

Diversity-Oriented Routes to Thiopeptide Antibiotics: Total Synthesis and Biological Evaluation of Micrococcin P2.

Hee-Jong Hwang,^{*†a,b} Young-Jin Son,^{†a,c} Dahyun Kim,^a Jusuk Lee,^a Yun-Jeong Shin,^c Yonghoon Kwon,^{*c} Marco A. Ciufolini^{*b}

^aA&J Science Co., Ltd., 80 Chumbok Ro, Dong Gu, Daegu, 41061, Republic of Korea.

^bDepartment of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, BC V6K 1Z1, Canada.

^cDepartment of Agricultural Biotechnology, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul, 08826, Republic of Korea

Supporting Information

¹H and ¹³C NMR Spectra

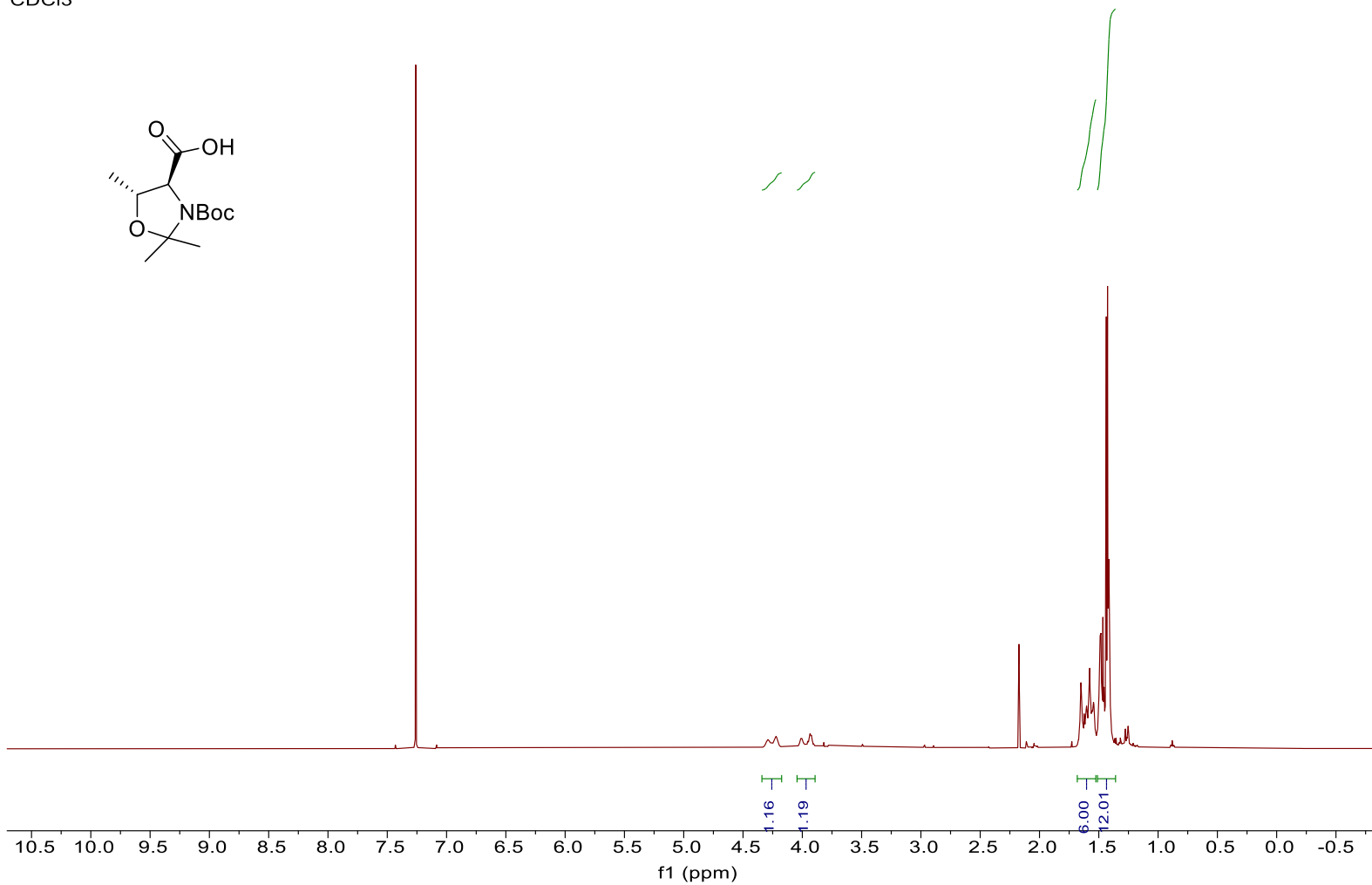
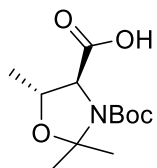
Table of Contents

¹ H NMR Spectrum of compound 8	p. 5
¹³ C NMR Spectrum of compound 8	p. 6
¹ H NMR Spectrum of compound 9	p. 7
¹³ C NMR Spectrum of compound 9	p. 8
¹ H NMR Spectrum of compound 10	p. 9
¹³ C NMR Spectrum of compound 10	p. 10
¹ H NMR Spectrum of compound 12	p. 11
¹³ C NMR Spectrum of compound 12	p. 12
¹ H NMR Spectrum of compound 15	p. 13
¹³ C NMR Spectrum of compound 15	p. 14
¹ H NMR Spectrum of compound 16	p. 15
¹³ C NMR Spectrum of compound 16	p. 16
HSQC Spectrum of compound 16	p. 17
HMBC Spectrum of compound 16	p. 18
¹ H NMR Spectrum of compound 17	p. 19
¹³ C NMR Spectrum of compound 17	p. 20
¹ H NMR Spectrum of compound 18	p. 21
¹³ C NMR Spectrum of compound 18	p. 22
¹ H NMR Spectrum of compound 6	p. 23
¹³ C NMR Spectrum of compound 6	p. 24
¹ H NMR Spectrum of compound 20	p. 25
¹³ C NMR Spectrum of compound 20	p. 26
¹ H NMR Spectrum of compound 3	p. 27
¹³ C NMR Spectrum of compound 3	p. 28
¹ H NMR Spectrum of compound 22a	p. 29

¹³ C NMR Spectrum of compound 22a	p. 30
¹ H NMR Spectrum of compound 22b	p. 31
¹³ C NMR Spectrum of compound 22b	p. 32
¹ H NMR Spectrum of compound 22c	p. 33
¹³ C NMR Spectrum of compound 22c	p. 34
¹ H NMR Spectrum of compound 22d	p. 35
¹³ C NMR Spectrum of compound 22d	p. 36
¹ H NMR Spectrum of compound 22e	p. 37
¹³ C NMR Spectrum of compound 22e	p. 38
HSQC Spectrum of compound 22e	p. 39
HMBC Spectrum of compound 22e	p. 40
¹ H NMR Spectrum of compound 22f	p. 41
¹³ C NMR Spectrum of compound 22f	p. 42
HSQC Spectrum of compound 22f	p. 43
HMBC Spectrum of compound 22f	p. 44
¹ H NMR Spectrum of compound 22g	p. 45
¹³ C NMR Spectrum of compound 22g	p. 46
¹ H NMR Spectrum of compound 22h	p. 47
¹³ C NMR Spectrum of compound 22h	p. 48
¹ H NMR Spectrum of compound 27	p. 49
¹³ C NMR Spectrum of compound 27	p. 50
¹ H NMR Spectrum of compound 28	p. 51
¹³ C NMR Spectrum of compound 28	p. 52
HSQC Spectrum of compound 28	p. 53
¹ H NMR Spectrum of compound 29	p. 54
¹³ C NMR Spectrum of compound 29	p. 55
HSQC Spectrum of compound 29	p. 56

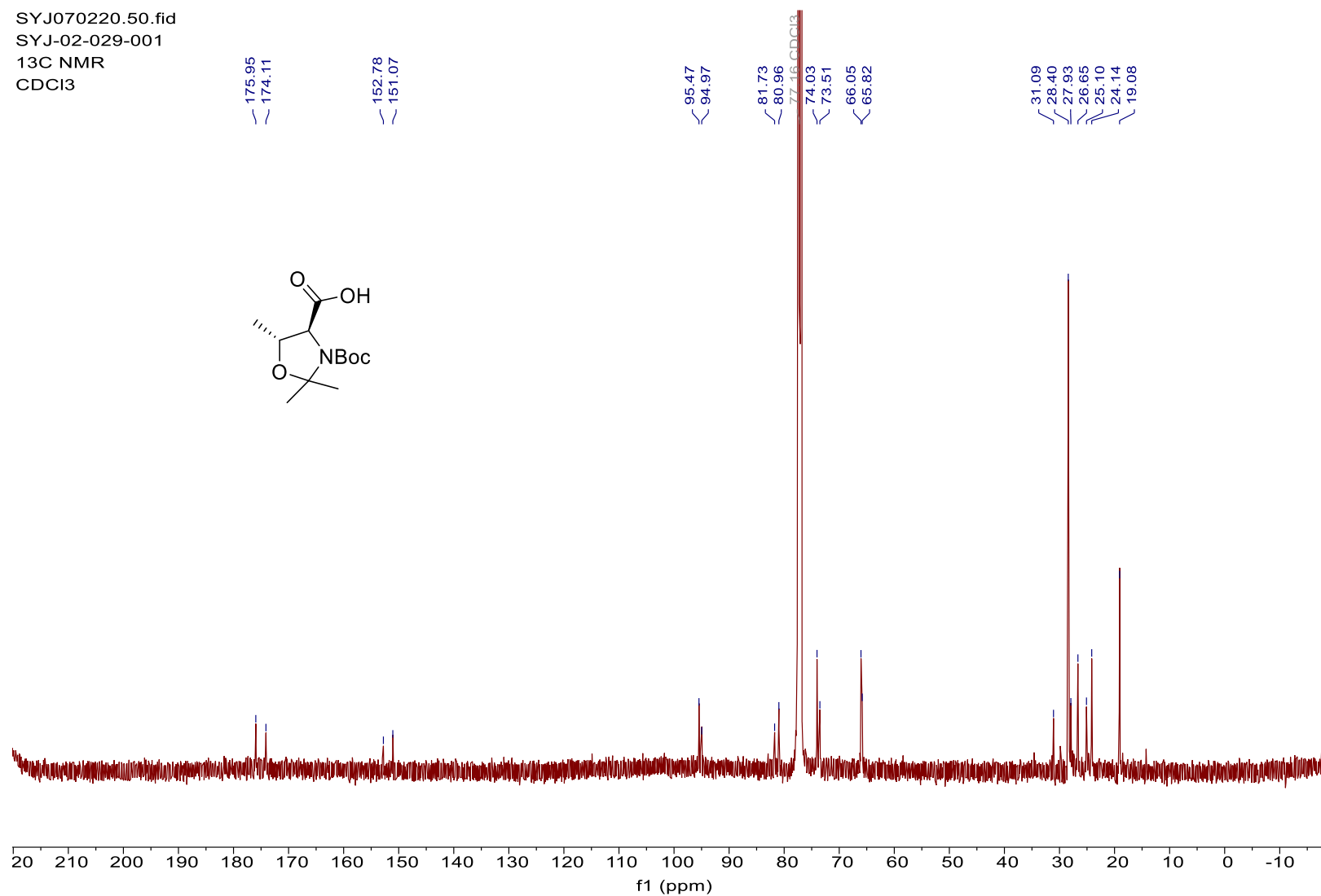
¹ H NMR Spectrum of compound 24	p. 57
¹³ C NMR Spectrum of compound 24	p. 58
HSQC Spectrum of compound 24	p. 59
¹ H NMR Spectrum of compound 25	p. 60
¹³ C NMR Spectrum of compound 25	p. 61
¹ H NMR Spectrum of synthetic micrococcin P2	p. 62
¹³ C NMR Spectrum of synthetic micrococcin P2	p. 63
¹ H NMR Spectrum of synthetic micrococcin P1	p. 64
¹ H NMR Spectrum of authentic micrococcin P1	p. 65
¹ H NMR Spectral comparison of reduced MP2 vs. MP1	p. 66
¹ H NMR Spectrum of reduced MP2 in DMSO- <i>d</i> ₆ : epimers not resolved	p. 67
¹ H NMR Spectrum of reduced MP2 in CDCl ₃ : epimers resolved	p. 68
¹ H NMR Spectrum of compound 30	p. 69
¹³ C NMR Spectrum of compound 30	p. 70
¹ H NMR Spectra of synthetic vs. fermented MP2	p. 71
¹³ C NMR Spectra of synthetic vs. fermented MP2	p. 72

SYJ070220.1.fid
SYJ-02-029-001
1H NMR
CDCl3



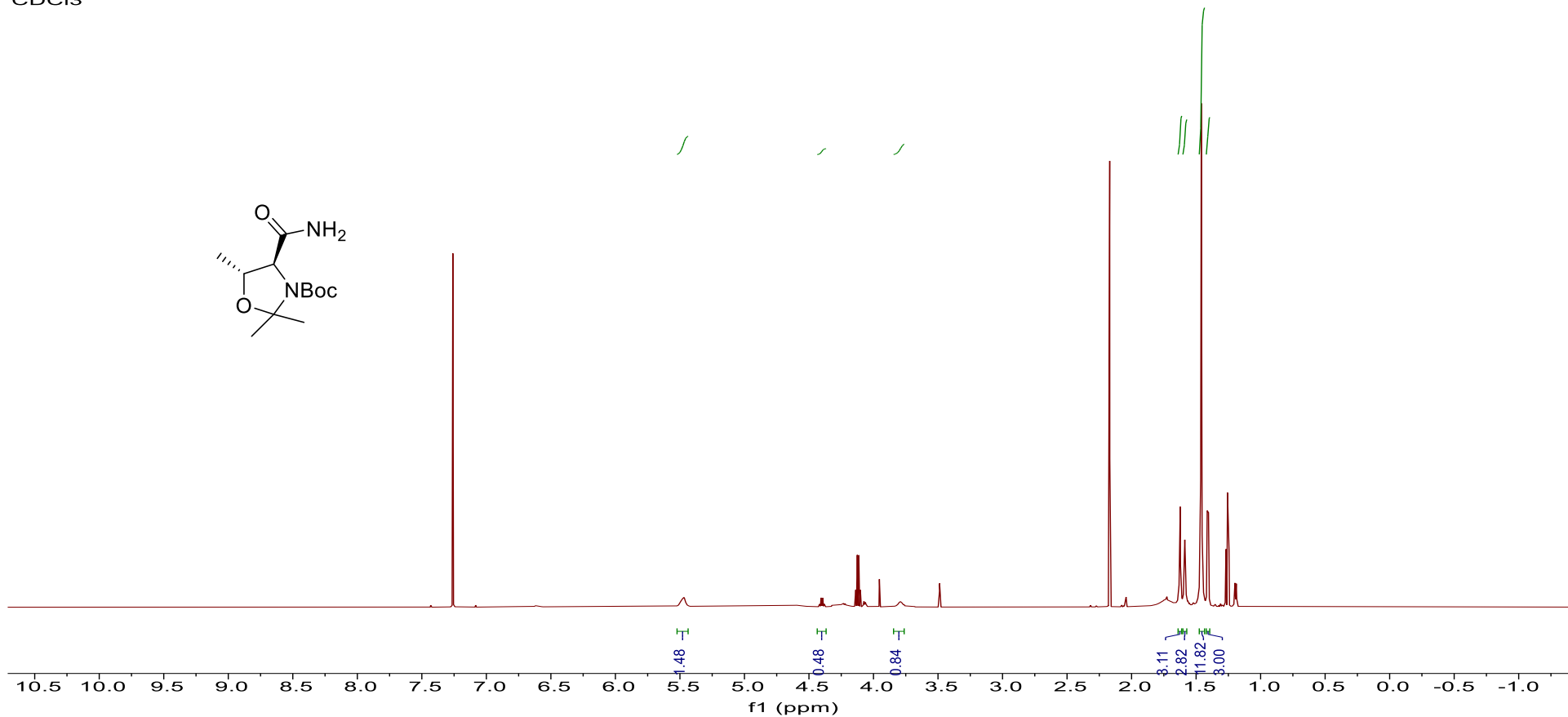
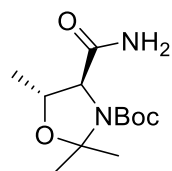
¹H-NMR Spectrum of Compound 8 (600 MHz, CDCl₃)

SYJ070220.50.fid
SYJ-02-029-001
13C NMR
CDCl3



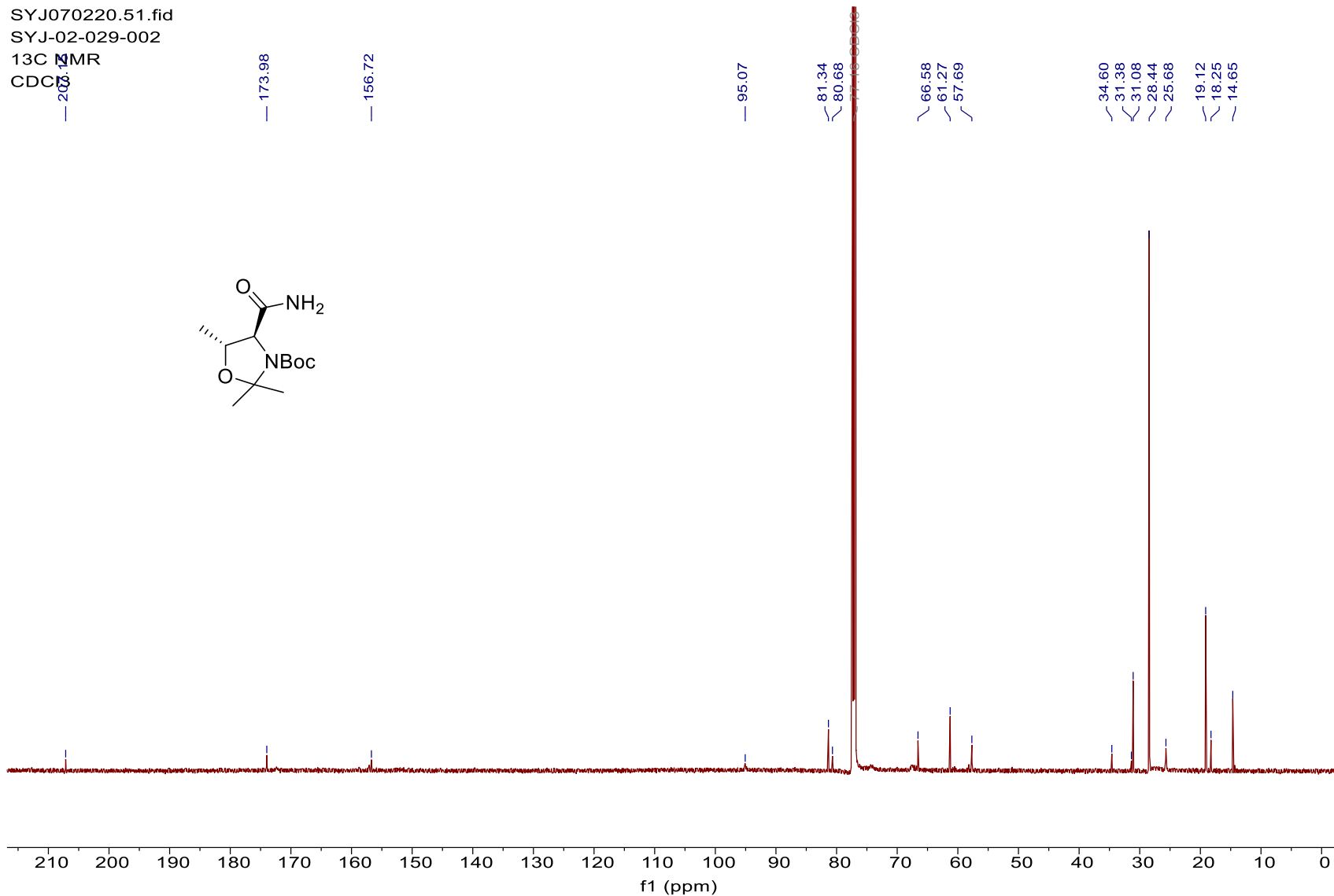
¹³C NMR Spectrum of Compound 8 (151 MHz, CDCl₃)

SYJ070220.10.fid
SYJ-02-029-002
1H NMR
CDCl₃



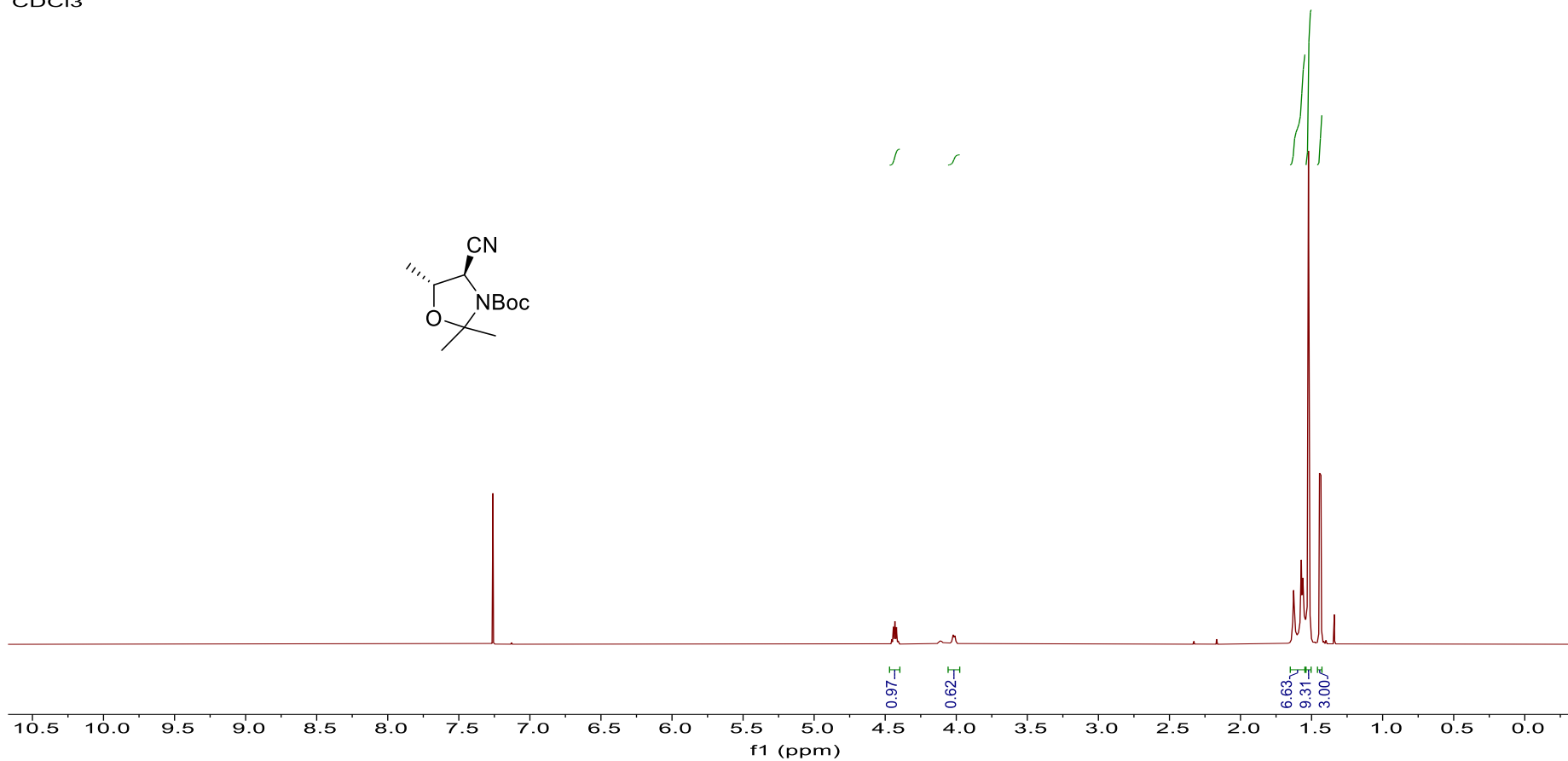
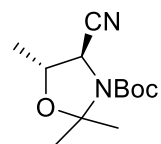
¹H-NMR Spectrum of Compound 9 (600 MHz, CDCl₃)

SYJ070220.51.fid
SYJ-02-029-002
13C NMR
CDCl₃



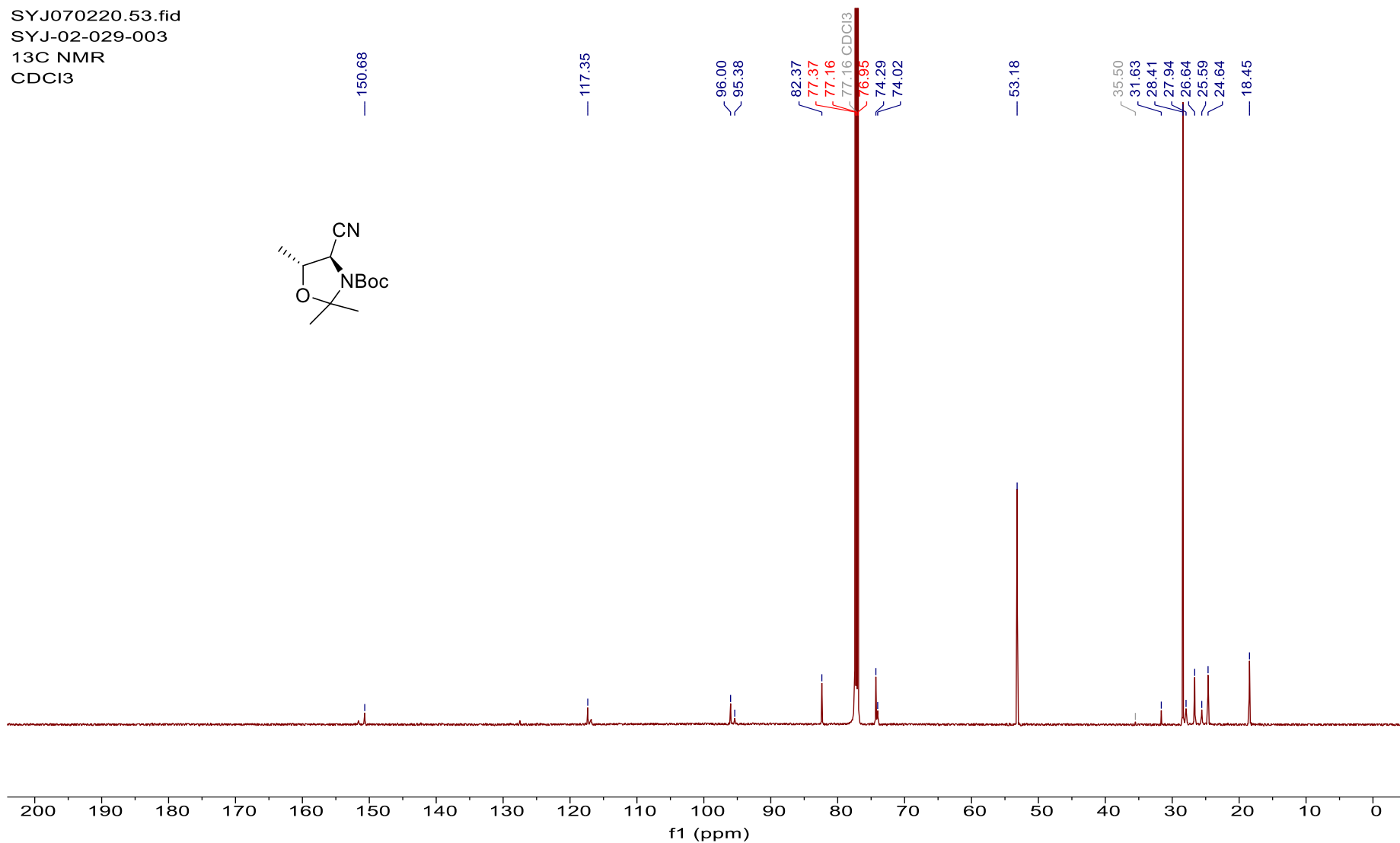
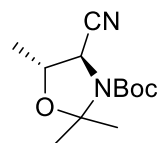
¹³C-NMR Spectrum of Compound 9 (151 MHz, CDCl₃)

SYJ070220.20.fid
SYJ-02-029-003
1H NMR
CDCl3



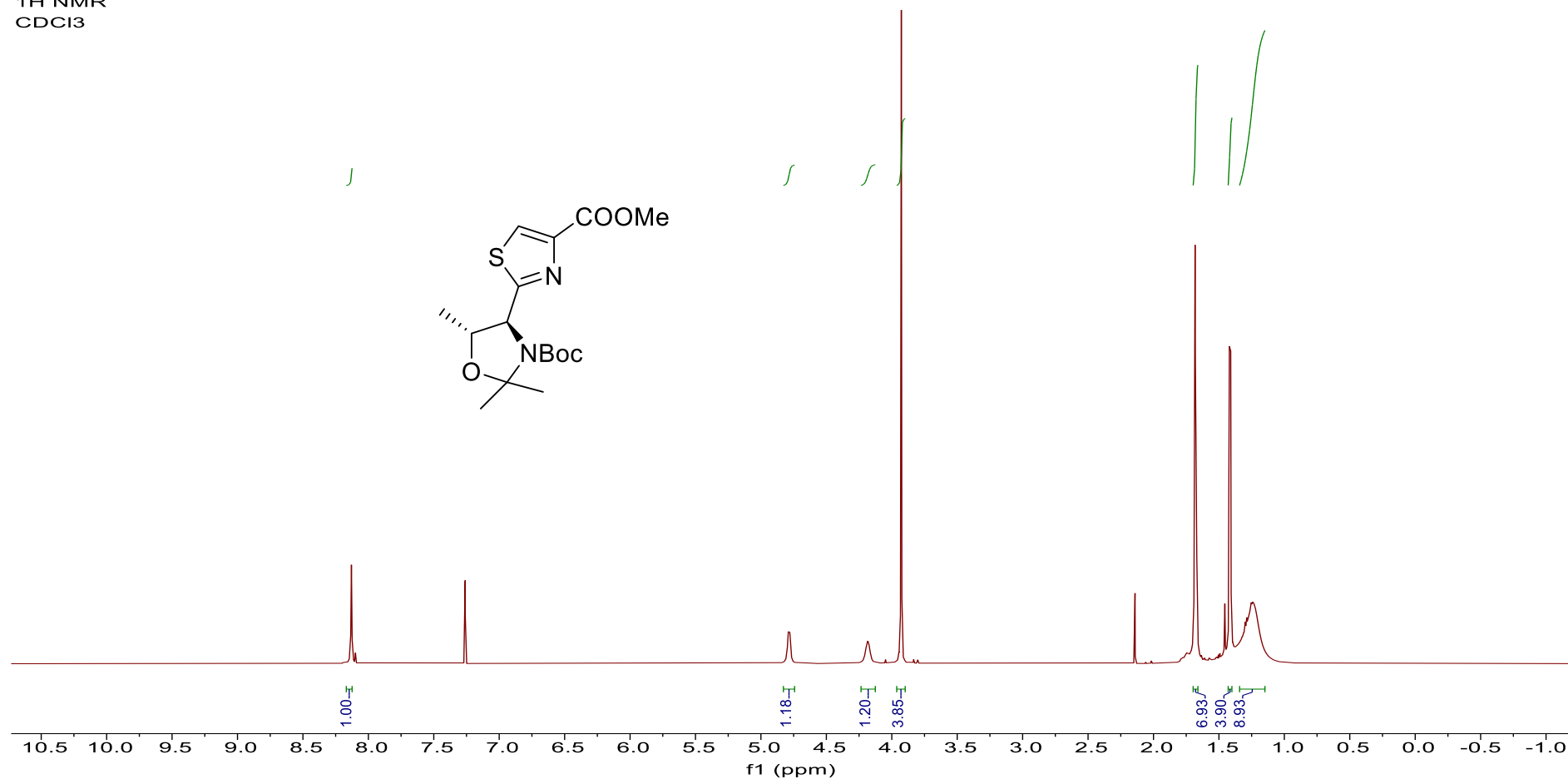
¹H-NMR Spectrum of Compound 10 (600 MHz, CDCl₃)

SYJ070220.53.fid
SYJ-02-029-003
13C NMR
CDCl3



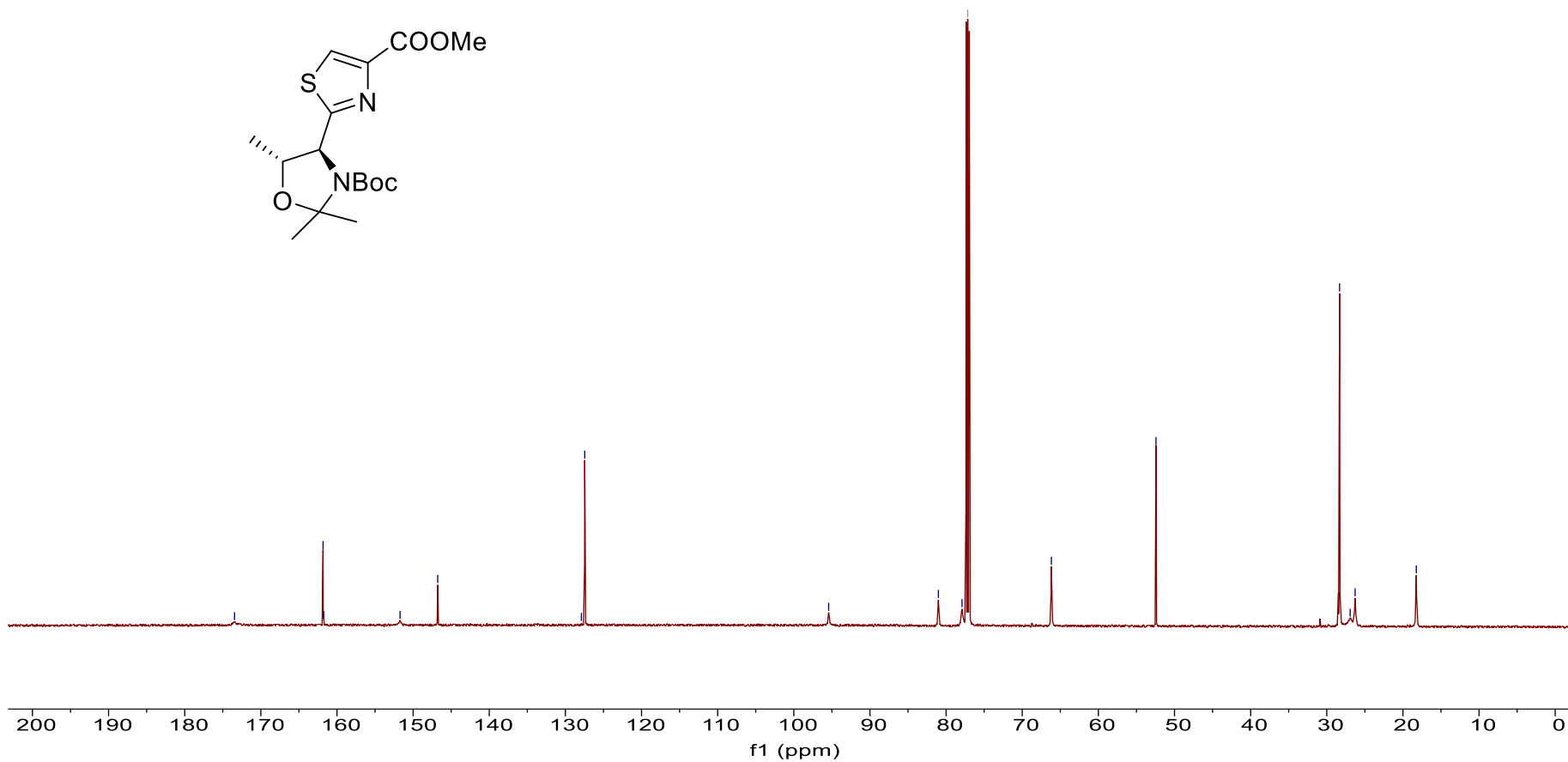
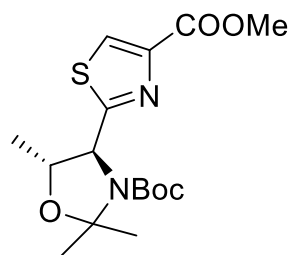
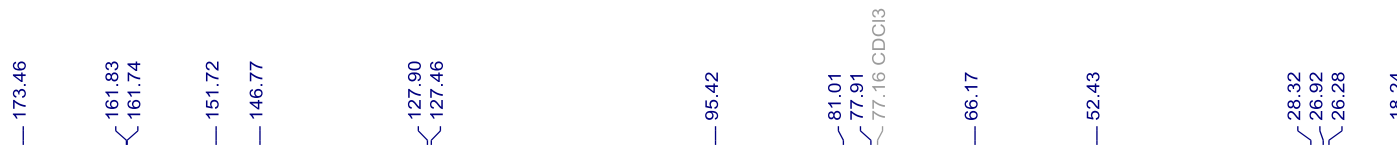
13C-NMR Spectrum of Compound 10 (151 MHz, CDCl3)

SYJ080620.30.fid
SYJ-02-029-004
1H NMR
CDCl3



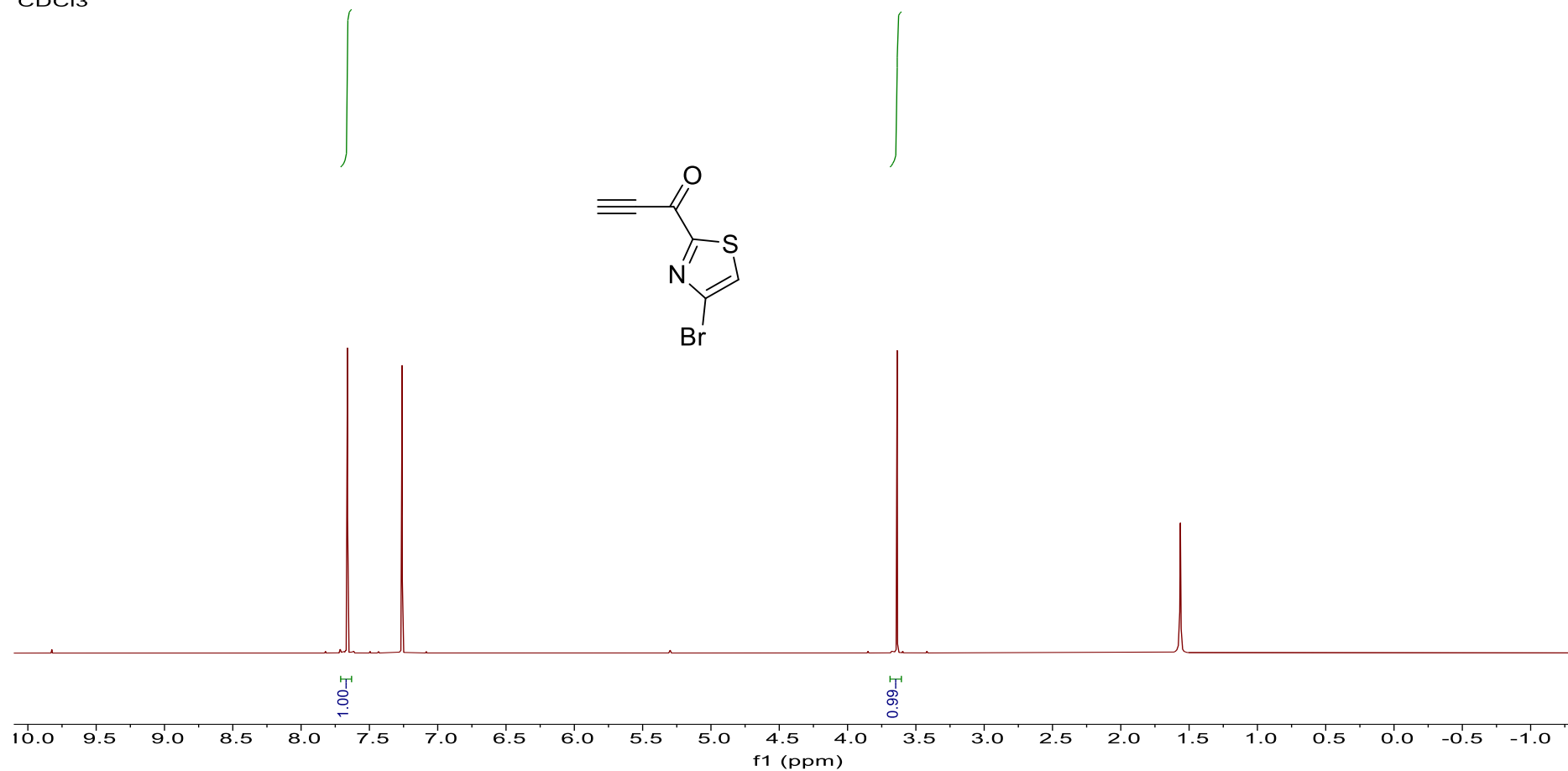
¹H-NMR Spectrum of Compound 12 (600 MHz, CDCl₃, 50 °C)

SYJ080620.31.fid
SYJ-02-029-004
13C NMR
CDCl3



¹³C-NMR Spectrum of Compound 12 (151 MHz, CDCl₃, 50 °C)

SYJ070220.60.fid
SYJ-02-029-006
1H NMR
CDCl3



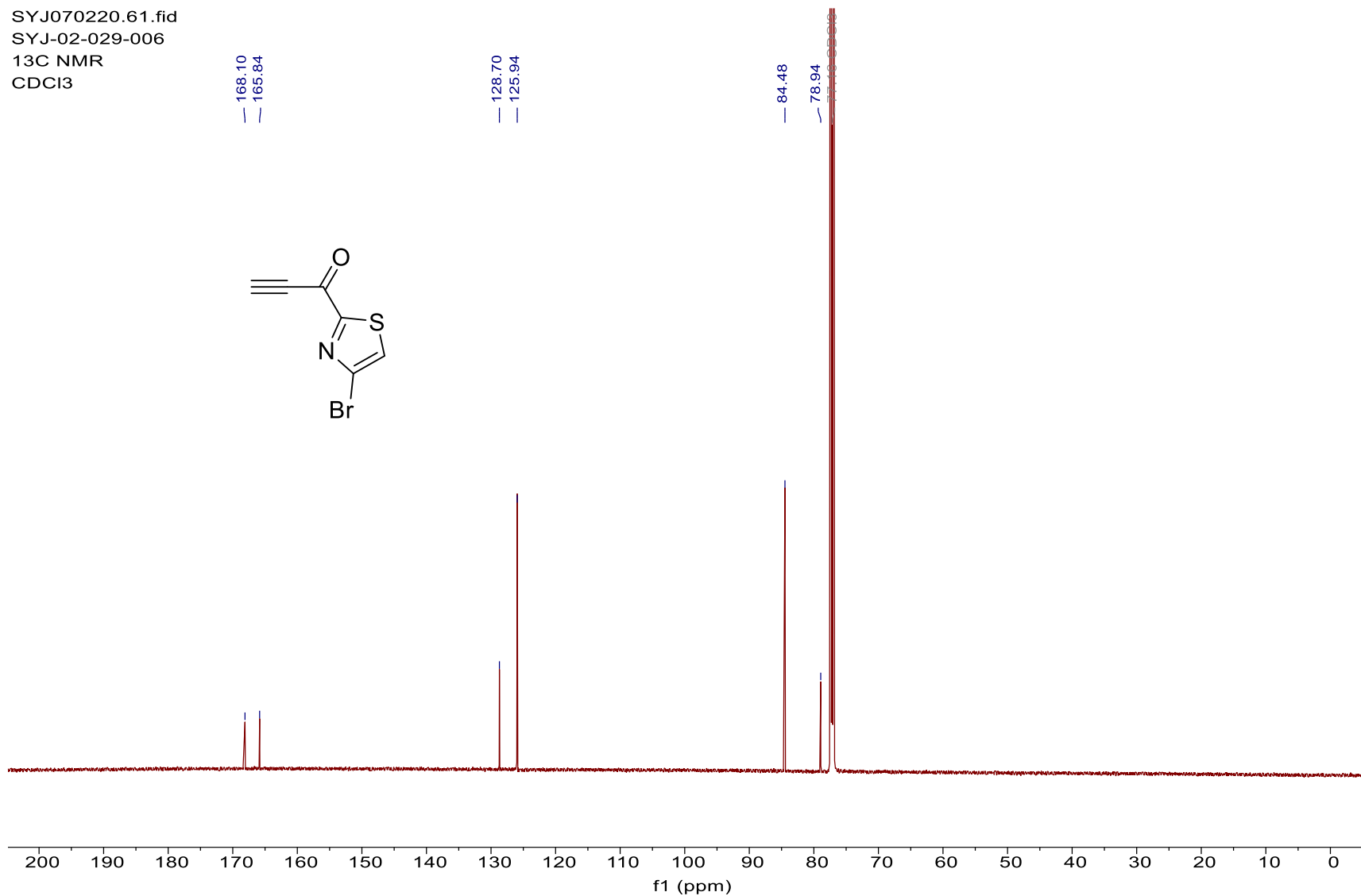
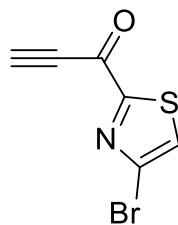
¹H-NMR Spectrum of Compound 15 (600 MHz, CDCl₃)

SYJ070220.61.fid
SYJ-02-029-006
13C NMR
CDCl3

168.10
165.84

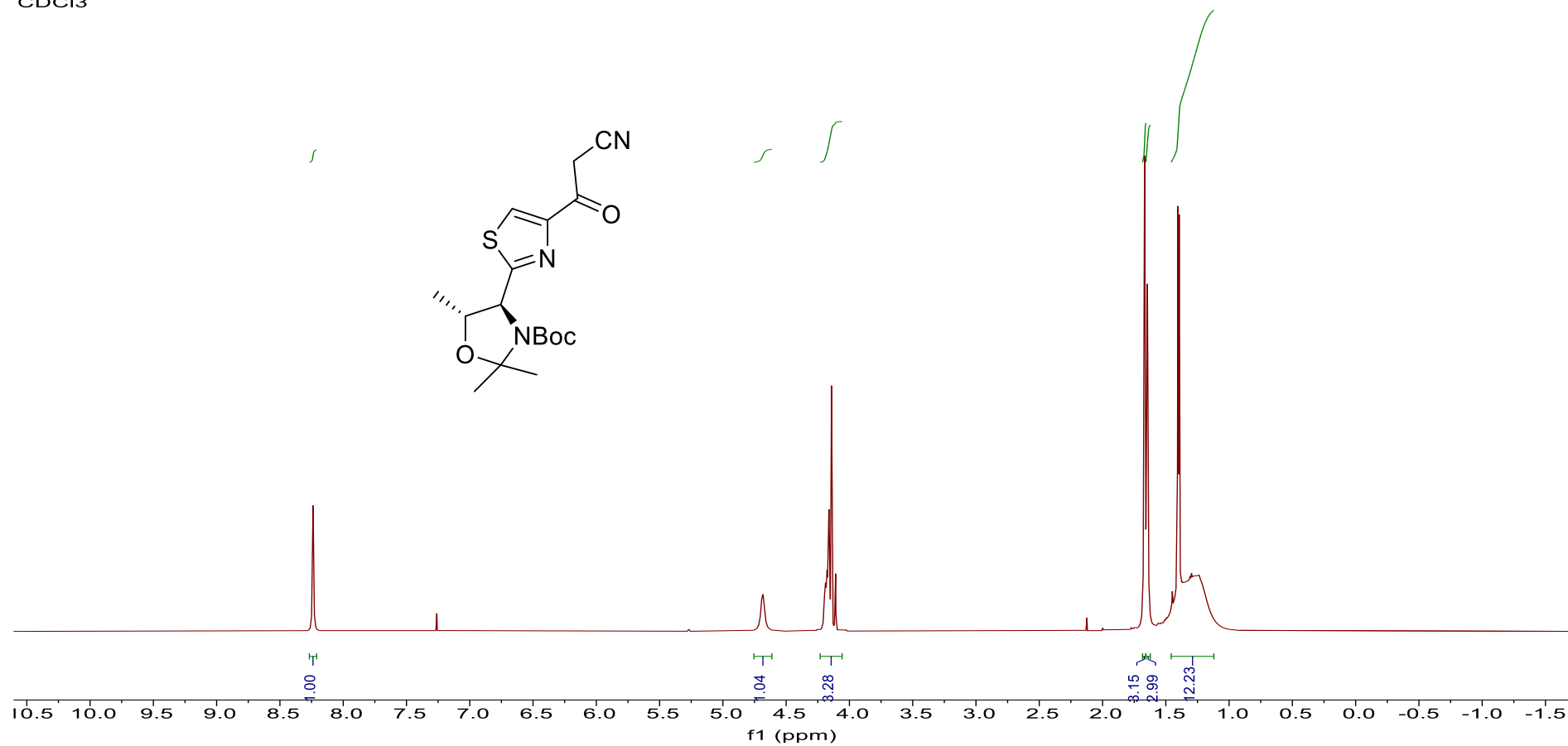
128.70
125.94

84.48
78.94



¹³C-NMR Spectrum of Compound 15 (151 MHz, CDCl₃)

SYJ091620.10.fid
SYJ-02-029-005
1H NMR
CDCl₃



¹H-NMR Spectrum of Compound 16 (600 MHz, CDCl₃, 50 °C)

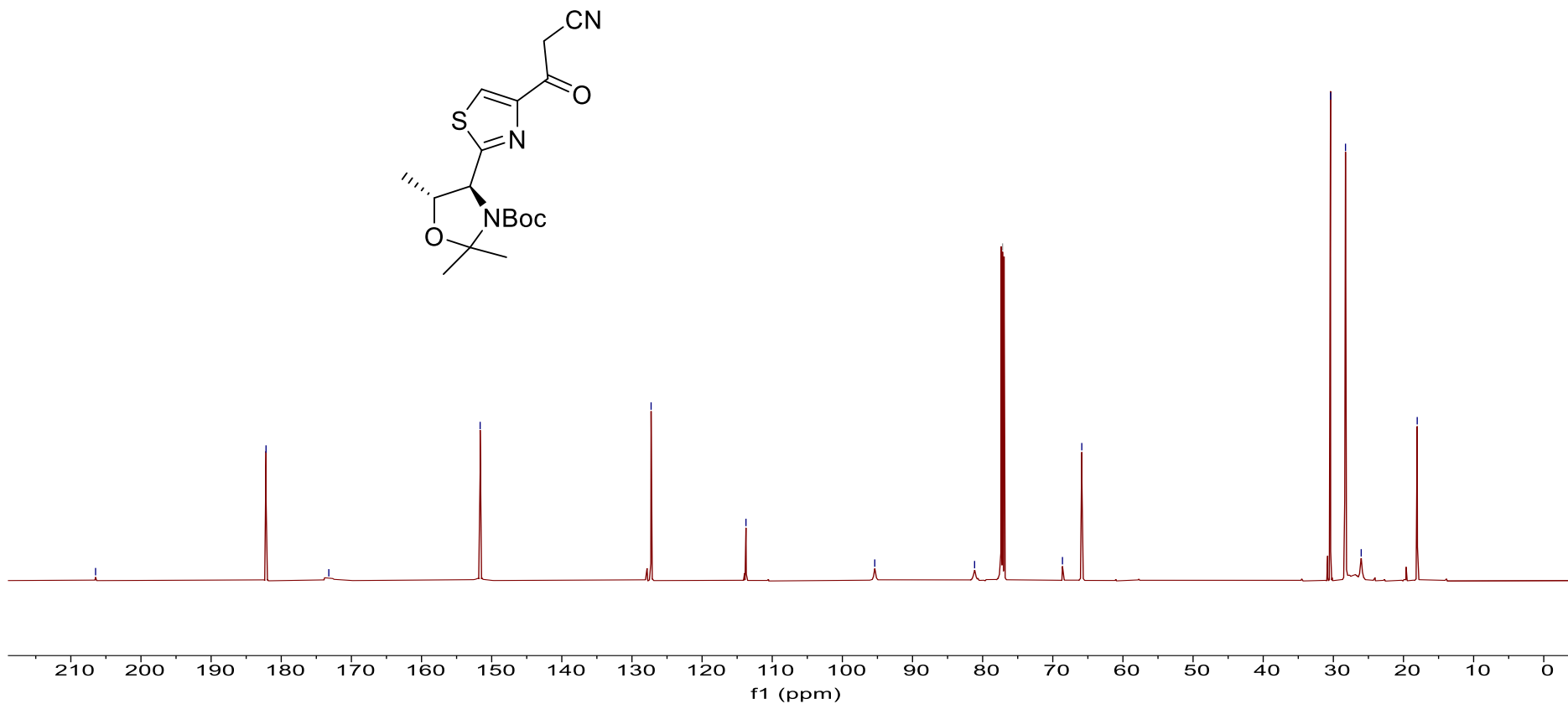
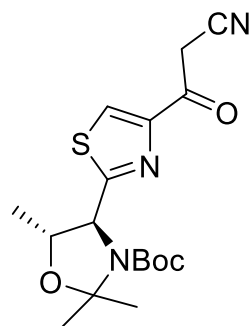
FPKBmGAmSt6XwmCMzTrFiw.12.fid

SYJ-02-029-005

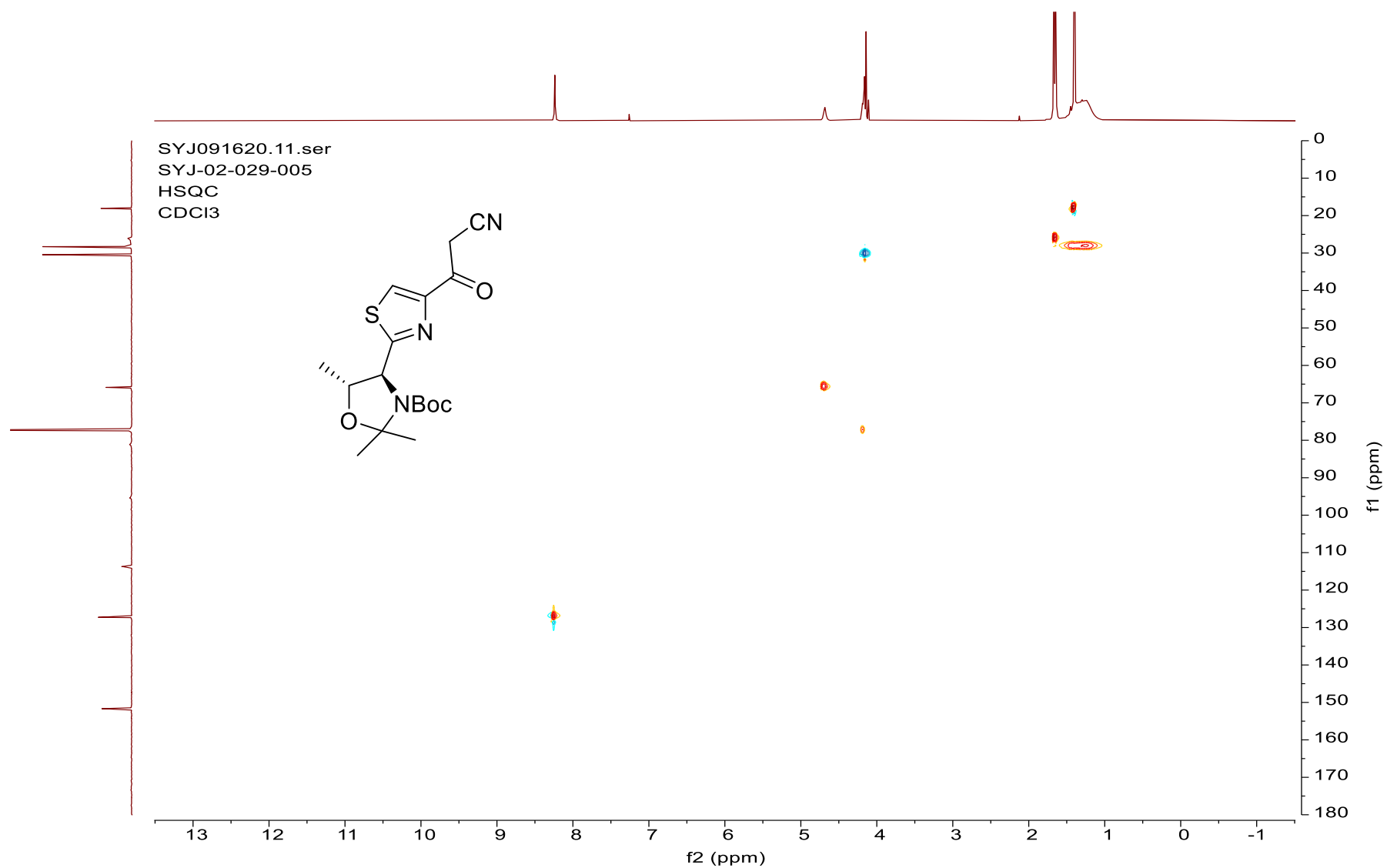
13C NMR

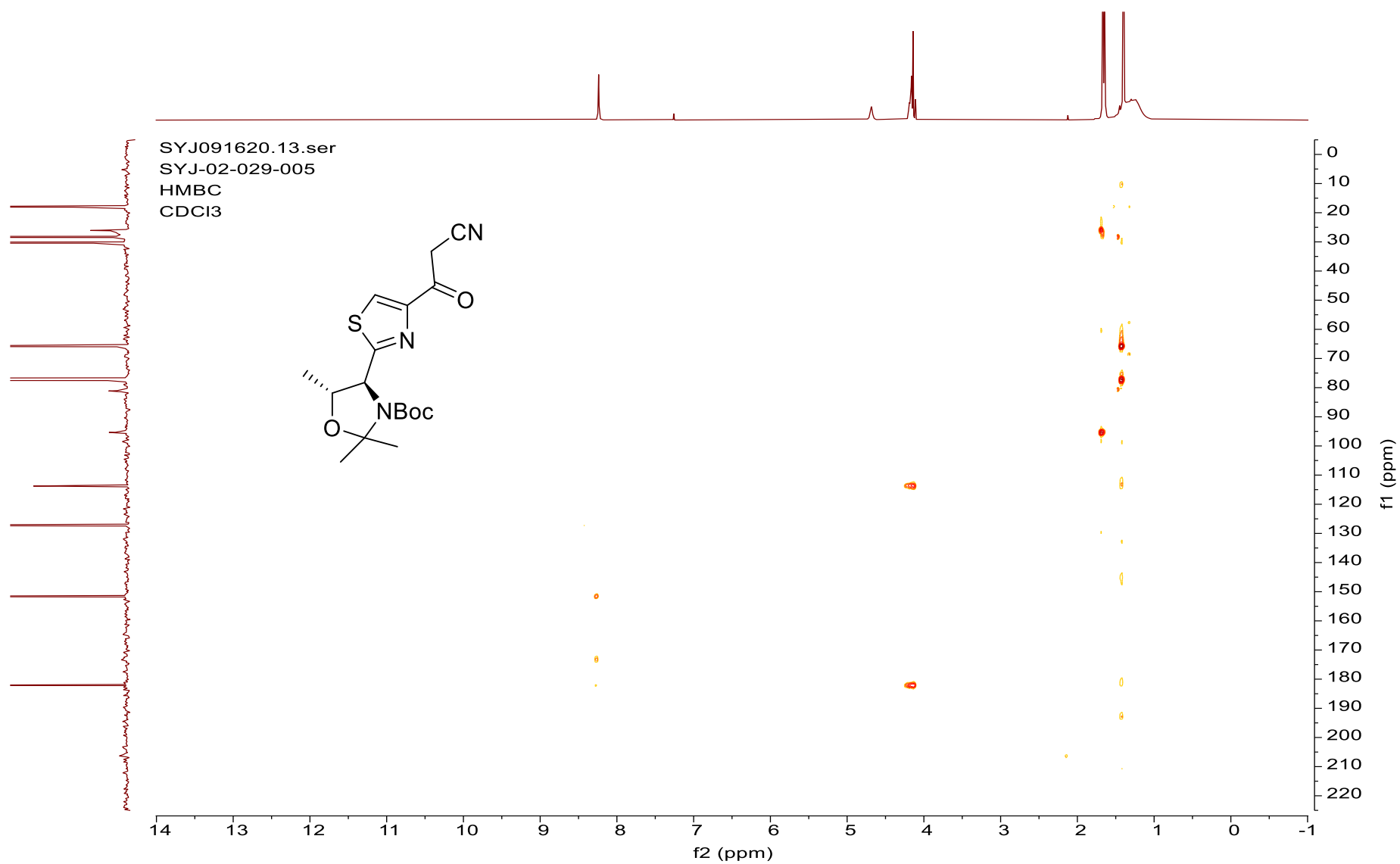
CDCl₃

206.48 182.17 173.22 151.64 127.27 113.74 95.38 81.15 77.16 CDCl₃ 68.62 65.87 30.40 28.27 26.03 18.04

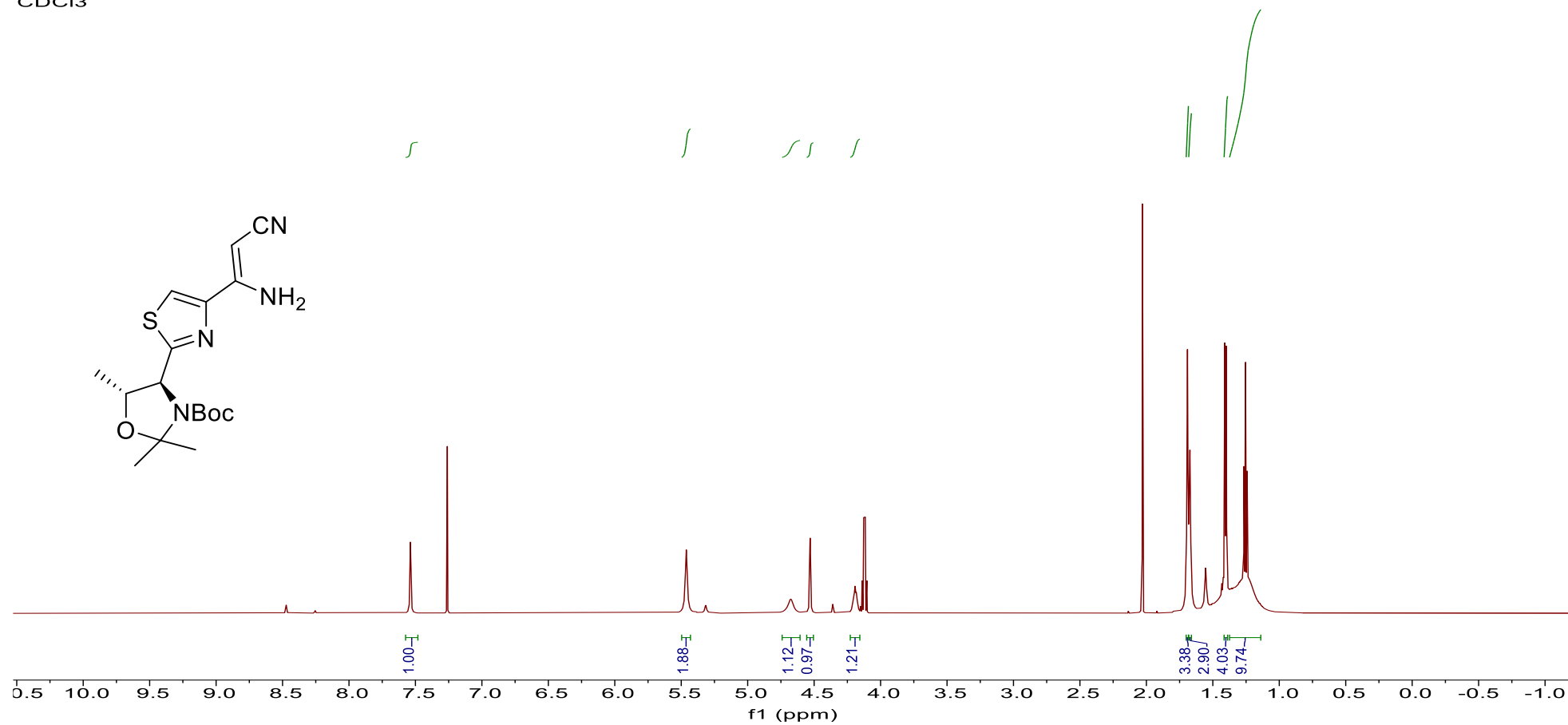


¹³C-NMR Spectrum of Compound 16 (151 MHz, CDCl₃, 50 °C)

**HSQC Spectrum of Compound 16 (600 MHz, CDCl₃)**

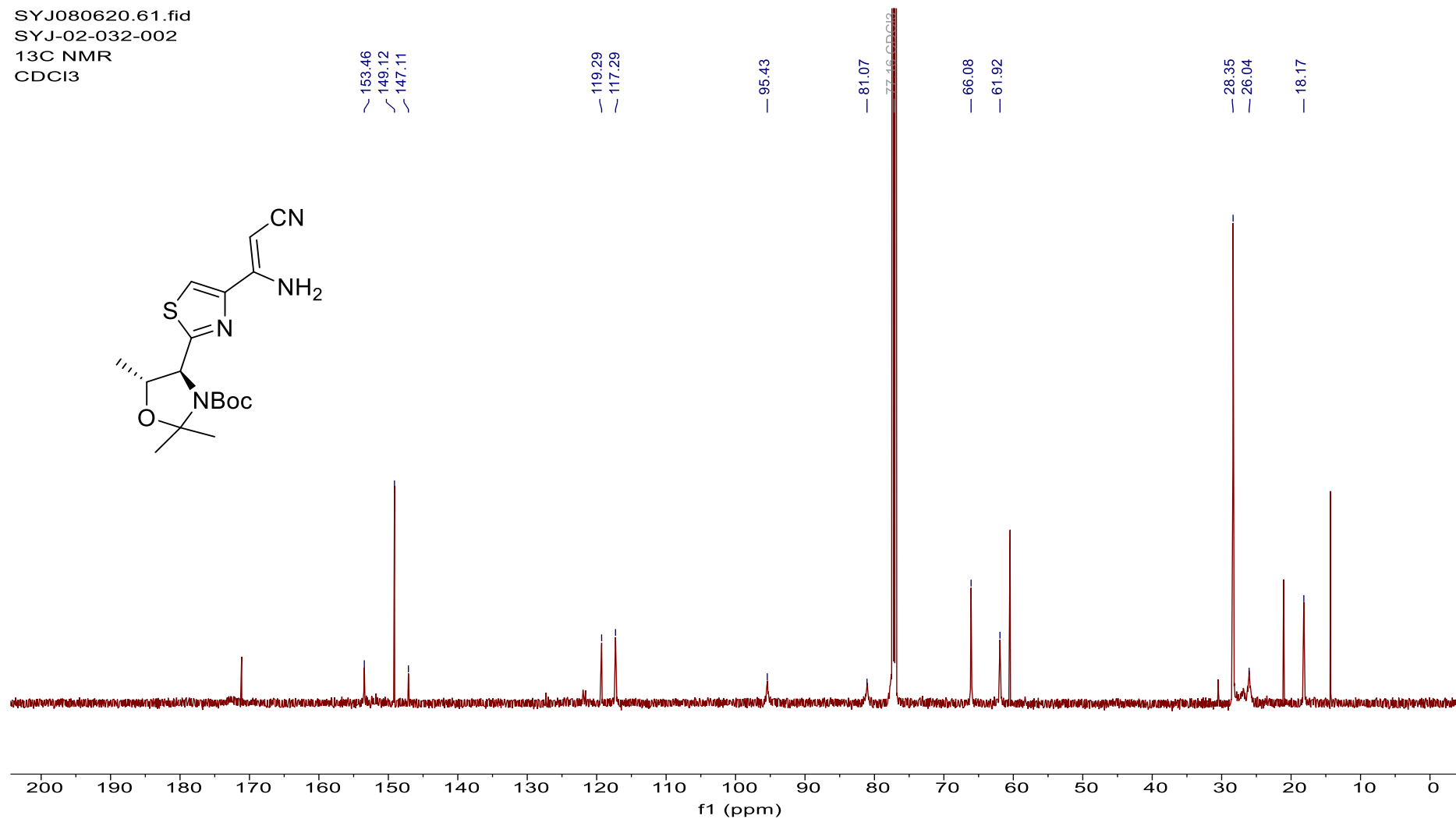
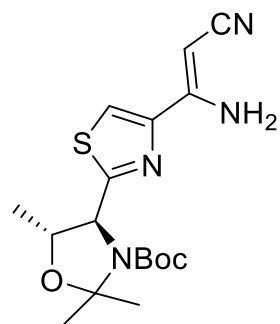
HMBC Spectrum of Compound 16 (600 MHz, CDCl₃)

SYJ080620.62.fid
SYJ-02-032-002
1H NMR
CDCl3



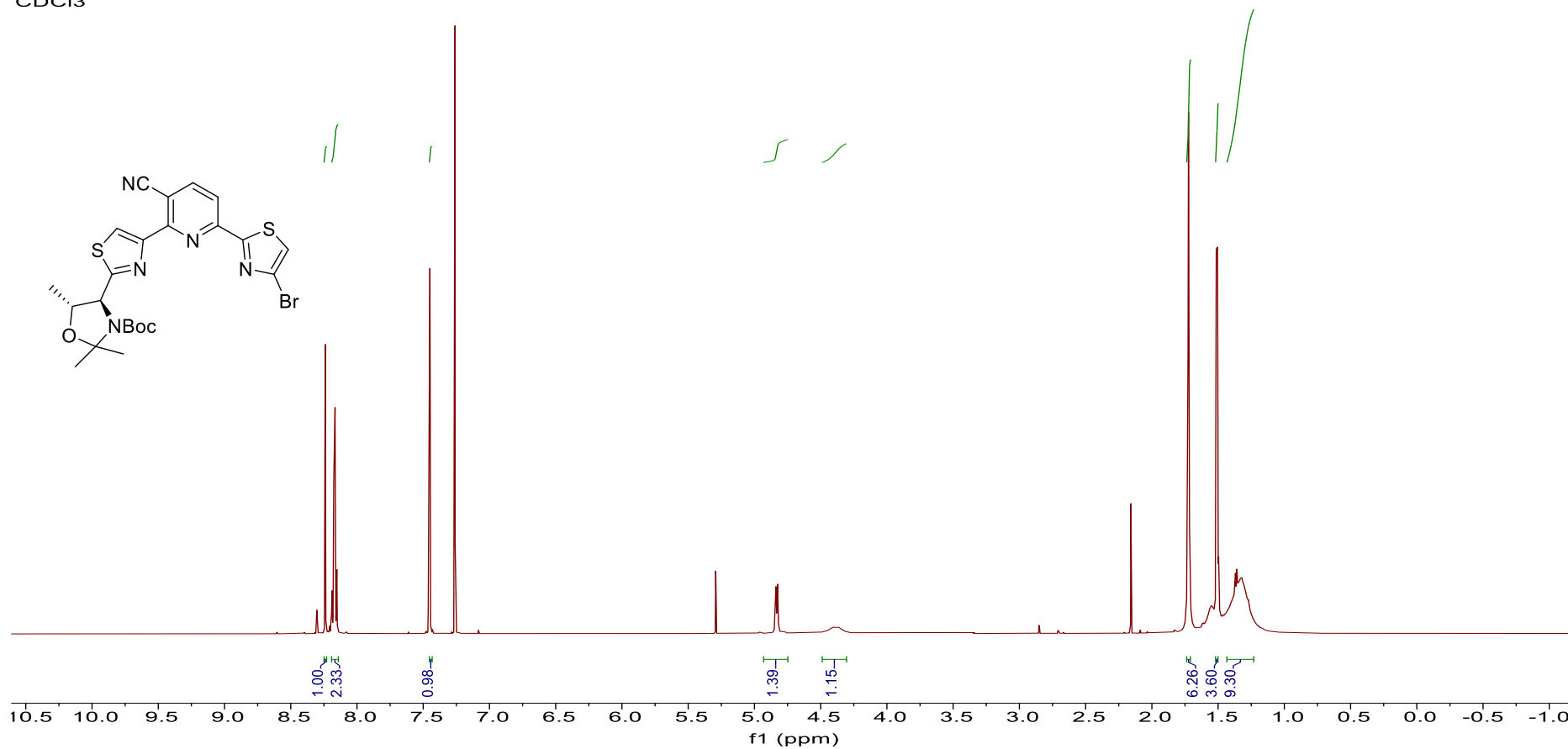
¹H-NMR Spectrum of Compound 17 (600 MHz, CDCl₃, 50 °C)

SYJ080620.61.fid
SYJ-02-032-002
13C NMR
CDCl3



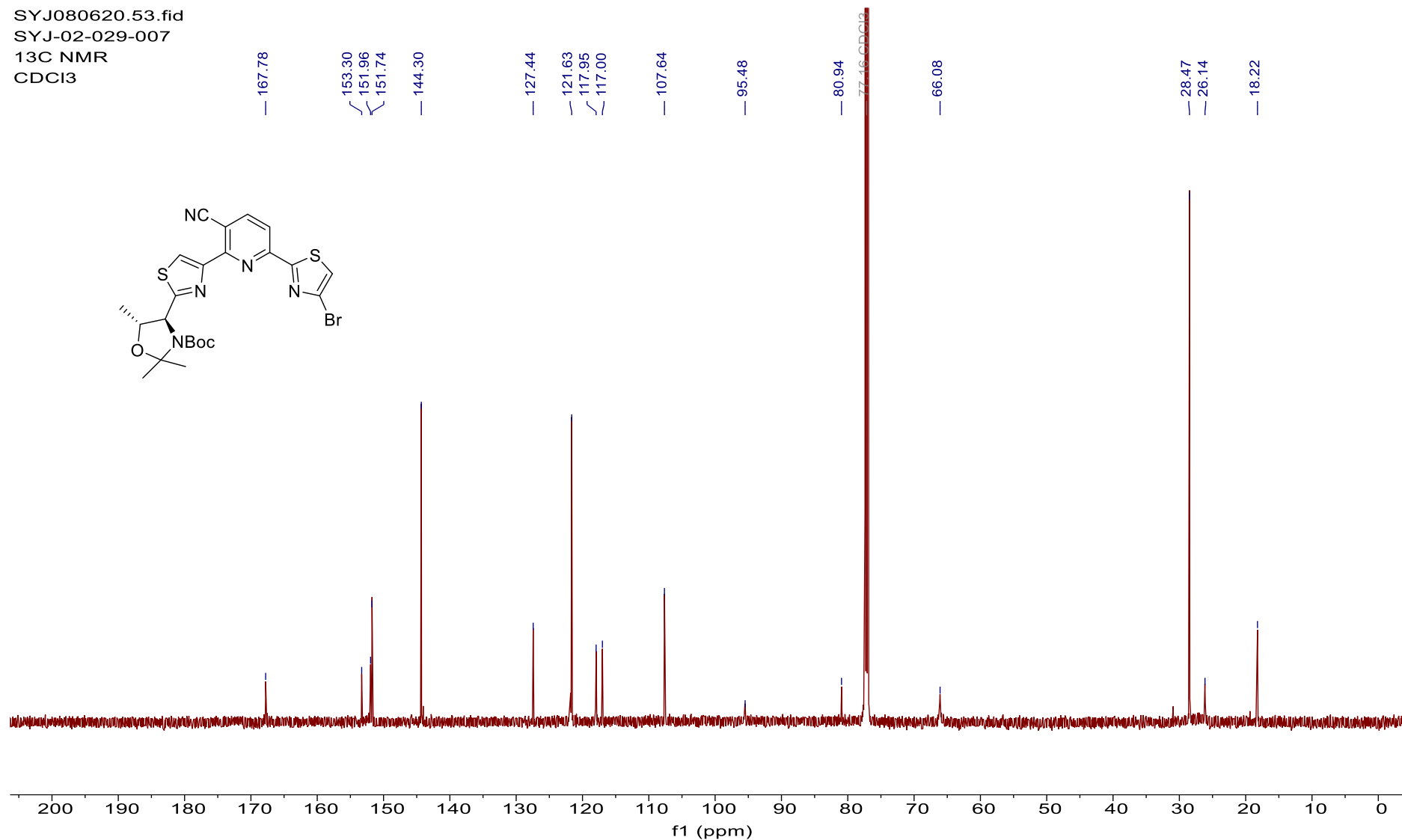
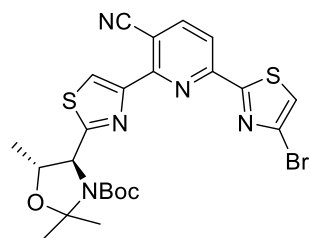
¹³C-NMR Spectrum of Compound 17 (151 MHz, CDCl₃, 50 °C)

SYJ080620.52.fid
SYJ-02-029-007
1H NMR
CDCl3



¹H-NMR Spectrum of Compound 18 (600 MHz, CDCl₃, 50 °C)

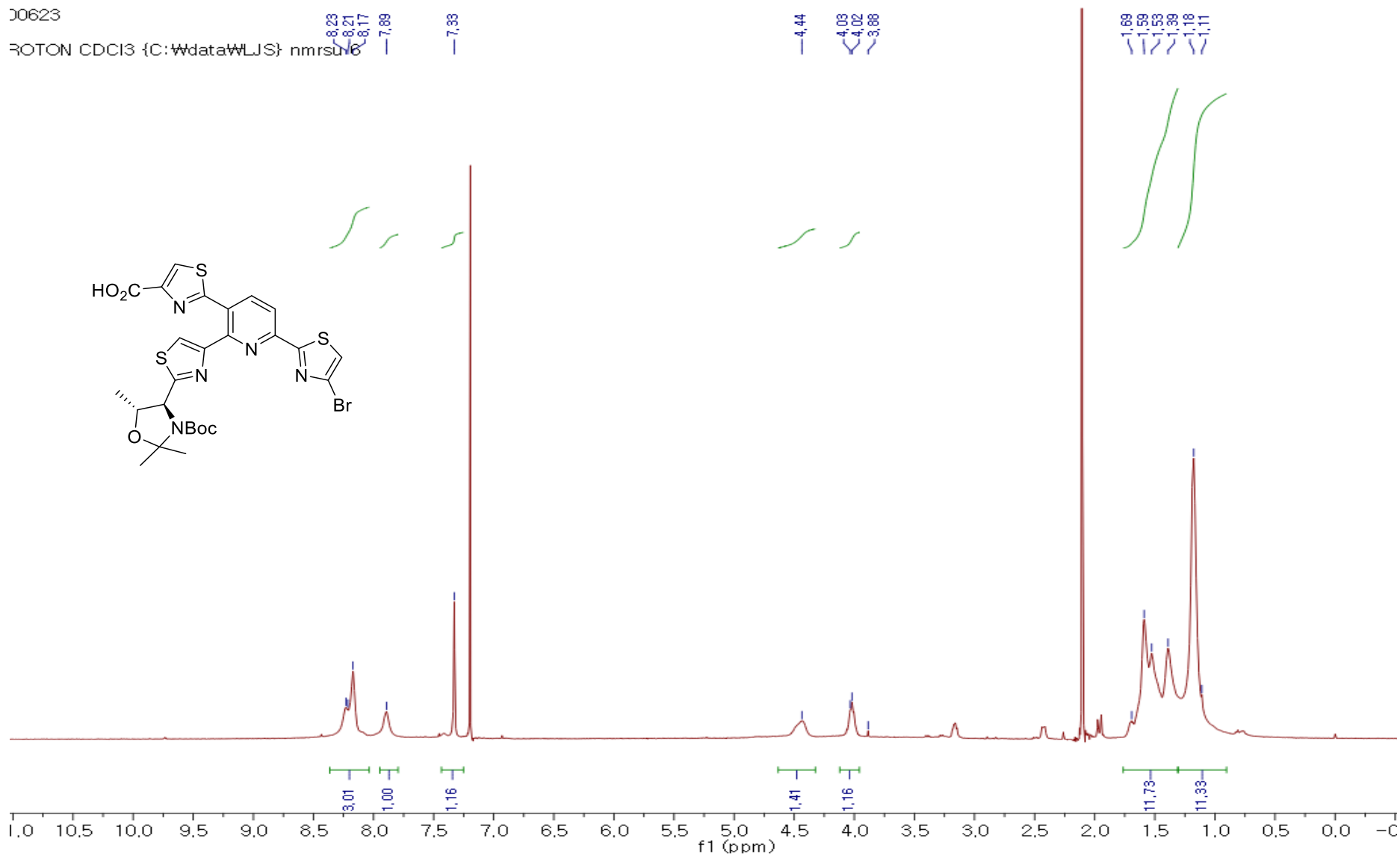
SYJ080620.53.fid
 SYJ-02-029-007
 13C NMR
 CDCl3



¹³C-NMR Spectrum of Compound 18 (151 MHz, CDCl₃, 50 °C)

00623

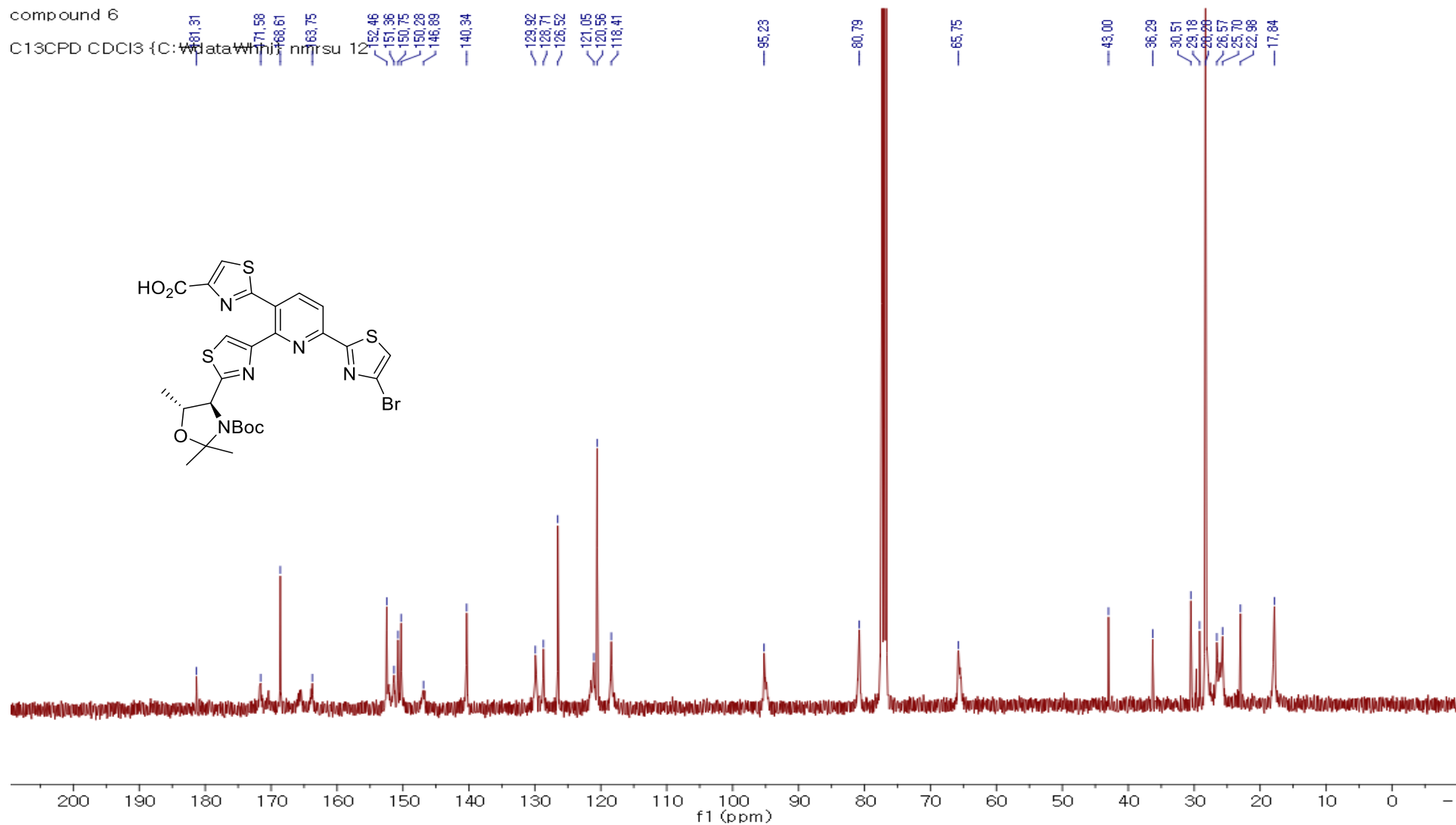
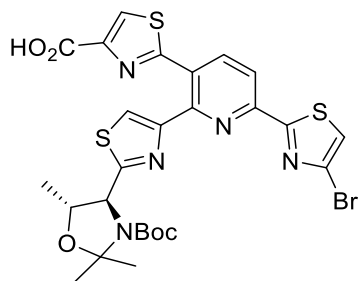
ROTUN CDCI3 {C:\wdata\WLS} nmrsun6



¹H-NMR Spectrum of Compound 6 (400 MHz, CDCl₃)

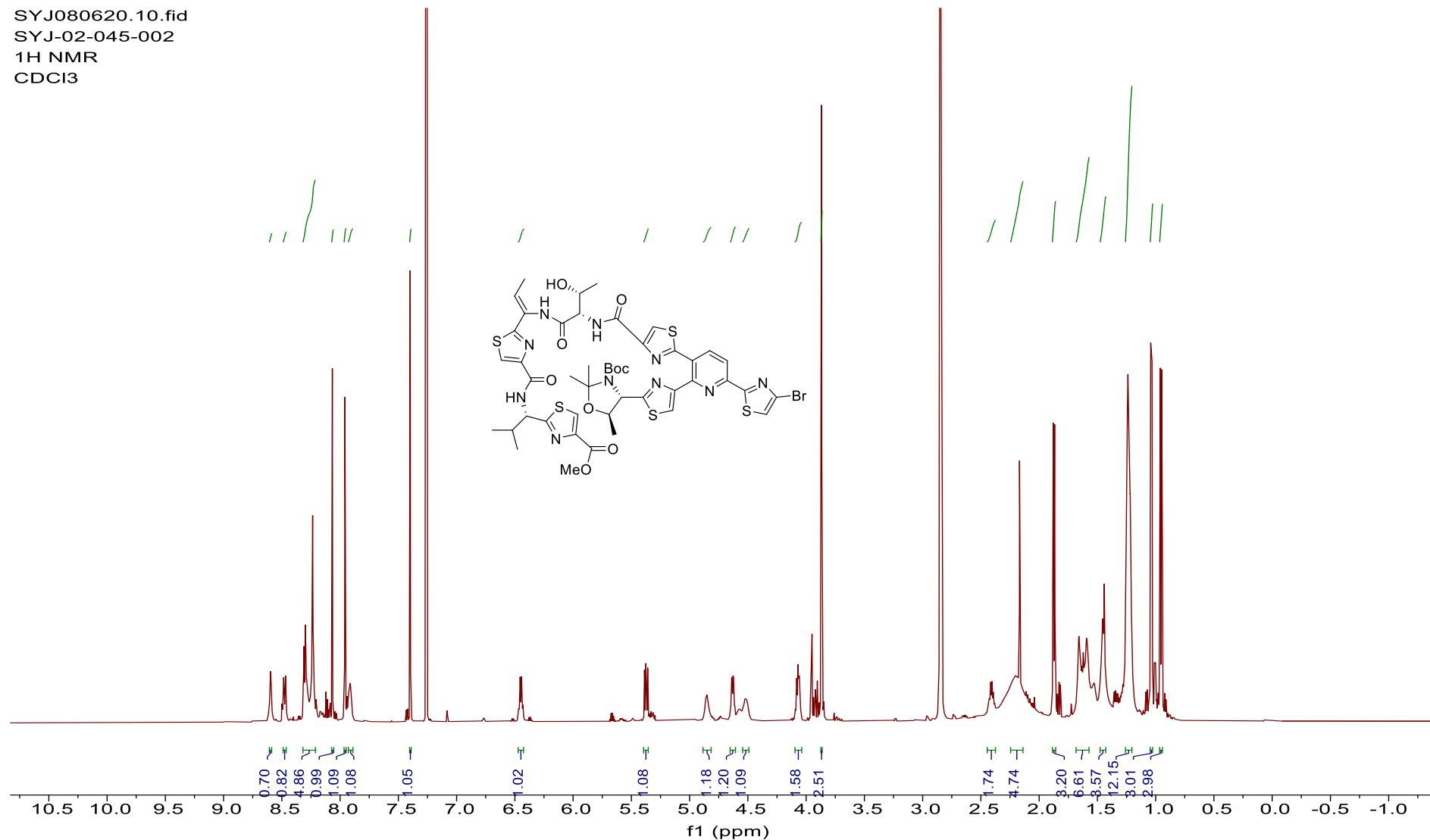
compound 6

C13CPD CDCl3 (C: wdata-whip1 nmr su 12



¹³C-NMR Spectrum of Compound 6 (100 MHz, CDCl₃)

SYJ080620.10.fid
 SYJ-02-045-002
 1H NMR
 CDCl3



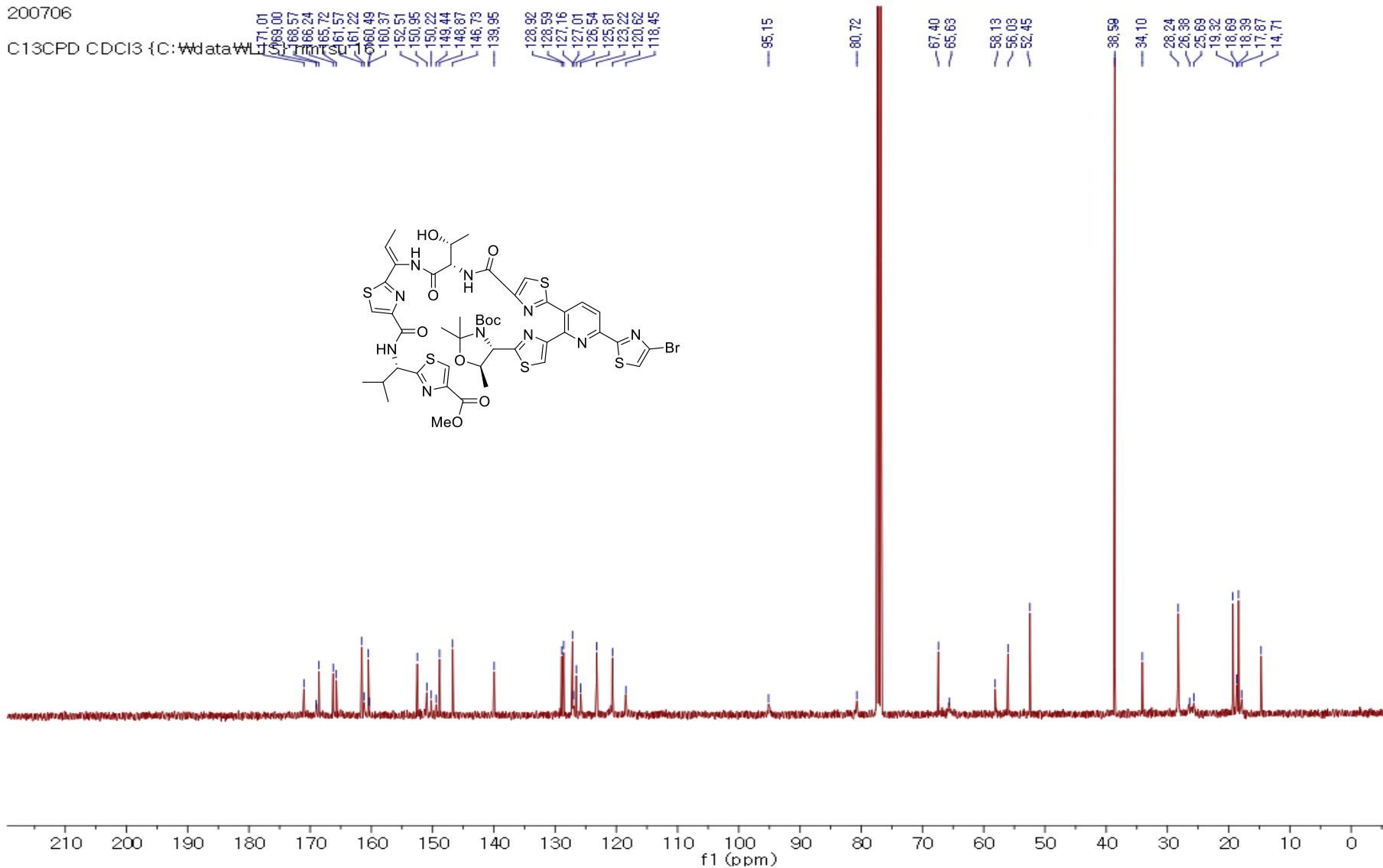
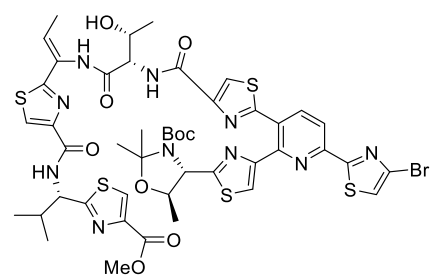
¹H-NMR Spectrum of Compound 20 (600 MHz, CDCl₃)

200706

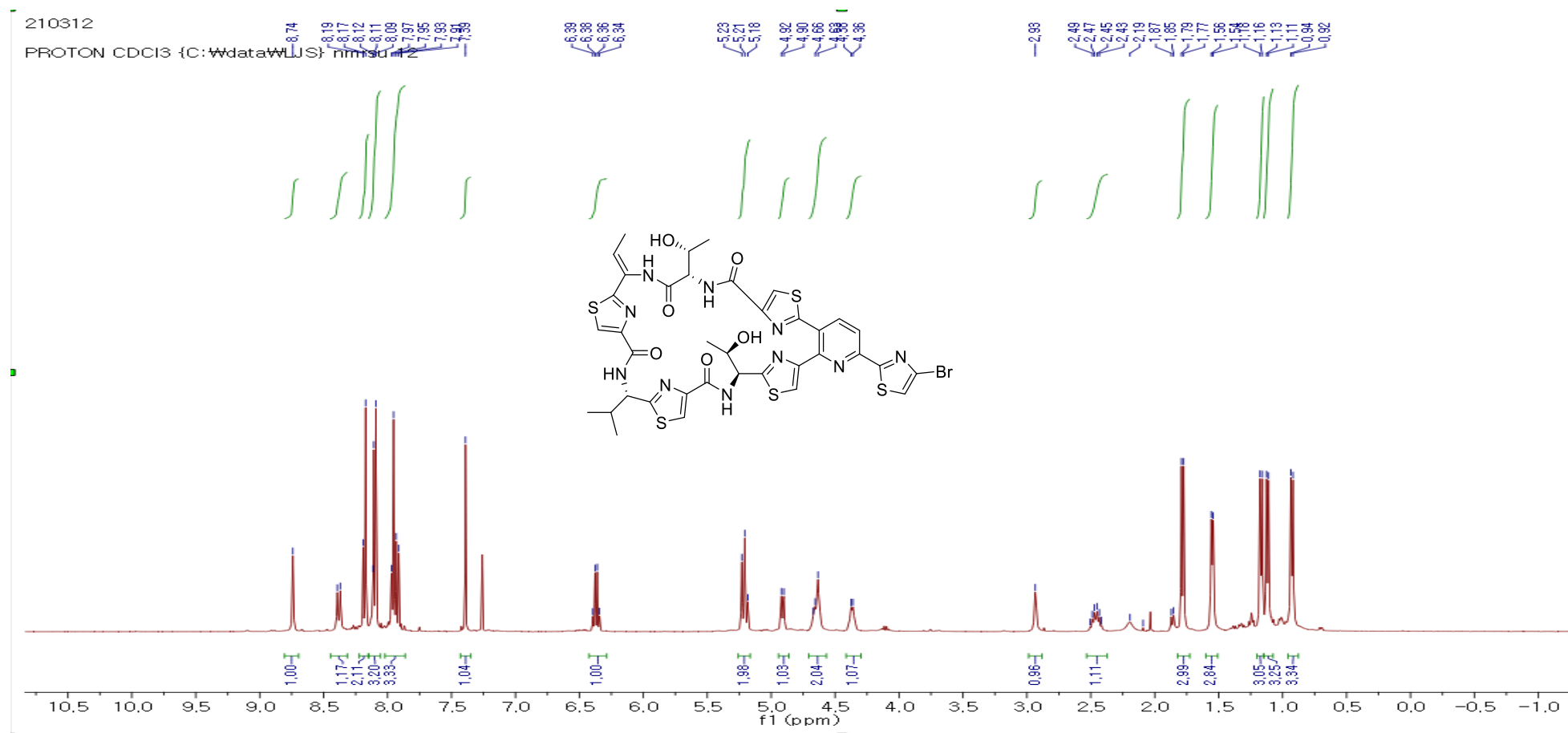
C13CPD CDCI3 {C:\wdata\WLI

171.01
168.00
168.57
166.24
165.72
161.57
161.22
160.49
160.37
152.51
150.95
150.22
149.44
148.87
146.73
139.95
128.92
128.99
127.16
127.01
126.54
125.81
123.22
120.62
118.45

95.15
80.72
67.40
65.63
58.13
56.03
52.45
38.59
34.10
28.24
26.38
25.69
19.32
18.69
18.39
17.87
14.71



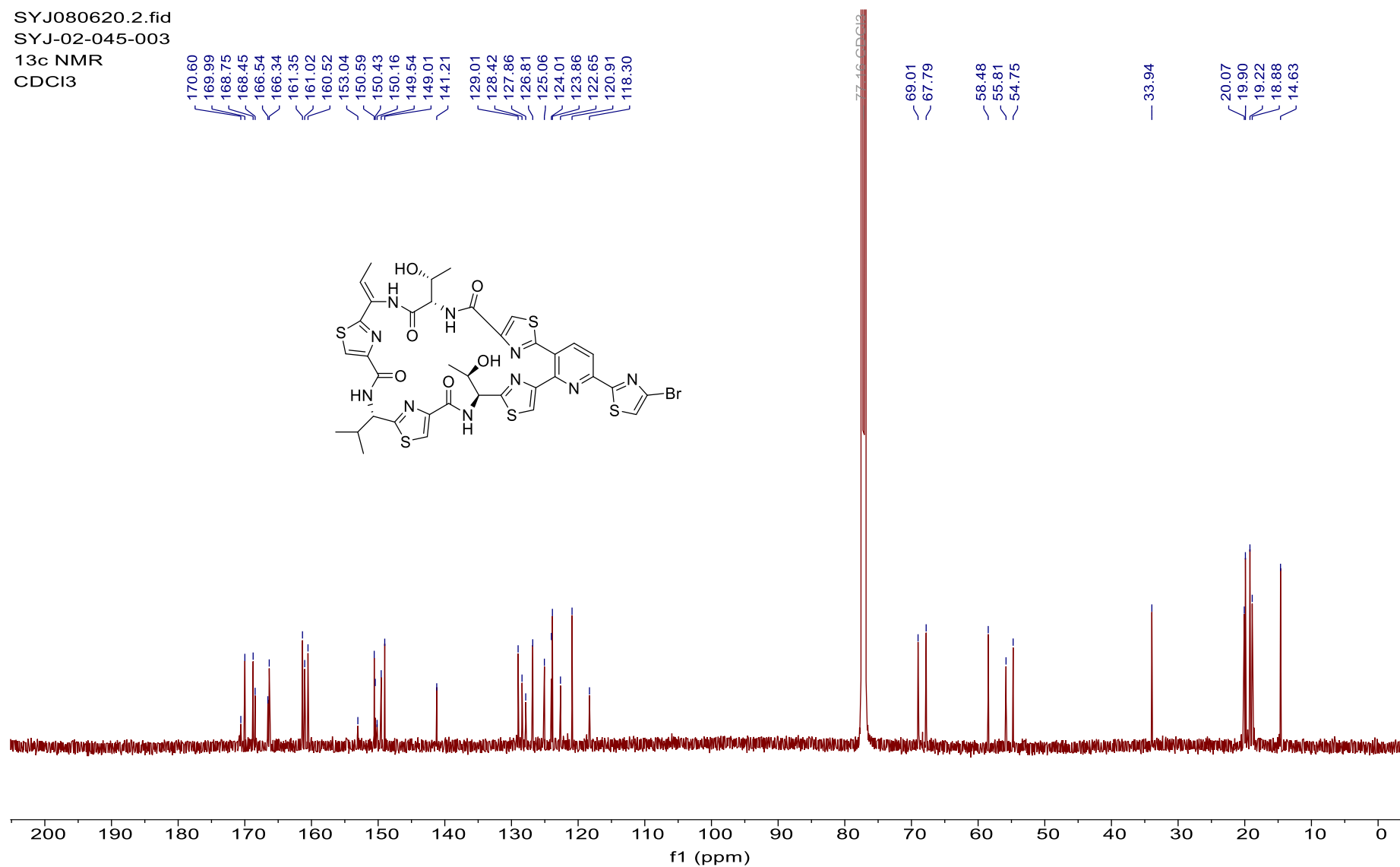
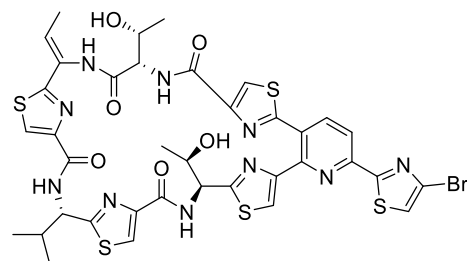
¹³C-NMR Spectrum of Compound 20 (100 MHz, CDCl₃)



¹H-NMR Spectrum of Compound 3 (400 MHz, CDCl₃)

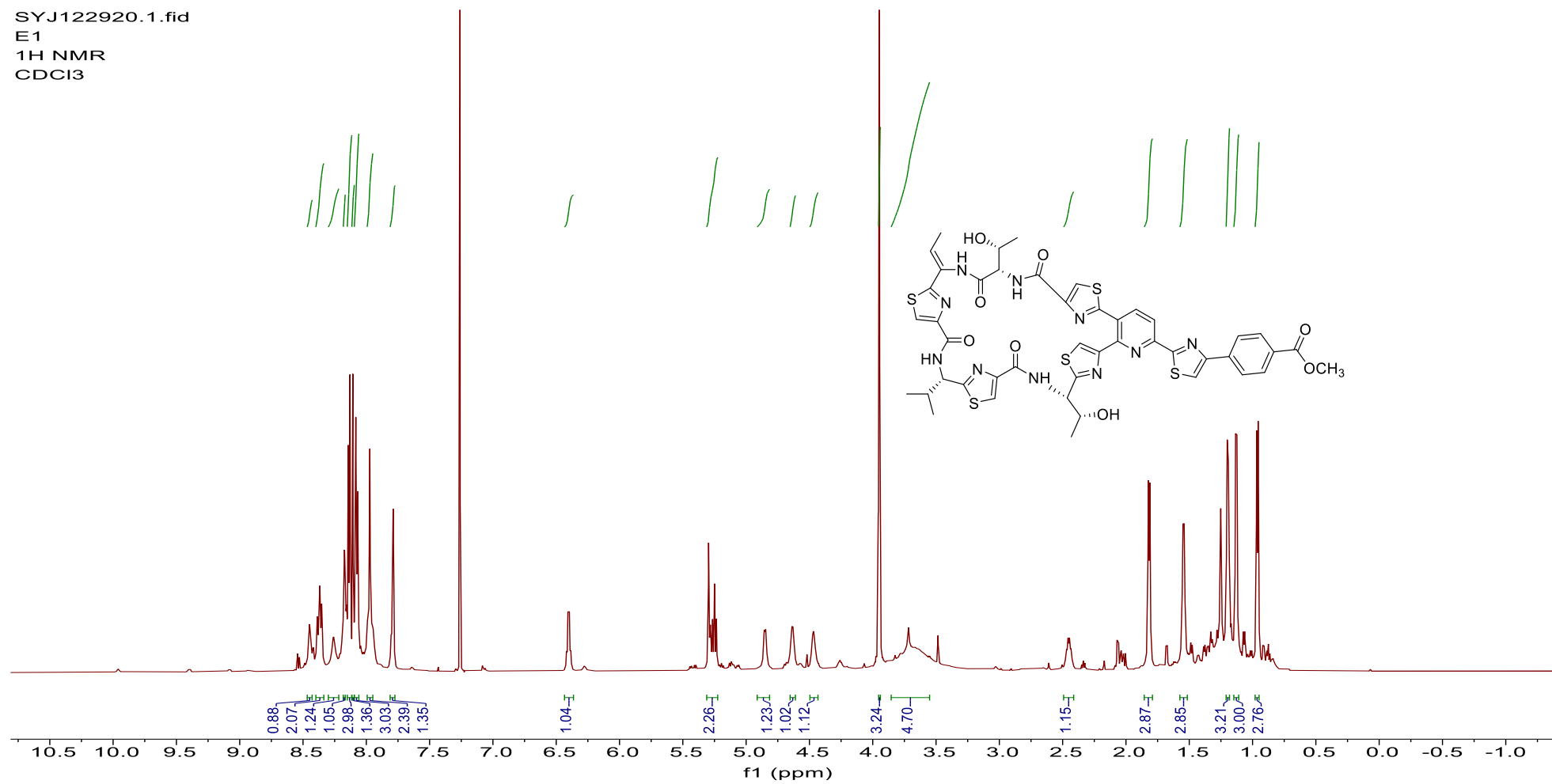
SYJ080620.2.fid
 SYJ-02-045-003
 13c NMR
 CDCl3

170.60 169.99 168.75 168.45 166.54 166.34 161.35 161.02 160.52 153.04 150.59 150.43 150.16 149.54 149.01 141.21 129.01 128.42 127.86 126.81 125.06 124.01 123.86 122.65 120.91 118.30 77.16 CDCl3 69.01 67.79 58.48 55.81 54.75 33.94 20.07 19.90 19.22 18.88 14.63



¹³C-NMR Spectrum of Compound 3 (151 MHz, CDCl₃)

SYJ122920.1.fid
E1
1H NMR
CDCl₃

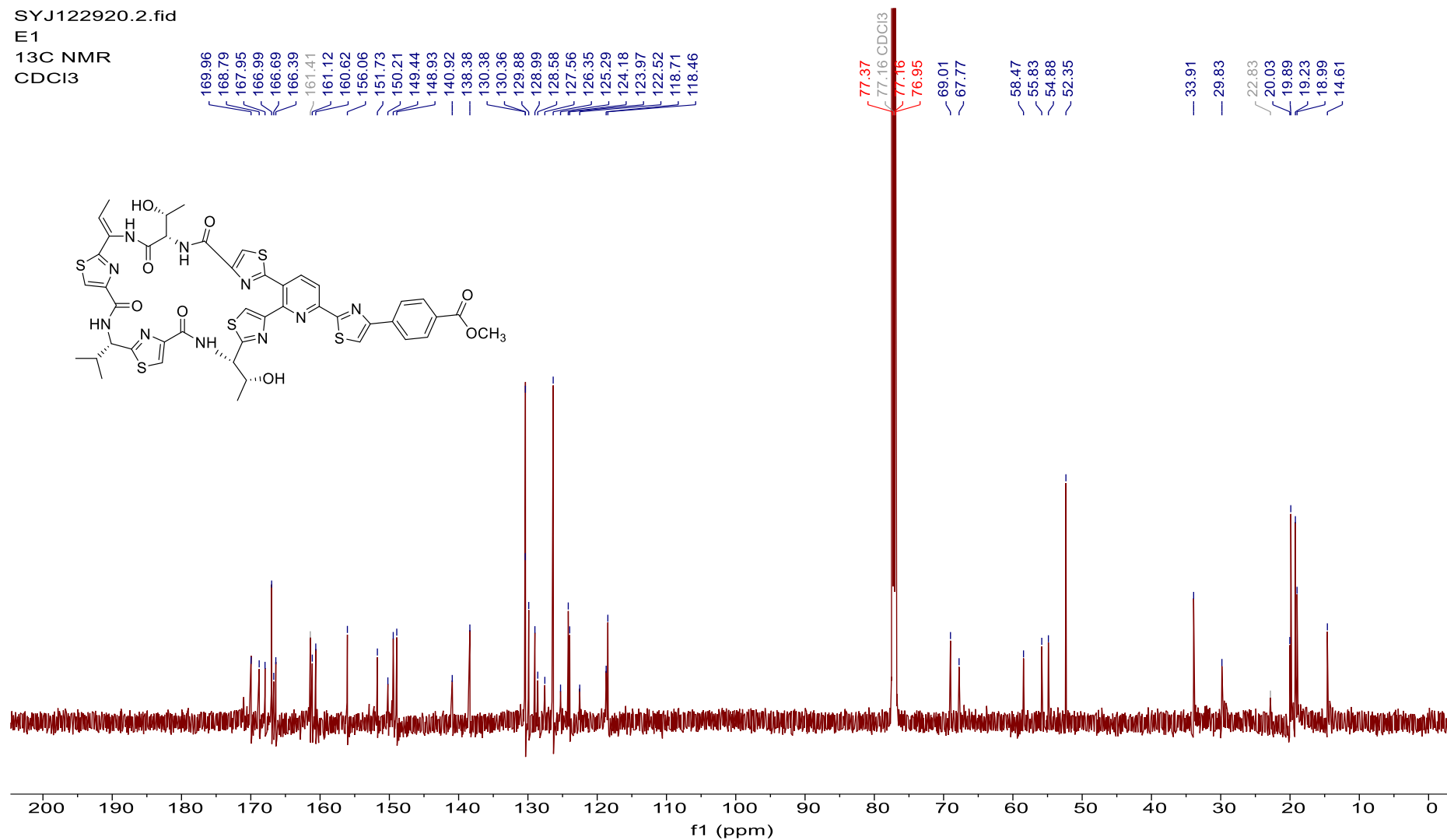
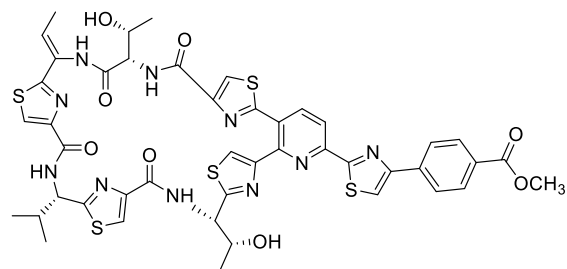


¹H-NMR Spectrum of Compound 22a (600 MHz, CDCl₃)

SYJ122920.2.fid
E1
13C NMR
CDCl3

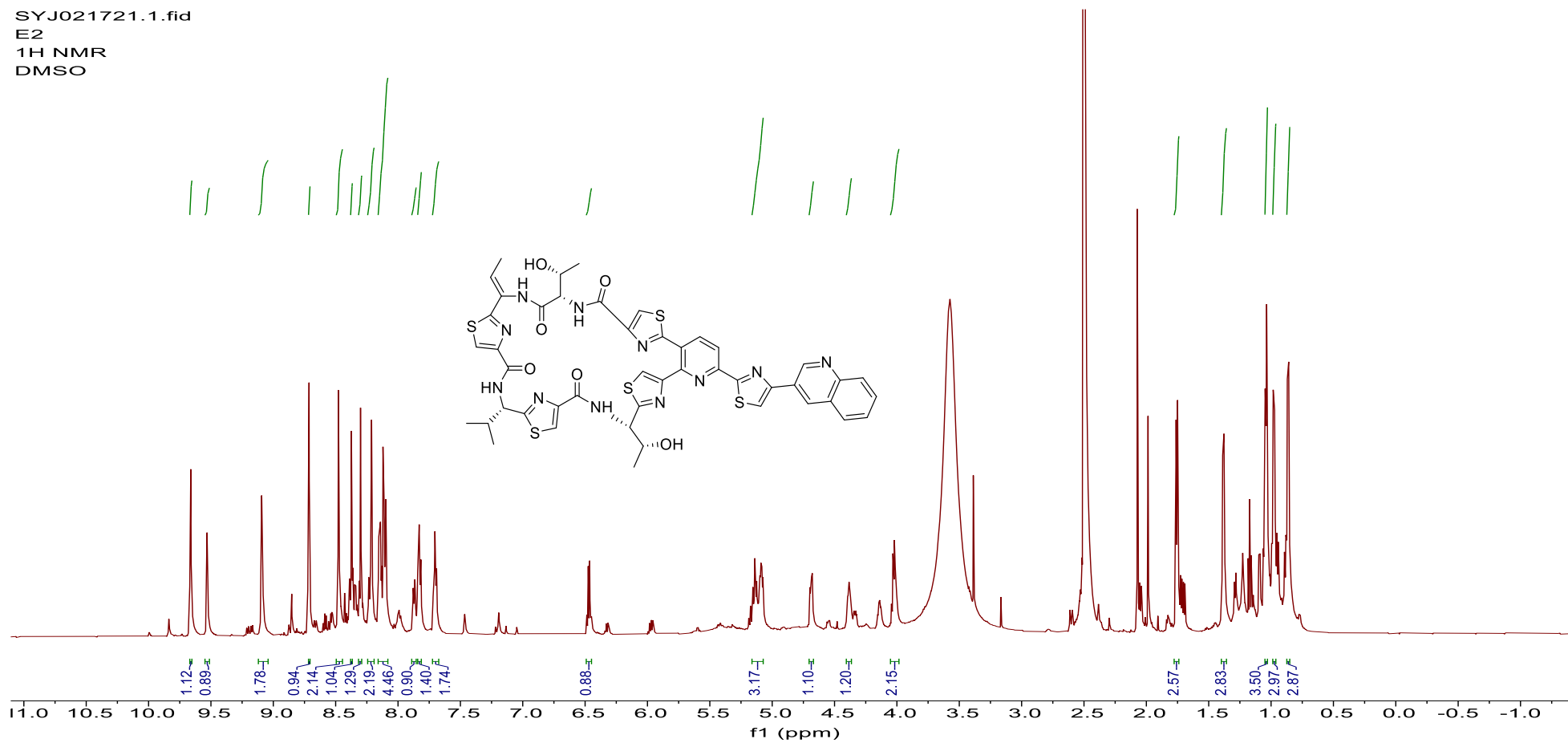
169.96
168.79
167.95
166.99
166.69
166.39
161.41
161.12
160.62
156.06
151.73
150.21
149.44
148.93
140.92
138.38
130.38
130.36
129.88
128.99
128.58
127.56
126.35
125.29
124.18
123.97
122.52
118.71
118.46

77.37
77.16 CDCl3
77.16
76.95
69.01
67.77
58.47
55.83
54.88
52.35
33.91
29.83
22.83
20.03
19.89
19.23
18.99
14.61



¹³C-NMR Spectrum of Compound 22a (151 MHz, CDCl₃)

SYJ021721.1.fid
E2
1H NMR
DMSO



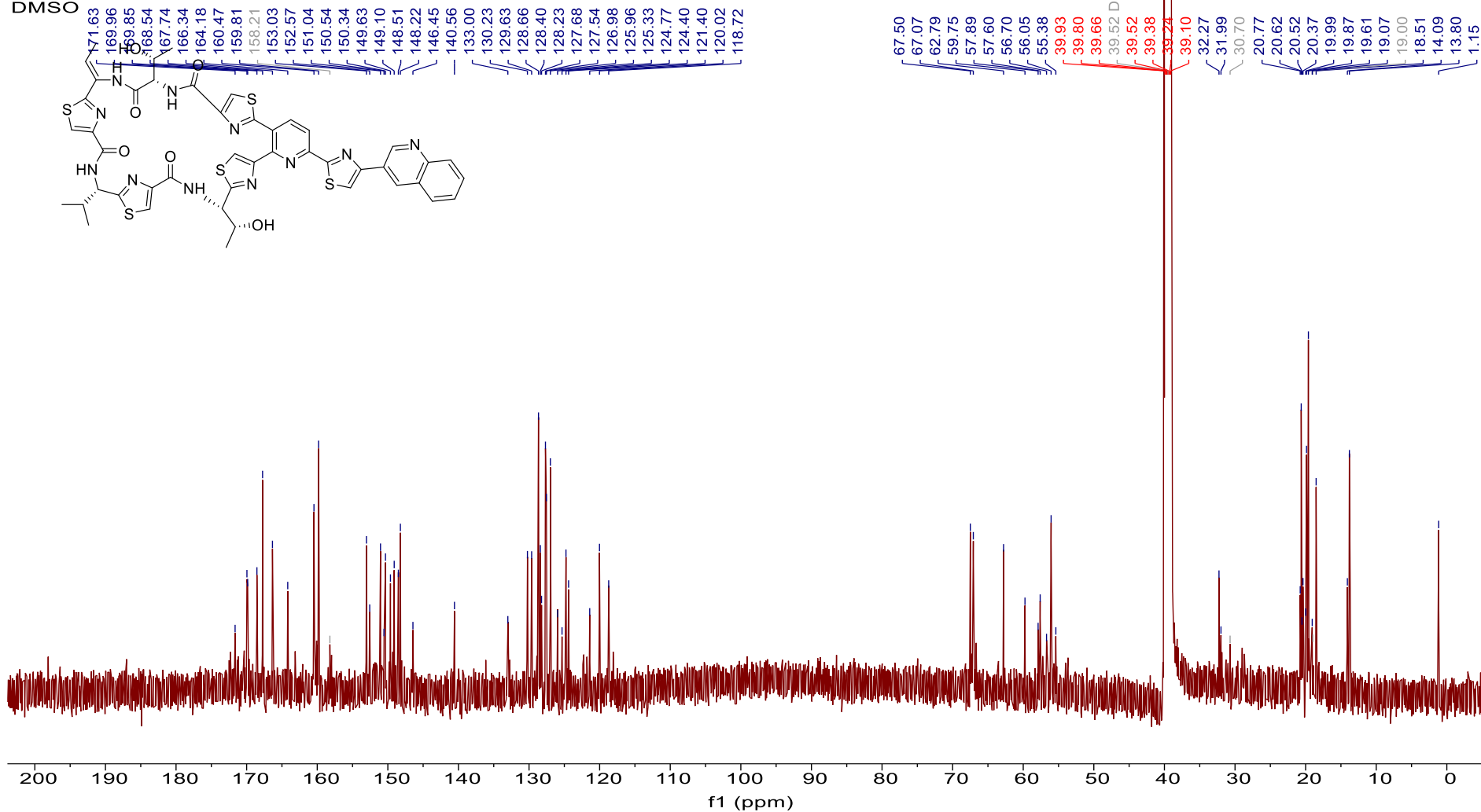
¹H-NMR Spectrum of Compound 22b (600 MHz, DMSO-d₆)

SYJ021821.10.fid

E2

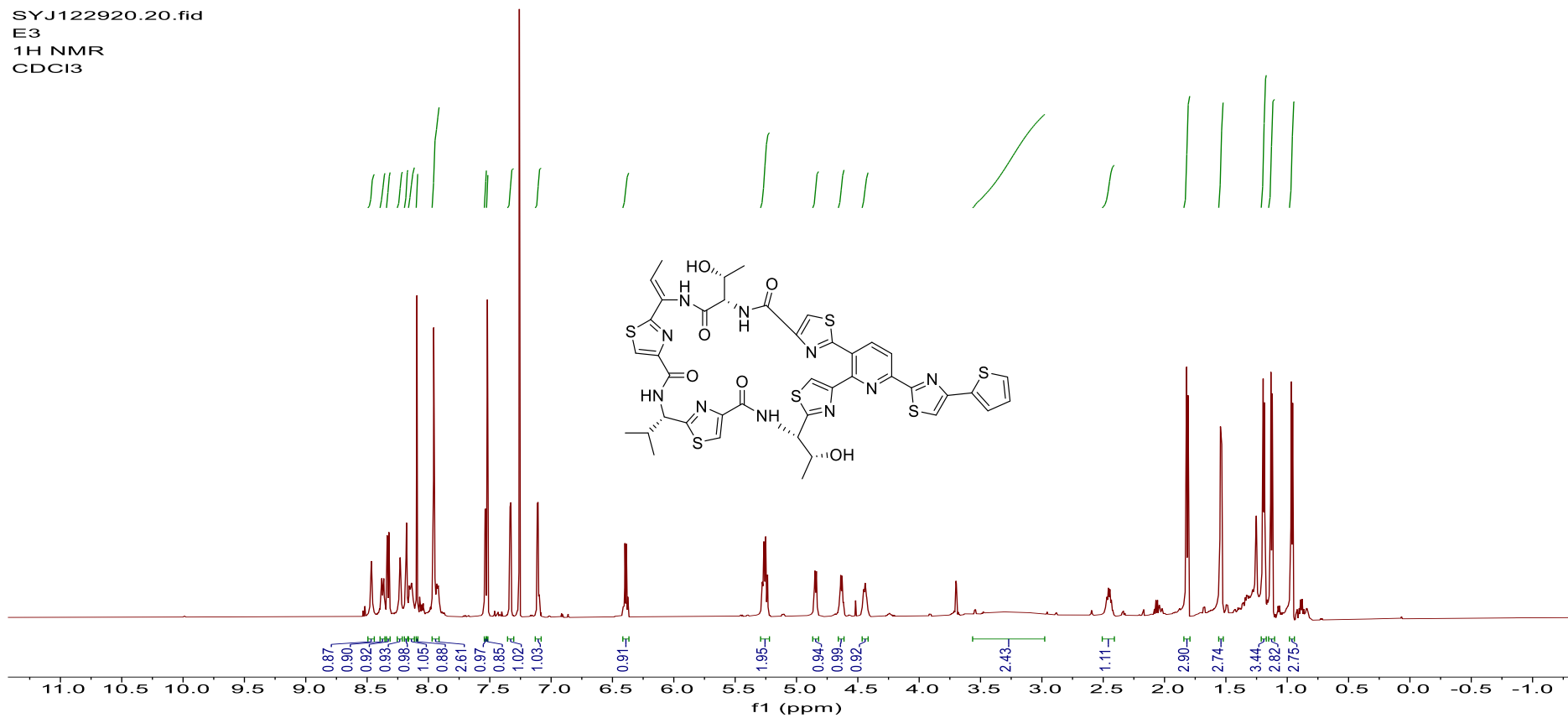
¹³C NMR

DMSO



¹³C-NMR Spectrum of Compound 22b (151 MHz, DMSO-*d*₆)

SYJ122920.20.fid
E3
1H NMR
CDCl3



¹H-NMR Spectrum of Compound 22c (600 MHz, CDCl₃)

SYJ122920.21.fid

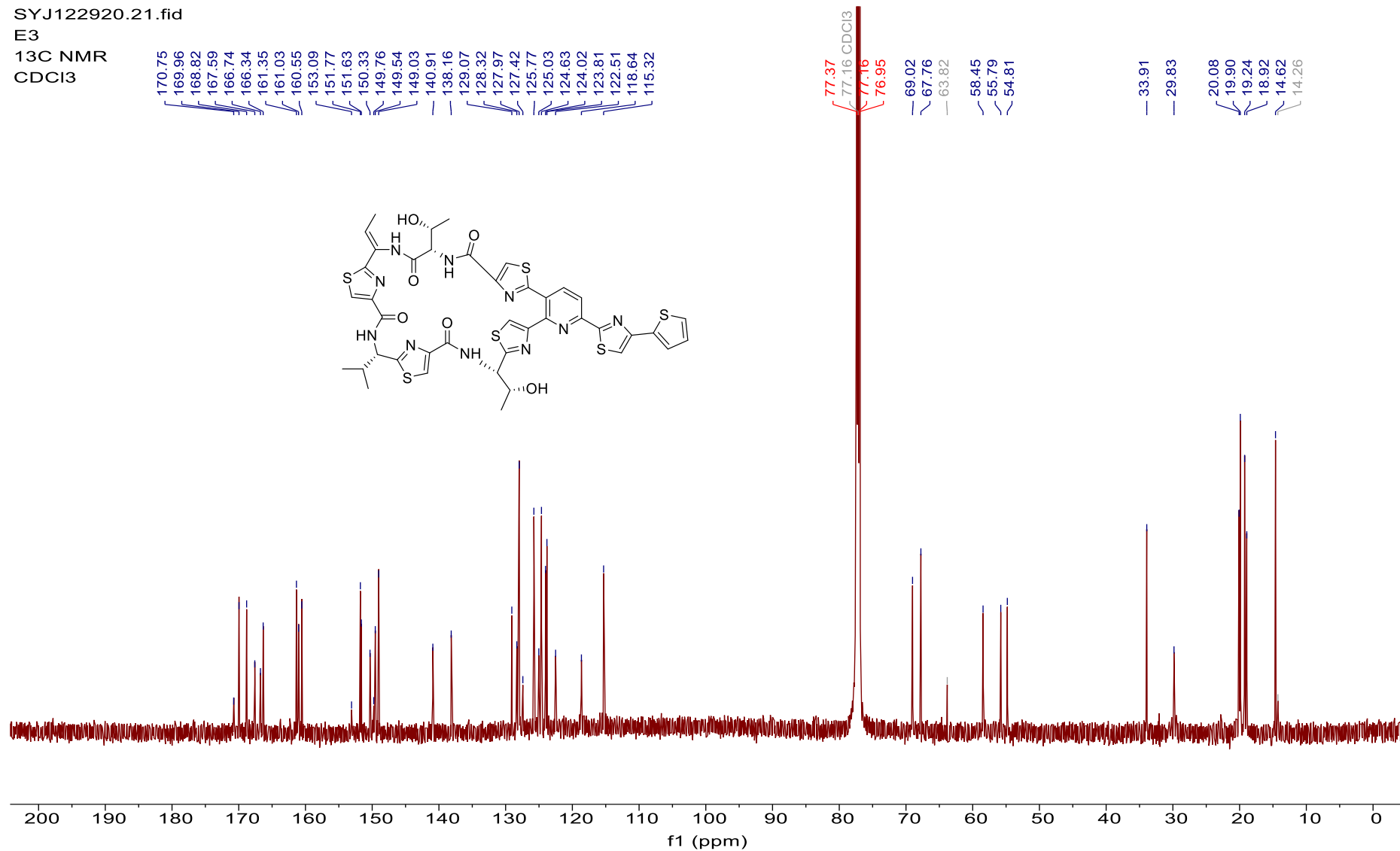
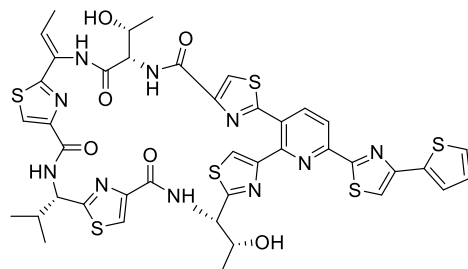
E3

¹³C NMR

CDCl₃

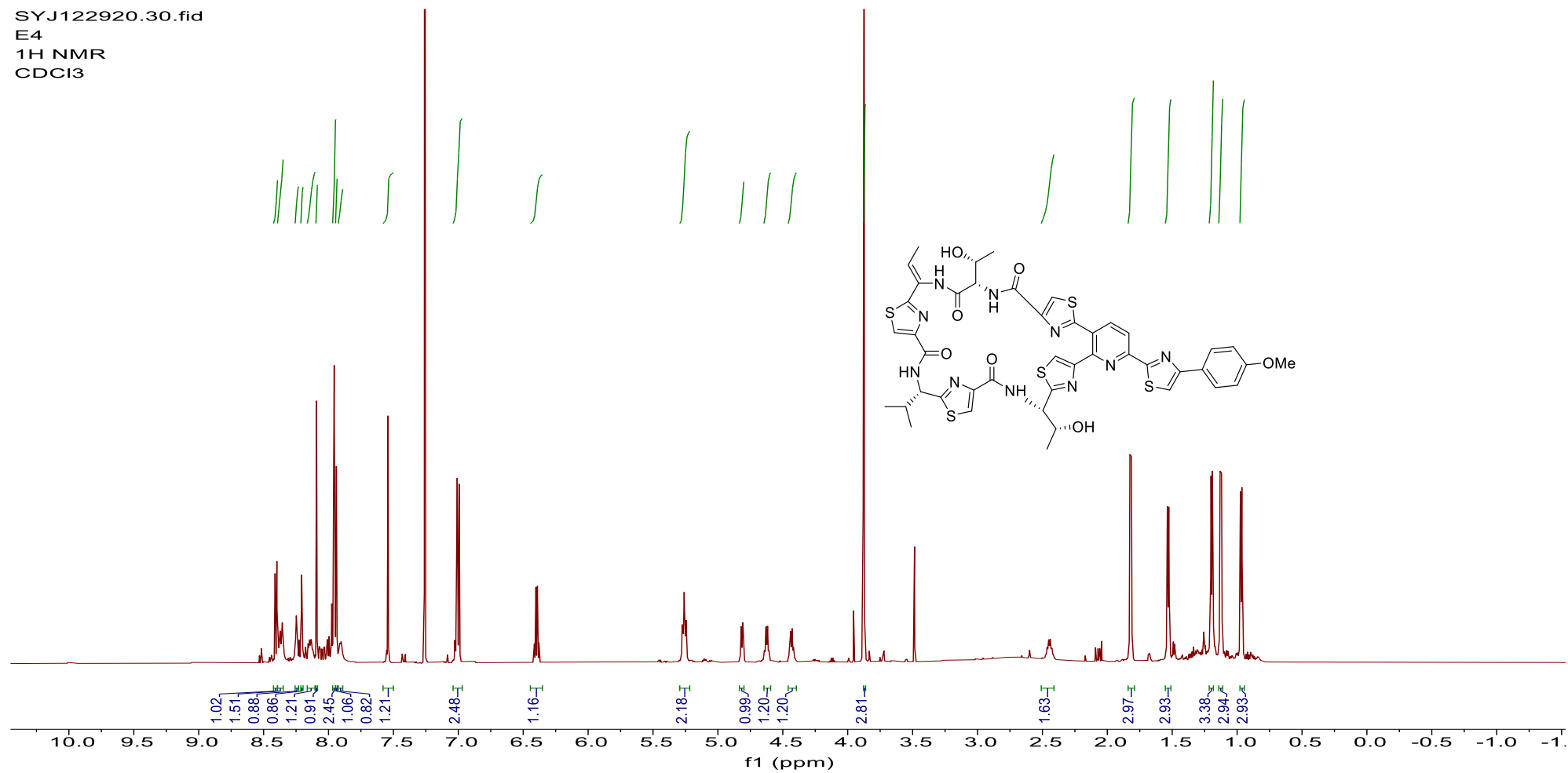
170.75
169.96
168.82
167.59
166.74
166.34
161.35
161.03
160.55
153.09
151.77
151.63
150.33
149.76
149.54
149.03
140.91
138.16
129.07
128.32
127.97
127.42
125.77
125.03
124.63
124.02
123.81
122.51
118.64
115.32

77.37
77.16 CDCl₃
77.16
76.95
69.02
67.76
63.82
58.45
55.79
54.81
33.91
29.83
20.08
19.90
19.24
18.92
14.62
14.26



¹³C-NMR Spectrum of Compound 22c (151 MHz, CDCl₃)

SYJ122920.30.fid
E4
1H NMR
CDCl3



¹H-NMR Spectrum of Compound 22d (600 MHz, CDCl₃)

SYJ122920.32.fid

E4

¹³C NMR

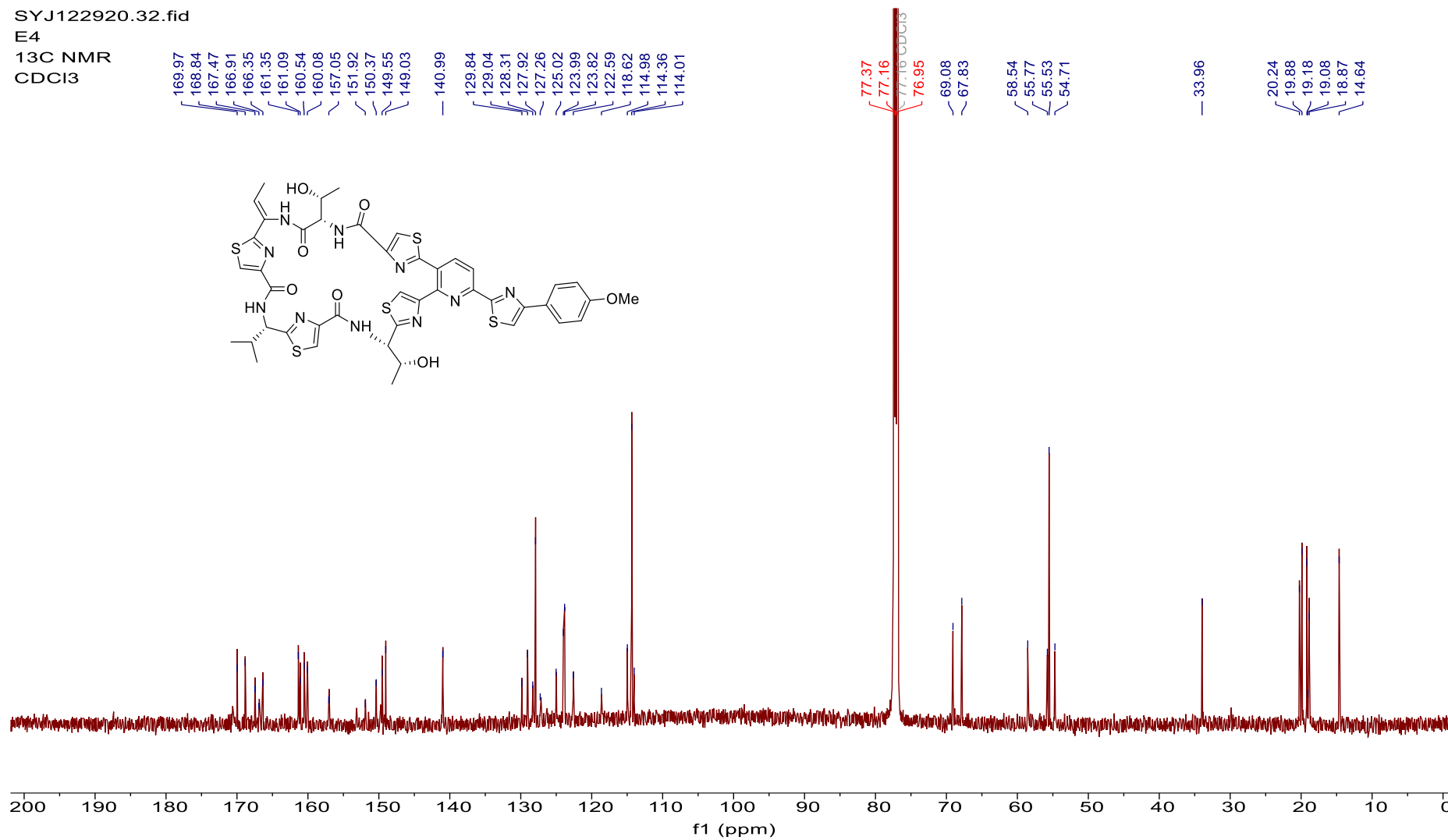
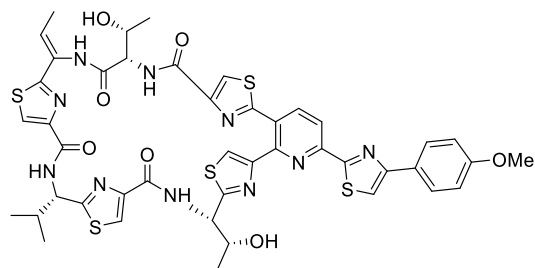
CDCl₃

169.97
168.84
167.47
166.91
166.35
161.35
161.09
160.54
160.08
157.05
151.92
150.37
149.55
149.03
— 140.99
129.84
129.04
128.31
127.92
127.26
125.02
123.99
123.82
122.59
118.62
114.98
114.36
114.01

77.37
77.16
77.16
76.95
69.08
67.83
58.54
55.77
55.53
54.71

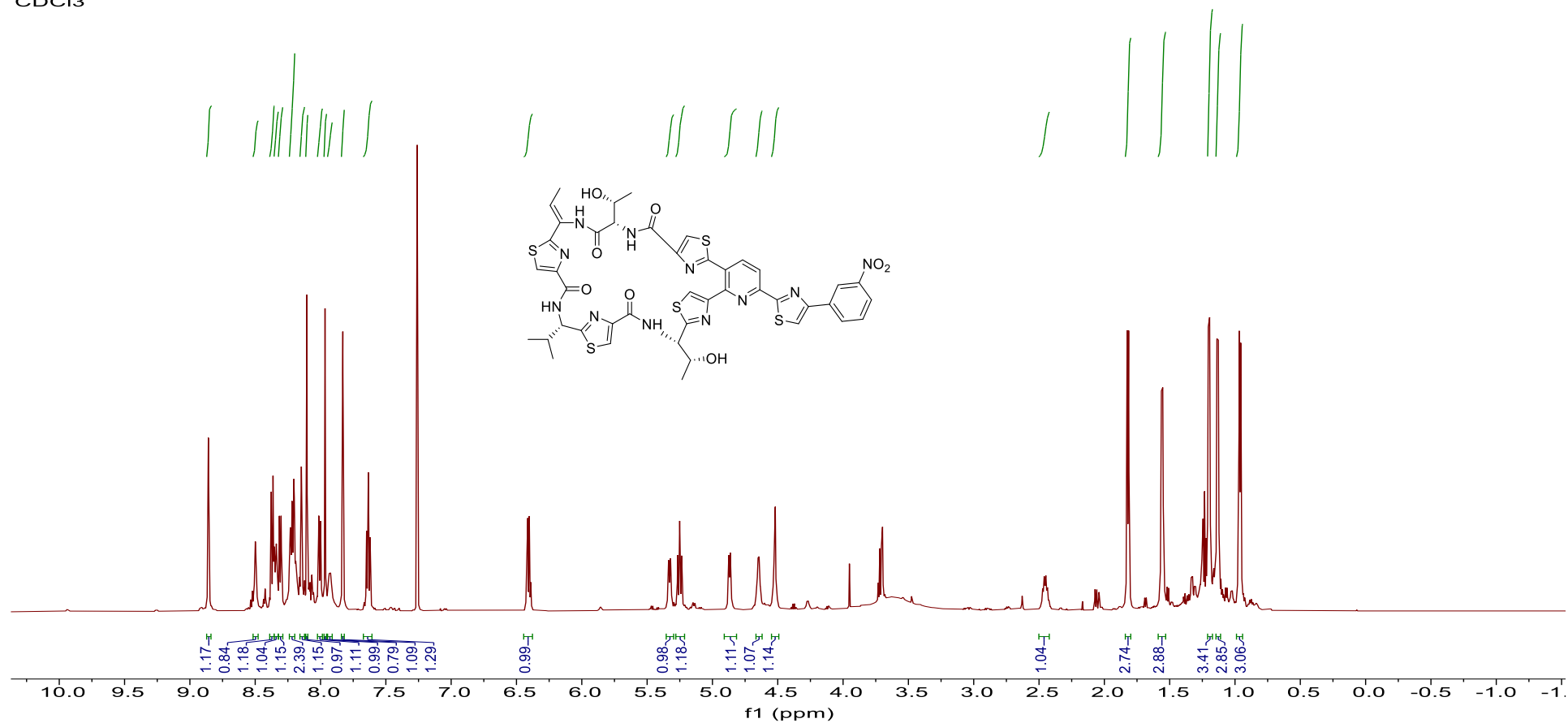
— 33.96

20.24
19.88
19.18
19.08
18.87
14.64



¹³C-NMR Spectrum of Compound 22d (151 MHz, CDCl₃)

SYJ012621.20.fid
E5
1H NMR
CDCl₃



¹H-NMR Spectrum of Compound 22e (600 MHz, CDCl₃)

SYJ012621.23.fid
E5
13C NMR
CDCl3

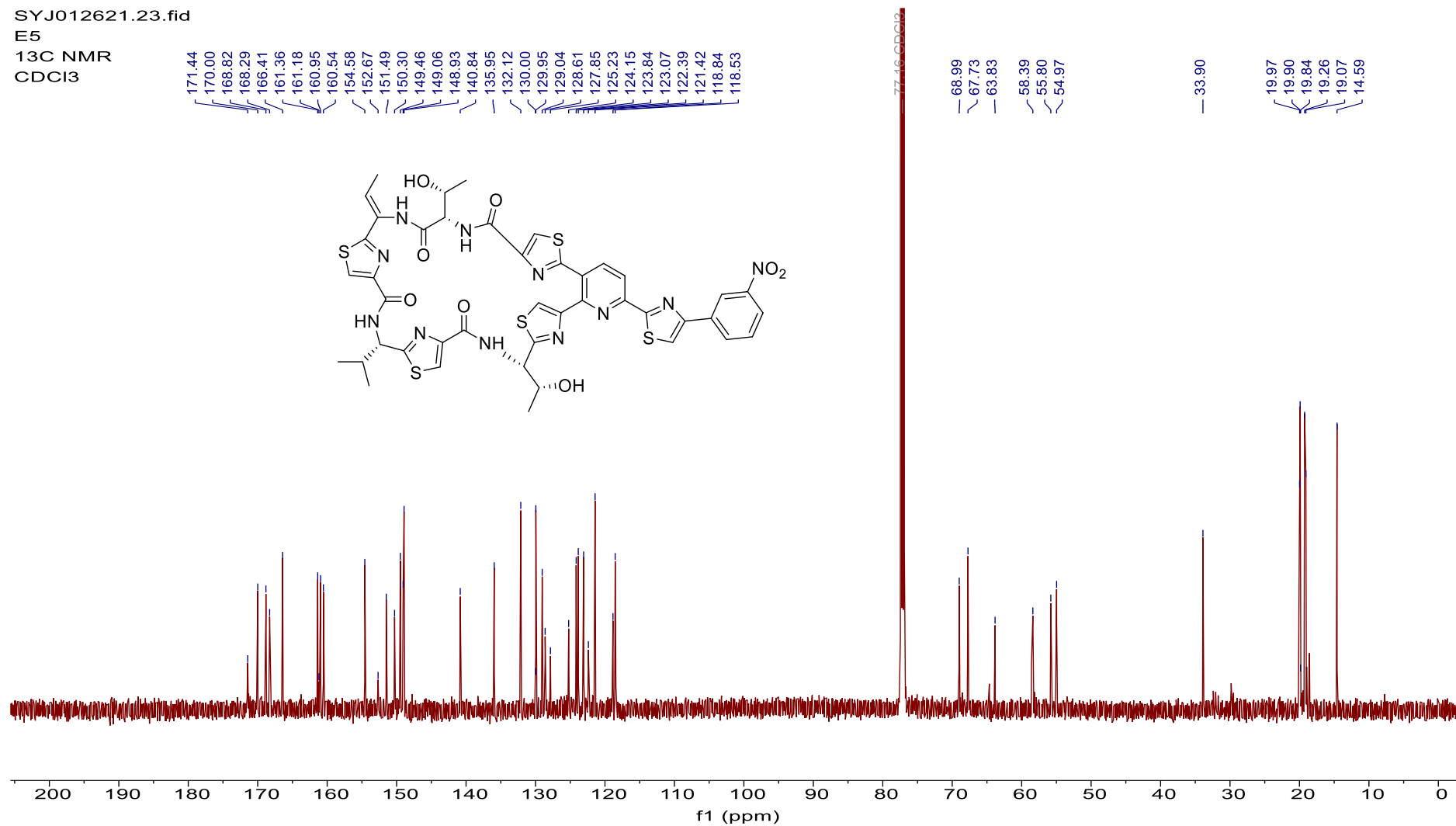
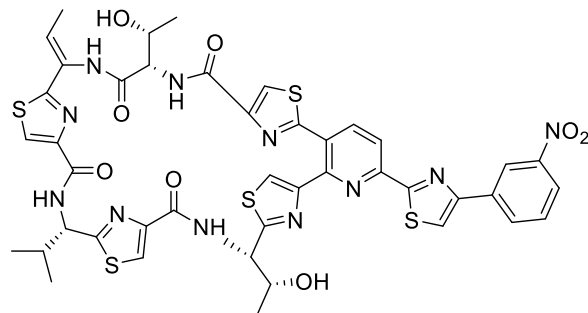
171.44
170.00
168.82
168.29
166.41
161.36
161.18
160.95
160.54
154.58
152.67
151.49
150.30
149.46
149.06
148.93
140.84
135.95
132.12
130.00
129.95
129.04
128.61
127.85
125.23
124.15
123.84
123.07
122.39
121.42
118.84
118.53

77.16-CDCl3

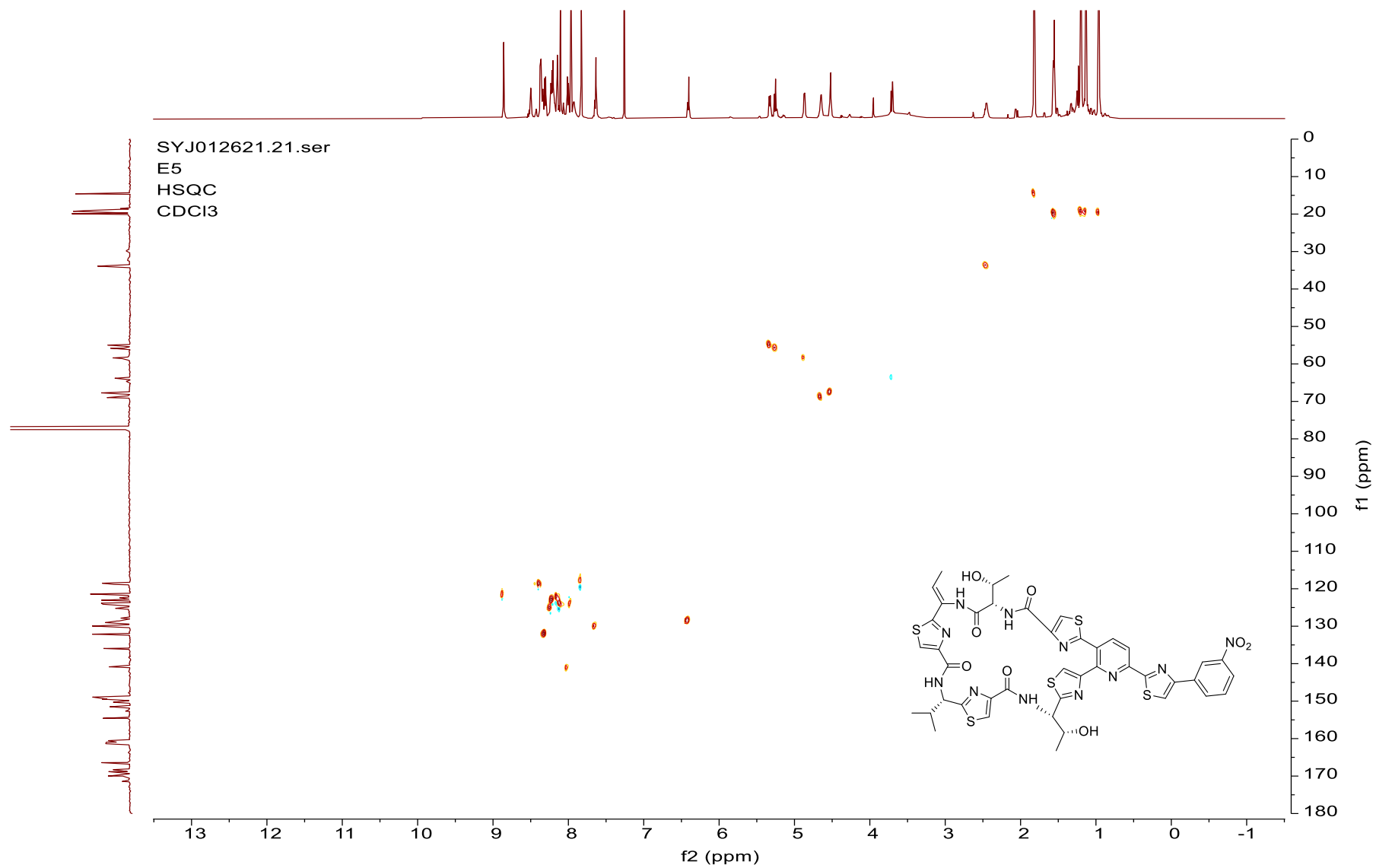
68.99
67.73
63.83
58.39
55.80
54.97

33.90

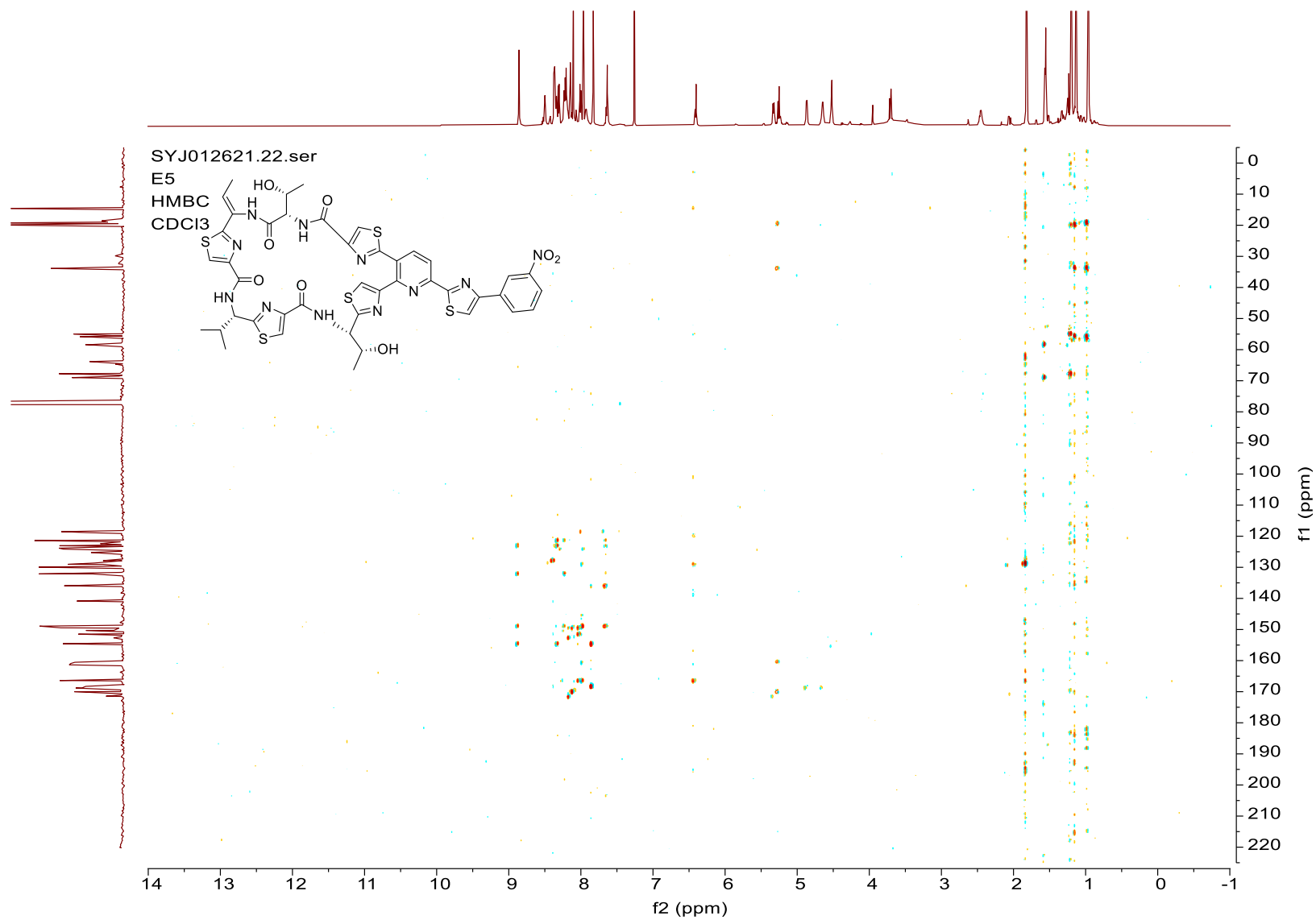
19.97
19.90
19.84
19.26
19.07
14.59



¹³C-NMR Spectrum of Compound 22e (151 MHz, CDCl₃)

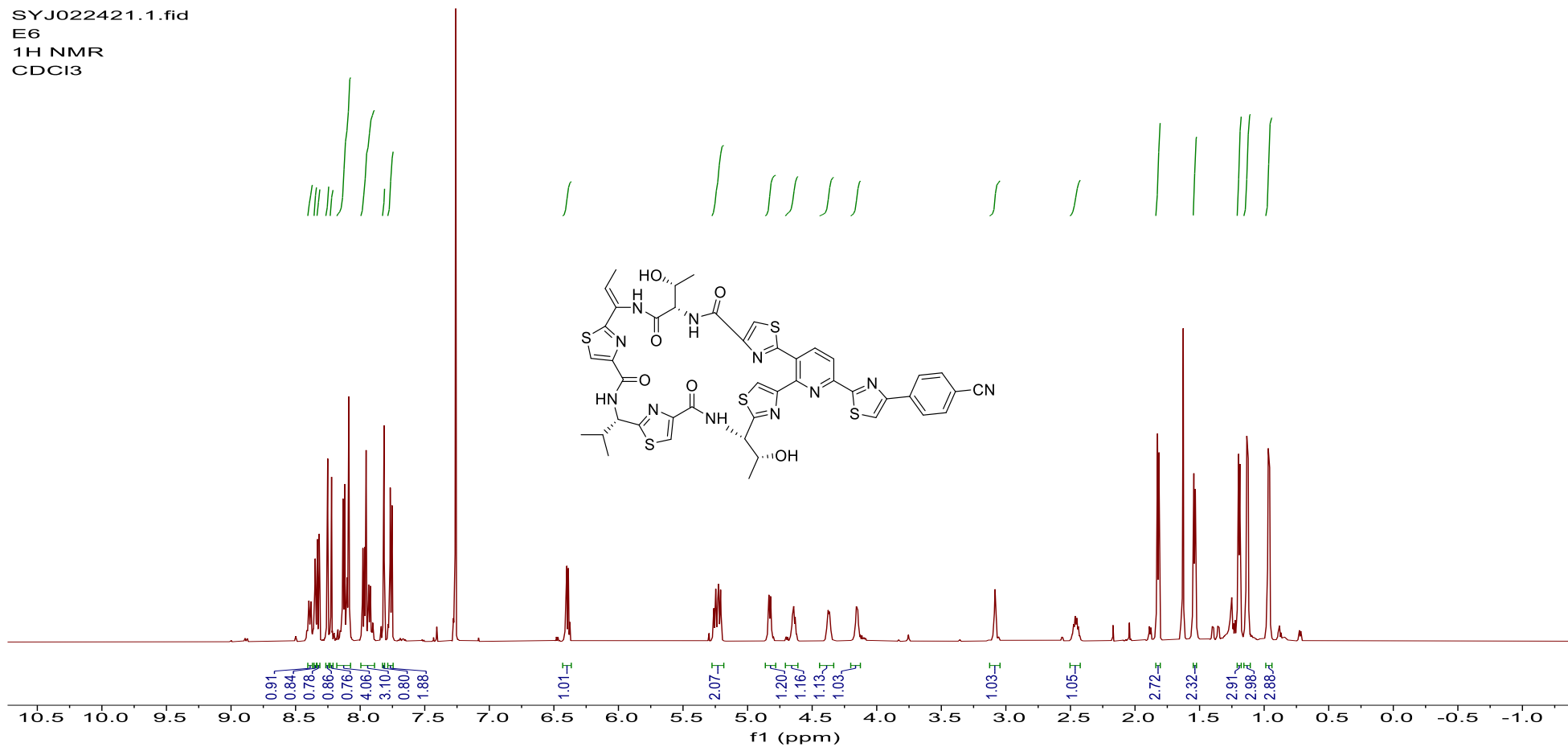


HSQC Spectrum of Compound 22e (600 MHz, CDCl₃)



HMBC Spectrum of Compound 22e (600 MHz, CDCl₃)

SYJ022421.1.fid
E6
1H NMR
CDCl3



¹H-NMR Spectrum of Compound 22f (600 MHz, CDCl₃)

SYJ022421.2.fid

E6

¹³C NMR

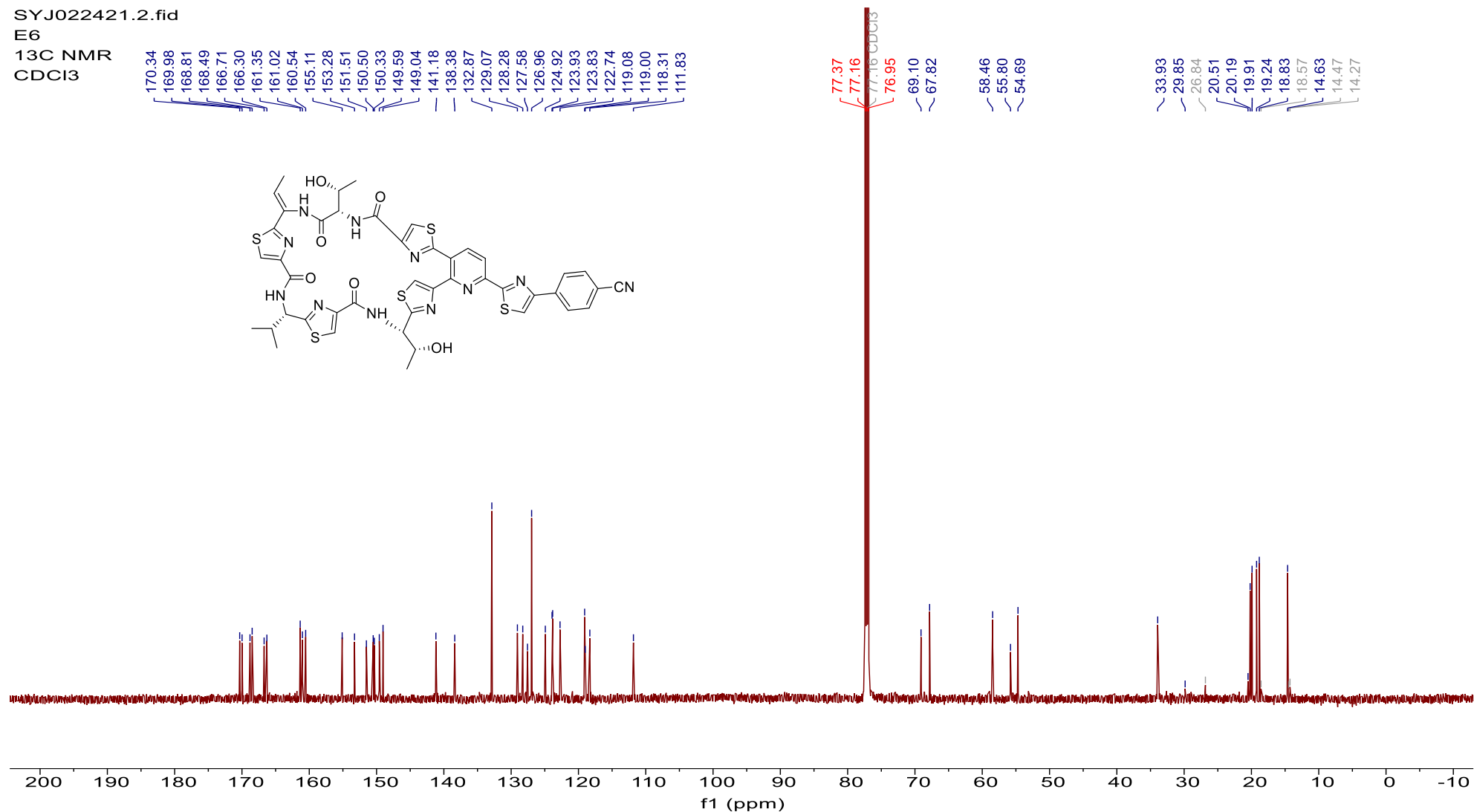
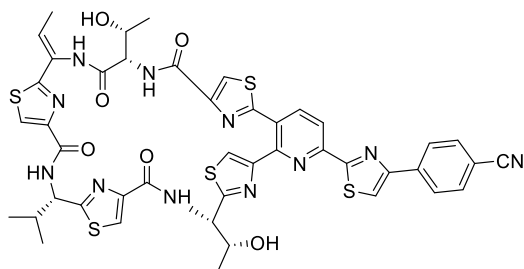
CDCl₃

170.34
169.98
168.81
168.49
166.71
166.30
161.35
161.02
160.54
155.11
153.28
151.51
150.50
150.33
149.59
149.04
141.18
138.38
132.87
129.07
128.28
127.58
126.96
124.92
123.93
123.83
122.74
119.08
119.00
118.31
111.83

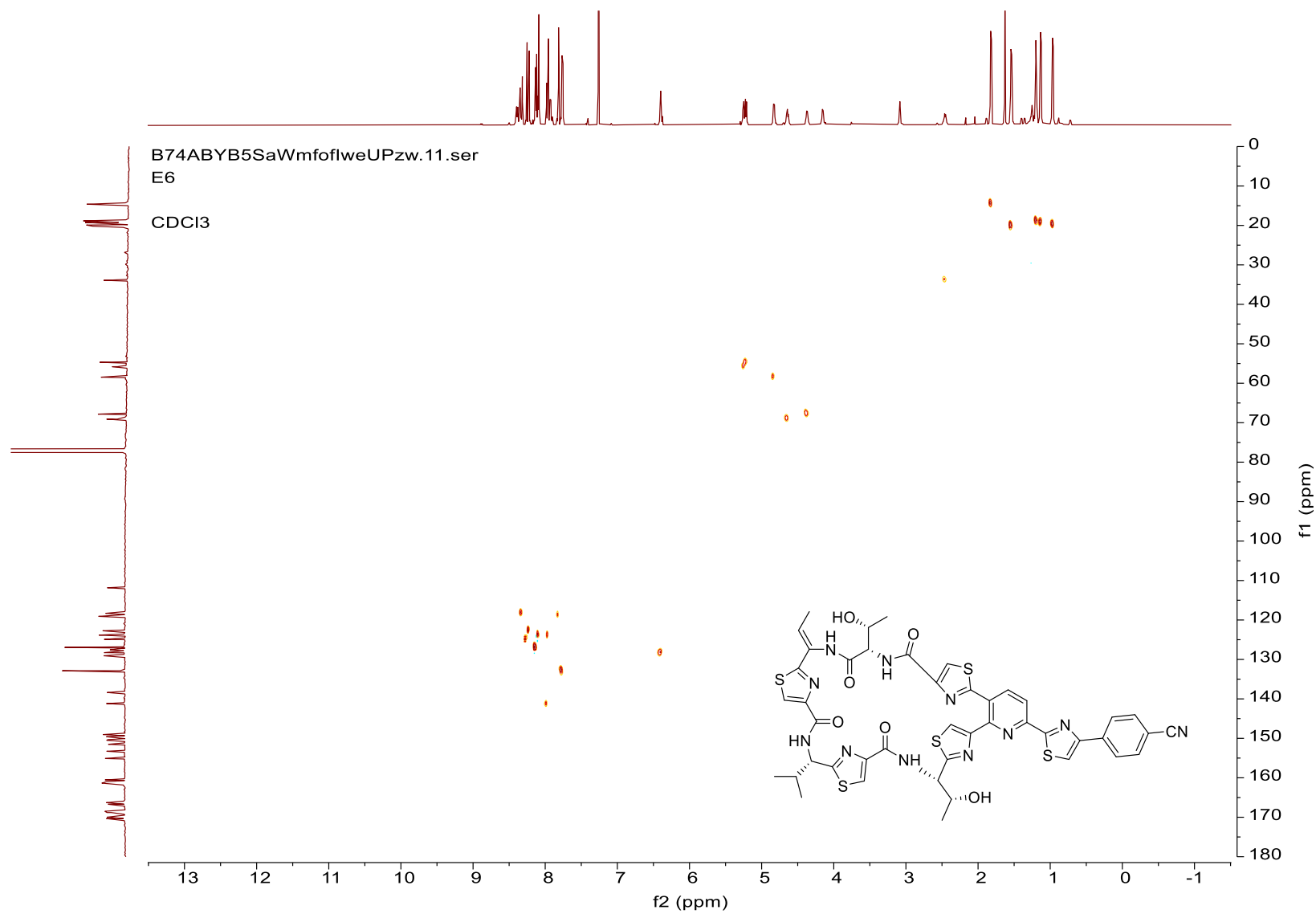
77.37
77.16
76.95
69.10
67.82

58.46
55.80
54.69

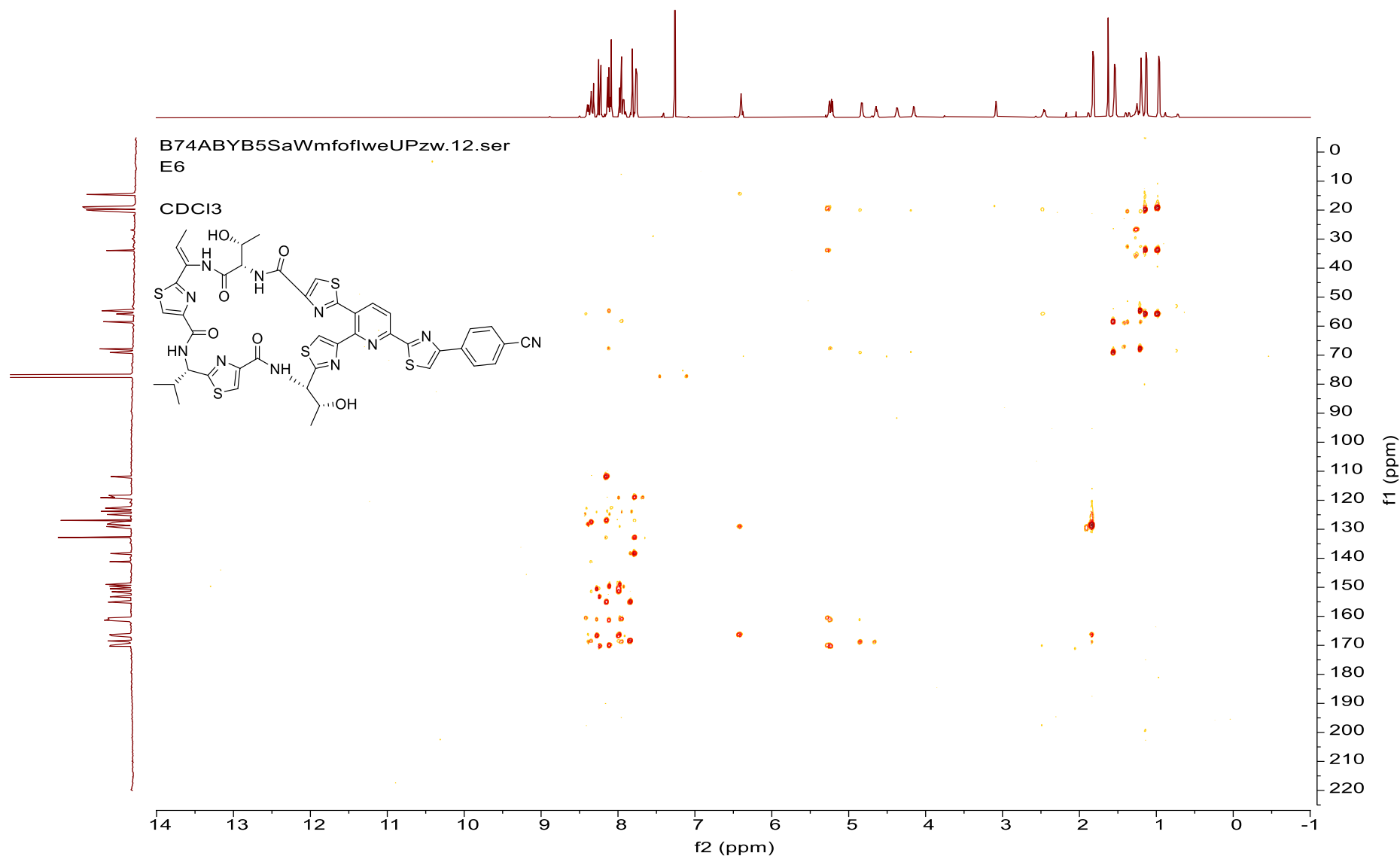
33.93
29.85
26.84
20.51
20.19
19.91
19.24
18.83
18.57
14.63
14.47
14.27

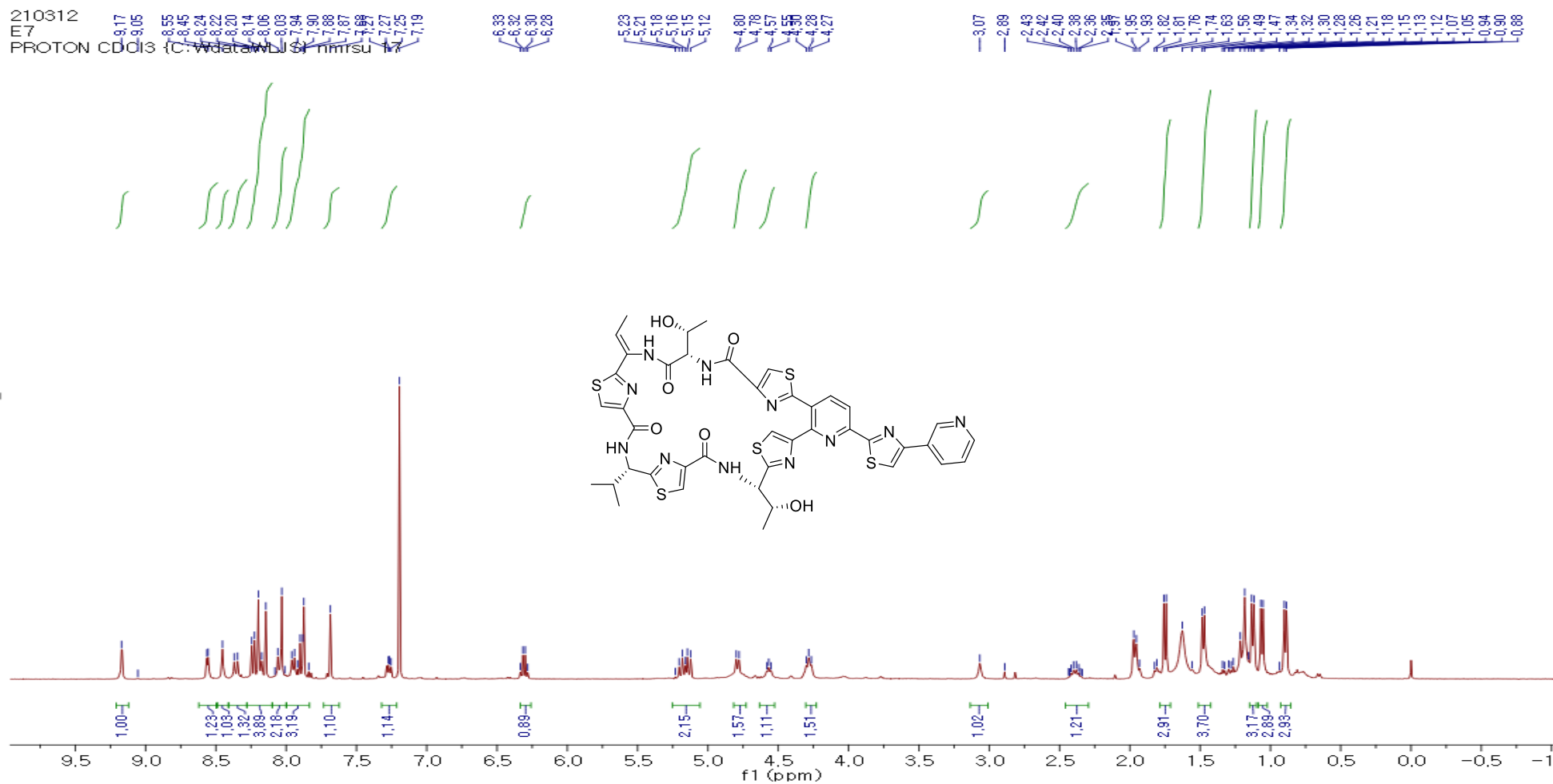


¹³C-NMR Spectrum of Compound 22f (151 MHz, CDCl₃)



HSQC Spectrum of Compound 22f (600 MHz, CDCl₃)





¹H-NMR Spectrum of Compound 22g (400 MHz, CDCl₃)

SYJ122920.61.fid

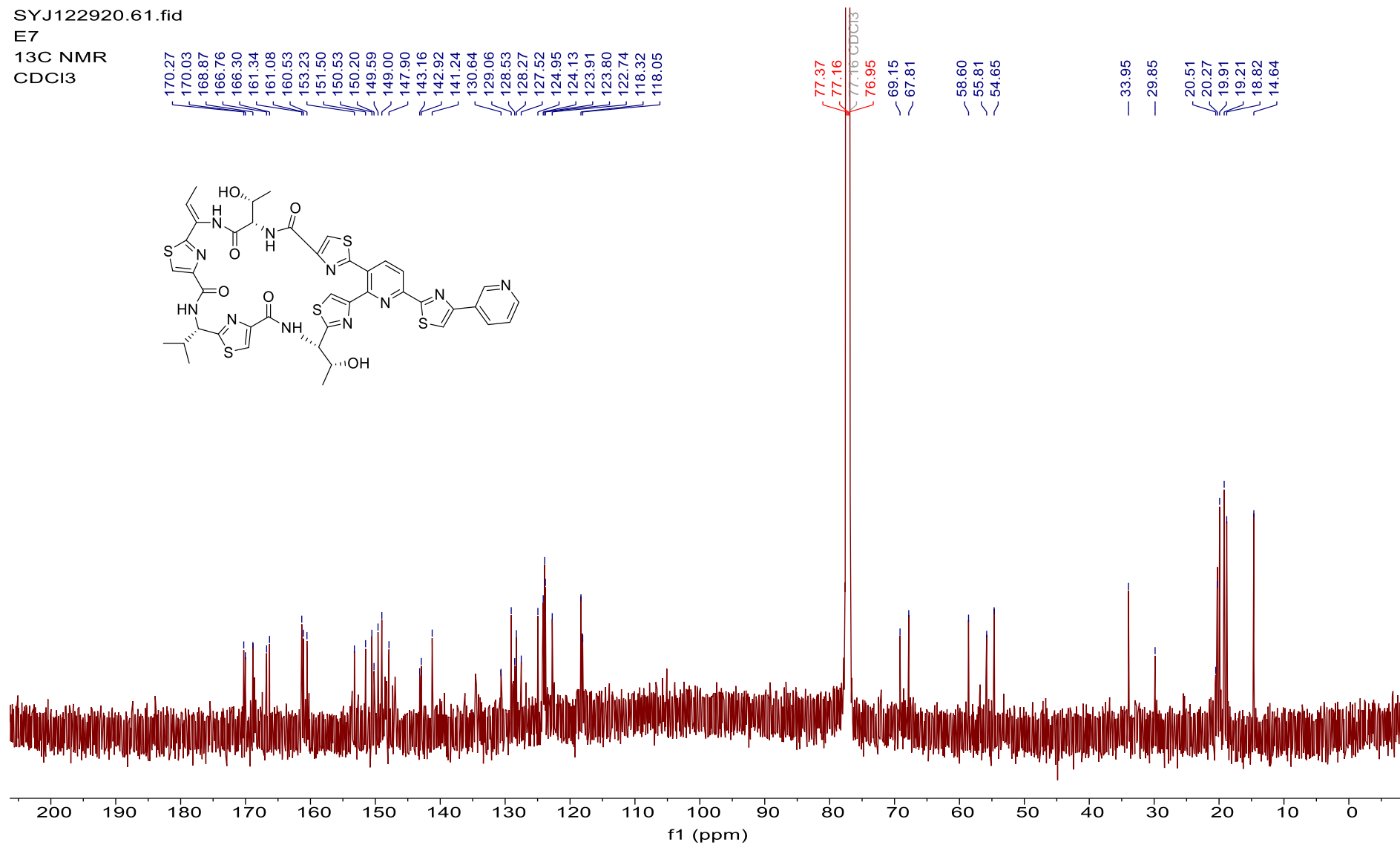
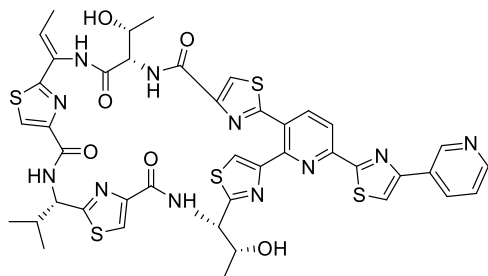
E7

¹³C NMR

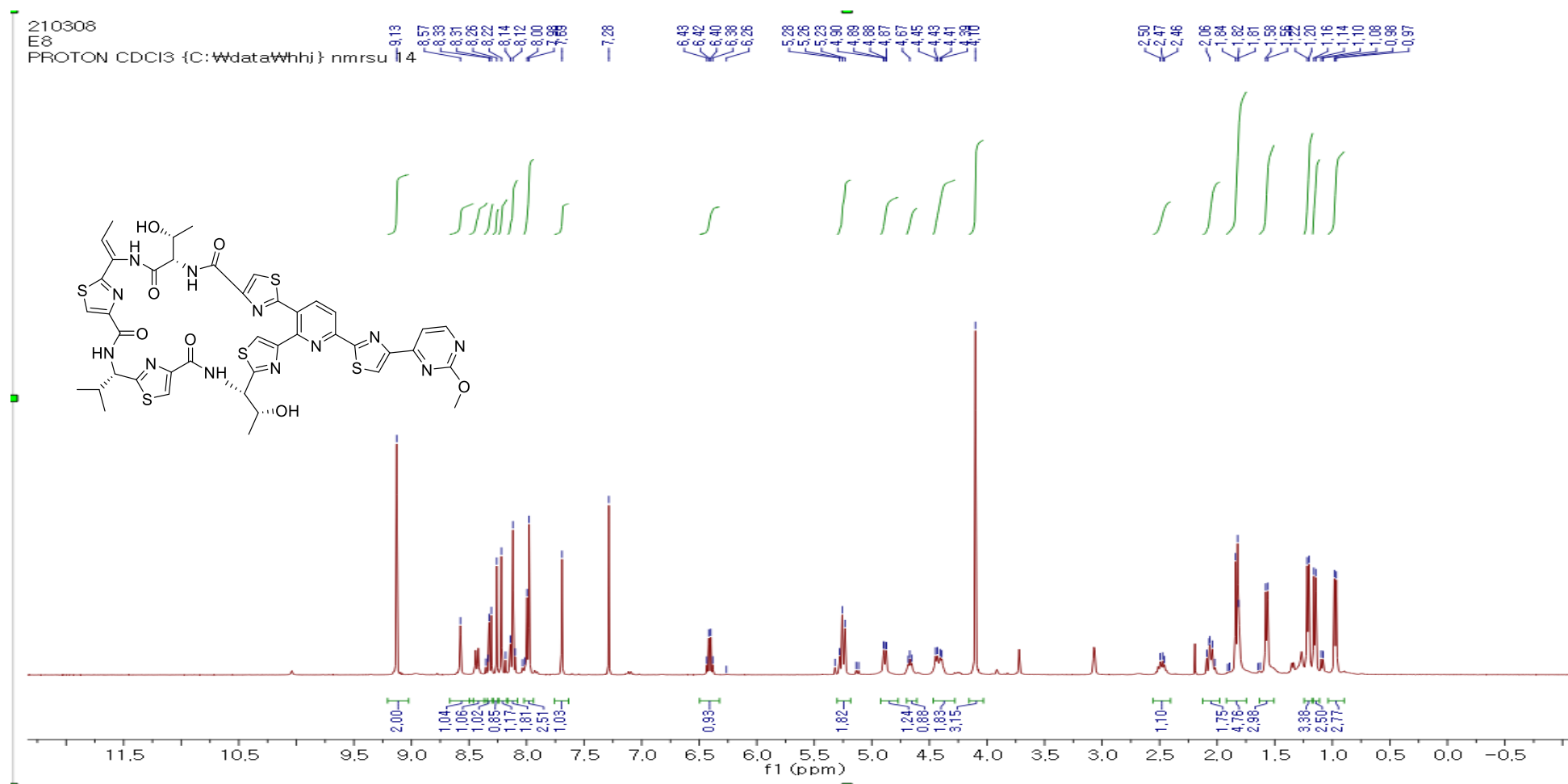
CDCl₃

170.27
170.03
168.87
166.76
166.30
161.34
161.08
160.53
153.23
151.50
150.53
150.20
149.59
149.00
147.90
143.16
142.92
141.24
130.64
129.06
128.53
128.27
127.52
124.95
124.13
123.91
123.80
122.74
118.32
118.05

77.37
77.16
77.16 CDCl₃
76.95
69.15
67.81
58.60
55.81
54.65
33.95
29.85
20.51
20.27
19.91
19.21
18.82
14.64



¹³C-NMR Spectrum of Compound 22g (151 MHz, CDCl₃)



¹H-NMR Spectrum of Compound 22h (400 MHz, CDCl₃)

210308

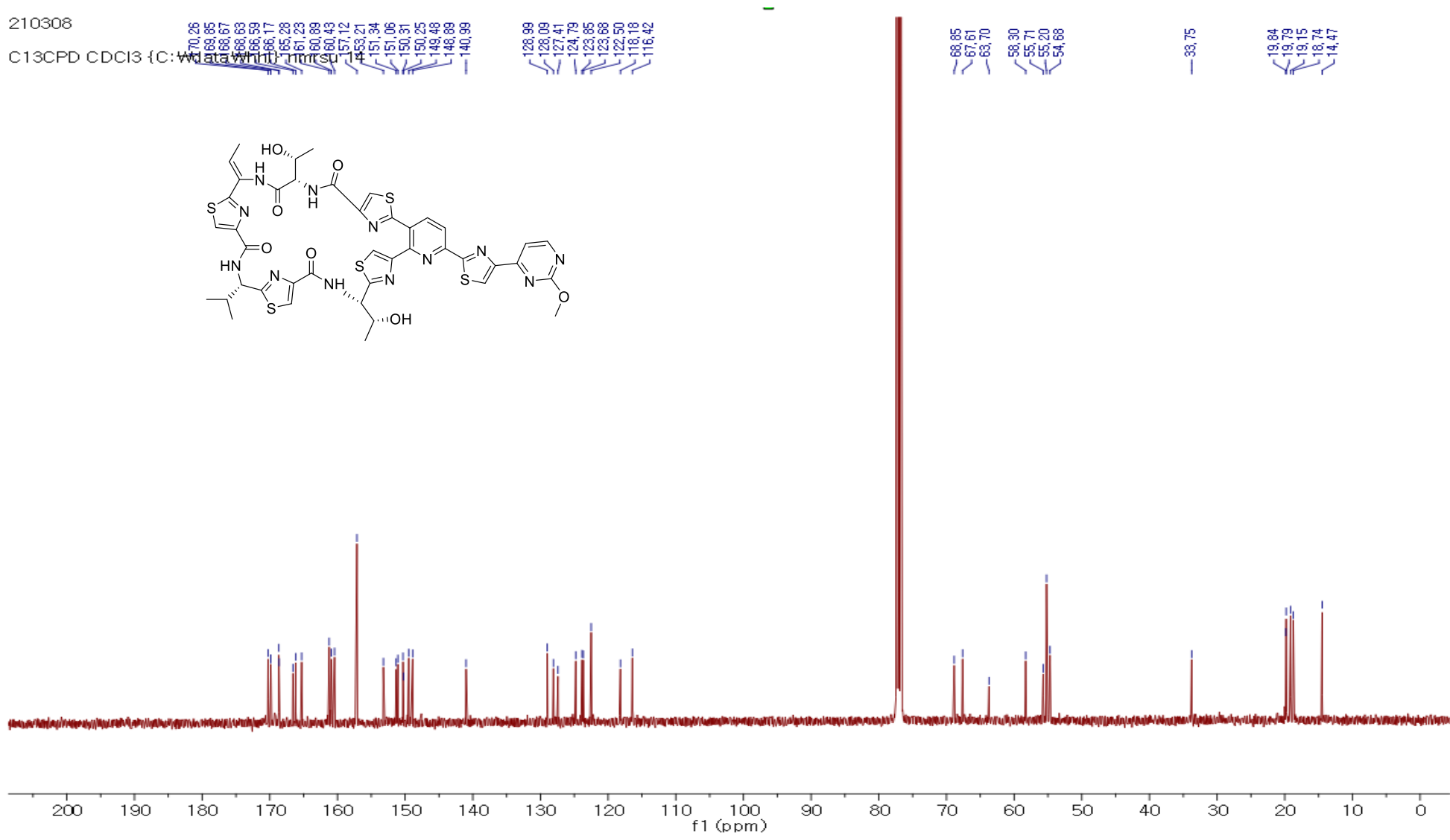
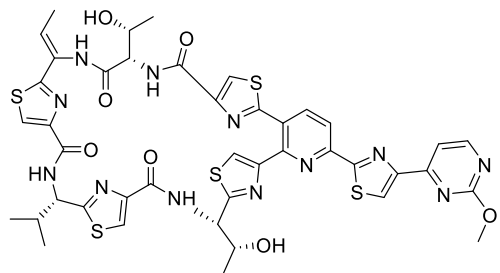
C13CPD CDCI3 {C:\data\whi\11m\su

170.26
169.85
168.67
168.63
166.59
166.17
165.28
161.23
160.89
160.43
157.12
153.21
151.34
151.06
150.31
150.25
149.48
148.89
140.99
128.99
128.09
127.41
124.79
123.85
123.88
122.50
118.18
116.42

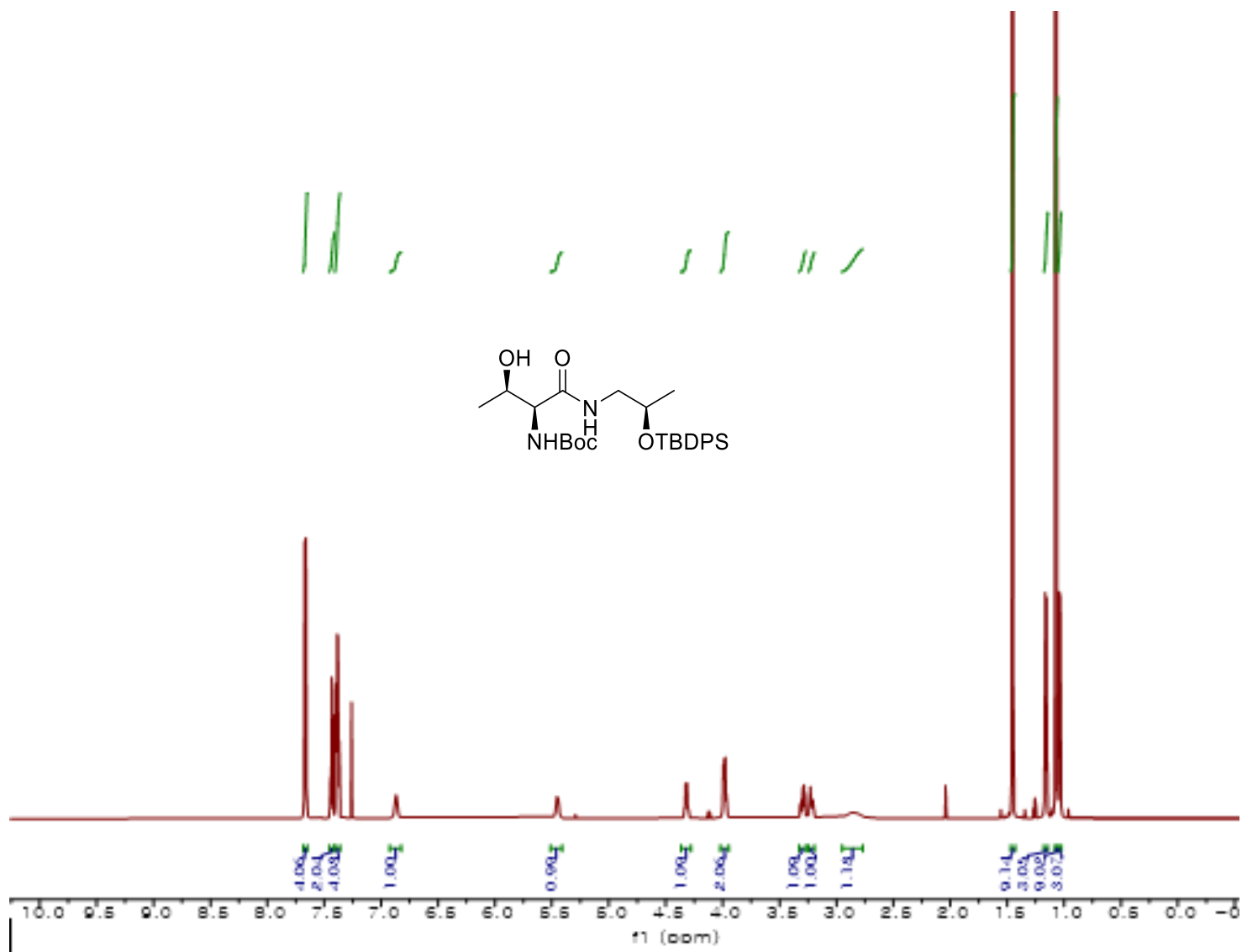
68.85
67.61
63.70
58.30
55.71
55.20
54.68

33.75

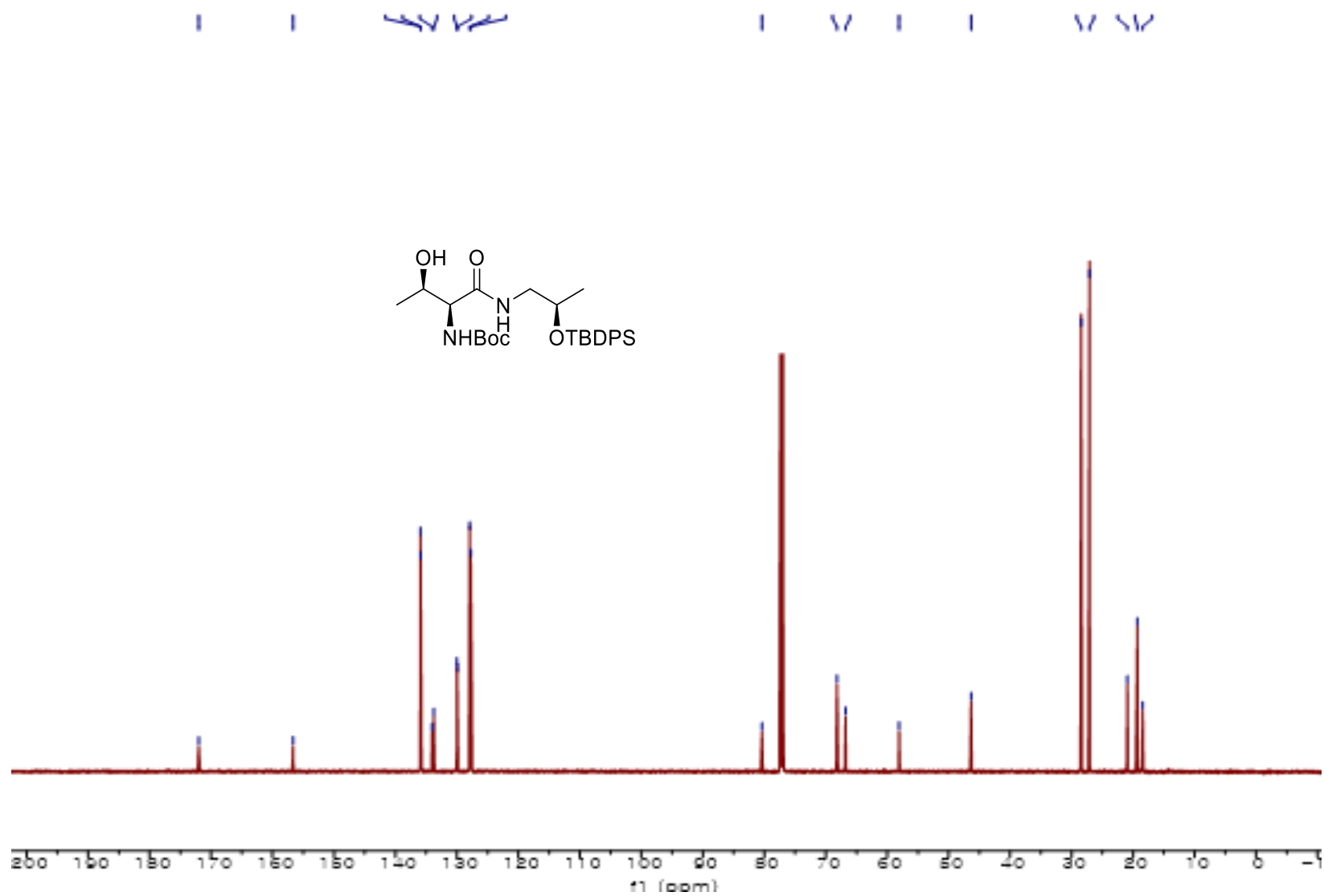
19.84
19.79
19.15
18.74
14.47

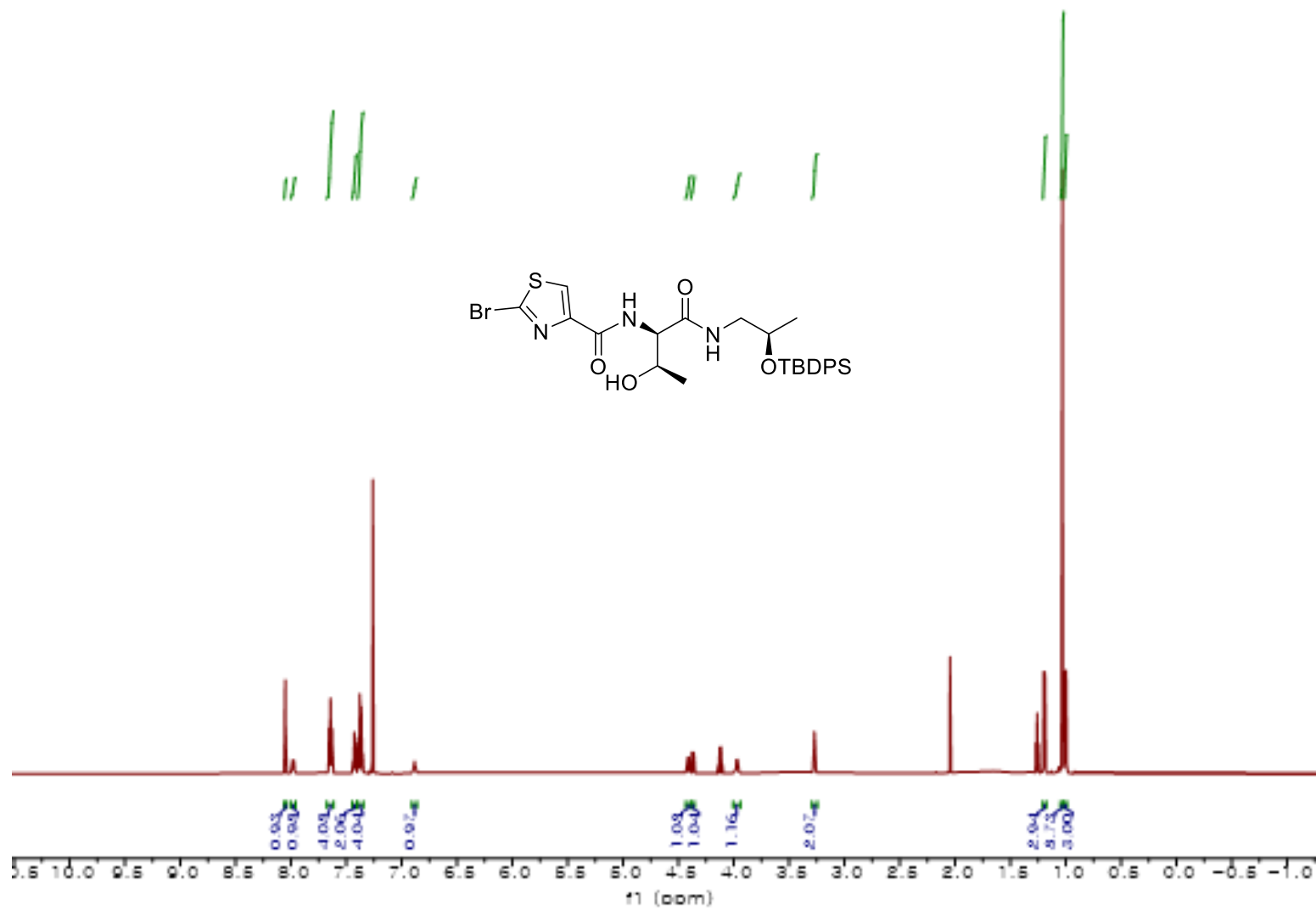


¹³C-NMR Spectrum of Compound 22h (100 MHz, CDCl₃)

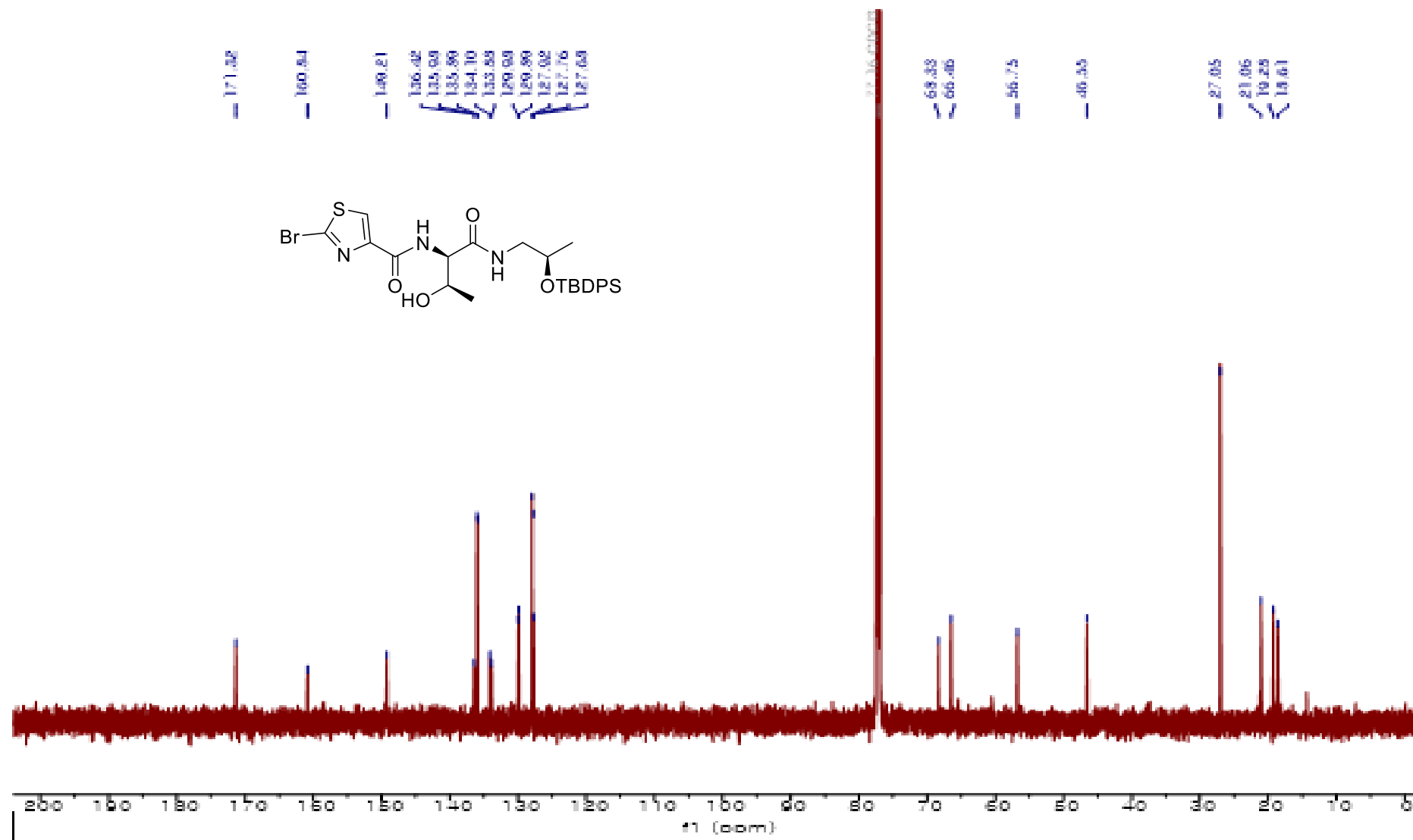


¹H-NMR Spectrum of Compound 27 (600 MHz, CDCl₃)

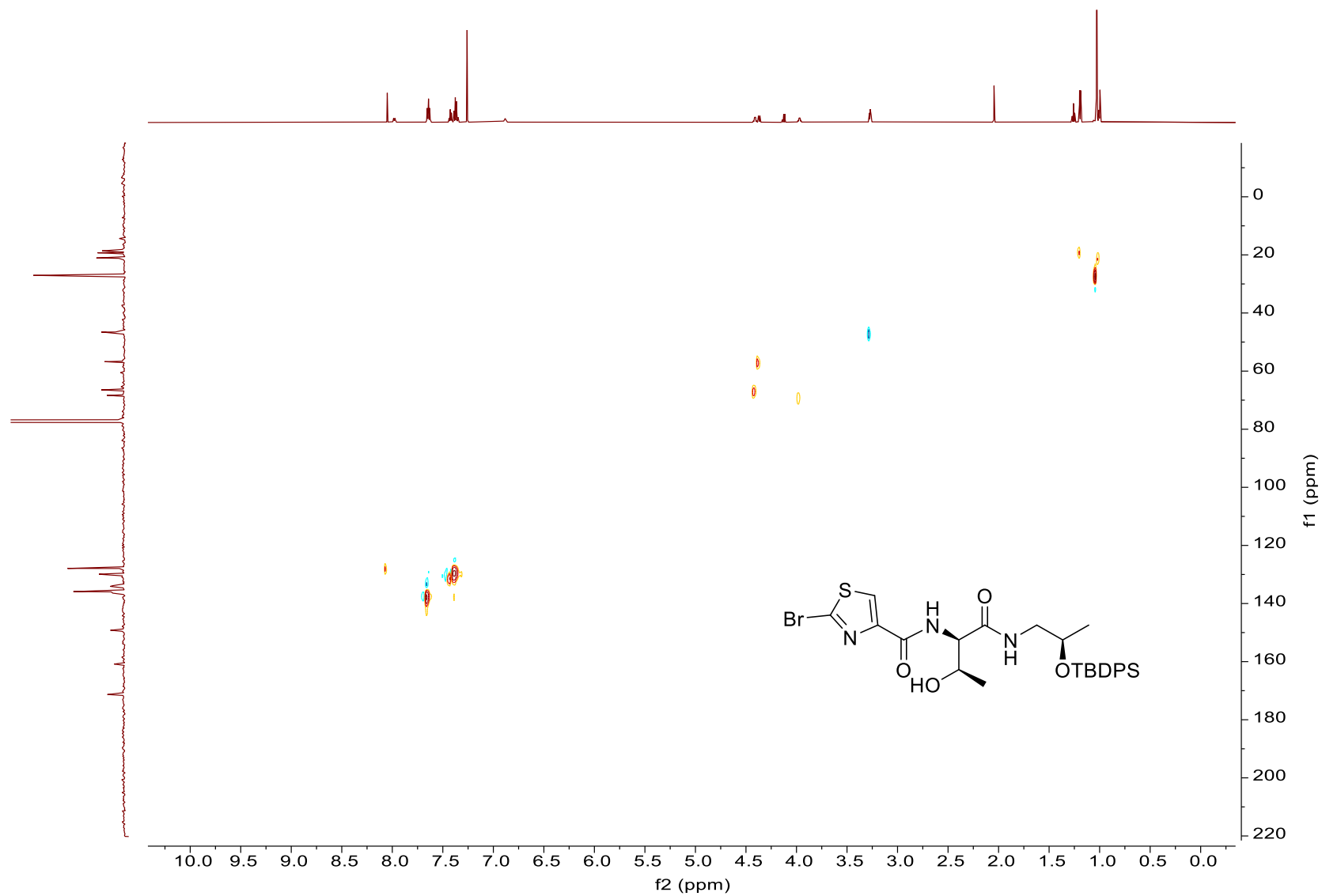




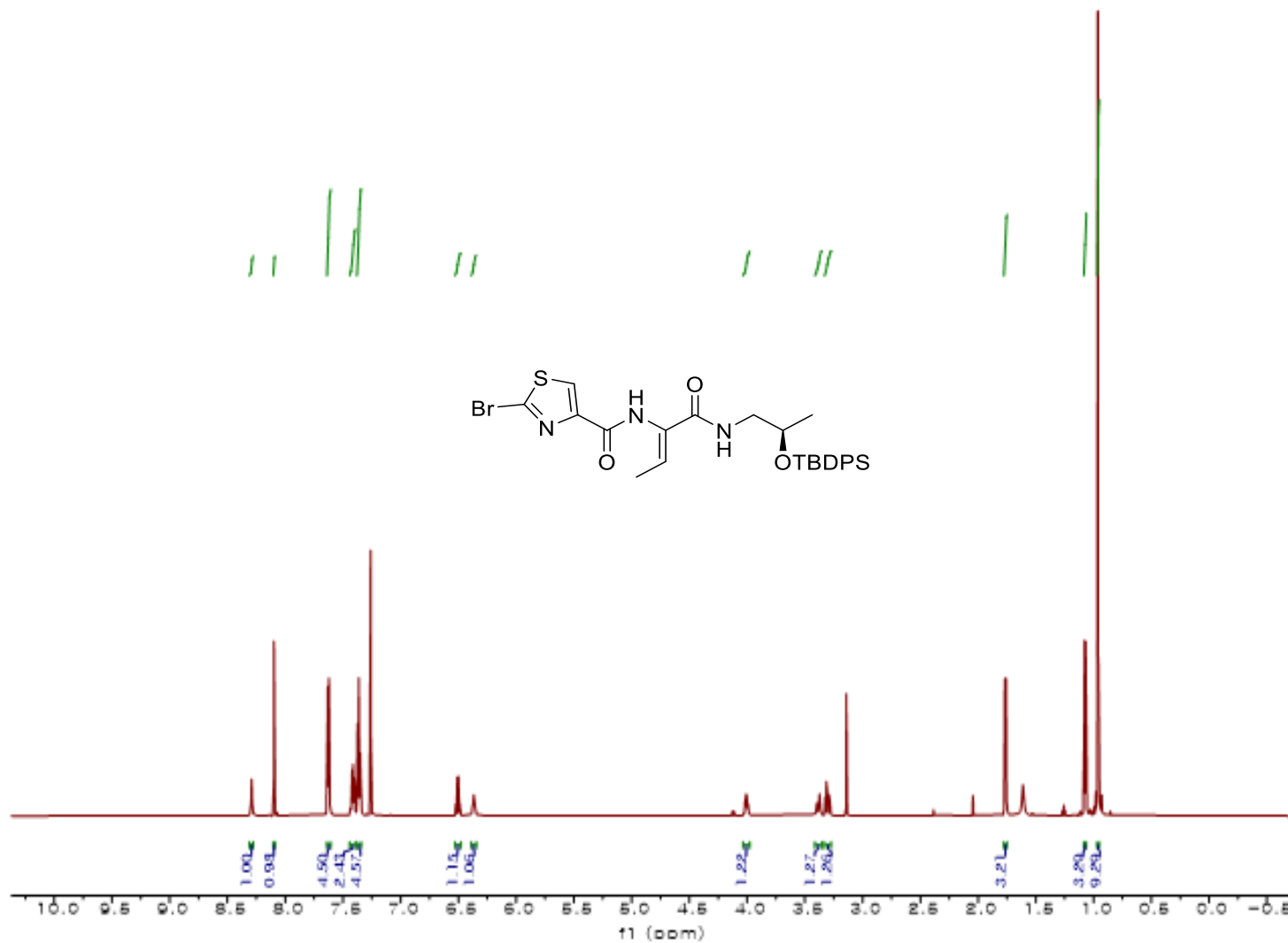
¹H-NMR Spectrum of Compound 28 (600 MHz, CDCl₃)



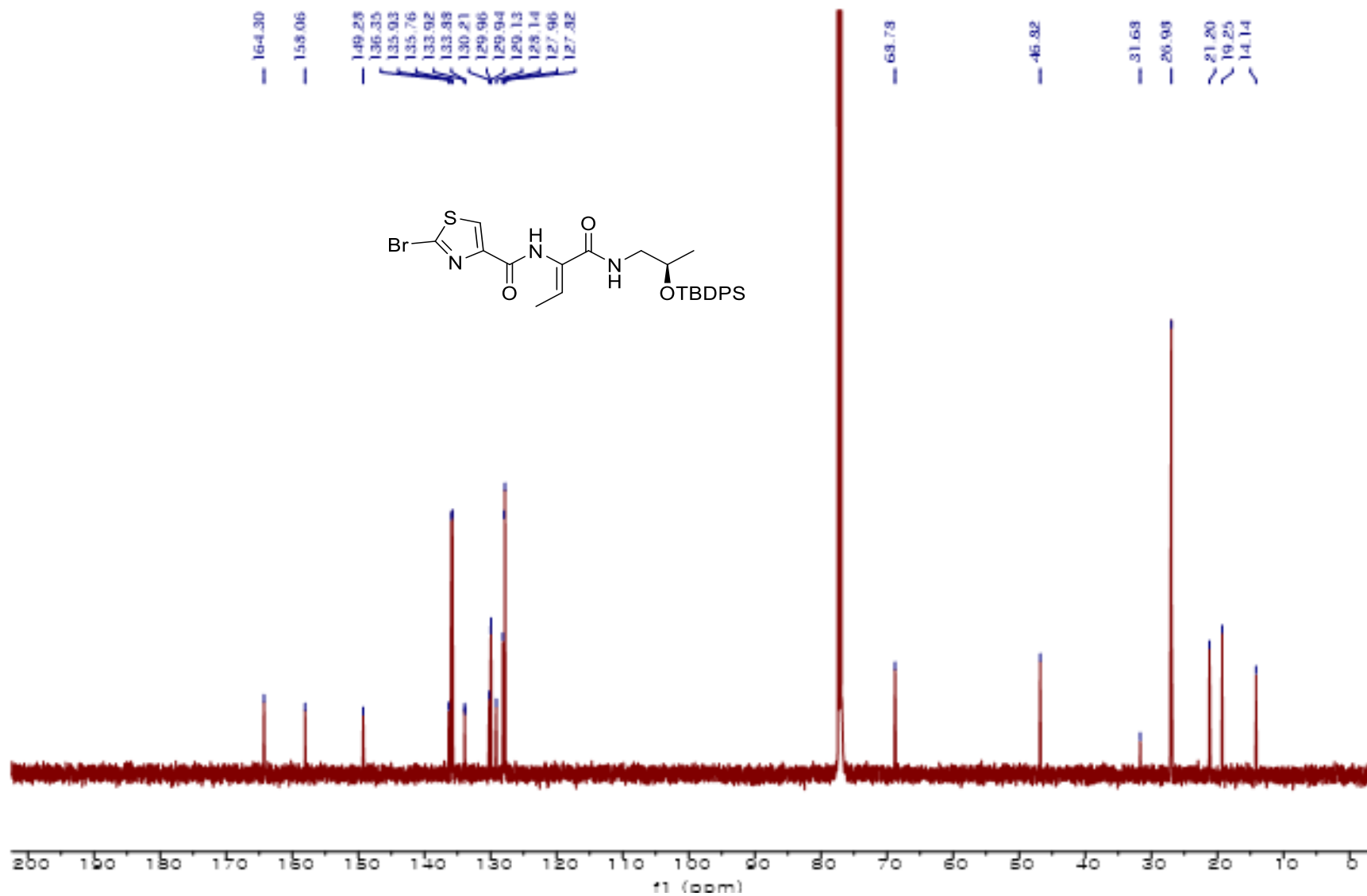
¹³C-NMR Spectrum of Compound 28 (151 MHz, CDCl₃)



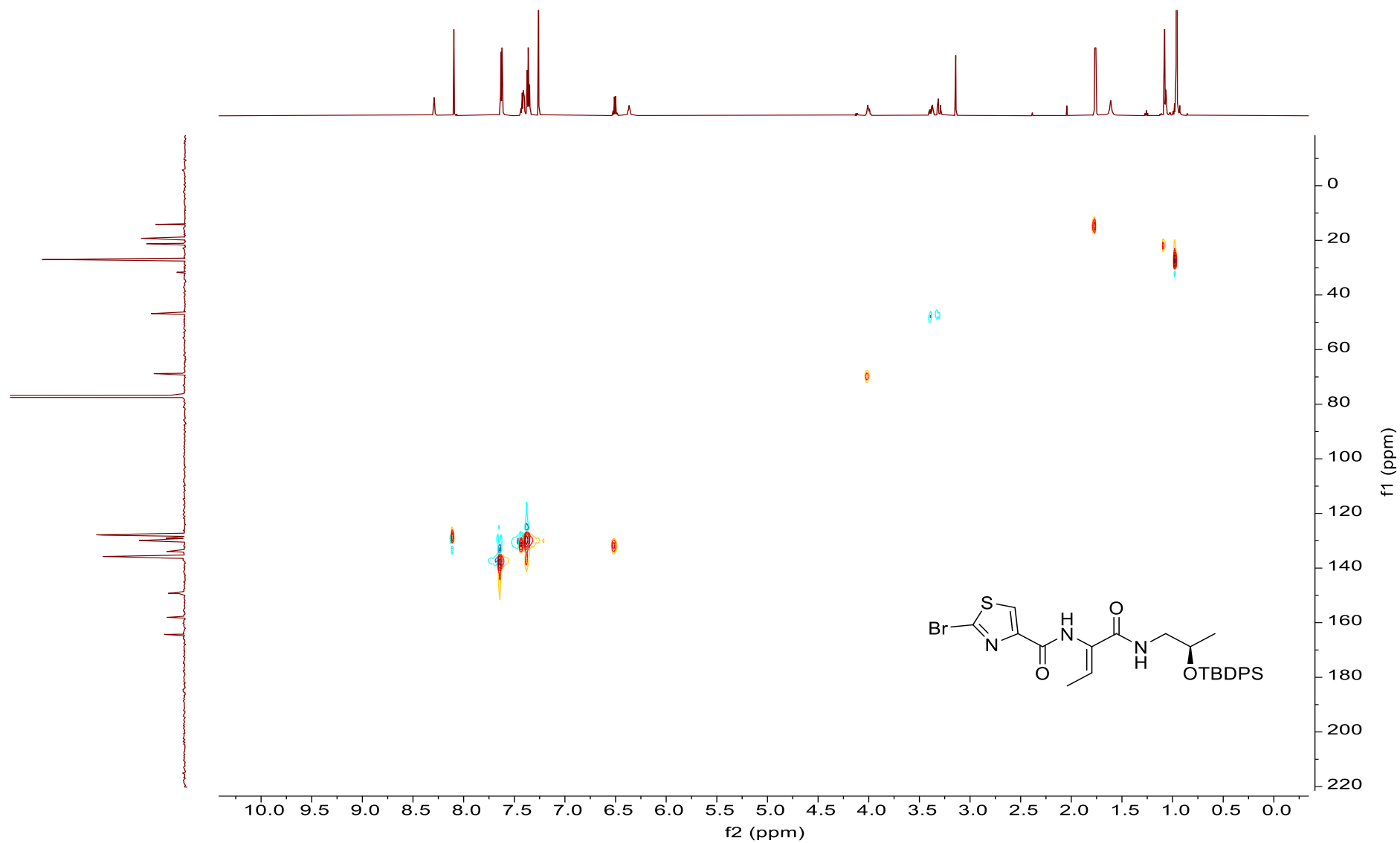
HSQC Spectrum of Compound 28 (600 MHz, CDCl₃)



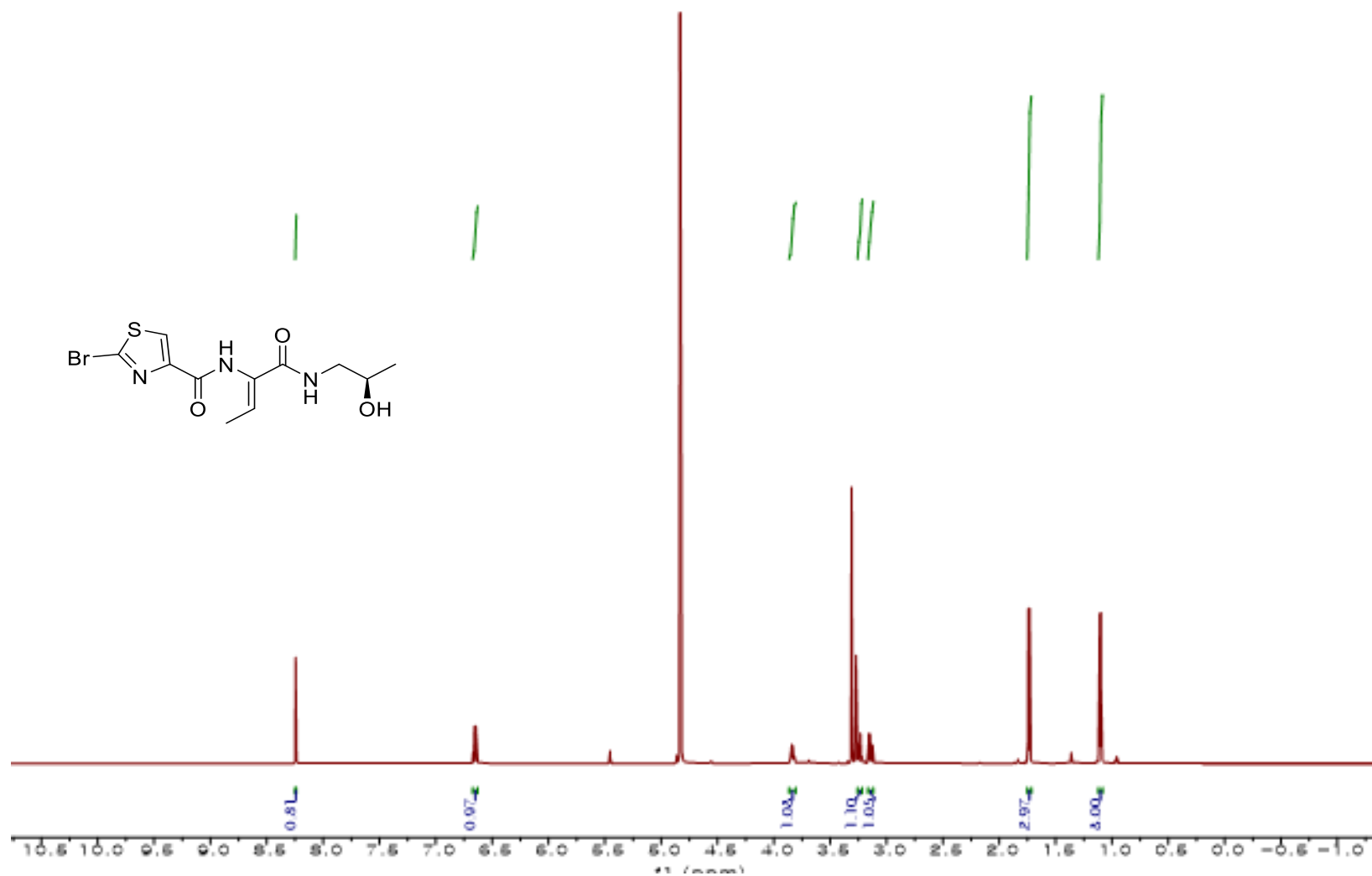
¹H-NMR Spectrum of Compound 29 (600 MHz, CDCl₃)



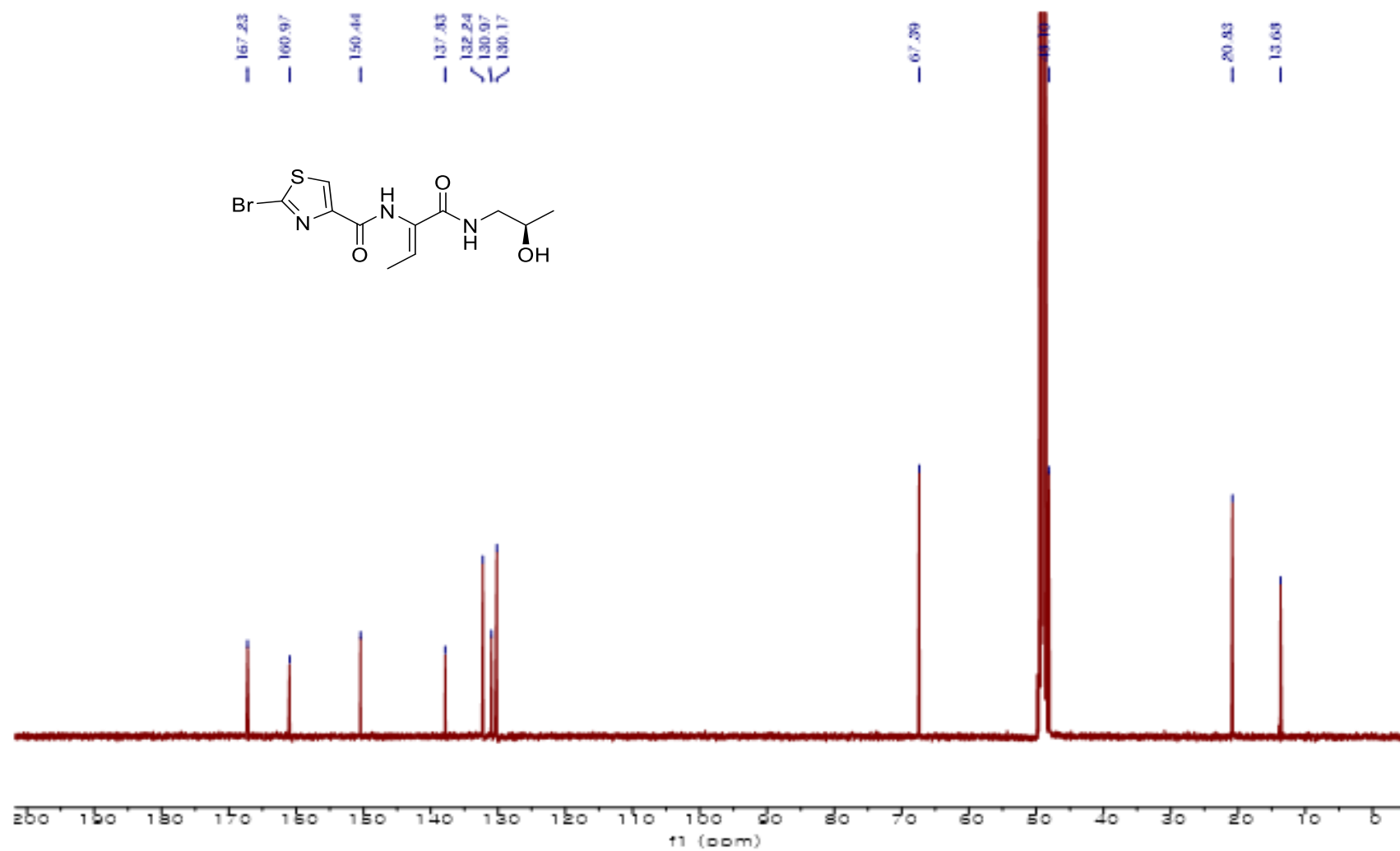
¹³C-NMR Spectrum of Compound 29 (151 MHz, CDCl₃)



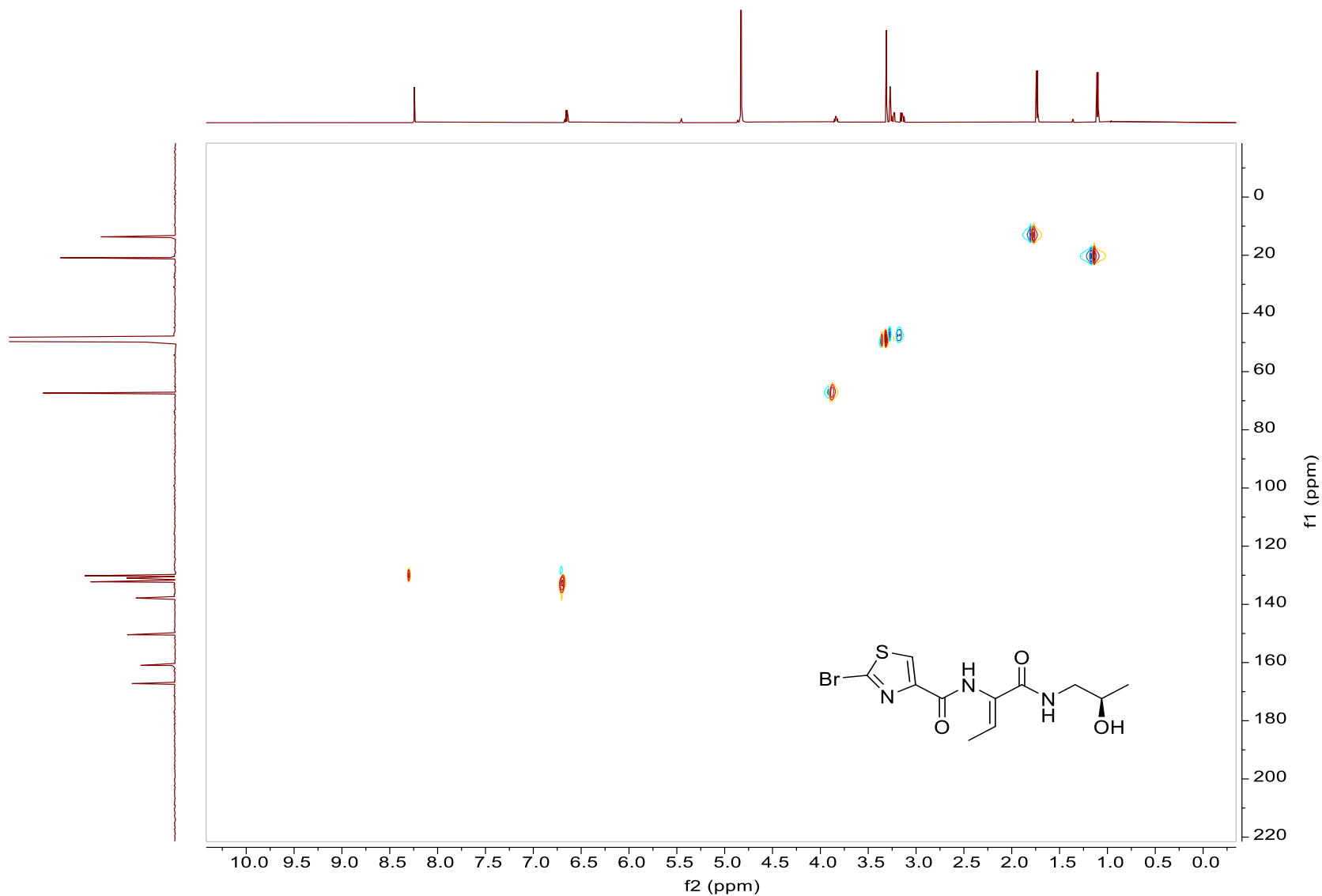
HSQC Spectrum of Compound 29 (600 MHz, CDCl₃)



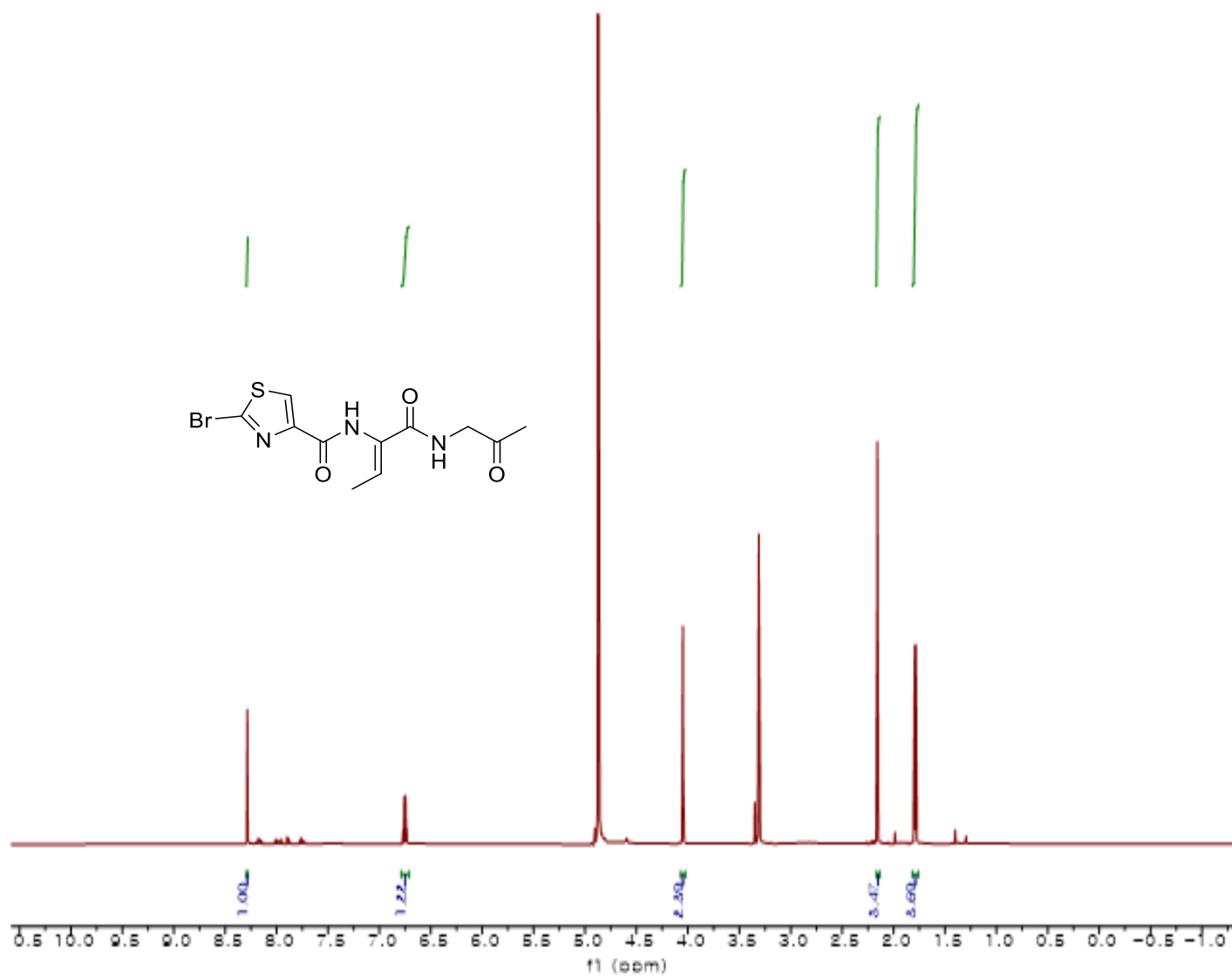
¹H-NMR Spectrum of Compound 24 (600 MHz, CDCl₃)



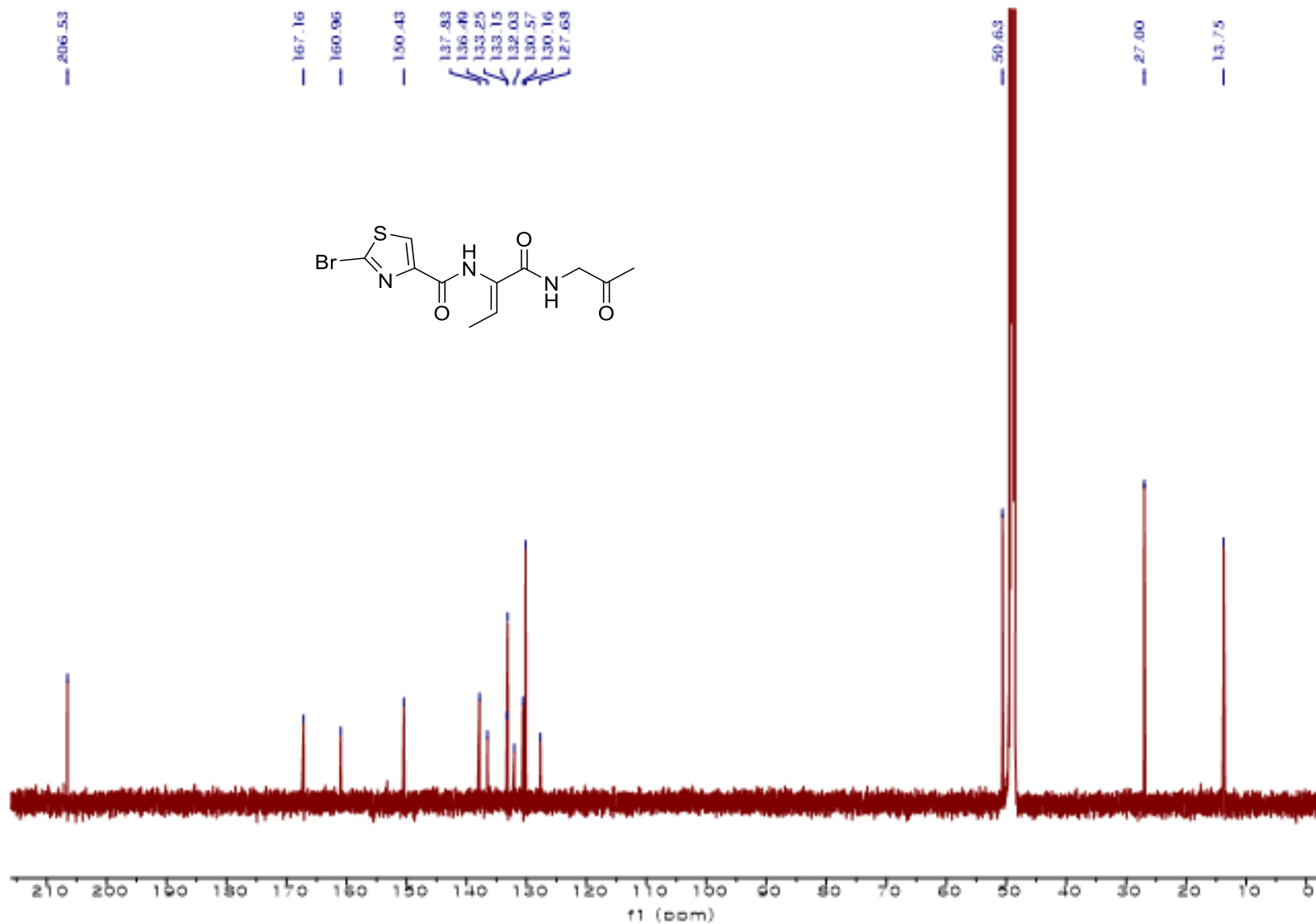
¹³C-NMR Spectrum of Compound 24 (151 MHz, CDCl₃)



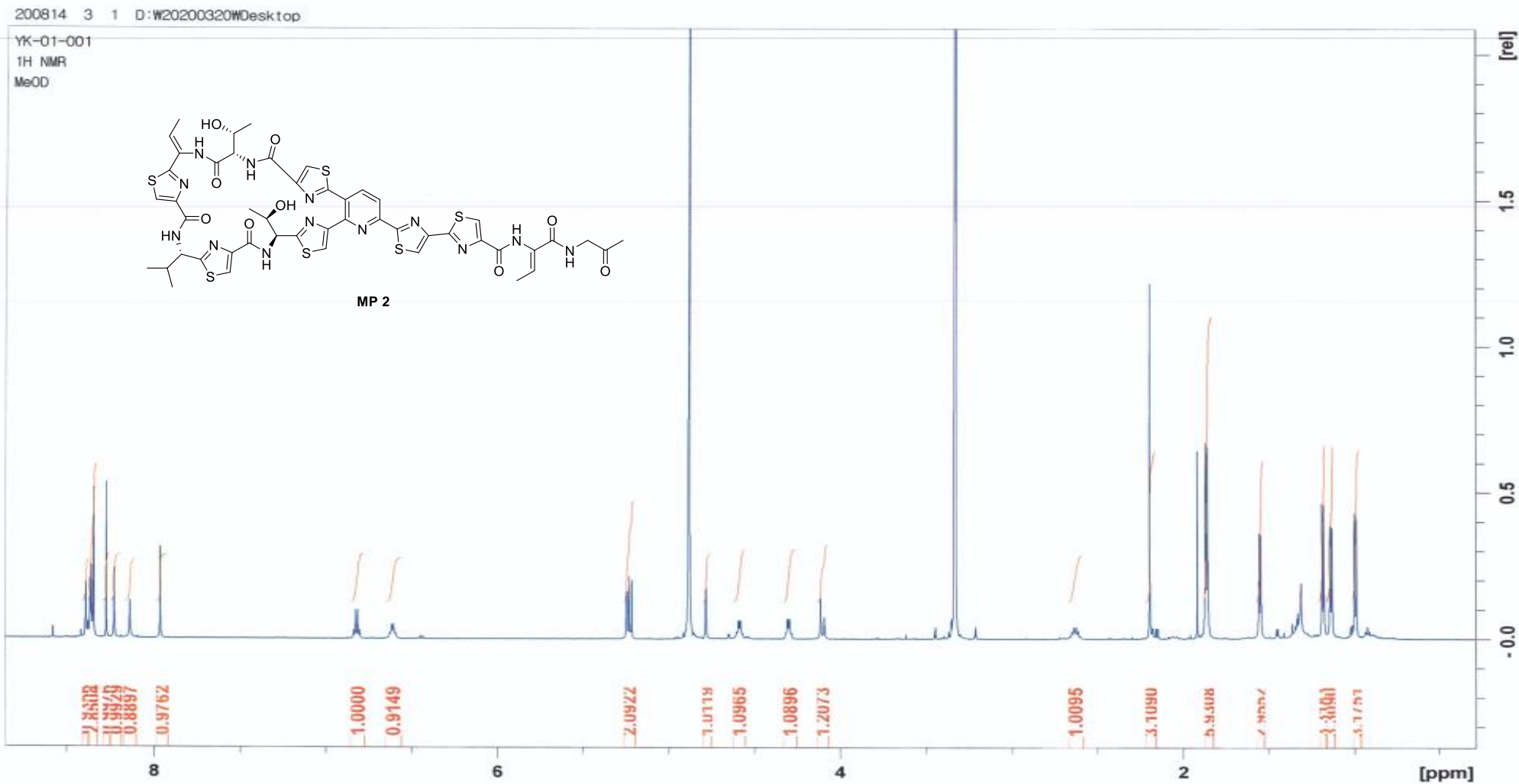
HSQC Spectrum of Compound 24 (600 MHz, CDCl₃)



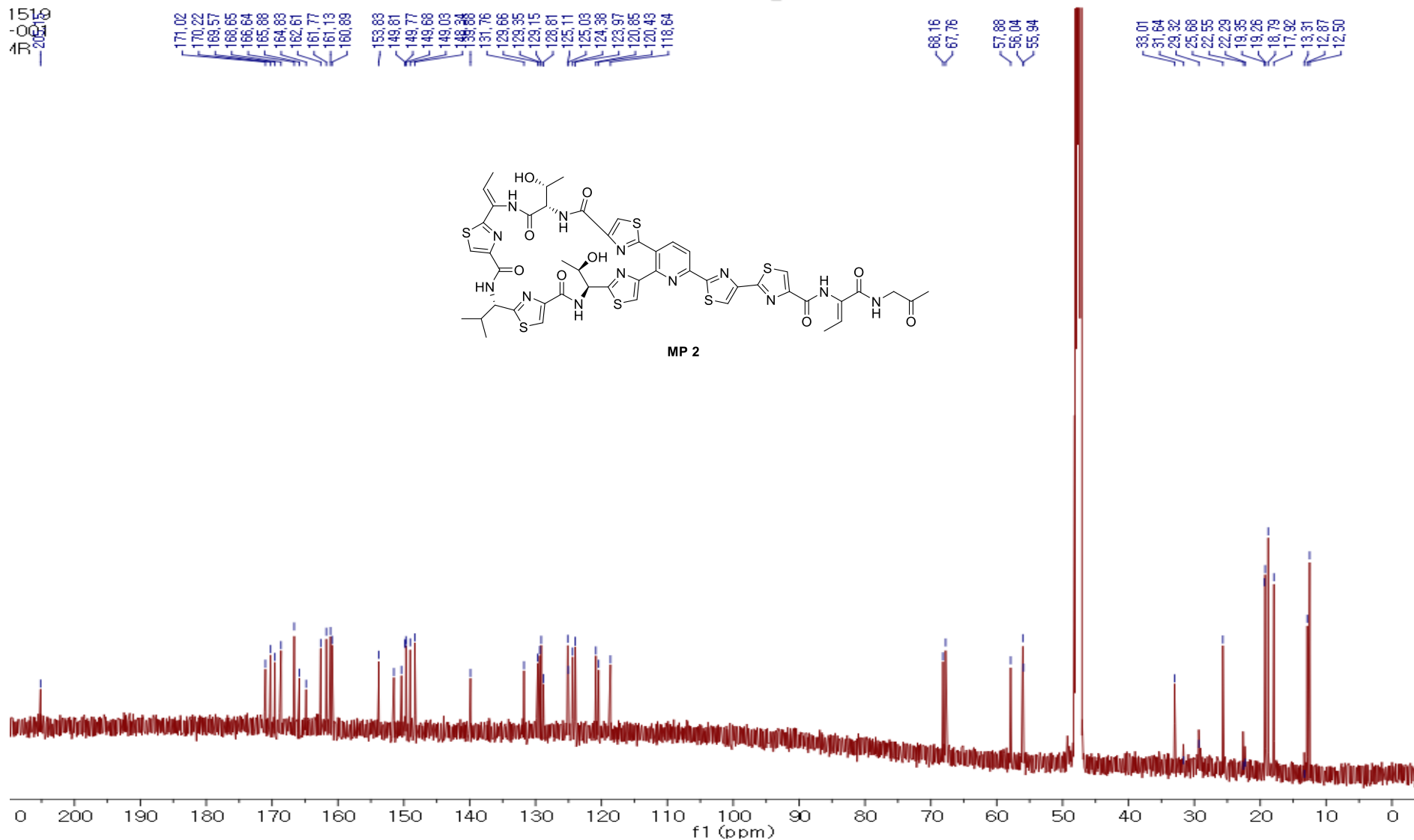
¹H-NMR Spectrum of Compound 25 (600 MHz, CDCl₃)



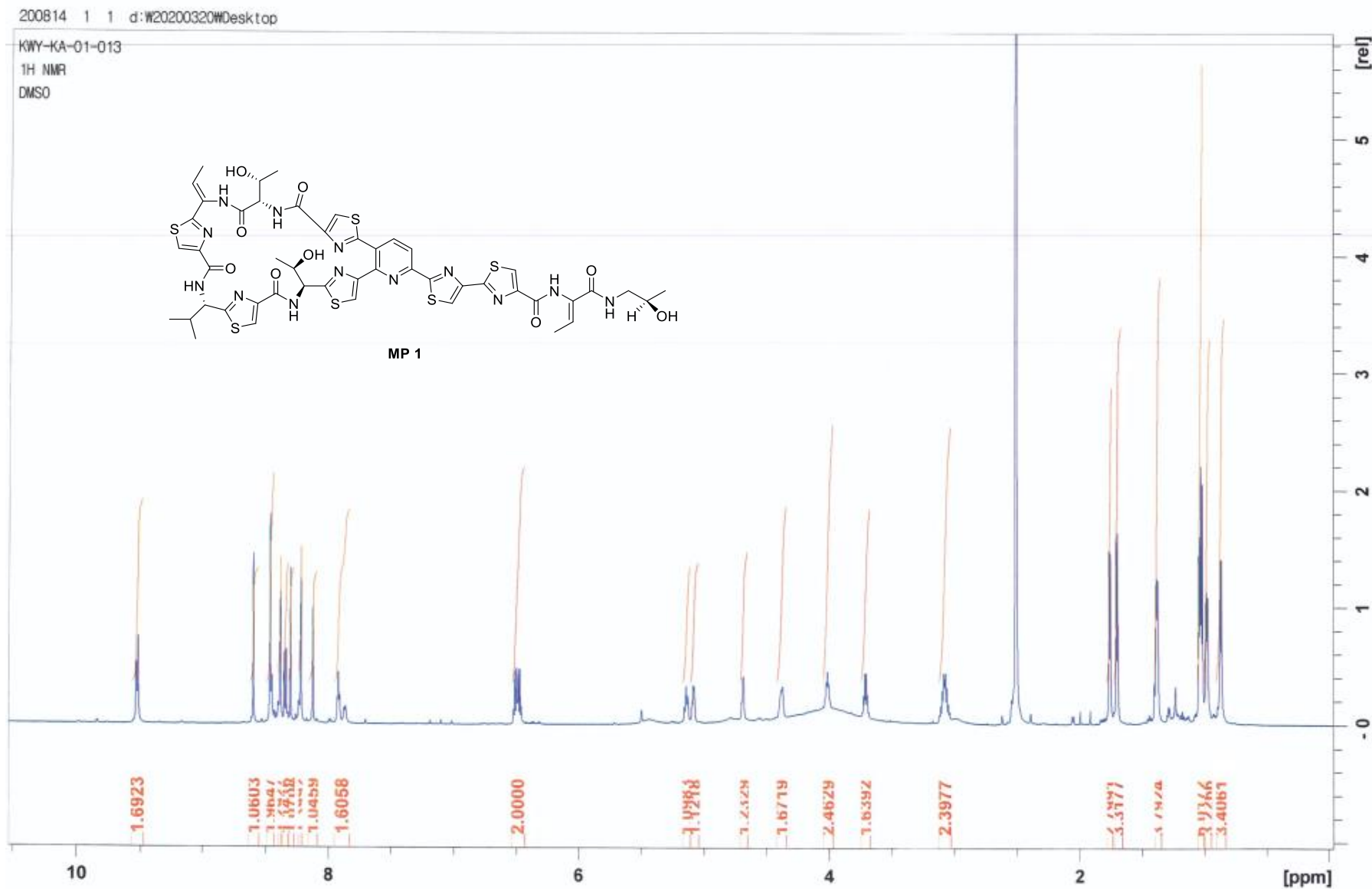
¹³C-NMR Spectrum of Compound 25 (151 MHz, CDCl₃)



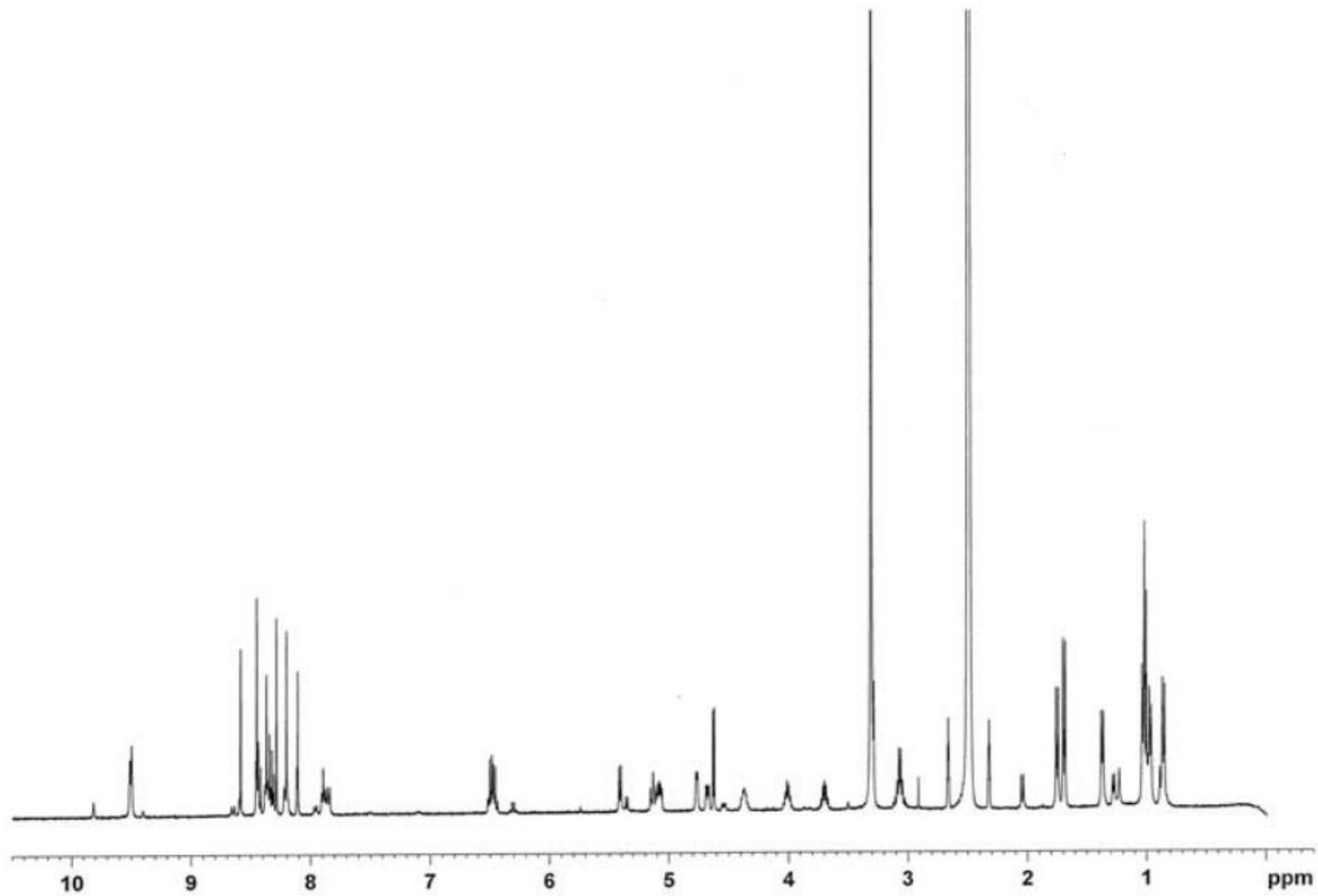
¹H-NMR Spectrum of Synthetic Micrococcin P2, 1 (600 MHz, CD₃OD)



¹³C-NMR Spectrum of Synthetic Micrococcin P2, 1 (151 MHz, CD₃OD)

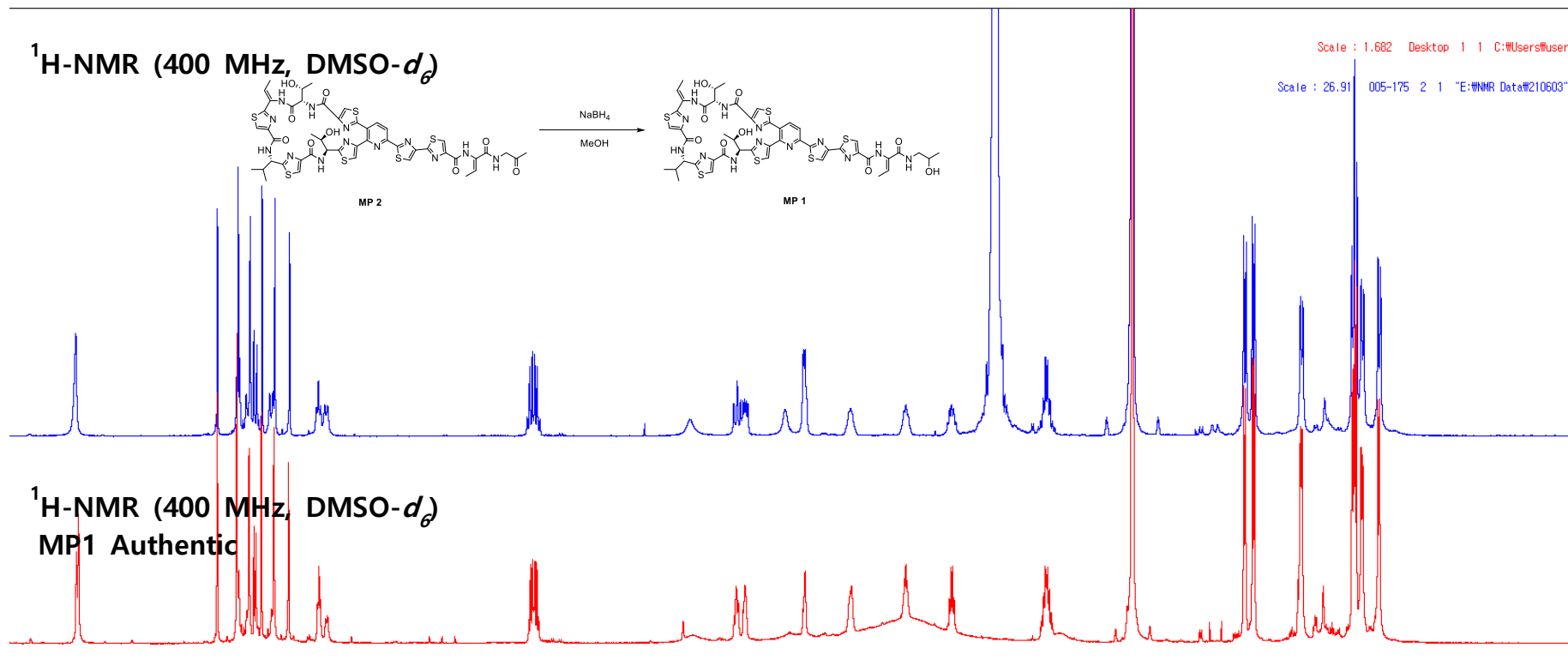


^1H NMR spectrum of synthetic MP1 (600 MHz, $\text{DMSO}-d_6$)

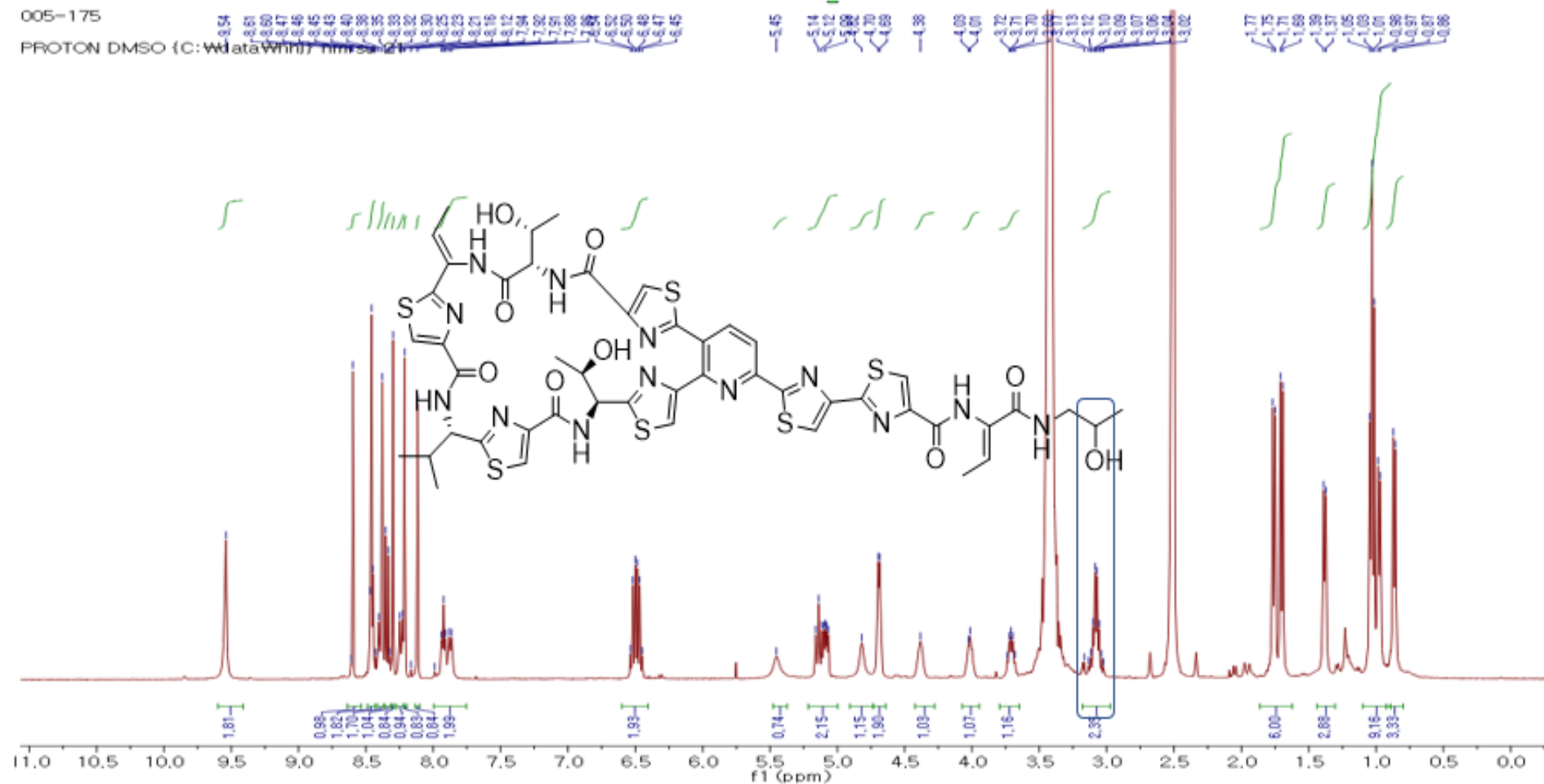


¹H NMR spectrum of authentic MP1 in DMSO-*d*₆¹ for comparison

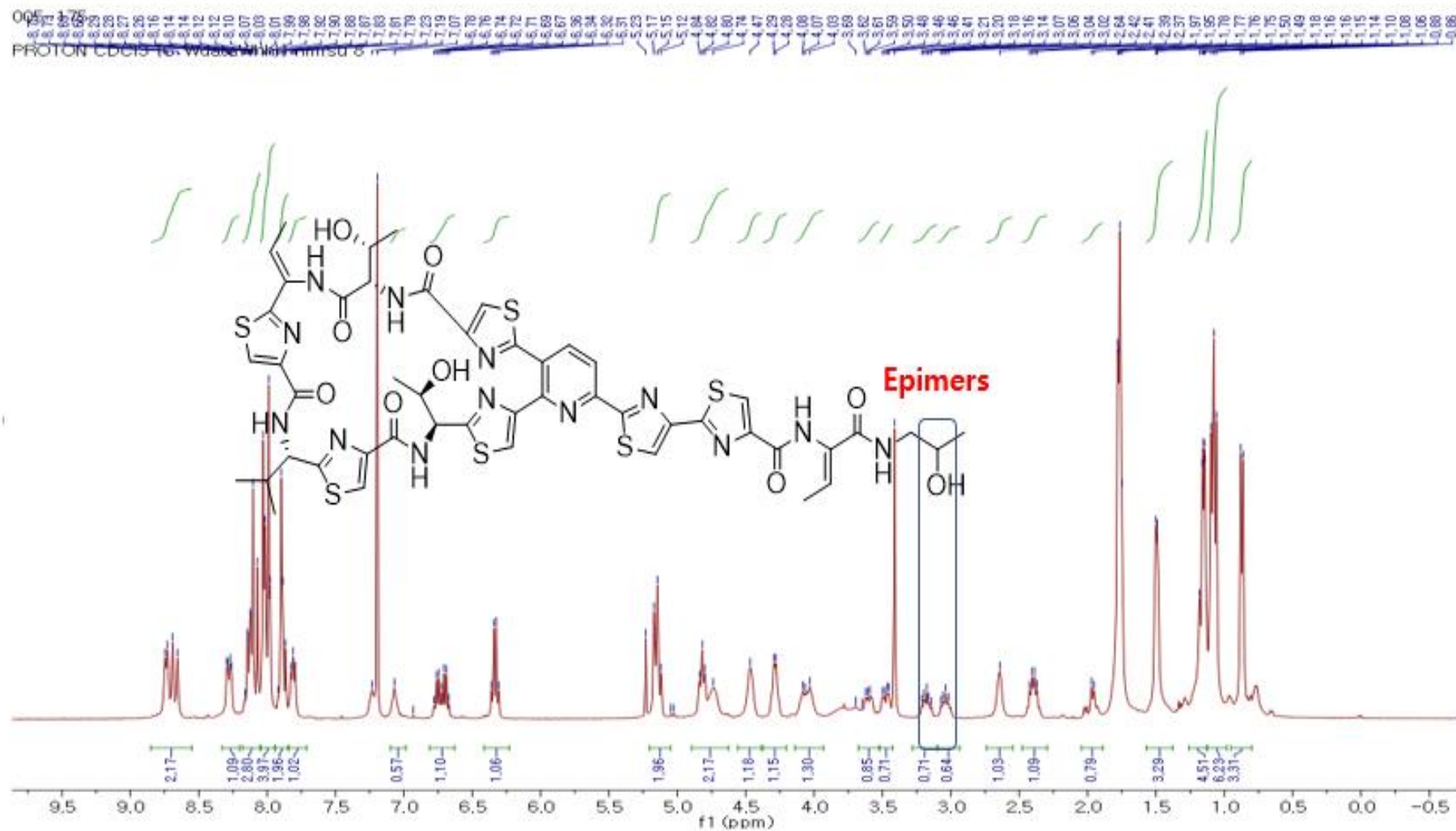
¹ This spectrum was reproduced from David Lefranc's dissertation (footnote 11).



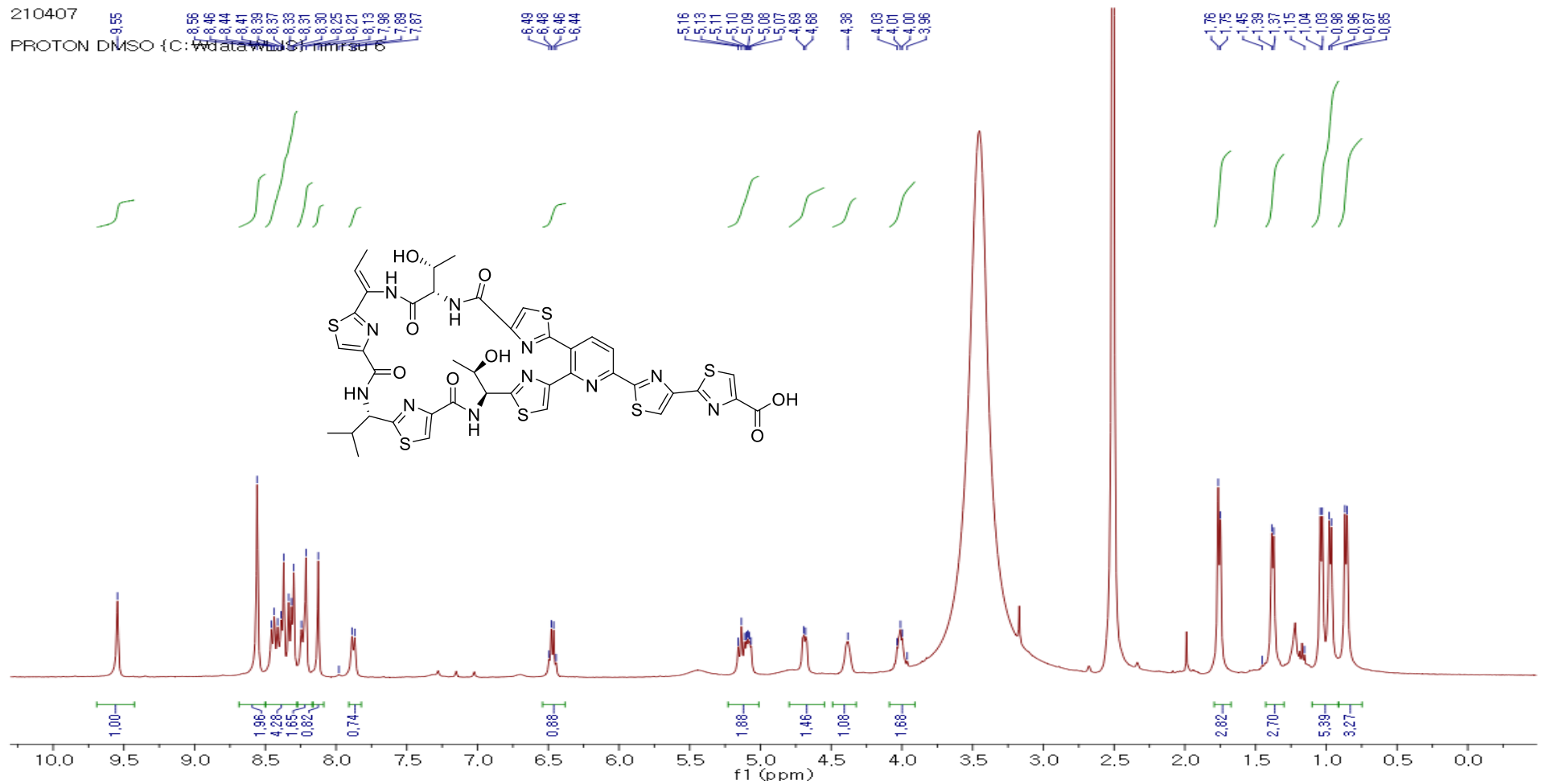
$^1\text{H NMR}$ spectral comparison of reduced MP2 vs. MP1 ($\text{DMSO-}d_6$)



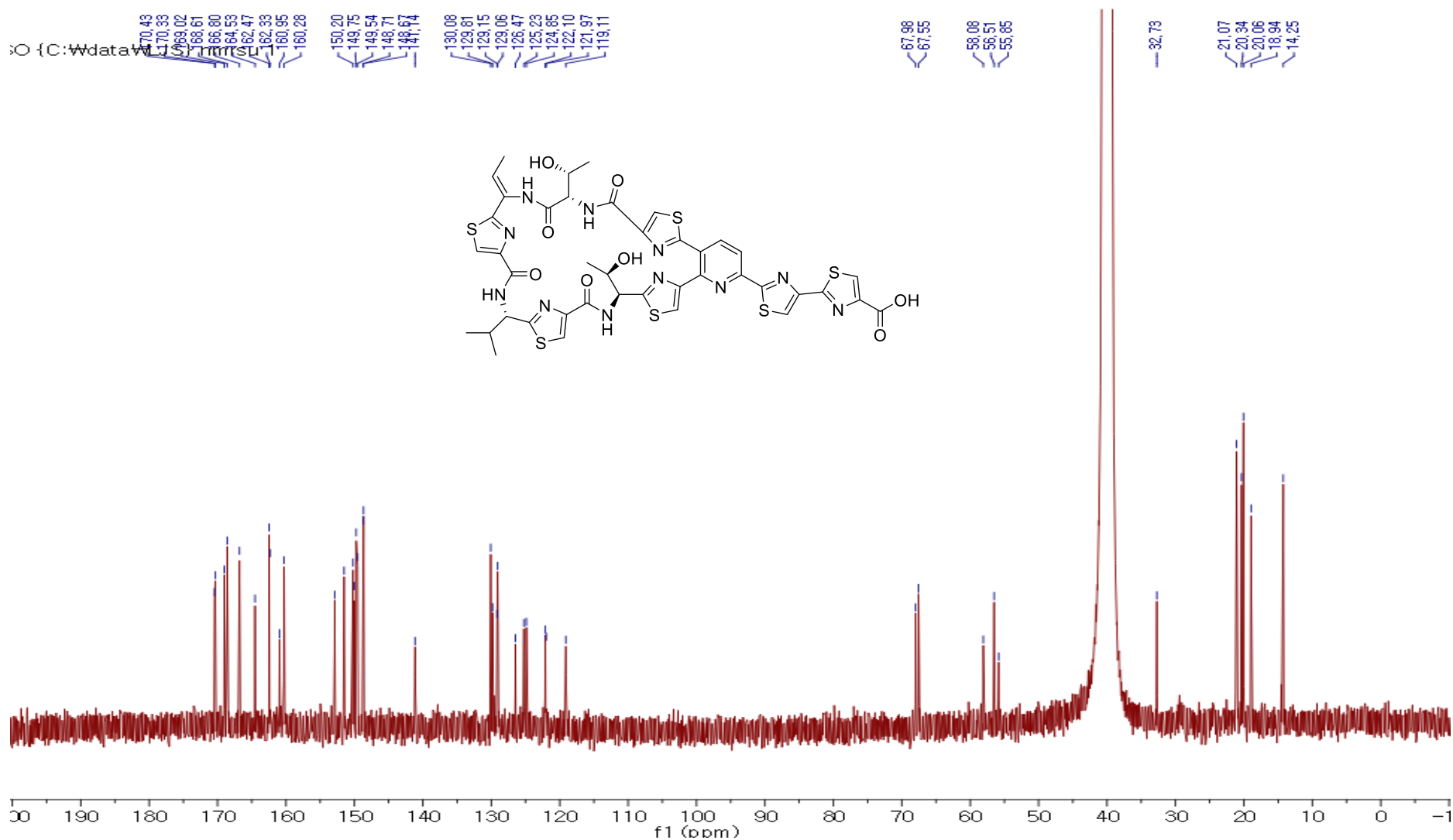
^1H NMR spectrum of reduced MP2 in $\text{DMSO}-d_6$ (600 MHz): the epimers are not resolved



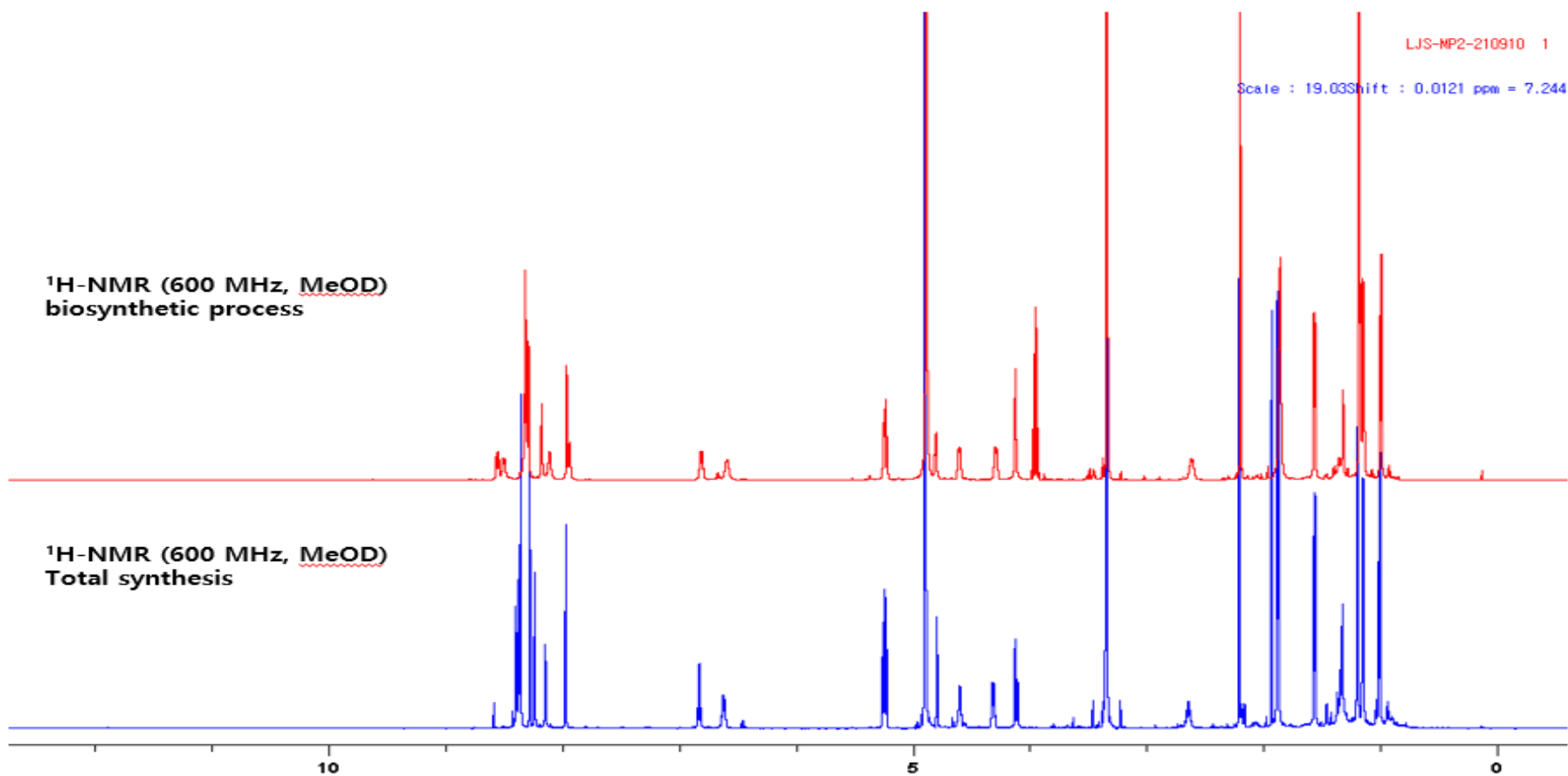
^1H NMR spectrum of reduced MP2 in CDCl_3 (600 MHz) clearly showing the presence of MP1 and *epi*-MP1



¹H-NMR Spectrum of Compound 30 (400 MHz, DMSO-*d*₆)

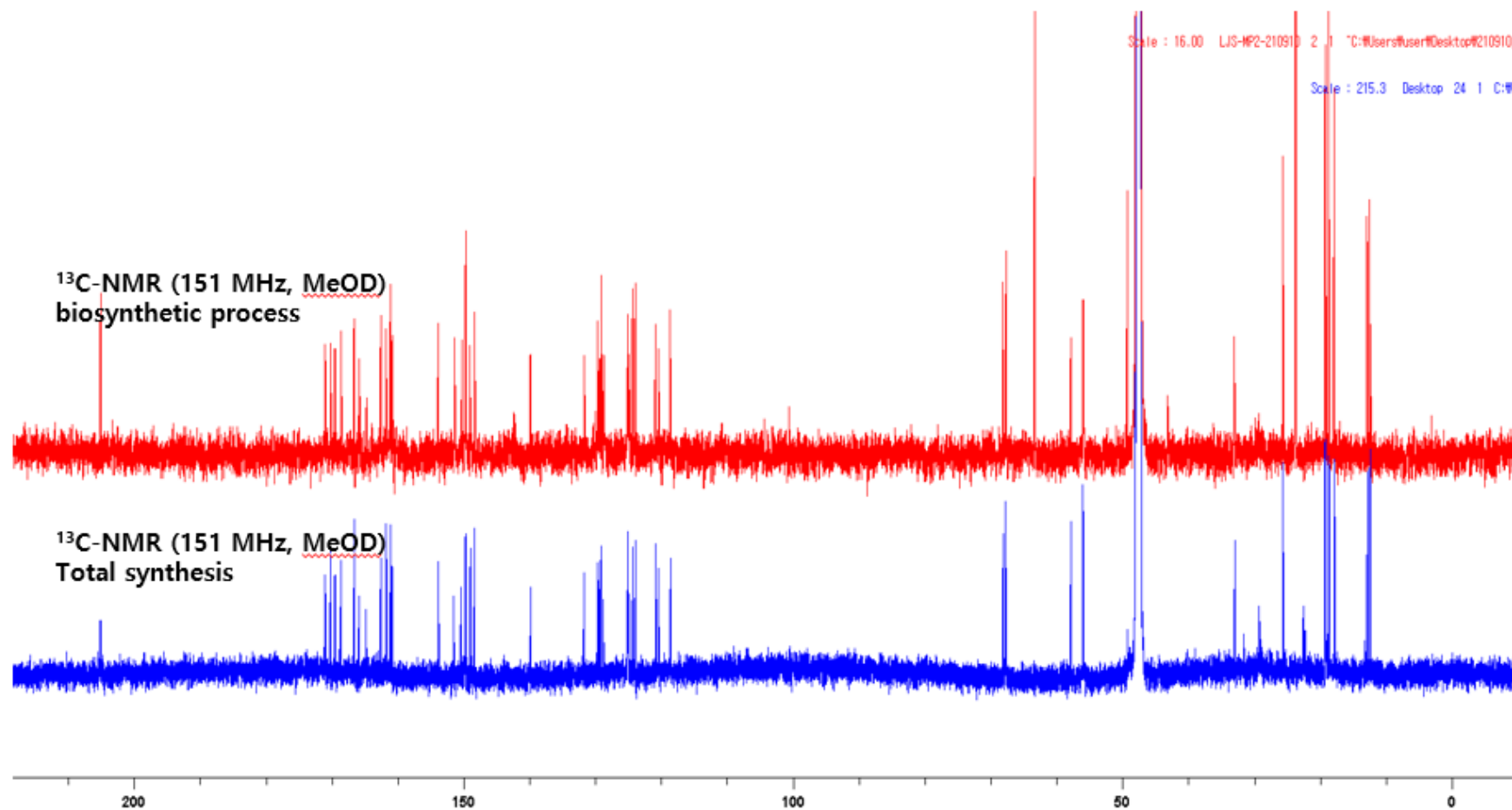


¹³C-NMR Spectrum of Compound 30 (100 MHz, DMSO-*d*₆)



¹H-NMR Spectra of Fermented (top) vs. Synthetic MP2 (150 MHz, CD₃OD)

small differences exist only at the level of exchangeable protons (OH and NH)



^{13}C -NMR Spectra of Fermented (top) vs. Synthetic MP2 (150 MHz, CD_3OD)