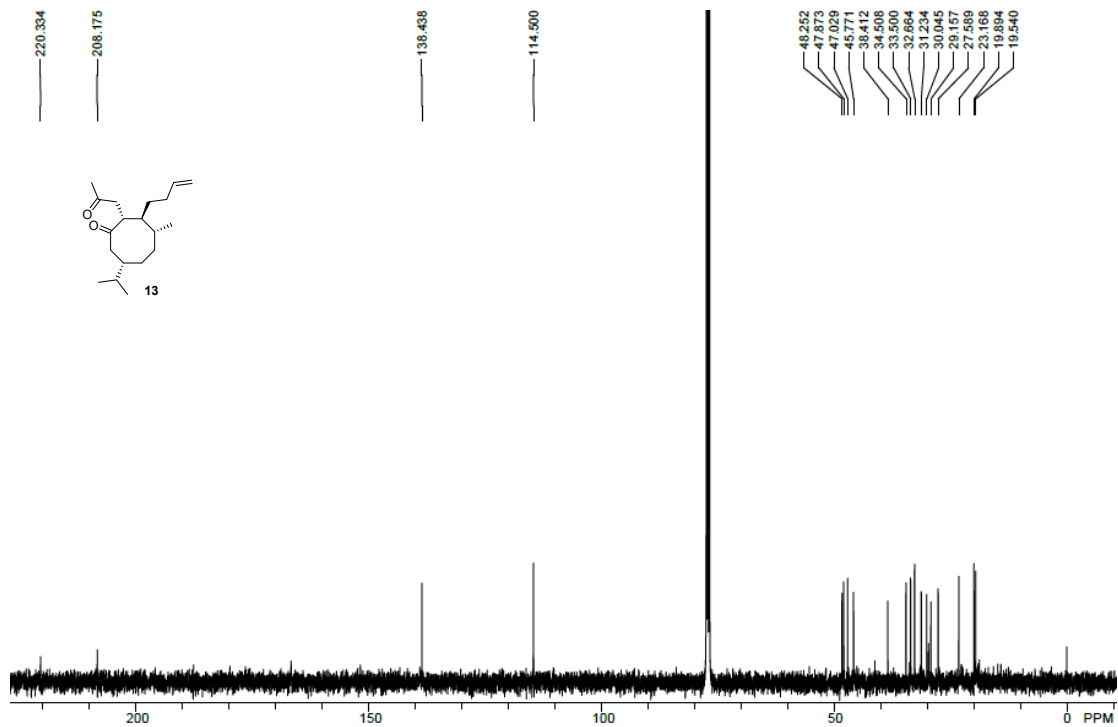
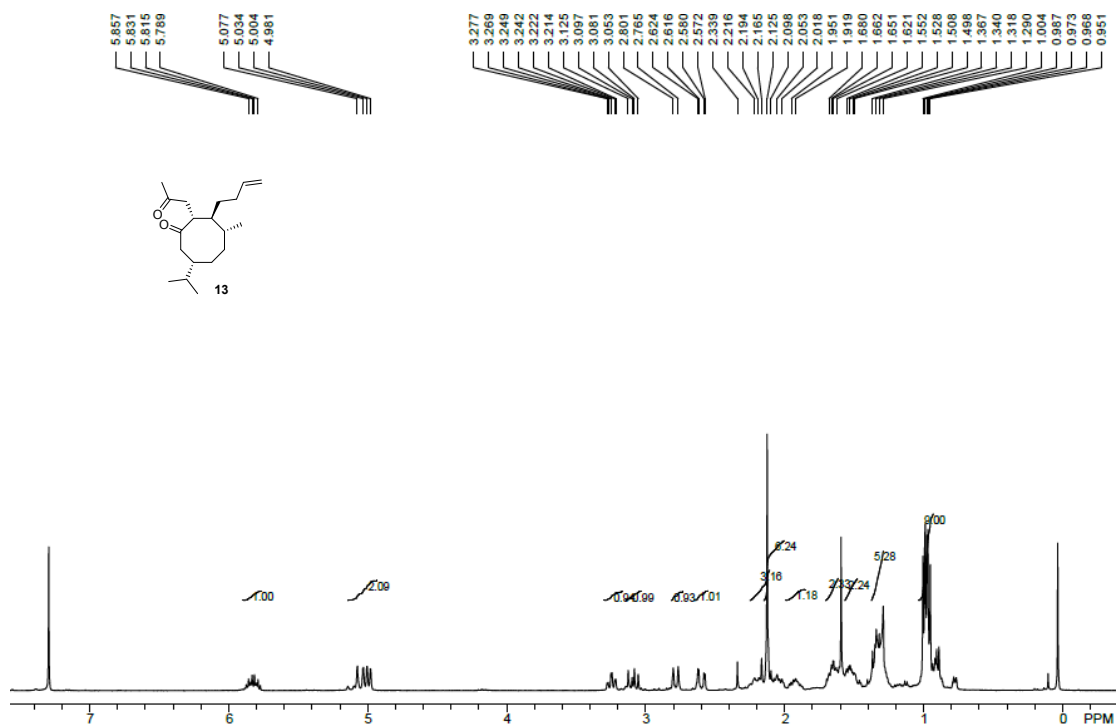


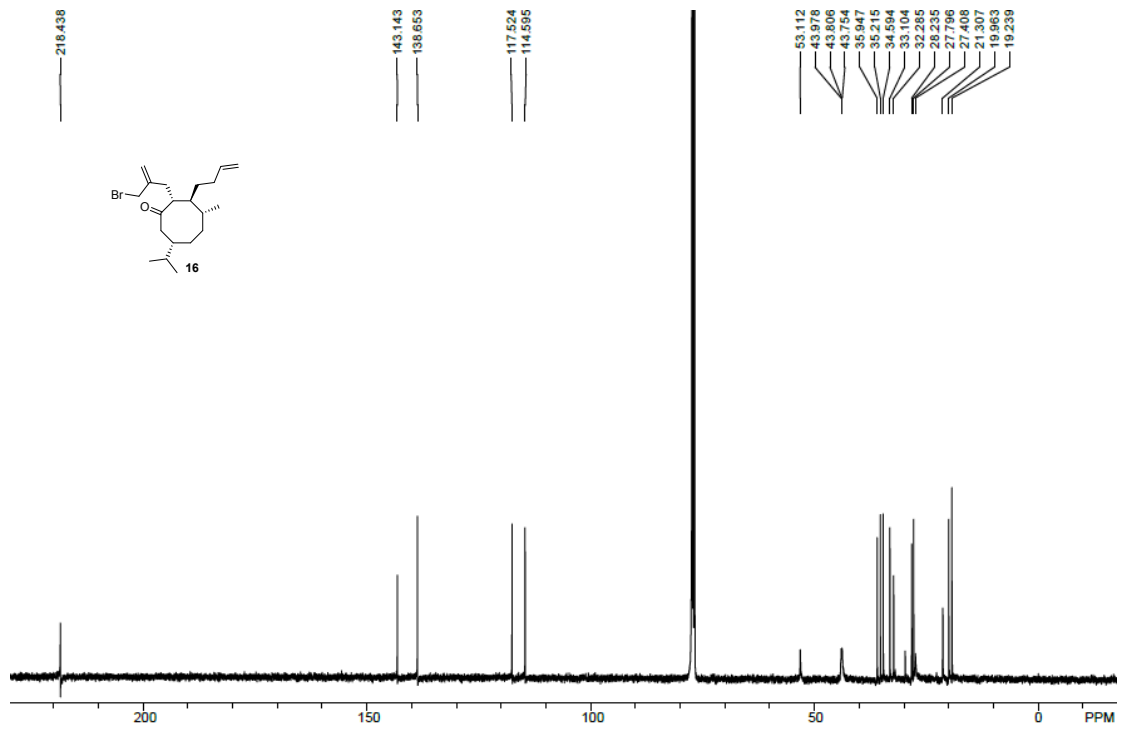
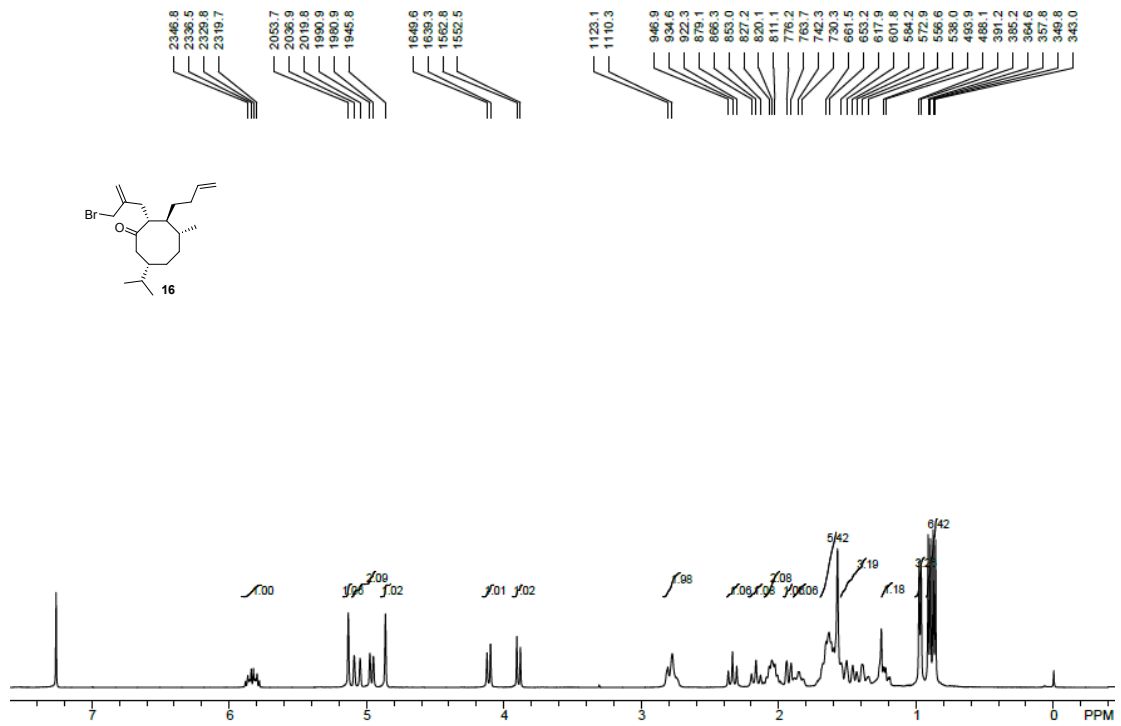


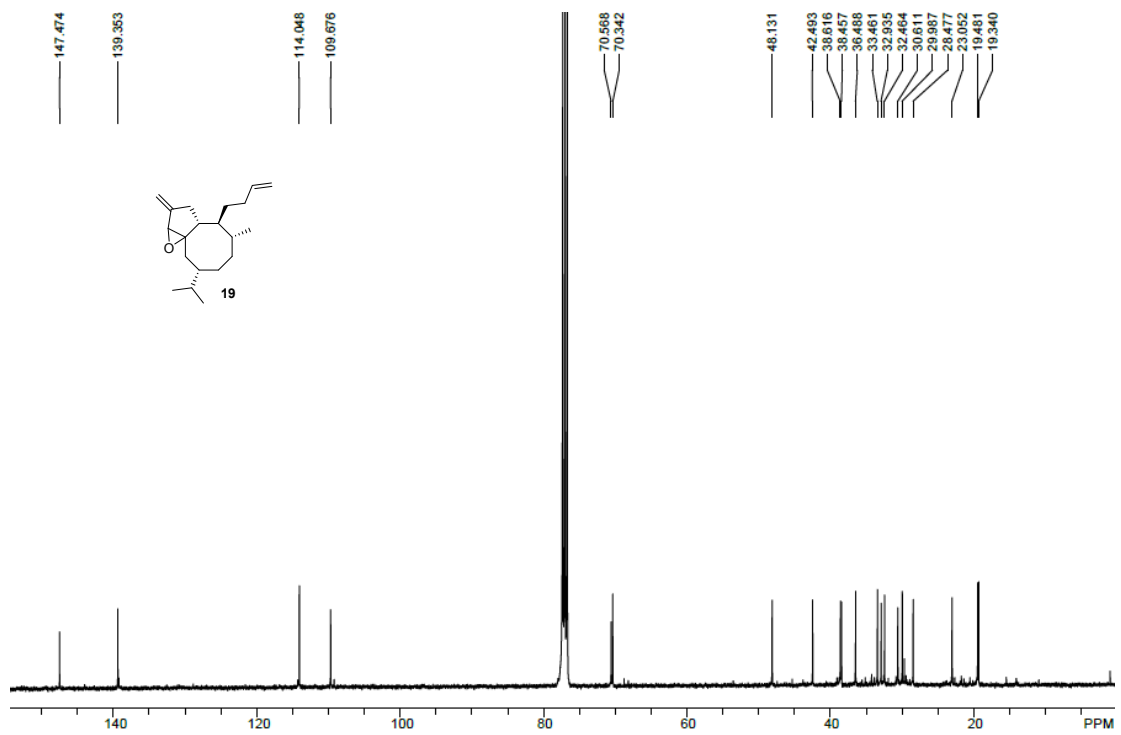
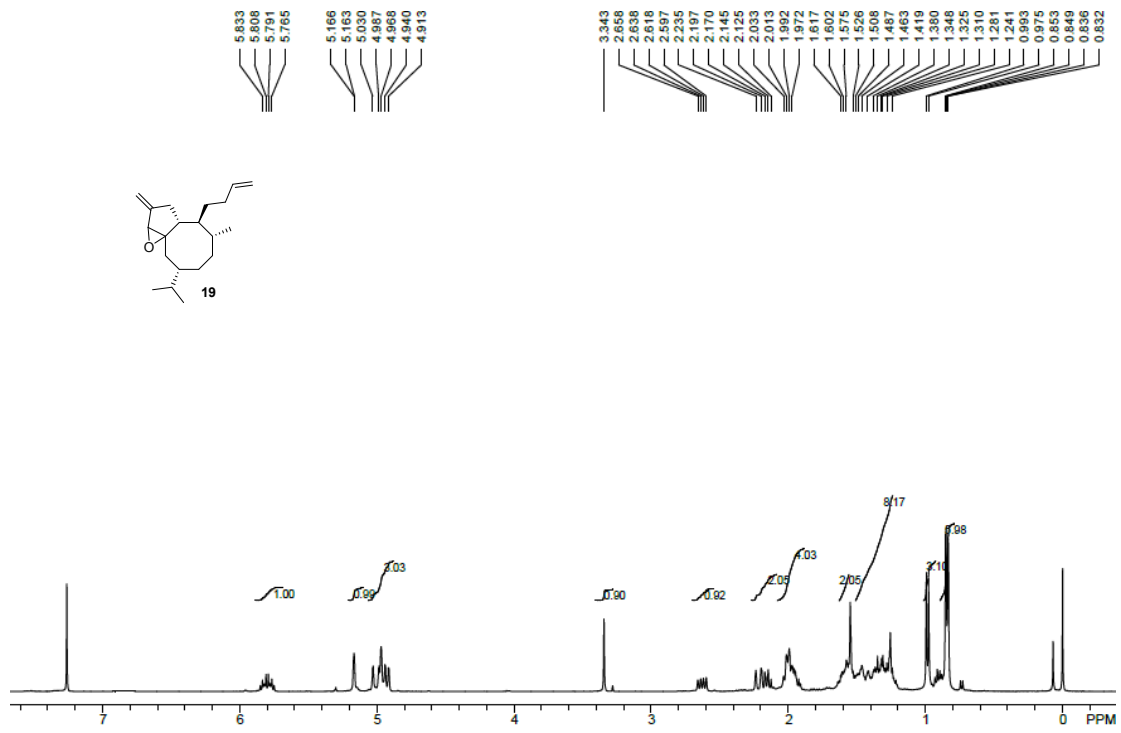


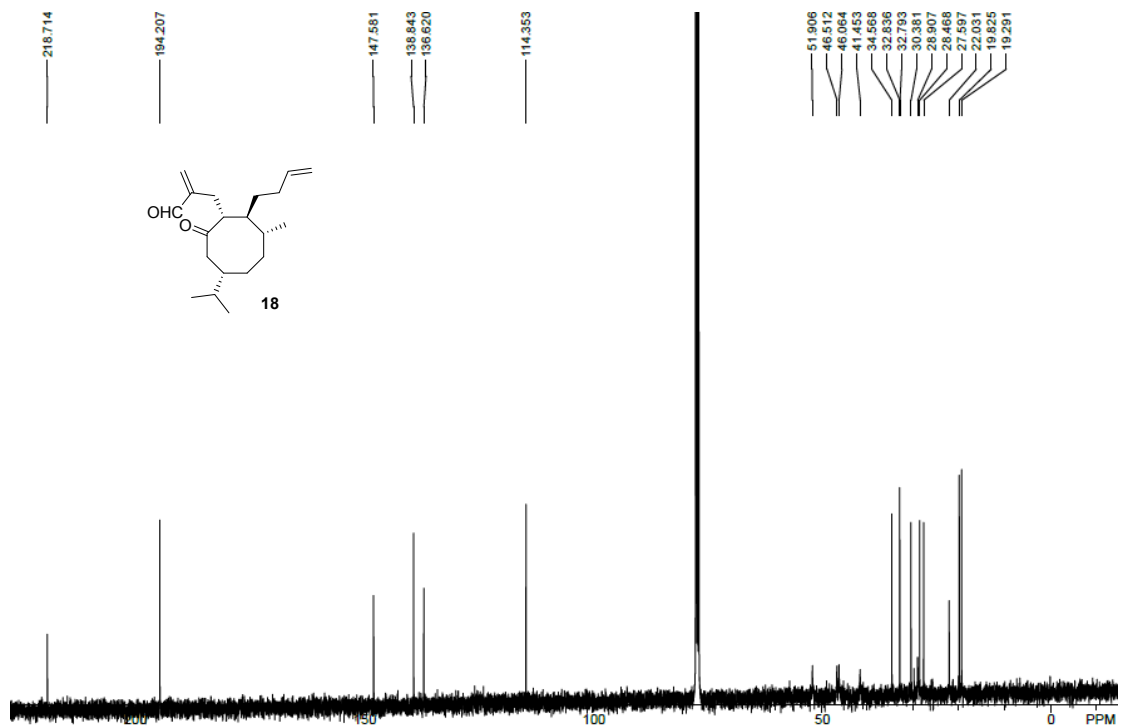
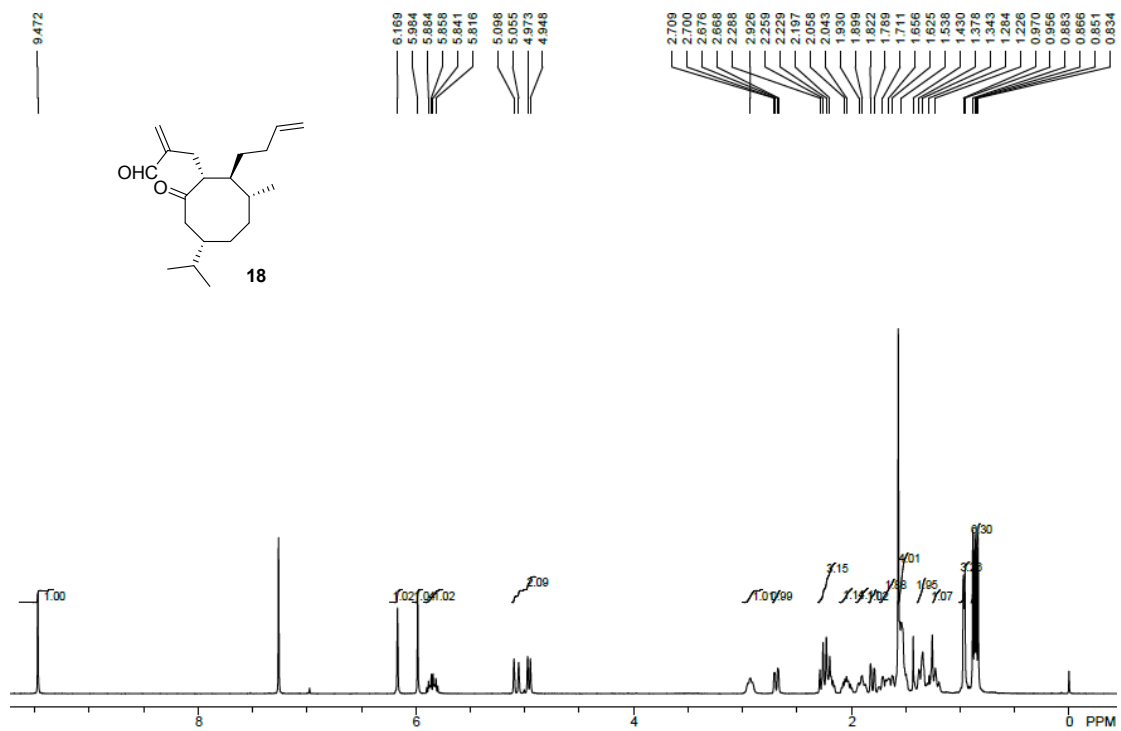


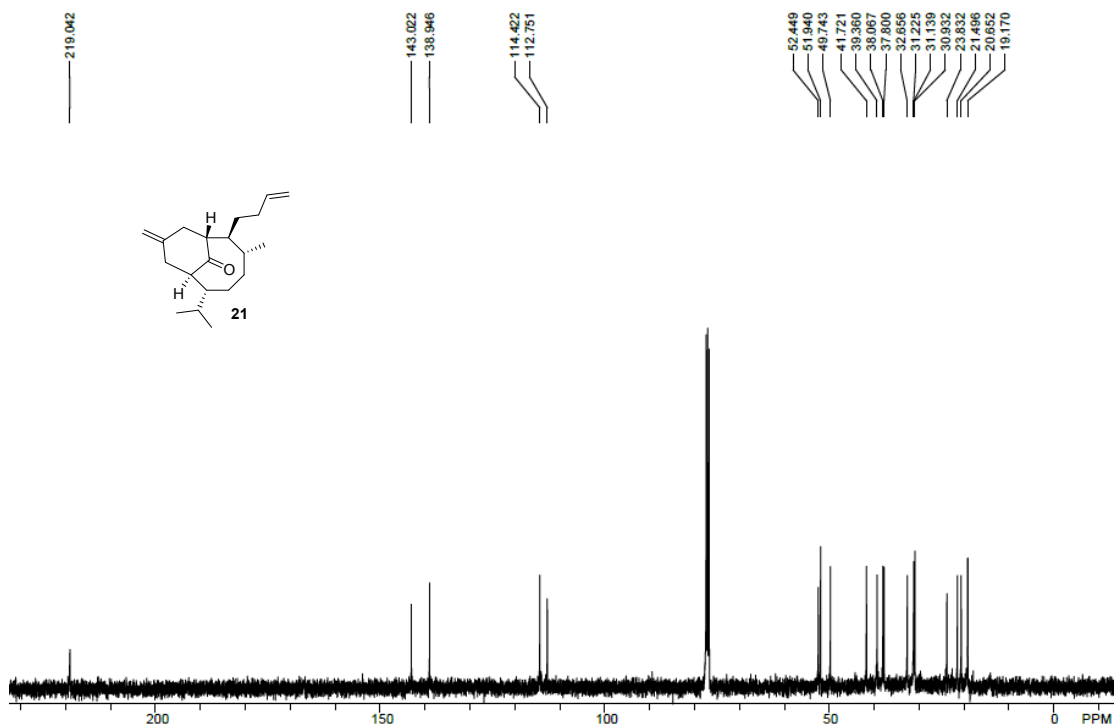
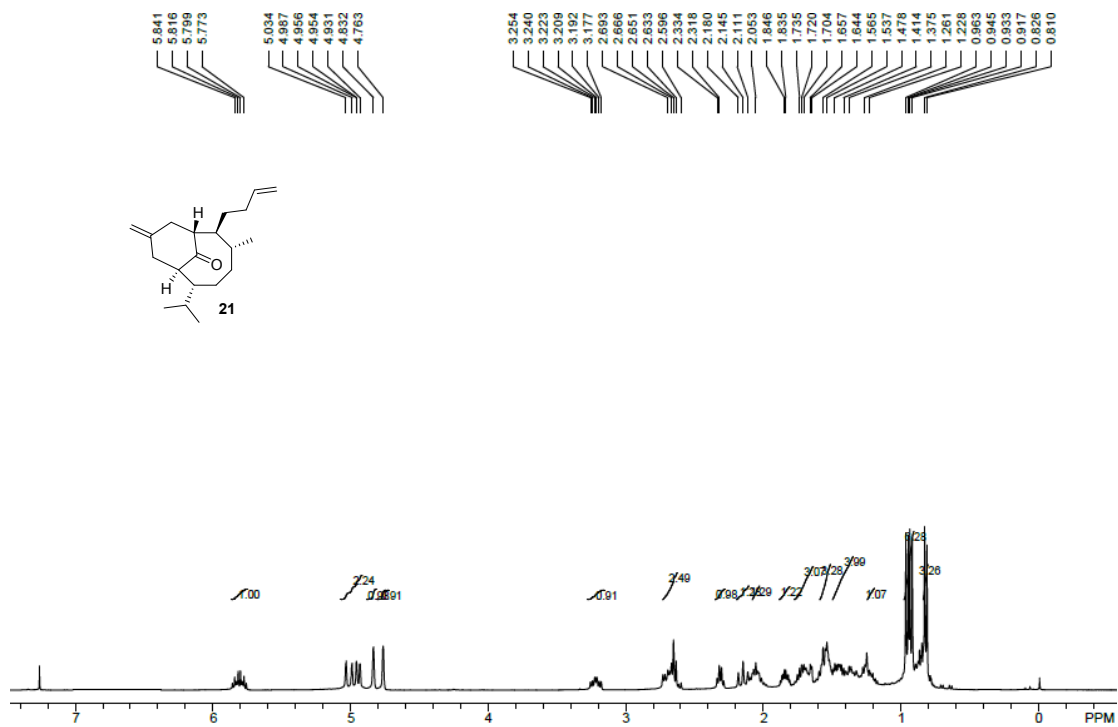


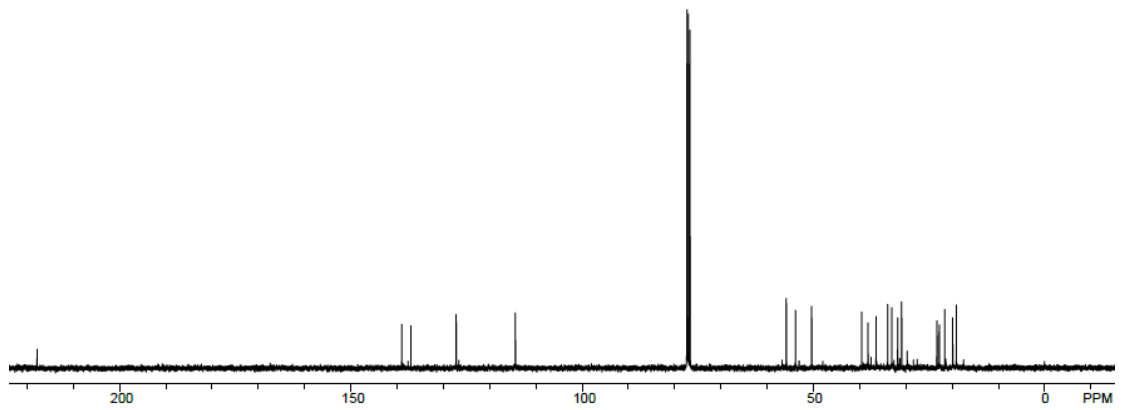
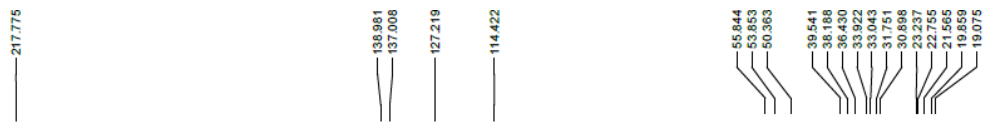
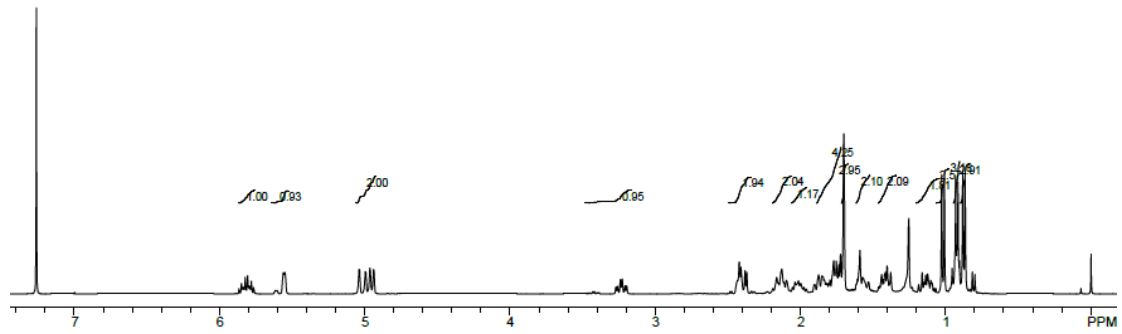
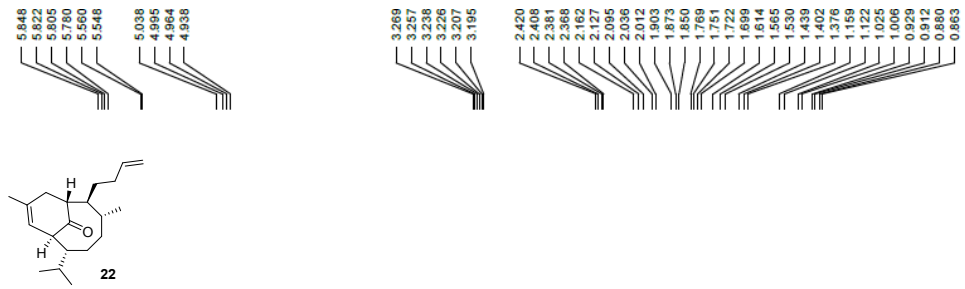




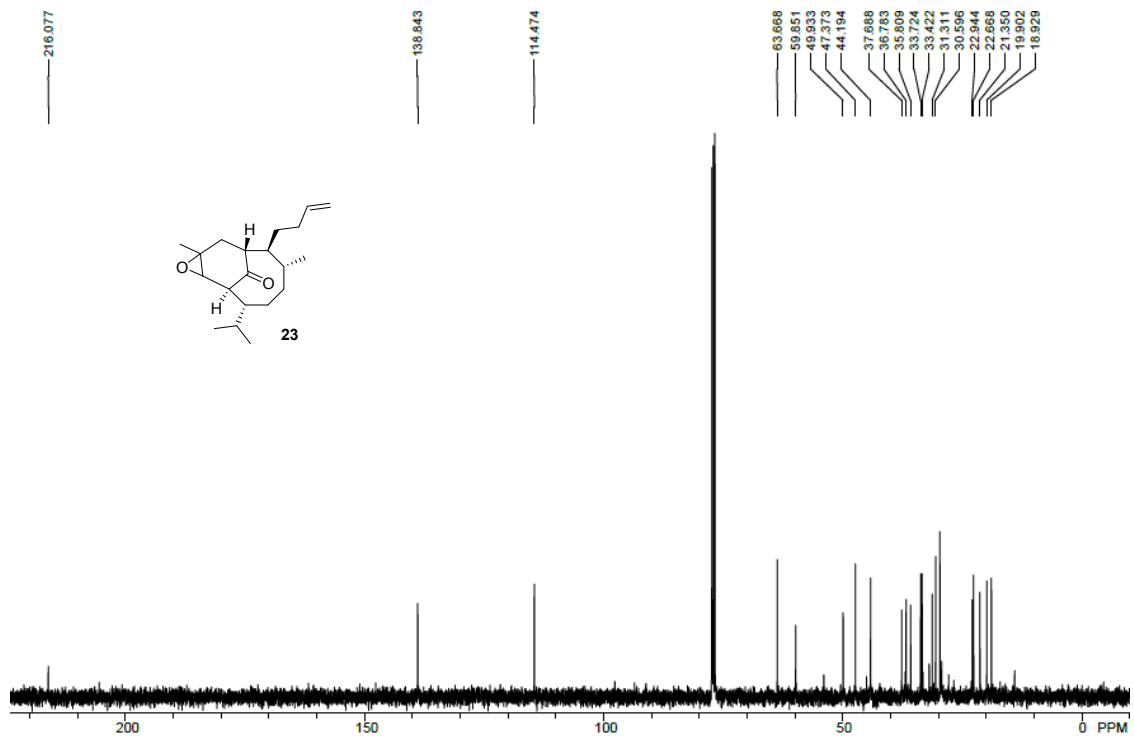
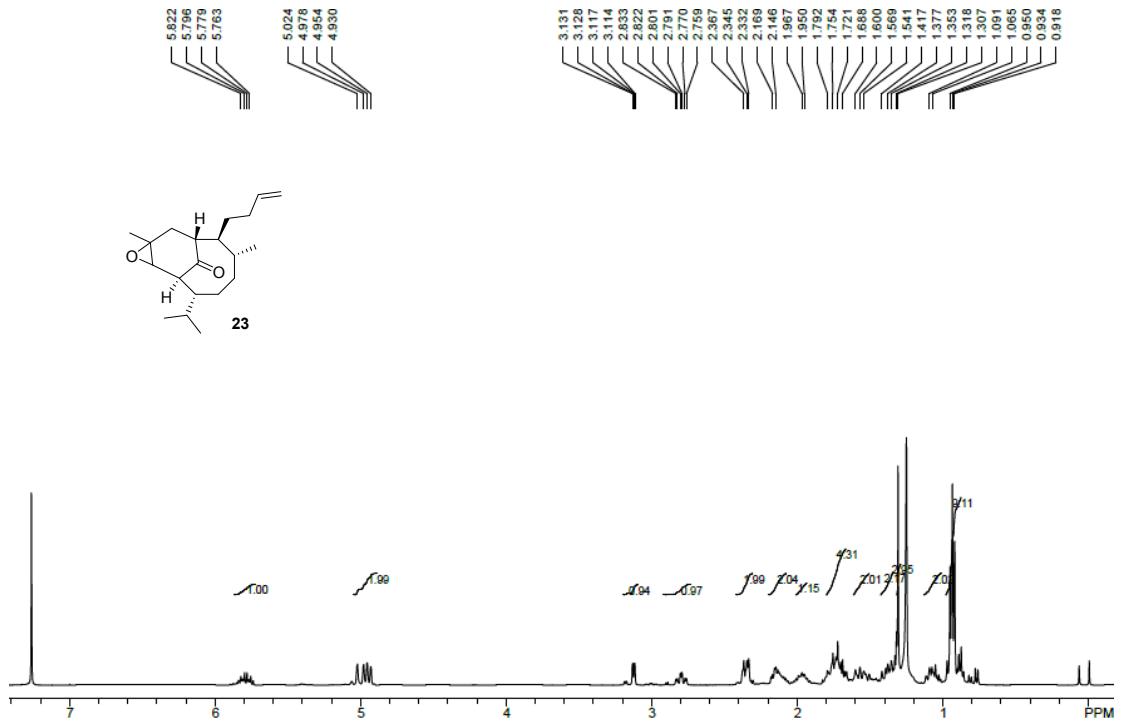
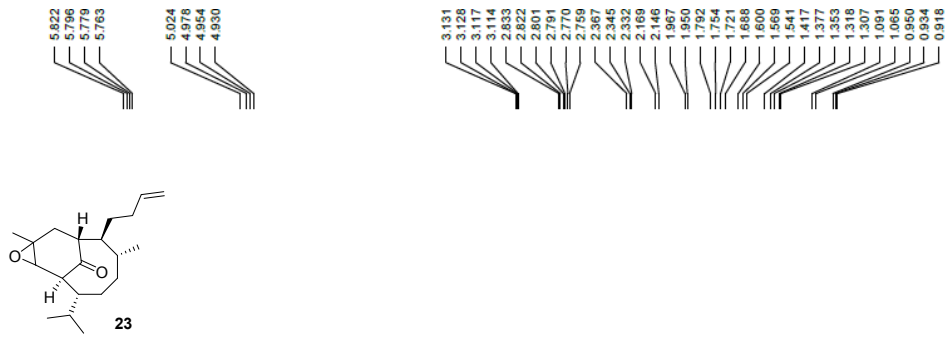














## Crystal Lattice Structure of 21

