

Supplementary Information

Divergent Asymmetric Synthesis of (–)-Ganocins A–C and (+)-Cochlearol B via a Non-biomimetic Strategy

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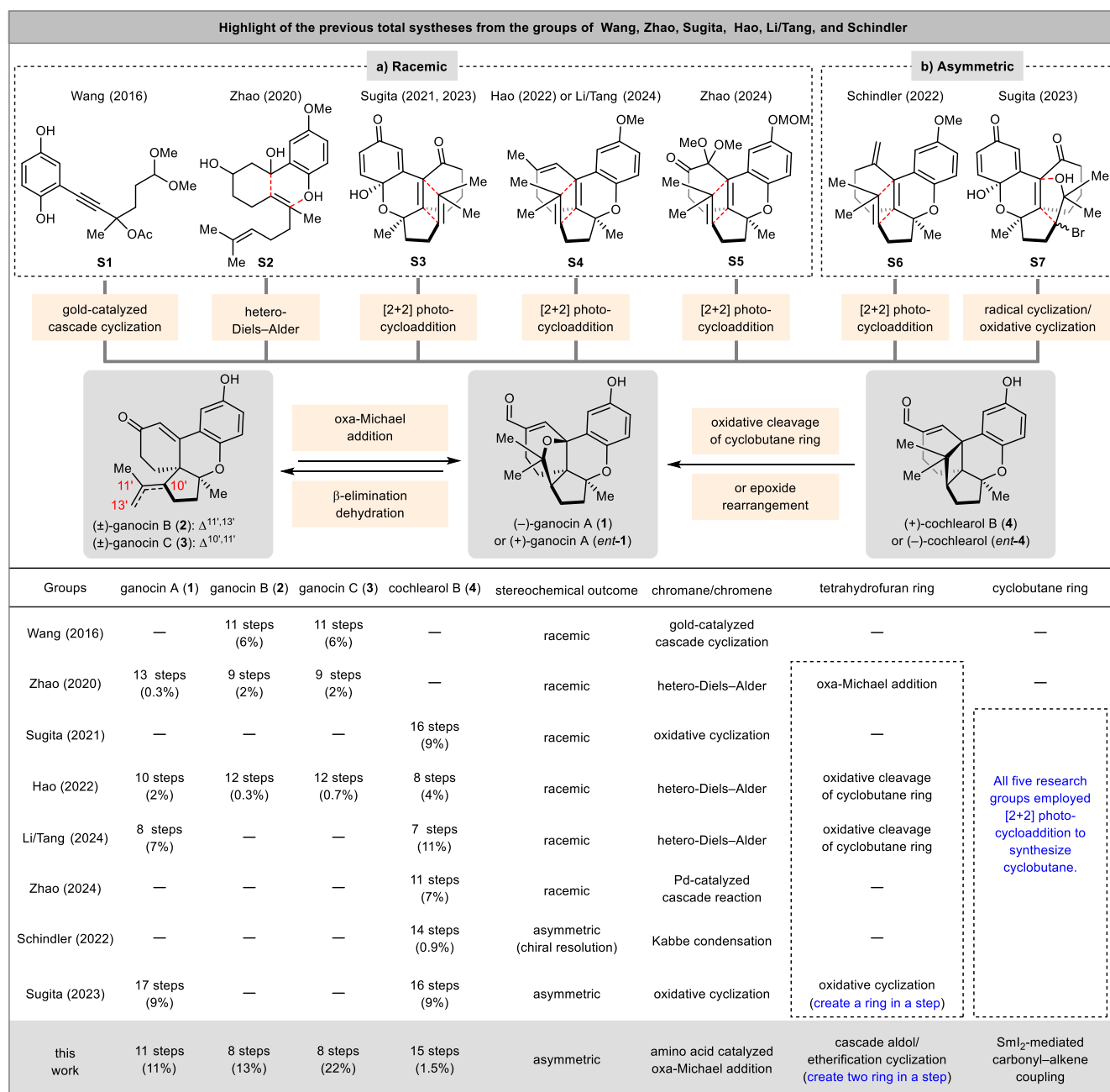
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1. General Experimental Procedures

All reactions were carried out under nitrogen atmosphere anhydrous conditions and all reagents were purchased from commercial suppliers without further purification. Unless stated otherwise, reactions were performed at 33 °C. Anhydrous THF (tetrahydrofuran), DCM (dichloromethane), PhMe (toluene), and DMF (*N,N*-dimethylformamide) were obtained from an Inert PS-MD-4 solvent system. Anhydrous CH₃CN (acetonitrile), benzene, PhCl (chlorobenzene), DMSO (dimethyl sulfoxide), MeOH (methanol), EtOH (ethanol), *t*-BuOH (*tert*-butanol), *i*-PrOH (isopropanol), EtOAc (ethyl acetate), and 1,4-dioxane were purchased from Energy Chemical, Ltd. HMPA (hexamethylphosphoramide), Et₃N (triethylamine) and Et₂O (diethyl ether) were obtained from commercial sources and subjected to anhydrous treatment prior to use. AcOH (acetic acid) was commercially available and was used without anhydrous treatment. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 400 MHz NMR spectrometer (400 MHz for ¹H, 100 MHz for ¹³C) or a Bruker Avance 500 MHz NMR spectrometer (500 MHz for ¹H, 125 MHz for ¹³C). Chemical shifts were referenced using residual undeuterated solvent (CDCl₃: δ 7.26, 77.16 ppm; C₆D₆: δ 7.16, 128.06 ppm; C₅D₅N: 7.19, 149.0 ppm; (CD₃)₂CO: δ 2.05, 29.84 ppm unless otherwise stated) at 298 K. HRMS(ESI) spectra were acquired on a Waters Xevo G3 QTof mass spectrometer. IR spectra were recorded on a Nicolet 210 spectrophotometer. Melting points were determined using a hot stage apparatus. Optical rotations were measured with a Rudolph Research Automatic Polarimeter IV. Single-crystal structures were measured on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. TLC was performed on commercially prepared silica gel plates (GF254, 200-300 mesh) and visualized under UV light at 254 nm or by staining with phosphomolybdic acid or potassium permanganate solution.

2. Summary of Prior Synthetic Reports



Supplementary Figure 1. Total synthesis of ganocins A–C (1–3) and cochlearol B (4). a Racemic. b Asymmetric.

In the past decade, numerous elegant racemic syntheses of ganocins A–C (1–3) and cochlearol B (4) have been achieved (Supplementary Figure 1a)^{1–6}. In 2016, Wang and Li et al. reported the first total synthesis of racemic ganocins B (2) and C (3) in 11 steps with 6% overall yields, which features a gold-catalyzed intramolecular cascade cyclization of propargyl acetate **S1** to construct the 6/6/5 tricyclic skeleton¹. In 2020, Zhao and co-workers achieved the divergent total synthesis of racemic ganocins A–C (1–3) in 13, 9, and 9 steps with 0.3%, 2%, and 2% overall yields, respectively². Notable steps in their synthesis include a biomimetic hetero-Diels–Alder annulation of **S2** to construct the tricyclic scaffold and an intramolecular oxa-Michael addition/triflation cascade reaction to forge the tetrahydrofuran ring. In the subsequent year, Sugita et al. reported the first total synthesis of racemic cochlearol B (4) in 16 steps with 9% overall yields³. The key steps include an oxidative cyclization and intramolecular [2+2] photocycloaddition of enone **S3** to construct the pentacyclic skeleton. In 2022, Hao et al. disclosed the unified and biomimetic synthesis of racemic ganocins A–C (1–3)

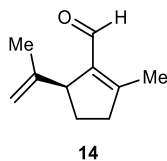
and cochlearol B (**4**) (10, 12, 12, and 8 steps with 2%, 0.3%, 0.7%, and 4% overall yields, respectively)⁴. They used an intramolecular [2+2] photocycloaddition of diene **S4** to construct the cyclobutane part of the pentacyclic skeleton, and either a complex carbocation rearrangement of epoxide or oxidative cleavage of cyclobutane to convert the cyclobutane intermediate into a tetrahydrofuran moiety present in ganocin A. In 2024, besides [2+2] photocycloaddition of diene **S4**, Li and Tang et al. utilized epoxide rearrangement or 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ)-induced oxidative cleavage of cyclobutane to efficiently convert cochlearol B (**4**) (7 steps with 11% overall yields) to ganocin A (**1**) (8 steps with 7% overall yields)⁵. In the same year, Zhao and co-workers reported the total synthesis of racemic cochlearol B (**4**) in 11 steps with 7% overall yields⁶. Their synthesis features a novel Pd-catalyzed Wacker-type/cross-coupling cascade reaction and an intramolecular [2+2] photocycloaddition of alkene **S5**.

So far, only one asymmetric synthesis of ganocin A (**1**) and two asymmetric syntheses of cochlearol B (**4**) have been reported, respectively (Supplementary Figure 1b)^{7,8}. For example, in 2022, Schindler and co-workers disclosed the first asymmetric total synthesis of (+)-cochlearol B (**4**) using chiral resolution in 14 steps with 0.9% overall yields⁷, including an organocatalytic Kabbe condensation and a visible-light-mediated [2+2] photocycloaddition of diene **S6** to construct the bicyclo[3.2.0]heptane core. One year later, Sugita and co-workers reported asymmetric syntheses of (+)-ganocin A (*ent*-**1**) and (–)-cochlearol B (*ent*-**4**) based on their previous racemic synthesis⁸. Using an asymmetric Corey–Bakshi–Shibata reduction to install the stereocenter, they completed the total synthesis of (–)-cochlearol B (*ent*-**4**) in 16 steps with 9% overall yields. Subsequently, they achieved the first asymmetric synthesis of (+)-ganocin A (*ent*-**1**) in 17 steps with 9% overall yields via intramolecular radical cyclization of bromohydrin **S7** and benzylic oxidative cyclization.

Our group accomplished the divergent asymmetric total synthesis of the (–)-ganocins A–C (**1–3**) and (+)-cochlearol B (**4**) from (*R*)-limonene in 11, 8, 8, and 15 steps with 11%, 13%, 22%, and 1.5% overall yields, respectively. The synthesis features an amino acid-catalyzed diastereoselective oxa-Michael addition to construct the chromanone framework, acid-dependent divergent reaction pathways of a common intermediate, wherein aldol/dehydration provides the 5/6/6/6 tetracyclic framework whereas an efficient cascade aldol/etherification cyclization leads to the 5/5/6/6/6 pentacyclic skeleton, and a Sml₂-mediated 4-*exo*-trig reductive cross-coupling reaction that rapidly forges the highly strained cyclobutanol ring.

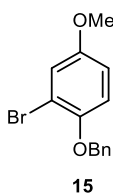
3. Experimental Procedures and Experimental Data

Preparation of Compound 14



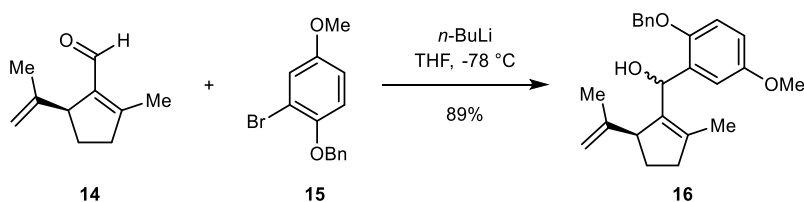
Compound **14** was prepared according to the literature procedure⁹. Analytical data matches with the literature.

Preparation of Compound 15



Compound **15** was prepared according to the literature procedure¹⁰. Analytical data matches with the literature.

Preparation of Compound 16



To a solution of **15** (17.5 g, 60.0 mmol, 1.5 equiv) in THF (250 mL) was added dropwise *n*-BuLi (2.5 M in hexane, 24.8 mL, 62.0 mmol, 1.55 equiv) at $-78\text{ }^{\circ}\text{C}$ and stirred at this temperature for 10 min, a solution of compound **14** (6.0 g, 40.0 mmol, 1.0 equiv) in THF (102 mL) was added dropwise. After stirring at same temperature for 2 h, the reaction was quenched with saturated aqueous NH_4Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 50:1→20:1→10:1→5:1) to afford **16** as a mixture of two diastereomers (12.9 g, 89% yield) as a yellow oil.

Note: The two diastereomers can be separated by preparative thin layer chromatography (PTLC, petroleum ether:EtOAc = 8:1) to afford **16a** and **16b**.

Data for 16a:

TLC: R_f = 0.6 (petroleum ether:EtOAc = 8:1).

$[\alpha]_D^{26}$ = +169 (c = 1.0, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ 7.40 – 7.28 (m, 5H), 7.09 (d, J = 3.1 Hz, 1H), 6.80 (d, J = 8.8 Hz, 1H), 6.72 (dd, J = 8.8, 3.1 Hz, 1H), 5.90 (d, J = 6.2 Hz, 1H), 5.00 (s, 2H), 4.80 (s, 1H), 4.73 (s, 1H), 3.79 (s, 3H), 3.18 (d, J = 9.5 Hz, 1H), 2.58 (d, J = 6.6 Hz, 1H), 2.44 (dt, J = 16.8, 8.5 Hz, 1H), 2.15 (ddd, J = 16.3, 9.8, 2.4 Hz, 1H), 1.97 – 1.87 (m, 1H), 1.73 (s, 3H), 1.61 (s, 3H), 1.59 – 1.52 (m, 1H).

^{13}C NMR (125 MHz, CDCl_3) δ 153.7, 152.1, 149.7, 139.0, 137.4, 135.3, 133.3, 128.5, 128.0, 127.7, 113.2, 112.7, 112.4, 110.2, 70.8, 67.2, 55.8, 52.9, 37.9, 29.3, 19.8, 14.3.

HRMS(ESI)⁺ calcd for $\text{C}_{24}\text{H}_{28}\text{O}_3\text{Na}^+$ $[\text{M}+\text{Na}]^+$: 387.1931; found: 387.1935.

FT-IR (cm⁻¹): 2923, 1494, 1454, 1209, 1045, 1021, 734, 696.

Data for 16b:

TLC: R_f = 0.5 (petroleum ether:EtOAc = 8:1).

$[\alpha]_D^{26} = +48$ (c = 0.5, CHCl₃).

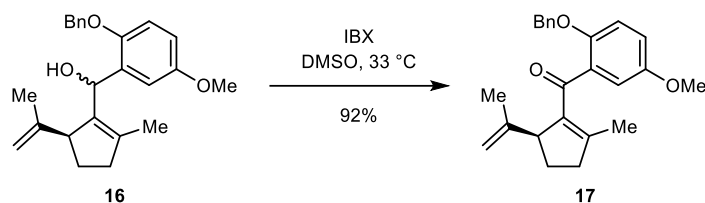
¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.29 (m, 5H), 7.00 (d, J = 3.1 Hz, 1H), 6.80 (d, J = 8.8 Hz, 1H), 6.71 (dd, J = 8.8, 3.1 Hz, 1H), 5.58 (s, 1H), 5.04 (d, J = 11.6 Hz, 1H), 5.01 (d, J = 11.6 Hz, 1H), 4.51 (s, 2H), 3.76 (s, 3H), 3.26 (d, J = 9.3 Hz, 1H), 2.50 – 2.35 (m, 1H), 2.29 – 2.17 (m, 1H), 2.07 – 1.93 (m, 1H), 1.76 (s, 3H), 1.64 – 1.55 (m, 1H), 1.50 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 153.7, 150.4, 148.7, 138.7, 137.2, 135.9, 132.4, 128.7, 128.1, 127.7, 114.2, 112.53, 112.50, 110.2, 70.8, 68.0, 55.9, 55.2, 38.7, 29.1, 19.3, 15.0.

HRMS(ESI)⁺ calcd for C₂₄H₂₆O₃Na⁺ [M+Na]⁺: 387.1931; found: 387.1932.

FT-IR (cm⁻¹): 3468, 2918, 2845, 1494, 1454, 1207, 1044, 1016, 733.

Preparation of Compound 17



To a solution of **16** (2.96 g, 8.13 mmol, 1.0 equiv) in DMSO (81.0 mL) was added 2-iodoxybenzoic acid (IBX, 2.73 g, 9.76 mmol, 1.2 equiv) at 33 °C. After stirring at same temperature for 1.5 h, the reaction was quenched with a mixture of saturated aqueous NaHCO₃ solution and saturated aqueous Na₂S₂O₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 20:1→10:1) to afford **17** (2.70 g, 92% yield) as a yellow oil.

TLC: R_f = 0.5 (petroleum ether:EtOAc = 10:1).

$[\alpha]_D^{25} = -21$ (c = 1.0, CHCl₃).

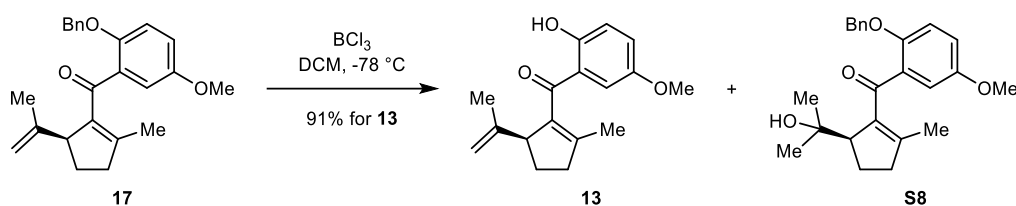
¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.27 (m, 5H), 6.94 – 6.85 (m, 3H), 5.00 (d, J = 11.5 Hz, 1H), 4.98 (d, J = 11.6 Hz, 1H), 4.54 (s, 1H), 4.50 (s, 1H), 3.76 (s, 3H), 3.73 – 3.65 (m, 1H), 2.48 (dt, J = 16.3, 7.4 Hz, 1H), 2.23 (ddd, J = 17.0, 8.9, 5.7 Hz, 1H), 2.02 – 1.91 (m, 1H), 1.80 (s, 3H), 1.61 – 1.51 (m, 1H), 1.54 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 195.0, 153.9, 153.8, 150.3, 147.9, 139.8, 137.0, 132.4, 128.5, 127.9, 127.4, 117.3, 114.4, 114.3, 110.2, 71.5, 55.9, 54.5, 39.6, 28.9, 20.4, 16.3.

HRMS(ESI)⁺ calcd for C₂₄H₂₆O₃Na⁺ [M+Na]⁺: 385.1774; found: 385.1779.

FT-IR (cm⁻¹): 2939, 2910, 1628, 1493, 1454, 1283, 1220, 1043, 736.

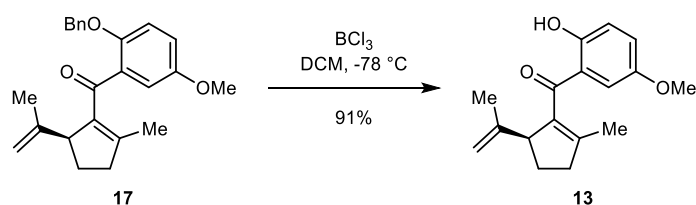
Supplementary Table 1. Optimization of selective debenzylation of compound 17



Entry	Conditions	13 (%) ^a	S8 (%) ^a
1	TiCl ₄ , DCM, 0 °C	0	28
2	TFA, toluene, 0 °C	0	<10
3	FeCl ₃ , DCM, 0 °C	0	53
4	BCl ₃ , DCM, -78 °C	91	0
5	DDQ, DCM/H ₂ O (10:1), 33 to 50 °C	complex mixture	

^aIsolated yield. TFA = trifluoroacetic acid. DDQ = 2,3-dichloro-5,6-dicyano-1,4 benzoquinone.

Preparation of Compound 13



To a solution of **17** (14.5 g, 40.1 mmol, 1.0 equiv) in DCM (400 mL) was added BCl₃ (1 M in hexane, 48.1 mL, 48.1 mmol, 1.2 equiv) at -78 °C. After stirring at same temperature for 1 h, the reaction was quenched with MeOH and saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with DCM and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 20:1→10:1) to afford **13** (9.92 g, 91% yield) as a yellow solid.

TLC: *R_f* = 0.7 (petroleum ether:EtOAc = 9:1).

M.p.: 61.1–62.2 °C.

$[\alpha]_D^{25}$ = +82 (c = 1.0, CHCl₃).

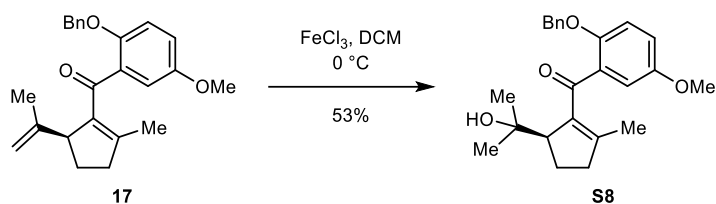
¹H NMR (500 MHz, CDCl₃) δ 11.85 (s, 1H), 7.15 (d, *J* = 3.1 Hz, 1H), 7.10 (dd, *J* = 9.1, 3.1 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 1H), 4.73 (s, 1H), 4.67 (s, 1H), 3.99 – 3.92 (m, 1H), 3.76 (s, 3H), 2.65 – 2.55 (m, 1H), 2.48 (dt, *J* = 17.1, 8.2 Hz, 1H), 2.29 – 2.20 (m, 1H), 1.83 – 1.73 (m, 1H), 1.74 (s, 3H), 1.66 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 201.9, 157.1, 151.8, 148.2, 146.8, 137.4, 123.9, 119.9, 119.2, 115.7, 111.5, 57.0, 56.1, 39.1, 29.2, 20.0, 17.0.

HRMS(ESI)⁺ calcd for C₁₇H₂₀O₃Na⁺ [M+Na]⁺: 295.1305; found: 295.1306.

FT-IR (cm⁻¹): 3647, 2939, 1635, 1586, 1483, 1282, 1209, 1039, 791.

Preparation of Compound S8



To a solution of **17** (5.4 mg, 0.0149 mmol, 1.0 equiv) in DCM (0.2 mL) was added FeCl_3 (8.0 mg, 0.0492 mmol, 3.3 equiv) at 0°C . After stirring at same temperature for 43 min, the reaction was quenched with saturated aqueous NaHCO_3 solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 5:1) to afford **S8** (3.0 mg, 53% yield) as a yellow oil.

TLC: R_f = 0.2 (petroleum ether:EtOAc = 5:1).

$[\alpha]_D^{24} = +10$ (c = 0.2, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ 7.39 – 7.30 (m, 5H), 7.00 (d, J = 3.0 Hz, 1H), 6.95 (dd, J = 8.9, 3.0 Hz, 1H), 6.92 (d, J = 8.9 Hz, 1H), 5.01 (d, J = 11.5 Hz, 1H), 4.98 (d, J = 11.6 Hz, 1H), 3.79 (s, 3H), 3.49 (brs, 1H), 3.28 – 3.17 (m, 1H), 2.52 – 2.40 (m, 1H), 2.21 – 2.09 (m, 1H), 1.88 – 1.76 (m, 1H), 1.61 (s, 3H), 1.60 – 1.55 (m, overlap with H_2O , 1H), 1.15 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 197.2, 156.0, 154.2, 150.7, 139.4, 136.8, 132.1, 128.7, 128.3, 127.7, 118.3, 114.7, 114.6, 73.7, 71.7, 59.2, 56.0, 40.1, 29.5, 26.2, 25.3, 16.7.

HRMS(ESI) $^+$ calcd for $\text{C}_{24}\text{H}_{29}\text{O}_4^+$ $[\text{M}+\text{H}]^+$: 381.2060; found: 381.2065.

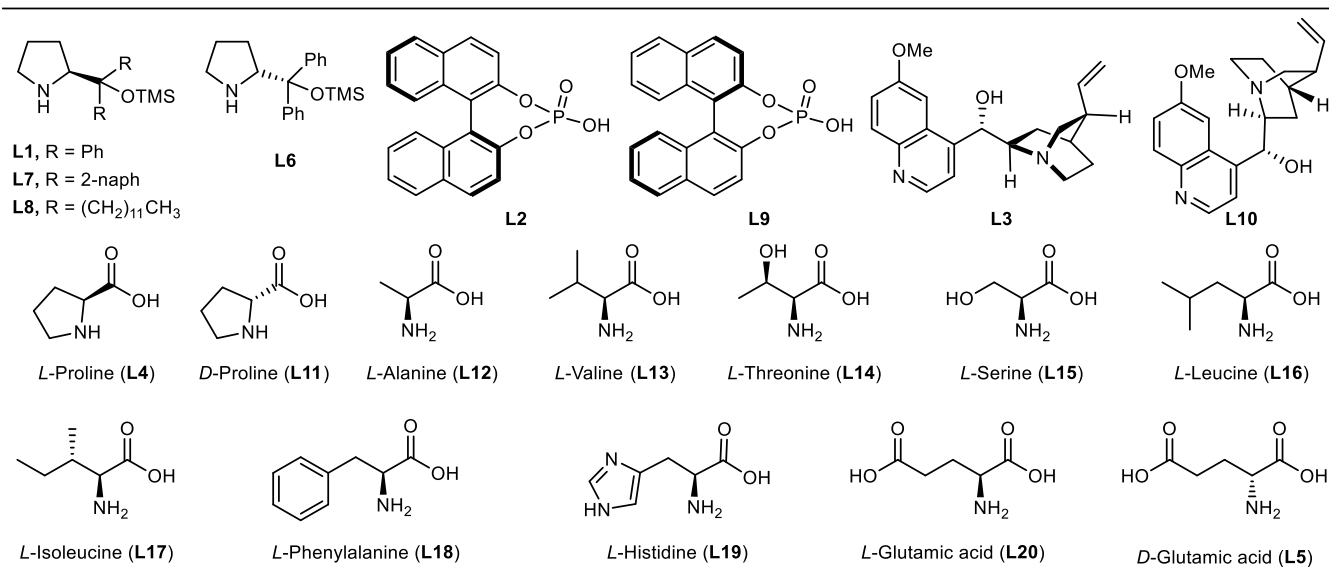
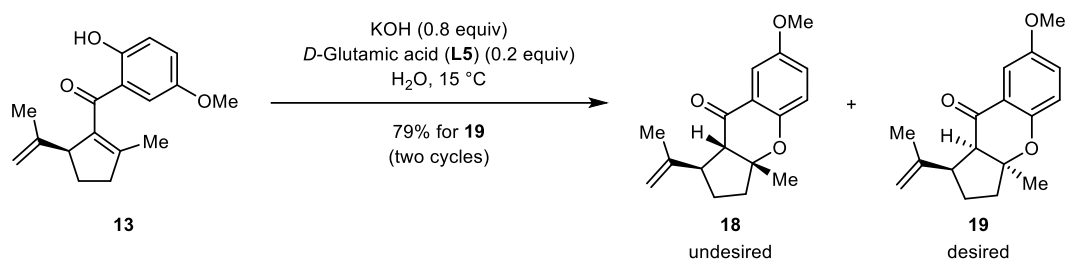
FT-IR (cm^{-1}): 3446, 2967, 2917, 1603, 1492, 1414, 1218, 1042, 737.

Preparation of Ligands

L1-L6 and **L9-L20** were commercially available and used as received.

L7¹¹ and **L8¹²** were synthesized according to literature procedures. Analytical data matches with the literature.

Supplementary Table 2. Optimization of oxa-Michael reaction of compound 13

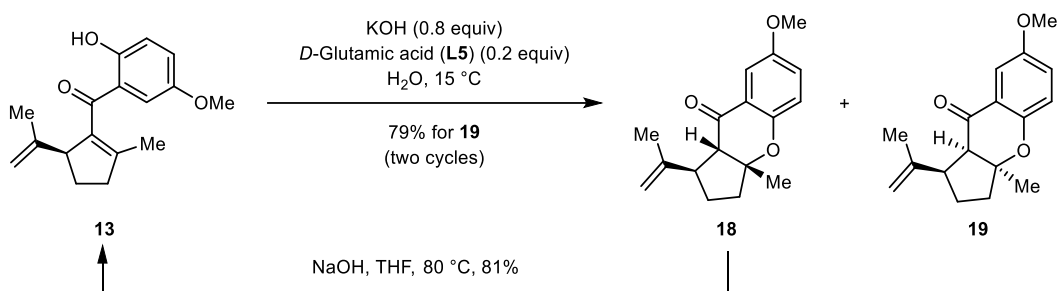


Entry	Conditions ^a	18 (%) ^b	19 (%) ^b	Ratio of 18:19
1	TFA, Toluene, 33 to 60 °C	0	0	-
2	TfOH, Toluene, 33 °C	0	0	-
3	KOH, DEG, 100 °C	97	0	1:0
4 ^c	N ₂ H ₄ •H ₂ O, DEG, 33 °C	48	18	1:0.4
5 ^{c,d}	N ₂ H ₄ •H ₂ O, DEG, 100 °C	48	16	1:0.3
6 ^{c,d}	N ₂ H ₄ •H ₂ O, DEG, 200 °C	36	0	1:0
7	PhNHNH ₂ , DEG, 33 °C	38	17	1:0.4
8	PhNH ₂ , DEG, 33 °C	54	26	1:0.5
9	L1 , DCM, 33 to 60 °C		NR	
10	L6 , DCM, 33 to 60 °C		NR	
11	L7 , DCM, 33 to 60 °C		NR	
12	L8 , DCM, 33 to 60 °C		NR	
13	L2 , toluene, 33 to 100 °C		NR	
14	L9 , toluene, 33 to 100 °C		NR	
15	L3 , toluene, 33 to 130 °C	49	23	1:0.5
16	L10 , toluene, 33 to 130 °C	59	23	1:0.4

17	KOH (1.1 equiv), <i>L</i> -Proline (L4) (0.2 equiv), H ₂ O, 33 °C	32	45	1:1.4
18	KOH (1.1 equiv), <i>D</i> -Proline (L11) (0.2 equiv), H ₂ O, 33 °C	70	23	1:0.3
19	KOH (1.1 equiv), <i>L</i> -Alanine (L12) (0.2 equiv), H ₂ O, 33 °C	49	42	1:0.9
20	KOH (1.1 equiv), <i>L</i> -Valine (L13) (0.2 equiv), H ₂ O, 33 °C	50	45	1:0.9
21	KOH (1.1 equiv), <i>L</i> -Threonine (L14) (0.2 equiv), H ₂ O, 33 °C	48	50	1:1.0
22	KOH (1.1 equiv), <i>L</i> -Serine (L15) (0.2 equiv), H ₂ O, 33 °C	59	35	1:0.6
23	KOH (1.1 equiv), <i>L</i> -Leucine (L16) (0.2 equiv), H ₂ O, 33 °C	49	51	1:1.0
24	KOH (1.1 equiv), <i>L</i> -Isoleucine (L17) (0.2 equiv), H ₂ O, 33 °C	49	47	1:1.0
25	KOH (1.1 equiv), <i>L</i> -Phenylalanine (L18) (0.2 equiv), H ₂ O, 33 °C	51	43	1:0.8
26	KOH (1.1 equiv), <i>L</i> -Histidine (L19) (0.2 equiv), H ₂ O, 33 °C	58	40	1:0.7
27	KOH (1.1 equiv), <i>L</i> -Glutamic acid (L20) (0.2 equiv), H ₂ O, 33 °C	44	52	1:1.2
28	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 33 °C	38	61	1:1.6
29 ^{c,e}	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 33 °C	53	45	1:0.8
30	KOH (1.1 equiv), PhNHNH ₂ (0.2 equiv), H ₂ O, 33 °C	63	16	1:0.3
31	KOH (1.1 equiv), PhNH ₂ (0.2 equiv), H ₂ O, 33 °C	67	19	1:0.3
32	KOH (1.1 equiv), L1 (0.2 equiv), H ₂ O, 33 °C	41	58	1:1.4
33	KOH (1.1 equiv), L6 (0.2 equiv), H ₂ O, 33 °C	40	57	1:1.4
34	KOH (1.1 equiv), L7 (0.2 equiv), H ₂ O, 33 °C	46	46	1:1.0
35	KOH (1.1 equiv), L8 (0.2 equiv), H ₂ O, 33 °C	47	51	1:1.1
36	KOH (1.1 equiv), L2 (0.2 equiv), H ₂ O, 33 °C	41	41	1:1.0
37	KOH (1.1 equiv), L9 (0.2 equiv), H ₂ O, 33 °C	43	38	1:0.9
38	KOH (1.1 equiv), L3 (0.2 equiv), H ₂ O, 33 °C	39	60	1:1.5
39	KOH (1.1 equiv), L10 (0.2 equiv), H ₂ O, 33 °C	41	48	1:1.2
40	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 23 °C	36	52	1:1.4
41	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 15 °C	26	56	1:2.2
42	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 5 °C	22	44	1:2.0
43	KOH (1.1 equiv), <i>D</i> -Glutamic acid (L5) (1.2 equiv), H ₂ O, 15 °C		NR	
44	KOH (0.8 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 15 °C	29	64	1:2.2
45	KOH (0.8 equiv), L1 (0.2 equiv), H ₂ O, 15 °C	31	62	1:2.0
46	KOH (0.8 equiv), L3 (0.2 equiv), H ₂ O, 15 °C	24	39	1:1.6
47 ^{c,f}	KOH (0.8 equiv), <i>D</i> -Glutamic acid (L5) (0.2 equiv), H ₂ O, 15 °C	34	62(79) ^g	1:1.8

^aall reactions were performed on a 20.0 mg scale in 0.74 mL solvent except as otherwise indicated. ^bYield determined by ¹H NMR with CH₂Br₂ as an internal standard. ^cIsolated yield. ^d**13** (5.0 mg). ^e**13** (500 mg). ^f**13** (1.0 g). ^gYield after two cycles (in parentheses). TfOH = trifluoromethanesulfonic acid. DEG = diethylene glycol. N₂H₄•H₂O = hydrazine hydrate. NR = No reaction.

Preparation of Compounds 18 and 19



To a suspension of **13** (1.0 g, 3.68 mmol, 1.0 equiv) in H₂O (18.4 mL) were added a solution of KOH (165 mg, 2.94 mmol, 0.8 equiv) in H₂O (18.4 mL) and *D*-glutamic acid (**L5**) (108 mg, 0.735 mmol, 0.2 equiv) at 15 °C. After stirring at same temperature for 59 h, the reaction was quenched with saturated aqueous NH₄Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 60:1→20:1) to afford desired **19** (620 mg, 62% yield) as a yellow solid and **18** (344 mg, 34% yield) as a yellow solid.

To a solution of **18** (344 mg, 1.26 mmol, 1.0 equiv) in THF (12.6 mL) was added NaOH (212 mg, 5.31 mmol, 4.2 equiv) at 33 °C. After stirring under reflux for 1.5 h, the reaction mixture was cooled to 33 °C and quenched with saturated aqueous NH₄Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 20:1) to afford desired **13** (278 mg, 81% yield) as a yellow solid. The first procedure was repeated with **13** one more time to give **19** as a yellow solid (168 mg, total 788 mg, 79% overall yield).

Data for **18**:

TLC: R_f = 0.4 (petroleum ether:EtOAc = 15:1).

M.p.: 62.7–63.0 °C.

$[\alpha]_D^{25}$ = –129 (c = 1.0, CHCl₃).

¹H NMR (500 MHz, CDCl₃) δ 7.29 (d, J = 3.2 Hz, 1H), 7.08 (dd, J = 9.0, 3.2 Hz, 1H), 6.84 (d, J = 9.0 Hz, 1H), 4.78 (s, 1H), 4.77 (s, 1H), 3.78 (s, 3H), 3.00 (dt, J = 11.2, 8.7 Hz, 1H), 2.57 (d, J = 11.6 Hz, 1H), 2.28 – 2.14 (m, 2H), 1.94 – 1.84 (m, 1H), 1.80 – 1.68 (m, 1H), 1.76 (s, 3H), 1.41 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 194.1, 153.8, 153.7, 144.5, 125.5, 119.8, 118.0, 112.3, 107.4, 91.0, 58.9, 55.8, 50.8, 39.0, 29.1, 21.8, 19.3.

HRMS (ESI)⁺ calcd for C₁₇H₂₀O₃Na⁺ [M+Na]⁺: 295.1305; found: 295.1303.

FT-IR (cm⁻¹): 2966, 1679, 1618, 1486, 1466, 1283, 1219, 1035, 894.

Data for **19**:

TLC: R_f = 0.3 (petroleum ether:EtOAc = 15:1).

M.p.: 63.3–63.4 °C.

$[\alpha]_D^{25}$ = +98 (c = 1.0, CHCl₃).

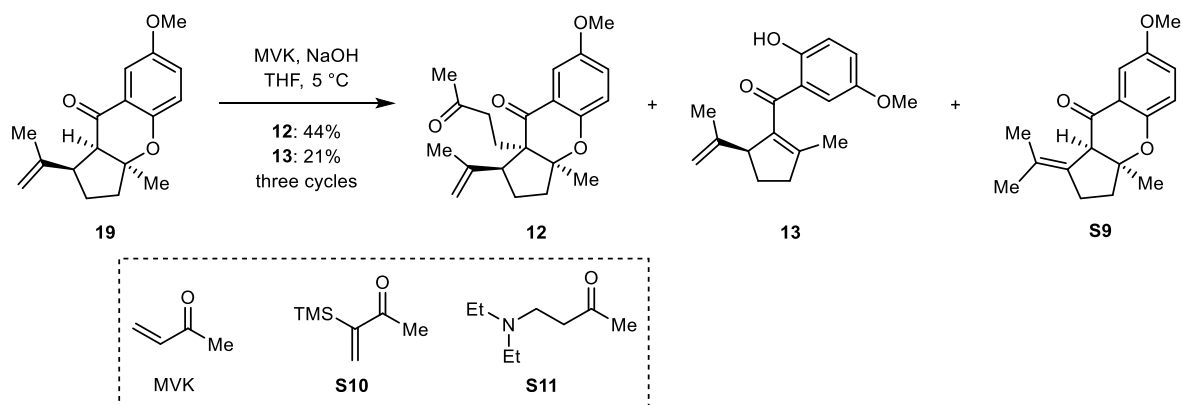
¹H NMR (500 MHz, CDCl₃) δ 7.23 (d, J = 3.2 Hz, 1H), 7.04 (dd, J = 9.0, 3.2 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 4.70 (s, 1H), 4.68 (s, 1H), 3.77 (s, 3H), 3.25 (dt, J = 11.9, 8.8 Hz, 1H), 2.86 (d, J = 12.0 Hz, 1H), 2.24 (ddd, J = 13.3, 7.3, 1.7 Hz, 1H), 2.19 – 2.08 (m, 1H), 2.01 – 1.93 (m, 1H), 1.85 – 1.71 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 193.7, 154.9, 153.7, 144.7, 125.4, 120.5, 119.8, 113.5, 106.8, 89.3, 58.4, 55.8, 50.4, 40.6, 30.3, 23.5, 23.0.

HRMS (ESI)⁺ calcd for C₁₇H₂₀O₃Na⁺ [M+Na]⁺: 295.1305; found: 295.1307.

FT-IR (cm⁻¹): 2925, 2854, 1676, 1487, 1431, 1279, 1036, 826.

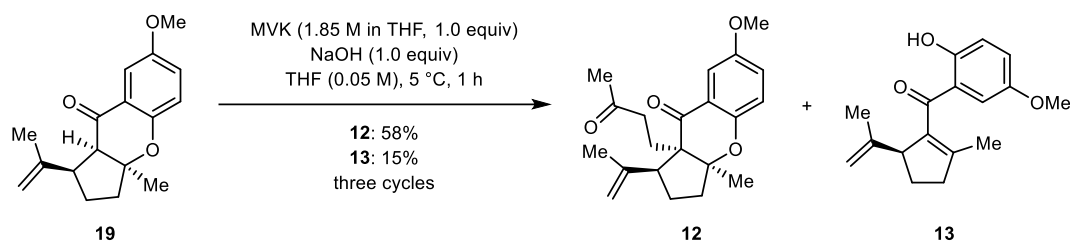
Supplementary Table 3. Optimization of Michael addition of compound 19



Entry	Conditions ^a	12 (%) ^b	13 (%) ^b	S9 (%) ^b
1	MVK, H ₂ SO ₄ , benzene, 33 to 60 °C	0	0	82
2	MVK, <i>p</i> -TsOH·H ₂ O, toluene, 33 to 60 °C	0	0	99
3	MVK, TiCl ₄ , DCM, 0 to 60 °C	0	0	72
4	MVK, BF ₃ ·Et ₂ O, DCM, 0 to 33 °C	0	0	0
5 ^d	MVK, LDA, THF, 0 °C	0	trace	0
6 ^d	MVK, LiHMDS, THF, 33 °C	0	0	0
7 ^d	MVK, DBU, THF, 50 °C	0	trace	0
8 ^d	MVK, NaOMe, MeOH, 33 °C	0	trace	0
9 ^d	MVK, EtONa, EtOH, 0 °C	0	31	0
10	MVK, <i>t</i> -BuOK, THF, 0 °C	0	80	0
11	MVK, <i>t</i> -BuOK, 18-Crown-6, THF, 0 °C	0	84	0
12	MVK, <i>t</i> -BuOLi, THF, 0 to 33 °C	complex mixture		
13	MVK, Piperidine, toluene, 60 °C		NR	
14	MVK, TMG, DCM, 55 °C		NR	
15	MVK, Et ₂ NH, CH ₃ CN, 80 °C		NR	
16	MVK, HMDS, DCM, 0 to 60 °C		NR	
17	MVK, K ₂ CO ₃ , THF, 60 °C		NR	
18 ^{c,e,f}	MVK, NaOH, THF, 5 °C	44	21	0
19 ^d	S10 , LDA, THF, -78 to 33 °C	0	<10	0
20 ^c	S10 , KOH, THF, -20 to 33 °C	16	26	0
21 ^{c,d}	S11 , KOH, THF/PhCl, -20 to 33 °C	<5	17	0
22	S11 , Et ₃ N, benzene, 100 °C		NR	

^aall reactions were performed on a 10.0 mg scale in 0.4 mL solvent except as otherwise indicated. ^bYield determined by ¹H NMR with CH₂Br₂ as an internal standard. ^cIsolated yield. ^dA large amount of **19** remains. ^e**19** (1.0 g). ^fYield of three cycles. MVK = methyl vinyl ketone. *p*-TsOH·H₂O = *p*-toluenesulfonic acid monohydrate. LDA = lithium diisopropylamide. LiHMDS = lithium bis(trimethylsilyl)amide. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene. TMG = 1,1,3,3-tetramethylguanidine. HMDS = hexamethyldisilazane.

Supplementary Table 4. Optimization of the Michael addition of compound **19 with MVK**



Entry	Conditions ^a	12 (%) ^b	13 (%) ^b	19 (%) ^b
1 ^c	MVK (1.85 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h	38	12	23
2 ^d	MVK (0.5 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h (Add dropwise via syringe pump over 20 min.)	26	12	35
3 ^d	MVK (0.5 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h (Add dropwise via syringe pump over 40 min.)	30	12	30
4 ^d	MVK (1.2 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 2 h (Add dropwise via syringe pump over 36 min.)	33	23	11
5 ^d	MVK (1.85 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h (Add dropwise via syringe pump over 30 min.)	34	12	37
6 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h (Add dropwise one portion via a syringe pump every 5 min.)	35	11	40
7 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.1 M), 5 °C, 1 h (Add dropwise one portion via a syringe pump every 20 min.)	37	12	36
8 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (0.5 equiv), THF (0.05 M), 5 °C, 1 h	32	8	48
9 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (1.0 equiv), THF (0.05 M), 5 °C, 1 h	34	8	47
10 ^{e,f,g}	MVK (1.85 M in THF, 1.0 equiv), NaOH (1.0 equiv), THF (0.05 M), 5 °C, 1 h	35 (58)	7 (15)	45 (7)
11 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (1.0 equiv), THF (0.05 M), 5 °C, 2 h	36	15	33
12 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (2.0 equiv), THF (0.05 M), 5 °C, 1 h	35	10	42
13 ^e	MVK (1.85 M in THF, 1.5 equiv), NaOH (1.0 equiv), THF (0.05 M), 5 °C, 1 h	38	9	27
14 ^e	MVK (1.85 M in THF, 2.0 equiv), NaOH (1.0 equiv), THF (0.05 M), 5 °C, 40 min	35	7	20
15 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (1.0 equiv), THF/PhMe (0.05 M), 5 °C, 1 h	31	4	51
16 ^e	MVK (1.85 M in THF, 1.0 equiv), NaOH (1.0 equiv), THF/PhCl (0.05 M), 5 °C, 1 h	31	6	52
17 ^e	MVK (1.85 M in THF, 1.0 equiv), KOH (1.0 equiv), THF/PhCl (0.05 M), 5 °C, 4 h	33	14	39
18 ^e	MVK (1.85 M in THF, 1.0 equiv), KOH (1.0 equiv), THF (0.05 M), 5 °C, 1 h	42	19	24

^aall reactions were performed on a 165 mg scale in 6.1 mL solvent except as otherwise indicated. ^bIsolated yield. ^cGeneral procedure A. ^dGeneral procedure B. ^eGeneral procedure C. ^f**19** (1.0 g). ^gYield of three cycles (in parentheses).

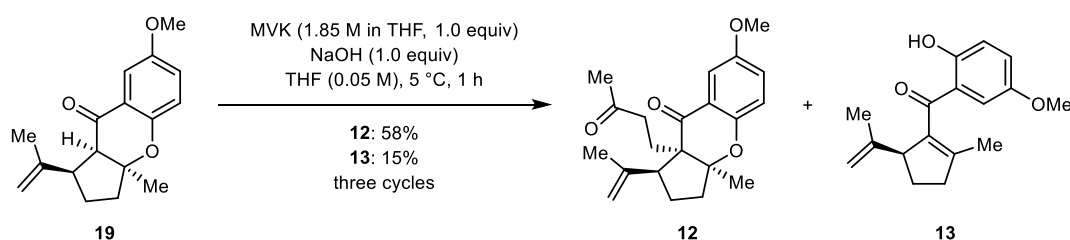
General procedure A: To a solution of **19** (165 mg, 0.606 mmol, 1.0 equiv) in THF (6.1 mL) was added solid NaOH (12.1 mg, 0.303 mmol, 0.5 equiv) at 5 °C, and the mixture was stirred at this temperature for 5 min. A solution of MVK (1.85 M in THF, 109 μ L, 0.202 mmol, 0.33 equiv) was added dropwise to the reaction mixture. After stirring for 5 min, another portion of the MVK solution (1.85 M in THF, 109 μ L, 0.202 mmol, 0.33 equiv) was added dropwise to the reaction mixture. After stirring for 5 min, a third portion of the MVK solution (1.85 M in THF, 109 μ L, 0.202 mmol, 0.33 equiv) was added dropwise to the reaction mixture, and stirring was continued for another 1 h at 5 °C. The reaction mixture was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue

was purified by silica gel column chromatography (petroleum ether:EtOAc = 60:1→30:1→8:1) to afford **12** (78.2 mg, 38% yield) as a yellow oil, **13** (20.4 mg, 12% yield) and **19** (38.0 mg, 23% yield).

General procedure B: To a solution of **19** (165 mg, 0.606 mmol, 1.0 equiv) in THF (6.1 mL) was added solid NaOH (12.1 mg, 0.303 mmol, 0.5 equiv) at 5 °C, and the mixture was stirred at this temperature for 5 min. A solution of MVK (1.85 M in THF, 327 µL, 0.606 mmol, 1.0 equiv) was added via syringe pump to the reaction mixture over 30 min, and stirring was continued for another 1 h at 5 °C. The reaction mixture was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 60:1→30:1→8:1) to afford **12** (70.1 mg, 34% yield) as a yellow oil, **13** (19.0 mg, 12% yield) and **19** (61.0 mg, 37% yield).

General procedure C: To a solution of **19** (165 mg, 0.606 mmol, 1.0 equiv) in THF (12.1 mL) was added solid NaOH (24.0 mg, 0.606 mmol, 1.0 equiv) at 5 °C, and the mixture was stirred at this temperature for 5 min. A solution of MVK (1.85 M in THF, 109 µL, 0.202 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min. After stirring for 5 min, another portion of the MVK solution (1.85 M in THF, 109 µL, 0.202 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min. After stirring for 5 min, a third portion of the MVK solution (1.85 M in THF, 109 µL, 0.202 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min, and stirring was continued for another 1 h at 5 °C. The reaction mixture was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 60:1→30:1→8:1) to afford **12** (69.9 mg, 34% yield) as a yellow oil, **13** (13.6 mg, 8% yield) and **19** (78.0 mg, 47% yield).

Preparation of Compound 12



To a solution of **19** (1.0 g, 3.68 mmol, 1.0 equiv) in THF (73.5 mL) was added solid NaOH (147 mg, 3.68 mmol, 1.0 equiv) at 5 °C, and the mixture was stirred at this temperature for 5 min. A solution of MVK (1.85 M in THF, 662 µL, 1.23 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min. After stirring for 5 min, another portion of the MVK solution (1.85 M in THF, 662 µL, 1.23 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min. After stirring for 5 min, a third portion of the MVK solution (1.85 M in THF, 662 µL, 1.23 mmol, 0.33 equiv) was added via syringe pump to the reaction mixture over 5 min, and stirring was continued for another 1 h at 5 °C. The reaction mixture was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 60:1→30:1→8:1) to afford **12** (441 mg, 35% yield) as a yellow oil, **13** (73.0 mg, 7% yield) and **19** (446 mg, 45% yield). This procedure was repeated another two times to give **12** as a yellow oil (294 mg, total 735 mg, 58% yield), **13** (74.3 mg, total 147 mg, 15% yield) and **19** (72.8 mg, 7% yield).

Data for 12:

TLC: R_f = 0.4 (petroleum ether:EtOAc = 5:1).

$[\alpha]_D^{25}$ = +65 (c = 1.0, CHCl₃).

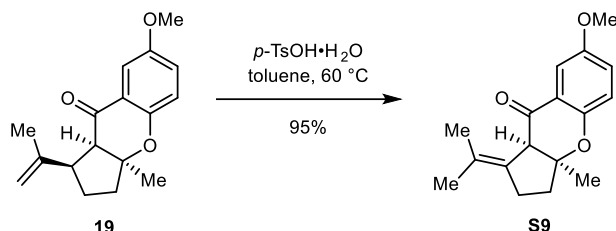
¹H NMR (500 MHz, CDCl₃) δ 7.18 (d, J = 3.1 Hz, 1H), 7.03 (dd, J = 9.0, 3.2 Hz, 1H), 6.77 (d, J = 9.0 Hz, 1H), 4.77 (s, 1H), 4.74 (s, 1H), 3.77 (s, 3H), 2.94 (ddd, J = 18.0, 10.6, 4.7 Hz, 1H), 2.73 (t, J = 8.8 Hz, 1H), 2.56 (ddd, J = 17.9, 10.4, 5.2 Hz, 1H), 2.17 – 2.09 (m, 1H), 2.12 (s, 3H), 2.06 – 1.92 (m, 3H), 1.92 – 1.83 (m, 2H), 1.60 (s, 3H), 1.42 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 208.5, 196.3, 154.0, 153.9, 144.8, 125.0, 121.9, 119.9, 114.0, 107.3, 92.2, 60.5, 55.84, 55.76, 39.6, 37.8, 30.2, 29.9, 28.1, 22.9, 21.6.

HRMS(ESI)⁺ calcd for C₂₁H₂₆O₄Na⁺ [M+Na]⁺: 365.1723; found: 365.1728.

FT-IR (cm⁻¹): 2952, 1716, 1670, 1488, 1429, 1277, 1153, 1034, 828.

Preparation of Compound S9



To a solution of **19** (20.0 mg, 0.0735 mmol, 1.0 equiv) in toluene (0.74 mL) was added *p*-TsOH·H₂O (42.0 mg, 0.221 mmol, 3.0 equiv) at 33 °C. After stirring at 60 °C for 3.5 h, the reaction was cooled down to 33 °C and quenched by saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 5:1) to afford **S9** (19.0 mg, 95% yield) as a colorless oil.

TLC: *R_f* = 0.9 (petroleum ether:EtOAc = 5:1).

[α]_D²⁴ = +239 (c = 0.2, CHCl₃).

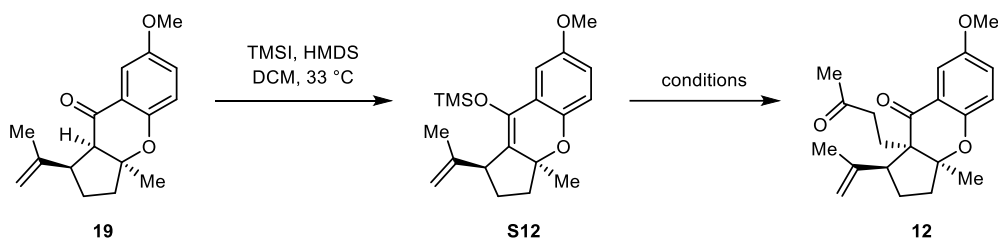
¹H NMR (500 MHz, CDCl₃) δ 7.27 (d, *J* = 3.2 Hz, 1H), 7.07 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.84 (d, *J* = 9.0 Hz, 1H), 3.78 (s, 3H), 3.37 – 3.32 (m, 1H), 2.46 – 3.36 (m, 1H), 2.36 – 2.27 (m, 1H), 2.14 (ddd, *J* = 12.8, 9.5, 6.8 Hz, 1H), 1.81 – 1.78 (m, 3H), 1.74 – 1.67 (m, 1H), 1.67 – 1.64 (m, 3H), 1.46 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 193.3, 154.1, 153.7, 130.0, 129.6, 125.4, 119.5, 119.0, 107.6, 87.9, 57.8, 55.9, 35.5, 27.8, 24.6, 21.8, 21.6.

HRMS(ESI)⁺ calcd for C₁₇H₂₀O₃Na⁺ [M+Na]⁺: 295.1305; found: 295.1308.

FT-IR (cm⁻¹): 2932, 1676, 1488, 1429, 1280, 1230, 1034, 824, 736.

Supplementary Table 5. Failed Michael addition of compound 19

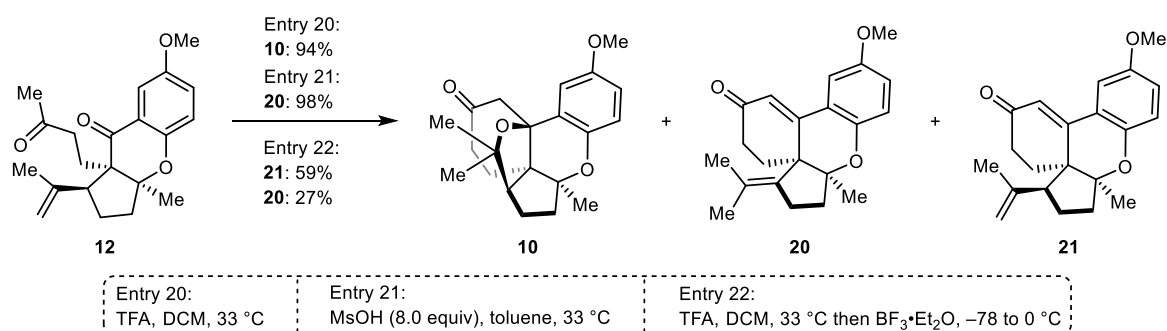


Entry	Conditions	Result
1	MVK, <i>i</i> -PrOH, BF ₃ ·Et ₂ O, MeNO ₂ , DCM, –78 to 0 °C	NP
2	MVK, MeLi, THF, –50 to –78 °C	NP
3	MVK, ZnCl ₂ , Et ₂ O, 0 to 33 °C	NP

NP = no product.

Note: Only the hydrolysis product **19** and the subsequent retro-oxa-Michael product **13** were observed.

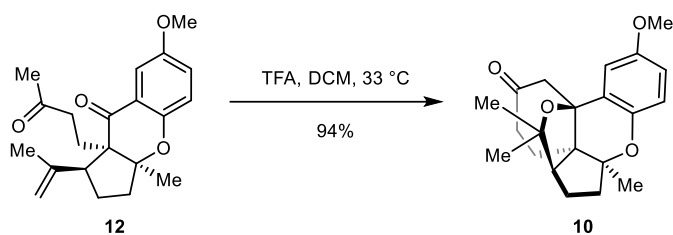
Supplementary Table 6. Optimization of acid-dependent divergent cyclization of compound 12



Entry	Conditions	10 (%) ^a	20 (%) ^a	21 (%) ^a
1	LiHMDS, THF, -78 °C	0	0	0
2	LDA, THF, -78 to 0 °C		NR	
3	<i>t</i> -BuOK, <i>t</i> -BuOH, 33 °C	0	0	0
4	<i>t</i> -BuOK, THF, 0 °C	0	0	0
5	NaOMe, MeOH, 0 to 100 °C	0	0	0
6	NaOH, EtOH, 0 to 100 °C	0	0	0
7	KOH, MeOH, 80 °C		complex mixture	
8	LiOH, <i>i</i> -PrOH, 100 °C		NR	
9	Cs ₂ CO ₃ , CH ₃ CN, 100 °C	0	0	0
10	K ₂ CO ₃ , MeOH, 100 °C		NR	
11	NaH, THF, 0 to 60 °C	0	0	0
12	Morpholine, EtOH, 100 °C		NR	
13	Piperidine, AcOH, benzene, 100 °C		NR	
14	Pyrrolidine, AcOH, benzene, 100 °C		NR	
15	<i>L</i> -proline, MeOH, 100 °C		NR	
16	H ₂ SO ₄ , DCM, 33 °C	0	0	0
17	MsOH (1.7 equiv), toluene, 33 °C	37	39	17
18	BF ₃ •Et ₂ O, THF, 0 to 80 °C	52	0	0
19	<i>p</i> -TsOH•H ₂ O, toluene, 50 °C	81	0	0
20	TFA, DCM, 33 °C	94	0	0
21	MsOH (8.0 equiv), toluene, 33 °C	0	98	0
22	TFA, DCM, 33 °C then BF ₃ •Et ₂ O, -78 to 0 °C	0	27	59

^aIsolated yield.

Preparation of Compound 10



To a solution of **12** (200 mg, 0.585 mmol, 1.0 equiv) in DCM (5.8 mL) was added trifluoroacetic acid (TFA, 52.0 μ L, 0.701 mmol, 1.2 equiv) at 33 $^{\circ}$ C. After stirring at same temperature for 29 h, another portion of TFA (9.0 μ L, 0.117 mmol, 0.2 equiv) was added at 33 $^{\circ}$ C. After stirring at same temperature for 14 h, a third portion of TFA (9.0 μ L, 0.117 mmol, 0.2 equiv) was added at 33 $^{\circ}$ C. After stirring at same temperature for 5.5 h, the reaction was quenched with saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 10:1 $\rightarrow$ 5:1) to afford **10** (188 mg, 94% yield) as a yellow solid.

TLC: $R_f = 0.7$ (petroleum ether:EtOAc = 3:1).

M.p.: 142.0–143.7 °C.

$$[\alpha]_D^{25} = +133 \text{ (c = 0.2, CHCl}_3\text{)}.$$

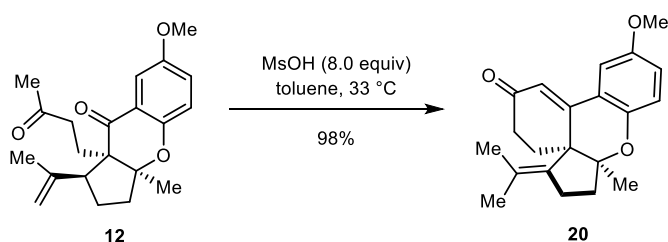
¹H NMR (500 MHz, CDCl₃) δ 6.98 (d, *J* = 2.8 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.9, 2.8 Hz, 1H), 3.75 (s, 3H), 2.61 (d, *J* = 16.2 Hz, 1H), 2.57 – 2.40 (m, 4H), 2.27 (td, *J* = 13.8, 4.3 Hz, 1H), 2.07 – 1.94 (m, 1H), 1.78 (dt, *J* = 13.8, 3.5 Hz, 1H), 1.70 – 1.58 (m, 3H), 1.48 (s, 3H), 1.28 (s, 3H), 0.98 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 210.0, 154.7, 145.4, 131.8, 119.1, 115.4, 110.5, 87.4, 82.9, 80.5, 61.5, 59.8, 55.8, 52.1, 39.1, 35.2, 31.2, 29.9, 24.7, 23.7, 23.1.

HRMS(ESI)⁺ calcd for C₂₁H₂₇O₄⁺ [M+H]⁺: 343.1904; found: 343.1906.

FT-IR (cm⁻¹): 2964, 1724, 1492, 1240, 1134, 1013, 941, 815.

Preparation of Compound 20



To a solution of **12** (20.0 mg, 0.0585 mmol, 1.0 equiv) in toluene (0.59 mL) was added methanesulfonic acid (MsOH, 30.0 μ L, 0.468 mmol, 8.0 equiv) at 33 $^{\circ}$ C. After stirring at same temperature for 1 h, the reaction was quenched with saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 8:1) to afford **20** (18.6 mg, 98%) as a yellow oil.

TLC: $R_f = 0.4$ (petroleum ether:EtOAc = 5:1).

$$[\alpha]_D^{26} = -663 \text{ (c = 1.0, CHCl}_3\text{)}.$$

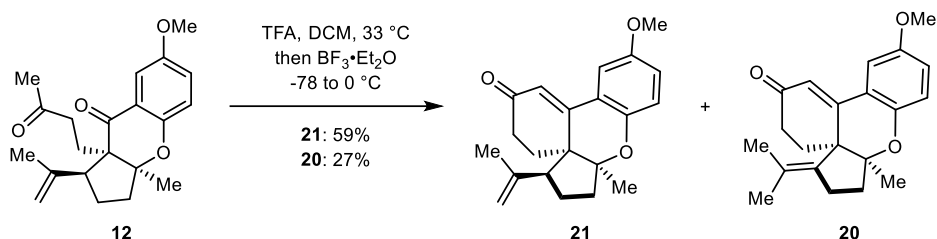
¹H NMR (400 MHz, CDCl₃) δ 7.01 (d, *J* = 2.9 Hz, 1H), 6.91 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 6.58 (s, 1H), 3.77 (s, 3H), 2.69 – 2.53 (m, 2H), 2.48 – 2.37 (m, 2H), 2.08 (ddd, *J* = 13.8, 9.2, 2.0 Hz, 1H), 2.01 – 1.90 (m, 2H), 1.83 (ddd, *J* = 12.9, 4.9, 2.9 Hz, 1H), 1.54 (s, 3H), 1.53 (s, 3H), 1.24 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 200.1, 155.4, 153.6, 149.1, 133.6, 127.3, 122.0, 121.0, 119.0, 118.0, 108.0, 91.0, 55.9, 52.0, 34.7, 34.4, 30.9, 28.4, 23.5, 19.1, 17.7.

HRMS(ESI)⁺ calcd for C₂₁H₂₄O₃Na⁺ [M+Na]⁺: 347.1618; found: 347.1620.

FT-IR (cm⁻¹): 2926, 2855, 1662, 1594, 1489, 1277, 1243, 1168, 1037, 795.

Preparation of Compound 21



To a solution of **12** (100 mg, 0.292 mmol, 1.0 equiv) in DCM (2.9 mL) was added TFA (26.0 μL, 0.351 mmol, 1.2 equiv) at 33 °C. After stirring at same temperature for 23 h, BF₃·Et₂O (148 μL, 1.17 mmol, 4.0 equiv) was added at –78 °C. After stirring at 0 °C for 40 min, the reaction was quenched with saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 30:1) to afford **21** (56.0 mg, 59% yield) as a yellow solid and **20** (25.4 mg, 27% yield) as a yellow oil.

Data for 21:

TLC: *R_f* = 0.7 (petroleum ether:EtOAc = 3:1).

M.p.: 116.9–118.3 °C.

[α]_D²⁵ = –133 (*c* = 0.2, CHCl₃).

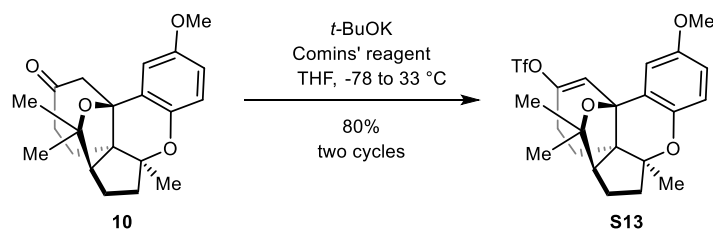
¹H NMR (500 MHz, CDCl₃) δ 7.00 (d, *J* = 2.9 Hz, 1H), 6.88 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.68 (d, *J* = 8.9 Hz, 1H), 6.55 (s, 1H), 4.61 (s, 2H), 3.75 (s, 3H), 3.13 (t, *J* = 8.0 Hz, 1H), 2.75 (ddd, *J* = 18.5, 14.1, 4.8 Hz, 1H), 2.53 (ddd, *J* = 17.8, 4.8, 2.3 Hz, 1H), 2.28 – 2.12 (m, 2H), 2.10 – 1.96 (m, 3H), 1.79 (ddd, *J* = 12.8, 4.9, 2.3 Hz, 1H), 1.40 (s, 3H), 1.27 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 199.1, 153.6, 152.5, 149.4, 145.1, 121.0, 120.6, 119.4, 114.4, 106.5, 89.0, 55.7, 52.9, 51.5, 37.9, 33.9, 33.4, 28.0, 23.0, 19.2 (one signal is missing due to insufficient relaxation time).

HRMS(ESI)⁺ calcd for C₂₁H₂₅O₃⁺ [M+H]⁺: 325.1798; found: 325.1799.

FT-IR (cm⁻¹): 2925, 2853, 1659, 1589, 1491, 1240, 1167, 1039, 819.

Preparation of Compound S13



To a solution of **10** (50.0 mg, 0.146 mmol, 1.0 equiv) in THF (1.5 mL) was added *t*-BuOK (1.0 M in THF, 0.18 mL, 0.175 mmol, 1.2 equiv) at –78 °C. The resulting solution was stirred at –78 °C for 10 min. A solution of Comins' reagent (68.8 mg, 0.175 mmol, 1.2 equiv)

in THF (0.75 mL) was added to the reaction mixture at $-78\text{ }^{\circ}\text{C}$. After stirring at $33\text{ }^{\circ}\text{C}$ for 1.5 h, the reaction was quenched by saturated aqueous NH_4Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 50:1→30:1→5:1) to afford **S13** (41.8 mg, 60% yield) as a yellow oil and **10** (17.0 mg, 34% yield). This procedure was repeated one more time to give **S13** as a yellow oil (13.8 mg, total 55.6 mg, 80% yield).

TLC: R_f = 0.8 (petroleum ether:EtOAc = 9:1).

$[\alpha]_D^{25}$ = +27 (c = 0.2, CHCl_3).

^1H NMR (500 MHz, C_6D_6) δ 7.09 (d, J = 2.9 Hz, 1H), 6.82 (d, J = 8.7 Hz, 1H), 6.60 (dd, J = 8.7, 3.0 Hz, 1H), 6.04 (s, 1H), 3.30 (s, 3H), 2.22 – 2.08 (m, 2H), 2.02 – 1.93 (m, 2H), 1.56 – 1.48 (m, 1H), 1.45 (ddd, J = 14.0, 7.0, 4.8 Hz, 1H), 1.41 – 1.27 (m, 3H), 1.22 (s, 3H), 1.09 (s, 3H), 1.05 (s, 3H).

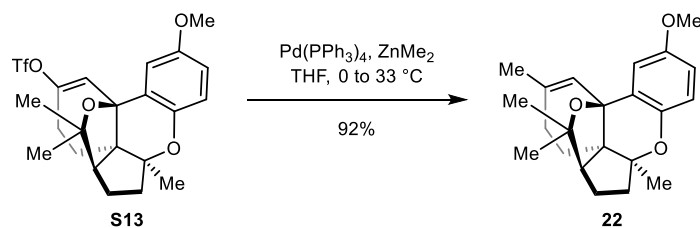
^{13}C NMR (125 MHz, C_6D_6) δ 155.3, 149.5, 147.4, 131.3, 123.1, 119.7, 119.1 (q, J = 318.6 Hz), 114.8, 111.9, 89.1, 83.4, 79.5, 60.8, 60.7, 55.2, 40.3, 32.6, 30.5, 26.0, 25.8, 24.5, 23.4.

^{19}F NMR (471 MHz, CDCl_3) δ -73.70.

HRMS(ESI) $^+$ calcd for $\text{C}_{22}\text{H}_{25}\text{F}_3\text{O}_6\text{SNa}^+$ [$\text{M}+\text{Na}$] $^+$: 497.1216; found: 497.1220.

FT-IR (cm^{-1}): 2922, 2850, 1491, 1419, 1212, 1141, 882, 758.

Preparation of Compound 22



To a suspension of anhydrous ZnCl_2 (546 mg, 4.01 mmol) in THF (8.0 mL) was added MeMgBr (3.0 M in Et_2O , 3.0 mL, 9.0 mmol) at $0\text{ }^{\circ}\text{C}$, and the mixture was stirred at this temperature for 1 h. The solids were allowed to settle before the solution was used¹³. To a solution of **S13** (26.7 mg, 0.0563 mmol, 1.0 equiv) in THF (0.56 mL) was added $\text{Pd(PPh}_3)_4$ (13.0 mg, 0.0113 mmol, 0.2 equiv) at $0\text{ }^{\circ}\text{C}$, and stirred at this temperature for 5 min, freshly prepared ZnMe_2 (0.364 M in THF, 1.5 mL, 0.563 mmol, 10.0 equiv) was added. After stirring at $33\text{ }^{\circ}\text{C}$ for 1.5 h, the reaction was quenched by careful addition of pH 7 buffer at $0\text{ }^{\circ}\text{C}$. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 50:1→20:1) to afford **22** (17.6 mg, 92% yield) as a yellow oil.

TLC: R_f = 0.7 (petroleum ether:EtOAc = 9:1).

$[\alpha]_D^{25}$ = +40 (c = 0.2, CHCl_3).

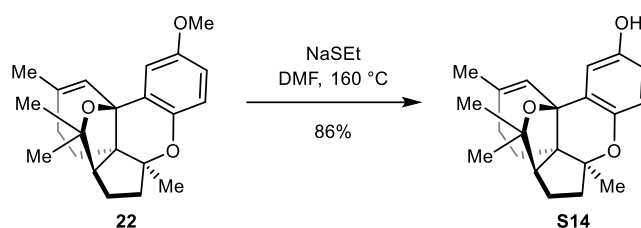
^1H NMR (500 MHz, CDCl_3) δ 7.07 (d, J = 2.9 Hz, 1H), 6.72 (d, J = 8.7 Hz, 1H), 6.67 (dd, J = 8.7, 2.9 Hz, 1H), 5.49 – 5.45 (m, 1H), 3.78 (s, 3H), 2.42 – 2.36 (m, 1H), 2.24 – 2.06 (m, 2H), 1.98 – 1.88 (m, 2H), 1.82 – 1.74 (m, 1H), 1.72 – 1.60 (m, 3H), 1.69 (s, 3H), 1.38 (s, 3H), 1.31 (s, 3H), 1.12 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 154.5, 147.1, 135.6, 133.7, 126.5, 118.9, 113.6, 111.8, 89.1, 82.5, 78.4, 62.5, 59.8, 55.9, 40.9, 33.0, 31.3, 28.2, 25.9, 24.5, 23.8, 23.7.

HRMS(ESI) $^+$ calcd for $\text{C}_{22}\text{H}_{29}\text{O}_3^+$ [$\text{M}+\text{H}$] $^+$: 341.2111; found: 341.2111.

FT-IR (cm^{-1}): 3053, 2924, 1491, 1265, 1147, 1042, 742.

Preparation of Compound S14



To a solution of **22** (5.0 mg, 0.0147 mmol, 1.0 equiv) in DMF (0.2 mL) was added a suspension of NaSEt (29.0 mg, 0.2939 mmol, 20.0 equiv) in DMF (0.4 mL) at 33 °C, the resulting mixture was degassed by freeze-pump-thaw cycling (three times). After stirring at 160 °C for 12 h, the reaction mixture was cooled down to 33 °C and quenched by brine. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 5:1) to afford **S14** (4.1 mg, 86% yield) as a yellow oil.

TLC: $R_f = 0.2$ (petroleum ether:EtOAc = 9:1).

$$[\alpha]_D^{25} = +56 \text{ (c = 0.2, CHCl}_3\text{)}.$$

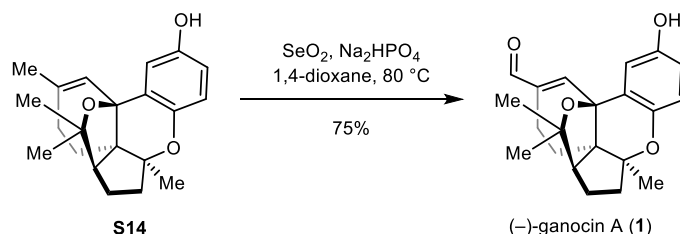
¹H NMR (500 MHz, CDCl₃) δ 7.01 (d, *J* = 3.0 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 6.56 (dd, *J* = 8.5, 2.9 Hz, 1H), 5.49 (s, 1H), 5.05 (brs, 1H), 2.44 – 2.38 (m, 1H), 2.21 – 2.09 (m, 2H), 1.99 – 1.86 (m, 2H), 1.81 – 1.56 (m, 4H), 1.69 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H), 1.15 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 150.3, 147.1, 135.9, 133.4, 126.3, 119.1, 114.9, 113.5, 89.3, 82.7, 78.4, 62.2, 59.9, 40.9, 32.9, 31.1, 28.1, 25.9, 24.6, 23.8, 23.5.

HRMS(ESI)⁺ calcd for C₂₁H₂₇O₃⁺ [M+H]⁺: 327.1955; found: 327.1960.

FT-IR (cm⁻¹): 3305, 2967, 2928, 1492, 1447, 1276, 1261, 971, 750.

Preparation of (–)-ganocin A (1)



To a solution of **S14** (4.8 mg, 0.0148 mmol, 1.0 equiv) in 1,4-dioxane (0.2 mL) were added SeO₂ (8.2 mg, 0.0740 mmol, 5.0 equiv) and Na₂HPO₄ (10.5 mg, 0.0740 mmol, 5.0 equiv) at 33 °C. After stirring at 80 °C for 3 h, another portion of SeO₂ (8.2 mg, 0.0740 mmol, 5.0 equiv) and Na₂HPO₄ (10.5 mg, 0.0740 mmol, 5.0 equiv) was added at 33 °C. After stirring at 80 °C for 1.5 h, a third portion of SeO₂ (4.9 mg, 0.0444 mmol, 3.0 equiv) and Na₂HPO₄ (6.3 mg, 0.0444 mmol, 3.0 equiv) was added at 33 °C. After stirring at 80 °C for 30 min, the reaction mixture was cooled to 33 °C and filtered through a pad of celite. The filtrate was concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 2:1) to afford (–)-ganocin A (**1**) (3.8 mg, 75% yield) as a colorless oil.

TLC: $R_f = 0.5$ (petroleum ether:EtOAc = 2:1).

$$[\alpha]_D^{26} = -8 \text{ (c = 0.1, CHCl}_3\text{)}.$$

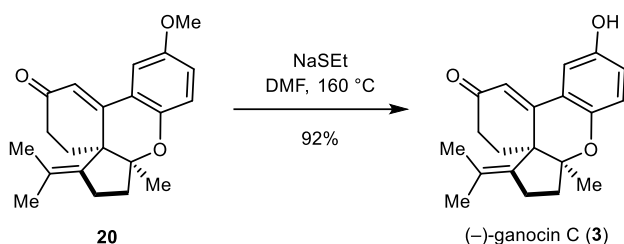
¹H NMR (500 MHz, CDCl₃) δ 9.44 (s, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 6.66 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.64 – 6.61 (m, 1H), 2.44 – 2.38 (m, 2H), 2.25 – 2.16 (m, 1H), 2.16 – 2.06 (m, 2H), 1.76 – 1.64 (m, 3H), 1.62 – 1.56 (m, overlap with H₂O, 1H), 1.45 (s, 3H), 1.32 (s, 3H), 1.18 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 193.5, 151.1, 150.3, 146.8, 139.3, 130.5, 119.5, 116.0, 113.5, 88.6, 84.0, 78.1, 62.2, 60.7, 39.5, 32.6, 31.1, 25.8, 24.0, 23.5, 19.3.

HRMS(ESI)⁺ calcd for C₂₁H₂₄O₄Na⁺ [M+Na]⁺: 363.1567; found: 363.1566.

FT-IR (cm⁻¹): 3345, 2923, 1685, 1493, 1449, 1182, 1144, 878, 790.

Preparation of (–)-ganocin C (3)



To a solution of **20** (20.0 mg, 0.0617 mmol, 1.0 equiv) in DMF (0.2 mL) was added a suspension of NaSEt (109 mg, 1.23 mmol, 20.0 equiv) in DMF (0.4 mL) at 33 °C, the resulting mixture was degassed by freeze-pump-thaw cycling (three times). After stirring at 160 °C for 7 h, the reaction was cooled down to 33 °C and quenched by brine. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 3:1) to afford (–)-ganocin C (**3**) (17.6 mg, 92% yield) as a yellow foam.

TLC: *R_f* = 0.2 (petroleum ether:EtOAc = 3:1).

$[\alpha]_D^{24} = -288$ (c = 0.13, MeOH).

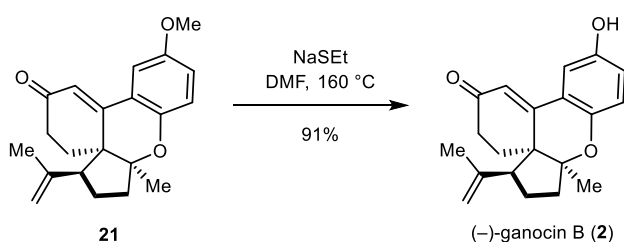
¹H NMR (500 MHz, C₅D₅N) δ 7.64 (d, *J* = 2.9 Hz, 1H), 7.15 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.97 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 2.68 – 2.56 (m, 2H), 2.49 (dt, *J* = 16.3, 3.5 Hz, 1H), 2.36 – 2.28 (m, 1H), 2.06 (ddd, *J* = 13.7, 9.3, 1.8 Hz, 1H), 1.92 – 1.82 (m, 2H), 1.68 (ddd, *J* = 13.0, 4.7, 2.9 Hz, 1H), 1.54 (s, 3H), 1.36 (s, 3H), 1.22 (s, 3H).

¹³C NMR (125 MHz, C₅D₅N) δ 198.6, 154.4, 152.5, 147.9, 134.4, 126.5, 122.4, 122.0, 118.90, 118.86, 111.3, 90.5, 52.2, 34.52, 34.46, 30.9, 28.4, 23.0, 18.7, 17.3.

HRMS(ESI)⁺ calcd for C₂₀H₂₃O₃⁺ [M+H]⁺: 311.1642; found: 311.1644.

FT-IR (cm⁻¹): 3304, 2917, 1641, 1585, 1490, 1458, 1170, 872, 736.

Preparation of (–)-ganocin B (2)



To a solution of **21** (30.0 mg, 0.0926 mmol, 1.0 equiv) in DMF (0.2 mL) was added a suspension of NaSEt (82.0 mg, 0.926 mmol, 10.0 equiv) in DMF (0.9 mL) at 33 °C, the resulting mixture was degassed by freeze-pump-thaw cycling (three times). After stirring at 160 °C for 5.5 h, the reaction was cooled down to 33 °C and quenched by brine. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 5:1→2:1) to afford (–)-ganocin B (**2**) (26.3 mg, 91% yield) as a yellow oil.

TLC: *R_f* = 0.2 (petroleum ether:EtOAc = 3:1).

$[\alpha]_D^{22} = -177$ (c = 0.13, MeOH).

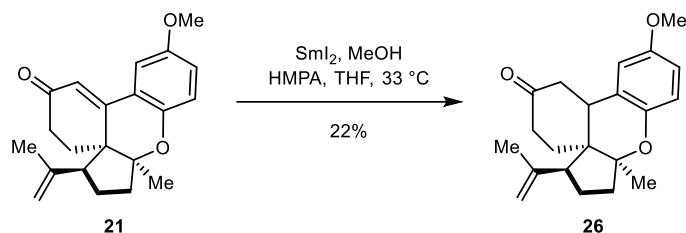
¹H NMR (500 MHz, C₅D₅N) δ 7.63 (d, *J* = 3.0 Hz, 1H), 7.20 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.91 (s, 1H), 4.79 (s, 1H), 4.72 – 4.68 (m, 1H), 3.12 (t, *J* = 8.1 Hz, 1H), 2.79 (ddd, *J* = 18.4, 14.0, 4.9 Hz, 1H), 2.55 (ddd, *J* = 18.0, 4.9, 2.2 Hz, 1H), 2.30 – 2.19 (m, 1H), 2.15 – 2.06 (m, 1H), 1.98 – 1.83 (m, 3H), 1.59 (ddd, *J* = 12.8, 4.9, 2.3 Hz, 1H), 1.46 (s, 3H), 1.24 (s, 3H).

¹³C NMR (125 MHz, C₅D₅N) δ 198.0, 152.7, 151.8, 148.4, 145.9, 121.9, 120.9, 120.5, 119.4, 114.3, 109.9, 88.6, 53.1, 51.7, 37.8, 34.0, 33.6, 28.2, 22.5, 18.9.

HRMS(ESI)⁺ calcd for C₂₀H₂₃O₃⁺ [M+H]⁺: 311.1642; found: 311.1645.

FT-IR (cm⁻¹): 3293, 2949, 1638, 1582, 1491, 1458, 1247, 1170, 871.

Preparation of Compound 26



To a solution of **21** (5.0 mg, 0.0154 mmol, 1.0 equiv) in THF (0.2 mL) were added HMPA (27.0 μL, 0.154 mmol, 10.0 equiv) and MeOH (3.0 μL, 0.0742 mmol, 4.8 equiv) at 33 °C, the resulting mixture was degassed by freeze-pump-thaw cycling (three times). SmI₂ (0.1 M in THF, 34.0 μL, 0.0339 mmol, 2.2 equiv) was added to the reaction mixture at 33 °C. After stirring at same temperature for 40 min, the reaction was quenched with saturated aqueous NH₄Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 5:1) to afford **26** (1.1 mg, 22% yield) as a colorless oil and **21** (1.7 mg, 34% yield).

Data for **26**:

TLC: *R_f* = 0.6 (petroleum ether:EtOAc = 5:1).

[α]_D²⁵ = +86 (c = 0.1, CHCl₃).

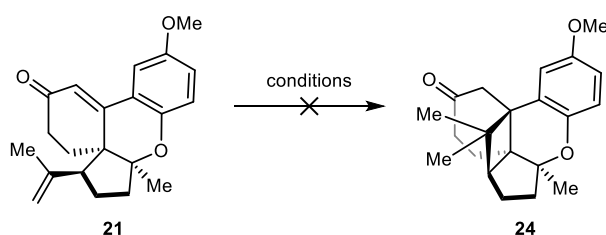
¹H NMR (500 MHz, CDCl₃) δ 6.72 – 6.66 (m, 2H), 6.52 – 6.49 (m, 1H), 4.69 – 4.65 (m, 2H), 3.73 (s, 3H), 3.13 (dd, *J* = 13.4, 4.8 Hz, 1H), 3.06 – 2.96 (m, 2H), 2.90 (ddd, *J* = 15.5, 4.8, 1.9 Hz, 1H), 2.80 (ddd, *J* = 16.2, 13.1, 7.0 Hz, 1H), 2.60 – 2.52 (m, 1H), 2.10 – 2.03 (m, 1H), 2.02 – 1.95 (m, 1H), 1.93 – 1.85 (m, 1H), 1.84 – 1.73 (m, 3H), 1.31 (s, 3H), 1.20 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 210.7, 153.4, 148.5, 146.6, 124.2, 117.0, 116.8, 113.2, 109.9, 88.4, 55.9, 53.5, 47.8, 40.7, 38.3, 37.9, 37.8, 36.5, 28.5, 20.8, 20.6.

HRMS(ESI)⁺ calcd for C₂₁H₂₆O₃Na⁺ [M+Na]⁺: 349.1774; found: 349.1773.

FT-IR (cm⁻¹): 3433, 2923, 2853, 1712, 1493, 1264, 1039, 803, 744.

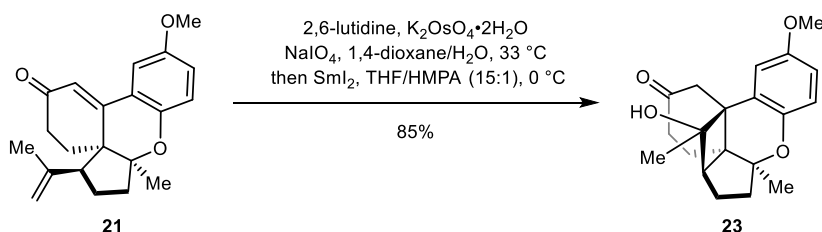
Supplementary Table 7. Failed attempts on radical-trapping reagents



Entry	Conditions	Result
1	Sml ₂ , 4-bromobenzenethiol, HMPA, THF, 0 °C	NP
2	Sml ₂ , <i>t</i> -BuOH, 4-bromobenzenethiol, HMPA, THF, 33 °C	NP
3	Sml ₂ , <i>t</i> -BuOH, 4-mercaptophenol, HMPA, THF, 33 °C	NP
4	Sml ₂ , <i>t</i> -BuOH, toluenethiol, HMPA, THF, 33 °C	NP
5	Sml ₂ , <i>t</i> -BuOH, 4-mercaptopyridine, HMPA, THF, 33 °C	NP
6	Sml ₂ , <i>t</i> -BuOH, CCl ₄ , HMPA, THF, 33 °C	NP
7	Sml ₂ , <i>t</i> -BuOH, BrCCl ₃ , HMPA, THF, 33 °C	NP
8	Sml ₂ , <i>t</i> -BuOH, C ₄ F ₉ I, HMPA, THF, 33 °C	NP

Note: NP = no detectable **24**. Only ketone **26** and compounds with unknown structures were observed.

Preparation of Compound 23



To a solution of **21** (160 mg, 0.494 mmol, 1.0 equiv) in 1,4-dioxane (18.5 mL) and H₂O (6.2 mL) were added 2,6-lutidine (118 μ L, 0.987 mmol, 2.0 equiv), K₂OsO₄·2H₂O (18.0 mg, 0.0494 mmol, 0.1 equiv) and NaIO₄ (422 mg, 1.97 mmol, 4.0 equiv) at 33 °C. After stirring at same temperature for 1.5 h, the reaction mixture was concentrated under reduced pressure and diluted with EtOAc. The resulting mixture was filtered through a pad of celite. The filtrate was concentrated under reduced pressure. The crude product was evenly divided into four portions, and each portion was dissolved in THF (4.0 mL) and HMPA (0.27 mL). The resulting mixture was degassed by freeze-pump-thaw cycling (three times). Sml₂ (0.1 M in THF, 2.5 mL, 0.247 mmol, 2.0 equiv) was added to the reaction mixture at 0 °C. After stirring at same temperature for 40 min, another portion of Sml₂ (0.1 M in THF, 1.25 mL, 0.125 mmol, 1.01 equiv) was added at 0 °C. After stirring for 30 min, a third portion of Sml₂ (0.1 M in THF, 1.25 mL, 0.125 mmol, 1.01 equiv) was added at 0 °C. After stirring for 40 min, a fourth portion of Sml₂ (0.1 M in THF, 0.6 mL, 0.0617 mmol, 0.5 equiv) was added at 0 °C. After stirring at same temperature for 1 h, the reaction was quenched by saturated aqueous NH₄Cl solution. The reaction was repeated another 3 times with same scale and the combined reaction mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 50:1→20:1) to afford **23** (137mg, 85% yield) as a yellow oil.

TLC: *R*_f = 0.7 (petroleum ether:EtOAc = 1:1).

[α]_D²⁵ = +5 (c = 0.2, CHCl₃).

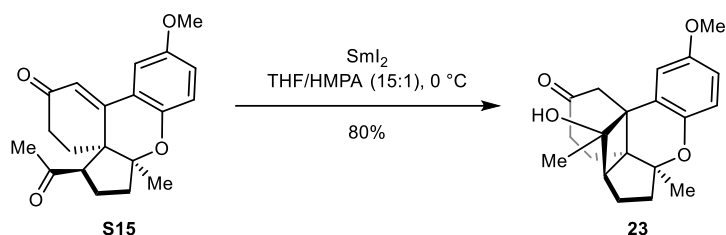
¹H NMR (500 MHz, CDCl₃) δ 6.87 (d, *J* = 8.8 Hz, 1H), 6.75 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.54 (d, *J* = 2.9 Hz, 1H), 3.76 (s, 3H), 3.11 (d, *J* = 16.1 Hz, 1H), 2.65 – 2.61 (m, 1H), 2.58 (d, *J* = 16.1 Hz, 1H), 2.50 (brs, 1H), 2.49 – 2.43 (m, 2H), 2.17 – 2.08 (m, 1H), 2.01 – 1.91 (m, 2H), 1.77 (dt, *J* = 14.4, 5.4 Hz, 1H), 1.73 – 1.65 (m, 2H), 1.29 (s, 3H), 1.28 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 211.7, 155.1, 146.7, 128.6, 120.1, 113.7, 112.3, 87.5, 75.1, 55.8, 51.5, 47.6, 47.2, 47.1, 39.2, 36.2, 25.5, 25.4, 21.95, 21.93.

HRMS(ESI)⁺ calcd for C₂₀H₂₄O₄Na⁺ [M+Na]⁺: 351.1567; found: 351.1568.

FT-IR (cm⁻¹): 3726, 3481, 2924, 2853, 1709, 1492, 1218, 960, 767.

Supplementary Table 8. Optimization of Sml₂-mediated 4-exo-trig reductive ketone–enone coupling of **S15**

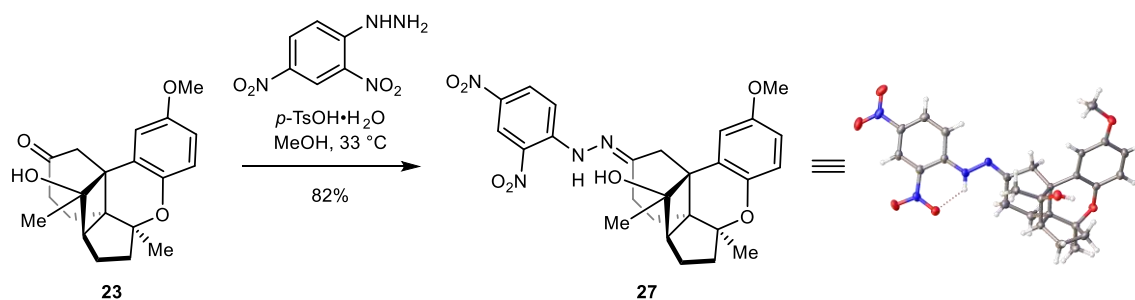


Entry	Conditions	23 (%) ^a
1	Sml ₂ , THF, 0 °C	42
2	Sml ₂ , THF/H ₂ O (15:1), 0 °C	36
3	Sml ₂ , THF/MeOH (3:1), 0 °C	33
4	Sml ₂ , THF/ <i>t</i> -BuOH (15:1), 0 °C	46
5	Sml ₂ , THF/ <i>t</i> -BuOH/HMPA (30:1:2), 0 °C	73
6	Sml ₂ , THF/HMPA (15:1), 0 °C	80

^aIsolated yield.

Note: Purified compound **S15** was employed for the optimization of the above reaction conditions.

Preparation of Compound 27



To a solution of **23** (8.0 mg, 0.0244 mmol, 1.0 equiv) in MeOH (0.41 mL) were added *p*-TsOH·H₂O (3.7 mg, 0.0195 mmol, 0.8 equiv) and 2,4-dinitrophenylhydrazine (7.2 mg, 0.0366 mmol, 1.5 equiv) at 33 °C. After stirring at same temperature for 1 h, the reaction mixture was concentrated under reduced pressure and diluted with EtOAc. The resulting mixture was quenched with saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 1:1) to afford **27** (10.1 mg, 82% yield) as a red solid.

TLC: *R_f* = 0.8 (petroleum ether:EtOAc = 1:1).

M.p.: 216–217 °C.

$[\alpha]_D^{23} = -84$ (c = 0.1 CHCl₃).

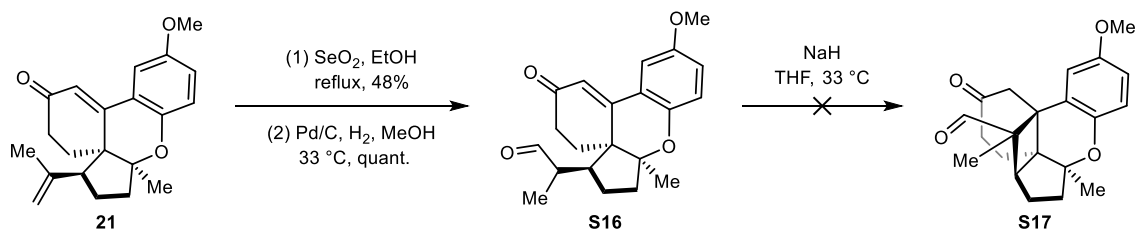
¹H NMR (500 MHz, CDCl₃) δ 10.97 (s, 1H), 9.12 (d, *J* = 2.6 Hz, 1H), 8.29 (dd, *J* = 9.6, 2.6 Hz, 1H), 7.90 (d, *J* = 9.6 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.74 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.70 (d, *J* = 3.0 Hz, 1H), 3.79 (s, 3H), 3.32 (d, *J* = 15.0 Hz, 1H), 2.85 (d, *J* = 15.0 Hz, 1H), 2.68 – 2.55 (m, 3H), 2.51 (dt, *J* = 18.6, 6.5 Hz, 1H), 2.16 – 2.06 (m, 1H), 2.02 – 1.91 (m, 2H), 1.89 – 1.81 (m, 1H), 1.75 – 1.65 (m, 2H), 1.40 (s, 3H), 1.28 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 158.7, 155.2, 147.3, 145.1, 138.1, 130.2, 129.4, 128.6, 123.6, 120.1, 116.5, 113.5, 112.7, 87.6, 75.4, 55.8, 47.4, 47.3, 39.4, 38.7, 25.6, 25.2, 24.5, 22.0, 21.7 (one signal is missing due to insufficient relaxation time).

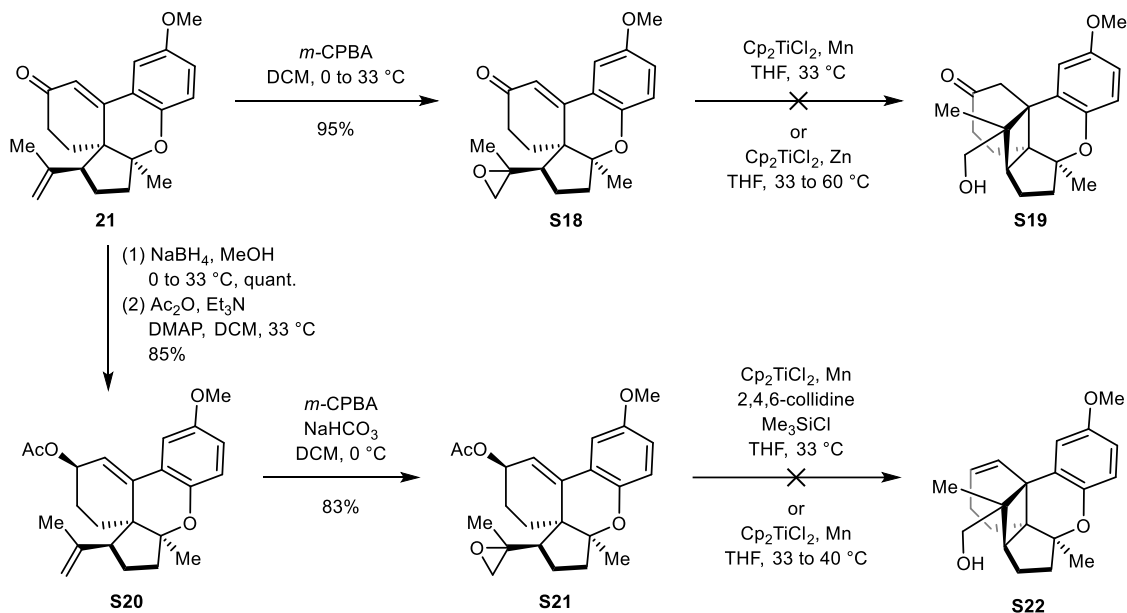
HRMS(ESI)⁺ calcd for C₂₆H₂₉O₇N₄⁺ [M+H]⁺: 509.2031; found: 509.2032.

FT-IR (cm⁻¹): 3528, 3316, 2926, 1618, 1517, 1334, 1137, 832, 743.

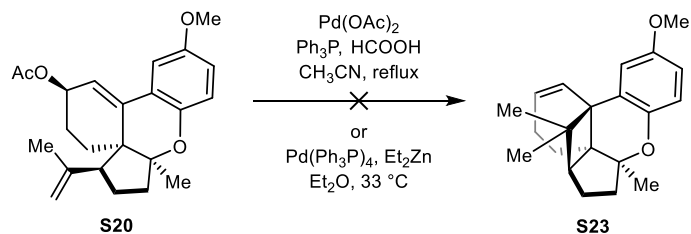
a) Michael addition of the aldehyde and the enone



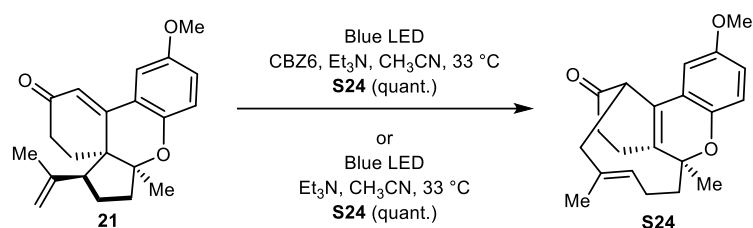
b) Titanium(III)-mediated radical cyclization of an epoxide



c) Oppolzer cyclization



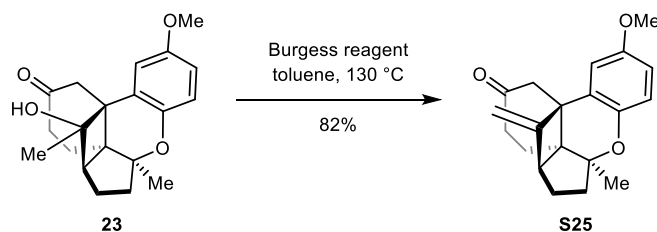
d) Photocatalytic reactions induced by the super photoreductant CBZ6



Note: Analytical data of compound **S24** matches the literature⁶.

Supplementary Figure 2. Failed attempts. **a** Michael addition of the aldehyde and the enone. **b** Titanium(III)-mediated radical cyclization of an epoxide. **c** Oppolzer cyclization. **d** Photocatalytic reactions induced by the super photoreductant CBZ6.

Preparation of Compound S25



To a solution of **23** (30.0 mg, 0.0914 mmol, 1.0 equiv) in toluene (0.91 mL) was added Burgess reagent (87.1 mg, 0.366 mmol, 4.0 equiv) at 33 °C. After stirring at 130 °C for 2 h, the reaction was cooled down to 33 °C and quenched by brine. The reaction was repeated another 9 times with same scale and the combined reaction mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:EtOAc = 15:1→10:1) to afford **S25** (233 mg, 82% yield) as a yellow oil.

TLC: R_f = 0.9 (petroleum ether:EtOAc = 2:1).

$[\alpha]_D^{26}$ = +52 (c = 0.2, CHCl₃).

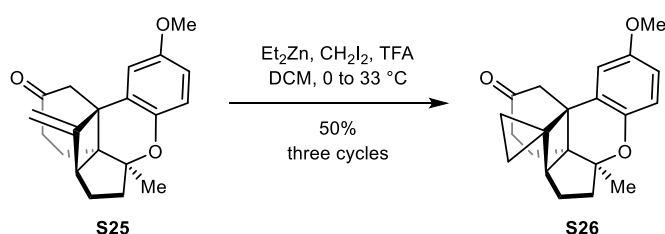
¹H NMR (500 MHz, CDCl₃) δ 6.78 – 6.75 (m, 1H), 6.71 – 6.66 (m, 2H), 5.19 – 5.15 (m, 1H), 4.95 – 4.91 (m, 1H), 3.74 (s, 3H), 3.11 (d, J = 7.1 Hz, 1H), 2.84 (d, J = 14.9 Hz, 1H), 2.57 (d, J = 15.0 Hz, 1H), 2.51 (ddd, J = 19.6, 5.9, 3.5 Hz, 1H), 2.42 (ddd, J = 19.6, 11.6, 5.7 Hz, 1H), 2.29 (td, J = 12.7, 7.1 Hz, 1H), 2.18 (ddd, J = 14.2, 11.7, 5.9 Hz, 1H), 1.91 (ddd, J = 14.3, 5.6, 3.5 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.63 (dd, J = 13.0, 7.1 Hz, 1H), 1.53 (dd, J = 12.9, 6.7 Hz, 1H), 1.39 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 211.3, 156.7, 154.4, 145.1, 130.4, 119.1, 113.2, 111.4, 109.1, 85.9, 55.7, 51.9, 47.6, 47.1, 46.0, 36.4, 35.8, 29.5, 23.7, 23.4.

HRMS(ESI)⁺ calcd for C₂₀H₂₃O₃⁺ [M+H]⁺: 311.1642; found: 311.1643.

FT-IR (cm⁻¹): 3732, 3626, 2938, 1715, 1493, 1140, 1037, 810.

Preparation of Compound S26



To a solution of Et₂Zn (2.0 M in hexanes, 0.6 mL, 1.19 mmol) in DCM (5.0 mL) was added slowly a solution of TFA (65.0 μ L, 0.865 mmol) in DCM (2.5 mL) at 0 °C. After stirring at this temperature for 10 min, CH₂I₂ (70.0 μ L, 0.865 mmol) was added and stirring was continued for another 20 min at 0 °C. To a solution of **S25** (9.0 mg, 0.0290 mmol, 1.0 equiv) in DCM (0.6 mL) was added freshly prepared CF₃CO₂ZnCH₂I (0.1 M in DCM, 2.9 mL, 0.290 mmol, 10.0 equiv) at 0 °C. After stirring at 33 °C for 1 h, the reaction was quenched with saturated aqueous NaHCO₃ solution and extracted with EtOAc. The reaction was repeated another 15 times with same scale and combined organic layers were washed with saturated aqueous NaHCO₃ solution and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by HPLC (SHIMADZU LC-20AR, Ultimate XB-C4, 10 $\times$ 250 mm, 5 μ m, eluent A: water, eluent B: acetonitrile, gradient: T = 0 min: 30% B, T = 30 min: 60% B, T = 45 min: 70% B, 3.8 mL/min; **S25**, retention time: 30.0 min; **S26**, retention time: 31.6 min) to afford **S26** (48.0 mg, 34% yield) as a yellow solid and **S25** (63.0 mg, 44% yield). This procedure was repeated another two times to give **S26** as a yellow solid (27.5 mg, total 75.5 mg, 50% yield).

TLC: R_f = 0.7 (petroleum ether:EtOAc = 3:1).

M.p.: 141.2–143.3 °C.

$[\alpha]_D^{25} = +50$ ($c = 0.2$, CHCl_3).

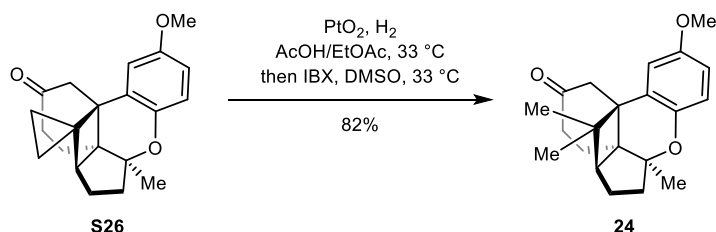
^1H NMR (500 MHz, CDCl_3) δ 6.81 (d, $J = 8.8$ Hz, 1H), 6.69 (dd, $J = 8.8, 2.9$ Hz, 1H), 6.04 (d, $J = 2.9$ Hz, 1H), 3.72 (s, 3H), 2.61 – 2.55 (m, 3H), 2.45 – 2.39 (m, 2H), 2.37 – 2.29 (m, 1H), 2.17 (ddd, $J = 14.2, 10.1, 7.5$ Hz, 1H), 1.90 (dt, $J = 14.3, 4.5$ Hz, 1H), 1.60 – 1.50 (m, overlap with H_2O , 2H), 1.41 (s, 3H), 1.36 (dd, $J = 12.0, 7.0$ Hz, 1H), 0.91 – 0.84 (m, 1H), 0.51 – 0.46 (m, 1H), 0.46 – 0.41 (m, 1H), 0.36 – 0.29 (m, 1H).

^{13}C NMR (125 MHz, CDCl_3) δ 212.2, 154.0, 145.4, 129.3, 119.0, 112.9, 112.0, 85.1, 55.8, 49.9, 46.8, 44.3, 40.8, 36.8, 36.1, 29.3, 26.0, 23.60, 23.56, 12.4, 7.1.

HRMS(ESI) $^+$ calcd for $\text{C}_{21}\text{H}_{24}\text{O}_3\text{Na}^+$ $[\text{M}+\text{Na}]^+$: 347.1618; found: 347.1620.

FT-IR (cm^{-1}): 2940, 2864, 1713, 1492, 1262, 1143, 1039, 804, 767.

Preparation of Compound 24



To a solution of **S26** (8.0 mg, 0.0247 mmol, 1.0 equiv) in EtOAc (0.3 mL) and AcOH (0.3 mL) was added PtO_2 (22.0 mg, 0.0987 mmol, 4.0 equiv) at 33 °C. The reaction mixture was degassed with H_2 for three times and equipped with a H_2 balloon. After stirring at same temperature for 1 h, the resulting mixture was filtered through a pad of celite and washed with EtOAc. The filtrate was concentrated under reduced pressure to give the crude product. To a solution of above crude product in DMSO (0.5 mL) was added 2-iodoxybenzoic acid (IBX, 14.0 mg, 0.0494 mmol, 2.0 equiv) at 33 °C. After stirring at same temperature for 45 min, the reaction was quenched with a mixture of saturated aqueous NaHCO_3 solution and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 4:1) to afford **24** (6.6 mg, 82% yield) as a colorless oil.

TLC: $R_f = 0.4$ (petroleum ether:EtOAc = 5:1).

$[\alpha]_D^{25} = +12$ ($c = 0.2$, CHCl_3).

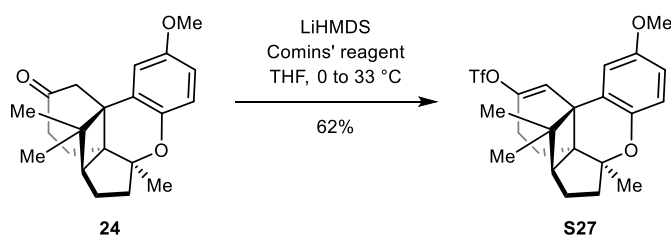
^1H NMR (500 MHz, CDCl_3) δ 6.77 (d, $J = 8.8$ Hz, 1H), 6.68 (dd, $J = 8.8, 2.9$ Hz, 1H), 6.43 (d, $J = 2.9$ Hz, 1H), 3.75 (s, 3H), 3.13 (d, $J = 16.4$ Hz, 1H), 2.60 – 2.44 (m, 2H), 2.31 (d, $J = 16.4$ Hz, 1H), 2.28 – 2.24 (m, 1H), 2.16 – 2.08 (m, 1H), 2.03 (ddd, $J = 14.7, 10.0, 4.9$ Hz, 1H), 1.86 (dt, $J = 14.3, 5.7$ Hz, 1H), 1.78 – 1.71 (m, 1H), 1.66 – 1.59 (m, 2H), 1.34 (s, 3H), 1.16 (s, 3H), 0.76 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 212.8, 154.0, 146.5, 130.7, 119.2, 113.1, 112.9, 85.9, 55.8, 49.9, 48.8, 46.3, 43.3, 40.3, 39.0, 36.5, 28.8, 26.2, 24.1, 23.5, 22.6.

HRMS(ESI) $^+$ calcd for $\text{C}_{21}\text{H}_{27}\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 327.1955; found: 327.1958.

FT-IR (cm^{-1}): 2923, 2856, 1711, 1492, 1223, 1135, 1041, 961, 767.

Preparation of Compound S27



To a solution of **24** (9.0 mg, 0.0276 mmol, 1.0 equiv) in THF (0.4 mL) was added LiHMDS (1.0 M in THF, 36.0 μ L, 0.0359 mmol, 1.3 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 10 min. A solution of Comins' reagent (54.0 mg, 0.138 mmol, 5.0 equiv) in THF (0.2 mL) was added to the reaction mixture at 0 °C. After stirring at 33 °C for 2 h, the reaction was quenched by saturated aqueous NH_4Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether:DCM = 3:1→petroleum ether:EtOAc = 8:1) to afford **S27** (7.8 mg, 62% yield) as a colorless oil.

TLC: R_f = 0.6 (petroleum ether:DCM = 3:1).

$[\alpha]_D^{21} = +132$ (c = 0.1, CHCl_3)

^1H NMR (500 MHz, CDCl_3) δ 6.80 (d, J = 8.7 Hz, 1H), 6.71 (dd, J = 8.8, 2.9 Hz, 1H), 6.54 (d, J = 2.9 Hz, 1H), 6.00 (d, J = 2.2 Hz, 1H), 3.78 (s, 3H), 2.57 – 2.42 (m, 2H), 2.17 – 2.08 (m, 1H), 2.04 – 1.99 (m, 1H), 1.80 – 1.68 (m, 2H), 1.66 – 1.59 (m, 3H), 1.27 (s, 3H), 1.08 (s, 3H), 0.80 (s, 3H).

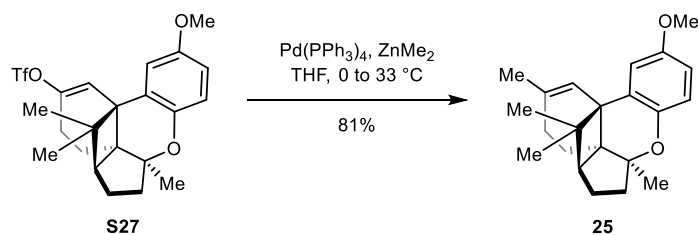
^{13}C NMR (125 MHz, CDCl_3) δ 154.2, 149.4, 147.1, 128.9, 124.1, 119.5, 118.7 (q, J = 318.4 Hz), 113.0, 112.7, 86.7, 55.9, 49.5, 46.3, 45.0, 44.9, 38.7, 29.5, 27.9, 26.3, 24.1, 23.3, 21.5.

^{19}F NMR (471 MHz, CDCl_3) δ –73.94.

HRMS(ESI) $^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{O}_5\text{F}_3\text{S}^+$ $[\text{M}+\text{H}]^+$: 459.1448; found: 459.1442.

FT-IR (cm^{-1}): 2951, 1493, 1419, 1211, 1141, 891, 851, 741.

Preparation of Compound 25



To a solution of **S27** (6.3 mg, 0.0138 mmol, 1.0 equiv) in THF (0.2 mL) was added $\text{Pd(PPh}_3)_4$ (3.2 mg, 0.00275 mmol, 0.2 equiv) at 0 °C, and stirred at this temperature for 5 min, ZnMe_2 (1 M in hexane, 0.28 mL, 0.275 mmol, 20.0 equiv) was added. After stirring at 33 °C for 2 h, the reaction was quenched by careful addition of pH 7 buffer at 0 °C. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 30:1) to afford **25** (3.6 mg, 81% yield) as a colorless oil.

TLC: R_f = 0.8 (petroleum ether:EtOAc = 30:1).

$[\alpha]_D^{21} = +112$ (c = 0.1, CHCl_3).

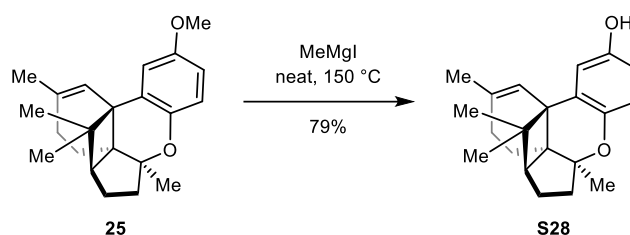
^1H NMR (500 MHz, CDCl_3) δ 6.75 (d, J = 8.3 Hz, 1H), 6.68 – 6.62 (m, 2H), 5.57 (s, 1H), 3.77 (s, 3H), 2.14 – 1.98 (m, 3H), 1.95 – 1.90 (m, 1H), 1.78 (s, 3H), 1.74 – 1.67 (m, 1H), 1.62 – 1.53 (m, overlap with H_2O , 2H), 1.45 (dd, J = 9.8, 5.2 Hz, 2H), 1.27 (s, 3H), 0.94 (s, 3H), 0.78 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ 153.8, 147.2, 135.4, 131.5, 127.6, 118.8, 113.6, 111.7, 86.8, 55.8, 49.2, 45.9, 43.8, 43.7, 38.6, 29.3, 28.1, 26.9, 24.3, 24.2, 23.6, 21.8.

HRMS(ESI) $^+$ calcd for $\text{C}_{22}\text{H}_{28}\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 347.1982; found: 347.1985.

FT-IR (cm^{-1}): 3477, 2921, 2852, 1491, 1226, 1140, 1045, 795.

Preparation of Compound S28



To a solution of **25** (3.7 mg, 0.0114 mmol, 1.0 equiv) in Et₂O (0.2 mL) was added MeMgI (3.0 M in Et₂O, 0.23 mL, 0.684 mmol, 60.0 equiv) at 0 °C. After gently removing Et₂O under vacuum, the resulting residue was heated to 150 °C under vacuum for 1 h. After cooling to 33 °C and then back to 0 °C, the residue was diluted in Et₂O. Then, the reaction mixture was carefully quenched with saturated aqueous NH₄Cl solution. The reaction mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 9:1) to afford **S28** (2.8 mg, 79% yield) as a yellow oil.

TLC: R_f = 0.3 (petroleum ether:EtOAc = 9:1).

$[\alpha]_D^{22}$ = +50 (c = 0.1, CHCl₃).

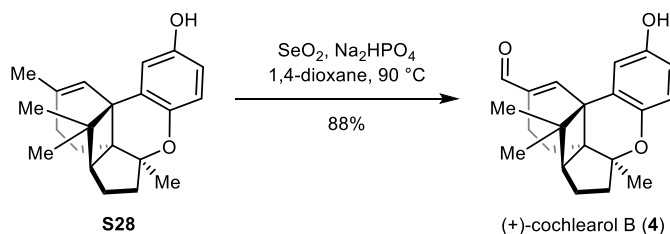
¹H NMR (500 MHz, CDCl₃) δ 6.70 (d, J = 8.5 Hz, 1H), 6.60 (d, J = 2.9 Hz, 1H), 6.56 (dd, J = 8.5, 3.0 Hz, 1H), 5.56 (s, 1H), 4.37 (brs, 1H), 2.15 – 1.97 (m, 3H), 1.93 (dd, J = 7.8, 2.9 Hz, 1H), 1.79 (s, 3H), 1.74 – 1.67 (m, 1H), 1.62 – 1.54 (m, overlap with H₂O, 2H), 1.47 – 1.41 (m, 2H), 1.26 (s, 3H), 0.93 (s, 3H), 0.77 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 149.5, 147.3, 135.5, 131.8, 127.5, 119.2, 114.4, 113.8, 86.9, 49.3, 46.1, 43.9, 43.7, 38.8, 29.4, 28.1, 27.0, 24.4, 24.3, 23.6, 21.8.

HRMS(ESI)⁺ calcd for C₂₁H₂₇O₂⁺ [M+H]⁺: 311.2006; found: 311.2010.

FT-IR (cm⁻¹): 3386, 2921, 2851, 1491, 1448, 1206, 1081, 815, 749.

Preparation of (+)-cochlearol B (4)



To a solution of **S28** (2.7 mg, 0.00870 mmol, 1.0 equiv) in 1,4-dioxane (0.2 mL) were added SeO₂ (1.3 mg, 0.0113 mmol, 1.3 equiv) and Na₂HPO₄ (6.2 mg, 0.0435 mmol, 5.0 equiv) at 33 °C. After stirring at 90 °C for 30 min, another portion of SeO₂ (1.3 mg, 0.0113 mmol, 1.3 equiv) and Na₂HPO₄ (6.2 mg, 0.0435 mmol, 5.0 equiv) was added at 33 °C. After stirring at 90 °C for 30 min, the reaction mixture was cooled to 33 °C and filtered through a pad of celite. The filtrate was concentrated under reduced pressure. The residue was purified by PTLC (petroleum ether:EtOAc = 2:1) to afford (+)-cochlearol B (**4**) (2.5 mg, 88% yield) as a colorless oil.

TLC: R_f = 0.4 (petroleum ether:EtOAc = 2:1).

$[\alpha]_D^{25}$ = +144 (c = 0.1, MeOH).

¹H NMR (500 MHz, (CD₃)₂CO) δ 9.55 (s, 1H), 7.87 (s, 1H), 7.07 (d, J = 2.3 Hz, 1H), 6.80 (d, J = 1.9 Hz, 1H), 6.70 – 6.63 (m, 2H), 2.64 (ddd, J = 16.6, 4.7, 3.6 Hz, 1H), 2.20 – 2.11 (m, 1H), 2.10 – 2.07 (m, overlap, 1H), 2.04 – 1.99 (m, 1H), 1.78 – 1.72 (m, 1H), 1.71 – 1.60 (m, 3H), 1.38 (ddd, J = 13.4, 11.5, 4.7 Hz, 1H), 1.29 (s, 3H), 1.01 (s, 3H), 0.89 (s, 3H).

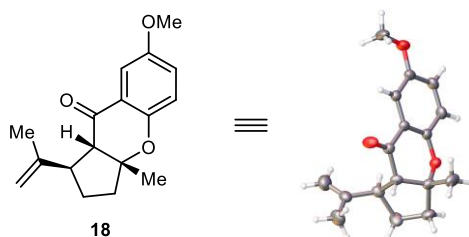
¹³C NMR (125 MHz, (CD₃)₂CO) δ 193.4, 156.4, 152.4, 147.3, 142.1, 129.1, 119.9, 115.4, 115.1, 87.2, 50.3, 48.2, 46.1, 45.1, 39.0, 29.1, 26.8, 24.6, 23.8, 21.8, 19.5.

HRMS(ESI)⁺ calcd for C₂₁H₂₅O₃⁺ [M+H]⁺: 325.1798; found: 325.1800.

FT-IR (cm⁻¹): 3414, 2923, 2851, 1676, 1631, 1492, 1449, 1209, 1134, 789, 751.

4. X-ray Crystallographic Data

X-ray crystallographic data for compound **18** (CCDC: 2492584)

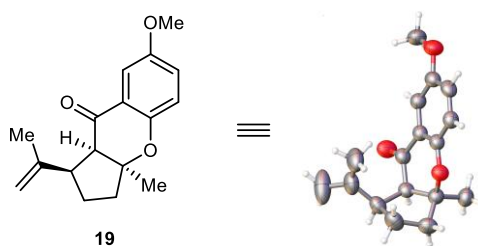


The crude product **18** was purified by silica gel column chromatography (petroleum ether/EtOAc). Concentration of the combined fractions containing **18** under reduced pressure using a rotary evaporator directly afforded colorless single crystals. The crystal structure of compound **18** was solved using OLEX2.

Supplementary Table 9. Crystal data and structure refinement for **18**

Empirical formula	C ₁₇ H ₂₀ O ₃
Formula weight	272.33
Temperature/K	169.99(10)
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	7.78061(12)
b/Å	10.93062(16)
c/Å	17.3290(2)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	1473.78(4)
Z	4
ρ _{calc} /g/cm ³	1.227
μ/mm ⁻¹	0.666
F(000)	584.0
Crystal size/mm ³	0.16 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2θ range for data collection/°	9.566 to 147.796
Index ranges	-8 ≤ h ≤ 9, -13 ≤ k ≤ 13, -21 ≤ l ≤ 21
Reflections collected	15707
Independent reflections	2959 [R _{int} = 0.0461, R _{sigma} = 0.0254]
Data/restraints/parameters	2959/0/193
Goodness-of-fit on F ²	1.038
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0350, wR ₂ = 0.0907
Final R indexes [all data]	R ₁ = 0.0359, wR ₂ = 0.0918
Largest diff. peak/hole / e Å ⁻³	0.15/-0.13
Flack/Hoof parameter	-0.09(8)/-0.09(8)

X-ray crystallographic data for compound **19** (CCDC: 2492585)

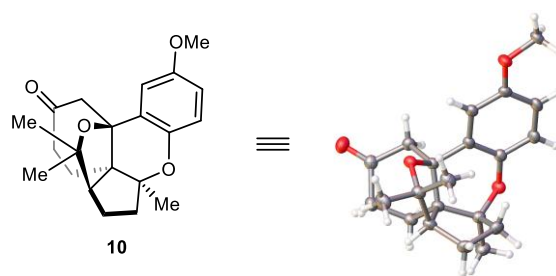


The crude product **19** was purified by silica gel column chromatography (petroleum ether/EtOAc). Concentration of the combined fractions containing **19** under reduced pressure using a rotary evaporator directly afforded colorless single crystals. The crystal structure of compound **19** was solved using OLEX2.

Supplementary Table 10. Crystal data and structure refinement for **19**

Empirical formula	C ₁₇ H ₂₀ O ₃
Formula weight	272.33
Temperature/K	170.00
Crystal system	monoclinic
Space group	P2 ₁
a/Å	7.6156(2)
b/Å	7.6565(2)
c/Å	12.4216(3)
α/°	90
β/°	90.1590(10)
γ/°	90
Volume/Å ³	724.29(3)
Z	2
ρ _{calc} /cm ³	1.249
μ/mm ⁻¹	0.677
F(000)	292.0
Crystal size/mm ³	0.15 × 0.12 × 0.09
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	7.116 to 136.404
Index ranges	-9 ≤ h ≤ 9, -9 ≤ k ≤ 9, -14 ≤ l ≤ 14
Reflections collected	21546
Independent reflections	2643 [R _{int} = 0.0448, R _{sigma} = 0.0308]
Data/restraints/parameters	2643/1/185
Goodness-of-fit on F ²	1.208
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0433, wR ₂ = 0.1248
Final R indexes [all data]	R ₁ = 0.0436, wR ₂ = 0.1249
Largest diff. peak/hole / e Å ⁻³	0.21/-0.18
Flack/Hooft parameter	0.09(4)/0.07(5)

X-ray crystallographic data for compound **10** (CCDC: 2492583)

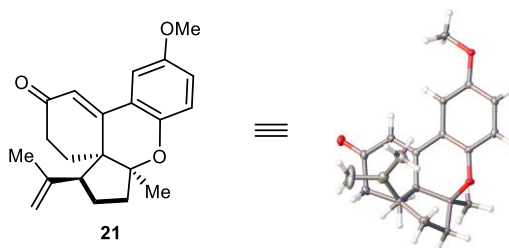


Anti-solvent vapor-assisted crystallization¹⁴: At room temperature, compound **10** was dissolved in ethyl ether. Single crystals of **10** were grown via slow diffusion of anti-solvent *n*-heptane vapor into the solution. The crystal structure of compound **10** was solved using OLEX2.

Supplementary Table 11. Crystal data and structure refinement for **10**

Empirical formula	C ₂₁ H ₂₆ O ₄
Formula weight	342.42
Temperature/K	150.00(10)
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
<i>a</i> /Å	8.3952(3)
<i>b</i> /Å	13.2868(4)
<i>c</i> /Å	15.9184(4)
α /°	90
β /°	90
γ /°	90
Volume/Å ³	1775.62(9)
<i>Z</i>	4
ρ_{calc} /cm ³	1.281
μ /mm ⁻¹	0.703
<i>F</i> (000)	736.0
Crystal size/mm ³	0.16 × 0.12 × 0.1
Radiation	Cu K α (λ = 1.54184)
2 θ range for data collection/°	8.668 to 147.998
Index ranges	-8 ≤ <i>h</i> ≤ 10, -16 ≤ <i>k</i> ≤ 14, -18 ≤ <i>l</i> ≤ 19
Reflections collected	6693
Independent reflections	3500 [<i>R</i> _{int} = 0.0396, <i>R</i> _{sigma} = 0.0486]
Data/restraints/parameters	3500/0/230
Goodness-of-fit on <i>F</i> ²	1.022
Final <i>R</i> indexes [<i>I</i> ≥ 2 σ (<i>I</i>)]	<i>R</i> ₁ = 0.0481, <i>wR</i> ₂ = 0.1267
Final <i>R</i> indexes [all data]	<i>R</i> ₁ = 0.0506, <i>wR</i> ₂ = 0.1308
Largest diff. peak/hole / e Å ⁻³	0.29/-0.28
Flack parameter	0.32(15)

X-ray crystallographic data for compound **21** (CCDC: 2492586)

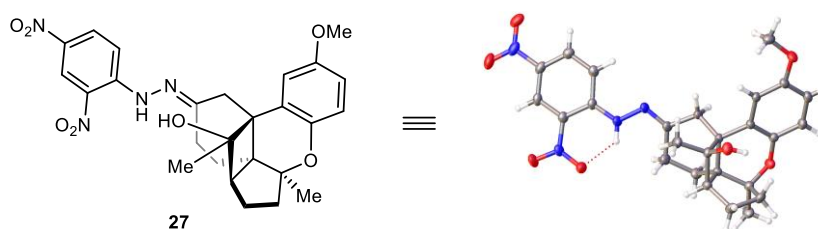


The crude product **21** was purified by silica gel column chromatography (petroleum ether/EtOAc). Concentration of the combined fractions containing **21** under reduced pressure using a rotary evaporator directly afforded colorless single crystals. The crystal structure of compound **21** was solved using OLEX2.

Supplementary Table 12. Crystal data and structure refinement for **21**

Empirical formula	C ₂₁ H ₂₄ O ₃
Formula weight	324.40
Temperature/K	100.00
Crystal system	monoclinic
Space group	P2 ₁
a/Å	7.3731(3)
b/Å	7.9107(4)
c/Å	14.7748(7)
α/°	90
β/°	101.009(2)
γ/°	90
Volume/Å ³	845.90(7)
Z	2
ρ _{calc} /cm ³	1.274
μ/mm ⁻¹	0.666
F(000)	348.0
Crystal size/mm ³	0.15 × 0.12 × 0.1
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	6.094 to 136.45
Index ranges	-8 ≤ h ≤ 8, -9 ≤ k ≤ 9, -17 ≤ l ≤ 17
Reflections collected	32484
Independent reflections	3069 [R _{int} = 0.0404, R _{sigma} = 0.0229]
Data/restraints/parameters	3069/1/220
Goodness-of-fit on F ²	1.110
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0331, wR ₂ = 0.0865
Final R indexes [all data]	R ₁ = 0.0331, wR ₂ = 0.0866
Largest diff. peak/hole / e Å ⁻³	0.22/-0.25
Flack/Hoof parameter	0.08(3)/0.10(3)

X-ray crystallographic data for compound **27** (CCDC: 2492587)



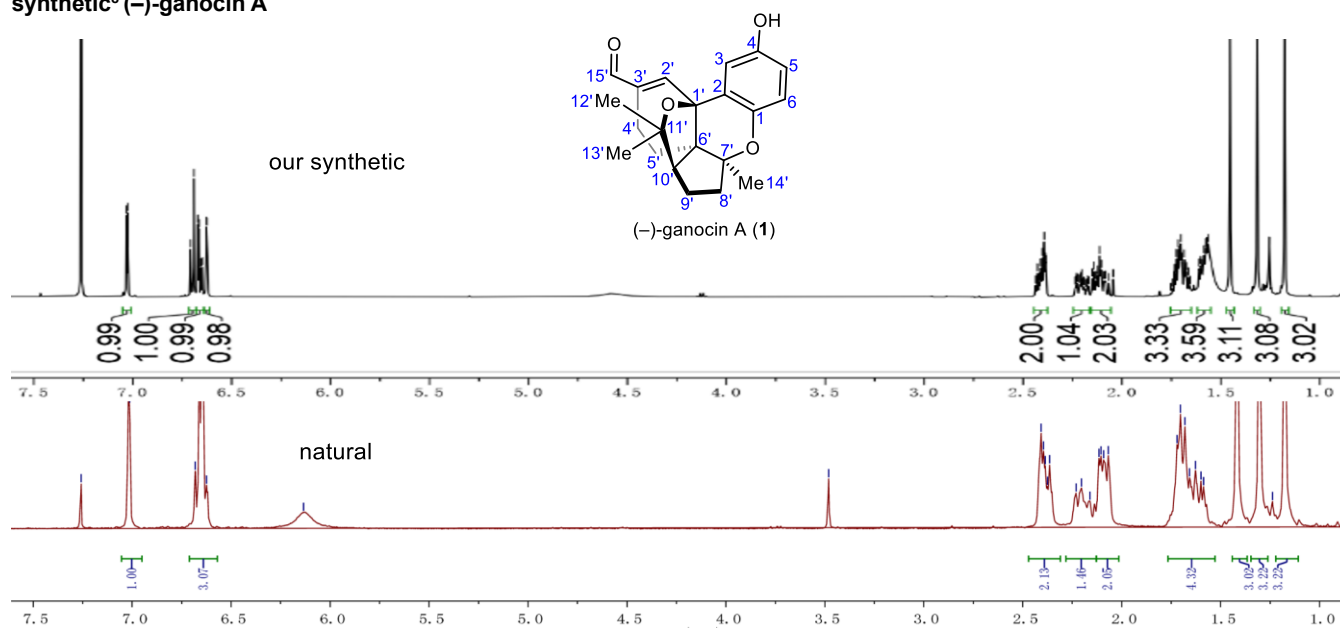
At room temperature, compound **27** was dissolved in a mixture of dichloromethane and petroleum ether. The solution was then allowed to evaporate slowly, yielding colorless crystals. The crystal structure of compound **27** was solved using OLEX2.

Supplementary Table 13. Crystal data and structure refinement for **27**

Empirical formula	C ₂₆ H ₂₈ N ₄ O ₇
Formula weight	508.52
Temperature/K	150.00
Crystal system	monoclinic
Space group	P2 ₁
a/Å	7.2940(5)
b/Å	15.9994(12)
c/Å	20.4598(15)
α/°	90
β/°	92.493(2)
γ/°	90
Volume/Å ³	2385.4(3)
Z	4
ρ _{calc} /g/cm ³	1.416
μ/mm ⁻¹	0.868
F(000)	1072.0
Crystal size/mm ³	0.15 × 0.13 × 0.11
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	4.322 to 136.42
Index ranges	-8 ≤ h ≤ 8, -19 ≤ k ≤ 19, -24 ≤ l ≤ 24
Reflections collected	77313
Independent reflections	8649 [R _{int} = 0.0457, R _{sigma} = 0.0333]
Data/restraints/parameters	8649/1/676
Goodness-of-fit on F ²	1.054
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0329, wR ₂ = 0.0836
Final R indexes [all data]	R ₁ = 0.0330, wR ₂ = 0.0837
Largest diff. peak/hole / e Å ⁻³	0.33/-0.25
Flack/Hoof parameter	0.08(2)/0.09(2)

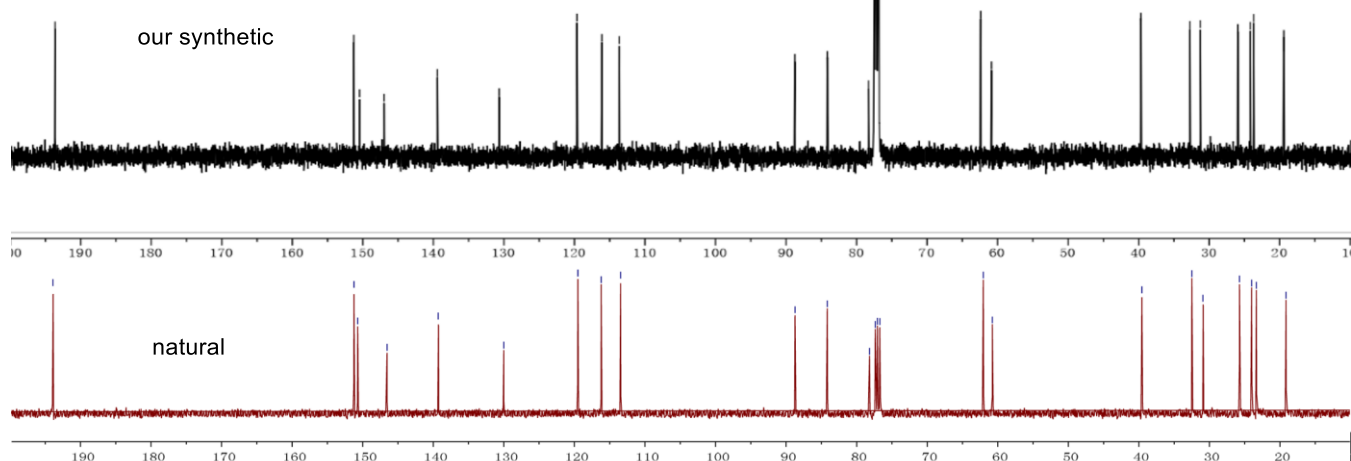
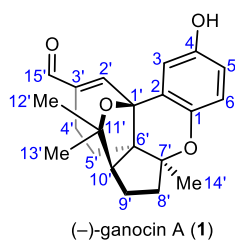
5. Comparison of the Spectra and Data of (–)-Ganocins A–C

¹H NMR spectra and data comparison of our synthetic, Natural¹⁵, Zhao's synthetic², Li and Tang's synthetic⁵, and Sugital's synthetic⁸ (–)-ganocin A



H	Our synthetic (500 MHz, CDCl ₃)	Natural ¹⁵ (400 MHz, CDCl ₃)	Zhao's synthetic ² (600 MHz, CDCl ₃)	Li and Tang's synthetic ⁵ (400 MHz, CDCl ₃)	Sugital's synthetic ⁸ (600 MHz, CDCl ₃)
1	-	-	-	-	-
2	-	-	-	-	-
3	7.03 (d, <i>J</i> = 2.8 Hz, 1H)	7.01 (d, <i>J</i> = 2.4 Hz, 1H)	7.03 (d, <i>J</i> = 2.8 Hz, 1H)	7.03 (d, <i>J</i> = 2.8 Hz, 1H)	7.03 (d, <i>J</i> = 2.4 Hz, 1H)
4	-	-	-	-	4.71 (s, 1H) (Ar-OH)
5	6.66 (dd, <i>J</i> = 8.6, 2.9 Hz, 1H)	6.64 (m, 1H)	6.66 (dd, <i>J</i> = 8.6, 2.8 Hz, 1H)	6.66 (dd, <i>J</i> = 8.6, 2.8 Hz, 1H)	6.66 (dd, <i>J</i> = 7.8, 2.4 Hz, 1H)
6	6.70 (d, <i>J</i> = 8.5 Hz, 1H)	6.64 (m, 1H)	6.70 (d, <i>J</i> = 8.6 Hz, 1H)	6.70 (d, <i>J</i> = 8.5 Hz, 1H)	6.69 (d, <i>J</i> = 7.8 Hz, 1H)
1'	-	-	-	-	-
2'	6.64 – 6.61 (m, 1H)	6.62 (m, 1H)	6.63 (s, 1H)	6.63 (m, 1H)	6.63 (brs, 1H)
3'	-	-	-	-	-
4'	2.44 – 2.38 (m, 1H); 2.25 – 2.16 (m, 1H)	2.37 (m, 1H); 2.18 (m, 1H)	2.39 (m, 1H); 2.20 (m, 1H)	2.39 (m, 1H); 2.21 (m, 1H)	2.39 (m, 1H); 2.20 (m, 1H)
5'	2.16 – 2.06 (m, 1H); 1.76 – 1.64 (m, 1H)	2.07 (m, 1H); 1.66 (m, 1H)	2.11 (m, 1H); 1.67 (m, 1H)	2.12 (m, 1H); 1.67 (m, 1H)	2.11 (m, 1H); 1.69 (m, 1H)
6'	-	-	-	-	-
7'	-	-	-	-	-
8'	2.16 – 2.06 (m, 1H); 1.62 – 1.56 (m, overlap with H ₂ O, 1H)	2.07 (m, 1H); 1.57 (m, 1H)	2.07 (m, 1H); 1.57 (m, 1H)	2.09 (m, 1H); 1.58 (m, 1H)	2.11 (m, 1H); 1.58 (m, 1H)
9'	1.76 – 1.64 (m, 2H)	1.69 (m, 2H)	1.69 (m, 2H)	1.70 (m, 2H)	1.69 (m, 2H)
10'	2.44 – 2.38 (m, 1H)	2.39 (m, 1H)	2.41 (m, 1H)	2.42 (m, 1H)	2.41 (m, 1H)
11'	-	-	-	-	-
12'	1.18 (s, 3H)	1.17 (s, 3H)	1.18 (s, 3H)	1.18 (s, 3H)	1.18 (s, 3H)
13'	1.32 (s, 3H)	1.30 (s, 3H)	1.32 (s, 3H)	1.32 (s, 3H)	1.32 (s, 3H)
14'	1.45 (s, 3H)	1.42 (s, 3H)	1.45 (s, 3H)	1.46 (s, 3H)	1.45 (s, 3H)
15'	9.44 (s, 1H)	9.40 (s, 1H)	9.44 (s, 1H)	9.44 (s, 1H)	9.44 (s, 1H)

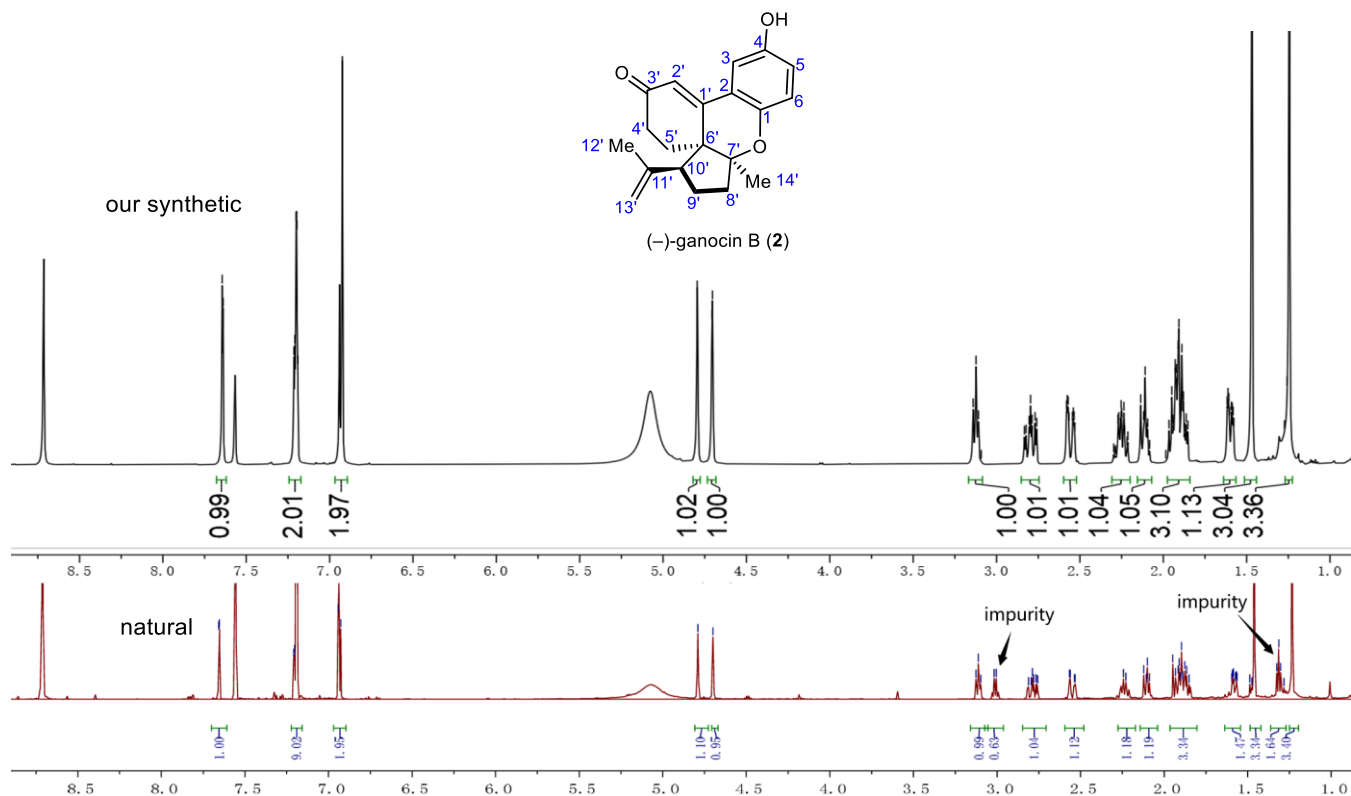
¹³C NMR spectra and data comparison of our synthetic, Natural¹⁵, Zhao's synthetic², Li and Tang's synthetic⁵, and Sugital's synthetic⁸ (–)-ganocin A



C	Our synthetic (125 MHz, CDCl ₃)	Natural ¹⁵ (100 MHz, CDCl ₃)	Zhao's synthetic ² (150 MHz, CDCl ₃)	Li and Tang's synthetic ⁵ (100 MHz, CDCl ₃)	Sugital's synthetic ⁸ (150 MHz, CDCl ₃)
1	146.8	146.5	146.8	146.7	146.7
2	130.5	129.9	130.5	130.3	130.2
3	113.5	113.4	113.5	113.5	113.4
4	150.3	151.2	151.2	151.3	151.1
5	116.0	116.1	116.0	116.2	116.0
6	119.5	119.5	119.5	119.6	119.5
1'	78.1	78.1	78.1	78.3	78.2
2'	151.1	150.6	150.3	150.7	150.5
3'	139.3	139.2	139.3	139.3	139.3
4'	19.3	19.1	19.3	19.3	19.2
5'	31.1	30.8	31.1	31.1	31.0
6'	60.7	60.7	60.7	60.8	60.7
7'	88.6	88.7	88.6	88.7	88.6
8'	39.5	39.5	39.5	39.6	39.5
9'	24.0	24.0	24.0	24.1	24.0
10'	62.2	62.0	62.2	62.2	62.1
11'	84.0	84.2	84.0	84.2	84.1
12'	25.8	25.8	25.8	25.9	25.7
13'	32.6	32.5	32.6	32.6	32.5
14'	23.5	23.3	23.5	23.5	23.4
15'	193.5	193.8	193.6	193.8	193.7

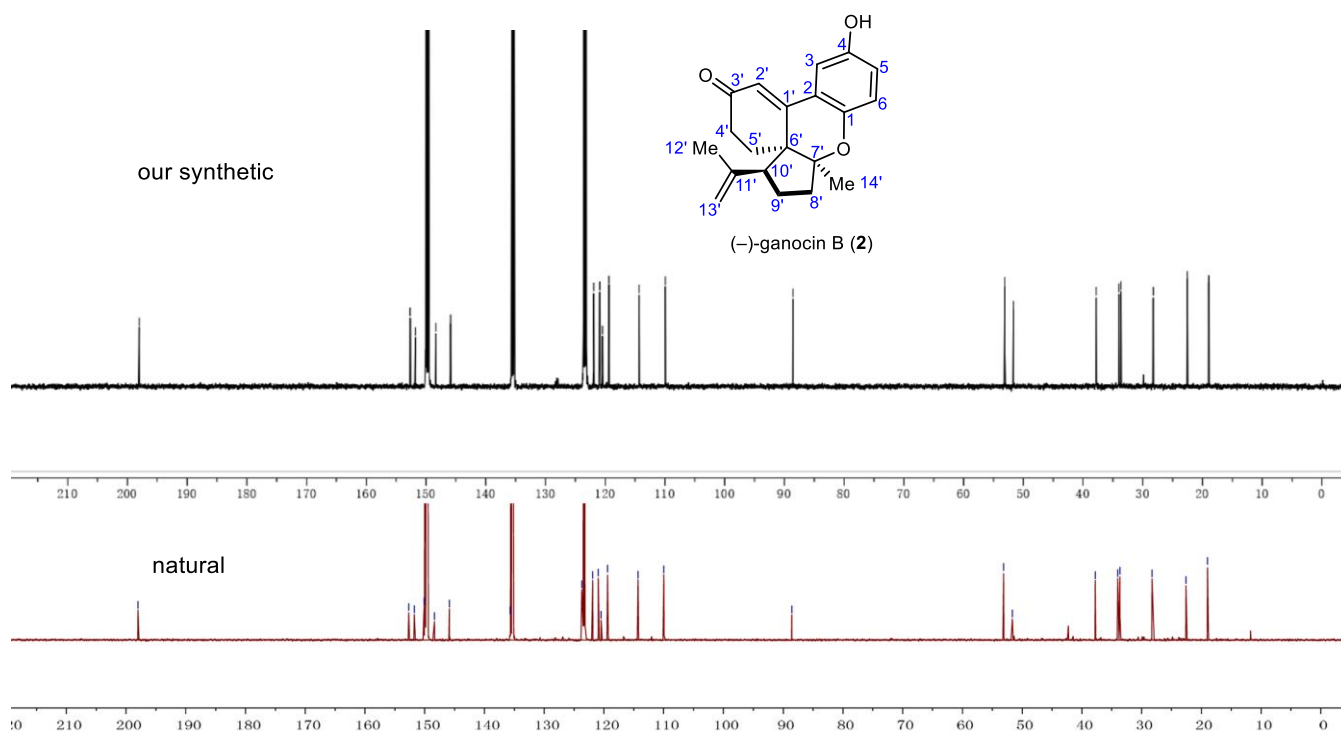
Note: we revised ¹³C assignments (C4, C2') from prior reports^{2,5,8,15}.

¹H NMR spectra and data comparison of our synthetic and natural¹⁵ (–)-ganocin B



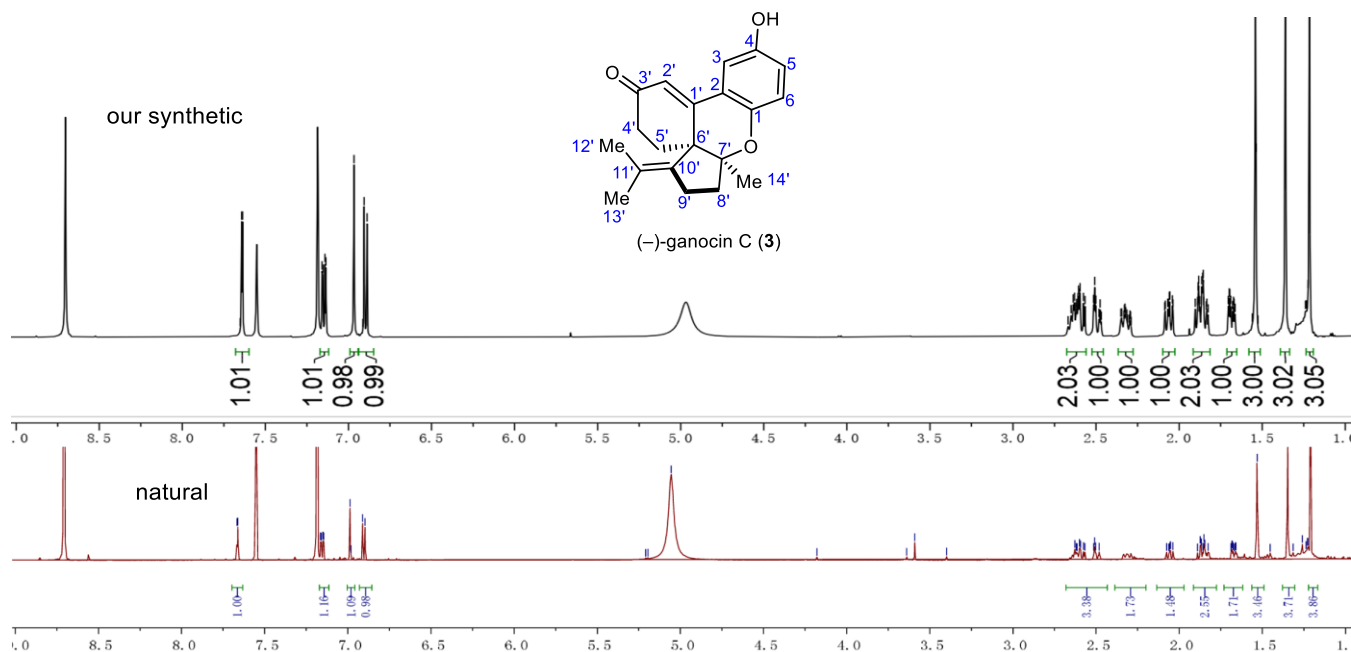
H	Our synthetic (500 MHz, C ₅ D ₅ N)	Natural ¹⁵ (600 MHz, C ₅ D ₅ N)	Δδ (Our synthetic – Natural)
1	-	-	-
2	-	-	-
3	7.63 (d, <i>J</i> = 3.0 Hz, 1H)	7.65 (d, <i>J</i> = 3.0 Hz, 1H)	–0.02
4	-	-	-
5	7.20 (dd, <i>J</i> = 8.7, 2.8 Hz, 1H)	7.20 (dd, <i>J</i> = 9.0, 3.0 Hz, 1H)	0
6	6.92 (d, <i>J</i> = 8.7 Hz, 1H)	6.93, (d, <i>J</i> = 9.0 Hz, 1H)	–0.01
1'	-	-	-
2'	6.91 (s, 1H)	6.94 (s, 1H)	–0.03
3'	-	-	-
4'	2.79 (ddd, <i>J</i> = 18.5, 14.0, 4.9 Hz, 1H); 2.55 (ddd, <i>J</i> = 18.0, 4.9, 2.2 Hz, 1H)	2.78 (m, 1H); 2.55 (m, 1H)	+0.01; 0
5'	1.98 – 1.83 (m, 1H); 1.59 (ddd, <i>J</i> = 12.8, 4.9, 2.3 Hz, 1H)	1.86 (m, 1H); 1.57 (m, 1H)	-; +0.02
6'	-	-	-
7'	-	-	-
8'	2.15 – 2.06 (m, 1H); 1.98 – 1.83 (m, 1H)	2.10 (m, 1H); 1.91 (m, 1H)	+0.01 (center); -
9'	2.30 – 2.19 (m, 1H); 1.98 – 1.83 (m, 1H)	2.23 (m, 1H); 1.89 (m, 1H)	+0.02 (center); -
10'	3.12 (t, <i>J</i> = 8.1 Hz, 1H)	3.11 (t, 1H)	+0.01
11'	-	-	-
12'	1.46 (s, 3H)	1.46 (s, 3H)	0
13'	4.79 (s, 1H); 4.72 – 4.68 (m, 1H)	4.79 (s, 1H); 4.70 (s, 1H)	0; +0.01 (center)
14'	1.24 (s, 3H)	1.23 (s, 3H)	+0.01

¹³C NMR spectra and data comparison of our synthetic and natural¹⁵ (-)-ganocin B



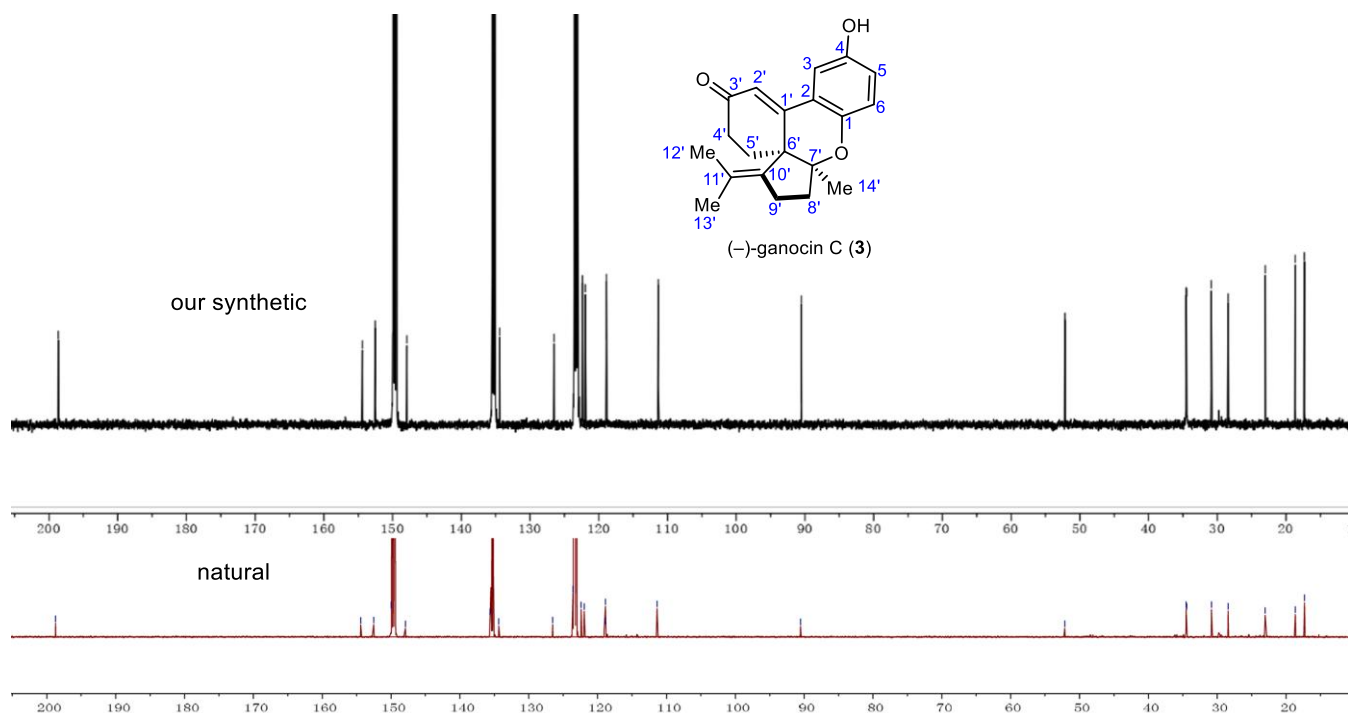
C	Our synthetic (125 MHz, C ₅ D ₅ N)	Natural ¹⁵ (150 MHz, C ₅ D ₅ N)	Δδ (Our synthetic – Natural)
1	148.4	148.4	0
2	120.5	120.4	+0.1
3	109.9	109.9	0
4	151.8	151.7	+0.1
5	121.9	121.9	0
6	119.4	119.4	0
1'	152.7	152.6	+0.1
2'	120.9	120.9	0
3'	198.0	198.0	0
4'	33.6	33.6	0
5'	34.0	33.9	+0.1
6'	51.7	51.6	+0.1
7'	88.6	88.5	+0.1
8'	37.8	37.7	+0.1
9'	28.2	28.2	0
10'	53.1	53.0	+0.1
11'	145.9	145.8	+0.1
12'	22.5	22.5	0
13'	114.3	114.3	0
14'	18.9	18.9	0

¹H NMR spectra and data comparison of our synthetic and natural¹⁵ (–)-ganocin C



H	Our synthetic (500 MHz, C ₅ D ₅ N)	Natural ¹⁵ (600 MHz, C ₅ D ₅ N)	Δδ (Our synthetic – Natural)
1	-	-	-
2	-	-	-
3	7.64 (d, <i>J</i> = 2.9 Hz, 1H)	7.66 (d, <i>J</i> = 3.0 Hz, 1H)	–0.02
4	-	-	-
5	7.15 (dd, <i>J</i> = 8.8, 2.9 Hz, 1H)	7.16 (dd, <i>J</i> = 9.0, 3.0 Hz, 1H)	–0.01
6	6.90 (d, <i>J</i> = 8.8 Hz, 1H)	6.91 (d, <i>J</i> = 9.0 Hz, 1H)	–0.01
1'	-	-	-
2'	6.97 (s, 1H)	6.99 (s, 1H)	–0.02
3'	-	-	-
4'	2.68 – 2.56 (m, 1H); 2.49 (dt, <i>J</i> = 16.3, 3.5 Hz, 1H)	2.59 (m, 1H); 2.49 (m, 1H)	–; 0
5'	1.92 – 1.82 (m, 1H); 1.68 (ddd, <i>J</i> = 13.0, 4.7, 2.9 Hz, 1H)	1.84 (m, 1H); 1.66 (m, 1H)	–; +0.02
6'	-	-	-
7'	-	-	-
8'	2.68 – 2.56 (m, 1H); 2.36 – 2.28 (m, 1H)	2.62 (m, 1H); 2.30 (m, 1H)	–; –
9'	2.06 (ddd, <i>J</i> = 13.7, 9.3, 1.8 Hz, 1H); 1.92 – 1.82 (m, 1H)	2.05 (m, 1H); 1.85 (m, 1H)	+0.01; –
10'	-	-	-
11'	-	-	-
12'	1.54 (s, 3H)	1.53 (s, 3H)	+0.01
13'	1.36 (s, 3H)	1.34 (s, 3H)	+0.02
14'	1.22 (s, 3H)	1.21 (s, 3H)	+0.01

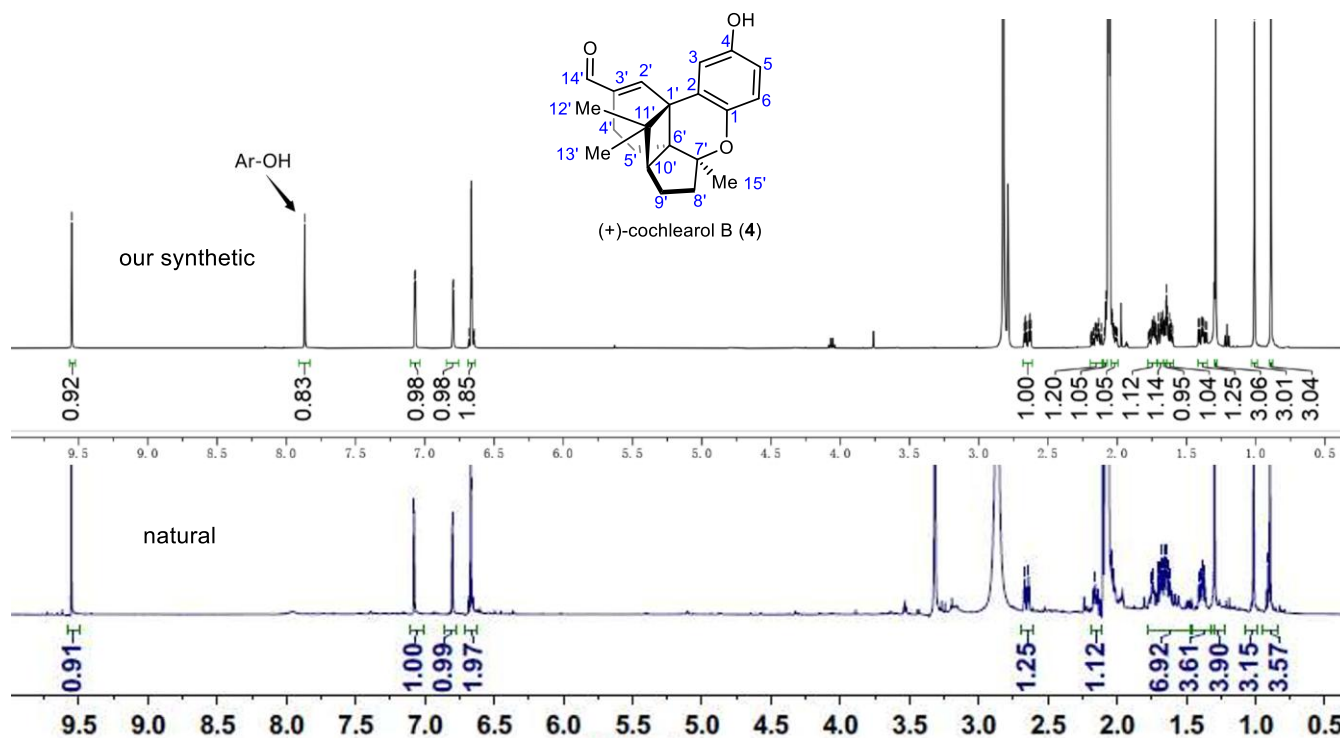
¹³C NMR spectra and data comparison of our synthetic and natural¹⁵ (–)-ganocin C



C	Our synthetic (125 MHz, C ₅ D ₅ N)	Natural ¹⁵ (150 MHz, C ₅ D ₅ N)	Δδ (Our synthetic – Natural)
1	147.9	147.9	0
2	118.9	118.9	0
3	111.3	111.4	–0.1
4	152.5	152.6	–0.1
5	122.0	122.1	–0.1
6	118.9	118.9	0
1'	154.4	154.5	–0.1
2'	122.4	122.5	–0.1
3'	198.6	198.8	–0.2
4'	34.52	34.6	–0.1
5'	30.9	30.9	0
6'	52.2	52.2	0
7'	90.5	90.6	–0.1
8'	28.4	28.5	–0.1
9'	34.46	34.5	0
10'	134.4	134.5	–0.1
11'	126.5	126.6	–0.1
12'	18.7	18.8	–0.1
13'	23.0	23.1	–0.1
14'	17.3	17.4	–0.1

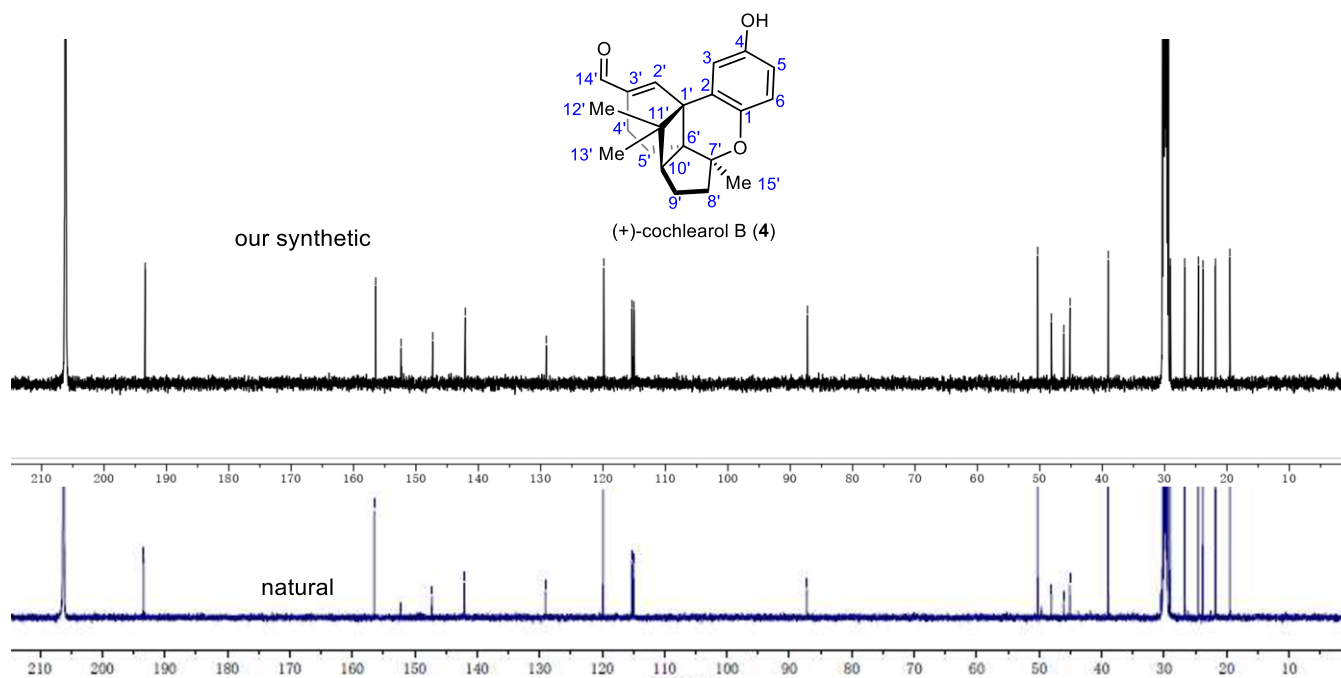
6. Comparison of the Spectra and Data of (+)-Cochlearol B

¹H NMR spectra and data comparison of our synthetic and natural¹⁶ (+)-cochlearol B



H	Our synthetic (500 MHz, (CD ₃) ₂ CO)	Natural ¹⁶ (600 MHz, (CD ₃) ₂ CO)	$\Delta\delta$ (Our synthetic – Natural)
1	-	-	-
2	-	-	-
3	6.80 (d, J = 1.9 Hz, 1H)	6.80 (d, J = 2.2 Hz, 1H)	0
Ar-OH	7.87 (s, 1H)	-	-
5	6.70 – 6.63 (m, 1H)	6.65 (dd, J = 8.5, 2.2 Hz, 1H)	-
6	6.70 – 6.63 (m, 1H)	6.68 (d, J = 8.5 Hz, 1H)	-
1'	-	-	-
2'	7.07 (d, J = 2.3 Hz, 1H)	7.08 (d, J = 2.0 Hz, 1H)	–0.01
3'	-	-	-
4'	2.64 (ddd, J = 16.6, 4.7, 3.6 Hz, 1H); 2.04 – 1.99 (m, 1H)	2.65 (m, 1H); 2.03 (m, 1H)	–0.01; –0.01 (center)
5'	1.71 – 1.60 (m, 1H); 1.38 (ddd, J = 13.4, 11.5, 4.7 Hz, 1H)	1.66 (m, 1H); 1.39 (m, 1H)	-; –0.01
6'	-	-	-
7'	-	-	-
8'	2.20 – 2.11 (m, 1H); 1.71 – 1.60 (m, 1H)	2.15 (m, 1H); 1.63 (m, 1H)	+0.01 (center); -
9'	1.78 – 1.72 (m, 1H); 1.71 – 1.60 (m, 1H)	1.75 (m, 1H); 1.69 (m, 1H)	–0.01 (center); -
10'	2.10 – 2.07 (m, overlap with H ₂ O, 1H)	2.09 (m, overlap with H ₂ O, 1H)	0 (center)
11'	-	-	-
12'	0.89 (s, 3H)	0.90 (s, 3H)	–0.01
13'	1.01 (s, 3H)	1.01 (s, 3H)	0
14'	9.55 (s, 1H)	9.55 (s, 1H)	0
15'	1.29 (s, 3H)	1.30 (s, 3H)	–0.01

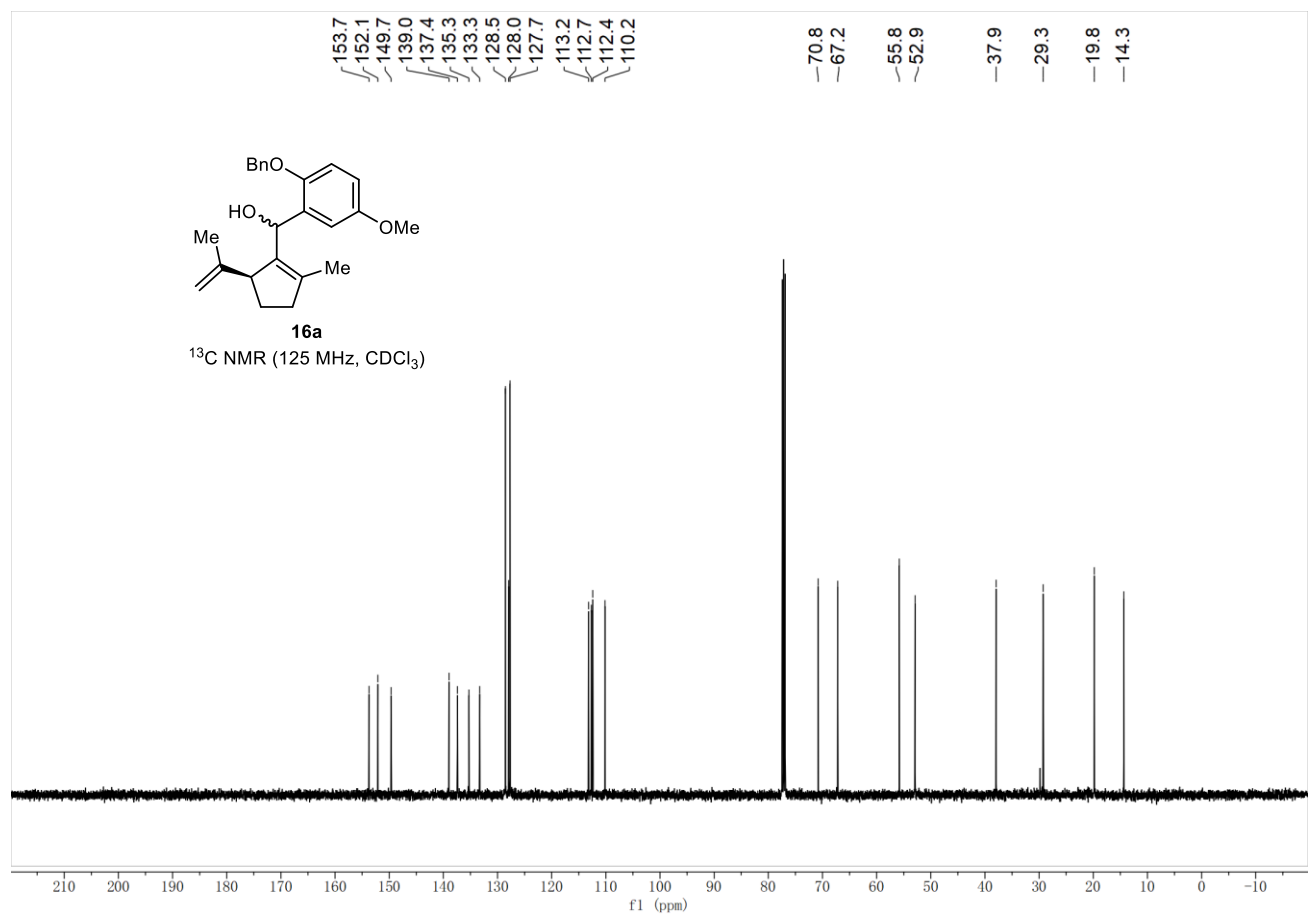
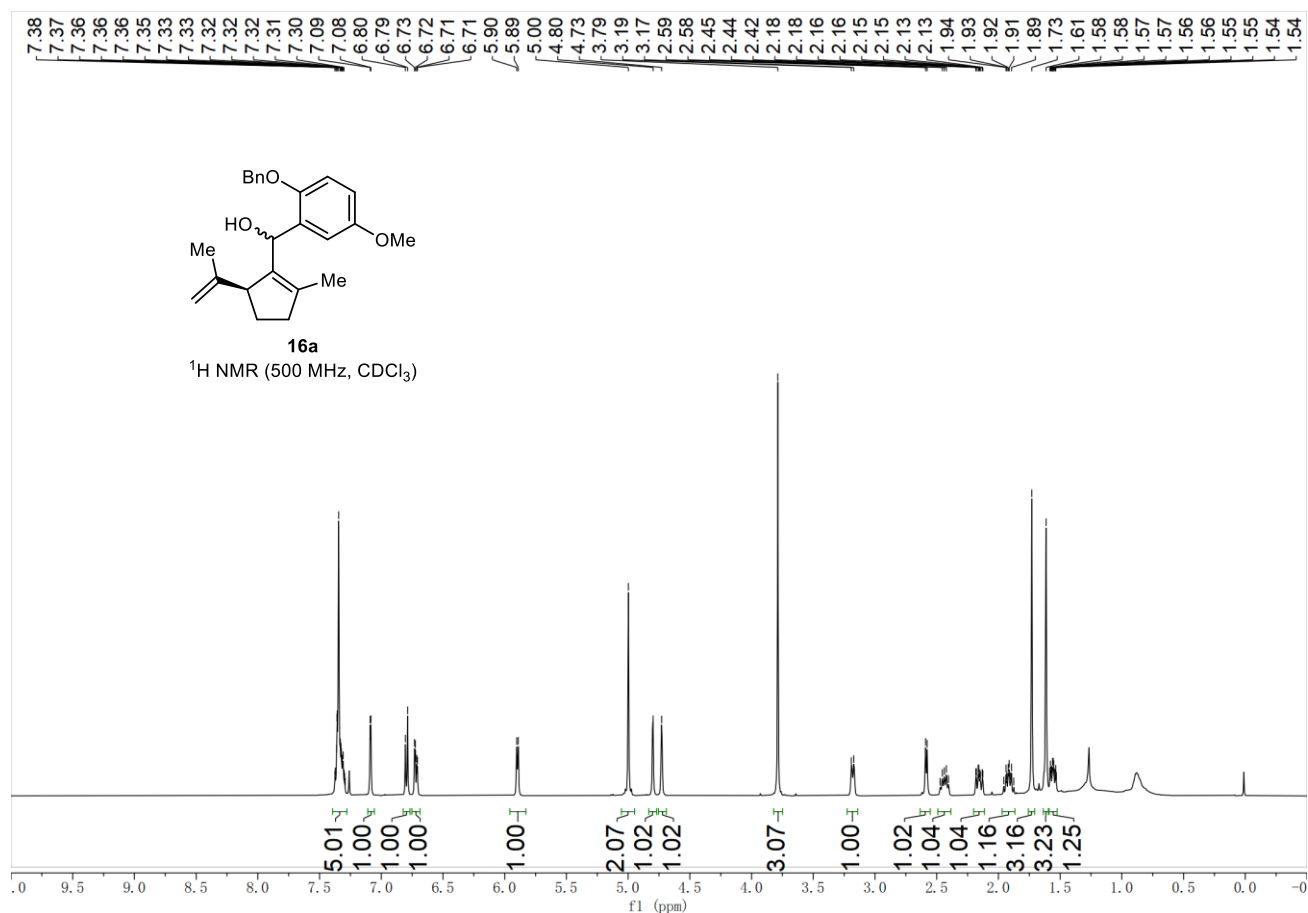
¹³C NMR spectra and data comparison of our synthetic and natural¹⁶ (+)-cochlearol B

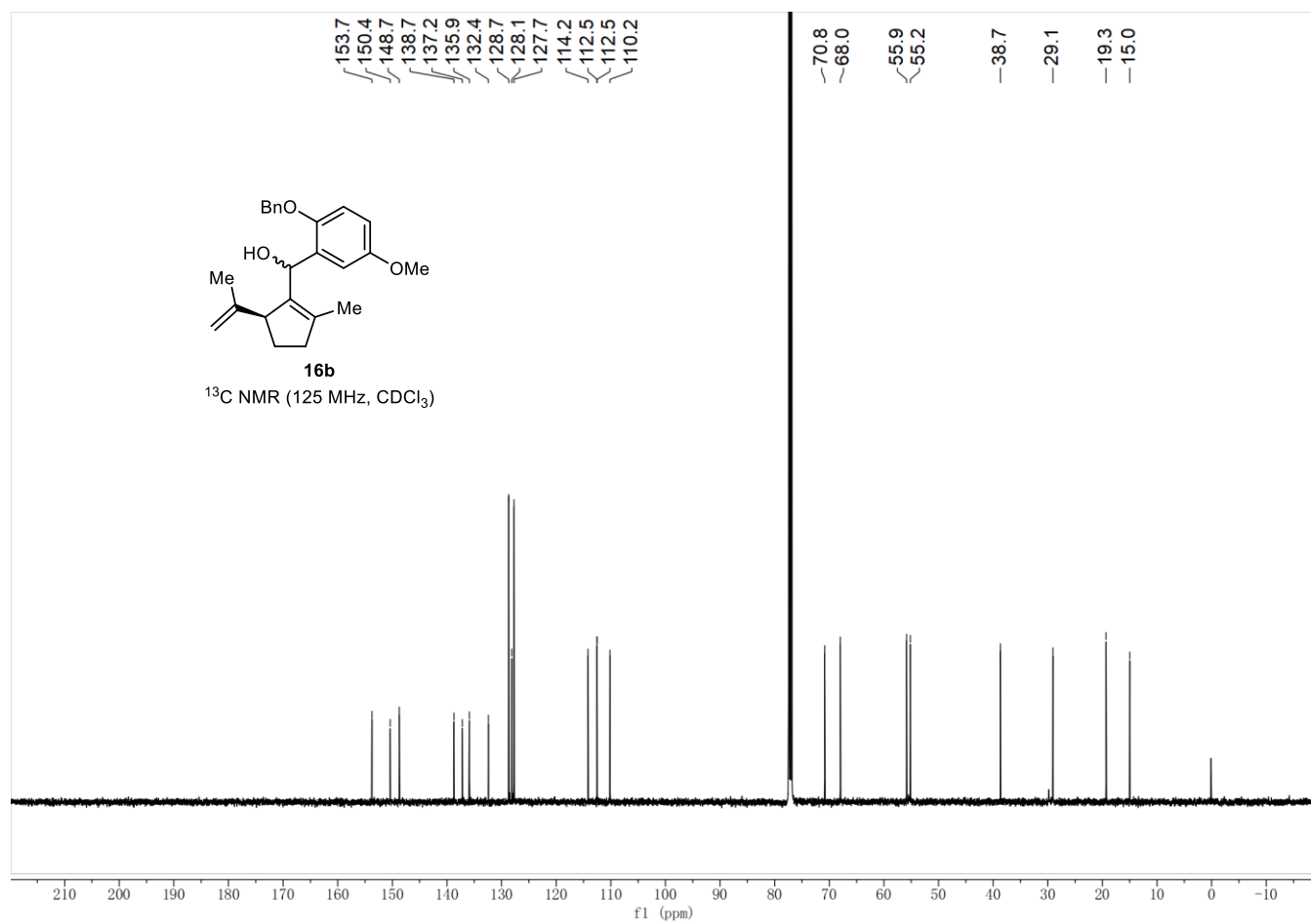
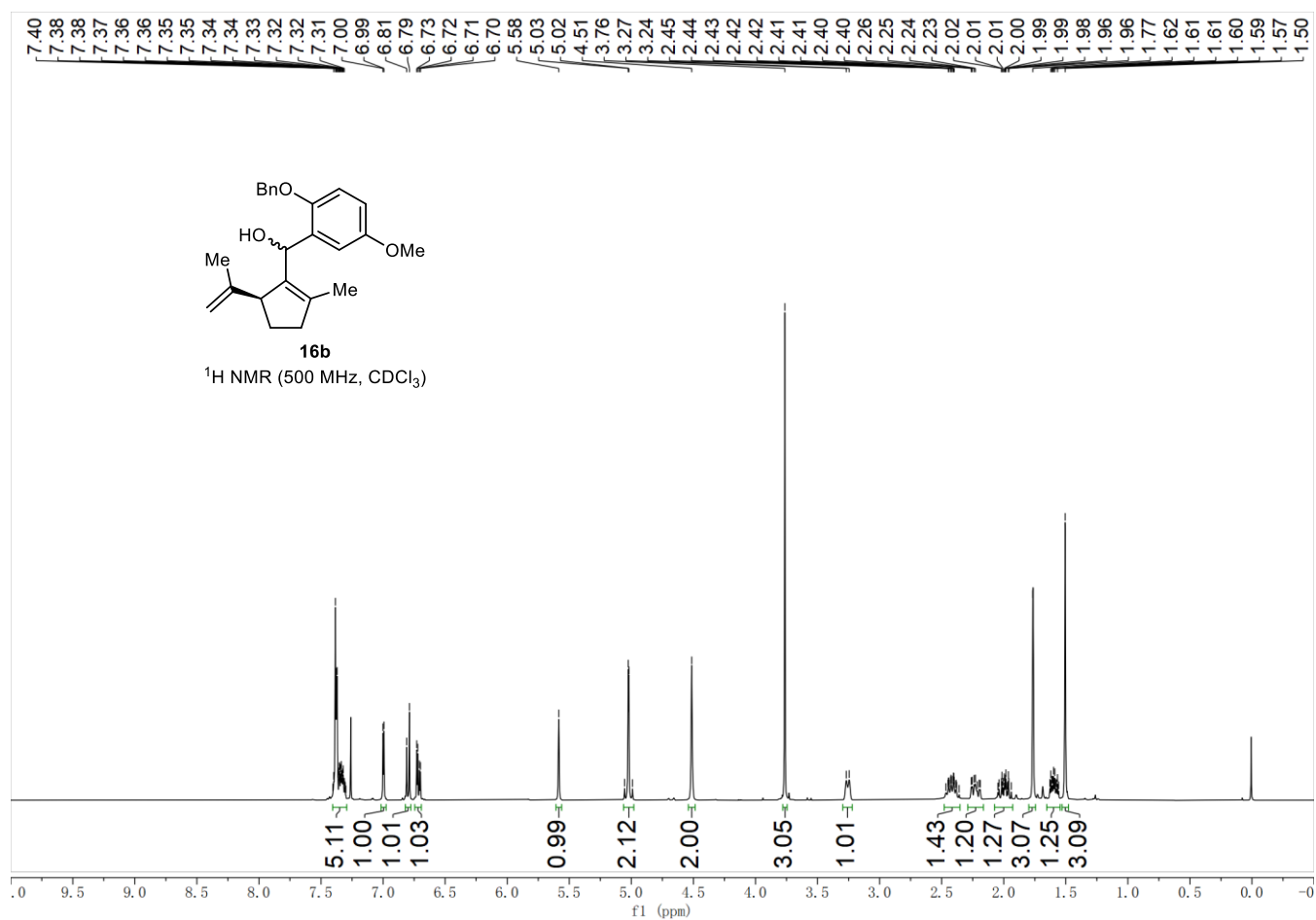


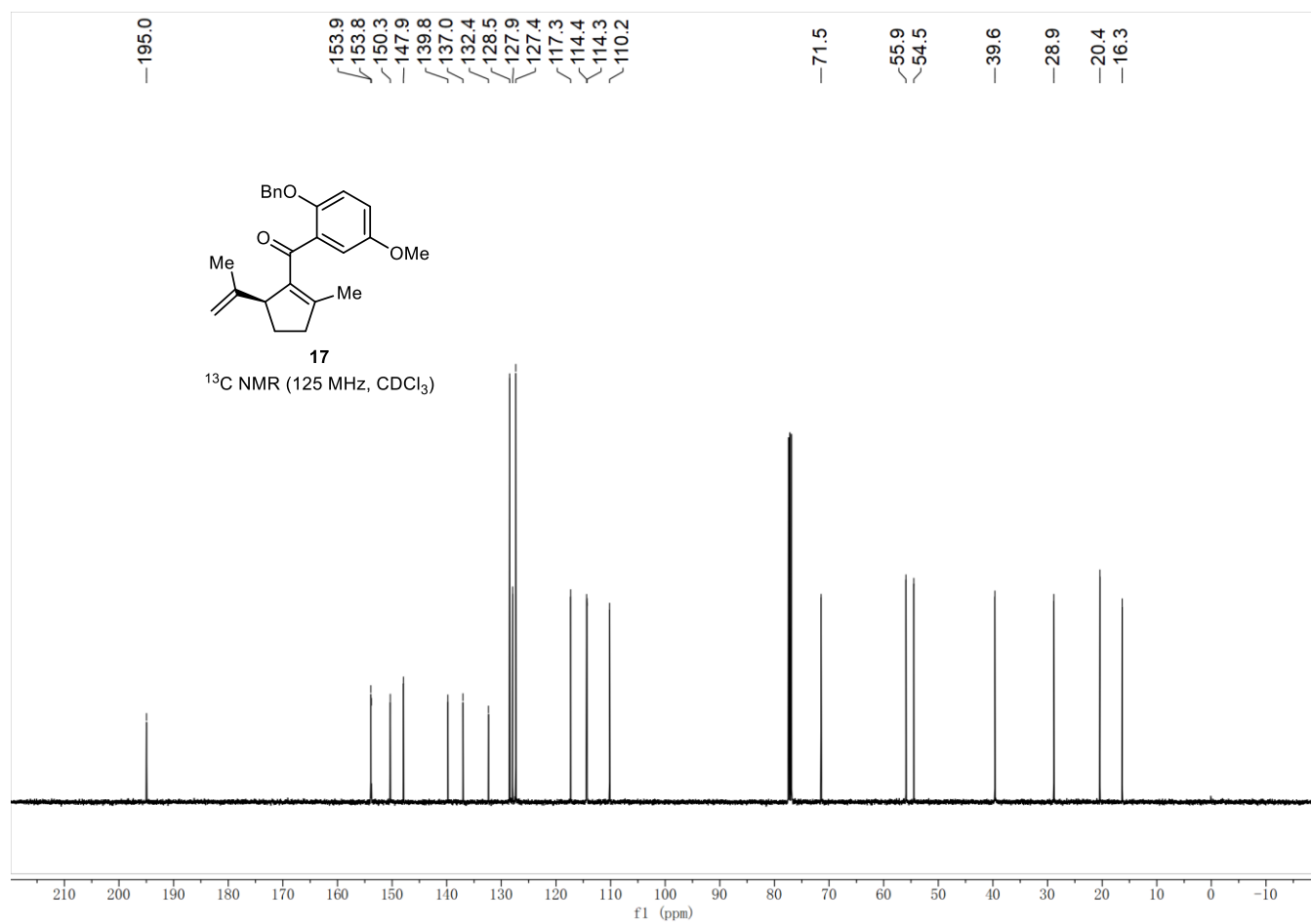
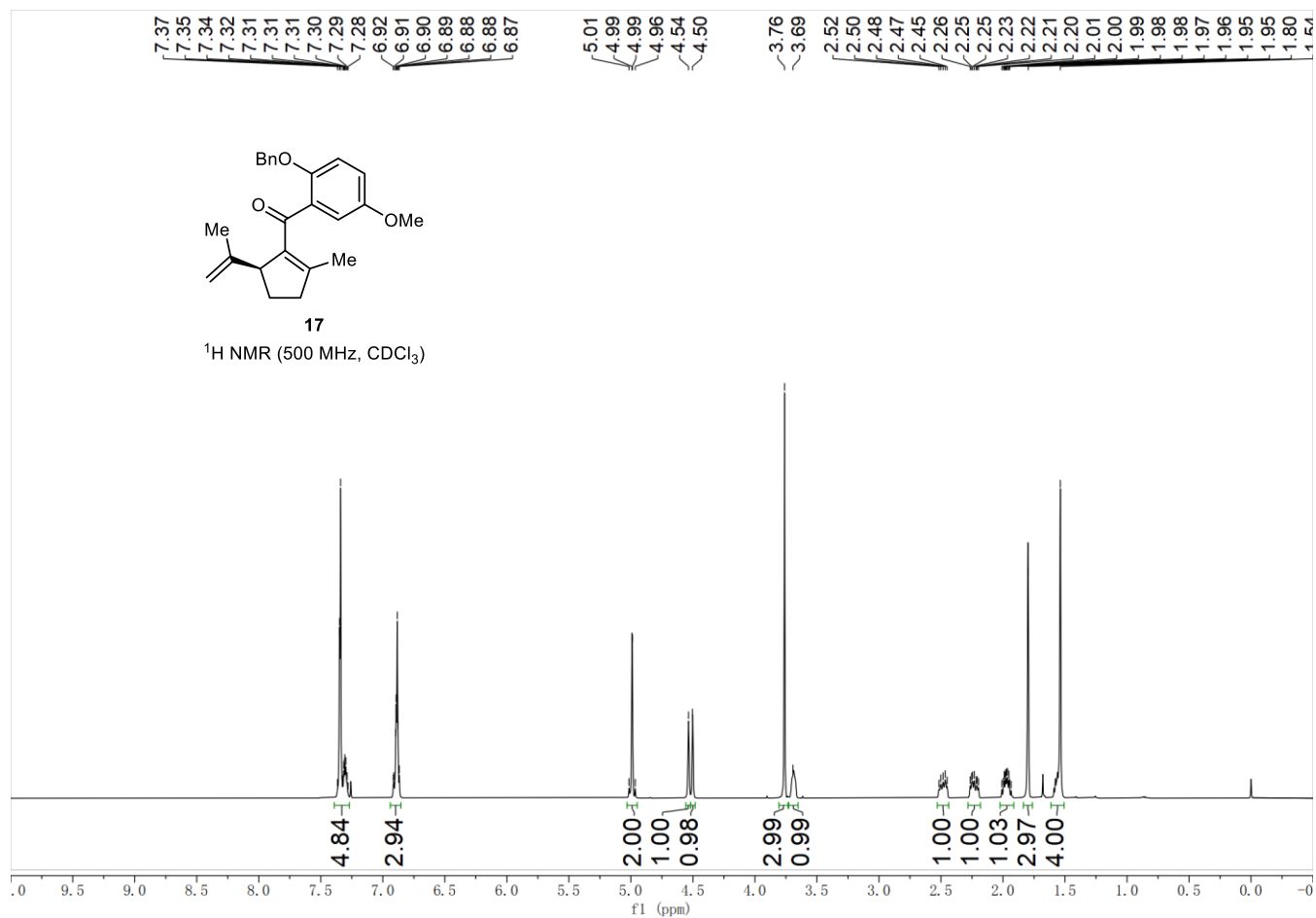
C	Our synthetic (125 MHz, (CD ₃) ₂ CO)	Natural ¹⁶ (150 MHz, (CD ₃) ₂ CO)	Δδ (Our synthetic – Natural)
1	152.4	156.4	-
2	129.1	129.0	+0.1
3	115.1	114.9	+0.2
4	147.3	147.2	+0.1
5	115.4	115.2	+0.2
6	119.9	119.8	+0.1
1'	46.1	46.1	0
2'	156.4	152.2	-
3'	142.1	142.0	+0.1
4'	19.5	19.5	0
5'	26.8	26.7	+0.1
6'	48.2	45.1	-
7'	87.2	87.2	0
8'	39.0	38.9	+0.1
9'	24.6	24.5	+0.1
10'	50.3	50.2	+0.1
11'	45.1	48.1	-
12'	21.8	21.8	0
13'	29.1	29.0	+0.1
14'	193.4	193.4	0
15'	23.8	23.8	0

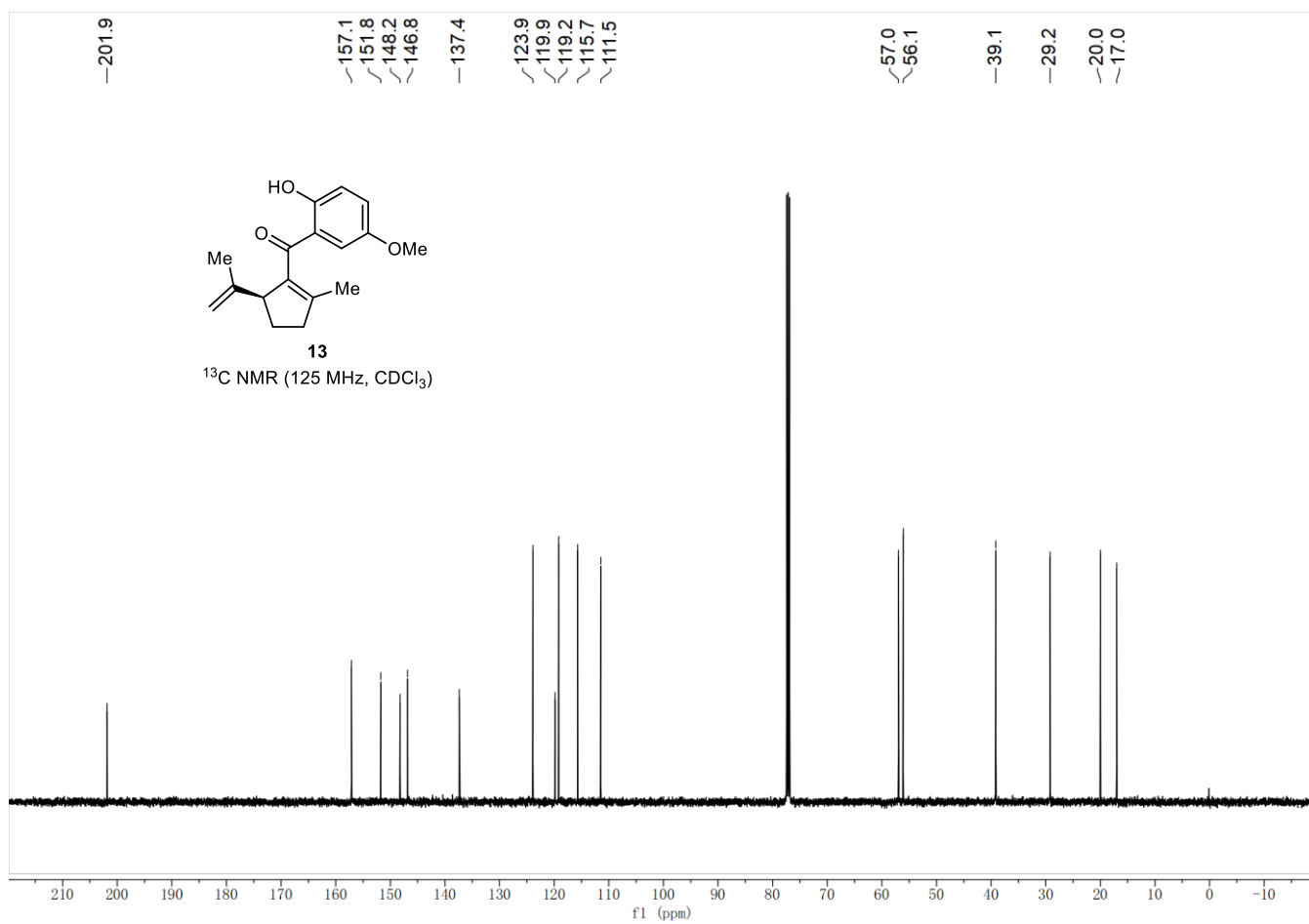
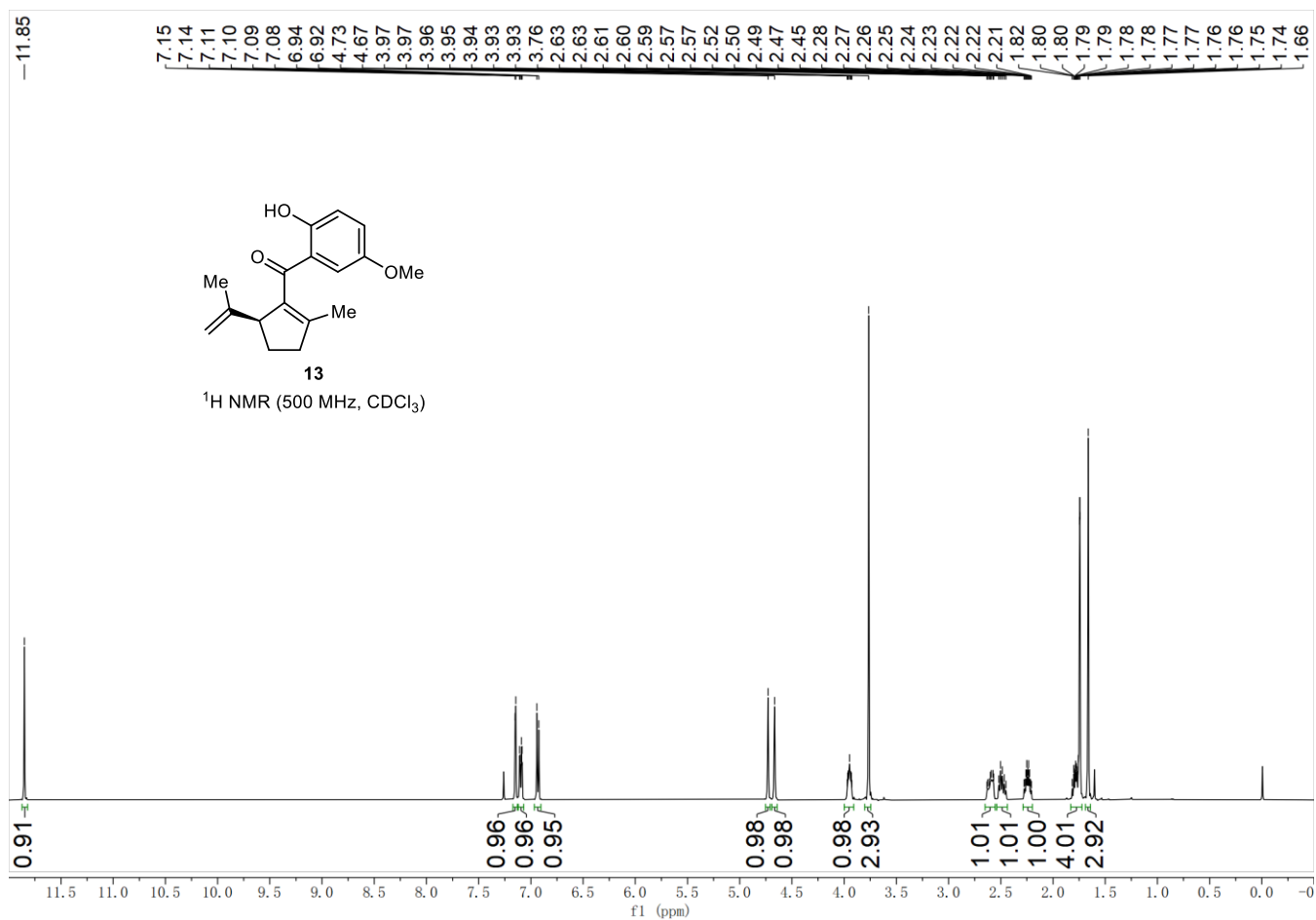
Note: The ¹H and ¹³C NMR spectra of our synthesized cochlearol B are in full agreement with those reported in the isolation literature¹⁶. We revised the ¹³C assignments (C1, C2', C6', and C11') from the isolation literature.

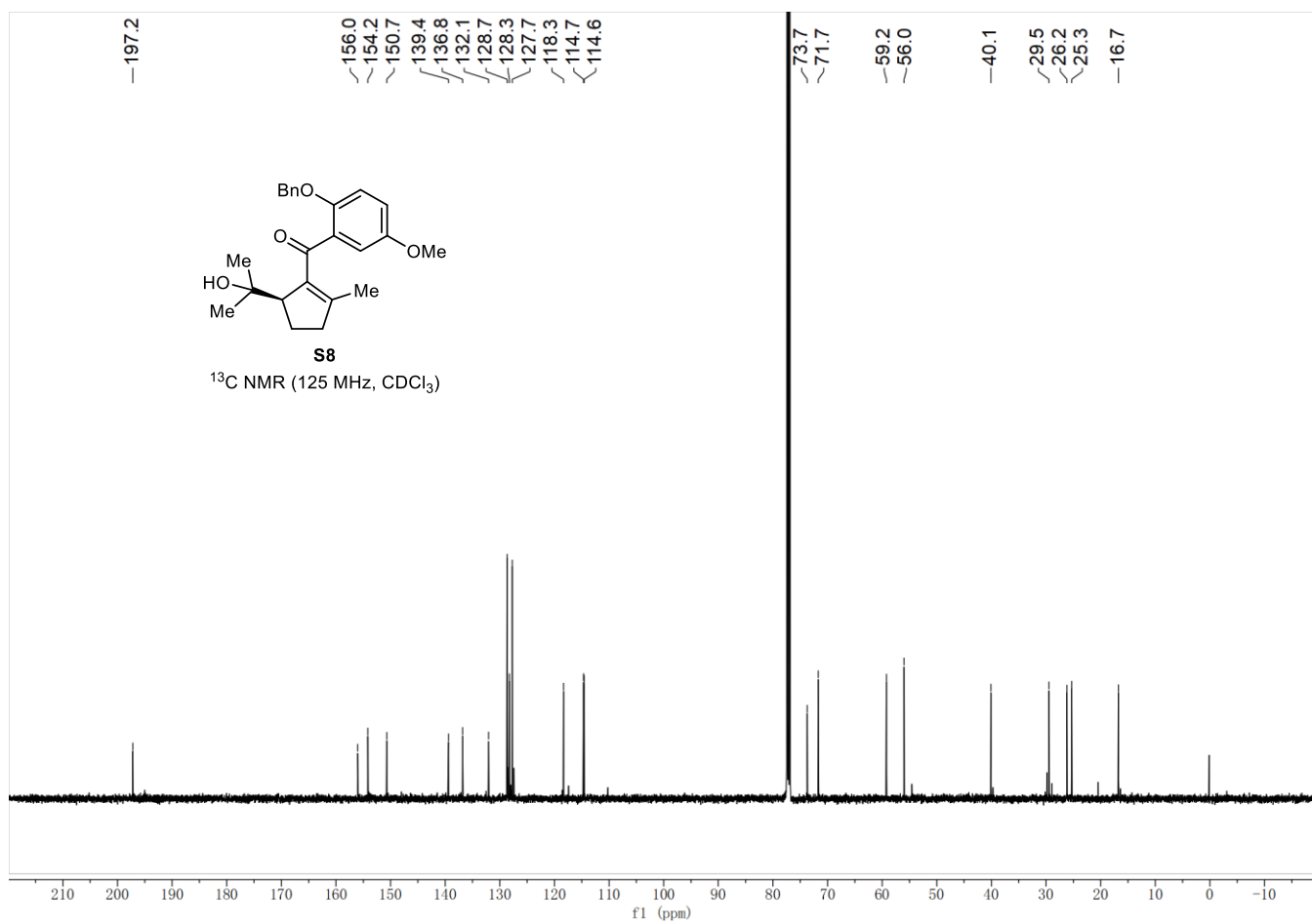
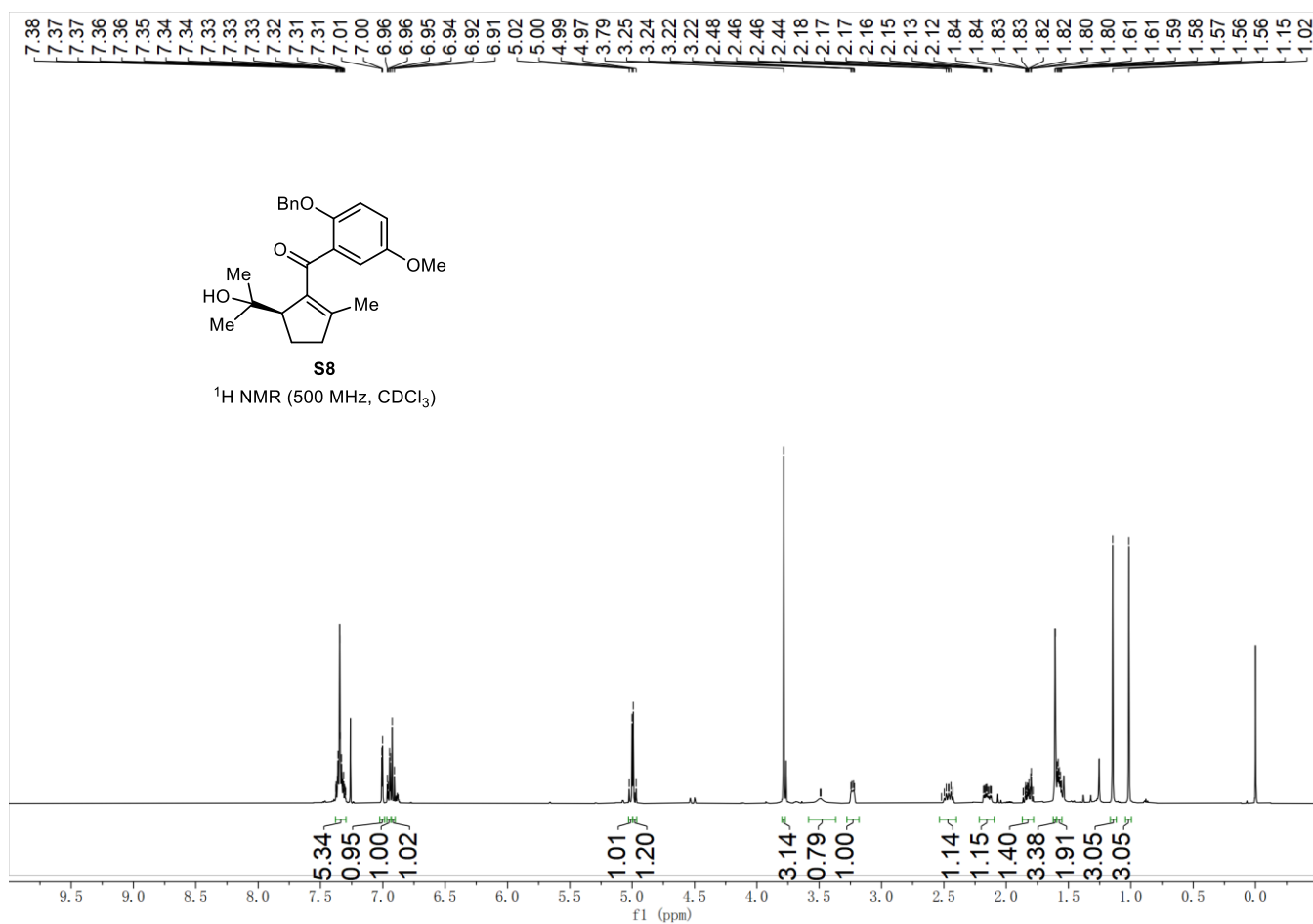
7. ^1H and ^{13}C NMR Spectra of the Synthetic Intermediates, Ganocins A–C and Cochlearol B

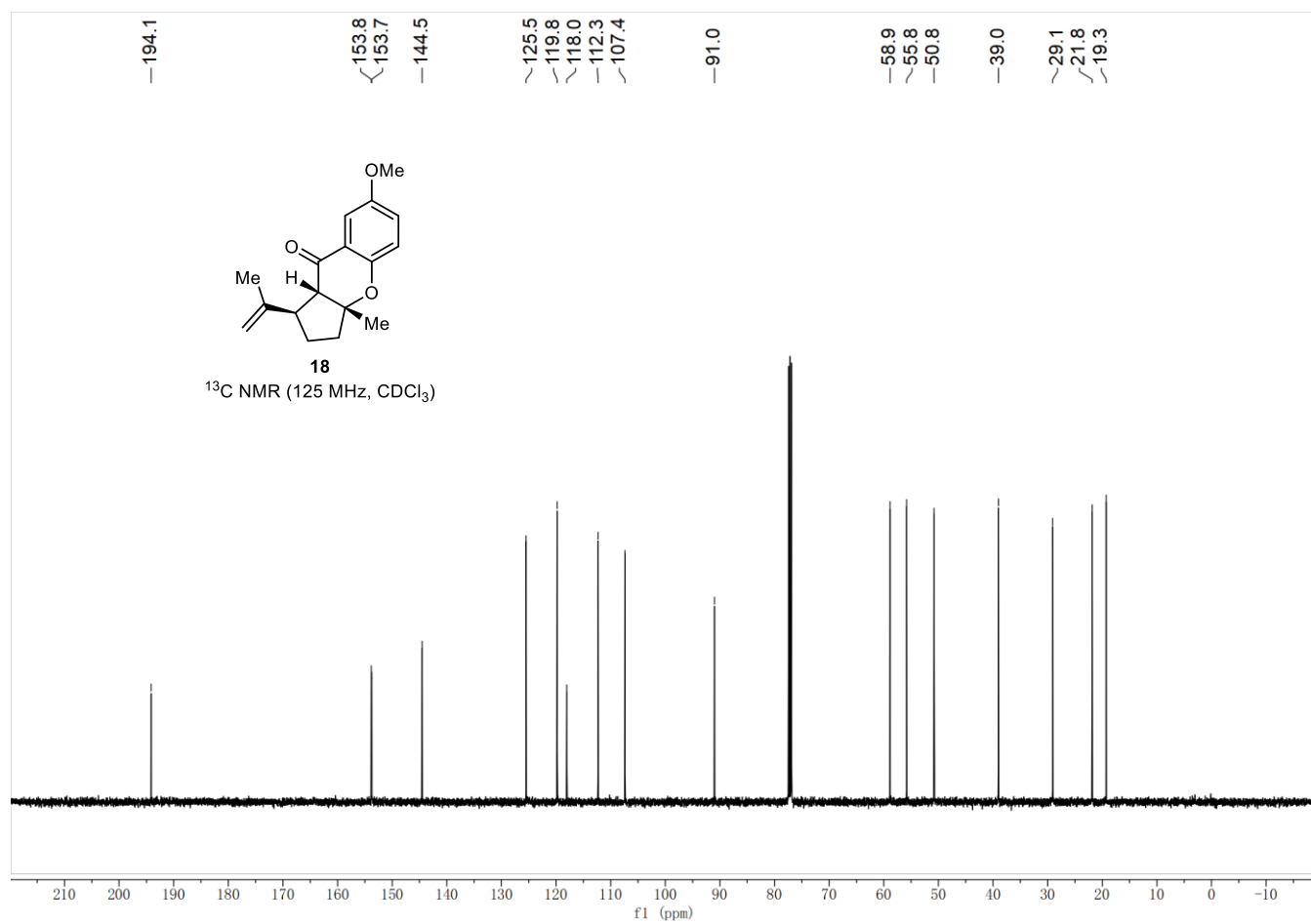
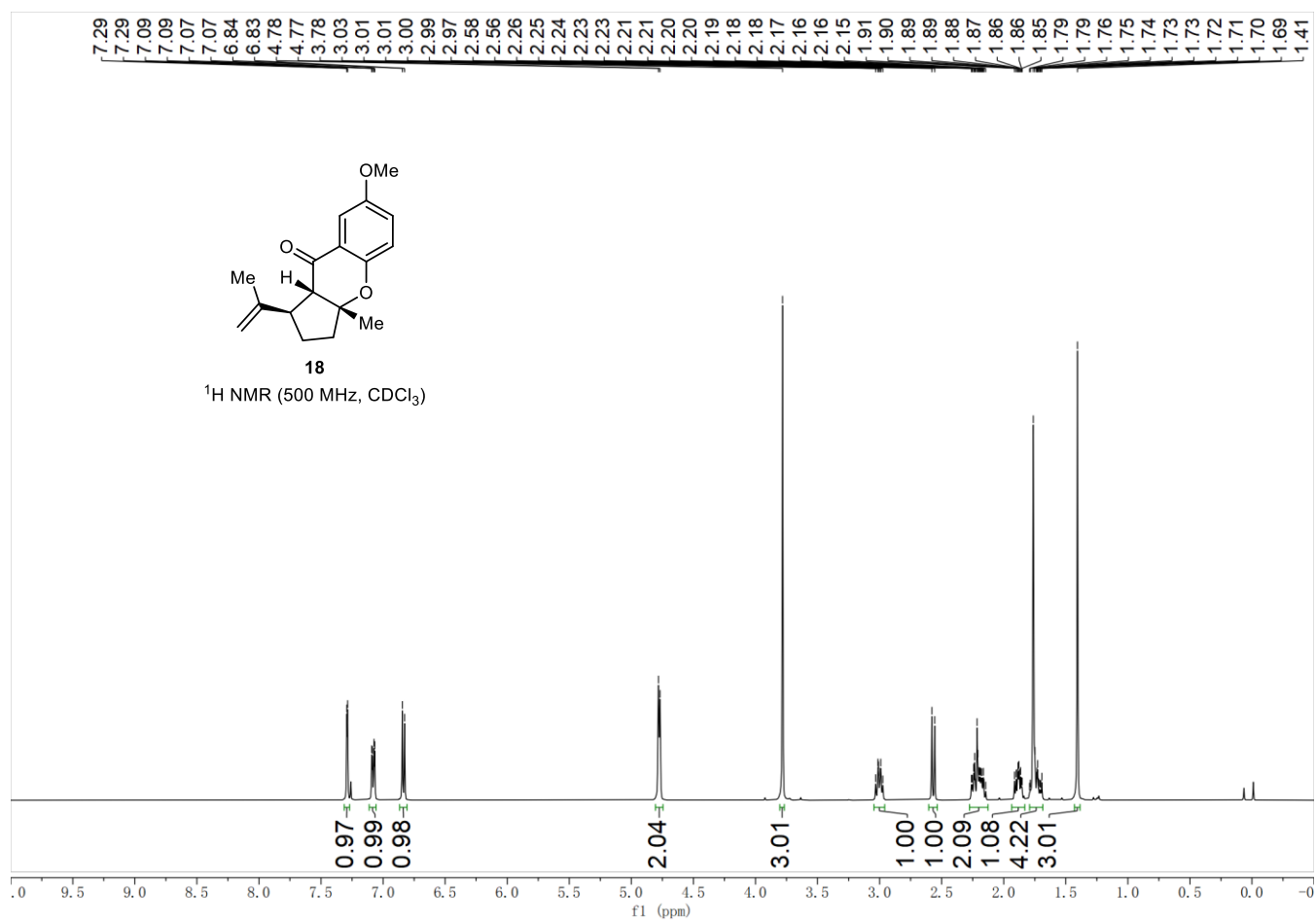


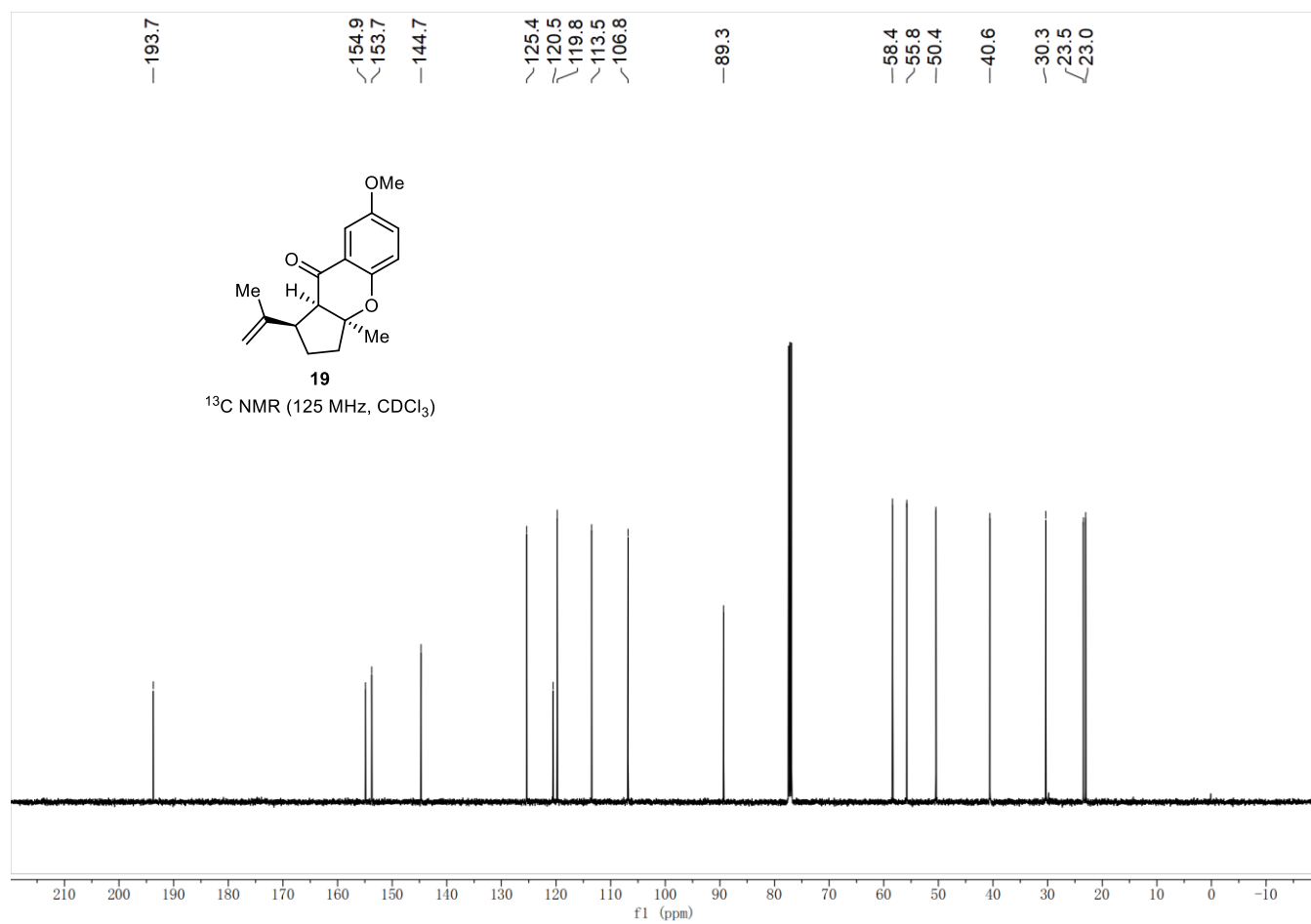
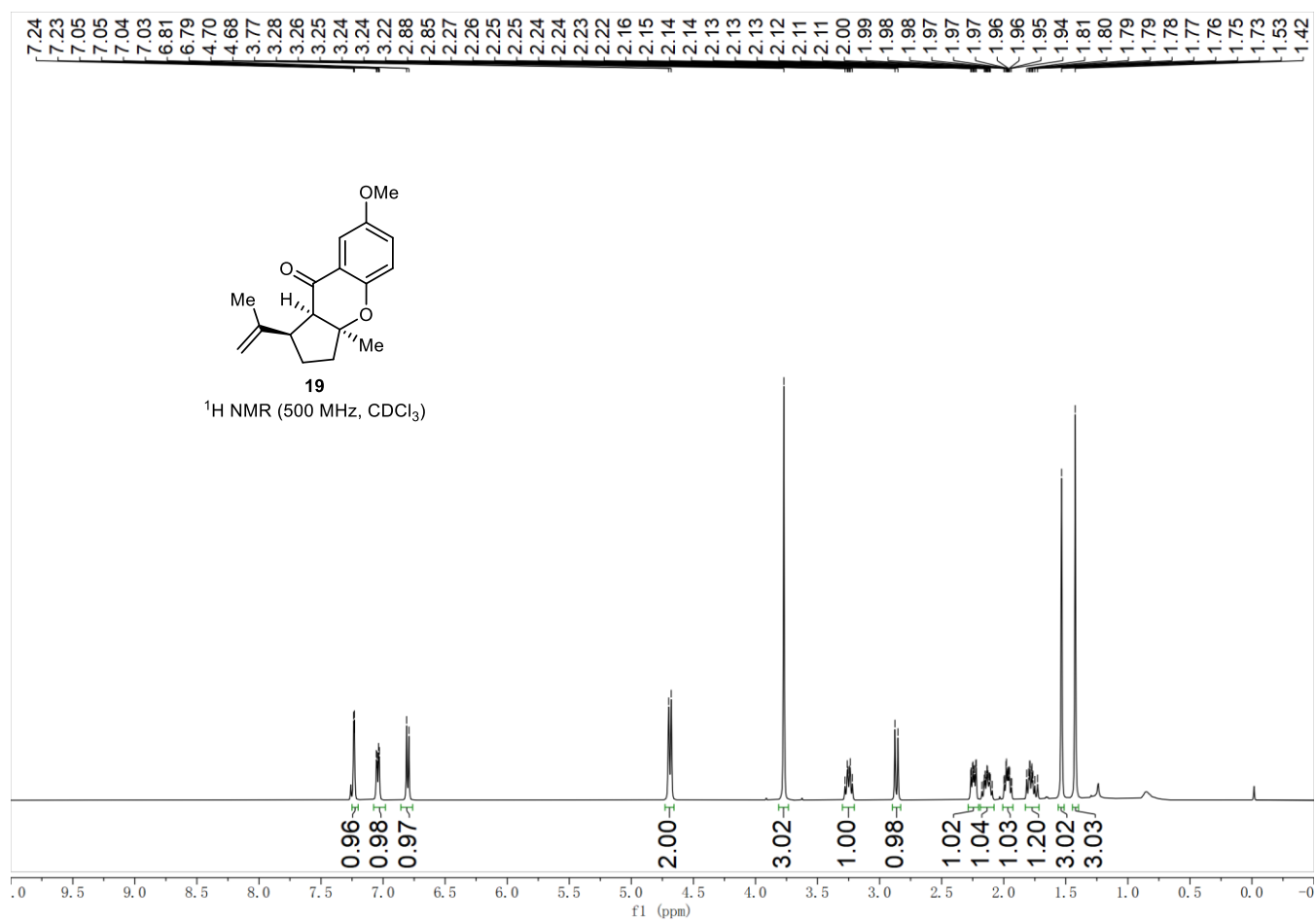


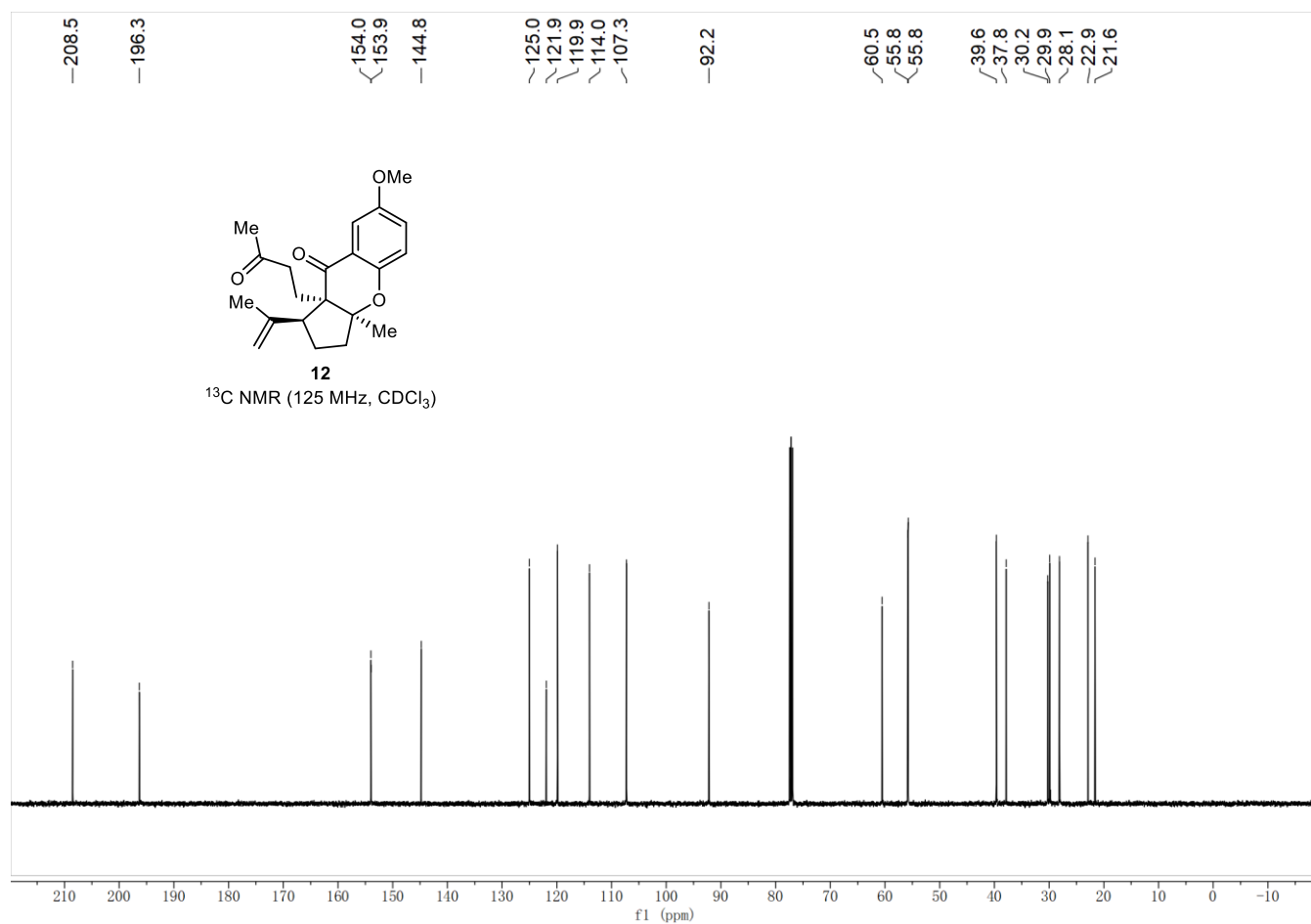
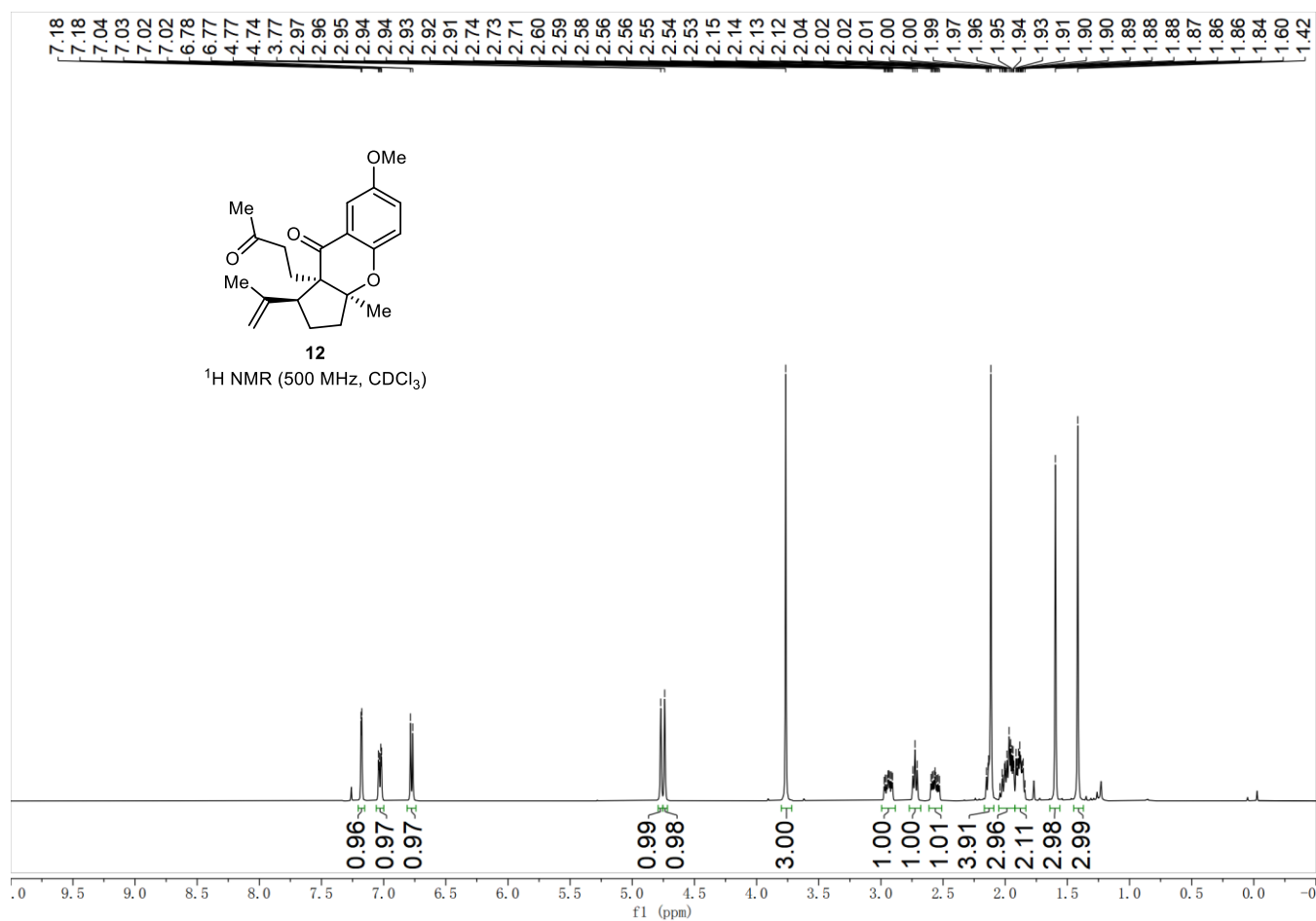


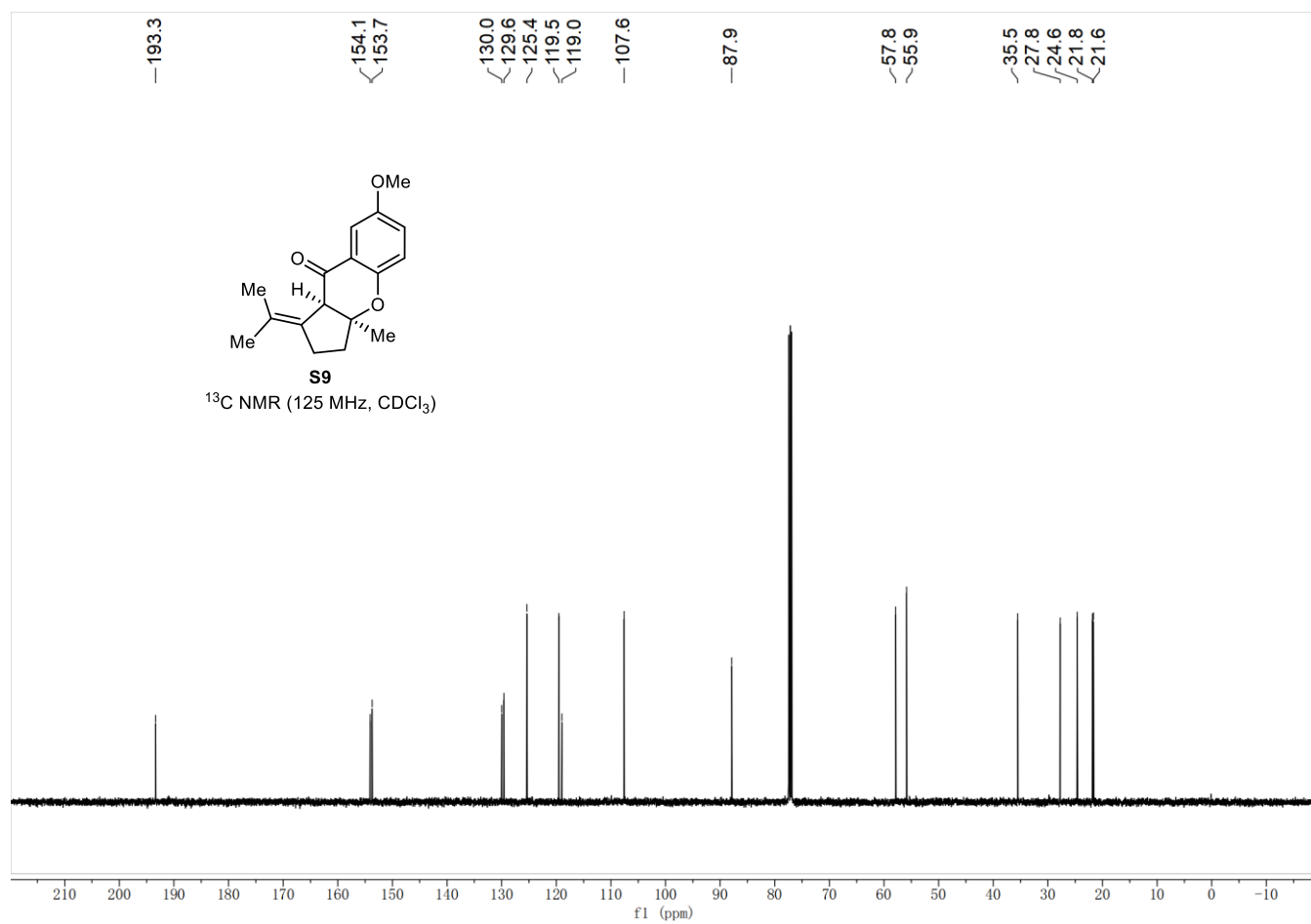
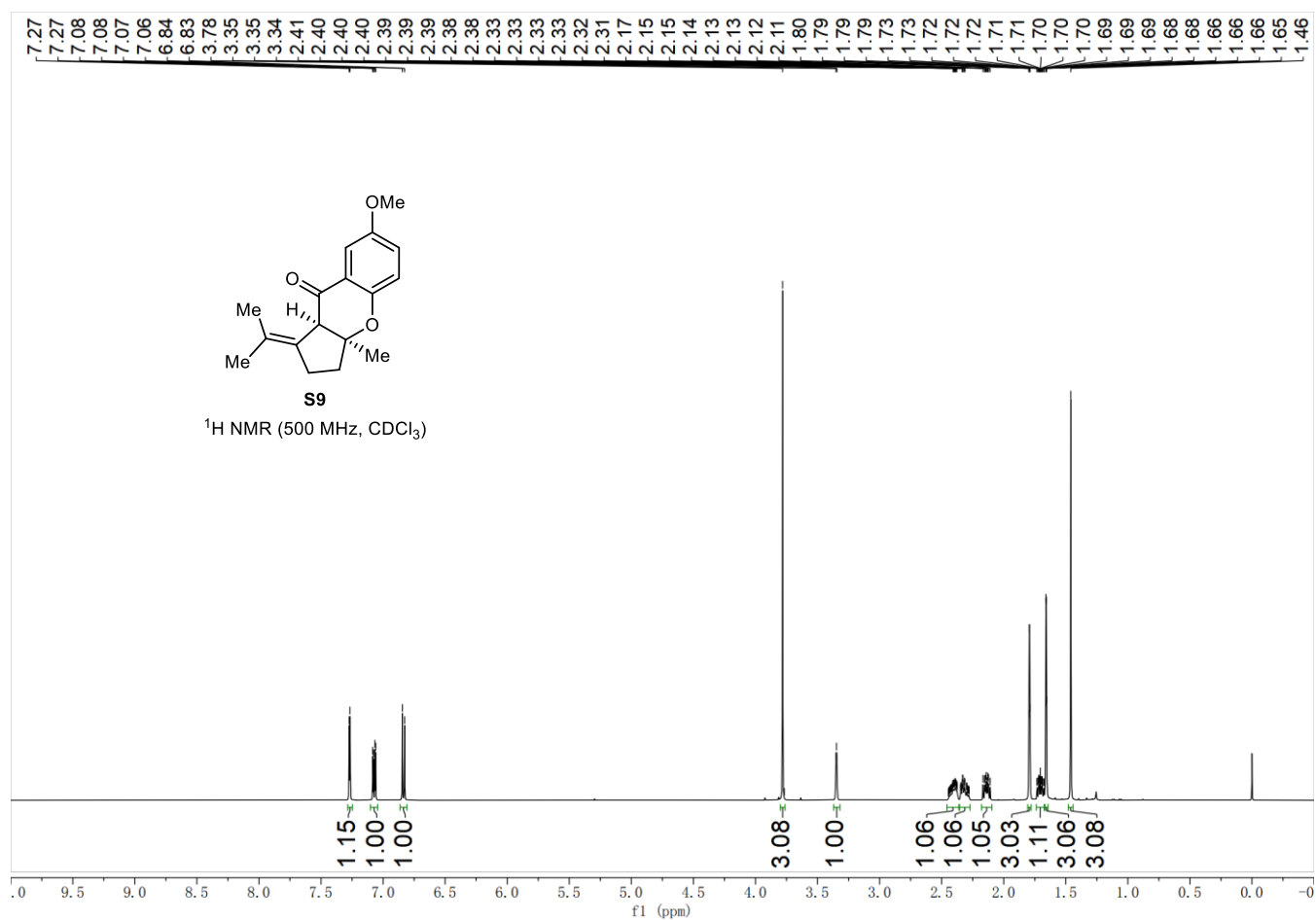


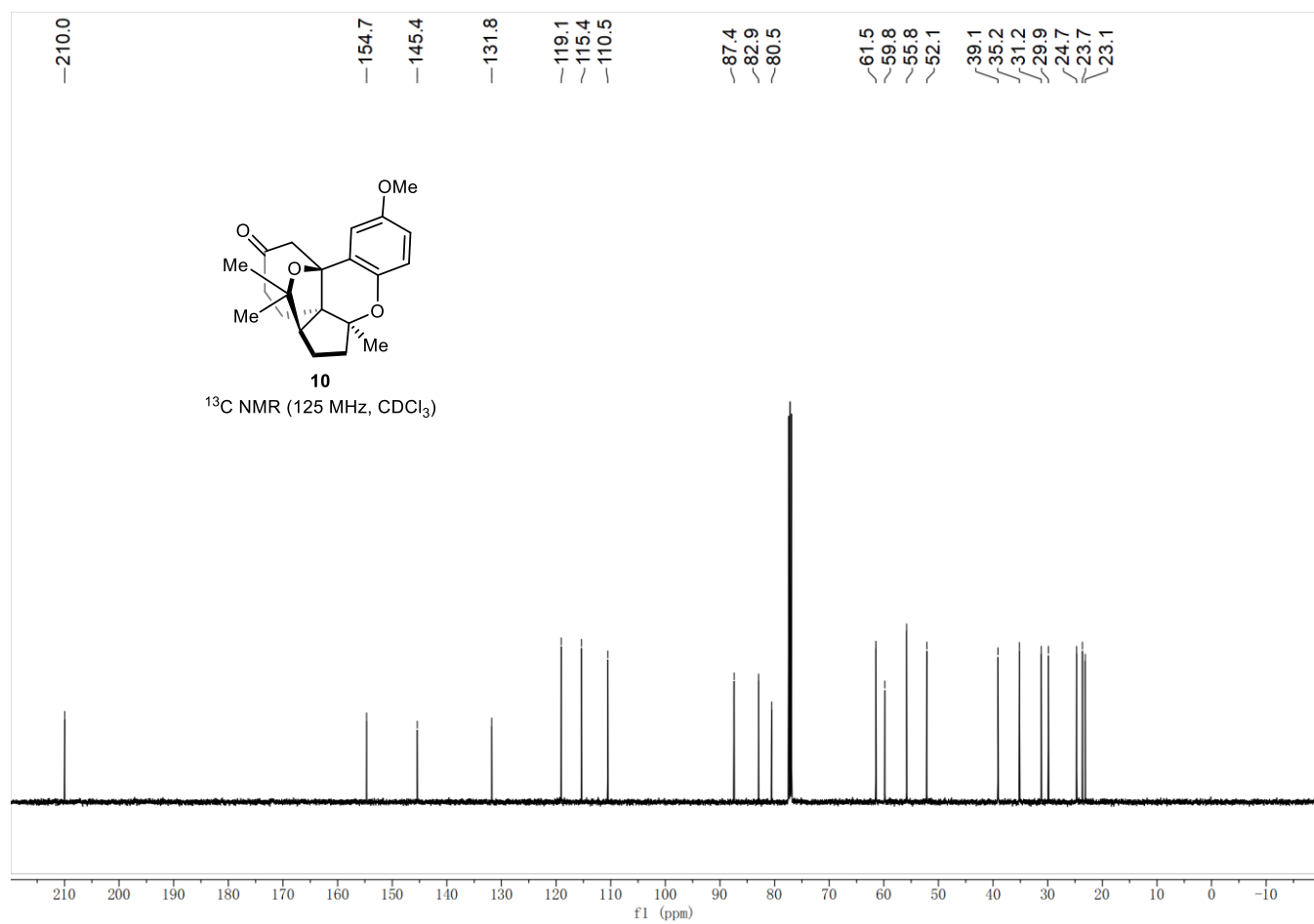
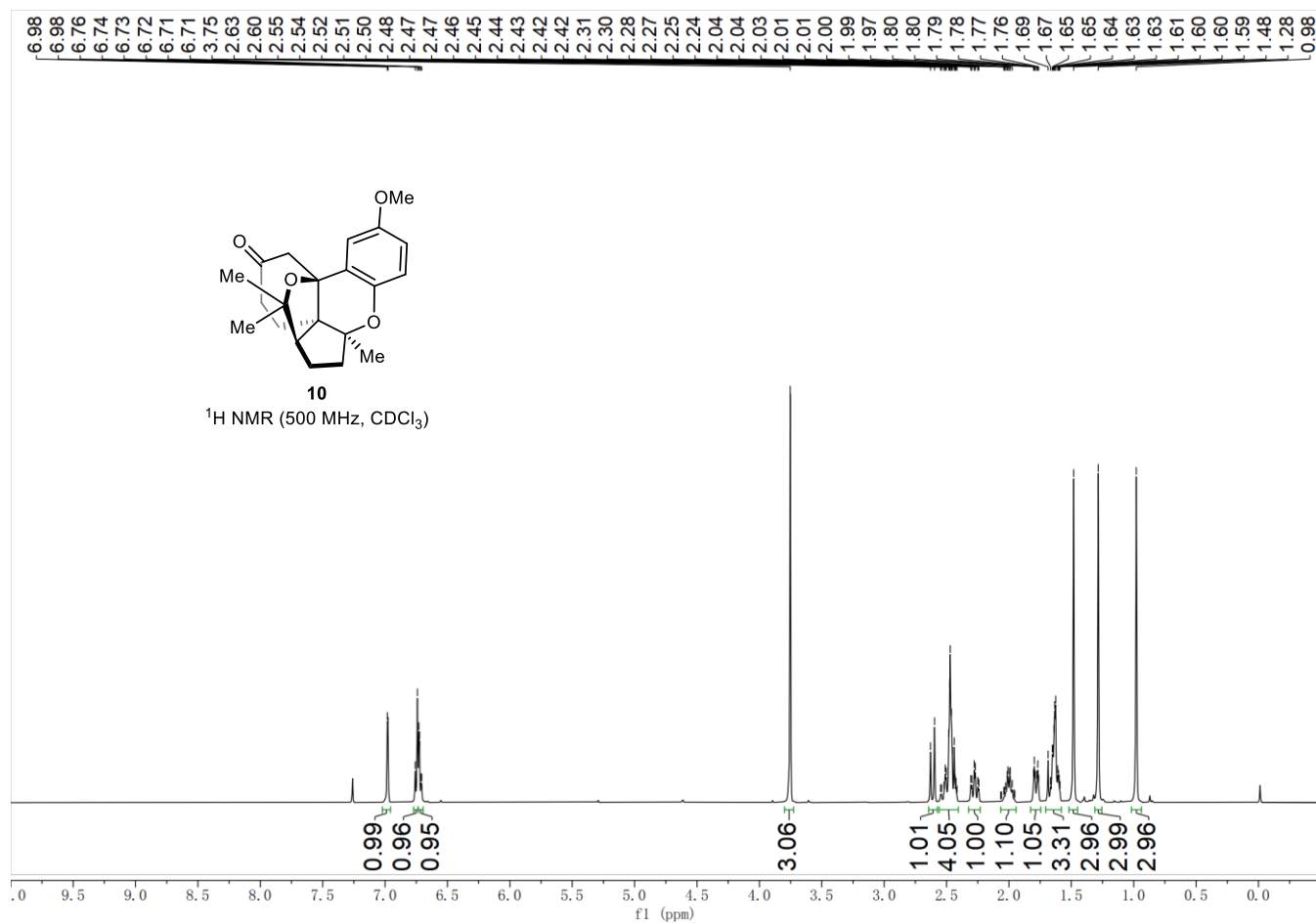


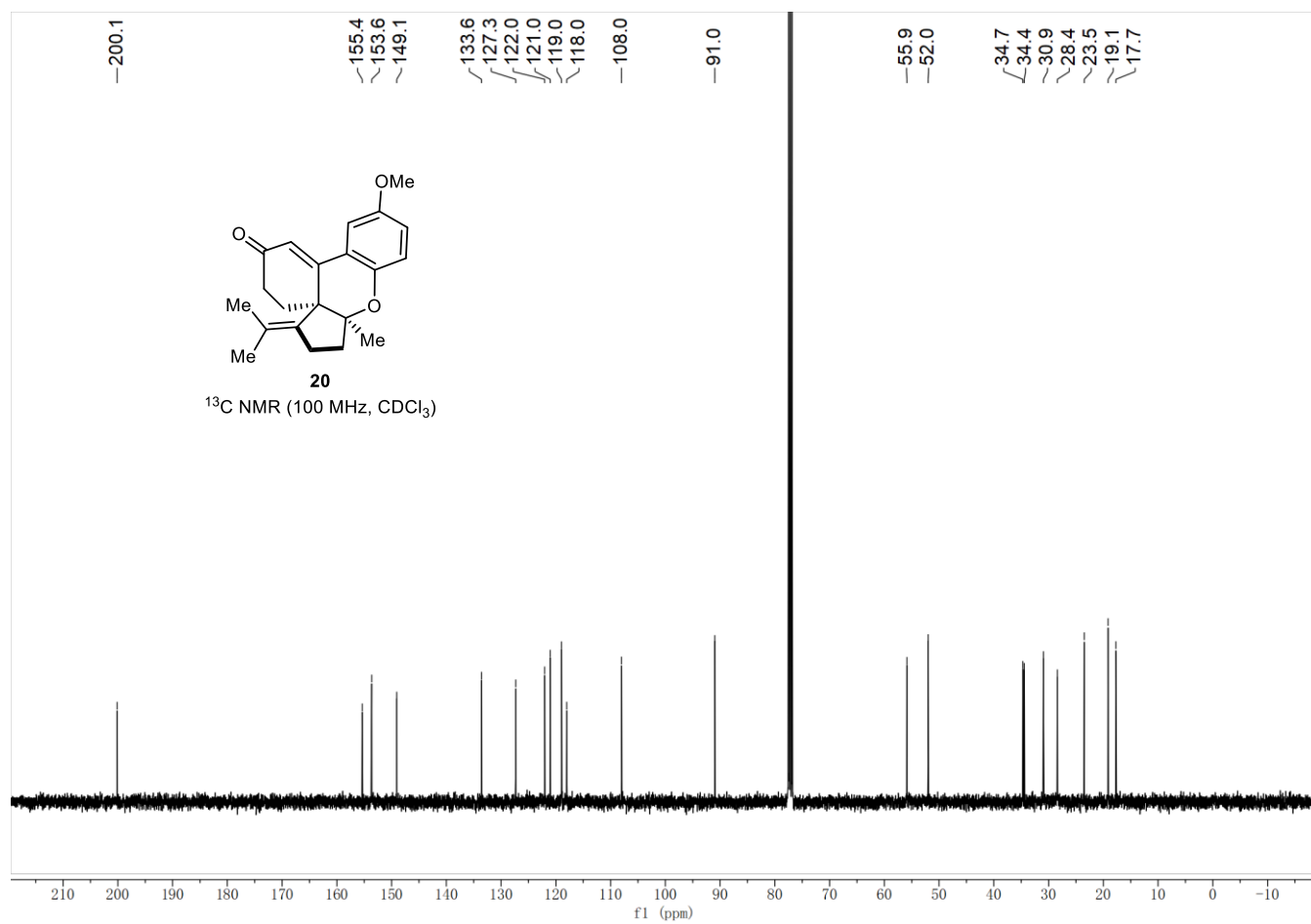
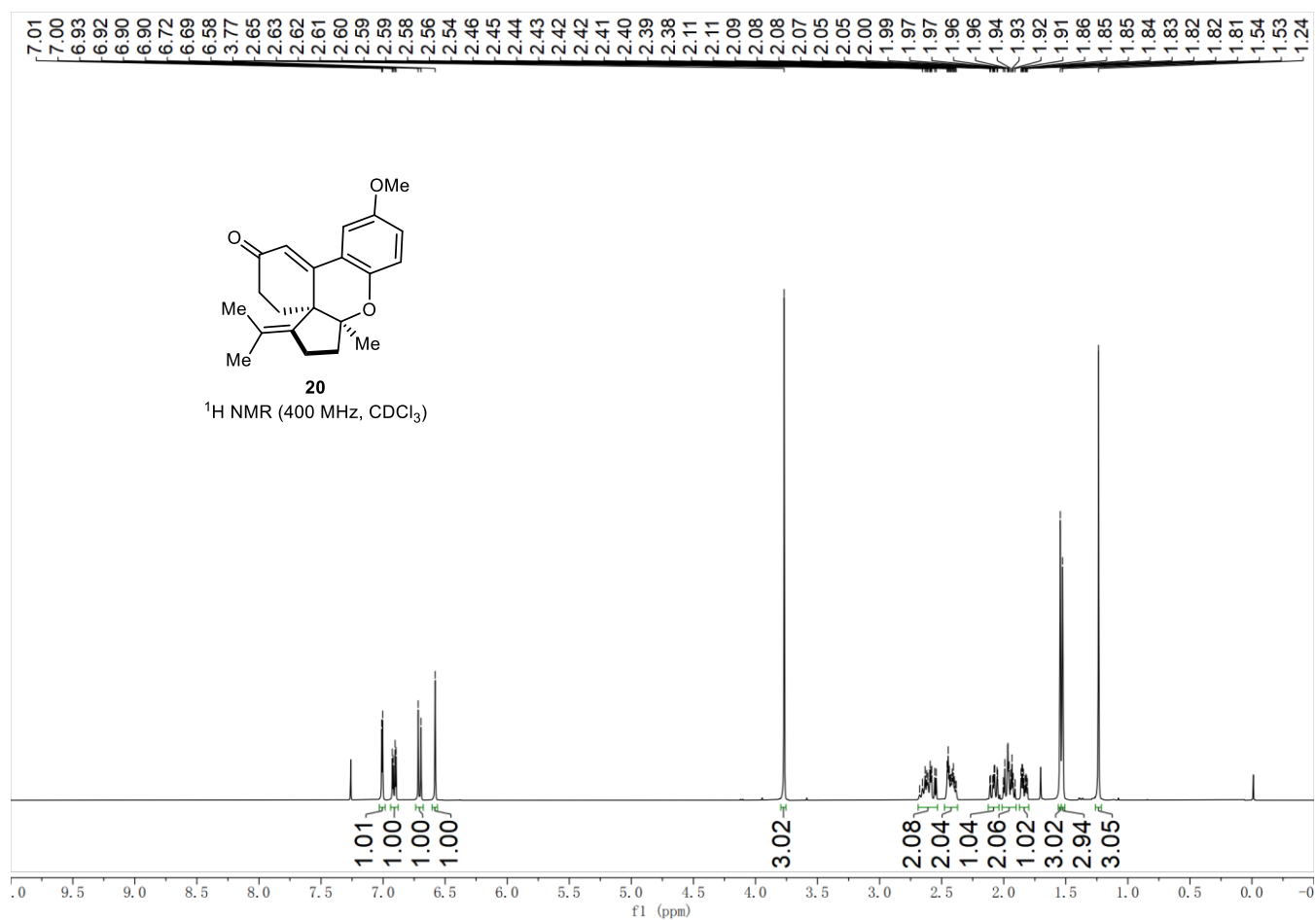


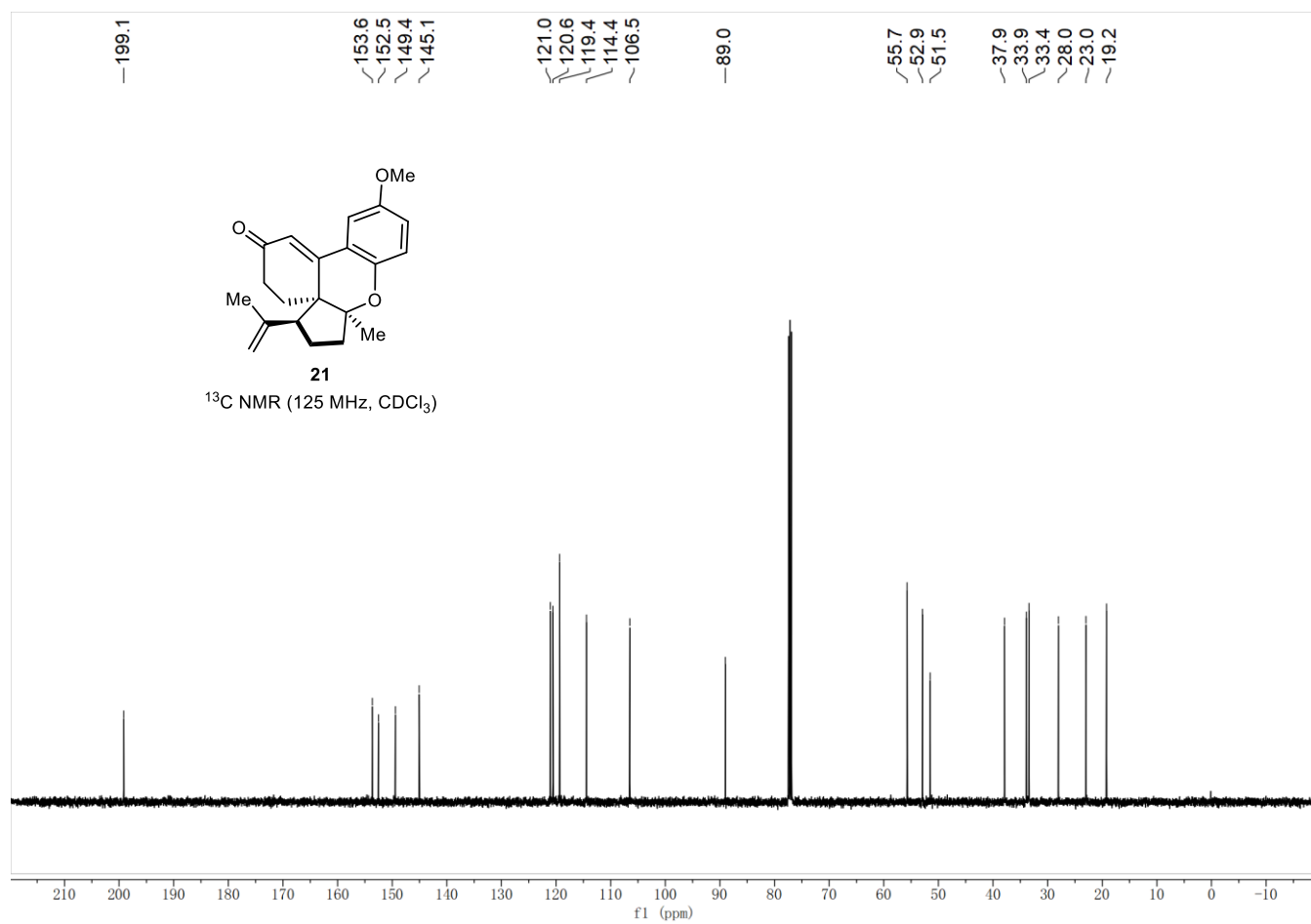
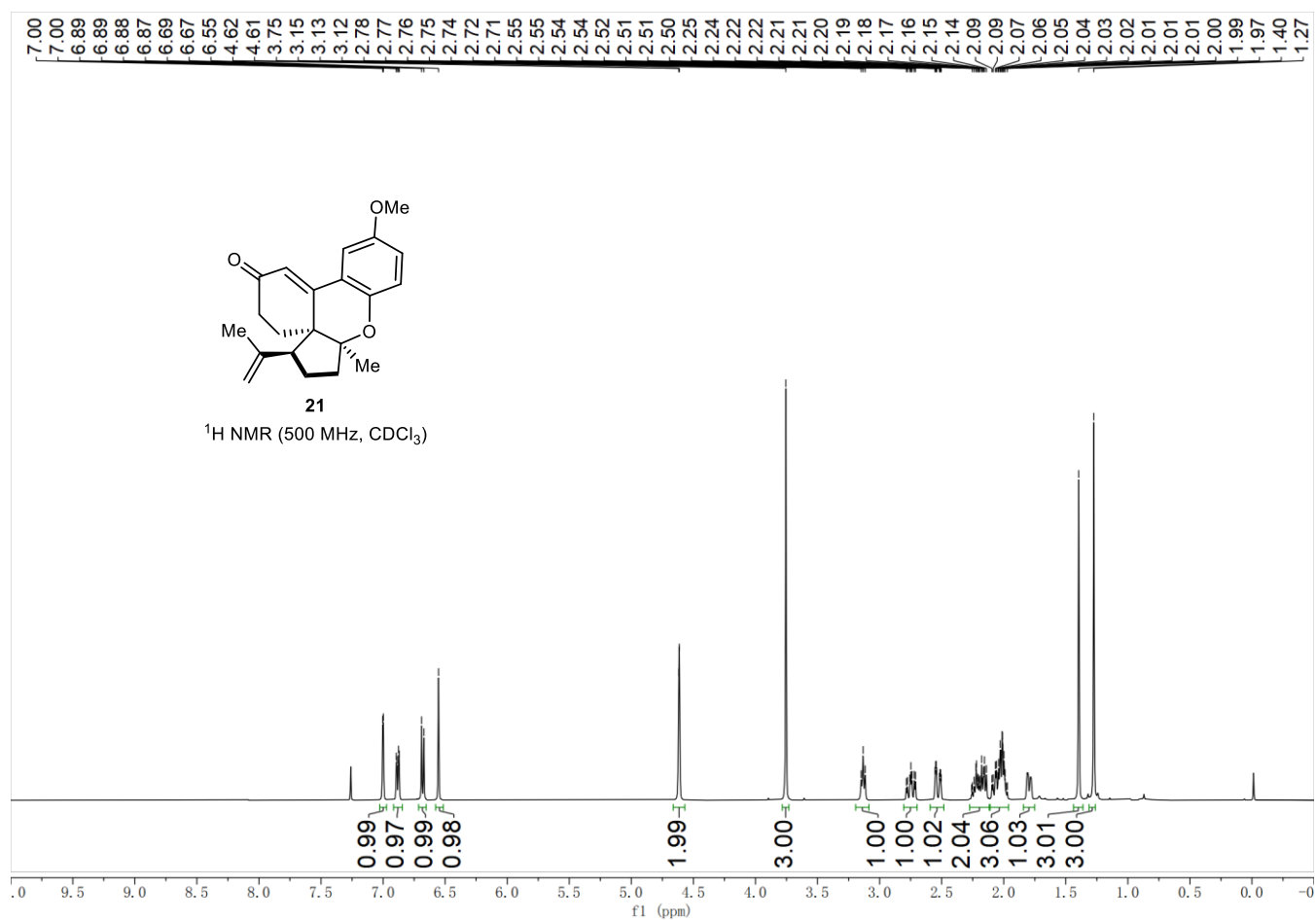


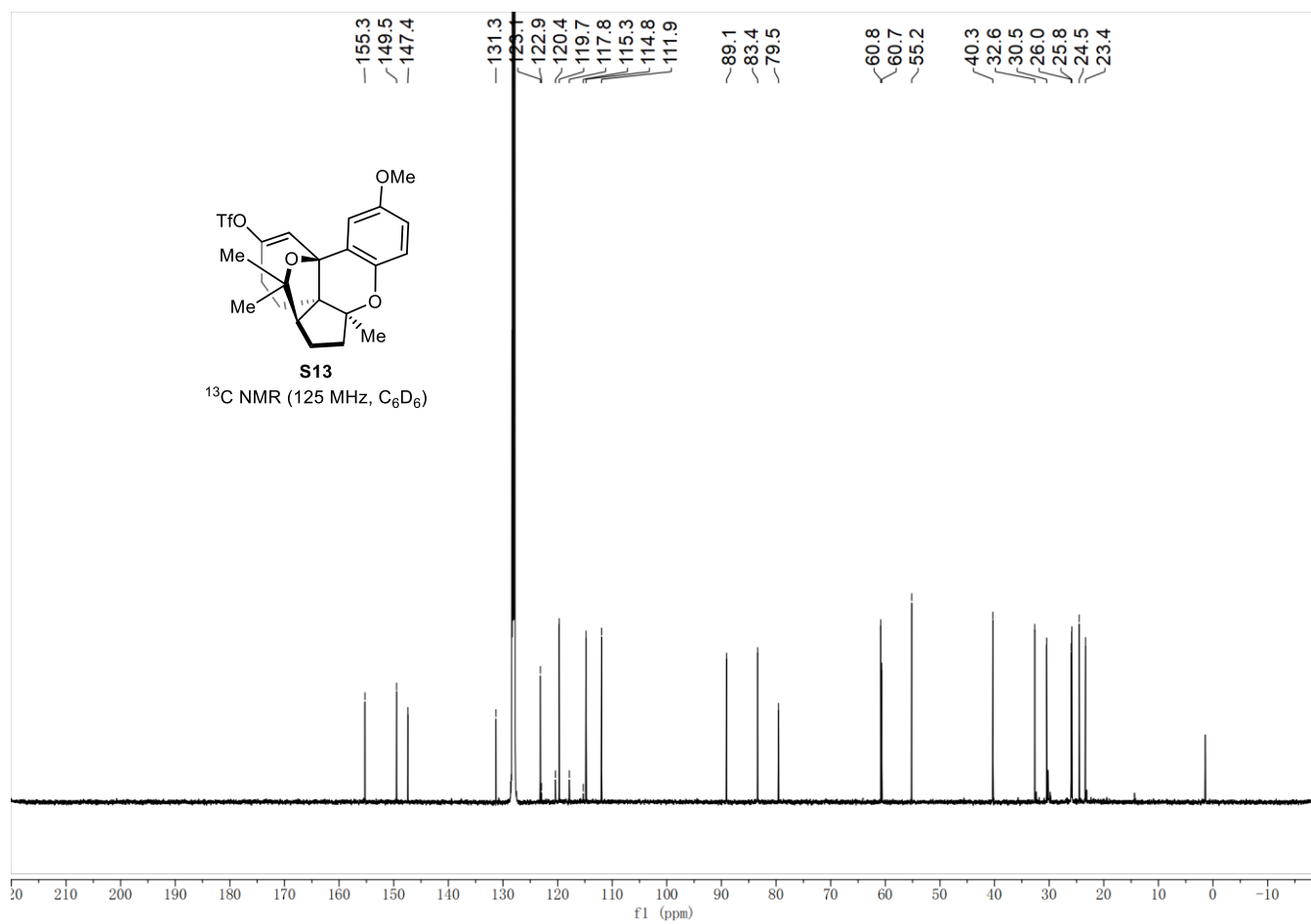
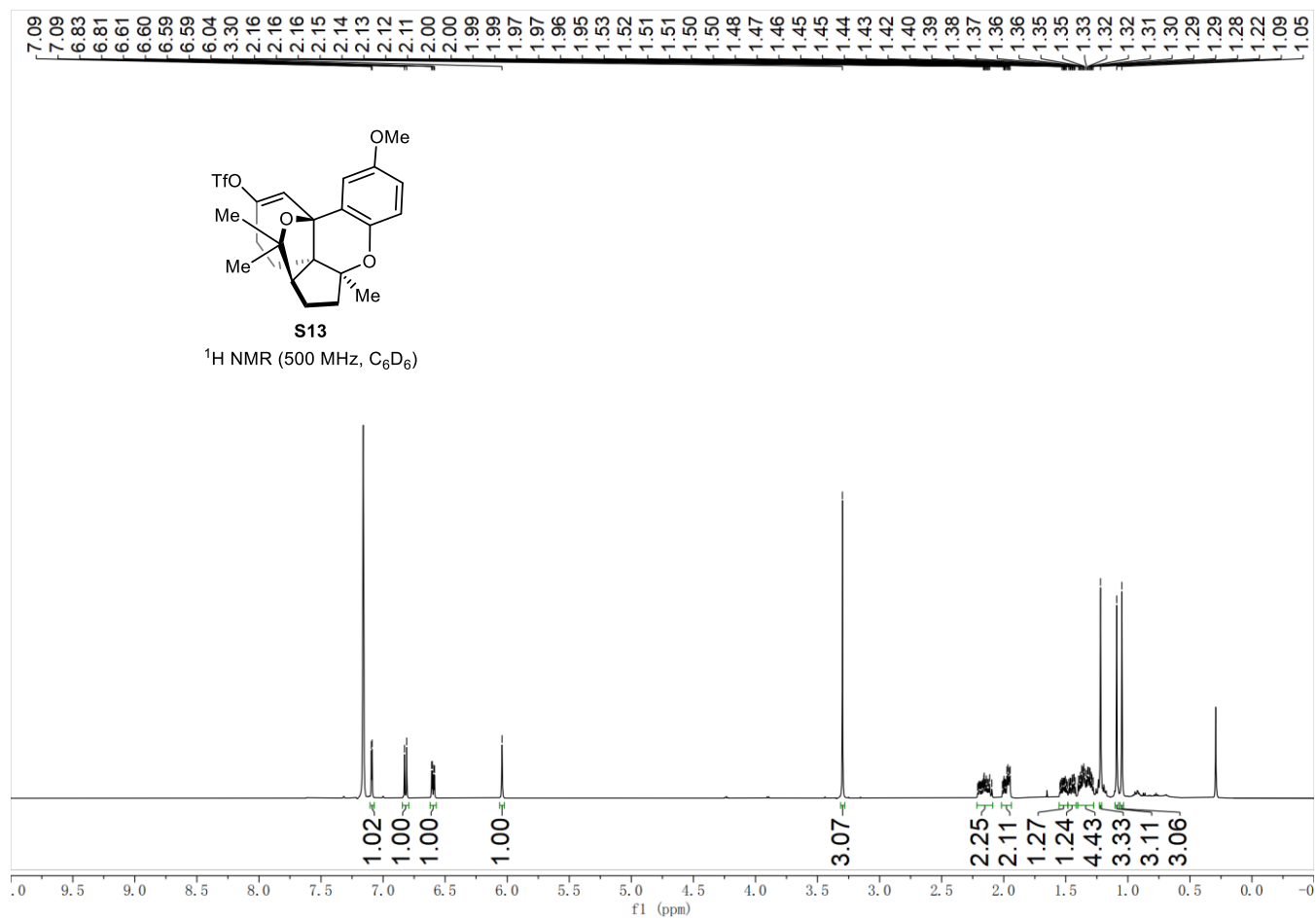


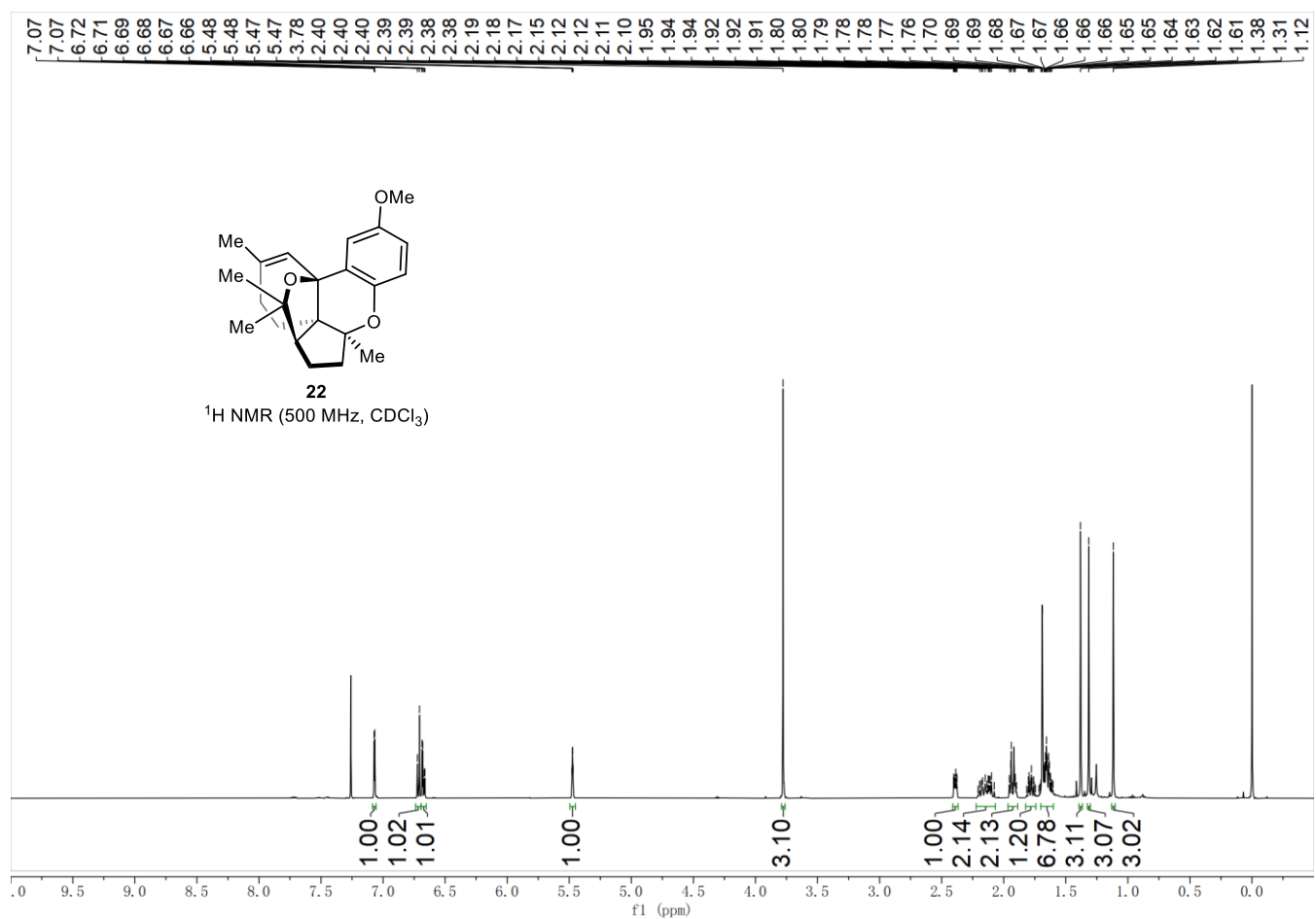
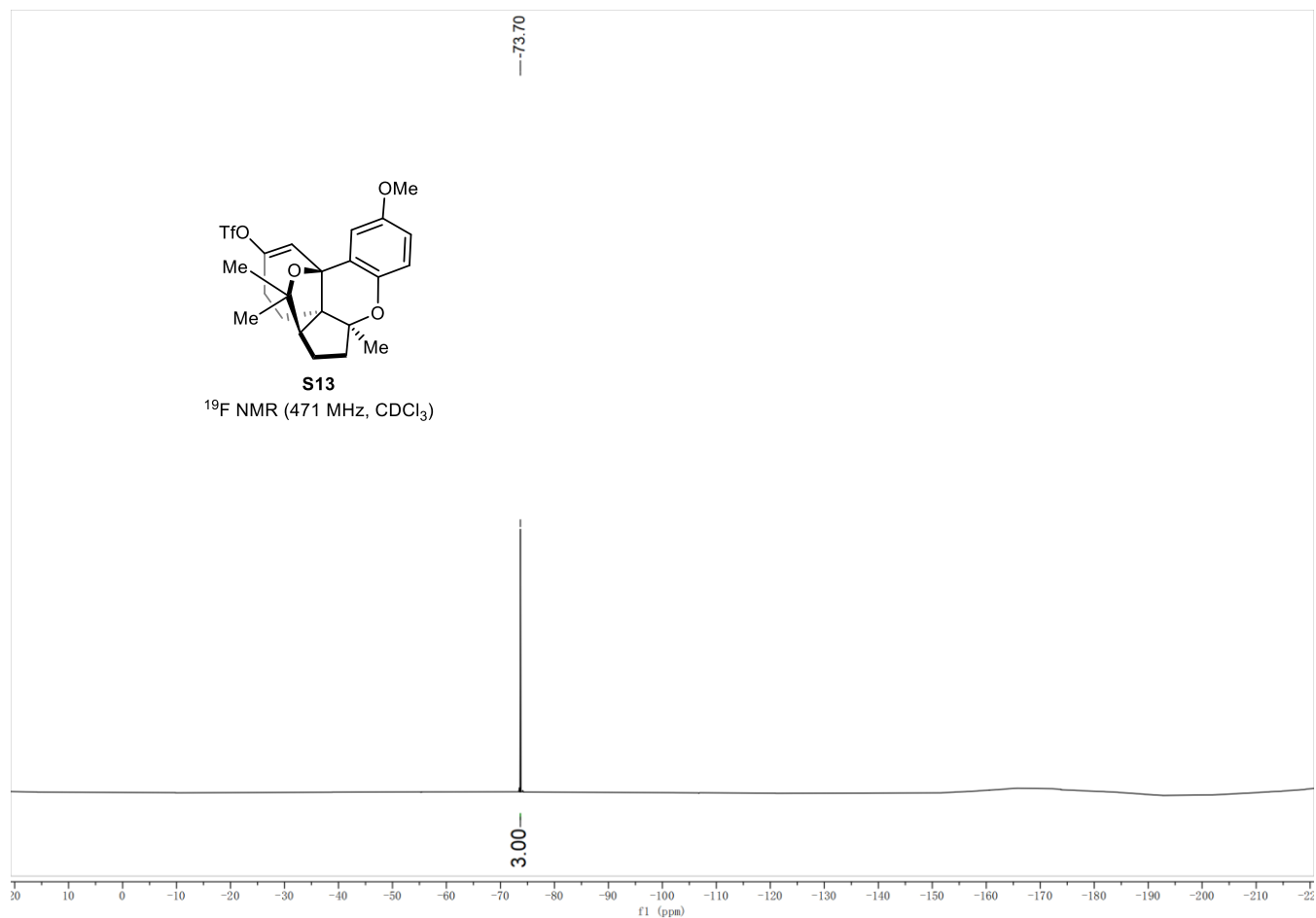


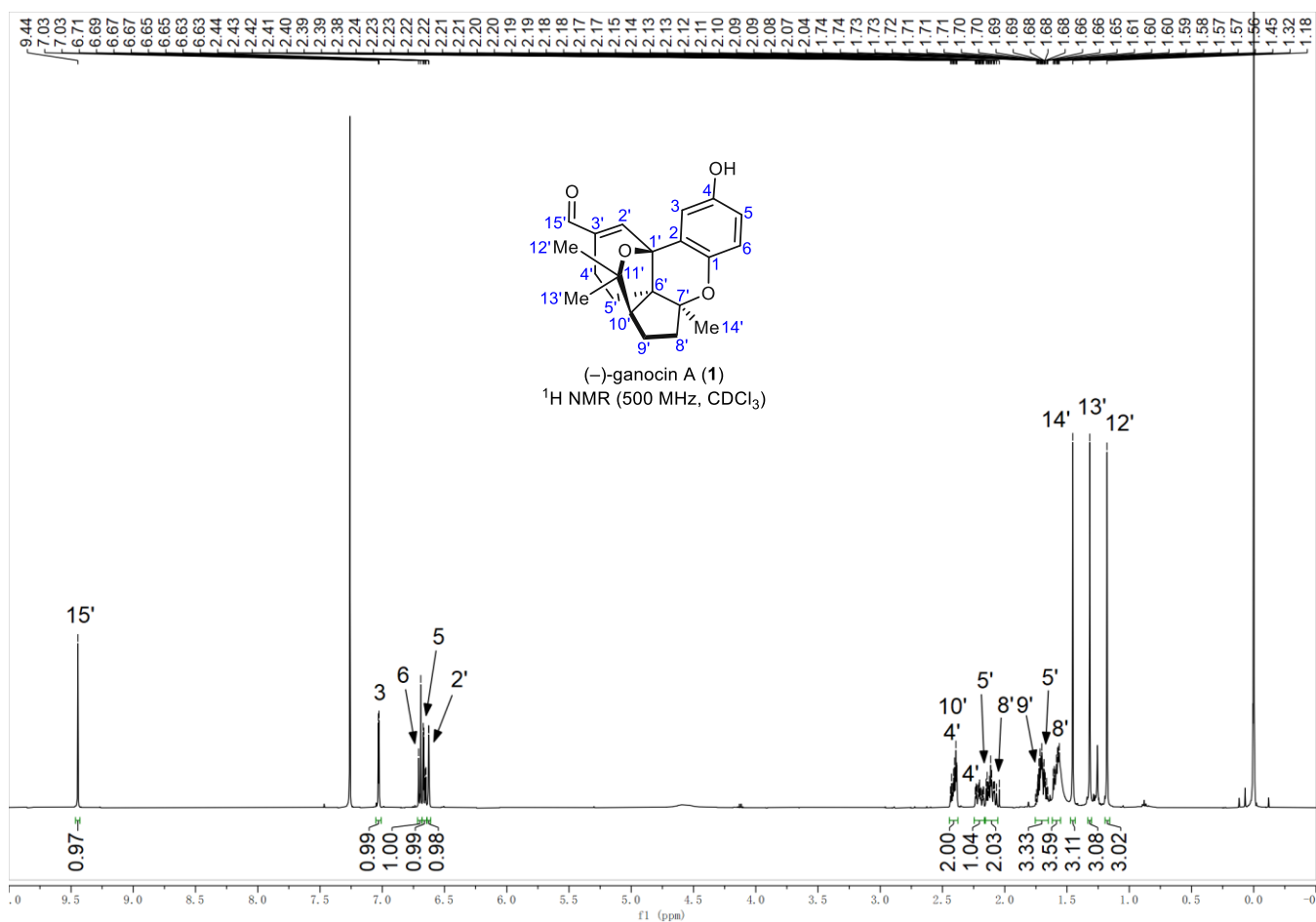
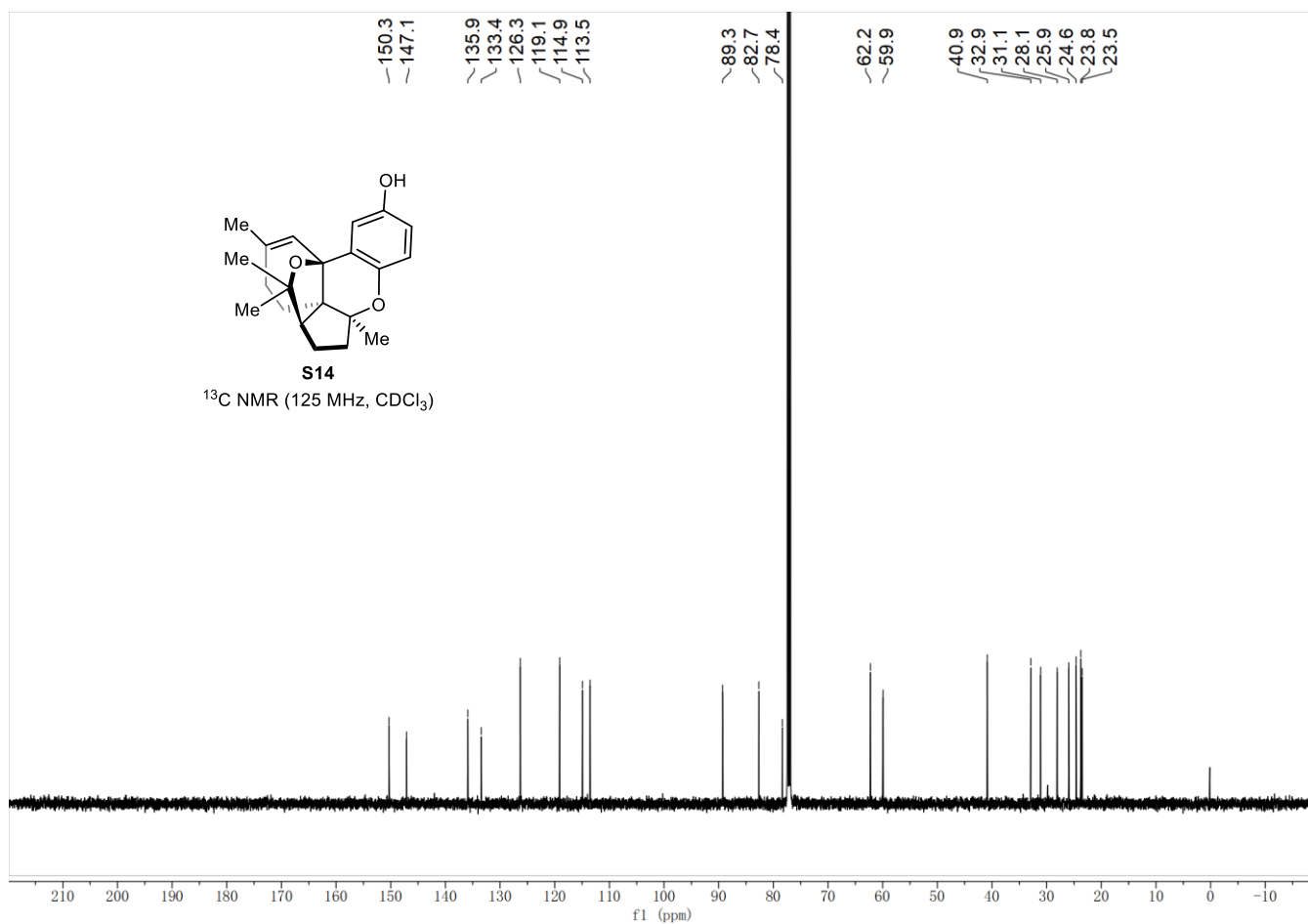


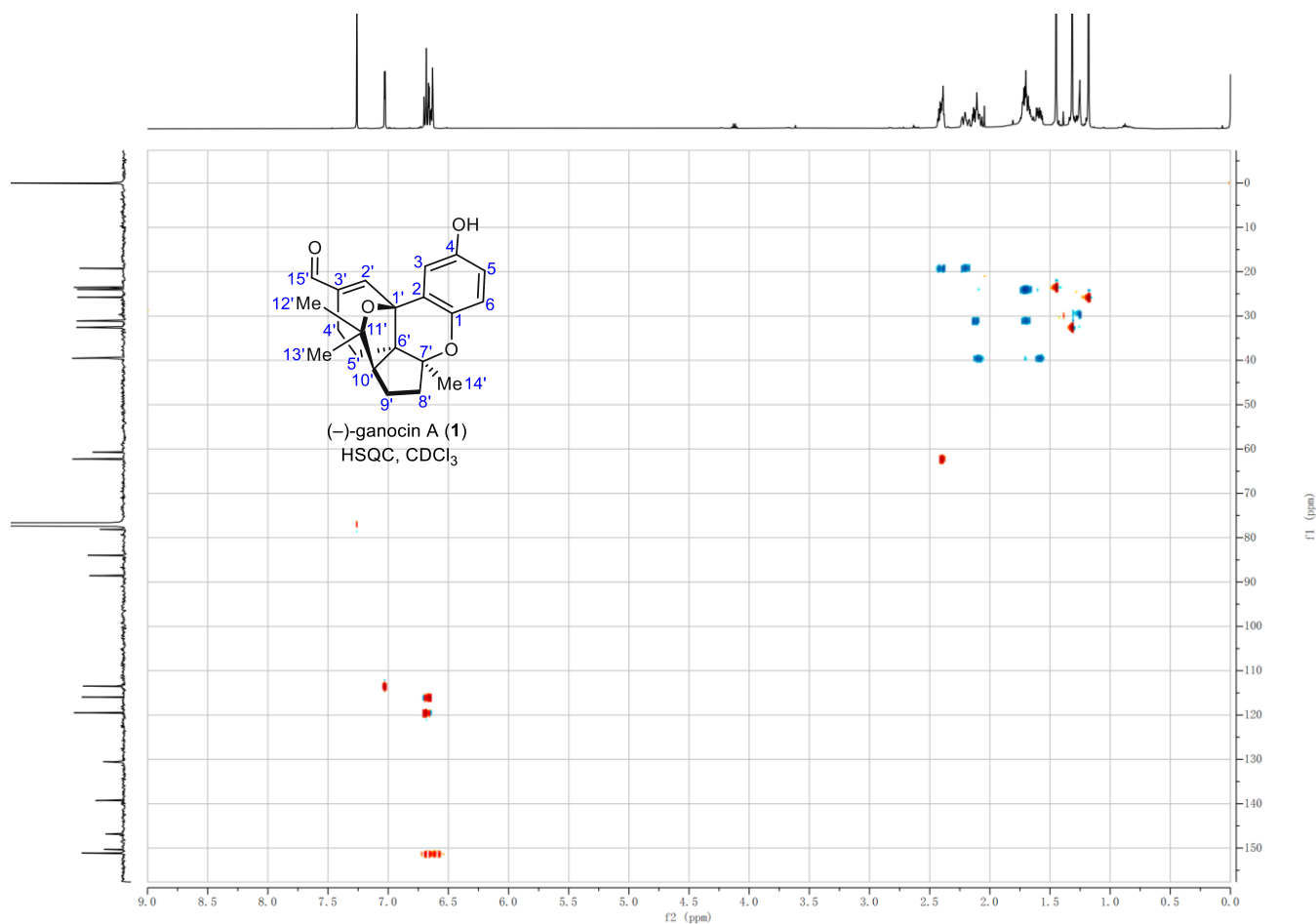
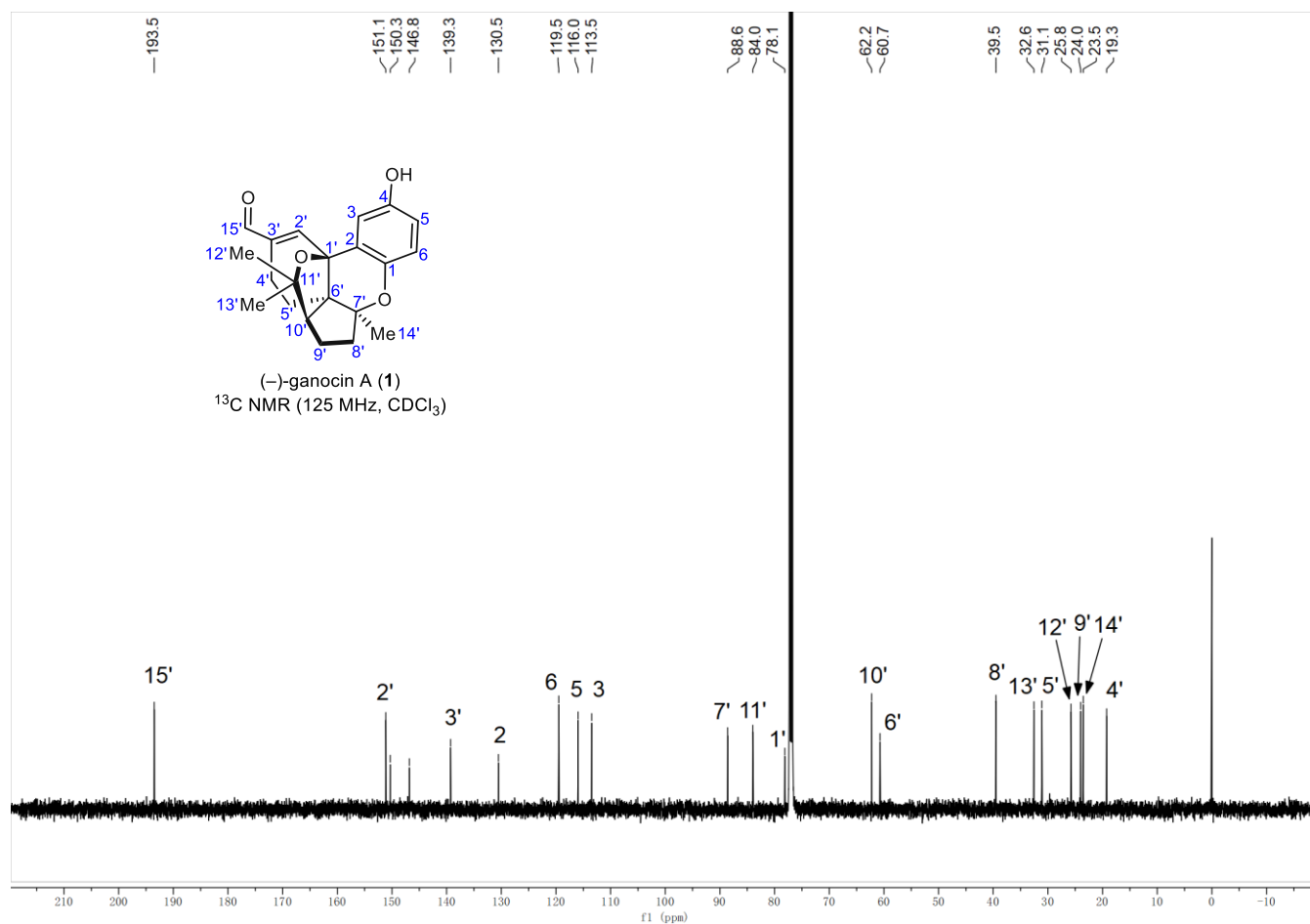


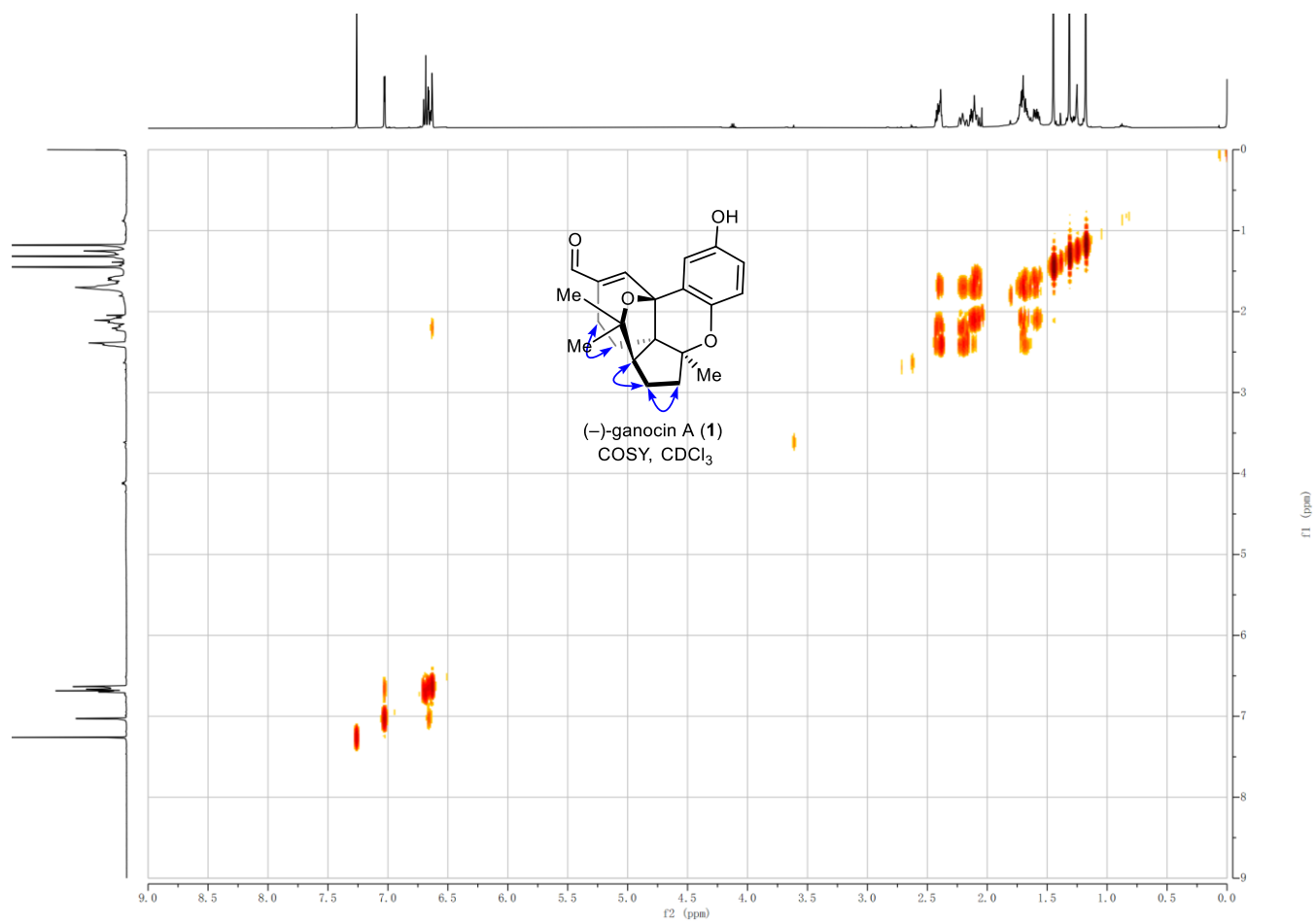
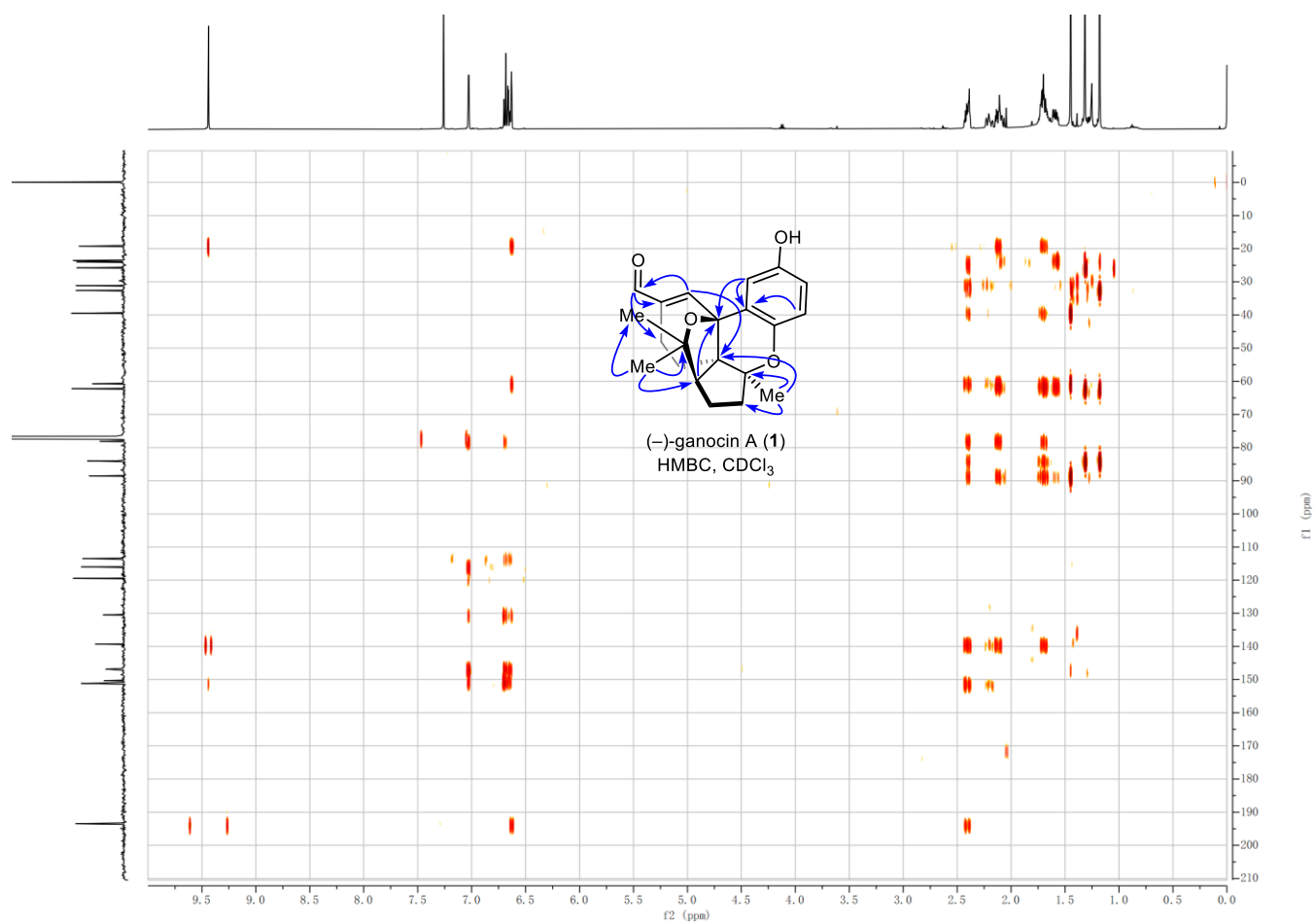


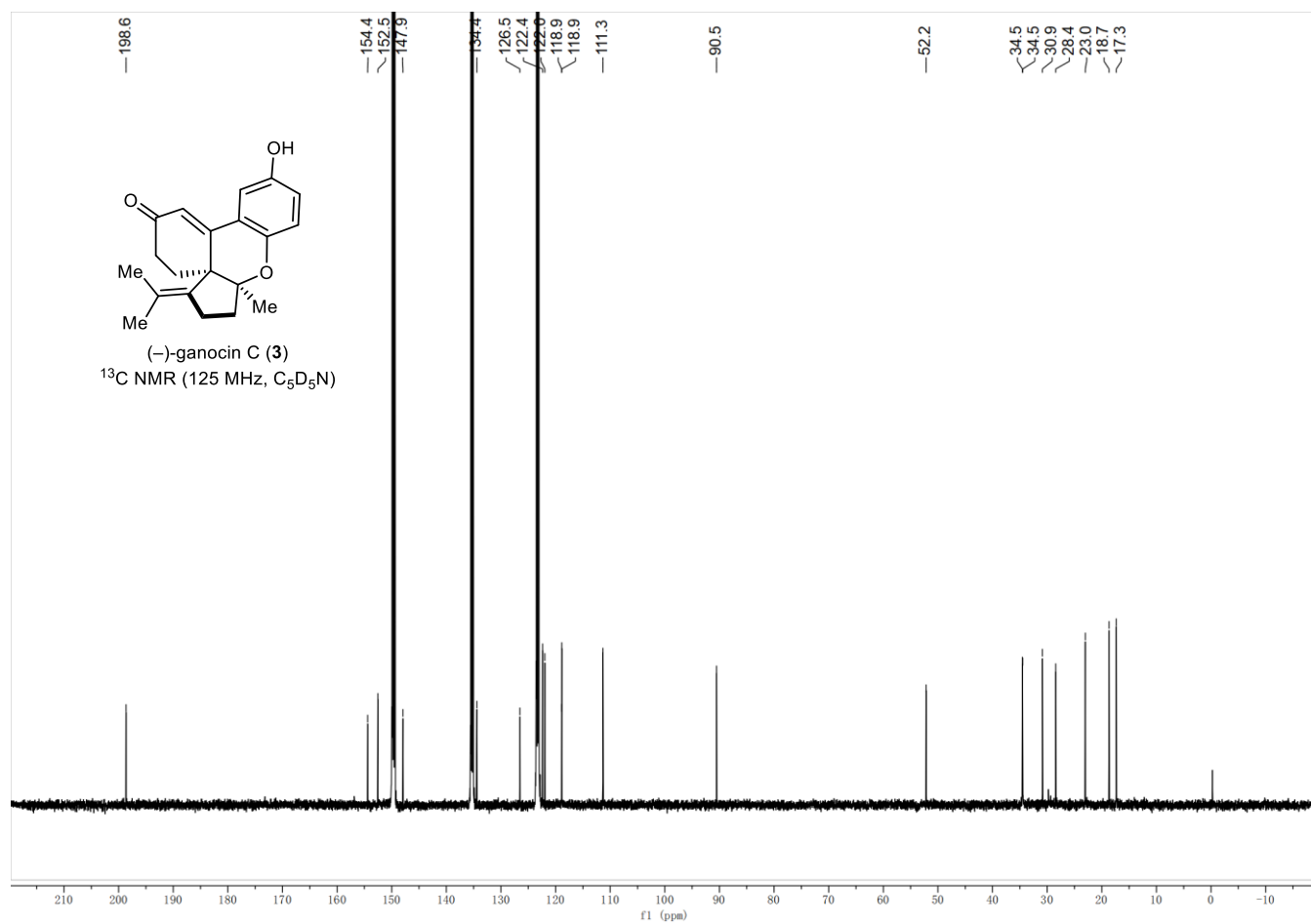
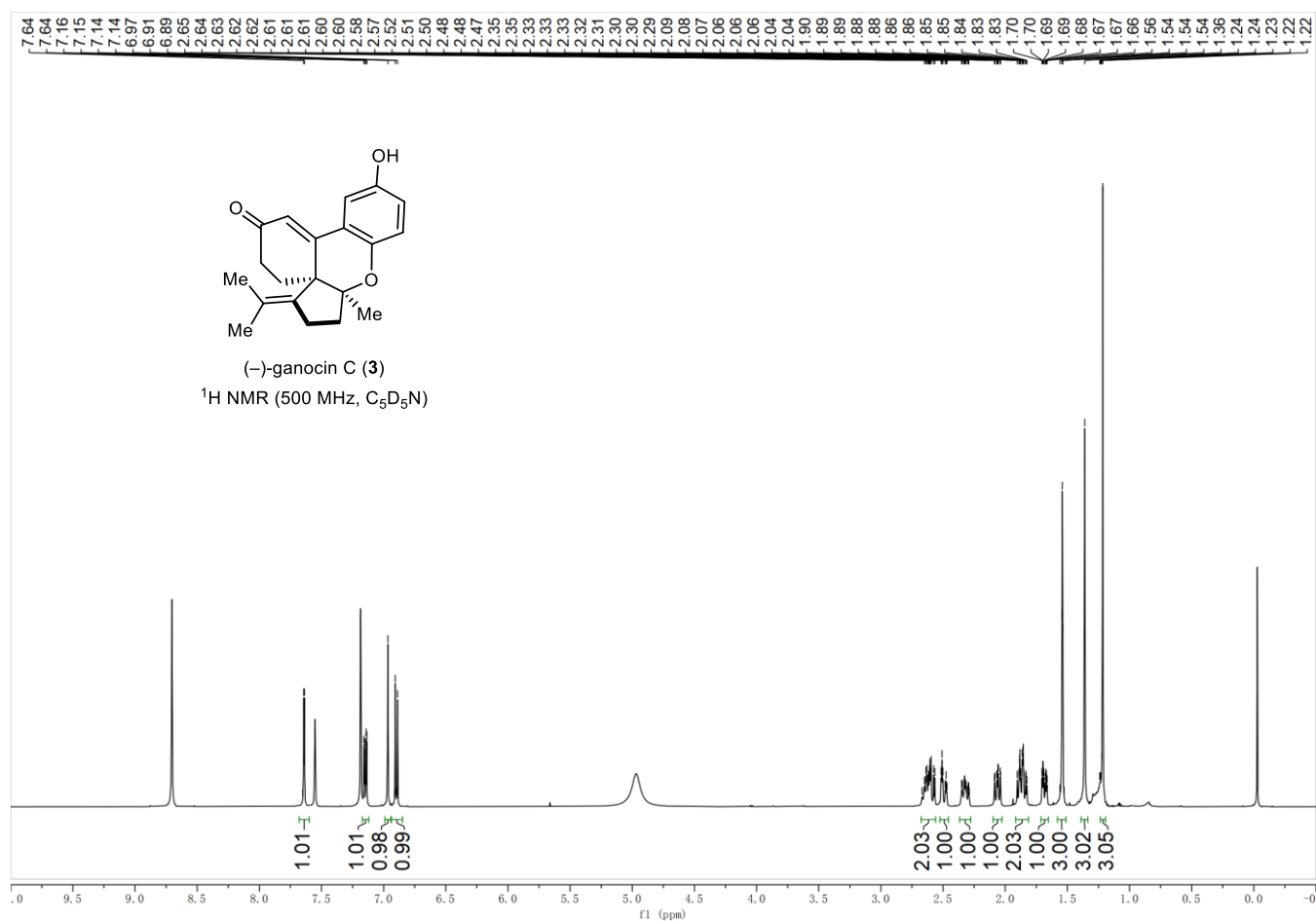


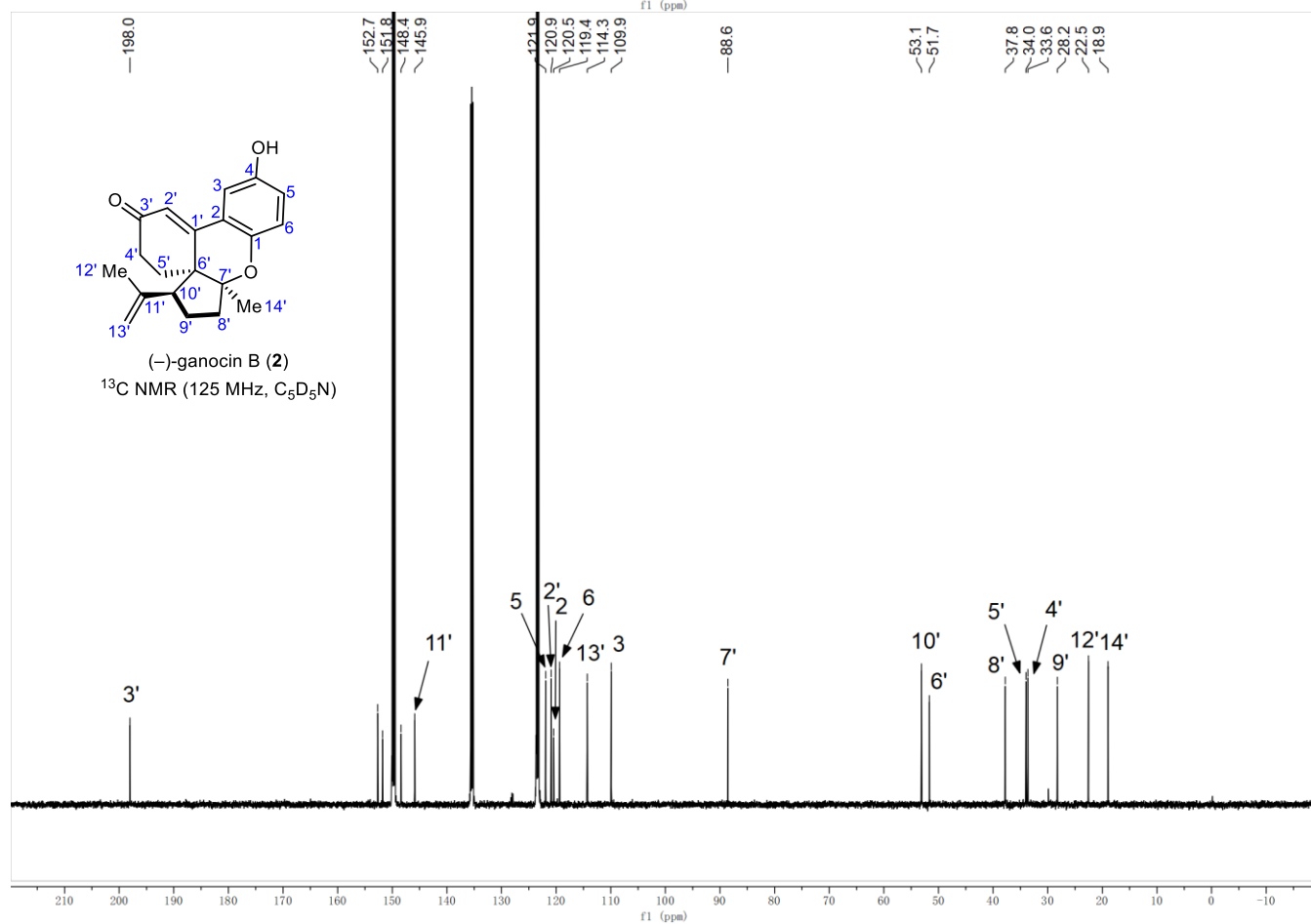
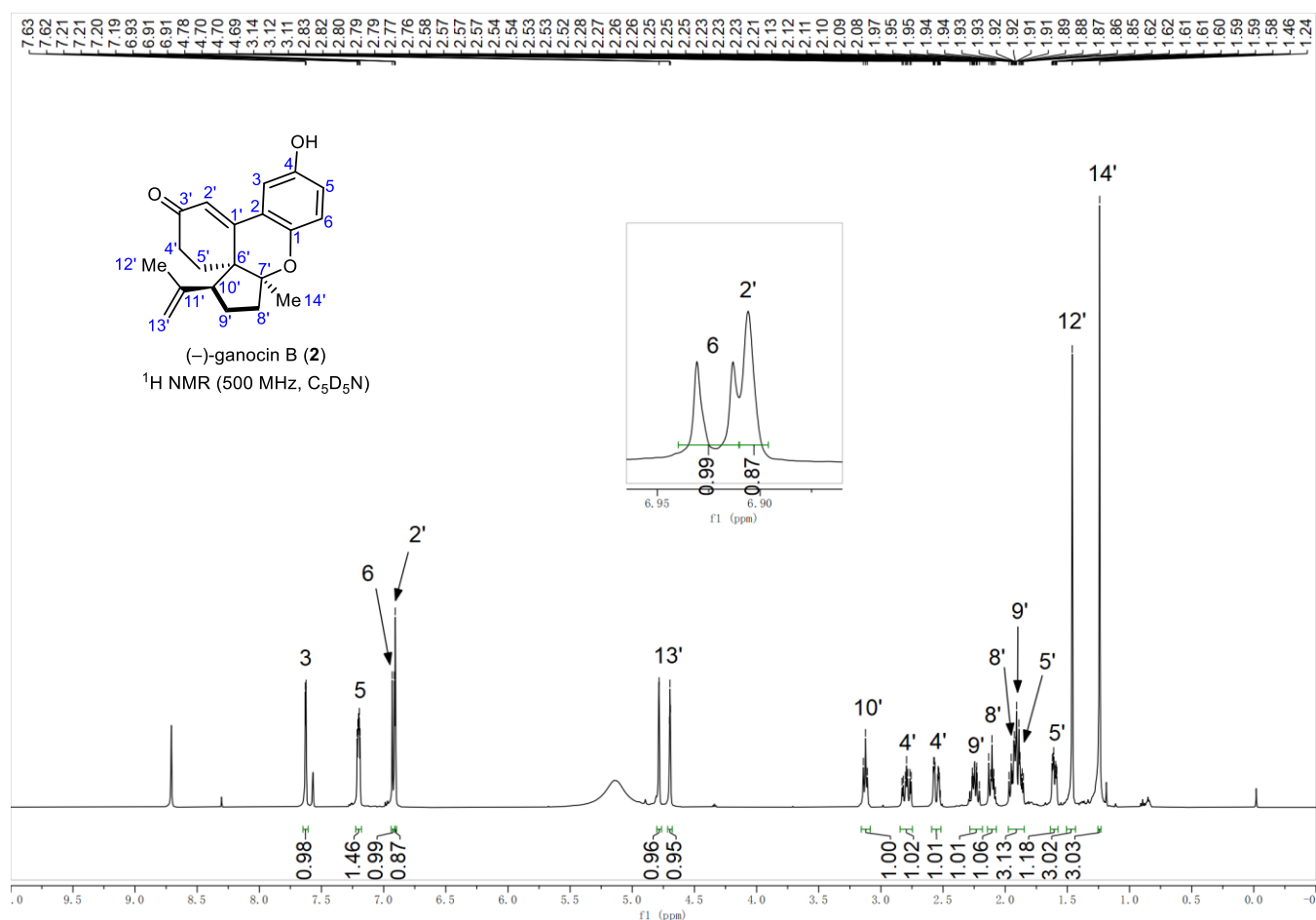


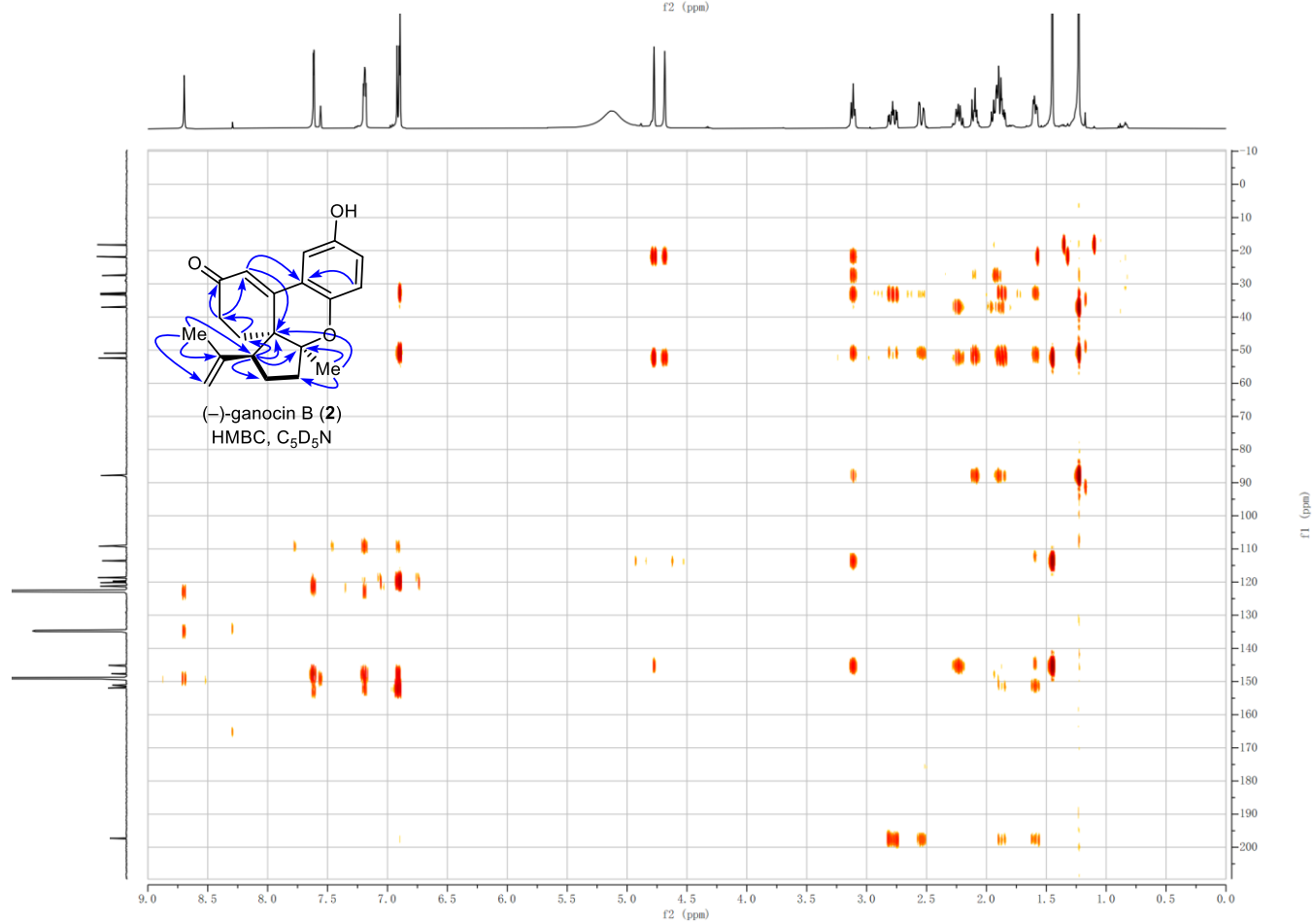
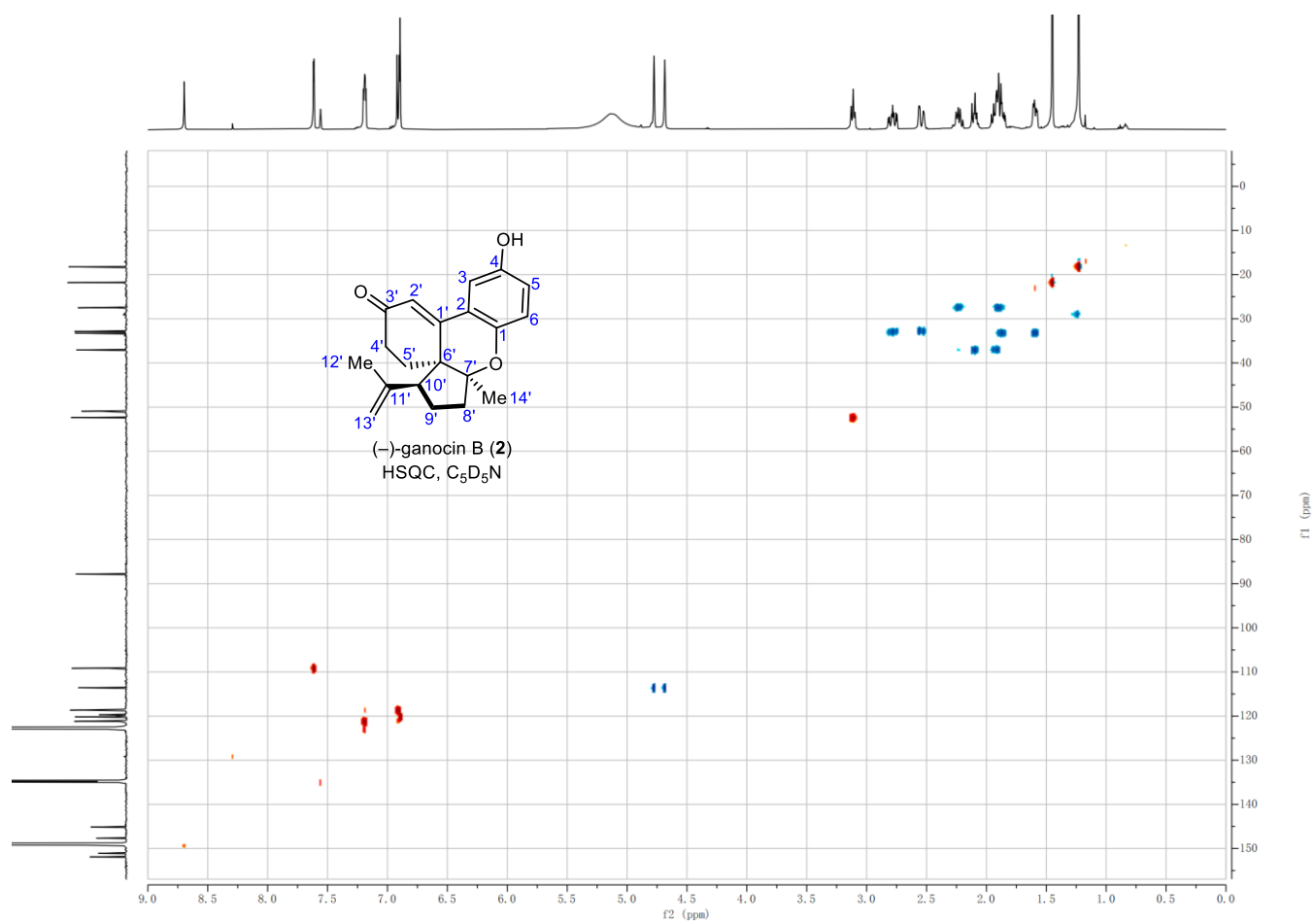


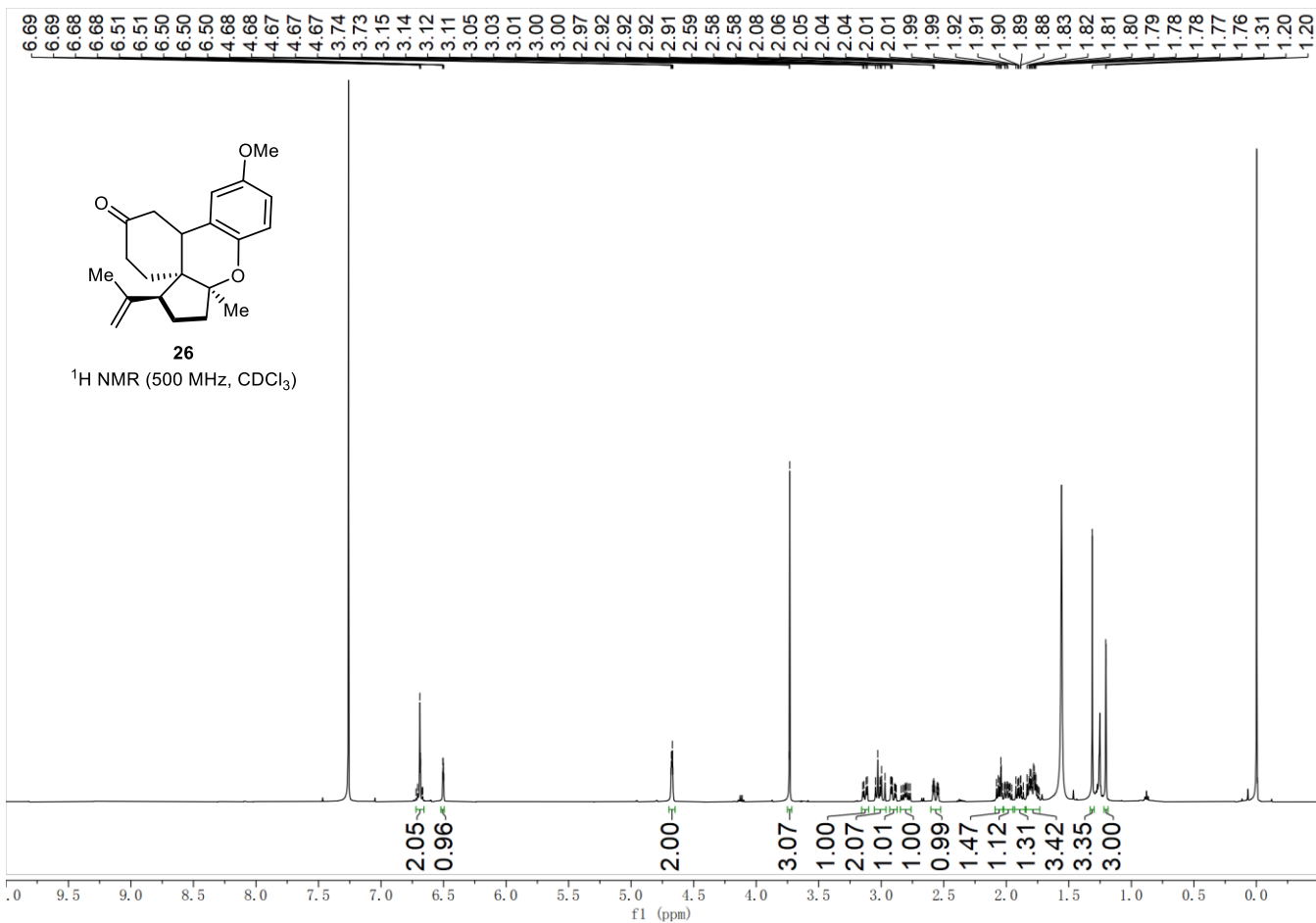


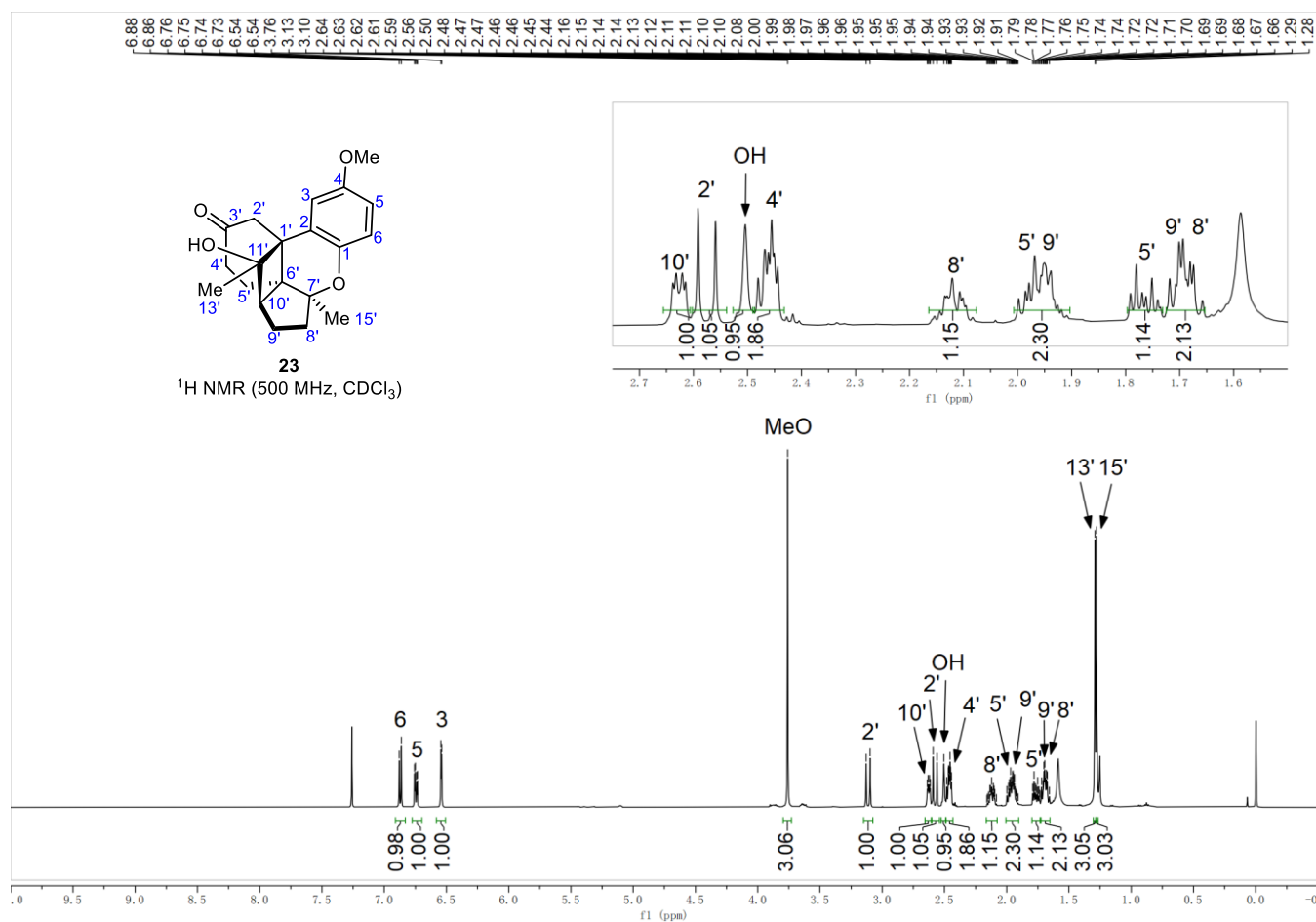
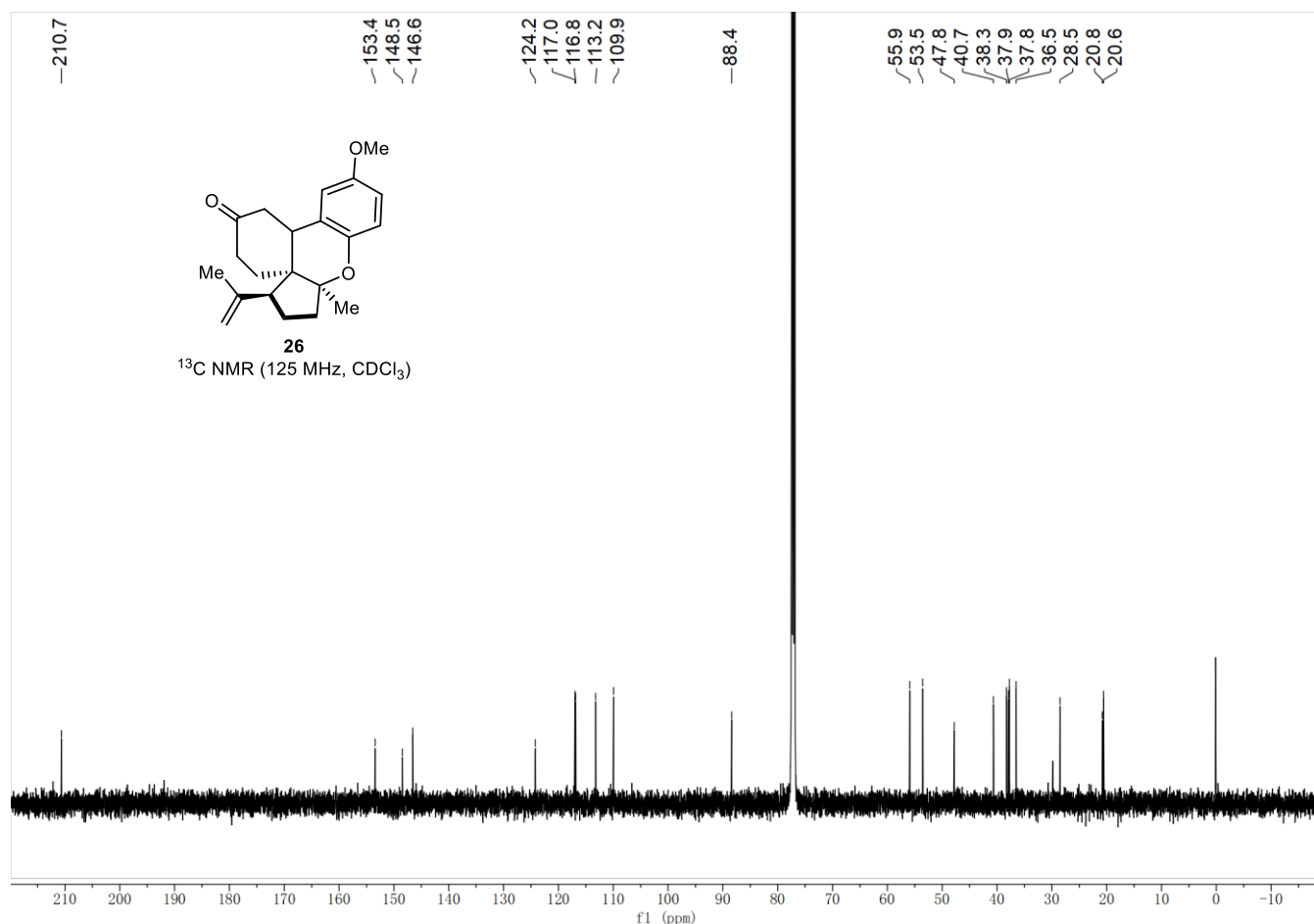


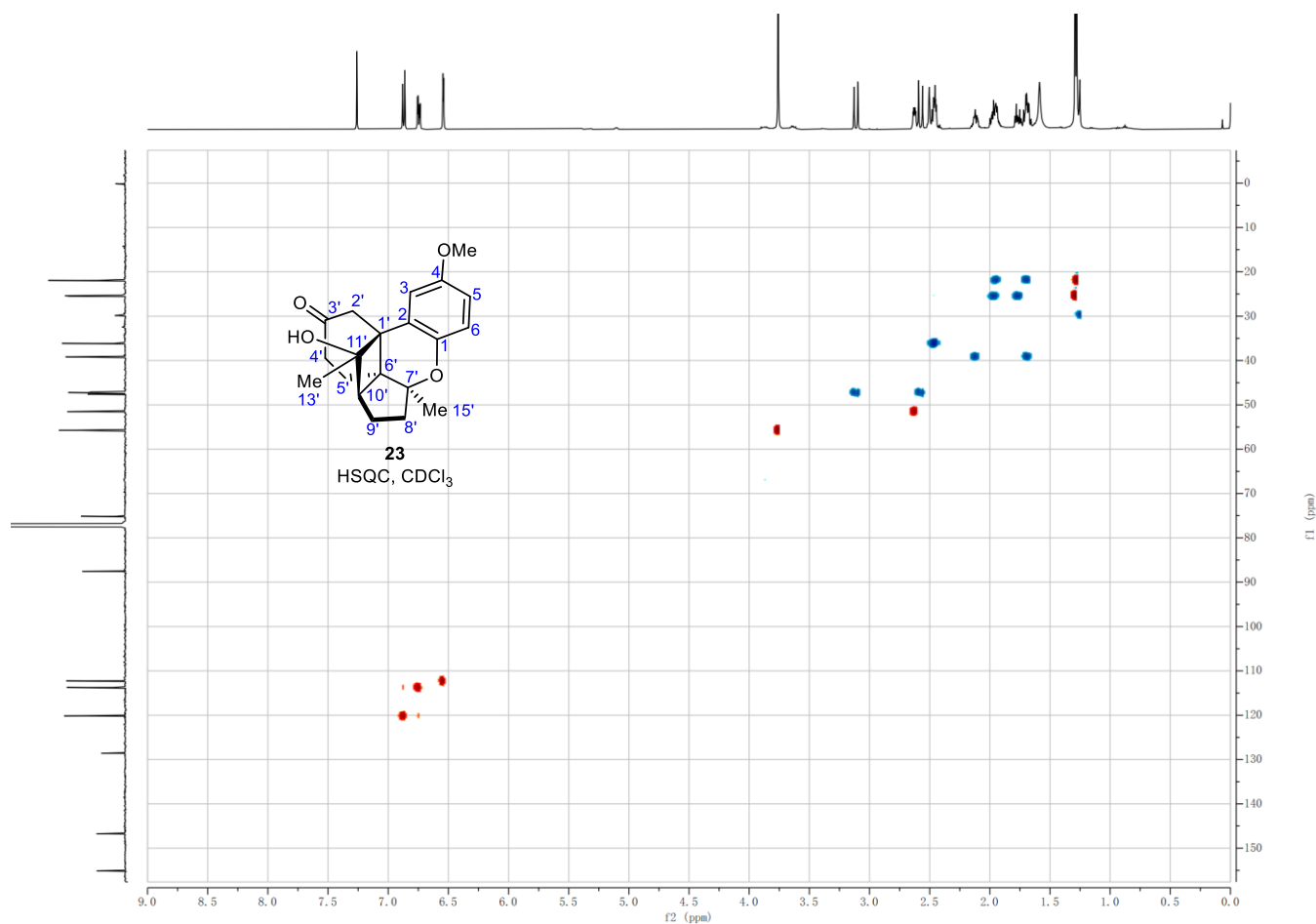
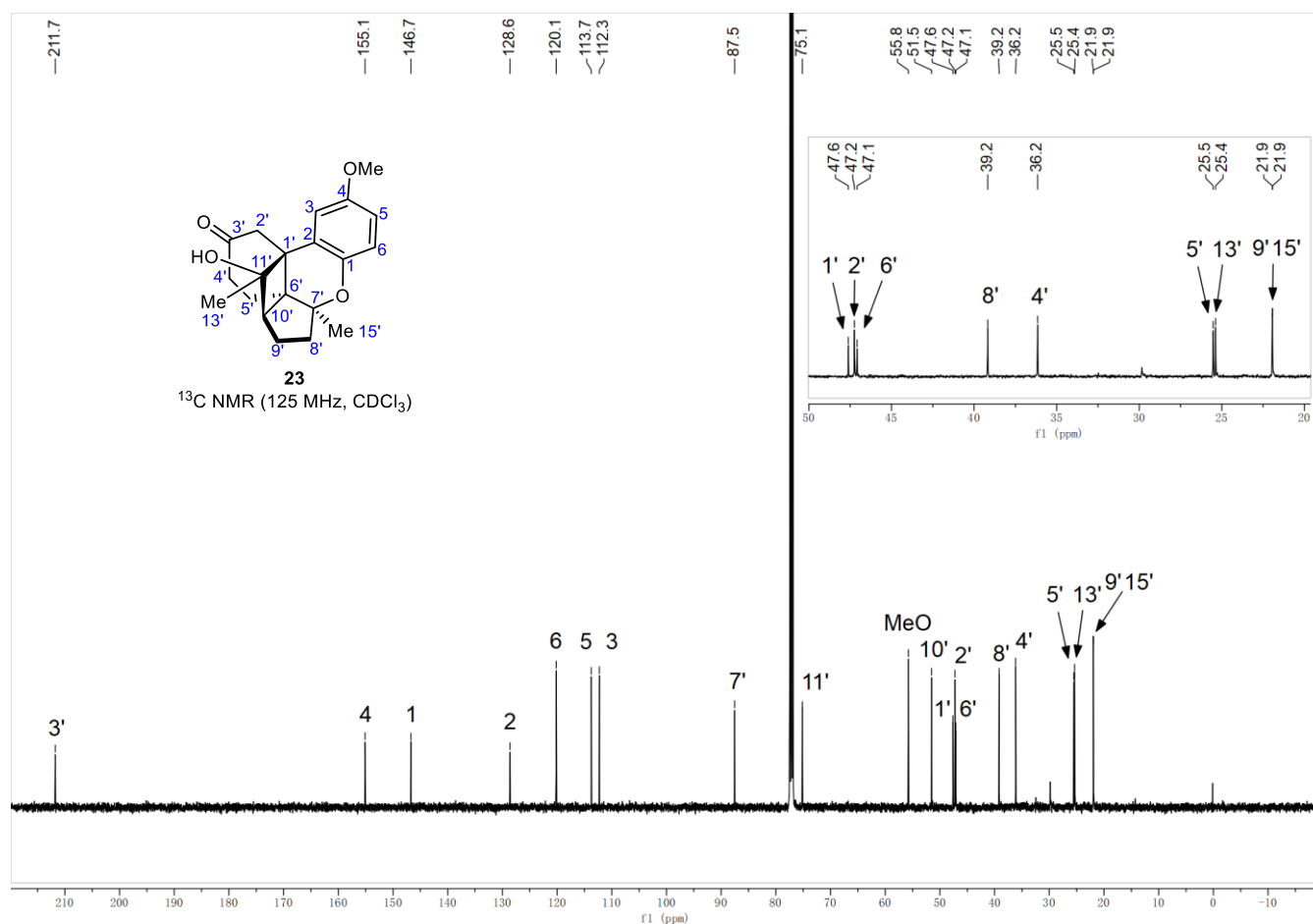


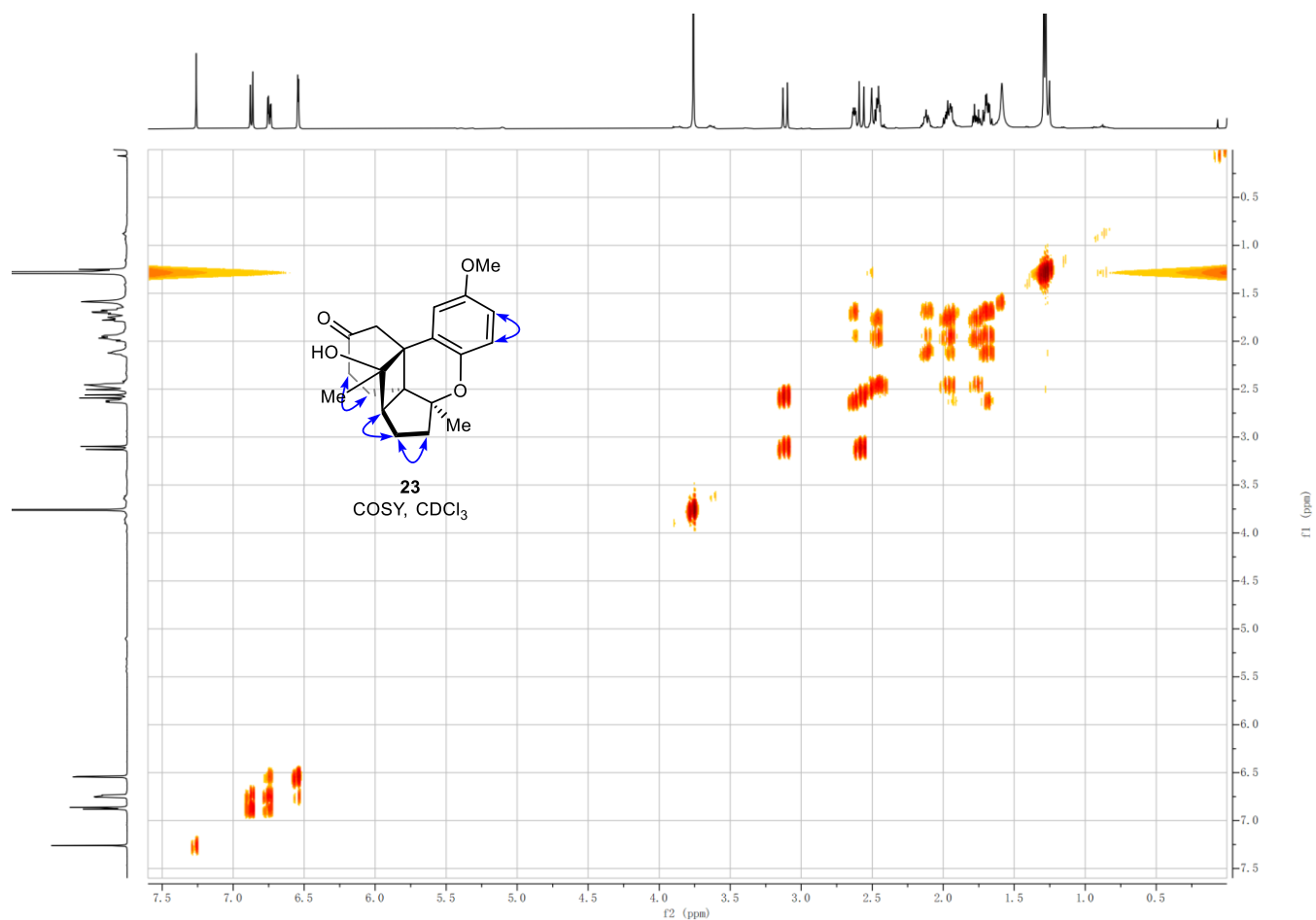
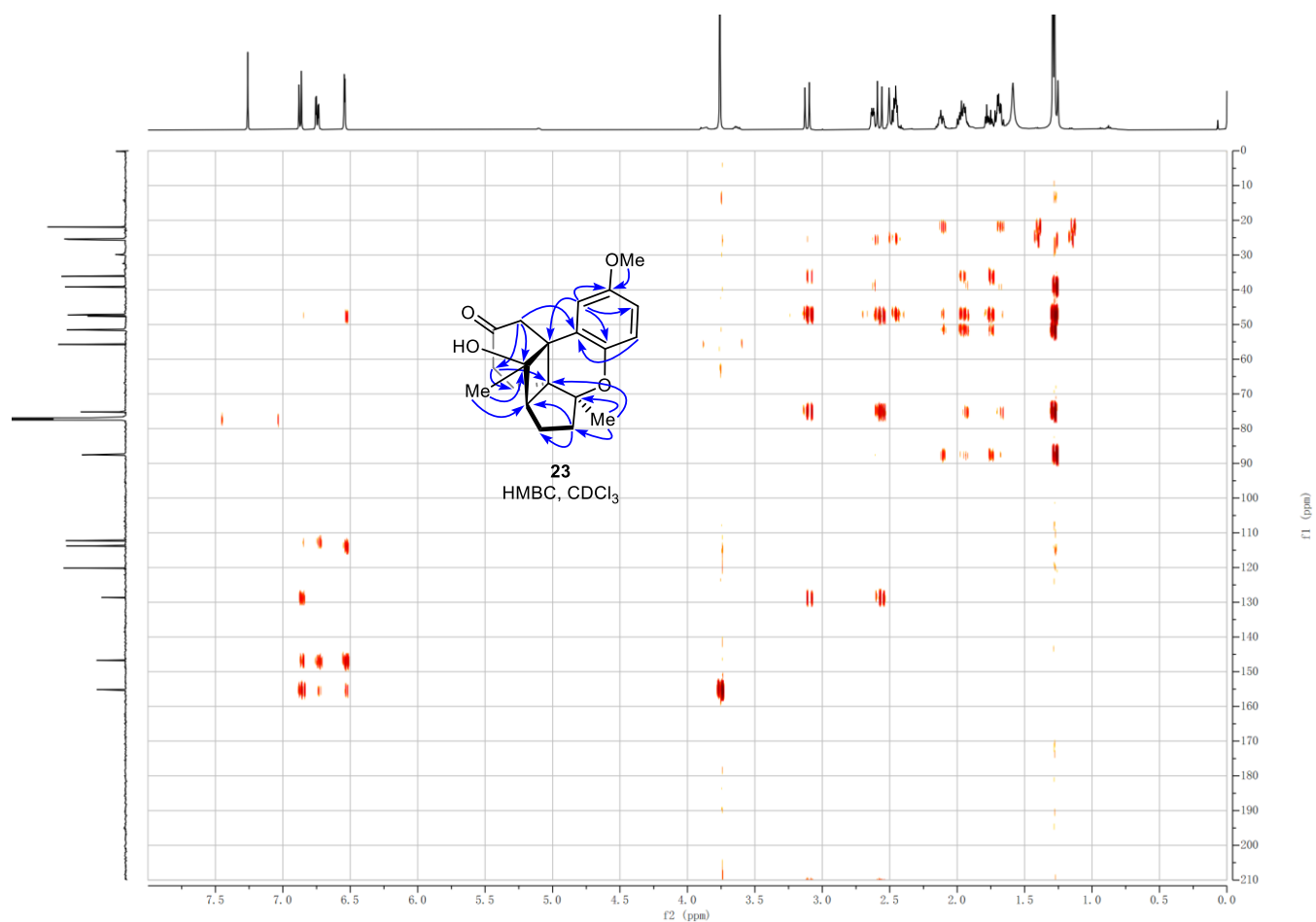


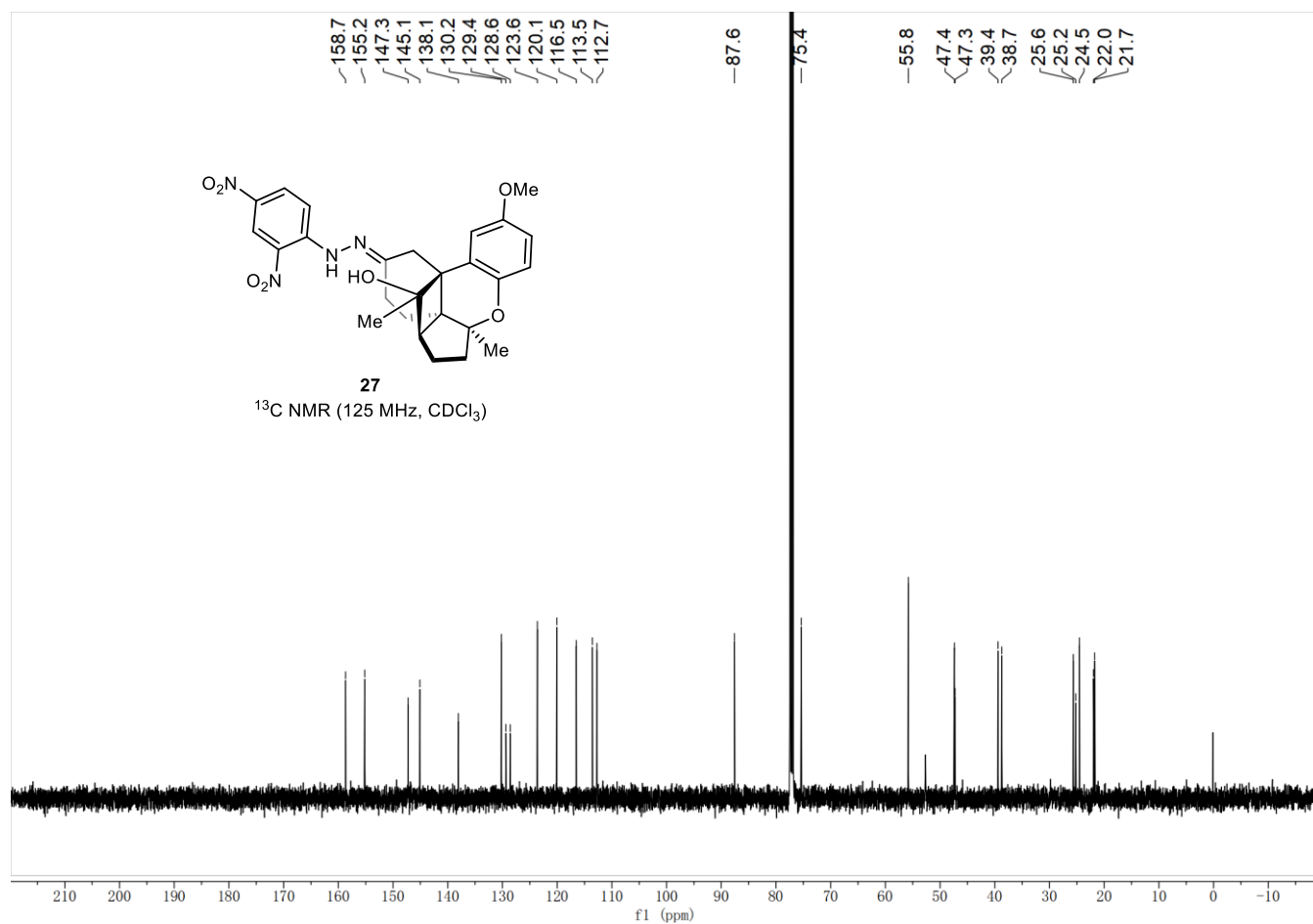
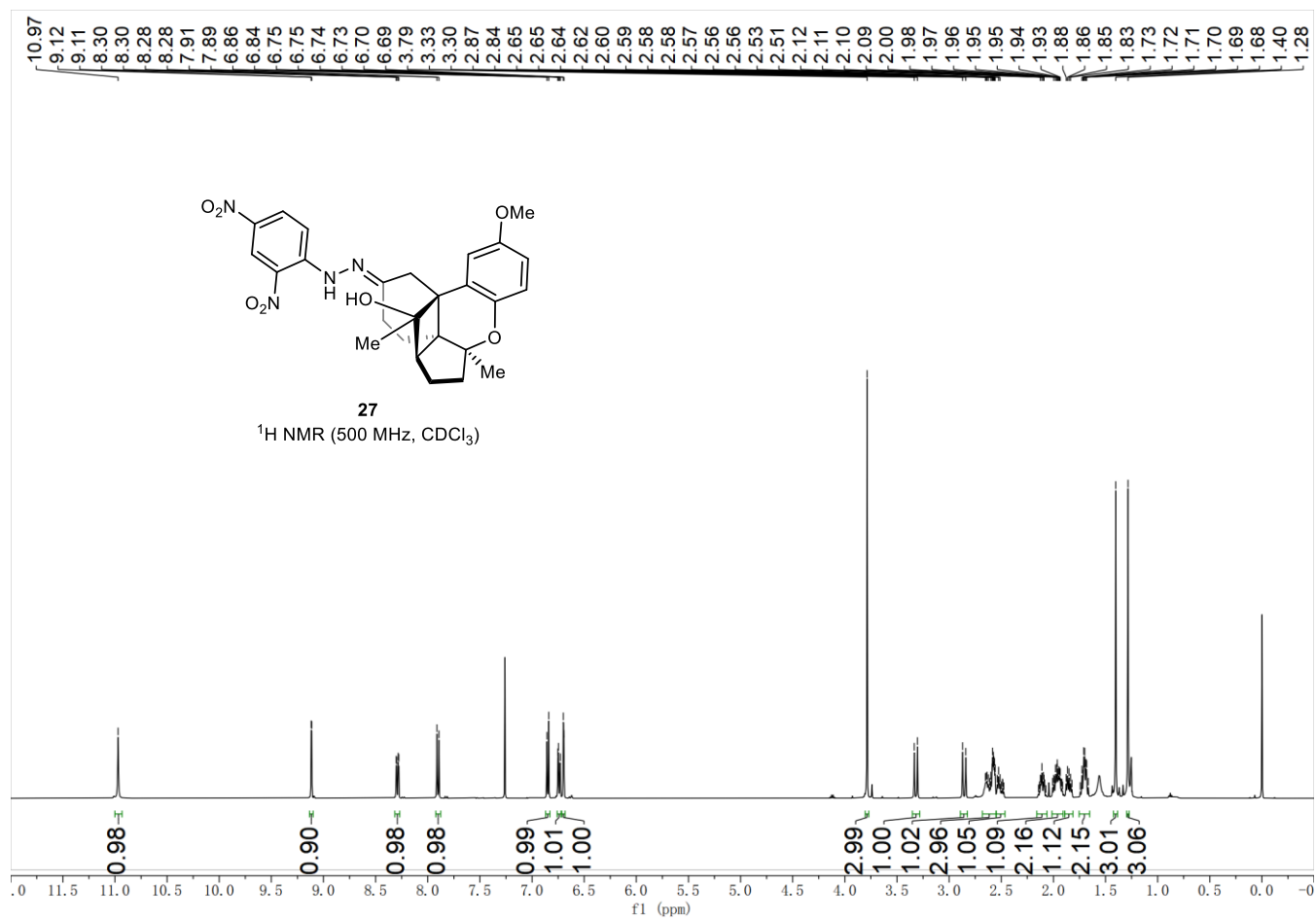


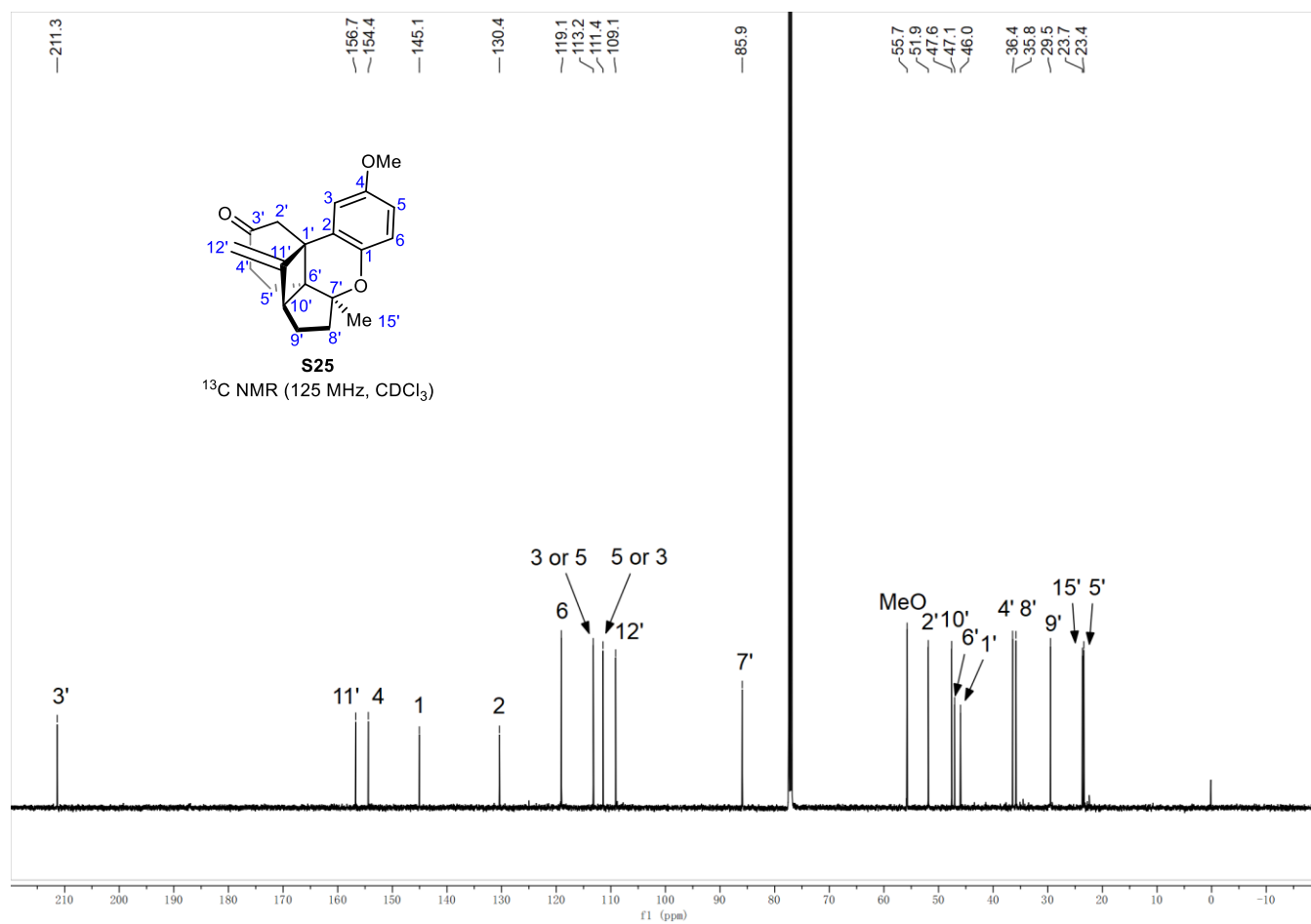
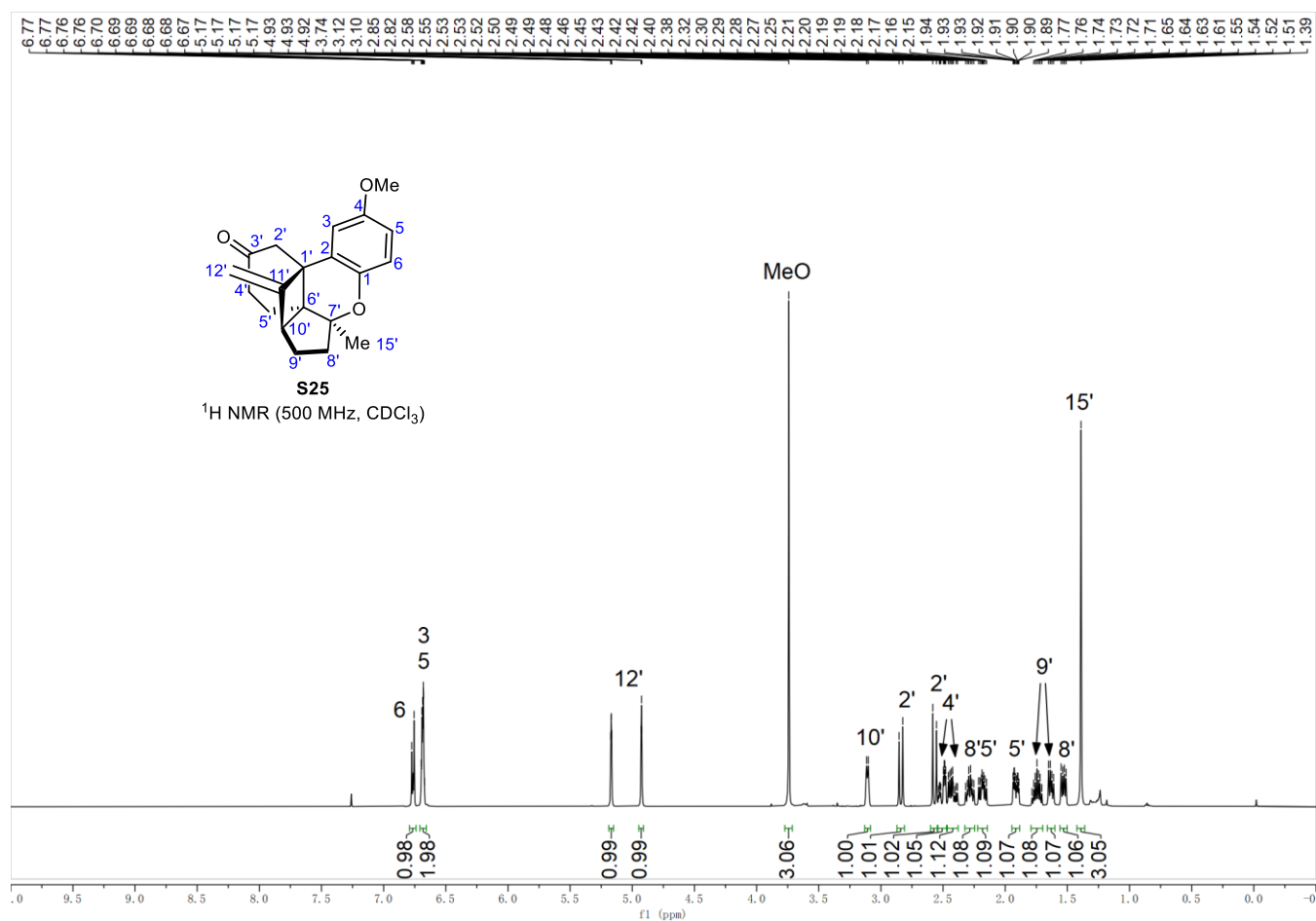


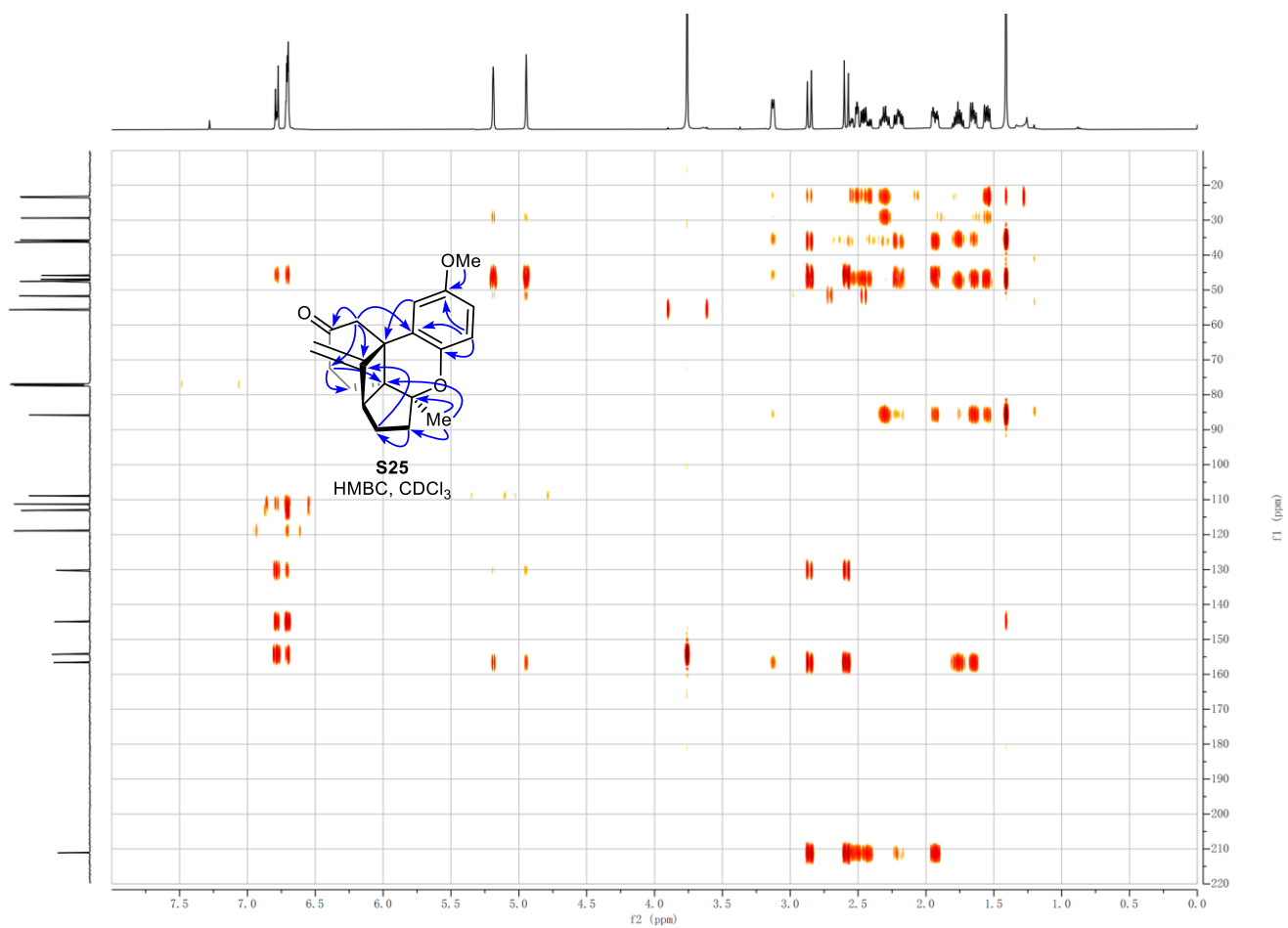
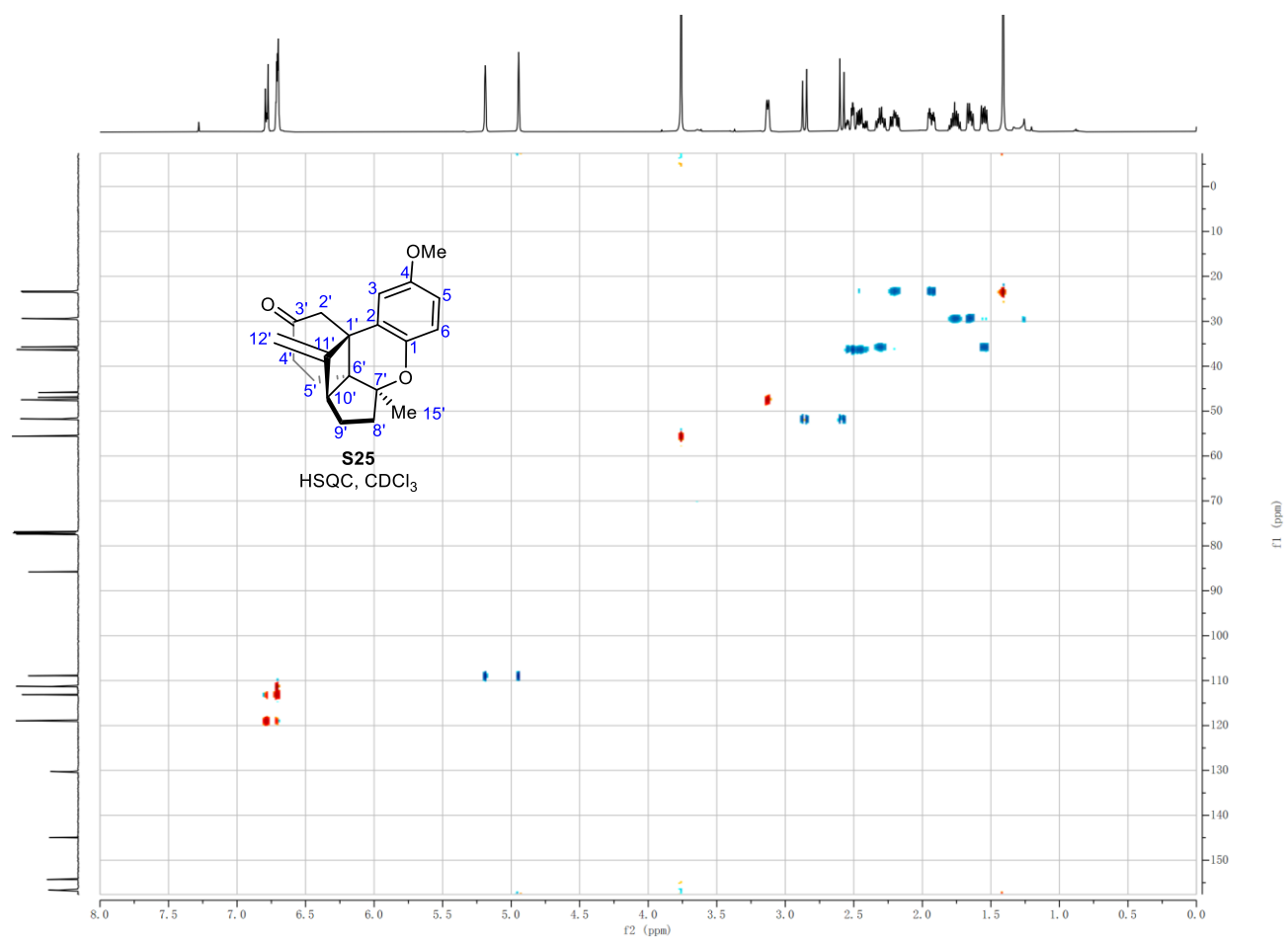


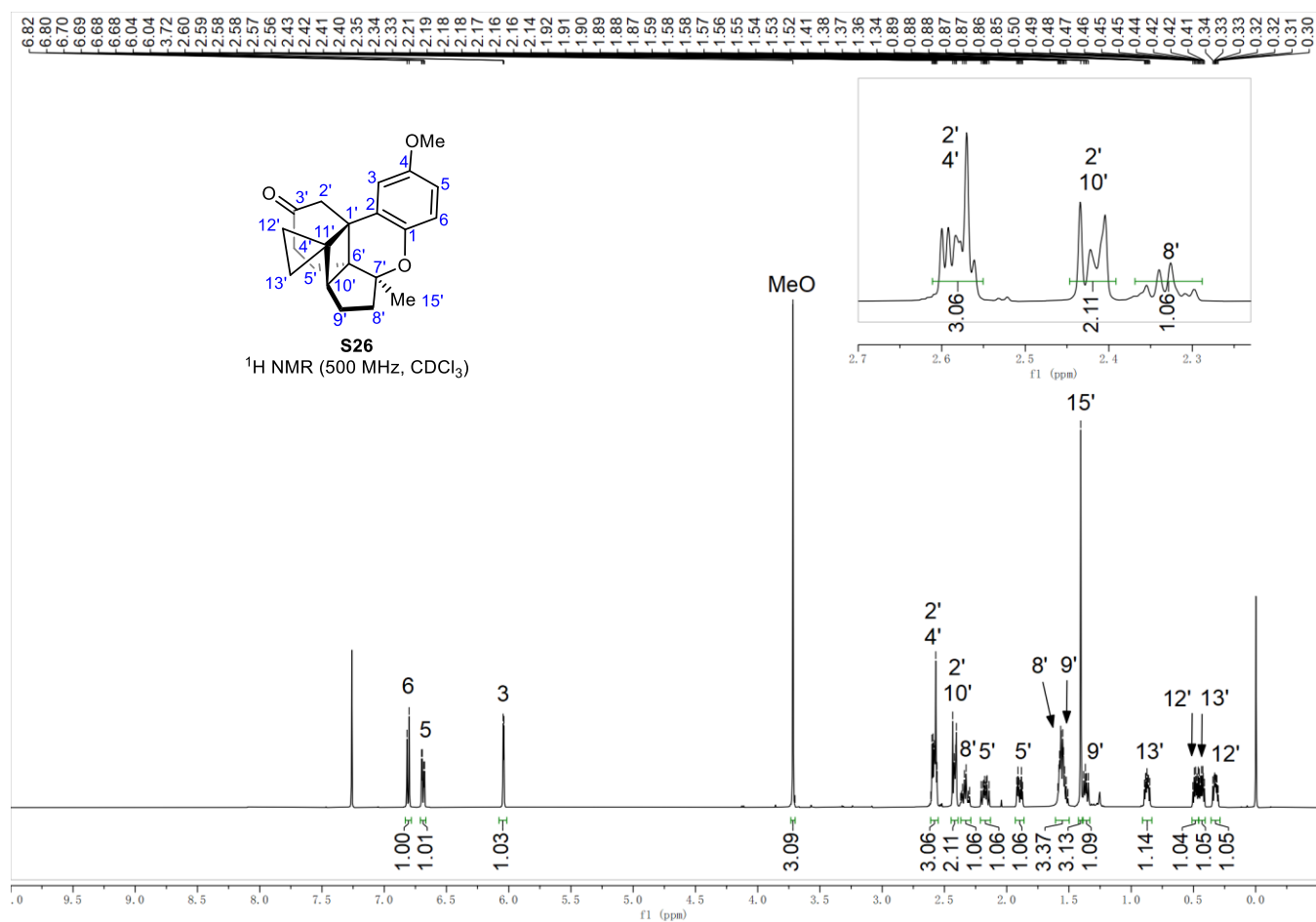
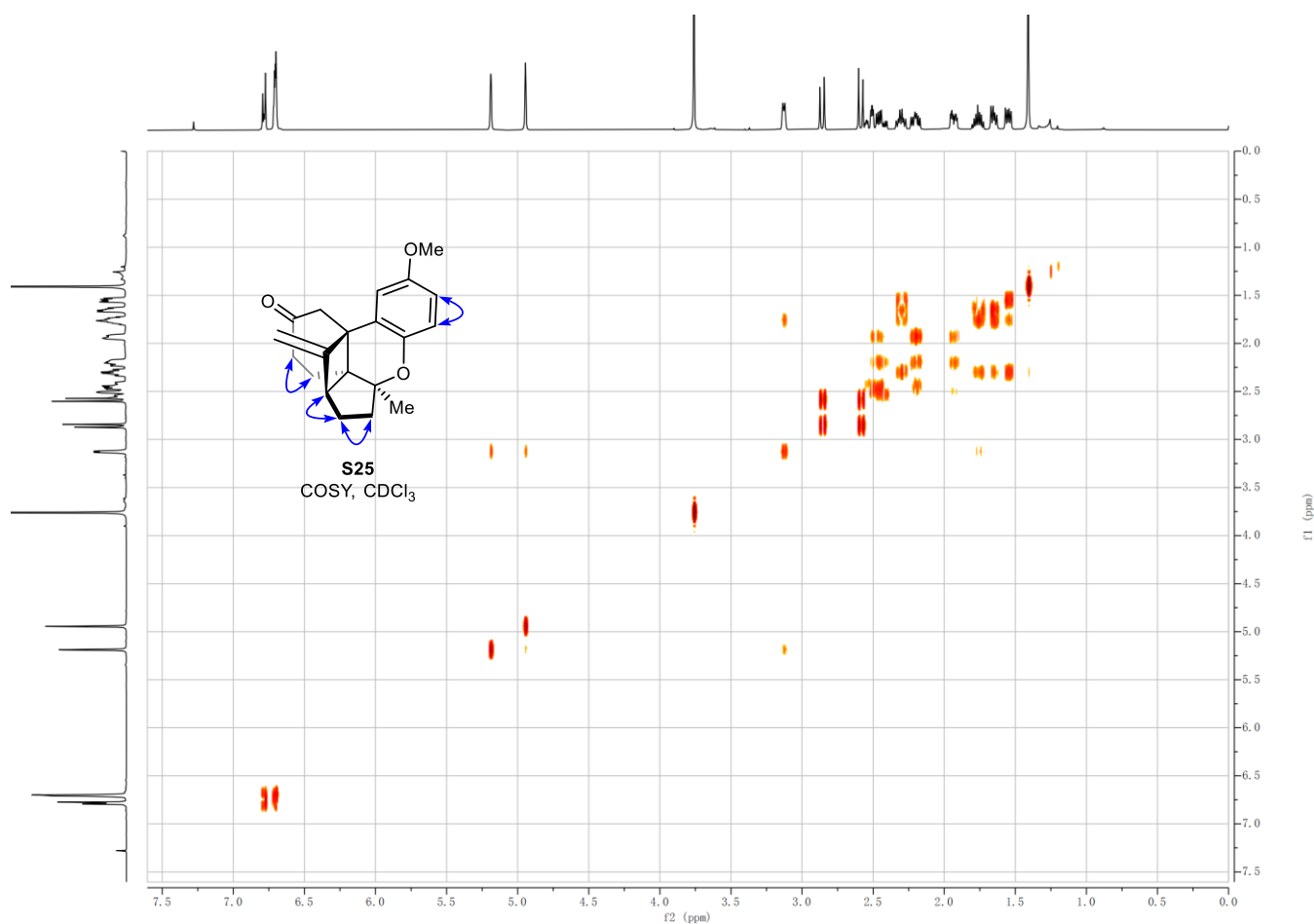


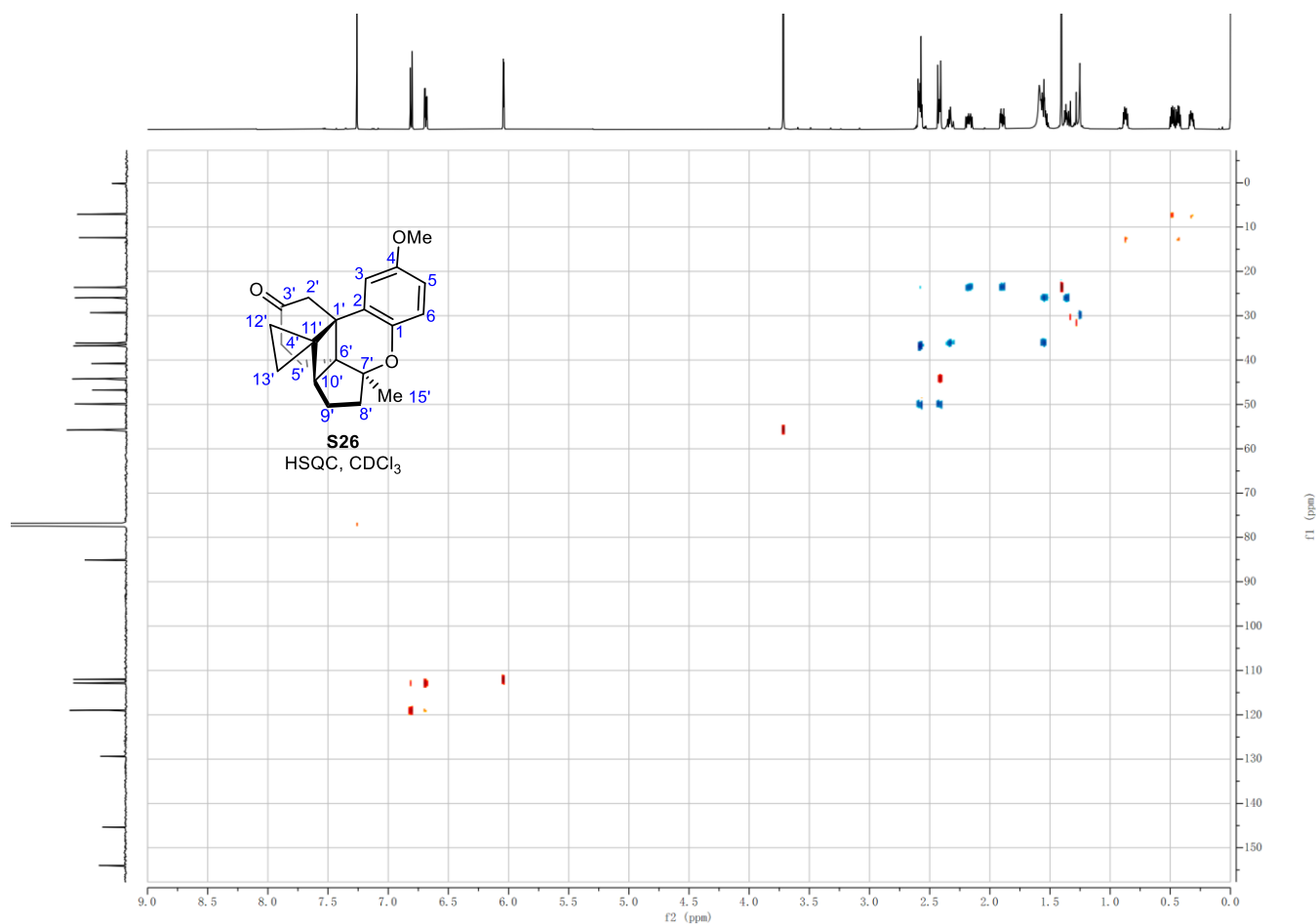
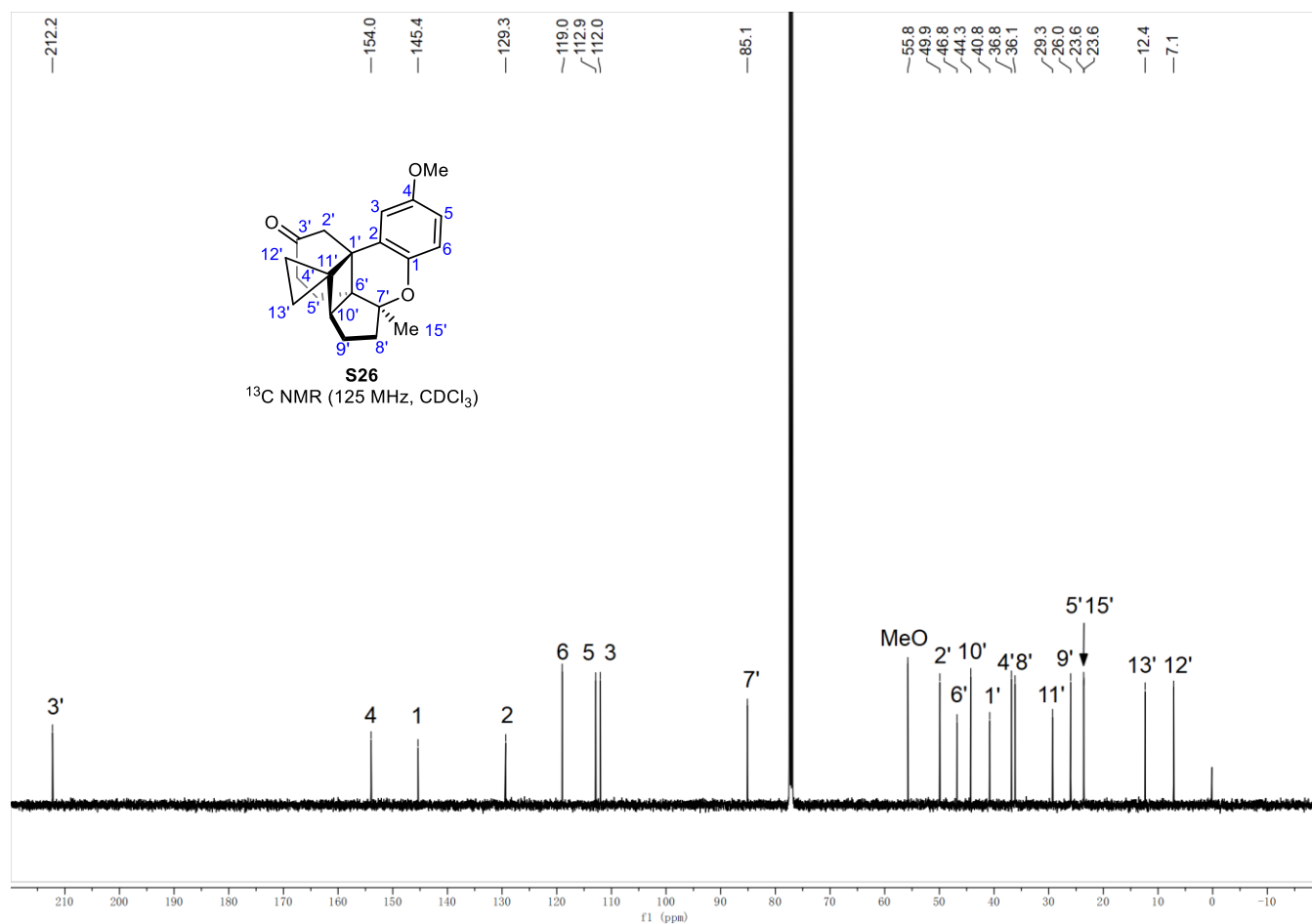


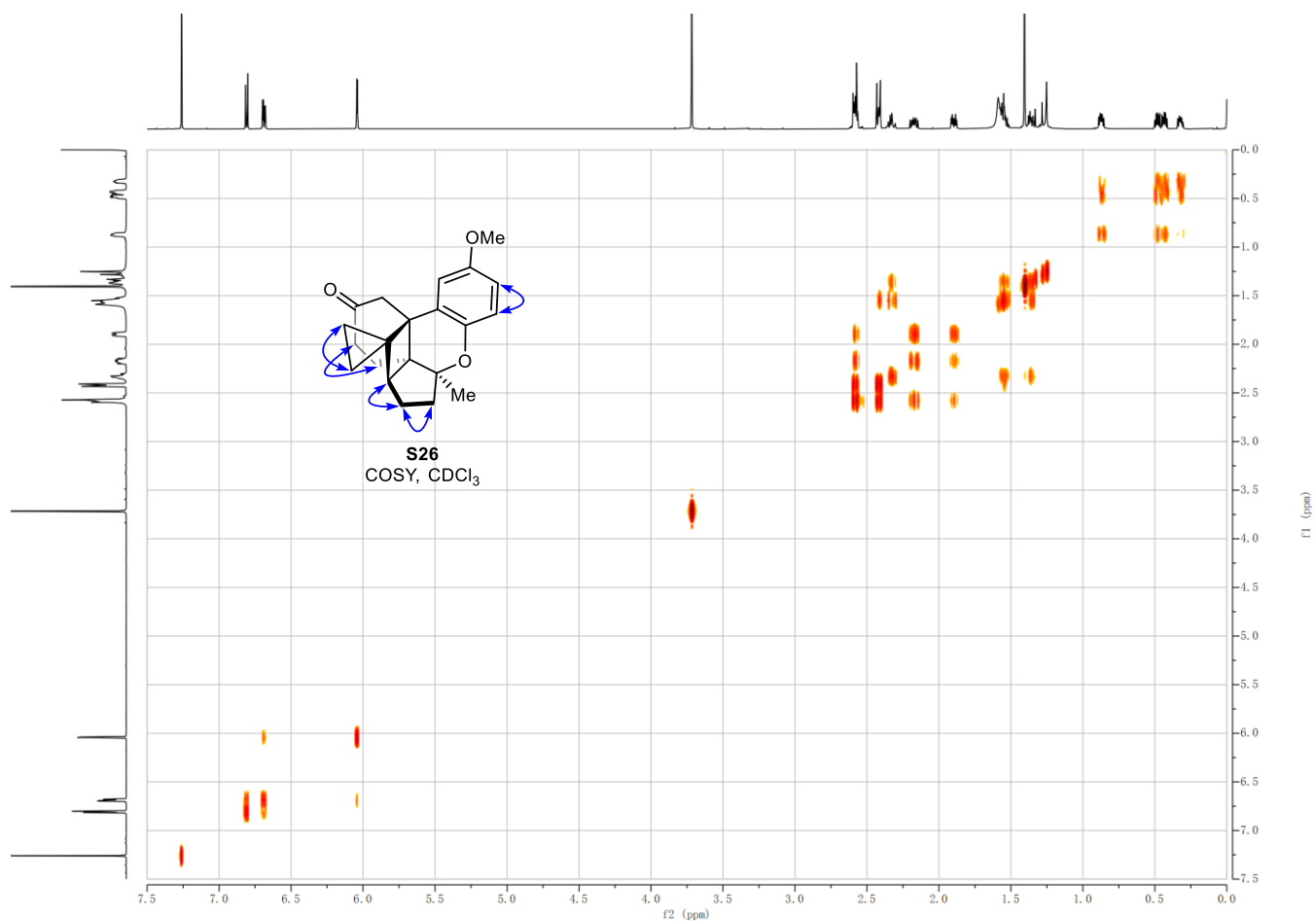
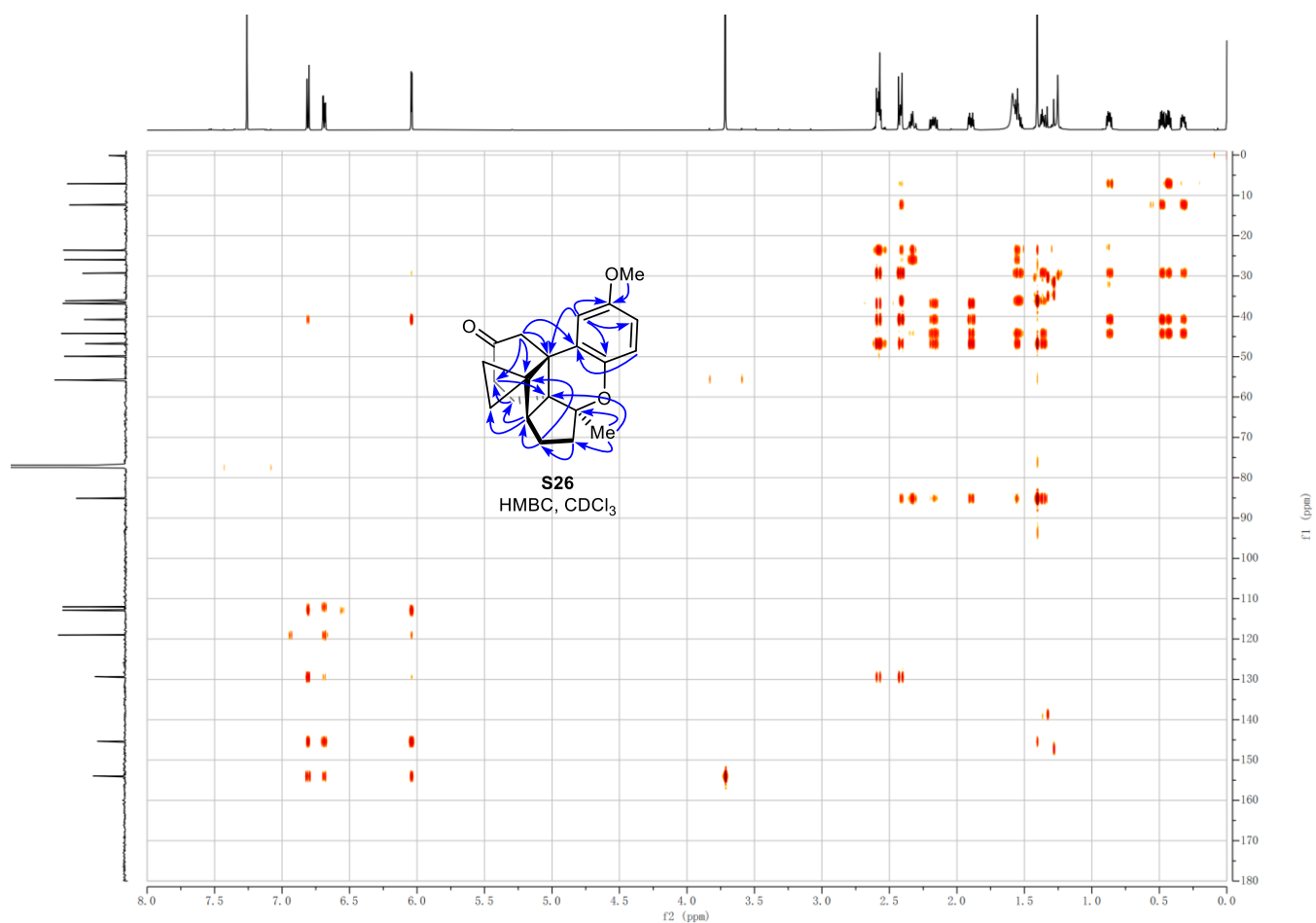


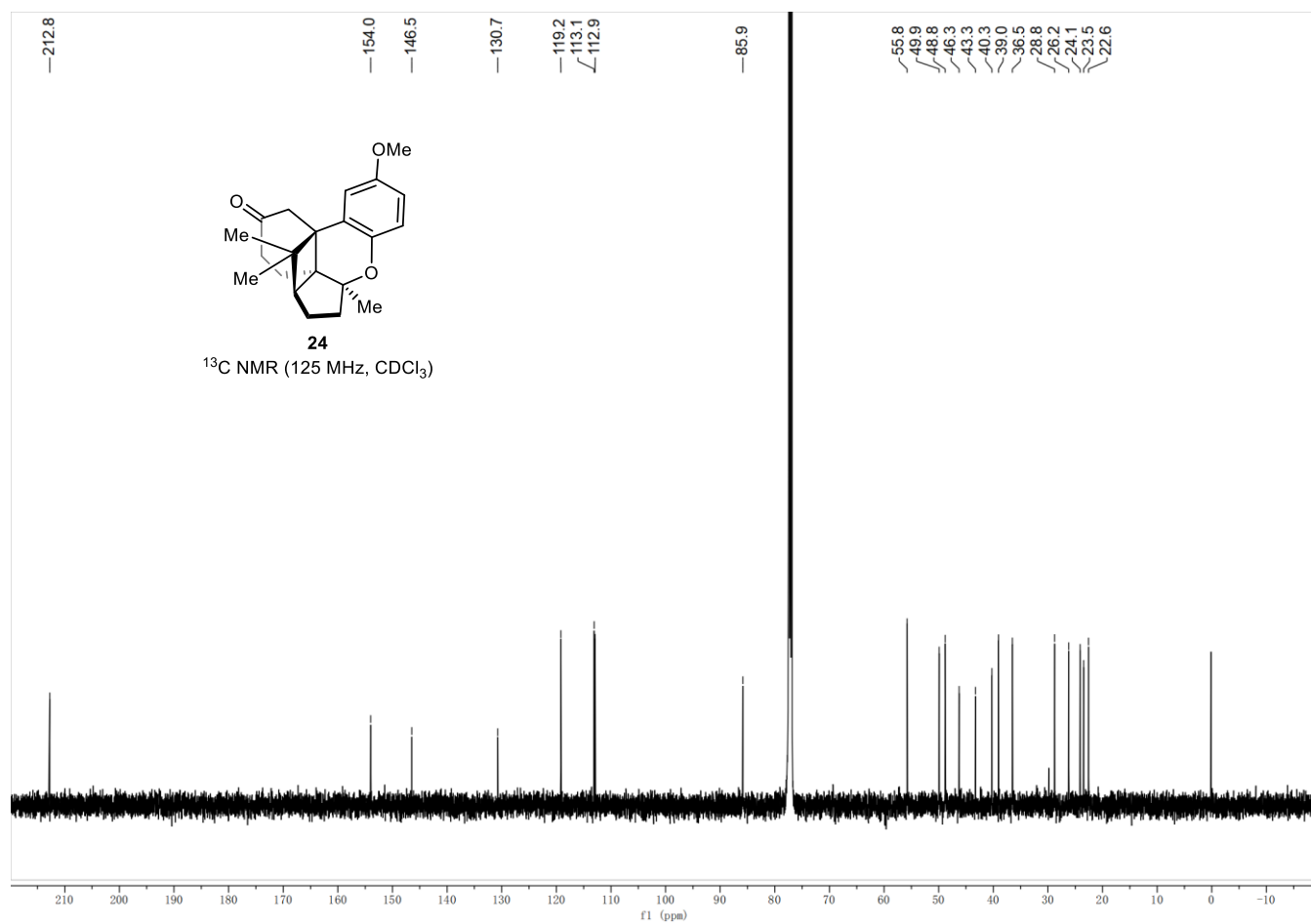
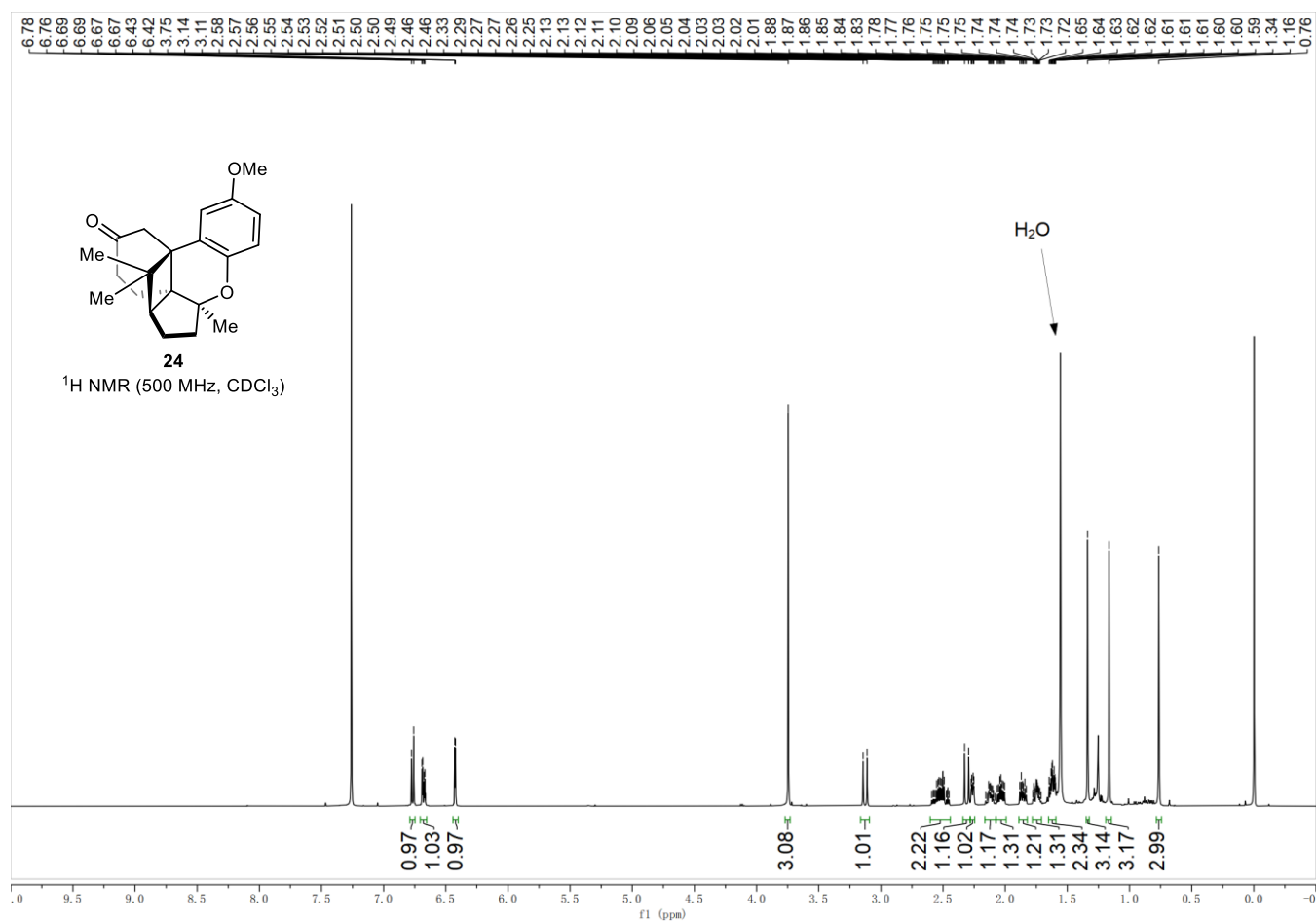


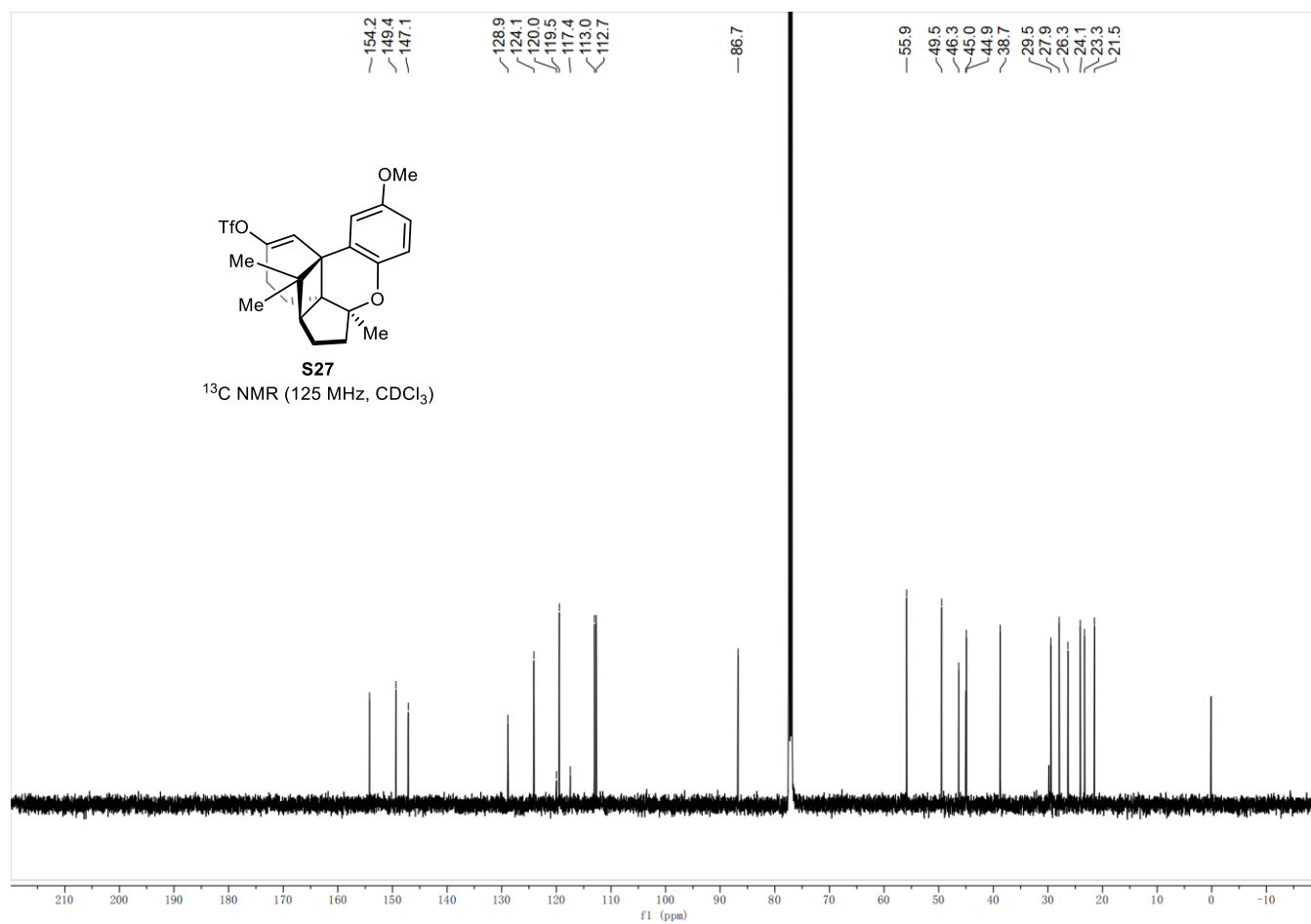
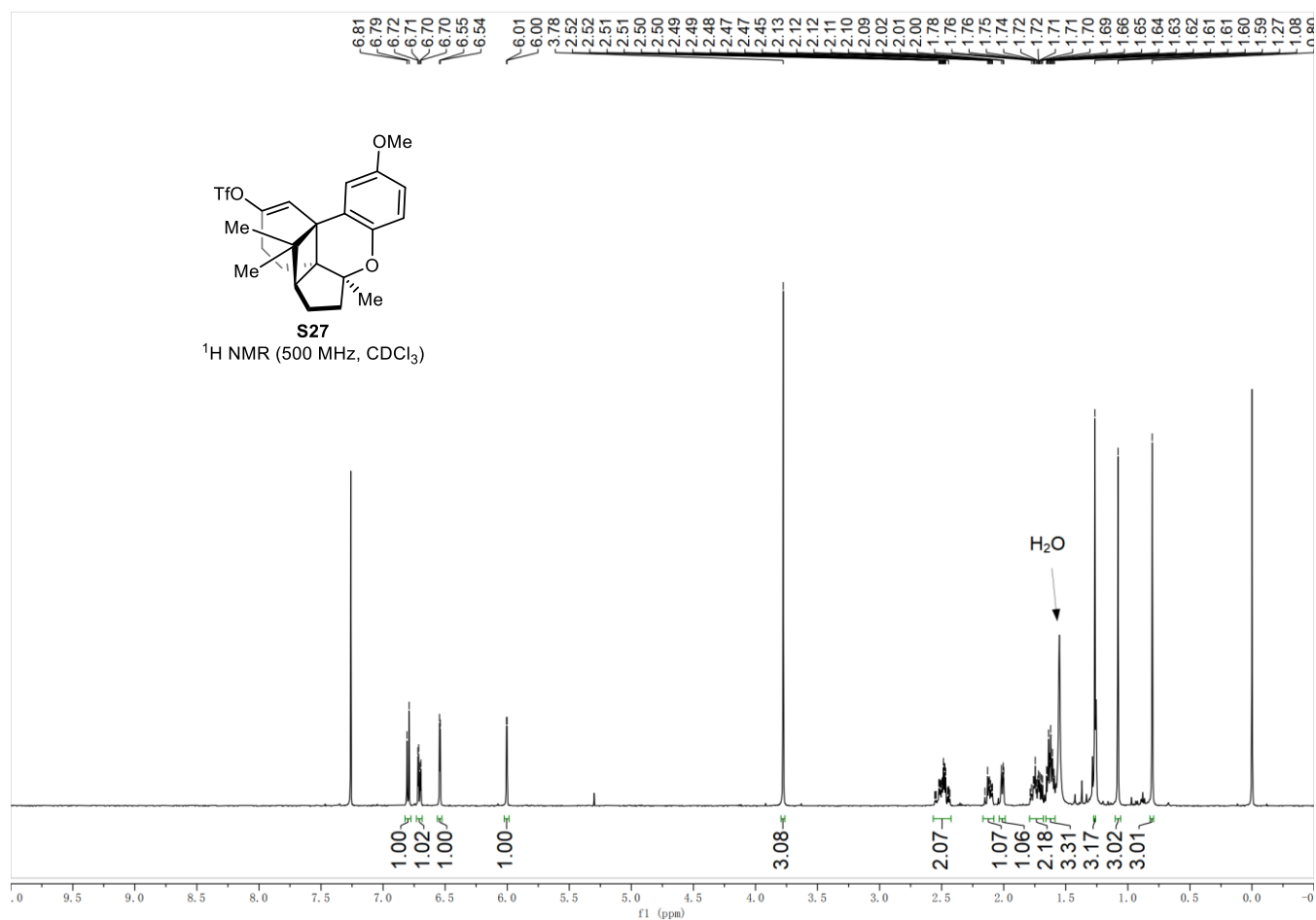


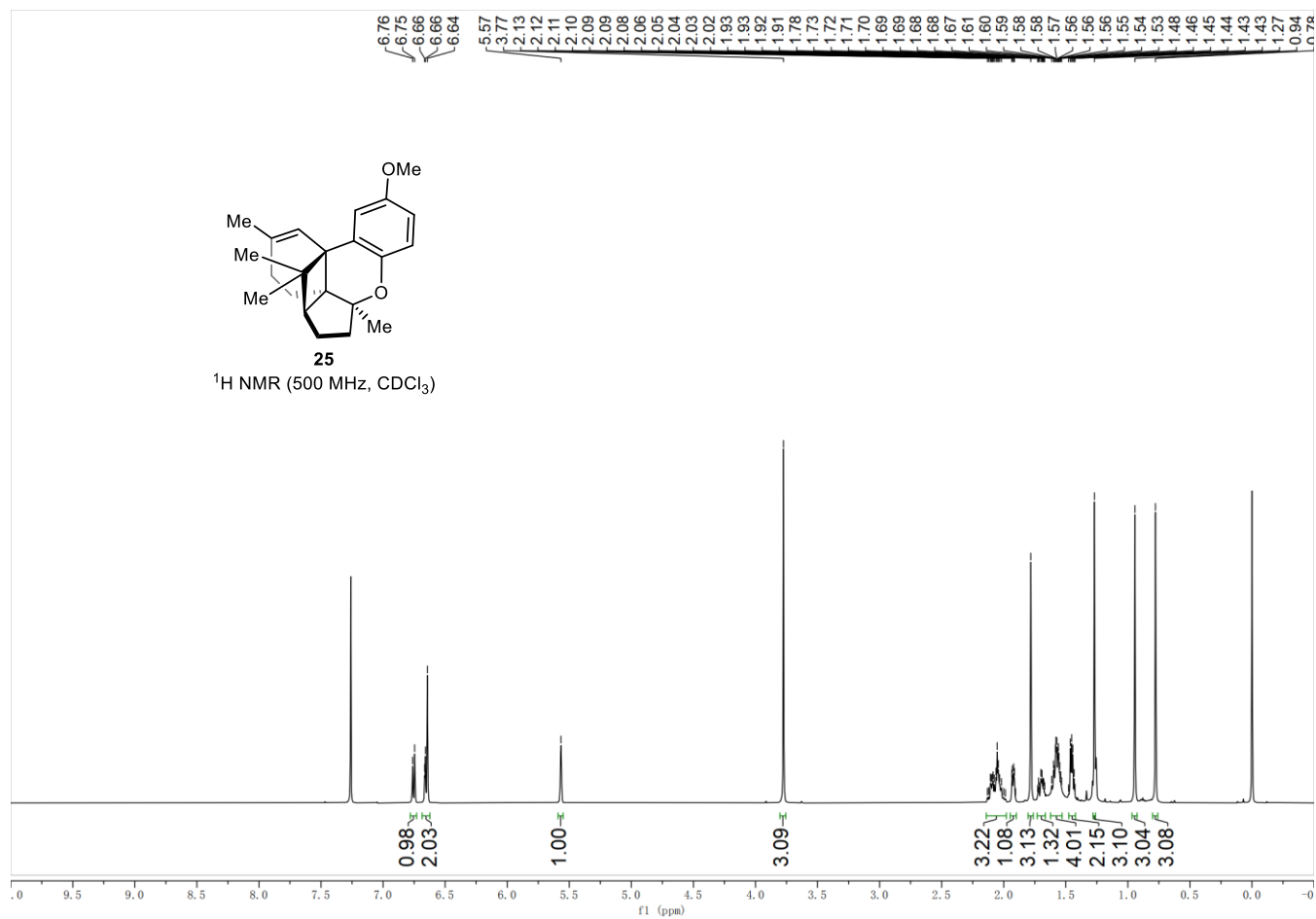
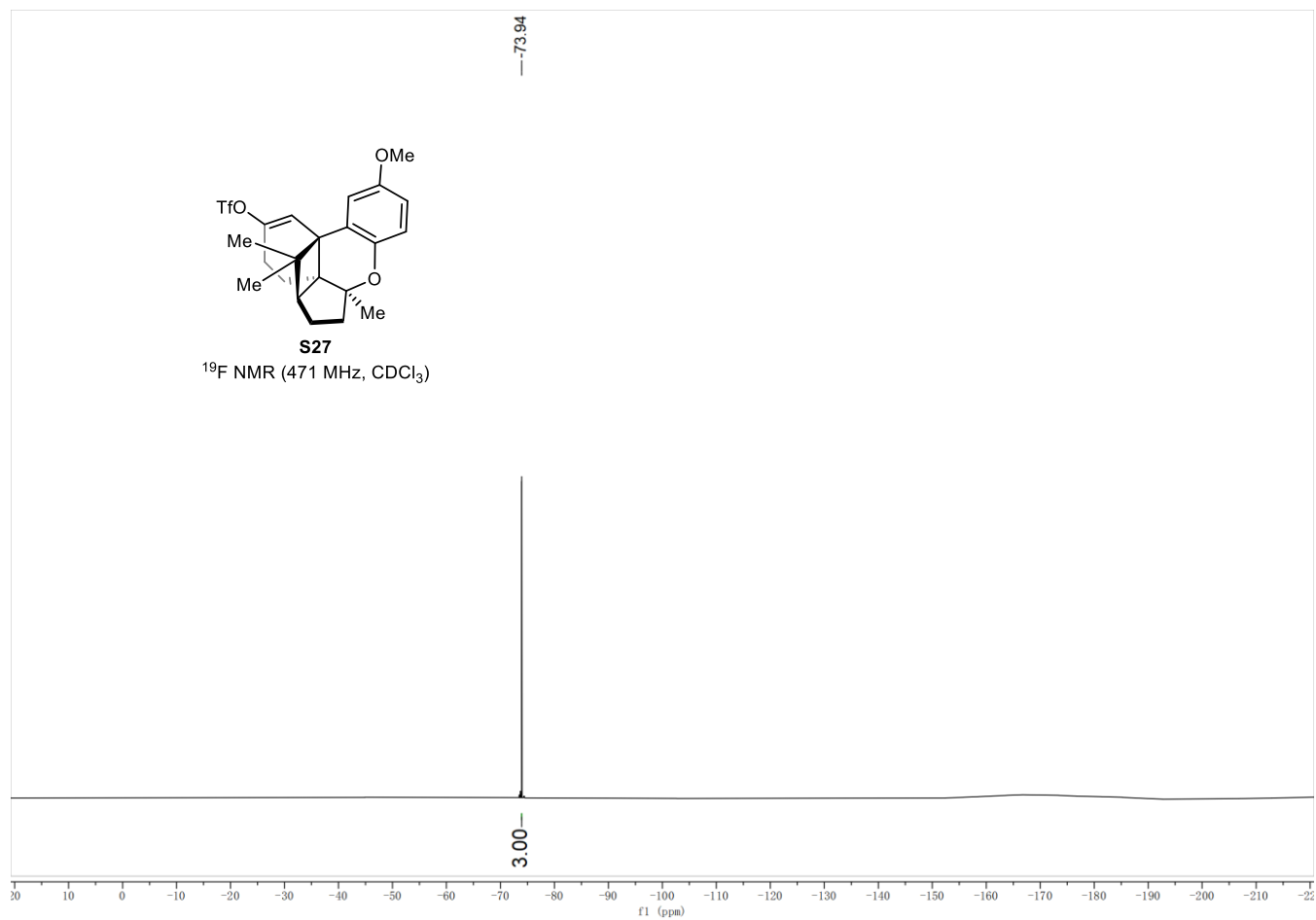


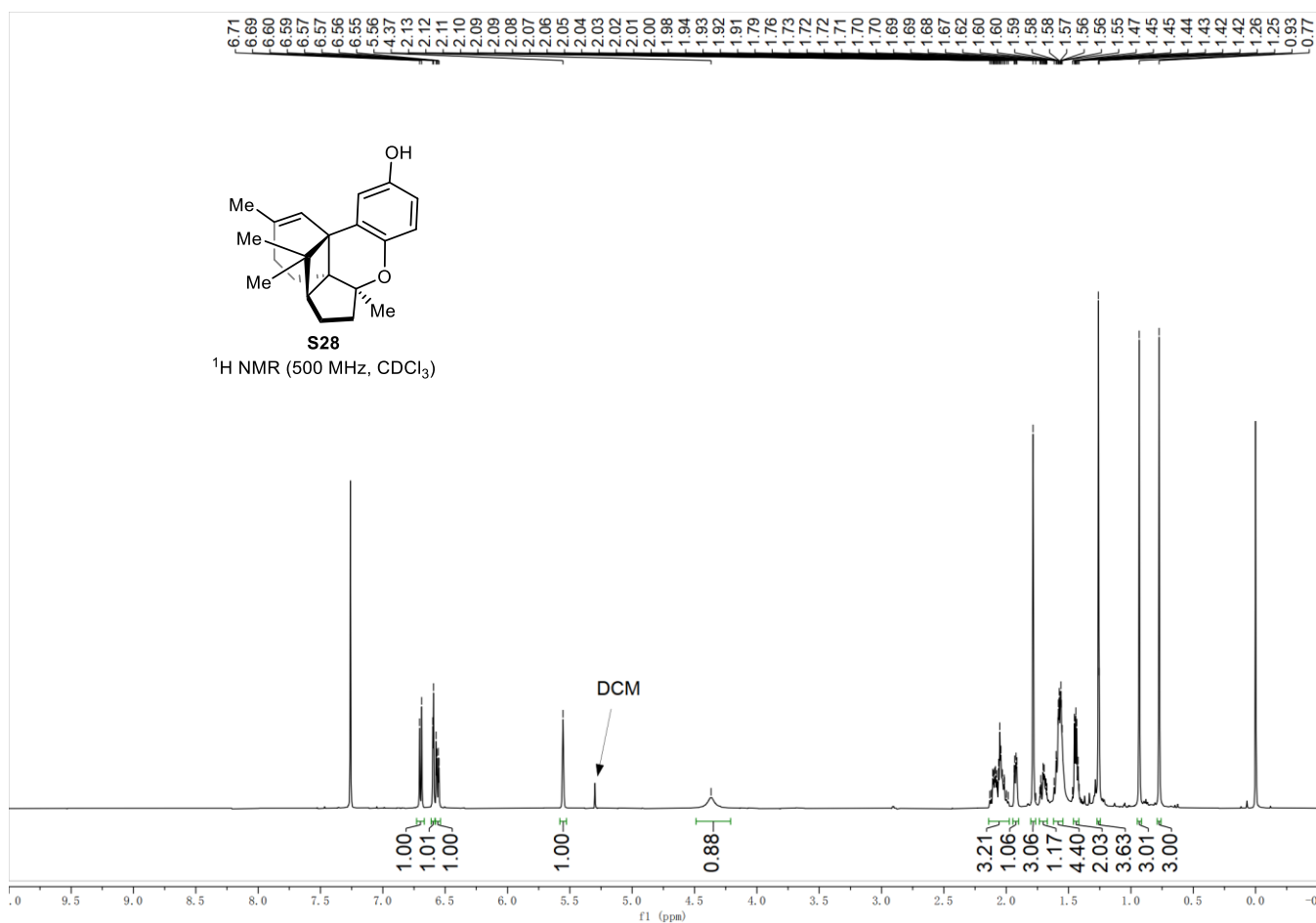
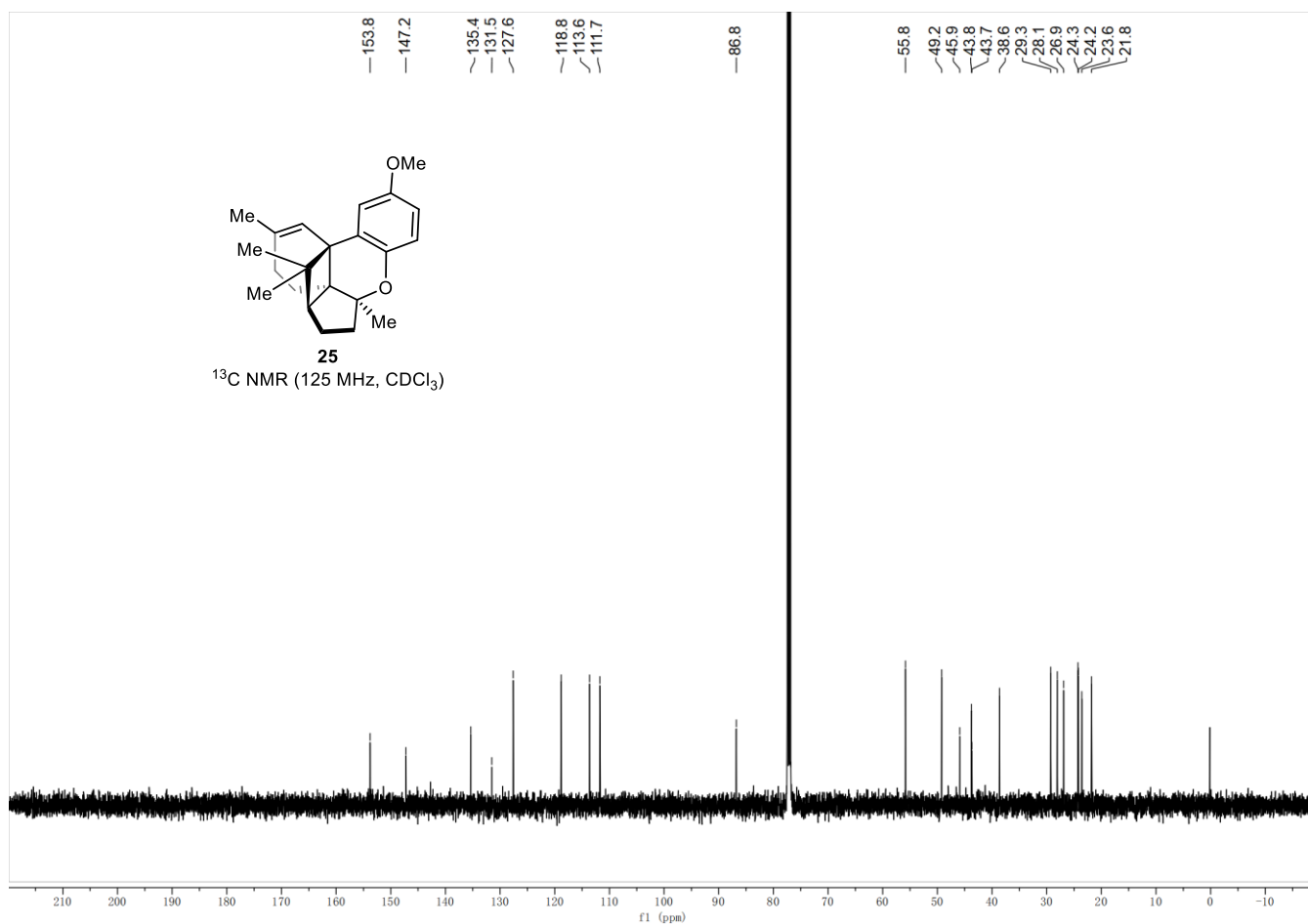


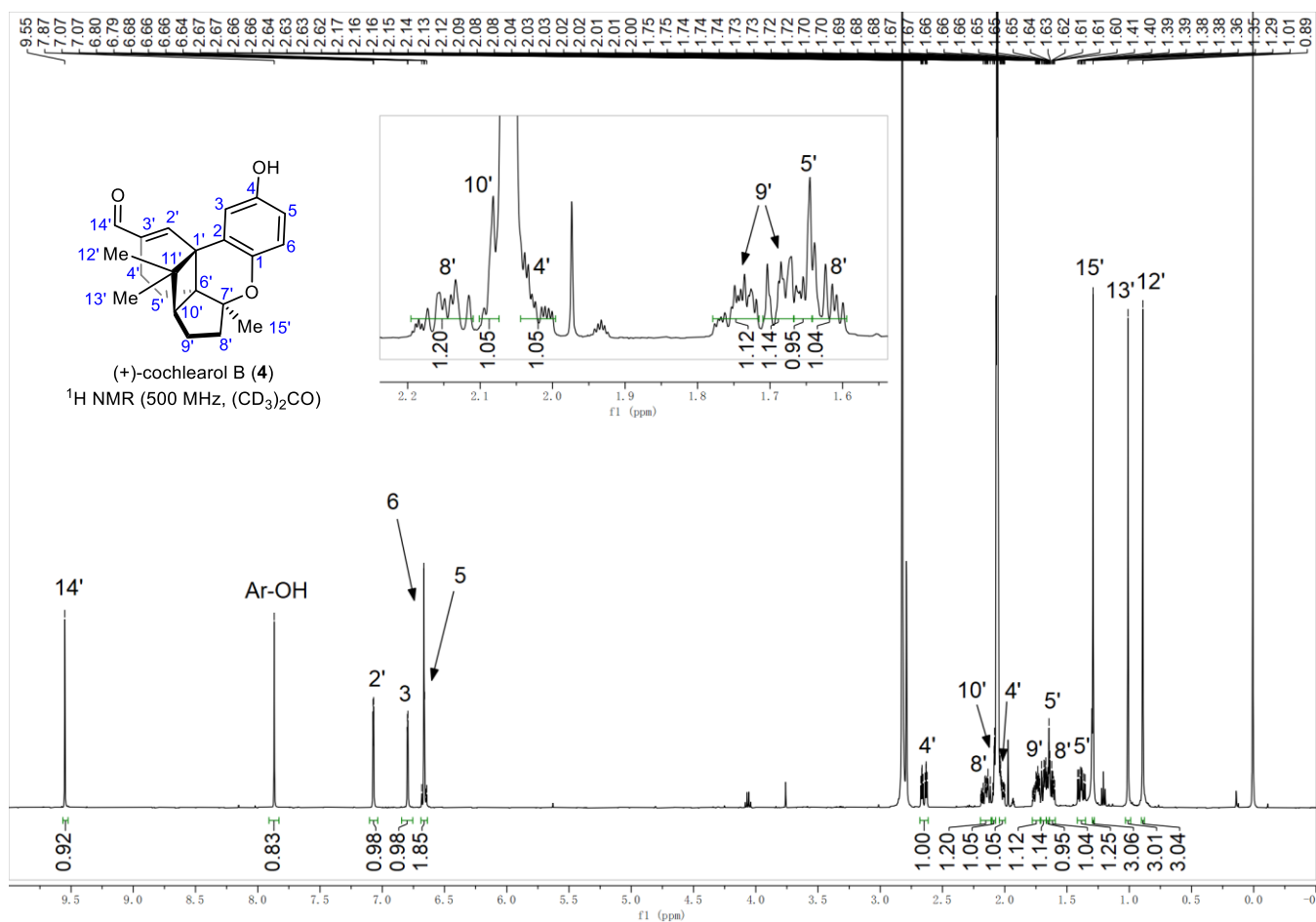
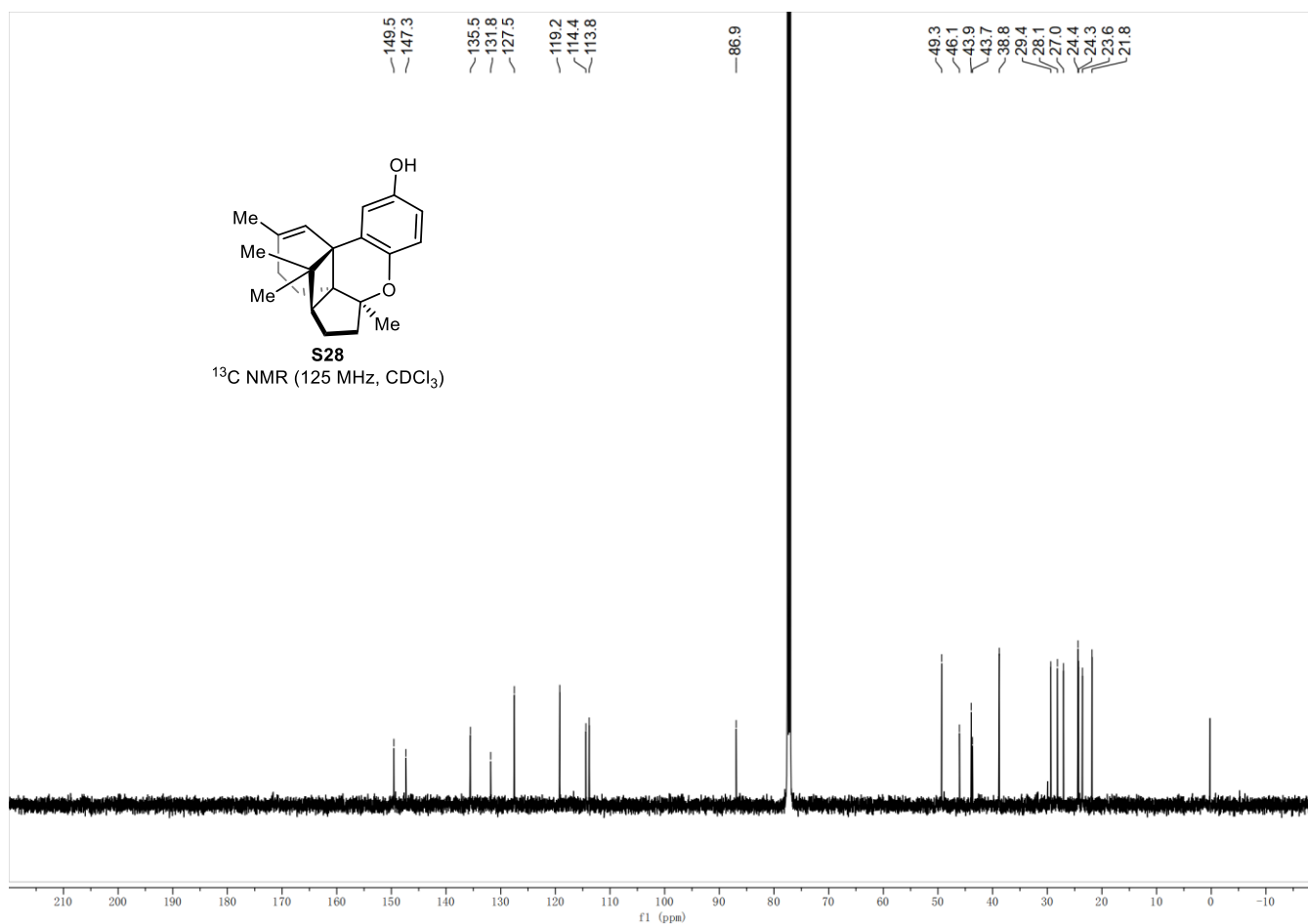


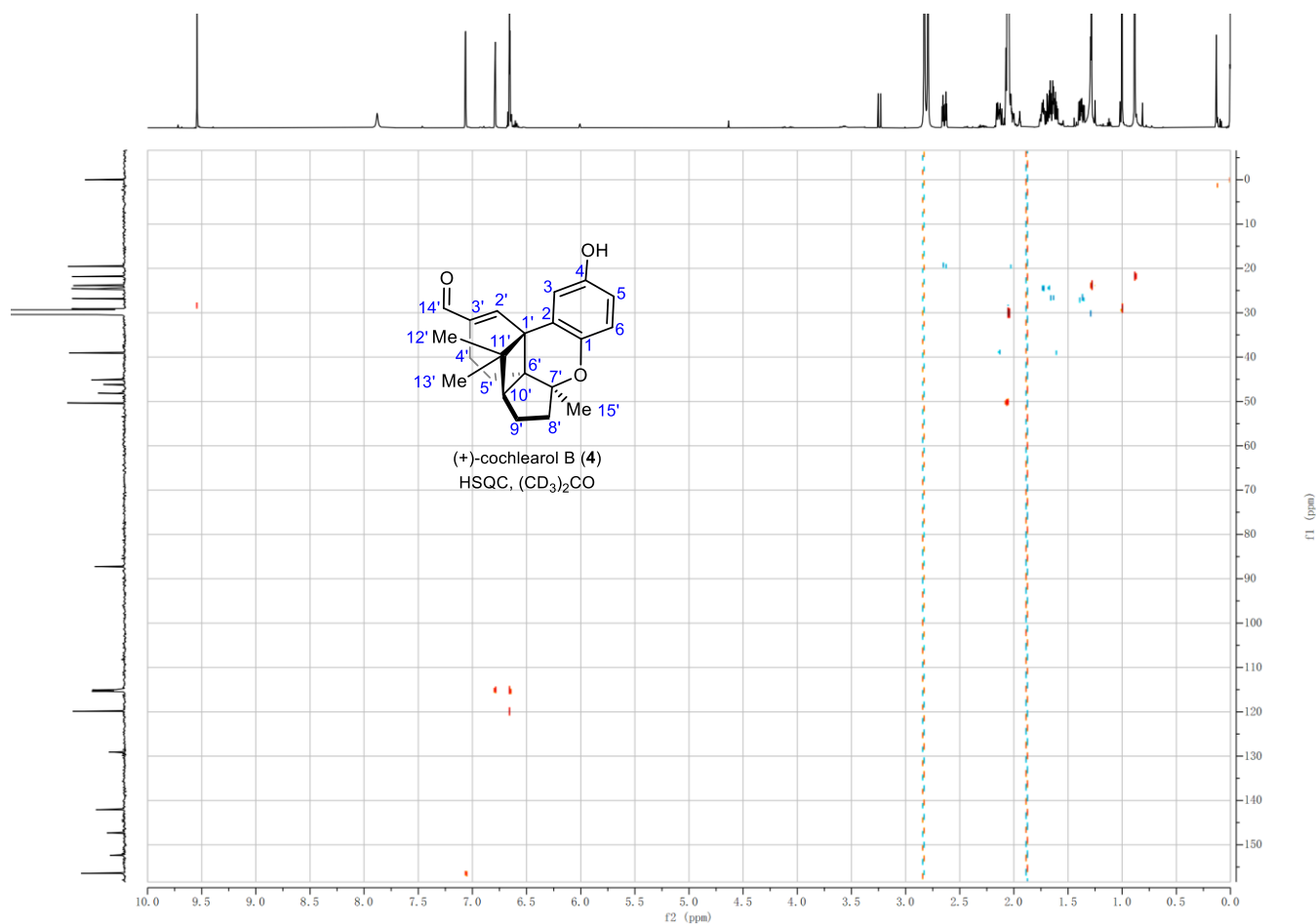
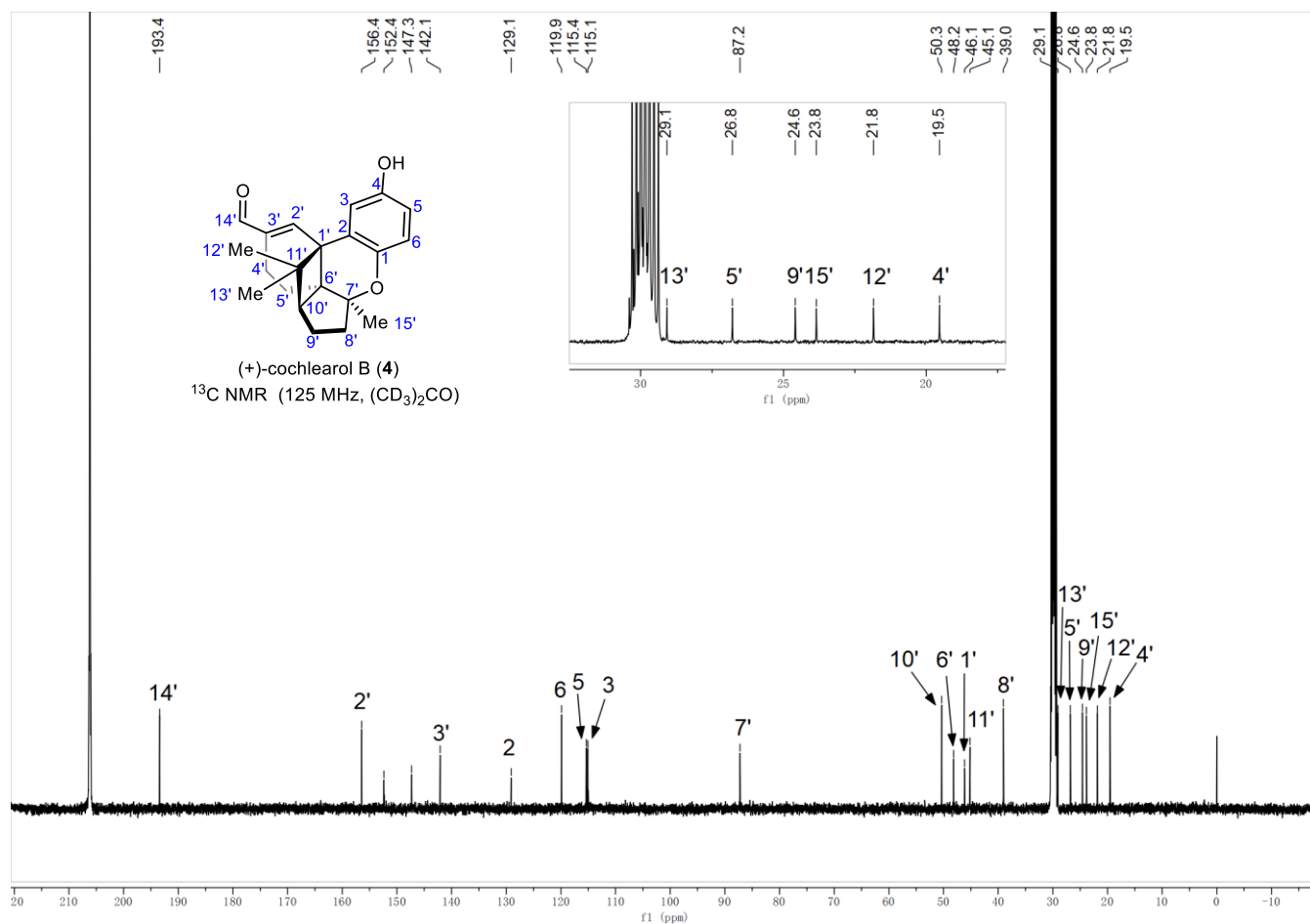


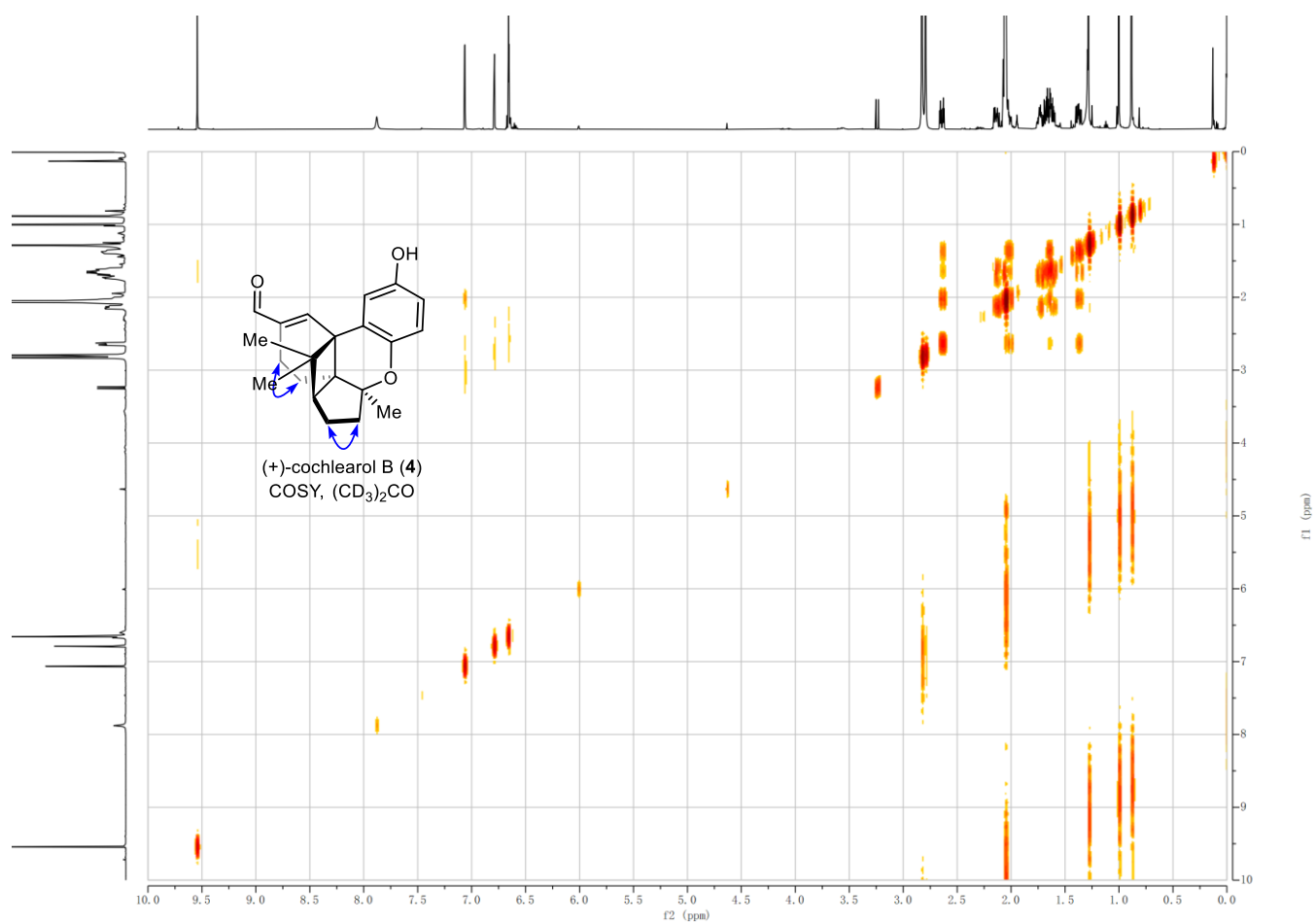
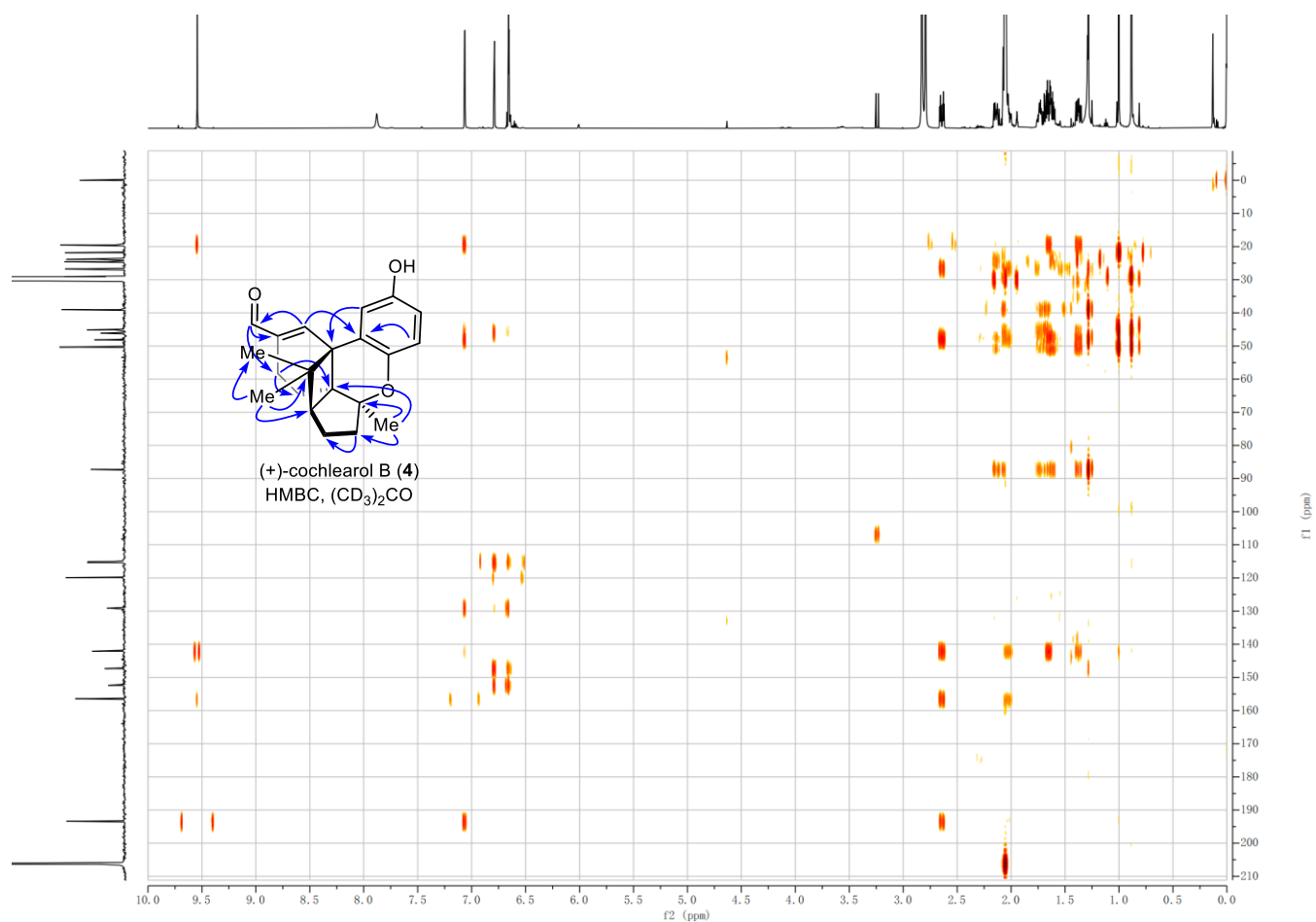












8. Supplementary References

- (1) Liu, Y., Zhou, C.-J., Li, Q. & Wang, H. Total synthesis of ($\pm$)-ganocins B and C. *Org. Biomol. Chem.* **14**, 10362–10365 (2016).
- (2) Shao, H., Gao, X., Wang, Z.-T., Gao, Z. & Zhao, Y.-M. Divergent biomimetic total syntheses of ganocins A–C, ganocochlearins C and D, and cochlearol T. *Angew. Chem. Int. Ed.* **59**, 7419–7424 (2020).
- (3) Mashiko, T. et al. Total synthesis of cochlearol B via intramolecular [2+2] photocycloaddition. *Angew. Chem. Int. Ed.* **60**, 24484–24487 (2021).
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