Supporting Information

Formal Total Synthesis of Macarpine via a Au(I)-Catalyzed 6-*endo*-dig Cycloisomerization Strategy

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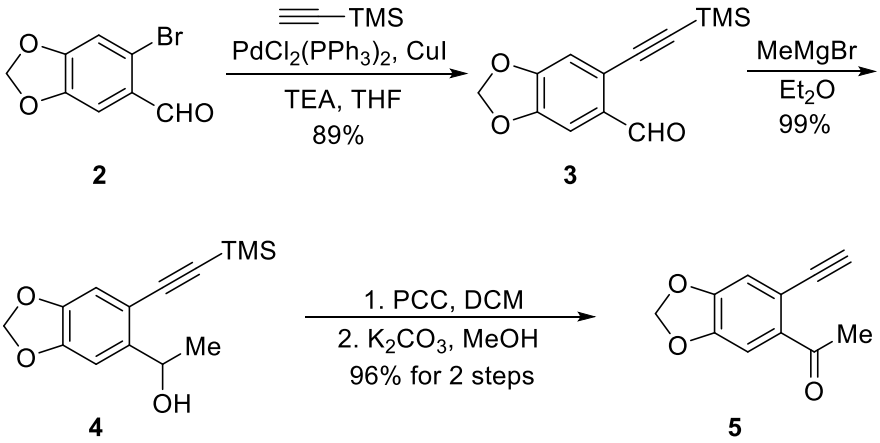
Contents

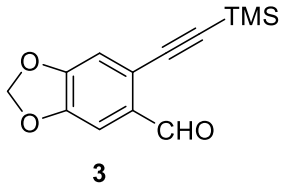
1. General Information

Unless otherwise stated, the reagents were commercially available and can be used without further purification. THF and Et_2O were distilled from sodium under a nitrogen atmosphere. DCM was distilled from calcium hydride (CaH) under a nitrogen atmosphere. TLC analysis of the reaction mixture was performed on Dynamicadsorbents silica F-254 TLC plates. Flash column chromatography was performed on Zeoprep 60 (200-300 mesh) silica gel. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-III 600 spectrometer with reference to $CDCl_3$ and DMSO-d_6. HR-ESI-MS were recorded on Bruker micro-TOFQ-Q instrument. IR spectra were recorded on Bruker IFS 55 spectrometer. Melting points were tested on Thomas Hoover capillary melting point apparatus.

2. General Procedures for the Preparation of 3-5, 8-12 and Characterization Data



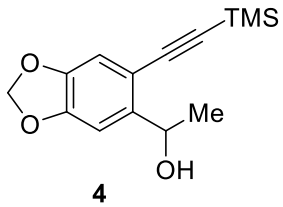
6-((Trimethylsilyl)ethynyl)benzo[d][1,3]dioxole-5-carbaldehyde (3)



3

In a manner analogous to literature[s1-s19] to afford the product **3** (14.40 g, 58.55 mmol, 89%) and data are in agreement with those reported in literature.[s14-s19]

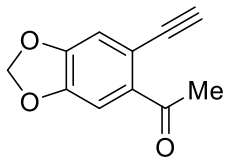
1-(6-((Trimethylsilyl)ethynyl)benzo[d][1,3]dioxol-5-yl)ethan-1-ol (4)



4

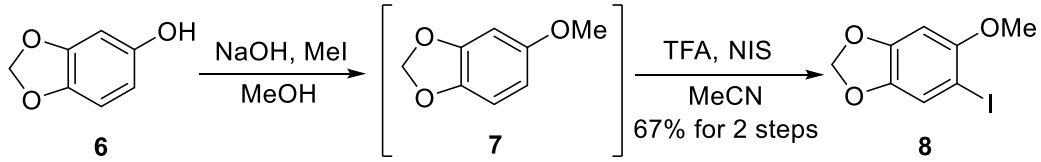
In a manner analogous to literature[s20] to afford the product **4** (2.02 g, 7.70 mmol, 99%) as a yellow oily liquid (EtOAc/petroleum ether = 1:10); ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.04 (s, 1H), 6.88 (s, 1H), 6.07 – 5.99 (m, 2H), 5.23 (d, *J* = 4.2 Hz, 1H), 5.03 (dd, *J* = 6.3, 4.3 Hz, 1H), 1.26 (d, *J* = 6.4 Hz, 3H), 0.26 – 0.17 (m, 9H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 147.95, 145.62, 145.11, 110.99, 110.07, 104.89, 102.87, 101.00, 96.79, 65.61, 39.58, 39.45, 39.24, 39.10, 38.89, 38.68, 24.43, -0.46; IR (thin film, cm^{-1}): 2944, 2832, 1663, 1483, 1449, 1371, 1252, 1114, 1020, 857, 846; HRMS (ESI): *m/z* Calcd. for $C_{14}H_{19}O_3Si$ $[M+H]^+$ 263.1098, Found 263.1090.

1-(6-Ethynylbenzo[d][1,3]dioxol-5-yl)ethan-1-one (5)



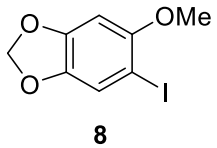
5

In a manner analogous to literature[s21] to afford the product **5** (487 mg, 2.60 mmol, 96% for 2 steps) as a yellow oily liquid (EtOAc/petroleum ether = 1:15); ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.32 (s, 1H), 7.10 (s, 1H), 6.15 (s, 2H), 4.34 (s, 1H), 2.58 (s, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 197.99, 150.21, 148.48, 136.65, 115.31, 113.71, 109.01, 103.06, 85.09, 82.94, 30.09; IR (thin film, cm^{-1}): 2937, 2852, 1674, 1582, 1457, 1121, 912, 891, 727; HRMS (ESI): *m/z* Calcd. for $C_{11}H_9O_3$ $[M+H]^+$ 189.0546, Found 189.0540.



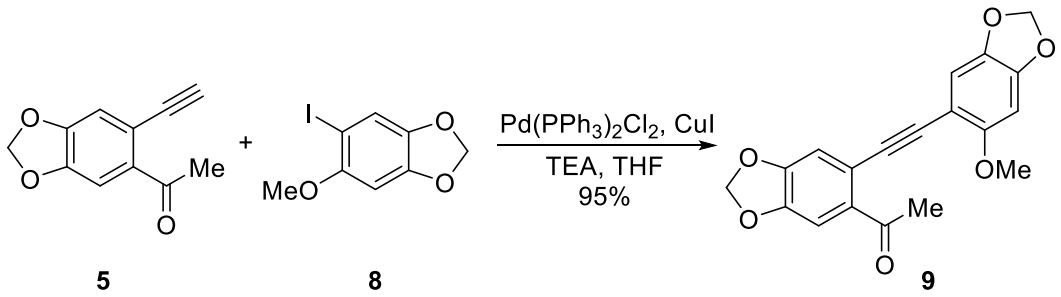
6 **7** **8**

5-Iodo-6-methoxybenzo[d][1,3]dioxole (8)



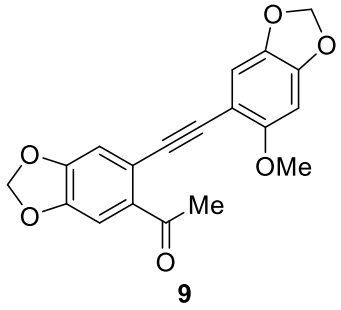
8

In a manner analogous to literature to afford the product **8** (3.71 g, 13.40 mmol, 67% for 2 steps) and data are in agreement with those reported in literature.[s22,s23]



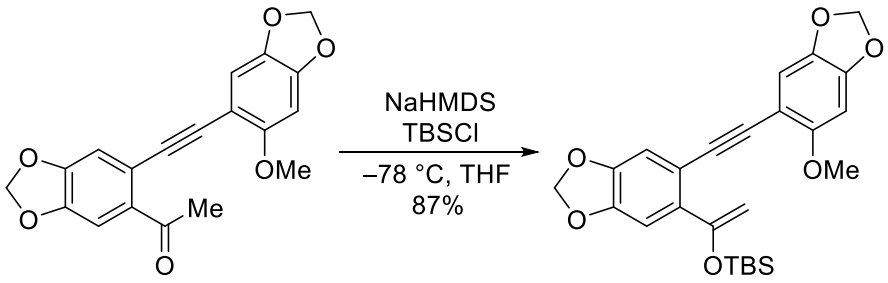
5 **8** **9**

1-(6-((6-Methoxybenzo[d][1,3]dioxol-5-yl)ethynyl)benzo[d][1,3]dioxol-5-yl)ethan-1-one (9)



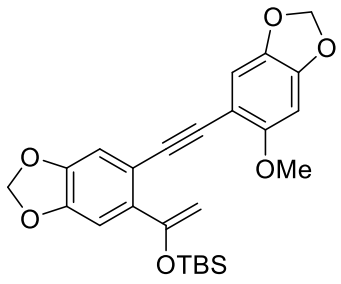
9

In a manner analogous to literature[s21] to afford the product **9** (3.50 g, 10.50 mmol, 95%) as a black solid (EtOAc/petroleum ether = 1:20); Mp 80.0 – 80.9 °C; ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.28 (s, 1H), 7.10 (s, 1H), 7.01 (s, 1H), 6.88 (s, 1H), 6.16 (s, 2H), 6.04 (s, 2H), 3.79 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 198.33, 157.32, 150.48, 149.74, 148.16, 141.08, 135.41, 117.28, 112.61, 111.50, 108.73, 103.01, 102.25, 95.76, 91.87, 91.61, 57.00, 30.47; IR (thin film, cm^{-1}): 2944, 2833, 1472, 1418, 1448, 1268, 1195, 1113, 1020; HRMS (ESI): *m/z* Calcd. for $C_{19}H_{15}O_6$ $[M+H]^+$ 339.0863, Found 339.0859.



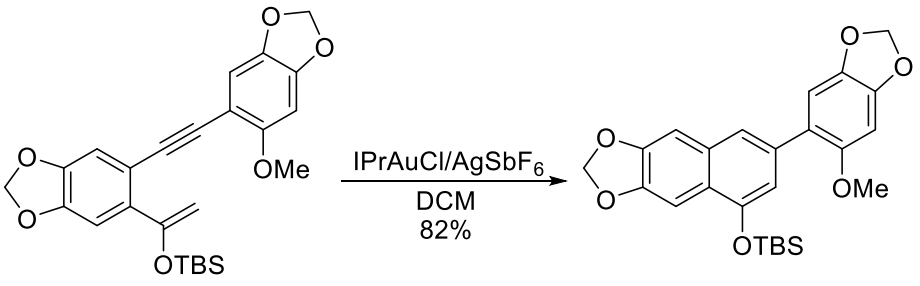
9 **10**

***tert*-Butyl((1-(6-((6-methoxybenzo[d][1,3]dioxol-5-yl)ethynyl)benzo[d][1,3]dioxol-5-yl)vinyl)oxy)dimethylsilane (10)**



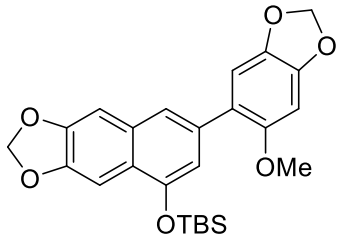
10

In a manner analogous to literature[s21] to afford the product **10** (1.10 g, 2.50 mmol, 87%) as a yellow solid (EtOAc/petroleum ether = 1:50); Mp 90.1 – 91.5 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.00 (s, 1H), 6.98 (s, 1H), 6.89 (s, 1H), 6.85 (s, 1H), 6.09 (s, 2H), 6.03 (s, 2H), 5.19 (d, J = 1.5 Hz, 1H), 4.69 (d, J = 1.5 Hz, 1H), 3.78 (s, 3H), 0.90 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.23, 155.75, 151.52, 150.08, 149.50, 143.21, 137.10, 116.45, 114.48, 113.56, 109.81, 105.89, 104.56, 104.38, 99.16, 98.04, 94.18, 91.97, 59.21, 28.30, 20.61, 2.07; IR (thin film, cm^{-1}): 2954, 2927, 2897, 2856, 2201, 1619, 1485, 1434, 1360, 1378, 1253, 1228, 1192, 1175, 1116, 1074, 1038, 937, 860, 831, 781, 760, 686; HRMS (ESI): *m/z* Calcd. for $C_{25}H_{29}O_6Si$ $[M+H]^+$ 453.1728, Found 453.1718.



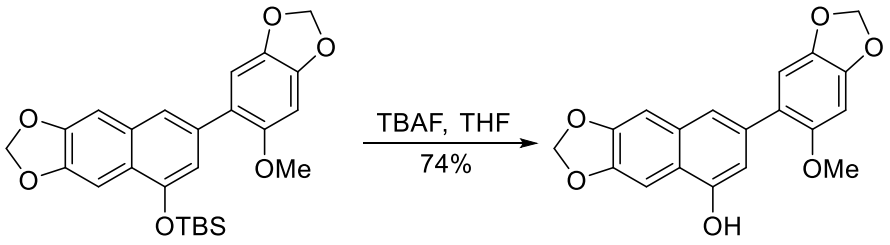
10 **11**

***tert*-Butyl((7-(6-methoxybenzo[d][1,3]dioxol-5-yl)naphtho[2,3-d][1,3]dioxol-5-yl)oxy)dimethylsilane (11)**



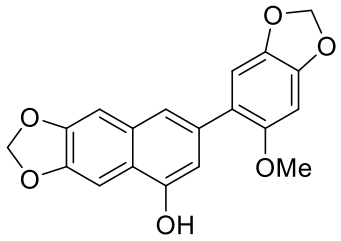
11

In a manner analogous to literature[s21] to afford the product **11** (371 mg, 0.82 mmol, 82%) as a yellow oily liquid (EtOAc/petroleum ether = 1:10); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.37 (d, J = 1.2 Hz, 1H), 7.28 (s, 2H), 6.96 – 6.93 (m, 2H), 6.90 (s, 1H), 6.12 (s, 2H), 6.02 (s, 2H), 3.71 (s, 3H), 1.04 (s, 9H), 0.27 (s, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 151.99, 149.83, 148.11, 147.78, 147.51, 141.59, 135.07, 132.01, 122.66, 122.36, 120.71, 114.47, 110.11, 104.43, 101.67, 98.27, 96.39, 57.01, 26.20, 18.59, 3.92; IR (thin film, cm^{-1}): 3032, 2990, 2877, 2865, 1460, 1431, 1352, 940, 757; HRMS (ESI): *m/z* Calcd. for $C_{25}H_{29}O_6Si$ $[M+H]^+$ 453.1728, Found 453.1725.



11 **12**

7-(6-Methoxybenzo[d][1,3]dioxol-5-yl)naphtho[2,3-d][1,3]dioxol-5-ol (12)



12

In a manner analogous to literature[s24] to afford the product **12** (200 mg, 0.59 mmol, 74%) and data are in agreement with those reported in literature.[s23,s25]

3. References

[s1]. Liu, X. J.; Zhou, S. Y.; Xiao, Y.; Sun, Q.; Lu, X.; Li, Y.; Li, J. H. *Org. Lett.*, **2021**, *23*, 7839–7844.

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[s18]. Takahashi, H.; Yoshida, K.; Yanagisawa, A. *J. Org. Chem.*, **2009**, *74*, 3632–3640.

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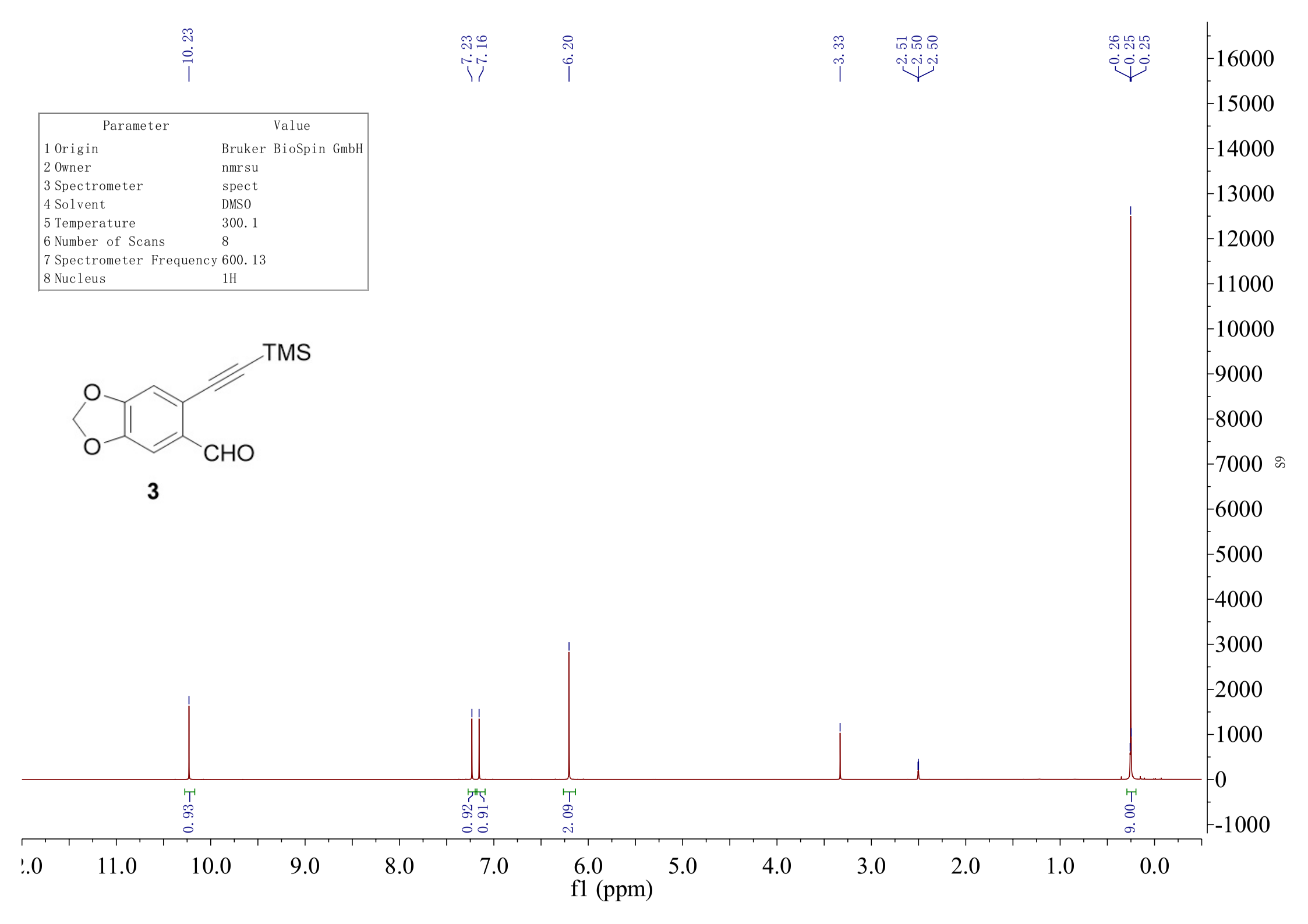
[s25]. Solorio-Alvarado, C. R.; Echavarren, A. M. *J. Am. Chem. Soc.*, **2010**, *132*, 11881–11883.

4. NMR Spectra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7.16
6.20
3.33
2.51
2.50
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4000
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0
-1000
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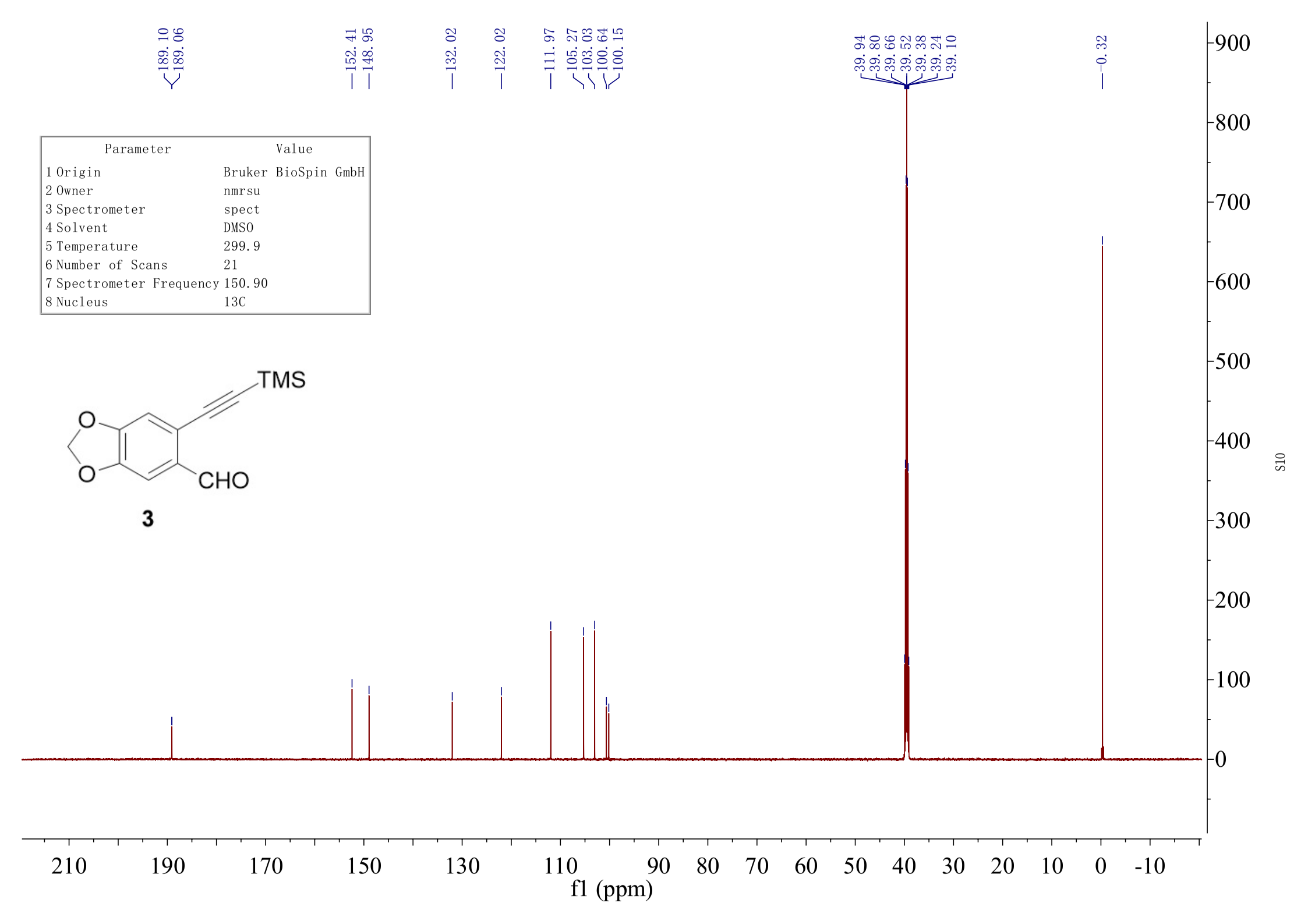
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189.06
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132.02
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111.97
105.27
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100.15
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39.66
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O
CHO
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700
600
500
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300
200
100
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S10
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150
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110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Parameter	Value
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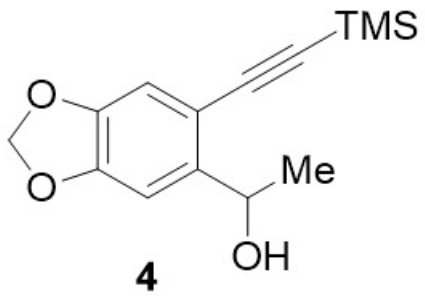

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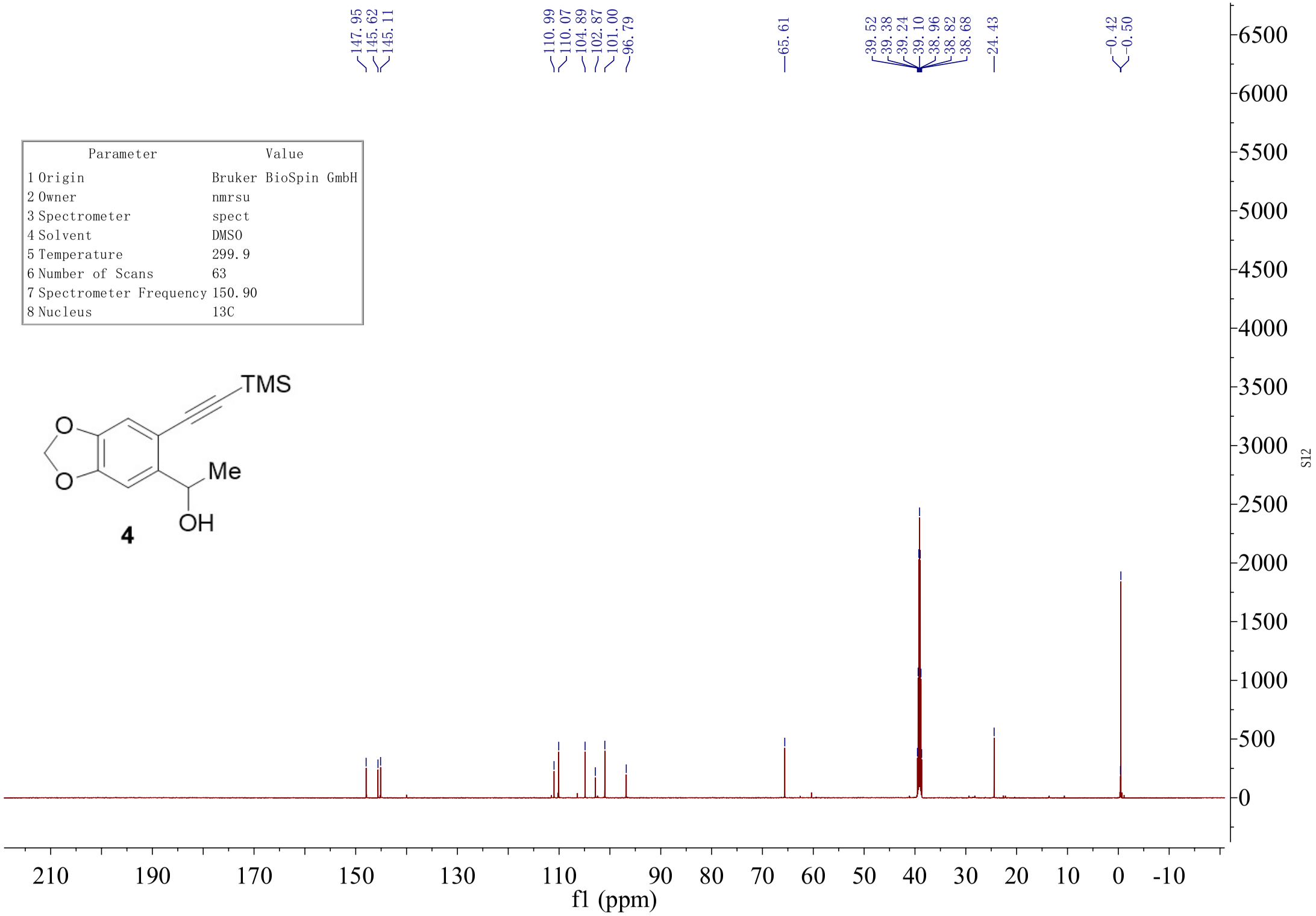
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110.07
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101.00
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65.61
39.52
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1500
1000
500
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80
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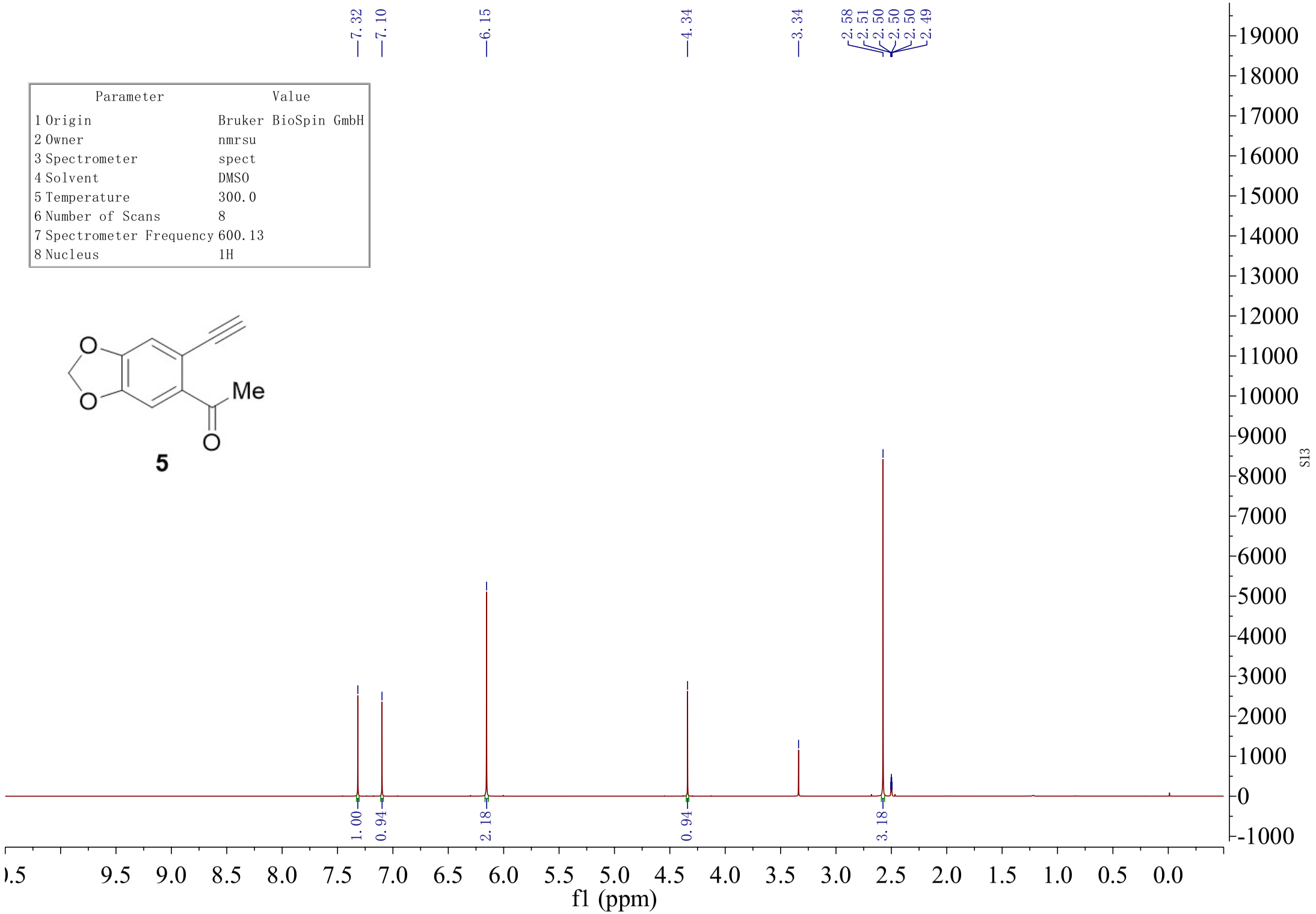
f1 (ppm)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2.50
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2.49
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3 Spectrometer spect
4 Solvent DMSO
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Me
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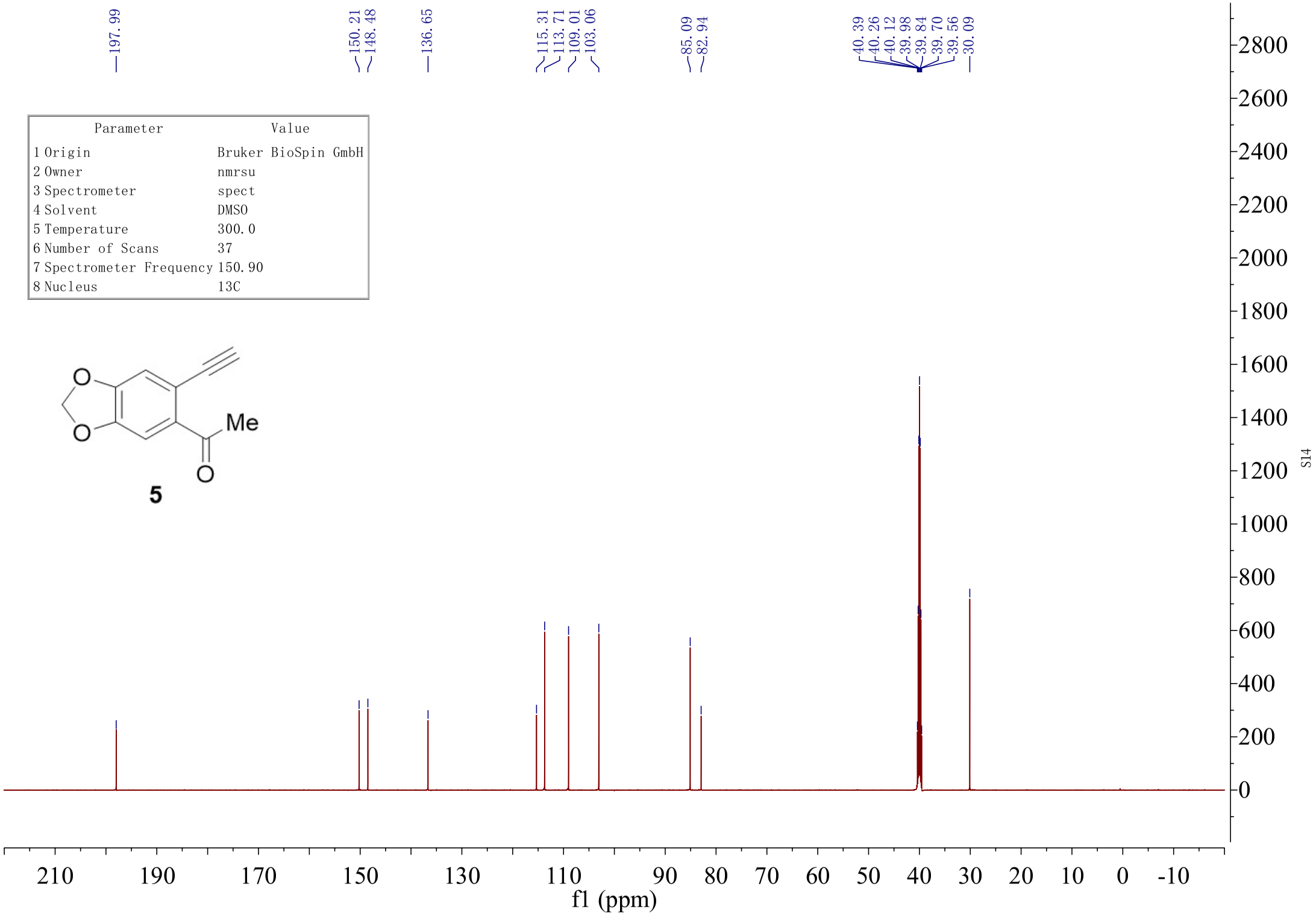
f1 (ppm)
S13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O
Me
O
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150
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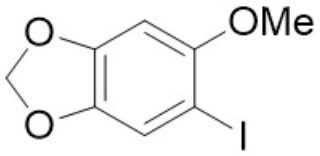
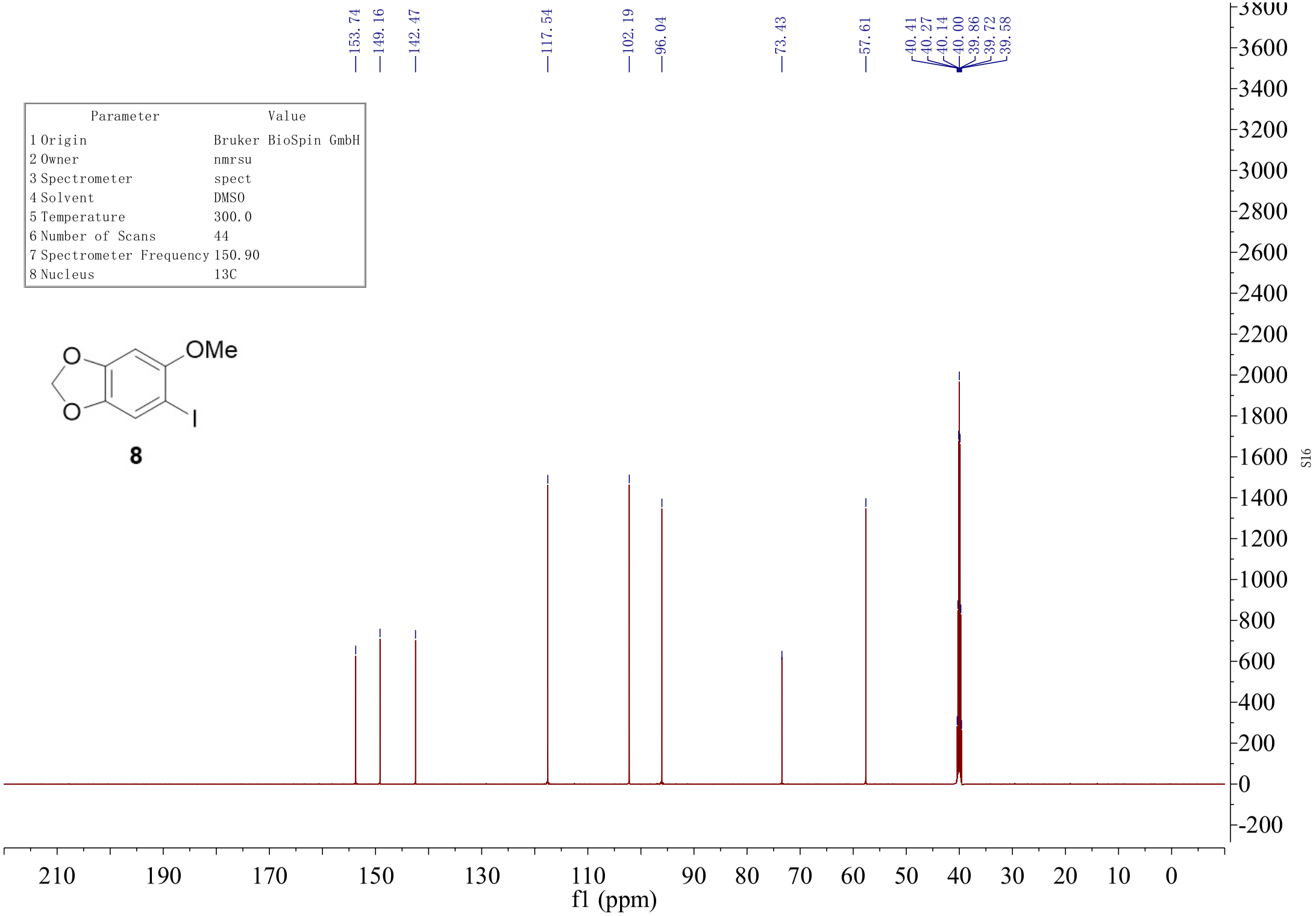
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
S14

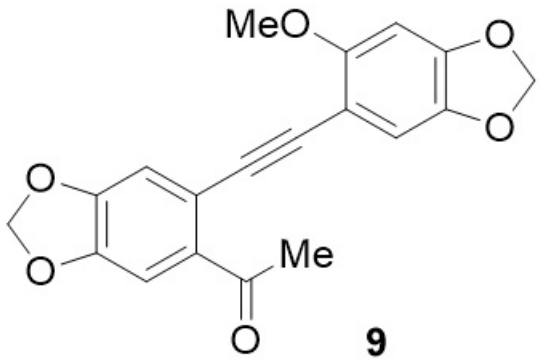
Parameter	Value
1 Origin	Bruker BioSpin GmbH
2 Owner	nmrsu
3 Spectrometer	spect
4 Solvent	DMSO
5 Temperature	300.0
6 Number of Scans	16
7 Spectrometer Frequency	600.13
8 Nucleus	1H



8


153.74
149.16
142.47
117.54
102.19
96.04
73.43
57.61
40.41
40.27
40.14
40.00
39.86
39.72
39.58
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 300.0
6 Number of Scans 44
7 Spectrometer Frequency 150.90
8 Nucleus 13C
O
OMe
O
I
8
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Parameter	Value
1 Origin	Bruker BioSpin GmbH
2 Owner	nmrsu
3 Spectrometer	spect
4 Solvent	DMSO
5 Temperature	300.0
6 Number of Scans	8
7 Spectrometer Frequency	600.13
8 Nucleus	1H



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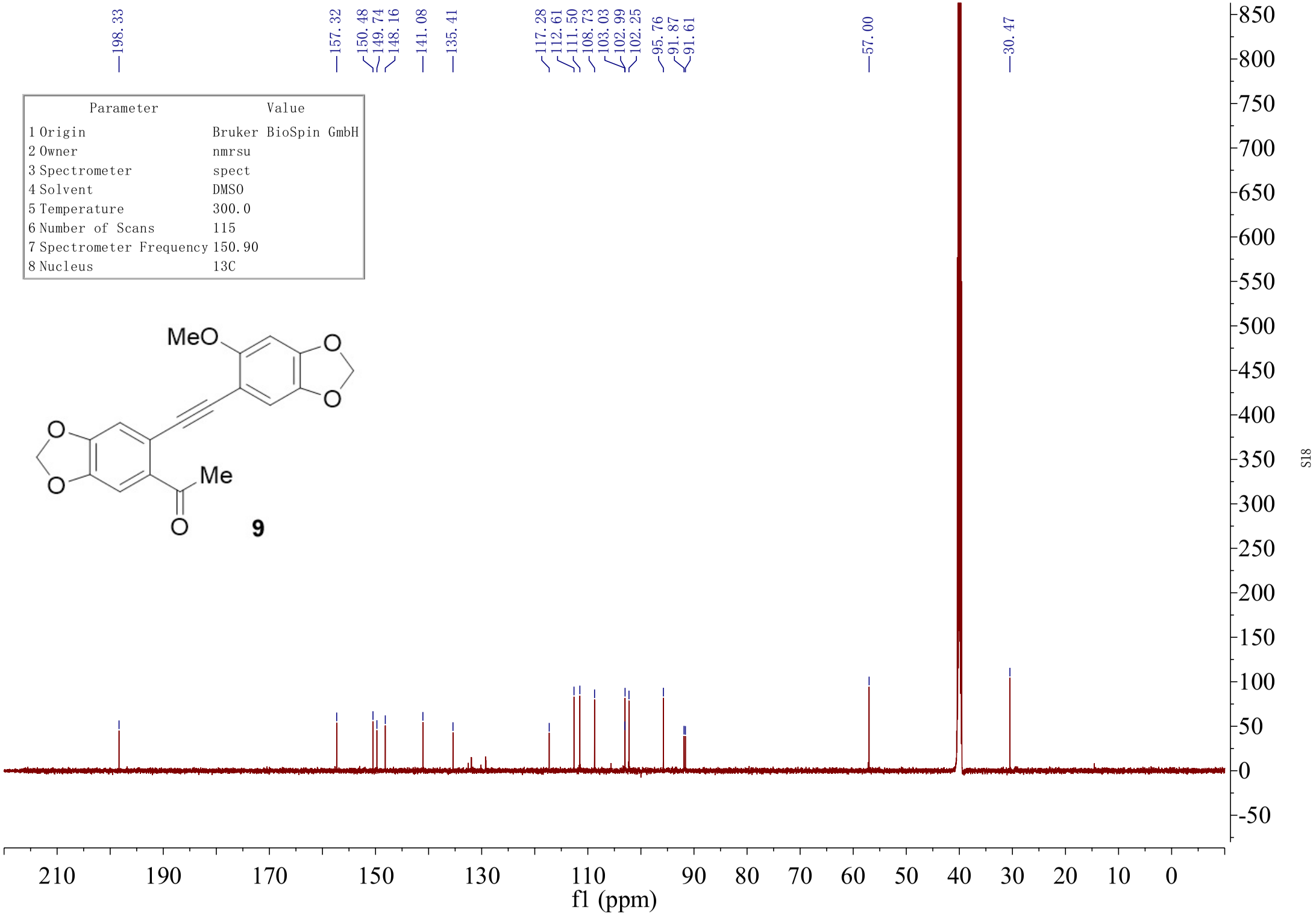
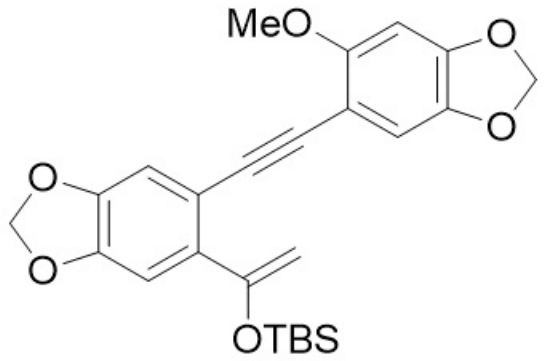

198.33
157.32
150.48
149.74
148.16
141.08
135.41
117.28
112.61
111.50
108.73
103.03
102.99
102.25
95.76
91.87
91.61
57.00
30.47
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 300.0
6 Number of Scans 115
7 Spectrometer Frequency 150.90
8 Nucleus 13C
MeO
O
O
O
O
Me
O
9
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Parameter	Value
1 Origin	Bruker BioSpin GmbH
2 Owner	nmrsu
3 Spectrometer	spect
4 Solvent	DMSO
5 Temperature	299.9
6 Number of Scans	8
7 Spectrometer Frequency	600.13
8 Nucleus	1H



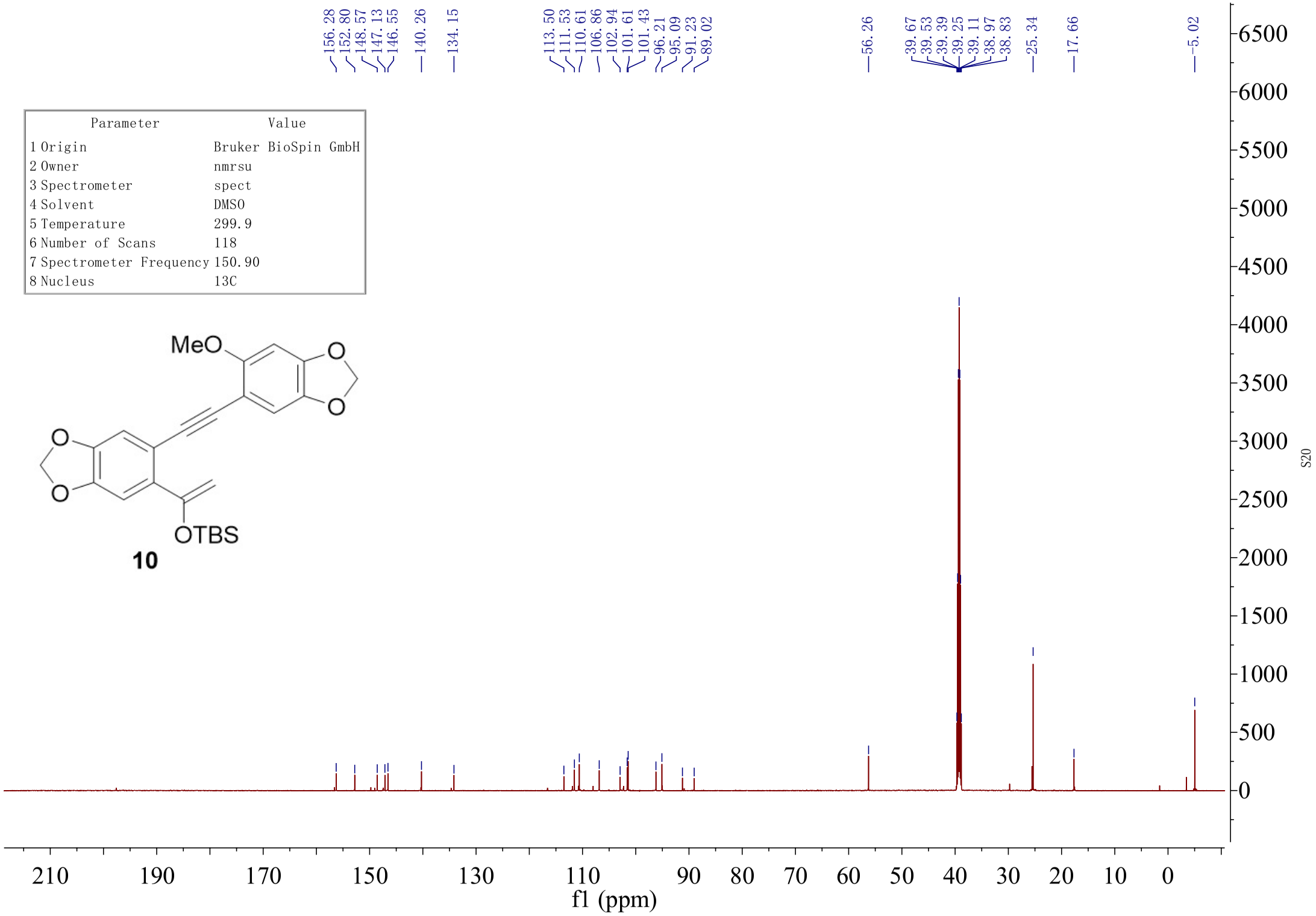
10

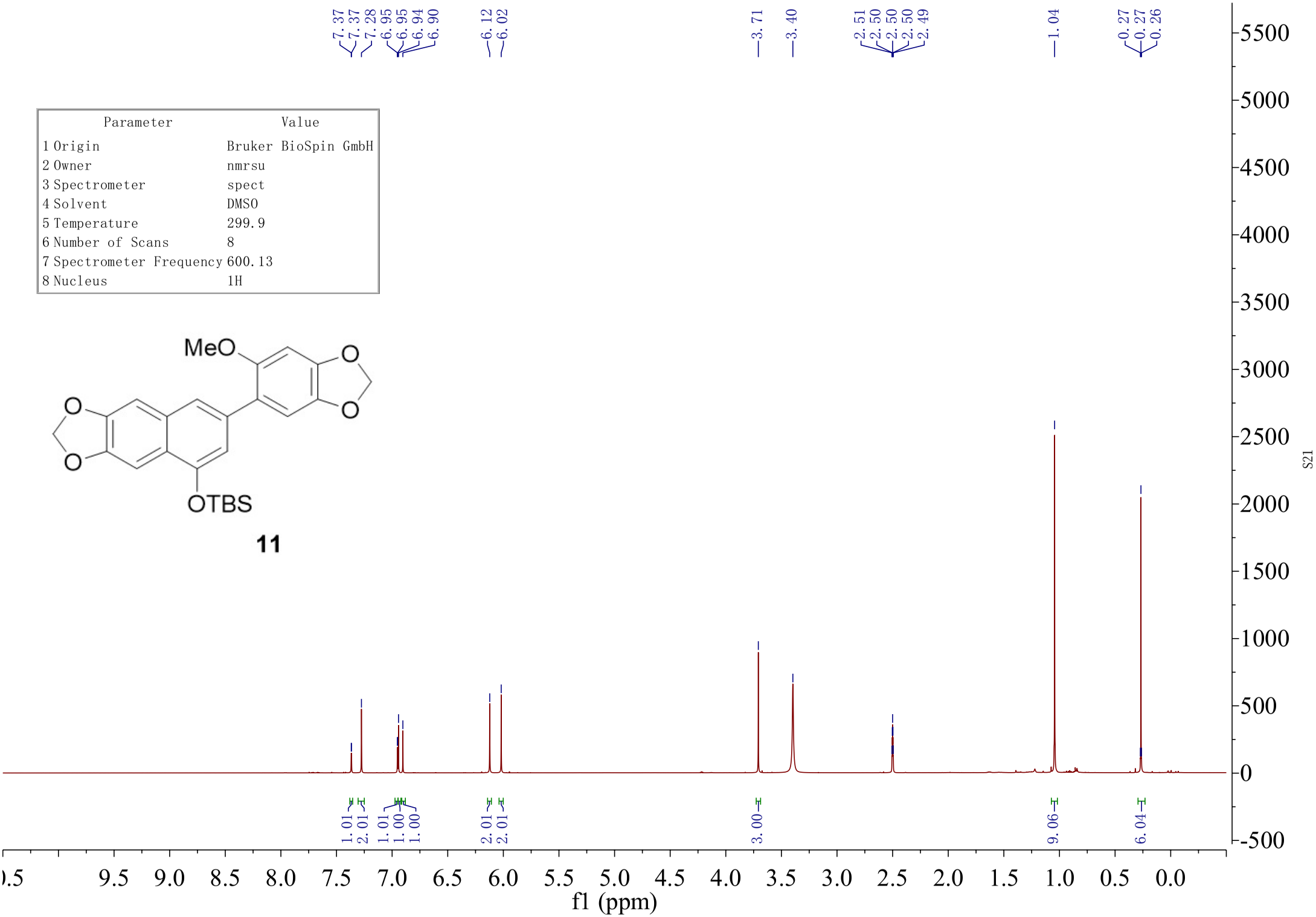
7.00 6.98 6.89 6.85 6.09 6.03 5.19 5.19 4.69 4.68 3.78 3.35 2.50 2.50 2.50 2.49 0.90 0.13

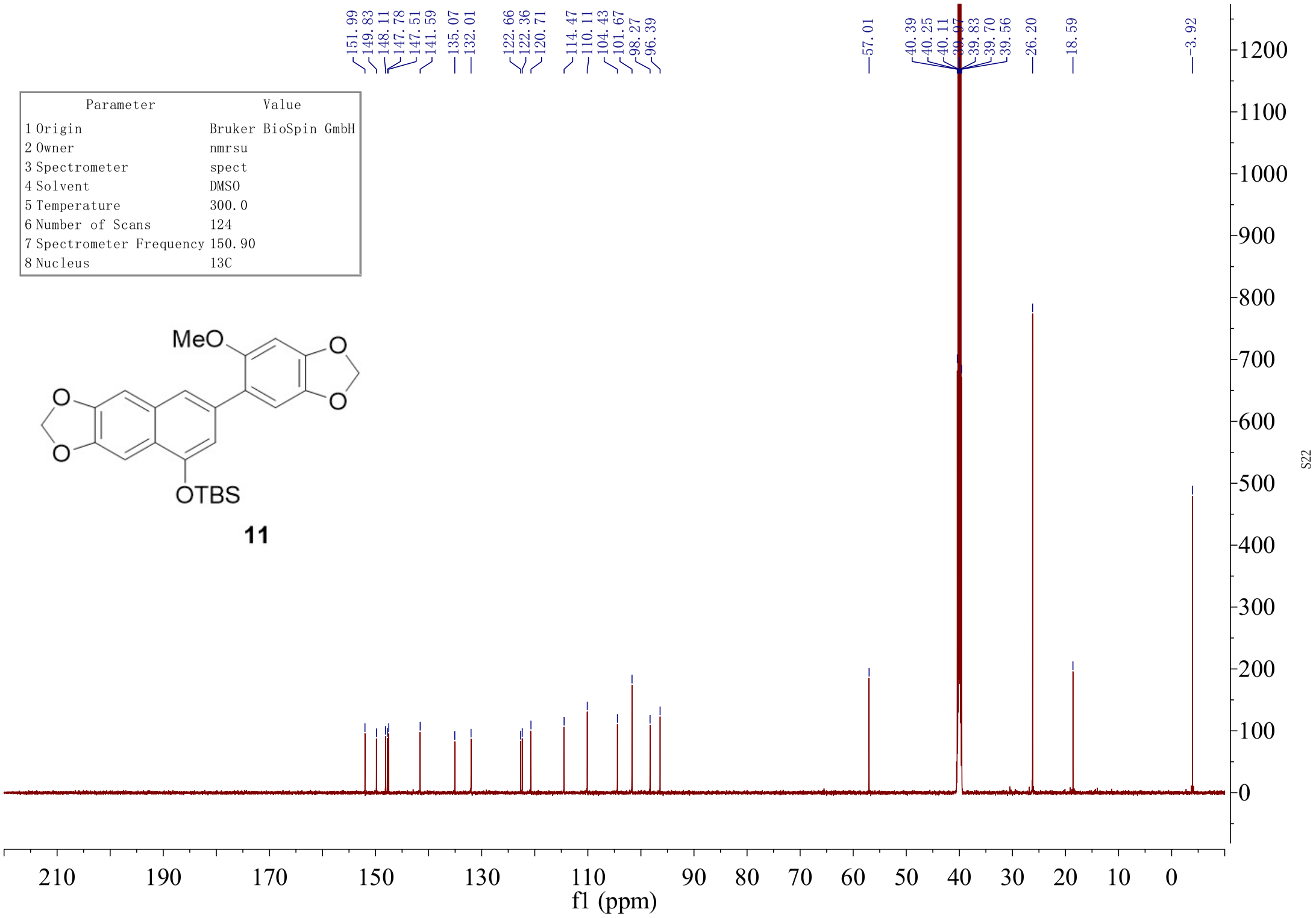
0.91 0.94 0.85 0.94 2.06 2.22 0.98 0.97 2.94 9.28 6.00

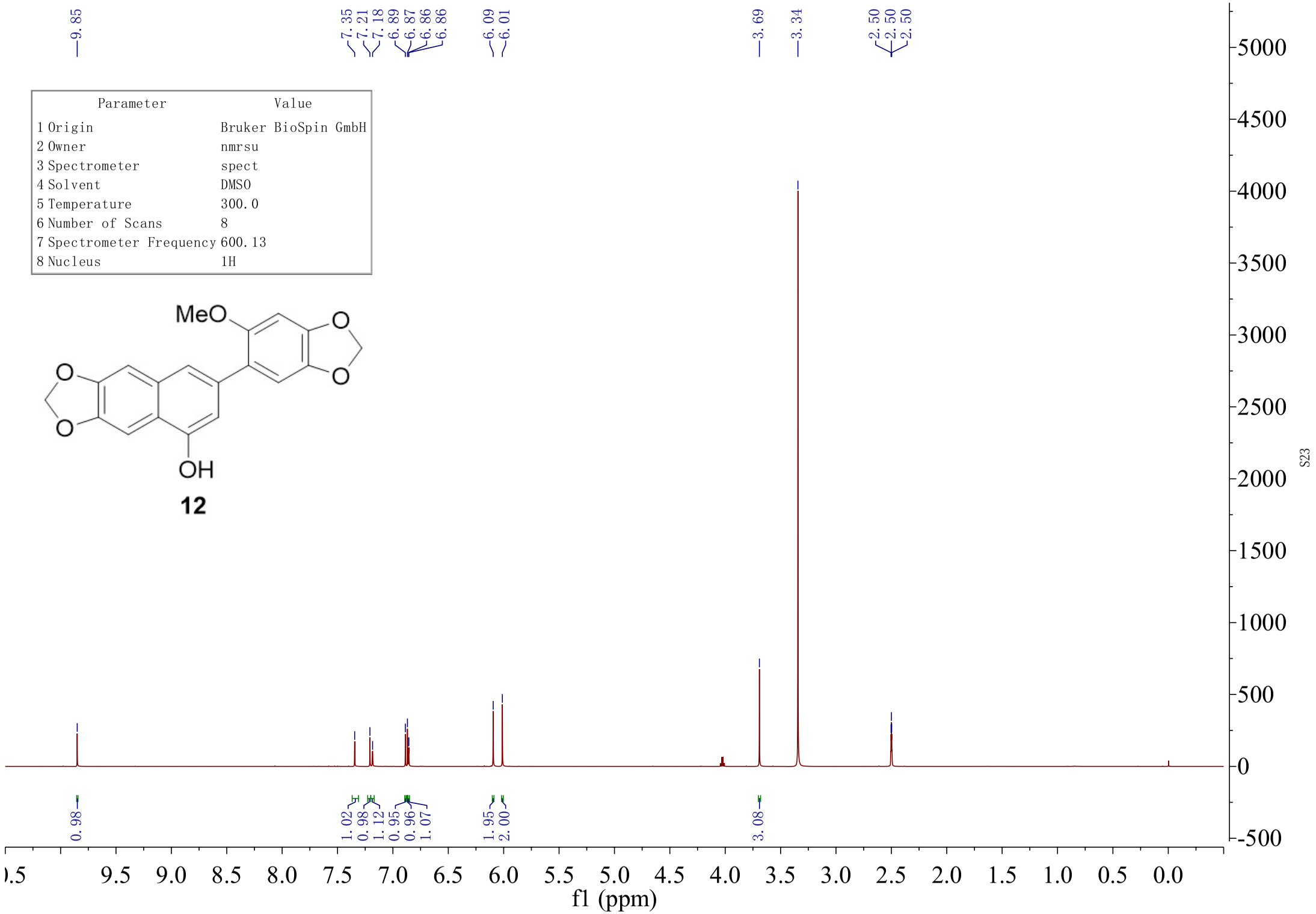
f1 (ppm)

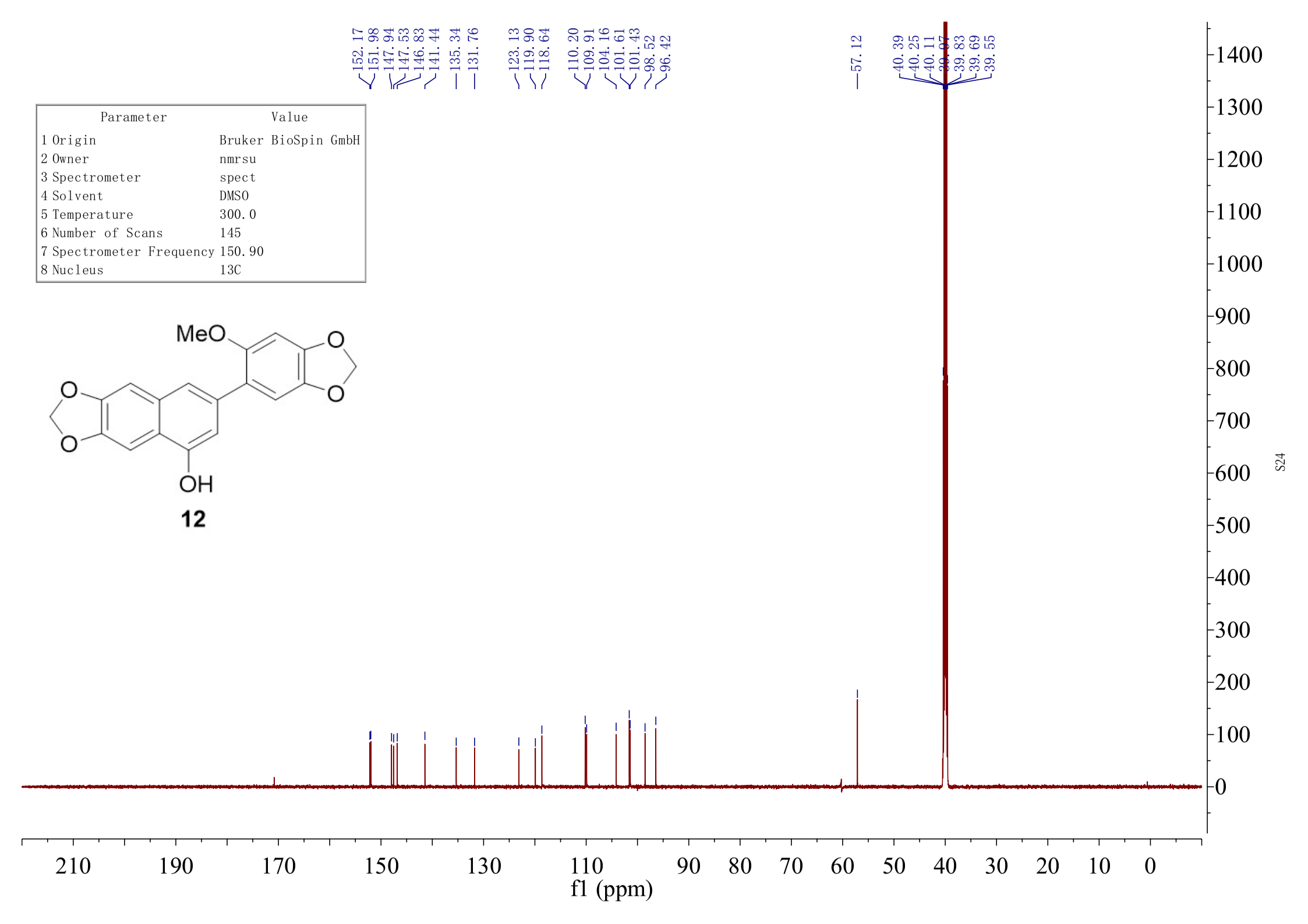
S19


156.28
152.80
148.57
147.13
146.55
140.26
134.15
113.50
111.53
110.61
106.86
102.94
101.61
101.43
96.21
95.09
91.23
89.02
56.26
39.67
39.53
39.39
39.25
39.11
38.97
38.83
25.34
17.66
-5.02
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 299.9
6 Number of Scans 118
7 Spectrometer Frequency 150.90
8 Nucleus 13C
MeO
O
O
O
O
OTBS
10
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
S20
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.37
7.37
7.28
6.95
6.95
6.94
6.90
6.12
6.02
3.71
3.40
2.51
2.50
2.50
2.50
2.49
1.04
0.27
0.27
0.26
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 299.9
6 Number of Scans 8
7 Spectrometer Frequency 600.13
8 Nucleus 1H
MeO
O
O
O
O
OTBS
11
1.01
2.01
1.01
1.00
1.00
2.01
2.01
3.00
9.06
6.04
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
S21
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)


151.99
149.83
148.11
147.78
147.51
141.59
135.07
132.01
122.66
122.36
120.71
114.47
110.11
104.43
101.67
98.27
96.39
57.01
40.39
40.25
40.11
39.83
39.70
39.56
26.20
18.59
-3.92
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 300.0
6 Number of Scans 124
7 Spectrometer Frequency 150.90
8 Nucleus 13C
MeO
O
O
O
O
OTBS
11
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
S22
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.85
7.35
7.21
7.18
6.89
6.87
6.86
6.86
6.09
6.01
3.69
3.34
2.50
2.50
2.50
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 300.0
6 Number of Scans 8
7 Spectrometer Frequency 600.13
8 Nucleus 1H
MeO
O
O
O
O
OH
12
0.98
1.02
0.98
1.12
0.95
0.96
1.07
1.95
2.00
3.08
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
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)
S23


152.17
151.98
147.94
147.53
146.83
141.44
135.34
131.76
123.13
119.90
118.64
110.20
109.91
104.16
101.61
101.43
98.52
96.42
57.12
40.39
40.25
40.11
39.97
39.83
39.69
39.55
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Owner nmrsu
3 Spectrometer spect
4 Solvent DMSO
5 Temperature 300.0
6 Number of Scans 145
7 Spectrometer Frequency 150.90
8 Nucleus 13C
MeO
O
O
O
O
OH
12
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
S24