Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Highly Efficient and Practical Resolution of 2,3:6,7-Dibenzobicyclo-[3.3.1]nona-2,6-diene-4,8-dione And Stereoselective Synthesis of It Chiral Diamine Derivatives

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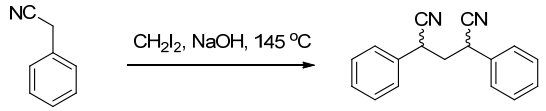
Supporting Information

List of Contents

General Information

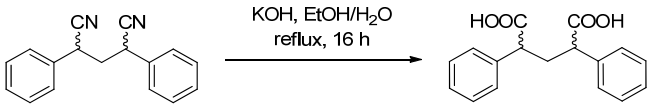
Proton nuclear magnetic resonance were recorded on Bruker-400MHz instruments internally referenced to tetramethylsilane (0.0 ppm) or the residue of $CDCl_3$ (7.26 ppm) signal and DMSO-d_6 (2.50 ppm) signal. HRMS spectra were recorded on P-SIMS-Gly of Bruker Daltonics Inc. Solvents were distilled using standard techniques. Tetrahydrofuran was distilled over sodium under an atmosphere of nitrogen. Toluene was distilled over calcium hydride under an atmosphere of nitrogen. Methanol was dried by magnesium.

Preparation of the diketone (±)-4



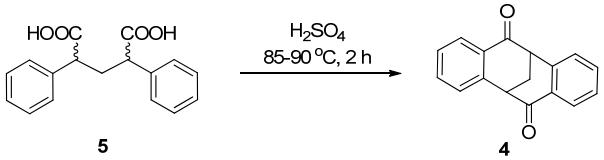
S1

The phenylacetonitrile (46.0 mL, 0.40 mol, 2.0 eq) and diiodomethane (16.1 mL, 0.20 mol, 1.0 eq) were added to the powder NaOH (16.0 g, 0.40 mol, 2.0 eq), and the mixture was stirred at 145 °C for 2 h. After cooling to room temperature, a mixture of water/diethyl ether (1:1, 100 mL) was added and the aqueous phase was extracted with Et_2O (3×100 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtrated and concentrated. Excess phenylacetonitrile was removed by distillation under reduced pressure (4 mmHg), and the resulting crude 2,4-diphenylpentanedinitrile (32.1 g, 65%) was used in next step without purification.



S1 5

A mixture of 2,4-diphenylpentanedinitrile (32.1 g, 0.13 mol) in EtOH (350 mL), 5 N KOH (350 mL) was stirred reflux for 16 h. After cooling to room temperature, ethanol was removed by evaporation, and the resulting mixture was extrated with Et_2O (3×100 mL) and the organic layers were discarded. The aqueous layer was acidified with concentrated hydrochloric acid to pH = 2-3 and extracted with EtOAc (3×200 mL). The combined organic layer was washed with water and brine, dried over Na_2SO_4, filtrated and concented. The resulting crude 2,4-diphenylpentanedioic acid (36.8 g, 99.7 %) was used in next step directly without purification.

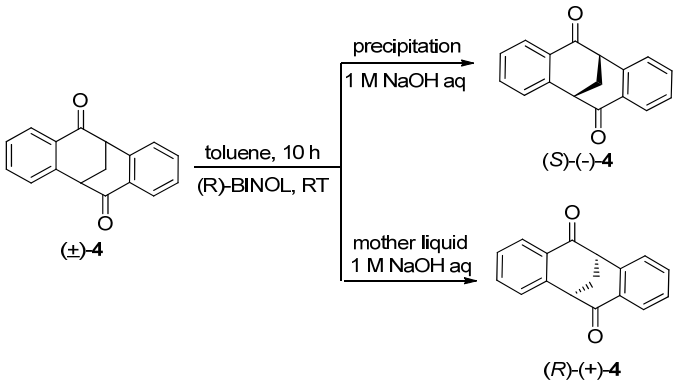


5 4

H_2SO_4 (98%, 49 ml) was added to 2,4-diphenylpentanedioic acid (7.30 g, 25.7 mmol) and the resulting mixture was stirred at 85-90 °C for 2 h. After cooling to room temperature the mixture was poured to a beach containing crashed ice. The yellowish

solid was collected by filtration and the filtrate was extracted with toluene three times. The combined organic layer was washed with brine and dried over Na_2SO_4 and concentrated with evaporation to give a yellowish solid. The combined solid diketone (±)-**4** (4.95 g, 78%) was pure enough for spectra characterization and was used in next step without purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 2 H), 7.54-7.40 (m, 4 H), 7.39-7.28 (m, 2 H), 4.00 (t, *J* = 2.8 Hz, 2 H), 2.97 (t, *J* = 2.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3, 140.0, 134.5, 128.82, 128.79, 128.76, 128.2, 48.8, 32.2; HRMS (ESI) calcd for $C_{17}H_{13}O_2$ [M^++H] 249.0910, found 249.0905.

Resolution of diketone (±)-4 with (R)-BINOL



(*R*)-(+)-1,1'-Bi-2-naphthol (8.50 g, 30.0 mmol, 0.60 eq) was added to a solution of diketone (±)-**4** (12.40 g, 50.0 mmol, 1.0 eq) and toluene (250 mL). The resulting mixture was stirred at room temperature for 10 h, filtrated and solid was washed with cold toluene.

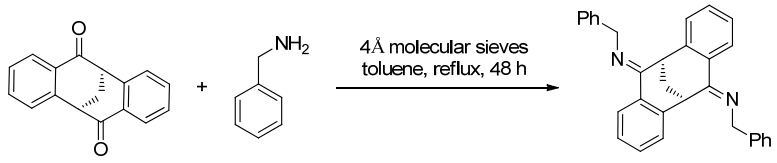
The inclusion complex solid was added to a mixture of toluene (250 mL) and aqueous NaOH solution (1 M, 250 mL) and stirred at room temperature until all solid was dissolved. After separation, the organic layer was washed with 1 N NaOH (2× 250 mL), and the combined aqueous phase was extracted with toluene (2×250 mL). The combined organic layer was washed with water and dried over Na_2SO_4, filtered and concentrated to give white solid (*S*)-(-)-**4** (6.03g, 49%, 94.1% ee). The solid was recrystallized from CH_2Cl_2/EtOAc to give (*S*)-(-)-**4** (5.25 g, 42%, 99.8% ee). $[\alpha]_D^{23}$ −383 (c 0.30, $CHCl_3$). HPLC (Chiralcel OD-H, iospropanol/hexane = 3:97, flow: 1.0 mL/min, λ = 254 nm).

The mother liquid was washed with 1 N NaOH (3×250 mL), the aqueous phase was extracted with toluene (2×250 mL), the combined organic layer was washed with water and dried over Na_2SO_4 , filtered and concentrated to afford (*R*)-(+)-**4** (6.37 g, 51%, 83.9% ee). The obtained solid was recrystallized from CH_2Cl_2/EtOAc to give (*R*)-(+)-**4** (5.43 g, 44%, 99.5% ee). $[\alpha]_D^{23}$ = +383 (c 0.30, $CHCl_3$). HPLC (Chiralcel OD-H, iospropanol/hexane = 3:97, flow: 1.0 mL/min, λ = 254 nm).

The combined aqueous phase was acidified with 1 N HCl to pH~4, and the solid

was collected by filtration, washed with H_2O and dried under air to give (*R*)-(+)-1,1'-Bi-2-naphthol (8.24 g, 97%, 99.1% ee). HPLC (Chiralcel AD-H, isopropanol/hexane = 10:90, flow: 0.5 mL/min, λ = 254 nm).

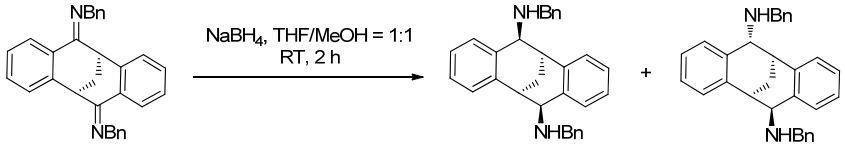
Preparation of the imine (*R*)-6



(*R*)-(+)-**4** (*R*)-**6**

Under nitrogen atmosphere, a mixture of (*R*)-(+)-**4** (1.24 g, 5.00 mmol, 1.0 eq), benzylamine (2.0 mL, 20.0 mmol, 4.0 eq), flame dried molecular sieves (4Å, powdered, 6.00 g) and toluene (15 mL) was stirred at reflux temperature for 48 h. After cooling to room temperature, the mixture was filtered through a pad of celite and the solid cake was washed with toluene. The filtrate was concentrated with evaporation and the resulting solid was recrystallized from EtOAc and CH_2Cl_2 to give the pure (*R*)-**6** (1.77 g, 83%). $[\alpha]_D^{23}$ = +530 (c 0.34, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 7.6 Hz, 2 H), 7.47 (d, *J* = 7.6 Hz, 4 H), 7.39 (t, *J* = 7.6 Hz, 4 H), 7.33-7.15 (m, 8 H), 5.24 (s, 4 H), 4.72 (t, *J* = 3.2 Hz, 2 H), 2.59 (t, *J* = 3.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 140.3, 137.8, 132.9, 130.6, 128.5, 128.2, 127.6, 127.5, 127.2, 126.8, 55.2, 35.2, 31.2; HRMS (ESI) calcd for $C_{31}H_{27}N_2$ [M^++H] 427.2169, found 427.2160.

Preparation of the amine 7a and 7b



(*R*)-**6** **7a** **7b**

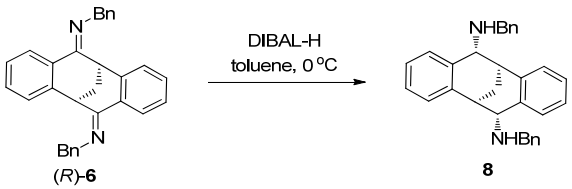
$NaBH_4$ (0.151 g, 4.00 mmol, 8.0 eq) was slowly added to a mixture of (*R*)-**6** (0.213 g, 0.50 mmol, 1.0 eq) in THF (3.0 mL) and MeOH (3.0 mL) at 0 °C and stirred at room temperature for 2 h. The mixture was quenched with 1 N HCl and neutralized with aqueous sat. $NaHCO_3$. The resulting mixture was extracted with EtOAc and the combined organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated with evaporation. The residue was purified by column chromatography on silica (5% ethyl acetate/hexanes) to afford the desired product **7a** (0.181 g, 84%) and **7b** (30 mg, 14%), as well as a small amount of uncharacterized mixtures.

7a, $[\alpha]_D^{23}$ = +20 (c 0.52, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.2 Hz, 2 H), 7.56 (d, *J* = 7.6 Hz, 4 H), 7.37 (t, *J* = 7.6 Hz, 4 H), 7.27 (t, *J* = 7.6 Hz, 2 H), 7.20-7.05 (m, 6 H), 4.38 (d, *J* = 13.6 Hz, 2 H), 4.17-4.06 (m, 4 H), 3.55-3.48 (m, 2 H),

2.42 (t, J = 3.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 139.8, 135.6, 128.9, 128.4, 128.2, 128.1, 127.0, 126.9, 126.3, 61.6, 51.1, 34.0, 30.6; HRMS (ESI) calcd for $C_{31}H_{31}N_2$ [M^++H] 431.2482, found 431.2473.

7b, $[\alpha]_D^{23}$ = +12 (c 0.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (t, J = 4.4 Hz, 1 H), 7.56 (d, J = 7.2 Hz, 2 H), 7.50 (d, J = 7.2 Hz, 2 H), 7.38 (q, J = 7.6 Hz, 4 H), 7.33-7.24 (m, 2 H), 7.16-7.05 (m, 6 H), 7.00 (s, 1 H), 4.38 (d, J = 13.6 Hz, 1 H), 4.20-4.07 (m, 3 H), 4.05 (d, J = 13.6 Hz, 1 H), 3.68 (s, 1 H), 3.55 (t, J = 4.4 Hz, 1 H), 3.32 (s, 1 H), 2.71 (dd, J = 2.8 Hz, 12.0 Hz, 1 H), 2.06 (dd, J = 3.6 Hz, 12.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 140.5, 139.1, 139.0, 138.1, 136.0, 130.7, 129.4, 128.6, 128.41, 128.39, 128.3, 128.1, 127.7, 127.2, 126.95, 126.93, 126.8, 126.6, 126.5, 63.6, 60.6, 52.5, 51.1, 36.4, 33.5, 24.3; HRMS (ESI) calcd for $C_{31}H_{31}N_2$ [M^++H] 431.2482, found 431.2482.

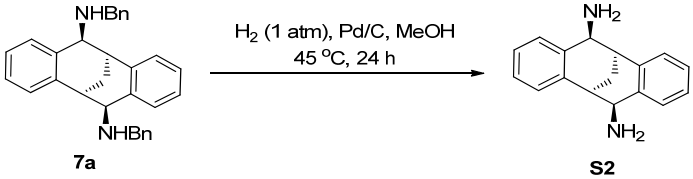
Preparation of the amine 8



(*R*)-**6** **8**

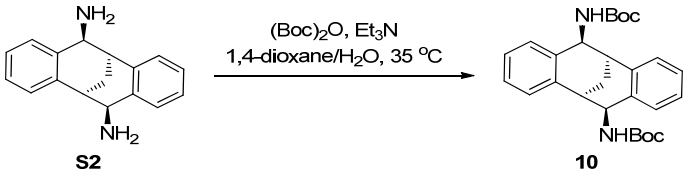
Under nitrogen atmosphere, the DIBAL-H (1.0 mol/L, 2.5 mL, 2.50 mmol, 5.0 eq) was slowly added to a mixture of (*R*)-**6** (0.213 g, 0.50 mmol, 1.0 eq) in toluene (5.0 mL) at 0 °C and stirred for 2 h. Saturated potassium sodium tartrate solution was slowly added to the mixture to quench this reaction, after stirred for another 30 min at rt. The solid was filtered off and washed with EtOAc. The mixture was extracted with EtOAc, and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product **8** (0.214 g, 99.5%) was pure enough for spectra characterization and was used in next step without purification. $[\alpha]_D^{23}$ = −24 (c 0.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.2 Hz, 4 H), 7.45-7.35 (m, 4 H), 7.30 (t, J = 7.2 Hz, 2 H), 7.16-7.09 (m, 2 H), 7.09-7.02 (m, 4 H), 7.02-6.96 (m, 2 H), 4.20 (d, J = 13.2 Hz, 2 H), 4.08 (d, J = 13.2 Hz, 2 H), 3.62 (d, J = 2.0 Hz, 2 H), 3.37-3.25 (m, 2 H), 2.39 (t, J = 2.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 139.7, 137.3, 130.2, 128.9, 128.5, 128.4, 127.2, 127.1, 126.6, 62.7, 52.4, 36.2, 18.4; HRMS (ESI) calcd for $C_{31}H_{31}N_2$ [M^++H] 431.2482, found 431.2474.

Preparation of the amine 10



7a **S2**

The reaction was conducted by following the known procedure with slight modification:[1] A 10 ml flask containing a mixture of 10% Pd/C (0.130 g), **7a** (0.213 g, 0.50 mmol) in MeOH (4 mL) was purged with H_2 and stirred at 45 ^oC for 24 h with a hydrogen balloon. After cooling to room temperature, the mixture was filtered through a pad of celite, washed with EtOAc and concentrated to afford the desired diamine **S2** (0.121 g, 97%) which was used in next step without further purification.



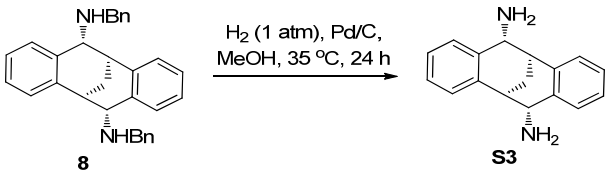
S2 **10**

A mixture of diamine **S2** (0.121 g, 0.48 mmol, 1.0 eq), di-tert-butyl dicarbonate ester (0.3 mL, 1.45 mmol, 3.0 eq), triethylamine (0.20 mL, 1.45 mmol, 3.0 eq) in 1,4-dioxane/H_2O (2:1, 7.5 mL) was stirred at 35 ^oC for 12 h. After cooling to room temperature, the 1,4-dioxane was removed by evaporation. The residue was extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography on silica (5% ethyl acetate/hexanes) to afford the desired product **10** (0.202 g, 93%). **A pair of stereomers (~7:1) was observed by ^{1}H NMR at room temperature presumable due to the partially inhibited rotation of the amide functionality. The high temperature (70 ^{o}C, DMSO-*d*$_6$) ^{1}H NMR clearly showed a single isomer.**

$[\alpha]_D^{23}$ = +65 (c 0.52, $CHCl_3$).

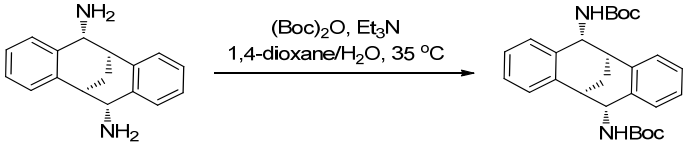
^{1}H NMR (400 MHz, ***CDCl*$_3$**): δ 7.35-7.26 (m, 2 H), 7.24-7.15 (m, 4 H), 7.14-7.01 (m, 2 H), 5.24 (dd, *J* = 5.6 Hz, 10.0 Hz, 2 H), 4.50 (d, *J* = 10.0 Hz, 2 H), 3.45-3.28 (m, 2 H), 2.44 (t, *J* = 3.2 Hz, 2 H), 1.55 (s, 18 H); ^{1}H NMR (400 MHz, ***70 ^{o}C, DMSO-d*$_6$**): δ 7.25-7.13 (m, 6 H), 7.05-6.97 (m, 2 H), 5.62 (s, 2 H), 5.08 (dd, *J* = 5.2 Hz, *J* = 8.8 Hz, 2 H), 3.36-3.25 (m, 2 H), 2.36 (t, *J* = 3.2 Hz, 2 H), 1.51 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.0, 136.7, 135.7, 130.6, 127.4, 127.2, 126.7, 79.7, 54.5, 36.7, 29.5, 28.6; HRMS (ESI) calcd for $C_{27}H_{35}O_4N_2$ [M^++H] 451.2591, found 451.2587.

Preparation of the amine 11



8 **S3**

A 10 ml flask containing a mixture of 10% Pd/C (0.130 g), **8** (0.215 g, 0.50 mmol) in MeOH (4 mL) was purged with H_2 and stirred at 45 ^oC for 24 h with a hydrogen balloon. After cooling to room temperature, the mixture was filtered through a pad of celite, washed with EtOAc and concentrated to afford the desired diamine **S3** (0.120 g, 96%) which was used in next step without further purification.



S3 11

A mixture of diamine **S3** (0.120 g, 0.48 mmol, 1.0 eq), di-tert-butyl dicarbonate ester (0.30 mL, 1.45 mmol, 3.0 eq), triethylamine (0.20 mL, 1.45 mmol, 3.0 eq) in 1,4-dioxane/H_2O (2:1, 7.5 mL) was stirred at 35 ^oC for 12 h. After cooling to room temperature, the 1,4-dioxane was removed by evaporation. The residue was extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography on silica (5% ethyl acetate/hexanes) to afford the product **11** (0.178 g, 83%). **A pair of isomers due to partially inhibited rotations were observed.**

$[\alpha]_D^{23}$ = +55 (c 0.32, $CHCl_3$).

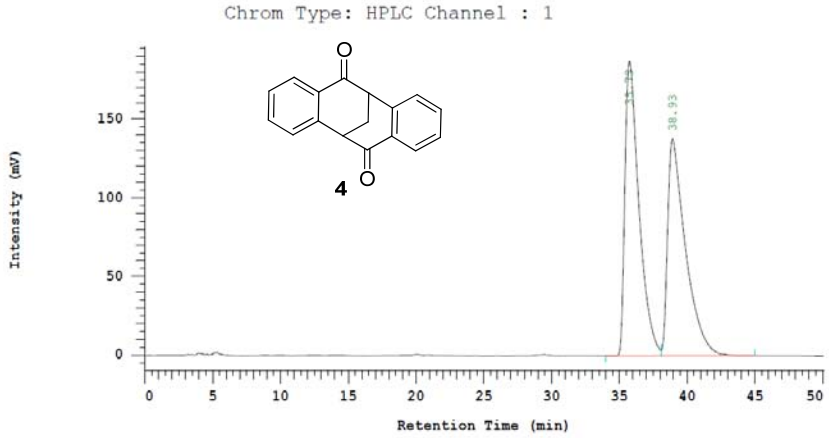
^{1}H NMR (400 MHz, ***CDCl$_3$***): δ 7.81 (d, *J* = 7.6 Hz 2 H), 7.58-7.50 (m, 2 H), 7.47 (d, *J* = 4.0 Hz, 4 H), 5.34 (d, *J* = 6.4 Hz, 2 H), 4.98 (d, *J* = 6.4 Hz, 2 H), 3.73 (s, 2 H), 2.46 (s, 2 H), 1.85 (s, 18 H); ^{1}H NMR (400 MHz, ***70 ^{o}C, DMSO-d$_6$***): δ 7.28 (dd, J = 0.7 Hz, J = 7.6 Hz, 2 H), 7.20 (td, J = 1.6 Hz, J = 7.6 Hz, 3 H), 7.11 (td, J = 1.6 Hz, J = 7.6 Hz, 3 H), 7.06 (dd, J = 1.2 Hz, J = 7.6 Hz, 2 H), 4.51 (d, J = 8.0 Hz, 2 H), 3.10 (s, 2 H), 2.22 (t, J = 2.8 Hz, 2 H), 1.49 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 139.1, 133.7, 130.5, 129.8, 128.1, 127.4, 79.6, 55.4, 38.1, 28.5, 19.3. HRMS (ESI) calcd for $C_{27}H_{35}O_4N_2$ [M^++H] 451.2591, found 451.2583.

References

[1] Thunberg, L.; Allenmark, S. ***Chirality***. **2004**, *16*, 614–624.

HPLC (Chiralcel OD-H, 3% 2-propanol in hexane, flow: 1.0 mL/min).

The diketone (±)-4



Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

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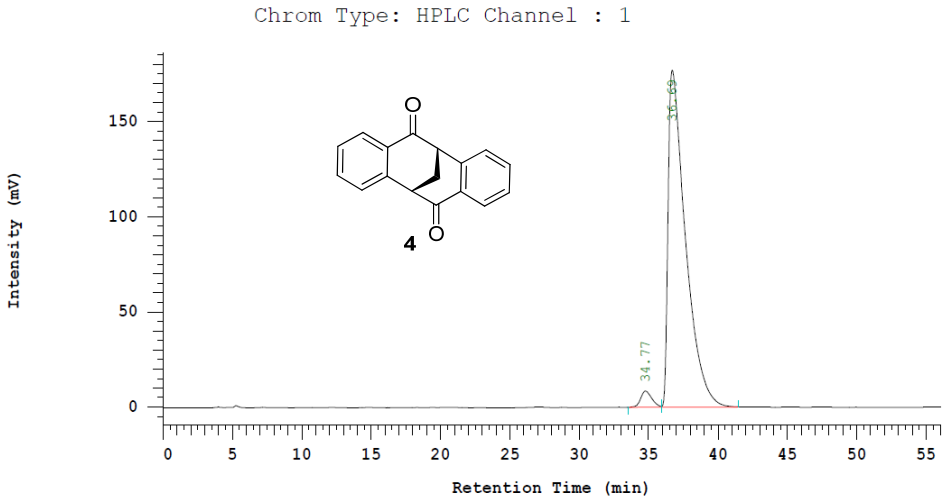
1	35.73	13554800	51.784	BV
2	38.93	12620939	48.216	VB
		26175739	100.000	

The diketone (-)-4 (94.1% ee)



Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

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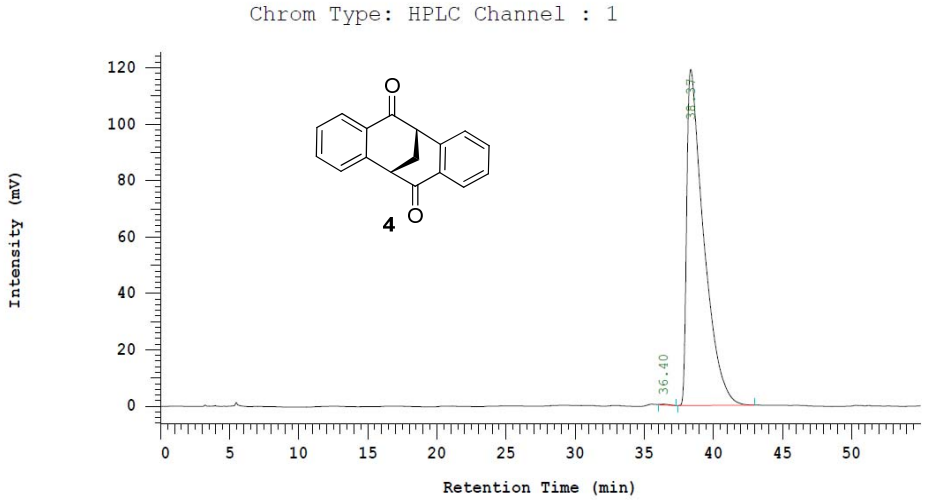
		15894984	100.000	

The diketone (-)-4 (99.8% ee)



Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

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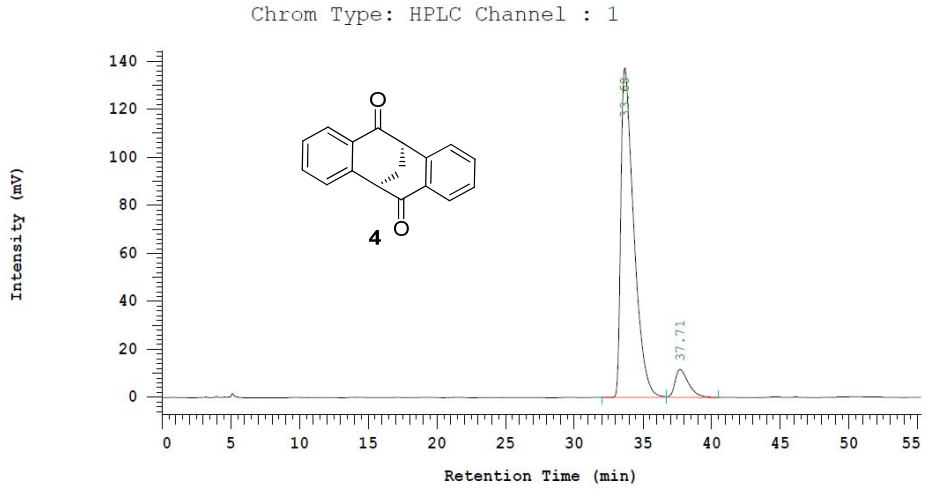
		10203002	100.000	

The diketone (+)-4 (83.9% ee)



Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

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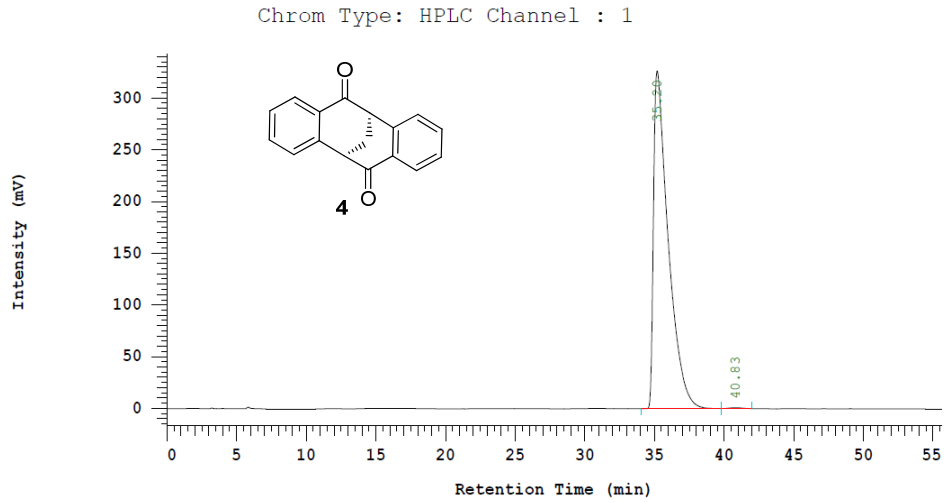
The diketone (+)-4 (99.5% ee)



Chrom Type: HPLC Channel : 1
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Calculation Method: AREA%

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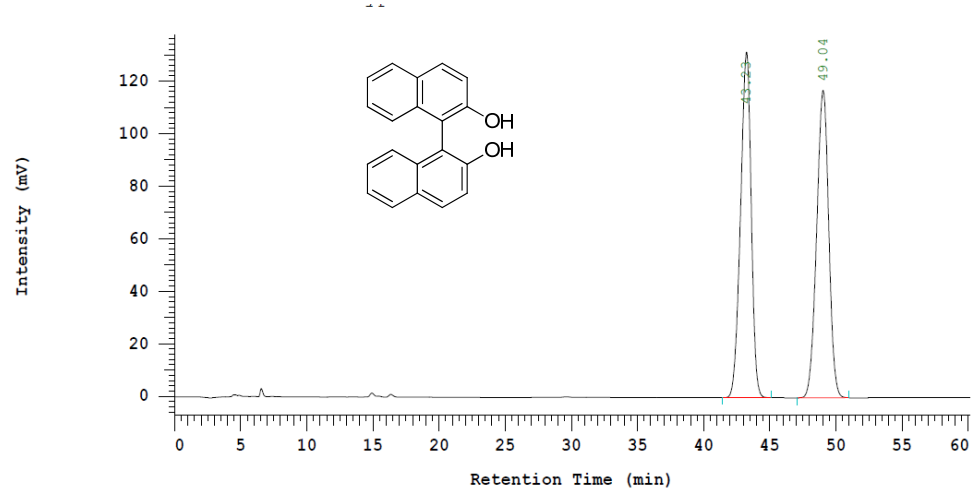
HPLC (Chiralcel AD-H, 10% 2-propanol in hexane, flow: 0.5 mL/min).

(±)-BINOL.



Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

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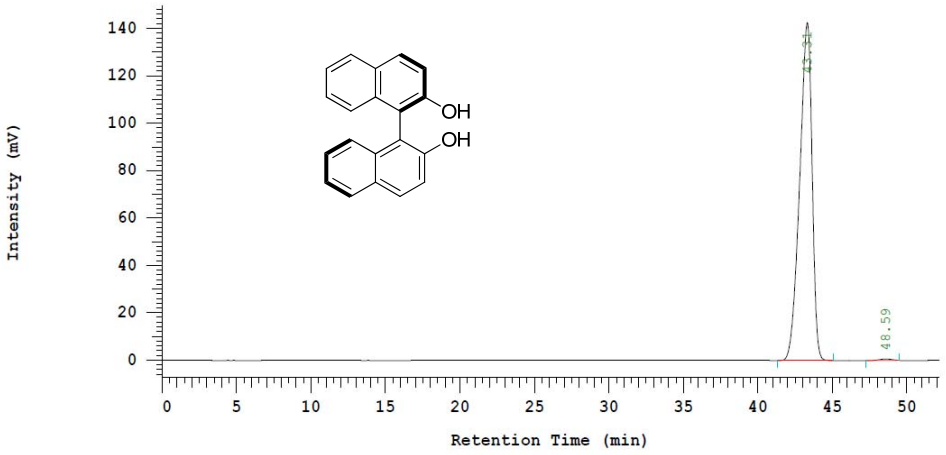
		14842819	100.000	

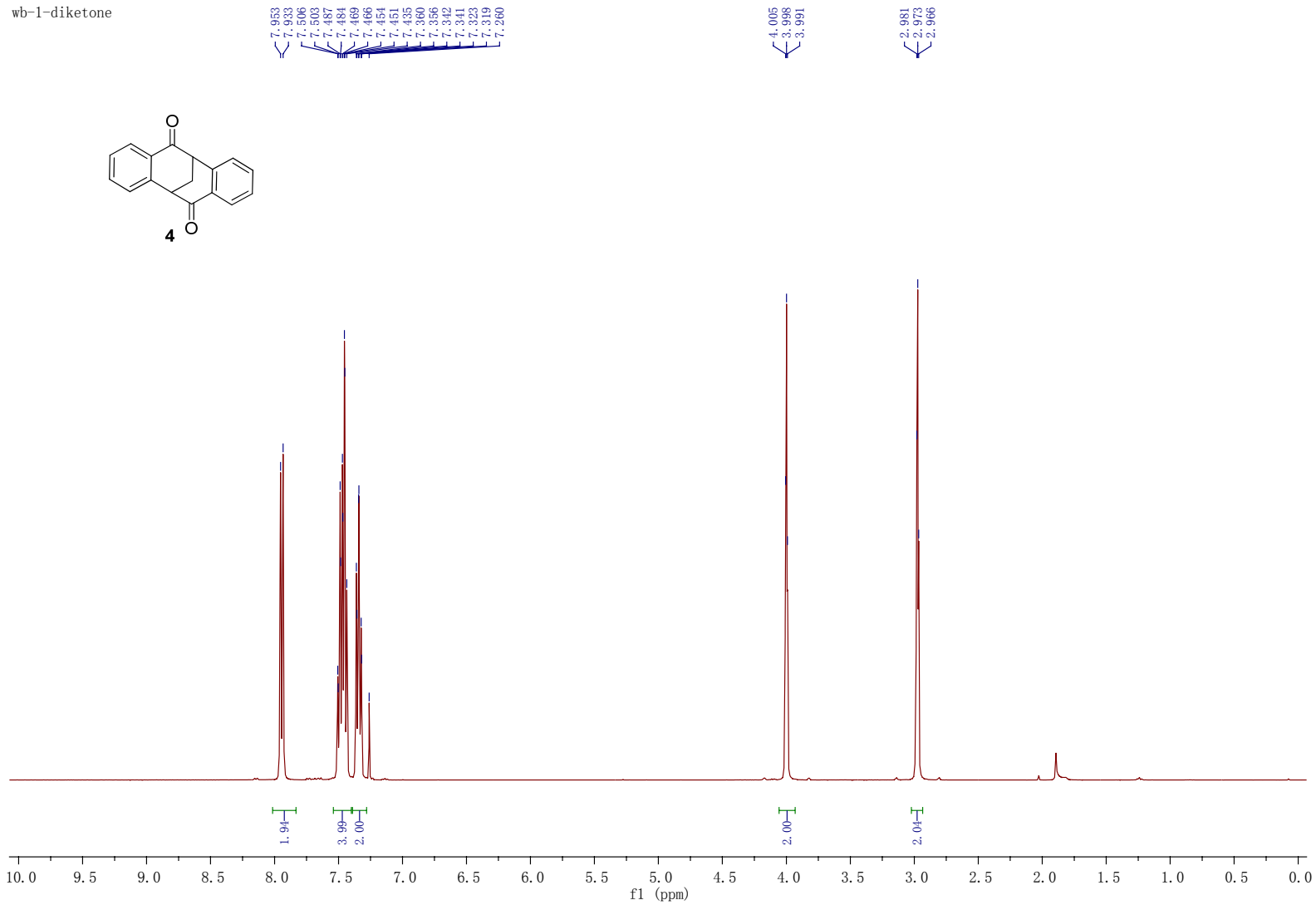
(R)-BINOL (99.1% ee).

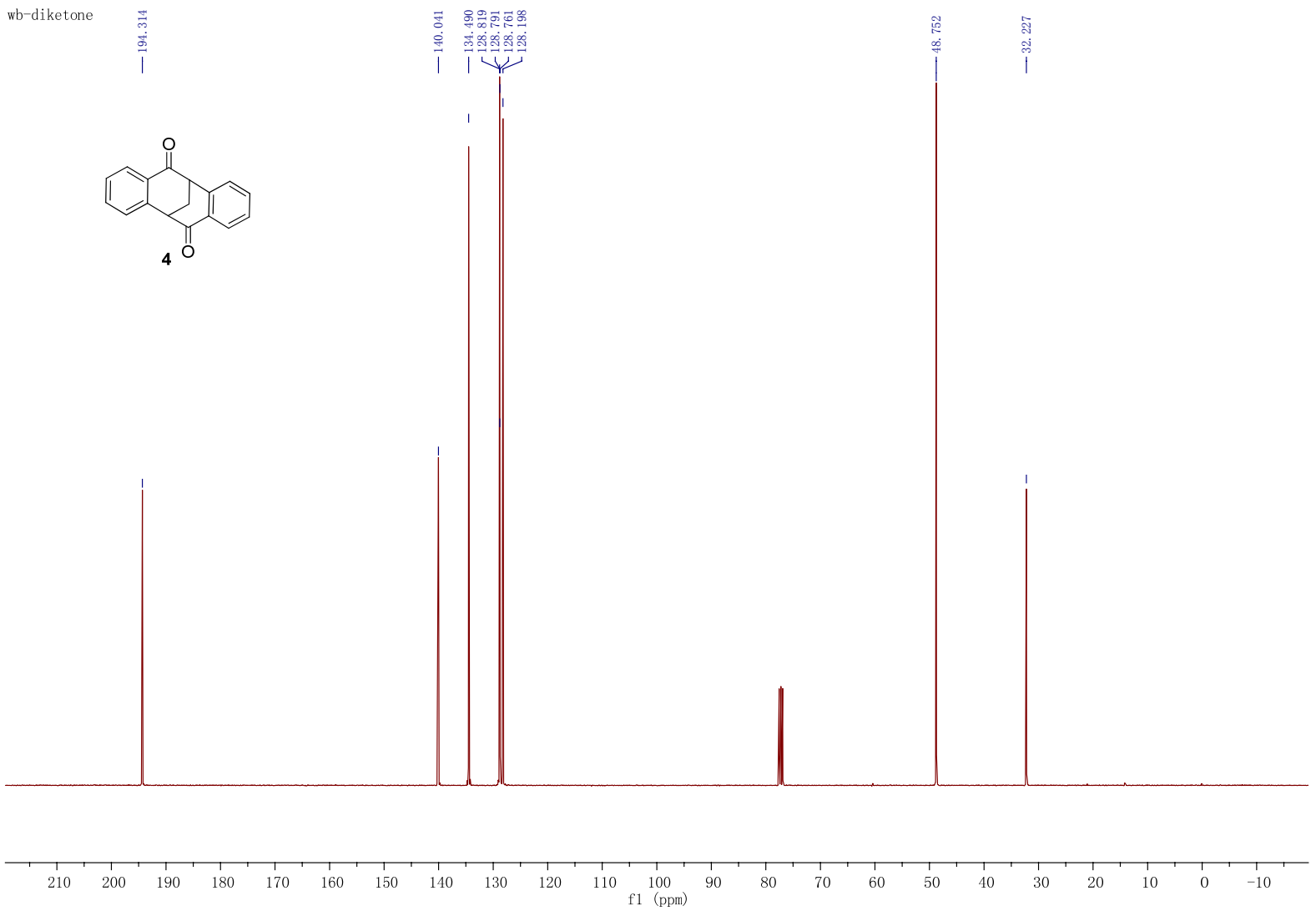


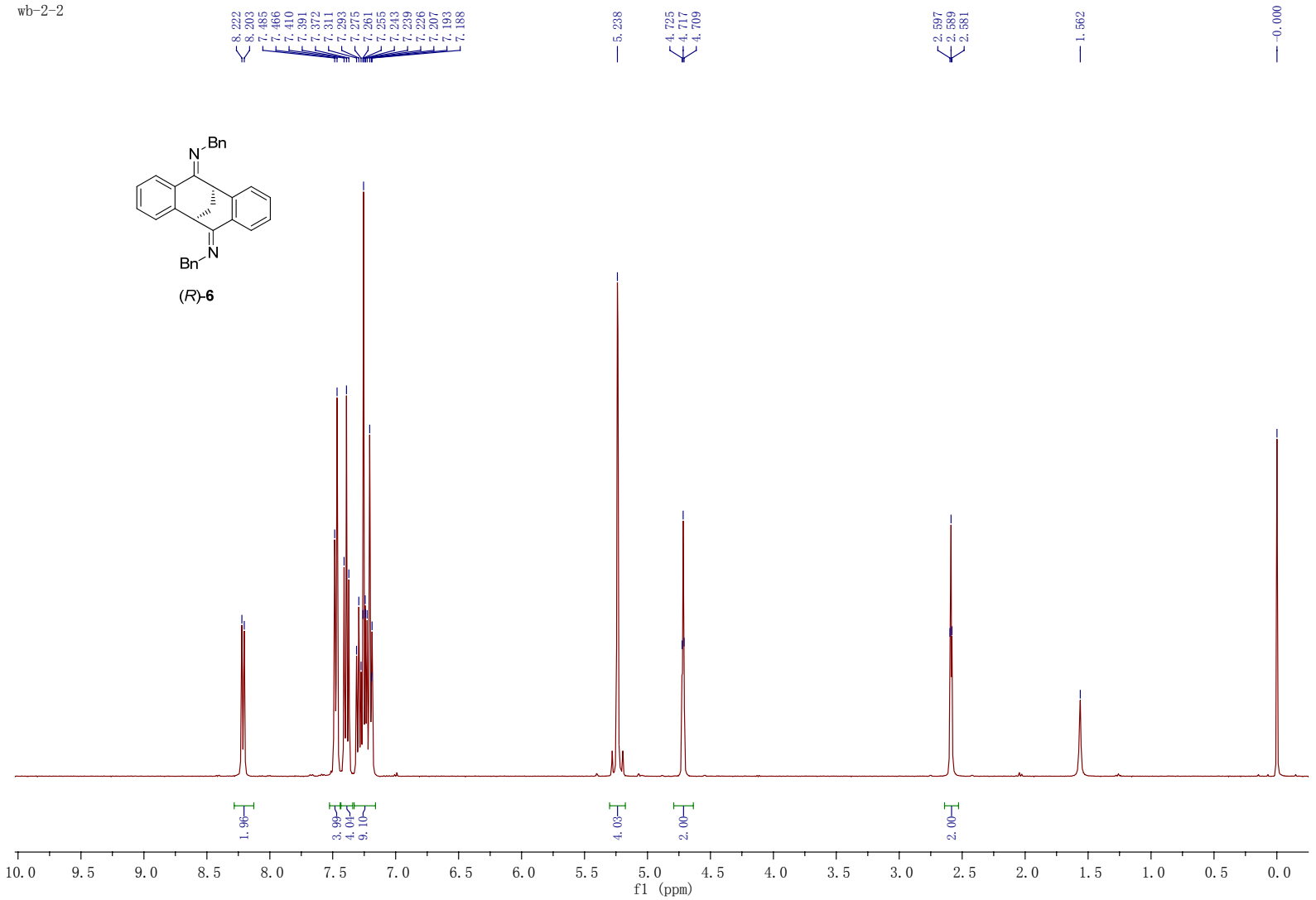
Chrom Type: HPLC Channel : 1
Peak Quantitation: AREA
Calculation Method: AREA%

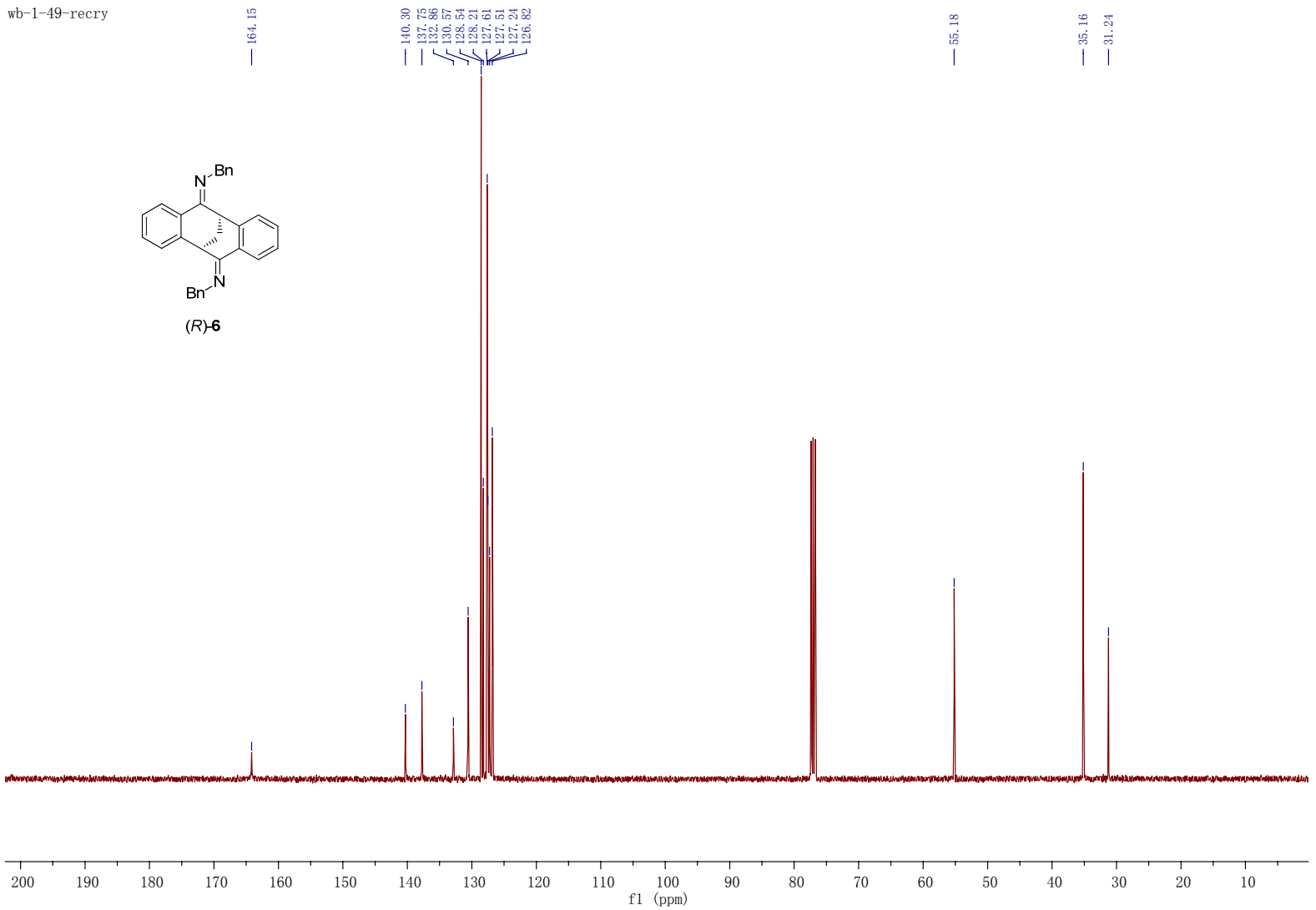
No.	RT	Area	Conc 1	BC
1	43.31	8286368	99.577	BB
2	48.59	35160	0.423	BB
		8321528	100.000	

wb-1-diketone

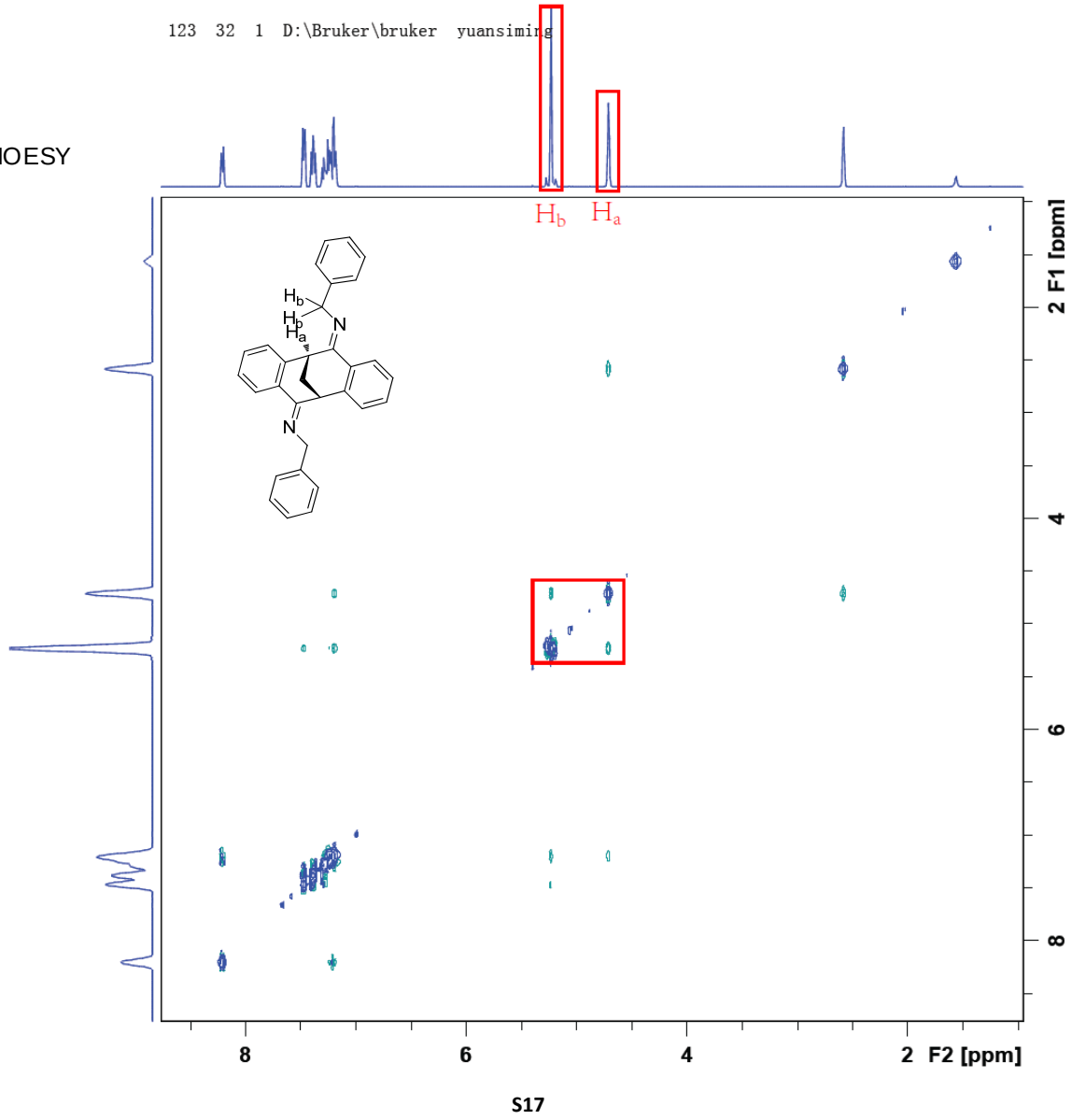


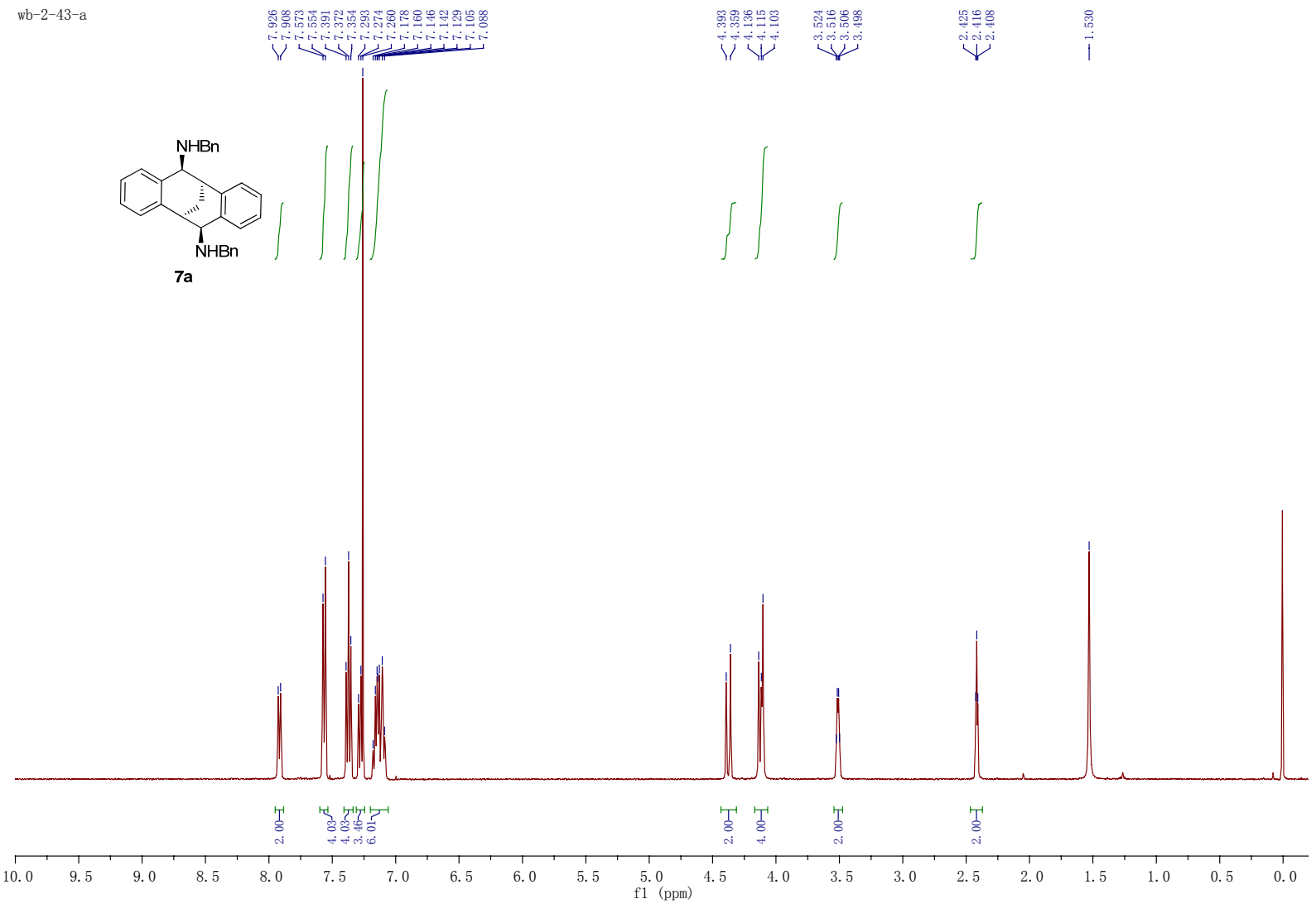

wb-diketone
194.314
140.041
134.490
128.819
128.791
128.761
128.198
48.752
32.227
O
O
4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

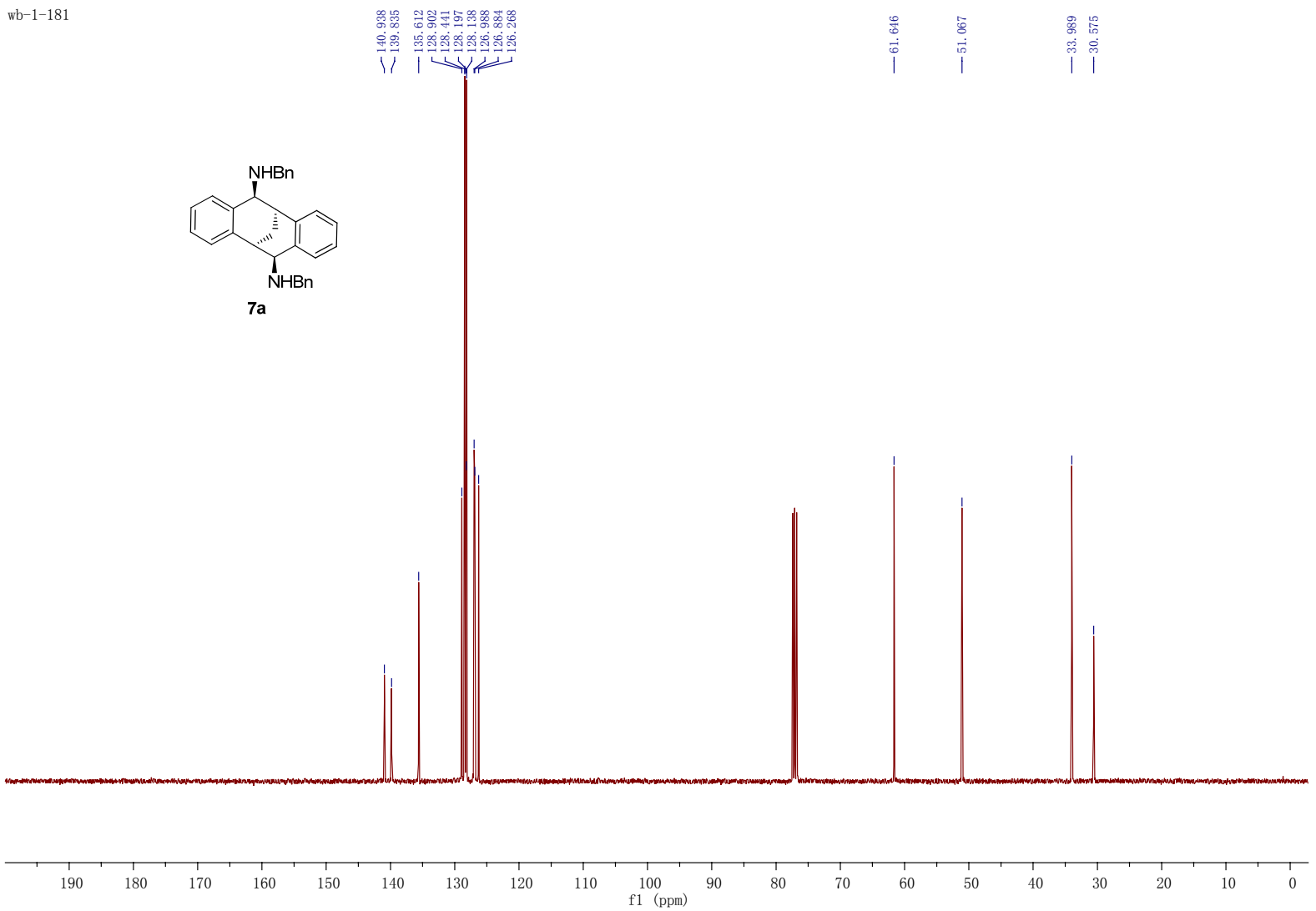

wb-2-2
8.222
8.203
7.485
7.466
7.410
7.391
7.372
7.311
7.293
7.275
7.261
7.255
7.243
7.239
7.226
7.207
7.193
7.188
5.238
4.725
4.717
4.709
2.597
2.589
2.581
1.562
-0.000
N
Bn
Bn
N
(R)-6
1.96
3.99
4.04
9.10
4.03
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

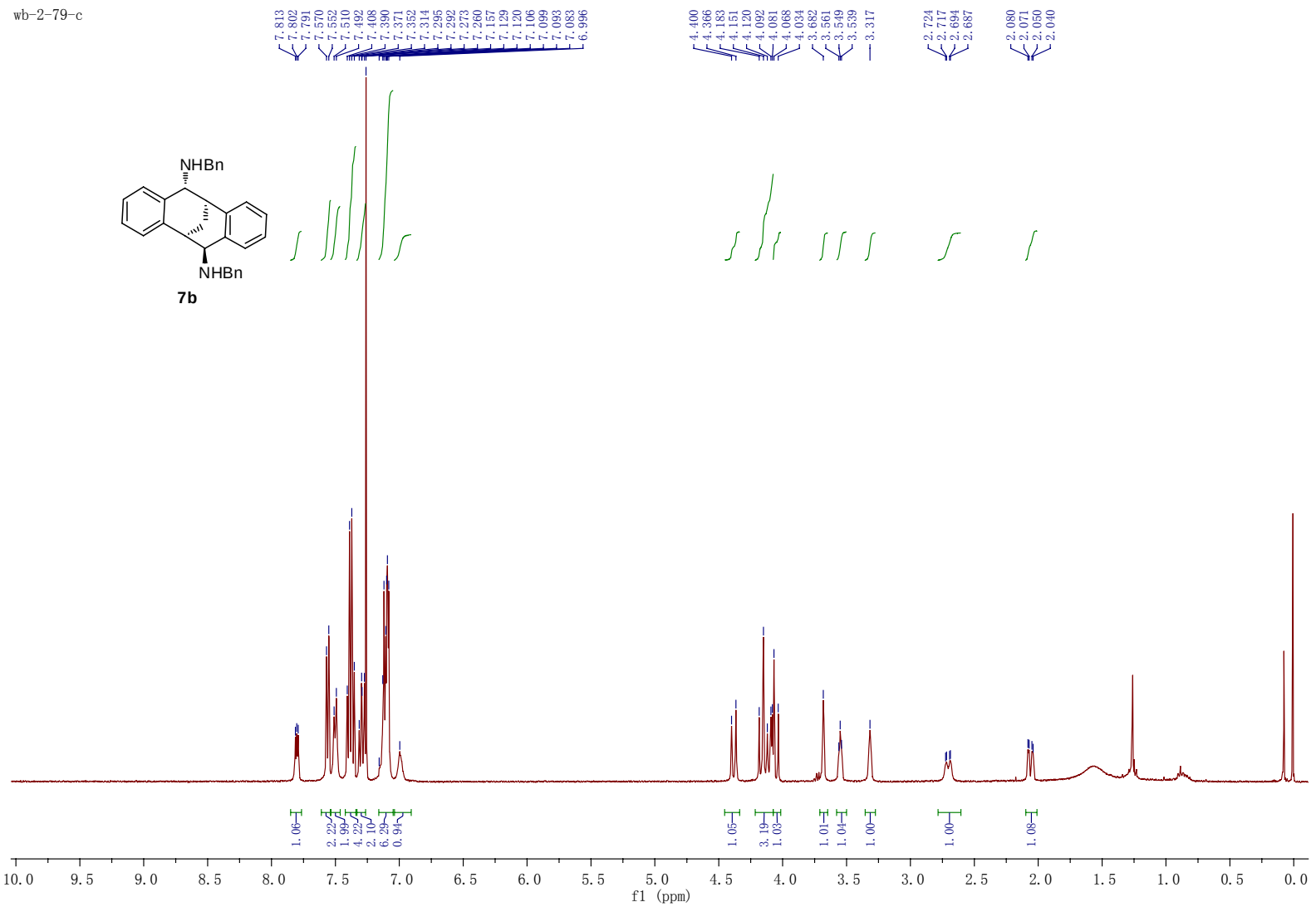

wb-1-49-recry
164.15
140.30
137.75
132.86
130.57
128.54
128.21
127.61
127.51
127.24
126.82
55.18
35.16
31.24
Bn
N
N
Bn
(R)-6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

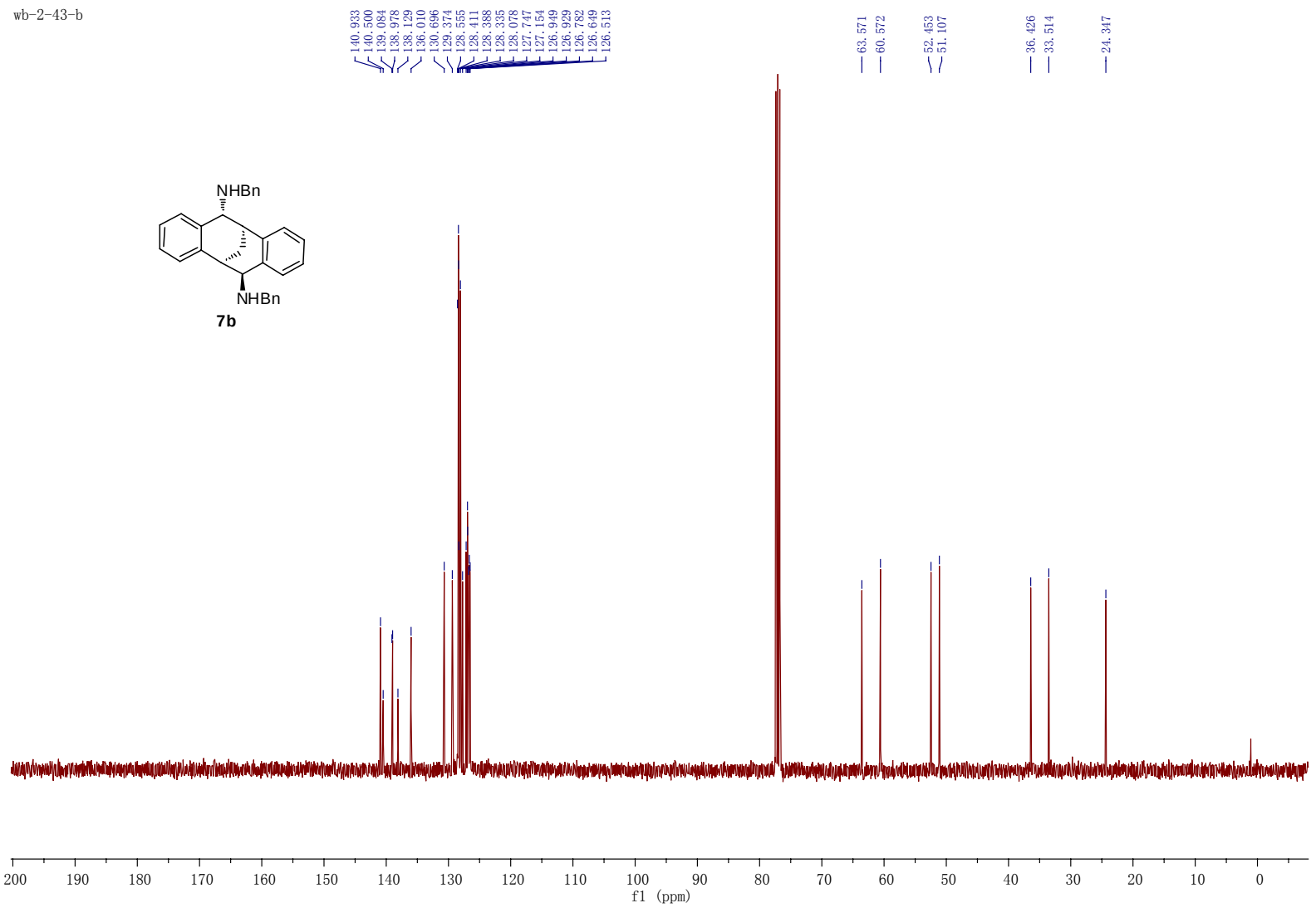
5-NOESY


123 32 1 D:\Bruker\bruker yuansiming
Hb
Ha
Hb
Hb
Ha
N
N
2 F1 [ppm]
4
6
8
8
6
4
2 F2 [ppm]

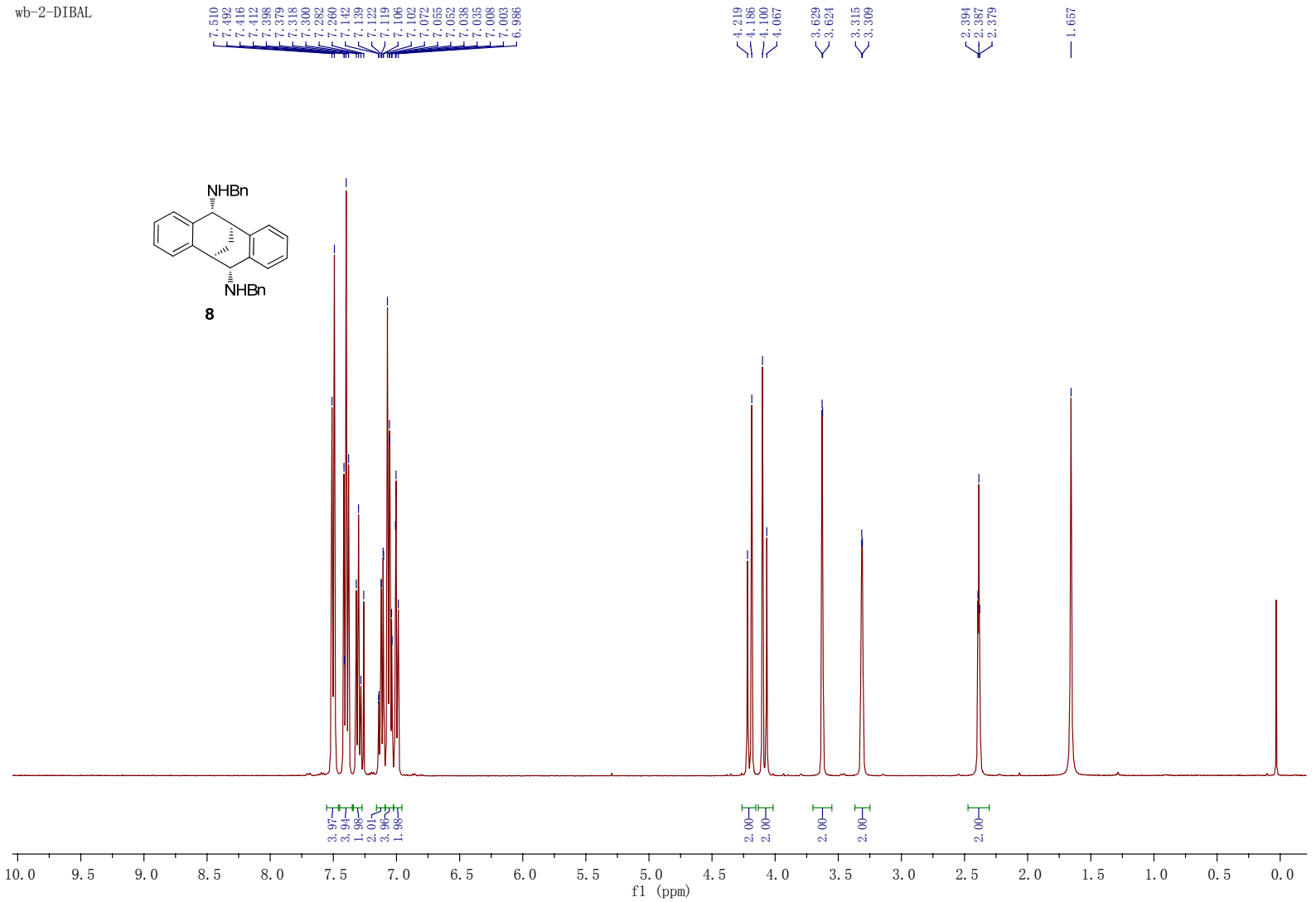

wb-2-43-a
7.926
7.908
7.573
7.554
7.391
7.372
7.354
7.293
7.274
7.260
7.178
7.160
7.146
7.142
7.129
7.105
7.088
4.393
4.359
4.136
4.115
4.103
3.524
3.516
3.506
3.498
2.425
2.416
2.408
1.530
NHBn
NHBn
7a
2.00
4.03
4.03
3.46
6.01
2.00
4.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

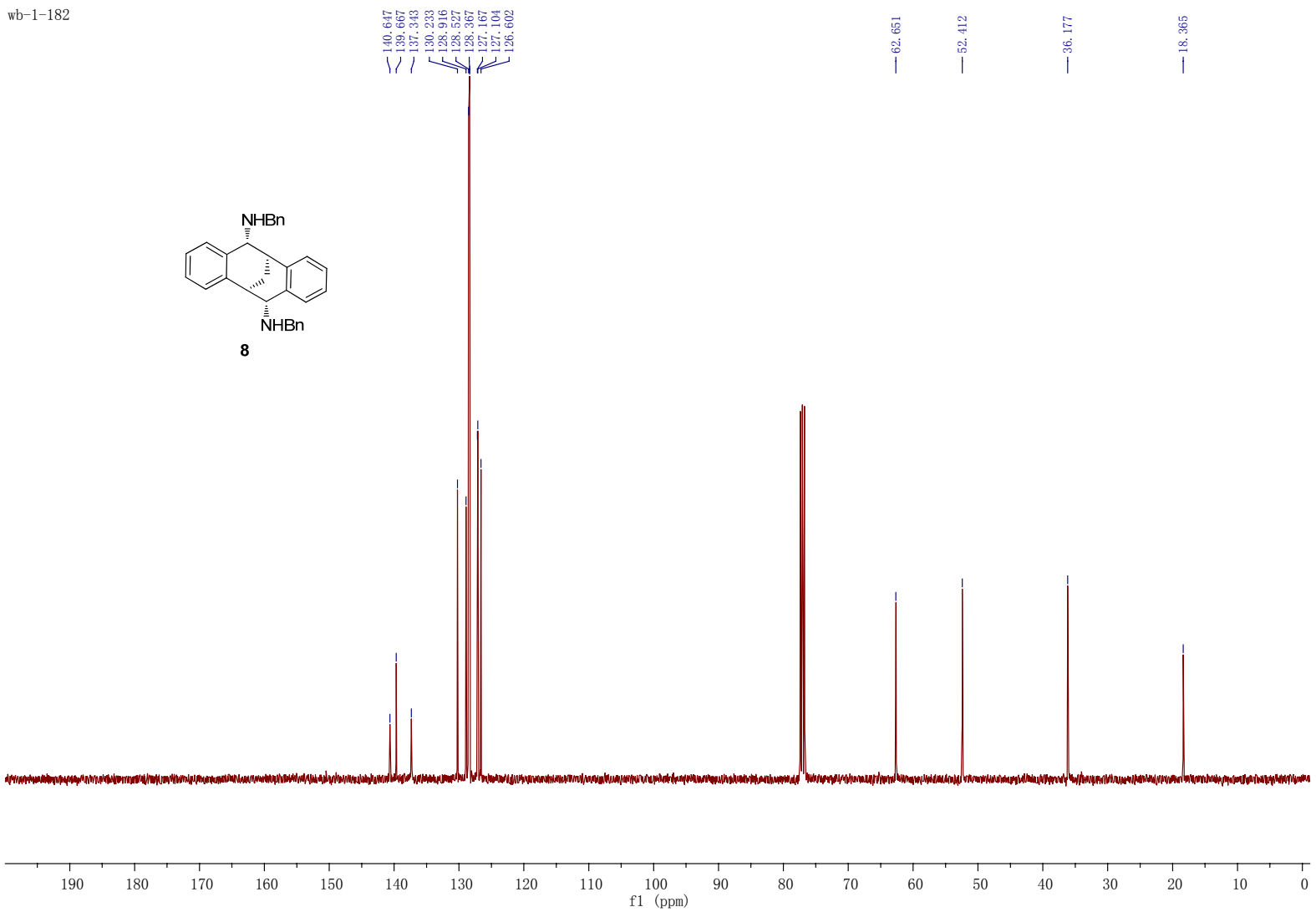

wb-1-181
140.938
139.835
135.612
128.902
128.441
128.197
128.138
126.988
126.884
126.268
61.646
51.067
33.989
30.575
NHBn
NHBn
7a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

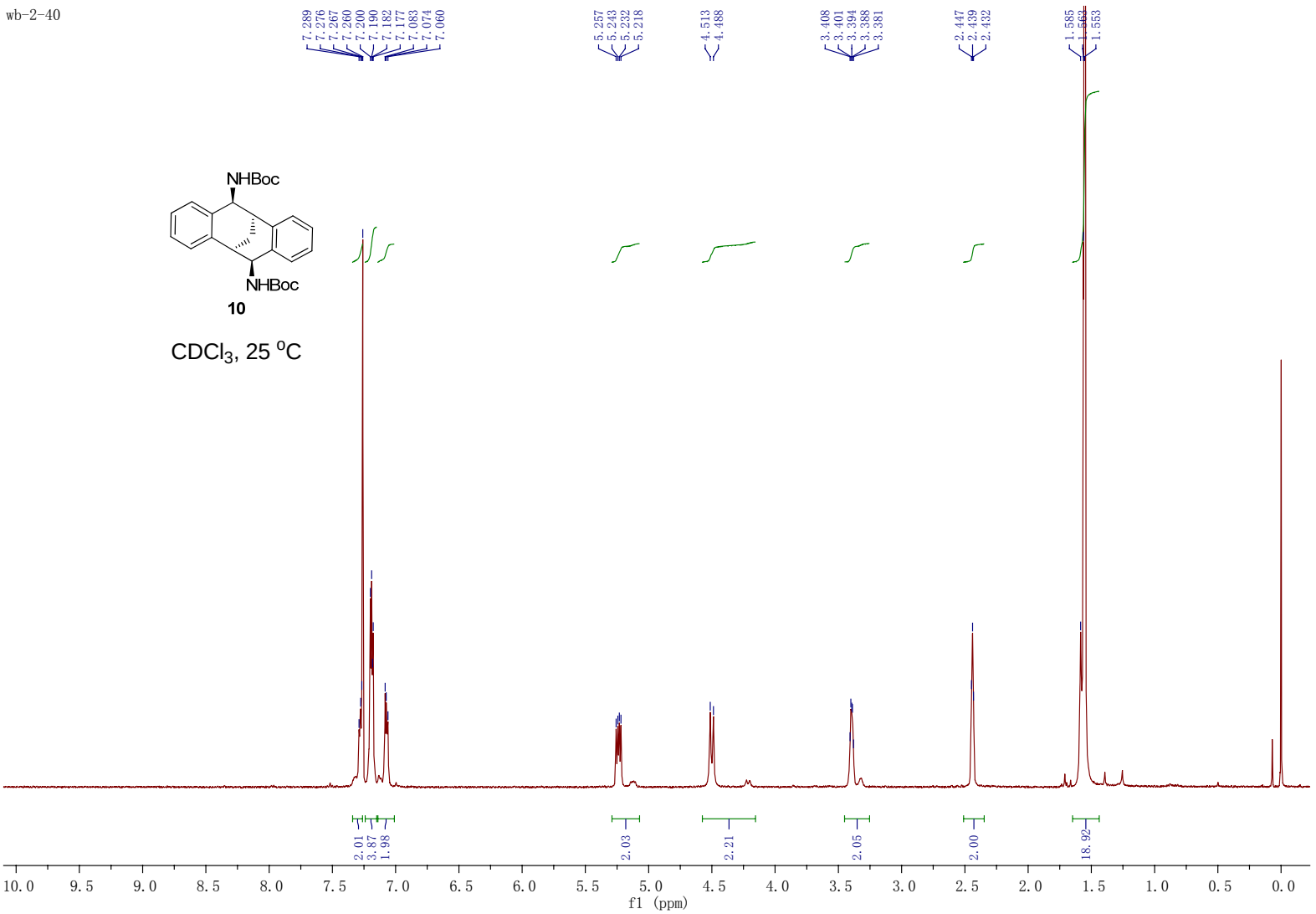

wb-2-79-c
7.813
7.802
7.791
7.570
7.552
7.510
7.492
7.408
7.390
7.371
7.352
7.314
7.295
7.292
7.273
7.260
7.157
7.129
7.120
7.106
7.099
7.093
7.083
6.996
4.400
4.366
4.183
4.151
4.120
4.092
4.081
4.068
4.034
3.682
3.561
3.549
3.539
3.317
2.724
2.717
2.694
2.687
2.080
2.071
2.050
2.040
NHBn
NHBn
7b
1.06
2.22
1.99
4.22
2.10
6.29
0.94
1.05
3.19
1.03
1.01
1.04
1.00
1.00
1.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

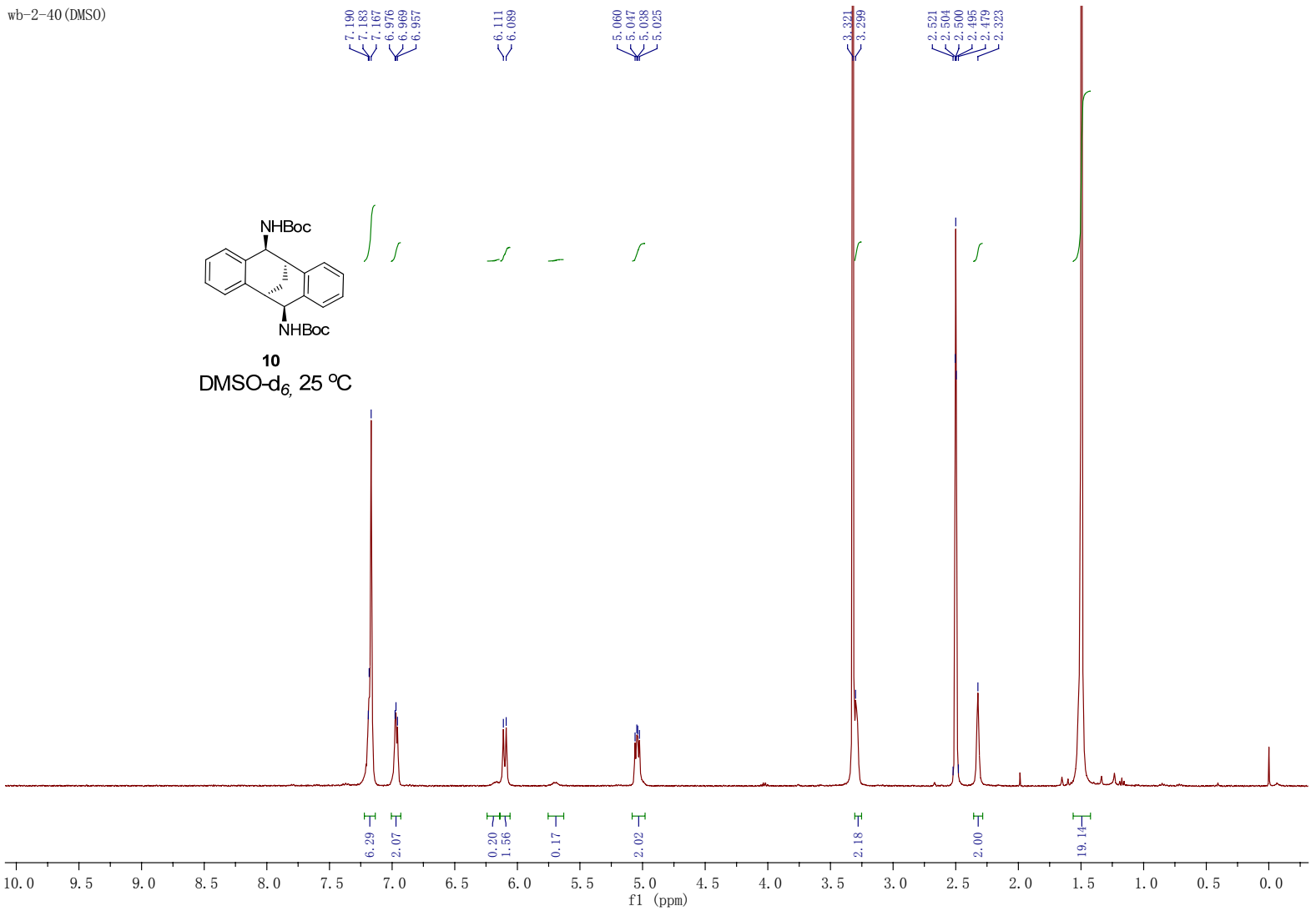

wb-2-43-b
140.933
140.500
139.084
138.978
138.129
136.010
130.696
129.374
128.555
128.411
128.388
128.335
128.078
127.747
127.154
126.949
126.929
126.782
126.649
126.513
63.571
60.572
52.453
51.107
36.426
33.514
24.347
NHBn
NHBn
7b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

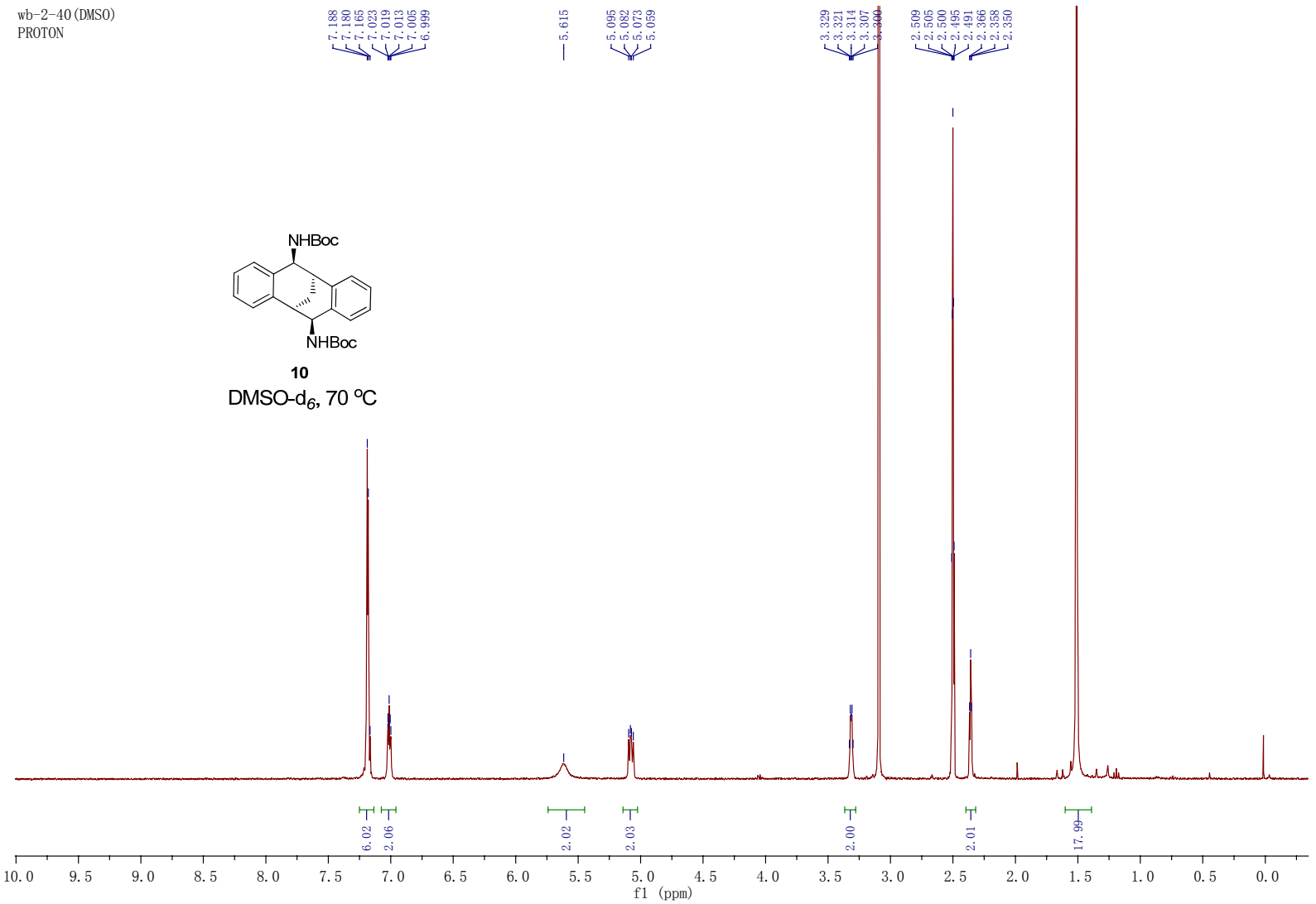
wb-2-DIBAL

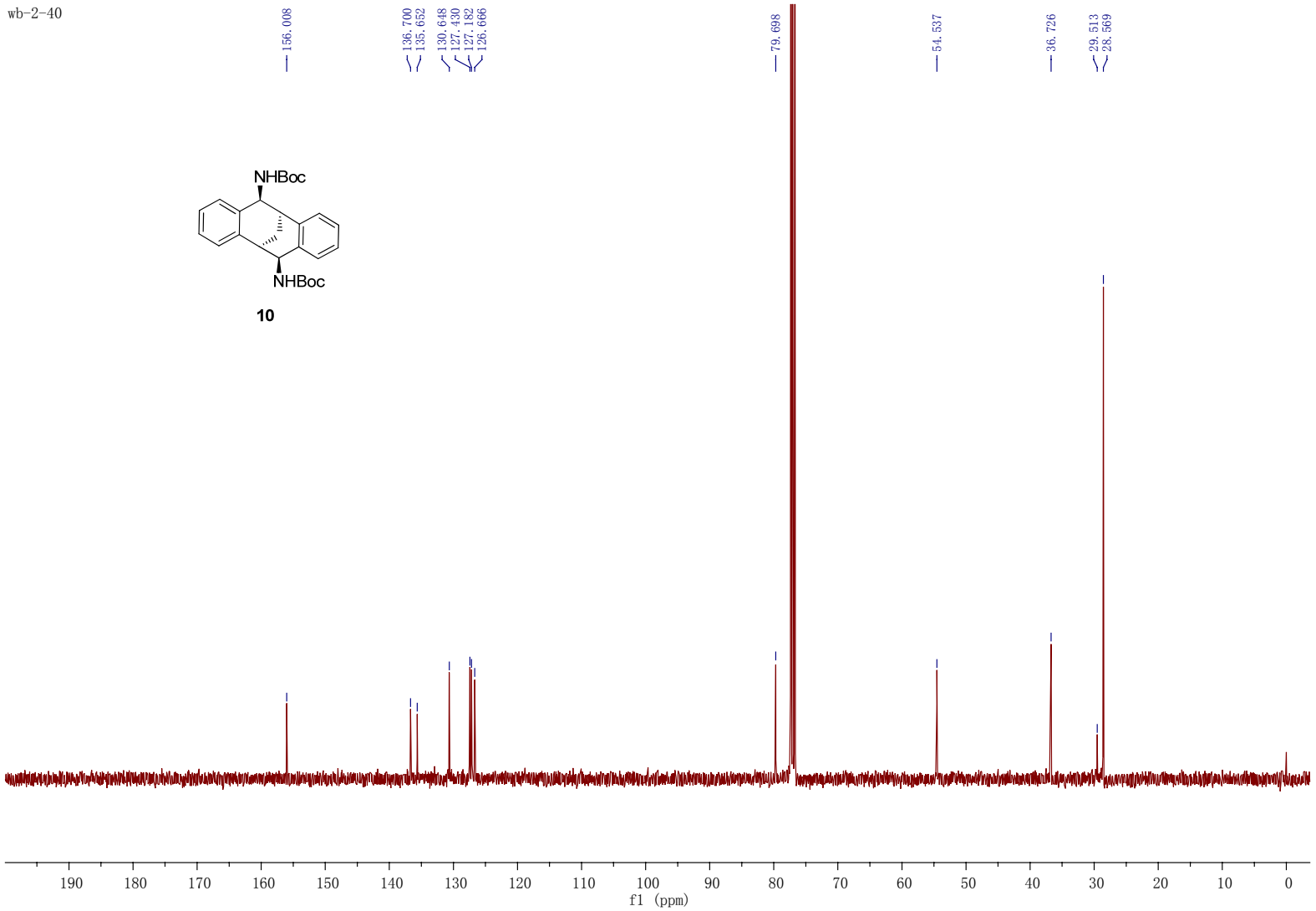

7.510
7.492
7.416
7.412
7.398
7.379
7.318
7.300
7.282
7.260
7.142
7.139
7.122
7.119
7.106
7.102
7.072
7.055
7.052
7.038
7.035
7.008
7.003
6.986
4.219
4.186
4.100
4.067
3.629
3.624
3.315
3.309
2.394
2.387
2.379
1.657
NHBn
NHBn
8
3.97
3.94
1.98
2.01
3.96
1.98
2.00
2.00
2.00
2.00
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

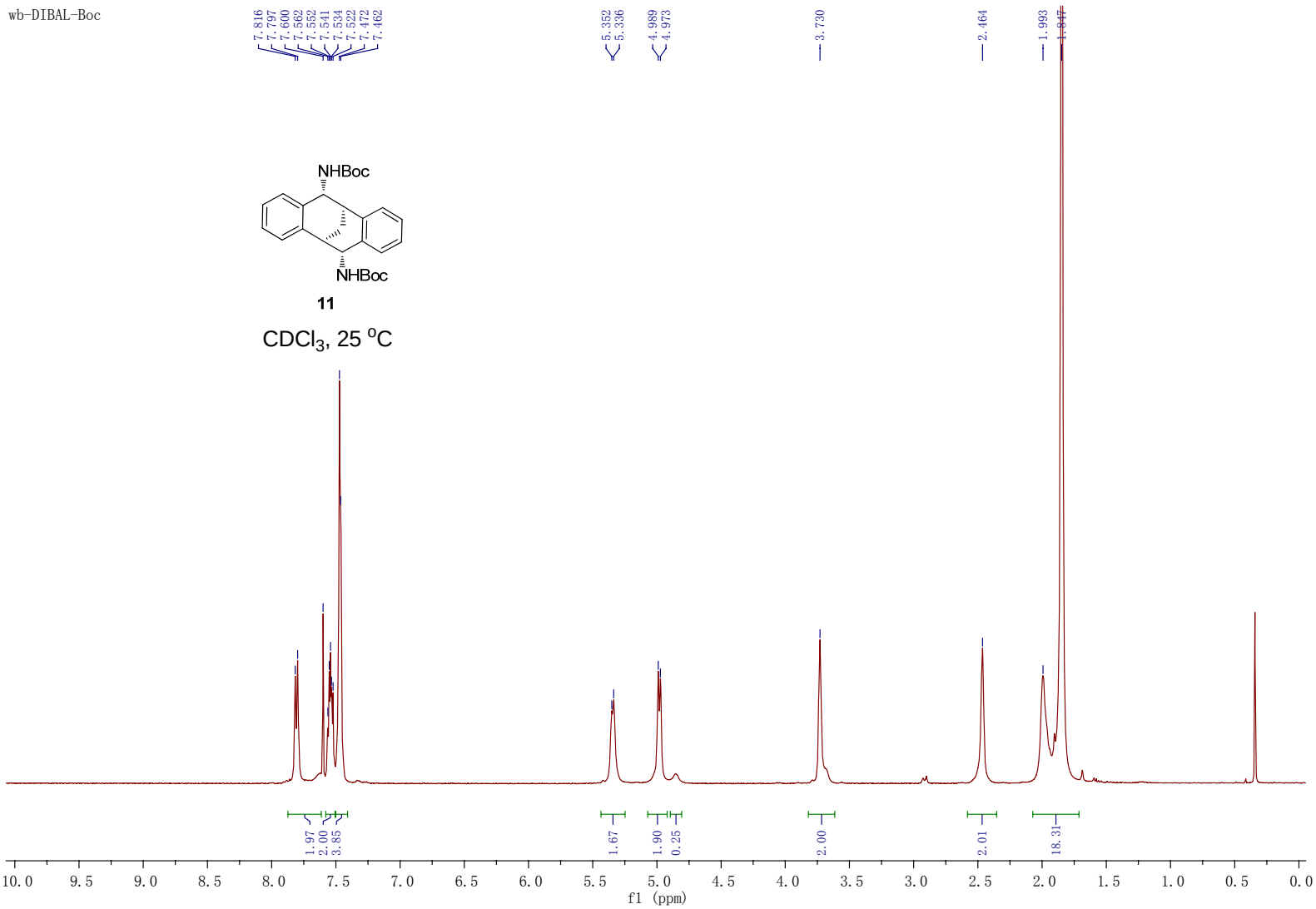

wb-1-182
140.647
139.667
137.343
130.233
128.916
128.527
128.367
127.167
127.104
126.602
62.651
52.412
36.177
18.365
NHBn
NHBn
8
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

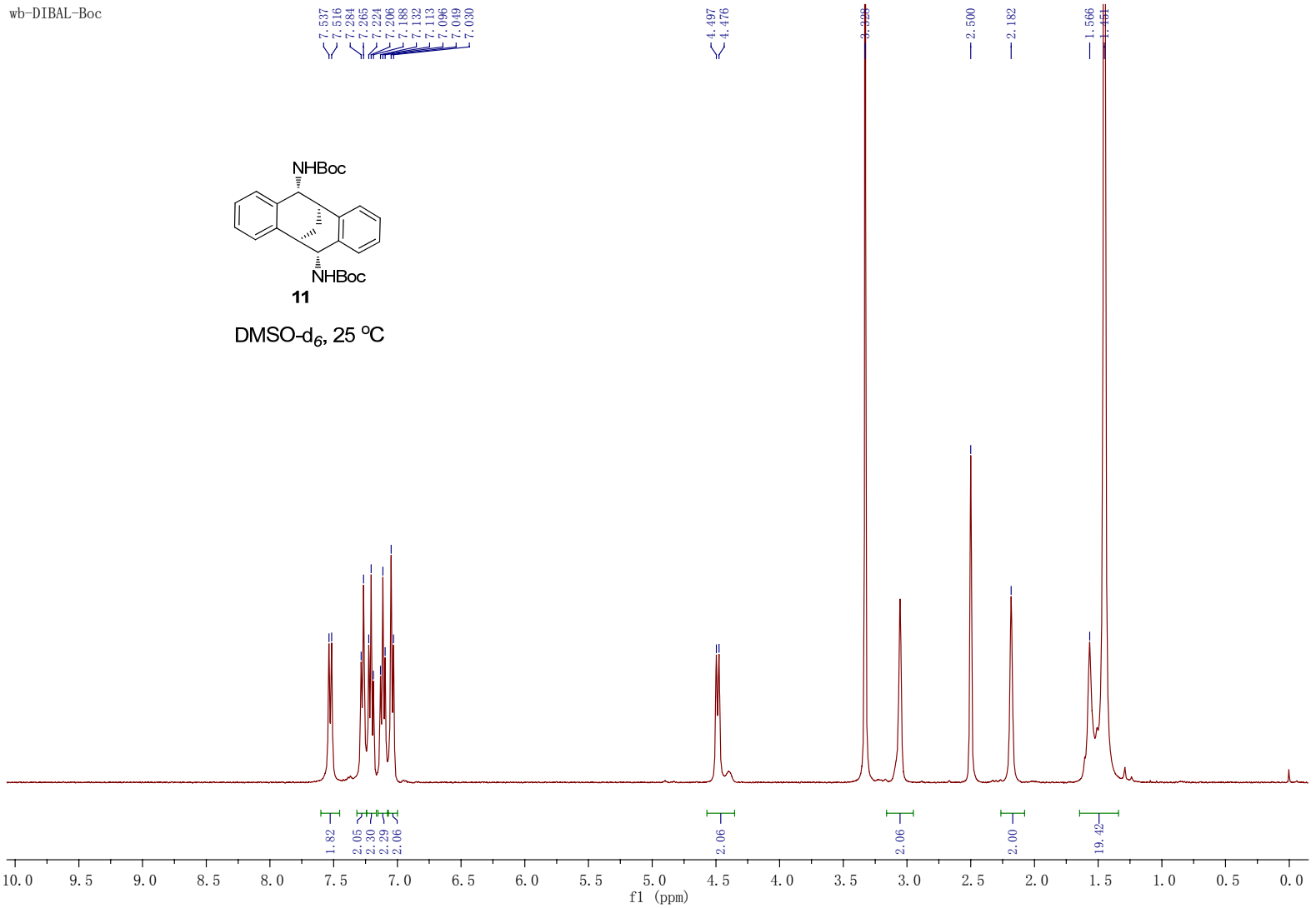

wb-2-40
7.289
7.276
7.267
7.260
7.200
7.190
7.182
7.177
7.083
7.074
7.060
5.257
5.243
5.232
5.218
4.513
4.488
3.408
3.401
3.394
3.388
3.381
2.447
2.439
2.432
1.585
1.563
1.553
NHBoc
NHBoc
10
CDCl3, 25 °C
2.01
3.87
1.98
2.03
2.21
2.05
2.00
18.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

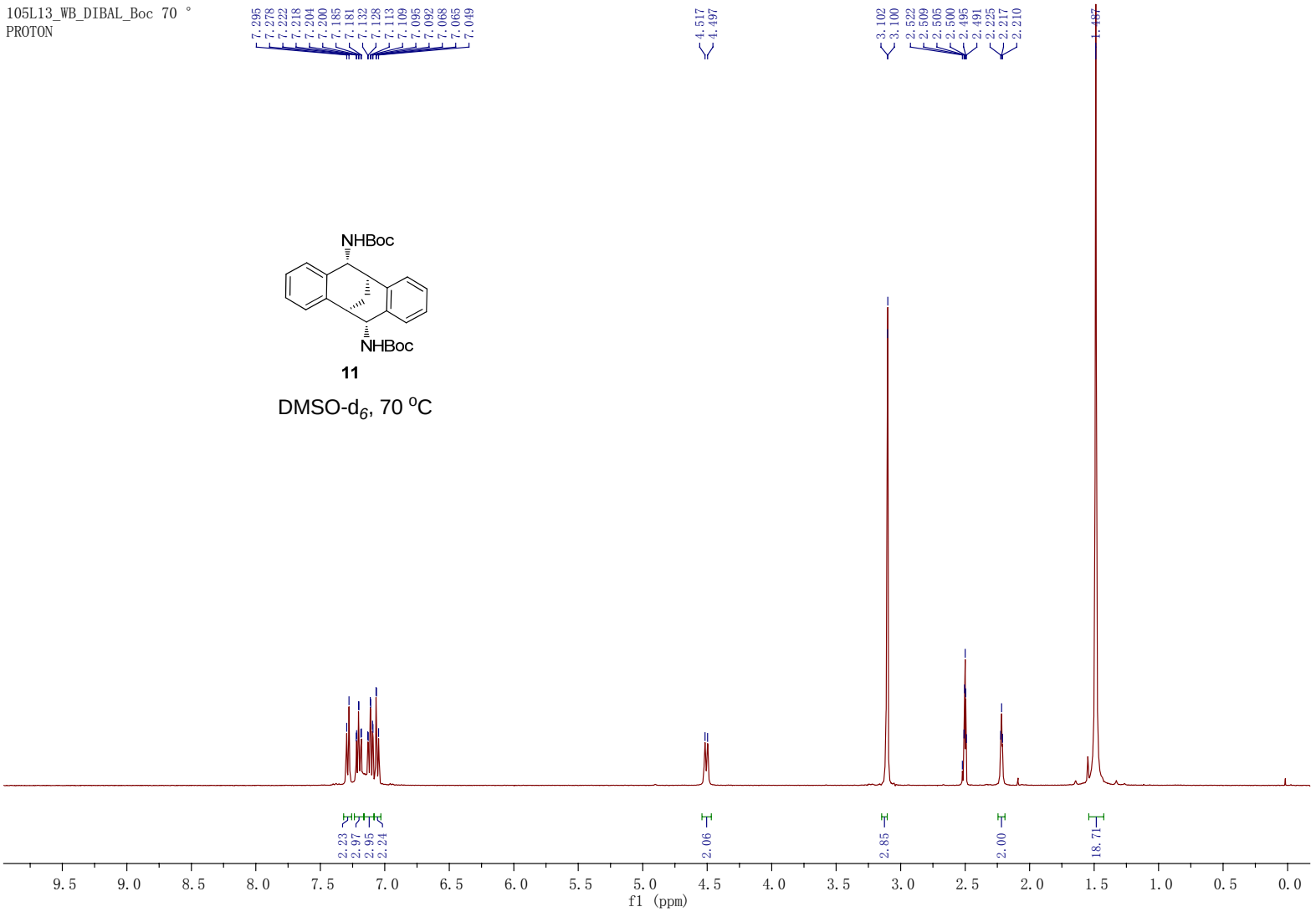

wb-2-40 (DMSO)
7.190
7.183
7.167
6.976
6.969
6.957
6.111
6.089
5.060
5.047
5.038
5.025
3.321
3.299
2.521
2.504
2.500
2.495
2.479
2.323
NHBoc
NHBoc
10
DMSO-d6, 25 °C
6.29
2.07
0.20
1.56
0.17
2.02
2.18
2.00
19.14
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

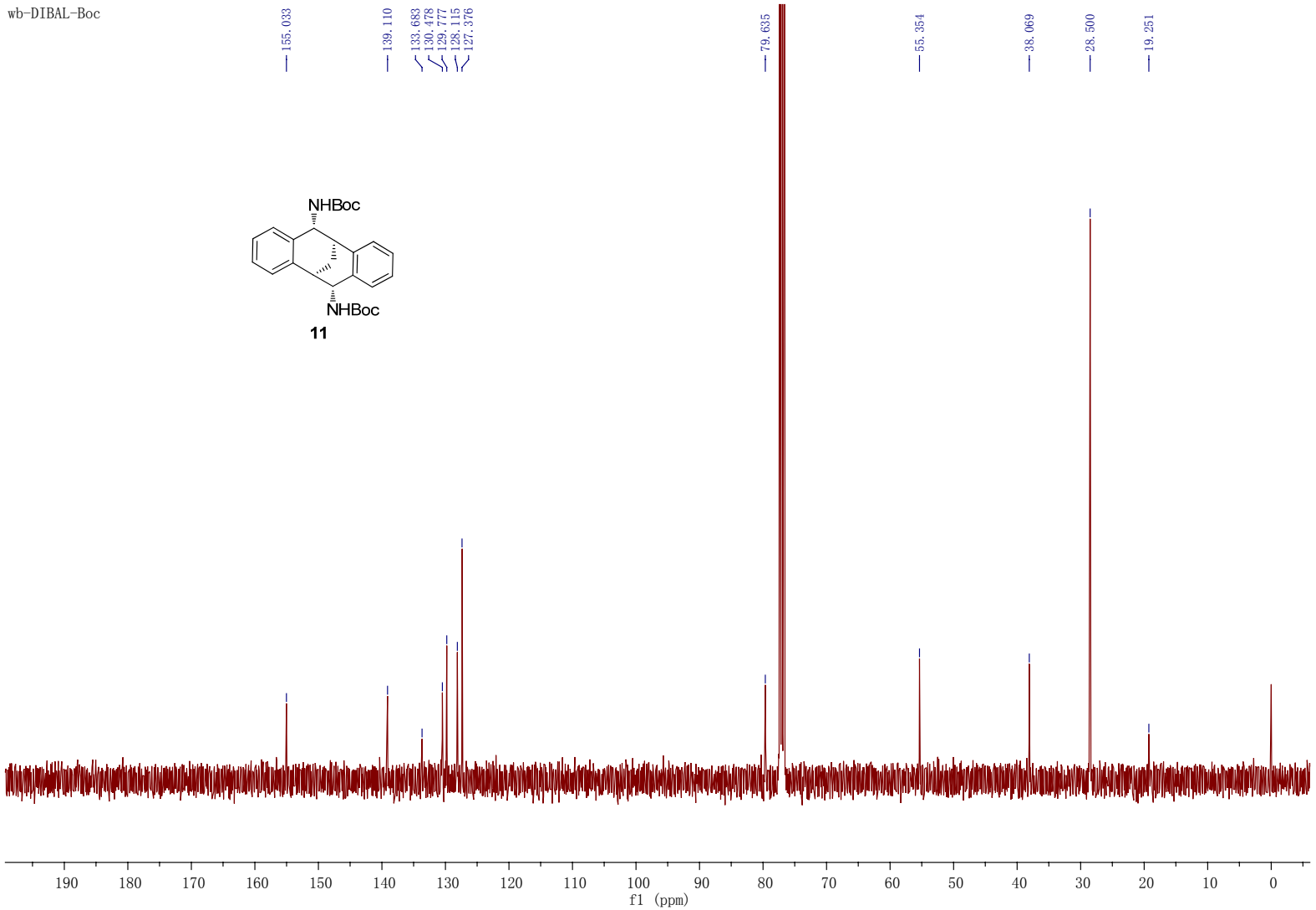

wb-2-40(DMSO)
PROTON
7.188
7.180
7.165
7.023
7.019
7.013
7.005
6.999
5.615
5.095
5.082
5.073
5.059
3.329
3.321
3.314
3.307
3.300
2.509
2.505
2.500
2.495
2.491
2.366
2.358
2.350
NHBoc
NHBoc
10
DMSO-d6, 70 °C
6.02
2.06
2.02
2.03
2.00
2.01
17.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


wb-2-40
156.008
136.700
135.652
130.648
127.430
127.182
126.666
79.698
54.537
36.726
29.513
28.569
NHBoc
NHBoc
10
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


wb-DIBAL-Boc
7.816
7.797
7.600
7.562
7.552
7.541
7.534
7.522
7.472
7.462
5.352
5.336
4.989
4.973
3.730
2.464
1.993
1.847
NHBoc
NHBoc
11
CDCl3, 25 °C
1.97
2.00
3.85
1.67
1.90
0.25
2.00
2.01
18.31
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


wb-DIBAL-Boc
7.537
7.516
7.284
7.265
7.224
7.206
7.188
7.132
7.113
7.096
7.049
7.030
4.497
4.476
3.398
2.500
2.182
1.566
1.461
NHBoc
NHBoc
11
DMSO-d6, 25 °C
1.82
2.05
2.30
2.29
2.06
2.06
2.06
2.00
19.42
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


105L13_WB_DIBAL_Boc 70 °
PROTON
7.295
7.278
7.222
7.218
7.204
7.200
7.185
7.181
7.132
7.128
7.113
7.109
7.095
7.092
7.068
7.065
7.049
4.517
4.497
3.102
3.100
2.522
2.509
2.505
2.500
2.495
2.491
2.225
2.217
2.210
1.487
NHBoc
NHBoc
11
DMSO-d6, 70 °C
2.23
2.97
2.95
2.24
2.06
2.85
2.00
18.71
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


wb-DIBAL-Boc
155.033
139.110
133.683
130.478
129.777
128.115
127.376
79.635
55.354
38.069
28.500
19.251
NHBoc
NHBoc
11
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)