Supporting Information for

Divergent Synthetic Studies Towards Bisabosqual A and Fargenone: Regio- and Stereoselective Construction of [6-5-6] and [6-7-6] Tricyclic Core via an Intramolecular S_N2 reaction

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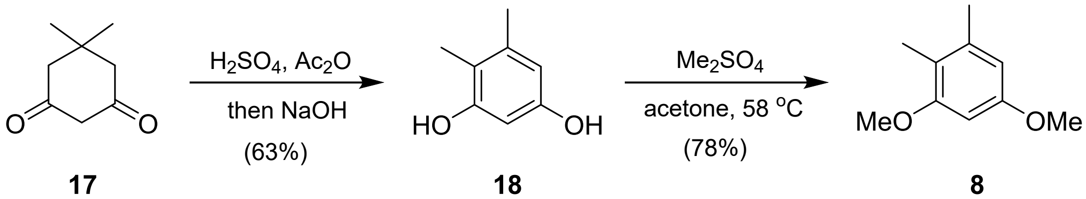
General Procedure

For product purification by flash column chromatography, silica gel (200−300 meshes) from the Qingdao Hailang silicon material company in China, and petroleum ether (bp. 60~90 °C) from Chengdu Lixinhe Chemical Co., Ltd. All solvents were purified and dried by standard techniques and distilled prior to use. The experiments were conducted under an argon or nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2±0.03 mm (HSGF5025) from Beijing Jianqiangweiye Chemical Co., +Ltd. Visualization on TLC was achieved by use of UV light at 254 nm. Organic extracts were dried over Na_2SO_4, unless otherwise noted. ^1H and ^{13}C NMR spectra were taken on a *Bruker* AM-400 and AM-600 spectrometer with TMS as an internal standard and $CDCl_3$ (^1H NMR: δ = 7.26; ^{13}C NMR: δ = 77.00) as solvent unless otherwise noted. IR spectra were recorded on an IR NICOLET iS10 spectrometer with a KBr disc. HRMS were determined on a AB SCIEX Triple TOF^{TM} 4600 spectrometer with ESI positive ion mode. The X-ray diffraction studies were carried out on a Bruker SMART Apex CCD area detector diffractometer equipped with graphite-monochromated Cu or Mo-Kα radiation source. The heat source of heating reactions is an oil bath.

Preparation of compound 8



17 **18** **8**

The compound **8** was prepared according to a general protocol described by Verheijen[1], Peng[2] and co-workers. To a 250 mL round-bottom flask containing 5,5-dimethylcyclohexane-1,3-dione **17** (10.00 g, 71.43 mmol) and Ac_2O (111 mL) under argon, followed by the addition of concentrated sulfuric acid (4.2 mL, 78.57 mmol, 1.1 equiv) at room temperature over 4 min. After 1 h of refluxing, the reaction temperature was cooled to room temperature again, and the majority of the volatiles were removed under reduced pressure. The reaction mixture was diluted with ice water (200 ml), and stirring for 20 minutes. Finally, this was extracted with CH_2Cl_2 (3 ×50 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL), water (30 mL) and brine (30 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product could be used directly for the next reaction without further purification.

To a 250 mL round-bottom flask containing the above 4,5-dimethyl-1,3-phenylene diacetate was added EtOH (100 mL), followed by the addition of NaOH (8.284 g, 207.1 mmol, 2.9 equiv) in H_2O (11 mL) under argon. The mixture was stirred for 1 h at 60 °C, and then cooled to room temperature. The solution was neutralized with 4*N* HCl and concentrated, and extracted with EtOAc (3 × 60 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL), water (30 mL) and brine (30 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 2 : 1) on silica gel to afford 4,5-dimethylbenzene-1,3-diol **18** (6.20 g, 63% yield) as a yellow solid. R_f = 0.4

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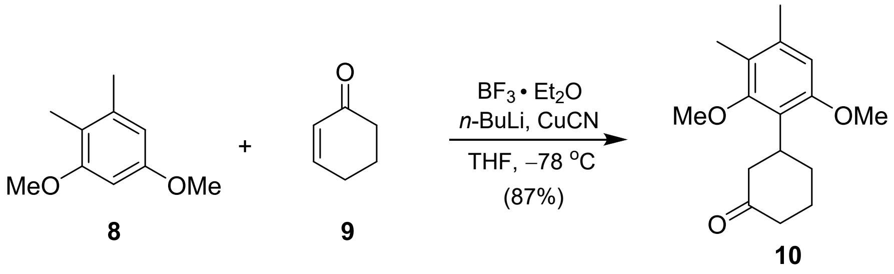
[1] McKinney, D. C.; Zhou, F.; Eyermann, C. J.; Ferguson, A. D.; Bryan Prince, D.; Breen, J.; Giacobbe, R. A.; Lahiri, S.; Verheijen, J. C. *ACS Infect. Dis.* **2015**, *1*, 310−316.

[2] Xiao, J.; Zhao, J.; Wang, Y.-W.; Luo, G.; Peng, Y. *Org. Biomol. Chem.***2021**,*19,*9840–9843.

(petroleum ether/EtOAc = 2 : 1).

In a 250 mL round-bottom flask, the above diphenol **18** (6.20 g, 44.93 mmol) and oven-dried K_2CO_3 (15.52 g, 112.3 mmol, 2.5 equiv) was dissolved in anhydrous acetone (80 mL). Me_2SO_4 (12.8 mL, 134.8 mmol, 3.0 equiv) was added dropwise over 5 min, and the reaction mixture was then stirred 10 h at 58 °C. After that, acetone was removed in vacuo and the resultant mixture was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL), water (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash columnchromatography (petroleum ether/EtOAc = 25 : 1) on silica gel to afford compound **8** (5.818 g, 78% yield) as a milky white oil (*based on dimethylsulfate as limiting reagent*). R_f = 0.7 (petroleum ether/EtOAc = 4 : 1); ^{1}H NMR (400 MHz, $CDCH_3$): δ = 6.35 (s, 1H), 6.33 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.26 (s, 3H), 2.07 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3, 158.0, 138.2, 117.2, 106.3, 95.9, 55.5, 55.3, 20.4, 10.9 ppm.

Synthesis of compound 10



In a 300 mL round-bottom flask, the compound **8** (13.03 g, 78.52 mmol, 2.0 equiv) was dissolved in anhydrous THF (60 mL), and the mixture was cooled to 0 °C. Then, the solution was added of *n*-BuLi (33 mL, 82.44 mmol, 2.1 equiv, 2.5 M in hexane) under argon over 10 min. After stirred 10 min, the reaction temperature was warmed to room temperature, and stirred for 2.5 h again. The fresh prepared aryl lithium reagent could be used directly for the next reaction.

To a 250 mL round-bottom flask containing the CuCN (5.274 g, 58.89 mmol, 1.5 equiv) and anhydrous THF (15 mL) under argon, and the mixture was cooled to −78

^{o}C. Then, the above aryl lithium reagent was added dropwise over 3 min, and the reaction mixture was then stirred 1 h. The fresh prepared aryl copper lithium reagent could be used directly for the next reaction.

To a 50 mL round-bottom flask containing the cyclohexanone **9** (3.769 g, 39.26 mmol), BF_3•Et_2O (4.9 mL, 39.26 mmol, 1.0 equiv) and anhydrous THF (10 mL) under argon. The solution was cooled to −78 ^{o}C, and stirred for 5 min. Then, this solution was added dropwise to the above aryl copper lithium reagent, and stirred for 1 h at −78 ^{o}C. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (10 mL), and extracted with EtOAc (3 × 70 mL). The organic layers were washed with water (2 × 25 mL) and brine (25 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 15 : 1) on silica gel to afford **10** (8.949 g, 87% yield) as a white solid. R_f = 0.5 (petroleum ether/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (s, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 3.58–3.49 (m, 1H), 3.23 (t, J = 13.6 Hz, 1H), 2.42–2.37 (m, 2H), 2.37–2.32 (m, 2H), 2.25 (s, 3H), 2.13 (s, 3H), 2.10–2.07 (m, 1H), 1.79–1.75 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.2, 156.6 (2C), 136.7, 122.2, 121.8, 109.1, 61.2, 55.2, 45.8, 41.3, 36.0, 29.3, 25.8, 20.3, 12.0 ppm. This product (8 mg) was dissolved in EtOAc (1 mL) and hexane (2 mL). After 4 days, the colorless single crystals were obtained by slow evaporation of solvent at room temperature. The crystal structure and the X-ray crystallographic data of **10** were described as follows:

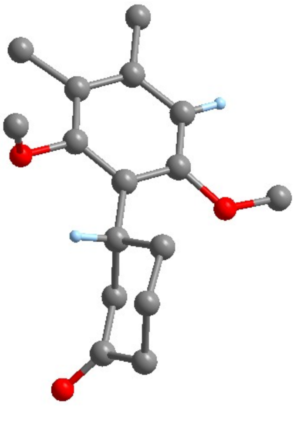
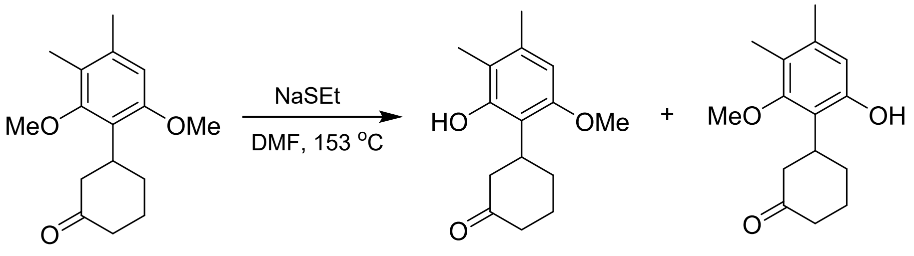


Table S1: X-ray crystal data of **10** (shown at the 50% probability level)

Empirical formula	$C_{16}H_{22}O_3$

Temperature (K)	149.99(10)
Crystal color	Colorless
Formula weight	262.33
Crystal system	orthorhombic
Space group	Pbca
a (Å)	15.7570(2)
b (Å)	10.12180(10)
c (Å)	18.1651(2)
α (°)	90
β (°)	90
γ (°)	90
V (Å^3)	2897.14(6)
Z	8
Density (calculated) (g/cm^3)	1.203
F (000)	1136.0
λ (Å)	1.54184
Reflections collected	11033
Independent reflections	2869
2θ Range for data collection (°)	11.23—154.826
Index range	$-16 \le h \le 19$ $-12 \le k \le 12$ $-22 \le l \le 17$
Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0439$, $wR_2 = 0.1128$
Largest difference peak and hole [e Å^{-3}]	0.27, –0.18

Synthesis of compound 11



10 **11** (74%) **11'** (10%)

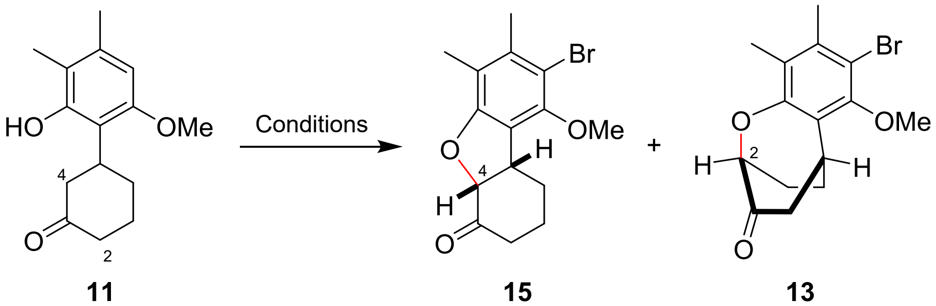
To a 100 mL round-bottom flask containing **10** (1.12 g, 4.27 mmol) in anhydrous

DMF (35 mL), followed by the addition of NaSEt (1.149 g, 13.66 mmol, 3.2 equiv) under argon. After being stirred for 6 h at 153 °C, the reaction mixture was cooled to room temperature. Then, it was quenched by the addition of 2*N* HCl (15 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL), water (2 × 15 mL) and brine (10 mL), then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 15 : 1) on silica gel to afford compound **11** (784 mg, 74% yield) as a white solid and **11′** (106 mg, 10% yield) as a pale yellow solid.

Data for **11**: R_f = 0.5 (petroleum ether/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.27 (s, 1H), 3.78 (s, 3H), 3.51 (t, J = 3.6 Hz, 1H), 3.00 (s, 1H), 2.25 (s, 3H), 2.08 (s, 3H), 2.05 (s, 1H), 2.00 (dd, J = 12.4, 2.8 Hz, 1H), 1.84–1.71 (m, 3H), 1.59–1.50 (m, 2H), 1.43–1.34 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0, 153.6, 135.4, 114.9, 110.8, 103.5, 98.3, 55.4, 39.1, 36.3, 29.7, 28.6, 20.3, 19.4, 11.2 ppm.

Data for **11′**: R_f = 0.4 (petroleum ether/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.47 (s, 1H), 3.72 (s, 3H), 3.45 (t, J = 3.6 Hz, 1H), 3.27 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H), 2.07–2.04 (m, 1H), 2.01 (dd, J = 12.4, 2.8 Hz, 1H), 1.89–1.84 (m, 1H), 1.78–1.71 (m, 2H), 1.66–1.55 (m, 2H), 1.46–1.40 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 153.8, 136.9, 120.5, 116.0, 112.2, 98.1, 61.1, 38.9, 36.5, 30.9, 29.4, 20.0, 19.1, 11.8 ppm.

Synthesis of compound 13 and 15



11 **15** **13**

Table S2: Optimization for divergent conversion from **11** to compound **13** and **15**

Entry[a]	Brominated regent	solvent	additives	**15**, Yield[b] (%)	**13**, Yield[b] (%)
1	Br_2	$AcOH/CH_3CN$	LiBr, Et_3N	3	50
2	$PyHBr_3$	$AcOH/CH_2Cl_2$	LiBr, Et_3N	2	54
3	Me_3PhNBr_3	THF/glycol, CH_3CN	LiBr, Et_3N	4	52
4	Me_3PhNBr_3	THF	Bu_4NI, H_2O_2	21	40
5	Me_3PhNBr_3	THF	NaOH	36	30

[a] The reaction take place under an argon atmosphere. [b] The isolated yield was shown.

To a 10 mL round-bottom flask containing **11** (500 mg, 2.02 mmol) in anhydrous THF (15 mL), and the solution was cooled to −78 °C. Then, followed by the addition of Me_3PhNBr_3 (2.353 g, 6.26 mmol, 3.1 equiv) in THF (20 mL) under argon. After being stirred for 3 h at −78 °C, the reaction mixture was warmed to room temperature and stirred for 12 h. The resulting crude bromide products was filtered and concentrated under reduced pressure to afford yellow solid, which could be used directly for the next reaction.

In a 100 mL round-bottom flask, the above bromide products was dissolved in CH_2Cl_2 (5 mL), and the solution was cooled to 0 °C. Then, followed by the addition 0.5 *N* NaOH (40 mL) dropwise over 5 min, and the reaction mixture was stirred 30 min at room temperature. After that, the resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 15 : 1) on silica gel to afford compound **15** (236 mg, 36% yield) as a yellow oil and **13** (196 mg, 30% yield) as a yellow solid.

Data for **15**: R_f = 0.7 (petroleum ether/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.84 (d, J = 9.2 Hz, 1H), 4.18–4.13 (m, 1H), 3.82 (s, 3H), 2.58–2.42 (m, 2H), 2.34 (s, 3H), 2.20 (s, 3H), 2.14–2.09 (m, 1H), 1.92−1.88 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.4, 158.1, 151.2, 138.2, 118.5, 116.3, 111.4, 85.0, 60.5, 44.7, 38.2, 26.4, 21.1, 19.7, 12.9 ppm;

Data for **13**: R_f = 0.5 (petroleum ether/EtOAc = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.44 (d, J = 6.8 Hz, 1H), 3.76 (s, 3H), 3.74−3.71 (m, 1H), 2.89 (dt, J =

18.8, 2.0 Hz, 1H), 2.76 (dd, J = 18.8, 6.0 Hz, 1H), 2.52–2.47 (m, 1H), 2.36 (s, 3H), 2.26–2.20 (m, 1H), 2.13 (s, 3H), 2.08–2.05 (m, 1H), 1.94-1.91 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.6, 151.7, 151.3, 136.8, 124.1, 123.1, 112.5, 80.4, 61.5, 45.8, 29.3, 27.3, 26.6, 20.0, 13.3 ppm; This product (4 mg) was dissolved in EtOAc (1 mL) and hexane (1 mL). After 3 days, the colorless single crystals were obtained by slow evaporation of solvent at room temperature. The crystal structure and the X-ray crystallographic data of **13** were described as follows:

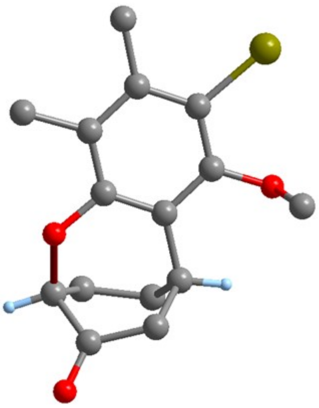
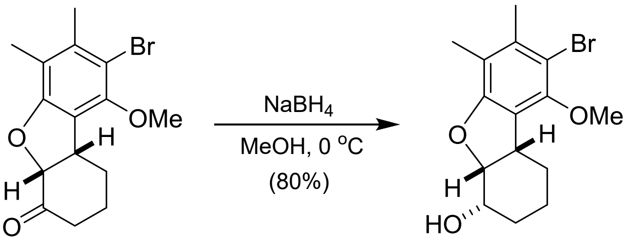


Table S3: X-ray crystal data of **13** (shown at the 50% probability level)

Empirical formula	$C_{15}H_{17}BrO_3$
Temperature (K)	149.97(10)
Crystal color	Colorless
Formula weight	325.20
Crystal system	monoclinic
Space group	$P2_1/n$
a (Å)	9.81899(16)
b (Å)	9.17658(16)
c (Å)	15.2660(3)
α (°)	90
β (°)	101.9390(17)
γ (°)	90
V (Å^3)	1345.78(4)
Z	4
Density (calculated) (g/cm^3)	1.605

F (000)	664.0
λ (Å)	1.54184
Reflections collected	8763
Independent reflections	2711
2θ Range for data collection (°)	9.864—154.902
Index range	$-10 \leq h \leq 12$ $-11 \leq k \leq 11$ $-19 \leq l \leq 18$
Final R indices [I>2σ(I)]	$R_1 = 0.0469$, $wR_2 = 0.1174$
Largest difference peak and hole [e Å $^{-3}$]	0.89, –0.64

Synthesis of compound 16



15 **16**

To a 10 mL round-bottom flask containing **15** (20 mg, 0.062 mmol) in anhydrous MeOH (2 mL), and the solution was cooled to 0 ^{o}C. Then, followed by the addition of NaBH$_4$ (2.8 mg, 0.074 mmol, 1.2 equiv) under argon. After being stirred for 30 min at 0 ^{o}C, the reaction mixture was was quenched by the addition of ice water (2 mL) and extracted with EtOAc (3 × 5 mL). The organic layers were washed with water (5 mL) and brine (5 mL), then dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 6 : 1) on silica gel to afford compound **16** (16.3 mg, 80% yield) as a white solid. $R_f = 0.4$ (petroleum ether/EtOAc = 4:1); ^{1}H NMR (600 MHz, CDCl$_3$): $\delta = 4.63$ (t, $J = 3.6$ Hz, 1H), 3.93-3.90 (m, 1H), 3.86 (s, 3H), 3.41–3.37 (m, 1H), 2.35 (s, 3H), 2.18 (s, 3H), 1.98–1.92 (m, 2H), 1.72 (dt, $J = 13.8$, 4.2 Hz, 1H), 1.59–1.54 (m, 1H), 1.39–1.30 (m, 1H), 1.18–1.10 (m, 1H), 0.86–0.84 (m, 1H) ppm; ^{13}C NMR (150 MHz, CDCl$_3$): $\delta = 157.1$, 150.6, 137.3, 123.0, 116.1, 110.6, 84.4, 69.7, 60.8, 41.0, 29.0, 28.2, 21.5, 19.7, 13.0 ppm. This product (5 mg) was dissolved in EtOAc (1 mL) and hexane (3 mL). After 5 days, the colorless single crystals were obtained by slow evaporation of solvent at room temperature. The crystal structure and the X-ray crystallographic data of **16** were described as follows:

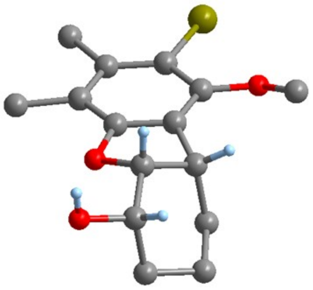
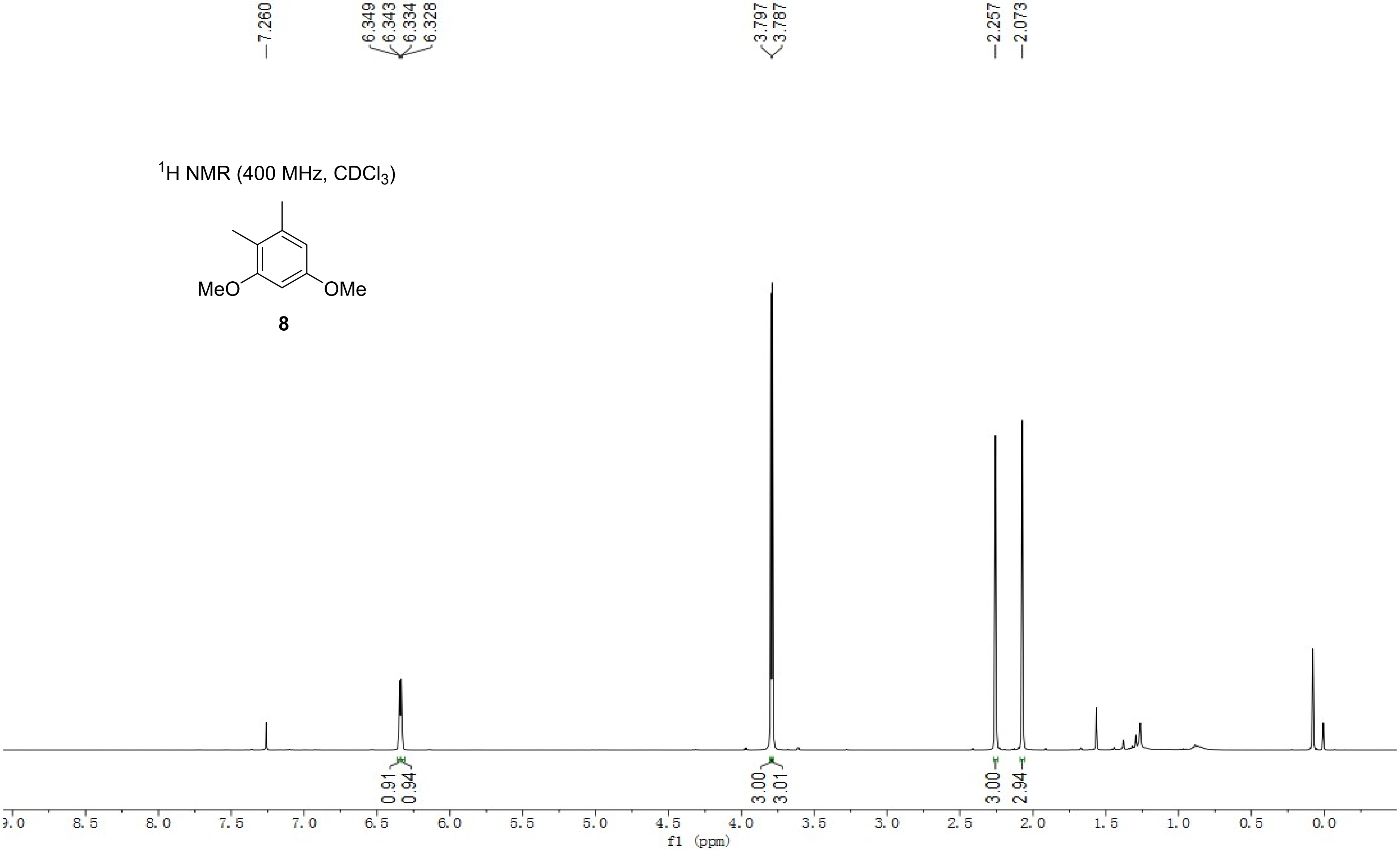


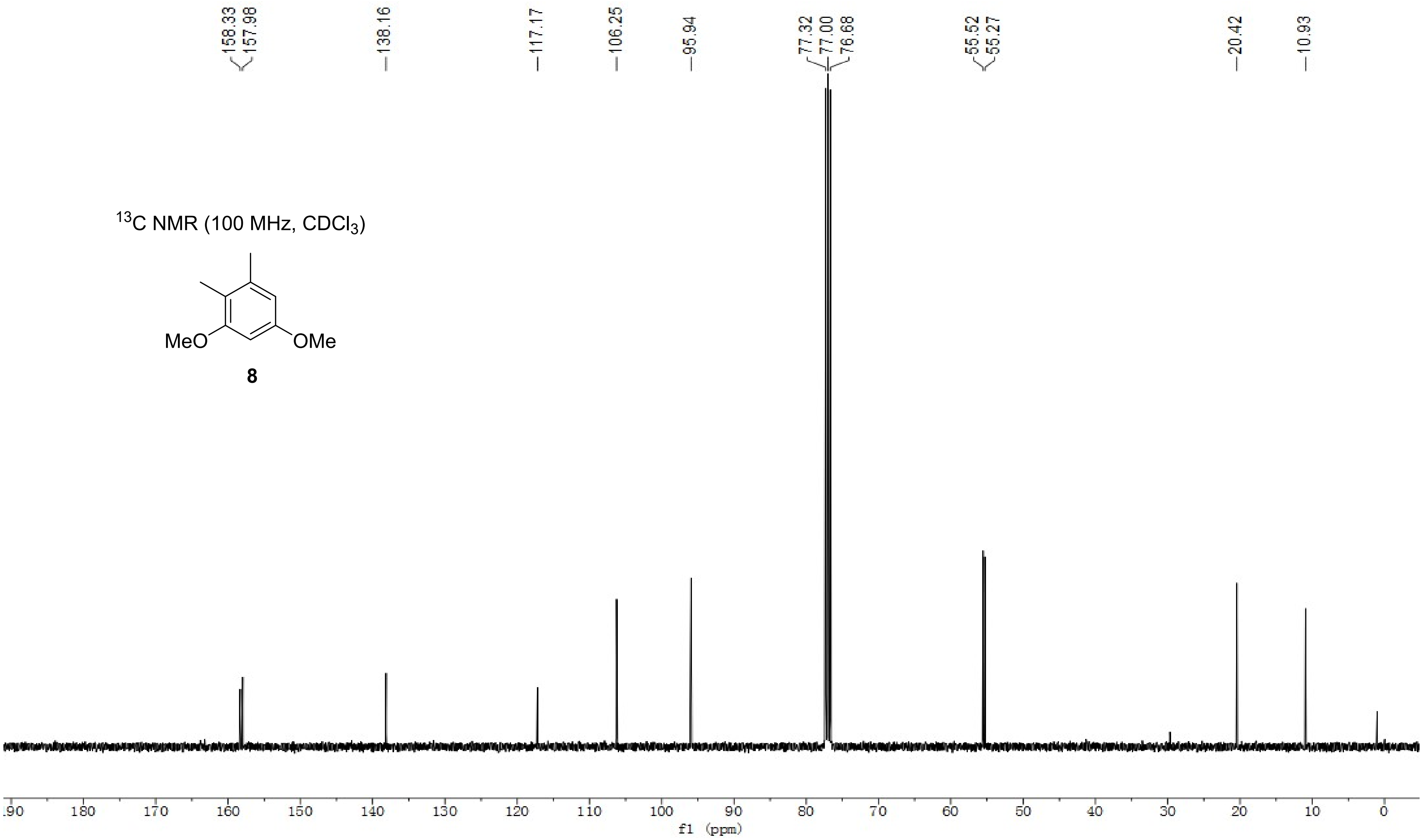
Table S4: X-ray crystal data of **16** (shown at the 50% probability level)

Empirical formula	$C_{15}H_{19}BrO_3$
Temperature (K)	293.15
Crystal color	Colorless
Formula weight	327.21
Crystal system	orthorhombic
Space group	$Pna2_1$
a (Å)	21.8523(12)
b (Å)	5.1108(4)
c (Å)	25.9585(19)
α (°)	90
β (°)	90
γ (°)	90
V (Å ^{3})	2899.1(3)
Z	8
Density (calculated) (g/cm ^{3})	1.499
F (000)	1344.0
λ (Å)	0.71073
Reflections collected	14892
Independent reflections	5527
2θ Range for data collection (°)	6.278—52.742
Index range	$-27 \leq h \leq 27$ $-6 \leq k \leq 6$ $-32 \leq l \leq 32$
Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0521$, $wR_2 = 0.0806$
Largest difference peak and hole [e Å $^{-3}$]	0.36, –0.34

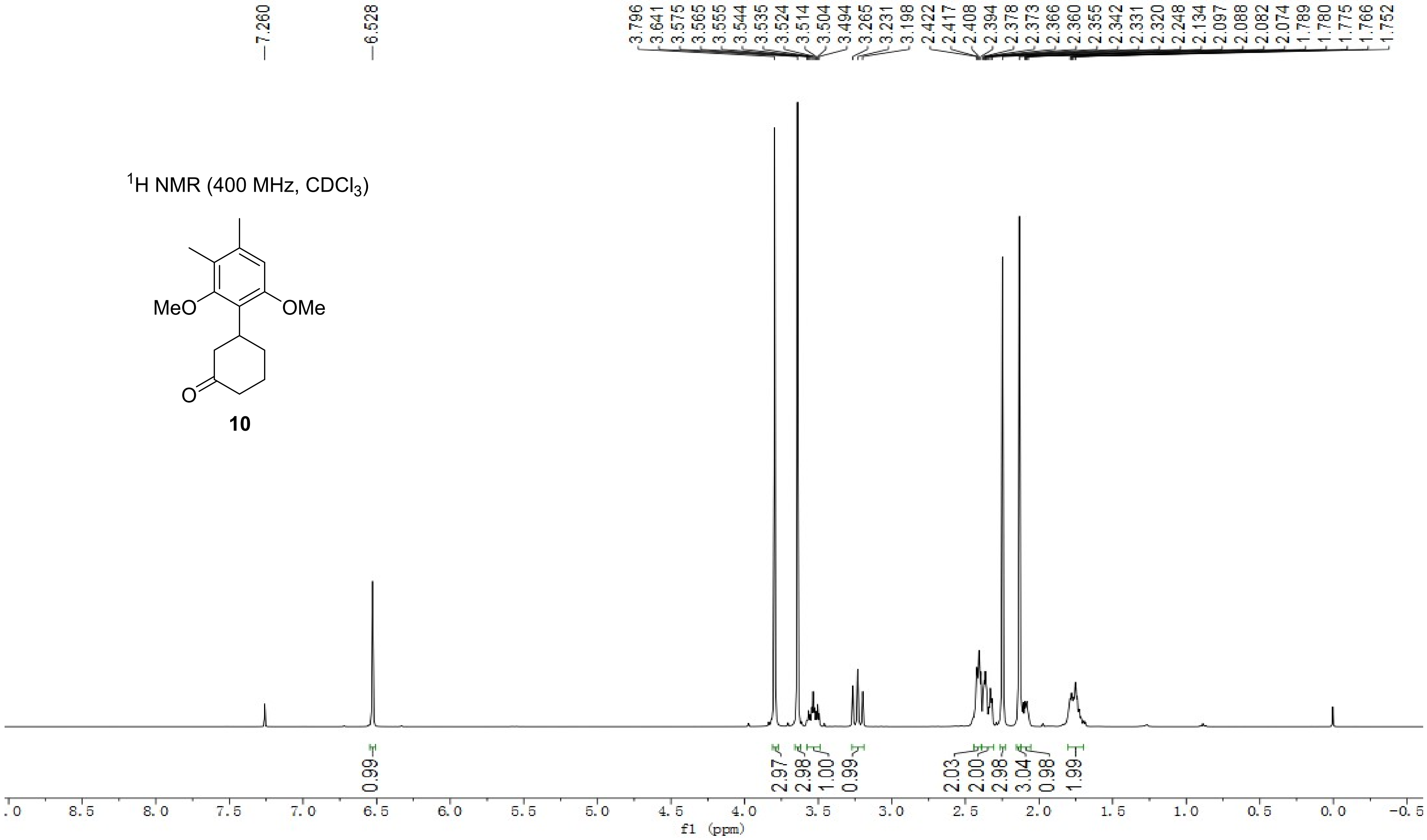
^{1}H NMR (400 MHz, $CDCl_3$)

8




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

8


1H NMR (400 MHz, CDCl3)
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OMe
O
10
7.260
6.528
3.796
3.641
3.575
3.565
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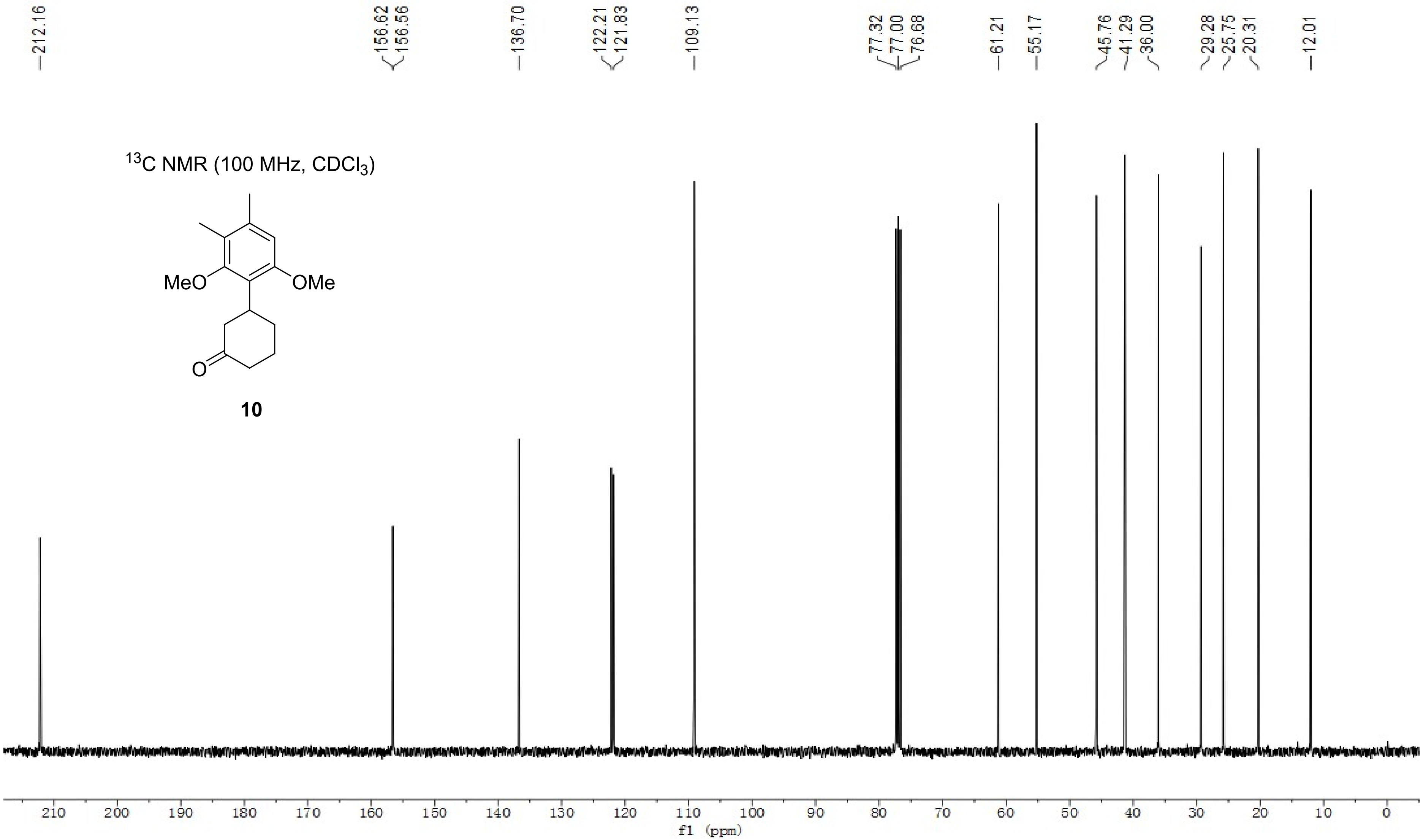
3.544
3.535
3.524
3.514
3.504
3.494
3.265
3.231
3.198
2.422
2.417
2.408
2.394
2.378
2.373
2.366
2.360
2.355
2.342
2.331
2.320
2.248
2.134
2.097
2.088
2.082
2.074
1.789
1.780
1.775
1.766
1.752
0.99
2.97
2.98
1.00
0.99
2.03
2.00
2.98
3.04
0.98
1.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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156.56
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122.21
121.83
109.13
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77.00
76.68
61.21
55.17
45.76
41.29
36.00
29.28
25.75
20.31
12.01
^{13}C NMR (100 MHz, CDCl$_3$)
MeO
OMe
O
210
200
190
180
170
160
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140
130
120
110
100
90
80
70
60
50
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30
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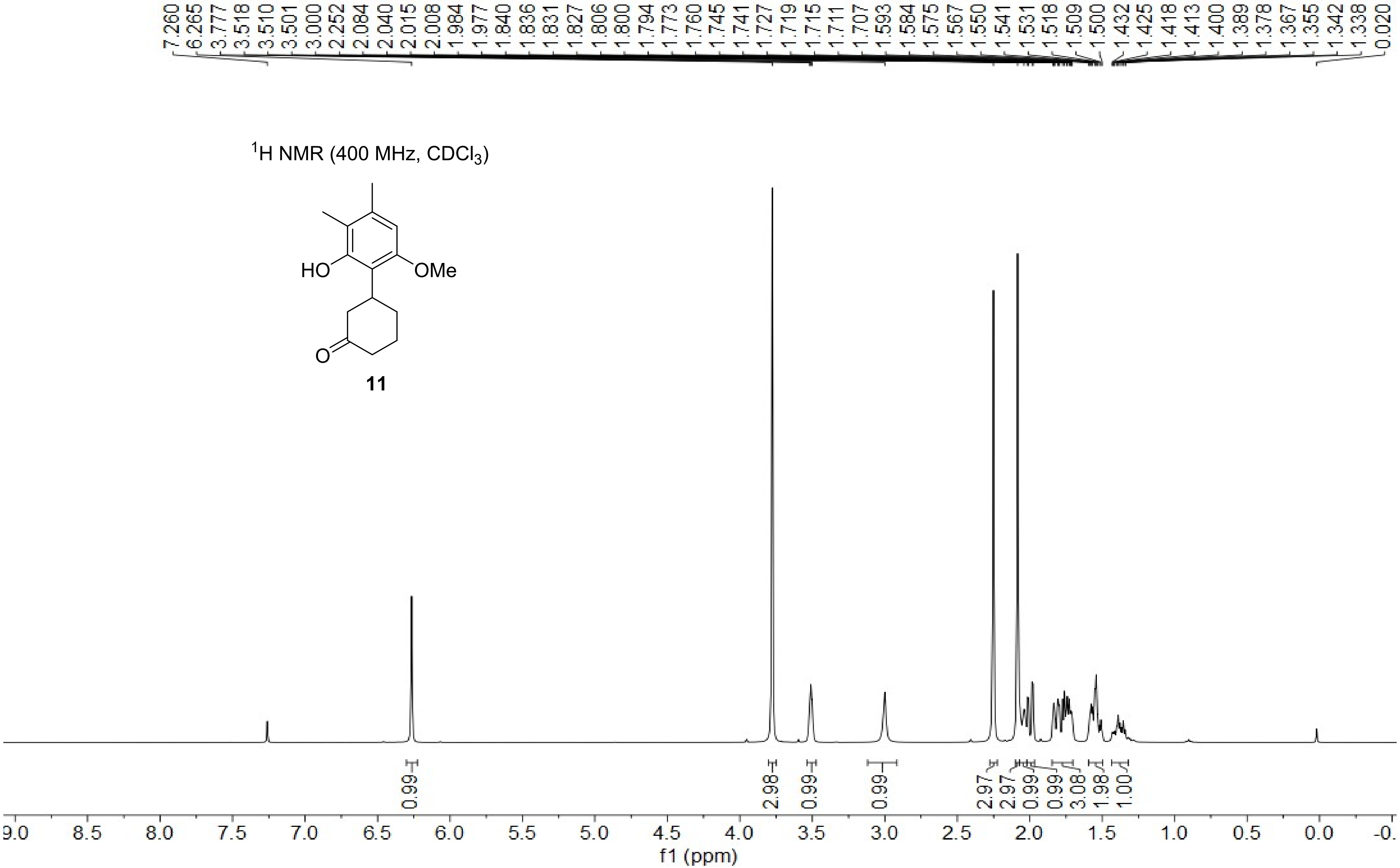
10
0
f1 (ppm)

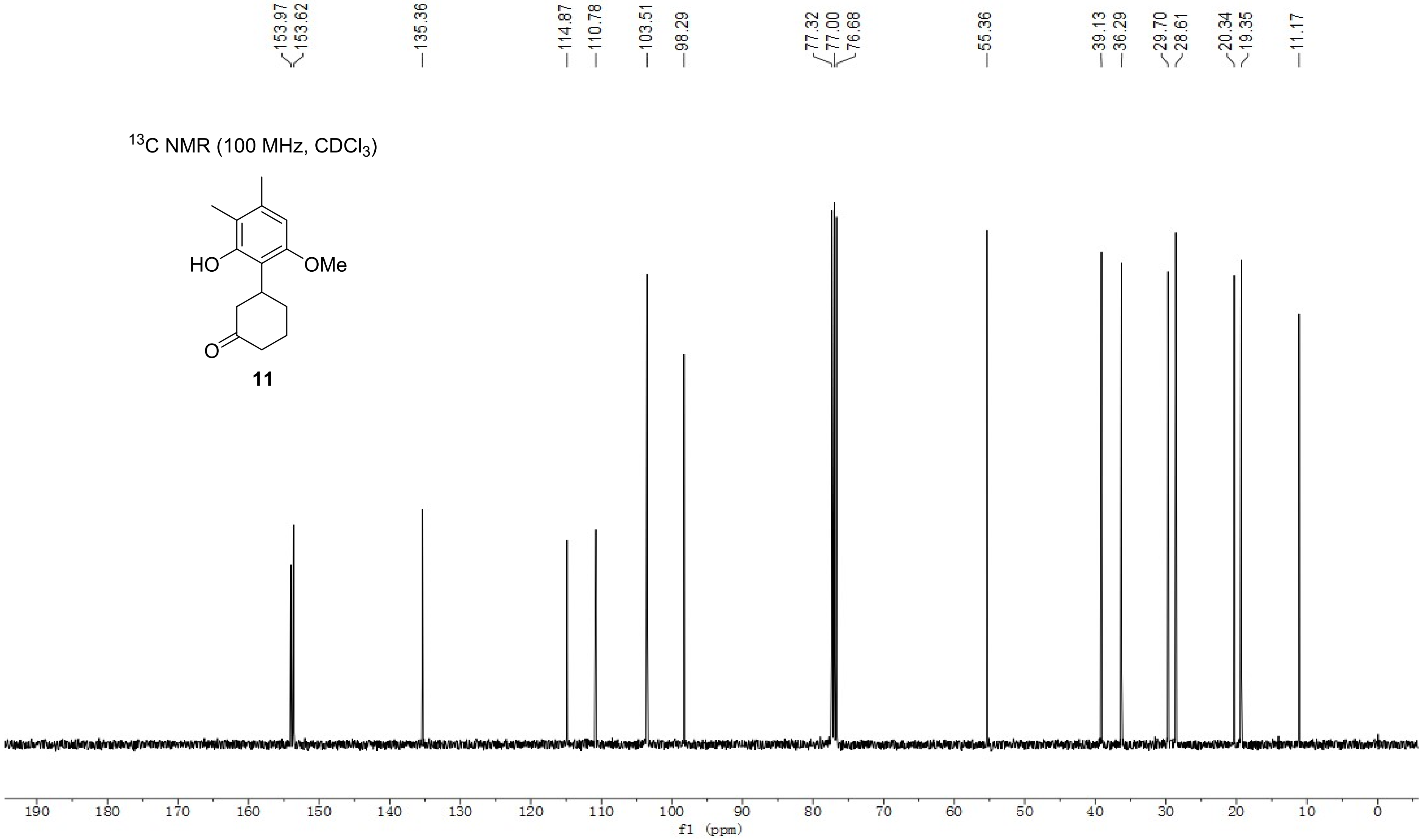
10



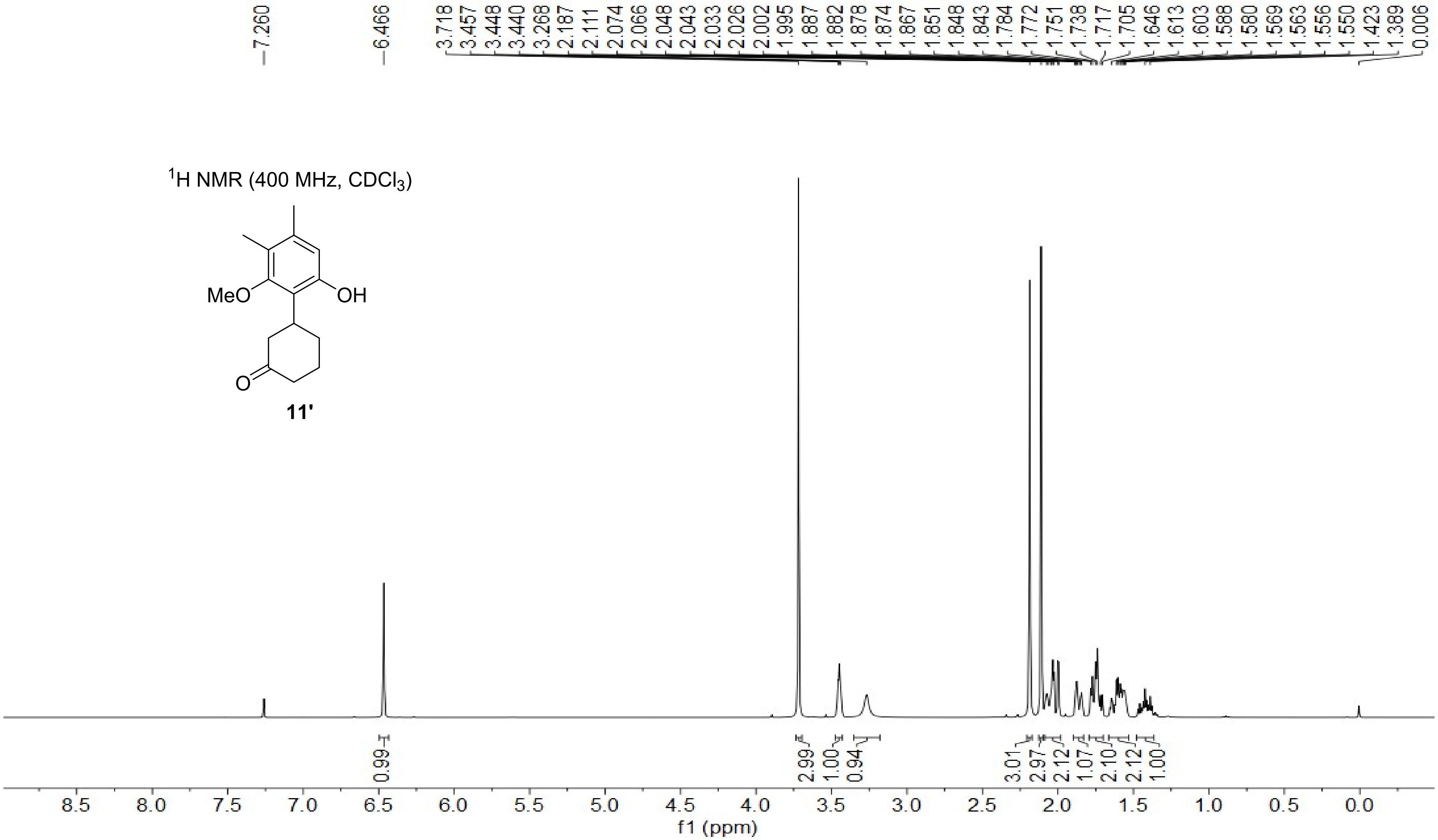
^{1}H NMR (400 MHz, CDCl$_3$)

11

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

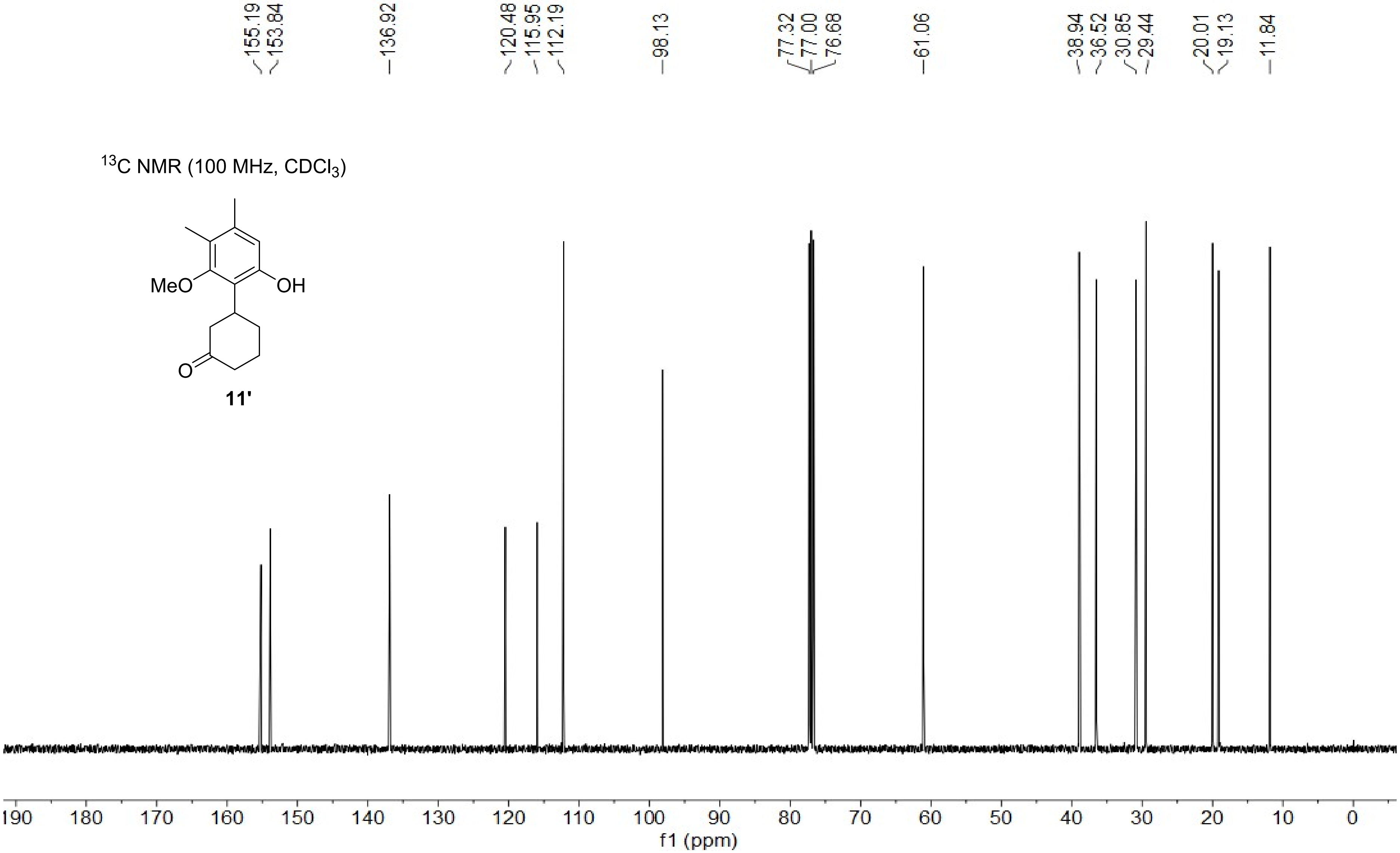


11

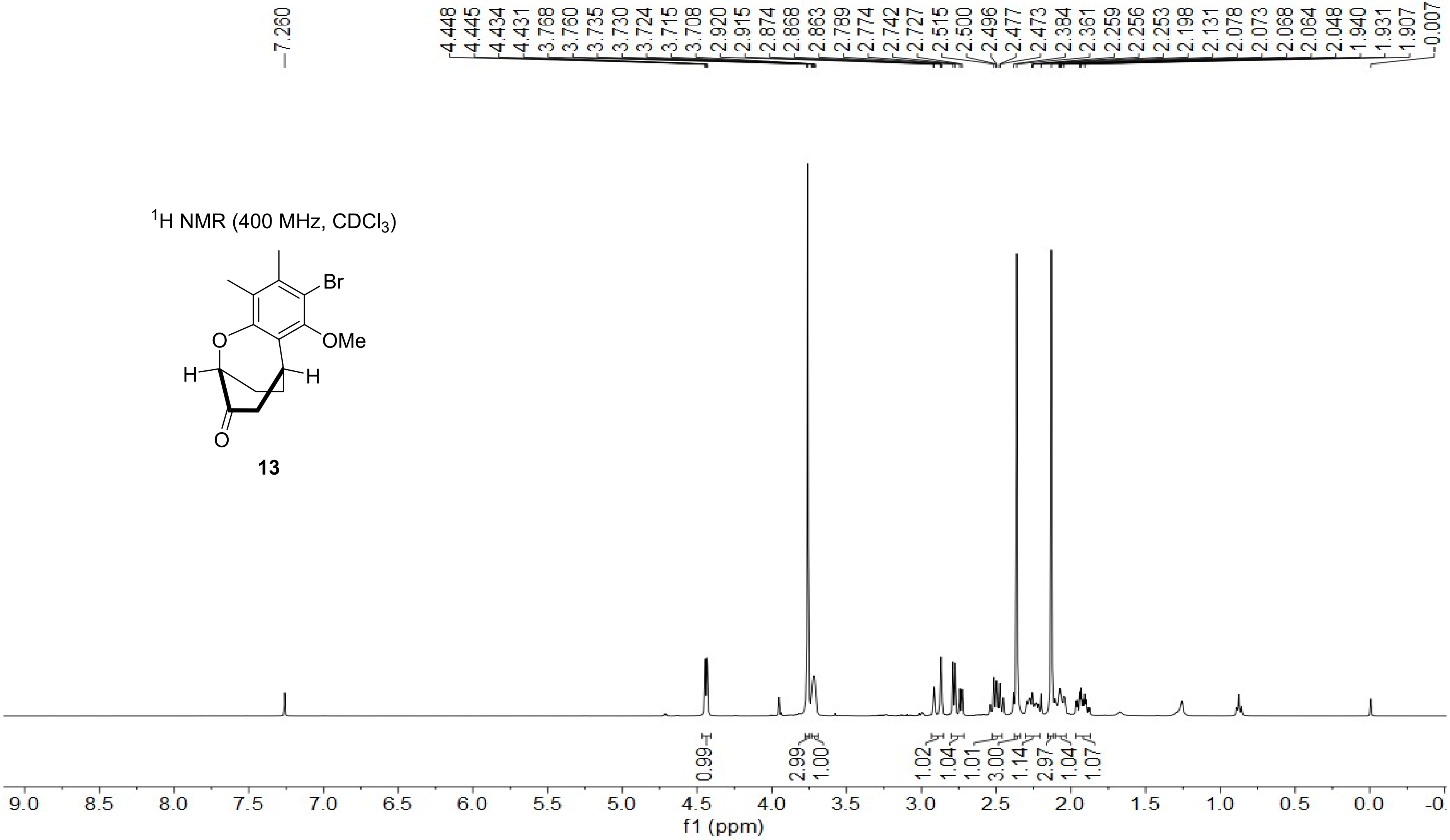


¹H NMR (400 MHz, CDCl₃)
MeO
OH
O
11'
7.260
6.466
3.718
3.457
3.448
3.440
3.268
2.187
2.111
2.074
2.066
2.048
2.043
2.033
2.026
2.002
1.995
1.887
1.882
1.878
1.874
1.867
1.851
1.848
1.843
1.784
1.772
1.751
1.738
1.717
1.705
1.646
1.613
1.603
1.588
1.580
1.569
1.563
1.556
1.550
1.423
1.389
0.006
0.99
2.99
1.00
0.94
3.01
2.97
2.12
1.07
2.10
2.12
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

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

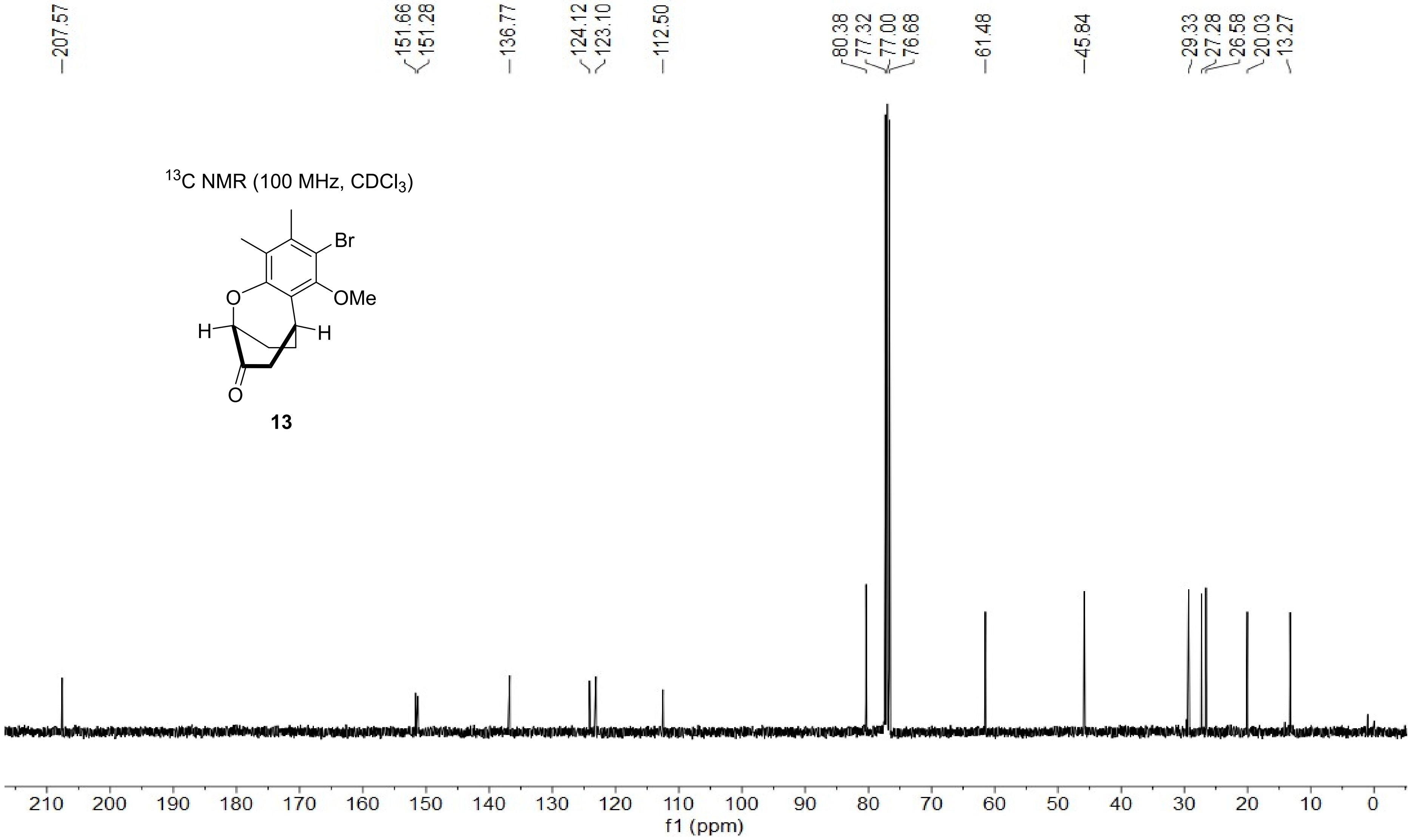


11'

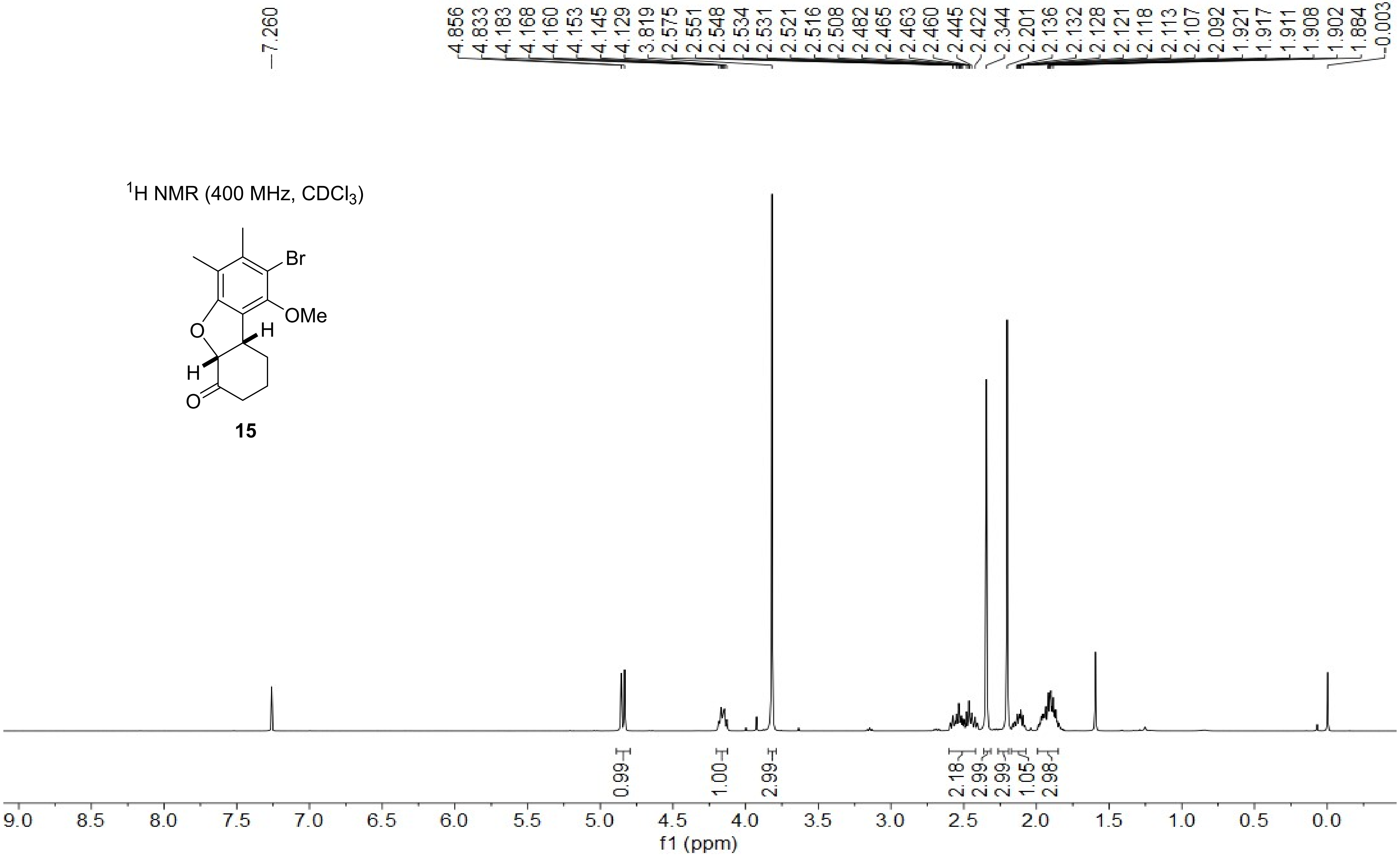


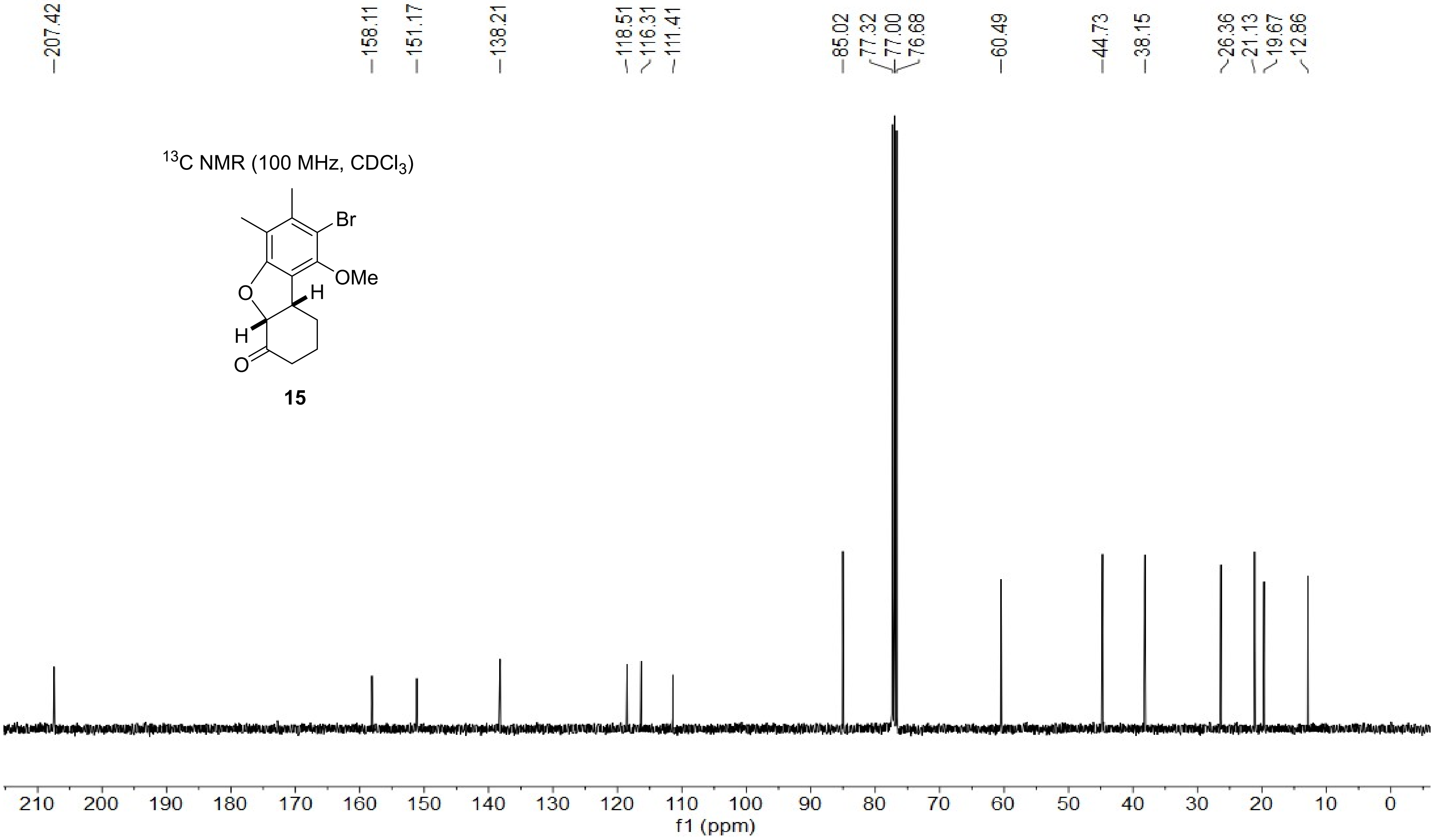
^{1}H NMR (400 MHz, $CDCl_3$)

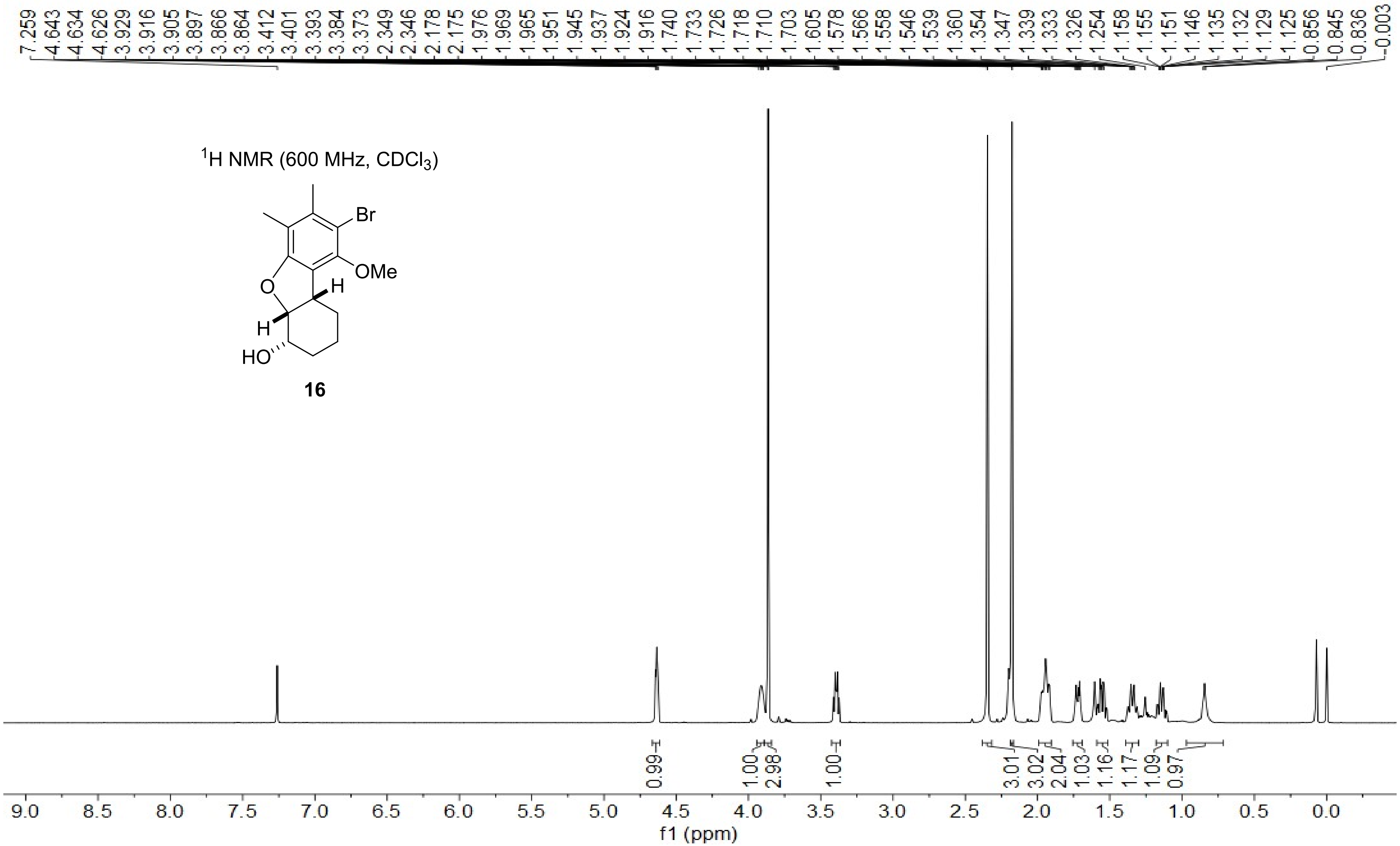
13

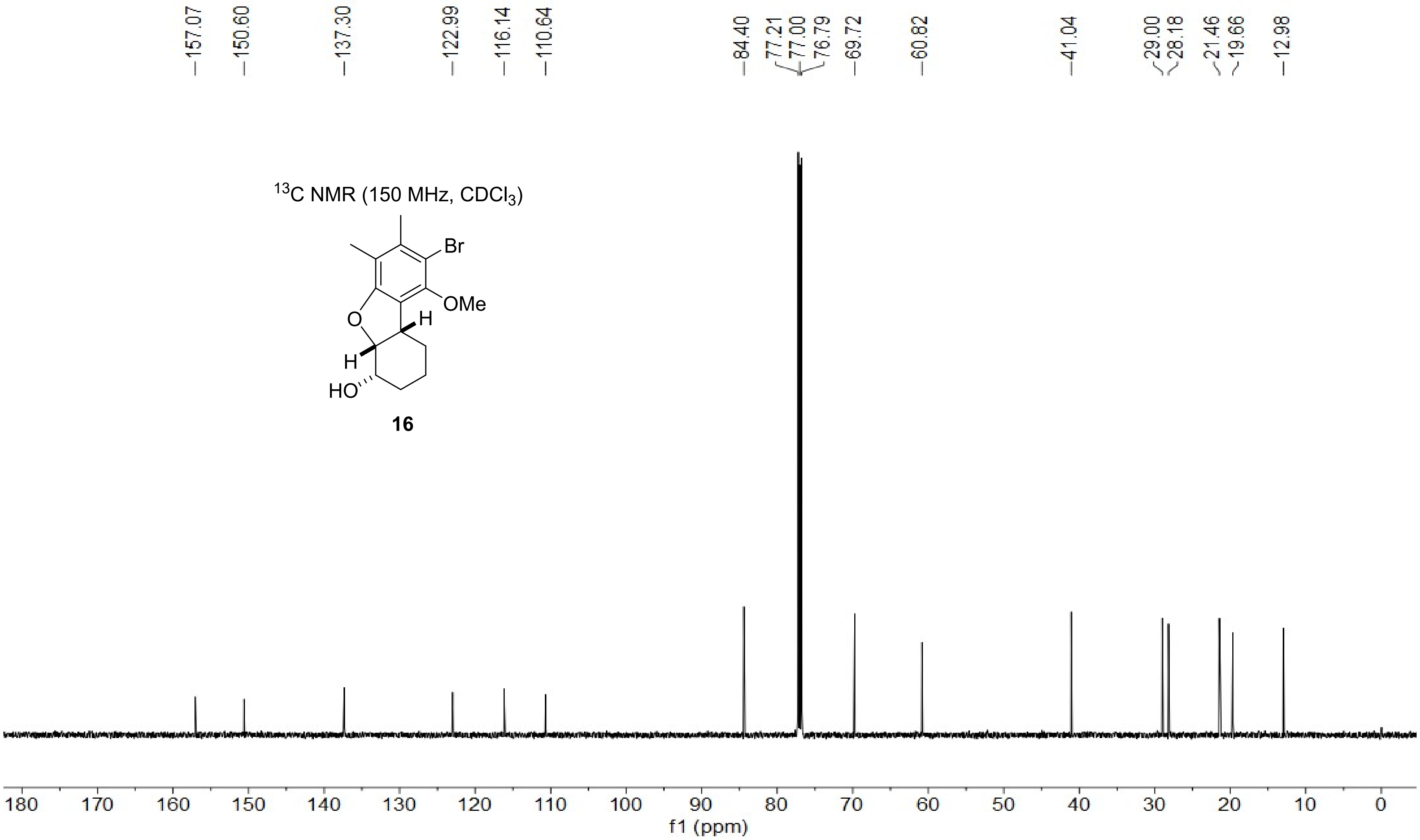

207.57
151.66
151.28
136.77
124.12
123.10
112.50
80.38
77.32
77.00
76.68
61.48
45.84
29.33
27.28
26.58
20.03
13.27
^{13}C NMR (100 MHz, CDCl$_3$)
Br
OMe
O
H
H
O
13
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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




207.42
158.11
151.17
138.21
118.51
116.31
111.41
85.02
77.32
77.00
76.68
60.49
44.73
38.15
26.36
21.13
19.67
12.86
^{13}C NMR (100 MHz, CDCl$_3$)
Br
OMe
O
H
H
O
15
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.259
4.643
4.634
4.626
3.929
3.916
3.905
3.897
3.866
3.864
3.412
3.401
3.393
3.384
3.373
2.349
2.346
2.178
2.175
1.976
1.969
1.965
1.951
1.945
1.937
1.924
1.916
1.740
1.733
1.726
1.718
1.710
1.703
1.605
1.578
1.566
1.558
1.546
1.539
1.360
1.354
1.347
1.339
1.333
1.326
1.254
1.158
1.155
1.151
1.146
1.135
1.132
1.129
1.125
0.856
0.845
0.836
-0.003
^{1}H NMR (600 MHz, CDCl$_3$)
Br
OMe
O
H
H
HO
16
0.99
1.00
2.98
1.00
3.01
3.02
2.04
1.03
1.16
1.17
1.09
0.97
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



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

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