Supporting Information

Enantioselective Syntheses and Application of 4-*epi*-Galiellalactone and the Corresponding Activity-Based Probe： From Strained Bicycles to Strained Tricycles

Yandong Lu,[†] Shan Zhao,[‡] Shijie Zhou,[‡] Si-Cong Chen,[†]and Tuoping Luo[†,‡,*]

[†]Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education and Beijing National Laboratory for Molecular Science (BNLMS), College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China
[‡]Peking – Tsinghua Center for Life Sciences, Academy for Advanced Interdisciplinary Studies, Peking University, Beijing 100871, China

Table of Contents

I: Supplementary Figures and Tables

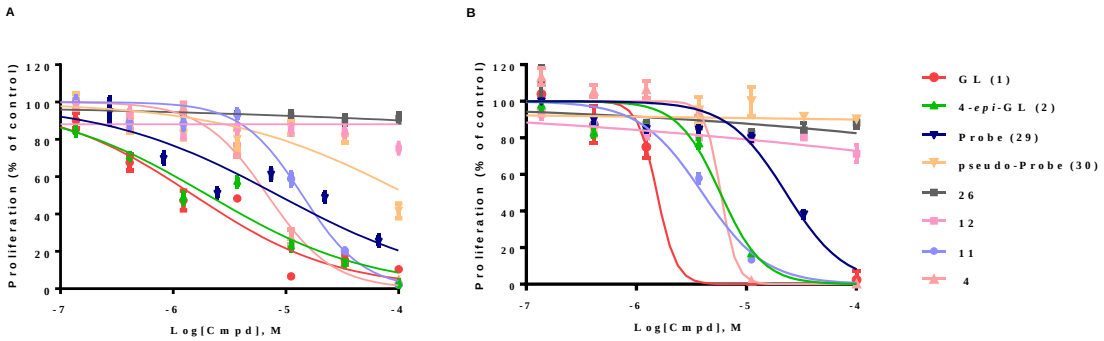


Figure S1. Cytotoxicity of galiellalactone and synthesized compounds against MOLT-4 (A) and Jurkat (B) cells (dose response curves).

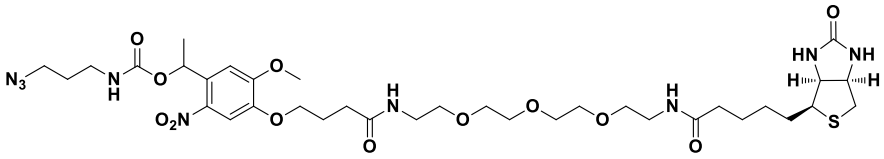


Figure S2. Stucture of the photocleavable biotin-azide used in the pull-down experiments for LC-MS/MS analysis

Probe (**29**) /µM	25	0	25
pseudo-Probe (**30**) /µM	0	25	0
4-*epi*-GL (**2**)/µM	0	0	25

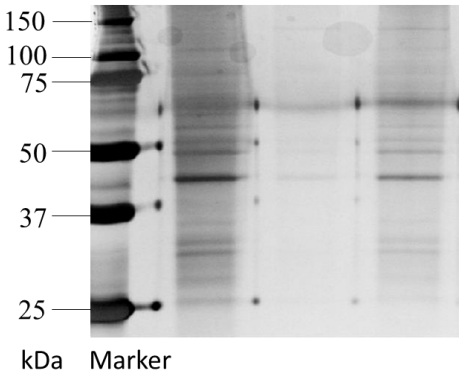
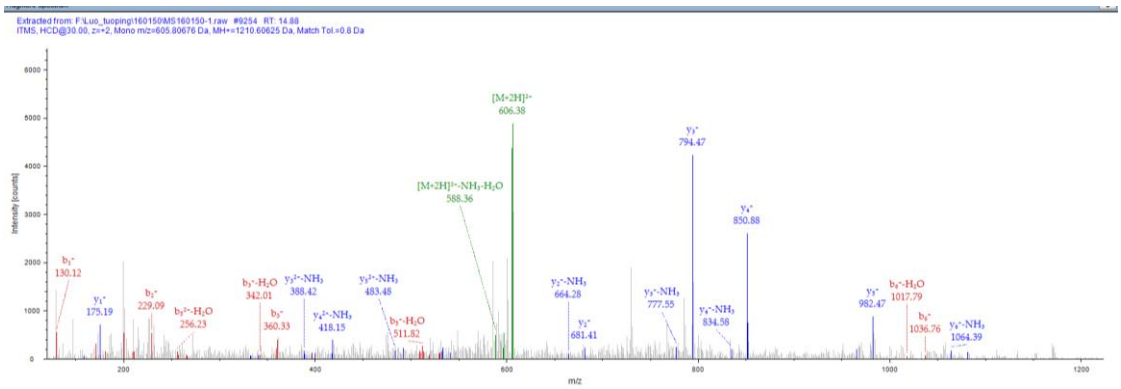


Figure S3. Silver staining after pull-down experiment using 4-*epi*-galiellalactone probe **29** on intact Molt cells. The pseudo probe **30** was used as a negative control, while pretreatment of cells with 4-*epi*-galiellalactone **2** diminished the binding ability of **29** with target proteins.



Res.	b ion	b++	y ion	y++
E	130.0	65.5		
V	229.1	115.1	1081.6	541.3
M	360.2	180.6	982.5	491.8
G	417.2	209.6	851.5	426.2
L	530.3	265.6	794.4	397.7
C_{probe}	1036.5	518.8	681.3	341.2
R			175.1	88.1

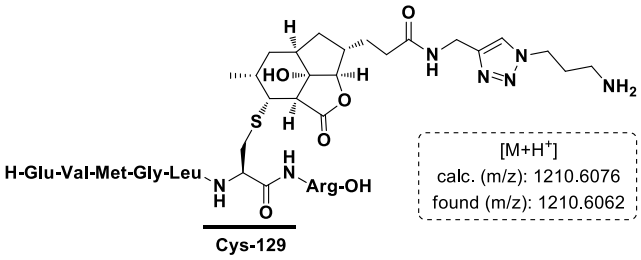


Figure S4. LC-MS/MS analysis and b/y ion assignments by Mascot confirming Ataxin 7 was labeled by probe **29**

Figure S5. Western blot analysis of freshly separated mouse brain cells treated with probe **29** (4–25 μM) for 2 h. The cell lysates were subjected to a $CuSO_4$-catalyzed click reaction with biotin-azide for 1 h and then the binding proteins were successively pulled down by streptavidin beads, separated by SDS-PAGE and immunoblotted with Ataxin-7 antibody. Competitive binding was demonstrated by pretreatment of cells with galiellalactone or 4-*epi*-galiellalactone prior to the addition of **29**.

All calculations were performed using the Gaussian 09 D.01 software package[1]. Geometries were optimized under B3LYP functional and 6-31G(d) basis set. Frequency analysis showed no imaginary frequencies, which indicated that each geometry below is at the minima of the potential energy surface.

Table S1. The calculated thermochemistry property and reaction Gibbs free energy change for **7** and **9**.

Compound	Enthalpy (a.u.)	Entropy ($Cal \cdot mol^{-1} \cdot K^{-1}$)	Free energy (a.u.)	ΔG Hydrogenation ($kCal \cdot mol^{-1}$)
H_2	-1.162021	31.130	-1.176812	–
9	-654.201615	112.073	-654.254864	-14.8
10	-655.400194	115.795	-655.455211	
7	-613.728595	98.573	-613.775430	-18.7
8	-614.935394	98.203	-614.982053	

Table S2. The calculated HOMO and LUMO energies, energy gap, dipole, and plotted LUMO surface of several typical unsaturated carbonyl compounds, **7** and **9**.

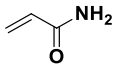
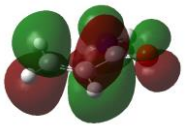
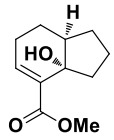
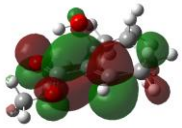
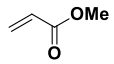
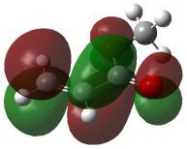
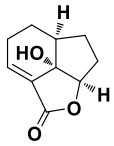
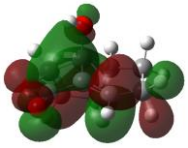
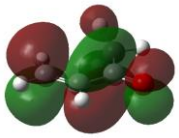
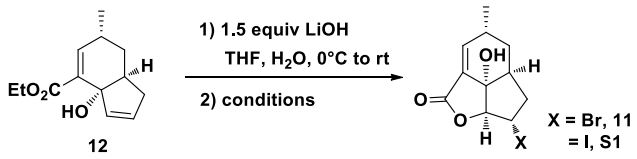
Compound	E_{HOMO} (a.u.)	E_{LUMO} (a.u.)	E_{LUMO} (eV)	ΔE (eV)	Dipole	LUMO Surface
 Acrylamide	-0.24929	-0.03681	-1.00	5.78	3.6966	
 **9**	-0.25061	-0.04098	-1.12	5.70	2.9928	
 Methyl Acrylate	-0.27186	-0.04523	-1.23	6.17	2.1140	
 **7**	-0.25885	-0.04625	-1.26	5.78	4.0378	
 Butenone	-0.24785	-0.05693	-1.55	5.19	3.1143	
 Acrolein	-0.25712	-0.06500	-1.77	5.23	3.1602	

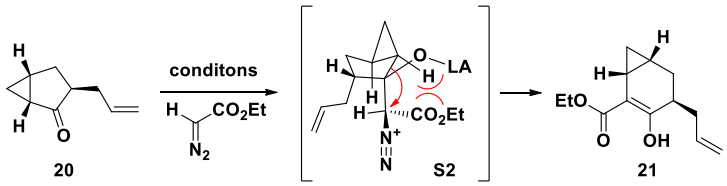
Table S3. Optimization of Conditions for the in-*situ* Bromolactonization of **12**



12

Entry	Conditions	Result
1	NBS, THF, 0°C to rt	<19%
2	NBS, DCM, 0°C	N.D.
3	NBS, DCM, $NaHCO_3$, 0°C	30%
4	NBS, DCM, $NaHCO_3$, TBAB, 0°C	6%
5	NIS, DCM, $NaHCO_3$, 0°C	9%

Table S4. Optimization of Conditions for the Ring Expansion of **20**[a]



20 S2 21

Entry	Conditions[a]	Result
1	$SnCl_4$, toluene, rt	sub recovered
2	$ZnCl_2$, toluene, rt	sub recovered
3	$Sc(OTf)_3$, toluene, rt	sub recovered
4	$ZnCl_2$, DCM, rt	partially decomposed
5	$Et_3O^+BF_4^-$, DCM, rt	decomposed
6	$BF_3{\cdot}Et_2O$, CH_2Cl_2, rt	41% yield
7	$BF_3{\cdot}Et_2O$, THF, rt	13% yield
8	$BF_3{\cdot}Et_2O$, toulene, rt	50% yield
9[b]	$BF_3{\cdot}Et_2O$, toluene, rt	64% yield

[a] All reactions were conducted with 2 equiv L.A. and 2 equiv ethyl diazoacetate at 50 mg scale unless otherwise stated. [b] 1g scale.

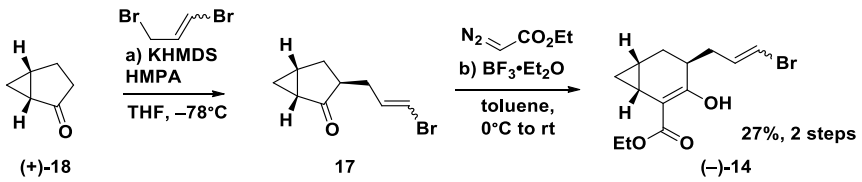
Table S5. Identification of modified proteins by probe **29** in Molt cells. See the accompanying excel spreadsheet.

II: Experimental Procedures and Spectroscopic Data

General Information

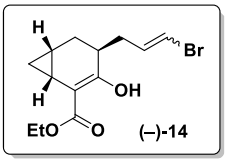
Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF was distilled from sodium-benzophenone, toluene was distilled from sodium, dichloroethane and dichloromethane were distilled from calcium hydride. Yields refer to chromatographically. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by Thin Layer Chromatography on plates (GF254) supplied by Yantai Chemicals (China) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. If not specially mentioned, flash column chromatography uses silica gel (200-300 mesh) supplied by Tsingtao Haiyang Chemicals (China). NMR spectra were recorded on Brüker Advance 500 (1H 500 MHz, 13C 125 MHz) and Brüker Advance 400 (1H 400 MHz, 13C 100 MHz). TMS was used as internal standard for 1H NMR (0.00 ppm), and solvent signal was used as reference for 13C NMR (CDCl3, 77.0 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Mass spectrometric data were obtained using Brüker Apex IV FTMS using ESI (electrospray ionization) and Waters GCT (GC-MS) using EI (electron impact ionization). Infrared spectra were recorded on a Thermo Nicolet iS5 spectrometer.

Synthesis of compound (−)-14



KHMDS (1.0 M in THF, 17.5 mL, 17.5 mmol, 1.04 equiv) was diluted with THF (60 mL) and cooled to −78 °C. Ketone (+)-**18**[2] (1.62 g, 16.9 mmol, 1 equiv) in 10 mL THF was added dropwise over a period of 10 min. After stirred for an additional 1 h at −78 °C, HMPA (6 mL) was added, followed by the rapid addition of 1,3-dibromo-1-propene (5.00 g, 25 mmol, 1.5 equiv). The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution after 10 min. The aqueous layer was extracted with Et_2O (3 x 100 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/50) to give a crude mixture of compound **17** (2.02 g, 9.40 mmol) as a colorless oil.

To a solution of the above crude product **17** in toluene (60 mL) was added $BF_3{\cdot}Et_2O$ (2.32 ml, 18.8 mmol, 2 equiv) at 0 °C. Ethyl diazoacetate (90%, 2.38 g, 18.8 mmol, 2 equiv) in toluene (5 mL) was added dropwise subsequently at the same temperature. After an additional 10 min at 0 °C, the mixture was warmed to room temperature and stirred for 6 h in dark. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and stirred for 30 min. The aqueous layer was extracted with Et_2O (3 x 50 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/100) to give compound **(−)-14** (1.36 g, 4.52 mmol) as a colorless oil in 27% yield (2 steps).



$\mathbf{R}_f$ = 0.75 (EtOAc/PE = 1/10);

$[\alpha]_D^{20}$ = −56.4 (*c* = 0.5, $CHCl_3$);

HRMS-ESI calc. for $C_{13}H_{17}BrNaO_3$ [M + Na^+]: 323.0253; Found: 323.0257;

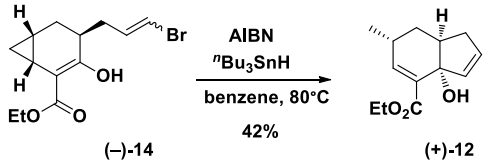
IR (neat, cm^{-1}): 3487, 3071, 2981, 2927, 2861, 1735, 1716, 1644, 1607, 1410, 1371, 1291, 1240, 1200, 1084, 1022, 834, 709, 661;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.30 (d, *J* = 3.0 Hz, 1H), 6.27 – 6.07 (m, 2H), 4.34 – 4.16 (m, 2H), 2.67 – 2.08 (m, 3H), 1.95 – 1.79 (m, 2H), 1.64 – 1.56 (m, 1H), 1.34 (t, *J* = 7.1 Hz,

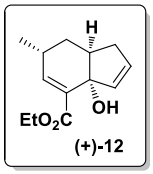
3H), 1.31 – 1.13 (m, 1H), 0.86 (td, *J* = 8.2, 4.5 Hz, 1H), 0.26 (dd, *J* = 9.7, 4.7 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.44, 172.95, 172.88, 135.67, 132.77, 109.42, 105.98, 99.36, 60.47, 60.44, 35.85, 35.79, 34.33, 31.37, 29.70, 27.79, 27.37, 14.34, 14.29, 14.02, 8.88, 8.85, 8.44, 8.38.

Synthesis of compound (+)-12



To a solution of compound **(−)-14** (1.36 g, 4.52 mmol) in benzene (70 mL, degassed with a balloon of N_2 for 30 min) was added dropwise a solution of ^{n}Bu$_3$SnH (2.39 mL, 9.04 mmol, 2 equiv) and 2,2'-Azobis(2-methylpropionitrile) (AIBN, 185 mg, 1.13 mmol, 0.25 equiv) in benzene (5 mL, degassed with a balloon of N_2 for 10 min) at 80 ºC. The reaction mixture was stirred at 80 ºC for 5 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/40 to 1/20) to give compound **(+)-12** (418 mg, 1.88 mmol) as a colorless oil in 42% yield.



R_f = 0.40 (EtOAc/PE = 1/5);

$[\alpha]_D^{20}$ = +5.4 (*c* = 0.59, $CHCl_3$);

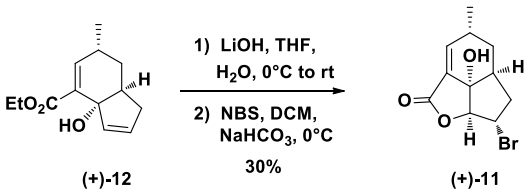
HRMS-ESI calc. for $C_{13}H_{18}NaO_3$ [M + Na^+]: 245.1148; Found: 245.1148;

IR (neat, cm^{-1}): 3529, 3048, 2959, 2925, 2871, 2853, 1691, 1637, 1456, 1370, 1258, 1222, 1085, 1038, 1026, 786, 768, 736;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 2.4 Hz, 1H), 5.98 (dt, *J* = 5.6, 1.8 Hz, 1H), 5.84 – 5.79 (m, 1H), 4.28 – 4.20 (m, 2H), 4.00 (s, 1H), 2.65 – 2.41 (m, 3H), 2.13 (ddt, *J* = 16.4, 7.3, 2.2 Hz, 1H), 1.77 (dt, *J* = 13.5, 4.9 Hz, 1H), 1.62 – 1.56 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.14 (d, *J* = 7.2 Hz, 3H);

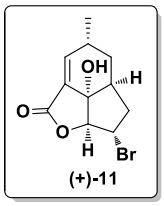
^{13}C NMR (126 MHz, $CDCl_3$) δ 167.64, 146.64, 136.32, 132.73, 132.61, 80.94, 60.75, 43.51, 35.31, 30.80, 27.59, 25.17, 20.28, 14.20.

Synthesis of compound (+)-11



(+)-12 (+)-11

To a solution of compound **(+)-12** (179 mg, 0.805 mmol) in THF/H_2O (3.6 ml/7.2 ml) was added $LiOH{\cdot}H_2O$ (51 mg, 1.21 mmol, 1.5 equiv) at room temperature. The reaction mixture was stirred overnight and then cooled to 0°C, followed by the addition of $NaHCO_3$ (135 mg, 1.61 mmol, 2 equiv) and CH_2Cl_2 (7.2 ml) subsequently. The reaction mixture was stirred at 0°C for 10 min, followed by the addition of NBS (172 mg, 0.97 mmol, 1.2 equiv). After an additional 2 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (3 x 20 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/5) to give compound **(+)-11** (67 mg, 0.245 mmol) as a colorless solid in 30% yield.



R_f = 0.50 (EtOAc/PE = 1/2);

$[\alpha]_D^{20}$ = +94.2 (*c* = 0.22, $CHCl_3$);

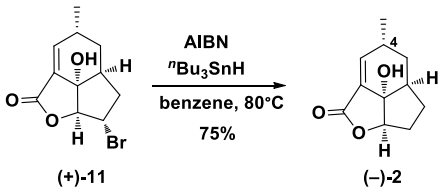
HRMS-EI calc. for $C_{11}H_{13}O_3Br$ [M – e^-]: 272.0048; Found: 272.0052;

IR (neat, cm^{-1}): 3402, 2962, 2925, 2871, 2855, 1750, 1668, 1455, 1337, 1283, 1192, 1076, 1047, 1002, 988, 944, 897;

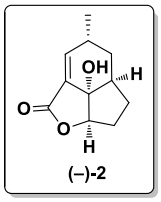
^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (d, *J* = 4.0 Hz, 1H), 5.07 (s, 1H), 4.09 (d, *J* = 6.3 Hz, 1H), 2.95 (dtd, *J* = 13.5, 4.3, 2.9 Hz, 1H), 2.43 (dtd, *J* = 9.7, 6.9, 4.1 Hz, 1H), 2.07 (dd, *J* = 15.0, 6.5 Hz, 1H), 1.97 – 1.85 (m, 2H), 1.74 (ddd, *J* = 14.5, 9.7, 4.5 Hz, 1H), 1.24 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.89, 148.23, 127.37, 94.72, 79.30, 48.54, 39.82, 37.97, 29.37, 27.32, 19.49.

Synthesis of compound (−)-2



To a solution of compound **(+)-11** (4.5 mg, 0.016 mmol) in benzene (1 mL, degassed with a balloon of N_2 for 5 min) was added $^{n}Bu_3SnH$ (22 µL, 0.08 mmol, 5 equiv) and 2,2'-Azobis(2-methylpropionitrile) (AIBN, 4.8 mg, 0.029 mmol, 1.8 equiv). The reaction mixture was stirred at 80 ºC for 5 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/4) to give compound **(−)-2** (2.4 mg, 0.012 mmol) as a colorless solid in 75% yield.



R_f = 0.33 (EtOAc/PE = 1/2);

$[\alpha]_D^{20}$ = +98.4 (*c* = 1.00, $CHCl_3$);

Melting point: 117-119 °C;

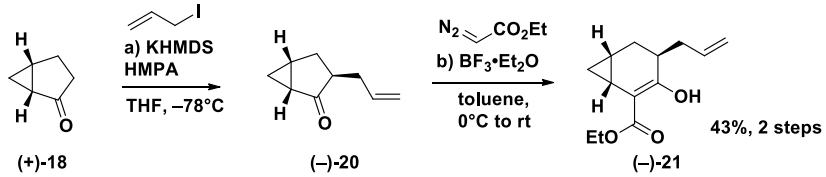
HRMS-ESI calc. for $C_{11}H_{14}NaO_3$ [M + Na^+]: 217.0835; Found: 217.0836;

IR (neat, cm^{-1}): 3421, 2959, 2926, 2873, 2855, 1740, 1669, 1458, 1344, 1240, 1195, 1070, 1017, 971, 901;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.91 (d, *J* = 3.9 Hz, 1H), 4.81 (d, *J* = 7.8 Hz, 1H), 2.41 (m, 3H), 2.12 (ddt, *J* = 15.6, 11.3, 8.8 Hz, 1H), 1.91 (ddd, *J* = 14.6, 6.6, 2.5 Hz, 1H), 1.76 – 1.56 (m, 3H), 1.33 (qd, *J* = 11.8, 8.8 Hz, 1H), 1.22 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.28, 146.92, 128.71, 88.57, 80.36, 41.80, 29.81, 29.09, 28.15, 26.16, 19.54.

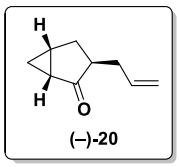
Synthesis of compound (−)-21



KHMDS (1.0 M in THF, 15.4 mL, 15.4 mmol, 1.05 equiv) was diluted with THF (140 mL) and cooled to −78 °C. Ketone (+)-**18** (1.41 g, 14.7 mmol, 1 equiv) in 30 mL THF

was added dropwise over a period of 10 min. After stirred for an additional 1 h at −78 °C, HMPA (7.4 mL) was added, followed by the rapid addition of allyl iodide (11 ml, 117 mmol, 8 equiv). The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution after 10 min. The aqueous layer was extracted with Et_2O (3 x 100 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo* to give a crude mixture of compound **(−)-20** as a colorless oil;

To a solution of the above crude product **(−)-20** in toluene (50 mL) was added $BF_3{\cdot}Et_2O$ (2.7 ml, 22.0 mmol, 1.5 equiv) at 0 °C. Ethyl diazoacetate (90%, 3.5 ml, 22.0 mmol, 1.5 equiv) in toluene (5 mL) was added dropwise subsequently at the same temperature. After an additional 10 min at 0 °C, the mixture was warmed to room temperature and stirred for 5 h in dark. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and stirred for 30 min. The aqueous layer was extracted with Et_2O (3 x 50 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/200 to 1/50) to give compound **(−)-21** (1.40 g, 6.29 mmol) as a colorless oil in 43% yield (2 steps).



R_f = 0.45 (EtOAc/PE = 1/10);

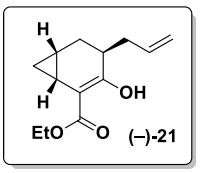
$[\alpha]_D^{20}$ = –53.1 (*c* = 1.37, $CHCl_3$);

HRMS-EI calc. for $C_9H_{12}O$ [M – e^-]: 136.0888; Found: 136.0890;

IR (neat, cm^{-1}): 3076, 2931, 2869, 1719, 1640, 1450, 1307, 1193, 1011, 913, 824, 642;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.72 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.08 – 4.97 (m, 2H), 2.55 – 2.47 (m, 1H), 2.23 (dd, *J* = 12.4, 8.1 Hz, 1H), 2.13 (qd, *J* = 8.9, 4.2 Hz, 1H), 2.04 – 1.88 (m, 2H), 1.81 (tt, *J* = 8.5, 4.7 Hz, 2H), 1.23 – 1.15 (m, 1H), 0.98 (td, *J* = 4.6, 3.3 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.20, 135.93, 116.35, 40.05, 33.84, 29.62, 27.54, 20.08, 14.63.



R_f = 0.70 (EtOAc/PE = 1/30);

$[\alpha]_D^{20}$ = –67.3 (*c* = 1.02, $CHCl_3$);

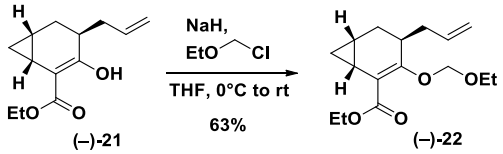
HRMS-ESI calc. for $C_{13}H_{19}O_3$ [M + H^+]: 223.1329; Found: 223.1325;

IR (neat, cm^{-1}): 3073, 2979, 2929, 2863, 1738, 1644, 1605, 1411, 1371, 1345, 1291, 1241, 1200, 1082, 1025, 914, 834;

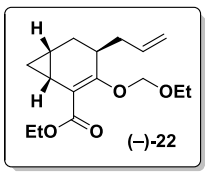
^{1}H NMR (400 MHz, Chloroform-*d*) δ 12.31 (s, 1H), 5.88 – 5.73 (m, 1H), 5.12 – 5.02 (m, 2H), 4.33 – 4.18 (m, 2H), 2.56 – 2.47 (m, 1H), 2.31 (dt, *J* = 13.9, 7.9 Hz, 1H), 2.22 – 2.13 (m, 1H), 1.91 (dt, *J* = 13.5, 6.6 Hz, 1H), 1.78 (ddd, *J* = 13.9, 5.8, 4.3 Hz, 1H), 1.56 (td, *J* = 8.4, 4.7 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.21 – 1.11 (m, 1H), 0.85 (td, *J* = 8.2, 4.4 Hz, 1H), 0.25 (q, *J* = 4.7 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.59, 173.05, 136.46, 116.69, 98.94, 60.36, 36.62, 35.58, 27.62, 14.75, 14.37, 8.67, 8.52.

Synthesis of compound (−)-22



NaH (95%, 175 mg, 6.93 mmol, 1.5 equiv) was diluted with THF (35 mL) and cooled to 0 °C. A solution of **(−)-21** (1030 mg, 4.63 mmol, 1 equiv) in 10 mL THF was added dropwise over a period of 15 min at 0 ºC and the mixture was stirred for 30 min. $EtOCH_2OCl$ (80%, 806 µl, 6.93 mmol, 1.5 equiv) was added to the mixture and the reaction mixture was stirred at room temperature. After 3 h, the reaction mixture was quenched by addition of water at 0 ºC and extracted with Et_2O (3 x 50 mL). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/PE = 1/100 to 1/50) to give compound **(−)-22** (817 mg, 2.91 mmol) as a colorless oil in 63% yield.



R_f = 0.50 (EtOAc/PE = 1/10);

$[\alpha]_D^{20}$ = –6.0 (*c* = 1.15, $CHCl_3$);

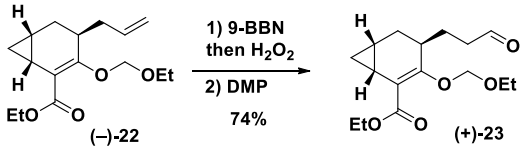
HRMS-ESI calc. for $C_{16}H_{24}NaO_4$ [M + Na^+]: 303.1567; Found: 303.1564;

IR (neat, cm^{-1}): 3073, 2977, 2930, 2905, 1712, 1619, 1445, 1392, 1366, 1277, 1244, 1200, 1152, 1104, 1071, 1021, 984, 916;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.64 – 5.52 (m, 1H), 4.91 – 4.72 (m, 4H), 3.98 (qq, *J* = 7.1, 3.8 Hz, 2H), 3.48 (q, *J* = 7.1 Hz, 2H), 2.30 – 2.22 (m, 1H), 2.15 – 2.02 (m, 2H), 1.90 (ddd, *J* = 14.1, 7.9, 3.7 Hz, 1H), 1.33 (m, 2H), 1.07 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H), 0.91 (tdd, *J* = 8.2, 5.3, 2.9 Hz, 1H), 0.76 (td, *J* = 8.3, 4.1 Hz, 1H), 0.01 (q, *J* = 4.7 Hz, 1H);

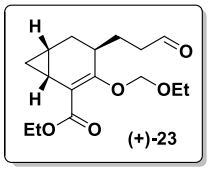
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.07, 166.66, 136.55, 116.68, 112.01, 95.07, 64.75, 59.97, 36.66, 36.42, 29.32, 18.64, 15.05, 14.35, 12.28, 8.09.

Synthesis of compound (+)-23



To a solution cooled at 0 ºC, containing compound **(−)-22** (640 mg, 2.28 mmol, 1 equiv) in THF (7 mL) under N_2, was added a solution of 9-BBN (0.5 M in THF, 13.7 ml, 6.84 mmol, 3 equiv), and the reaction mixture was stirred at room temperature for 4 h. After cooling the mixture to 0 ºC, ethanol (5 mL) and a solution of 6 M NaOH (2.5 mL) were added followed by the addition of H_2O_2 (30%, 1.6 mL). The mixture was left under stirring at 0 °C for 3 h. The mixture was then extracted with Et_2O (3×20 mL) and dried over Na_2SO_4. The solution was filtered, and concentrated *in vacuo* to give a crude mixture of alcohol;

To a solution of the above crude product in dry DCM (30 mL) was added $NaHCO_3$ (766 mg, 9.12 mmol, 4 equiv) and DMP (1.45 g, 3.42 mmol, 1.5 equiv) at 0 °C. The mixture was stirred at room temperature for 3 h and quenched with saturated aqueous $NaHCO_3$ solution. The reaction mixture was extracted with CH_2Cl_2 (3×50 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/PE = 1/6) to give compound **(+)-23** (500 mg, 1.69 mmol) as a colorless oil in 74% yield (2 steps).



R_f = 0.20 (EtOAc/PE = 1/5);

$[\alpha]_D^{20}$ = +21.5 (*c* = 1.15, $CHCl_3$);

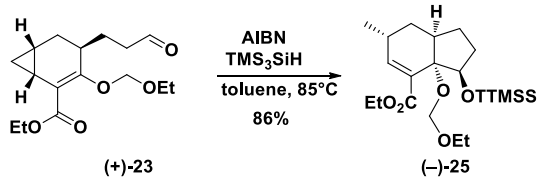
HRMS-ESI calc. for $C_{16}H_{24}NaO_5$ [M + Na^+]: 319.1521; Found: 319.1517;

IR (neat, cm^{-1}): 2977, 2929, 2902, 2866, 1712, 1697, 1627, 1447, 1391, 1247, 1200, 1150, 1104, 1073, 1019, 958, 916, 845, 787;

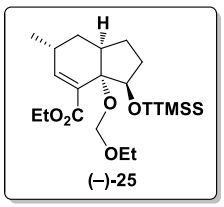
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.81 (s, 1H), 5.01 (dd, *J* = 42.9, 6.8 Hz, 2H), 4.21 (qq, *J* = 7.3, 3.8 Hz, 2H), 3.70 (q, *J* = 7.1 Hz, 2H), 2.67 – 2.49 (m, 2H), 2.33 (dq, *J* = 9.7, 4.9 Hz, 1H), 2.07 (ddd, *J* = 12.4, 7.7, 4.4 Hz, 2H), 1.92 (td, *J* = 14.4, 8.1 Hz, 1H), 1.60 (td, *J* = 8.5, 4.9 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.02 (td, *J* = 8.3, 4.2 Hz, 1H), 0.26 (q, *J* = 4.6 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.06, 166.90, 166.23, 112.80, 95.49, 64.90, 60.06, 41.73, 36.00, 30.17, 24.59, 19.00, 15.03, 14.33, 12.36, 8.18.

Synthesis of compound (−)-25



To a solution of compound **(+)-23** (180 mg, 0.609 mmol, 1 equiv) in toluene (15 ml, degassed with a balloon of N_2 for 10 min) was added dropwise a solution of TMS_3SiH (376 μL, 1.22 mmol, 2 equiv) and 2,2'-Azobis(2-methylpropionitrile) (AIBN, 25 mg, 0.152 mmol, 0.25 equiv) in toluene (5 ml, degassed with a balloon of N_2 for 5 min) at 85 ºC. The reaction mixture was stirred at the same temperature for 10 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/100 to 1/50) to give compound **(−)-25** (285 mg, 0.523 mmol) as a colorless oil in 86% yield.



R_f = 0.50 (EtOAc/PE = 1/20);

$[\alpha]_D^{20}$ = −45.0 (*c* = 0.81, $CHCl_3$);

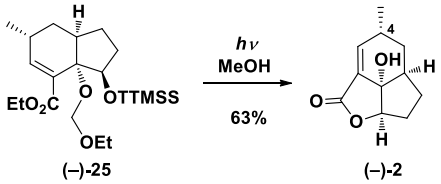
HRMS-ESI calc. for $C_{25}H_{52}NaO_5Si_4$ [M + Na^+]: 567.2784; Found: 567.2768;

IR (neat, cm^{-1}): 2948, 2893, 2873, 1721, 1456, 1392, 1244, 1222, 1100, 1064, 1033, 956, 835, 743, 687, 624;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 5.3 Hz, 1H), 4.65 – 4.55 (dd, *J* = 18.8, 7.4 Hz, 2H), 4.37 (d, *J* = 3.4 Hz, 1H), 4.21 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.10 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.59 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.47 (dq, *J* = 9.5, 7.1 Hz, 1H), 2.62 – 2.47 (m, 1H), 2.36 (m, 1H), 2.12 – 1.92 (m, 3H), 1.75 – 1.66 (m, 1H), 1.44 – 1.35 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.17 – 1.10 (m, 6H), 0.15 (s, 27H);

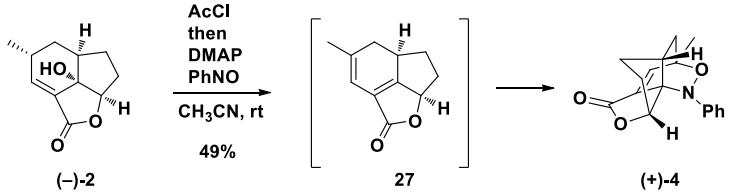
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.86, 150.13, 129.07, 89.88, 88.43, 82.71, 62.94, 59.42, 36.35, 34.84, 31.27, 29.34, 28.18, 18.52, 14.65, 13.86, 0.00.

Synthesis of compound (−)-2



A stirred solution of compound **(−)-25** (248 mg, 0.455 mmol, 1 equiv) in CH_2Cl_2 (2.5 mL) and MeOH (2.5 mL) in a quartz flask was placed upon a portable UV analyzer (254nm, 6W) at room temperature and irradiated for 9 h. After additional 12 h without irradiation, the reaction mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel (EtOAc/PE = 1/10 to 1/4) to give compound **(−)-2** (56 mg, 0.288 mmol) as a colorless solid in 63% yield.

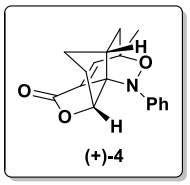
Synthesis of compound (+)-4[3]



Acetyl chloride (140 µL, 2.0 mmol, 35 equiv) was added dropwise to a solution of **(−)-2** (11 mg, 0.057 mmol, 1 equiv) in dry acetonitrile (1 mL) at room temperature. The

reaction mixture was stirred for an additional 3 h and concentrated *in vacuo* to give a crude mixture of compound **27**;

DMAP (7 mg, 0.057 mmol, 1 equiv) was added to the above crude product **27** and nitrosobenzene (61 mg, 0.57 mmol, 10 equiv) in dry acetonitrile (1 mL) at room temperature. The reaction mixture was stirred for an additional 1 h and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (EtOAc/PE = 1/100 to 1/4) to give compound **(+)-4** (7.9 mg, 0.028 mmol) as a colorless oil in 49% yield.



(+)-4

R_f = 0.40 (EtOAc/PE = 1/2);

$[\alpha]_D^{20}$ = +38.8 (*c* = 0.69, $CHCl_3$);

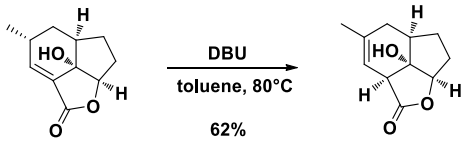
HRMS-ESI calc. for $C_{17}H_{18}NO_3$ [M + H^+]: 284.1281; Found: 284.1283;

IR (neat, cm^{-1}): 2957, 2922, 2851, 1762, 1665, 1593, 1485, 1309, 1213, 1143, 1093, 1015, 975, 761, 701;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (s, 1H), 7.25 – 7.19 (m, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.99 – 6.93 (m, 2H), 5.26 (d, *J* = 6.7 Hz, 1H), 2.70 – 2.60 (m, 1H), 2.33 (dd, *J* = 12.9, 8.9 Hz, 1H), 2.26 – 2.03 (m, 2H), 1.93 (dt, *J* = 12.8, 6.3 Hz, 1H), 1.70 (s, 3H), 1.35 (dd, *J* = 12.9, 5.2 Hz, 1H), 1.05 (qd, *J* = 12.8, 6.5 Hz, 1H);

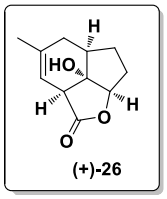
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.61, 148.01, 140.05, 130.31, 128.53, 125.66, 121.05, 82.49, 77.12, 76.02, 41.00, 39.01, 34.38, 29.74, 21.27.

Synthesis of compound (+)-26



(–)-2 (+)-26

To a solution of compound **(−)-2** (12.6 mg, 0.065 mmol) in toluene (1 mL) was added DBU (48 μL, 0.324 mmol, 5 equiv). The reaction mixture was stirred at 80 ºC for 7 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel ((EtOAc/PE = 1/3 to 1/2) to give compound **(+)-26** (7.8 mg, 0.040 mmol) as a colorless oil in 62% yield;



R_f = 0.33 (EtOAc/PE = 1/2);

$[\alpha]_D^{20}$ = +68.0 (*c* = 0.5, $CHCl_3$);

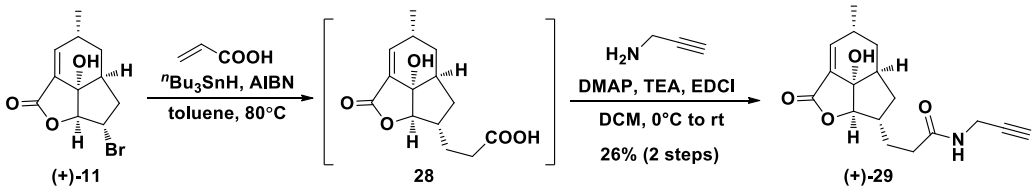
HRMS-ESI calc. for $C_{11}H_{14}NaO_3$ [M + Na^+]: 217.0835; Found: 217.0838.

IR (neat, cm^{-1}): 3426, 2965, 2924, 2853, 1765, 1743, 1439, 1190, 1071, 1016, 996, 984;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.59 (s, 1H), 4.77 (d, *J* = 5.0 Hz, 1H), 3.18 (q, *J* = 3.1 Hz, 1H), 2.42 – 2.30 (m, 1H), 2.19 (dt, *J* = 12.9, 6.4 Hz, 1H), 1.98 – 1.86 (m, 3H), 1.77 (s, 3H), 1.71 – 1.63 (m, 1H), 1.46 (qd, *J* = 12.7, 6.8 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.84, 133.51, 113.22, 90.80, 82.23, 48.13, 45.38, 31.29, 28.57, 28.47, 23.81.

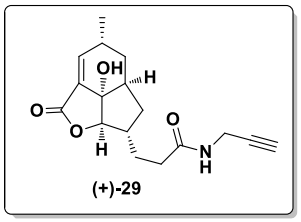
Synthesis of compound (+)-29



To a solution of compound **(+)-11** (20 mg, 0.073 mmol) and acrylic acid (50 µl, 0.73 mmol, 10 equiv) in toluene (4 mL, degassed with a balloon of N_2 for 10 min) was added dropwise a solution of ^{n}Bu_3SnH (39 µl, 0.146 mmol, 2 equiv) and 2,2'-Azobis(2-methylpropionitrile) (AIBN, 6 mg, 0.036 mmol, 0.5 equiv) in toluene (2 mL, degassed with a balloon of N_2 for 10 min) at 80 ºC for 2h. Subsequently, the reaction mixture was stirred at the same temperature for an additional 3 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (MeOH/CH_2Cl_2 = 1/20 to 1/10) to give a crude mixture of compound **28** (20 mg) as a colorless oil.

To a solution of the above crude product **28** (20 mg) in CH_2Cl_2 (2 mL) was consecutively added Et_3N (42µl, 0.30 mmol, 4 equiv), 2-propynylamine (10µl, 0.15 mmol, 2 equiv), DMAP (1.8 mg, 0.015 mmol, 0.2 equiv), EDC·HCl (29 mg, 0.15 mmol, 2 equiv). The reaction mixture was stirred at room temperature for 3 h, quenched by MeOH and then concentrated *in vacuo.* The residue was purified by PTLC on silica gel (MeOH/CH_2Cl_2 = 1/15) to give compound **(+)-29** (5.8 mg, 0.019 mmol) as a colorless oil in 26% yield (2

steps).



$\mathbf{R_f}$ = 0.55 (EtOAc);

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ = +58.8 (*c* = 0.25, $CHCl_3$);

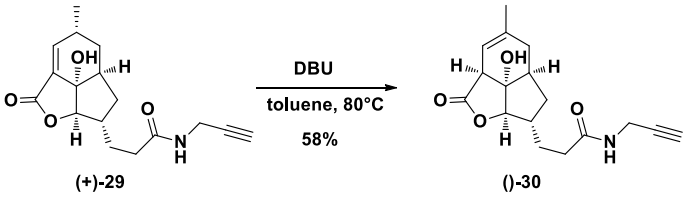
HRMS-ESI calc. for $C_{17}H_{22}NO_4$ [M + H^+]: 304.1543; Found: 304.1547;

IR (neat, cm^{-1}): 3289, 2958, 2925, 2872, 2854, 1747, 1648, 1541, 1454, 1236, 1200, 1077, 1004, 753;

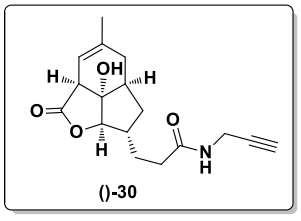
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.95 (d, *J* = 4.1 Hz, 1H), 5.81 (s, 1H), 4.42 (d, *J* = 2.3 Hz, 1H), 4.04 (ddd, *J* = 5.3, 2.6, 1.3 Hz, 2H), 2.50 (m, 2H), 2.35 – 2.19 (m, 2H), 2.23 (t, *J* = 2.5 Hz, 1H), 1.87 – 1.75 (m, 4H), 1.65 (ddd, *J* = 14.6, 9.3, 4.8 Hz, 1H), 1.58 (m, 3H), 1.50 (ddd, *J* = 11.3, 8.2, 4.4 Hz, 1H), 1.22 (d, *J* = 7.2 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.76, 169.67, 147.25, 129.00, 93.31, 80.47, 79.44, 71.68, 42.59, 39.31, 34.31, 32.24, 30.29, 29.36, 29.27, 29.05, 19.36.

Synthesis of compound (+)-30



To a solution of compound **(+)-29** (5.2 mg, 0.017 mmol) in toluene (1 mL) was added DBU (13 μL, 0.085 mmol, 5 equiv). The reaction mixture was stirred at 80 ºC for 9 h and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (MeOH/CH_2Cl_2 = 1/40) to give compound **(+)-30** (3.0 mg, 0.010 mmol) as a colorless oil in 58% yield.



$\mathbf{R_f}$ = 0.35 (MeOH/CH_2Cl_2 = 1/20);

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ = +34.0 (*c* = 0.20, $CHCl_3$);

HRMS-ESI calc. for $C_{17}H_{22}NO_4$ [M + H^+]: 304.1543; Found: 304.1546;

IR (neat, cm^{-1}): 3288, 2919, 2850, 1750, 1647, 1540, 1454, 1379, 1339, 1262, 1245, 1184, 1072, 1014, 915;

^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.81 (s, 1H), 5.59 (s, 1H), 4.44 (s, 1H), 4.05 (dt, *J* = 4.9, 2.3 Hz, 2H), 3.19 (dt, *J* = 4.6, 2.5 Hz, 1H), 2.47 (dtd, *J* = 9.7, 6.4, 2.9 Hz, 1H), 2.33 (m, 3H), 2.25 (t, *J* = 2.6 Hz, 1H), 2.03 – 1.80 (m, 4H), 1.77 (s, 3H), 1.72 – 1.61 (m, 2H), 1.55 (dd, *J* = 12.9, 6.4 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.14, 172.25, 134.36, 113.93, 94.41, 82.89, 79.21, 71.85, 48.44, 43.47, 42.66, 34.17, 34.08, 29.38, 29.16, 27.27, 23.82.

III. Procedures of Biological Assays

1. General Information

Human cell lines MOLT-4, Jurkat and SK-N-SH were obtained from Cell Resource Center, Peking Union Medical College (the headquarter of National Infrastructure of Cell Line Resource, NSTI) and checked free of mycoplasma contamination by PCR and culture. MOLT-4 and Jurkat cells were cultured at 37 °C under 5% CO_2 in RPMI medium 1640 (Gibco) containing 10% FBS(PVN) and 1% PS (Gibco). SK-N-SH cells were maintained in DMEM containing 10% FBS and 1% PS. For Western Blotting experiments, the samples were run on tris-glycine gels and transferred to polyvinylidene fluoride. The blots were blocked with 5% BSA in TBST, probed with primary antibody (1:10000 in TBST, Cell Signaling Technology, Danvers, MA) overnight at 4 °C, washed with TBST, incubated with the second antibody (1:10000, Cell Signaling Technology, Danvers, MA) for 1 h at room temperature, washed again in TBST, and visualized using Chemi system (Bio-Red) after treated with Enhanced chemiluminescent reagent.

2. Activity of synthesized galiellalactone analogues against cell proliferation

The functional activity of galiellalactone analogues were evaluated using CellTiter 96® AQueous One Solution Cell Proliferation Assay (MTS, Promega) on MOLT-4 and Jurkat cells. Cells were cultured in 96-well plates (3000 cells/well in 50 µl of medium) and allowed to set for 24 h. The cells were treated with 0-100 µM galiellalactone or analogues for 72 h. Samples were made in triplicate. 20 µl MTS solution was added per well and incubated at 37°C for 3 h. The absorbance of each well was measured using a scanning multi-well spectrophotometer at 490 nm. The results are presented as percent of untreated control cells.

3. In-*situ* Proteome labelling

Cells (2×10^7/sample) were subjected to Probe **29**, 4-*epi*-galiellalatone (**2**) or galiellalactone (**1**) (different concentrations in 10 mL complete medium) for 2 h at 37 °C under 5% CO_2, and washed with PBS (3 x 10 mL). Cell pellets were re-suspended in 0.1% NP-40 containing complete protease inhibitors (Roche), sonicated and separated into soluble and insoluble fractions by ultracentrifugation at 210,000g for 30 min. The soluble

protein concentration was determined using the BCA protein assay on a microplate reader and diluted with PBS into 1 mg/mL.

For in-gel fluorescence analysis, 40 μL of the solution was mixed with 20 μM rhodamine-azide, 1 mM Tris(2-carboxyethyl)phosphine (TCEP, Sigma-Aldrich), 100 μM Tris((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)amine (TBTA) (Sigma-Aldrich), and 1 mM $CuSO_4$ in PBS at room temperature (~25 °C). After 1 h, samples were mixed with SDS sample loading buffer and loaded with boiling by 10% SDS-PAGE. The results were visualized by fluorescent scanning using a Bio-RAD ChemiDocMP Imager.

For Western Blotting analysis, 80 μL sample as input samples in each set of experiments, the re-suspended proteome was combined with 500 μM biotin-azide, 100 μM TBTA, 1 mM TCEP, and 1 mM $CuSO_4$ in 2.88 ml PBS for 1 h. After this reaction, the proteomes were extracted with chloroform-methanol to remove redundant reagents. The protein interphase was then washed with cold methanol, then solubilized with PBS (1.2% SDS) and diluted with 5x PBS. Streptavidin beads (Thermo Fisher Scientific) (200 μL of slurry) were added and rotated at room temperature for 3 h. The solutions were centrifuged at 1400 g for 3 min and removed the supernatant. We washed the beads by adding 5 mL of 0.2% SDS/PBS, placed on a rotator for 10 min, then centrifuged at 1400 g for 3 min and remove the supernatant. Then we repeated the PBS and water washes three times. Then SDS loading buffer was added to the beads for heating at 90 °C for 5-10 min. The samples were separated by SDS-PAGE and immunoblotted with STAT3 and p-STAT3 antibodies.

For proteomic analysis, in each set of experiments, the re-suspended proteome was combined with 500 μM photocleavable biotin-azide, 100 μM TBTA, 1 mM TCEP, and 1 mM $CuSO_4$ in 3 ml PBS for 1 h. Following pull-down protocol by streptavidin beads as mentioned above. Beads in 200 μL water were radiated with UV light at 365nm for 2 h. The supernatants were dried by centrifugation and separated by SDS-PAGE. The results were visualized by Ag staining. Furthermore, the supernatants were dried by centrifugation. Then the samples were denatured in 8 M urea (150 μL of 100mg urea in PBS was added), reduced by 10 mM of dithiothreitol for 30 min at room temperature (10 μL of 200 mM stock in water was added) and alkylated by 10 mM iodoacetamide for 30 min at room temperature in dark (20 μL of 100 mM stock in water was added). The samples were diluted

with ammonium bicarbonate (25 mM, 460 µL) to 2 M urea and subjected to trypsin digestion (Promega; 4 µL of 0.5 µg/µL) overnight at 37 °C in the presence of 2 mM $CaCl_2$. Digested peptide samples were desalted and re-solubilized in 50uL Buffer A (95% water, 5% acetonitrile, 0.1% formic acid). 25 µL of each sample was analyzed by LC-MS/MS on a Ultimate 3000 LC system coupled with Q-Exactive Orbitrap mass spectrometer (Thermo Scientific Inc.). Peptides were eluted from the C18 column using a 75 min gradient of 96.3%-0 Buffer B (80% acetonitrile, 20% water, 0.1% formic acid) and 3.7%-100% Buffer C (95% water, 5% acetonitrile, 0.1% formic acid, 500mM ammonium acetate). The flow rate through the column was 5 µL/min and the spray voltage was 2.0 kV. The QE-Orbitrap was operated in data-dependent scanning mode, with one full MS scan (400–1800 m/z) in the orbitrap followed by MS/MS scans of the 20 most abundant ions using the linear ion trap with dynamic exclusion enabled. The MS data was analyzed by Mascot v2.3.02 using a SwissProt database. Modification of $C_{20}H_{29}N_5O_4$ on cysteine (C) was identified.

IV. Cartesian Coordinates of Various Michael Acceptors

Acrylamide

G_{gas} = -247.237836 a.u.

C	1.93852900	0.11150400	-0.12307000
C	0.84652600	-0.60137000	0.16501600
H	2.93343800	-0.31527600	-0.03172800
H	1.88538600	1.13384500	-0.48955500
H	0.92177000	-1.64033400	0.47461600
C	-0.56599600	-0.13198600	0.02225700
O	-1.48410000	-0.92823200	-0.12362400
N	-0.76464700	1.23067700	0.01905800
H	-1.73140200	1.52747000	0.04133000
H	-0.09821800	1.83652500	0.47571300

Butenone

G_{gas} = -231.173628 a.u.

C	-1.94259100	0.17216900	-0.00004100
C	-0.87639700	-0.63520700	-0.00005000
H	-2.95399900	-0.22483100	-0.00008500
H	-1.85226100	1.25518900	0.00001200
H	-0.99345400	-1.71685900	-0.00010400
C	0.54461300	-0.18920200	0.00000700
O	1.43591500	-1.02488100	-0.00001200
C	0.85824300	1.29848600	0.00008000
H	0.43374800	1.78972700	-0.88348700
H	0.43370700	1.78964900	0.88367200
H	1.94173400	1.42869700	0.00011100

Methyl Acrylate

G_{gas} = -306.401233 a.u.

C	2.17462900	-0.76423900	-0.00005900
C	1.49032600	0.38241900	0.00003900
H	3.26097500	-0.77102800	-0.00003600
H	1.67105400	-1.72556900	-0.00016500
H	1.98842900	1.34752900	0.00014600
C	0.01041600	0.48490800	0.00000700
O	-0.58829300	1.54273700	0.00013100
O	-0.60555200	-0.72039900	-0.00005100
C	-2.03976400	-0.67181400	-0.00005700
H	-2.36784200	-1.71179000	-0.00044200
H	-2.40775800	-0.15308000	0.88936300
H	-2.40773700	-0.15240600	-0.88908600

Acrolein

G_{gas} = -191.876602 a.u.

C	-1.76427600	0.14024400	0.00000200
C	-0.56269300	-0.44829800	-0.00002900
H	-2.69005100	-0.42730600	-0.00001400
H	-1.85840700	1.22481700	0.00004400
H	-0.44331100	-1.52928700	-0.00007000
C	0.67718700	0.35093300	-0.00001100
O	1.79658500	-0.12235600	0.00002200
H	0.51778600	1.45335300	0.00009200

H_2

G_{gas} = -1.176812 a.u.

H	0.00000000	0.00000000	0.37121700
H	0.00000000	0.00000000	-0.37121700

Compound 9

G_{gas} = -654.254864 a.u.

H	-3.77903100	-0.78577700	0.81234100
C	-3.12250400	-0.49783000	-0.01427000
H	-3.74685400	0.03757100	-0.74058700
C	0.58313200	0.45038700	0.07554800
C	1.87036800	-0.29203400	0.03987700
O	2.93717700	0.47281500	-0.27330200
O	1.97751500	-1.49101500	0.26655200
C	-2.45813700	-1.73742300	-0.66868100
H	-2.99203100	-2.08132700	-1.56084200
H	-2.43235500	-2.56700900	0.04357100
C	-1.01958300	-1.29008700	-0.97300000
H	-0.31447400	-2.11872200	-1.09014100
C	-0.67168100	-0.40323600	0.24549400
C	-1.92906800	1.76023300	-0.29012300
H	-1.91415800	1.56650800	-1.37183600
H	-2.85025600	2.32140600	-0.08968200
C	-1.96335900	0.42523200	0.46732000
H	-2.03675000	0.62981500	1.54172900
C	0.56203900	1.79358400	0.02949700
H	1.50300100	2.33396200	-0.03671000

C	-0.70249900	2.60106600	0.07843300
H	-0.81235000	3.02116000	1.09159100
H	-0.60996300	3.46880200	-0.58845800
O	-0.53639800	-1.22267200	1.41474300
H	0.26747200	-1.75480400	1.26342400
H	-0.98249400	-0.69013500	-1.89259100
C	4.20331000	-0.20533600	-0.28513400
H	4.42157200	-0.63198000	0.69740600
H	4.20210400	-1.00713400	-1.02807300
H	4.93809700	0.55729900	-0.54485300

Compound 10

G_{gas} = -655.455211 a.u.

H	3.27430000	-1.47634900	-0.79835700
C	3.01450800	-0.76295400	-0.01194900
H	3.94277400	-0.27792900	0.31193500
C	-0.58075000	0.48626900	-0.53032900
C	-1.87518800	-0.26659700	-0.24869000
O	-2.83920900	0.50572600	0.28215000
O	-2.05390800	-1.44909300	-0.49712900
C	2.28905400	-1.49759700	1.15467600
H	2.71427100	-1.23317400	2.12872400
H	2.39476200	-2.58106000	1.04848000
C	0.79825300	-1.07570100	1.06907900
H	0.10916800	-1.91511700	1.20214700
C	0.64430300	-0.45533300	-0.34020800
C	2.07401700	1.61591600	0.16817000

H	2.12097400	1.45558500	1.25526500
H	3.01328400	2.11358700	-0.10536600
C	1.99604500	0.26154200	-0.55863000
H	2.13145400	0.42710200	-1.63492300
C	-0.44881100	1.83298100	0.20360900
H	-0.50309700	1.67513100	1.28877000
C	0.87690200	2.51850300	-0.15261700
H	0.88101500	2.76736600	-1.22418800
H	0.95922600	3.46948700	0.38851600
O	0.60139900	-1.49346100	-1.32083500
H	-0.26505900	-1.92668000	-1.20253100
H	0.55992400	-0.33774000	1.84528900
C	-4.09856300	-0.14760500	0.52661900
H	-4.51478300	-0.53558400	-0.40645700
H	-3.96978600	-0.97411800	1.22976800
H	-4.74648900	0.62083000	0.94848900
H	-1.29645000	2.47536000	-0.05510600
H	-0.61036300	0.69138700	-1.61232000

Compound 7

G_{gas} = -613.775430 a.u.

C	0.13786300	0.35904500	0.76970100
C	1.45403400	0.80032200	0.12422500
C	2.45519000	-0.37035600	0.12526600
C	1.91647600	-1.67011300	-0.51830300
C	0.42592900	-1.83785300	-0.42323900
C	-0.36234400	-0.91223700	0.13497900

C	-0.95732500	1.35442700	0.30831400
C	-0.34452100	2.10440900	-0.89665800
C	0.99237300	1.38559000	-1.22762700
H	3.38881900	-0.07915200	-0.37002800
H	2.16387700	-1.70505100	-1.59077200
H	-0.03149100	-2.68389800	-0.93553200
H	-1.27223200	2.02425900	1.11078000
H	-0.14509600	3.14057700	-0.60052300
H	0.82371200	0.58491800	-1.95678200
H	2.42745400	-2.54210600	-0.08676300
H	2.70372200	-0.56990400	1.17367300
H	1.87103800	1.61015400	0.73830700
H	1.73197700	2.06589200	-1.66230700
H	-1.04187000	2.13610400	-1.73882000
C	-1.81885800	-0.77633600	-0.12668600
O	-2.63395300	-1.61300700	-0.42748100
O	-2.12568800	0.55792000	-0.03398600
O	0.30900300	0.26494100	2.18120300
H	-0.40771100	-0.28201800	2.54104200

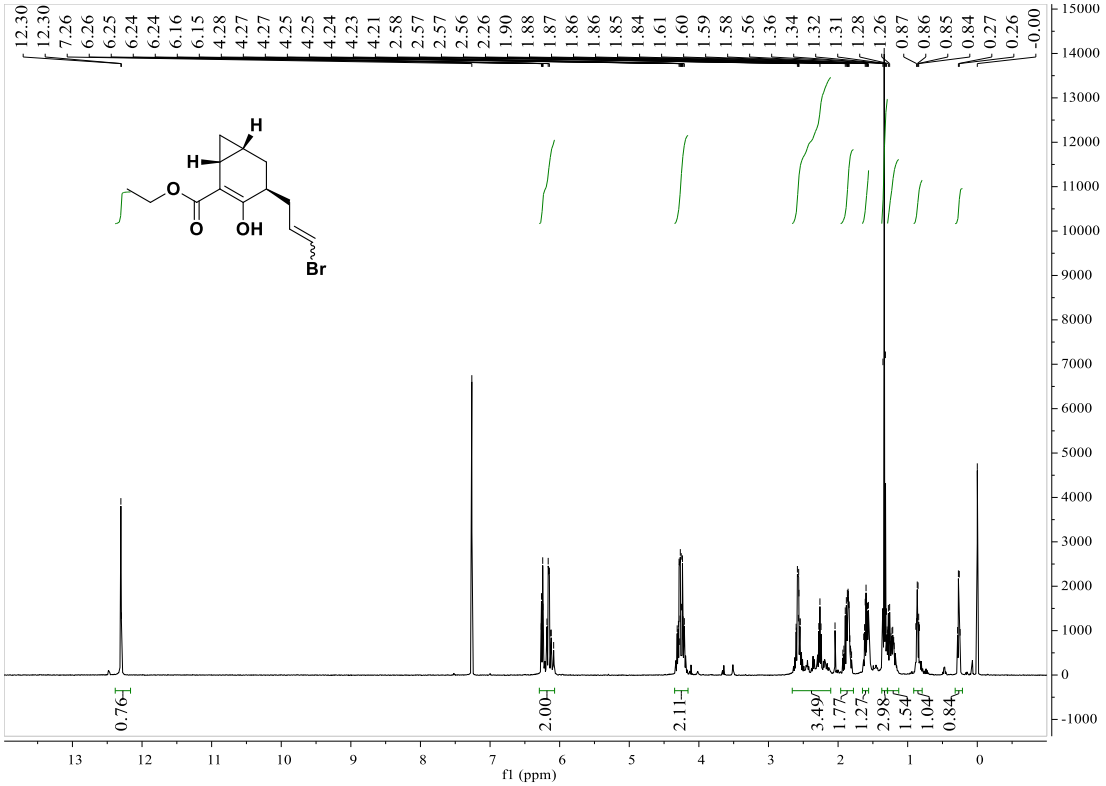
Compound 8

G_{gas} = -614.982053 a.u.

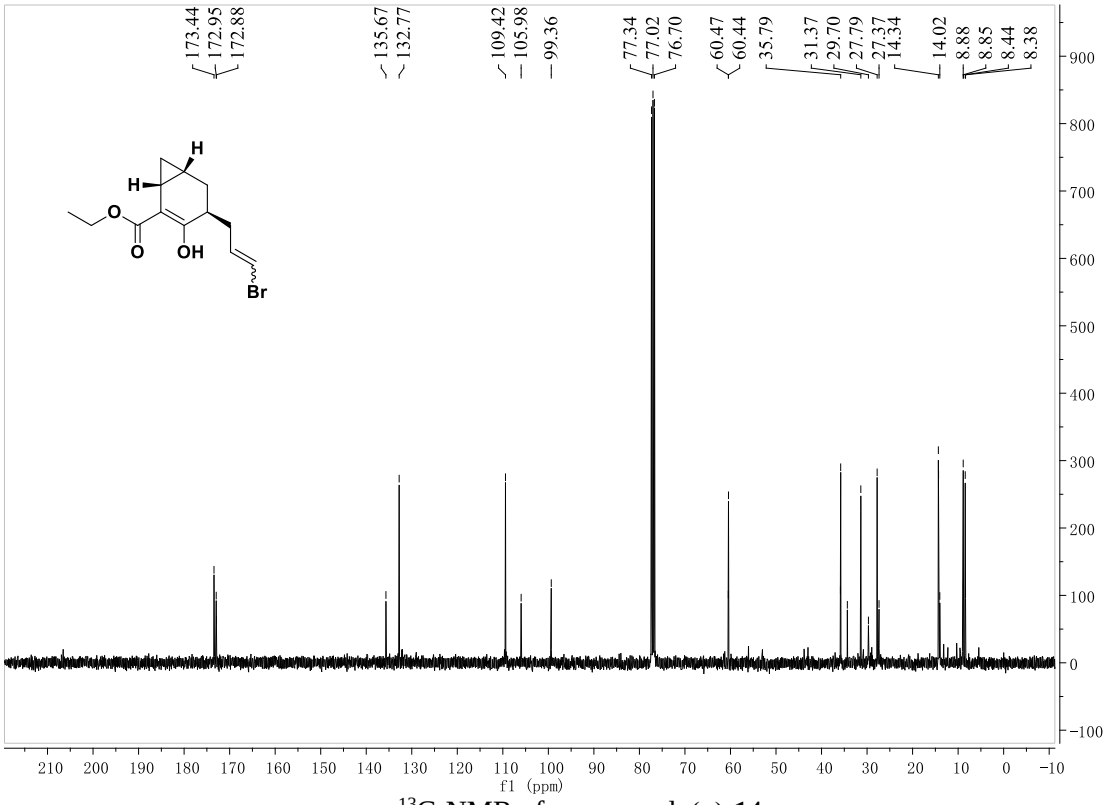
C	0.45431800	-0.23748300	0.84362600
C	0.61631600	-1.41853800	-0.16436100
C	-0.68352800	-2.16445300	-0.50988800
C	-1.86287000	-1.22520400	-0.79432300
C	-2.13703300	-0.33015800	0.41877800

C	-0.90295600	0.49591100	0.80092000
C	1.46401300	0.85253100	0.34723200
C	2.34815200	0.17914200	-0.69901800
C	1.39638800	-0.83034200	-1.36043200
H	-0.50051900	-2.82544400	-1.36685300
H	-1.65831200	-0.60065800	-1.67479000
H	-2.96347200	0.36034100	0.21916800
H	2.01371800	1.32624600	1.16753900
H	3.16400500	-0.34728500	-0.18768000
H	0.72686100	-0.31397100	-2.05971200
H	-2.75802100	-1.81164200	-1.03328600
H	-0.95273700	-2.81568500	0.33278700
H	1.29012000	-2.11853500	0.34516200
H	1.91943400	-1.60764900	-1.92699500
H	2.78997700	0.90516900	-1.38783900
C	-0.66403100	1.67507800	-0.13983500
O	-1.49034800	2.37491400	-0.66697900
O	0.67147900	1.87641200	-0.30422300
O	0.77322200	-0.75945400	2.12924300
H	0.62032900	-0.06244700	2.78797300
H	-1.07284500	0.95206900	1.79002800
H	-2.42597700	-0.95439100	1.27397300

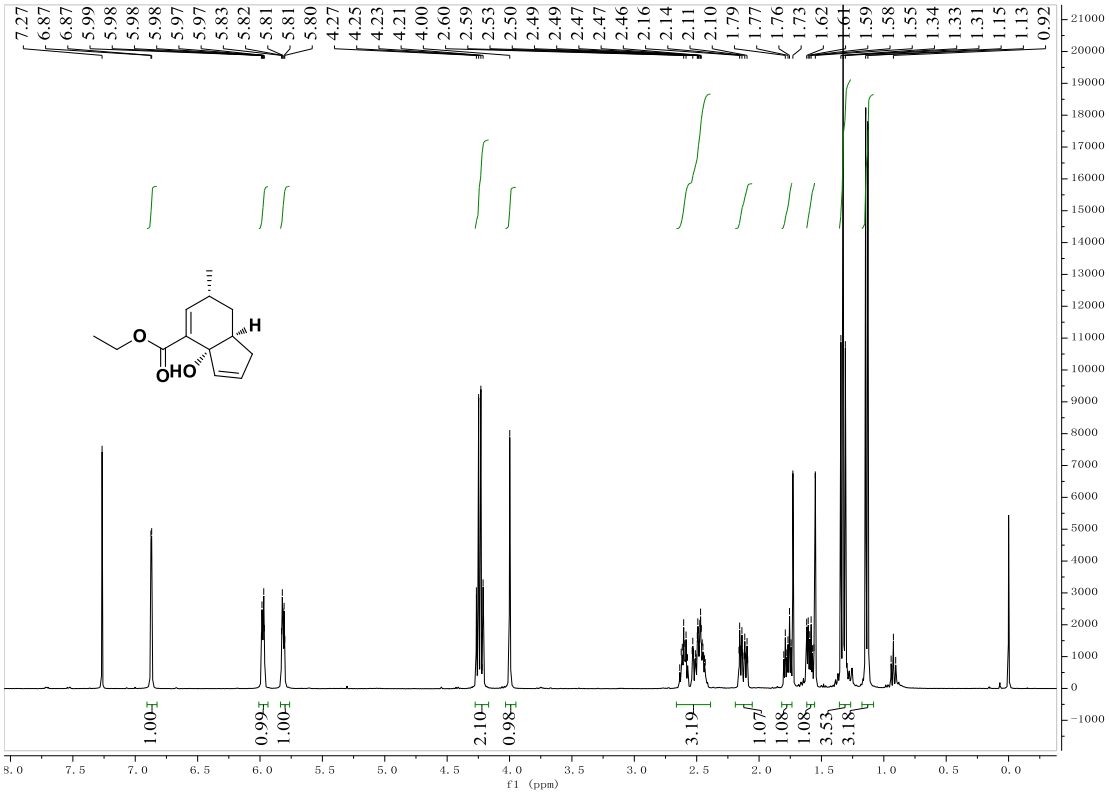
V: ^{1}H, and ^{13}C NMR Spectra of Compounds



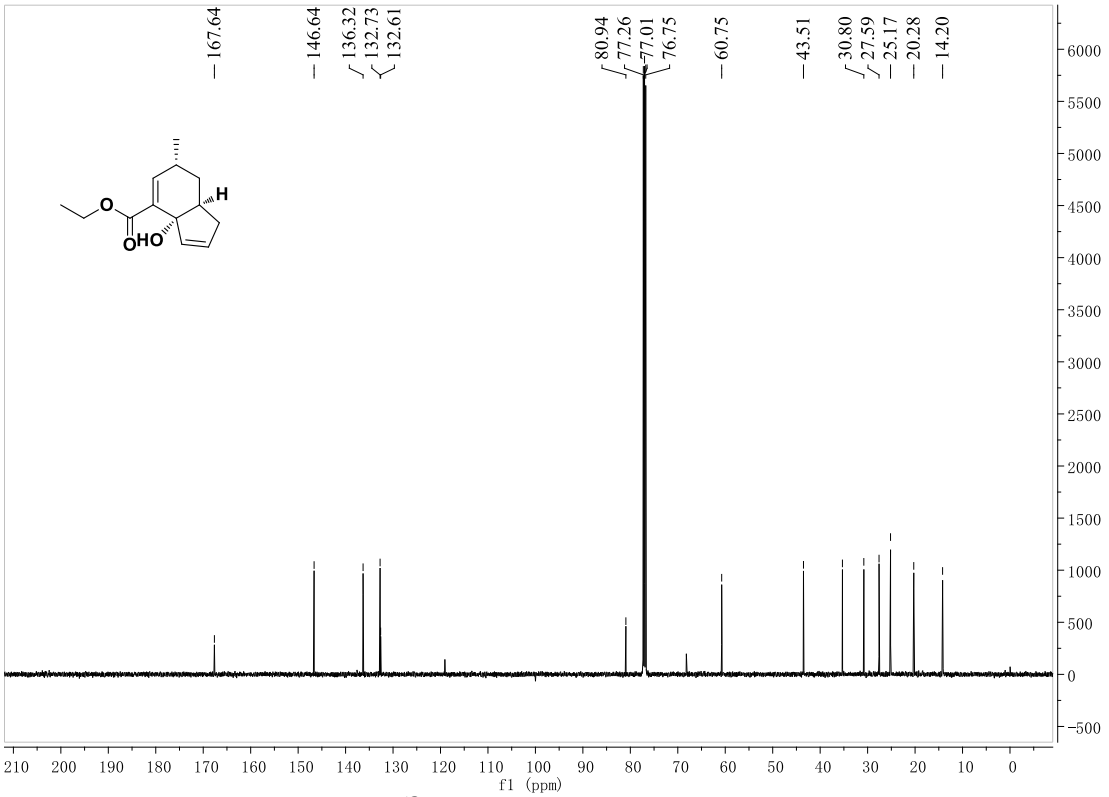
^{1}H-NMR of compound **(−)-14**



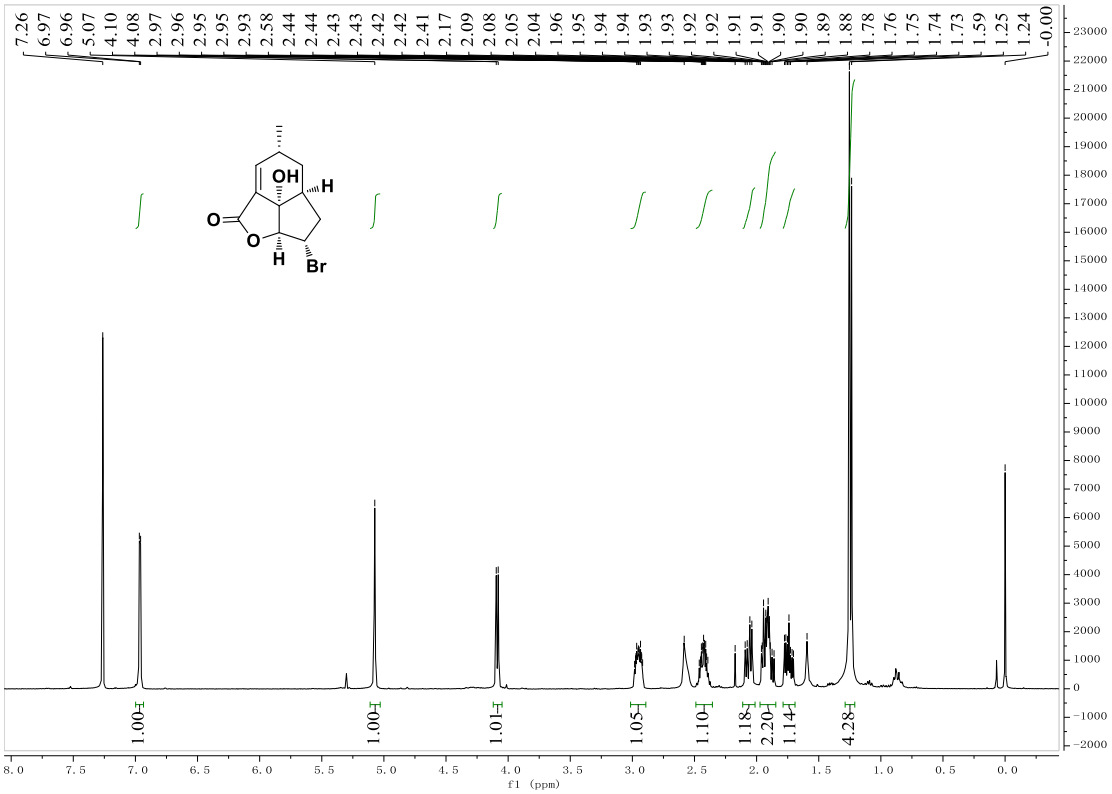
^{13}C-NMR of compound **(−)-14**



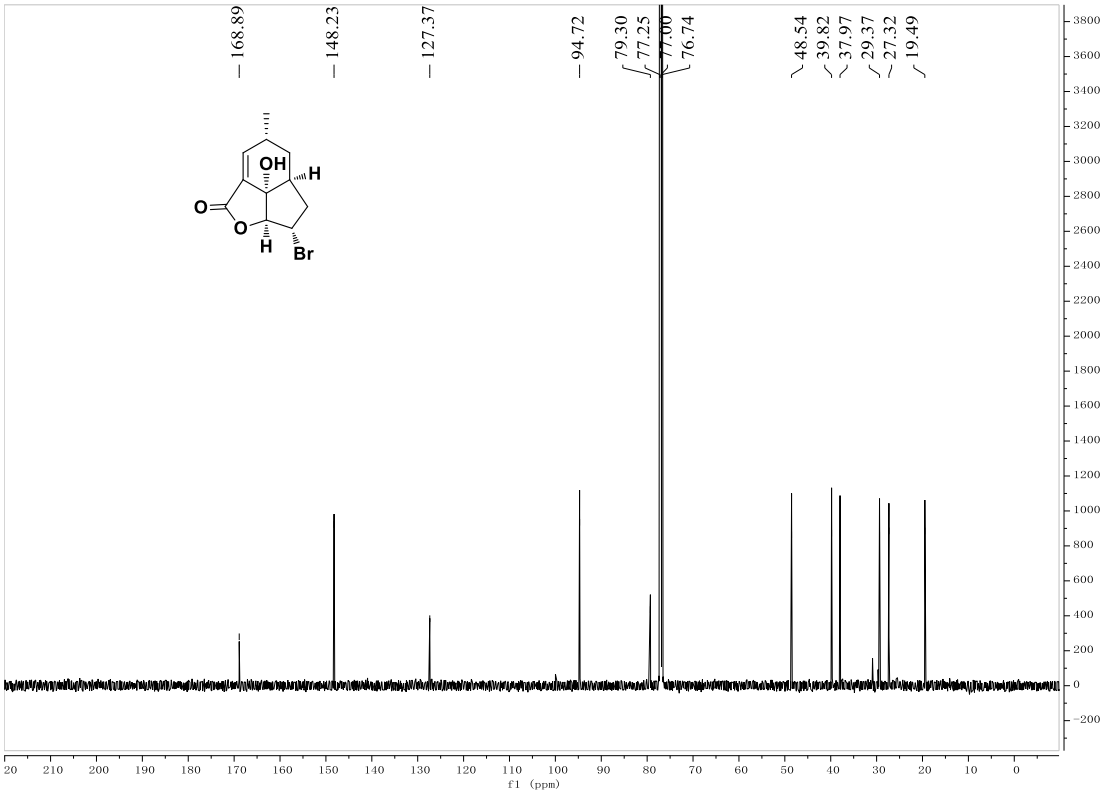
^{1}H-NMR of compound **(+)-12**



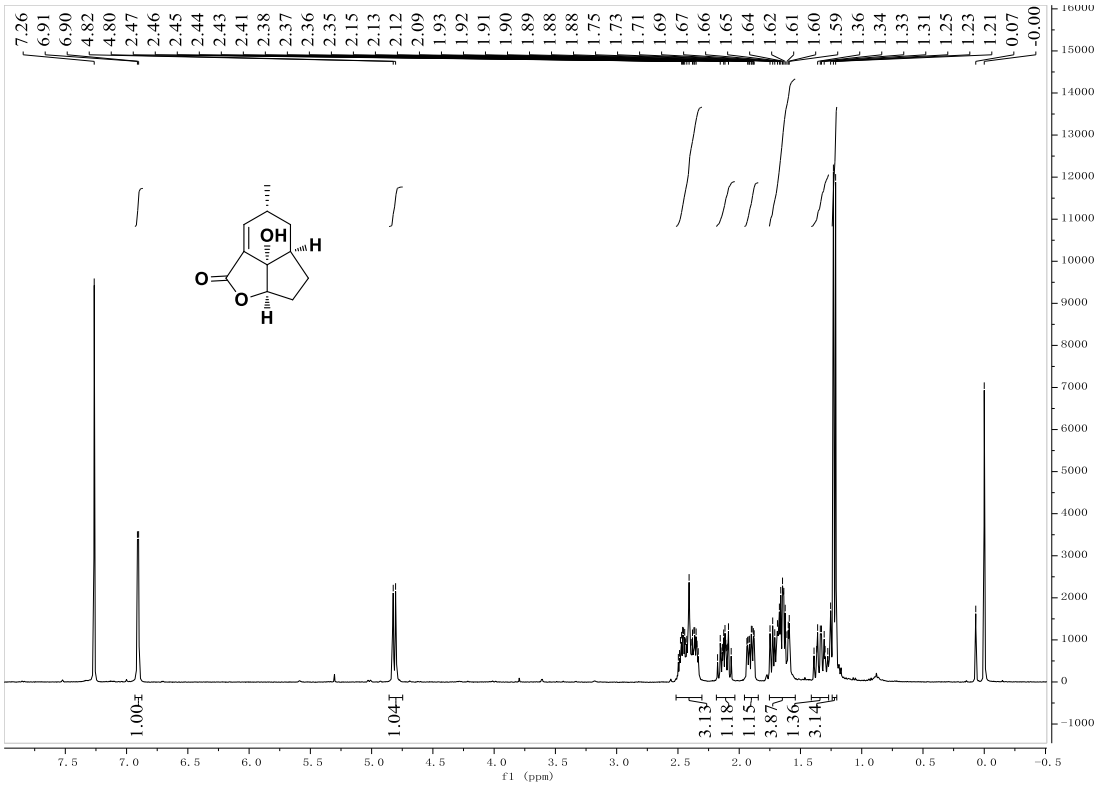
^{13}C-NMR of compound **(+)-12**



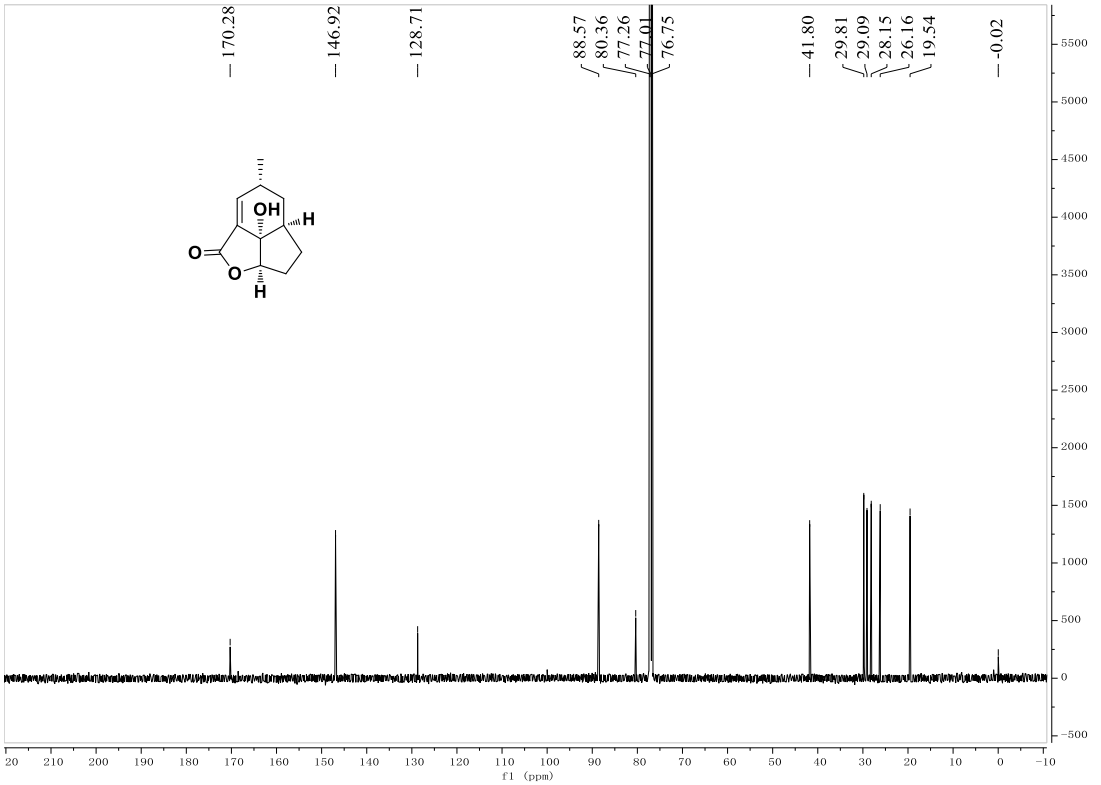
^{1}H-NMR of compound **(+)-11**



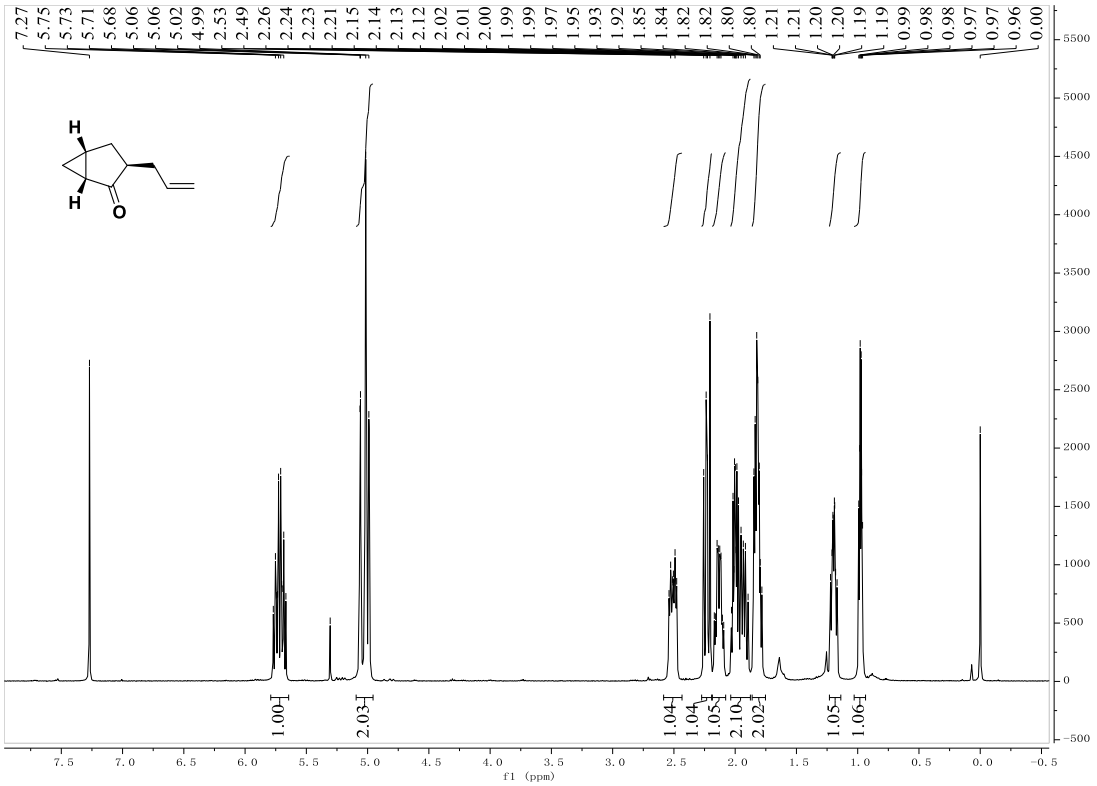
^{13}C-NMR of compound **(+)-11**



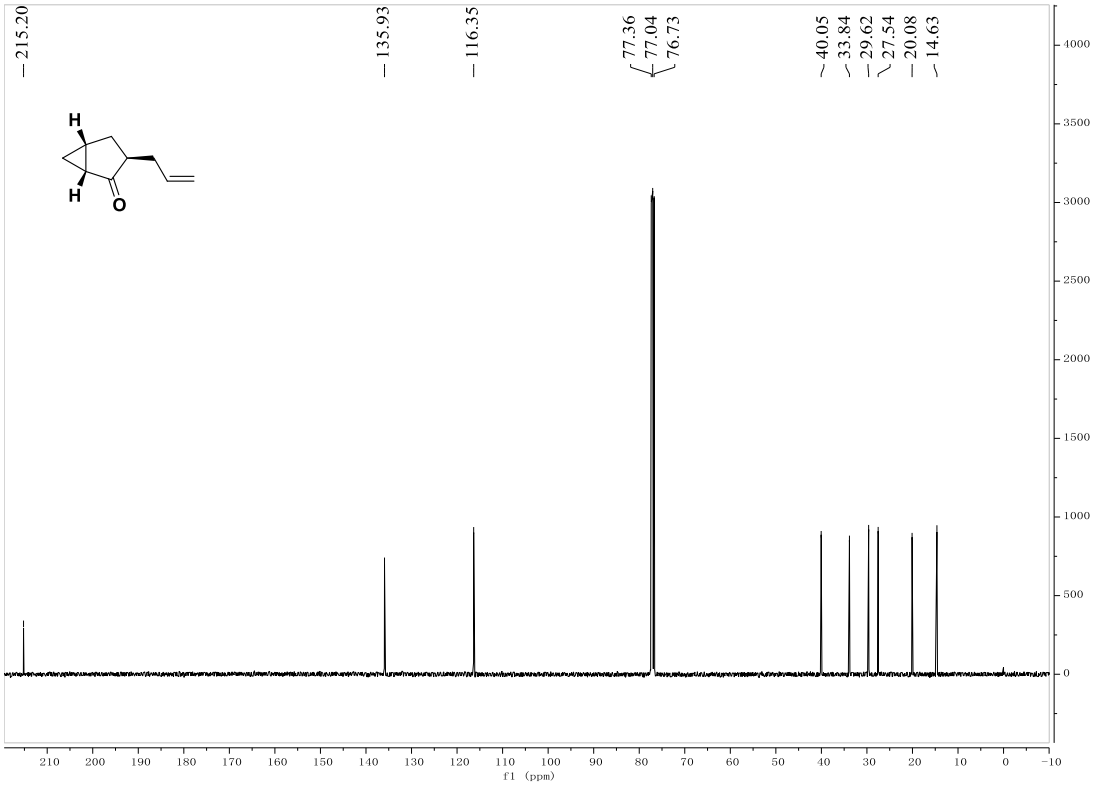
^{1}H-NMR of compound **(−)-2**



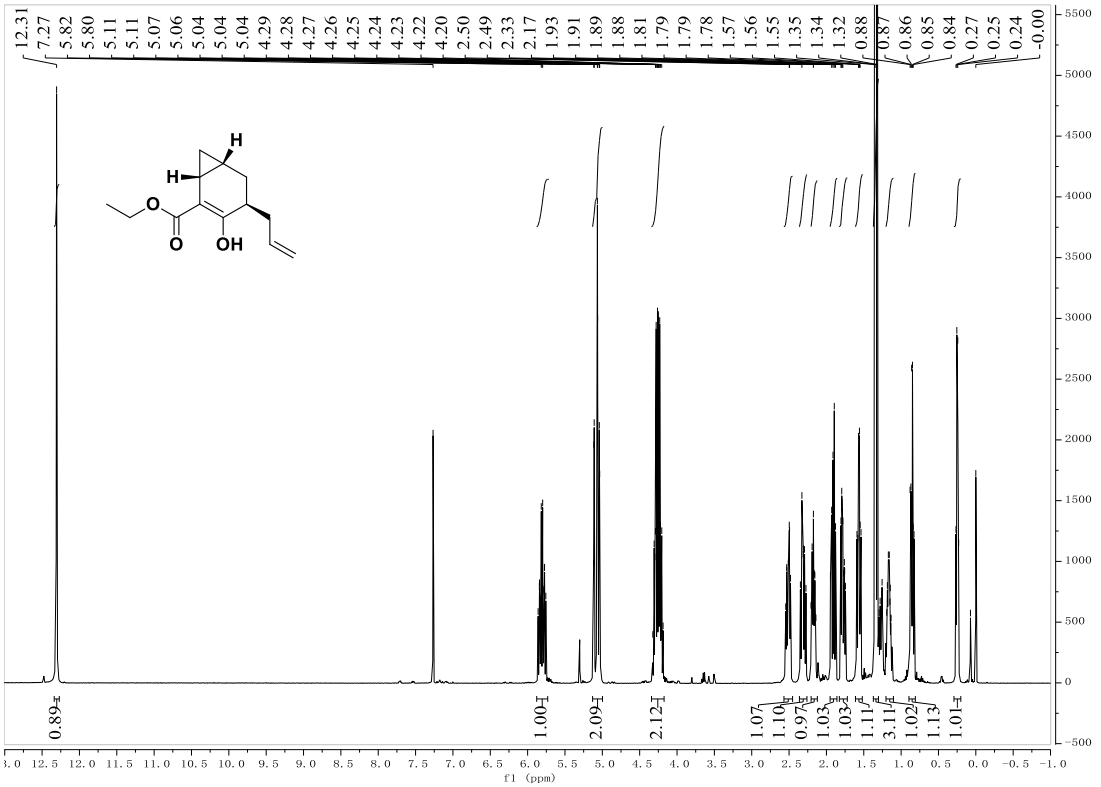
^{13}C-NMR of compound **(−)-2**



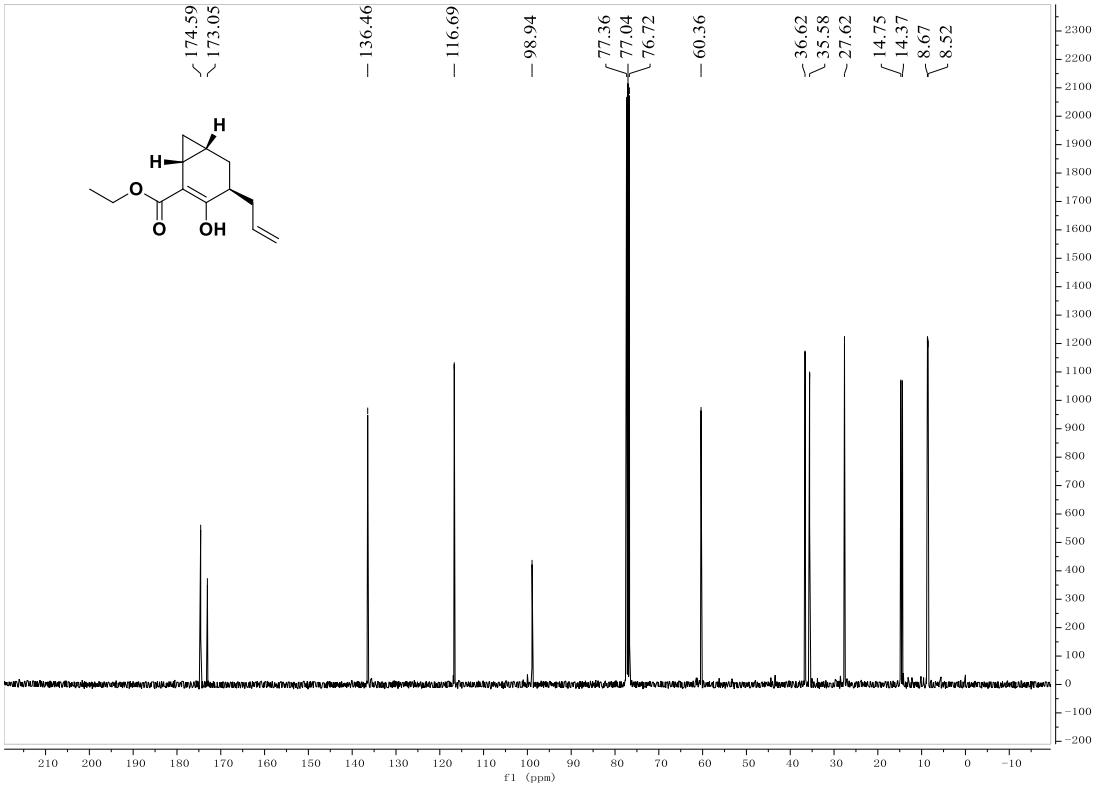
^{1}H-NMR of compound **(−)-20**



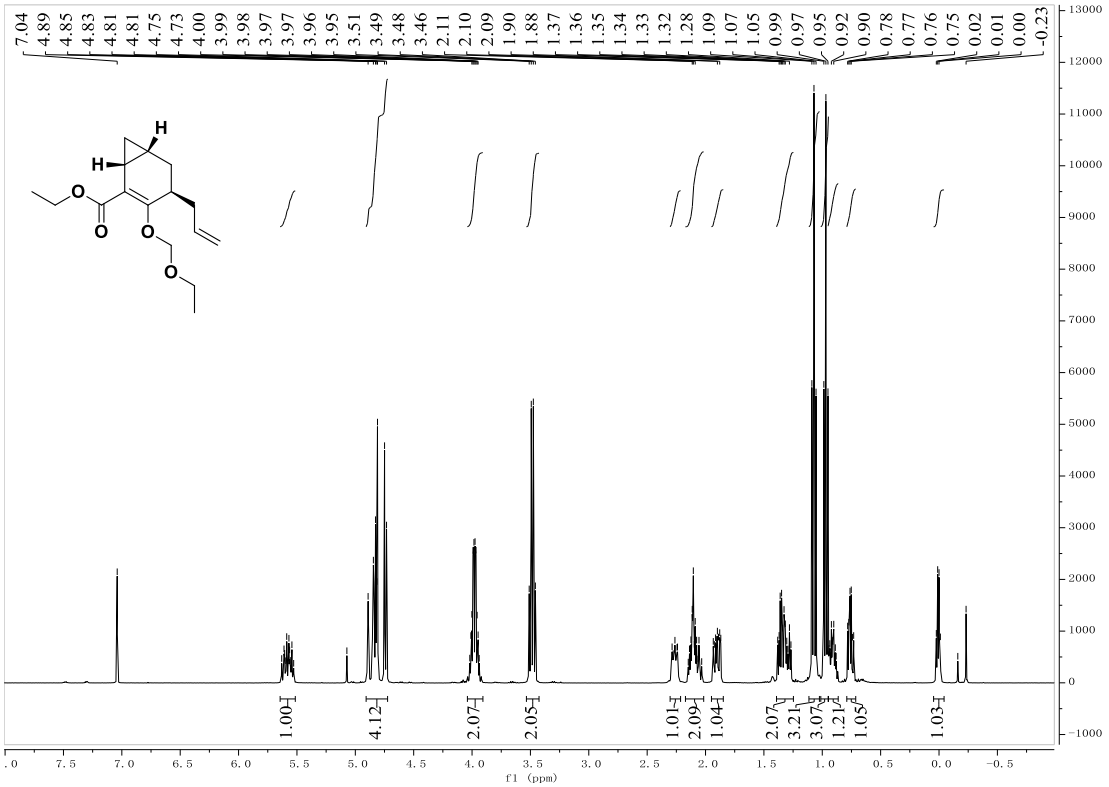
^{13}C-NMR of compound **(−)-20**



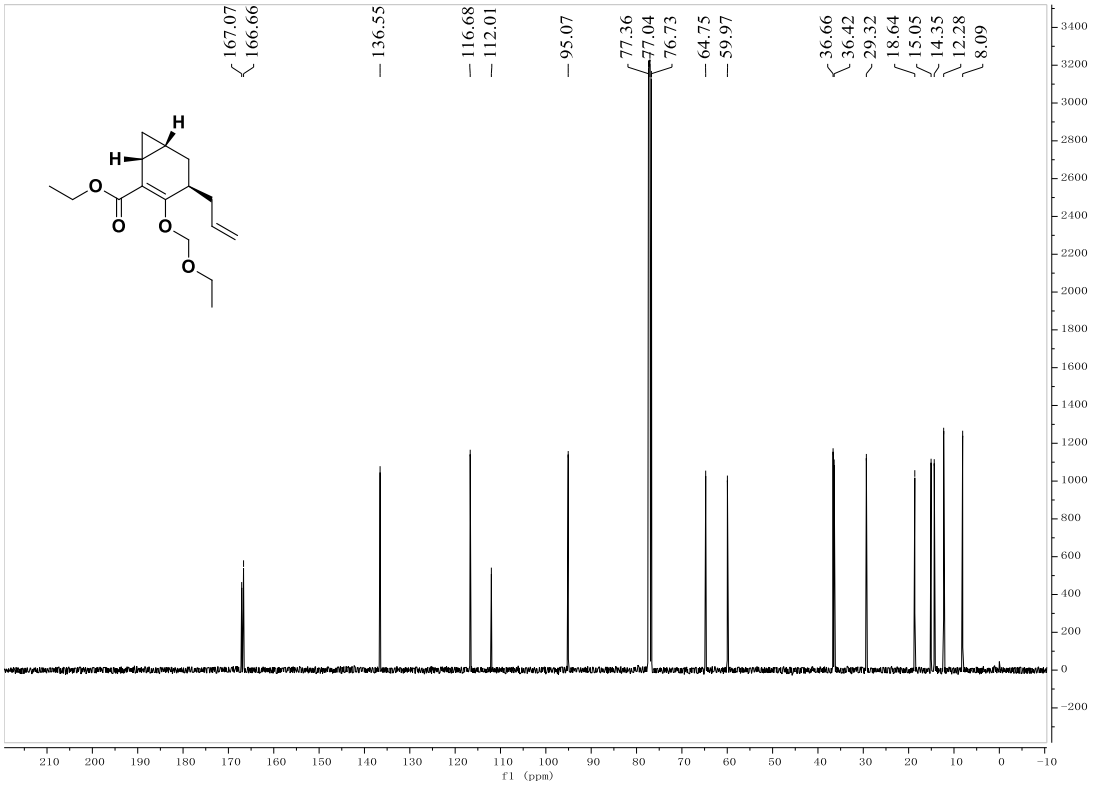
^{1}H-NMR of compound **(−)-21**



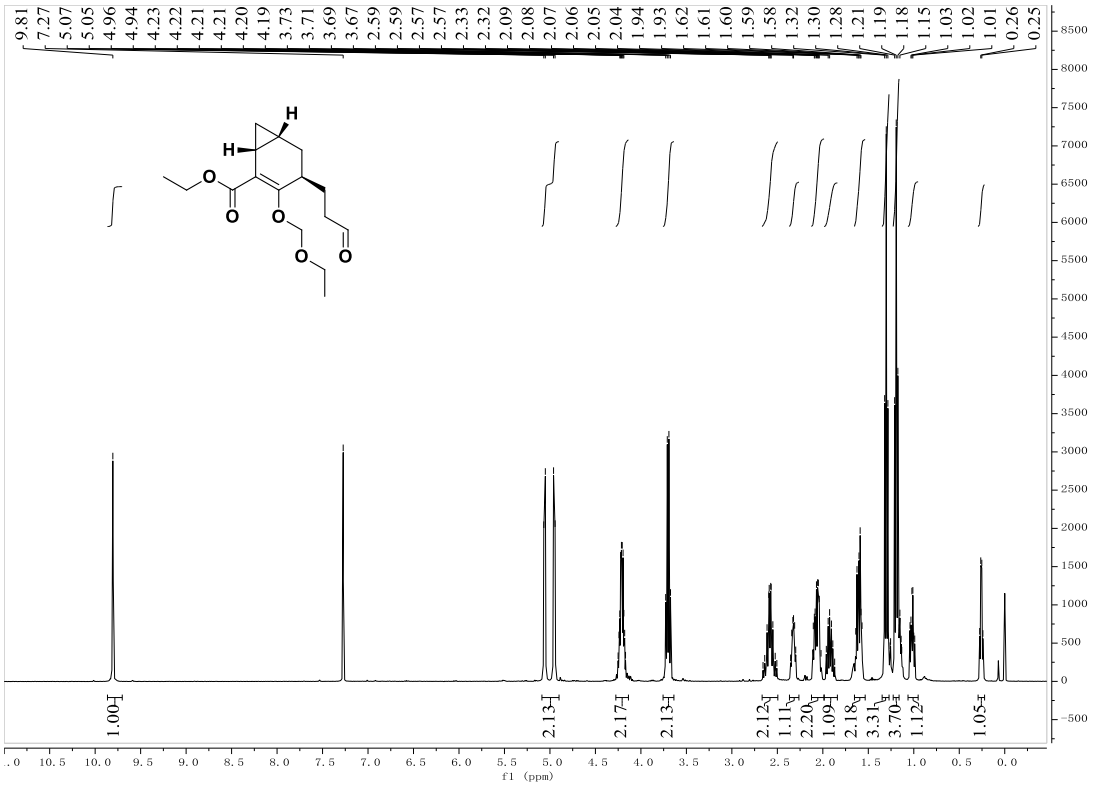
^{13}C-NMR of compound **(−)-21**



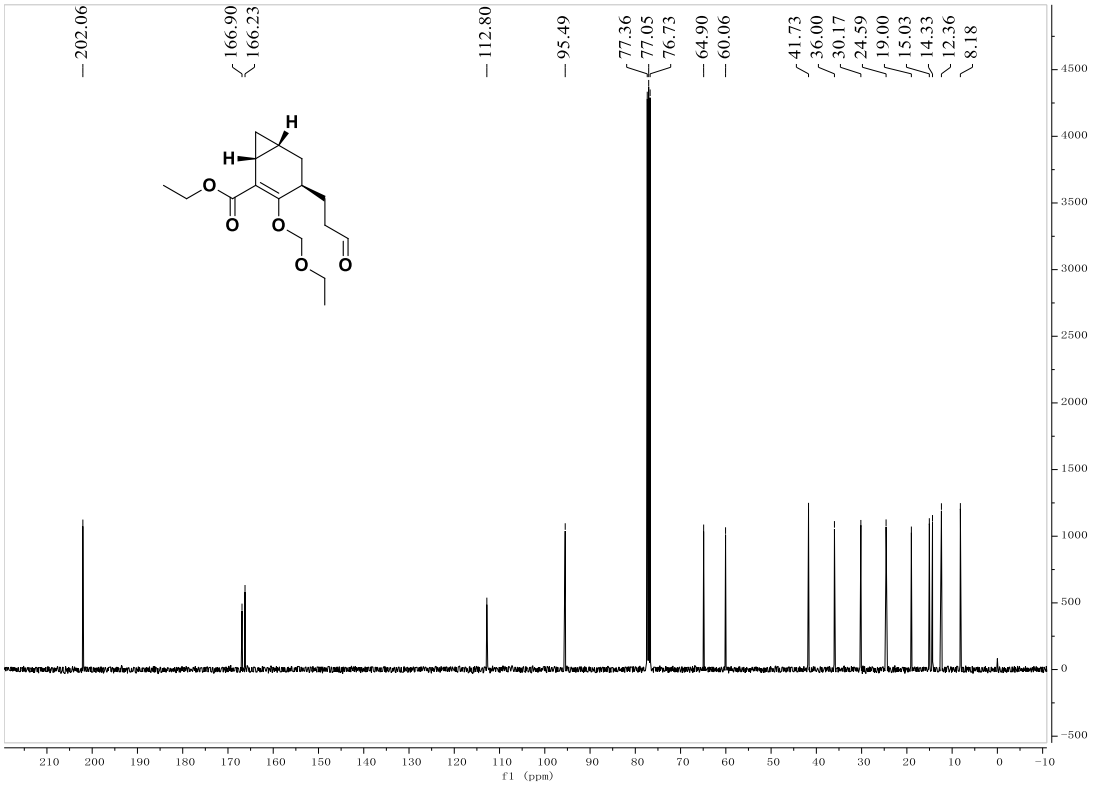
^{1}H-NMR of compound **(−)-22**



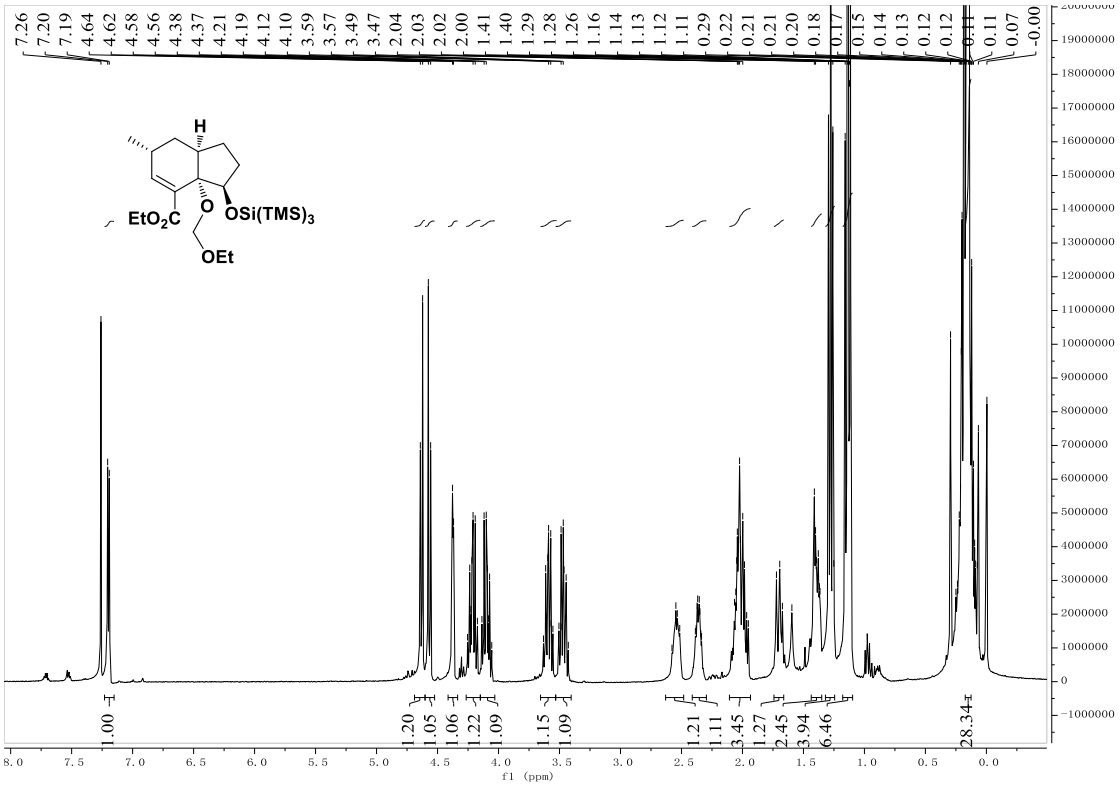
^{13}C-NMR of compound **(−)-22**



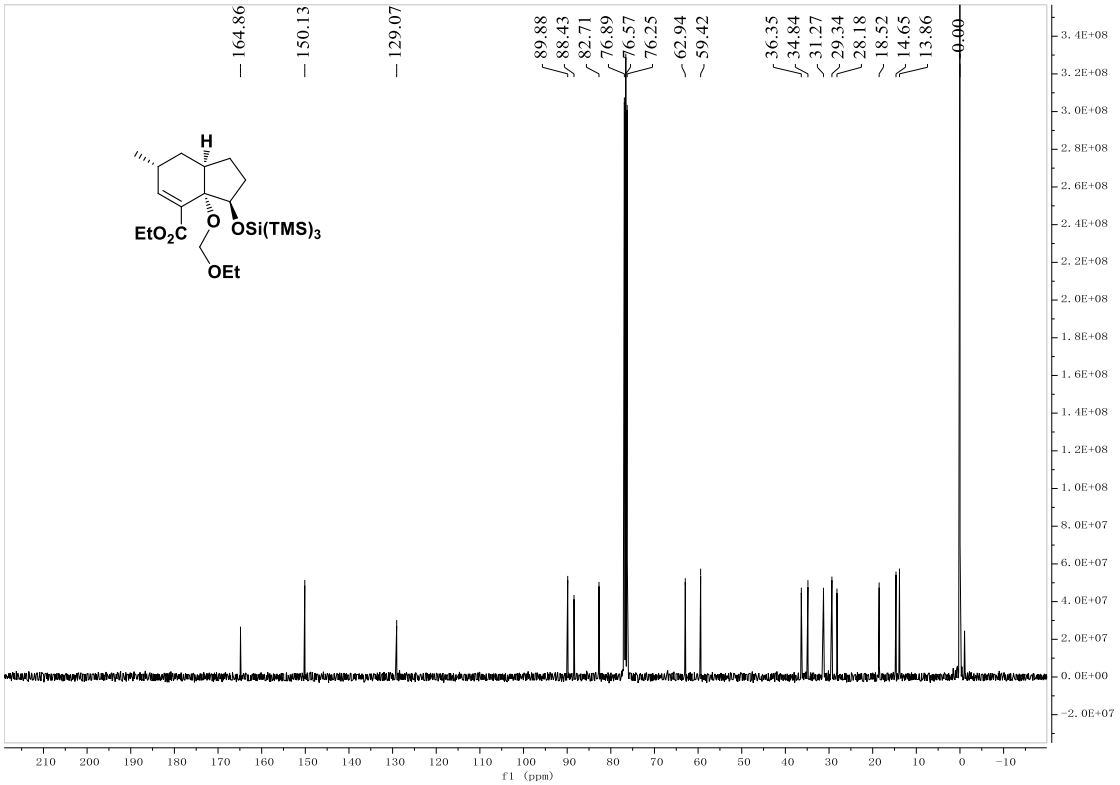
^{1}H-NMR of compound **(+)-23**



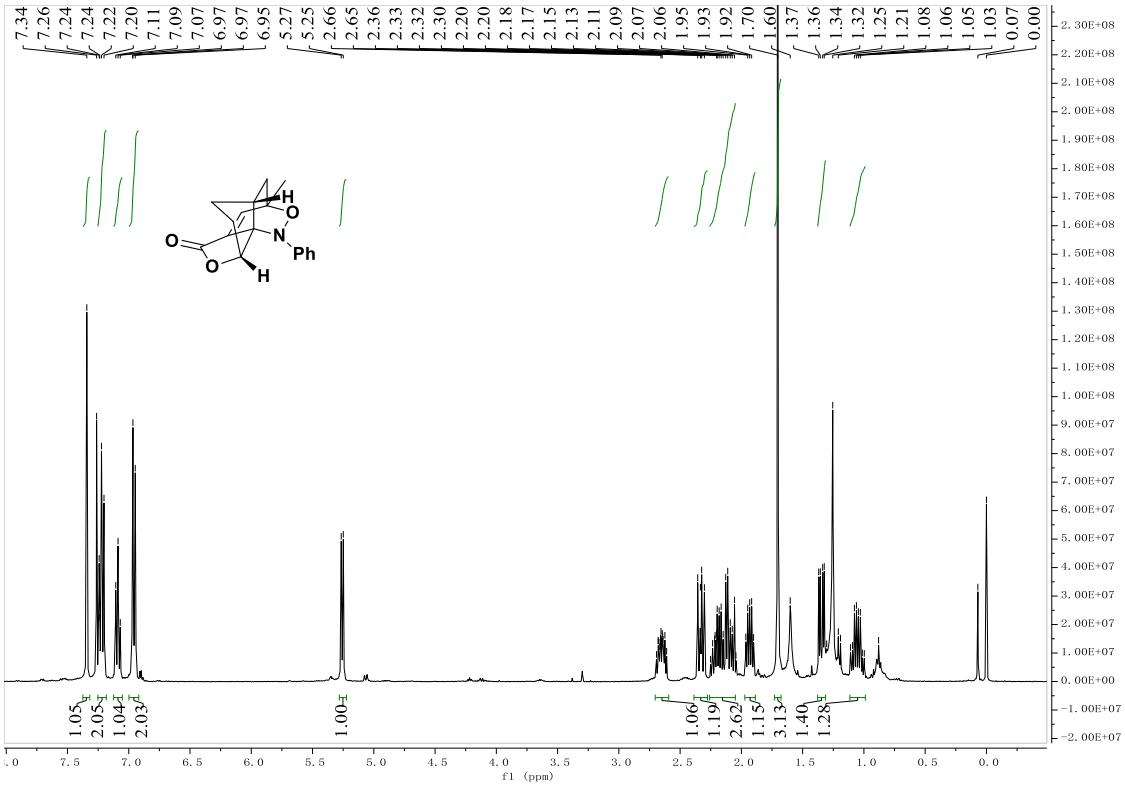
^{13}C-NMR of compound **(+)-23**



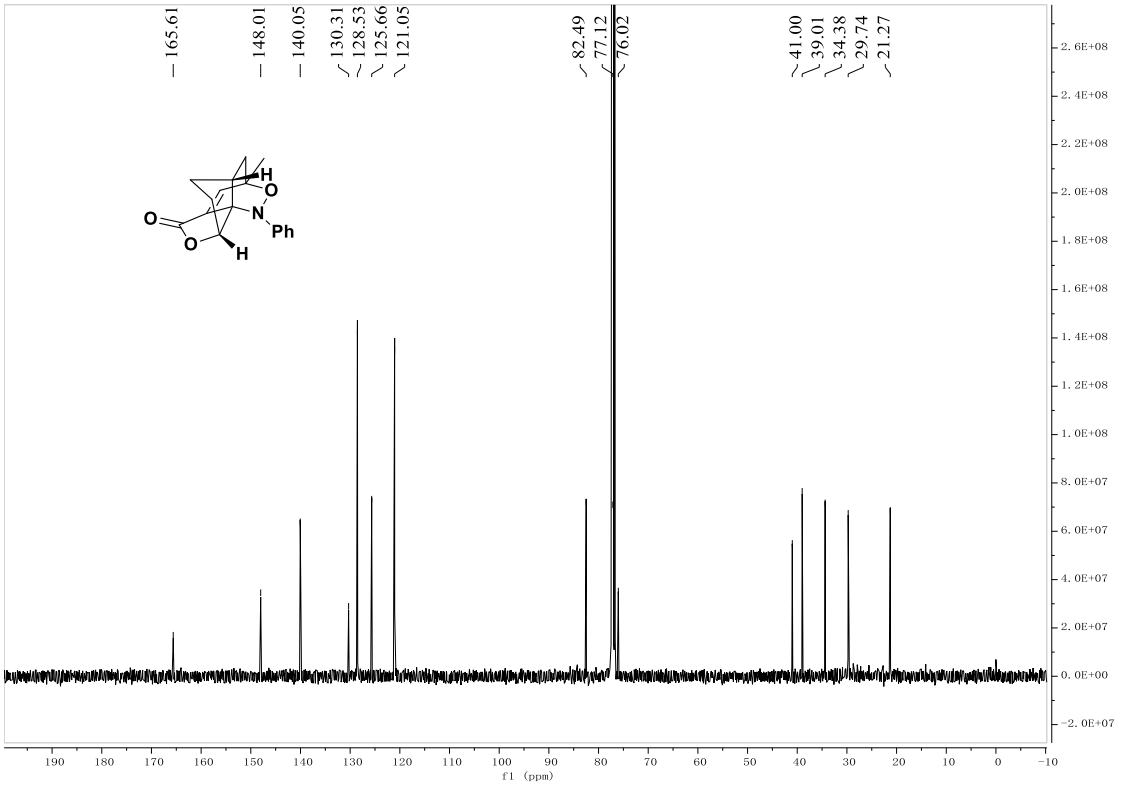
^{1}H-NMR of compound **(−)-25**



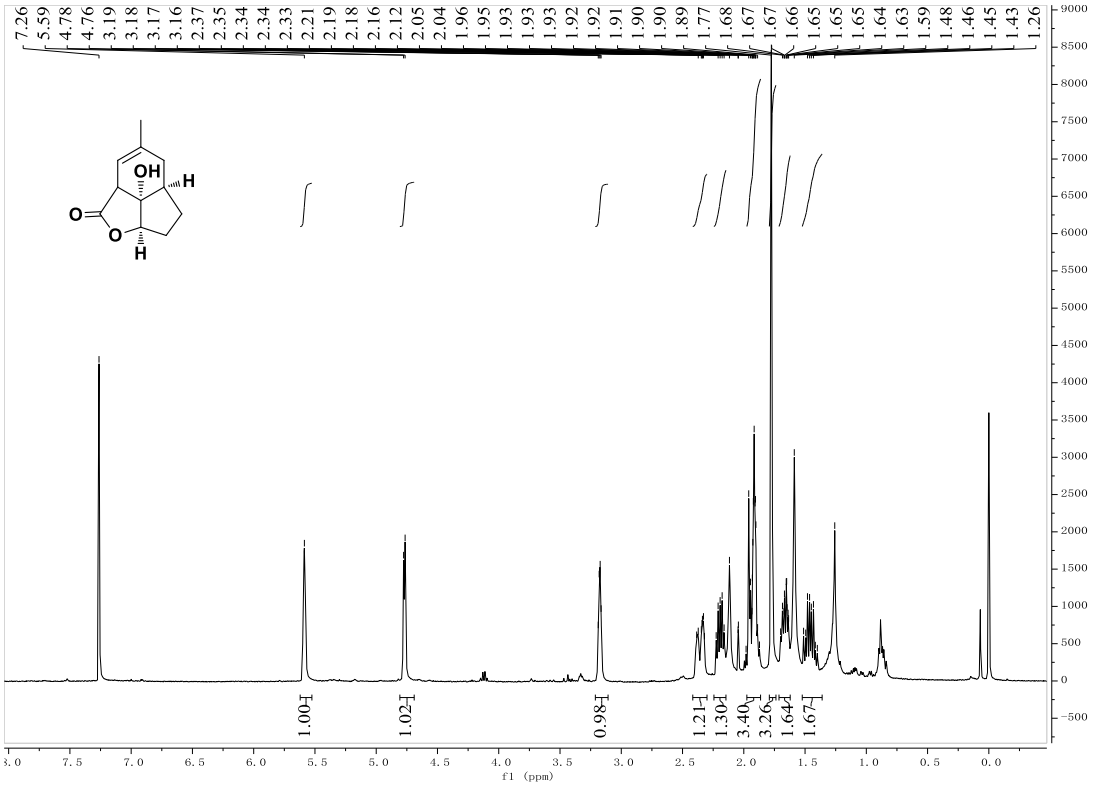
^{13}C-NMR of compound **(−)-25**



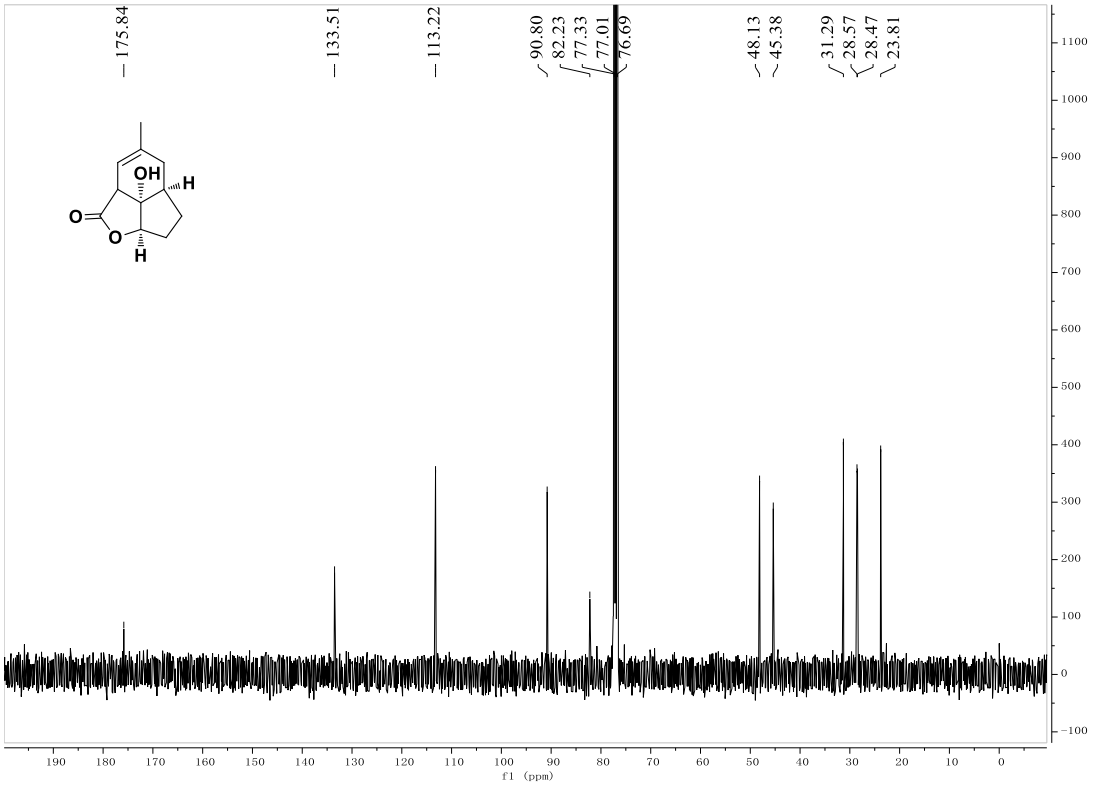
^{1}H-NMR of compound **(+)-4**



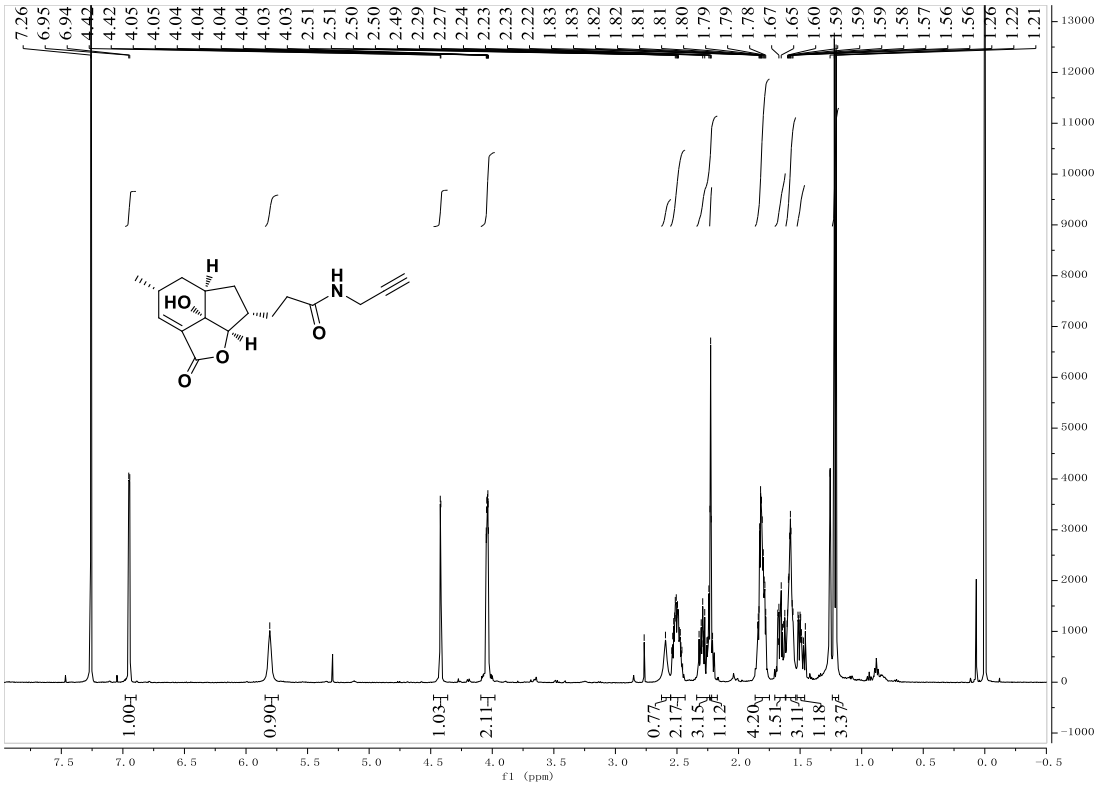
^{13}C-NMR of compound **(+)-4**



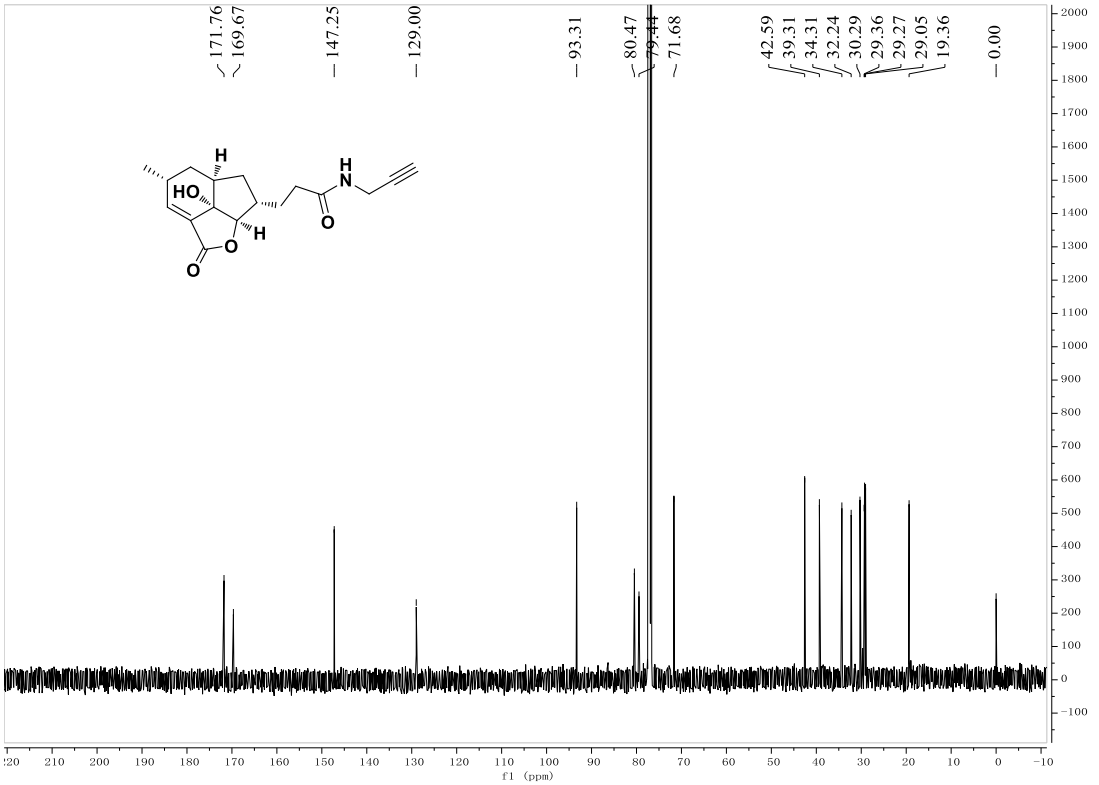
^{1}H-NMR of compound **(+)-26**



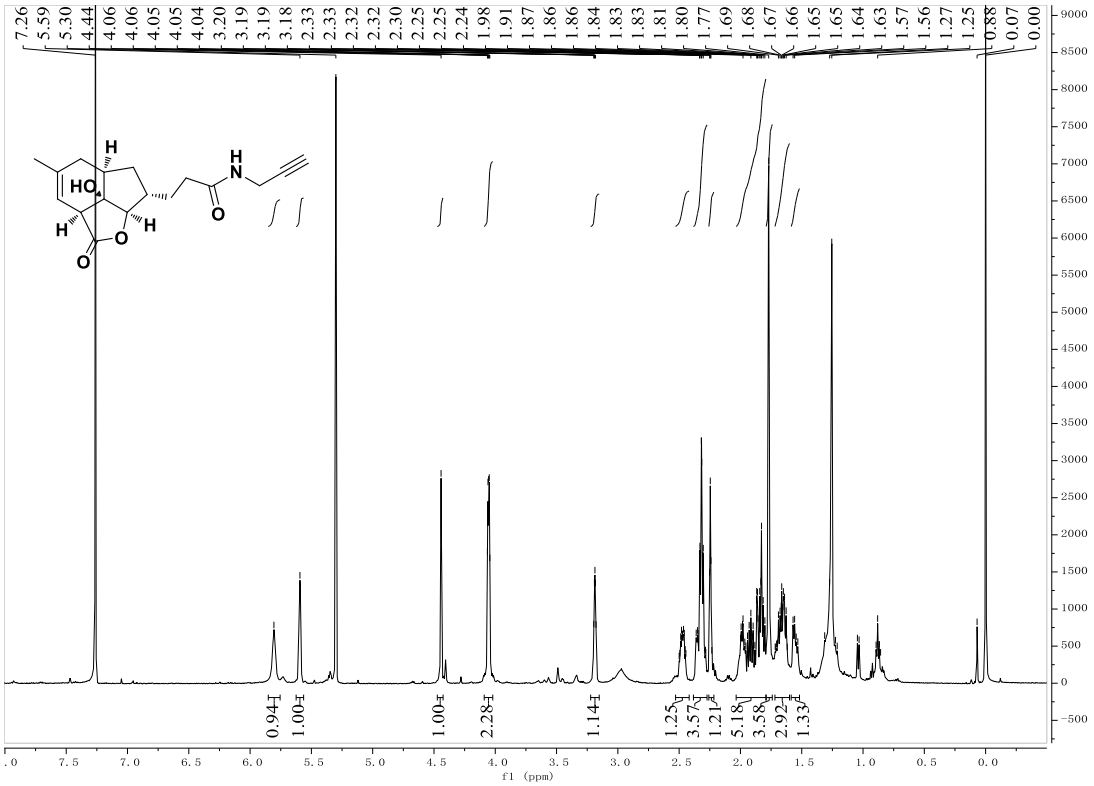
^{13}C-NMR of compound **(+)-26**



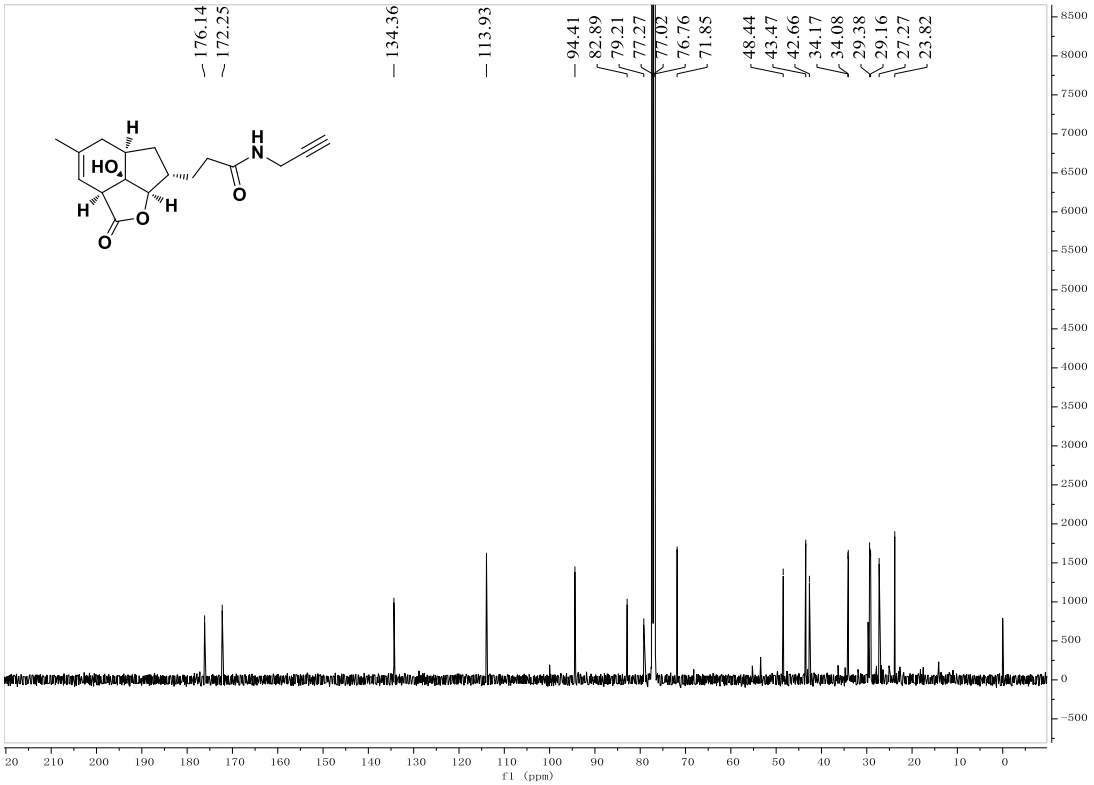
^{1}H-NMR of compound **(+)-29**



^{13}C-NMR of compound **(+)-29**



^{1}H-NMR of compound **(+)-30**



^{13}C-NMR of compound **(+)-30**

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