Supporting Information

Asymmetric synthesis of penostatins A-D from L-ascorbic acid

Maolin Wang, Yuanliang Jia, Folei Wu, Zupei Li, Lijun Shao and Xiaochuan Chen*

Key Laboratory of Green Chemistry & Technology of Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, PR China

E-mail:chenxc@scu.edu.cn

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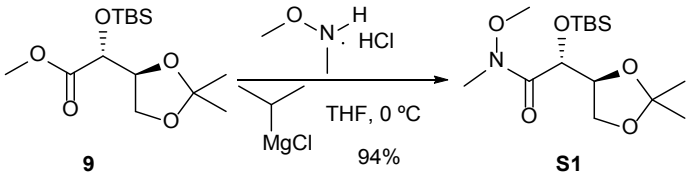
1. Experimental Procedures

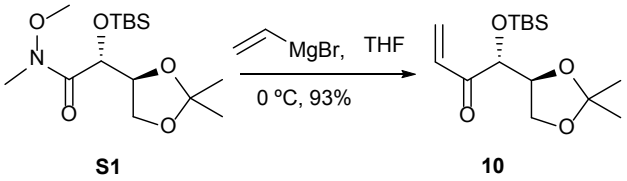
1.1 Synthesis of compound S1



To a solution of **9** (6.08 g, 20 mmol, 1 equiv.) and *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30 mmol, 1.5 equiv.) in THF (60 mL), a 2 M solution of *i*PrMgCl in THF (60 mmol, 3 equiv.) was added at 0 °C. The reaction mixture was stirred for 2 h at 0 °C. The reaction was then quenched with an aqueous saturated solution of NH_4Cl (200 mL) and extracted with EtOAc (3 × 200 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 80/20) to obtain **S1** (6.26 g, 94%) as a colorless oil.

$[\alpha]_D^{25}$ +12.3 (c 0.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (brs, 1H), 4.36 (q, *J* = 6.4 Hz, 1H), 3.99 (dd, *J* = 8.6, 6.5, Hz, 1H), 3.92 (dd, *J* = 8.6, 6.5 Hz, 1H), 3.71 (s, 3H), 3.21 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.8, 77.4, 70.9, 65.6, 61.3, 26.6, 25.9, 25.5, 18.5, −4.7, −4.8; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{15}H_{31}O_5NSiNa$ 356.1864, found 356.1850.

1.2 Synthesis of compound 10

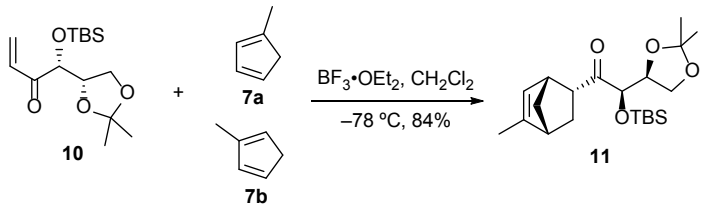


To a solution of **S1** (6.7 g, 20 mmol, 1 equiv.) in THF (100 mL), a solution of vinylmagnesium bromide (1.0 M in THF; 30 mL, 30 mmol, 1.5 equiv.) was added at 0 °C, and the resulting mixture was stirred at 25 ºC for 2 h. The reaction mixture was

slowly added to a solution of HCl (1 N, 150 mL) and extracted with EtOAc (3 × 200 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 95/5) to obtain **10** (5.58 g, 93%) as a colorless oil.

$[\alpha]_D^{25}$ +51.3 (c 0.73, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (dd, *J* = 17.4, 10.6 Hz, 1H), 6.37 (dd, *J* = 17.4, 1.9 Hz, 1H), 5.74 (dd, *J* = 10.6, 1.9 Hz, 1H), 4.24 (td, *J* = 6.6, 4.8 Hz, 1H), 4.14 (d, *J* = 4.8 Hz, 1H), 3.99 (dd, *J* = 8.5, 6.6 Hz, 1H), 3.86 (dd, *J* = 8.5, 6.6 Hz, 1H), 1.40 (s, 3H), 1.31 (s, 3H), 0.91 (s, 9H), 0.06 (d, *J* = 13.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 132.2, 129.3, 109.9, 78.8, 77.4, 65.5, 26.3, 25.9, 25.6, 18.4, −4.8, −4.9; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{15}H_{28}O_4SiNa$ 323.1649, found 323.1624.

1.3 Synthesis of compound 11

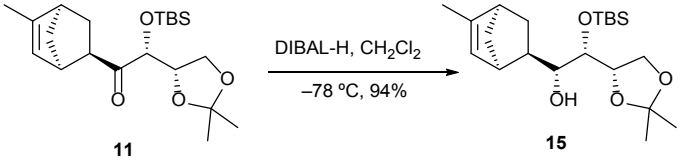


To a stirred solution of **10** (1.28 g, 4.3 mmol, 1 equiv.) in CH_2Cl_2 (43 mL) at −78 °C was slowly added **7a b** (2.5 mL, 26 mmol, 6 equiv.). Then, to the reaction mixture was added $BF_3 \cdot OEt_2$ (54 μL, 0.43 mmol, 0.1 equiv.) and stirred at −78 °C for additional 0.5 h. The reaction was quenched with an aqueous saturated solution of $NaHCO_3$ (50 mL). The organic phase was added to MeCN (200 mL) and filtered through a pad of Celite. The filtrate was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 95/5) to obtain **11** (1.37 g, 84%) as a colorless oil.

$[\alpha]_D^{25}$ +36.7 (c 1.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (s, 1H), 4.26 (q, *J* = 6.5 Hz, 1H), 4.12 (d, *J* = 5.5 Hz, 1H), 3.94 (dd, *J* = 8.5, 6.5 Hz, 1H), 3.84 (dd, *J* = 8.5, 7.4 Hz, 1H), 3.53 (dt, *J* = 8.4, 4.2 Hz, 1H), 3.27 (s, 1H), 2.65 (s, 1H), 1.76 (d, *J* = 1.6

Hz, 3H), 1.64 (ddd, *J* = 12.1, 8.6, 3.9 Hz, 1H), 1.49–1.42 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H), 1.30 (d, *J* = 8.2 Hz, 1H), 0.94 (s, 9H), 0.09 (d, *J* = 1.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.8, 148.5, 123.8, 109.4, 79.4, 77.4, 65.9, 50.2, 49.5, 47.8, 47.3, 27.4, 26.5, 26.0, 25.8, 18.5, 15.2, −4.57, −4.64; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{21}H_{36}O_4SiNa$ 403.2275, found 403.2276.

1.4 Synthesis of compound 15



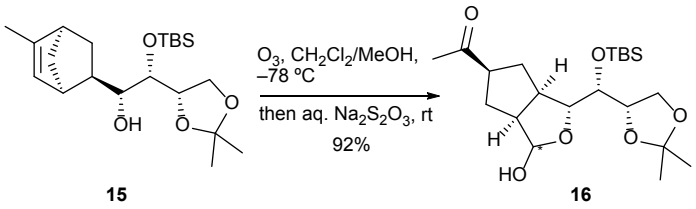
11 15

To a stirred solution of **11** (3.8 g, 10 mmol, 1 equiv.) in CH_2Cl_2 (100 mL) at −78 °C was added diisobutylaluminum hydride (DIBAL-H, 1.5 M in toluene; 16.7 mL, 25 mmol, 2.5 equiv.). The reaction mixture was stirred at −78 °C for additional 0.5 h. Excess DIBAL-H was then quenched at −40 °C rotate by dropwise addition of anhydrous MeOH until evolution of gas had ceased. The reaction solution was poured into a vigorously stirred mixture of a saturated aqueous solution of Rochelle's salt (200 mL). Vigorous stirring was maintained until the phases became clear, at which point the aqueous and organic layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 90/10) to obtain **15** (3.59 g, 94%) as a colorless oil.

$[\alpha]_D^{25}$ +30.0 (c 0.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (s, 1H), 4.14 (q, *J* = 7.2 Hz, 1H), 3.95 (dd, *J* = 8.2, 6.6 Hz, 1H), 3.59 (t, *J* = 7.9 Hz, 1H), 3.53 (d, *J* = 7.2 Hz, 1H), 2.90 (dq, *J* = 3.2, 1.6 Hz, 1H), 2.66 (t, *J* = 10.6 Hz, 1H), 2.57–2.50 (m, 1H), 2.33 (d, *J* = 10.6 Hz, 1H), 2.30–2.18 (m, 1H), 1.74 (d, *J* = 1.6 Hz, 3H), 1.72–1.64 (m, 1H), 1.52–1.44 (m, 1H), 1.38 (s, 3H), 1.32 (s, 3H), 1.20 (d, *J* = 8.2, Hz, 1H), 0.92 (s, 9H), 0.44 (ddd, *J* = 11.5, 4.7, 2.5 Hz, 1H), 0.12 (d, *J* = 11.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 126.0, 109.2, 77.8, 75.0, 74.9, 65.9, 48.8, 47.0, 45.5, 44.5, 28.7,

26.7, 26.2, 25.4, 18.6, 15.0, −3.7, −4.7; HRMS (ESI - TOF) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{38}O_4SiNa$ 405.2432, found 405.2422.

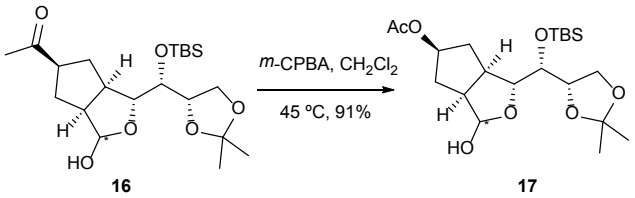
1.5 Synthesis of compound 16



A solution of **15** (3.4 g, 9 mmol, 1.0 equiv.) in CH_2Cl_2/MeOH (1:1, 30 mL) was cooled to −78 °C. A stream of O_3 was bubbled through the solution until a pale blue color persisted (about 0.5 h). A stream of N_2 was bubbled through the solution to remove residual O_3 until the solution become colorless. Then, the mixture was allowed to warm to room temperature and added an aqueous saturated solution of $Na_2S_2O_3$ (50 mL). The reaction mixture was stirred overnight. The reaction was extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 70/30) to obtain **16** (3.42 g, 92%) as a colorless oil.

$[\alpha]_D^{25}$ −21.2 (c 0.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (d, *J* = 12.0 Hz, 1H), 4.86 (d, *J* = 12.0 Hz, 1H), 4.23 (ddd, *J* = 8.4, 7.5, 6.1 Hz, 1H), 4.10 (dd, *J* = 7.9, 6.1 Hz, 1H), 3.91 (t, *J* = 2.4 Hz, 1H), 3.69–3.62 (m, 2H), 2.86–2.68 (m, 2H), 2.63 (q, *J* = 9.1 Hz, 1H), 2.35–2.19 (m, 2H), 2.15 (s, 3H), 1.64 (ddd, *J* = 12.8, 11.1, 8.1 Hz, 1H), 1.51 (td, *J* = 12.1, 9.7 Hz, 1H), 1.41 (s, 3H), 1.34 (s, 3H), 0.94 (s, 9H), 0.20 (d, *J* = 13.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 109.2, 104.5, 87.8, 78.1, 66.1, 54.3, 54.1, 44.5, 35.9, 34.5, 29.1, 26.8, 26.2, 25.6, 18.7, −3.9, −4.4; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{38}O_6SiNa$ 437.2330, found 437.2325

1.6 Synthesis of compound 17

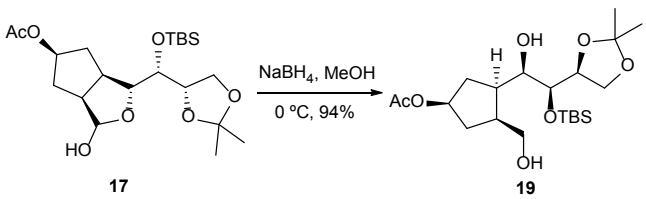


16 17

A solution of **16** (2.9 g, 7 mmol, 1.0 equiv.) in CH_2Cl_2 (70 mL) was treated with *m*-CPBA (85%; 2.9 g, 14 mmol, 2.0 equiv.). The mixture was stirred at 45 °C for 48 h. The mixture was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (30 mL), diluted with saturated aqueous $NaHCO_3$ solution (30 mL) and extracted with CH_2Cl_2 (3 × 70 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 75/25) to obtain **17** (2.74 g, 91%) as a colorless oil.

$[\alpha]_D^{25}$ −16.9 (c 0.86, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (d, *J* = 11.8 Hz, 1H), 4.97 (p, *J* = 6.3 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.23 (ddd, *J* = 8.5, 7.3, 6.3 Hz, 1H), 4.09 (dd, *J* = 7.9, 6.1 Hz, 1H), 3.97 (t, *J* = 2.5 Hz, 1H), 3.68 (t, *J* = 8.3 Hz, 1H), 3.64 (dd, *J* = 7.4, 2.1 Hz, 1H), 2.69 (tdd, *J* = 8.8, 5.9, 2.8 Hz, 1H), 2.56 (q, *J* = 8.8 Hz, 1H), 2.36–2.21 (m, 2H), 2.00 (s, 3H), 1.63–1.54 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H), 0.93 (s, 9H), 0.19 (d, *J* = 14.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 109.3, 105.6, 88.2, 78.1, 76.7, 75.7, 66.1, 51.6, 42.4, 38.7, 36.7, 26.8, 26.2, 25.7, 21.3, 18.7, −3.9, −4.4; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{38}O_7SiNa$ 453.2279, found 453.2275.

1.7 Synthesis of compound 19



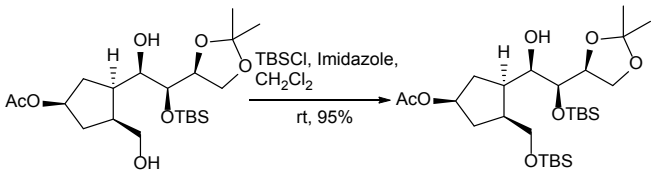
17 19

To a solution of **17** (1.2 g, 2.8 mmol, 1 equiv.) in MeOH (30 mL) was added $NaBH_4$ (320 mg, 8.4 mmol, 3 equiv.) at 0 °C and the mixture was stirred at the same temperature for 1 h. The reaction mixture was quenched with aqueous HCl (1 N; 50 mL), and the resulting solution was extracted with CH_2Cl_2 (3 × 50 mL). The

combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain **19** (1.14 g, 94%) as a colorless oil.

$[\alpha]_D^{25}$ −4.9 (c 1.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11–4.98 (m, 1H), 4.18 (q, *J* = 7.4 Hz, 1H), 4.03 (dd, *J* = 8.1, 6.4 Hz, 1H), 3.78 (dd, *J* = 11.5, 9.1 Hz, 1H), 3.65 (t, *J* = 7.9 Hz, 1H), 3.61 (d, *J* = 7.4 Hz, 1H), 3.56–3.47 (m, 2H), 2.41–2.31 (m, 1H), 2.26 (tt, *J* = 10.0, 7.3 Hz, 1H), 2.17 (dt, *J* = 14.3, 7.9 Hz, 1H), 2.07 (dt, *J* = 14.3, 7.3 Hz, 1H), 1.99 (s, 3H), 1.48–1.42 (m, 1H), 1.40 (s, 3H), 1.39–1.34 (m, 1H), 1.32 (s, 3H), 0.88 (s, 9H), 0.11 (d, *J* = 17.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 109.4, 77.8, 74.9, 74.6, 72.2, 65.9, 63.4, 43.4, 42.1, 35.7, 34.8, 26.7, 26.1, 25.4, 21.3, 18.5, −3.8, −4.8; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{21}H_{40}O_7SiNa$ 455.2436, found 455.2427.

1.8 Synthesis of compound 20

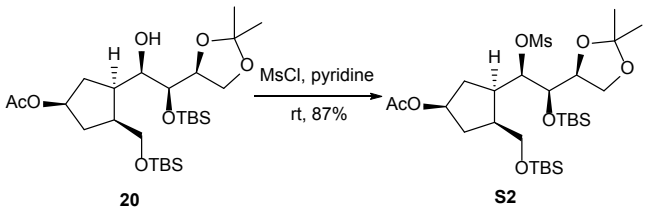


19 **20**

To a stirred solution of **19** (1.2 g, 2.7 mmol, 1 equiv.) in anhydrous CH_2Cl_2 (27 mL) at 0 °C were added imidazole (367 mg, 5.4 mmol, 2 equiv.) and *tert*-butyldimethylsilyl chloride (610 mg, 4.1 mmol, 1.5 equiv.). The reaction mixture was stirred at room temperature for 12 h. Then the reaction mixture was quenched by addition of water (25 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 90/10) to obtain **20** (1.4 g, 95%) as a colorless oil.

$[\alpha]_D^{25}$ −8.6 (c 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (qd, *J* = 7.2, 4.1 Hz, 1H), 4.26 (td, *J* = 8.1, 6.3 Hz, 1H), 4.04 (dd, *J* = 7.9, 6.2 Hz, 1H), 3.74 (dd, *J* = 10.3, 7.6 Hz, 1H), 3.62–3.54 (m, 3H), 3.50–3.42 (m, 2H), 2.38–2.27 (m, 2H), 2.21 (dt, *J* = 14.8, 8.1 Hz, 1H), 2.14–2.04 (m, 1H), 2.00 (s, 3H), 1.47 (dt, *J* = 14.8, 3.1 Hz, 1H), 1.36–1.43 (m, 4H), 1.34 (s, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (d, *J* = 17.0 Hz, 6H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 109.0, 78.3, 76.1, 75.1, 72.9, 66.2, 64.2, 43.6, 41.0, 35.4, 34.0, 26.9, 26.2, 26.0, 25.7, 21.4, 18.7, 18.3, −3.7, −4.9, −5.4, −5.5; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{27}H_{54}O_7Si_2Na$ 569.3300, found 569.3308.

1.9 Synthesis of compound S2



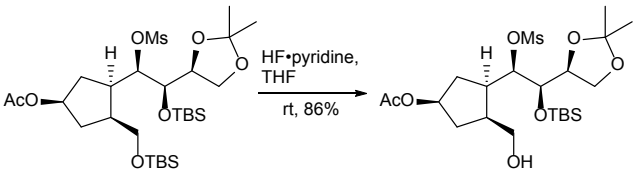
20 **S2**

A solution of **20** (5.46 g, 10 mmol, 1 equiv.) in anhydrous pyridine (16 mL) was treated at 0°C with MsCl (3.87 mL, 50 mmol, 5 equiv.) and the rection mixture was stirred 18 h at room temperature. The reaction was concentrated under vacuum and then quenched by addition of water (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 85/15) to obtain **S2** (5.43 g, 87%) as a colorless oil.

$[\alpha]_D^{25}$ +23.6 (c 1.33, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (qd, *J* = 7.2, 3.4 Hz, 1H), 4.68 (dd, *J* = 10.6, 2.2 Hz, 1H), 4.22–4.09 (m, 2H), 3.80 (dd, *J* = 6.9, 2.2 Hz, 1H), 3.77–3.70 (m, 2H), 3.64 (t, *J* = 7.7 Hz, 1H), 3.04 (s, 3H), 2.44–2.34 (m, 1H), 2.29 (dt, *J* = 14.0, 7.2 Hz, 1H), 2.14 (dq, *J* = 22.1, 8.0, 7.7 Hz, 2H), 2.00 (s, 3H), 1.92–1.83 (m, 1H), 1.74–1.61 (m, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 6H), 0.07 (d, *J* = 5.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 109.3, 82.7, 76.5,

75.0, 66.1, 62.1, 42.0, 40.6, 39.4, 35.0, 34.7, 26.7, 26.2, 26.1, 26.0, 25.7, 21.3, 18.5, 18.5, −4.1, −4.6, −5.27, −5.33; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{28}H_{56}O_9Si_2SNa$ 647.3076, found 647.3077.

1.10 Synthesis of compound S3

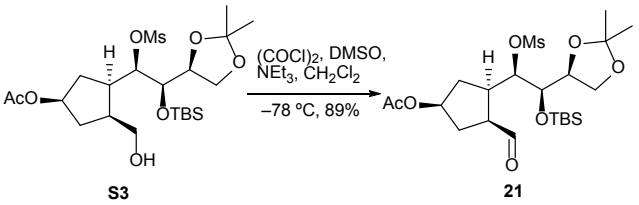


S2 **S3**

To a stirred solution of **S2** (3.6 g, 5.8 mmol, 1 equiv.) in THF (58 mL) in a Teflon® sample tube was added a solution of HF-pyridine (HF content ~70%; 1.5 mL, 58 mmol, 10 equiv.) at 0 °C under argon. The resulting mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (100 mL), and the whole mixture was extracted with EtOAc (3 × 100 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain **S3** (2.54 g, 86%) as a colorless oil.

$[\alpha]_D^{25}$ +12.1 (*c* 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20–5.09 (m, 1H), 4.83 (dd, *J* = 10.4, 2.6 Hz, 1H), 4.16 (q, *J* = 6.5 Hz, 1H), 4.09 (dd, *J* = 8.3, 6.5 Hz, 1H), 3.87 (dd, *J* = 11.0, 5.7 Hz, 1H), 3.83 (dd, *J* = 6.5, 2.5 Hz, 1H), 3.68 (t, *J* = 7.9 Hz, 1H), 3.62 (dd, *J* = 10.4, 7.0 Hz, 1H), 3.09 (s, 3H), 2.48–2.30 (m, 2H), 2.25 (p, *J* = 6.3 Hz, 1H), 2.12–2.03 (m, 1H), 2.01 (s, 3H), 1.92 (s, 1H), 1.76 (dt, *J* = 14.9, 1.8 Hz, 1H), 1.59 (td, *J* = 12.3, 6.0 Hz, 1H), 1.39 (s, 3H), 1.33 (s, 3H), 0.88 (s, 9H), 0.12 (d, *J* = 3.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 109.3, 82.4, 76.1, 74.8, 74.7, 66.0, 62.3, 42.9, 41.4, 39.3, 35.5, 34.6, 26.6, 26.0, 25.7, 21.4, 18.4, −4.3, −4.5; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{42}O_9SiSNa$ 533.2211, found 533.2212.

1.11 Synthesis of compound 21

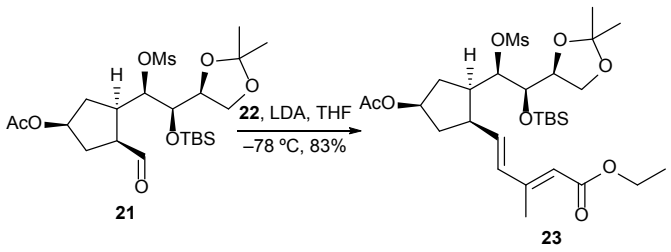


S3 **21**

A solution of DMSO (5.7 mL, 80 mmol, 4 equiv.) in CH_2Cl_2 (20 mL) was added dropwise under nitrogen at −78 °C to a solution of oxalyl chloride (3.5 mL, 40 mmol, 2 equiv.) in CH_2Cl_2 (140 mL). After the system had been kept for an additional 20 min at −78 °C, a solution of **S3** (10.2 g, 20 mmol, 1 equiv.) in CH_2Cl_2 (40 mL) was added dropwise. After the system had then been kept for an additional 45 min at −78 °C, triethylamine (11.2 mL, 80 mmol, 4 equiv.) was added dropwise. After the system had been kept for an additional 5 min at −78 °C, the temperature was raised to 25 °C and stirring was continued for 30 min. The reaction mixture was then partitioned between water (200 mL) and CH_2Cl_2. The organic extract was washed with a saturated aqueous solution of NH_4Cl, dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 65/35) to obtain **21** (9.04 g, 89%) as a colorless oil.

$[\alpha]_D^{25}$ +13.9 (c 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (dd, *J* = 2.6, 1.2 Hz, 1H), 5.23–5.13 (m, 1H), 5.08 (dd, *J* = 10.0, 2.8 Hz, 1H), 4.22–4.14 (m, 1H), 4.09 (dd, *J* = 8.3, 6.5 Hz, 1H), 3.87 (dd, *J* = 5.6, 2.8 Hz, 1H), 3.71 (t, *J* = 7.9 Hz, 1H), 3.04 (s, 3H), 2.97 (tt, *J* = 5.6, 2.8 Hz, 1H), 2.68–2.54 (m, 1H), 2.48 (dt, *J* = 14.5, 7.4 Hz, 1H), 2.22 (dt, *J* = 15.0, 8.2 Hz, 1H), 2.03 (t, *J* = 2.5 Hz, 1H), 2.00 (s, 3H), 1.81 (td, *J* = 13.0, 5.8 Hz, 1H), 1.40 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.13 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.8, 109.5, 80.9, 75.7, 74.4, 74.2, 66.1, 51.0, 42.9, 38.9, 35.3, 33.5, 26.5, 26.0, 25.7, 21.2, 18.4, −4.35, −4.43; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{40}O_9SiSNa$ 531.2055, found 531.2058.

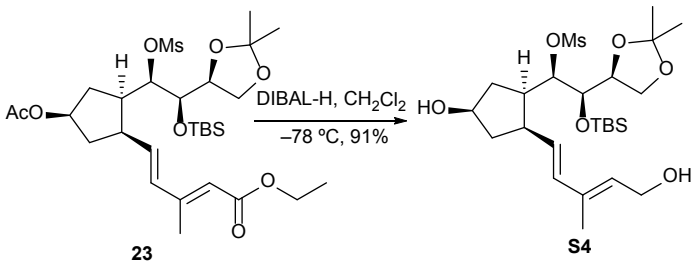
1.12 Synthesis of compound 23



To a solution of **22** (198 mg, 0.75 mmol, 1.5 equiv.) in THF (5 mL) was added LDA (2 M in THF; 0.325 mL, 0.65 mmol, 1.3 equiv.) under nitrogen at −78 °C. After 30 min, a solution of **21** (255 mg, 0.5 mmol, 1 equiv.) in THF (2.5 mL) was dropped slowly to the mixture and the reaction was stirred for 1 h at −78 °C. The reaction was then quenched with an aqueous saturated solution of NH_4Cl (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 80/20) to obtain **23** (256 mg, 83%) as a colorless oil.

$[\alpha]_D^{25}$ +28.5 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30–6.13 (m, 2H), 5.72 (d, *J* = 1.3 Hz, 1H), 5.19 (tdd, *J* = 7.8, 5.6, 2.2 Hz, 1H), 4.55 (dd, *J* = 10.6, 3.1 Hz, 1H), 4.22–4.12 (m, 3H), 4.04 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.92 (dd, *J* = 5.6, 3.1 Hz, 1H), 3.77–3.69 (m, 1H), 2.98 (s, 3H), 2.95–2.87 (m, 1H), 2.53 (dt, *J* = 14.4, 7.4 Hz, 1H), 2.40 (dddd, *J* = 12.9, 10.5, 7.4, 5.8 Hz, 1H), 2.29 (d, *J* = 1.2 Hz, 3H), 2.22 (ddd, *J* = 15.1, 8.1, 7.1 Hz, 1H), 2.03 (s, 3H), 1.78–1.66 (m, 2H), 1.40 (s, 3H), 1.36–1.33 (m, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.12 (d, *J* = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 167.2, 151.7, 136.0, 135.5, 119.2, 109.4, 83.0, 75.7, 74.9, 74.0, 66.0, 59.9, 44.2, 43.7, 39.5, 39.0, 34.4, 26.6, 26.0, 25.8, 21.4, 18.4, 14.5, 13.8, −4.3, −4.6; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{50}O_{10}SiSNa$ 641.2786, found 641.2783.

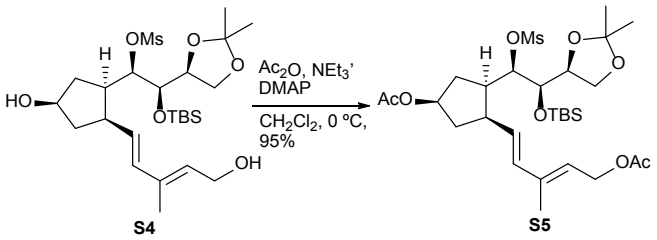
1.13 Synthesis of compound S4



To a stirred solution of **23** (1.2 g, 2 mmol, 1 equiv.) in CH_2Cl_2 (20 mL) at −78 °C was added DIBAL-H (1.5 in toluene; 6.4 mL, 9.6 mmol, 4.8 equiv.). The reaction mixture was stirred at −78 °C for additional 0.5 h. Excess DIBAL-H was then quenched at −40 °C rotate by dropwise addition of anhydrous MeOH until evolution of gas had ceased. The reaction solution was poured into a vigorously stirred mixture of a saturated aqueous solution of Rochelle's salt (40 mL). Vigorous stirring was maintained until the phases became clear, at which point the aqueous and organic layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain **S4** (970 mg, 91%) as a colorless oil.

$[\alpha]_D^{25}$ +50.3 (*c* 0.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (d, *J* = 15.6 Hz, 1H), 5.88 (dd, *J* = 15.6, 9.5 Hz, 1H), 5.57 (t, *J* = 6.9 Hz, 1H), 4.58 (dd, *J* = 10.6, 3.0 Hz, 1H), 4.39 (tt, *J* = 6.9, 3.5 Hz, 1H), 4.26 (d, *J* = 6.9 Hz, 2H), 4.18 (dt, *J* = 7.7, 6.1 Hz, 1H), 4.04 (dd, *J* = 8.4, 6.3 Hz, 1H), 3.94 (dd, *J* = 6.0, 3.0 Hz, 1H), 3.73 (t, *J* = 8.1 Hz, 1H), 2.97 (s, 3H), 2.79 (q, *J* = 7.5 Hz, 1H), 2.40 (dt, *J* = 13.3, 6.9 Hz, 1H), 2.36–2.25 (m, 1H), 2.25–2.13 (m, 1H), 1.90–1.84 (m, 2H), 1.81–1.77 (m, 3H), 1.64–1.52 (m, 2H), 1.39 (s, 3H), 1.34 (s, 3H), 0.91 (s, 9H), 0.12 (d, *J* = 8.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 136.0, 129.7, 129.3, 109.1, 83.8, 75.9, 74.3, 72.5, 66.0, 59.4, 44.0, 43.6, 42.2, 39.4, 37.7, 26.6, 26.0, 25.9, 18.4, 12.8, −4.3, −4.6; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{46}O_8SiSNa$ 557.2575, found 557.2580.

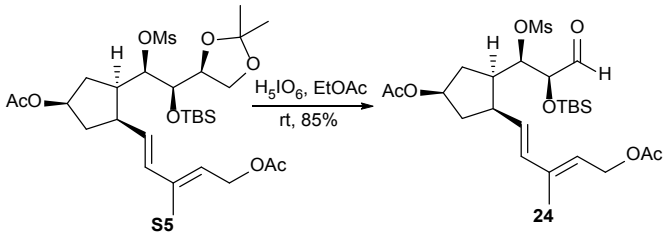
1.14 Synthesis of compound S5



To a solution of **S4** (634 mg, 1.2 mmol, 1 equiv.) in CH_2Cl_2 (12 ml) was added triethylamine (1 mL, 7.2 mmol, 6 equiv.), Ac_2O (450 µL, 4.8 mmol, 4 equiv.) and DMAP (12 mg, 0.1 mmol, 0.1 equiv.) at 0 ºC. The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with a saturated aqueous $NaHCO_3$ (10 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 80/20) to obtain **S5** (704 mg, 95%) as a colorless oil.

$[\alpha]_D^{25}$ +45.0 (*c* 0.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (d, *J* = 15.6 Hz, 1H), 5.84 (dd, *J* = 15.6, 9.5 Hz, 1H), 5.51 (t, *J* = 7.1 Hz, 1H), 5.15 (tdd, *J* = 8.0, 5.8, 2.2 Hz, 1H), 4.69 (qd, *J* = 13.0, 7.1 Hz, 2H), 4.55 (dd, *J* = 10.6, 3.1 Hz, 1H), 4.18 (dt, *J* = 7.6, 6.0 Hz, 1H), 4.03 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.92 (dd, *J* = 5.7, 3.1 Hz, 1H), 3.72 (t, *J* = 8.0 Hz, 1H), 2.97 (s, 3H), 2.83 (dt, *J* = 9.5, 6.4 Hz, 1H), 2.49 (dt, *J* = 14.4, 7.4 Hz, 1H), 2.34 (ddt, *J* = 13.0, 10.7, 7.1 Hz, 1H), 2.25–2.14 (m, 1H), 2.04 (s, 3H), 2.01 (s, 3H), 1.81 (d, *J* = 1.2 Hz, 3H), 1.73–1.61 (m, 2H), 1.38 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.11 (d, *J* = 8.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.7, 138.2, 135.9, 129.5, 124.1, 109.2, 83.4, 75.7, 75.0, 74.1, 66.0, 61.2, 43.9, 43.5, 39.4, 39.1, 34.4, 26.5, 26.0, 25.8, 21.3, 21.1, 18.3, 12.8, −4.4, −4.6; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{29}H_{50}O_{10}SiSNa$ 641.2786, found 641.2785.

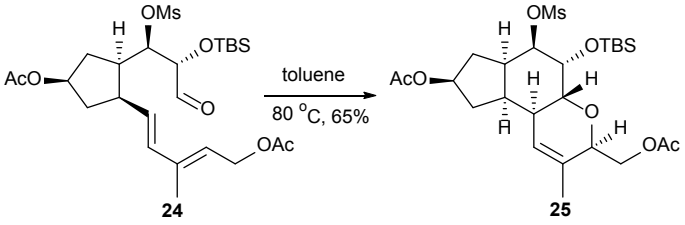
1.15 Synthesis of compound 24



To a stirred solution of **S5** (618 mg, 1 mmol, 1 equiv.) in EtOAc (10 mL) was added orthoperiodic acid (274 mg, 1.2 mmol, 1.2 equiv.) at room temperature. After being stirred at the same temperature for 1.5 h, the reaction mixture was quenched with an aqueous saturated solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 80/20) to obtain **24** (464 mg, 85%) as a colorless oil.

$[\alpha]_D^{25}$ +24.1 (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 6.20 (d, *J* = 15.6 Hz, 1H), 5.84 (dd, *J* = 15.6, 9.7 Hz, 1H), 5.55 (t, *J* = 7.1 Hz, 1H), 5.16 (tdd, *J* = 7.9, 6.0, 2.4 Hz, 1H), 4.81 (dd, *J* = 9.7, 3.0 Hz, 1H), 4.70 (qd, *J* = 13.0, 7.1 Hz, 2H), 4.29 (d, *J* = 3.0 Hz, 1H), 2.97 (s, 3H), 2.90 (q, *J* = 7.1 Hz, 1H), 2.41–2.31 (m, 1H), 2.24 (tt, *J* = 15.0, 7.3 Hz, 2H), 2.05 (s, 3H), 2.04 (s, 3H), 1.84 (d, *J* = 1.1 Hz, 3H), 1.77–1.67 (m, 2H), 0.93 (s, 9H), 0.09 (d, *J* = 16.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 171.2, 170.7, 138.1, 136.4, 128.6, 124.4, 81.1, 78.4, 74.6, 61.3, 43.9, 43.0, 39.4, 39.2, 34.1, 25.8, 21.4, 21.1, 18.3, 12.9, −4.4, −4.9; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{42}O_9SiSNa$ 569.2211, found 569.2213.

1.16 Synthesis of compound 25

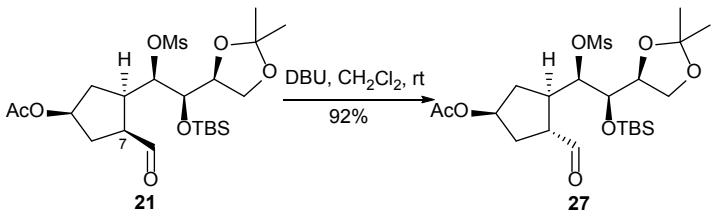


A solution of **24** (765 mg, 1.4 mmol) in toluene (14 mL) was heated to 80 °C under nitrogen. The reaction mixture was stirred at 80 °C for 24 h. The solvent was

concentrated under vacuum. The mixture was purified by flash column chromatography (eluent hexane/ethyl acetate 75/25) to obtain **25** (496 mg, 65%) as a white solid.

m.p. = 153–154 °C; $[\alpha]_D^{25}$ +41.6 (*c* 0.27, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 (s, 1H), 5.11 (dtd, *J* = 9.9, 7.9, 3.4 Hz, 1H), 4.68 (dd, *J* = 11.8, 8.8 Hz, 1H), 4.64 (t, *J* = 4.3 Hz, 1H), 4.16 (d, *J* = 8.2 Hz, 1H), 4.08 (s, 1H), 3.88 (dd, *J* = 11.8, 2.8 Hz, 1H), 3.83 (dd, *J* = 10.6, 2.0 Hz, 1H), 3.16 (s, 3H), 2.88–2.75 (m, 1H), 2.57–2.45 (m, 1H), 2.36 (dt, *J* = 15.2, 9.6 Hz, 1H), 2.20 (dq, *J* = 13.2, 6.5 Hz, 1H), 2.07 (s, 3H), 2.03 (s, 3H), 1.80 (ddd, *J* = 15.3, 3.4, 1.4 Hz, 1H), 1.66 (s, 3H), 1.60 (s, 1H), 1.50 (ddd, *J* = 14.6, 12.5, 8.0 Hz, 1H), 0.87 (s, 9H), 0.08 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.7, 130.9, 126.6, 82.1, 75.6, 75.1, 70.6, 65.3, 62.8, 41.1, 38.6, 36.5, 33.3, 32.8, 30.8, 25.8, 21.2, 21.0, 19.6, 18.1, −4.6, −5.2; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{42}O_9SiSNa$ 569.2211, found 569.2210.

1.17 Synthesis of compound 27

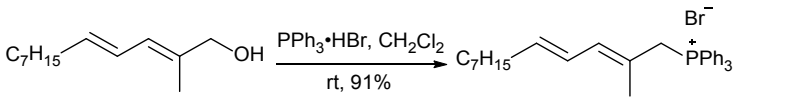


DBU (20 μL, 0.14 mmol, 0.1 equiv.) was added to a stirred solution of **21** (720 mg, 1.42 mmol, 1 equiv.) in CH_2Cl_2 (15 mL). Stirring at room temperature was continued for 1 h, and the solution was then washed with diluted hydrochloric acid (1 N, 8 mL), water (10 mL) and brine (10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 75/25) to obtain **27** (662 mg, 92%) as a white solid.

m.p. = 159–160 °C; $[\alpha]_D^{25}$ +11.8 (*c* 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (d, *J* = 3.1 Hz, 1H), 5.24–5.11 (m, 1H), 4.56 (dd, *J* = 10.3, 2.6 Hz, 1H), 4.22 (td, *J* = 7.0, 5.5 Hz, 1H), 4.10 (dd, *J* = 8.3, 6.5 Hz, 1H), 3.91 (dd, *J* = 5.5, 2.5 Hz, 1H), 3.68

(dd, J = 8.3, 7.0 Hz, 1H), 3.04 (s, 3H), 3.03–2.89 (m, 2H), 2.31 (ddd, J = 15.0, 9.0, 5.8 Hz, 1H), 2.04 (s, 3H), 2.01 (dd, J = 9.0, 4.6 Hz, 2H), 1.91 (ddt, J = 13.2, 6.7, 3.4 Hz, 1H), 1.41 (s, 3H), 1.35 (s, 3H), 0.91 (s, 9H), 0.14 (d, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 170.5, 109.5, 84.0, 75.8, 75.4, 74.2, 66.0, 54.3, 39.8, 38.6, 35.4, 33.5, 26.6, 26.0, 25.7, 21.3, 18.4, −4.38, −4.42; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{40}O_9SiSNa$ 531.2055, found 531.2056.

1.18 Synthesis of compound 28

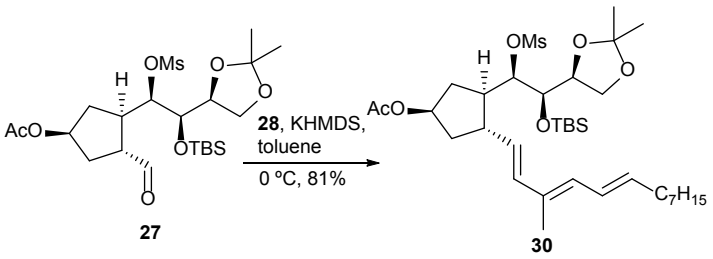


29 **28**

To a stirred solution of **29** (196 mg, 1.0 mmol, 1 equiv.) in CH_2Cl_2 (10 mL) was added triphenylphosphine hydrobromide (410 mg, 1.2 mmol, 1.2 equiv.). The reaction mixture was stirred for 8 h and the solvent was concentrated under vacuum. The mixture was purified by flash column chromatography (eluent dichloromethane/methanol 95/5) to obtain **28** (473 mg, 91%) as a white solid.

m.p. = 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.72 (m, 9H), 7.71–7.60 (m, 6H), 6.09–5.93 (m, 1H), 5.75 (dd, J = 10.8, 5.5 Hz, 1H), 5.44 (dtd, J = 16.8, 9.4, 8.1, 4.2 Hz, 1H), 4.65 (t, J = 13.8 Hz, 2H), 2.06–1.95 (m, 2H), 1.56 (d, J = 4.3 Hz, 3H), 1.34–1.15 (m, 10H), 0.89–0.80 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9 (d, J = 5.0 Hz), 135.7 (d, J = 12.2 Hz), 135.1, 134.3 (d, J = 9.9 Hz), 130.3 (d, J = 12.4 Hz), 125.1 (d, J = 5.5 Hz), 120.4 (d, J = 12.2 Hz), 118.5 (d, J = 85.1 Hz), 34.8 (d, J = 45.9 Hz), 33.0, 31.9, 29.2, 22.7, 19.0, 19.0, 14.2; HRMS (ESI-TOF) *m/z* $[M - Br]^+$ calcd for $C_{31}H_{38}P$ 441.2706, found 441.2726.

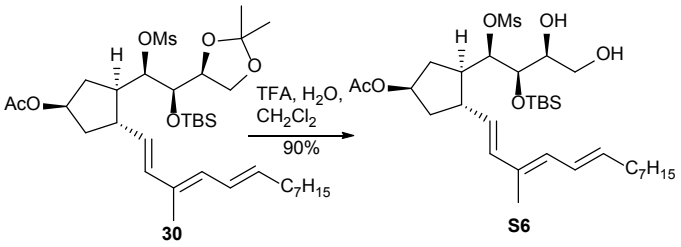
1.19 Synthesis of compound 30



To a suspension of **28** (1.04 g, 2.0 mmol, 2.0 equiv.) in toluene (15 mL) was added dropwise KHMDS (1.0 M in THF; 2.0 mL, 2.0 mmol, 2.0 equiv.) via syringe at 0 ºC. After the solution was stirred for 10 min at this temperature, a solution of **27** (508 mg, 1.0 mmol, 1.0 equiv.) in toluene (3 mL) was added slowly. The mixture was stirred for 4 h at 0 ºC and then quenched with an aqueous saturated solution of NH_4Cl (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 90/10) to obtain **30** (543 mg, 81%) as a colorless oil.

$[\alpha]_D^{25}$ +28.9 (*c* 0.96, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32 (ddt, *J* = 15.0, 11.1, 1.5 Hz, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 5.95 (d, *J* = 11.1 Hz, 1H), 5.71 (dt, *J* = 14.6, 7.1 Hz, 1H), 5.52 (dd, *J* = 15.6, 8.1 Hz, 1H), 5.14 (dp, *J* = 5.5, 2.7 Hz, 1H), 4.56 (dd, *J* = 9.8, 2.5 Hz, 1H), 4.19 (dt, *J* = 7.5, 6.4 Hz, 1H), 4.08 (dd, *J* = 8.3, 6.3 Hz, 1H), 3.90 (dd, *J* = 6.5, 2.4 Hz, 1H), 3.66 (t, *J* = 7.9 Hz, 1H), 2.90 (s, 3H), 2.84 (dq, *J* = 10.7, 7.4 Hz, 1H), 2.40–2.25 (m, 2H), 2.11 (q, *J* = 7.5 Hz, 2H), 2.03 (s, 3H), 1.96 (ddt, *J* = 14.0, 7.5, 2.1 Hz, 1H), 1.89–1.83 (m, 1H), 1.80 (d, *J* = 1.1 Hz, 3H), 1.71–1.64 (m, 1H), 1.40 (s, 3H), 1.39–1.36 (m, 2H), 1.34 (s, 3H), 1.27 (d, *J* = 4.6 Hz, 8H), 0.91 (s, 9H), 0.89–0.83 (m, 3H), 0.13 (d, *J* = 8.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 136.1, 134.6, 132.2, 132.0, 130.5, 126.6, 109.3, 84.5, 76.3, 75.4, 74.8, 66.0, 44.6, 40.7, 38.3, 36.0, 33.3, 32.0, 29.6, 29.3, 29.3, 26.6, 26.1, 25.7, 22.8, 21.5, 18.4, 14.2, 12.8, −4.3, −4.5; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{35}H_{62}O_8SiSNa$ 693.3827, found 693.3828.

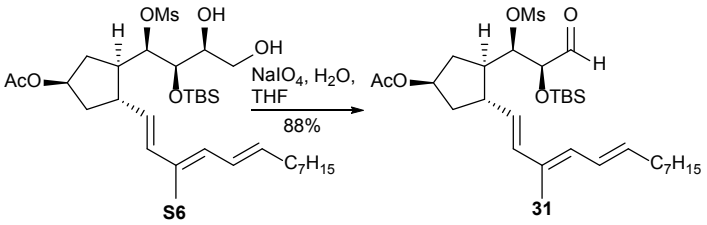
1.20 Synthesis of compound S6



To a stirred solution of **30** (74 mg, 0.11 mmol) in CH_2Cl_2 (3.6 mL) were added TFA (0.20 mL) and H_2O (0.20 mL) at room temperature. The solution was stirred at room temperature for 1 h. The reaction was then quenched with an aqueous saturated solution of $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain **S6** (62 mg, 90%) as a colorless oil.

$[\alpha]_D^{25}$ +24.4 (*c* 0.52, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32 (ddd, *J* = 15.0, 11.1, 1.5 Hz, 1H), 6.13 (d, *J* = 15.5 Hz, 1H), 5.95 (d, *J* = 11.0 Hz, 1H), 5.71 (dt, *J* = 14.6, 7.1 Hz, 1H), 5.52 (dd, *J* = 15.5, 8.3 Hz, 1H), 5.14 (td, *J* = 5.4, 2.6 Hz, 1H), 4.67 (dd, *J* = 10.1, 3.4 Hz, 1H), 4.10 (q, *J* = 2.7 Hz, 1H), 3.84 (ddd, *J* = 7.4, 5.2, 2.6 Hz, 1H), 3.54 (qd, *J* = 11.1, 6.2 Hz, 2H), 2.91 (s, 3H), 2.81 (dq, *J* = 11.1, 8.1 Hz, 1H), 2.43–2.34 (m, 1H), 2.29 (ddd, *J* = 15.6, 10.0, 5.8 Hz, 1H), 2.11 (q, *J* = 7.0 Hz, 2H), 2.03 (s, 3H), 1.98–1.88 (m, 2H), 1.80 (s, 3H), 1.61 (ddd, *J* = 14.0, 11.3, 5.4 Hz, 1H), 1.43–1.35 (m, 2H), 1.31–1.23 (m, 8H), 0.92 (s, 9H), 0.90–0.84 (m, 3H), 0.18 (d, *J* = 33.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 136.1, 134.6, 132.3, 132.0, 130.4, 126.7, 84.3, 75.8, 72.0, 69.9, 64.7, 46.8, 44.2, 40.5, 38.5, 36.1, 33.3, 32.0, 29.6, 29.34, 29.30, 26.0, 22.8, 21.5, 18.1, 14.2, 12.8, −3.8, −5.1; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{32}H_{58}O_8SiSNa$ 653.3514, found 653.3515.

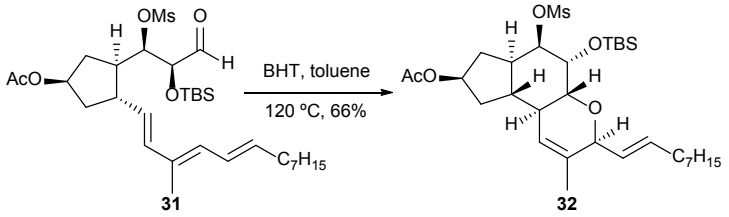
1.21 Synthesis of compound 31



To a stirred solution of **S6** (233 mg, 0.37 mmol) in THF/H_2O (1:1, 6 mL) was added $NaIO_4$ (792 mg, 3.7 mmol). The reaction mixture was stirred for 0.5 h. The reaction was then quenched with an aqueous saturated solution of $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 80/20) to obtain **31** (195 mg, 88%) as a colorless oil.

$[\alpha]_D^{25}$ +19.8 (*c* 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 1.0 Hz, 1H), 6.39–6.27 (m, 1H), 6.15 (d, *J* = 15.5 Hz, 1H), 5.97 (d, *J* = 11.0 Hz, 1H), 5.72 (dt, *J* = 14.6, 7.1 Hz, 1H), 5.50 (dd, *J* = 15.5, 8.3 Hz, 1H), 5.14 (dq, *J* = 5.8, 2.8 Hz, 1H), 4.83 (dd, *J* = 8.1, 3.8 Hz, 1H), 4.34 (dd, *J* = 3.8, 1.0 Hz, 1H), 2.96 (s, 3H), 2.90 (dd, *J* = 10.4, 7.6 Hz, 1H), 2.29–2.22 (m, 2H), 2.12 (q, *J* = 7.2 Hz, 2H), 2.05 (s, 3H), 2.03–1.94 (m, 2H), 1.81 (s, 3H), 1.70 (ddd, *J* = 14.0, 10.6, 5.8 Hz, 1H), 1.41–1.35 (m, 2H), 1.31–1.25 (m, 8H), 0.93 (s, 9H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.10 (d, *J* = 0.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 170.8, 136.2, 135.3, 132.2, 131.1, 130.8, 126.7, 82.3, 78.0, 75.0, 44.8, 44.4, 40.8, 38.6, 35.8, 33.3, 32.0, 29.6, 29.34, 29.31, 25.9, 22.8, 21.5, 18.3, 14.2, 12.8, −4.4, −4.8; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{31}H_{54}O_7SiSNa$ 621.3252, found 621.3255.

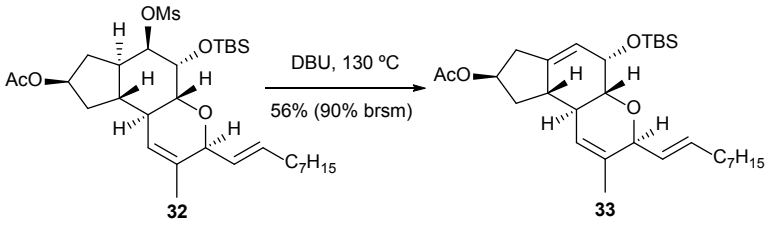
1.22 Synthesis of compound 32



To a stirred solution of **31** (246 mg, 0.41 mmol) in toluene (10 mL) was added BHT (9 mg, 0.04 mmol) at room temperature. The solution was stirred at 120 ºC for 6 h. Concentration of the solution followed by flash column chromatography (eluent hexane/ethyl acetate 85/15) to obtain **32** (162 mg, 66%) as a colorless oil.

$[\alpha]_D^{25}$ +18.1 (*c* 0.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.56–5.44 (m, 2H), 5.23 (td, *J* = 7.5, 3.2 Hz, 1H), 4.62 (t, *J* = 3.0 Hz, 1H), 4.36 (d, *J* = 6.5 Hz, 1H), 4.13 (t, *J* = 3.0 Hz, 1H), 3.45 (dd, *J* = 9.8, 2.4 Hz, 1H), 3.00 (s, 3H), 2.23 (dt, *J* = 13.2, 7.3 Hz, 1H), 2.19–2.12 (m, 1H), 2.09–2.02 (m, 2H), 2.01 (s, 3H), 2.00–1.91 (m, 2H), 1.59 (s, 3H), 1.57–1.46 (m, 2H), 1.39 (h, *J* = 6.9, 6.0 Hz, 3H), 1.31–1.25 (m, 8H), 0.87 (d, *J* = 2.9 Hz, 12H), 0.10 (d, *J* = 2.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 135.0, 134.3, 127.5, 123.0, 80.3, 77.7, 74.7, 71.1, 70.7, 42.4, 39.8, 38.3, 37.7, 35.9, 33.2, 32.5, 32.0, 29.4, 29.32, 29.25, 26.0, 22.8, 21.4, 20.1, 18.3, 14.2, −4.3, −5.0; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{31}H_{54}O_7SiSNa$ 621.3252, found 621.3255.

1.23 Synthesis of compound 33

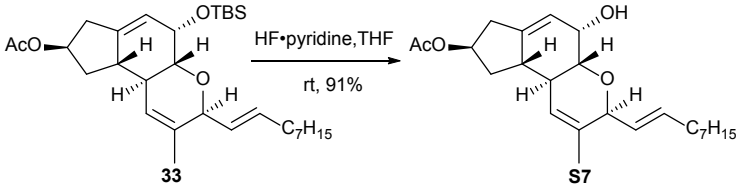


A stirred solution of **32** (191 mg, 0.32 mmol) in 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.5 mL) was heated to 120 °C for 3 h. The resulting mixture was purified by flash column chromatography (eluent hexane/ethyl acetate 95/5) to give product **33** (90 mg, 56%) as a colorless oil and recovered **32** (72 mg, 38%).

$[\alpha]_D^{25}$ +119.2 (*c* 0.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (dt, *J* = 15.4, 6.1 Hz, 1H), 5.57–5.50 (m, 2H), 5.26 (td, *J* = 5.7, 4.9, 1.6 Hz, 1H), 4.39 (d, *J* = 6.1 Hz, 1H), 4.19 (t, *J* = 4.2 Hz, 1H), 3.38 (dd, *J* = 9.3, 3.9 Hz, 1H), 2.82–2.70 (m, 1H), 2.38 (d, *J* = 18.1 Hz, 1H), 2.20–2.09 (m, 3H), 2.05 (q, *J* = 6.8 Hz, 2H), 2.01 (s, 3H), 1.63 (s,

3H), 1.56–1.47 (m, 1H), 1.41–1.34 (m, 2H), 1.31–1.21 (m, 9H), 0.88 (s, 12H), 0.08 (d, J = 5.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 144.1, 135.1, 134.3, 127.9, 123.2, 121.5, 76.7, 75.0, 71.8, 66.8, 44.5, 38.0, 37.0, 36.1, 32.5, 32.0, 29.3, 29.3, 29.2, 26.3, 22.8, 21.5, 20.3, 18.8, 14.3, −3.9, −4.3; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{30}H_{50}O_4SiNa$ 525.3371, found 525.3372.

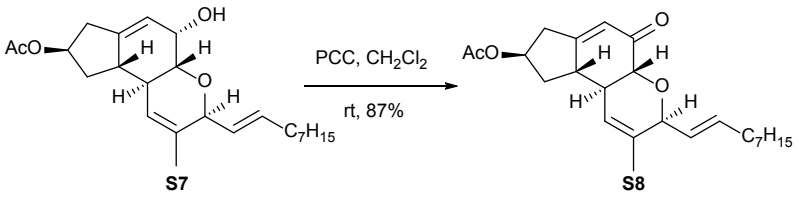
1.24 Synthesis of compound S7



To a stirred solution of **33** (200 mg, 0.4 mmol, 1 equiv.) in dry THF (4 mL) in a Teflon® sample tube was added a solution of HF-pyridine (HF content ~70%; 0.63 mL, 24 mmol, 60 equiv.) at 0 °C under argon. The resulting mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), and the whole mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 65/35) to obtain **S7** (141 mg, 91%) as a colorless oil.

$[\alpha]_D^{25}$ +81.7 (*c* 0.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72–5.63 (m, 2H), 5.62–5.54 (m, 2H), 5.26 (t, J = 5.4 Hz, 1H), 4.48 (dd, J = 21.1, 7.1 Hz, 1H), 4.24 (s, 1H), 3.51 (dd, J = 9.7, 4.0 Hz, 1H), 2.79 (dd, J = 18.5, 6.2 Hz, 1H), 2.52–2.38 (m, 2H), 2.25–2.14 (m, 3H), 2.07 (qd, J = 7.0, 3.4 Hz, 2H), 2.02 (s, 3H), 1.64 (s, 3H), 1.57–1.46 (m, 1H), 1.40 (q, J = 6.1 Hz, 2H), 1.30–1.25 (m, 8H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 147.0, 135.5, 135.1, 127.2, 122.7, 119.4, 77.8, 74.8, 71.5, 65.7, 44.1, 38.0, 37.1, 36.2, 32.5, 32.0, 29.3, 29.2, 22.8, 21.5, 20.2, 14.2; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{36}O_4Na$ 411.2506, found 411.2510.

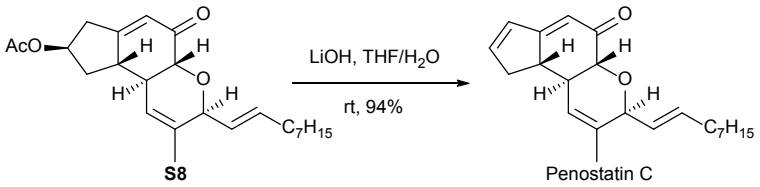
1.25 Synthesis of compound S8



To a stirred solution of **S7** (88.0 mg, 0.23 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) was added pyridinium chlorochromate (PCC, 992 mg, 4.6 mmol, 20 equiv.). The reaction mixture was added PCC (992 mg, 4.6 mmol, 20 equiv.) again after 3 h. The resulting dark mixture was stirred for additional 3 h and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 75/25) to obtain **S8** (76 mg, 87%) as a colorless oil.

$[\alpha]_D^{25}$ +55.3 (*c* 0.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (q, *J* = 2.3 Hz, 1H), 5.75–5.64 (m, 1H), 5.62–5.50 (m, 2H), 5.42–5.33 (m, 1H), 4.60 (d, *J* = 6.4 Hz, 1H), 4.07 (d, *J* = 11.5 Hz, 1H), 2.93 (ddt, *J* = 20.3, 5.9, 2.2 Hz, 1H), 2.79–2.67 (m, 2H), 2.48–2.33 (m, 2H), 2.13–1.99 (m, 5H), 1.67 (s, 3H), 1.63 (dd, *J* = 5.1, 1.2 Hz, 1H), 1.40–1.34 (m, 2H), 1.30–1.23 (m, 8H), 0.87 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 170.6, 168.4, 136.7, 136.5, 126.1, 122.8, 121.6, 77.6, 74.1, 73.9, 45.3, 44.8, 39.0, 36.6, 32.5, 31.9, 29.29, 29.25, 29.15, 22.8, 21.4, 20.2, 14.2; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{34}O_4Na$ 409.2349, found 409.2350.

1.26 Synthesis of (+)-Penostatin C

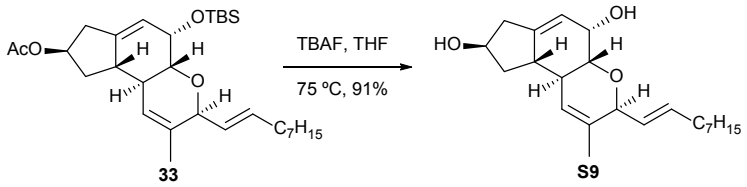


To a solution of **S8** (39 mg, 0.1 mmol, 1 equiv.) in THF/H_2O (1:1, 2 mL) was added LiOH·H_2O (4.2 mg, 0.1 mmol, 1 equiv.) and stirred for 15 min. The reaction mixture was quenched with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the

crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 65/35) to obtain (+)-penostatin C (30 mg, 94%) as a colorless oil.

$[\alpha]_D^{25}$ +172.0 (*c* 0.33, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (dt, *J* = 5.4, 2.6 Hz, 1H), 6.44 (dt, *J* = 5.6, 2.0 Hz, 1H), 5.91 (d, *J* = 2.6 Hz, 1H), 5.77–5.65 (m, 1H), 5.64–5.55 (m, 2H), 4.62 (d, *J* = 6.2 Hz, 1H), 4.04 (d, *J* = 10.9 Hz, 1H), 2.86 (dddd, *J* = 17.8, 7.0, 2.8, 1.7 Hz, 1H), 2.70 (dddd, *J* = 11.4, 6.9, 4.2, 2.6 Hz, 1H), 2.56–2.39 (m, 2H), 2.14–2.00 (m, 2H), 1.68 (s, 3H), 1.41–1.33 (m, 2H), 1.31–1.21 (m, 8H), 0.91–0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 170.8, 147.7, 136.7, 136.2, 132.3, 126.1, 121.7, 117.2, 77.6, 75.1, 45.8, 44.6, 36.5, 32.4, 31.8, 29.16, 29.12, 29.06, 22.7, 20.1, 14.1; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{30}O_2Na$ 349.2138, found 349.2139.

1.27 Synthesis of compound S9

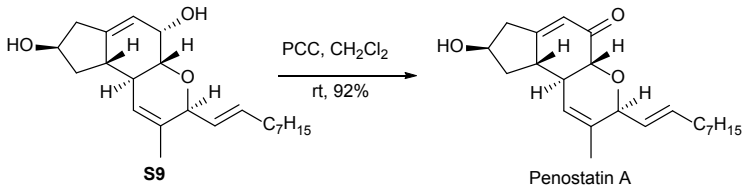


To a stirred solution of **33** (50 mg, 0.1 mmol, 1 equiv.) in THF (2 mL) was added TBAF (1 M in THF; 2 mL, 2 mmol, 20 equiv.). The resulting mixture was stirred for 25 h at 80 °C. The reaction was then quenched with an aqueous saturated solution of NH_4Cl (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were dried with Na_2SO_4. After filtration the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain **S9** (31 mg, 91%) as a colorless oil.

$[\alpha]_D^{25}$ +84.4 (*c* 0.44, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74–5.52 (m, 4H), 4.48 (tt, *J* = 5.4, 1.7 Hz, 2H), 4.23 (d, *J* = 4.3 Hz, 1H), 3.51 (dd, *J* = 10.2, 4.0 Hz, 1H), 2.78–2.65 (m, 1H), 2.46 (s, 1H), 2.39–2.27 (m, 2H), 2.20–2.02 (m, 4H), 1.63 (d, *J* = 1.9 Hz, 3H), 1.40 (d, *J* = 9.2 Hz, 2H), 1.28–1.23 (m, 8H), 0.92–0.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 135.6, 134.8, 127.3, 123.0, 119.1, 77.8, 71.7, 71.6,

65.8, 43.6, 40.9, 39.8, 36.2, 32.5, 32.0, 29.28, 29.25, 29.23, 22.8, 20.2, 14.3; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{34}O_3Na$ 369.2400, found 369.2401.

1.28 Synthesis of (+)-Penostatin A

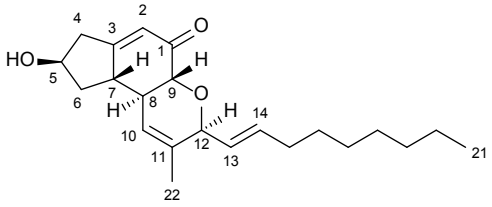


To a stirred solution of **S9** (45.0 mg, 0.13 mmol, 1 equiv.) in CH_2Cl_2 (2 mL) was added pyridinium chlorochromate (PCC, 140 mg, 0.65 mmol, 5 equiv.). The resulting dark mixture was stirred for 3 h and filtered through a pad of Celite. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent hexane/ethyl acetate 50/50) to obtain (+)-penostatin A (41 mg, 92%) as a colorless oil.

$[\alpha]_D^{25}$ +87.3 (*c* 0.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (d, *J* = 2.4 Hz, 1H), 5.68 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.61–5.52 (m, 2H), 4.64–4.56 (m, 2H), 4.08 (d, *J* = 11.5 Hz, 1H), 2.92–2.78 (m, 2H), 2.63 (d, *J* = 19.8 Hz, 1H), 2.46–2.37 (m, 1H), 2.27 (ddd, *J* = 13.4, 7.2, 2.4 Hz, 1H), 2.06 (q, *J* = 7.1 Hz, 2H), 1.66 (s, 3H), 1.56–1.51 (m, 1H), 1.37 (t, *J* = 6.7 Hz, 2H), 1.26 (s, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 169.7, 136.4, 136.3, 126.0, 122.5, 121.8, 77.2, 73.8, 71.1, 44.80, 44.76, 41.7, 39.2, 32.4, 31.8, 29.0, 22.6, 20.1, 14.1; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{32}O_3Na$ 367.2244, found 367.2245.

2. Comparison of NMR Spectroscopic Data

2.1 Comparison of NMR Spectroscopic Data of (+)-penostatins A ($CDCl_3$)



(+)-Penostatin A

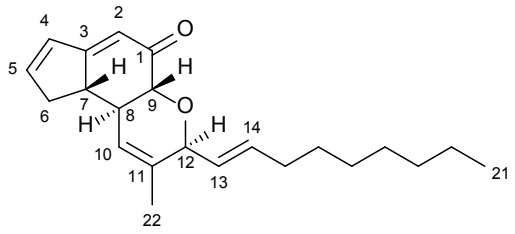
Table S1. Comparison of ^{1}H NMR Data for Natural and Synthetic (+)-penostatins A

Position	δ_H (**Natural**)	δ_H (**Tong's synthetic**)	δ_H (**Our synthetic**)
2	5.95	5.95	5.95
4 A	2.64	2.64	2.63
B	2.84	2.83	2.84
5	4.61	4.61	4.61
6 A	2.28	2.28	2.27
B	1.55	1.55	1.55
7	2.86	2.85	2.86
8	2.41	2.41	2.41
9	4.08	4.08	4.08
10	5.55	5.55	5.55
12	4.60	4.60	4.60
13	5.57	5.57	5.57
14	5.68	5.68	5.68
15	2.06	2.06	2.06
16	1.37	1.37	1.37
17	1.26	1.26	1.26
18	1.26	1.26	1.26
19	1.26	1.26	1.26
20	1.31	1.31	1.31
21	0.87	0.87	0.87
22	1.66	1.66	1.66

Table S2. Comparison of ^{13}C NMR Data for Natural and Synthetic (+)-penostatins A

Position	δ_C (**Natural**)	δ_H (**Tong's synthetic**)	δ_H (**Our synthetic**)
1	196.36	196.15	196.12
2	122.37	122.54	122.53
3	170.39	169.79	169.73
4	41.67	41.66	41.66
5	70.92	71.07	71.08
6	39.15	39.22	39.23
7	44.84	44.80	44.80
8	44.75	44.76	44.76
9	73.78	73.80	73.80
10	121.83	121.78	121.77
11	136.11	136.26	136.26
12	77.49	77.22	77.22
13	125.91	125.96	125.96
14	136.49	136.45	136.44
15	32.37	32.38	32.38
16	29.08	29.16	29.04
17	29.08	29.10	29.04
18	29.08	29.03	29.04
19	31.78	31.80	31.80
20	22.62	22.63	22.64
21	14.10	14.10	14.10
22	20.06	20.06	20.06

2.2 Comparison of NMR Spectroscopic Data of (+)-penostatins C ($CDCl_3$)



(+)-Penostatin C

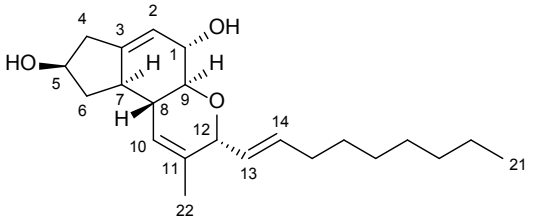
Table S3. Comparison of ^{1}H NMR Data for Natural and Synthetic (+)-penostatins C

Position	δ_H (**Natural**)	δ_H (**Tong's synthetic**)	δ_H (**Our synthetic**)
2	5.91	5.92	5.91
4	6.45	6.46	6.44
5	6.69	6.68	6.68
6 A	2.86	2.86	2.86
B	2.45	2.45	2.45
7	2.70	2.70	2.70
8	2.53	2.52	2.53
9	4.45	4.05	4.04
10	5.58	5.58	5.58
12	4.62	4.62	4.62
13	5.59	5.59	5.59
14	5.70	5.70	5.70
15	2.06	2.06	2.07
16	1.38	1.38	1.38
17	1.26	1.26	1.26
18	1.26	1.26	1.26
19	1.26	1.26	1.26
20	1.31	1.31	1.31
21	0.87	0.87	0.87
22	1.68	1.68	1.68

Table S4. Comparison of ^{13}C NMR Data for Natural and Synthetic (+)-penostatins C

Position	δ_C (**Natural**)	δ_H (**Tong's synthetic**)	δ_H (**Our synthetic**)
1	196.59	196.58	196.54
2	117.14	117.23	117.24
3	170.96	170.87	170.82
4	132.23	132.29	132.29
5	147.82	147.69	147.67
6	36.44	36.45	36.46
7	45.71	45.75	45.76
8	44.56	44.59	44.60
9	75.05	75.09	75.10
10	121.66	121.66	121.66
11	136.64	136.71	136.71
12	77.58	77.62	77.62
13	126.02	126.06	126.07
14	136.22	136.24	136.22
15	32.37	32.39	32.40
16	29.01	29.04	29.06
17	29.12	29.10	29.12
18	29.12	29.17	29.16
19	31.78	31.80	31.81
20	22.62	22.63	22.65
21	14.10	14.09	14.11
22	20.09	20.08	20.09

2.3 Comparison of NMR Spectroscopic Data of (-)-penostatins D ($CDCl_3$)



(-)-Penostatin D

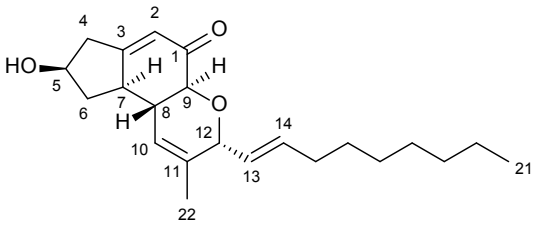
Table S5. Comparison of ^{1}H NMR Data for Natural and Synthetic (-)-penostatins D

Position	δ_H (**Natural**)	δ_H (**Our synthetic**)
1	4.34	4.33
2	5.47	5.46
4 A	2.71	2.70
B	2.19	2.18
5	4.37	4.37
6 A	2.40	2.40
B	1.33	1.33
7	2.07	2.07
8	2.03	2.03
9	3.45	3.45
10	5.50	5.50
12	4.41	4.41
13	5.57	5.57
14	5.69	5.68
15	2.06	2.06
16	1.37	1.37
17	1.27	1.27
18	1.27	1.27
19	1.27	1.27
20	1.30	1.30
21	0.88	0.87
22	1.63	1.63

Table S6. Comparison of ^{13}C NMR Data for Natural and Synthetic (-)-penostatins D

Position	δ_C (**Natural**)	δ_H (**Our synthetic**)
1	71.73	71.75
2	120.13	120.16
3	145.18	145.15
4	40.30	40.33
5	71.87	71.89
6	39.53	39.56
7	43.43	43.45
8	41.50	41.53
9	75.50	75.53
10	122.00	122.00
11	135.05	135.06
12	77.27	77.26
13	126.84	126.85
14	135.56	135.54
15	32.39	32.39
16	29.13	29.15
17	29.13	29.13
18	29.13	29.13
19	31.81	31.82
20	22.65	22.65
21	14.10	14.10
22	20.06	20.05

2.4 Comparison of NMR Spectroscopic Data of (-)-penostatins B ($CDCl_3$)



(-)-Penostatin B

Table S7. Comparison of ^{1}H NMR Data for Natural and Synthetic (-)-penostatins B

Position	δ_H (**Natural**)	δ_H (**Shishido's synthetic**)	δ_H (**Our synthetic**)
2	5.96	5.96	5.96
4 A	2.97	2.97	2.96
B	2.46	2.44	2.45
5	4.52	4.51	4.51
6 A	2.54	2.52	2.54
B	1.54	1.54	1.54
7	2.51	2.51	2.51
8	2.49	2.50	2.49
9	4.00	4.00	3.99
10	5.54	5.53	5.53
12	4.59	4.58	4.59
13	5.55	5.55	5.55
14	5.67	5.65	5.67
15	2.05	2.04	2.04
16	1.39	1.37	1.39
17	1.25	1.25	1.25
18	1.25	1.25	1.25
19	1.25	1.25	1.25
20	1.31	1.31	1.32
21	0.87	0.87	0.87
22	1.66	1.66	1.66

Table S8. Comparison of ^{13}C NMR Data for Natural and Synthetic (-)-penostatins B

Position	δ_C (**Natural**)	δ_H (**Shishido's synthetic**)	δ_H (**Our synthetic**)
1	196.07	195.92	195.93
2	122.68	122.72	122.73
3	168.82	168.60	168.57
4	41.47	41.51	41.49
5	71.23	71.25	71.28
6	38.61	38.67	38.67
7	45.12	45.18	45.16
8	45.27	45.27	45.28
9	73.93	73.96	73.96
10	121.60	121.59	121.58
11	136.42	136.45	136.46
12	77.24	77.21	77.22
13	125.95	126.02	125.99
14	136.33	136.25	136.28
15	32.37	32.35	32.37
16	29.02	29.03	29.03
17	29.12	29.13	29.14
18	29.12	29.08	29.10
19	31.80	31.79	31.81
20	22.64	22.61	22.63
21	14.12	14.07	14.10
22	20.06	20.02	20.05

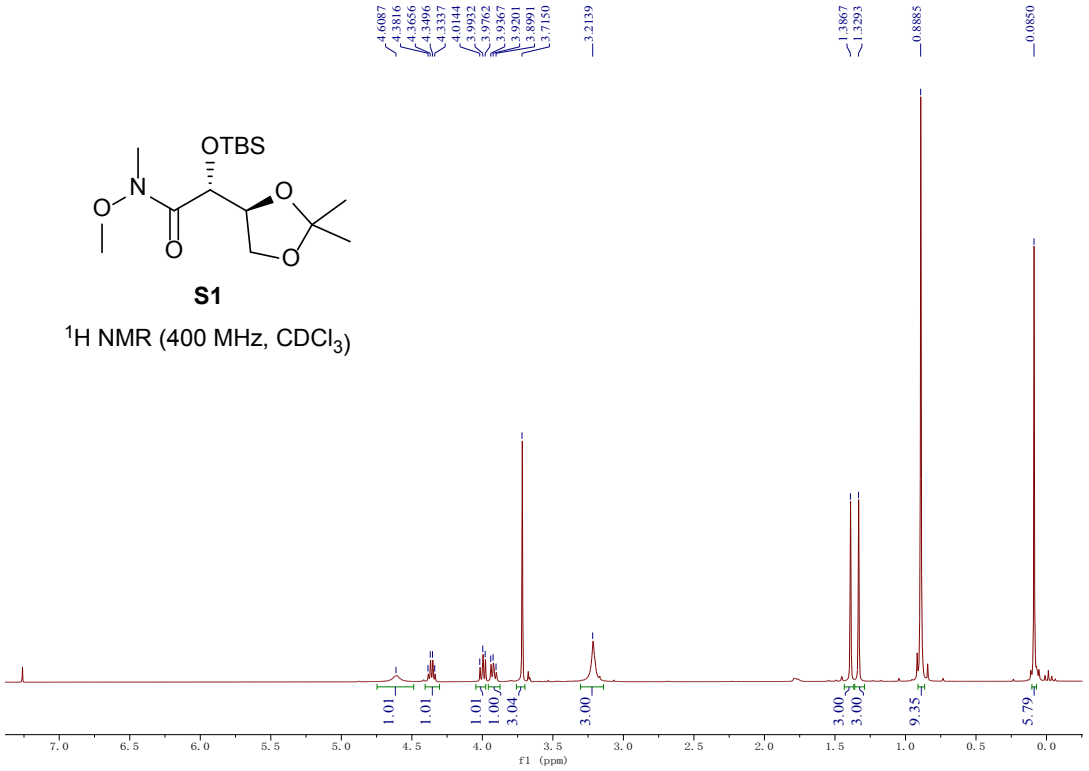
3. Comparison of Optical Rotation Data

Table S9. Comparison of Optical Rotation Data for Natural and Synthetic penostatins A-D

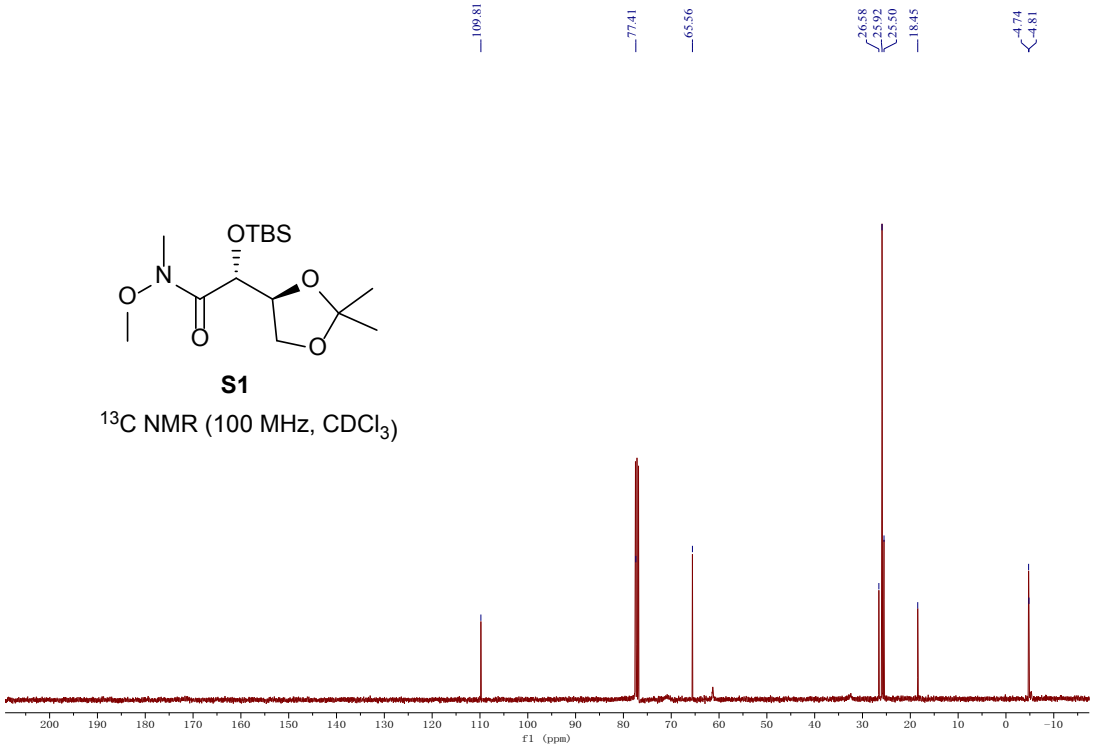
Compound	**Natural**	**Tong's synthetic**	**Our synthetic**
(+)-penostatins A	$[\alpha]_D$ +133.3 (*c* 0.18, $CHCl_3$)	$[\alpha]_D^{25}$ +54.4 (*c* 0.16, $CHCl_3$)	$[\alpha]_D^{25}$ +87.3 (*c* 0.14, $CHCl_3$)
(-)-penostatins B	$[\alpha]_D$ -103.1 (*c* 0.49, $CHCl_3$)	-	$[\alpha]_D^{25}$ -98.7 (*c* 0.07, $CHCl_3$)
(+)-penostatins C	$[\alpha]_D$ +120.0 (*c* 1.0, $CHCl_3$)	$[\alpha]_D^{25}$ +79.3 (*c* 0.16, $CHCl_3$)	$[\alpha]_D^{25}$ +172.0 (*c* 0.33, $CHCl_3$)
(-)-penostatins D	$[\alpha]_D$ -26.7 (*c* 0.14, $CHCl_3$)	-	$[\alpha]_D^{25}$ -23.3 (*c* 0.13, $CHCl_3$)

4. NMR spectra of the compounds

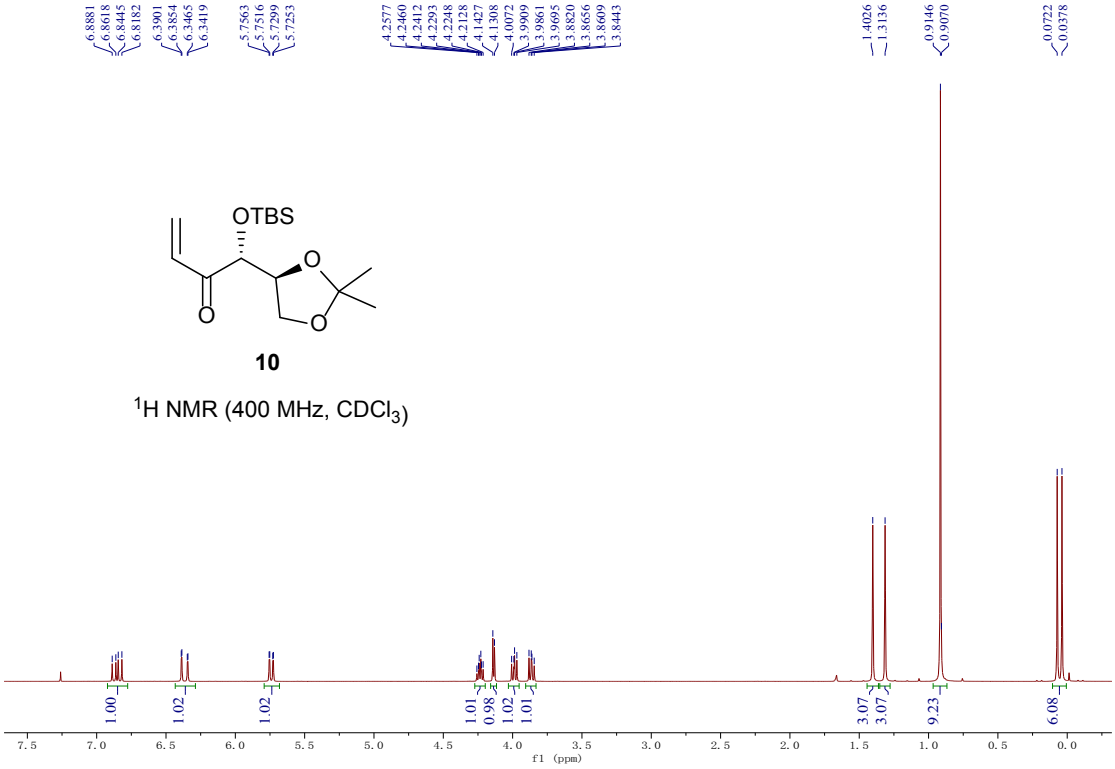
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S1**



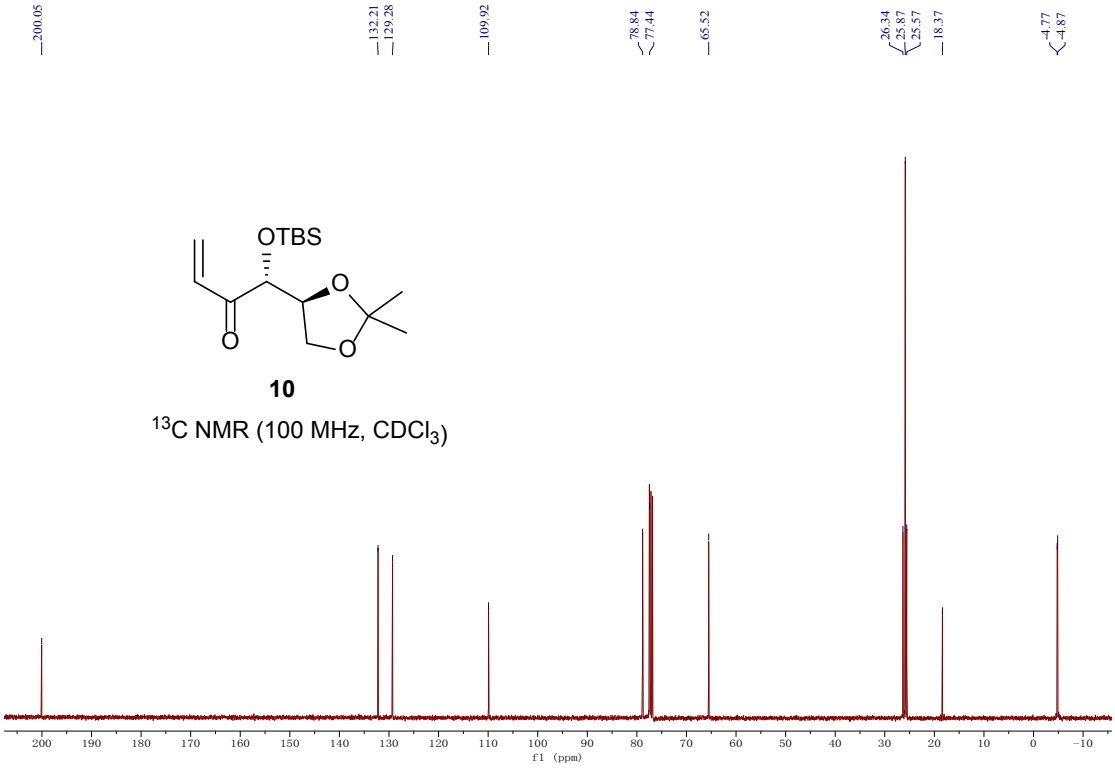
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S1**



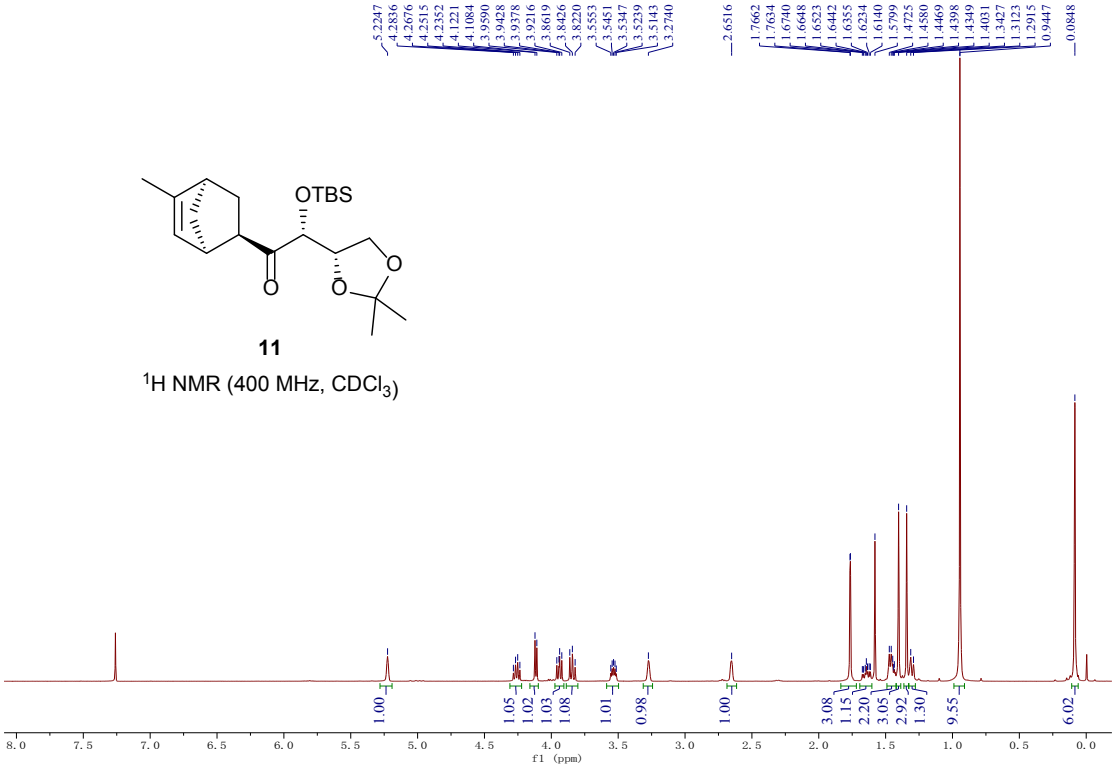
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **10**



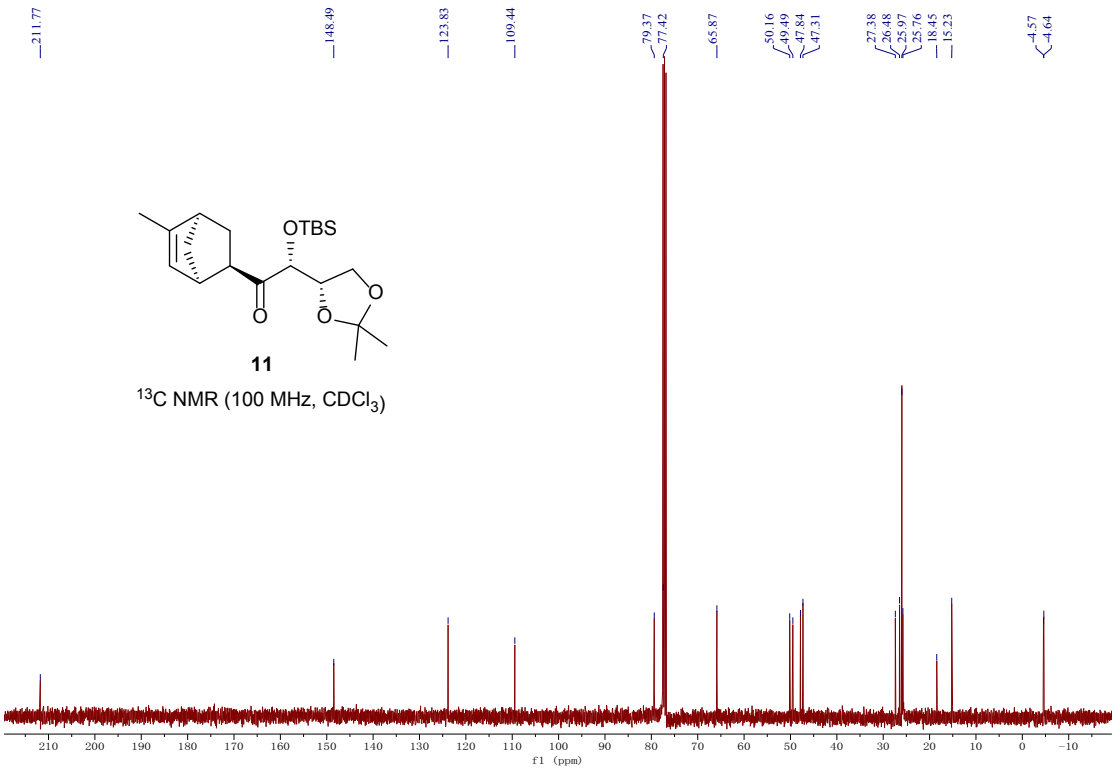
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **10**



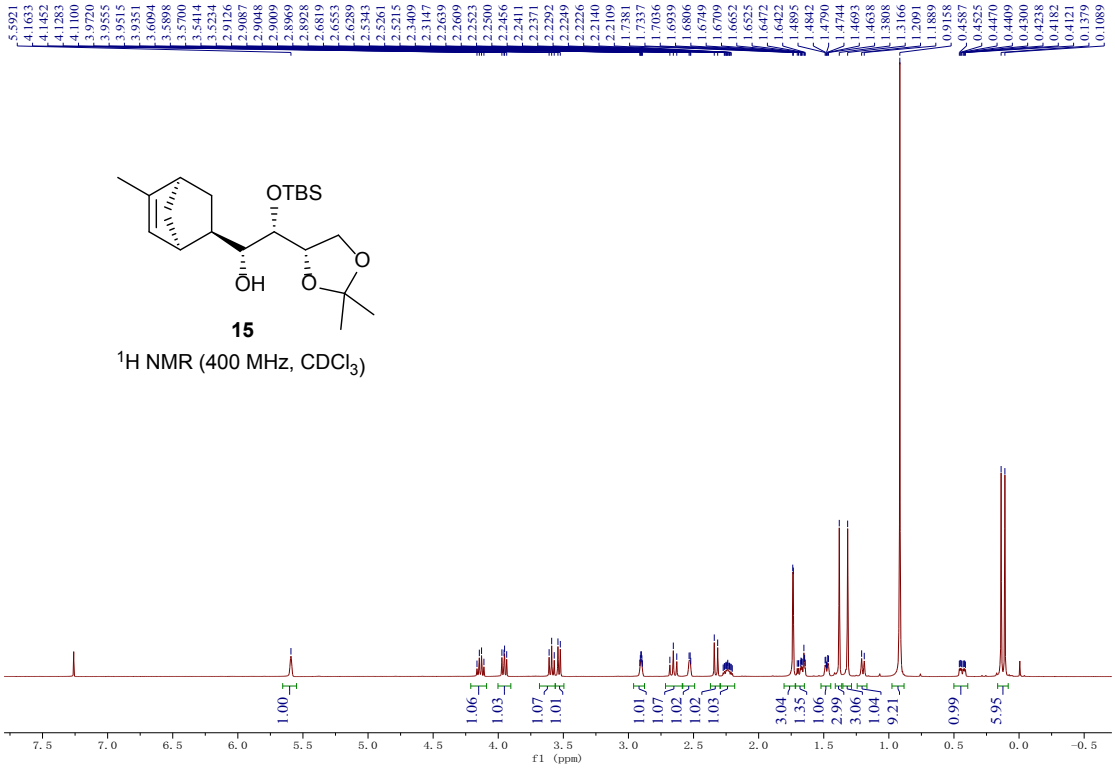
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **11**



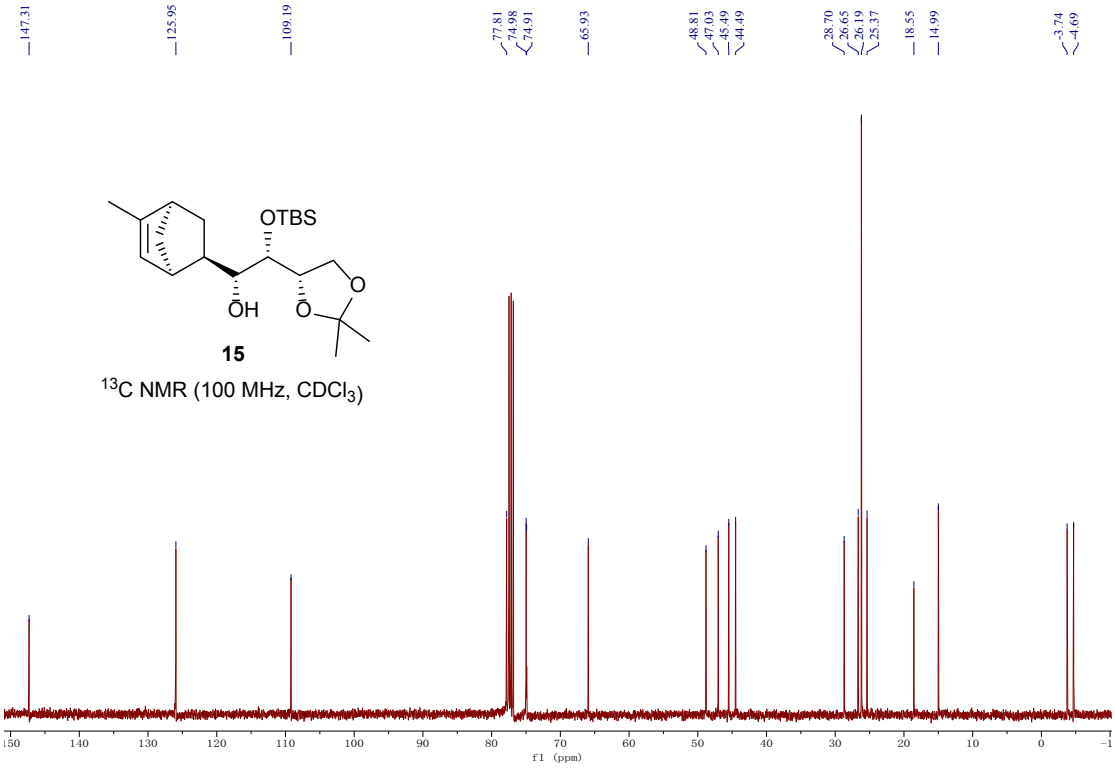
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **11**



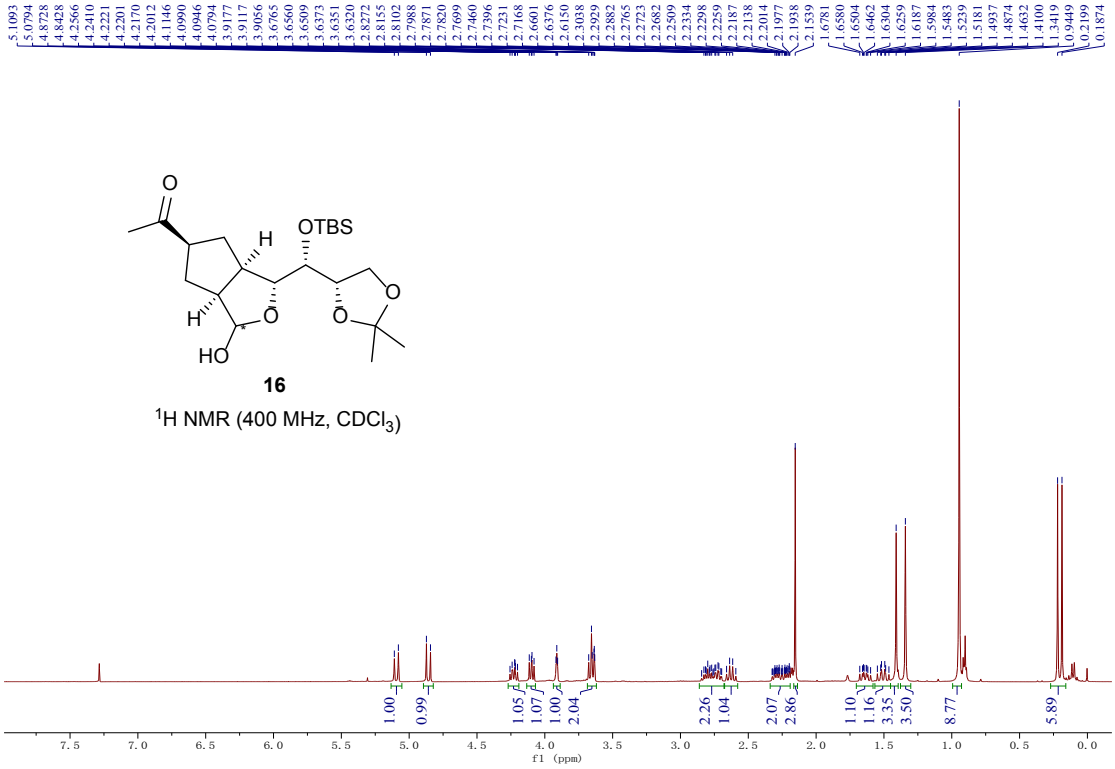
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **15**



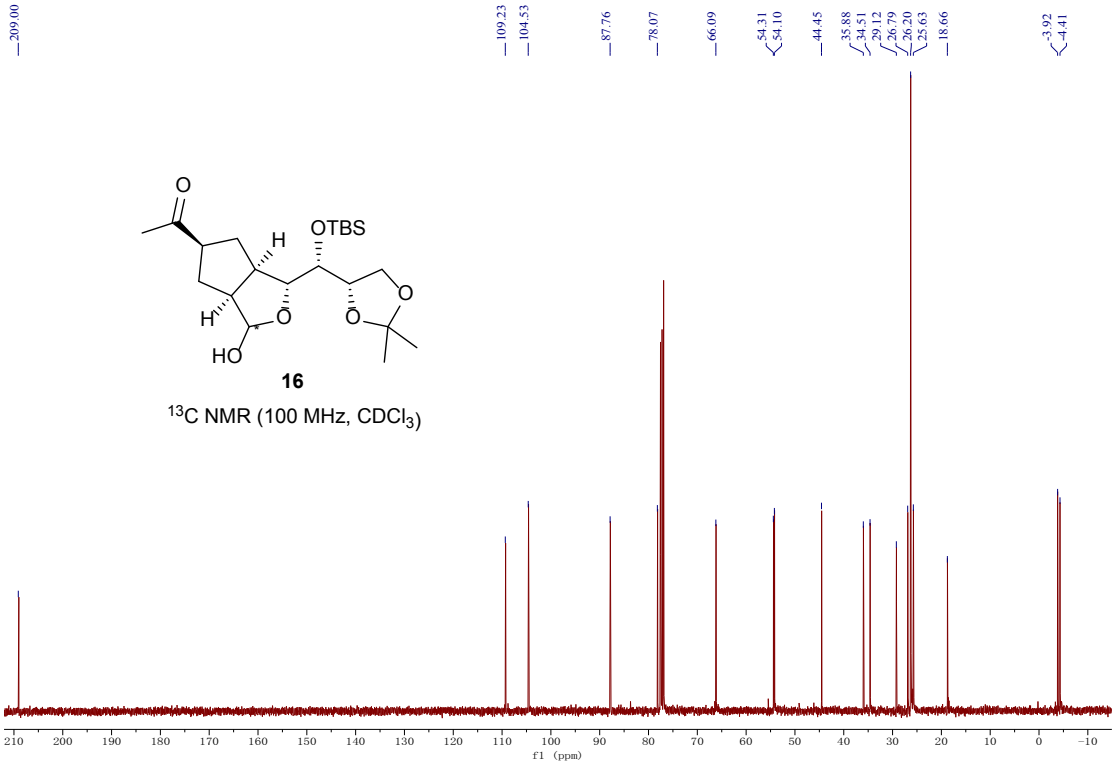
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **15**



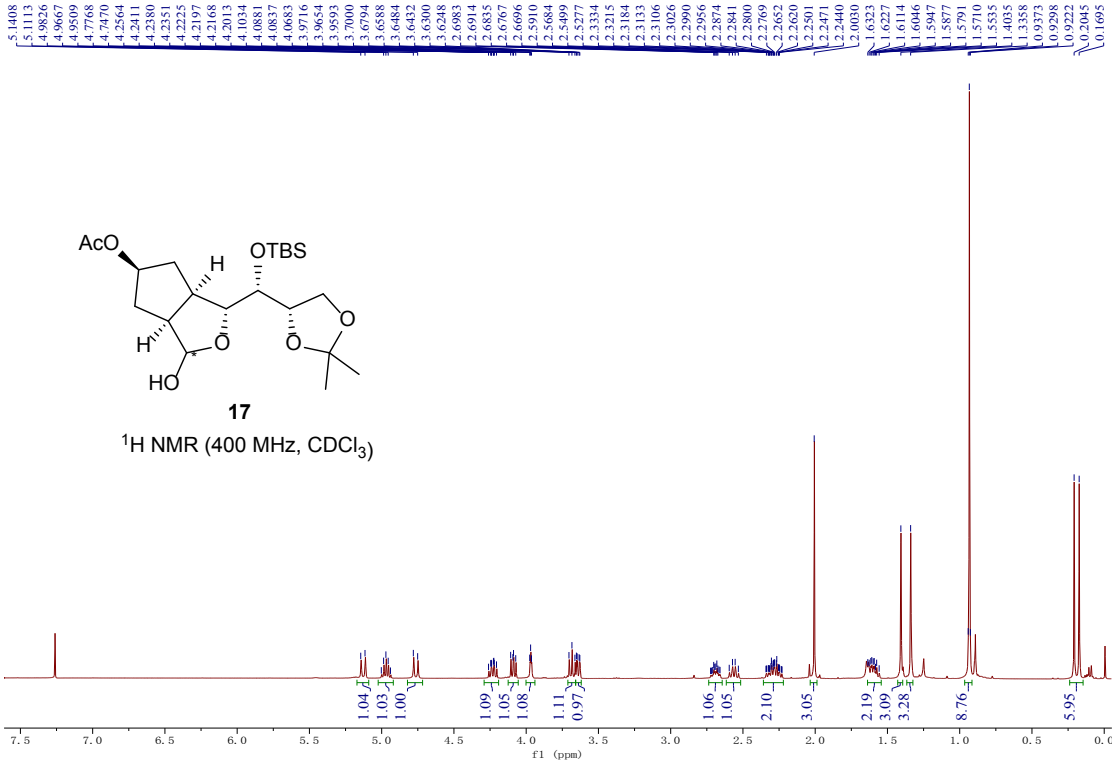
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **16**



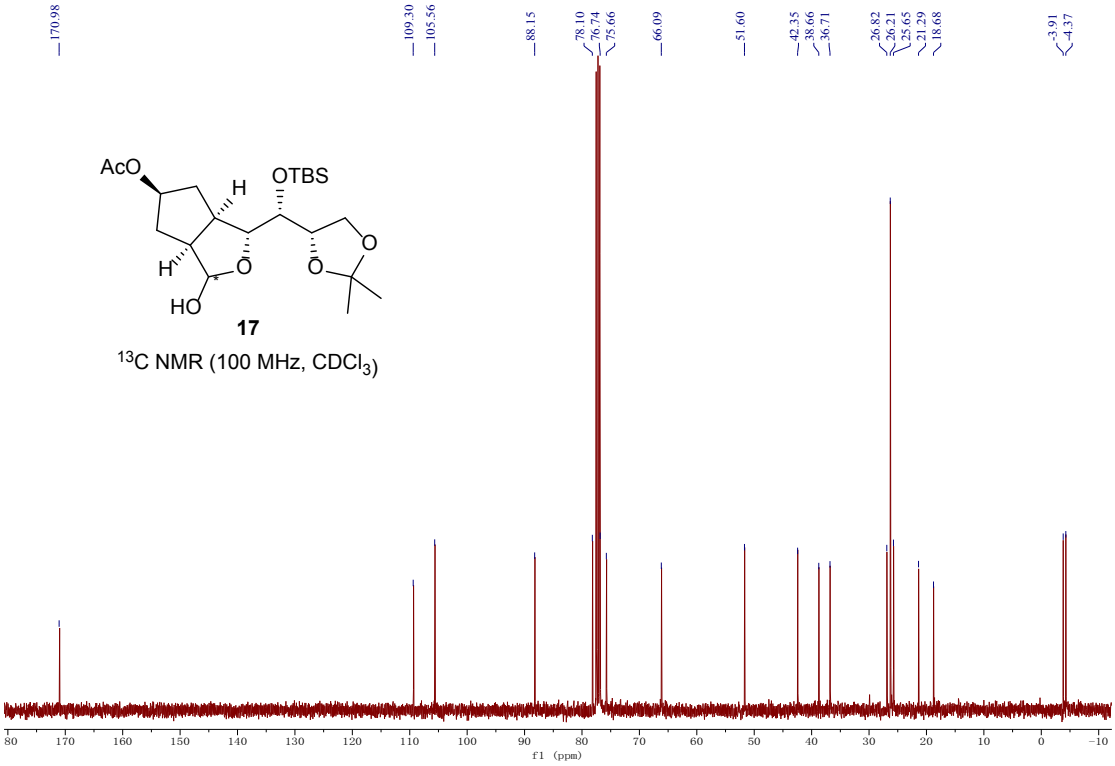
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **16**



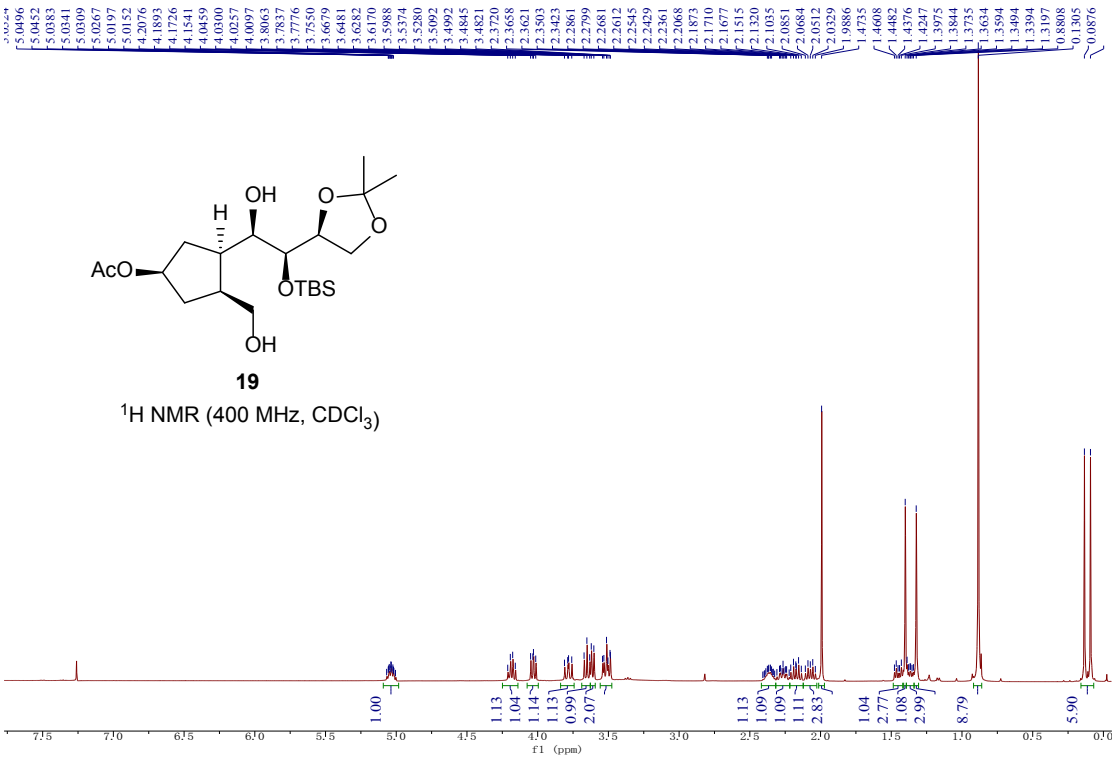
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **17**



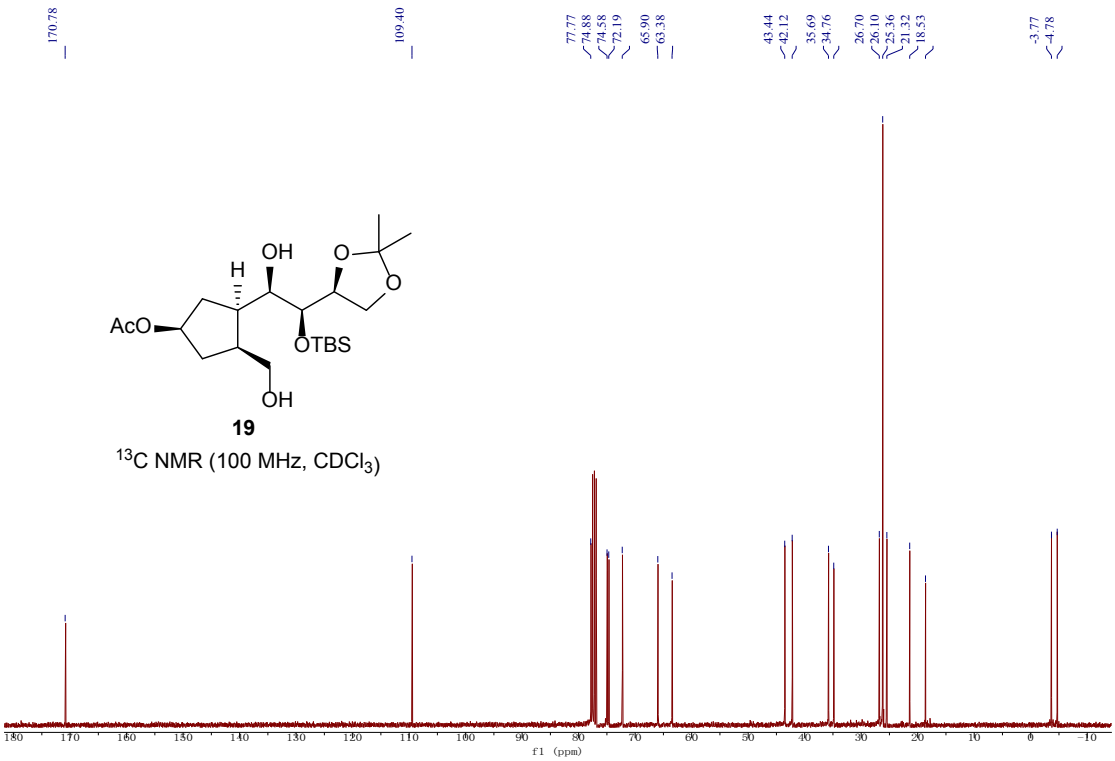
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **17**



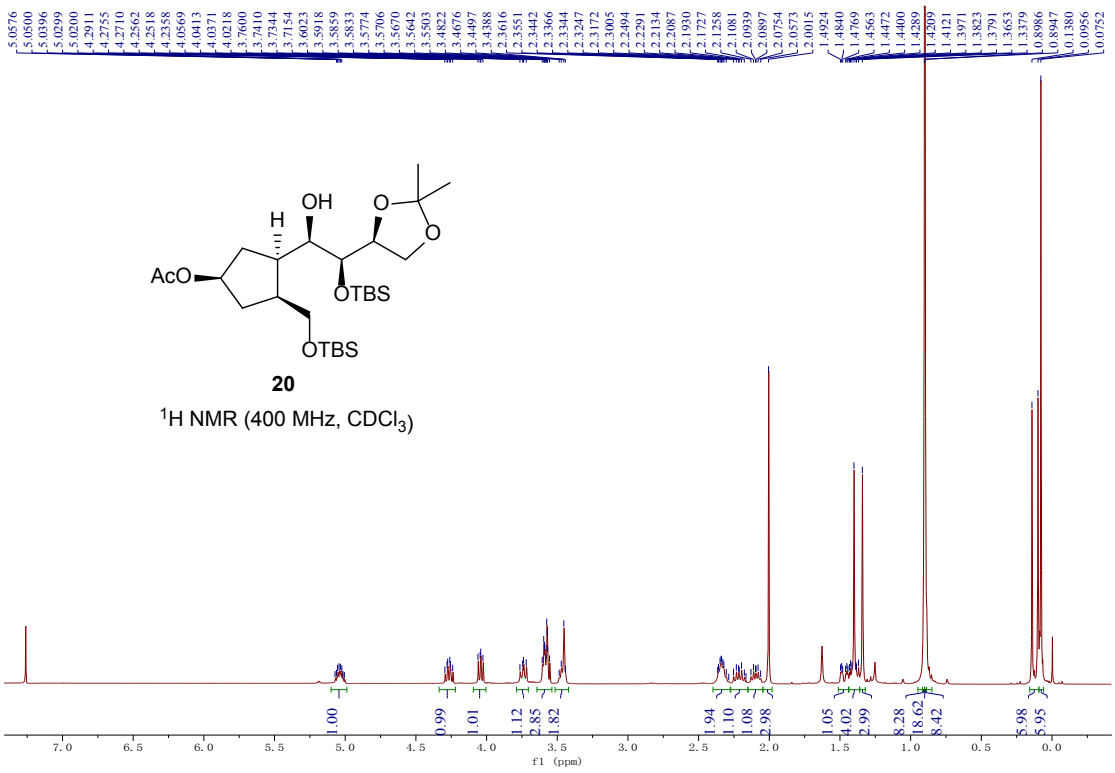
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **19**



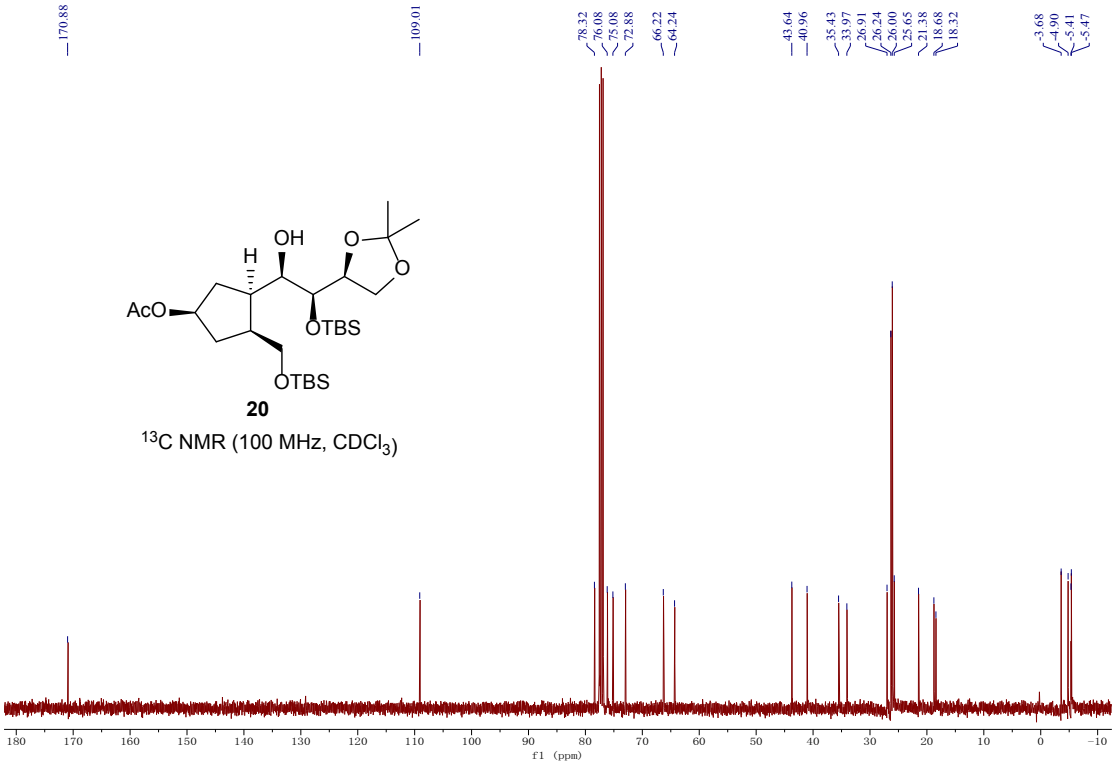
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **19**



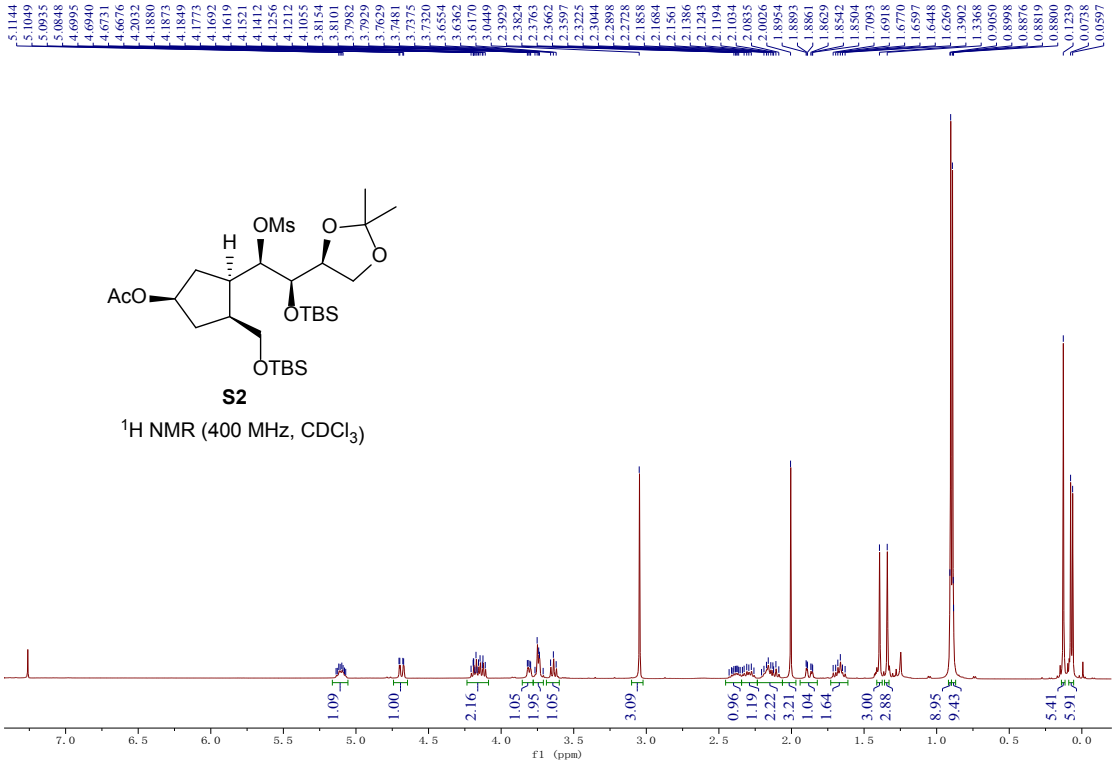
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **20**



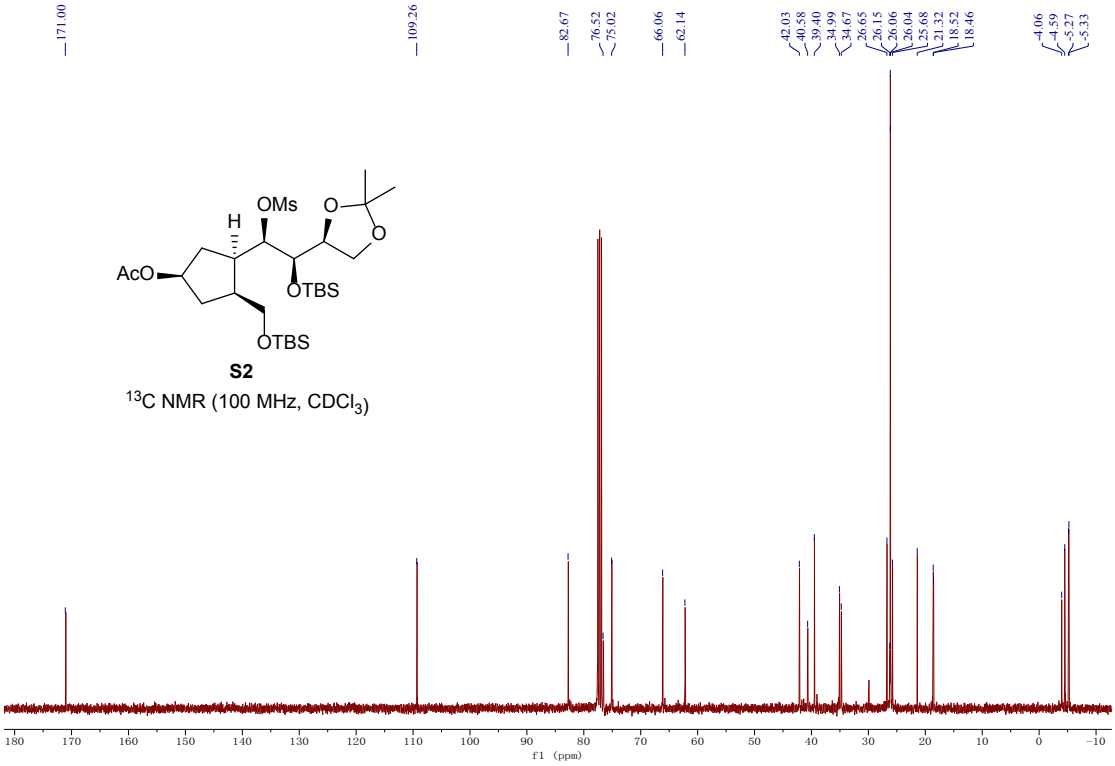
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **20**



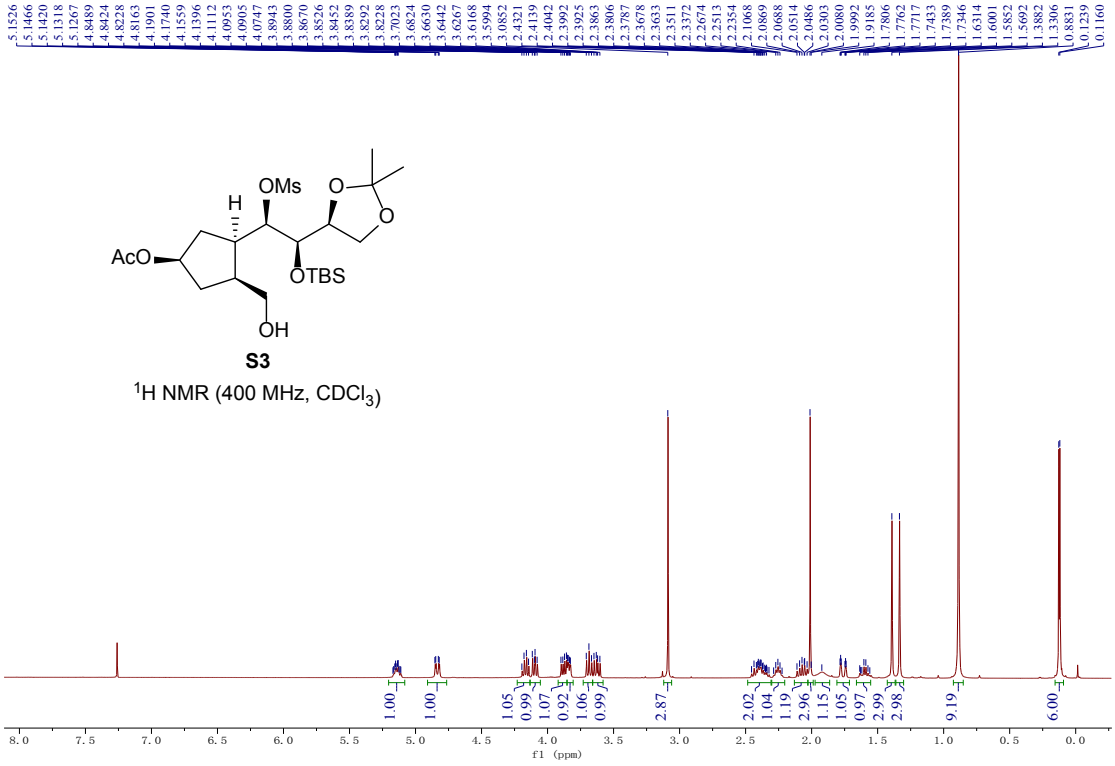
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S2**



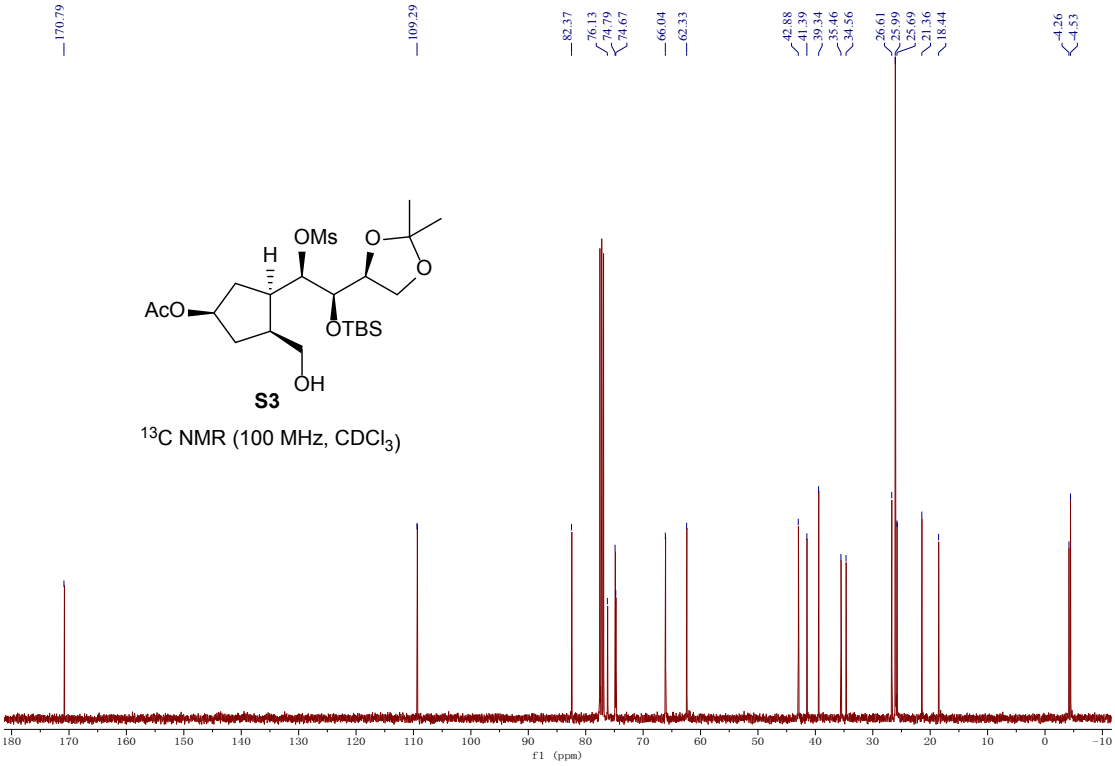
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S2**



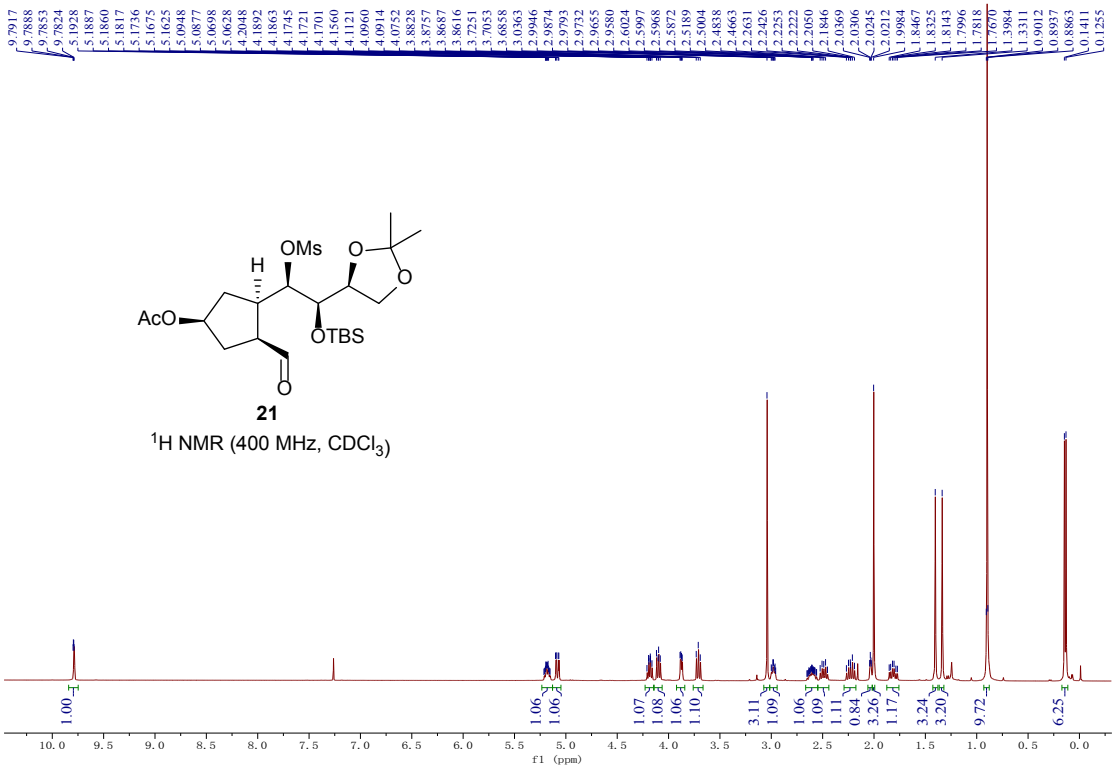
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S3**



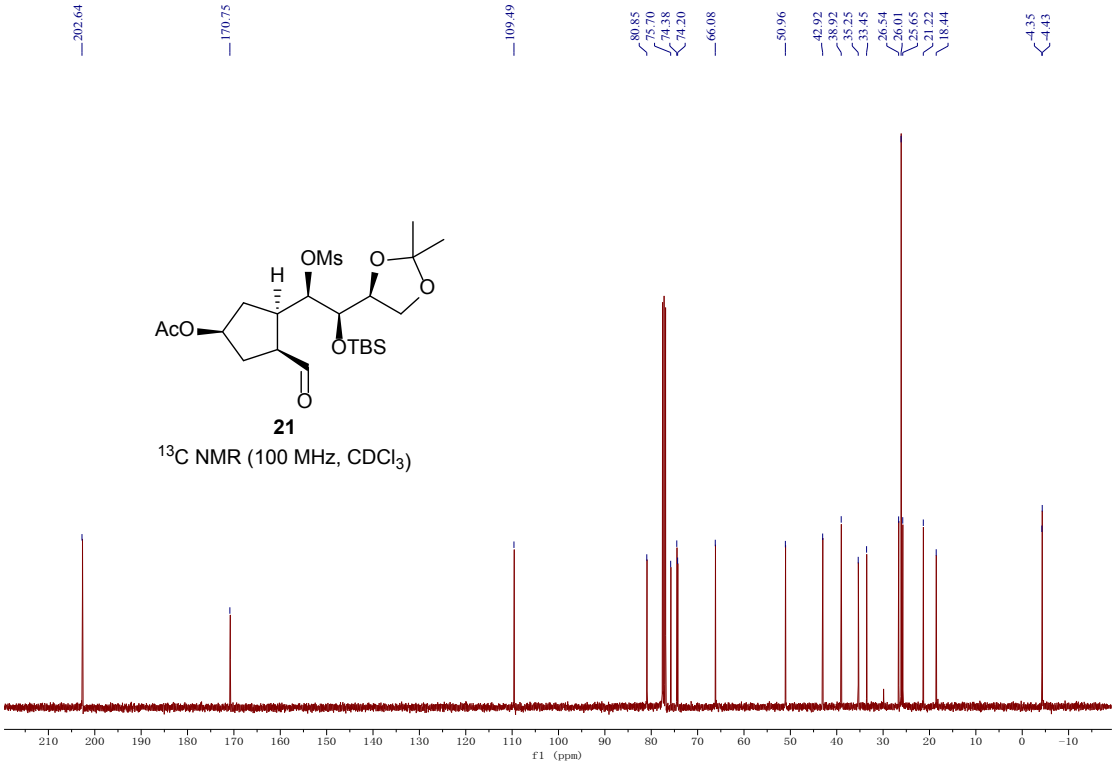
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S3**



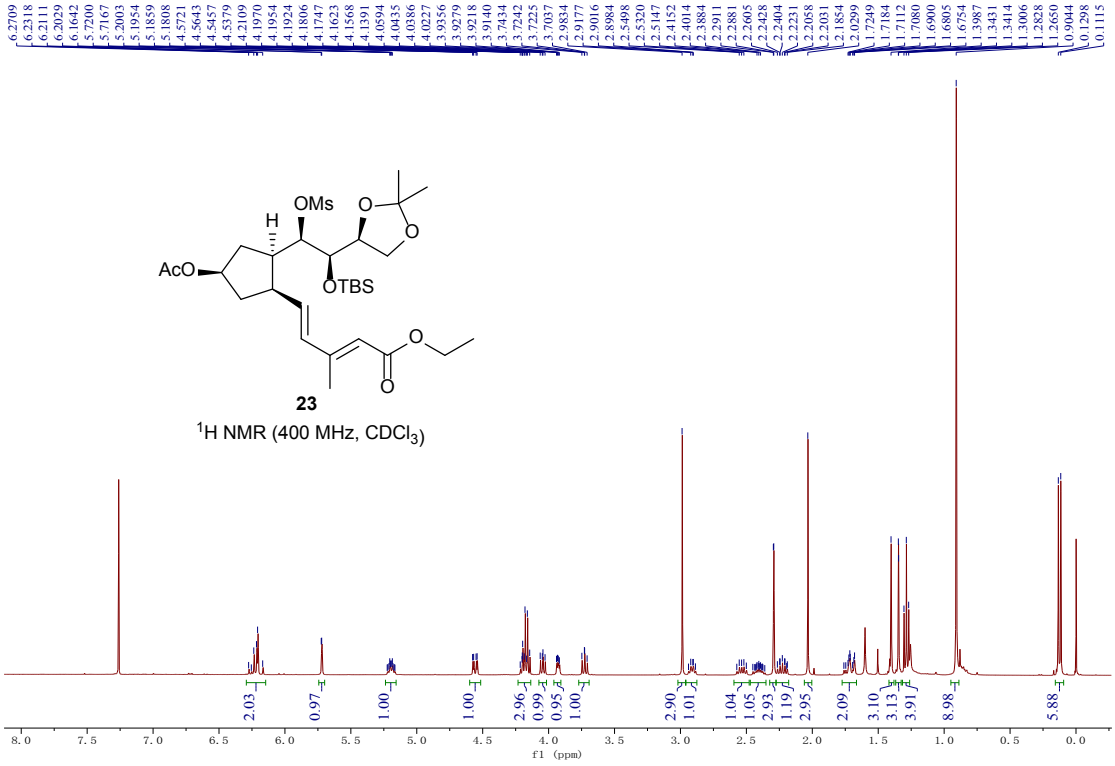
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **21**



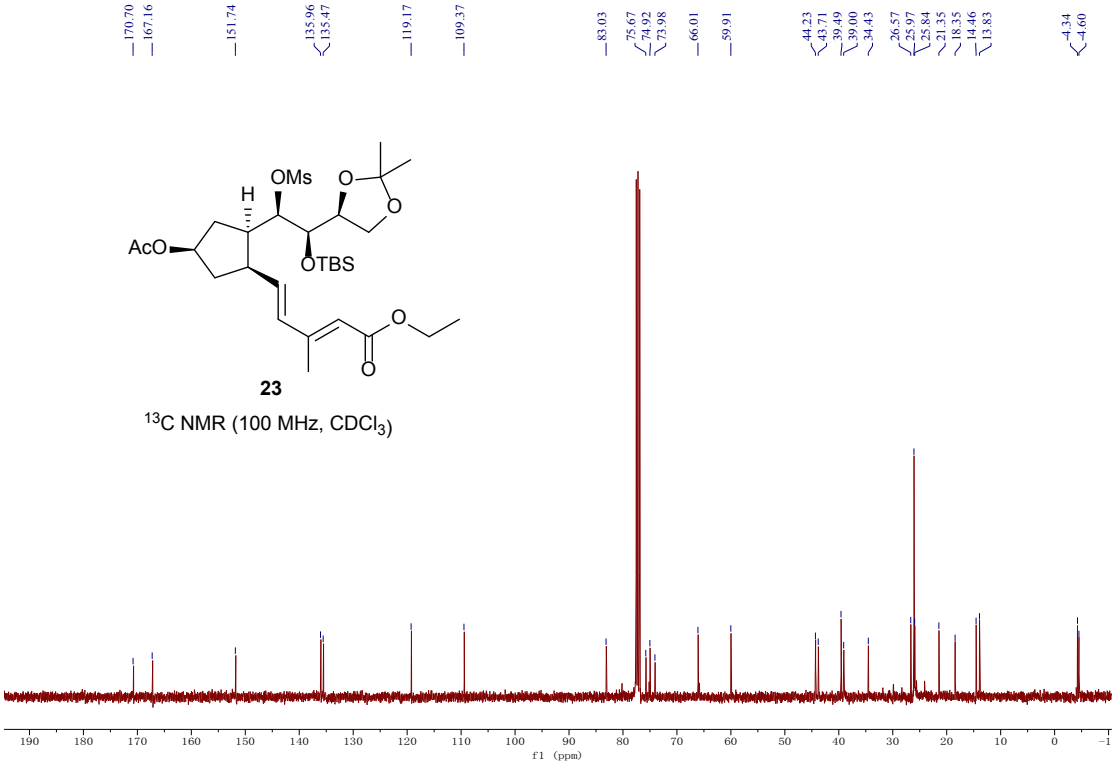
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **21**



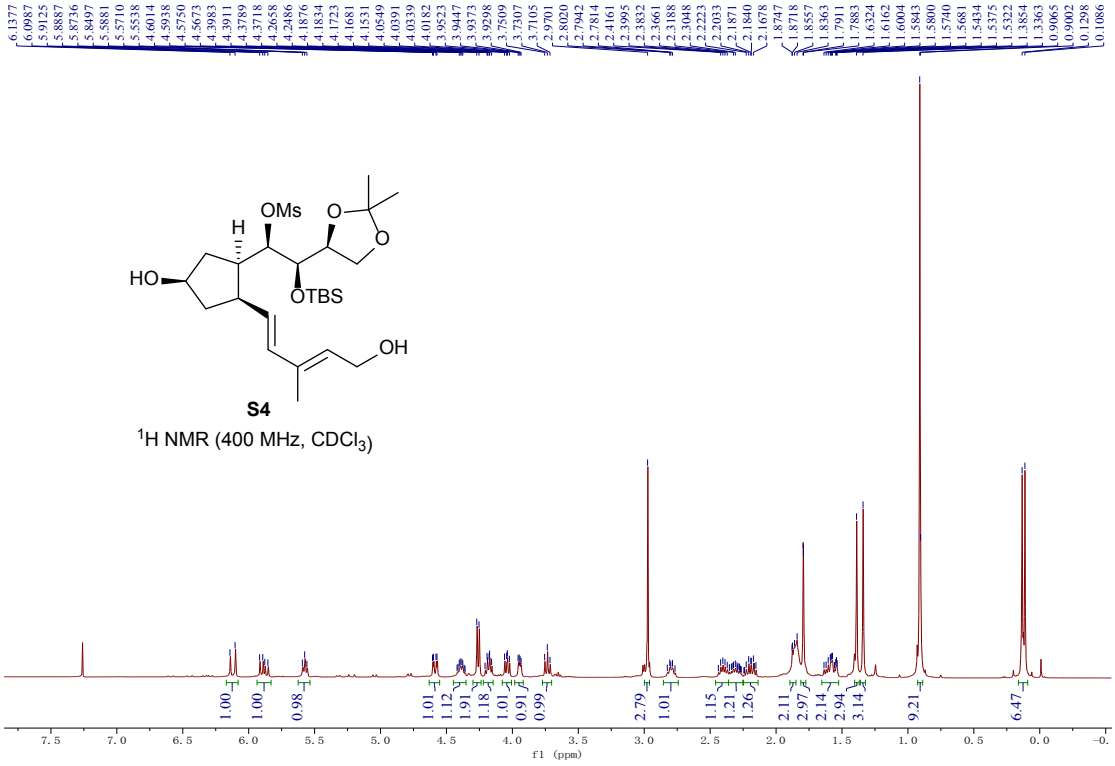
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **23**



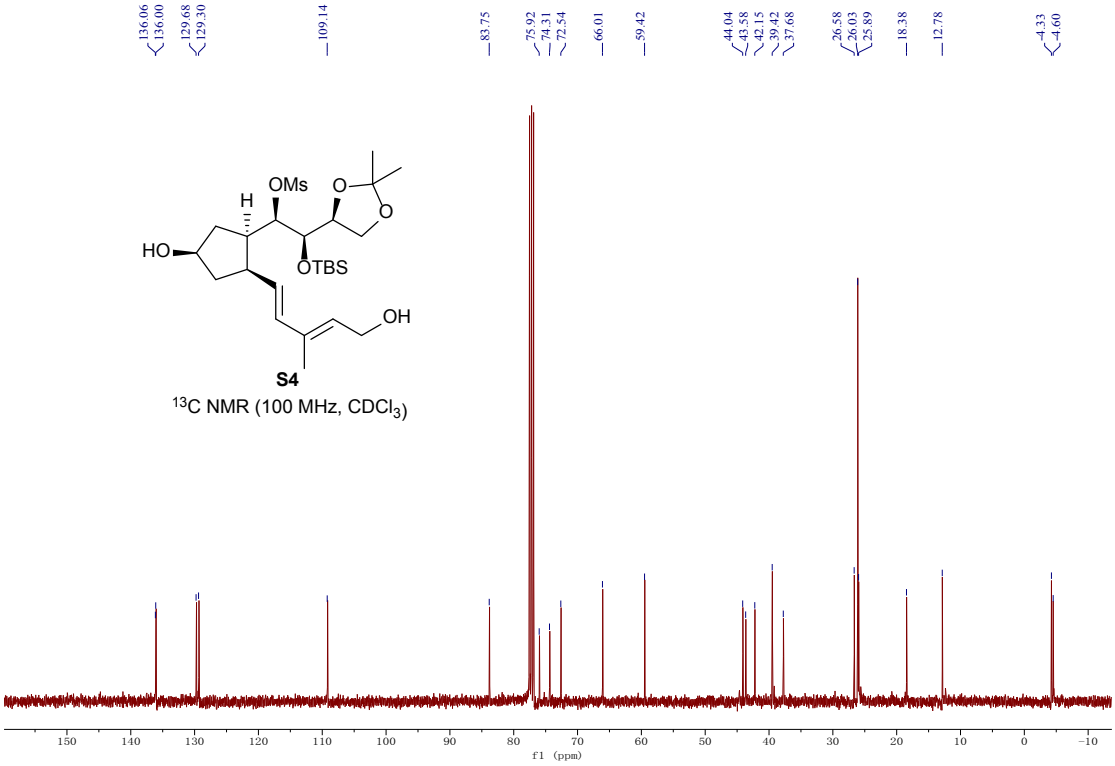
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **23**



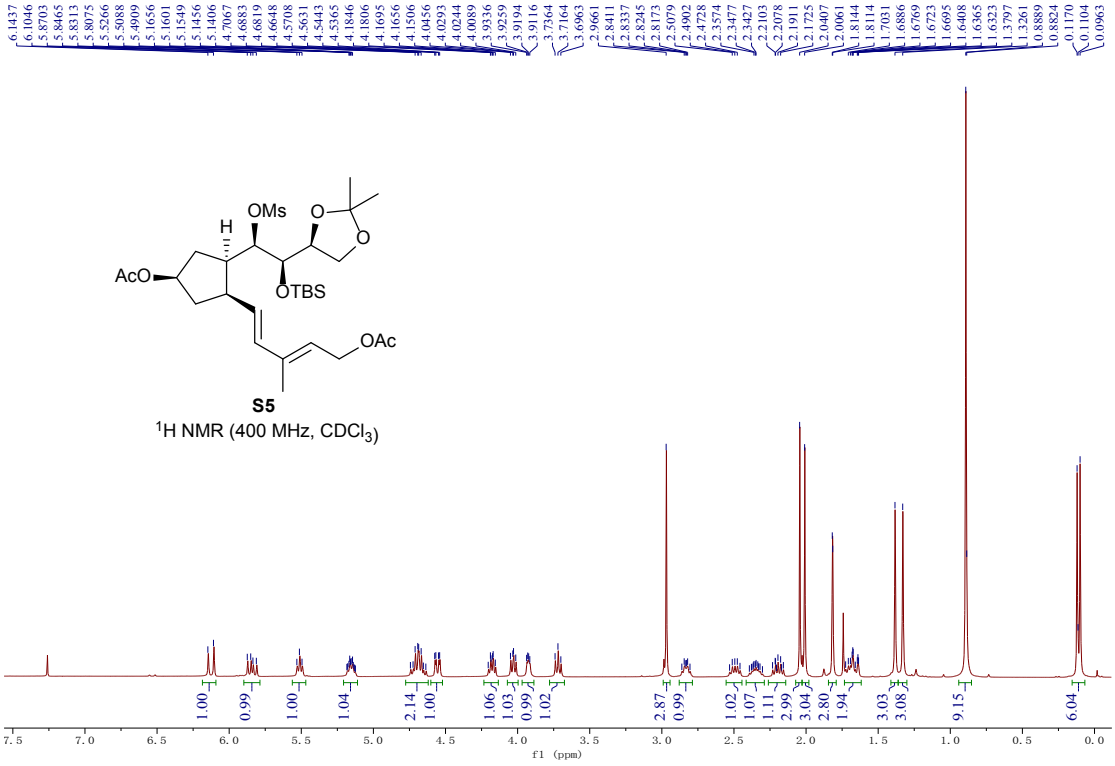
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S4**



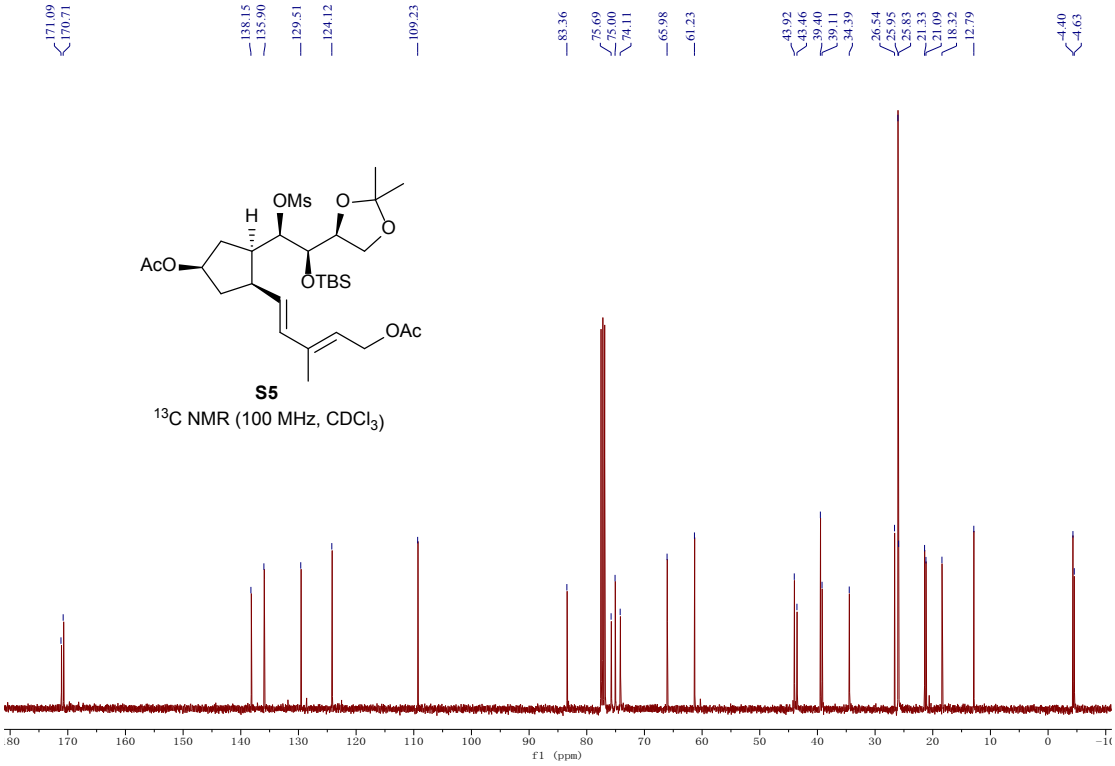
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S4**



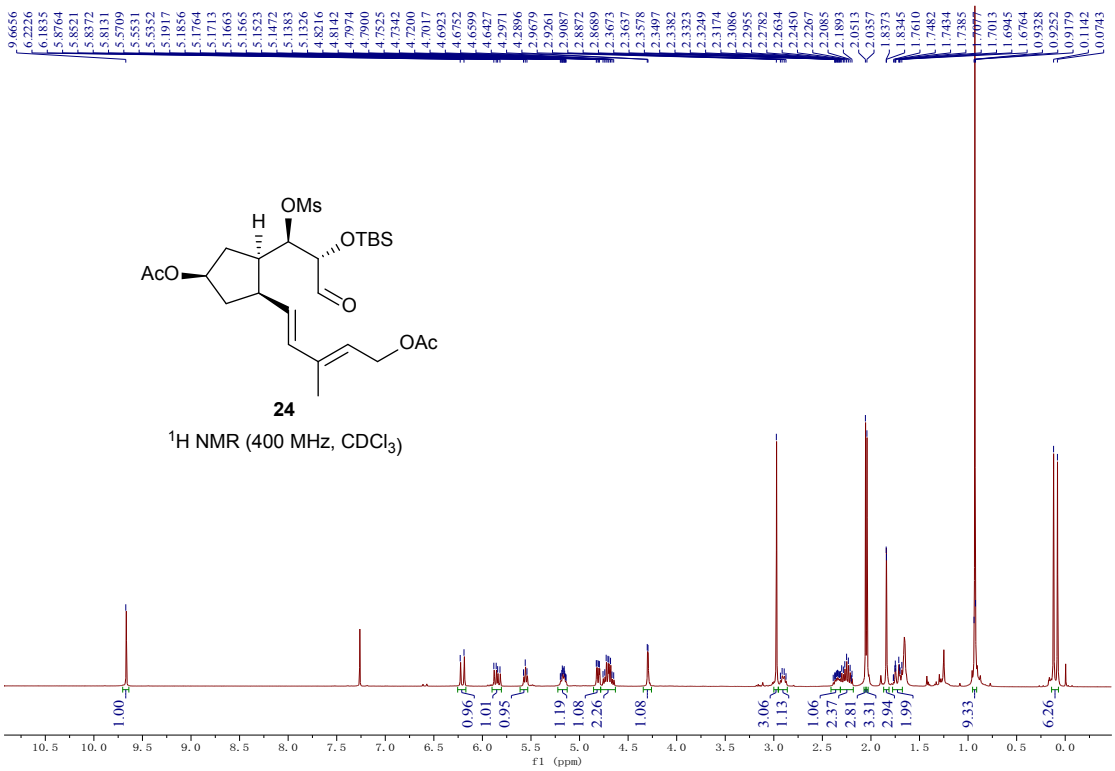
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S5**



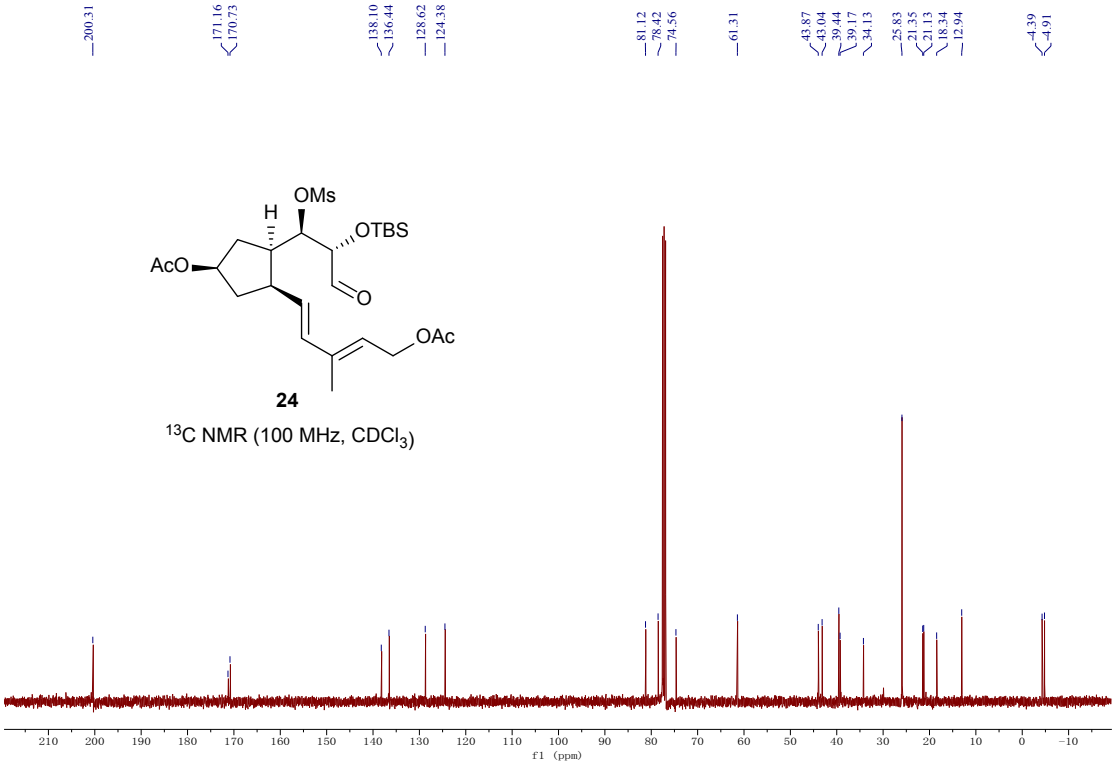
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S5**



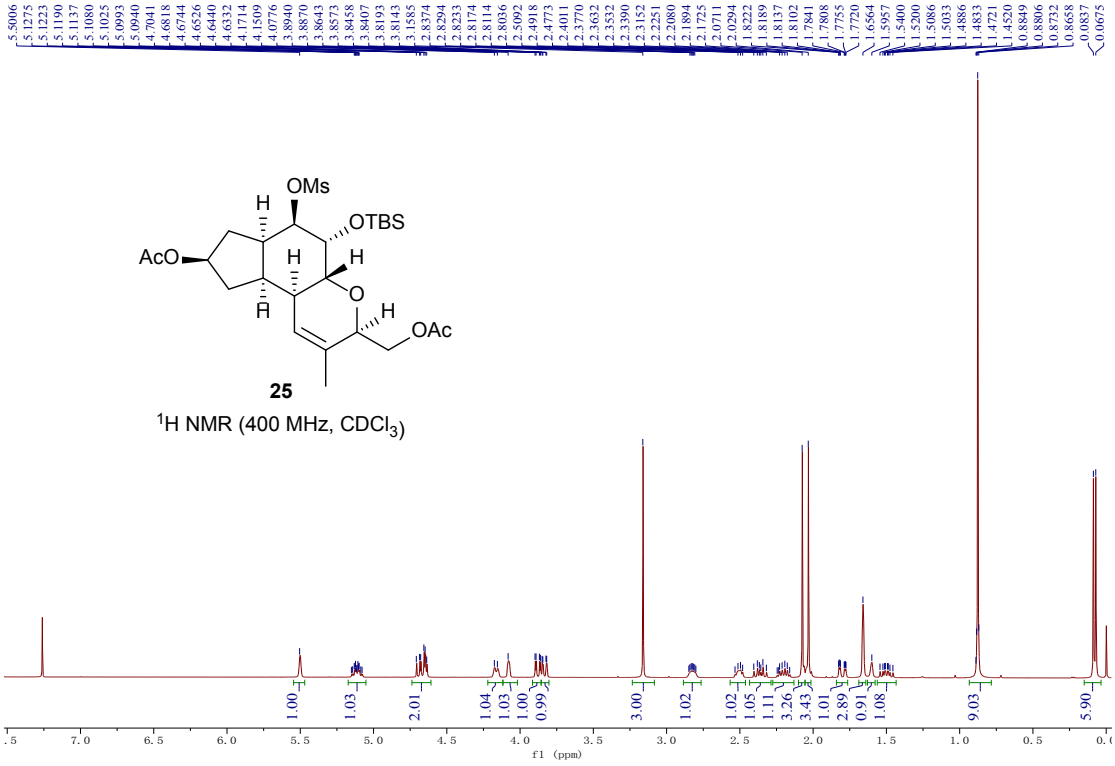
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **24**



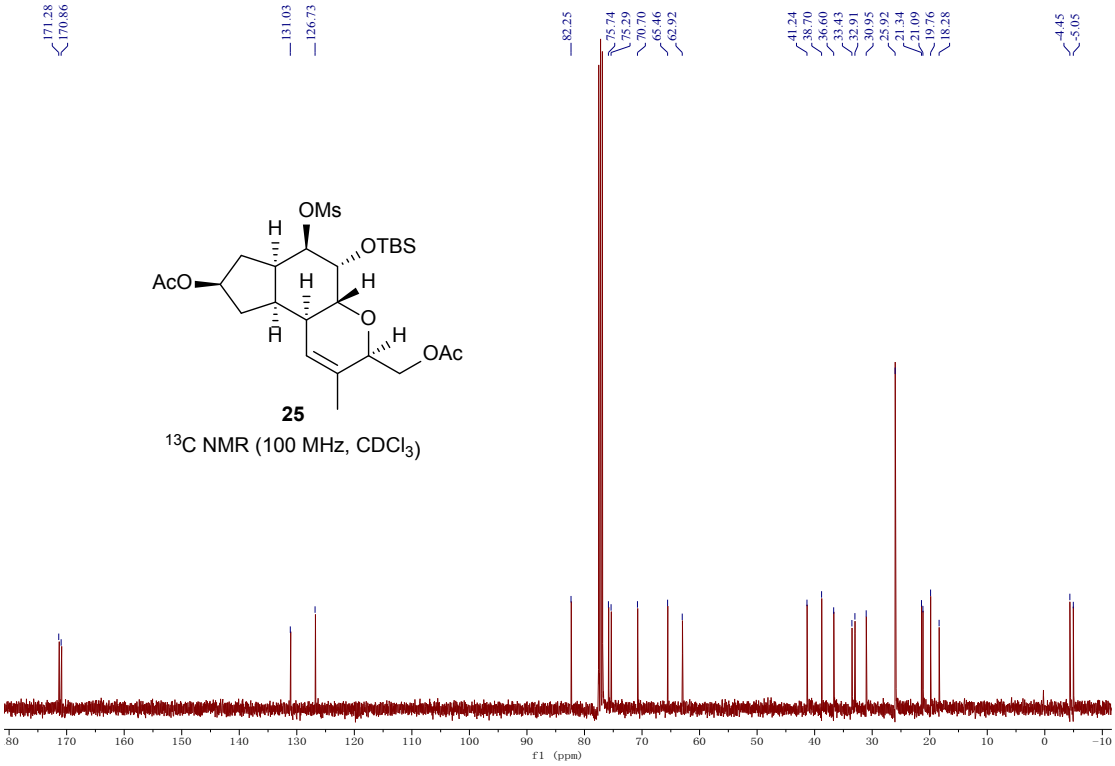
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **24**



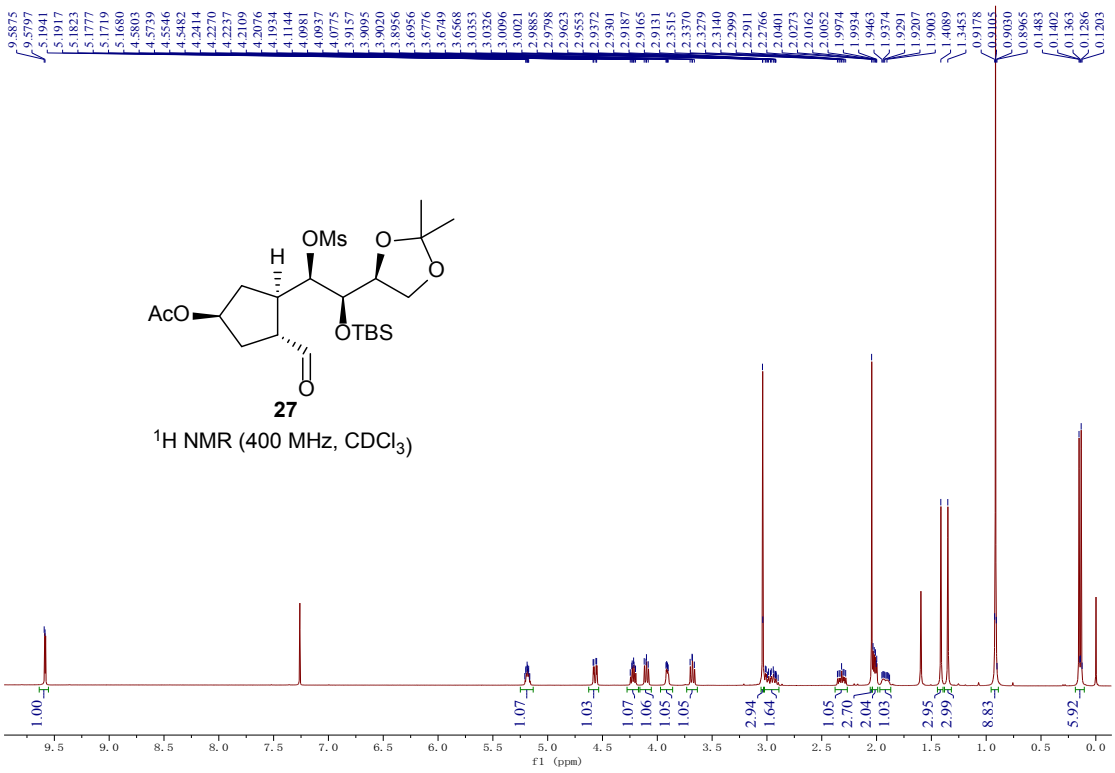
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **25**



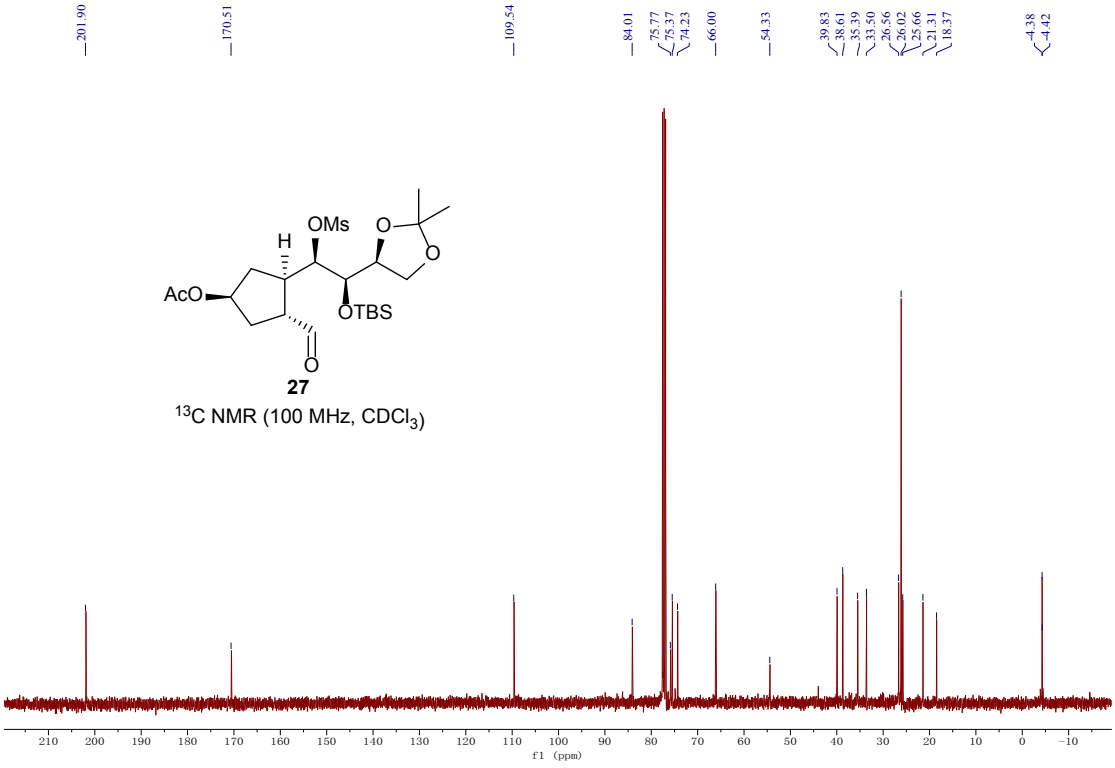
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **25**



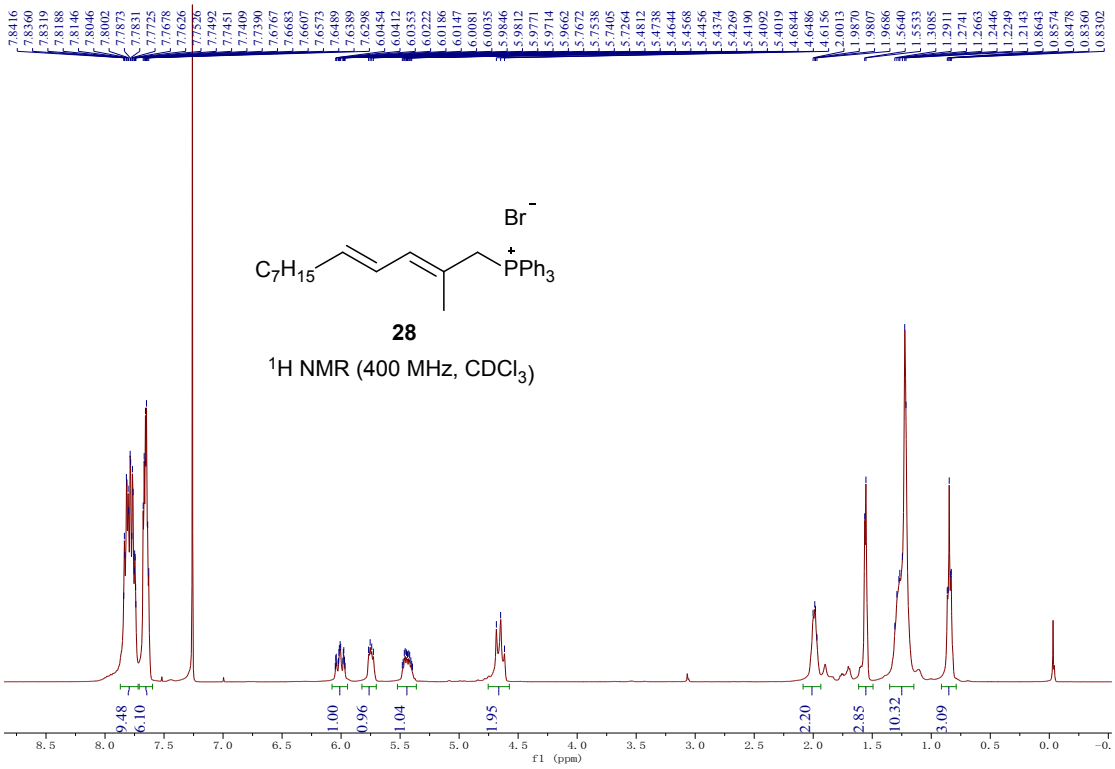
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **27**



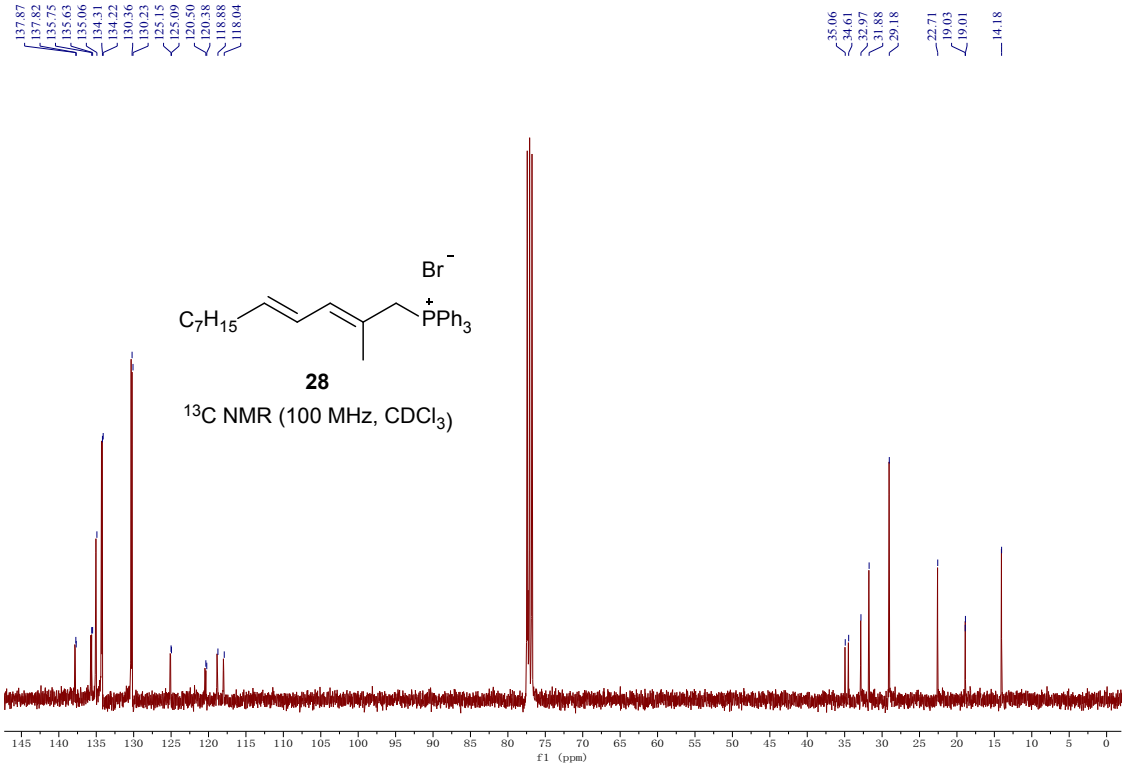
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **27**



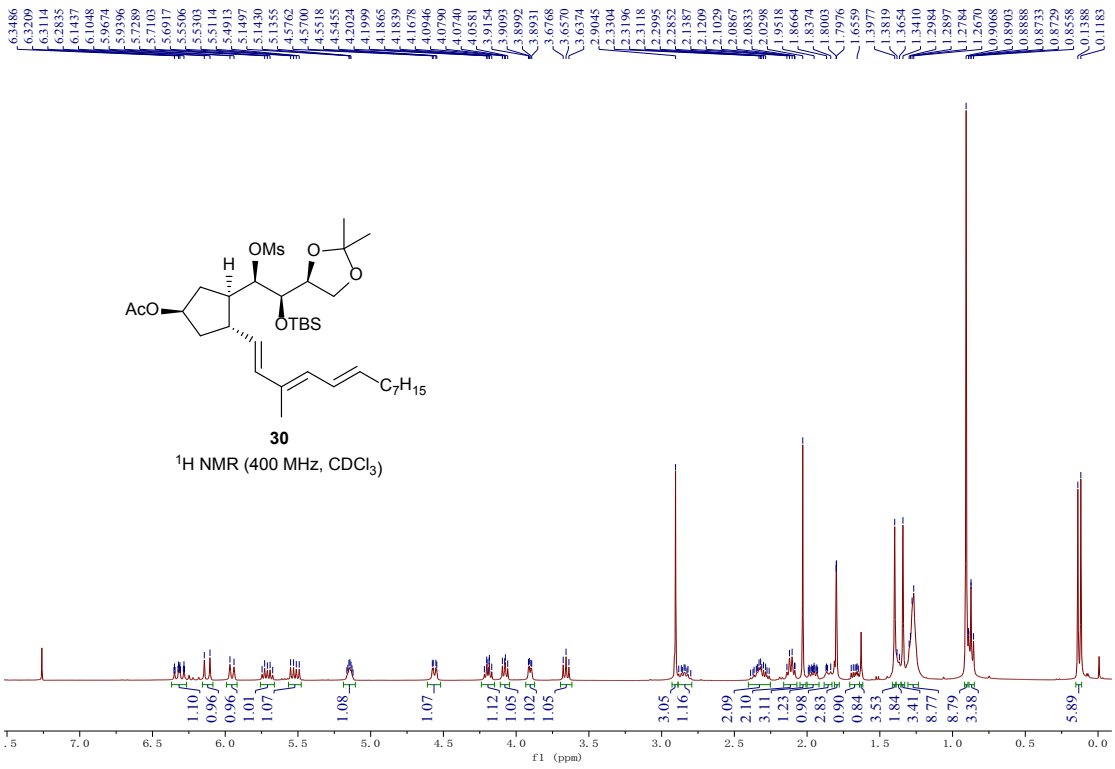
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **28**



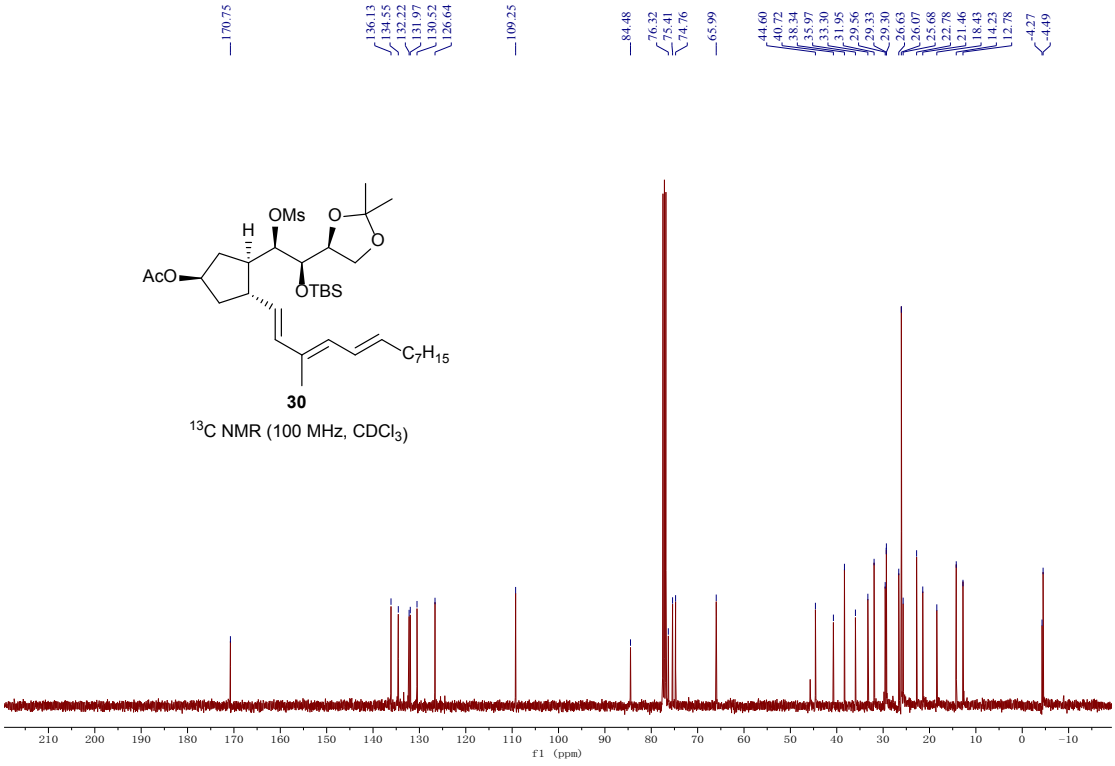
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **28**



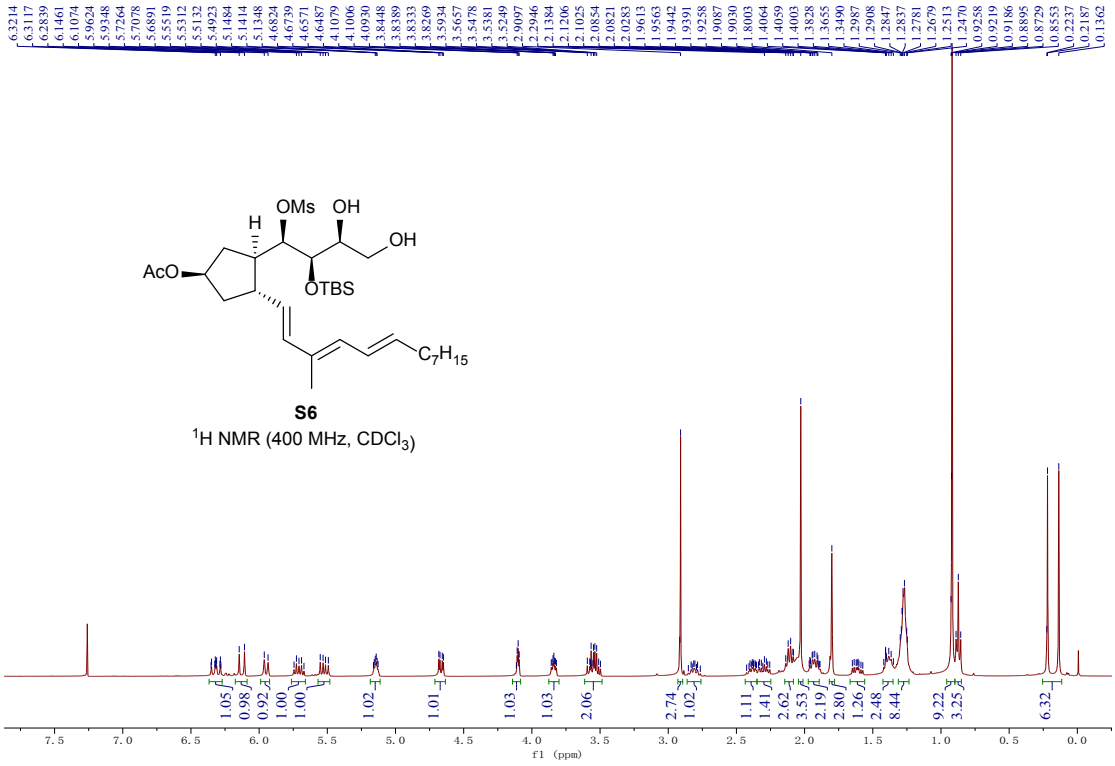
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **30**



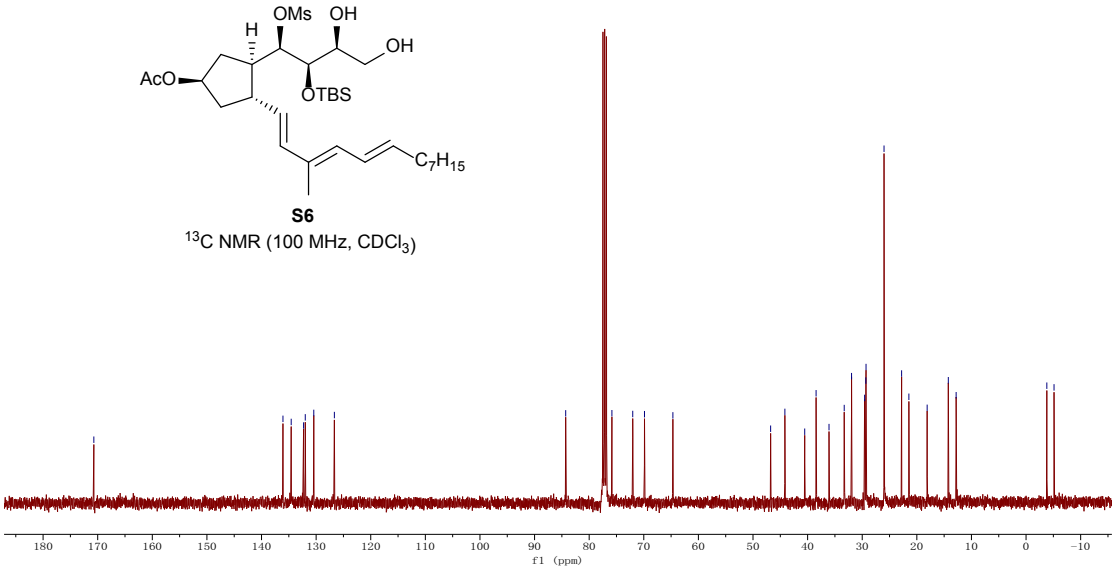
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **30**



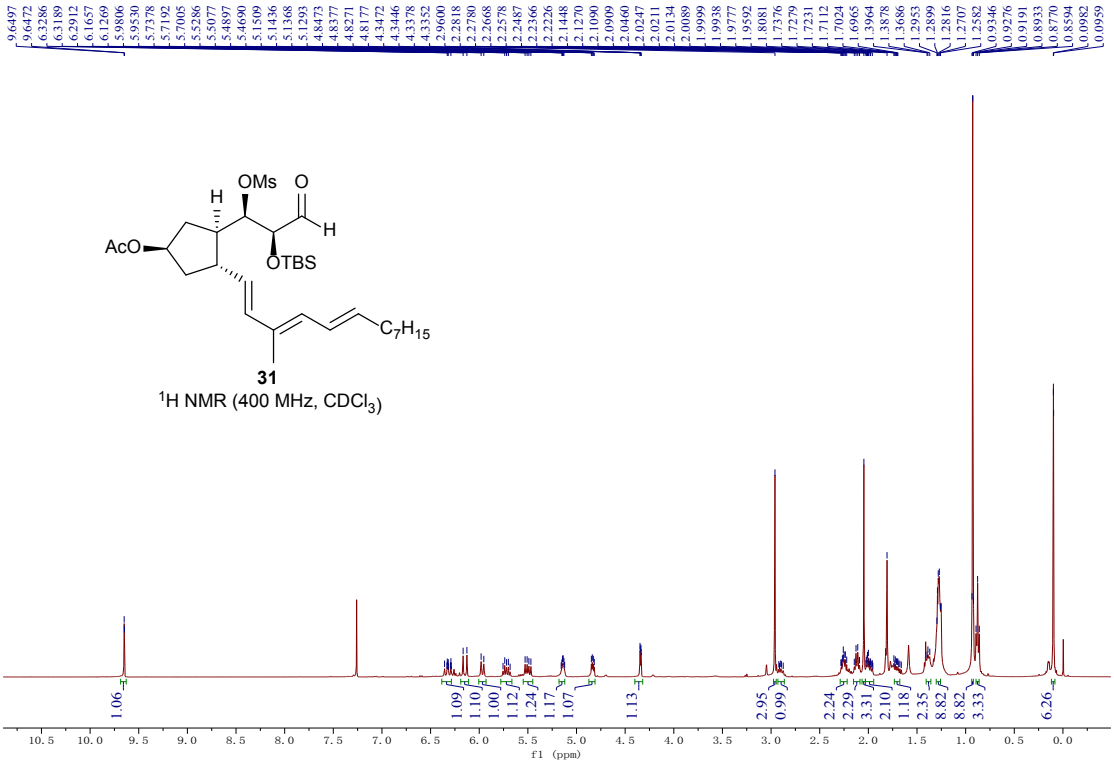
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S6**



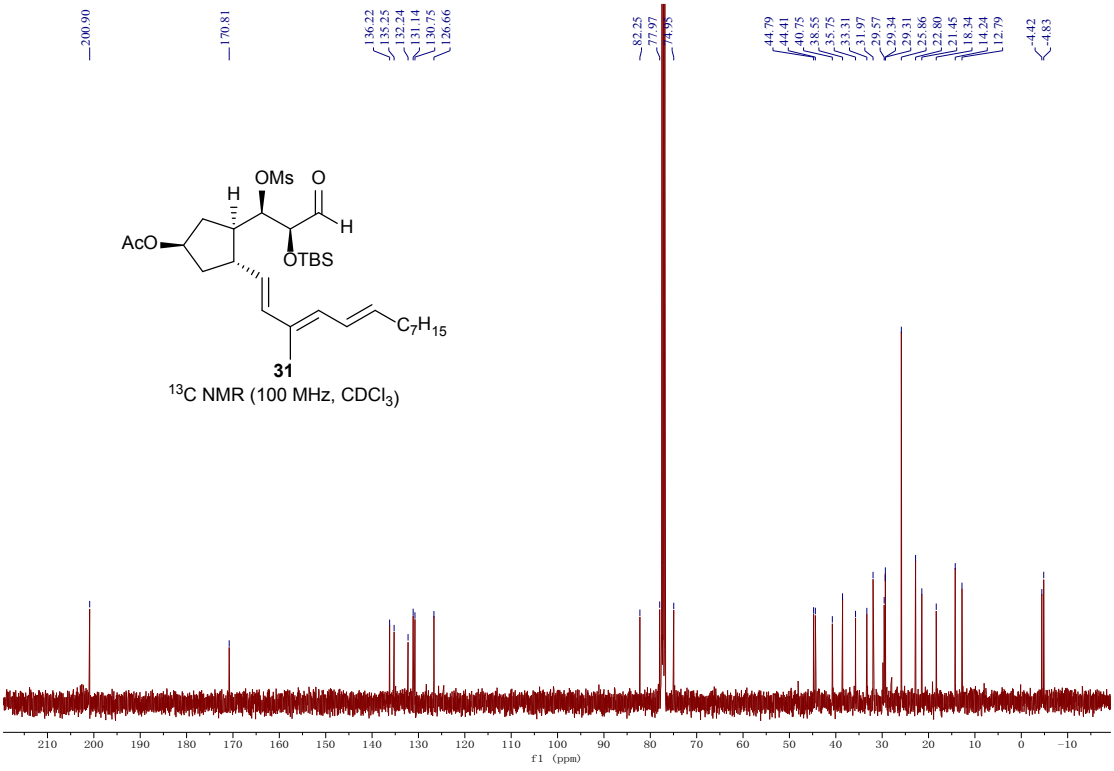
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S6**



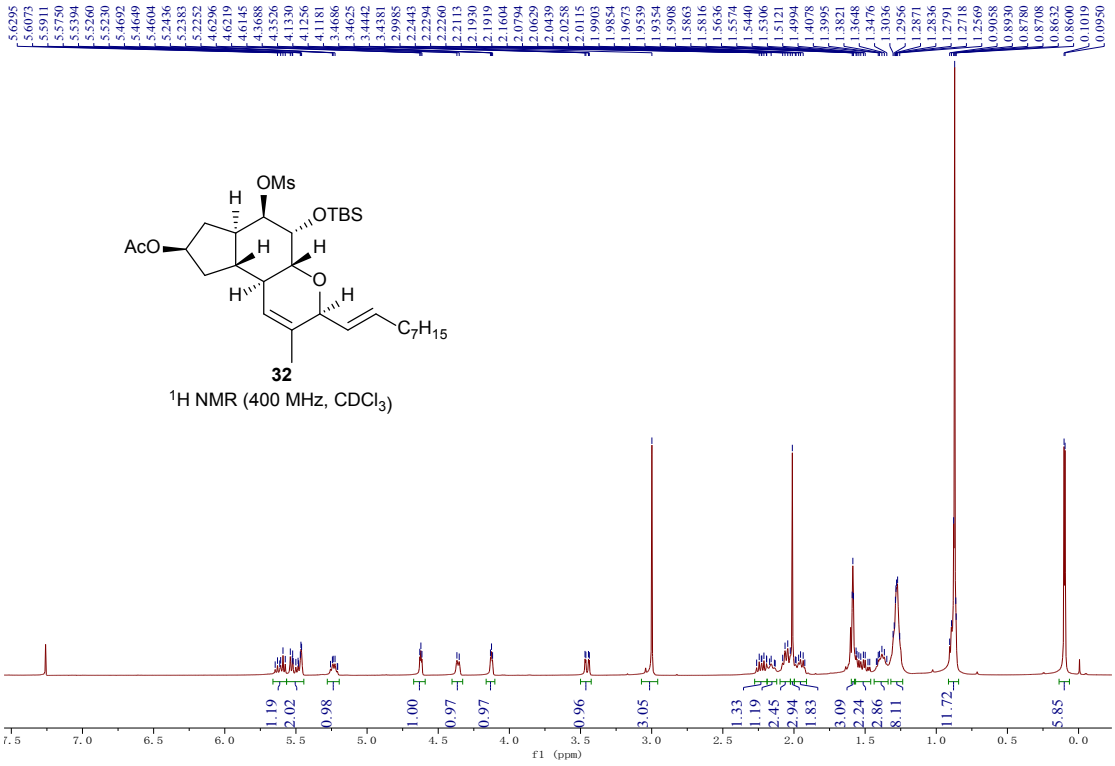
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **31**



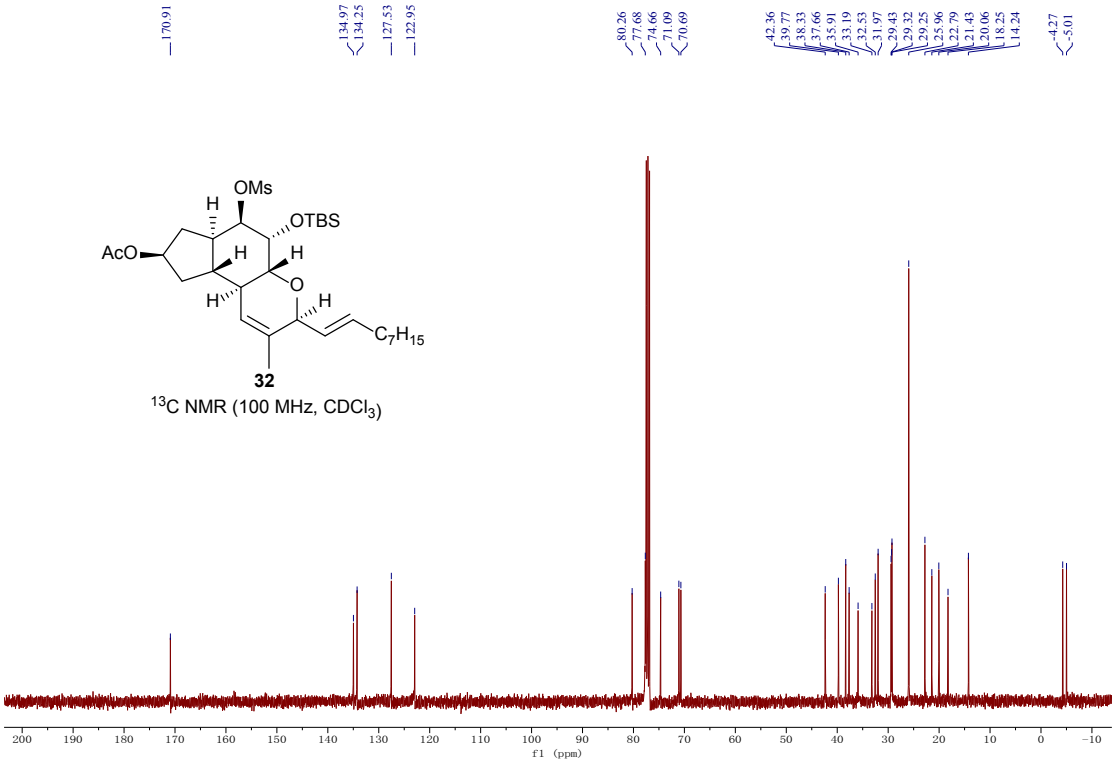
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **31**



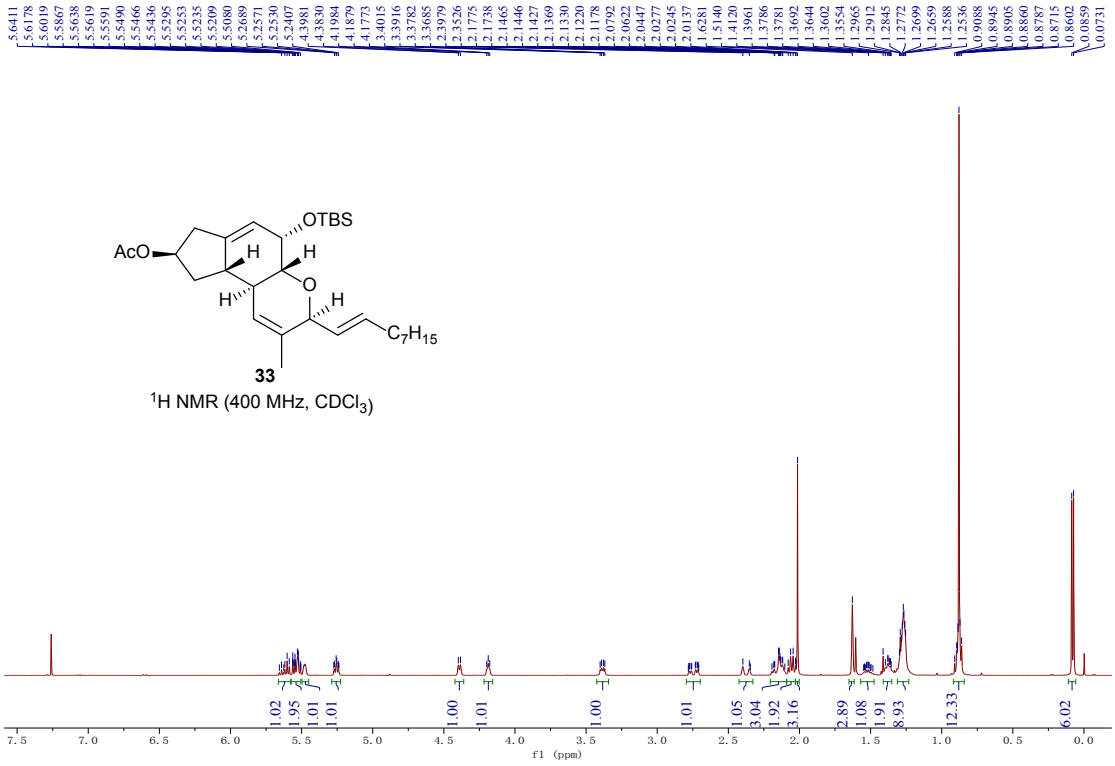
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **32**



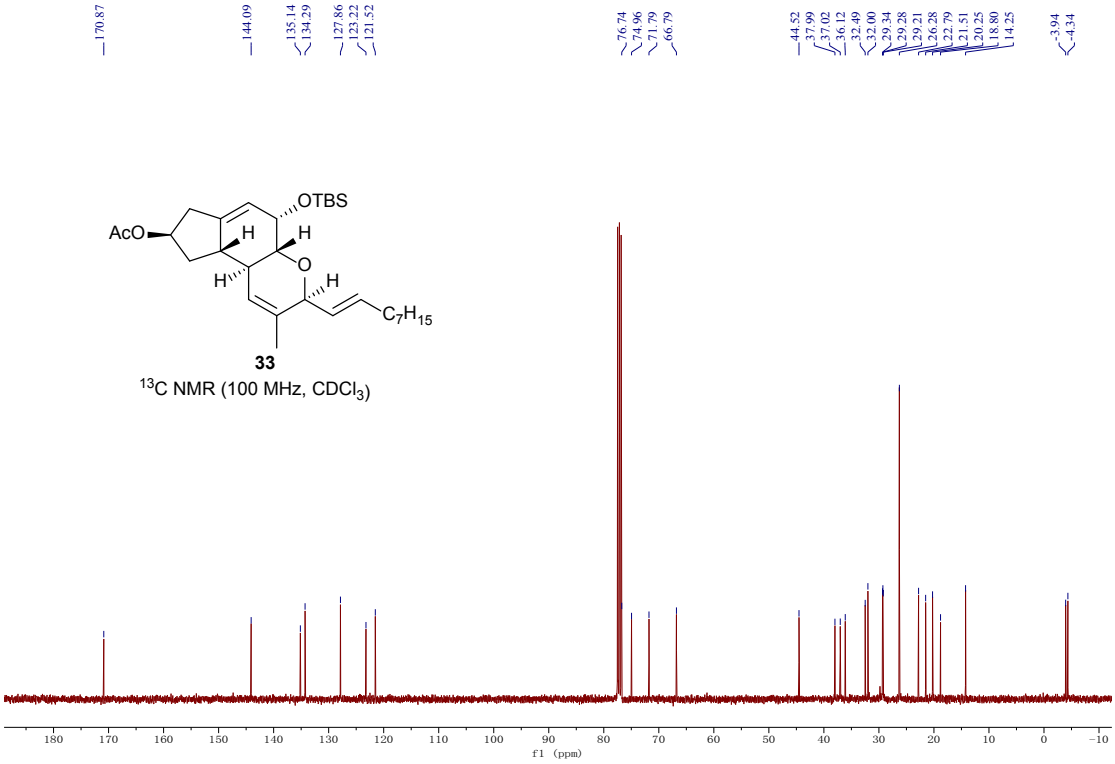
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **32**



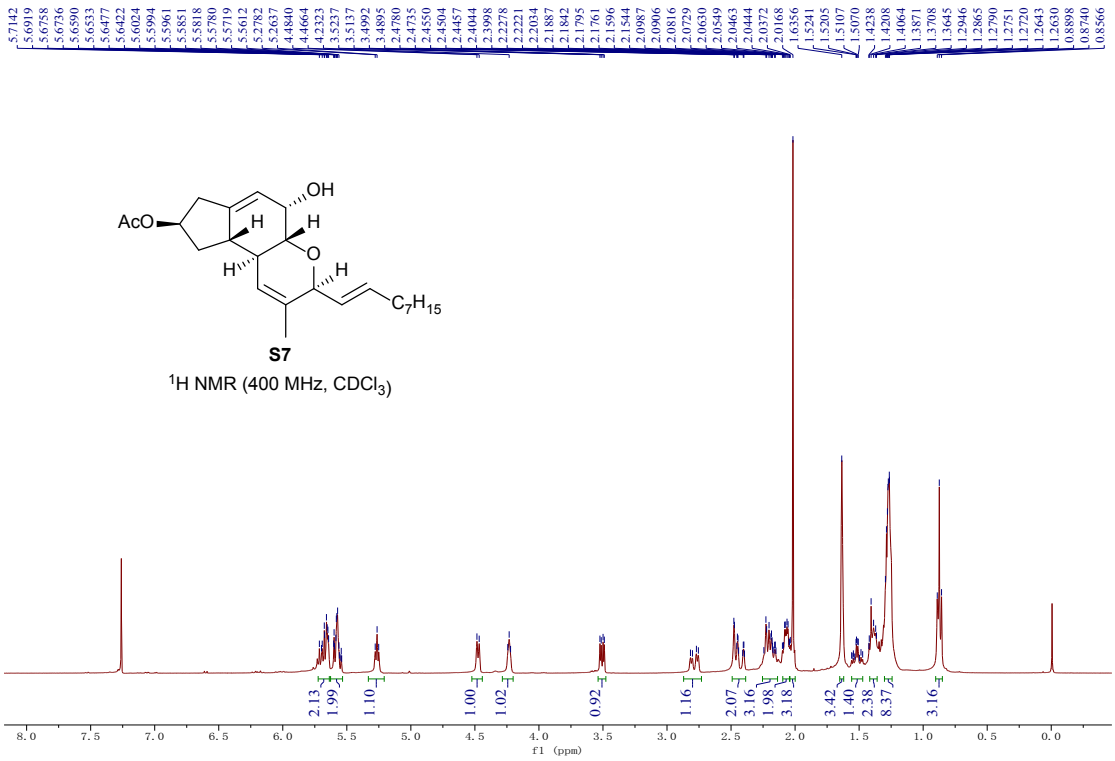
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **33**



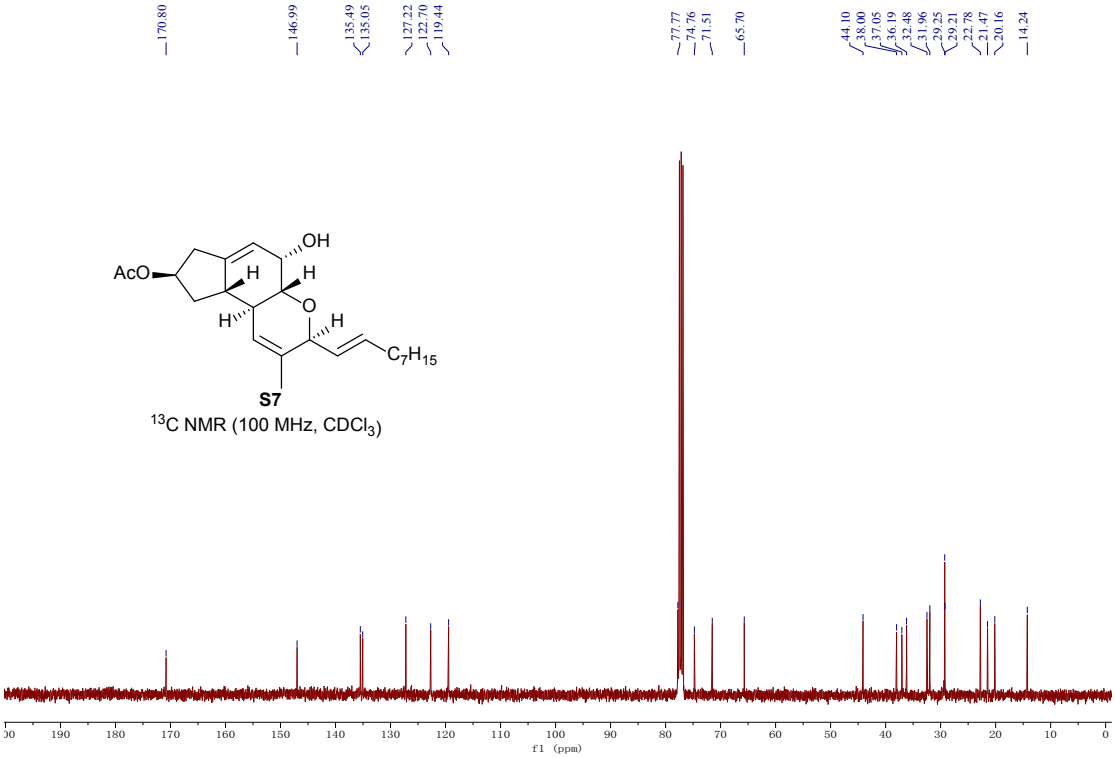
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **33**



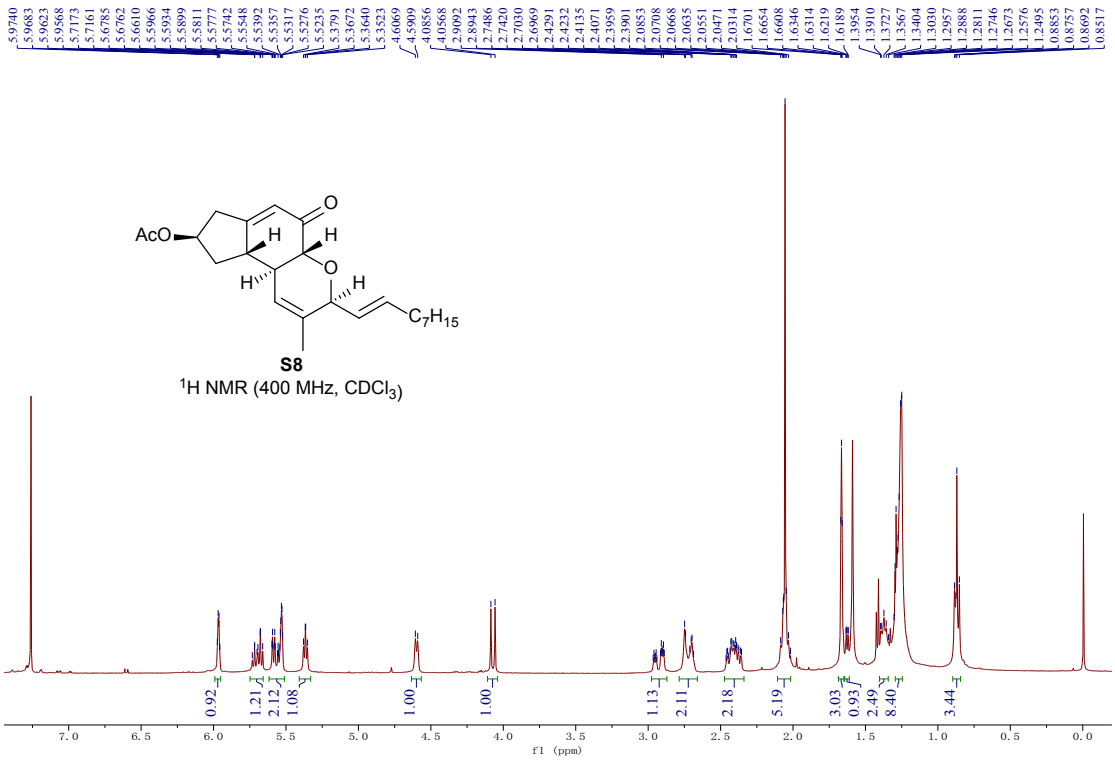
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S7**



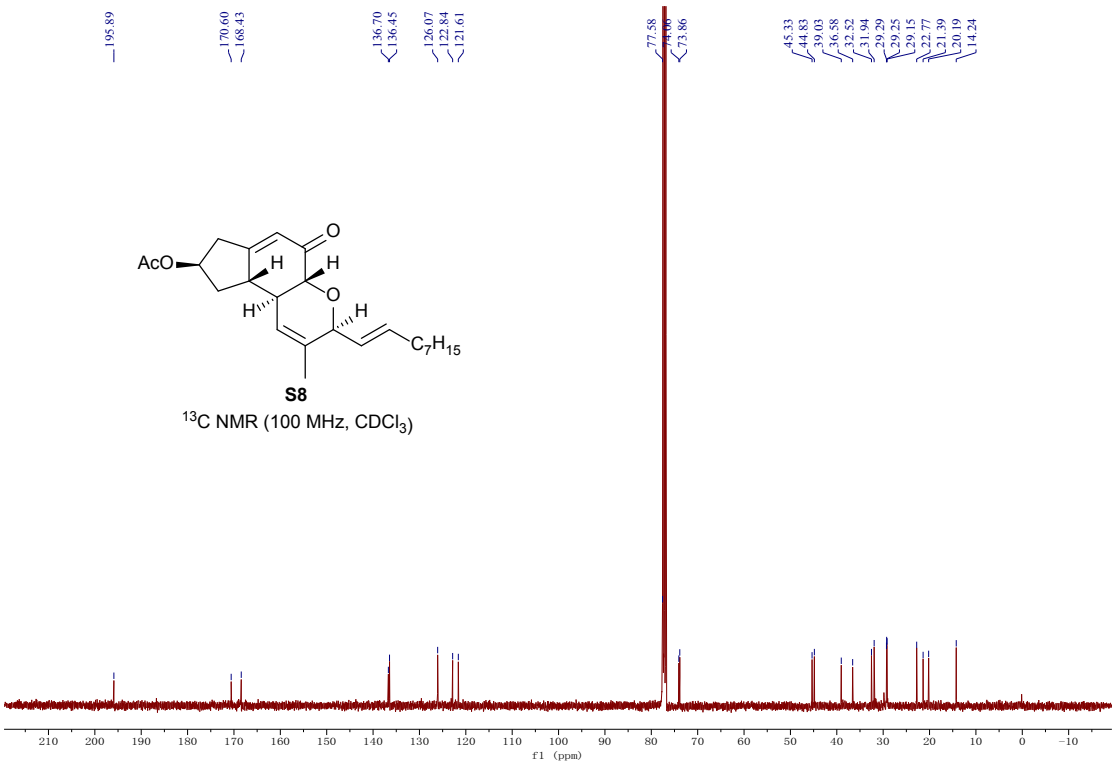
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S7**



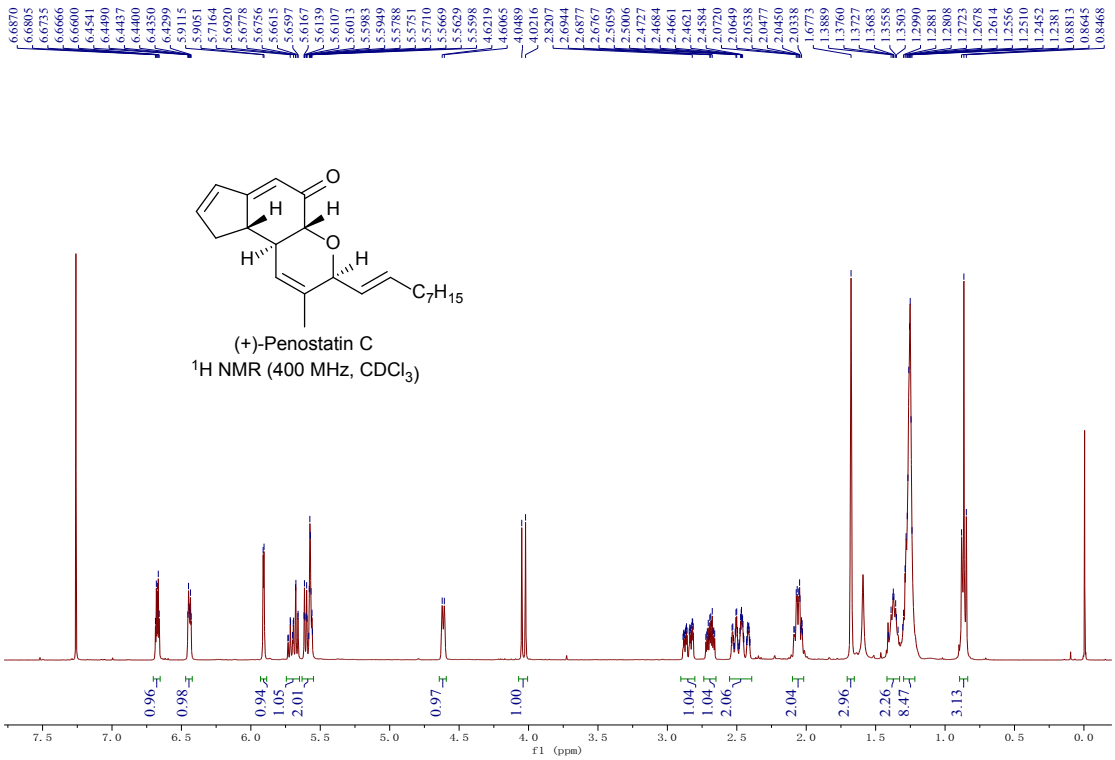
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S8**



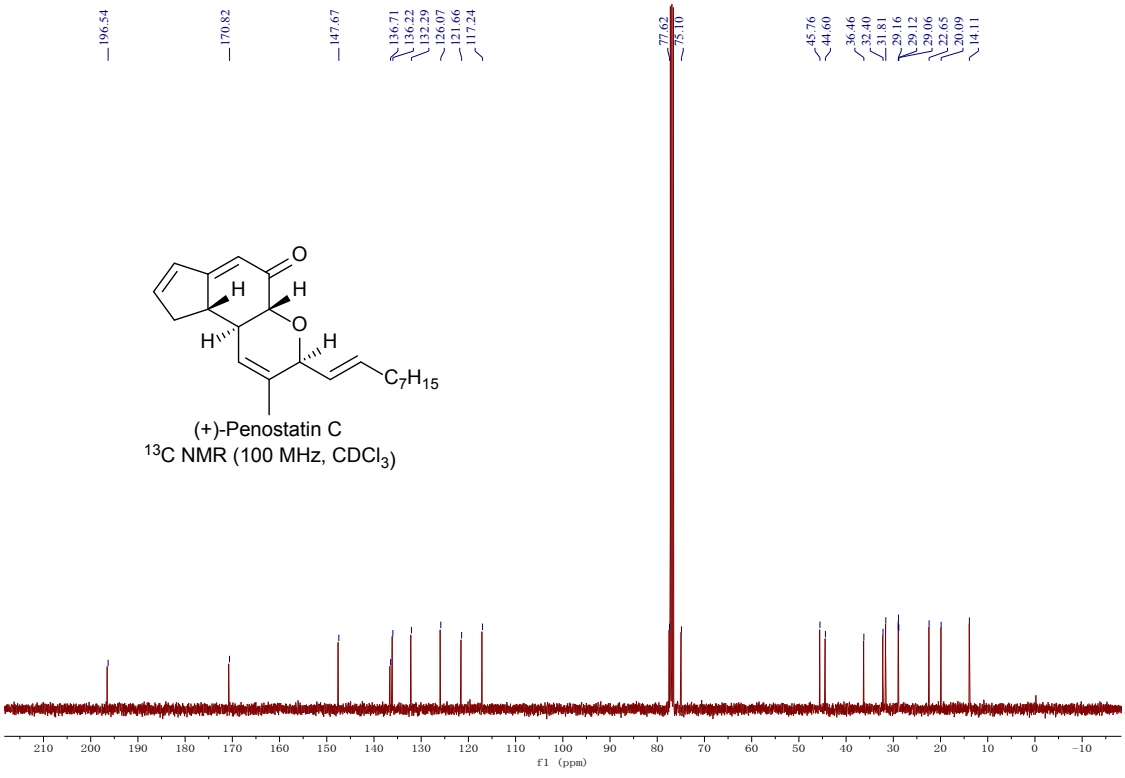
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S8**



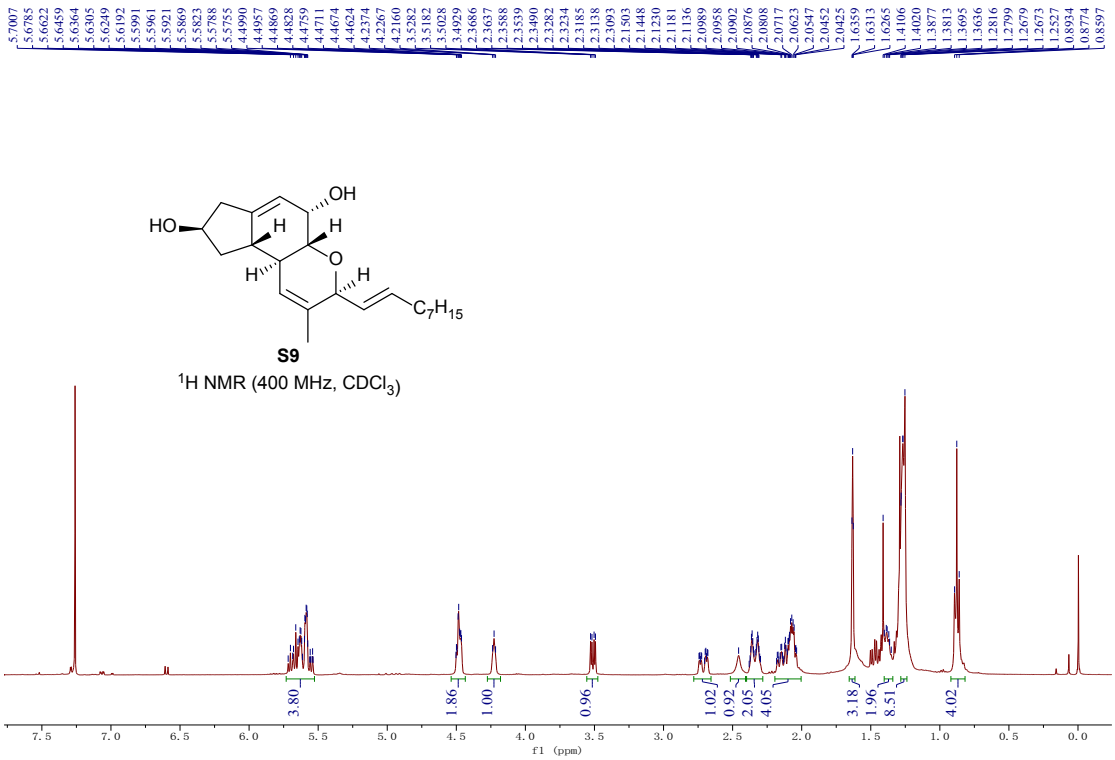
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **(+)-Penostatin C**



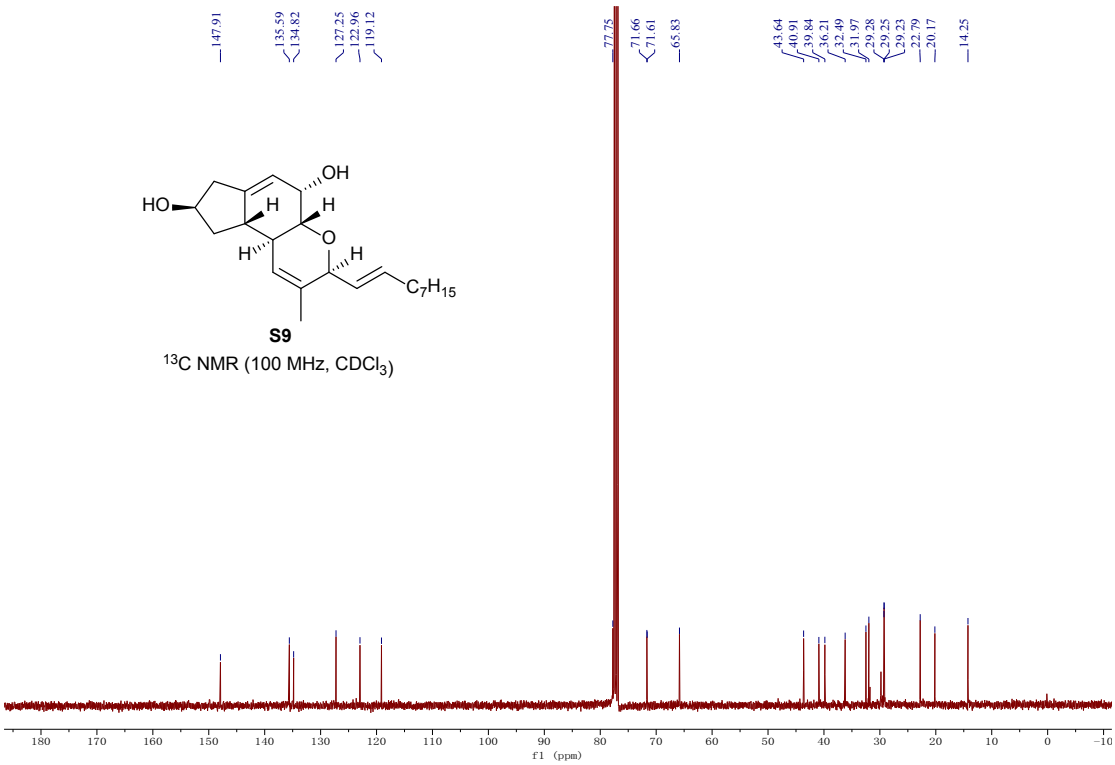
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of **(+)-Penostatin C**



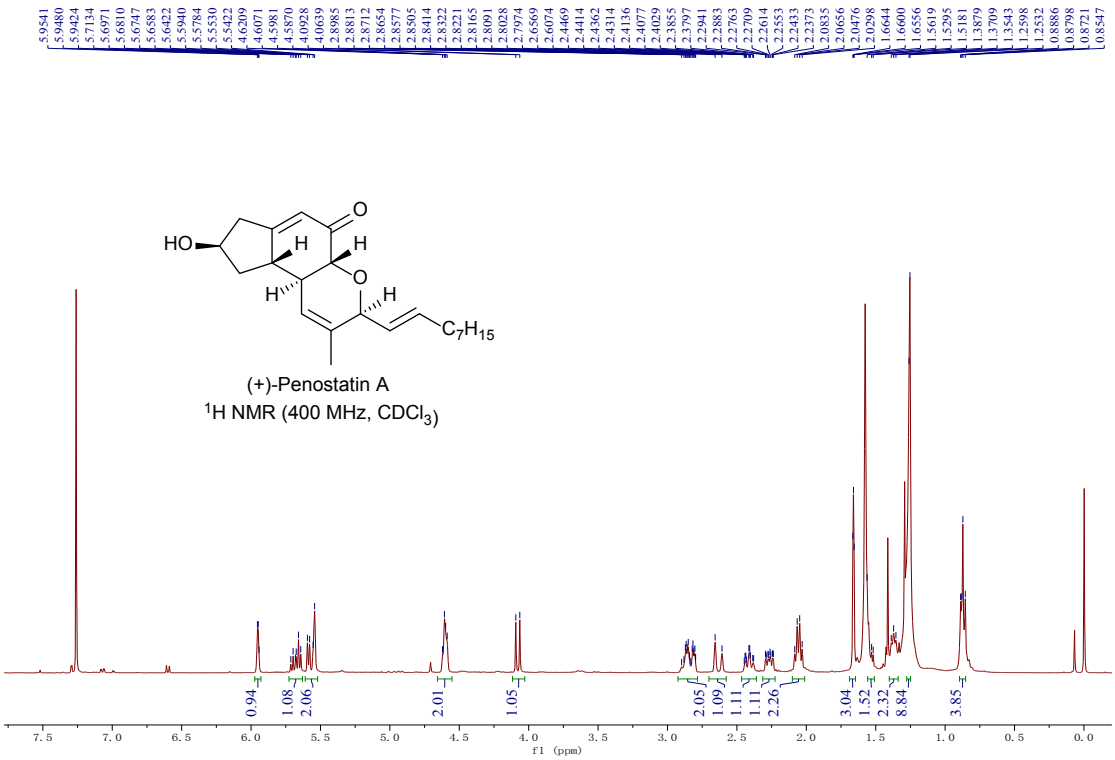
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **S9**



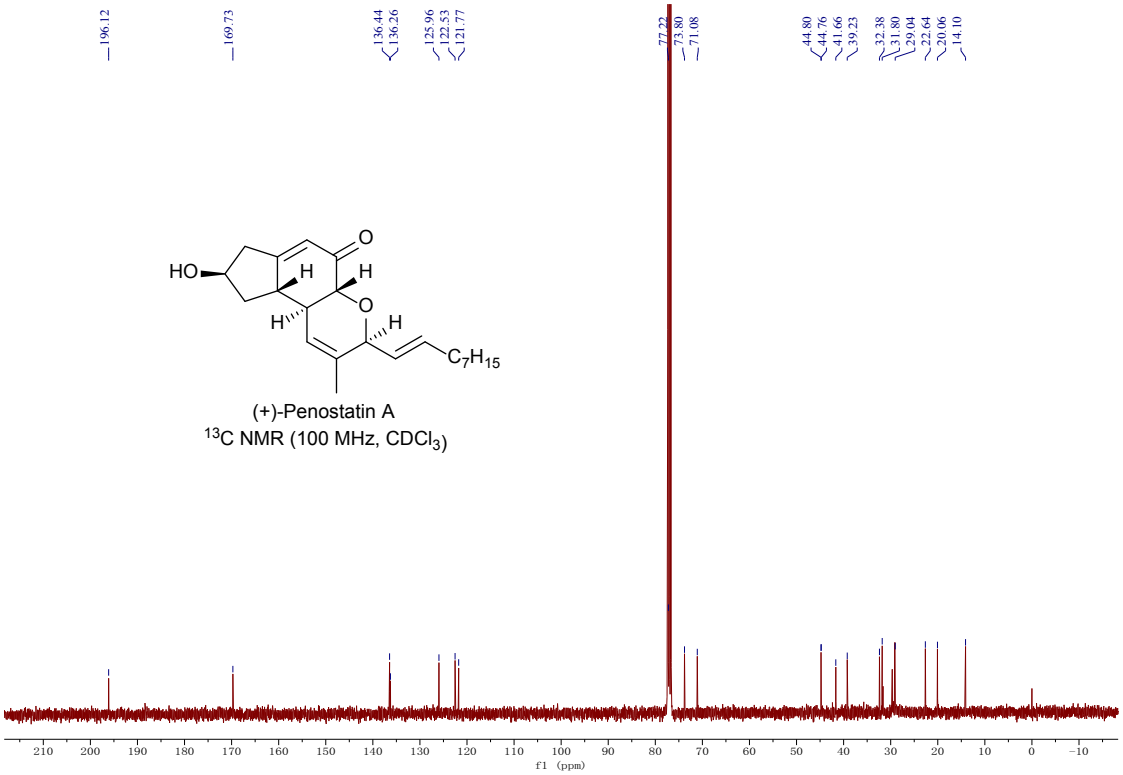
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **S9**



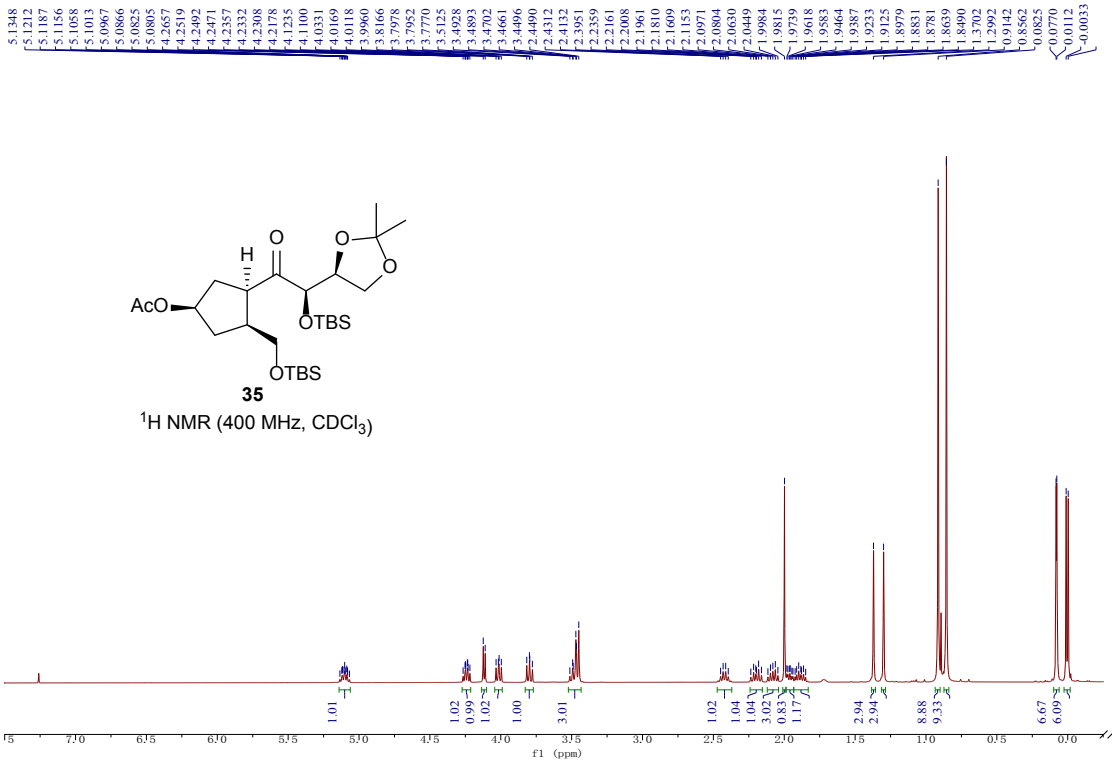
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **(+)-Penostatin A**



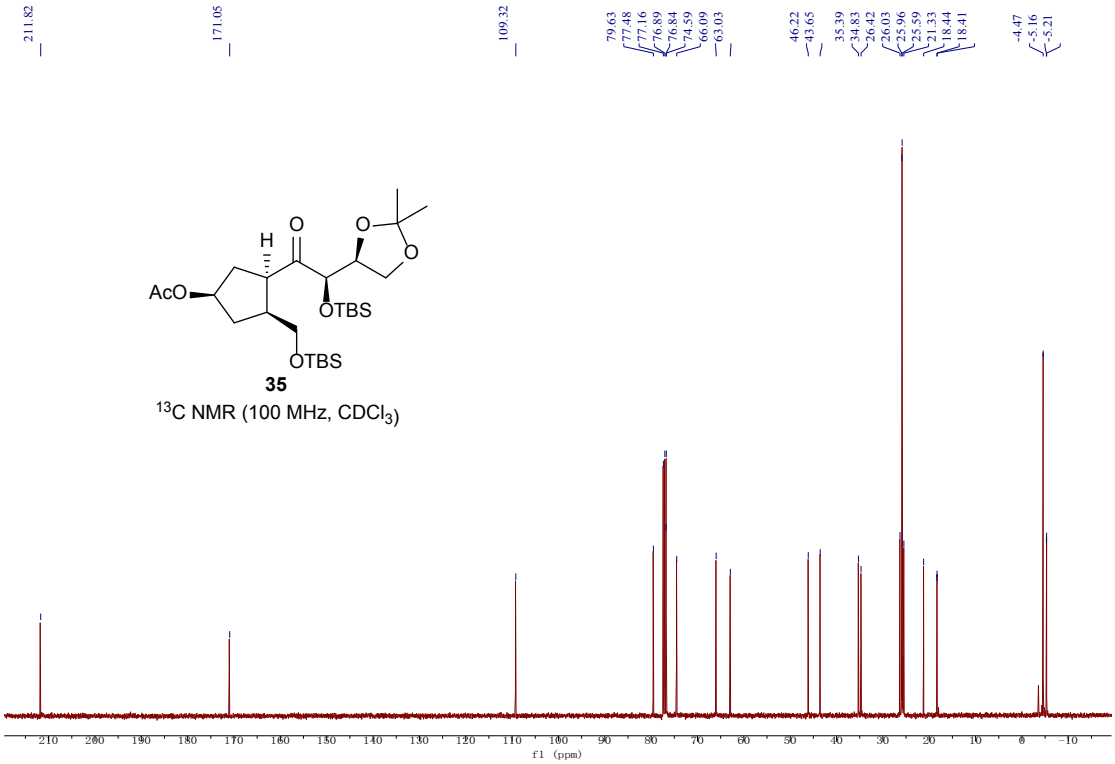
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of **(+)-Penostatin A**



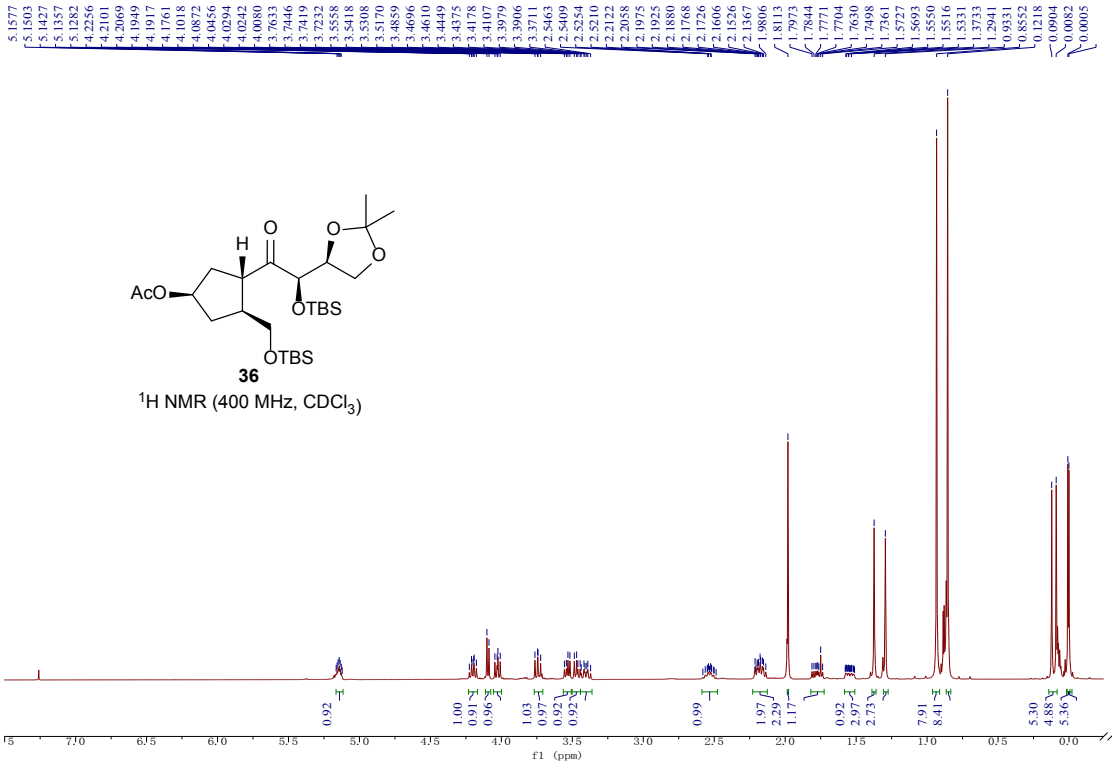
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **35**



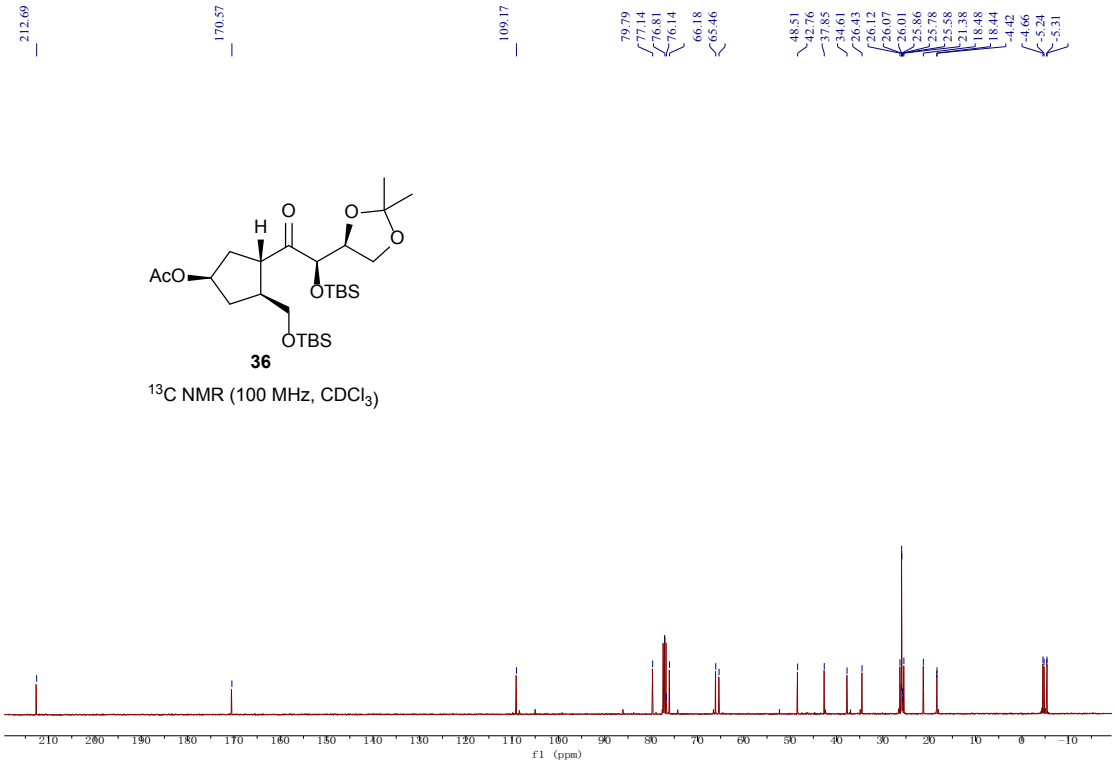
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **35**



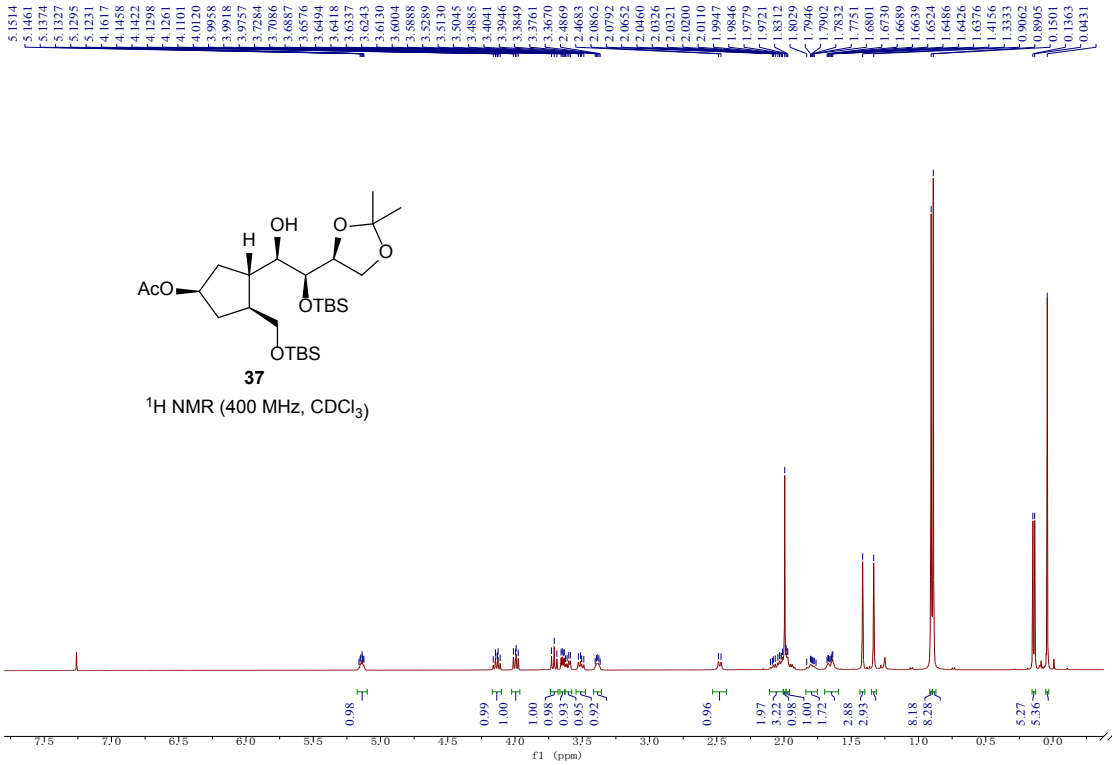
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **36**



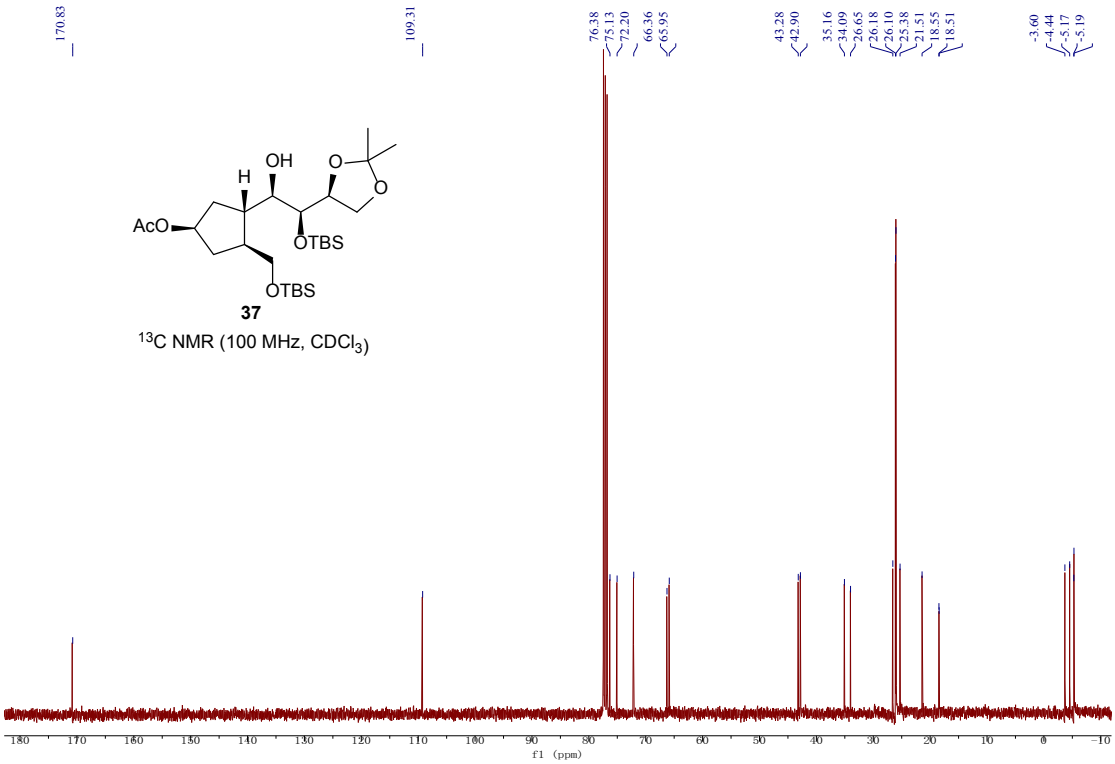
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **36**



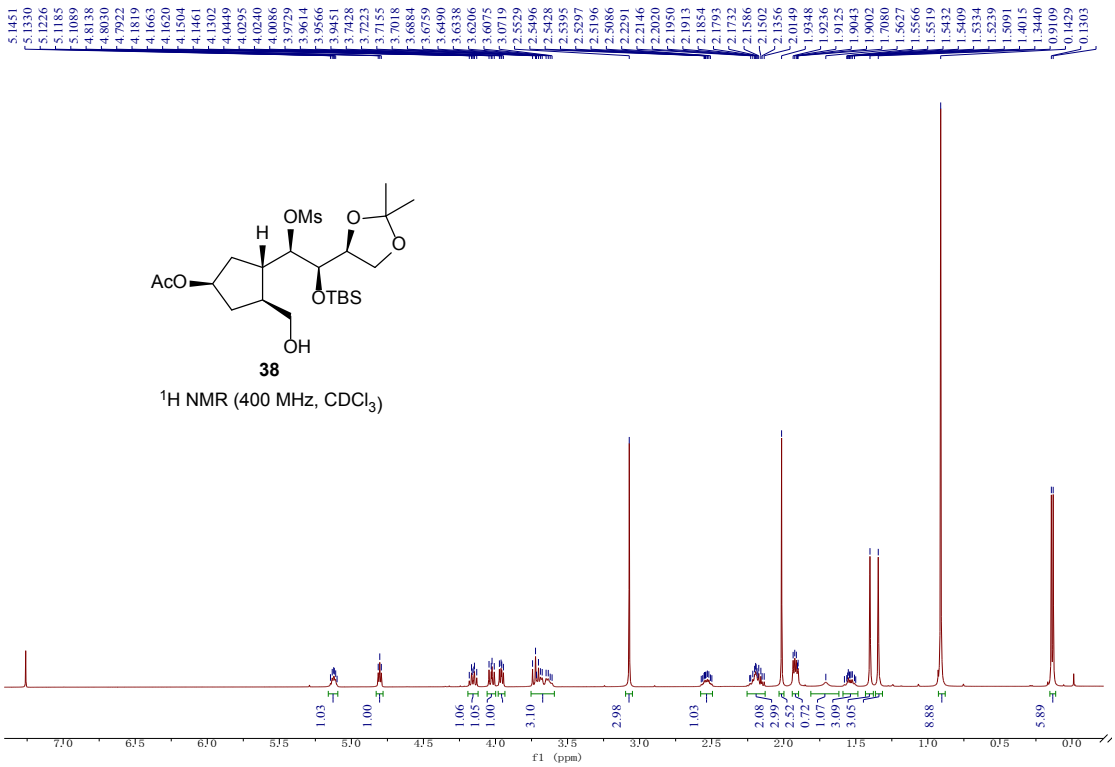
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **37**



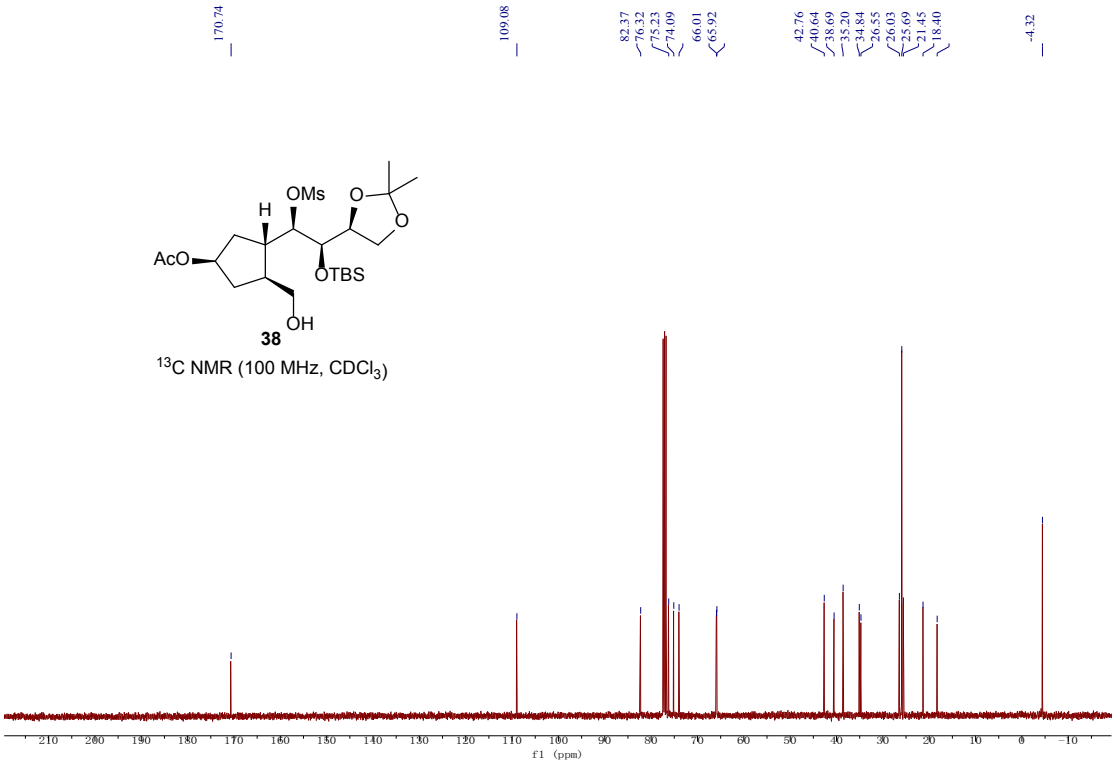
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **37**



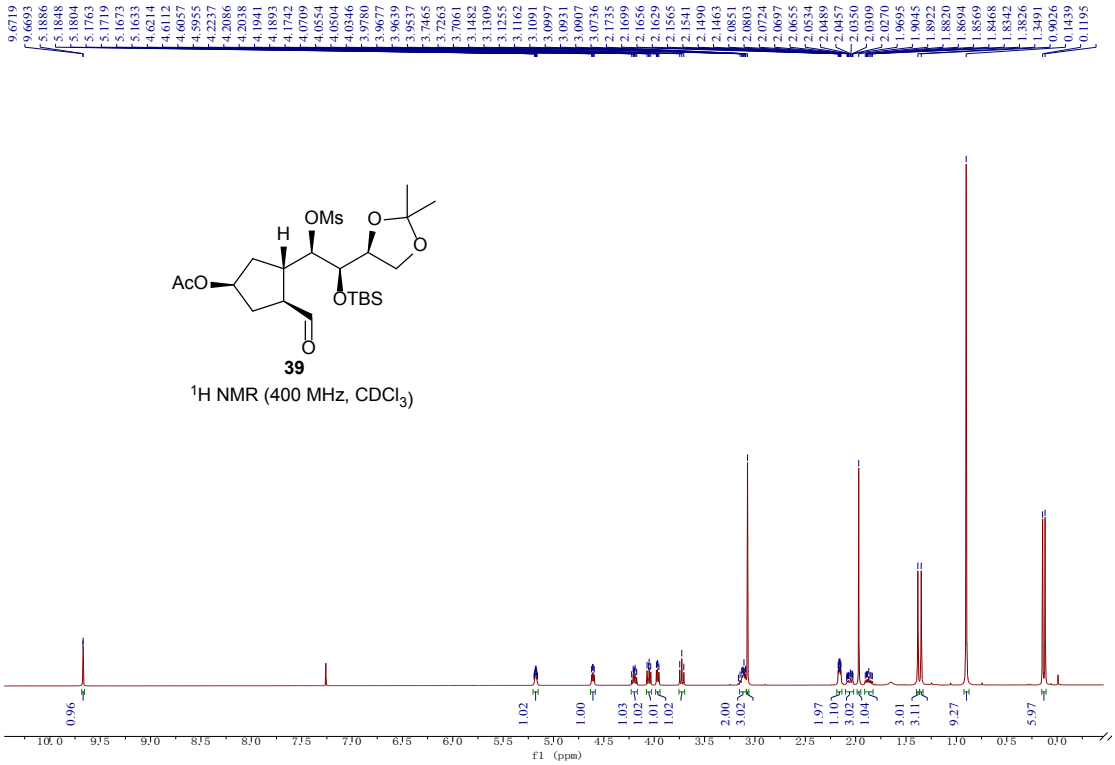
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **38**



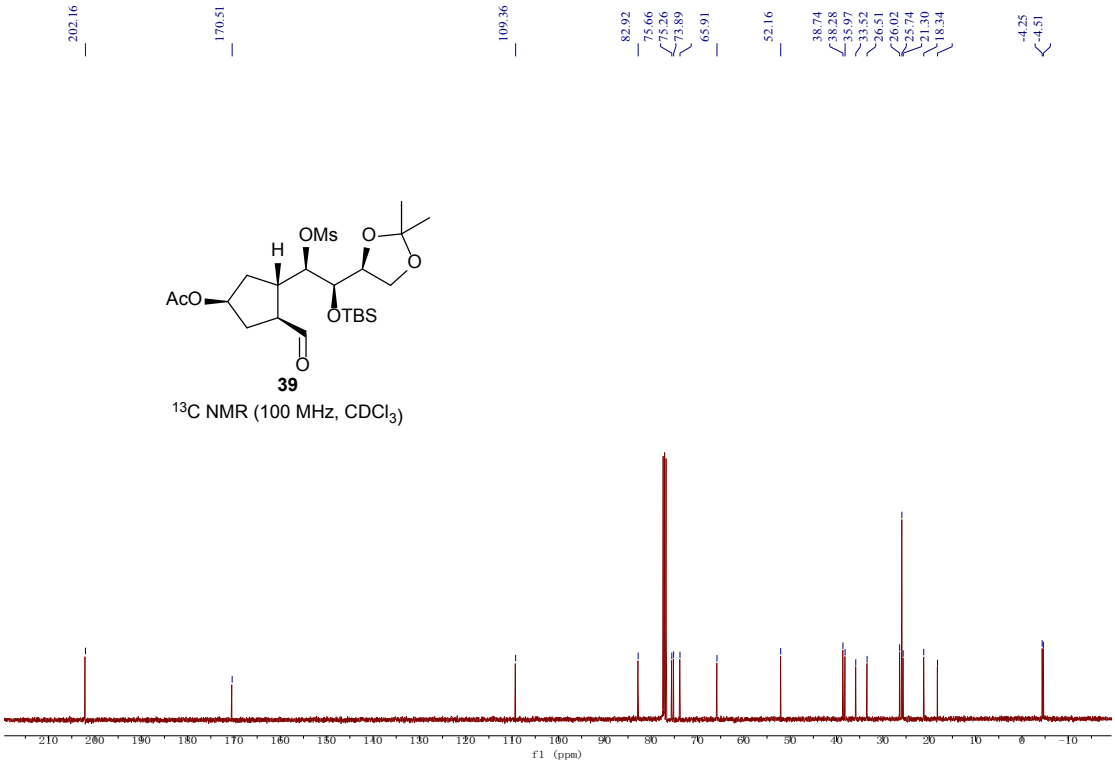
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **38**



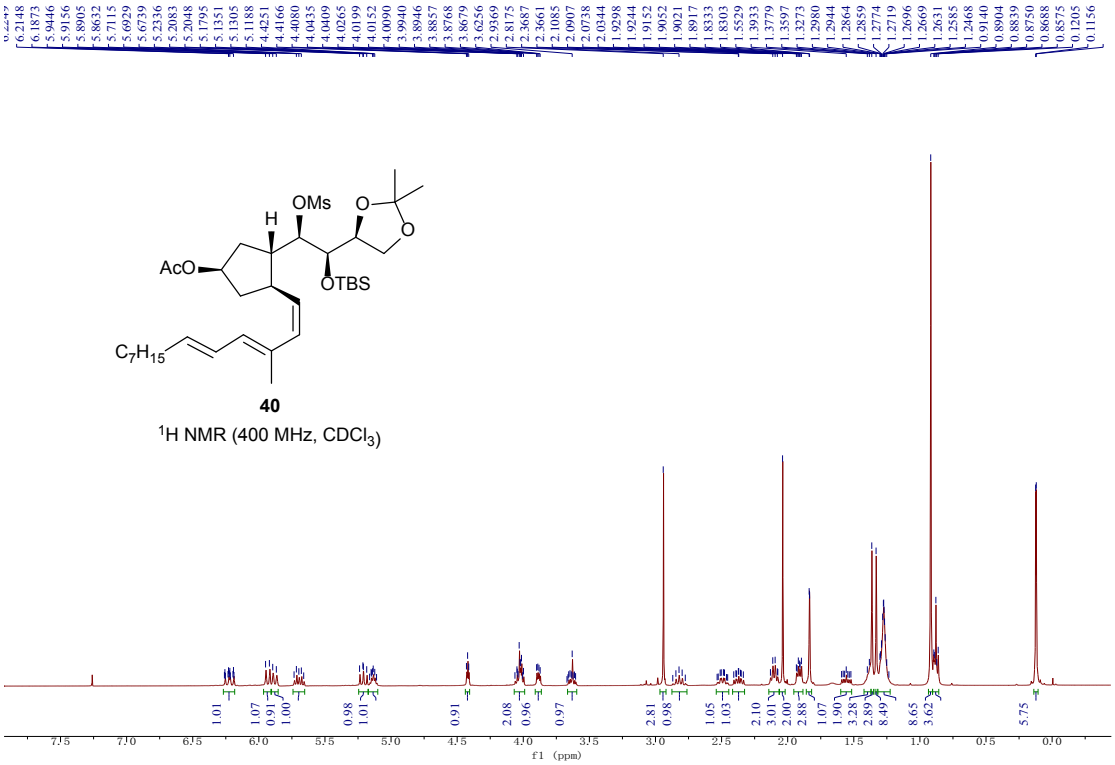
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **39**



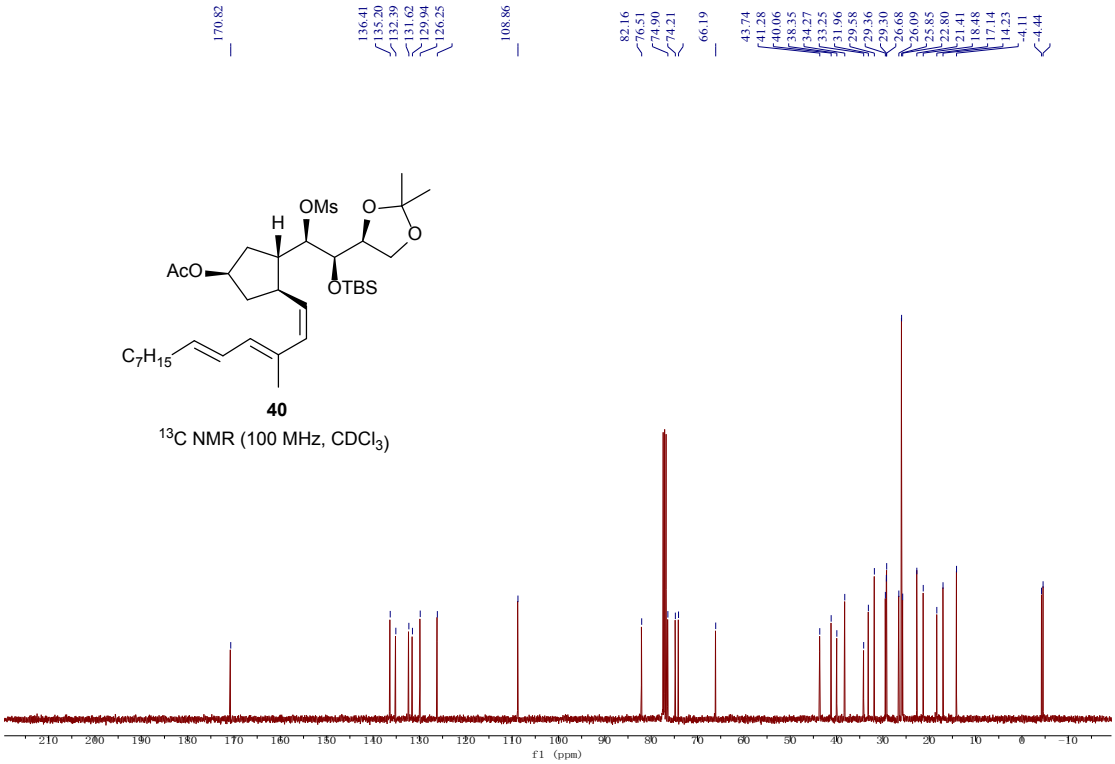
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **39**



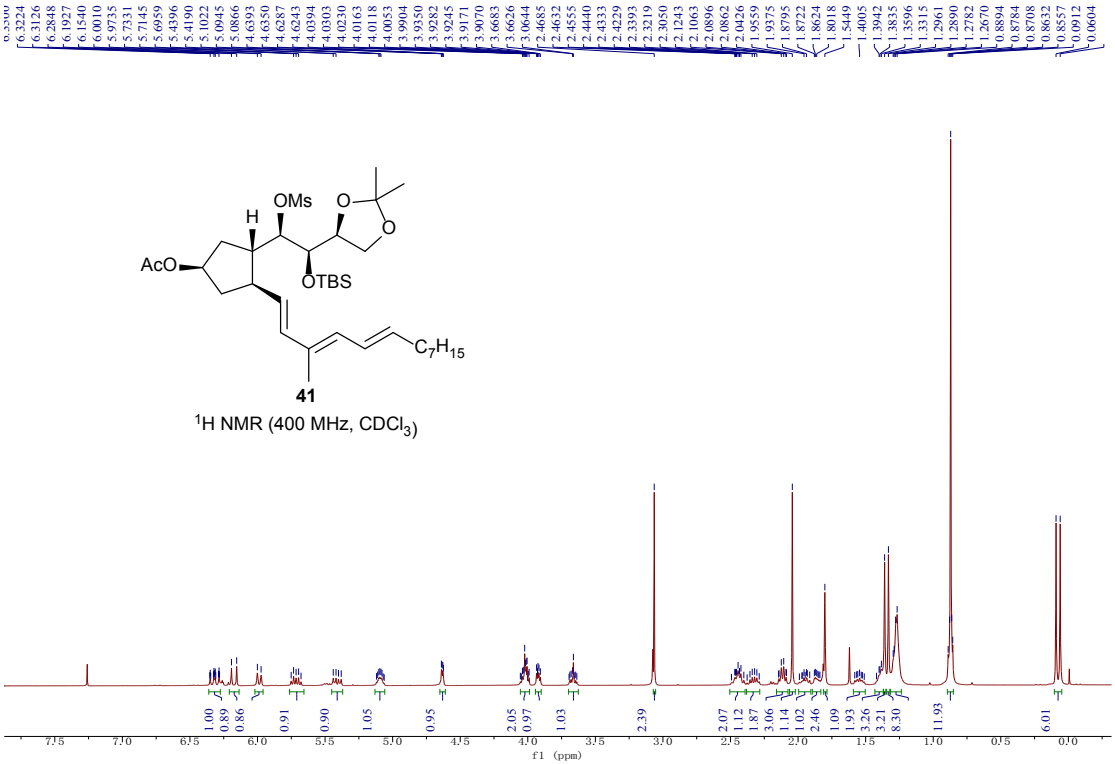
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **40**



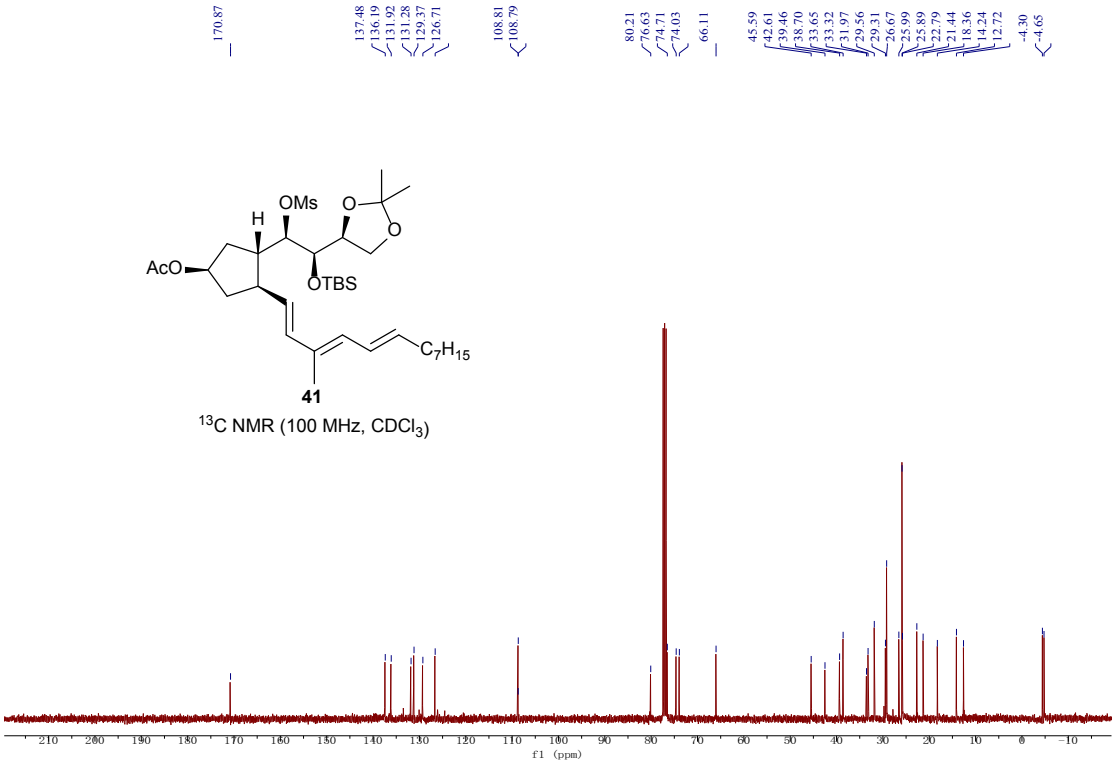
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **40**



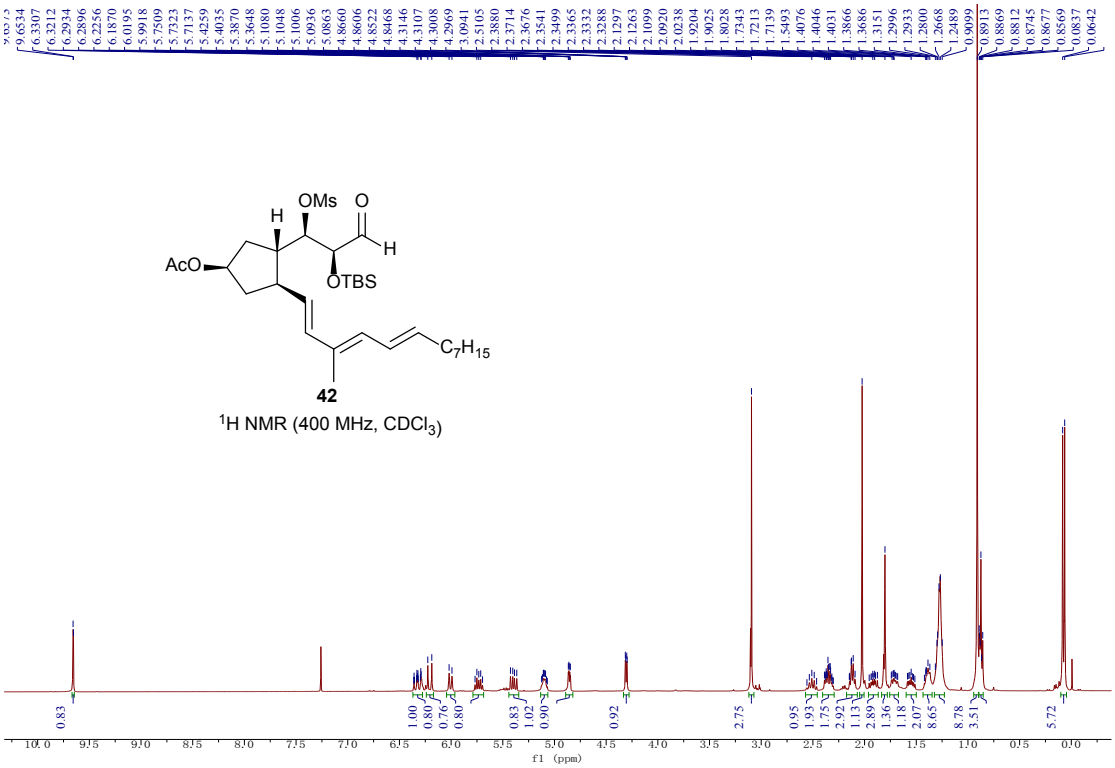
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **41**



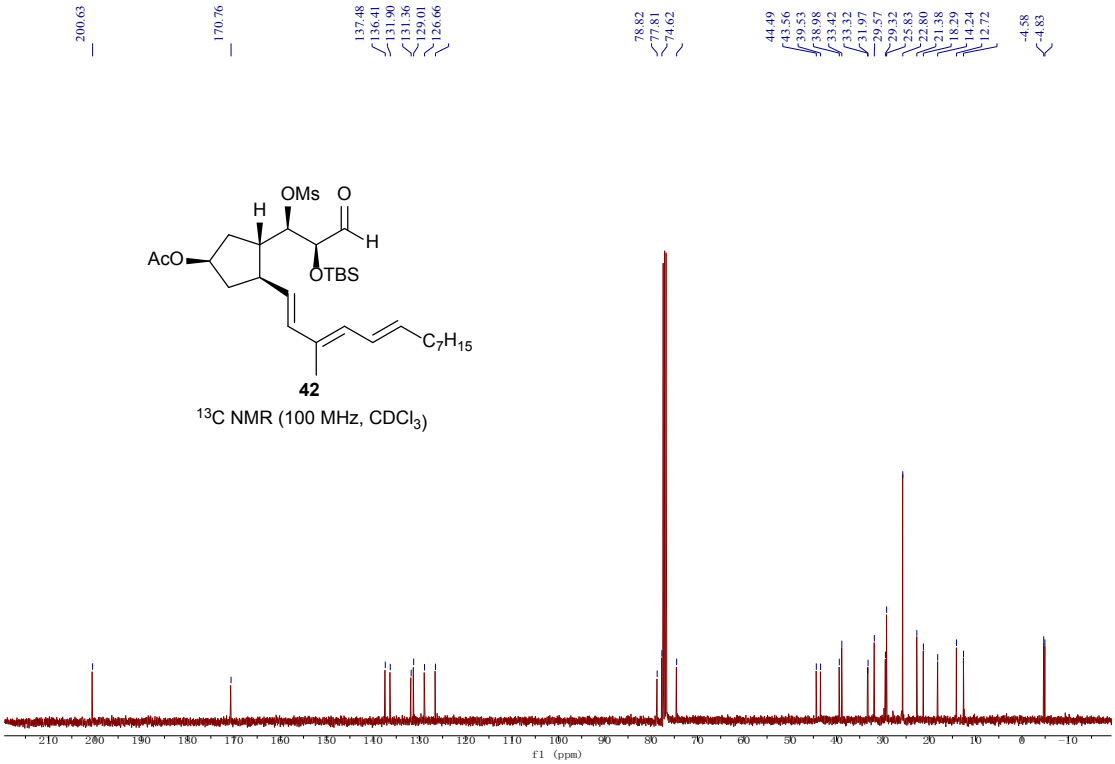
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **41**



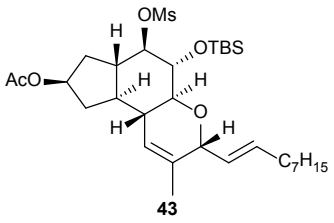
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **42**



^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **42**



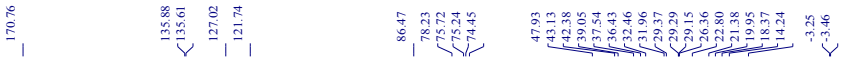
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **43**

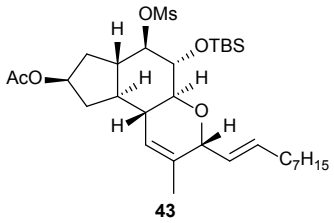


43

^{1}H NMR (400 MHz, $CDCl_3$)

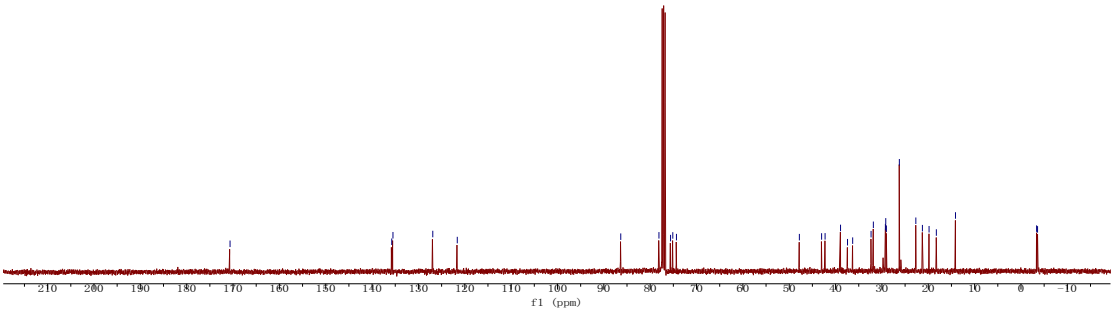
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **43**



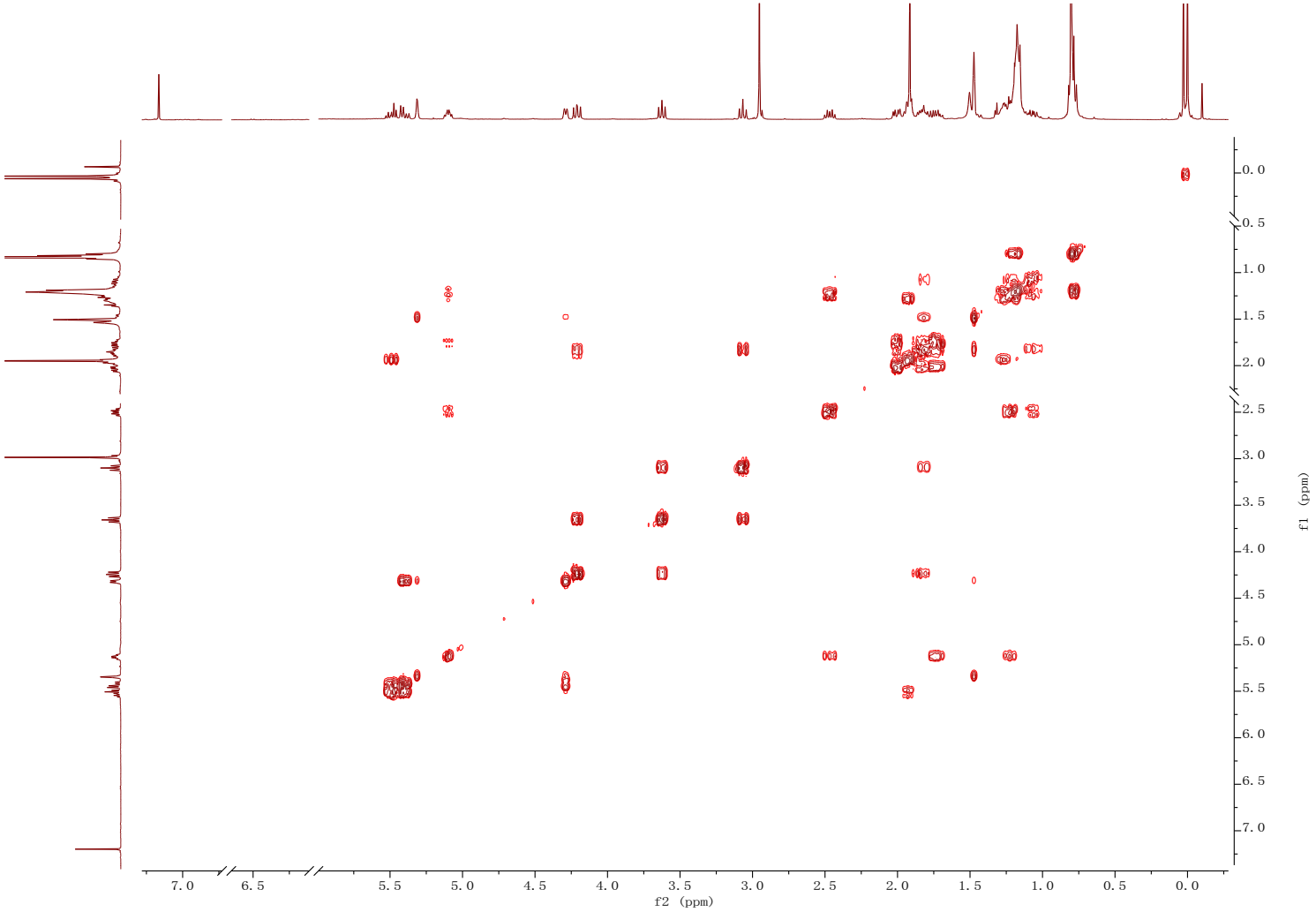


43

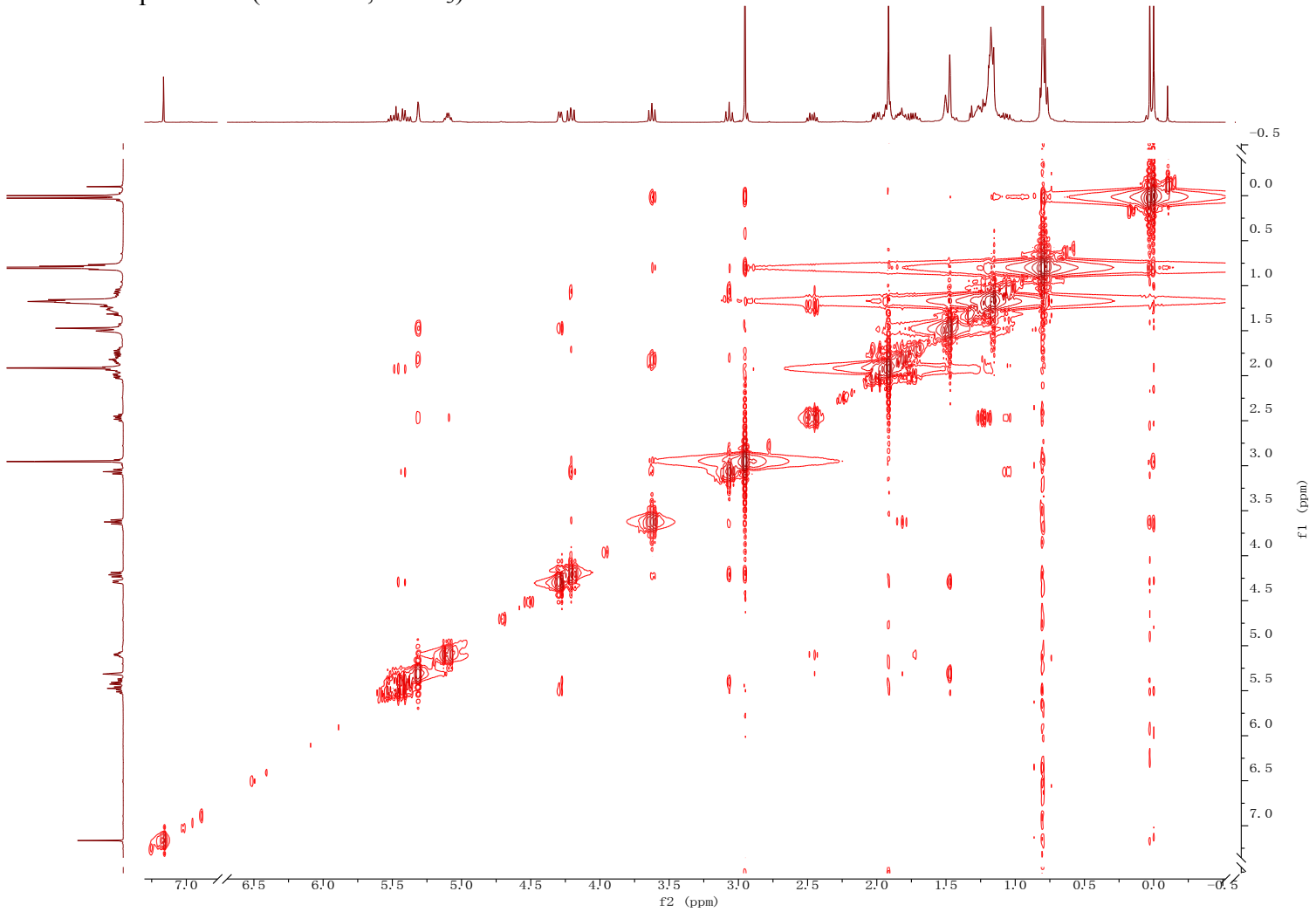
^{13}C NMR (100 MHz, $CDCl_3$)



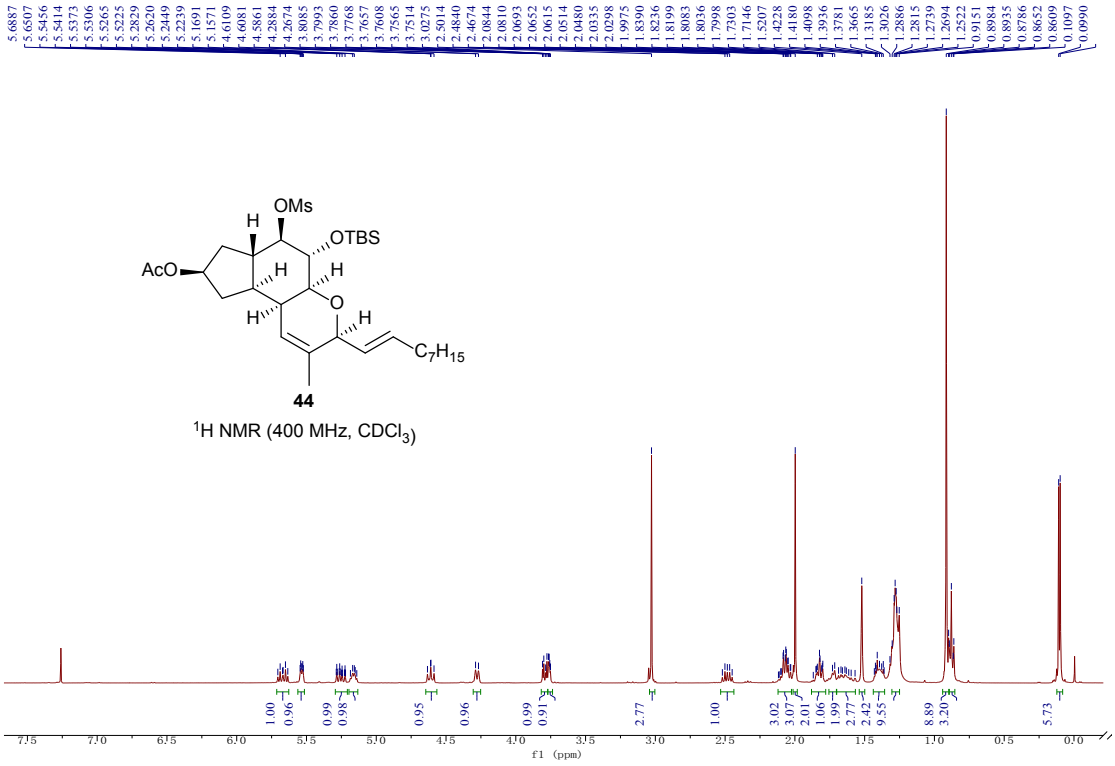
^{1}H-^{1}H COSY spectrum of compound **43** (400 MHz, $CDCl_3$)



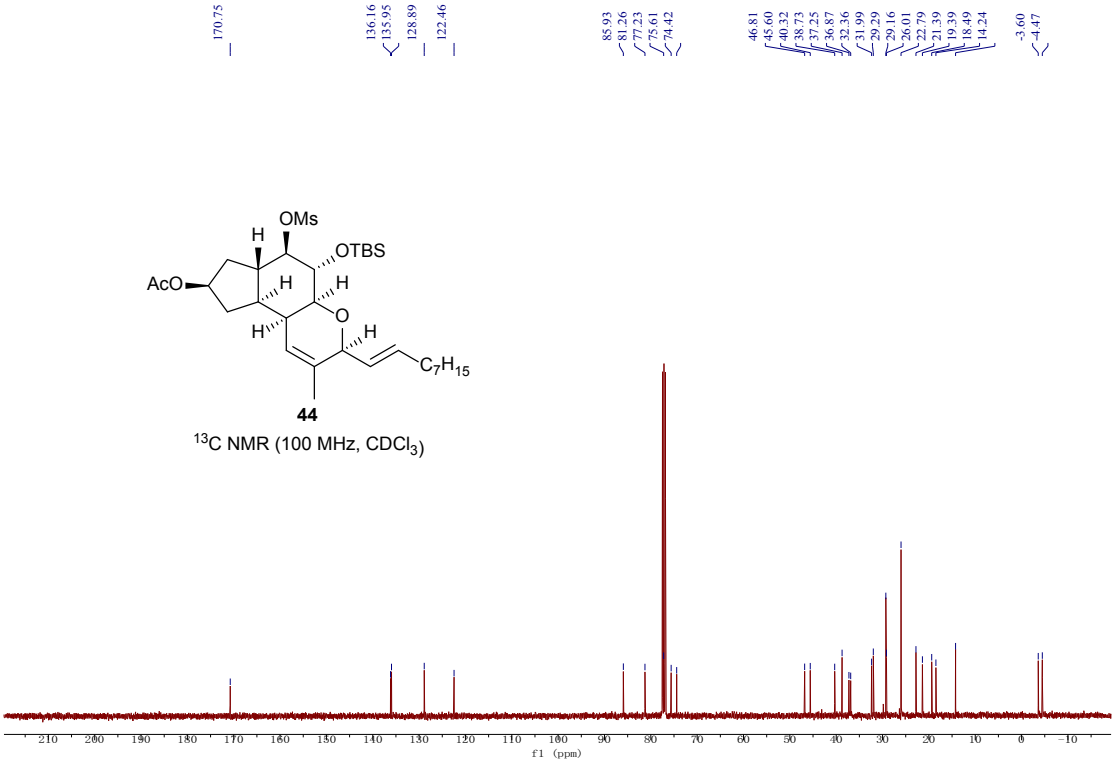
NOESY spectrum of compound **43** (400 MHz, $CDCl_3$)



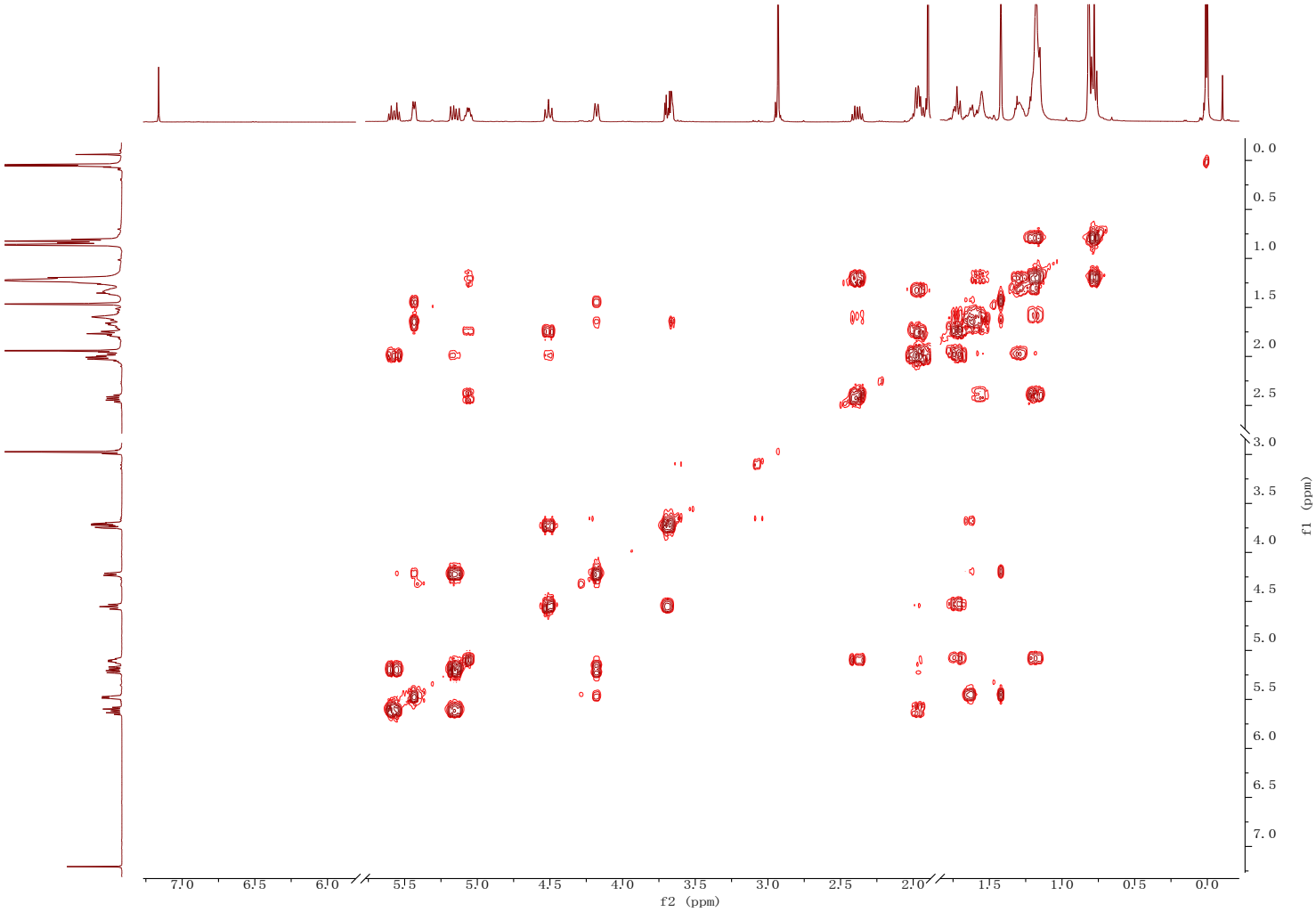
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **44**



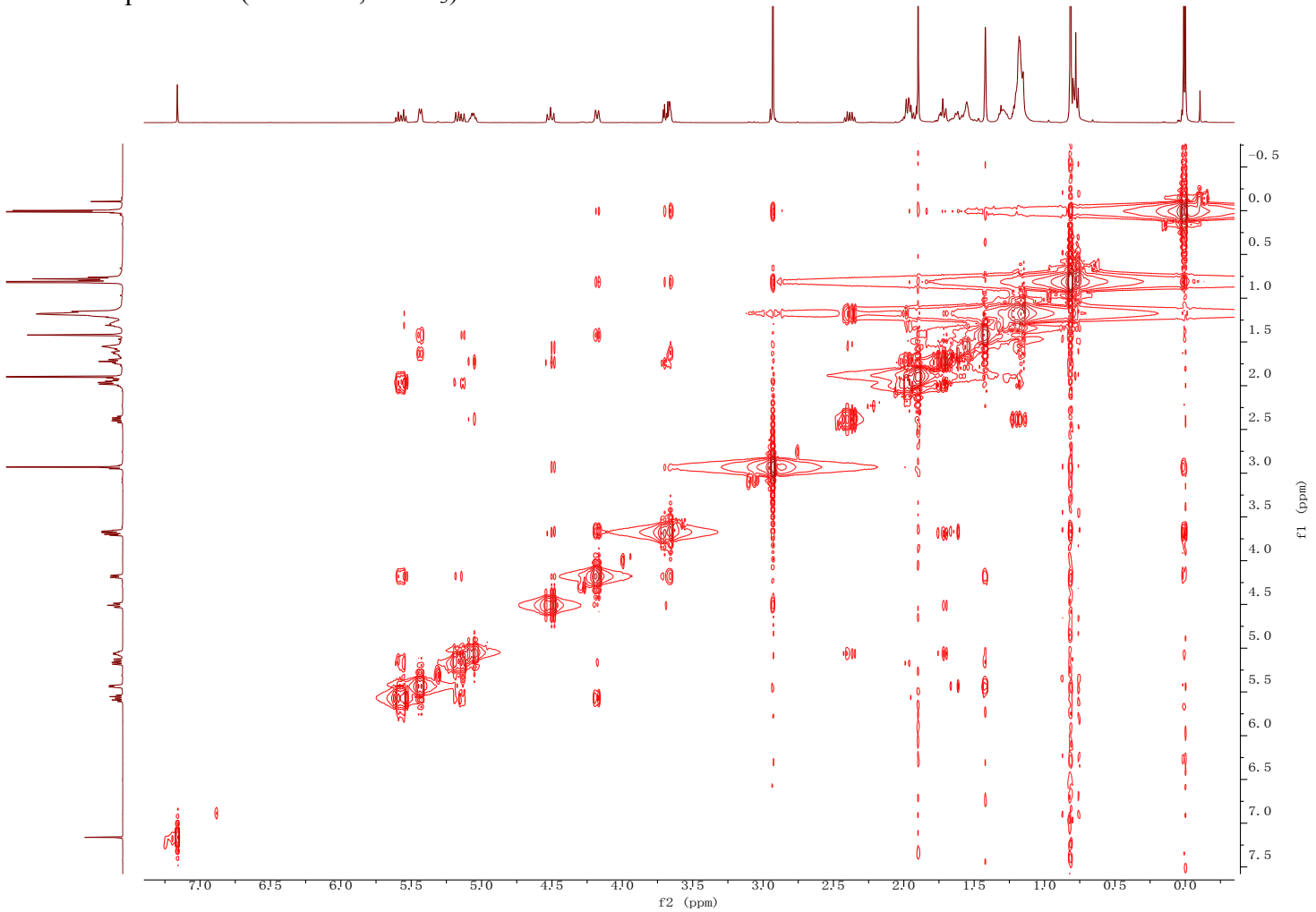
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **44**



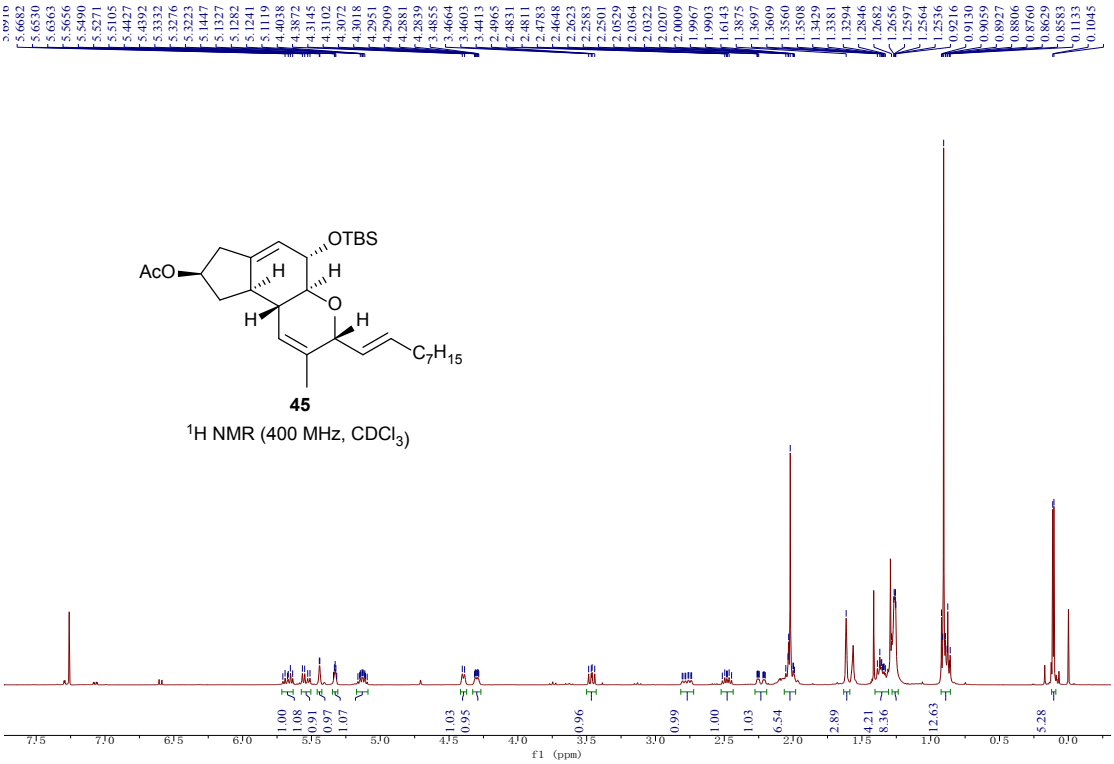
^{1}H-^{1}H COSY spectrum of compound **44** (400 MHz, $CDCl_3$)



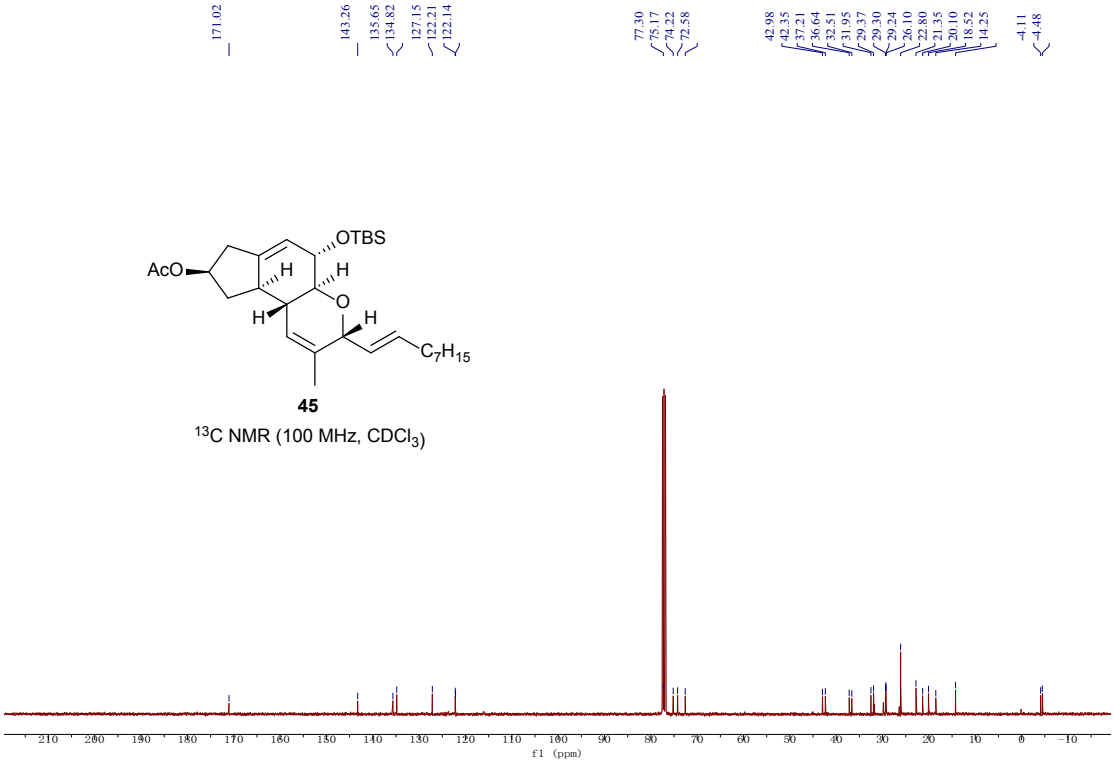
NOESY spectrum of compound **44** (400 MHz, $CDCl_3$)



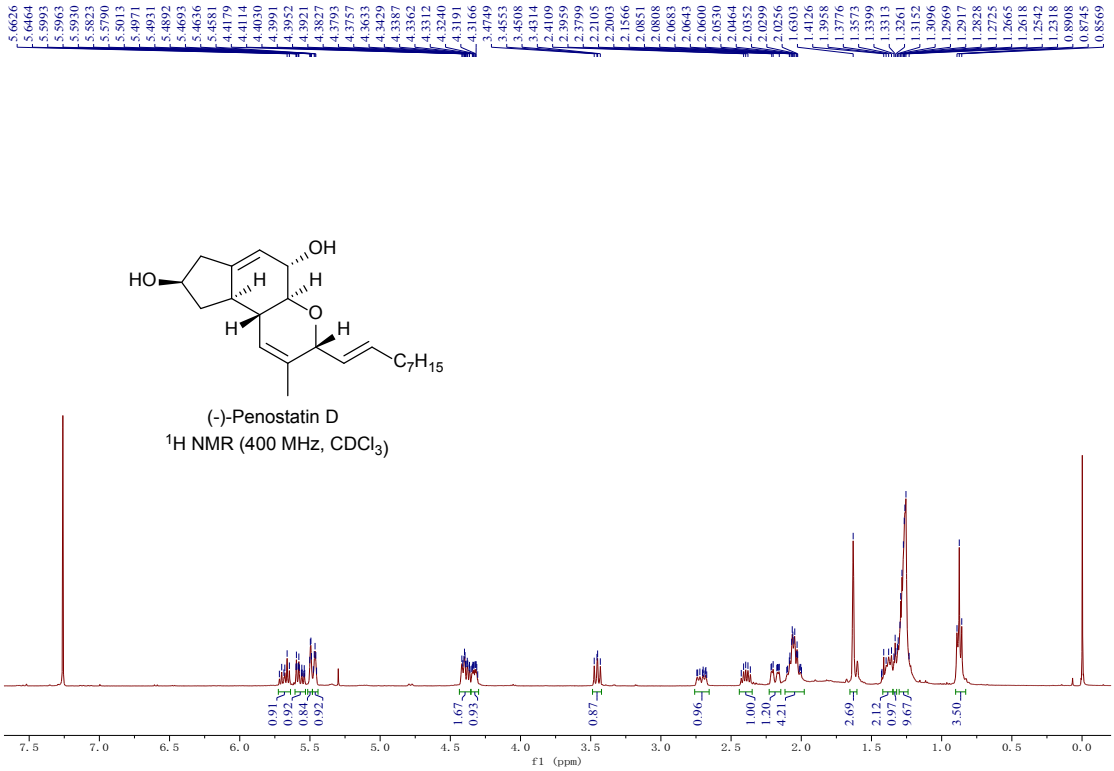
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **45**



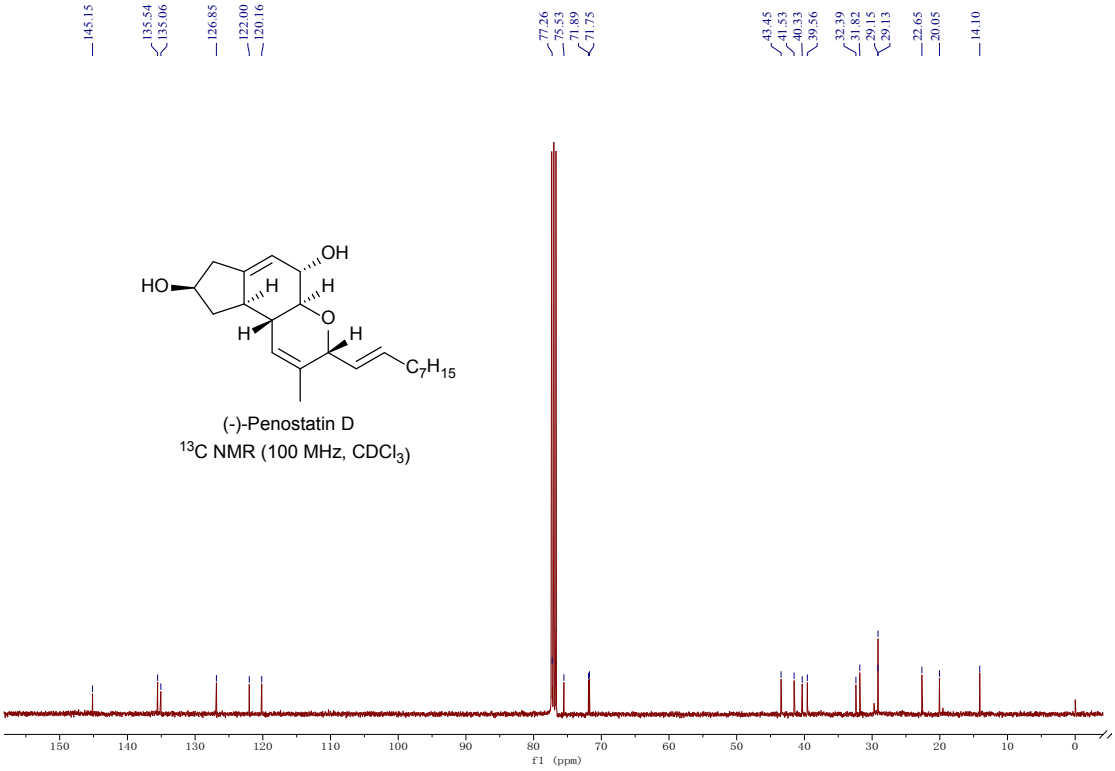
^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **45**



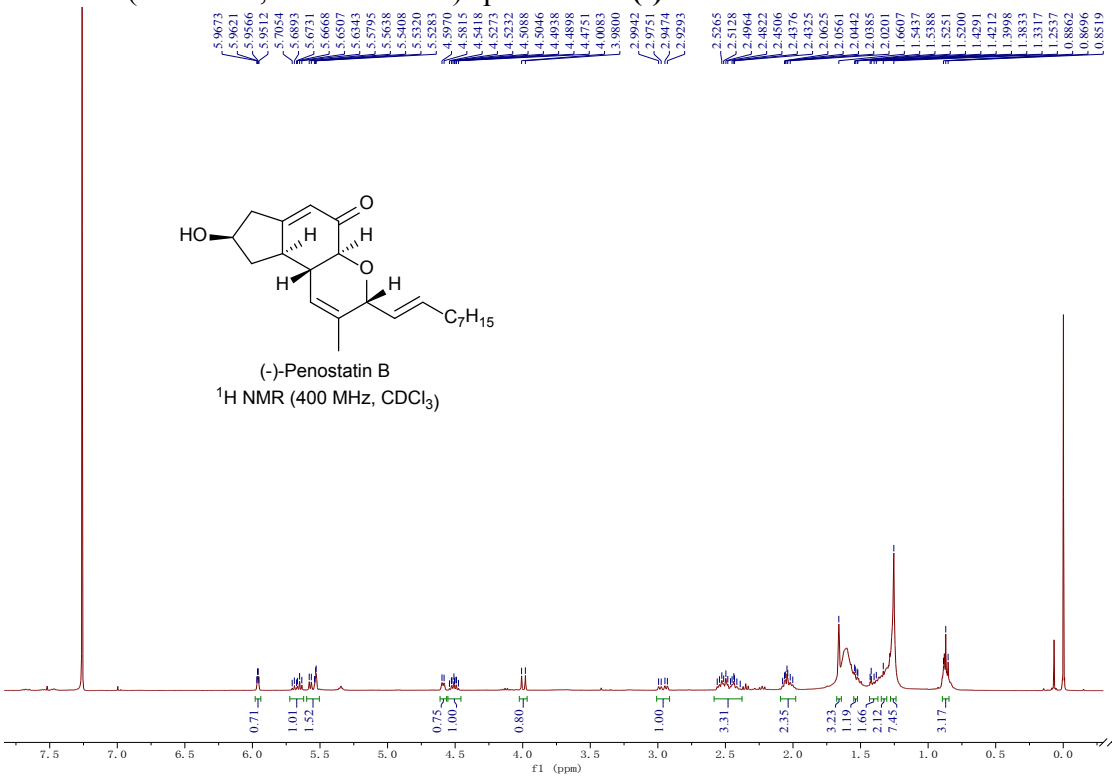
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **(-)-Penostatin D**



^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of **(-)-Penostatin D**



^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **(-)-Penostatin B**



^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of **(-)-Penostatin B**