Electronic Supplementary Information

Prins Cyclization of 1,3-Dioxinone: Synthesis of 11-*Epi*-Badkhysin

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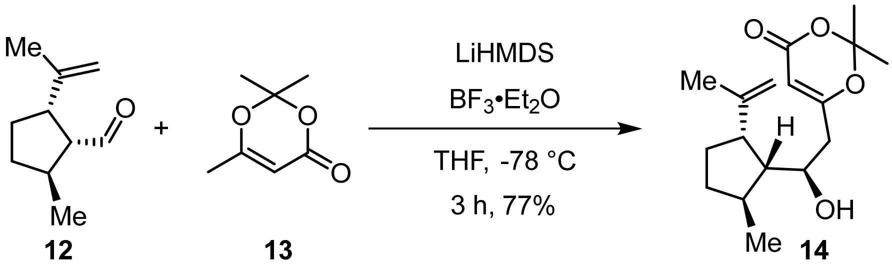
1. General Information

Unless otherwise stated, all chemicals were purchased from commercial suppliers without further purification. Anhydrous MeOH, EtOH and DMF solvents were directly purchased from commercial suppliers, other anhydrous solvents were distilled prior to use (THF and Et_2O were distilled from metallic sodium/benzophenone; DCM, DCE, pyridine and MeCN were distilled from CaH_2). All reactions were conducted in dried glassware, and reaction temperatures refer to the external temperature and are uncorrected. Microwave-assisted heating reactions were conducted on a CEM DISCOVER SP microwave synthesizer. Reaction progress was monitored by thin-layer chromatography (TLC). Silica gel (200 – 300 mesh) for column chromatography and silica GF_{254} for TLC were obtained from Merck Chemicals Co. Ltd. (Shanghai). The boiling range of petroleum ether for column chromatography is 60 – 90 °C. Yields are isolated yields unless otherwise mentioned.

All synthetic new compounds were characterized by melting point (crystal), optical rotation, ^1H NMR, ^{13}C NMR and HRMS. The melting points were measured on a Hanon MP 430 auto melting-point system and were uncorrected. The optical rotations were recorded on a JASCO P-2000 polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 400 (^1H NMR: 400 MHz, ^{13}C NMR: 100 MHz) or Bruker Avance 600 (^1H NMR: 600 MHz, ^{13}C NMR: 150 MHz) spectrometers and calibrated using undeuterated solvent as an internal reference ($CHCl_3$, δ 7.26 ppm ^1H NMR, δ 77.16 ppm ^{13}C NMR; MeOH, δ 3.31 ppm ^1H NMR, δ 49 ppm ^{13}C NMR); The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. To make copies of the ^1H-NMR spectra as clear as possible, multiplet peaks mark only the three major peaks. High Resolution Mass spectra (HRMS) were taken on AB QSTAR Pulsar mass spectrometer or Aglient LC/MSD TOF mass spectrometer.

2. Experimental Section

2.1 Synthesis of Secondary Alcohol 14



The starting material (1*R*,2*S*,5*S*)-2-methyl-5-(prop-1-en-2-yl)cyclopentane-1-carbaldehyde (**12**) was prepared from the commercially available (*S*)-Carvone according to the procedure reported by Meyer.[1]

To a solution of aldehyde **12** (10.00 g, 66.0 mmol) in anhydrous THF (220 mL) was added BF_3•Et_2O (8.25 mL, 66.0 mmol) at -78 °C. In the meantime, to a stirred solution of dioxinone **13** (18.7 g, 131.0 mmol) in THF (300 mL) was added lithium bis(trimethylsilyl)amide (1.0 M in THF, 131 mL, 131.0 mmol) at -78 °C. The resulting mixtures were stirred respectively at -78 °C for 1 hour. The solution of dioxinone-derived lithium dienolate was cannulated to the solution of aldehyde at -78 °C. The reaction mixture was allowed to stir at -78 °C for 2 hours. After TLC analysis, the reaction was quenched with a saturated aqueous solution of NH_4Cl (300 mL) at -78 °C. The resulting mixture was then diluted with water (300 mL), and extracted with EtOAc (3×500 mL). The combined organic phases were washed with brine (400 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1) to give secondary alcohol **14** (14.9 g, 77%, a single diastereoisomer) as colorless oil.

R_f = 0.43 (petroleum ether : ethyl acetate = 5:1).

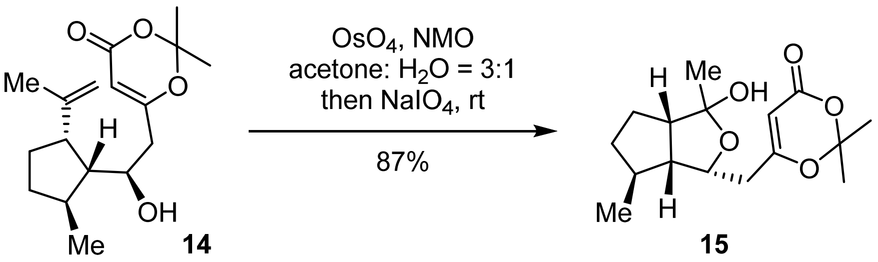
$[\alpha]_D^{20}$ = +9.9 (*c* 0.25, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.32 (s, 1H), 4.94 (s, 1H), 4.86 (s, 1H), 4.02 – 3.97 (m, 1H), 2.60 – 2.54 (m, 1H), 2.41 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.31 – 2.24 (m, 2H), 2.04 – 1.97 (m, 1H),1.83 (s, 3H), 1.76 – 1.71 (m, 2H), 1.69 (s, 3H), 1.67 (s, 3H), 1.65 – 1.62 (m, 1H), 1.19 – 1.12 (m, 1H), 1.09 (d, *J* = 6.88 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.76, 161.36, 147.77, 110.60, 106.61, 94.87, 69.20, 52.12, 50.16, 39.49, 34.80, 32.29, 30.87, 25.45, 24.91, 24.21, 23.31.

HRMS (ESI): Calcd for $C_{17}H_{27}O_4$ $[M+H]^+$: 295.1904, found: 295.1902

2.2 Synthesis of Hemiketone 15



To a solution of alcohol **14** (20.0 mg, 0.07 mmol) in a mixed solvent (0.68 mL, acetone: H_2O = 3:1) was added NMO (9.6 mg, 0.082 mmol) and OsO_4 (0.35 mg, 20 mg/mL in H_2O, 0.001 mmol) at room temperature. After being stirred at ambient temperature for 12 hours, $NaIO_4$ (43.6 mg, 0.2 mmol) was added. The reaction mixture was then stirred for another 5 hours. Upon completion, the suspension was filtered and the residue was washed with EtOAc (3×5 mL). The combined organic phases were successively washed with saturated aqueous solution of $Na_2S_2O_3$ (10 mL), brine (10 mL), and the organic phases were dried over anhydrous Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1) to give acid sensitive hemiketone **15** (17.6 mg, 87%) as a yellow oil.

R*f* = 0.56 (petroleum ether : ethyl acetate = 5:1).

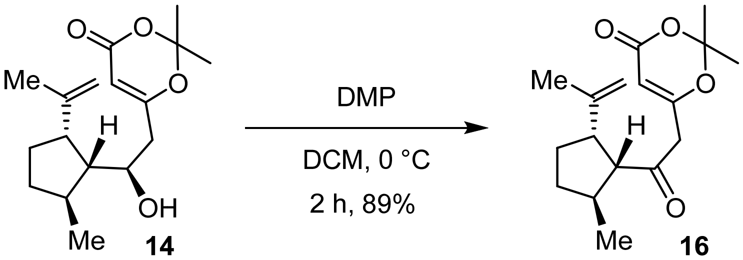
$[\alpha]_D^{20}$ = +94.3 (*c* 0.12, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (s, 1H), 4.47 (q, *J* = 6.8 Hz, 1H), 2.68 (q, *J* = 8.8 Hz, 1H), 2.47 (d, *J* = 6.4 Hz, 2H), 2.30 – 2.24 (m, 1H), 2.01 (s, 1H), 1.84 – 1.73 (m, 3H), 1.68 (d, *J* = 2.4 Hz, 6H), 1.43 (s, 3H), 1.32 – 1.26 (m, 1H), 1.19 – 1.11 (m, 1H), 0.99 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.86, 161.53, 106.61, 105.44, 94.59, 73.74, 54.71, 53.91, 36.70, 35.27, 34.89, 29.02, 25.50, 24.85, 24.51, 20.51.

HRMS (ESI): Calcd for $C_{16}H_{25}O_5$ $[M+H]^+$: 297.1697, found: 297.1694.

2.3 Synthesis of Ketone 16



Dess-Martin periodinane (24.20 g, 57 mmol) was added to a solution of secondary alcohol **14** (14 g, 47 mmol) in DCM (317 mL) at 0 °C. After addition, the reaction mixture was stirred at this temperature for 2 hours. After TLC analysis, a saturated aqueous solution of $Na_2S_2O_3$ (200 mL) was added slowly, and the resulting suspension was stirred for another 30 minutes. The resulting mixture was then extracted with DCM (3×200 mL). The combined organic phases were washed with brine (500 mL) and dried over Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1) to give ketone **16** (12.40 g, 89%) as a white solid.

M.p.= 46.2 – 48.3 ºC

R*f* = 0.64 (petroleum ether : ethyl acetate = 5:1).

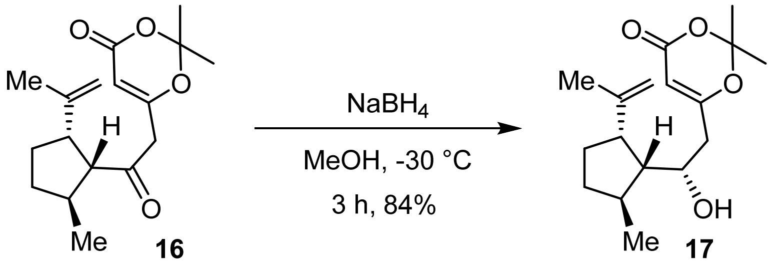
$[\alpha]_D^{20}$ = –37.5 (*c* 0.16, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.27 (s, 1H), 4.81 (s, 1H), 4.76 (s, 1H), 3.34 (d, *J* = 16.4 Hz, 1H), 3.23 (d, *J* = 16.4 Hz, 1H), 3.03 (q, *J* = 9.0 Hz, 1H), 2.68 (t, *J* = 8.4 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.03 – 1.98 (m, 1H), 1.89 – 1.84 (m, 1H), 1.77 – 1.72 (m, 1H), 1.69 (d, *J* = 4.6 Hz, 6H), 1.67 (s, 3H), 1.24 – 1.17 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 205.05, 165.21, 161.06, 145.54, 113.14, 107.21, 96.63, 63.55, 50.22, 47.99, 36.01, 33.71, 30.30, 25.33, 25.00, 21.69, 20.80.

HRMS (ESI): Calcd for $C_{17}H_{25}O_4$ $[M+H]^+$: 293.1747, found: 293.1744.

2.4 Synthesis of Alcohol 17



To a stirred solution of ketone **16** (12.00 g, 41 mmol) in MeOH (205 mL) was added NaBH$_4$ (2.33 g, 61.6 mmol) in one portion at -30 °C, and the resultant mixture was then stirred at this temperature for 3 hours. Upon completion, the reaction was carefully quenched with saturated aqueous solution of NH$_4$Cl (100 mL) and diluted with water (100 mL). The mixture was extracted with DCM (3×300 mL). The combined organic phases were washed with brine (500 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to afford secondary alcohol **17** (10.08 g, 84%) as a colorless oil.

R*f* = 0.41 (petroleum ether : ethyl acetate = 5:1).

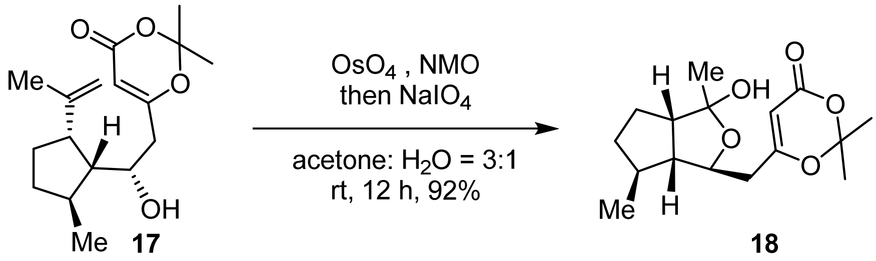
$[\alpha]_D^{20}$ = –48.8 (*c* 0.14, CHCl$_3$).

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.29 (s, 1H), 4.87 (s, 2H), 3.81 (td, *J* = 10.0, 2.8 Hz, 1H), 2.64 – 2.57 (m, 2H), 2.46 (dd, *J* = 14.8, 2.4 Hz, 1H), 2.20 (dd, *J* = 14.4, 10.0 Hz, 1H), 1.98 – 1.91 (m, 1H), 1.85 (s, 3H), 1.83 – 1.78 (m, 1H), 1.77 – 1.72 (m, 1H), 1.72 – 1.68 (m, 1H), 1.65 (s, 3H), 1.63 (s, 3H), 1.15 – 1.10 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 170.20, 161.44, 148.89, 111.80, 106.55, 94.93, 70.19, 55.50, 49.08, 39.14, 35.58, 33.38, 29.37, 25.61, 24.49, 23.97, 22.73.

HRMS (ESI): Calcd for $C_{17}H_{27}O_4$ [M+H]$^+$: 295.1904, found: 295.1904.

2.5 Synthesis of Hemiketone 18



To a solution of alcohol **17** (10.00 g, 34 mmol) in a mixed solvent (230 mL, acetone: H_2O = 3:1) was added NMO (4.78 g, 40.76 mmol), OsO_4 (86 mg, 20 mg/mL in H_2O, 0.34 mmol) at room temperature. After being stirred at ambient temperature for 12 hours, $NaIO_4$ (21.8 g, 102 mmol) was added. The reaction mixture was then stirred for another 5 hours. Upon completion, the suspension was filtered and the residue was washed with EtOAc (3×300 mL). The combined organic phases were successively washed with saturated aqueous solution of $Na_2S_2O_3$ (800 mL) and brine (800 mL). The organic phases were dried over anhydrous Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1) to give hemiketone **18** (9.20 g, 92%) as a white solid.

$\mathbf{R}_f$ = 0.57 (petroleum ether : ethyl acetate = 5:1).

$[\alpha]_D^{20}$ = –27.2 (*c* 0.54, $CHCl_3$).

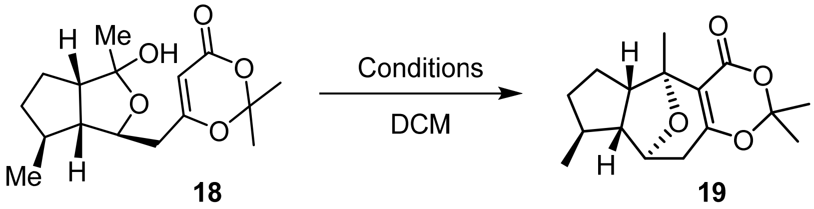
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 – 5.29 (m, 1H), 4.01 – 3.96 (m, 1H), 2.73 – 2.57 (m, 2H), 2.48 – 2.34 (m, 2H), 2.21 – 2.17 (m, 1H), 1.95 – 1.91 (m, 1H), 1.85 – 1.77(m, 2H), 1.66 (s, 6H), 1.41 (s, 3H), 1.36 – 1.28 (m, 1H), 1.22 – 1.14 (m, 1H), 0.98 – 0.88 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.63, 169.19, 161.54, 161.46, 108.03, 106.63, 105.11, 94.94, 94.88, 83.09, 78.73, 59.39, 57.88, 54.63, 53.96, 43.07, 41.33, 39.78, 38.30, 36.37, 35.47, 28.60, 28.15, 25.50, 25.48, 24.82, 24.77, 24.73, 24.61, 20.62, 19.96.

HRMS (ESI): Calcd for $C_{16}H_{24}NaO_5$ $[M+Na]^+$: 319.1516, found: 319.1515.

2.6 Optimization for the Prins Cyclization of 18

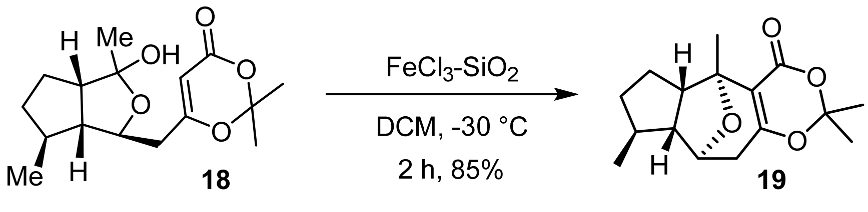
Table S1 Optimization for the Prins Cyclization of **18**



Entry	Lewis Acids	Additives	C (M)	T (°C)	Results[a]
1	$BF_3 \cdot OEt_2$ (1.2 eq.)	-	0.1	RT	31 %
2	$BF_3 \cdot OEt_2$ (1.2 eq.)	-	0.08	-20	52 %
3	$BF_3 \cdot OEt_2$ (1.2 eq.)	-	0.03	0	67 %
4	$Sc(OTf)_3$ (0.5 eq.)	-	0.05	-30	32 %
5	$Yb(OTf)_3$ (0.5 eq.)	-	0.1	0	42 %
6	$Cu(OTf)_2$ (0.5 eq.)	-	0.05	-30	41 %
7	$Fe(OTf)_3$ (0.5 eq.)	-	0.05	-30	46 %
8	$FeCl_3$-SiO_2[b] (0.5 eq.)	-	0.05	-78	NR
9	$FeCl_3$ (1.5 eq.)	$MgSO_4$[c]	0.03	-30	75 %
10	$FeCl_3$ (1.5 eq.)	-	0.05	-30	67 %
11	$FeCl_3$ (0.3 eq.)	$MgSO_4$[c]	0.03	-30	63 %
12	$FeCl_3$-SiO_2[b] (0.5 eq.)	-	0.05	-30	85 %

[a] Isolated yield after purification by silica gel chromatography. [b] SiO_2:$FeCl_3$ = 50:3 (m/m). [c] $MgSO_4$:$FeCl_3$ = 10:1 (m/m).

2.7 Synthesis of Ether 19



To a stirred solution of hemiketone **18** (9.00 g, 19.8 mmol) in DCM (660 mL) was added $FeCl_3$-SiO_2 (64.00 g, $FeCl_3$: SiO_2 = 3 : 50 m/m) in one portion at -30 °C. The brown mixture was stirred at -30 °C for 3 hours. Upon completion, the suspension The resulting suspension was filtered through a short column of silica gel and washed with

DCM (ca. 500 mL). The combined organic phases were washed with saturated aqueous solution of brine (800 mL), the organic phases were dried over anhydrous Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to give ether **19** (4.68 g, 85%) as a white solid.

M.p.= 124.9 – 126.1 ºC

R_f = 0.51 (petroleum ether : ethyl acetate = 5:1).

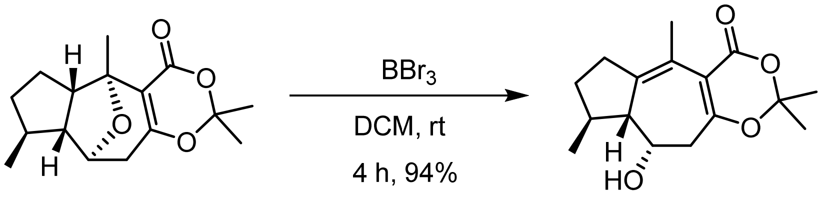
$[\alpha]_D^{20}$ = +98.1 (*c* 0.38, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.15 (d, *J* = 5.4 Hz, 1H), 2.81 (q, *J* = 9.0 Hz, 1H), 2.71 (dd, *J* = 18.6, 5.4 Hz, 1H), 2.02 (d, *J* = 18.0 Hz, 1H), 1.98 – 1.96 (m, 1H), 1.78 – 1.66 (m, 6H), 1.64 (s, 3H), 1.60 (s, 3H), 1.45 – 1.38 (m, 1H), 1.09 – 1.06 (m, 1H), 1.04 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 162.62, 159.16, 112.35, 105.61, 80.48, 78.94, 58.48, 58.16, 43.07, 36.22, 35.69, 28.12, 27.69, 22.11, 19.98, 18.51.

HRMS (ESI): Calcd for $C_{16}H_{23}O_4$ $[M+H]^+$: 279.1591, found: 279.1589.

2.8 Synthesis of Alcohol 20



19 **20**

To a stirred solution of ether **19** (5.00 g, 17.96 mmol) in DCM (600 mL) was added BBr_3 (2.1 mL, 21.6 mmol) in one portion at ambient temperature and the mixture was stirred for 4 hours. Upon completion, MeOH (50 mL) was added to the reaction mixture and stirred for 10 minutes. The reaction was quenched with saturated aqueous solution of $NaHCO_3$ (500 mL) and extracted with DCM (3×500 mL). The combined organic phases were washed with brine (900 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 2:1) to give alcohol **20** (4.72 g, 94%) as a yellow oil.

R*f* = 0.32 (petroleum ether : ethyl acetate = 2:1).

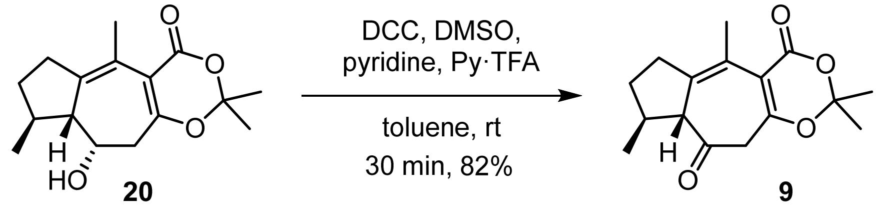
$[\alpha]_D^{20}$ = –36.0 (*c* 0.34, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (br s, 1H), 2.56 – 2.45 (m, 2H), 2.35 – 2.23 (m, 3H), 2.16 (br s, 1H), 2.01 – 1.95 (m, 5H), 1.66 (s, 6H), 1.30 – 1.21 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.26, 160.34, 145.05, 122.10, 108.73, 105.22, 79.67, 55.38, 40.71, 34.86, 34.07, 30.80, 25.48, 24.70, 20.41, 18.28.

HRMS (ESI): Calcd for $C_{16}H_{23}O_4$ $[M+H]^+$: 279.1591, found: 279.1587.

2.9 Synthesis of Ketone 9



To a stirred solution of alcohol **20** (4.7 g, 16.9 mmol) in anhydrous toluene (340 mL) was sequentially added DCC (11.15 g, 54 mmol), pyridine (1.74 g, 22 mmol), DMSO (19.79 g, 253 mmol) and pyridinium trifluoroacetate (3.91 g, 20.3 mmol) at ambient temperature under nitrogen and the mixture was stirred for 30 minutes. Upon completion, the reaction was diluted with petroleum ether (300 mL). The suspension was filtered and the residue was washed with EtOAc (3×500 mL). The combined organic phases were washed with brine (900 mL), the organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 20:1 to 10:1) to give ketone **9** (3.82 g, 82%) as a brown oil.

R*f* = 0.57 (petroleum ether : ethyl acetate = 5:1).

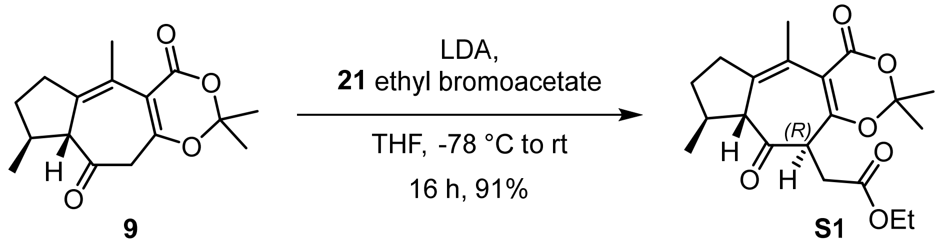
$[\alpha]_D^{20}$ = –209.7 (*c* 0.29, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.35 (d, *J* = 16.8 Hz, 1H), 3.13 (d, *J* = 16.8 Hz, 1H), 2.72 (s, 1H), 2.69 - 2.65 (m, 1H), 2.56 – 2.51 (m, 1H), 2.28 – 2.23 (m, 1H), 2.04 (s, 3H), 1.88 – 1.83 (m, 1H), 1.73 (s, 3H), 1.68 (s, 3H), 1.41 – 1.35 (m, 1H), 1.03 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 206.26, 160.27, 159.04, 139.89, 123.22, 110.07, 105.86, 64.62, 47.50, 34.17, 32.81, 29.90, 25.76, 24.58, 19.93, 18.69.

HRMS (ESI): Calcd for $C_{16}H_{21}O_4$ $[M+H]^+$: 277.1434, found: 277.1437.

2.10 Synthesis of Ester S1



To a stirred solution of diisopropylamine (2.24 mL, 15.95 mmol) in anhydrous THF (100 mL) was added *n*-BuLi (6.33 mL, 2.5 M, 15.81 mmol) dropwise through a syringe at -78 °C under nitrogen. After addition, the reaction flask was removed from the cold trap and warmed up to 0 °C. After being stirred at 0 °C for 30 minutes, the reaction flask was moved to the cold trap and cooled down to -78 °C. Then ketone **9** (3.80 g, 13.75 mmol) was introduced to the flask in one portion, and the reaction mixture was then stirred for 1 hour. Ethyl bromoacetate **21** (2.48 g, 14.85 mmol) was cannulated to the solution of ketone at -78 °C. The reaction mixture was allowed to stir at room temperature for about 16 hours. After TLC analysis, saturated aqueous solution of NH_4Cl (200 mL) was added to the reaction mixture, and the resulting suspension was extracted with EA (3×300 mL). The combined organic phases were washed with brine (800 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 20:1) to give ethyl ester **S1** (4.53 g, 91%) as a colorless oil.

R_f = 0.63 (petroleum ether : ethyl acetate = 5:1).

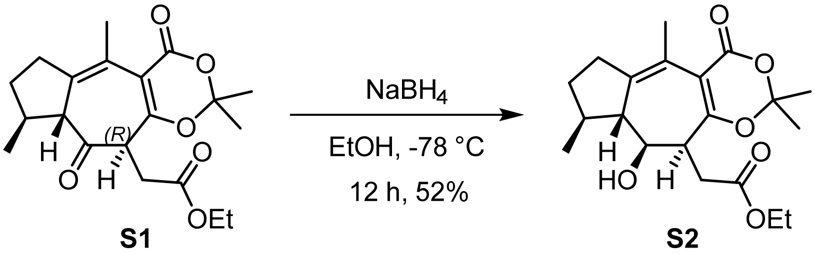
$[\alpha]_D^{20}$ = –160.7 (*c* 0.42, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.13 (q, *J* = 6.6 Hz, 2H), 3.83 (td, *J* = 6.6, 1.8 Hz, 1H), 2.92 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.76 (dd, *J* = 17.4, 7.2 Hz, 1H), 2.69 – 2.65 (m, 1H), 2.59 – 2.54 (m, 1H), 2.49 – 2.45 (m, 1H), 2.33 – 2.29 (m, 1H), 2.05 (s, 3H), 1.92 – 1.86 (m, 1H), 1.67 (s, 3H), 1.61 (s, 3H), 1.39 – 1.32 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 206.79, 171.88, 160.18, 158.85, 142.02, 123.22, 109.95, 106.17, 63.39, 61.00, 51.08, 36.77, 33.21, 30.58, 29.18, 25.31, 24.67, 19.91, 18.71, 14.34.

HRMS (ESI): Calcd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802, found: 363.1797.

2.11 Synthesis of Alcohol S2



To a stirred solution of ester **S1** (4.5 g, 12.42 mmol) in EtOH (124 mL) was added $NaBH_4$ (705 mg, 18.6 mmol) in one portion at -78 °C, and the resultant mixture was then stirred at this temperature for 12 hours. Upon completion, the reaction was carefully quenched with saturated aqueous solution of NH_4Cl (100 mL). The mixture was extracted with DCM (3×200 mL). The combined organic phases were washed with brine (600 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 2:1) to afford alcohol **S2** (2.08 g, 52%) as a colorless oil.

R*f* = 0.26 (petroleum ether : ethyl acetate = 2:1).

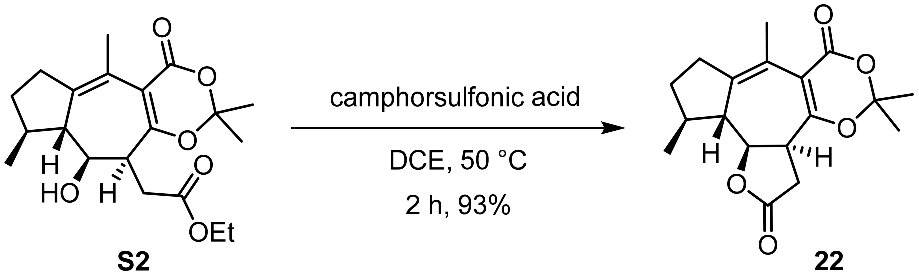
$[\alpha]_D^{20}$ = –44.2 (*c* 0.24, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (qd, *J* = 7.2, 1.2 Hz, 2H), 4.06 – 4.03 (m, 1H), 3.11 – 3.06 (m, 1H), 2.77 (dd, *J* = 16.4, 8.8 Hz, 1H), 2.53 – 2.42 (m, 2H), 2.38 – 2.30 (m, 1H), 2.10 – 2.06 (m, 2H), 1.99 – 1.94 (m, 3H), 1.92 – 1.85 (m, 2H), 1.72 (s, 3H), 1.65 (s, 3H), 1.49 – 1.42 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.53, 167.50, 160.23, 144.44, 123.21, 109.12, 106.08, 88.32, 60.86, 58.55, 42.88, 39.13, 33.02, 30.86, 28.71, 25.80, 24.51, 20.72, 18.21, 14.33.

HRMS (ESI): Calcd for $C_{20}H_{29}O_6$ $[M+H]^+$: 365.1959, found: 365.1956.

2.12 Synthesis of Lactone 22



To a stirred solution of alcohol **S2** (2.00 g, 6.31 mmol) in DCE (130 mL) was added camphorsulfonic acid (293.0 mg, 1.26 mmol) in one portion. The mixture was stirred for 2 hours at 50 °C. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (150 mL). The mixture was extracted with DCM (3×100 mL). The combined organic phases were washed with brine (300 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 5:1) to afford lactone **22** (1.87 g, 93%) as a white solid.

M.p.= 121.3 – 123.6 °C.

R*f* = 0.45 (petroleum ether : ethyl acetate = 5:1).

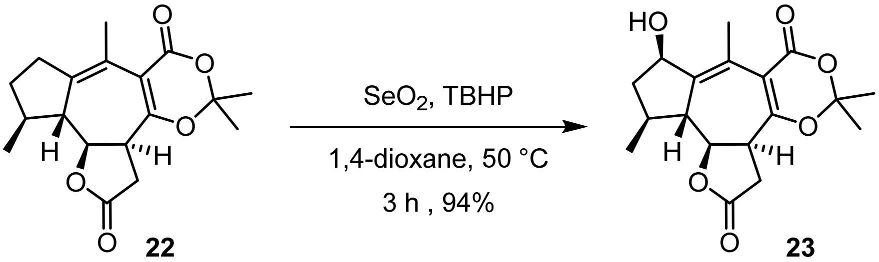
$[\alpha]_D^{20}$ = –185.1 (*c* 0.12, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.35 – 3.31 (m, 1H), 2.99 (dd, *J* = 17.6, 1.6 Hz, 1H), 2.54 (dd, *J* = 17.6, 9.2 Hz, 1H), 2.49 – 2.40 (m, 1H), 2.37 – 2.29 (m, 1H), 2.21 – 2.16 (m, 2H), 1.97 – 1.88 (m, 4H), 1.69 (d, *J* = 5.6 Hz, 6H), 1.52 – 1.45 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.10, 163.75, 159.60, 142.90, 123.30, 109.63, 106.33, 92.89, 53.40, 40.63, 37.97, 32.48, 29.34, 28.57, 25.47, 24.74, 20.05, 18.26.

HRMS (ESI): Calcd for $C_{18}H_{23}O_5$ $[M+H]^+$: 319.1540, found: 319.1540.

2.13 Synthesis of Alcohol 23



To a stirred solution of lactone **22** (1.87 g, 5.87 mmol) in 1,4-dioxane (60 mL) was added SeO_2 (717 mg, 6.46 mmol) and TBHP (2.35 mL, 5.5 M in pentane, 12.92 mmol) at room temperature. The reaction mixture was stirred at 50 °C for 3 hours before being quenched with saturated aqueous solution of $Na_2S_2O_3$ (100 mL). The aqueous layer was extracted with EtOAc (3×200 mL). The combined organic phases were washed with brine (600 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 5:1 to 3:1) to afford alcohol **23** (1.84 g, 94%) as a white solid.

M.p.= 154.6 – 158.1 °C.

R*f* = 0.15 (petroleum ether : ethyl acetate = 3:1).

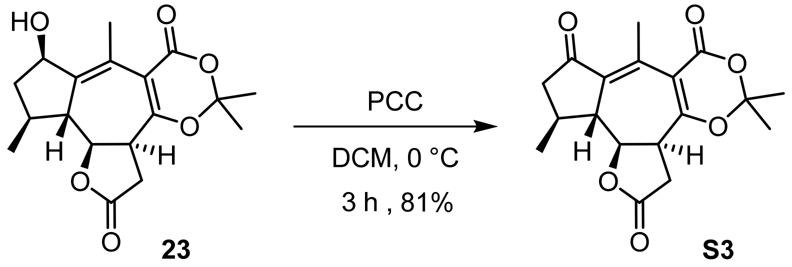
$[\alpha]_D^{20}$ = –198.4 (*c* 0.23, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (s, 1H), 4.54 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.37 – 3.32 (m, 1H), 3.05 (dd, *J* = 17.6, 1.2 Hz, 1H), 2.57 (dd, *J* = 18, 9.2 Hz, 1H), 2.42 (d, *J* = 11.2 Hz, 1H), 2.30 – 2.22 (m, 2H), 2.17 (d, *J* = 0.8 Hz, 3H), 1.74 (d, *J* = 7.6 Hz, 6H), 1.69 – 1.66 (m, 2H), 1.19 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.72, 164.48, 159.21, 144.90, 130.05, 109.76, 106.82, 92.43, 72.42, 53.88, 41.84, 40.64, 36.19, 29.35, 25.85, 24.64, 22.44, 18.57.

HRMS (ESI): Calcd for $C_{18}H_{26}NO_6$ $[M+NH_4]^+$: 352.1755, found: 352.1749.

2.14 Synthesis of Ketone S3



To the mixture of alcohol **23** (1.84 g, 5.5 mmol) and Al_2O_3 (9.48 g, basic) in anhydrous DCM (110 mL) was added PCC (2.37 g, 11 mmol) in one portion at 0 °C. After stirring 3 hours, the reaction was diluted with DCM (100 mL), the suspension was filtered and the residue was washed with DCM (3×100 mL). The combined filtrate was washed sequentially with saturated aqueous solution of $Na_2S_2O_3$ (300 mL), HCl (300 mL, 1 M) and brine (500 mL). The organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1) to give ketone **S3** (1.48 g, 81%) as a yellow solid.

M.p.= 183.1 – 184.2 °C.

R*f*= 0.33 (petroleum ether : ethyl acetate = 5:1).

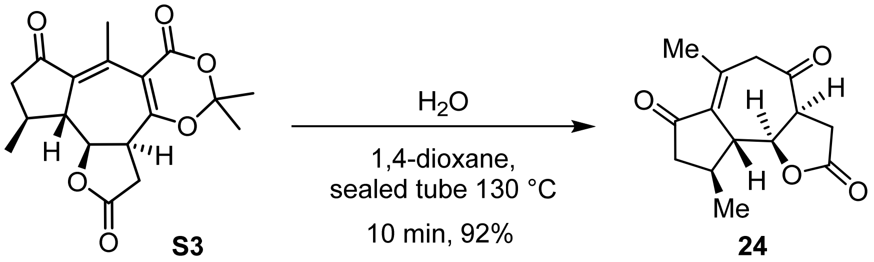
$[\alpha]_D^{20}$ = –407.4 (*c* 0.23, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (dd, *J* = 11.6, 6.8 Hz, 1H), 3.41 – 3.37 (m, 1H), 3.07 (d, *J* = 17.6 Hz, 1H), 2.75 (dd, *J* = 18.4, 8.4 Hz, 1H), 2.62 (dd, *J* = 18.0, 9.2 Hz, 1H), 2.50 – 2.42 (m, 5H), 2.16 (d, *J* = 18.4 Hz, 1H), 1.75 (d, *J* = 4.0 Hz, 6H), 1.05 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 205.09, 174.09, 166.72, 158.17, 145.79, 131.99, 109.92, 107.40, 91.83, 52.74, 46.94, 41.07, 29.67, 29.22, 25.74, 24.72, 22.49, 17.81.

HRMS (ESI): Calcd for $C_{18}H_{20}NaO_6^+$ $[M+Na]^+$: 355.1152, found: 355.1157.

2.15 Synthesis of Ketone 24



Ketone **S3** (1.48 g, 4.45 mmol) was dissolved in 1,4-dioxane (148 mL) at room temperature in a sealed tube and then H_2O (1.2 mL, 66.8 mmol) was added. The reaction mixture was stirred at 130 °C for 10 minutes. Upon completion, the reaction was cooled by ice-bath and poured to a saturated aqueous solution of $NaHCO_3$ (200 mL). The aqueous layer was extracted with EtOAc (3×300 mL). The combined organic phases were washed with brine (900 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 5:1 to 2:1) to afford ketone **24** (1.02 g, 92%) as a white solid.

M.p.= 146.4 – 151.1 °C.

R*f* = 0.34 (petroleum ether : ethyl acetate = 3:1).

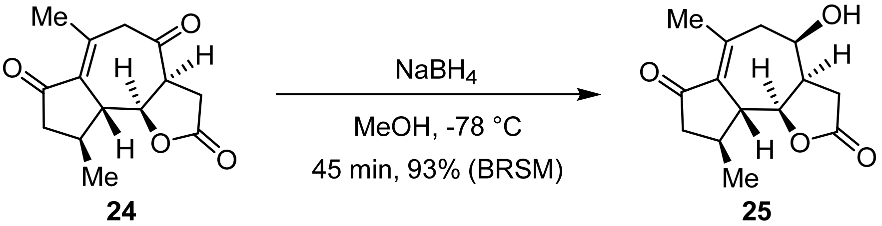
$[\alpha]_D^{20}$ = –202.4 (*c* 0.08, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.74 (dd, *J* = 12.0, 8.4 Hz, 1H), 3.65 – 3.61 (m, 2H), 3.17 – 3.09 (m, 2H), 2.68 (dd, *J* = 18.0, 8.4 Hz, 1H), 2.63 (d, *J* = 12.0 Hz, 1H), 2.56 (dd, *J* = 18.0, 9.0 Hz, 1H), 2.47 – 2.45 (m, 1H), 2.32 (s, 3H), 2.11 (dd, *J* = 18.6, 3.0 Hz, 1H), 1.06 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 205.31, 203.77, 174.75, 147.58, 130.59, 83.40, 53.59, 50.88, 48.33, 46.00, 30.04, 29.33, 22.09, 20.30.

HRMS (ESI): Calcd for $C_{14}H_{17}O_4$ $[M+H]^+$: 249.1121, found: 249.1118.

2.16 Synthesis of Alcohol 25



To a stirred solution of ketone **24** (1.02 g, 4.11 mmol) in MeOH (82 mL) was added $NaBH_4$ (124.2 mg, 3.29 mmol) in one portion at -78 °C. The mixture was stirred for 45 minutes at -78 °C. Upon completion, the reaction was quenched with saturated aqueous solution of NH_4Cl (100 mL). The mixture was extracted with DCM (3×200 mL). The combined organic phases were washed with brine (600 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 5:1 to 1:1) to afford alcohol **25** (451.1 mg, 44%, BRSM 93%) as a white solid as well as ketone **24** (480.2 mg, 47%).

M.p.= 113.7 – 116.1 °C.

R*f* = 0.23 (petroleum ether : ethyl acetate = 1:1).

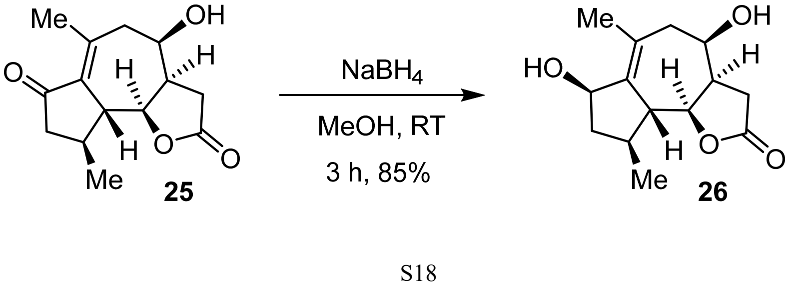
$[\alpha]_D^{20}$ = +39.3 (*c* 0.09, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.47 (dd, *J* = 11.4, 7.8 Hz, 1H), 4.06 (br s, 1H), 3.15 (d, *J* = 8.4 Hz, 1H), 2.92– 2.79 (m, 3H), 2.65 – 2.56 (m, 2H), 2.50 (d, *J* = 17.4 Hz, 1H), 2.30 – 2.25 (m, 5H), 2.04 (dd, *J* = 18.0, 7.2 Hz, 1H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 206.48, 176.29, 150.28, 131.09, 83.65, 66.99, 49.28, 47.14, 44.36, 42.87, 31.27, 30.48, 22.23, 21.67.

HRMS (ESI): Calcd for $C_{14}H_{19}O_4$ $[M+H]^+$: 251.1278, found: 251.1272.

2.17 Synthesis of Alcohol 26



To a stirred solution of ketone **25** (6.8 mg, 0.027 mmol) in MeOH (0.6 mL) was added $NaBH_4$ (2.1 mg, 0.054 mmol) in one portion at 0 °C. The mixture was stirred for 3 hours at ambient temperature. Upon completion, the reaction was quenched with saturated aqueous solution of NH_4Cl (5 mL). The mixture was extracted with DCM (3×5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 3:1 to 1:2) to afford alcohol **26** (5.8 mg, 85%) as a white solid.

M.p.= 145.6 – 148.5 °C.

R_f = 0.22 (petroleum ether : ethyl acetate = 1:2).

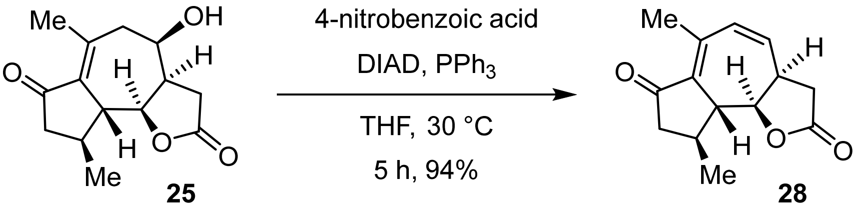
$[\alpha]_D^{20}$ = +27.3 (*c* 0.09, MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.71 (t, *J* = 6.0 Hz, 1H), 4.35 (dd, *J* = 10.8, 8.4 Hz, 1H), 4.01 (s, 1H), 2.90 (dd, *J* = 17.4, 11.4 Hz, 1H), 2.83 – 2.77 (m, 2H), 2.66 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.55 (br s, 1H), 2.49 (dd, *J* = 17.4, 9.0 Hz, 1H), 2.37 (d, *J* = 17.4 Hz, 1H), 2.28 – 2.23 (m, 1H), 2.00 (br s, 1H), 1.95 – 1.90 (m, 1H), 1.85 (s, 3H), 1.37 – 1.32 (m, 1H), 1.19 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.73, 139.53, 130.92, 84.90, 73.49, 66.46, 50.17, 43.83, 43.60, 41.20, 36.94, 29.67, 22.16, 21.80.

HRMS (ESI): Calcd for $C_{14}H_{21}O_4$ $[M+H]^+$: 253.1434, found: 253.1437.

2.18 Synthesis of Diene 28



To a stirred solution of alcohol **25** (6.0 mg, 0.024 mmol) in anhydrous THF (0.16 mL) was sequentially added PPh_3 (18.9 mg, 0.072 mmol), 4-nitrobenzoic acid (12.0 mg, 0.072 mmol) and DIAD (13 μL, 0.072 mmol) at ambient temperature, and the mixture was stirred for 5 hours under nitrogen atmosphere. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (5 mL). The mixture was extracted with EtOAc (3×5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 20:1 to 10:1) to give diene **28** (5.2 mg, 94%) as a white solid.

M.p.= 131.4 – 133.4 °C.

R*f* = 0.62 (petroleum ether : ethyl acetate = 5:1).

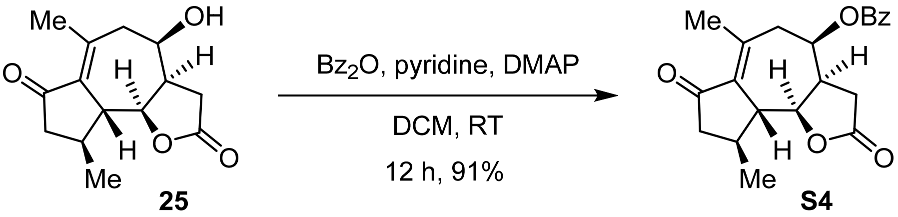
$[\alpha]_D^{20}$ = –318.1 (*c* 0.19, MeOH).

^{1}H NMR (600 MHz, CD_3OD) δ 6.20 (dd, *J* = 11.4, 1.8 Hz, 1H), 6.09 (dd, *J* = 11.4, 3.0 Hz, 1H), 4.79 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.28 – 3.23 (m, 1H), 2.94 (dd, *J* = 17.4, 9.6 Hz, 1H), 2.79 (dd, *J* = 18.0, 8.4 Hz, 1H), 2.62 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.50 (d, *J* = 12.0 Hz, 1H), 2.48 – 2.44 (m, 1H), 2.25 (d, *J* = 1.8 Hz, 3H), 2.09 (dd, *J* = 18.0, 4.2 Hz, 1H), 1.10 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, CD_3OD) δ 208.42, 177.78, 149.00, 138.74, 135.31, 132.27, 92.79, 54.10, 47.95, 39.73, 36.24, 30.97, 22.74, 18.68.

HRMS (ESI): Calcd for $C_{14}H_{17}O_3$ $[M+H]^+$: 233.1172, found: 233.1177.

2.19 Synthesis of Ester S4



To a stirred solution of ketone **25** (988.0 mg, 3.95 mmol) in DCM (79 mL) was added Bz_2O (1.79 g, 7.89 mmol), pyridine (1.27 mL, 15.79 mmol) and DMAP (144.7 mg, 1.18 mmol) at 0 °C. The mixture was stirred for 12 hours at ambient temperature. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (80 mL). The mixture was extracted with DCM (3×80 mL). The combined organic phases were washed with brine (200 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 20:1 to 10:1) to afford ester **S4** (1.28 g, 91%) as a white solid.

M.p.= 133.2 – 136.8 °C.

R*f* = 0.27 (petroleum ether : ethyl acetate = 10:1).

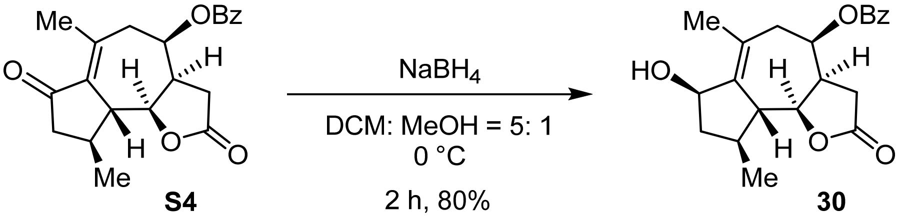
$[\alpha]_D^{20}$ = –71.5 (*c* 0.31, $CHCl_3$).

^{1}H NMR (400 MHz, CD_3OD) δ 8.02 – 7.99 (m, 2H), 7.65 – 7.61 (m, 1H), 7.52 – 7.48 (m, 2H), 5.32 (q, *J* = 4.4 Hz, 1H), 4.73 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.28 (br s, 1H), 3.18 – 3.07 (m, 2H), 2.85 (dd, *J* = 17.6, 9.2 Hz, 1H), 2.77 – 2.66 (m, 3H), 2.42 – 2.36 (m, 1H), 2.26 (d, *J* = 1.6 Hz, 3H), 2.05 (dd, *J* = 17.6, 5.2 Hz, 1H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, CD_3OD) δ 207.99, 178.28, 166.98, 152.73, 134.67, 131.40, 130.96, 130.56, 129.79, 84.32, 72.11, 50.73, 47.41, 41.84, 41.82, 32.57, 32.04, 22.44, 21.17.

HRMS (ESI): Calcd for $C_{21}H_{22}NaO_5$ $[M+Na]^+$: 377.1359, found: 377.1356.

2.20 Synthesis of Alcohol 30



To a stirred solution of ester **S4** (1.20 g, 3.39 mmol) in a mixture solvent (68 mL, DCM: MeOH = 5:1, v/v) was added $NaBH_4$ (192 mg, 5.08 mmol) in one portion at 0 °C, and the mixture was stirred for 2 hours. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (50 mL). The mixture was extracted with DCM (3×100 mL). The combined organic phases were washed with brine (300 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 20:1 to 10:1) to afford alcohol **30** (966.1 mg, 80%) as a white solid.

M.p.= 145.5 – 152.4 °C.

R*f* = 0.25 (petroleum ether : ethyl acetate = 10:1).

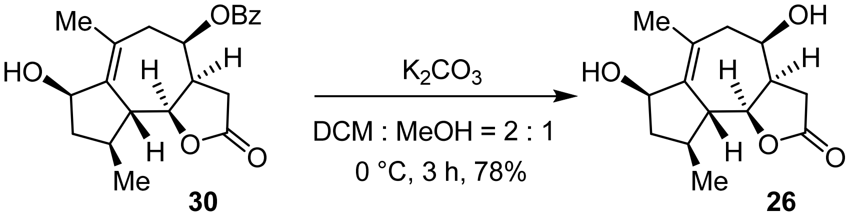
$[\alpha]_D^{20}$ = –23.5 (*c* 0.11, $CHCl_3$).

^{1}H NMR (600 MHz, CD_3OD) δ 8.01 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 5.31 (q, *J* = 4.2 Hz, 1H), 4.72 (s, 1H), 4.51 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.14 – 3.07 (m, 2H), 2.90 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.76 (dd, *J* = 18.0, 9.0 Hz, 1H), 2.66 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.46 (dd, *J* = 17.4, 2.4 Hz, 1H), 2.21 – 2.14 (m, 2H), 1.88 (s, 3H), 1.49 (dt, *J* = 12.6, 5.4 Hz, 1H), 1.24 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, CD_3OD) δ 178.58, 167.20, 139.37, 134.53, 132.92, 131.20, 130.57, 129.73, 85.82, 74.26, 72.69, 51.92, 43.16, 42.20, 39.50, 38.08, 32.36, 22.60, 21.67.

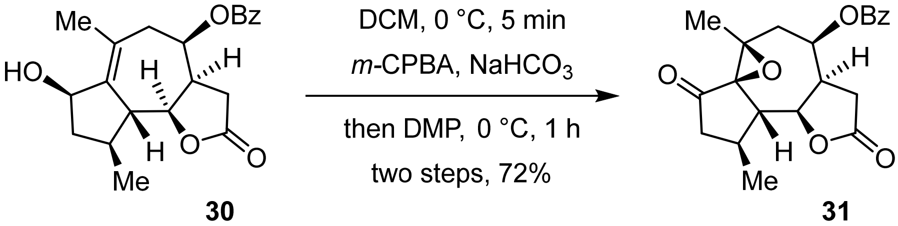
HRMS (ESI): Calcd for $C_{21}H_{24}NaO_5$ $[M+Na]^+$: 379.1516, found: 379.1515.

2.21 Hydrolysis of Alcohol 30



To a stirred solution of alcohol **30** (7.8 mg, 0.022 mmol) in a mixture solvent (400 μL, DCM: MeOH = 2:1, v/v) was added K_2CO_3 (30.3 mg, 0.22 mmol) in one portion at 0 °C, and the mixture was stirred for 3 hours. Upon completion, the reaction was quenched with saturated aqueous solution of NH_4Cl (2 mL). The mixture was extracted with EtOAc (3×5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 1:1 to 1:5) to afford alcohol **26** (4.3 mg, 78%) as a white solid. The NMR spectra of this compound agree well with the intermediate **26** which was obtained from the reduction of enone **25**.

2.22 Synthesis of Ketone 31



To a stirred solution of alcohol **30** (960.0 mg, 2.69 mmol) in DCM (54 mL) was added $NaHCO_3$ (905.1 mg, 10.8 mmol) and *m*-CPBA (1.09 g, 85%, 5.39 mmol) sequentially at 0 °C. The resultant mixture was then stirred at 0 °C for 5 minutes. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (50 mL). The mixture was extracted with DCM (3×50 mL). The combined organic phases were washed with brine (150 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was used for next step without further purification.

To a stirred solution of above crude product in DCM (43 mL) was added DMP (1.82 g, 4.3 mmol) at 0 °C, and the mixture was stirred for 1 hour. Upon completion, the reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (50 mL). The mixture was extracted with DCM (3×50 mL). The combined organic phases were washed with brine (150 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to afford ketone **31** (723.1 mg, 72%) as a white solid.

M.p.= 183.8 – 190.5 °C.

R*f* = 0.21 (petroleum ether : ethyl acetate = 10:1).

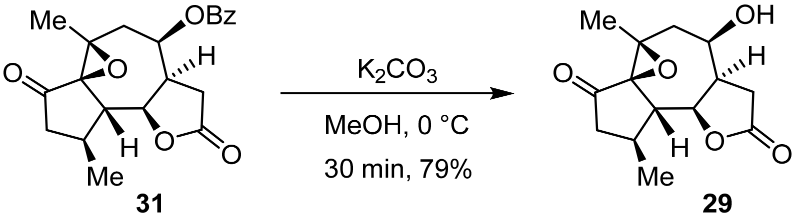
$[\alpha]_D^{20}$ = –95.2 (*c* 0.17, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 15.2 Hz, 2H), 5.42 – 5.37 (m, 1H), 4.74 (dd, *J* = 11.6, 7.2 Hz, 1H), 3.42 – 3.34 (m, 1H), 2.81 – 2.59 (m, 4H), 2.36 – 2.23 (m, 4H), 1.69 (s, 3H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 212.44, 174.38, 165.53, 133.82, 129.78, 129.35, 128.79, 78.36, 67.60, 64.29, 63.71, 49.09, 44.32, 42.46, 38.74, 29.56, 28.54, 21.35, 17.19.

HRMS (ESI): Calcd for $C_{21}H_{22}NaO_6$ $[M+Na]^+$: 393.1309, found: 393.1311.

2.23 Synthesis of Alcohol 29



To a stirred solution of ketone **31** (720.2 mg, 1.94 mmol) in MeOH (38 mL) was added K_2CO_3 (537.1 mg, 3.89 mmol) in one portion at 0 °C, and the mixture was stirred for 30 minutes. Upon completion, the suspension was filtered and the residue was washed with EtOAc (3×30 mL). The combined filtrate was washed with saturated aqueous solution of NH_4Cl (100 mL), brine (100 mL), the organic phases were dried over anhydrous Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1 to 1:1) to give alcohol **29** (409 mg, 79%) as a pale-yellow oil.

R_f = 0.15 (petroleum ether : ethyl acetate = 2:1).

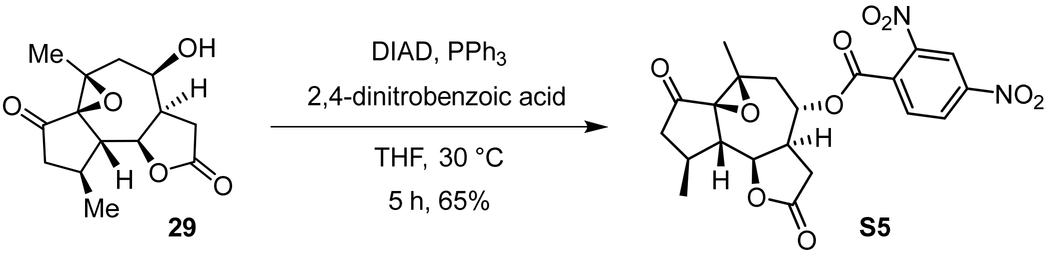
$[\alpha]^{20}_{D}$ = –83.1 (*c* 0.18, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.71 (dd, J = 12.0, 8.0 Hz, 1H), 3.99 (d, J = 4.0 Hz, 1H), 3.53 (d, J = 5.6 Hz, 1H), 3.03 – 2.96 (m, 1H), 2.91 – 2.83 (m, 1H), 2.79 – 2.68 (m, 3H), 2.57 (d, J = 12.0 Hz, 1H), 2.46 (dd, J = 17.2, 8.0 Hz, 1H), 2.16 (d, J = 16.0 Hz, 2H), 1.46 (s, 3H), 1.08 (d, J = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 210.53, 175.66, 79.05, 68.00, 67.15, 65.34, 46.87, 44.33, 43.86, 38.04, 28.70, 28.28, 22.16, 19.20.

HRMS (ESI): Calcd for $C_{14}H_{18}NaO_5$ $[M+Na]^+$: 289.1046, found: 289.1050.

2.24 Synthesis of Ester S5



To a stirred solution of alcohol **29** (400.0 mg, 1.94 mmol) in anhydrous THF (15 mL) was sequentially added PPh_3 (1.18 g, 4.51 mmol), 2,4-dinitrobenzoic acid (956 mg, 4.51 mmol) and DIAD (885 µL, 4.51 mmol) at 30 °C, and the mixture was stirred for 5 hours under nitrogen atmosphere. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL). The mixture was extracted with EtOAc (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to give ester **S5** (451.1 mg, 65%) as a colorless oil.

R*f* = 0.38 (petroleum ether : ethyl acetate = 5:1).

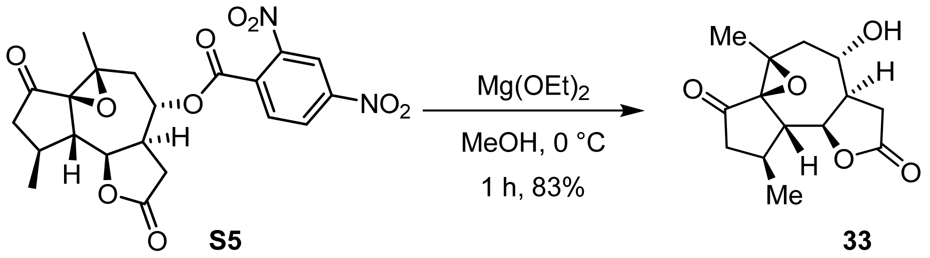
$[\alpha]_D^{20}$ = –70.9 (*c* 0.08, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 2.0 Hz, 1H), 8.57 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 5.18 – 5.13 (m, 1H), 4.72 (dd, *J* = 12.4, 8.4 Hz, 1H), 3.11 – 3.01 (m, 1H), 2.83 – 2.78 (m, 1H), 2.74 – 2.68 (m, 2H), 2.65 – 2.58 (m, 2H), 2.35 – 2.28 (m, 2H), 2.18 (d, *J* = 16.8 Hz, 1H), 1.47 (s, 3H), 1.14 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 210.44, 173.95, 162.80, 149.32, 147.94, 132.26, 131.57, 127.98, 119.87, 77.12, 72.20, 66.36, 64.33, 46.91, 44.35, 44.00, 39.68, 31.54, 28.25, 22.31, 18.62.

HRMS (ESI): Calcd for $C_{21}H_{20}N_2NaO_{10}$ $[M+Na]^+$: 483.1010, found: 483.1009.

2.25 Synthesis of Alcohol 33



To a stirred solution of ester **S5** (450.0 mg, 0.98 mmol) in MeOH (15 mL) was added $Mg(OEt)_2$ (559.2 mg, 4.89 mmol) at 0 °C, and the mixture was stirred for 1 hour. Upon completion, the suspension was filtered and the residue was washed with EtOAc (3×20 mL). The combined filtrate was washed with saturated aqueous solution of NH_4Cl (50 mL), brine (50 mL), the organic phases were dried over anhydrous Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5:1 to 1:1) to give alcohol **33** (216.2 mg, 83%) as a pale-yellow oil.

R*f* = 0.13 (petroleum ether : ethyl acetate = 2:1).

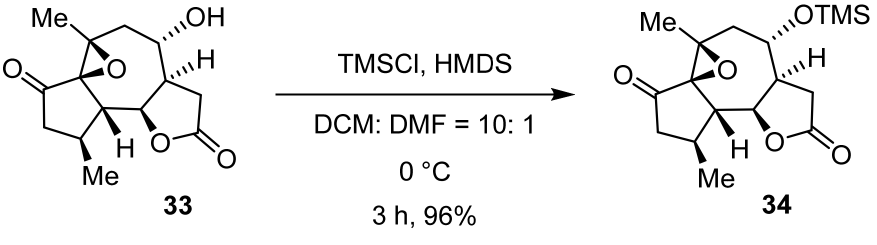
[α]$^{20}_{D}$ = –75.2 (*c* 0.15, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.65 (dd, *J* = 12.0, 7.8 Hz, 1H), 3.69 (t, *J* = 9.6 Hz, 1H), 2.84 – 2.76 (m, 3H), 2.69 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.51 – 2.47 (m, 1H), 2.43 (d, *J* = 15.6 Hz, 1H), 2.20 (dd, *J* = 15.6, 10.8 Hz, 1H), 2.16 – 2.13 (m, 2H), 1.99 (br s, 1H), 1.43 (s, 3H), 1.09 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 211.14, 175.17, 77.58, 66.74, 66.62, 64.78, 47.16, 46.64, 44.23, 43.96, 32.31, 28.18, 22.21, 18.81.

HRMS (ESI): Calcd for $C_{14}H_{18}NaO_5$ $[M+Na]^+$: 289.1046, found: 289.1047.

2.26 Synthesis of Silyl Ether 34



To a stirred solution of alcohol **33** (210.0 mg, 0.79 mmol) in a mixture solvent (15 mL, DCM: DMF = 10:1, v/v) were added TMSCl (150 μL, 1.18 mmol) and HMDS (493 μL, 2.37 mmol) at 0 °C, and the mixture was stirred for 3 hours. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL). The mixture was extracted with DCM (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 20:1 to 10:1) to give silyl ether **34** (257 mg, 96%) as a white solid.

M.p.= 158.5 – 161.1 °C.

R*f* = 0.44 (petroleum ether : ethyl acetate = 10: 1).

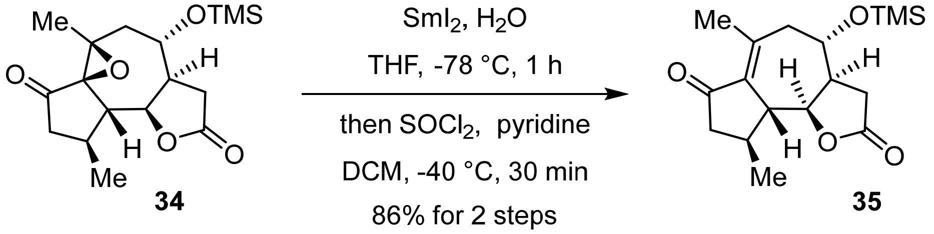
$[\alpha]_D^{20}$ = –73.6 (*c* 0.07, $CHCl_3$).

^{1}H NMR (400 MHz, CD_3OD) δ 4.89 – 4.83 (m, 1H), 3.71 (td, *J* = 10.0, 2.8 Hz, 1H), 2.88 – 2.79 (m, 2H), 2.73 – 2.65 (m, 1H), 2.59 (dd, *J* = 10.0, 0.8 Hz, 2H), 2.38 – 2.20 (m, 3H), 2.06 – 2.01 (m, 1H), 1.36 (s, 3H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.14 (s, 9H).

^{13}C NMR (100 MHz, CD_3OD) δ 213.42, 177.89, 79.25, 68.50, 68.25, 66.21, 48.40, 47.68, 44.98, 44.67, 33.38, 29.38, 22.08, 18.86, 0.18.

HRMS (ESI): Calcd for $C_{17}H_{26}NaO_5Si$ $[M+Na]^+$: 361.1442, found: 361.1442.

2.27 Synthesis of Unsaturated Ketone 35



To a stirred solution of silyl ether **34** (250.0 mg, 0.74 mmol) and H_2O (1.33 mL, 74 mmol) in THF (25 mL) was added SmI_2 (0.1 M in THF, 37 mL, 3.69 mmol) dropwise under nitrogen at -78 °C. The resultant mixture was stirred at -78 °C for 1 hour. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (50 mL). The mixture was extracted with EtOAc (3×80 mL). The combined organic phases were washed with brine (250 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was used for next step without further purification.

To a stirred solution of above crude product in DCM (15 mL) were added pyridine (475 μL, 5.9 mmol) and $SOCl_2$ (161 μL, 2.21 mmol) at -40 °C, and the mixture was stirred for 30 minutes. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL). The mixture was extracted with DCM (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to afford unsaturated ketone **35** (204.1mg, 86%) as a yellow solid.

M.p.= 111.4 – 114.0 °C.

R_f = 0.41 (petroleum ether : ethyl acetate = 5:1).

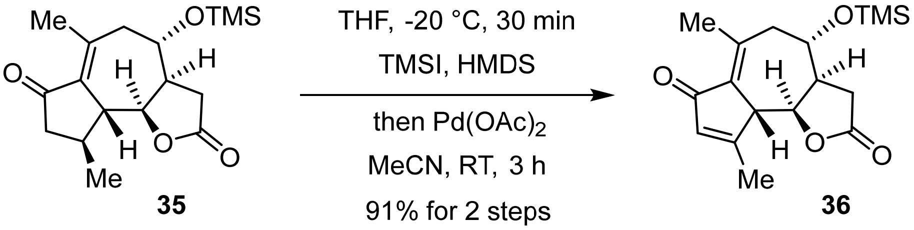
$[\alpha]_D^{20}$ = +106 (*c* 0.07, $CHCl_3$).

^{1}H NMR (600 MHz, CD_3OD) δ 4.62 (dd, *J* = 11.4, 7.8 Hz, 1H), 4.18 (td, *J* = 10.2, 3.6 Hz, 1H), 2.97 – 2.94 (m, 1H), 2.79 – 2.73 (m, 1H), 2.72 – 2.62 (m, 3H), 2.60 – 2.52 (m, 2H), 2.19 – 2.15 (m, 4H), 2.01 (dd, *J* = 17.4, 9.0 Hz, 1H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.15 (s, 9H).

^{13}C NMR (150 MHz, CD_3OD) δ 208.08, 178.36, 152.73, 131.62, 85.33, 69.57, 49.34, 48.81, 47.97, 46.88, 33.48, 33.39, 21.88, 21.83, 0.11.

HRMS (ESI): Calcd for $C_{17}H_{27}O_4Si$ $[M+H]^+$: 323.1673, found: 323.1675.

2.28 Synthesis of enone 36



To a stirred solution of unsaturated ketone **35** (200.0 mg, 0.62 mmol) in anhydrous THF (13 mL) were sequentially added HMDS (647 μL, 3.1 mmol) and TMSI (308 μL, 2.17 mmol) at -20 °C. The resultant mixture was stirred at -20 °C for 30 minutes. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL). The mixture was extracted with EtOAc (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was used for next step without further purification.

To a stirred solution of above crude product in MeCN (12 mL) was added $Pd(OAc)_2$ (208.0 mg, 0.93 mmol) at room temperature, and the mixture was stirred for 3 hours. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL). The mixture was extracted with EtOAc (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to afford enone **36** (181.2 mg, 91%) as a brown oil.

R*f* = 0.32 (petroleum ether : ethyl acetate = 5:1).

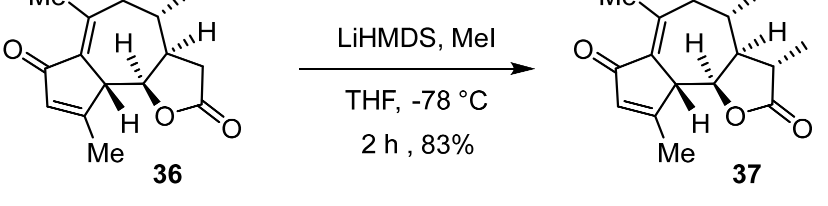
$[\alpha]_D^{20}$ = –56.9 (*c* 0.13, $CHCl_3$).

^{1}H NMR (600 MHz, CD_3OD) δ 6.11 (s, 1H), 4.48 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.35 (td, *J* = 9.6, 4.8 Hz, 1H), 3.81 (d, *J* = 10.8 Hz, 1H), 3.00 (dd, *J* = 19.2, 4.8 Hz, 1H), 2.77 – 2.69 (m, 2H), 2.67 – 2.62 (m, 1H), 2.41 (dd, *J* = 19.2, 9.6 Hz, 1H), 2.25 (d, *J* = 6.0 Hz, 6H), 0.17 (s, 9H).

^{13}C NMR (150 MHz, CD_3OD) δ 198.25, 178.29, 174.62, 149.48, 134.94, 129.29, 84.55, 67.09, 49.99, 49.49, 45.86, 32.42, 20.41, 19.15, 0.03.

HRMS (ESI): Calcd for $C_{17}H_{25}O_4Si$ $[M+H]^+$: 321.1517, found: 321.1520.

2.29 Synthesis of α-methyl Lactone 37



To a stirred solution of enone **36** (50.0 mg, 0.16 mmol) in anhydrous THF (3.2 mL) was added LiHMDS (468 μL, 1 M in THF, 0.47 mmol) dropwise under nitrogen at -78 °C. The resultant mixture was stirred at -78 °C for 1 hour, MeI (97 μL, 1.56 mmol) was added via a syringe and the reaction mixture was stirred at -78 °C for 1 hour. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (30 mL). The mixture was extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine (60 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to afford α-methyl lactone **37** (44.1 mg, 83%) as a white solid.

M.p.= 98.8 – 101.5 °C.

R_f = 0.53 (petroleum ether : ethyl acetate = 5:1).

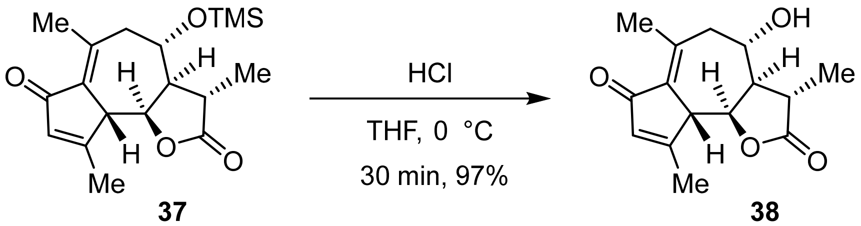
$[\alpha]_D^{20}$ = –11.4 (*c* 0.07, $CHCl_3$).

^{1}H NMR (600 MHz, CD_3OD) δ 6.13 (s, 1H), 4.44 (dd, *J* = 10.8, 7.8 Hz, 1H), 4.38 (td, *J* = 9.6, 3.6 Hz, 1H), 3.81 (d, *J* = 10.8 Hz, 1H), 2.89 (dd, *J* = 18.6, 3.6 Hz, 1H), 2.86 – 2.82 (m, 1H), 2.46 (dd, *J* = 18.0, 9.0 Hz, 1H), 2.40 (q, *J* = 7.8 Hz, 1H), 2.26 (d, *J* = 10.2 Hz, 6H), 1.32 (d, *J* = 7.2 Hz, 3H), 0.18 (s, 9H).

^{13}C NMR (150 MHz, CD_3OD) δ 198.15, 180.78, 174.85, 149.80, 135.52, 130.13, 82.29, 68.80, 54.14, 49.48, 47.31, 38.71, 20.99, 19.79, 16.26, 0.05.

HRMS (ESI): Calcd for $C_{18}H_{27}O_4Si$ $[M+H]^+$: 335.1673, found: 335.1667.

2.30 Synthesis of Alcohol 38



37 **38**

To a stirred solution of α-methyl lactone **37** (40.0 mg, 0.12 mmol) in THF (2.4 mL) was added HCl (60 μL, 4 M in dioxane, 0.24 mmol) at 0 °C, and the mixture was stirred for 30 minutes. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (5 mL). The mixture was extracted with EtOAc (3×10 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 3:1 to 1:2) to give alcohol **38** (30.2 mg, 97%) as a white solid.

M.p.= 155.8 – 159.0 °C.

R*f* = 0.17 (petroleum ether : ethyl acetate = 1:1).

$[\alpha]_D^{20}$ = –48.1 (*c* 0.13, $CHCl_3$).

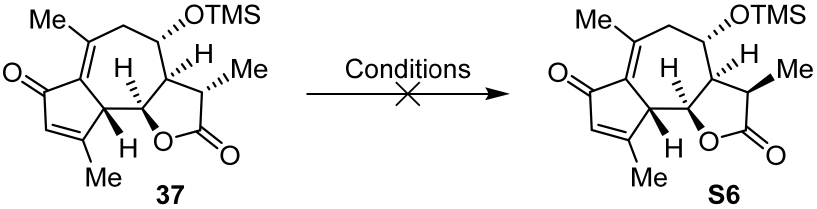
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.15 (s, 1H), 4.42 (t, *J* = 10.2 Hz, 1H), 4.30 (s, 1H), 3.49 (d, *J* = 10.8 Hz, 1H), 2.95 – 2.93 (m, 2H), 2.46 (dd, *J* = 18.6, 10.2 Hz, 1H), 2.35 – 2.32 (m, 1H), 2.30 (s, 3H), 2.24 (s, 3H), 1.82 (d, *J* = 5.4 Hz, 1H), 1.39 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 195.72, 178.64, 170.98, 146.31, 135.42, 128.81, 80.50, 66.87, 52.18, 48.49, 48.03, 37.67, 20.47, 19.80, 16.78.

HRMS (ESI): Calcd for $C_{15}H_{19}O_4$ $[M+H]^+$: 263.1278, found: 263.1268.

2.31 Studies on the Epimerization of the C-11 Stereochemistry from 37

Table S2 Attempted conditions for epimerization of the C-11 stereochemistry from **37**



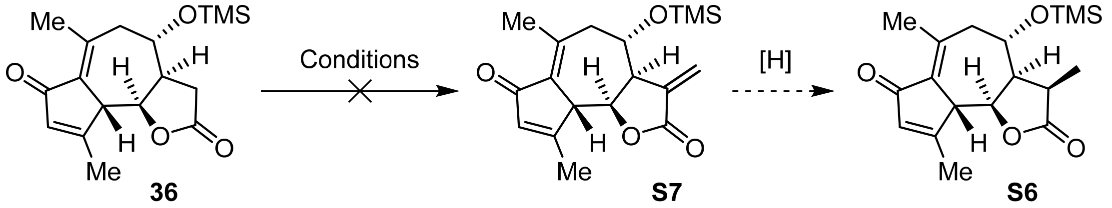
Entry[a]	Base[b]	Additive	Proton source[c]	Temperature	Results
1	KHMDS	-	AcOH	-78 °C to 0 °C	Recovery of **37**
2	NaHMDS	-	AcOH	-78 °C to 0 °C	Recovery of **37**
3	NaHMDS	TBAF[d]	AcOH	-78 °C to 0 °C	Recovery of **37**
4	NaHMDS	-	Benzoic acid	-78 °C to 0 °C	Recovery of **37**
5	NaHMDS	-	Phenol	-78 °C to 0 °C	Recovery of **37**
6	LiHMDS	-	BHT	-78 °C to 0 °C	Recovery of **37**
7	LiHMDS	-	TFA·Py	-78 °C to 0 °C	Recovery of **37**
8	LiHMDS	-	Benzoic acid	-78 °C to 0 °C	Recovery of **37**
9	LiHMDS	-	AcOH	-78 °C to 0 °C	Recovery of **37**
10	LDA	-	AcOH	-78 °C to 0 °C	Recovery of **37**
11	LiTMP	-	BHT	-78 °C to 0 °C	Recovery of **37**

12	$LiNEt_2$	-	BHT	-78 °C to 0 °C	Recovery of **37**
13	$LiNEt_2$	-	Phenol	-78 °C to 0 °C	Recovery of **37**
14	DBU[e]	-	MeOH	0 °C to 80 °C	Decomposed
15	K_2CO_3[e]	-	Phenol	Reflux	Decomposed

[a] Reactions conducted on a 5 mg scale under nitrogen atmosphere in 0.05 M THF. [b] Base (3 equiv). [c] proton source (10 equiv). [d] additive (2 eq.). [e] solvent (toluene)

2.32 Studies on the Methylenation of C-11 Position from 36

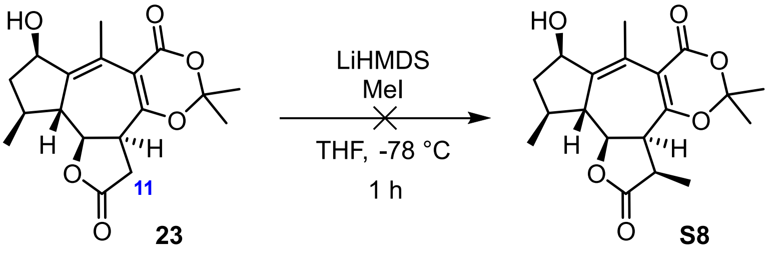
Table S3 Attempted conditions for alkylation at C11 from **36**



Entry[a]	Conditions	Result
1	LiHMDS[b], eschenmoser's salt (5 eq.)	Recovery of **36**
2	LiHMDS[c], eschenmoser's salt (10 eq.)	Recovery of **36**
3	LDA[c], eschenmoser's salt (10 eq.)	Recovery of **36**
4	NaHMDS[b], eschenmoser's salt (5 eq.)	Recovery of **36**
5	KHMDS[b], eschenmoser's salt (5 eq.)	Recovery of **36**
6	LiTMP[b], eschenmoser's salt (5 eq.)	Recovery of **36**
7	LiHMDS[b], 2-(hydroxymethyl)isoindoline-1,3-dione (3 eq.)	Recovery of **36**
8	LiHMDS[b]methyl formate (5 eq.)	Recovery of **36**
9	LiHMDS[b]paraformaldehyde (5 eq.)	Recovery of **36**
10	LiHMDS[b]diethyl chlorophosphate (5 eq.)	Recovery of **36**

[a] Reactions conducted on a 5 mg scale under nitrogen atmosphere in 0.05 M THF at -78 °C. [b] Base (2 equiv). [c] Base (5 equiv).

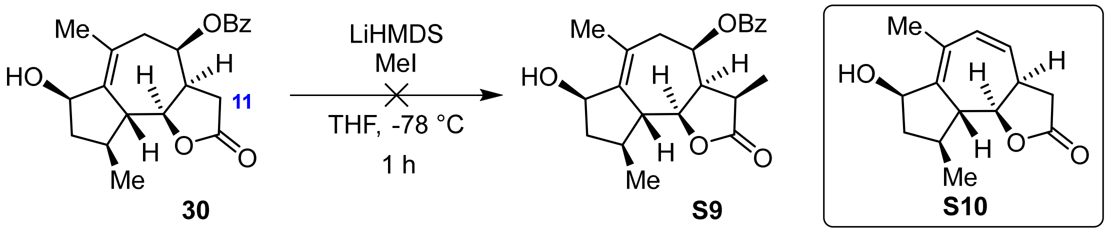
2.33 Studies on the Methylation of C11 Position from 23



To a stirred solution of alcohol **23** (5.0 mg, 0.015 mmol) in anhydrous THF (0.3

mL) was added LiHMDS (45 µL, 1 M in THF, 0.045 mmol) dropwise under nitrogen at -78 °C. The resultant mixture was stirred at -78 °C for 1 hour, MeI (9.3 µL, 0.149 mmol) was added via a syringe and the reaction mixture was stirred at -78 °C for 1 hour. Upon completion, this reaction unfortunately provided a complex mixture.

2.34 Studies on the Methylation of C11 Position from 30



To a stirred solution of alcohol **30** (5 mg, 0.014 mmol) in anhydrous THF (0.28 mL) was added LiHMDS (42 µL, 1 M in THF, 0.042 mmol) dropwise under nitrogen at -78 °C. The resultant mixture was stirred at -78 °C for 1 hour, MeI (8.7 µL, 0.140 mmol) was added via a syringe and the reaction mixture was stirred at -78 °C for 1 hour. Upon completion, the reaction was quenched with H_2O (1 mL). The mixture was washed with EtOAc (3×2 mL). The combined organic phases were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 3:1 to 1:1) to afford conjugated diene **S10** (2.6 mg, 79%) as a yellow oil.

R_f = 0.21 (petroleum ether : ethyl acetate = 2:1).

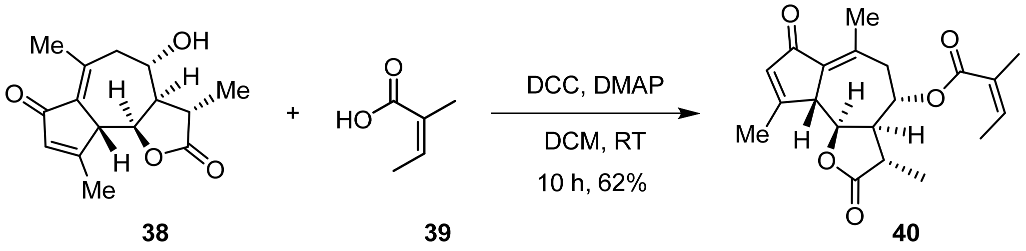
$[\alpha]_D^{20}$ = –35.5 (*c* 0.33, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (dd, *J* = 11.2, 2.2 Hz, 1H), 5.68 (dd, *J* = 11.2, 3.2 Hz, 1H), 4.82 (s, 1H), 4.43 (dd, *J* = 10.8, 9.6 Hz, 1H), 3.19 – 3.11 (m, 1H), 2.79 (dd, *J* = 18.0, 9.6 Hz, 1H), 2.49 (dd, *J* = 17.6, 6.8 Hz, 1H), 2.36 (d, *J* = 11.6 Hz, 1H), 2.33 – 2.29 (m, 1H), 2.27 – 2.20 (m, 1H), 1.93 (s, 3H), 1.62 – 1.57 (m, 2H), 1.19 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.70, 141.91, 134.03, 132.90, 130.44, 90.73, 73.63, 53.51, 42.67, 38.21, 35.77, 35.17, 22.73, 19.00.

HRMS (ESI): Calcd for $C_{14}H_{19}O_3$ $[M+H]^+$: 235.1329, found: 235.1333.

2.35 Synthesis of 11-*epi*-badkhysin 40



11-*epi*-badkhysin

To a stirred solution of alcohol **38** (10.0 mg, 0.04 mmol) in DCM (0.38 mL) were added DCC (15.7 mg, 0.08 mmol), angelica acid **39** (7.6 mg, 0.08 mmol) and DMAP (9.3 mg, 0.08 mmol) at ambient temperature, and the mixture was stirred for 10 hours. Upon completion, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (5 mL). The mixture was extracted with DCM (3×5 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to 5:1) to give **40** (8.2 mg, 62 %) as a colorless oil.

R*f* = 0.64 (petroleum ether : ethyl acetate = 5:1).

$[\alpha]_D^{20}$ = +21.3 (*c* 0.16, $CHCl_3$).

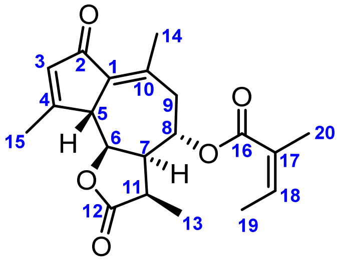
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.88 (q, *J* = 6.6 Hz, 1H), 6.18 (s, 1H), 5.47 (t, *J* = 8.4 Hz, 1H), 4.44 – 4.41 (m, 1H), 3.60 (d, *J* = 10.8 Hz, 1H), 2.95 (d, *J* = 17.4 Hz, 1H), 2.69 (p, *J* = 7.2 Hz, 1H), 2.59 (q, *J* = 8.4 Hz, 1H), 2.47 (dd, *J* = 18.0, 9.6 Hz, 1H), 2.27 (d, *J* = 11.4 Hz, 6H), 1.84 (s, 3H), 1.82 (s, 3H), 1.36 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 195.50, 177.63, 170.82, 166.96, 146.09, 139.08, 135.70, 129.09, 128.19, 80.22, 69.00, 50.15, 48.50, 42.63, 37.30, 20.44, 19.93, 16.10, 14.72, 12.20.

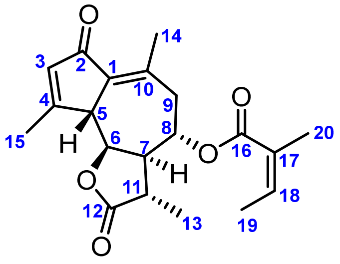
HRMS (ESI): Calcd for $C_{20}H_{25}O_5$ $[M+H]^+$: 345.1697, found: 345.1691.

3. Spectral Data Comparison

Table S4. Comparison of ^{1}H NMR spectra



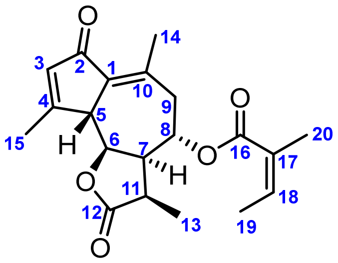
badkhysin



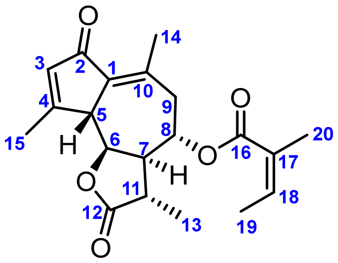
11-*epi*-badkhysin

Position	Natural sample **badkhysin** Dračínský (2012)[2] (600 MHz, $CDCl_3$) δ_H	Semi-synthetic sample **badkhysin** Alejandro (1994)[3] (300 MHz, $CDCl_3$) δ_H, mult (*J* in Hz)	Synthetic sample **11-*epi*-badkhysin** This work (600 MHz, $CDCl_3$) δ_H, mult (*J* in Hz)
H-3	6.17	6.09, m	6.18, s
H-5	3.60	3.54, d (10.9)	3.60, d (11)
H-6	4.46	4.39, dd (10.6, 8.2)	4.43, m
H-7	3.08	3.04, dt (10.5, 8.4)	2.59, q (8.1)
H-8	5.50	5.43, ddd (10.5, 9.5, 3.7)	5.47, t (9.1)
H-9α	2.52	2.46, dd (18.3, 9.4)	2.47, dd (17.9, 9.7)
H-9β	2.94	2.87, dd (18.4, 3.7)	2.95, d (17.8)
H-11	2.86	2.78, dq (8.4, 7.8)	2.69, p (7.3)
H-13	1.35	1.28, d	1.36, d (7.1)
H-14	2.29	2.21, s	2.28, s
H-15	2.26	2.19, s	2.26, s
H-18	6.18	6.10, qq (7.3, 1.5)	6.88, q (6.5)
H-19	2.01	1.93, dq (7.3, 1.5)	1.84, s
H-20	1.89	1.82, dq (1.5)	1.82, s

Table S5. Comparison of ^{13}C NMR spectra



badkhysin



11-*epi*-badkhysin

Position	Natural sample **badkhysin** Dračínský (2012)[2] (150 MHz, $CDCl_3$) δ_C	Semi-synthetic sample **Badkhysin** Alejandro (1994)[3] (100 MHz, $CDCl_3$) δ_C	Synthetic sample **11-*epi*-badkhysin** This work (150 MHz, $CDCl_3$) δ_C
C-1	129.75	129.7	129.09
C-2	195.22	195.1	195.50
C-3	135.39	139.8	135.70
C-4	169.64	169.7	170.82
C-5	49.04	48.9	48.50
C-6	80.74	80.6	80.21
C-7	45.09	37.1	50.15
C-8	67.02	67.0	69.00
C-9	43.52	43.4	42.63
C-10	145.19	145.1	146.08
C-11	37.19	45.0	37.30
C-12	176.02	177.9	177.63
C-13	13.26	13.1	16.10
C-14	20.19	19.5	20.44
C-15	19.66	20.3	19.93
C-16	166.57	166.5	166.96
C-17	126.95	126.9	128.19
C-18	140.05	135.2	139.08
C-19	15.89	15.7	12.20
C-20	20.48	20.0	14.72

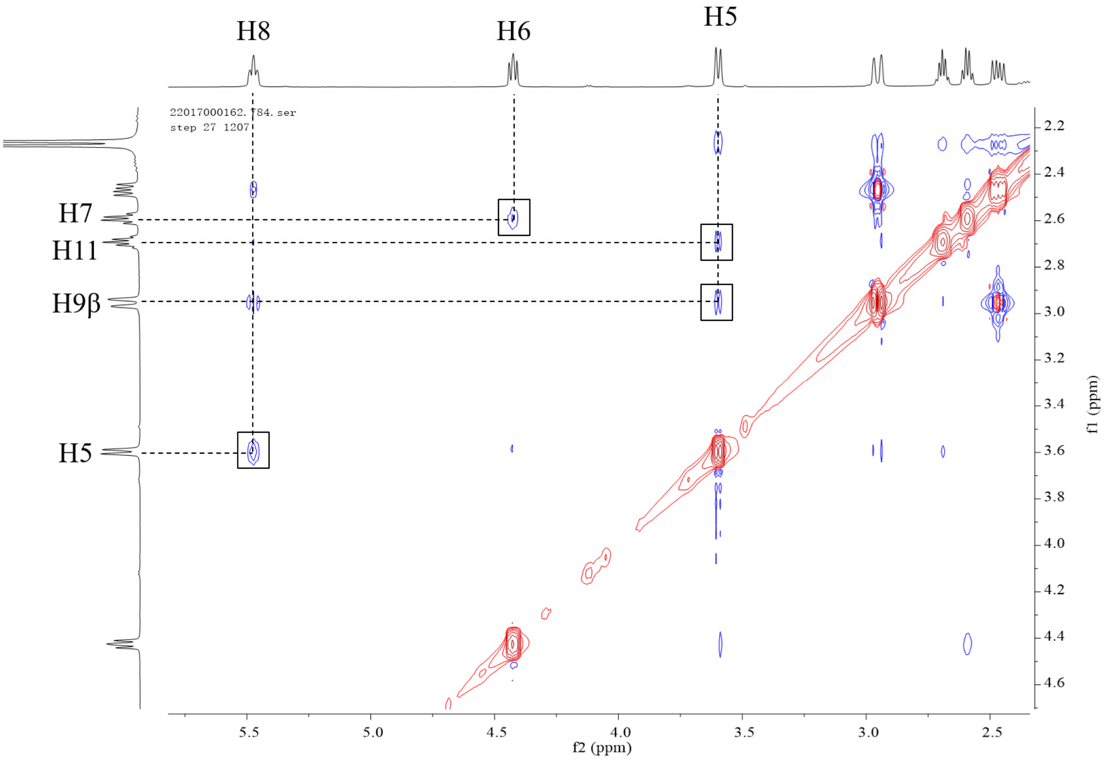
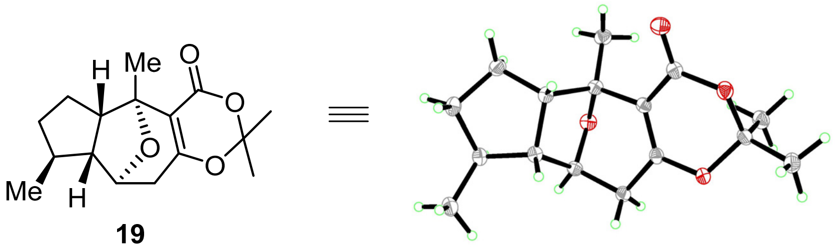


Figure S1. NOE signals for H5/H8, H5/H11, H5/H9β and H7/H6

4. X-Ray Single Crystal Diffraction Data

4.1 Compound 19 (CCDC: 2322258)



19

A specimen of $C_{16}H_{22}O_4$, approximate dimensions 0.310 mm x 0.360 mm x 0.380 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å). The integration of the data using a monoclinic unit cell yielded a total of 7551 reflections to a maximum θ angle of 67.09° (0.84 Å resolution), of which 2507 were independent (average redundancy 3.012, completeness = 98.5%, R_{int} = 4.95%, R_{sig} = 4.75%) and 2451 (97.77%) were greater than $2\sigma(F^2)$.

The final cell constants of a = 7.6552(16) Å, b = 5.6610(12) Å, c = 17.132(4) Å, β = 101.164(7)°, volume = 728.4(3) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.5218 and 0.7528. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21 1, with Z = 2 for the formula unit, $C_{16}H_{22}O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 185 variables converged at R1 = 3.71%, for the observed data and wR2 = 9.49% for all data. The goodness-of-fit was 1.060. The largest peak in the final difference electron density synthesis was 0.154 $e^-/Å^3$ and the largest hole was -0.183 $e^-/Å^3$ with an RMS deviation of 0.040 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.269 g/cm^3 and F(000), 300 e^-.

Table S6. Sample and crystal data for 2322258

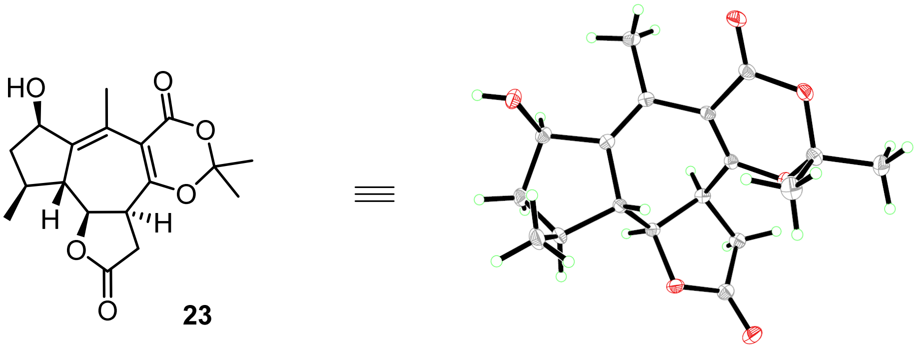
Identification code	**2322258**	
Chemical formula	$C_{16}H_{22}O_4$	
Formula weight	278.33 g/mol	
Wavelength	1.54178 Å	
Crystal size	0.310 x 0.360 x 0.380 mm	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 7.6552(16) Å	α = 90°
	b = 5.6610(12) Å	β = 101.164(7)°
	c = 17.132(4) Å	γ = 90°
Volume	728.4(3) $Å^3$	
Z	2	
Density (calculated)	1.269 g/cm^3	
Absorption coefficient	0.733 mm^{-1}	
F(000)	300	

Table S7. Data collection and structure refinement for 2322258

Theta range for data collection	2.63 to 67.09°	
Index ranges	-9<=h<=9, -6<=k<=6, -20<=l<=20	
Reflections collected	7551	
Independent reflections	2507 [R(int) = 0.0495]	
Max. and min. transmission	0.7528 and 0.5218	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	2507 / 1 / 185	
Goodness-of-fit on F^2	1.060	
Final R indices	2451 data; I>2σ(I)	R1 = 0.0371, wR2 = 0.0939

	all data	R1 = 0.0380, wR2 = 0.0949
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0306P)^2+0.2425P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.11(10)	
Largest diff. peak and hole	0.154 and -0.183 eÅ^{-3}	
R.M.S. deviation from mean	0.040 eÅ^{-3}	

4.2 Compound 23 (CCDC: 2322305)



23

A specimen of $C_{18}H_{22}O_6$, approximate dimensions 0.350 mm x 0.400 mm x 0.420 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å).The integration of the data using an orthorhombic unit cell yielded a total of 22371 reflections to a maximum θ angle of 68.18° (0.83 Å resolution), of which 3023 were independent (average redundancy 7.400, completeness = 99.3%, R_{int} = 3.85%, R_{sig} = 2.34%) and 3001 (99.27%) were greater than $2\sigma(F^2)$.

The final cell constants of a = 7.3182(12) Å, b = 11.8250(19) Å, c = 19.235(3) Å, volume = 1664.6(5) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 $\sigma(I)$. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6807 and 0.7531.The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with Z = 4 for the formula unit, $C_{18}H_{22}O_6$. The final anisotropic full-matrix least-squares refinement on F^2 with 221 variables converged at R1 = 2.72%, for the observed data and wR2 = 7.33% for all data. The goodness-of-fit was 1.024. The largest peak in the final difference electron density synthesis was 0.138 e$^-$/Å^3 and the largest hole was -0.173 e$^-$/Å^3 with an RMS deviation of 0.034 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.334 g/cm^3 and F(000), 712 e$^-$.

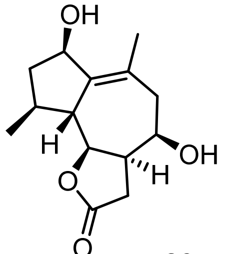
Table S8. Sample and crystal data for 2322305

Identification code	**2322305**	
Chemical formula	$C_{18}H_{22}O_6$	
Formula weight	334.35 g/mol	
Wavelength	1.54178 Å	
Crystal size	0.350 x 0.400 x 0.420 mm	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.3182(12) Å	$\alpha = 90°$
	b = 11.8250(19) Å	$\beta = 90°$
	c = 19.235(3) Å	$\gamma = 90°$
Volume	1664.6(5) $Å^3$	
Z	4	
Density (calculated)	1.334 g/cm^3	
Absorption coefficient	0.831 mm^{-1}	
F(000)	712	

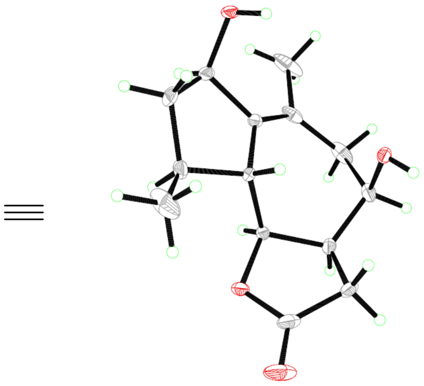
Table S9. Data collection and structure refinement for 2322305

Theta range for data collection	4.60 to 68.18°	
Index ranges	-8<=h<=8, -14<=k<=14, -23<=l<=22	
Reflections collected	22371	
Independent reflections	3023 [R(int) = 0.0385]	
Max. and min. transmission	0.7531 and 0.6807	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	3023 / 0 / 221	
Goodness-of-fit on F^2	1.024	
Final R indices	3001 data; $I>2\sigma(I)$	R1 = 0.0272, wR2 = 0.0731
	all data	R1 = 0.0274, wR2 = 0.0733
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0464P)^2+0.2874P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.11(4)	
Largest diff. peak and hole	0.138 and -0.173 $eÅ^{-3}$	
R.M.S. deviation from mean	0.034 $eÅ^{-3}$	

4.3 Compound 26 (CCDC: 2322268)



26



A specimen of $C_{14}H_{20}O_4$, approximate dimensions 0.160 mm x 0.170 mm x 0.190 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured ($\lambda = 1.54178$ Å).The integration of the data using a trigonal unit cell yielded a total of 58155 reflections to a maximum θ angle of 77.37° (0.79 Å resolution), of which 5704 were independent (average redundancy 10.195, completeness = 99.9%, $R_{int} = 3.28\%$, $R_{sig} = 1.38\%$) and 5682 (99.61%) were greater than $2\sigma(F^2)$.

The final cell constants of $\underline{a} = 9.3343(3)$ Å, $\underline{b} = 9.3343(3)$ Å, $\underline{c} = 26.7238(16)$ Å, volume = 2016.47(18) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 $\sigma(I)$. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6781 and 0.7541. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 32, with Z = 6 for the formula unit, $C_{14}H_{20}O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 333 variables converged at R1 = 2.93%, for the observed data and wR2 = 7.73% for all data. The goodness-of-fit was 1.049. The largest peak in the final difference electron density synthesis was 0.157 e$^-$/Å^3 and the largest hole was -0.193 e$^-$/Å^3 with an RMS deviation of 0.034 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.247 g/cm^3 and F(000), 816 e$^-$.

Table S10. Sample and crystal data for 2322268

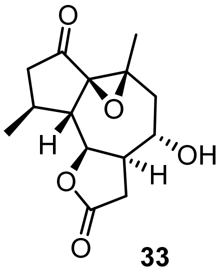
Identification code	**2322268**
Chemical formula	$C_{14}H_{20}O_4$
Formula weight	252.30 g/mol
Wavelength	1.54178 Å

Crystal size	0.160 x 0.170 x 0.190 mm	
Crystal system	trigonal	
Space group	P 32	
Unit cell dimensions	a = 9.3343(3) Å	α = 90°
	b = 9.3343(3) Å	β = 90°
	c = 26.7238(16) Å	γ = 120°
Volume	2016.47(18) Å^3	
Z	6	
Density (calculated)	1.247 g/cm^3	
Absorption coefficient	0.740 mm^{-1}	
F(000)	816	

Table S11. Data collection and structure refinement for 2322268

Theta range for data collection	4.96 to 77.37°	
Index ranges	-11<=h<=10, -11<=k<=11, -33<=l<=33	
Reflections collected	58155	
Independent reflections	5704 [R(int) = 0.0328]	
Max. and min. transmission	0.7541 and 0.6781	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)	
Function minimized	Σ w(F$_o^2$ - F$_c^2$)^2	
Data / restraints / parameters	5704 / 1 / 333	
Goodness-of-fit on F^2	1.049	
Final R indices	5682 data; I>2σ(I)	R1 = 0.0293, wR2 = 0.0772
	all data	R1 = 0.0294, wR2 = 0.0773
Weighting scheme	w=1/[σ^2(F$_o^2$)+(0.0449P)^2+0.3760P] where P=(F$_o^2$+2F$_c^2$)/3	
Absolute structure parameter	0.00(2)	
Largest diff. peak and hole	0.157 and -0.193 eÅ^{-3}	
R.M.S. deviation from mean	0.034 eÅ^{-3}	

4.4 Compound 33 (CCDC: 2324246)



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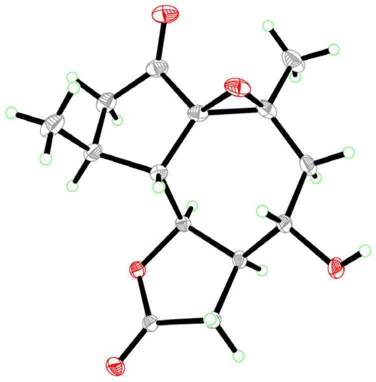


A specimen of $C_{14}H_{18}O_5$, approximate dimensions 0.200 mm x 0.230 mm x 0.240 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å). The integration of the data using a monoclinic unit cell yielded a total of 19174 reflections to a maximum θ angle of 77.59° (0.79 Å resolution), of which 2907 were independent (average redundancy 6.596, completeness = 99.6%, R_{int} = 3.25%, R_{sig} = 2.28%) and 2858 (98.31%) were greater than $2\sigma(F^2)$.

The final cell constants of a = 7.83220(10) Å, b = 6.90300(10) Å, c = 13.3006(3) Å, β = 104.2910(10)°, volume = 696.85(2) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6457 and 0.7541. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21 1, with Z = 2 for the formula unit, $C_{14}H_{18}O_5$. The final anisotropic full-matrix least-squares refinement on F^2 with 176 variables converged at R1 = 3.41%, for the observed data and wR2 = 10.18% for all data. The goodness-of-fit was 1.035. The largest peak in the final difference electron density synthesis was 0.169 e$^-$/Å^3 and the largest hole was -0.119 e$^-$/Å^3 with an RMS deviation of 0.032 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.269 g/cm^3 and F(000), 284 e$^-$.

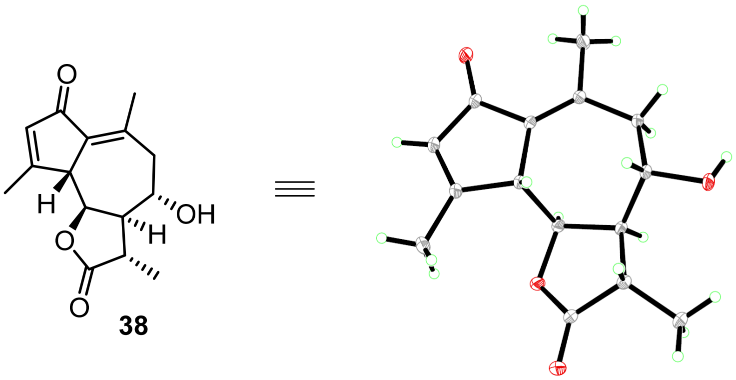
Table S12. Sample and crystal data for 2324246

Identification code	**2324246**	
Chemical formula	$C_{14}H_{18}O_5$	
Formula weight	266.28 g/mol	
Wavelength	1.54178 Å	
Crystal size	0.200 x 0.230 x 0.240 mm	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 7.83220(10) Å	α = 90°
	b = 6.90300(10) Å	β = 104.2910(10)°
	c = 13.3006(3) Å	γ = 90°
Volume	696.85(2) Å^3	
Z	2	
Density (calculated)	1.269 g/cm^3	
Absorption coefficient	0.801 mm^{-1}	
F(000)	284	

Table S13. Data collection and structure refinement for 2324246

Theta range for data collection	3.43 to 77.59°	
Index ranges	-9<=h<=9, -8<=k<=8, -16<=l<=16	
Reflections collected	19174	
Independent reflections	2907 [R(int) = 0.0325]	
Max. and min. transmission	0.7541 and 0.6457	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)	
Function minimized	Σ w(F_o^2 - F_c^2)^2	
Data / restraints / parameters	2907 / 1 / 176	
Goodness-of-fit on F^2	1.035	
Final R indices	2858 data; I>2σ(I)	R1 = 0.0341, wR2 = 0.1011
	all data	R1 = 0.0350, wR2 = 0.1018
Weighting scheme	w=1/[$\sigma^2(F_o^2)+(0.0726P)^2+0.0251P$] where P=($F_o^2+2F_c^2$)/3	
Absolute structure parameter	0.09(3)	
Extinction coefficient	0.0230(40)	
Largest diff. peak and hole	0.169 and -0.119 eÅ^{-3}	
R.M.S. deviation from mean	0.032 eÅ^{-3}	

4.5 Compound 38 (CCDC: 2324247)



38

A specimen of $C_{15}H_{20}O_5$, approximate dimensions 0.130 mm x 0.180 mm x 0.240 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å).The integration of the data using a monoclinic unit cell yielded a total of 19587 reflections to a maximum θ angle of 77.76° (0.79 Å resolution), of which 3028 were independent (average redundancy 6.469, completeness = 99.4%, R_{int} = 2.99%, R_{sig} = 2.16%) and 2986 (98.61%) were greater than 2σ(F^2).

The final cell constants of a = 9.5642(3) Å, b = 7.7285(2) Å, c = 10.2740(3) Å, β = 103.7530(10)°, volume = 737.65(4) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.5877 and 0.7541.The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21 1, with Z = 2 for the formula unit, $C_{15}H_{20}O_5$. The final anisotropic full-matrix least-squares refinement on F^2 with 188 variables converged at R1 = 3.90%, for the observed data and wR2 = 11.03% for all data. The goodness-of-fit was 1.048. The largest peak in the final difference electron density synthesis was 0.209 $e^-/Å^3$ and the largest hole was -0.168 $e^-/Å^3$ with an RMS deviation of 0.033 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.262 g/cm^3 and F(000), 300 e^-.

Table S14. Sample and crystal data for 2324247

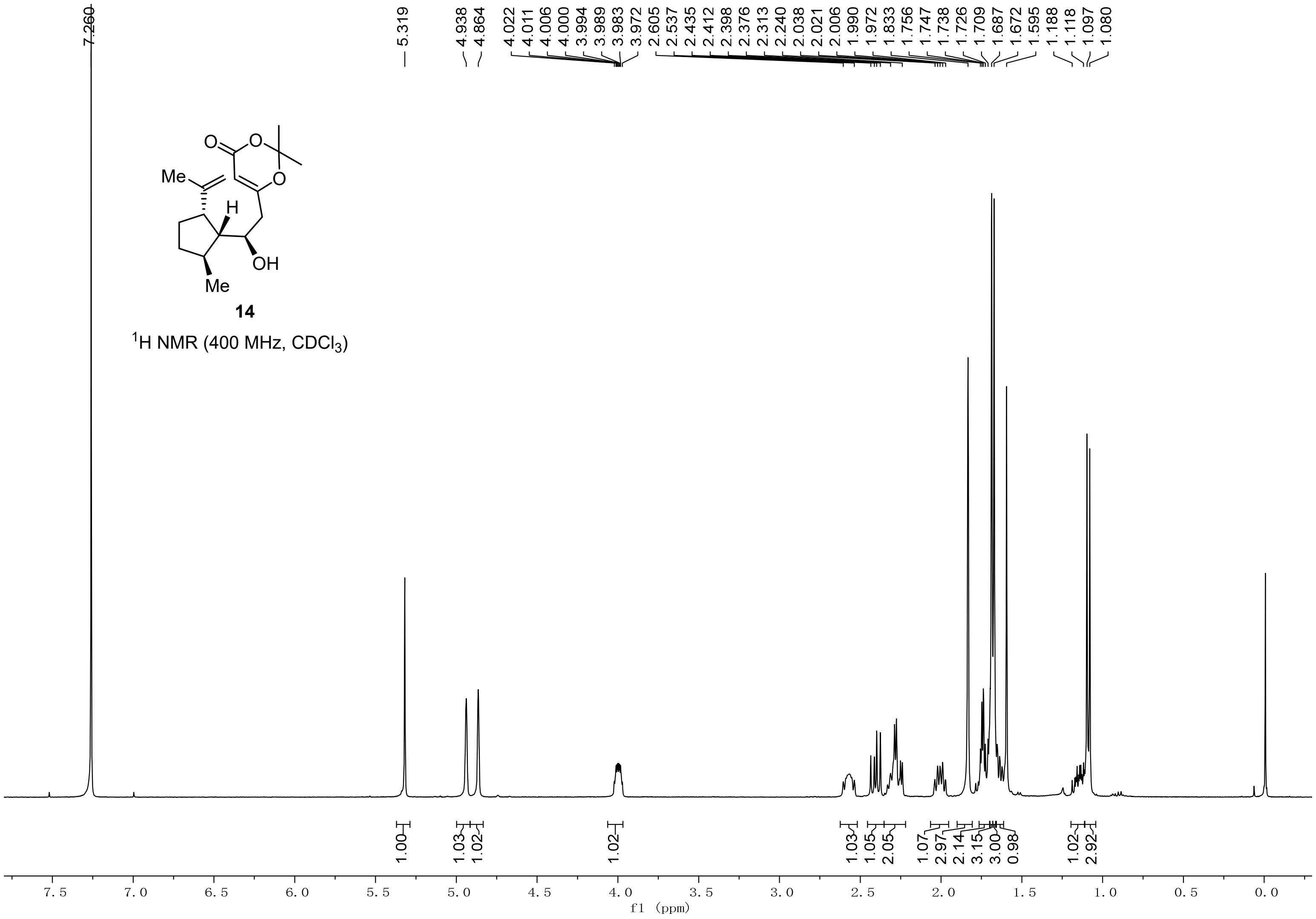
Identification code	**2324247**	
Chemical formula	$C_{15}H_{20}O_5$	
Formula weight	280.31 g/mol	
Wavelength	1.54178 Å	
Crystal size	0.130 x 0.180 x 0.240 mm	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 9.5642(3) Å	α = 90°
	b = 7.7285(2) Å	β = 103.7530(10)°
	c = 10.2740(3) Å	γ = 90°
Volume	737.65(4) $Å^3$	
Z	2	
Density (calculated)	1.262 g/cm^3	
Absorption coefficient	0.781 mm^{-1}	
F(000)	300	

Table S15. Data collection and structure refinement for 2324247

Theta range for data collection	7.24 to 77.76°	
Index ranges	-12<=h<=12, -9<=k<=8, -13<=l<=12	
Reflections collected	19587	
Independent reflections	3028 [R(int) = 0.0299]	
Max. and min. transmission	0.7541 and 0.5877	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	3028 / 1 / 188	
Goodness-of-fit on F^2	1.048	
Final R indices	2986 data; I>2σ(I)	R1 = 0.0390, wR2 = 0.1094

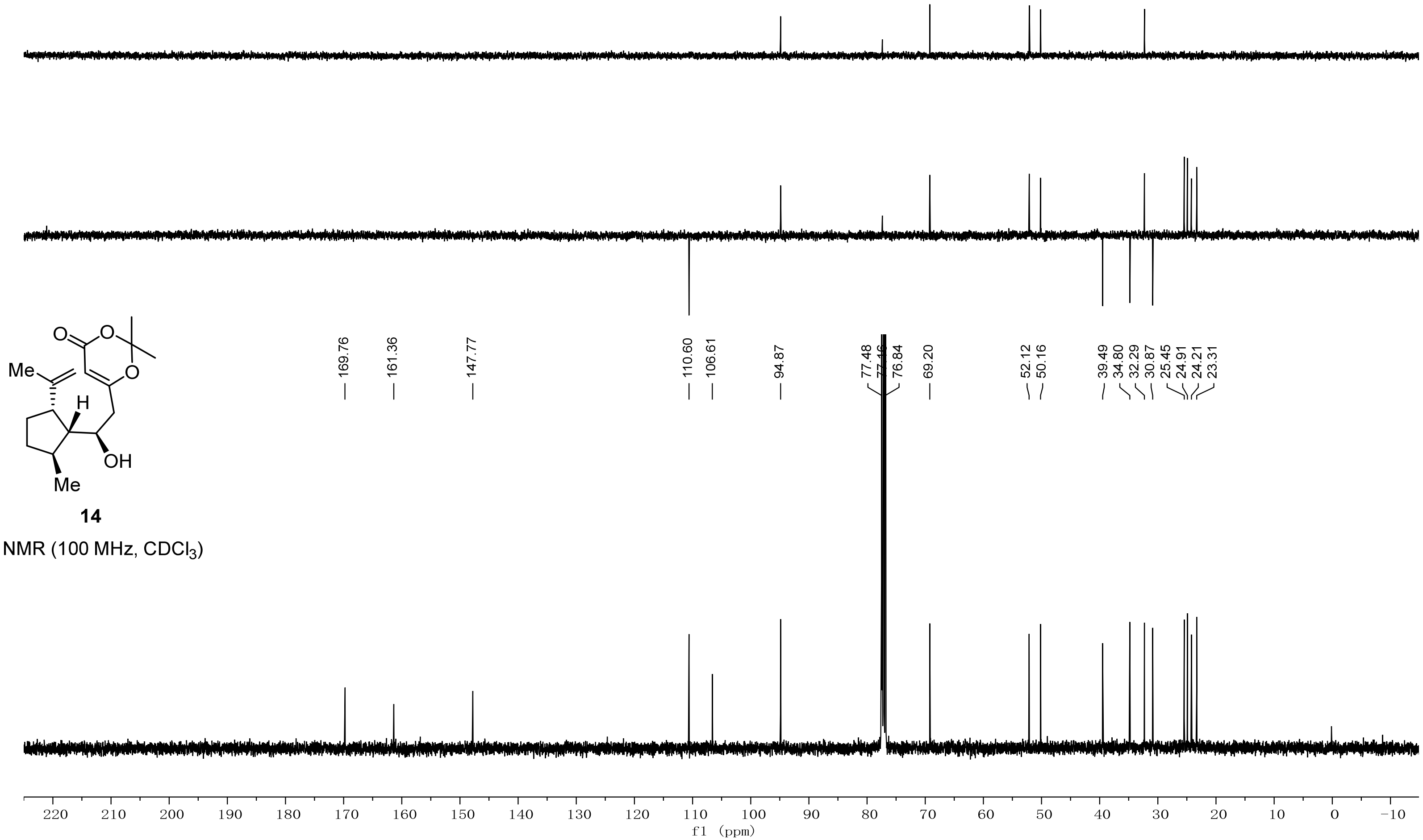
	all data	R1 = 0.0395, wR2 = 0.1103
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0675P)^2+0.0773P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	-0.05(10)	
Largest diff. peak and hole	0.209 and -0.168 eÅ^{-3}	
R.M.S. deviation from mean	0.033 eÅ^{-3}	

5. Copies of ^{1}H NMR, ^{13}C NMR and 2D NMR Spectra



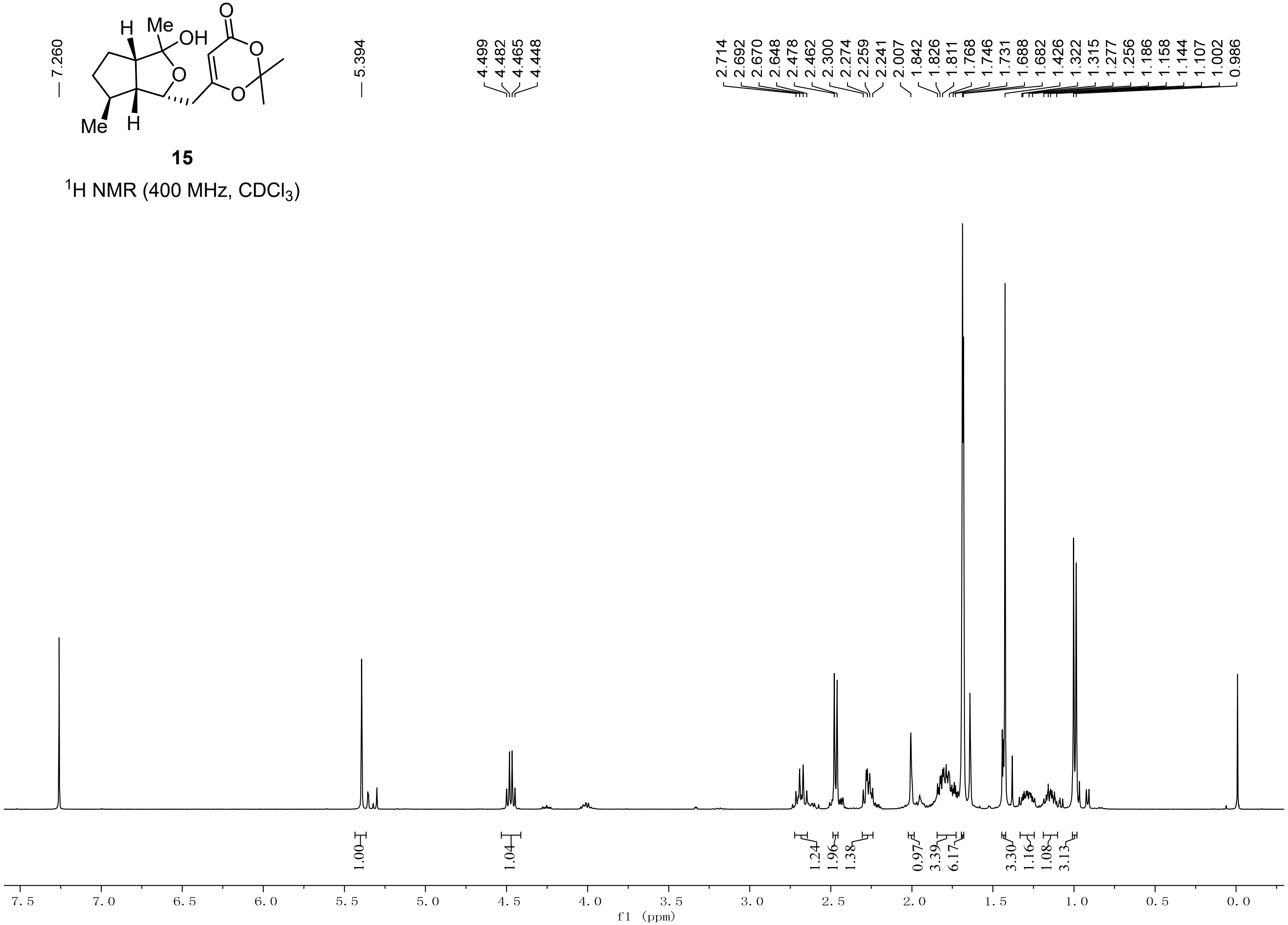
14

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



14

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



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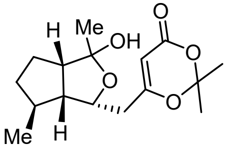
^{1}H NMR (400 MHz, CDCl$_3$)



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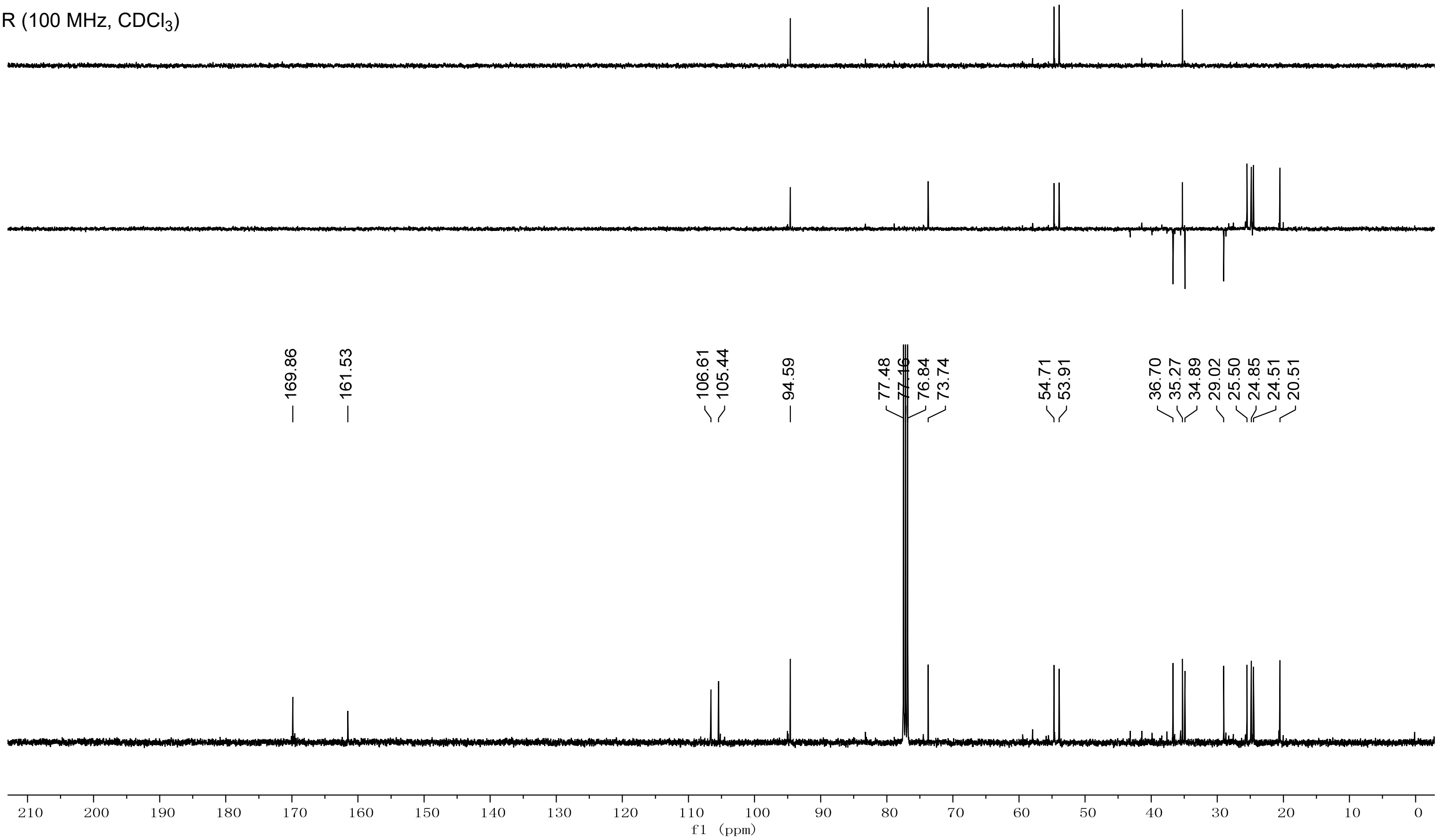
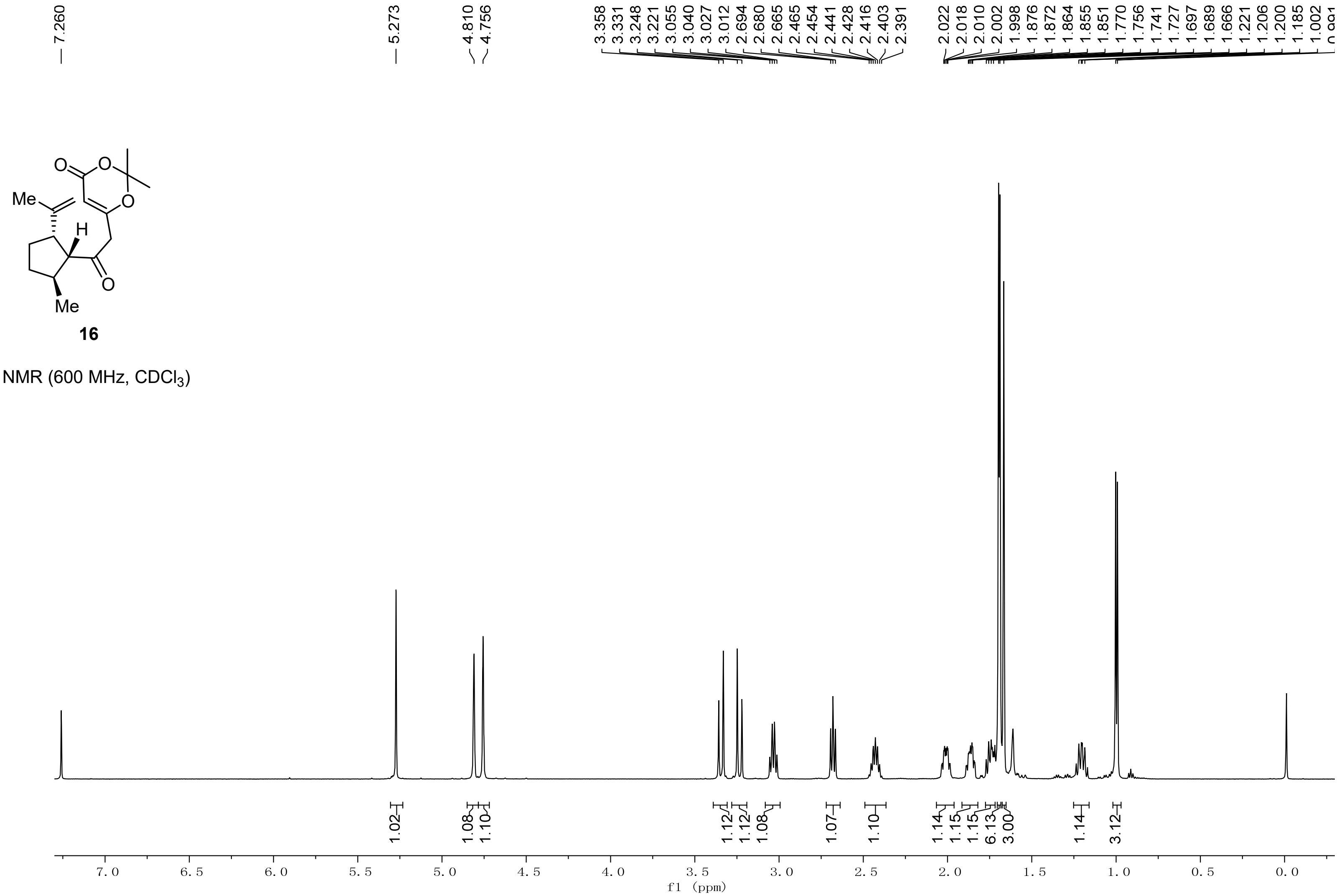
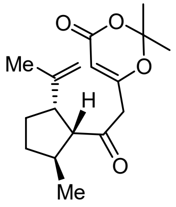
^{13}C NMR (100 MHz, $CDCl_3$)





16

^{1}H NMR (600 MHz, CDCl$_3$)



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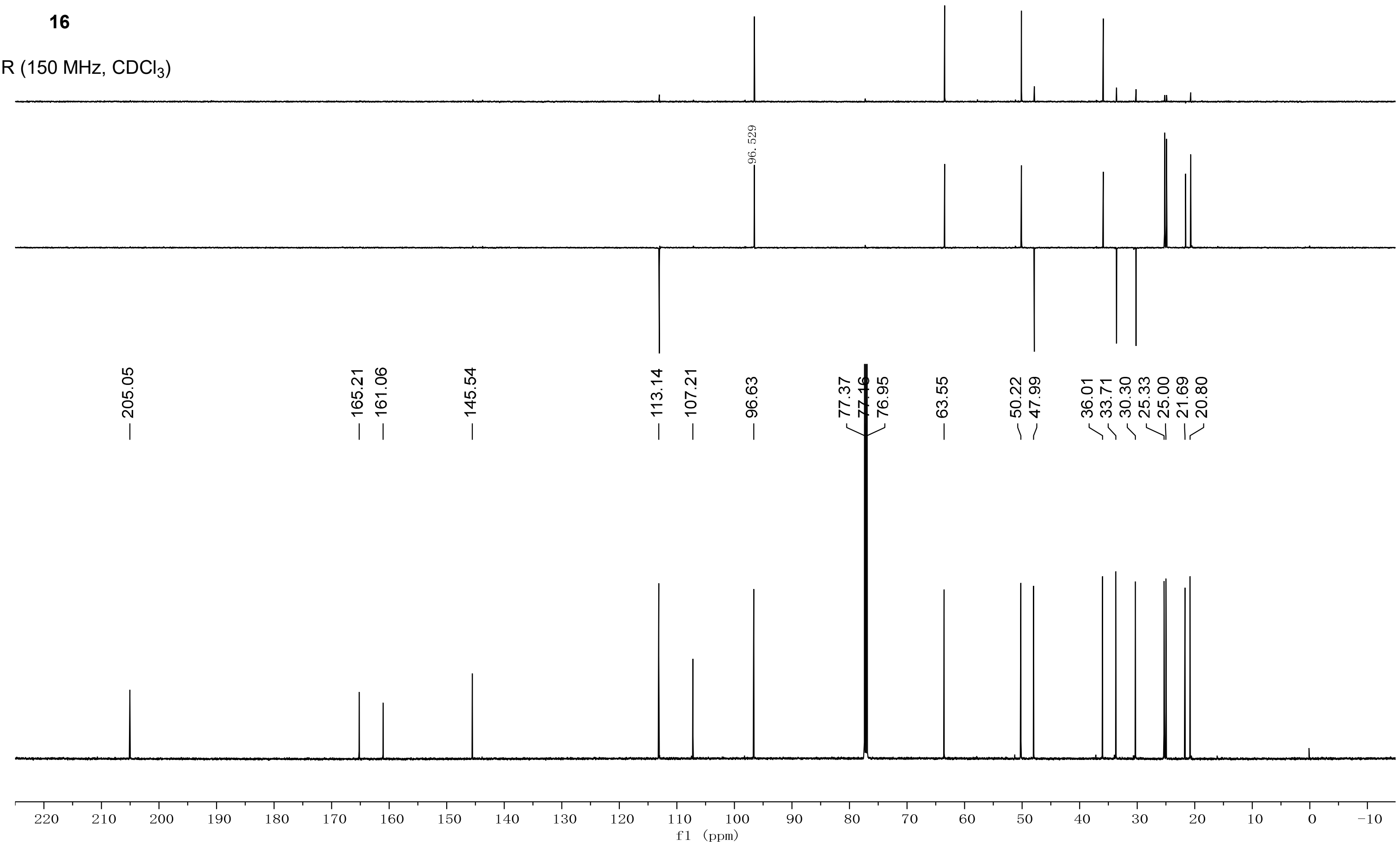
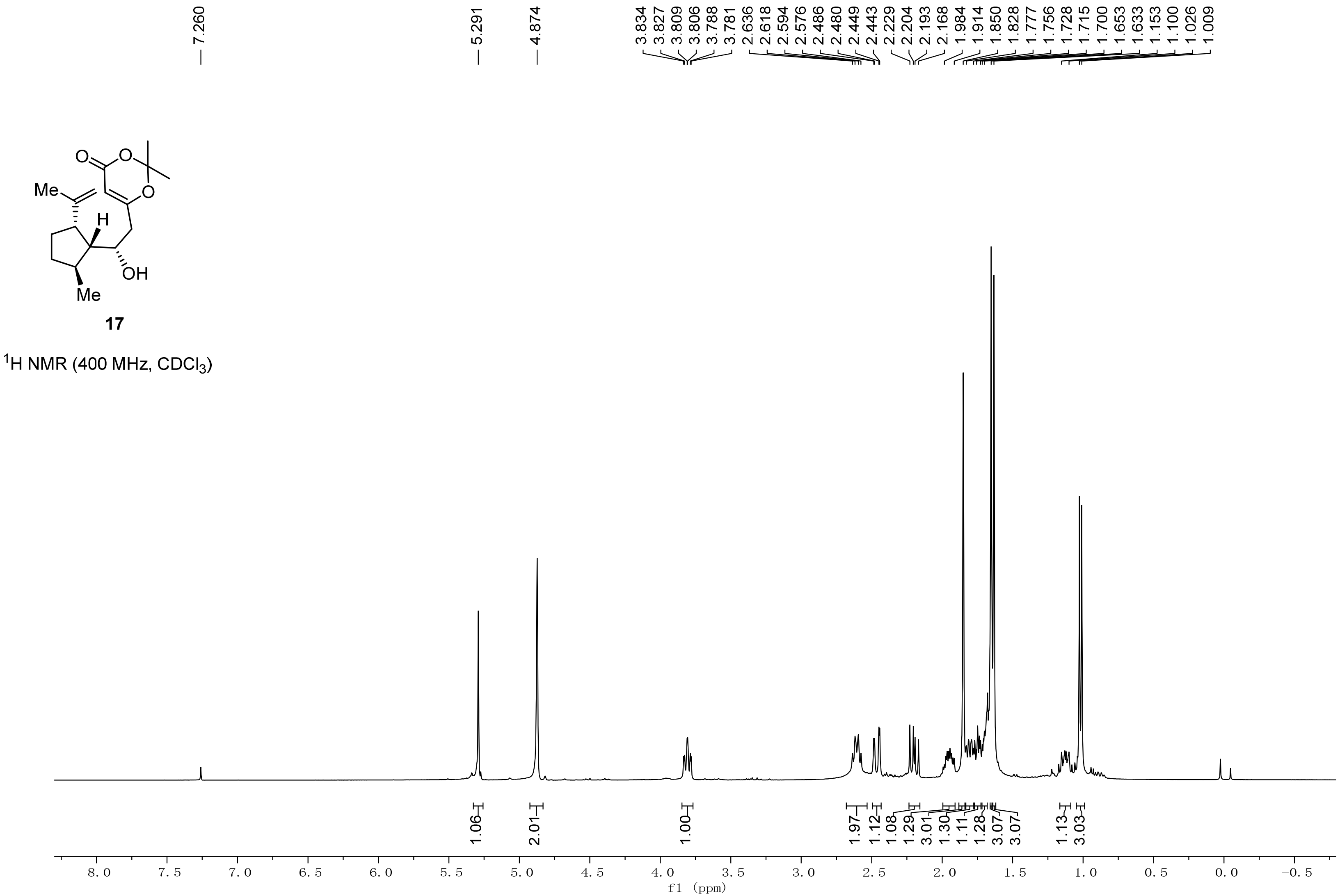
^{13}C NMR (150 MHz, CDCl$_3$)





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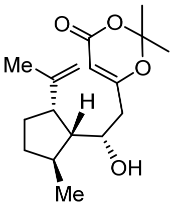
^{1}H NMR (400 MHz, $CDCl_3$)



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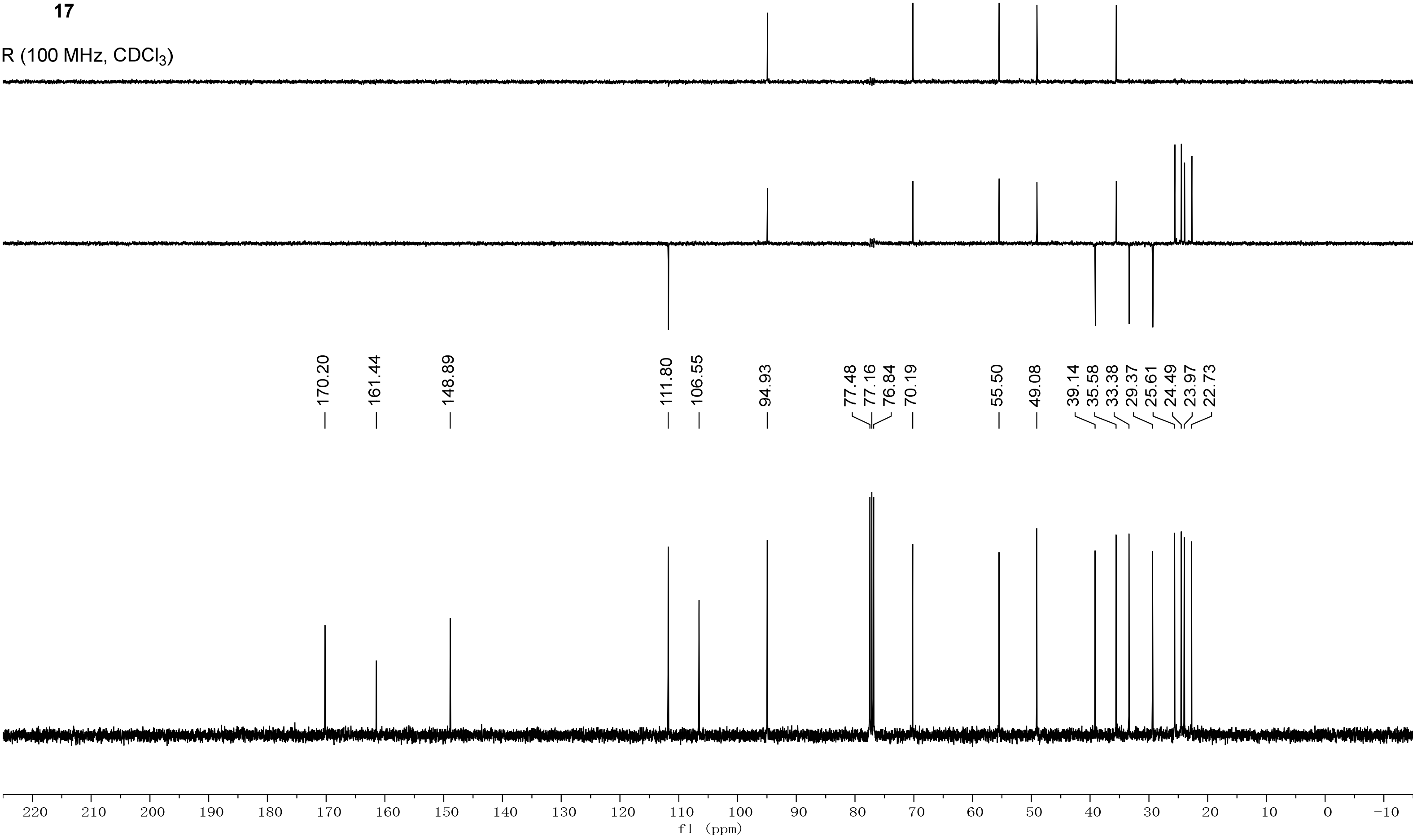
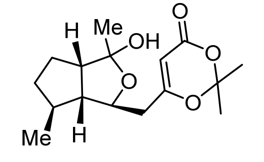
^{13}C NMR (100 MHz, CDCl$_3$)





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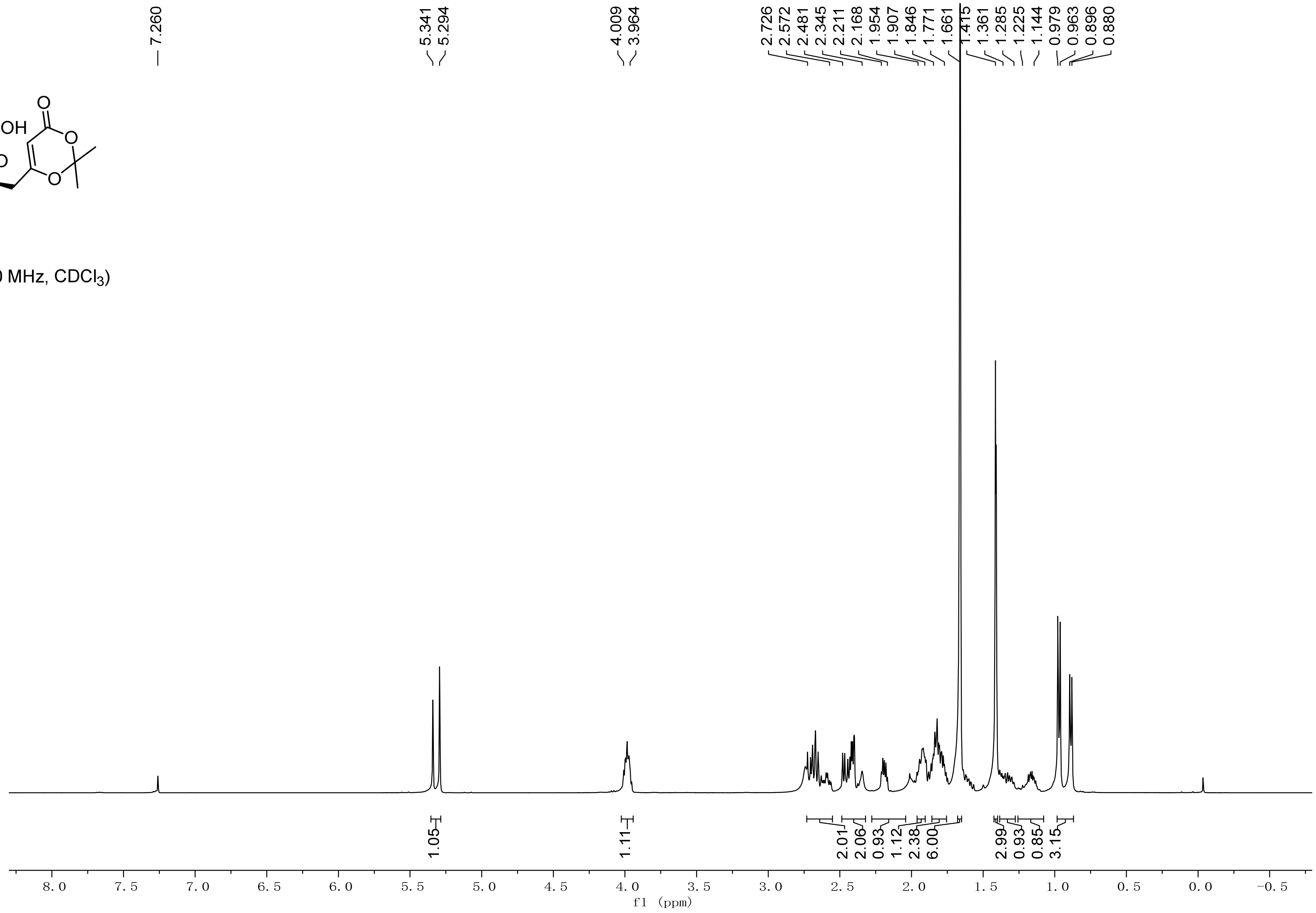

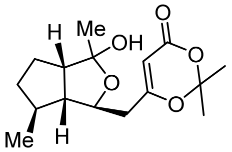

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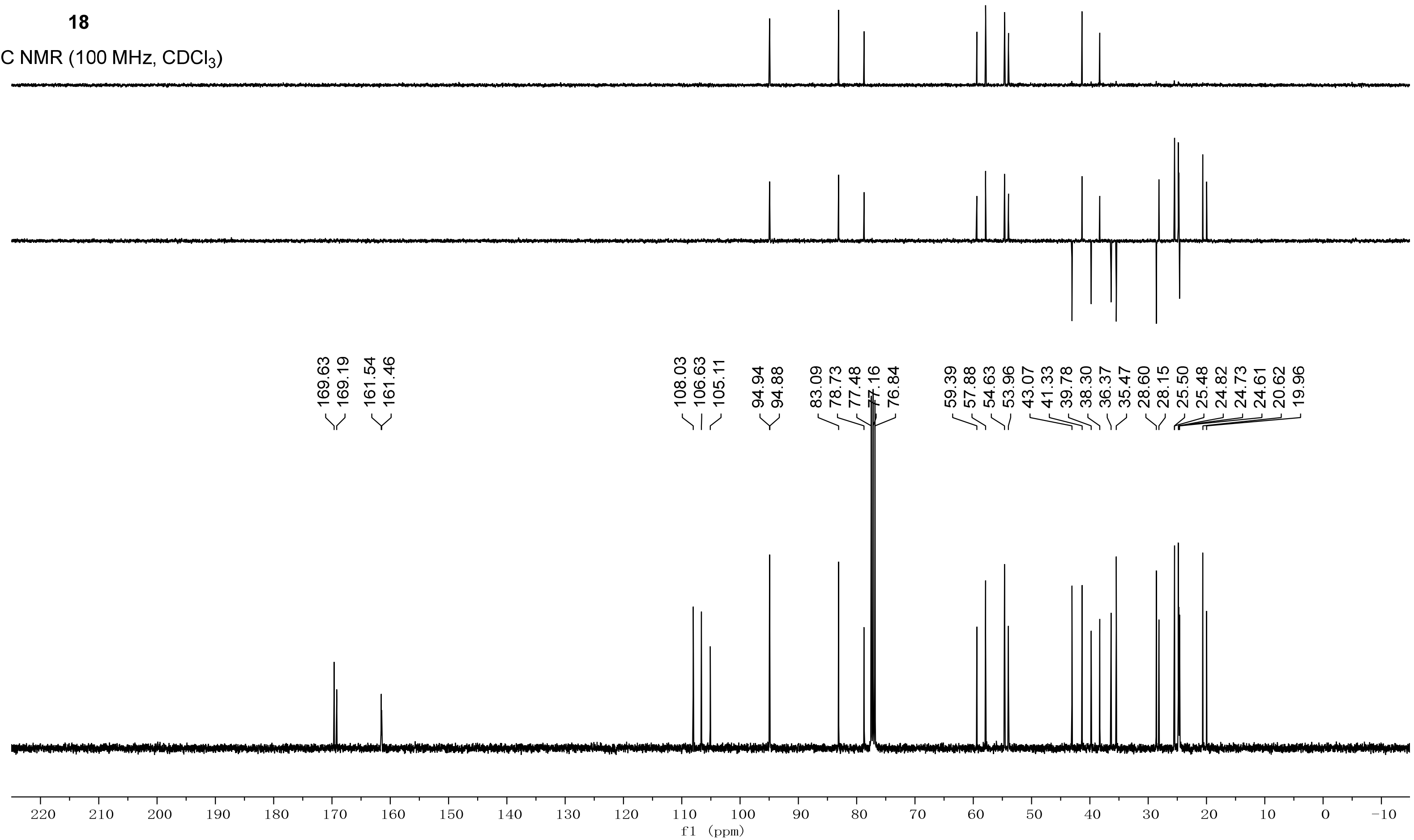

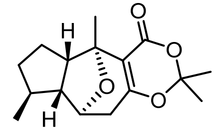

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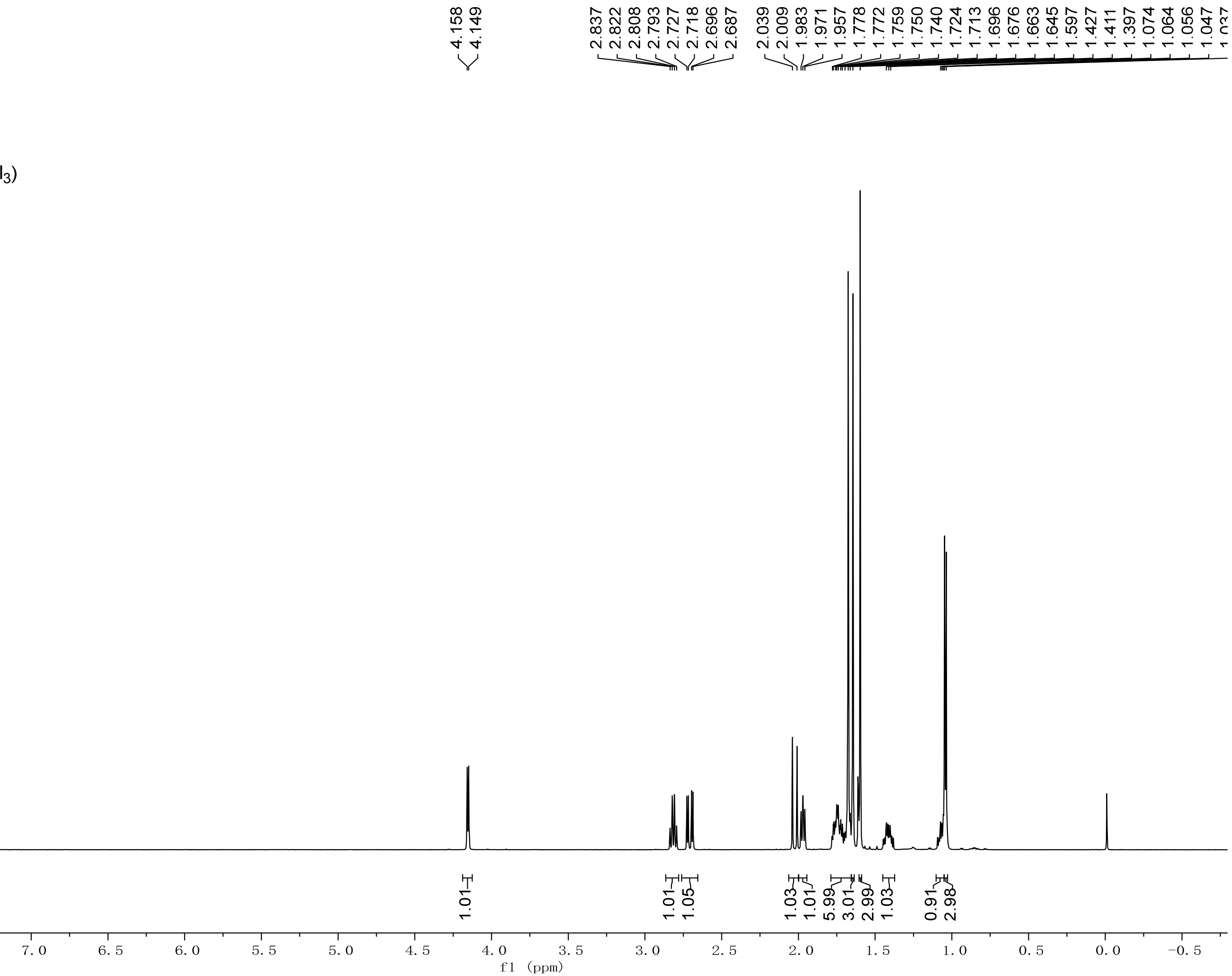

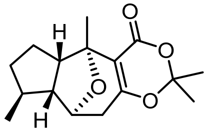

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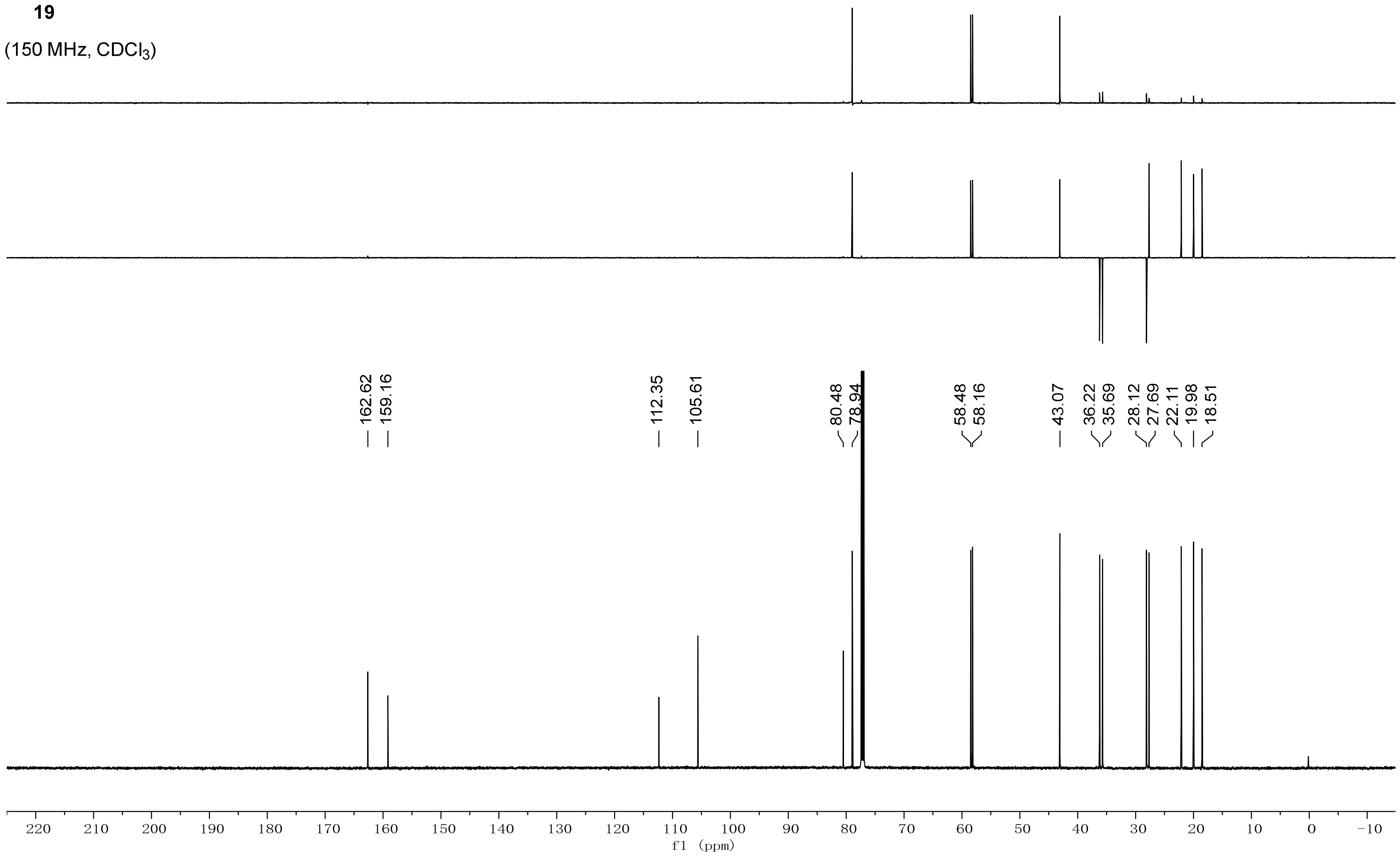
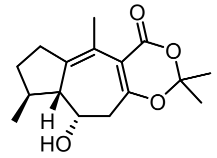
^{13}C NMR (150 MHz, CDCl$_3$)





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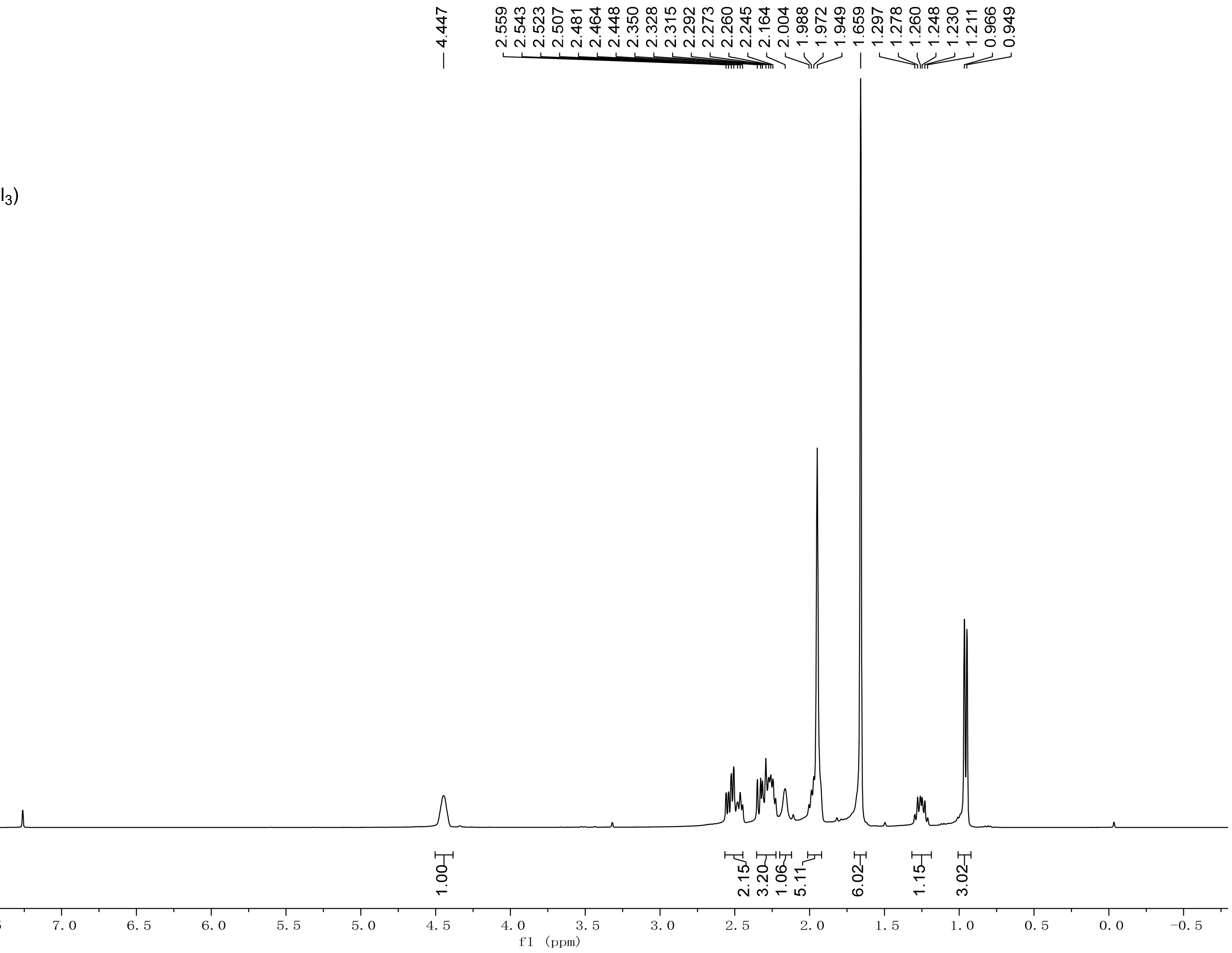
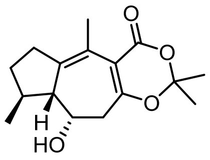
^{1}H NMR (400 MHz, $CDCl_3$)





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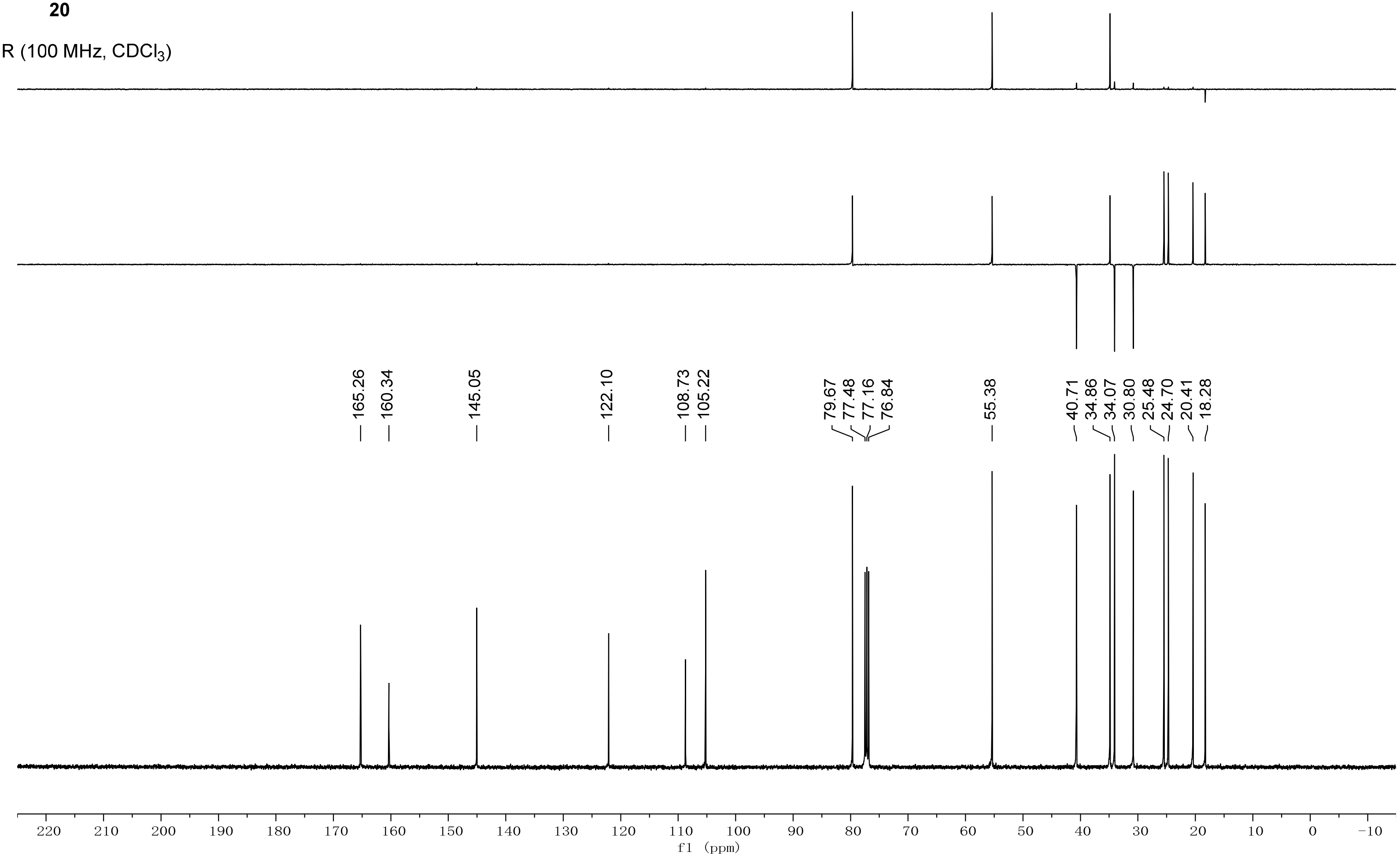
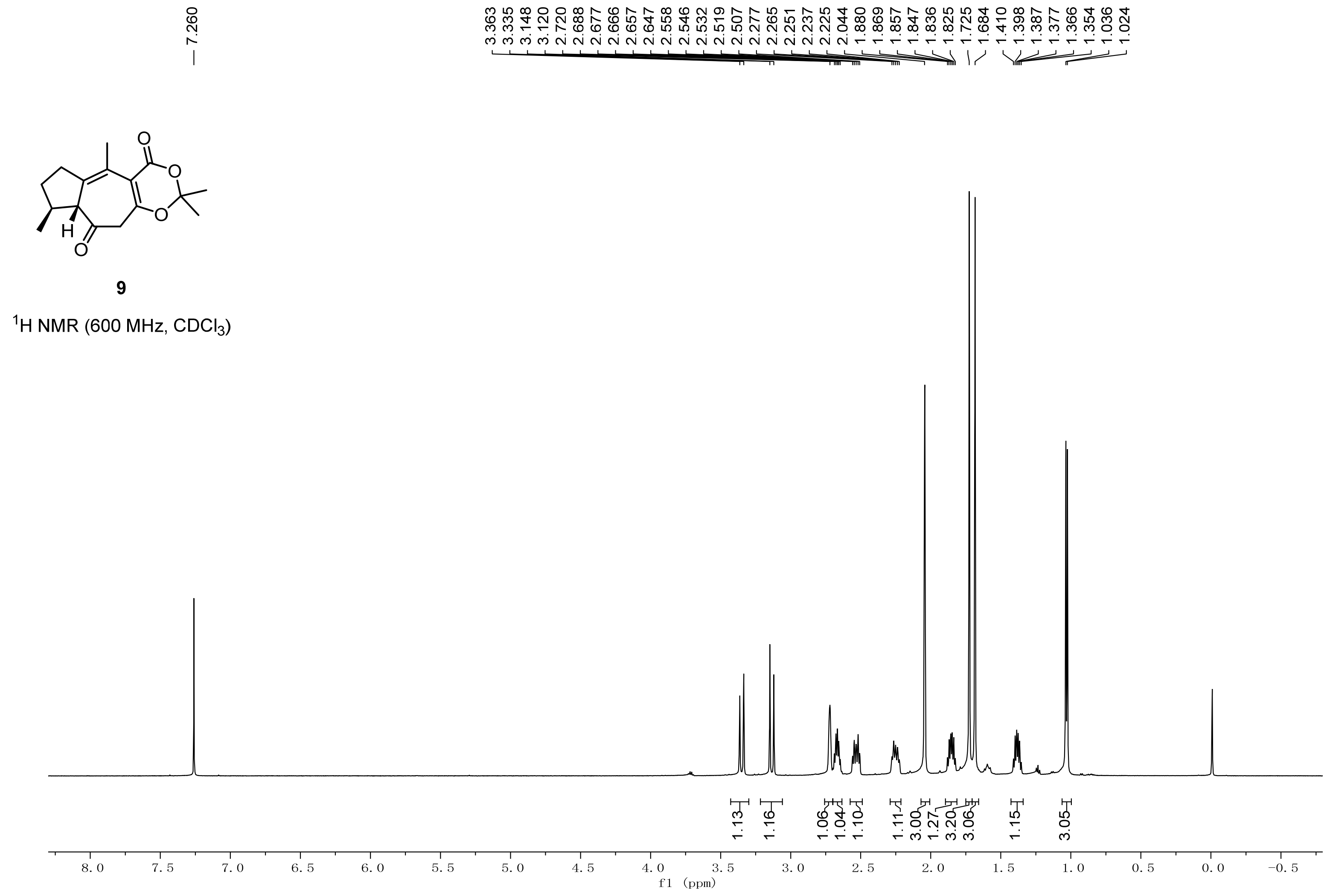
^{13}C NMR (100 MHz, CDCl$_3$)





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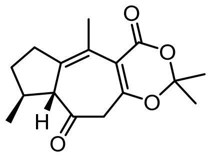
^{1}H NMR (600 MHz, CDCl$_3$)



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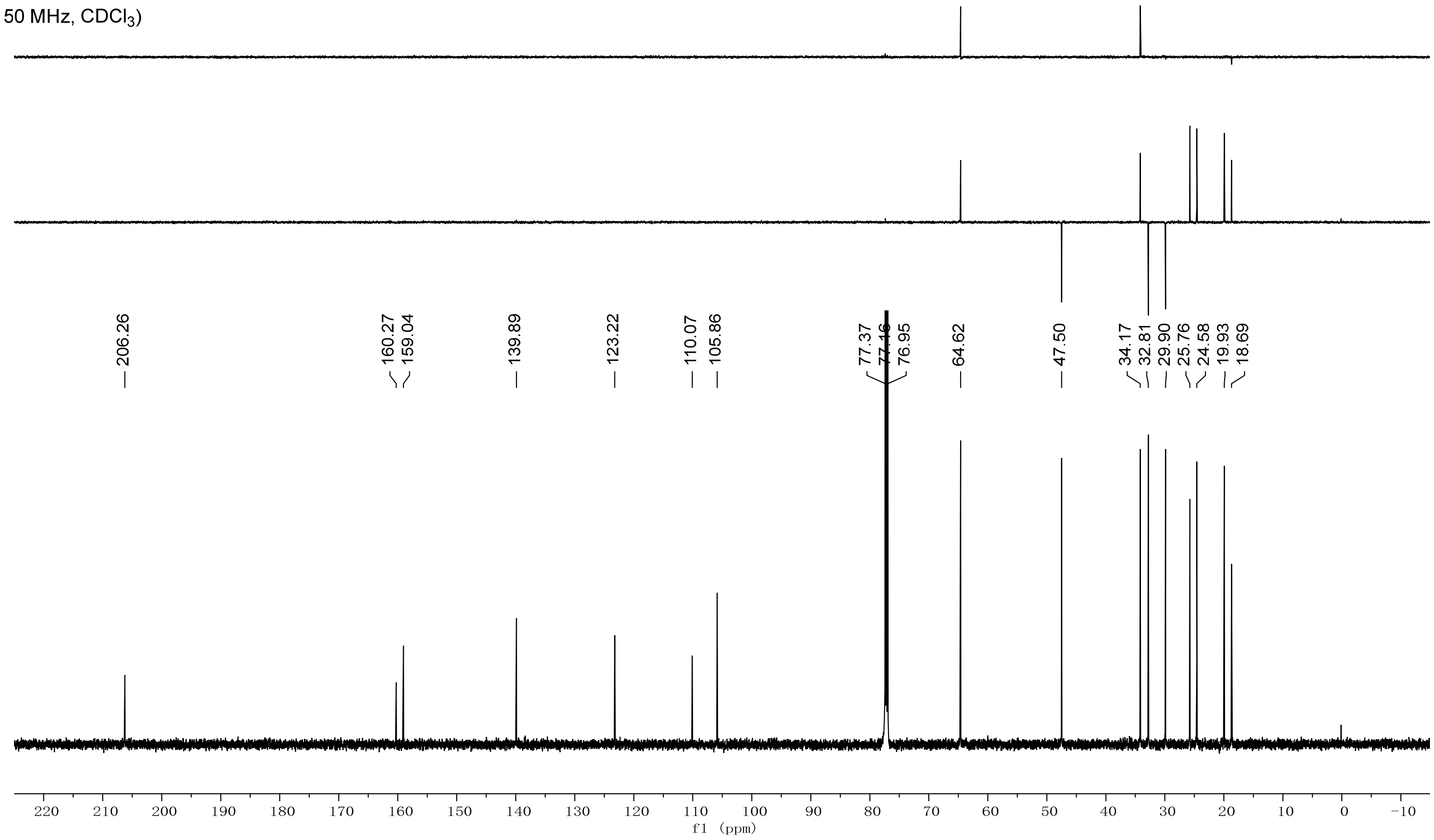
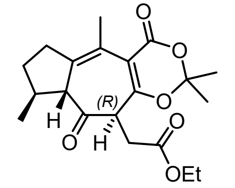
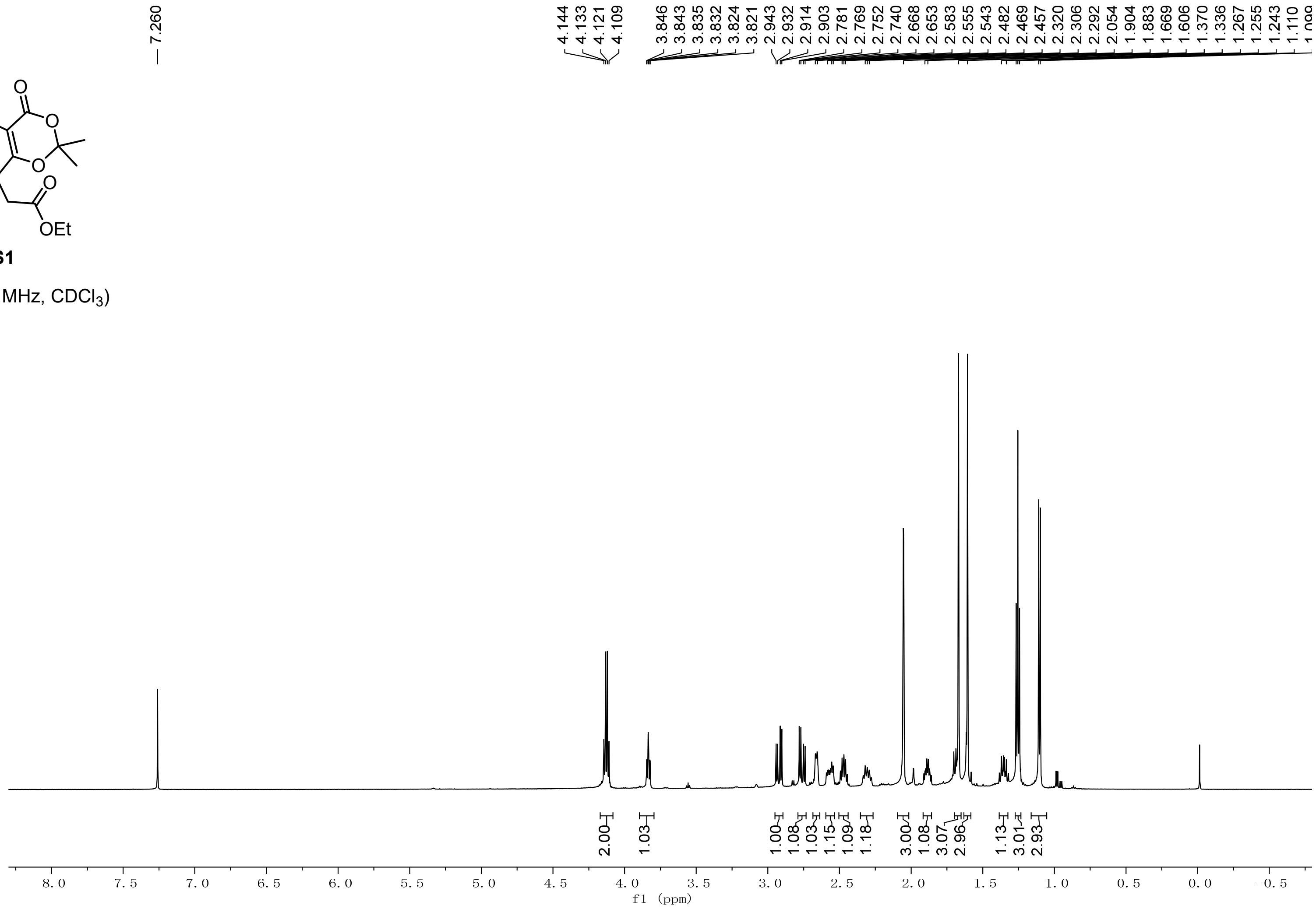
^{13}C NMR (150 MHz, CDCl$_3$)

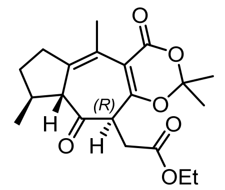




S1

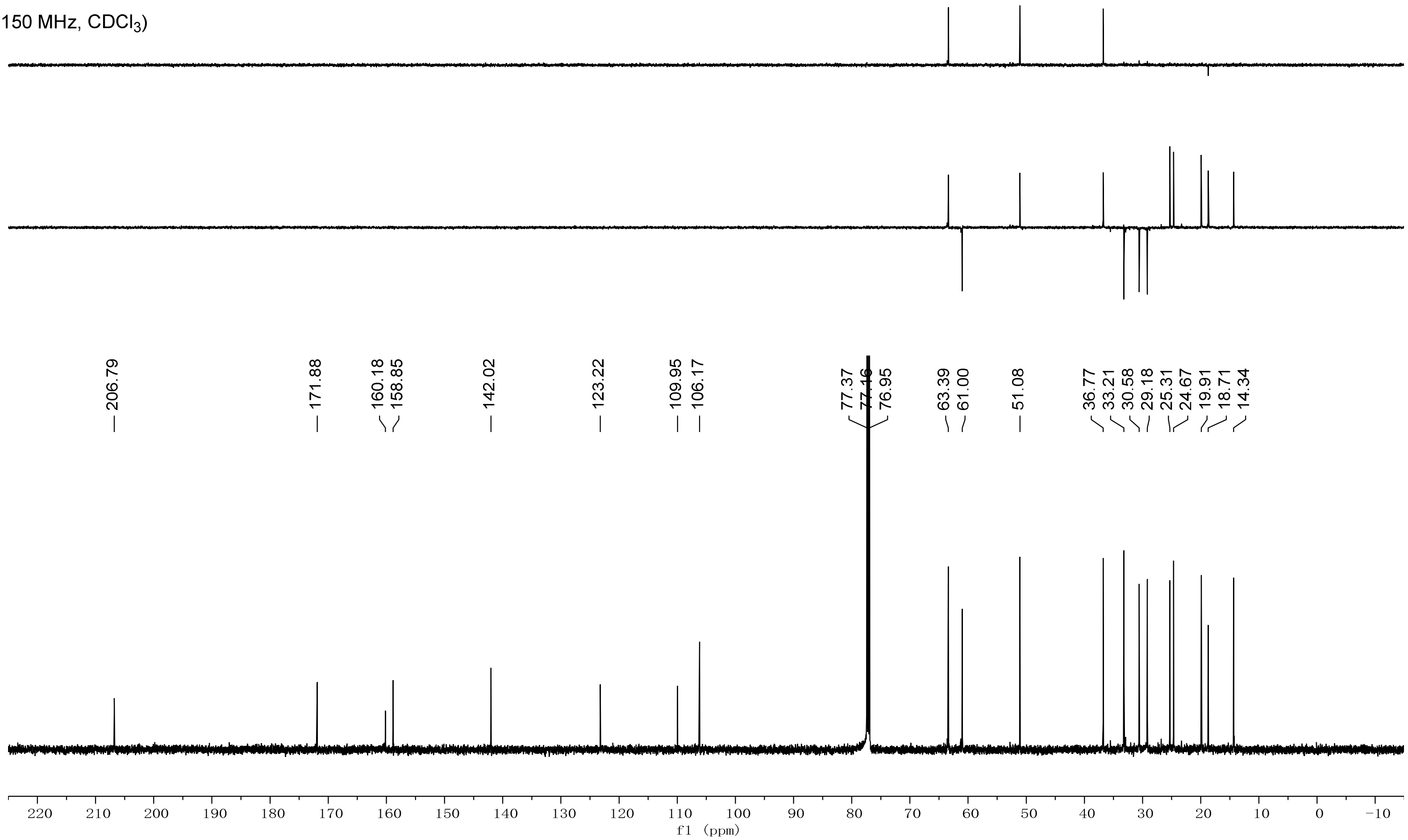
^{1}H NMR (600 MHz, CDCl$_3$)

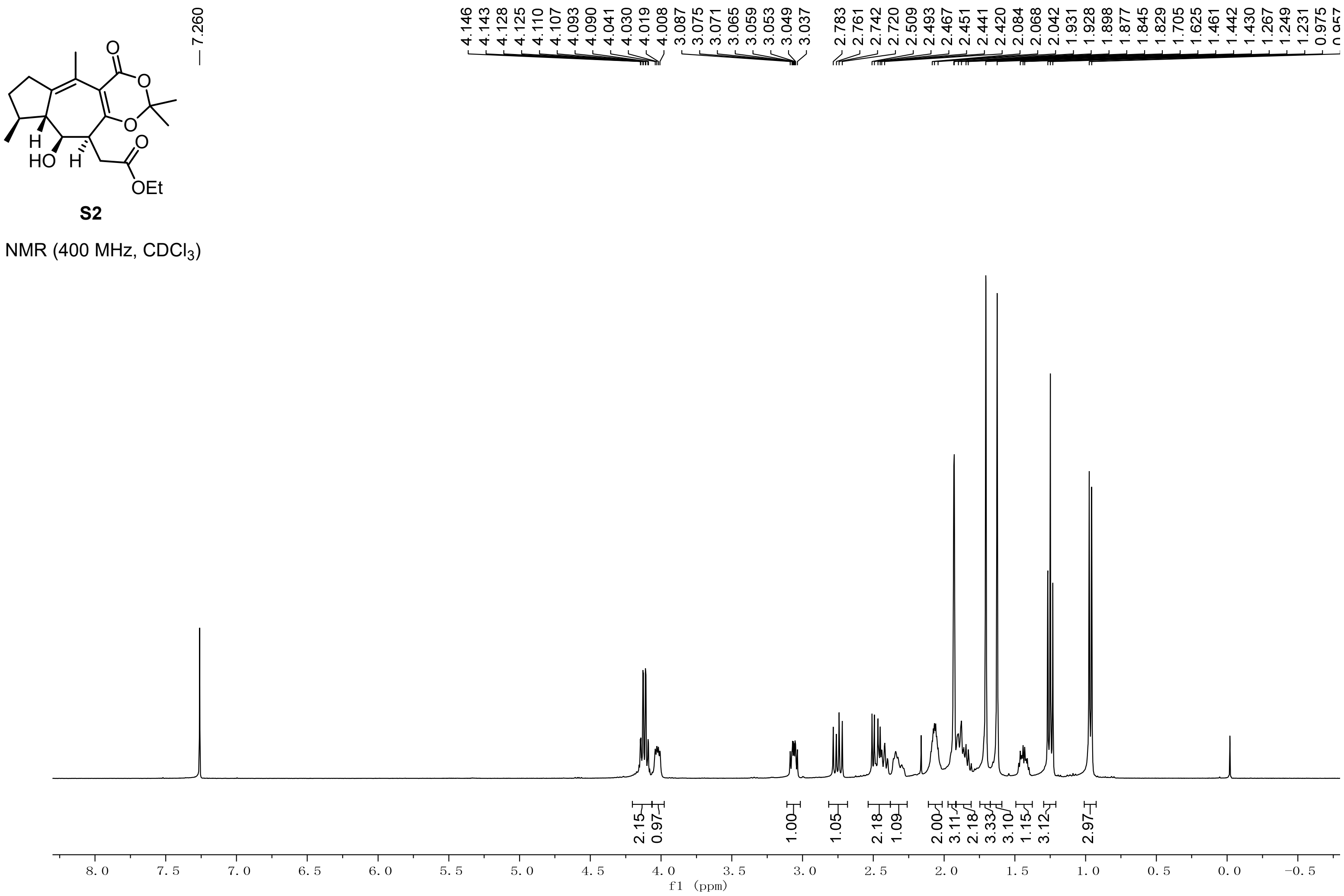




S1

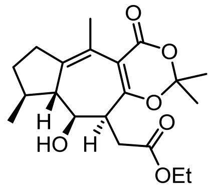
^{13}C NMR (150 MHz, CDCl$_3$)





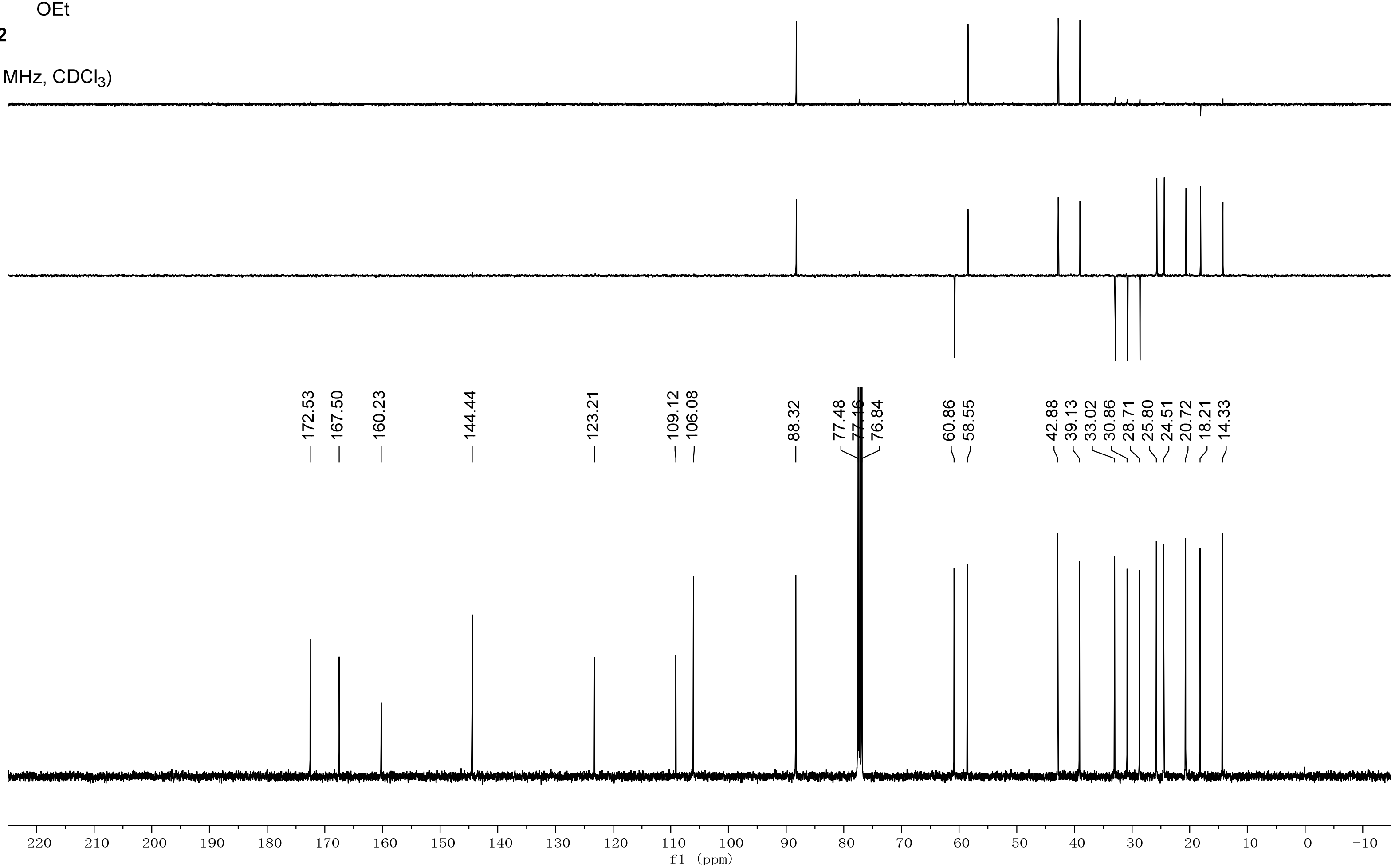
S2

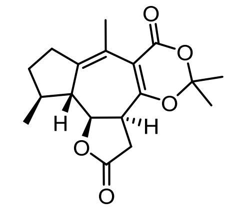
^{1}H NMR (400 MHz, $CDCl_3$)



S2

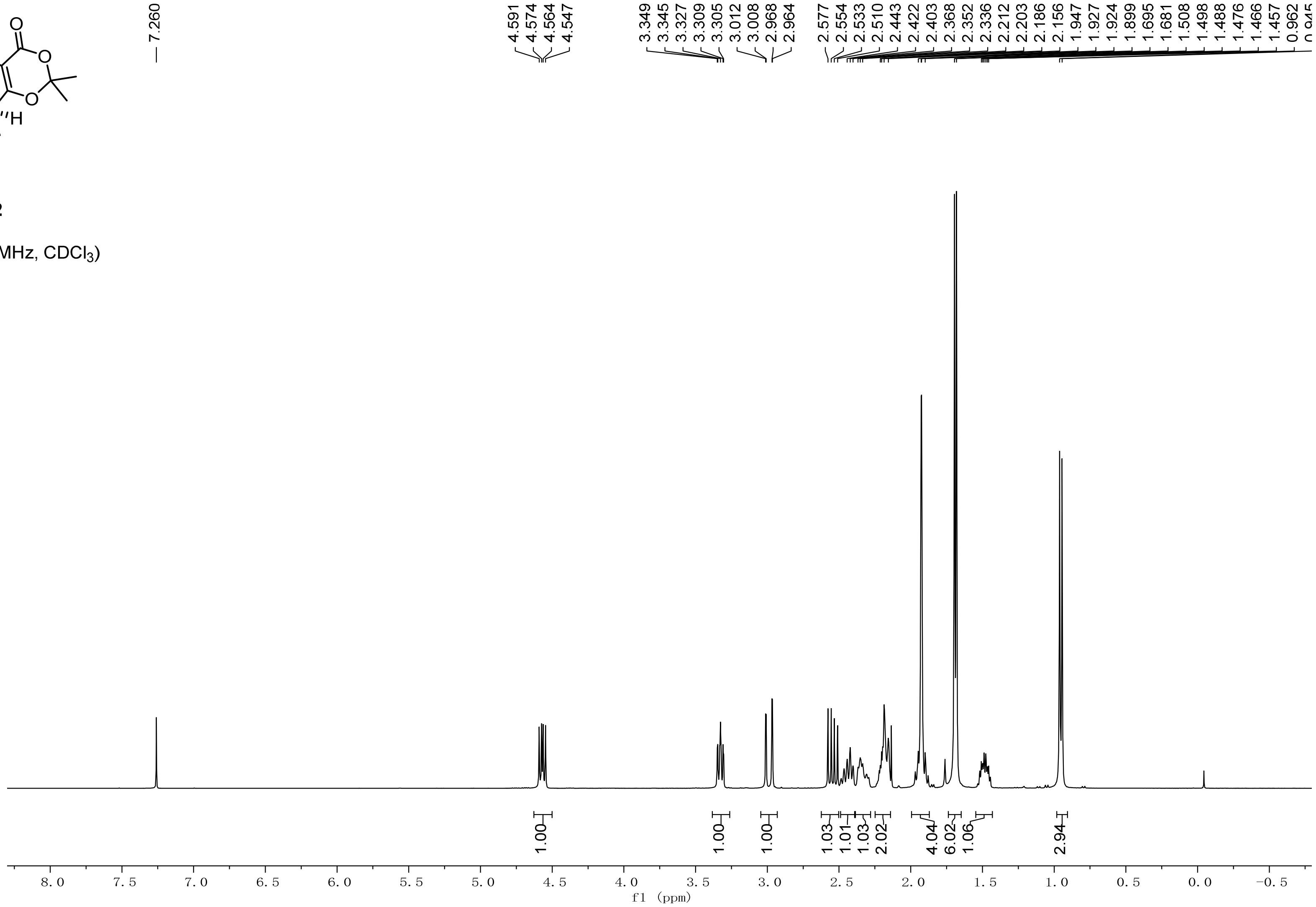
^{13}C NMR (100 MHz, $CDCl_3$)

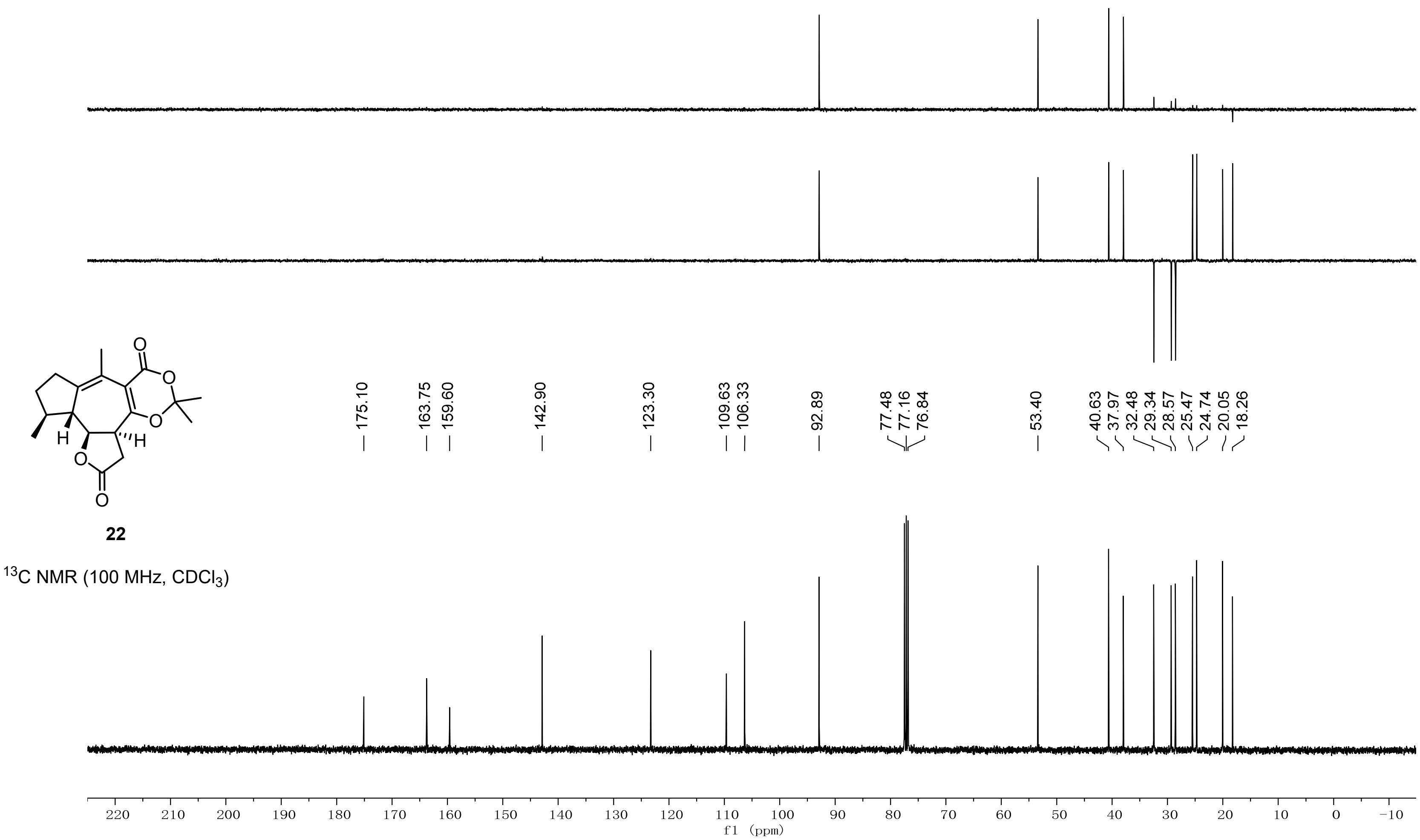




22

^{1}H NMR (400 MHz, CDCl$_3$)





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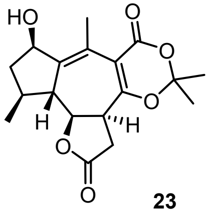

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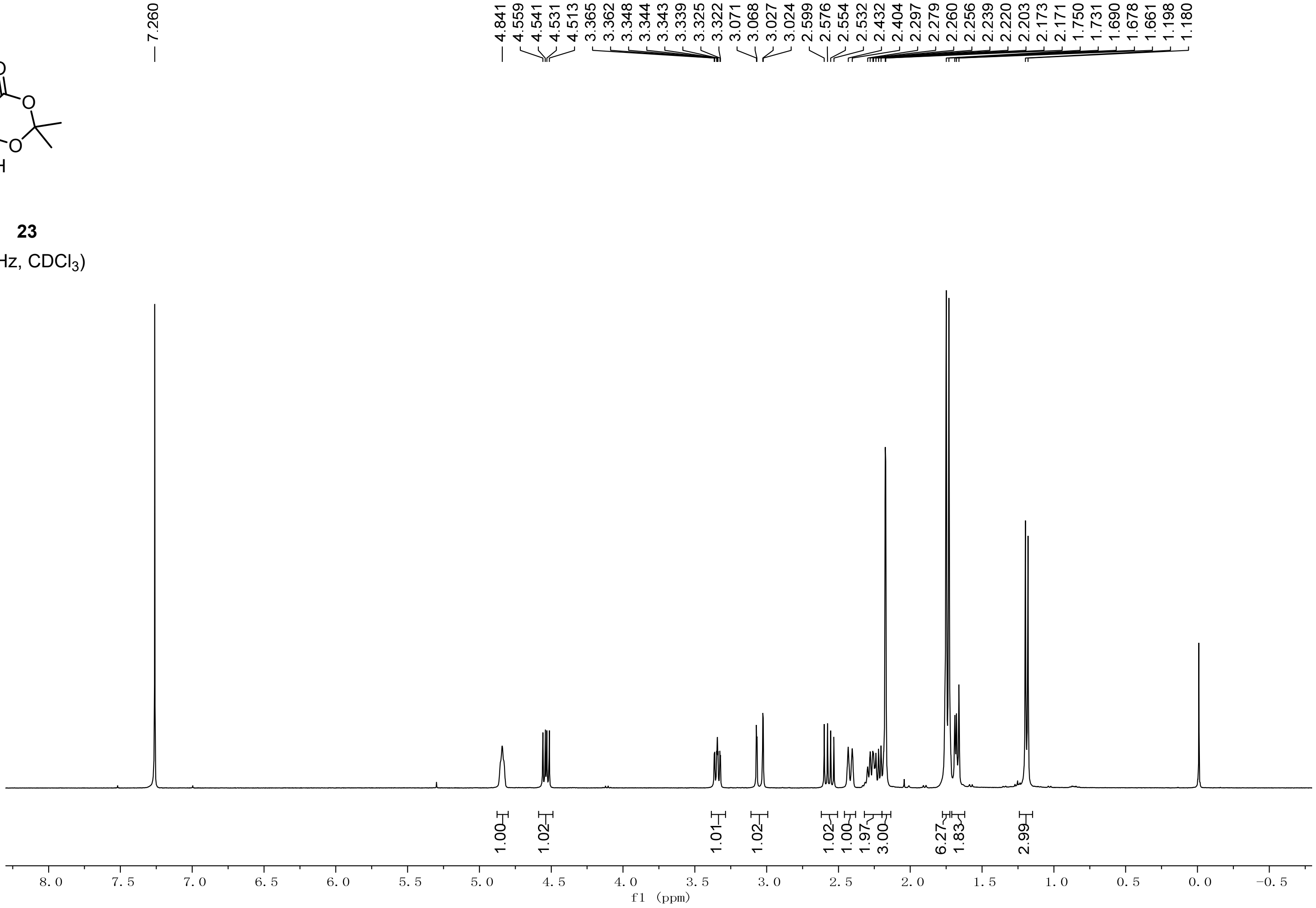

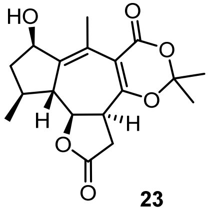

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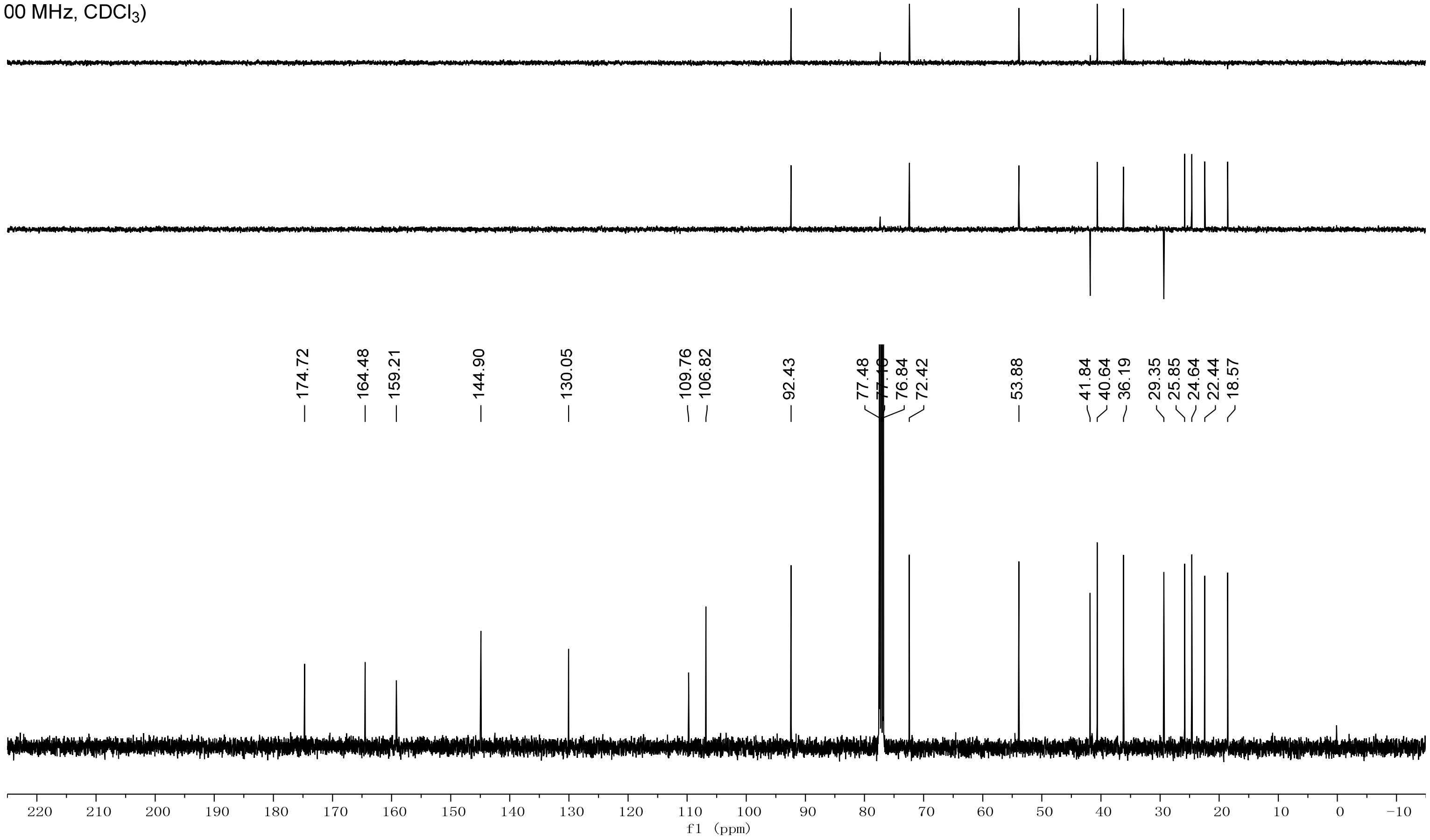
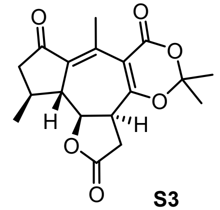
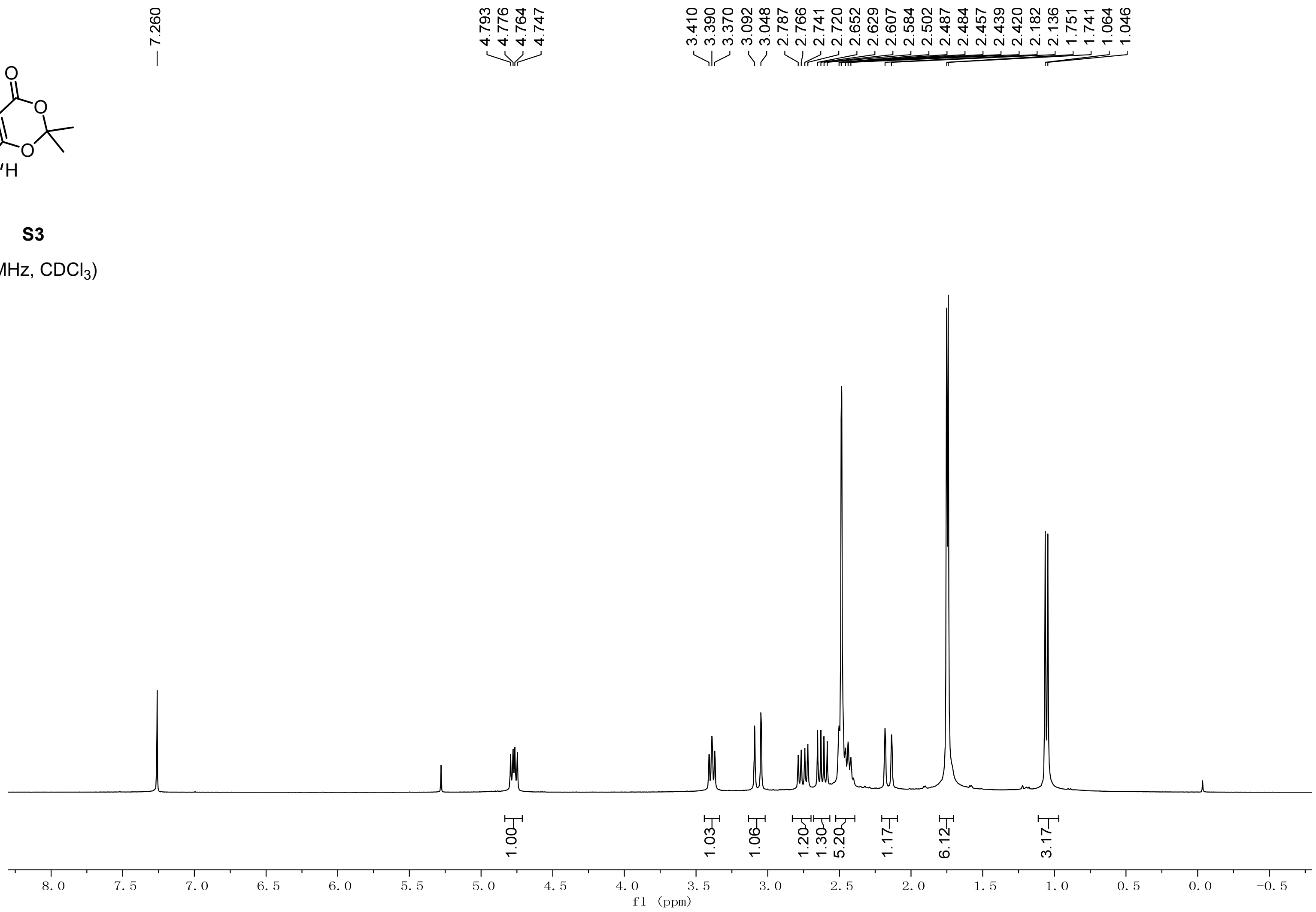
^{13}C NMR (100 MHz, CDCl$_3$)

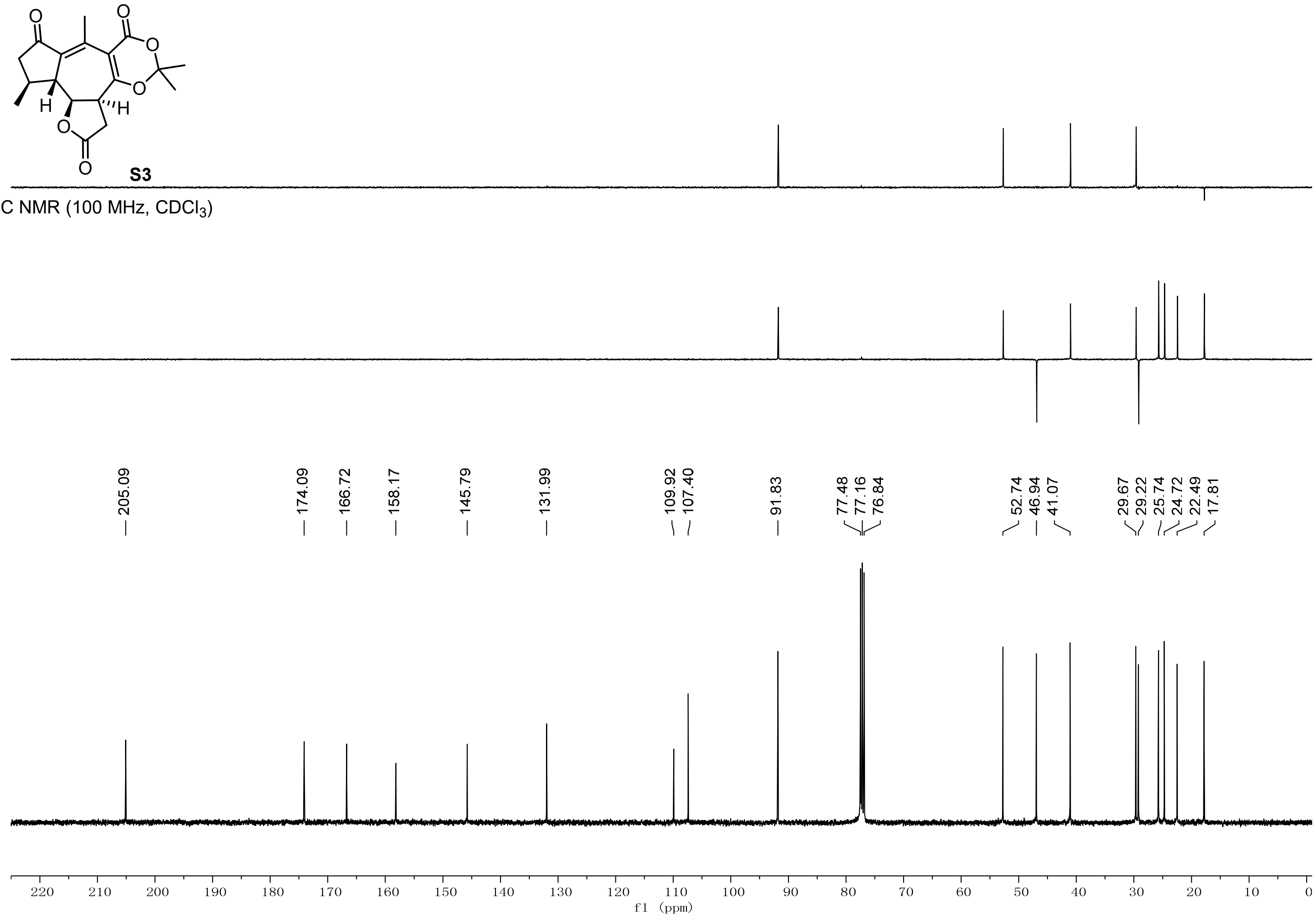




S3

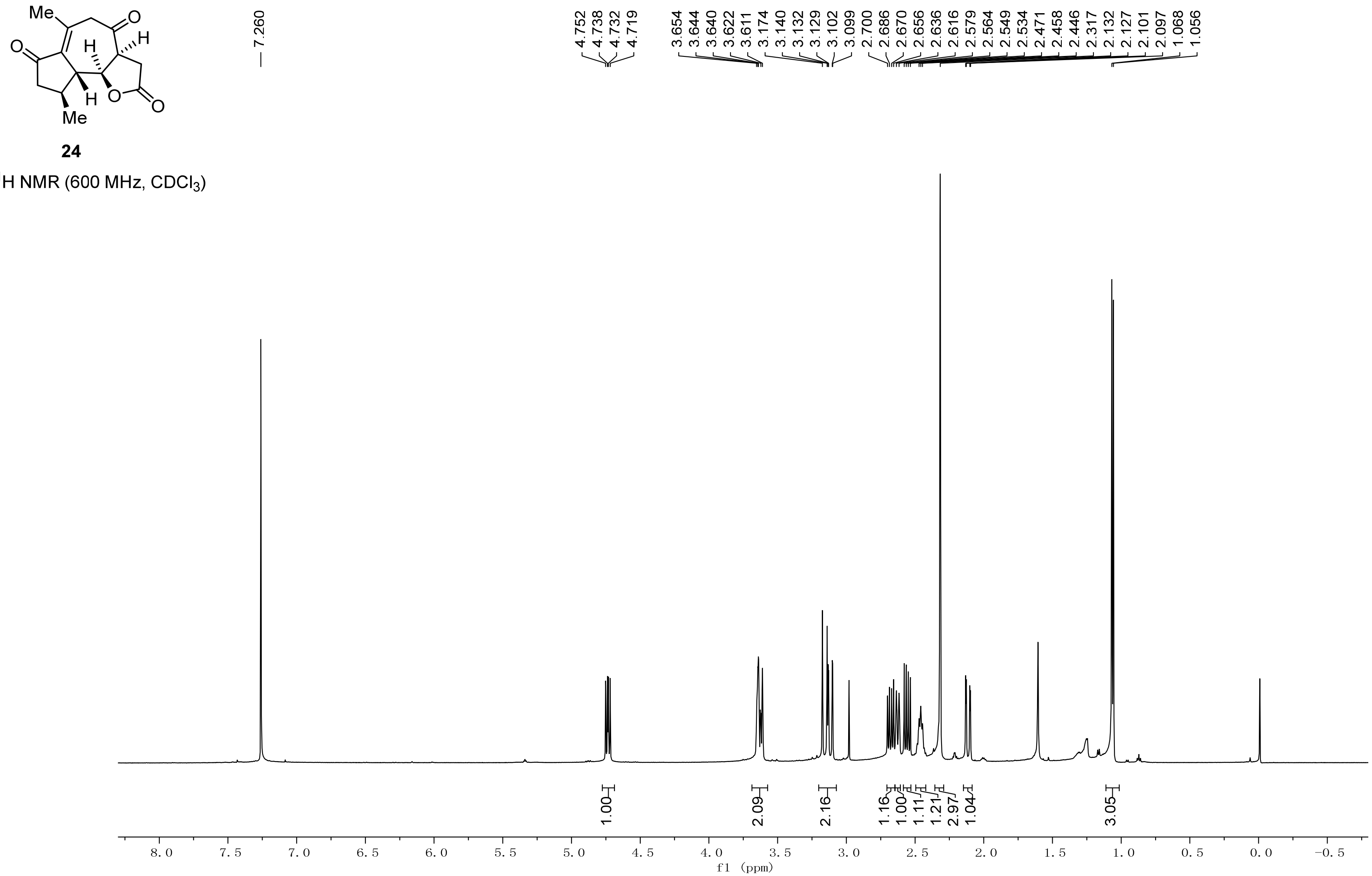
^{1}H NMR (400 MHz, CDCl$_3$)





S3

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



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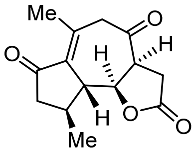
^{1}H NMR (600 MHz, CDCl$_3$)



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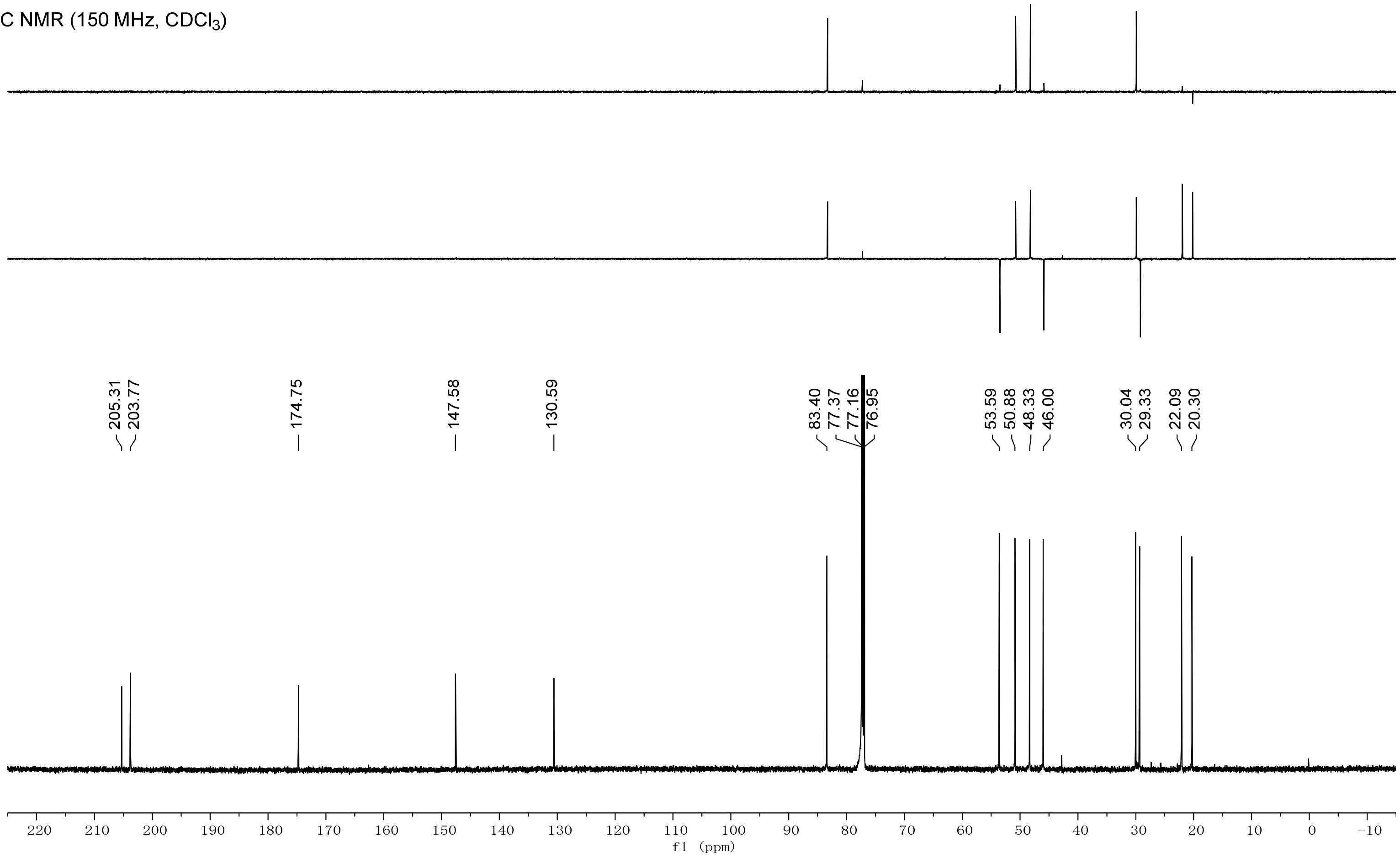
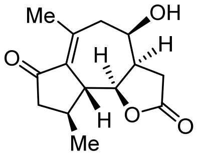
^{13}C NMR (150 MHz, $CDCl_3$)





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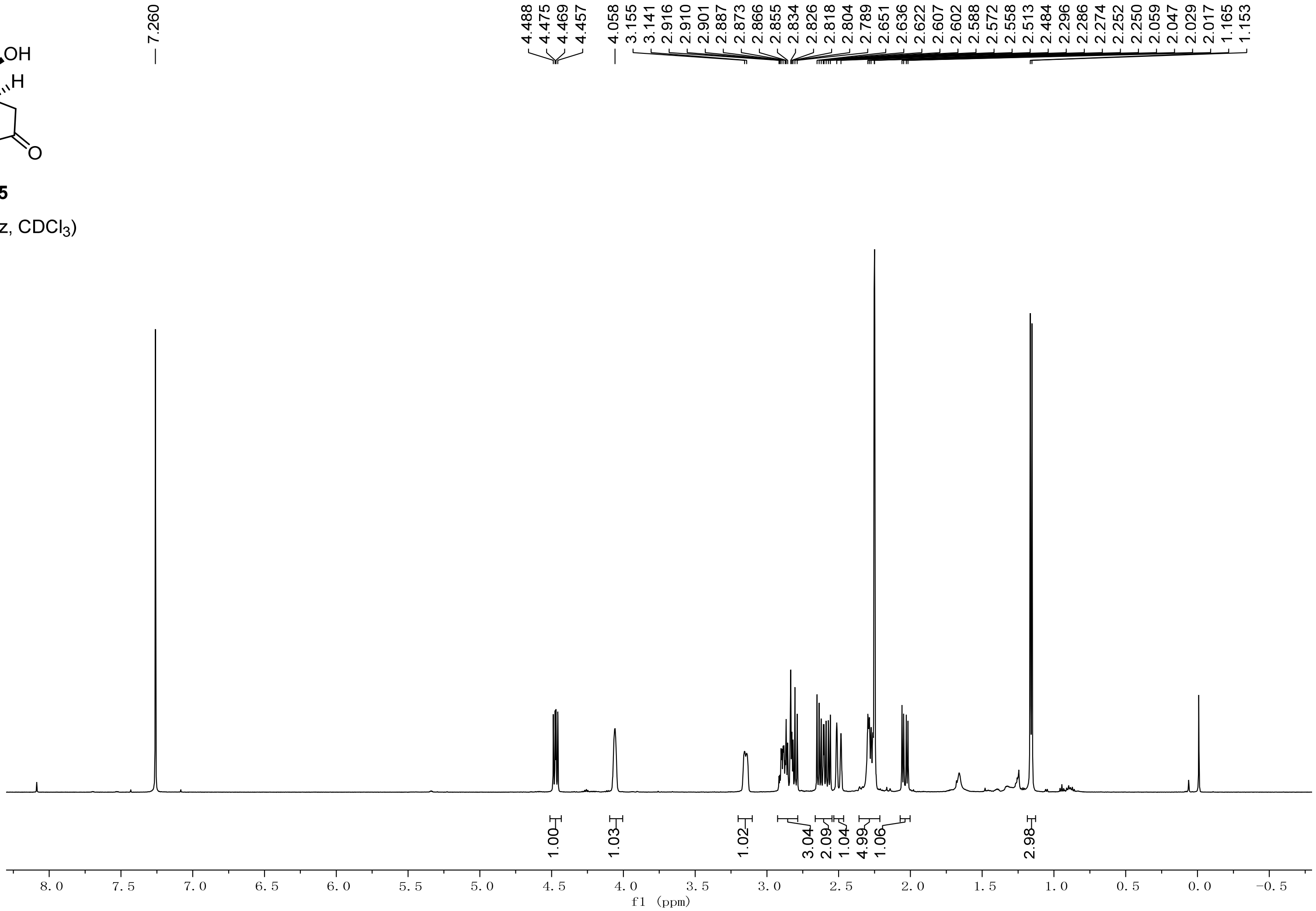

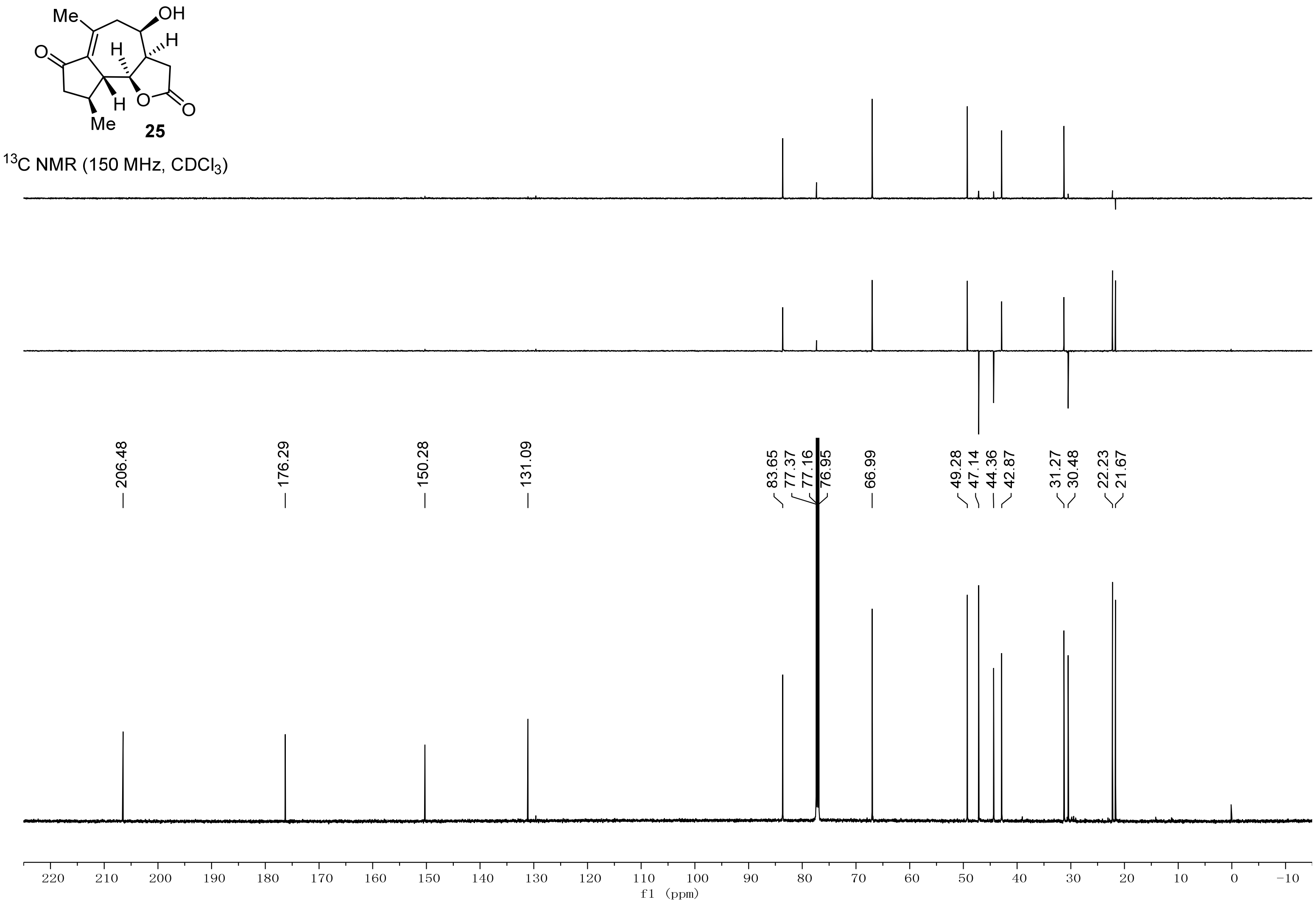

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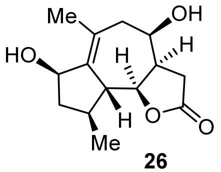

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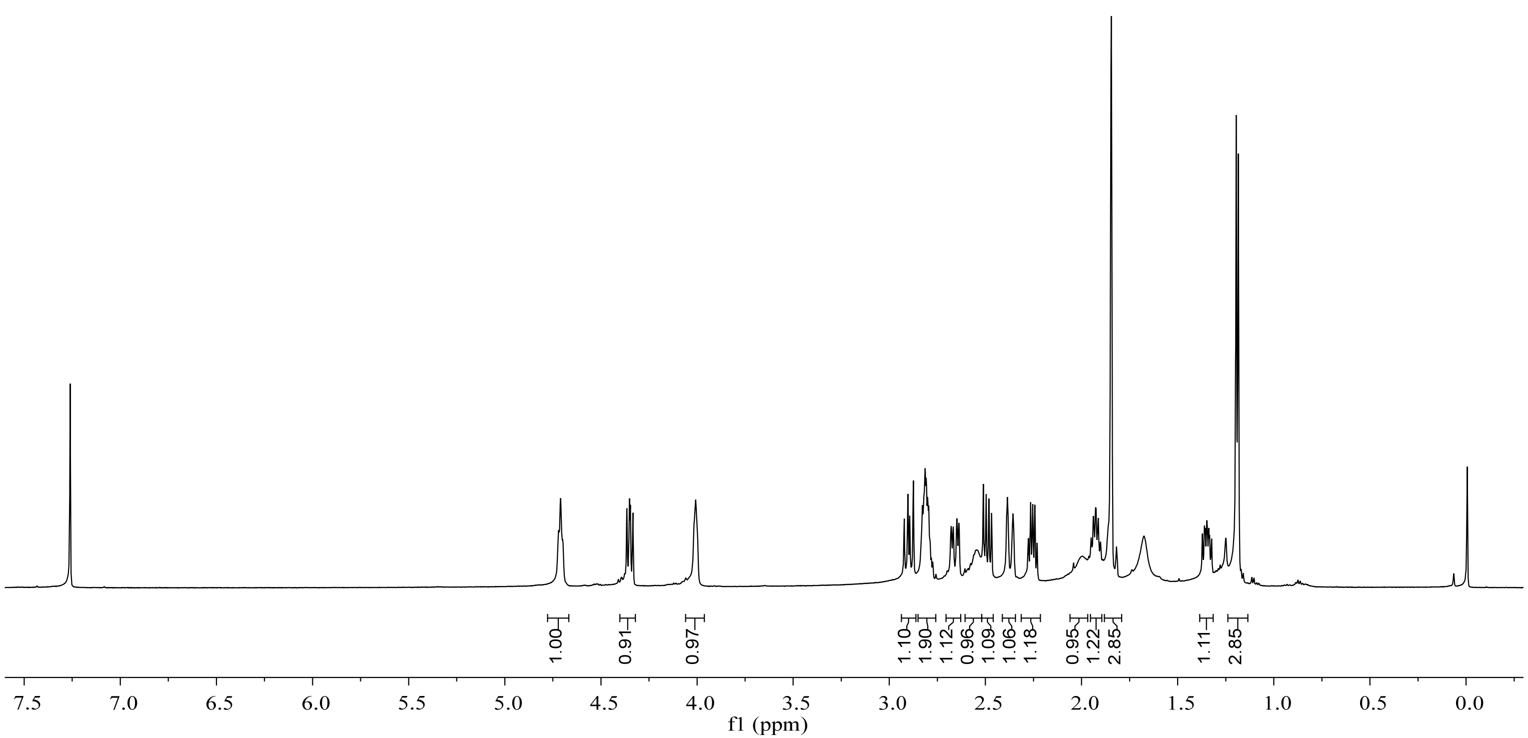

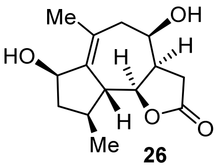

26

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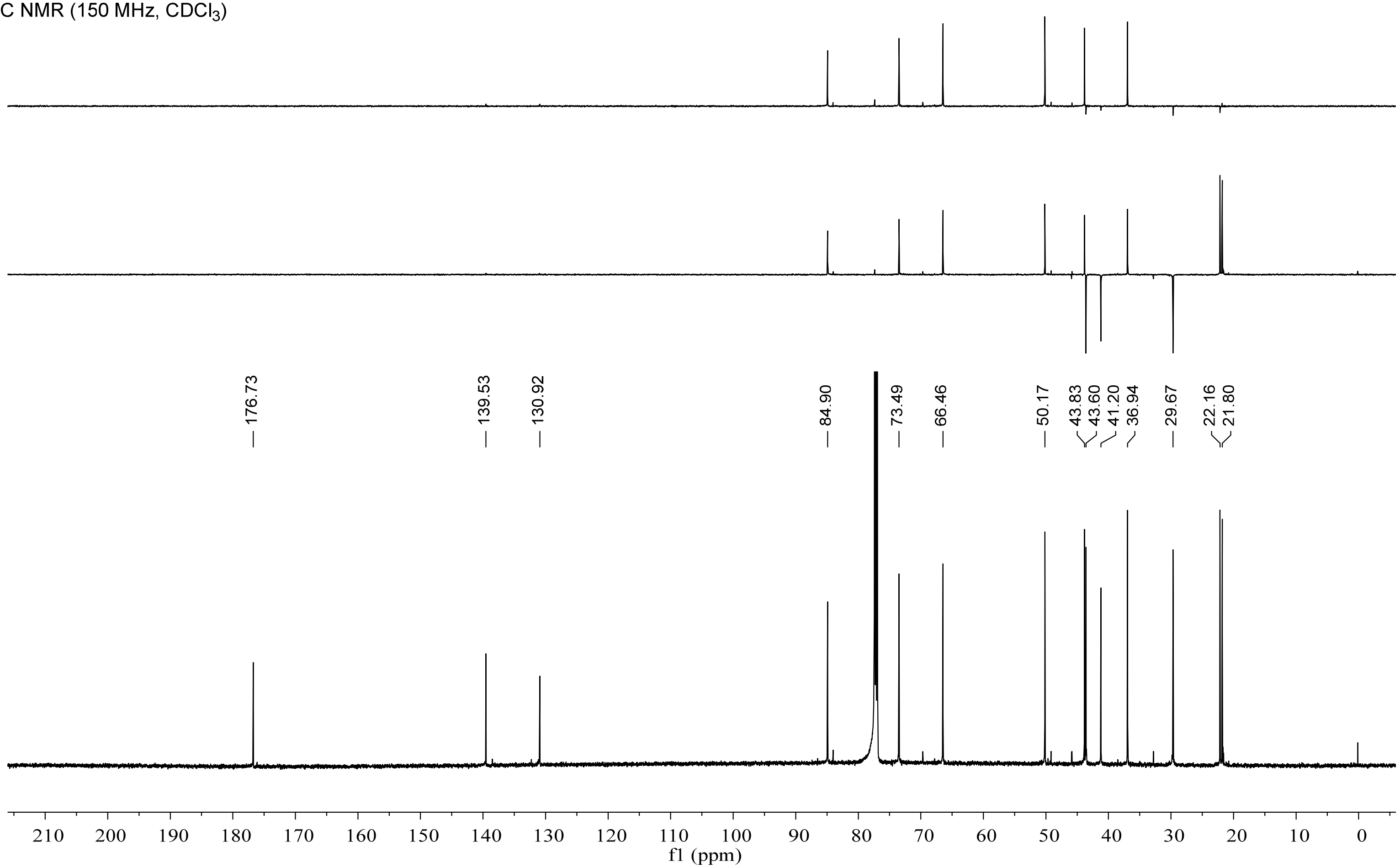
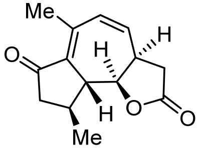
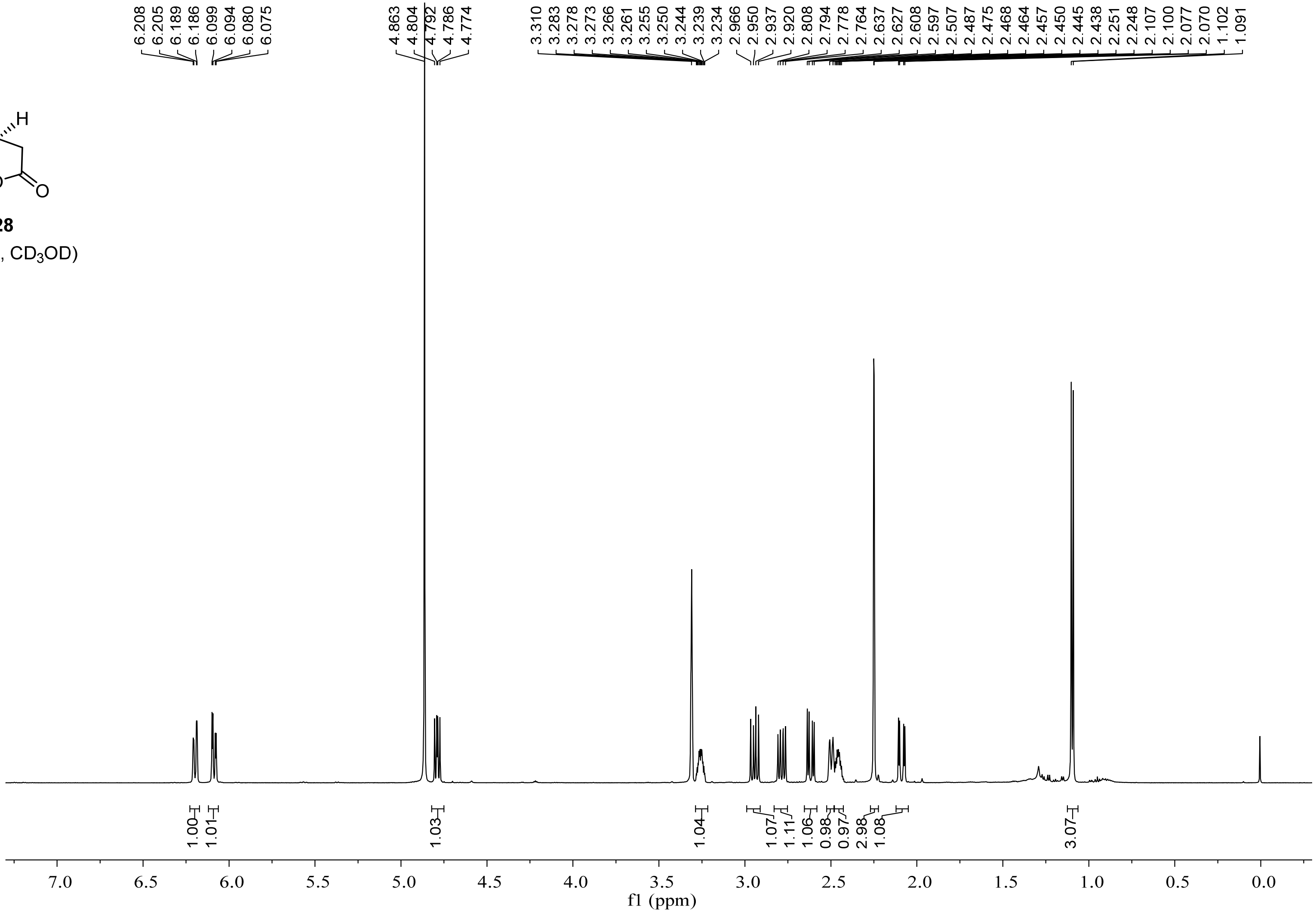
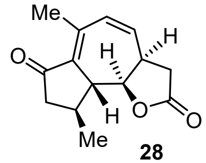




28

^{1}H NMR (600 MHz, CD_3OD)





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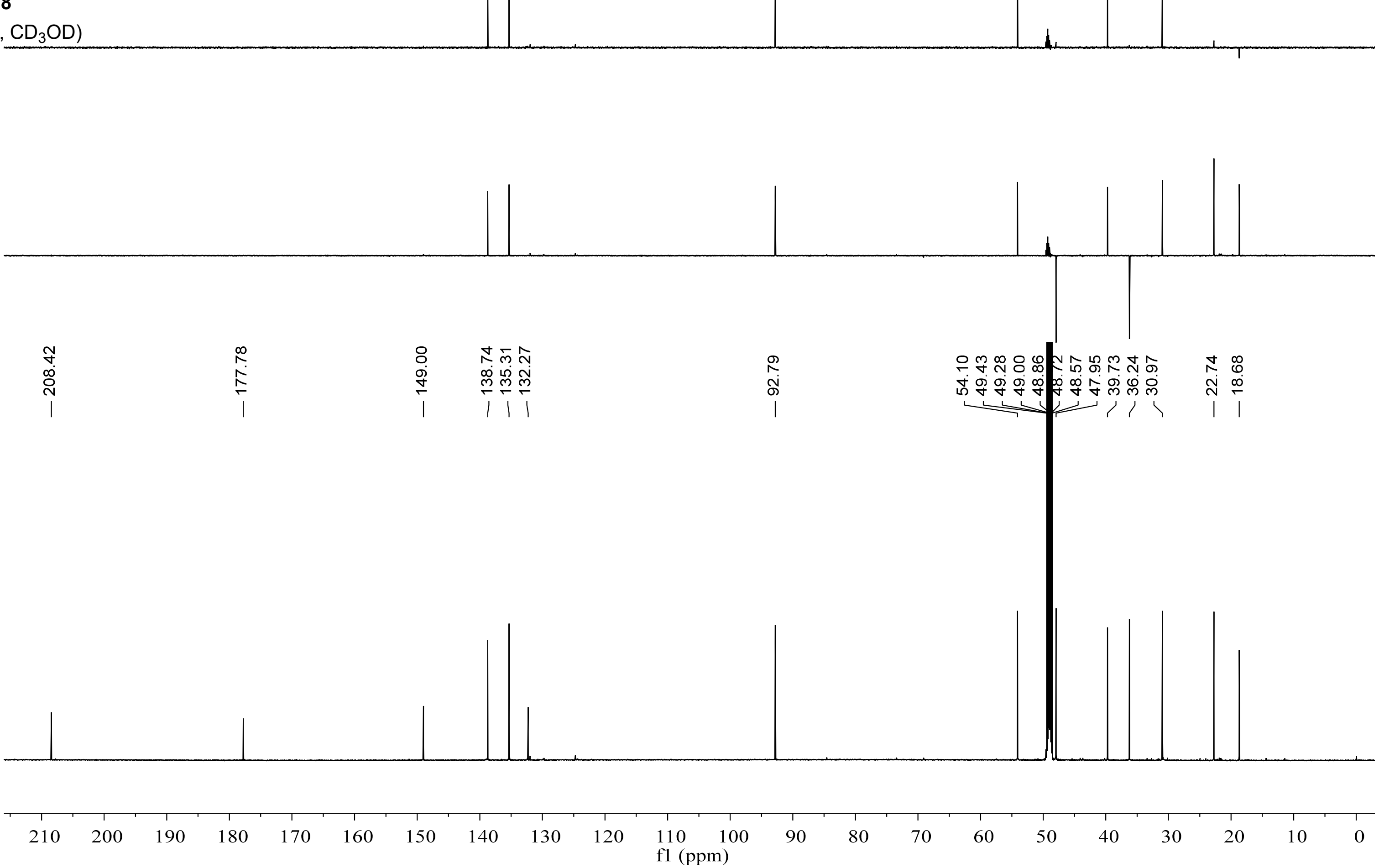
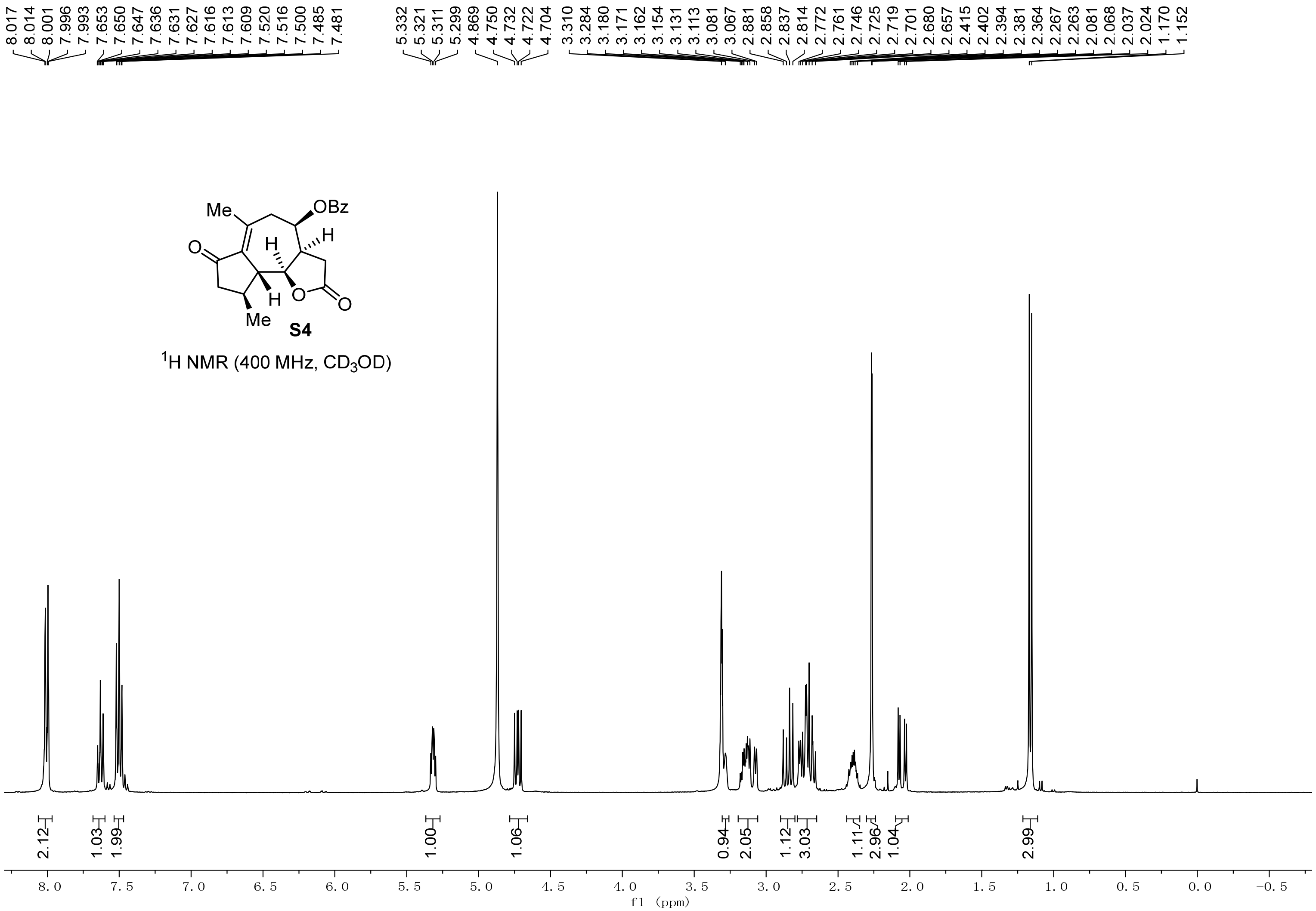
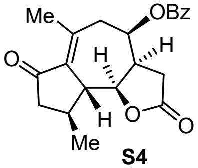




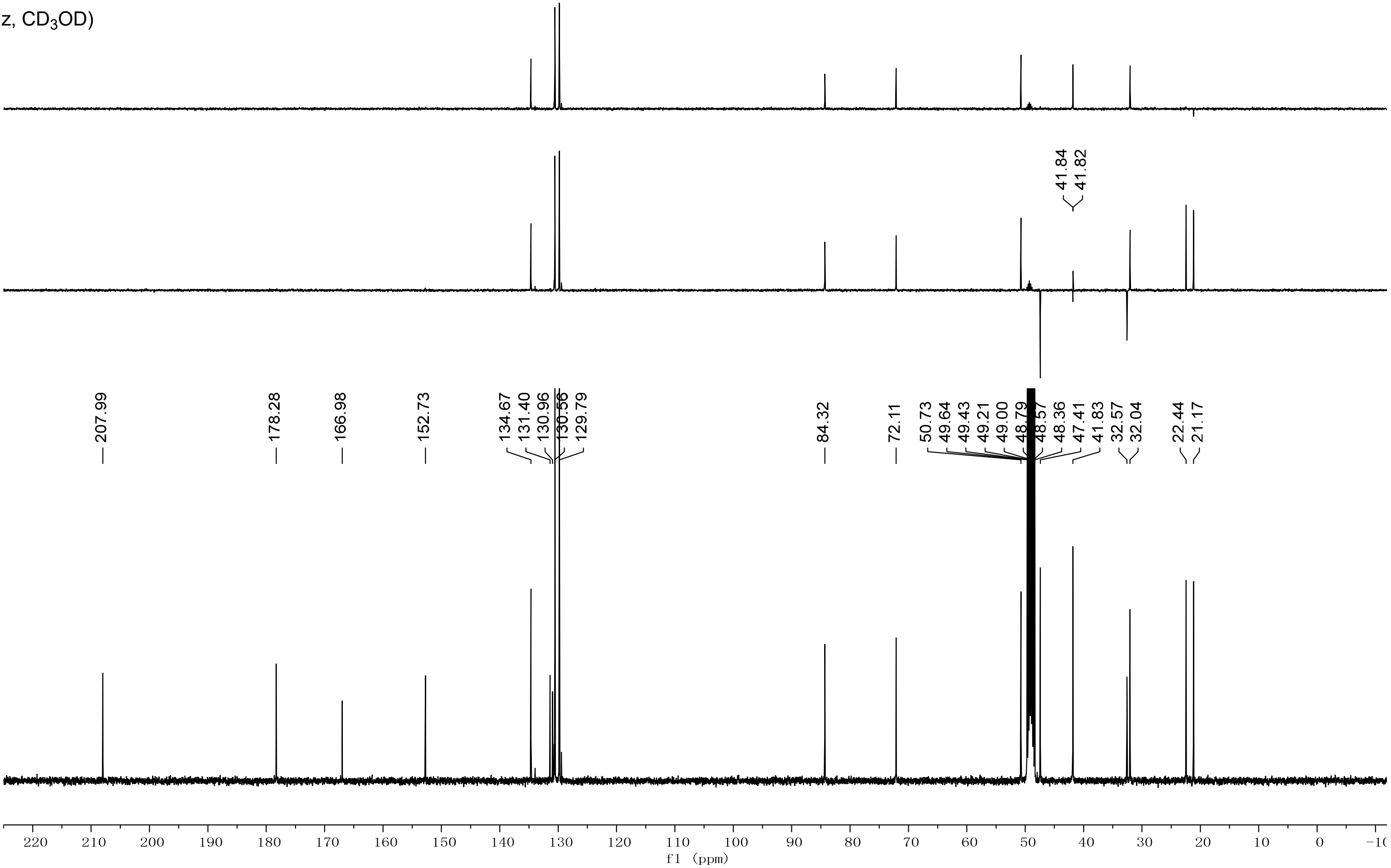
S4

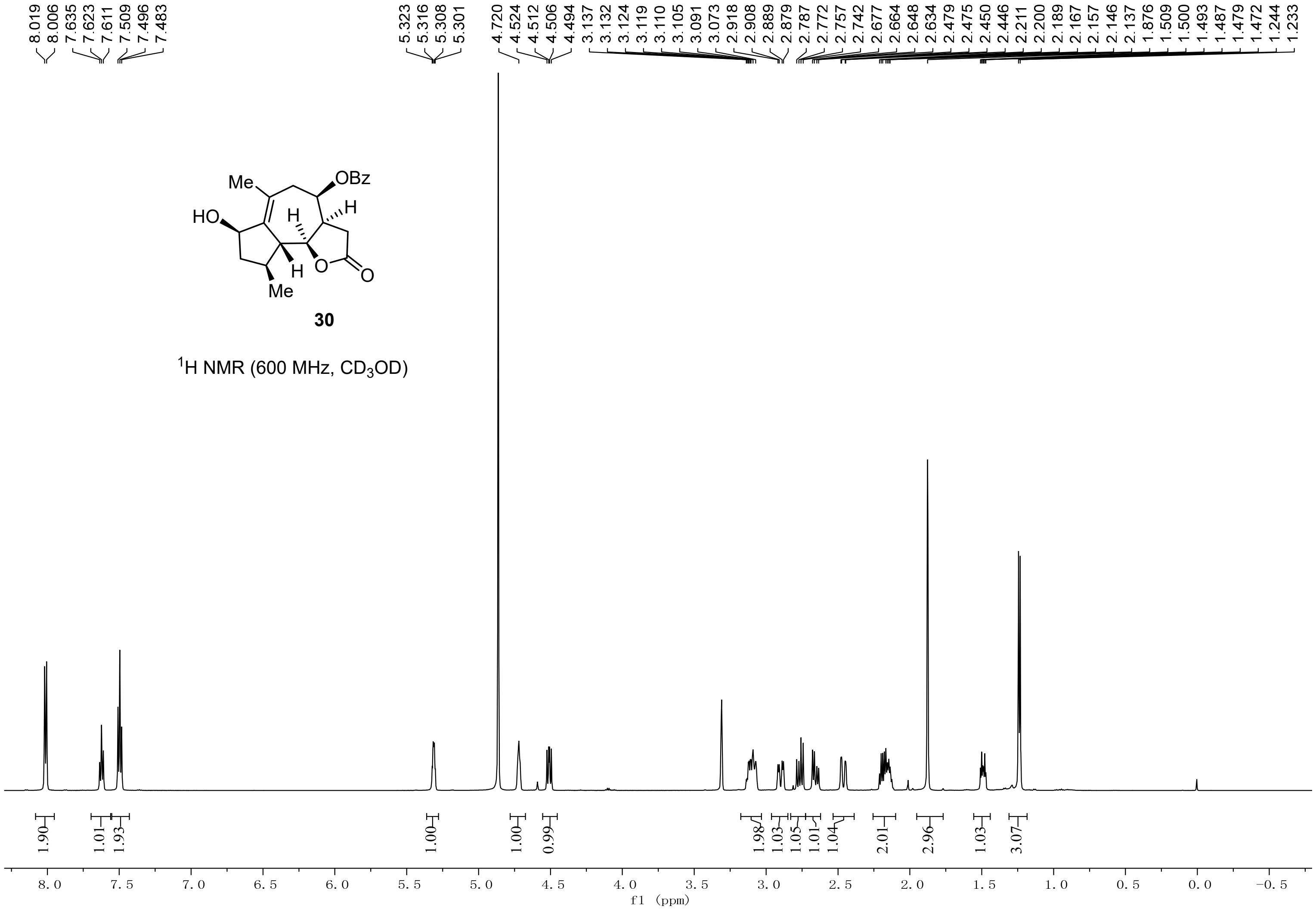
^{1}H NMR (400 MHz, CD$_3$OD)



S4

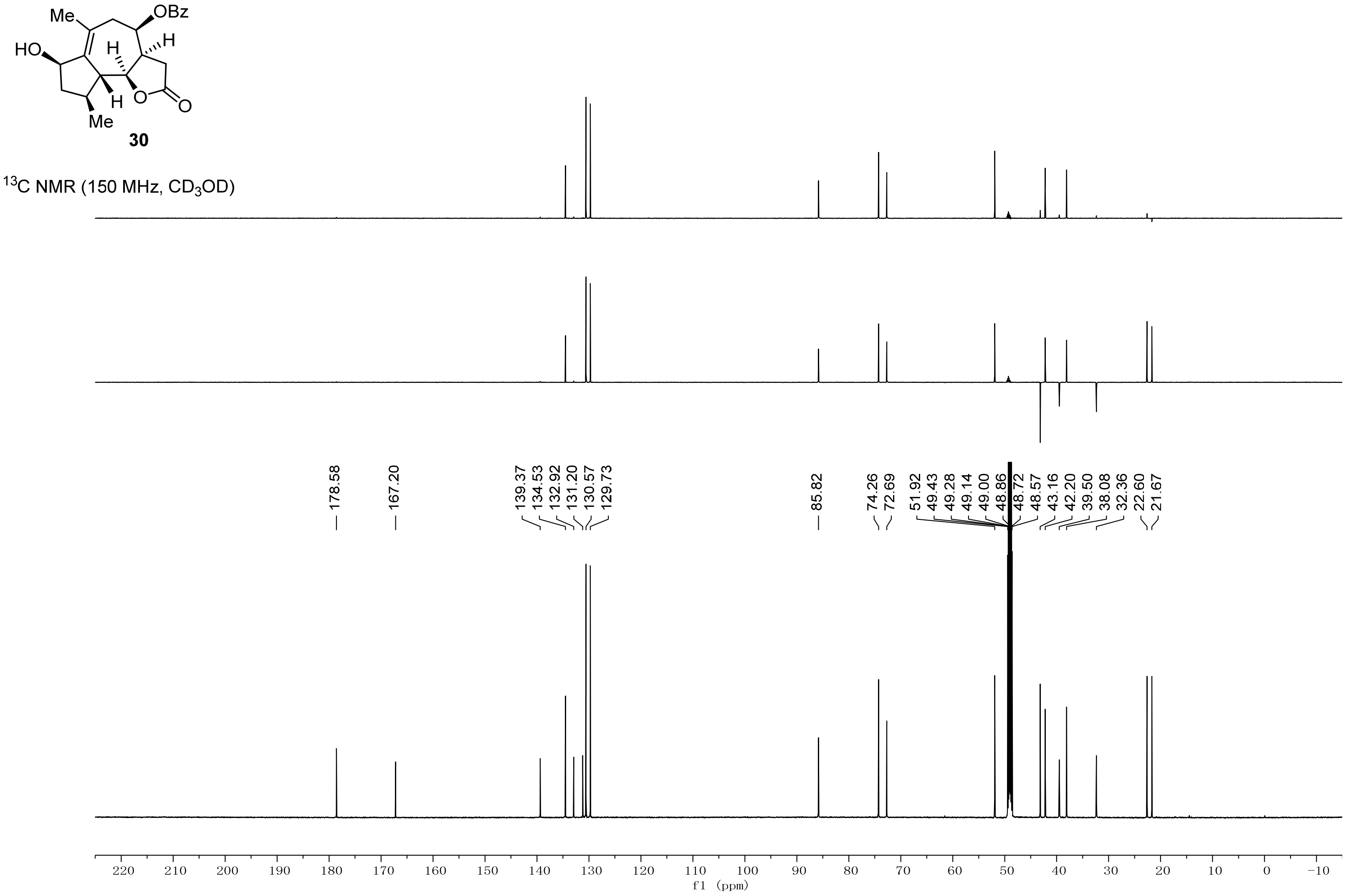
^{13}C NMR (100 MHz, CD_3OD)





30

^{1}H NMR (600 MHz, CD_3OD)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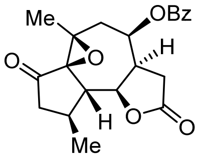
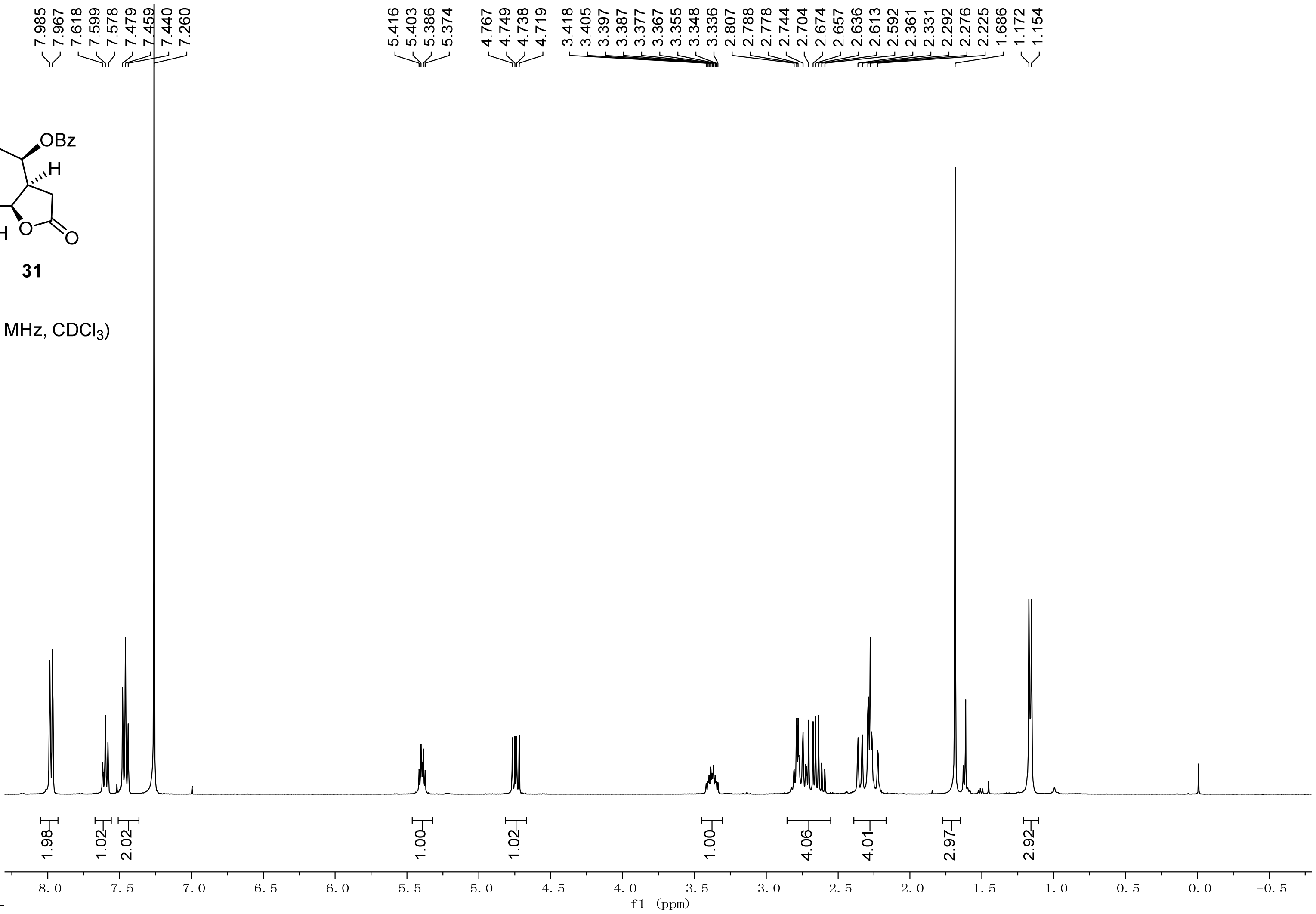
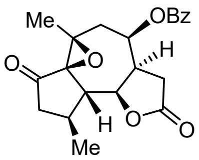
^{13}C NMR (150 MHz, CD_3OD)



31

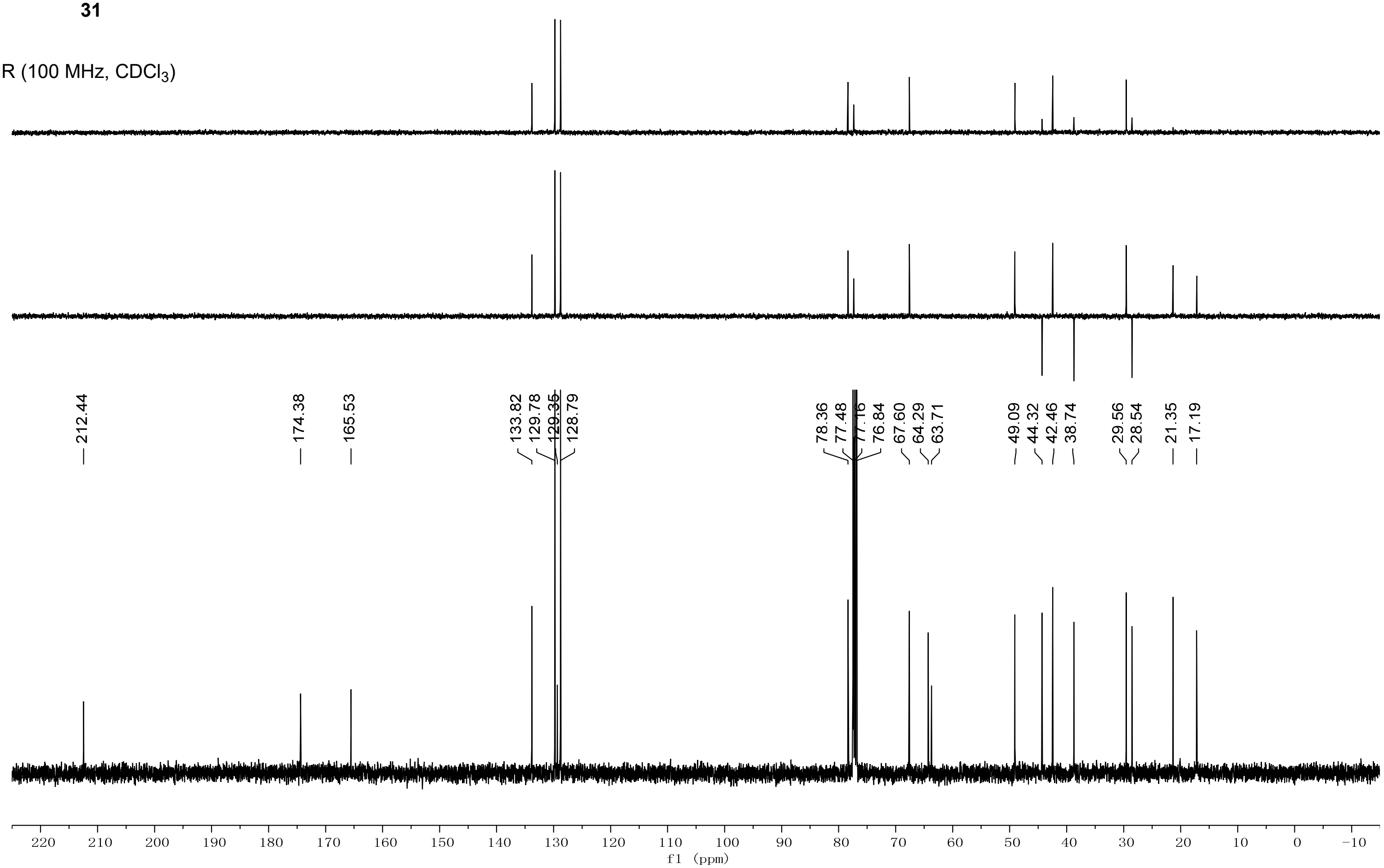
^{1}H NMR (400 MHz, CDCl$_3$)

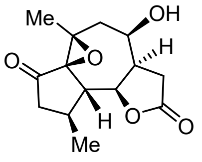




31

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





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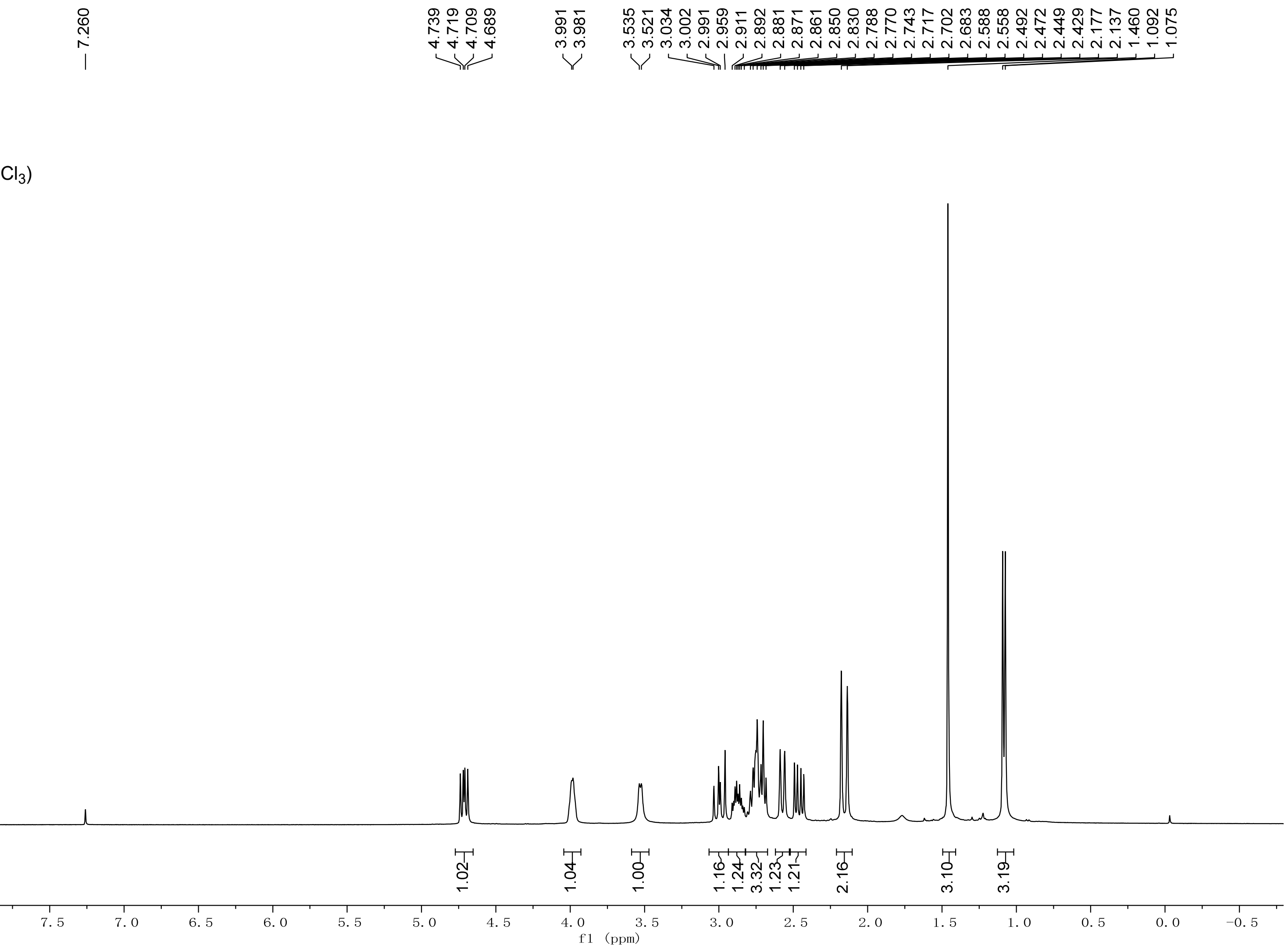
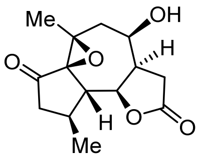
^{1}H NMR (400 MHz, $CDCl_3$)





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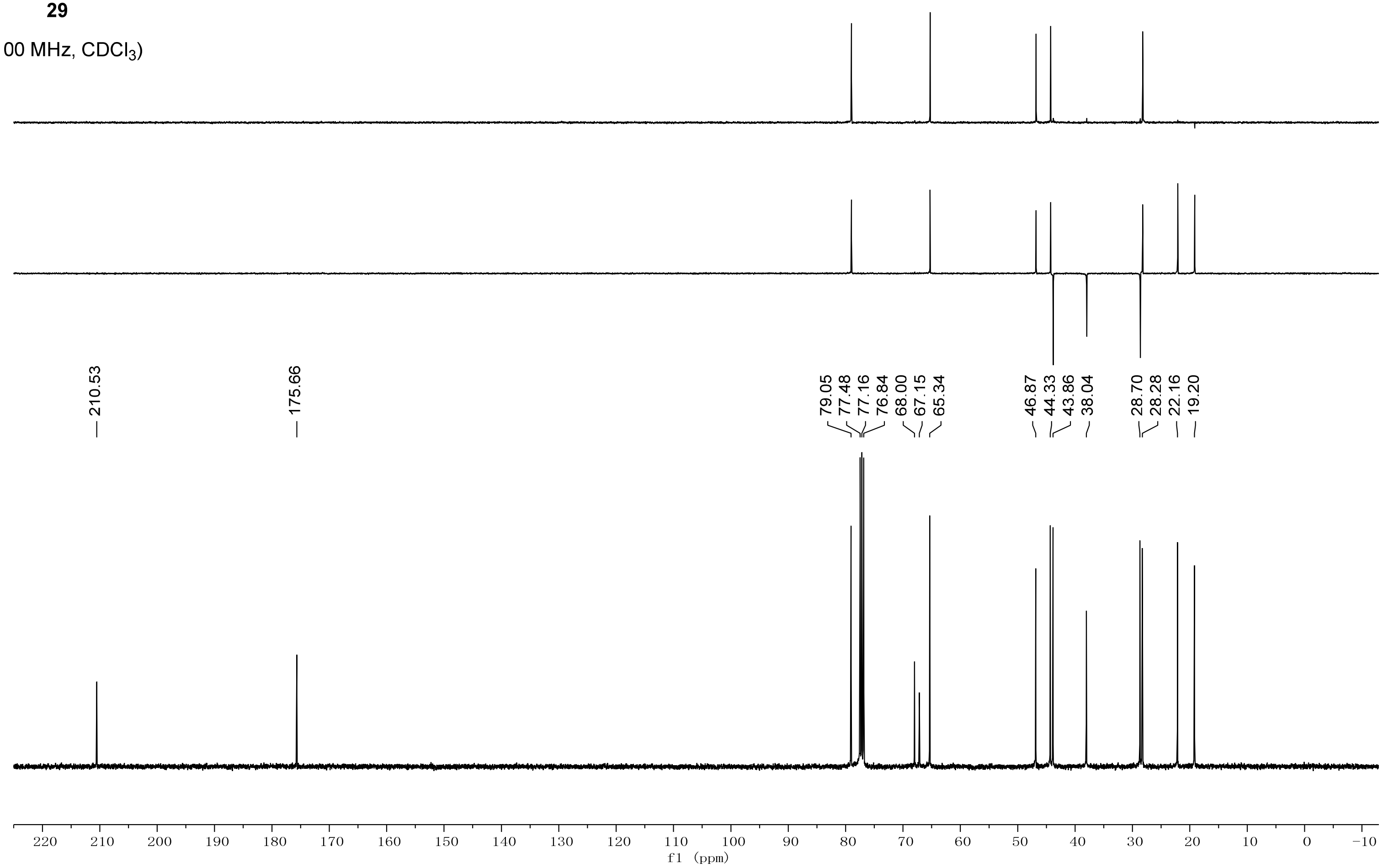
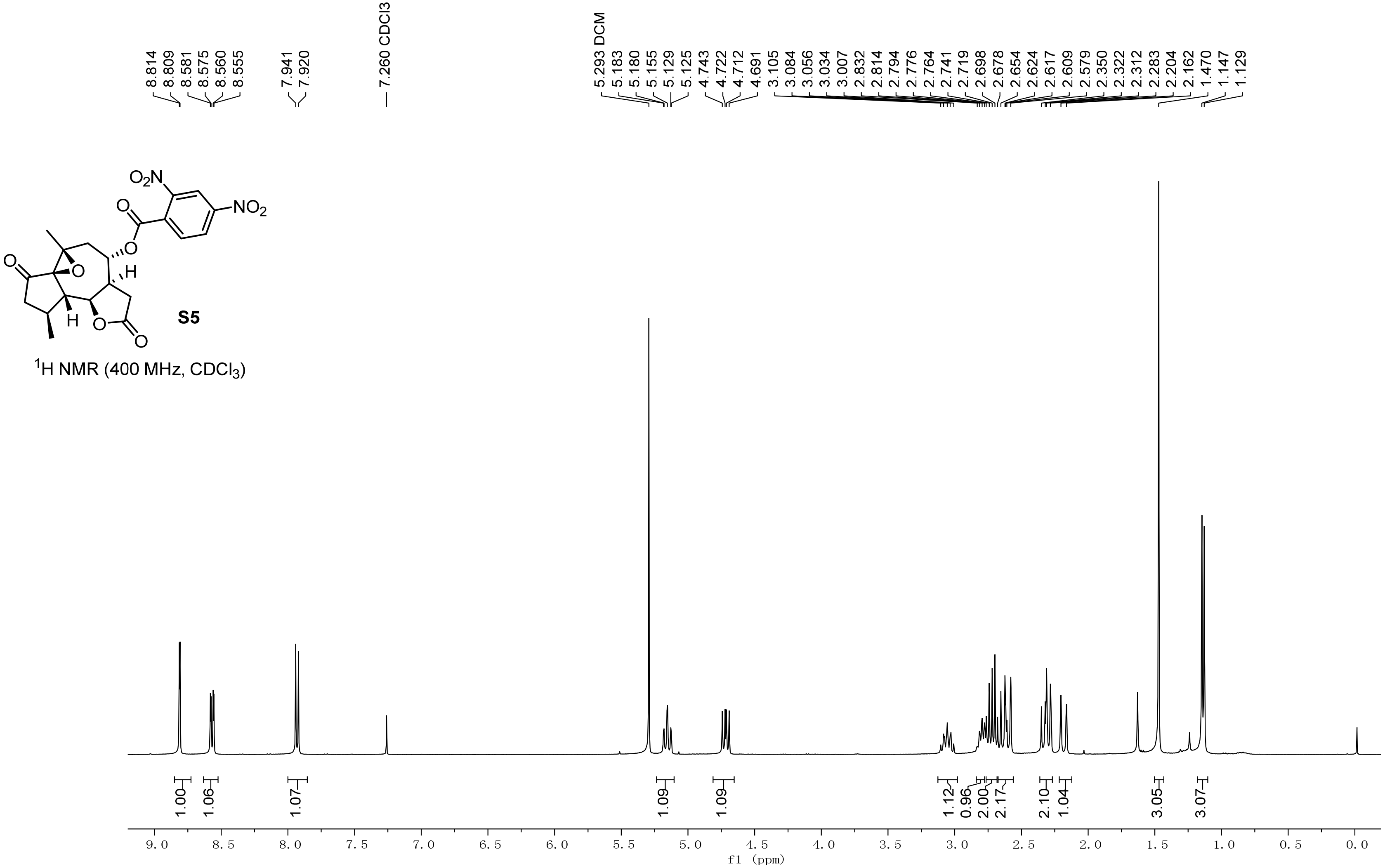
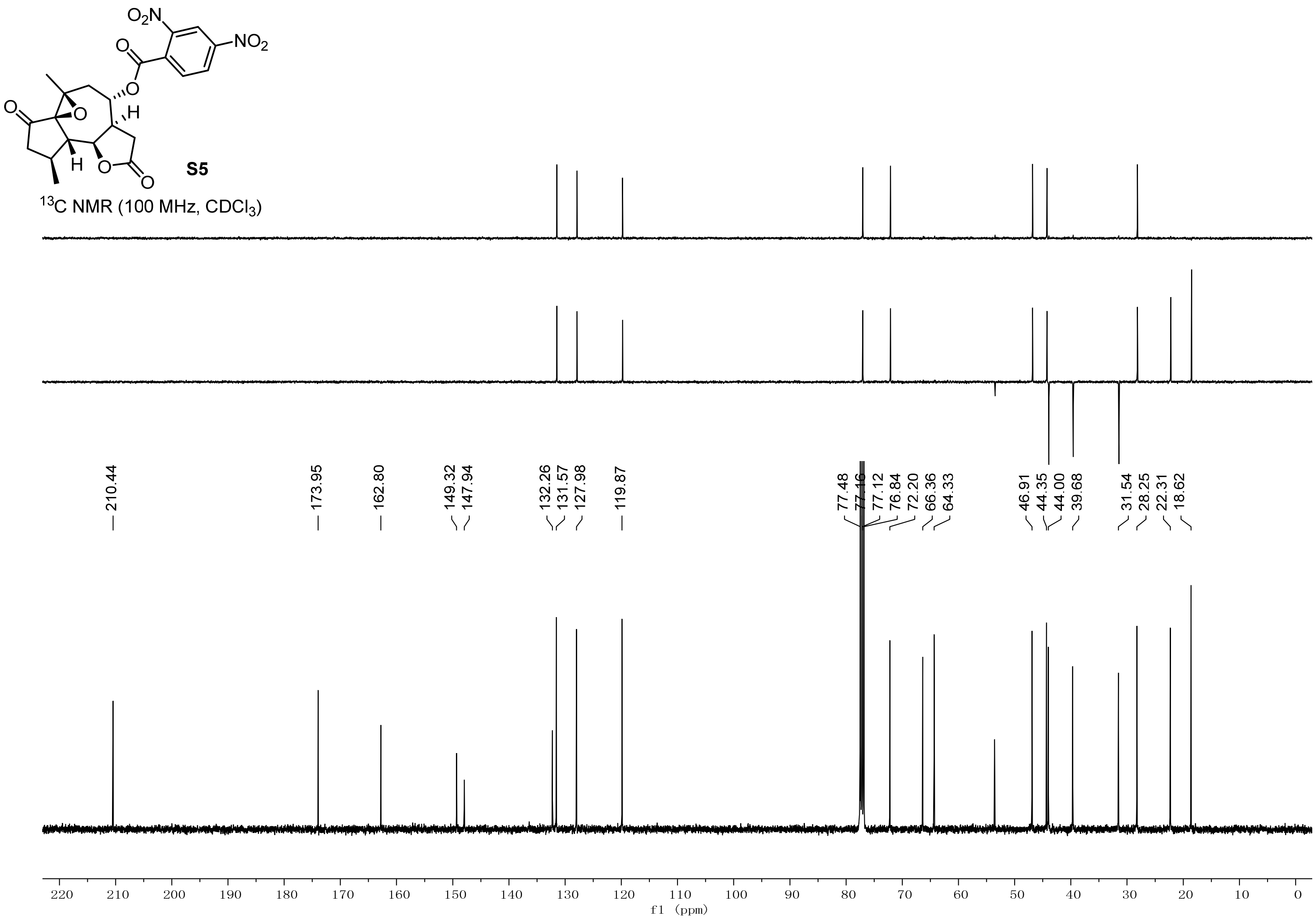
^{13}C NMR (100 MHz, CDCl$_3$)





S5

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

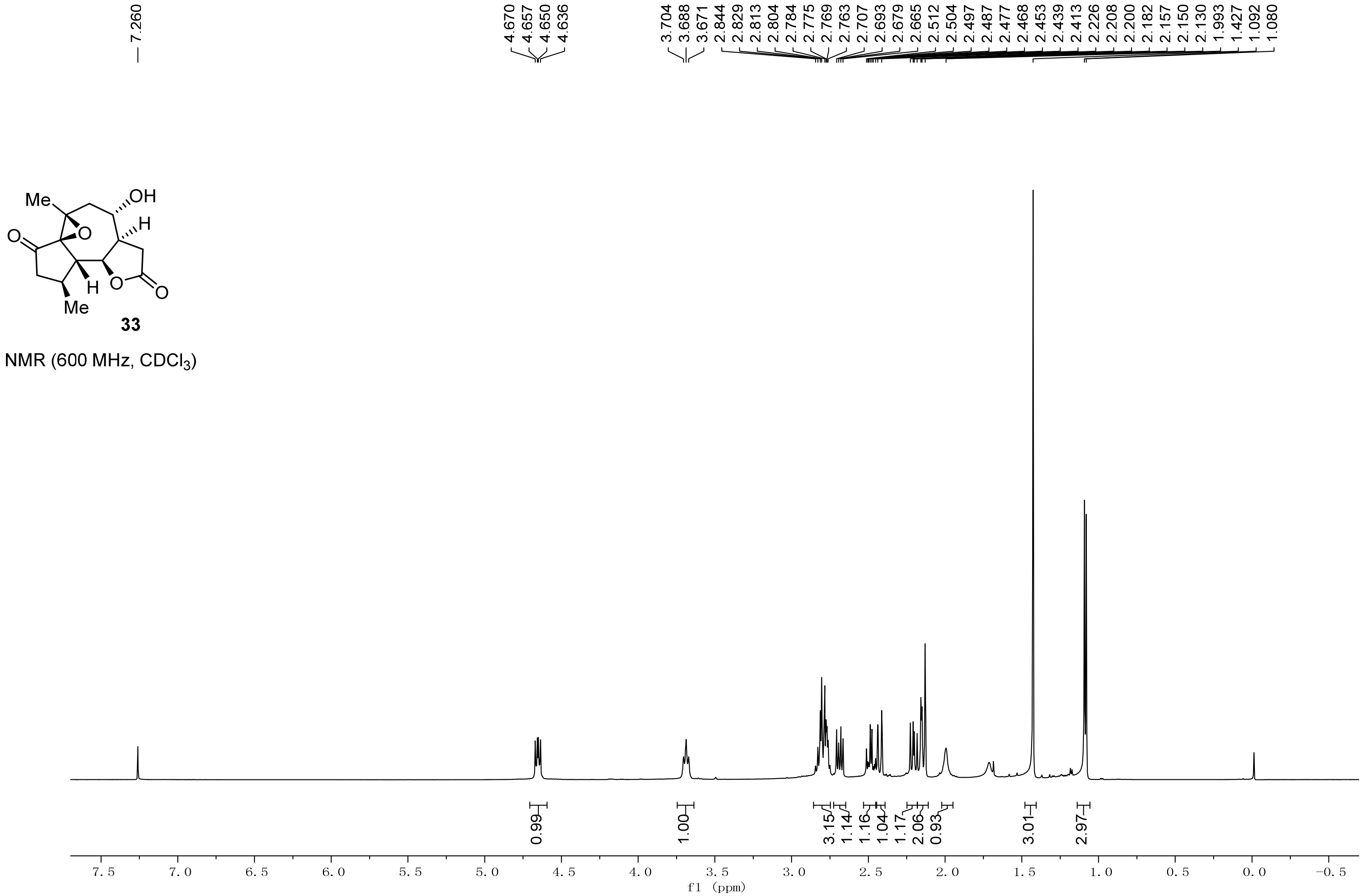


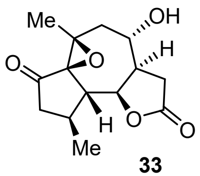
S5

^{13}C NMR (100 MHz, CDCl$_3$)

33

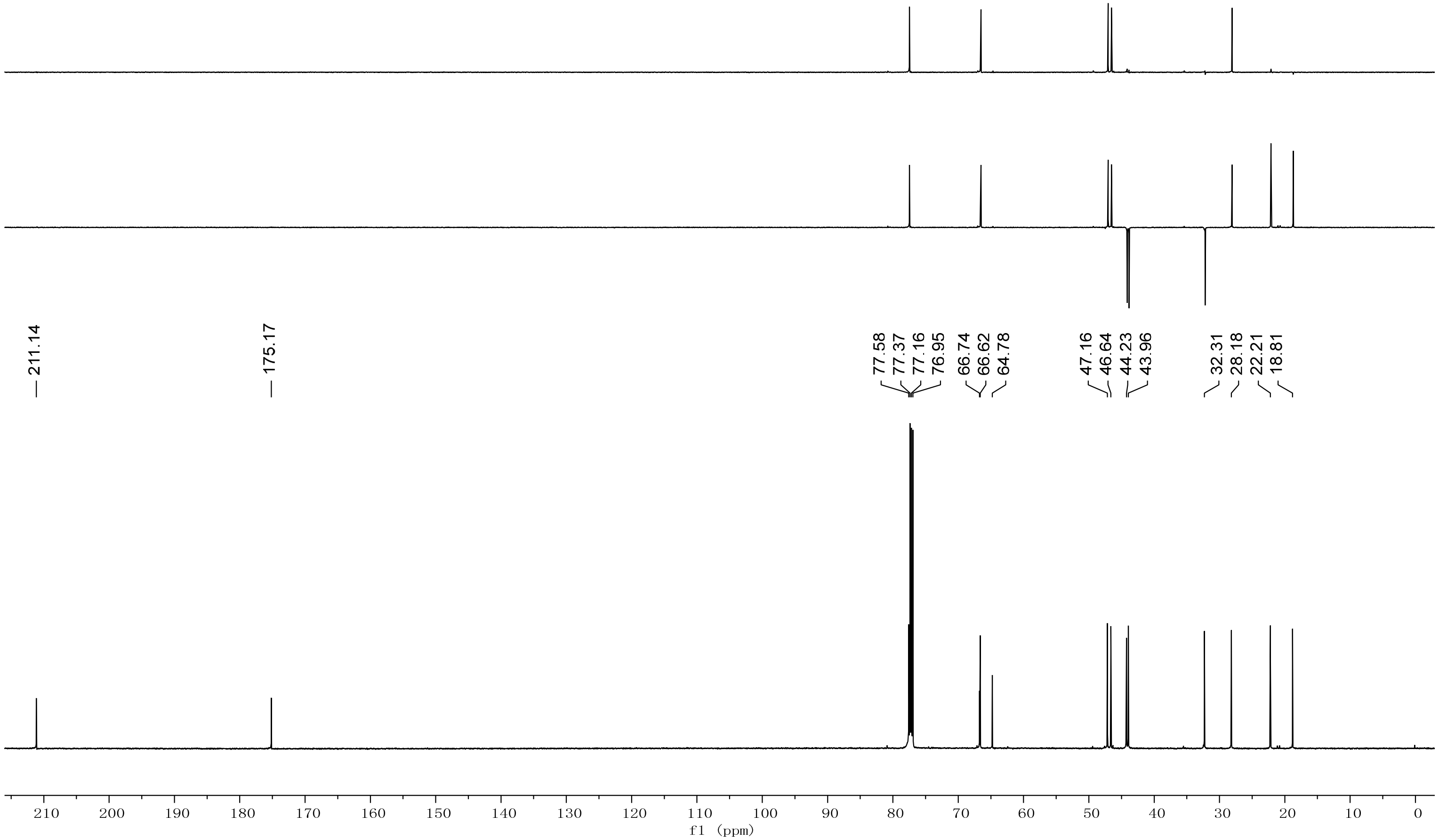
^{1}H NMR (600 MHz, CDCl$_3$)

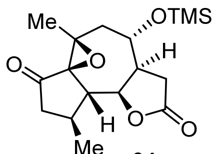




33

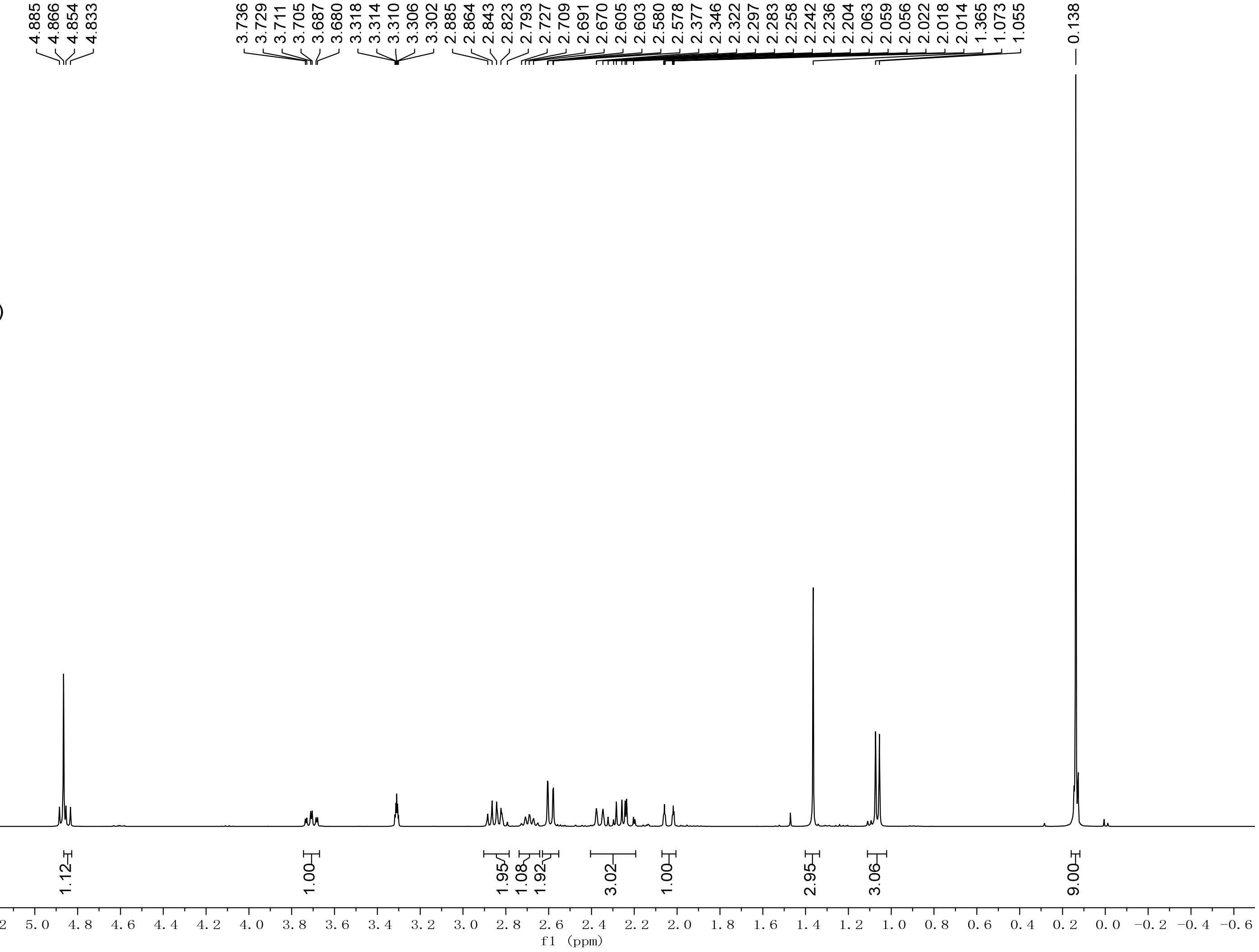
^{13}C NMR (150 MHz, CDCl$_3$)

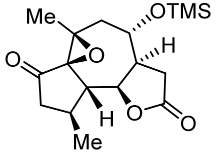




34

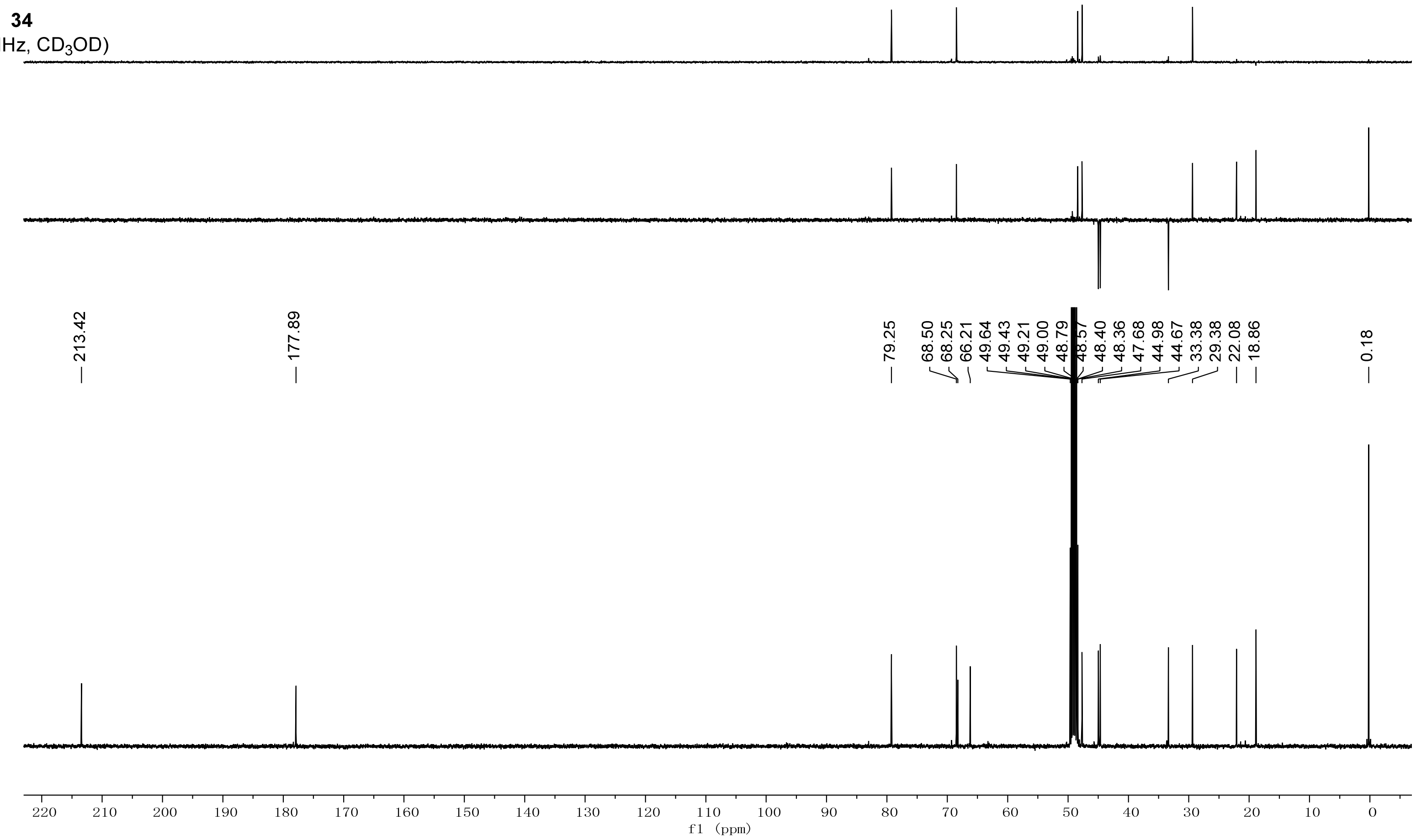
^{1}H NMR (400 MHz, CD_3OD)

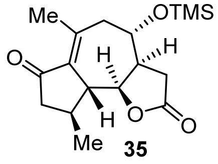




34

^{13}C NMR (100 MHz, CD$_3$OD)





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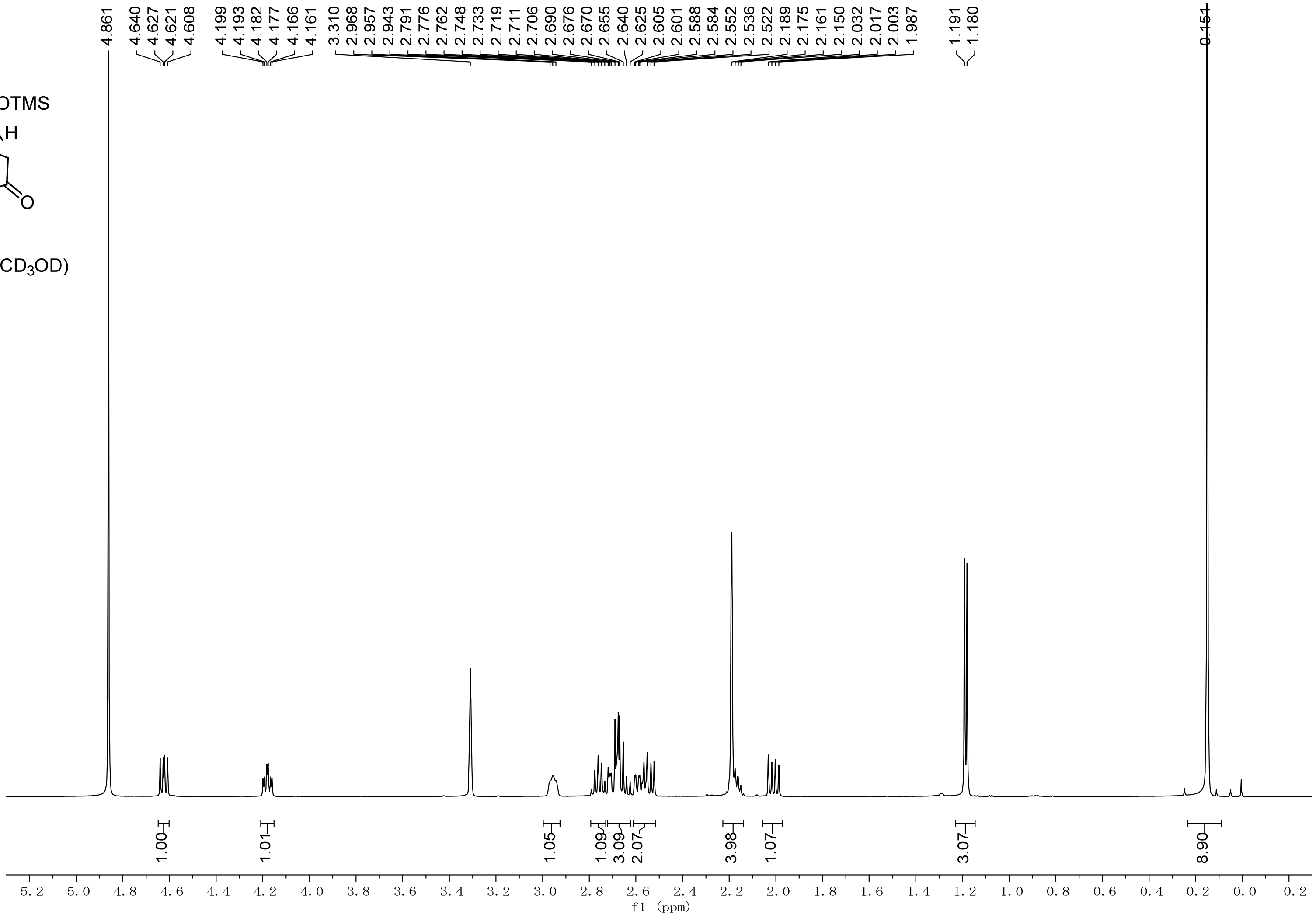
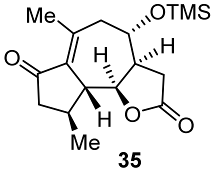
^{1}H NMR (600 MHz, CD_3OD)





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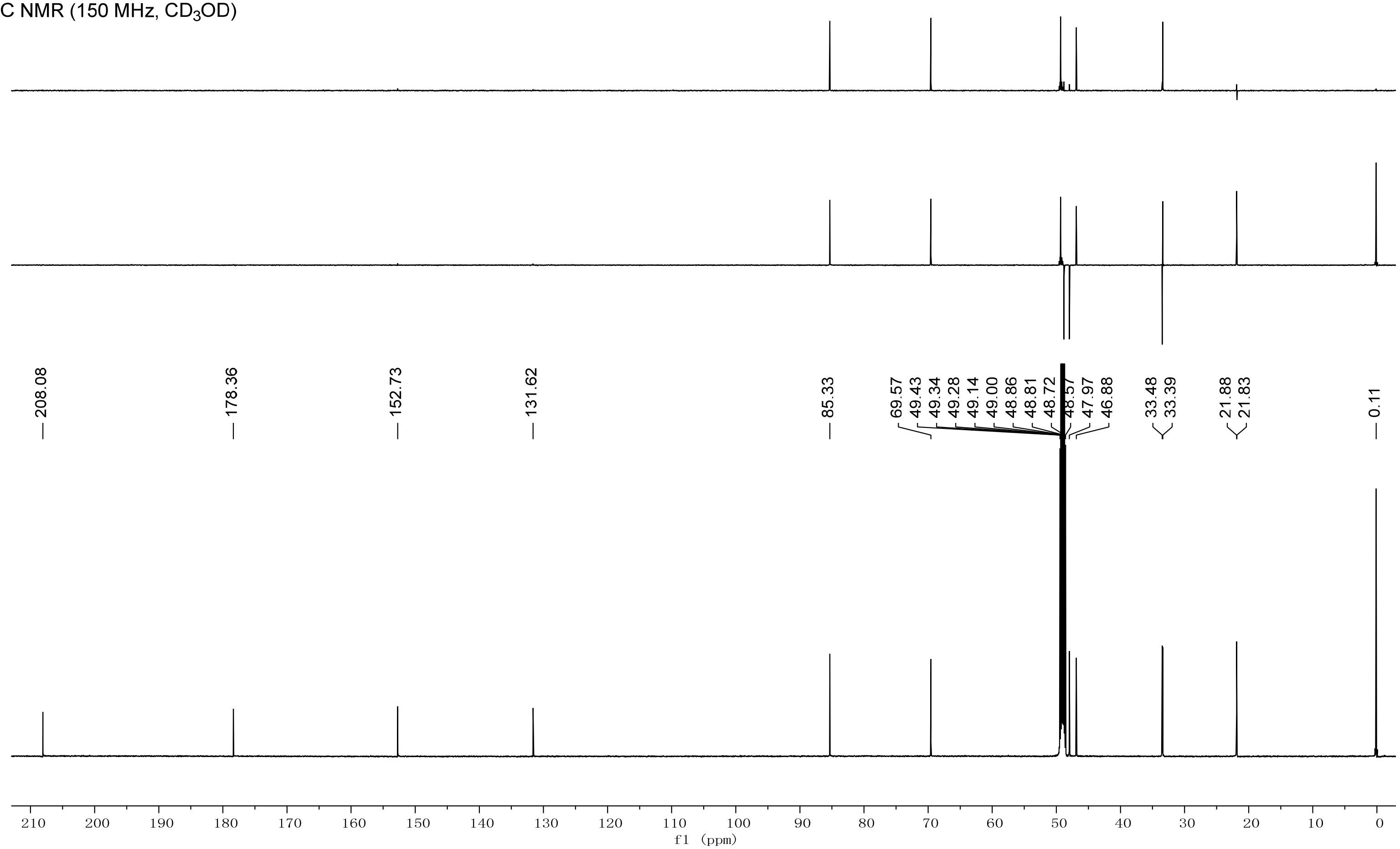
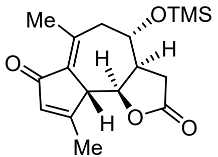
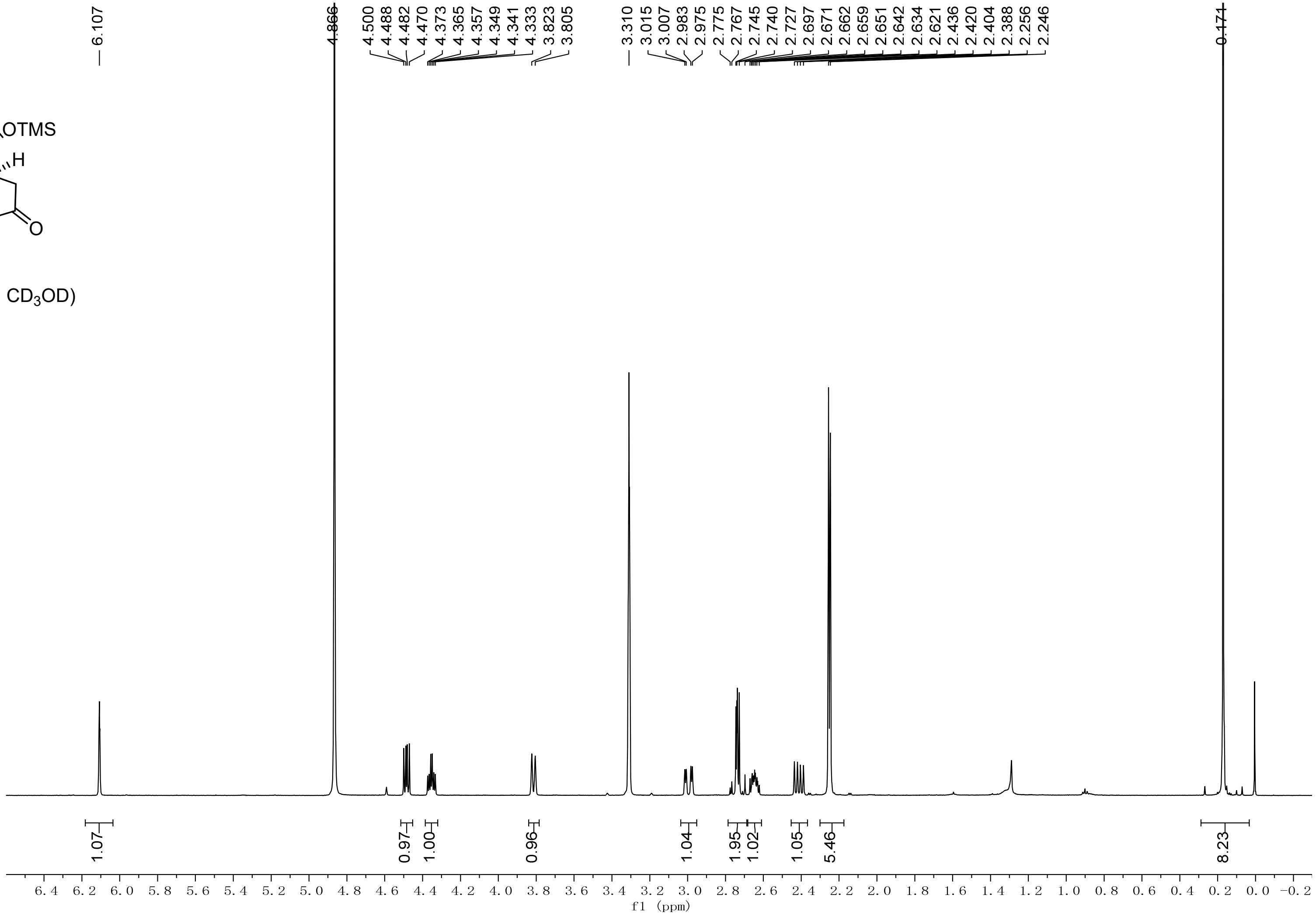
^{13}C NMR (150 MHz, CD$_3$OD)

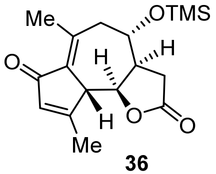




36

^{1}H NMR (600 MHz, CD_3OD)





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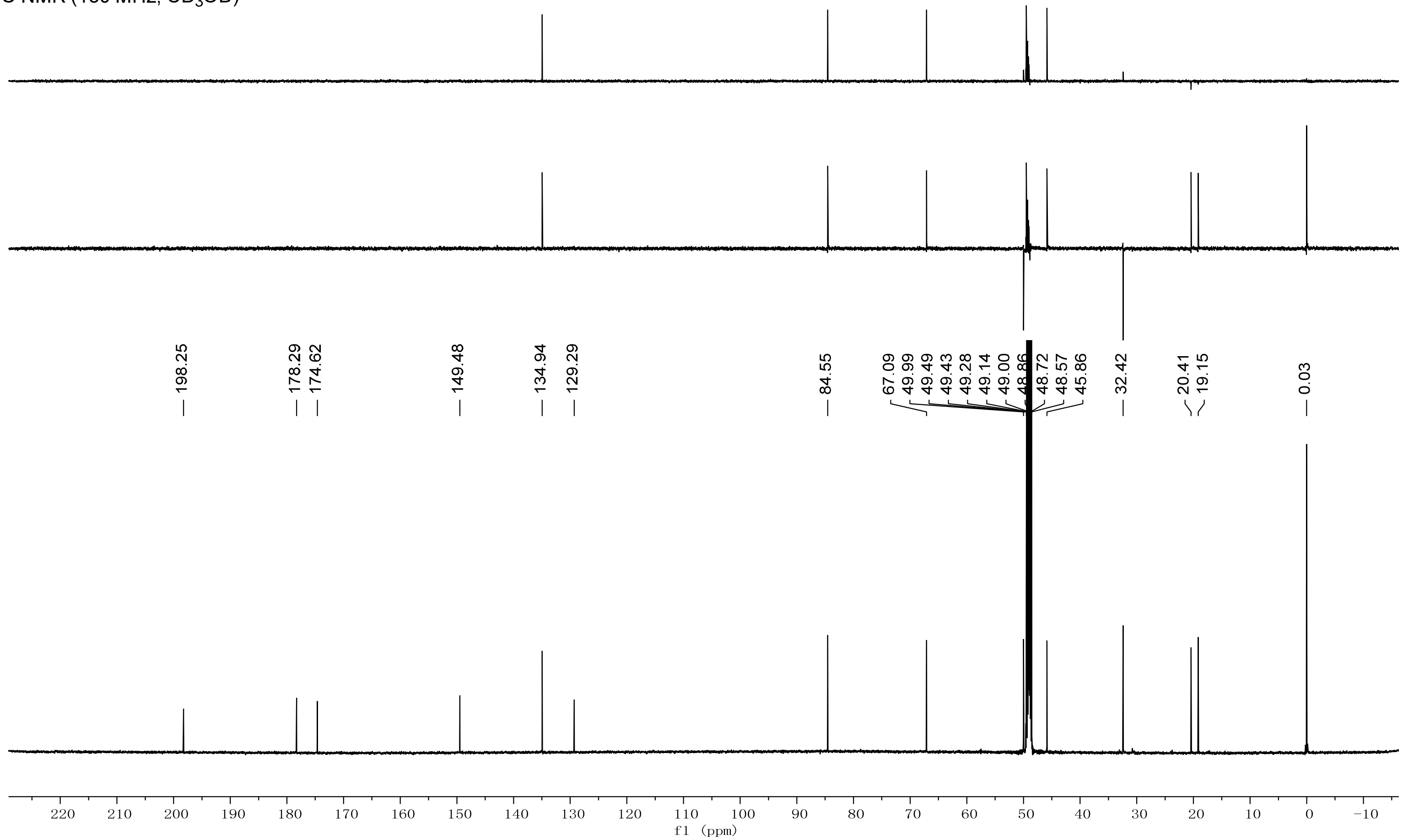
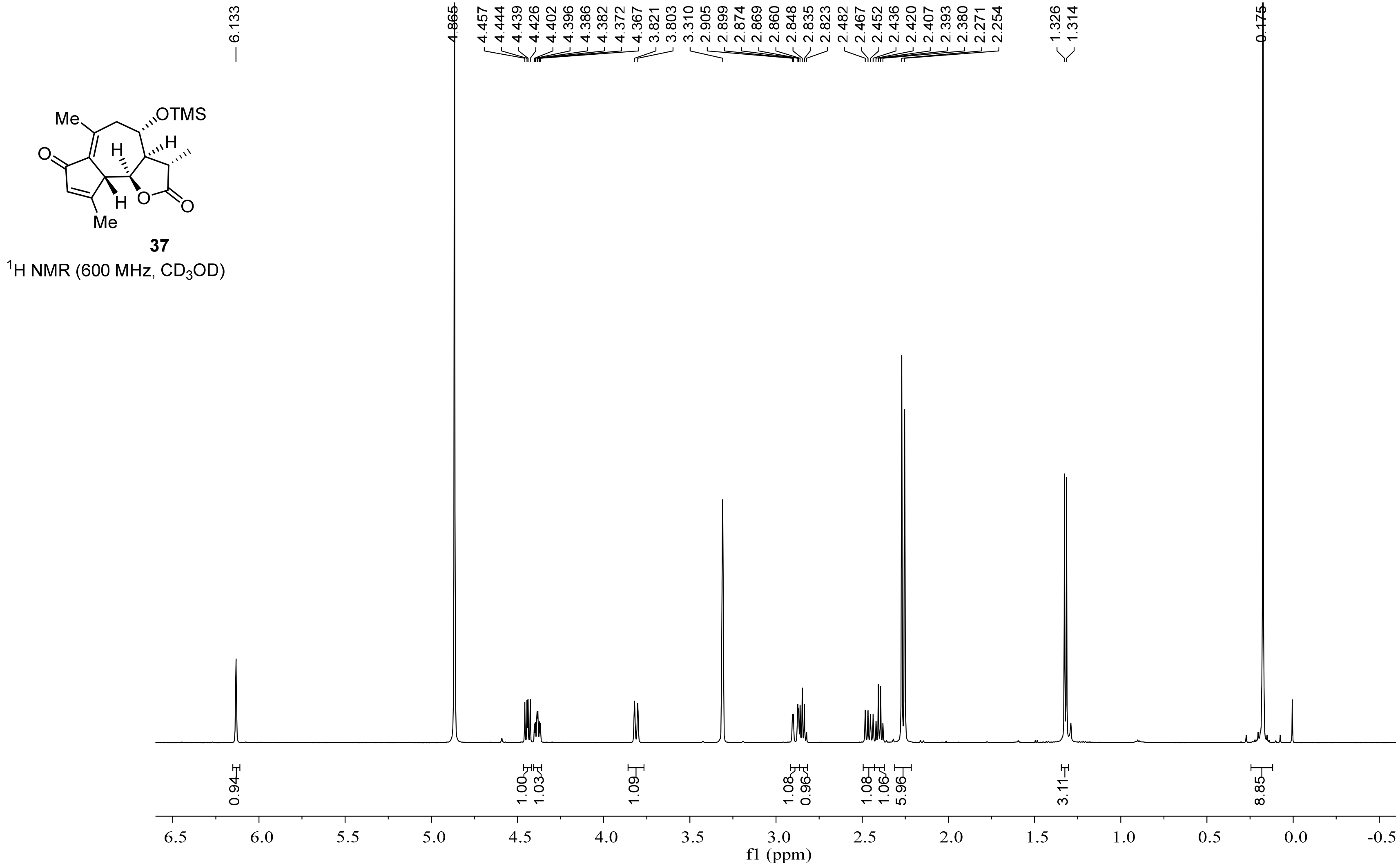
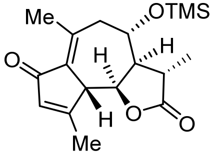




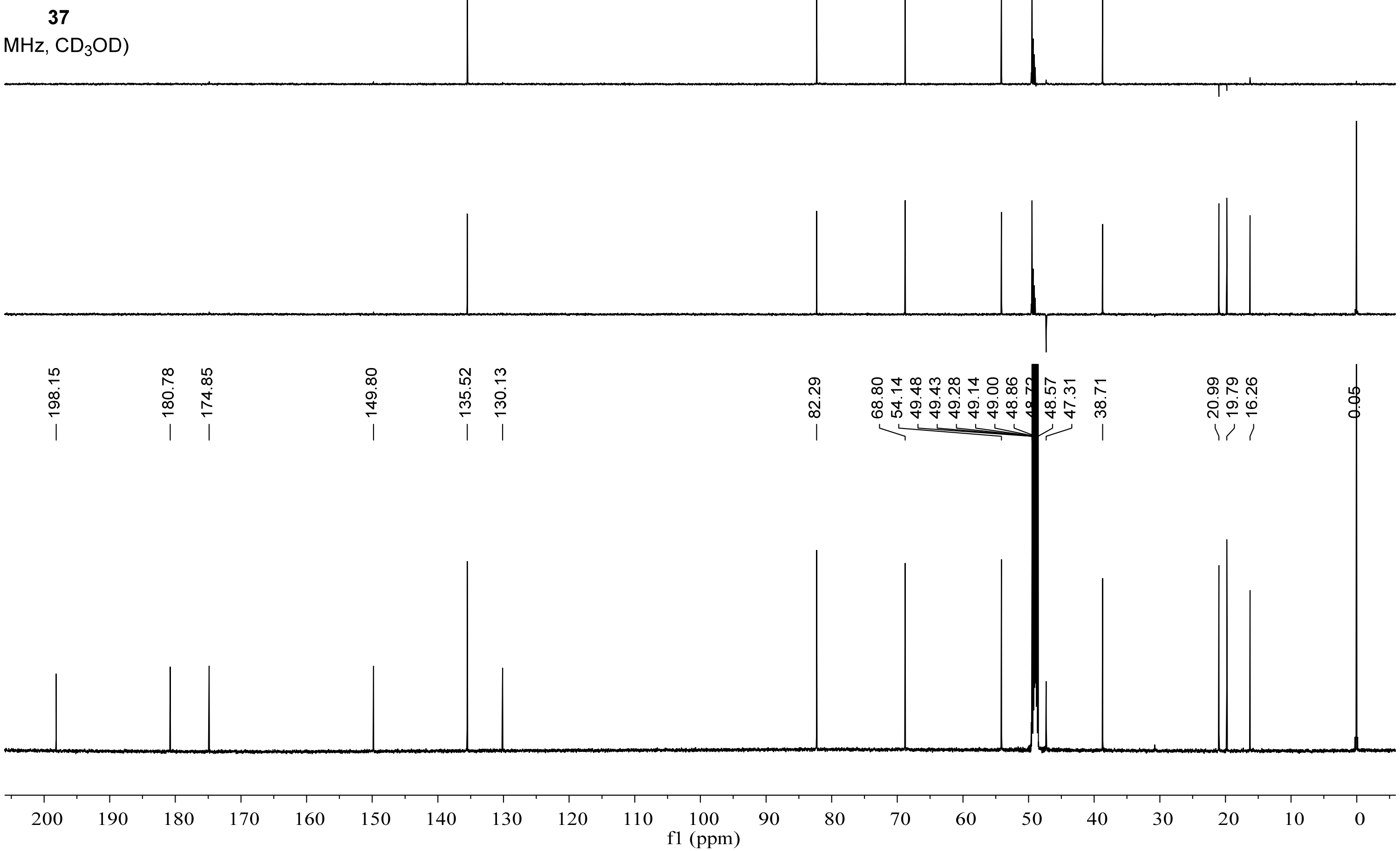
37

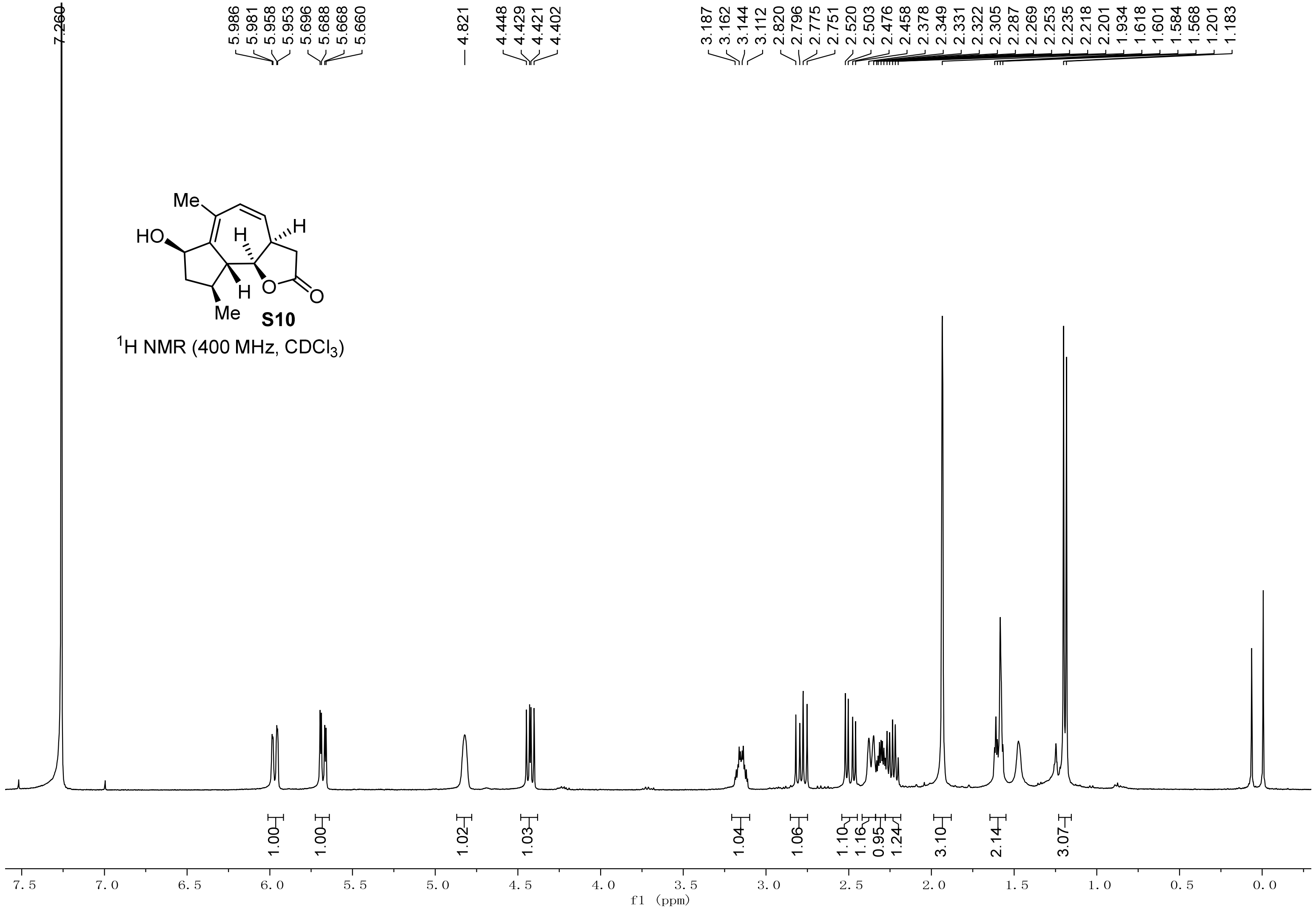
^{1}H NMR (600 MHz, CD_3OD)



37

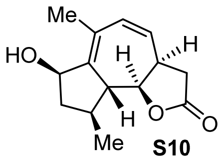
^{13}C NMR (150 MHz, CD$_3$OD)





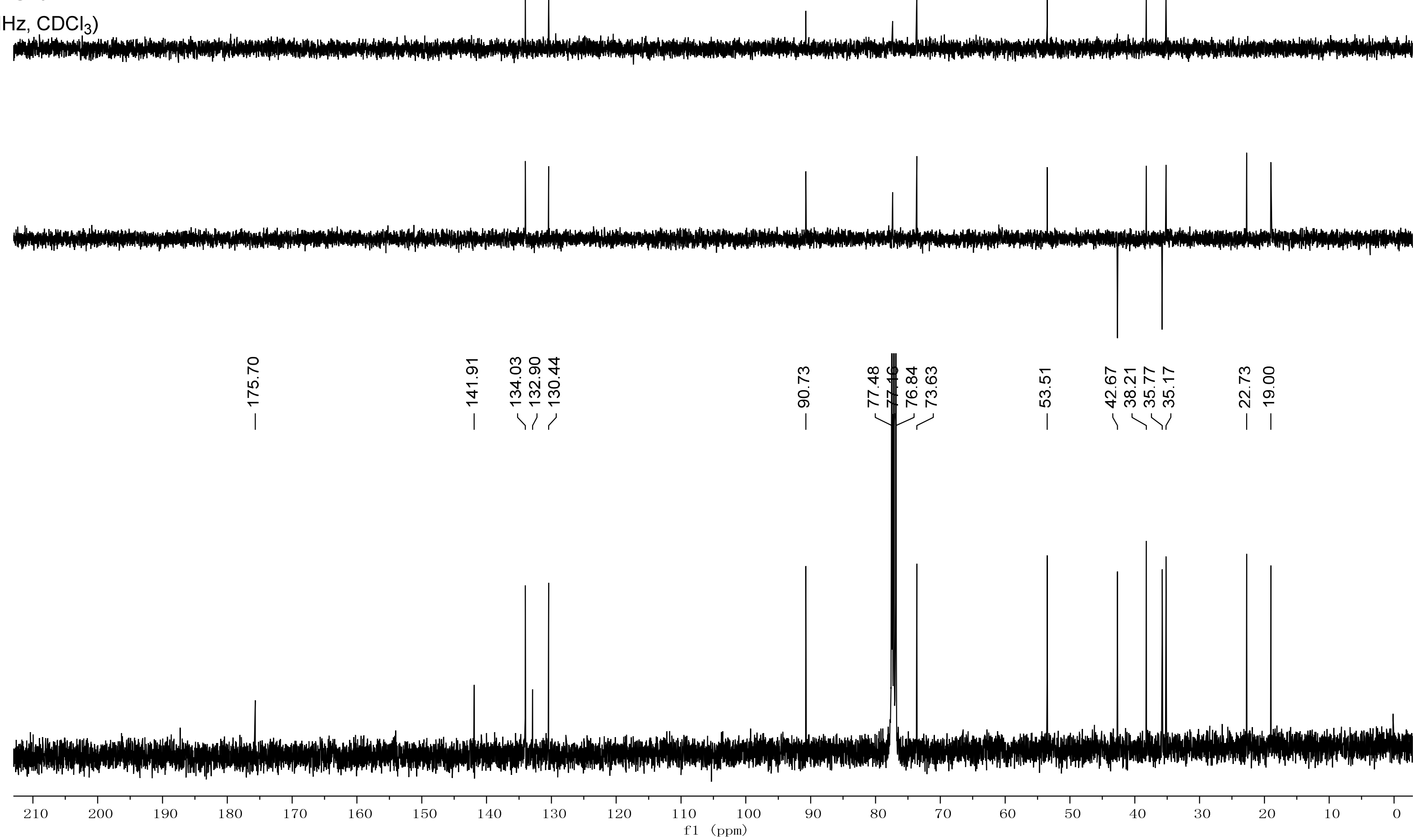
S10

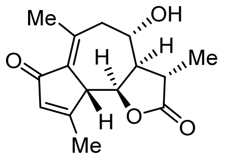
^{1}H NMR (400 MHz, CDCl$_3$)



S10

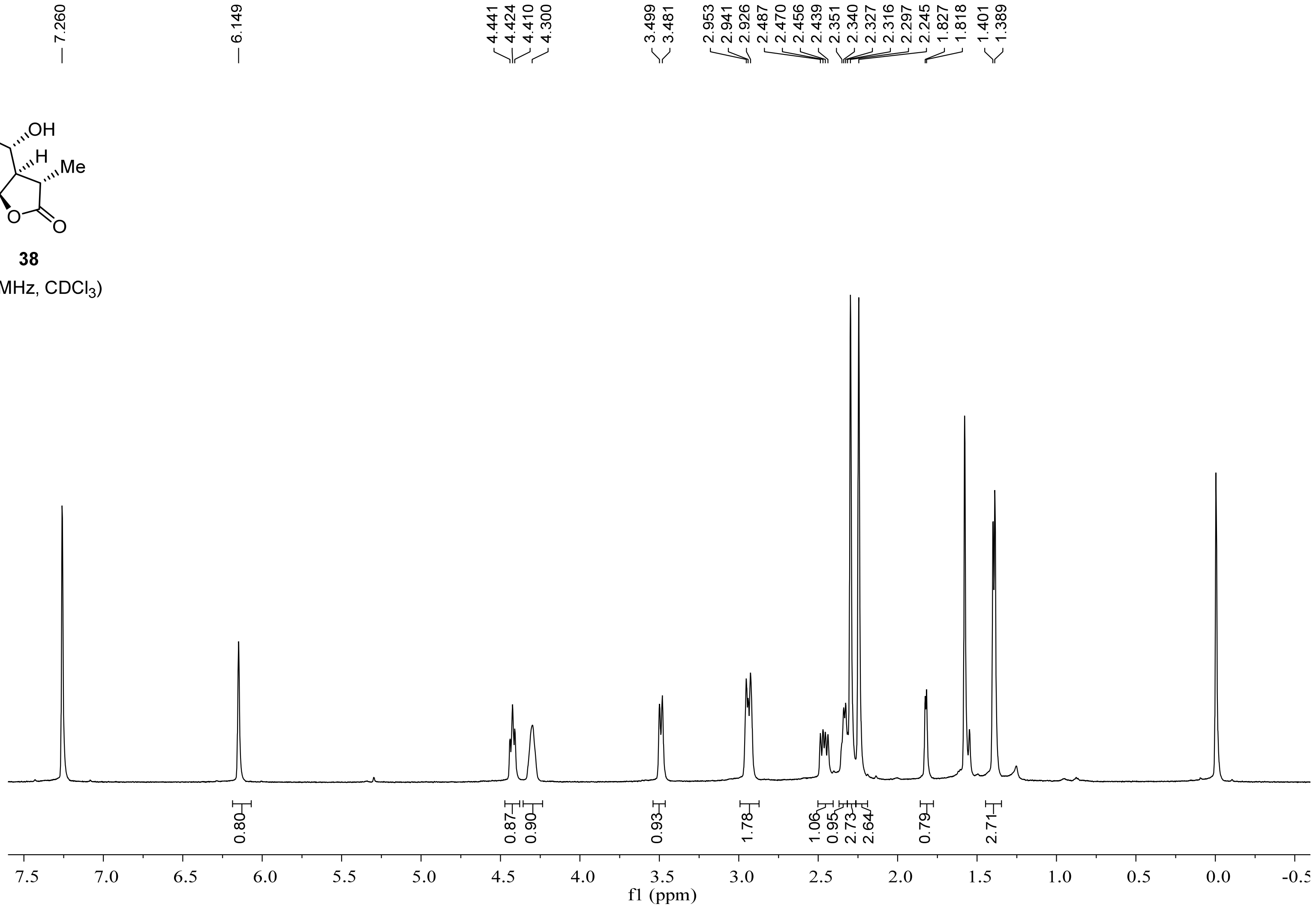
^{13}C NMR (100 MHz, CDCl$_3$)

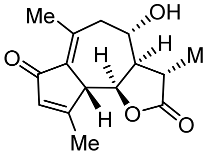




38

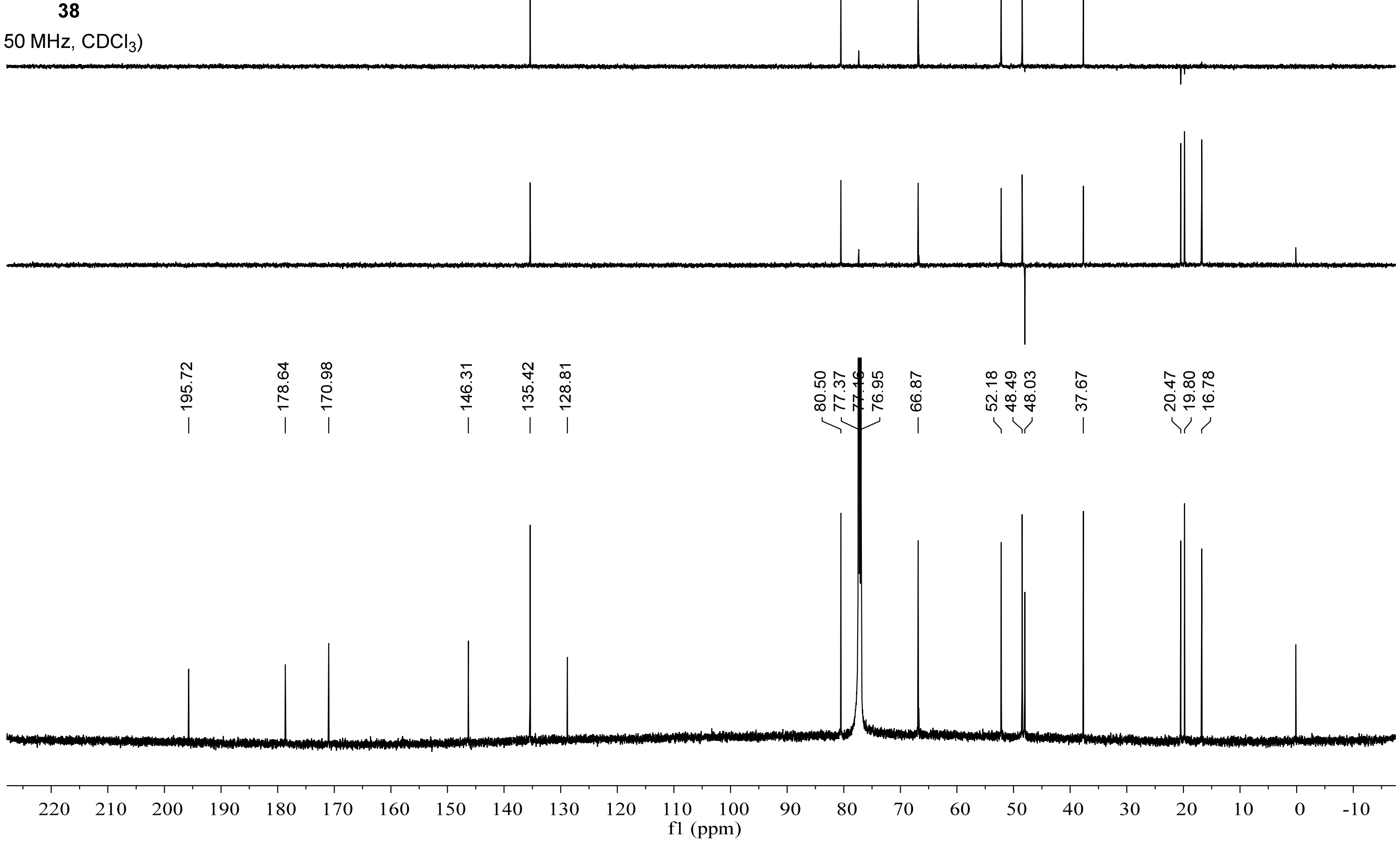
^{1}H NMR (600 MHz, CDCl$_3$)

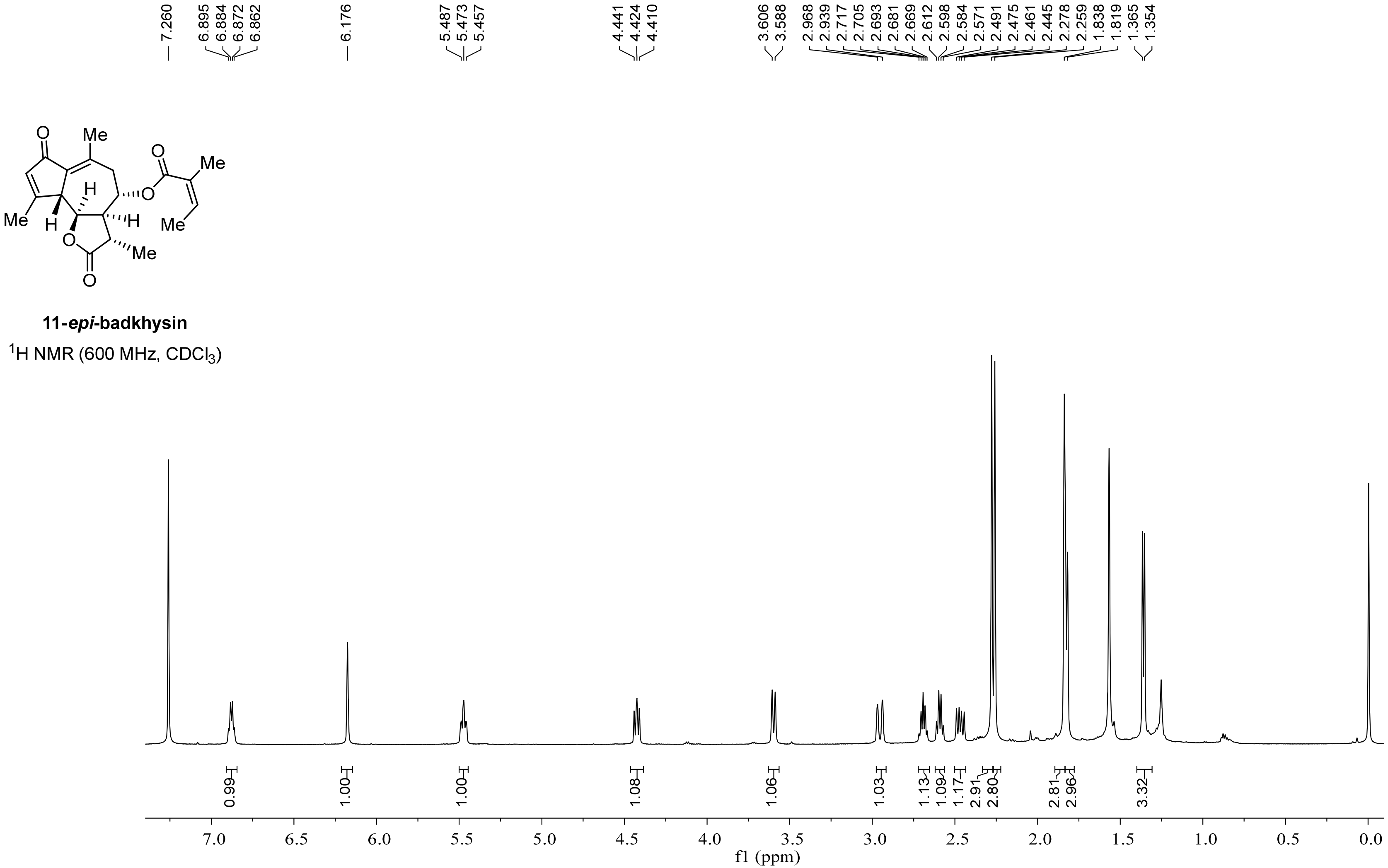




38

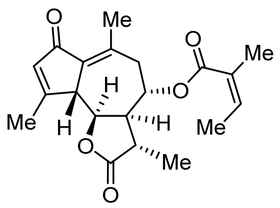
^{13}C NMR (150 MHz, CDCl$_3$)





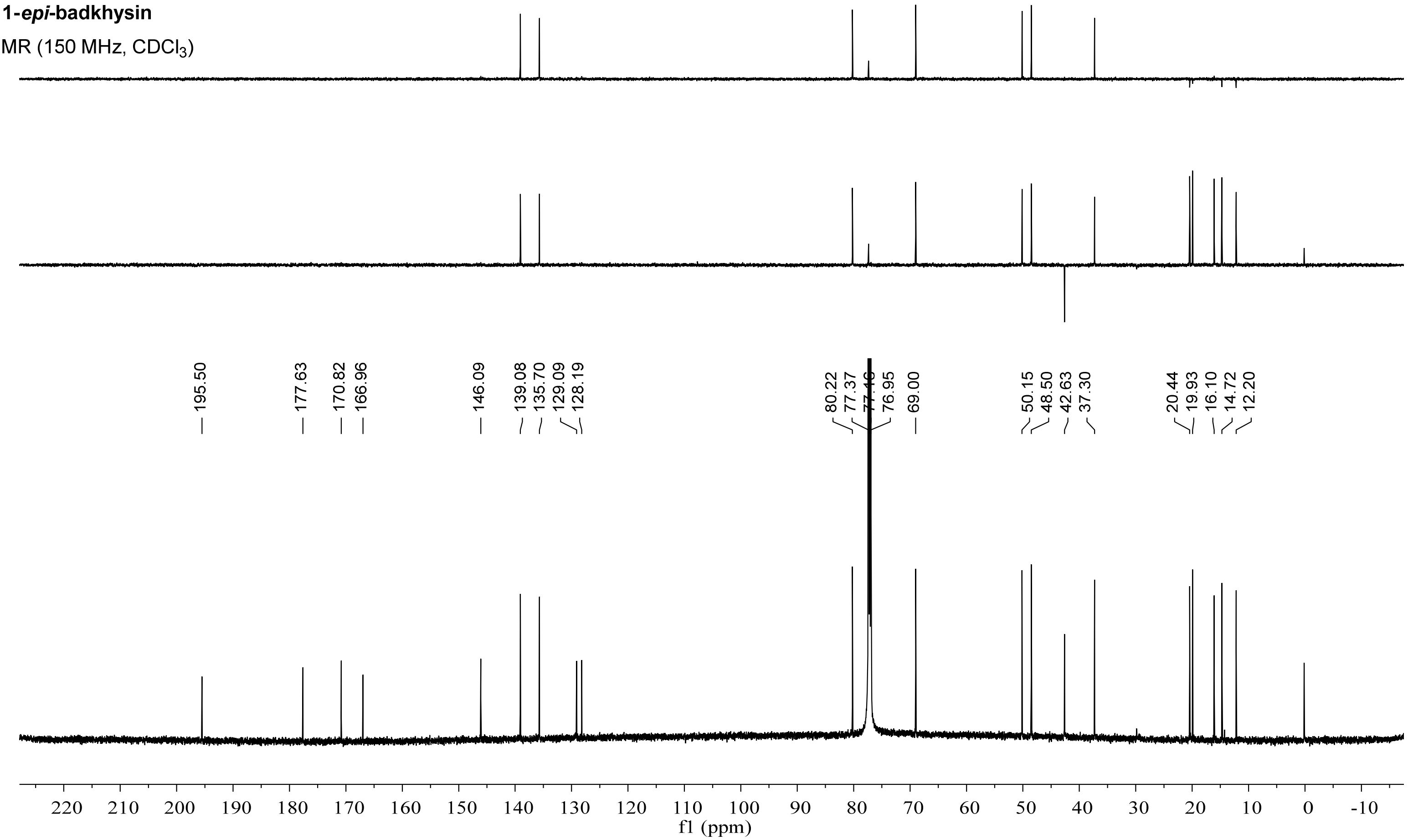
11-*epi*-badkhysin

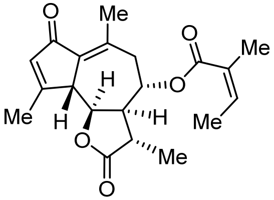
^{1}H NMR (600 MHz, CDCl$_3$)



11-*epi*-badkhysin

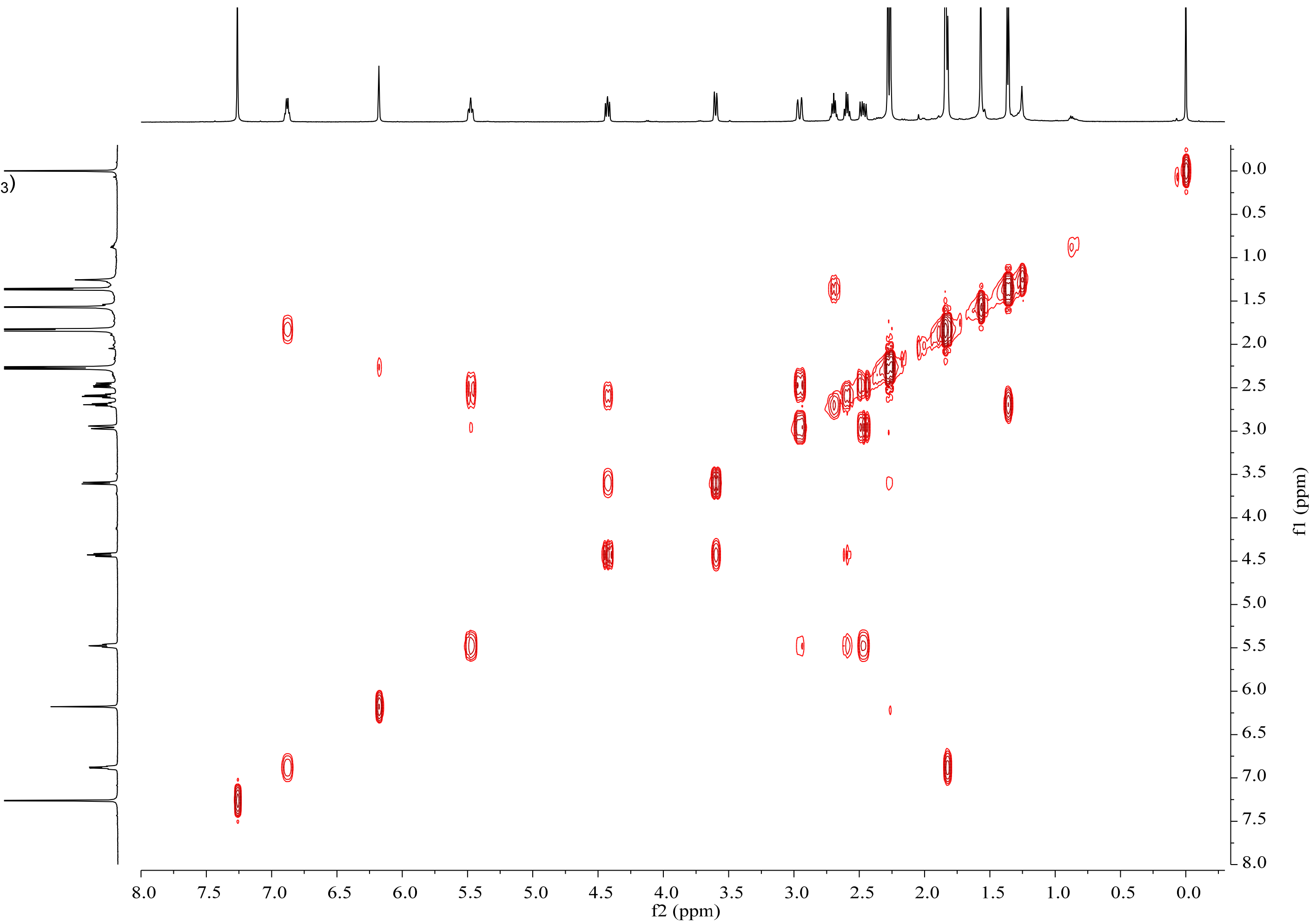
^{13}C NMR (150 MHz, CDCl$_3$)

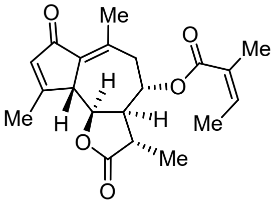




11-*epi*-badkhysin

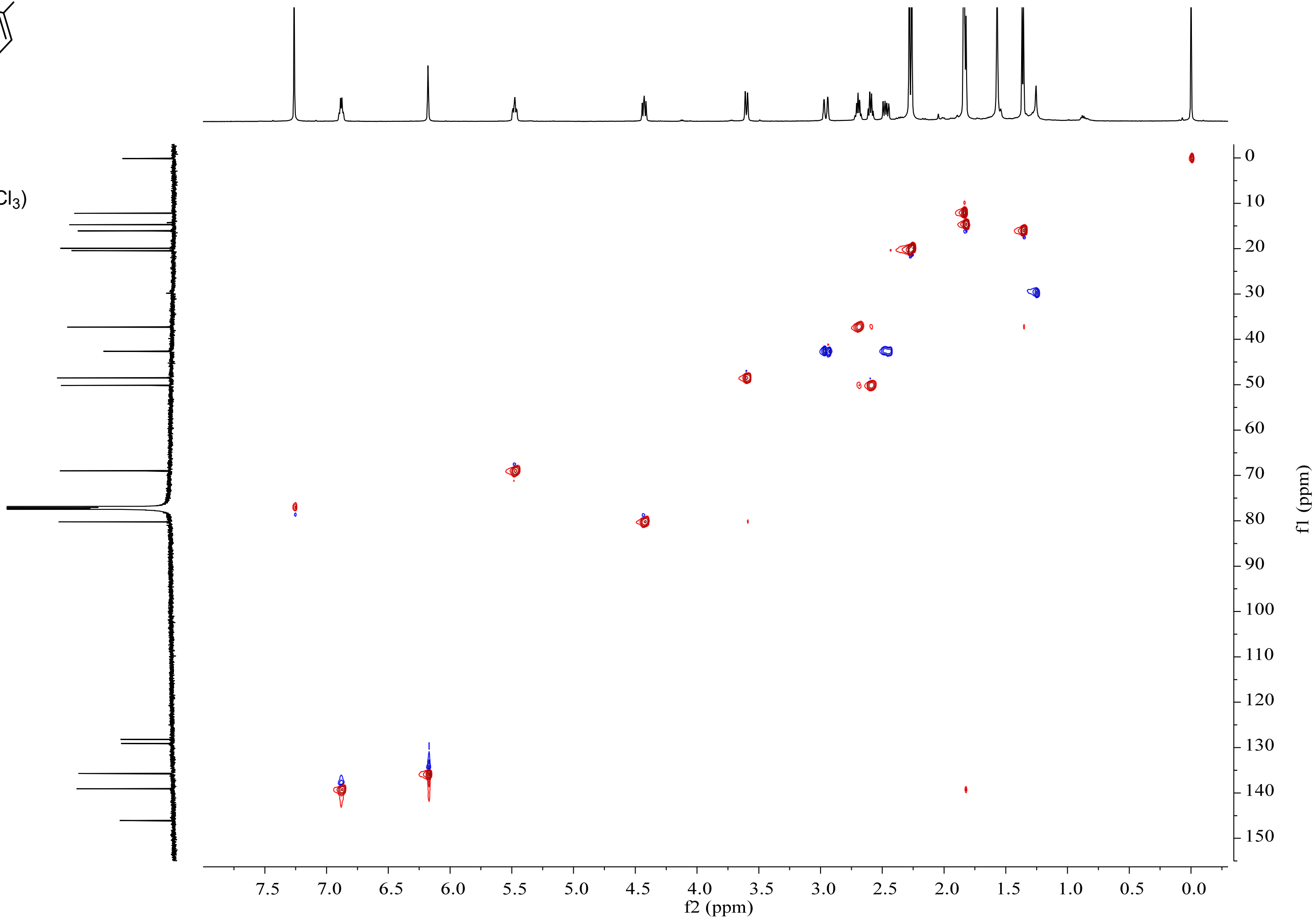
2D NMR (COSY, $CDCl_3$)

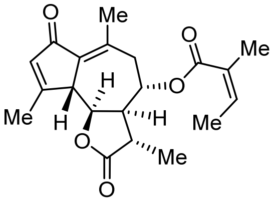




11-*epi*-badkhysin

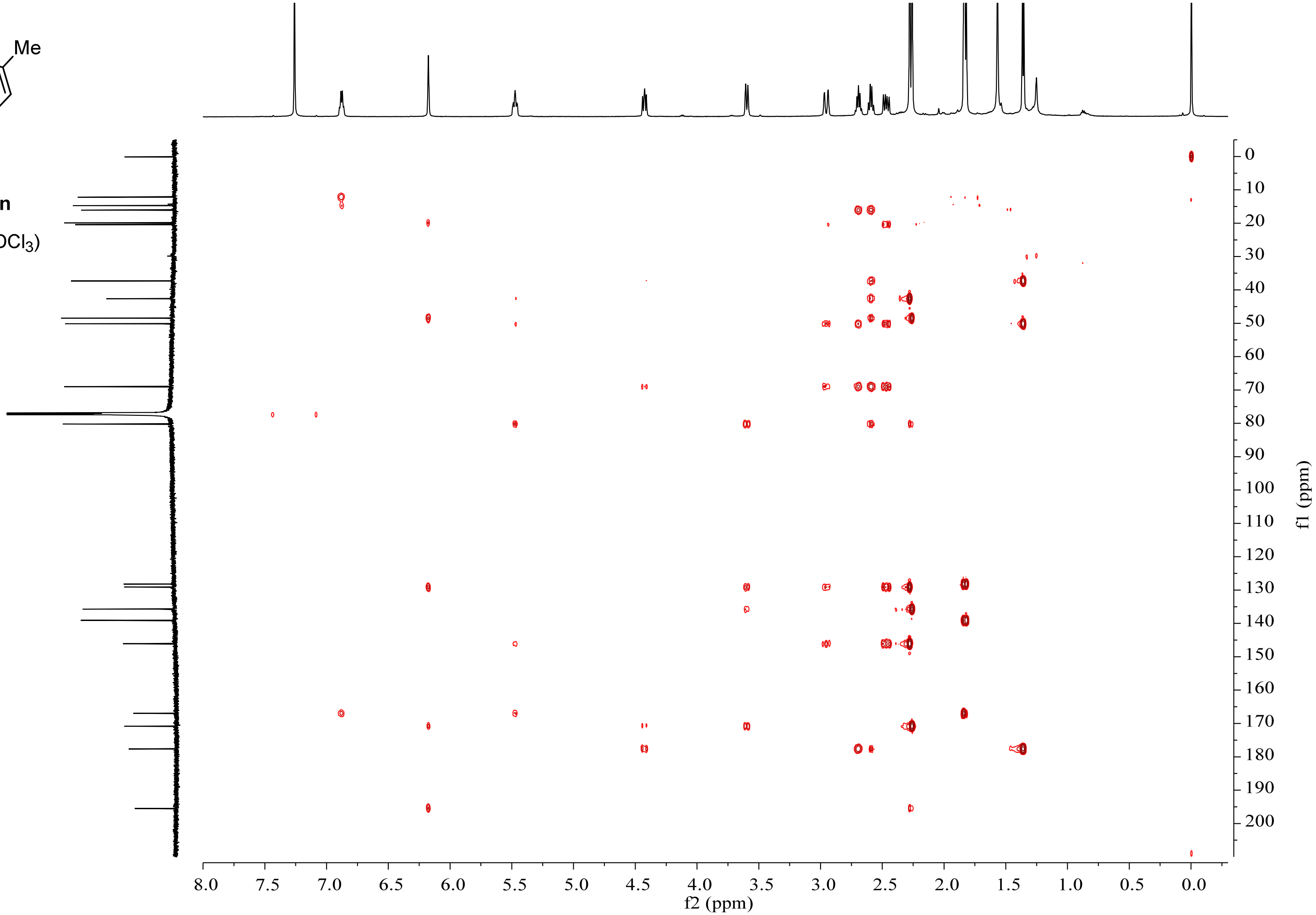
2D NMR (HSQC, $CDCl_3$)

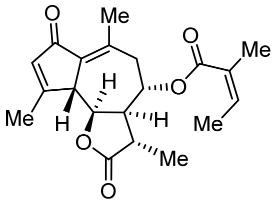




11-*epi*-badkhysin

2D NMR (HMBC, $CDCl_3$)





11-*epi*-badkhysin

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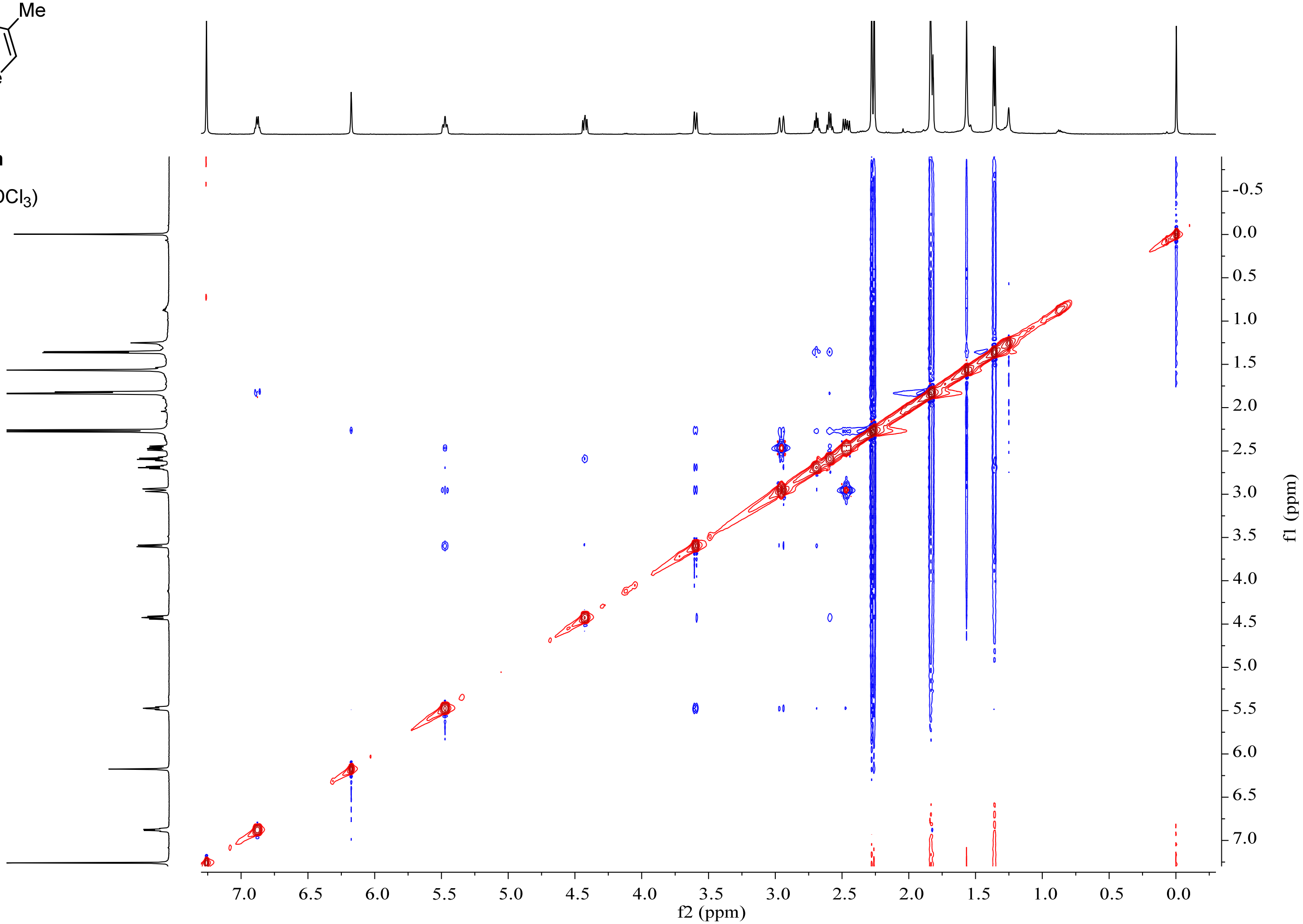

6. Supplementary References

1. Vaidotas Navickas, Dmitry B. Ushakov, Martin E. Maier, Markus Ströbele, and H.-Jürgen Meyer, Synthesis of the Guaianolide Ring System via Cycloaddition of a Bicyclic Carbonyl Ylide with Allyl Propiolate, *Organic Letters*, **2010**, 12, 3418-3421.
2. Martin Dračínský, Miloš Buděšínský, and Beata Warżajtis, Urszula Rychlewska, Solution and Solid-State Effects on NMR Chemical Shifts in Sesquiterpene Lactones: NMR, X-ray, and Theoretical Methods, |*J. Phys. Chem. A*, **2012**, 116, 680-688.
3. Alejandro F. Barrero, M. Mar Herrador, and Pilar Arteaga, Sesquiterpene Lactones and Other Constituents of *Seseli vayredanum*, *Phytochemistry*, **1994**, 37, 1351-1358.