

# Bioinspired Synthesis of Nortriterpenoid Propindilactone G

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## Supporting Information

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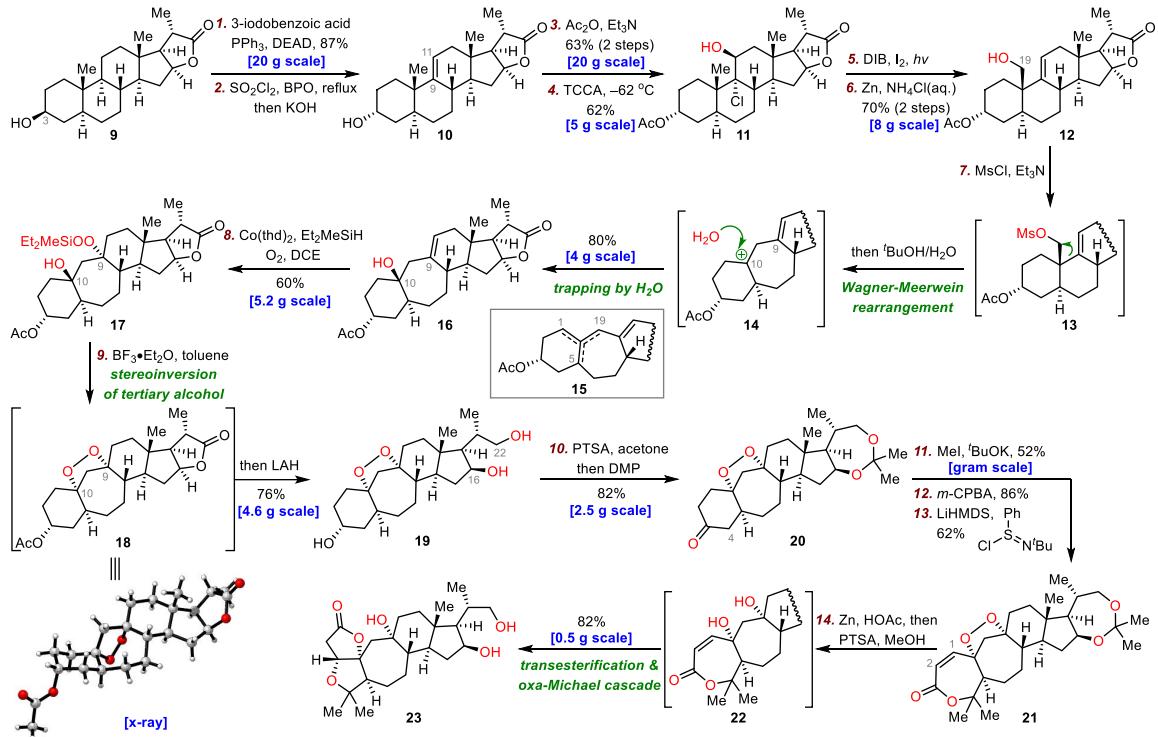
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## **1. General experimental**

All reactions utilizing air- or moisture-sensitive reagents were carried out in flame-dried glassware under an argon atmosphere, unless otherwise stated. Dry tetrahydrofuran (THF), dichloromethane (DCM), toluene (PhMe), diethyl ether (Et<sub>2</sub>O) were obtained by passing the HPLC grade or pre-dried solvents through activated alumina columns. Tetrachloromethane (CCl<sub>4</sub>), 1,2-dichloroethane (DCE), cyclohexane, 'BuOH, triethylamine (Et<sub>3</sub>N) and hexamethylphosphoramide (HMPA) were distilled from CaH<sub>2</sub>. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.15-0.2 mm pre-coated silica gel (10-40 μm) plates, using UV light as the visualizing agent or ethanolic phosphomolybdic acid and heating as developing agents. Flash chromatography was performed with silica gel (200-300 mesh) under pressure. Yields refer to chromatographically and spectroscopically (<sup>1</sup>H NMR) homogeneous material, unless otherwise stated. NMR spectra were recorded on Bruker-400 and Bruker-600 spectrometers. <sup>1</sup>H NMR spectra were calibrated using residual undeuterated solvent as an internal reference (CDCl<sub>3</sub>: 7.26 ppm; MeOH-*d*<sub>4</sub>: 3.31 ppm; C<sub>5</sub>D<sub>5</sub>N: 8.74 ppm) and <sup>13</sup>C NMR spectra were calibrated against the deuterated solvent peak (CDCl<sub>3</sub>: 77.2 ppm; MeOH-*d*<sub>4</sub>: 49.0 ppm; C<sub>5</sub>D<sub>5</sub>N: 150.3 ppm). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were collected on Avatar 330 FT-IR spectrometer. Melting points were determined on SGW X-4 microscopic melting point apparatus and were uncorrected. Optical rotations were determined on JASCO P-1030 Polarimeter in the solvent indicated. High-resolution mass spectra were recorded on IonSpec 4.7 Tesla FTMS or Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS.

## 2. Full synthetic sequence

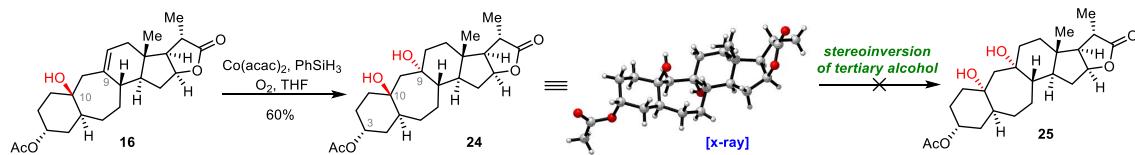
**Scheme S1. Bioinspired Synthesis of Advanced Intermediate Lactone 23**



Reagents and conditions: (1) 3-iodobenzoic acid (1.2 equiv), PPh<sub>3</sub> (1.5 equiv), DEAD (1.5 equiv), THF, 0 °C to rt, 2.5 h, 87%; (2) SO<sub>2</sub>Cl<sub>2</sub> (1.6 equiv), BPO (0.2 equiv), CCl<sub>4</sub>, reflux, 5 h; then KOH (18.5 equiv), MeOH, reflux, 2 h; then 2.4 M HCl (aq.), rt, 0.5 h; (3) Ac<sub>2</sub>O (1.3 equiv), Et<sub>3</sub>N (1.3 equiv), DMAP (0.16 equiv), DCM, rt, 2 h, 63% (2 steps); (4) TCCA (0.8 equiv), diglyme/H<sub>2</sub>O (9/1), -62 °C, 2.5 h, 62%; (5) DIB (3.0 equiv), I<sub>2</sub> (3.0 equiv), cyclohexane, *hν* (275 W), reflux, 4 h; (6) Zn (25.0 equiv), NH<sub>4</sub>Cl (10.0 equiv), sat. NH<sub>4</sub>Cl (aq.), DMF, 140 °C, 4 h, 70% (2 steps); (7) MsCl (2.0 equiv), DMAP (0.2 equiv), Et<sub>3</sub>N (3.0 equiv), DCM, rt, 1 h; then *t*BuOH/H<sub>2</sub>O (1/2), 20 to 30 °C, 24 h, 80%; (8) Et<sub>2</sub>MeSiH (1.5 equiv), Co(thd)<sub>2</sub> (0.2 equiv), O<sub>2</sub>, DCE, rt to 0 °C, 9.5 h, 60%; (9) BF<sub>3</sub>·Et<sub>2</sub>O (0.4 equiv), toluene, 50 °C, 2 h; then NaHCO<sub>3</sub> (0.5 equiv); then LiAlH<sub>4</sub> (5.0 equiv), THF, 0 °C to rt, 70 min, 76%; (10) 2,2-dimethoxypropane (18.0 equiv), PTSA (0.25 equiv), acetone, rt, 0.5 h; then Et<sub>3</sub>N (2.0 equiv); then DMP (2.5 equiv), NaHCO<sub>3</sub> (5.0 equiv), DCM, rt, 1 h, 82%; (11) *t*BuOK (8.5 equiv), MeI (8.5 equiv), *t*BuOH/cyclohexane/HMPA (2.8/2.2/1), 0 °C, 125 min, 52%; (12) *m*-CPBA (4.0 equiv), NaHCO<sub>3</sub> (6.3 equiv), toluene, rt, 5 h, 86%; (13) LiHMDS (1.4 equiv), *N*-*tert*-butyl phenylsulfinimidoyl chloride (1.4 equiv), THF, -78 °C to 0 °C, 80 min, 62%; (14) Zn (6.0 equiv), AcOH (6.0 equiv), DCM, rt, 22 h; then PTSA (15.0 equiv), MeOH, rt, 50 min, 82%. Abbreviations: DEAD = diethyl azodicarboxylate; THF = tetrahydrofuran; BPO = benzoyl peroxide; DMAP = 4-dimethylaminopyridine; DCM = dichloromethane; TCCA = trichloroisocyanuric acid; DIB = (diacetoxyiodo)benzene; DMF = *N,N*-dimethylformamide; thd = 2,2,6,6-tetramethyl-3,5-heptanedionato; DCE = 1,2-dichloroethane; LAH = lithium aluminum hydride; PTSA = *p*-toluenesulfonic acid; DMP = Dess-Martin periodinane; HMPA = hexamethylphosphoramide; *m*-

CPBA = *meta*-chloroperbenzoic acid; LHMDS = lithium *bis*(trimethylsilyl)amide.

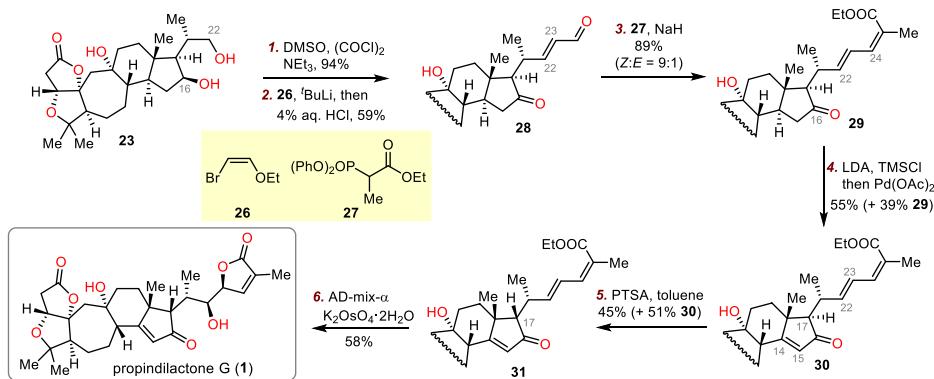
### Scheme S2. Mukaiyama Hydration of Homoallylic Alcohol 16



Reagents and conditions:  $\text{Co}(\text{acac})_2$  (0.3 equiv),  $\text{PhSiH}_3$  (4.0 equiv),  $\text{O}_2$  (1 atm), THF, rt, 5 h, 60%.

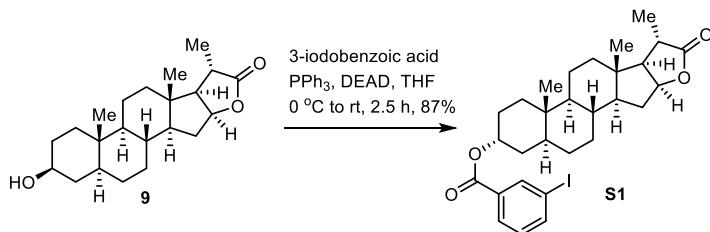
Abbreviation: acac = acetylacetone.

### Scheme S3. Completion of the Synthesis of Propindilactone G (1)



Reagents and conditions: (1)  $(\text{COCl})_2$  (5.0 equiv),  $\text{DMSO}$  (7.5 equiv),  $\text{Et}_3\text{N}$  (12.0 equiv),  $\text{DCM}$ ,  $-78^\circ\text{C}$  to  $0^\circ\text{C}$ , 3 h, 94%; (2) **26** (3.5 equiv),  ${}^t\text{BuLi}$  (7.0 equiv),  $\text{Et}_2\text{O}/\text{THF}$  (3.5/1),  $-78^\circ\text{C}$ , 110 min; then 4%  $\text{HCl}$  (aq.),  $\text{H}_2\text{O}$ , rt, 0.5 h, 59%; (3) **27** (2.5 equiv),  $\text{NaH}$  (2.8 equiv),  $\text{THF}$ ,  $0^\circ\text{C}$  to  $-78^\circ\text{C}$ , 2.5 h, 89% ( $Z:E = 9:1$ ); (4)  $\text{LDA}$  (3.0 equiv),  $\text{TMSCl}$  (4.0 equiv),  $\text{DME}/\text{THF}$  (8/1),  $-78^\circ\text{C}$ , 2 h; then  $\text{Pd}(\text{OAc})_2$  (1.0 equiv),  $\text{DMSO}$ ,  $50^\circ\text{C}$ , 1 h, 55% **30** + 39% **29**; (5)  $\text{PTSA}$  (0.2 equiv),  $\text{toluene}$ ,  $80^\circ\text{C}$ , 1 h, 45% **31** + 51% **30**; (6)  $\text{AD}-\text{mix-}\alpha$  (1.0 equiv),  $\text{MeSO}_2\text{NH}_2$  (1.0 equiv),  $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$  (0.03 equiv),  ${}^t\text{BuOH}/\text{H}_2\text{O}$  (1/1), rt to  $0^\circ\text{C}$ , 22.5 h, 58%. Abbreviations: DMSO = dimethylsulfoxide; LDA = lithium diisopropylamide; TMS = trimethylsilyl; DME = 1,2-dimethoxyethane.

### 3. Experimental procedures and characterization data for compounds 10-31.



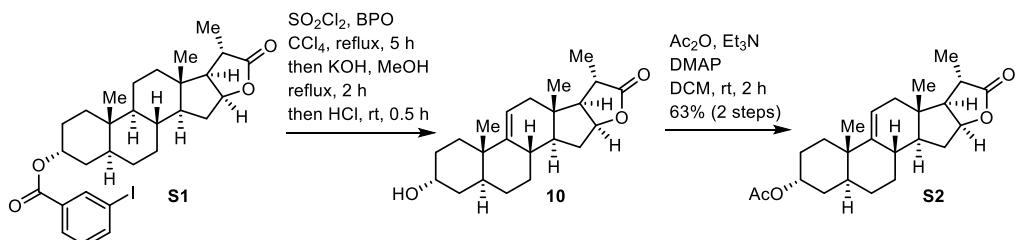
Compound **9** was synthesized from commercially available tigogenin (CAS: 77-60-1) according to a procedure reported by Tian and co-workers.<sup>1</sup>

To a solution of **9** (20.0 g, 57.8 mmol, 1.0 equiv), 3-iodobenzoic acid (17.2 g, 69.4 mmol, 1.2 equiv) and  $\text{PPh}_3$  (22.8 g, 86.7 mmol, 1.5 equiv) in 300 mL dry  $\text{THF}$  was added  $\text{DEAD}$  (13.6 mL, 86.7 mmol, 1.5 equiv) dropwise at  $0\text{ }^\circ\text{C}$ . The reaction mixture was stirred at room temperature for 2.5 h and quenched by 10 mL  $\text{H}_2\text{O}$ .  $\text{THF}$  was removed under reduced pressure and the resulting mixture was treated with 260 mL  $\text{EtOH}$ . Stirring was continued for 2.5 h at room temperature to afford a suspension which was filtered, washed with 100 mL  $\text{EtOH}$  twice. The filter cake was dried using an infrared lamp to afford compound **S1** (20.0 g, 60%) as a white solid, which is sufficiently pure for direct use in the next step.

The mother liquor was concentrated under reduced pressure to give a brown oil, which was dissolved in 300 mL  $\text{EtOAc}$ , and filtered to remove diethyl hydrazodicarboxylate. Then  $\text{ZnCl}_2$  (15.0 g, 110.0 mmol, 1.9 equiv) was added to the filtrate to give a suspension, which was filtered to remove another by-product triphenylphosphine oxide. The mother liquor was concentrated under reduced pressure and purification by flash chromatography ( $\text{SiO}_2$ , 5:5:1 DCM:petroleum ether: $\text{EtOAc}$ ) provided compound **S1** (9.0 g, 27%) as a white solid.

**Compound S1:** mp: 192.1 – 194.4 °C; TLC (petroleum ether: $\text{EtOAc}$ , 2:1 v/v):  $R_f$  = 0.85;  $[\alpha]_D^{30} -16.3$  (*c* 1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.34 (t, *J* = 1.7 Hz, 1H), 8.00 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.87 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 5.28 – 5.21 (m, 1H), 4.93 (td, *J* = 7.8, 4.6 Hz, 1H), 2.57 (q, *J* = 7.6 Hz, 1H), 2.26 (dt, *J* = 13.9, 7.3 Hz, 1H), 1.89 – 1.81 (m, 2H), 1.80 – 1.63 (m, 4H), 1.62 – 1.43 (m,

7H), 1.37 – 1.18 (m, 4H), 1.30 (d,  $J$  = 7.6 Hz, 3H), 1.17 – 1.05 (m, 2H), 1.03 – 0.90 (m, 1H), 0.84 (s, 3H), 0.74 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  181.4, 164.5, 141.7, 138.5, 133.1, 130.1, 128.8, 93.9, 82.9, 71.4, 59.2, 54.7, 54.4, 41.8, 40.5, 38.4, 36.2, 36.1, 35.0, 33.2, 33.1, 32.9, 32.1, 28.2, 26.3, 20.3, 18.1, 14.0, 11.5; IR (KBr):  $\nu$  = 2932, 2853, 1769, 1714, 1263, 1182, 973, 747  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+H] $^+$  calcd for  $\text{C}_{29}\text{H}_{38}\text{IO}_4$ , 577.1809; found, 577.1800.



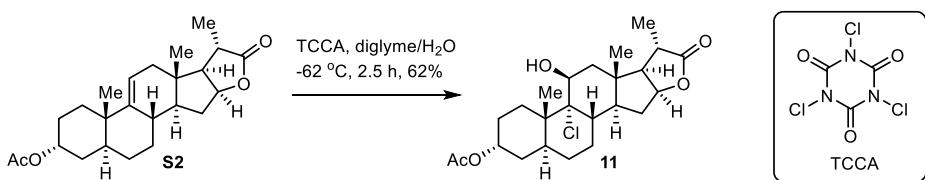
To a solution of **S1** (20.0 g, 34.7 mmol, 1.0 equiv) and BPO (1.7 g, 6.9 mmol, 0.2 equiv) in 700 mL dry  $\text{CCl}_4$  was added  $\text{SO}_2\text{Cl}_2$  (4.5 mL, 55.6 mmol, 1.6 equiv) under argon. The solution was refluxed for 5 h before cooled to room temperature, and concentration under reduced pressure afforded a yellow foam. The crude mixture was dissolved in 300 mL MeOH and a solution of KOH (36.0 g, 642.9 mmol, 18.5 equiv) in 300 mL MeOH was added. The reaction mixture was refluxed for 2 h before cooled to room temperature. Concentration under reduced pressure afforded the crude reaction mixture which was neutralized with aq. HCl (2.4 M, 300 mL) to pH 2-3. Stirring was continued for 0.5 h at room temperature and the reaction mixture was extracted with EtOAc ( $2 \times 150$  mL). The combined organic layers were washed successively with sat. aq.  $\text{NaHCO}_3$  ( $2 \times 200$  mL),  $\text{H}_2\text{O}$  (200 mL), brine (50 mL) and dried over  $\text{Na}_2\text{SO}_4$ . Removal of the solvent under reduced pressure afforded the crude product **10** which was used in the next step without further purification.

To a solution of the crude **10** obtained above in 150 mL dry DCM was added DMAP (690.0 mg, 5.7 mmol, 0.16 equiv),  $\text{Et}_3\text{N}$  (6.3 mL, 45.3 mmol, 1.3 equiv) and  $\text{Ac}_2\text{O}$  (4.3 mL, 45.3 mmol, 1.3 equiv) at room temperature. After stirred at this temperature for 2 h, the reaction mixture was quenched with  $\text{H}_2\text{O}$  (50 mL) and extracted with DCM

(3×100 mL). The combined organic layers were washed successively with sat. aq. NaHCO<sub>3</sub> (200 mL), H<sub>2</sub>O (200 mL), brine (200 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The resulting residue was treated with a mixed solvent of petroleum ether and <sup>i</sup>BuOH (35 mL, 3:1, v/v). The suspension was stirred at room temperature for 2 h, filtered, and the filter cake was washed with petroleum ether and <sup>i</sup>BuOH (30 mL, 3:1, v/v). The residue was dried using an infrared lamp to afford **S2** (8.5 g, 63% over 2 steps) as a light yellow solid, which was sufficiently pure for direct use in the next step.

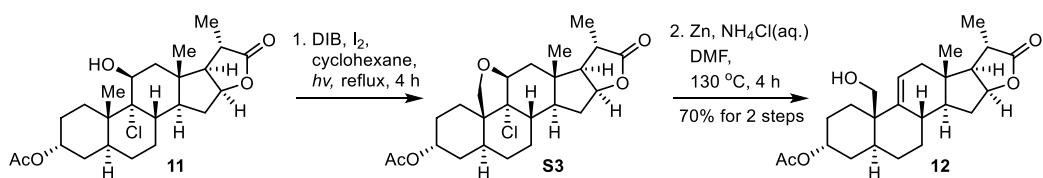
**Compound 10:** mp: 214.0 – 216.0 °C; TLC (petroleum ether:EtOAc, 2:1 v/v): *R<sub>f</sub>* = 0.31; [α]<sub>D</sub><sup>30</sup> –30.4 (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.29 (d, *J* = 5.8 Hz, 1H), 4.95 (td, *J* = 7.7, 4.4 Hz, 1H), 4.04 – 4.00 (m, 1H), 2.61 (q, *J* = 7.6 Hz, 1H), 2.37 (dt, *J* = 14.3, 7.5 Hz, 1H), 2.13 – 2.04 (m, 1H), 2.02 – 1.95 (m, 1H), 1.95 – 1.84 (m, 3H), 1.75 – 1.67 (m, 2H), 1.65 – 1.54 (m, 2H), 1.54 – 1.35 (m, 5H), 1.34 – 1.21 (m, 3H), 1.29 (d, *J* = 7.6 Hz, 3H), 1.06 – 0.96 (m, 1H), 0.88 (s, 3H), 0.66 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 181.3, 147.5, 114.7, 83.2, 66.3, 58.8, 52.4, 40.3, 40.0, 38.5, 37.7, 36.5, 36.0 (2C), 34.1, 33.2, 30.7, 29.1, 28.2, 17.9, 16.9, 13.4; IR (KBr): ν = 3521, 2917, 2856, 1754, 1196, 1004, 963, 918 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>Na, 367.2244; found, 367.2240.

**Compound S2:** mp: 121.1 – 123.5 °C; TLC (petroleum ether:EtOAc, 2:1 v/v): *R<sub>f</sub>* = 0.88; [α]<sub>D</sub><sup>27</sup> –14.6 (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.30 (d, *J* = 5.8 Hz, 1H), 5.02 – 4.93 (m, 2H), 2.62 (q, *J* = 7.6 Hz, 1H), 2.39 (dt, *J* = 14.0, 7.4 Hz, 1H), 2.15 – 2.06 (m, 1H), 2.05 – 1.97 (m, 1H), 2.00 (s, 3H), 1.96 – 1.87 (m, 3H), 1.86 – 1.78 (m, 1H), 1.76 – 1.59 (m, 2H), 1.57 – 1.45 (m, 5H), 1.37 – 1.25 (m, 3H), 1.30 (d, *J* = 7.6 Hz, 3H), 1.00 (qd, *J* = 12.8, 4.9 Hz, 1H), 0.91 (s, 3H), 0.67 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 181.2, 170.7, 147.5, 114.9, 83.1, 69.9, 58.9, 52.4, 40.4, 40.0, 38.7, 38.3, 36.5, 36.1, 34.1, 33.14, 33.11, 31.5, 28.0, 26.3, 21.6, 17.9, 17.1, 13.4; IR (KBr): ν = 2933, 2873, 1768, 1723, 1240, 1182, 1025, 968 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>35</sub>O<sub>4</sub>, 387.2530; found, 387.2532.



To a solution of **S2** (5.0 g, 13.0 mmol, 1.0 equiv) in diglyme (diethylene glycol dimethyl ether)/H<sub>2</sub>O (600 mL, 9:1, v/v) was added a solution of TCCA (2.5 g, 10.7 mmol, 0.8 equiv) in 5 mL diglyme at -62 °C. After stirred at the same temperature for 2.5 h, the reaction mixture was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (40 mL) and warmed to room temperature. Stirring was continued for another 10 h until the solution became clear. The reaction mixture was extracted with EtOAc (3×200 mL) and the combined organic layers were washed with aq. NaCl (sat. aq. NaCl/H<sub>2</sub>O, 1:1, 3×200 mL) and brine. Concentration under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO<sub>2</sub>, 7:7:1 petroleum ether:DCM:EtOAc) to provide compound **11** (3.6 g, 62%) as a white solid.

**Compound 11:** mp: 180.9 – 184.1 °C; TLC (petroleum ether:acetone, 4:1 v/v): *R*<sub>f</sub> = 0.37; [α]<sub>D</sub><sup>27</sup> -7.4 (*c* 0.65, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.00 – 4.90 (m, 2H), 4.41 – 4.37 (m, 1H), 2.58 (q, *J* = 7.6 Hz, 1H), 2.53 – 2.41 (m, 2H), 2.28 – 2.20 (m, 1H), 2.19 – 2.09 (m, 1H), 2.05 (s, 3H), 1.94 (d, *J* = 7.8 Hz, 1H), 1.92 – 1.84 (m, 1H), 1.82 – 1.73 (m, 3H), 1.72 – 1.67 (m, 1H), 1.66 – 1.59 (m, 1H), 1.58 – 1.47 (m, 4H), 1.46 – 1.35 (m, 2H), 1.30 (d, *J* = 7.6 Hz, 3H), 1.27 (s, 3H), 1.26 – 1.19 (m, 2H), 0.99 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 181.5, 170.9, 91.2, 82.5, 73.7, 69.5, 59.2, 48.2, 43.1, 42.2, 41.3, 36.1, 35.3, 33.0, 32.5, 32.4, 27.4, 27.2, 26.7, 25.7, 21.6, 18.1, 17.6, 16.5; IR (KBr): ν = 3463, 2936, 2879, 1748, 1730, 1265, 1027, 736 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>36</sub>ClO<sub>5</sub>, 439.2246; found, 439.2252.



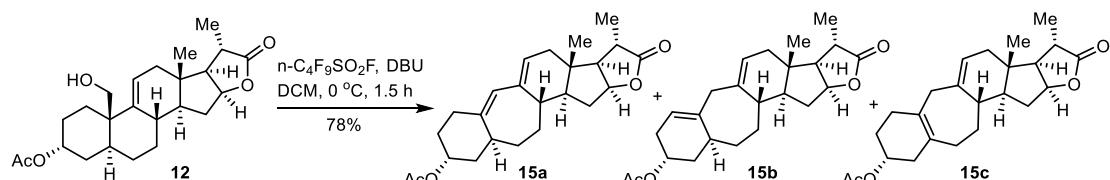
To a solution of **11** (8.0 g, 18.2 mmol, 1.0 equiv) and DIB (11.7 g, 36.4 mmol, 2.0 equiv) in 800 mL dry cyclohexane was added I<sub>2</sub> (9.2 g, 36.4 mmol, 2.0 equiv). The reaction mixture was heated to reflux by irradiation with an infrared lamp (275 W) for 2 h. Another portion of DIB (5.9 g, 18.2 mmol, 1.0 equiv) and I<sub>2</sub> (4.6 g, 18.2 mmol, 1.0 equiv) was added and stirring was continued for another 2 h under the same condition. The reaction mixture was cooled to room temperature, quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (100 mL), and extracted with EtOAc (3×200 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO<sub>2</sub>, 13:5:1→3:1:1 petroleum ether:DCM:EtOAc) to provide crude **S3** (7.5 g).

To a solution of **S3** (7.5 g, 17.2 mmol, 1.0 equiv) in 113 mL DMF and 47 mL sat. aq. NH<sub>4</sub>Cl was added zinc powder (16.7 g, 257.4 mmol, 15.0 equiv) and NH<sub>4</sub>Cl<sub>(s)</sub> (9.2 g, 171.6 mmol, 10.0 equiv). After the reaction mixture was refluxed at 140 °C for 2 h, another portion of zinc powder (11.1 g, 171.6 mmol, 10.0 equiv) and 47 mL sat. aq. NH<sub>4</sub>Cl was added. After stirred for 2 h under the same condition, the reaction mixture was cooled to room temperature and filtered through celite. The filtrate was extracted with EtOAc (3 × 200 mL) and the combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO<sub>2</sub>, 11:3:1→3:2:1 petroleum ether:DCM:EtOAc) to provide **12** (5.1 g, 70% for 2 steps) as a white solid.

**Compound S3:** mp: 251.3 – 255.6 °C; TLC (petroleum ether:acetone, 4:1 v/v): *R<sub>f</sub>* = 0.41; [α]<sub>D</sub><sup>27</sup> -10.3 (*c* 0.54, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.03 – 4.09 (m, 1H), 4.97 (td, *J* = 7.8, 4.7 Hz, 1H), 4.19 (t, *J* = 3.0 Hz, 1H), 3.94 (dd, *J* = 8.7, 1.9 Hz, 1H), 3.88 (d, *J* = 8.7 Hz, 1H), 2.63 (q, *J* = 7.6 Hz, 1H), 2.20 (dt, *J* = 14.0, 7.2 Hz, 1H), 2.07 (s, 3H), 2.05 (d, *J* = 1.9 Hz, 1H), 2.01 (d, *J* = 2.2 Hz, 1H), 1.97 – 1.85 (m, 4H), 1.74 (dt, *J* = 15.0, 2.7 Hz, 1H), 1.70 – 1.63 (m, 2H), 1.62 – 1.43 (m, 6H), 1.31 (d, *J* = 7.6 Hz, 3H), 1.35 – 1.23 (m, 1H), 1.17 (td, *J* = 14.2, 2.8 Hz, 1H), 0.94 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 181.0, 170.7, 82.6, 80.3, 78.1, 68.9, 67.7, 59.4, 49.1, 45.8, 42.9, 38.5,

36.9, 36.3, 35.0, 32.1, 31.9, 30.2, 27.6, 26.6, 24.0, 21.6, 18.1, 16.3; IR (KBr):  $\nu$  = 2938, 2882, 1761, 1738, 1256, 1235, 947, 735  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>34</sub>ClO<sub>5</sub>, 437.2089; found, 437.2090.

**Compound 12:** mp: 195.3 – 197.7 °C; TLC (petroleum ether:EtOAc, 1:1 v/v):  $R_f$  = 0.35;  $[\alpha]_D^{27}$  –10.4 ( $c$  0.73, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.47 (d,  $J$  = 5.3 Hz, 1H), 5.11 – 5.03 (m, 1H), 4.99 (td,  $J$  = 7.7, 4.3 Hz, 1H), 3.73 – 3.63 (m, 2H), 2.65 (q,  $J$  = 7.6 Hz, 1H), 2.43 (dt,  $J$  = 14.4, 7.4 Hz, 1H), 2.21 – 2.08 (m, 2H), 2.04 (s, 3H), 2.03 – 1.94 (m, 3H), 1.94 – 1.70 (m, 4H), 1.59 – 1.49 (m, 3H), 1.46 – 1.29 (m, 4H), 1.34 (d,  $J$  = 7.6 Hz, 3H), 1.11 (qd,  $J$  = 12.7, 4.5 Hz, 1H), 0.84 – 0.77 (m, 1H), 0.72 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  181.0, 170.7, 142.3, 120.8, 82.9, 69.5, 58.9, 58.1, 52.4, 43.8, 40.3, 40.2, 38.5, 36.5, 35.9, 34.1, 33.1, 32.8, 27.5, 25.9, 25.0, 21.6, 18.0, 14.0; IR (KBr):  $\nu$  = 3527, 2932, 2871, 1768, 1731, 1256, 962, 734  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>35</sub>O<sub>5</sub>, 403.2479; found, 403.2482.



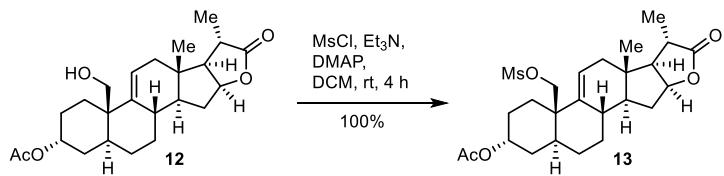
To a stirred solution of **12** (100.0 mg, 0.25 mmol, 1.0 equiv) and DBU (148  $\mu\text{L}$ , 1.00 mmol, 4.0 equiv) in 5 mL dry DCM was added *n*-C<sub>4</sub>F<sub>9</sub>SO<sub>2</sub>F (133  $\mu\text{L}$ , 0.75 mmol, 3.0 equiv) at 0 °C. The reaction mixture was stirred at the same temperature for 1.5 h, quenched with sat. aq. NH<sub>4</sub>Cl (5 mL) and extracted with DCM (3×10 mL). The combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash chromatography (SiO<sub>2</sub>, 10:1 petroleum ether: EtOAc) to afford a 1.4:2.2:1.0 mixture of **15a**, **15b** and **15c** in 78% combined yield (75.0 mg).

**Compound 15a:** white foam; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f$  = 0.73;  $[\alpha]_D^{25}$  –47.4 ( $c$  1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.89 (s, 1H), 5.56 (d,  $J$  = 5.2 Hz, 1H), 5.12 – 5.07 (m, 1H), 4.98 (td,  $J$  = 7.7, 4.2 Hz, 1H), 2.66 (q,  $J$  = 7.8 Hz, 1H), 2.53

– 2.33 (m, 3H), 2.20 – 1.96 (m, 6H), 2.06 (s, 3H), 1.96 – 1.87 (m, 2H), 1.77 (dd,  $J$  = 12.7, 7.8 Hz, 1H), 1.67 – 1.59 (m, 1H), 1.53 – 1.42 (m, 1H), 1.38 – 1.19 (m, 4H), 1.33 (d,  $J$  = 7.6 Hz, 3H), 0.79 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  181.0, 170.8, 139.2, 138.6, 128.3, 127.3, 82.9, 69.8, 59.0, 51.0, 44.1, 40.8, 40.7, 39.2, 37.3, 37.0, 36.7, 34.5, 34.3, 31.2, 29.3, 21.6, 17.9, 14.2; IR (KBr):  $\nu$  = 2930, 2852, 1771, 1733, 1249, 1180, 1037, 734  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+Na] $^+$  calcd for  $\text{C}_{24}\text{H}_{32}\text{O}_4\text{Na}$ , 407.2193; found, 407.2192.

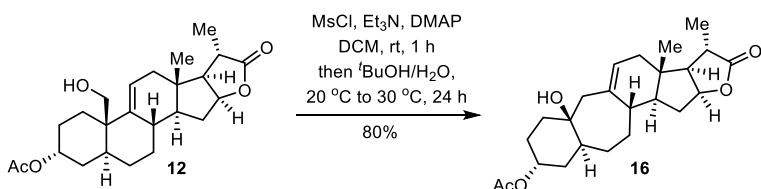
**Compound 15b:** mp: 185.2 – 187.1 °C; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f$  = 0.73;  $[\alpha]_D^{25}$  –137.5 ( $c$  0.87,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.33 (brs, 1H), 5.27 (d,  $J$  = 2.8 Hz, 1H), 5.06 – 4.93 (m, 2H), 2.97 (d,  $J$  = 15.4 Hz, 1H), 2.87 (d,  $J$  = 15.3 Hz, 1H), 2.64 (q,  $J$  = 7.5 Hz, 1H), 2.46 – 2.36 (m, 2H), 2.36 – 2.26 (m, 1H), 2.04 (s, 3H), 2.01 – 1.95 (m, 2H), 1.95 – 1.81 (m, 3H), 1.80 – 1.69 (m, 3H), 1.61 – 1.51 (m, 2H), 1.50 – 1.35 (m, 3H), 1.32 (d,  $J$  = 7.6 Hz, 3H), 0.73 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  181.1, 171.0, 139.8, 139.2, 119.9, 119.3, 82.8, 68.1, 59.1, 50.6, 43.7, 41.4, 40.8, 40.0, 39.8, 36.6, 35.8, 34.7, 34.2, 31.7, 29.5, 21.6, 18.0, 13.9; IR (KBr):  $\nu$  = 2923, 2853, 1770, 1727, 1245, 1033, 804, 734  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+Na] $^+$  calcd for  $\text{C}_{24}\text{H}_{32}\text{O}_4\text{Na}$ , 407.2193; found, 407.2191.

**Compound 15c:** colorless oil; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f$  = 0.73;  $[\alpha]_D^{25}$  –4.4 ( $c$  0.50,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.30 (d,  $J$  = 4.7 Hz, 1H), 5.01 – 4.90 (m, 2H), 2.94 (d,  $J$  = 14.9 Hz, 1H), 2.64 (q,  $J$  = 7.6 Hz, 1H), 2.42 (d,  $J$  = 14.9 Hz, 1H), 2.39 (ddd,  $J$  = 13.2, 7.6, 6.0 Hz, 1H), 2.27 – 2.07 (m, 5H), 2.03 (s, 3H), 2.01 – 1.84 (m, 5H), 1.83 – 1.74 (m, 1H), 1.73 – 1.62 (m, 1H), 1.61 – 1.41 (m, 3H), 1.32 (d,  $J$  = 7.6 Hz, 3H), 1.29 – 1.20 (m, 1H), 0.76 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  181.2, 171.0, 137.5, 130.1, 129.2, 121.1, 83.0, 70.2, 59.0, 50.6, 42.5, 41.7, 41.1, 39.8, 37.0, 36.6, 34.0, 31.2, 30.3, 29.2, 27.8, 21.6, 18.0, 13.8; IR (KBr):  $\nu$  = 2923, 2838, 1770, 1732, 1244, 1031, 801, 734  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+Na] $^+$  calcd for  $\text{C}_{24}\text{H}_{32}\text{O}_4\text{Na}$ , 407.2193; found, 407.2191.



To a solution of **12** (3.6 g, 9.0 mmol, 1.0 equiv) and DMAP (110.0 mg, 0.9 mmol, 0.1 equiv) in 130 mL dry DCM was added Et<sub>3</sub>N (3.7 mL, 27.0 mmol, 3.0 equiv) and MsCl (1.4 mL, 18.0 mmol, 2.0 equiv). The reaction mixture was stirred at room temperature for 4 h and concentrated in vacuo to provide the crude residue which was purified by flash chromatography (SiO<sub>2</sub>, 8:1→5:1 petroleum ehter:acetone) to provide **13** (4.3 g, 100%) as a white foam.

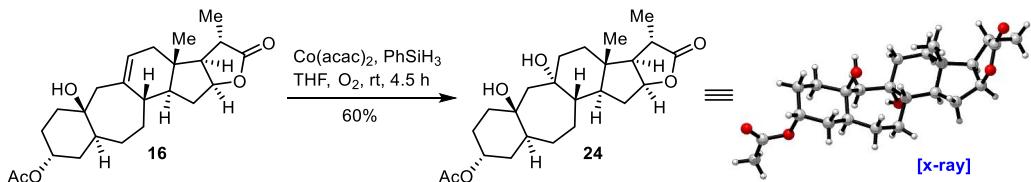
**Compound 13:** TLC (petroleum ether:EtOAc, 1:1 v/v):  $R_f = 0.35$ ;  $[\alpha]_D^{27} -11.5$  (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.45 (d, *J* = 5.8 Hz, 1H), 5.09 – 5.05 (m, 1H), 4.99 (td, *J* = 7.6, 4.3 Hz, 1H), 4.38 (d, *J* = 9.7 Hz, 1H), 4.33 (d, *J* = 9.7 Hz, 1H), 2.93 (s, 3H), 2.64 (q, *J* = 7.4 Hz, 1H), 2.43 (dt, *J* = 14.3, 7.4 Hz, 1H), 2.18 – 2.08 (m, 2H), 2.04 (s, 3H), 2.01 – 1.85 (m, 5H), 1.82 – 1.71 (m, 2H), 1.69 – 1.63 (m, 1H), 1.59 – 1.48 (m, 3H), 1.44 – 1.36 (m, 3H), 1.33 (d, *J* = 7.7 Hz, 3H), 1.11 (qd, *J* = 12.2, 5.9 Hz, 1H), 0.74 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  181.0, 170.5, 140.5, 120.7, 82.9, 69.0, 65.9, 58.7, 52.6, 41.6, 40.4, 40.1, 38.8, 37.4, 36.6, 35.8, 34.1, 33.1, 32.8, 27.6, 25.7, 25.1, 21.6, 17.9, 13.3; IR (KBr):  $\nu$  = 2936, 2874, 1766, 1731, 1449, 1237, 1175, 735 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>37</sub>O<sub>7</sub>S, 481.2255; found, 481.2252.



To a solution of **12** (4.0 g, 9.9 mmol, 1.0 equiv) and DMAP (242.8 mg, 2.0 mmol, 0.2 equiv) in 81 mL dry DCM was added Et<sub>3</sub>N (4.14 mL, 29.8 mmol, 3.0 equiv) and MsCl (1.54 mL, 19.9 mmol, 2.0 equiv). The reaction mixture was stirred at room temperature for 1 h and concentrated in vacuo to provide the crude mesylate **13**. After **13** was dissolved in H<sub>2</sub>O/'BuOH (820 mL, 2:1, v/v), the reaction mixture was stirred at 20 °C

for 21 h and 30 °C for 3 h. The reaction mixture was extracted with EtOAc ( $3 \times 200$  mL) and the combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude residue which was purified by flash chromatography (SiO<sub>2</sub>, 8:1→5:1 petroleum ether: EtOAc) to furnish compound **16** (3.2 g, 80%) as a white solid.

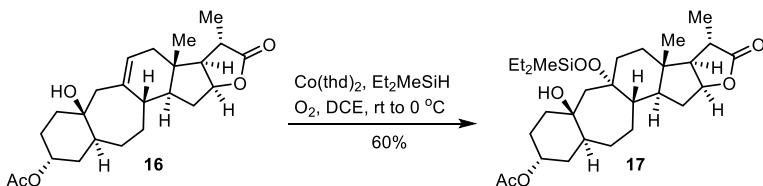
**Compound 16:** mp: 177.1 – 179.5 °C; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f = 0.51$ ; [α]<sub>D</sub><sup>27</sup> –49.0 (*c* 0.47, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.35 – 5.30 (m, 1H), 5.04 – 5.00 (m, 1H), 4.96 (td, *J* = 7.7, 4.2 Hz, 1H), 2.71 – 2.61 (m, 2H), 2.40 (dt, *J* = 14.0, 7.4 Hz, 1H), 2.30 (d, *J* = 15.8 Hz, 1H), 2.18 – 2.09 (m, 1H), 2.08 – 2.00 (m, 1H), 2.04 (s, 3H), 1.98 (d, *J* = 7.4 Hz, 1H), 1.90 – 1.72 (m, 3H), 1.72 – 1.65 (m, 3H), 1.63 – 1.52 (m, 4H), 1.50 – 1.35 (m, 3H), 1.34 – 1.29 (m, 1H), 1.31 (d, *J* = 7.6 Hz, 3H), 1.06 (s, 1H), 0.78 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 181.1, 170.8, 138.0, 122.7, 82.9, 72.2, 69.8, 59.2, 50.8, 50.7, 43.1, 41.4, 40.9, 40.2, 36.7, 36.5, 34.9, 34.3, 33.8, 29.2, 25.3, 21.6, 17.9, 14.4; IR (KBr):  $\nu$  = 3496, 2921, 2874, 1767, 1731, 1259, 1240, 735 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M-H]<sup>-</sup> calcd for C<sub>24</sub>H<sub>33</sub>O<sub>5</sub>, 401.2333; found, 401.2341.



A stirred solution of **16** (300.0 mg, 0.75 mmol, 1.0 equiv) and Co(acac)<sub>2</sub> (57.8 mg, 0.23 mmol, 0.3 equiv) in 21 mL dry THF was bubbled with O<sub>2</sub> for 0.5 h at room temperature. Then PhSiH<sub>3</sub> (0.37 mL, 3.00 mmol, 4.0 equiv) was added over 1 h. Stirring was continued for 3 h at the same temperature under an O<sub>2</sub> atmosphere (no bubbling). The reaction mixture was quenched with aq. HCl (1M, 5 mL) and extracted with EtOAc ( $3 \times 15$  mL). The combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude residue, which was purified by flash chromatography (SiO<sub>2</sub>, 2:1→1:1 petroleum ether: EtOAc) to furnish compound **24** (187.0 mg, 60%) as a white solid.

The single crystal of compound **24** suitable for X-ray determination was obtained by slow evaporation of a solution of **24** in hexanes and acetone at room temperature.

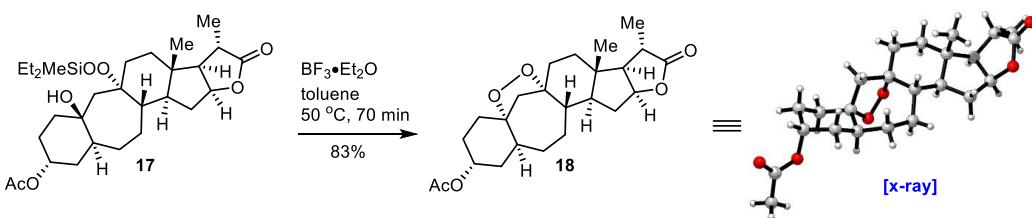
**Compound 24:** mp: 141.0 – 143.0 °C; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f = 0.14$ ;  $[\alpha]_D^{25} -30.4$  ( $c$  1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.02 – 4.98 (m, 1H), 4.94 (td,  $J$  = 7.7, 4.6 Hz, 1H), 2.56 (q,  $J$  = 7.4 Hz, 1H), 2.25 (dt,  $J$  = 13.6, 7.1 Hz, 1H), 2.03 (s, 3H), 2.00 – 1.95 (m, 1H), 1.91 (s, 2H), 1.86 – 1.73 (m, 4H), 1.70 – 1.61 (m, 4H), 1.59 – 1.46 (m, 5H), 1.47 – 1.34 (m, 5H), 1.30 (d,  $J$  = 7.6 Hz, 3H), 1.24 (s, 1H), 1.17 (s, 1H), 0.77 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  181.4, 170.8, 82.7, 73.8, 72.8, 69.9, 58.9, 57.5, 48.1, 45.3, 42.0, 40.2, 38.9, 37.2, 36.2, 34.1, 33.8, 33.2, 31.8, 28.8, 25.5, 21.6, 18.0, 13.2; IR (KBr):  $\nu$  = 3541, 3467, 2929, 1737, 1710, 1434, 734, 694 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>37</sub>O<sub>6</sub>, 421.2585; found, 421.2582.



To a solution of **16** (5.2 g, 12.9 mmol, 1.0 equiv) and Co(thd)<sub>2</sub> (1.1 g, 2.6 mmol, 0.2 equiv) in 260 mL dry DCE was added Et<sub>2</sub>MeSiH (2.8 mL, 19.4 mmol, 1.5 equiv) under O<sub>2</sub> atmosphere (1 atm). The reaction mixture was stirred at room temperature for 15 min and then at 0 °C for 9 h under O<sub>2</sub> (balloon). The reaction mixture was quenched with sat. aq. NaHCO<sub>3</sub> (40 mL) and extracted with DCM (3×50 mL). The combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash chromatography (SiO<sub>2</sub>, 7:1→6:1→5:1 petroleum ether:EtOAc) to provide compound **17** (4.1 g, 60%) as a white solid.

**Compound 17:** mp: 170.9 – 173.8 °C; TLC (petroleum ether:EtOAc, 2:1 v/v):  $R_f = 0.61$ ;  $[\alpha]_D^{25} -11.5$  ( $c$  0.30, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.03 – 4.99 (m, 1H), 4.94 (td,  $J$  = 7.7, 4.5 Hz, 1H), 2.56 (q,  $J$  = 7.6 Hz, 1H), 2.28 (d,  $J$  = 15.7 Hz, 1H), 2.25 – 2.12 (m, 2H), 2.04 (s, 3H), 2.08 – 1.95 (m, 2H), 1.85 (d,  $J$  = 7.8 Hz, 2H), 1.76 (d,  $J$  = 15.9

Hz, 1H), 1.79 – 1.73 (m, 1H), 1.71 – 1.50 (m, 6H), 1.50 – 1.34 (m, 8H), 1.31 (d,  $J$  = 7.6 Hz, 3H), 0.99 (t,  $J$  = 7.9 Hz, 6H), 0.77 (s, 3H), 0.70 (q,  $J$  = 7.6 Hz, 2H), 0.68 (q,  $J$  = 7.6 Hz, 2H), 0.17 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  181.5, 170.9, 84.7, 82.7, 73.1, 69.8, 59.1, 53.3, 47.9, 45.4, 42.0, 40.1, 36.9, 36.3, 34.3, 34.2, 33.6, 33.1, 32.1, 27.6, 25.4, 21.7, 18.1, 13.4, 7.0, 5.8, 5.6, –5.0 (one  $\text{CH}_3$  carbon was overlapped); IR (KBr):  $\nu$  = 3458, 2945, 2874, 1760, 1734, 1243, 826, 804  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+Na] $^+$  calcd for  $\text{C}_{29}\text{H}_{48}\text{O}_7\text{SiNa}$ , 559.3062; found, 559.3061.

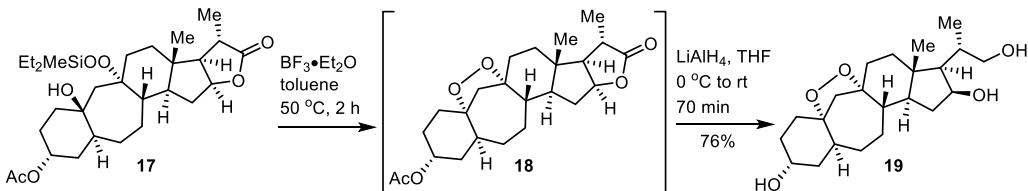


To a solution of **17** (0.8 g, 1.45 mmol, 1.0 equiv) in 29 mL dry toluene was added  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (54  $\mu\text{L}$ , 0.44 mmol, 0.3 equiv). The reaction mixture was stirred at  $50^\circ\text{C}$  for 70 min and quenched with sat. aq.  $\text{NaHCO}_3$  (8 mL). The aqueous layer was extracted with  $\text{EtOAc}$  ( $3 \times 15$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash chromatography ( $\text{SiO}_2$ , 10:1 → 8:1 petroleum ether:acetone) to provide compound **18** (505.0 mg, 83%) as a white solid.

The single crystal of compound **18** suitable for X-ray determination was obtained by slow evaporation of a solution of **18** in petroleum ether and  $\text{EtOAc}$  at room temperature.

**Compound 18:** mp: 222.4 – 224.0  $^\circ\text{C}$ ; TLC (petroleum ether: $\text{EtOAc}$ , 2:1 v/v):  $R_f$  = 0.53;  $[\alpha]_D^{25}$  +25.6 ( $c$  1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.99 – 4.91 (m, 2H), 2.57 (d,  $J$  = 11.8 Hz, 1H), 2.55 (q,  $J$  = 7.7 Hz, 1H), 2.30 (dt,  $J$  = 13.6, 7.2 Hz, 1H), 2.06 – 1.97 (m, 4H), 2.03 (s, 3H), 1.97 – 1.90 (m, 3H), 1.90 – 1.81 (m, 3H), 1.75 – 1.67 (m, 1H), 1.66 – 1.60 (m, 1H), 1.59 – 1.46 (m, 4H), 1.43 – 1.35 (m, 1H), 1.33 – 1.26 (m, 1H), 1.30 (d,  $J$  = 7.6 Hz, 3H), 1.10 (td,  $J$  = 12.6, 3.4 Hz, 2H), 0.77 (s, 3H);  $^{13}\text{C}$  NMR

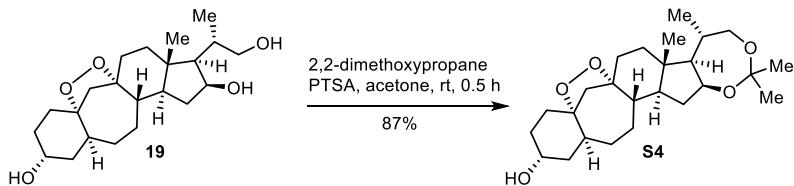
(101 MHz, CDCl<sub>3</sub>) δ 181.3, 170.7, 87.8, 86.0, 82.6, 68.1, 58.8, 50.1, 48.5, 45.7, 41.6, 37.6, 36.3, 35.7, 35.5, 33.3, 33.2, 32.4, 31.8, 28.6, 27.6, 21.5, 18.0, 13.0; IR (KBr): ν = 2937, 2863, 2769, 1733, 1254, 1237, 1183, 1021 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>35</sub>O<sub>6</sub>, 419.2428; found, 419.2423.



To a solution of **17** (4.6 g, 8.7 mmol, 1.0 equiv) in 218 mL dry toluene was added BF<sub>3</sub>·Et<sub>2</sub>O (0.32 mL, 2.6 mmol, 0.3 equiv). After stirred at 50 °C for 1 h, another portion of BF<sub>3</sub>·Et<sub>2</sub>O (0.11 mL, 0.9 mmol, 0.1 equiv) was added and stirring was continued for another 1 h. The reaction mixture was quenched with solid NaHCO<sub>3</sub> (366.0 mg, 4.4 mmol, 0.5 equiv) and stirred at room temperature for 10 min. Removal of the solvent under reduced pressure afforded the crude **18**, which was dissolved in 435 mL dry THF. LiAlH<sub>4</sub> (1.7 g, 43.5 mmol, 5.0 equiv) was added in 5 min at 0 °C. After stirred at room temperature for another 65 min, the reaction mixture was quenched slowly with 1.7 mL H<sub>2</sub>O, 1.7 mL 15% aq. NaOH and 5.1 mL H<sub>2</sub>O. The mixture was then filtered through celite and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography (SiO<sub>2</sub>, 30:1→20:1 DCM:MeOH) to provide compound **19** (2.5 g, 76%) as a white solid.

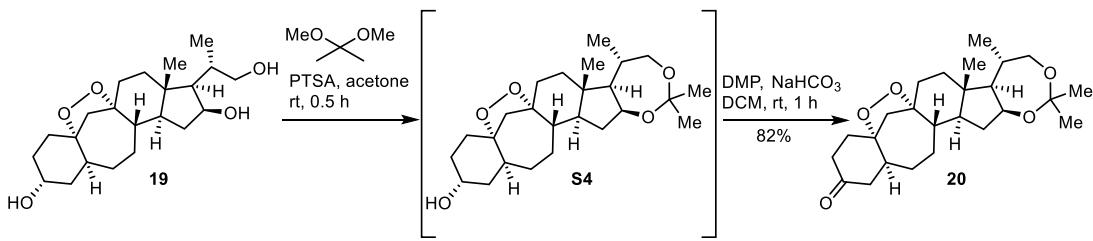
**Compound 19:** mp: 234.2 – 236.4 °C; TLC (petroleum ether:acetone, 2:1 v/v): *R*<sub>f</sub> = 0.29; [α]<sub>D</sub><sup>25</sup> +170.9 (*c* 0.07, MeOH); <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 4.37 (td, *J* = 7.7, 4.7 Hz, 1H), 3.96 – 3.91 (m, 1H), 3.64 (dd, *J* = 10.5, 5.8 Hz, 1H), 3.48 (dd, *J* = 10.5, 4.8 Hz, 1H), 2.71 (d, *J* = 12.1 Hz, 1H), 2.25 (dt, *J* = 13.1, 7.6 Hz, 1H), 2.18 – 2.04 (m, 3H), 1.99 (d, *J* = 12.1 Hz, 1H), 1.94 – 1.75 (m, 6H), 1.66 – 1.40 (m, 6H), 1.29 – 1.16 (m, 4H), 1.16 – 1.09 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.97 (s, 3H); <sup>13</sup>C NMR (101 MHz, CD<sub>3</sub>OD) δ 88.0, 85.9, 71.2, 67.8, 64.3, 59.6, 49.5, 45.5, 42.1, 39.8, 37.2, 36.0, 35.1, 32.5, 32.2, 31.5, 30.5, 27.1, 15.6, 11.1; (In CD<sub>3</sub>OD, two carbon peaks were

overlapped, so C<sub>5</sub>D<sub>5</sub>N was used instead) <sup>13</sup>C NMR (101 MHz, C<sub>5</sub>D<sub>5</sub>N) δ 88.1, 85.8, 71.3, 68.8, 64.0, 60.9, 50.1, 48.1, 45.9, 42.6, 41.3, 37.7, 37.0, 35.7, 33.4, 33.3, 32.9, 32.2, 31.9, 27.8, 17.0, 12.4; IR (KBr): ν = 3735, 3354, 2969, 2926, 1559, 1507, 1364, 668 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>36</sub>O<sub>5</sub>Na, 403.2455; found, 403.2462.



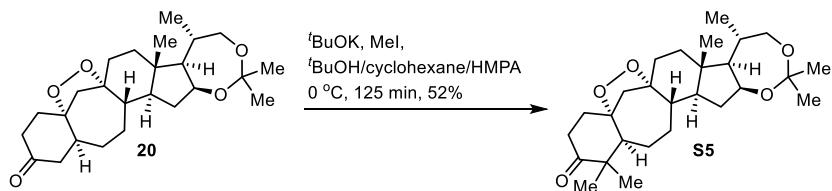
To a stirred solution of **19** (445.0 mg, 1.2 mmol, 1.0 equiv) and 2,2-dimethoxypropane (2.6 mL, 21.6 mmol, 18.0 equiv) in 90 mL acetone was added PTSA (56.0 mg, 0.3 mmol, 0.25 equiv). After stirred at room temperature for 0.5 h, Et<sub>3</sub>N (0.32 mL, 2.4 mmol, 2.0 equiv) was added and stirring was continued for another 10 min. Acetone was removed under reduced pressure to afford the crude residue which was purified by flash chromatography (SiO<sub>2</sub>, 4:1→3:1 petroleum ether:EtOAc) to furnish compound **S4** as a white solid (430.0 mg, 87%).

**Compound S4:** mp: 204.7 – 205.9 °C; TLC (petroleum ether:EtOAc, 2:1 v/v): *R*<sub>f</sub> = 0.35; [α]<sub>D</sub><sup>25</sup> +36.0 (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.52 (q, *J* = 7.9 Hz, 1H), 4.02 – 3.98 (m, 1H), 3.80 (dd, *J* = 11.9, 5.7 Hz, 1H), 3.19 (t, *J* = 11.4 Hz, 1H), 2.55 (d, *J* = 11.8 Hz, 1H), 2.32 (tq, *J* = 12.7, 6.4 Hz, 1H), 2.13 (td, *J* = 13.0, 3.8 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.99 – 1.80 (m, 7H), 1.71 – 1.61 (m, 3H), 1.60 – 1.51 (m, 2H), 1.49 – 1.42 (m, 2H), 1.39 (s, 3H), 1.32 – 1.18 (m, 3H), 1.27 (s, 3H), 1.11 (t, *J* = 13.2 Hz, 2H), 0.86 (s, 3H), 0.82 (d, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 100.5, 88.0, 85.9, 71.8, 70.0, 64.9, 58.6, 50.1, 46.8, 45.4, 42.2, 40.6, 37.0, 35.1, 33.8, 32.7, 32.4, 32.1, 31.3, 31.2, 27.6, 25.8, 23.6, 16.8, 12.6; IR (KBr): ν = 3496, 2938, 2871, 1374, 1092, 935, 806, 743 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>25</sub>H<sub>40</sub>O<sub>5</sub>Na, 443.2768; found, 443.2768.



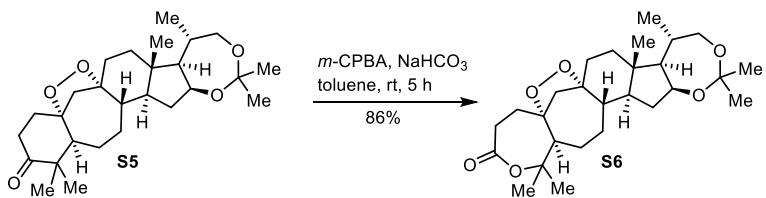
To a stirred solution of **19** (2.5 g, 6.6 mmol, 1.0 equiv) and 2,2-dimethoxypropane (14.5 mL, 118.5 mmol, 18.0 equiv) in 506 mL acetone was added PTSA (0.3 g, 1.6 mmol, 0.25 equiv). After stirred at room temperature for 0.5 h, Et<sub>3</sub>N (1.8 mL, 13.2 mmol, 2.0 equiv) was added and stirring was continued for another 10 min. Acetone was removed under reduced pressure and the crude product was dissolved in 165 mL DCM. Then NaHCO<sub>3</sub> (2.8 g, 33.0 mmol, 5.0 equiv) and DMP (5.6 g, 13.2 mmol, 2.0 equiv) were added successively. After stirred at room temperature for 0.5 h, another portion of DMP (1.4 g, 3.3 mmol, 0.5 equiv) was added and stirring was continued for another 0.5 h at the same temperature. The reaction mixture was filtered through celite and quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (40 mL). The organic layer was separated and the aqueous layer was further extracted with DCM (2×50 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was purified by flash chromatography (SiO<sub>2</sub>, 6:1→4:1 petroleum ether:EtOAc) to furnish compound **20** as a white solid (2.3 g, 82%).

**Compound 20:** mp: 186.3 – 187.7 °C; TLC (petroleum ether:EtOAc, 2:1 v/v): *R*<sub>f</sub> = 0.61; [α]<sub>D</sub><sup>25</sup> +38.6 (*c* 0.63, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.52 (q, *J* = 7.9 Hz, 1H), 3.80 (dd, *J* = 12.0, 5.8 Hz, 1H), 3.19 (t, *J* = 11.4 Hz, 1H), 2.79 (d, *J* = 12.0 Hz, 1H), 2.46 – 2.22 (m, 4H), 2.15 (d, *J* = 12.4 Hz, 1H), 2.13 – 2.05 (m, 3H), 2.05 – 1.93 (m, 3H), 1.93 – 1.84 (m, 1H), 1.84 – 1.73 (m, 1H), 1.73 – 1.61 (m, 3H), 1.58 – 1.51 (m, 2H), 1.38 (s, 3H), 1.35 – 1.18 (m, 4H), 1.26 (s, 3H), 0.87 (s, 3H), 0.82 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 209.9, 100.6, 86.3, 86.2, 71.7, 70.0, 58.7, 51.6, 47.2, 45.9, 44.7, 42.2, 41.6, 37.8, 37.0, 35.7, 33.9, 32.7, 32.6, 31.3, 27.9, 25.9, 23.7, 16.9, 12.6; IR (KBr): ν = 2940, 2855, 1712, 1454, 1220, 1092, 1045, 895 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>25</sub>H<sub>38</sub>O<sub>5</sub>Na, 441.2611; found, 441.2613.



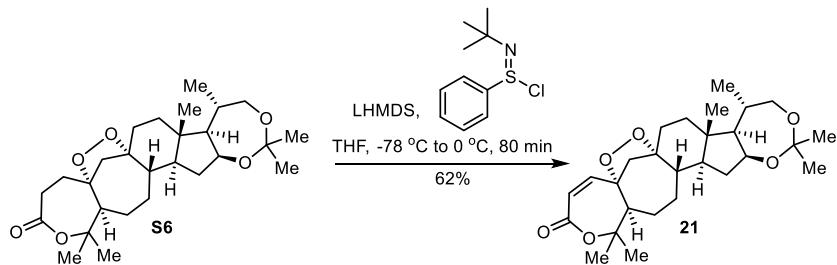
To a solution of **20** (1.1 g, 2.6 mmol, 1.0 equiv) in 'BuOH/ cyclohexane/HMPA (61.0 mL, 2.8:2.2:1, v/v) was added 'BuOK (1.0 M in THF, 7.9 mL, 7.9 mmol, 3.0 equiv) and MeI (0.49 mL, 7.9 mmol, 3.0 equiv) at 0 °C. After stirred at 0 °C for 25 min, 'BuOK (5.3 mL×2, 5.3 mmol×2, 2.0 equiv×2) and MeI (0.33 mL×2, 5.3 mmol×2, 2.0 equiv×2) were added in two portions every 25 min. 'BuOK (2.6 mL, 2.6 mmol, 1.0 equiv) and MeI (0.16 mL, 2.6 mmol, 1.0 equiv) were added and stirring was continued for another 25 min under the same condition. Finally, another portion of 'BuOK (1.3 mL, 1.3 mmol, 0.5 equiv) and MeI (0.08 mL, 1.3 mmol, 0.5 equiv) were added and stirring was continued for 25 min at 0 °C. The reaction mixture was quenched with water (20 mL) and extracted with EtOAc (3×40 mL). The combined organic layers were washed with aq. NaCl (water/brine=1:1, v/v, 30 mL) for 8 times and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash chromatography (SiO<sub>2</sub>, 31:6:1→25:6:1 petroleum ether:DCM: EtOAc) to provide compound **S5** (610.0 mg, 52%) as a white solid.

**Compound S5:** mp: 183.9 – 185.4 °C; TLC (petroleum ether:EtOAc, 4:1 v/v): *R*<sub>f</sub> = 0.57; [α]<sub>D</sub><sup>25</sup> +99.7 (*c* 0.31, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.53 (q, *J* = 7.9 Hz, 1H), 3.80 (dd, *J* = 12.0, 5.8 Hz, 1H), 3.20 (t, *J* = 11.4 Hz, 1H), 2.76 (d, *J* = 12.2 Hz, 1H), 2.63 – 2.48 (m, 1H), 2.42 – 2.26 (m, 3H), 2.08 (d, *J* = 12.4 Hz, 1H), 2.06 – 1.99 (m, 2H), 1.98 – 1.85 (m, 3H), 1.82 – 1.66 (m, 3H), 1.64 – 1.48 (m, 3H), 1.39 (s, 3H), 1.34 – 1.20 (m, 4H), 1.27 (s, 3H), 1.08 (s, 3H), 0.99 (s, 3H), 0.88 (s, 3H), 0.82 (d, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 215.8, 100.5, 86.4, 86.2, 71.8, 70.0, 58.7, 53.7, 48.2, 46.8, 46.5, 44.4, 42.4, 36.9, 35.8, 35.6, 33.7, 31.8, 31.3, 28.4, 25.9, 24.4, 24.2, 23.7, 20.7, 16.8, 12.7; IR (KBr): ν = 2944, 2870, 1709, 1454, 1224, 1092, 1075, 895 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>42</sub>O<sub>5</sub>Na, 469.2924; found,



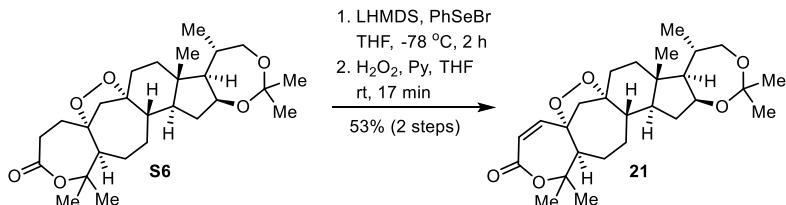
To a stirred solution of **S5** (585.0 mg, 1.3 mmol, 1.0 equiv) and NaHCO<sub>3</sub> (687.8 mg, 8.2 mmol, 6.3 equiv) in 33 mL toluene was added 85% *m*-CPBA (800.0 mg, 3.9 mmol, 3.0 equiv) at room temperature. After stirred at the same temperature for 3.5 h, another portion of 85% *m*-CPBA (270.0 mg, 1.3 mmol, 1.0 equiv) was added and stirring was continued for another 1.5 h at room temperature. The reaction mixture was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was purified by flash chromatography (SiO<sub>2</sub>, 5:1 petroleum ether:EtOAc) to furnish compound **S6** (520.1 mg, 86%) as a white solid.

**Compound S6:** mp: 208.9 – 211.4 °C; TLC (petroleum ether:EtOAc, 4:1 v/v): *R*<sub>f</sub> = 0.25; [α]<sub>D</sub><sup>25</sup> +76.2 (*c* 0.60, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.53 (q, *J* = 7.9 Hz, 1H), 3.79 (dd, *J* = 11.9, 5.8 Hz, 1H), 3.18 (t, *J* = 11.4 Hz, 1H), 2.80 – 2.56 (m, 2H), 2.65 (d, *J* = 12.0 Hz, 1H), 2.40 – 2.25 (m, 1H), 2.16 – 1.93 (m, 6H), 1.97 (d, *J* = 12.4 Hz, 1H), 1.89 (t, *J* = 12.4 Hz, 1H), 1.73 – 1.61 (m, 3H), 1.61 – 1.54 (m, 1H), 1.53 – 1.44 (m, 2H), 1.413 (s, 3H), 1.405 (s, 3H), 1.38 (s, 3H), 1.32 – 1.20 (m, 3H), 1.26 (s, 3H), 0.86 (s, 3H), 0.81 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 173.8, 100.6, 87.6, 86.9, 85.8, 71.8, 70.0, 58.7, 52.0, 48.6, 46.6, 44.6, 42.4, 36.8, 34.9, 33.7, 31.9, 31.7, 31.3, 31.2, 28.8, 28.4, 25.9, 23.7, 23.3, 16.8, 12.7; IR (KBr): ν = 2948, 2871, 1719, 1253, 1223, 1097, 1044, 901 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>42</sub>O<sub>6</sub>Na, 485.2874; found, 485.2872.



To a stirred solution of **S6** (100.0 mg, 0.22 mmol, 1.0 equiv) in 5.4 mL dry THF was added LHMDS (1.0 M solution in THF, 0.3 mL, 0.31 mmol, 1.4 equiv) at  $-78^{\circ}\text{C}$  under argon. After stirring at  $-78^{\circ}\text{C}$  for 0.5 h, a solution of *N*-*tert*-butylbenzenesulfinimidoyl chloride (64.0 mg, 0.31 mmol, 1.4 equiv) in 1.0 mL dry THF was added dropwise. Stirring was continued for 40 min at  $-78^{\circ}\text{C}$  and 10 min at  $0^{\circ}\text{C}$ . The reaction mixture was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  and extracted with EtOAc ( $3\times 15$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ , 19:1  $\rightarrow$  16:1 petroleum ether:acetone) to furnish compound **21** (61.7 mg, 62%) as a white solid.

Alternatively, compound **21** could be prepared in two steps, as shown below:

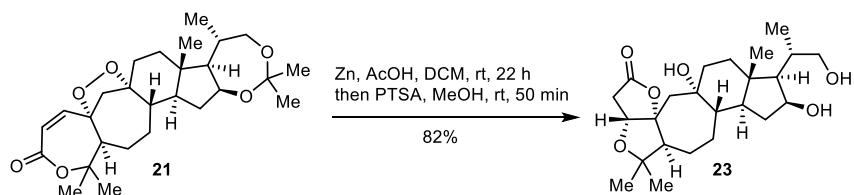


LHMDS (1.3 M solution in THF, 1.6 mL, 2.04 mmol, 2.0 equiv) was added to a stirred solution of **S6** (475.0 mg, 1.02 mmol, 1.0 equiv) in 20 mL dry THF at  $-78^{\circ}\text{C}$  under argon. After stirring at  $-78^{\circ}\text{C}$  for 0.5 h, a solution of PhSeBr (606.5 mg, 2.57 mmol, 2.5 equiv) in 5 mL dry THF was added. After an additional 1.5 h, the reaction mixture was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  and extracted with EtOAc ( $3\times 20$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash column chromatography to afford the desired phenylseleno lactone.

To a solution of the above selenylated lactone in 25 mL THF was added pyridine (0.49

mL, 6.12 mmol, 6.0 equiv) and H<sub>2</sub>O<sub>2</sub> (30% solution in H<sub>2</sub>O, 0.21 mL, 2.04 mmol, 2.0 equiv) at room temperature. After stirring at the same temperature for 5 min, another portion of H<sub>2</sub>O<sub>2</sub> (30% solution in H<sub>2</sub>O, 0.31 mL, 3.06 mmol, 3.0 equiv) was added and stirring was continued for another 12 min. The reaction mixture was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was purified by flash chromatography (SiO<sub>2</sub>, 20:1→4:1 petroleum ether:acetone) to furnish compound **21** as a white solid (250.7 mg, 53%).

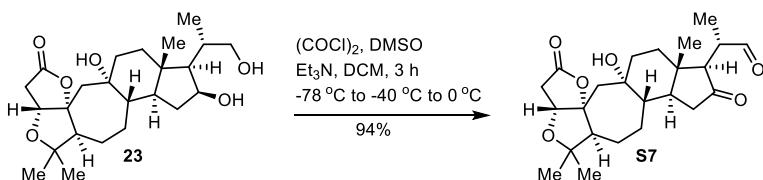
**Compound 21:** mp: 165.1 – 166.9 °C; TLC (petroleum ether:EtOAc, 4:1 v/v): *R*<sub>f</sub> = 0.23; [α]<sub>D</sub><sup>25</sup> +165.8 (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.24 (d, *J* = 12.5 Hz, 1H), 5.93 (d, *J* = 12.5 Hz, 1H), 4.53 (q, *J* = 7.9 Hz, 1H), 3.80 (dd, *J* = 12.0, 5.8 Hz, 1H), 3.19 (t, *J* = 11.4 Hz, 1H), 2.78 (d, *J* = 12.3 Hz, 1H), 2.40 (dd, *J* = 11.7, 5.8 Hz, 1H), 2.36 – 2.27 (m, 1H), 2.19 – 2.09 (m, 1H), 2.15 (d, *J* = 12.5 Hz, 1H), 2.08 – 1.95 (m, 2H), 1.87 (q, *J* = 12.7 Hz, 1H), 1.74 – 1.66 (m, 2H), 1.66 – 1.53 (m, 3H), 1.49 (td, *J* = 11.7, 4.7 Hz, 1H), 1.41 (s, 3H), 1.38 (s, 6H), 1.32 – 1.18 (m, 3H), 1.26 (s, 3H), 0.86 (s, 3H), 0.81 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.4, 146.8, 119.6, 100.6, 87.5, 87.3, 82.9, 71.7, 70.0, 58.7, 53.1, 49.2, 46.6, 44.5, 42.4, 36.9, 33.6, 31.31, 31.28, 30.2, 28.8, 28.1, 25.9, 23.7, 21.6, 16.8, 12.7; IR (KBr): ν = 2953, 2900, 1693, 1644, 1262, 1016, 985, 809 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>27</sub>H<sub>40</sub>O<sub>6</sub>Na, 483.2717; found, 483.2722.



To a solution of **21** (489.0 mg, 1.06 mmol, 1.0 equiv) in 22 mL DCM was added zinc powder (414.1 mg, 6.37 mmol, 6.0 equiv) and AcOH (0.19 mL, 3.19 mmol, 3.0 equiv). After stirring at room temperature for 11 h, another portion of AcOH (0.19 mL, 3.19 mmol, 3.0 equiv) was added and stirring was continued for 11 h under the same

condition. MeOH (21.5 mL) and PTSA (3.03 g, 15.93 mmol, 15.0 equiv) were added. After stirred at room temperature for 50 min, the reaction was quenched with Et<sub>3</sub>N (6 mL). After stirred at room temperature for another 10 min, solvent was removed under reduced pressure. Sat. aq. NH<sub>4</sub>Cl (20 mL) was added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash chromatography (SiO<sub>2</sub>, 5:1 → 2:1 petroleum ether: EtOAc) to provide compound **23** (367.9 mg, 82%) as a white solid.

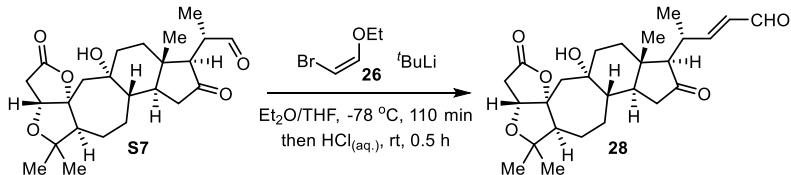
**Compound 23:** mp: 230.1 – 231.5 °C; TLC (petroleum ether:acetone, 3:1 v/v): *R*<sub>f</sub> = 0.21; [α]<sub>D</sub><sup>25</sup> +43.0 (*c* 0.62, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.40 (q, *J* = 7.6 Hz, 1H), 4.15 (d, *J* = 4.2 Hz, 1H), 3.74 – 3.48 (m, 3H), 2.94 (s, 1H), 2.75 – 2.47 (m, 3H), 2.35 (dd, *J* = 13.3, 4.0 Hz, 1H), 2.26 – 2.13 (m, 2H), 1.91 (d, *J* = 15.1 Hz, 1H), 1.80 (d, *J* = 15.1 Hz, 1H), 1.76 – 1.67 (m, 3H), 1.66 – 1.54 (m, 3H), 1.46 – 1.34 (m, 3H), 1.31 (s, 3H), 1.27 – 1.15 (m, 2H), 1.10 (s, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 174.1, 100.0, 85.0, 81.0, 72.8, 72.5, 71.0, 62.2, 59.4, 49.5, 46.2, 45.7, 42.9, 38.9, 35.8, 35.6, 35.4, 32.5, 28.9, 27.9, 26.4, 22.4, 16.9, 12.5; IR (KBr): ν = 3579, 3392, 2932, 2862, 1777, 1263, 911, 736 cm<sup>-1</sup>; HRMS (ESI, *m/z*): [M+Na]<sup>+</sup> calcd for C<sub>24</sub>H<sub>38</sub>O<sub>6</sub>Na, 445.2561; found, 445.2566.



To a solution of (COCl)<sub>2</sub> (361 μL, 4.25 mmol, 5.0 equiv) in 22 mL dry DCM was added DMSO (454 μL, 6.38 mmol, 7.5 equiv) at –78 °C. After stirring at the same temperature for 45 min, a solution of **23** (360.0 mg, 0.85 mmol, 1.0 equiv) in 28 mL DCM was added and stirring was continued for 35 min at –78 °C. The reaction mixture was warmed to –40 °C and stirring was continued for another 45 min at the same temperature. Et<sub>3</sub>N (1.42 mL, 10.20 mmol, 12.0 equiv) was added and stirring was

continued for 50 min at  $-40\text{ }^{\circ}\text{C}$  and finally 5 min at  $0\text{ }^{\circ}\text{C}$ . The reaction mixture was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  and extracted with DCM ( $3\times20$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ ,  $6:1\rightarrow5:1$  petroleum ether:acetone) to furnish compound **S7** (335.2 mg, 94%) as a white foam.

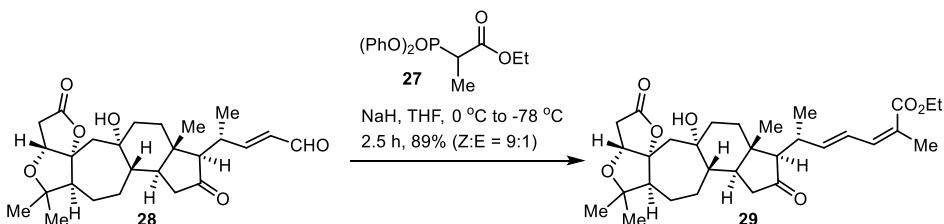
**Compound S7:** TLC (petroleum ether:acetone, 3:1 v/v):  $R_f = 0.32$ ;  $[\alpha]_D^{25} -58.6$  ( $c 1.00$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.79 (d,  $J = 2.1$  Hz, 1H), 4.17 (dd,  $J = 4.2, 1.5$  Hz, 1H), 3.17 (s, 1H), 2.74 – 2.66 (m, 2H), 2.56 – 2.49 (m, 2H), 2.45 – 2.33 (m, 2H), 2.24 (dd,  $J = 18.3, 7.9$  Hz, 1H), 2.02 – 1.91 (m, 1H), 1.95 (d,  $J = 15.2$  Hz, 1H), 1.82 (d,  $J = 15.2$  Hz, 1H), 1.82 – 1.73 (m, 2H), 1.73 – 1.63 (m, 2H), 1.56 – 1.41 (m, 3H), 1.32 (s, 3H), 1.31 – 1.22 (m, 1H), 1.115 (d,  $J = 6.8$  Hz, 3H), 1.11 (s, 3H), 0.82 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  217.1, 203.5, 173.9, 99.6, 85.0, 81.0, 72.4, 65.1, 59.4, 48.8, 45.7, 43.7, 43.5, 42.3, 38.4, 37.7, 35.7, 33.8, 28.8, 27.7, 26.7, 22.4, 13.3, 13.0; IR (KBr):  $\nu = 3574, 2971, 2933, 1779, 1734, 1188, 911, 734$   $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{24}\text{H}_{34}\text{O}_6\text{Na}$ , 441.2248; found, 441.2249.



To a solution of (*Z*)-1-bromo-2-ethoxyethylene (**26**) (157.4 mg, 1.05 mmol, 3.5 equiv) in 7.2 mL dry  $\text{Et}_2\text{O}$  was added  $^{\prime}\text{BuLi}$  (1.3 M in pentane, 1.62 mL, 2.10 mmol, 7.0 equiv) dropwise. After the reaction was stirred at  $-78\text{ }^{\circ}\text{C}$  for 50 min, a solution of aldehyde **S7** (125.0 mg, 0.30 mmol, 1.0 equiv) in 4.2 mL  $\text{Et}_2\text{O}$  and 3.3 mL THF was added. The reaction mixture was stirred at  $-78\text{ }^{\circ}\text{C}$  for another 1 h before being quenched with 5 mL 4% aq.  $\text{HCl}$  and 5 mL  $\text{H}_2\text{O}$ . The resulting mixture was stirred at room temperature for 0.5 h and quenched with sat. aq.  $\text{NaHCO}_3$ . The aqueous layer was extracted with  $\text{EtOAc}$  ( $3\times15$  mL) and the combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ ,

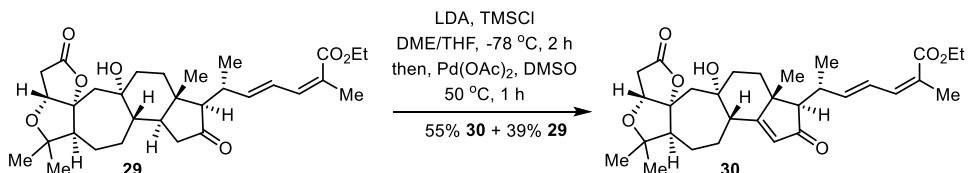
6:1→5:1 petroleum ether:acetone) to furnish compound **28** (78.6 mg, 59%) as a colorless oil.

**Compound 28:** TLC (petroleum ether:acetone, 3:1 v/v):  $R_f = 0.32$ ;  $[\alpha]_D^{25} -29.9$  ( $c$  0.35,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.50 (d,  $J = 7.9$  Hz, 1H), 7.18 (dd,  $J = 15.7, 8.0$  Hz, 1H), 6.07 (dd,  $J = 15.7, 7.9$  Hz, 1H), 4.17 (dd,  $J = 4.3, 1.5$  Hz, 1H), 3.18 (s, 1H), 2.80 – 2.64 (m, 3H), 2.37 (dd,  $J = 13.3, 4.4$  Hz, 1H), 2.29 – 2.18 (m, 2H), 2.11 (d,  $J = 6.5$  Hz, 1H), 1.95 (d,  $J = 15.2$  Hz, 1H), 1.91 – 1.74 (m, 3H), 1.82 (d,  $J = 15.2$  Hz, 1H), 1.72 – 1.64 (m, 2H), 1.57 – 1.40 (m, 5H), 1.32 (s, 3H), 1.22 (d,  $J = 7.0$  Hz, 3H), 1.11 (s, 3H), 0.79 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  216.6, 194.6, 173.8, 163.4, 131.6, 99.6, 85.0, 81.0, 72.5, 68.3, 59.4, 48.7, 45.7, 43.3, 43.0, 38.7, 38.4, 35.7, 34.7, 33.7, 28.8, 27.7, 26.6, 22.3, 20.0, 13.6; IR (KBr):  $\nu = 3574, 2929, 2853, 1779, 1732, 1682, 1631, 734$   $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{26}\text{H}_{37}\text{O}_6$ , 445.2585; found, 445.2579.



To a suspension of sodium hydride (60% dispersion in mineral oil, 29.6 mg, 0.74 mmol, 2.8 equiv) in 2.6 mL dry THF was added dropwise phosphonate **27** (216.3 mg, 0.65 mmol, 2.5 equiv) at 0 °C. After stirred for 0.5 h at the same temperature, the reaction mixture was cooled to –78 °C and a solution of enal **28** (115.0 mg, 0.26 mmol, 1.0 equiv) in 4.0 mL THF was added. The reaction mixture was stirred for 2 h at –78 °C before quenched with sat. aq.  $\text{NH}_4\text{Cl}$ . The reaction mixture was extracted with  $\text{EtOAc}$  ( $3 \times 10$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ , 10:1→8:1 petroleum ether: acetone) to furnish compound **29** (122.2 mg, 89%,  $Z:E = 9:1$ ) as a white foam.

**Compound 29:** TLC (petroleum ether:acetone, 3:1 v/v):  $R_f = 0.45$ ;  $[\alpha]_{D}^{25} -23.9$  ( $c$  1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.09 (dd,  $J = 15.3, 11.1$  Hz, 1H), 6.40 (d,  $J = 11.1$  Hz, 1H), 6.21 (dd,  $J = 15.3, 8.1$  Hz, 1H), 4.20 (q,  $J = 7.2$  Hz, 2H), 4.16 (d,  $J = 4.0$  Hz, 1H), 3.10 (s, 1H), 2.76 – 2.54 (m, 3H), 2.36 (dd,  $J = 13.3, 4.3$  Hz, 1H), 2.22 – 2.11 (m, 2H), 2.02 (d,  $J = 5.3$  Hz, 1H), 1.93 (d,  $J = 16.0$  Hz, 1H), 1.92 (s, 3H), 1.86 – 1.71 (m, 3H), 1.82 (d,  $J = 16.0$  Hz, 1H), 1.70 – 1.59 (m, 3H), 1.58 – 1.46 (m, 3H), 1.45 – 1.36 (m, 1H), 1.31 (s, 3H), 1.30 (t,  $J = 7.2$  Hz, 3H), 1.18 (d,  $J = 7.0$  Hz, 3H), 1.10 (s, 3H), 0.77 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  217.1, 173.9, 167.9, 146.1, 141.3, 126.6, 124.2, 99.6, 85.0, 81.0, 72.6, 68.8, 60.2, 59.4, 48.6, 45.8, 43.2, 43.0, 39.0, 38.4, 35.7, 34.7, 33.6, 28.8, 27.7, 26.7, 22.4, 21.1, 20.8, 14.5, 13.9; IR (KBr):  $\nu = 3576, 2974, 2932, 1782, 1734, 1700, 1634, 733$   $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{31}\text{H}_{45}\text{O}_7$ , 529.3160; found, 529.3156.

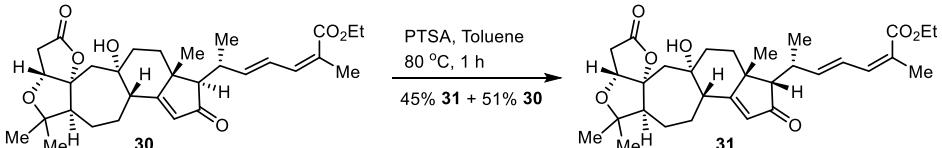


To a solution of ester **29** (90.0 mg, 0.17 mmol, 1.0 equiv) in 2.4 mL DME was added dropwise freshly prepared LDA (1.0 M in THF, 0.51 mL, 0.51 mmol, 3.0 equiv) at -78 °C. After stirred at -78 °C for 0.5 h, 0.3 mL dry THF was added (to avoid freezing of the reaction mixture) and stirring was continued for another 0.5 h. TMSCl (89  $\mu\text{L}$ , 0.68 mmol, 4.0 equiv) was added and the reaction mixture was stirred for 1 h at -78 °C. The reaction mixture was quenched with sat. aq.  $\text{NaHCO}_3$  and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was used directly in the next step.

A solution of the crude silyl enol ether obtained above and  $\text{Pd}(\text{OAc})_2$  (38.2 mg, 0.17 mmol, 1.0 equiv) in 3.0 mL DMSO was stirred at 50 °C for 1 h before quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (5 mL). The reaction mixture was extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated

in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ , 8:1 $\rightarrow$ 6:1 $\rightarrow$ 5:1 petroleum ether:acetone) to furnish compound **30** (49.2 mg, 55%) as a white foam and recovered **29** (35.1 mg, 39%).

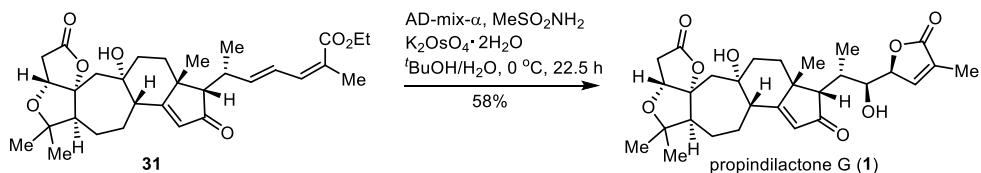
**Compound 30:** TLC (petroleum ether:acetone, 3:1 v/v):  $R_f = 0.29$ ;  $[\alpha]_D^{25} +124.5$  ( $c$  0.47,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.13 (dd,  $J = 15.3, 11.1$  Hz, 1H), 6.42 (d,  $J = 11.1$  Hz, 1H), 6.15 (dd,  $J = 15.3, 8.1$  Hz, 1H), 5.80 (s, 1H), 4.21 (q,  $J = 7.1$  Hz, 2H), 4.18 (d,  $J = 2.2$  Hz, 1H), 3.33 (s, 1H), 2.88 – 2.78 (m, 1H), 2.74 – 2.64 (m, 2H), 2.39 (d,  $J = 13.6$  Hz, 1H), 2.37 (d,  $J = 12.4$  Hz, 1H), 2.28 (d,  $J = 4.3$  Hz, 1H), 2.07 (d,  $J = 15.2$  Hz, 1H), 2.03 – 1.96 (m, 1H), 1.93 (s, 3H), 1.91 – 1.74 (m, 5H), 1.88 (d,  $J = 15.2$  Hz, 1H), 1.58 – 1.52 (m, 1H), 1.34 (s, 3H), 1.31 (t,  $J = 7.2$  Hz, 3H), 1.29 (d,  $J = 7.2$  Hz, 3H), 1.19 (s, 3H), 1.12 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.8, 186.2, 173.6, 167.9, 145.4, 141.1, 127.1, 126.9, 124.3, 98.9, 84.7, 80.9, 75.2, 64.7, 60.3, 60.0, 50.1, 47.2, 45.2, 38.0, 35.8, 35.5, 35.3, 28.5, 26.8, 25.3, 22.0, 21.8, 21.3, 20.8, 14.5; IR (KBr):  $\nu = 3570, 2927, 2868, 1781, 1693, 1633, 1614, 738$   $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{31}\text{H}_{43}\text{O}_7$ , 527.3003; found, 527.3008.



To a solution of **30** (60.0 mg, 0.11 mmol, 1.0 equiv) in 5.7 mL toluene was added PTSA (4.3 mg, 0.023 mmol, 0.2 equiv). After the reaction mixture was stirred at 80 °C for 1 h, the reaction mixture was quenched with sat. aq.  $\text{NaHCO}_3$  (4 mL) and extracted with  $\text{EtOAc}$  ( $3 \times 10$  mL). The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ , 30:1 $\rightarrow$ 25:1 DCM:acetone) to furnish compound **31** (27.0 mg, 45%) as a yellow foam and recovered **30** (30.6 mg, 51%).

**Compound 31:** TLC (DCM:acetone, 8:1 v/v):  $R_f = 0.64$ ;  $[\alpha]_D^{25} +153.6$  ( $c$  0.41,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.10 (dd,  $J = 15.3, 11.1$  Hz, 1H), 6.43 (d,  $J = 11.2$  Hz, 1H), 6.13 (dd,  $J = 15.3, 7.9$  Hz, 1H), 5.79 (s, 1H), 4.21 (q,  $J = 7.1$  Hz, 2H), 4.18 (d,  $J =$

4.7 Hz, 1H), 3.33 (s, 1H), 2.84 – 2.74 (m, 1H), 2.73 – 2.64 (m, 2H), 2.43 – 2.34 (m, 2H), 2.23 (d,  $J$  = 4.6 Hz, 1H), 2.15 (td,  $J$  = 13.1, 4.3 Hz, 1H), 2.07 (d,  $J$  = 15.2 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.94 (s, 3H), 1.92 – 1.78 (m, 3H), 1.89 (d,  $J$  = 15.2 Hz, 1H), 1.65 – 1.60 (m, 1H), 1.51 (dt,  $J$  = 12.9, 2.6 Hz, 1H), 1.34 (s, 3H), 1.31 (t,  $J$  = 7.1 Hz, 3H), 1.26 (s, 3H), 1.13 (d,  $J$  = 6.8 Hz, 3H), 1.12 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  209.1, 187.3, 173.5, 167.9, 146.2, 141.0, 127.1, 126.1, 124.7, 98.9, 84.7, 80.9, 75.5, 62.7, 60.3, 60.1, 50.4, 46.1, 45.2, 38.2, 36.2, 35.3, 29.1, 28.4, 27.3, 26.8, 25.4, 21.9, 20.8, 17.6, 14.5; IR (KBr):  $\nu$  = 3570, 2926, 1782, 1693, 1614, 1455, 808, 736  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ): [M+H] $^+$  calcd for  $\text{C}_{31}\text{H}_{43}\text{O}_7$ , 527.3003; found, 527.3004.



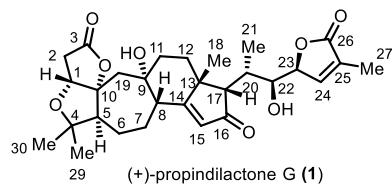
A solution of AD-mix- $\alpha$  (41.0 mg, 0.03 mmol, 1.0 equiv),  $\text{MeSO}_2\text{NH}_2$  (2.9 mg, 0.03 mmol, 1.0 equiv) and  $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$  (0.3 mg, 0.9  $\mu\text{mol}$ , 0.03 equiv) in  ${}^{\prime}\text{BuOH}$  and water (2.4 mL, 1:1, v/v) was stirred at room temperature for 10 min and 0  $^{\circ}\text{C}$  for 10 min. The yellow reaction mixture was transferred into a reaction tube containing **31** (16.0 mg, 0.03 mmol, 1.0 equiv) at 0  $^{\circ}\text{C}$ . The reaction mixture was stirred at 0  $^{\circ}\text{C}$  for 22.5 h and quenched with sat. aq.  $\text{Na}_2\text{S}_2\text{O}_3$ . The aqueous layer was extracted with  $\text{EtOAc}$  ( $3 \times 15$  mL) and the combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuo. The residue was purified by flash chromatography ( $\text{SiO}_2$ , 60:1 → 50:1 DCM:MeOH) to furnish propindilactone **G** (**1**) (9.1 mg, 58%) as a white solid.

**Propindilactone G (1):** mp: 241.4 – 242.5  $^{\circ}\text{C}$ ; TLC (DCM:acetone, 6:1 v/v):  $R_f$  = 0.14;  $[\alpha]_D^{25}$  +59.6 ( $c$  0.15, MeOH);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.11 (s, 1H), 5.83 (s, 1H), 4.99 (q,  $J$  = 2.2 Hz, 1H), 4.24 (d,  $J$  = 5.5 Hz, 1H), 4.19 (d,  $J$  = 4.2 Hz, 1H), 4.00 (dd,  $J$  = 6.4, 4.8 Hz, 1H), 3.42 (s, 1H), 2.85 (s, 1H), 2.80 – 2.64 (m, 2H), 2.44 (d,  $J$  = 11.5 Hz, 1H), 2.37 (dd,  $J$  = 13.4, 4.5 Hz, 1H), 2.23 – 2.14 (m, 2H), 2.10 (d,  $J$  = 15.1 Hz, 1H),

2.06 – 1.98 (m, 1H), 1.95 (s, 3H), 1.94 – 1.77 (m, 4H), 1.70 – 1.62 (m, 1H), 1.47 – 1.35 (m, 2H), 1.35 (s, 3H), 1.29 (s, 3H), 1.13 (s, 3H), 0.99 (d,  $J$  = 7.0 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  211.7, 191.3, 174.6, 173.6, 147.3, 130.7, 126.6, 98.8, 84.7, 83.0, 80.9, 75.8, 74.0, 60.1, 57.5, 50.7, 45.7, 45.0, 38.1, 35.2, 34.3, 28.37, 28.39, 27.3, 26.7, 25.3, 21.9, 15.5, 11.0;  $^1\text{H}$  NMR (400 MHz,  $\text{C}_5\text{D}_5\text{N}$ )  $\delta$  7.12 (brs, 1H), 6.83 (d,  $J$  = 7.5 Hz, 1H), 6.08 (d,  $J$  = 1.5 Hz, 1H), 5.26 (s, 1H), 5.06 (s, 1H), 4.72 (t,  $J$  = 7.5 Hz, 1H), 4.25 (d,  $J$  = 4.9 Hz, 1H), 3.40 (d,  $J$  = 1.6 Hz, 1H), 3.01 (dd,  $J$  = 18.0, 5.1 Hz, 1H), 2.76 (d,  $J$  = 18.0 Hz, 1H), 2.64 – 2.55 (m, 1H), 2.53 – 2.47 (m, 1H), 2.46 (dd,  $J$  = 13.5, 4.0 Hz, 1H), 2.46 – 2.39 (m, 1H), 2.22 (ABd,  $J$  = 15.3 Hz, 1H), 2.08 (ABd,  $J$  = 15.4 Hz, 1H), 1.98 – 1.92 (m, 1H), 1.94 – 1.85 (m, 1H), 1.90 – 1.83 (m, 1H), 1.83 (s, 3H), 1.69 – 1.62 (m, 1H), 1.63 – 1.58 (m, 1H), 1.39 – 1.31 (m, 1H), 1.29 (s, 3H), 1.26 (d,  $J$  = 6.8 Hz, 3H), 1.25 (s, 3H), 1.22 – 1.16 (m, 1H), 1.09 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{C}_5\text{D}_5\text{N}$ )  $\delta$  211.0, 191.0, 175.2, 175.2, 149.3, 130.1, 127.3, 99.3, 84.7, 82.3, 81.8, 75.6, 72.1, 60.1, 57.7, 50.2, 45.7, 45.6, 38.1, 36.6, 36.1, 29.1, 28.3, 28.0, 26.8, 26.6, 22.5, 14.1, 10.9. IR (KBr):  $\nu$  = 3563, 3457, 2971, 2927, 1749, 1667, 1608, 734  $\text{cm}^{-1}$ ; HRMS (ESI,  $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{29}\text{H}_{39}\text{O}_8$ , 515.2639; found, 515.2643.

#### 4. NMR comparison of synthetic and natural propindilactone G

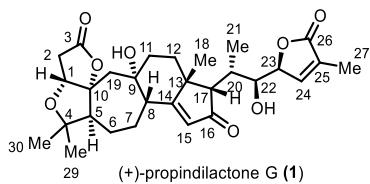
##### <sup>1</sup>H NMR data comparison of synthetic and natural propindilactone G



position	natural sample <sup>2</sup> (500 MHz in C <sub>5</sub> D <sub>5</sub> N)	our synthetic sample (400 MHz in C <sub>5</sub> D <sub>5</sub> N)	$\Delta \delta$	Yang's synthetic sample <sup>3</sup> (400 MHz in C <sub>5</sub> D <sub>5</sub> N)
1	4.25 (d, 4.5)	4.25 (d, 4.9)	0	4.25 (d, 5.0)
2 $\alpha$	2.75 (d, 17.5)	2.76 (d, 18.0)	0.01	2.75 (d, 18.0)
2 $\beta$	3.01 (dd, 17.5, 4.5)	3.01 (dd, 18.0, 5.1)	0	3.01 (dd, 18.0, 5.1)
5	2.45 (dd, 13.5, 4.0)	2.46 (dd, 13.5, 4.0)	0.01	2.46 (dd, 13.5, 3.9)
6 $\alpha$	1.63 – 1.55 (m)	1.63 – 1.58 (m)	0.01	1.63 – 1.59 (m)
6 $\beta$	1.34 – 1.32 (m)	1.39 – 1.31 (m)	0.02	1.38 – 1.33 (m)
7 $\alpha$	1.92 (m)	1.98 – 1.92 (m)	0.03	1.97 – 1.92 (m)
7 $\beta$	1.88 (m)	1.94 – 1.85 (m)	0.02	1.92 – 1.88 (m)
8	2.51 – 2.46 (m)	2.53 – 2.47 (m)	0.01	2.52 – 2.47 (m)
11 $\alpha$	1.91 – 1.83 (m)	1.90 – 1.83 (m)	0	1.96 – 1.85 (m)
11 $\beta$	1.66 – 1.60 (m)	1.69 – 1.62 (m)	0.02	1.69 – 1.63 (m)
12 $\alpha$	2.34 (m)	2.46 – 2.39 (m)	0.08	2.43 – 2.34 (m)
12 $\beta$	1.64 – 1.61 (m)	1.22 – 1.16 (m) <sup>a</sup>	-	1.64 – 1.61 (m)
15	6.07 (s)	6.08 (d, 1.5)	0.01	6.08 (d, 1.1)
17	3.38 (s)	3.40 (d, 1.6)	0.02	3.39 (d, 1.3)
18	1.24 (s)	1.25 (s)	0.01	1.24 (s)
19 $\alpha$	2.20 (ABd, 15.5)	2.22 (ABd, 15.3)	0.02	2.22 (ABd, 15.3)
19 $\beta$	2.10 (ABd, 15.5)	2.08 (ABd, 15.4)	-	2.08 (ABd, 15.3)
20	2.60 – 2.55 (m)	2.64 – 2.55 (m)	0.02	2.63 – 2.55 (m)
21	1.25 (d, 7.5)	1.26 (d, 6.8)	0.01	1.26 (d, 6.7)
22	4.72 (d, 9.0)	4.72 (t, 7.5) <sup>b</sup>	0	4.71 (d, 8.3)
23	5.26 (brs)	5.26 (s)	0	5.26 (d, 8.3)
24	7.12 (brs)	7.12 (brs)	0	7.11-7.12
27	1.83 (s)	1.83 (s)	0	1.83 (s)
29	1.09 (s)	1.09 (s)	0	1.09 (s)
30	1.28 (s)	1.29 (s)	0.01	1.29 (s)
9-OH	-	5.06 (s)	-	-
22-OH	-	6.83 (d, 7.5)	-	-

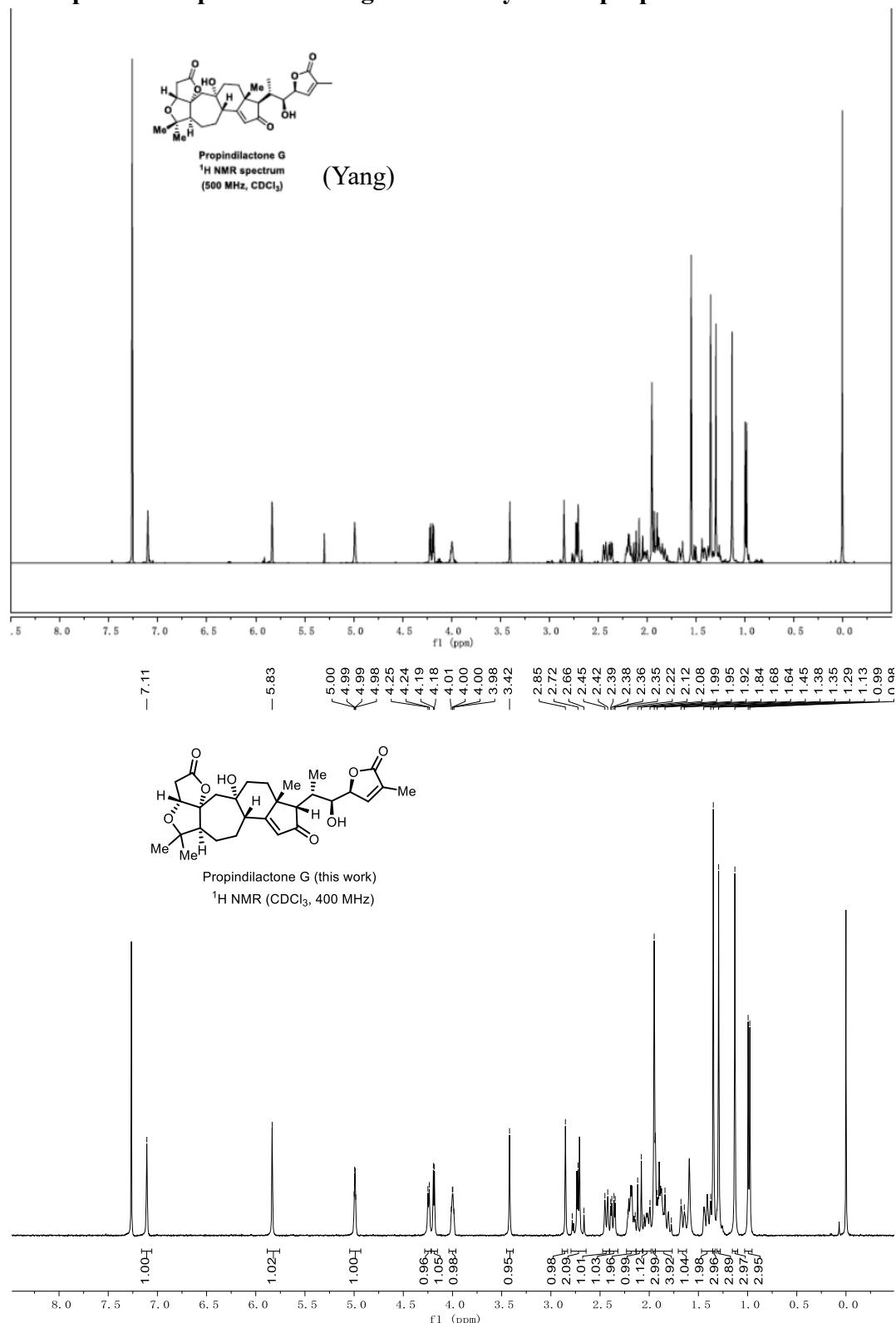
<sup>a</sup>The chemical shift of 12 $\beta$ -H, despite different from literature's reported value, was determined by HSQC spectrum (see page S108 for details). <sup>b</sup>When D<sub>2</sub>O was added to the synthetic sample of propindilactone G in C<sub>5</sub>D<sub>5</sub>N, the signal of C22-H changed from triplet ( $J = 7.5$  Hz) to doublet ( $J = 8.8$  Hz).

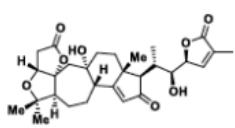
**<sup>13</sup>C NMR data comparison of synthetic and natural (+)-propindilactone G**



position	natural sample <sup>2</sup> (126 MHz in C <sub>5</sub> D <sub>5</sub> N)	our synthetic sample (151 MHz in C <sub>5</sub> D <sub>5</sub> N)	Δ δ	Yang's synthetic sample <sup>3</sup> (126 MHz in C <sub>5</sub> D <sub>5</sub> N)
1	81.8	81.8	0	81.9
2	36.1	36.1	0	36.2
3	175.3	175.2	-0.1	175.2
4	84.7	84.7	0	84.8
5	60.1	60.1	0	60.2
6	26.5	26.8	0.3	26.7
7	26.8	26.6	-0.2	26.9
8	50.1	50.2	0.1	50.3
9	75.7	75.6	-0.1	75.8
10	99.4	99.3	-0.1	99.4
11	38.0	38.1	0.1	38.2
12	28.4	28.3	-0.1	28.5
13	45.7	45.7	0	45.8
14	191.1	191.0	-0.1	191.0
15	127.2	127.3	0.1	127.4
16	211.2	211.0	-0.2	211.0
17	57.8	57.7	-0.1	57.9
18	27.9	28.0	0.1	28.0
19	45.6	45.6	0	45.8
20	36.5	36.6	0.1	36.6
21	14.1	14.1	0	14.3
22	72.2	72.1	-0.1	72.4
23	82.3	82.3	0	82.4
24	149.3	149.3	0	149.3
25	130.1	130.1	0	130.2
26	175.3	175.2	-0.1	175.2
27	10.8	10.9	0.1	10.9
29	22.5	22.5	0	22.6
30	29.0	29.1	0.1	29.2

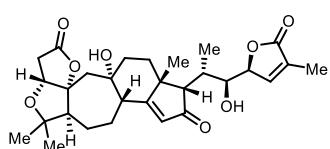
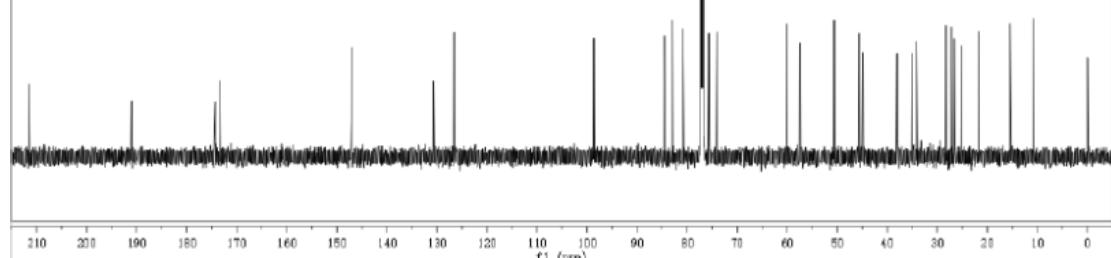
**NMR spectra comparison of Yang's and our synthetic propindilactone G in  $\text{CDCl}_3$**



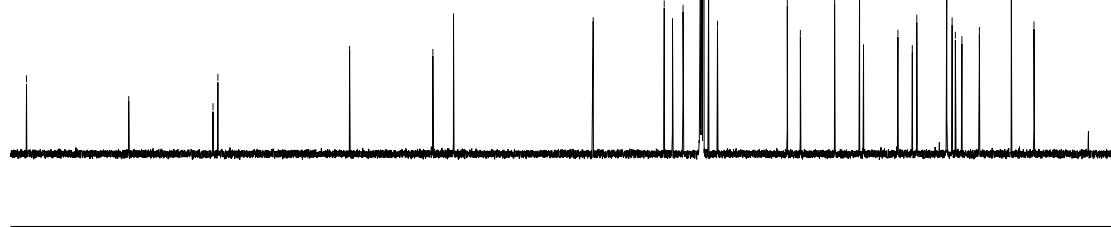


Propindilactone G  
 $^{13}\text{C}$  NMR spectrum  
(126 MHz,  $\text{CDCl}_3$ )

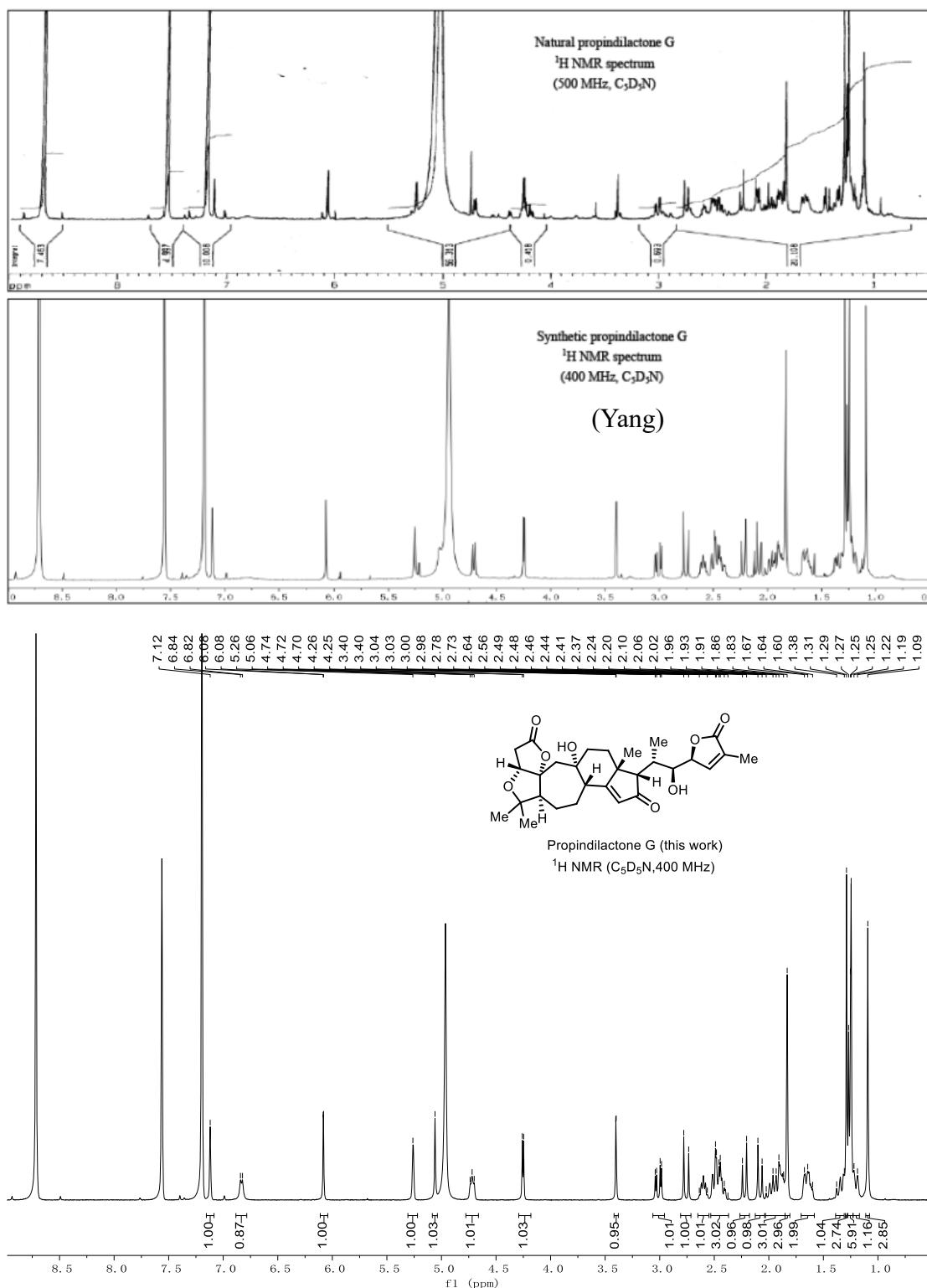
(Yang)



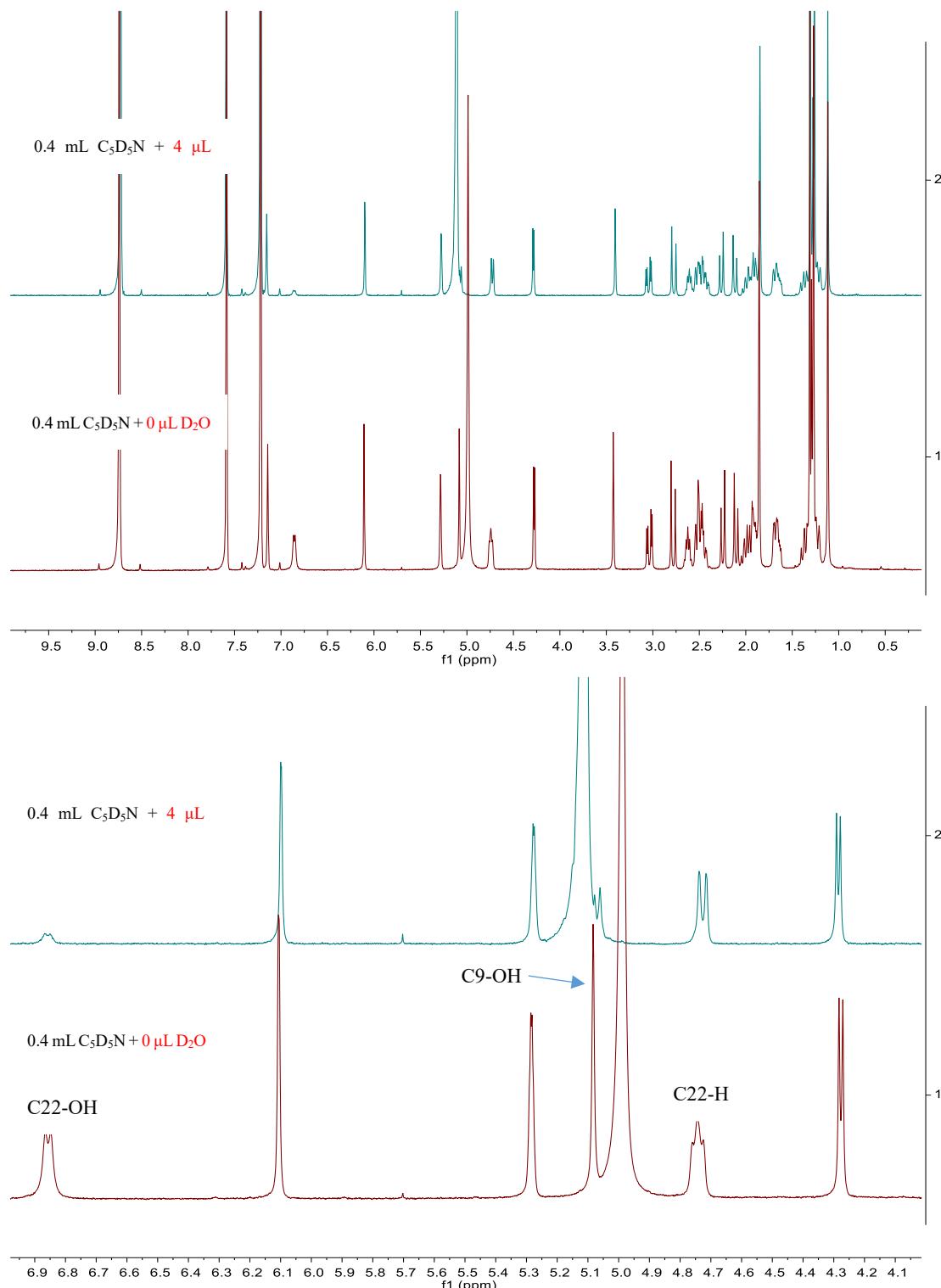
Propindilactone G (this work)  
 $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 101 MHz)

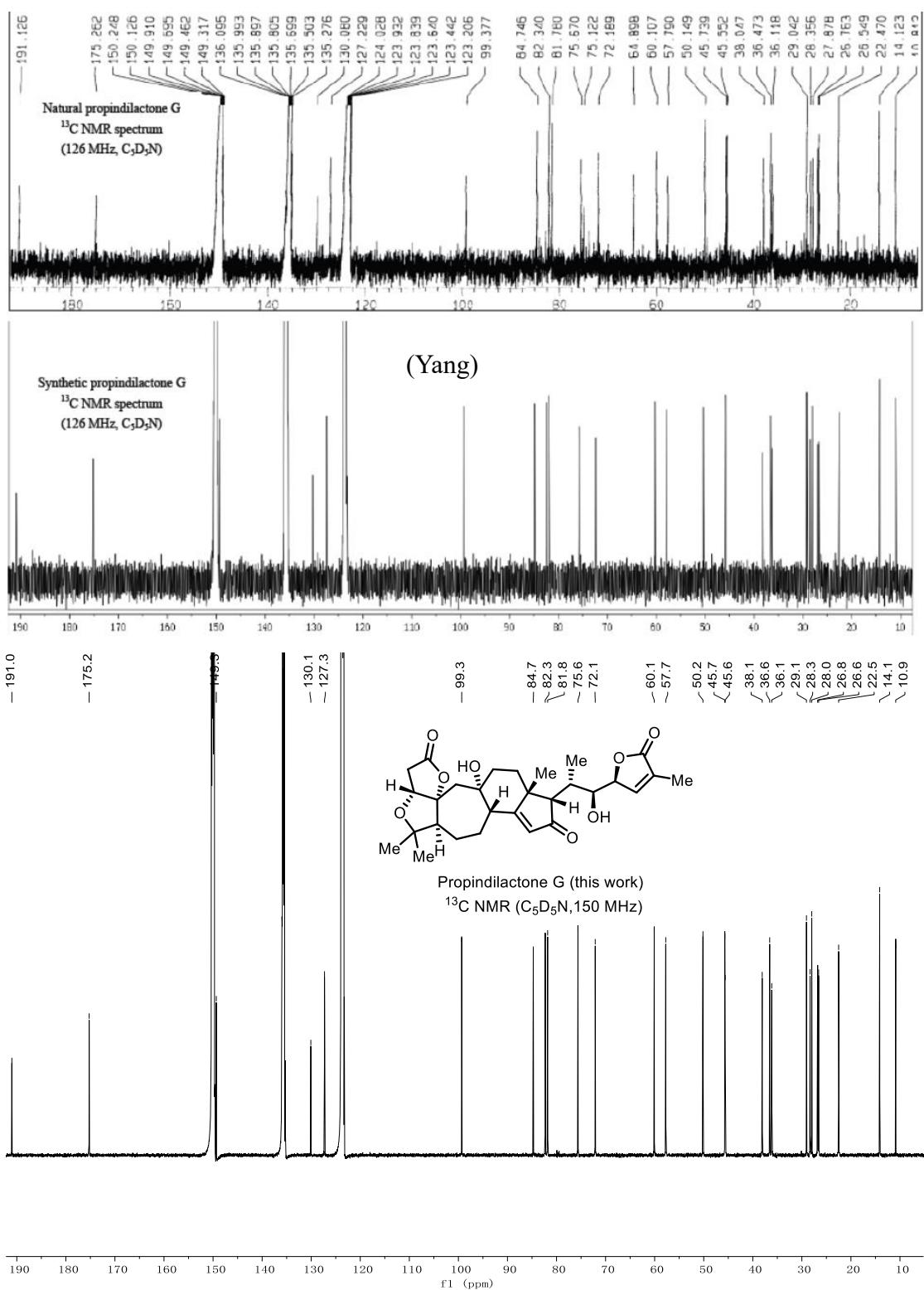


## NMR spectra comparison of natural and synthetic propindilactone G in C<sub>5</sub>D<sub>5</sub>N

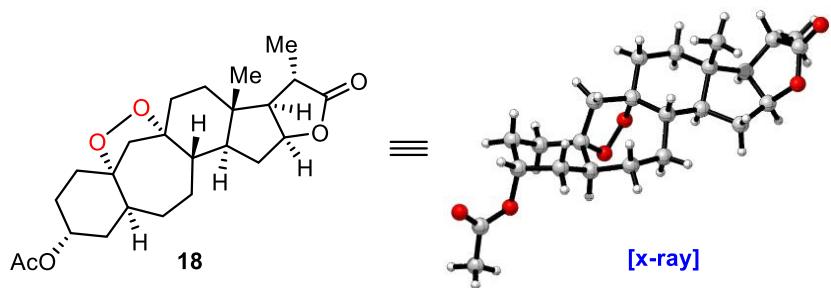


**Note:** When D<sub>2</sub>O was added to the synthetic sample of propindilactone G in C<sub>5</sub>D<sub>5</sub>N, the <sup>1</sup>H NMR signals of C22-OH ( $\delta$  6.83 ppm) and C9-OH ( $\delta$  5.06 ppm) disappeared and the signal of C22-H changed from triplet ( $J = 7.5$  Hz) to doublet ( $J = 8.8$  Hz).





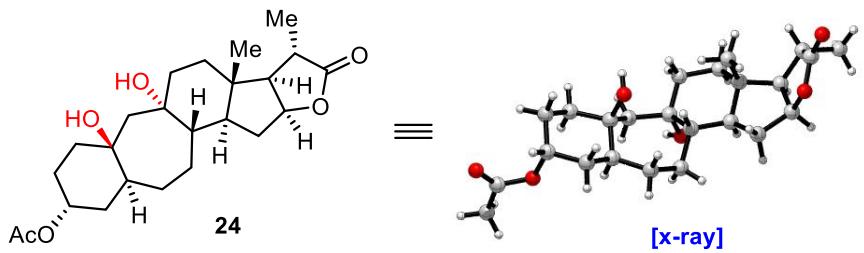
## 5. X-ray crystallographic data for compounds 18 and 24



**Table S1. Crystal data and structure refinement for CCDC 1970045**

Identification code	CCDC 1970045	
Empirical formula	C <sub>24</sub> H <sub>34</sub> O <sub>6</sub>	
Formula weight	418.51	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.7822(5) Å	a= 90°.
	b = 14.2070(11) Å	b= 90°.
	c = 26.733(2) Å	g = 90°.
Volume	2196.1(3) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.266 Mg/m <sup>3</sup>	
Absorption coefficient	0.729 mm <sup>-1</sup>	
F(000)	904	
Crystal size	0.190 x 0.100 x 0.060 mm <sup>3</sup>	
Theta range for data collection	3.523 to 64.979°.	
Index ranges	-5<=h<=6, -16<=k<=16, -31<=l<=29	
Reflections collected	10368	
Independent reflections	3676 [R(int) = 0.0782]	
Completeness to theta = 67.679°	93.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7533 and 0.4242	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	3676 / 0 / 274	
Goodness-of-fit on F <sup>2</sup>	1.037	
Final R indices [I>2sigma(I)]	R1 = 0.0805, wR2 = 0.2093	
R indices (all data)	R1 = 0.0930, wR2 = 0.2270	

Absolute structure parameter	0.3(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.350 and -0.308 e. $\text{\AA}^{-3}$

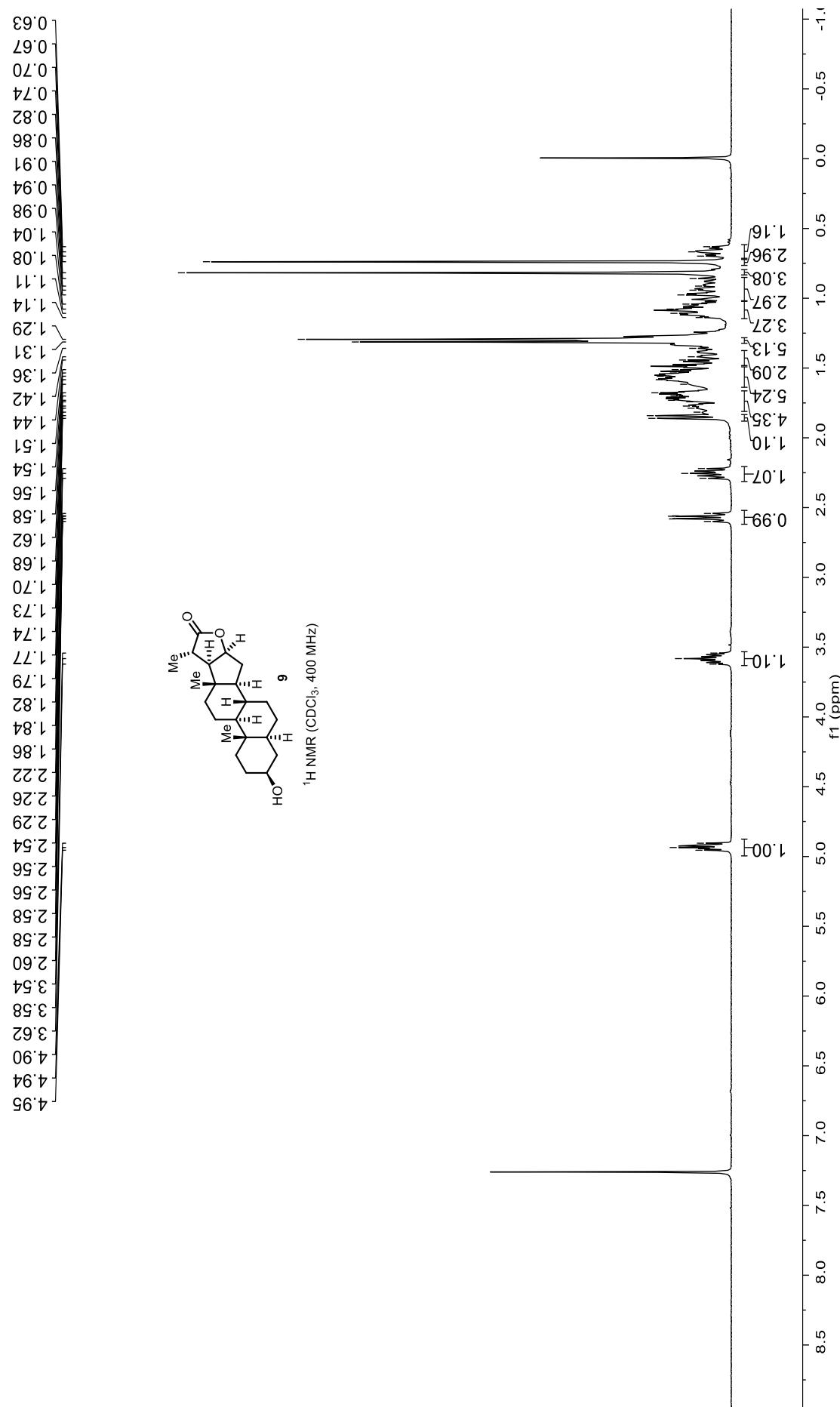


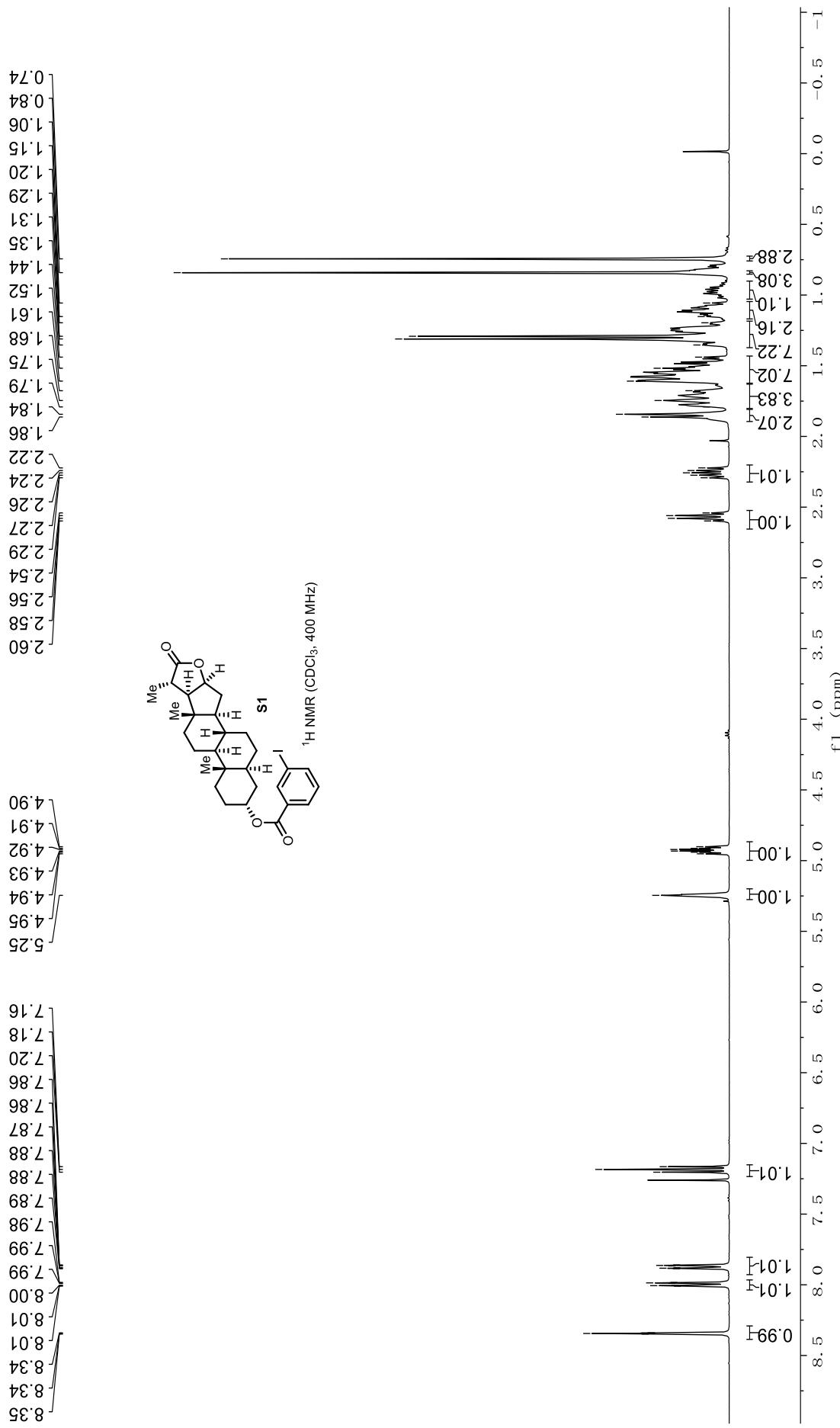
**Table S2. Crystal data and structure refinement for CCDC 1970046**

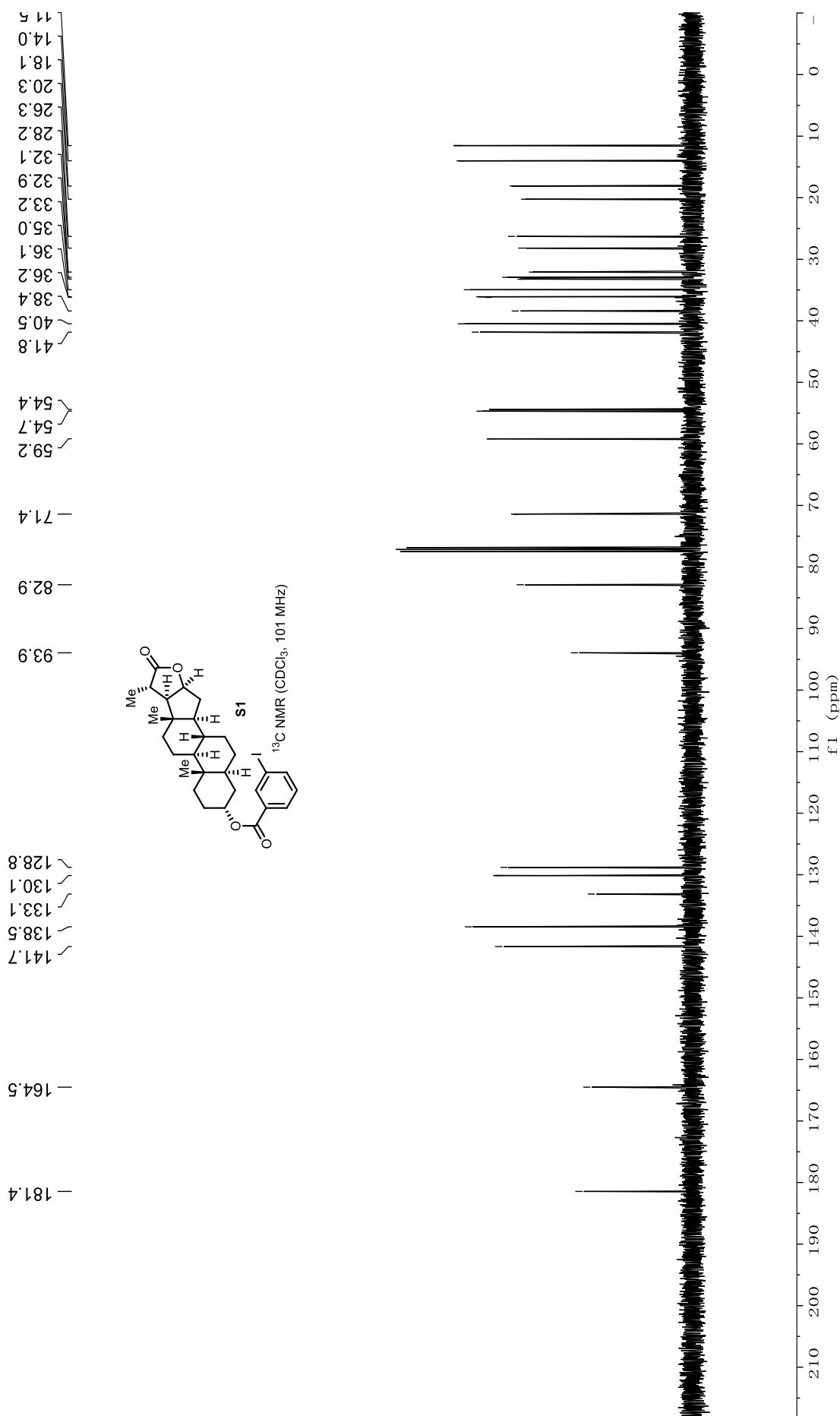
Identification code	CCDC 1970046					
Empirical formula	C <sub>24</sub> H <sub>38</sub> O <sub>7</sub>					
Formula weight	438.54					
Temperature	293(2) K					
Wavelength	1.54178 Å					
Crystal system	Orthorhombic					
Space group	P 21 21 21					
Unit cell dimensions	a = 6.2210(4) Å	a= 90°.	b = 18.4005(11) Å	b= 90°.	c = 20.3992(15) Å	g = 90°.
Volume	2335.1(3) Å <sup>3</sup>					
Z	4					
Density (calculated)	1.247 Mg/m <sup>3</sup>					
Absorption coefficient	0.738 mm <sup>-1</sup>					
F(000)	952					
Crystal size	0.140 x 0.100 x 0.050 mm <sup>3</sup>					
Theta range for data collection	3.234 to 65.462°.					
Index ranges	-7<=h<=7, -21<=k<=21, -23<=l<=24					
Reflections collected	15047					
Independent reflections	4001 [R(int) = 0.2107]					
Completeness to theta = 67.679°	94.8 %					
Absorption correction	Semi-empirical from equivalents					
Max. and min. transmission	0.7533 and 0.4035					
Refinement method	Full-matrix least-squares on F <sup>2</sup>					
Data / restraints / parameters	4001 / 0 / 289					
Goodness-of-fit on F <sup>2</sup>	1.044					
Final R indices [I>2sigma(I)]	R1 = 0.0667, wR2 = 0.1709					
R indices (all data)	R1 = 0.1384, wR2 = 0.2302					
Absolute structure parameter	-0.2(3)					

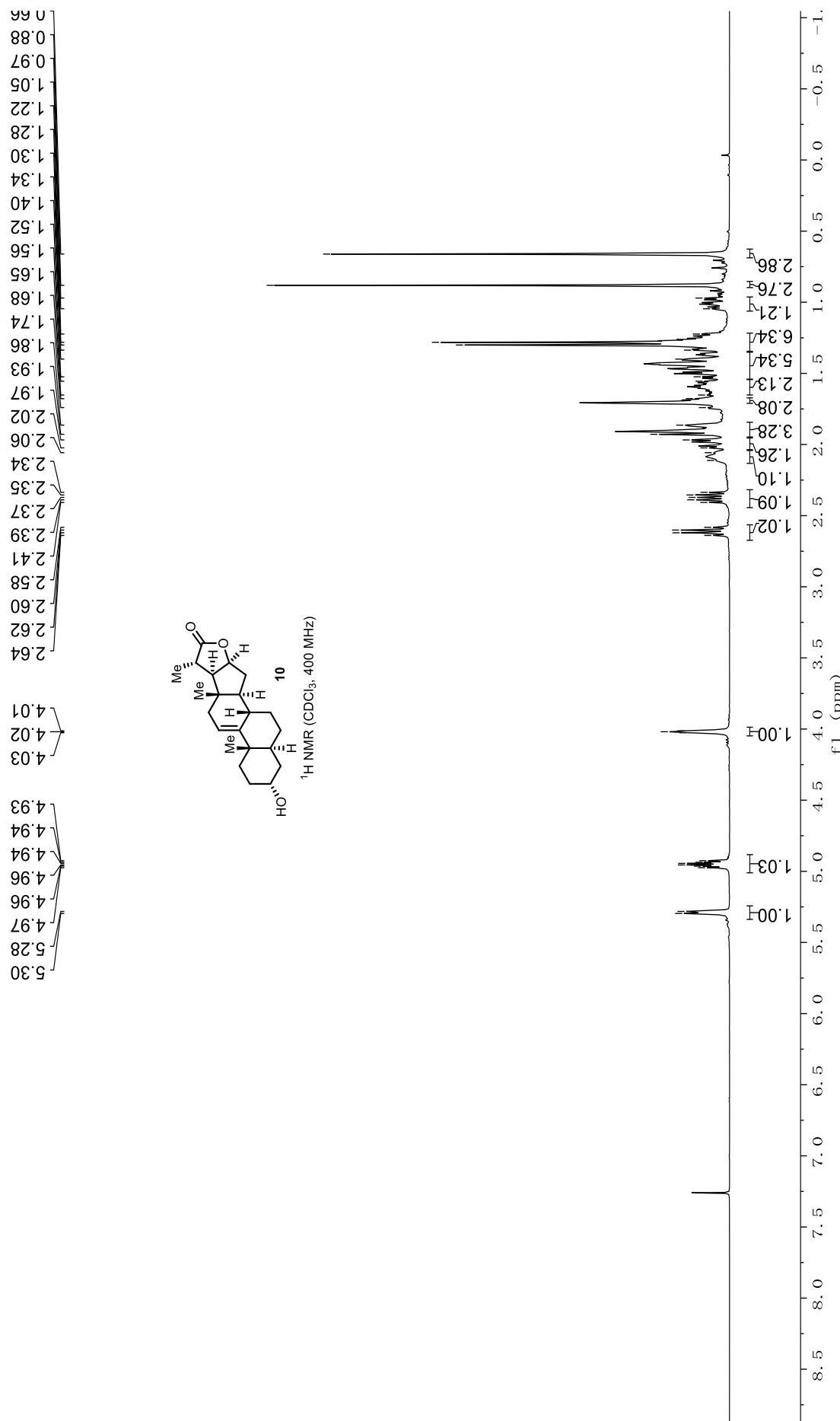
Extinction coefficient	0.0081(15)
Largest diff. peak and hole	0.343 and -0.290 e. $\text{\AA}^{-3}$

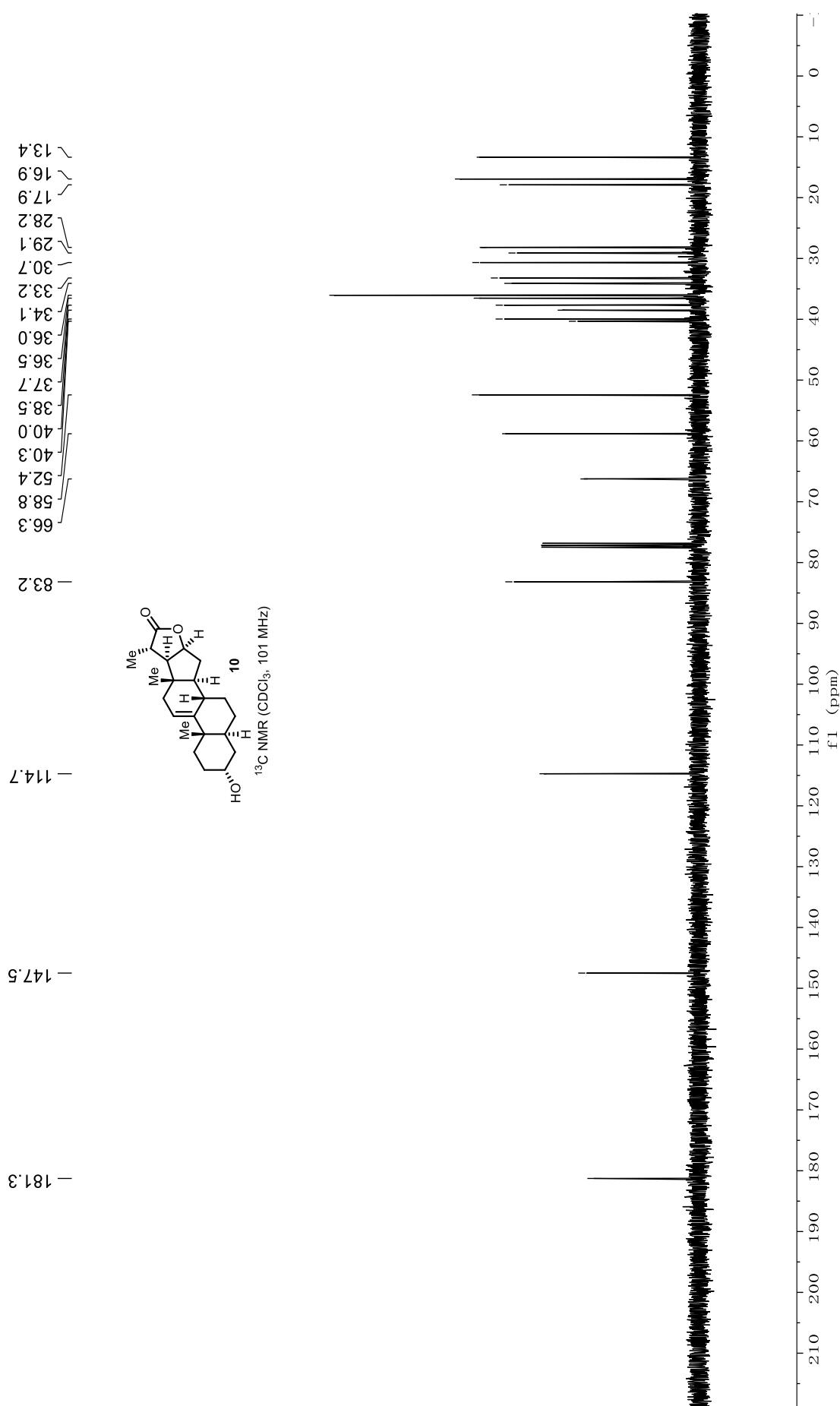
## 6. NMR spectra

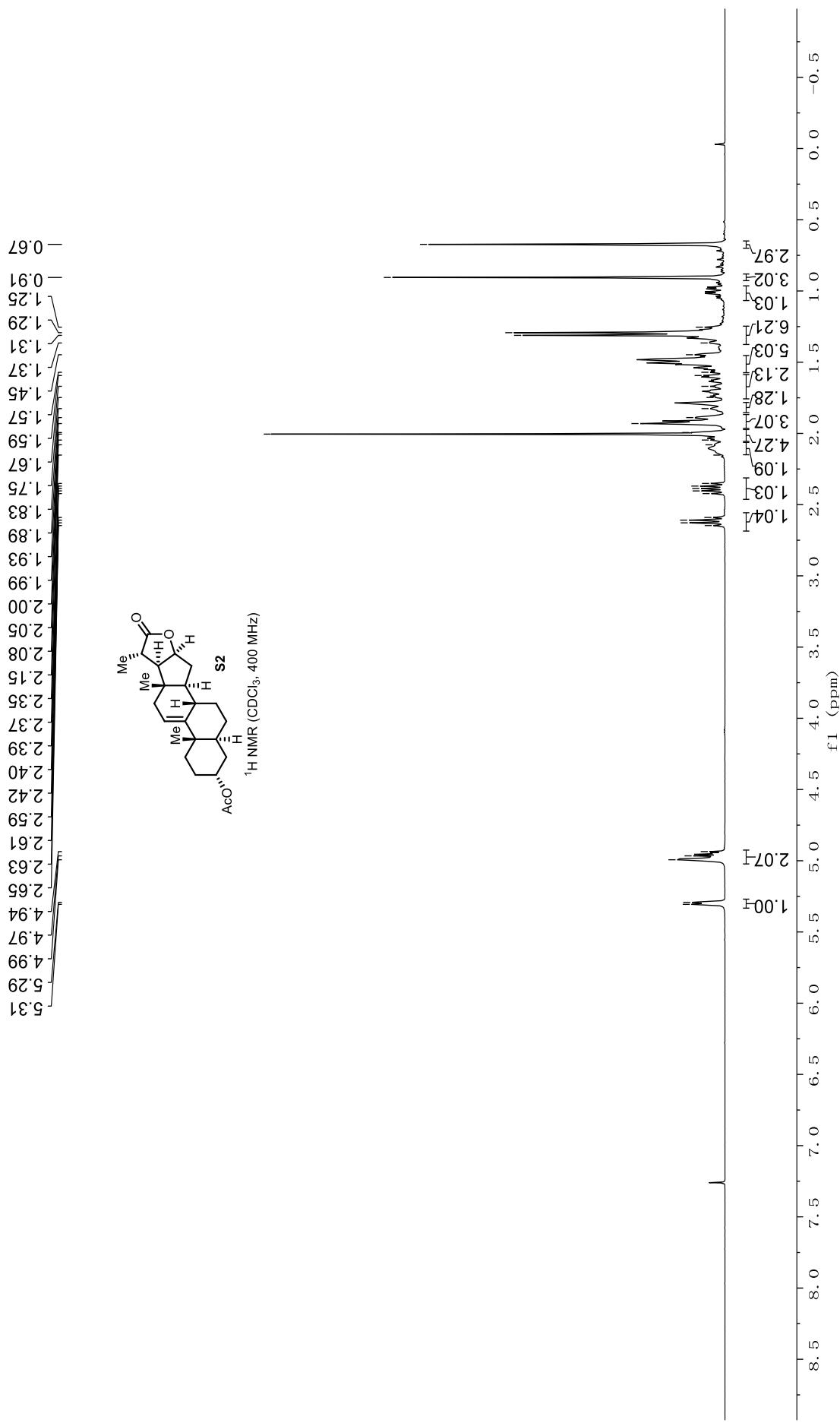


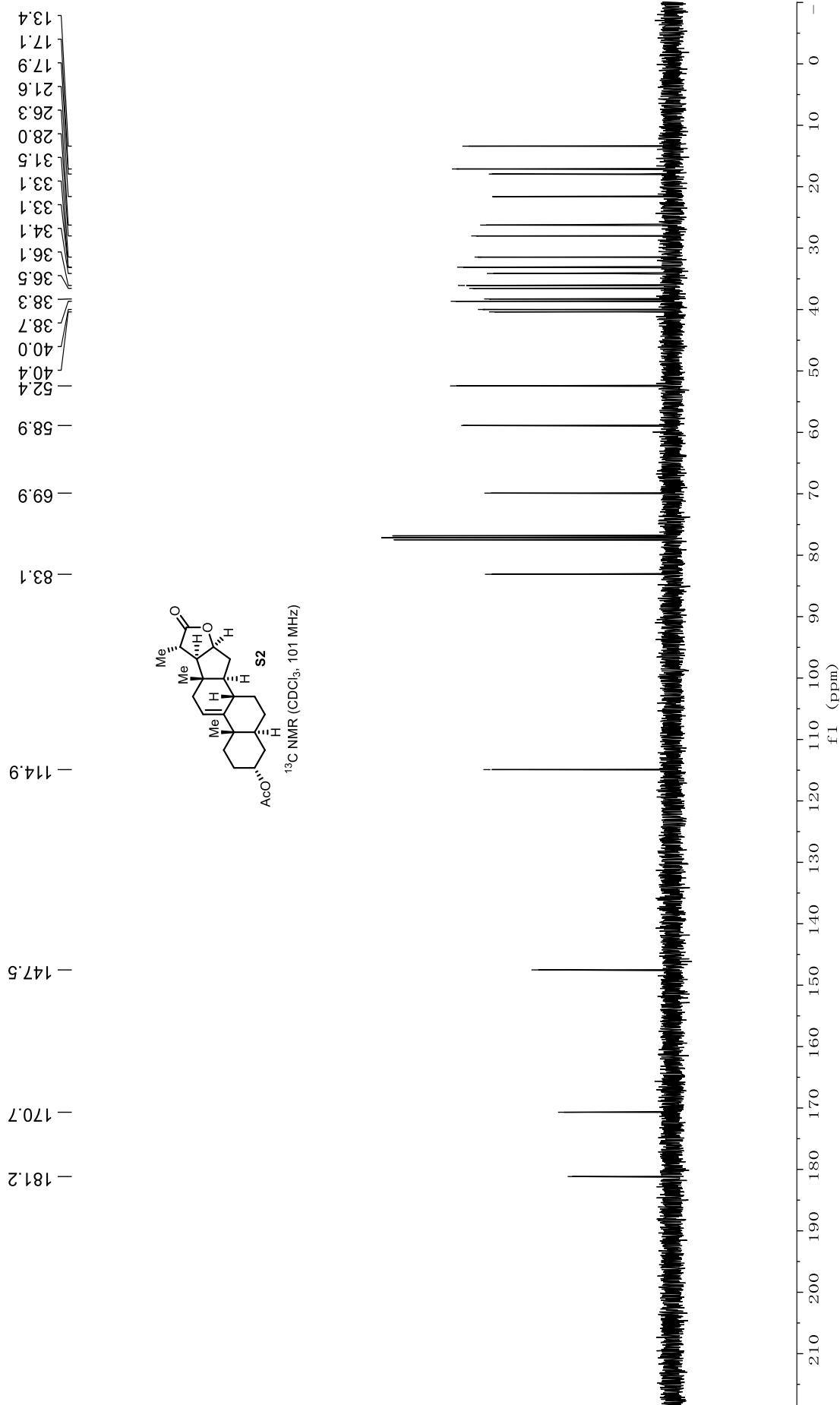


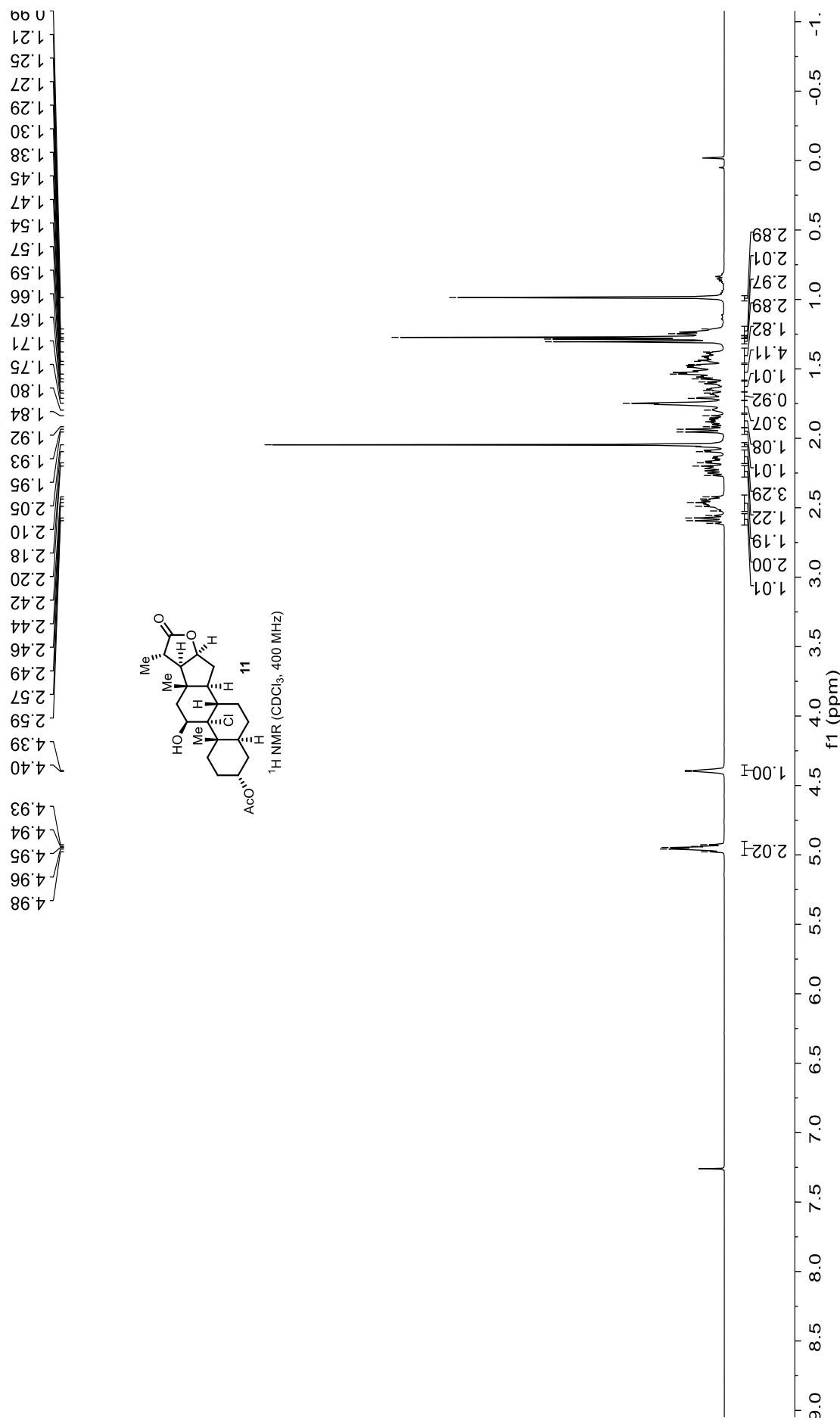


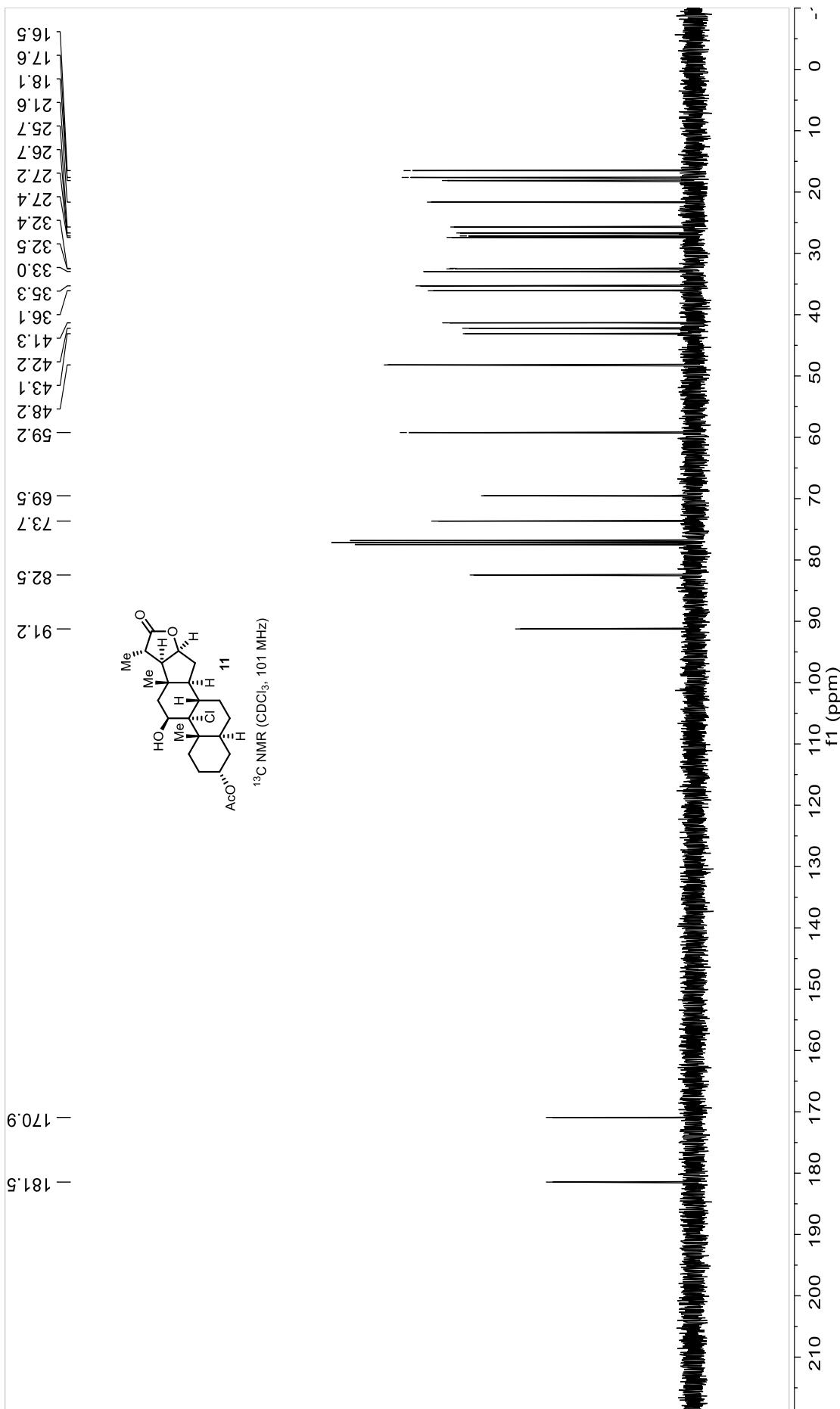


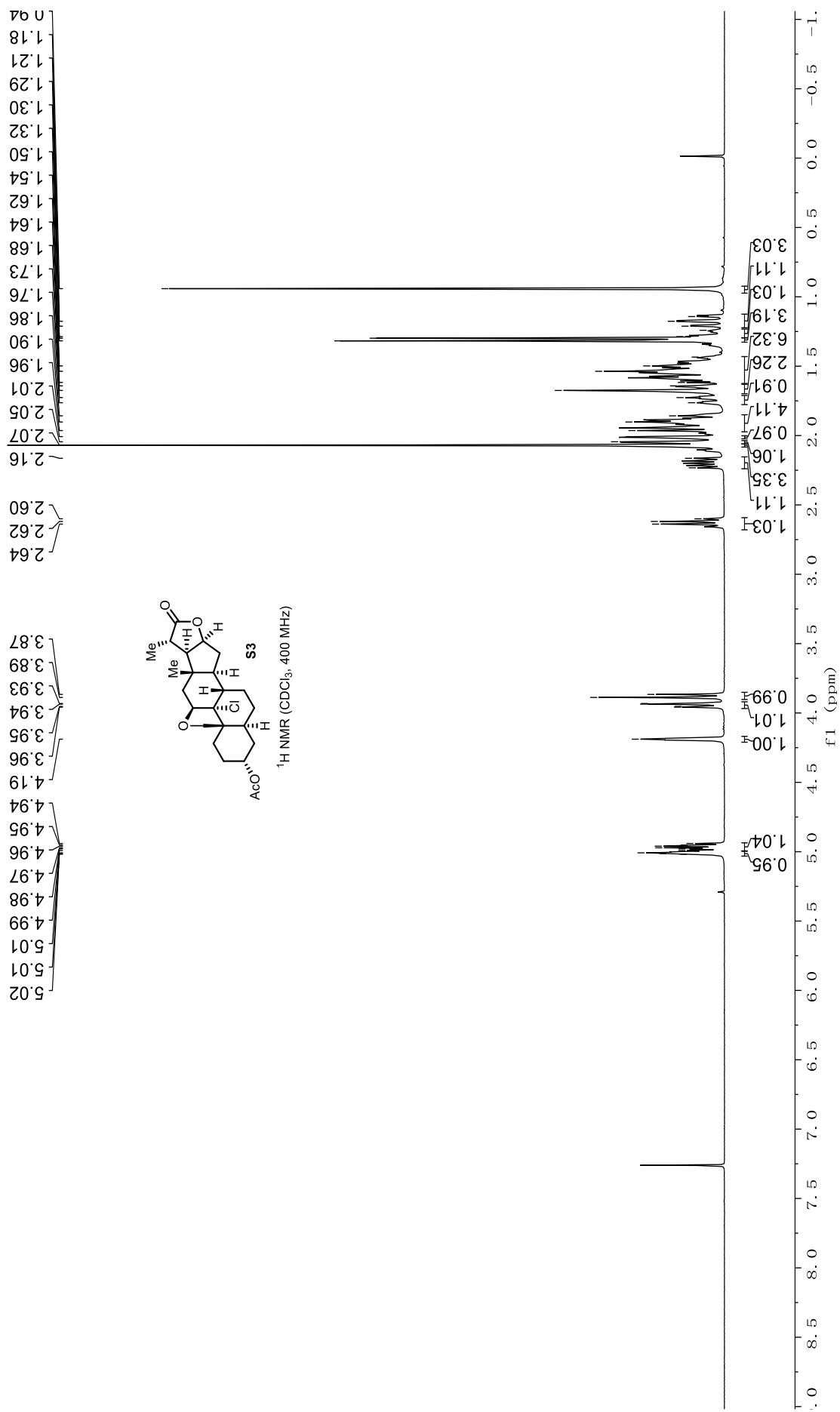


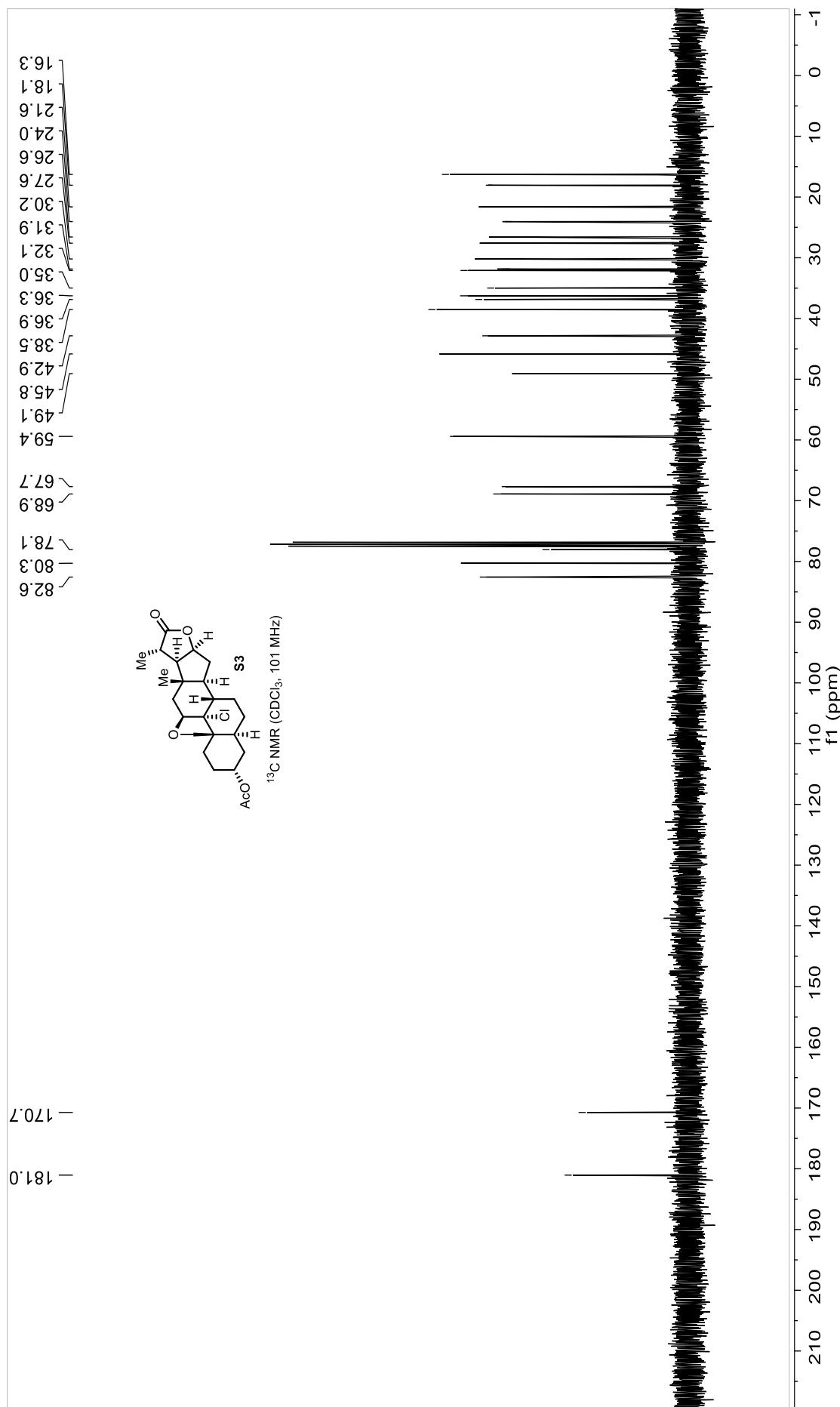


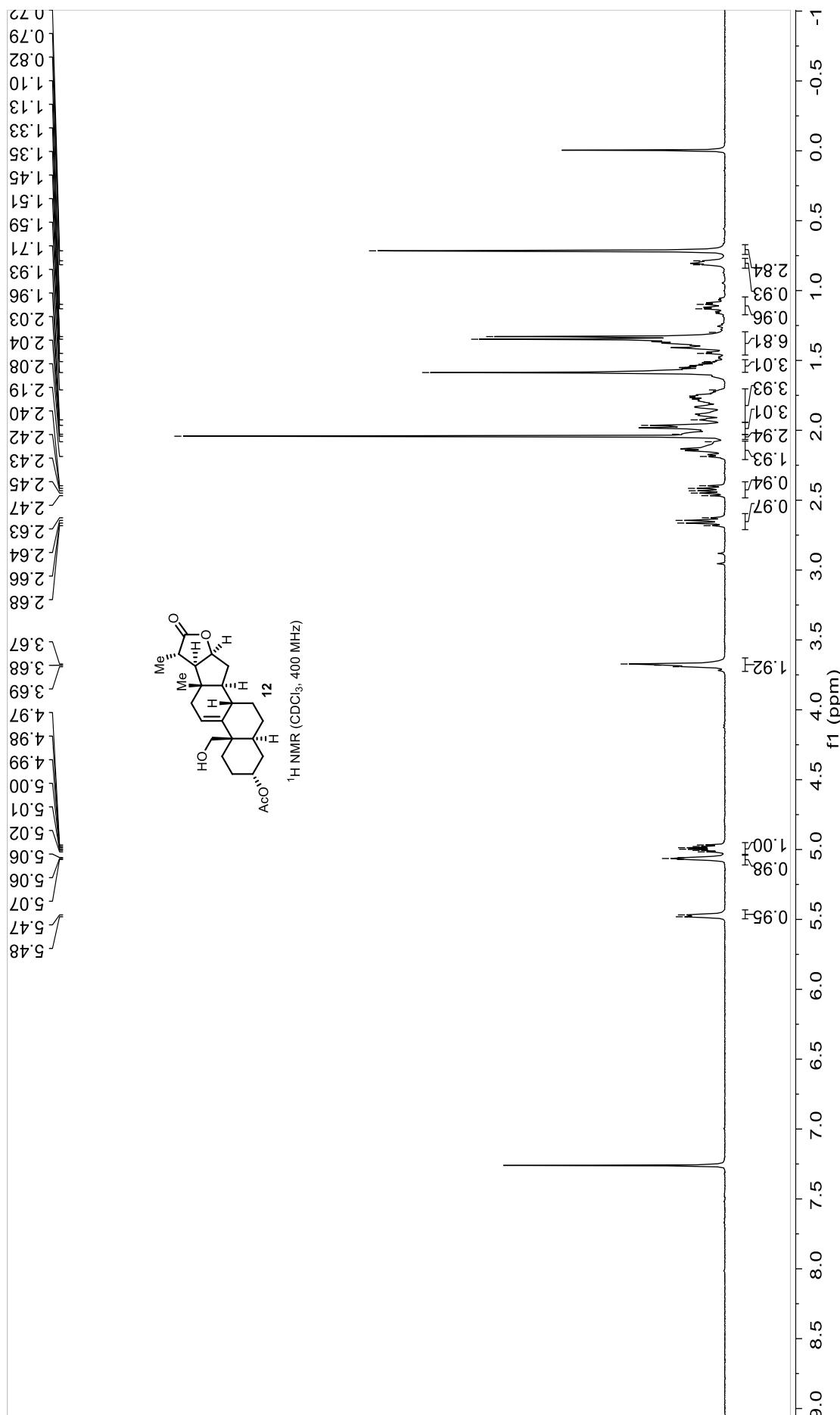


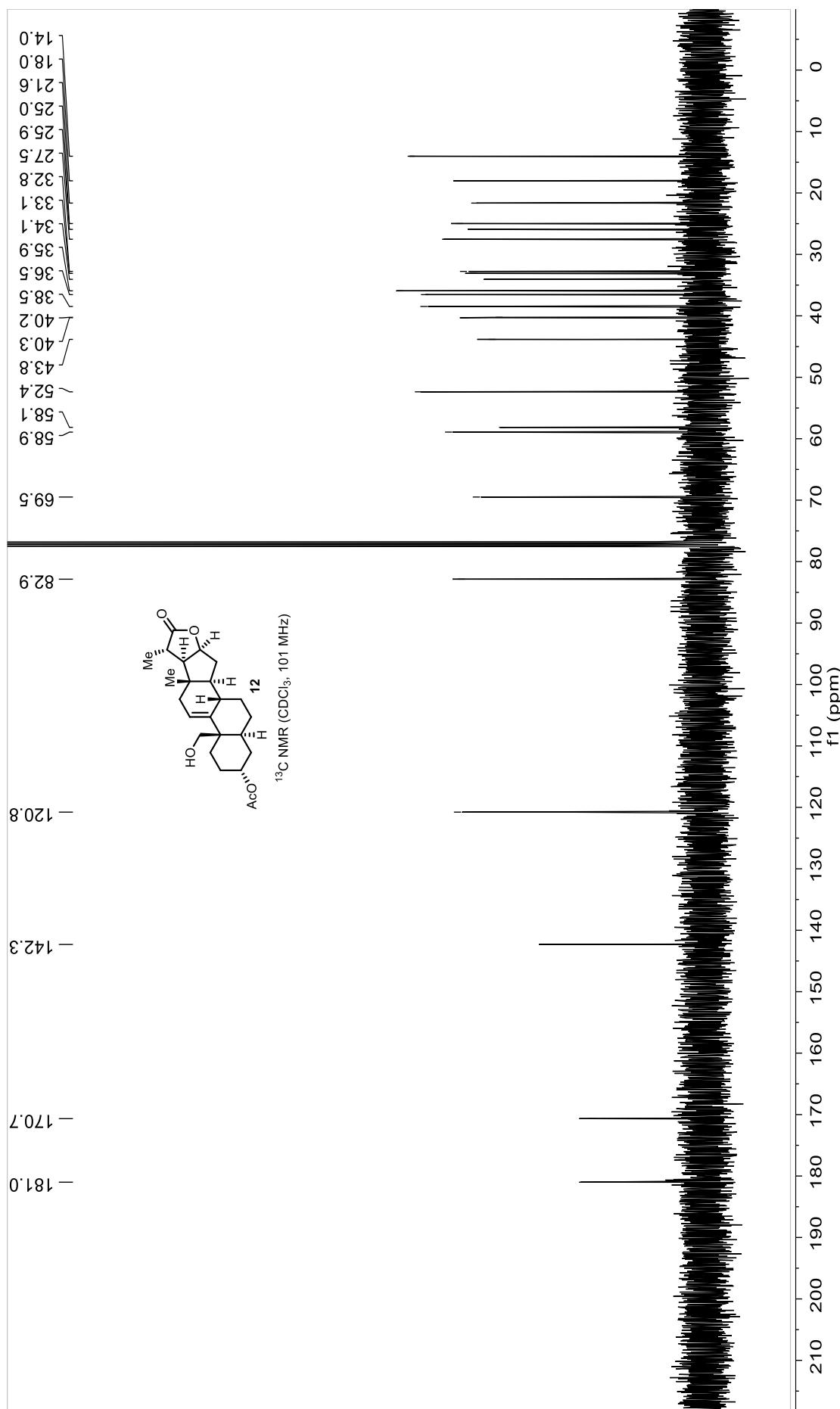


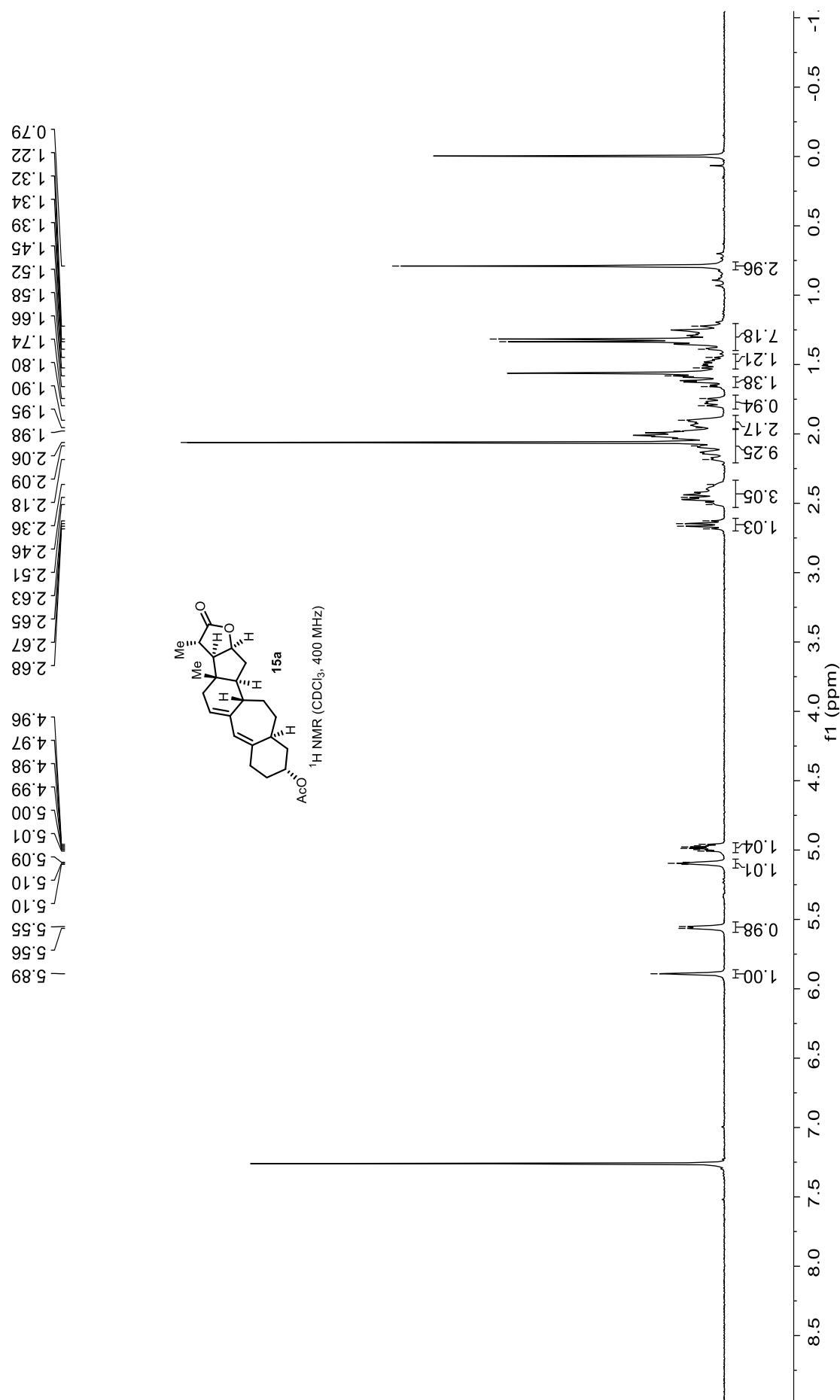


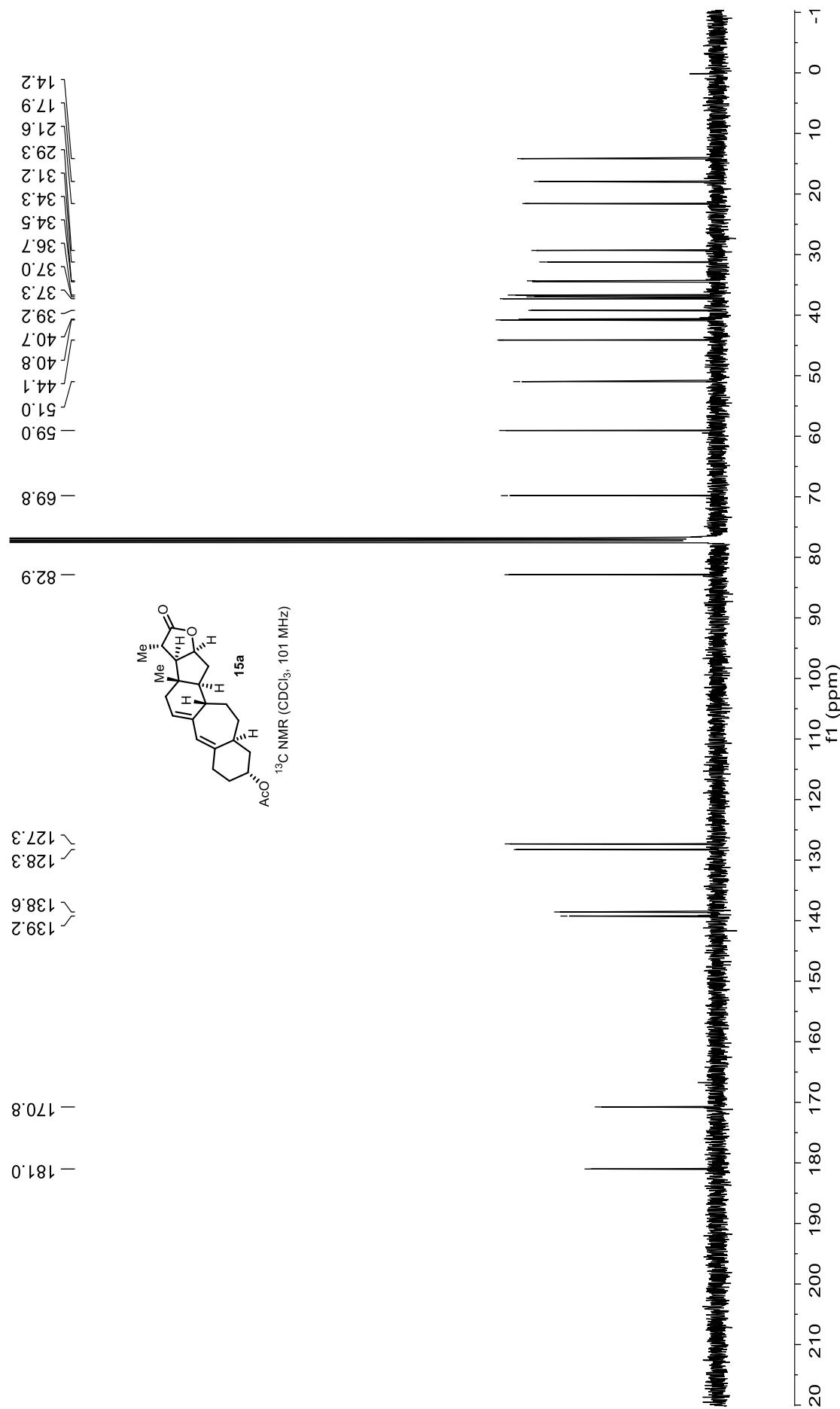


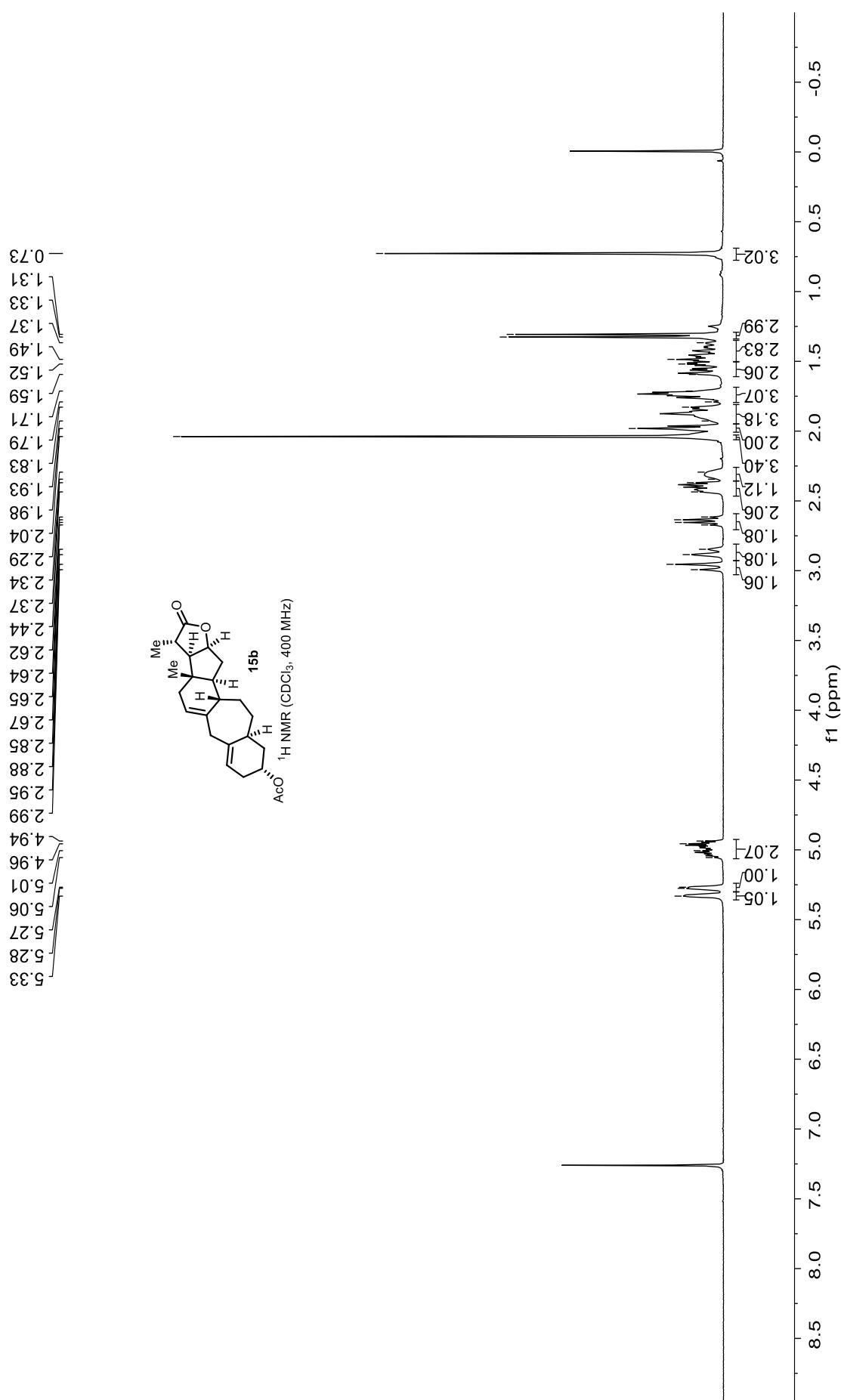


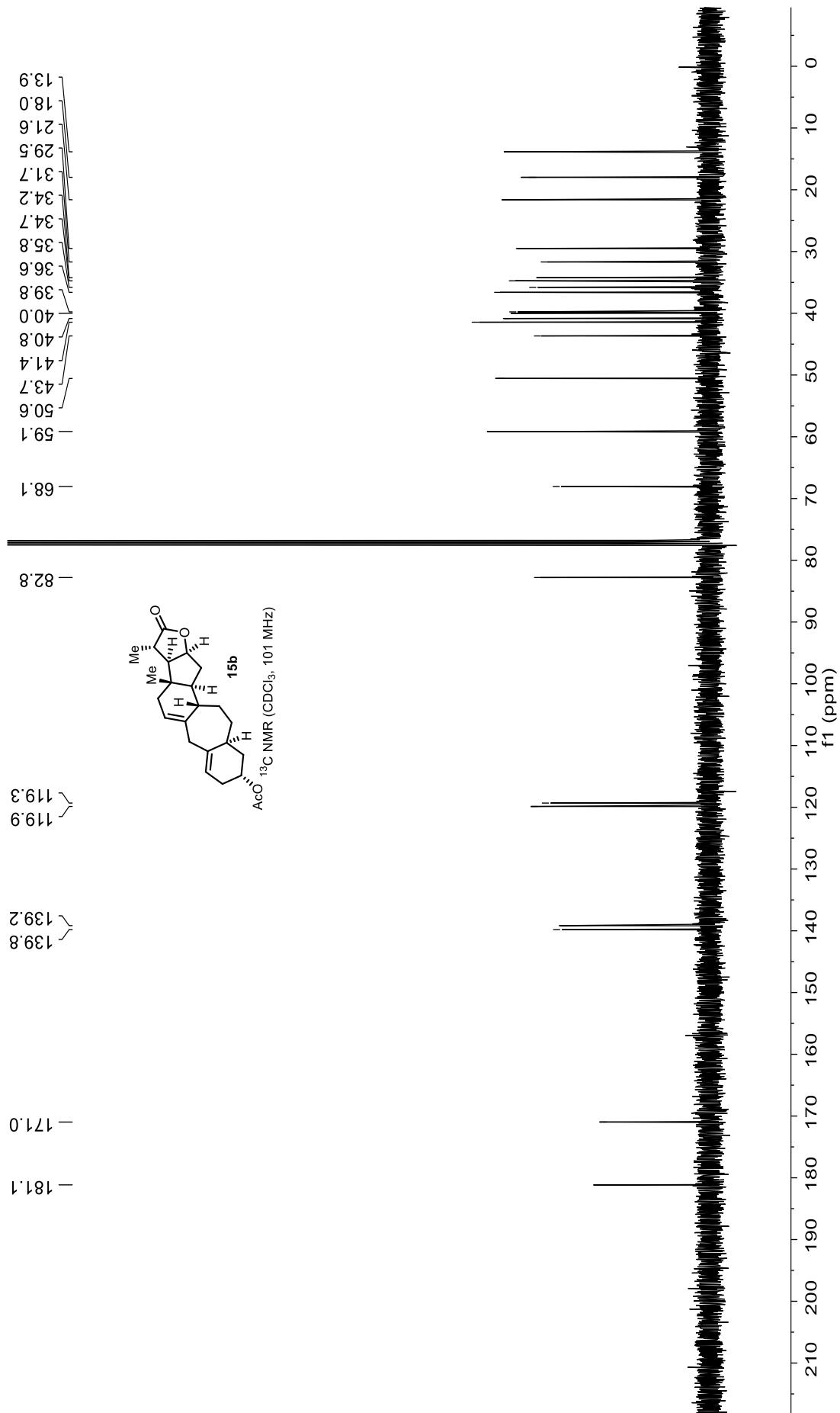


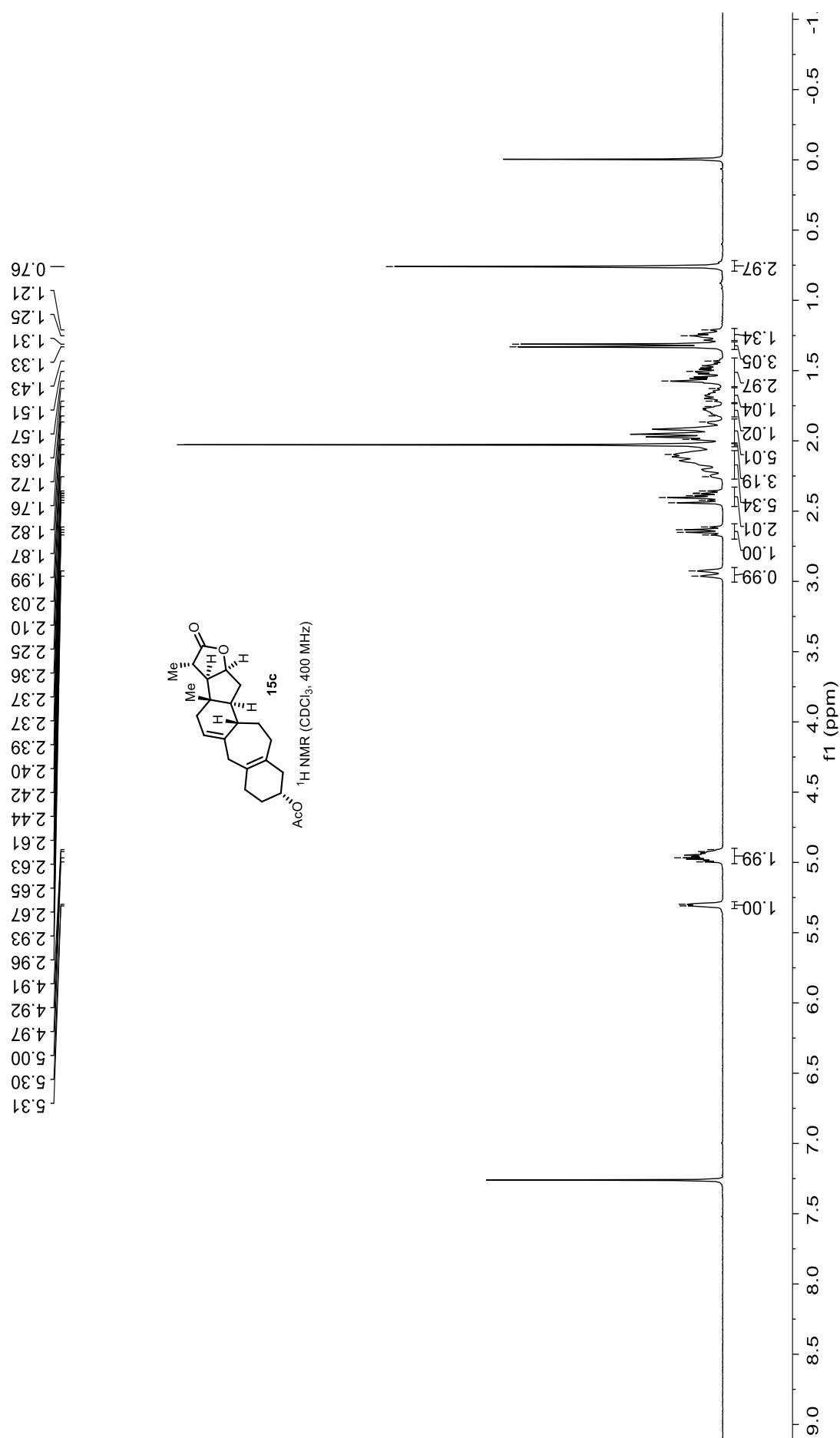


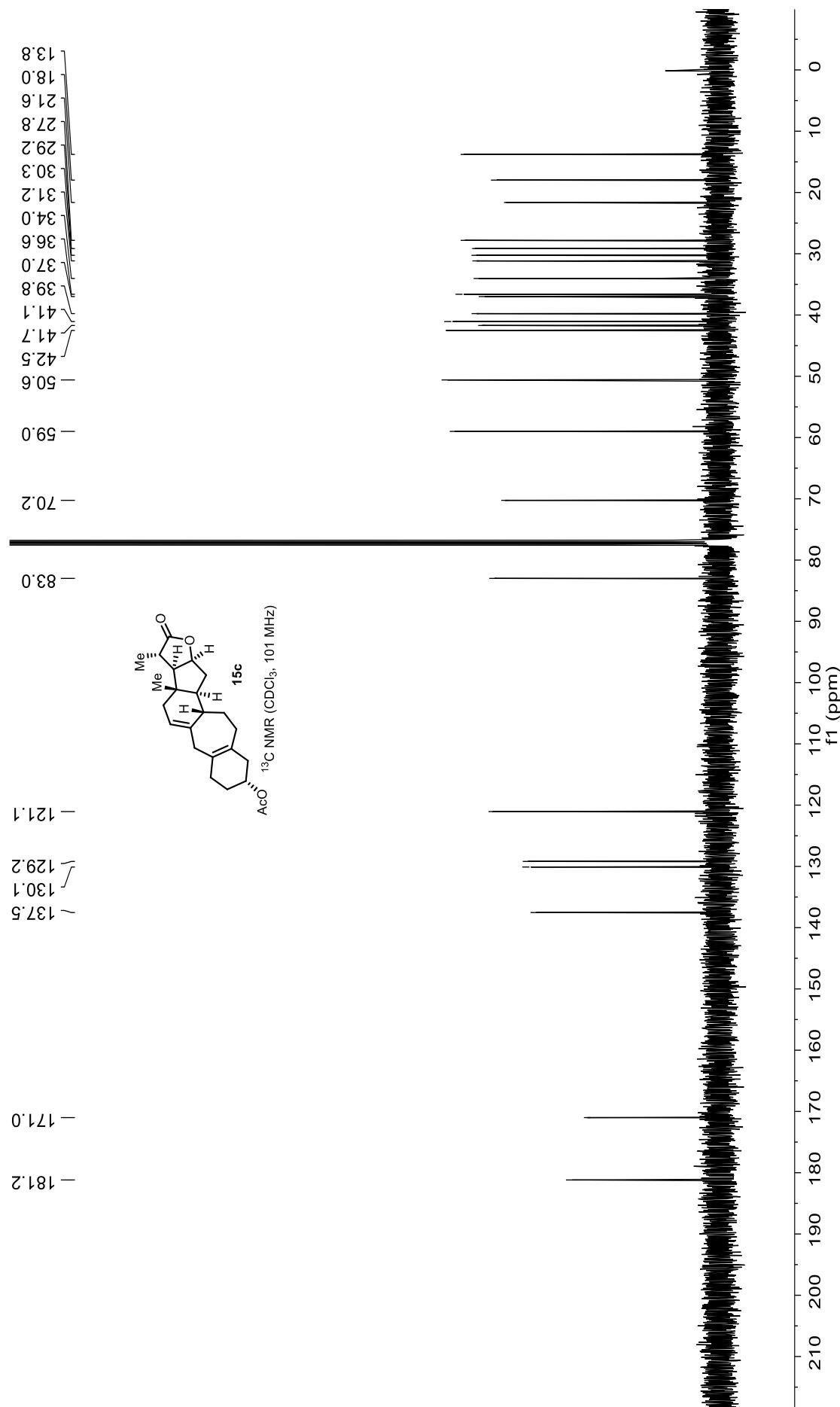


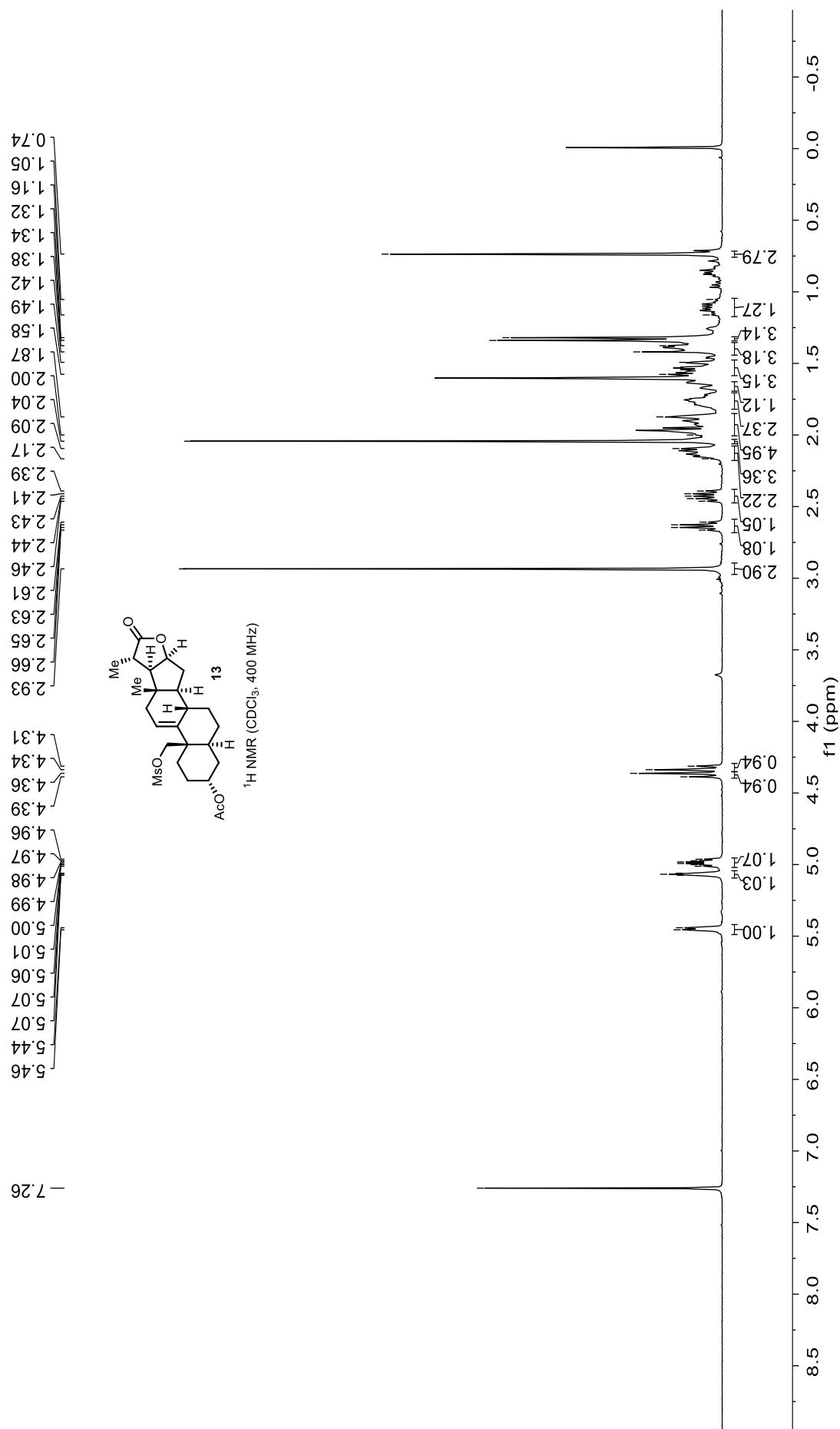


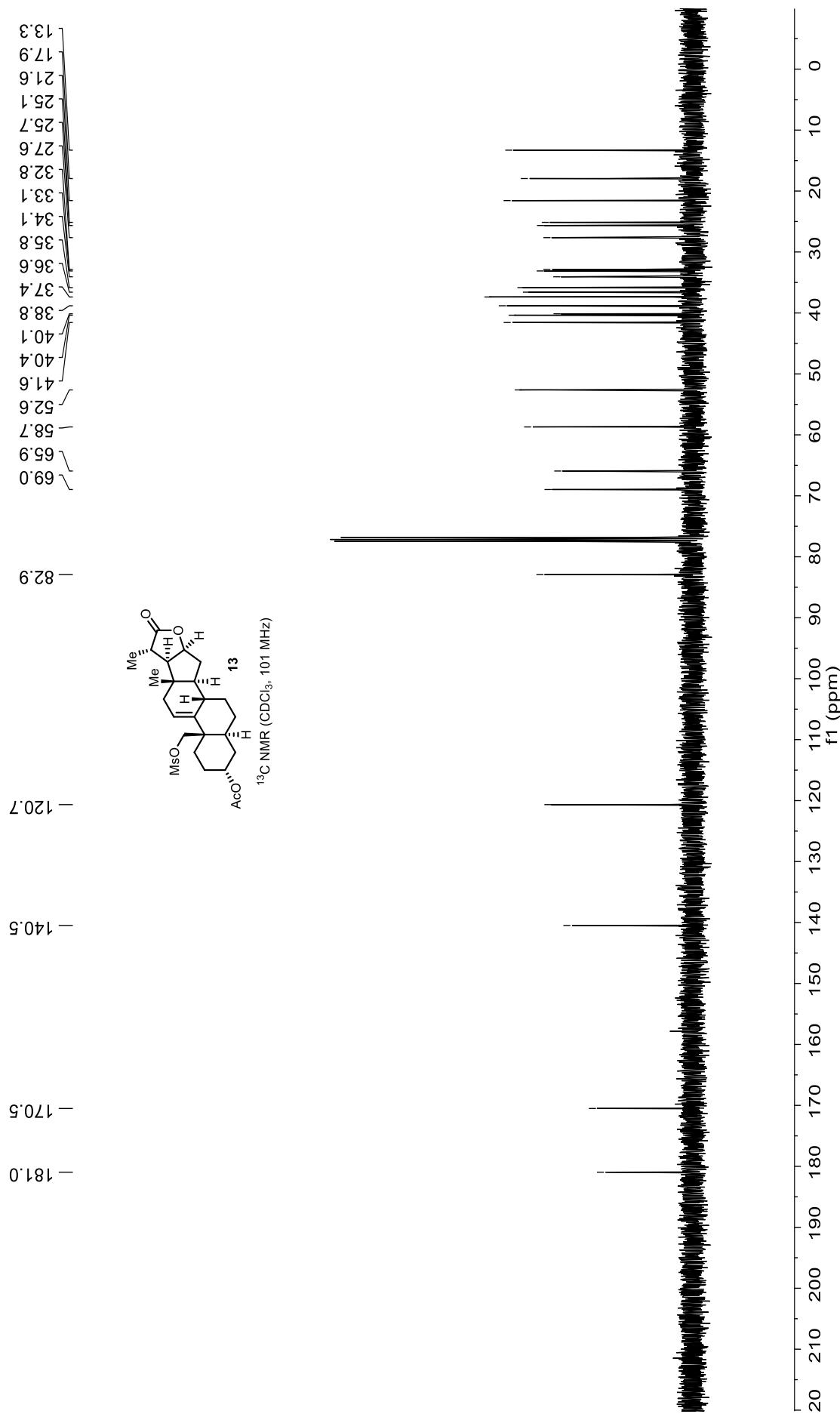


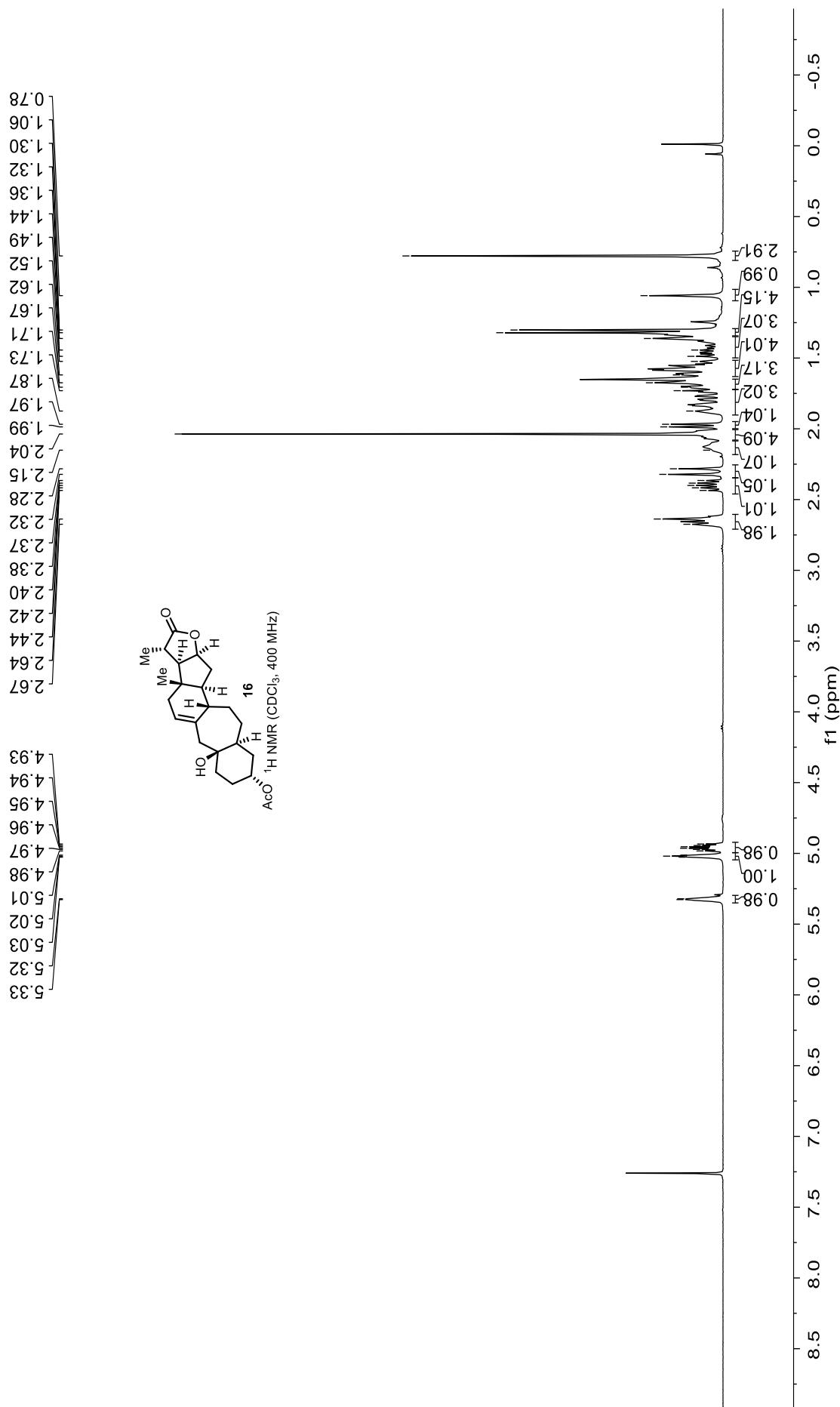


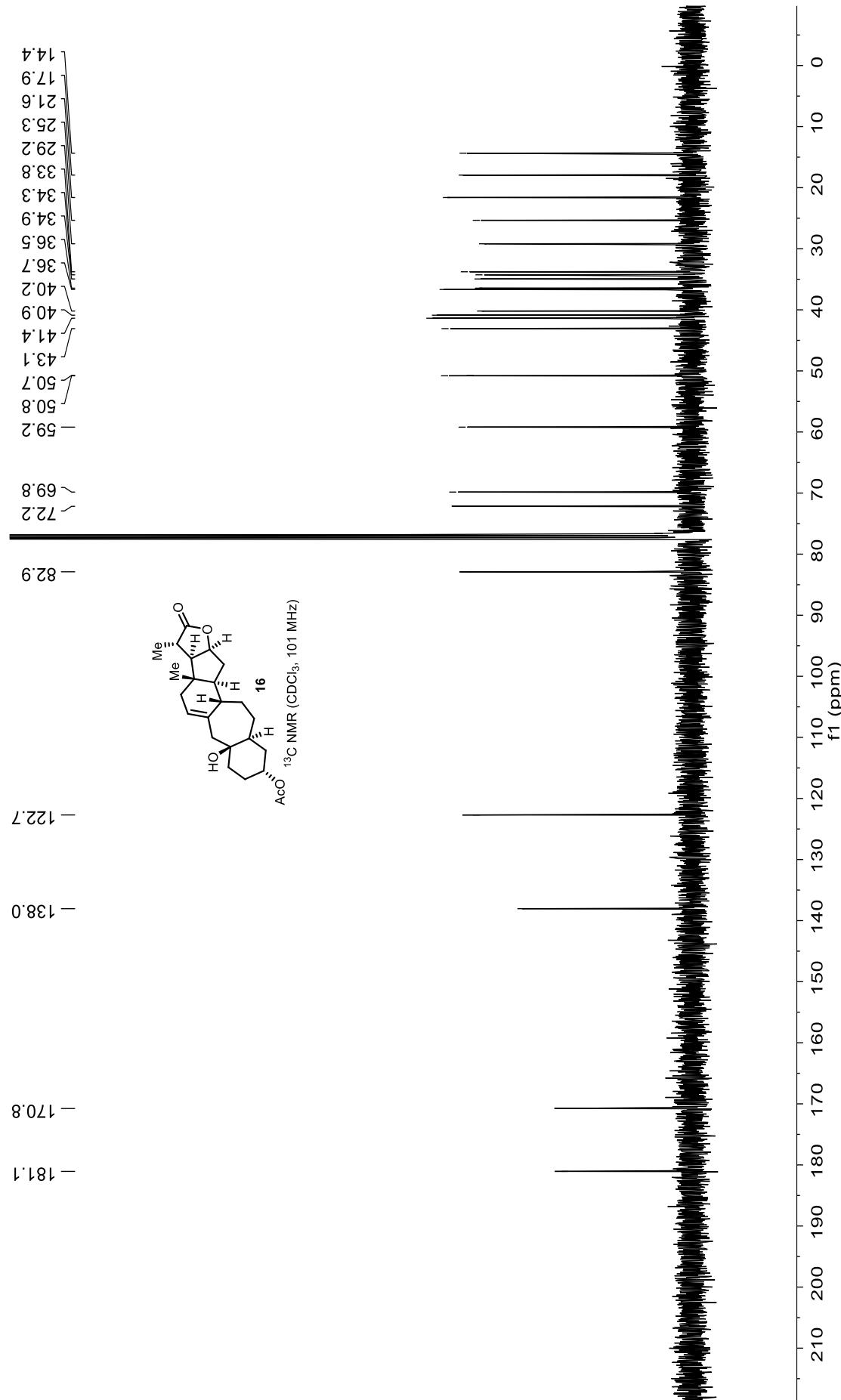


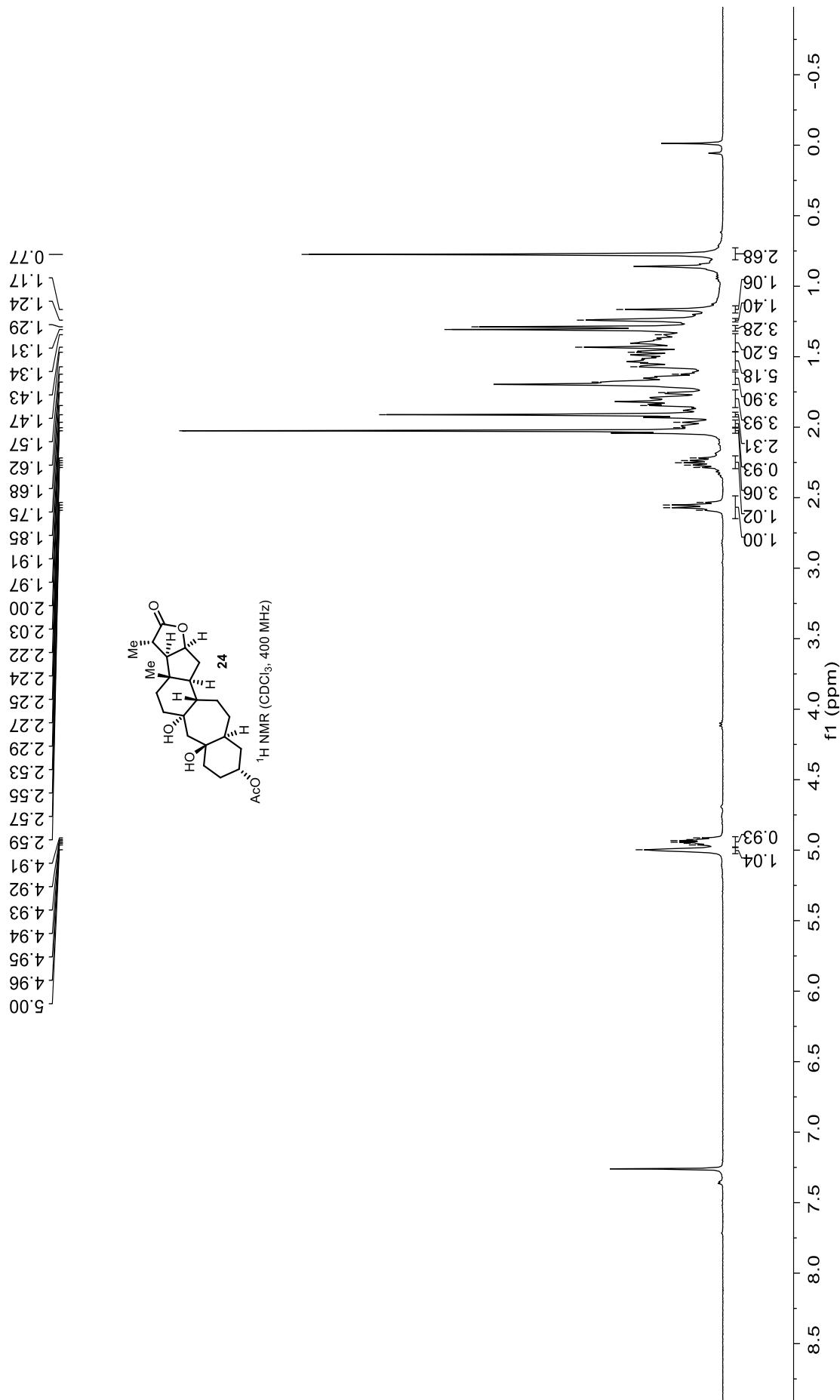


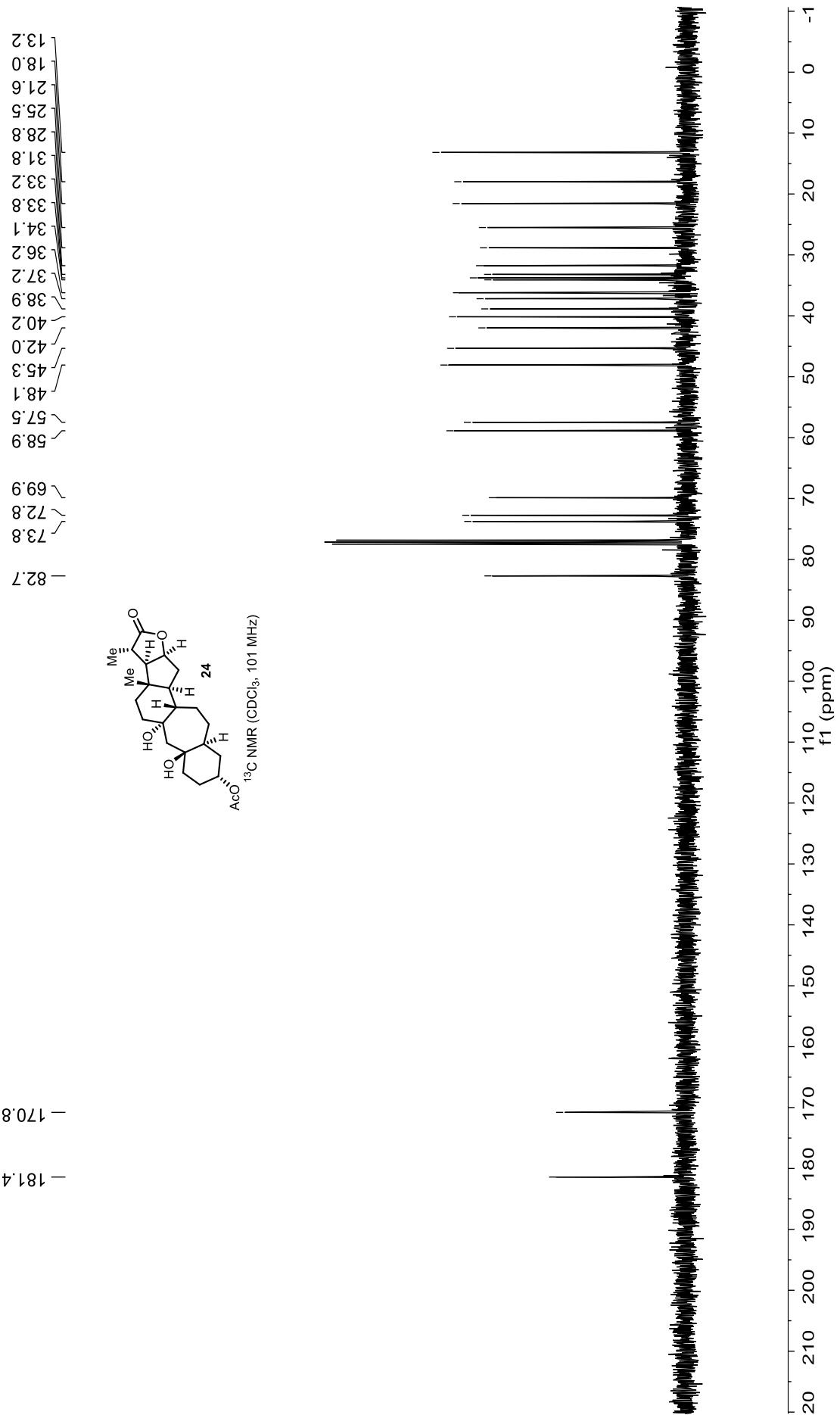


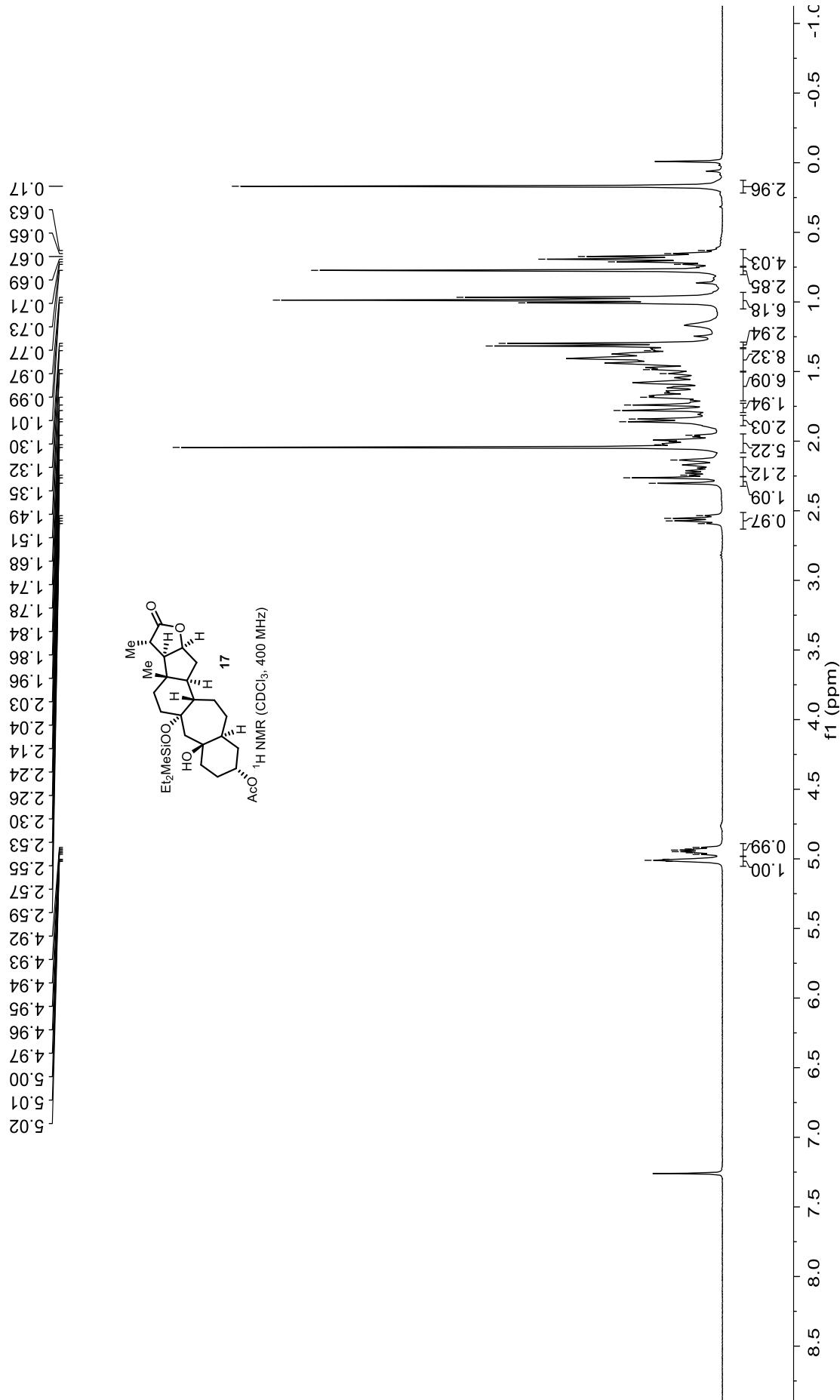


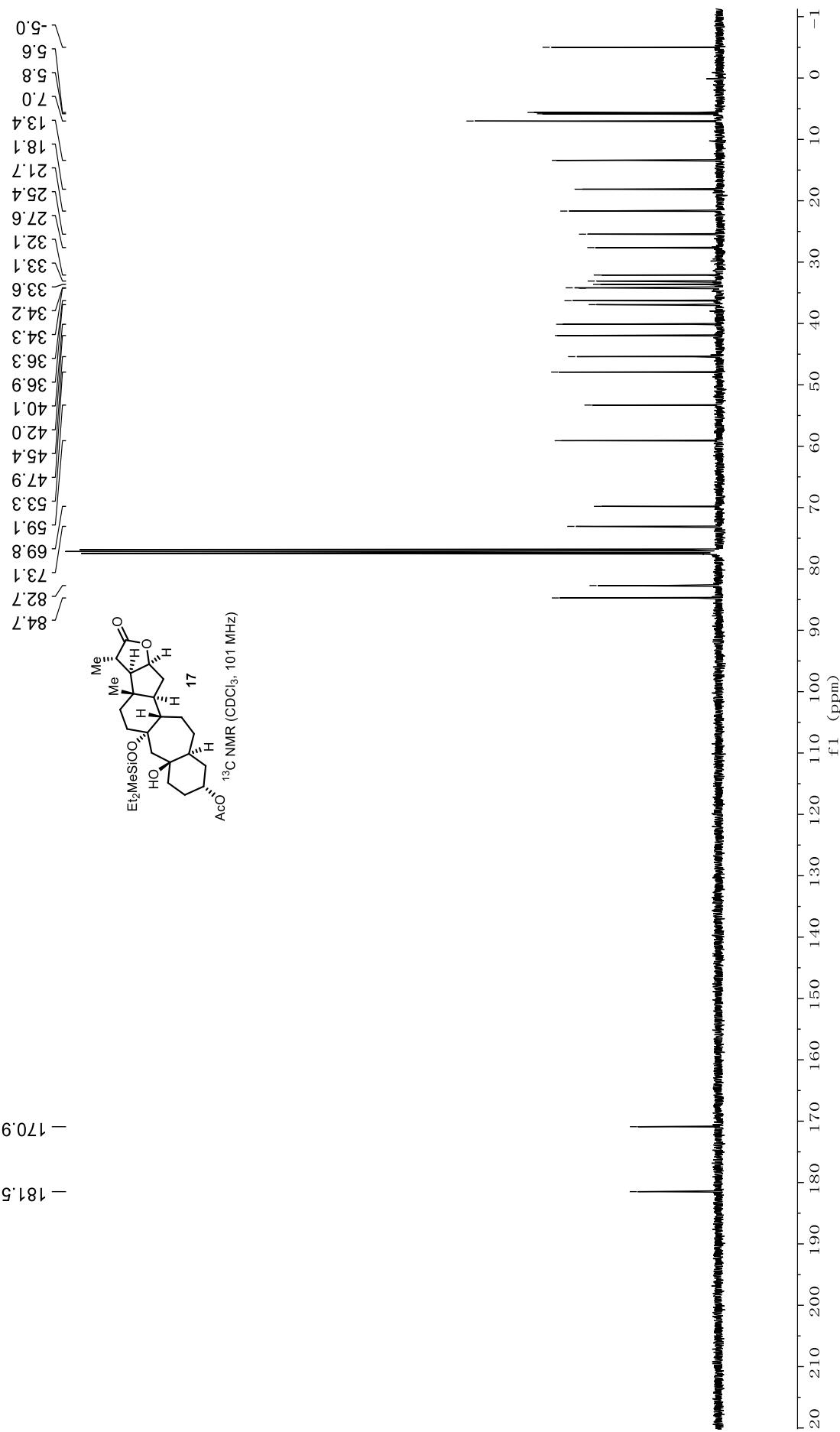


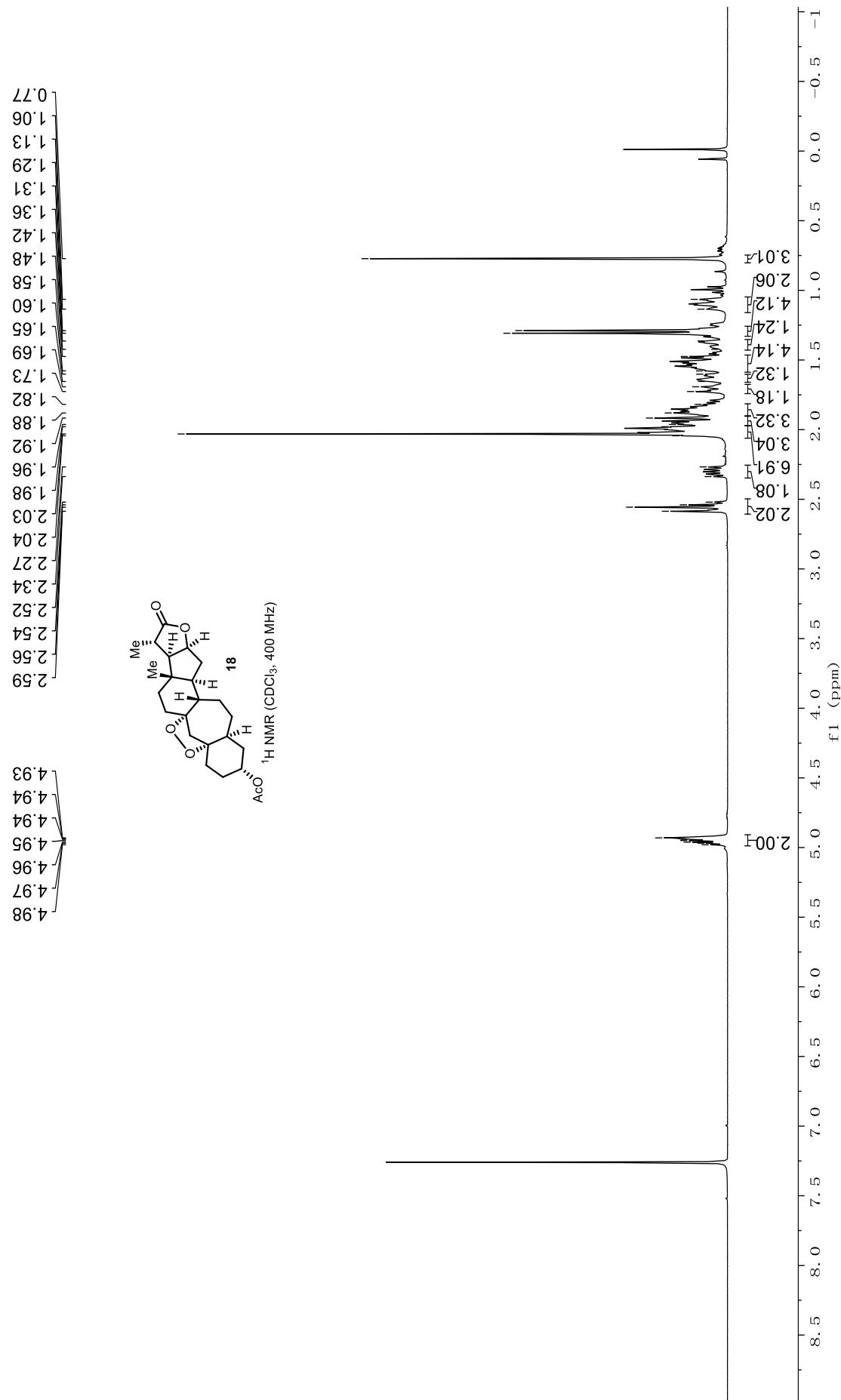


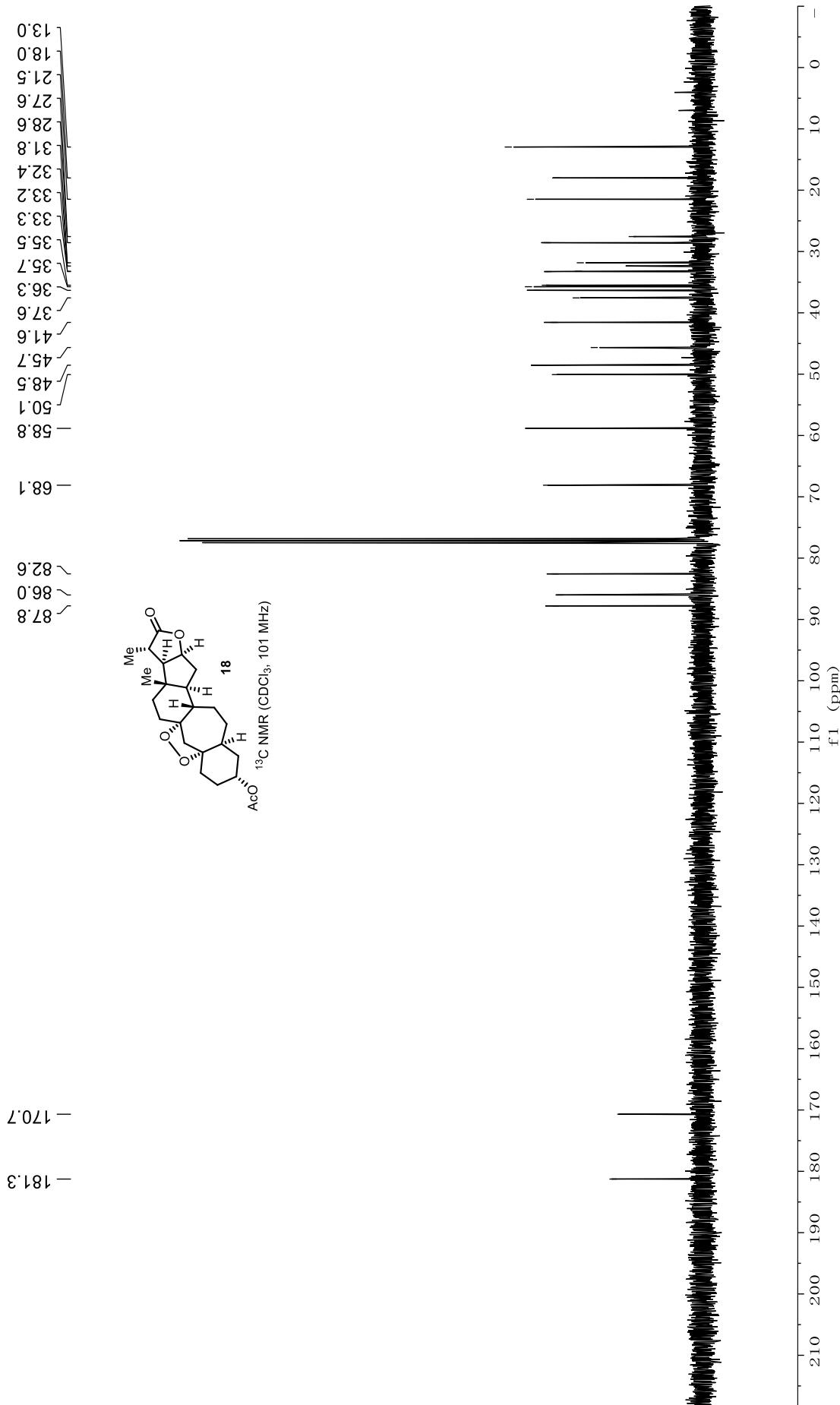


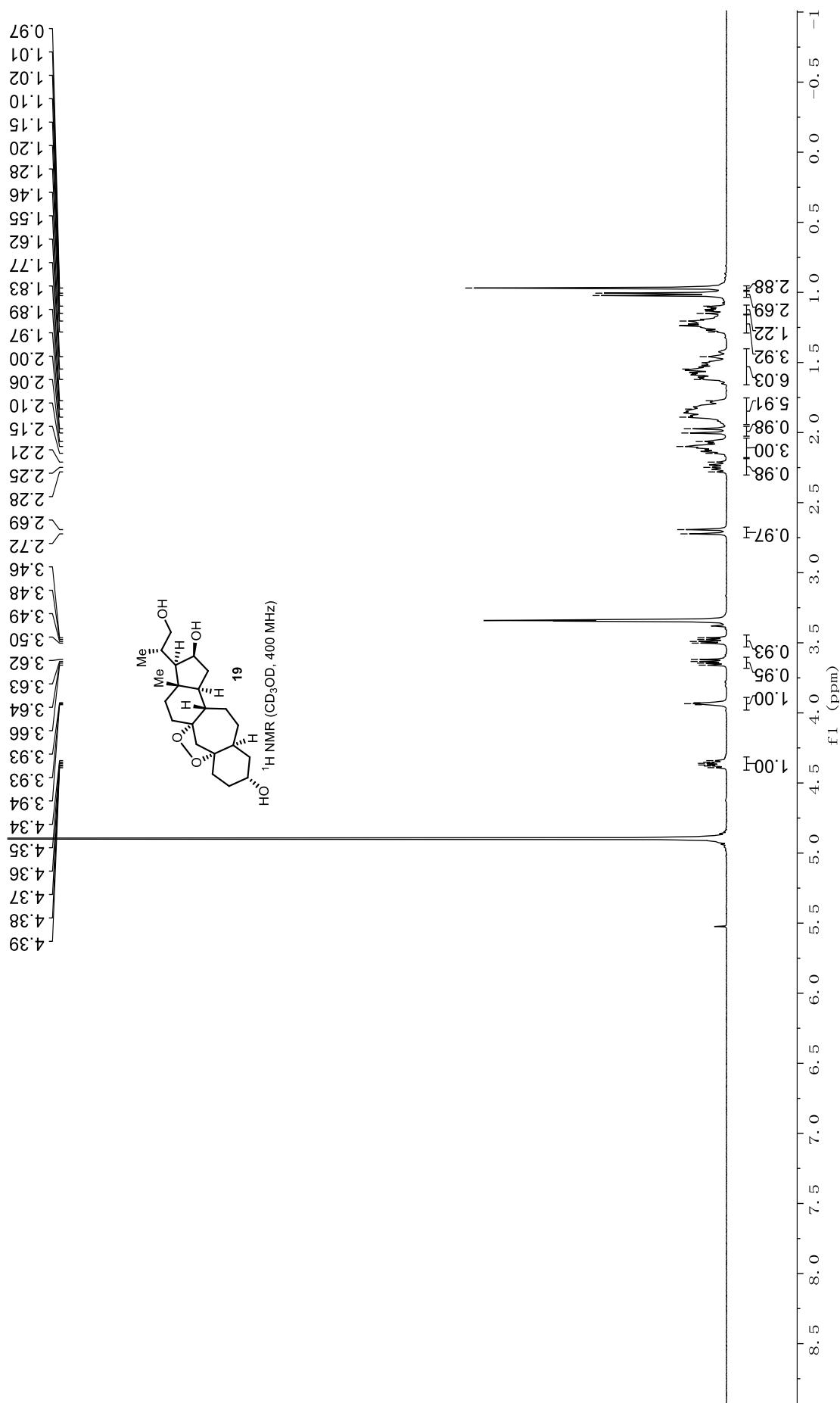


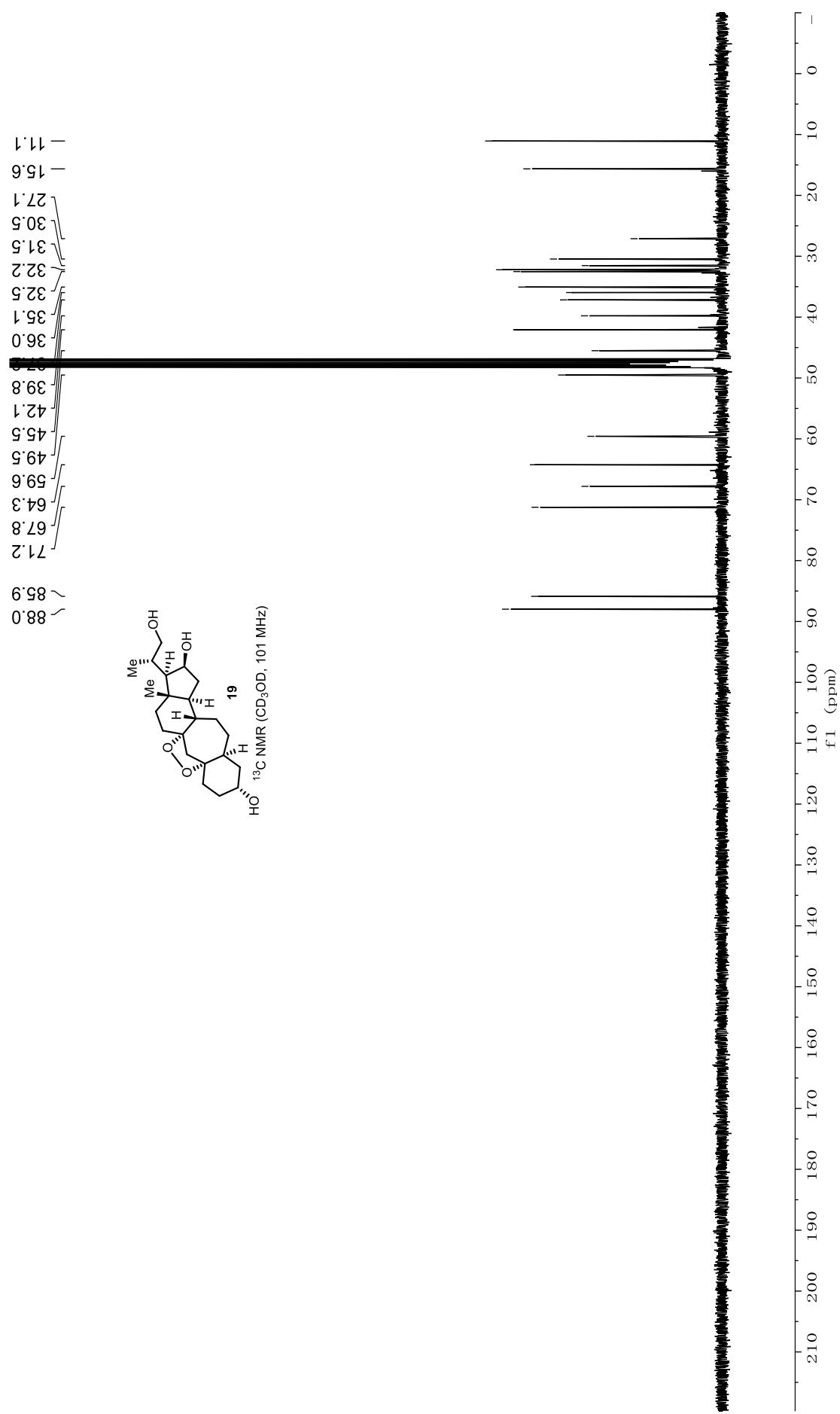


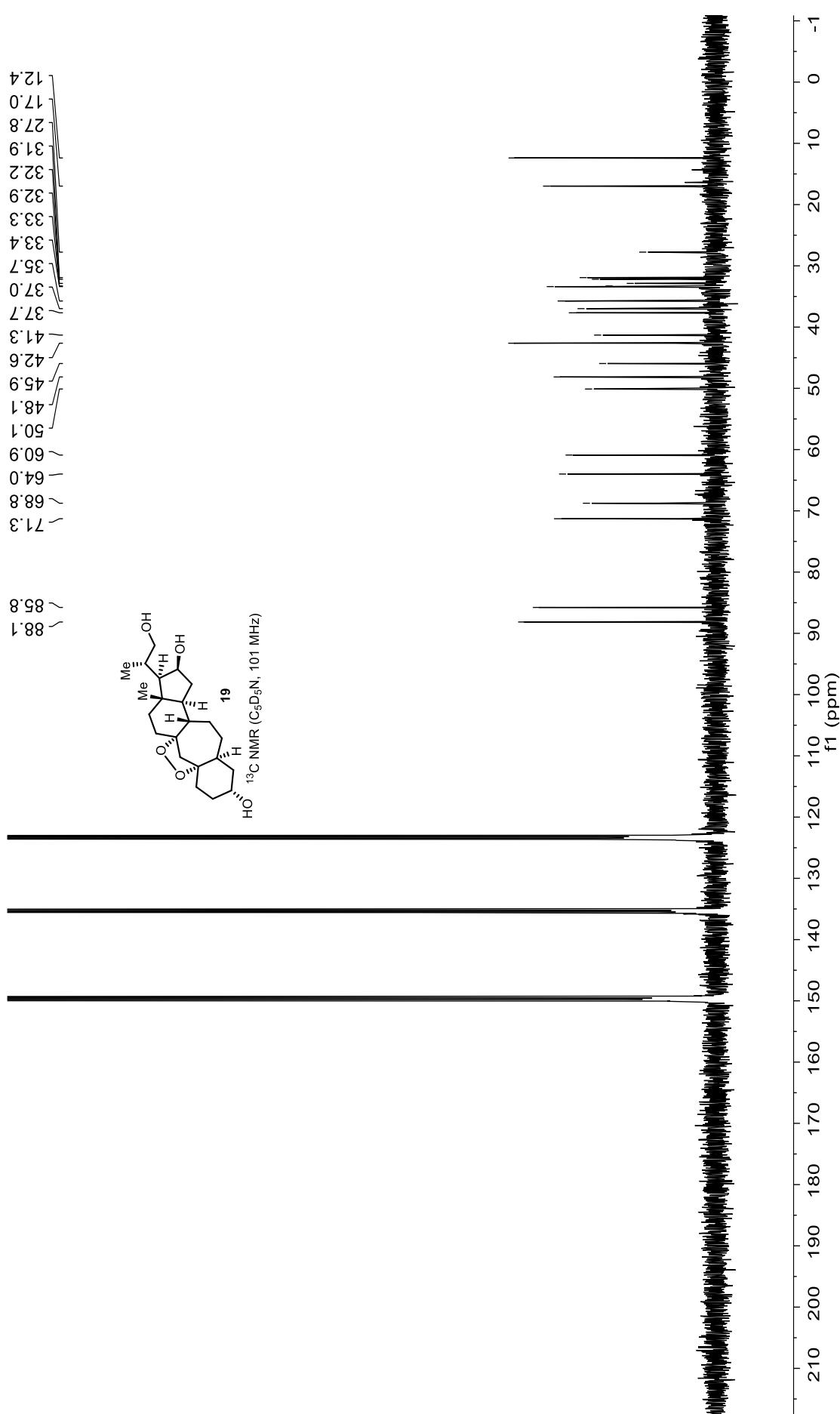


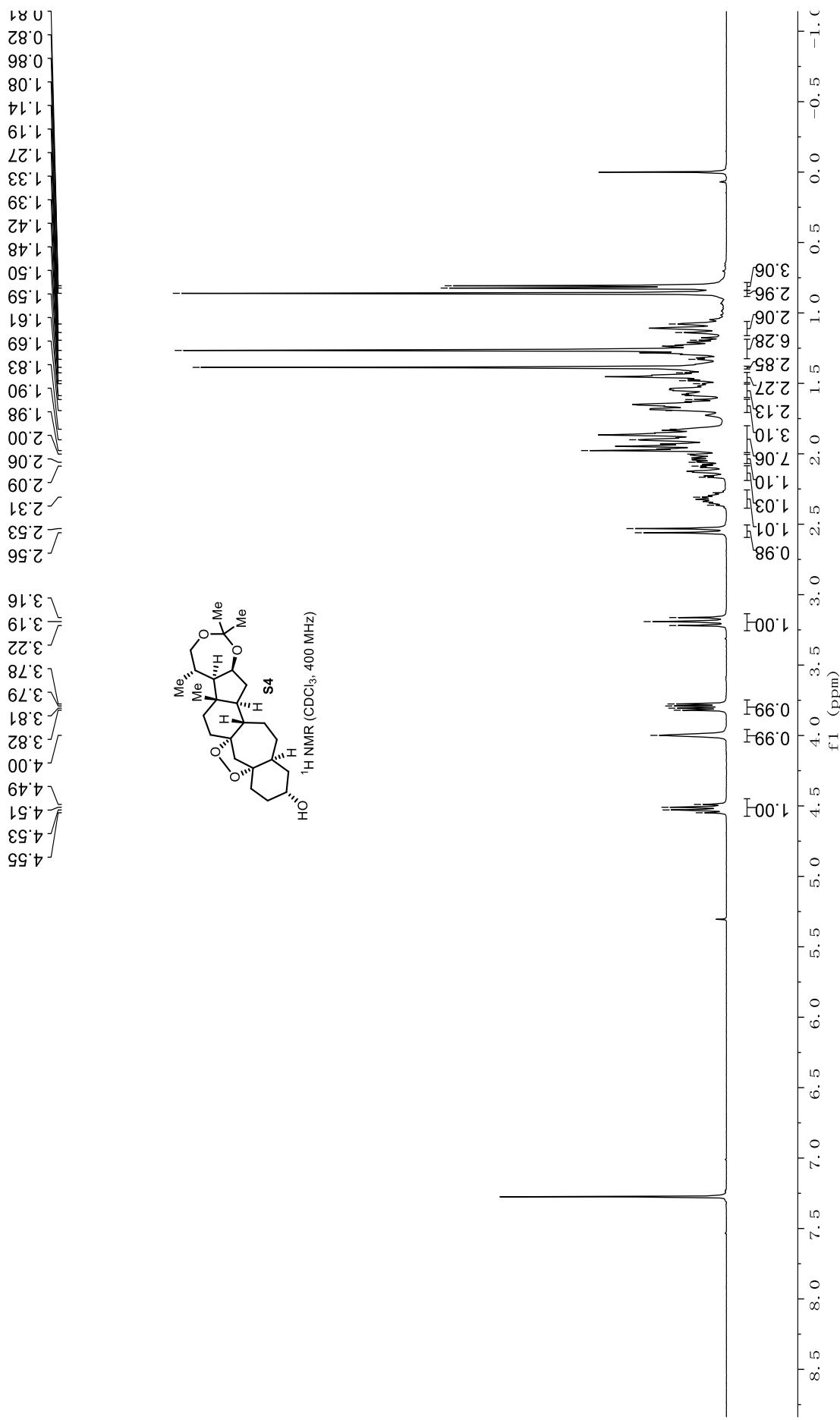


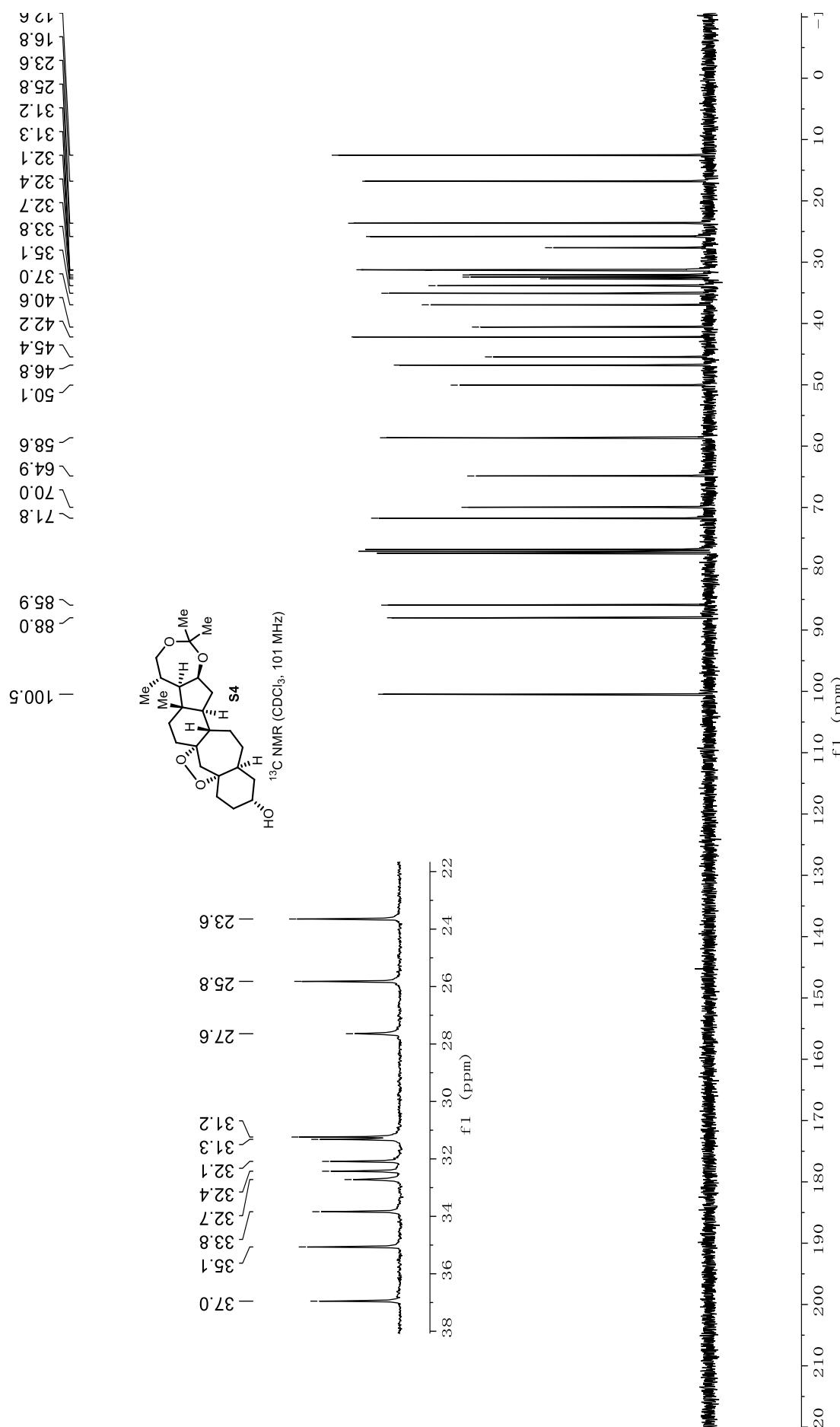


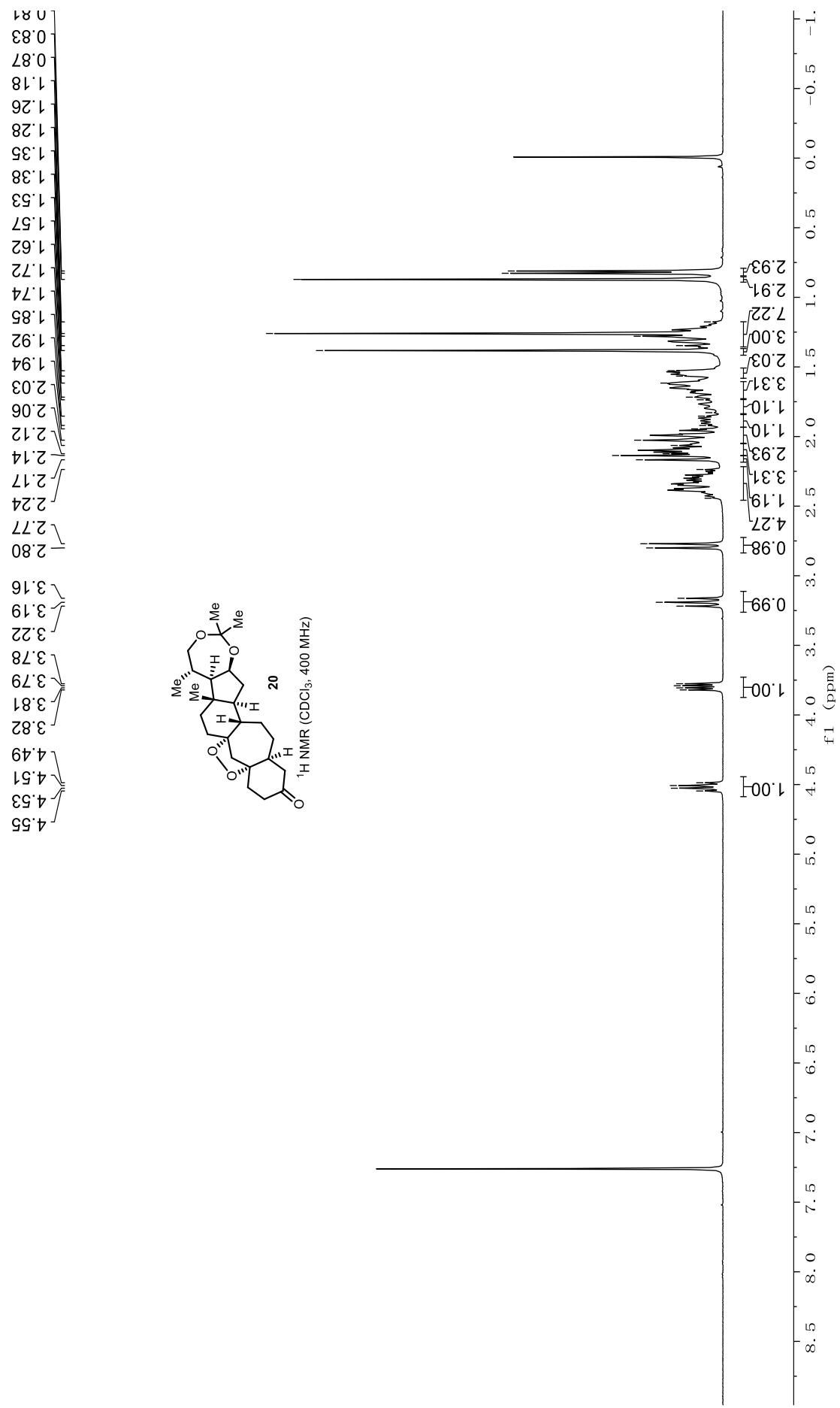


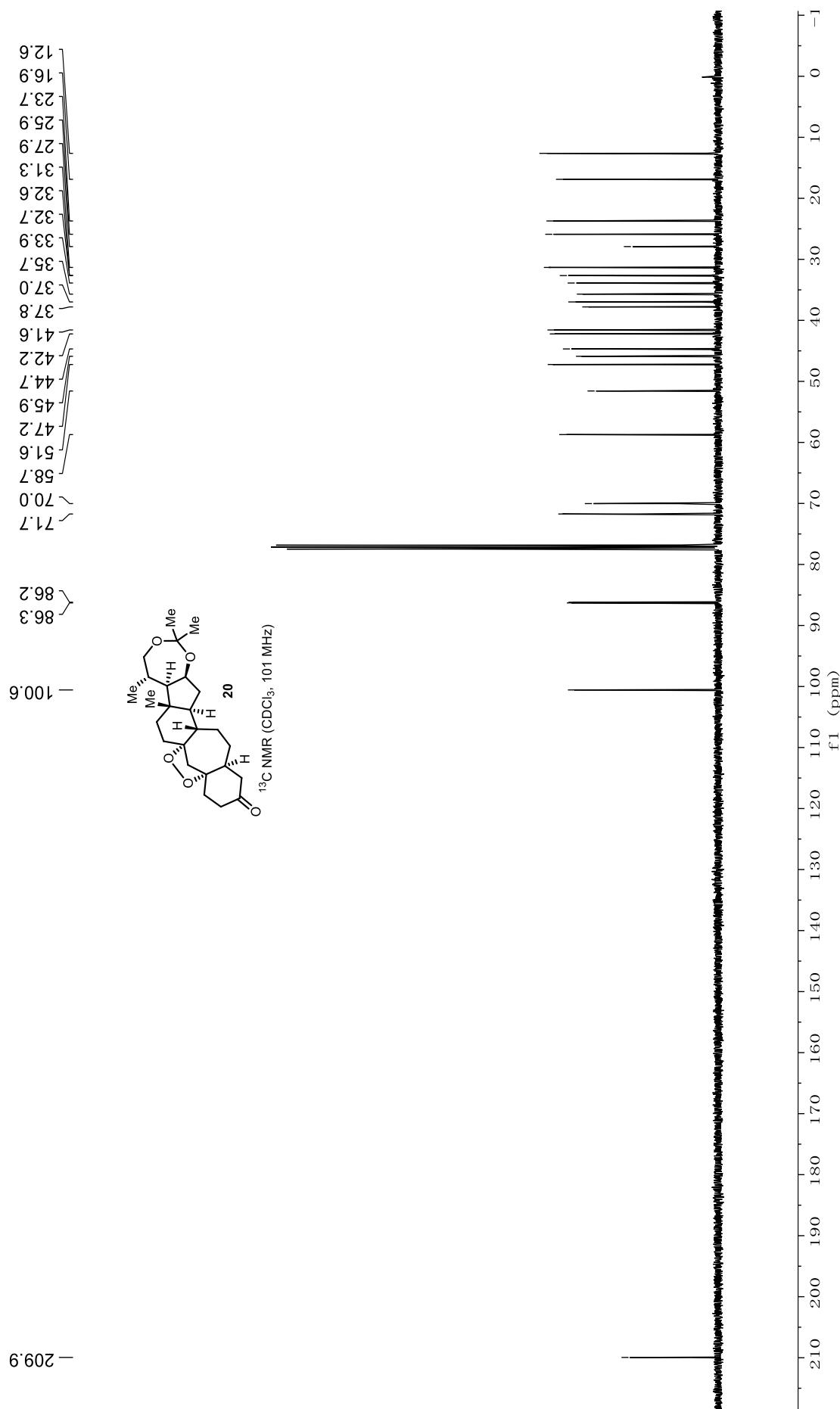


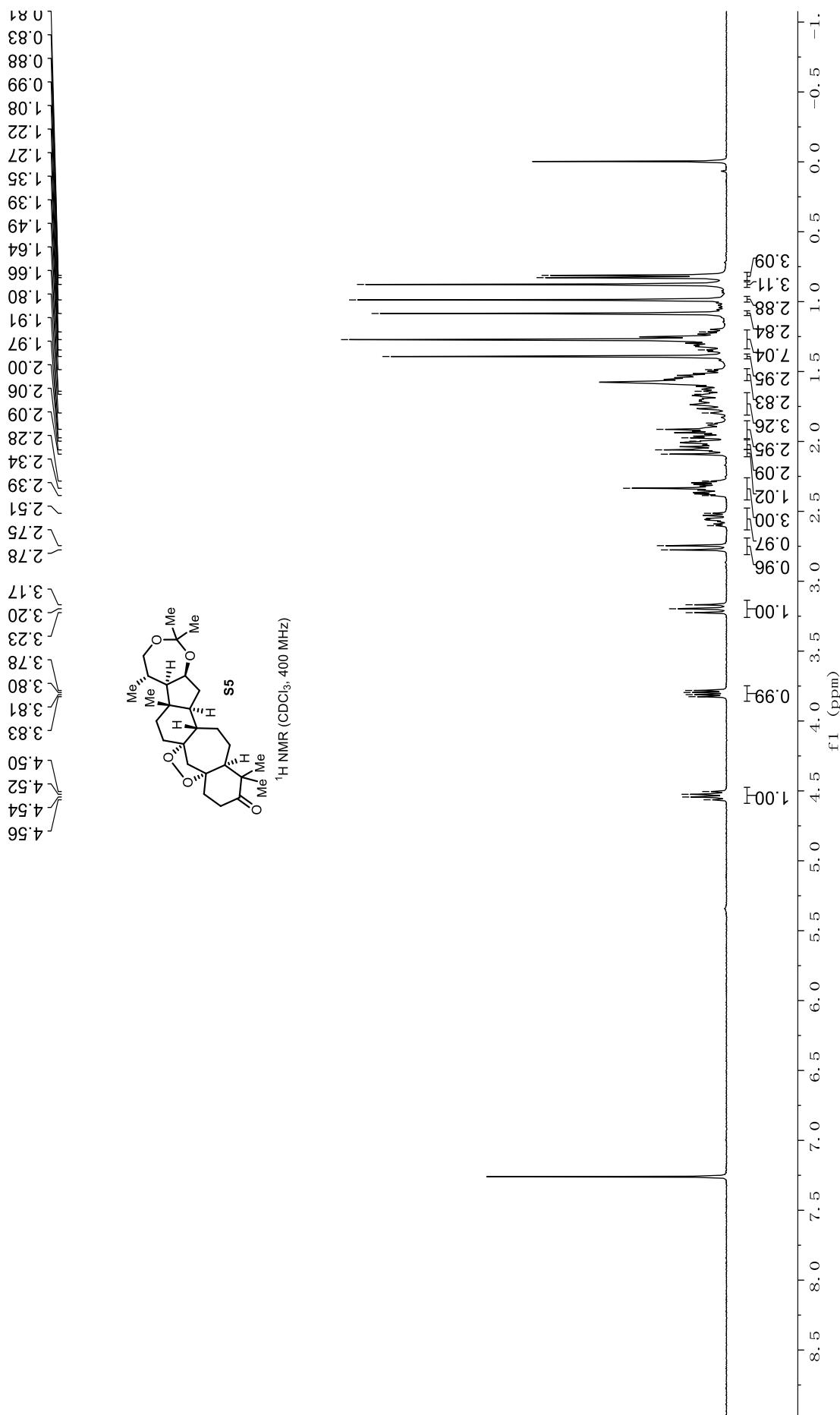


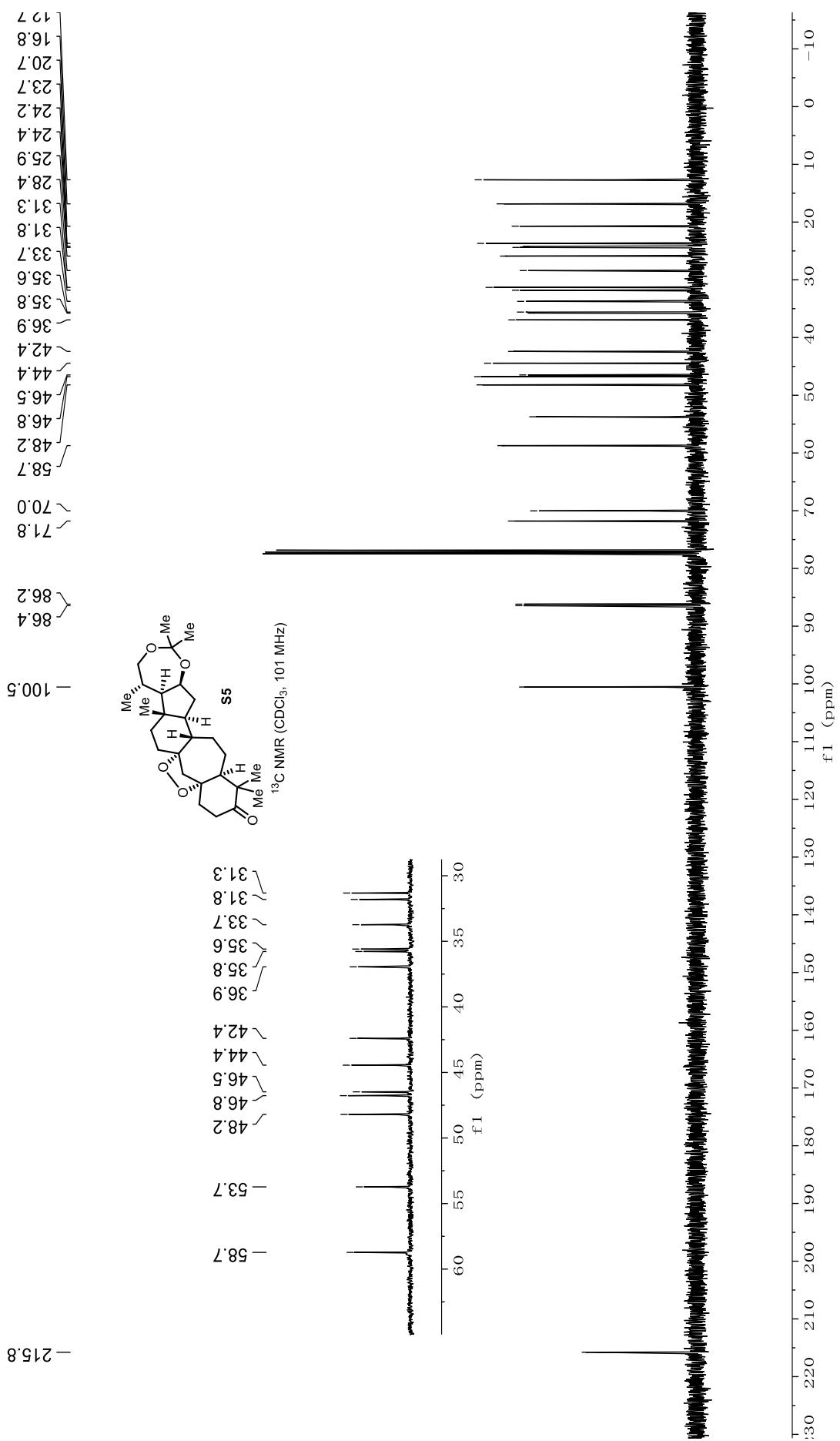


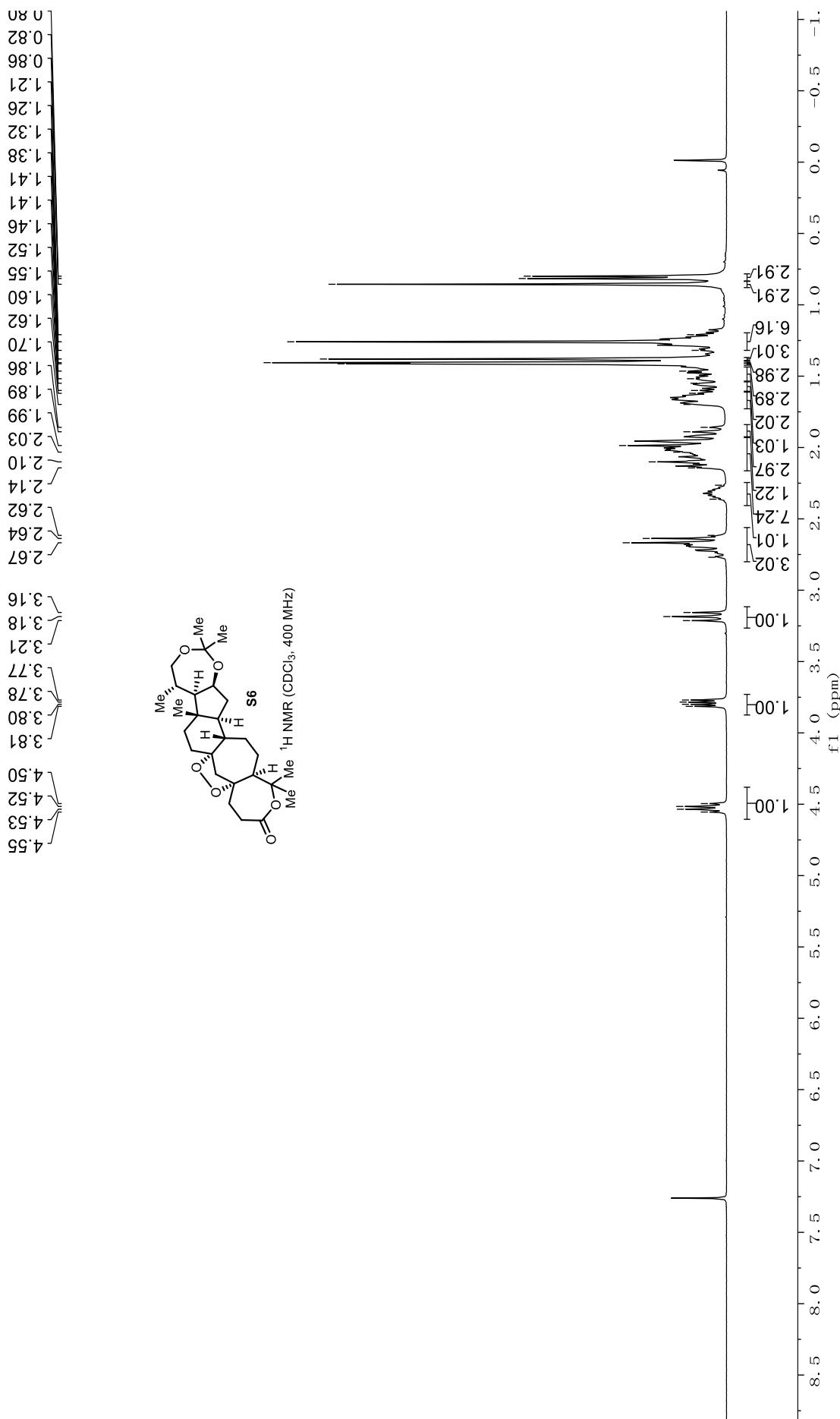


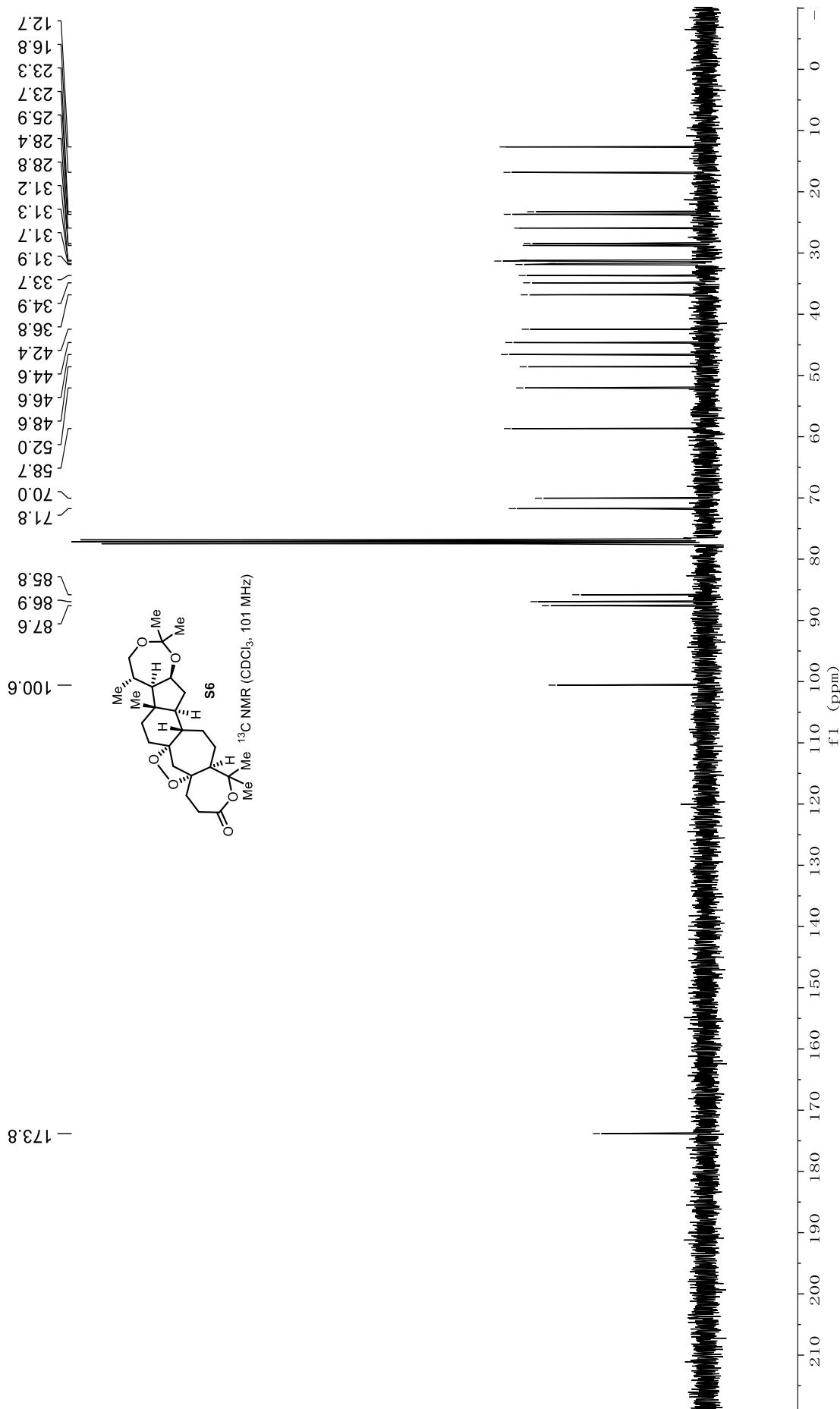


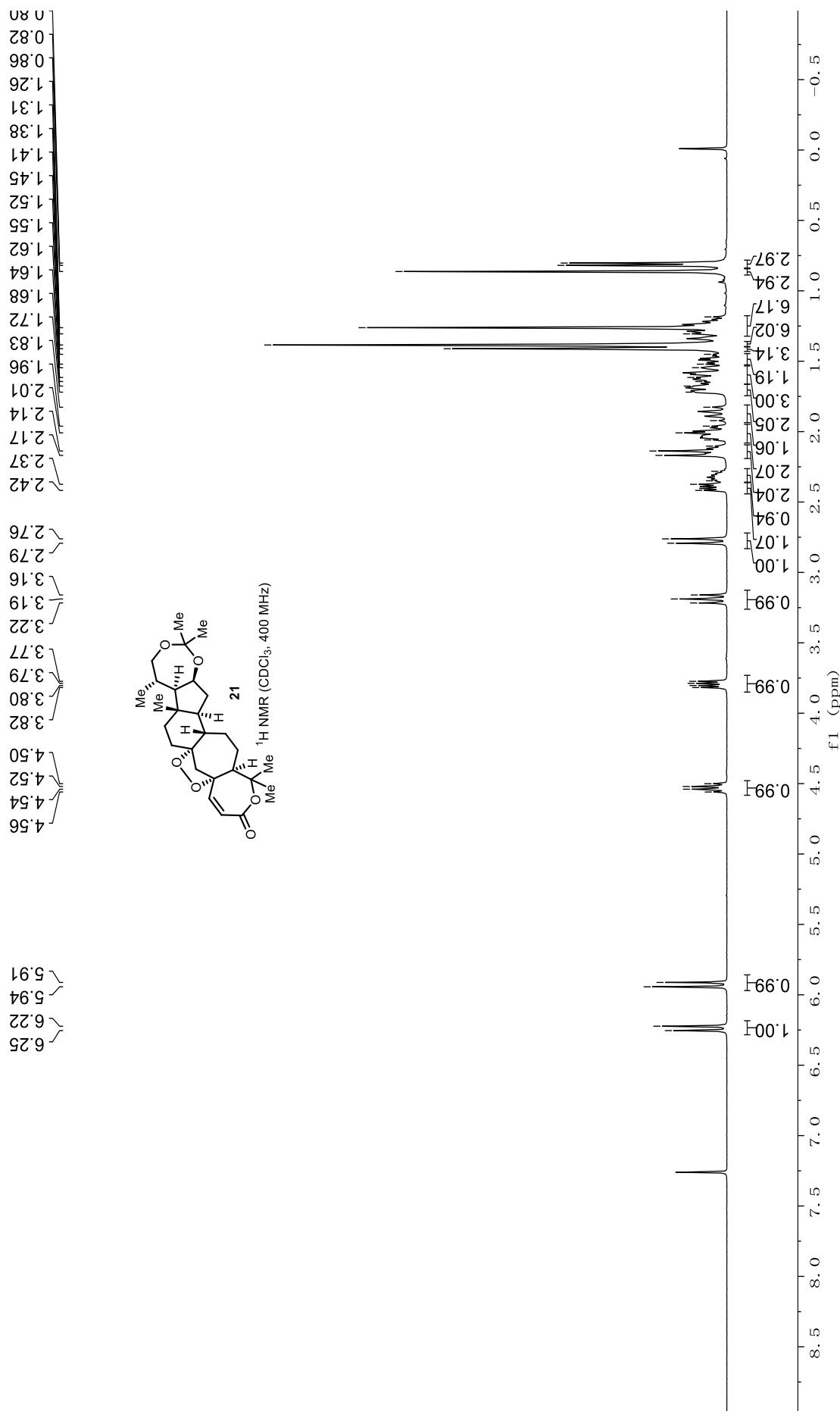


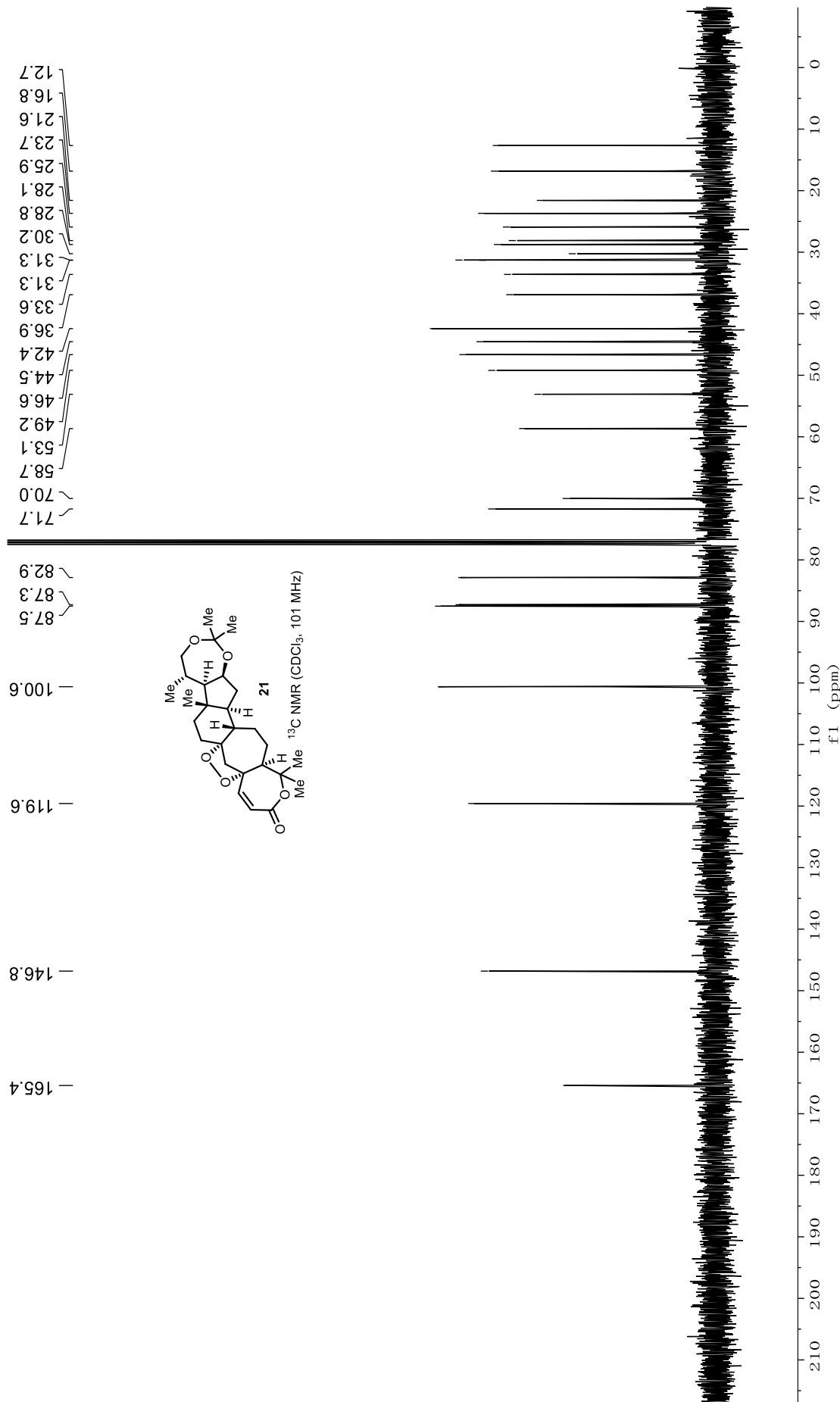


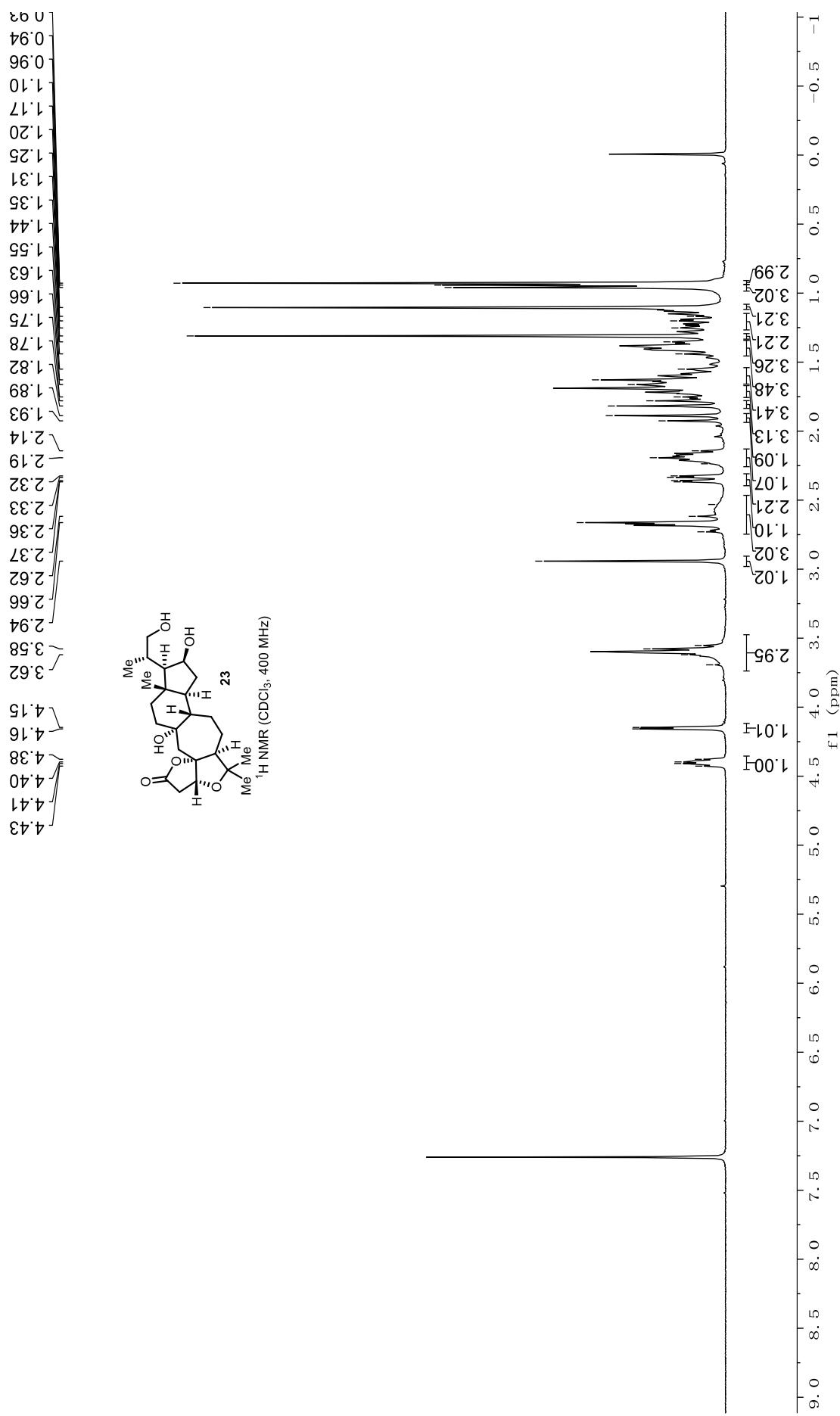


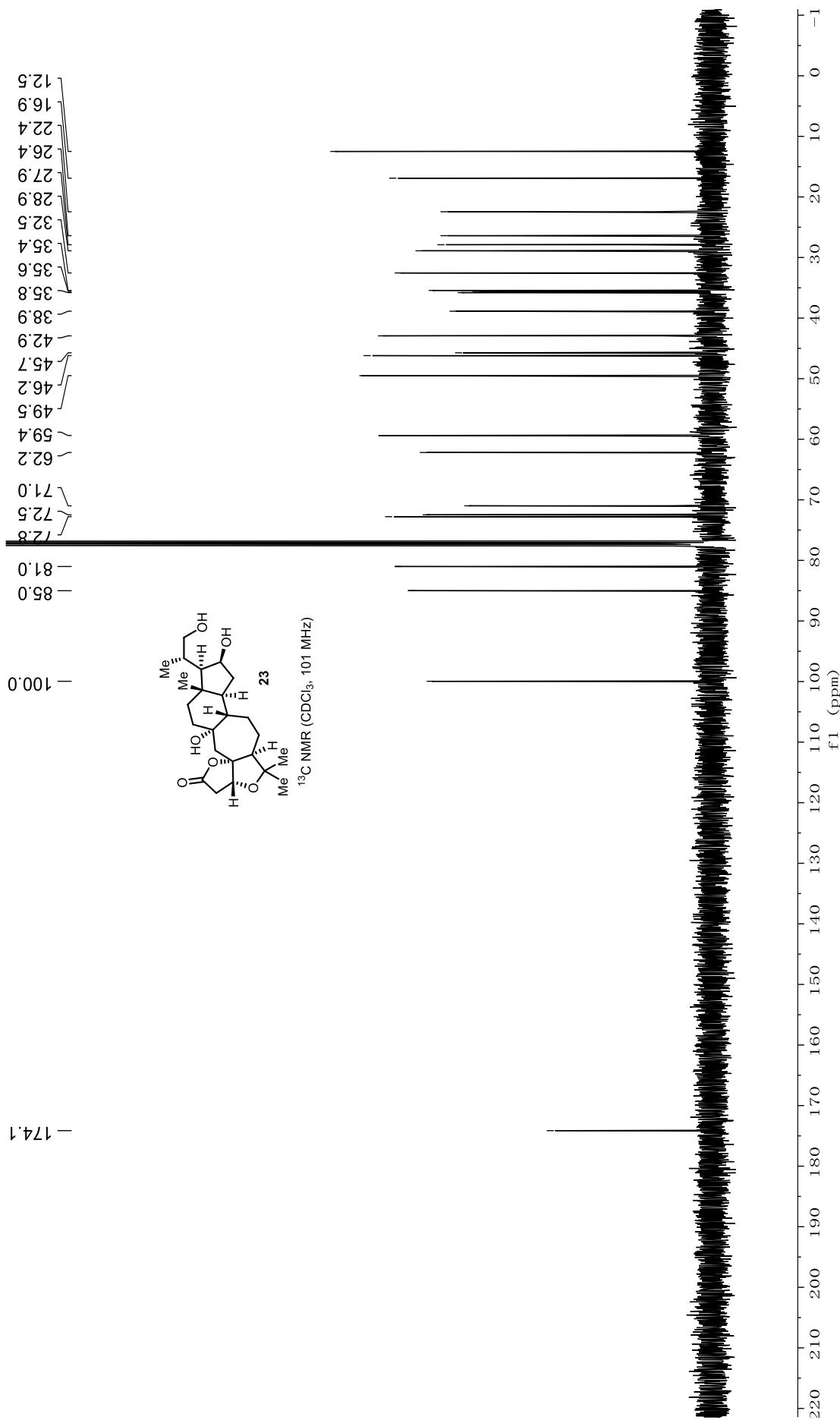


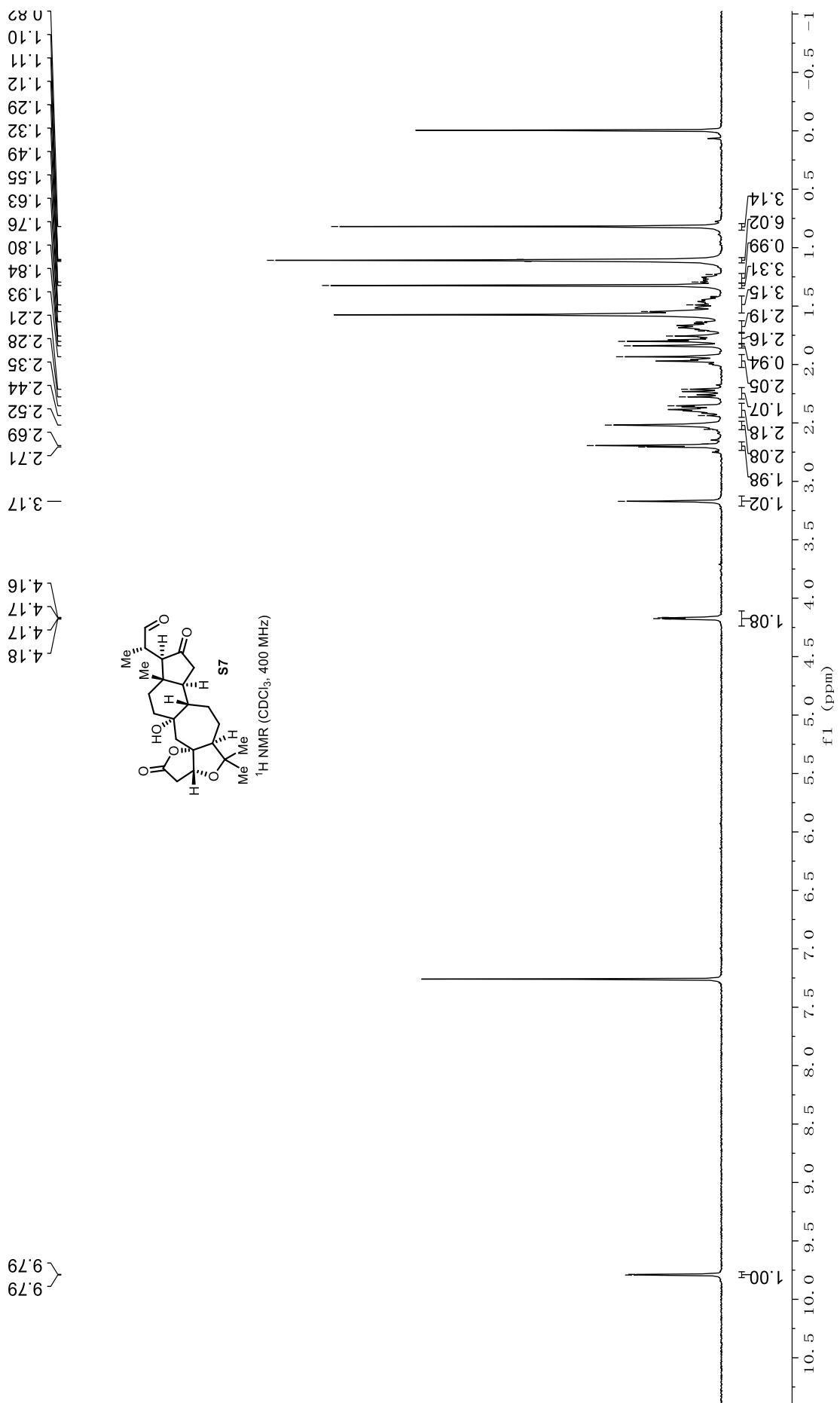


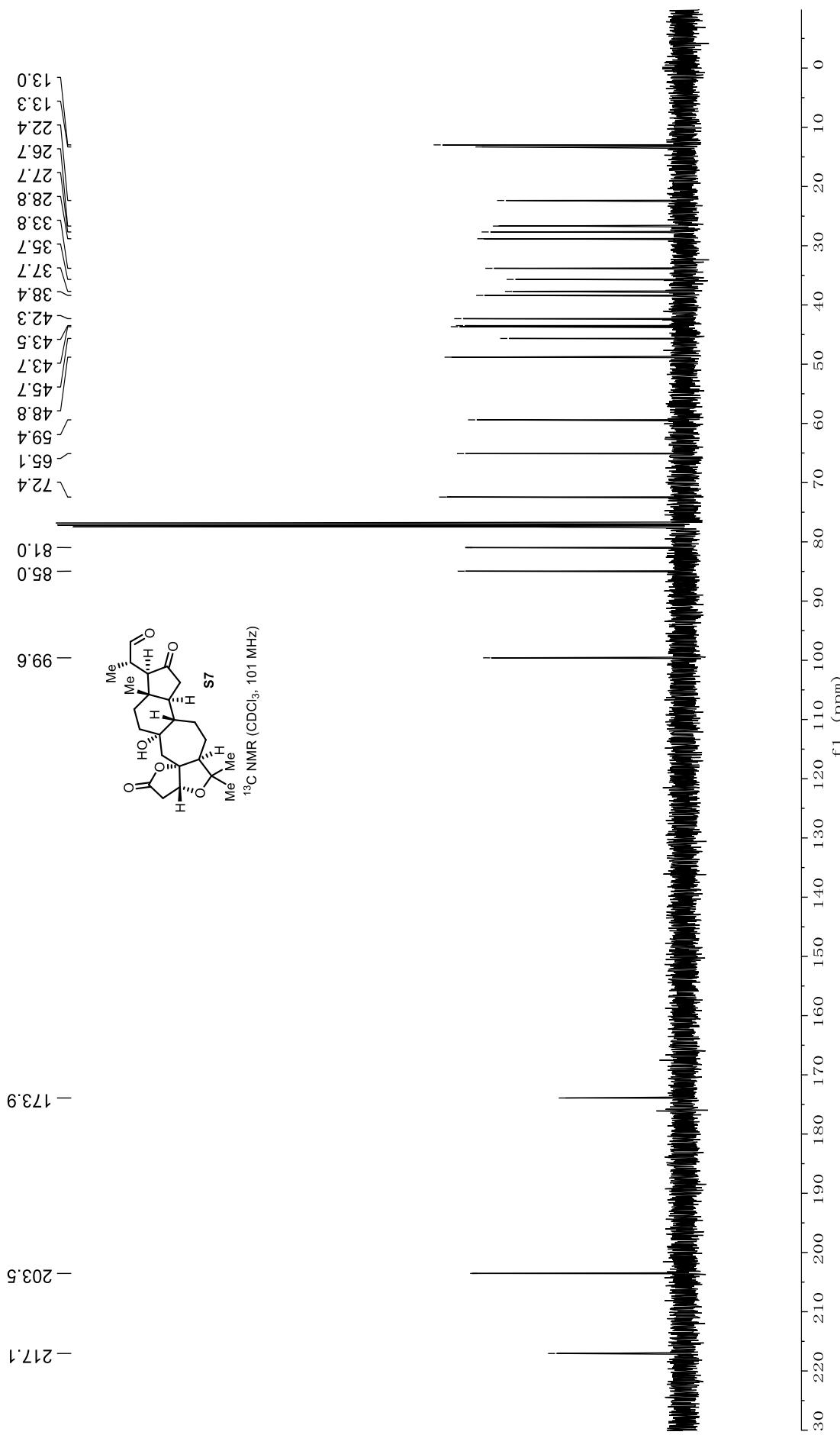


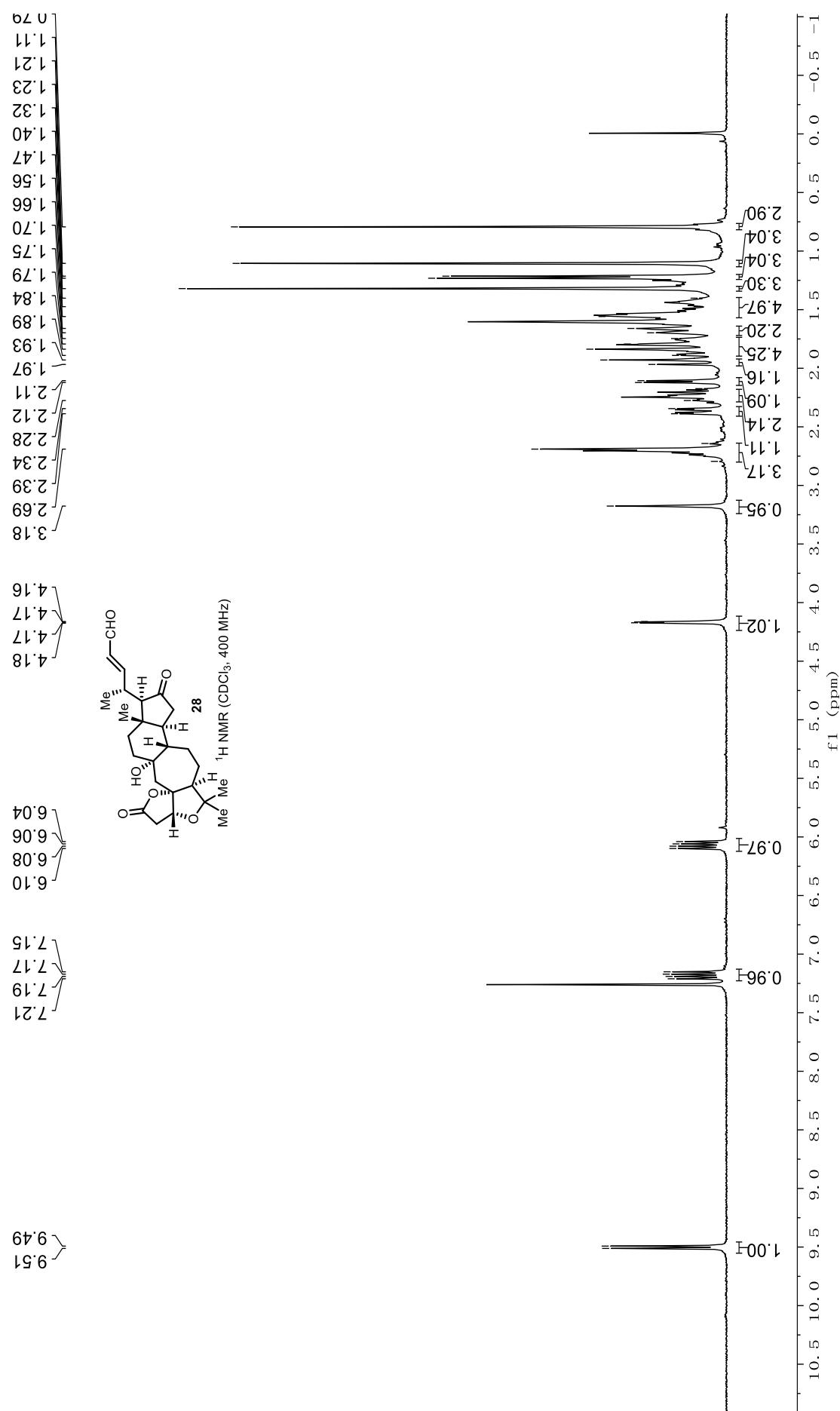


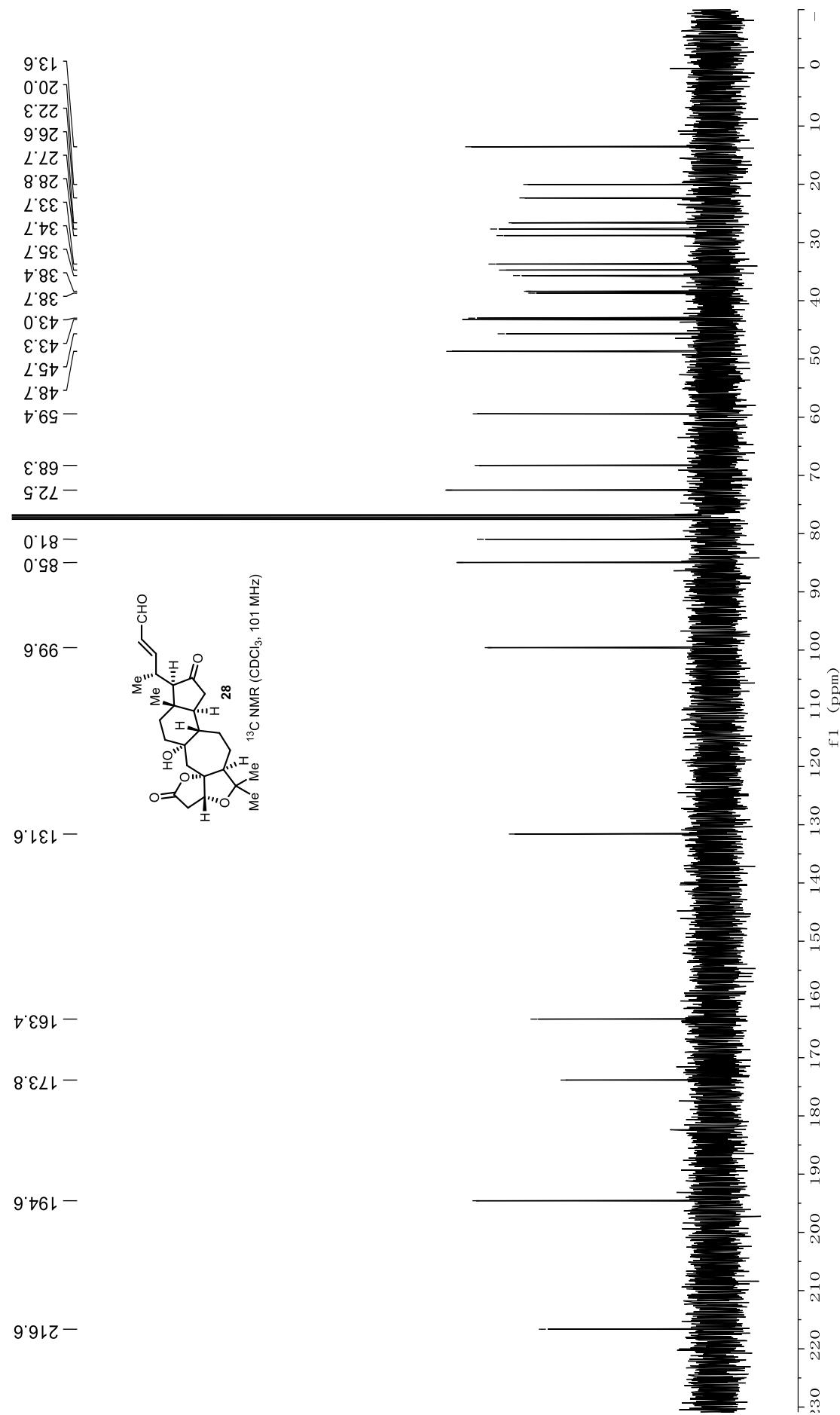


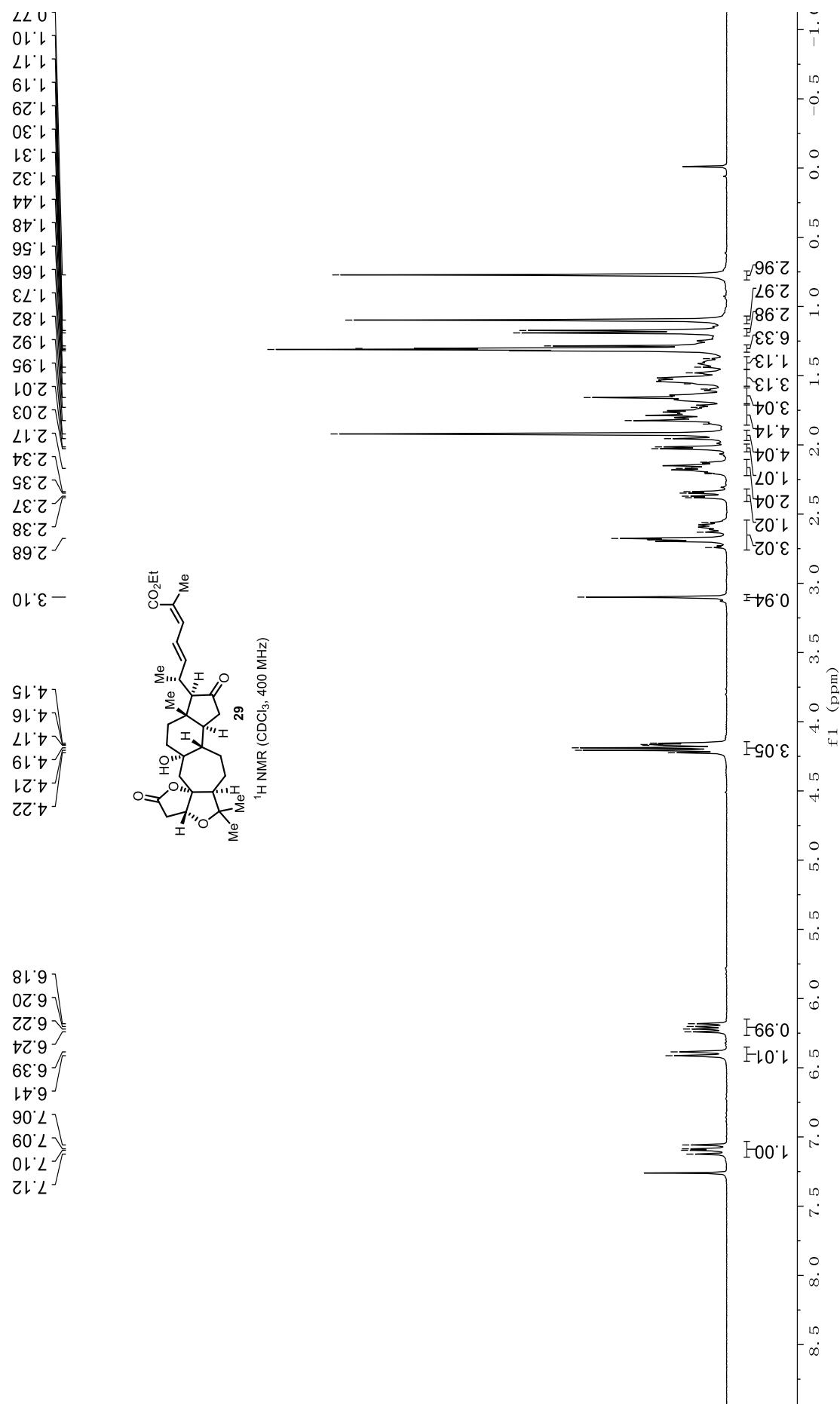


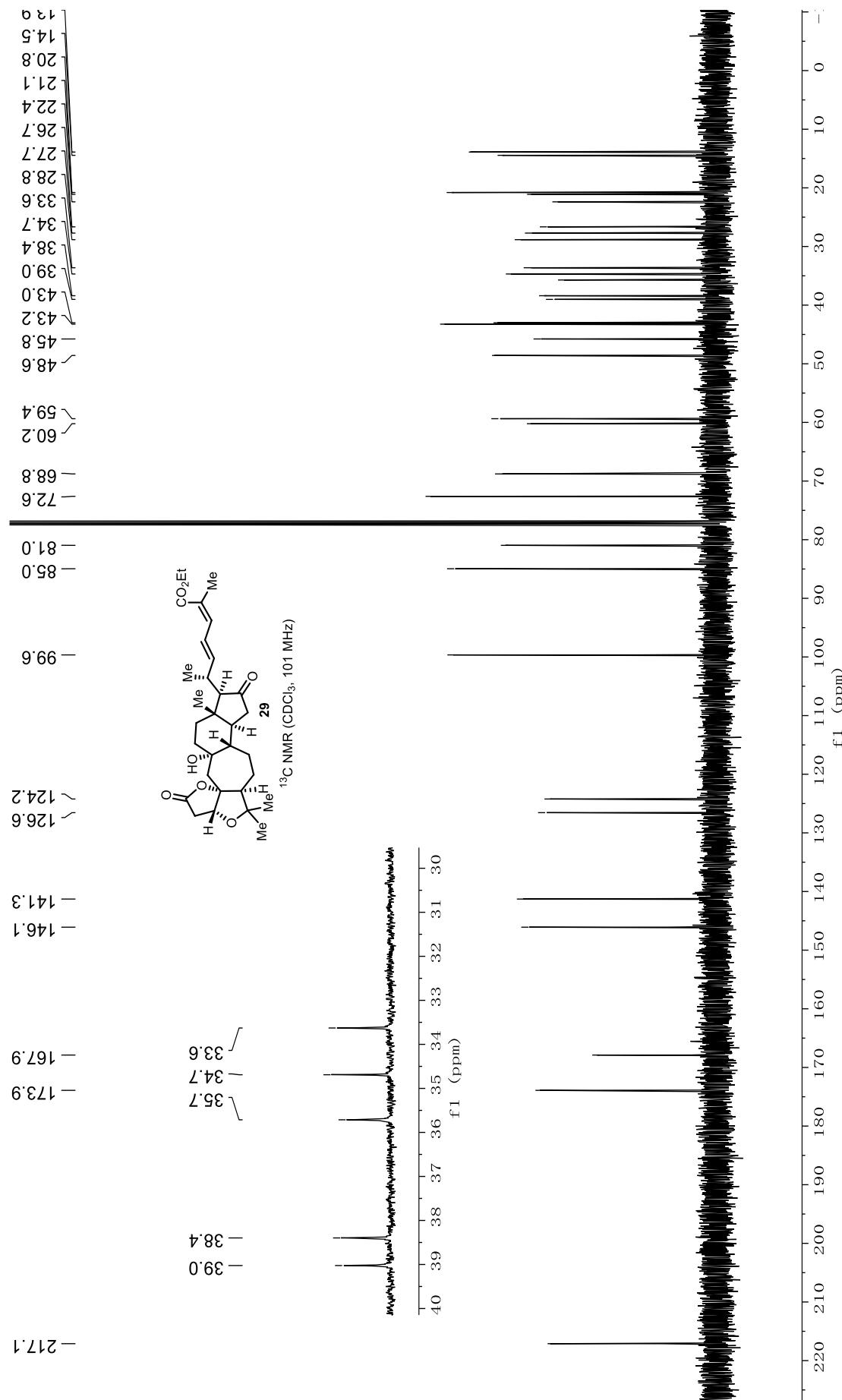


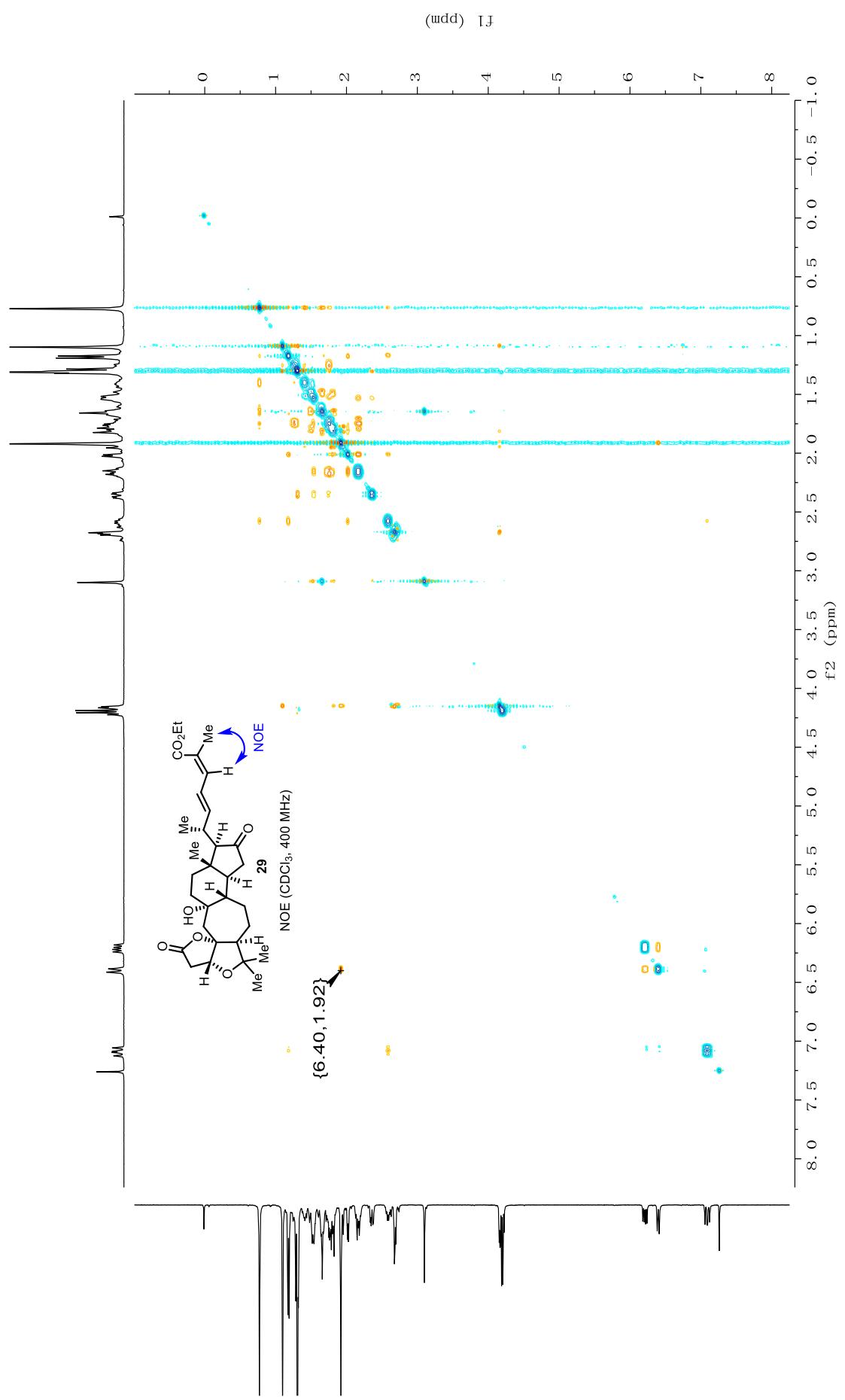


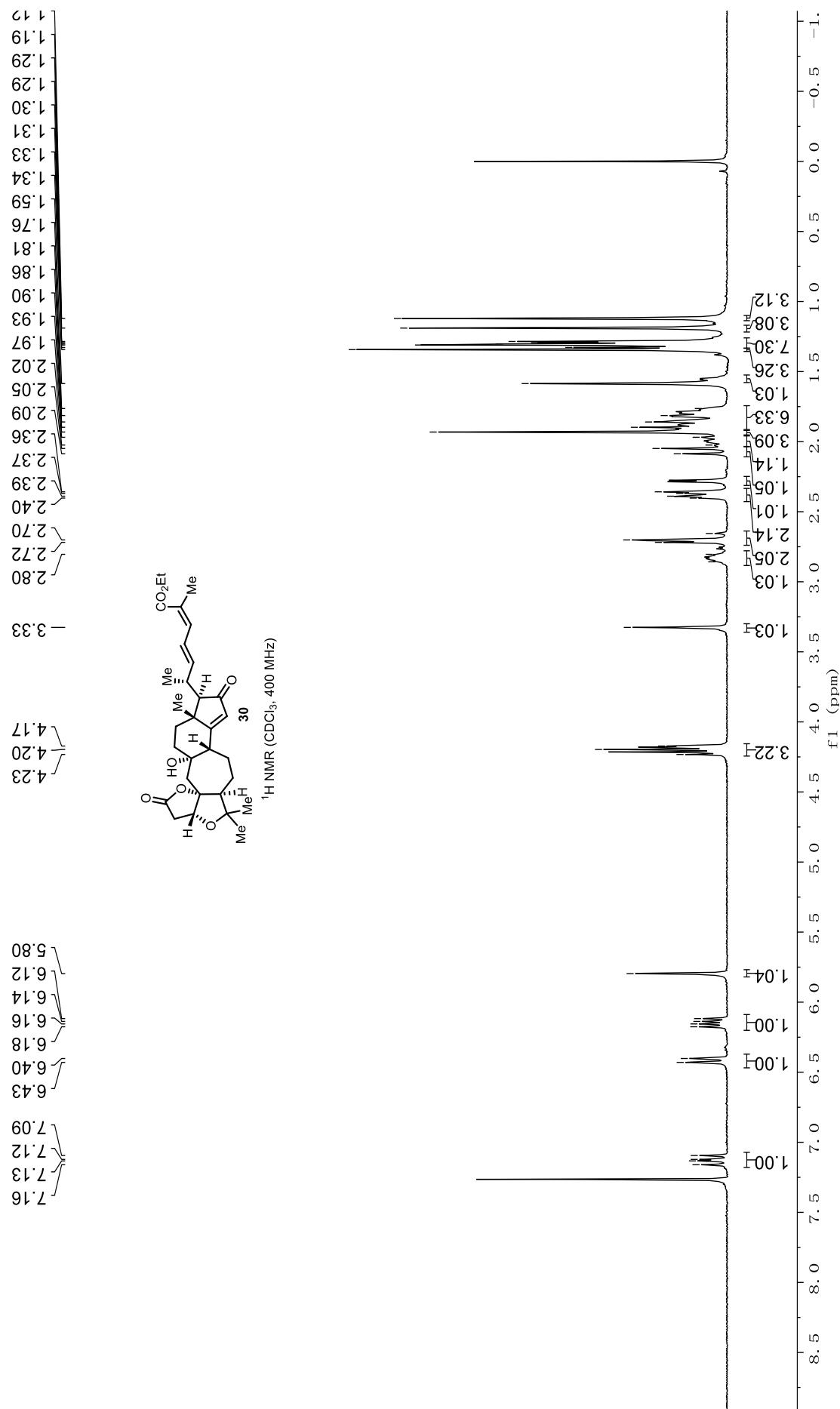


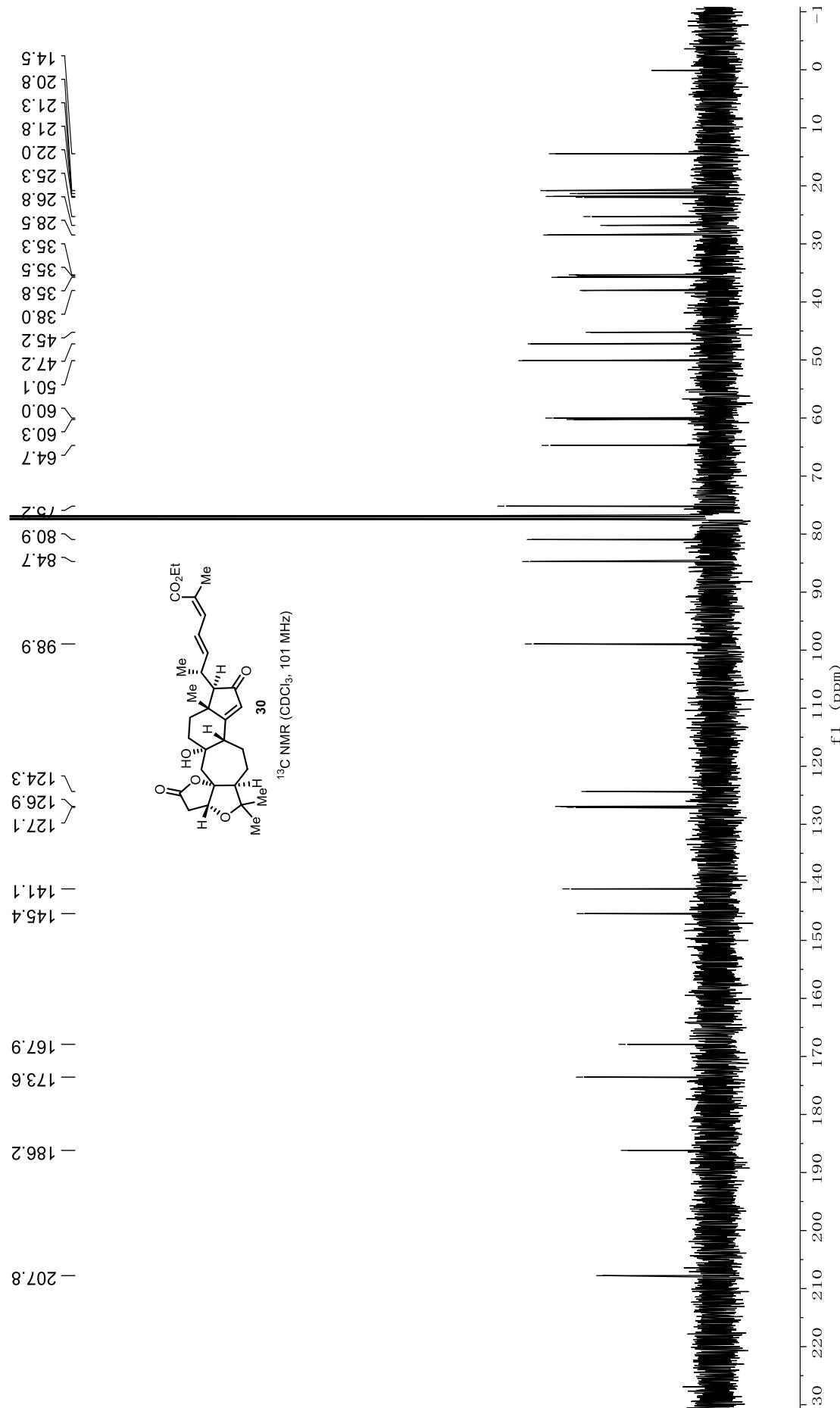


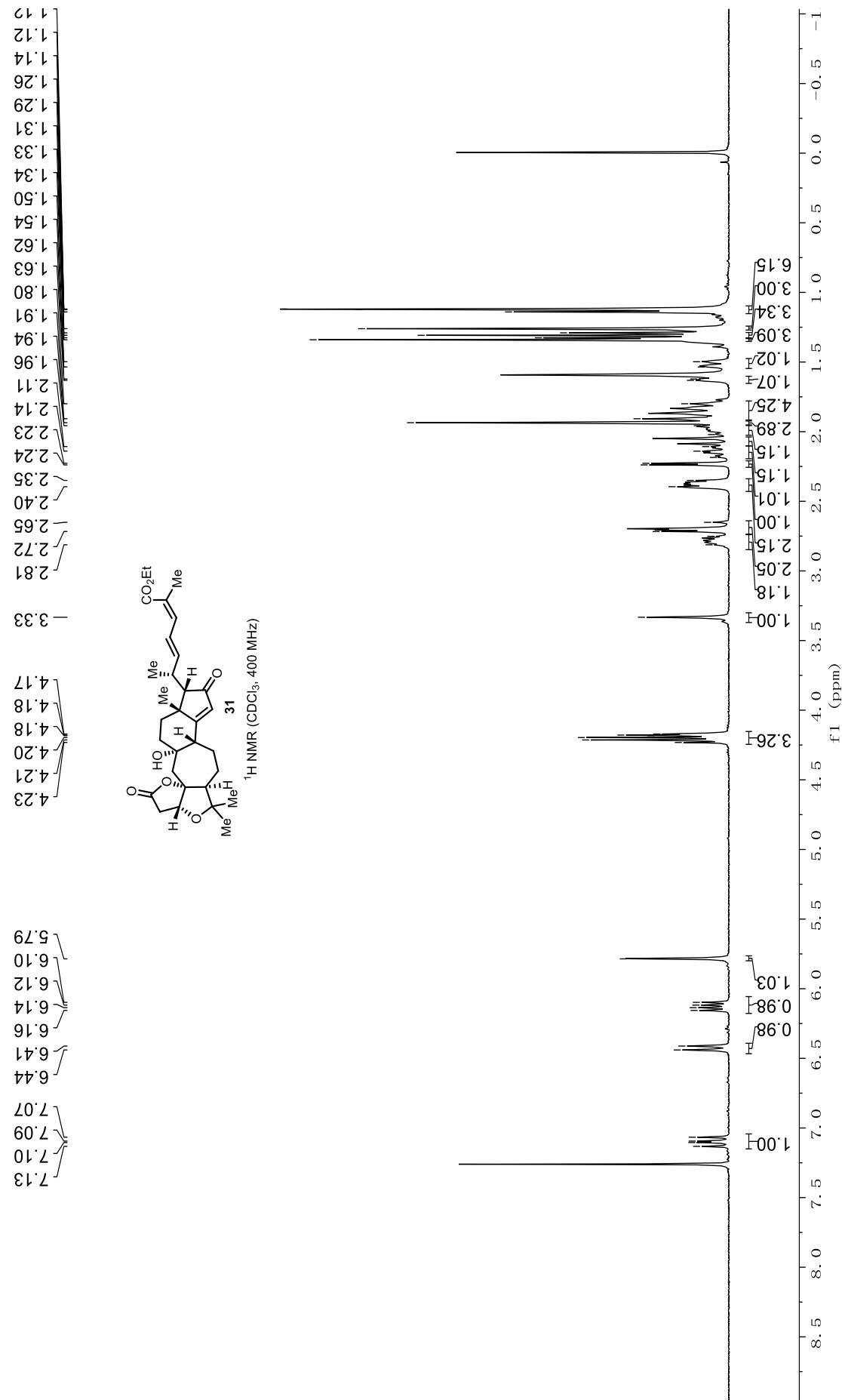


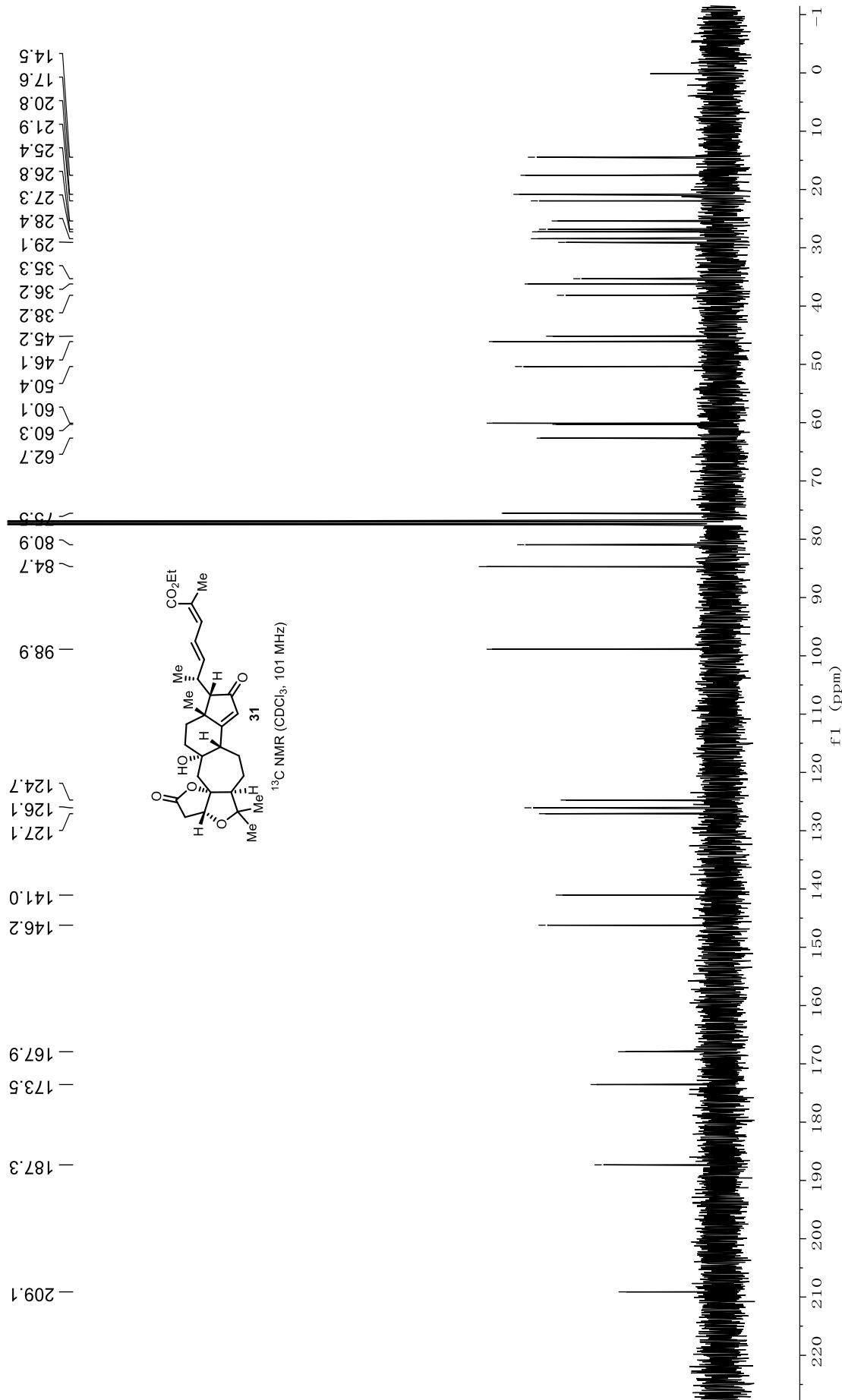


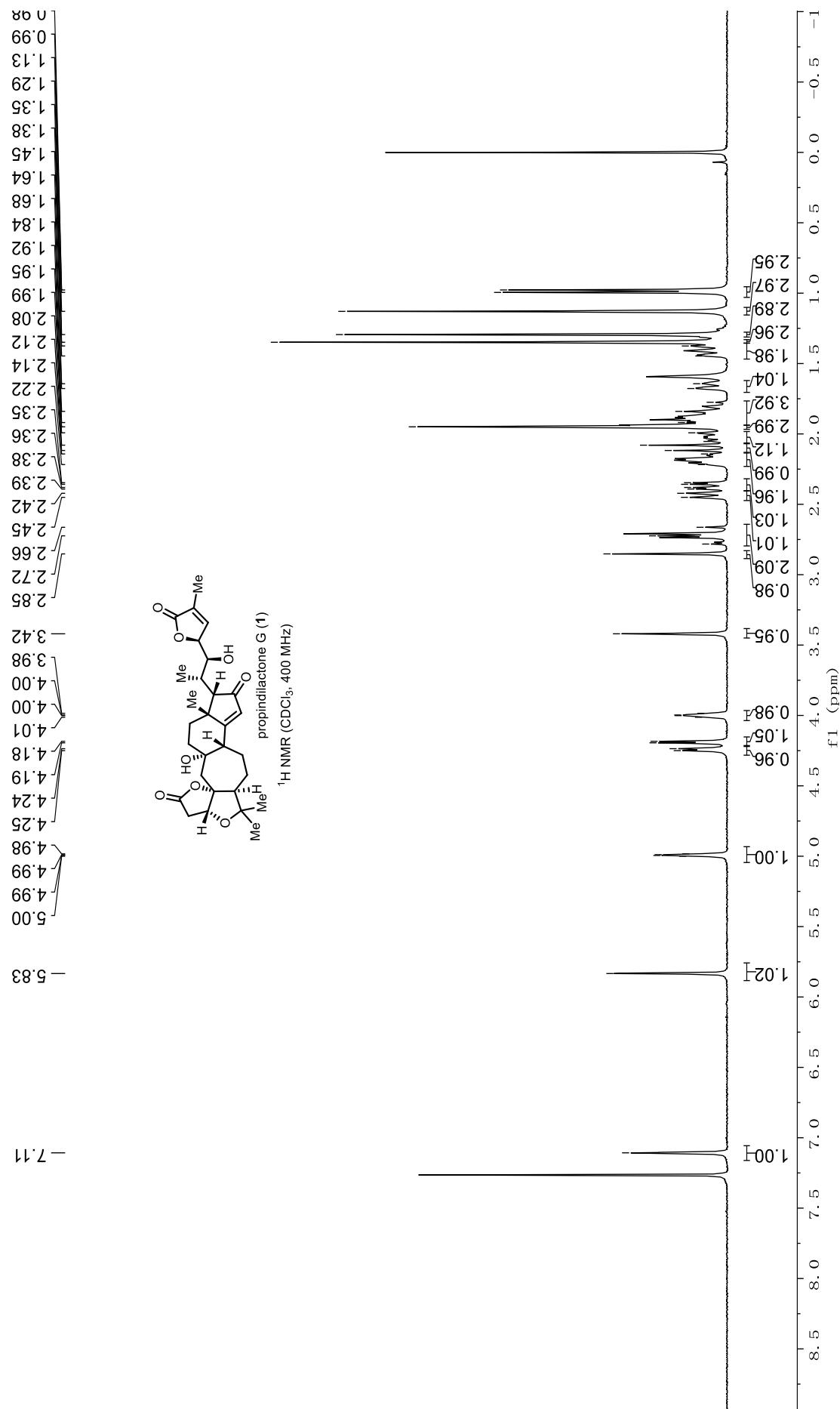


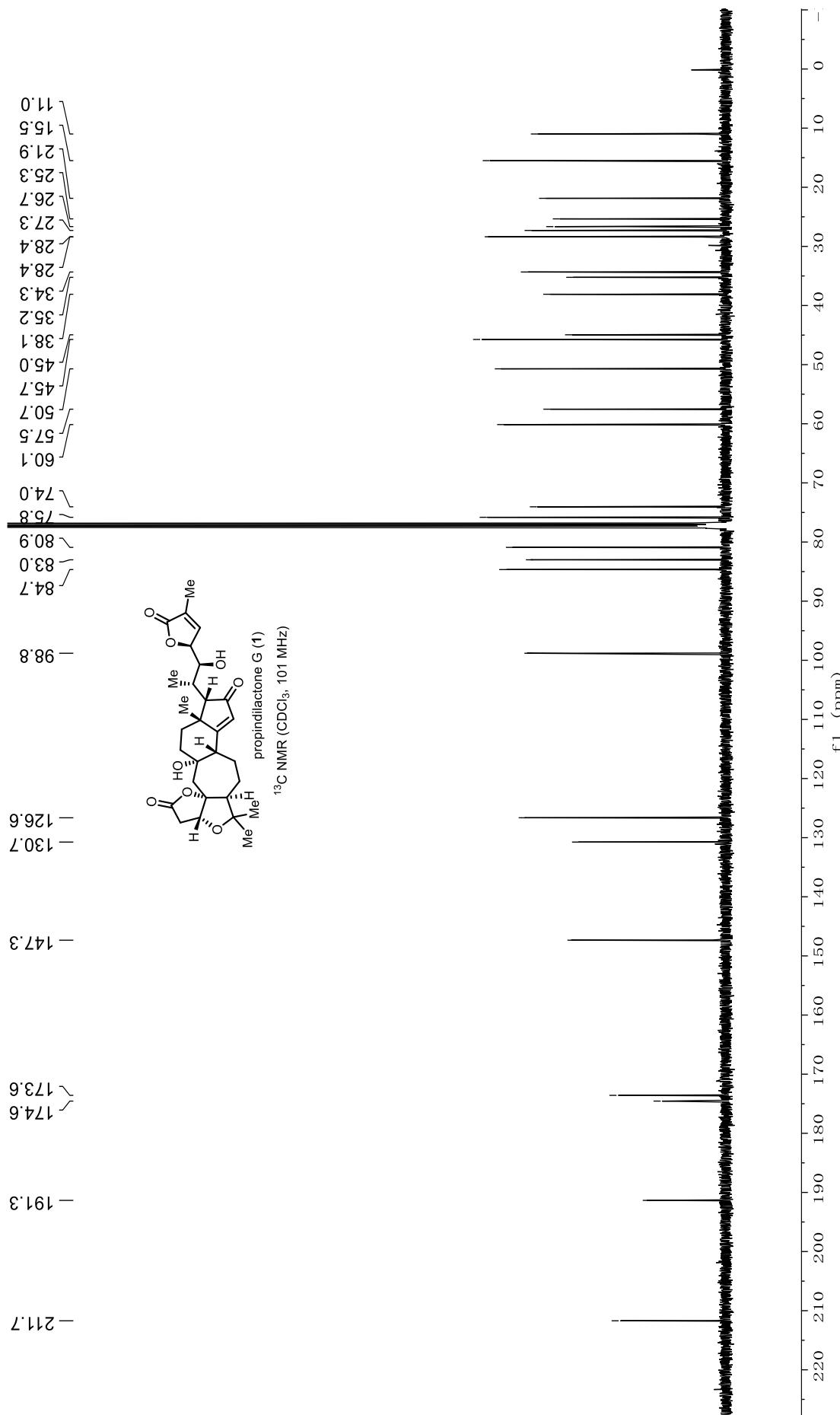


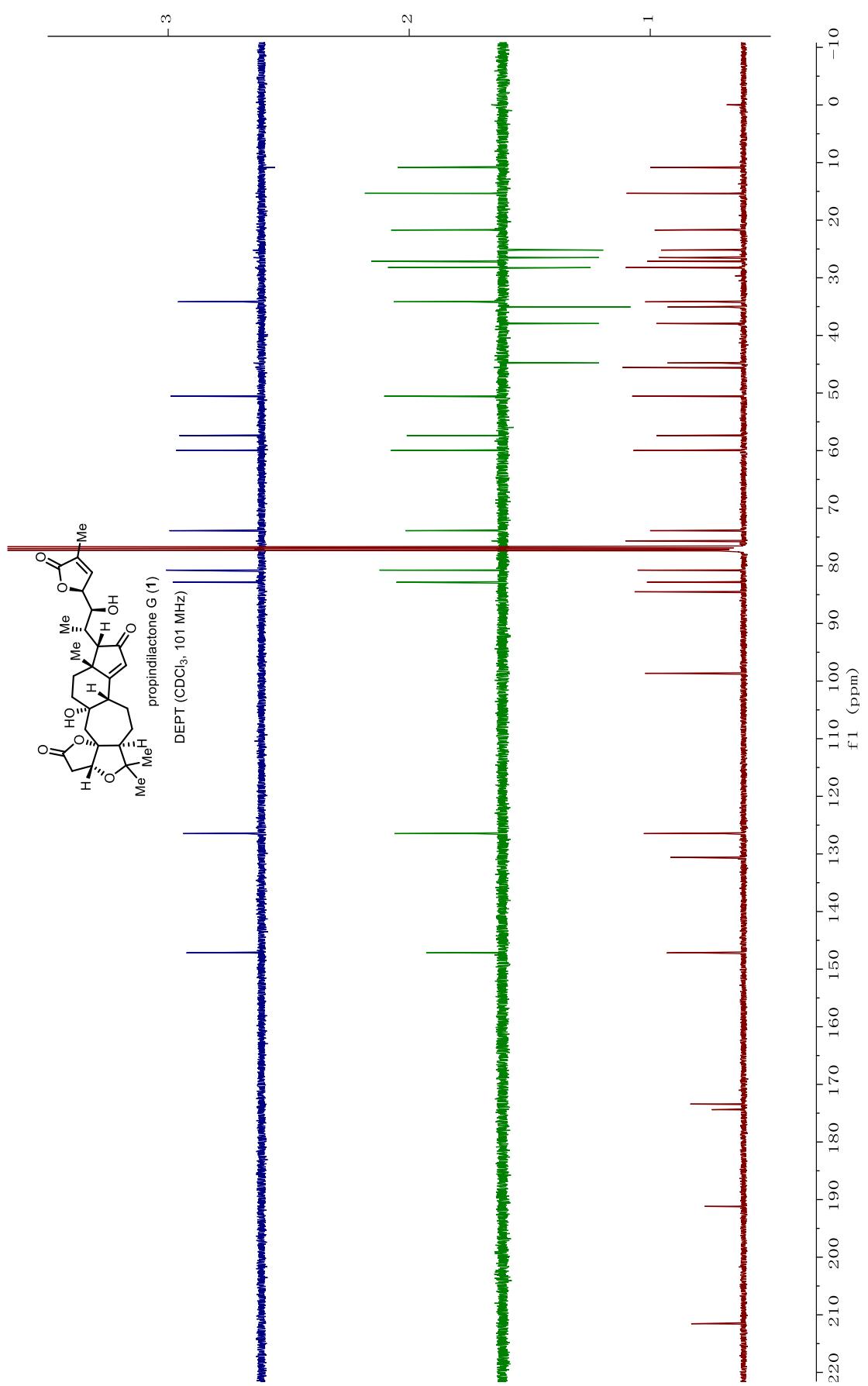


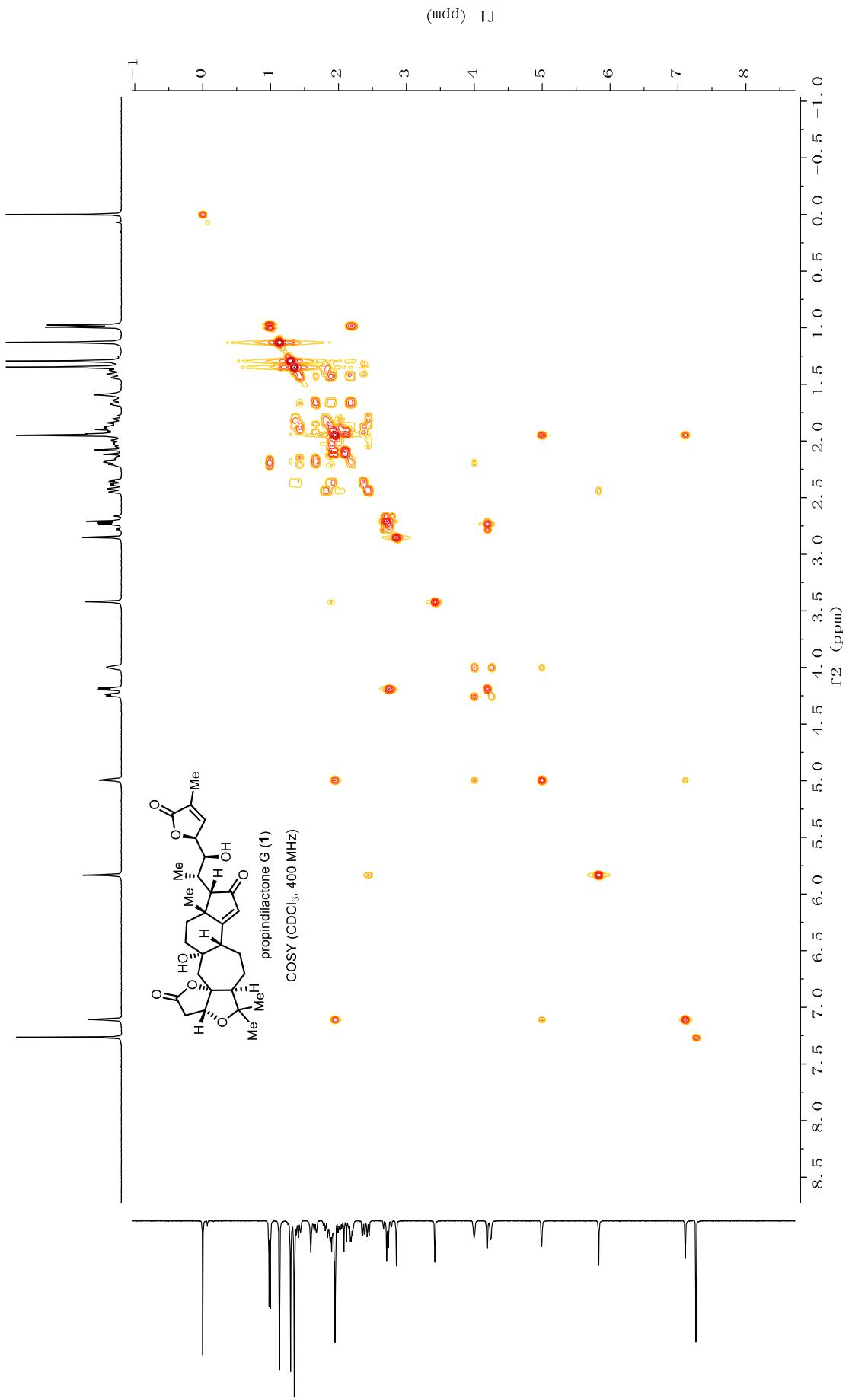


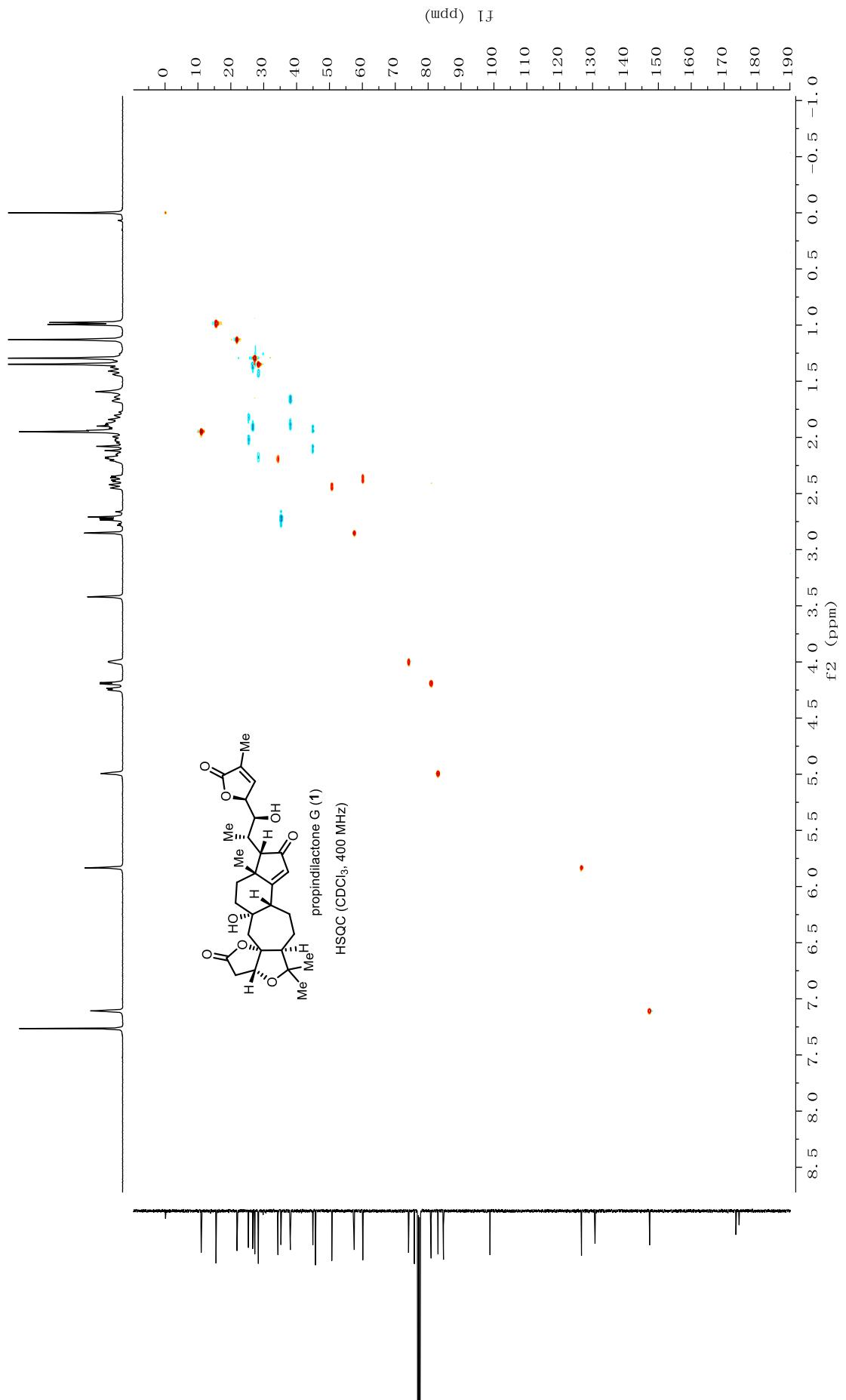


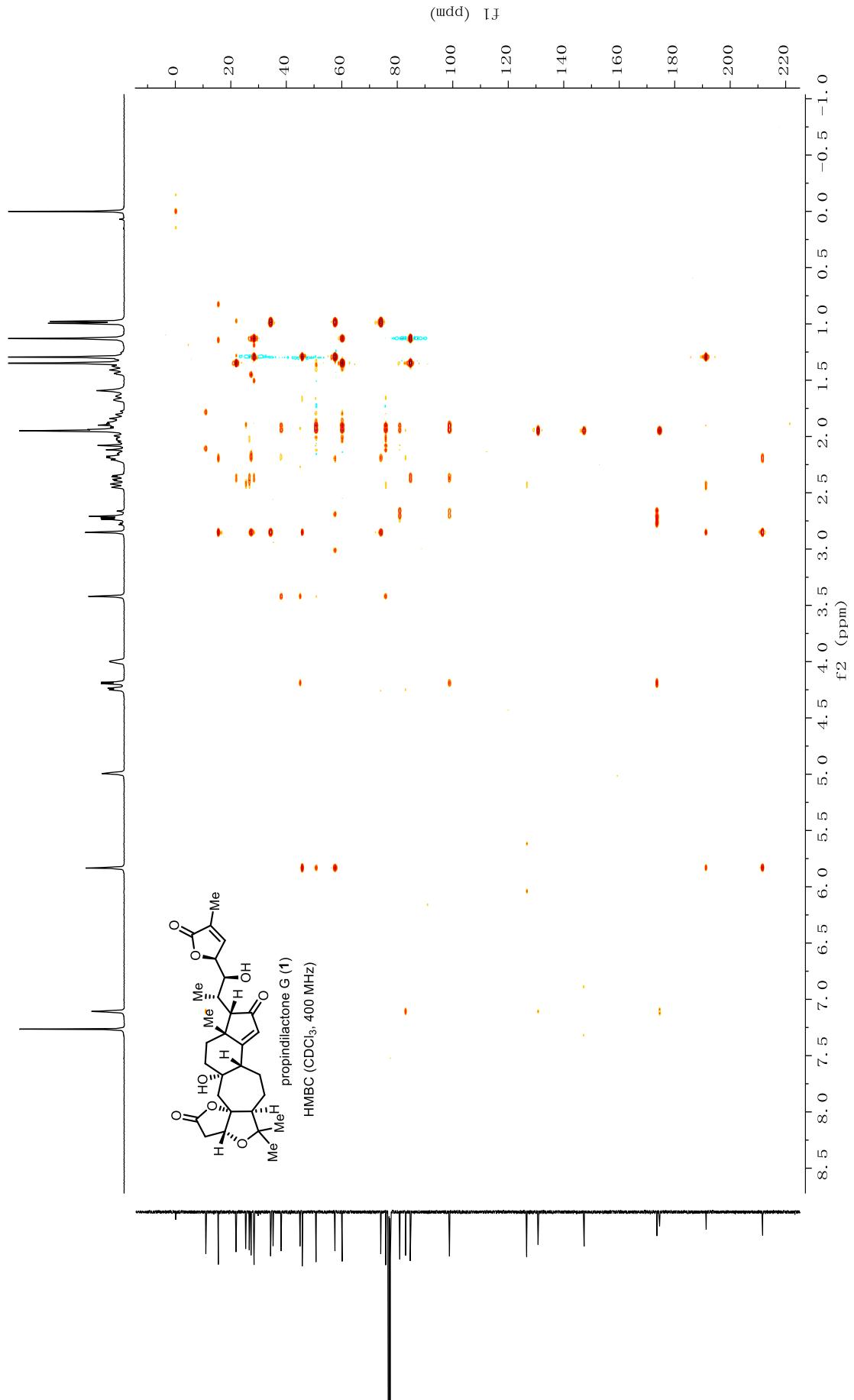


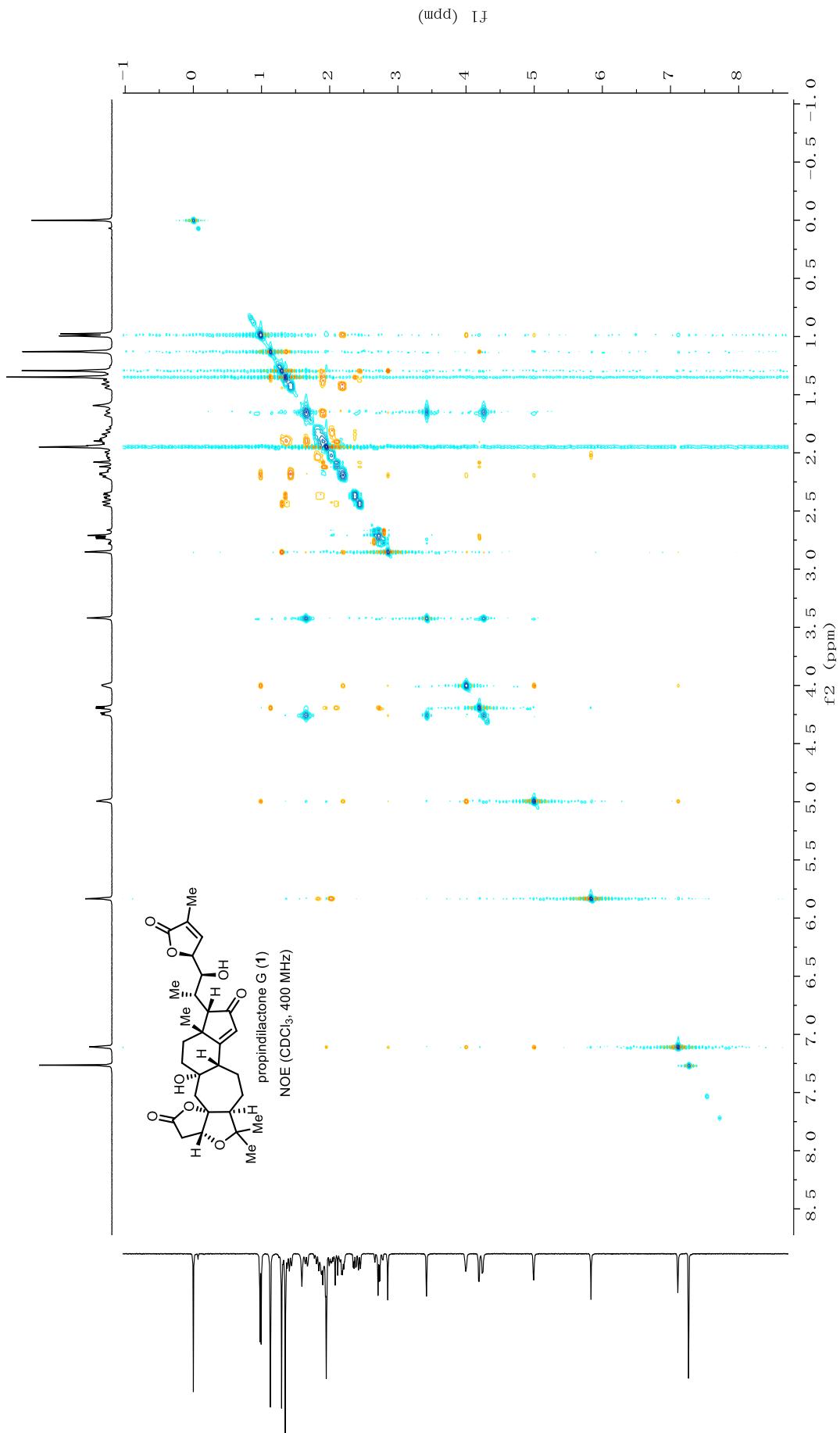


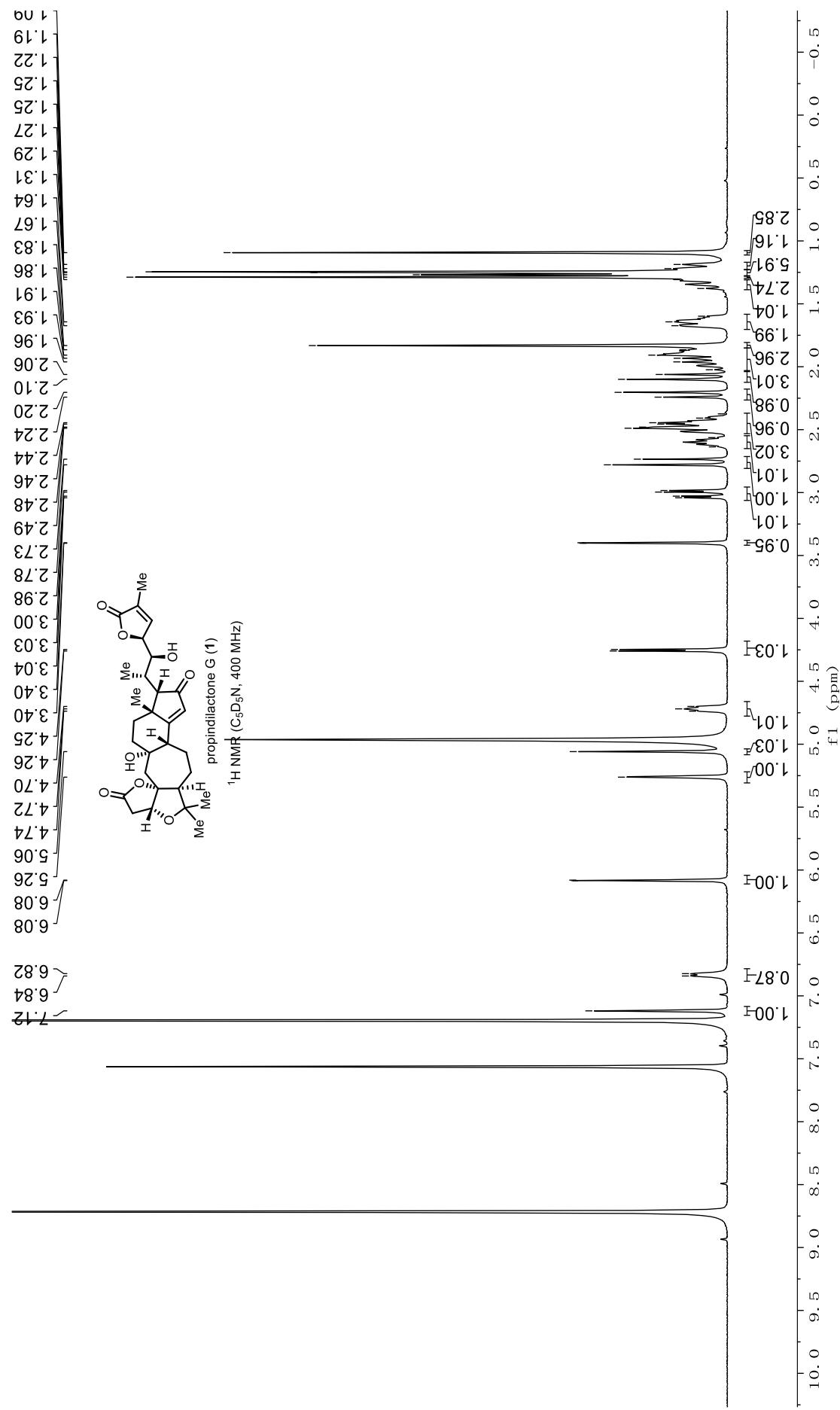


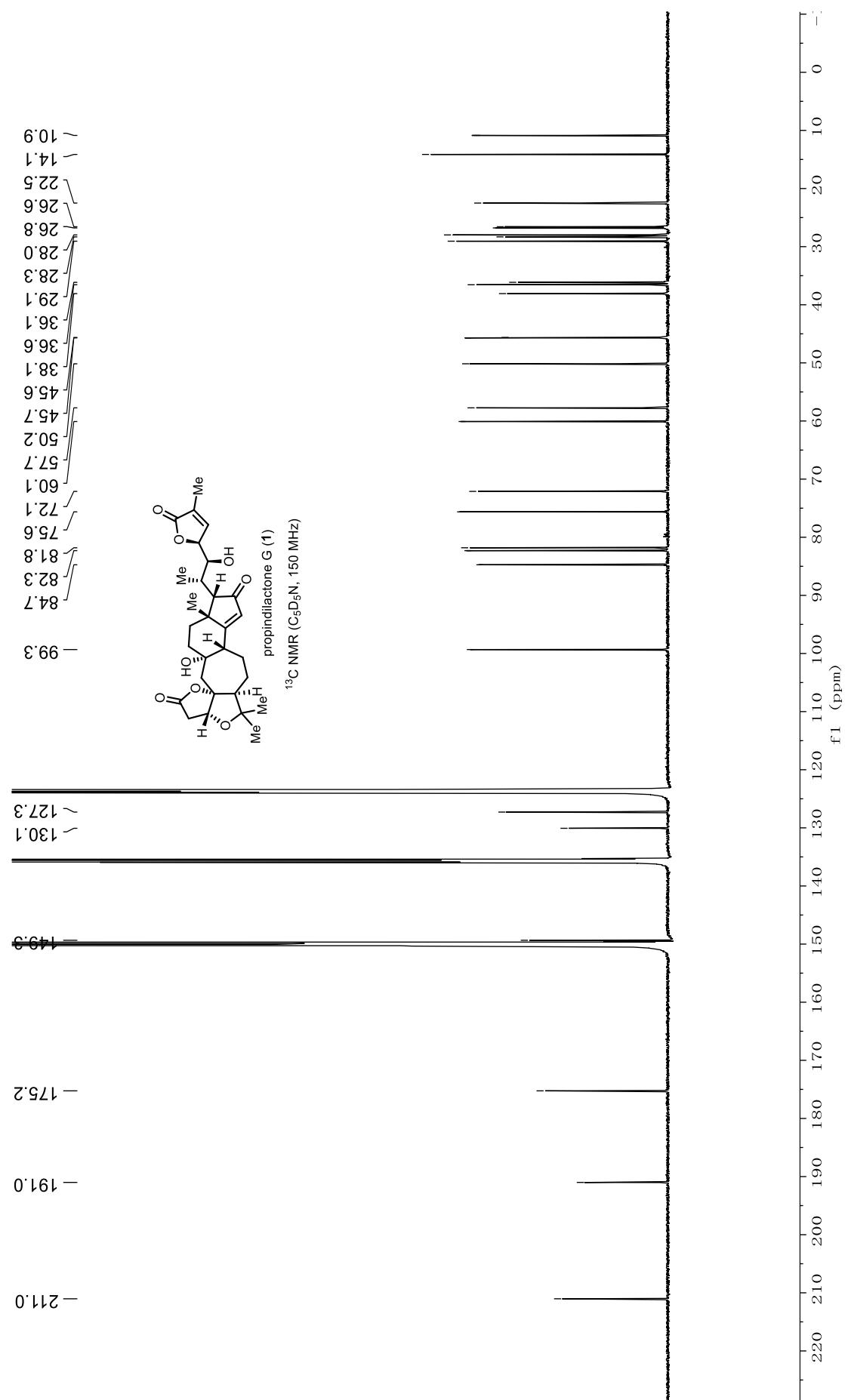


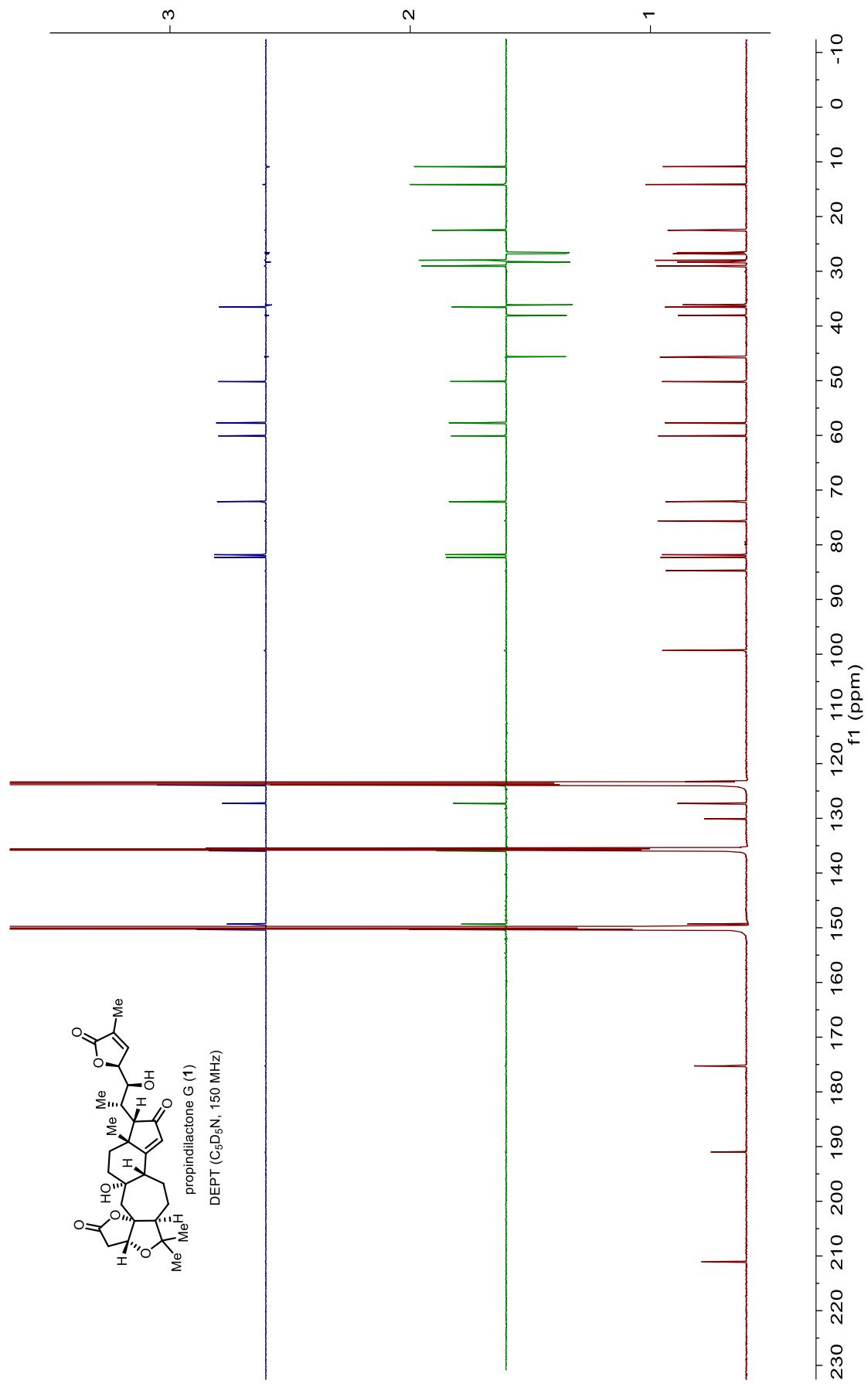


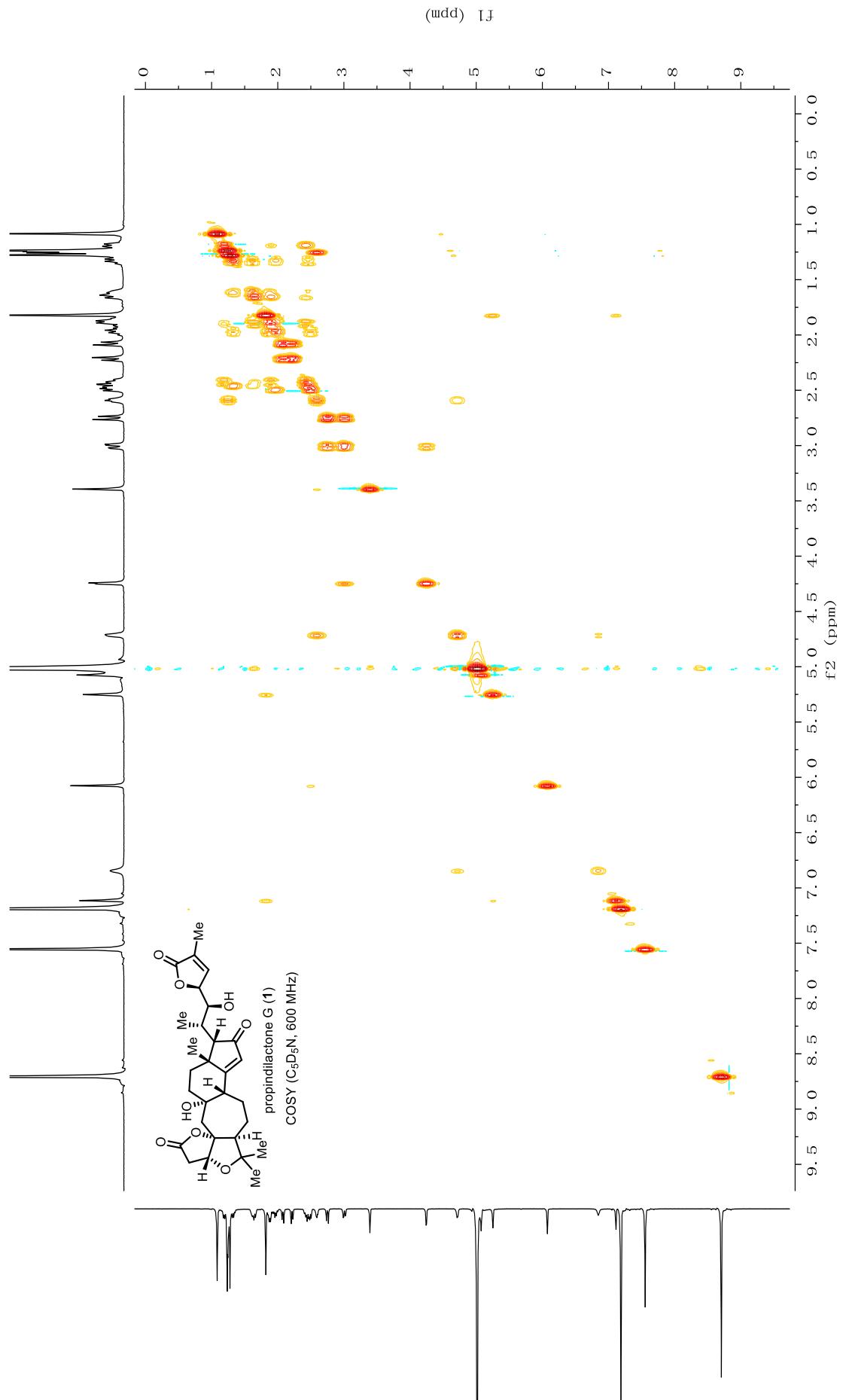


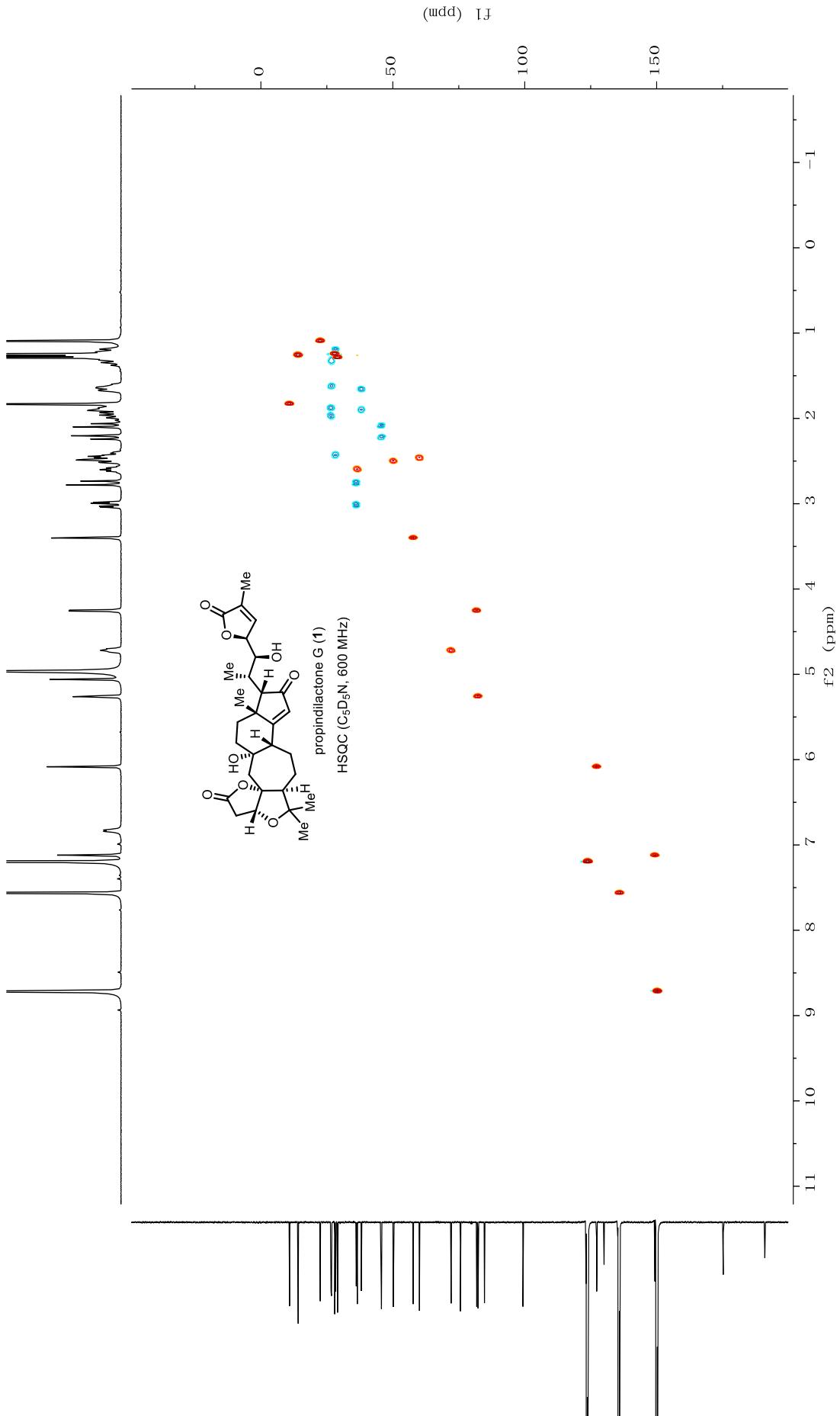


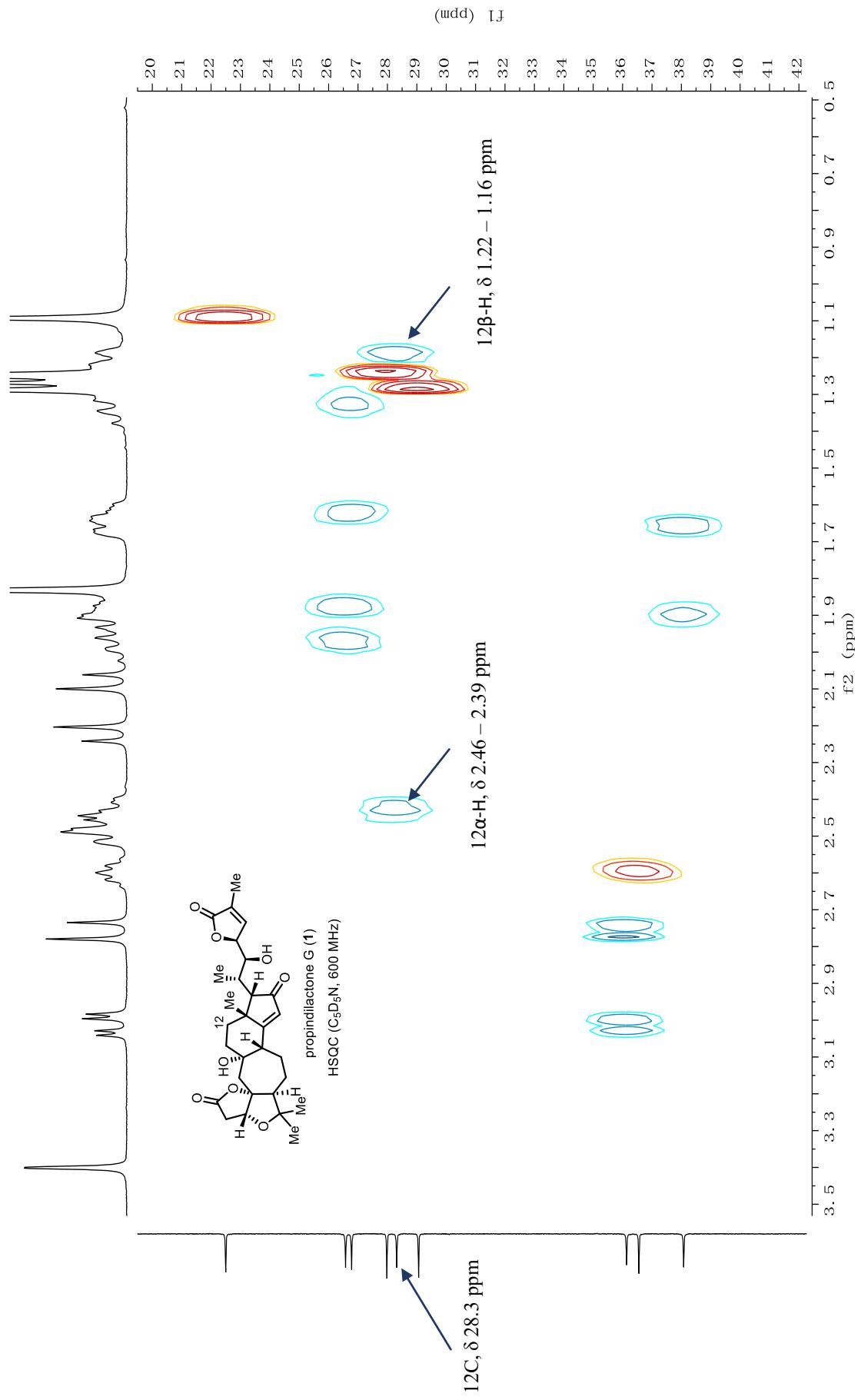


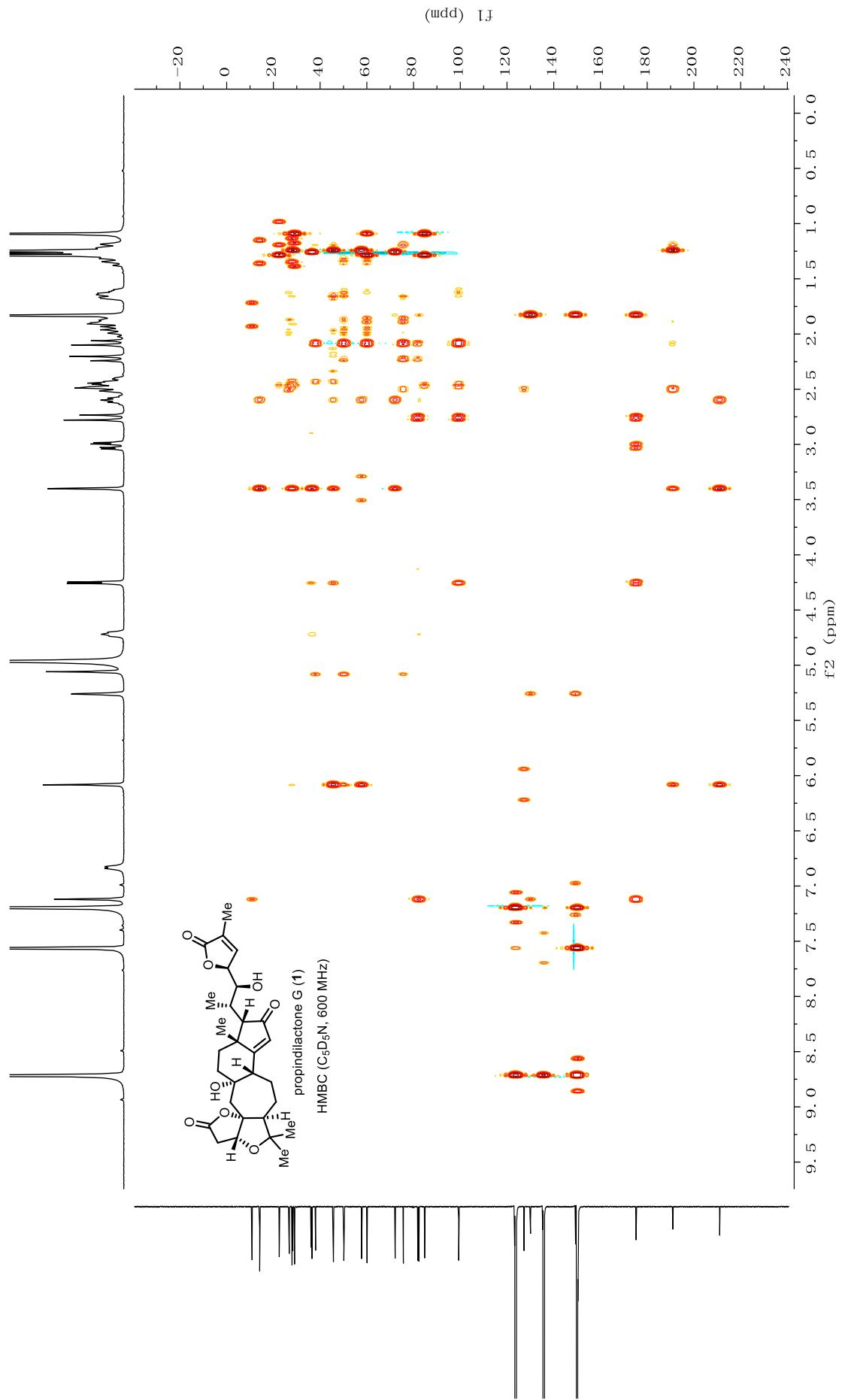


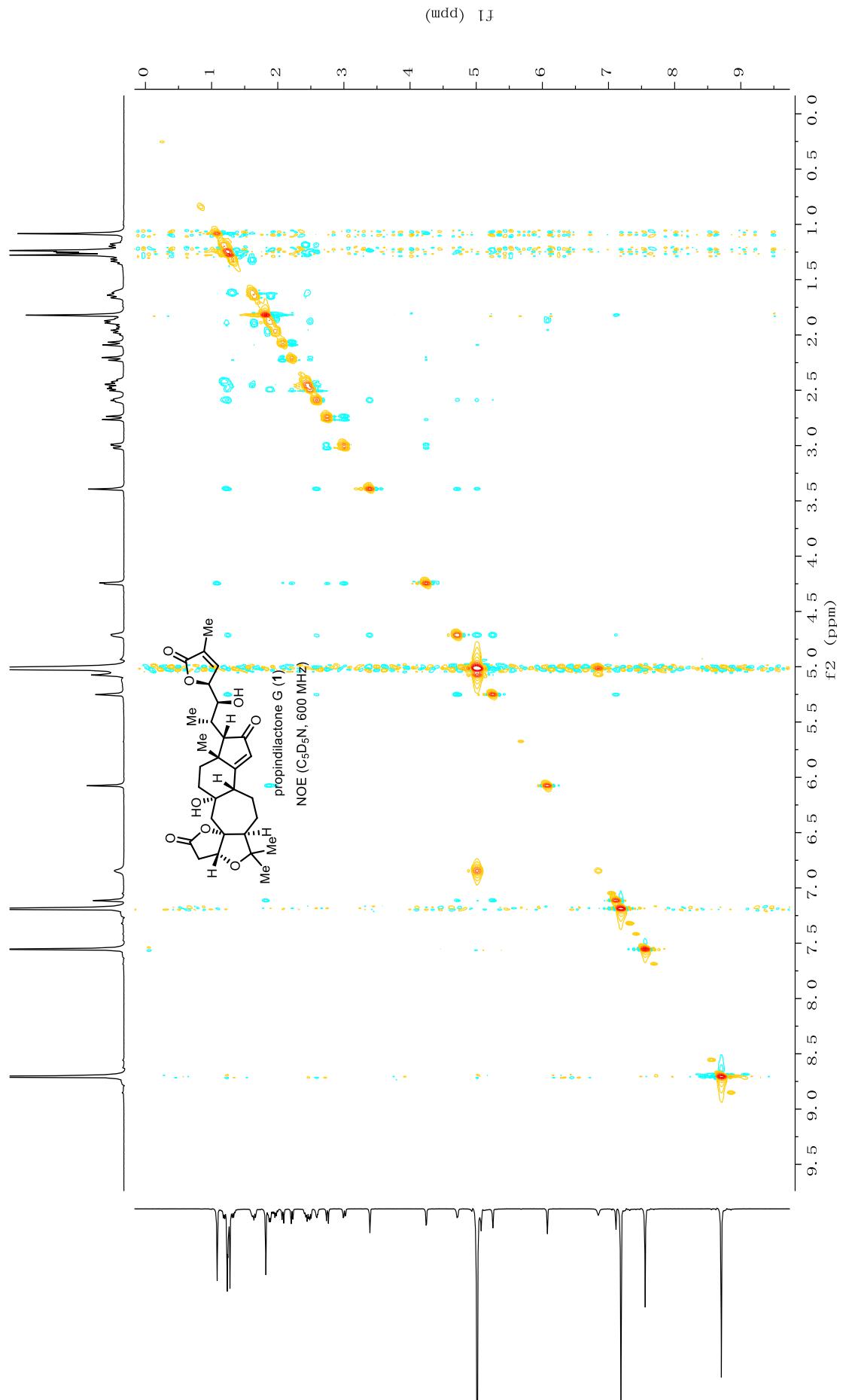












## 7. References

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