Supplementary information for

Synthesis of Portimines Reveals the Basis of Their Anti-cancer Activity

Junchen Tang*, Weichao Li*, Tzu-Yuan Chiu, Francisco Martínez-Peña, Zengwei Luo, Christine T. Chong, Qijia Wei, Nathalia Gazaniga, Thomas J. West, Yi Yang See, Luke L. Lairson†, Christopher G. Parker† and Phil S. Baran†

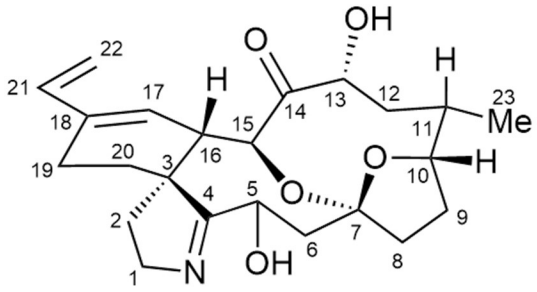
Correspondence to: llairson@scripps.edu, cparker@scripps.edu, pbaran@scripps.edu

This PDF file includes:

Table of Contents

Overview of Synthesis

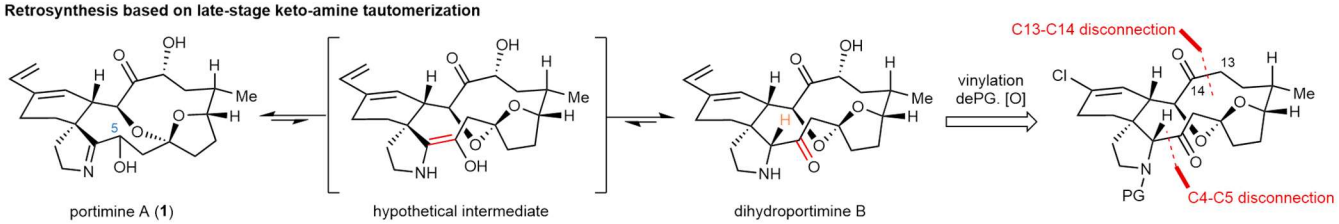
Skeletal numbering system of portimine A (1)



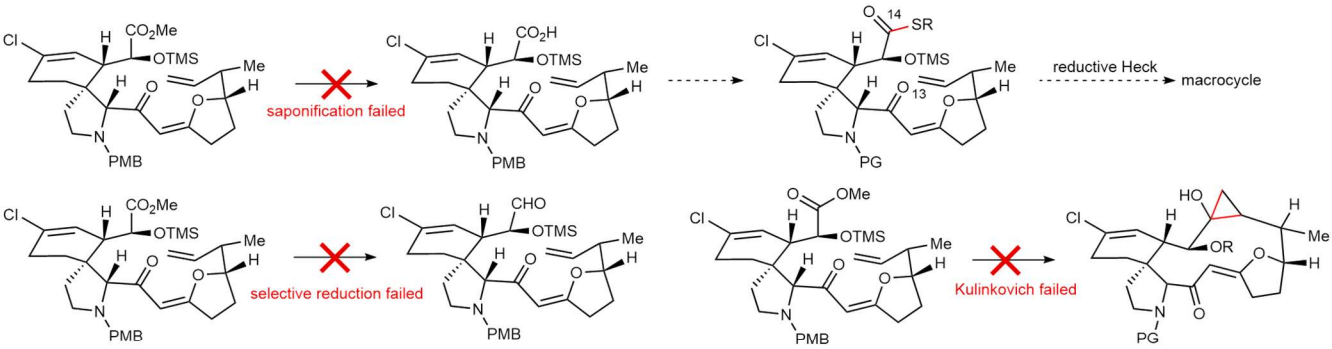
portimine A (**1**)

Summary of failed approaches to macrocyclization.

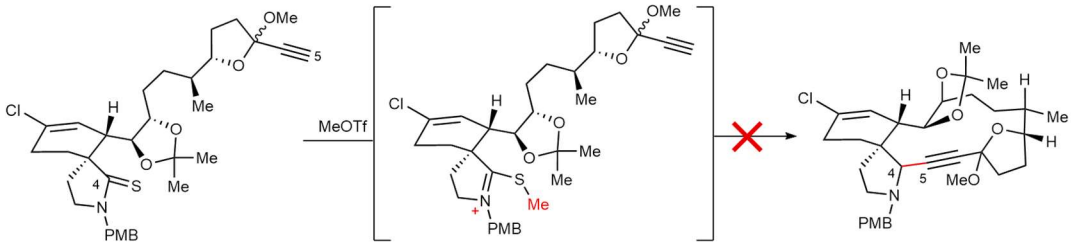
Retrosynthesis based on late-stage keto-amine tautomerization



Failed macrocyclization attempts based on C13-C14 disconnection

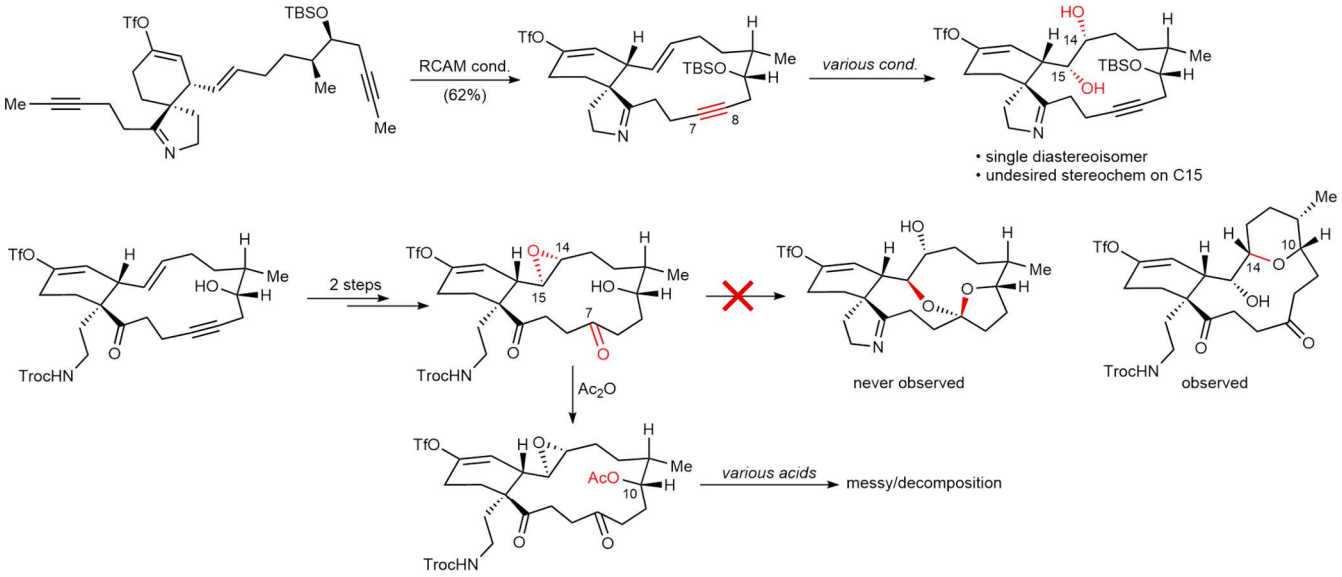


Failed macrocyclization attempts based on C4-C5 disconnection

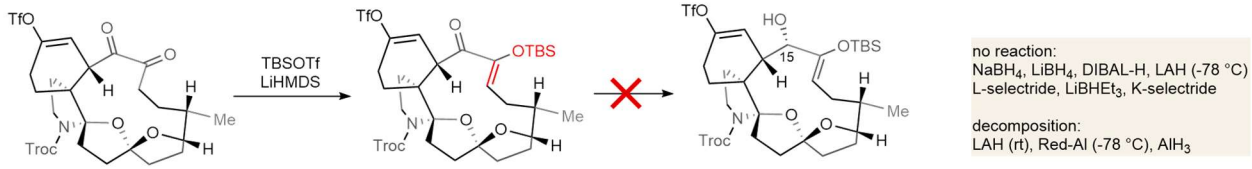


Summary of failed approaches to ketalization.

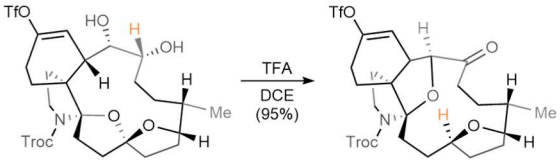
Undesired stereochem outcome from direct oxidation of C-14/C-15 olefin



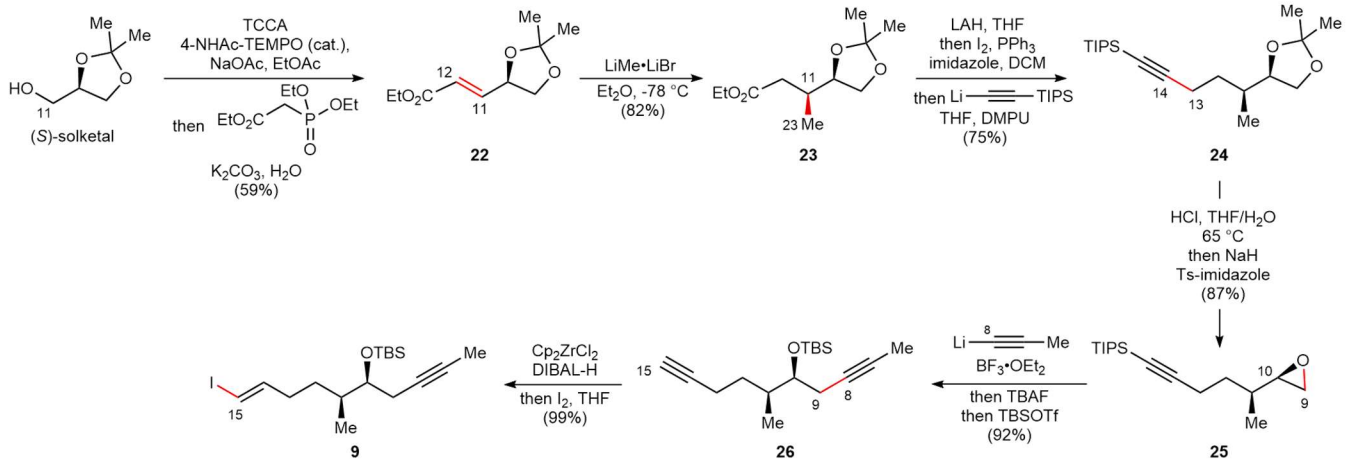
Failed approach to reduce C-15 carbonyl



An observed undesired hydride shift



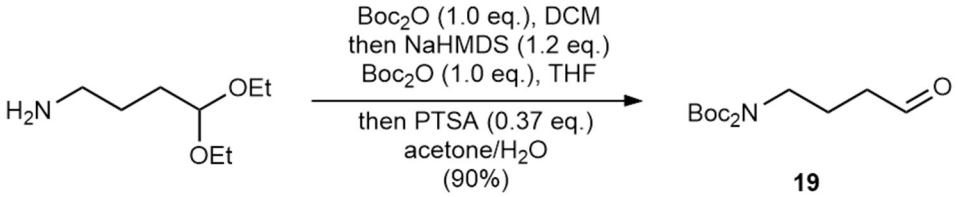
Detailed route to compound 9.



General Experimental

All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), toluene (PhMe), dimethylformamide (DMF), benzene, and triethylamine (TEA) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F254). Silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043 – 0.063 mm). NMR spectra were recorded on Bruker DRX600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (chloroform-*d*: ^{1}H NMR δ = 7.26 ppm, ^{13}C NMR δ = 77.2 ppm, acetonitrile-*d3*: ^{1}H NMR δ = 1.94 ppm, ^{13}C NMR δ = 118.3, 1.3 ppm, methanol-*d4*: ^{1}H NMR δ = 3.31 ppm, ^{13}C NMR δ =49.0 ppm, benzene-*d6*: ^{1}H NMR δ = 7.16 ppm, ^{13}C NMR δ = 128.1 ppm). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qt = quint, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time-of-flight (ESI-TOF) reflectron experiments.

Compound **19**

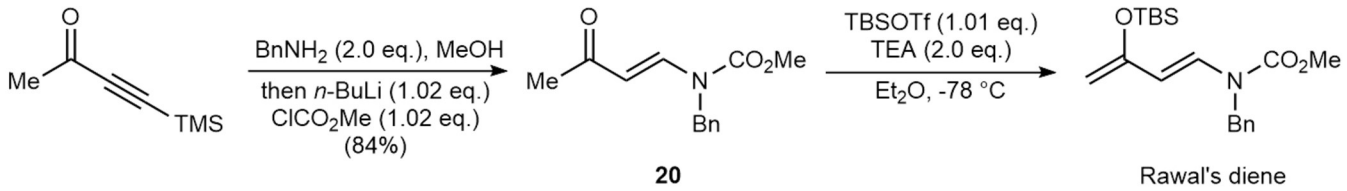


To a solution of 4-aminobutyraldehyde diethyl acetal (32.2 g, 200 mmol) in DCM (200 mL), was added Boc_2O (43.8 g, 201 mmol) dropwise at rt. The reaction was monitored by TLC (stain: 1% ninhydrin in ethanol). Upon completion, the solvent was removed under reduced pressure, and the residue was dissolved in THF (200 mL) at 0 ºC under argon. To this solution, NaHMDS (0.6 M in toluene, 400 ml, 240 mmol) was added dropwise with vigorous stirring. The resulting solution was kept stirring at the same temperature, followed by a slow addition of Boc_2O (43.8 g, 201 mmol). After completion, sat. aq. NH_4Cl (500 ml) was added and stirred overnight. The organic layer was separated, while the aqueous layer was extracted with Et_2O (3x 300 ml). The combined organic layer was dried over $MgSO_4$, followed by concentration to give the crude Boc-imide as product.

The crude carbamate obtained above was dissolved in acetone/H_2O (4:1, 500 ml). PTSA monohydrate (14.0 g, 73.6 mmol) was added and stirred at rt for 16 h. The mixture was neutralized with sat. aq. $NaHCO_3$ (500 ml) and extracted with Et_2O (3x 300 ml). The combined organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by chromatography (5% EtOAc in hexanes to 15% EtOAc in hexanes) to afford compound **19** (51.7 g, 90%) as colorless oil.

Physical state: colorless oil
TLC: R_f = 0.41 (25% EtOAc in hexanes, $KMnO_4$ staining)
^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 2.2 Hz, 1H), 3.58 (t, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.2 Hz, 2 H), 1.86 (qt, *J* = 7.2 Hz, 2H), 1.47 (s, 18H)
^{13}C-NMR (125 MHz, $CDCl_3$) δ 201.6, 152.7 (2C), 82.6 (2C), 45.5, 41.1, 28.1(6C), 21.6
All spectral data meet with that previously reported.[1]

Compound **20** and Rawal's diene



20 Rawal's diene

To a solution of $BnNH_2$ (30.6 g, 286 mmol) in MeOH (200 mL) at 0 °C was added 4-(trimetylsilyl)-3-butyn-2-one (21.6 mL, 143 mmol) dropwise. After stirring for 1.0 h at rt, the solvent was removed in vacuo. The crude product was suspended in EtOAc (200 ml) and rinsed by aq. sat. NaH_2PO_4 (200 ml) to remove benzylamine. The organic layer was separated and the aqueous phase was extracted with EtOAc(3x 200 ml). The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure to give the crude enamine[2], which was directly used for next step.

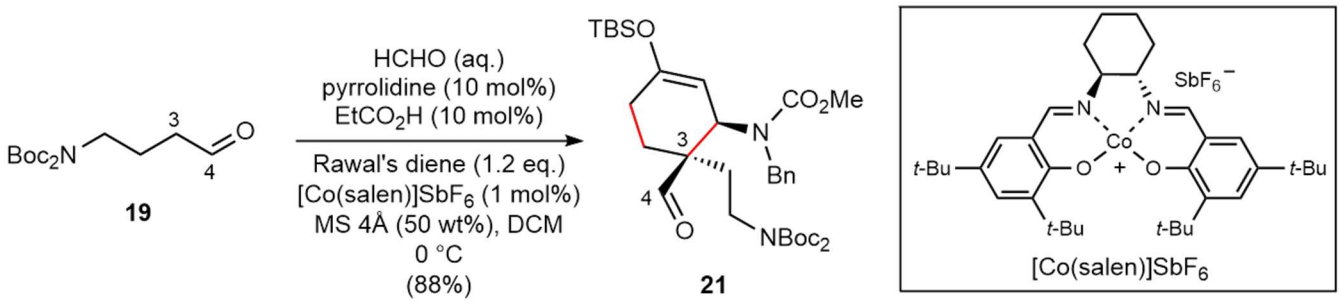
The crude enamine obtained above was dissolved in THF (10 ml/g), and and *n*-BuLi (2.5 M, 60 ml, 150 mmol) was added at 0 °C under argon over 30 min. After 10 min, $ClCO_2Me$ (11.6 ml, 14.2 g, 150 mmol) was added slowly, and the solution was stirred for 2 h. Upon completion, the mixture was poured into H_2O (500 ml). The mixture was extracted with EtOAc (3x 200 ml) and dried over $MgSO_4$. Compound **20** (27.9 g, 120 mmol, 84%) can be obtained by chromatography (0-40% EtOAc in hexanes).

Physical state: pale yellow oil
TLC: R_f = 0.28 (30% EtOAc in hexanes, UV active, $KMnO_4$ staining)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 14.4 Hz, 1H), 7.36 – 7.03 (m, 5H), 5.50 (d, *J* = 14.4 Hz, 1H), 4.76 (s, 2H), 3.84 (s, 3H), 2.13 (s, 3H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.3, 154.6, 142.0, 135.4, 129.0 (2C), 127.3 (2C), 126.6, 110.0, 54.6, 48.4, 27.7
HRMS (ESI-TOF): calc'd for $C_{13}H_{15}NO_3$ $[M+H]^+$: 234.1125, found: 234.1126

The pure compound **20** (52 g, 223 mmol) was dissolved in Et_2O (650 ml) under argon. To this solution, TEA (45.5 g, 450 mmol) was added in one portion at -78 °C. TBSOTf (59.5 g, 225 mmol) was dropped into this solution slowly. A cloudy mixture was generated during addition. After stirring at -78 °C for 30 min, the flask was gradually warmed to 0 °C for another 30 min. The reaction was quenched by a mixture of hexanes (200 ml) and sat. aq. $NaHCO_3$ (500 ml), followed by extraction with hexanes (3x 400 ml). The organic phase was dried over $MgSO_4$, and concentrated to give Rawal's diene (purity was determined by NMR, used directly for next step).

Physical state: pale yellow solid
TLC: R_f = 0.43 (hexanes+1% TEA, UV active, $KMnO_4$ staining)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.42 (m, 1H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.27 – 7.13 (m, 3H), 5.36 (d, *J* = 14.1 Hz, 2H), 4.80 (s, 2H), 4.13 (s, 1H), 4.07 (s, 1H), 3.83 (s, 3H), 1.00 (s, 9H), 0.18 (s, 6H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.1, 154.5, 136.9, 128.8 (2C), 127.3 (2C), 126.7, 126.3, 108.4, 93.0, 53.8, 48.2, 25.9 (3C), 18.4, -4.5 (2C)
HRMS (ESI-TOF): calc'd for $C_{19}H_{29}NO_3Si$ $[M+H]^+$: 348.1990, found: 348.1986

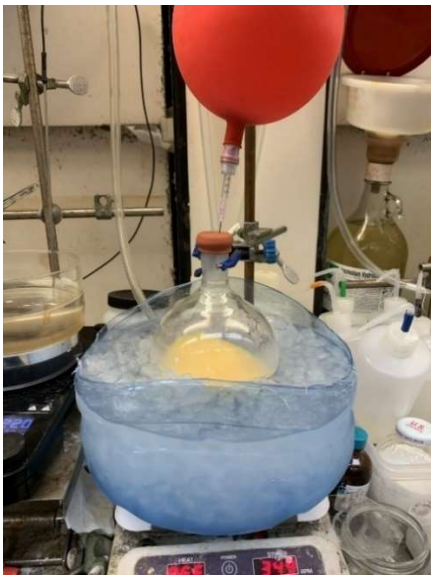
Compound **21**



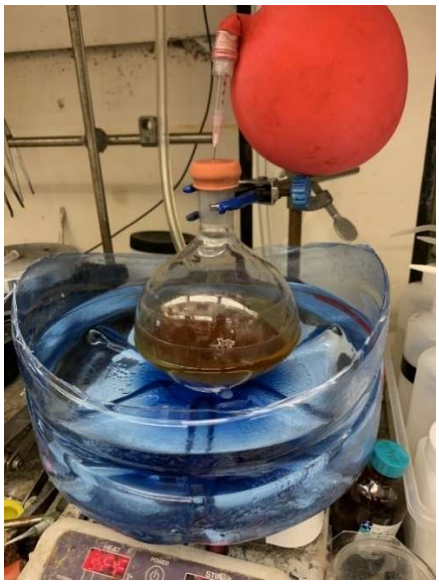
To a mixture of aqueous formaldehyde solution (13 ml, 37% formaldehyde in water) and compound **19** (46.8 g, 162.9 mmol) in *i*-PrOH (95 mL) were added propionic acid (1.20 g, 16.2 mmol, 0.1 eq.) and pyrrolidine (1.15 g, 16.2 mmol, 0.1 equiv.). The reaction mixture was stirred at 55 °C for 1.0 h. Upon completion, sat. aq. $NaHCO_3$ (20 ml) and brine (100 ml) was added, and the mixture was extracted with Et_2O (3x 100 ml). The combined organic layer was dried over $MgSO_4$, and concentrated in vacuo to remove all volatiles. The crude acrolein (compound **4**) obtained was directly used for Diels-Alder cycloaddition.

Compound **4** was dissolved in DCM (200 mL), followed by adding MS4Å (25 g, dried in oven overnight, 110 °C) and Rawal's diene (70.5 g, 10.7 mmol, 1.2 equiv.) under argon. After stirring the mixture at 0 °C for 15 min, [Co(salen)]SbF_6 (984 mg, 1.63 mmol, 0.01 equiv.) was added in one portion. The reaction mixture was stirred at 0 °C and allowed to warm up to rt overnight. Upon completion, silica gel (ca. 150 g) was added. After concentration in vacuo, the crude was purified with chromatography (dry loading, 0-20% EtOAc in hexanes) to afford compound **21** (92.7 g, 143.3 mmol, 88%).

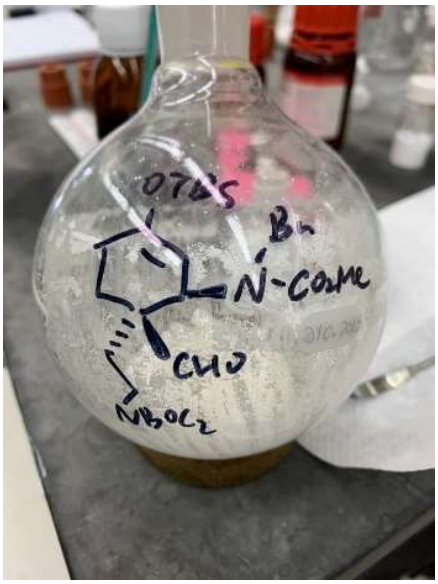
Physical state: white powder
TLC: R_f = 0.35 (20% EtOAc in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -55.4 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 9.89-9.59 (m, 1H), 7.28 – 7.24 (m, 2H), 7.21 – 7.14 (m, 1H), 7.14 – 6.98 (m, 2H), 5.12 – 4.75 (m, 1H), 4.59 (d, *J* = 5.7 Hz, 1H), 4.52 (d, *J* = 16.4 Hz, 1H), 4.37 (d, *J* = 16.4 Hz, 1H), 3.79 – 3.47 (m, 4H), 3.40 – 3.30 (m, 1H), 2.23 – 2.02 (m, 3H), 2.01 – 1.83 (m, 2H), 1.63 – 1.56 (m, 1H), 1.51 (s, 18H), 0.83 (s, 9H), -0.04 (s, 3H), -0.13 (s, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 204.8, 158.2, 155.7, 152.2, 152.1, 139.5, 128.3 (2C),126.7, 126.2, 126.1, 99.4, 82.8, 57.4, 53.0, 48.1, 42.2, 30.9, 29.8, 28.3 (6C), 25.8, 25.6 (3C), 22.8, 20.3, 18.0, -4.7 (2C)
HRMS (ESI-TOF): calc'd for $C_{34}H_{54}N_2O_8Si$ $[M+H]^+$: 647.3728, found: 647.3736



before adding [Co] catalyst

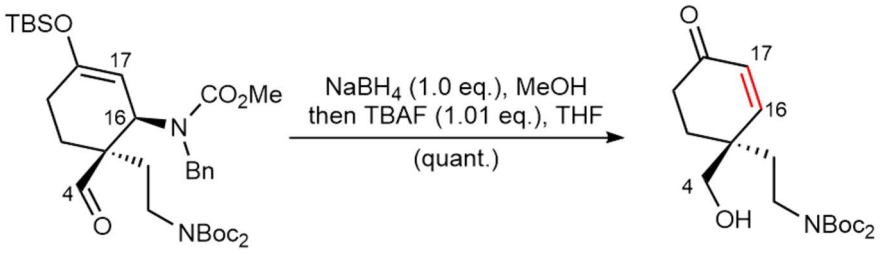


after completion



product after purification

Compound **6**



21 **6** (94% ee)

Reduction

To a solution of compound **21** (81.4 g, 126 mmol) in a mixture of MeOH (400 ml) and DCM (100 ml) was added $NaBH_4$ (4.7 g, 124 mmol) portionwise at 0 °C. The reaction was kept stirring for 1 h, and was quenched by sat. aq. NH_4Cl (300 ml). The mixture was extracted with DCM (3x 400 ml) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure to afford the crude product, which was directly used for next step.

E1cb

The crude product was dissolved in THF (500 ml), and added TBAF (130 ml, 1.0 M in THF). The reaction mixture was stirred for 30 min, and quenched by sat. aq. NH_4Cl (200 ml). The mixture was extracted with DCM (3x 300 ml) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure. The crude product was purified by chromatography (30% EtOAc in hexanes to 80% EtOAc in hexanes) to yield compound **6** (46 g, 126 mmol, quantitative yield).

Note: Compound **6 is bench-stable.*

Physical state: pale yellow oil

TLC: R_f = 0.25 (30% EtOAc in hexanes, UV active, $KMnO_4$ staining)

$[\alpha]^{25}_D$: +37.8 (c = 1.0, $CHCl_3$)

^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.82 (d, J = 10.2 Hz, 1H), 6.01 (d, J = 10.2 Hz, 1H), 3.71 – 3.61 (m, 3H), 3.56 (d, J = 11.6 Hz, 1H), 2.93 (t, J = 6.4 Hz, 1H), 2.55 – 2.38 (m, 2H), 1.95 – 1.76 (m, 4H), 1.51 (s, 18H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 199.3, 154.3, 152.8 (2C), 129.5, 83.2 (2C), 66.8, 42.0, 40.3, 33.9, 33.1, 28.4, 28.2 (6C)

HRMS (ESI-TOF): calc'd for $C_{19}H_{31}NO_6$ $[M\text{-}Boc+2H]^+$: 270.1705, found: 270.1704

CHIRAL REPORT

Sample Set Name: TANG_BARAN

Acq. Method Set: J1_BAR0447
Processing Method: J1_BAR0447

Date Acquired: 8/25/2022 5:13:43 PM PDT, 8/25/2022 5:18:39 PM PDT
Date Processed: 8/25/2022 5:17:48 PM PDT, 8/25/2022 5:22:42 PM PDT

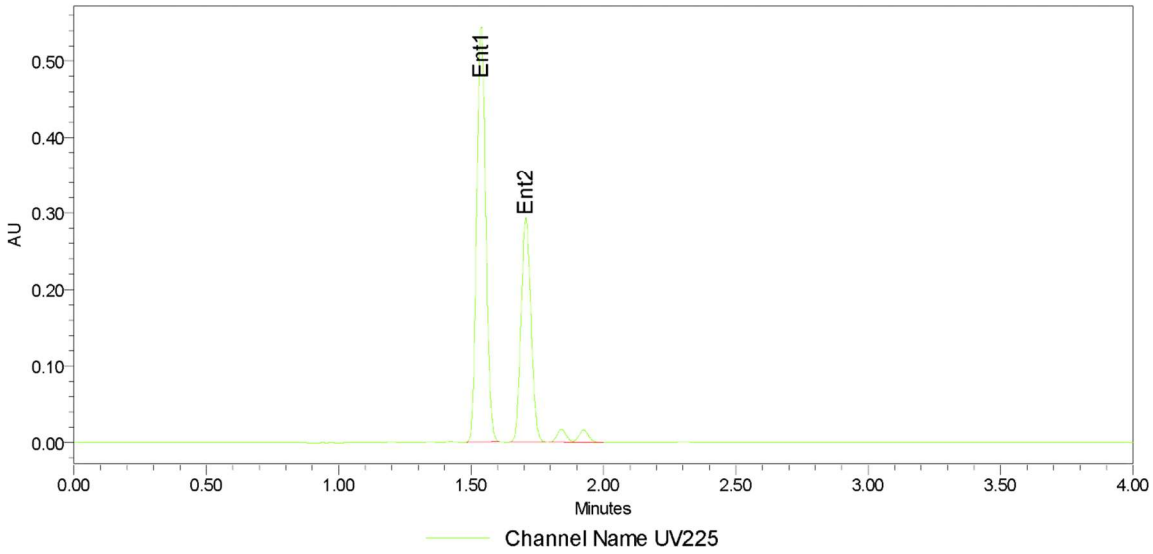
Peak Areas Summary
Area Summarized by Name

	SampleName	Vial	Date Acquired	ent1	ent2	ee	Ent1 (µV*sec)	Ent2 (µV*sec)
1	JT-SI-RACEMIC	2:E,2	8/25/2022 5:13:43 PM PDT	62.84	37.16	25.68	1295499	766160
2	JT-SI-CHIRAL	2:E,3	8/25/2022 5:18:39 PM PDT	3.03	96.97	-93.95	47822	1532828

CHIRAL REPORT

Sample Name:	JT-SI-RACEMIC	Acq. Method Set:	J1_BAR0447
Vial:	2:E,2	Processing Method:	J1_BAR0447
Date Acquired:	8/25/2022 5:13:43 PM PDT		
Date Processed:	8/25/2022 5:17:48 PM PDT		

Chromatogram(s)

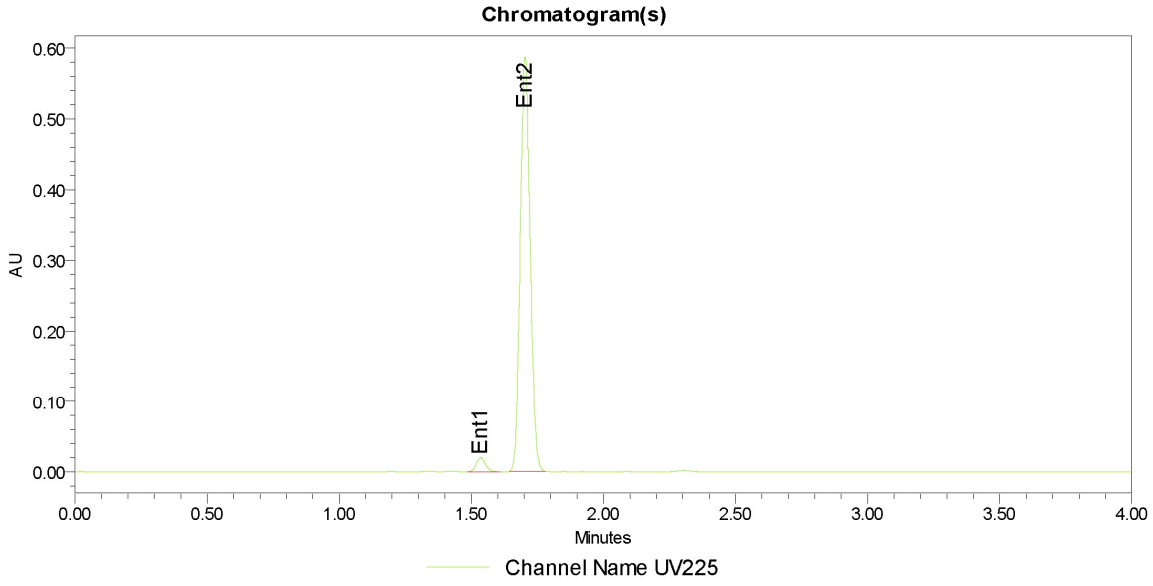


Peak Info

	Channel Name	Name	RT	Area	Height (µV)	ent1	ent2	ee
1	UV225	Ent1	1.54	1295499	545071	62.84	37.16	25.68
2	UV225	Ent2	1.71	766160	293514	62.84	37.16	25.68
3	UV225		1.84	40470	16874	62.84	37.16	25.68
4	UV225		1.93	41110	16300	62.84	37.16	25.68

CHIRAL REPORT

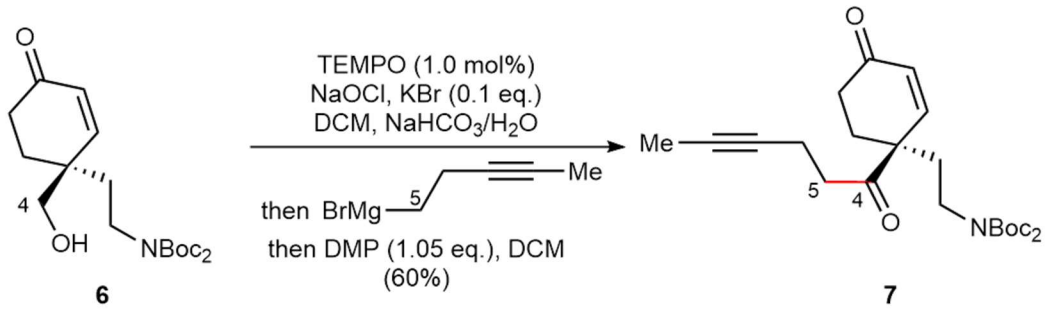
Sample Name:	JT-SI-CHIRAL	Acq. Method Set:	J1_BAR0447
Vial:	2:E,3	Processing Method:	J1_BAR0447
Date Acquired:	8/25/2022 5:18:39 PM PDT		
Date Processed:	8/25/2022 5:22:42 PM PDT		



Peak Info

	Channel Name	Name	RT	Area	Height (µV)	ent1	ent2	ee
1	UV225	Ent1	1.54	47822	19778	3.03	96.97	-93.95
2	UV225	Ent2	1.70	1532828	587756	3.03	96.97	-93.95

Compound **7**



Alcohol oxidation

To a solution of compound **6** (16.1 g, 43.6 mmol) in DCM (60 ml) was added $NaHCO_3$ (15 g) and water (50 ml). The resulting mixture was added KBr (539 mg, 4.5 mmol) and TEMPO (68 mg, 0.44 mmol) at rt (open air). The reaction was cooled to 0 °C, and a solution of NaOCl (6 wt%, 105 ml) was added slowly at the same temperature. The reaction mixture turned red immediately, and the ice bath was removed. The reaction mixture was quenched by sat. aq. $Na_2S_2O_3$ (100 ml), and extracted with DCM (3x 200 ml). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The product (ca. 16 g) was used directly to next step without purification.

Grignard reagent preparation[3]

To a suspension of Mg powder (3.1 g,129 mmol) and LiCl (6.0 g, 141 mmol) in THF (29 ml), DIBAL-H (1.3 ml, 1.0 M in toluene) was added dropwise under argon at 0 °C.

Meanwhile, a solution of 3-pentynyl bromide (19.0 g, 129 mmol, in 72.8 ml THF) was prepared at rt. A small portion of this stock solution (8.7 ml) was added to the above suspension at 0 °C to initiate the Grignard reaction. After 15 min, the rest of the stock solution was added slowly. The residual bromide was rinsed by THF (3x 10 ml). The reaction mixture was stirred vigorously at 0 °C for 30 min and warmed up to rt for an extra 30 min. The Grignard reagent was obtained as 0.54 M (theo. 0.95 M) indicated by titration with I_2 in THF.

Grignard addition

To a solution of the freshly-made aldehyde (16 g, 43.6 mmol, in 320 ml THF) at -78 °C was added the freshly-prepared Grignard reagent (110 ml, 59.4 mmol) dropwise in 1 h (under argon). The reaction mixture was kept stirring at the same temperature for an extra hour, and AcOH (10 ml) was added to quench the reaction. The resulting solution was warmed up to rt gradually, followed by adding brine (250 ml) and sat. aq. $NaHCO_3$ (50 ml) The mixture was extracted with EtOAc (4x 400 ml) and dried over $MgSO_4$. The obtained organic phase was concentrated under reduced pressure to obtain the crude product, which was used in next step without purification.

Alcohol oxidation

The crude product obtained from Grignard addition was dissolved in DCM (100 ml, open air), and cooled to 0 °C. $NaHCO_3$ (10 g) was added to the solution, followed by adding Dess-martin periodinane (19.0 g, 44.8 mmol). The reaction mixture was warmed to rt. After 1 h, the reaction mixture was diluted

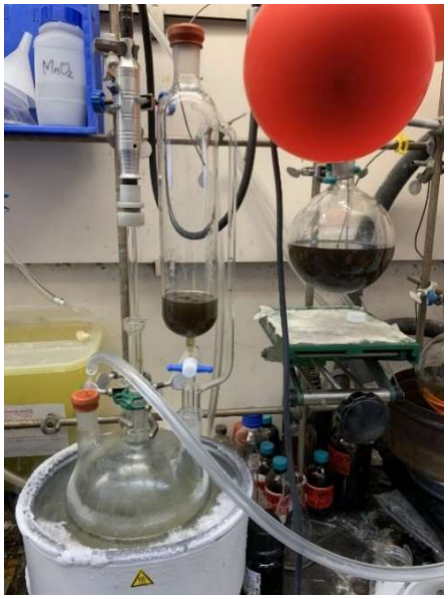
with DCM (ca. 50 ml), and was quenched by sat. aq. $Na_2S_2O_3$ (90 ml) and sat. aq. $NaHCO_3$ (150 ml). The resulting mixture was kept stirring for 45 min. The mixture was extracted with DCM (3x 100 ml) and dried over $MgSO_4$. The organic phase was concentrated under reduced pressure. The crude product was purified by chromatography (5% EtOAc in hexanes to 20% EtOAc in hexanes) to yield compound **7** (11.3 g, 26.1 mmol, 60%).

**Note: Compound 7 is bench-stable.*

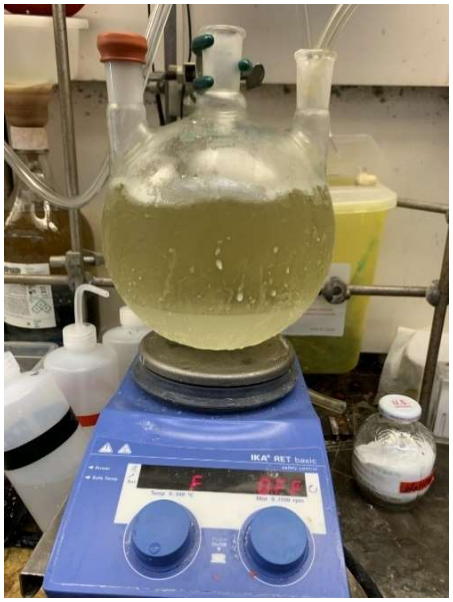
Physical state: light yellow oil
TLC: R_f = 0.60 (30% EtOAc in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -32.2 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.01 (d, J = 10.3 Hz, 1H), 6.09 (d, J = 10.3 Hz, 1H), 3.60 – 3.45 (m, 2H), 2.81 – 2.68 (m, 2H), 2.54 – 2.35 (m, 5H), 2.06 – 1.93 (m, 3H), 1.72, (s, 3H), 1.50 (s, 18H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 207.5, 198.3, 152.4 (2C), 150.1, 130.6, 83.0 (2C), 77.6, 76.6, 52.4, 42.1, 38.8, 36.5, 34.8, 29.8, 28.3 (6C), 13.6, 3.6
HRMS (ESI-TOF): calc'd for $C_{24}H_{35}NO_6$ $[M+Na]^+$: 456.2362, found: 456.2350

Pictures were based on 60 g scale

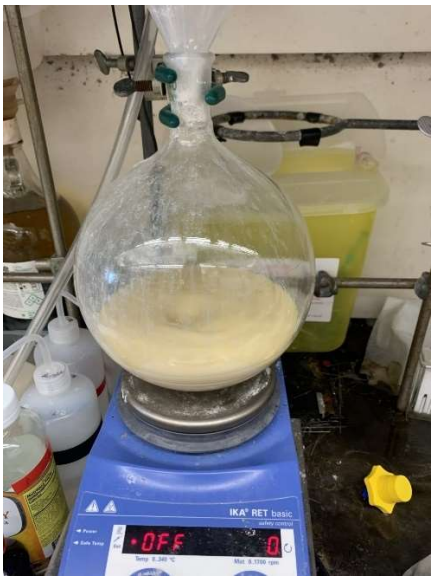
dropping bleach into **6**



adding Grignard reagent



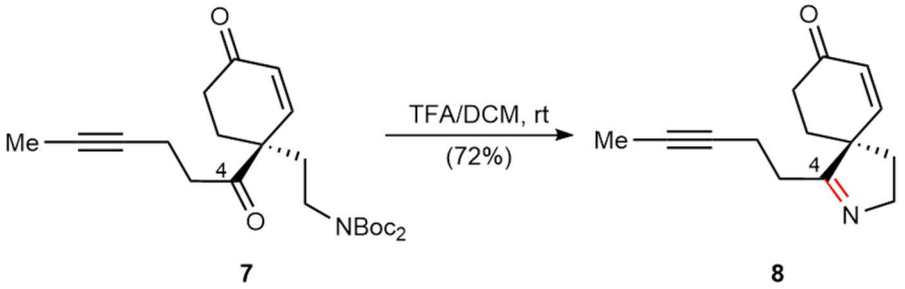
after quenching



DMP oxidation

pure product

Compound **8**



7 **8**

To a solution of compound **7** (8.8 g, 20.3 mmol) in DCM (62.8 ml) was added TFA (31.4 ml) at rt. The resulting red solution was stirred for 1.5 h at the same temperature. The reaction mixture was added carefully (via dropping funnel) to a mixture of Na_2CO_3 (64 g, in 120 ml H_2O) and 4 M NaOH (24 ml), then stirred vigorously for 36 h. The mixture was extracted with Et_2O (for the first time, 100 ml) and DCM (5x 50 ml). The organic layer was dried over $MgSO_4$, and was concentrated under reduced pressure. The crude product was purified by chromatography (Et_2O to 5% MeOH +1% TEA in Et_2O) to yield compound **8** (3.14 g, 14.6 mmol, 72%).

Note: Compound **8 is unstable for long-term storage (partial decomposition even took place after 1 week at -20 °C), should be used as soon as possible.*

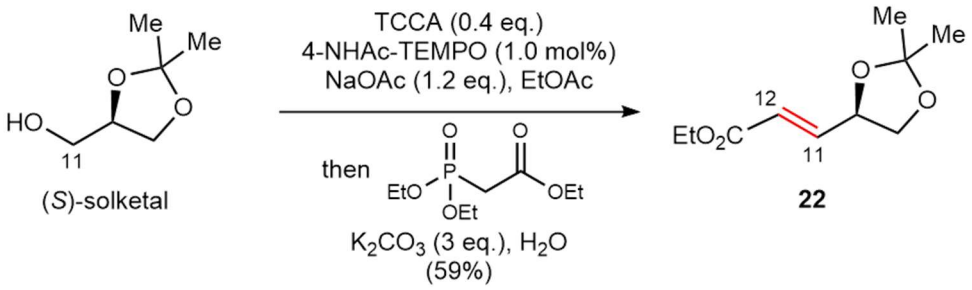
Physical state: sticky orange oil
TLC: R_f = 0.37 (pure EtOAc, highly UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -155.8 (c = 0.5, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.62 (dd, J = 10.1, 1.6 Hz, 1H), 6.05 (d, J = 10.1 Hz, 1H), 3.96 (dddt, J = 16.0, 8.6, 3.8, 1.9 Hz, 1H), 3.81 (dtt, J = 15.6, 7.6, 2.4 Hz, 1H), 2.58 – 2.48 (m, 4H), 2.48 – 2.34 (m, 2H), 2.20 – 2.09 (m, 2H), 1.96 (dddd, J = 13.0, 8.7, 7.7, 1.0 Hz, 1H), 1.86 (dtd, J = 13.5, 4.9, 1.7 Hz, 1H), 1.75 (t, J = 2.5 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 198.3, 178.0, 152.0, 129.7, 78.4, 76.2, 58.3, 55.7, 35.4, 35.2, 30.1, 29.3, 16.0, 3.7
HRMS (ESI-TOF): calc'd for $C_{14}H_{17}NO$ $[M+H]^+$: 216.1388, found: 216.1382

reaction mixture

work up

purified compound **8**

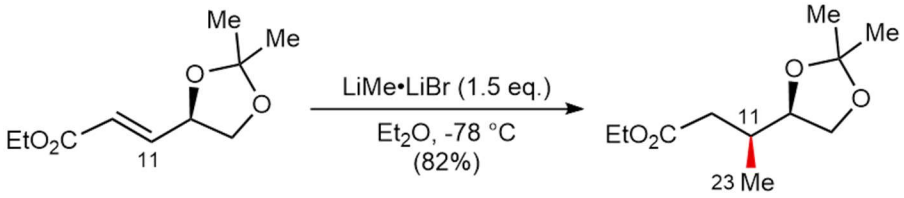
Compound **22**



To a solution of (*S*)-solketal (50.0 g, 378 mmol) in EtOAc (500 ml) was added NaOAc (37 g, 451 mmol) and 4-NHAc-TEMPO (0.81 g, 3.8 mmol) under argon. TCCA (35 g, 151 mmol) was added by portions at 0 °C. The mixture was stirring at the same temperature for 1.5 h, then filtered through a Büchner funnel. The residue was rinsed with EtOAc, and the resulting filtrate was added water (190 ml), K_2CO_3 (157 g, 1.14 mol), and triethyl phosphonoacetate (81.5 ml, 92.1 g, 411 mmol) at 0 °C. The reaction mixture was stirred overnight at rt, and a mixture of Et_2O (200 ml) and water (100 ml) was added. The organic layer was separated and the aqueous phase was extracted with Et_2O (3x 200 ml). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure (100 mbar, 25 °C). The residue was purified by chromatography (20% Et_2O in pentane) to yield compound **22** (44.8 g, 224 mmol, 59%).

Physical state: colorless oil
TLC: R_f = 0.40 (10% EtOAc in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -36.4 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 15.6, 5.6 Hz, 1H), 6.10 (dd, *J* = 15.6, 1.4 Hz, 1H), 4.66 (tdd, *J* = 7.0, 5.6, 1.4 Hz, 1H), 4.26 – 4.14 (m, 3H), 3.68 (dd, *J* = 8.3, 7.0 Hz, 1H), 1.48 – 1.43 (m, 3H), 1.41 (d, *J* = 0.8 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 166.3, 144.8, 122.7, 110.4, 75.1, 69.0, 60.8, 26.6, 25.9, 14.4
HRMS (ESI-TOF): calc'd for $C_{10}H_{16}O_4$ $[M+Na]^+$: 223.0941, found: 223.0942

Compound **23** (Ref. 4)

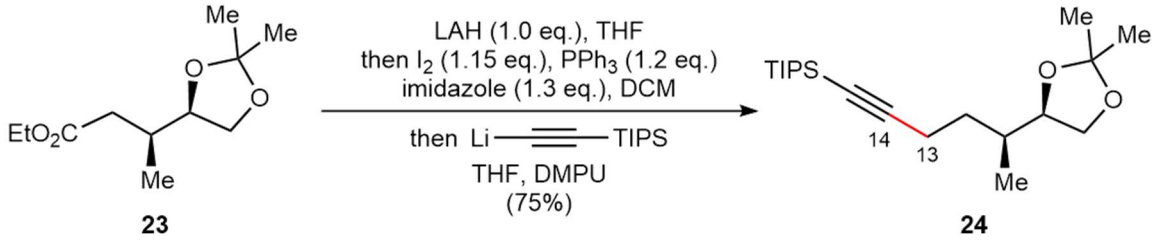


22 **23**

To a solution of compound **22** (21.0 g, 104 mmol) in Et_2O (550 ml) was added MeLi·LiBr (1.6 M in Et_2O, 71.5 ml, 157 mmol) dropwise via syringe pump (or dropping funnel) under -78 °C over 2.5 h. Upon completion, the solution was quenched by MeOH (10 ml) and sat. aq. $NaHCO_3$ (200 ml) at -78 °C, then warmed to rt slowly. The resulting mixture was extracted with Et_2O (3x 200 ml) and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the crude product was purified by chromatography (0% to 20% EtOAc in hexanes) to obtain compound **23** (18.5 g, 85.5 mmol, 82%).

Physical state: colorless oil
TLC: R_f = 0.47 (20% EtOAc in hexanes)
$[\alpha]^{25}_D$: -9.60 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 4.14 (q, J = 7.2 Hz, 2H), 4.05 – 3.96 (m, 2H), 3.66 – 3.61 (m, 1H), 2.40 (dd, J = 14.9, 5.0 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.13 (dd, J = 14.9, 8.8 Hz, 1H), 1.25 (s, 3H), 1.22 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.00 (d, J = 6.8, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 172.8, 109.1, 79.0, 67.0, 60.6, 37.8, 33.2, 26.6, 25.4, 15.6, 14.4
HRMS (ESI-TOF): calc'd for $C_{11}H_{20}O_4$ $[M+Na]^+$: 239.1259, found: 239.1254

Compound **24**



To a solution of compound **23** (10.4 g, 48.1 mmol) in THF (90 ml) was added LAH (1.83 mg, 48.2 mmol) by portions at 0 °C. The ice bath was removed, then the reaction mixture was allowed to stir at rt for 2 h. Upon completion, EtOAc (100 ml) was added slowly, then water (2 ml) was added to quench the remaining LAH. After stirring for 30 min, sat. aq. Rochelle's salt (200 mL) was added to this mixture and stirred overnight. After separating the organic layer, the aqueous phase was extracted with EtOAc (3x 100 ml). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to yield the crude alcohol.

The alcohol obtained from above was dissolved in DCM (50 ml) under argon, imidazole (4.25 g, 62.5 mmol) and PPh_3 (15.1 g, 57.7 mmol) was added. To this mixture, I_2 (14.0 g, 55.3 mmol) was added slowly. The red color faded since all I_2 was consumed. Upon completion (indicated by TLC), methanol was added to quench the excess iodine, followed by blowing air over the solution to quench the excess PPh_3 (normally takes 30 min). The volatiles were then removed by reduced pressure, and pentane (150 ml) was added and stirred vigorously (sonication if necessary). After 1 h, the solids were removed by filtration through a Büchner funnel, and the residue was washed with pentane (2x 150 ml). Subsequently, the filtrate was collected, and the pentane was removed under reduced pressure to give the crude iodide (contained ~6% TPPO).

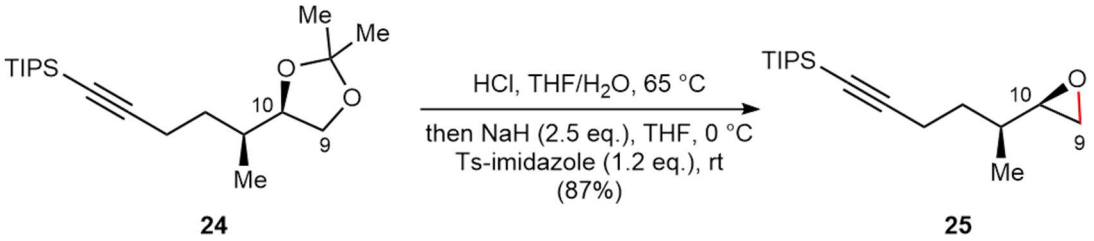
In another flame-dried round bottom flask, TIPS acetylene (9.65 g, 52.9 mmol) was dissolved in THF (86 ml), and *n*-BuLi (2.5 M in hexanes, 19.2 ml, 48.1 mmol) was added dropwise under argon. The mixture was then stirred at 0 °C for 30 min and cooled to -78 °C. DMPU (12 ml) was added to this solution in one portion. Subsequently, a solution of the freshly prepared iodide (in 20 ml THF) was added dropwise to the freshly prepared lithium acetylide. The mixture was stirred at rt overnight and quenched with water. The aqueous phase was extracted with Et_2O (3x 100 ml) and combined. The combined organic phase was rinsed with water (3x 100 ml) to remove the residual DMPU and dried over $MgSO_4$. After removal of the solvents, the residue was purified with chromatography (hexanes to 5% EtOAc in hexanes) to give compound **24** (12.2 g, 36.1 mmol, 75%).

Physical state: colorless oil
TLC: R_f = 0.21 (30% DCM in hexanes, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -16.5 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 4.02 (dd, J = 7.6, 6.3 Hz, 1H), 3.92 (q, J = 6.3 Hz, 1H), 3.64 (t, J = 7.6 Hz, 1H), 2.35 (ddd, J = 17.0, 7.5, 5.7 Hz, 1H), 2.27 (ddd, J = 17.0, 8.2, 7.3 Hz, 1H), 1.87 – 1.75 (m, 1H), 1.61 – 1.54 (m, 1H), 1.39 (s, 3H), 1.35 (s, 3H), 1.36 – 1.29 (m, 1H), 1.10 – 1.00 (m, 21H), 0.99 (d, J = 6.6 Hz, 3H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 108.9, 108.6, 80.8, 79.9, 67.9, 35.6, 32.2, 26.7, 25.7, 18.8 (6C), 17.8, 15.0, 11.5 (3C)

HRMS (ESI-TOF): calc'd for $C_{20}H_{38}O_2Si$ $[M+H]^+$: 339.2719, found: 339.2711

Compound **25**



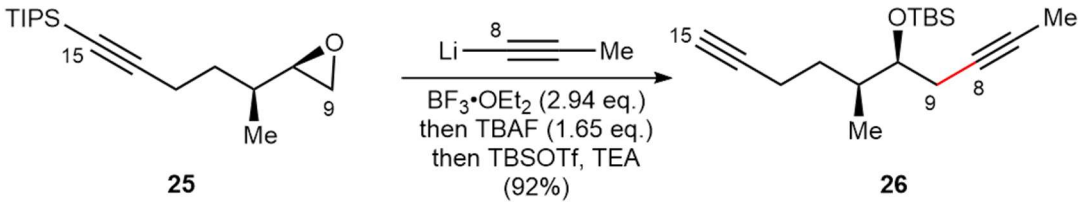
24 **25**

A solution of compound **24** (18.5 g, 54.5 mmol) in a mixture of HCl (3 M, 50 ml) and THF (100 ml) was heated at 75 °C for 12 h. The mixture was then cooled down to rt, and sat. aq. $NaHCO_3$ (100 ml) was slowly added to neutralize the HCl. The mixture was extracted with Et_2O (3x 100 ml) and the organic phase was dried over $MgSO_4$. The crude was obtained from concentrating under reduced pressure and used directly.

NaH (5.4 g, 60 wt% in mineral oil, 135 mmol) was suspended in THF (100 ml) under argon atmosphere. This mixture was then cooled to 0 °C. To this solution, the crude product obtained above (dissolved in 20 ml THF) was added dropwise. Upon completion, ice bath was removed to allow the mixture to warm up. The mixture was then stirred under rt for 1.5 h, and Ts-imidazole (14.4 g, 65 mmol) was added by portion. The resulting mixture was stirred vigorously at the same temperature for 45 min. Upon completion, H_2O (100 mL) was added in and the mixture was stirred for 15 min. The organic layer was separated and the aqueous phase was extracted with Et_2O (3x 100 ml). The combined organic phase was dried over $MgSO_4$ and concentrated. The crude product was purified by chromatography (hexanes to 30% DCM in hexanes) to yield epoxide **25** (13.3 g, 47.4 mmol, 87%).

Physical state: colorless oil
TLC: R_f = 0.33 (40% DCM in hexanes, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +13.3 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 2.77 (dd, *J* = 5.0, 3.2 Hz, 1H), 2.70 (dt, *J* = 6.8, 3.2 Hz, 1H), 2.59 (dd, *J* = 5.0, 3.2 Hz, 1H), 2.39 – 2.26 (m, 2H), 1.64 (tt, *J* = 11.3, 4.7 Hz, 1H), 1.56 – 1.47 (m, 2H), 1.13 – 0.96 (m, 24H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 108.4, 80.9, 56.7, 47.1, 35.3, 32.8, 18.8 (6C), 17.9, 16.9, 11.4 (3C)
HRMS (ESI-TOF): calc'd for $C_{17}H_{32}OSi$ $[M+H]^+$: 281.2301, found: 281.2296

Compound **26**



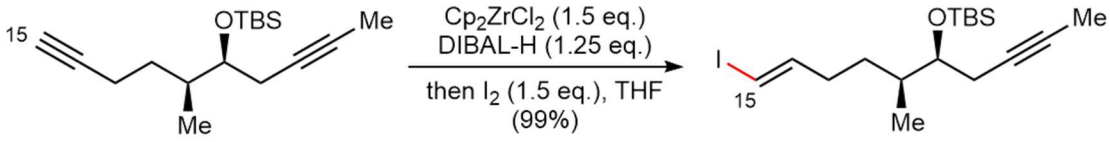
A solution of *n*-BuLi (73.0 ml, 182 mmol in hexanes) in THF (300 ml) was cooled to -78 °C under argon. To this solution, a balloon of propyne was added via needle, and the solution began to absorb the gas. Upon completion (the solution turned cloudy), the balloon was removed. The generated mixture was allowed to stir at -78 °C for 30 min.

To this freshly prepared propynyllithium, a solution of compound **25** (17.0 g, 60.6 mmol) in THF (30 ml) was added slowly at the same temperature. BF_3 etherate (22.0 ml, 178 mmol) was added subsequently, and the reaction mixture was allowed to stir at -78 °C for 1 h. The reaction was quenched with sat. aq. $NaHCO_3$ (100 mL) and diluted with Et_2O (50 mL), then stirred for 1 h. The mixture was extracted with EtOAc (3x 150 ml) and the organic layer was dried over $MgSO_4$. The solvents were removed in vacuo and the crude product was directly used for next transformation.

The crude product obtained from above was added TBAF (100 ml, 1.0 M in THF, 100 mmol) under argon. The resulting mixture was stirred at 45 °C overnight. Upon completion, sat. aq. NH_4Cl (80 mL) and EtOAc (50 mL) was added. The mixture was extracted with EtOAc (3x 100 ml) and dried over $MgSO_4$. After removing solvents under reduced pressure, the crude was dissolved in DCM (120 ml), then added TEA (18.2 g, 25.1 ml, 180 mmol). To this solution, TBSOTf (31.7 g, 27.6 ml, 120 mmol) was slowly added under rt. The mixture was stirred at the same temperature for 30 min, then heated to reflux for 1 h. Upon completion, sat. aq. $NaHCO_3$ (120 mL) was added and the mixture was extracted with DCM (3x 100 ml). The combined organic layer was dried over $MgSO_4$ and concentrated. The crude was purified by chromatography (0-5% EtOAc in hexanes) to yield compound **26** (15.5 g, 55.7 mmol, 92%).

Physical state: colorless oil
TLC: R_f = 0.50 (5% EtOAc in hexanes, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -10.5 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 3.71 (td, J = 6.7, 2.8 Hz, 1H), 2.30 – 2.22 (m, 2H), 2.18 (dtd, J = 16.9, 7.8, 2.6 Hz, 1H), 1.93 (t, J = 2.6 Hz, 1H), 1.92 – 1.85 (m, 1H), 1.77 (t, J = 2.6 Hz, 3H), 1.67 (dtd, J = 13.3, 7.9, 5.3 Hz, 1H), 1.38 (dtd, J = 13.3, 8.4, 6.0 Hz, 1H), 0.88 (s, 9H), 0.85 (d, J = 6.8 Hz, 3H), 0.08 (s, 3H), 0.06 (s, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 84.8, 77.2, 76.8, 74.5, 68.3, 36.4, 32.3, 26.0 (3C), 25.0, 18.3, 16.7, 13.0, 3.70, -4.1, -4.6
HRMS (ESI-TOF): calc'd for $C_{17}H_{30}OSi$ $[M+H]^+$: 279.2139, found: 279.2142

Compound **9**

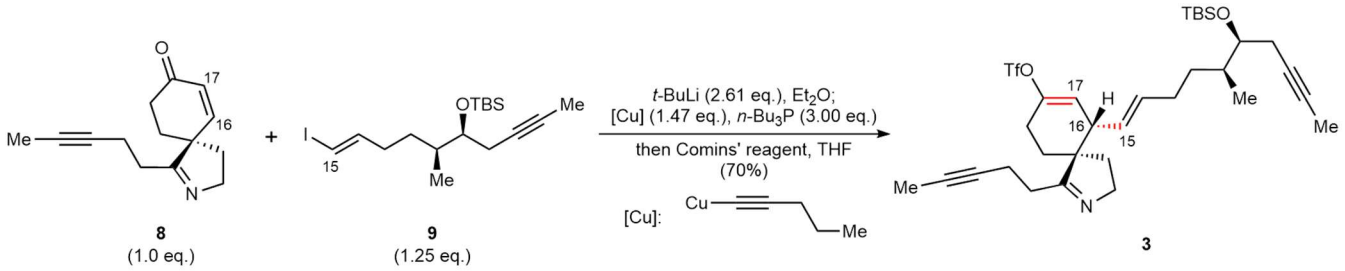


26 **9**

To a solution of Cp_2ZrCl_2 (13.6 g, 46.5 mmol) in THF (100 ml) was added DIBAL-H (38.6 ml, 38.6 mmol, 1.0 M in hexanes) dropwise at 0 °C. A white precipitation was formed. The mixture was allowed to stir for 1 h, and a solution of compound **26** (8.58 g, 30.8 mmol) in THF (10 ml) was added slowly. The reaction mixture (cloudy) was warmed up to rt slowly, and kept stirring overnight. A solution of I_2 (12.0 g, 47.2 mmol) in THF (20 ml) was added at 0 °C, the resulting dark solution was stirred for 1 h at the same temperature. The reaction was quenched with sat. aq. $Na_2S_2O_3$ (150 mL), and filtered to remove undissolved impurities (if needed). The obtained mixture was extracted with Et_2O (3x 100 ml), and the organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude product. Pure compound **9** (12.4 g, 30.4 mmol, 99%) was obtained by chromatography (2% EtOAc in hexanes).
Note: Compound **9 is highly stable and can be stored as neat (at 5 °C) for a couple of months.*

Physical state: pale yellow oil
TLC: R_f = 0.44 (3% EtOAc in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -13.6 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.51 (dt, *J* = 14.3, 7.2 Hz, 1H), 5.99 (dd, *J* = 14.3, 1.5 Hz, 1H), 3.68 (td, *J* = 6.8, 2.8 Hz, 1H), 2.29 – 2.18 (m, 2H), 2.17 – 1.99 (m, 2H), 1.78 (t, *J* = 2.6 Hz, 3H), 1.77 – 1.70 (m, 1H), 1.55 – 1.46 (m, 1H), 1.28 – 1.18 (m, 1H), 0.88 (s, 9H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.07 (s, 3H), 0.04 (s, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 146.8, 77.3, 76.7, 74.6, 74.4, 36.4, 34.1, 32.0, 26.0 (3C), 25.0, 18.3, 13.3, 3.8, -4.1, -4.5
HRMS (ESI-TOF): calc'd for $C_{17}H_{31}IOSi$ $[M+H]^+$: 407.1267, found: 407.1260

Compound **3**



Lithium-halogen exchange

To a solution of compound **9** (7.42 g, 18.3 mmol, in 46 ml Et_2O) at -78 °C, *t*-BuLi (23.8 ml, 1.6 M in pentane, 38.1 mmol) was added dropwise. A bright yellow solution was formed immediately, followed by a formation of precipitation. Reaction was kept stirring under -78 °C for at least 2.5 h to give the solution of vinyllithium.

Preparation of [Cu] [5]

To a 1L round-bottom flask charged CuI (38.0 g, 200 mmol), an aqueous ammonia solution (28-30 %, 500 ml) was added under argon. A blue solution was generated (indicating the oxidation of Cu (I)) and the dissolution of CuI took place. To reduce the amount of Cu (II) as much as possible, solid hydroxylammonium chloride was added (ca. 7 g) portionwise until the color of the solution did not fade.

Subsequently, ethanol (300 ml) was added to the solution, followed by the addition of 1-pentyne (14 ml, 142 mmol) in one portion. The solution turned dark quickly and was stirred vigorously overnight. The yellow slurry was collected by a Büchner funnel, followed by washing with water, methanol, and finally ether. After drying in vacuo for 24 h, [Cu] was obtained as a light, yellow powder (12.1 g, 93 mmol, 47% based on CuI, 65% based on 1-pentyne).

Copper (I)-phosphine complex preparation[5]

Meanwhile, [Cu] (2.86 g, 21.5 mmol) was suspended in THF (16 ml) under argon. To this suspension, *n*-Bu_3P (10.9 ml, 8.82 g, 43.6 mmol) was added dropwise. Dissolution of the yellow precipitate took place and completed in 15-30 min.

Transmetallation and conjugate addition

To the generated vinyllithium solution at -78 °C, the prepared Cu (I)-phosphine complex was added dropwise in 5 min. After addition, the orange mixture was stirred for 1 h at -78 °C.

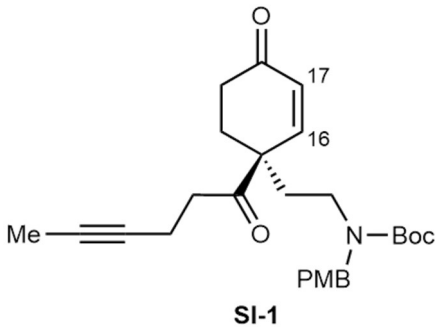
A solution of compound **8** (3.14 g, 14.6 mmol, in 10 ml THF) was added to the above solution dropwise at -78 °C. The resulting mixture was kept stirring at the same temperature for 40 min. Then a solution of Comins' reagent (8.59 g, 21.9 mmol, in 20 ml THF) was added and the resulting solution was warmed to 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and quenched by 5% aq. NH_3 (100 ml), Na_2CO_3 (10 g), and blew with air for 1 h. The resulting mixture was stirred vigorously for 45 min, and extracted with Et_2O (3x 150 ml). The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by gradient chromatography (20% Et_2O in hexanes to 40% Et_2O + 1% TEA in hexanes) to yield compound **3** (6.41 g, 10.2 mmol, 70%).

Note: Compound **3 gradually decomposed in crude, it is therefore preferable to purify the crude product as soon as possible (in the same day). The RCAM step will not work if any impurities are present.*

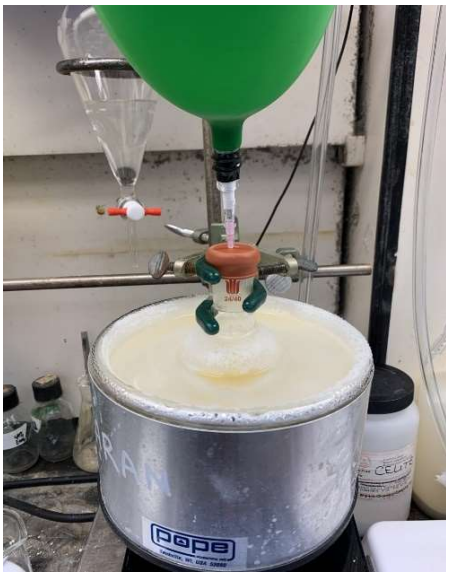
Physical state: pale yellow oil
TLC: R_f = 0.58 (50% Et_2O in hexanes, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -53.1 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.68 (d, J = 2.0 Hz, 1H), 5.46 (dt, J = 14.3, 6.8 Hz, 1H), 5.21 (ddt, J = 14.3, 7.44, 1.49 Hz, 1H), 3.85 – 3.77 (m, 1H), 3.67 (td, J = 6.96, 2.80 Hz, 1H), 3.52 (tdd, J = 10.3, 8.3, 4.1 Hz, 1H), 3.17 – 3.06 (m, 1H), 2.56 – 2.51 (m, 2H), 2.50 – 2.34 (m, 4H), 2.28 – 2.18 (m, 2H), 2.10 – 1.93 (m, 3H), 1.93 – 1.86 (m, 1H), 1.71 – 1.65 (m, 1H), 1.81 – 1.73 (m, 6H), 1.65 – 1.53 (m, 2H), 1.46 – 1.39 (m, 1H), 1.21 – 1.12 (m, 1H), 0.88 (s, 9H), 0.81 (d, J = 6.8 Hz, 3H), 0.07 (s, 3H), 0.04 (s, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 177.8, 148.9, 134.4, 126.3, 120.6, 118.7 (q, $J_{C\text{-}F}$ = 316 Hz), 78.9, 77.1, 76.9, 75.9, 74.7, 58.7, 56.7, 43.1, 37.0, 33.1, 31.5, 30.9, 30.0, 29.0, 26.0 (3C), 25.5, 25.1, 18.3, 15.9, 13.2, 3.7 (2C), -4.0, -4.5
^{1}H-COSY, ^{1}H-^{13}C-HSQC, ^{1}H-^{13}C-HMBC, NOESY spectra are available
HRMS (ESI-TOF): calc'd for $C_{32}H_{48}F_3NO_4SSi$ $[M+H]^+$: 628.3104, found: 628.3093

Supplementary Table 1. Screened conditions for conjugate addition

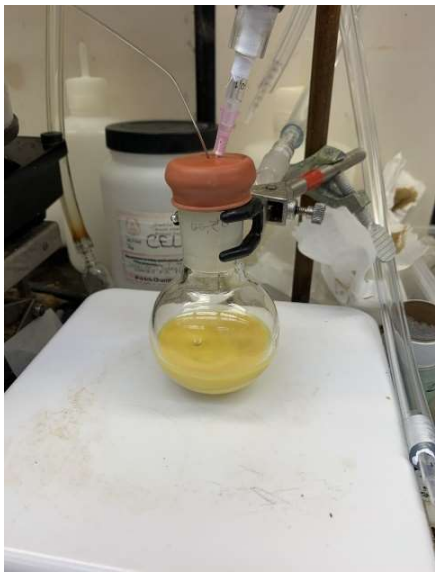
entry	enone	RLi precursor	condition	result (dr = desired:undesired)
1	**SI-1**	vinylMgBr	CuI	low yield
2	**SI-1**	vinylMgBr	CuBr	no reaction
3	**SI-1**	$vinylSnBu_3$	CuCN, LiMe, Comins' reagent	81%, dr = 1:7
4	**8**	$vinylSnBu_3$	CuCN, LiMe	messy
5	**8**	$(vinyl)_4Sn$	PhLi, CuI, Me_2S	30-54%, dr > 20:1
6	**8**	$(vinyl)_4Sn$	PhLi, CuI, n-Bu_3P, Comins' reagent	80%, dr > 20:1
7	**8**	**26**	$HZrCp_2Cl$, CuCN, LiMe	decomposed
8	**8**	**9**	n-BuLi, CuI, n-Bu_3P	no reaction
9	**8**	**9**	n-BuLi, [Cu], n-Bu_3P, $PhNTf_2$	25%, dr > 20:1
10	**8**	**9**	n-BuLi, [Cu], $P(NMe_2)_3$, $PhNTf_2$	<20% conv.
11	**8**	**9**	t-BuLi, [Cu], n-Bu_3P, $PhNTf_2$	54-70%, dr > 20:1
12	**8**	**9**	t-BuLi, [Cu], n-Bu_3P, Comins' reagent	70-83%, dr > 20:1



SI-1



after adding *t*-BuLi

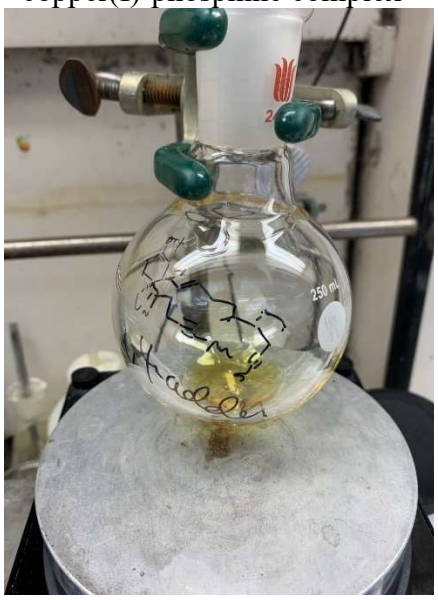


[Cu] in THF

copper(I)-phosphine complex

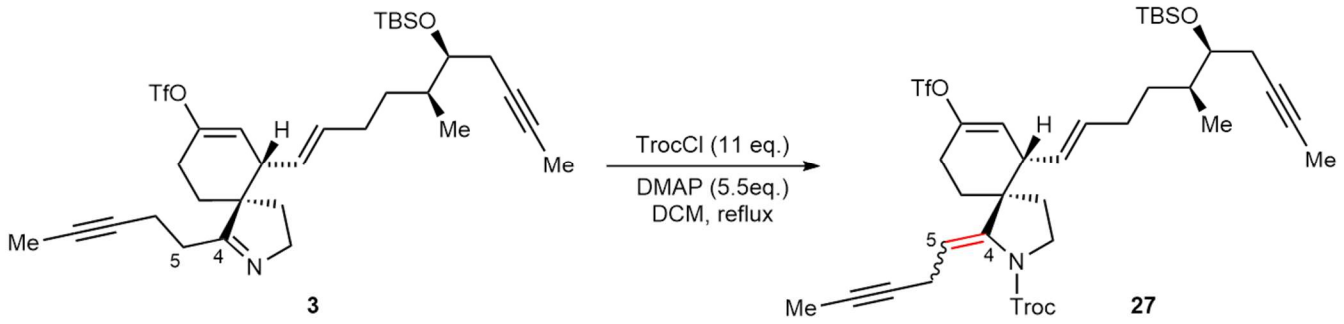
transmetalation

adding Comins' reagent



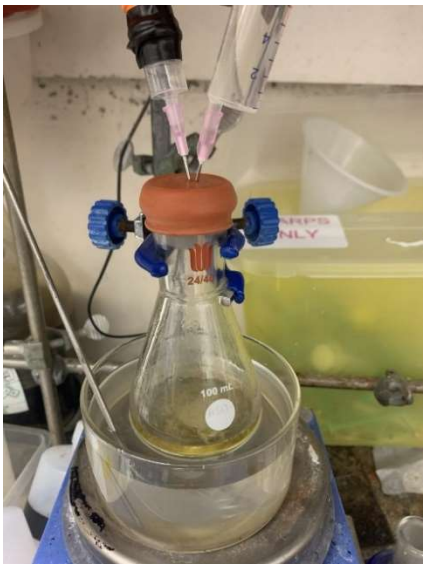
pure compound **3**

Compound **27**

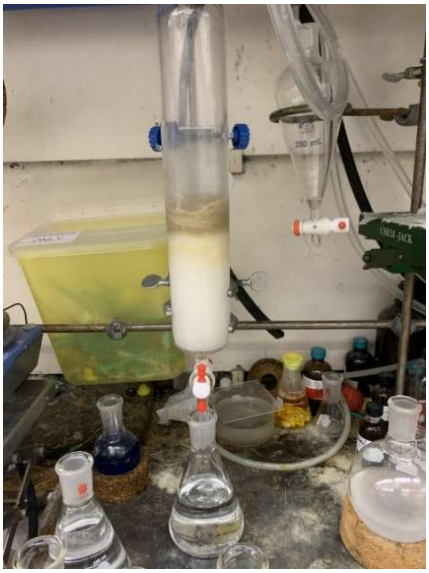


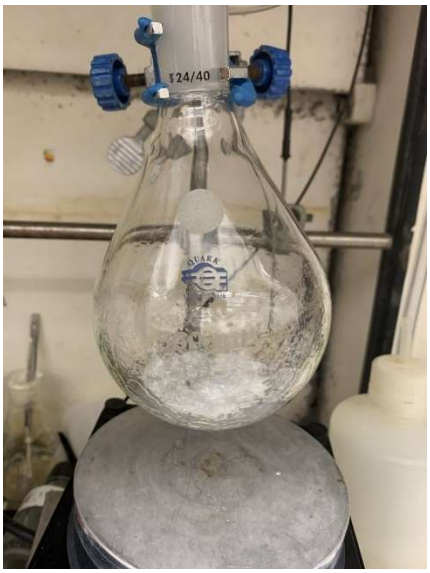
To a solution of freshly prepared compound **3** (3.33 g, 5.31 mmol) in DCM (34.0 ml) was added DMAP (3.54 g, 29.0 mmol) and heat to reflux. Subsequently, TrocCl (8.1 ml, 12.5 g, 58.8 mmol) was added dropwise, and the resulting solution was allowed to stir at the same temperature for 30 min. Upon completion, the reaction mixture (might be slurry) was added to a vigorously stirred sat. aq. $NaHCO_3$ (100 mL) The mixture was then stirred at rt for 1.5 h, and extracted with hexanes (3x 50 ml), dried over $MgSO_4$ and concentrated. Pure compound **27** (4.09 g, 5.11 mmol, 96%) was obtained by chromatography (pentane to 40% DCM in pentane).

Physical state: colorless oil
TLC: R_f = 0.44 (50% DCM in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +82.1 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.71 (d, *J* = 4.7 Hz, 1H), 5.54 (dt, *J* = 15.4, 6.7 Hz, 1H), 5.33 (dd, *J* = 15.4, 8.0 Hz, 1H), 5.00 (s, 1H), 5.20 – 4.41 (br s, 2H), 3.73 – 3.64 (m, 2H), 3.62 – 3.50 (m, 1H), 3.01 – 2.87 (m, 2H), 2.87 – 2.70 (m, 1H), 2.43 – 2.29 (m, 1H), 2.29 – 2.18 (m, 3H), 2.08 (ddt, *J* = 15.5, 10.9, 6.0 Hz, 1H), 2.04 – 1.95 (m, 1H), 1.81 (dt, *J* = 13.3, 9.7 Hz, 1H), 1.77 (t, *J* = 2.6 Hz, 3H), 1.76 (t, *J* = 2.6 Hz, 3H), 1.74 – 1.65 (m, 1H), 1.63 – 1.50 (m, 3H), 1.45 (ddt, *J* = 12.8, 9.5, 5.6 Hz, 1H), 1.24 – 1.16 (m, 1H), 0.87 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.07 (s, 3H), 0.03 (s, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ 148.8, 141.0, 135.1, 127.5, 121.8, 120.3, 118.7 (q, $J_{C\text{-}F}$ = 320.4 Hz), 95.6, 77.1, 76.9, 75.1, 74.5, 66.0, 45.7, 45.5, 45.0, 36.9, 33.3, 31.5, 30.7, 26.0, 25.1, 19.4, 18.3, 13.1, 3.7 (2C), -4.0, -4.6
(a few carbons are missing in ^{13}C-NMR; geometry of the double bond is not assigned due to rotamers)
HRMS (ESI-TOF): calc'd for $C_{35}H_{49}Cl_3F_3NO_6SSi$ $[M+H]^+$: 802.2140, found: 802.2124



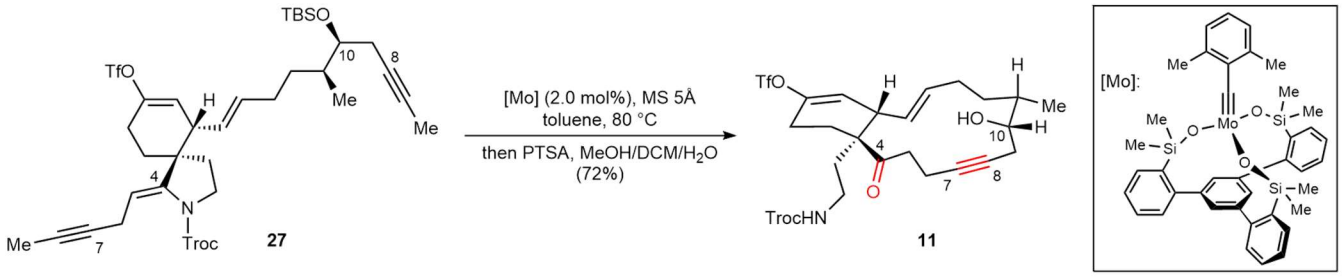
reaction mixture


chromatography



product after purification

Compound **11**



A 250 ml round bottom flask charged freshly prepared compound **27** (2.35 g, 2.93 mmol) was added MS 5Å (7.01 g, 250 wt% to SM, dried at >200 °C under high vacuum overnight) and cat. (43 mg, 0.058 mmol) in glovebox. Then the flask was taken out from glovebox, and toluene (140 ml) was added under argon. The mixture was pre-stirred for 5 min, and heated to 80 °C. After 45 min, TLC (60% DCM in hexanes) indicated the full conversion. The reaction mixture was allowed to filter over a Celite® plug to remove the molecular sieves, and rinsed with DCM. The filtrate was concentrated under reduced pressure and gave a pale-yellow foam as crude product.

The crude product was dissolved in a mixture of DCM (2.4 ml), MeOH (24 ml) and H_2O (1.2 ml). To this solution, PTSA (1.0 g, 5.3 mmol) was added, and the solution was heated to 50 °C and stirred overnight. Upon completion, the reaction mixture was quenched with sat. aq. $NaHCO_3$ (30 mL) and brine (20 mL), and was extracted with DCM (3x 50 ml). The resulting organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by chromatography (DCM to 20% Et_2O in DCM) to yield compound **11** (1.38 g, 2.11 mmol, 72%).

Note: Compound **11 is bench-stable.*

Physical state: white solid

TLC: R_f = 0.45 (20% Et_2O in hexanes, $KMnO_4$ staining)

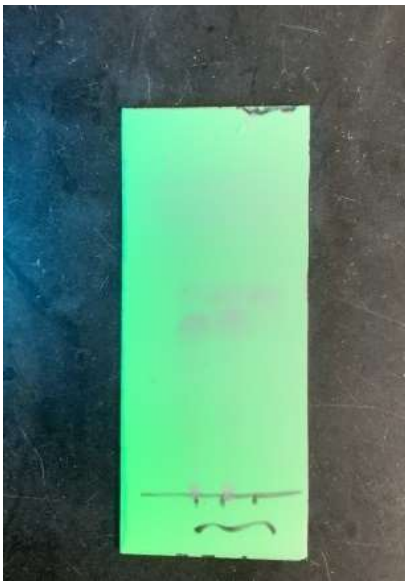
$[\alpha]^{25}_D$: -41.4 (c = 0.5, $CHCl_3$)

^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.65 (ddd, J = 15.3, 9.7, 4.7 Hz, 1H), 5.60 (d, J = 2.3 Hz, 1H), 5.27 (dd, J = 15.3, 8.6 Hz, 1H), 5.17 (t, J = 5.8 Hz, 1H), 4.74 (d, J = 12.0 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 3.56 – 3.50 (m, 1H), 3.45 (s, 1H), 3.34 – 3.27 (m, 1H), 3.26 – 3.20 (m, 1H), 2.80 (ddd, J = 18.8, 11.2, 3.0 Hz, 1H), 2.64 – 2.46 (m, 4H), 2.46 – 2.28 (m, 3H), 2.20 – 2.01 (m, 4H), 1.95 (dd, J = 14.0, 5.8 Hz, 1H), 1.85 (dq, J = 9.4, 6.6 Hz, 1H), 1.64 (ddd, J = 14.0, 9.4, 5.0 Hz, 1H), 1.50 – 1.39 (m, 2H), 1.23 – 1.15 (m, 1H), 0.93 (d, J = 6.6 Hz, 3H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 209.9, 154.7, 147.6, 133.9, 126.5, 120.5, 118.6 (q, $J_{C\text{-}F}$ = 320 Hz), 95.7, 81.5, 75.8, 74.7, 73.0, 52.0, 46.2, 37.7, 35.7, 33.0, 32.3, 28.3, 28.0, 27.2, 25.6, 24.9, 13.6, 13.1

HRMS (ESI-TOF): calc'd for $C_{25}H_{31}Cl_3F_3NO_7S$ $[M+H]^+$: 652.0917, found: 652.0919

reaction mixture

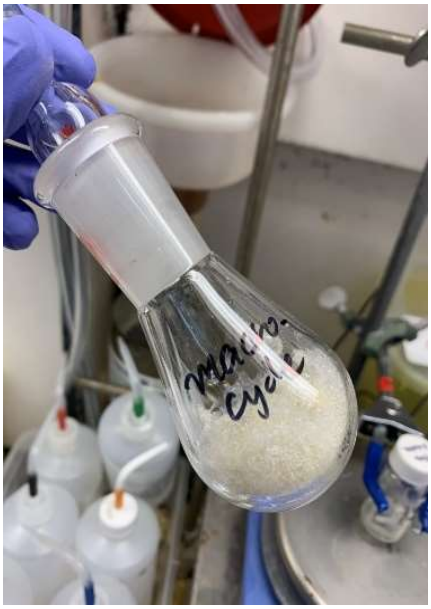


TLC (left: reaction)

TLC (under $KMnO_4$)

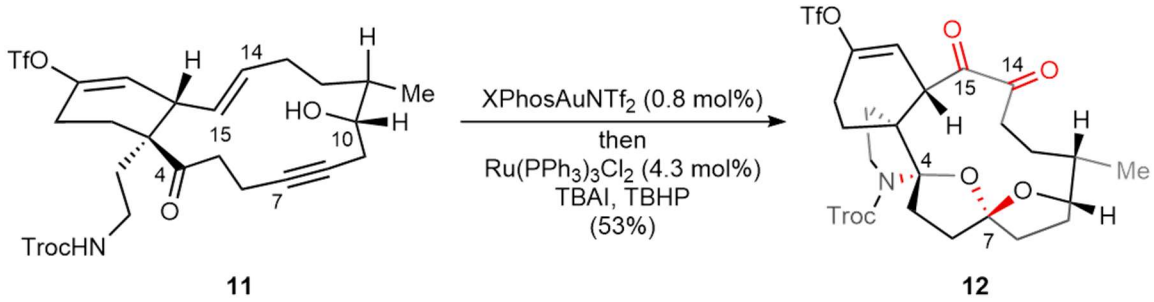
hydrolysis

TLC (after hydrolysis)



pure compound **11**

Compound **12**



11 **12**

To a solution of compound **11** (3.02 g, 4.62 mmol, azeotroped with benzene to remove residual H_2O) in DCM (30 ml) was added $XPhosAuNTf_2$ (30.2 mg, 0.032 mmol) under argon. The mixture was refluxed for 2 h. Upon completion (indicated by TLC, 20% Et_2O in DCM), it was cooled to rt, and TEA (0.05 ml) was added to quench the gold catalyst. Subsequently, the solvent was removed under reduced pressure to give a white foam.

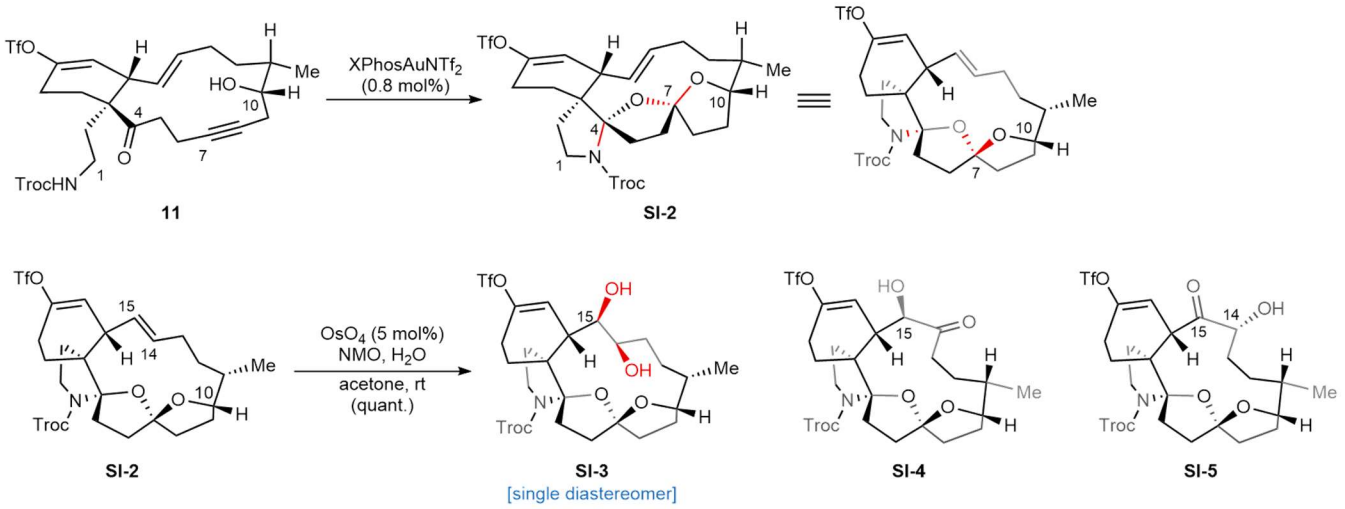
The resulting polycyclic compound was dissolved in MeCN/PhMe/H_2O (5:5:1, 112 ml), and TBAI (808 mg, 2.19 mmol) was added in one portion to give a clear solution. $Ru(PPh_3)_3Cl_2$ (191 mg, 0.2 mmol) was added to this solution subsequently. A gray-green mixture was generated. Subsequently, TBHP (5-6 M in decane, 10.9 ml) was added dropwise. The yellow green solution turned dark (ca. 15 min, protected from light with foil). The reaction was allowed to stir at rt for 1.5 h (open air, water bath to maintain a constant temperature). Upon completion, the reaction was diluted by Et_2O (50 ml), and quenched by a mixture of water (100 ml), $NaHSO_3$ (12 g) and NaCl (30 g). The resulting cloudy mixture was stirred for 1 h to give a good phase separation. After collecting the organic phase, the aqueous phase was extracted with Et_2O (4x 100 ml). The combined organic phase was dried over $MgSO_4$, and concentrated under reduced pressure, The crude product was purified by chromatography (DCM to 5% Et_2O in DCM) to yield compound **12** (1.67 g, 2.44 mmol, 53%).

Note: Compound **12 is light-sensitive and very unstable in solvents ($CHCl_3$, benzene, etc.). It is necessary to remove the solvents for storage.*

Physical state: yellow foam
TLC: R_f = 0.45 (20% Et_2O in hexanes, yellow under light, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +40.4 (c = 1.0, MeOH)
^{1}H-NMR (600 MHz, CD_3CN) δ 5.57 (m, 1H), 4.82 (d, J = 12.3 Hz, 1H), 4.70 (d, J = 12.3 Hz, 1H), 4.48 (dt, J = 4.9, 2.5 Hz, 1H), 3.78 (ddd, J = 10.1, 6.1, 3.8 Hz, 1H), 3.68 – 3.53 (m, 1H), 3.47 (td, J = 11.1, 7.1 Hz, 1H), 3.15 – 3.06 (m, 1H), 2.77 (dt, J = 12.6, 10.0 Hz, 1H), 2.68 (dddd, J = 13.6, 11.5, 9.7, 1.8 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.38 (ddt, J = 18.3, 5.3, 2.3 Hz, 1H), 2.32 – 2.20 (m, 3H), 2.02 (ddd, J = 13.6, 8.6, 3.0 Hz, 1H), 1.96 – 1.93 (m, 1H), 1.88 (dd, J = 13.2, 7.0 Hz, 1H), 1.81 – 1.73 (m, 1H), 1.72 – 1.64 (m, 3H), 1.63 – 1.53 (m, 2H), 0.83 (d, J = 7.2 Hz, 3H)
^{13}C-NMR (150 MHz, CD_3CN) δ 199.8, 199.0, 152.7, 150.6, 119.7 (q, $J_{C\text{-}F}$ = 320 Hz), 119.0, 117.9, 105.5, 96.9, 84.3, 75.0, 52.4, 45.2, 40.4, 37.6, 37.4, 37.0, 32.9, 29.1, 27.4, 25.4, 25.4, 24.1, 23.8, 18.9
HRMS (ESI-TOF): calc'd for $C_{25}H_{29}Cl_3F_3NO_9S$ $[M+H]^+$: 682.0659, found: 682.0668

Supplementary Table 2. Screened conditions for 1,2-diketone formation. (From compound SI-2)

entry	condition	result (based on **16**)
1	NMO, OsO_4, *then* DMSO, $(COCl)_2$ (>10 eq.), TEA	**SI-4** as product (83%)
2	NMO, OsO_4, *then* DMSO, TFAA (10 eq.)	trace **12**
3	NMO, OsO_4, *then* DMSO, TFAA (>45 eq.)	20% + messy byproducts
4	NMO, OsO_4, *then* CrO_3, H_2SO_4	decomposed
5	NMO, OsO_4, *then* DMP, DCE, 60 °C	**SI-4** + **SI-5** + trace **12**
6	NMO, OsO_4, *then* DMP, Py, DCE, 40 °C	no **12** observed, messy
7	NMO, OsO_4, *then* IBX, DMSO, rt	no **12** observed, SM
8	$NaBrO_3$ (excess), $RuCl_3$ (10 mol%), buffer (pH = 8)	trace **12**
9	TBHP, $[Ru(cymene)Cl_2]_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	35-55%
10	TBHP, $RuCl_3$ (8 mol%), TBAI, MeCN/PhMe/H_2O	trace **12** + decomposed
11	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	50–65%
12	TBHP, Ru(BINAP)Cl_2 (8 mol%), TBAI, MeCN/PhMe/H_2O	50%
13	TBHP, $Ru_3(CO)_{12}$ (8 mol%), TBAI, MeCN/PhMe/H_2O	35%
14	TBHP, $Ru(DMSO)_4Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	30%
15	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, $MeNO_2$/PhMe/H_2O	sluggish, messy
16	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe (dry)	sluggish, low conv.
17	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TMAI, MeCN/PhMe/H_2O	no **12** observed, SM
18	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), MeCN/PhMe/H_2O	no **12** observed, SM
19	*m*-CPBA, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	no **12** observed, SM
20	H_2O_2, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	no **12** observed, SM
21	$NaBrO_3$, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	no **12** observed, SM
22	$K_2S_2O_8$, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	no **12** observed, SM
23	cymene hydroperoxide, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O	no **12** observed, SM
24	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O, $NaHCO_3$	sluggish, low conv.
25	TBHP, $Ru(PPh_3)_3Cl_2$ (8 mol%), TBAI, MeCN/PhMe/H_2O, NaH_2PO_4	sluggish, low conv.



NMR spectra of **SI-2** (crude ^{1}H NMR from [Au] step), **SI-3** (^{1}H NMR, ^{13}C NMR, HSQC, HMBC), **SI-4** (^{1}H NMR, COSY, NOESY), and **SI-5** (^{1}H NMR, ^{13}C NMR, HSQC, HMBC, NOESY) are available.

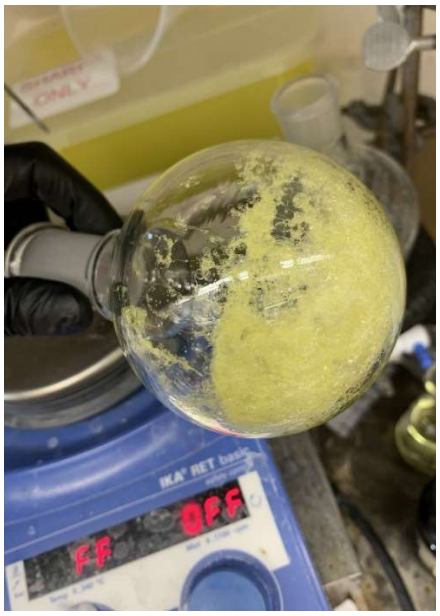
reaction mixture (w/ Au)

crude olefin

dropping TBHP into reaction

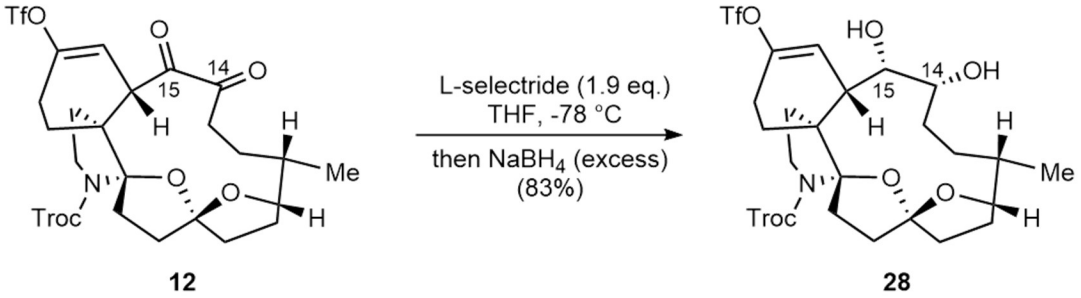
dark solution indicates completion

chromatography



pure compound **12**

Compound **28**



12 **28**

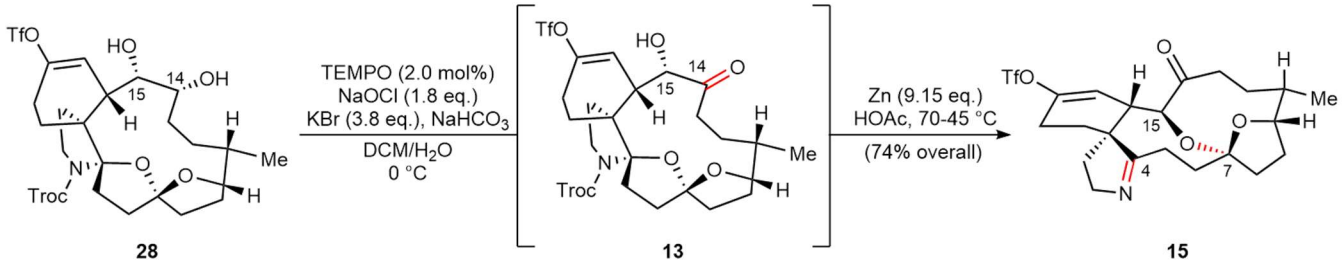
To a solution of compound **12** (2.43 g, 3.53 mmol) in THF (135 ml) was added L-selectride (1.0 M in THF, 6.7 ml) at -78 °C under argon. The yellow solution turned to colorless as completion (usually takes 30 min). The reaction was quenched according to the following procedure:

i. Adding MeOH (3.8 ml) to the mixture at -78 °C and stirred at this temperature for 5 min.
ii. The cooling bath was removed, and a mixture of water (50 ml), EtOAc (10 ml) and Na_2CO_3 (3.0 g) was added subsequently. The resulting mixture was allowed to stir for 5 min.
iii. A solution of H_2O_2 (50 wt% in H_2O, 2 ml) was added dropwise, and the mixture was stirred for 60 min at rt.

After work up, the mixture was extracted with EtOAc (3x 50 ml), and the combined organic layer was dried over $MgSO_4$. After concentrating under reduced pressure, the residue was dissolved in MeOH (100 ml) and cooled to 0 °C. $NaBH_4$ (large excess, around 500 mg) was added portionwise at this temperature. The reaction was stirred for 1 h. Upon completion (indicated by TLC), sat. aq. NH_4Cl (50 ml) and water (100 ml) was added, and the mixture was extracted with DCM (3x 150 ml). The combined organic phase was dried over $MgSO_4$ and concentrated, the crude product was purified by chromatography (5% EtOAc in DCM to 15% EtOAc in DCM) to yield compound **28** (2.03 g, 83%).

Physical state: white foam
TLC: R_f = 0.23 (30% EtOAc in hexanes, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +17.9 (*c* = 1.0, $CHCl_3$)
^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.86 (s, 1H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.06 (td, *J* = 8.9, 8.3, 4.0 Hz, 1H), 3.92 – 3.82 (m, 1H), 3,60 (t, *J* = 10.4 Hz, 1H), 3.56 – 3.10 (m, 3H), 3.03 – 2.81 (m, 1H), 2.57 – 2.22 (m, 5H), 2.11 – 1.74 (m, 10H), 1.73 – 1.52 (m, 4H), 0.86 (d, *J* = 7.2 Hz, 3H)
^{13}C-NMR (125 MHz, $CDCl_3$) δ 152.3, 149.3, 124.0, 118.7 (q, $J_{C\text{-}F}$ = 320 Hz), 116.2, 106.5, 96.0, 86.2, 81.4, 75.0, 74.6, 66.0, 49.7, 44.8, 38.0, 36.4, 35.8, 34.5, 29.9 (2C), 28.7, 26.6, 25.1, 24.1,18.1
HRMS (ESI-TOF): calc'd for $C_{25}H_{33}Cl_3F_3NO_9S$ $[M\text{-}OH]^+$: 668.0866, found: 668.0869

Compound **15**



To a solution of compound **28** (1.95 g, 2.84 mmol) in DCM (37 ml) was added TEMPO (55.5 mg, 0.059 mmol), KBr (1.3 g, 10.9 mmol) and sat. $NaHCO_3$ aq. (9.3 ml), then cooled to 0 °C. The mixture was then stirred for 5 min and a solution of NaOCl (6%, ca. 0.8 M, 5.1 ml) was added dropwise. The resulting red biphasic solution was stirred at the same temperature for 3.5 h, then quenched by adding sat. aq. $Na_2S_2O_3$ (10 ml). The yellow mixture turned colorless in a few seconds, followed by extraction with DCM for couple of times. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give a white foam (C-14 oxidized product **13**).

The crude compound **13** obtained above was mixed with zinc powder (1.7 g, 26 mmol), then dissolved in a mixture of AcOH (70 ml) and H_2O (23 ml), heated at 70 °C under argon. The mixture was stirred for 3 h at the same temperature, then cooled down to 45 °C. After stirring at 45 °C for 2 h, the mixture was cooled down to rt, and dropped into a solution of K_2CO_3 (70 g in 100 ml H_2O). After quenching the acetic acid, the biphasic mixture was extracted with DCM (4x 50 ml), and dried over $MgSO_4$. After removal of the solvents, the crude product was purified with chromatography (EtOAc to 10% MeOH + 1% TEA in EtOAc) to give compound **15** (1.03 g, 2.10 mmol, 74%).

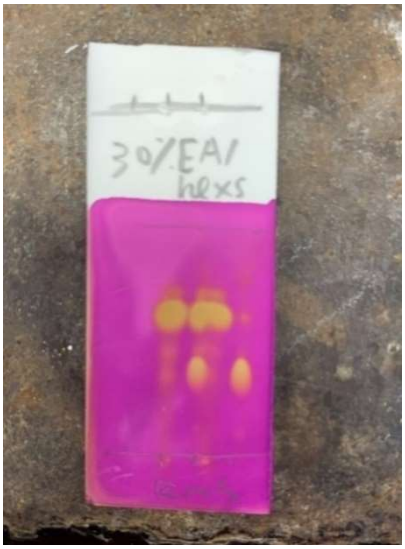
Note: Imine **15 is bench-stable.*

Physical state: pale yellow powder
TLC: R_f = 0.23 (3% MeOH in EtOAc, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -35.6 (c = 0.5, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.09 (q, J = 1.7 Hz, 1H), 4.29 (dt, J = 10.3, 6.2 Hz, 1H), 4.04 (d, J = 12.0 Hz, 1H), 4.00 – 3.94 (m, 1H), 3.89 – 3.81 (m, 1H), 3.65 – 3.58 (dtt, J = 17.2, 6.9, 3.6 Hz, 1H), 2.74 – 2.56 (m, 3H), 2.55 – 2.43 (m, 4H), 2.38 – 2.28 (m, 1H), 2.19 – 2.07 (m, 2H), 2.00 – 1.80 (m, 4H), 1.79 – 1.68 (m, 3H), 1.49 (dt, J = 12.6, 6.3 Hz, 1H), 1.43 (dd, J = 14.6, 8.1 Hz, 1H), 0.83 (d, J = 7.1 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 206.5, 182.0, 148.4, 119.1, 118.6 (q, $J_{C\text{-}F}$ = 320 Hz), 110.7, 84.6, 75.9, 56.0, 53.6, 48.7, 40.4, 37.2, 36.5, 34.1, 28.6, 28.3, 27.0, 26.3, 24.8, 24.4, 17.7
HRMS (ESI-TOF): calc'd for $C_{22}H_{28}F_3NO_6S$ $[M+H]^+$: 492.1668, found: 492.1663

Supplementary Table 3. Screened conditions for selective C-14 oxidation from compound 28.

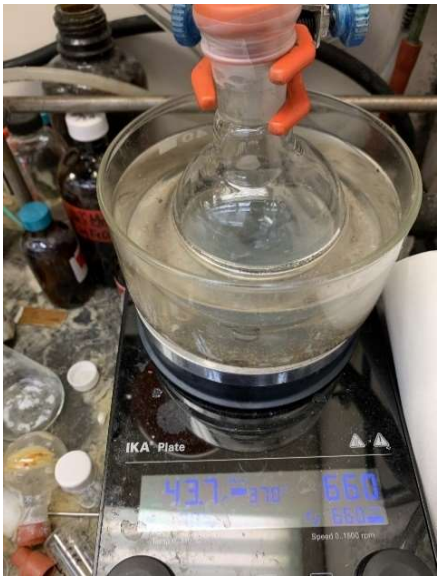
entry	condition	result
1	DMP, DCM, 0 °C	C-15 oxidized only (**SI-5**)
2	DMP, DCM, rt	**SI-5** + **12**
3	Collins reagent	messy
4	Jones' reagent	decomposed
5	PCC, DCM, 0 °C	messy
6	Fetizon's reagent, benzene, reflux	no reaction
7	DMSO, $(COCl)_2$, TEA, -78 °C to 0 °C	SM + **13** + **SI-5** + **12** + **SI-4**
8	DMSO, $(COCl)_2$, TEA, -78 °C	SM + **SI-5**:**17** (1:1) + **12**
9	DMSO, $(COCl)_2$, DIPEA, -78 °C to rt	**SI-5** + **13** + **12**
10	DMSO, DCC, Py, TFA, benzene, rt	no reaction
11	$Py{\cdot}SO_3$, DIPEA, DCM:DMSO = 1:1	no reaction
12	Ac_2O, DMSO, rt	**12** (major)
13	NCS, Me_2S, benzene	messy
14	DMSO, TFAA, TEA, -78 °C	**12** as major product
15	DMSO, TFAA, DIPEA, -78 °C	**SI-5** + **13**
16	DMSO, TFAA, morpholine, -78 °C to -50 °C	**SI-5** + **13**
17	DMSO, $(COCl)_2$, DIPEA, -78 °C to -50 °C	**SI-5** + **13**
18	DMSO, $(COCl)_2$, morpholine, -78 °C to -50 °C	**SI-5** (major) + **13**
19	TBSOTf, 2,6-lutidine, DCM	C-14 silylated only
20	DMDO, acetone, 0 °C	decomposed
21	NMO, TPAP, MS 4Å, DCM	**12** (major)
22	TEMPO, NaOCl (large excess), KBr, DCM, $NaHCO_3$	**13** (major) + **12**
23	TEMPO, NaOCl (ca. 2.0 eq.), KBr, DCM, $NaHCO_3$	**13** (93-99%)


oxidation step



TLC after completion (oxidation)


crude hydroxyl ketone



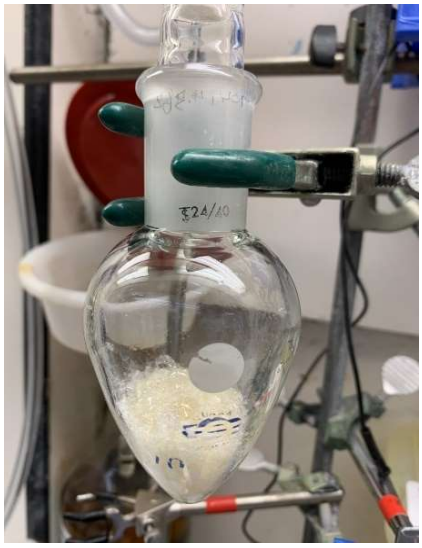
reaction mixture (ring reconstitution)

TLC of reaction (5% MeOH/EA)

quench by K_2CO_3

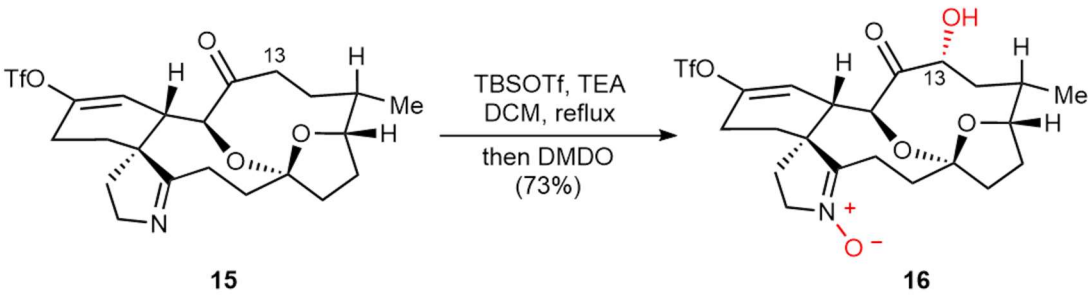
crude product

chromatography



pure compound **15**

Compound **16**



Silylation

To a solution of compound **15** (505 mg, 1.03 mmol) in refluxing DCM (5.0 ml) was added TEA (1.07 ml, 777 mg, 7.68 mmol) and TBSOTf (0.75 ml, 862 mg, 3.26 mmol). The reaction mixture was then allowed to stir for 45 min. Upon completion, the mixture was rinsed with sat. aq. $NaHCO_3$ (5 ml), followed by extraction with DCM (3x 10 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated to give crude silyl enol ether as product.

DMDO oxidation

The crude product from above was dissolved in DCM (3 ml), and added DMDO solution (freshly prepared, ca. 0.08 M in acetone, 50 ml) at 0 °C dropwise. After stirring at 0 °C for 1 h, the solvent was removed in vacuo. The residual was redissolved in acetone/H_2O (v/v = 1:1, 20 ml) and added $NaHCO_3$ solid. Oxone® (550 mg) was added to this mixture, and the reaction was stirred at rt for 1 h. Upon completion, a mixture of brine (10 ml) and DCM (5 ml) was added. The aqueous phase was extracted with DCM (4x 10 ml), and the organic layer was dried and concentrated. The crude product was purified by chromatography (EtOAc to 10% MeOH in EtOAc) to give compound **16** (387.1 mg, 0.74 mmol, 73%).
Note: Nitrone **16 is stable for long-term storage under -20 °C.*

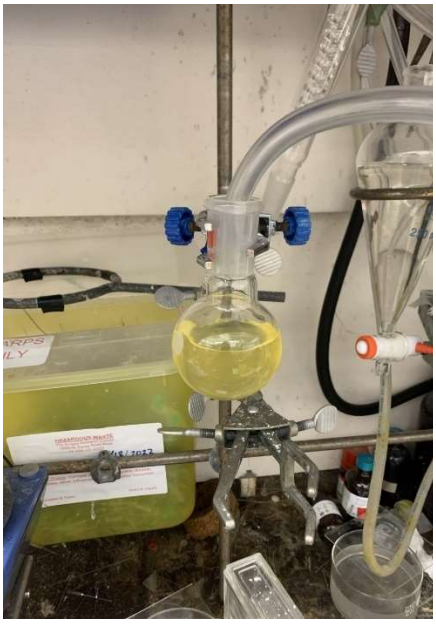
Physical state: white powder
TLC: R_f = 0.30 (10% MeOH in EtOAc, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +49.0 (*c* = 0.1, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.23 (s, 1H), 4.78 (br s, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.25 (dt, *J* = 11.2, 6.0 Hz, 1H), 4.09 – 4.02 (m, 1H), 4.00 (dd, *J* = 11.3, 2.8 Hz, 1H), 3.95 – 3.86 (dt, *J* = 13.4, 6.4 Hz, 2H), 3.45 (td, *J* = 14.3, 7.3 Hz, 1H), 2.60 – 2.43 (m, 3H), 2.30 (dt, *J* = 14.1, 11.0 Hz, 1H), 2.26 – 2.18 (m, 2H), 2.14 – 2.04 (m, 2H), 2.04 – 1.92 (m, 2H), 1.92 – 1.84 (m, 2H), 1.82 (dd, *J* = 15.2, 7.2 Hz, 1H), 1.73 (dt, *J* = 12.7, 7.0 Hz, 1H), 1.59 (dt, *J* = 12.7, 6.3 Hz, 1H), 1.54 (dd, *J* = 14.1, 2.8 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 204.2, 153.4, 147.8, 118.6 (q, $J_{C\text{-}F}$ = 320 Hz), 118.0, 110.7, 84.9, 78.7, 70.9, 59.5, 49.3, 40.2, 37.7, 34.3, 33.9, 33.6, 29.0, 25.6, 24.4, 22.7, 18.4, 17.6
HRMS (ESI-TOF): calc'd for: $C_{22}H_{28}F_3NO_8S$ $[M+H]^+$: 524.1561, found: 524.1561

charge SM in flask

silylation

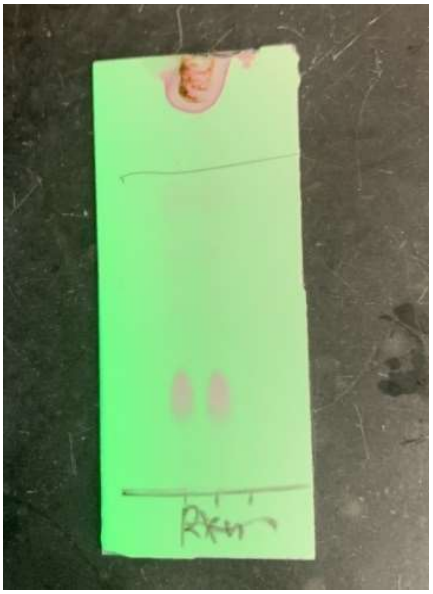
TLC (5% MeOH in EA, right: SM)

silyl enol ether with DMDO



removal of acetone

treated with Oxone®



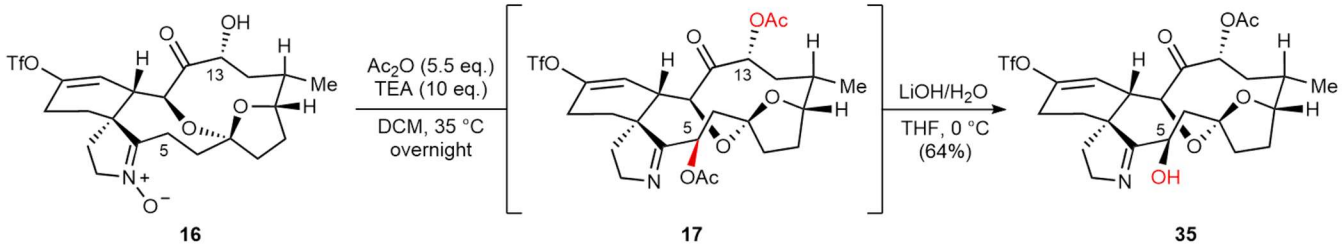
TLC (under UV, 10% MeOH in EA)

TLC (upon $KMnO_4$)

chromatography

pure nitrone **16**

Compound **17** and **35**



Compound **16** (339 mg, 0.65 mmol) was dissolved in DCM (6.0 ml), and TEA (0.9 ml, 660 mg, 6.5 mmol) was added. The mixture was then heated to 35 °C, and Ac_2O (0.34 ml, 365 mg, 3.58 mmol) was added dropwise. The mixture was stirred overnight (monitored with TLC using 5% MeOH in DCM). Upon completion, the reaction was quenched with sat. aq. $NaHCO_3$ (2.0 ml) at rt. The mixture was extracted with DCM (3x 10 ml), and the combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give crude compound **17** (purity determined by NMR of crude product).

Physical state: white solid
TLC: R_f = 0.42 (5% MeOH in DCM, $KMnO_4$ staining)
[α]$^{25}_D$: +5.30 (c = 1.0, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.78 (dd, J = 10.9, 8.0 Hz, 1H), 5.19 (dd, J = 11.1, 2.8 Hz, 1H), 5.05 (q, J = 1.7 Hz, 1H), 4.36 (d, J = 12.0 Hz, 1H), 4.25 (dt, J = 10.0, 6.0 Hz, 1H), 4.18 – 4.08 (m, 1H), 3.92 (dd, J = 16.2, 9.1 Hz, 1H), 3.77 (ddd, 16.2, 10.2, 6.9 Hz, 1H), 2.64 – 2.41 (m, 3H), 2.41 – 2.26 (m, 3H), 2.23-2.13 (m, 1H), 2.12 – 1.95 (m, 2H), 2.08 (s, 3H), 2.05 (s, 3H), 1.93-1.73 (m, 4H), 1.60 (td, J = 12.5, 7.6 Hz, 1H), 1.52 (dd, J = 13.2, 2.8 Hz, 1H), 0.88 (d, J = 6.5 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 199.8, 177.2, 169.3, 169.0, 148.8, 118.6 (q, $J_{C\text{-}F}$ = 320 Hz), 117.8, 108.1, 84.0, 79.9, 73.0, 72.1, 56.4, 53.7, 40.4, 39.1, 36.7, 34.0, 31.6, 29.4, 28.7, 26.5, 24.5, 21.3, 20.9, 17.4
^{1}H-^{13}C-HSQC, ^{1}H-^{13}C-HMBC spectra are available
HRMS (ESI-TOF): calc'd for $C_{26}H_{32}F_3NO_{10}S$ $[M+H]^+$: 608.1777, found: 608.1776

The crude **17** obtained above was dissolved in THF (8.1 ml) and H_2O (0.95 ml), and a solution of LiOH (1.4 M in H_2O, 1.0 ml) was added dropwise at 0 °C. The resulting solution was then stirred at 0 °C, and carefully monitored by TLC (5% MeOH in DCM). The reaction was quenched by a mixture of sat. aq. $NaHCO_3$ (10 ml) and DCM (10 ml), followed by extraction with DCM (3x 10 ml). The organic layer was combined and dried over $MgSO_4$. After removal of the solvents, the crude product was purified by chromatography (pure DCM to 5% MeOH in DCM) to afford compound **35** (226 mg, 0.41 mmol, 64%).
Note: Compound **35 was made since it was the start point to all portimine-related analogs described below.*

Physical state: white powder
TLC: R_f = 0.25 (5% MeOH in DCM, $KMnO_4$ staining)
[α]$^{25}_D$: +14.0 (c = 0.1, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.19 (dd, J = 11.4, 2.7 Hz, 1H), 5.06 (q, J = 1.7 Hz, 1H), 4.75 (dd, J =

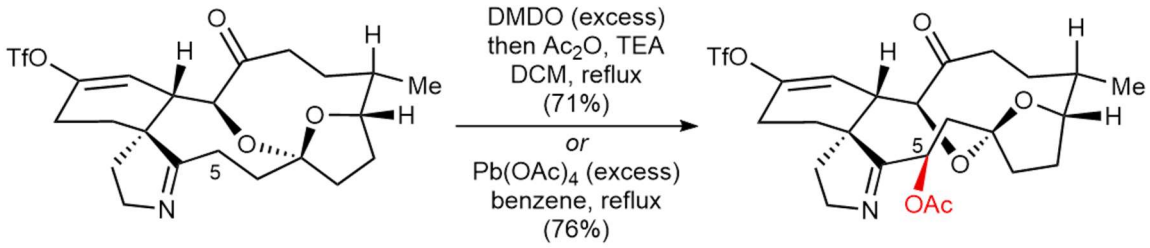
11.1, 7.6 Hz, 1H), 4.34 (d, J = 12.2 Hz, 1H), 4.29 – 4.20 (m, 2H), 3.81 (dd, J = 15.7, 8.9 Hz, 1H), 3.61 (ddt, J = 16.2, 10.5, 5.8 Hz, 1H), 2.72 (dd, J = 14.9, 11.2 Hz, 1H), 2.57 – 2.25 (m, 5H), 2.19 (dd, J = 15.0, 7.6 Hz, 1H), 2.04 (s, 3H), 2.03 – 1.98 (m, 1H), 1.98 – 1.93 (m, 1H), 1.91 – 1.81 (m, 2H), 1.77 (dt, J = 12.1, 7.1 Hz, 1H), 1.70 – 1.67 (m, 1H), 1.58 (dd, J = 12.6, 7.7 Hz, 1H), 1.52 (dd, J = 13.6, 2.8 Hz, 1H), 0.88 (d, J = 6.9 Hz, 3H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 199.6, 183.2, 169.1, 148.6,118.7 (q, J_{C-F} = 319 Hz), 118.0, 108.4, 84.0, 80.0, 72.9, 70.3, 55.4, 53.5, 42.7, 38.9, 37.0, 34.0, 31.5, 29.5, 29.1, 26.5, 24.4, 21.0, 17.5

HRMS (ESI-TOF): calc'd for $C_{24}H_{30}F_3NO_9S$ $[M+H]^+$: 566.1666, found: 566.1658

For stereochemistry assignment of compound **35**, see spectra data of compound **SI-6**.

Synthesis of compound **SI-6**



15 **SI-6**

Procedure I (DMDO oxidation followed by acetylation)

To a solution of compound **15** (3.7 mg, 0.0075 mmol) in DCM (0.1 ml) was added DMDO solution (freshly prepared, ca. 0.08 M in acetone, 0.25 ml) at 0 °C in one portion. After stirring at 0 °C for 1 h, the volatiles were removed in vacuo. The residual was redissolved in DCM (0.2 ml) and added Ac_2O (ca. 0.05 ml) and TEA (ca. 0.05 ml), followed by heating to reflux overnight. The mixture was quenched with sat. aq. $NaHCO_3$ (1.0 ml) at rt and extracted with DCM (3x 1 ml). The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. Pure compound **SI-6** (2.9 mg, 0.0053 mmol, 71%) was obtained by PTLC (10% MeOH in DCM)

Procedure II (Lead (IV) acetate oxidation)

To a solution of compound **15** (20.1 mg, 0.041 mmol) in benzene (1.0 ml) was added $Pb(OAc)_4$ (25 mg, contains AcOH as stabilizer, white crystals) under argon at room temperature. The reaction mixture was then heated to reflux and stirred for 1 h. The yellow solution was then quenched by adding sat. aq. $NaHCO_3$ (2 ml) and extracted with DCM (3x 2 ml). The combined organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Pure compound **SI-6** (17.3 mg, 0.031mmol, 76%) was obtained by PTLC described above.

Physical state: white powder

TLC: R_f = 0.35 (5% MeOH in DCM, $KMnO_4$ staining)

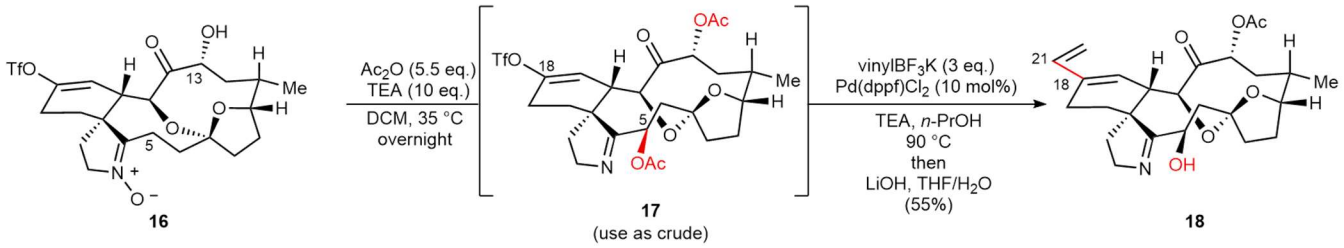
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.79 (dd, J = 10.9, 8.1 Hz, 1H), 5.10 (t, J = 1.7 Hz, 1H), 4.29 (dt, J = 10.2, 6.2 Hz, 1H), 4.15 (d, J = 10.9 Hz, 1H), 4.06 (d, J = 12.0 Hz, 1H), 3.96 – 3.88 (m, 1H), 3.76 (ddd, J = 16.4, 10.3, 6.8 Hz, 1H), 2.68 – 2.58 (m, 2H), 2.49 (dddd, J = 23.0, 14.7, 11.1, 6.0 Hz, 3H), 2.37 – 2.26 (m, 2H),

2.24 – 2.14 (m, 1H), 2.14 – 2.09 (m, 1H), 2.07 (s, 3H), 2.07 – 2.04 (m, 1H), 1.99 – 1.90 (m, 2H), 1.87 (dd, J = 12.6, 6.7 Hz, 1H), 1.78 (dtd, J = 11.6, 6.9, 6.2, 2.7 Hz, 2H), 1.57 (td, J = 12.6, 7.7 Hz, 1H), 1.45 (dd, J = 14.9, 7.8 Hz, 1H), 0.84 (d, J = 7.1 Hz, 3H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 206.1, 177.6, 169.4, 148.6, 118.8, 118.4 (q, $J_{C\text{-}F}$ = 320 Hz), 108.1, 84.6, 76.0, 72.1, 56.3, 53.7, 48.7, 40.4, 39.6, 37.1, 36.6, 29.4, 28.7, 26.4, 24.8, 24.6, 21.3, 17.7

^{1}H-^{13}C-HSQC, ^{1}H-^{13}C-HMBC, NOESY spectra are available

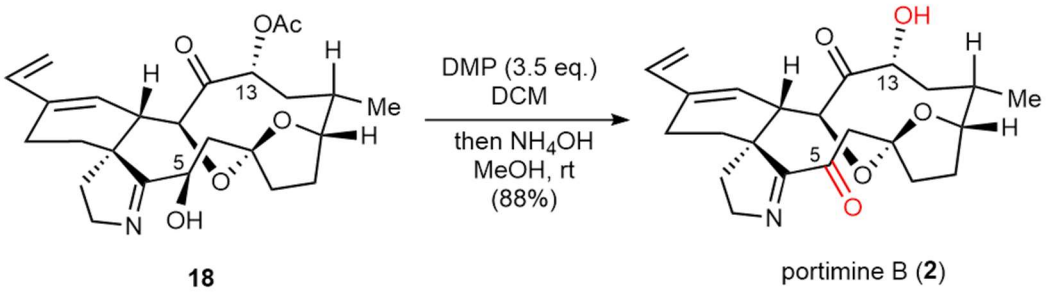
Compound **18**



To a solution of crude compound **17** (39.3 mg, 0.065 mol, synthesized by the aforementioned procedure) in *n*-PrOH (2.0 ml) was added vinylBF_3K (30 mg, 0.22 mol) and Pd(dppf)Cl_2·DCM (5.1 mg, 0.007 mol) at rt. The mixture was then heated to 90 °C, and TEA (0.05 ml) was added dropwise. The resulting red solution became yellow gradually, ended a brown solution. The reaction was monitored by TLC (40% acetone in hexanes). Upon completion, the volatiles were removed by reduced pressure, and the residue was redissolved in a mixture of THF/H_2O (v/v = 8:1, 1 ml), and added LiOH (1.4 M in H_2O, 0.1 ml) at 0 °C. The reaction was carefully monitored by TLC (5% MeOH in DCM). Upon completion, the reaction was quenched by a mixture of sat. aq. $NaHCO_3$ (1 ml) and DCM (1 ml), followed by extraction with DCM (3x 1 ml). The organic layer was combined and dried over $MgSO_4$. After removal of the solvents, the crude product was purified by PTLC (5% MeOH in DCM) to afford compound **18** (15.4 mg, 55%).

Physical state: white solid
TLC: R_f = 0.43 (40% acetone in hexanes, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +18.0 (*c* = 0.1, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.18 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.24 – 5.19 (m, 1H), 5.10 (d, *J* = 17.5 Hz, 1H), 4.91 – 4.99 (m, 2H), 4.75 (dd, *J* = 11.2, 7.4 Hz, 1H), 4.31 (d, *J* = 12.1 Hz, 1H), 4.26 (dt, *J* = 10.7, 5.6 Hz, 1H), 4.16 (d, *J* = 12.1 Hz, 1H), 3.76 (dd, *J* = 16.2, 8.8 Hz, 1H), 3.61 (ddd, *J* = 16.2, 10.4, 6.8 Hz, 1H), 2.81 (dd, *J* = 14.8, 11.3 Hz, 1H), 2.42 – 2.22 (m, 5H), 2.19 – 2.14 (m, 1H), 2.07 (s, 3H), 2.03 (dd, *J* = 12.3, 7.0 Hz, 1H), 1.91 – 1.71 (m, 4H), 1.71 – 1.63 (m, 1H), 1.57 (td, *J* = 12.5, 7.6 Hz, 1H), 1.53 – 1.46 (m, 1H), 0.87 (d, *J* = 7.0 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 200.1, 184.0, 168.9, 139.0, 135.4, 127.7, 111.6, 108.2, 83.7, 80.1, 73.7, 70.8, 55.4, 54.2, 42.5, 39.8, 36.9, 34.0, 31.6, 29.6, 29.2, 24.3, 22.7, 21.1, 17.4
HRMS (ESI-TOF): calc'd for $C_{25}H_{33}NO_6$ $[M+H]^+$: 444.2381, found: 444.2377

Compound **2** (portimine B)



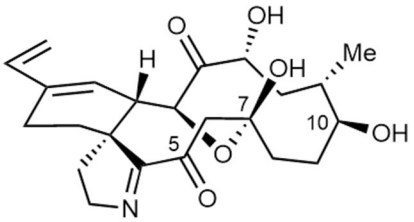
18 portimine B (**2**)

To a solution of compound **18** (16.7 mg, 0.038 mol) in DCM (0.3 ml) was added DMP (55.1 mg, 0.13 mmol) and $NaHCO_3$ powder (25 mg). The resulting mixture was allowed to stir at rt for 1 h. Upon completion, sat. aq. K_2CO_3 (0.2 ml) and sat. aq. $Na_2S_2O_3$ (0.2 ml) was added, followed by dilution with DCM (2 ml) and water (2 ml). The biphasic mixture was stirred vigorously for 30 min, and the organic layer was separated. The aqueous phase was extracted with DCM (3x 2 ml), and the combined DCM phase was dried over $MgSO_4$ and filter. After concentration, the residue was dissolved in MeOH (0.2 ml) and added aq. NH_3 (37%, 0.1 ml). The progress of hydrolysis can be monitored by TLC (5% MeOH in DCM). After completion, the mixture was added brine to facilitate phase separation. DCM was chosen to extract the solution (3x 2 ml), and the combined DCM layer was dried and concentrated. Portimine B (**2**) (13.3 mg, mmol, 88%) was obtained by chromatography (pure DCM to 5% MeOH in DCM).

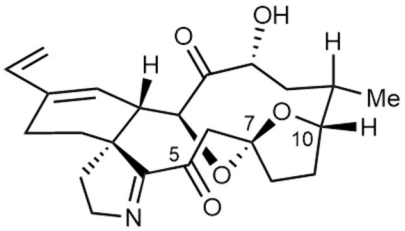
Physical state: white solid
TLC: R_f = 0.22 (3% MeOH in DCM, UV active, $KMnO_4$ staining)
$[\alpha]^{25}_D$: +42.9 (c = 0.08, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.21 (dd, J = 17.4, 10.8 Hz, 1H), 5.11 (d, J = 17.4 Hz, 1H), 5.07 (d, J = 2.0 Hz, 1H), 4.97 (d, J = 10.8 Hz, 1H), 4.62 (d, J = 12.2 Hz, 1H), 4.281 (dt, J = 10.1, 6.0 Hz, 1H), 4.15 (d, J = 11.3 Hz, 1H), 4.08 (dd, J = 16.2, 9.1 Hz, 1H), 3.83 (ddd, J = 16.6, 10.4, 6.7 Hz, 1H), 3.78 (d, J = 12.8 Hz, 1H), 3.43 (d, J = 17.5 Hz, 1H), 2.79 (d, J = 17.5 Hz, 1H), 2.50 (s, 1H), 2.42 – 2.24 (m, 4H), 2.12 (dd, J = 12.5, 7.1 Hz, 1H), 2.03 – 1.90 (m, 2H), 1.87 (dd, J = 12.5, 6.6 Hz, 1H), 1.78 (dt, J = 12.4, 6.4 Hz, 2H), 1.73 – 1.65 (m, 1H), 1.63 – 1.53 (m, 1H), 0.91 (d, J = 7.1 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 204.4, 200.9, 182.5, 138.6, 136.0, 126.7, 112.4, 107.1, 84.7, 78.9, 72.2, 58.1, 54.7, 53.0, 40.9, 38.2, 34.3, 34.1, 28.7, 28.6, 24.4, 22.6, 17.7
HRMS (ESI-TOF): calc'd for $C_{23}H_{29}NO_5$ $[M+H]^+$: 400.2119, found: 400.2117

Supplementary Table 4. Comparison of ^{13}C shift in $CDCl_3$ and chemical structure between synthetic 2 and previously reported 2 (Ref. 6).

position	chemical shift in reported **2**	chemical shift in synthetic **2**
C1	58.1	58.4
C2	28.7	28.8
C3	54.7	55.1
C4	182.5	182.9
C5	200.9	201.4
C6	53.0	53.2
C7	107.1	107.2
C8	38.2	38.5
C9	24.4	24.6
C10	84.7	85.0
C11	34.3	34.7
C12	34.1	34.3
C13	78.9	79.1
C14	204.4	204.8
C15	72.2	72.4
C16	40.9	41.2
C17	126.7	126.9
C18	136.0	135.8
C19	22.6	22.8
C20	28.6	28.8
C21	138.6	138.8
C22	112.4	112.5
C23	17.7	18.0

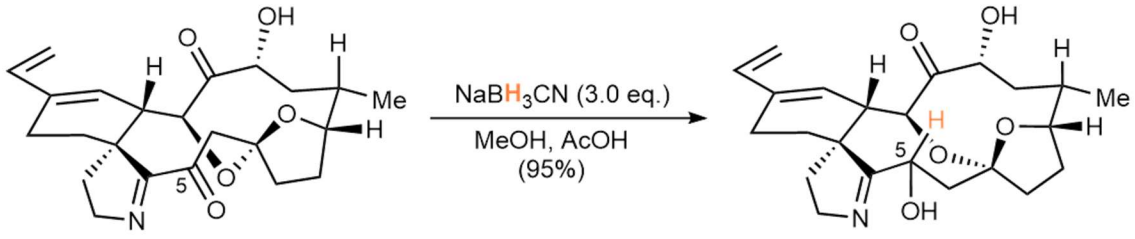


portimine B (**2**)
reported structure



portimine B (**2**)
revised structure

Compound **1** (portimine A)



portimine B (**2**) portimine A (**1**)

To a solution of crude compound **2** (ca. 20 mg, 0.05 mmol) in MeOH (0.5 ml) was added $NaBH_3CN$ (10 mg, 0.16 mol) and AcOH (0.025 ml) at rt. The resulting mixture was stirred at the same temperature for 1.5 h, and quenched with sat. $NaHCO_3$ aq. The mixture was extracted with DCM (4x), and the organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified with chromatography (DCM to 10% MeOH in DCM) to obtain compound **1** (19.2 mg, 0.048 mol, 95%).

**Note: Portimine A can be auto-oxidized to portimine B under air.*

Physical state: white solid

TLC: R_f = 0.54 (10% MeOH in DCM, UV active, $KMnO_4$ staining)

$[\alpha]^{25}_D$: +5.8 (*c* = 1.0, $CHCl_3$)

^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.21 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.17 – 5.01 (m, 2H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.71 (br s, 1H), 4.52 (s, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.18 (dt, *J* = 11.2, 5.6 Hz, 1H), 4.08 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.86 (dd, *J* = 15.2, 8.8 Hz, 1H), 2.81 (dd, *J* = 15.9, 5.1 Hz, 1H), 2.43 – 2.19 (m, 4H), 2.09 (d, *J* = 15.8 Hz, 1H), 2.01 – 1.92 (m, 2H), 1.93 – 1.79 (m, 2H), 1.79 – 1.61 (m, 5H), 1.50 (dd, *J* = 13.7, 2.6 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H)

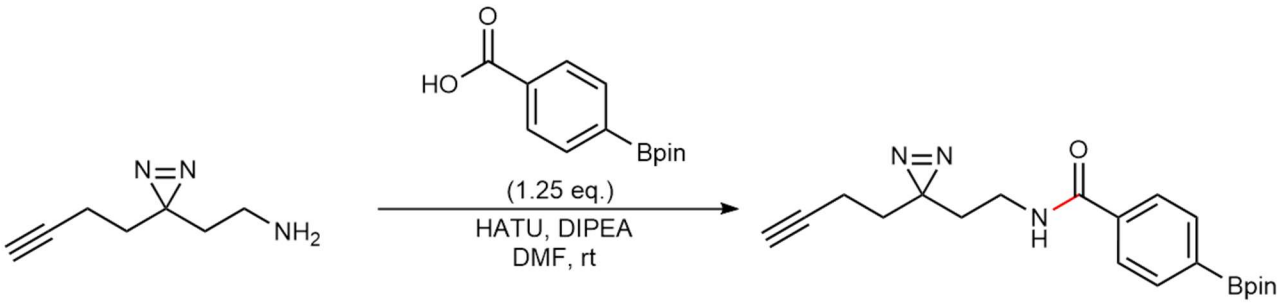
^{13}C-NMR (150 MHz, $CDCl_3$) δ 204.6, 185.0, 138.8, 135.2, 127.8, 111.7, 109.1, 83.2, 79.3, 71.6, 65.6, 54.9, 52.7, 43.1, 40.6, 37.6, 34.3, 33.8, 29.6, 29.0, 24.6, 22.6, 17.6

HRMS (ESI-TOF): calc'd for $C_{23}H_{31}NO_5$ $[M+H]^+$: 402.2275, found: 402.2265

Supplementary Table 5. Comparison of ^{13}C shift in $CDCl_3$ and chemical structure between synthetic 1 and previously reported 1.

position	chemical shift in authentic **1**	chemical shift in synthetic **1**
C1	54.9	54.9
C2	29.4	29.6
C3	52.7	52.7
C4	185.0	185.0
C5	65.6	65.6
C6	43.1	43.1
C7	109.1	109.1
C8	37.6	37.6
C9	24.6	24.6
C10	83.2	83.2
C11	34.3	34.3
C12	33.8	33.8
C13	79.3	79.3
C14	204.6	204.6
C15	71.6	71.6
C16	40.7	40.6
C17	127.8	127.8
C18	135.2	135.2
C19	22.6	22.6
C20	29.1	29.0
C21	138.8	138.8
C22	111.7	111.7
C23	17.6	17.6

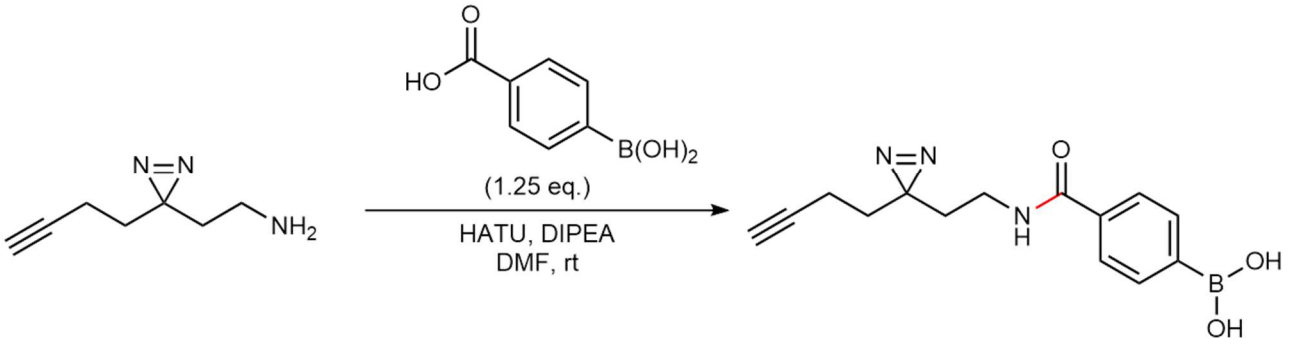
Compound **29-1**



To a solution of amine (16 mg, 0.12 mmol) in DMF (0.2 ml) was added HATU (44 mg, 0.12 mmol) and acid (38 mg, 0.15 mmol). The mixture was stirred at rt, followed by an addition of DIPEA (10 drops). The resulting yellow solution was stirred under argon for 16 h, and diluted with Et_2O (1 ml). Sat. $NaHCO_3$ aq. (1 ml) was added to this mixture to quench the excess benzoic acid. The resulting biphasic mixture was extracted with Et_2O (3x 1 ml), dried over $MgSO_4$, and concentrated under reduced pressure. Pure compound **29-1** (32 mg, 0.087 mmol, 73%) was obtained by PTLC (12% Et_2O in DCM).

Physical state: colorless oil
TLC: R_f = 0.55 (30% EtOAc in hexanes, UV active, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 6.35 (t, *J* = 5.8 Hz, 1H), 3.31 (q, *J* = 6.6 Hz, 2H), 2.03 (td, *J* = 7.2, 2.6 Hz, 2H), 1.98 (t, *J* = 2.6 Hz, 1H), 1.82 (t, *J* = 6.6 Hz, 2H), 1.68 (t, *J* = 7.2 Hz, 2H), 1.35 (s, 12H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 167.7, 136.7, 135.2 (2C), 126.2 (2C), 84.3 (2C), 82.9, 69.6, 35.1, 32.7, 32.3, 29.9, 27.1, 25.0 (4C), 13.4
HRMS (ESI-TOF): calc'd for $C_{20}H_{26}BN_3O_3$ $[M+H]^+$: 368.2140, found: 368.2136

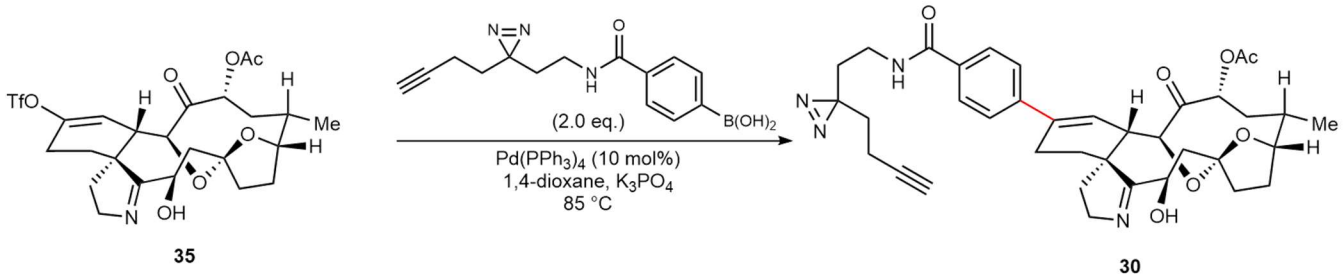
Compound **29-2**



To a solution of amine (10.0 mg, 0.12 mmol) in DMF (0.2 ml) was added HATU (36 mg, 0.12 mmol) and acid (16 mg, 0.15 mmol). The mixture was stirred at rt, followed by an addition of DIPEA (0.05 ml). The resulting yellow solution was stirred under argon for 16 h, followed by adding H_2O (1 ml). The resulting biphasic mixture was extracted with EtOAc (3x 1 ml), dried over $MgSO_4$, and concentrated under reduced pressure. Pure compound **29-2** (17.2 mg, 0.087 mmol, 73%) was obtained by PTLC (60% EtOAc in hexanes).

Physical state: white solid
TLC: R_f = 0.65 (60% EtOAc in hexanes, UV active, $KMnO_4$ staining)
^{1}H-NMR (500 MHz, CD_3OD) δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 2H), 2.27 (t, *J* = 2.7 Hz, 1H), 2.05 (td, *J* = 7.4, 2.7 Hz, 2H), 1.75 (t, *J* = 7.1 Hz, 2H), 1.68 (t, *J* = 7.4 Hz, 2H)
^{13}C-NMR (126 MHz, CD_3OD) δ 169.0, 133.5 (2C), 125.8 (2C), 82.2, 69.0, 37.5, 34.6, 32.1, 31.8, 26.6, 12.5
(1 aromatic carbon was missing in ^{13}C NMR)
HRMS (ESI-TOF): calc'd for $C_{14}H_{16}BN_3O_3$ $[M+H]^+$: 286.1363, found: 286.1354

Compound **30**

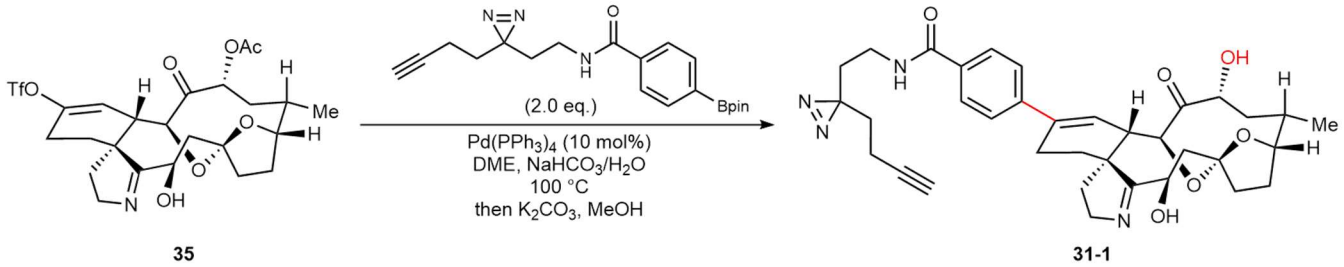


35 **30**

To a solution of compound **35** (5.0 mg, 0.0088 mmol) and compound **29-2** (5.1 mg, 0.018 mmol) in 1,4-dioxane (0.35 ml) was added $Pd(PPh_3)_4$ (0.7 mg, 0.00091 mmol) and K_3PO_4 (3 mg). The resulting yellow solution was heated to 85 °C. Upon completion (normally 2 h), H_2O (0.2 mL) was added to the mixture followed by extraction with DCM (3x 1 ml). The pure compound **30** (4.5 mg, 0.0069 mmol, 78%) was obtained by PTLC (45% acetone in hexanes).

Physical state: white solid
TLC: R_f = 0.25 (10% MeOH in DCM, UV active, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 6.29 (t, *J* = 5.9 Hz, 1H), 5.41 (s, 1H), 5.25 – 5.20 (m, 1H), 4.80 (dd, *J* = 11.1, 7.5 Hz, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 4.29 – 4.20 (m, 2H), 3.82 (dd, *J* = 15.6, 8.6 Hz, 1H), 3.68 (ddd, *J* = 16.0, 10.1, 7.0 Hz, 1H), 3.31 (q, *J* = 6.4 Hz, 2H), 2.84 (dd, *J* = 14.8, 11.2 Hz, 1H), 2.64 – 2.52 (m, 2H), 2.47 – 2.32 (m, 3H), 2.21 (dd, *J* = 14.9, 7.5 Hz, 1H), 2.04 (s, 3H), 2.04 – 2.02 (m, 2H), 1.98 (t, *J* = 2.6 Hz, 2H), 1.98 – 1.84 (m, 3H), 1.82 (t, *J* = 6.6 Hz, 2H), 1.81 – 1.74 (m, 3H), 1.68 (t, *J* = 7.3 Hz, 2H), 1.59 (td, *J* = 12.6, 7.7 Hz, 1H), 1.53 (dd, *J* = 13.1, 2.9 Hz, 1H), 0.89 (d, *J* = 6.2 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 200.3, 184.5, 169.1, 167.3, 144.1, 135.6, 133.1 (2C), 127.2, 125.1, 124.9, 108.4, 83.9, 82.9, 80.3, 73.8, 70.8, 69.7, 55.4, 53.8, 42.7, 40.1, 37.0, 35.1, 34.2, 32.7, 32.3, 31.7, 30.1, 29.9, 29.3, 27.1, 26.0, 24.5, 21.3, 17.6, 13.4
HRMS (ESI-TOF): calc'd for $C_{37}H_{44}N_4O_7$ $[M+H]^+$: 657.3283, found: 657.3291

Compound **31-1** (ePA-DA)



To a solution of compound **35** (5.1 mg, 0.0091 mmol) and compound **29-1** (6.6 mg, 0.018 mmol) in DME (0.2 ml) was added $Pd(PPh_3)_4$ (1.0 mg, 0.00091 mmol). The resulting yellow solution was added sat. aq. $NaHCO_3$ (0.05 ml) while stirring, followed by heating to 100 °C. Upon completion (normally 2 h), water (0.5 ml) was added and the mixture was extracted with DCM (3x 1ml). The combined organic layer was dried over $MgSO_4$ and concentrated. The residue was dissolved in MeOH (0.1 ml) and treated with K_2CO_3 (10 mg). After vigorous stirring at rt for 30 min, the mixture was extracted with DCM (3x 1 ml) and purified by PTLC (8% MeOH in DCM) to afford compound **31-1** (4.4 mg, 0.0072 mmol, 79%) as product.

Note: Hydrolysis of the acetate was occasionally observed under Suzuki condition described here, directly delivered compound **31-1.*

Physical state: white solid

TLC: R_f = 0.21 (10% MeOH in DCM, UV active, $KMnO_4$ staining)

^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.12 (br s, 1H), 5.63 (s, 1H), 4.74 (t, *J* = 9.3 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.31 (s, 1H), 4.14 – 4.03 (m, 1H), 3.92 (d, *J* = 12.0 Hz, 1H), 3.59 (q, *J* = 6.5 Hz, 1H), 3.54 – 3.45 (m, 1H), 3.42 – 3.30 (m, 1H), 2.96 (q, *J* = 9.1 Hz, 1H), 2.85 (t, *J* = 12.9 Hz, 1H), 2.43 – 2.29 (m, 2H), 2.29 – 2.20 (m, 2H), 2.18 – 2.09 (m, 1H), 2.05 – 1.87 (m, 6H), 1.86 – 1.70 (m, 4H), 1.68 (td, *J* = 7.2, 4.5 Hz, 2H), 1.65 – 1.55 (m, 3H), 1.54 – 1.44 (m, 1H), 0.95 (d, *J* = 6.5 Hz, 3H)

^{13}C-NMR (150 MHz, $CDCl_3$) δ 207.8, 185.1, 167.7, 142.3, 133.8, 132.9 (2C), 127.4, 124.7, 124.4, 108.1, 84.3, 82.9, 79.6, 71.5, 70.8, 69.6, 54.7, 53.8, 42.4, 40.3, 37.1, 34.9, 34.6, 33.0, 32.8, 32.3, 29.9, 29.7, 28.9, 27.2, 25.1, 24.4, 17.8, 13.5

HRMS (ESI-TOF): calc'd for $C_{35}H_{42}N_4O_6$ $[M+H]^+$: 615.3177, found: 615.3170

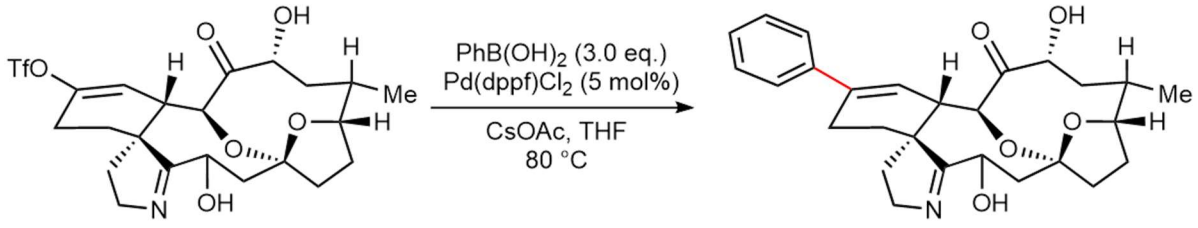
Compound **31-2** (PA-DA)

30 **31-2**

To a solution of compound **30** (4.5 mg, 0.0069 mmol) in DCM (0.8 ml) was added DMP (5.9 mg, 0.014 mmol) and $NaHCO_3$ (10 mg) at rt. The mixture was then stirred for 2 h, followed by quenching with sat. aq. $Na_2S_2O_3$ (0.5 ml) and solid Na_2CO_3 (10 mg). The mixture was then stirred for 30 min to give a clear biphasic liquid. The DCM layer was collected and the aqueous layer was extracted with DCM (3x 1 ml). The organic phase was dried over $MgSO_4$ and concentrated to give the crude product, which was dissolved in MeOH (0.15 ml) and treated with AcOH (5 drops). The solution was cooled to 0 °C, and $NaBH_3CN$ (ca. 5 mg, large excess) was added in one portion. The colorless solution was stirred at the same temperature for 1.5 h. Upon completion, K_2CO_3 (100 mg) and H_2O (0.1 ml) was added subsequently, which gave a slightly yellow mixture. The hydrolysis was carried out at rt for 1 h, and the mixture was extracted with DCM (4x 1 ml). The combined organic layer was dried over $MgSO_4$ and concentrated. Pure compound **31-2** (2.1 mg, 0.0034, 49%) was obtained by PTLC (10% MeOH in DCM).

Physical state: white solid
TLC: R_f = 0.23 (10% MeOH in DCM, UV active, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 6.31 (s, 1H), 5.54 (d, *J* = 2.2 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.43 (s, 1H), 4.21 (dt, *J* = 11.2, 5.9 Hz, 1H), 4.10 (dd, *J* = 11.3, 2.7 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.72 – 3.62 (m, 2H), 3.30 (q, *J* = 6.4 Hz, 2H), 2.80 (dd, *J* = 15.9, 5.1 Hz, 1H), 2.54 (d, *J* = 7.8 Hz, 2H), 2.39 – 2.32 (m, 1H), 2.31 – 2.25 (m, 1H), 2.13 (d, *J* = 15.9 Hz, 1H), 2.07 – 1.96 (m, 5H), 1.92 (dd, *J* = 12.6, 6.7 Hz, 1H), 1.89 – 1.83 (m, 1H), 1.81 (t, *J* = 6.6 Hz, 2H), 1.75 (td, *J* = 12.3, 5.1 Hz, 2H), 1.72 – 1.63 (m, 3H), 1.61 – 1.51 (m, 2H), 0.90 (d, *J* = 6.9 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 205.5, 185.2, 167.3, 143.7, 135.0, 133.0 (2C), 127.1, 125.4, 109.2, 83.5, 82.9, 79.4, 71.6, 69.7, 65.7, 55.0, 52.1, 43.2, 40.8, 37.8, 35.1, 34.5, 33.8, 32.6, 32.3, 29.9, 29.5, 29.3, 27.2, 25.7, 24.8, 17.8. 13.4
HRMS (ESI-TOF): calc'd for $C_{35}H_{42}N_4O_6$ $[M+H]^+$: 615.3177, found: 615.3193

Compound **32** (PhPA)

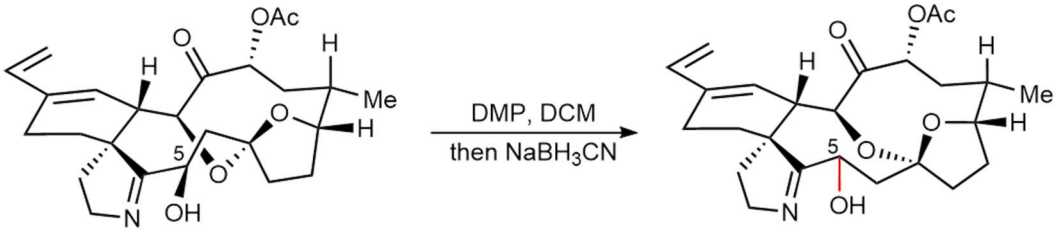


37 **32**

To a mixture of compound **37** (2.3 mg, 0.0044 mmol), $PhB(OH)_2$ (1.6 mg, 0.013 mmol), CsOAc (5 mg), and $Pd(dppf)Cl_2 \cdot DCM$ (0.18 mg, 0.0002 mmol) was added THF (0.3 ml) and heated to reflux. After 20 h, TLC indicated the full completion (monitored by 40% acetone in hexanes), and a mixture of sat. aq. Na_2CO_3 (0.5 ml) and DCM (1 ml) was added. The mixture was extracted with DCM (4x 1ml), dried over $MgSO_4$, and concentrated. Pure compound **32** (1.7 mg, 0.0037 mmol, 84%) was obtained by PTLC (10% MeOH in DCM).

Physical state: white powder
TLC: R_f = 0.46 (10% MeOH in DCM, UV active, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 5.47 (s, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.37 (s, 1H2), 4.21 (dt, *J* = 11.2, 6.0 Hz, 1H), 4.09 (dd, *J* = 11.2, 2.6 Hz, 1H), 3.84 (dd, *J* = 15.3, 9.0 Hz, 1H), 3.71 – 3.61 (m, 1H), 3.55 (d, *J* = 12.1 Hz, 1H), 2.78 (dd, *J* = 15.9, 5.1 Hz, 1H), 2.58 – 2.41 (m, 2H), 2.39 – 2.24 (m, 2H), 2.11 (d, *J* = 15.9 Hz, 1H), 2.01 – 1.93 (m, 2H), 1.93 – 1.81 (m, 2H), 1.76 – 1.70 (m, 1H), 1.71 – 1.63 (m, 3H), 1.55 (dd, *J* = 14.1, 2.7 Hz, 1H), 0.91 (d, *J* = 6.9 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 206.1, 140.4, 135.4, 128.5, 127.6, 125.2, 123.4, 109.2, 83.4, 79.6, 71.7, 65.7, 54.8, 52.1, 43.1, 40.5, 37.7, 34.5, 33.5, 29.9, 29.4, 29.1, 25.6, 24.8, 17.8
(1 carbon (C=N) was missing in ^{13}C NMR)
HRMS (ESI-TOF): calc'd for $C_{27}H_{33}NO_5$ $[M+H]^+$: 452.2432, found: 452.2435

Compound **33**

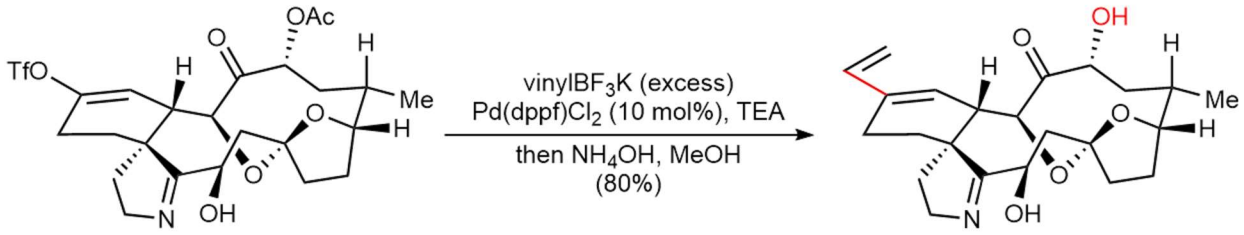


18 **33**

Compound **33** (6.3 mg, 0.014 mmol) was prepared from compound **18** (9.0 mg, 0.020 mmol) by oxidation with DMP (excess, ca. 10 mg) and reduction with $NaBH_3CN$ (same as the synthesis of **1**). Purified by PTLC (5% *i*-PrOH in DCM).

Physical state: white powder
TLC: R_f = 0.58 (10% MeOH in DCM, UV active, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 6.16 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.21 – 5.16 (m, 1H), 5.10 (d, *J* = 17.5 Hz, 1H), 4.96 (d, *J* = 10.8 Hz, 1H), 4.90 (s, 1H), 4.52 (t, *J* = 4.2 Hz, 1H), 4.29 (d, *J* = 11.9 Hz, 1H), 4.20 (dt, *J* = 10.8, 5.4 Hz, 1H), 3.88 (dd, *J* = 15.3, 8.9 Hz, 1H), 3.75 (d, *J* = 12.4 Hz, 1H), 3.70 (ddd, *J* = 14.7, 7.1, 3.7 Hz, 1H), 2.81 (dd, *J* = 16.0, 5.1 Hz, 1H), 2.45 – 2.26 (m, 4H), 2.11 (dd, *J* = 16.1, 1.9 Hz, 1H), 2.06 (s, 3H), 1.99 (dd, *J* = 12.2, 7.1 Hz, 2H), 1.93 (dd, *J* = 12.5, 6.9 Hz, 1H), 1.88 – 1.63 (m, 5H), 1.49 (dd, *J* = 12.9, 2.8 Hz, 1H), 0.87 (d, *J* = 6.6 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 200.5, 185.8, 169.0, 138.8, 135.6, 127.3, 112.2, 109.4, 83.3, 80.2, 73.6, 65.7, 54.8, 52.8, 43.3, 40.7, 37.8, 34.1, 31.6, 29.5, 29.0, 24.7, 22.7, 21.3, 17.6
HRMS (ESI-TOF): calc'd for $C_{25}H_{33}NO_6$ $[M+H]^+$: 444.2381, found: 444.2379

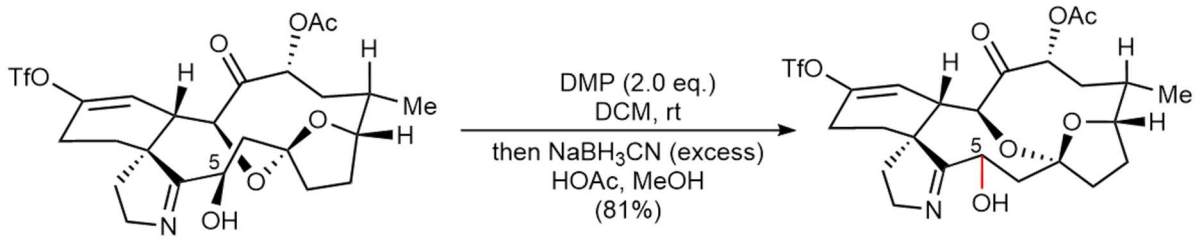
Compound **34** (ePA)



Compound **35** (2.2 mg, 0.005 mmol) was dissolved in *n*-PrOH (0.1 ml), followed by addition of vinylBF$_3$K (1.5 mg, 0.011 mmol) and Pd(dppf)Cl$_2$ (0.4 mg, 0.0005 mmol) under argon. TEA (1 drop) was added to this solution. Subsequently, the reaction was heated to 80 °C for 1 h. Upon completion (monitored by TLC), the solvent was removed under vacuo, and the residue was dissolved in MeOH (0.1 ml). Aq. NH$_3$ (37%, 0.1 ml) was added to this solution. The resulting solution was stirred for 2 h, and concentrated. The residue was purified by PTLC (10% *i*-PrOH in DCM) to give compound **34** (*epi*-portimine A) (1.8 mg, 0.004 mmol, ca. 80%) as single product.

Physical state: white solid
TLC: R_f = 0.44 (10% MeOH in DCM, UV active, KMnO$_4$ staining)
[α]^{25}D: -8.0 (*c* = 0.1, CHCl$_3$)
^{1}H-NMR (600 MHz, CDCl$_3$) δ 6.21 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.08 (d, *J* = 17.5 Hz, 1H), 5.04 (s, 1H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.78 (dd, *J* = 11.1, 7.5 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.23 (dt, *J* = 10.4, 6.0 Hz, 1H), 4.14 (d, *J* = 12.0 Hz, 1H), 4.08 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.75 (dd, *J* = 16.0, 8.8 Hz, 1H), 3.63 (ddd, *J* = 16.0, 10.3, 7.0 Hz, 1H), 2.80 (dd, *J* = 14.6, 11.1 Hz, 1H), 2.40 – 2.21 (m, 5H), 2.15 (dd, *J* = 14.0, 6.7 Hz, 1H), 2.01 (dd, *J* = 12.1, 7.1 Hz, 1H), 1.92 – 1.82 (m, 2H), 1.79 (dd, *J* = 12.5, 6.7 Hz, 1H), 1.76 – 1.66 (m, 2H), 1.58 – 1.49 (m, 2H), 0.88 (d, *J* = 6.0 Hz, 3H)
^{13}C-NMR (150 MHz, CDCl$_3$) δ 204.7, 184.8, 139.1, 135.3, 128.2, 111.6, 108.2, 83.9, 79.3, 71.9, 70.7, 55.3, 54.5, 42.5, 40.1, 37.0, 34.6, 33.9, 29.8, 29.2, 24.5, 22.8, 17.7
HRMS (ESI-TOF): calc'd for $C_{23}H_{31}NO_5$ $[M+H]^+$: 402.2275, found: 402.2266

Compound **36**

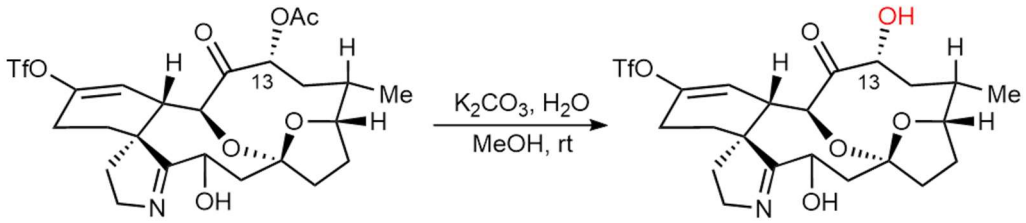


35 **36**

Compound **35** (15.4 mg, 0.027 mmol) was dissolved in DCM (0.15 ml), followed by addition of Dess-Martin periodinane (27.2 mg, mmol). After stirring under rt for 1.5 h, the mixture was added DCM and sat. $Na_2S_2O_3$ aq., and solid Na_2CO_3. The heterogenous, cloudy mixture was stirred at the same temperature for 30 min to give a clear biphasic mixture. The DCM layer was collected, and the aqueous phase was extracted with DCM (3x 1 ml). After concentration, the crude product was dissolved in MeOH (0.3 ml), followed by adding AcOH (0.05 ml) at rt. $NaBH_3CN$ (ca. 10 mg) was added to this solution in one portion, and the resulting clear solution was stirred at the same temperature for 1 h. Upon completion (indicated by TLC, 5% MeOH in DCM), K_2CO_3 (55 mg) was added in one portion to give a slightly yellow mixture. The mixture was stirred for 30 min, then quenched by adding water (0.3 mL). The mixture was extracted with DCM (3x 1 ml) and dried over $MgSO_4$. Pure compound **36** (11.1 mg, 0.021 mmol, 78%) was obtained by PTLC (6% *i*-PrOH in DCM).

Physical state: white solid
TLC: R_f = 0.53 (10% MeOH in DCM, $KMnO_4$ staining)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.18 (dd, *J* = 11.3, 2.8 Hz, 1H), 5.04 (s, 1H), 4.66 (br s, 1H), 4.48 (s, 1H), 4.34 (d, *J* = 12.0 Hz, 1H), 4.21 (dt, *J* = 11.1, 5.9 Hz, 1H), 3.94 (dd, *J* = 15.5, 9.0 Hz, 1H), 3.86 (d, *J* = 12.3 Hz, 1H), 3.79 – 3.70 (m, 1H), 2.74 (dd, *J* = 16.2, 5.1 Hz, 1H), 2.60 – 2.46 (m, 2H), 2.38 – 2.25 (m, 2H), 2.18 – 2.05 (m, 3H), 2.04 (s, 3H), 2.01 (dt, *J* = 12.4, 6.3 Hz, 1H), 1.88 – 1.78 (m, 3H), 1.78 – 1.66 (m, 2H), 1.52 (dd, *J* = 13.6, 2.9 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 200.0, 169.1, 148.5, 117.9, 109.5, 83.6, 80.0, 72.8, 65.6, 55.0, 52.0, 43.4, 39.6, 37.8, 34.0, 31.5, 29.6, 28.8, 26.4, 24.7, 21.0, 17.6
*(2 carbons (C=N and CF_3) were missing in ^{13}C NMR but shown in compound **37**)*
HRMS (ESI-TOF): calc'd for $C_{24}H_{30}F_3NO_9S$ $[M+H]^+$: 566.1666, found: 566.1641

Compound **37**

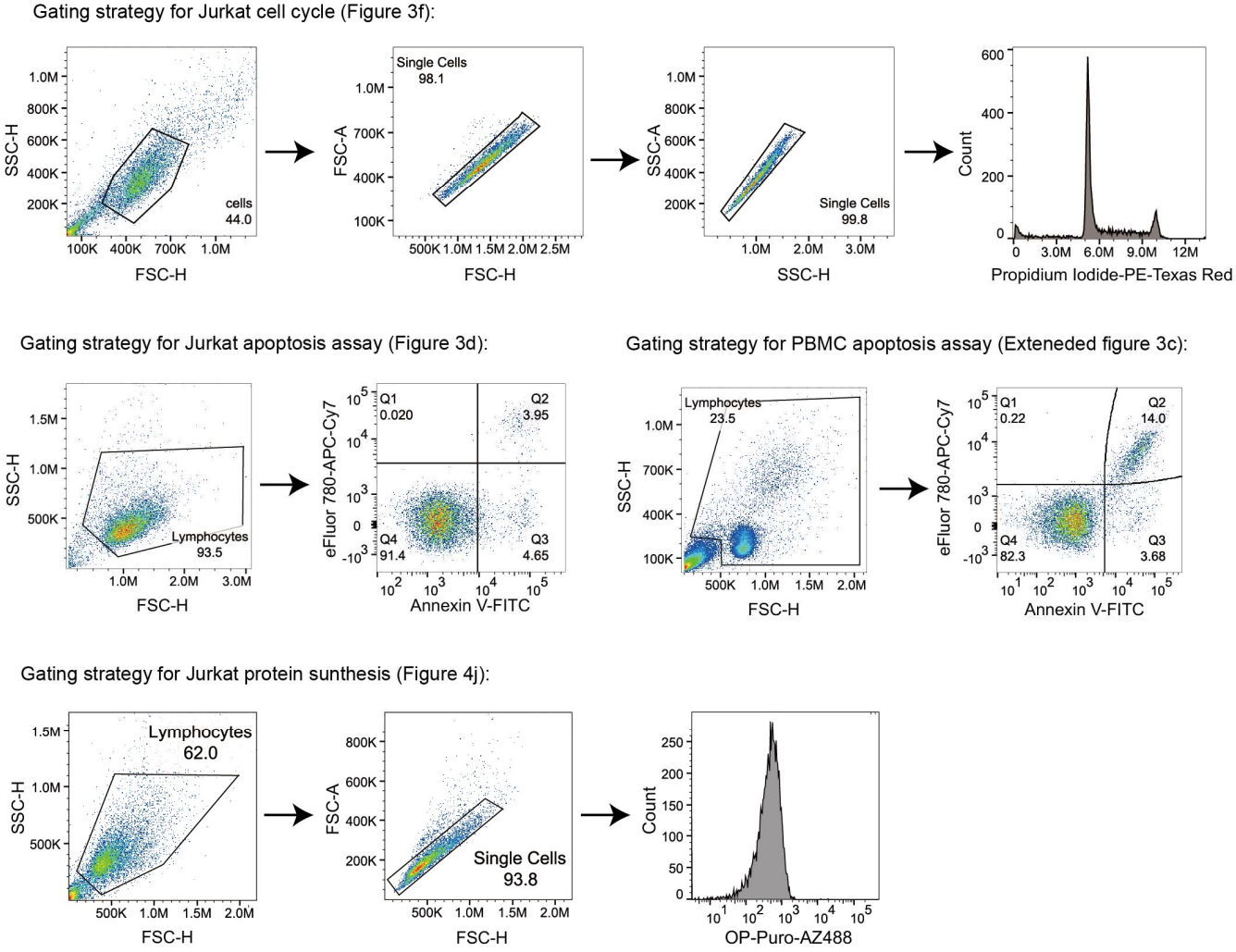


36 **37**

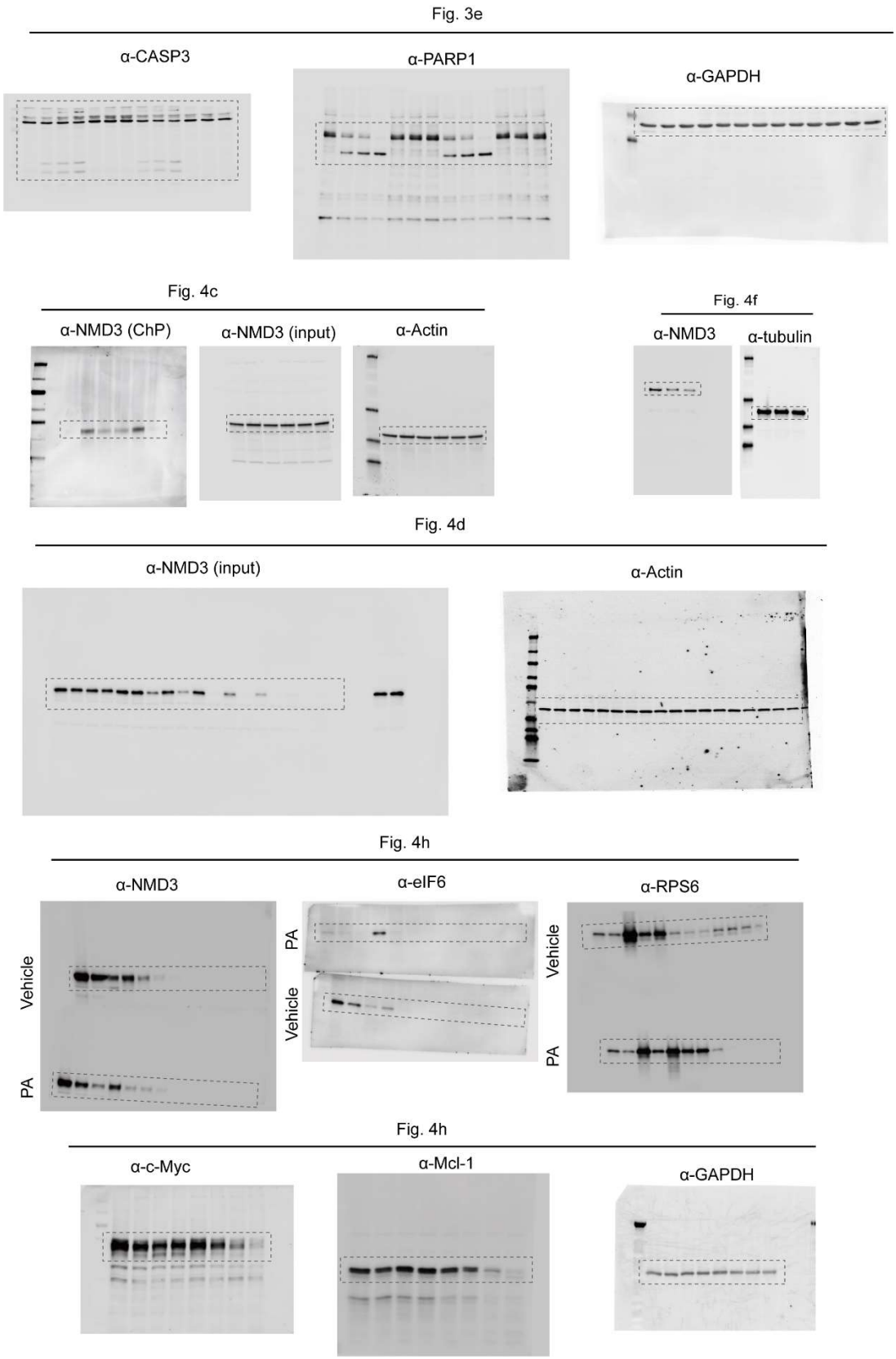
Compound **36** (15.5 mg, 0.027 mmol) was with MeOH (1.0 ml) and K_2CO_3 (58 mg) in a test tube. Upon completion, DCM (1 ml) was added, and the aqueous phase was extracted by DCM (3x 1 ml). The combined organic phase was dried over $MgSO_4$, followed by the removal of the solvents *in vacuo*. Pure compound **37** (11.1 mg, 0.021 mmol, 78%) was obtained by PTLC (8% MeOH in DCM).

Physical state: white solid
TLC: R_f = 0.50 (10% MeOH in DCM, $KMnO_4$ staining)
$[\alpha]^{25}_D$: -15.0 (c = 0.1, $CHCl_3$)
^{1}H-NMR (600 MHz, $CDCl_3$) δ 5.16 (s, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.48 (s, 1H), 4.19 (dt, J = 11.1, 5.8 Hz, 1H), 4.08 – 4.00 (m, 1H), 3.92 (dd, J = 15.5, 9.0 Hz, 1H), 3.81 (d, J = 12.0 Hz, 1H), 3.78 – 3.68 (m, 1H), 2.71 (dd, J = 16.1, 5.1 Hz, 1H), 2.63 – 2.52 (m, 1H), 2.50 – 2.42 (m, 1H), 2.32 – 2.20 (m, 2H), 2.15 – 2.04 (m, 2H), 2.04 – 1.93 (m, 2H), 1.84 (dq, J = 13.1, 8.9, 6.2 Hz, 3H), 1.73 (dt, J = 12.2, 6.9 Hz, 1H), 1.66 (td, J = 12.7, 7.6 Hz, 1H), 1.52 (dd, J = 13.2, 2.7 Hz, 1H), 0.89 (d, J = 6.5 Hz, 3H)
^{13}C-NMR (150 MHz, $CDCl_3$) δ 204.8, 148.3, 118.7, 118.6 (q, $J_{C\text{-}F}$ = 320 Hz), 109.3, 83.6, 79.0, 70.6, 65.6, 54.8, 52.0, 43.2, 39.7, 37.7, 34.2, 33.4, 29.9, 29.4, 28.7, 26.2, 24.7, 17.7
HRMS (ESI-TOF): calc'd for $C_{22}H_{28}F_3NO_8S$ $[M+H]^+$: 524.1561, found: 524.1547

Gating Strategies:

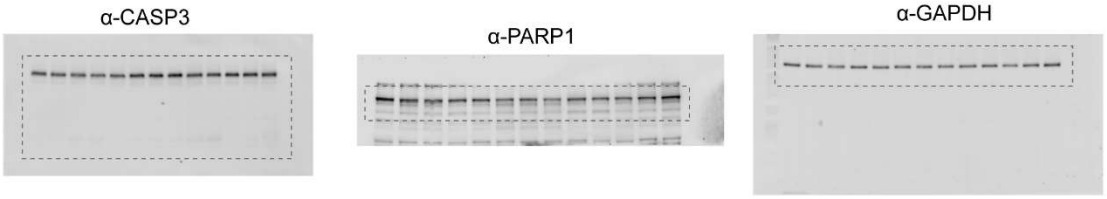


Supplementary Fig. 1. Gating strategy for flow cytometry experiments.

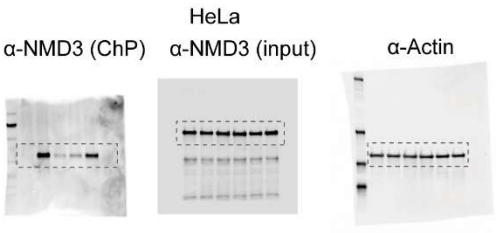


Supplementary Fig. 2. Uncropped western blot images in Fig. 3 and 4.

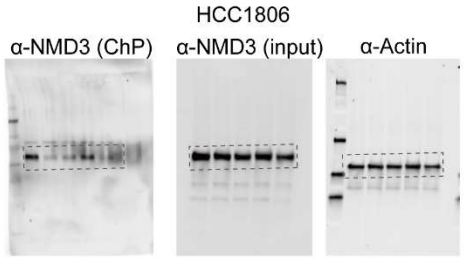
Extended Data Fig. 3c



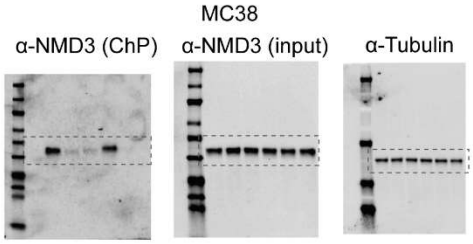
Extended Data Fig. 5b



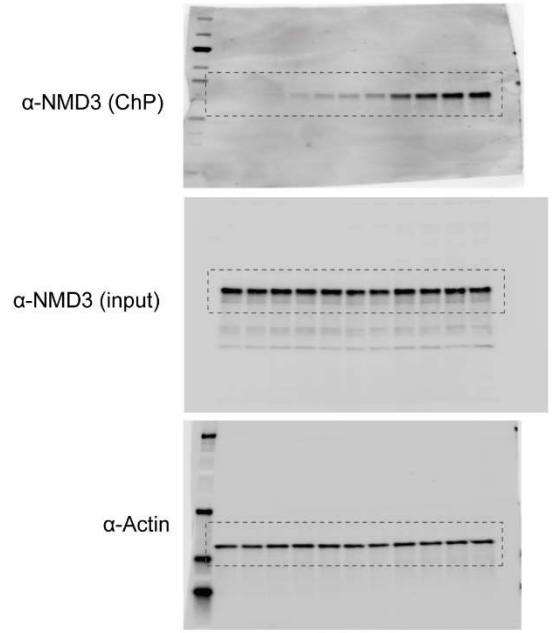
Extended Data Fig. 5c



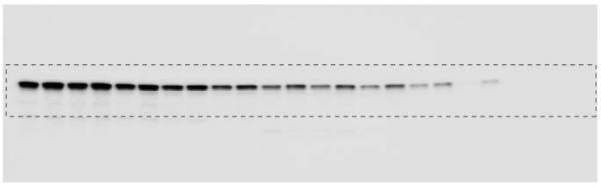
Extended Data Fig. 5d



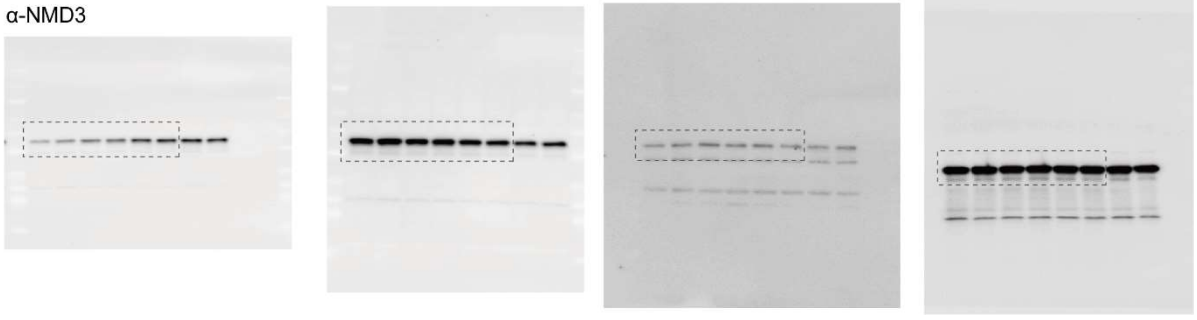
Extended Data Fig. 5e

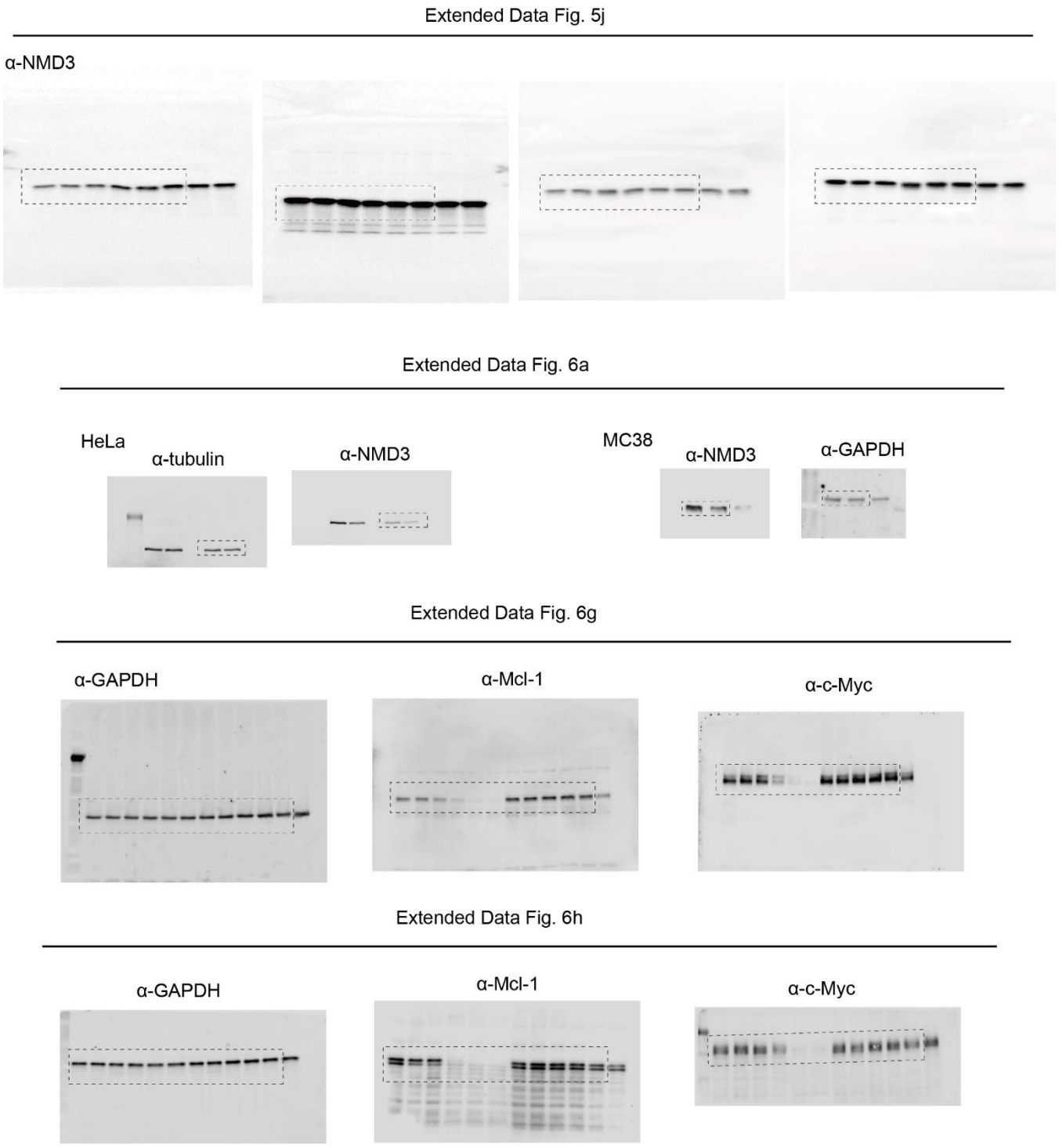


Extended Data Fig. 5f



Extended Data Fig. 5h





Supplementary Fig. 3. Uncropped western blot images in Extended Data Fig. 3, 5, 6.

Supplementary Table 6. Pharmacokinetic (PK) evaluation of portimine A in mice.[a]

Parameter	i.p. 1 mg kg^{-1}	p.o. 5 mg kg^{-1}
$AUC_{0\text{-}last}$ (ng.h/mL)	42.30 ± 2.60	5.85 ± 2.14
$AUC_{0\text{-}inf}$ (ng.h/mL)	45.50 ± 2.70	9.35 ± 2.09
$t_{½}$ (h)	0.57 ± 0.06	0.59 ± 0.15
t_{max} (h)	0.08	0.25
t_{last} (h)	2.00	1.00
C_{max} (ng/mL)	118.37 ± 21.33	12.40 ± 4.86

[a]The value of mice represented the results (mean ± s.d.) from three independent experiments.

Supplementary Table 7. Chemical proteomics data in Jurkat cells

Proteomics data of PA-DA, PA, ePA, and ePA-DA engagement in Jurkat cells corresponding to Figures 4a. *P*-values for the abundance ratios were calculated using two-tailed *t*-test.

Supplementary Table 8. Chemical proteomics data in MC38 cells

Proteomics data of PA-DA, PA, ePA, and ePA-DA engagement in Jurkat cells corresponding to Figures 4b. *P*-values for the abundance ratios were calculated using two-tailed *t*-test.

Supplementary Table 9. Chemical proteomics data in HCC1806 cells

Proteomics data of PA-DA, PA, ePA, and ePA-DA engagement in Jurkat cells corresponding to Extended Figure 5a. *P*-values for the abundance ratios were calculated using two-tailed *t*-test.

Reagent or Resource summary

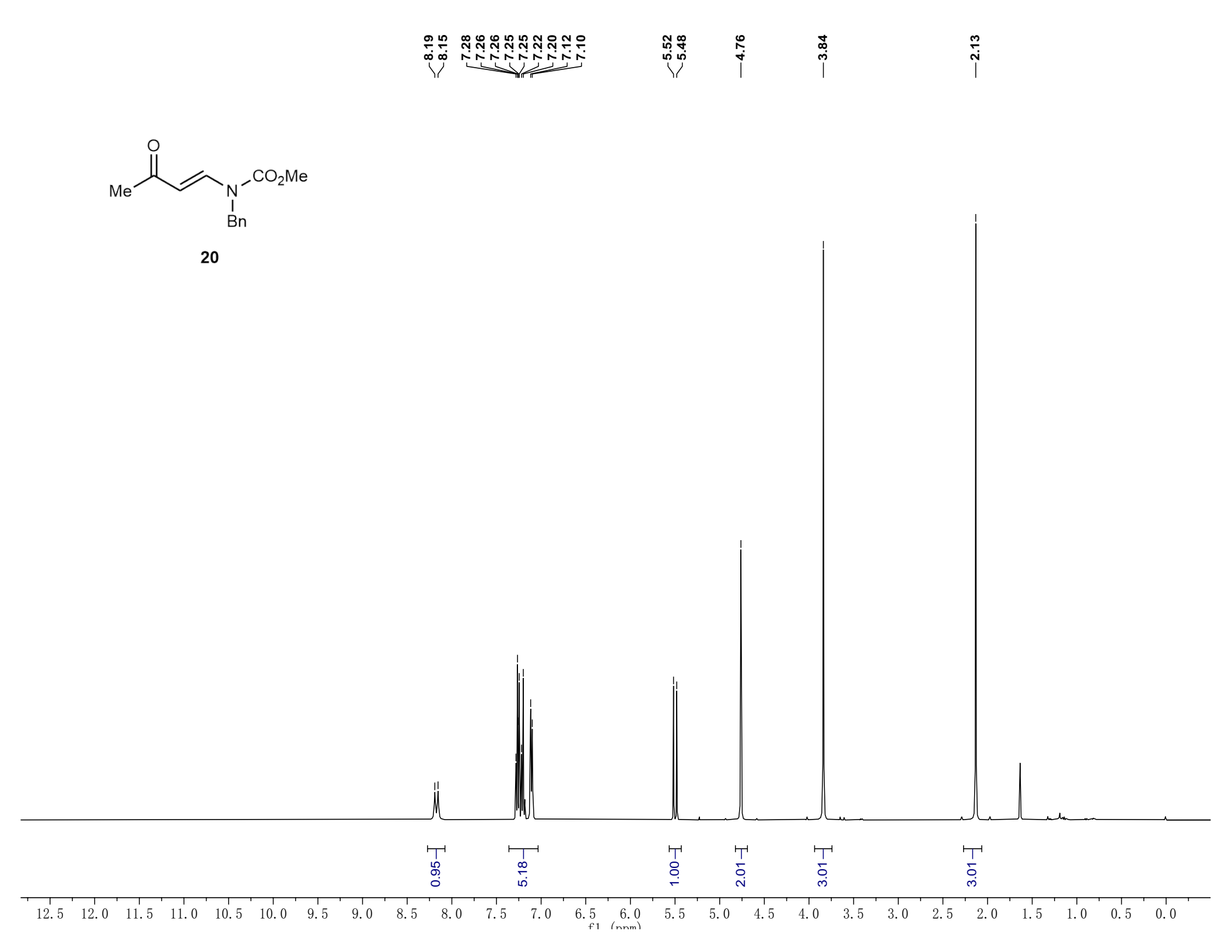
Reagent or resource	Source	Catalog number
Antibodies		
Anti-NMD3 antibody (1:5000)	ProteinTech	#16060-1-AP
Anti-EIF6 antibody (1:1000)	ProteinTech	#10291-1-AP
Anti-PARP1 antibody (1:2000)	ProteinTech	#66520-1-Ig
Anti-CASP3 antibody (1:1000)	Cell Signaling Technology	# 9662
Anti-Mcl-1 antibody (1:1000)	Cell Signaling Technology	# 5453
Anti-c-Myc antibody (1:1000)	Cell Signaling Technology	# 9402
Anti-RPS6 antibody (1:2000)	Cell Signaling Technology	#2217
Anti-GAPDH hFAB (1:10000)	Bio-Rad	#12004168
Anti-Actin hFAB (1:10000)	Bio-Rad	#12004164
Anti-Tubulin hFAB (1:10000)	Bio-Rad	#12004165
Goat anti-Mouse IgG, HRP	Abcam	ab6789
Goat anti-Rabbit IgG, HRP	Abcam	ab6721
Cell Lines		
Jurkat	ATCC	CRL-3216
HCC1806	ATCC	CCL-185
HeLa	ATCC	CCL-2
MC38	Derived and provided by the laboratory of Dr. Jeff Schlom, NCI	
Lenti-X™ 293T cells	Takara Bio	632180
RD	ATCC	CCL-136
HT-1080	ATCC	CCL-121
A673	ATCC	CRL-1598
MCF-7	ATCC	HTB-22
MDA-MB-231	ATCC	CRM-HTB-26
SUM159	Laboratory of Dr. Sendurai Mani, Brown University	
HepG2	ATCC	HB-8065
B16-F10	ATCC	CRL-6475
LNCaP	ATCC	CRL-1740
786-O	ATCC	CRL-1932
4T1	ATCC	CRL-2539
GBM-A	Laboratory of Dr. Stephen Skirboll, Stanford Medical Center	
GBM-F	Laboratory of Dr. Stephen Skirboll, Stanford Medical Center	
U87EGFRvIII	Laboratory of Dr. Paul Mischel, Stanford University. Derived by	

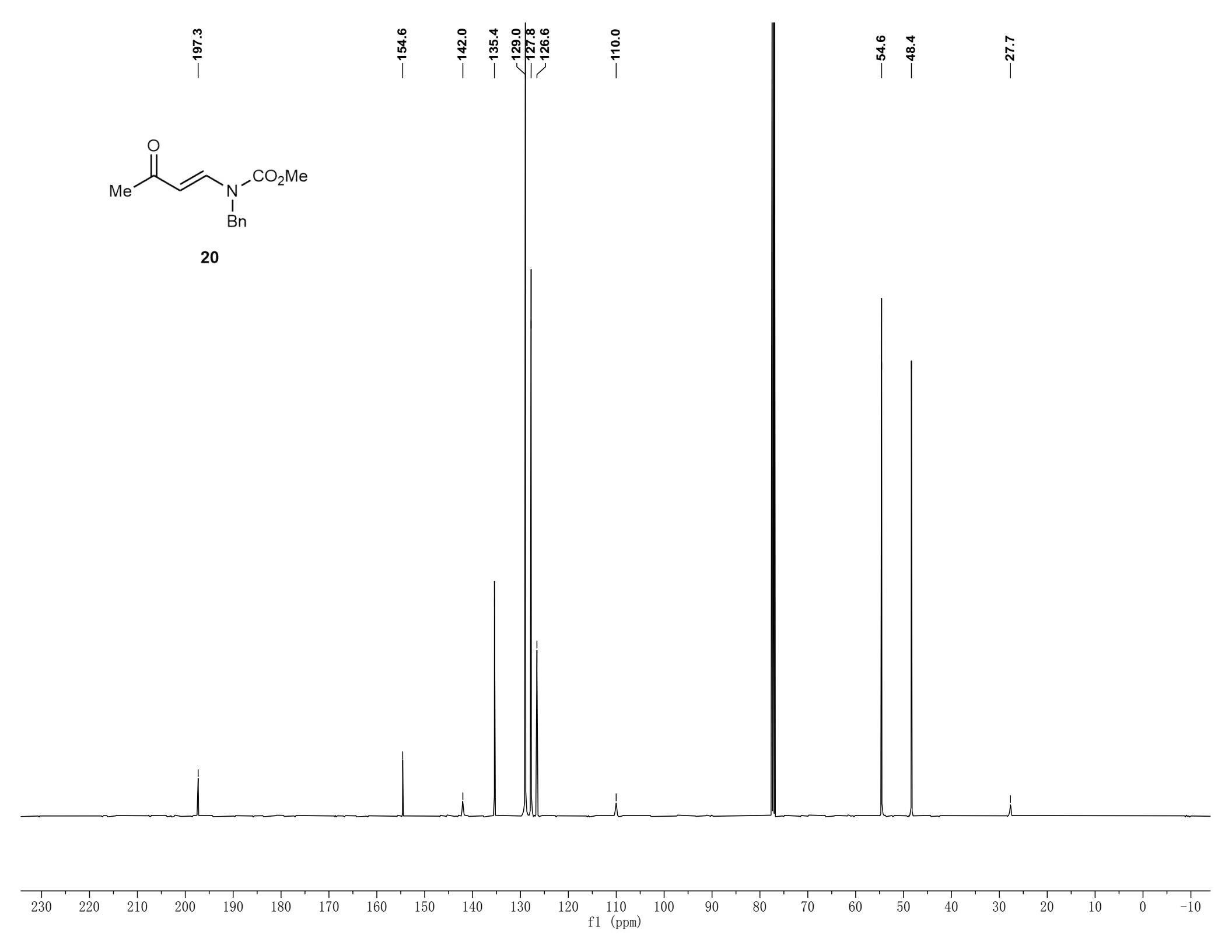
	retroviral transduction of U87 cell line with pLPCX construct that contains human EGFRvIII cDNA.	
LN229	ATCC	CRL-2611
U118MG	ATCC	HTB-15
Critical commercial assays		
Trans-Blot Turbo RTA transfer Kit, LF, PVDF	BioRad	#1704275
CellTiter-Glo Luminescent Cell Viability Assay	Promega	G7570
Reagents		
Biotin-PEG_3-Azide	Click Chemistry Tools	AZ104
o-propargyl puromycin	Click Chemistry Tools	1407
AZDye 488 Azide	Click Chemistry Tools	1275
tris(3-hydroxypropyltriazolylmethyl)amine; THPTA	Click Chemistry Tools	1010
Rhodamine-azide	Synthesized in lab	-
Pierce Streptavidin Agarose	Thermo Fisher Scientific	20353
Pierce High pH Reversed-Phase Fractionation Kit	Thermo Fisher Scientific	84868
PEI MAX	Polysciences Inc.	24765-1
Sequencing Grade Modified Trypsin	Promega	V5111
TMT10plex™ Isobaric Label Reagent Set	Thermo Fisher Scientific	90406
TMTpro™ 16plex Label Reagent Set	Thermo Fisher Scientific	A44520
Halt Protease Inhibitor	Thermo Fisher Scientific	78438
RNaseA	Thermo Fisher Scientific	R1253
Cycloheximide	RPI Corp.	C81040
Tris	Fisher	BP152-5
NaCl	Sigma	S7653
$MgCl_2$	Sigma	M8266
DTT	Sigma	D0632
RiboLock RNase Inhibitor	Thermo Fisher Scientific	EO0381
polybrene	Sigma	TR-1003-G
SuperSignal™ West Femto Maximum Sensitivity Substrate	Thermo Fisher Scientific	34095
Recombinant DNA		
scrambled shRNA	Addgene	#1864
Software and Algorithms		

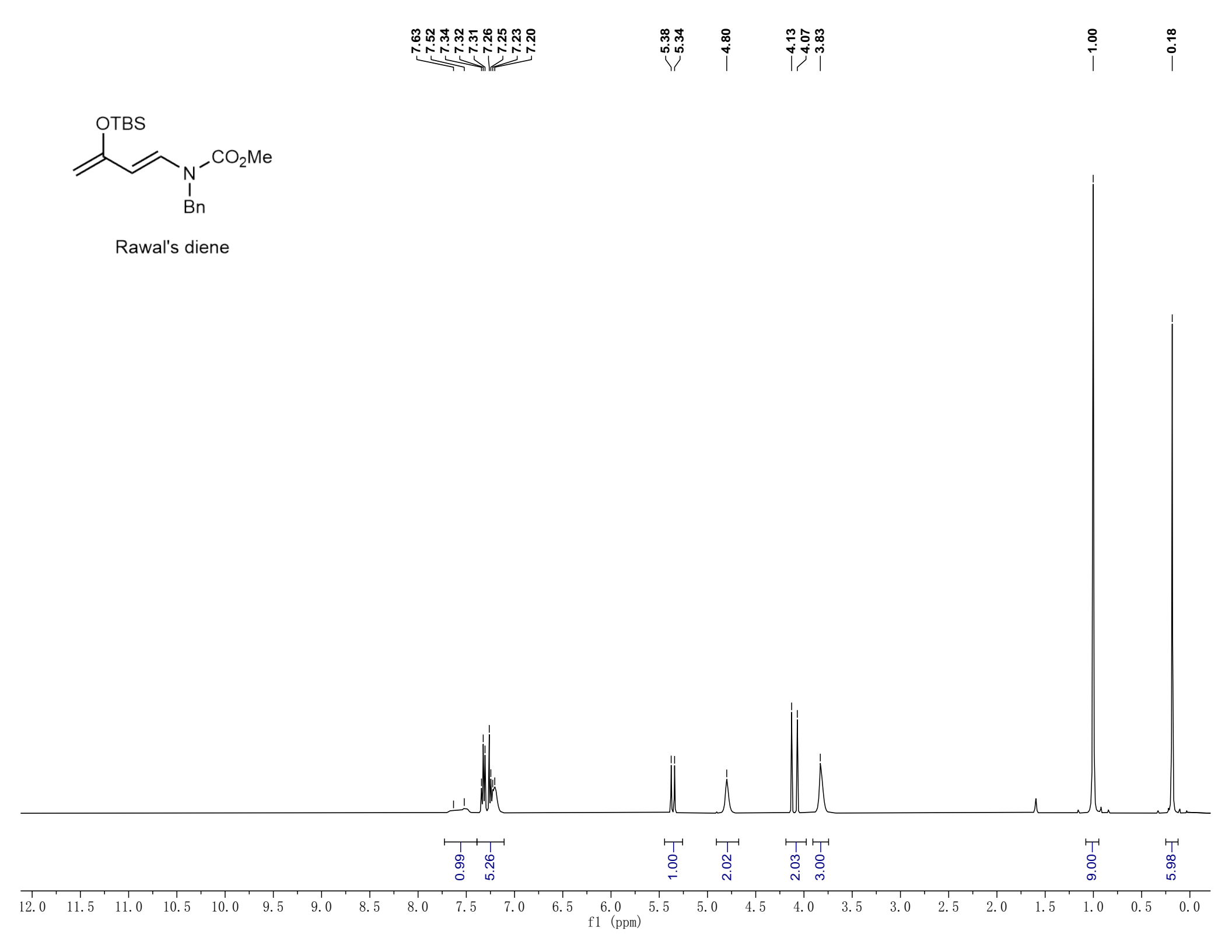
Proteome Discoverer	Thermo Fisher Scientific	Opton
GraphPad 9.0	Dotmatics	-
FlowJo™ v10	FlowJo	-
Phoenix WinNonlin 6.3	Certara	-
BD FACS Diva 6.0	BD Biosciences	-
Illustrator v26.1	Adobe	-
ImageJ v1.53r17	NIH	-

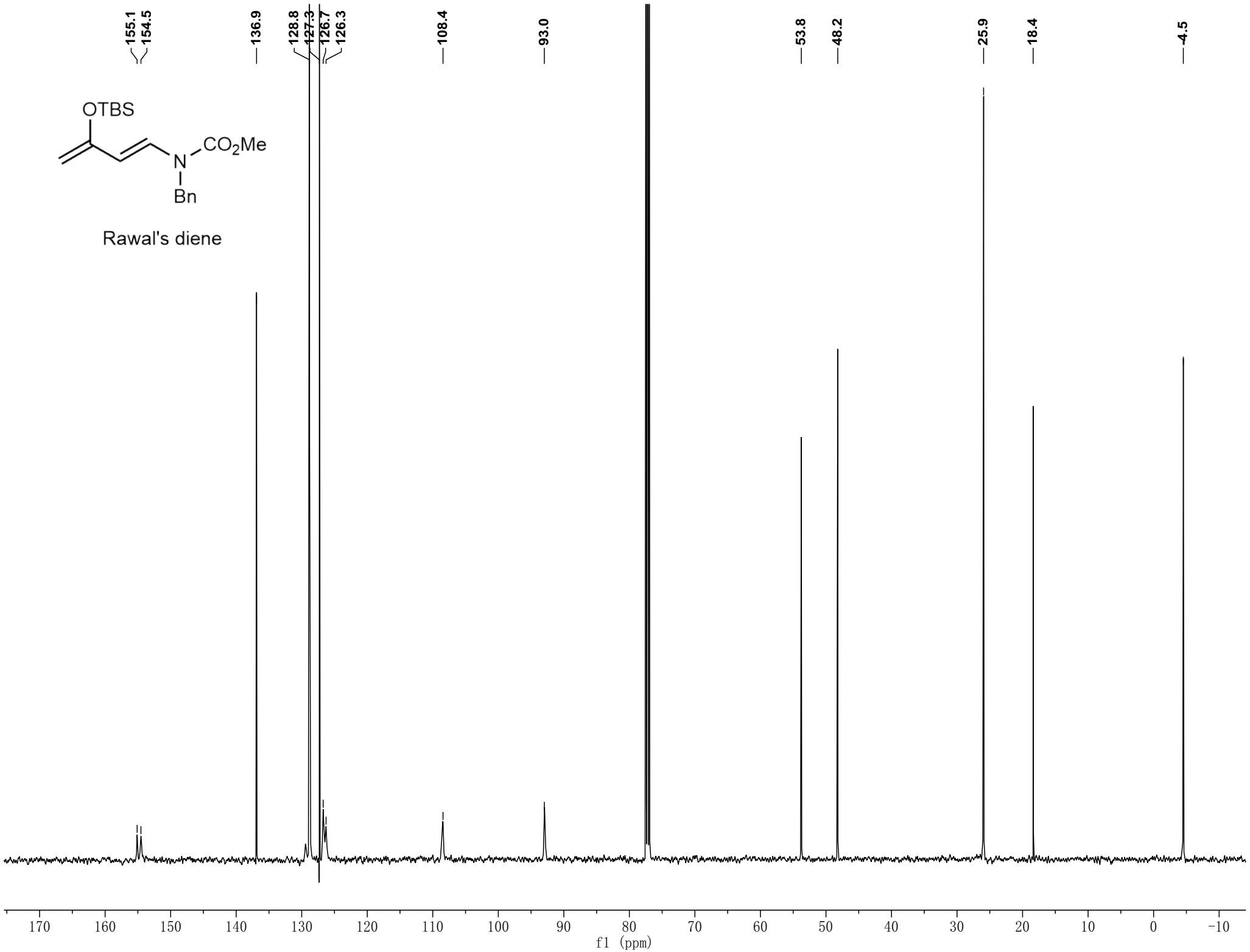
References

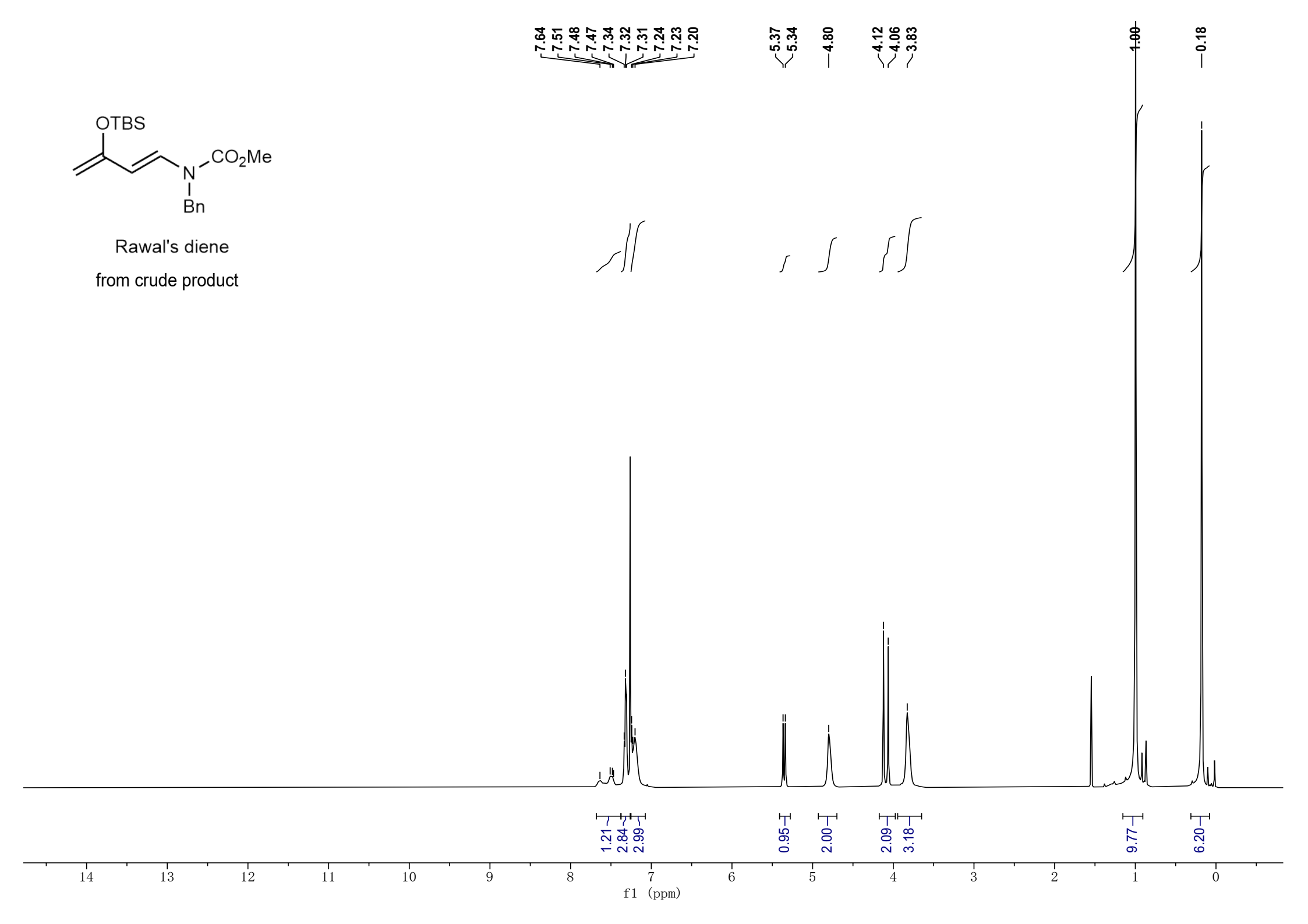
1. Synthesis of Medium-Sized Cyclic Amines by Selective Ring Cleavage of Sulfonylated Bicyclic Amines. Iradier, F.; Gomez Arrayas, R.; Carretero, J. C. *Org. Lett.* **2001**, *3*, 2957−2960.
2. Microwave-Assisted Palladium-Catalyzed Allylation of β-Enaminones. Erray, I.; Rezgui, F.; Oble, J.; Poli, G. *Synlett* **2014**, *25*, 2196–2200.
3. Activation of Mg Metal for Safe Formation of Grignard Reagents on Plant Scale. Tilstam, U.; Weinmann, H. *Organic Process Research & Development* **2002**, *6*, 906−910.
4. The First Syntheses of Single Enantiomers of The Major Methoxymycolic Acid of Mycobacterium Tuberculosis. Al Dulayymi, J. R.; Baird, M. S.; Roberts, E.; Deysel, M.; Verschoor, J. *Tetrahedron* **2007**, *63*, 2571−2592.
5. Convenient and Practical Alkynylation of Heteronucleophiles with Copper Acetylides. Theunissen, C.; Lecomte, M.; Jouvin, K.; Laouiti, A.; Guissart, C.; Heimburger, J.; Loire, E.; Evano, G. *Synthesis* **2014**, *46*, 1157−1166.
6. Identification of Portimine B, a New Cell Permeable Spiroimine That Induces Apoptosis in Oral Squamous Cell Carcinoma. Fribley, A. M.; Xi, Y.; Makris, C.; Alves-de-Souza, C.; York, R.; Tomas, C.; Wright, J. L. C.; Strangman, W. K. *ACS Med. Chem. Lett.* **2019**, *10*, 2, 175–179.

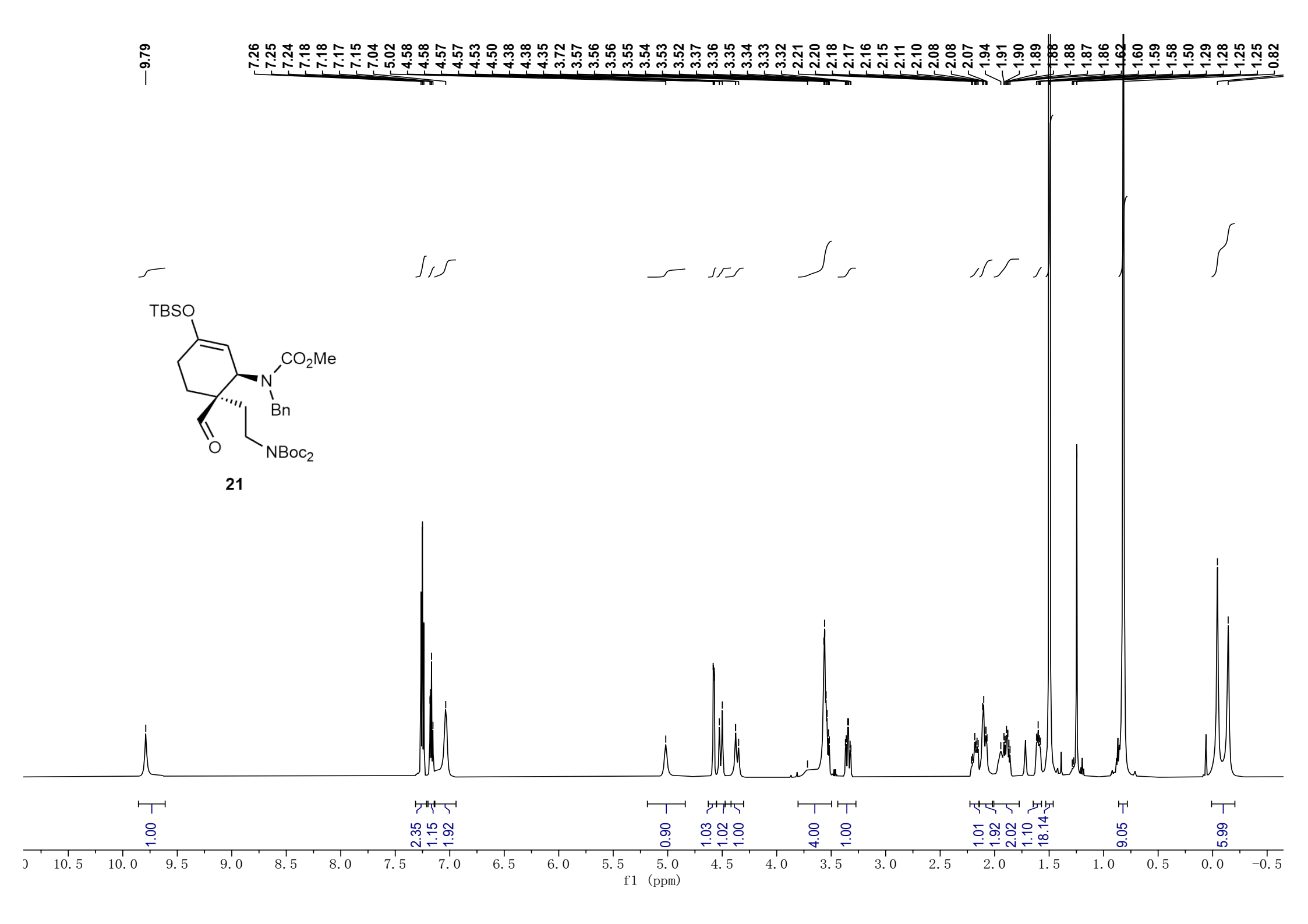

8.19
8.15
7.28
7.26
7.26
7.25
7.25
7.22
7.20
7.12
7.10
5.52
5.48
4.76
3.84
2.13
O
Me
N
CO2Me
Bn
20
0.95
5.18
1.00
2.01
3.01
3.01
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

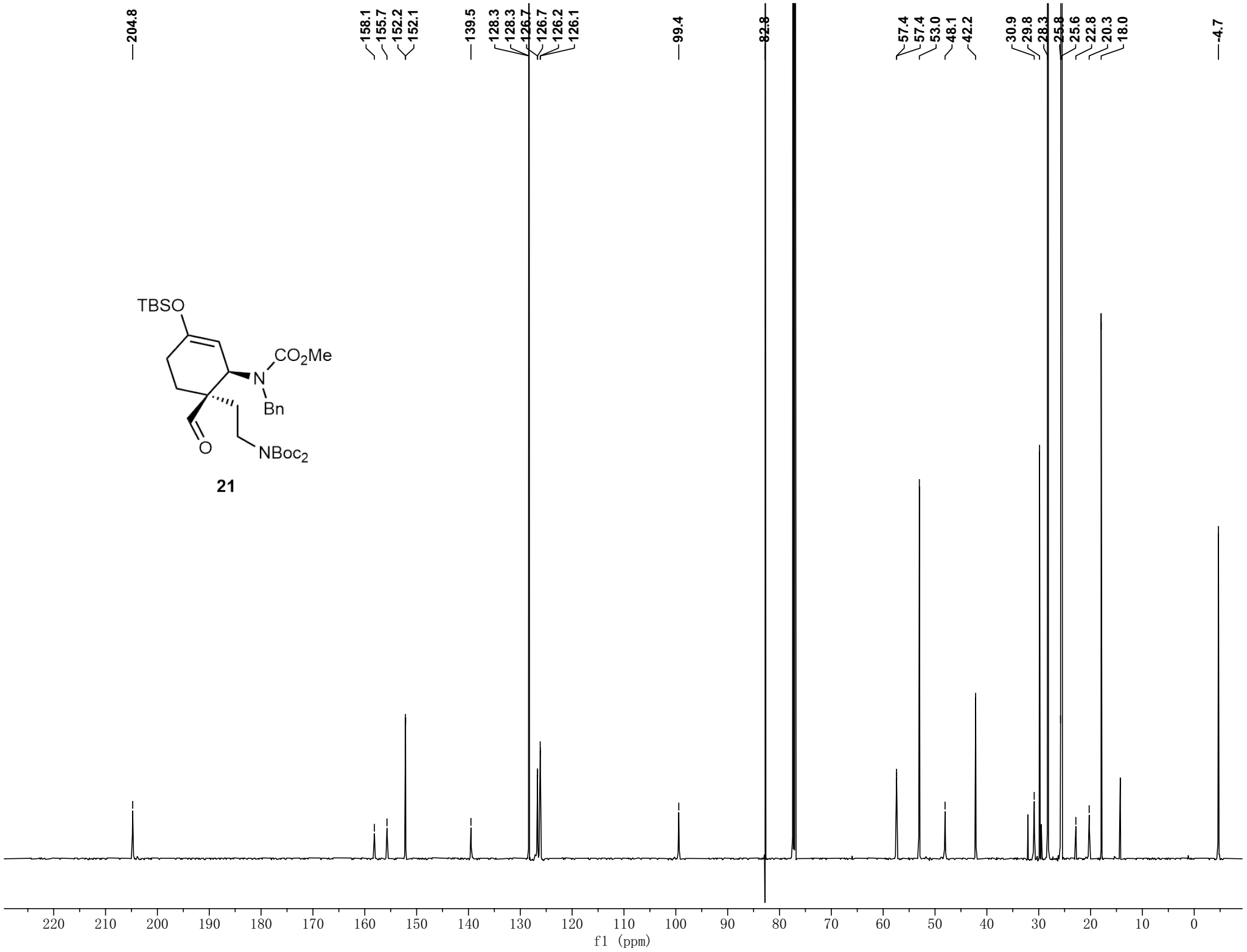

197.3
154.6
142.0
135.4
129.0
127.8
126.6
110.0
54.6
48.4
27.7
O
Me
N
CO2Me
Bn
20
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

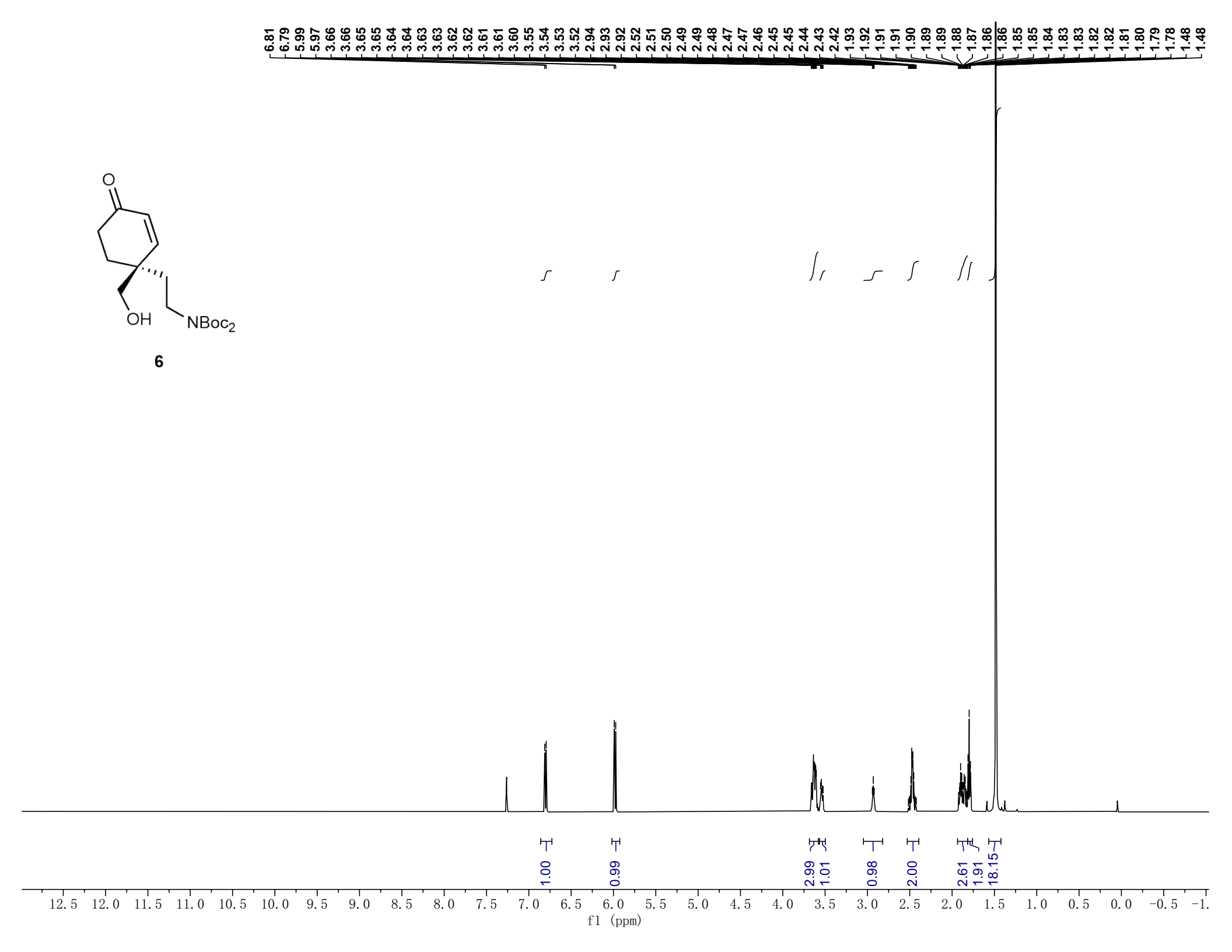

7.63
7.52
7.34
7.32
7.31
7.26
7.25
7.23
7.20
5.38
5.34
4.80
4.13
4.07
3.83
1.00
0.18
OTBS
CO2Me
N
Bn
Rawal's diene
0.99
5.26
1.00
2.02
2.03
3.00
9.00
5.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

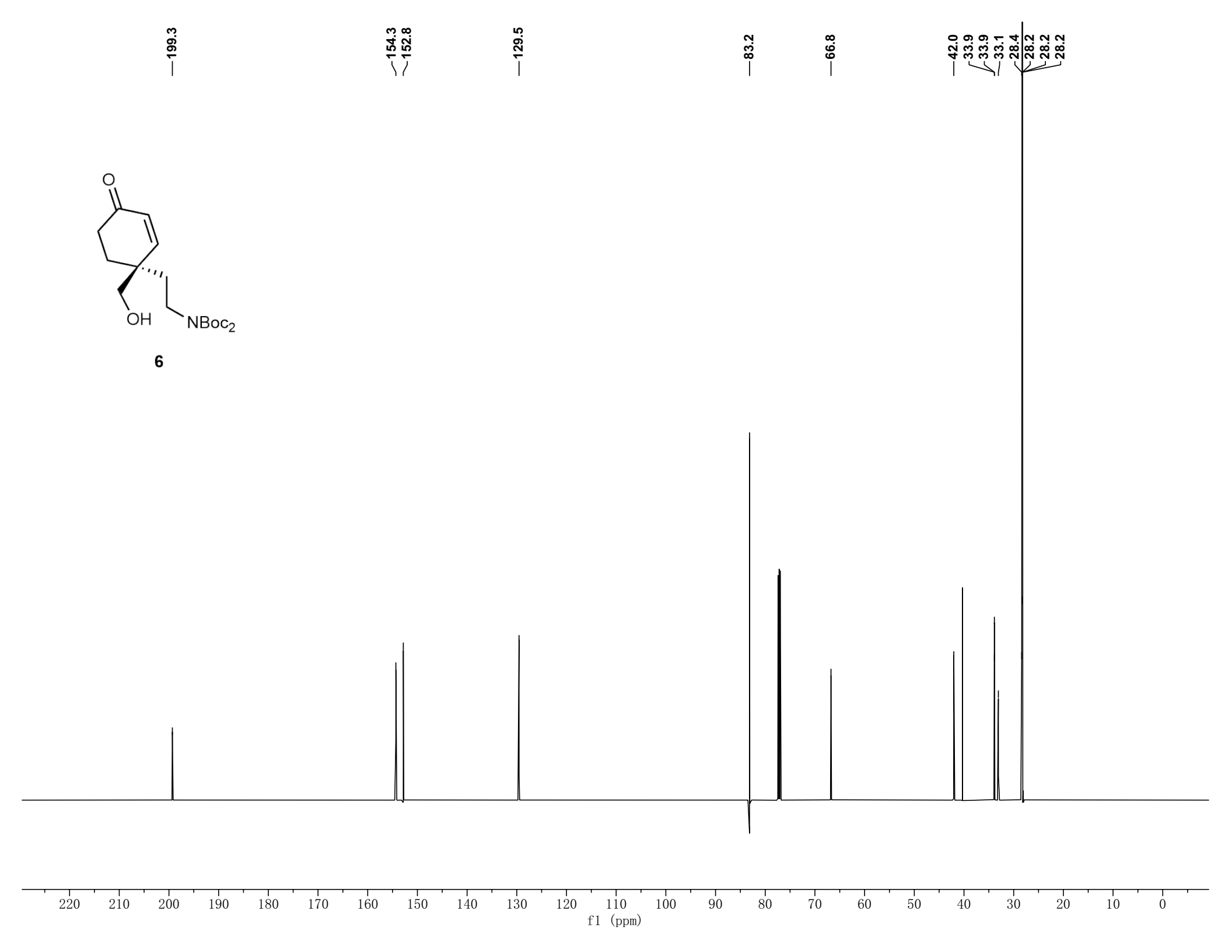

155.1
154.5
136.9
128.8
127.3
126.7
126.3
108.4
93.0
53.8
48.2
25.9
18.4
-4.5
OTBS
CO2Me
N
Bn
Rawal's diene
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

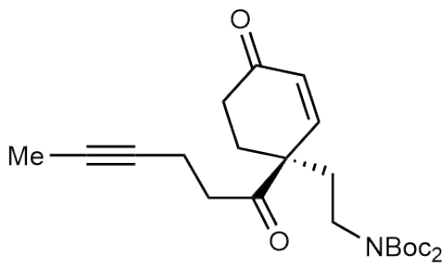

OTBS
CO2Me
N
Bn
Rawal's diene
from crude product
7.64
7.51
7.48
7.47
7.34
7.32
7.31
7.24
7.23
7.20
5.37
5.34
4.80
4.12
4.06
3.83
1.00
0.18
1.21
2.84
2.99
0.95
2.00
2.09
3.18
9.77
6.20
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


9.79
7.26 7.25 7.24 7.18 7.18 7.17 7.15 7.04 5.02 4.58 4.58 4.57 4.57 4.53 4.50 4.38 4.38 4.35 3.72 3.57 3.56 3.56 3.55 3.54 3.53 3.52 3.37 3.36 3.35 3.34 3.33 3.32 2.21 2.20 2.18 2.17 2.16 2.15 2.11 2.10 2.08 2.08 2.07 1.94 1.91 1.90 1.89 1.88 1.88 1.87 1.86 1.62 1.60 1.59 1.58 1.50 1.29 1.28 1.25 1.25 0.82
TBSO
CO2Me
N
Bn
O
NBoc2
21
1.00
2.35
1.15
1.92
0.90
1.03
1.02
1.00
4.00
1.00
1.01
1.92
2.02
1.10
18.14
9.05
5.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


204.8
158.1
155.7
152.2
152.1
139.5
128.3
128.3
126.7
126.7
126.2
126.1
99.4
82.8
57.4
57.4
53.0
48.1
42.2
30.9
29.8
28.3
25.8
25.6
22.8
20.3
18.0
-4.7
TBSO
CO2Me
N
Bn
O
NBoc2
21
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

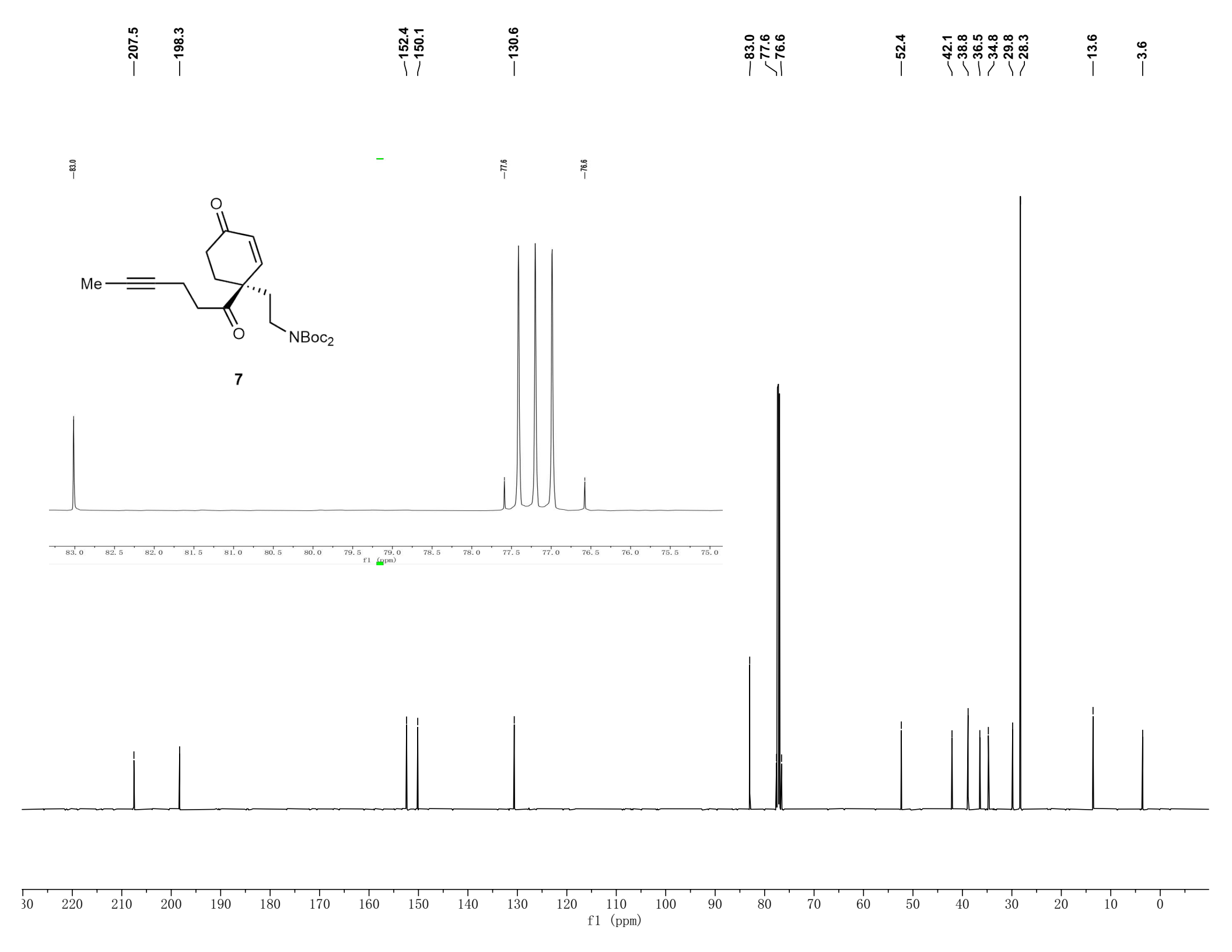

6.81 6.79 5.99 5.97 3.66 3.65 3.65 3.64 3.64 3.63 3.63 3.62 3.62 3.61 3.61 3.60 3.55 3.54 3.53 3.52 2.94 2.93 2.92 2.52 2.51 2.50 2.49 2.49 2.48 2.47 2.47 2.46 2.45 2.45 2.44 2.43 2.42 1.93 1.92 1.91 1.91 1.90 1.89 1.89 1.88 1.87 1.86 1.86 1.85 1.84 1.83 1.83 1.82 1.82 1.81 1.80 1.79 1.78 1.48 1.48
O
OH
NBoc2
6
1.00 0.99 2.99 1.01 0.98 2.00 2.61 1.91 18.15
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

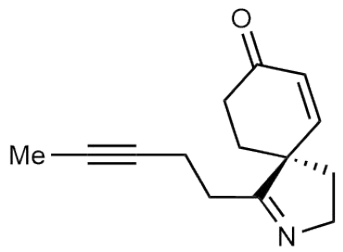

199.3
154.3
152.8
129.5
83.2
66.8
42.0
33.9
33.9
33.1
28.4
28.2
28.2
28.2
O
OH
NBoc2
6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
O
O
NBoc2

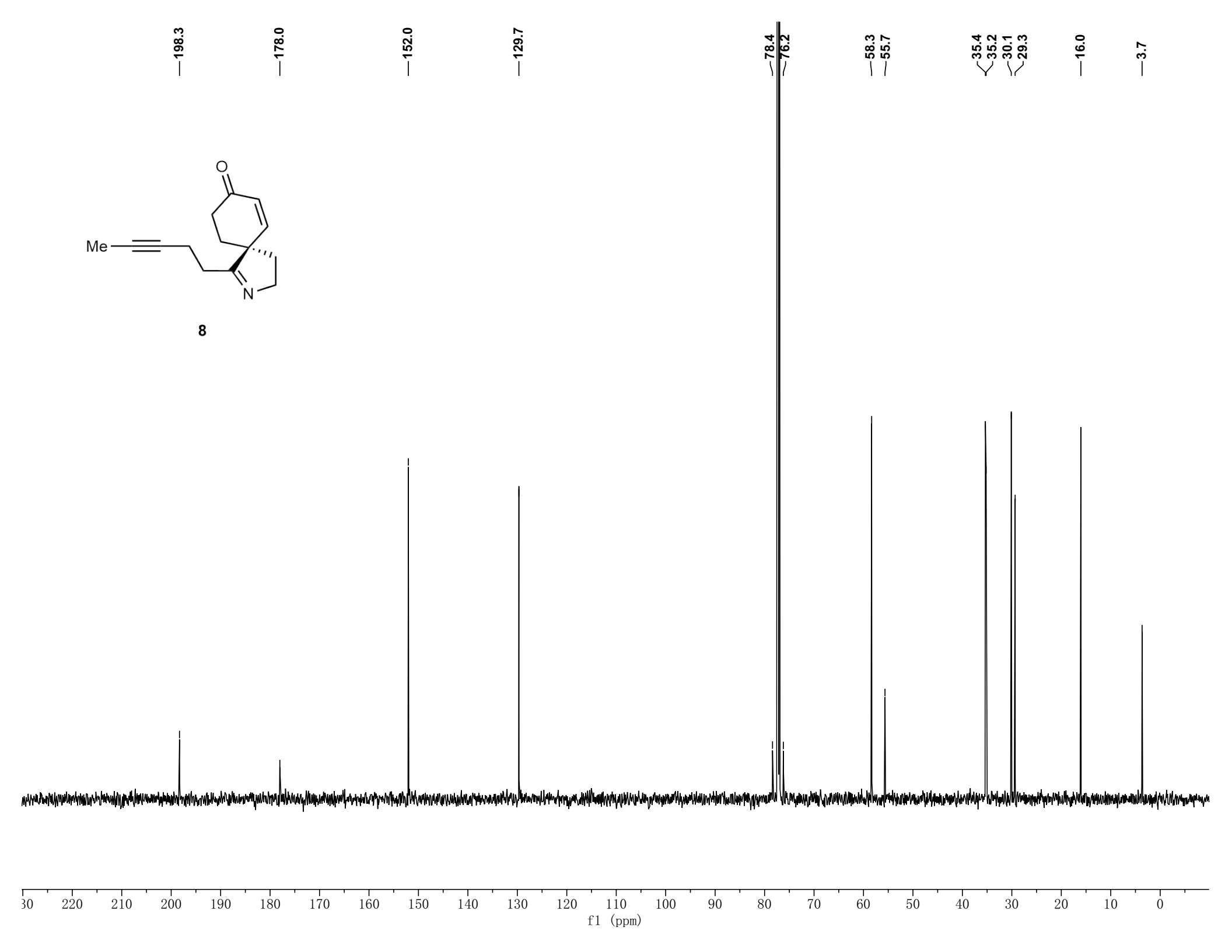
7

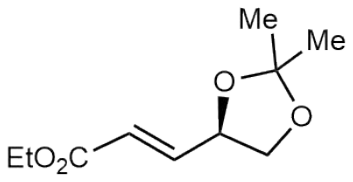
7.01
7.00
6.10
6.08
3.60
3.59
3.58
3.56
3.55
3.54
3.54
3.53
3.52
3.51
3.50
3.49
2.79
2.77
2.77
2.76
2.74
2.73
2.72
2.70
2.51
2.50
2.49
2.48
2.47
2.45
2.44
2.43
2.42
2.41
2.40
2.01
2.00
1.98
1.01
1.00
2.08
2.09
5.02
2.95
19.83
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


207.5
198.3
152.4
150.1
130.6
83.0
77.6
76.6
52.4
42.1
38.8
36.5
34.8
29.8
28.3
13.6
3.6
Me
O
O
NBoc2
7
f1 (ppm)



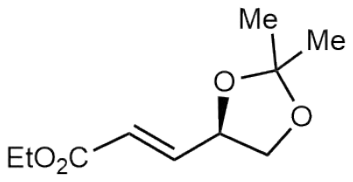
8


198.3
178.0
152.0
129.7
78.4
76.2
58.3
55.7
35.4
35.2
30.1
29.3
16.0
3.7
O
Me
N
8
f1 (ppm)


Me
Me
O
O
EtO2C

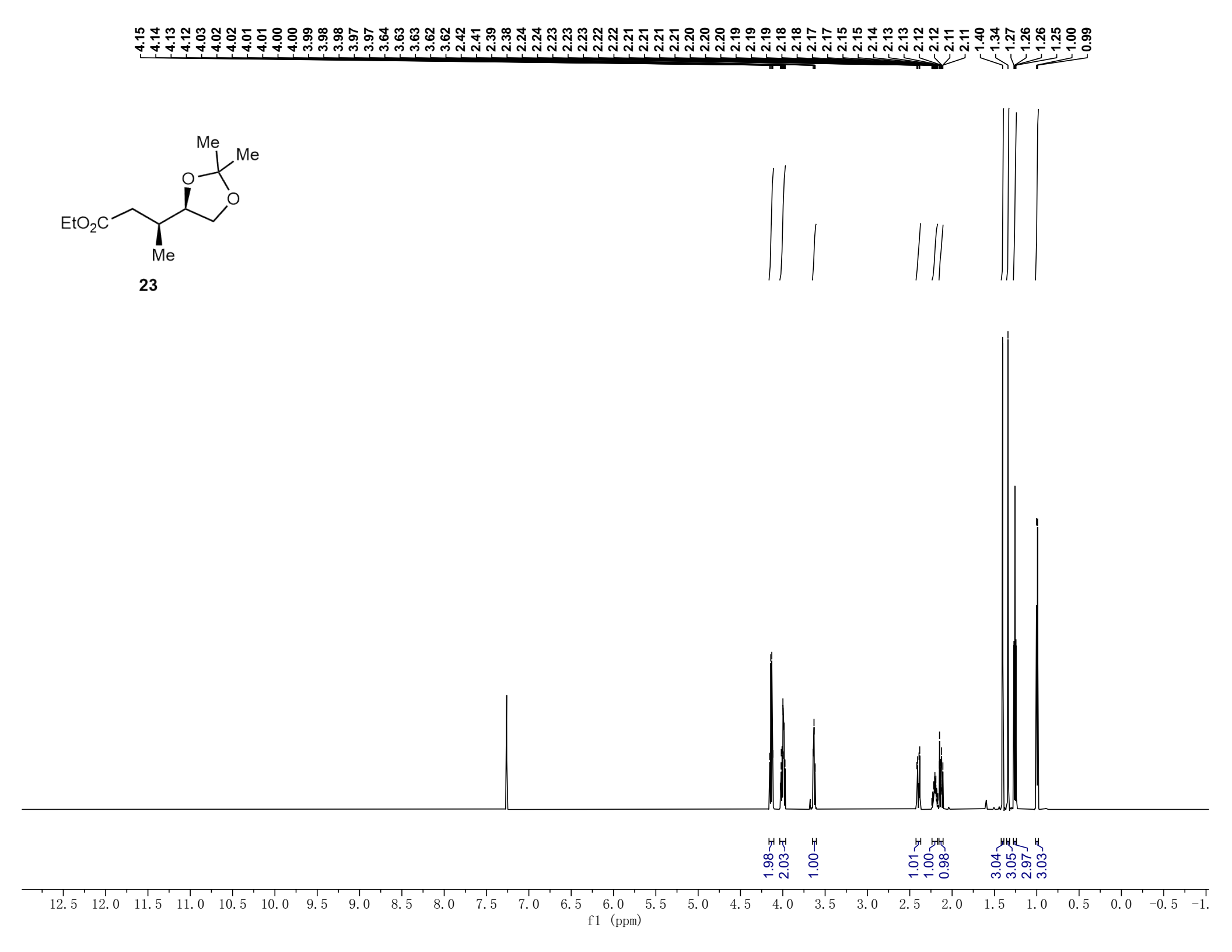
22

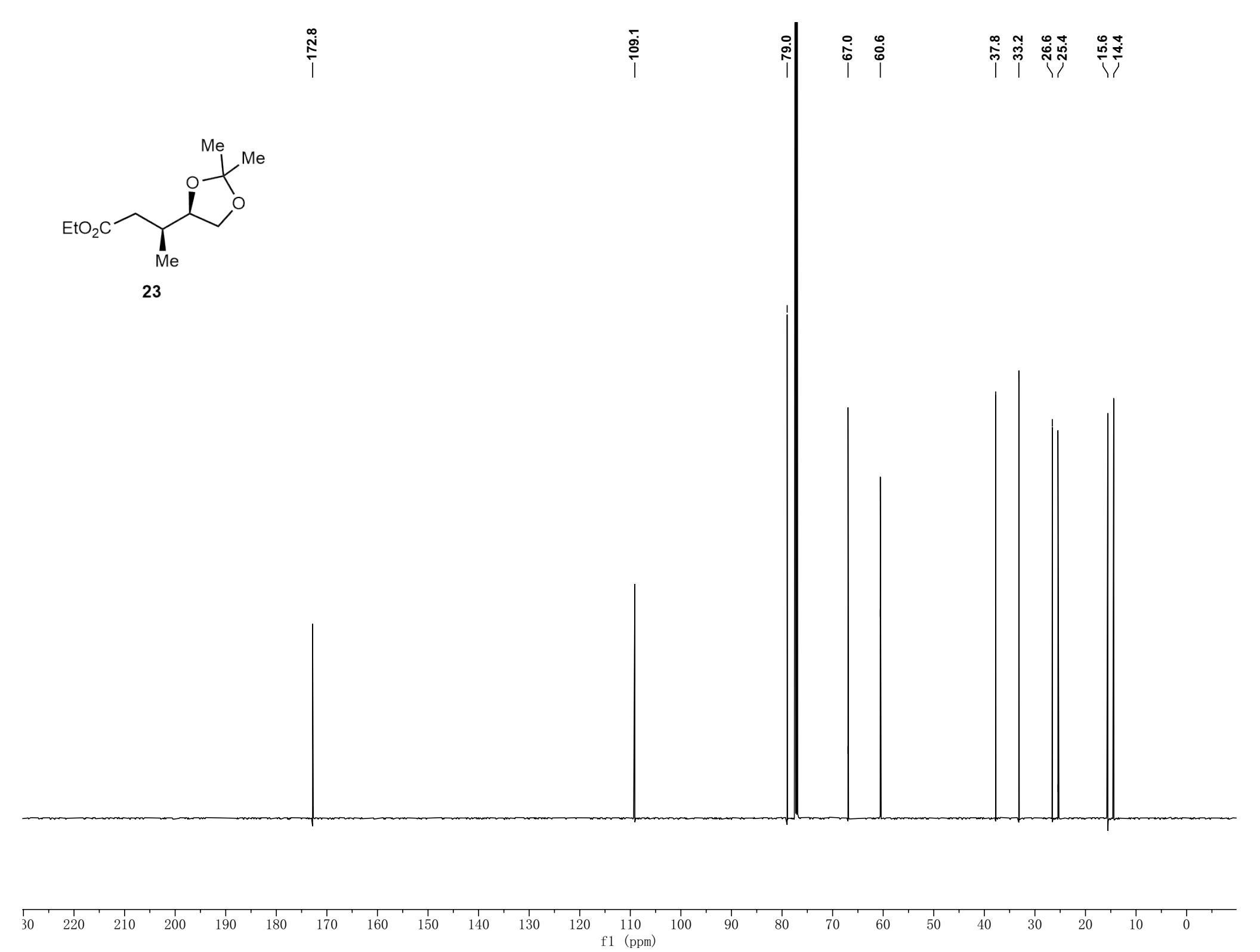
6.89
6.88
6.87
6.86
6.11
6.11
6.08
6.08
4.68
4.68
4.67
4.67
4.67
4.66
4.66
4.66
4.65
4.22
4.21
4.20
4.19
4.19
4.18
4.18
4.17
3.69
3.68
3.67
3.66
1.45
1.45
1.41
1.41
1.30
1.29
1.28
0.97
0.97
0.98
3.01
0.99
3.06
2.96
3.05
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

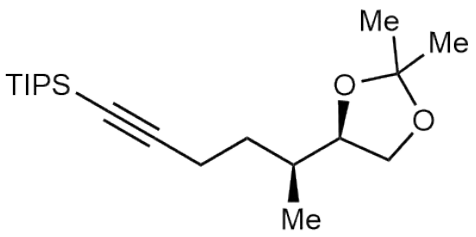

Me
Me
O
O
EtO2C

22

166.3
144.8
122.7
110.4
75.1
69.0
60.8
26.6
25.9
14.4
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

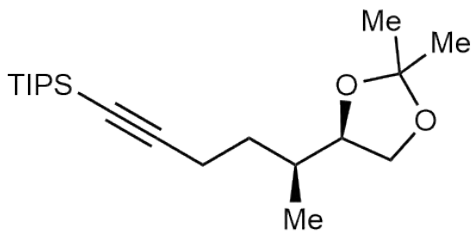

4.15 4.14 4.13 4.12 4.03 4.02 4.02 4.01 4.01 4.00 4.00 3.99 3.98 3.98 3.97 3.97 3.64 3.63 3.63 3.62 3.62 2.42 2.41 2.39 2.38 2.24 2.24 2.23 2.23 2.23 2.22 2.22 2.21 2.21 2.21 2.21 2.20 2.20 2.19 2.19 2.19 2.18 2.18 2.17 2.17 2.15 2.15 2.14 2.13 2.13 2.12 2.12 2.11 2.11 1.40 1.34 1.27 1.26 1.26 1.25 1.00 0.99
Me
Me
O
O
EtO2C
Me
23
1.98
2.03
1.00
1.01
1.00
0.98
3.04
3.05
2.97
3.03
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


172.8
109.1
79.0
67.0
60.6
37.8
33.2
26.6
25.4
15.6
14.4
Me
Me
O
O
EtO2C
Me
23
f1 (ppm)


TIPS
Me
Me
O
O
Me

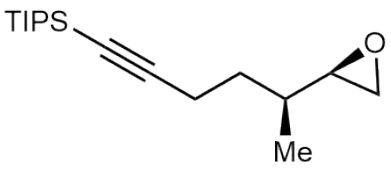
24

4.03 4.02 4.02 4.01 3.94 3.92 3.91 3.91 3.90 3.65 3.64 3.62 2.38 2.37 2.37 2.36 2.35 2.34 2.34 2.33 2.30 2.29 2.29 2.28 2.27 2.26 2.26 2.25 1.85 1.84 1.84 1.83 1.83 1.82 1.82 1.82 1.81 1.81 1.80 1.80 1.80 1.79 1.79 1.79 1.78 1.78 1.60 1.59 1.59 1.58 1.58 1.57 1.57 1.57 1.56 1.56 1.55 1.55 1.53 1.39 1.35 1.07 1.06 1.05 1.04 1.03 1.02 1.01 1.01 1.00 1.00 0.99 0.98
1.00 1.00 1.00 1.00 1.00 1.00 1.27 3.02 4.08 21.06 3.08
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


TIPS
Me
Me
O
O
Me

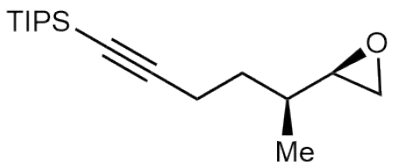
24

108.9
108.6
80.8
79.9
67.9
35.6
32.2
26.7
25.7
18.8
17.8
15.0
11.5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TIPS
O
Me

25

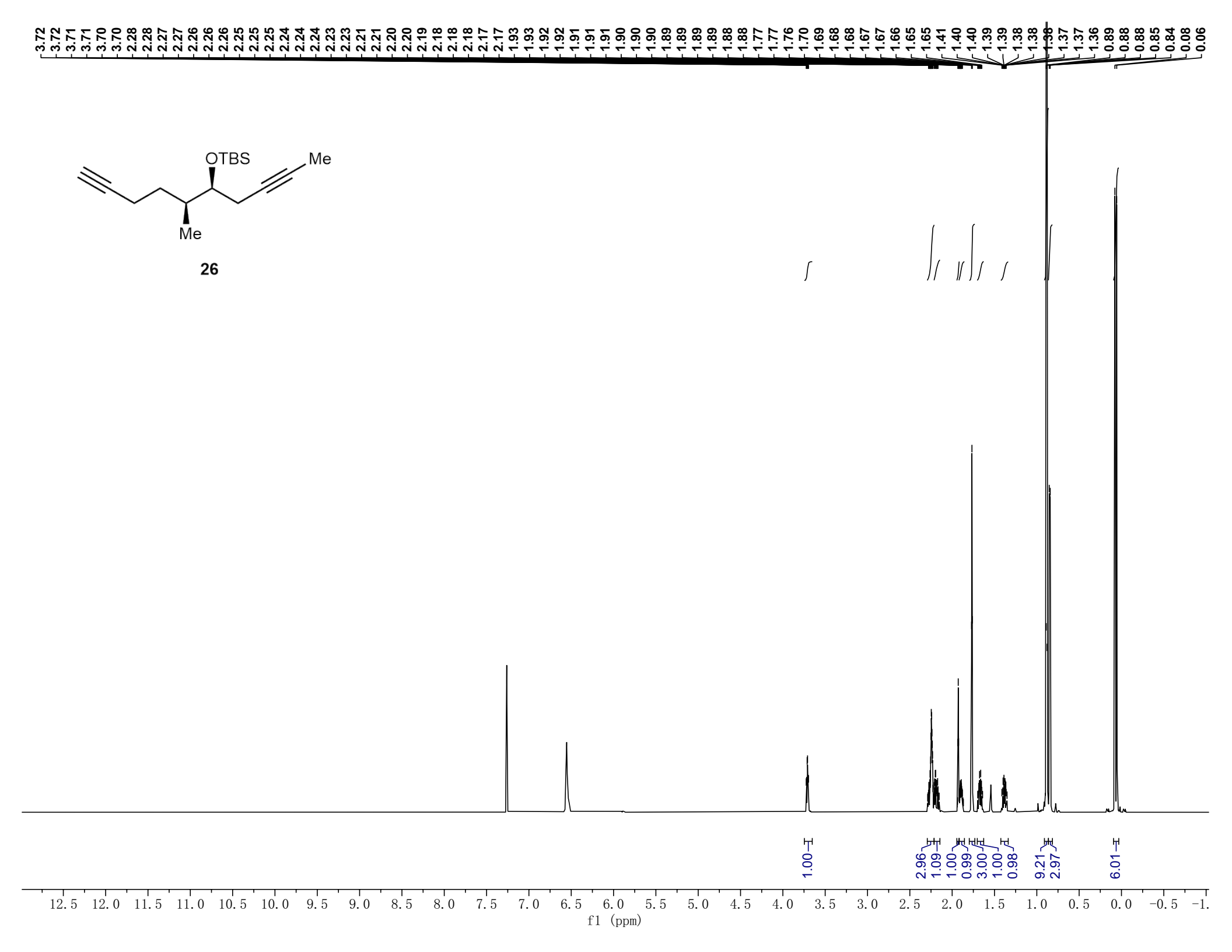
2.78 2.78 2.77 2.76 2.71 2.71 2.70 2.69 2.69 2.59 2.59 2.58 2.58 2.39 2.38 2.38 2.37 2.36 2.35 2.35 2.34 2.34 2.33 2.32 2.32 2.31 2.30 2.30 2.29 2.29 2.27 1.68 1.68 1.67 1.67 1.66 1.66 1.65 1.64 1.63 1.63 1.63 1.62 1.61 1.56 1.55 1.53 1.53 1.53 1.52 1.52 1.51 1.51 1.50 1.50 1.49 1.10 1.09 1.09 1.06 1.06 1.05 1.03 1.02 1.01 1.01 1.00 1.00 0.99 0.98
1.00 1.01 0.99 2.04 1.02 2.03 24.00
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

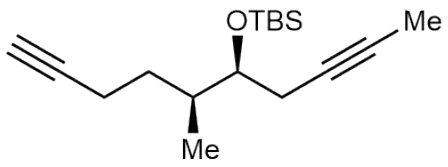


25

108.4
80.9
56.7
47.4
35.3
32.8
18.8
17.9
16.9
11.4

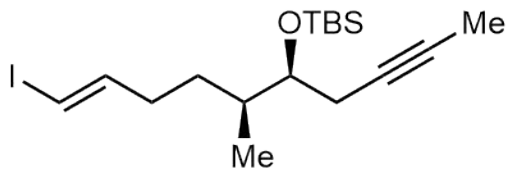
f1 (ppm)


OTBS
Me
Me
26
f1 (ppm)


OTBS
Me
Me

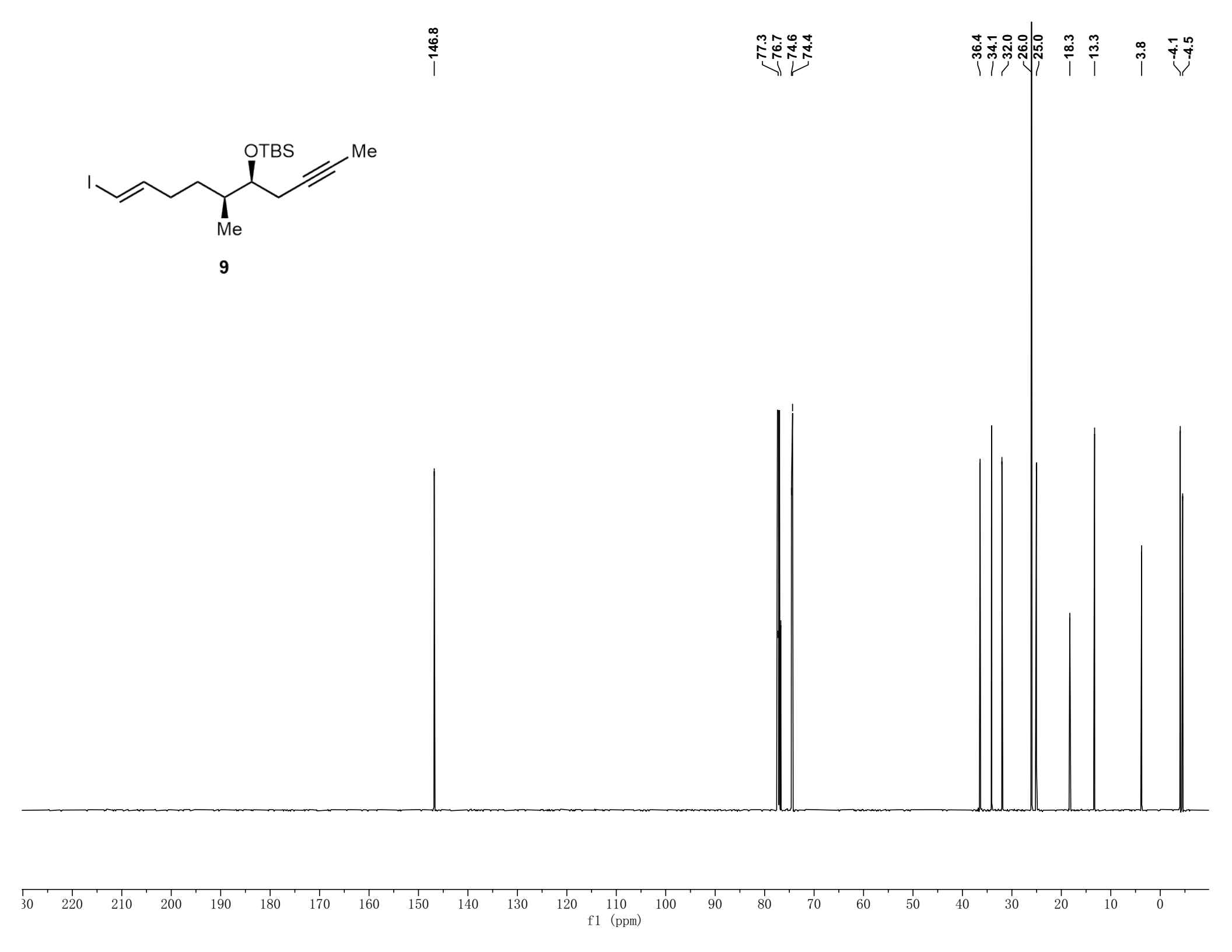
26

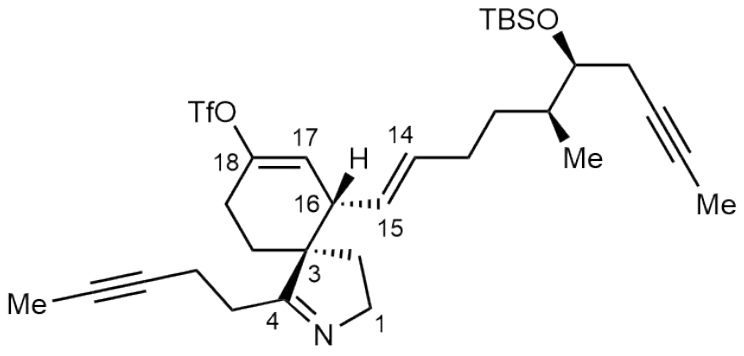
84.8
77.2
76.8
74.5
68.3
36.4
32.3
26.0
25.0
18.3
16.7
13.0
3.7
-4.1
-4.6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OTBS
Me
I
Me

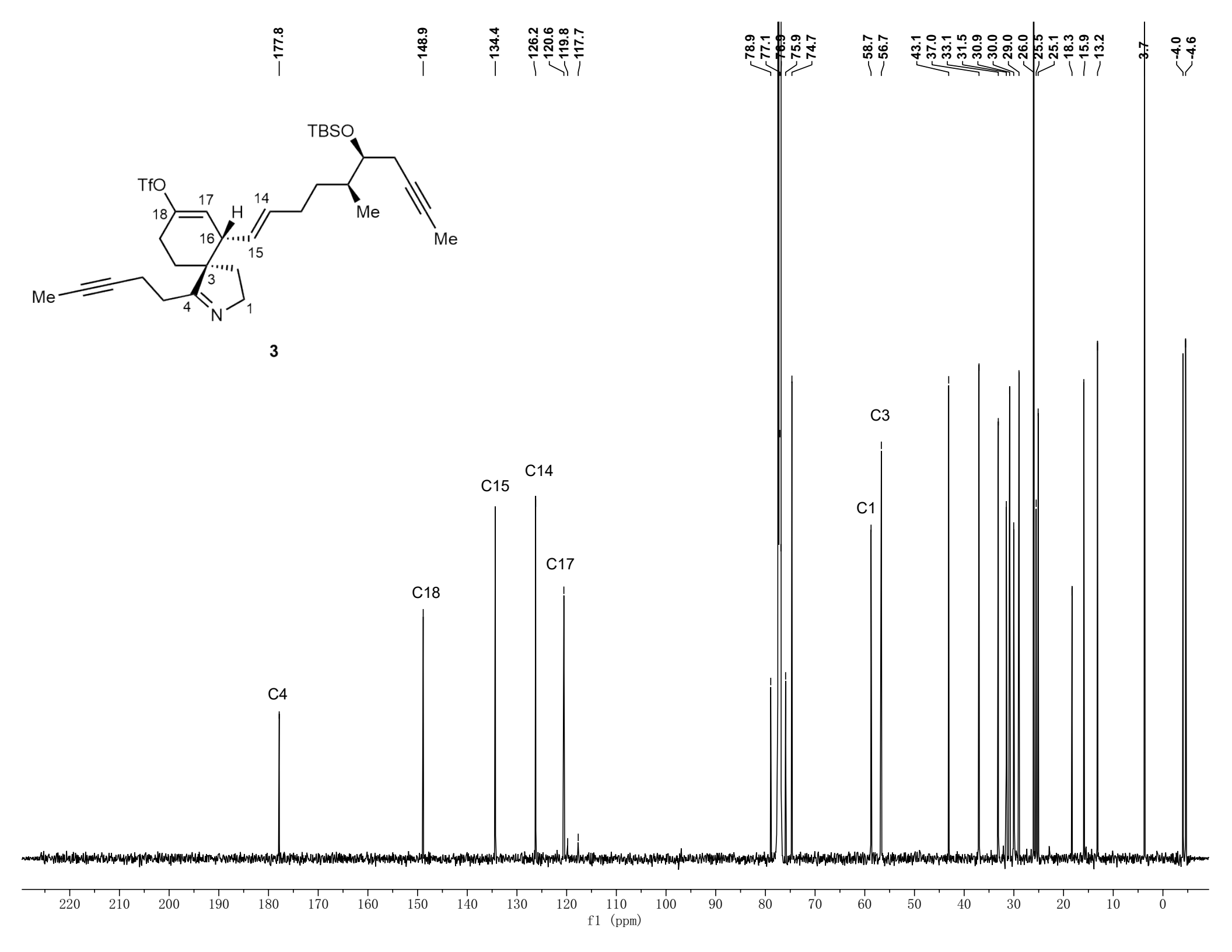
9

6.53 6.52 6.50 6.49 6.48 6.01 6.00 5.98 3.69 3.69 3.68 3.68 3.67 3.67 2.25 2.24 2.24 2.23 2.23 2.22 2.22 2.21 2.13 2.13 2.12 2.12 2.11 2.11 2.10 2.10 2.07 2.06 2.05 2.05 2.04 2.04 2.03 1.78 1.78 1.77 1.77 1.76 1.76 1.75 1.75 1.74 1.73 1.73 1.72 1.53 1.52 1.52 1.51 1.51 1.51 1.50 1.50 1.49 1.26 1.25 1.24 1.23 1.23 1.22 1.21 0.88 0.88 0.88 0.87 0.83 0.82 0.07 0.04
1.00 1.01 1.01 2.07 1.04 1.01 3.05 1.02 1.00 1.08 9.36 3.06 3.09 3.10
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

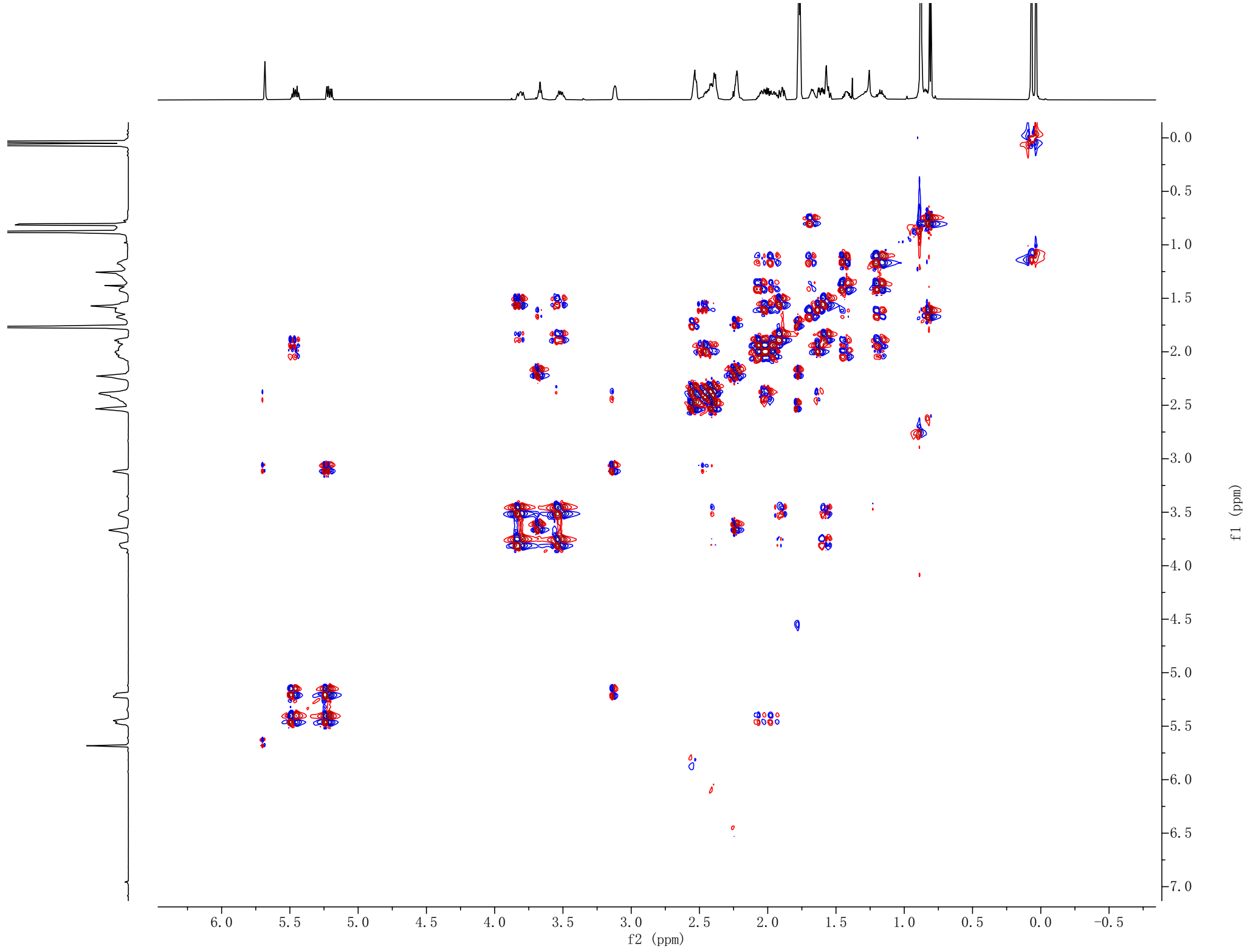

146.8
77.3
76.7
74.6
74.4
36.4
34.1
32.0
26.0
25.0
18.3
13.3
3.8
-4.1
-4.5
OTBS
Me
I
Me
9
f1 (ppm)

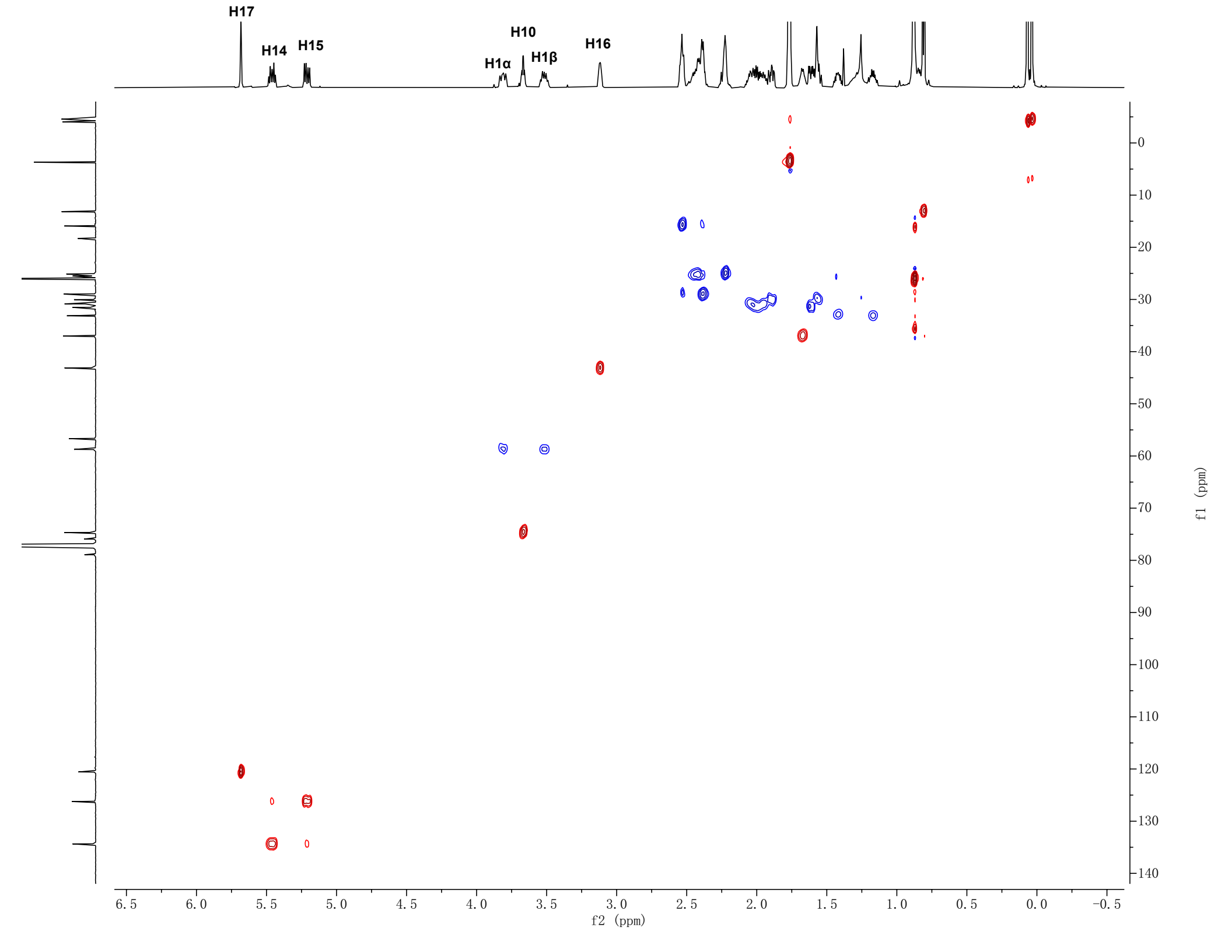


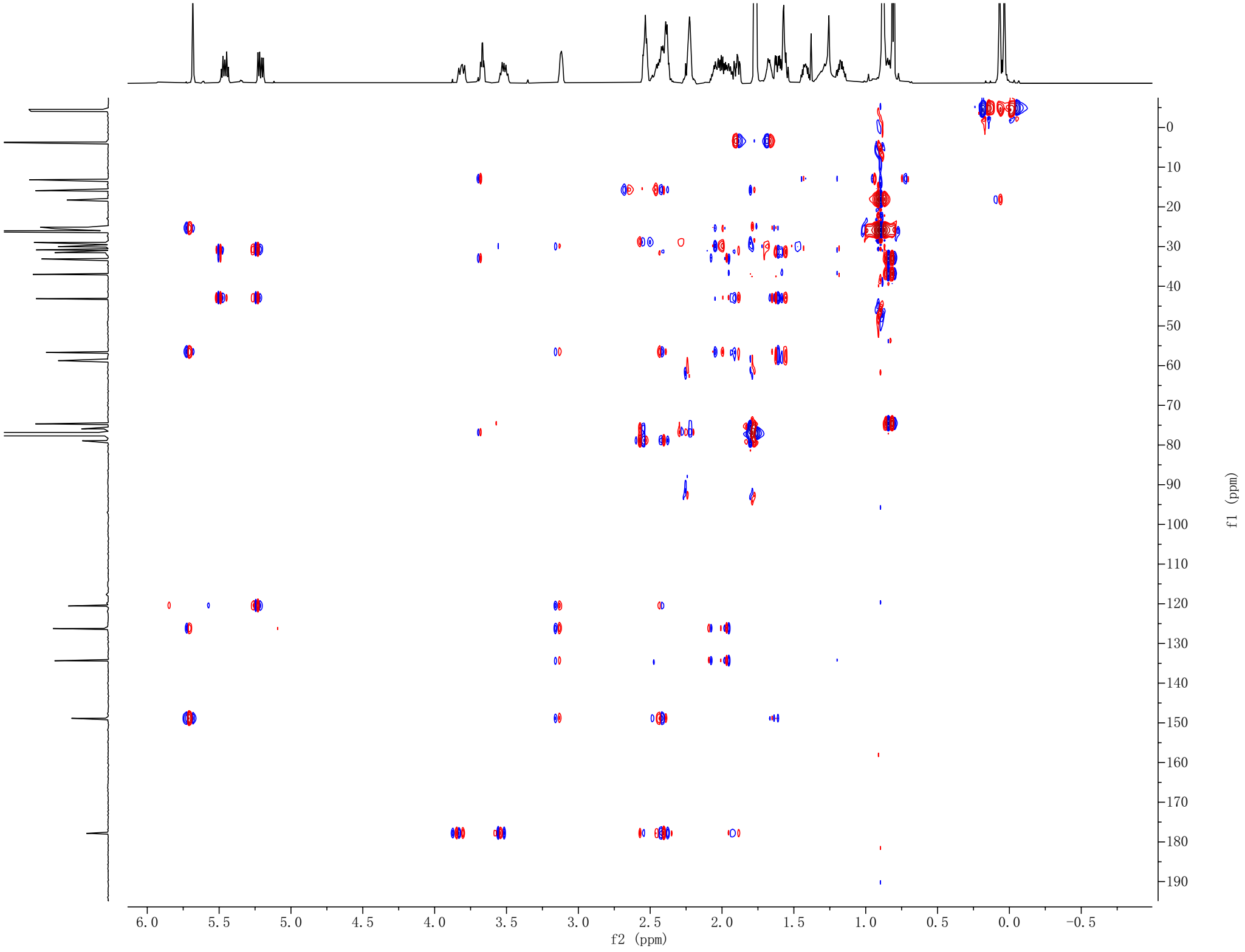
3

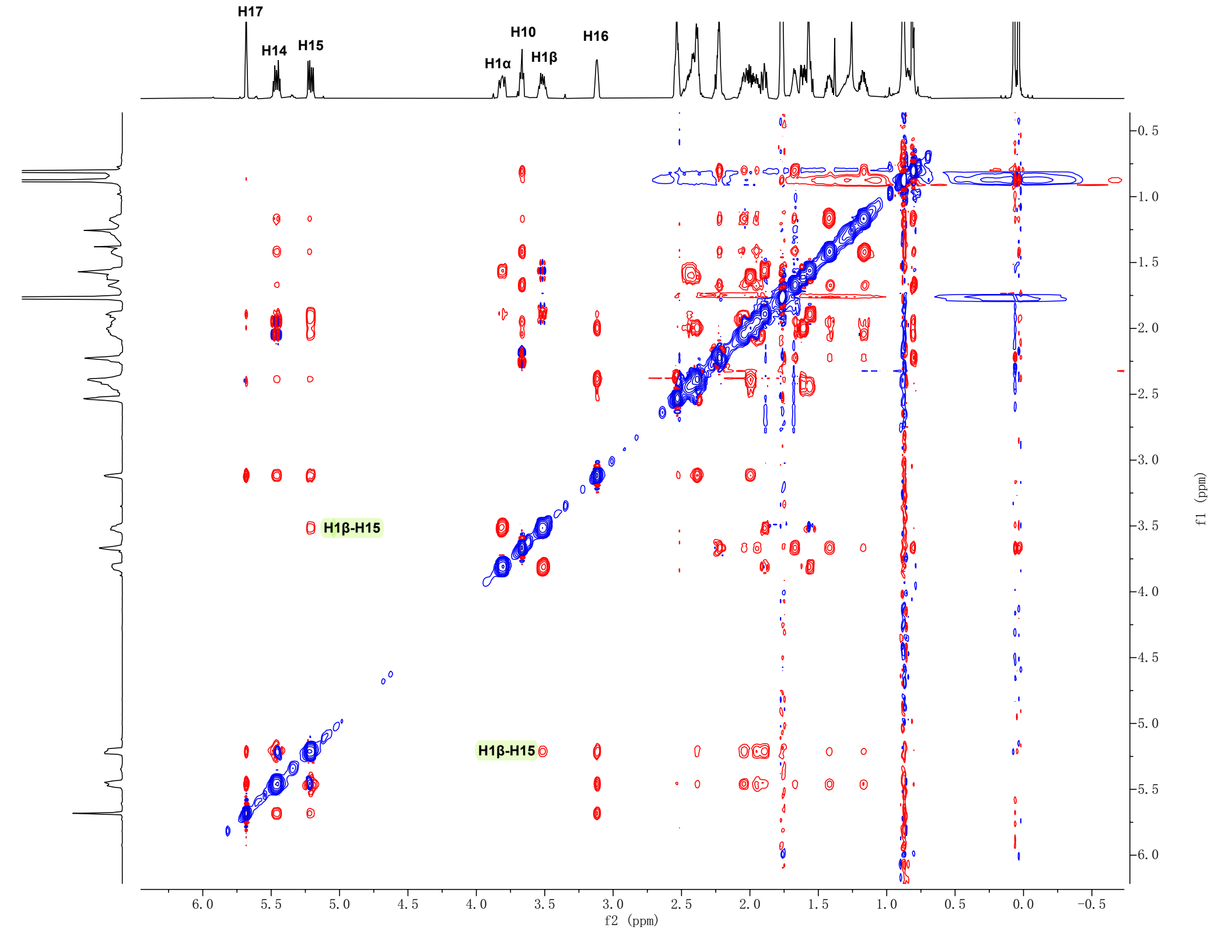

177.8
148.9
134.4
126.2
120.6
119.8
117.7
78.9
77.1
76.9
75.9
74.7
58.7
56.7
43.1
37.0
33.1
31.5
30.9
30.0
29.0
26.0
25.5
25.1
18.3
15.9
13.2
3.7
-4.0
-4.6
TBSO
TfO
17
14
18
H
Me
16
Me
15
3
Me
4
N
1
C4
C18
C15
C14
C17
C1
C3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

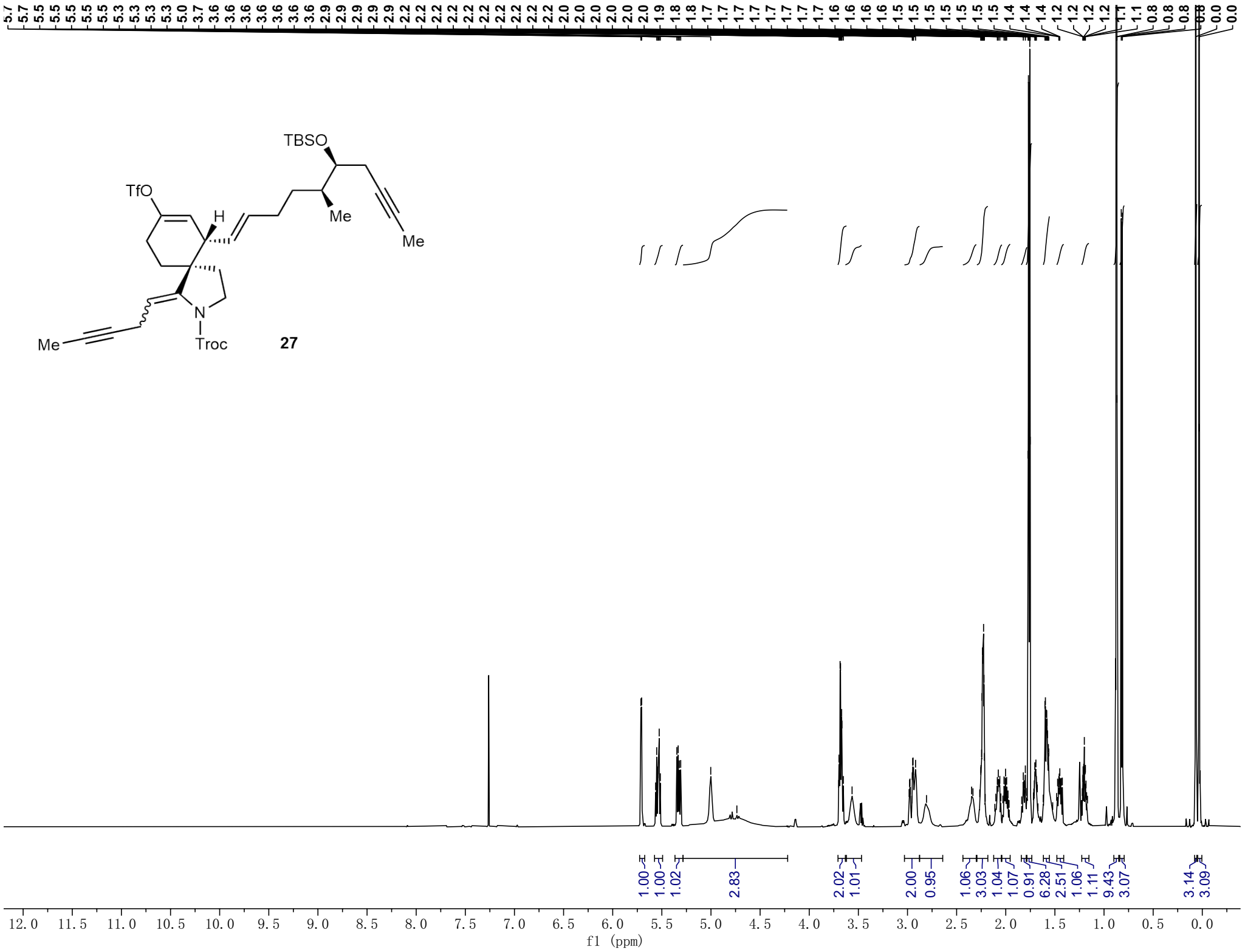
3

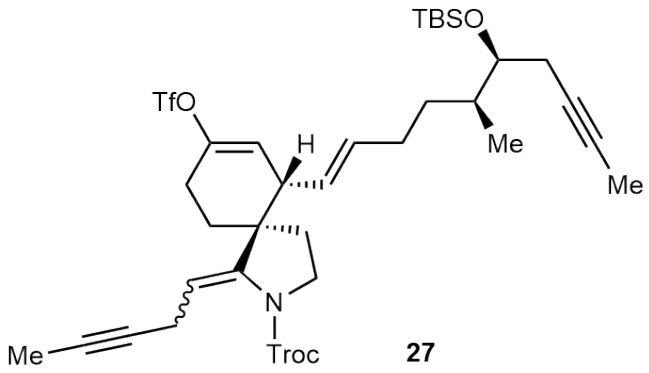

6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
f1 (ppm)


H17
H14
H15
H1α
H10
H1β
H16
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)


6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
f1 (ppm)


H17
H14
H15
H1α
H10
H1β
H16
H1β-H15
H1β-H15
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
f1 (ppm)

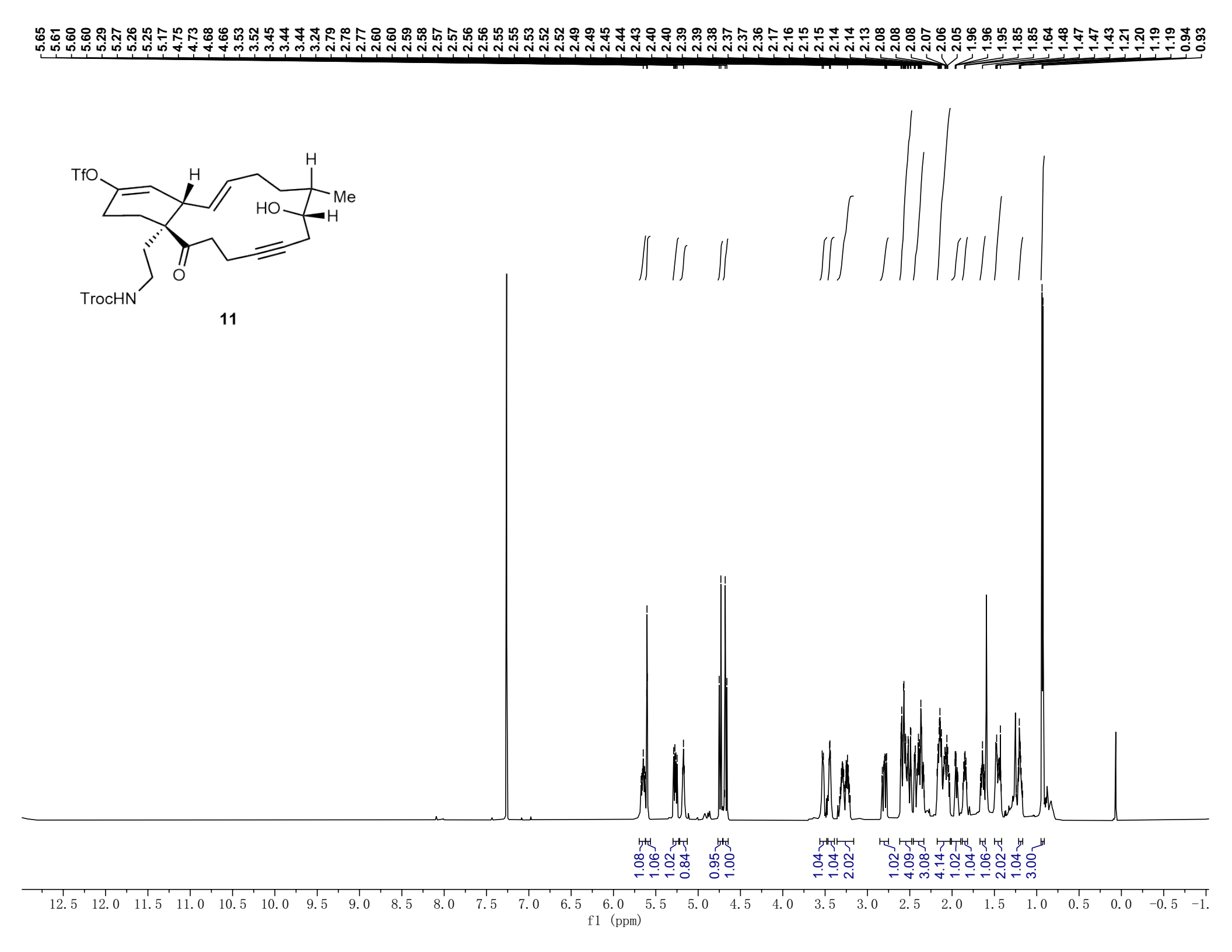

TBSO
TfO
H
Me
Me
N
Troc
Me
27
1.00
1.00
1.02
2.83
2.02
1.01
2.00
0.95
1.06
3.03
1.04
1.07
0.91
6.28
2.51
1.06
1.11
9.43
3.07
3.14
3.09
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

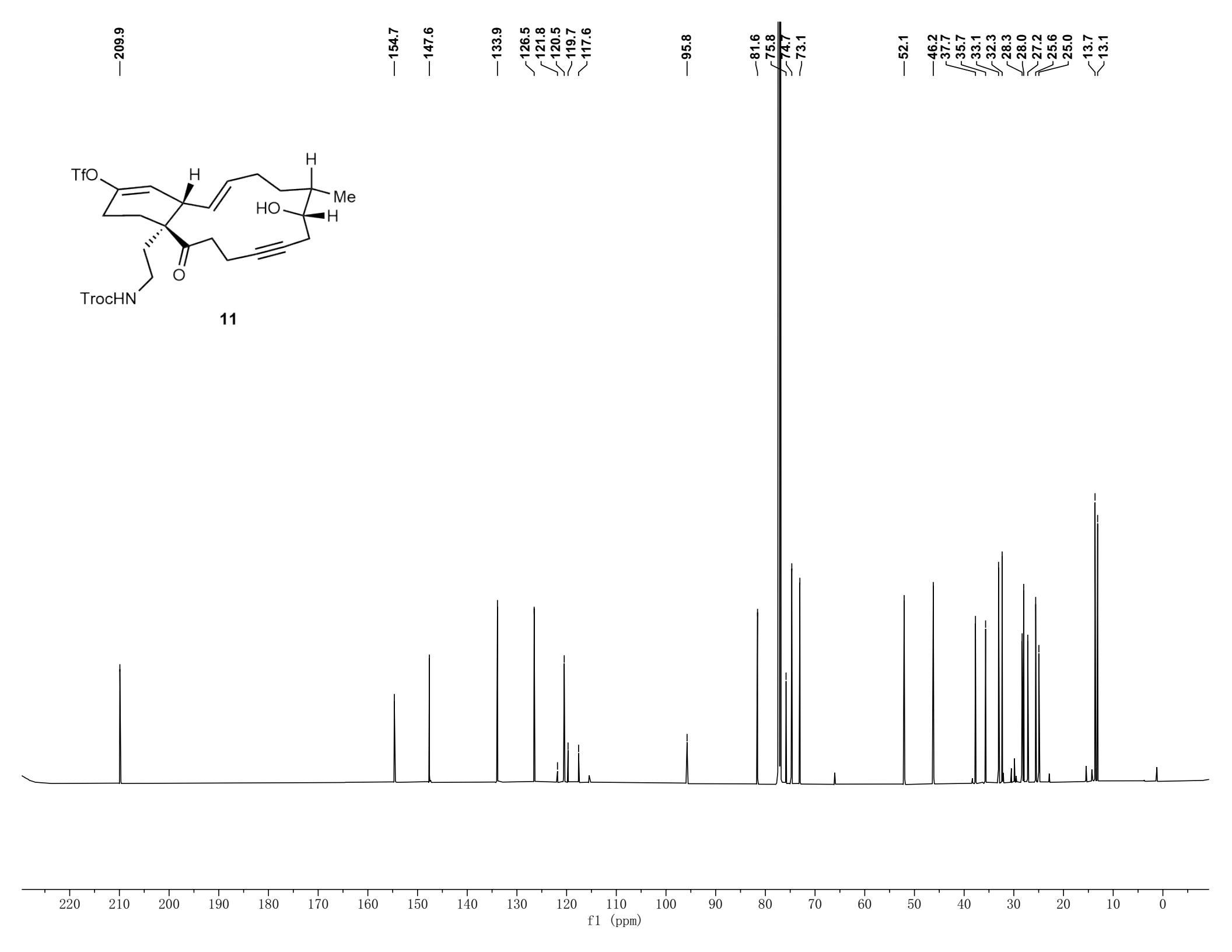


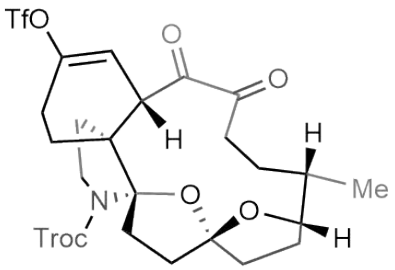
27

148.8 141.0 135.1 127.5 121.8 120.3 119.7 117.6 115.5 95.6 77.1 76.9 75.5 75.1 74.5 66.0 45.7 45.5 45.0 36.9 33.3 31.5 30.7 26.0 25.9 25.1 19.4 18.3 13.1 3.7 3.7 -4.0 -4.6

f1 (ppm)

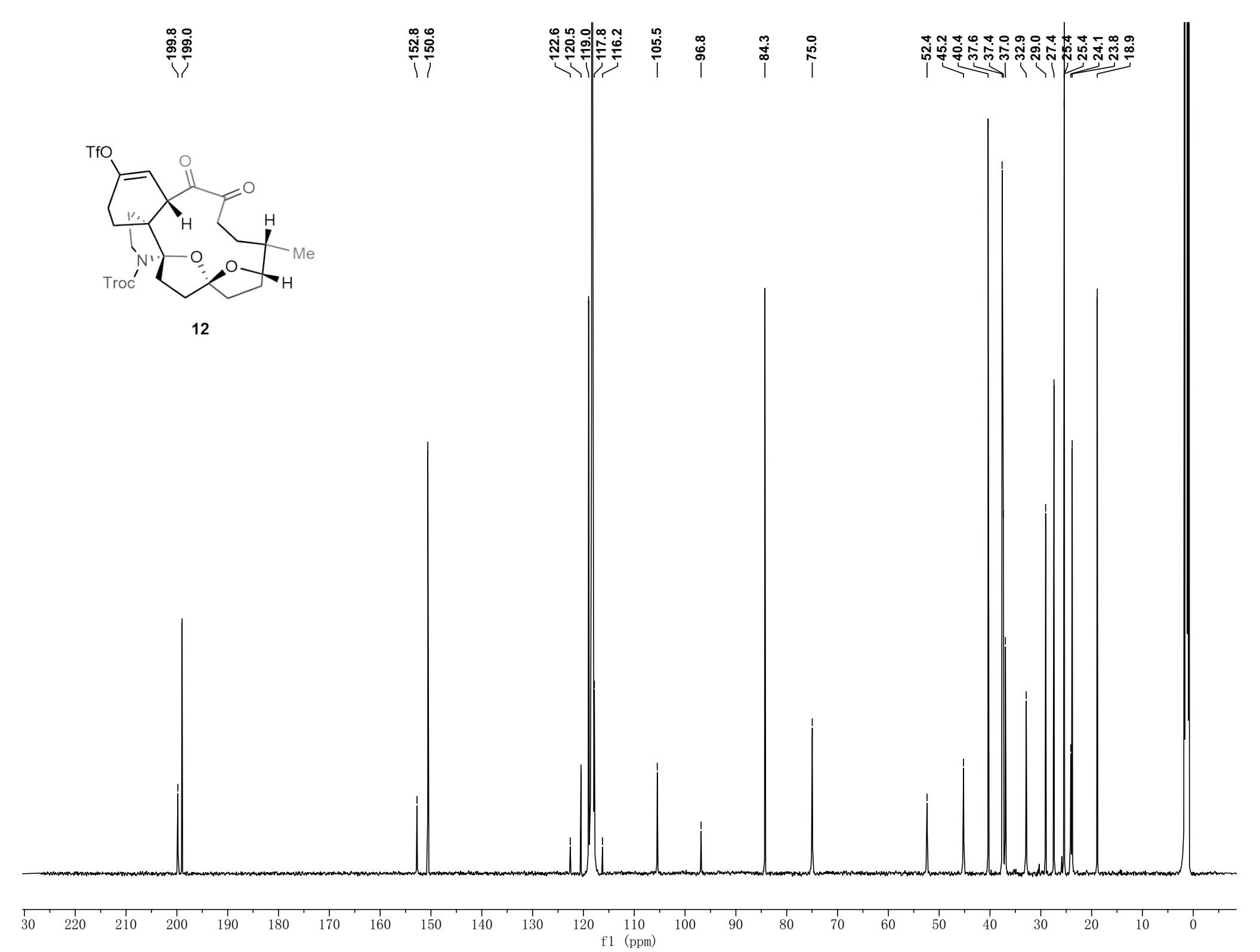

5.65 5.61 5.60 5.60 5.29 5.27 5.26 5.25 5.17 4.75 4.73 4.68 4.66 3.53 3.52 3.45 3.44 3.44 3.24 2.79 2.78 2.77 2.60 2.60 2.59 2.58 2.57 2.57 2.56 2.56 2.55 2.55 2.53 2.52 2.52 2.49 2.49 2.45 2.44 2.43 2.40 2.40 2.39 2.39 2.38 2.37 2.37 2.36 2.17 2.16 2.15 2.14 2.14 2.13 2.08 2.08 2.08 2.07 2.06 2.05 1.96 1.96 1.95 1.85 1.85 1.64 1.48 1.47 1.47 1.43 1.21 1.20 1.19 1.19 0.94 0.93
TfO
H
H
Me
HO
H
O
TrocHN
11
1.08 1.06 1.02 0.84 0.95 1.00 1.04 1.04 2.02 1.02 4.09 3.08 4.14 1.02 1.04 1.06 2.02 1.04 3.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

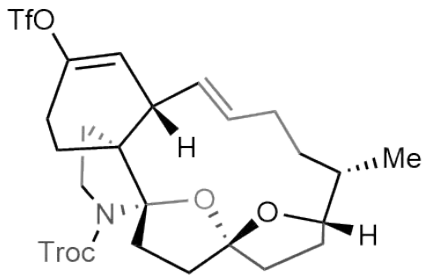

209.9
154.7
147.6
133.9
126.5
121.8
120.5
119.7
117.6
95.8
81.6
75.8
74.7
73.1
52.1
46.2
37.7
35.7
33.1
32.3
28.3
28.0
27.2
25.6
25.0
13.7
13.1
TfO
H
H
Me
HO
H
O
TrocHN
11
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TfO
O
O
H
H
Me
N
O
O
H
Troc

12

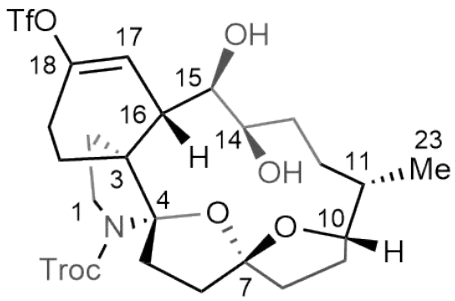
5.59 5.59 5.59 5.58 4.73 4.71 4.51 4.50 4.50 4.50 4.50 3.80 3.49 3.48 3.12 3.12 3.11 3.11 2.31 2.31 2.30 2.30 2.29 2.28 2.28 2.28 2.27 2.17 2.16 2.16 2.16 2.15 2.14 2.04 2.04 2.03 2.03 2.02 1.99 1.98 1.98 1.92 1.91 1.90 1.90 1.89 1.89 1.88 1.88 1.72 1.71 1.71 1.71 1.70 1.70 1.70 1.69 1.69 1.68 1.68 1.63 1.63 1.63 1.62 1.62 1.62 1.62 1.61 1.61 1.61 1.59 1.59 0.86 0.85
1.00 1.01 1.09 0.98 0.99 0.97 1.02 0.99 1.00 1.04 0.99 1.10 3.13 3.07 1.30 1.15 1.11 1.05 3.05 2.03 3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


199.8
199.0
152.8
150.6
122.6
120.5
119.0
117.8
116.2
105.5
96.8
84.3
75.0
52.4
45.2
40.4
37.6
37.4
37.0
32.9
29.0
27.4
25.4
25.4
24.1
23.8
18.9
TfO
O
O
H
H
Me
N
O
O
H
Troc
12
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

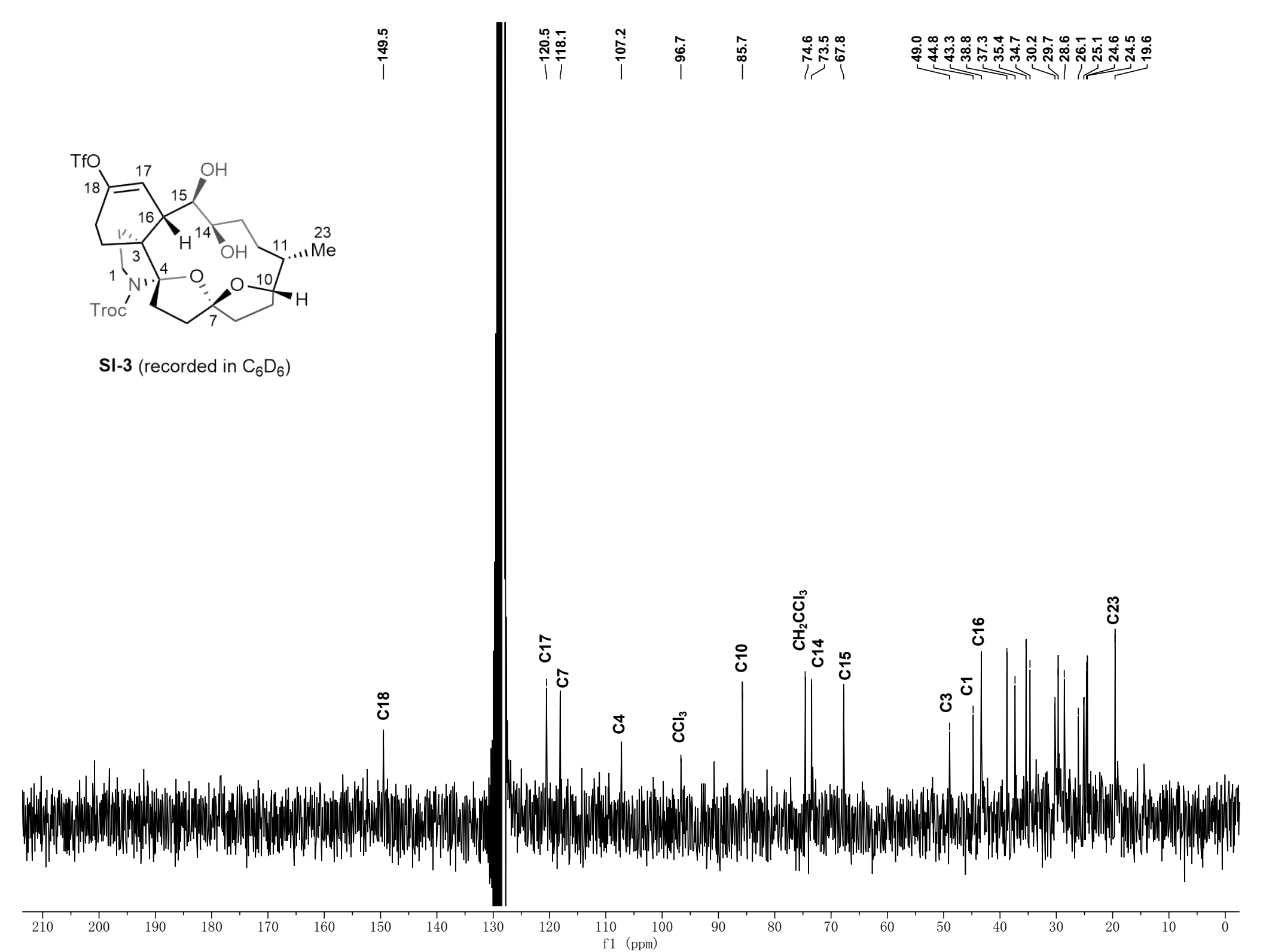

TfO
H
Me
N
O
O
H
Troc

SI-2 (crude)

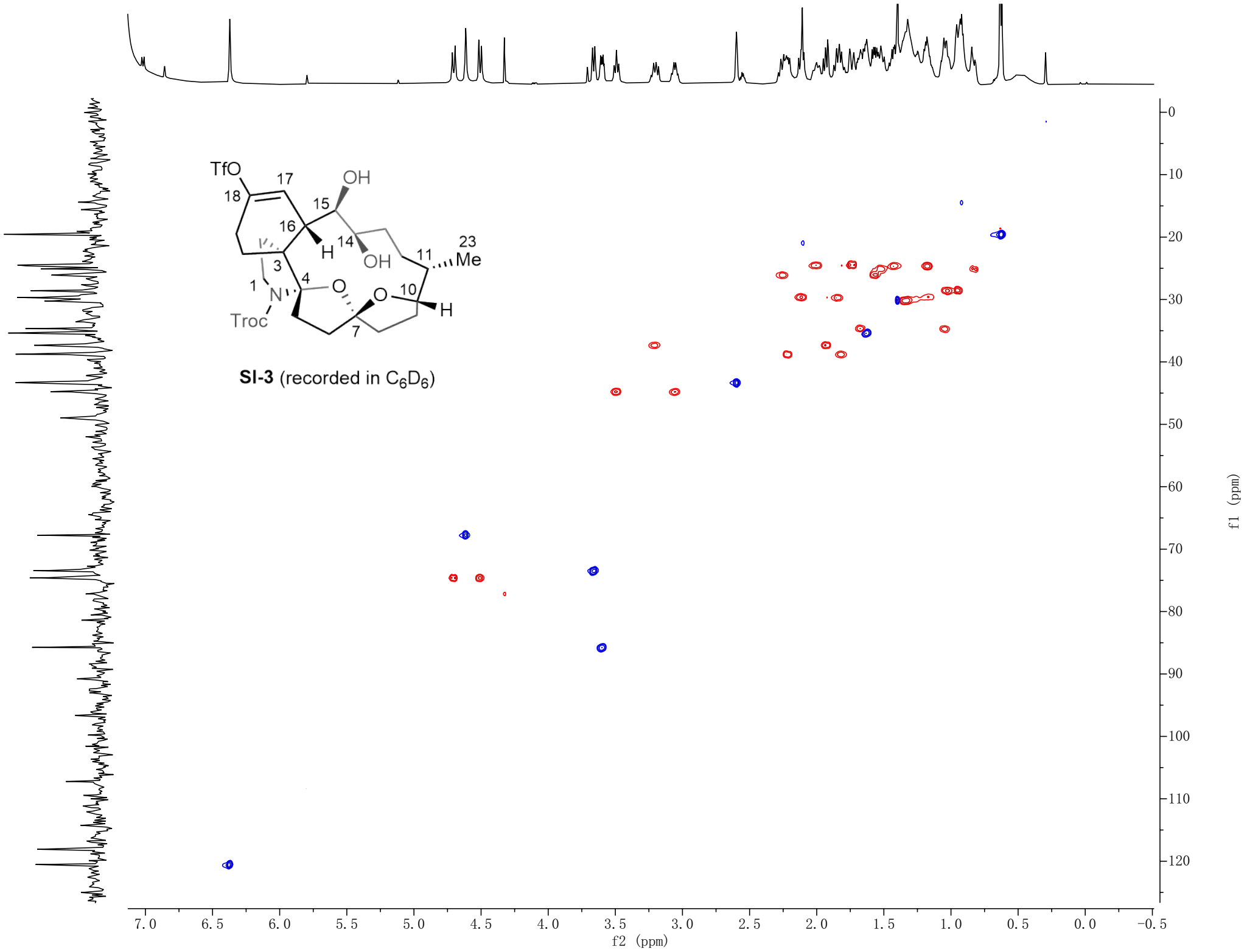
5.88 5.87 5.86 5.85 5.84 5.83 5.82 5.49 5.48 5.48 5.21 5.19 5.18 5.16 4.83 4.80 4.64 4.61 3.92 3.92 3.91 3.90 3.88 3.69 3.66 3.64 3.43 3.41 3.41 3.39 3.38 3.37 3.19 3.17 2.97 2.94 2.40 2.38 2.30 2.28 2.26 2.24 2.16 2.14 2.11 2.09 2.08 2.06 2.05 2.03 1.95 1.93 1.92 1.91 1.90 1.88 1.86 1.85 1.84 1.83 1.70 1.68 1.67 1.66 1.64 1.62 1.61 1.59 1.58 1.57 1.31 1.28 0.87 0.85
1.00 1.09 1.05 1.03 1.06 1.02 1.01 1.21 0.95 0.96 5.09 5.22 4.08 7.87 1.28 3.06
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

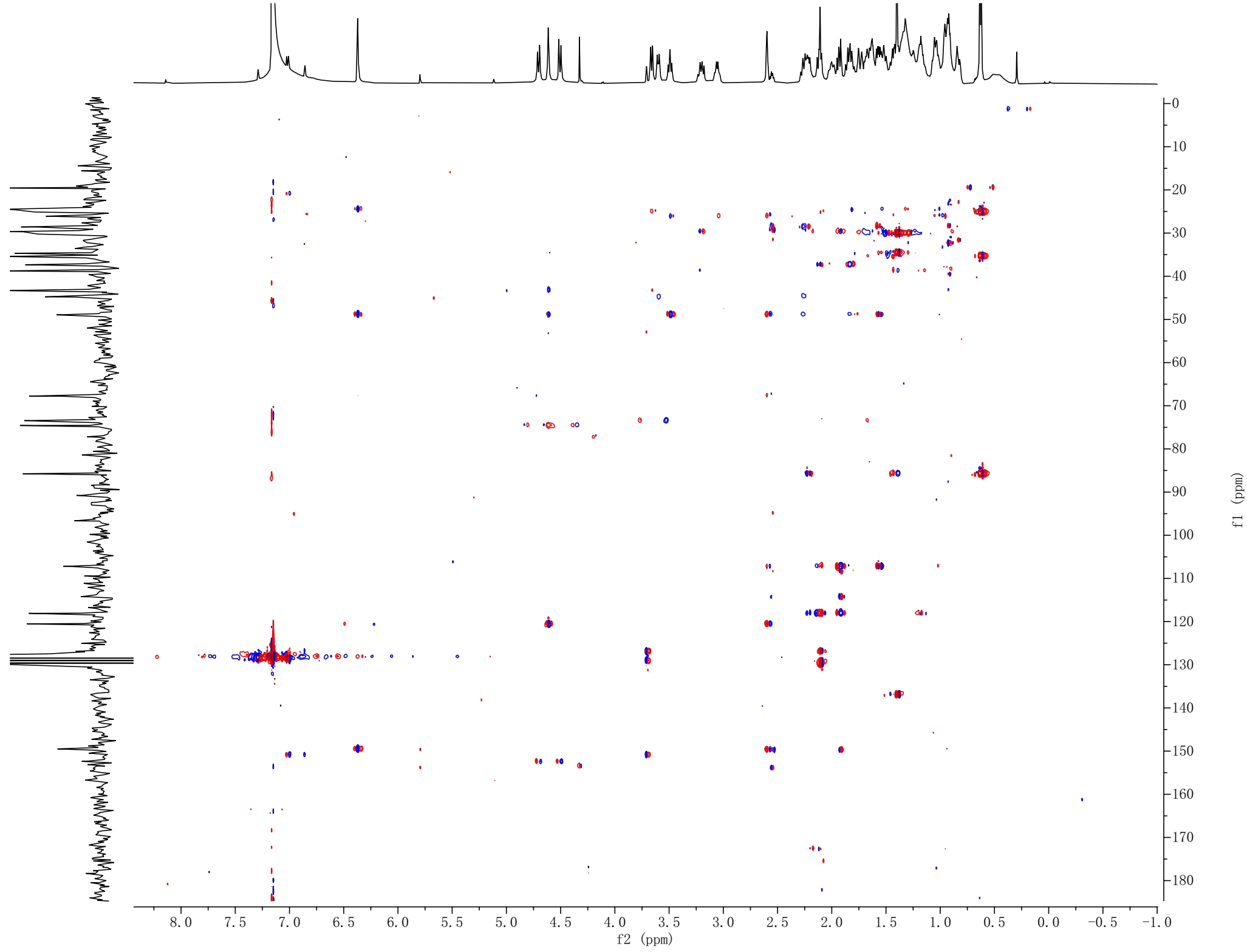


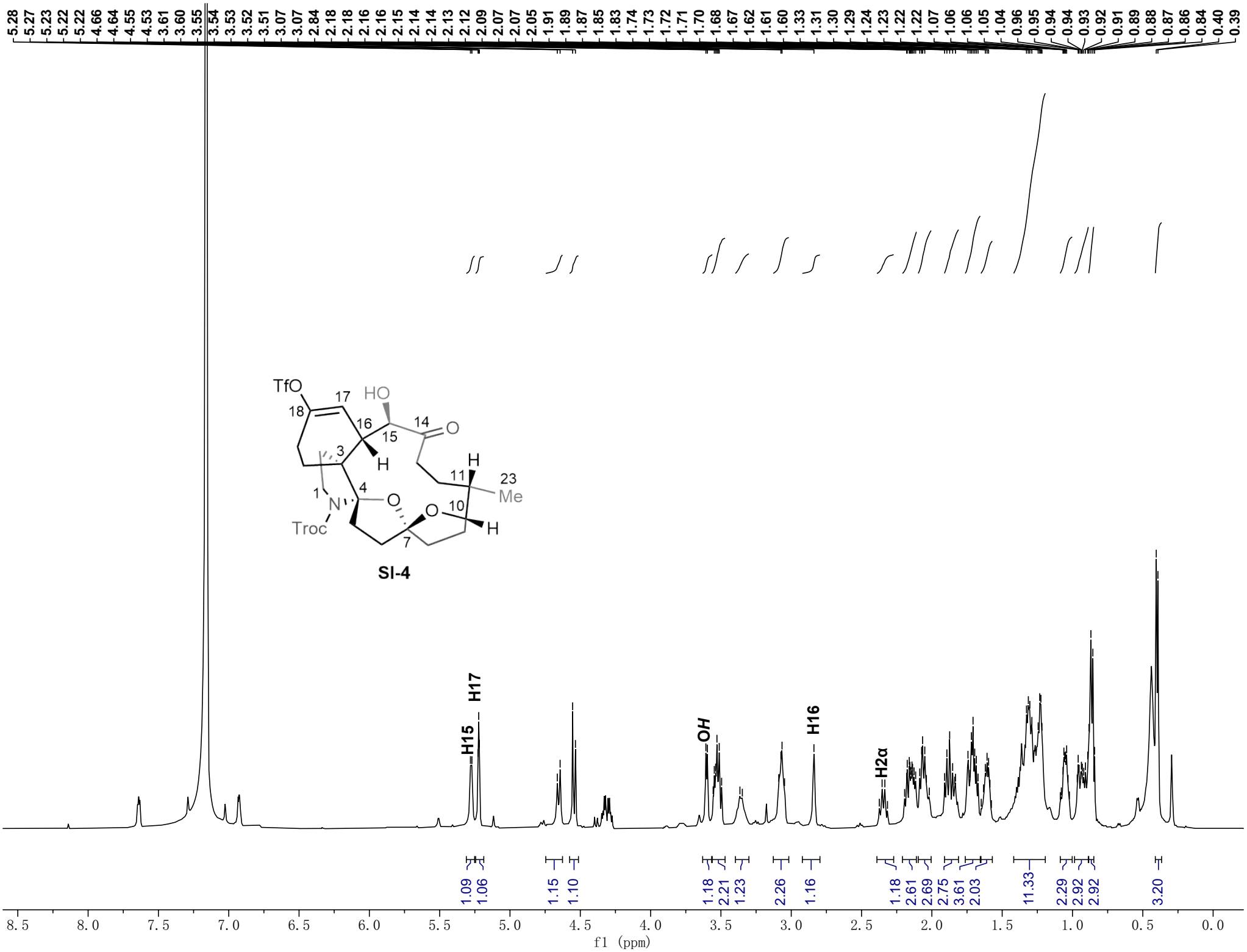
SI-3 (recorded in C_6D_6)



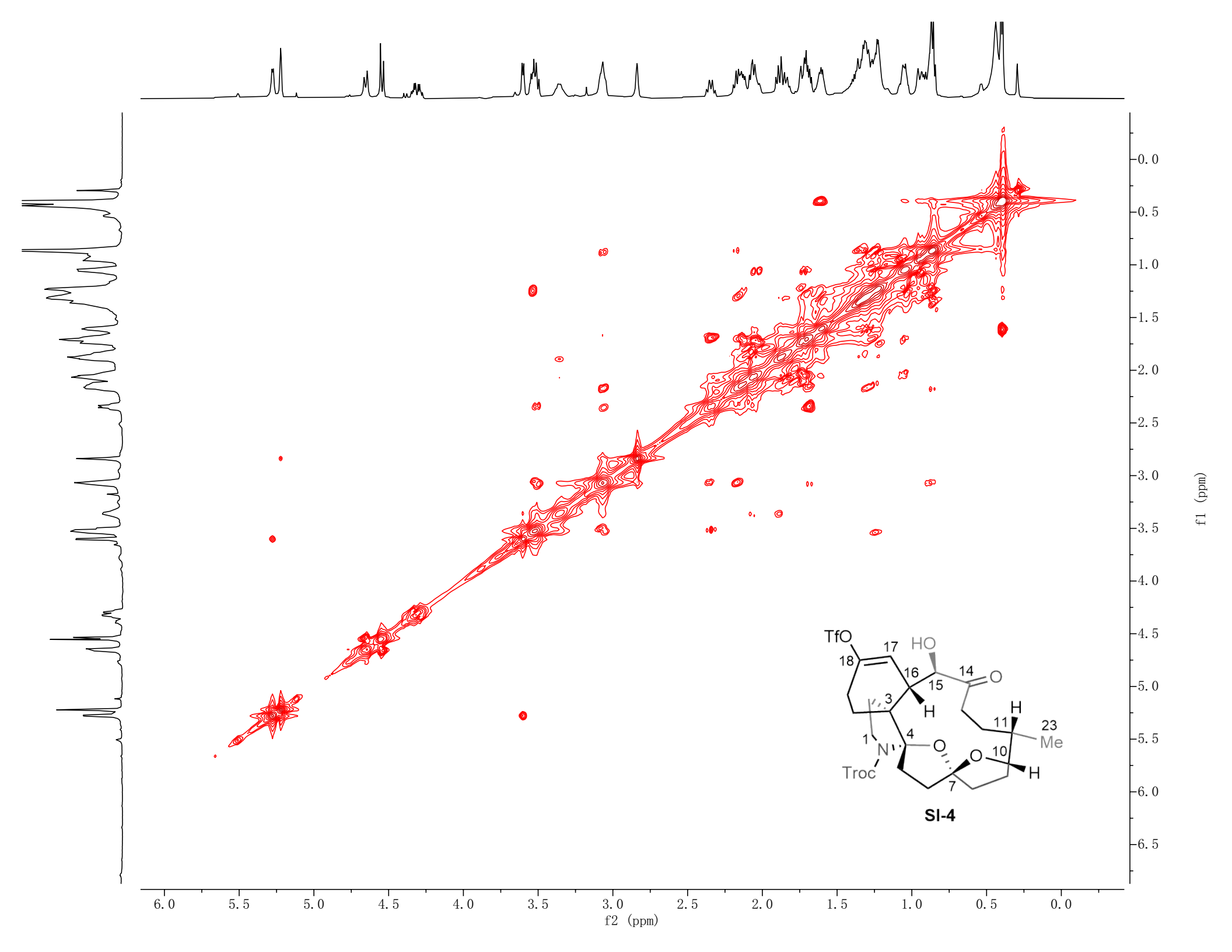
SI-3 (recorded in C_6D_6)

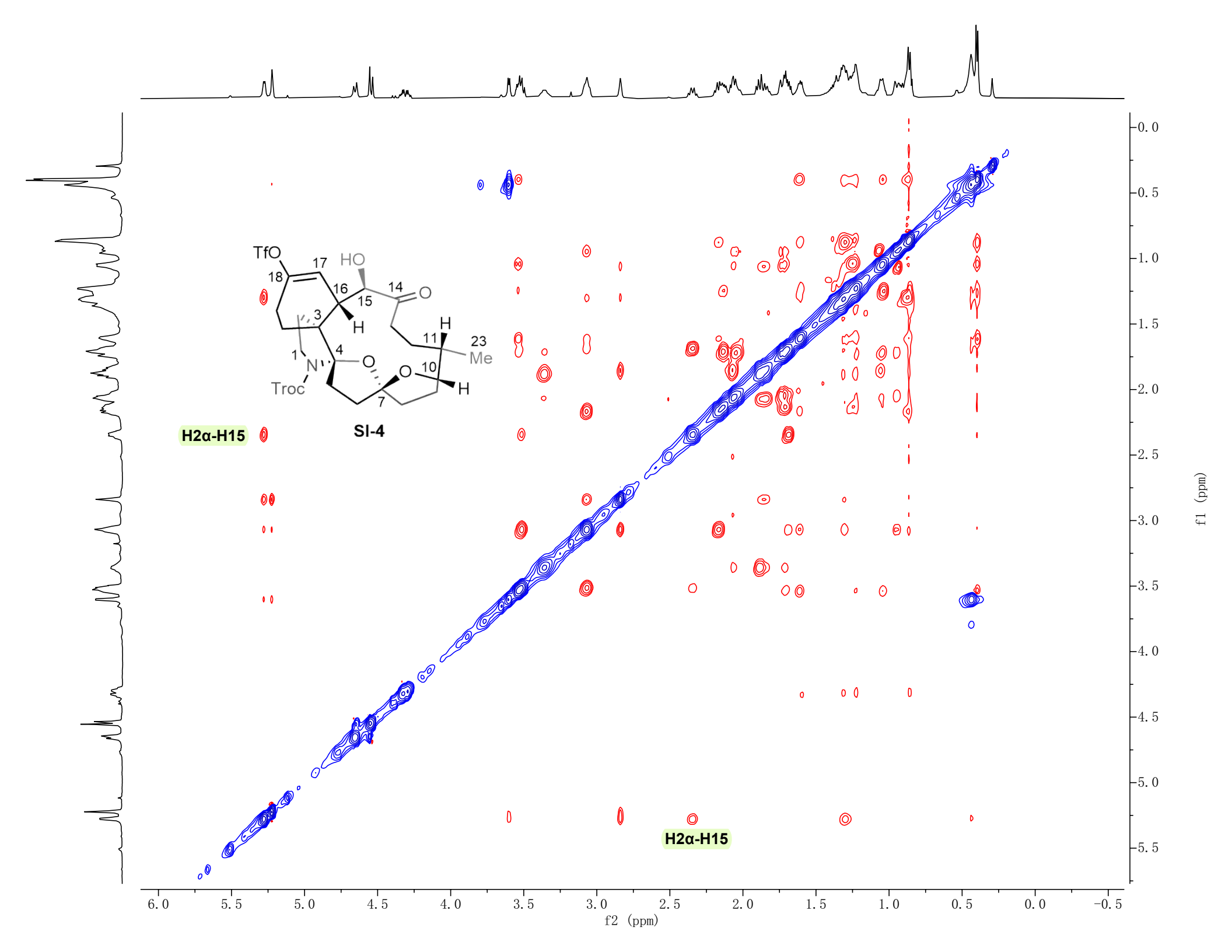

TfO
17
OH
18
15
16
H
14
OH
11
23
Me
3
1
4
O
O
10
N
H
Troc
7
SI-3 (recorded in C6D6)
f2 (ppm)
f1 (ppm)

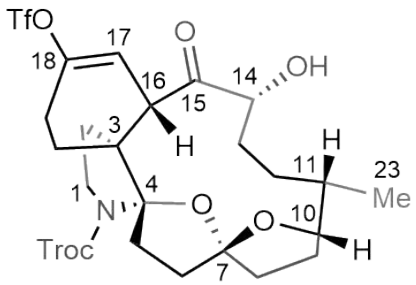

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)


5.28 5.27 5.23 5.22 5.22 4.66 4.64 4.55 4.53 3.61 3.60 3.55 3.54 3.53 3.52 3.51 3.07 3.07 2.84 2.18 2.18 2.16 2.16 2.15 2.14 2.14 2.13 2.12 2.09 2.07 2.07 2.05 1.91 1.89 1.87 1.85 1.83 1.74 1.73 1.72 1.71 1.70 1.68 1.67 1.62 1.61 1.60 1.33 1.31 1.30 1.29 1.24 1.23 1.22 1.22 1.07 1.06 1.06 1.05 1.04 0.96 0.95 0.94 0.94 0.93 0.92 0.91 0.89 0.88 0.87 0.86 0.84 0.40 0.39
TfO
HO
17
18
16
15
14
O
3
H
11
H
23
Me
1
N
4
O
O
10
H
Troc
7
H15
H17
OH
H16
H2α
1.09 1.06 1.15 1.10 1.18 2.21 1.23 2.26 1.16 1.18 2.61 2.69 2.75 3.61 2.03 11.33 2.29 2.92 2.92 3.20
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

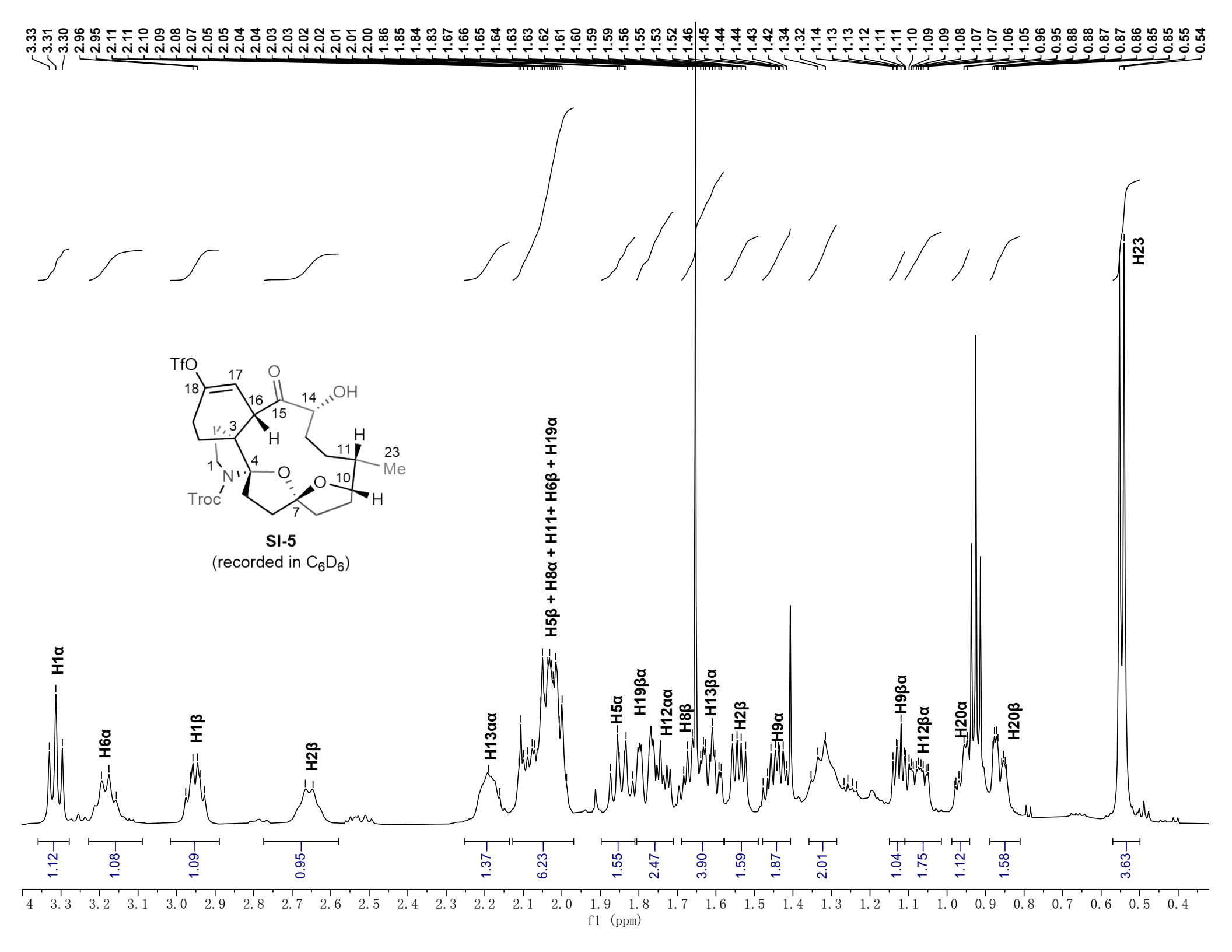
SI-4

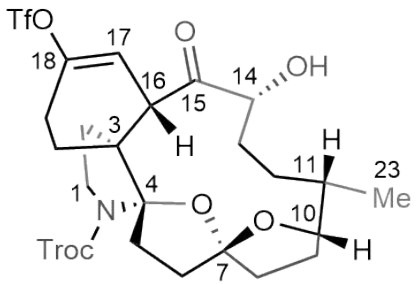

6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
f1 (ppm)
TfO
17
HO
18
16
14
O
15
3
H
11
H
23
Me
1
N
4
O
O
10
H
Troc
7
SI-4


TfO
17
HO
18
16
14
O
15
H
3
H
11
23
Me
1
4
O
O
10
N
Troc
H
7
SI-4
H2α-H15
H2α-H15
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
f1 (ppm)

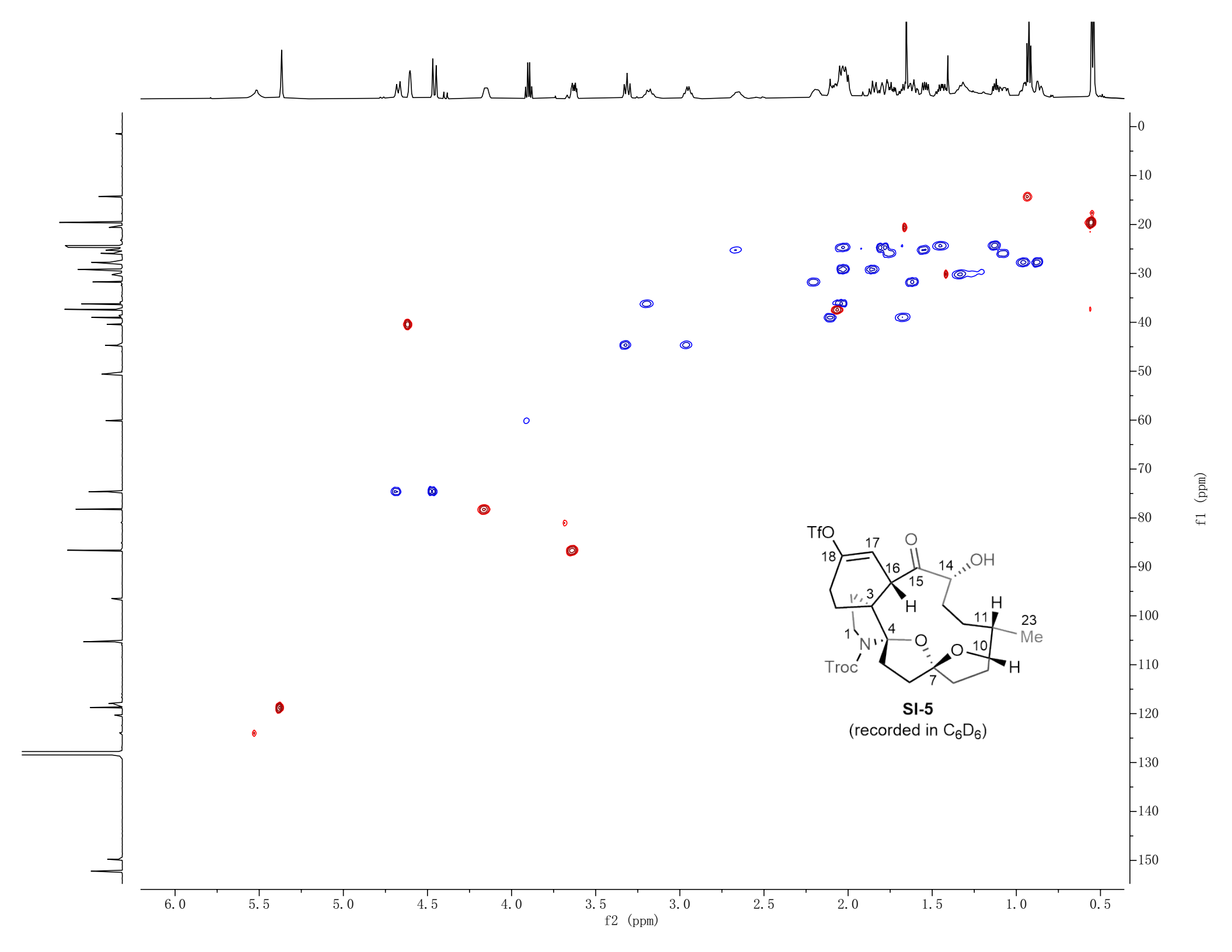


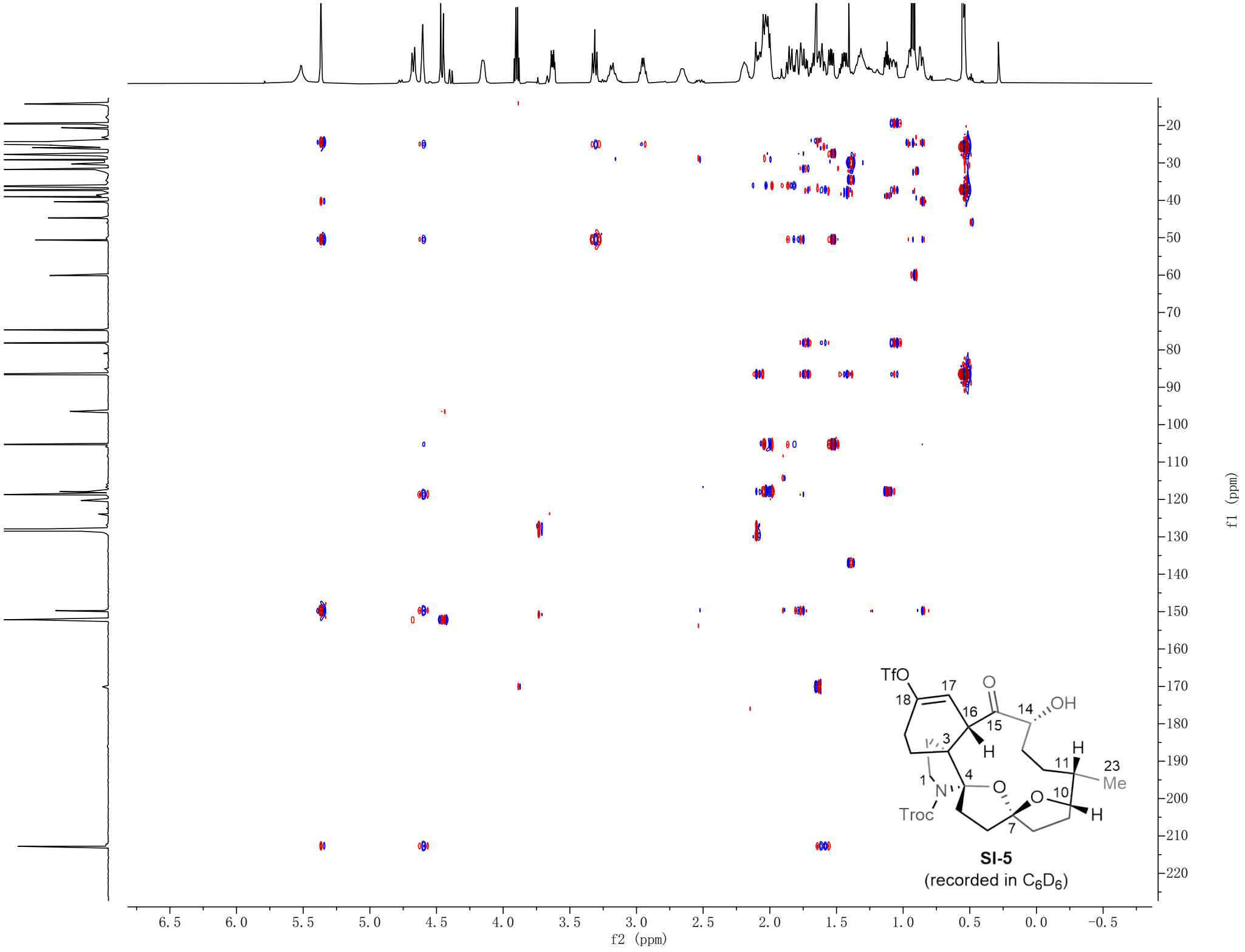
SI-5
(recorded in C_6D_6)

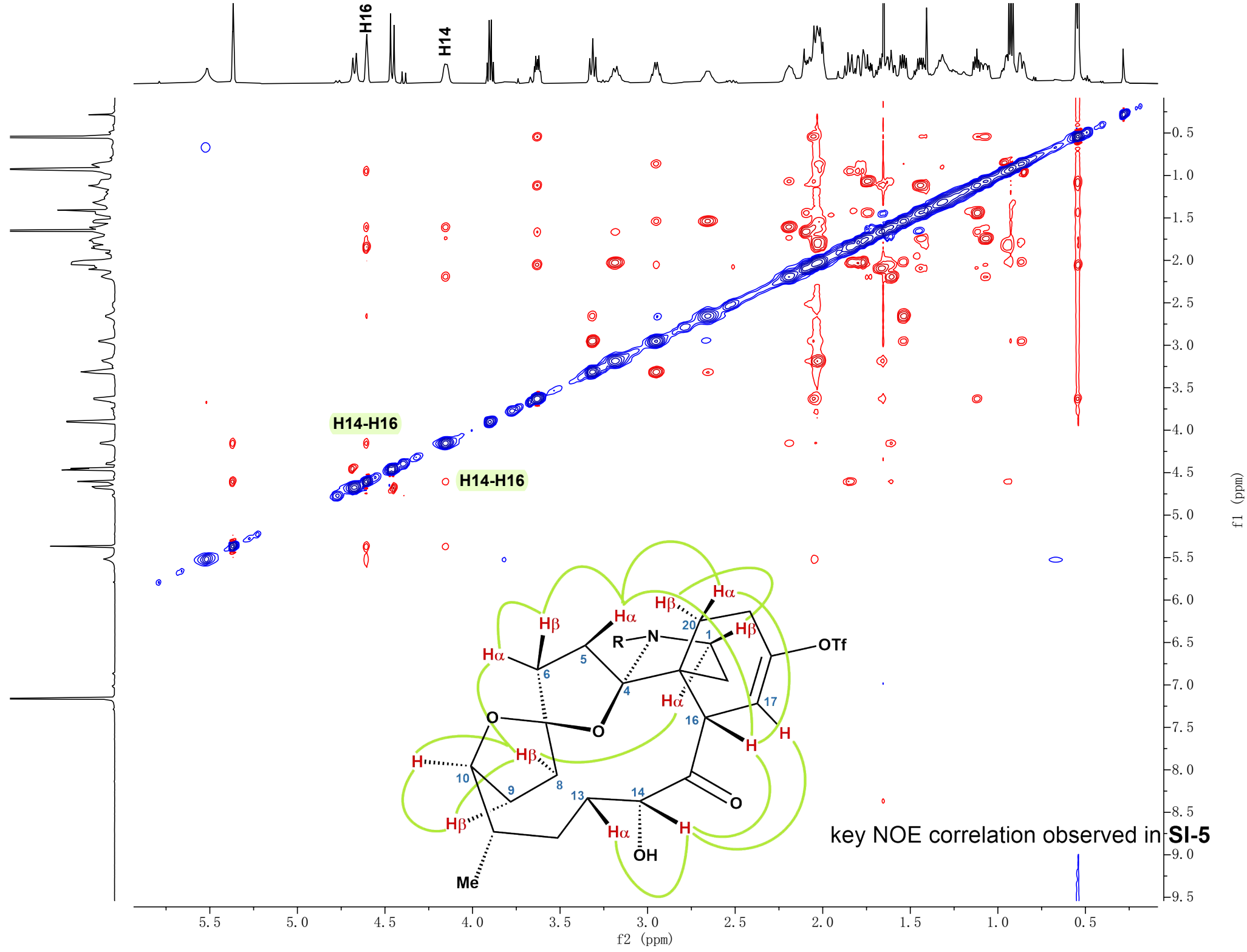

TfO
17
O
18
16
14
OH
15
3
H
H
11
23
Me
1
4
O
N
O
10
Troc
H
7
SI-5
(recorded in C6D6)
H1α
H6α
H1β
H2β
H13αα
H5β + H8α + H11+ H6β + H19α
H5α
H19βα
H12αα
H8β
H13βα
H2β
H9α
H9βα
H12βα
H20α
H20β
H23
1.12
1.08
1.09
0.95
1.37
6.23
1.55
2.47
3.90
1.59
1.87
2.01
1.04
1.75
1.12
1.58
3.63
f1 (ppm)

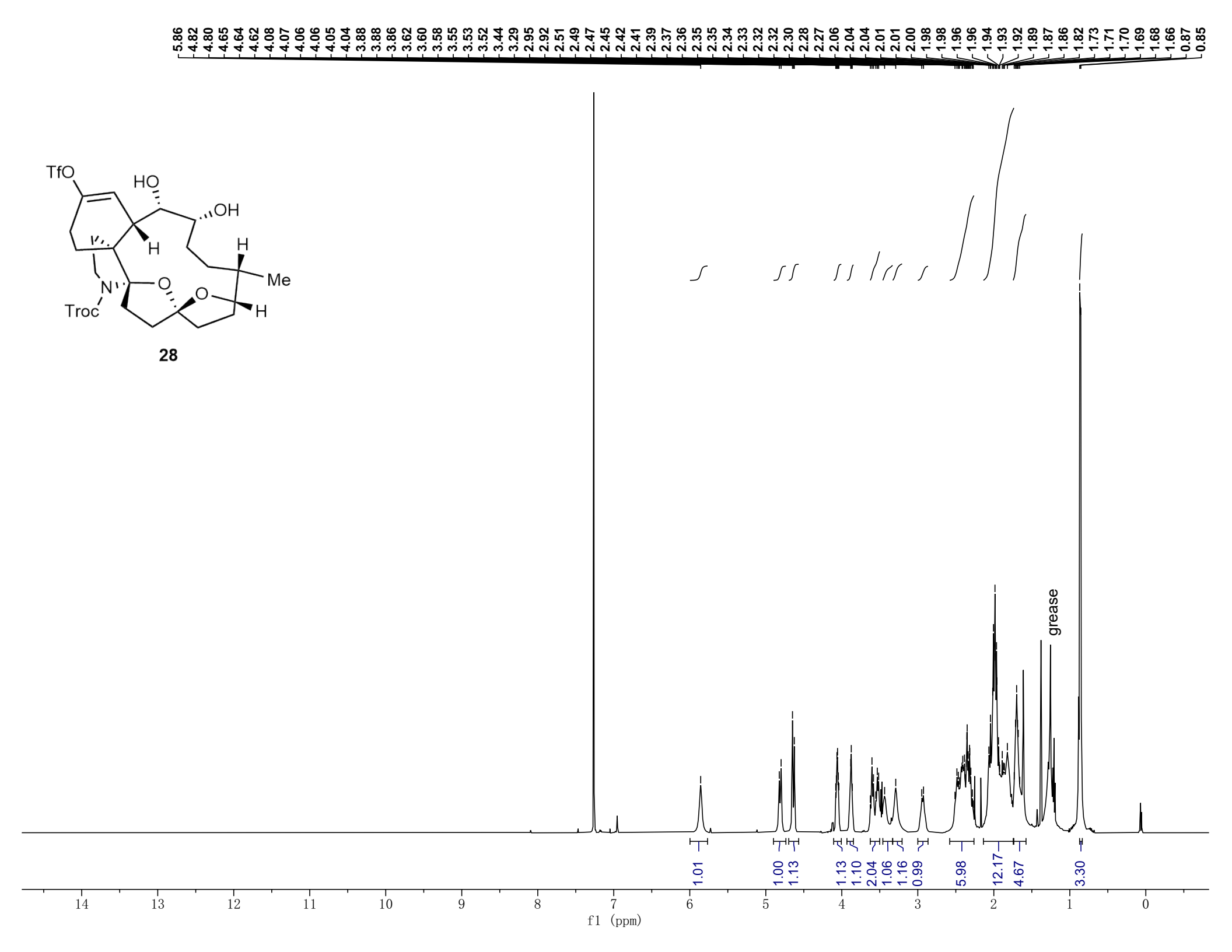


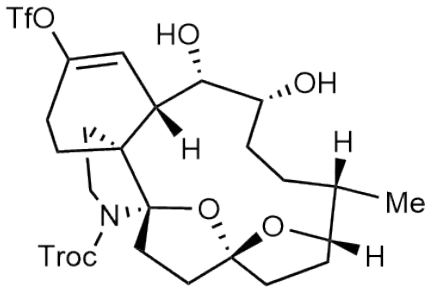
SI-5
(recorded in C_6D_6)


TfO
17
O
18
16
14
OH
15
H
3
H
11
23
Me
1
4
O
N
O
10
Troc
O
H
7
SI-5
(recorded in C6D6)
f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)
TfO
OH
Me
Troc
SI-5
(recorded in C6D6)

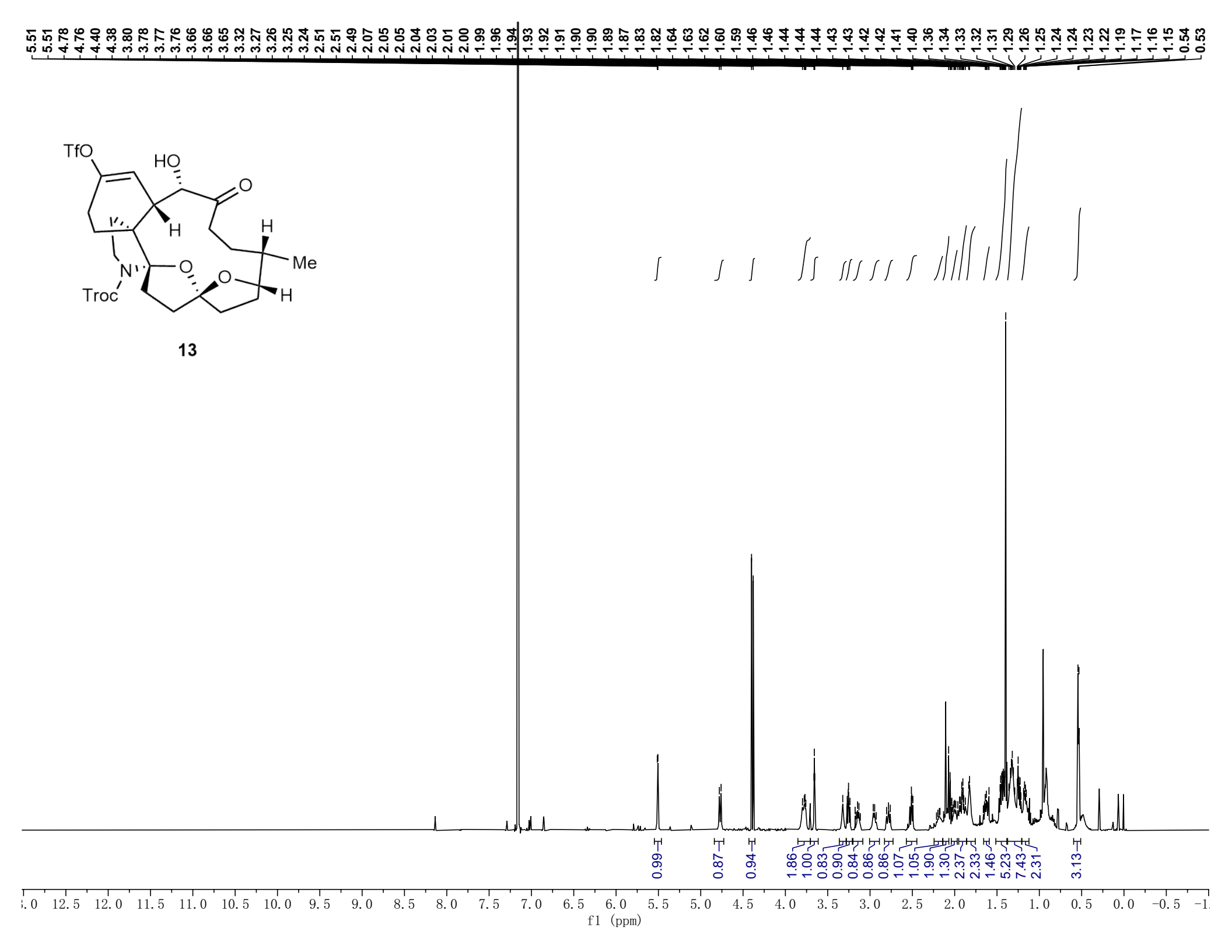

H16
H14
H14-H16
H14-H16
f2 (ppm)
f1 (ppm)
key NOE correlation observed in SI-5
OTf
Me
OH

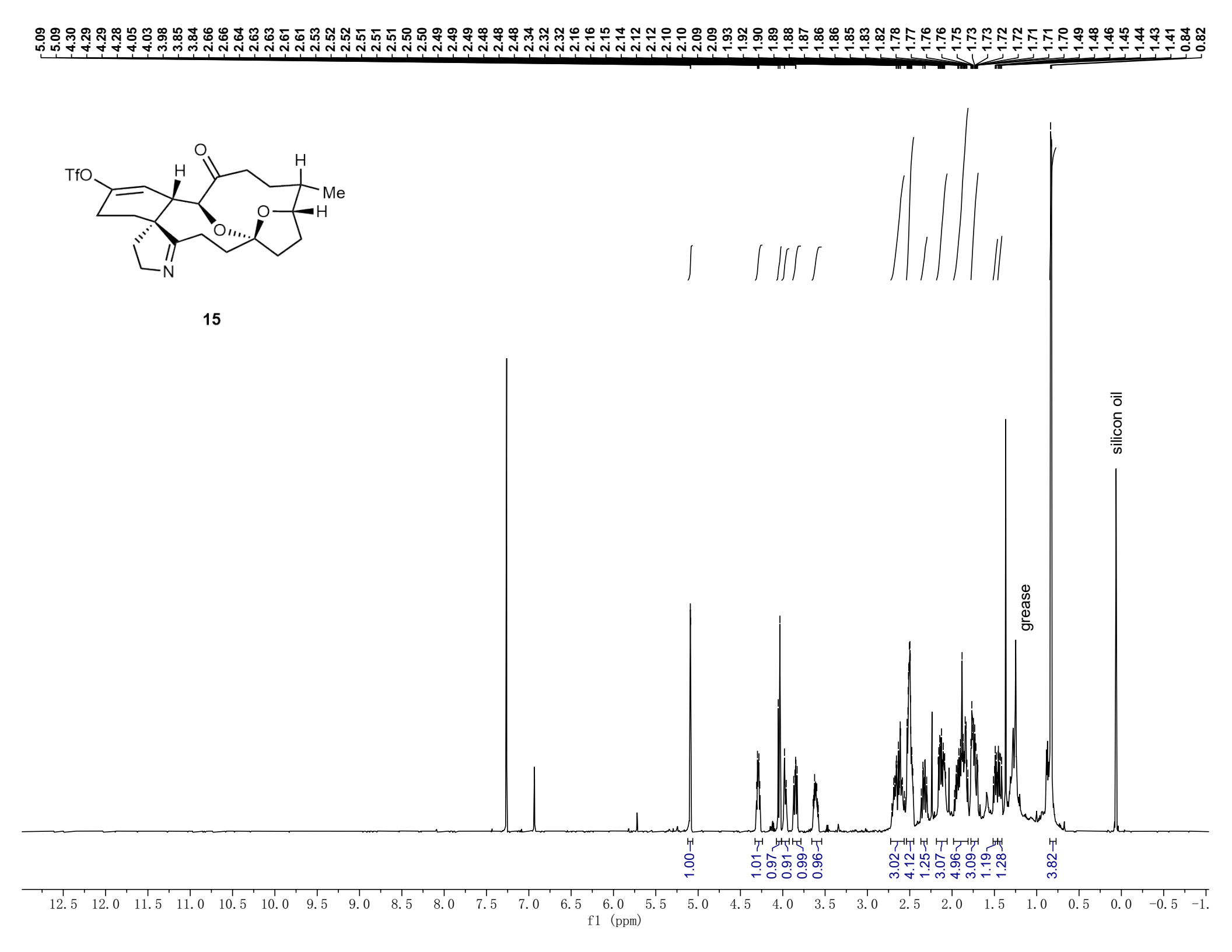

5.86 4.82 4.80 4.65 4.64 4.62 4.08 4.07 4.06 4.06 4.05 4.04 3.88 3.88 3.86 3.62 3.60 3.58 3.55 3.53 3.52 3.44 3.29 2.95 2.92 2.51 2.49 2.47 2.45 2.42 2.41 2.39 2.37 2.36 2.35 2.35 2.34 2.33 2.32 2.32 2.30 2.28 2.27 2.06 2.04 2.04 2.01 2.01 2.00 1.98 1.98 1.96 1.96 1.94 1.93 1.92 1.89 1.87 1.86 1.82 1.73 1.71 1.70 1.69 1.68 1.66 0.87 0.85
TfO
HO
OH
H
H
Me
N
O
O
H
Troc
28
grease
1.01
1.00
1.13
1.13
1.10
2.04
1.06
1.16
0.99
5.98
12.17
4.67
3.30
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

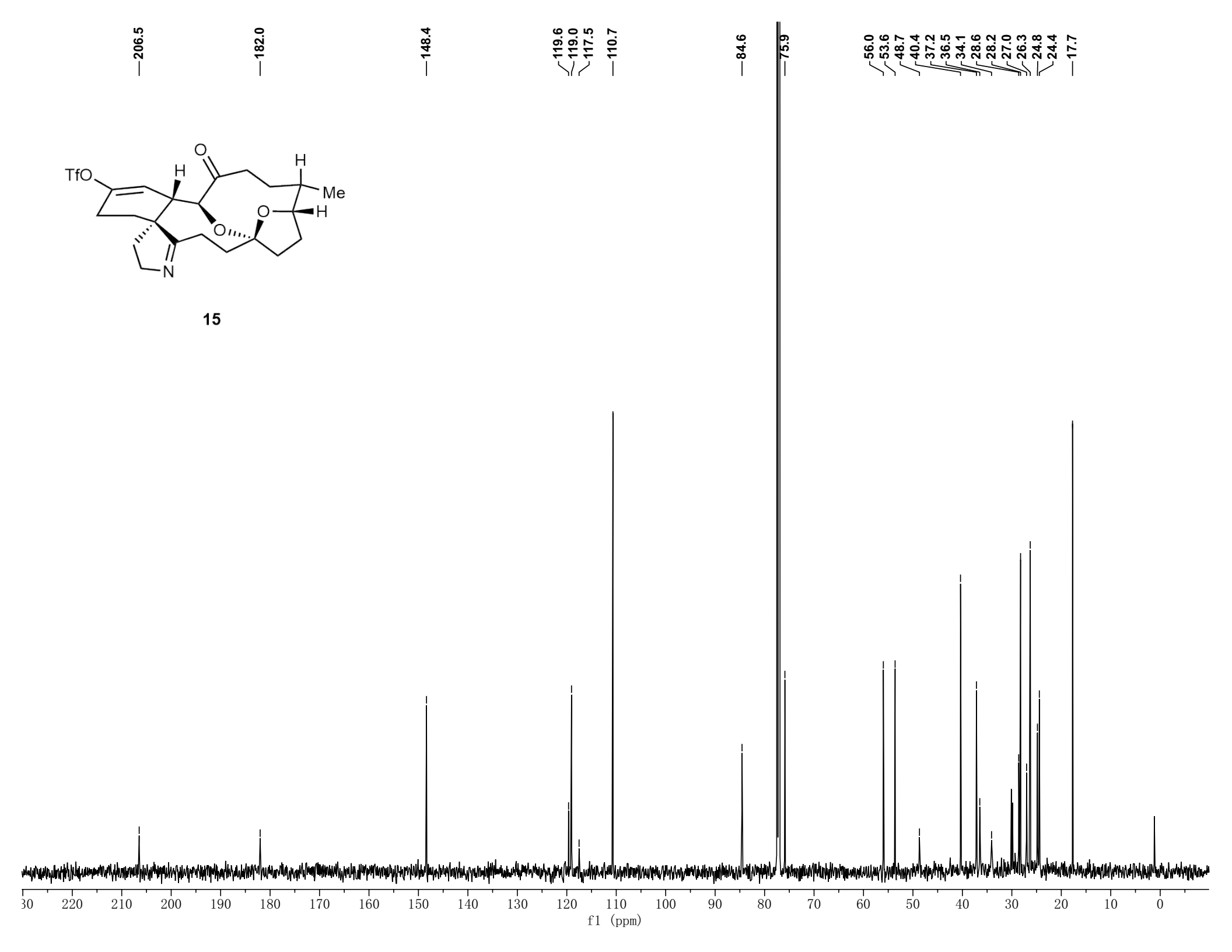

TfO
HO
OH
H
H
Me
N
O
O
H
Troc

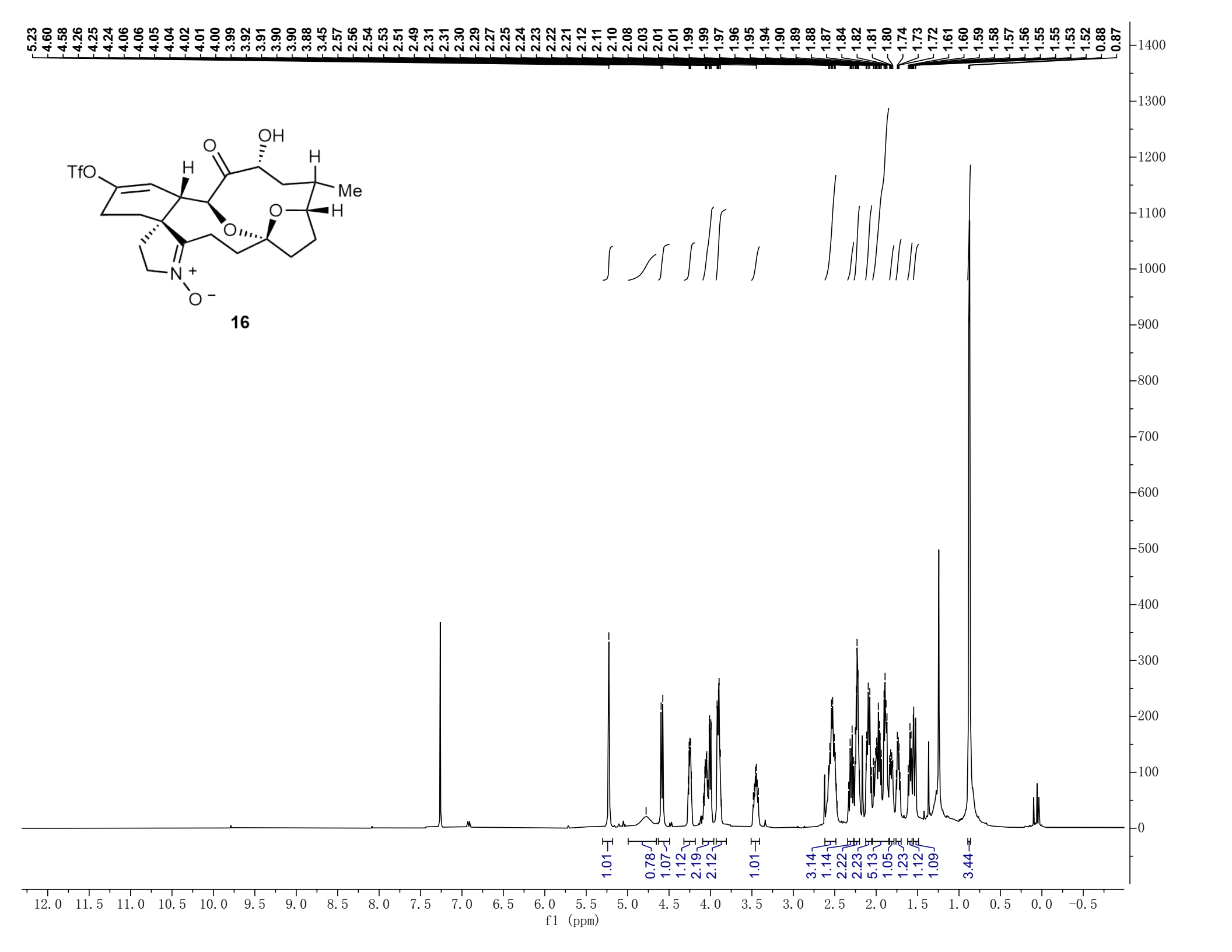
28

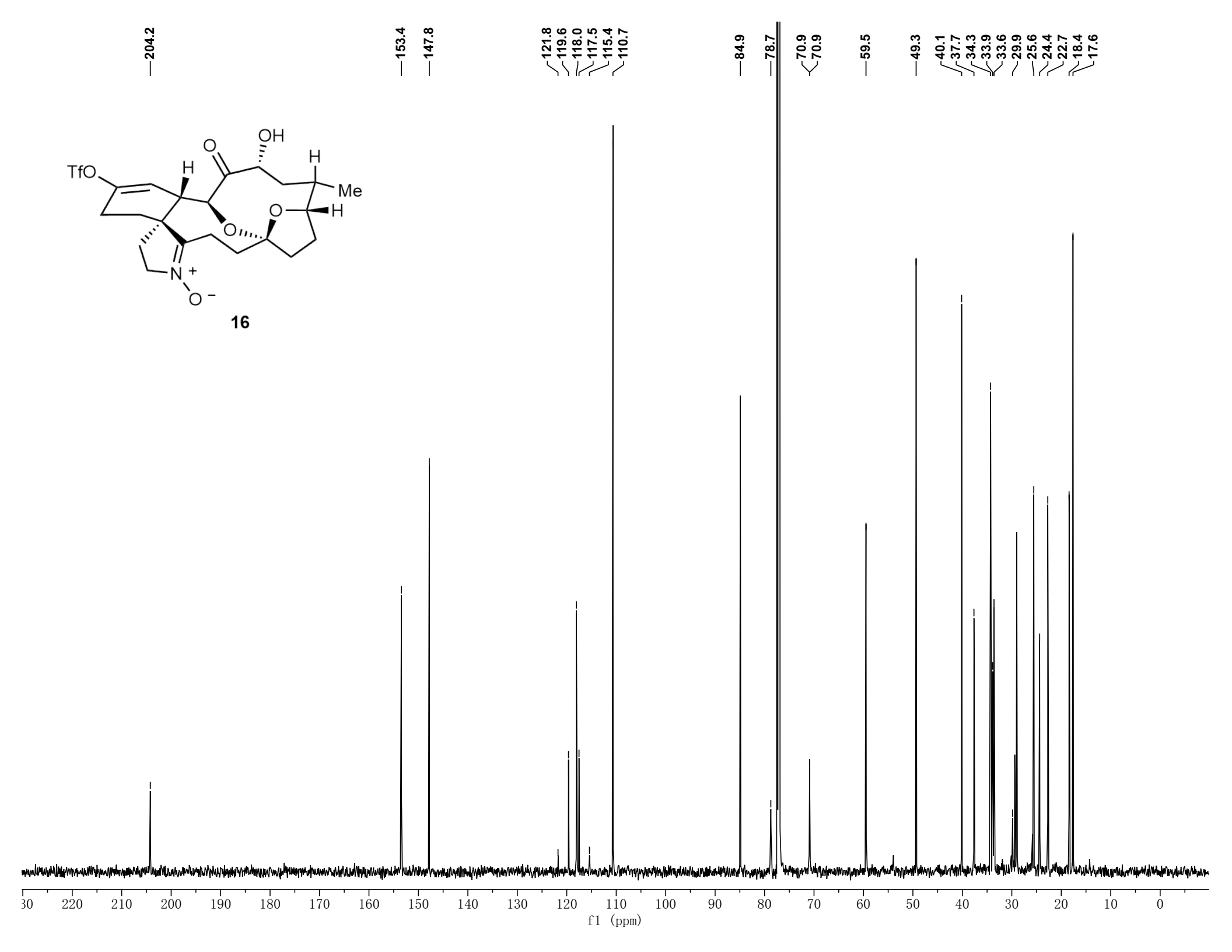
152.3
149.3
124.0
122.5
119.9
117.4
116.2
114.9
106.5
96.0
86.2
81.4
77.4
75.0
74.6
74.6
49.7
44.8
38.0
36.4
35.8
35.8
34.6
29.9
29.9
29.9
28.7
26.6
26.0
25.1
24.1
18.1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

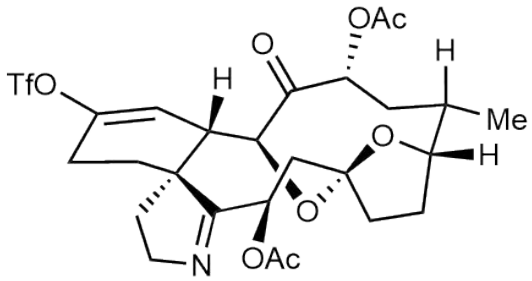

5.51 5.51 4.78 4.76 4.40 4.38 3.80 3.78 3.77 3.76 3.66 3.66 3.65 3.32 3.27 3.26 3.25 3.24 2.51 2.51 2.49 2.07 2.05 2.05 2.04 2.03 2.01 2.00 1.99 1.96 1.94 1.93 1.92 1.91 1.90 1.90 1.89 1.87 1.83 1.82 1.64 1.63 1.62 1.60 1.59 1.46 1.46 1.44 1.44 1.44 1.43 1.43 1.42 1.42 1.41 1.40 1.36 1.34 1.33 1.32 1.31 1.29 1.26 1.25 1.24 1.24 1.23 1.22 1.19 1.17 1.16 1.15 0.54 0.53
TfO
HO
O
H
H
Me
N
O
O
H
Troc
13
0.99 0.87 0.94 1.86 1.00 0.83 0.90 0.84 0.86 0.86 1.07 1.05 1.90 1.30 2.37 2.33 1.46 5.23 7.43 2.31 3.13
f1 (ppm)


5.09 5.09 4.30 4.29 4.28 4.05 4.03 3.98 3.85 3.84 2.66 2.66 2.64 2.63 2.63 2.61 2.61 2.53 2.52 2.52 2.51 2.51 2.51 2.50 2.50 2.49 2.49 2.49 2.48 2.48 2.48 2.34 2.32 2.32 2.16 2.16 2.15 2.14 2.12 2.12 2.10 2.10 2.09 2.09 1.93 1.92 1.90 1.89 1.88 1.87 1.86 1.86 1.85 1.83 1.82 1.78 1.77 1.76 1.76 1.75 1.73 1.73 1.72 1.72 1.71 1.71 1.70 1.49 1.48 1.46 1.45 1.44 1.43 1.41 0.84 0.82
TfO
H
O
H
Me
O
H
O
N
15
silicon oil
grease
1.00
1.01
0.97
0.91
0.99
0.96
3.02
4.12
1.25
3.07
4.96
3.09
1.19
1.28
3.82
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


206.5
182.0
148.4
119.6
119.0
117.5
110.7
84.6
75.9
56.0
53.6
48.7
40.4
37.2
36.5
34.1
28.6
28.2
27.0
26.3
24.8
24.4
17.7
TfO
H
O
H
Me
O
O
N
15
f1 (ppm)

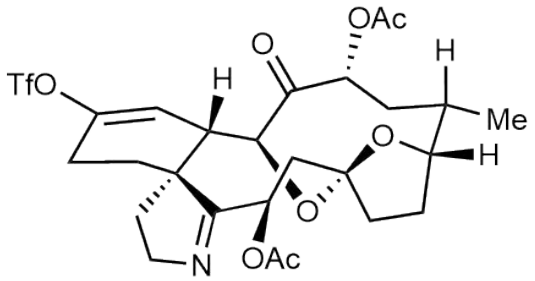

5.23 4.60 4.58 4.26 4.25 4.24 4.06 4.06 4.05 4.04 4.02 4.01 4.00 3.99 3.92 3.91 3.90 3.90 3.88 3.45 2.57 2.56 2.54 2.53 2.51 2.49 2.31 2.31 2.30 2.29 2.27 2.25 2.24 2.23 2.22 2.21 2.12 2.11 2.10 2.08 2.03 2.01 2.01 1.99 1.99 1.97 1.96 1.95 1.94 1.90 1.89 1.88 1.87 1.84 1.82 1.81 1.80 1.74 1.73 1.72 1.61 1.60 1.59 1.58 1.57 1.56 1.55 1.55 1.53 1.52 0.88 0.87
TfO
H
O
OH
H
Me
O
H
O
N +
O −
16
1.01 0.78 1.07 1.12 2.19 2.12 1.01 3.14 1.14 2.22 2.23 5.13 1.05 1.23 1.12 1.09 3.44
f1 (ppm)


204.2
153.4
147.8
121.8
119.6
118.0
117.5
115.4
110.7
84.9
78.7
70.9
70.9
59.5
49.3
40.1
37.7
34.3
33.9
33.6
29.9
25.6
24.4
22.7
18.4
17.6
TfO
H
O
OH
H
Me
O
H
O
N +
O −
16
f1 (ppm)


OAc
O
H
TfO
H
Me
O
H
O
N
OAc

17

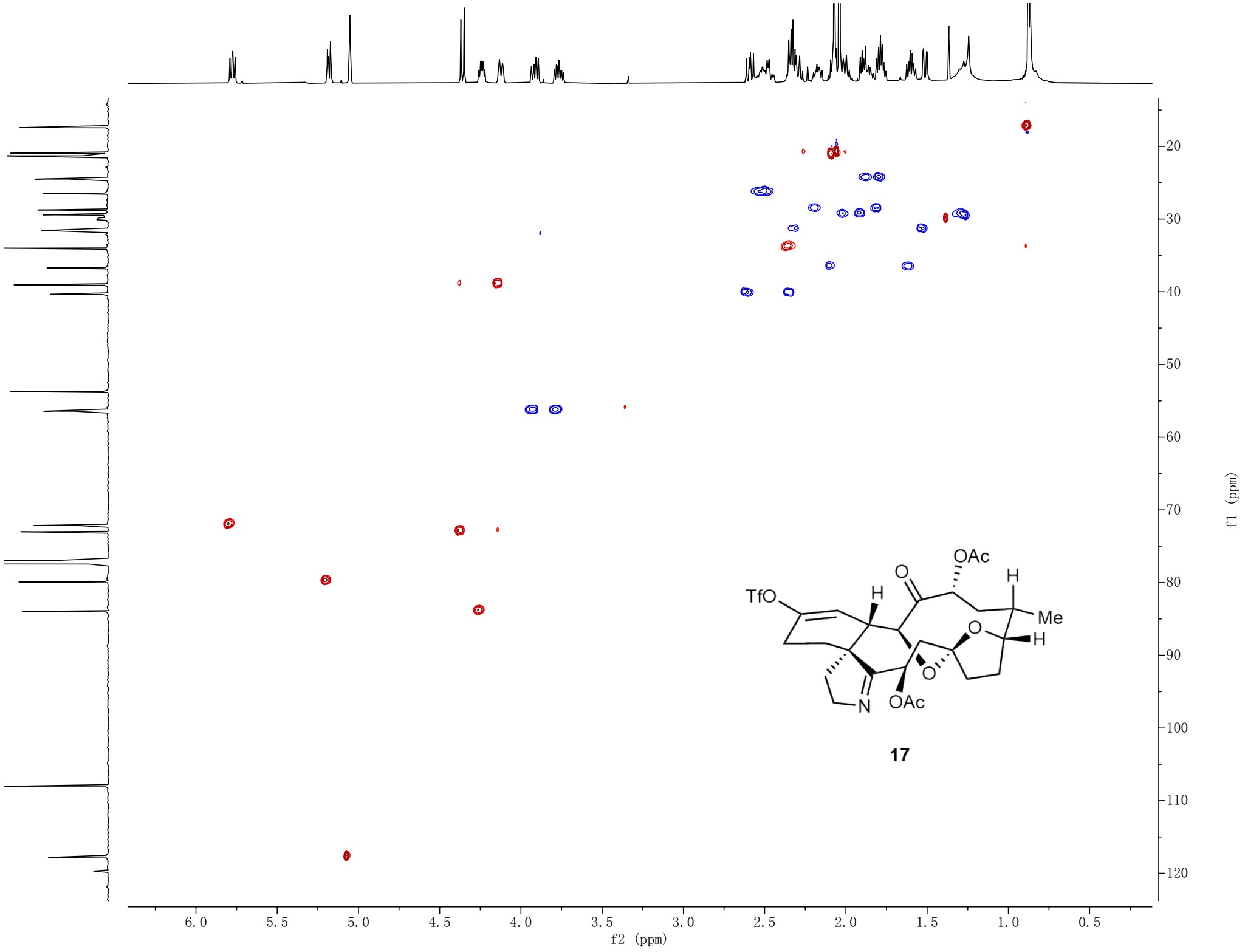
5.79 5.78 5.77 5.76 5.19 5.19 5.17 5.17 5.06 5.05 5.05 5.05 4.37 4.35 4.25 4.24 4.23 4.14 4.13 4.11 3.91 3.89 3.77 2.61 2.59 2.59 2.57 2.48 2.48 2.48 2.47 2.47 2.35 2.35 2.34 2.33 2.31 2.31 2.30 2.28 2.18 2.09 2.08 2.07 2.06 2.04 2.03 2.02 2.02 2.01 2.00 2.00 1.99 1.91 1.90 1.89 1.88 1.81 1.81 1.80 1.80 1.79 1.79 1.78 1.78 1.77 1.61 1.60 1.59 1.58 1.53 1.52 1.50 1.50 0.88 0.87
1.00 1.01 1.01 1.00 1.06 1.03 1.00 0.99 1.09 2.19 3.18 1.14 4.24 4.58 2.19 2.07 1.51 1.10 3.13
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)



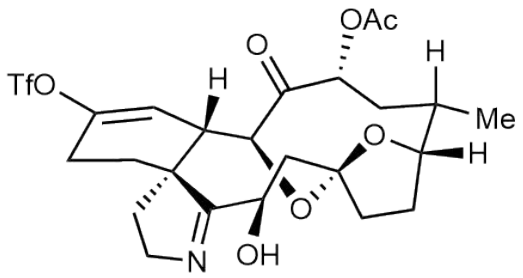
17

199.8
177.2
169.3
169.0
148.8
119.7
117.8
117.6
108.1
84.0
79.9
73.0
72.1
56.4
53.7
40.4
39.1
36.7
34.0
31.6
29.4
28.7
26.5
24.5
21.3
21.0
17.4

f1 (ppm)

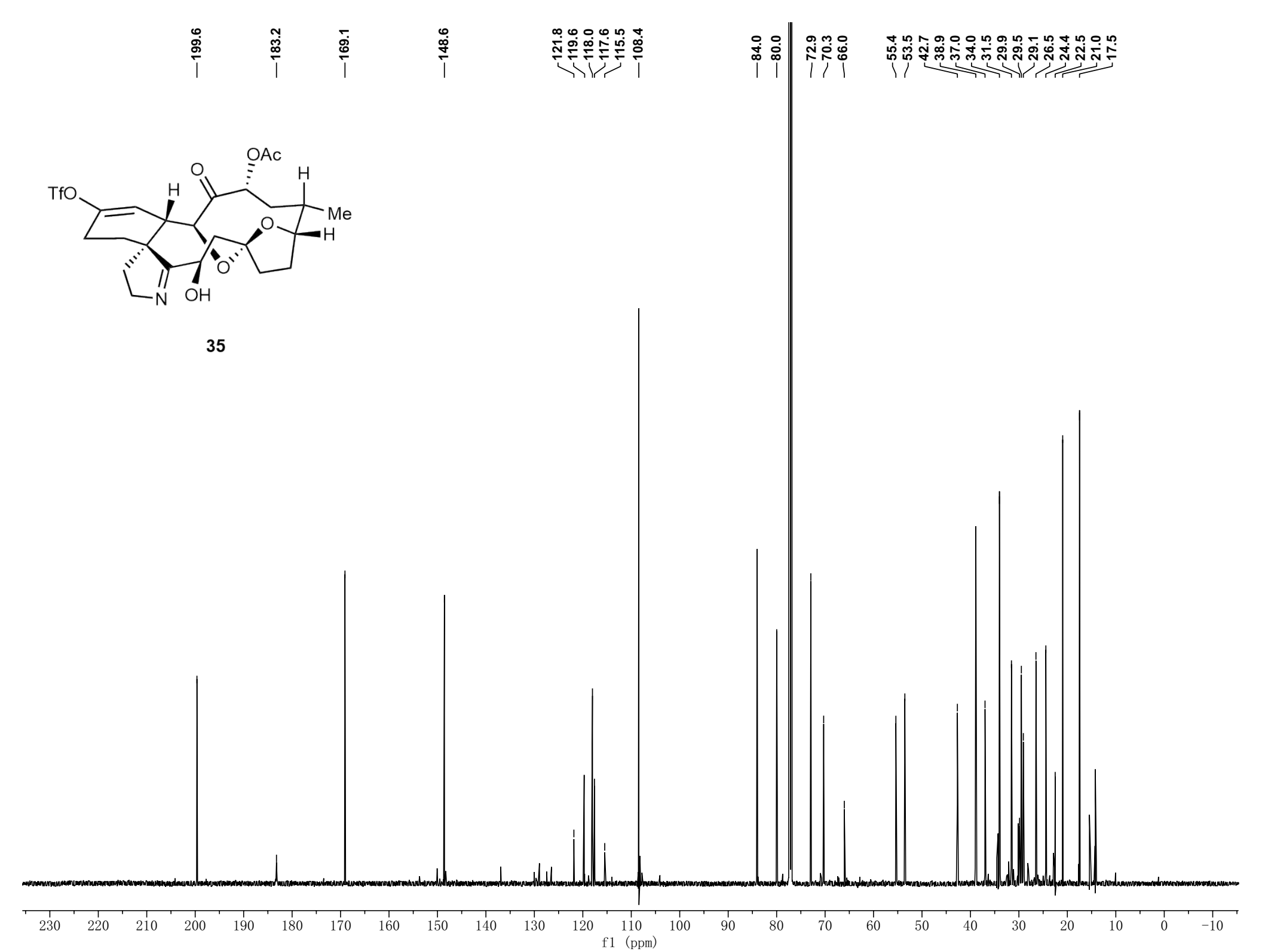

6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
20
30
40
50
60
70
80
90
100
110
120
f1 (ppm)
TfO
H
O
OAc
H
Me
O
H
O
N
OAc

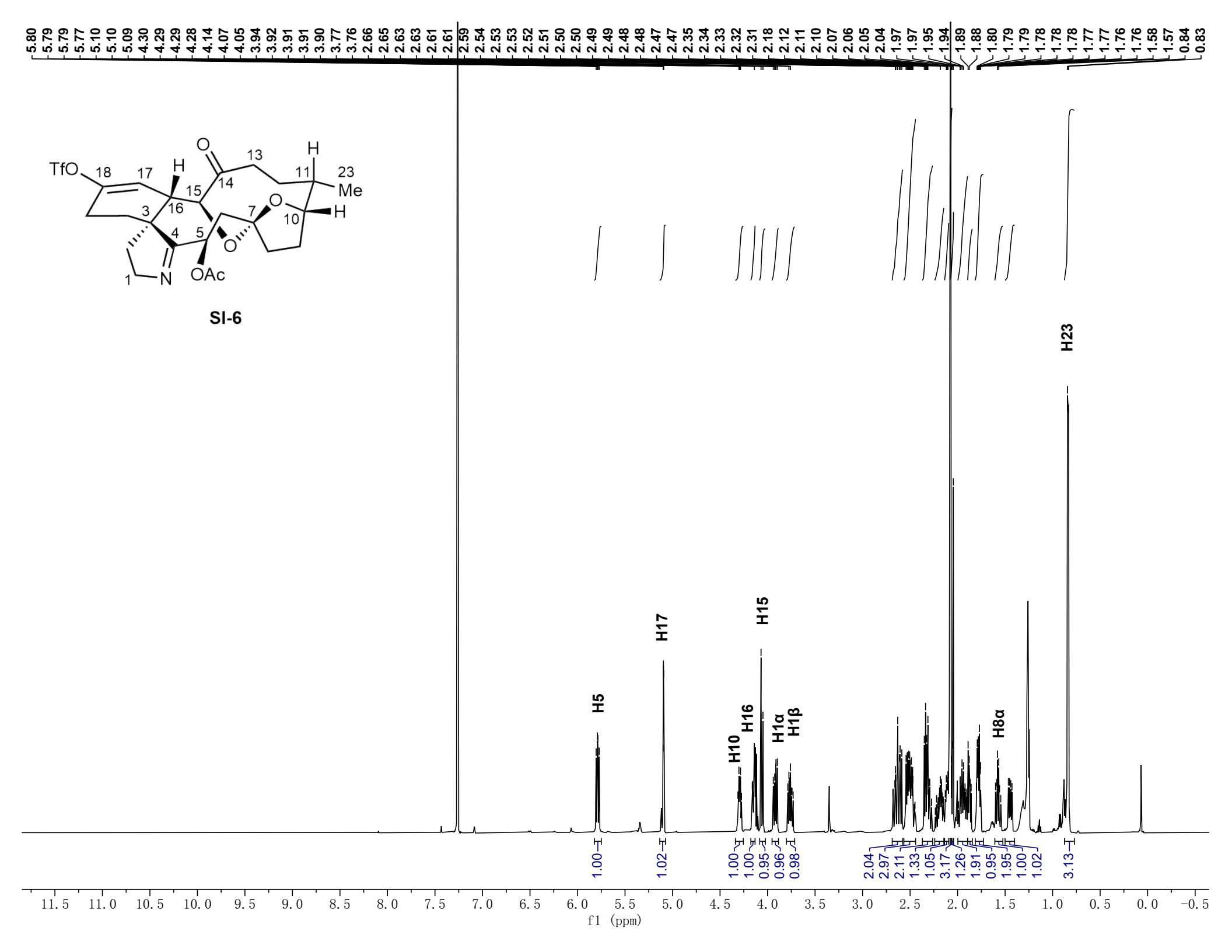
17

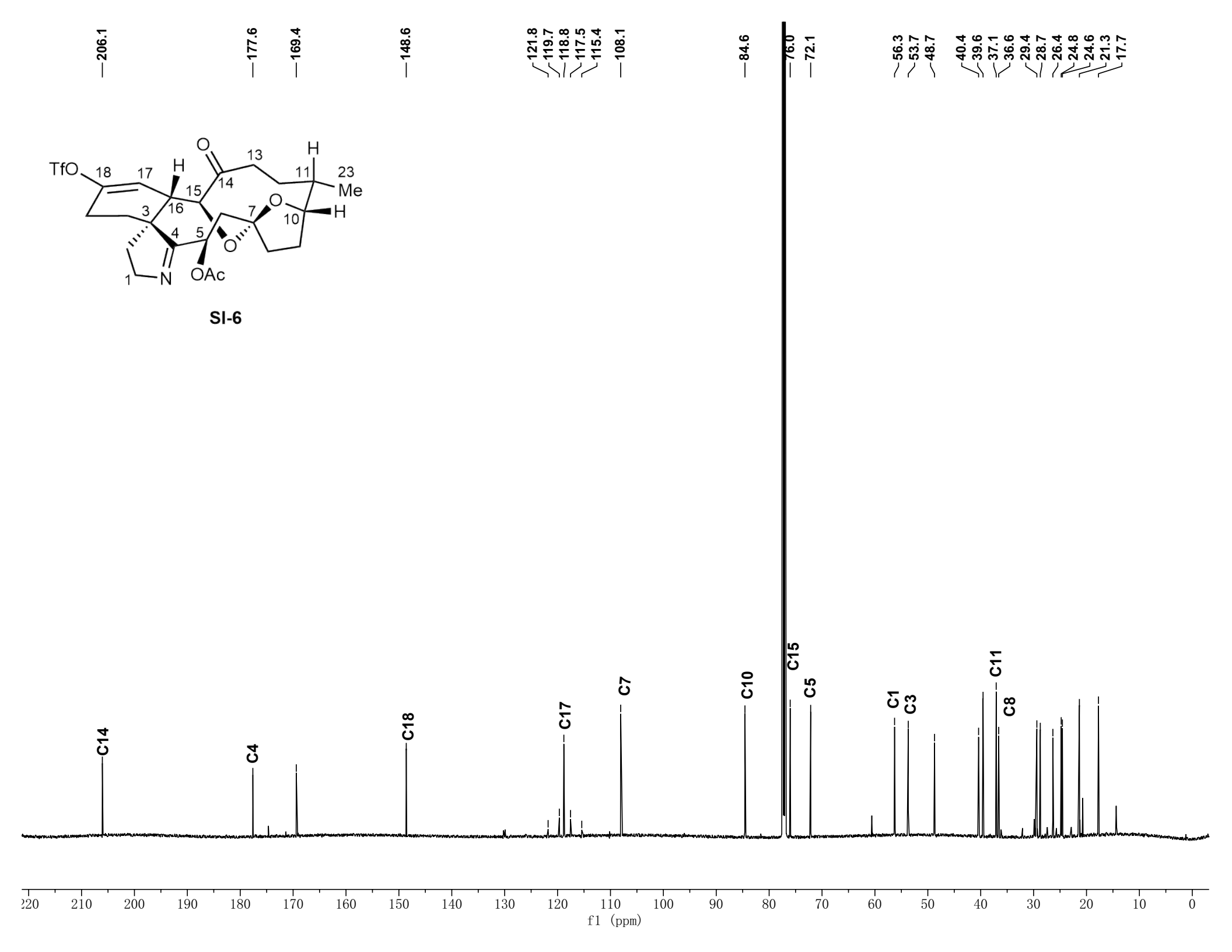

OAc
O
H
TfO
H
Me
O
H
O
OH
N

35

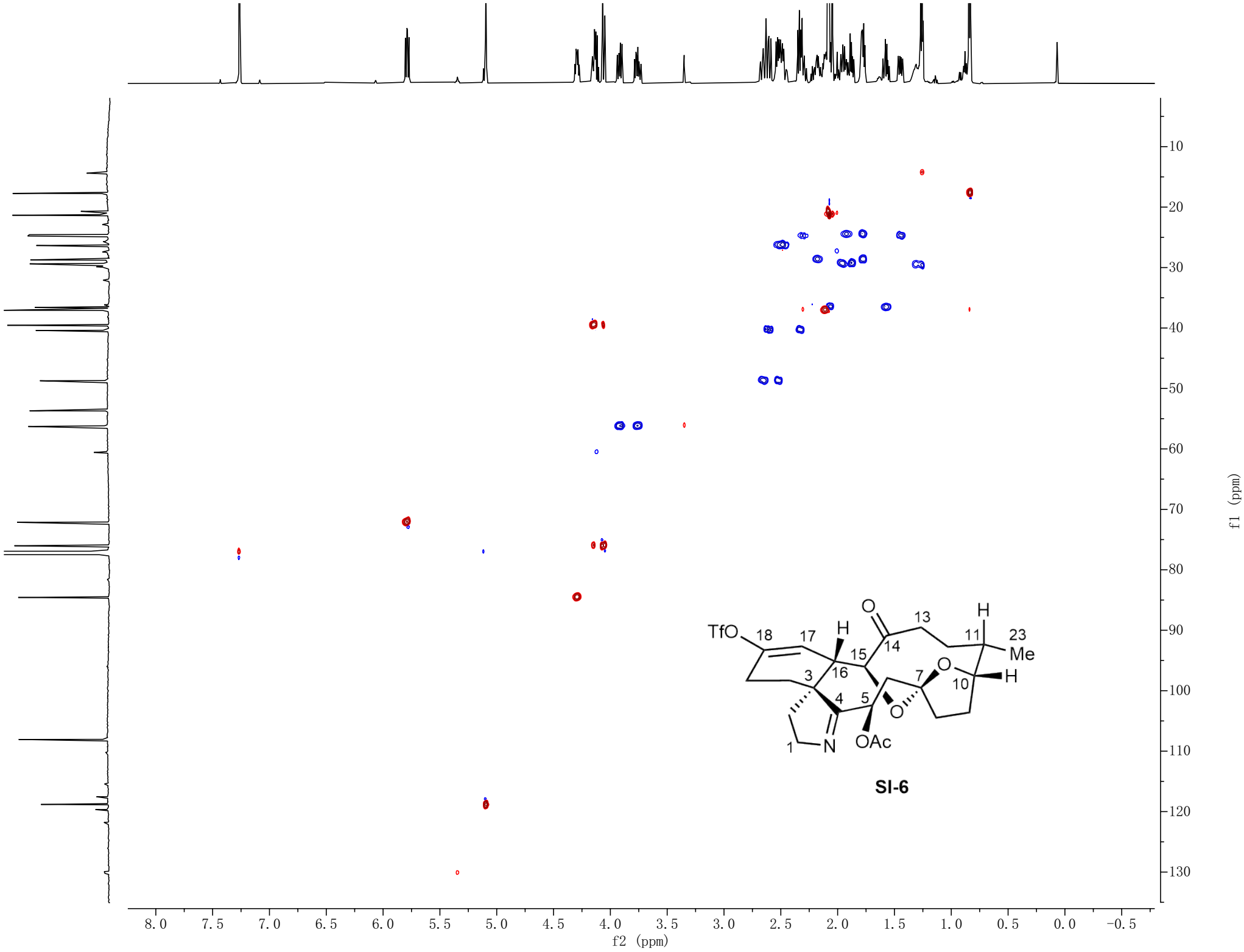
5.20 5.19 5.18 5.18 5.06 5.05 5.05 4.75 4.73 4.35 4.33 4.27 4.26 4.25 4.24 4.23 3.83 3.82 3.81 3.79 3.62 3.61 2.74 2.72 2.71 2.69 2.51 2.49 2.48 2.48 2.42 2.36 2.35 2.34 2.32 2.31 2.30 2.28 2.21 2.20 2.18 2.17 2.17 2.04 2.03 2.02 2.01 2.00 1.97 1.96 1.90 1.89 1.88 1.88 1.87 1.87 1.86 1.86 1.85 1.78 1.77 1.76 1.70 1.69 1.68 1.67 1.59 1.58 1.57 1.56 1.55 1.53 1.53 1.51 1.50 0.88 0.87
1.01 1.00 1.01 0.99 2.14 1.02 1.05 1.00 1.95 1.24 1.07 1.05 1.06 3.25 1.04 0.96 2.05 0.96 1.03 1.13 1.10 3.02
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


199.6
183.2
169.1
148.6
121.8
119.6
118.0
117.6
115.5
108.4
84.0
80.0
72.9
70.3
66.0
55.4
53.5
42.7
38.9
37.0
34.0
31.5
29.9
29.5
29.1
26.5
24.4
22.5
21.0
17.5
OAc
O
H
TfO
H
Me
O
H
O
OH
N
35
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

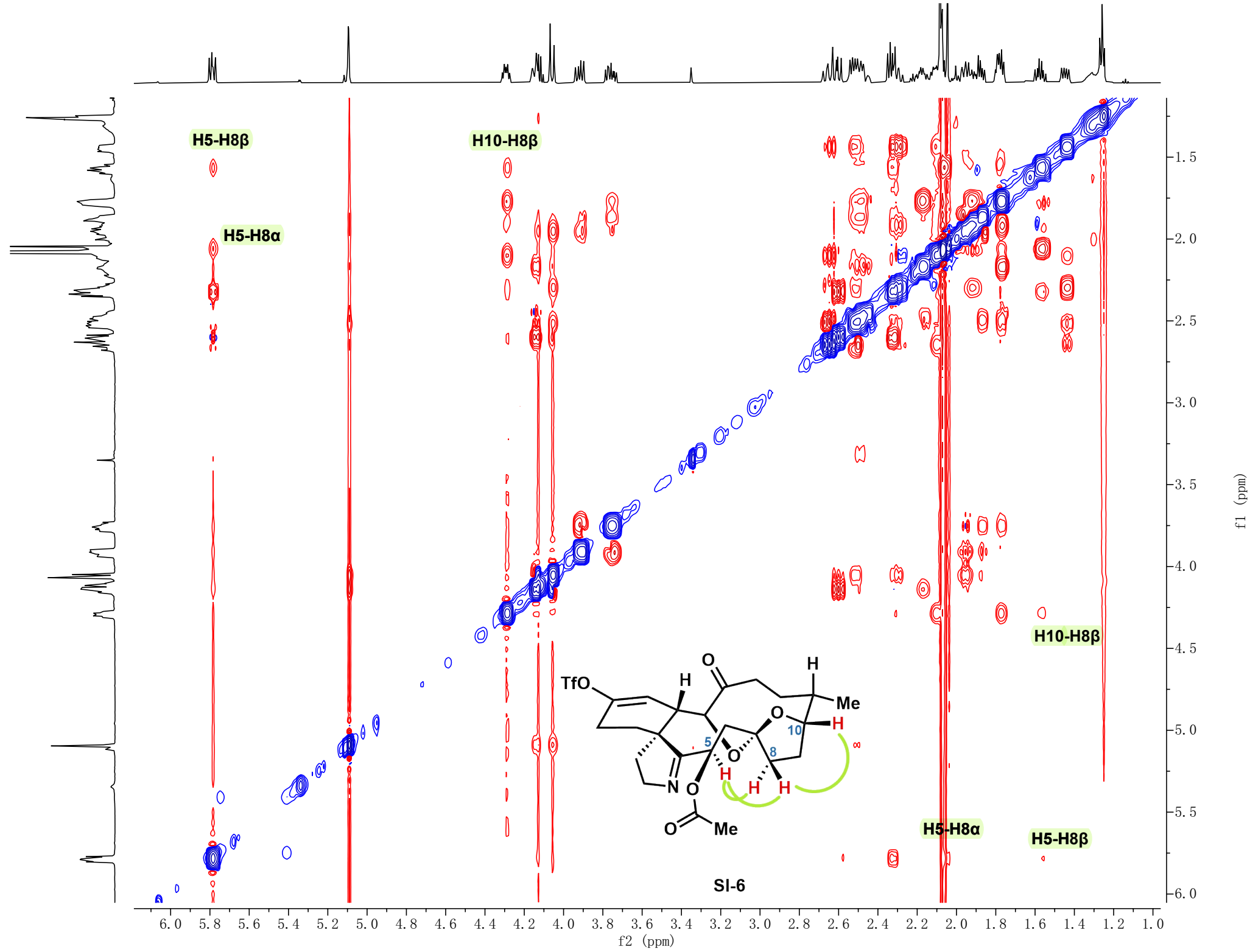

5.80 5.79 5.79 5.77 5.10 5.10 5.09 4.30 4.29 4.29 4.28 4.14 4.07 4.05 3.94 3.92 3.91 3.91 3.90 3.77 3.76 2.66 2.65 2.63 2.63 2.61 2.61 2.59 2.54 2.53 2.53 2.52 2.51 2.50 2.50 2.49 2.49 2.48 2.48 2.47 2.47 2.35 2.34 2.33 2.32 2.31 2.18 2.12 2.11 2.10 2.07 2.06 2.05 2.04 1.97 1.97 1.95 1.94 1.89 1.88 1.80 1.79 1.79 1.78 1.78 1.78 1.77 1.77 1.76 1.76 1.58 1.57 0.84 0.83
TfO
18
17
H
15
16
3
4
5
14
O
13
H
11
23
Me
7
O
10
H
O
1
N
OAc
SI-6
H5
H17
H10
H16
H15
H1α
H1β
H8α
H23
1.00
1.02
1.00
1.00
0.95
0.96
0.98
2.04
2.97
2.11
1.33
1.05
3.17
1.26
1.91
0.95
1.95
1.00
1.02
3.13
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

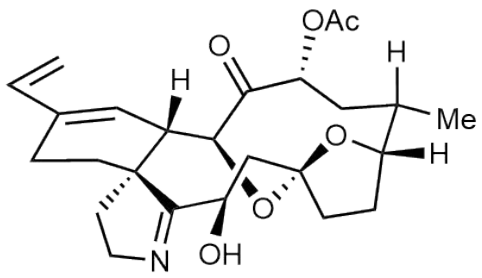

206.1
177.6
169.4
148.6
121.8
119.7
118.8
117.5
115.4
108.1
84.6
76.0
72.1
56.3
53.7
48.7
40.4
39.6
37.1
36.6
29.4
28.7
26.4
24.8
24.6
21.3
17.7
TfO
18
17
H
15
14
O
13
H
11
23
Me
3
16
7
O
10
H
4
5
O
1
N
OAc
C14
C4
C18
C17
C7
C10
C15
C5
C1
C3
C11
C8
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SI-6


f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
10
20
30
40
50
60
70
80
90
100
110
120
130
TfO
18
17
H
O
13
H
11
23
Me
14
15
16
3
4
5
7
O
10
H
O
1
N
OAc

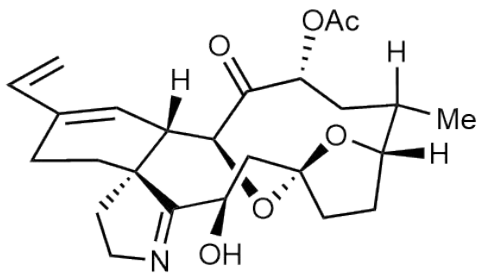
SI-6


H5-Hβ
H5-Hα
H10-Hβ
H10-Hβ
H5-Hα
H5-Hβ
TfO
O
H
H
Me
O
H
10
5
8
O
H
H
H
N
O
O
Me
SI-6
f2 (ppm)
f1 (ppm)


OAc
O
H
H
Me
O
H
O
N
OH

18

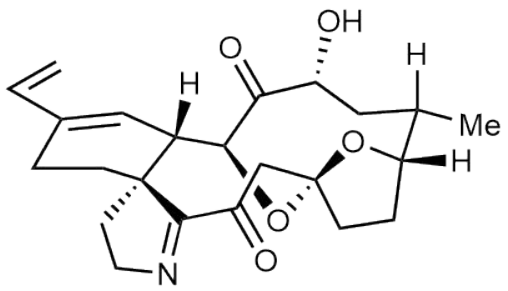
6.21 6.19 6.18 6.16 5.22 5.20 5.20 5.12 5.09 4.96 4.95 4.94 4.77 4.76 4.75 4.74 4.32 4.32 4.30 4.30 4.27 4.26 4.25 4.24 4.17 4.15 3.80 3.78 3.77 3.76 3.64 3.64 3.63 2.83 2.81 2.80 2.79 2.37 2.35 2.34 2.32 2.30 2.28 2.19 2.18 2.18 2.17 2.17 2.16 2.07 2.07 2.05 2.04 2.03 2.02 1.89 1.87 1.86 1.84 1.83 1.82 1.81 1.77 1.76 1.75 1.70 1.69 1.57 1.56 1.51 1.51 1.51 1.49 1.49 0.88 0.87
1.02 1.00 1.04 2.03 1.01 1.02 1.13 1.02 0.98 1.03 1.00 5.28 1.46 2.89 1.19 2.64 0.94 1.05 0.94 0.84 3.26
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)



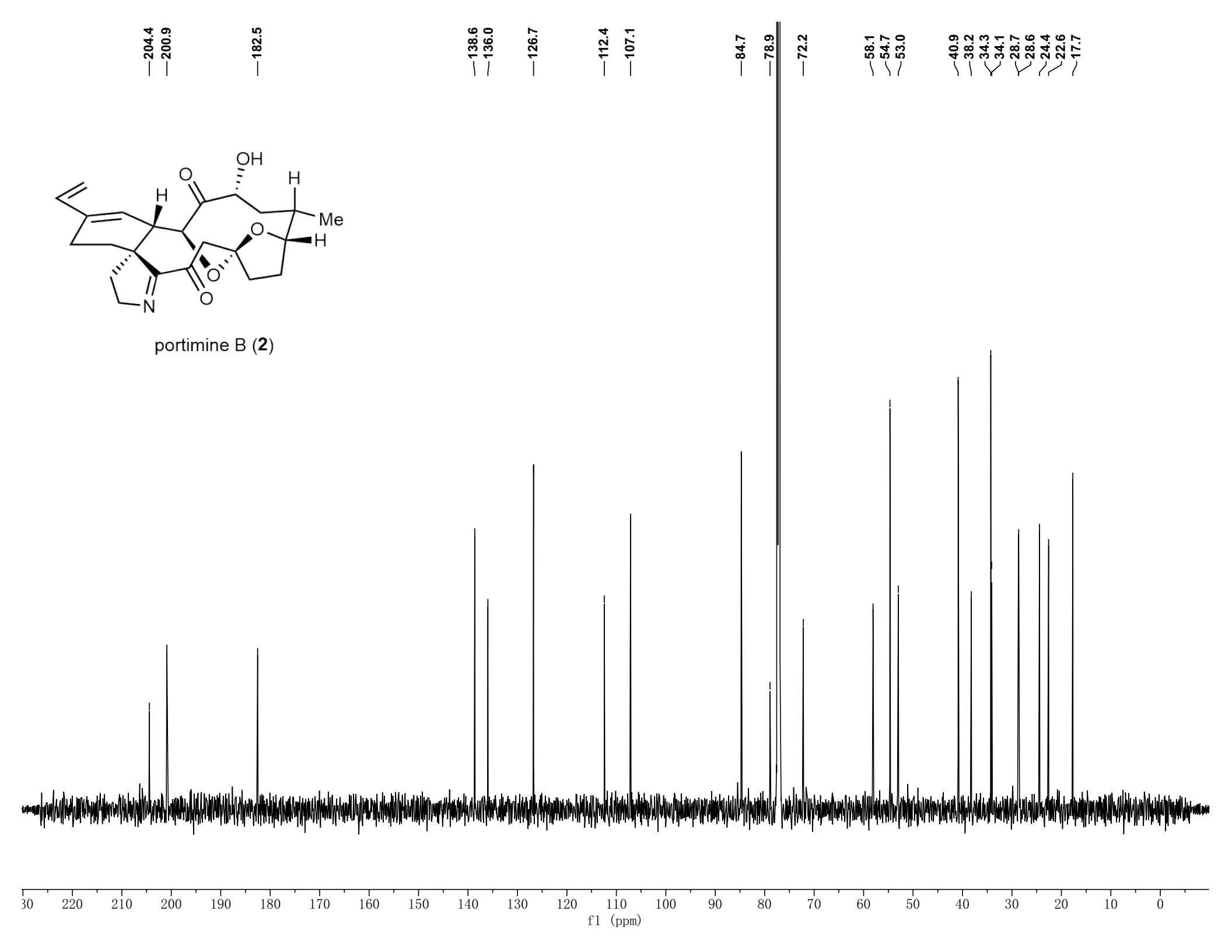
18

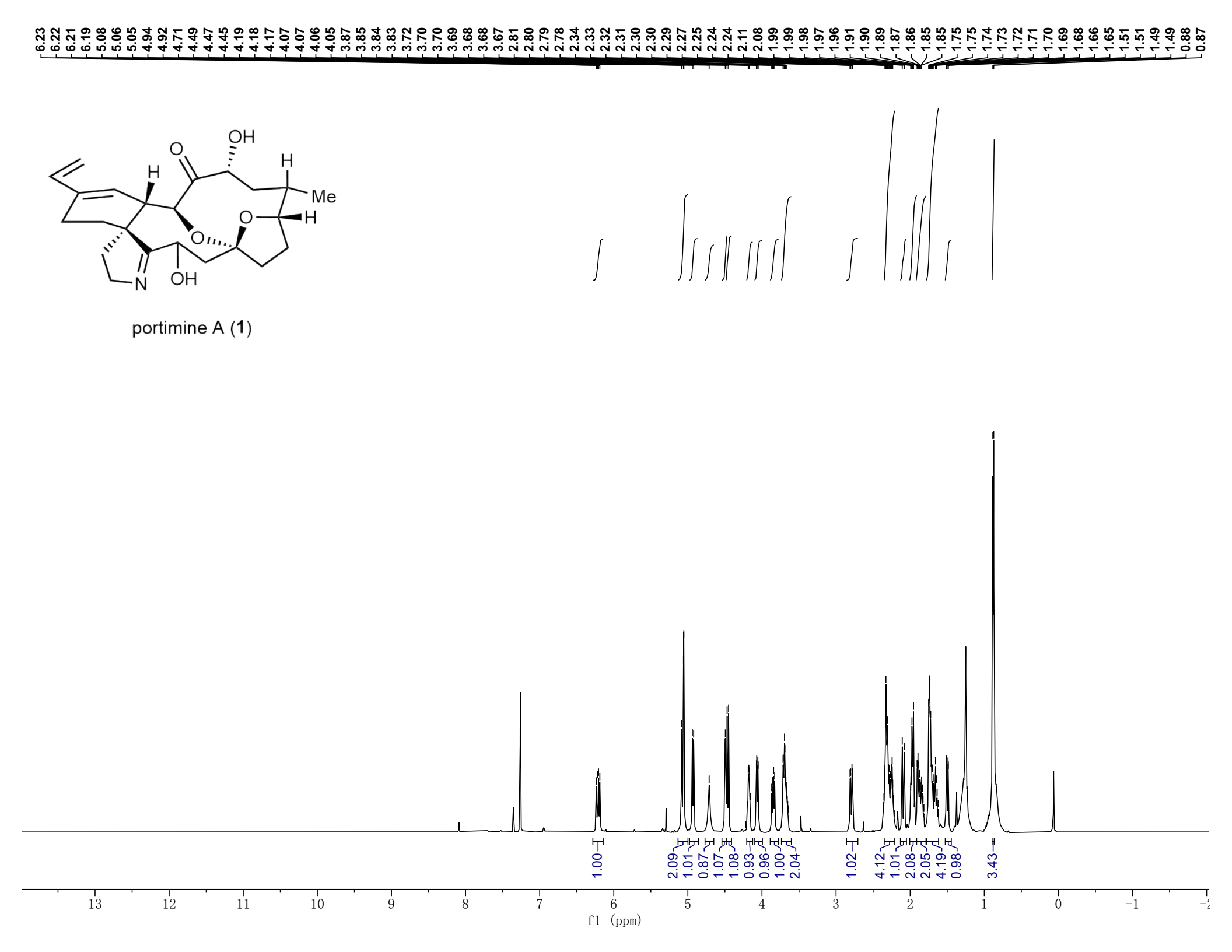
200.3
184.2
169.1
139.2
135.6
127.9
111.8
108.4
83.8
80.3
73.9
71.0
55.6
54.4
42.7
40.0
37.1
34.2
31.8
29.8
29.3
24.5
22.9
21.3
17.6

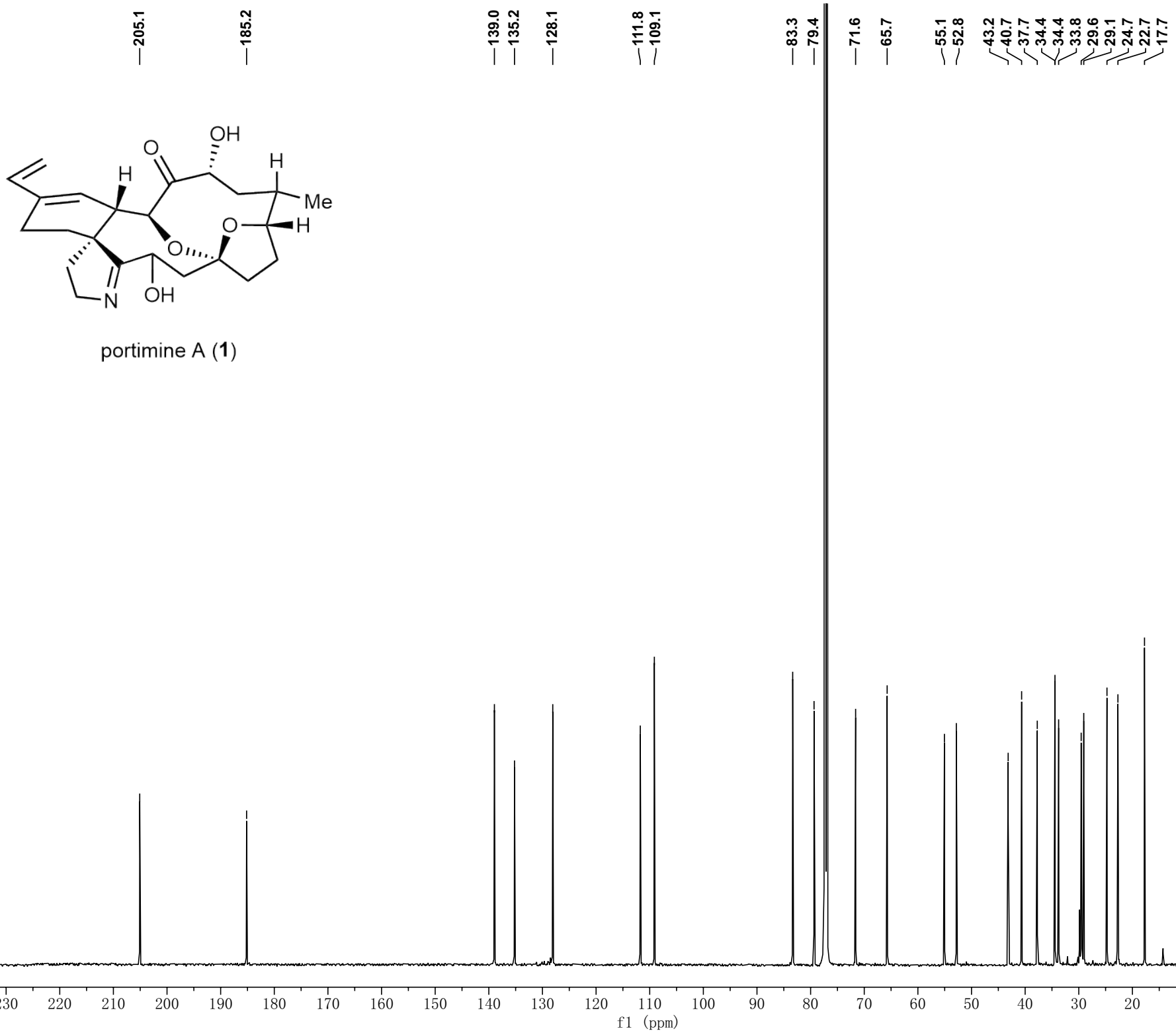
f1 (ppm)



portimine B (**2**)


204.4
200.9
182.5
138.6
136.0
126.7
112.4
107.1
84.7
78.9
72.2
58.1
54.7
53.0
40.9
38.2
34.3
34.1
28.7
28.6
24.4
22.6
17.7
OH
H
O
H
Me
O
H
O
O
N
portimine B (2)
f1 (ppm)

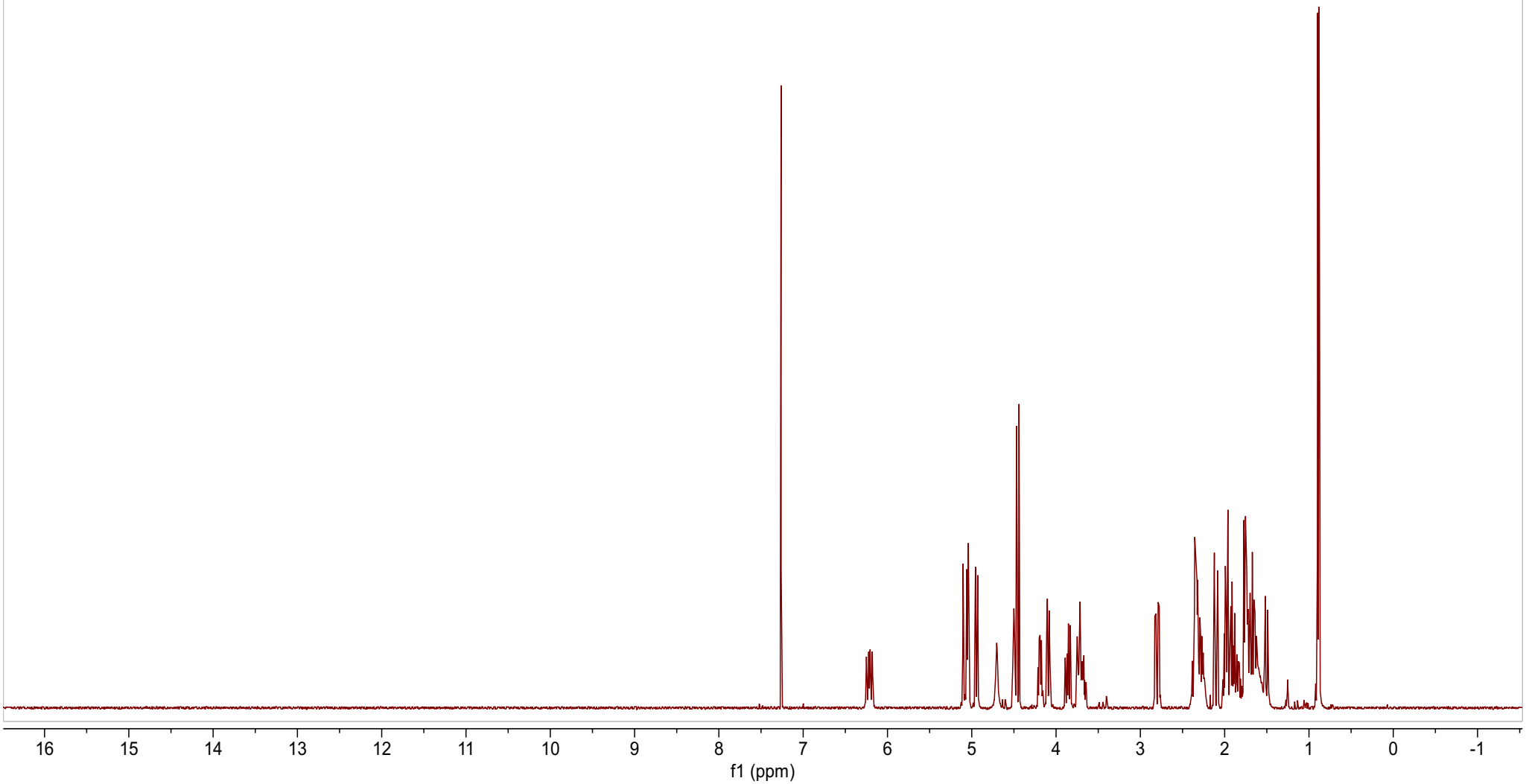

6.23 6.22 6.21 6.19 5.08 5.06 5.05 4.94 4.92 4.71 4.49 4.47 4.45 4.19 4.18 4.17 4.07 4.07 4.06 4.05 3.87 3.85 3.84 3.83 3.72 3.70 3.70 3.69 3.68 3.68 3.67 2.81 2.80 2.79 2.78 2.34 2.33 2.32 2.31 2.30 2.30 2.29 2.27 2.25 2.24 2.24 2.11 2.08 1.99 1.99 1.98 1.97 1.96 1.91 1.90 1.89 1.87 1.86 1.85 1.85 1.75 1.75 1.74 1.73 1.72 1.71 1.70 1.69 1.68 1.66 1.65 1.51 1.51 1.49 1.49 0.88 0.87
OH
O
H
H
Me
O
H
O
N
OH
portimine A (1)
1.00 2.09 1.01 0.87 1.07 1.08 0.93 0.96 1.00 2.04 1.02 4.12 1.01 2.08 2.05 4.19 0.98 3.43
13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2
f1 (ppm)

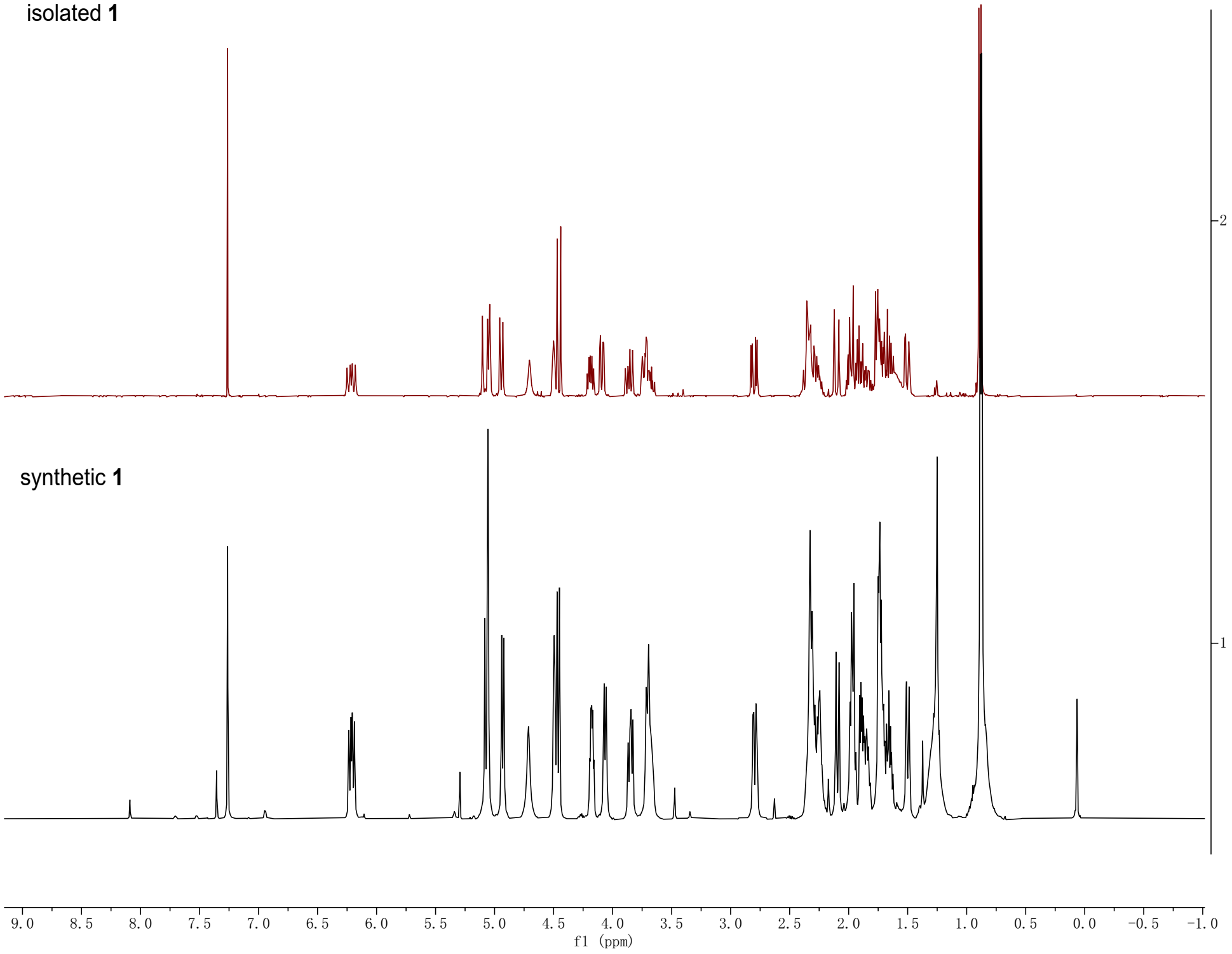


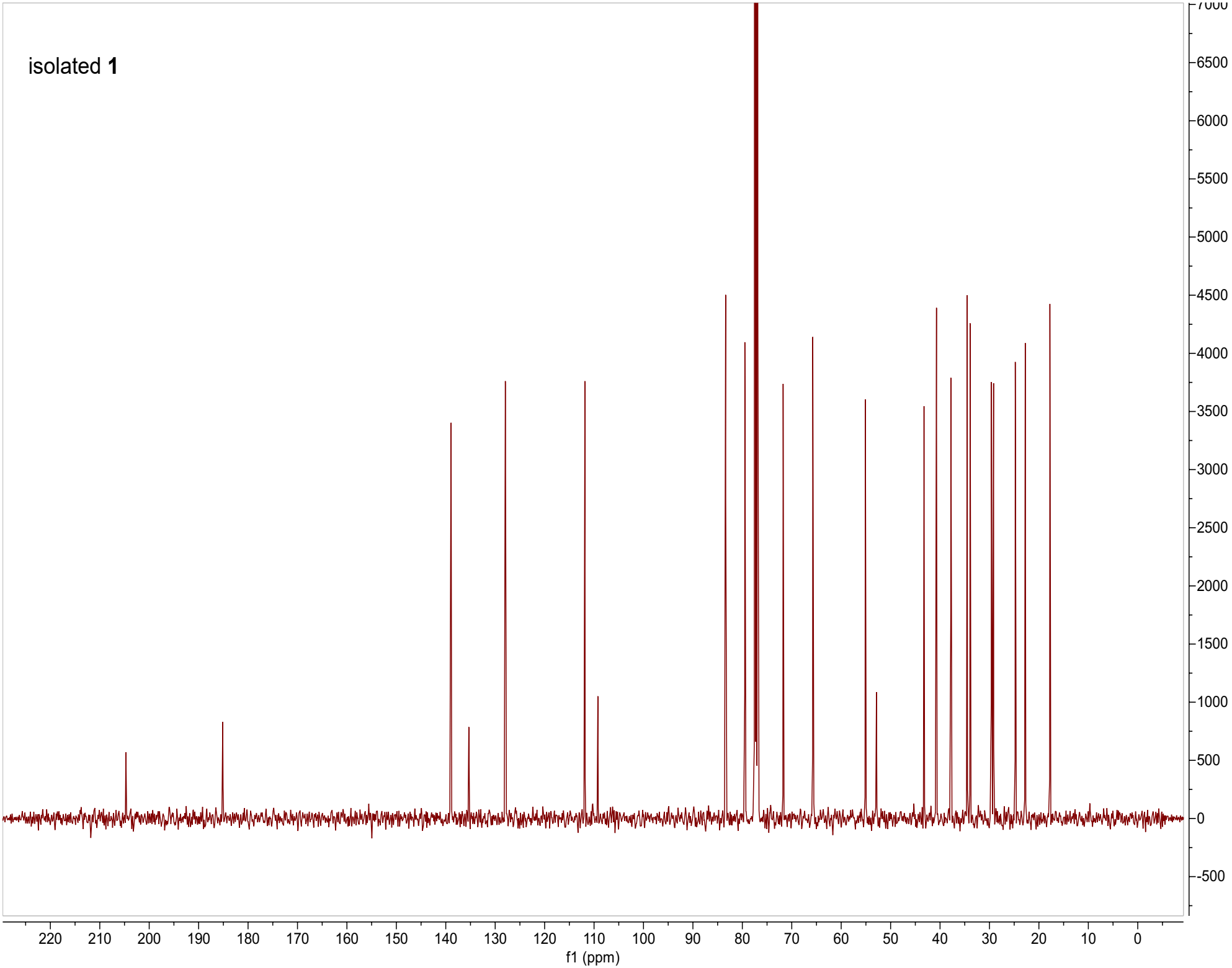
portimine A (**1**)

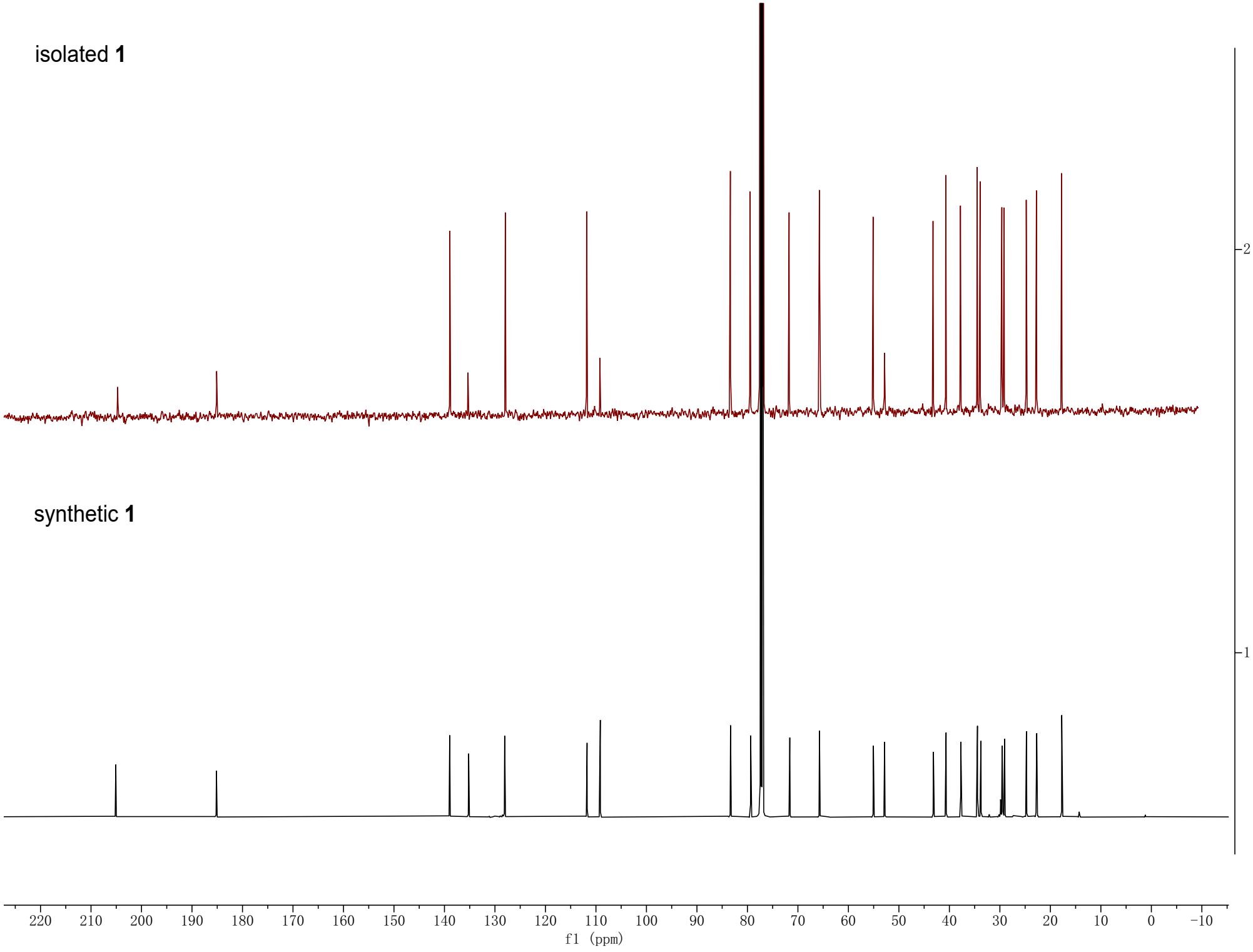
Portimine NMR data_1.1.fid
1H

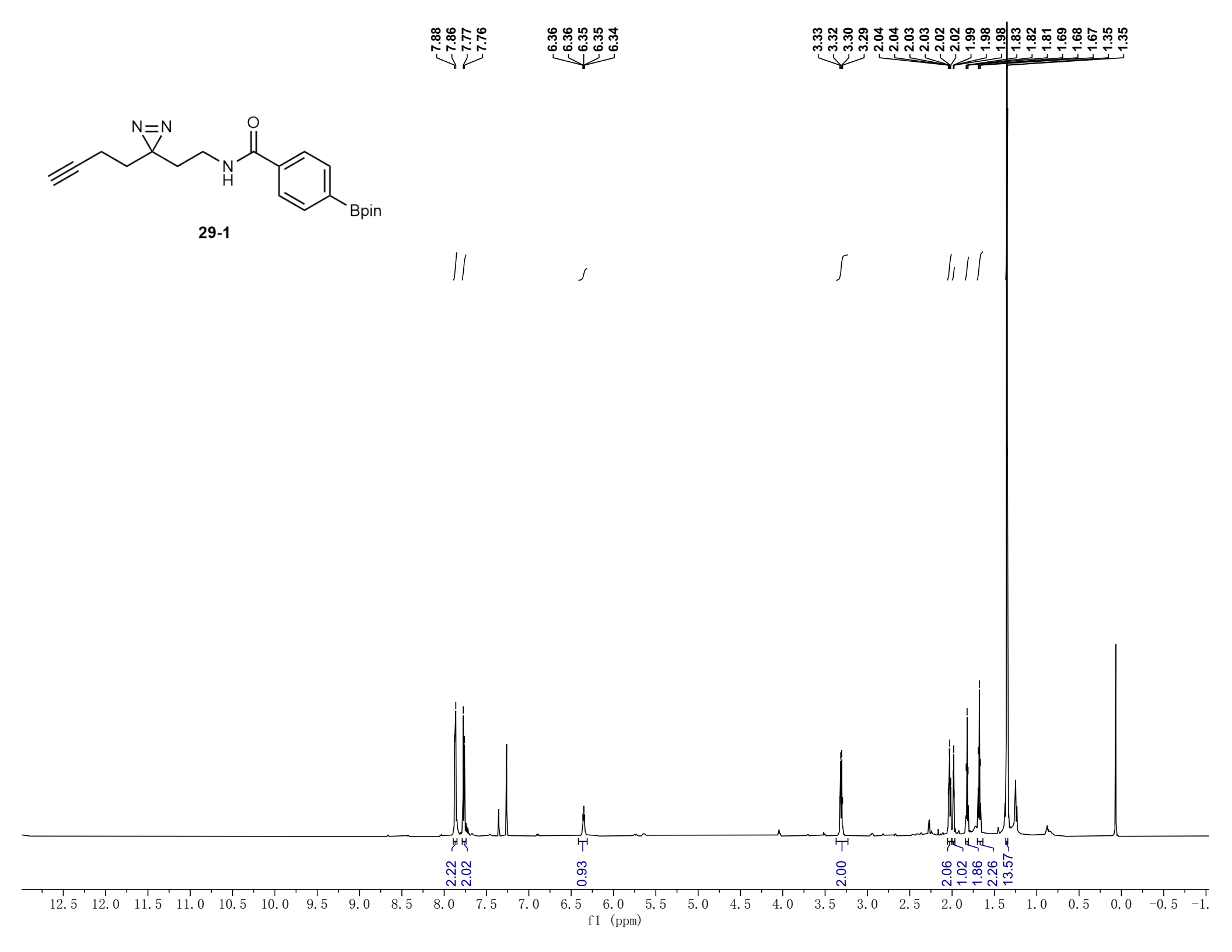
isolated **1**

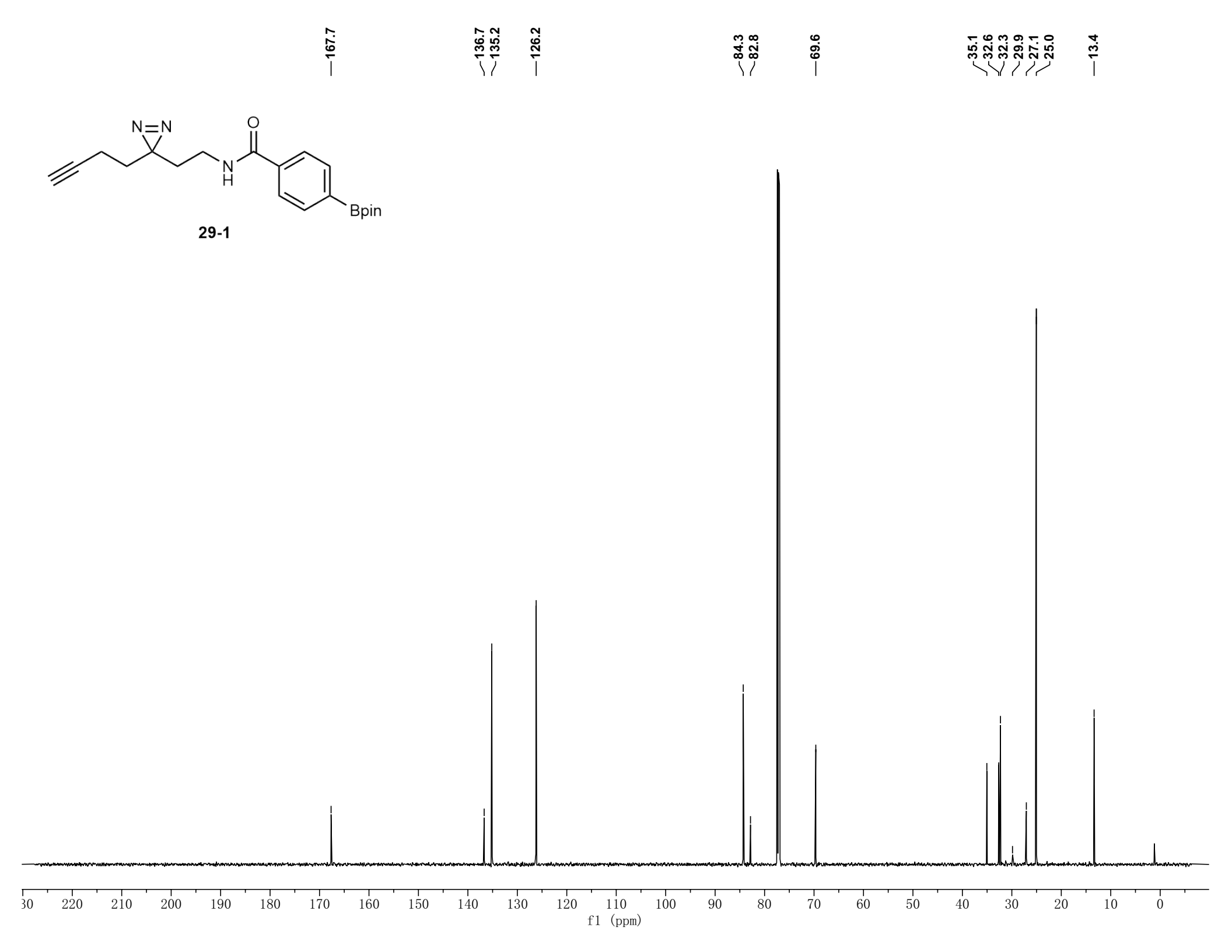


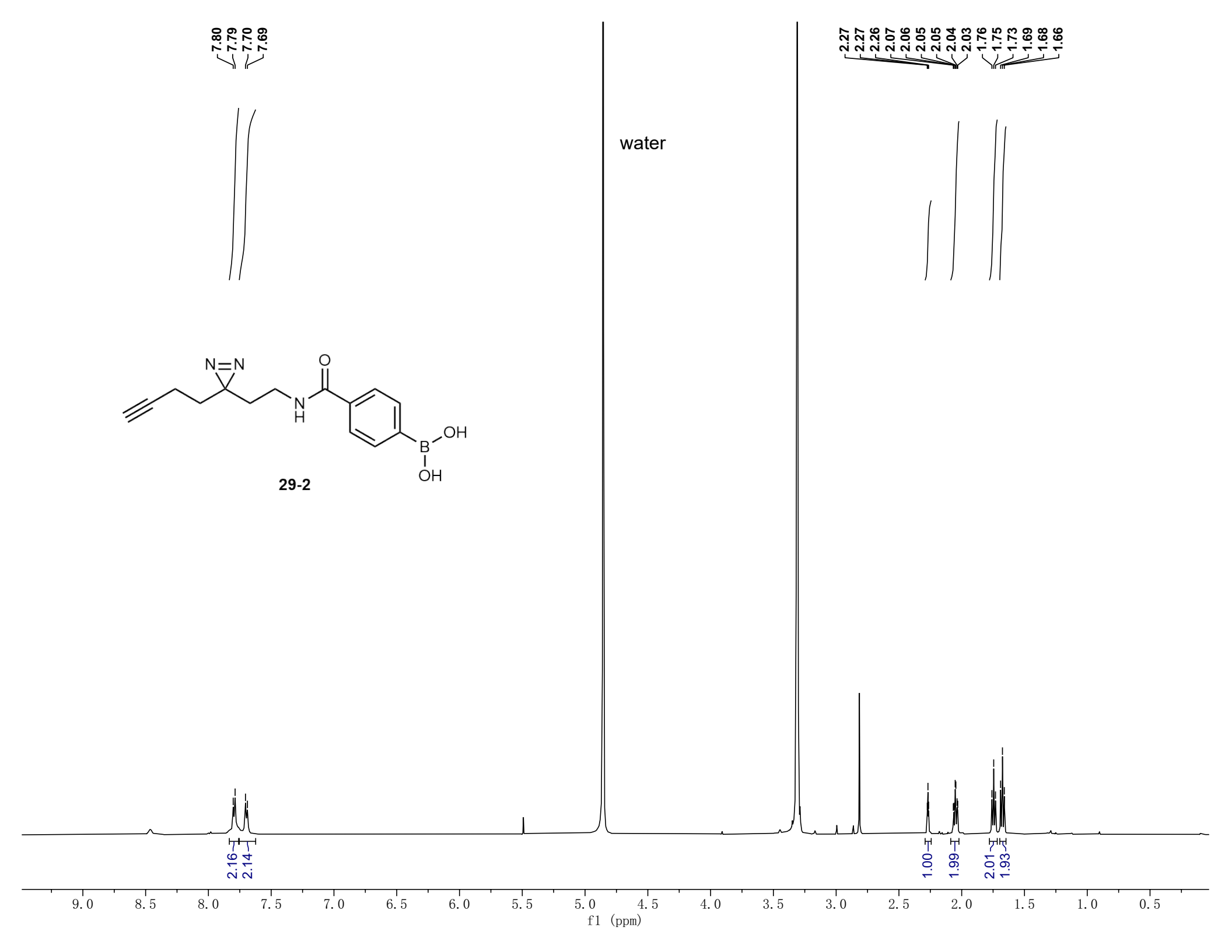

isolated 1
synthetic 1
2
1
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

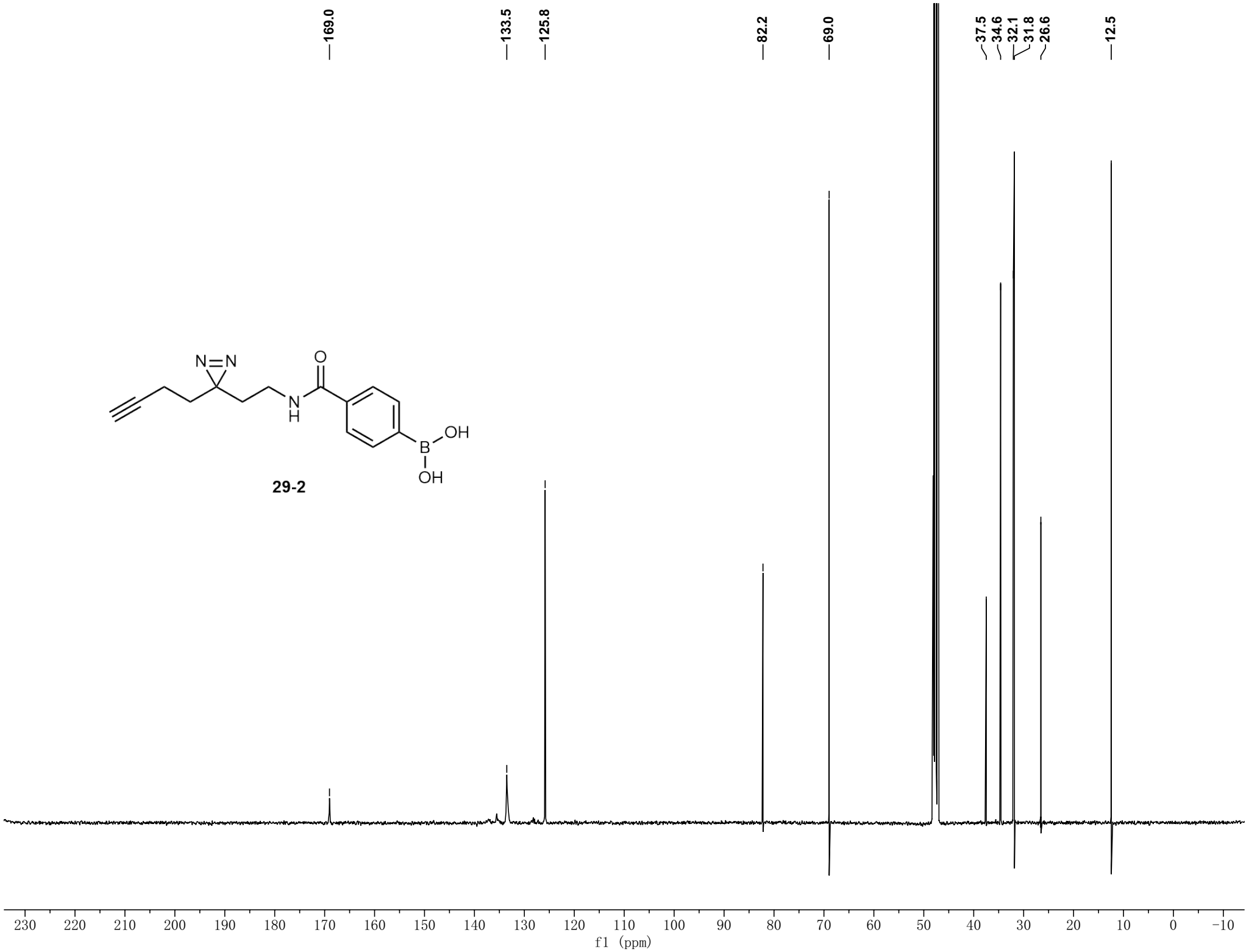

isolated 1
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

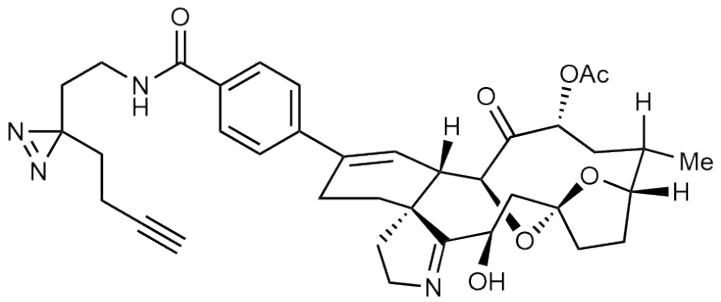

isolated 1
synthetic 1
2
1
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


7.88
7.86
7.77
7.76
6.36
6.36
6.35
6.35
6.34
3.33
3.32
3.30
3.29
2.04
2.04
2.03
2.03
2.02
2.02
1.99
1.98
1.98
1.83
1.82
1.81
1.69
1.68
1.67
1.35
1.35
N=N
O
N
H
Bpin
29-1
2.22
2.02
0.93
2.00
2.06
1.02
1.86
2.26
13.57
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


167.7
136.7
135.2
126.2
84.3
82.8
69.6
35.1
32.6
32.3
29.9
27.1
25.0
13.4
N=N
O
N
H
Bpin
29-1
f1 (ppm)

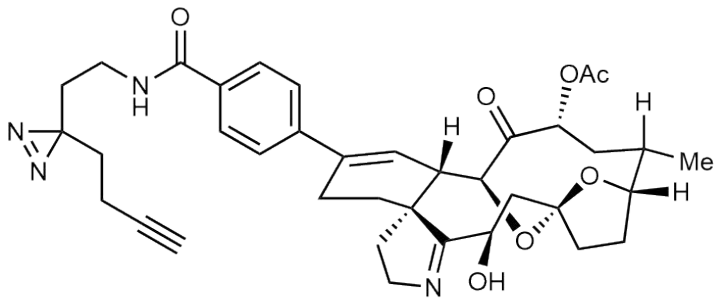

7.80
7.79
7.70
7.69
2.27
2.27
2.26
2.07
2.06
2.05
2.05
2.04
2.03
1.76
1.75
1.73
1.69
1.68
1.66
water
N=N
O
N
H
OH
B
OH
29-2
2.16
2.14
1.00
1.99
2.01
1.93
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


169.0
133.5
125.8
82.2
69.0
37.5
34.6
32.1
31.8
26.6
12.5
N=N
O
N
H
OH
B
OH
29-2
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
N
N
OAc
O
H
H
Me
O
H
O
N
OH

30

7.71 7.70 7.37 7.35 6.29 5.41 5.41 5.24 5.24 5.22 5.22 4.81 4.80 4.79 4.40 4.38 4.28 4.27 4.27 4.26 4.26 4.25 4.22 3.81 3.33 3.32 3.31 3.29 2.85 2.84 2.82 2.60 2.59 2.38 2.37 2.35 2.23 2.22 2.20 2.19 2.05 2.05 2.04 2.04 2.03 2.03 2.02 1.99 1.98 1.98 1.95 1.93 1.92 1.91 1.90 1.89 1.88 1.84 1.82 1.81 1.80 1.79 1.78 1.78 1.77 1.70 1.68 1.67 1.59 1.58 1.54 1.54 1.52 1.51 0.90 0.88
2.01 2.05 0.91 1.00 1.04 1.15 1.06 2.12 1.03 1.10 2.00 1.09 2.13 3.65 1.38 6.13 1.12 3.91 2.19 3.03 2.10 1.18 1.09 3.45
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

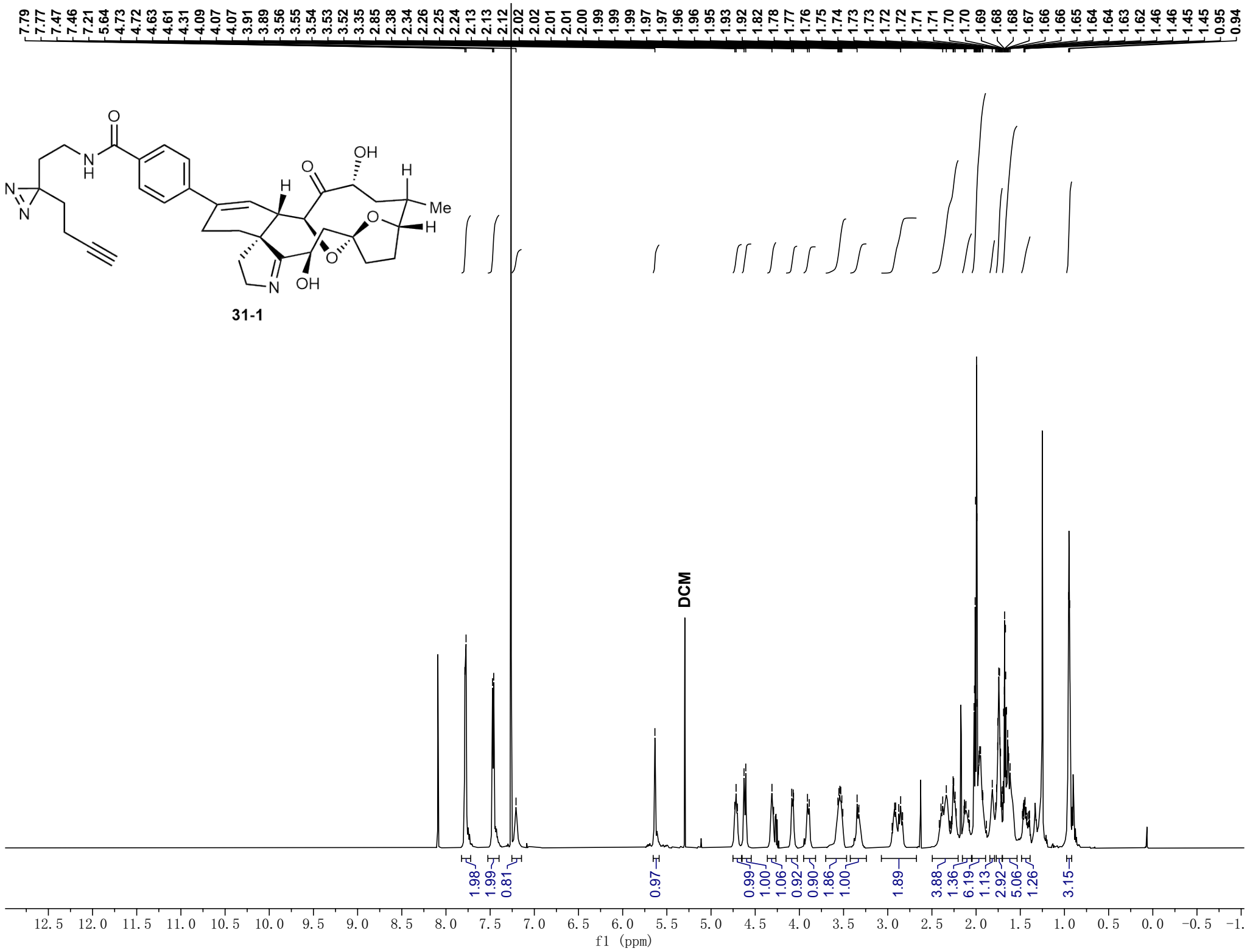


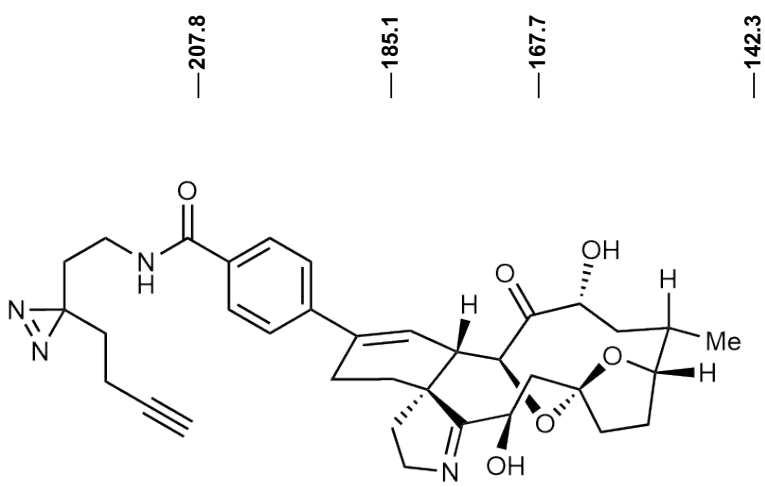
30

200.3
184.5
169.1
167.3
144.1
135.6
133.1
127.2
125.2
124.9
108.4
83.9
82.9
80.3
73.8
70.8
69.7
69.6
55.4
53.8
42.7
40.1
37.0
35.1
34.2
32.7
32.3
31.7
30.1
29.9
29.3
27.1
26.0
24.5
21.3
17.6
13.4

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

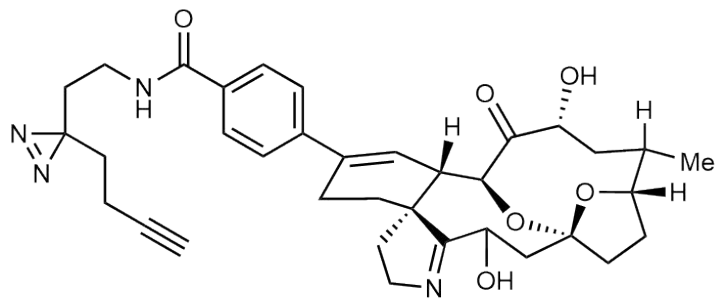
f1 (ppm)


7.79 7.77 7.47 7.46 7.21 5.64 4.73 4.72 4.63 4.61 4.31 4.09 4.07 4.07 3.91 3.89 3.56 3.55 3.54 3.53 3.52 3.35 2.85 2.38 2.34 2.26 2.25 2.24 2.13 2.13 2.12 2.02 2.02 2.01 2.01 2.00 1.99 1.99 1.99 1.97 1.97 1.96 1.96 1.95 1.93 1.92 1.82 1.78 1.77 1.76 1.75 1.74 1.73 1.73 1.72 1.72 1.71 1.71 1.70 1.70 1.69 1.68 1.68 1.67 1.66 1.65 1.64 1.64 1.63 1.62 1.46 1.46 1.45 1.45 0.95 0.94
O
N
H
N
N
OH
O
H
H
Me
O
O
OH
N
31-1
DCM
1.98 1.99 0.81 0.97 0.99 1.00 1.06 0.92 0.90 1.86 1.00 1.89 3.88 1.36 6.19 1.13 2.92 5.06 1.26 3.15
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


O
N
H
N
N
H
O
OH
H
Me
O
H
O
OH
N

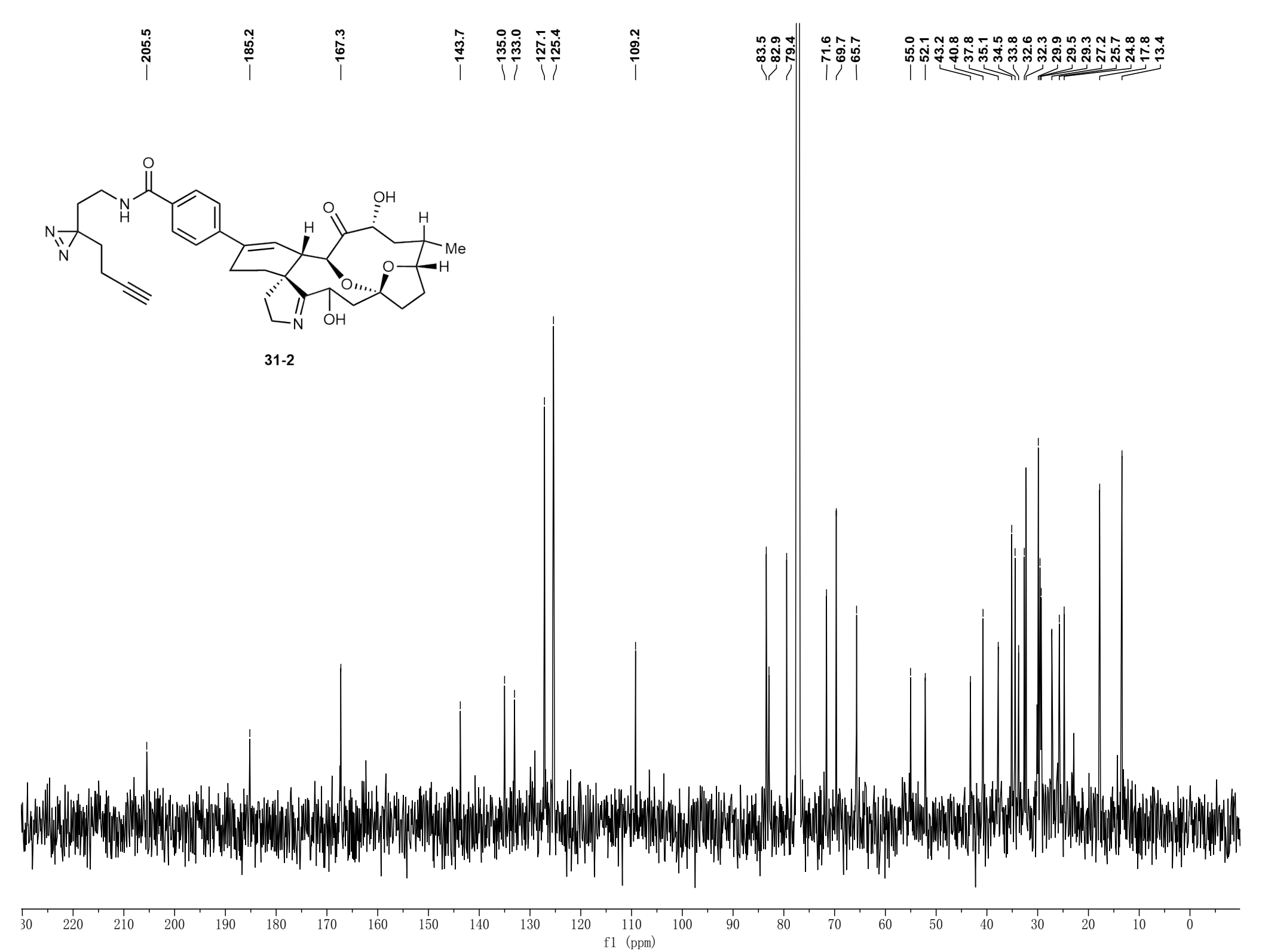
31-1

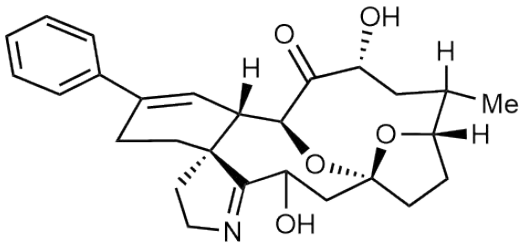
207.8
185.1
167.7
142.3
133.8
132.9
127.4
124.7
124.4
108.1
84.3
82.9
79.6
71.5
70.9
69.6
68.0
54.7
53.8
42.4
40.3
37.1
34.9
34.6
33.0
32.8
32.3
32.3
29.9
29.7
28.9
27.2
27.2
25.1
24.4
17.8
13.5
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
N
H
N
N
O
H
OH
H
Me
O
O
O
H
N
OH

31-2

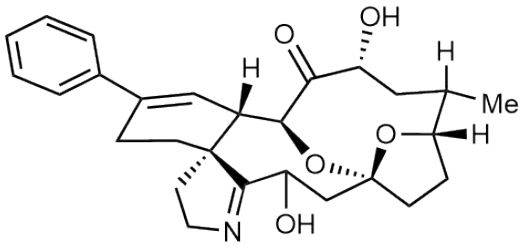
grease
2.01
2.05
0.78
1.00
1.00
0.95
1.05
1.12
1.08
2.22
2.07
1.02
1.99
1.23
1.75
1.03
5.72
1.03
1.08
1.87
4.56
1.93
3.66
f1 (ppm)


205.5
185.2
167.3
143.7
135.0
133.0
127.1
125.4
109.2
83.5
82.9
79.4
71.6
69.7
65.7
55.0
52.1
43.2
40.8
37.8
35.1
34.5
33.8
32.6
32.3
29.9
29.5
29.3
27.2
25.7
24.8
17.8
13.4
O
N
H
N
N
H
O
OH
H
Me
O
H
O
O
OH
N
31-2
f1 (ppm)


OH
O
H
H
Me
O
O
H
OH
N

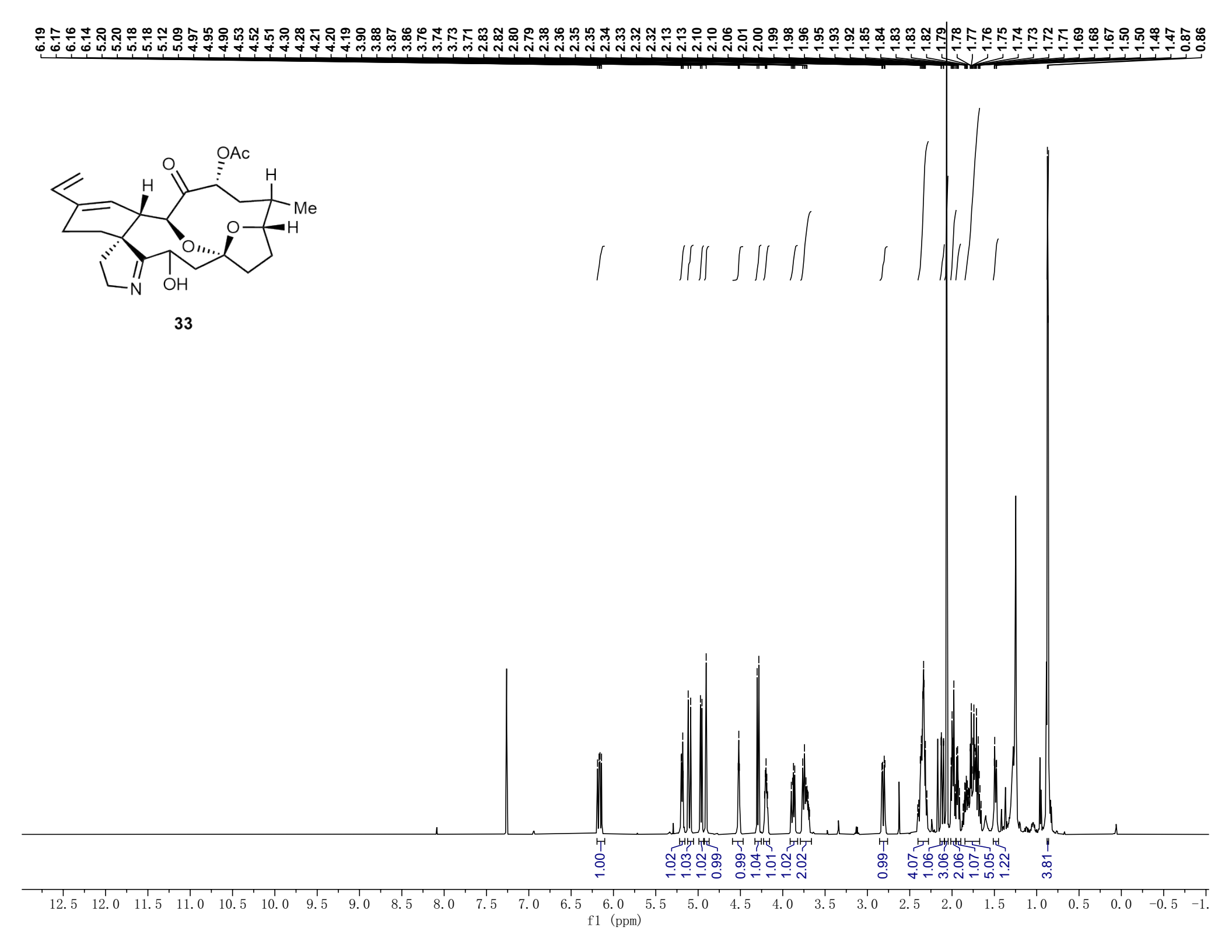
32

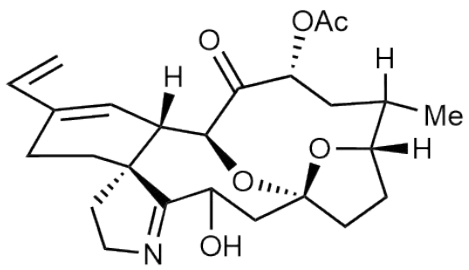
7.40 7.38 7.30 7.29 7.28 7.26 7.25 7.24 7.23 5.47 4.54 4.52 4.37 4.22 4.21 4.21 4.20 4.10 4.10 4.08 4.08 3.86 3.84 3.83 3.82 3.68 3.67 3.65 3.56 3.54 2.80 2.79 2.78 2.77 2.51 2.50 2.47 2.36 2.34 2.34 2.32 2.30 2.29 2.28 2.26 2.12 2.09 2.00 1.98 1.97 1.96 1.95 1.91 1.90 1.89 1.88 1.86 1.85 1.84 1.83 1.76 1.74 1.73 1.72 1.71 1.69 1.68 1.67 1.66 1.65 1.64 1.56 1.56 1.54 1.54 0.91 0.90
contains water
grease
2.17 2.61 0.90 0.99 1.00 0.98 1.04 1.00 1.16 0.93 0.93 2.18 2.61 1.45 2.64 2.91 15.36 1.60 3.07
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


OH
O
H
H
Me
O
O
H
OH
N

32

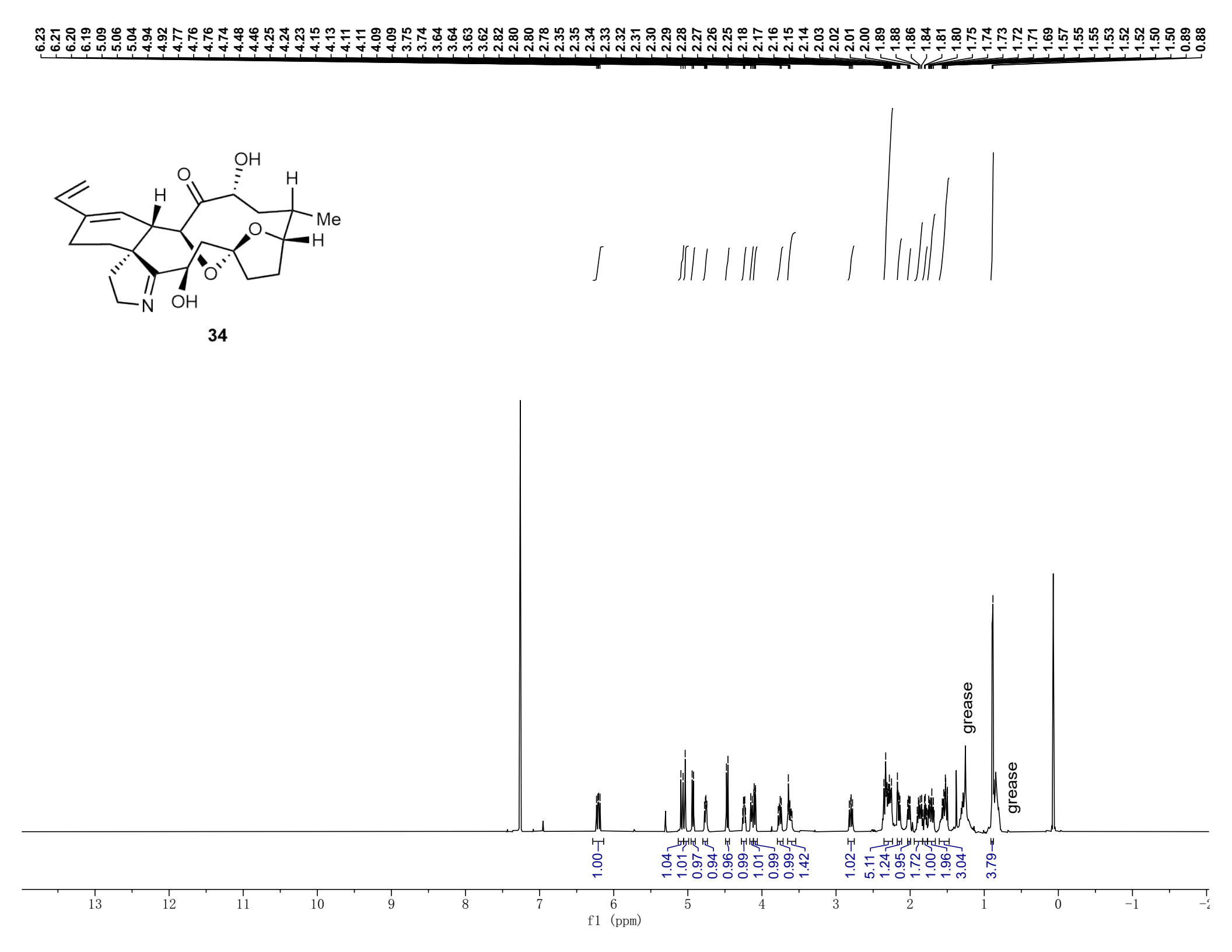
206.1
140.4
135.4
128.5
127.6
125.2
123.4
109.2
83.4
79.6
71.7
65.7
54.8
52.1
43.1
40.5
37.7
34.5
33.5
29.9
29.4
29.1
25.6
24.8
17.8
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

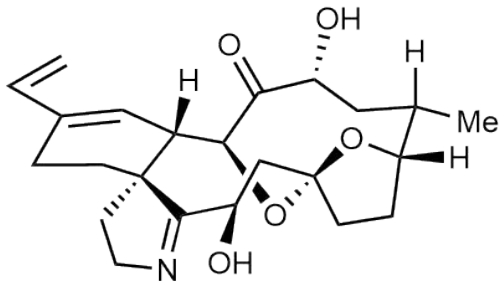

6.19 6.17 6.16 6.14 5.20 5.18 5.18 5.12 5.09 4.97 4.95 4.90 4.53 4.52 4.51 4.30 4.28 4.21 4.20 4.19 3.90 3.88 3.87 3.86 3.76 3.74 3.73 3.71 2.83 2.82 2.80 2.79 2.38 2.36 2.35 2.35 2.34 2.33 2.32 2.32 2.13 2.13 2.10 2.10 2.06 2.01 2.00 1.99 1.98 1.96 1.95 1.93 1.92 1.85 1.84 1.83 1.83 1.82 1.79 1.78 1.77 1.76 1.75 1.74 1.73 1.72 1.71 1.69 1.68 1.67 1.50 1.50 1.48 1.47 0.87 0.86
OAc
O
H
Me
O
H
O
O
N
OH
33
1.00 1.02 1.03 1.02 0.99 0.99 1.04 1.01 1.02 2.02 0.99 4.07 1.06 3.06 2.06 1.07 5.05 1.22 3.81
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)



33

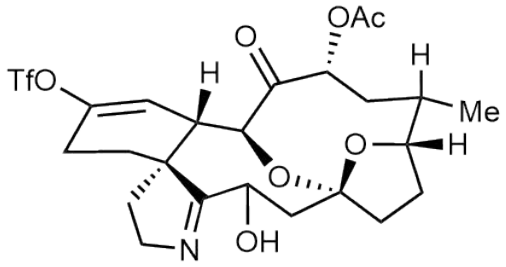
200.5
200.4
185.8
169.0
138.8
135.6
127.3
112.2
109.4
83.3
80.2
73.6
65.7
54.8
54.8
54.8
52.8
43.3
40.7
37.8
34.1
31.7
31.6
29.5
29.0
24.7
22.8
22.7
21.3
17.6


6.23 6.21 6.20 6.19 5.09 5.06 5.04 4.94 4.92 4.77 4.76 4.76 4.74 4.48 4.46 4.25 4.24 4.23 4.15 4.13 4.11 4.11 4.09 4.09 3.75 3.74 3.64 3.64 3.63 3.62 2.82 2.80 2.80 2.78 2.35 2.34 2.33 2.32 2.31 2.30 2.29 2.28 2.27 2.26 2.25 2.18 2.17 2.16 2.15 2.14 2.03 2.02 2.01 2.00 1.89 1.88 1.86 1.84 1.81 1.80 1.75 1.74 1.73 1.72 1.71 1.69 1.57 1.55 1.55 1.53 1.52 1.52 1.50 1.50 0.89 0.88
OH
O
H
H
Me
O
H
O
OH
N
34
grease
grease
1.00 1.04 1.01 0.97 0.94 0.96 0.99 1.01 0.99 0.99 1.42 1.02 5.11 1.24 0.95 1.72 1.00 1.96 3.04 3.79
13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2
f1 (ppm)


OH
O
H
H
Me
O
H
O
OH
N

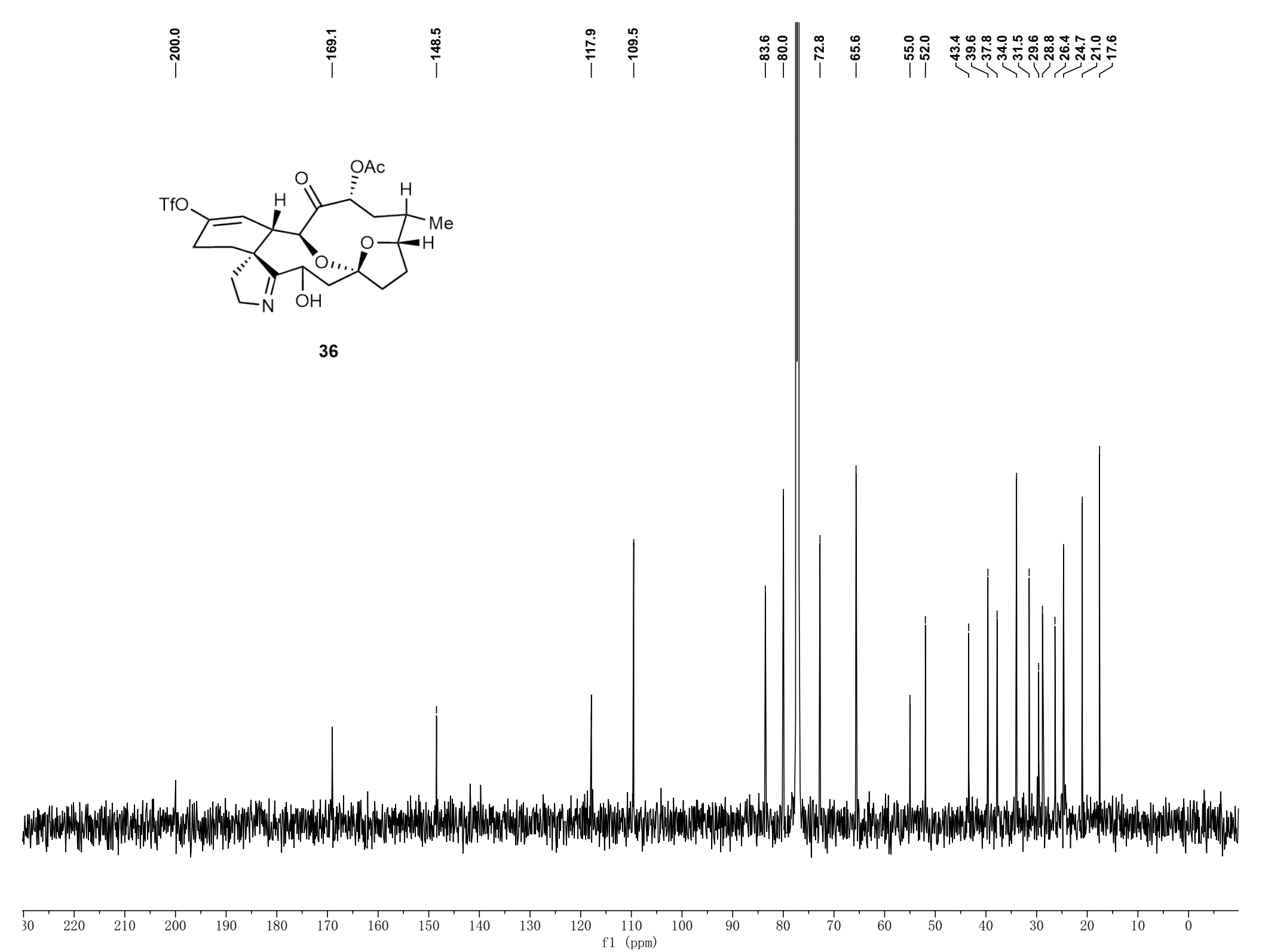
34

204.7
184.8
139.1
135.3
128.2
111.6
108.2
83.9
79.3
71.9
70.7
55.3
54.5
42.5
40.1
37.0
34.6
33.9
29.8
29.2
24.5
22.8
17.7
silicon oil
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

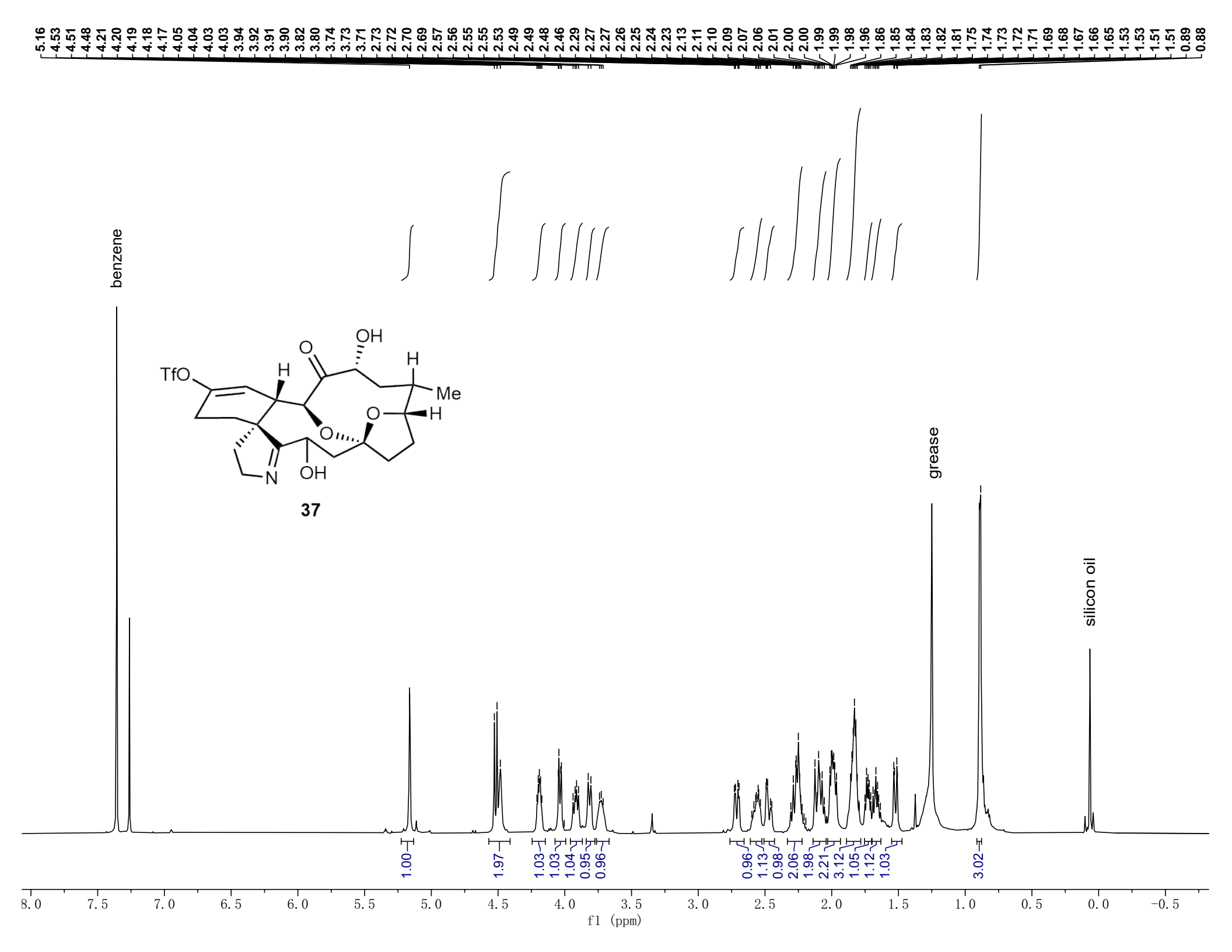

OAc
O
H
TfO
H
Me
O
H
O
N
OH

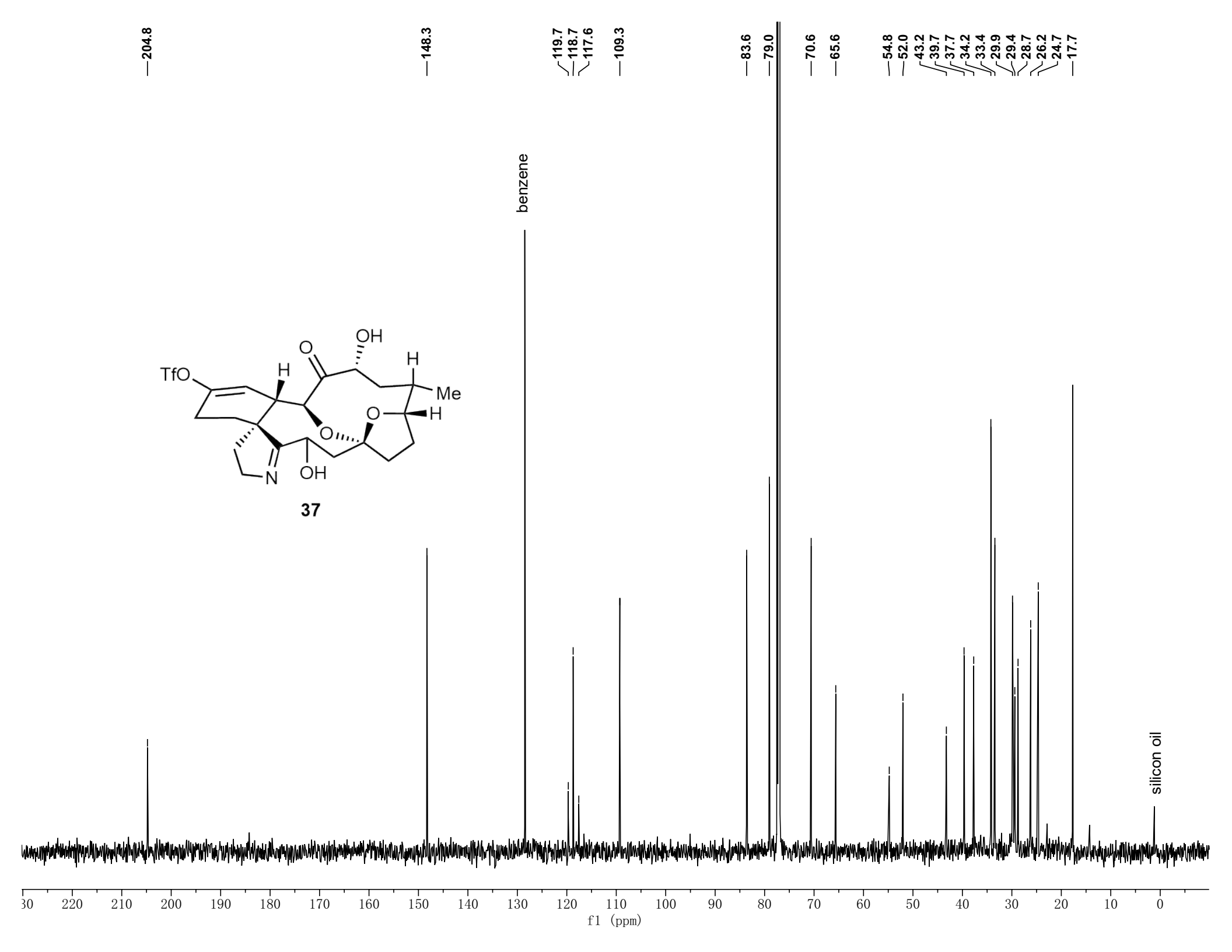
36

5.20 5.19 5.18 5.17 5.04 4.48 4.35 4.33 4.23 4.22 4.21 4.21 4.20 3.96 3.94 3.93 3.91 3.87 3.85 3.75 3.74 3.73 2.76 2.75 2.73 2.72 2.58 2.56 2.53 2.49 2.37 2.36 2.35 2.34 2.33 2.32 2.30 2.30 2.28 2.26 2.25 2.16 2.16 2.13 2.11 2.09 2.09 2.08 2.04 2.03 2.02 2.01 2.00 1.99 1.84 1.84 1.83 1.82 1.81 1.80 1.77 1.76 1.75 1.74 1.73 1.72 1.71 1.70 1.69 1.68 1.67 1.53 1.53 1.51 1.50 0.89 0.87
1.08 0.99 0.86 1.10 1.03 1.04 1.09 1.03 1.10 1.00 2.11 2.23 2.87 1.04 3.08 1.14 1.28 1.41 3.51
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


200.0
169.1
148.5
117.9
109.5
83.6
80.0
72.8
65.6
55.0
52.0
43.4
39.6
37.8
34.0
31.5
29.6
28.8
26.4
24.7
21.0
17.6
TfO
H
O
OAc
H
Me
O
H
O
N
OH
f1 (ppm)

36


5.16 4.53 4.51 4.48 4.21 4.20 4.19 4.18 4.17 4.05 4.04 4.03 4.03 3.94 3.92 3.91 3.90 3.82 3.80 3.74 3.73 3.71 2.73 2.72 2.70 2.69 2.57 2.56 2.55 2.55 2.53 2.49 2.49 2.48 2.46 2.29 2.27 2.27 2.26 2.25 2.24 2.23 2.13 2.11 2.10 2.09 2.07 2.06 2.01 2.00 2.00 1.99 1.99 1.98 1.96 1.86 1.85 1.84 1.83 1.82 1.81 1.75 1.74 1.73 1.72 1.71 1.69 1.68 1.67 1.66 1.65 1.53 1.53 1.51 1.51 0.89 0.88
benzene
TfO
H
O
OH
H
Me
O
H
O
N
OH
37
grease
silicon oil
1.00
1.97
1.03
1.03
1.04
0.95
0.96
0.96
1.13
0.98
2.06
1.98
2.21
3.12
1.05
1.12
1.03
3.02
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


204.8
148.3
119.7
118.7
117.6
109.3
83.6
79.0
70.6
65.6
54.8
52.0
43.2
39.7
37.7
34.2
33.4
29.9
29.4
28.7
26.2
24.7
17.7
benzene
silicon oil
TfO
OH
O
H
Me
O
H
O
N
OH
37
f1 (ppm)