

# Synthesis of the Guaianolide Ring System via Cycloaddition of a Bicyclic Carbonyl Ylide with Allyl Propiolate

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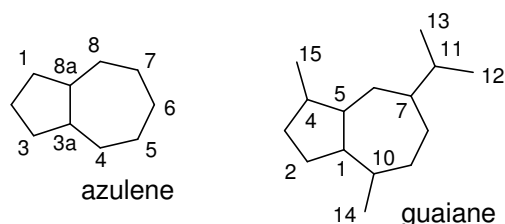
## Supporting Information

### Contents

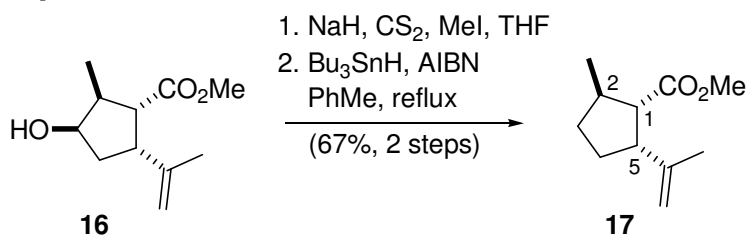
	Page
1. General methods	S2
2. Experimental procedures	S2
3. Copies of <sup>1</sup> H- and <sup>13</sup> C NMR spectra	S13
4. Calculated structure of the cyclic dipole	S28
5. Rendering of the X-ray structure of tricyclic compound <b>34</b>	S29

## 1. General methods

Unless otherwise noted, all reactions were performed in oven-dried glassware. All solvents used in the reactions were purified before use. Dry diethyl ether, tetrahydrofuran, and toluene were distilled from sodium and benzophenone, whereas dry  $\text{CH}_2\text{Cl}_2$ , dimethylformamide, methanol, ethyl acetate, benzene, and triethylamine were distilled from  $\text{CaH}_2$ . Petroleum ether with a boiling range of 40–60 °C was used. Reactions were generally run under nitrogen atmosphere. All commercially available compounds (Acros, Aldrich, Fluka, Merck) were used without purification.  $^1\text{H}$  and  $^{13}\text{C}$  NMR: Bruker Avance 400, spectra were recorded at 295 K in  $\text{CDCl}_3$  or in DMSO; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent:  $\text{CDCl}_3$  ( $^1\text{H}$  7.25,  $^{13}\text{C}$  77.0 ppm), DMSO ( $^1\text{H}$  2.49,  $^{13}\text{C}$  39.5 ppm).<sup>1</sup> HRMS (FT-ICR): Bruker Daltonic APEX 2 with electron spray ionization (ESI). Analytical LC-MS: HP 1100 Series connected with an ESI MS detector Agilent G1946C, positive mode with fragmentor voltage of 40 eV, column: Nucleosil 100-5, C-18 HD, 5  $\mu\text{m}$ , 70  $\times$  3 mm Machery Nagel, eluent: NaCl solution (5 mM)/acetonitrile, gradient: 0–10–15–17–20 min with 20–80–80–99–99% acetonitrile, flow: 0.5 mL  $\text{min}^{-1}$ . Flash chromatography: J. T. Baker silica gel 43–60  $\mu\text{m}$ . Thin-layer chromatography Machery-Nagel Polygram Sil G/UV<sub>254</sub>. Optical rotations: JASCO Polarimeter P-1020, sodium D line (589 nm),  $c$  = g per 100 mL. The azulene system was used for atom numbering of bi- or tricyclic compounds:



## 2. Experimental procedures



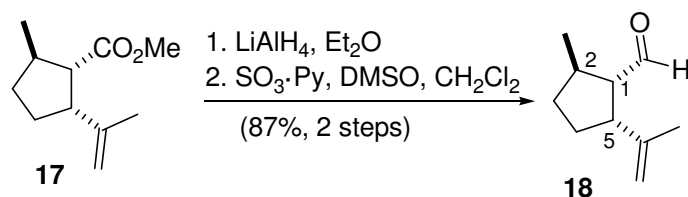
**(1S,2R,5R)-Methyl 2-methyl-5-(prop-1-en-2-yl)cyclopentanecarboxylate (17).** NaH (60% dispersion in oil, 22.0 g, 550 mmol) was added to a stirred solution of alcohol<sup>2</sup> **16** (11.2 g, 57.0 mmol) and imidazole (ca. 300 mg) in THF (200 mL) at 0 °C. The cooling bath was removed. After 15 min reaction was recooled to 0 °C and  $\text{CS}_2$  (38 mL, 612 mmol) was added dropwise. The mixture was allowed to warm to ambient temperature and after 1 h recooled to 0 °C before MeI (40 mL, 600 mmol) was added dropwise. After 3 h the reaction was quenched by careful addition of water (200 mL) at 0 °C. The mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  100 mL). The combined organic layers were washed with water (2  $\times$  200 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo. The residue was purified by flash

<sup>1</sup> Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.

<sup>2</sup> Andrews, S. P.; Ball, M.; Wierschem, F.; Cleator, E.; Oliver, S.; Högenauer, K.; Simic, O.; Antonello, A.; Hüniger, U.; Smith, M. D.; Ley, S. V. *Chem. Eur. J.* **2007**, *13*, 5688-5712.

chromatography (5% ethyl acetate in petroleum ether) to give the titled xanthate (16.2 g, 98%) as a yellow oil which was directly introduced to the next step.  $R_f = 0.43$  (petroleum ether/EtOAc, 9:1).

Tributylstannane (20.0 mL, 77.0 mmol) was added to a stirred solution of xanthate (16.2 g, 56.0 mmol) in dry toluene (200 mL) under  $N_2$ . The mixture was stirred for 5 min, and then AIBN (ca. 100 mg) was added. The resulting mixture was heated under reflux for 1 h and then the reaction was allowed to cool to ambient temperature, washed with water ( $3 \times 100$  mL) and saturated NaCl solution (100 mL). The organic layer was dried over  $MgSO_4$ , filtered, and concentrated in vacuo. The resulting colorless oil was distilled under reduced pressure (b.p. 90–95 °C, 25 mbar) to afford the title compound **17** (6.9 g, 67%, over 2 steps).  $R_f = 0.60$  (petroleum ether/EtOAc, 9:1);  $[\alpha]_D^{20} = +19.8$  (c 1.00,  $Et_2O$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta = 1.02$  (d,  $J = 6.9$  Hz, 3H,  $CHCH_3$ ), 1.16 (dddd,  $J = 12.5, 10.5, 8.7, 7.8$  Hz, 1H, 3-H), 1.71 (s, 3H,  $CH_2=CCH_3$ ), 1.71–1.77 (m, 1H, 4-H), 1.83 (dddd,  $J = 12.6, 10.2, 10.2, 7.6$  Hz, 1H, 4-H), 2.02 (dddd,  $J = 12.5, 7.7, 7.7, 2.4$  Hz, 1H, 3-H), 2.41 (dddq,  $J = 14.2, 14.2, 6.6, 6.6$  Hz, 1H, 2-H), 2.56 (dd,  $J = 8.9, 6.1$  Hz, 1H, 1-H), 2.76 (ddd,  $J = 9.4, 9.4, 6.7$  Hz, 1H, 5-H), 3.55 (s, 3H,  $OCH_3$ ), 4.67 (br s, 1H,  $CH_2=CCH_3$ ), 4.72 (br s, 1H,  $CH_2=CCH_3$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta = 21.2$  ( $CHCH_3$ ), 22.6 ( $CH_2=CCH_3$ ), 29.7 (C-4), 33.7 (C-3), 36.9 (C-2), 49.7 (C-5), 51.0 ( $OCH_3$ ), 55.6 (C-1), 110.7 ( $CH_2=CCH_3$ ), 145.5 ( $CH_2=CCH_3$ ), 175.1 ( $CO_2CH_3$ ); HRMS (ESI):  $[M+Na]^+$  calcd for  $C_{11}H_{18}O_2Na$  205.11990, found 205.11972; The spectral data are identical to those previously reported.<sup>3</sup>

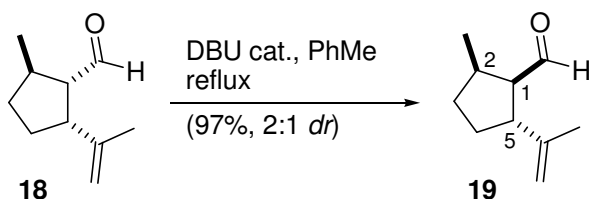


**(1S,2R,5R)-2-Methyl-5-(prop-1-en-2-yl)cyclopentanecarbaldehyde (18).** A solution of ester **17** (25.1 g, 0.14 mol) in diethyl ether (200 mL) was added dropwise to the suspension of lithium aluminium hydride (6.3 g, 0.17 mol) in diethyl ether (300 mL) at 0 °C. The mixture was stirred at room temperature for 2 d and then was quenched by careful addition of 15% NaOH (70 mL) and water (200 mL). Stirring was continued for 15 min, before  $MgSO_4$  was added, the mixture stirred for additional 15 min, and filtered to remove salts. Evaporation of the solvent yielded crude alcohol (21.0 g), which was introduced to the next reaction without further purification.  $R_f = 0.25$  (petroleum ether/EtOAc, 9:1).

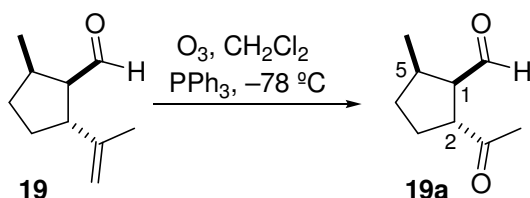
To a stirred solution of the foregoing alcohol (21.0 g, 0.14 mol) in  $CH_2Cl_2$  (700 mL) were added at room temperature  $Et_3N$  (230 mL, 1.66 mol) and a solution of  $SO_3 \cdot Py$  (125 g, 0.78 mol) in DMSO (400 mL). The reaction mixture was stirred for 1 h before it was quenched with water (300 mL) and extracted with ethyl acetate ( $3 \times 200$  mL). The combined organic layers were washed with water (200 mL), 1 N HCl ( $2 \times 200$  mL), water ( $2 \times 200$  mL), saturated NaCl solution (200 mL), dried over  $MgSO_4$ , filtered, and concentrated in vacuo. The residue was distilled at low pressure (b.p. 100–105 °C, 25 mbar) to give aldehyde **18** as a colorless oil (18.0 g, 87%, over 2 steps).  $R_f = 0.65$  (petroleum ether/EtOAc, 9:1); The spectral data are identical to those previously reported.<sup>4</sup>

<sup>3</sup> Dawson, G. W.; Pickett, J. A.; Smiley, D. W. M. *Bioorg. Med. Chem.* **1996**, *4*, 351-361.

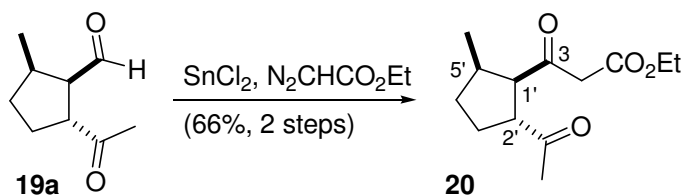
<sup>4</sup> Sakai, T.; Morita, K.; Matsumura, C.; Sudo, A.; Tsuboi, S.; Takeda, A. *J. Org. Chem.* **1981**, *46*, 4774-4779.



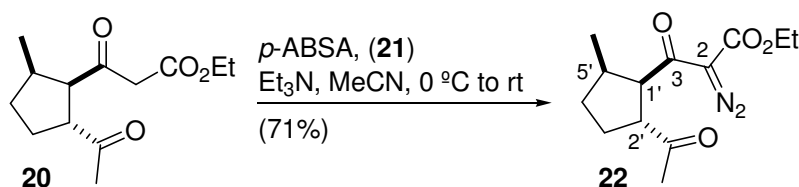
**(1R,2R,5R)-2-Methyl-5-(prop-1-en-2-yl)cyclopentanecarbaldehyde (19).** DBU (0.2 mL) was added to a stirred solution of aldehyde **18** (17.0 g, 0.11 mol) in toluene (150 mL). The resulting mixture was stirred under reflux for 2 d. Then solvent was carefully evaporated to afford a mixture of two stereoisomers **19/18** in a ratio of 2:1 (16.5 g, 97%) [as determined by  $^1\text{H}$  NMR spectroscopy via integration of the aldehyde signals (**18**: 9.48 ppm, **19**: 9.72 ppm)].  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.98 (d,  $J$  = 7.1 Hz, 3H,  $\text{CHCH}_3$ ), 1.13–1.34 (m, 2H), 1.43–1.54 (m, 1H), 1.84–2.02 (m, 1H), 1.63 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}_2$ ), 2.41–2.49 (m, 1H, 2-H), 2.62 (ddd,  $J$  = 8.7, 8.7, 3.4 Hz, 1H, 1-H), 2.98 (ddd,  $J$  = 8.5, 8.5, 8.5 Hz, 1H, 5-H), 4.64 (br s, 1H,  $\text{CH}_3\text{C}=\text{CH}_2$ ), 4.65 (br s, 1H,  $\text{CH}_3\text{C}=\text{CH}_2$ ), 9.72 (d,  $J$  = 3.8 Hz, 1H,  $\text{CH}=\text{O}$ ).



**(1R,2R,5R)-2-Acetyl-5-methylcyclopentanecarbaldehyde (19a).** Nitrogen was bubbled through a solution of aldehyde **19** (4 g, 27 mmol) in  $\text{CH}_2\text{Cl}_2$  (40 ml) at  $-78^\circ\text{C}$  before ozone was bubbled until a deep blue color was observed. Nitrogen was again applied until no blue color remained. After the addition of  $\text{PPh}_3$  (10.5 g, 40 mmol) the reaction mixture was stirred overnight at room temperature.  $R_f$  (ketoaldehyde **19a**) = 0.43 (petroleum ether/ $\text{EtOAc}$ , 4:1). This solution was used as such for the subsequent keto ester formation. An analytical sample was prepared after evaporation of the solvent followed by flash chromatography (petroleum ether/ $\text{Et}_2\text{O}$ , 9:1).  $[\alpha]_D^{20}$  = +25.5 ( $c$  0.85,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.03 (d,  $J$  = 7.1 Hz, 3H,  $\text{CHCH}_3$ ), 1.32 (ddd,  $J$  = 15.4, 12.5, 7.6 Hz, 1H, 4-H), 1.65 (ddd,  $J$  = 16.1, 12.8, 8.0 Hz, 1H, 3-H), 1.88 (dddd,  $J$  = 12.6, 7.8, 6.4, 5.0 Hz, 1H, 4-H), 2.10 (dddd,  $J$  = 9.9, 7.5, 5.0, 2.5 Hz, 1H, 3-H), 2.17 (s, 3H,  $\text{CH}_3\text{C}=\text{O}$ ), 2.56 (app dddq,  $J$  = 14.5, 14.5, 7.4, 7.1 Hz, 1H, 5-H), 3.25 (ddd,  $J$  = 8.4, 7.0, 1.1 Hz, 1H, 1-H), 3.48 (ddd,  $J$  = 9.5, 7.6, 7.5 Hz, 1H, 2-H), 9.81 (d,  $J$  = 0.8 Hz, 1H,  $\text{CH}=\text{O}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 16.4 ( $\text{CHCH}_3$ ), 27.7 (C-3), 29.1 ( $\text{CH}_3\text{C}=\text{O}$ ), 34.2 (C-4), 36.6 (C-5), 49.5 (C-2), 56.4 (C-1), 203.1 ( $\text{CH}=\text{O}$ ), 209.0 ( $\text{CH}_3\text{C}=\text{O}$ ); HRMS (ESI):  $[\text{M}+\text{Na}+\text{MeOH}]^+$  calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_3\text{Na}$  209.11429, found 209.11450.



**Ethyl 3-((1'*R*,2'*R*,5'*R*)-2'-acetyl-5'-methylcyclopentyl)-3-oxopropanoate (20).** Anhydrous tin (II) chloride<sup>5</sup> (9.0 g, 47 mmol) was added, followed by dropwise addition of ethyl diazoacetate (8 mL, 73 mmol) to the foregoing solution of crude ketoaldehyde **19a** in CH<sub>2</sub>Cl<sub>2</sub> (the quenched ozonolysis solution). Stirring was continued for 2 h, and then the mixture was transferred to a separatory funnel, containing saturated NaCl (100 mL) and diethyl ether (200 mL). After separation of the layers, the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with water (100 mL), saturated NaCl solution (100 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/Et<sub>2</sub>O, 4:1) to give β-keto ester **20** (2.5 g, 66%, over 2 steps) as a colorless oil. *R*<sub>f</sub> = 0.30 (petroleum ether/EtOAc, 4:1); [α]<sub>D</sub><sup>20</sup> = −11.7 (*c* 1.02, MeOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.83 (d, *J* = 7.3 Hz, 3H, CHCH<sub>3</sub>), 1.24 (dd, *J* = 7.3, 7.3 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.42–1.50 (m, 1H, 4'-H), 1.58–1.67 (m, 1H, 3'-H), 1.82–1.92 (m, 1H, 4'-H), 2.07–2.20 (m, 1H, 3'-H), 2.13 (s, 3H, CH<sub>3</sub>C=O), 2.54 (app dddq, *J* = 13.7, 11.3, 7.0, 7.0 Hz, 1H, 5'-H), 3.40–3.48 (m, 2H, 1'-H, 2'-H), 3.47 (s, 2H, 2-H), 4.11–4.30 (m, 2H, OCH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.0 (OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (CHCH<sub>3</sub>), 27.0 (C-3'), 29.3 (CH<sub>3</sub>C=O), 33.8 (C-4'), 37.0 (C-5'), 49.8 (C-3), 51.2 (C-1'), 57.0 (C-2'), 61.3 (OCH<sub>2</sub>CH<sub>3</sub>), 166.8 (C-1), 203.3 (C-3), 209.2 (CH<sub>3</sub>C=O); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>13</sub>H<sub>20</sub>O<sub>4</sub>Na 263.12538, found 263.12538.

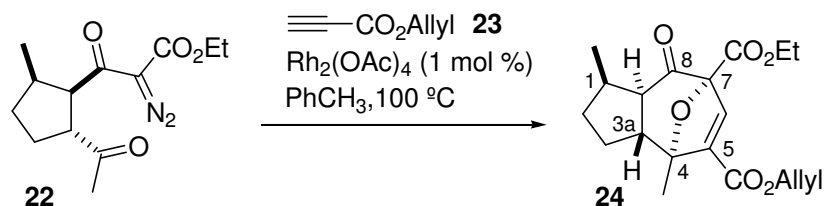


**Ethyl 3-((1'*R*,2'*R*,5'*R*)-2'-acetyl-5'-methylcyclopentyl)-2-diazo-3-oxopropanoate (22).** Triethylamine (3.9 mL, 28.0 mmol) was added dropwise at 0 °C to a solution of β-keto ester **20** (3.4 g, 14 mmol) and *p*-acetamidobenzenesulfonyl azide<sup>6</sup> (*p*-ABSA, **21**) (4.3 g, 18 mmol) in acetonitrile (60 mL). The mixture was stirred for 2 h and quenched with saturated NH<sub>4</sub>Cl solution (30 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with water (100 mL) and saturated NaCl solution (100 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 9:1) to give diazo compound **22** (2.7 g, 71%) as a yellow oil. *R*<sub>f</sub> = 0.70 (petroleum ether/EtOAc, 2:1); [α]<sub>D</sub><sup>20</sup> = −39.2 (*c* 1.76, MeOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.80 (d, *J* = 7.1 Hz, 3H, CHCH<sub>3</sub>), 1.30 (dd, *J* = 7.2, 7.2 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.39 (dddd, *J* = 12.8, 7.6, 7.4, 5.8 Hz, 1H, 4'-H), 1.63 (dddd, *J* = 12.5, 8.9, 8.8, 8.2 Hz, 1H, 3'-H), 1.94 (dddd, *J* = 12.4, 8.6, 6.8, 5.0 Hz, 1H, 4'-H), 2.07–2.13 (m, 1H, 3'-H), 2.12 (s, 3H, CH<sub>3</sub>C=O), 2.61 (app dddq, *J* = 14.2, 14.2, 6.9, 6.8 Hz, 1H, 5'-H), 3.56 (ddd, *J* = 18.7, 9.4, 9.4 Hz, 1H, 2'-H), 4.07 (dd, *J* = 8.6 Hz, 1H, 1'-H), 4.23–4.31 (m, 2H, OCH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.2 (OCH<sub>2</sub>CH<sub>3</sub>), 16.8 (CHCH<sub>3</sub>), 27.4 (C-3'), 29.1 (CH<sub>3</sub>C=O), 34.0 (C-4'), 36.2 (C-5'), 52.6 (C-2'), 53.1 (C-1'), 61.4 (OCH<sub>2</sub>CH<sub>3</sub>), 160.9 (C-1), 192.9 (C-3), 209.2 (CH<sub>3</sub>C=O); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>13</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub>Na 289.11588, found 289.11592.

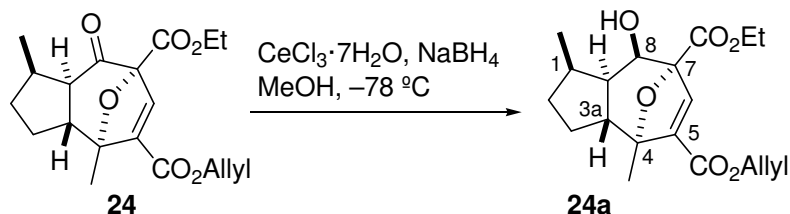
<sup>5</sup> SnCl<sub>2</sub>·xH<sub>2</sub>O was dehydrated by slow addition to a vigorously stirred solution of acetic anhydride (120 g salt per 100 g anhydride). After 1 h, the anhydrous SnCl<sub>2</sub> was filtered, washed with anhydrous Et<sub>2</sub>O to removed acetic acid and anhydride, and dried under vacuum.

Armarego, W.L.F., Chai, C.L.L., Purification of laboratory chemicals, **2003**, 5<sup>th</sup> edition, p 478.

<sup>6</sup> Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, 17, 1709-1716.



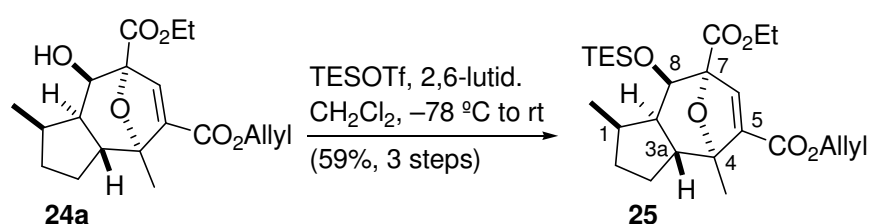
**(1*R*,3*aR*,4*R*,7*R*,8*aR*)-5-Allyl 7-ethyl 1,4-dimethyl-8-oxo-1,2,3,3*a*,4,7,8,8*a*-octahydro-4,7-epoxyazulene-5,7-dicarboxylate (**24**).**  $\text{Rh}_2(\text{OAc})_4$  (30 mg, 1 mol%) was added to a mixture of diazo compound **22** (1.0 g, 3.8 mmol) and allyl propiolate<sup>7</sup> **23** (2 mL) in toluene (50 mL) at room temperature. Then the closed Schlenck tube was transferred to a preheated oil bath (100 °C) and kept with stirring at this temperature for 15 min. The mixture was allowed to cool to room temperature and filtered through a pad of Celite, using diethyl ether as a rinse. The filtrate was concentrated in vacuo to afford crude cycloadduct **24** (1.32 g) as a yellowish oil, which was used in the next step without further purification.  $R_f = 0.50$  (petroleum ether/EtOAc, 4:1);  $[\alpha]_D^{20} = +74.4$  ( $c$  1.84,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 0.95 (d,  $J = 6.9$  Hz, 3H,  $\text{CHCH}_3$ ), 1.31 (dd,  $J = 7.1, 7.1$  Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.69 (s, 3H,  $\text{OCCH}_3$ ), 3.28 (dd,  $J = 11.7, 6.4$  Hz, 8*a*-H), 1.27–1.42 (m, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.67 (dd,  $J = 5.8, 5.8$  Hz, 2H,  $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 5.26 (dd,  $J = 10.4, 1.0$  Hz, 1H,  $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 5.33 (dd,  $J = 17.0, 1.3$  Hz, 1H,  $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 5.92 (dddd,  $J = 16.8, 10.9, 5.8, 5.5$  Hz, 1H,  $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 6.93 (s, 1H, 6-H); further protons could not be assigned.  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 14.1$  ( $\text{OCH}_2\text{CH}_3$ ), 17.7 ( $\text{OCCH}_3$ ), 18.8 ( $\text{CHCH}_3$ ), 27.0 (C-3), 29.0 (C-2), 29.8 (C-1), 47.1 (C-3*a*), 57.0 (C-8*a*), 62.5 ( $\text{OCH}_2\text{CH}_3$ ), 65.6 ( $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 87.2 (C-4), 93.2 (C-7), 118.9 ( $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 131.4 ( $\text{OCH}_2\text{CH}=\text{CH}_2$ ), 137.2 (C-6), 146.0 (C-5), 162.0 ( $\text{CO}_2\text{Allyl}$ ), 164.3 ( $\text{CO}_2\text{Et}$ ), 201.4 (C=O); HRMS (ESI):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{19}\text{H}_{24}\text{O}_6\text{Na}$  371.14651, found 371.14627.



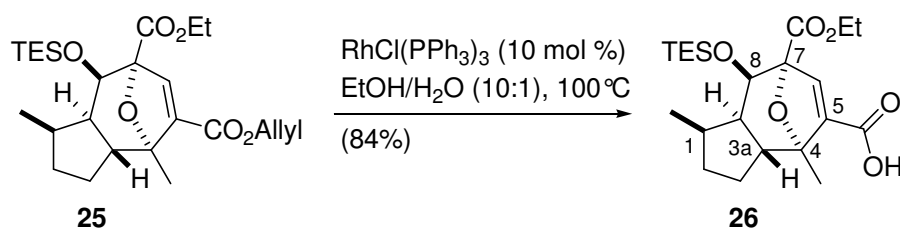
**(1*R*,3*aR*,4*R*,7*R*,8*S*,8*aR*)-5-Allyl 7-ethyl 8-hydroxy-1,4-dimethyl-1,2,3,3*a*,4,7,8,8*a*-octahydro-4,7-epoxyazulene-5,7-dicarboxylate (**24a**).** Cerium (III) chloride heptahydrate (3.5 g, 9.5 mmol) was added to the solution of crude ketone **24** (1.1 g, 3.2 mmol) in methanol (20 mL) and the mixture stirred for 30 min at room temperature, before it was cooled to  $-78$  °C and sodium borohydride (240 mg, 6.4 mmol) was added in portions. Stirring was continued for 2 h at the same temperature. The reaction was quenched by slow addition of water, and most of methanol was removed in vacuo. Diethyl ether (100 mL) and water (100 mL) were added, the layers separated, and the aqueous layer was extracted with diethyl ether (4  $\times$  50 mL). The combined organic layers were washed with saturated NaCl solution, dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo to give crude alcohol **24a** (1.1 g) as a yellowish oil, which was used in the next step without further purification.  $R_f = 0.20$  (petroleum ether/EtOAc, 4:1); An analytical sample was obtained by flash chromatography (petroleum ether/EtOAc, 9:1).  $[\alpha]_D^{20} = +17.0$  ( $c$  2.38,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):

<sup>7</sup> For the preparation of allyl propiolate **23** see: Feray, L.; Bertrand, M. P. *Eur. J. Org. Chem.* **2008**, 3164-3170.

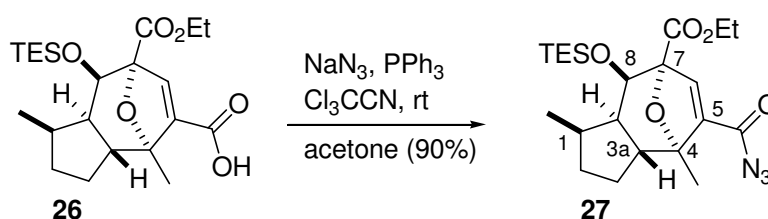
$\delta$  = 0.95 (d,  $J$  = 7.1 Hz, 3H, CHCH<sub>3</sub>), 0.98–1.03 (m, 1H, 2-H), 1.23–1.34 (m, 1H, 3-H), 1.31 (dd,  $J$  = 7.1, 7.1 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.56 (s, 1H, OCCH<sub>3</sub>), 1.72–1.78 (m, 1H, 3-H), 1.87 (ddd,  $J$  = 12.1, 12.1, 6.5 Hz, 1H, 3a-H), 1.94–2.02 (m, 2H, 2-H, OH), 2.17 (ddd,  $J$  = 12.5, 7.4, 4.6 Hz, 1H, 8a-H), 2.25 (app dddq,  $J$  = 7.4, 7.4, 2.9 Hz, 1H, 1-H), 4.28 (2 app dq,  $J$  = 14.2, 7.1, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.51 (dd,  $J$  = 4.7, 4.7 Hz, 1H, 9-H), 4.66 (dd,  $J$  = 13.3, 5.7 Hz, 2H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.24 (dd,  $J$  = 10.4, 1.0 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.33 (dd,  $J$  = 17.0, 1.3 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.93 (dddd,  $J$  = 16.8, 10.9, 5.8, 5.5 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 7.02 (s, 1H, 6-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.2 (OCH<sub>2</sub>CH<sub>3</sub>), 19.1 (OCCH<sub>3</sub>), 20.1 (CHCH<sub>3</sub>), 25.8 (C-3), 31.1 (C-2), 32.5 (C-1), 35.7 (C-3a), 47.8 (C-8a), 61.9 (OCH<sub>2</sub>CH<sub>3</sub>), 65.3 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 73.5 (C-8), 87.2 (C-4), 88.4 (C-7), 118.5 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 131.7 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 141.9 (C-6), 144.6 (C-5), 162.6 (CO<sub>2</sub>Allyl), 170.2 (CO<sub>2</sub>Et); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>26</sub>O<sub>6</sub>Na 373.16216, found 373.16217.



**(1R,3aR,4R,7R,8R,8aR)-5-Allyl 7-ethyl 1,4-dimethyl-8-((triethylsilyl)oxy)-1,2,3,3a,4,7,8,8a-octahydro-4,7-epoxyazulene-5,7-dicarboxylate (25).** 2,6-Lutidine (0.2 mL, 1.7 mmol) was added dropwise to a solution of alcohol **24a** (150 mg, 0.43 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at –78 °C. Then TES-triflate (0.2 mL, 0.8 mmol) was added at the same temperature. The mixture was allowed to warm to room temperature, filtered through a pad of silica gel, washed with 50% solution of ethyl acetate in petroleum ether, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 25:1) to give TES-ether **25** (118 mg, 59% over 3 steps) as a colorless oil.  $R_f$  = 0.53 (petroleum ether/EtOAc, 9:1);  $[\alpha]_D^{20}$  = +28.2 ( $c$  2.36, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.61 (ddd,  $J$  = 15.8, 7.6, 7.6 Hz, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.88 (d,  $J$  = 6.9 Hz, 3H, CHCH<sub>3</sub>), 0.93 (dd,  $J$  = 7.9, 7.9 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.97–1.05 (m, 1H, 2-H), 1.24–1.33 (m, 1H, 3-H), 1.33 (dd,  $J$  = 7.4, 7.4 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.54 (s, 3H, OCCH<sub>3</sub>), 1.68–1.75 (m, 1H, 3-H), 1.87–1.96 (m, 2H, H-2, 3a-H), 2.07 (ddd,  $J$  = 12.5, 6.4, 4.3 Hz, 1H, 8a-H), 2.15–2.25 (m, 1H, 1-H), 4.28 (2 app dq,  $J$  = 10.9, 7.4 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.60–4.75 (m, 3H, 8-H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.24 (dd,  $J$  = 10.4, 0.8 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.33 (dd,  $J$  = 17.3, 1.3 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 5.93 (dddd,  $J$  = 16.8, 10.9, 5.8, 5.5 Hz, 1H, OCH<sub>2</sub>CH=CH<sub>2</sub>), 6.98 (s, 1H, 6-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.8 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 6.8 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 14.2 (OCH<sub>2</sub>CH<sub>3</sub>), 19.4 (OCCH<sub>3</sub>), 19.6 (CHCH<sub>3</sub>), 24.8 (C-3), 31.1 (C-2), 32.9 (C-1), 35.2 (C-3a), 48.3 (C-8a), 61.9 (OCH<sub>2</sub>CH<sub>3</sub>), 65.0 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 73.3 (C-8), 86.8 (C-4), 89.2 (C-7), 118.0 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 132.0 (OCH<sub>2</sub>CH=CH<sub>2</sub>), 142.8 (C-6), 143.1 (C-5), 162.8 (CO<sub>2</sub>Allyl), 170.1 (CO<sub>2</sub>Et); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>25</sub>H<sub>40</sub>O<sub>6</sub>SiNa 487.24864, found 487.24857.

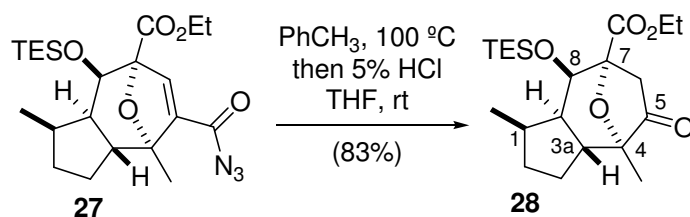


**(1*R*,3*aR*,4*R*,7*R*,8*R*,8*aR*)-7-(Ethoxycarbonyl)-1,4-dimethyl-8-((triethylsilyl)oxy)-1,2,3,3*a*,4,7,8,8*a*-octahydro-4,7-epoxyazulene-5-carboxylic acid (**26**).** RhCl(PPh<sub>3</sub>)<sub>3</sub> (10 mg) was added to a solution of allyl ester **25** (42 mg, 0.09 mmol) in a mixture of water/ethanol (2 mL, 1:10). Then the closed flask was transferred to a preheated (100 °C) oil bath. The mixture was stirred for 1 h at this temperature, cooled, and then the solvents were removed in vacuo. The residue was purified by flash chromatography (petroleum ether/Et<sub>2</sub>O/AcOH (glac.), 4:1:0.01) to give carboxylic acid **26** (32 mg, 84%) as a colorless oil. *R*<sub>f</sub> = 0.2 (petroleum ether/Et<sub>2</sub>O/AcOH (glac.), 4:1:0.01); [α]<sup>20</sup><sub>D</sub> = +50.6 (*c* 3.48, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.62 (ddd, *J* = 15.9, 7.8, 7.8 Hz, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.90 (d, *J* = 7.1 Hz, 3H, CHCH<sub>3</sub>), 0.94 (dd, *J* = 8.1, 8.1 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.99–1.07 (m, 1H, 2-H), 1.26–1.37 (m, 1H, 3-H), 1.33 (dd, *J* = 7.1, 7.1 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.55 (s, 3H, OCCH<sub>3</sub>), 1.68–1.76 (m, 1H, 3-H), 1.88–1.96 (m, 2H, 3*a*-H, 2-H), 2.09 (ddd, *J* = 12.4, 6.4, 4.4 Hz, 1H, 8*a*-H), 2.17–2.26 (m, 1H, 1-H), 4.29 (2 app dq, *J* = 10.9, 7.4 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.67 (d, *J* = 4.3 Hz, 1H, 8-H), 7.14 (s, 1H, 6-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 4.8 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 6.9 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 14.1 (OCH<sub>2</sub>CH<sub>3</sub>), 19.4 (OCCH<sub>3</sub>), 19.6 (CHCH<sub>3</sub>), 24.8 (C-3), 31.0 (C-2), 32.9 (C-1), 35.2 (C-3*a*), 48.4 (C-8*a*), 61.9 (OCH<sub>2</sub>CH<sub>3</sub>), 73.4 (C-8), 86.7 (C-4), 89.2 (C-7), 142.8 (C-5), 145.7 (C-6), 168.2 (CO<sub>2</sub>Et), 169.9 (CO<sub>2</sub>H); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>36</sub>O<sub>6</sub>SiNa 447.21734, found 447.21730.

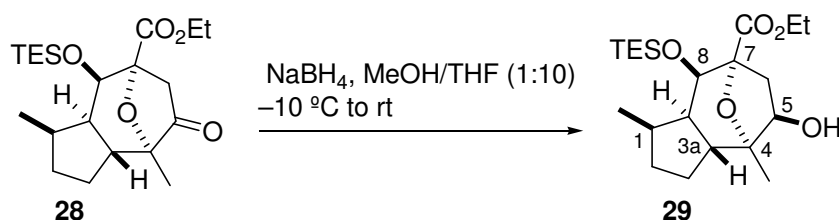


**(1*R*,3*aR*,4*R*,7*R*,8*R*,8*aR*)-Ethyl 5-(azidocarbonyl)-1,4-dimethyl-8-((triethylsilyl)oxy)-1,2,3,3*a*,4,7,8,8*a*-octahydro-4,7-epoxyazulene-7-carboxylate (**27**).** Trichloroacetonitrile (0.03 mL, 0.33 mmol) was added dropwise to a stirred solution of carboxylic acid **26** (70 mg, 0.16 mmol), sodium azide (16 mg, 0.25 mmol), PPh<sub>3</sub> (86 mg, 0.33 mmol) in acetone (2 mL) at room temperature. After 30 min the solvent was removed by a flow of nitrogen and the residue was purified by flash chromatography (petroleum ether/EtOAc, 25:1) to give azide **27** (66 mg, 90%) as a colorless oil. *R*<sub>f</sub> = 0.37 (petroleum ether/EtOAc, 9:1); [α]<sup>20</sup><sub>D</sub> = +40.1 (*c* 1.63, MeOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.61 (ddd, *J* = 15.9, 7.8, 7.8 Hz, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.88 (d, *J* = 7.1 Hz, 3H, CHCH<sub>3</sub>), 0.94 (dd, *J* = 8.1, 8.1 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.97–1.05 (m, 1H, 2-H), 1.25–1.37 (m, 1H, 3-H), 1.32 (dd, *J* = 7.1, 7.1 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.54 (s, 3H, OCCH<sub>3</sub>), 1.68–1.76 (m, 1H, 3-H), 1.81–1.95 (m, 2H, 3*a*-H, 2-H), 2.06 (ddd, *J* = 12.4, 6.4, 4.4 Hz, 1H, 8*a*-H), 2.15–2.25 (m, 1H, 1-H), 4.28 (2 app dq, *J* = 10.9, 7.4 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.66 (d, *J* = 4.3 Hz, 1H, 8-H), 7.06 (s, 1H, 6-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 4.8 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 6.8 (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 14.1 (OCH<sub>2</sub>CH<sub>3</sub>), 19.2 (OCCH<sub>3</sub>), 19.5 (CHCH<sub>3</sub>), 24.7 (C-3), 31.0 (C-2), 32.9 (C-1), 35.2 (C-3*a*), 48.3 (C-8*a*), 62.0 (OCH<sub>2</sub>CH<sub>3</sub>), 73.4 (C-8), 86.9 (C-4), 89.2 (C-7), 144.4 (C-5), 145.8 (C-6), 168.4 (CO<sub>2</sub>Et), 169.7 (CON<sub>3</sub>); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>35</sub>N<sub>3</sub>O<sub>5</sub>SiNa 472.22382, found 472.22384.



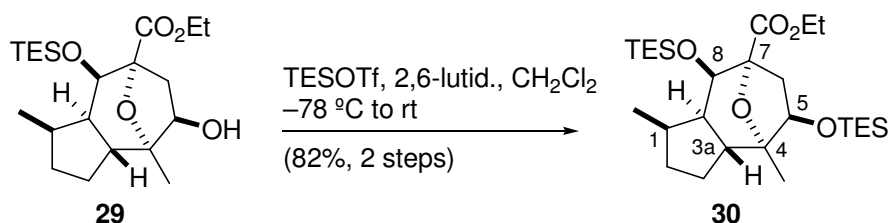


**(1*R*,3*aR*,4*R*,7*R*,8*R*,8*aR*)-Ethyl 1,4-dimethyl-5-oxo-8-((triethylsilyl)oxy)decahydro-4,7-epoxyazulene-7-carboxylate (28).** Azide **27** (66 mg, 0.15 mmol) was dissolved in toluene (2 mL) and stirred for 1 h at 100 °C. Then the solvent was removed in vacuo, the residue was dissolved in THF (2 mL) followed by the addition of 5% HCl (0.5 mL) and THF (0.5 mL). Stirring was continued for 15 min, then the reaction was quenched with triethylamine (0.5 mL) and the solvents were evaporated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 25:1) to give ketone **28** (48 mg, 83%) as a colorless oil.  $R_f = 0.53$  (petroleum ether/EtOAc, 9:1);  $[\alpha]_D^{20} = +0.5$  ( $c$  0.98,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.60$  (dddd,  $J = 16.8, 9.9, 8.4, 1.8$  Hz, 6H,  $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 0.92 (d,  $J = 9.4$  Hz, 3H,  $\text{CHCH}_3$ ), 0.93 (dd,  $J = 8.1, 8.1$  Hz, 9H,  $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 1.13–1.21 (m, 1H, 2-H), 1.26 (s, 3H,  $\text{OCCH}_3$ ), 1.32 (dd,  $J = 7.1, 7.1$  Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.40 (ddd,  $J = 10.9, 7.2, 1.3$  Hz, 1H, 3-H), 1.60–1.68 (m, 1H, 3-H), 1.85 (ddd,  $J = 13.2, 10.7, 7.4$  Hz, 1H, 3a-H), 1.92–2.02 (m, 2H, 2-H, 8a-H), 2.22–2.31 (m, 1H, 1-H), 2.60 (d,  $J = 18.1$  Hz, 1H, 6-H), 3.10 (d,  $J = 18.1$  Hz, 1H, 6-H), 4.28 (2 app dq,  $J = 10.8, 7.1$  Hz, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.73 (d,  $J = 4.1$  Hz, 1H, 8-H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 4.8$  ( $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 6.9 ( $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 14.1 ( $\text{OCH}_2\text{CH}_3$ ), 16.5 ( $\text{OCCH}_3$ ), 19.2 ( $\text{CHCH}_3$ ), 24.0 (C-3), 32.4 (C-1), 32.6 (C-2), 36.4 (C-3a), 38.8 (C-6), 45.2 (C-8a), 62.0 ( $\text{OCH}_2\text{CH}_3$ ), 71.2 (C-8), 83.0 (C-4), 84.2 (C-7), 171.4 ( $\text{CO}_2\text{Et}$ ), 214.6 (C=O); HRMS (ESI):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{21}\text{H}_{36}\text{O}_5\text{SiNa}$  419.22242, found 419.22238.

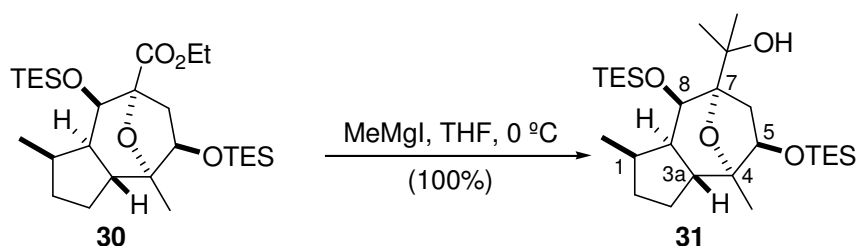


**(1*R*,3*aR*,4*R*,5*R*,7*R*,8*R*,8*aR*)-Ethyl 5-hydroxy-1,4-dimethyl-8-((triethylsilyl)oxy)decahydro-4,7-epoxyazulene-7-carboxylate (29).** Sodium borohydride (21 mg, 0.55 mmol) was added in portions to a stirred solution of ketone **28** (150 mg, 0.38 mmol) in methanol/THF (6.6 mL, 1:10) at  $-10\text{ }^\circ\text{C}$ . The mixture was allowed to warm to room temperature, and then quenched by careful addition of water. Most of the organic solvents were evaporated in vacuo, the residue was diluted with water (10 mL), and the mixture extracted with ethyl acetate ( $3 \times 10$  mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 4:1) to give alcohol **29** (150 mg, 85%) as a colorless oil.  $R_f = 0.37$  (petroleum ether/EtOAc, 4:1);  $[\alpha]_D^{20} = +5.8$  ( $c$  2.46,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz, DMSO):  $\delta = 0.48$ –0.55 (m, 6H,  $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 0.88 (dd,  $J = 8.1, 8.1$  Hz, 9H,  $\text{Si}(\text{CH}_2\text{CH}_3)_3$ ), 0.96 (d,  $J = 6.8$  Hz, 3H,  $\text{CHCH}_3$ ), 1.09 (s, 3H,  $\text{OCCH}_3$ ), 1.10–1.35 (m, 2H, 2-H, 3-H), 1.21 (dd,  $J = 7.1, 7.1$  Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.47 (dddd,  $J = 12.4, 8.3, 8.3, 4.3$  Hz, 1H, 3-H), 1.71 (ddd,  $J = 13.8, 6.2, 6.1$ , 1H, 8a-H), 1.87–1.96 (m, 1H, 2-H), 2.14 (dd,  $J = 13.3, 8.0$  Hz, 1H, 6-H), 2.19–2.35 (m, 3H, 1-H, 3a-H, 6-H), 3.60 (ddd,  $J = 8.6, 8.6, 4.3$  Hz, 1H, 5-H), 4.10 (2 app dq,  $J = 10.9, 7.1$  Hz, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.63 (d,  $J = 6.1$  Hz, 1H, 8-H), 5.20 (d,  $J = 4.3$  Hz, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 4.3$  ( $\text{SiCH}_2\text{CH}_3$ ), 6.7 ( $\text{SiCH}_2\text{CH}_3$ ), 13.9 ( $\text{OCH}_2\text{CH}_3$ ), 18.8 ( $\text{CHCH}_3$ ), 19.9

(OCCH<sub>3</sub>), 23.8 (C-3), 32.0 (C-1), 32.7 (C-3a), 32.8 (C-6), 33.6 (C-2), 44.2 (C-8a), 61.0 (OCH<sub>2</sub>CH<sub>3</sub>), 70.8 (C-8), 76.8 (C-5), 82.5 (C-4), 83.3 (C-7), 171.8 (CO<sub>2</sub>Et); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>21</sub>H<sub>38</sub>O<sub>5</sub>SiNa 421.23807, found 421.23845.

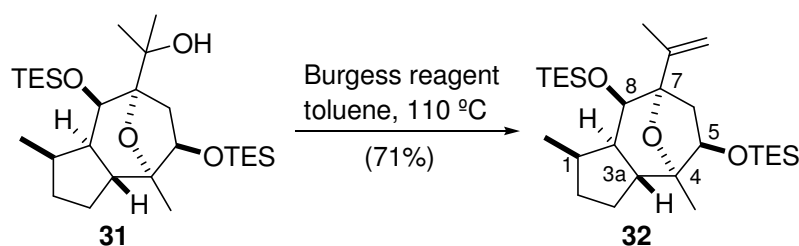


**(1*R*,3*aR*,4*R*,5*R*,7*R*,8*R*,8*aR*)-Ethyl 1,4-dimethyl-5,8-bis((triethylsilyl)oxy)decahydro-4,7-epoxyazulene-7-carboxylate (30).** 2,6-Lutidine (0.13 mL, 1.15 mmol) was added dropwise to a solution of alcohol **29** (150 mg, 0.38 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -78 °C. Then TES-triflate (0.13 mL, 0.58 mmol) was added at the same temperature. The mixture was allowed to warm to room temperature (ca 3 h), filtered through a pad of silica gel, the filter cake was washed with mixture of petroleum ether/EtOAc (1:1), and the filtrates concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 25:1) to afford TES-ether **30** (159 mg, 82% over 2 steps). *R*<sub>f</sub> = 0.55 (petroleum ether/EtOAc, 9:1); [α]<sub>D</sub><sup>20</sup> = +2.0 (*c* 6.00, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.51–0.61 (m, 12H, (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>)<sub>2</sub>), 0.92 (dd, *J* = 7.9, 7.9 Hz, 9H, (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.95 (dd, *J* = 8.1, 8.1 Hz, 9H, (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 1.00 (d, *J* = 7.1 Hz, 3H, CHCH<sub>3</sub>), 1.18–1.26 (m, 1H, 2-H), 1.20 (s, 3H, OCCH<sub>3</sub>), 1.30 (dd, *J* = 7.1, 7.1 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.30–1.39 (m, 1H, 3-H), 1.53 (dddd, *J* = 16.9, 8.8, 8.5, 4.7 Hz, 1H, 3-H), 1.81 (ddd, *J* = 14.0, 6.1, 6.1 Hz, 1H, 8a-H), 1.87–1.96 (m, 1H, 2-H), 2.22–2.51 (m, 4H, 1-H, 3a-H, 6-H, 6-H), 3.77 (dd, *J* = 9.3, 7.5 Hz, 1H, 5-H), 4.21 (2 app dq, *J* = 10.8, 7.1 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.66 (d, *J* = 5.8 Hz, 1H, 8-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 4.8 (SiCH<sub>2</sub>CH<sub>3</sub>), 4.9 (SiCH<sub>2</sub>CH<sub>3</sub>), 6.7 (SiCH<sub>2</sub>CH<sub>3</sub>), 6.8 (SiCH<sub>2</sub>CH<sub>3</sub>), 14.1 (OCH<sub>2</sub>CH<sub>3</sub>), 18.7 (CHCH<sub>3</sub>), 20.2 (OCCH<sub>3</sub>), 24.2 (C-3), 32.7 (C-1), 33.2 (C-3a), 34.1 (C-6), 44.6 (C-2), 61.5 (OCH<sub>2</sub>CH<sub>3</sub>), 71.6 (C-8), 78.1 (C-5), 83.2 (C-4), 84.4 (C-7), 172.7 (CO<sub>2</sub>Et); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>52</sub>O<sub>5</sub>Si<sub>2</sub>Na 535.32455, found 535.325022.

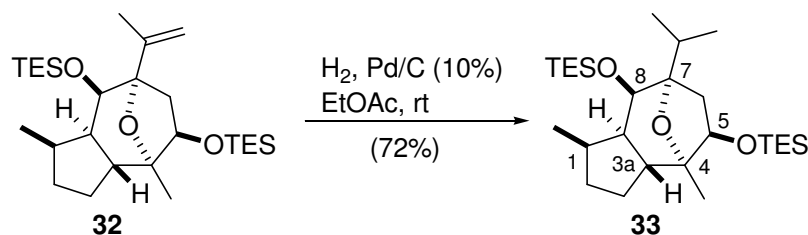


**2-((1*R*,3*aR*,4*R*,5*R*,7*R*,8*R*,8*aR*)-1,4-Dimethyl-5,8-bis((triethylsilyl)oxy)decahydro-4,7-epoxyazulen-7-yl)propan-2-ol (31).** Freshly prepared methylmagnesium iodide (0.12 mL, 1M solution in Et<sub>2</sub>O, 0.12 mmol) was added dropwise to a stirred solution of ester **30** (10 mg, 0.019 mmol) in THF (1 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and quenched with saturated NH<sub>4</sub>Cl (0.5 mL), diluted with water (2 mL) and extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with saturated NaCl solution (2 × 10 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 25:1) to give tertiary alcohol **31** (9.7 mg, 100%) as a colorless oil. *R*<sub>f</sub> = 0.48 (petroleum ether/EtOAc, 9:1); [α]<sub>D</sub><sup>20</sup> = +3.4 (*c* 1.00, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.57 (ddd, *J* = 16.7, 8.6, 1.3

Hz, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.65 (ddd, *J* = 15.9, 7.9, 2.3 Hz, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.94 (dd, *J* = 7.8, 7.8 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.96 (dd, *J* = 8.1, 8.1 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 1.00 (d, *J* = 7.1 Hz, 3H, CHCH<sub>3</sub>), 1.14 (s, 3H, OCCH<sub>3</sub>), 1.16 (s, 3H, C(CH<sub>3</sub>)<sub>2</sub>), 1.18 (s, 3H, C(CH<sub>3</sub>)<sub>2</sub>), 1.22–1.28 (m, 1H, 2-H), 1.35 (dddd, *J* = 12.2, 10.3, 10.3, 6.2 Hz, 1H, 3-H), 1.49–1.58 (m, 1H, 3-H), 1.69 (ddd, *J* = 13.6, 6.4, 4.7 Hz, 1H, 8a-H), 1.88 (dddd, *J* = 12.1, 10.5, 7.1, 4.9 Hz, 1H, 2-H), 1.98 (dd, *J* = 13.0, 9.7 Hz, 1H, 6-H), 2.15–2.24 (m, 2H, 1-H, 6-H), 2.55 (ddd, *J* = 13.6, 10.0, 9.0 Hz, 1H, 3a-H), 3.66 (dd, *J* = 9.6, 6.6 Hz, 1H, 5-H), 4.45 (d, *J* = 4.6 Hz, 1H, 8-H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 4.9 (SiCH<sub>2</sub>CH<sub>3</sub>), 5.9 (SiCH<sub>2</sub>CH<sub>3</sub>), 6.8 (SiCH<sub>2</sub>CH<sub>3</sub>), 7.2 (SiCH<sub>2</sub>CH<sub>3</sub>), 18.6 (CHCH<sub>3</sub>), 21.2 (OCCH<sub>3</sub>), 24.0 (C-3), 24.8 (C(CH<sub>3</sub>)<sub>2</sub>), 24.8 (C(CH<sub>3</sub>)<sub>2</sub>), 32.6 (C-1), 32.7 (C-6), 33.1 (C-3a), 34.9 (C-2), 45.9 (C-8a), 71.0 (C-8), 73.3 (C(CH<sub>3</sub>)<sub>2</sub>), 79.6 (C-5), 81.4 (C-4), 89.1 (C-7); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>54</sub>O<sub>4</sub>Si<sub>2</sub>Na 521.34528, found 521.345436.

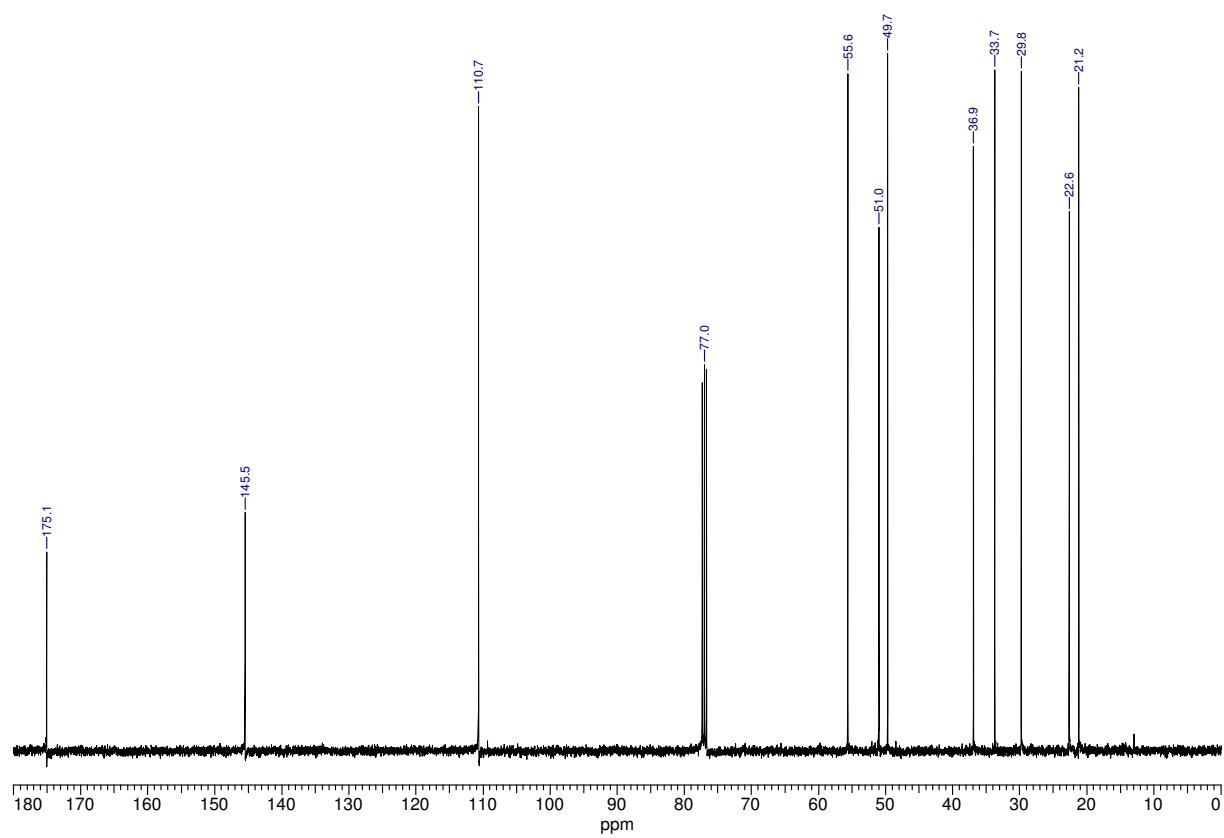
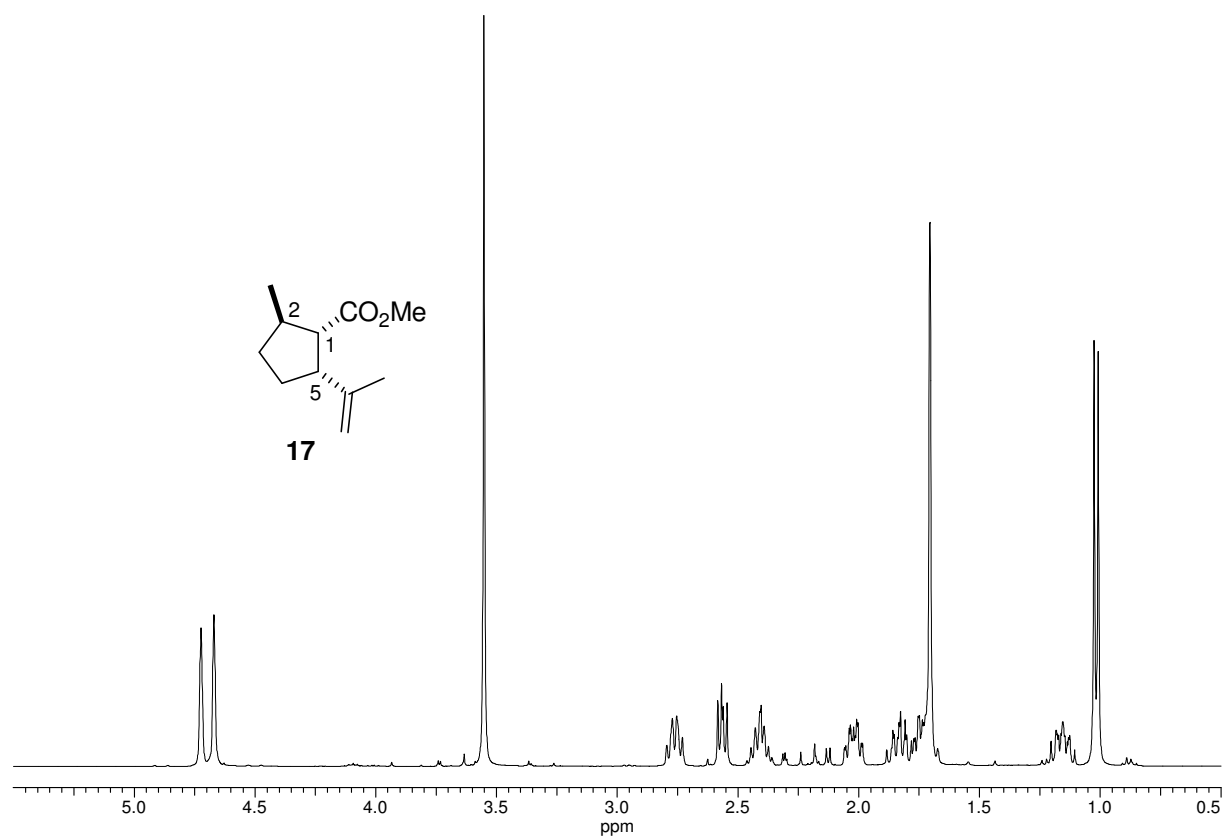


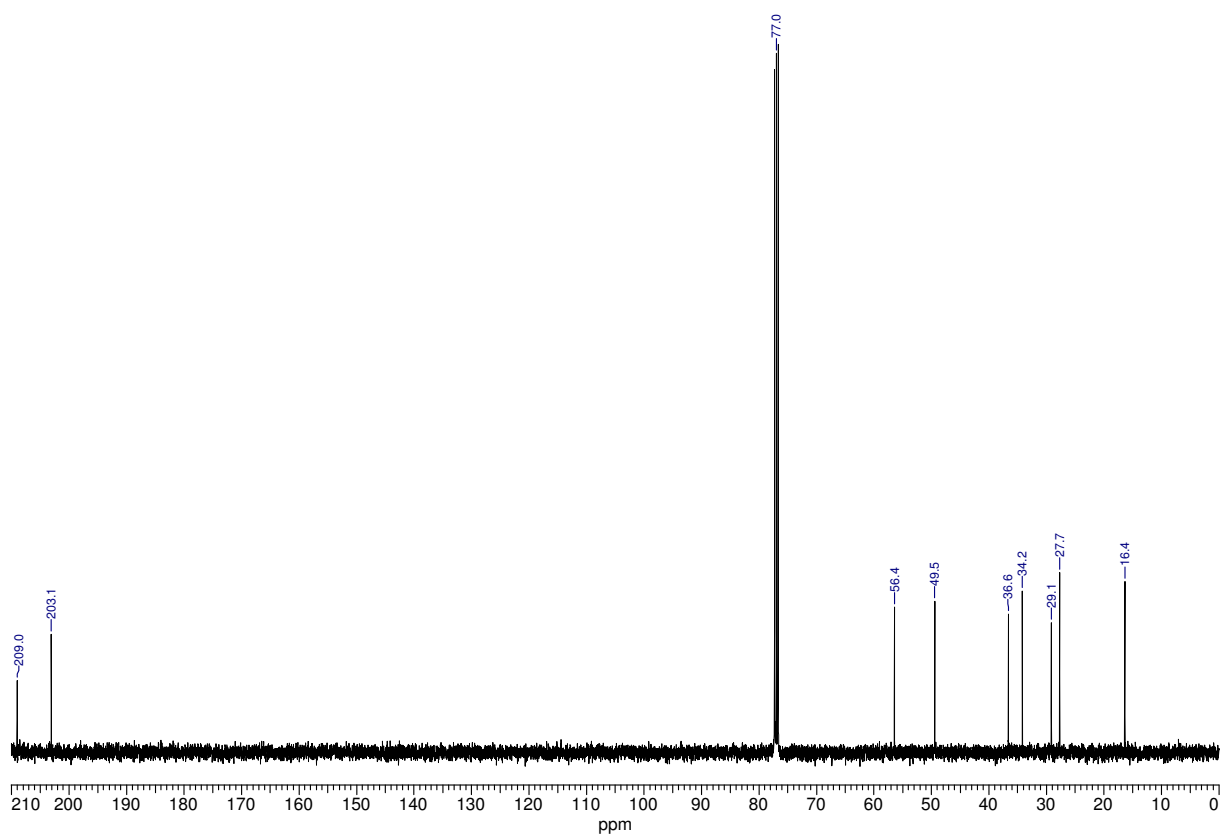
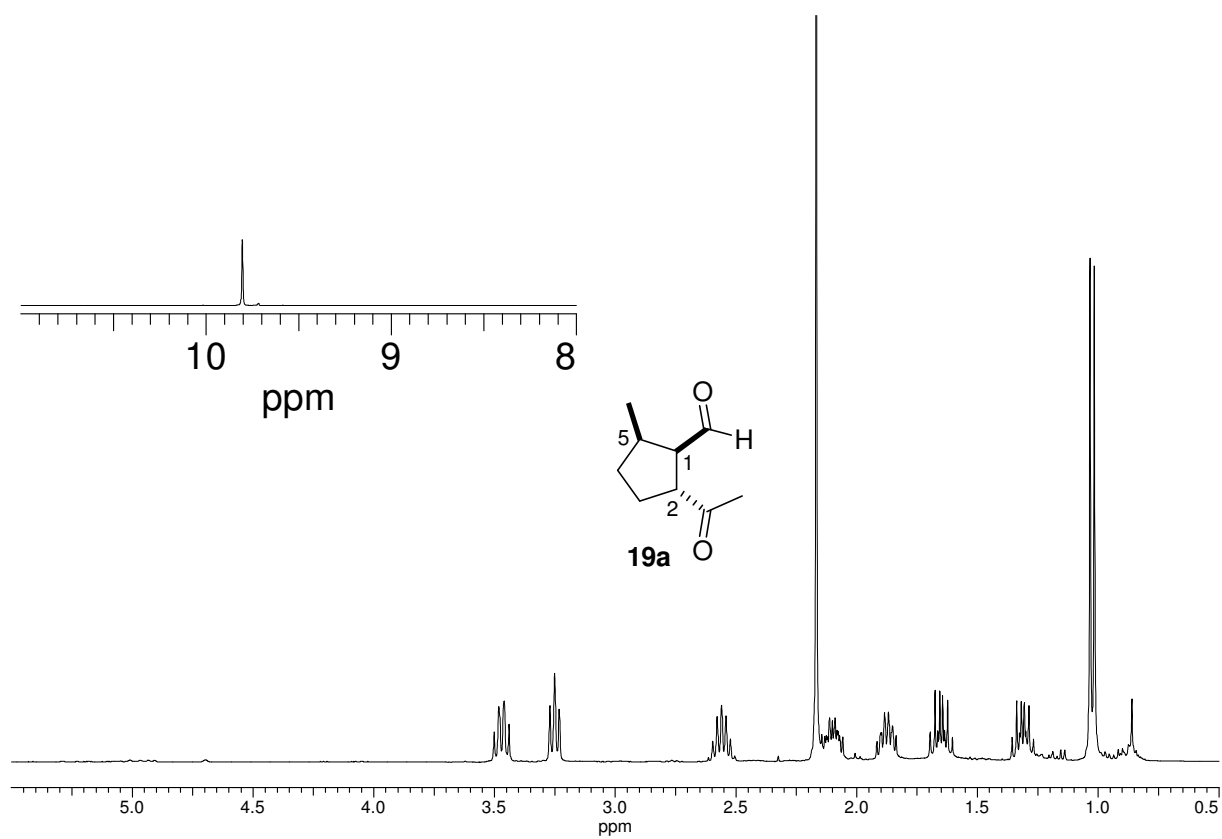
**(((1*R*,3*aR*,4*R*,5*R*,7*S*,8*R*,8*aR*)-1,4-Dimethyl-7-(prop-1-en-2-yl)decahydro-4,7-epoxyazulene-5,8-diyl)bis(oxy))bis(triethylsilane) (32).** Burgess reagent<sup>8</sup> (10 mg, 0.040 mmol) was added to a stirred solution of alcohol **31** (5 mg, 0.010 mmol) in toluene (1 mL) and the mixture stirred at 110 °C for 5 min. Then the solvent was evaporated and the residue purified by flash chromatography (petroleum ether/EtOAc, 30:1) providing alkene **32** (3.4 mg, 71%) as a colorless oil. *R*<sub>f</sub> = 0.31 (petroleum ether/EtOAc, 33:1); [α]<sub>D</sub><sup>20</sup> = +4.8 (*c* 0.31, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.50–0.60 (m, 12H, (Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>)<sub>2</sub>), 0.92 (dd, *J* = 7.8, 7.8 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.95 (dd, *J* = 8.1, 8.1 Hz, 9H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 1.00 (d, *J* = 6.8 Hz, 3H, CHCH<sub>3</sub>), 1.16 (s, 3H, OCCH<sub>3</sub>), 1.21–1.27 (m, 1H, 2-H), 1.30–1.39 (m, 1H, 3-H), 1.49–1.58 (m, 1H, 3-H), 1.73 (ddd, *J* = 14.0, 5.9, 5.8 Hz, 1H, 8a-H), 1.77 (s, 3H, CH<sub>2</sub>=CCH<sub>3</sub>), 1.84–1.93 (m, 1H, 2-H), 2.04 (dd, *J* = 13.0, 9.2 Hz, 1H, 6-H), 2.19–2.24 (m, 1H, 1-H), 2.29 (dd, *J* = 13.1, 7.3 Hz, 1H, 6-H), 2.49 (ddd, *J* = 14.0, 10.1, 8.7 Hz, 1H, 3a-H), 3.68 (dd, *J* = 9.3, 7.3 Hz, 1H, 5-H), 4.25 (d, *J* = 6.1 Hz, 1H, 8-H), 4.88 (dd, *J* = 1.4, 1.4 Hz, 1H, C=CH<sub>2</sub>), 4.91 (br.s, 1H, C=CH<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 5.0 (SiCH<sub>2</sub>CH<sub>3</sub>), 5.4 (SiCH<sub>2</sub>CH<sub>3</sub>), 6.8 (SiCH<sub>2</sub>CH<sub>3</sub>), 7.0 (SiCH<sub>2</sub>CH<sub>3</sub>), 18.4 (CH<sub>3</sub>C=CH<sub>2</sub>), 18.6 (CHCH<sub>3</sub>), 20.7 (OCCH<sub>3</sub>), 23.9 (C-3), 32.8 (C-3a), 32.9 (C-1), 34.0 (C-2), 35.0 (C-6), 45.7 (C-8a), 72.4 (C-8), 78.7 (C-5), 80.9 (C-4), 85.9 (C-7), 112.1 (CH<sub>3</sub>C=CH<sub>2</sub>), 147.0 (CH<sub>3</sub>C=CH<sub>2</sub>); HRMS (ESI): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>52</sub>O<sub>3</sub>Si<sub>2</sub>Na 503.33472, found 503.33510.

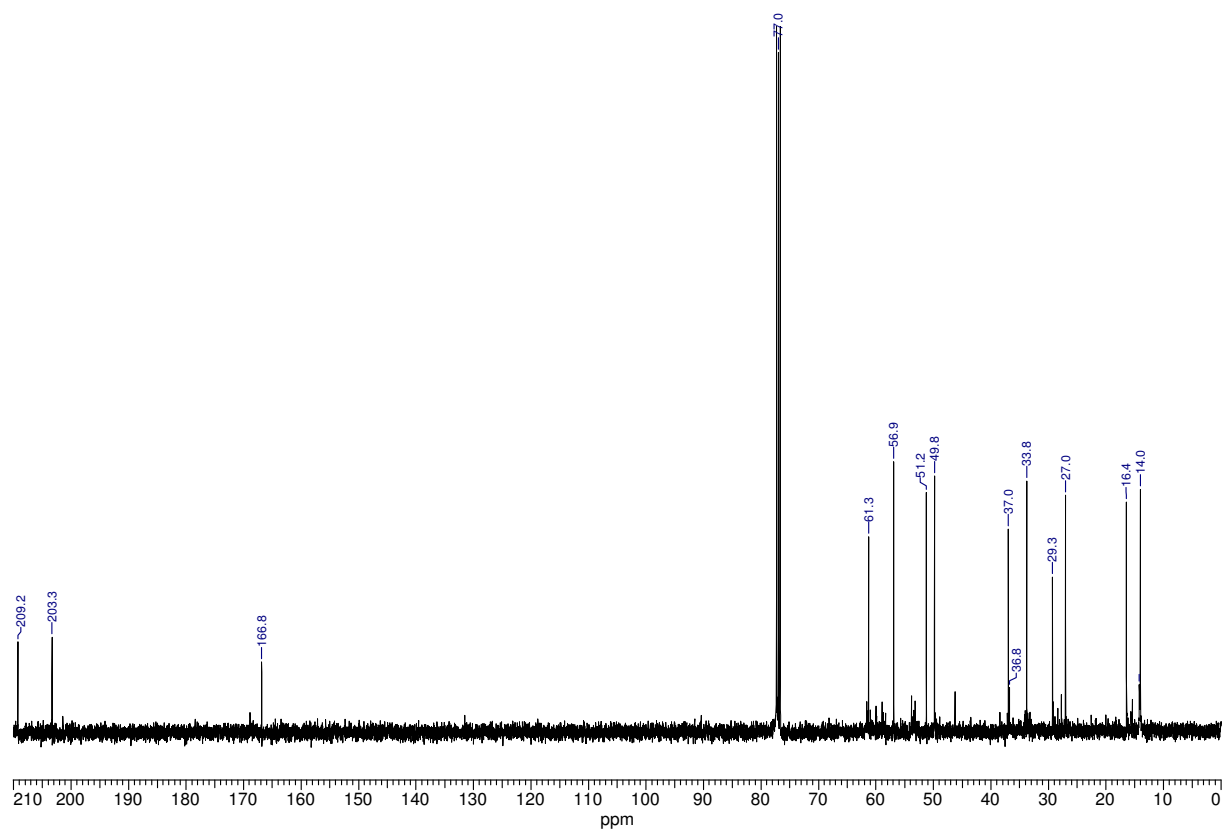
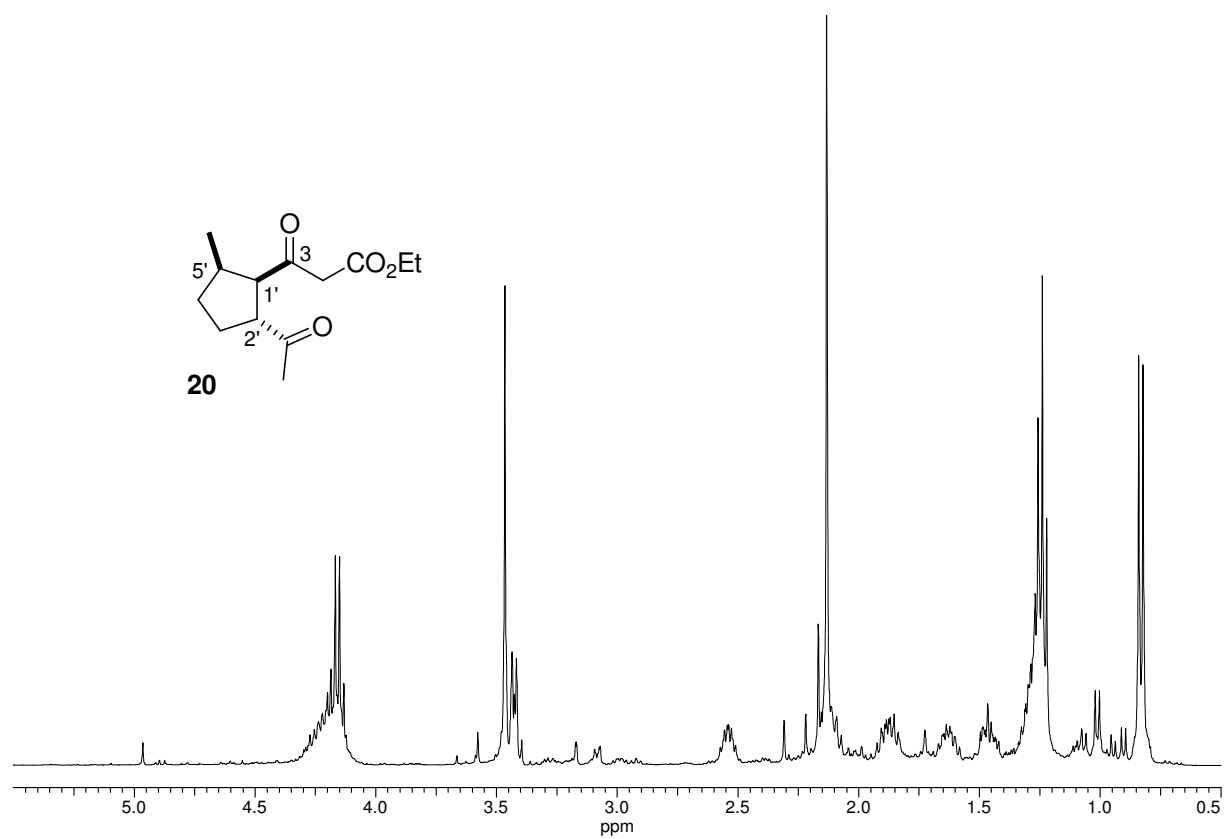


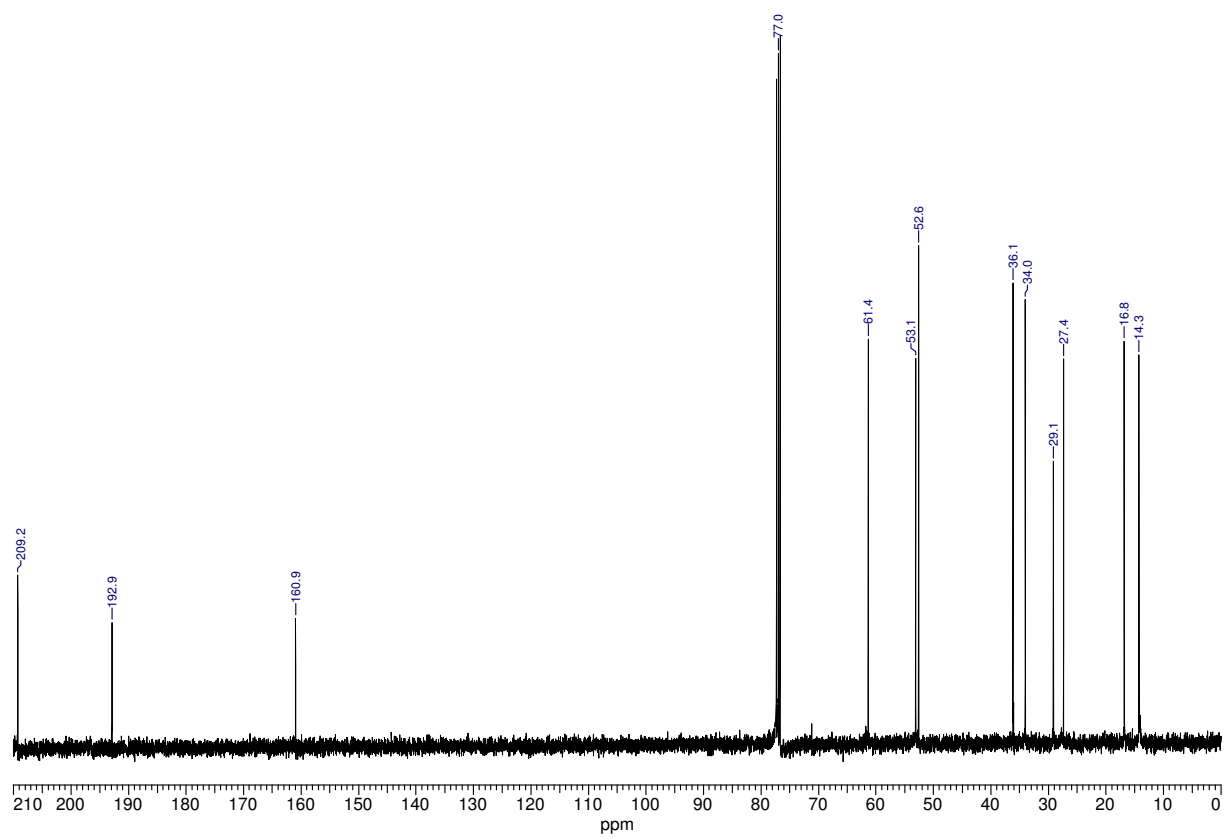
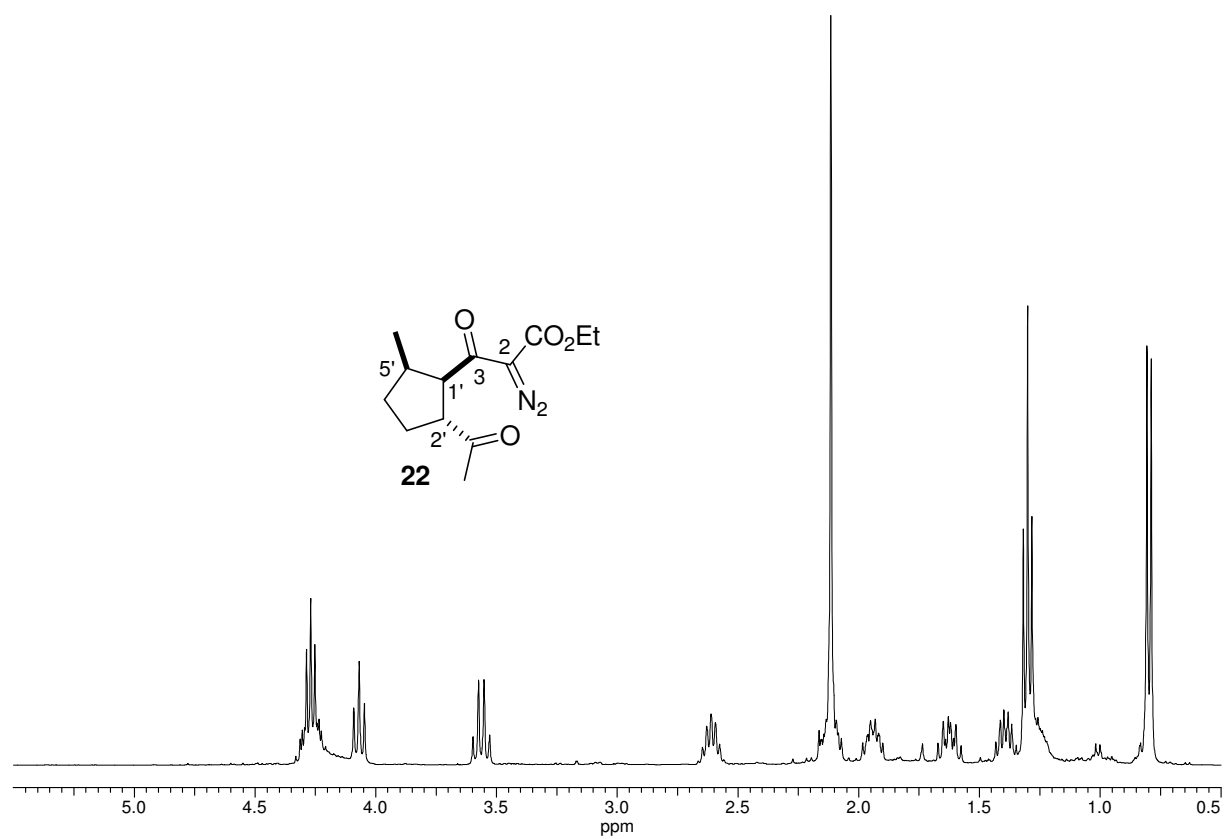
<sup>8</sup> For the preparation of Burgess reagent see: Burgess, E.M., Penton, H.R., Taylor, E.A. *J. Org. Chem.* **1973**, *38*, 26-31.



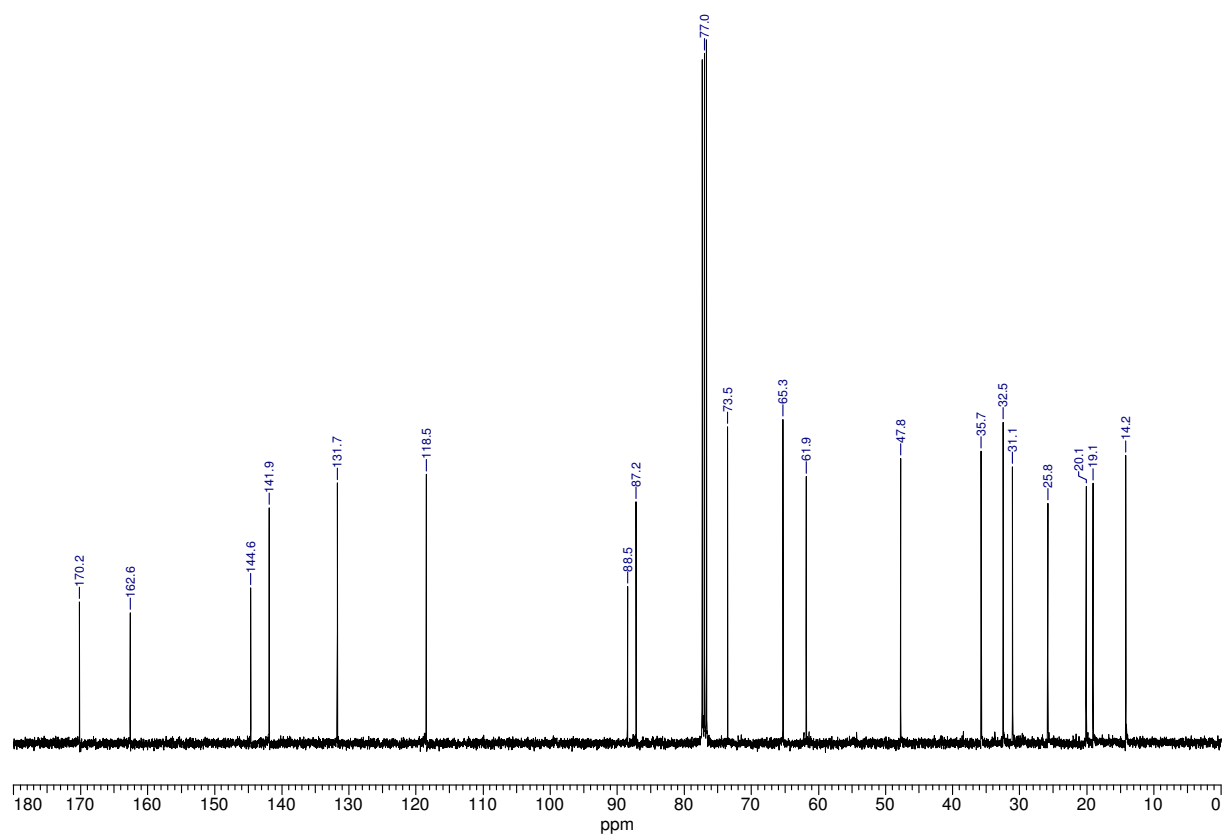
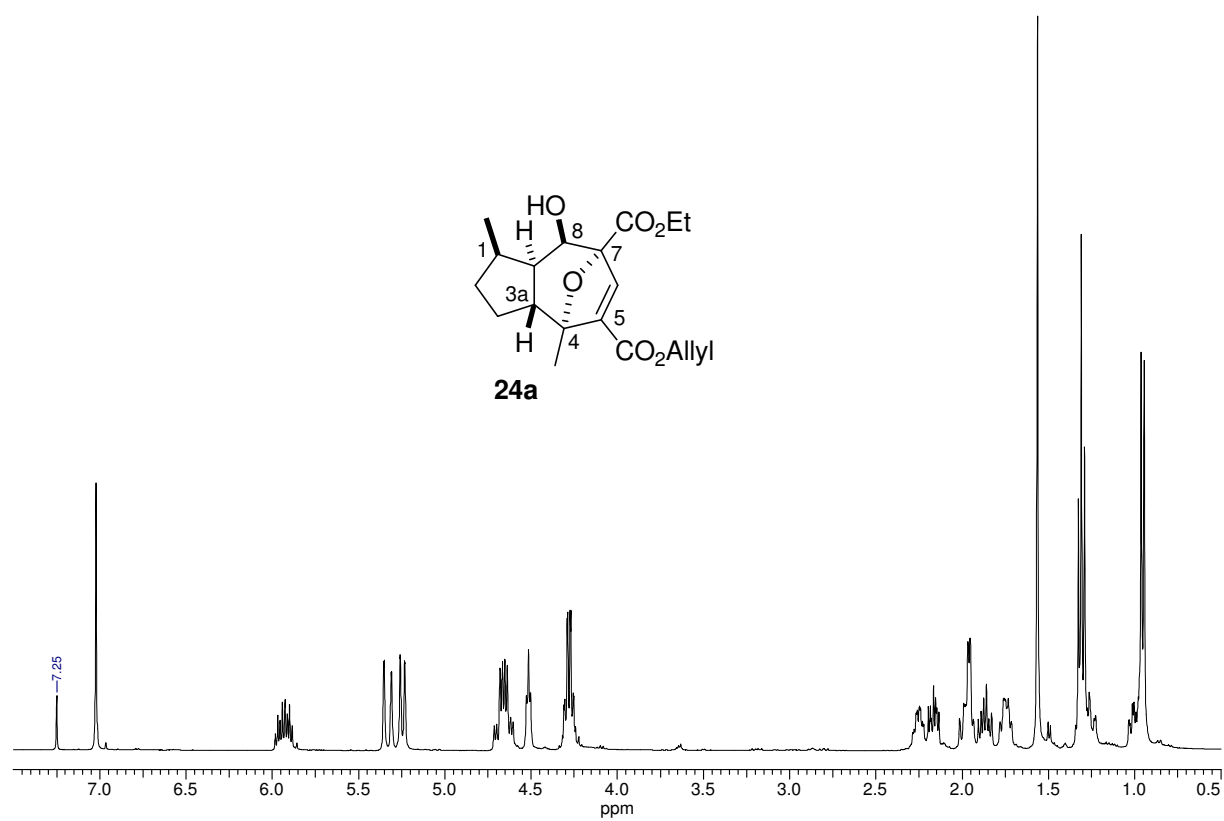


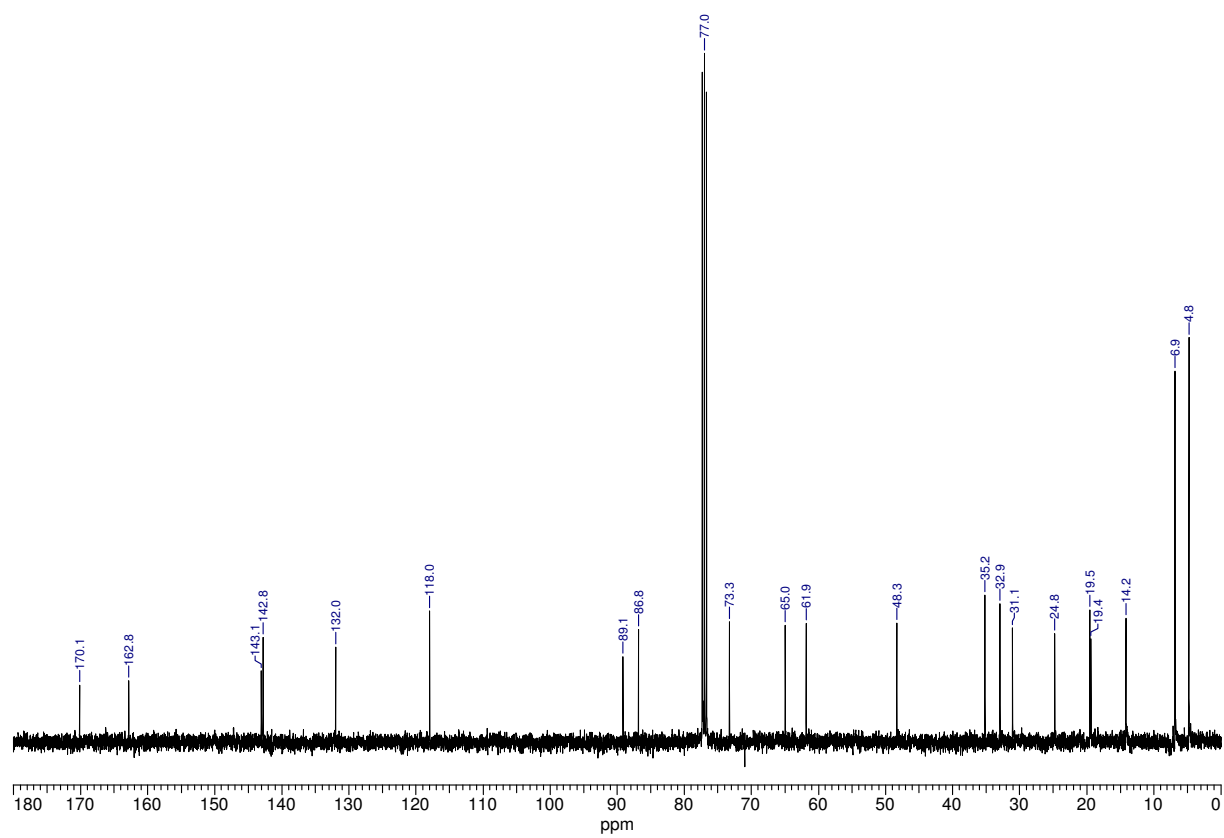
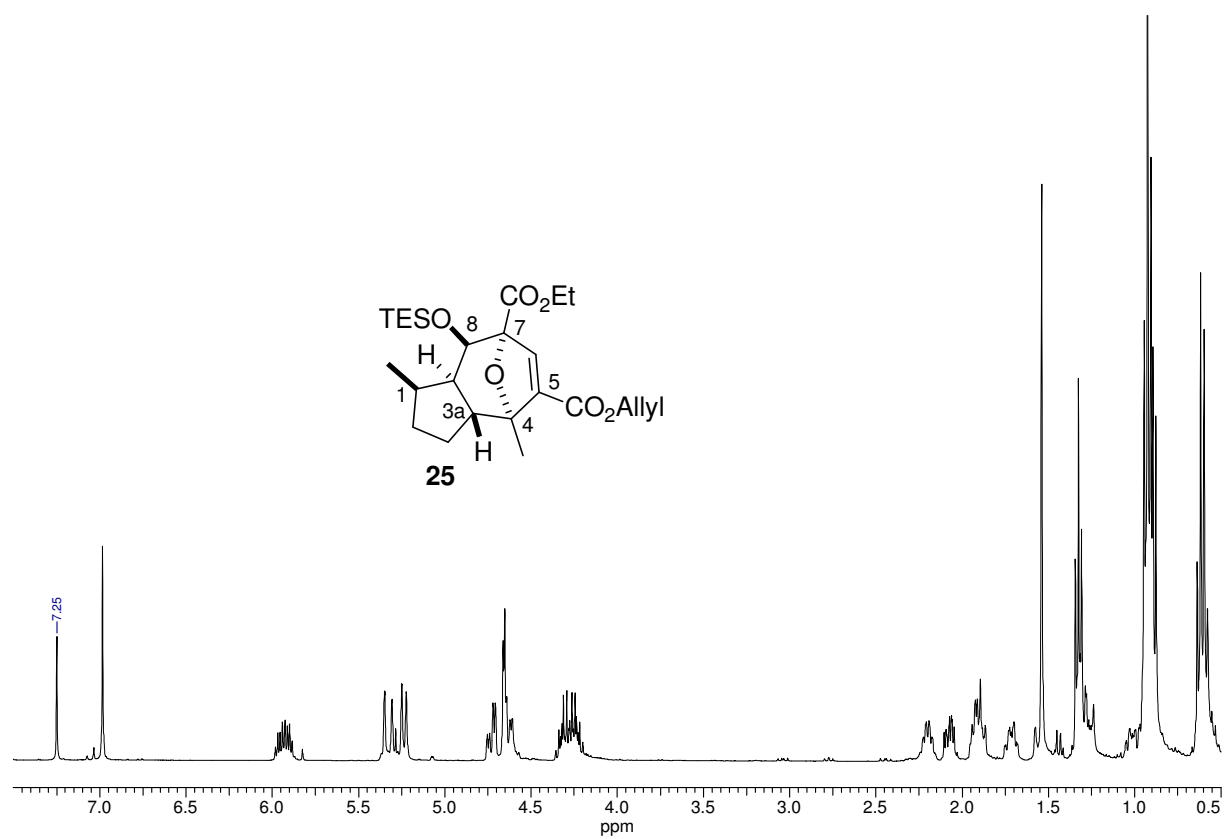


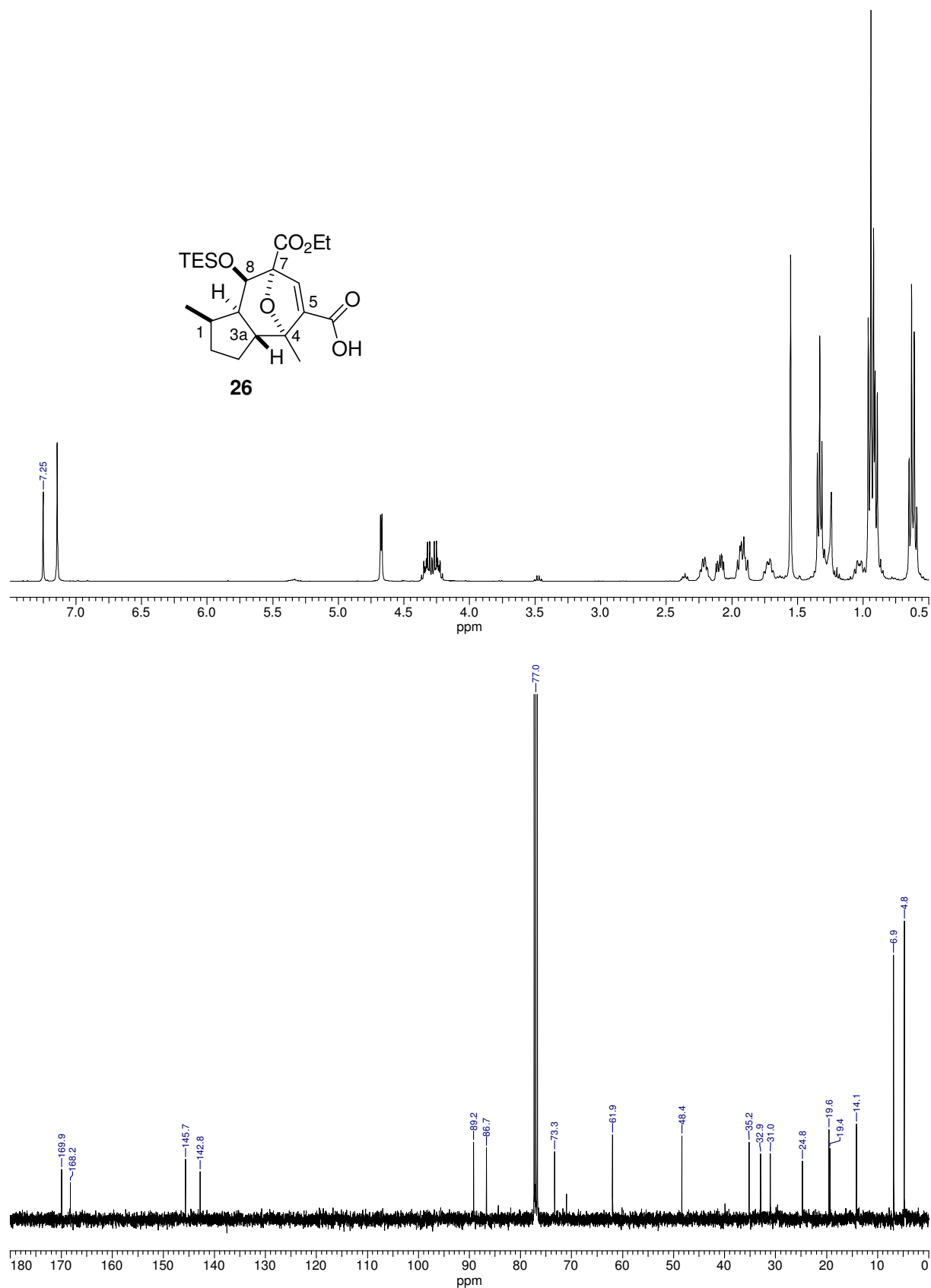


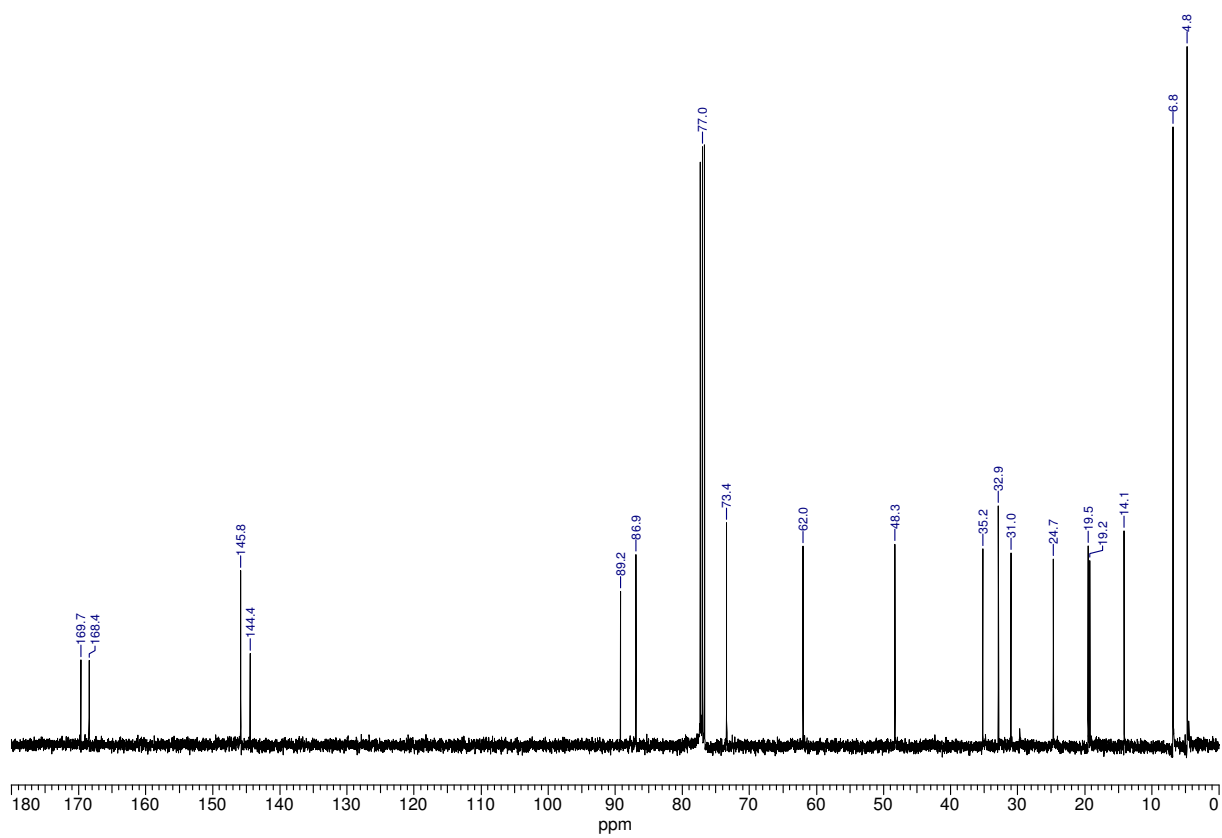
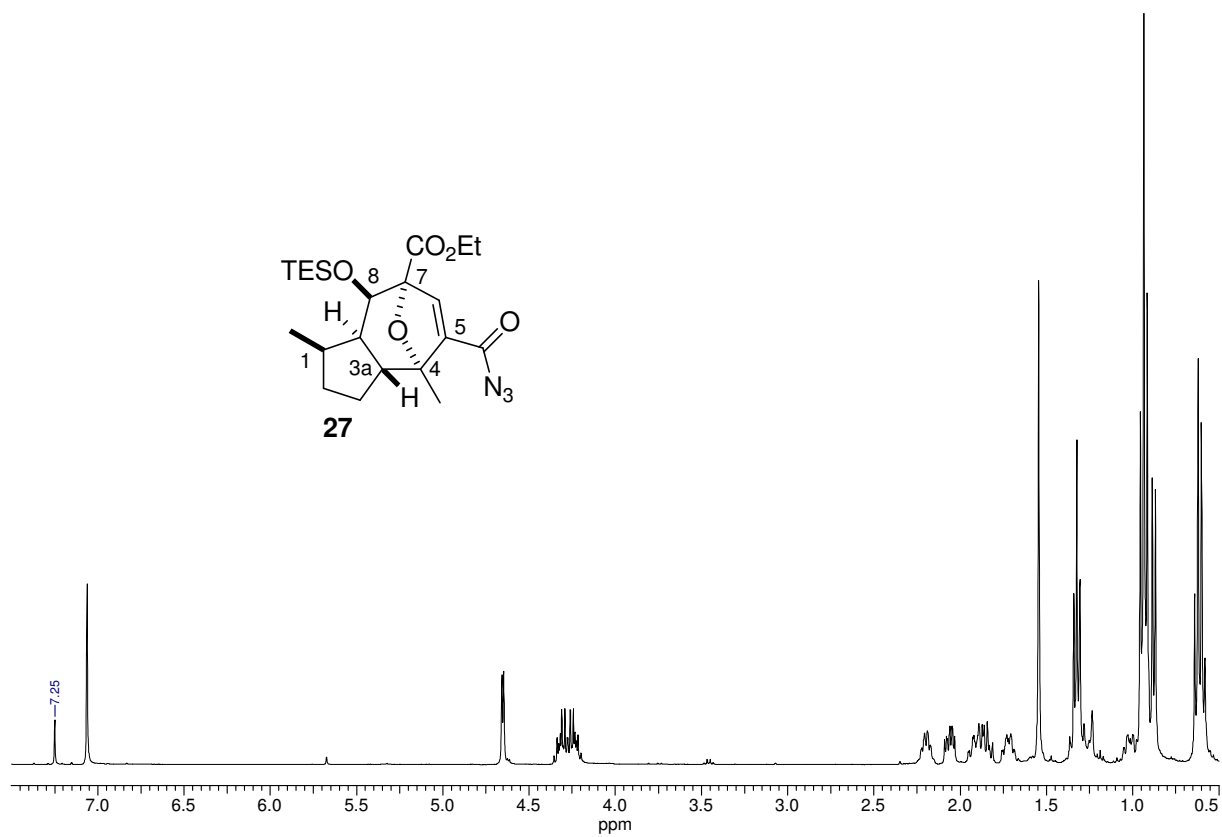
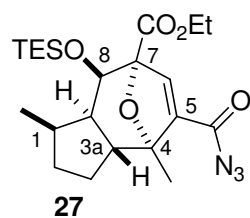


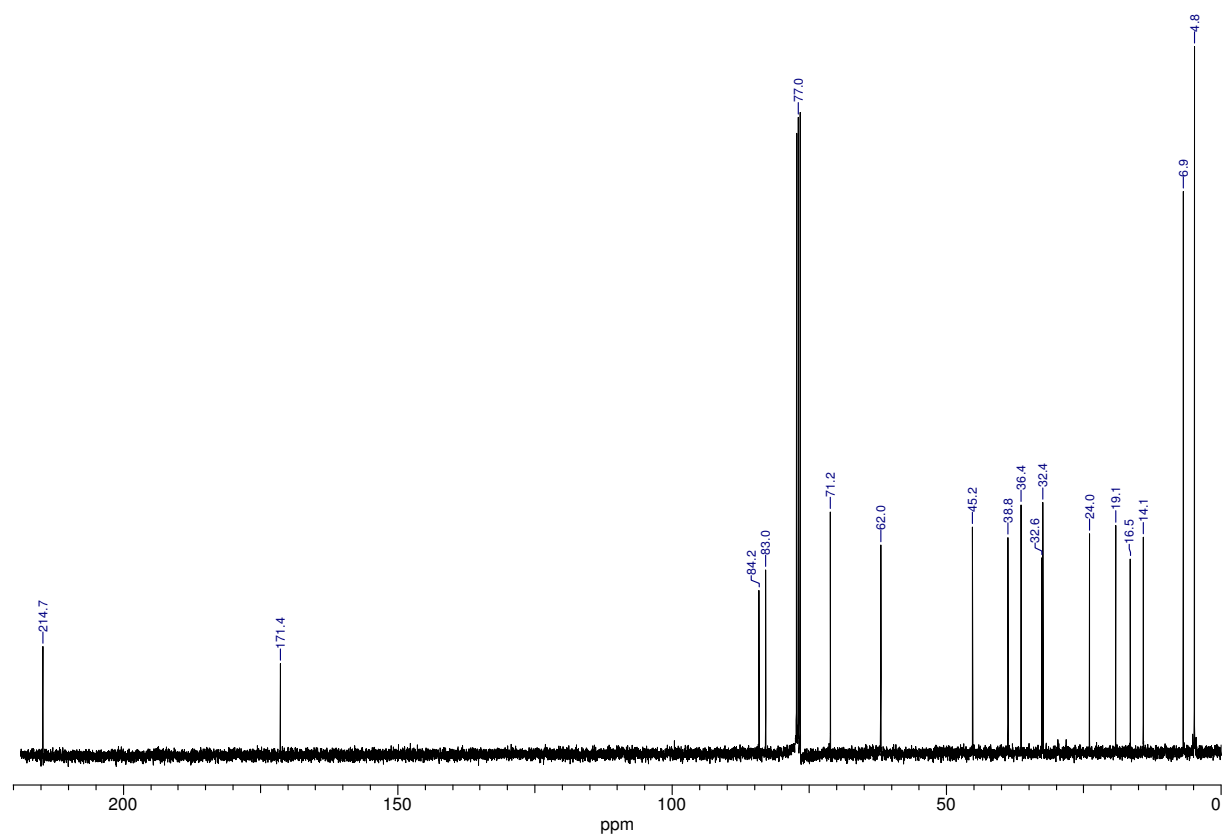
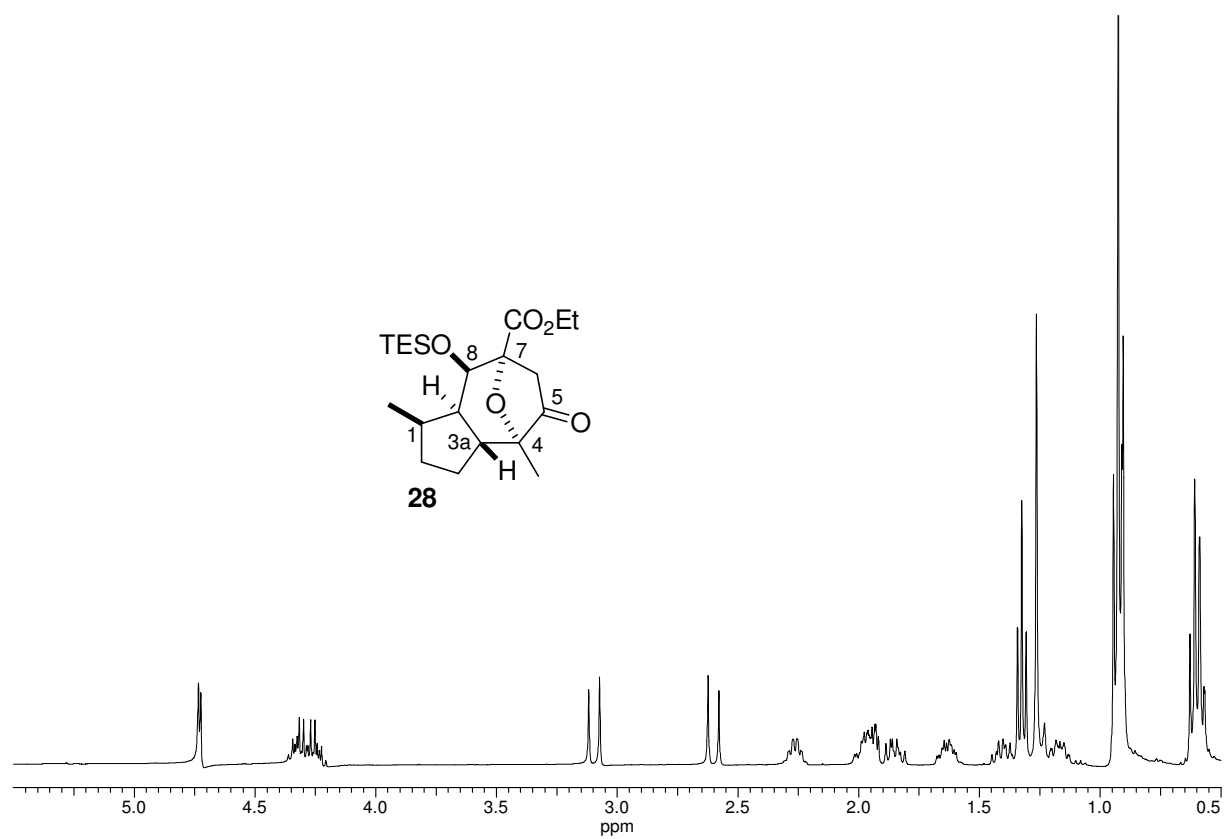


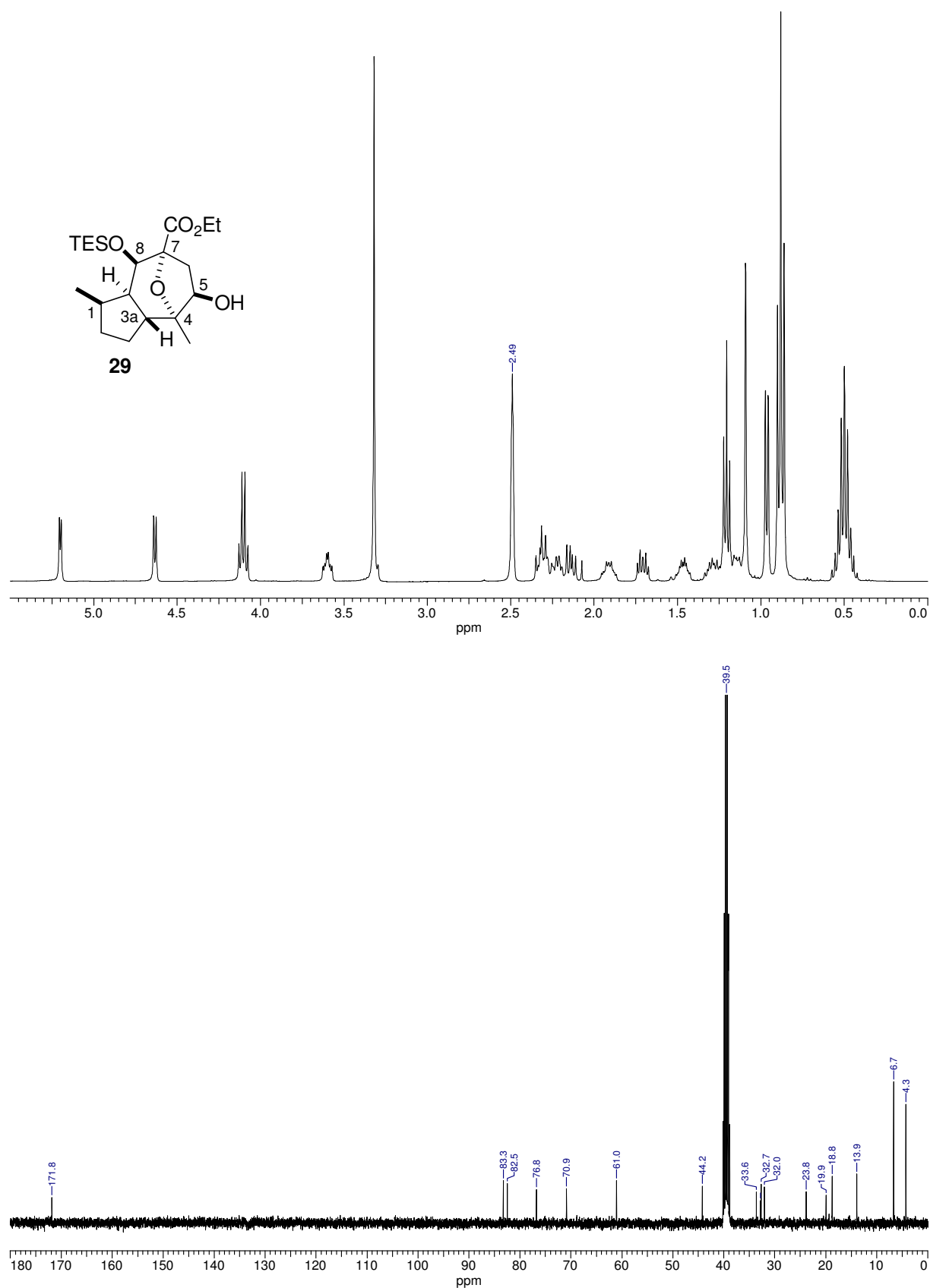


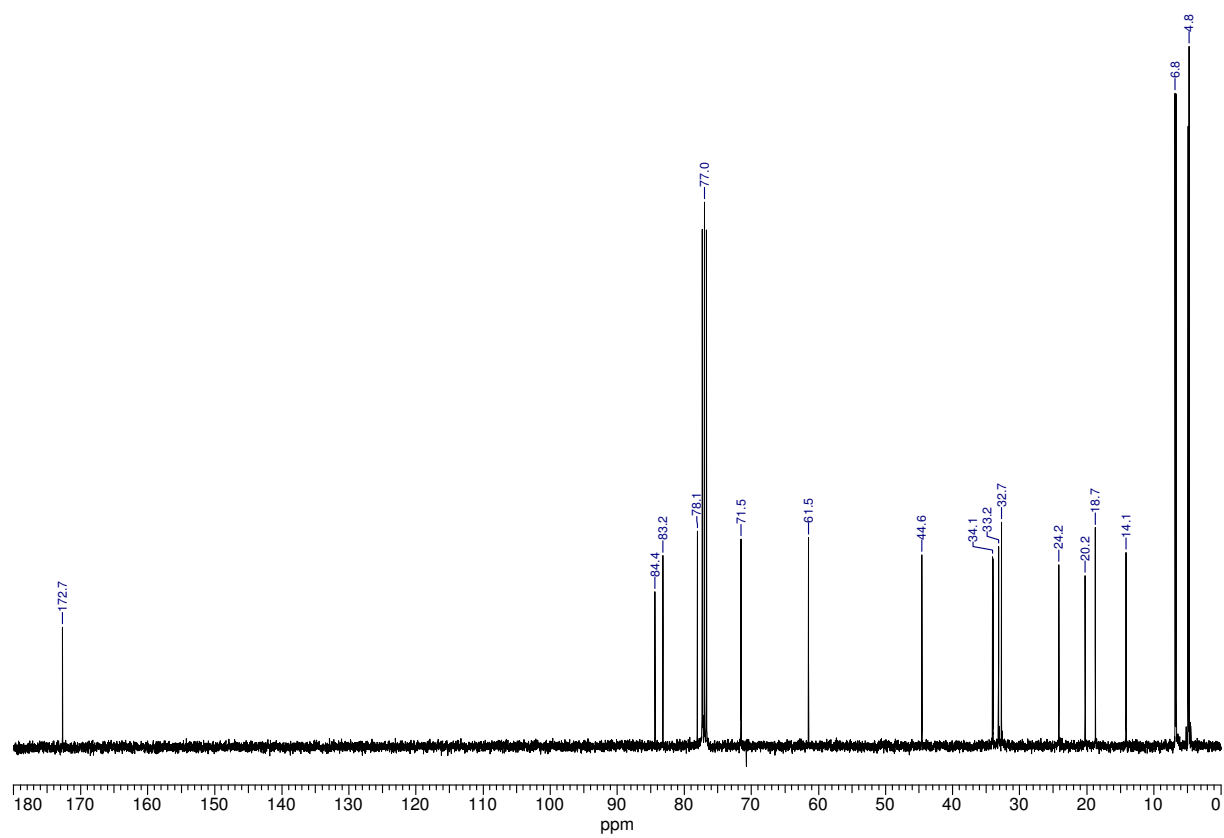
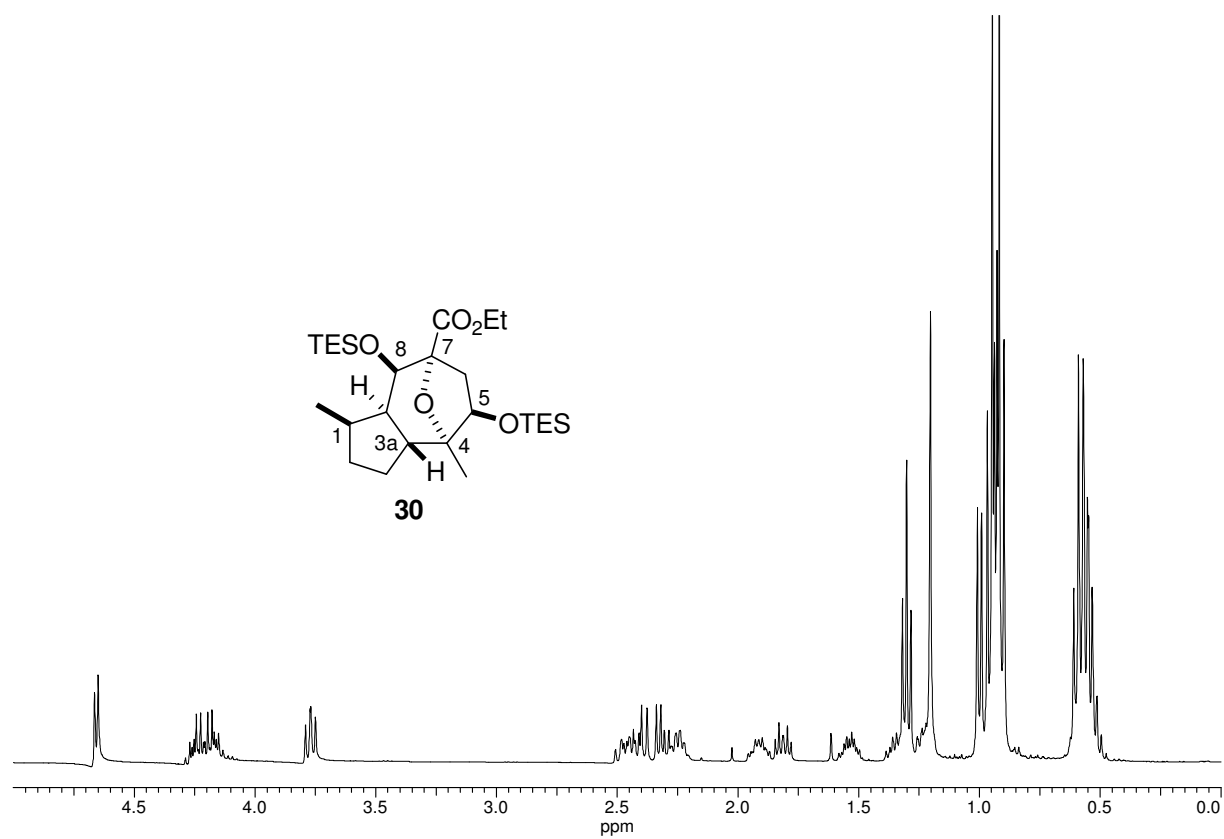


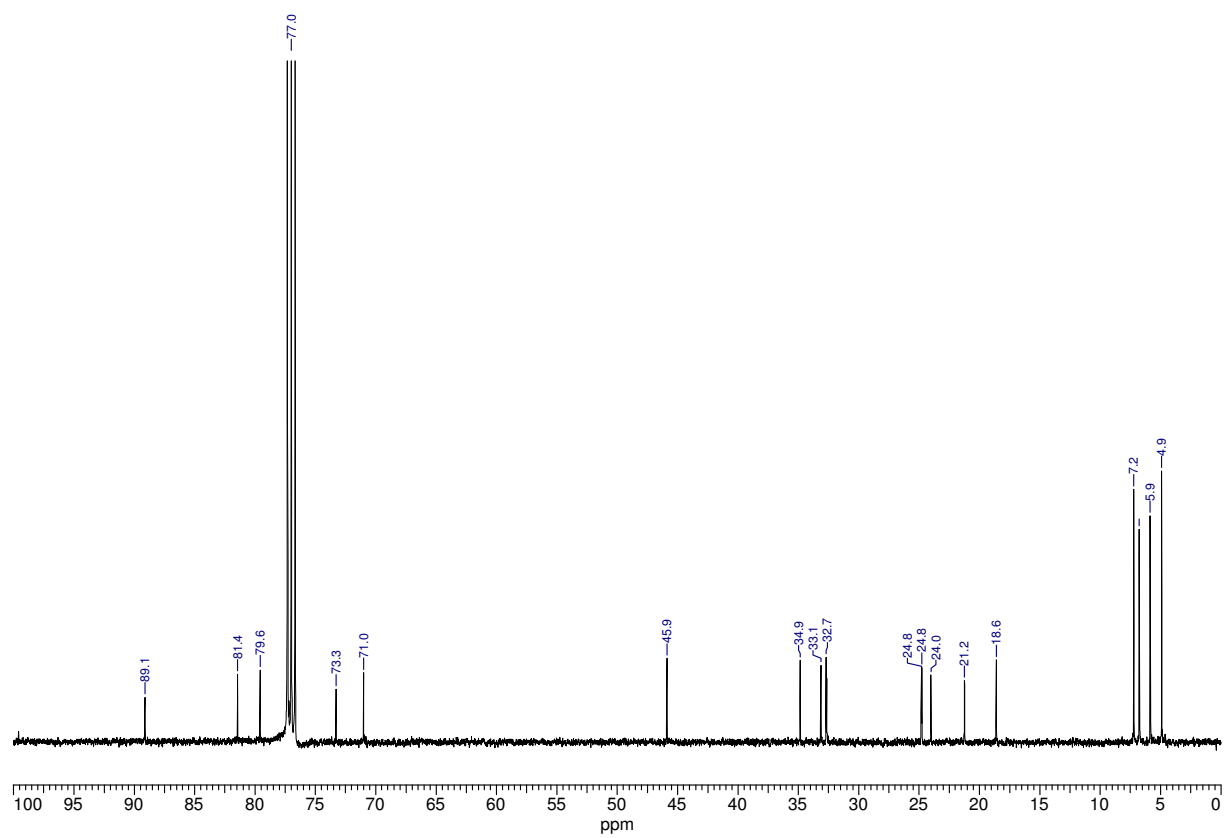
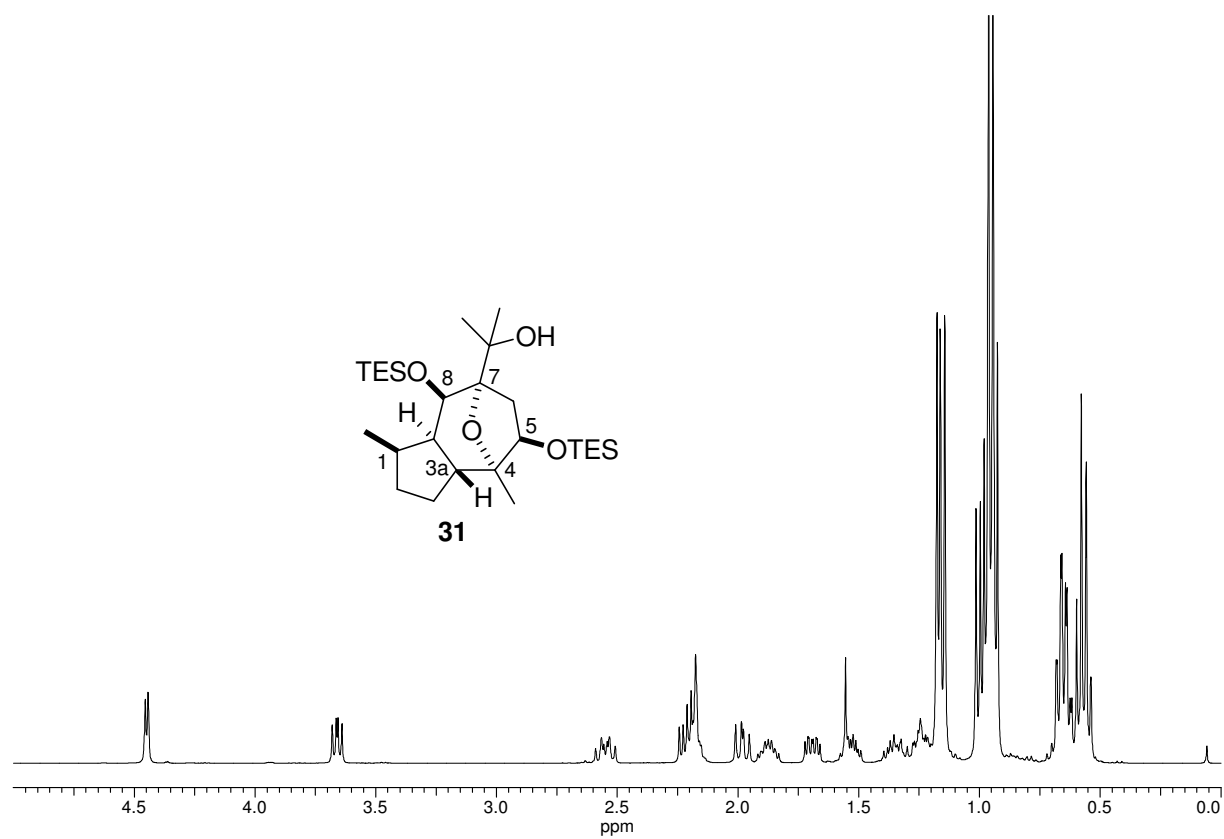




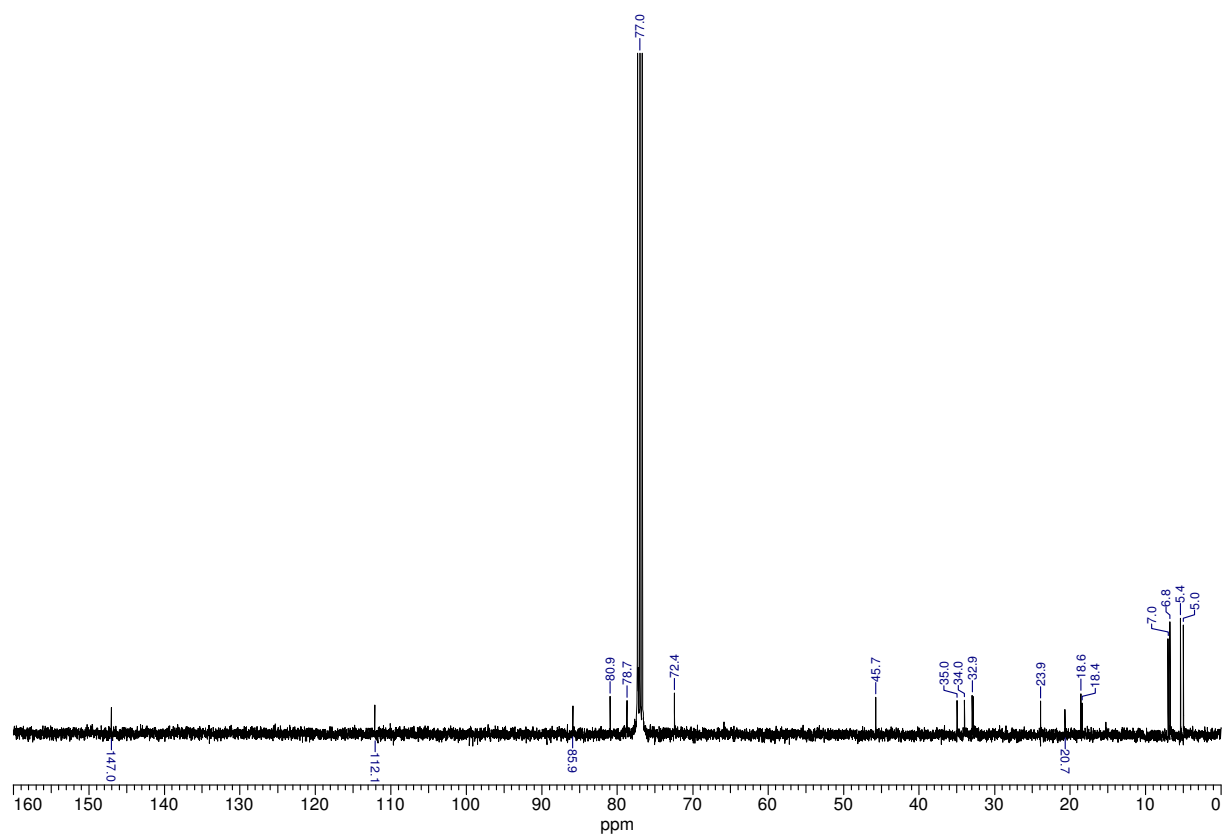
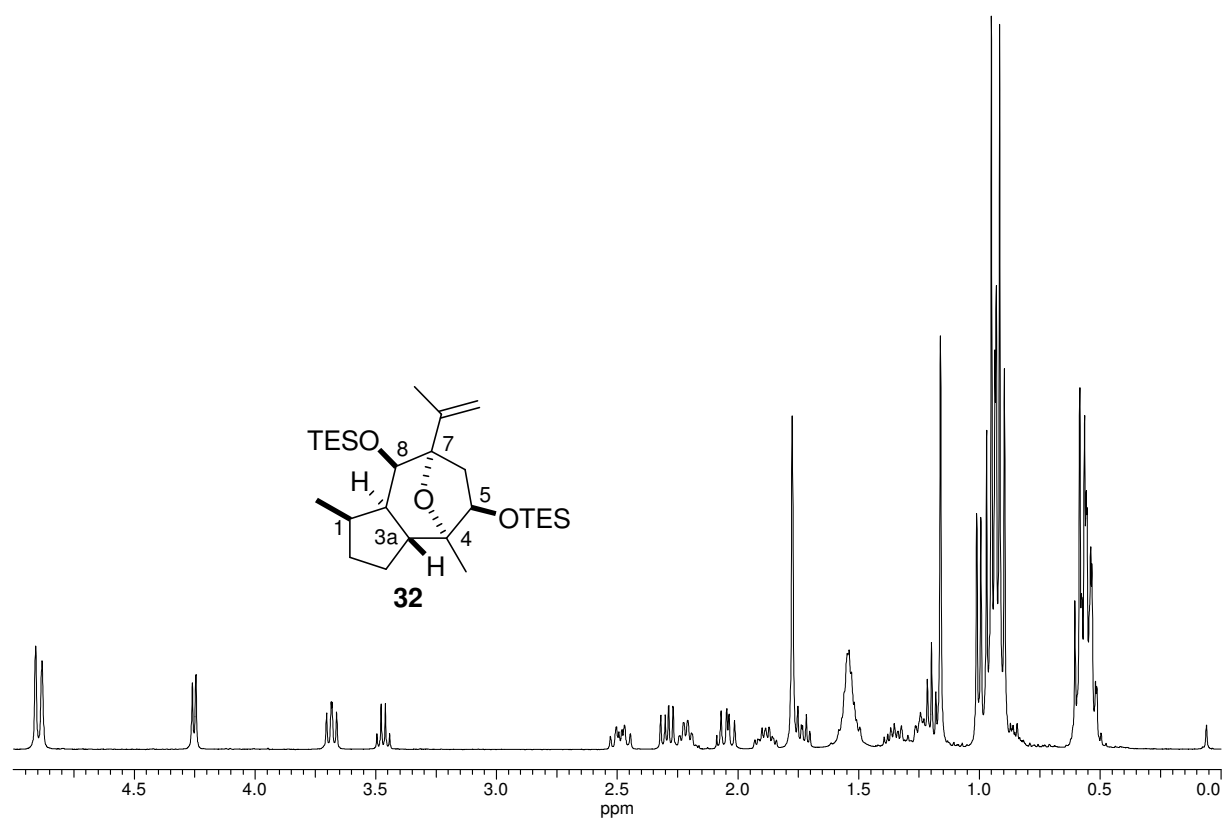


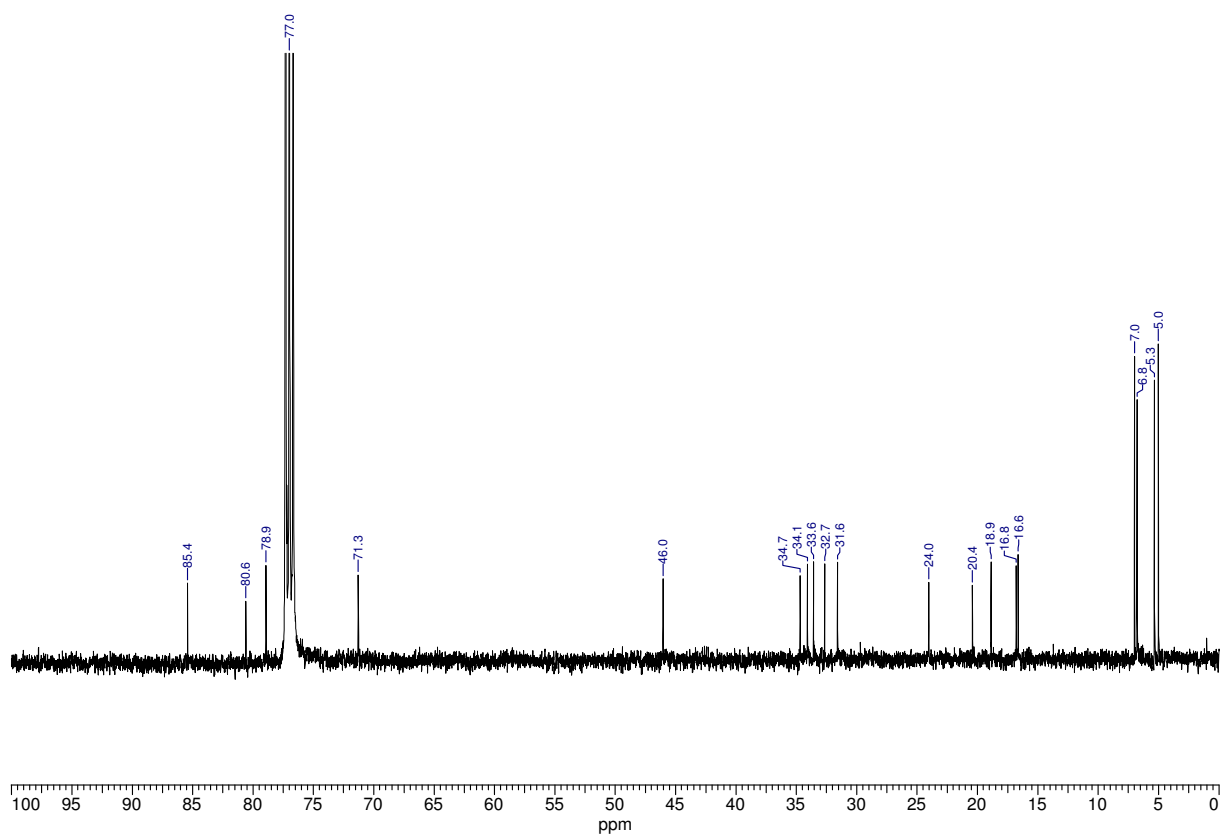
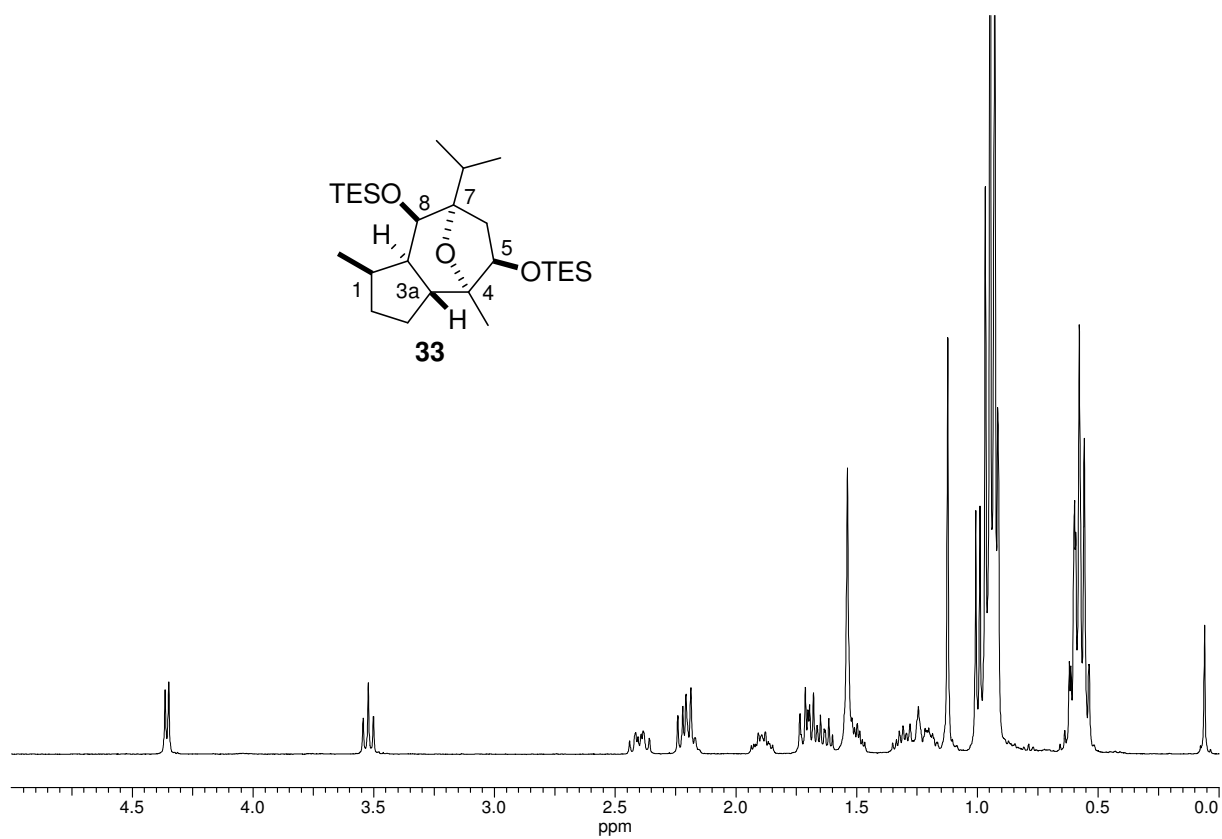
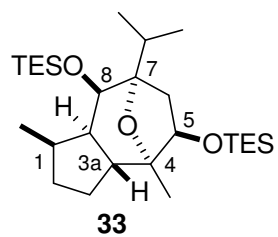


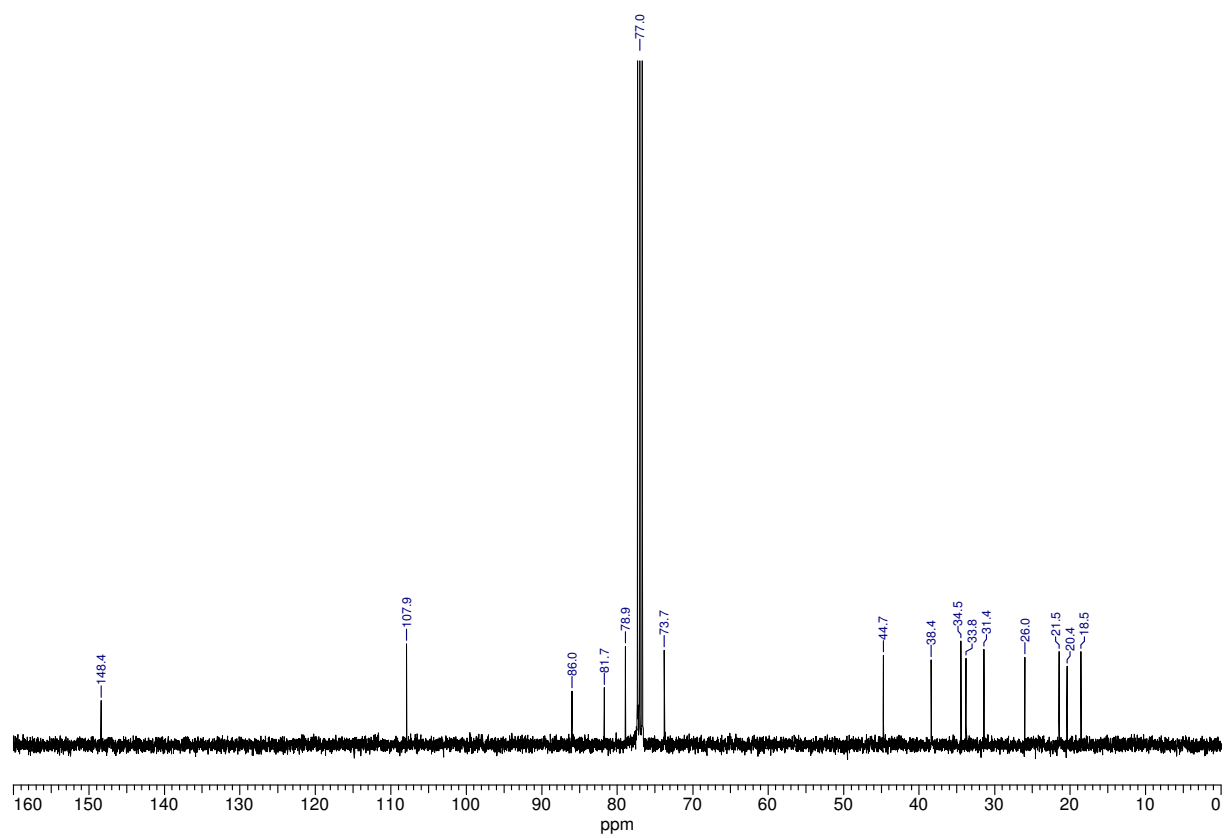
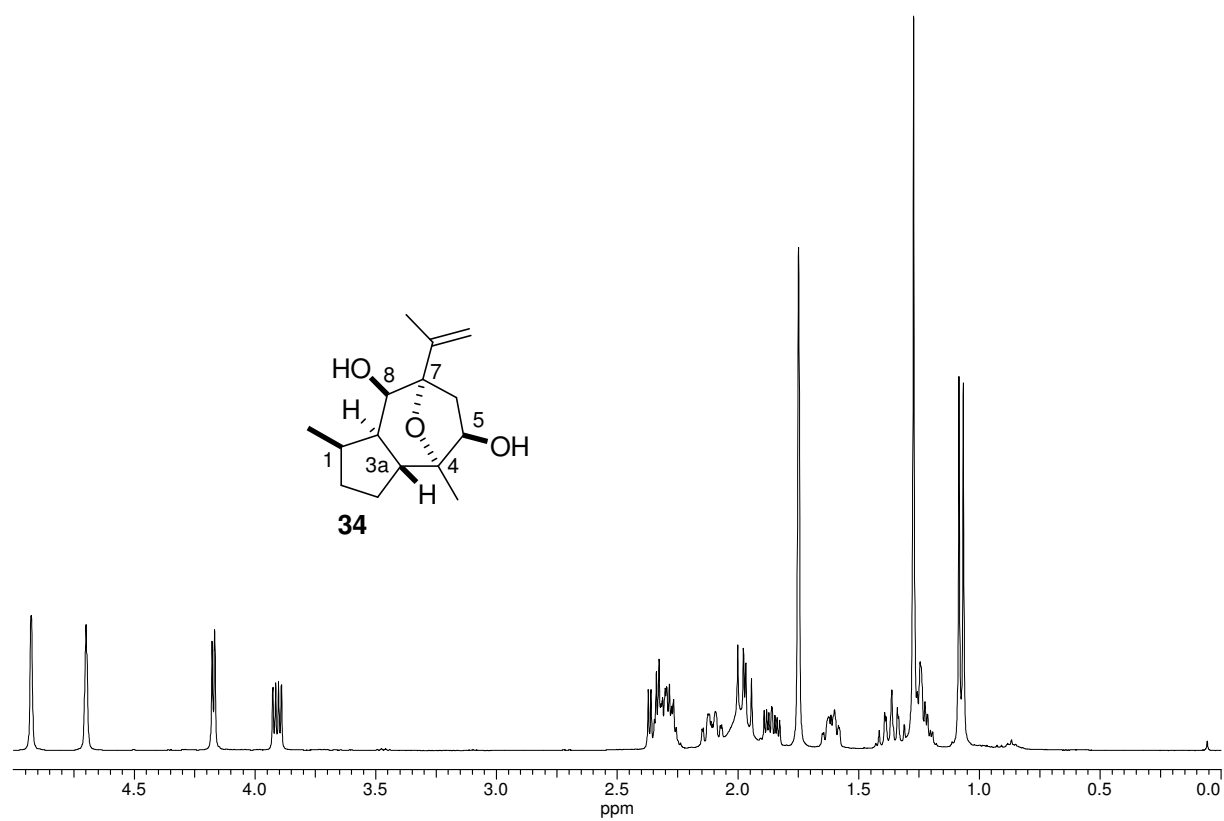


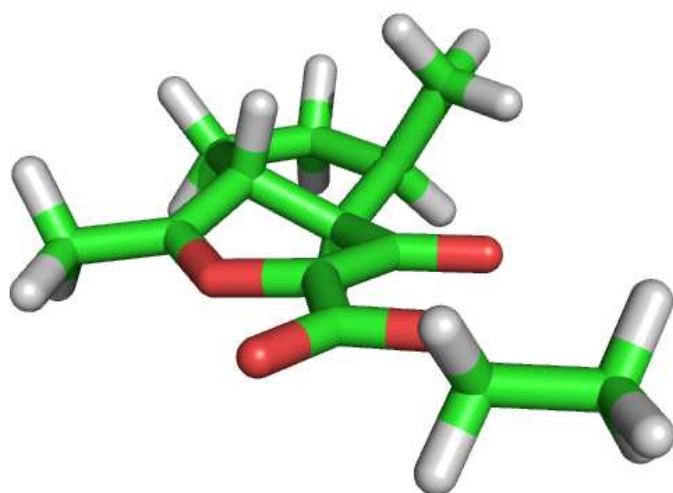
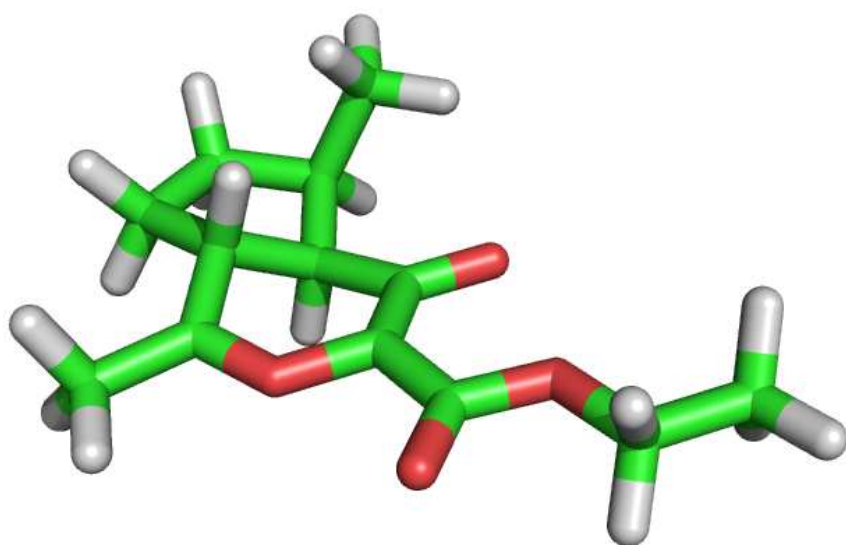




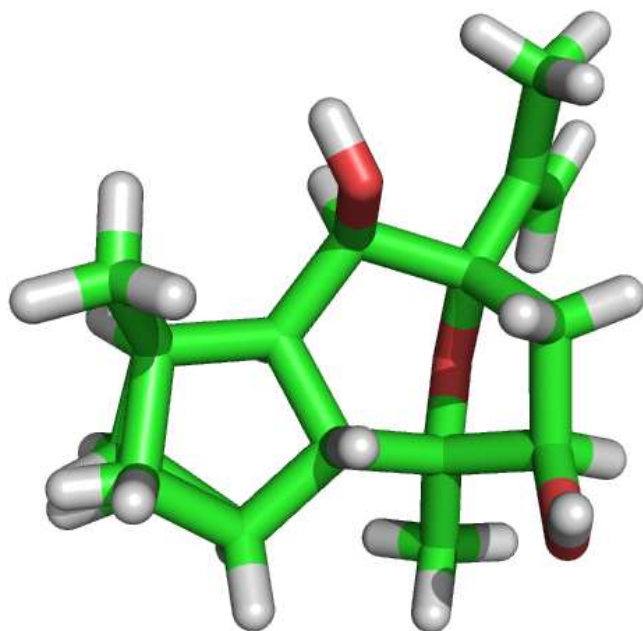








**Figure S1.** Calculated structure of the cyclic carbonyl ylide (Spartan 08) showing the half-chair conformation in the six-membered ring.



**Figure S2.** Rendering of the X-ray structure of tricyclic compound **34**.