Supporting Information

Total synthesis of (+)-haperforin G

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Part I: General Information

Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere under anhydrous conditions using freshly distilled solvent. Solvent purification was conducted according to Purification of Laboratory Chemicals (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials.

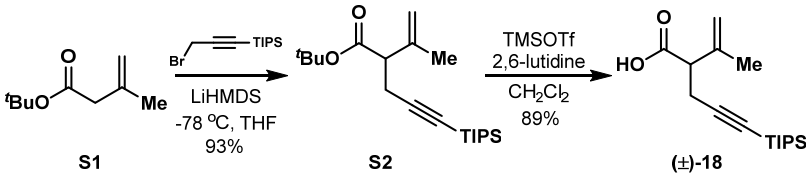
Reactions were monitored by thin layer chromatography (TLC) on plates (GF254) supplied by Yantai Chemicals (China) and visualized by UV or alternatively stained with iodine vapor or basic solution of $KMnO_4$. If not specially mentioned, flash column chromatography was performed using E. Merck silica gel (60, particle size 0.040-0.063 mm).

NMR spectra were recorded on Bruker AV400, Bruker AV500 instruments and calibrated by using residual undeuterated chloroform (δ_H = 7.26 ppm) and $CDCl_3$ (δ_C = 77.0 ppm) as internal references. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, b = broad, td = triple doublet, dt = double triplet, dq = double quartet, m = multiplet. Infrared (IR) spectra were recorded on a Thermo Nicolet Avatar iS5 spectrometer. High-resolution mass spectra (HRMS) were recorded on a Bruker Solarix XR FTMS mass spectrometer using ESI (electrospray ionization) or EI as ionization method. Unless otherwise noted, sample for ESI ionization was dissolved in methanol containing 10% (v/v) HCOOH.

Commercial grade reagents and solvents were used without further purification except as indicated below. Anhydrous tetrahydrofuran (THF) were distilled from sodium-benzophenone. Dichloromethane was distilled from calcium hydride. Toluene and benzene were distilled from sodium.

Part II: Experimental Procedures

Synthesis of compound (±)-18

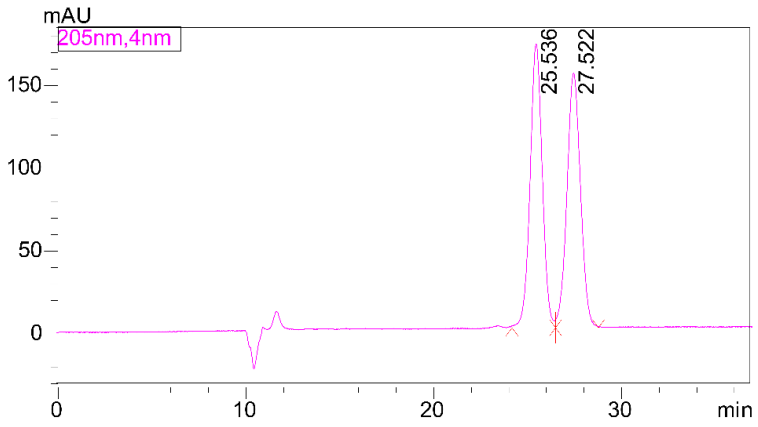


To a stirred solution of LiHMDS (0.39 mL, 1.0 M in THF, 0.39 mmol) in THF (1 mL) was added a solution of **S1**[1] (50 mg, 0.32 mmol) in THF (1 mL) over 2 min. at -78 °C, and the resultant mixture was stirred at the same temperature for 20 min. To this solution was added a solution of (3-bromoprop-1-yn-1-yl)triisopropylsilane (114 mg, 0.42 mmol) in THF (1 mL) over 5 min at -78 °C, and the resultant mixture was stirred at the same temperature for 5 min. The reaction mixture was quenched by addition of a saturated solution of NH_4Cl (10 mL), and the resultant mixture was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with a solution of brine (30 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 400:1 to 200:1) to give **S2** (104 mg, 93%) as colorless oil.

Characterization data of **S2**: R_f = 0.60 (silica gel, petroleum ether : EtOAc = 20:1); IR (neat): ν_{max} = 2942, 2865, 2363, 2175, 1731, 1463, 1368, 1256, 1149, 995, 883, 668 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 4.98 – 4.83 (m, 2H), 3.15 (dd, *J* = 7.7, 7.6 Hz, 1H), 2.69 (dd, *J* = 16.9, 7.6 Hz, 1H), 2.49 (dd, *J* = 16.9, 7.7 Hz, 1H), 1.76 (t, *J* = 1.2 Hz, 3H), 1.43 (s, 9H), 1.15 – 0.93 (m, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 141.7, 114.2, 106.1, 81.7, 80.9, 53.6, 28.1, 21.7, 20.4, 18.7, 11.4. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{21}H_{39}O_2Si$, 351.2714; found 351.2710.

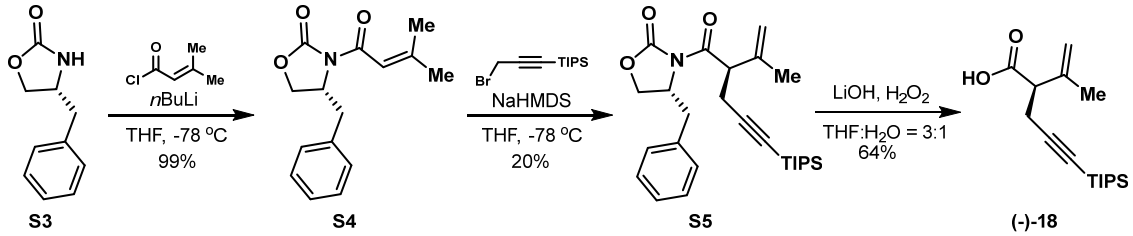
To a stirred solution of **S2** (100 mg, 0.29 mmol) and 2,6-lutidine (306 mg, 2.86 mmol) in CH_2Cl_2 (14 mL) was added TMSOTf (318 mg, 1.43 mmol) at 0 °C in a dropwise manner, and the resultant mixture was stirred at room temperature 3 h. The mixture was quenched by addition of a solution of $NaHSO_4$ (5%, 30 mL), and the resultant mixture was extracted with EtOAc (2 x 25 mL). The combined organic layer was washed with brine (2 x 15 mL), and then dried over sodium sulfate. The extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (CH_2Cl_2 : MeOH = 100:1 to 20:1) to give **(±)-18** (75 mg, 89%) as white solid.

(±)-18 was analyzed with chiral HPLC (0.05% solution of CF_3COOH : MeOH = 20 : 80, 0.3 mL/min, λ = 205 nm, chiralpak IG-3, 4.6 mmφ × 250 mmL, particle size 3 μm).



	Ret. Time (min)		Area%
	25.536	7595416	49.921
	27.522	7619520	50.079
		15214936	100.00

Synthesis of compound (-)-18 (Method A)



To a stirred solution of **S3** (1.77 g, 10.0 mmol) in THF (35 mL) at -78 °C was added *n*BuLi (4.2 mL, 2.5 M in hexane, 10.5 mmol) in a dropwise manner, and the mixture was stirred at the same temperature for 10 min. To this solution was added 3-methylbut-2-enoyl chloride (1.42 g, 12.0 mmol) at -78 °C in a dropwise manner, and the resultant mixture was then stirred at 0 °C for 30 min. The reaction was worked up by addition of a solution of K_2CO_3 (10 mL, 1.0 M in water, 10.0 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. After addition of water (100 mL), the mixture was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with brine (200 mL), and dried over sodium sulfate. The solvent of the extract ws concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 10:1 to 4:1) to give **S4** (2.58 g, 99%) as white solid.

Characterization data of **S4**: R_f = 0.50 (silica gel, petroleum ether : EtOAc = 4:1); IR (neat): ν_{max} = 2915, 1770, 1675, 1629, 1446, 1385, 1348, 1255, 1213, 1183, 1105, 1004, 846, 751, 701 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.23 (m, 2H), 7.22 – 7.13 (m, 3H), 6.88 (brs, 1H), 4.79 – 4.50 (m, 1H), 4.27 – 3.85 (m, 2H), 3.26 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.70 (dd, *J* = 13.3, 9.6 Hz, 1H), 2.15 (d, *J* = 1.3 Hz, 3H), 1.93 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 159.6, 153.5, 135.7, 129.6, 129.0, 127.3, 115.9, 66.0, 55.3, 38.1, 28.2, 21.5. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{15}H_{18}NO_3$, 260.1281; found 260.1274.

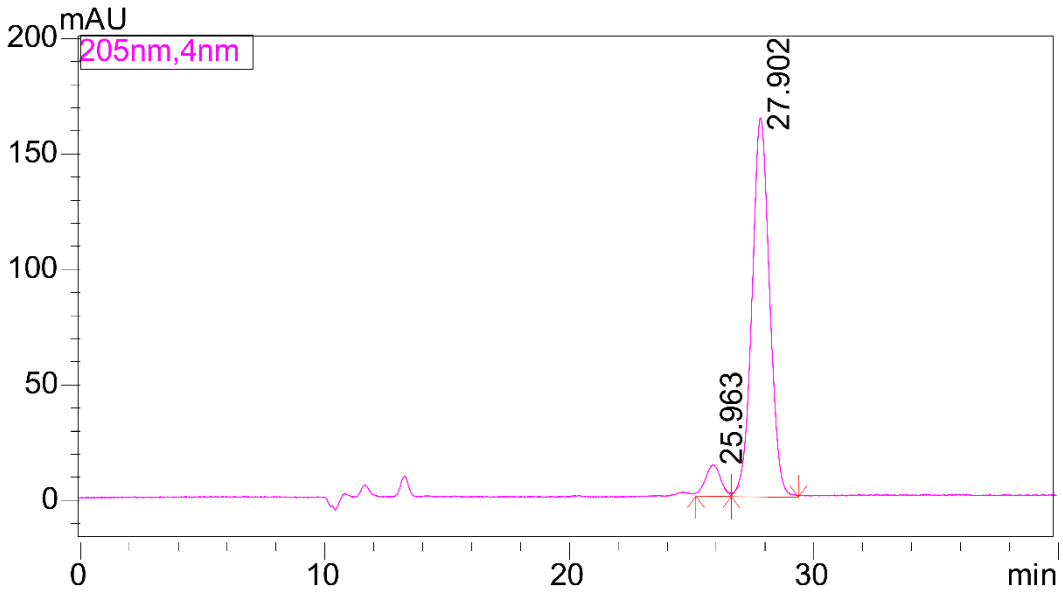
To a stirred solution of **S4** (2.58 g, 9.96 mmol) in THF (35 mL) was added NaHMDS (5.5 mL, 2.0 M in THF, 10.96 mmol) at -78 °C in a dropwise manner, and the resultant mixture was stirred at the same temperature for 1 h. To this solution was added a solution of (3-bromoprop-1-yn-1-yl)triisopropylsilane (2.87 g, 10.46 mmol) in THF (5 mL) -78 °C in a dropwise manner, and the mixture was stirred at the same temperature for 5 h. The reaction was quenched by addition of a saturated NH_4Cl (100 mL), and the mixture was extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with brine (200 mL), and then dried over sodium sulfate. The solvent of the extract was concentrated in vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 10:1 to 4:1) to give **S5** (902 mg, 20%, *dr* = 14:1) as colorless oil.

Characterization data of **S5**: R_f = 0.60 (silica gel, petroleum ether : EtOAc = 4:1); IR (neat): ν_{max} = 2941, 2863, 2173, 1782, 1697, 1454, 1381, 1363, 1287, 1206, 1191, 1106, 1013, 905, 882, 700, 676, 661 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.18 (m, 5H), 4.98 – 4.89 (m, 2H), 4.73 – 4.59 (m, 2H), 4.19 – 4.08 (m, 2H), 3.39 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.82 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.73 – 2.58 (m, 2H), 1.85 (s, 3H), 1.04 (d, *J* = 4.9 Hz, 21H).^{13}C NMR (101 MHz, $CDCl_3$) δ

172.1, 153.0, 142.1, 135.6, 129.5, 129.1, 127.5, 114.6, 106.0, 82.0, 66.0, 55.9, 50.2, 38.2, 22.1, 21.2, 18.7, 11.4. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{27}H_{40}NO_3Si$, 454.2772; found 454.2773.

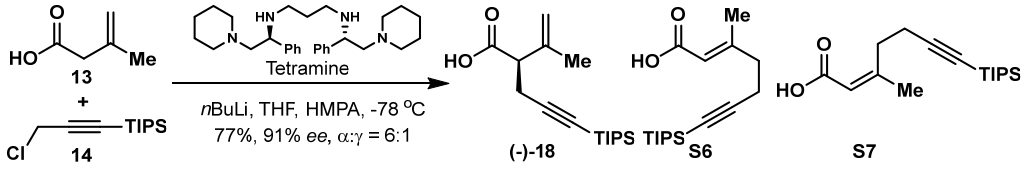
To a stirred solution of **S5** (131 mg, 0.29 mmol) in THF (2.1 mL) and water (0.7 mL) was sequentially added LiOH (0.58 mL, 2.0 M in water, 1.16 mmol) and H_2O_2 (0.26 mL, 30% in water, 2.32 mmol) at 0 °C, and the resultant mixture was stirred at room temperature for 5 h. The reaction was quenched by addition of a saturated solution of Na_2SO_3 (20 mL), and the mixture was extracted with EtOAc (2 x 30 mL). The combined organic extract was washed with brine (50 mL), and dried over sodium sulfate. The solvent of extract was concentrated in vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 4:1 to 2:1) to give (-)-**18** (54 mg, 64%, 88% *ee*) as colorless oil.

(-)-18 was analyzed with chiral HPLC (0.05% solution of CF_3COOH : MeOH = 20 : 80, 0.3 mL/min, λ = 205 nm, chiralpak IG-3, 4.6 mmφ × 250 mmL, particle size 3 μm).



	Ret. Time (min)		Area%
	25.963	511684	5.973
	27.902	8055069	94.027
		8566753	100.00

Synthesis of compound (-)-18 (Method B):



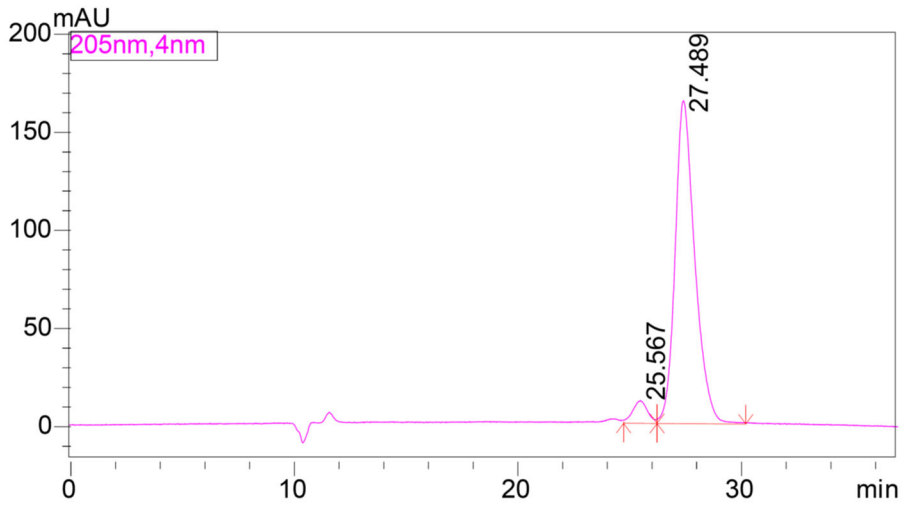
To a stirred solution of **13** (3.0 g, 30 mmol) and tetramine[2] (14.1 g, 31.5 mmol) in THF (200 mL) was added *n*BuLi (48 mL, 2.5 M in hexane, 120 mmol) at 0 °C in a dropwise manner, and the resultant mixture was first stirred at room temperature for 45 min. and then cooled to -78 °C. To this solution was added HMPA (23 mL), and the resultant mixture was stirred at the same temperature for 10 min. To this solution was added a solution of **14** (8.28 g, 36 mmol) in THF (30 mL) at -78 °C

in a dropwise manner during 20 min, the resultant mixture was stirred the same temperature for 4 h. The reaction was quenched by addition of a mixed solvent of THF (29.25 mL) and MeOH (9.75 mL) -78 ºC, and the resultant mixture was allowed to warm up to 0 ºC, and stirred at the same temperature for 5 min. To this solution was added a solution of HCl (1 N, 270 mL), and the mixture was extracted with EtOAc (3 x 150 mL). The combined organic layers were sequentially washed with a solution of HCl (1 N, 150 mL) and brine (2 x 350 mL), and dried over sodium sulfate. The solvent of extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc : AcOH = 20:1:0.04) to give (-)-**18** (6.81 g, 77%, 91% *ee*) as colorless oil, together with **S6** and **S7** as a mixture in a ratio of 1:1 (1.13 g, 13%).

Recovery of tetramine: The aqueous layer was washed with EtOAc, and then adjusted with a solution of sodium hydroxide (3 N) at room temperature to pH>12. The mixture was then extracted with EtOAc (3 x 150 mL). The combined organic layers were washed with brine, and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum to afford tetramine, which contains a small amount of HMPA. The residue was purified by flash chromatography on silica gel (CH_2Cl_2 : MeOH : Ammonia = 10:1:0.05) to give pure tetramine (12.5 g, 89%).

Characterization data of **(-)-18**: R_f = 0.25 (silica gel, CH_2Cl_2 : MeOH = 20:1). $[\alpha]_D^{30}$ = -23.8 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2942, 2864, 2176, 1709, 1648 1463, 1382, 1286, 1247, 995, 901, 883, 676, 630 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.12 – 4.86 (m, 2H), 3.33 (dd, *J* = 8.1, 7.5 Hz, 1H), 2.76 (dd, *J* = 16.9, 7.5 Hz, 1H), 2.57 (dd, *J* = 16.9, 8.1 Hz, 1H), 1.81 (t, *J* = 1.2 Hz, 3H), 1.20 – 0.97 (m, 21H).^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 140.5, 115.5, 105.2, 82.6, 52.6, 21.5, 20.2, 18.7, 11.3. HRMS (ESI, m/z): $[M-H]^+$ calcd for $C_{17}H_{29}O_2Si$, 293.1942; found 293.1948.

(-)-18 was analyzed with chiral HPLC (0.05% solution of CF_3COOH : MeOH = 20 : 80, 0.3 mL/min, λ = 205 nm, chiralpak IG-3, 4.6 mmφ × 250 mmL, particle size 3 μm).



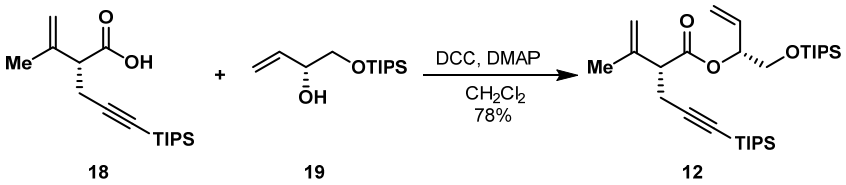
	Ret. Time (min)		Area%
	25.567	460512	4.434
	27.489	9926310	95.566
		10386822	100.00

Characterization data of **S6**: R_f = 0.35 (silica gel, CH_2Cl_2 : MeOH = 20:1). IR (neat): ν_{max} = 2941, 2864, 2171, 1690, 1638, 1462, 1414, 1260, 1199, 1055, 919, 882, 676, 661, 620 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.76 (q, *J* = 1.3 Hz, 1H), 2.47 (td, *J* = 6.8, 1.4 Hz, 2H), 2.40 (td,

J = 6.9, 1.3 Hz, 2H), 2.20 (d, J = 1.3 Hz, 3H), 1.12 – 0.99 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 160.6, 116.4, 106.8, 82.0, 40.1, 18.9, 18.7, 18.4, 11.4. HRMS (ESI, m/z): $[M-H]^+$ calcd for $C_{17}H_{29}O_2Si$, 293.1942; found 293.1939.

Characterization data of **S7**: R_f = 0.38 (silica gel, CH_2Cl_2 : MeOH = 20:1). IR (neat): ν_{max} = 2941, 2864, 2172, 1690, 1642, 1462, 1427, 1292, 1250, 1166, 1052, 995, 919, 882, 676, 660, 621 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.75 (brs, 1H), 2.87 (t, J = 7.1 Hz, 2H), 2.50 (t, J = 7.1 Hz, 2H), 2.02 (d, J = 1.4 Hz, 3H), 1.30 – 0.72 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 161.9, 116.7, 107.8, 81.3, 32.4, 26.1, 18.8, 18.7, 11.4. HRMS (ESI, m/z): $[M-H]^+$ calcd for $C_{17}H_{29}O_2Si$, 293.1942; found 293.1940.

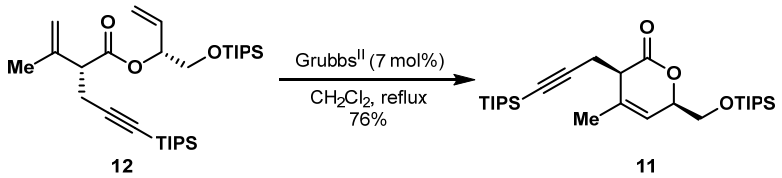
Synthesis of compound 12



To a stirred solution of **18** (8.10 g, 27.55 mmol) and **19**[3] (6.72 g, 27.55 mmol) in CH_2Cl_2 (250 mL) was sequentially added DCC (6.82, 33.06 mmol) and DMAP (337 mg, 2.76 mmol) at 0 °C, and the reaction mixture was slowly warmed to room temperature and stirred for 12 h. The reaction was worked up by filtered of the reaction mixture through a pad of celite, and washed with petroleum ether (3×30 mL). the filtrate was concentrated in vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 200:1) to give **12** (11.21 g, 78%, *dr* = 18:1) as colorless oil.

Characterization data of **12**: R_f = 0.60 (silica gel, petroleum ether : EtOAc = 20:1); IR (neat): ν_{max} = 2942, 2892, 2865, 2176, 1739, 1647, 1463, 1382, 1163, 1131, 995, 920, 882, 789, 678, 661 cm^{-1}; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.85 (ddd, J = 17.0, 10.6, 6.0 Hz, 1H), 5.31 (dd, J = 17.0, 1.3 Hz, 1H), 5.33 – 5.30 (m, 1H), 5.21 (dd, J = 10.6, 1.3 Hz, 1H), 4.96 – 4.94 (m, 1H), 4.93 (t, J = 1.5 Hz, 1H), 3.88 – 3.67 (m, 2H), 3.30 (dd, J = 8.4, 7.0 Hz, 1H), 2.75 (dd, J = 17.0, 7.0 Hz, 1H), 2.58 (dd, J = 17.0, 8.4 Hz, 1H), 1.77 (t, J = 1.2 Hz, 3H), 1.11 – 0.93 (m, 42H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6, 140.9, 133.7, 118.0, 115.1, 105.8, 82.1, 76.0, 65.1, 52.8, 21.7, 20.3, 18.7, 18.0, 12.0, 11.4. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{30}H_{57}O_3Si_2$, 521.3841; found 521.3841.

Synthesis of compound 11

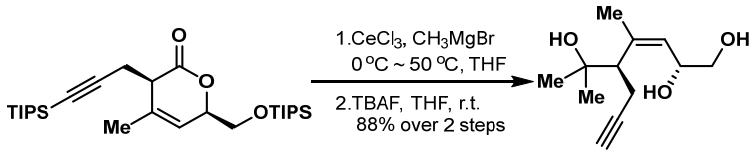


To a stirred solution of **12** (6.70 g, *dr* = 18:1, 12.88 mmol) in CH_2Cl_2 (1.3 L) was added Grubbs^{II} (546 mg, 0.644 mmol) at room temperature, and the resultant mixture was then stirred 43 °C 12 h. To this solution was added a second portion of Grubbs^{II} (219 mg, 0.258 mmol), and resultant mixture was stirred for 15 h. The reaction was worked up by removal of the solvent of the reaction mixture under vacuum, and the residue was purified by a flash chromatography on silica gel

(petroleum ether : EtOAc = 100:1 to 50:1) to give lactone **11** (4.82 g, 76%, *dr* > 20:1) as a colorless oil.

Characterization data of **11**: R_f = 0.25 (silica gel, petroleum ether : EtOAc = 20:1); $[\alpha]_D^{30}$ = -41.8 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2941, 2891, 2864, 2174, 1739, 1462, 1383, 1324, 1217, 1196, 1121, 1070, 1013, 996, 919, 882, 786, 677, 660, 505 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.85 – 5.67 (m, 1H), 4.87 (brs, 1H), 3.91 (dd, *J* = 9.9, 5.0 Hz, 1H), 3.73 (dd, *J* = 9.9, 6.7 Hz, 1H), 3.11 (dd, *J* = 5.9, 4.9 Hz, 1H), 2.94 (dd, *J* = 17.1, 5.9 Hz, 1H), 2.87 (dd, *J* = 17.1, 4.9 Hz, 1H), 1.94 (d, *J* = 1.6 Hz, 3H), 1.13 – 0.97 (m, 42H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 133.1, 120.0, 104.7, 83.4, 79.1, 66.1, 43.3, 22.3, 20.5, 18.7, 18.0, 12.0, 11.4. HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{28}H_{56}NO_3Si_2$, 510.3793; found 510.3793.

Synthesis of compound 20



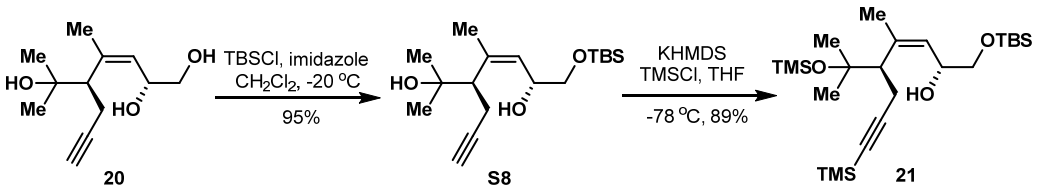
11 **20**

$CeCl_3$ (24.05 g, 97.60 mmol) in a 1 litter of flask was pre-treated by heating at 150 °C under vacuum for 2 h. To this flask was added THF (580 mL) at room temperature in a dropwise manner, the resultant mixture was stirred at the same temperature for 3 h. To this solution was added CH_3MgBr (32.5 mL, 3 M in Et_2O, 97.60 mmol) at 0 °C in a dropwise manner, and the resultant mixture was stirred at the same temperature for 4 h. To this solution was added a solution of **11** (4.80 g, 9.76 mmol) in THF (50 mL) at 0 °C over 5 min. and the resultant mixture was stirred at the same temperature for 10 min, and then stirred at 50 °C for 10 min. The reaction was quenched by addition of a solution of CH_3COOH (10%, 150 mL), and the mixture was then extracted with EtOAc (3 x 150 mL). The combined organic extracts was washed with brine (500 mL), and dried over sodium sulfate. The solvent was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 10:1) to give a colorless oil.

To a solution of the colorless oil made above in THF (100 mL) was added TBAF (30 mL, 1 M in THF, 30 mmol) at 0 °C in a dropwise manner, the resultant mixture was stirred at room temperature for 3 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (150 mL), and the mixture was extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with brine (200 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 1:1 to 1:2) to give triol **20** (1.82 g, 88% over 2 steps) as colorless oil.

Characterization data of **20**: R_f = 0.15 (silica gel, petroleum ether : EtOAc = 1:2); $[\alpha]_D^{30}$ = +45.4 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3294, 2971, 1658, 1380, 1152, 1066, 931, 873, 804, 630 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.49 (dd, *J* = 8.5, 1.6 Hz, 1H), 4.62 – 4.42 (m, 1H), 3.65 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.52 (dd, *J* = 11.2, 7.4 Hz, 1H), 3.33 (brs, 1H), 2.90 (dd, *J* = 11.3, 4.3 Hz, 1H), 2.61 (brs, 1H), 2.54 – 2.31 (m, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.81 (d, *J* = 1.4 Hz, 3H), 1.29 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 129.8, 83.1, 72.2, 69.5, 68.5, 66.5, 50.5, 29.4, 27.5, 20.7, 18.0. HRMS (ESI, m/z): $[M+Na]^+$ calcd for $C_{12}H_{20}NaO_3$, 235.1305; found 235.1298.

Synthesis of compound 21



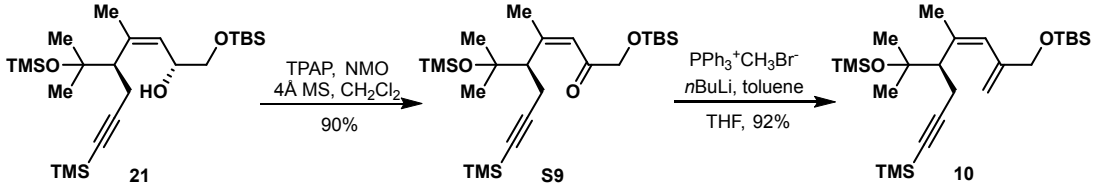
To a stirred solution of **20** (5.01 g, 23.63 mmol) and imidazole (3.21 g, 47.20 mmol) in CH_2Cl_2 (100 mL) was added TBSCl (3.73 g, 24.78 mmol) at -20 °C in portions, and the resultant mixture was stirred at the same temperature for 5 min. The reaction was quenched by addition of water (150 mL), and the mixture was extracted with EtOAc (500 mL). The combined organic extracts were dried over sodium sulfate, and the solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 10:1 to 4:1) to give diol **S8** (7.31 g, 95%) as colorless oil.

Characterization data of **S8**: R_f = 0.2 (silica gel, petroleum ether : EtOAc = 10:1); $[\alpha]_D^{30}$ = +17.6 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3312, 2954, 2928, 2857, 1471, 1378, 1253, 1105, 1051, 1006, 888, 835, 777, 668, 631 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.40 (dd, *J* = 8.2, 1.5 Hz, 1H), 4.54 – 4.37 (m, 1H), 3.69 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.51 – 3.33 (m, 1H), 2.98 – 2.82 (m, 1H), 2.78 (brs, 1H), 2.59 – 2.33 (m, 2H), 2.22 (brs, 1H), 1.91 (t, *J* = 2.7 Hz, 1H), 1.81 (d, *J* = 1.4 Hz, 3H), 1.29 (s, 3H), 1.24 (s, 3H), 0.91 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 128.8, 83.4, 71.8, 69.2, 68.4, 67.2, 29.6, 28.1, 26.1, 18.5, 17.9, -5.1, -5.2. HRMS (ESI, m/z): $[M+Na]^+$ calcd for $C_{18}H_{34}NaO_3Si$, 349.2169; found 349.2164.

To a stirred solution of **S8** (7.10 g, 21.78 mmol) and TMSCl (18.93 g, 174.24 mmol) in THF (220 mL) at 0 ℃ was added KHMDS (130.7 mL, 1.0 M in THF, 130.70 mmol) over 1 h. The reaction mixture was quenched with a saturated solution of NH_4Cl (500 mL) and the mixture was extracted with EtOAc (800 mL), the organic layer was washed with HCl (500 mL, 0.5 M in water) and brine (2 x 500 mL), dried over sodium sulfate, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleum ether : EtOAc = 100:1 to 50:1) to give **21** (9.11 g, 89%) as colorless oil.

Characterization data of **21**: R_f = 0.50 (silica gel, petroleum ether : EtOAc = 10:1); $[\alpha]_D^{30}$ = +21.0 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2956, 2929, 2858, 2175, 1462, 1384, 1250, 1198, 1151, 1108, 1040, 895, 838, 777, 758, 644 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.27 (dd, *J* = 8.6, 1.5 Hz, 1H), 4.39 (m, 1H), 3.67 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.35 (dd, *J* = 10.1, 9.0 Hz, 1H), 2.61 (dd, *J* = 9.2, 5.9 Hz, 1H), 2.57 (d, *J* = 1.9 Hz, 1H), 2.53 – 2.49 (m, 2H), 1.73 (d, *J* = 1.5 Hz, 3H), 1.29 (s, 3H), 1.25 (s, 3H), 0.92 (s, 9H), 0.11 (s, 9H), 0.09 (s, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 127.2, 107.2, 84.8, 74.9, 68.8, 67.3, 50.9, 29.9, 29.6, 26.0, 20.3, 18.4, 18.4, 2.5, 0.3, -5.0, -5.1. HRMS (ESI, m/z): $[M+Na]^+$ calcd for $C_{24}H_{50}NaO_3Si_3$, 493.2960; found 493.2961.

Synthesis of compound 10



To a solution of dried 4Å molecular sieve (6.50 g), **21** (6.30 g, 13.40 mmol) and NMO (3.51 g,

29.50 mmol) in CH_2Cl_2 (200 mL) was added TPAP (471 mg, 1.34 mmol) at 0 °C in one portion, and the resultant mixture was then stirred 40 °C for 2 h. The reaction mixture was purified directly by a flash chromatography on silica gel (petroleum ether : EtOAc = 200:1 to 100:1) to give **S9** (5.83 g, 93%) as colorless oil.

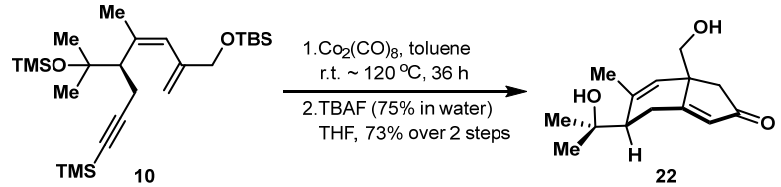
Characterization data of **S9**: R_f = 0.5 (silica gel, petroleum ether : EtOAc = 20:1); $[\alpha]_D^{30}$ = +7.8 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2956, 2857, 2176, 1705, 1684, 1610, 1250, 1154, 1091, 1036, 897, 839, 778, 758, 643 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 6.35 (d, *J* = 1.7 Hz, 1H), 4.19 (s, 2H), 4.10 (dd, *J* = 11.0, 4.8 Hz, 1H), 2.56 (dd, *J* = 17.1, 11.0 Hz, 1H), 2.45 (dd, *J* = 17.1, 4.8 Hz, 1H), 1.93 (d, *J* = 1.3 Hz, 3H), 1.32 (s, 3H), 1.19 (s, 3H), 0.93 (s, 9H), 0.09 (s, 9H), 0.09 (d, *J* = 2.9 Hz, 6H), 0.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.6, 161.2, 123.1, 106.7, 85.1, 75.4, 70.4, 49.6, 29.8, 29.3, 26.0, 21.9, 18.6, 18.5, 2.5, 0.3, -5.2, -5.3. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{24}H_{49}O_3Si_3$, 469.2984; found 469.2971.

To a suspension of methyltriphenyl phosphonium bromide (35.40 g, 99.20 mmol) in anhydrous toluene (500 mL) was added *n*BuLi (37.2 mL, 2.5 M in hexane, 93.01 mmol) at room temperature in a dropwise manner, and the resultant mixture was then stirred at the same temperature for 1 h.

To a solution of **S9** (5.81 g, 12.40 mmol) in THF (150 mL) was added the solution prepared above at 0 °C via a syringe in a dropwise manner, and the reaction mixture was stirred at 0 °C for for 30 min. the reaction was quenched by addition of a saturated solution of NH_4Cl (300 mL), and the mixture was extracted with EtOAc (2 x 200 mL) The combined organic layers were washed with brine (500 mL), and dried over sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether:EtOAc = 400:1 to 200 :1) to give **10** (5.31 g, 92%) as colorless oil.

Characterization data of **10**: R_f = 0.65 (silica gel, petroleum ether : EtOAc = 20:1); $[\alpha]_D^{30}$ = +164.5 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2955, 2856, 2175, 1382, 1365, 1250, 1198, 1157, 1105, 1034, 895, 835, 775, 758, 643, 610 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.72 (s, 1H), 5.29 – 5.19 (m, 1H), 5.13 (brs, 1H), 4.09 (d, *J* = 15.2 Hz, 1H), 4.00 (d, *J* = 15.2 Hz, 1H), 2.96 (dd, *J* = 9.7, 5.7 Hz, 1H), 2.64 – 2.46 (m, 2H), 1.75 (d, *J* = 1.5 Hz, 3H), 1.21 (s, 3H), 1.14 (s, 3H), 0.93 (s, 9H), 0.11 (s, 9H), 0.08 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 139.8, 127.1, 111.0, 107.7, 85.2, 75.0, 66.0, 49.8, 30.0, 29.9, 26.1, 20.5, 18.6, 18.6, 2.5, 0.3, -5.2. HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{25}H_{54}NO_2Si_3$, 484.3457; found 484.3450.

Synthesis of compound 22

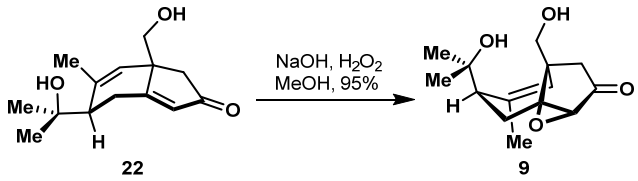


To a stirred solution of **10** (6.02 g, 12.87 mmol) in toluene (1.0 L) was added $Co_2(CO)_8$ (880 mg, 2.57 mmol) at room temperature in one portion under nitrogen, and the resultant mixture was stirred at the same temperature for 1.5 h. The reaction mixture was then stirred at 120 °C under balloon pressure of CO for 36 h. The reaction was worked up by filtered of the reaction mixture through a pad of celite, and washed with EtOAc (3 x 150 mL), The filtrate was concentrated under vacuum to give a dark brown oil.

To a solution of the oil made above in THF (150 mL) was added TBAF (17.95 g, 75% in water, 51.48 mmol) at room temperature in a dropwise manner, the resultant mixture was stirred at room temperature for 5 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (100 mL), and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (100 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 2:1 to 1:2) to give diol **22** (2.22 g, 73% over 2 steps) as a colorless oil.

Characterization data of **22**: R_f = 0.15 (silica gel, petroleum ether : EtOAc = 1:2); $[\alpha]_D^{30}$ = +97.1 (*c* =1.0 in MeOH); IR (neat): ν_{max} = 3361, 2969, 2921, 1675, 1622, 1380, 1257, 1134, 1059, 931, 827, 621 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 5.85 (d, *J* = 1.5 Hz, 1H), 5.41 (d, *J* = 1.6 Hz, 1H), 4.85 (t, *J* = 6.0 Hz, 1H), 4.44 (s, 1H), 3.37 (d, *J* = 6.0 Hz, 2H), 2.77 (dd, *J* = 12.5, 6.1 Hz, 1H), 2.43 (d, *J* = 17.7 Hz, 1H), 2.39 – 2.24 (m, 2H), 1.97 (d, *J* = 17.7 Hz, 1H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.17 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 206.0, 182.1, 137.9, 128.7, 127.0, 72.3, 66.0, 52.5, 49.9, 45.6, 29.8, 28.2, 25.2, 24.1. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{14}H_{21}O_3$, 237.1485; found 237.1484.

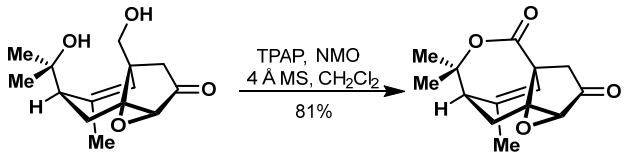
Synthesis of compound 9



To a stirred solution of **22** (5.03 g, 21.18 mmol) in methanol (150 mL) was sequentially added NaOH (7 mL, 6 M in water, 42.37 mmol) and H_2O_2 (7 mL, 30% in water, 63.54 mmol) at 0 ºC, and the resultant mixture was stirred at rthe same temperature for 10 min. The reaction was quenched by addition of a saturated NH_4Cl (150 mL), and the mixture was extracted with EtOAc (4 x 150 mL). The combined organic layers was washed with brine (100 mL), and dried over sodium sulfate. The solvent of the extract was concentrated in vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 2:1 to 1:2) to give **9** (5.07 g, 95%) as colorless oil.

Characterization data of **9**: R_f = 0.45 (silica gel, petroleum ether : EtOAc = 1:2); $[\alpha]_D^{30}$ = -94.0 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3416, 2971, 2927, 2870, 1735, 1402, 1380, 1256, 1200, 1126, 1030, 918, 810, 731, 648, 541 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.28 (t, *J* = 1.6 Hz, 1H), 3.85 – 3.65 (m, 2H), 3.20 (s, 1H), 2.51 (d, *J* = 18.0 Hz, 1H), 2.54 – 2.47 (m, 1H), 2.33 (dd, *J* = 13.5, 10.9 Hz, 1H), 1.95 (t, *J* = 1.2 Hz, 3H), 1.91 (d, *J* = 18.0 Hz, 1H), 1.83 (brs, 1H), 1.65 (dd, *J* = 13.5, 7.1 Hz, 1H), 1.39 (brs, 1H), 1.26 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.1, 141.4, 129.0, 73.7, 71.3, 65.2, 61.5, 50.8, 43.9, 42.6, 30.4, 26.9, 25.6, 24.4. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{14}H_{21}O_4$, 253.1434; found 253.1434.

Synthesis of compound 23

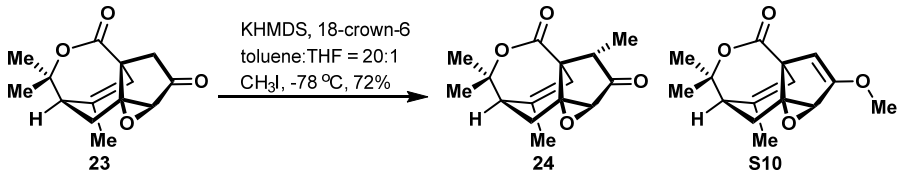


9 **23**

To a solution of dried 4Å molecular sieve (6.02 g), **9** (5.07 g, 20.12 mmol) and NMO (9.42 g, 80.48 mmol) in CH_2Cl_2 (260 mL) was added TPAP (707 mg, 2.01 mmol) at 0 °C in one portion, and the resultant mixture was then stirred at 30 °C for 30 min. The reaction mixture was purified directly by a flash chromatography on silica gel (CH_2Cl_2 : Methanol = 100:1) to give a colorless oil, which was purified again by flash chromatography on silica gel (petroleum ether : EtOAc = 5:1 to 2:1) to give **23** (4.04 g, 81%) as a semi-solid.

Characterization data of **23**: R_f = 0.4 (silica gel, petroleum ether : EtOAc = 2:1); $[\alpha]_D^{30}$ = -150.9 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3358, 2920, 2850, 1747, 1708, 1659, 1632, 1271, 1199, 1105, 1072, 1024, 921, 879, 826, 733, 703, 550 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.55 (brs, 1H), 3.43 (d, *J* = 19.0 Hz, 1H), 3.32 (s, 1H), 2.54 (dd, *J* = 15.3, 1.8 Hz, 1H), 2.46 (dd, *J* = 5.0, 1.8 Hz, 1H), 2.35 (dd, *J* = 15.3, 5.0 Hz, 1H), 2.25 (d, *J* = 19.0 Hz, 1H), 1.97 (d, *J* = 1.7 Hz, 3H), 1.57 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.5, 166.9, 145.7, 125.0, 87.2, 70.1, 61.5, 51.2, 48.7, 43.6, 28.6, 28.2, 25.4, 23.9. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{14}H_{17}O_4$, 249.1121; found 249.1121.

Synthesis of compound 24



23 **24** **S10**

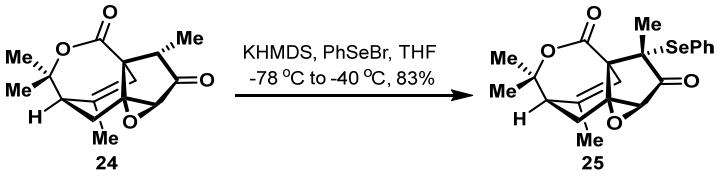
To a stirred solution of KHMDS (28.5 mL, 1 M in THF, 28.50 mmol) in toluene (300 mL) was added a solution of **23** (5.90 g, 23.80 mmol) in toluene (200 mL) at -78 °C over 80 min via a syringe pump. To this solution was added a solution of 18-crown-6 (9.21 g, 35.70 mmol) in toluene (40 mL) at the same temperature with stirring, and the resultant mixture was stirred for 5 min. To this solution was added a solution of CH_3I (6.77 g, 47.61 mmol) -78 °C over 10 min, and the resultant mixture was stirred at the same temperature for 5 min. The reaction mixture was quenched by addition of a saturated solution of NH_4Cl (500 mL), and the mixture was extracted with EtOAc (3 x 300 mL). The combined organic layers were washed with brine (500 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (CH_2Cl_2:EtOAc = 30:1 to 20 :1) to give **24** (4.49 g, 72%) and **S10** (1.04 g, 17%) as colorless oils.

Characterization data of **24**: R_f = 0.60 (silica gel, CH_2Cl_2 : EtOAc = 20:1); $[\alpha]_D^{30}$ = -72.5 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3360, 2980, 2920, 2850, 1747, 1710, 1274, 1255, 1200, 1116, 1016, 908, 875, 854, 831, 588cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.64 (t, *J* = 1.6 Hz, 1H), 3.30 (q, *J* = 7.2 Hz, 1H), 3.29 (s, 1H), 2.58 (dd, *J* = 15.4, 1.5 Hz, 1H), 2.41 (dt, *J* = 5.4, 1.5 Hz, 1H), 2.31 (dd, *J* = 15.4, 5.4 Hz, 1H), 1.96 (d, *J* = 1.7 Hz, 3H), 1.57 (s, 3H), 1.49 (s, 3H), 1.15 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.3, 167.4, 145.8, 118.9, 87.1, 68.8, 61.0, 53.7, 47.8, 42.8, 28.5, 28.3, 25.3, 24.4, 9.1. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{15}H_{19}O_4$, 263.1278; found

263.1276.

Characterization data of **S10**: R_f = 0.25 (silica gel, CH_2Cl_2 : EtOAc = 20:1); $[\alpha]_D^{30}$ = -156.4 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2979, 2922, 1716, 1634, 1447, 1356, 1301, 1268, 1211, 1117, 1084, 1041, 1025, 904, 880, 828, 782 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 5.66 – 5.62 (m, 1H), 4.87 (d, *J* = 2.6 Hz, 1H), 3.65 (s, 3H), 3.63 (d, *J* = 2.6 Hz, 1H), 2.47 – 2.43 (m, 1H), 2.40 (dd, *J* = 15.0, 2.7 Hz, 1H), 2.29 (dd, *J* = 15.0, 3.8 Hz, 1H), 1.95 (d, *J* = 1.7 Hz, 3H), 1.58 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 161.8, 142.7, 124.2, 101.4, 86.7, 66.4, 61.8, 57.5, 57.3, 48.5, 29.5, 28.2, 27.9, 23.7. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{15}H_{19}O_4$, 263.1278; found 263.1271.

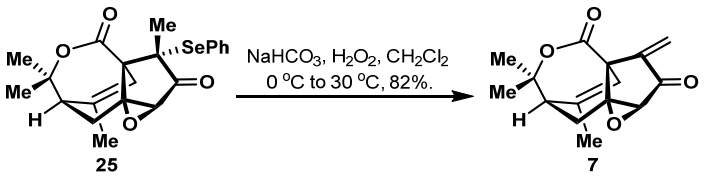
Synthesis of compound 25



To a stirred solution of KHMDS (18.2 mL, 1.0 M in THF, 18.2 mmol) in THF (60 mL) was added a solution of **24** (3.96 g, 15.10 mmol) in THF (60 mL) at -78 °C over 10 min via a syringe, and the resultant mixture was then stirred at -40 °C for 1 h. To this solution was added a solution of PhSeBr (4.65 g, 19.70 mmol) in THF (30 mL) at -78 °C over 10 min and stirred at the same temperature for 5 min. The reaction mixture was quenched by addition of a saturated solution of NH_4Cl (150 mL), and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed brine (200 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 5:1 to 2:1) to give **25** (5.22 g, 83%) as a semi-solid.

Characterization data of **25**: R_f = 0.5 (silica gel, petroleum ether : EtOAc = 2:1); $[\alpha]_D^{30}$ = -180.4 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3055, 2980, 2931, 1723, 1438, 1371, 1250, 1194, 1173, 1111, 1009, 963, 942, 884, 832, 812, 780, 732, 692, 598, 530, 473 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.51 – 7.41 (m, 3H), 7.38 – 7.33 (m, 2H), 6.15 (t, *J* = 1.6 Hz, 1H), 4.05 (s, 1H), 2.58 – 2.47 (m, 1H), 2.32 (dd, *J* = 14.8, 3.2 Hz, 1H), 2.27 (dd, *J* = 14.8, 3.1 Hz, 1H), 2.10 (d, *J* = 1.6 Hz, 3H), 1.79 (s, 3H), 1.59 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.0, 163.6, 144.6, 139.0, 130.6, 129.4, 125.9, 120.4, 87.8, 69.7, 65.6, 61.4, 56.6, 47.4, 29.9, 27.5, 26.9, 24.1, 16.1. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{21}H_{23}O_4Se$, 419.0756; found 419.0755.

Synthesis of compound 7

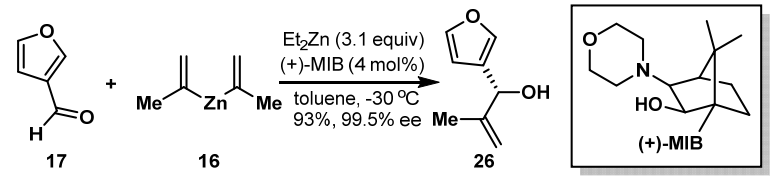


To a stirred solution of **25** (5.21 g, 12.44 mmol) and $NaHCO_3$ (6.27 g, 74.64 mmol) in CH_2Cl_2 (80 mL) was added H_2O_2 (4.1 mL, 30% in water, 37.32 mmol) at 0 °C, and the reaction mixture was then stirred at 30 °C for 1 h. To this solution was added additional H_2O_2 (2.7 mL, 30% in water, 24.90 mmol) at 0 °C, and the mixture wasstirred at room temperature for 30 min. The reaction mixture was quenched by addition of water (100 mL), and the mixture was extracted with CH_2Cl_2

(2 x 100 mL). The combined organic layers were dried over sodium sulfate, and the solvent of extract was concentrated in vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 4:1 to 1:1) to give **7** (2.65 g, 82%) as a semi-solid.

Characterization data of **7**: R_f = 0.4 (silica gel, petroleum ether : EtOAc = 1:1); $[\alpha]_D^{30}$ = -205.4 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2982, 1719, 1639, 1438, 1388, 1370, 1345, 1301, 1256, 1189, 1115, 1021, 951, 908, 884, 825, 793, 772, 730, 662, 585, 478 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 6.55 (s, 1H), 5.91 (s, 1H), 5.55 (brs, 1H), 3.57 (s, 1H), 2.86 – 2.28 (m, 3H), 1.98 (d, *J* = 1.7 Hz, 3H), 1.60 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.8, 165.0, 145.4, 143.8, 127.9, 124.9, 87.7, 66.9, 60.7, 55.9, 48.5, 28.8, 27.9, 26.2, 23.7. HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{15}H_{20}NO_4$, 278.1387; found 278.1387.

Synthesis of compound 26

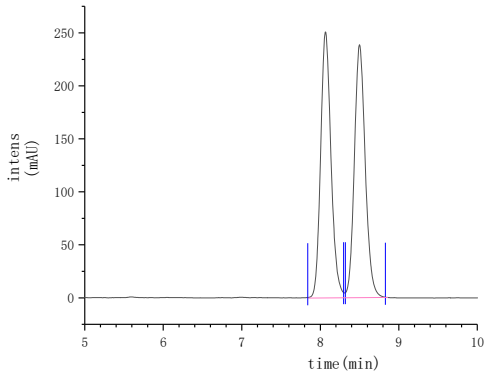


To a solution of (+)-MIB[4] (306 mg, 1.28 mmol) in toluene (90 mL) was added fresh diisopropenylzinc[5] (12.8 mL, 1.1 M in toluene, 14.08 mmol) at 15 °C. To this solution was diethylzinc (19.9 mL, 2.0 M in toluene, 39.68 mmol) was added -30 °C in a dropwise manner, and stirred another 10 min. To this solution was added a solution of aldehyde **17** (1.23 g, 12.80 mmol) in toluene (38 mL) -30 °C over 30 min. The reaction was quenched by slowly addition of a saturated solution of NH_4Cl (100 mL), and stirred strongly at 16 °C over 1h. The reaction was worked up by filtration of the mixture through a celite pad, and wahsed with EtOAc. The filtrate was extracted by EtOAc (2 × 50 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent of extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 20:1; 10:1) to give product **26** (1.65 g, 93%, 99.5% *ee*) as a colorless oil

Characterization data of **26**: R_f = 0.45 (silica gel, petroleum ether : EtOAc = 4:1); $[\alpha]_D^{20}$ = +4.4 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3368, 2974, 2917, 1654, 1593, 1502, 1449, 1373, 1265, 1157, 1046, 1019, 904, 875, 773, 734, 600 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 1.4 Hz, 1H), 7.38 (t, *J* = 1.7 Hz, 1H), 6.34 (d, *J* = 1.8 Hz, 1H), 5.15 (d, *J* = 1.9 Hz, 1H), 5.10 (d, *J* = 3.9 Hz, 1H), 4.94 (t, *J* = 1.7 Hz, 1H), 1.99 (d, *J* = 4.0 Hz, 1H), 1.69 (t, *J* = 1.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 143.4, 139.9, 127.1, 111.3, 109.1, 71.0, 18.3; HRMS (ESI, m/z): $[M+Na]^+$ calcd for $C_8H_{10}NaO_2$, 161.0573; found 161.0574.

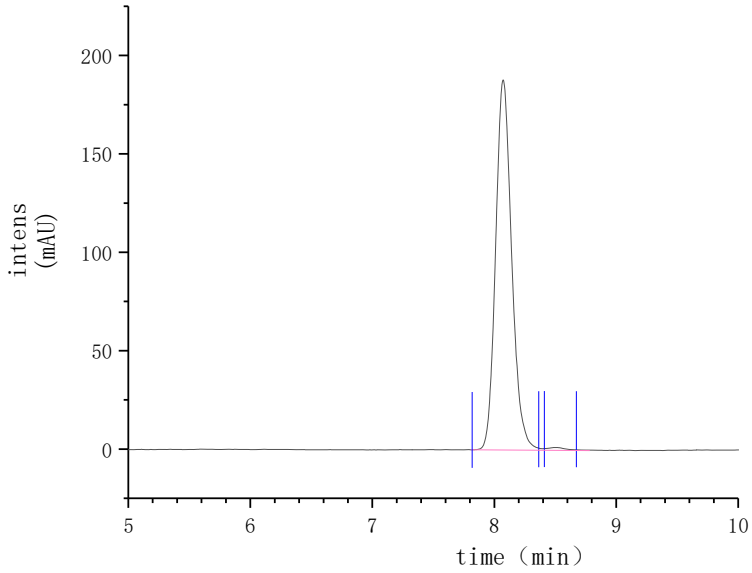
26 was analyzed with chiral HPLC (hexane/*i*-PrOH = 97:3, 1.0 mL/min, λ = 220 nm, chiralpak IC, 4.6 mmφ × 250 mmL, particle size 5 μm).

Racemic sample:



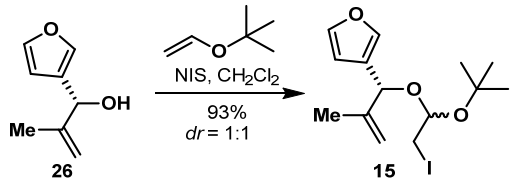
	Ret. Time (min)	Area	Area%
	8.07	11471.82	49.87
	8.50	11533.43	50.13
		23005.25	100.00

Asymmetric sample:



	Time (min)	Area	Area%
	8.07	8521.48	99.75
	8.53	21.17	0.25
		8642.65	100.00

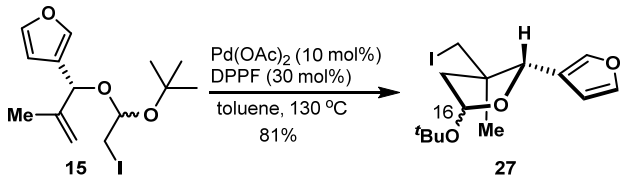
Synthesis of compound **15**



To a solution of **26** (1.63 g, 11.80 mmol) in CH_2Cl_2 (24 mL) was added *t*-butyl vinyl ether (1.42 g, 14.20 mmol). To this mixture was added NIS (3.19 g, 14.20 mmol) at -30 °C in portion-wise manner, and the resultant mixture was stirred at the same temperature for 20 min. The reaction mixture was quenched by slowly addition of a saturated solution of NH_4Cl (50 mL), and the mixture was extracted with EtOAc (2 x 100 mL). The combined organic layer was sequentially washed by $Na_2S_2O_3$ (20 mL) and brine (2 × 50 mL), and dried over anhydrous Na_2SO_4. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 100:1) to give product **15** (4.02 g, 93%, *dr* = 1:1) as a mixture of diastereoisomers.

Characterization data of **15**: R_f = 0.3 (silica gel, petroleum ether : EtOAc = 20:1); IR (neat): ν_{max} = 2973, 1651, 1500, 1450, 1411, 1391, 1366, 1313, 1260, 1158, 1100, 1000, 902, 873, 779, 728, 600 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 1.7, 0.9 Hz, 0.5H), 7.42 – 7.36 (m, 0.5H), 7.37 (t, *J* = 1.7 Hz, 0.5H), 7.34 (t, *J* = 1.7 Hz, 0.5H), 6.35 (dd, *J* = 1.9, 0.9 Hz, 0.5H), 6.29 (dd, *J* = 1.7, 0.9 Hz, 0.5H), 5.15 (dt, *J* = 1.9, 0.9 Hz, 0.5H), 5.10 (dt, *J* = 2.0, 1.0 Hz, 0.5H), 5.03 (s, 0.5H), 5.02 (s, 0.5H), 4.99 (t, *J* = 1.6 Hz, 0.5H), 4.89 (t, *J* = 1.7 Hz, 0.5H), 4.80 (dt, *J* = 10.3, 5.1 Hz, 1H), 3.27 – 3.11 (m, 2H), 1.71 – 1.63 (m, 3H), 1.25 (s, 4.5H), 1.23 (s, 4.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 144.8, 143.2, 143.0, 140.3, 140.0, 125.7, 125.4, 113.7, 112.4, 109.7, 109.4, 95.6, 95.5, 74.8, 74.8, 74.8, 73.5, 28.9, 28.9, 18.3, 17.6, 9.2, 9.2; HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{14}H_{25}INO_3$, 382.0874; found 382.0874.

Synthesis of compound 27

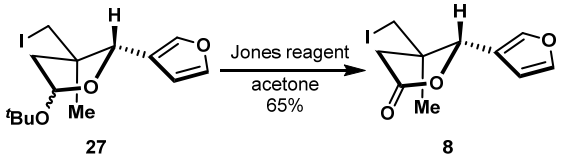


To a solution of **15** (100 mg, 0.27 mmol) in toluene (1.5 mL) was added DPPF (46 mg, 0.08 mmol), $Pd(OAc)_2$ (6 mg, 0.03 mmol), the resulting mixture was degassed with N_2 over 10 min. The reaction mixture was stirred at 130 °C for 36 h. The reaction was worked by a direct purification via a flash chromatography on silica gel (petroleum ether : CH_2Cl_2 = 1:1) to give product **27** (60 mg, *dr* = 2:1) as a pair of C16-diastereoisomers, and substrate **15** (26 mg), *brsm* = 81%.

Characterization data of **27**: R_f = 0.2~0.3 (silica gel, petroleum ether : CH_2Cl_2 = 1:1); IR (neat): ν_{max} = 3674, 2971, 2900, 2360, 1501, 1455, 1393, 1379, 1364, 1258, 1233, 1195, 1160, 1066, 1057, 1036, 1027, 1016, 1000, 874, 796, 600 cm^{-1};^1H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.34 (m, 2H), 6.42 (dd, *J* = 1.9, 0.9 Hz, 0.33H), 6.33 (t, *J* = 1.3 Hz, 0.66H), 5.50 (dd, *J* = 5.8, 3.9 Hz, 0.66H), 5.45 (dd, *J* = 6.3, 3.9 Hz, 0.33H), 4.92 (s, 0.66H), 4.78 (s, 0.33H), 3.47 – 3.22 (m, 2H), 2.25 (dd, *J* = 13.5, 6.3 Hz, 0.33H), 2.10 (dd, *J* = 13.4, 5.8 Hz, 0.66H), 1.97 (dd, *J* = 13.4, 3.9 Hz, 0.66H), 1.86 (dd, *J* = 13.5, 3.9 Hz, 0.33H), 1.27 (s, 3H), 1.25 (s, 6H), 1.02 (s, 1H), 0.91 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 142.9, 140.6, 140.1, 124.6, 122.9, 110.1, 109.4, 97.8, 96.8, 80.5, 78.0, 74.6,

74.5, 48.7, 46.0, 45.8, 45.3, 29.1, 29.0, 22.8, 22.5, 19.6, 17.9; HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{14}H_{22}IO_3$, 365.0608; found 365.0607.

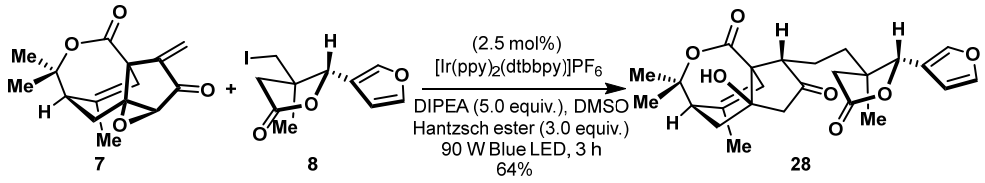
Synthesis of compound 8



To a solution of **27** (950 mg, 2.61 mmol) in acetone (20 mL) was added Jones reagent (8.7 mL, 1.2 M in water, 10.44 mmol) at 0 °C, and the resultant reaction mixture was first stirred at 0 °C for 1 h, and then at room temperature for 2 h. The reaction mixture was worked up by solid $NaHCO_3$ slowly until no bubbles are generated. The reaction mixture was filtered off through a celite pad, and then washed with EtOAc. The filtrate was concentrated under vacuum, and the residue was extracted with EtOAc (3 × 50 mL). The combined extracts were washed with brine (3 × 50 mL), dried over Na_2SO_4. The solvent of the extract was removed under reduced pressure, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 30:1) to deliver the lactone product **8** (519 mg, 65%) as a clear oil.

Characterization data of **8**: R_f = 0.4 (silica gel, petroleum ether : EtOAc = 4:1); $[\alpha]_D^{20}$ = -67.2 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 2967, 2919, 2848, 1744, 1502, 1454, 1416, 1382, 1285, 1161, 1024, 1012, 991, 874, 799, 599, 531 cm^{-1}; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.60 – 7.39 (m, 2H), 6.34 (dd, *J* = 1.9, 1.0 Hz, 1H), 5.39 (s, 1H), 3.31 (s, 2H), 2.82 (d, *J* = 17.1 Hz, 1H), 2.44 (d, *J* = 17.1 Hz, 1H), 1.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 144.1, 140.3, 119.8, 108.6, 81.0, 44.1, 42.8, 21.2, 14.3; HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{10}H_{15}INO_3$, 324.0091; found 324.0083.

Synthesis of compound 28

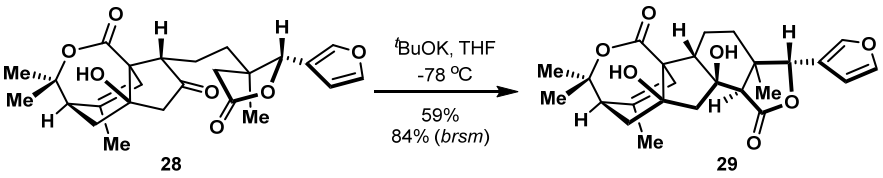


To a stirred solution of **7** (50.0 mg, 0.192 mmol) and **8** (70.1 mg, 0.231 mmol) in DMSO (2.0 mL) was added DIPEA (124.0 mg, 0.960 mmol) and Hantzsch ester (146.0 mg, 0.576 mmol) at rt under nitrogen atmosphere, followed by addition of $[Ir(ppy)_2(dtbbpy)]PF_6$ (5.3 mg, 0.006 mmol), and the resultant mixture was stirred under Blue LED (90 W, kessil A360We) for 4 h. The reaction mixture was quenched with water (25 mL), and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed brine (30 mL), and dried over sodium sulfate. The solvent of extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 2:1 to 1:1) to give a yellowish oil, which was purified again by a flash chromatography on silica gel (CH_2Cl_2 : EtOAc = 20:1 to 4:1) to give **28** (54.1 mg, 64%) as yellowish oil.

Characterization data of **28**: R_f = 0.2 (silica gel, petroleum ether : EtOAc = 1:1); $[\alpha]_D^{30}$ = -24.2 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3451, 2931, 1776, 1737, 1704, 1504, 1457, 1386, 1292, 1233, 1206, 1163, 1137, 1095, 1027, 912, 875, 809, 765, 730, 647, 602, 541, cm^{-1}; ^1H NMR (500

MHz, Chloroform-*d*) δ 7.49 (brs, 1H), 7.44 – 7.41 (m, 1H), 6.44 – 6.40 (m, 1H), 5.51 (brs, 1H), 5.25 (s, 1H), 3.21 (ddd, *J* = 8.1, 3.3, 1.4 Hz, 1H), 2.72 (dd, *J* = 18.9, 2.0 Hz, 1H), 2.71 (d, *J* = 16.9 Hz, 1H), 2.62 (dd, *J* = 15.0, 2.0 Hz, 1H), 2.40 (d, *J* = 16.9 Hz, 1H), 2.34 (dt, *J* = 5.0, 1.7 Hz, 1H), 2.27 (d, *J* = 18.9 Hz, 1H), 2.26 (s, 1H), 2.13 – 2.03 (m, 2H), 1.95 (d, *J* = 1.6 Hz, 3H), 1.75 – 1.59 (m, 3H), 1.57 (s, 3H), 1.46 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.5, 176.2, 168.1, 146.4, 143.6, 140.3, 120.5, 119.4, 109.1, 86.5, 83.1, 79.1, 62.0, 54.7, 54.0, 48.9, 44.1, 41.9, 38.3, 37.1, 28.9, 28.2, 24.0, 21.9, 20.6. HRMS (ESI, m/z): $[M+NH_4]^+$ calcd for $C_{25}H_{27}O_6$, 460.2330; found 460.2324.

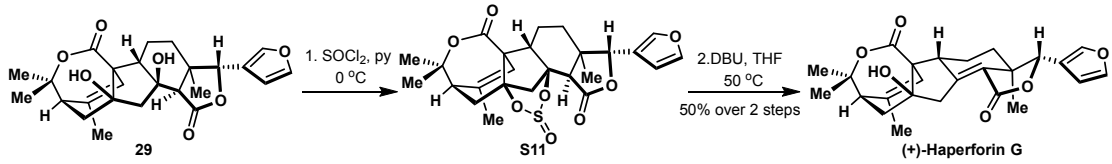
Synthesis of compound 29



To a stirred solution of **28** (28.0 mg, 0.063 mmol) in THF (1.3 mL) was added ^{t}BuOK (0.19 mL, 1.0 M in THF, 0.189 mmol) at -78 °C under nitrogen, and the resultant mixture was stirred at the same temperature for 4 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (15 mL), and the mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers was washed with brine (20 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 2:1 to 1:1) to give **29** (16.5 mg, 59%) and **28** (8.4 mg, 30%) as yellowish oils.

Characterization data of **29**: R_f = 0.25 (silica gel, petroleum ether : EtOAc = 1:1); $[\alpha]_D^{30}$ = -66.5 (*c* =1.0 in CH_2Cl_2); IR (neat): ν_{max} = 3480, 2935, 2871, 1760, 1702, 1504, 1457, 1383, 1341, 1269, 1206, 1161, 1086, 1041, 904, 875, 801, 763, 731, 598 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.54 – 7.35 (m, 2H), 6.31 (brs, 1H), 5.60 – 5.57 (m, 1H), 5.56 (s, 1H), 3.17 (dd, *J* = 12.4, 6.5 Hz, 1H), 2.82 (d, *J* = 1.8 Hz, 1H), 2.64 (s, 1H), 2.42 (dd, *J* = 14.9, 1.9 Hz, 1H), 2.41 (d, *J* = 14.8 Hz, 1H), 2.25 (dt, *J* = 5.2, 1.6 Hz, 1H), 2.09 (d, *J* = 14.9 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.99 – 1.88 (m, 3H), 1.91 (d, *J* = 1.6 Hz, 3H), 1.77 – 1.70 (m, 1H), 1.54 (s, 3H), 1.42 (s, 3H), 1.41 – 1.33 (m, 1H), 0.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 168.9, 144.1, 143.6, 139.6, 120.9, 120.3, 108.6, 86.5, 85.4, 84.3, 80.8, 63.6, 59.2, 56.2, 55.1, 48.3, 42.7, 35.5, 31.6, 28.8, 28.2, 24.2, 23.5, 20.7. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{25}H_{31}O_7$, 443.2064; found 443.2060.

Synthesis of (+)-Haperforin G



To a stirred solution of **29** (4.5 mg, 0.010 mmol) in pyridine (2.0 mL) was added $SOCl_2$ (0.2 mL) at rt, the resultant mixture was stirred at the same temperature for 30 min. The reaction was quenched by addition of a solution of HCl (1 N, 30 mL), and the mixture was extracted with EtOAc (3 x 15 mL). The combined organic layer was washed with brine (30 mL), and dried over sodium

sulfate. The solvent of extract was concentrated under vacuum to give **S11** as a diastereoisomers as an oil.

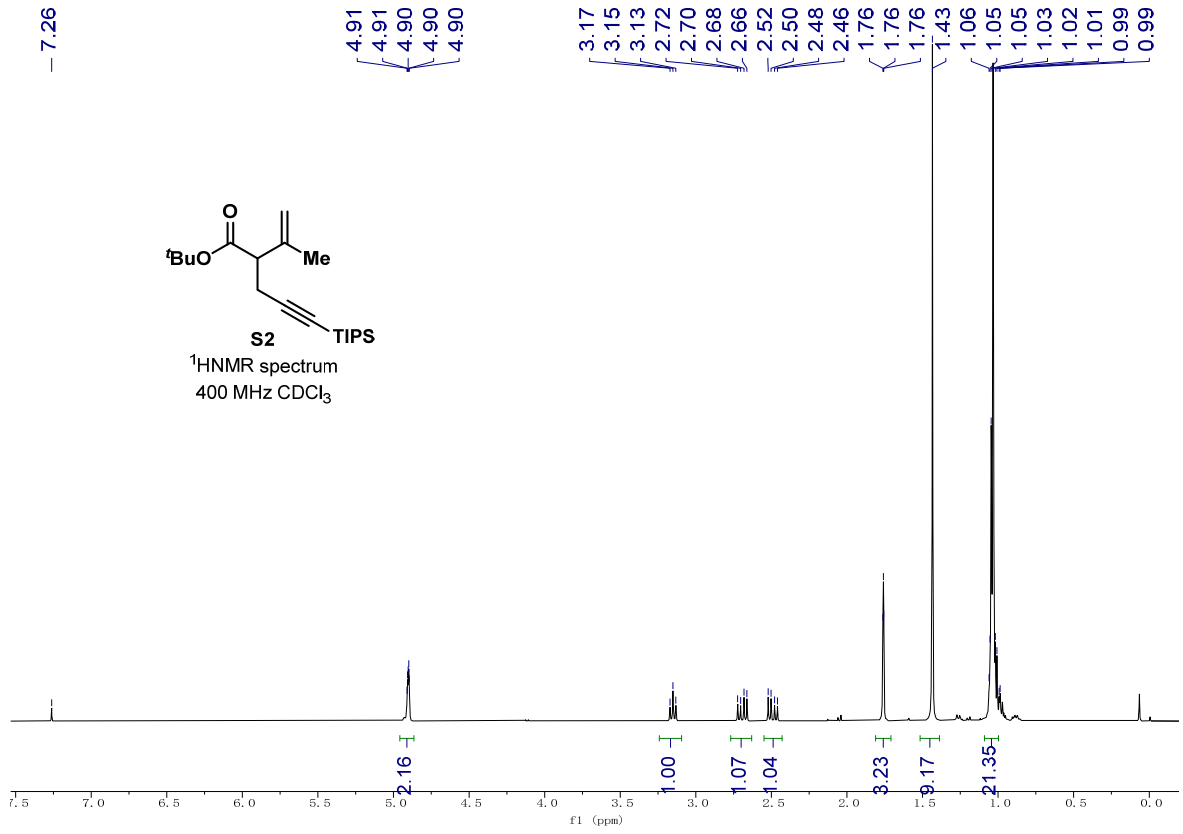
The above oil was dissolved in a fresh DBU solution (0.5 mL, 0.1 M in THF, 0.05 mmol), and the resultant mixture was stirred at 50 °C for 17 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (10 mL), and the mixture was extracted with EtOAc (2 x 10 mL). The combined extract was washed with brine (20 mL), and dried over sodium sulfate. The solvent of the extract was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (petroleum ether : EtOAc = 2:1 to 1:1) to give **(+)-Haperforin G** (2.1 mg, 50% over 2 steps) as a semi-solid.

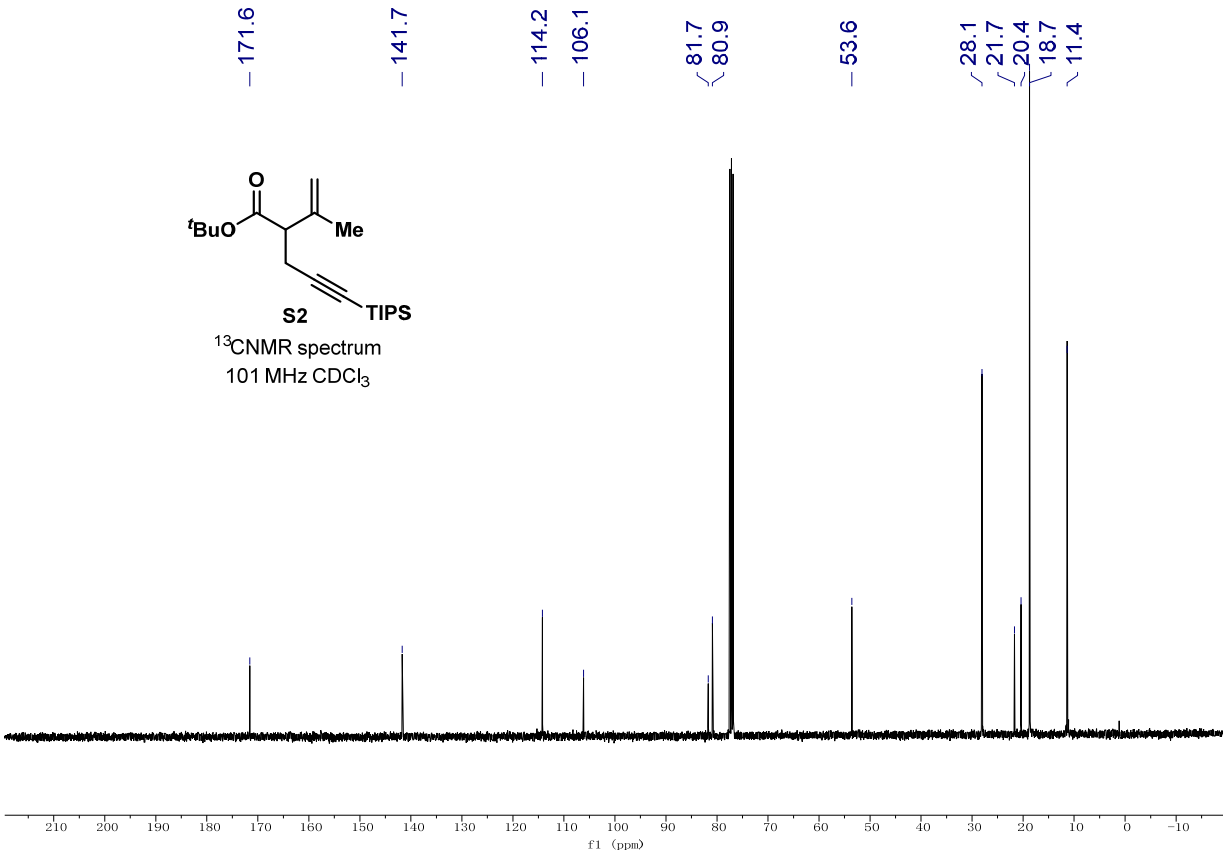
Characterization data of synthetic **(+)-Haperforin G**: R_f = 0.30 (silica gel, petroleum ether : EtOAc = 1:1); $[\alpha]_D^{30}$ = +11.4 (*c* =0.21 in $CHCl_3$); [literature: $[\alpha]_D$ = +24.1 (*c* =0.9 in $CHCl_3$)]; IR (neat): ν_{max} = 2920, 2851, 1752, 1701, 1263, 1197, 1164, 1087, 1036, 902, 875, 766, 729, 601 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.49 (brs, 1H), 7.47 – 7.44 (m, 1H), 6.35 (brs, 1H), 5.40 (s, 1H), 4.98 (s, 1H), 3.56 – 3.41 (m, 1H), 3.01 (dd, *J* = 19.8, 1.4 Hz, 1H), 2.94 (dd, *J* = 19.8, 2.2 Hz, 1H), 2.60 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.43 – 2.24 (m, 2H), 2.07 (dd, *J* = 14.9, 5.0 Hz, 1H), 2.00 (brs, 1H), 1.97 – 1.90 (m, 1H), 1.92 (d, *J* = 1.6 Hz, 3H), 1.80 – 1.67 (m, 2H), 1.56 (s, 3H), 1.44 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 168.5, 151.5, 146.1, 143.7, 140.0, 126.7, 120.5, 119.3, 108.5, 86.0, 84.2, 83.7, 62.0, 48.8, 47.5, 46.9, 43.1, 38.9, 31.9, 29.1, 28.1, 24.1, 22.0, 19.2. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{25}H_{29}O_6$, 425.1959; found 425.1963.

References:

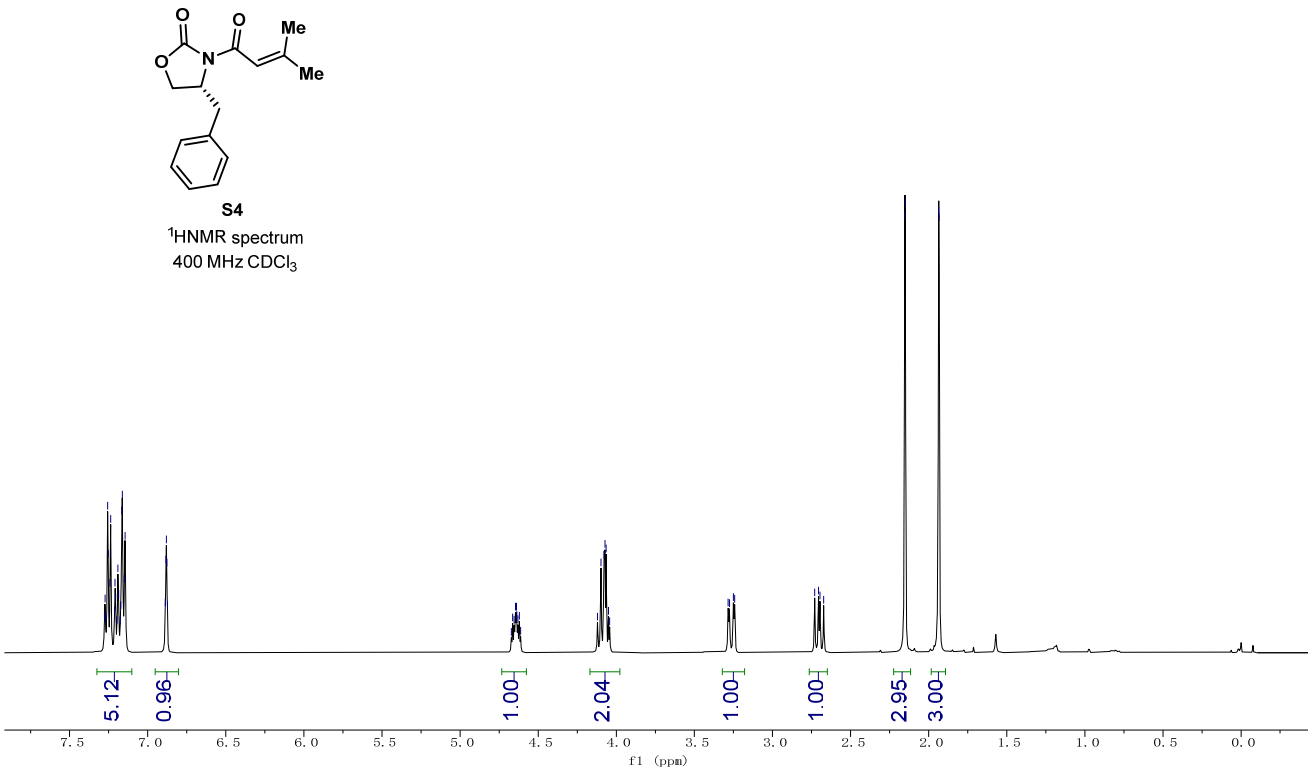
1. Smith, S. M.; Hoang, G. L.; Pal, R.; Bani Khaled, M. O.; Pelter, L. S. W.; Zeng, X. C.; Takacs, J. M. *Chem. Commun*. **2012**, *48*, 12180.
2. Frizzle, M. J.; Caille, S.; Marshall, T. L.; McRae, K.; Nadeau, K.; Guo, G.; Wu, S.; Martinelli, M. J.; Moniz, G. A. *Org. Process Res. Dev*. **2007**, *11*, 215.
3. Kim, M. J.; Sohn, T. I.; Kim, D.; Paton, R. S. *J. Am. Chem. Soc*. **2012**, *134*, 20178.
4. Nugent, W. A. *Chem. Commun.*, **1999**, 1369-1370.
5. Shibata, T.; Nakatsui, K.; Soai, K. *Inorganica Chimica Acta.* **1999**, *296*, 33-36.

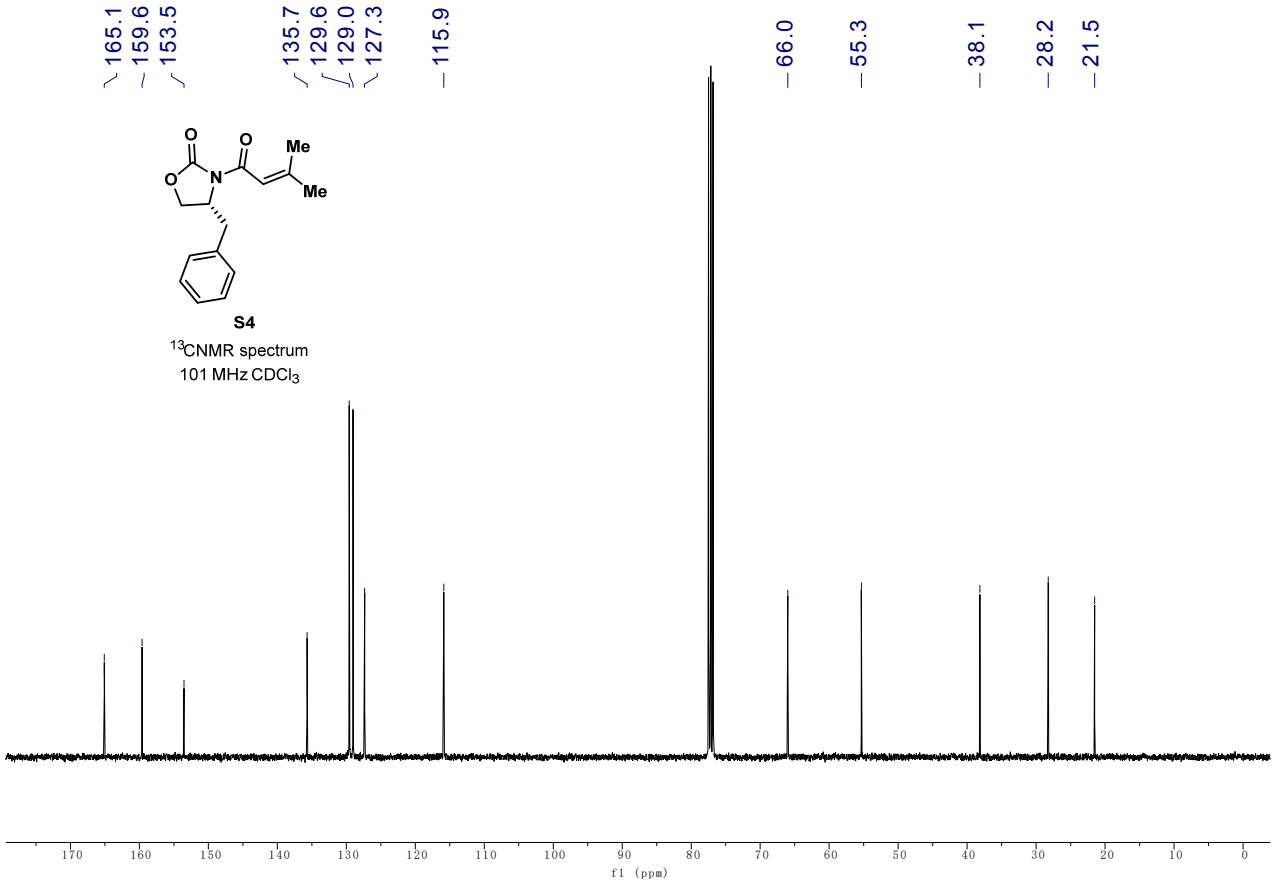
Part III: ^{1}H NMR and ^{13}C NMR spectrums




171.6
141.7
114.2
106.1
81.7
80.9
53.6
28.1
21.7
20.4
18.7
11.4
O
tBuO
Me
TIPS
S2
13CNMR spectrum
101 MHz CDCl3
f1 (ppm)

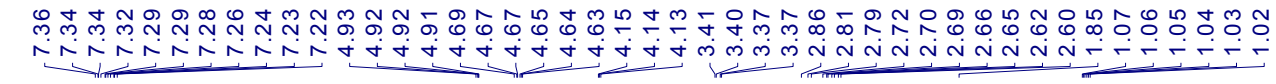

7.28
7.27
7.27
7.26
7.25
7.24
7.24
7.21
7.21
7.21
7.19
7.19
7.17
7.17
7.16
7.15
7.14
6.89
6.88
6.88
6.88
6.87
4.66
4.65
4.64
4.64
4.62
4.12
4.10
4.08
4.07
4.06
4.05
3.28
3.28
3.25
3.24
2.73
2.71
2.70
2.67
2.15
2.15
1.94
1.93

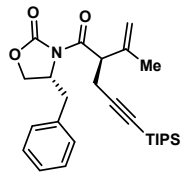

O
O
N
O
Me
Me
S4
1HNMR spectrum
400 MHz CDCl3
5.12
0.96
1.00
2.04
1.00
1.00
2.95
3.00
f1 (ppm)



S4

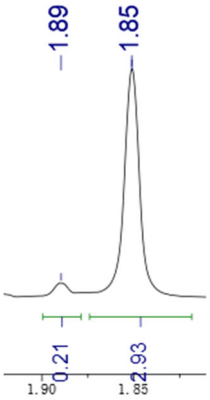
^{13}CNMR spectrum
101 MHz $CDCl_3$

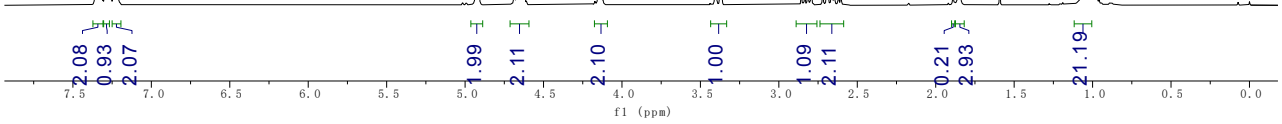


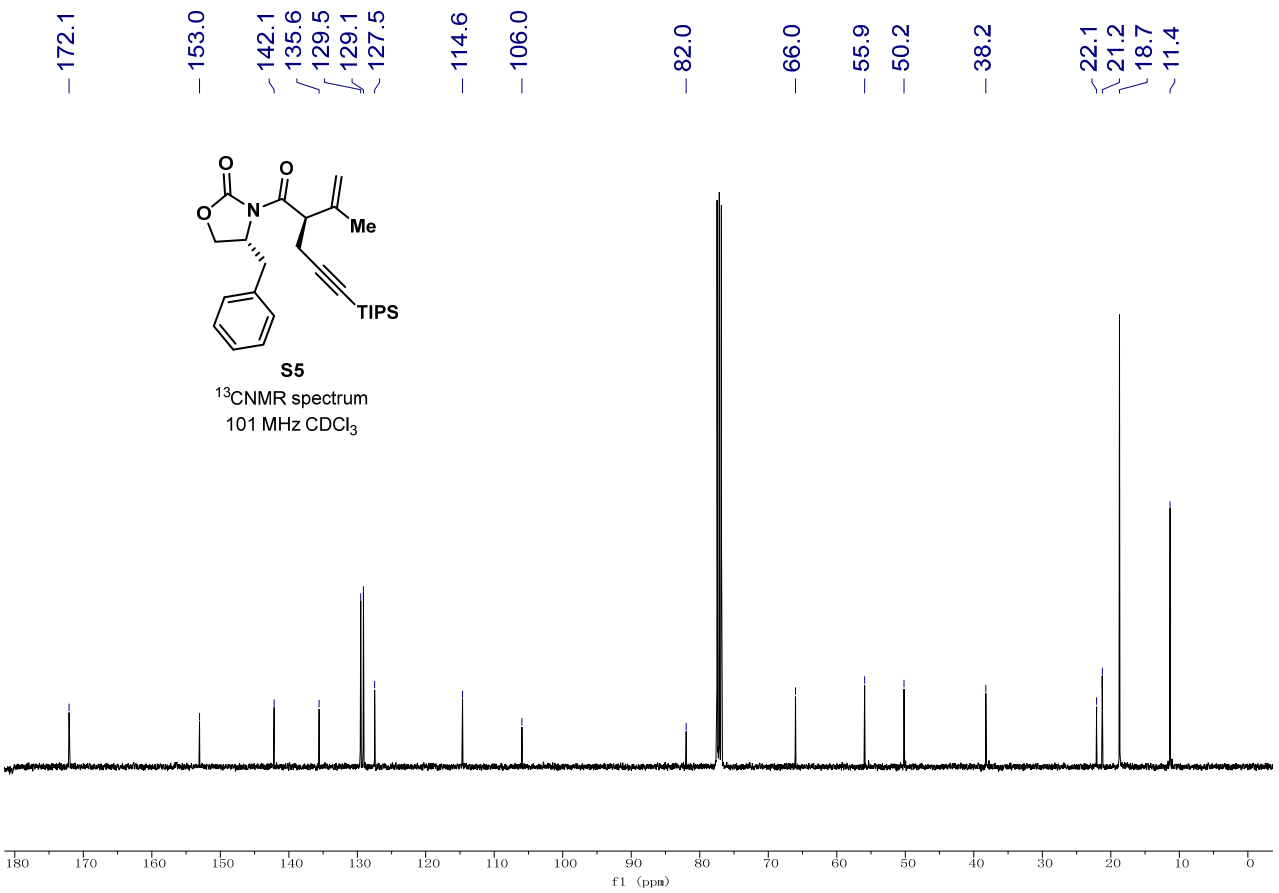


S5

^{1}HNMR spectrum
400 MHz $CDCl_3$



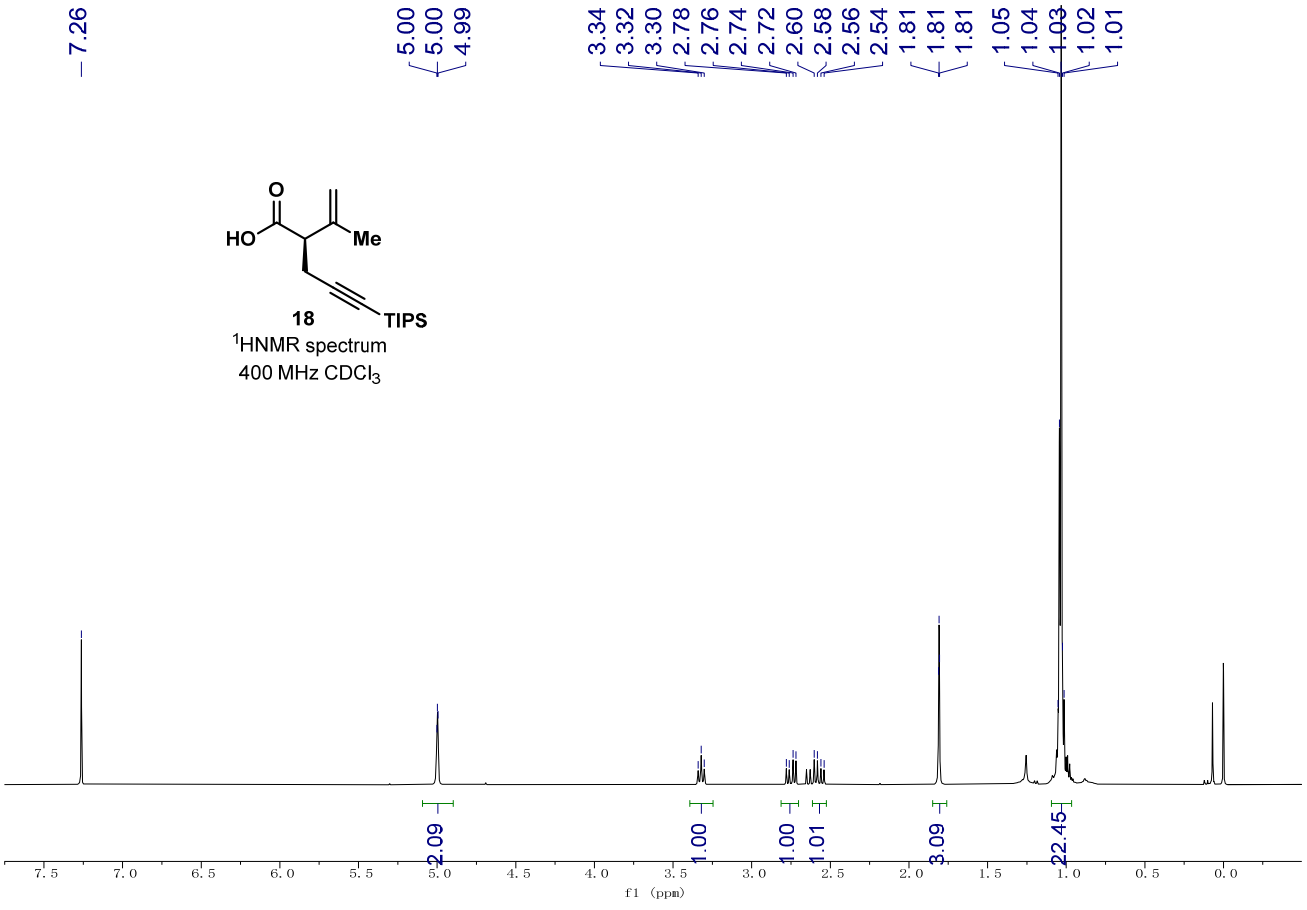




S5

^{13}CNMR spectrum

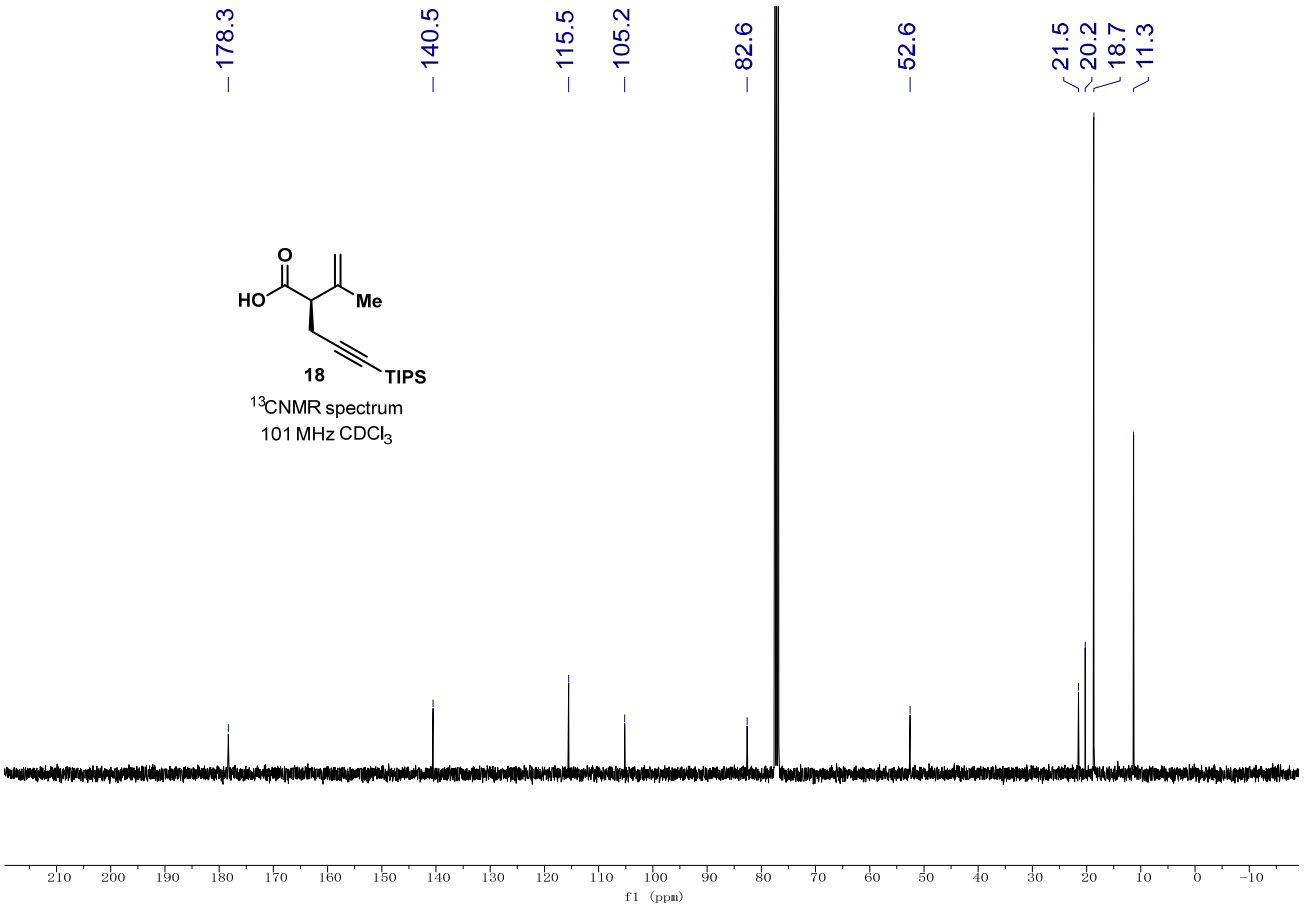
101 MHz $CDCl_3$



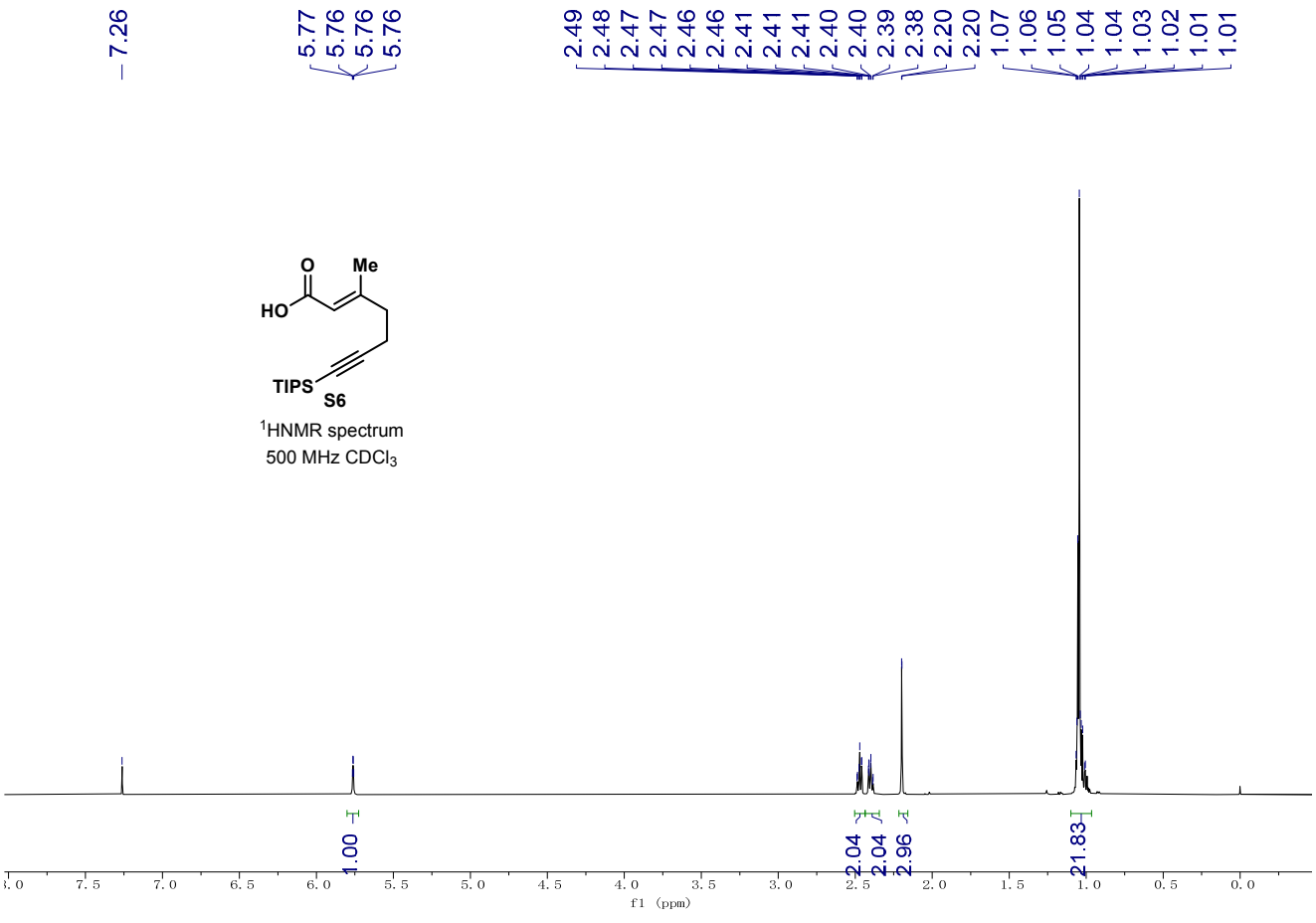
18

^{1}HNMR spectrum

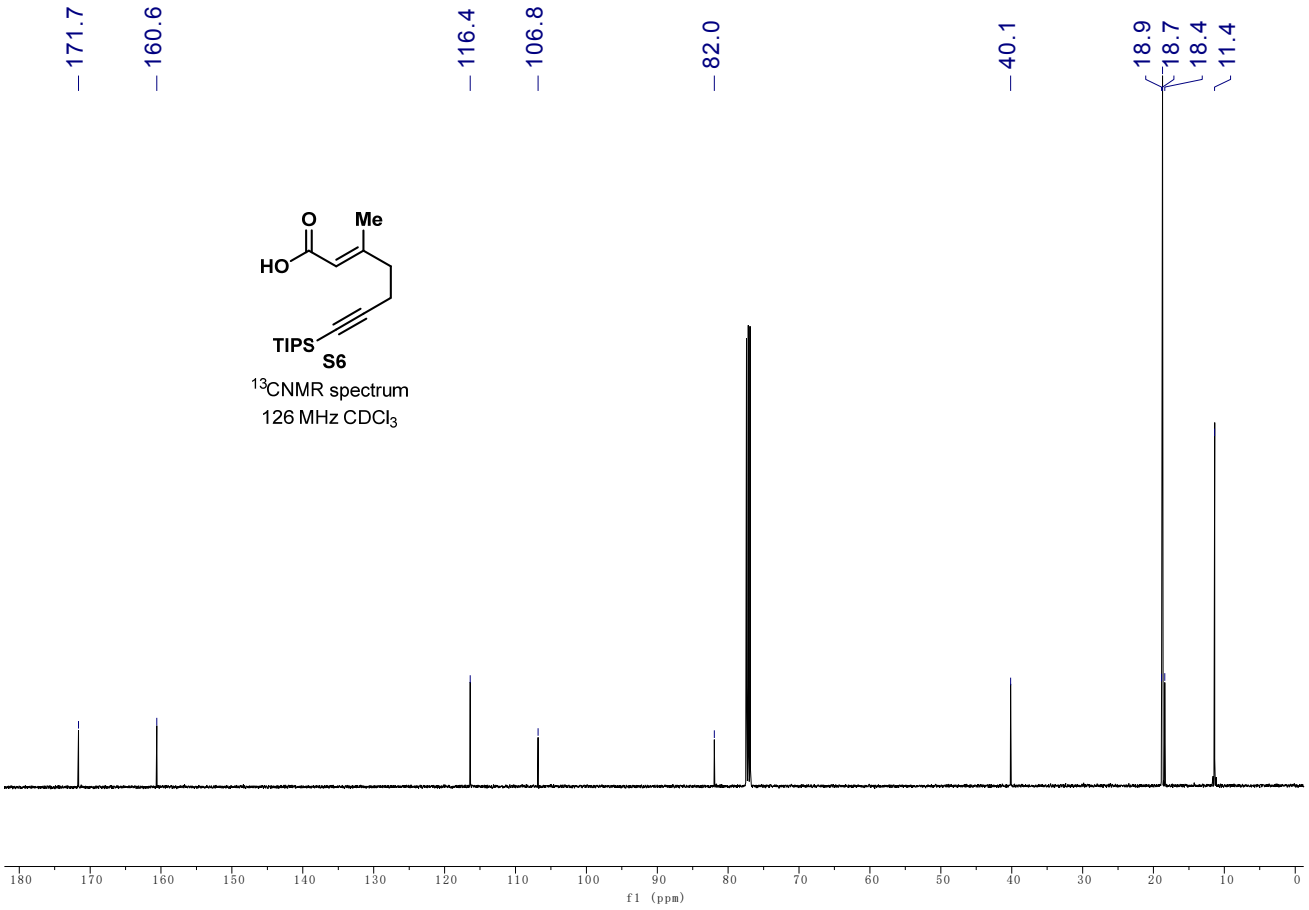
400 MHz $CDCl_3$

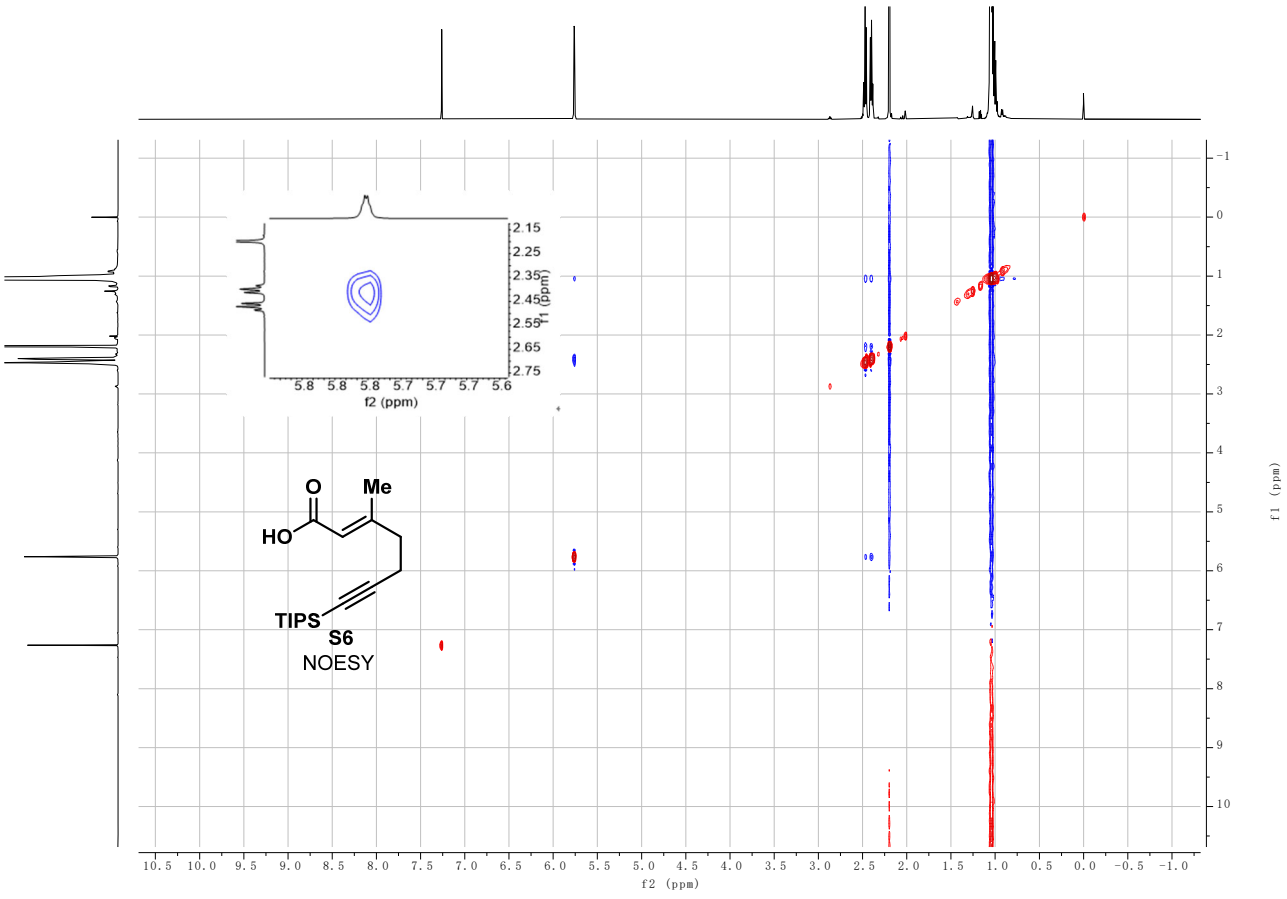


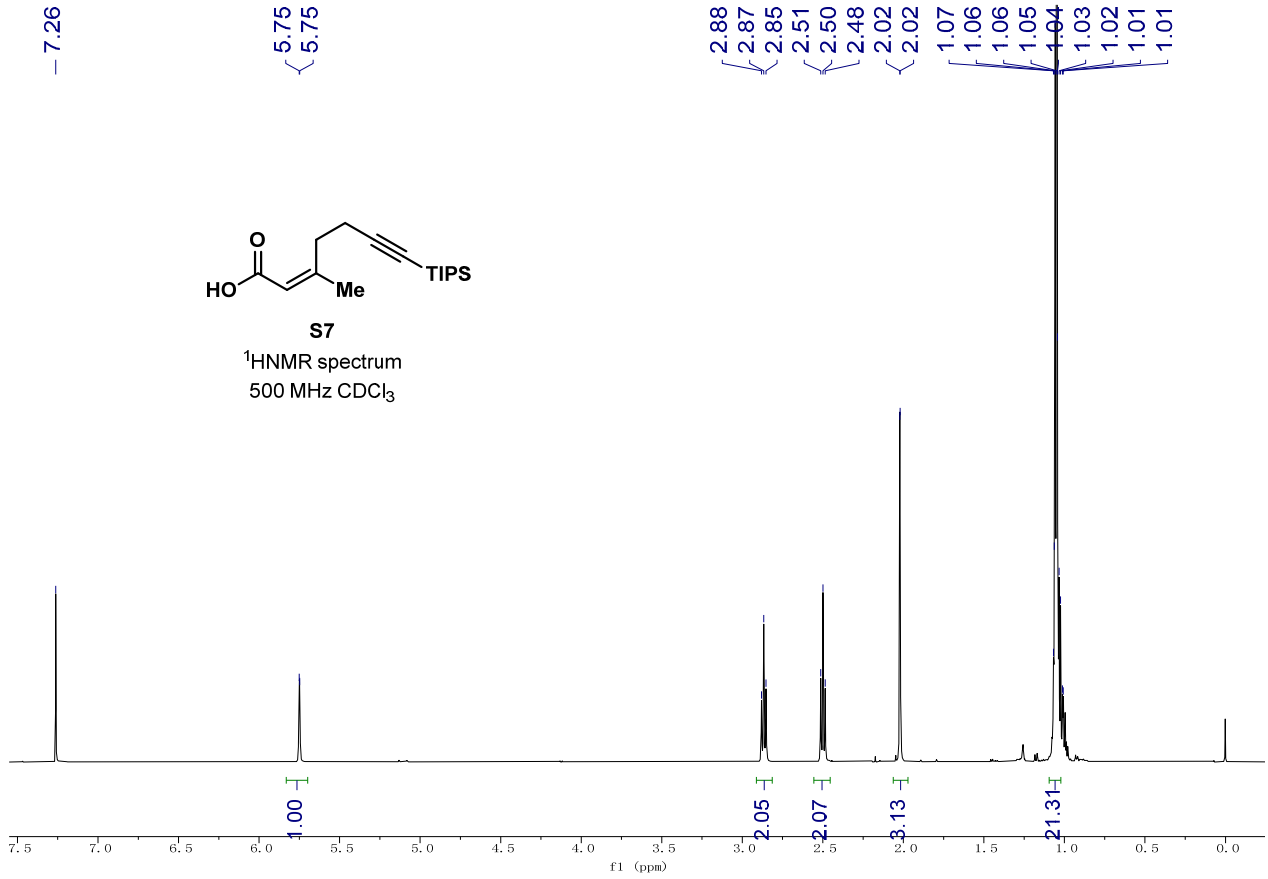
^{13}CNMR spectrum
101 MHz $CDCl_3$



^{1}HNMR spectrum
500 MHz $CDCl_3$


171.7
160.6
116.4
106.8
82.0
40.1
18.9
18.7
18.4
11.4
O
Me
HO
TIPS
S6
13CNMR spectrum
126 MHz CDCl3
f1 (ppm)

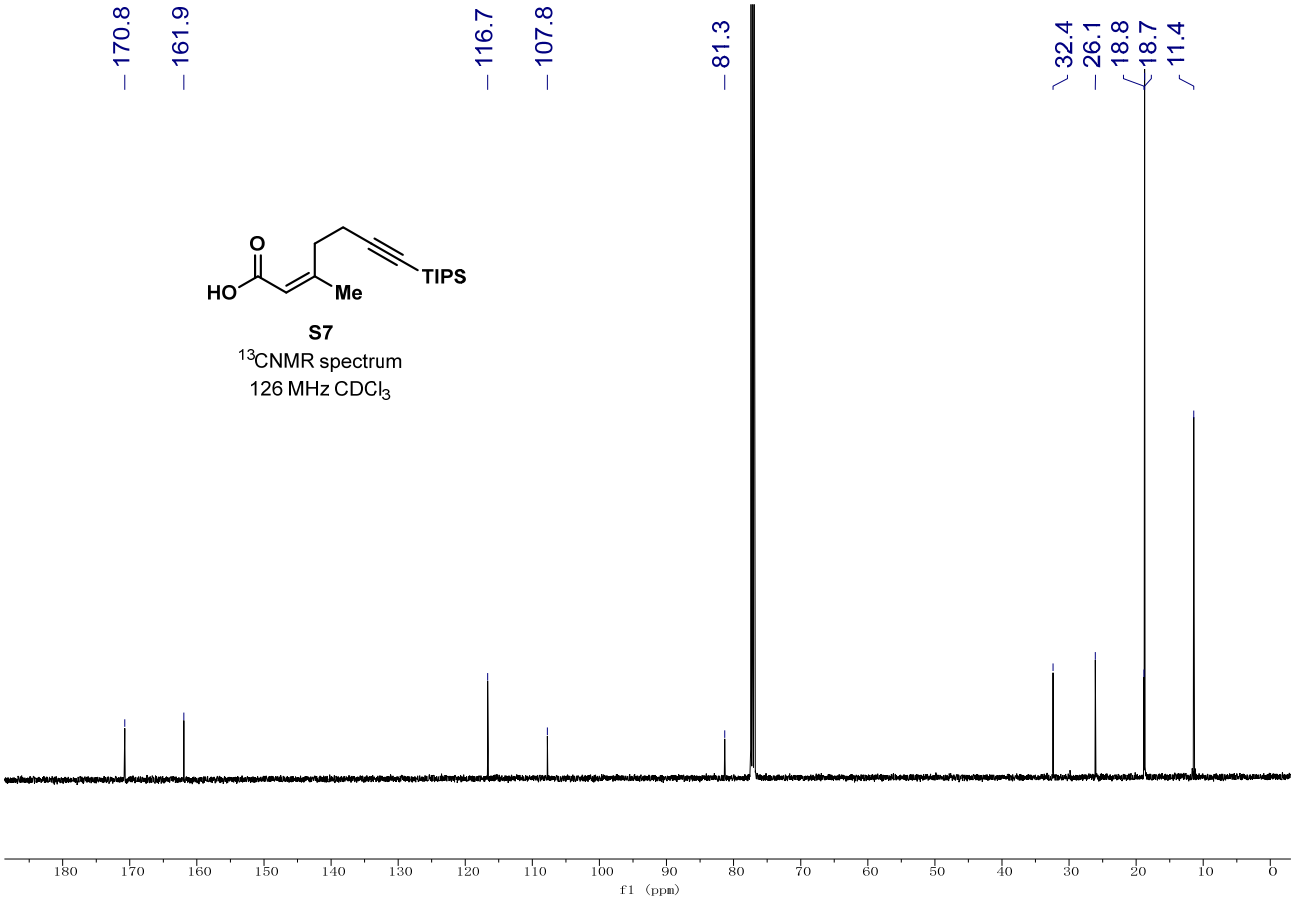

f1 (ppm)
f2 (ppm)
O
Me
HO
TIPS
S6
NOESY



S7

^{1}HNMR spectrum

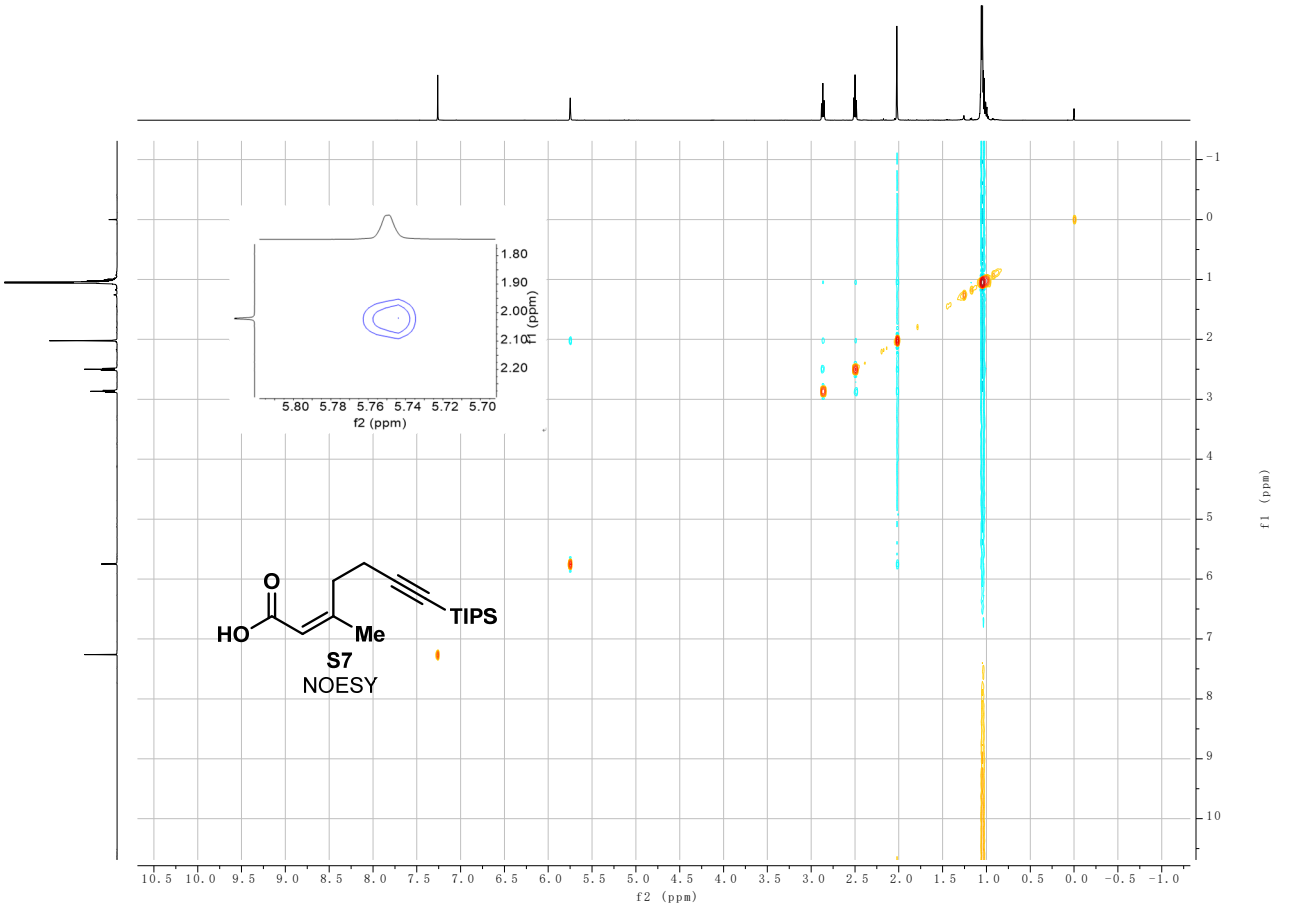
500 MHz $CDCl_3$

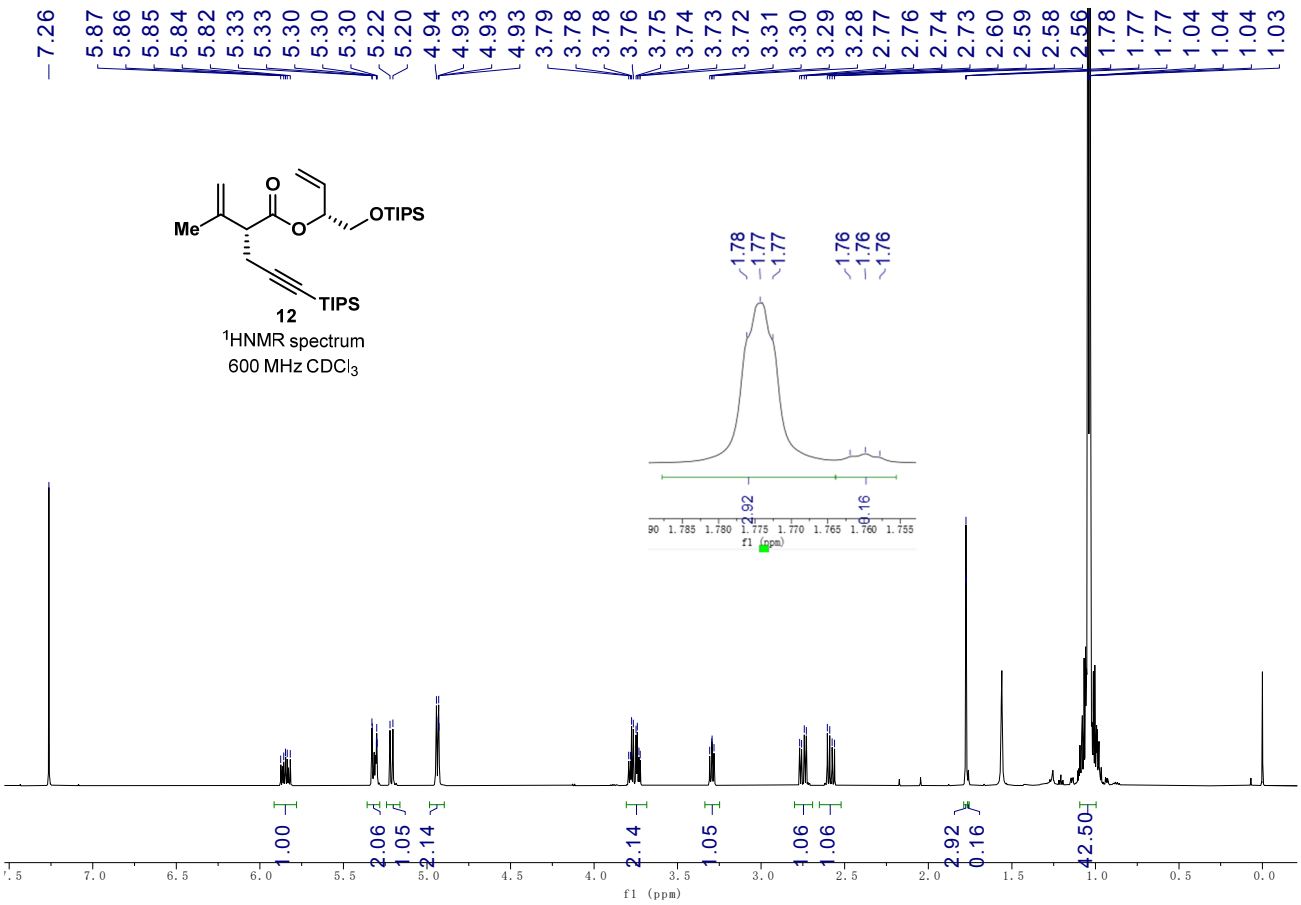


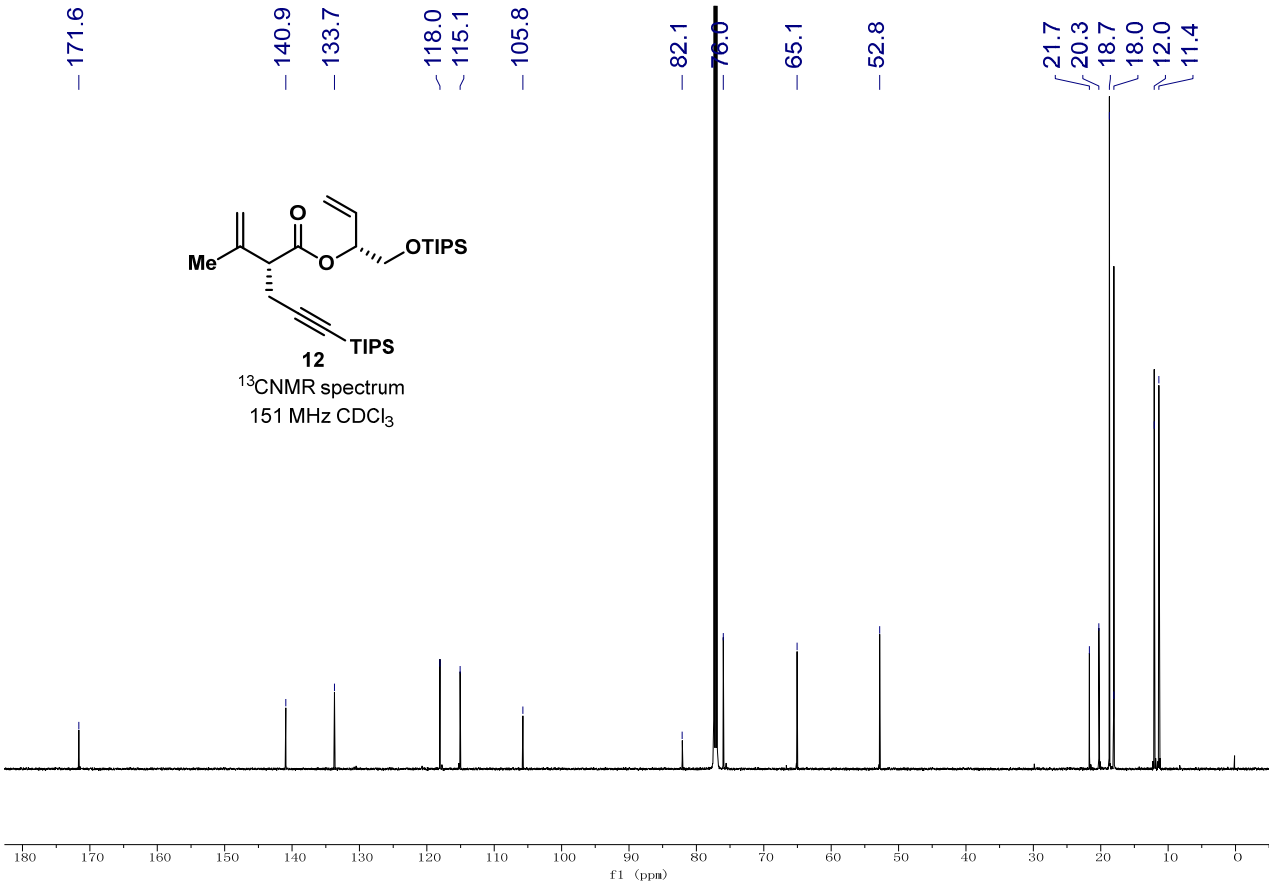
S7

^{13}CNMR spectrum

126 MHz $CDCl_3$


HO
O
Me
TIPS
S7
NOESY
f2 (ppm)
f1 (ppm)

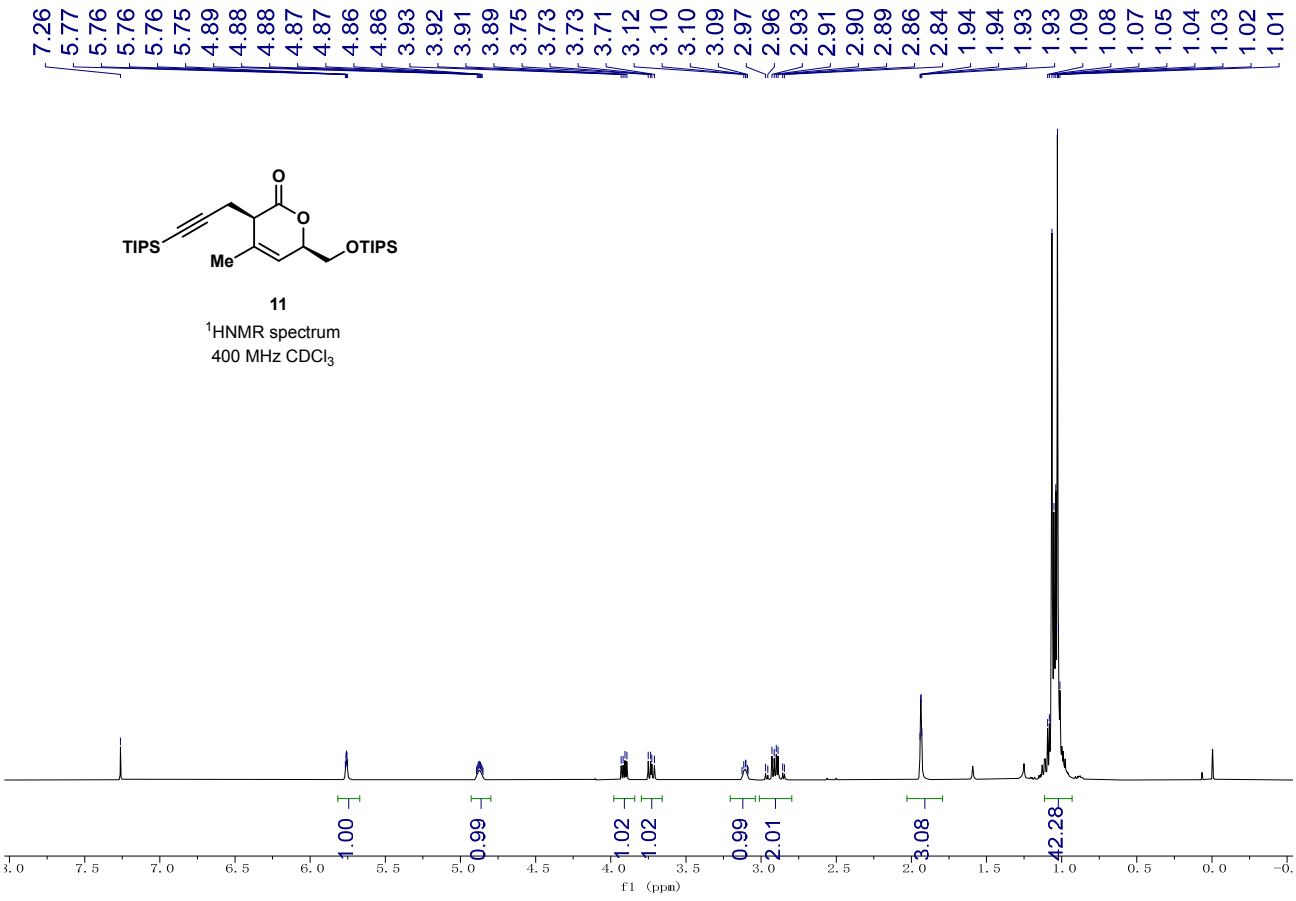

Me
O
O
OTIPS
TIPS
12
1HNMR spectrum
600 MHz CDCl3
f1 (ppm)



12

^{13}CNMR spectrum

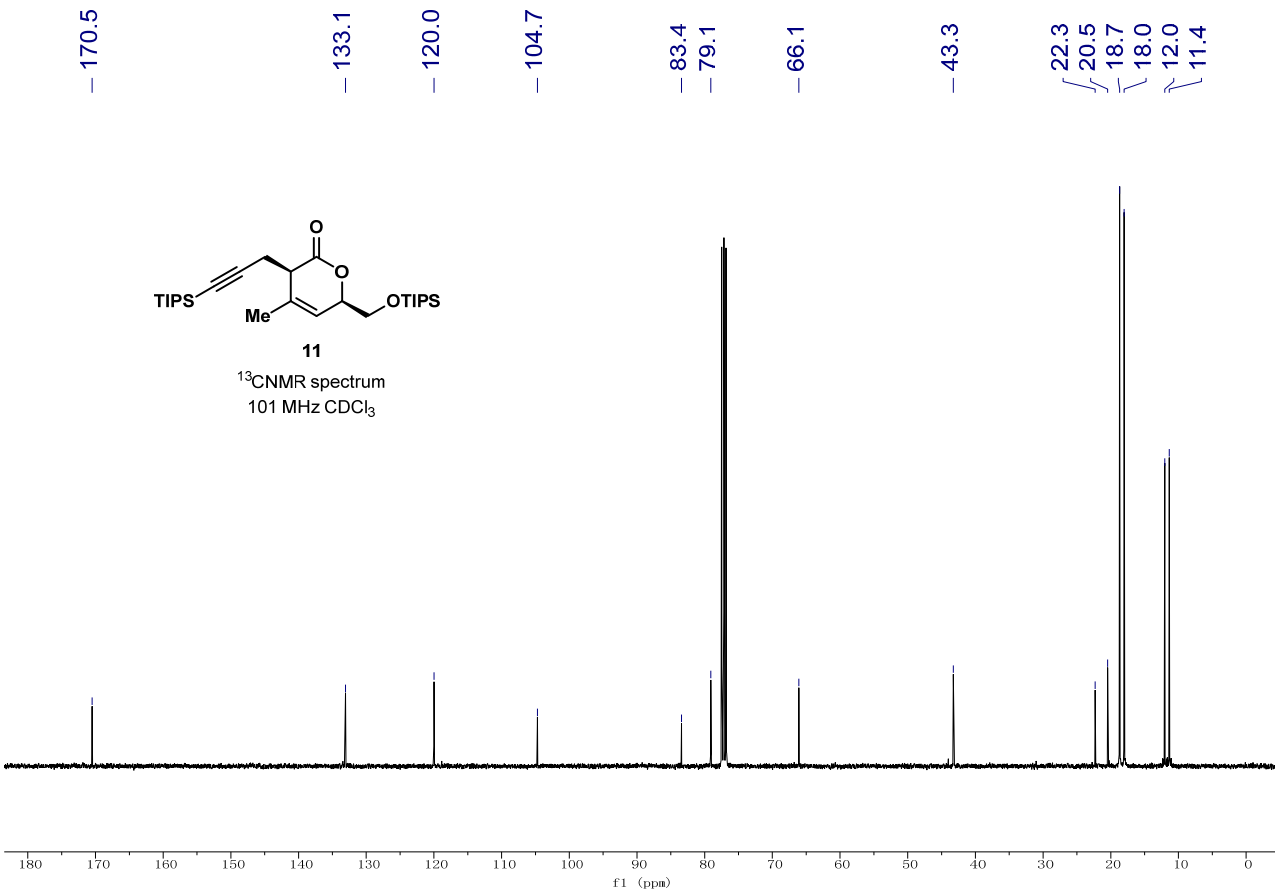
151 MHz $CDCl_3$



11

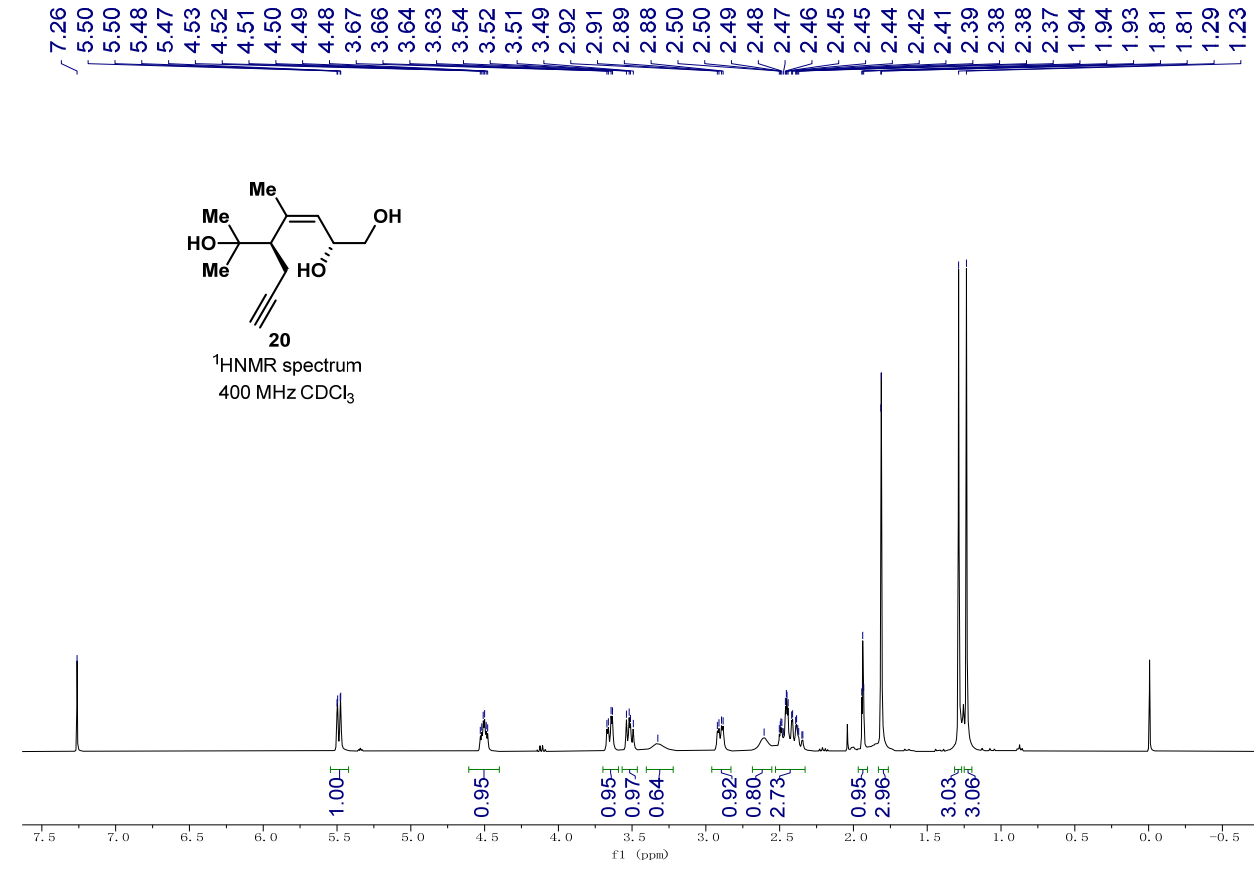
^{1}HNMR spectrum

400 MHz $CDCl_3$



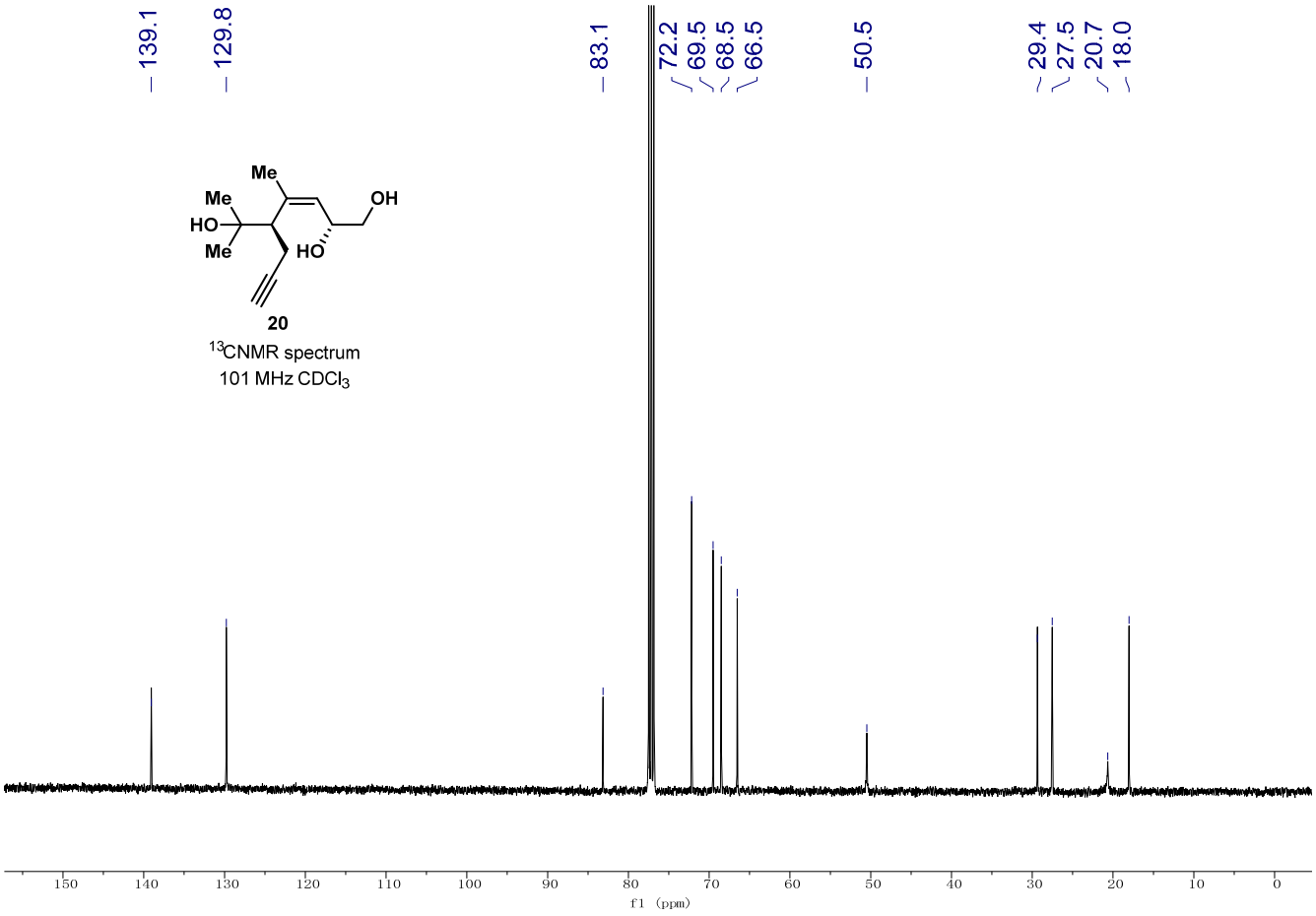
11

^{13}CNMR spectrum
101 MHz $CDCl_3$



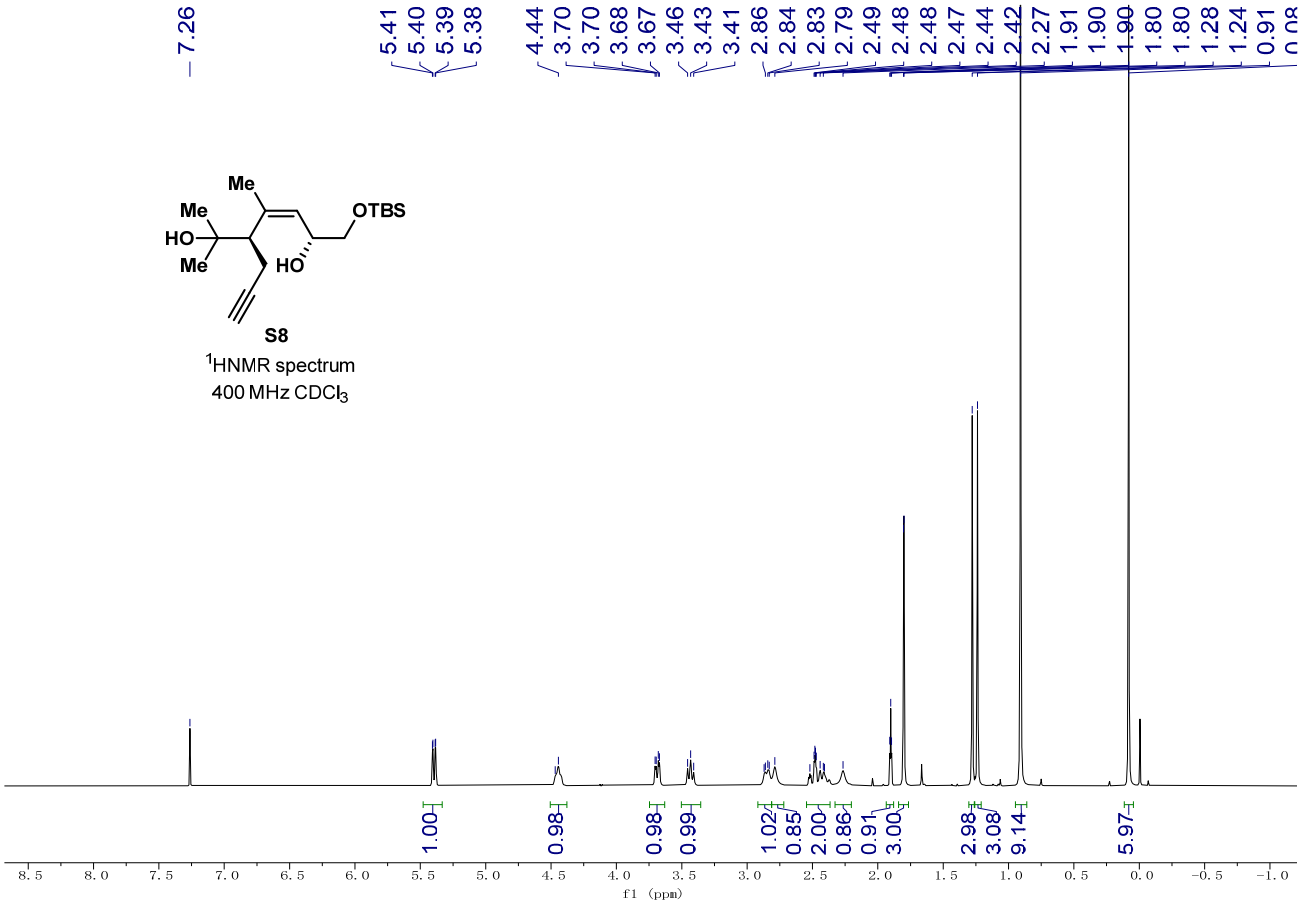
20

^{1}HNMR spectrum
400 MHz $CDCl_3$



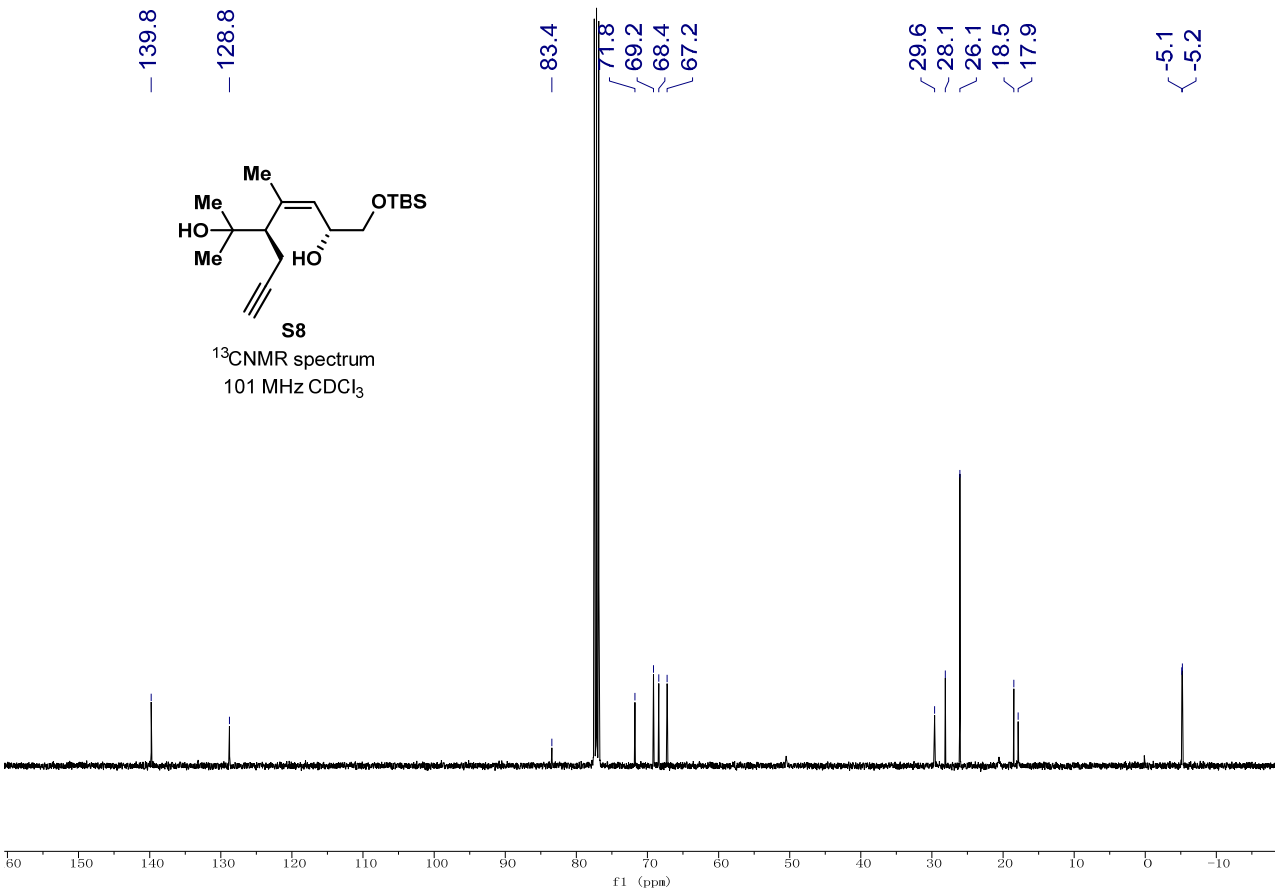
20

^{13}CNMR spectrum
101 MHz $CDCl_3$



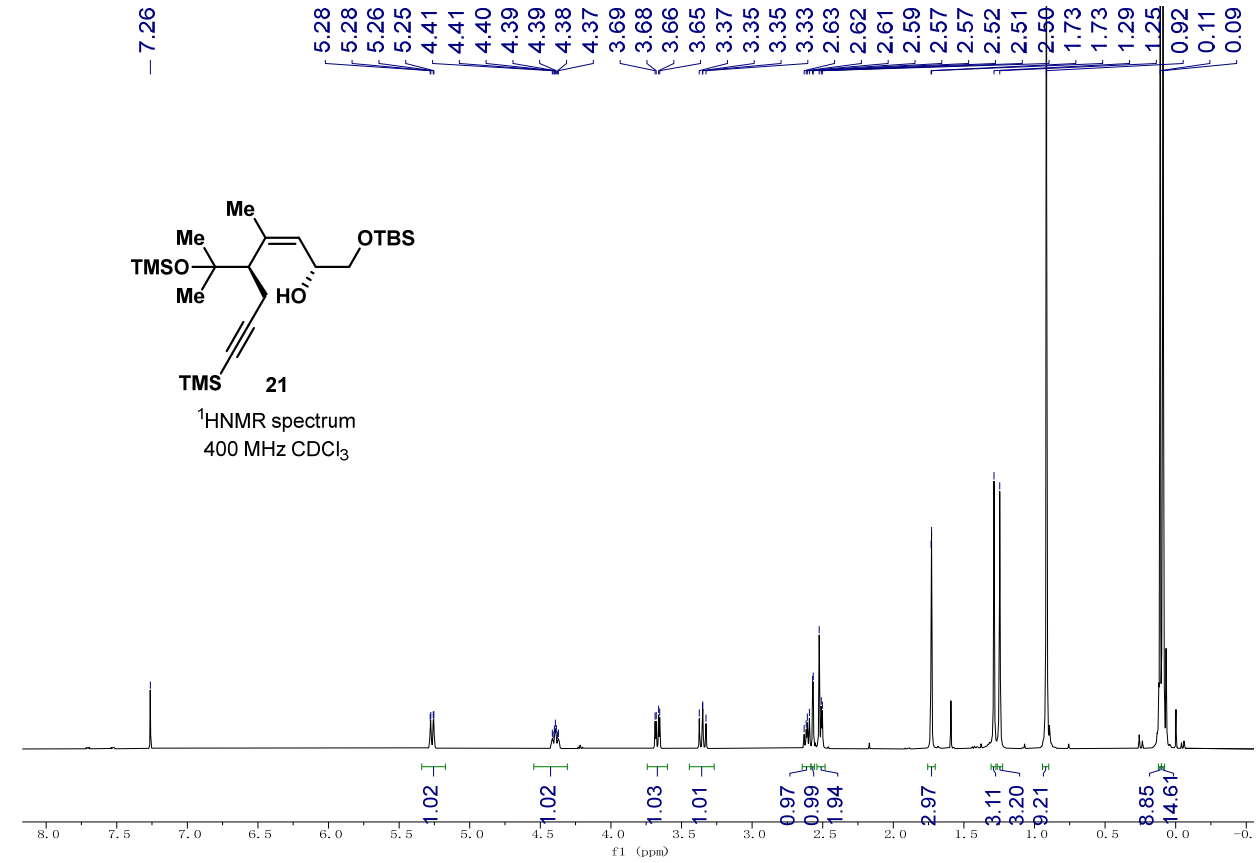
S8

^{1}HNMR spectrum
400 MHz $CDCl_3$

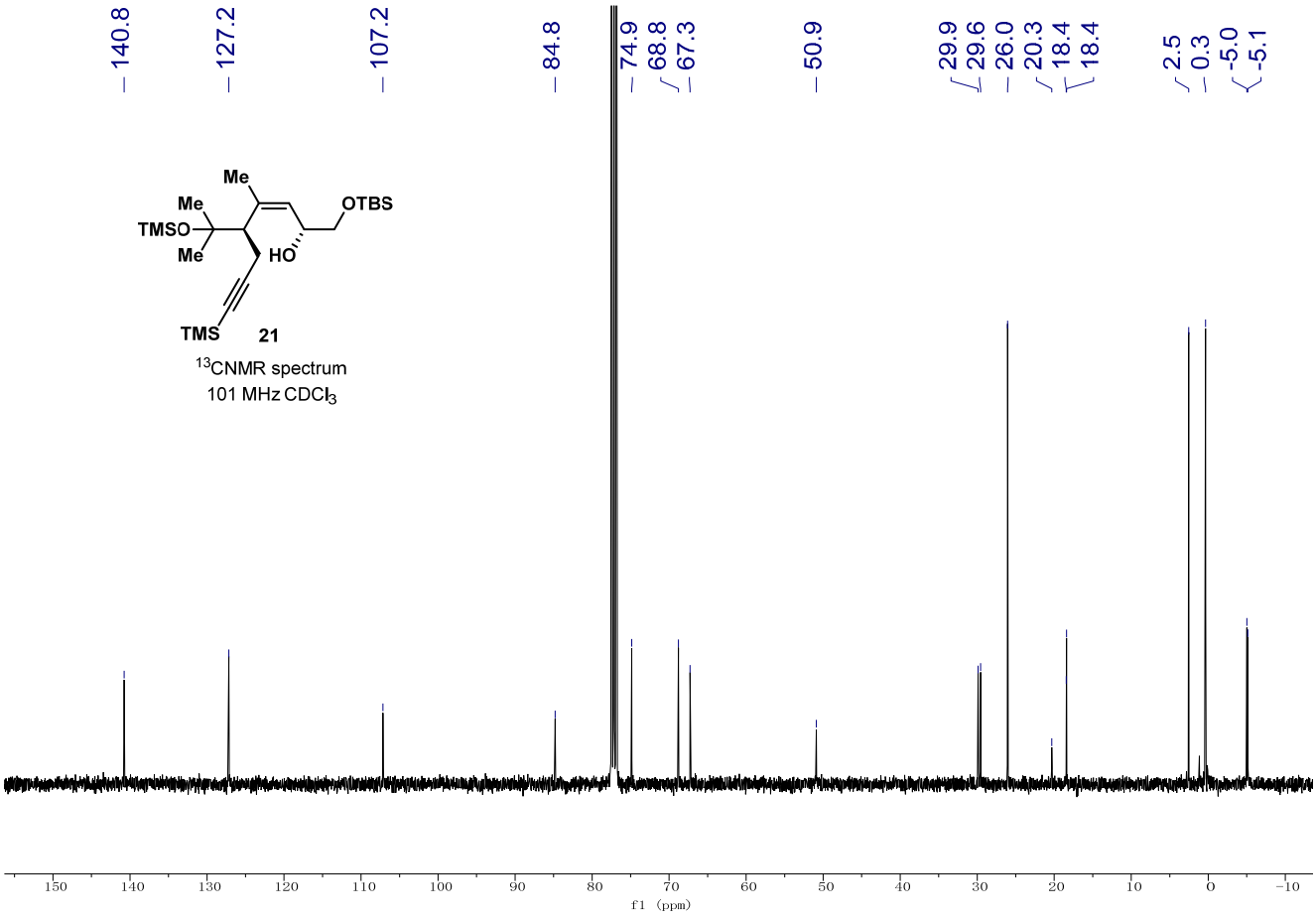


S8

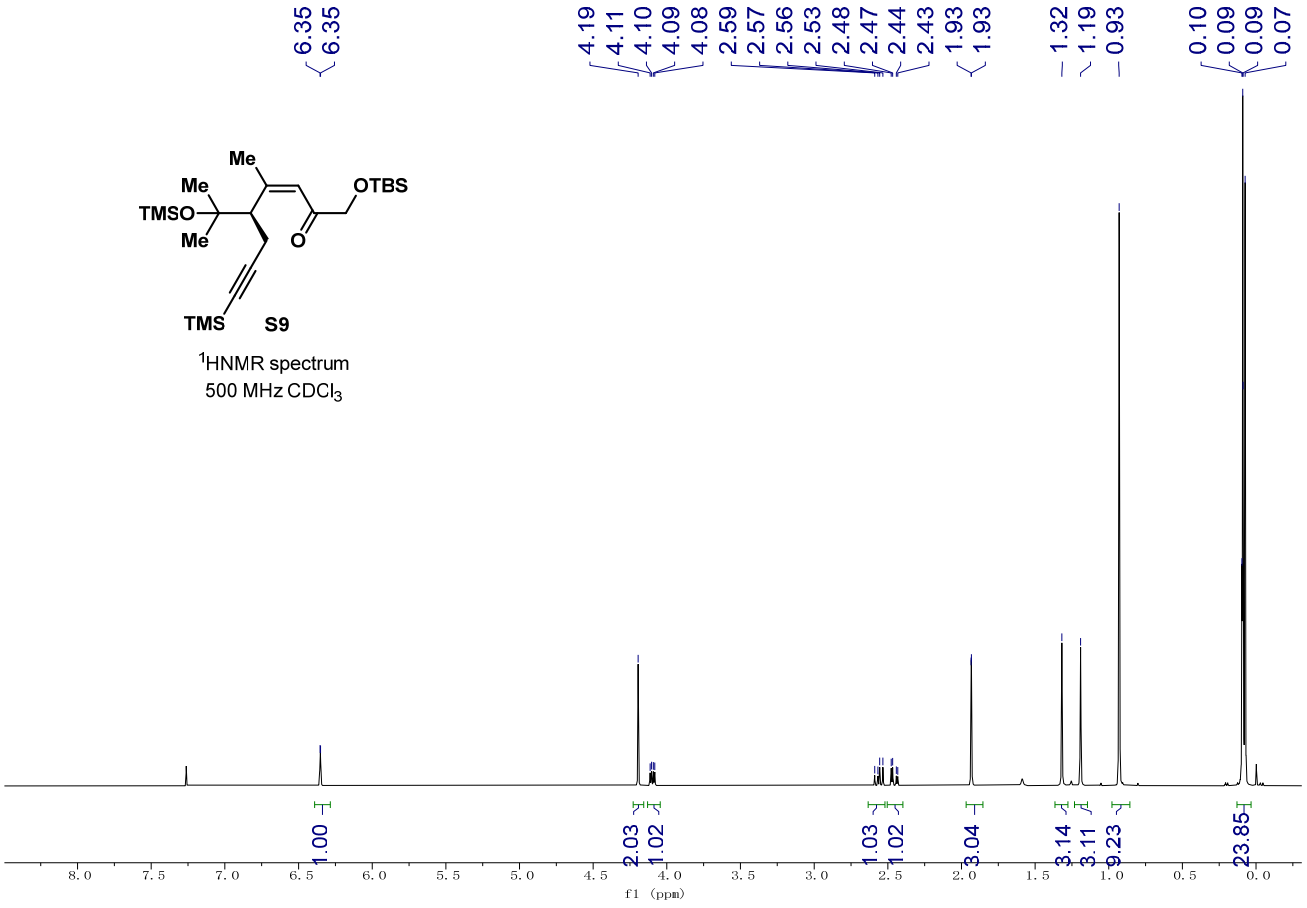
^{13}CNMR spectrum
101 MHz $CDCl_3$



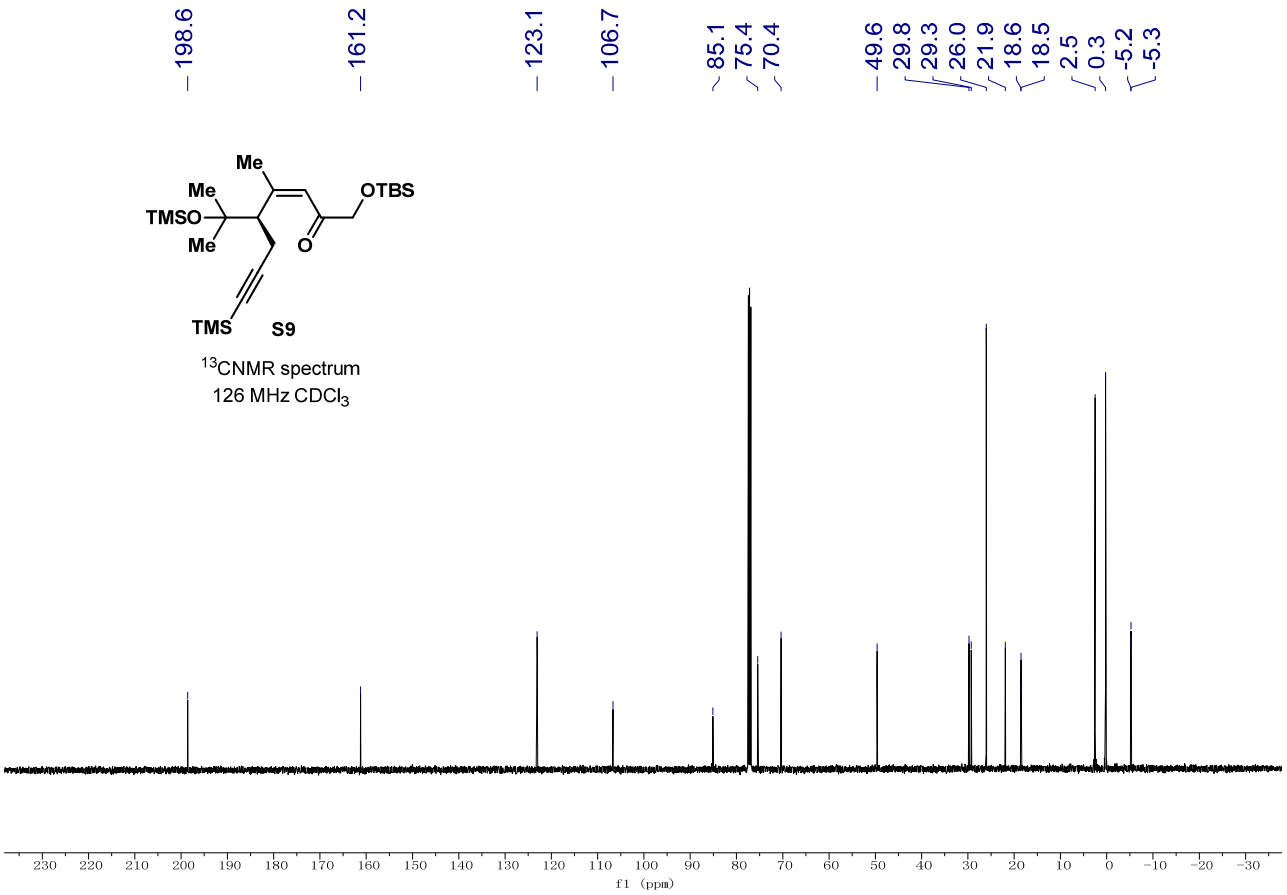
^{1}HNMR spectrum
400 MHz $CDCl_3$



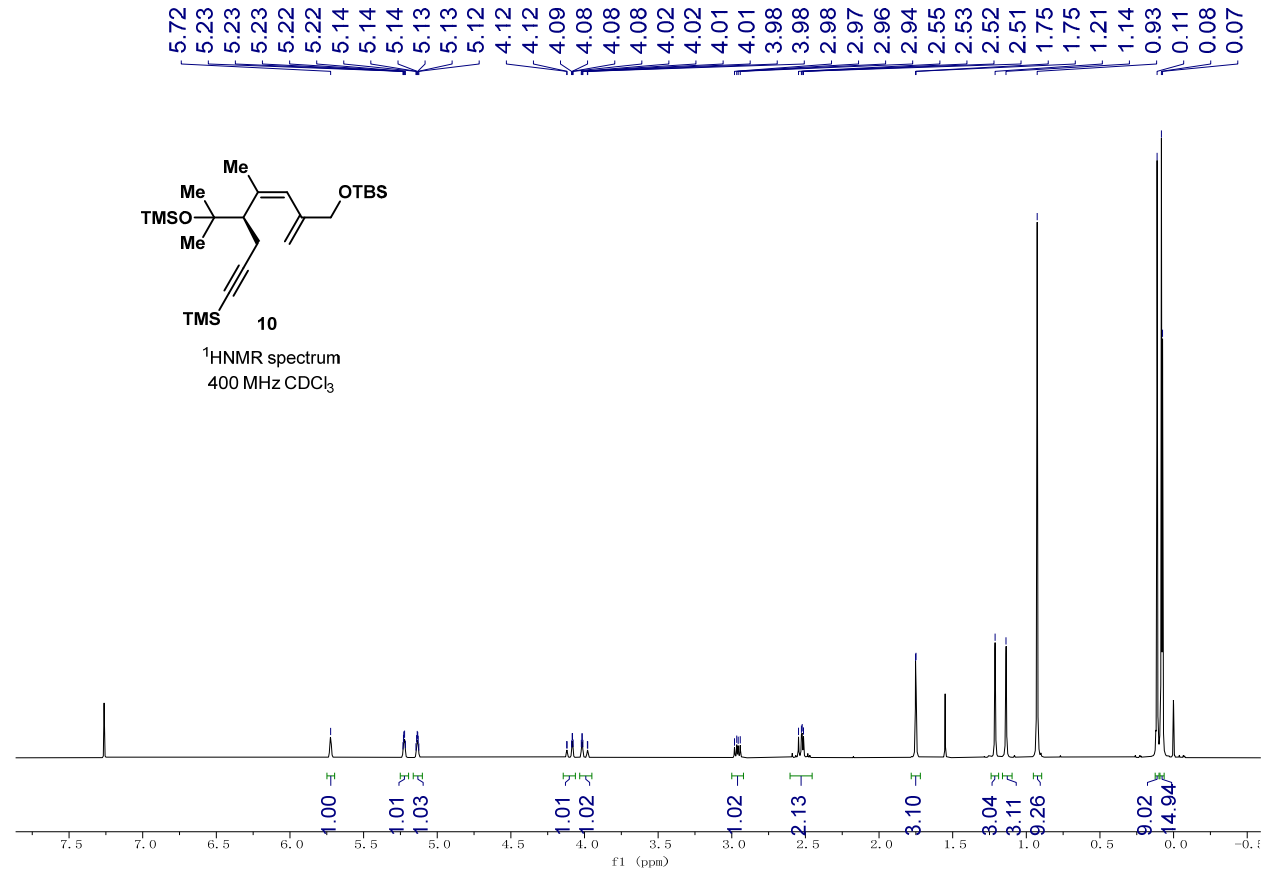
^{13}CNMR spectrum
101 MHz $CDCl_3$



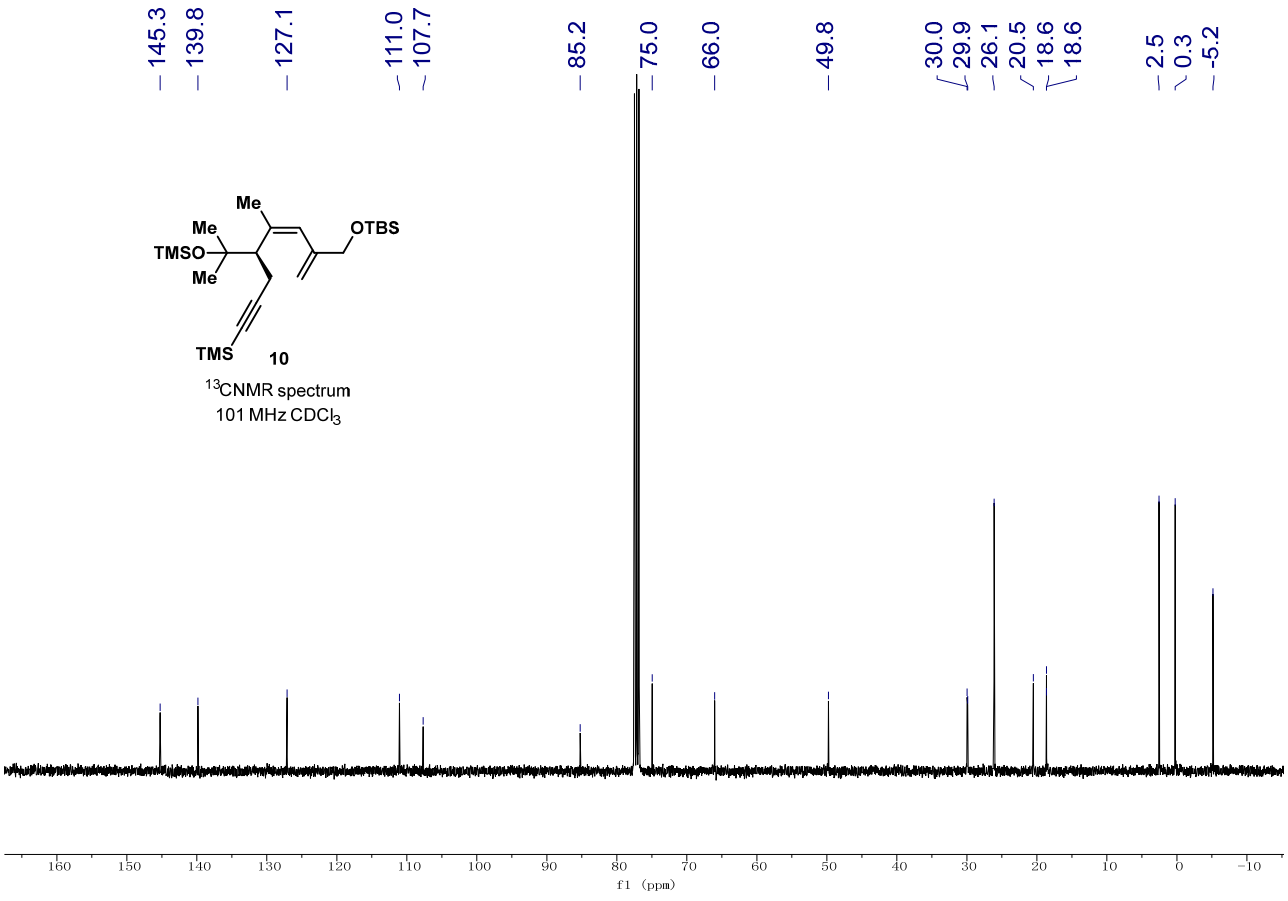
^{1}HNMR spectrum
500 MHz $CDCl_3$



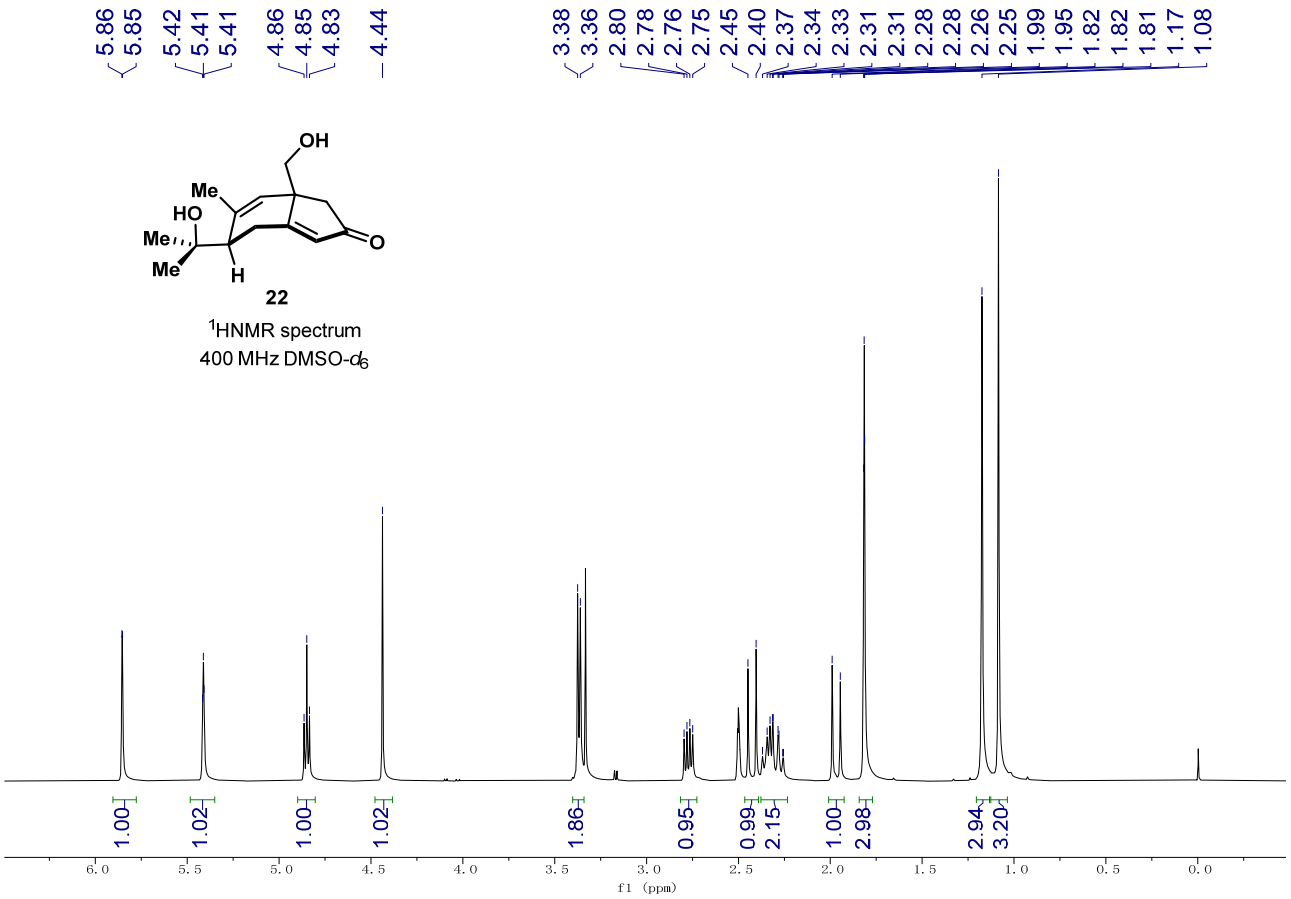
^{13}CNMR spectrum
126 MHz $CDCl_3$



^{1}HNMR spectrum
400 MHz $CDCl_3$

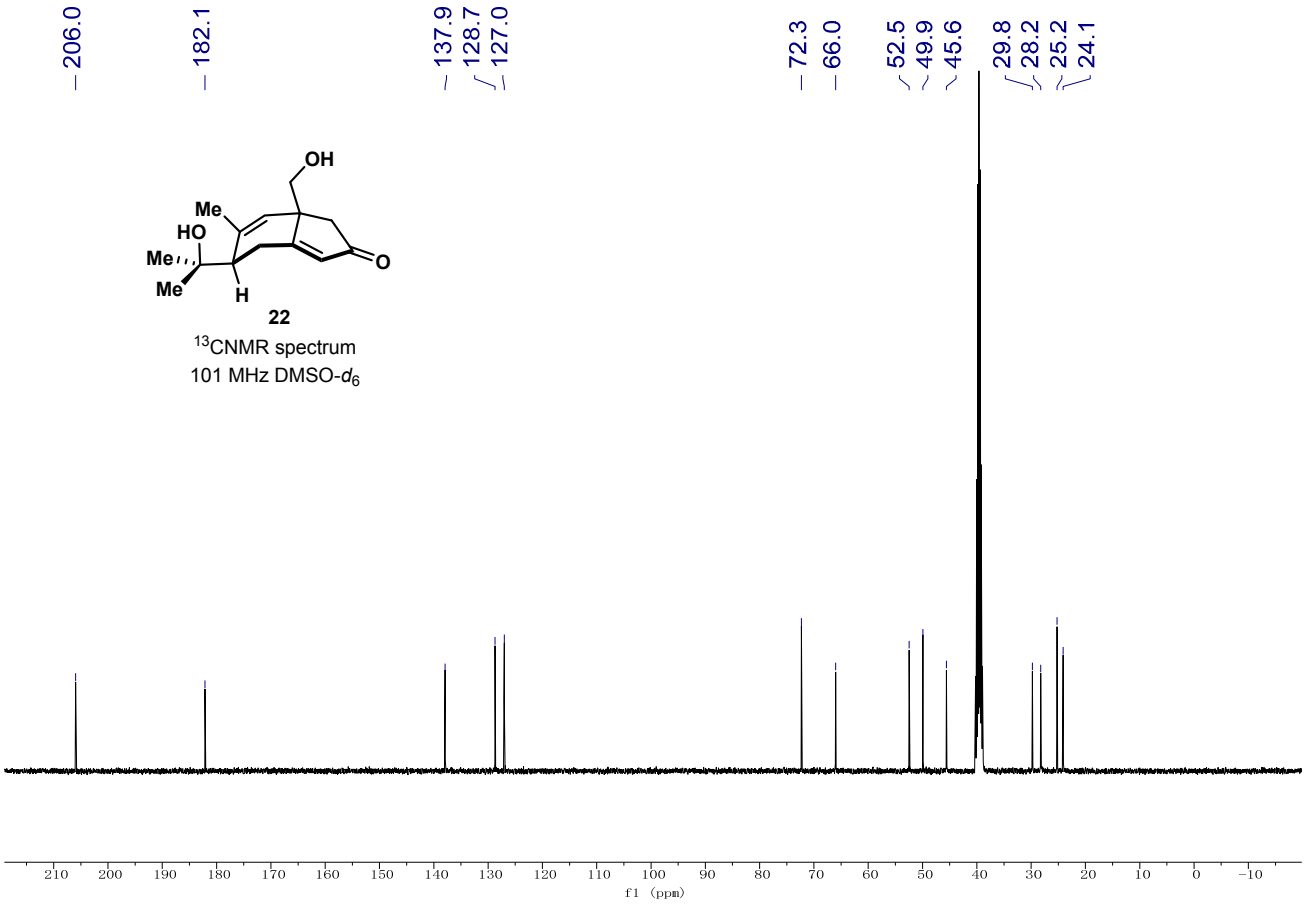


^{13}CNMR spectrum
101 MHz $CDCl_3$



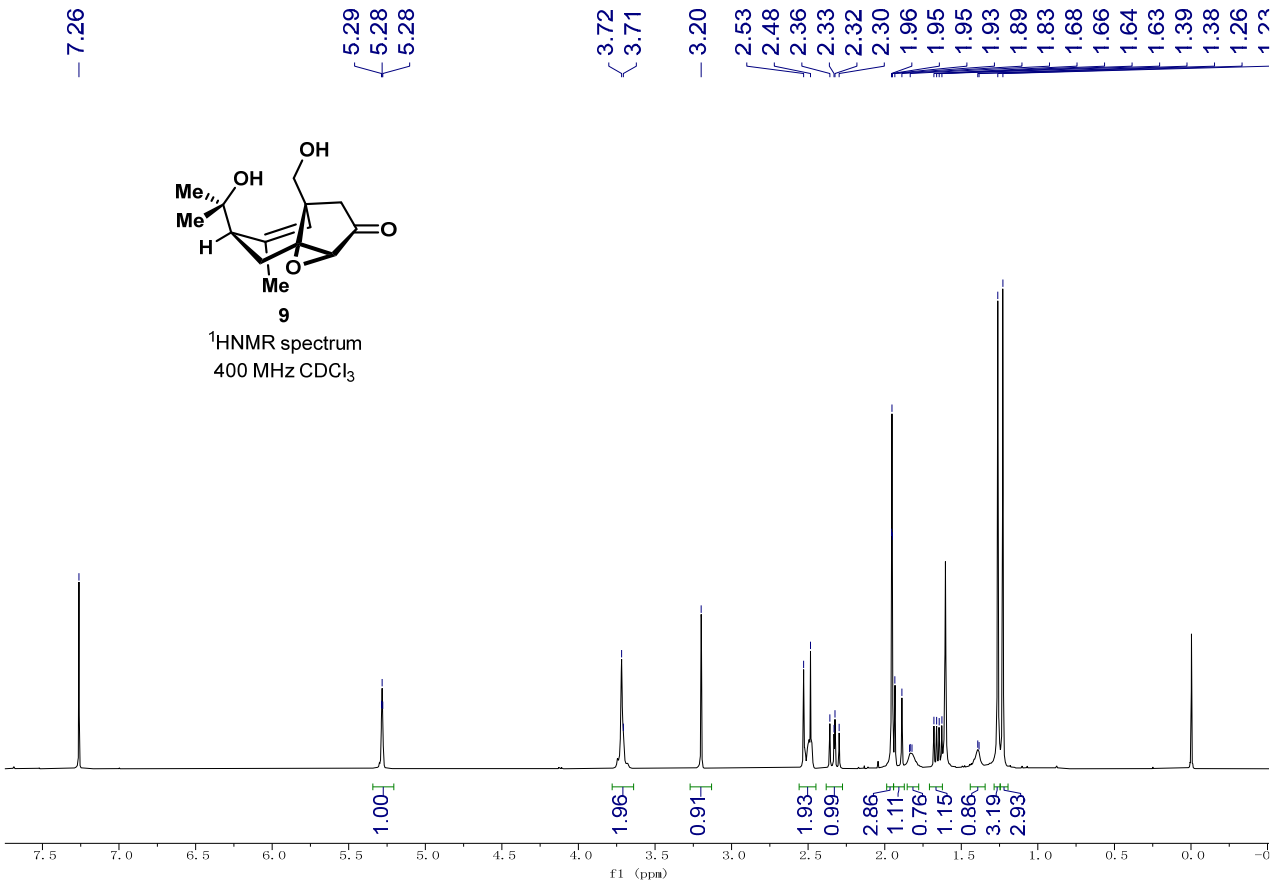
22

^{1}HNMR spectrum
400 MHz DMSO-d_6



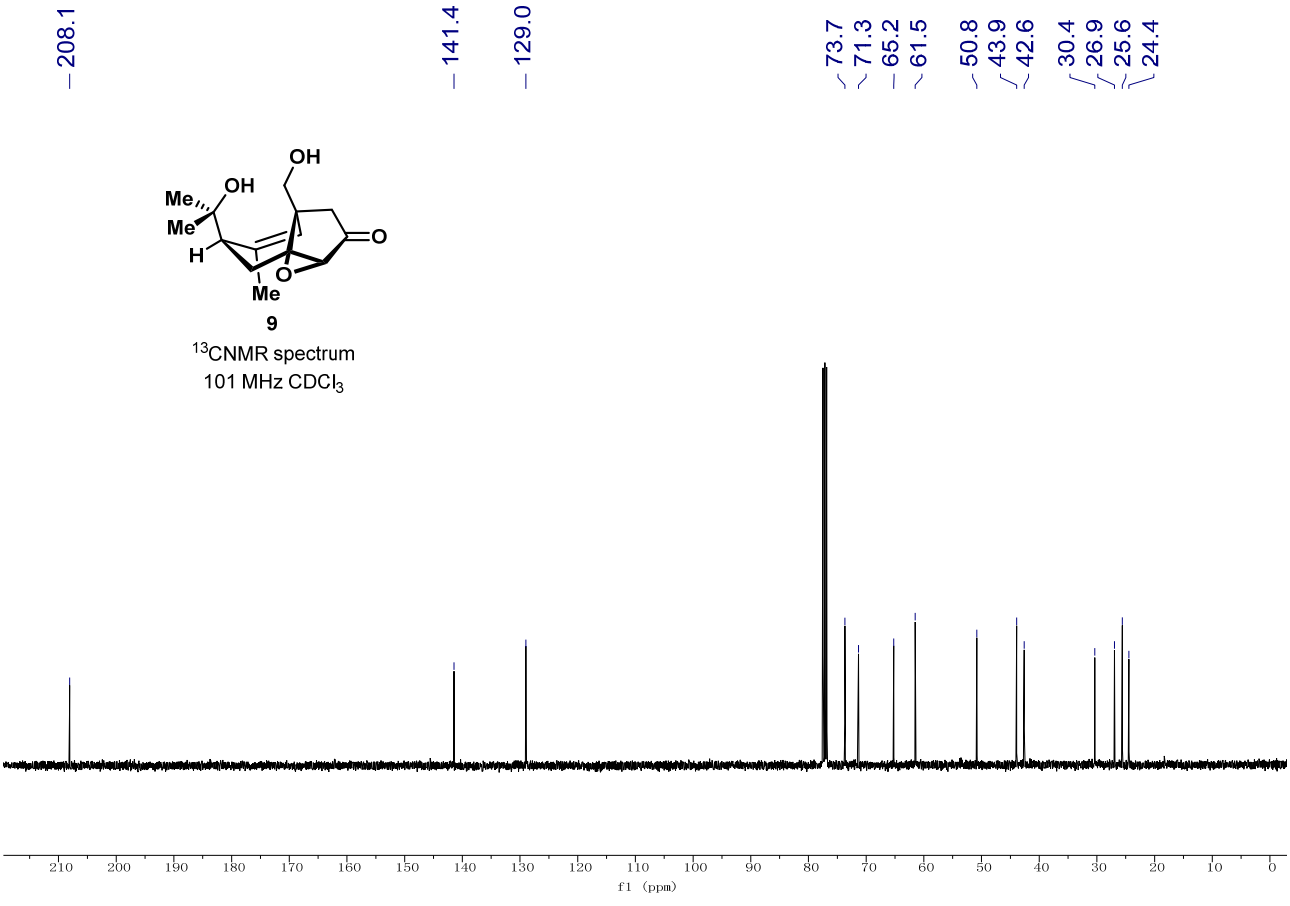
22

^{13}CNMR spectrum
101 MHz DMSO-d_6



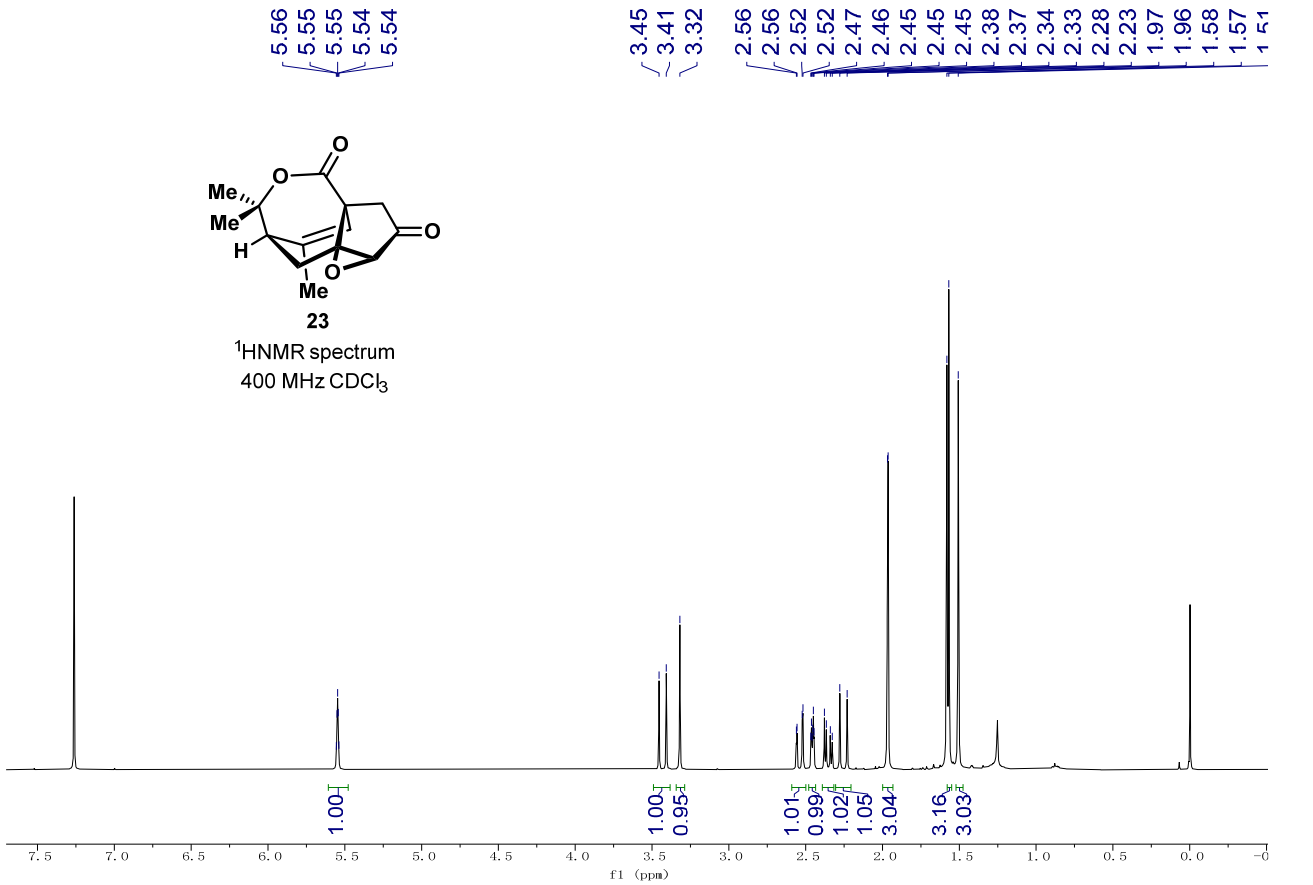
9

^{1}HNMR spectrum
400 MHz $CDCl_3$



9

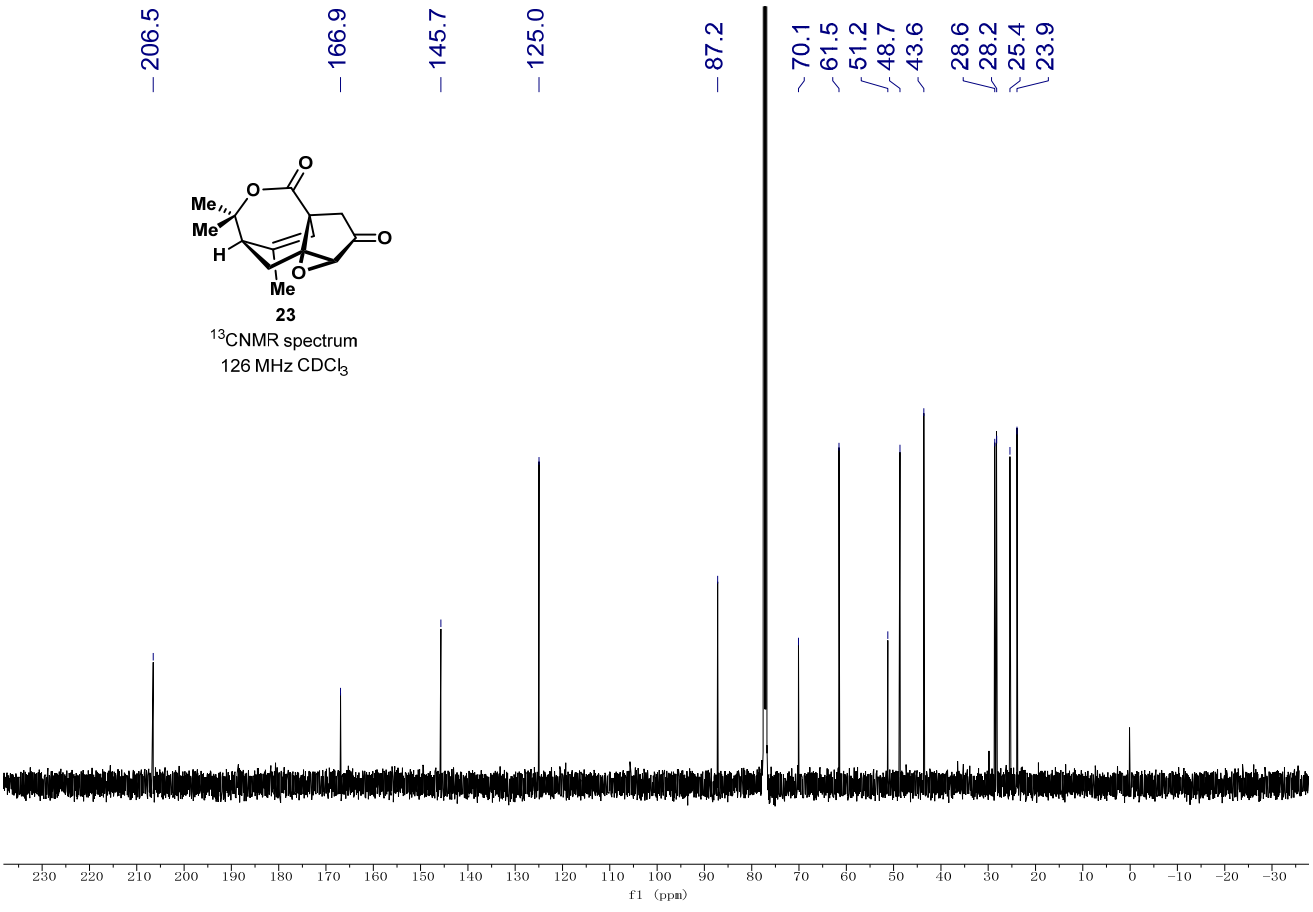
^{13}CNMR spectrum
101 MHz $CDCl_3$



23

^{1}HNMR spectrum

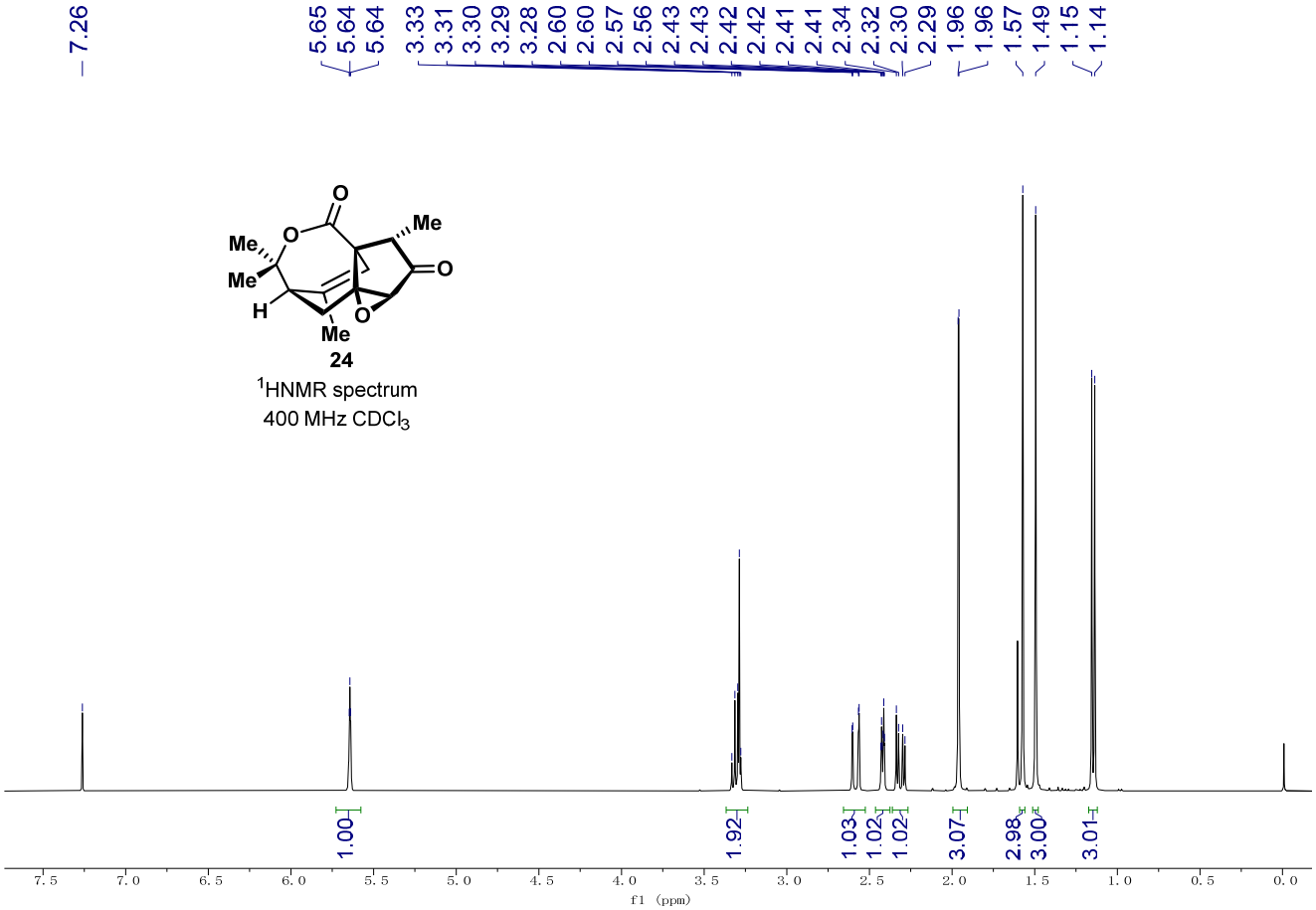
400 MHz $CDCl_3$



23

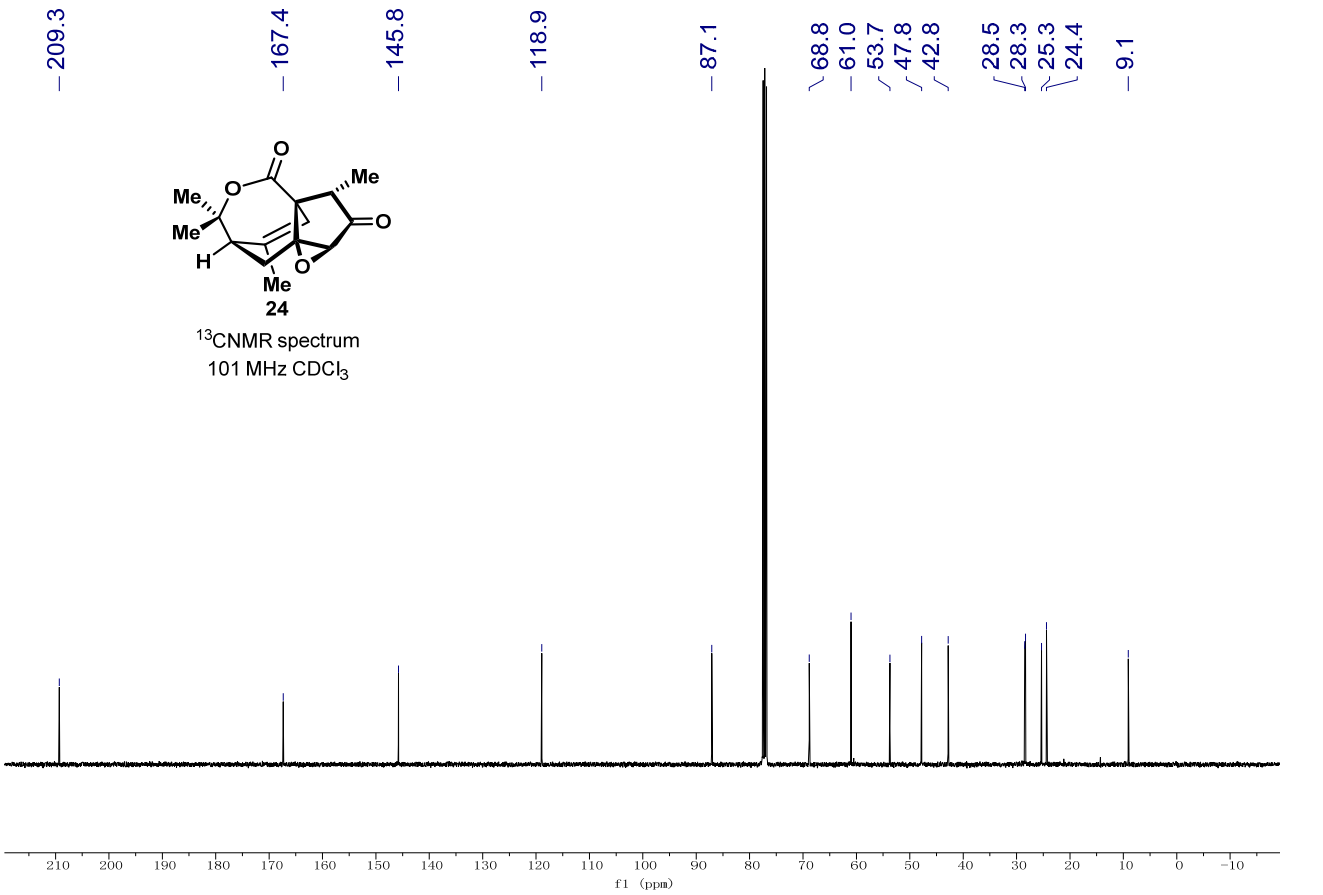
^{13}CNMR spectrum

126 MHz $CDCl_3$



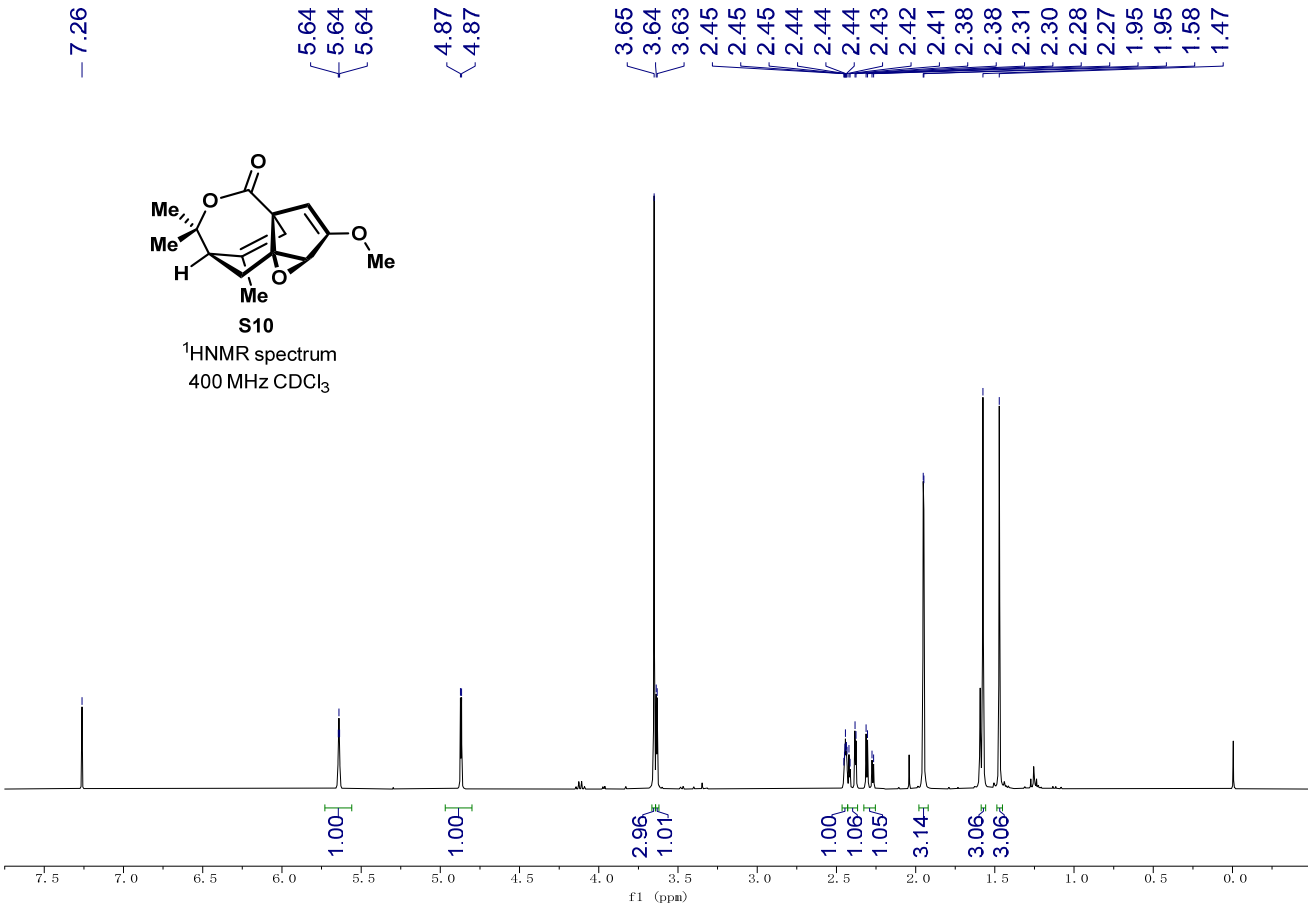
24

^{1}HNMR spectrum
400 MHz $CDCl_3$



24

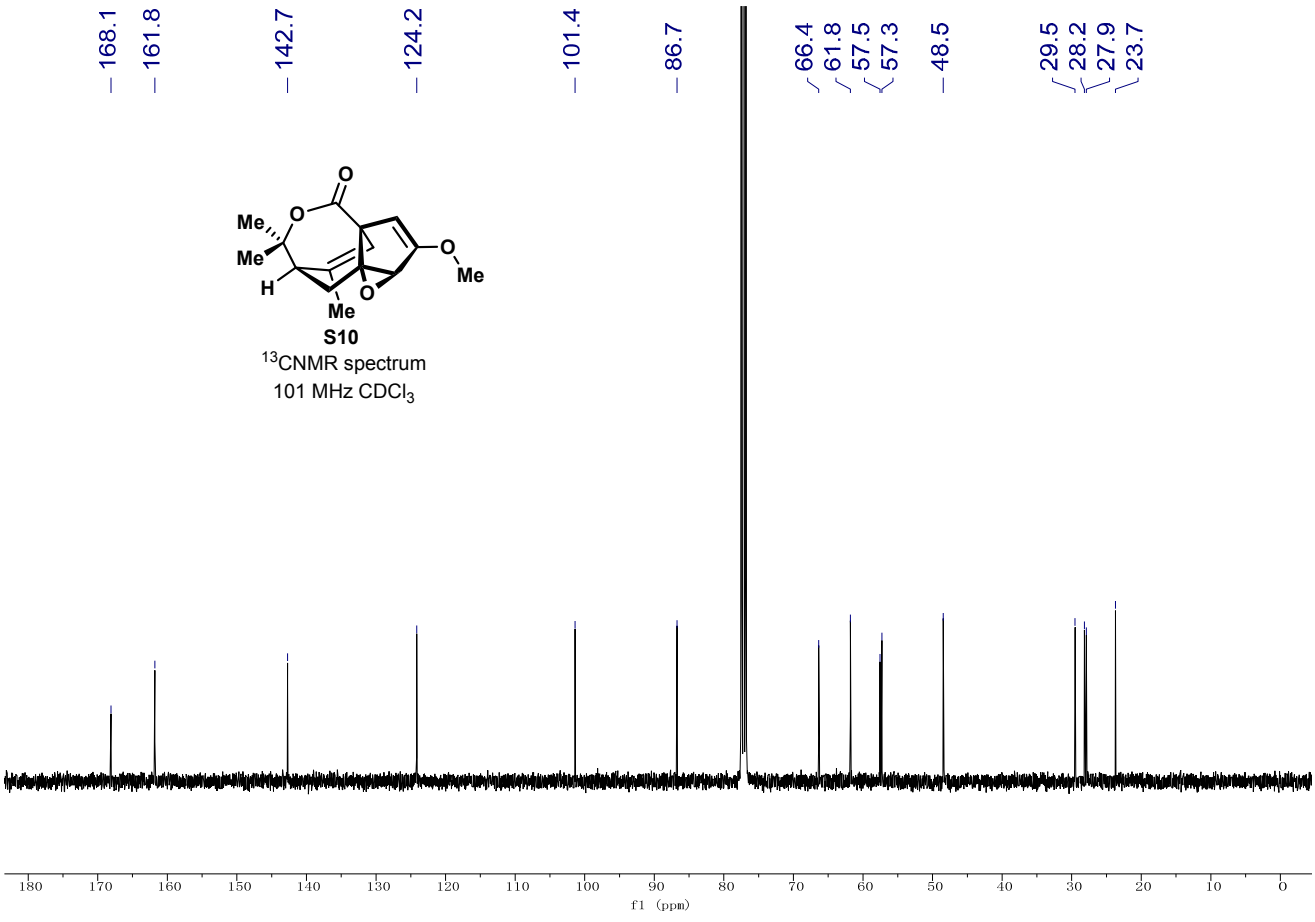
^{13}CNMR spectrum
101 MHz $CDCl_3$



S10

^{1}HNMR spectrum

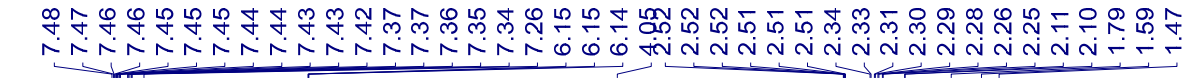
400 MHz $CDCl_3$

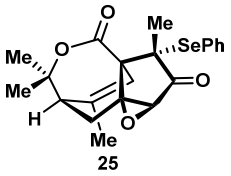


S10

^{13}CNMR spectrum

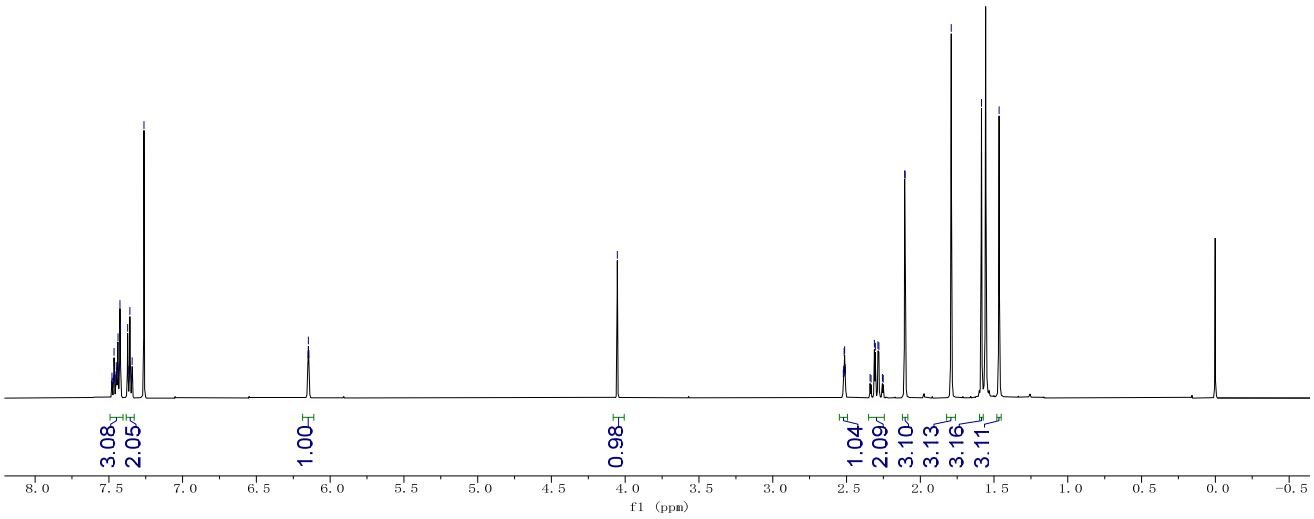
101 MHz $CDCl_3$

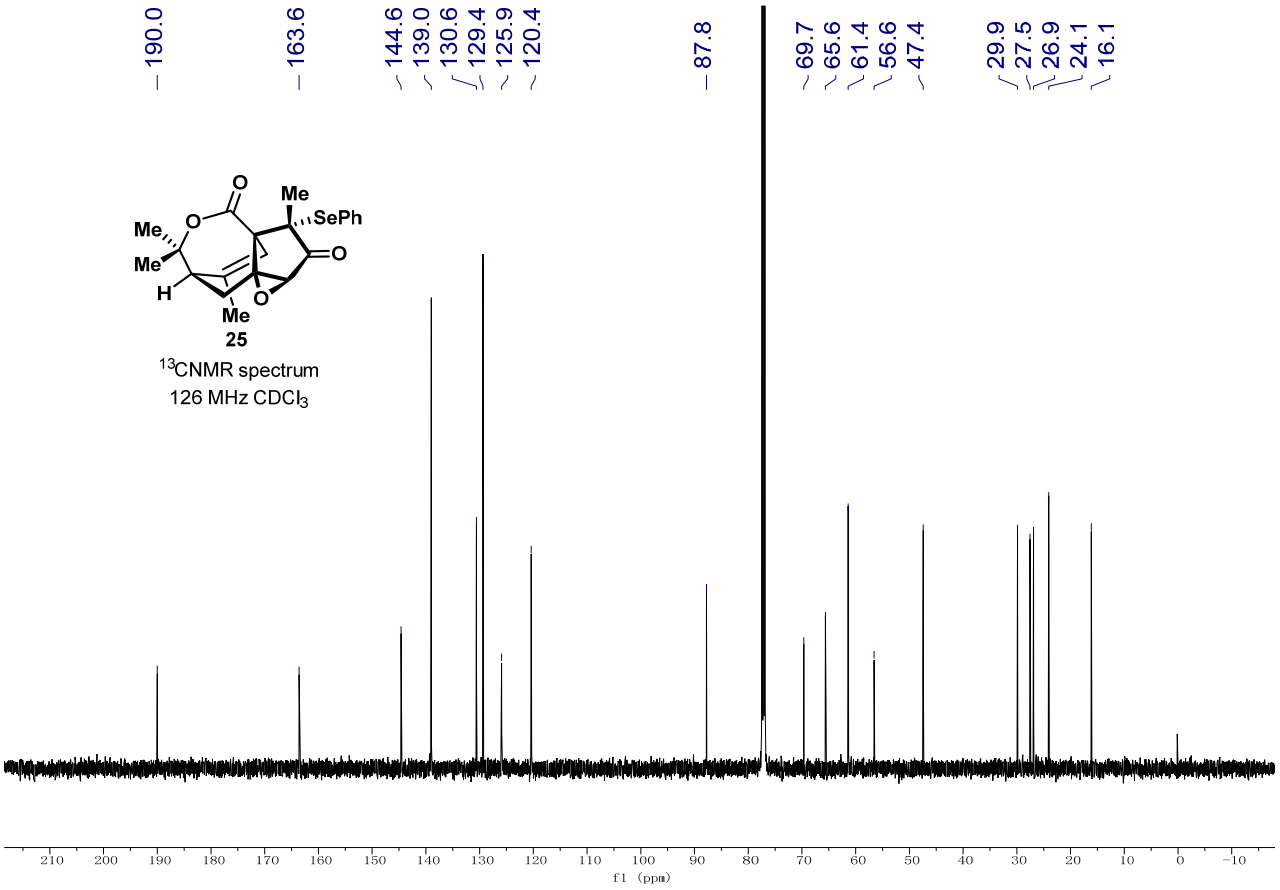




25

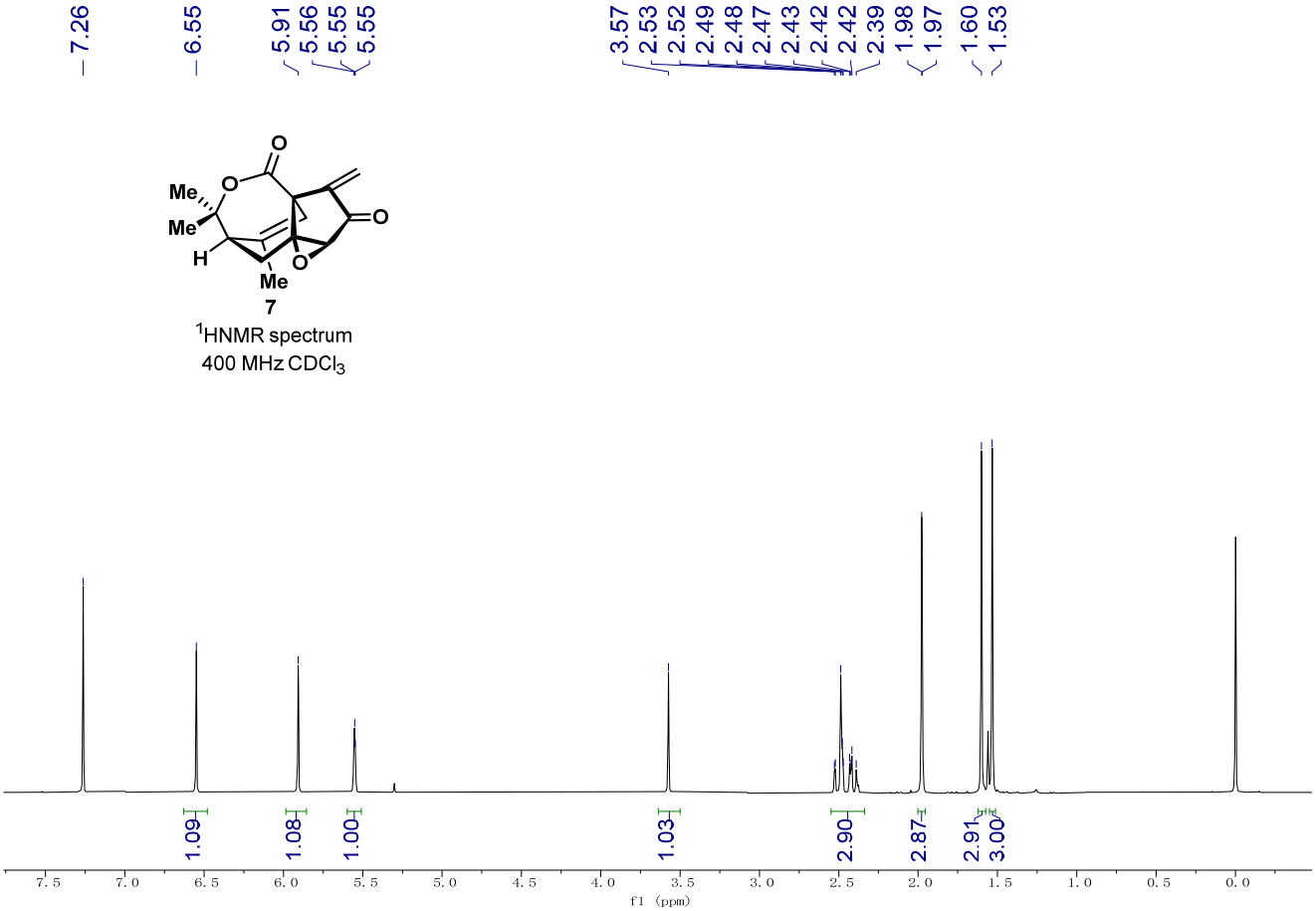
^{1}HNMR spectrum
500 MHz $CDCl_3$





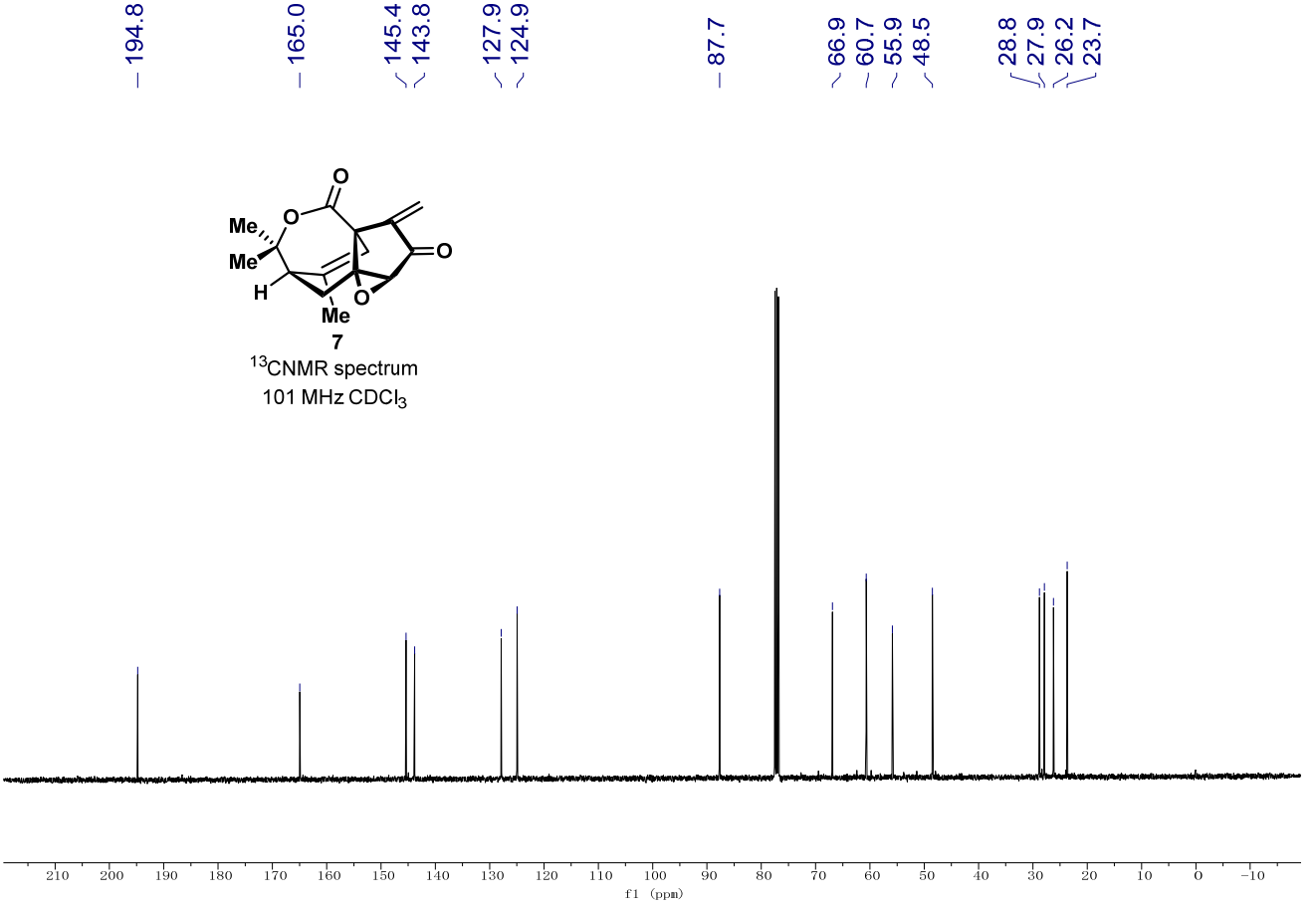
25

^{13}CNMR spectrum
126 MHz $CDCl_3$



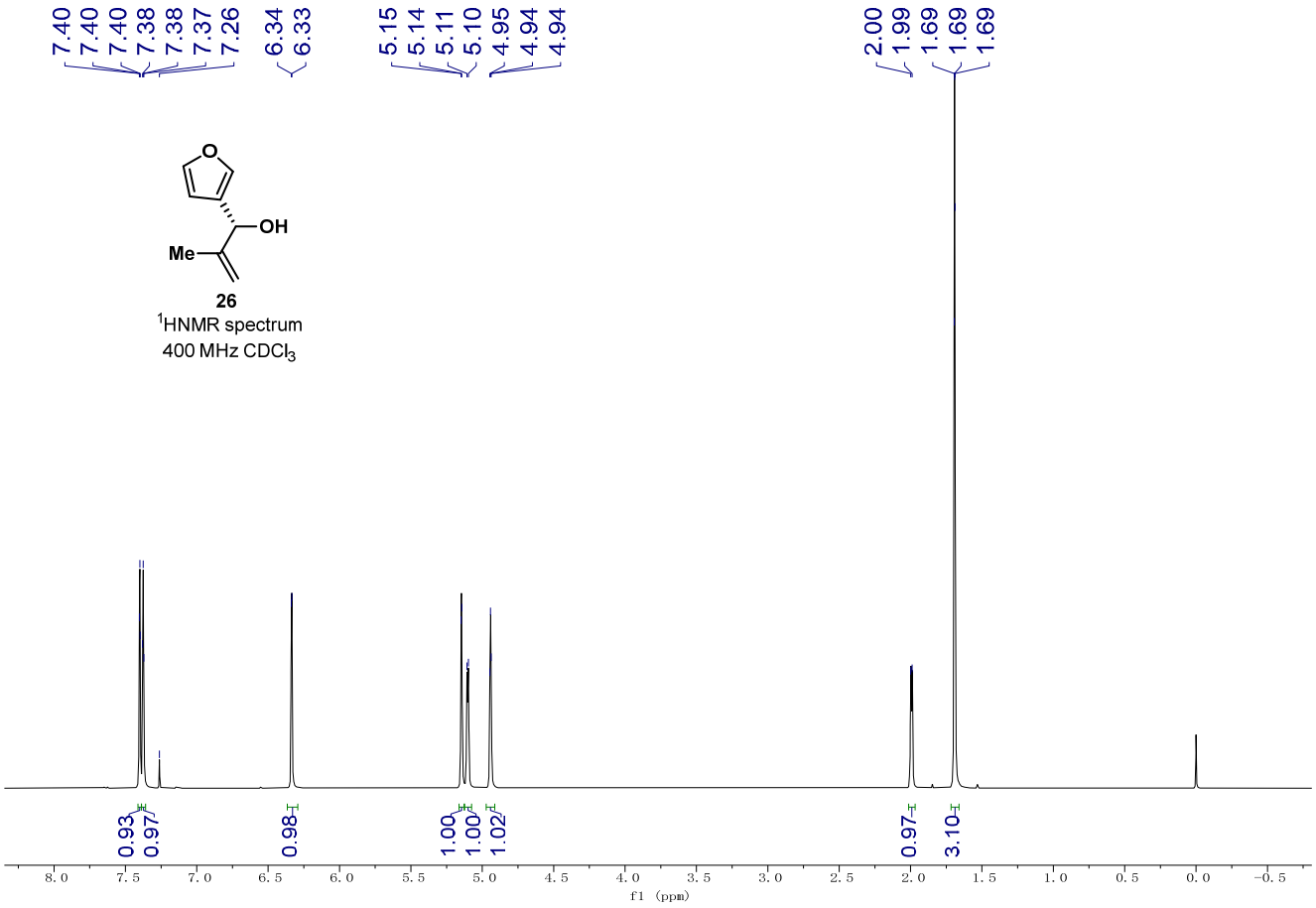
7

^{1}HNMR spectrum
400 MHz $CDCl_3$



7

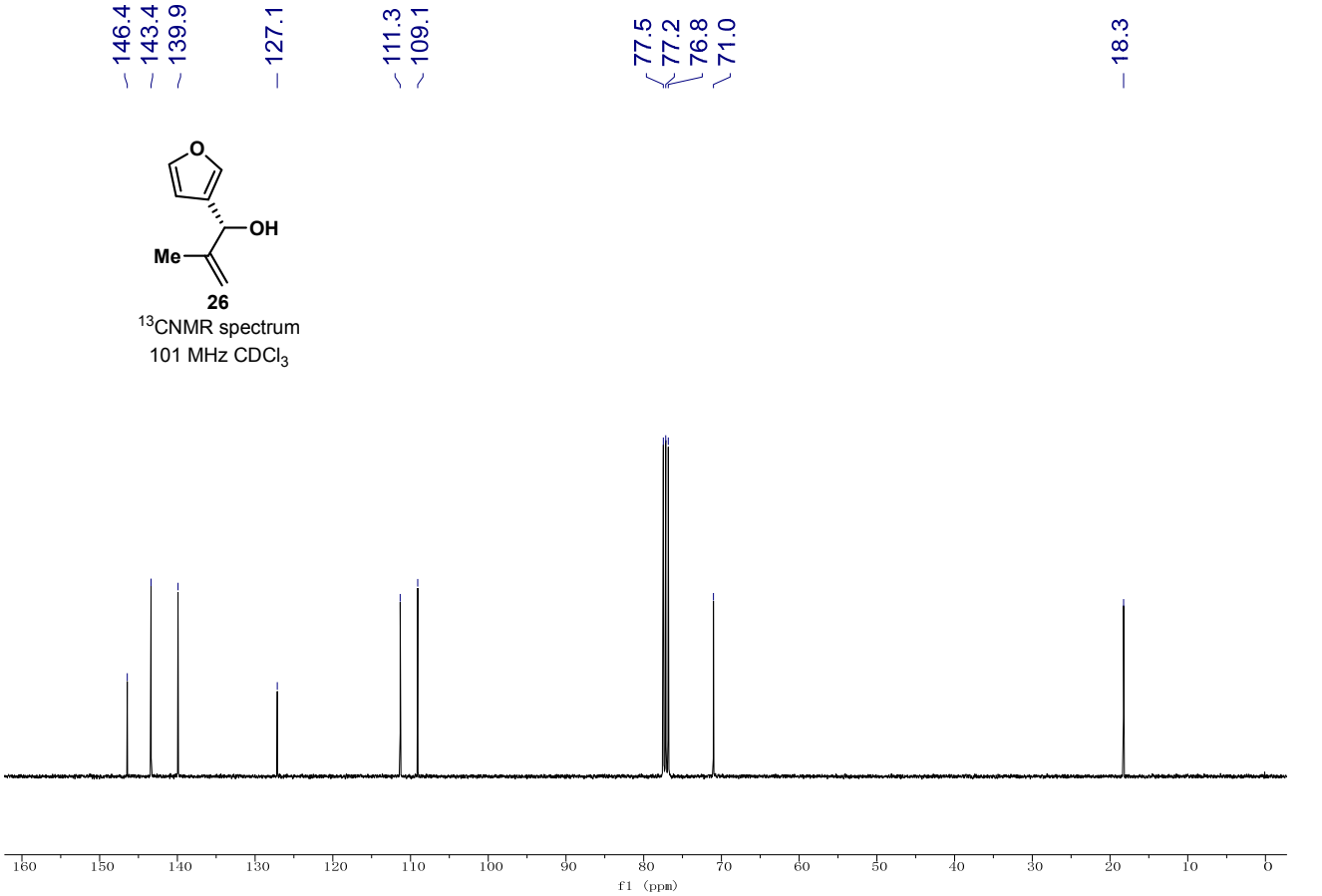
^{13}CNMR spectrum
101 MHz $CDCl_3$



26

^{1}HNMR spectrum

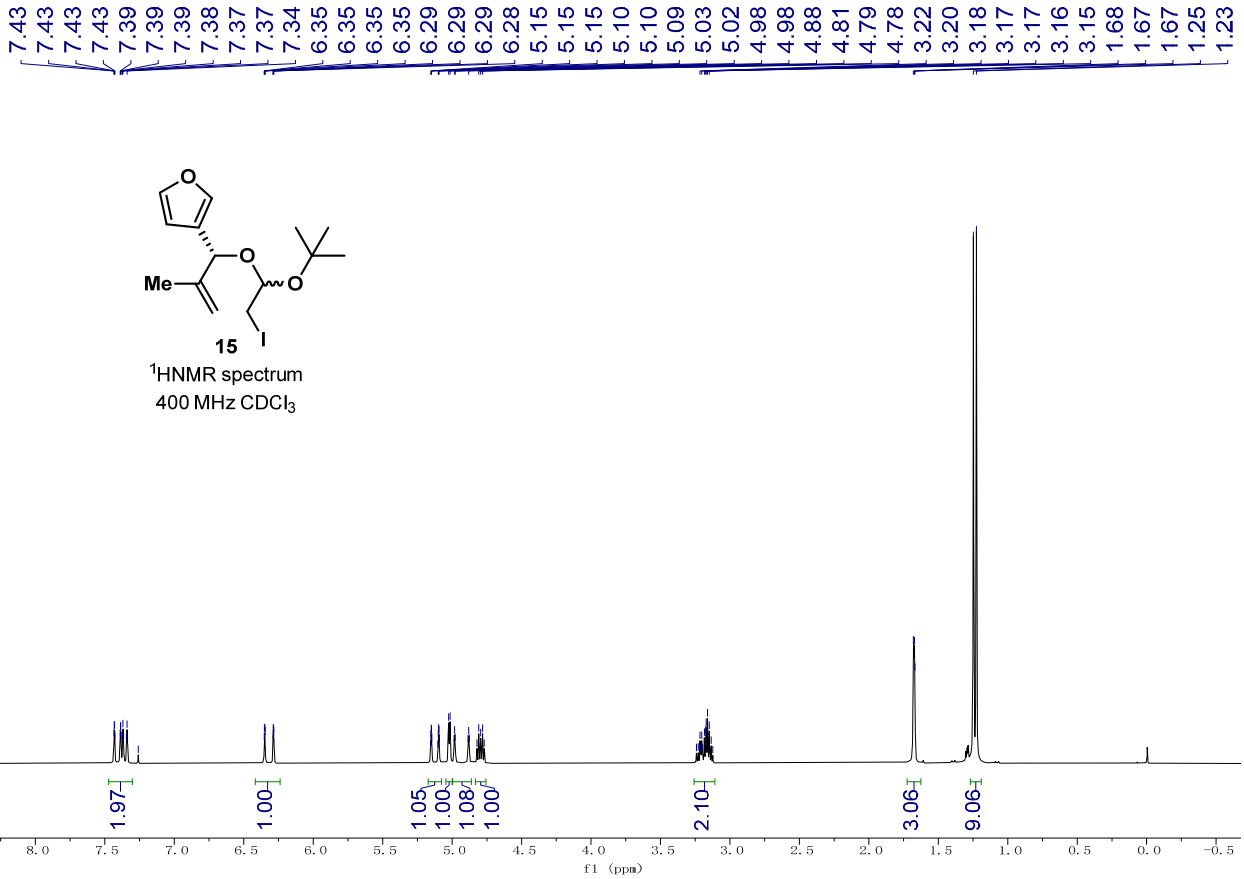
400 MHz $CDCl_3$

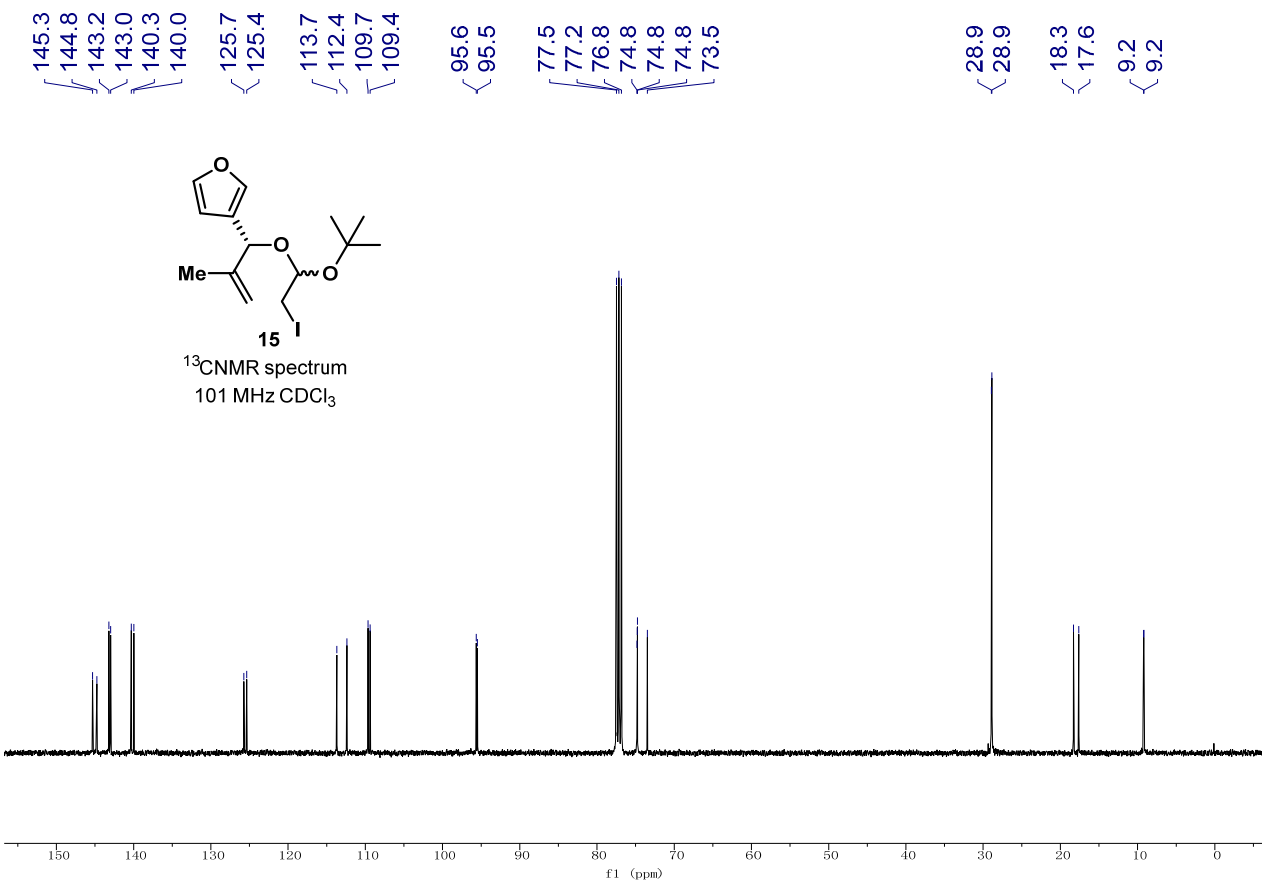


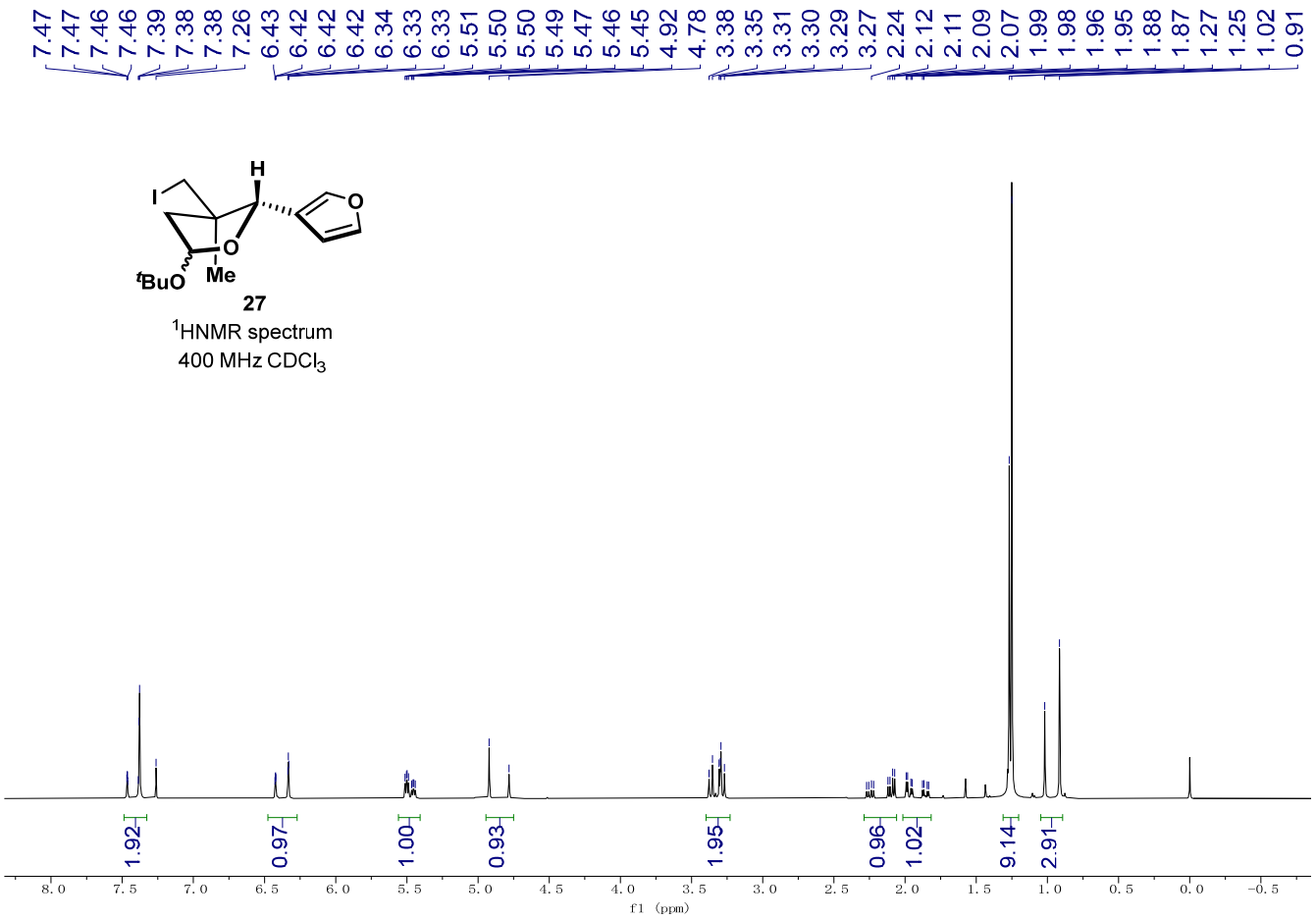
26

^{13}CNMR spectrum

101 MHz $CDCl_3$


7.43 7.43 7.43 7.43 7.39 7.39 7.39 7.38 7.37 7.37 7.34 6.35 6.35 6.35 6.35 6.29 6.29 6.29 6.28 5.15 5.15 5.15 5.10 5.10 5.09 5.03 5.02 4.98 4.98 4.88 4.81 4.79 4.78 3.22 3.20 3.18 3.17 3.17 3.16 3.15 1.68 1.67 1.67 1.25 1.23
Me
O
O
O
I
15
1HNMR spectrum
400 MHz CDCl3
1.97 1.00 1.05 1.00 1.08 1.00 2.10 3.06 9.06
f1 (ppm)

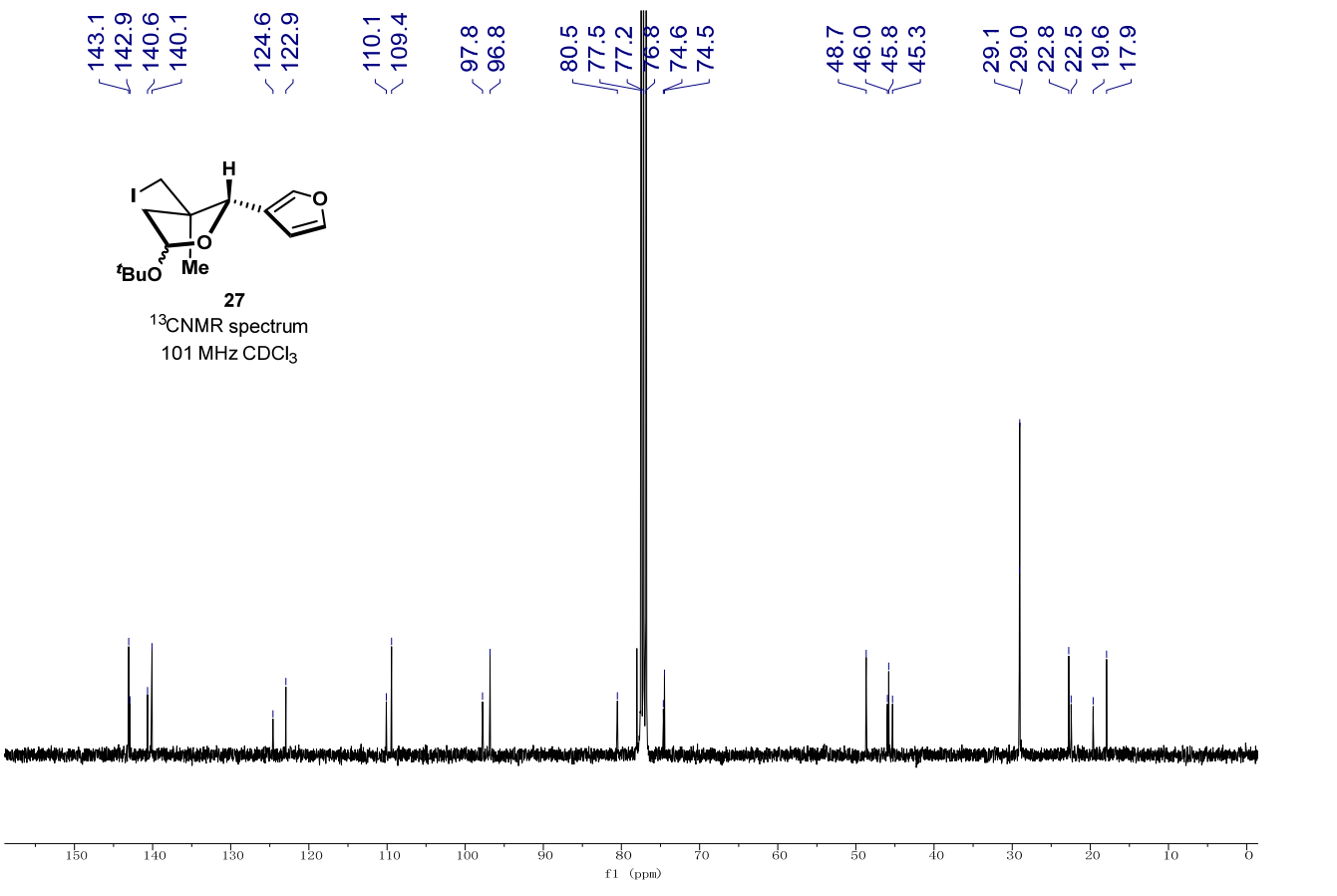

145.3 144.8 143.2 143.0 140.3 140.0 125.7 125.4 113.7 112.4 109.7 109.4 95.6 95.5 77.5 77.2 76.8 74.8 74.8 74.8 73.5 28.9 28.9 18.3 17.6 9.2 9.2
Me
O
O
O
I
15
13CNMR spectrum
101 MHz CDCl3
f1 (ppm)



27

^{1}HNMR spectrum

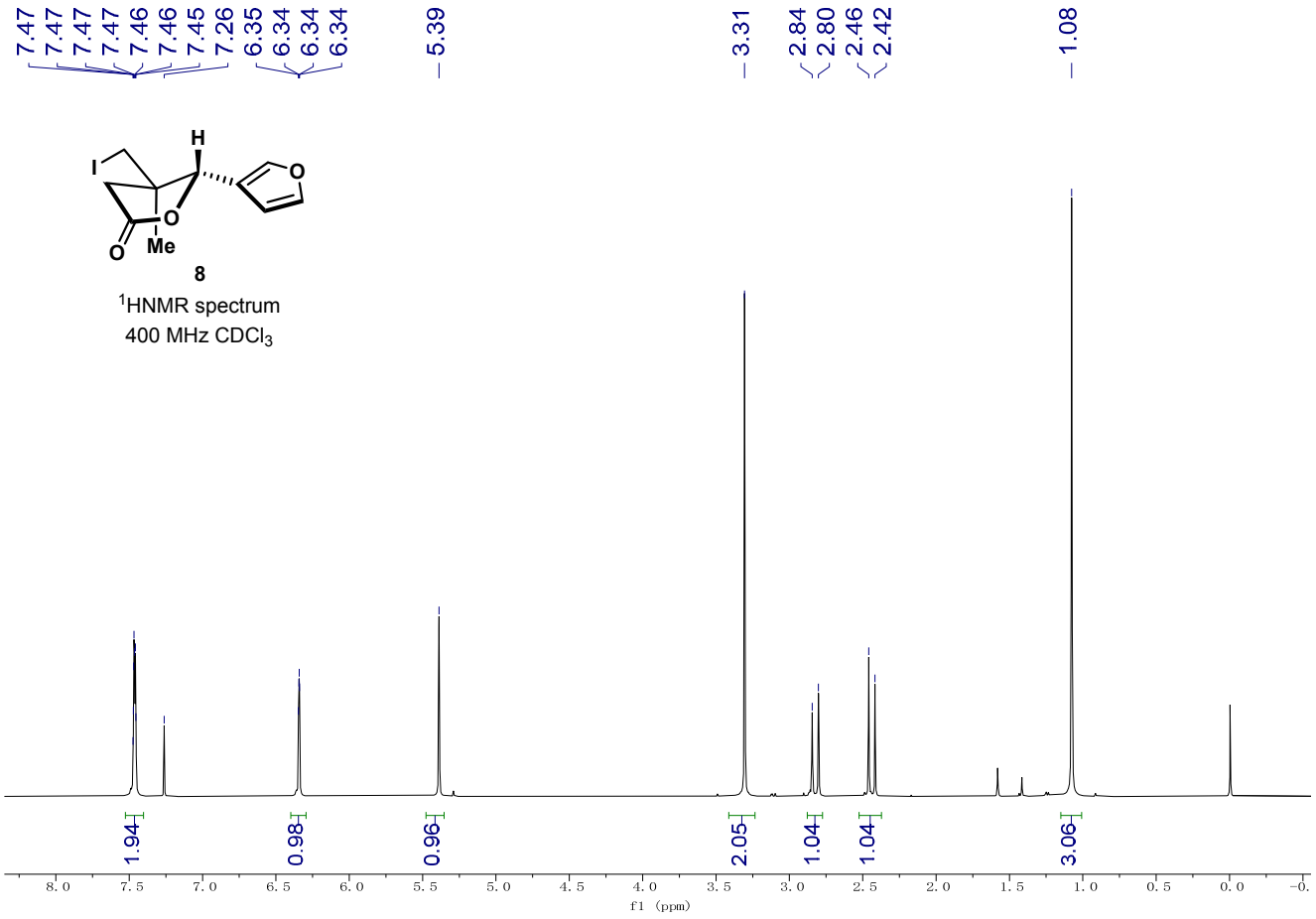
400 MHz $CDCl_3$



27

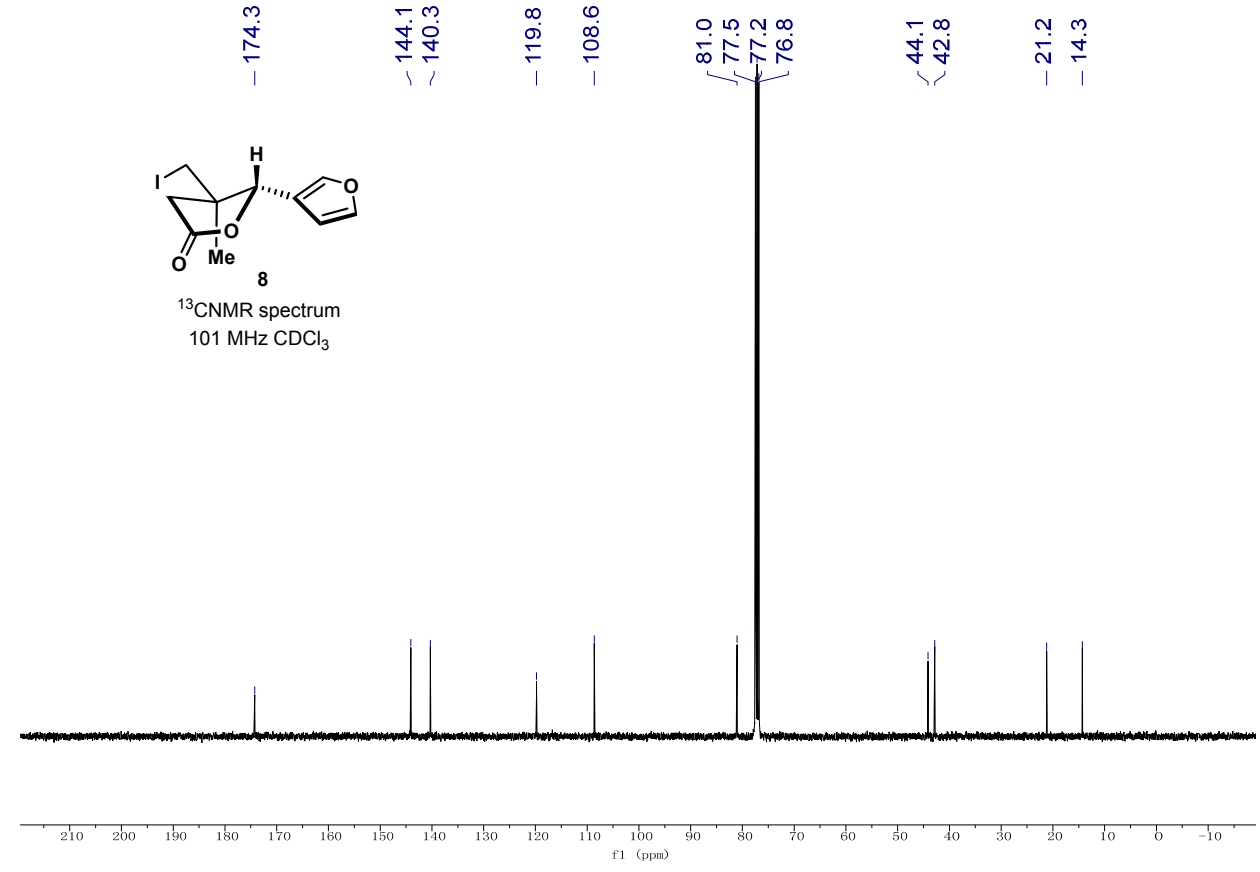
^{13}CNMR spectrum

101 MHz $CDCl_3$



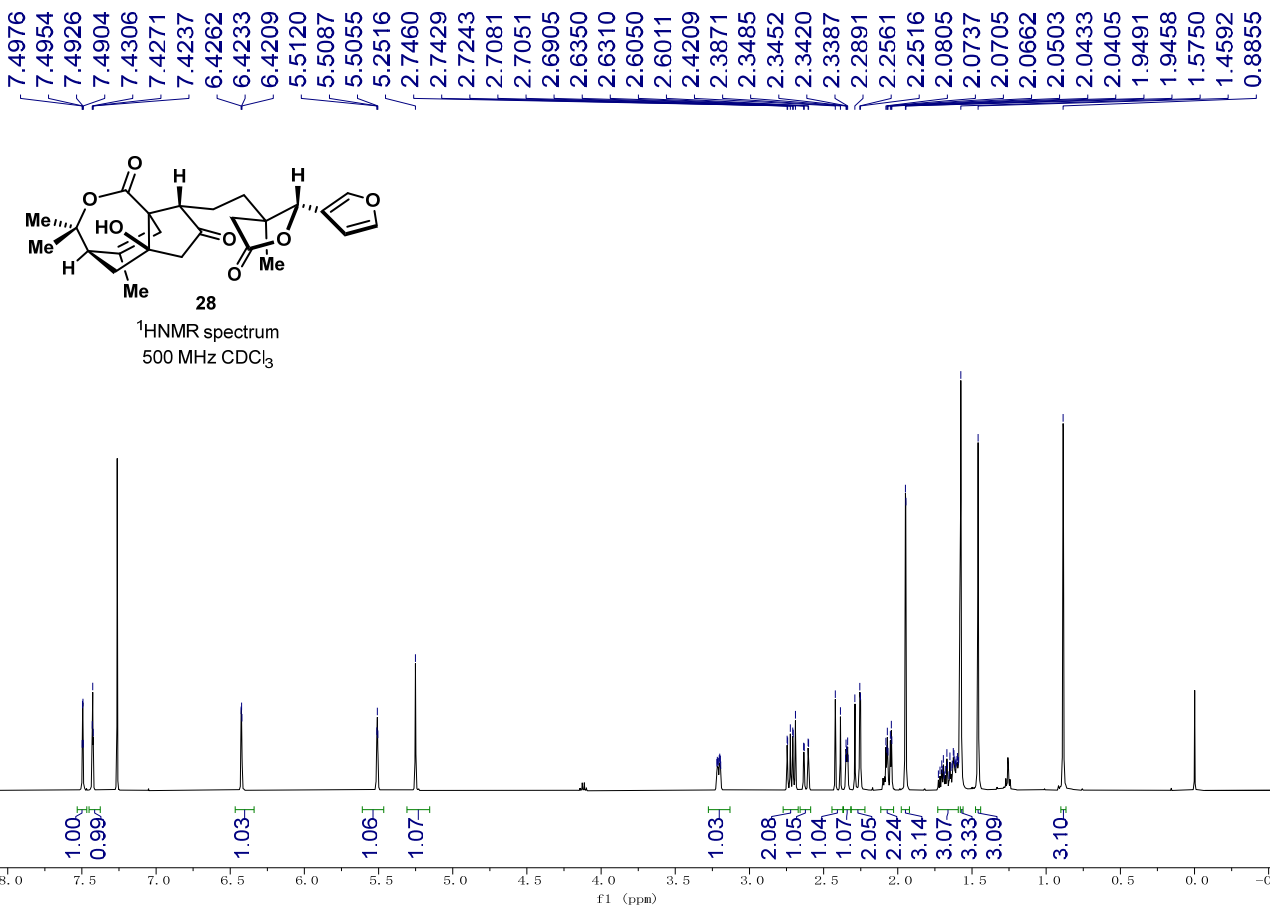
8

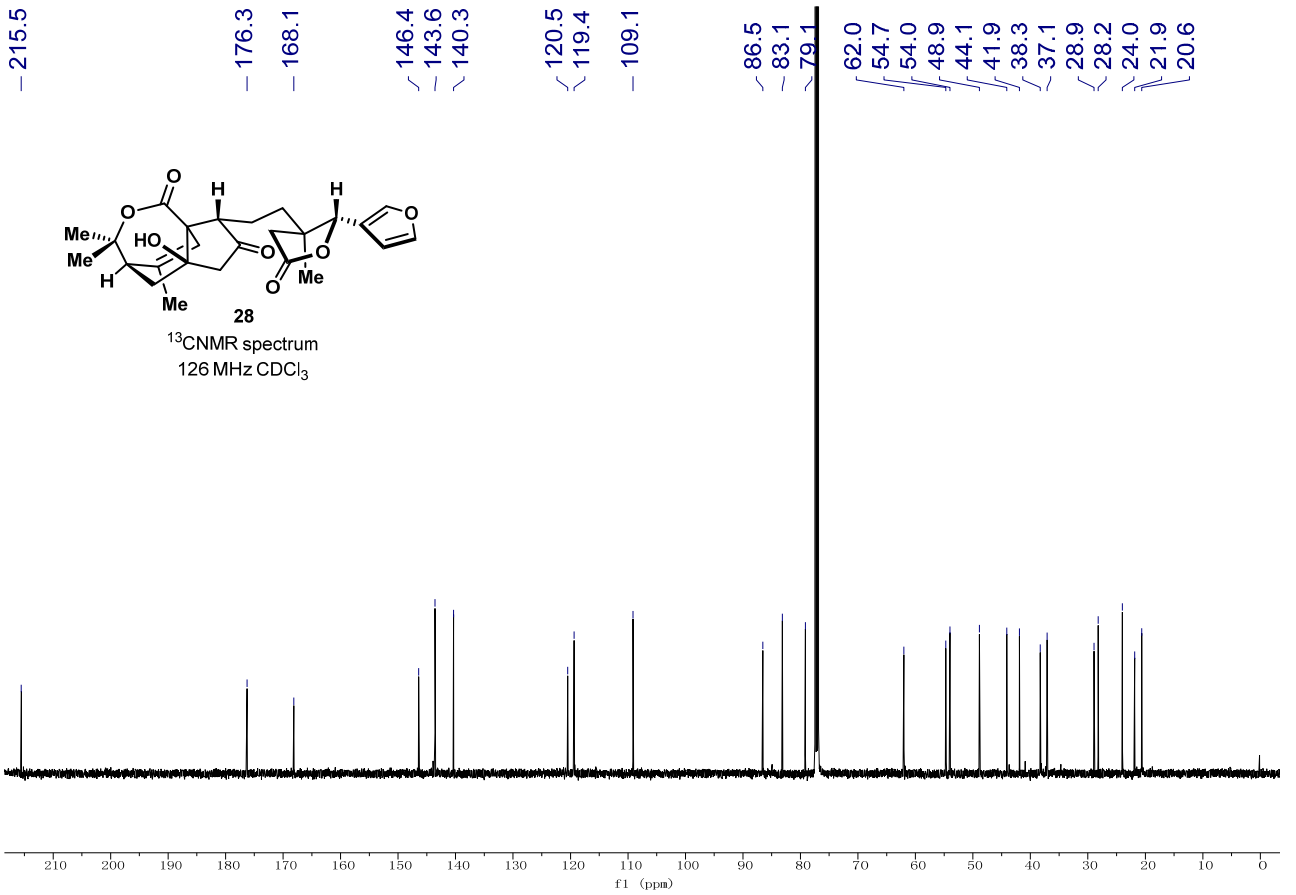
^{1}HNMR spectrum
400 MHz $CDCl_3$

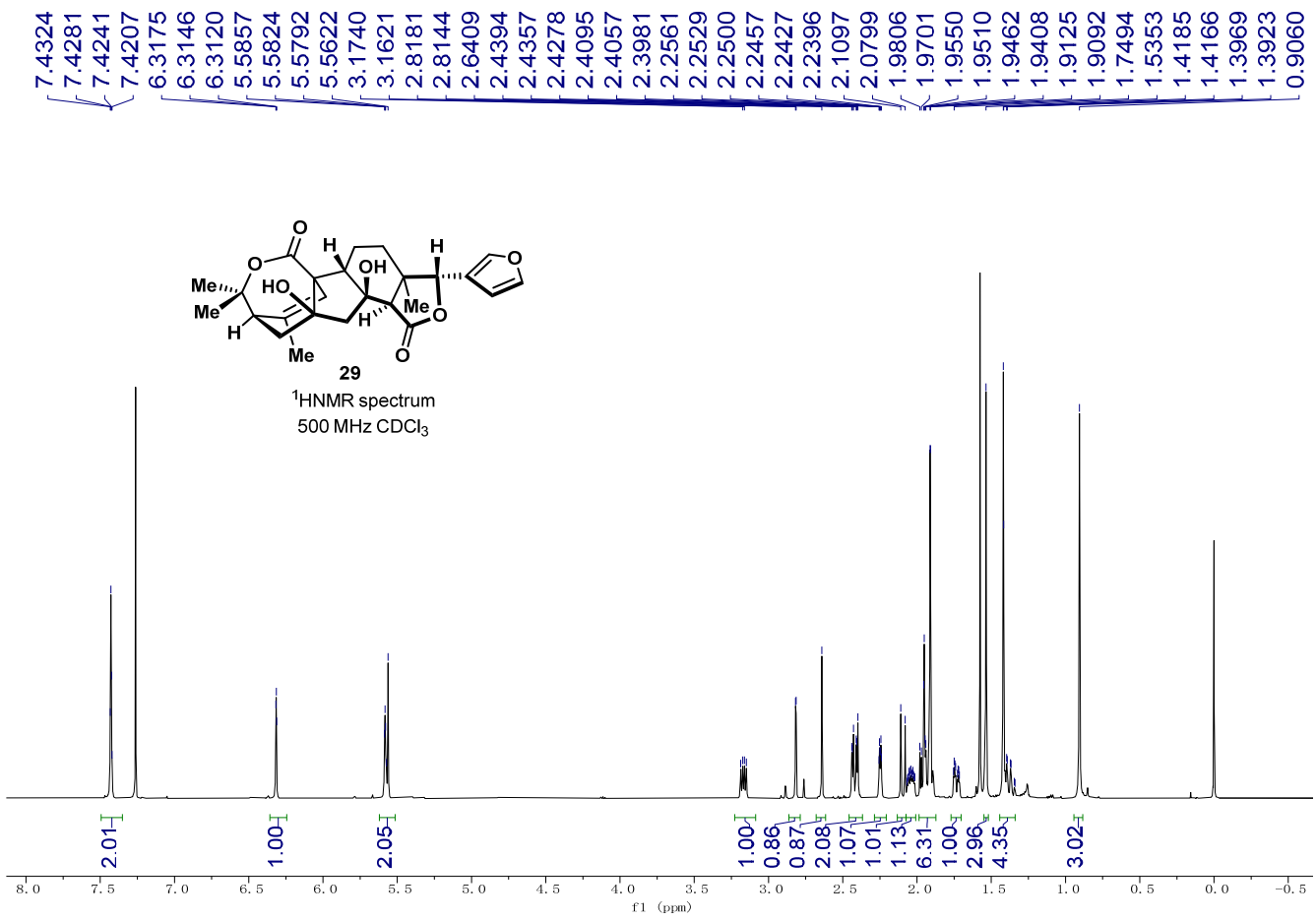


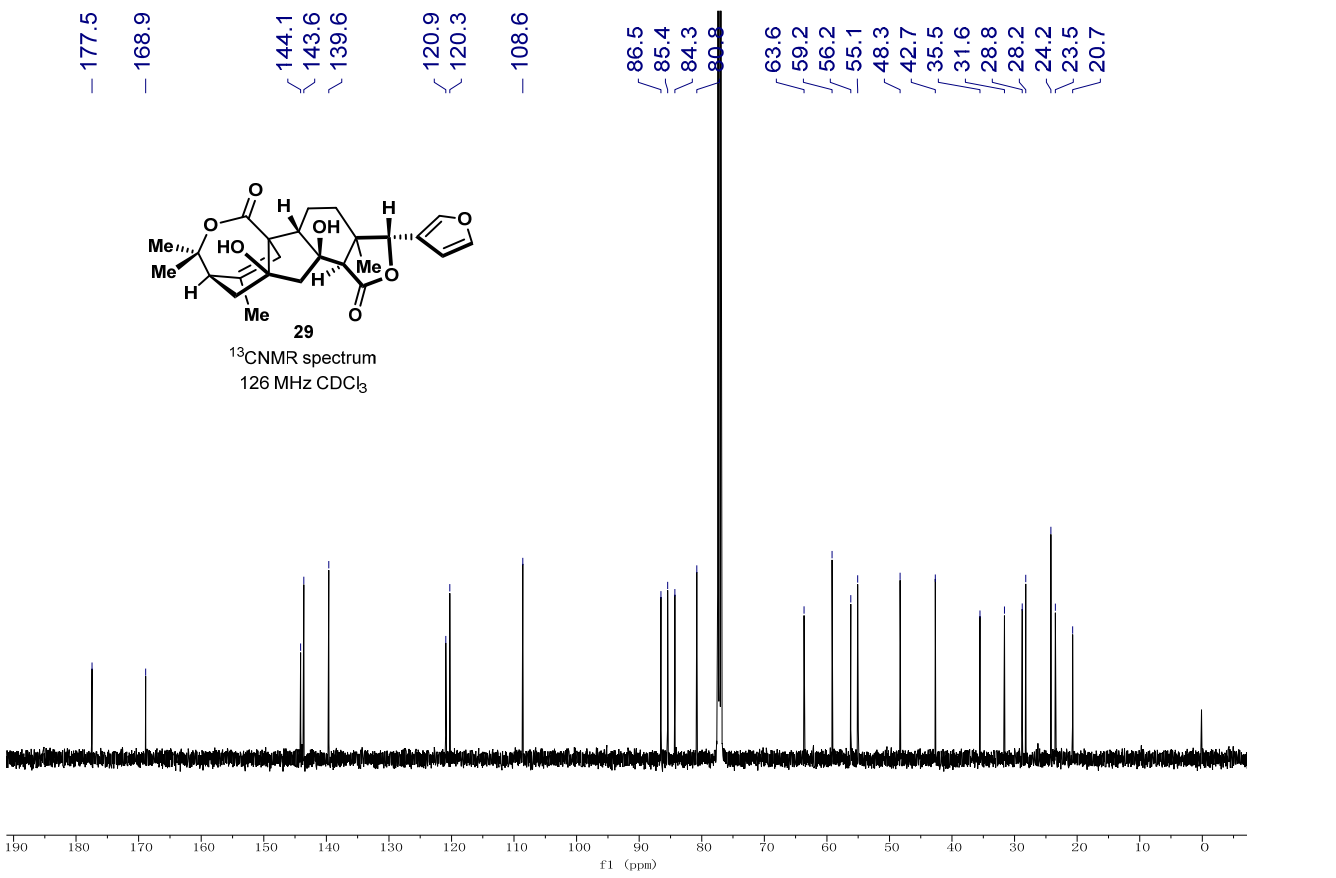
8

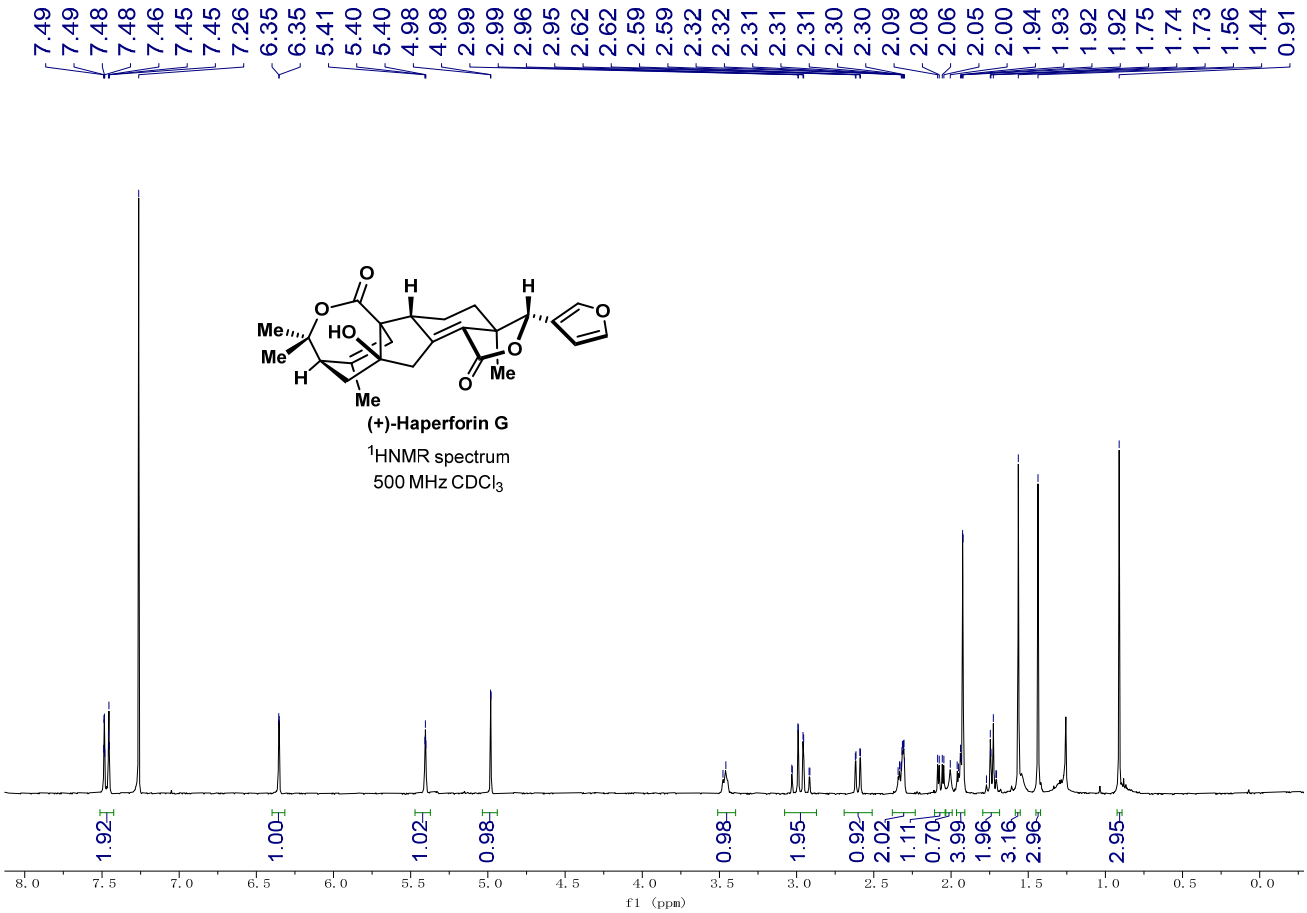
^{13}CNMR spectrum
101 MHz $CDCl_3$

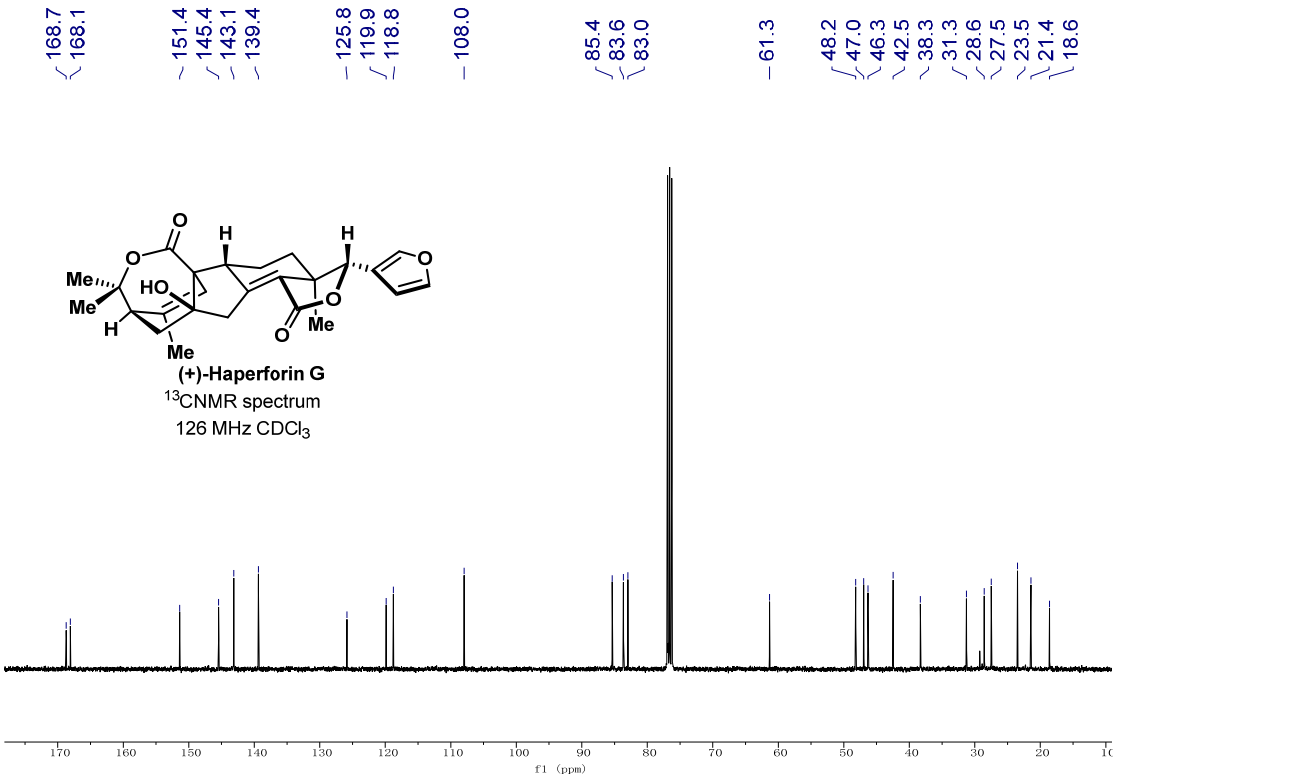

7.4976
7.4954
7.4926
7.4904
7.4306
7.4271
7.4237
6.4262
6.4233
6.4209
5.5120
5.5087
5.5055
5.2516
2.7460
2.7429
2.7243
2.7081
2.7051
2.6905
2.6350
2.6310
2.6050
2.6011
2.4209
2.3871
2.3485
2.3452
2.3420
2.3387
2.2891
2.2561
2.2516
2.0805
2.0737
2.0705
2.0662
2.0503
2.0433
2.0405
1.9491
1.9458
1.5750
1.4592
0.8855
Me
Me
HO
H
Me
O
H
H
O
O
O
O
Me
28
1HNMR spectrum
500 MHz CDCl3
1.00
0.99
1.03
1.06
1.07
1.03
2.08
1.05
1.04
1.07
2.05
2.24
3.14
3.07
3.33
3.09
3.10
f1 (ppm)


215.5
176.3
168.1
146.4
143.6
140.3
120.5
119.4
109.1
86.5
83.1
79.1
62.0
54.7
54.0
48.9
44.1
41.9
38.3
37.1
28.9
28.2
24.0
21.9
20.6
Me
Me
HO
H
Me
O
H
H
O
O
O
O
Me
28
13CNMR spectrum
126 MHz CDCl3
f1 (ppm)

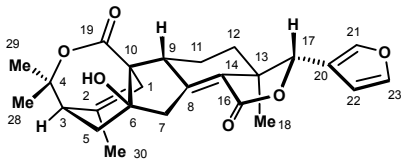

7.4324
7.4281
7.4241
7.4207
6.3175
6.3146
6.3120
5.5857
5.5824
5.5792
5.5622
3.1740
3.1621
2.8181
2.8144
2.6409
2.4394
2.4357
2.4278
2.4095
2.4057
2.3981
2.2561
2.2529
2.2500
2.2457
2.2427
2.2396
2.1097
2.0799
1.9806
1.9701
1.9550
1.9510
1.9462
1.9408
1.9125
1.9092
1.7494
1.5353
1.4185
1.4166
1.3969
1.3923
0.9060
29
1HNMR spectrum
500 MHz CDCl3
2.01
1.00
2.05
1.00
0.86
0.87
2.08
1.07
1.01
1.13
6.31
1.00
2.96
4.35
3.02
f1 (ppm)


177.5
168.9
144.1
143.6
139.6
120.9
120.3
108.6
86.5
85.4
84.3
80.8
63.6
59.2
56.2
55.1
48.3
42.7
35.5
31.6
28.8
28.2
24.2
23.5
20.7
29
13CNMR spectrum
126 MHz CDCl3
f1 (ppm)


7.49 7.49 7.48 7.48 7.46 7.45 7.45 7.26 6.35 6.35 5.41 5.40 5.40 4.98 4.98 2.99 2.99 2.96 2.95 2.62 2.62 2.59 2.59 2.32 2.32 2.31 2.31 2.31 2.30 2.30 2.09 2.08 2.06 2.05 2.00 1.94 1.93 1.92 1.92 1.75 1.74 1.73 1.56 1.44 0.91
(+)-Haperforin G
1HNMR spectrum
500 MHz CDCl3
1.92 1.00 1.02 0.98 0.98 1.95 0.92 2.02 1.11 0.70 3.99 1.96 3.16 2.96 2.95
f1 (ppm)


168.7 168.1 151.4 145.4 143.1 139.4 125.8 119.9 118.8 108.0 85.4 83.6 83.0 61.3 48.2 47.0 46.3 42.5 38.3 31.3 28.6 27.5 23.5 21.4 18.6
(+)-Haperforin G
13CNMR spectrum
126 MHz CDCl3
f1 (ppm)

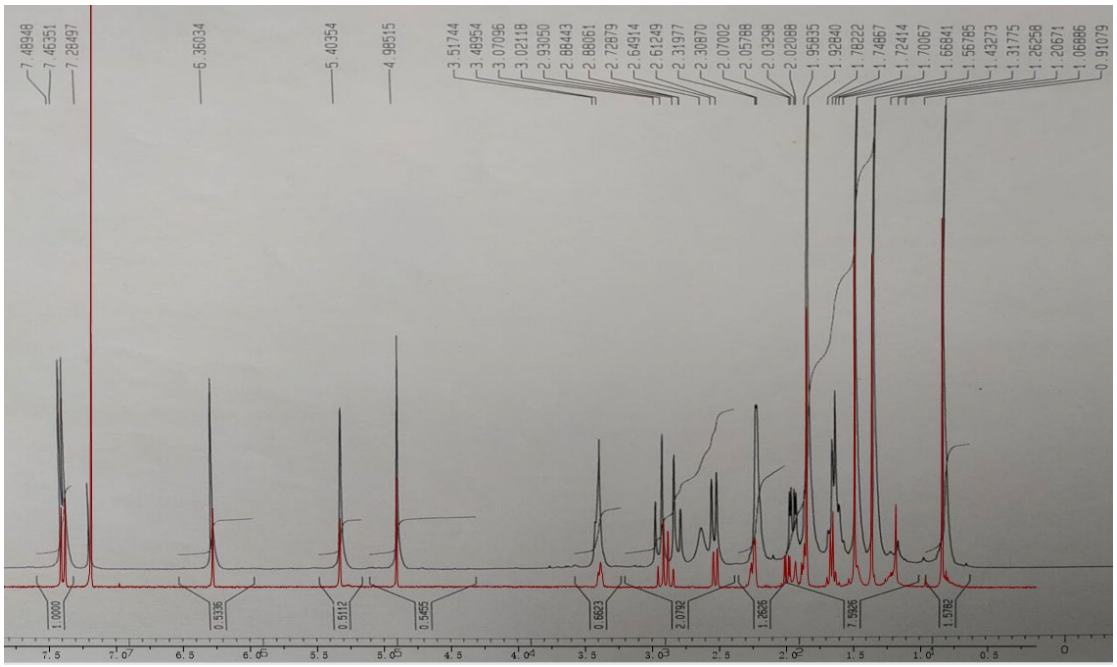
Part IV: NMR Comparison of Synthetic and Natural Haperforin G



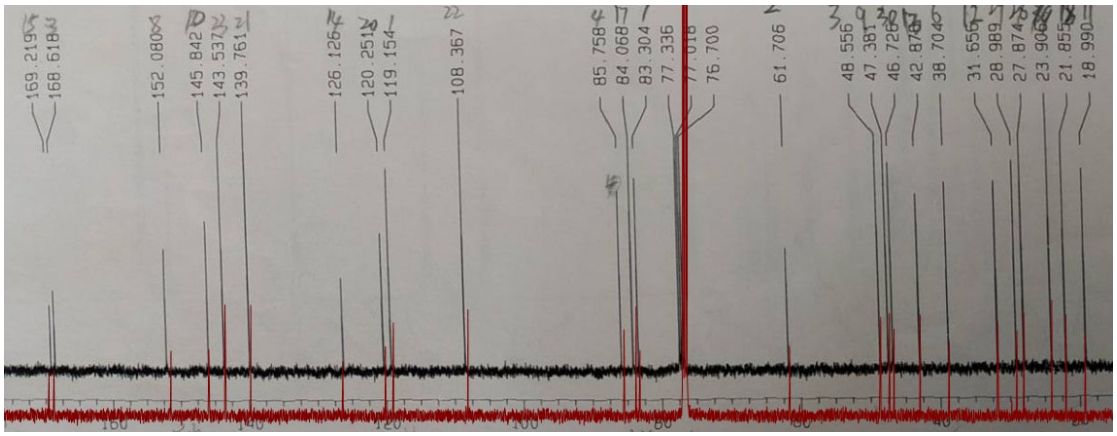
No	Natural δH [ppm, mult, *J* (Hz)] 300 MHz	Synthetic δH [ppm, mult, *J* (Hz)] 500 MHz	Err (Natural - Synthetic) Δδ [ppm]
1	5.39 (s)	5.40 (s)	-0.01
11b, 3	2.26 (m), 2.30 (m)	2.24 - 2.43 (m)	-
5a	2.04 (dd, 14, 4.5)	2.07 (dd, 14.9, 5.0)	-0.03
5b	2.61 (dd, 14, 1.5)	2.60 (dd, 14.9, 2.0)	0.01
7	2.88 and 3.04 (AB, 21)	2.94 (dd, 19.8, 2.2) 3.01 (dd, 19.8, 1.4)	-
9	3.48 (m)	3.56 - 3.41 (m)	-
11a, 12a	1.72 (m)	1.80 - 1.67 (m)	-
12b	-	1.97 - 1.90 (m)	-
OH	2.35 (s)	2.00 (brs)	-
17	4.96 (s)	4.98 (s)	-0.02
18	0.89 (s)	0.91 (s)	-0.02
21	7.45 (s)	7.49 (brs)	-0.04
22	6.38 (s)	6.35 (brs)	0.03
23	7.45 (s)	7.47 - 7.44 (m)	-
28	1.55 (s)	1.56 (s)	-0.01
29	1.42 (s)	1.44 (s)	-0.02
30	1.91	1.92 (d, 1.6)	-0.01

No	Natural δC [ppm], 75 MHz	Synthetic δC [ppm], 126 MHz	Err (Natural - Synthetic) Δδ [ppm]
1	118.8	118.8	0
2	145.4	145.4	0
3	48.2	48.2	0
4	85.3	86.3	0
5	38.3	38.3	0
6	82.8	83.0	-0.2
7	46.3	46.3	0
8	151.8	151.4	+0.4
9	46.9	47.0	-0.1
10	61.3	61.3	0
11	18.6	18.6	0
12	31.3	31.3	0
13	42.4	42.5	-0.1
14	125.6	125.8	-0.2
16	168.8	168.7	+0.1
17	83.6	83.6	0
18	21.4	21.4	0
19	168.1	168.1	0
20	119.8	119.9	-0.1
21	143.1	143.1	0
22	108.0	108.0	0
23	139.3	139.4	-0.1
28	27.4	27.5	-0.1
29	28.6	28.6	0
30	23.4	23.5	-0.1

^{1}H NMR Spectrum Comparison of Natural and Synthetic Haperforin G



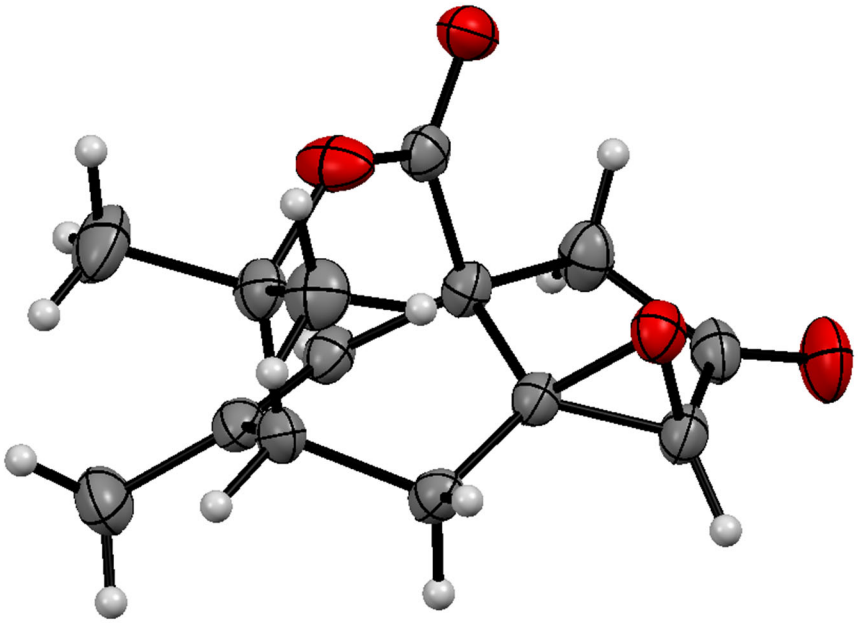
^{13}C NMR Spectrum Comparison of Natural and Synthetic Haperforin G



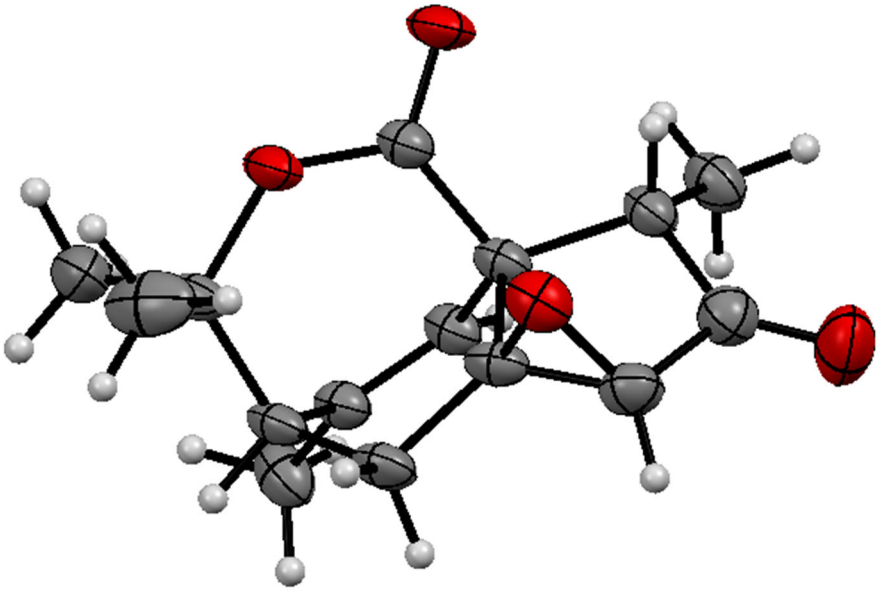
Dark: natural Haperforin G (This spectrum was provided by Hao Xiaojiang)

Red: synthetic Haperforin G

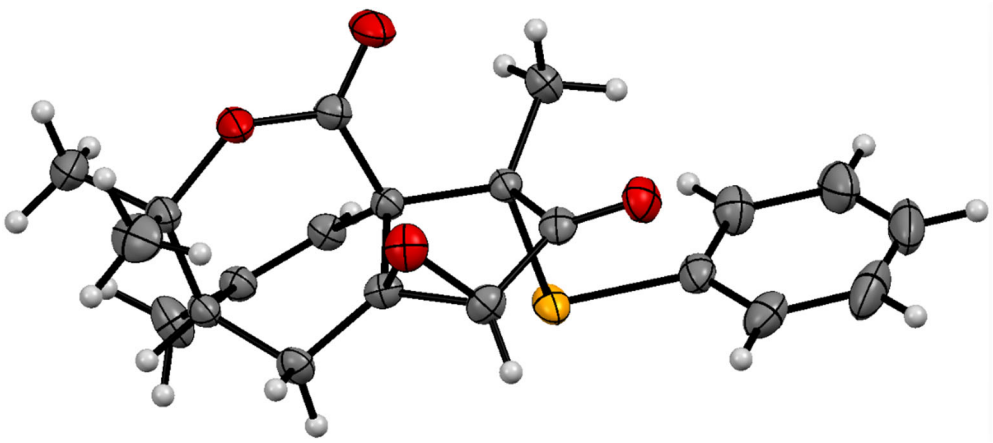
Part V: ORTEP Diagrams:



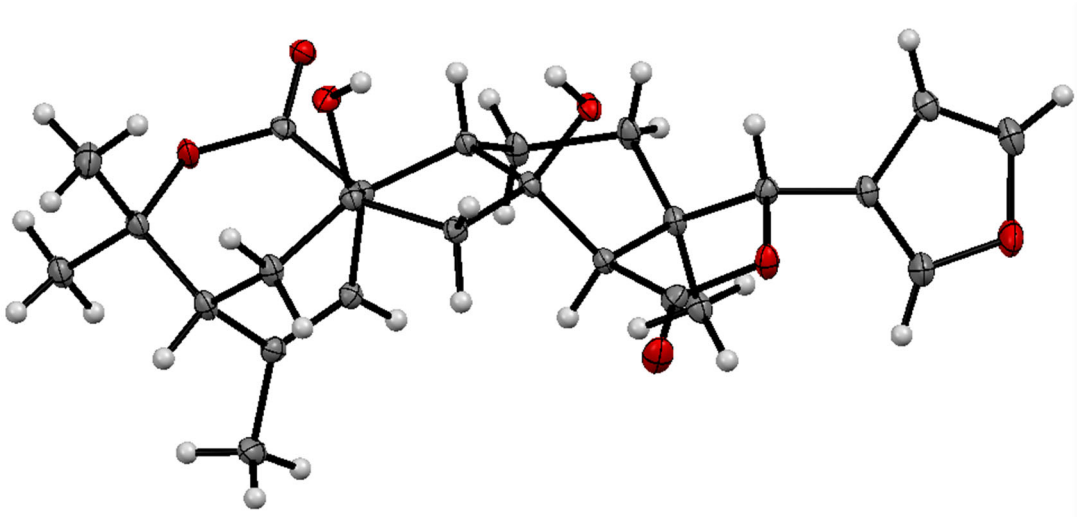
ORTEP diagram of compound **23**



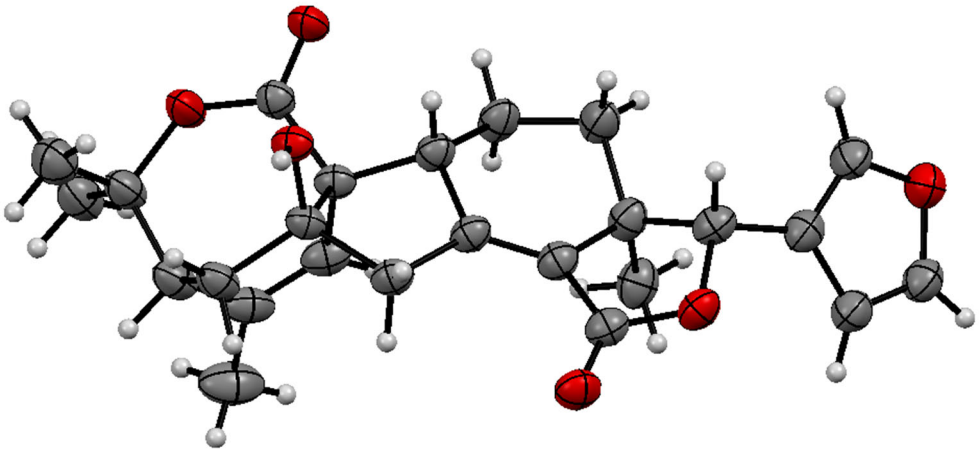
ORTEP diagram of compound **24**



ORTEP diagram of compound **25**



ORTEP diagram of compound **29**



ORTEP diagram of **(+)-Haperforin G**