

# Bioinspired Enantioselective Total Syntheses of Antibacterial Callistrilones Enabled by Double S<sub>N</sub>2' Cascade

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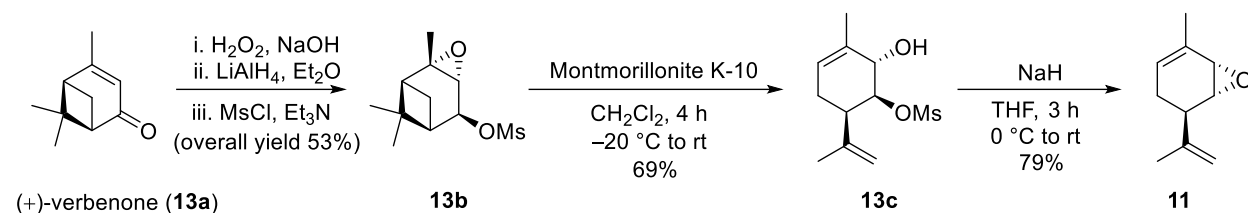
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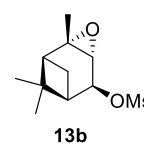
**1. General Information:** All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise mentioned. All the chemicals were purchased commercially and used without further purification. Anhydrous THF and diethyl ether were distilled from sodium benzophenone, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically pure compounds, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (60F-254) using UV light as a visualizing agent and a p-anisaldehyde or ninhydrin stain, and heat as developing agents. Silica gel (particle size: 100–200 and 230–400 mesh) was used for flash column chromatography. Neat compounds were used for recording IR spectra. NMR spectra were recorded on either 400 (<sup>1</sup>H, 400 MHz; <sup>13</sup>C, 100 MHz) or 500 (<sup>1</sup>H, 500 MHz; <sup>13</sup>C, 125 MHz). Chemical shifts of residual solvent in CDCl<sub>3</sub> were recorded 7.27 ppm for <sup>1</sup>H and 77.0 ppm for <sup>13</sup>C. Mass spectrometric data were obtained using Q-TofPremier-HAB213 and Q-Tof-Premier-ESI-MS instruments. Melting points measurements were made using a hot stage apparatus. Optical rotations were measured using a polarimeter at 28°C. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet, dt = doublet of a triplet, td = triplet of a doublet, m = multiplet, br = broad.

## 2. Experimental Procedures:

### Synthesis of epoxide **11**:

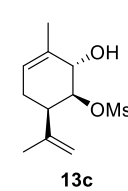


### Synthesis of compound **13b**:<sup>1</sup>



(+)-Verbenone (**13a**) (10.0 g, 66.66 mmol) was dissolved in MeOH (120 mL) and cooled to 0 °C. 30 % H<sub>2</sub>O<sub>2</sub> (9.0 mL) followed by 4 N NaOH (5.0 mL) was added, and the mixture was stirred for 2 h at rt, diluted with H<sub>2</sub>O (60 mL), and extracted with EtOAc (4 x 80 mL). Combined organic layers were washed with H<sub>2</sub>O (2 x 50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated to give verbenone epoxide which was dissolved in Et<sub>2</sub>O (80 mL), cooled at -78 °C, added to a suspension of LiAlH<sub>4</sub> (1.97 g, 51.91 mmol) for 10 min with stirring. The mixture was stirred for 3 h at -78 °C, and then H<sub>2</sub>O (10 mL) was slowly added. The reaction mixture was extracted with EtOAc (4 x 25 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was distilled off and subsequently verbenol epoxide was dissolved in anhydrous THF (70 mL). To the reaction mixture was added Et<sub>3</sub>N (12.18 mL, 87.37 mmol) and MsCl (4.0 mL, 52.42 mmol) under N<sub>2</sub> atmosphere slowly over a period of 5 min at 0 °C. The solution was allowed to warm to rt for about 1 h. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:9) as eluent furnished epoxide **13b** (8.7 g, 53%).  $[\alpha]_D^{28} = +40.00$  (*c* 0.55, CHCl<sub>3</sub>); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  2923, 2853, 1350, 1174, 959, 912, 528; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta = 5.00$  (d, *J* = 3.1 Hz, 1H), 3.26 (d, *J* = 1.8 Hz, 1H), 3.05 (s, 3H), 2.22 - 2.16 (m, 1H), 2.11 (td, *J* = 11.0, 6.7 Hz, 1H), 2.05 - 2.01 (m, 1H), 1.53 (d, *J* = 10.4 Hz, 1H), 1.42 (s, 3H), 1.35 (s, 3H), 1.12 (s, 3H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz)  $\delta = 78.5, 60.7, 57.5, 45.2, 44.8, 40.8, 38.5, 26.8, 22.0, 21.9, 21.6$ ; **HRMS**: *m/z* calcd for C<sub>11</sub>H<sub>18</sub>O<sub>4</sub>S [M+Na]<sup>+</sup>: 269.0823; found: 269.0823.

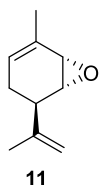
### Synthesis of compound **13c**:



To a magnetically stirred solution of compound **13b** (1.0 g, 4.06 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added montmorillonite K-10 (1 g) portion wise at -20 °C and allowed to warm at rt. The reaction mixture was stirred for 4 h at ambient temperature and monitored via TLC. Then reaction mixture was filtered through celite, solvent was evaporated and residue was purified by flash chromatography using EtOAc-hexane (1:4) as eluent which furnished alcohol **13c** (0.69

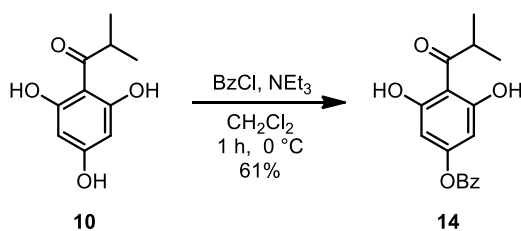
g, 69%).  $R_f = 0.50$  (EtOAc–hexane 2:3);  $[\alpha]_D^{28} = +29.90$  ( $c$  4.75,  $\text{CHCl}_3$ ); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  3513 (br.), 2968, 2918, 1351, 1174, 927, 915, 507;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta = 5.67$  (br. s., 1H), 4.97 (br. s., 1H), 4.85 (br. s., 2H), 4.11 (br. s., 1H), 2.96 - 2.89 (m, 3H), 2.55 - 2.51 (m, 1H), 2.35 - 2.22 (m, 1H), 2.10 - 1.98 (m, 1H), 1.89 - 1.75 (m, 6H)  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz)  $\delta = 143.7, 130.7, 125.5, 112.7, 81.5, 70.1, 38.5, 38.2, 24.9, 22.3, 20.4$  **HRMS**:  $m/z$  calcd for  $\text{C}_{11}\text{H}_{22}\text{NO}_4\text{S}$   $[\text{M}+\text{H}]^+$ : 264.1270; found: 264.1272.

#### Synthesis of compound epoxide **11**:



A magnetically stirred solution of NaH (0.243 g, 6.00 mmol, 60% suspension in mineral oil) in THF (15 mL) was cooled to 0 °C and added dropwise a solution of compound **13c** (1.25 g, 5.00 mmol) in THF. After 15 min the reaction mixture was allowed to warm at rt and stirred for 3 h. Then reaction mixture was cooled to 0 °C, water was added to the reaction mixture and extracted with EtOAc. Solvent was evaporated and residue was purified by flash chromatography using EtOAc–hexane (1:30) as eluent to furnish the product **11** (0.602 g, 79%) as a liquid.  $R_f = 0.50$  (EtOAc–hexane 1:9);  $[\alpha]_D^{28} = -20.00$  ( $c$  1.00,  $\text{CHCl}_3$ ); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  2925, 1645, 1451, 1377, 1206, 892, 784;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta = 5.49$  (td,  $J = 6.7, 1.9$  Hz, 1H), 4.80 (dd,  $J = 2.9, 1.6$  Hz, 1H), 4.72 (s, 1H), 3.39 (qd,  $J = 4.2, 2.1$  Hz, 1H), 3.18 (dd,  $J = 4.1, 2.3$  Hz, 1H), 2.85 (d,  $J = 8.6$  Hz, 1H), 2.27 (ddt,  $J = 11.3, 5.4, 2.7$  Hz, 1H), 1.97 (dd,  $J = 17.2, 6.3$  Hz, 1H), 1.91 - 1.87 (m, 3H), 1.78 - 1.74 (m, 3H);  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz)  $\delta = 145.2, 130.3, 123.1, 111.6, 57.7, 51.2, 37.4, 25.5, 22.5, 21.7$ ; **HRMS**:  $m/z$  calcd for  $\text{C}_{10}\text{H}_{13}$   $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$ : 133.1017; found: 133.1019.

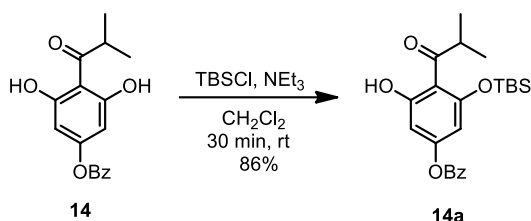
#### Synthesis of compound **14**:



To an ice cooled magnetically stirred solution of compound **10** (5.0 g, 25.48 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was added  $\text{Et}_3\text{N}$  (3.53 mL, 25.48 mmol) and kept for 10 min. Then benzoyl chloride (2.96 mL, 25.48 mmol) was added to reaction mixture and stirred for 1 hr at the same temperature. After completion of reaction indicated by TLC, the reaction was quenched by water. Then it was extracted with  $\text{CH}_2\text{Cl}_2$  and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent and purification of the residue on silica gel column using EtOAc–hexane (1:8) as eluent to furnish the product **14** (4.66 g, 61%);  $R_f = 0.5$  (EtOAc–hexane 1:3); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  3365 (br.), 2923, 2852, 1744, 1600, 1425, 1258, 1138, 1061, 705;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400

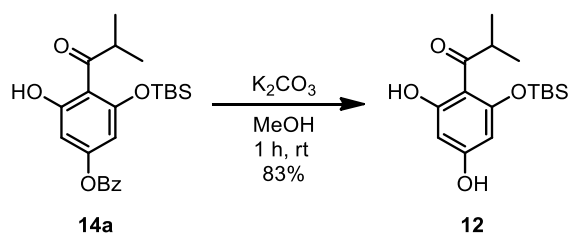
MHz)  $\delta$  = 10.62 (br. s., 1H), 8.19 (dd,  $J$  = 8.5, 1.2 Hz, 2H), 7.71 - 7.65 (m, 1H), 7.53 (t,  $J$  = 7.6 Hz, 2H), 6.27 (s, 2H), 3.74 (sep,  $J$  = 6.7 Hz, 1H), 1.13 (d,  $J$  = 6.7 Hz, 6H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  = 211.6, 165.8, 163.1, 155.7, 134.4, 130.5, 130.3, 128.8, 128.5, 107.8, 101.9, 39.8, 29.7, 18.9; **HRMS**:  $m/z$  calcd for  $\text{C}_{17}\text{H}_{17}\text{O}_5$   $[\text{M}+\text{H}]^+$ : 301.1076; found: 301.1072.

#### Synthesis of compound 14a:



To an ice cooled solution of magnetically stirred compound **14** (4.0 g, 13.31 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was added  $\text{Et}_3\text{N}$  (1.84 mL, 13.31 mmol) and stirred for 10 min. After that TBSCl (2.02 g, 13.31 mmol) was added portion wise to the reaction mixture was at the same temperature and warmed to rt and stirred for 30 min. After completion of reaction indicated by TLC, the reaction was quenched by water. Then it was extracted with  $\text{CH}_2\text{Cl}_2$  and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:33) as eluent furnished **14a** (4.74 g, 86 %) as a colourless liquid.  $R_f$  = 0.6 (EtOAc-hexane 1:6); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  2958, 2931, 2859, 1745, 1625, 1598, 1421, 1257, 1137, 1060, 829, 705;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  = 12.98 (s, 1H), 8.23 - 8.16 (m, 2H), 7.66 (t,  $J$  = 7.6 Hz, 1H), 7.53 (t,  $J$  = 7.6 Hz, 2H), 6.48 (d,  $J$  = 2.4 Hz, 1H), 6.35 (d,  $J$  = 2.4 Hz, 1H), 3.98 (sep,  $J$  = 6.7 Hz, 1H), 1.19 (d,  $J$  = 6.7 Hz, 6H), 1.02 (s, 9H), 0.36 (s, 6H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  = 211.6, 165.4, 164.0, 158.1, 155.8, 133.8, 130.3, 129.1, 128.6, 110.8, 104.3, 104.0, 39.2, 26.0, 19.1, 18.8, -3.9; **HRMS**:  $m/z$  calcd for  $\text{C}_{23}\text{H}_{31}\text{O}_5\text{Si}$   $[\text{M}+\text{H}]^+$ : 415.1941; found: 415.1944.

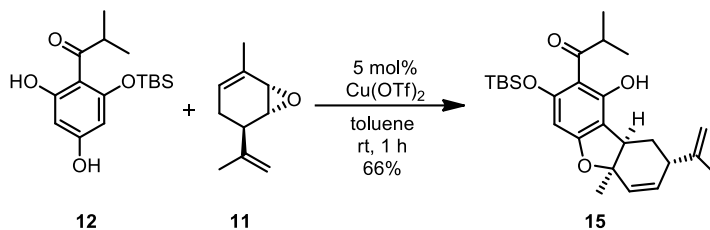
#### Synthesis of compound 12:



To a magnetically stirred solution of compound **14a** (3.5 g, 8.44 mmol) in MeOH (30 mL) was added  $\text{K}_2\text{CO}_3$  (1.16 g, 8.44 mmol) at rt and stirred for 1 h. Then it was extracted with EtOAc and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-

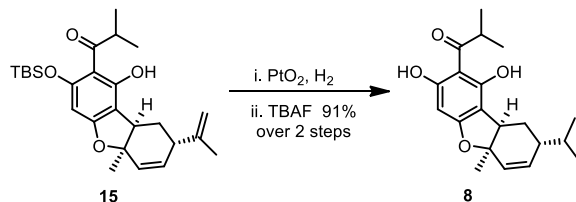
hexane (1:9) as eluent to furnish the product **12** (2.17 g, 83%) as a white solid.  $R_f = 0.4$  (EtOAc–hexane 1:4); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  3333 (br.), 2959, 2931, 2859, 1624, 1594, 1445, 1224, 1162, 1105, 830; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta = 13.67$  (s, 1H), 6.02 (d,  $J = 2.4$  Hz, 1H), 5.98 (s, 1H), 5.88 (d,  $J = 2.4$  Hz, 1H), 3.93 (sep,  $J = 7.0$  Hz, 1H), 1.15 (d,  $J = 7.0$  Hz, 6H), 1.00 (s, 9H), 0.34 (s, 6H). **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz)  $\delta = 210.8, 166.9, 161.7, 159.4, 107.1, 98.7, 97.2, 38.6, 26.0, 19.3, 18.9, -3.8$ ; **HRMS**:  $m/z$  calcd for C<sub>16</sub>H<sub>27</sub>O<sub>4</sub>Si [M+H]<sup>+</sup>: 311.1679; found: 311.1675.

### Synthesis of compound **15**:



To a solution of the acyl phloroglucinol derivative **12** (150 mg, 0.483 mmol) and allyl epoxide **11** (79 mg, 0.531 mmol) in toluene (5 mL) was added Cu(OTf)<sub>2</sub> (9 mg, 24  $\mu\text{mol}$ ) and stirred magnetically for 1 h at rt. The progress of reaction was monitored by TLC. Reaction was quenched using NaHCO<sub>3</sub>, extracted with EtOAc (3 x 5 mL), washed with brine (5 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc–hexane (1:99) as eluent furnished compound **15** (141 mg, 66 %) as colorless liquid.  $R_f = 0.7$  (EtOAc–hexane 1:9);  $[\alpha]_D^{28} = +26.4$  ( $c$  0.85, MeOH); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  2924, 2853, 1633, 1601, 1428, 1229, 1117, 1057, 839; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 500 MHz)  $\delta = 13.70$  (s, 1H), 5.92 (dd,  $J = 10.1, 3.3$  Hz, 1H), 5.83 (s, 1H), 5.74 (dd,  $J = 10.1, 1.9$  Hz, 1H), 4.81 (s, 1H), 4.71 (s, 1H), 3.93 (sep,  $J = 6.7$  Hz, 1H), 3.38 (dd,  $J = 6.8, 4.4$  Hz, 1H), 2.79 (br. s., 1H), 2.34 - 2.26 (m, 1H), 1.92 - 1.85 (m, 1H), 1.79 (s, 3H), 1.52 (s, 3H), 1.15 (dd,  $J = 6.7, 2.7$  Hz, 6H), 1.00 (s, 9H), 0.33 (d,  $J = 3.8$  Hz, 6H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 125 MHz)  $\delta = 210.9, 164.7, 162.4, 159.7, 147.0, 134.1, 129.1, 110.9, 108.8, 107.1, 93.8, 88.3, 43.2, 39.5, 38.4, 28.5, 26.2, 26.1, 21.4, 19.5, 19.4, 18.9, -3.7$ ; **HRMS**:  $m/z$  calcd for C<sub>26</sub>H<sub>39</sub>O<sub>4</sub>Si [M+H]<sup>+</sup>: 443.2618; found: 443.2617.

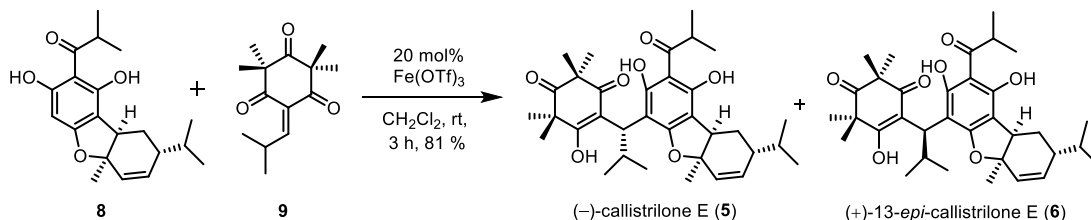
### Synthesis of compound **8**:



*Step I*- To a magnetically stirred solution of compound **15** (100 mg, 0.226 mmol) in MeOH (3 mL) was added PtO<sub>2</sub> (2 mg, 8 μmol) and reaction was continued at same temperature under hydrogen bladder pressure. The reaction was monitored by <sup>1</sup>H NMR of crude sample. After completion of reaction, reaction mixture was passed through celite pad and concentrated in vacuo.

*Step II*- To a magnetically stirred solution of above crude material in THF (3 mL) at 0 °C tetrabutylammonium fluoride (0.292 mL, 0.292 mmol, 1 M solution in THF) was added dropwise and the resulting mixture was stirred for 15 min at the same temperature. The reaction mixture was then quenched with water, extracted with EtOAc and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:15) as eluent furnished compound **8** (67 mg, 91% over two steps) as a colourless liquid. *R<sub>f</sub>* = 0.6 (EtOAc-hexane 1:9); [ $\alpha$ ]<sub>D</sub><sup>28</sup> = +48.34 (*c* 0.18, MeOH); **IR** (neat):  $\nu_{\max}$ /cm<sup>-1</sup> 3370, 2960, 2926, 1637, 1433, 1382, 1234, 1102, 1055, 849; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  = 13.09 (br. s., 1H), 6.58 (br. s., 1H), 5.89 (dd, *J* = 10.2, 2.5 Hz, 1H), 5.74 (s, 1H), 5.59 (dd, *J* = 10.2, 2.5 Hz, 1H), 3.85 (sep, *J* = 6.7 Hz, 1H), 3.46 (t, *J* = 4.8 Hz, 1H), 2.41 (dt, *J* = 13.2, 4.8 Hz, 1H), 2.02-1.96 (m, 1H), 1.66–1.60 (m, 2H), 1.56 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 6H), 0.92 (d, *J* = 6.7 Hz, 6H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz)  $\delta$  = 210.5, 165.3, 162.0, 160.7, 135.3, 128.9, 108.1, 104.1, 90.6, 89.3, 44.2, 39.2, 37.7, 31.4, 26.2, 25.9, 19.6 (2C), 19.4, 19.3; **HRMS**: *m/z* calcd for C<sub>20</sub>H<sub>27</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 331.1909; found: 331.1909.

### Synthesis of (–)-callistrilone E (**5**) and (+)-13-*epi*-callistrilone E (**6**):



To a magnetically stirred solution of compound **8** (140 mg, 0.423 mmol) and Michael acceptor **9** (100 mg, 0.423 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (5 mL), was added 20 mol% of Fe(OTf)<sub>3</sub> (42 mg, 84 μmol) and stirring was continued for additional 3 h and progress of the reaction was monitored by TLC. Then the reaction mixture was quenched with NaHCO<sub>3</sub> stirred for 15 min. and extracted with CH<sub>2</sub>Cl<sub>2</sub> and dried with Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:99) as eluent furnished (–)-callistrilone E (**5**) and (+)-13-*epi*-callistrilone E (**6**) (194 mg, 81%, *dr* = 3:1) as a colourless liquid. (–)-callistrilone E (**5**): (146 mg, 61 %); *R<sub>f</sub>* = 0.31 (EtOAc-hexane 1:19); [ $\alpha$ ]<sub>D</sub><sup>28</sup> = –17.2 (*c* 0.50, MeOH); **IR** (neat):  $\nu_{\max}$ /cm<sup>-1</sup> 2923, 2852, 1720, 1624, 1446, 1381, 1236, 1060, 838; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  = 13.80 (s, 1H), 13.75 (s, 1H), 11.16 (s, 1H), 10.20

(s, 1H), 9.70 (s, 1H), 9.23 (s, 1H), 5.91 (dd,  $J = 10.2, 2.2$  Hz, 1H), 5.77 (d,  $J = 10.4$  Hz, 1H), 5.59 (dd,  $J = 10.2, 2.2$  Hz, 1H), 5.48 (dd,  $J = 10.3, 2.3$  Hz, 1H), 4.04 - 3.96 (m, 2H), 3.69 (d,  $J = 11.5$  Hz, 1H), 3.53 (t,  $J = 4.0$  Hz, 1H), 3.44 - 3.41 (m, 1H), 3.29 (d,  $J = 10.9$  Hz, 1H), 2.95 (dt,  $J = 12.0, 6.6$  Hz, 1H), 2.82 (dt,  $J = 12.2, 6.4$  Hz, 1H), 2.52 (dt,  $J = 13.3, 4.0$  Hz, 1H), 2.37 (dt,  $J = 13.2, 4.7$  Hz, 1H), 1.96 - 1.93 (m, 1H), 1.92 - 1.88 (m, 1H), 1.64 (br. s., 1H), 1.62 (s, 3H), 1.59 (d,  $J = 6.2$  Hz, 2H), 1.56 (s, 3H), 1.54 - 1.50 (m, 3H), 1.46 - 1.44 (m, 6H), 1.37 (s, 3H), 1.34 (s, 3H), 1.31 (s, 3H), 1.29 - 1.27 (m, 9H), 1.15 (dd,  $J = 6.7, 1.8$  Hz, 6H), 1.09 (d,  $J = 6.7$  Hz, 3H), 1.10 (d,  $J = 6.7$  Hz, 3H), 0.88 (br. s., 3H), 0.86 (br. s., 6H), 0.82 (d,  $J = 6.5$  Hz, 6H), 0.81 (d,  $J = 6.5$  Hz, 3H), 0.79 (d,  $J = 6.3$  Hz, 3H), 0.76 (d,  $J = 6.5$  Hz, 3H), 0.70 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta = 212.6, 212.4, 204.0, 202.9, 176.2, 174.9, 161.9, 161.5, 161.4, 160.4, 160.1, 160.0, 137.0, 128.1, 128.0, 115.0, 114.8, 107.3, 107.1, 106.9, 105.9, 103.7, 103.4, 91.3, 91.2, 55.3, 54.6, 49.0, 48.6, 45.4, 44.1, 41.1, 40.3, 39.7, 38.0, 37.6, 31.5, 31.5, 27.4, 27.2, 26.5, 26.2, 26.1, 26.0, 25.8, 25.8, 25.6, 25.5, 24.8, 24.7, 23.8, 22.7, 22.1, 22.0, 20.3, 19.9, 19.8, 19.7, 19.6, 19.5, 19.5, 18.9$ ; **HRMS**:  $m/z$  calcd for  $\text{C}_{34}\text{H}_{47}\text{O}_7$   $[\text{M}+\text{H}]^+$ : 567.3322; found: 567.3320.

**\*13-*epi*-callistrilone E (6)**: (48 mg, 20 %);  $R_f = 0.3$  (EtOAc–hexane 1:19);  $[\alpha]_D^{28} = +20.6$  (c 0.23, MeOH); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  3294, 2925, 2856, 1724, 1620, 1456, 1400, 1098, 1013;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta = 13.80$  (s, 1H), 13.79 (s, 1H), 11.15 (s, 1H), 10.27 (s, 1H), 9.84 (s, 1H), 9.10 (s, 1H), 5.91 (dd,  $J = 10.2, 2.5$  Hz, 1H), 5.81 (d,  $J = 10.2$  Hz, 1H), 5.61 (dd,  $J = 10.2, 2.1$  Hz, 1H), 5.53 (dd,  $J = 10.3, 2.2$  Hz, 1H), 4.08 - 3.84 (m, 2H), 3.70 (d,  $J = 11.6$  Hz, 1H), 3.53 - 3.44 (m, 2H), 3.33 (d,  $J = 10.7$  Hz, 1H), 3.00 - 2.90 (m, 1H), 2.88 - 2.77 (m, 1H), 2.53 (dt,  $J = 13.3, 4.2$  Hz, 1H), 2.33 (dt,  $J = 13.3, 4.9$  Hz, 1H), 2.01 - 1.87 (m, 2H), 1.64 (s, 6H), 1.59 - 1.53 (m, 6H), 1.47 (s, 3H), 1.46 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 1.30 (s, 6H), 1.29 (s, 3H), 1.17 (d,  $J = 6.9$  Hz, 6H), 1.15-1.09 (m, 6H), 0.91 - 0.87 (m, 6H), 0.87 (d,  $J = 6.9$  Hz, 3H), 0.84 (d,  $J = 6.7$  Hz, 3H), 0.83 (d,  $J = 6.7$  Hz, 3H), 0.77 (d,  $J = 6.6$  Hz, 6H), 0.72 (d,  $J = 6.1$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta = 212.5, 212.3, 212.2, 203.9, 202.9, 176.2, 174.6, 161.6, 161.3, 161.1, 160.3, 160.0, 159.8, 137.0, 136.6, 127.9, 127.6, 114.7, 106.9, 106.8, 106.0, 103.9, 103.0, 91.6, 90.4, 55.0, 54.6, 48.7, 48.5, 44.7, 44.4, 41.0, 40.2, 39.5, 39.5, 37.9, 37.4, 31.4, 31.3, 27.3, 27.1, 26.6, 26.1, 25.9, 25.9, 25.8, 25.7, 25.3, 25.3, 24.7, 24.5, 23.1, 22.8, 22.0, 21.8, 21.8, 19.9, 19.8, 19.8, 19.7, 19.5, 19.3, 19.1, 19.0$ ; **HRMS**:  $m/z$  calcd for  $\text{C}_{34}\text{H}_{45}\text{O}_7$   $[\text{M}-\text{H}]^-$ : 565.3171; found: 565.3166.

\*In 13-*epi*-callistrilone E (6) NMR spectras minor peaks are there due to presence of rotamer. This rotameric peaks was also present in isolation spectras but these was not reported.

\* <sup>1</sup>H and <sup>13</sup>C NMR comparison Table between natural and synthetic 13-*epi*-callistrilone E (6)

<sup>1</sup> H-NMR in CDCl <sub>3</sub>		<sup>13</sup> C-NMR in CDCl <sub>3</sub>	
Natural 13- <i>epi</i> -Callistrilone E (6) 500 MHz	Synthetic 13- <i>epi</i> -Callistrilone C (6) 400 MHz	Nat. 13- <i>epi</i> -Callistrilone E(6) 125 MHz	Syn. 13- <i>epi</i> -Callistrilone E (6) 100 MHz
13.79	13.80 (s, 1H) 13.79 (s, 1H)	212.6	212.5
10.27	11.15 (s, 1H) 10.27 (s, 1H)	212.4	212.3 212.2
9.85	9.84 (s, 1H) 9.10 (s, 1H)	204.1	203.9 202.9
5.82 (dd, <i>J</i> = 10.3, 3.3 Hz)	5.81 (d, <i>J</i> = 10.2 Hz, 1H) 5.91 (dd, <i>J</i> = 10.2, 2.5 Hz, 1H)	174.8	174.6 176.2
5.54 (dd, <i>J</i> = 10.2, 2.1 Hz)	5.53 (dd, <i>J</i> = 10.3, 2.2 Hz, 1H) 5.61 (dd, <i>J</i> = 10.2, 2.1 Hz, 1H)	161.3	161.3 161.6
4.03 (m)	4.08 - 3.84 (m, 2H)	160.4	160.3 161.1
3.71 (d, <i>J</i> = 11.4 Hz)	3.70 (d, <i>J</i> = 11.6 Hz, 1H)	159.9	159.8 160.0
3.51 (dd, <i>J</i> = 5.6, 4.5 Hz)	3.53 - 3.44 (m, 2H) 3.33 (d, <i>J</i> = 10.7 Hz, 1H)	137.1	137.0 136.6
2.84 (m)	2.88 - 2.77 (m, 1H) 3.00 - 2.90 (m, 1H)	127.8	127.9 127.6
2.54 (m)	2.53 (dt, <i>J</i> = 13.3, 4.2 Hz, 1H) 2.33 (dt, <i>J</i> = 13.3, 4.9 Hz, 1H)	114.8	114.7
1.94 (m)	2.01 - 1.87 (m, 2H)	106.9	106.9
1.65 (s)	1.64 (s, 6H)	106.9	106.8 106.0
1.58 (m)	1.59 - 1.53 (m, 6H)	104.1	103.9 103.0
1.57 (m)		91.8	91.6



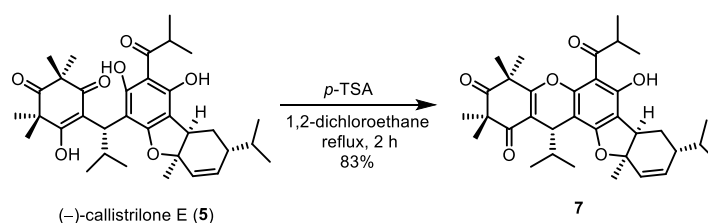
			90.4
1.48 (s)	1.47 (s, 3H) 1.46 (s, 3H)	54.8	55.0 54.6
1.36 (s)	1.35 (s, 3H) 1.39 (s, 3H)	48.9	48.7 48.5
1.31 (s)	1.33 (s, 3H)	44.5	44.4 44.7
1.30 (s)	1.30 (s, 6H) 1.29 (s, 3H)	40.4	40.2 41.0
1.18 (d, $J = 6.9$ Hz)	1.17 (d, $J = 6.9$ Hz, 6H)	39.6	39.5 39.5
1.14 (d, $J = 6.9$ Hz)	1.15-1.09 (m, 6H)	37.6	37.5 37.9
0.89 (d, $J = 6.5$ Hz)	0.91 - 0.87 (m, 6H)	31.5	31.4 31.3
0.86 (d, $J = 6.9$ Hz)	0.87 (d, $J = 6.9$ Hz, 3H)	27.5	27.3 27.1
0.84 (d, $J = 6.5$ Hz)	0.84 (d, $J = 6.7$ Hz, 3H) 0.83 (d, $J = 6.7$ Hz, 3H)	27.2	26.6 26.1
0.78 (d, $J = 6.9$ Hz)	0.77 (d, $J = 6.6$ Hz, 6H) 0.72 (d, $J = 6.1$ Hz, 3H)	26.3	25.9 25.9
		25.5	25.8 25.3
		25.5	25.7 25.3
		24.7	24.7 24.5
		23.0	23.1 22.8
		22.1	22.0
		22.0	21.8 21.8
		20.1	19.9

			19.8
		19.6	19.8 19.7
		19.5	19.5 19.3
		19.1	19.1 19.0

\*In 13-*epi*-callistrilone E (**6**) NMR spectras minor peaks are there due to presence of rotamer.

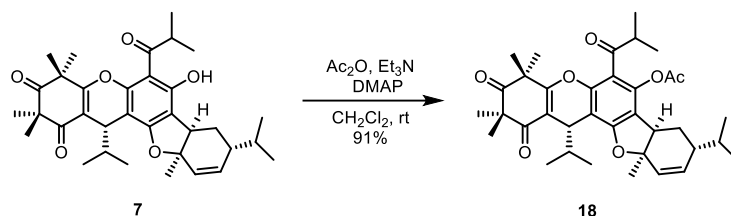
This rotameric peaks was also present in isolation spectras but these was not reported.

### Synthesis of compound 7:



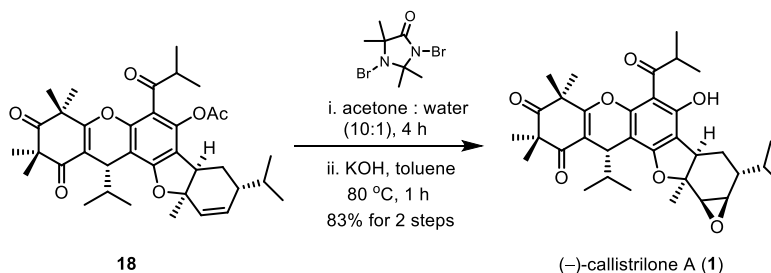
To a magnetically stirred solution of (-)-callistrilone E (**5**) (140 mg, 0.247 mmol) in dry 1,2-dichloroethane (15 mL) was added *para*-toluenesulfonic acid (94 mg, 0.494 mmol) and the mixture was refluxed for 2 h. After cooling to rt, the mixture was washed with a saturated solution of NaHCO<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub> and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc–hexane (1:9) as eluent furnished compound **7** (112 mg, 83%) as a crystalline solid, mp: 242–244°C;  $R_f = 0.6$  (EtOAc–hexane 1:9);  $[\alpha]_D^{28} = -119.13$  ( $c$  0.38, MeOH); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  2926, 1719, 1654, 1461, 1382, 1156, 1060; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  13.42 (s, 1H), 5.87 (dd,  $J = 10.1, 2.7$  Hz, 1H), 5.63 (dd,  $J = 10.1, 2.7$  Hz, 1H), 4.09 (d,  $J = 3.6$  Hz, 1H), 3.91 (sep,  $J = 6.8$  Hz, 1H), 3.55 (t,  $J = 4.6$  Hz, 1H), 2.48–2.42 (m, 1H), 1.97–1.90 (m, 1H), 1.89–1.82 (m, 1H), 1.70 – 1.65 (m, 1H), 1.64 – 1.61 (m, 1H), 1.60 (s, 3H), 1.59 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.25 (d,  $J = 6.8$  Hz, 3H), 1.23 (d,  $J = 6.8$  Hz, 3H), 0.91 (d,  $J = 6.8$  Hz, 6H), 0.84 (d,  $J = 6.8$  Hz, 3H), 0.73 (d,  $J = 6.7$  Hz, 3H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz)  $\delta$  212.1, 209.1, 197.4, 167.3, 163.0, 160.5, 153.4, 135.2, 129.1, 112.1, 112.1, 103.7, 99.3, 89.3, 56.1, 47.2, 44.8, 39.4, 37.8, 34.6, 32.2, 31.4, 26.4, 25.6, 25.0 (2C), 24.5, 24.3, 21.1, 19.6, 19.6, 19.4, 18.1, 17.8; **HRMS**:  $m/z$  calcd for C<sub>34</sub>H<sub>45</sub>O<sub>6</sub> [M+H]<sup>+</sup>: 549.3216; found: 549.3212.

### Synthesis of compound 18:



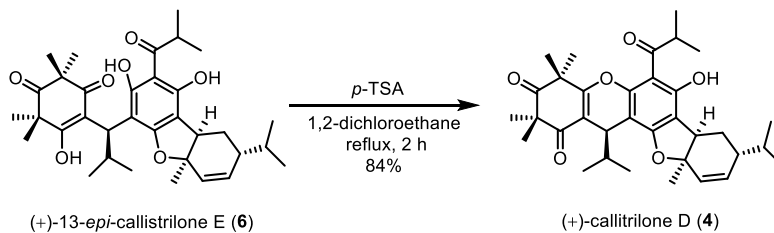
To a magnetically stirred solution of compound **7** (95 mg, 0.173 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) was added  $\text{Et}_3\text{N}$  (72  $\mu\text{L}$ , 0.520 mmol), DMAP (3 mg, 26  $\mu\text{mol}$ ) and acetic anhydride (33  $\mu\text{L}$ , 0.346 mmol) drop-wise and the resulting mixture was then stirred at rt. After completion of reaction, indicated by TLC, the reaction mixture was washed with a saturated solution of  $\text{NaHCO}_3$  and extracted with EtOAc. The combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:12) as eluent furnished acetate **18** (93 mg, 91%) as a colourless liquid;  $R_f = 0.30$  (EtOAc-hexane 1:9);  $[\alpha]_D^{28} = -80.12$  ( $c$  0.166, MeOH); **IR** (neat):  $\nu_{\text{max}}/\text{cm}^{-1}$  2961, 2927, 1773, 1703, 1647, 1460, 1383, 1188, 1157, 1060;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  5.78 (d,  $J = 10.3$  Hz, 1H), 5.58 (dd,  $J = 10.3, 2.3$  Hz, 1H), 4.13 (d,  $J = 3.6$  Hz, 1H), 3.47 (t,  $J = 4.3$  Hz, 1H), 3.01 (sep,  $J = 7.0$  Hz, 1H), 2.26 (s, 3H), 1.96-1.88 (m, 3H), 1.64-1.60 (m, 1H), 1.59 (s, 3H), 1.49 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.18 (d,  $J = 6.7$  Hz, 3H), 1.16 (d,  $J = 7.2$  Hz, 3H), 0.97-0.94 (m, 1H), 0.90 (d,  $J = 6.9$  Hz, 3H), 0.86 (d,  $J = 6.7$  Hz, 3H), 0.85 (d,  $J = 6.7$  Hz, 3H), 0.74 (d,  $J = 6.9$  Hz, 3H);  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  212.2, 205.1, 197.5, 168.0, 167.8, 158.6, 149.0, 142.7, 134.4, 129.5, 118.8, 114.8, 111.1, 106.0, 88.6, 56.0, 47.4, 46.0, 42.5, 37.5, 34.8, 33.0, 31.4, 25.9, 25.1, 25.0, 24.7, 24.6, 24.2, 20.5, 19.7, 19.3, 19.0, 18.5, 18.0 (2C); **HRMS**:  $m/z$  calcd for  $\text{C}_{36}\text{H}_{47}\text{O}_7$   $[\text{M}+\text{H}]^+$ : 591.3322; found: 591.3324.

### Synthesis of (-)-callistrilone A (1):



To a magnetically stirred solution of acetate **18** (56 mg, 0.094 mmol) in acetone/H<sub>2</sub>O (10:1, 3 mL) was added 1,3-dibromo-5,5-dimethylhydantoin (55 mg, 0.19 mmol) in small portions over 5 min. The entire set-up was covered with aluminum foil, placed in the dark and stirred for 4 h until all the starting material was consumed by TLC. The reaction mixture was quenched with saturated NH<sub>4</sub>Cl (2 mL), diluted with water (2 mL) and extracted with EtOAc (3 x 5 mL). The combined extracts were washed with brine (5 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:7) as eluent liquid furnished bromohydrin;  $R_f = 0.50$  (EtOAc-hexane 1:5). To a magnetically stirred solution of the bromohydrin in toluene (3 mL) was added solid powdered KOH (37 mg, 0.66 mmol) and the mixture was heated at 80 °C for 1 h until all the starting material was consumed by TLC. The reaction mixture was cooled and diluted with water (3 mL) and extracted with Et<sub>2</sub>O (3 x 5 mL). The combined organic layer were washed with brine (5 mL) and dried with Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:15) as eluent furnished (–)-callistrilone A (**1**) (44 mg, 83%, (2 steps)),  $R_f = 0.60$  (EtOAc-hexane 1:5);  $[\alpha]_D^{28} = -98.00$  ( $c$  0.125, MeOH); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  3436 (br), 2924, 1655, 1462, 1383, 1154, 1070; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 500 MHz)  $\delta$  13.31 (s, 1H), 4.14 (d,  $J = 3.6$  Hz, 1H), 3.86 (sep,  $J = 6.6$  Hz, 1H), 3.45 (dd,  $J = 4.1$ , 3.6 Hz, 1H), 3.28 (d,  $J = 4.1$  Hz, 1H), 3.02 (dd,  $J = 12.4$ , 6.0 Hz, 1H), 2.13-2.09 (m, 1H), 1.88-1.83 (m, 1H), 1.82 – 1.78 (m, 1H), 1.66 – 1.60 (m, 1H), 1.60 – 1.56 (m, 1H), 1.55 (s, 3H), 1.48 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H), 1.21 (d,  $J = 6.5$  Hz, 3H), 1.19 (d,  $J = 7.1$  Hz, 3H), 1.08 (d,  $J = 6.5$  Hz, 3H), 1.06 (d,  $J = 6.5$  Hz, 3H), 0.84 (d,  $J = 6.9$  Hz, 3H), 0.68 (d,  $J = 6.9$  Hz, 3H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 125 MHz)  $\delta$  212.3, 209.3, 197.3, 167.7, 161.9, 160.5, 154.1, 113.6, 112.6, 104.3, 99.3, 88.6, 56.4, 56.1, 55.1, 47.4, 40.5, 39.7, 39.3, 34.7, 32.6, 28.5, 26.3, 25.4 (2C), 25.1, 23.9, 23.6, 22.1, 21.5, 21.2, 20.1, 18.0 (2C); **HRMS**:  $m/z$  calcd for C<sub>34</sub>H<sub>45</sub>O<sub>7</sub> [M+H]<sup>+</sup>: 565.3160; found: 565.3162.

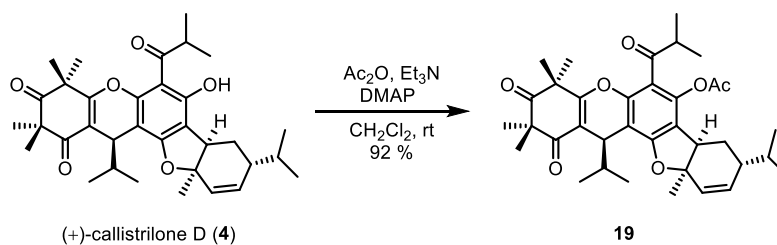
#### Synthesis of (+)-callistrilone D (**4**):



To a magnetically stirred solution of (+)-13-*epi*-callistrilone E (**6**) (90 mg, 0.159 mmol) in dry 1, 2-dichloroethane (15 mL) was added *para*-toluenesulfonic acid (60 mg, 0.318 mmol) and the mixture was refluxed for 2 h. After cooling to rt, the mixture was washed with a saturated solution of NaHCO<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub> and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue

on silica gel column using EtOAc–hexane (1:99) as eluent furnished (+)-callistrilone D (**4**) (73 mg, 84%).  $R_f = 0.6$  (EtOAc–hexane 1:9);  $[\alpha]_D^{28} = +88.3$  ( $c$  0.83, MeOH); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  2962, 1719, 1655, 1462, 1383, 1244, 1156, 1060, 844;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  13.43 (s, 1H), 5.88 (dd,  $J = 10.5, 2.4$  Hz, 1H), 5.61 (dd,  $J = 10.3, 2.4$  Hz, 1H), 4.08 (d,  $J = 3.7$  Hz, 1H), 3.90 (sep,  $J = 6.8$  Hz, 1H), 3.51 (t,  $J = 4.8$  Hz, 1H), 2.48–2.42 (m, 1H), 2.02 (br. s., 1H), 1.83 (m, 1H), 1.68 – 1.62 (m, 2H), 1.59 (s, 3H), 1.56 (s, 3H), 1.42 (s, 6H), 1.38 (s, 3H), 1.26 (s, 3H), 1.25 (s, 3H), 0.94 (d,  $J = 6.8$  Hz, 3H), 0.93 (d,  $J = 6.8$  Hz, 3H), 0.83 (d,  $J = 6.8$  Hz, 3H), 0.71 (d,  $J = 6.8$  Hz, 3H);  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  212.1, 209.0, 197.4, 167.5, 163.0, 160.9, 153.7, 135.1, 128.9, 112.4, 112.1, 103.7, 99.2, 89.7, 56.1, 47.2, 44.8, 39.5, 37.8, 34.5, 32.1, 31.4, 26.3, 25.5, 25.1, 24.9, 24.5, 24.2, 21.1, 19.7 (2C), 19.5, 17.9 (2C); **HRMS**:  $m/z$  calcd for  $\text{C}_{34}\text{H}_{45}\text{O}_6$   $[\text{M}+\text{H}]^+$ : 549.3216; found: 549.3217.

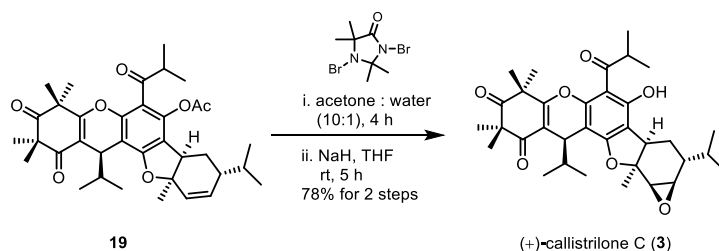
### Synthesis of compound **19**:



To a magnetically stirred solution of (+)-callistrilone D (**4**) (70 mg, 0.13 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) was added  $\text{Et}_3\text{N}$  (53  $\mu\text{L}$ , 0.382 mol), DMAP (2 mg, 0.013 mmol) and acetic anhydride (24  $\mu\text{L}$ , 0.255 mmol) dropwise and the resulting mixture was then stirred at rt. After completion of reaction, indicated by TLC, the reaction mixture was washed with a saturated solution of  $\text{NaHCO}_3$  and extracted with ethyl acetate. The combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent and purification of the residue on silica gel column using EtOAc–hexane (1:12) as eluent furnished acetate **19** (69 mg, 92%) as a colourless liquid;  $R_f = 0.30$  (EtOAc–hexane 1:9);  $[\alpha]_D^{28} = +56.0$  ( $c$  1.5, MeOH); **IR** (neat):  $\nu_{\max}/\text{cm}^{-1}$  2962, 2931, 1776, 1704, 1650, 1469, 1383, 1188, 1156, 1061;  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  5.83 (d,  $J = 9.7$  Hz, 1H), 5.60 (dd,  $J = 10.3, 1.7$  Hz, 1H), 4.13 (d,  $J = 3.4$  Hz, 1H), 3.45 (t,  $J = 4.3$  Hz, 1H), 3.16 (sep,  $J = 6.9$  Hz, 1H), 2.28 – 2.22 (m, 4H), 1.97 – 1.92 (m, 2H), 1.91–1.89 (m, 1H), 1.64 – 1.61 (m, 1H), 1.56 (s, 3H), 1.50 (s, 3H), 1.38 (s, 3H), 1.35 (s, 6H), 1.22 (d,  $J = 6.9$  Hz, 3H), 1.19 (d,  $J = 6.9$  Hz, 3H), 0.94 (d,  $J = 6.3$  Hz, 3H), 0.90 (d,  $J = 6.9$  Hz, 3H), 0.86 (d,  $J = 6.9$  Hz, 3H), 0.71 (d,  $J = 6.9$  Hz, 3H);  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 212.1, 204.7, 197.3, 168.1, 168.0, 158.7, 149.5, 143.3, 134.4, 129.4, 119.3, 114.8, 111.5, 105.7, 89.1, 56.1, 47.4, 45.7, 42.2, 37.8, 34.7, 32.9, 31.4, 25.9, 25.3, 25.0

(2C), 24.7, 23.5, 20.4, 19.9 (2C), 19.0, 18.6, 18.1, 17.6; **HRMS**:  $m/z$  calcd for  $C_{36}H_{47}O_7$   $[M+H]^+$ : 591.3322; found: 591.3322

### Synthesis of (+)-callistrilone C (**3**):



To a magnetically stirred solution of acetate **19** (64 mg, 0.11 mmol) in acetone/H<sub>2</sub>O (10:1, 3 mL) was added 1,3-dibromo-5,5-dimethylhydantoin (64 mg, 0.22 mmol) in small portions over 5 min. The entire set-up was covered with aluminum foil, placed in the dark and stirred for 4 h until all the starting material was consumed by TLC. The reaction mixture was quenched with saturated NH<sub>4</sub>Cl (2 mL), diluted with water (2 mL) and extracted with EtOAc (3 x 5 mL). The combined extracts were washed with brine (5 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:7) as eluent liquid furnished bromohydrin;  $R_f = 0.50$  (EtOAc-hexane 1:5). To a magnetically stirred solution of the bromohydrin in dry THF (3 mL) was added NaH (21 mg, 0.54 mmol) at rt. The resulting reaction mixture was then stirred for 5 h at same temperature. After completion of reaction indicated by TLC, diluted with water (3 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layer were washed with brine (5 mL) and dried with Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent and purification of the residue on silica gel column using EtOAc-hexane (1:24) as eluent furnished (+)-callistrilone C (**3**) (47 mg, 78%, (over 2 steps) (94% <sup>1</sup>H NMR purity using 1,3,5-trimethoxybenzene as an internal standard),  $R_f = 0.60$  (EtOAc-hexane 1:5);  $[\alpha]_D^{28} = +108.43$  ( $c$  0.17, MeOH); **IR** (neat):  $\nu_{max}/cm^{-1}$  2962, 2929, 2827, 1718, 1655, 1383, 1155, 1071, 844; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 500 MHz)  $\delta$  13.31 (s, 1H), 4.11 (d,  $J = 3.6$  Hz, 1H), 3.87 (sep,  $J = 6.8$  Hz, 1H), 3.43 (t,  $J = 3.3$  Hz, 1H), 3.27 (d,  $J = 4.0$  Hz, 1H), 3.02 (dd,  $J = 12.1, 6.0$  Hz, 1H), 2.13 - 2.08 (m, 1H), 1.91 - 1.85 (m, 1H), 1.84 - 1.80 (m, 1H), 1.70 - 1.60 (m, 2H), 1.58 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.21 (d,  $J = 6.9$  Hz, 3H), 1.21 (d,  $J = 6.9$  Hz, 3H), 1.08 (d,  $J = 6.3$  Hz, 3H), 1.08 (d,  $J = 6.3$  Hz, 3H), 0.91 (d,  $J = 6.9$  Hz, 3H), 0.71 (d,  $J = 6.9$  Hz, 3H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz)  $\delta = 212.2, 209.2, 197.7, 167.5, 162.1, 160.4, 153.6, 113.5, 112.4, 104.1, 99.2, 88.4, 56.3, 56.0, 55.1, 47.4, 40.6, 39.7, 39.2, 34.9, 32.6,$

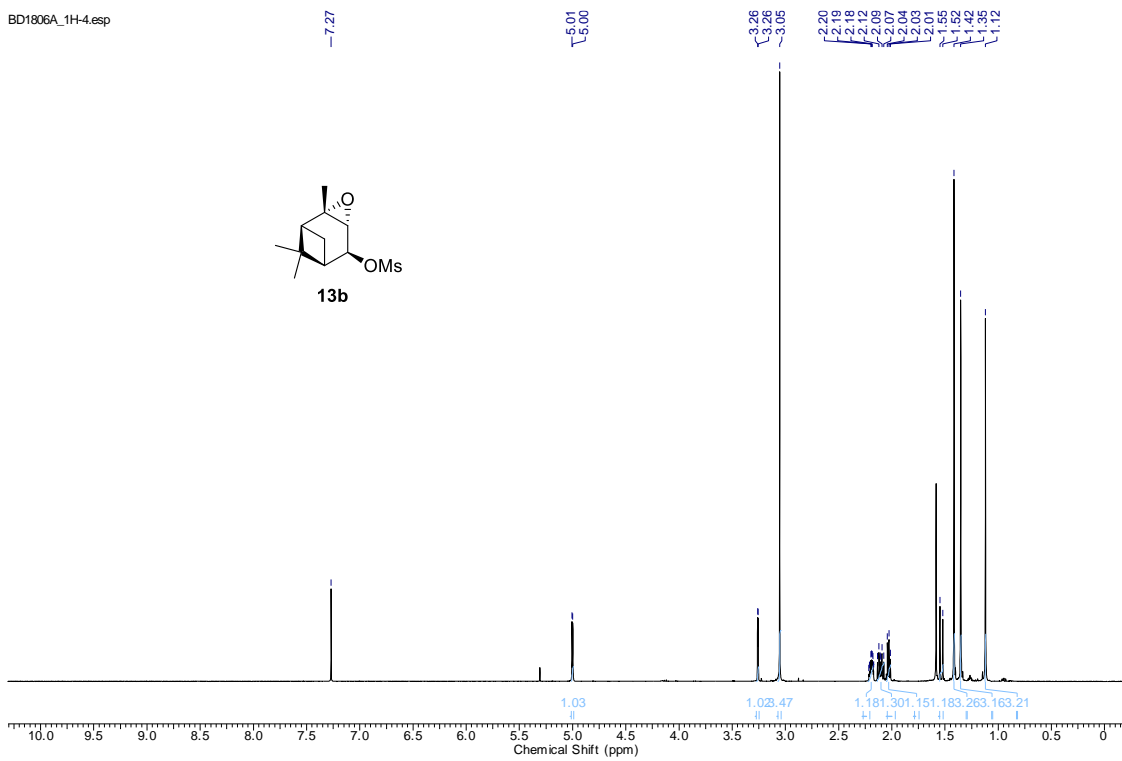
28.5, 26.2, 25.2, 25.2, 24.8, 24.3, 23.7, 22.1, 21.4, 21.2, 19.7, 18.1, 18.0; **HRMS**: m/z calcd for C<sub>34</sub>H<sub>45</sub>O<sub>7</sub> [M+H]<sup>+</sup>: 565.3160; found: 565.3154.

**Comparison table for optical rotation of Callistriones:**

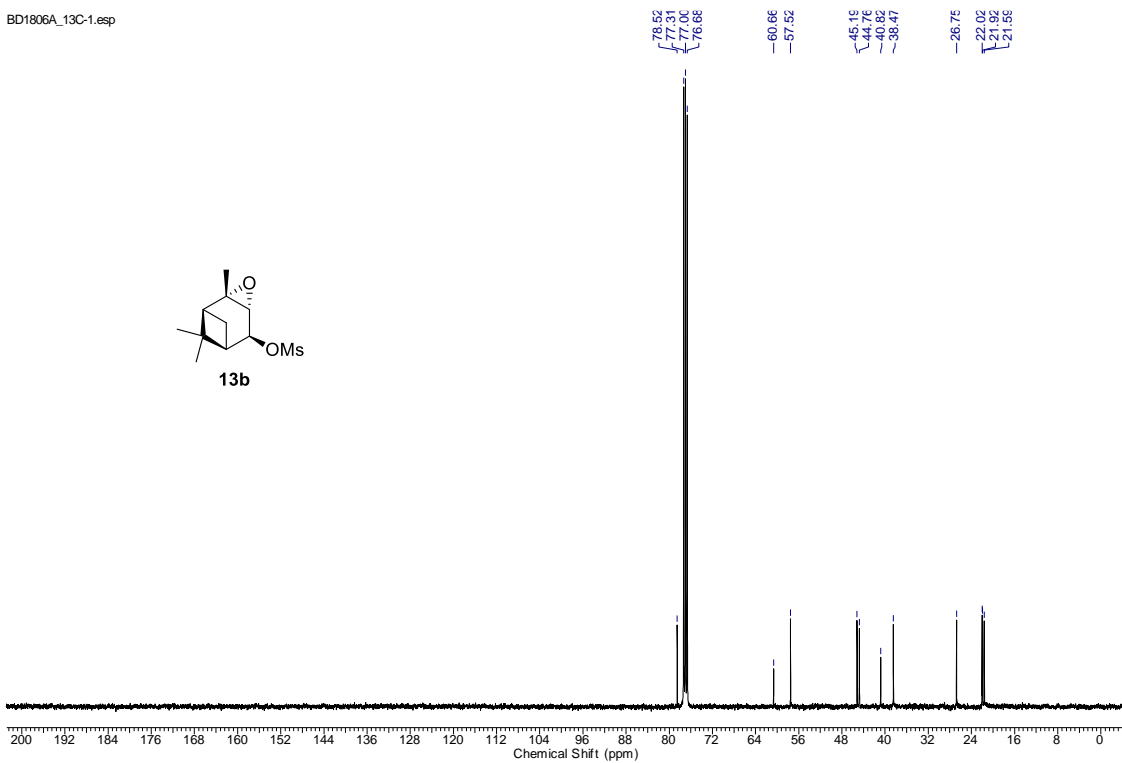
Compound	Natural	Synthetic (Previously reported)	Synthetic (This work)
<b>Callistrilone A</b>	$[\alpha]_D^{27} = -98.5$ (c 0.2 in MeOH)	$[\alpha]_D^{27} = -103.3$ (c 0.2 in MeOH) ( <i>Chem. Sci.</i> , <b>2018</b> , 9, 1488-1495) $[\alpha]_D^{235} = -105.0$ (c 0.2, MeOH) ( <i>Org. Lett.</i> <b>2018</b> , 20, 2509–2512)	$[\alpha]_D^{28} = -98.00$ (c 0.125, MeOH)
<b>Callistrilone C</b>	-----	$[\alpha]_D^{25} = +91.5$ (c 0.1, MeOH) ( <i>Chem. Sci.</i> , <b>2018</b> , 9, 1488-1495) $[\alpha]_D^{235} = +110.0$ (c 0.1, MeOH) ( <i>Org. Lett.</i> <b>2018</b> , 20, 2509–2512)	$[\alpha]_D^{28} = +108.43$ (c 0.17, MeOH)
<b>Callistrilone D</b>	----	$[\alpha]_D^{25} = +112.1$ (c 0.1, MeOH) ( <i>Chem. Sci.</i> , <b>2018</b> , 9, 1488-1495) $[\alpha]_D^{24} = +70.0$ (c 0.1, MeOH) ( <i>Org. Lett.</i> <b>2018</b> , 20, 2509–2512)	$[\alpha]_D^{28} = +88.3$ (c 0.83, MeOH)
<b>Callistrilone E</b>	----	$[\alpha]_D^{25} = -22.5$ (c 0.1, MeOH) ( <i>Chem. Sci.</i> , <b>2018</b> , 9, 1488-1495) $[\alpha]_D^{235} = -10.0$ (c 0.1, MeOH) ( <i>Org. Lett.</i> <b>2018</b> , 20, 2509–2512)	$[\alpha]_D^{28} = -17.2$ (c 0.50, MeOH)
<b>13-<i>epi</i>-Callistrilone E</b>	----	-----  -----	$[\alpha]_D^{28} = +20.6$ (c 0.23, MeOH)

### 3. $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra

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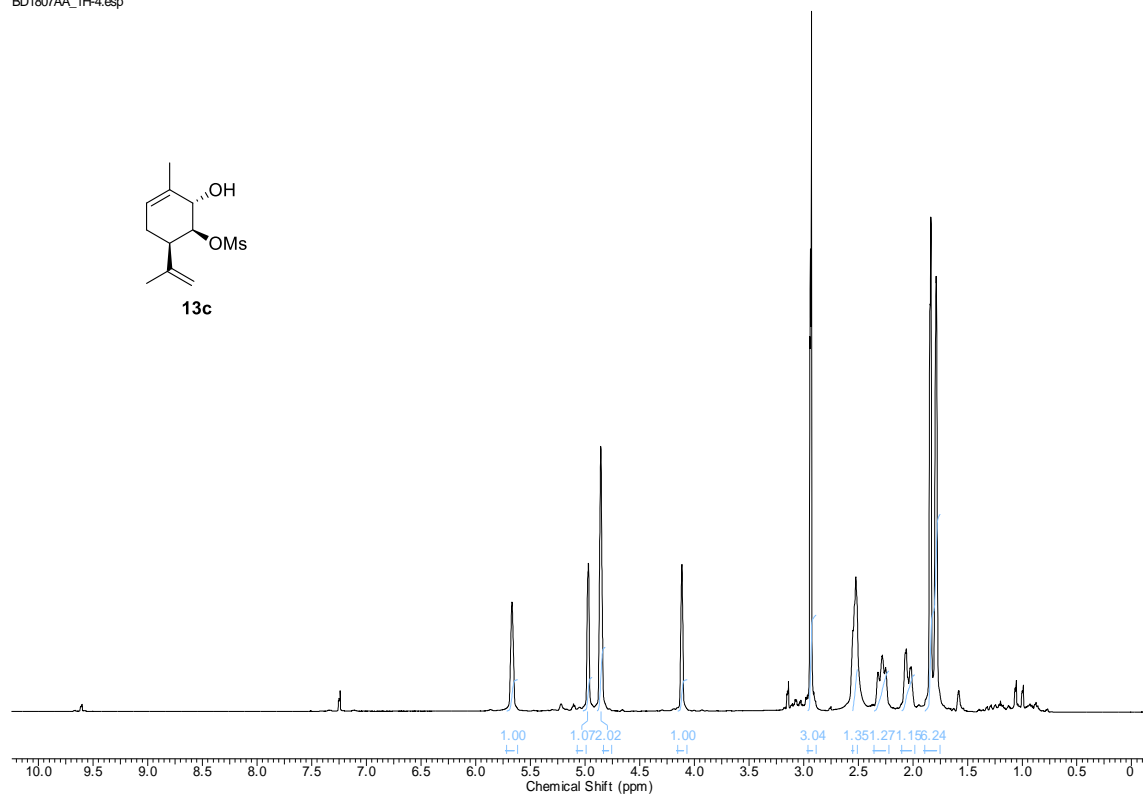
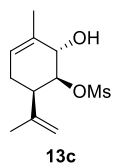


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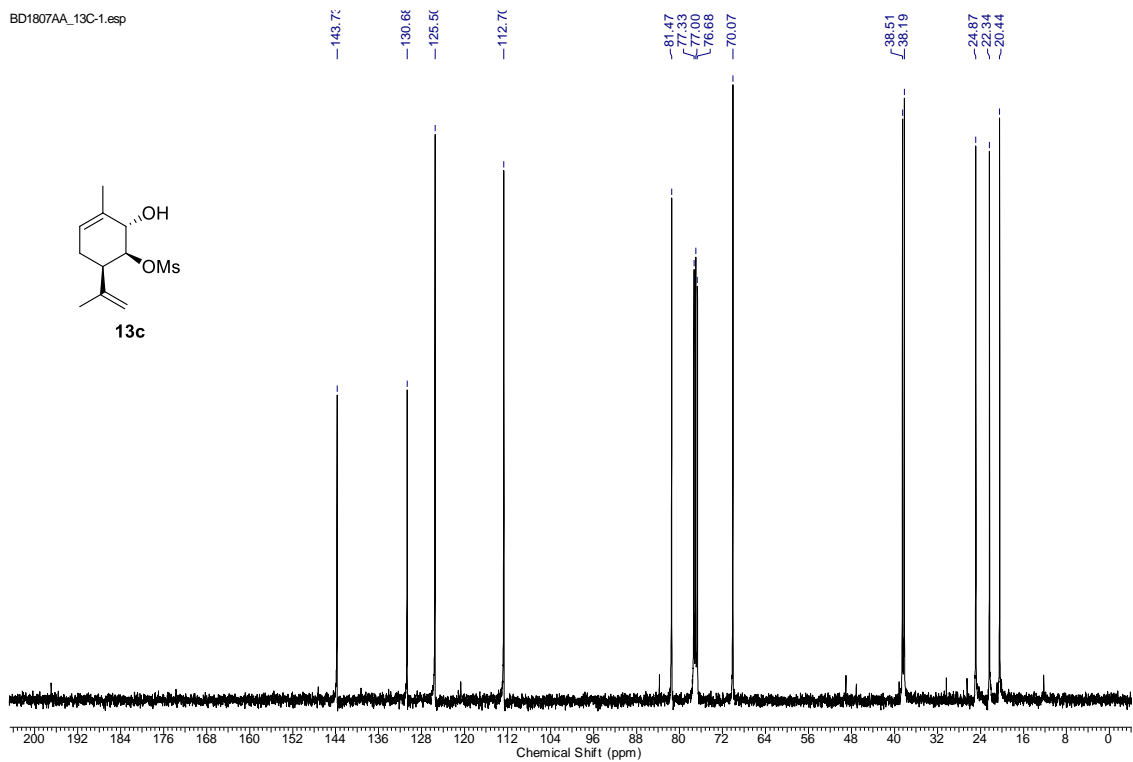
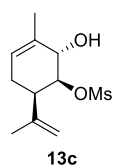




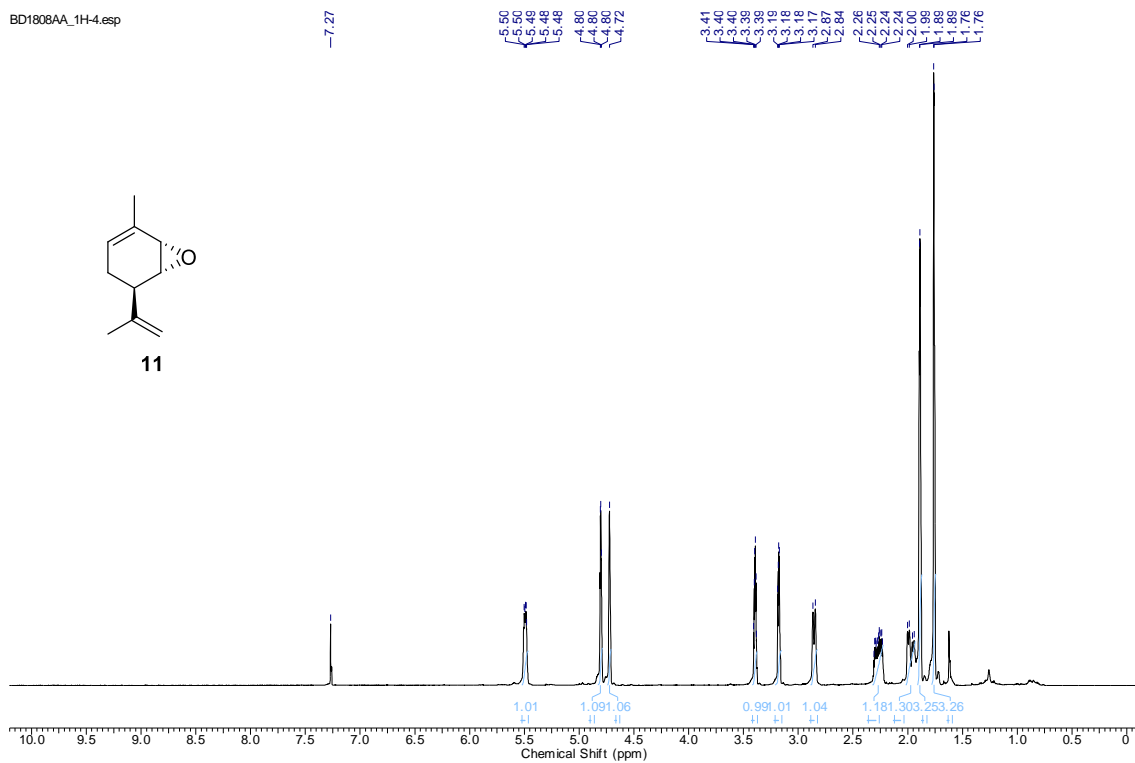
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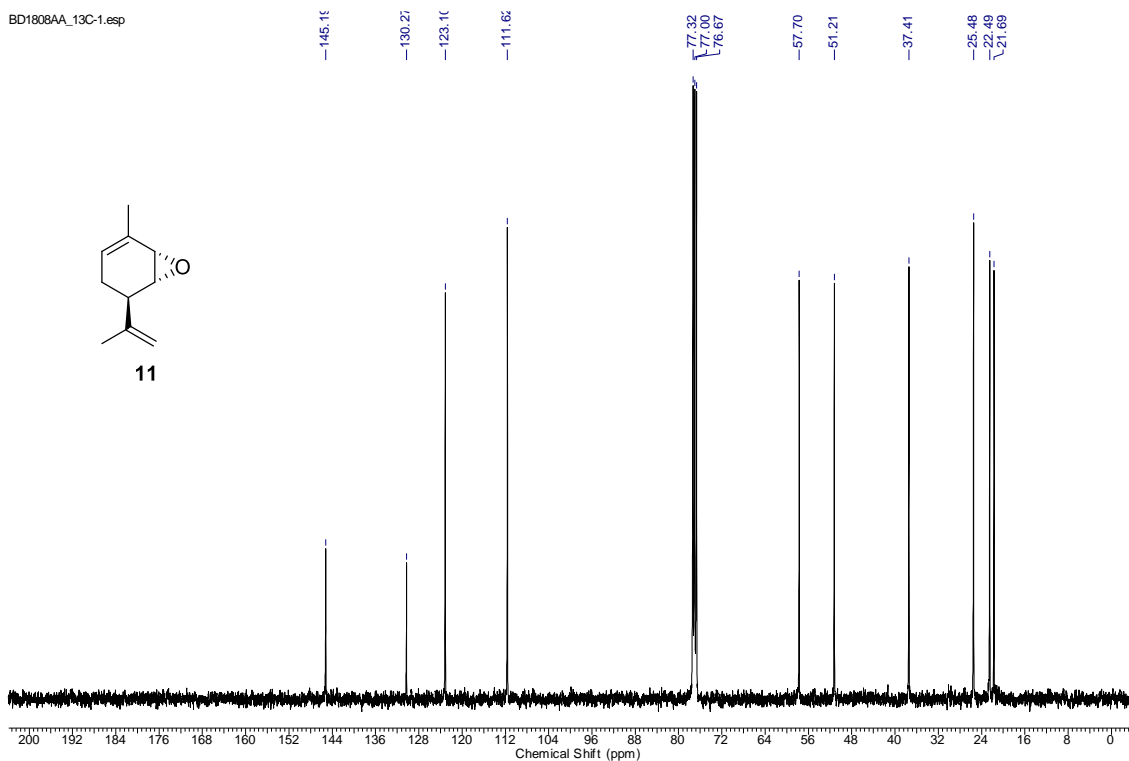
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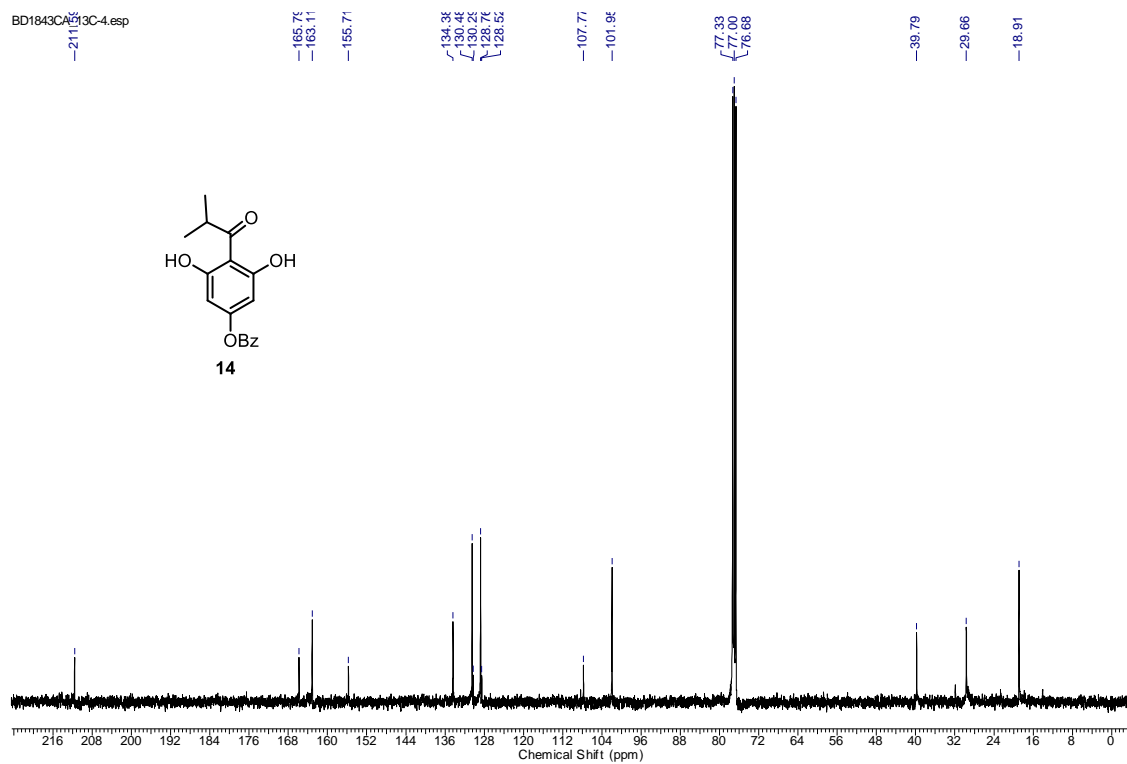
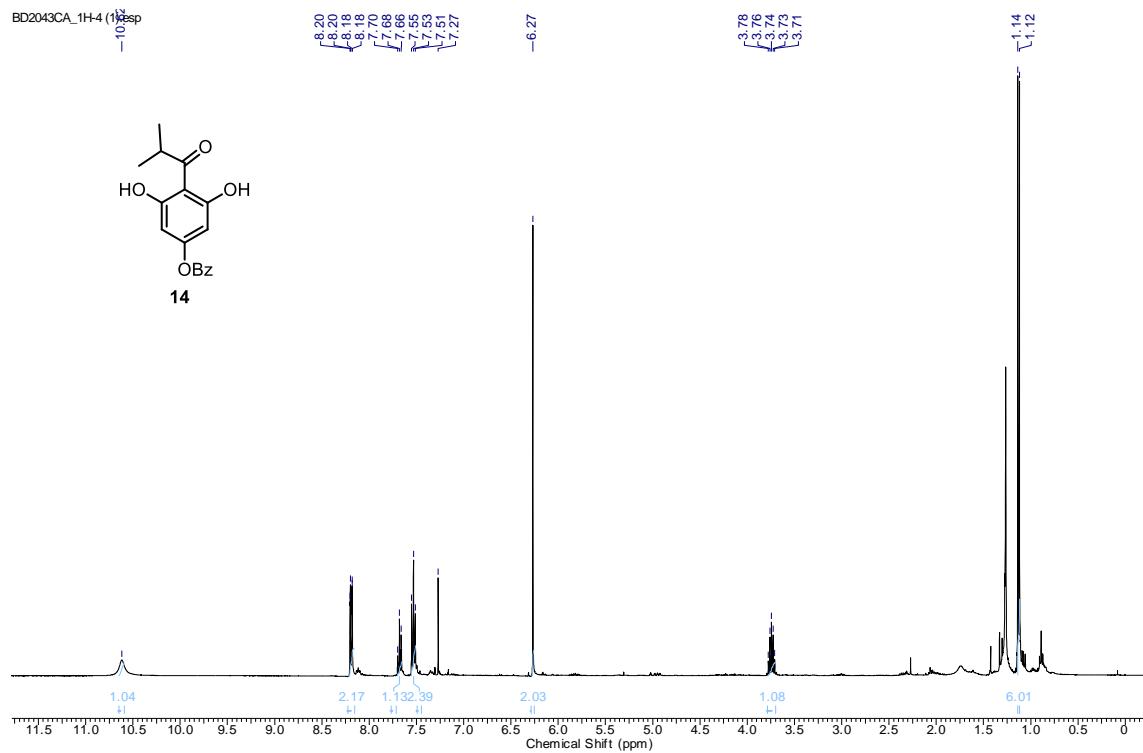


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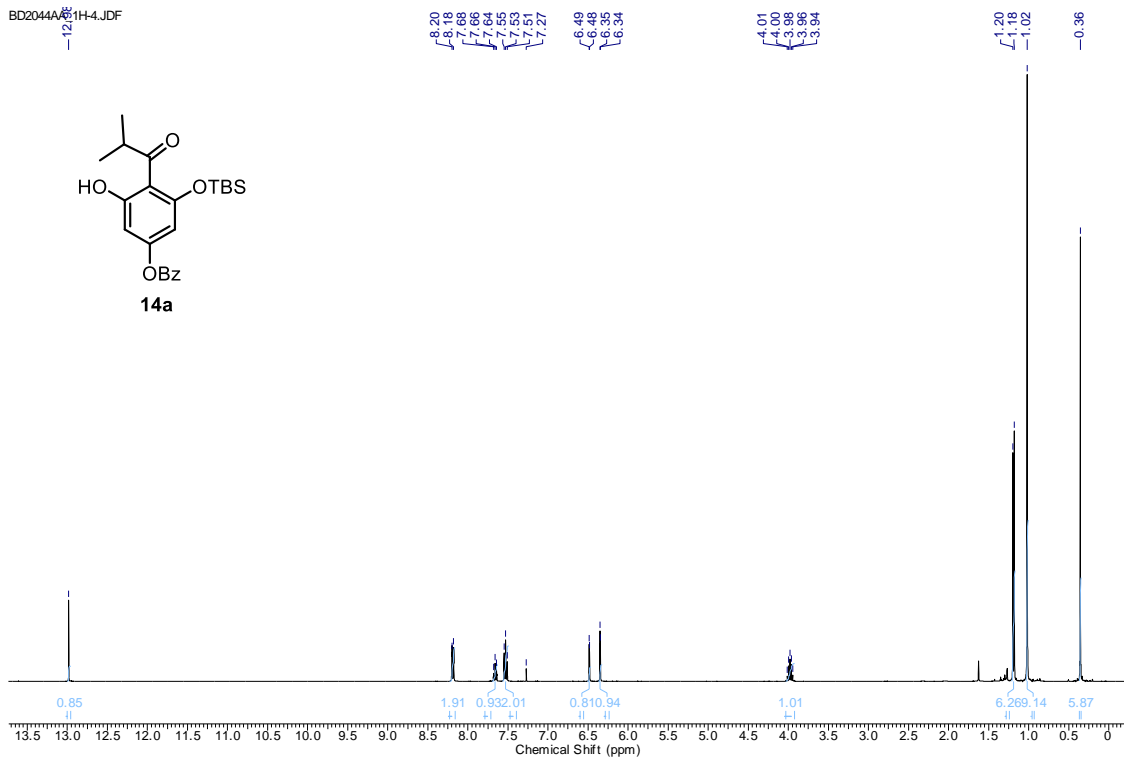


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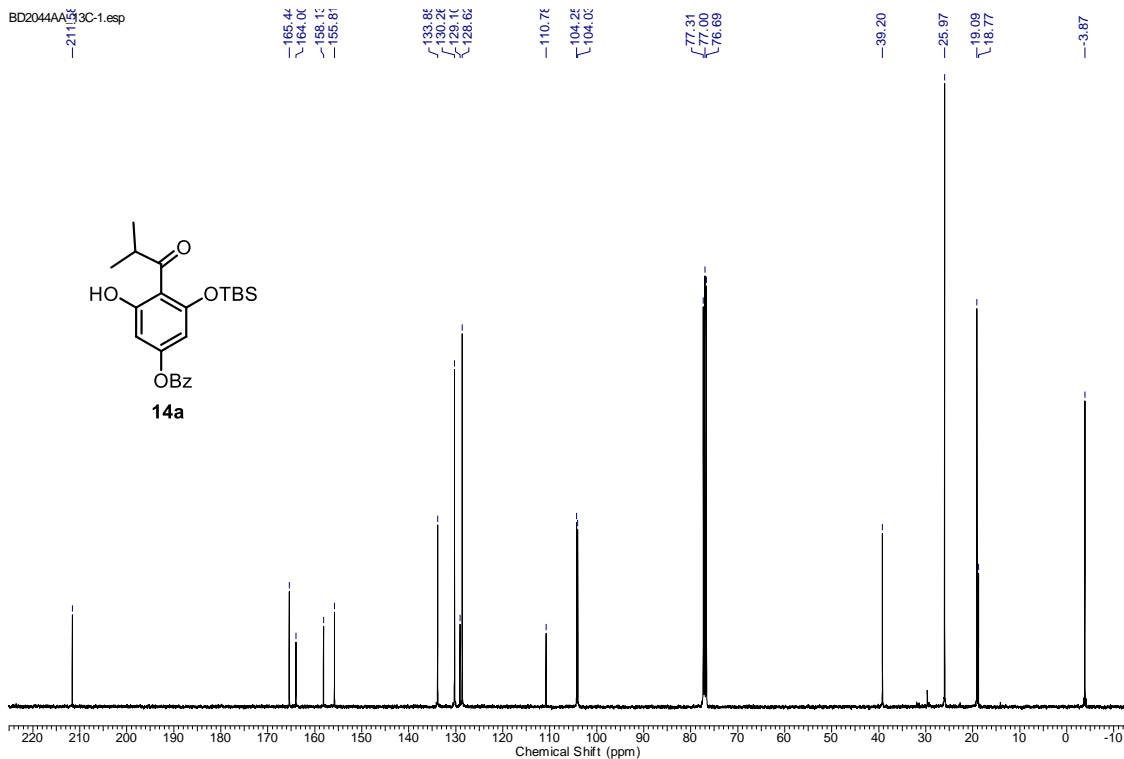


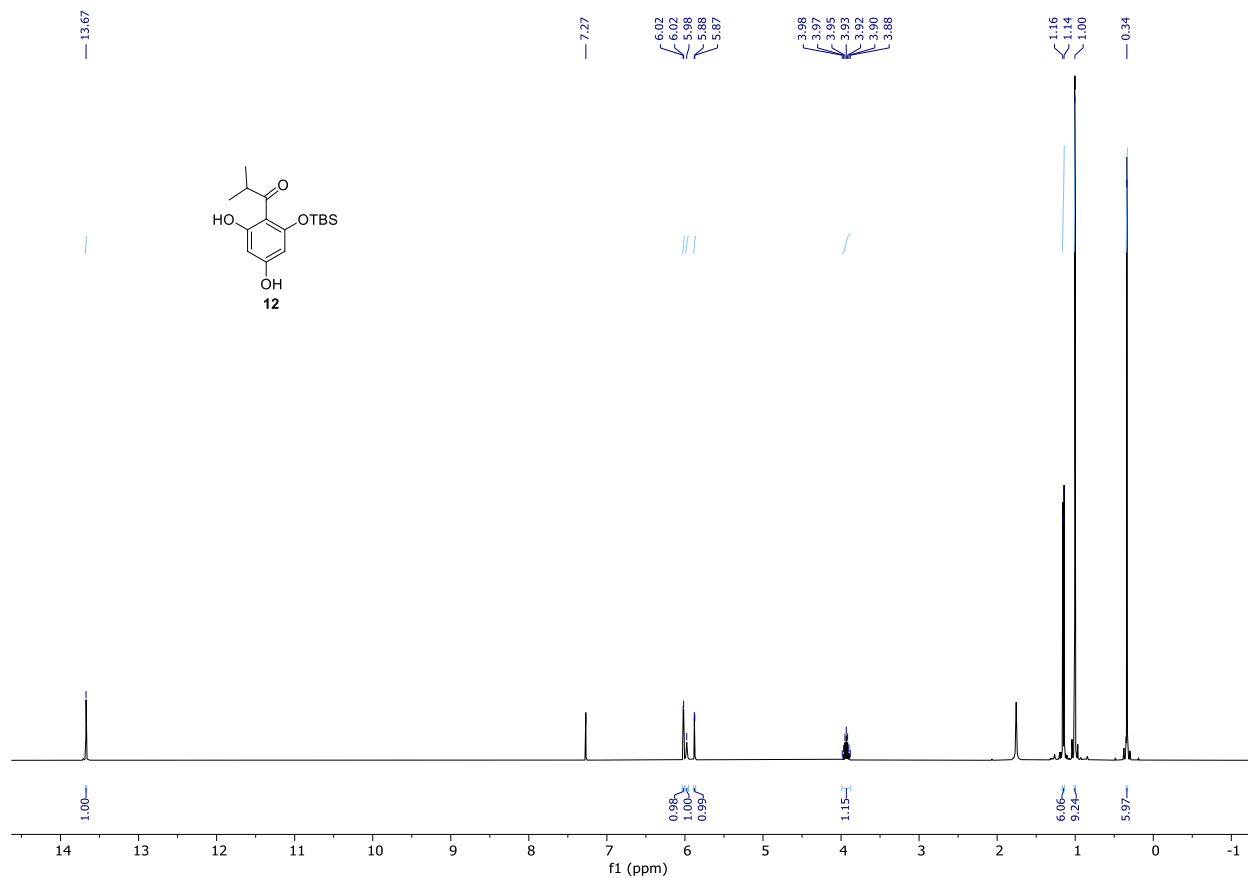


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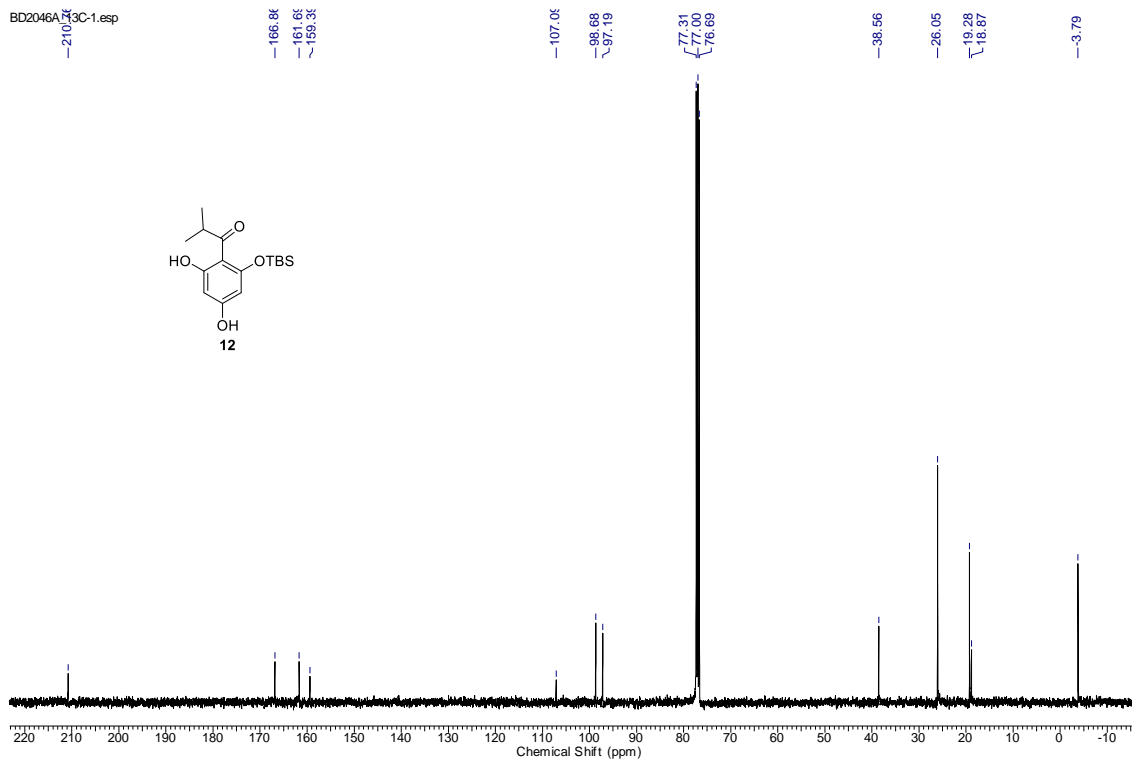


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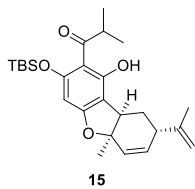
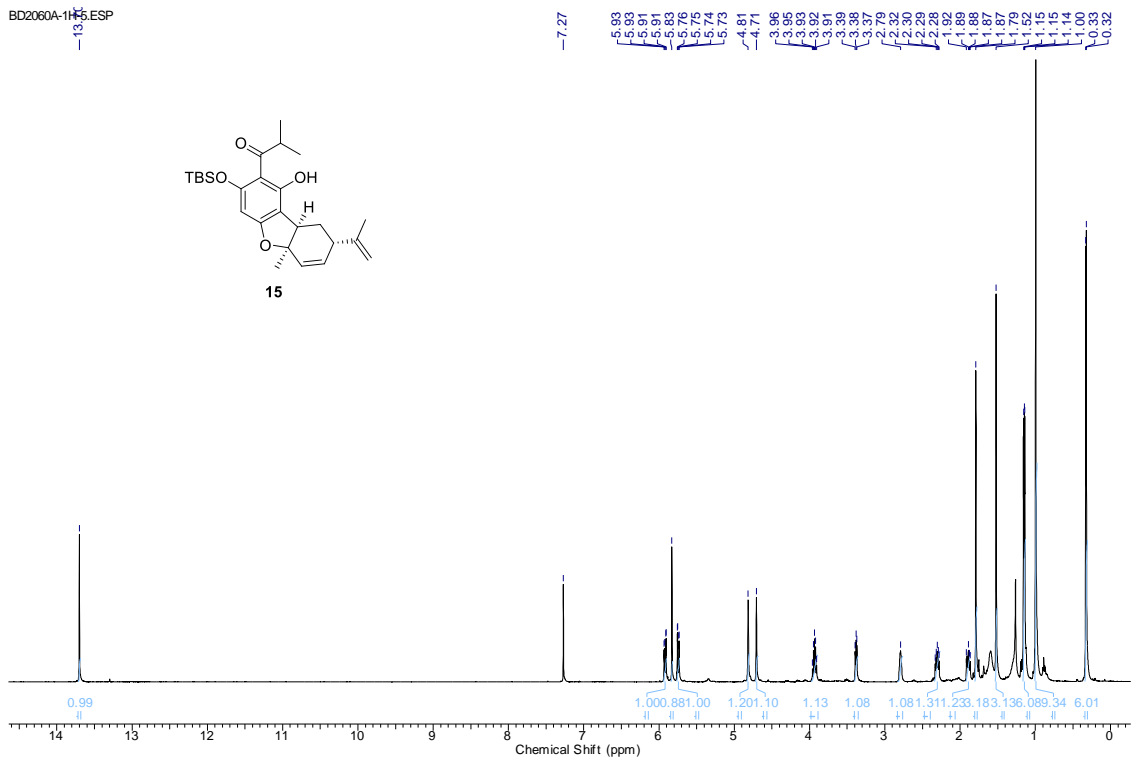




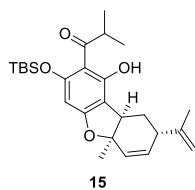
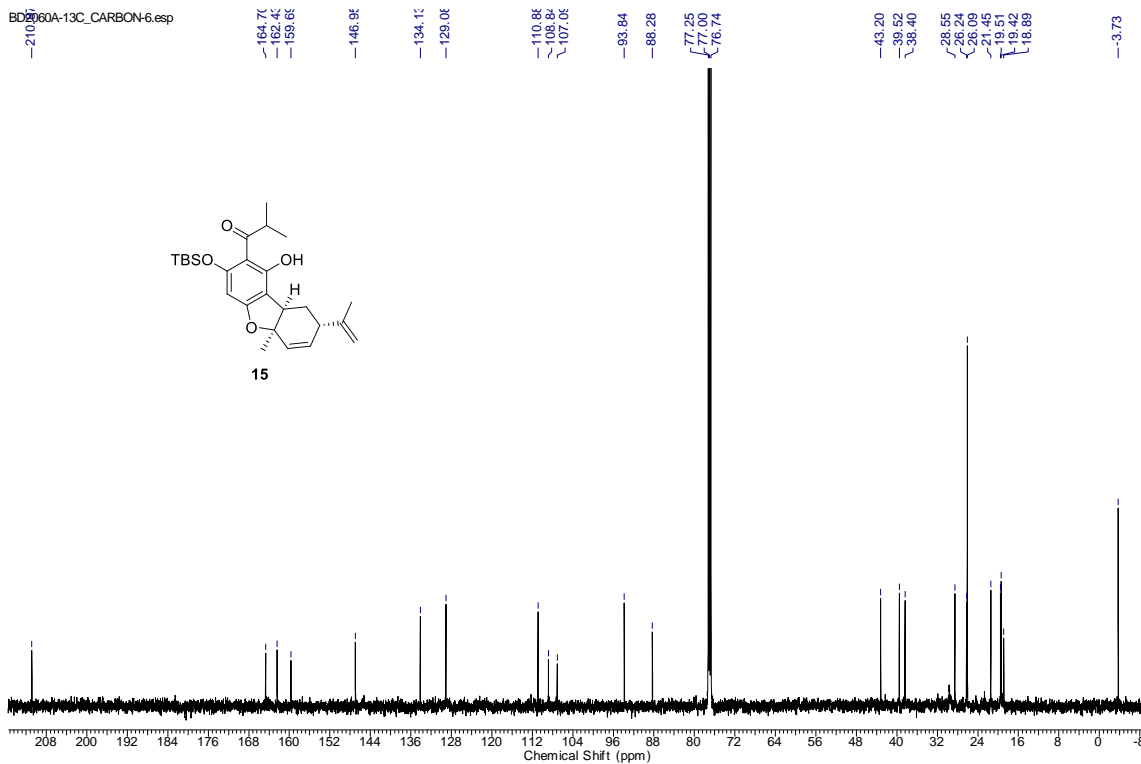
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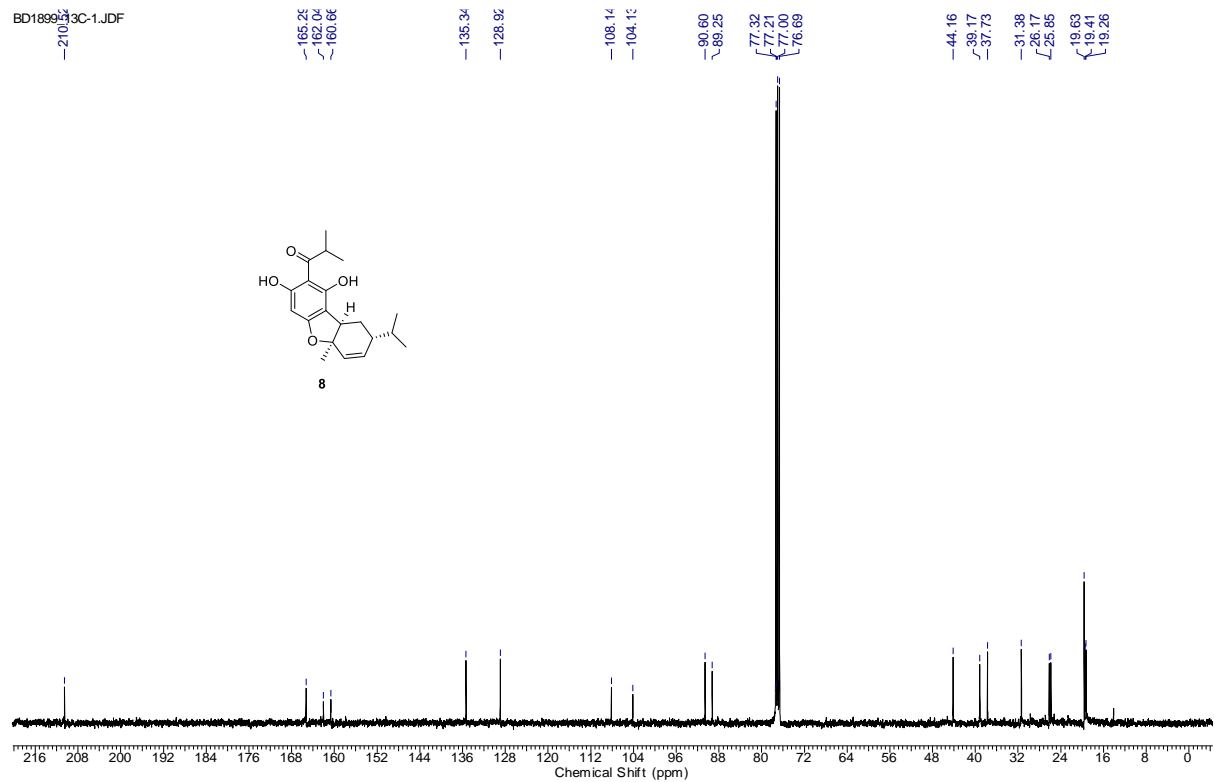
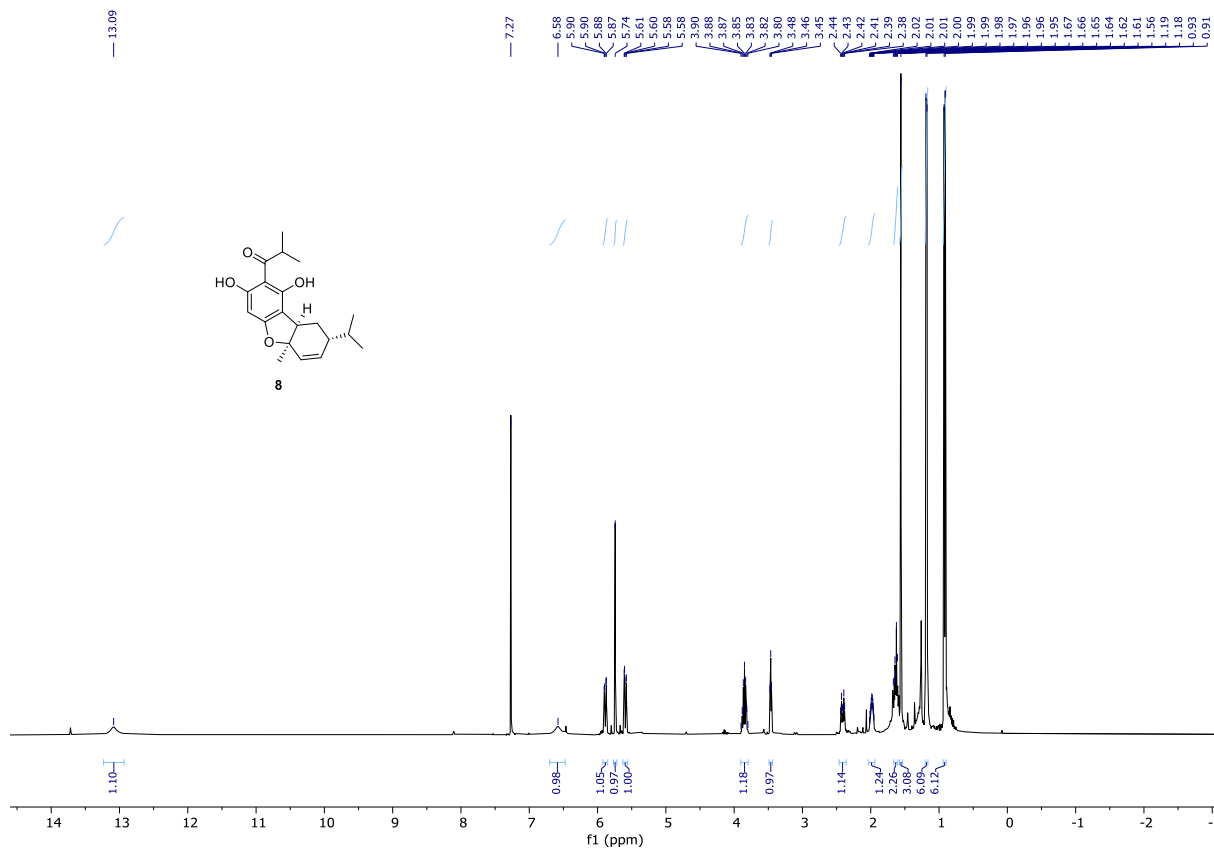


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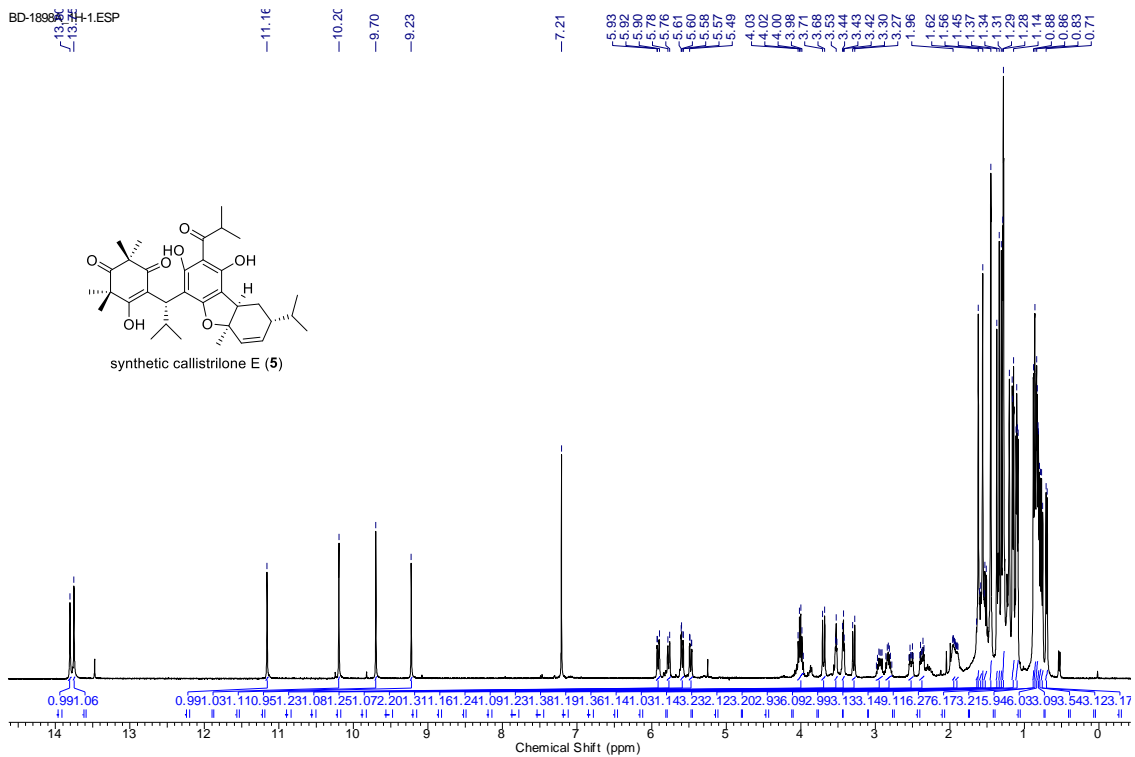


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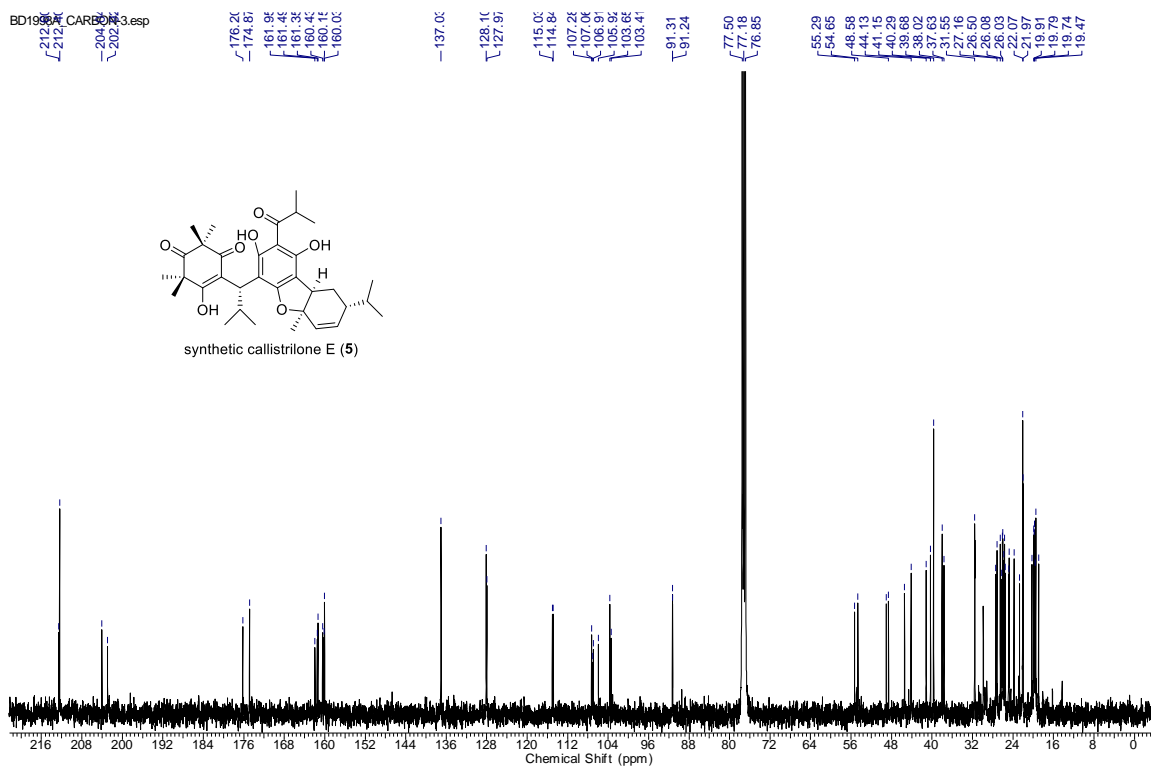




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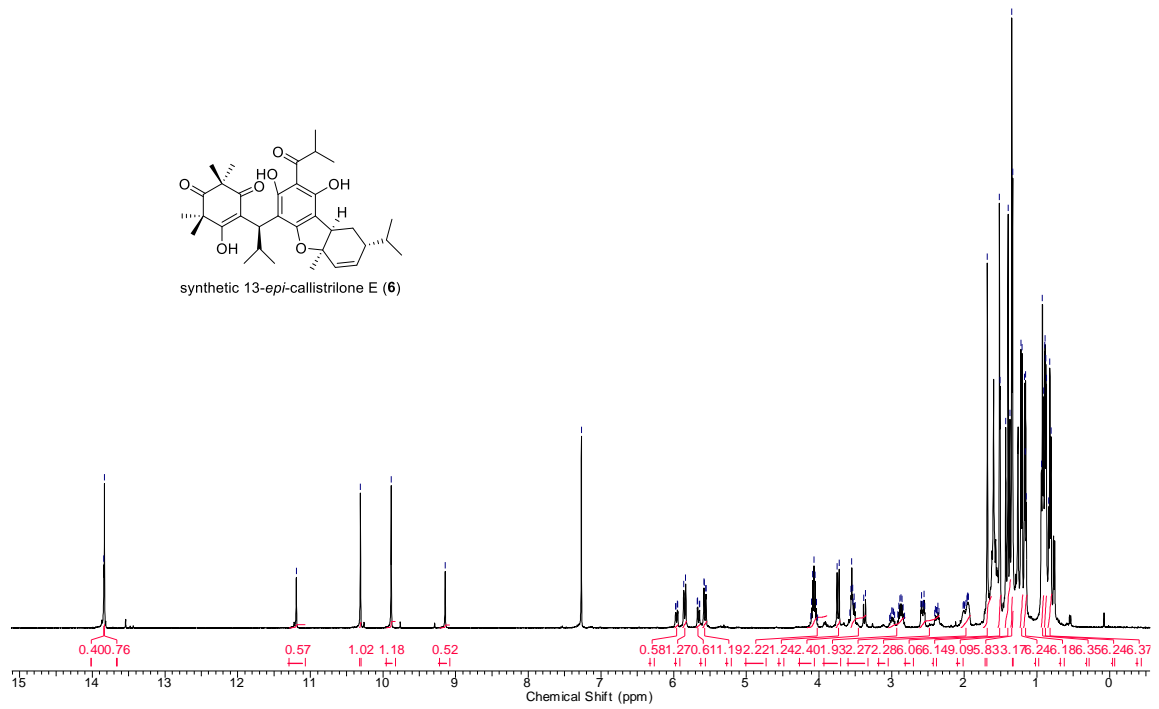
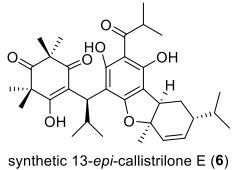




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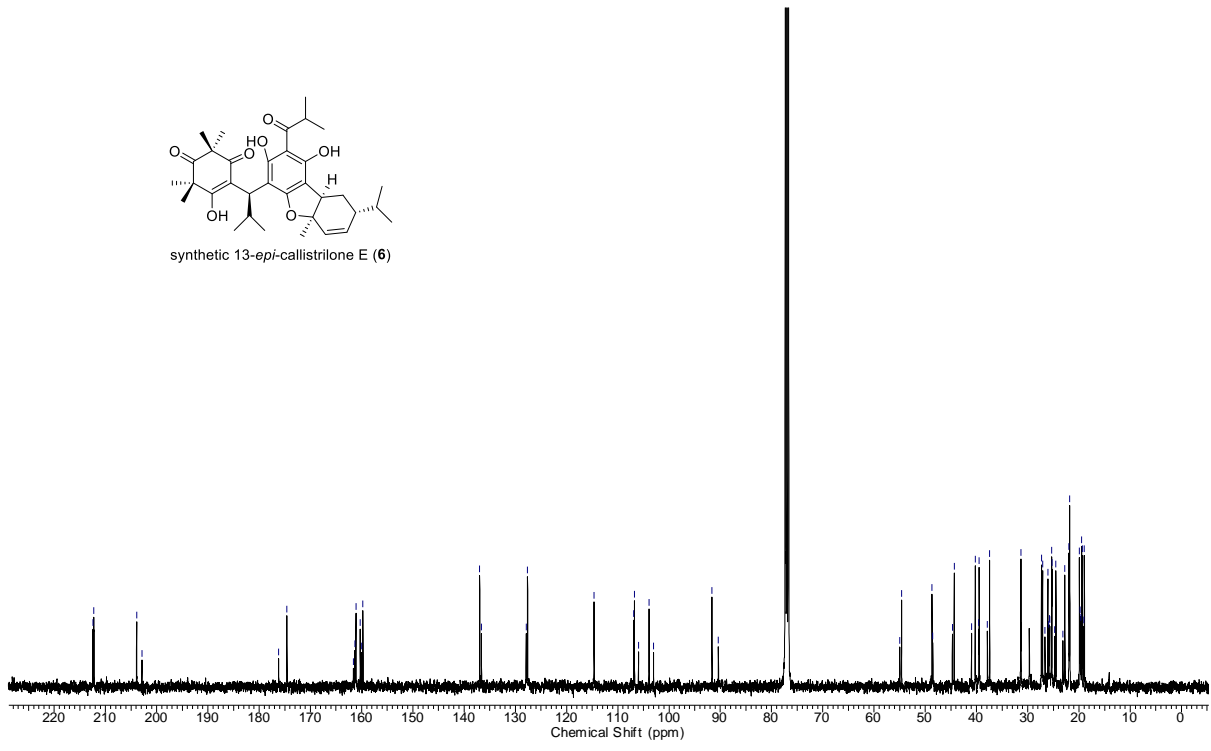
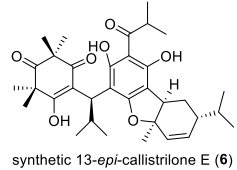
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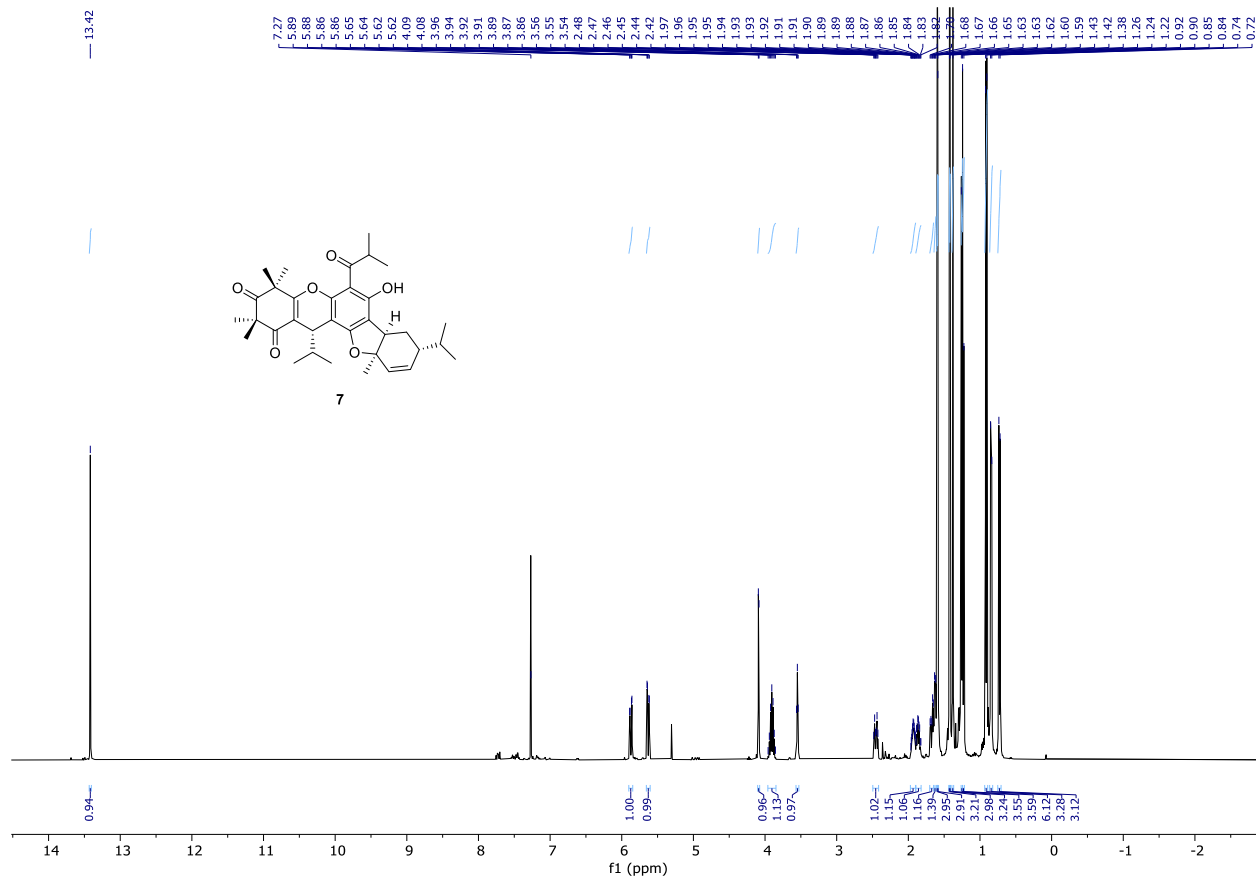
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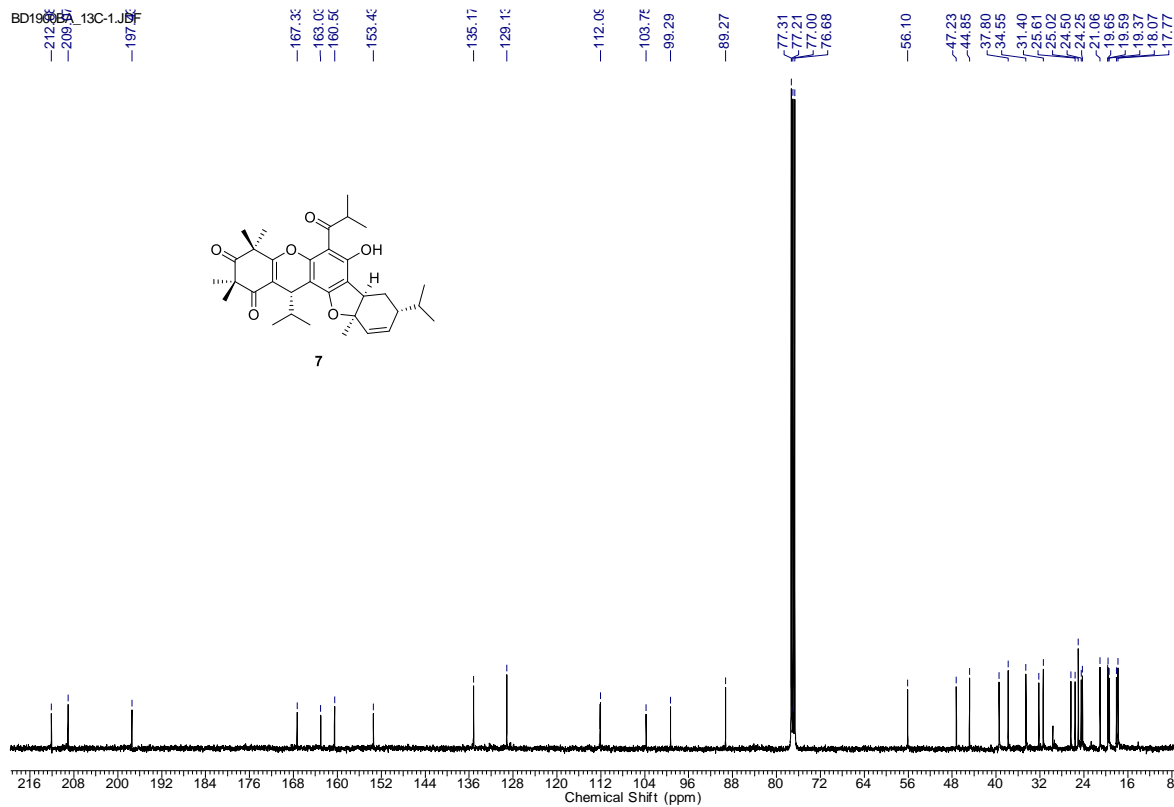
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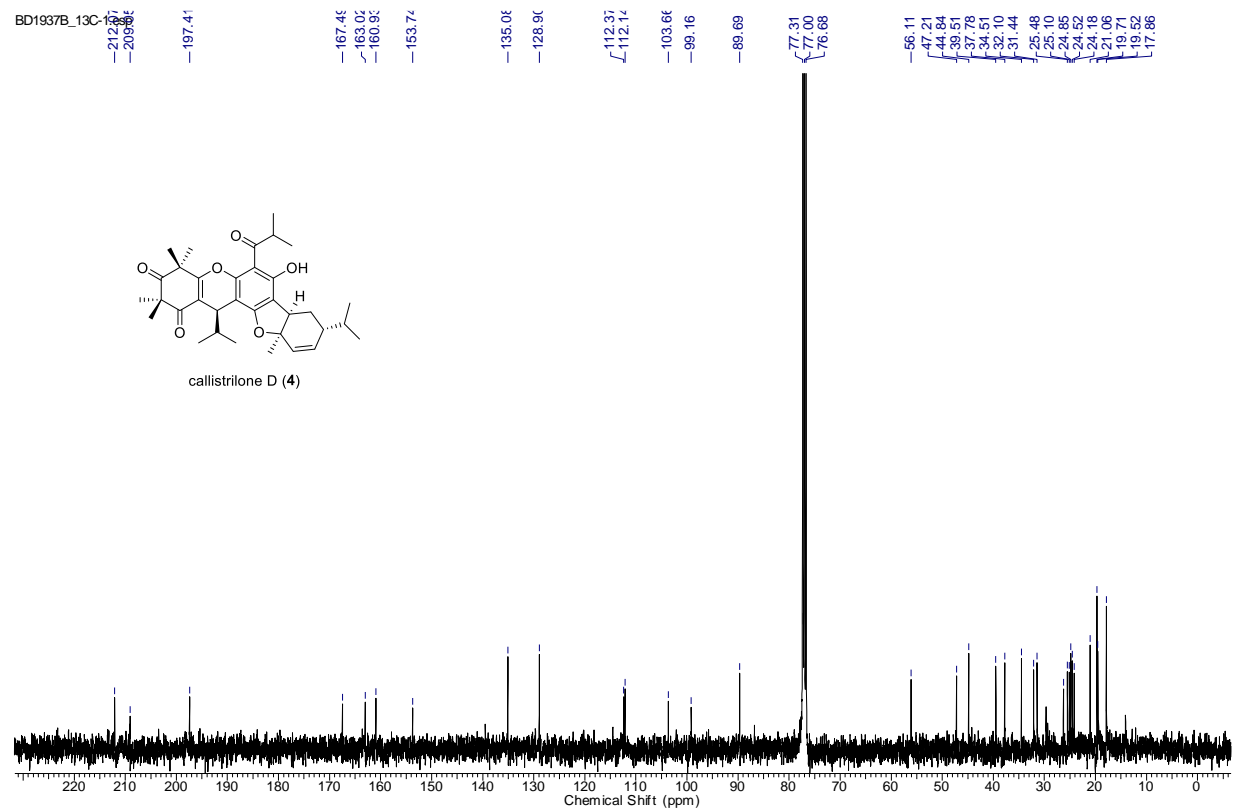
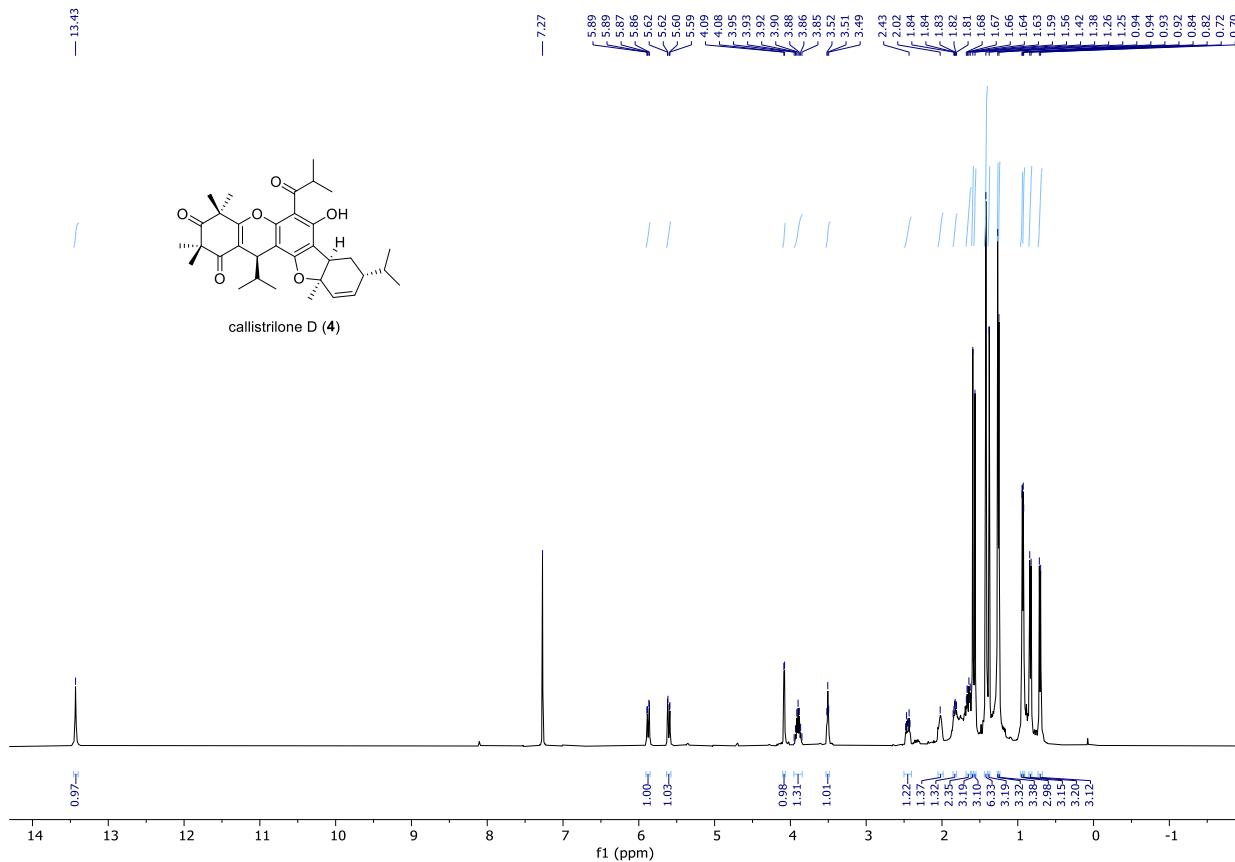
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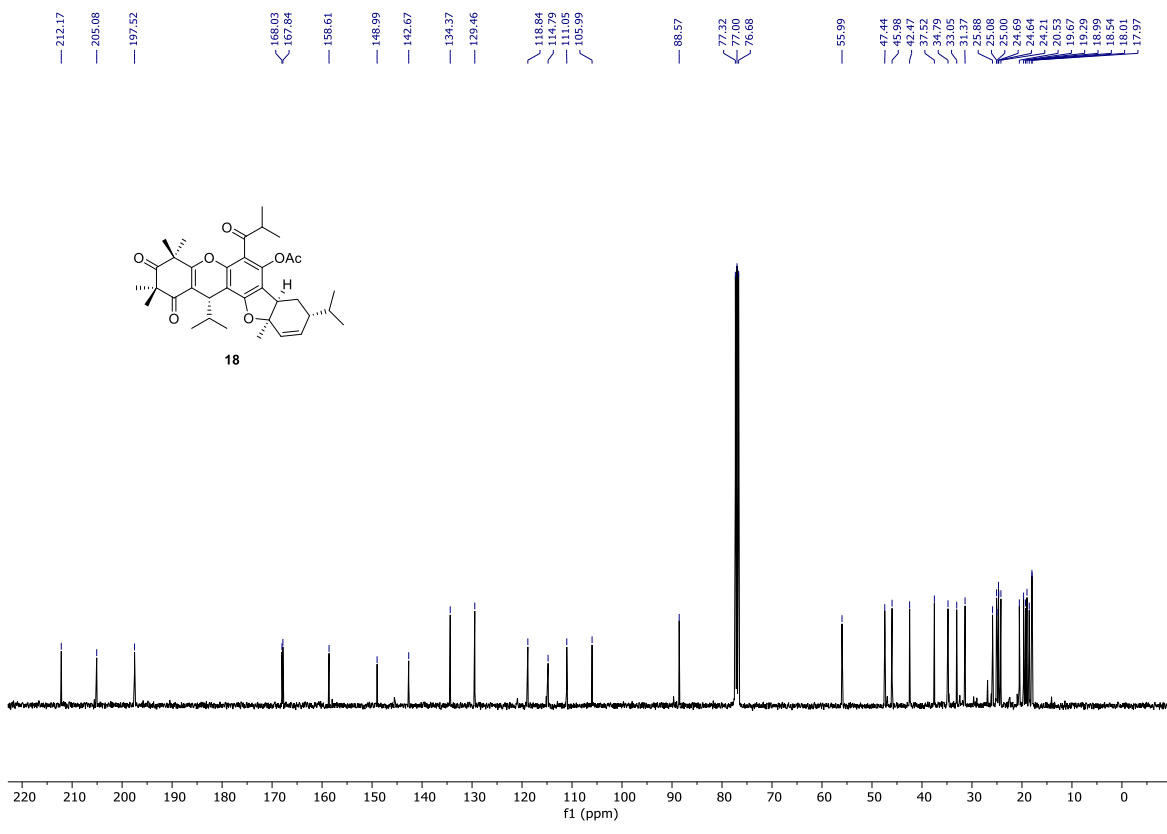
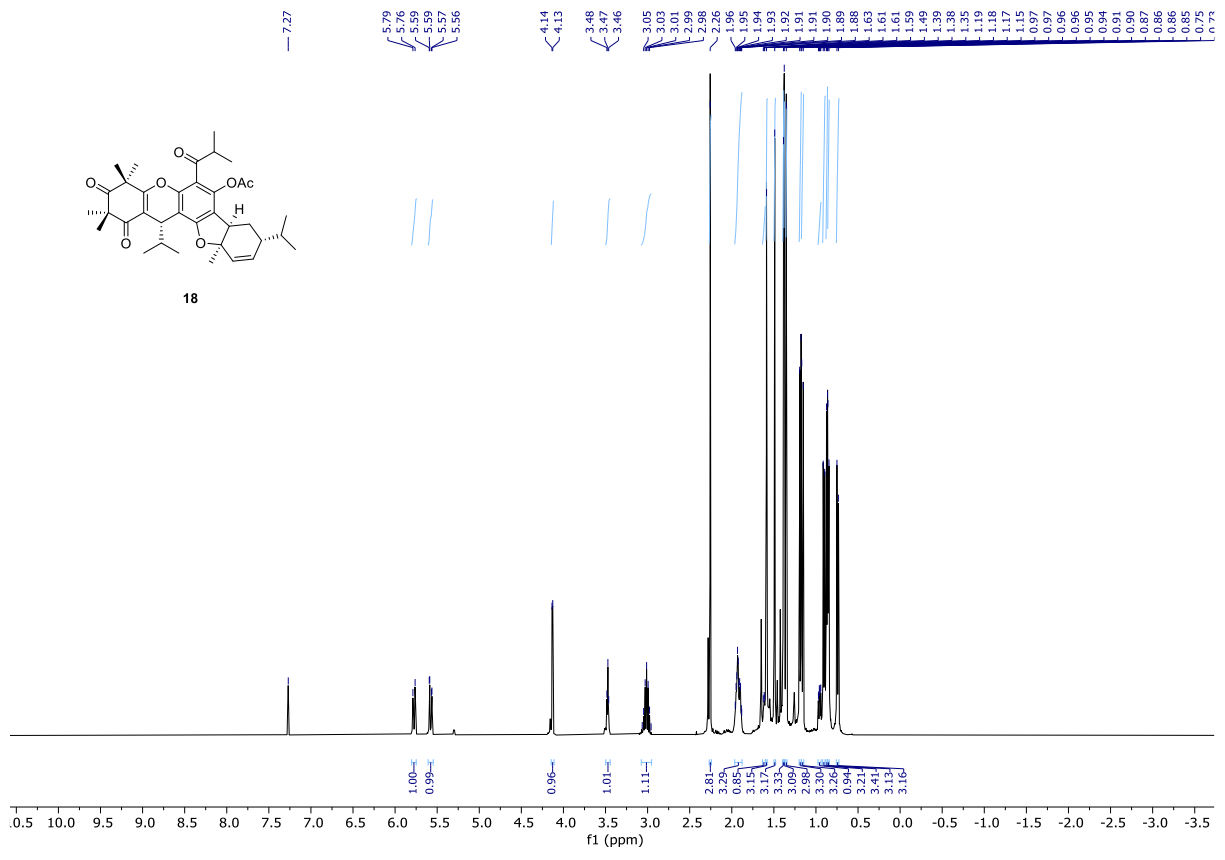


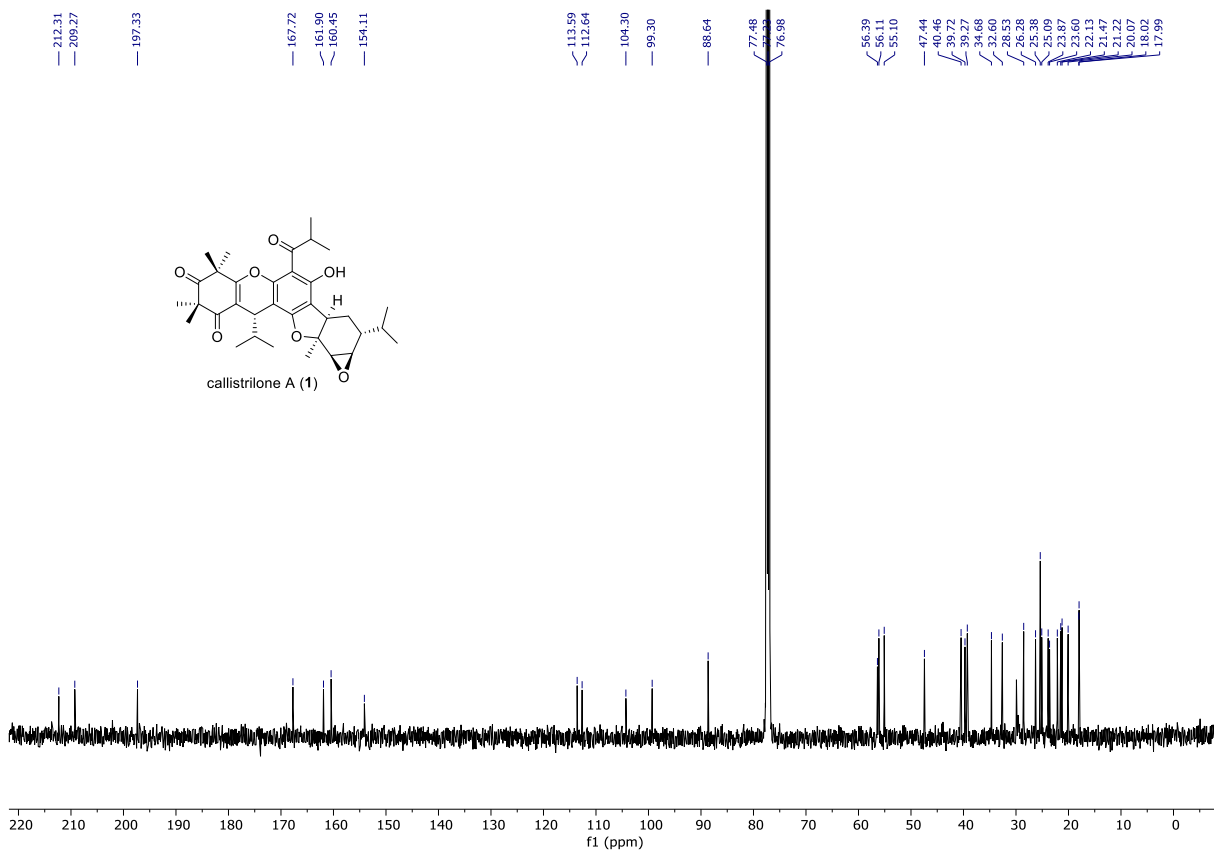
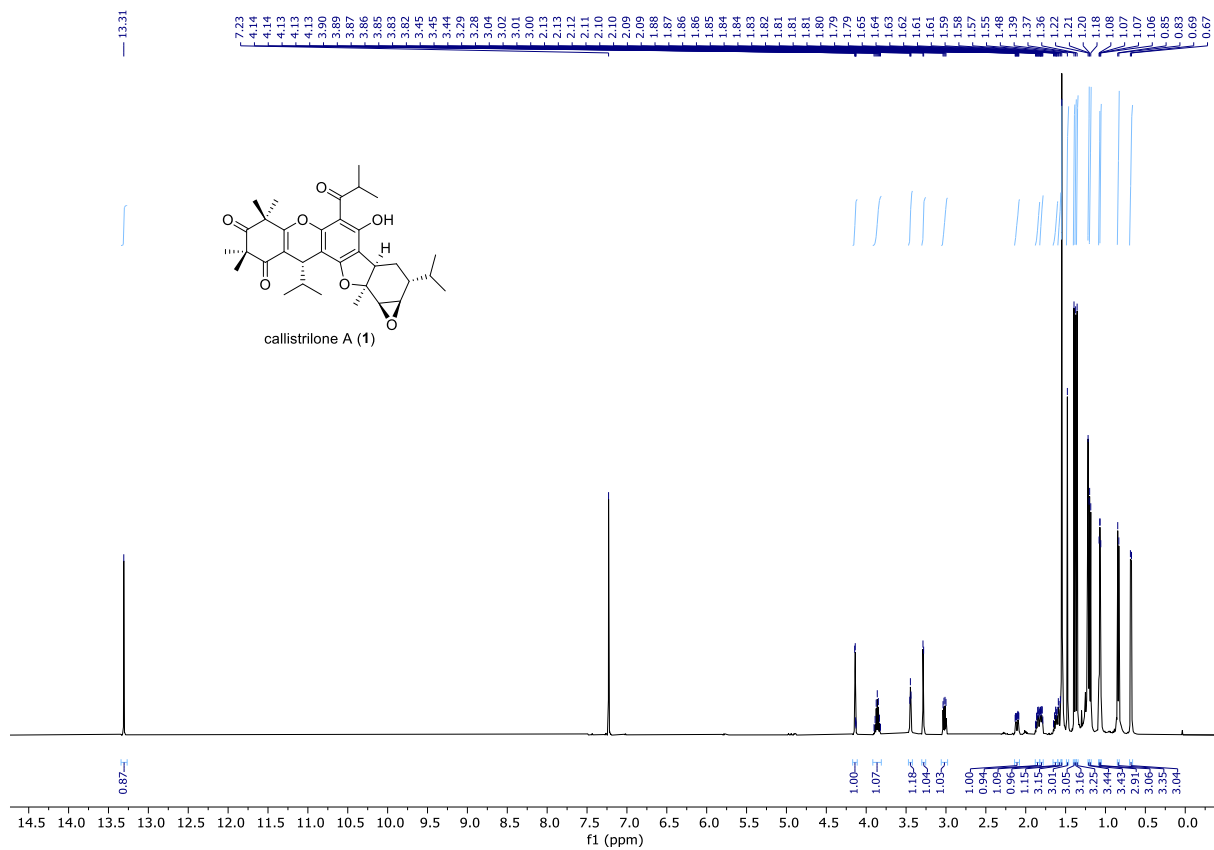


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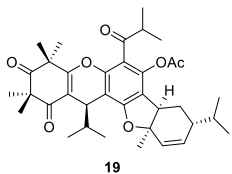
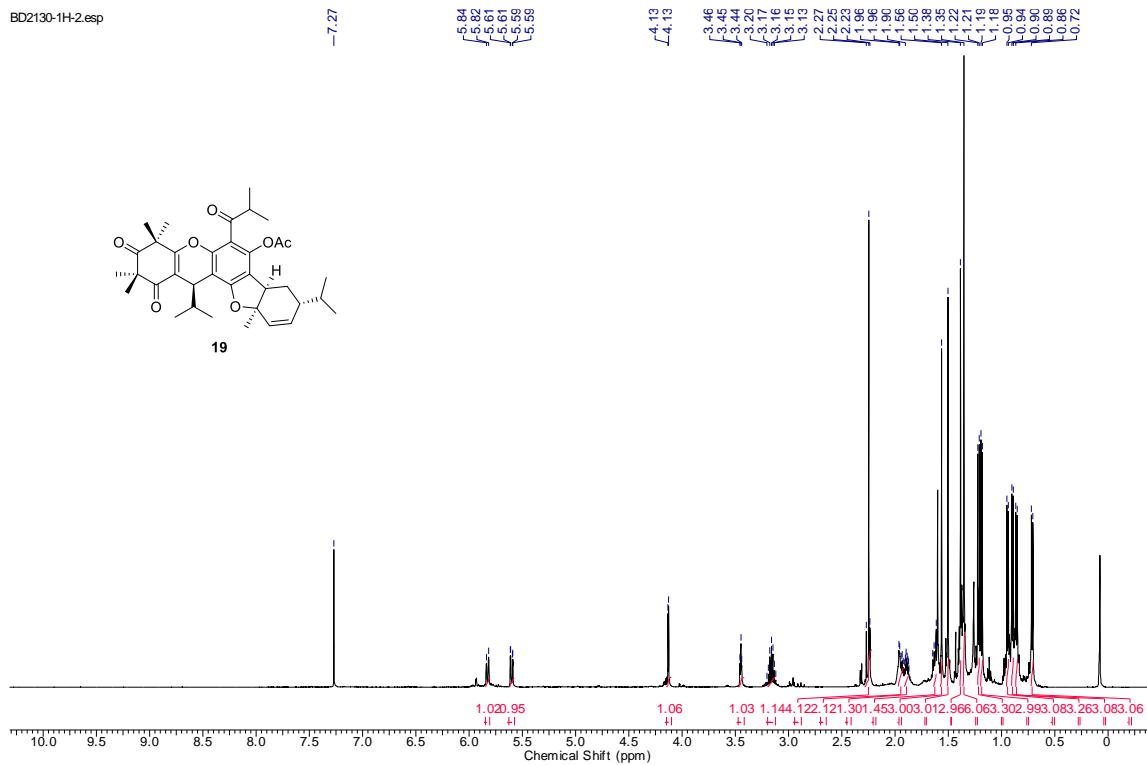




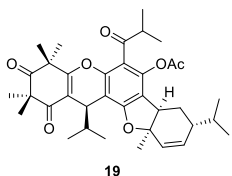
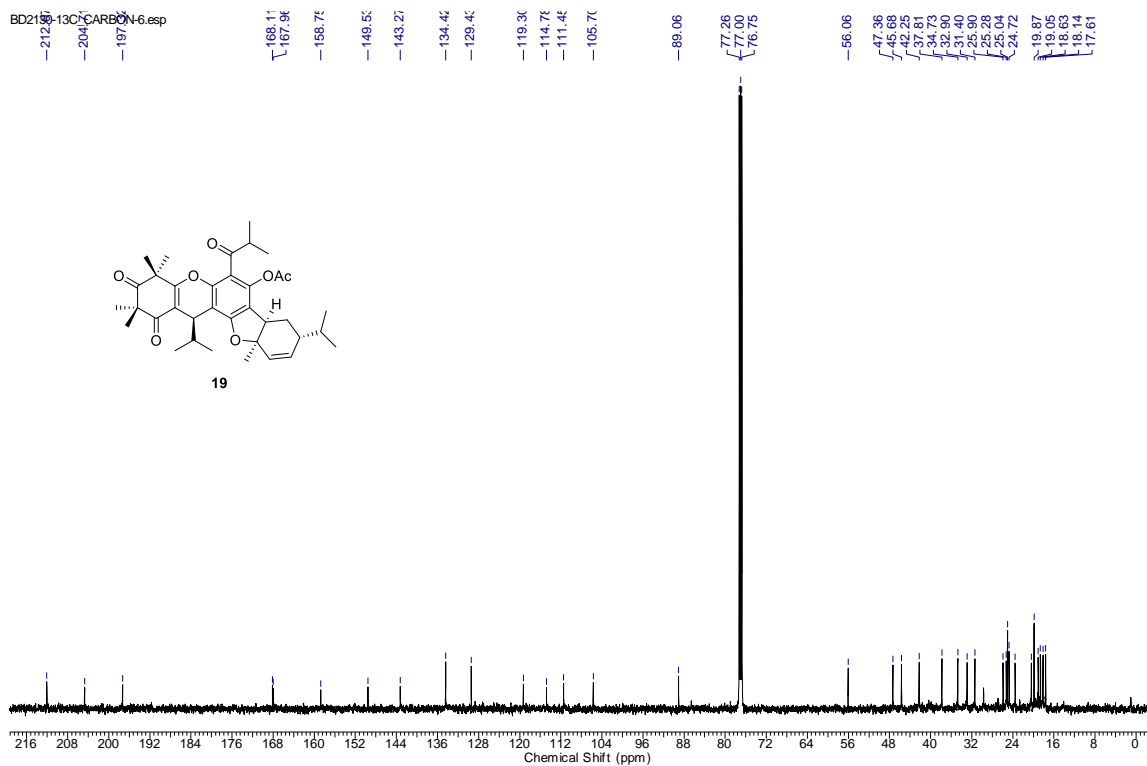




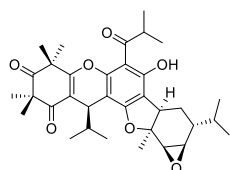
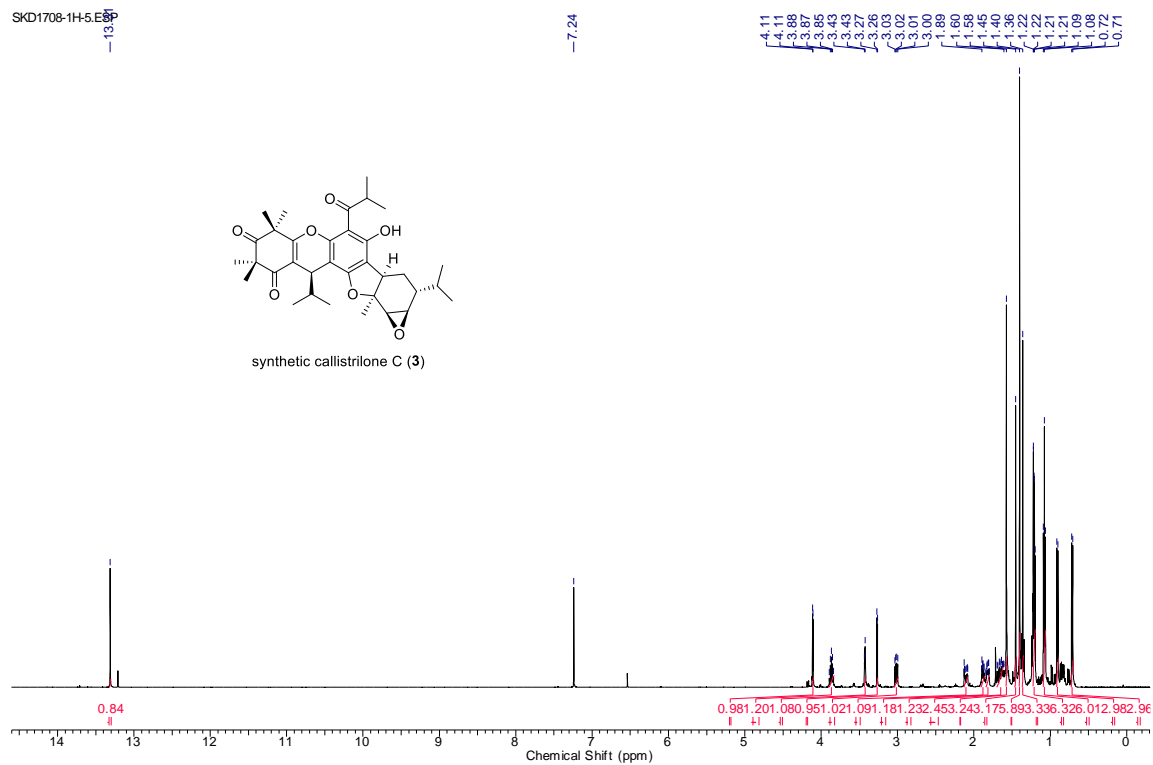
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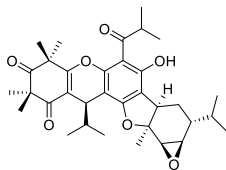
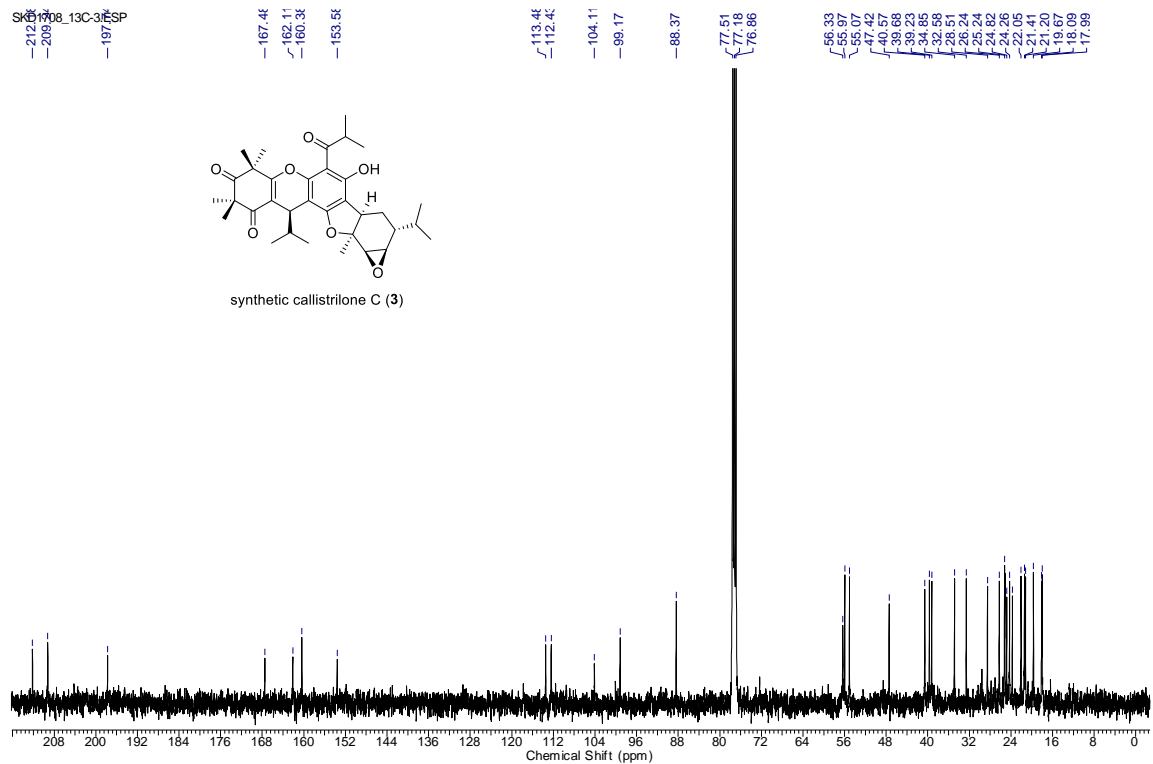


SKD1708-1H-5.E5P



synthetic callistrilone C (3)

SKD1708-13C-3P



synthetic callistrilone C (3)

#### 4. References:

[1] Ardashov, O. V.; Pavlova, A. V.; Il'ina, I.V.; Morozova, E. A.; Korchagina, D. V.; Karpova, E. V.; Volcho, K. P.; Tolstikova, T. G.; Salakhutdinov N. F. *J. Med. Chem.* **2011**, *54*, 3866.