

# Supporting Information

## Synthesis and Assignment of absolute Configuration of the Iridoid 9-Deoxygelsemide

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## General Procedures

All solvents were of commercial quality and were purified by distillation over the drying agents indicated: THF (Na/benzophenone), CH<sub>2</sub>Cl<sub>2</sub>, hexane, Et<sub>3</sub>N (CaH<sub>2</sub>), toluene (Na/K). All other reagents were used as supplied. All moisture-sensitive reactions were carried out under a positive static atmosphere of Ar in flame-dried glassware. Syringes and needles for the transfer of reagents were dried at 140 °C and allowed to cool in a desiccator over P<sub>2</sub>O<sub>5</sub> before use. Routine monitoring of reactions was performed using silica gel 60 (0.25 mm), aluminum-supported TLC plates. Compounds were visualized by UV irradiation at a wavelength of 254 nm, or stained by exposure to a 0.5% soln. of vanillin in H<sub>2</sub>SO<sub>4</sub>/EtOH, followed by charring. Flash column chromatography (FCC) was performed on silica gel (40–63 μm). Yields are reported for isolated compounds with >96% purity established by NMR unless otherwise indicated. <sup>1</sup>H and <sup>13</sup>C NMR spectra at 300 MHz and 75 MHz, respectively, in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl<sub>3</sub>: δ<sub>C</sub> 77.16; residual CHCl<sub>3</sub> in CDCl<sub>3</sub>: δ<sub>H</sub> 7.26; CD<sub>2</sub>Cl<sub>2</sub>: δ<sub>C</sub> 53.8; residual <sup>1</sup>H: δ<sub>H</sub> 5.32 ppm. COSY, DEPT, HSQC, NOESY spectra were recorded using a standard pulse program library. The number of H-atoms attached to each C-atom (s = 0H, d = 1H, t = 2H, q = 3H) was determined by DEPT experiments. Optical rotations were recorded on a digital polarimeter at 589 nm, concentration (*c*) is in g/100 mL.

**(4aR, 5R, 6S, 7R, 7aR)-hexahydro-5,6-epoxy-7-methylcyclopenta[*c*]pyran-3(1H)-one (10).** DBU (866 μL, 5.79 mmol) was added dropwise to a stirred solution of iodolactone **12**<sup>1</sup> (572 mg, 1.93 mmol) in dry toluene (13 mL) at rt, then the solution was heated at 50 °C. After stirring for 1 h, the solution was cooled to rt, then was added a saturated solution of NH<sub>4</sub>Cl (8 mL). The aq layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 5 mL). Combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum to give a residue which was purified by FCC on silica gel. Elution with hexane/AcOEt (7:3 v/v) gave **10** as a colorless solid (275 mg, 85 %), followed by olefin **13** (28 mg, about 8%). Mp 105-107 °C; [α]<sub>D</sub><sup>20</sup> = – 85.39 (*c* = 2.2, CH<sub>2</sub>Cl<sub>2</sub>). IR (nujol mull): 2919, 1722, 1478, 1391, 1342, 1293, 1250, 1166,

1064, 1045, 1024, 1005, 940, 897, 858, 826, 725  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.20–3.90 (m, 2H), 3.58 (br s, 1H), 3.4 (d,  $J = 2.2$ , 1H), 2.80–2.50 (m, 3H), 2.20–2.00 (m, 2H), 1.06 (d,  $J = 7.3$ , 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  172.7 (s, CO), 70.3 (t), 64.7 (d), 61.7 (d), 43.9 (d), 36.1 (d), 34.2 (d), 29.5 (t), 17.0 (q). LCMS  $m/z$  191.29  $[(\text{M}+\text{Na})^+, 91]$ , 169.13  $[(\text{M}+\text{H})^+, 100]$ . Elemental analysis calcd (%) for  $\text{C}_9\text{H}_{12}\text{O}_3$ : C 64.27, H 7.19; found: C 64.36, H 7.13.

**(4aR, 5R, 6R, 7R, 7aS)-hexahydro-5-hydroxy-6-iodo-7-methylcyclopenta[c]pyran-3(1H)-one (14)** and **(4aR, 5S, 6S, 7R, 7aR)-hexahydro-6-hydroxy-5-iodo-7-methylcyclopenta[c]pyran-3(1H)-one (15)**. 57% aq HI (380  $\mu\text{L}$ , 2.86 mmol), precooled at  $-20\text{ }^\circ\text{C}$ , was added to a stirred solution of epoxide **10** (437mg, 2.60 mmol) in THF (30 mL) at  $-78\text{ }^\circ\text{C}$ ; subsequently, the solution was allowed to reach rt. After stirring for 1 h, the solution was diluted with  $\text{CH}_2\text{Cl}_2$  (30 mL) and saturated aq  $\text{Na}_2\text{S}_2\text{O}_3$  (15 mL). The aq layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 8\text{ mL}$ ) and combined organic layers were dried with  $\text{MgSO}_4$ . The solvent was removed under vacuum and the residue was purified by FCC on silica gel. Elution with hexane/EtOAc (4:1 v/v) yielded a mixture of iodohydrins **14** and **15**, and lactone **12** in  $\geq 95\%$  yield. The amount of compound **14** was  $\leq 5\%$  **15**, and the ratio (**14** + **15**) : **12** was about 6 : 1 ( $^1\text{H}$  NMR spectrum of crude mixture). An analytical sample of **15**, colorless solid, was obtained by further chromatographic separation of the mixture. Mp  $130\text{--}131\text{ }^\circ\text{C}$ ;  $[\alpha]_{\text{D}}^{20} = +12.9$  ( $c = 0.86$ ,  $\text{CH}_2\text{Cl}_2$ ). IR (nujol mull): 3467, 1715, 1392, 1172, 1065, 961, 707  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 4.29 (dd,  $J = 4.3, 11.8$ , 1H), 4.17 (dd,  $J = 4.1, 11.8$ , 1H), 3.75 (td,  $J = 9.9, 4.1$ , 1H), 3.56 (t,  $J = 10.0$ , 1H), 2.90–2.75 (m, 1H), 2.68 (dd,  $J = 6.9, 15.4$ , 1H), 2.65–2.50 (m, 2H), 2.12–2.00 (m, 1H), 1.77–1.62 (m, 1H), 1.20 (d,  $J = 6.5$ , 3H).  $^{13}\text{C}$ -NMR: (75MHz,  $\text{CDCl}_3$ )  $\delta$ : 171.8 (s), 84.1 (d), 67.8 (t), 41.3 ( $2 \times$  d), 39.8 (d), 36.4 (d), 31.7 (t), 16.2 (q). Elemental analysis calcd (%) for  $\text{C}_9\text{H}_{13}\text{IO}_3$ : C 36.51, H 4.43; found: C 36.66, H 4.53.

**(4aR, 5R, 6R, 7R, 7aS)-octahydro-6-iodo-7-methyl-3-oxocyclopenta[c]pyran-5-yl acetate (16)**, **(4aR, 5S, 6S, 7R, 7aR)-octahydro-5-iodo-7-methyl-3-oxocyclopenta[c]pyran-6-yl acetate (17)**, and **((3aR, 4S, 5R, 6R, 6aR)-hexahydro-6-iodo-5-methyl-2-oxo-2H-cyclopenta[b]furan-4-yl)methyl acetate (12b)**. Pyridine (206  $\mu\text{L}$ , 2.1 mmol), followed by  $\text{Ac}_2\text{O}$  (183  $\mu\text{L}$ , 1.9 mmol) and a catalytic amount of DMAP (3 mg) were added to a stirred solution of the above mixture of **12**, **14**, and **15** (305 mg, 1.03 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10 mL)

at 0 °C. After 5 h of stirring at rt, the solution was concentrated under vacuum. The residue was purified by FCC on silica gel. Elution with hexane/EtOAc (7:3 v/v) gave lactone-acetate **17** (279 mg, 78 %), followed by a mixture of **16** and **17** (18 mg, 5%), and then pure **12b** (50 mg, 14%). Compound **17**, colorless solid, mp 80 – 83 °C;  $[\alpha]_D^{20} = +17.0$  ( $c = 0.87$ , CH<sub>2</sub>Cl<sub>2</sub>). IR (nujol mull): 3410, 1712, 1363, 1270, 1222, 735 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 5.16 (t,  $J = 10.1$ , 1H), 4.29 (dd,  $J = 4.1, 11.9$ , 1H), 4.18 (dd,  $J = 3.2, 11.9$ , 1H), 3.64 (t,  $J = 10.1$ , 1H), 3.00–2.80 (m, 1H), 2.75–2.55 (m, 2H), 2.13 (s, 3H), 2.20–2.05 (m, 1H), 1.90–1.80 (m, 1H), 1.13 (d,  $J = 6.6$ , 3H). <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$ : 171.3 (s), 170.2 (s), 82.5 (d), 67.3 (t), 41.7 (d), 41.1 (d), 39.1 (d), 31.5 (t), 28.7 (d), 20.8 (d), 15.8 (q). Elemental analysis calcd (%) for C<sub>11</sub>H<sub>15</sub>IO<sub>4</sub>: C 39.07, H 4.47; found: C 39.21, H 4.57. Lactone **12b**: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$ : 5.30 (d,  $J = 6$  Hz, 1H), 4.60 (d,  $J = 4.5$  Hz, 1H), 4.35–4.05 (m, 2H), 3.40–3.20 (m, 1H), 2.70 (dd,  $J = 10, 18.6$  Hz, 1H), 2.55 (dd,  $J = 1.8, 18.6$  Hz, 1H), 2.40–2.20 (m, 1H), 2.08 (s, 3H), 1.50–1.20 (m, 1H), 1.08 (d,  $J = 6.2$  Hz, 3H).

**(3aR, 4R, 5R, 6S, 6aR)-hexahydro-6-hydroxy-4-(hydroxymethyl)-5-methylcyclopenta[b]furan-2-one (25)** and **(4aR, 5R, 6S, 7R, 7aR)-hexahydro-5,6-dihydroxy-7-methylcyclopenta[c]pyran-3(1H)-one (26)**. 70% *m*-CPBA (477 mg, 1.93 mmol) was added at rt to a stirred solution of acetates **16** and **17** (about 5:95 mixture, 268 mg, 0.79 mmol), in CH<sub>2</sub>Cl<sub>2</sub> (10 mL). Solution's color changed during reaction from rose to 'red wine' with formation of a white precipitate. The reaction was monitored by TLC and after 3 h the solution was diluted with EtOAc (10 mL) and poured into saturated aq NaHCO<sub>3</sub> (5 mL) and Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (5 mL). After stirring for 1 h, the aq layer was extracted with EtOAc (5 × 5 mL) and combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was filtered on a short pad of silica gel. Elution with hexane/EtOAc (6:4, v/v) afforded an inseparable 2:1:5 mixture (NMR) of three compounds **22**, **23**, and **24** (130 mg, 72 %), which was directly submitted to the next step.

Resin Dowex 1 X 8 (OH<sup>-</sup> form) (186 mg) was added to a stirred solution of the above mixture (125 mg, 0.55 mmol) in MeOH (8 mL) at rt. After 3 h the resin was filtered off and washed exhaustively with methanol. Solvent was removed under vacuum to give a colorless solid, composed by isomeric lactones **25** and **26** (87 mg, combined yield = 85 %; **25** : **26**, 6 : 1). IR (nujol mull): 3392, 1752, 1654, 1196, 1174, 1070 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz,

MeOH-*d*<sub>4</sub>)  $\delta$  : 4.87 (dd, *J* = 4.8, 6.4, 1H), 4.30 (dd, *J* = 4.3, 11.4, 1H)\*, 4.16 (dd, *J* = 5.4, 11.4, 1H)\*, 3.96 (dd, *J* = 4.2, 4.5, 1H)\*, 3.80 (dd, *J* = 4.0, 11.2, 1H), 3.58 (dd, *J* = 4.9, 10.4, 1H), 3.55 (dd, *J* = 8.9, 11.2, 1H), 3.12–3.02 (m, 1H), 2.76–2.74 (m, 2H), 2.65–2.55 (m, 1H)\*, 2.65–2.55 (m, 1H)\*, 2.51 (dd, *J* = 7.6, 14.8, 1H)\*, 2.80–1.65 (m, 1H), 1.95–1.80 (m, 1H)\*, 1.80–1.65 (m, 1H), 1.65–1.50 (m, 1H), 1.11 (d, *J* = 6.3, 3H)\*, 1.07 (d, *J* = 6.3, 3H). <sup>13</sup>C NMR (75 MHz, MeOH-*d*<sub>4</sub>)  $\delta$  : 180.9 (s), 86.5 (d), 81.3\*(d), 80.6 (d), 75.3\*(d), 70.1\*(t), 61.4 (t), 47.1 (d), 42.5\*(d), 40.1\*(d), 39.4 (d), 38.3 (d), 37.0\*(d), 31.0 (t), 29.8\*(t), 16.8\*(q), 16.0 (q).

\*signal of minor product **26**.

Elemental analysis calcd (%) for C<sub>9</sub>H<sub>14</sub>O<sub>4</sub>: C 58.05, H 7.58; found: C 58.27, H 7.43.

**(1R, 2S, 3R, 4R, 7S, 8S, 11S)-2,7-dihydroxy-3-methyl-6,10-dioxatricyclo[6.2.1.0<sup>4,11</sup>]undecan-9-one (28)**. A 6 : 1 mixture of lactones **25** and **26** (56 mg, 0.30 mmol) dissolved in THF (3 mL) was added *via canula* to a stirred solution of sodium bis(trimethylsilyl)amide (NaHDMS, 1M in THF, 996  $\mu$ L, 0.996 mmol) in dry THF (2 mL) under Ar at -78 °C. After stirring the green solution at -78 °C for 1 h, freshly distilled HCOOEt (170  $\mu$ L, 2.04 mmol) was added and stirring was continued at -78 °C for 3 h, followed by a period of 12 h at -20 °C. The reaction was quenched by adding 1.2 N HCl dropwise until the pH was about 2, then the solution was diluted with CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and brine (5 mL). The separated aq layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5  $\times$  5 mL); combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was separated by FCC on silica gel. Elution with AcOEt gave compound **28** as colorless solid (40 mg, 62%). Mp 41–44 °C. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -22.56 (*c* = 0.86, CH<sub>3</sub>OH). <sup>1</sup>H NMR\* (300 MHz, MeOH-*d*<sub>4</sub>)  $\delta$  : 5.4 (br s, 1H), 4.78 (dd, *J* = 6.0, 4.3, 1H), 4.25 (dd, *J* = 4.1, 12.3, 1H), 3.49 (dd, *J* = 4.2, 11.0, 1H), 3.45 (1H, d, *J* = 12.2), 3.19 (td, *J* = 10.2, 6.0, 1H), 2.79 (d, *J* = 10.5, 1H), 1.87–1.70 (m, 1H), 1.50–1.37 (m, 1H), 1.07 (d, *J* = 6.3, 3H). <sup>13</sup>C NMR\* (75 MHz, MeOH-*d*<sub>4</sub>)  $\delta$  : 178.6 (s), 91.4 (d), 85.1 (d), 80.7 (d), 55.3 (t), 43.1 (d), 38.6 (d), 38.5 (d), 33.7 (d), 14.9 (q).

\*Signals of major ( $\geq$  90%)  $\beta$ -hemiacetal

Elemental analysis calcd (%) for C<sub>10</sub>H<sub>14</sub>O<sub>5</sub>: C 56.07, H 6.59; found: C 56.27, H 6.42.

**9-Deoxy-GEIR-1 (5)**. A solution of compound **28** (19 mg, 0.089 mmol) in acetic acid (200  $\mu$ L) was heated at 110 °C for 3 h. The solvent was removed under vacuum and the residue

was purified by FCC on silica gel. Elution with EtOAc yielded compound **5** as a colorless solid (6.1 mg, 35%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 5.35 (s, 1H), 5.09 (dd,  $J$  = 2.7, 6.6, 1H), 3.94 (d,  $J$  = 2.2, 1H), 3.88 (dd,  $J$  = 2.4, 10.5, 1H), 3.69 (dd,  $J$  = 1.5, 10.5, 1H), 3.25 (q,  $J$  = 6.9, 1H), 2.77 (dd,  $J$  = 2.3, 6.8, 1H), 2.66 (q,  $J$  = 7.6, 1H), 2.27 (dd,  $J$  = 1.0, 8.1, 1H), 1.1 (d,  $J$  = 7.7, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 174.3 (s), 92.70 (d), 83.1 (d), 80.84 (d), 64.3 (t), 43.9 (d), 42.8 (d), 40.4 (d), 38.7 (d), 18.2 (q). Elemental analysis calcd (%) for C<sub>10</sub>H<sub>12</sub>O<sub>4</sub>: C 61.22, H 6.16; found: C 61.40, H 6.30.

**(3aR, 4R, 5R, 6S, 6aR)-hexahydro-6-(tert-butyldimethylsilyloxy)-4-(tert-butyldimethylsilyloxy methyl)-5-methylcyclopenta[b]furan-2-one (30)**. Imidazole (328 mg, 4.83 mmol), followed by *tert*-butyldimethylsilyl chloride (485 mg, 3.22 mmol) and a catalytic amount of 4-(dimethylamino)pyridine (2 mg), were added to a stirred solution of compounds **25** and **26** (6 : 1 mixture, 60 mg, 0.322 mmol) in DMF (3 mL) at rt under Ar. The solution was heated at 60 °C and after 12 h was cooled to rt and diluted with Et<sub>2</sub>O (5 mL), saturated aq NaHCO<sub>3</sub> (3 mL), and water (10 mL). The aq layer was extracted with Et<sub>2</sub>O (3  $\times$  5 mL) and combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was purified by FCC on silica gel. Elution with hexane/EtOAc (9 : 1 v/v) afforded compound **30** as a colorless oil (115 mg, 100 % with respect to **25**). [ $\alpha$ ]<sub>D</sub> = -40.6 ( $c$  = 1.05, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 4.71 (dd,  $J$  = 4.9, 6.7, 1H), 3.75 (dd,  $J$  = 3.7, 10.6, 1H), 3.62–3.50 (m, 2H), 3.0–2.87 (m, 1H), 2.72 (dd,  $J$  = 4.2, 18.6, 1H), 2.54 (dd,  $J$  = 10.6, 18.6, 1H), 1.77–1.65 (m, 2H), 1.00 (d,  $J$  = 6.0, 3H), 0.93 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H), 0.06 (s, 6H). <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$ : 178.0 (s), 83.6 (d), 80.0 (d), 61.6 (t), 45.4 (d), 38.7 (d), 37.4 (d), 29.9 (t), 25.7 (3 $\times$ q), 25.6 (3 $\times$ q), 18.1 (2 $\times$ s), 15.9 (d), -4.6 (q), -4.9 (q), -5.5 (q), -5.6 (q). Elemental analysis calcd (%) for C<sub>21</sub>H<sub>42</sub>O<sub>4</sub>Si<sub>2</sub>: C 60.82, H 10.21; found: C 60.65, H 10.30.

**(3aR, 4R, 5R, 6S, 6aR)-hexahydro-6-(tert-butyldimethylsilyloxy)-4-(hydroxymethyl)-5-methylcyclopenta[b]furan-2-one (31)**. Pyridinium *p*-toluenesulfonate (PPTS) (70 mg, 0.28 mmol) was added to a stirred solution of compound **30** (116 mg, 0.28 mmol) in DCM/*i*-PrOH (1:1 v/v, 4 mL) at rt. After stirring for 24 h, KHCO<sub>3</sub> (29 mg, 0.29 mmol) was added and the mixture was stirred for an additional 1 h. The solid was filtered off and the filtrate was evaporated under vacuum. The residue was purified by flash column chromatography on

silica gel. Elution with a hexane/EtOAc gradient (from 9:1 to 100% EtOAc) yielded compound **31** as a colorless oil (42 mg, 50 %), followed by recovered **25** (18 mg, 35%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 4.75 (dd,  $J$  = 5.0, 6.4, 1H), 3.82 (dd,  $J$  = 3.5, 10.7, 1H), 3.72–3.55 (m, 2H), 3.05–2.90 (m, 1H), 2.74 (dd,  $J$  = 4.3, 18.7, 1H), 2.62 (dd,  $J$  = 10.4, 18.7, 1H), 1.90–1.63 (m, 2H), 1.03 (d,  $J$  = 5.7, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$ : 178.1 (s), 83.9 (d), 79.8 (d), 61.5 (t), 45.2 (d), 39.3 (d), 37.1 (d), 29.9 (t), 25.7 (3 $\times$ q), 18.1 (s), 16.1 (q), -4.6 (q), -4.9 (q). Elemental analysis calcd (%) for C<sub>15</sub>H<sub>28</sub>O<sub>4</sub>Si: C 59.96, H 9.39; found: C 59.78, H 9.50.

**(1R, 2S, 3R, 4R, 7S, 8S, 11S)-2-(tert-butyldimethylsilyloxy)-7-hydroxy-3-methyl-6,10-dioxo-tricyclo[6.2.1.0<sup>4,11</sup>]undecan-9-one (32).** Lactone **31** (28 mg, 0.093 mmol) dissolved in THF (1.5 mL) was added *via canula* to a stirred solution of sodium bis(trimethylsilyl)amide (NaHDMS, 1M in THF, 308  $\mu$ L, 0.308 mmol) in dry THF (1 mL) at -78 °C under Ar. After stirring at -78 °C for 1 h, freshly distilled HCOOEt (53  $\mu$ L, 0.653 mmol) was added. The solution was left at -78 °C for 3 h, then at -20 °C for 12 h. The reaction was quenched by addition of a phosphate buffered solution (pH = 6.8, 5 mL) at -20 °C, then the solution was warmed to rt, and diluted with EtOAc (3 mL) and brine (3 mL). Aq layer was extracted with EtOAc (5 $\times$ 5 mL); combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was separated by FCC on silica gel. Elution with hexane/EtOAc (4:1 v/v ) afforded compound **32** as a colorless solid (18.9 mg, 62 %). Mp 197-198 °C. [ $\alpha$ ]<sub>D</sub> = - 46.62 ( $c$  = 0.72, CH<sub>2</sub>Cl<sub>2</sub>). IR (nujol mull): 3410, 2930, 2901, 2858, 1734, 1461, 1369, 1252, 1200, 1112, 1046, 918, 837, 777, 712 cm<sup>-1</sup>. <sup>1</sup>H NMR\* (300 MHz, Me<sub>2</sub>CO-*d*<sub>6</sub>)  $\delta$ : 5.43 (s, 1H), 4.77 (dd,  $J$  = 4.2, 6.1, 1H), 4.24 (dd,  $J$  = 4.1, 12.2, 1H), 3.68 (dd,  $J$  = 4.2, 10.7, 1H), 3.40 (d,  $J$  = 12.2, 1H), 3.23 (td,  $J$  = 10.1, 6.2, 1H), 2.76 (d,  $J$  = 10.5, 1H), 1.92–1.75 (m, 1H), 1.44 (ddd,  $J$  = 4.1, 9.7, 12.8, 1H), 1.01 (d,  $J$  = 6.4, 3H), 0.95 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H). <sup>13</sup>C NMR\* (75 MHz, Me<sub>2</sub>CO-*d*<sub>6</sub>)  $\delta$ : 176.6 (s), 91.8 (d), 83.3 (d), 80.8 (d), 54.4 (t), 42.1 (d), 38.3 (d), 36.9 (d), 33.1 (d), 26.1 (3 $\times$ q), 18.7 (s), 14.8 (q), -4.4 (q), -4.7 (q).

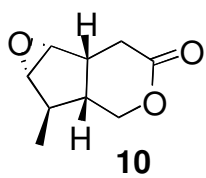
\*Signals of major ( $\geq$  90%)  $\beta$ -hemiacetal.

Elemental analysis calcd (%) for C<sub>16</sub>H<sub>28</sub>O<sub>5</sub>Si: C 59.20, H 8.97; found: C 59.42, H 9.15.

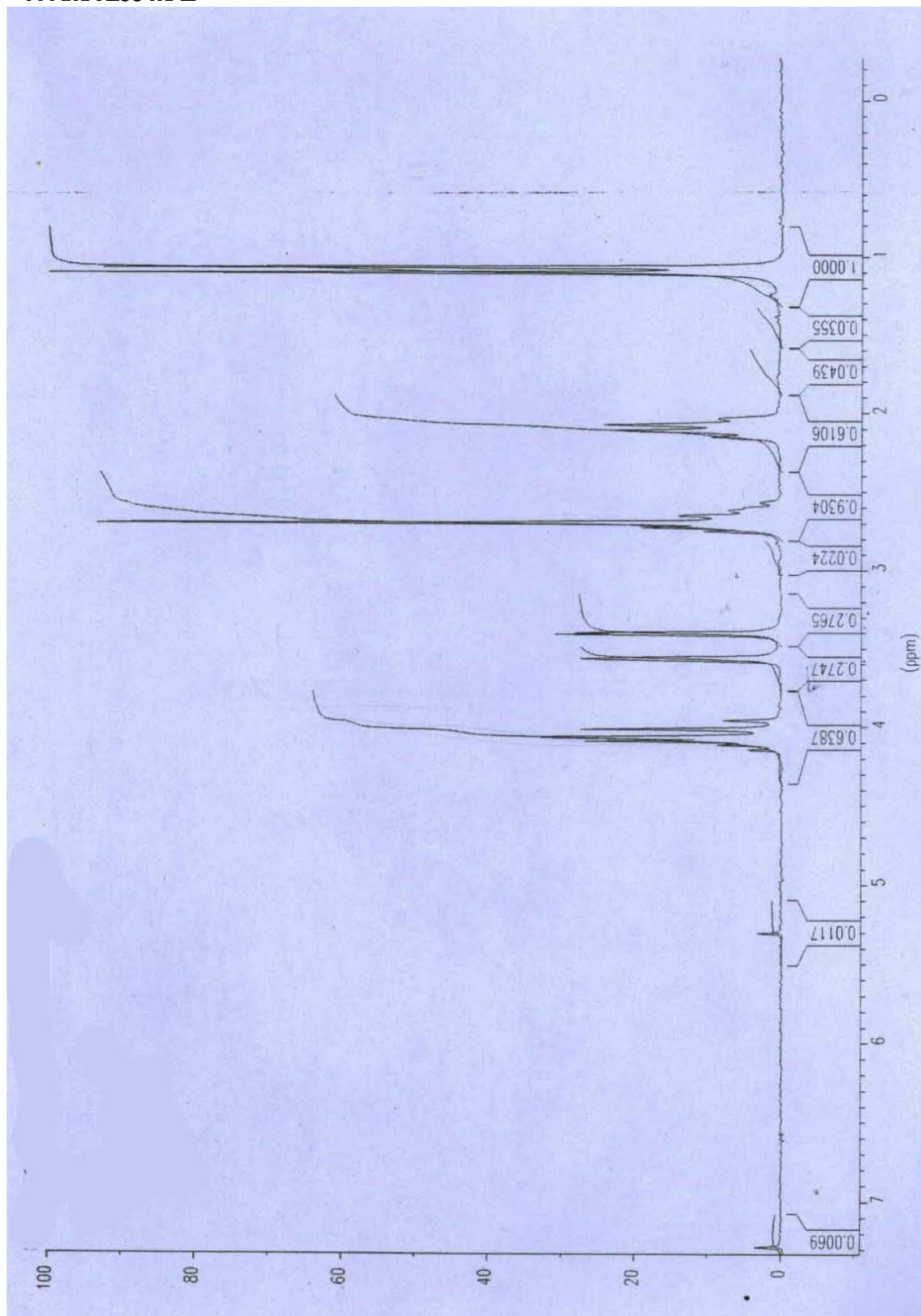
**(1R, 2S, 3R, 4R, 11S)-2-(tert-butyldimethylsilyloxy)-3-methyl-6,10-dioxatricyclo[6.2.1.0<sup>4,11</sup>] undec-7-en-9-one (33).** Freshly distilled anhydrous Et<sub>3</sub>N (18  $\mu$ L, 0.130 mmol), followed by MsCl (56  $\mu$ L, 0.056 mmol) were added to a stirred solution of compound **32** (14.3 mg, 0.043 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) at -30 °C under Ar. After 30 min the temperature was set at -15 °C. After 90 min the solution was diluted with CH<sub>2</sub>Cl<sub>2</sub> (3 mL) and aq phosphate buffer (pH = 6.8, 3 mL). The aq layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  3 mL) and combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was purified by FCC on silica gel. Elution with hexane/EtOAc (4:1 v/v) gave compound **33** (9.5 mg, 71 %) as colorless oil. <sup>1</sup>H NMR (300 MHz, Me<sub>2</sub>CO-*d*<sub>6</sub>)  $\delta$ : 7.32 (d, *J* = 2.3, 1H), 4.80 (t, *J* = 7.2, 1H), 4.32 (dd, *J* = 1.0, 12.3, 1H), 4.16 (dd, *J* = 3.4, 12.3, 1H), 3.86 (dd, *J* = 7.1, 9.4, 1H), 3.36 (td, *J* = 7.0, 2.4, 1H), 2.10–1.90 (m, 1H), 1.75–1.62 (m, 1H), 1.09 (d, *J* = 6.5, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H). <sup>13</sup>C NMR (75 MHz, Me<sub>2</sub>CO-*d*<sub>6</sub>)  $\delta$ : 176.60 (s), 151.9 (d), 102.5 (s), 82.1 (d), 79.1 (d), 64.9 (t), 39.6 (d), 39.3 (d), 36.4 (d), 26.2 (3 $\times$ q), 18.8 (s), 15.4 (q), -4.4 (q), -4.9 (q). HREIMS, *m/z* for C<sub>16</sub>H<sub>26</sub>O<sub>4</sub>Si (M<sup>+</sup>) calcd 310.16004, found 310.16064.

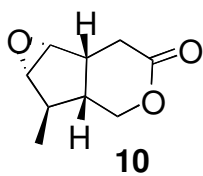
**9-Deoxygelsemide (1).** TBAF (1 M in THF, 39  $\mu$ L, 0.039 mmol) was added to a stirred cooled (0 °C) solution of compound **33** (8.3 mg, 0.027 mmol) in THF (1 mL) containing 1% H<sub>2</sub>O. After stirring for 1 h, the solution was diluted with EtOAc (2 mL) and aq phosphate buffer (pH = 6.8, 3 mL). The aq layer was extracted with EtOAc (3  $\times$  2 mL) and combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was purified by FCC on silica gel. Elution with hexane/EtOAc (1:1 v/v) gave a trace of compound **5**, followed by 9-deoxygelsemide (**1**)<sup>2</sup> as an amorphous powder (3.9 mg, 74%). CD [ $\Delta\epsilon$  (*c* 0.51 $\times$ 10<sup>-3</sup> mmol/L, MeOH, 20 °C) -10.0 (247 nm)]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.43 (d, *J* = 2.0, 1H), 4.89 (t, *J* = 7.3, 1H), 4.30 (d, *J* = 12.4, 1H), 4.14 (dd, *J* = 3.5, 12.4, 1H), 3.70 (q, *J* = 8.3, 1H), 3.35 (td, *J* = 7.8, 2.2, 1H), 2.14 (d, *J* = 8.6, 1H, OH), 1.95–1.80 (m, 1H), 1.76–1.55 (m, 1H), 1.16 (d, *J* = 6.4, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 170.84 (s), 152.81 (d), 100.09 (s), 80.51 (d), 78.06 (d), 64.08 (t), 38.44 (d), 38.11 (d), 36.51 (d), 15.01 (q). HREIMS, *m/z* for C<sub>10</sub>H<sub>12</sub>O<sub>4</sub> (M<sup>+</sup>) calcd 196.07356, found 196.07426. No authentic sample was available. However, our NMR spectra matched up peak for peak with the NMR spectra of 9-deoxygelsemide listed in ref. 2.



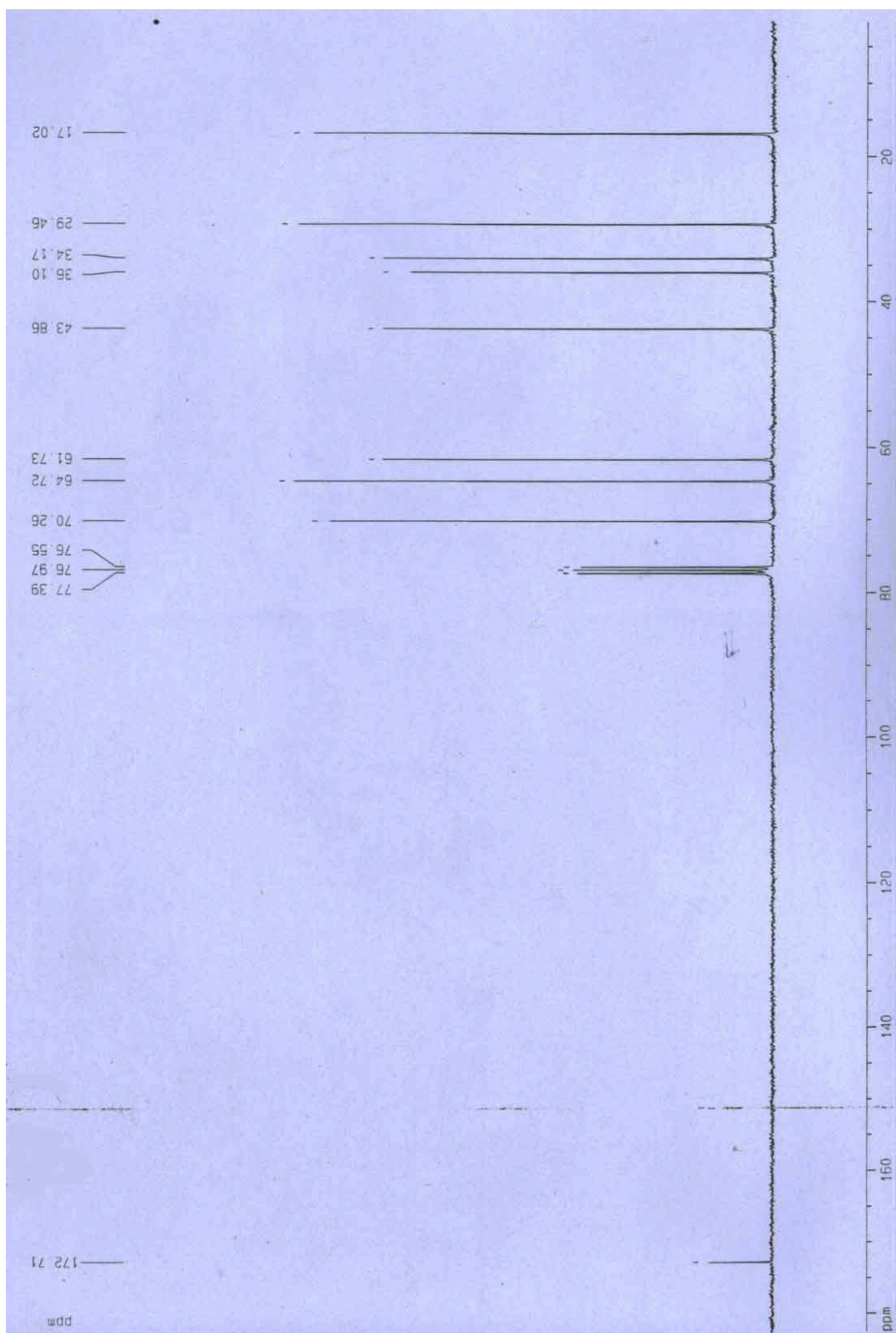


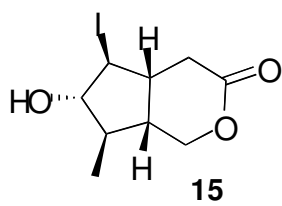
<sup>1</sup>H-NMR 200 MHz



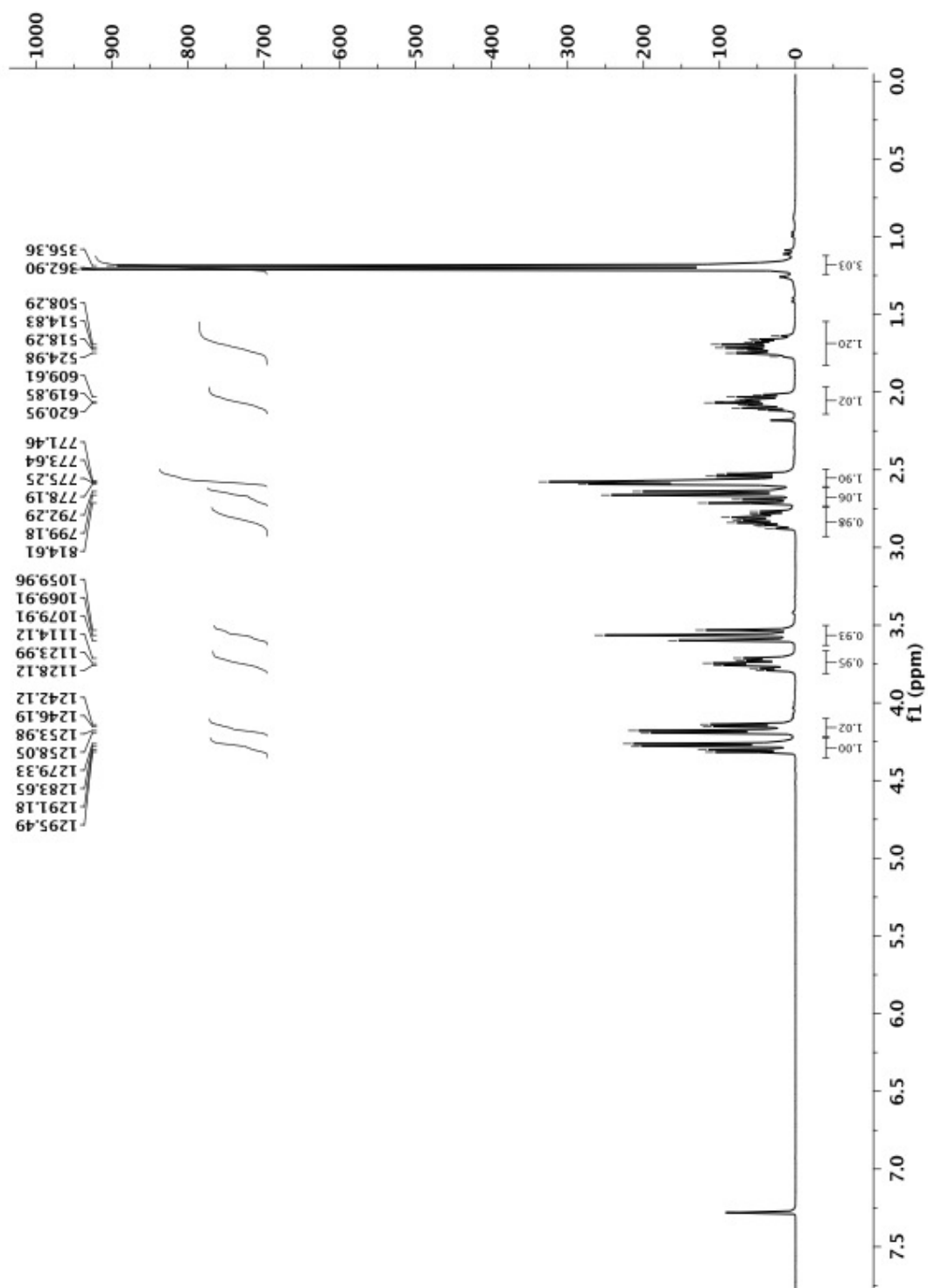


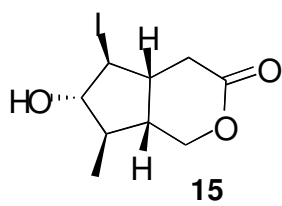
<sup>13</sup>C-NMR 75 MHz



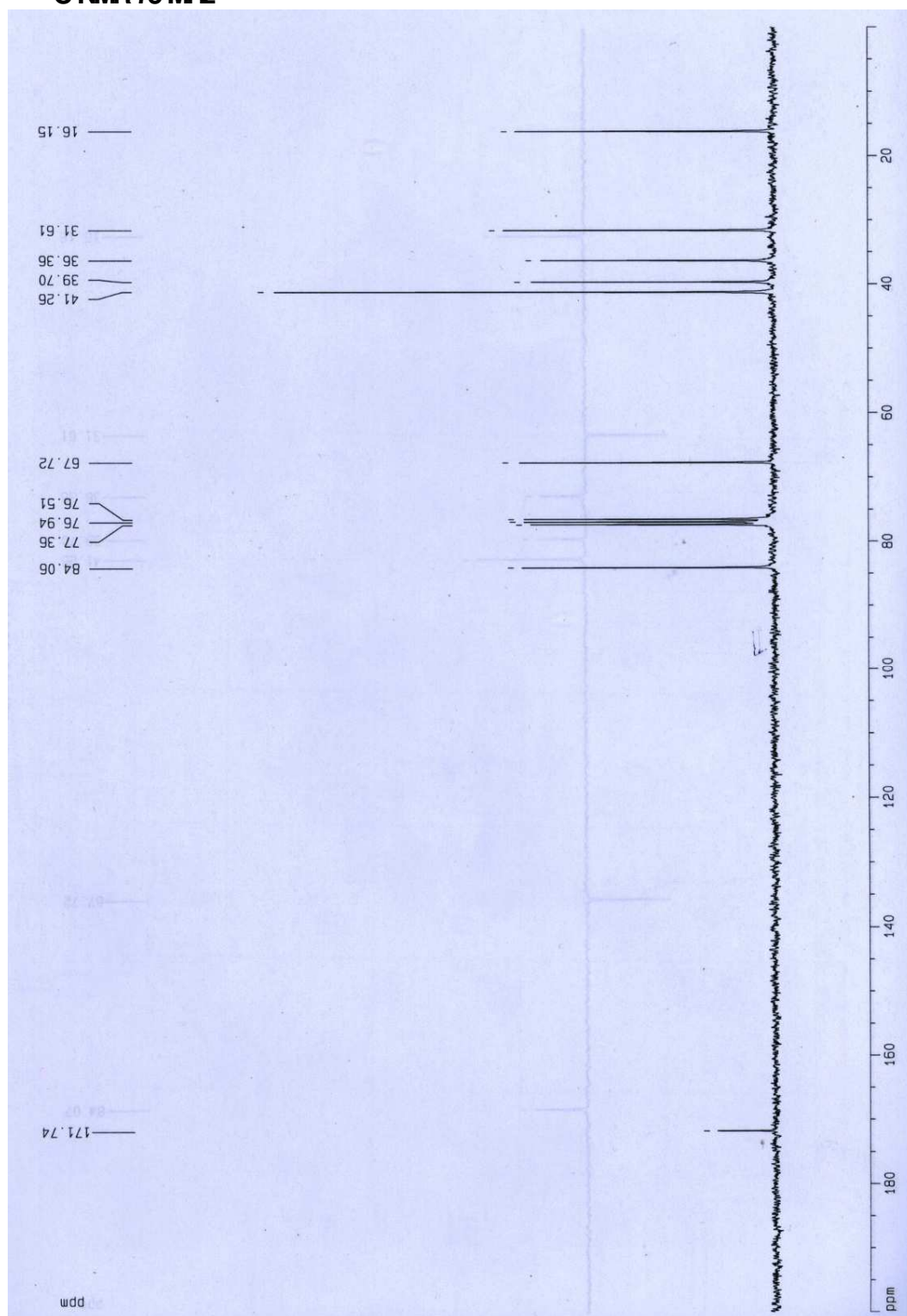


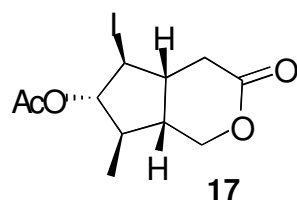
$^1\text{H-NMR}$  300 MHz



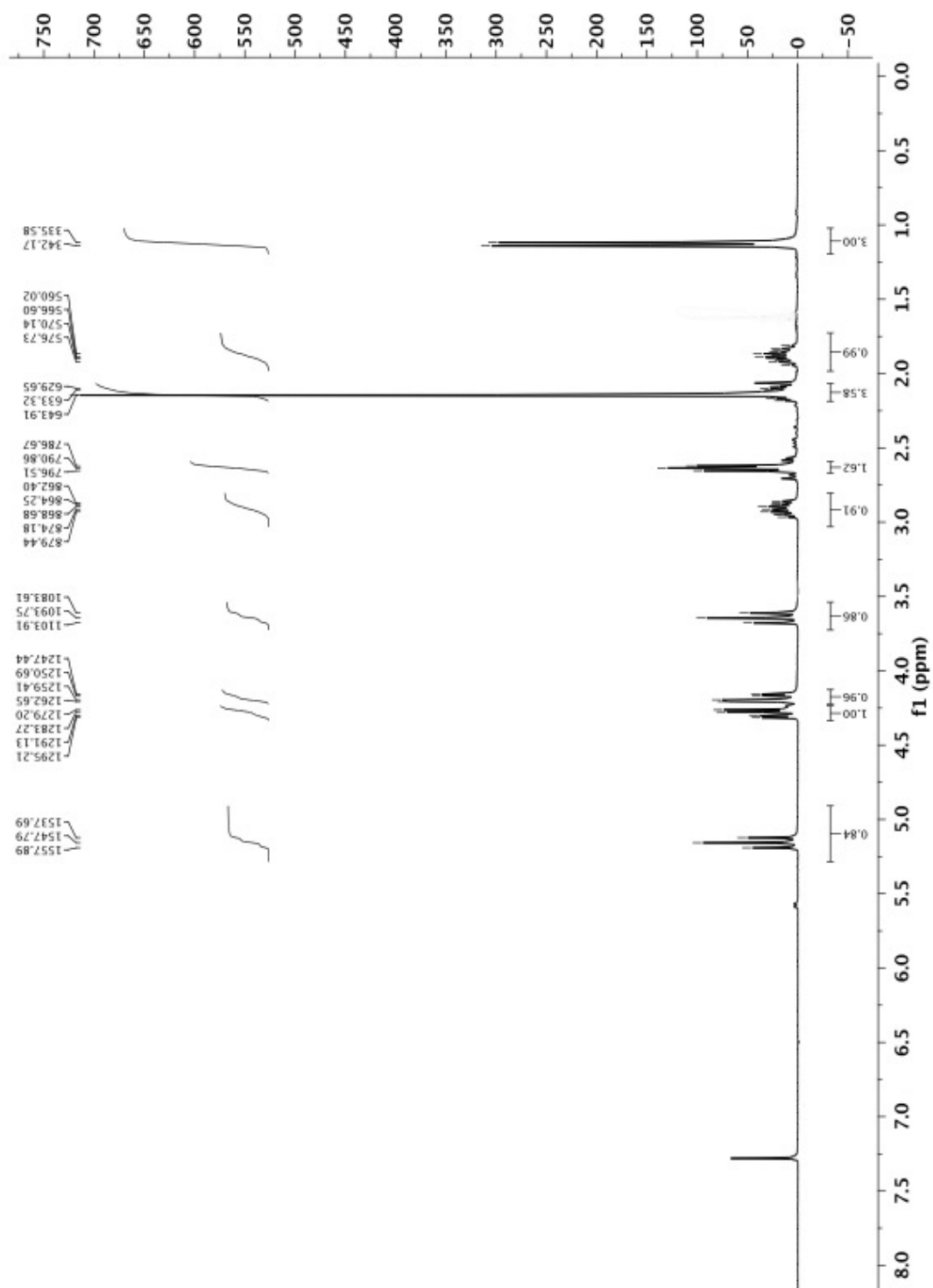


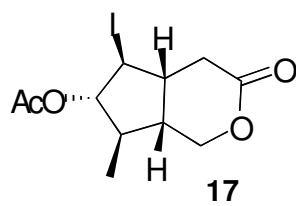
$^{13}\text{C-NMR}$  75 MHz



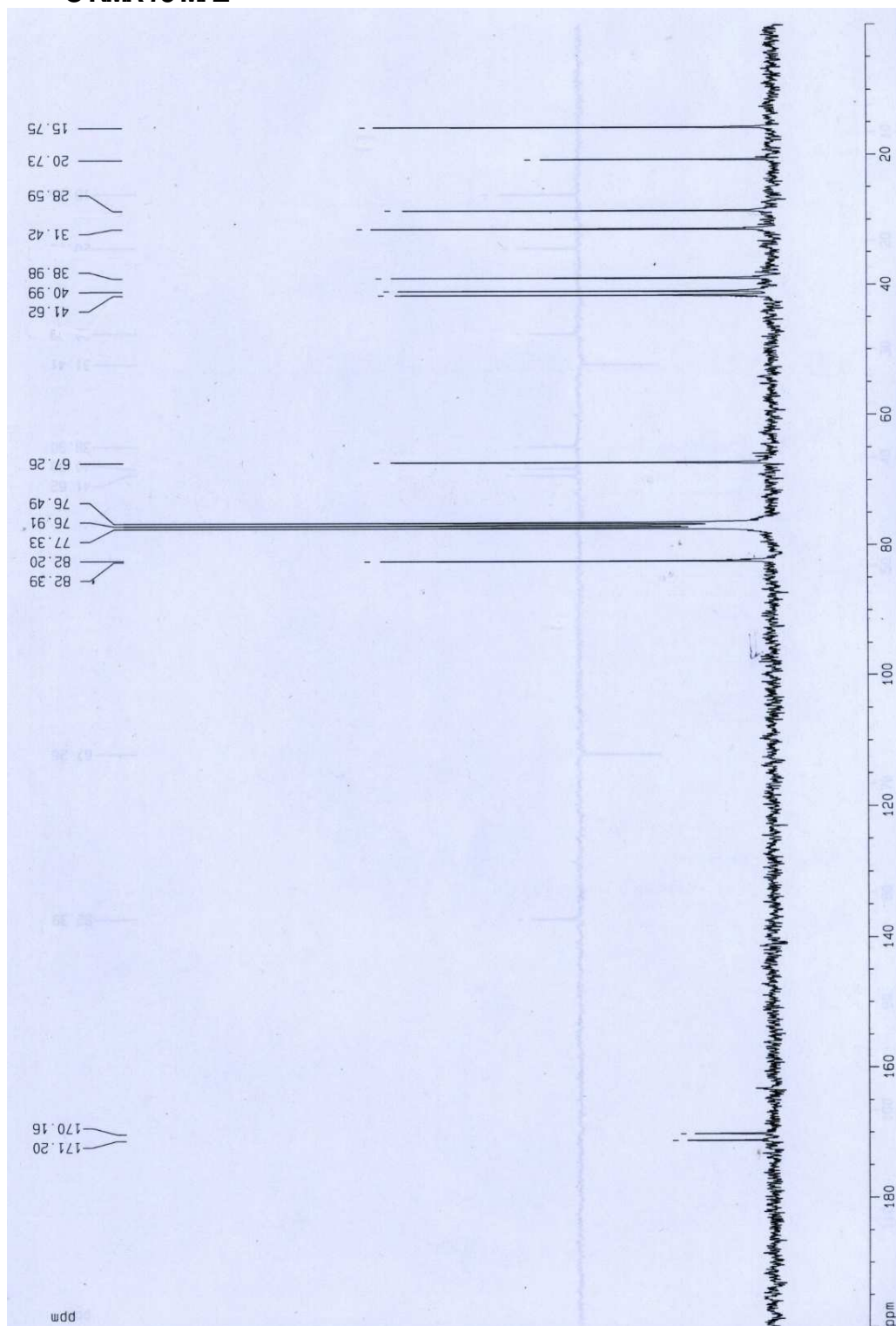


<sup>1</sup>H-NMR 300 MHz

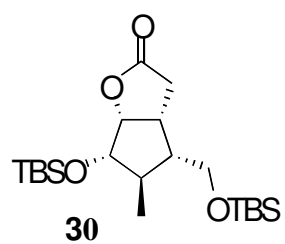




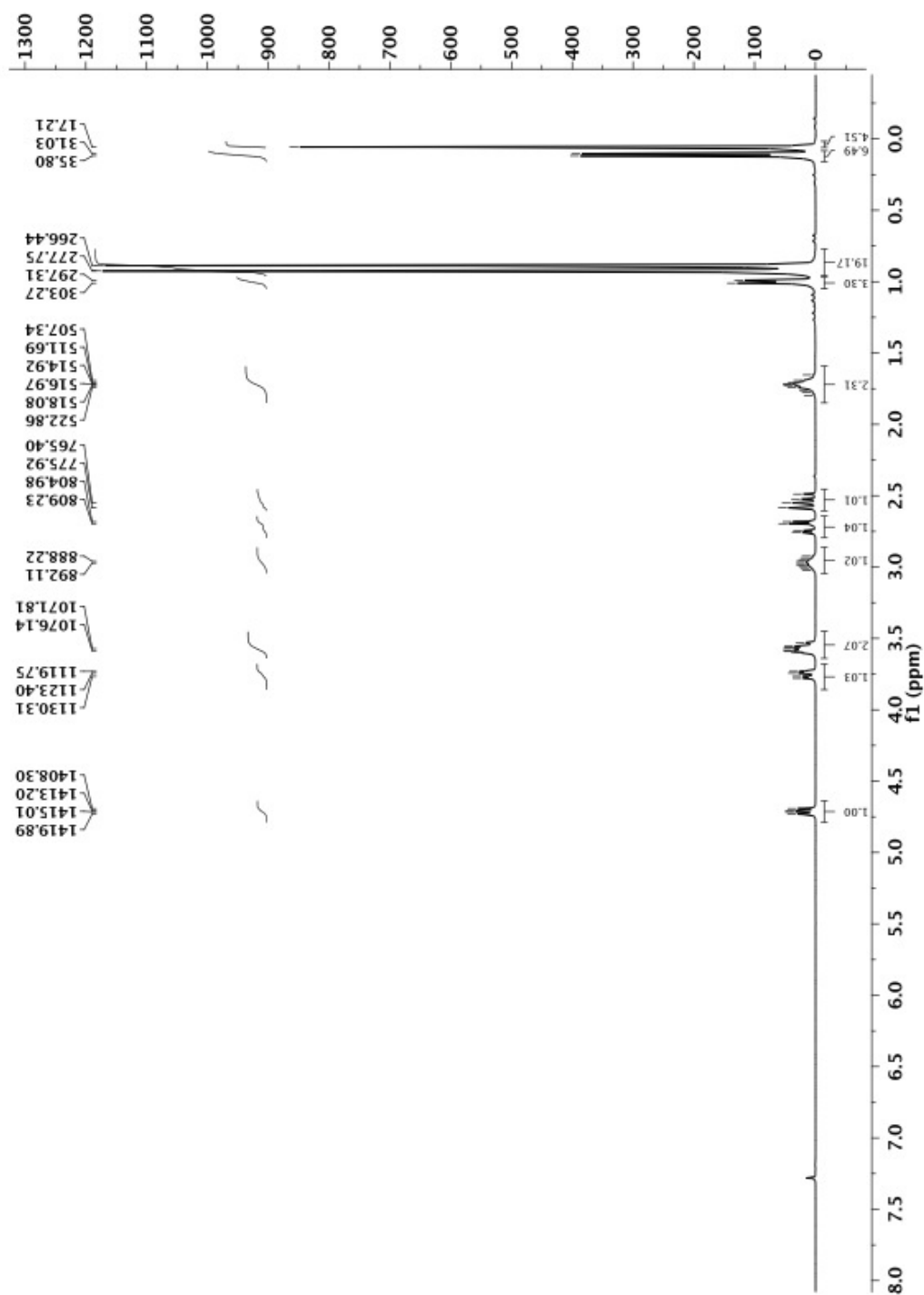
<sup>13</sup>C-NMR 75 MHz

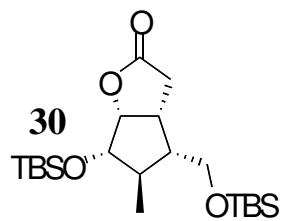




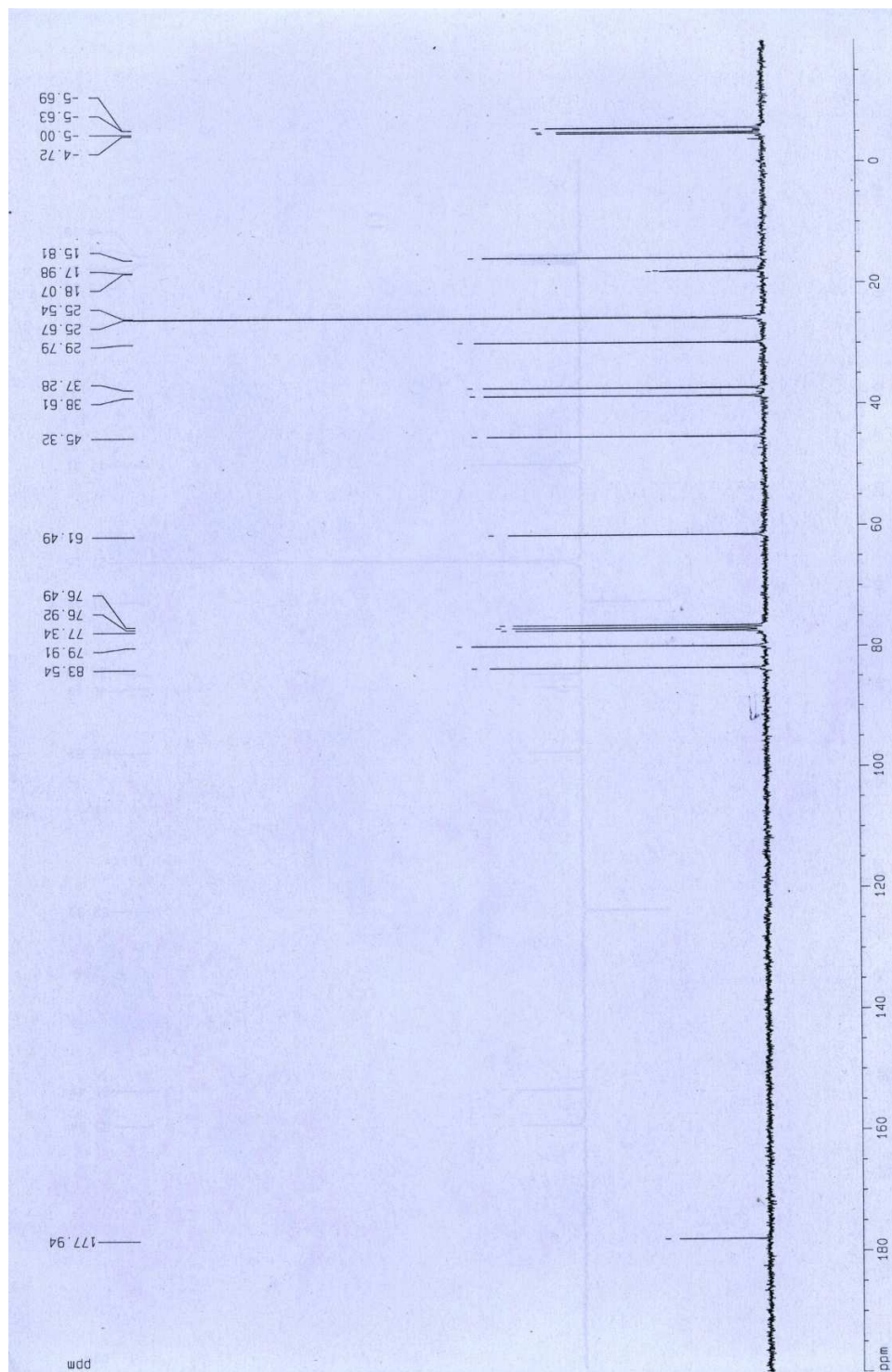


<sup>1</sup>H-NMR 300 MHz

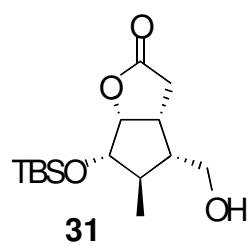




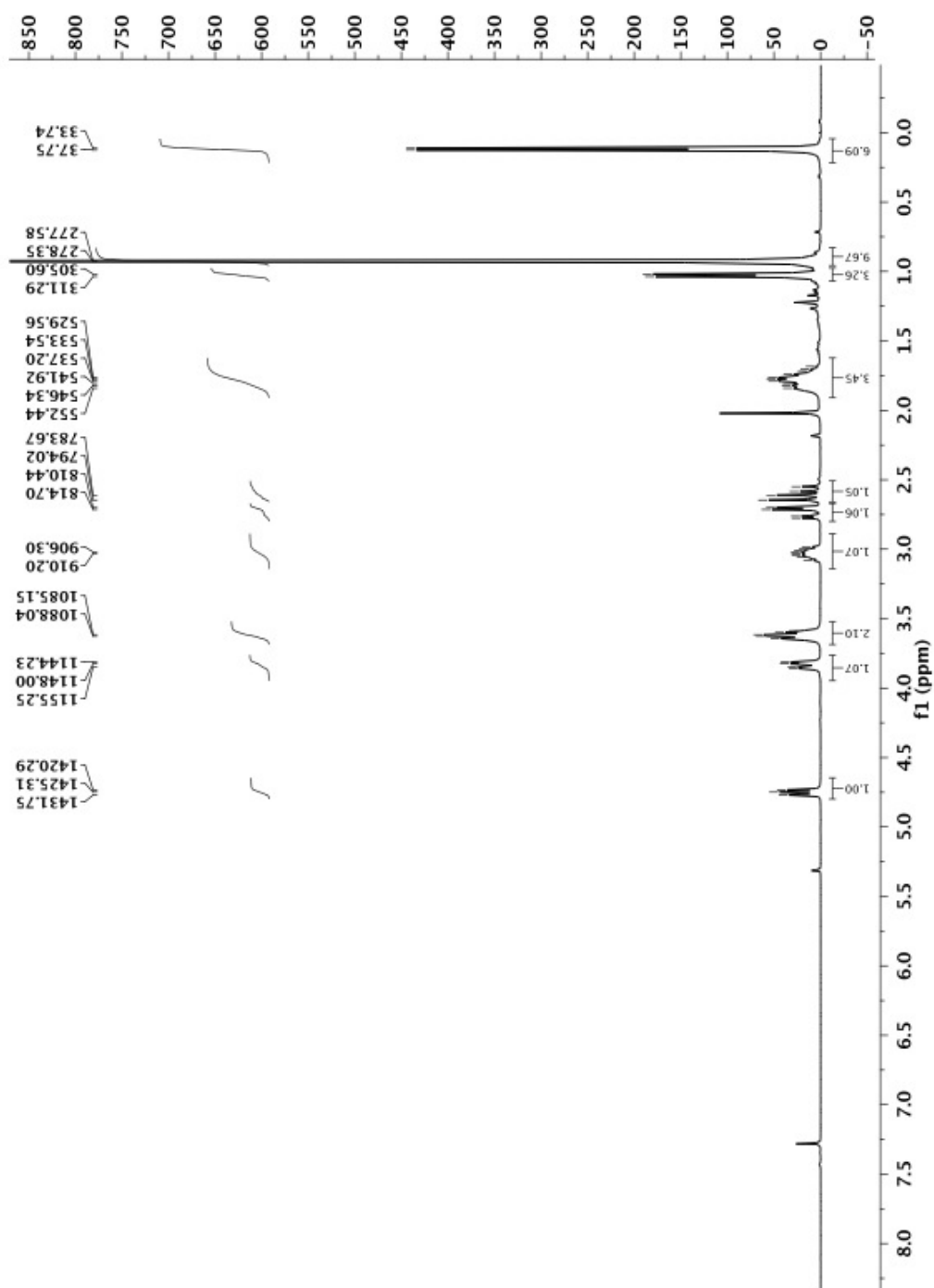
<sup>13</sup>C-NMR 75 MHz

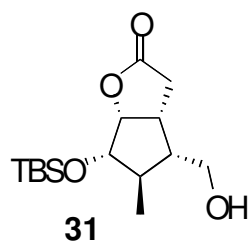




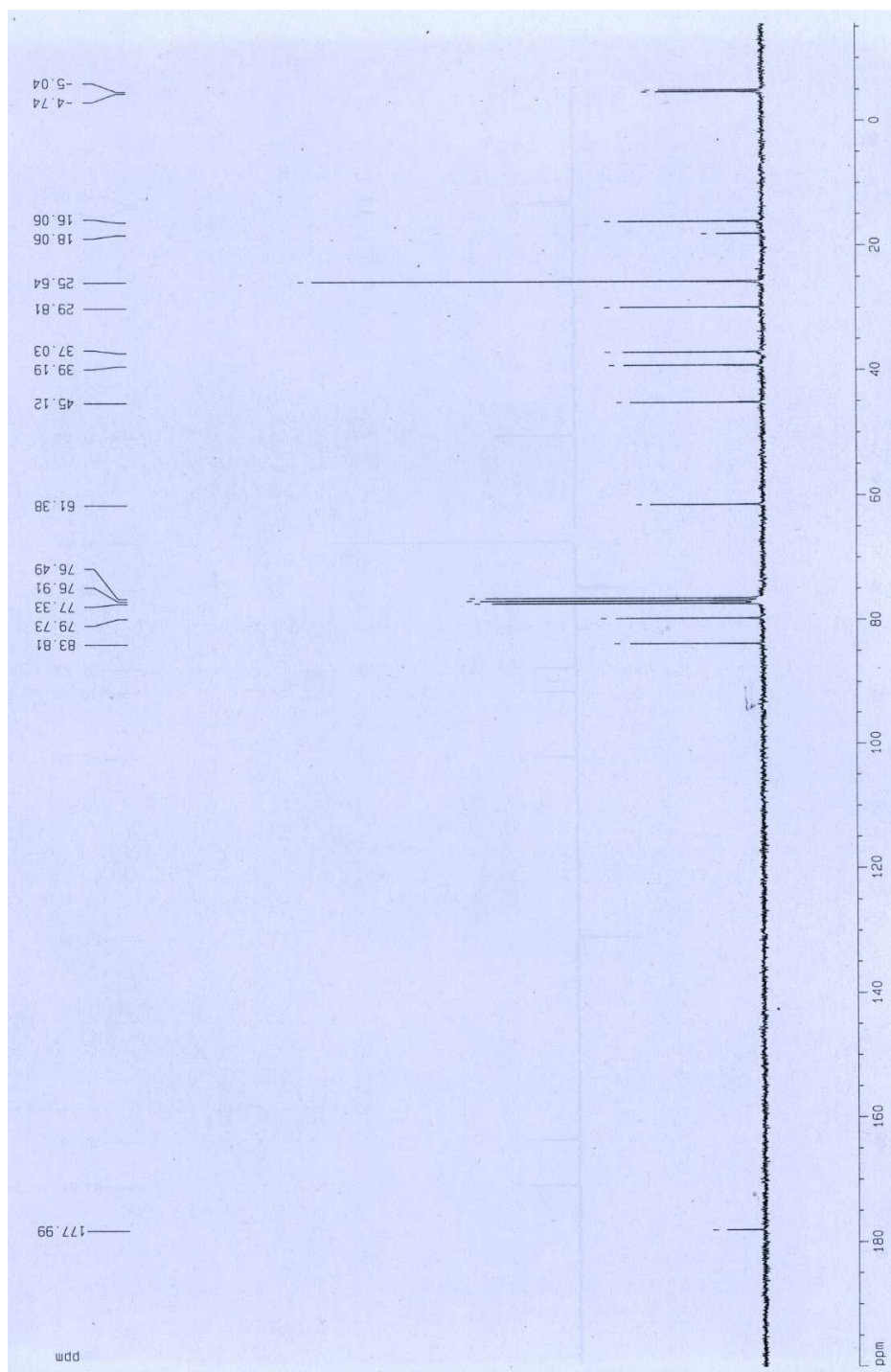


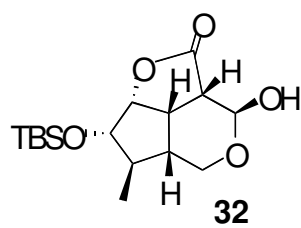
<sup>1</sup>H-NMR 300 MHz



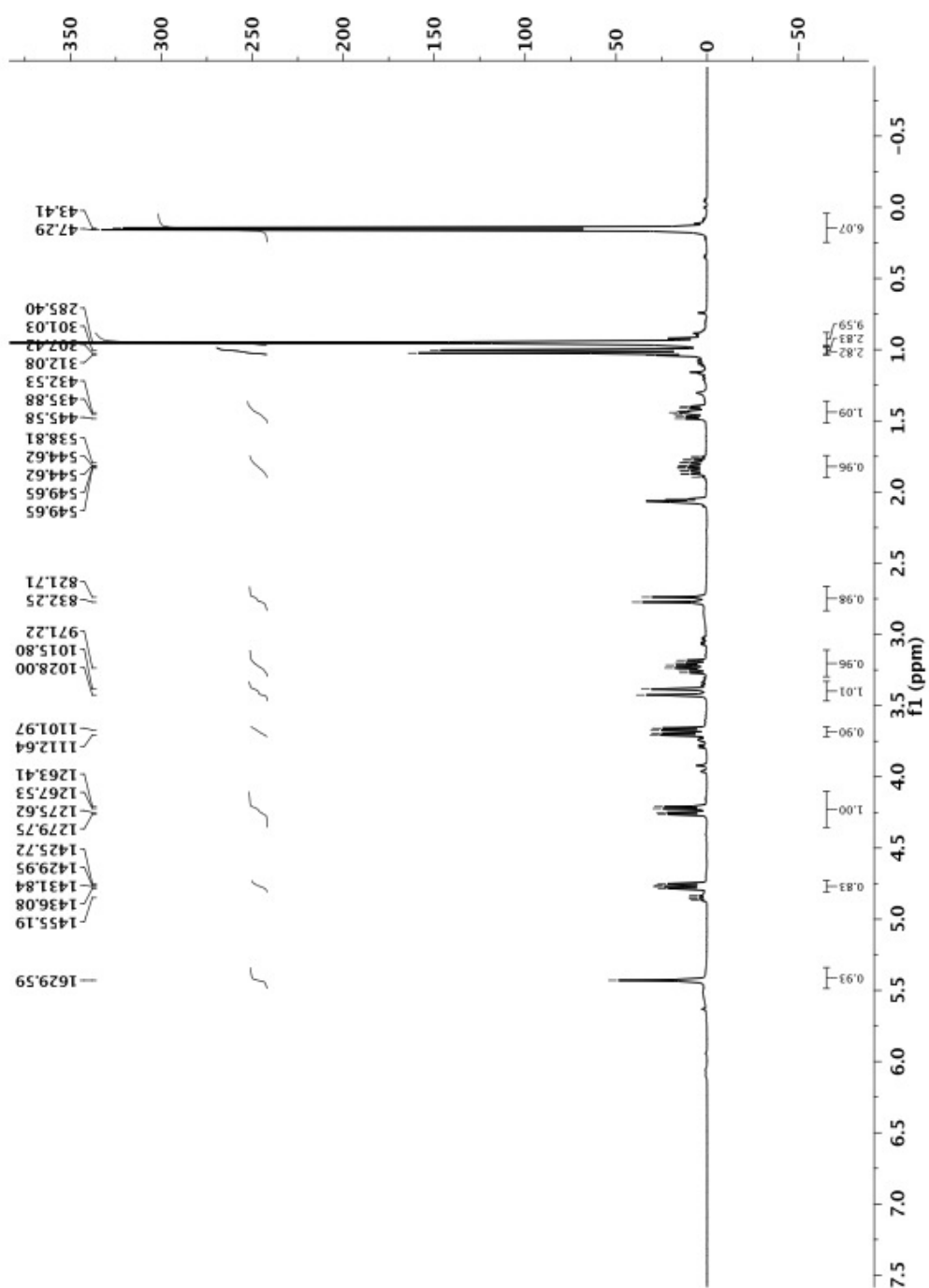


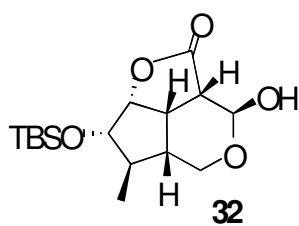
<sup>13</sup>C-NMR 75 MHz



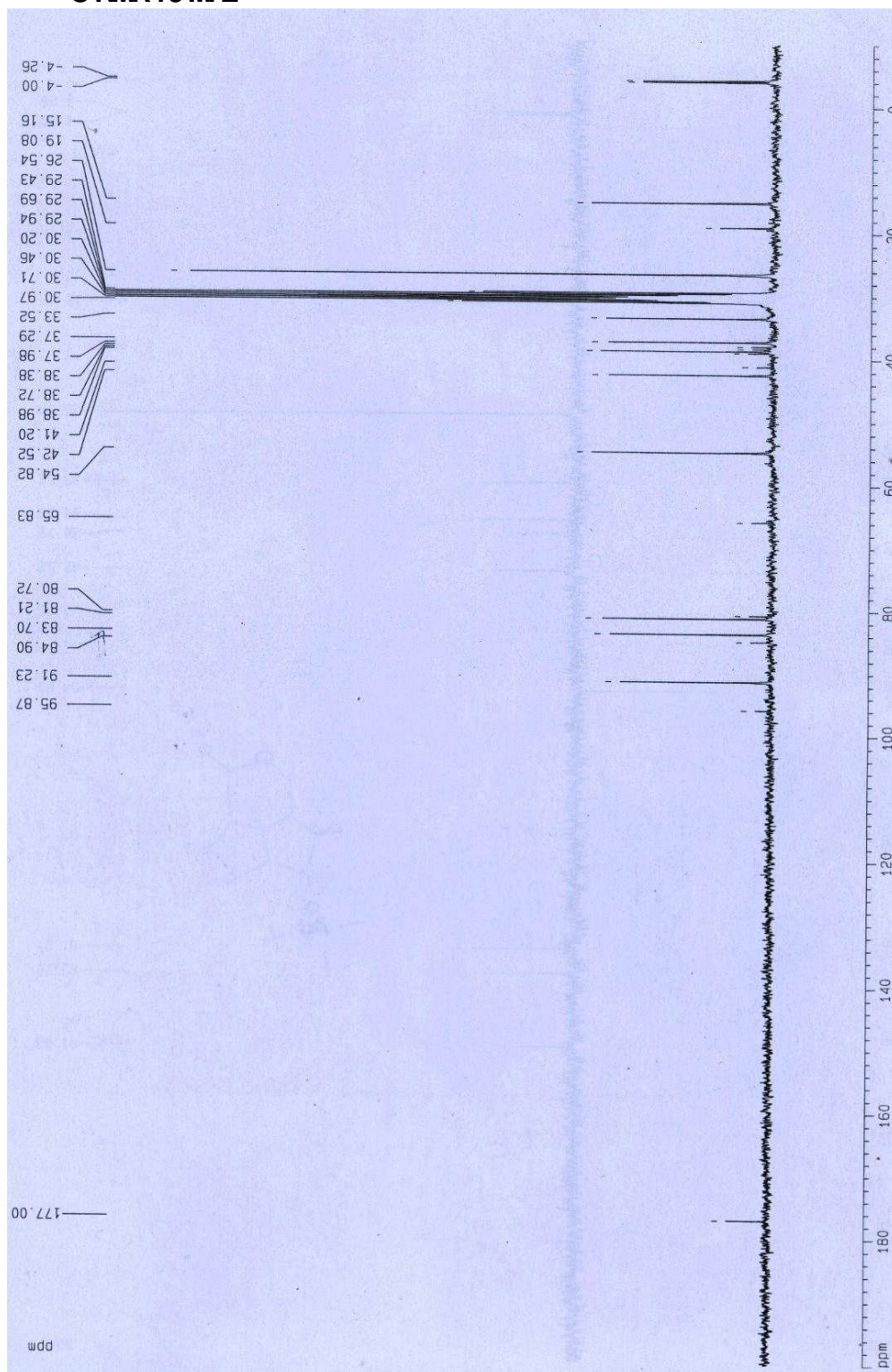


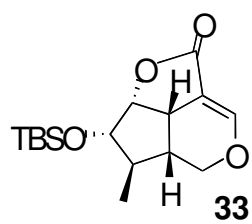
$^1\text{H-NMR}$  300 MHz



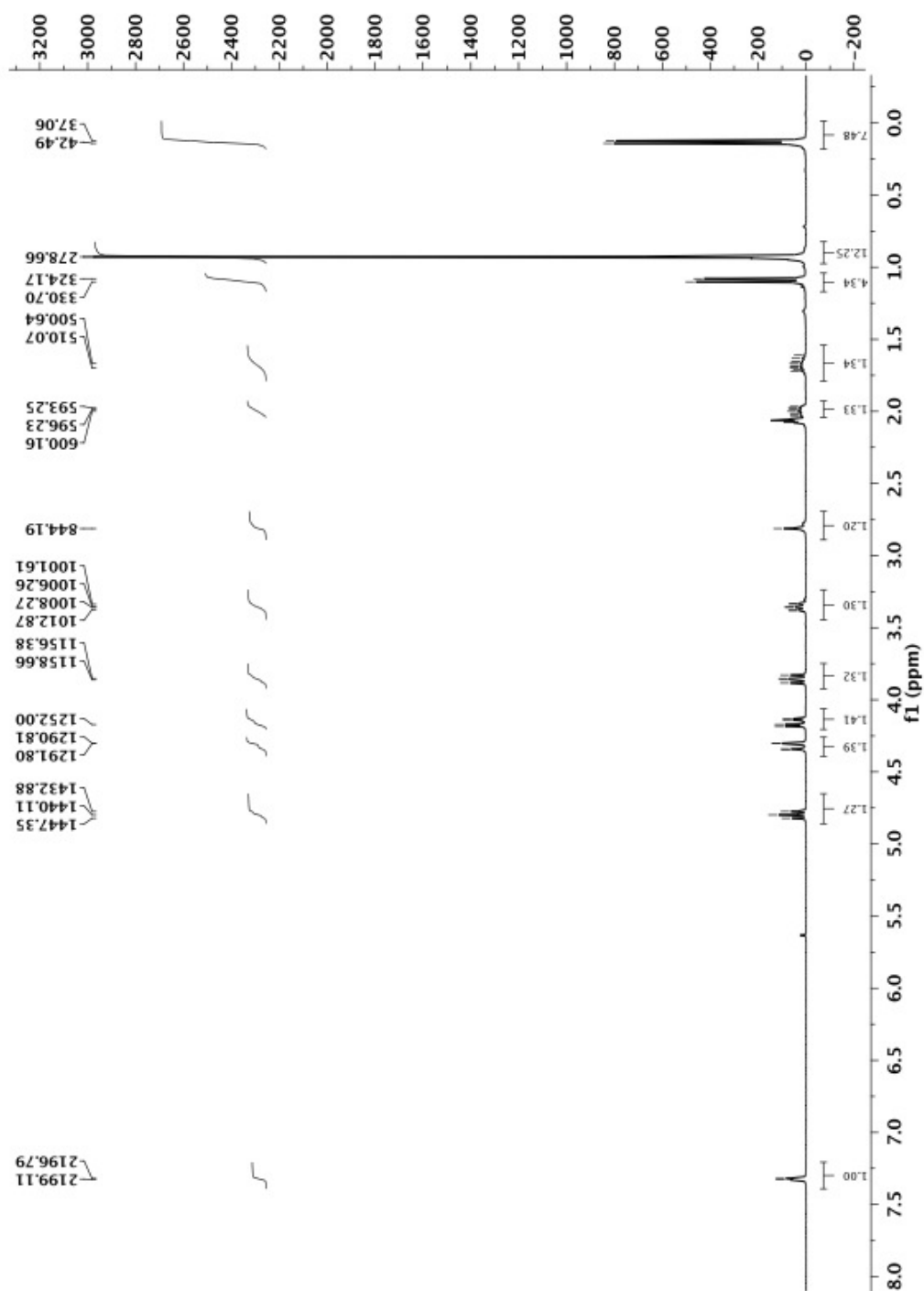


$^{13}\text{C-NMR}$  75 MHz

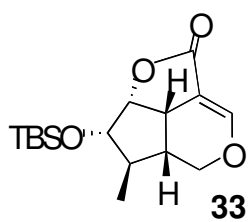




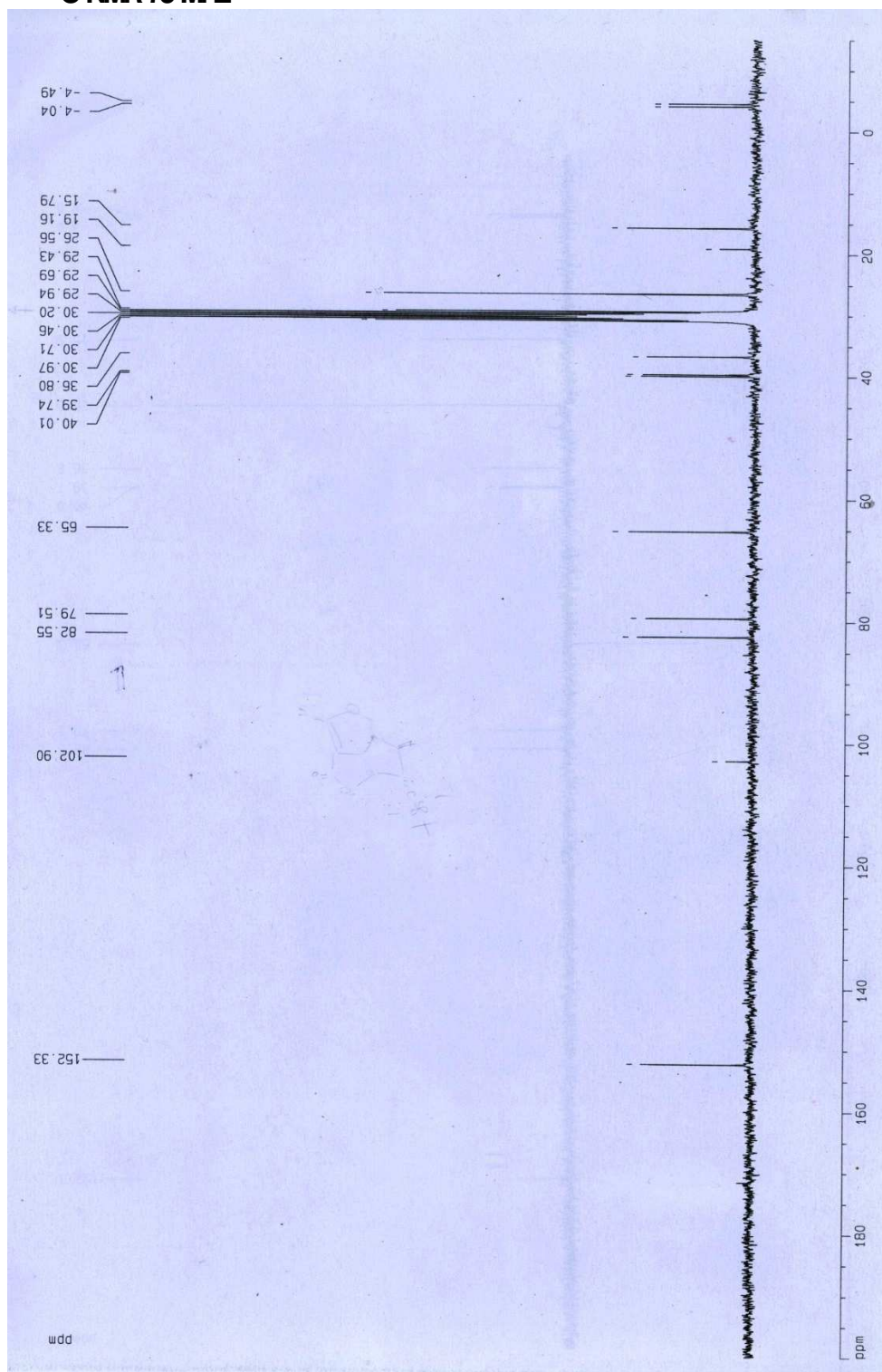
$^1\text{H-NMR}$  300 MHz

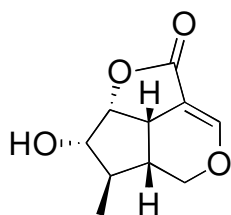






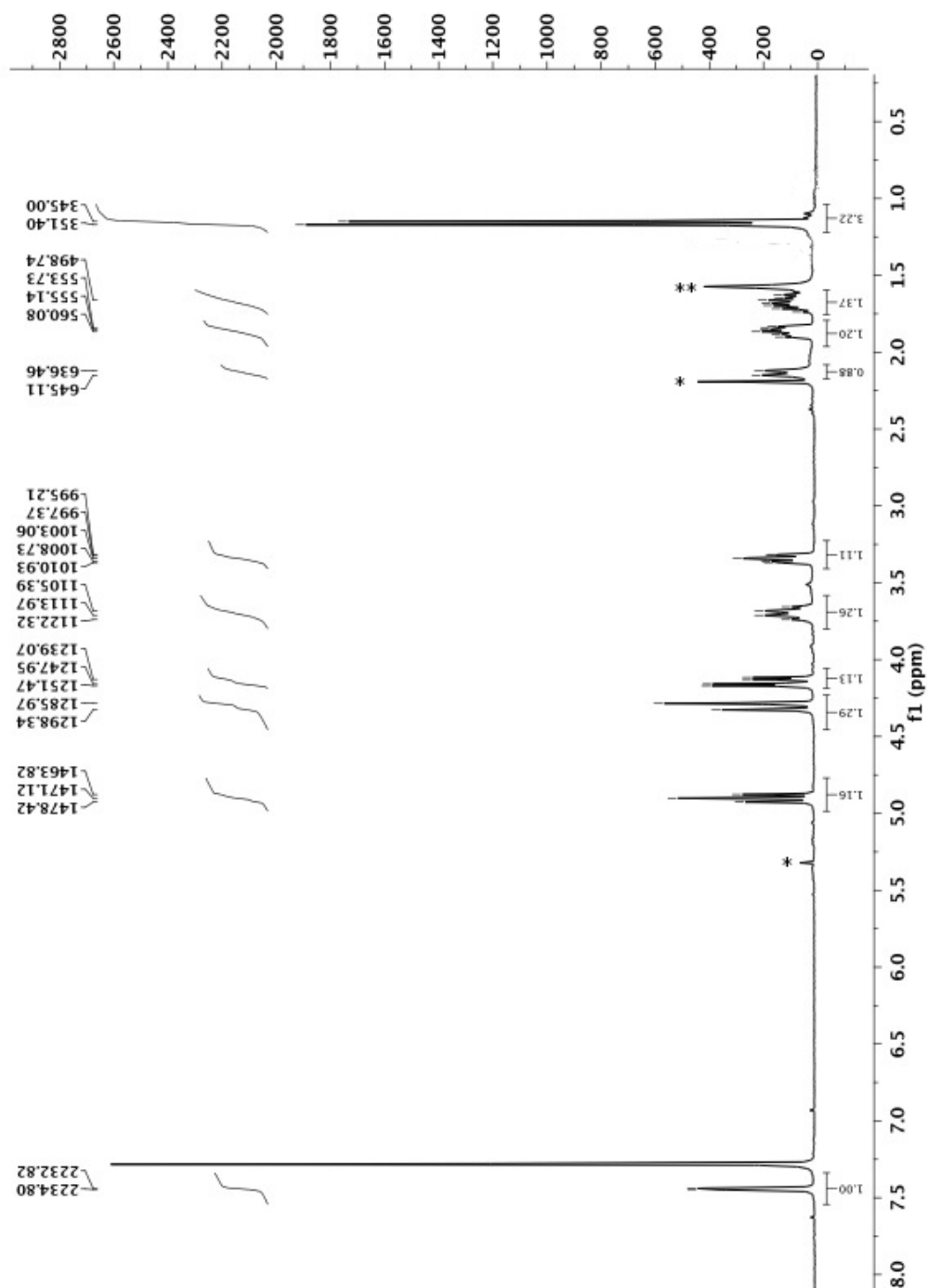
<sup>13</sup>C-NMR 75 MHz



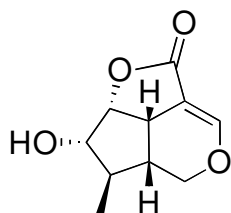


9-Deoxygelsemide (1)

$^1\text{H-NMR}$  300 MHz

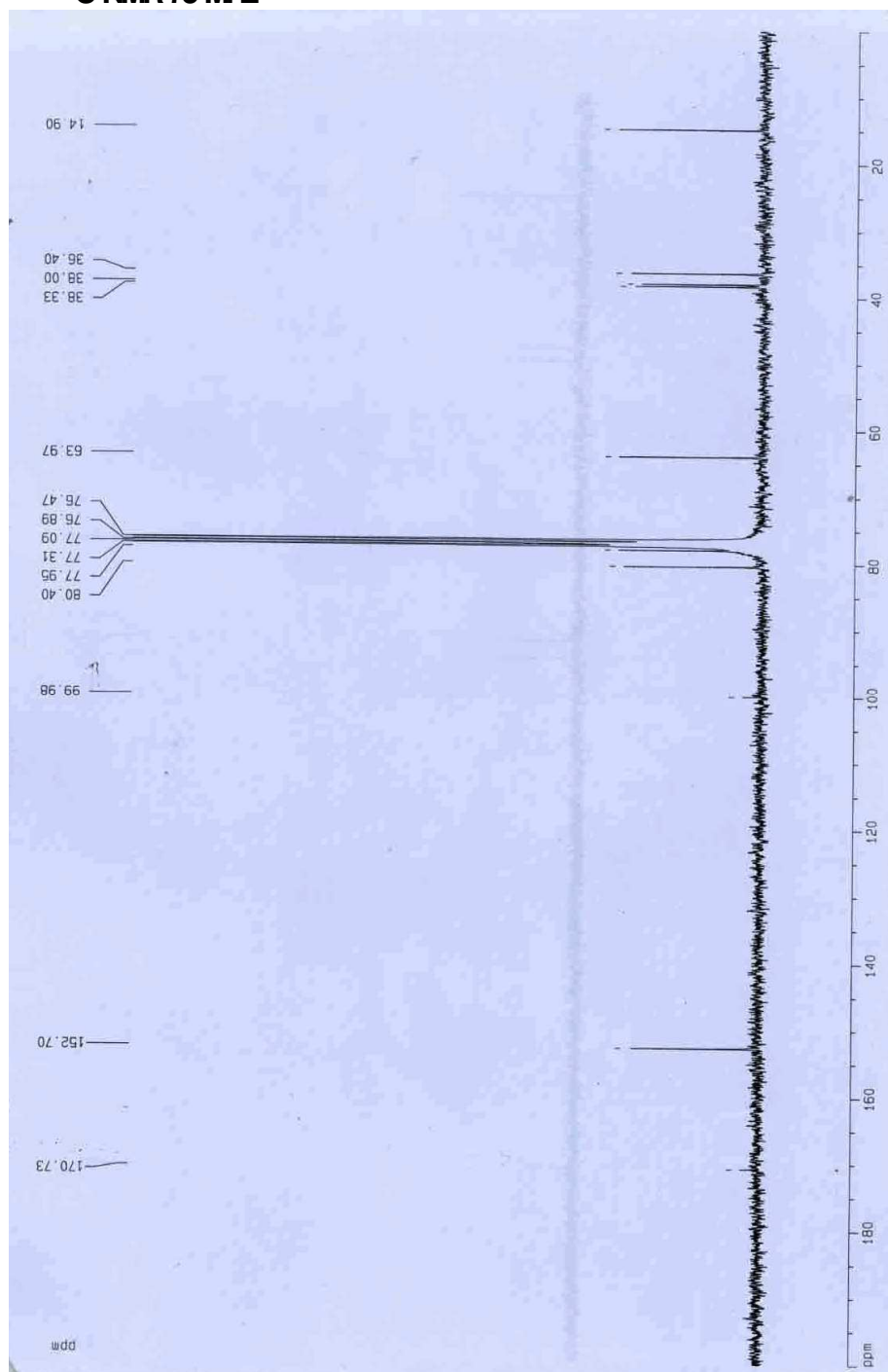


\* solvents \*\* H<sub>2</sub>O



9-Deoxygelsemide (1)

$^{13}\text{C-NMR}$  75 MHz





## References

- (1) Piccinini, P.; Vidari, G.; Zanoni, G. *J. Am. Chem. Soc.* **2004**, *126*, 5088–5089.
- (2) Takayama, H.; Morohoshi, Y.; Kitajima, M.; Aimi, N.; Wongseripipatana, S.; Ponglux, D.; Sakai, S. *Nat. Prod. Lett.* **1994**, *5*, 15–20.