Development of Chiral DMAP Catalyst for Dynamic Kinetic Resolution of Azole Hemiaminals

Artis Kinens,[†] Marcis Sejejs,[†§] Adam S. Kamlet,[‡] David W. Piotrowski,*[‡] Edwin Vedejs[†] and Edgars Suna*[†§]

[†] *Latvian Institute of Organic Synthesis, Aizkraukles 21, LV-1006, Riga, Latvia*

[§] *University of Latvia, Department of Chemistry, Jelgavas 1, LV-1006, Riga, Latvia*

[‡] *Worldwide Medicinal Chemistry, Pfizer, Inc., Eastern Point Road, Groton, Connecticut 06340, USA*

edgars@osi.lv, david.w.piotrowski@pfizer.com

CONTENTS

NMR titration of catalysts (*S*,*S*)–1a,e,m

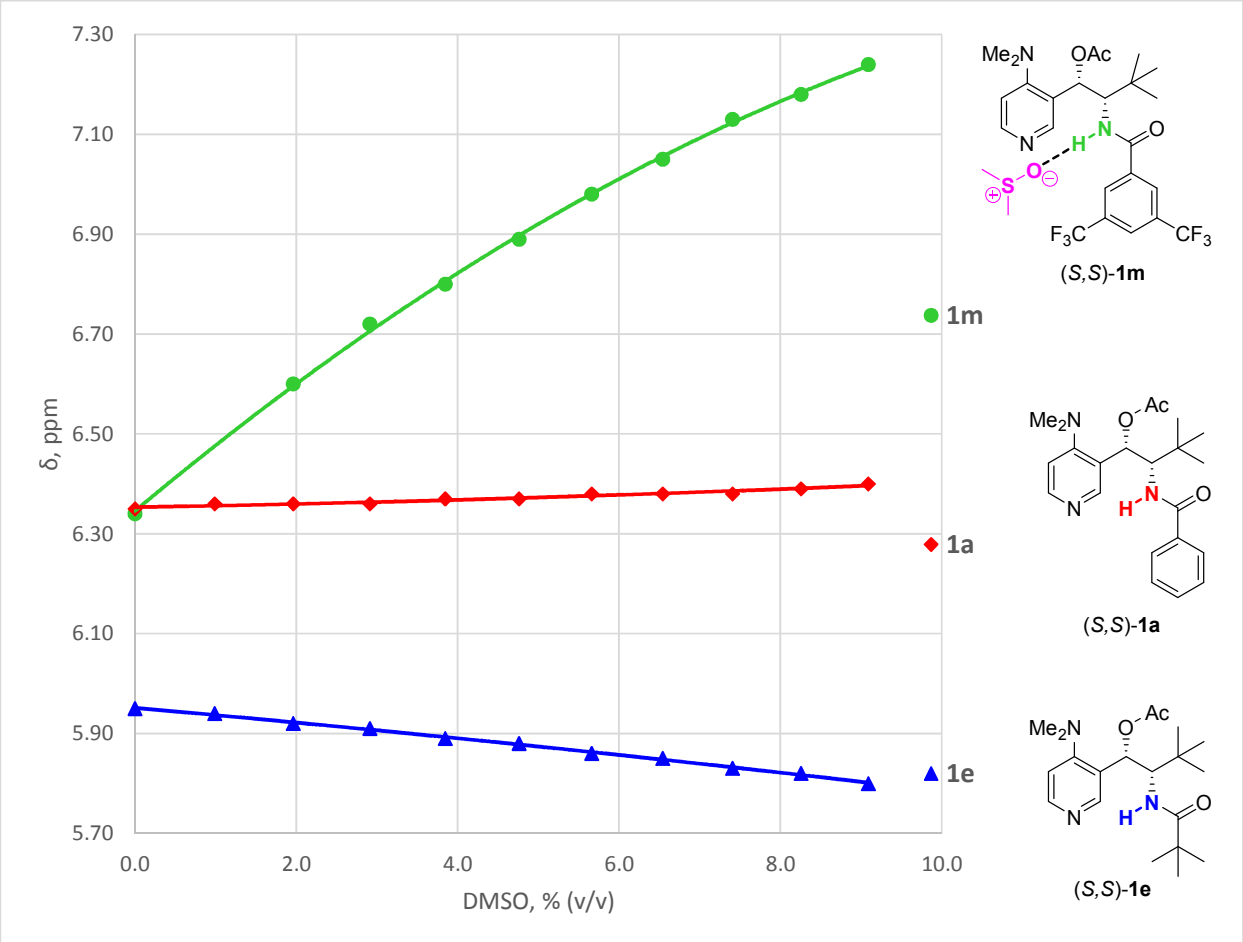


Figure S1. NMR titration of (*S*,*S*)–**1a,e,m** with DMSO-d_6 in $CHCl_3$-*d* at 298 K.

H-bond formation ability of catalysts (*S*,*S*)–**1a,e,m** was evaluated by NMR titration of their $CHCl_3$-*d* solution with DMSO-d_6.[1] Accordingly, DMSO-d_6 was added portionwise (1 vol% increment) to the $CHCl_3$-*d* solution of DMAP species (*S*,*S*)–**1a,e,m** and change of the amide N-H chemical shifts was monitored. The amide ^{1}H chemical shifts for each of the catalyst (*S*,*S*)–**1a,e,m** was plotted versus amount of the added DMSO-d_6 (Scheme S8). Negligible changes of ^{1}H chemical shifts were observed for catalysts (*S*,*S*)–**1a,e** indicating that these DMAP species feature weak H-bonding interactions with DMSO. In contrast, a relatively large downfield shift

(1) (a) Wagner, G.; Pardi, A.; Wuethrich, K. *J. Am. Chem. Soc.* **1983**, *105*, 5948–5949; (b) Jansma, A.; Zhang, Q.; Li, B.; Ding, Q.; Uno, T.; Bursulaya, B.; Liu, Y.; Furet, P.; Gray, N. S.; Geierstanger, B. H. *J. Med. Chem.* **2007**, *50*, 5875–5877.

of the amide N-H was observed for chiral pyridine (*S*,*S*)–**1m** suggesting an increased H-bonding interactions with DMSO.

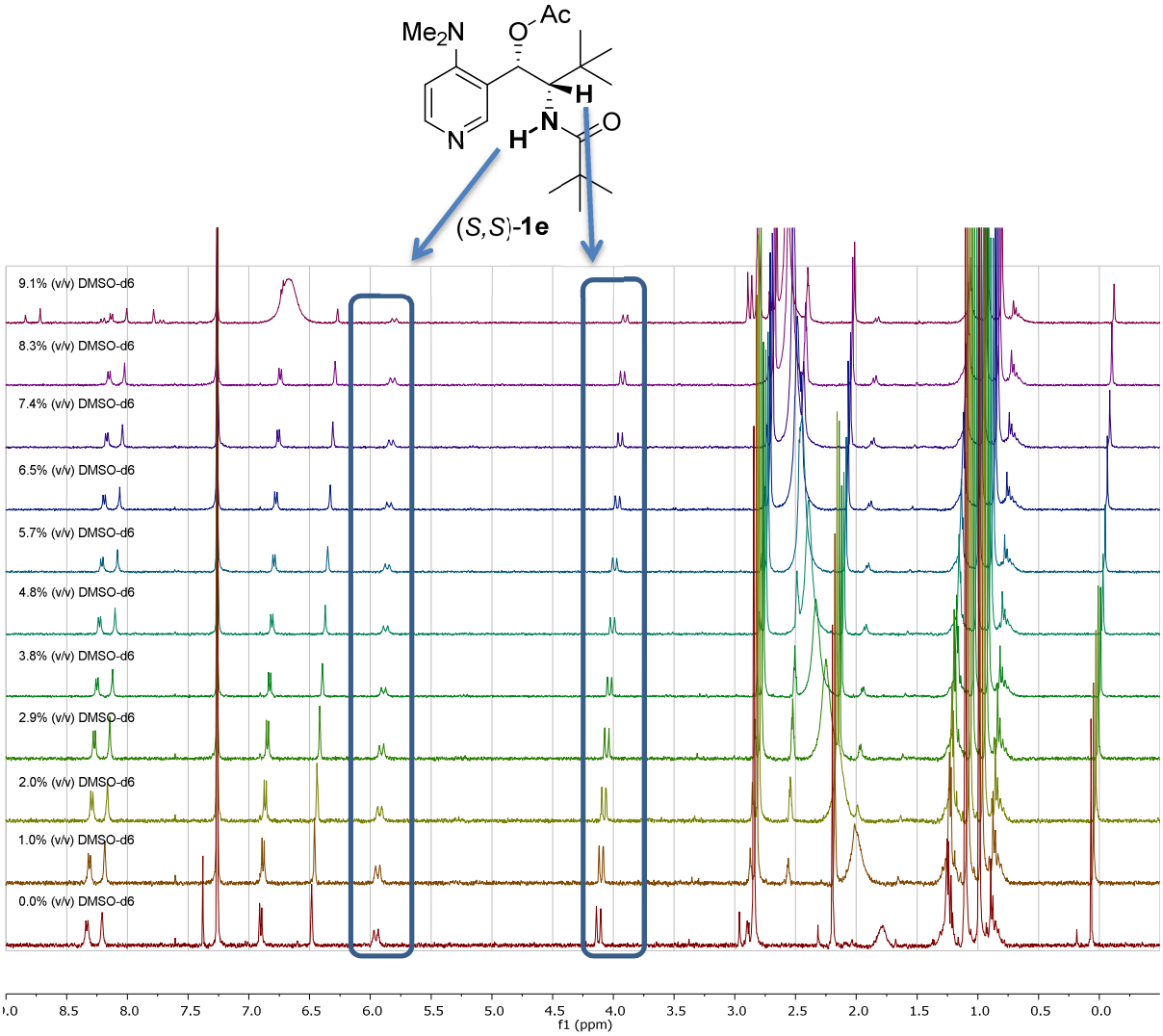


Figure S2. ^{1}H-NMR spectra for titration of (*S*,*S*)-**1e** with DMSO-d_6

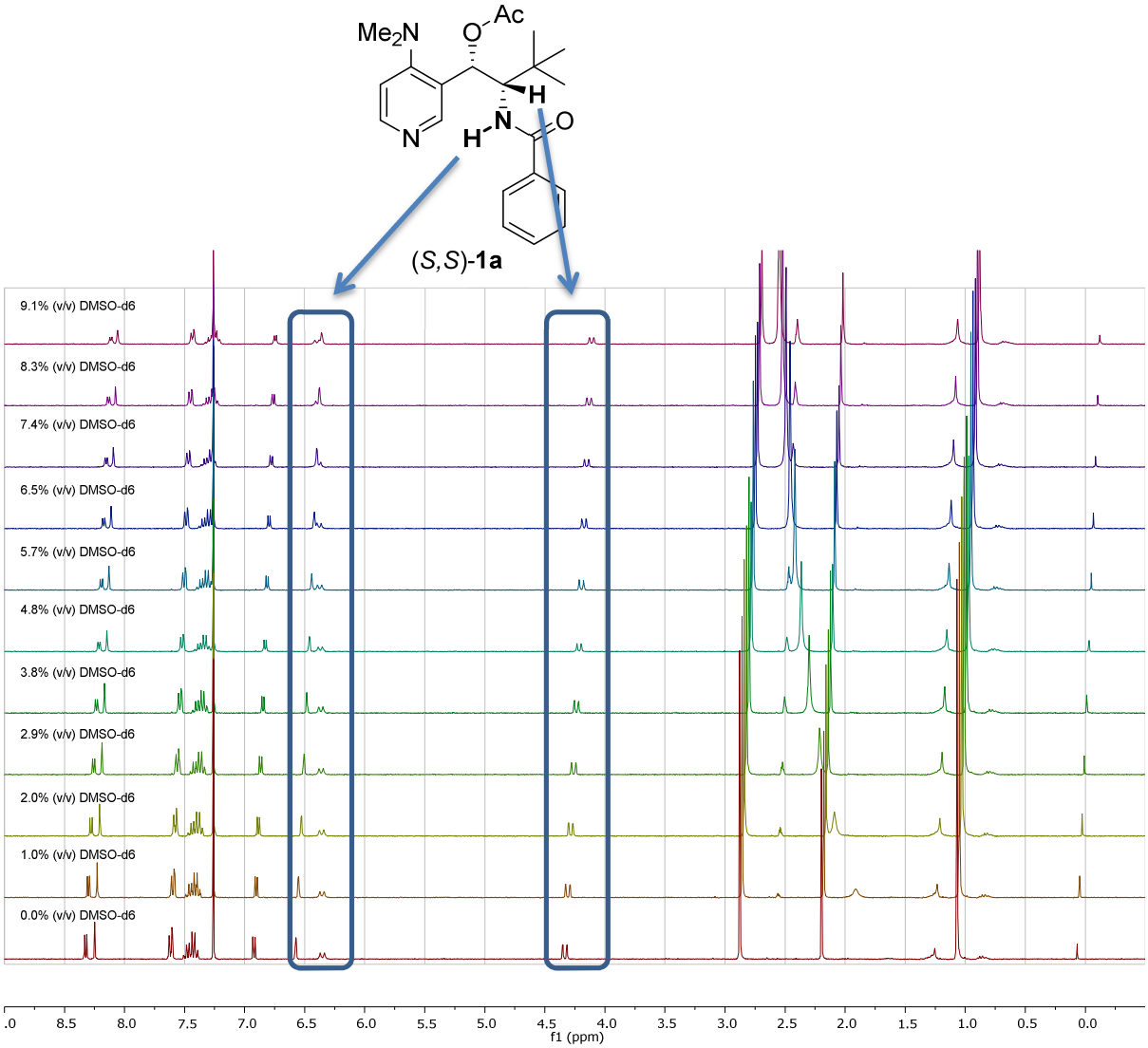


Figure S3. ^{1}H-NMR spectra for titration of (*S*,*S*)-**1a** with DMSO-d_6

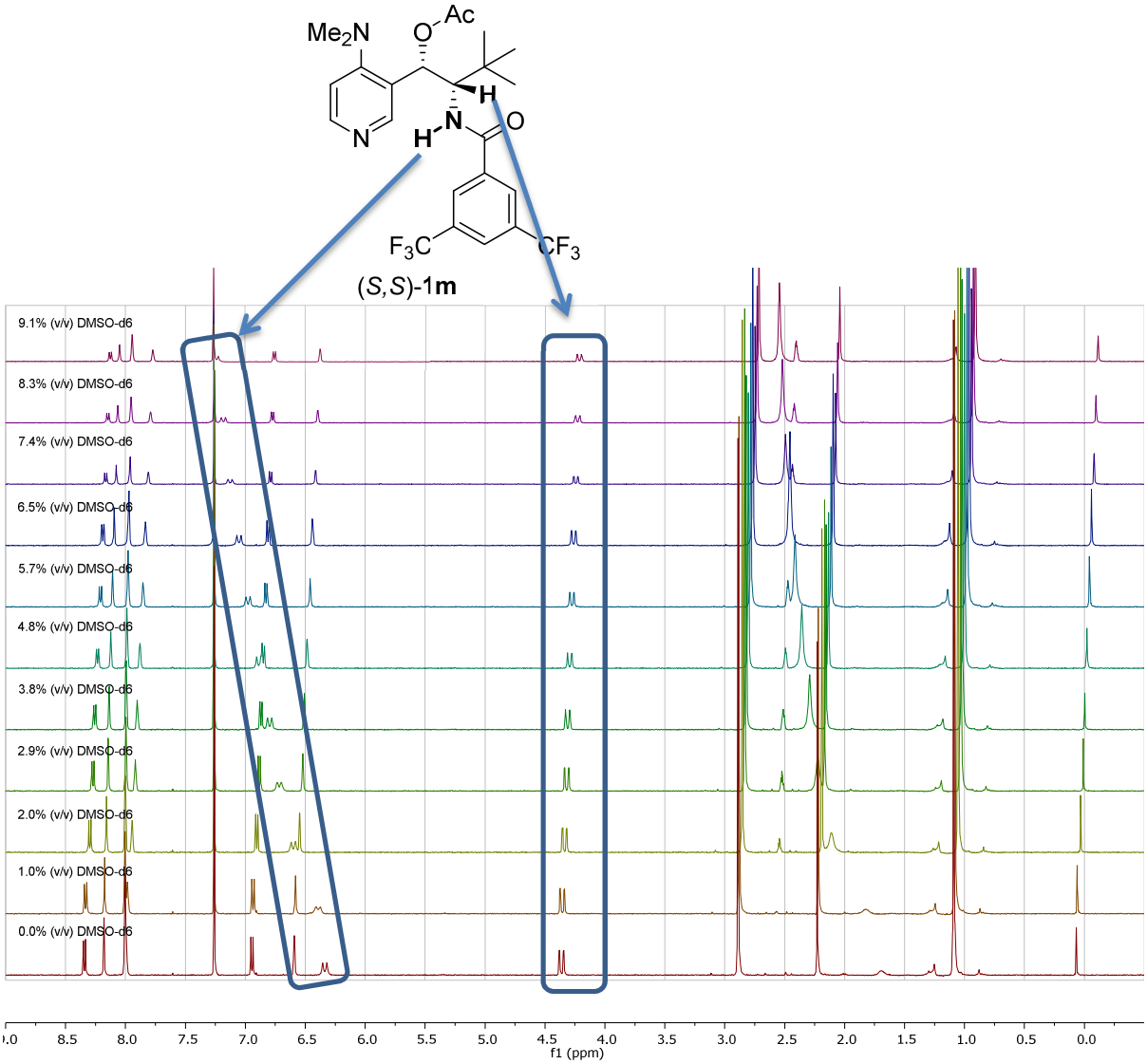
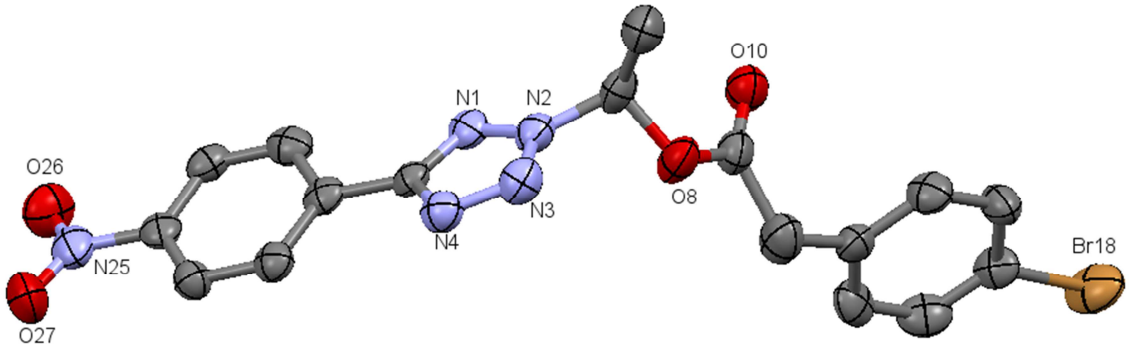


Figure S4. ^{1}H-NMR spectra for titration of (*S*,*S*)-**1m** with DMSO-d_6

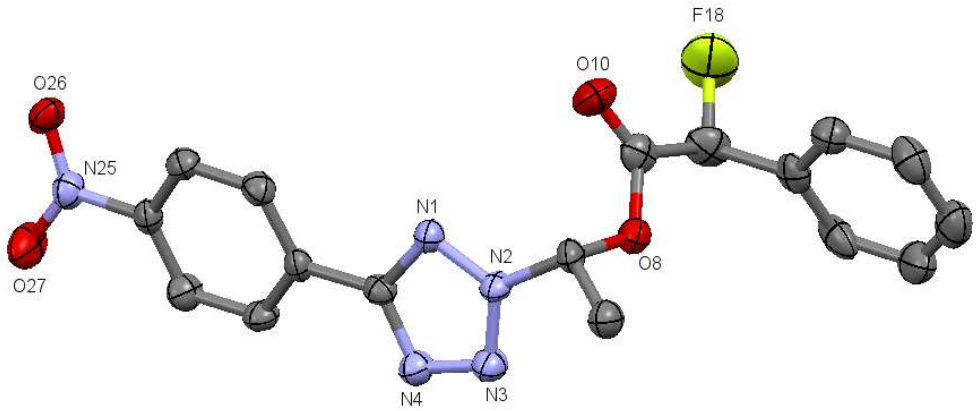
X-Ray Structure, Crystal Data and Structure Refinements for (*R*)–**12x**



(ellipsoids at 50% probability; hydrogen atoms are omitted for clarity)

Empirical formula	$C_{17}H_{14}BrN_5O_4$
Formula weight	432.24
Temperature	193(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21
Unit cell dimensions	a = 13.5743(5) A alpha = 90 deg.
	b = 7.6627(4) A beta = 107.8219(17) deg.
	c = 18.0825(11) A gamma = 90 deg.
Volume	1790.61(16) A^3
Z, Calculated density	4, 1.603 Mg/m^3
Absorption coefficient	2.330 mm^-1
F(000)	872
Crystal size	0.24 x 0.16 x 0.11 mm
Two-theta max. for data	56.0 deg.
Limiting indices	=-17<=h<=17 -8<=k<=10 -23<=l<=23
Reflections collected / uniqu	e 7401 / 7394 [R(int) = 0.0127]
Completeness to theta = 28.0	98%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameter	s 7394 / 1 / 487
Goodness-of-fit on F^2	1.096
Final R indices [I>2sigma(I)]	R1 = 0.0797, wR2 = 0.1501
R indices (all data)	R1 = 0.1263, wR2 = 0.1697
Absolute structure parameter	0.032(13)
Largest diff. peak and hole	0.848 and -0.797 e.A^-3

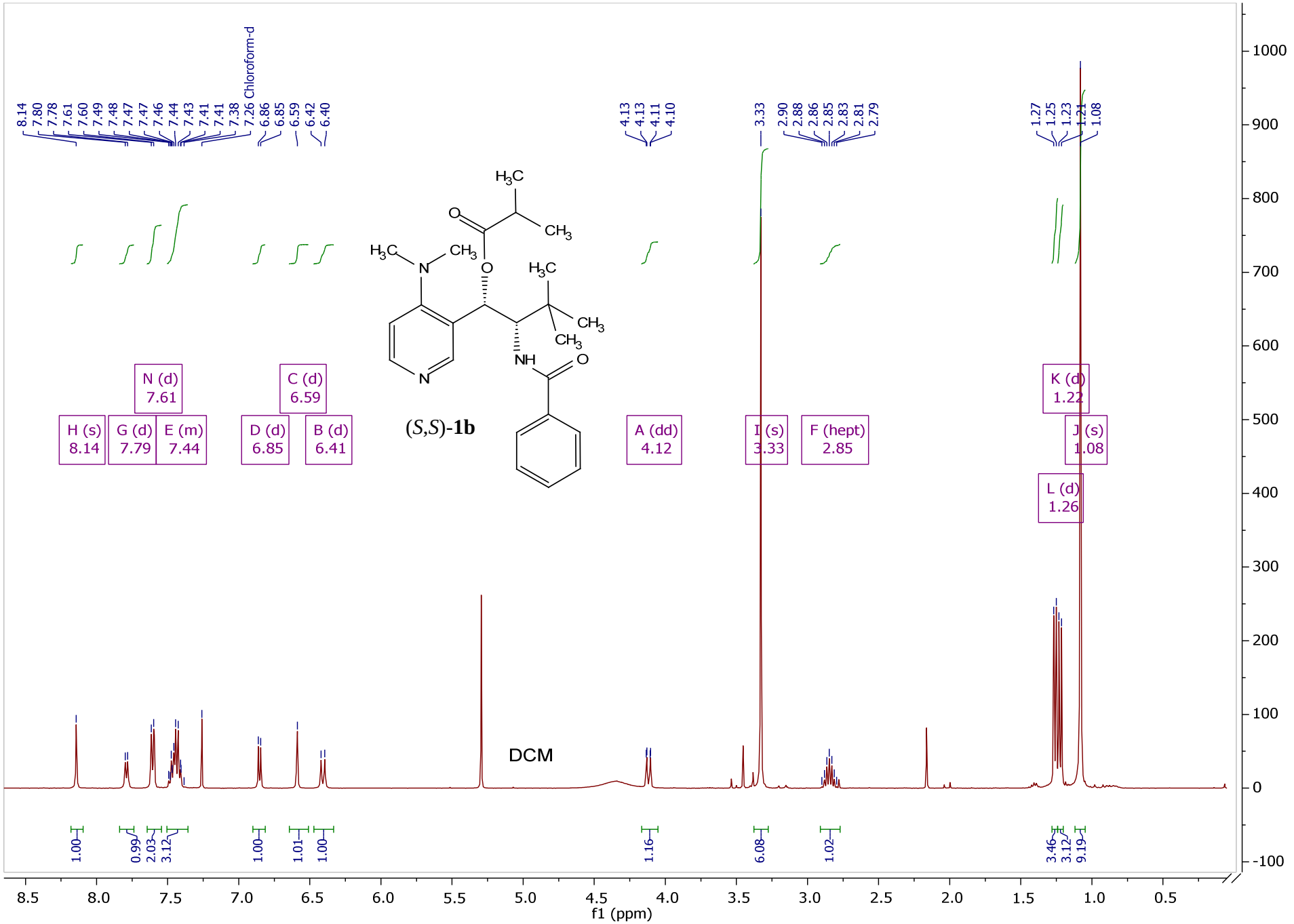
X-Ray Structure, Crystal Data and Structure Refinements for (*R*,*S*)–**14**

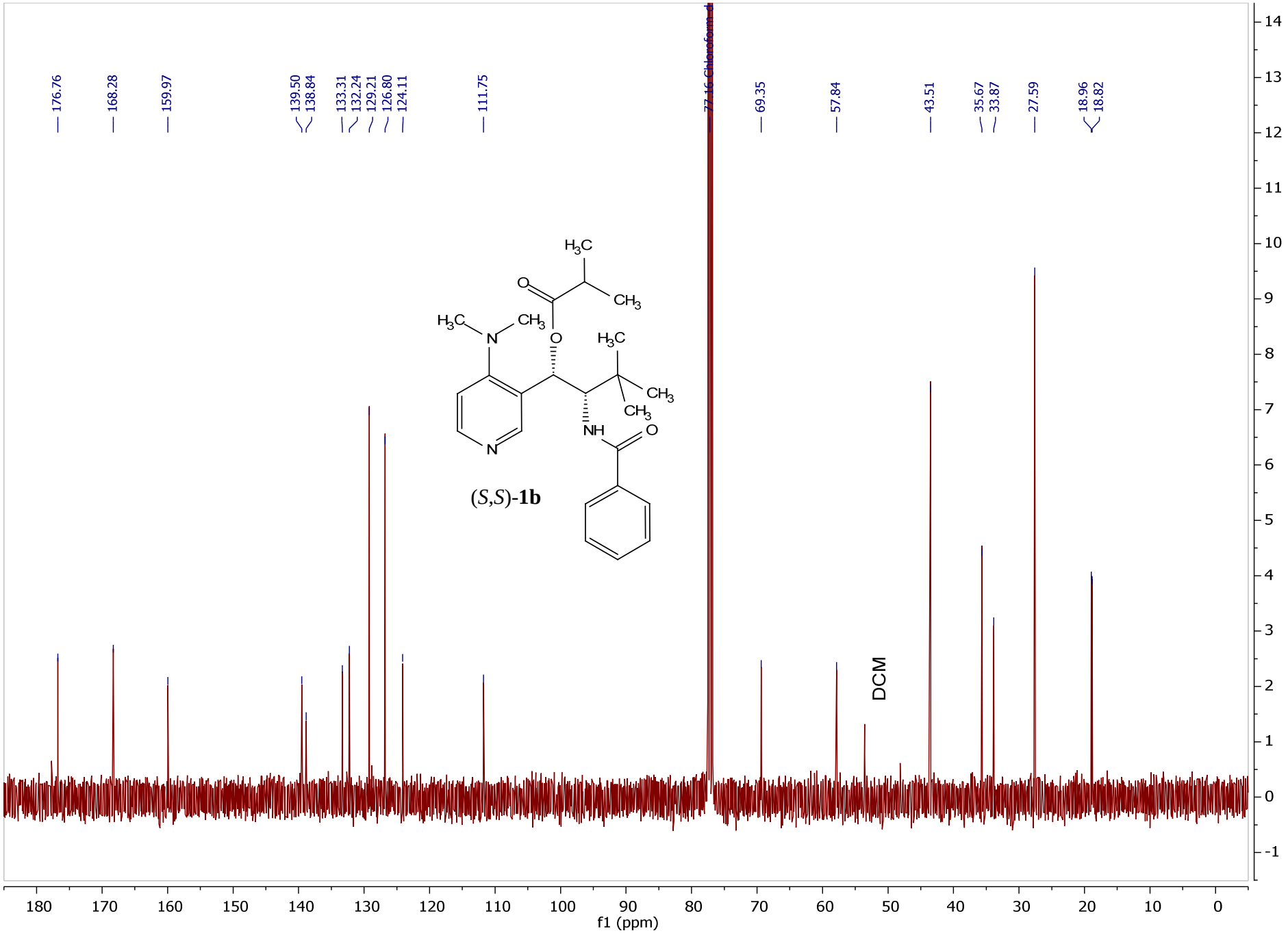


(ellipsoids at 50% probability; hydrogen atoms are omitted for clarity)

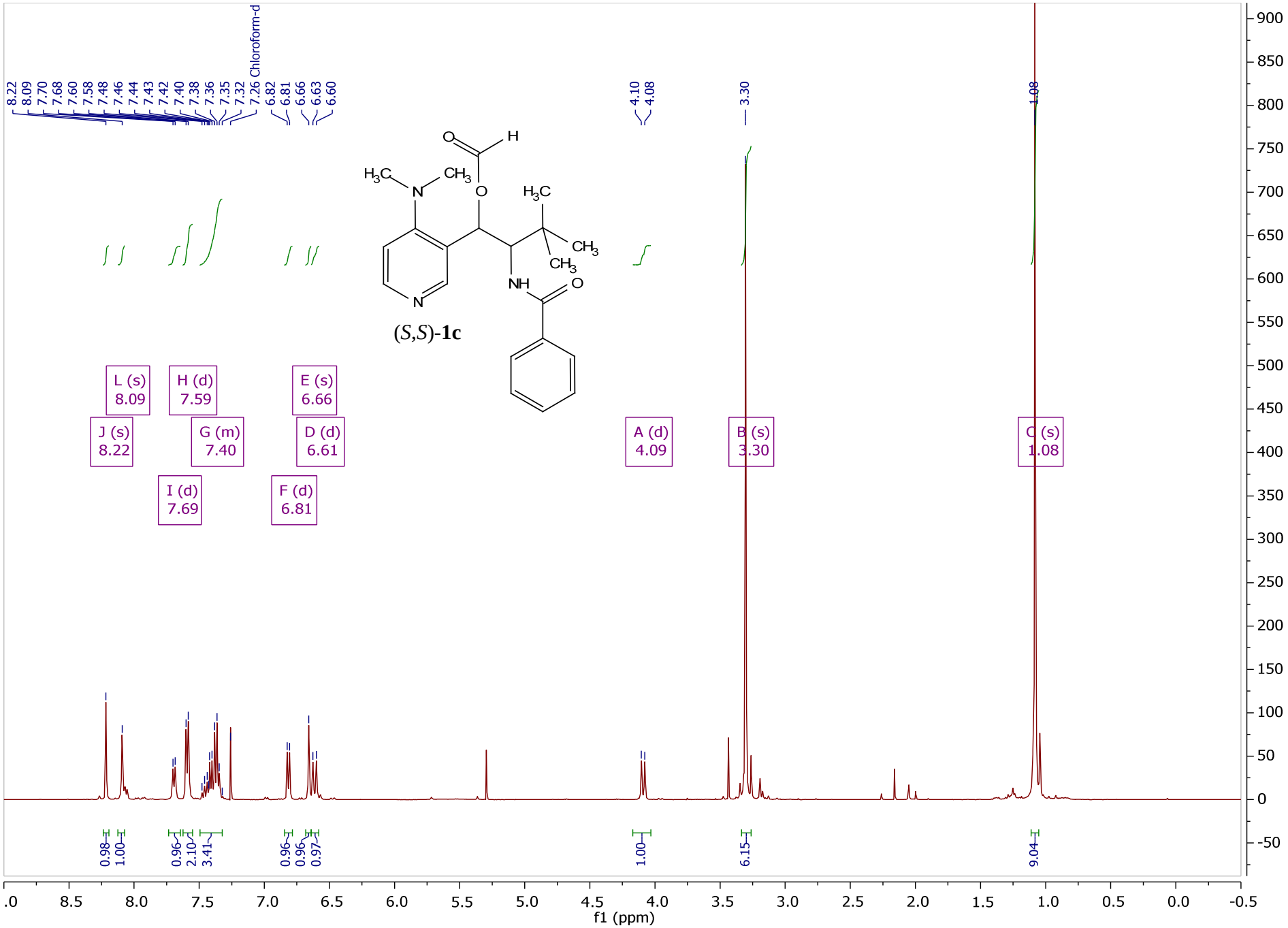
Empirical formula	$C_{17}H_{14}FN_5O_4$
Formula weight	371.33
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21
Unit cell dimensions	a = 6.5366(4) A alpha = 90 deg.
	b = 9.8897(6) A beta = 96.641(2) deg.
	c = 13.2763(10) A gamma = 90 deg.
Volume	852.49(10) A^3
Z, Calculated density	2, 1.447 Mg/m^3
Absorption coefficient	0.113 mm^-1
F(000)	384
Crystal size	0.47 x 0.07 x 0.02 mm
Two-theta max. for data	58.0 deg.
Limiting indices	=-8<=h<=8 -12<=k<=13 -17<=l<=14
Reflections collected / unique	6374 / 2316 [R(int) = 0.0945]
Completeness to theta = 29.0	98%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2316 / 1 / 244
Goodness-of-fit on F^2	1.008
Final R indices [I>2sigma(I)]	R1 = 0.0662, wR2 = 0.1143
R indices (all data)	R1 = 0.1331, wR2 = 0.1362
Largest diff. peak and hole	0.212 and -0.219 e.A^-3

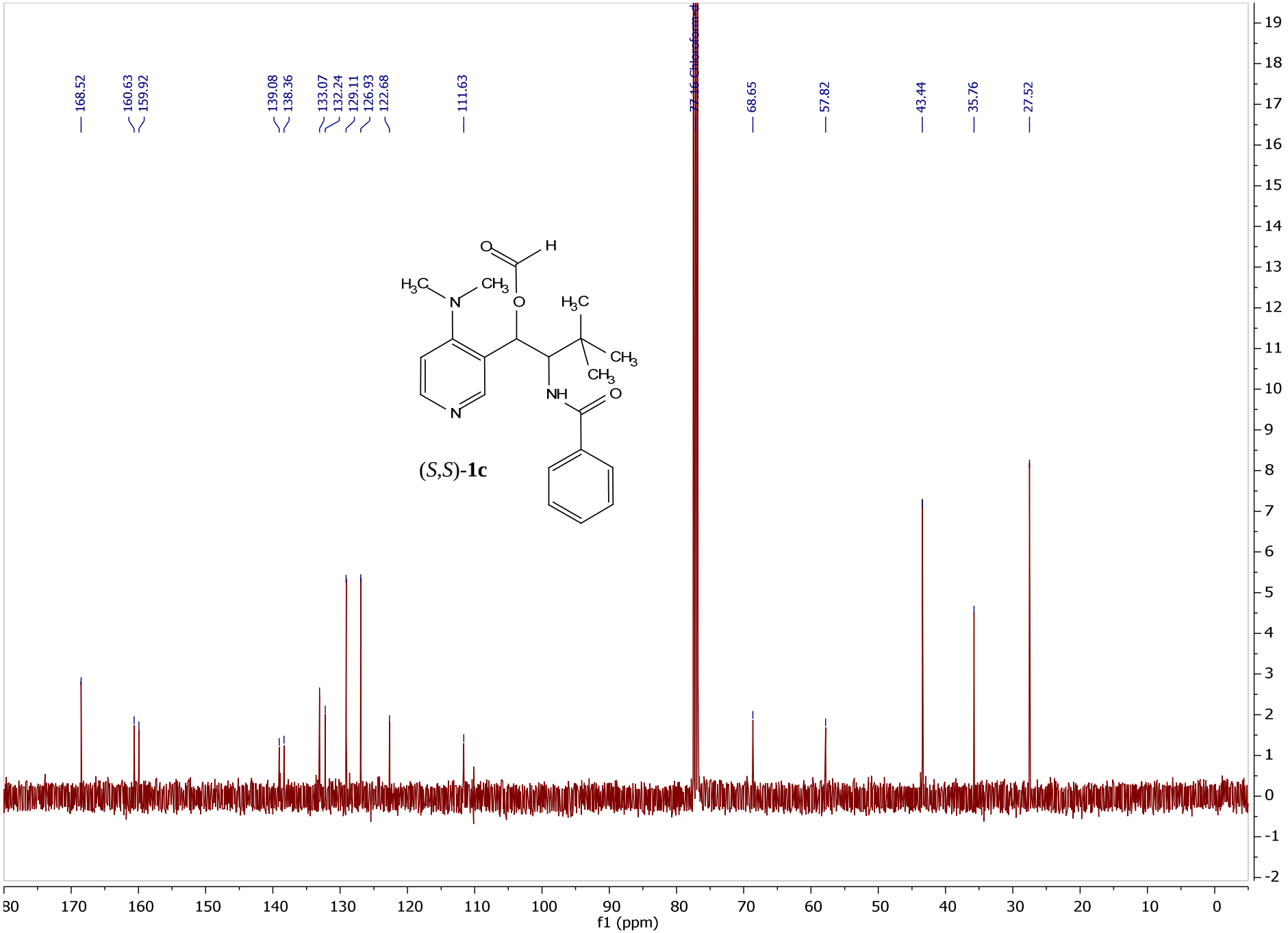
Spectroscopic Data

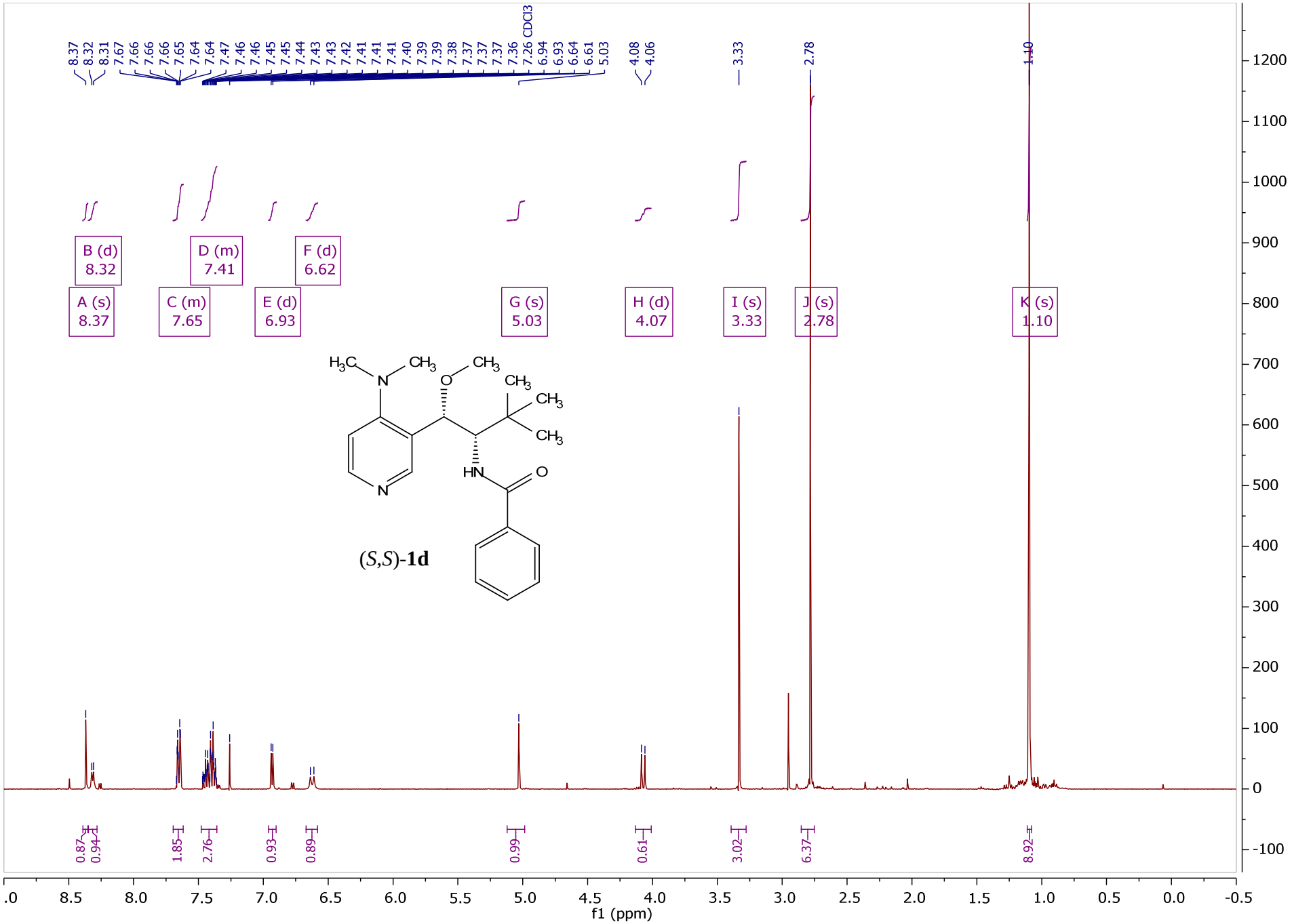

8.14
7.80
7.78
7.61
7.60
7.49
7.48
7.47
7.47
7.46
7.44
7.43
7.41
7.41
7.38
7.26 Chloroform-d
6.86
6.85
6.59
6.42
6.40
4.13
4.13
4.11
4.10
3.33
2.90
2.88
2.86
2.85
2.83
2.81
2.79
1.27
1.25
1.23
1.21
1.08
N (d) 7.61
C (d) 6.59
K (d) 1.22
H (s) 8.14
G (d) 7.79
E (m) 7.44
D (d) 6.85
B (d) 6.41
A (dd) 4.12
I (s) 3.33
F (hept) 2.85
J (s) 1.08
L (d) 1.26
(S,S)-1b
DCM
1.00
0.99
2.03
3.12
1.00
1.01
1.00
1.16
6.08
1.02
3.46
3.12
9.19
f1 (ppm)

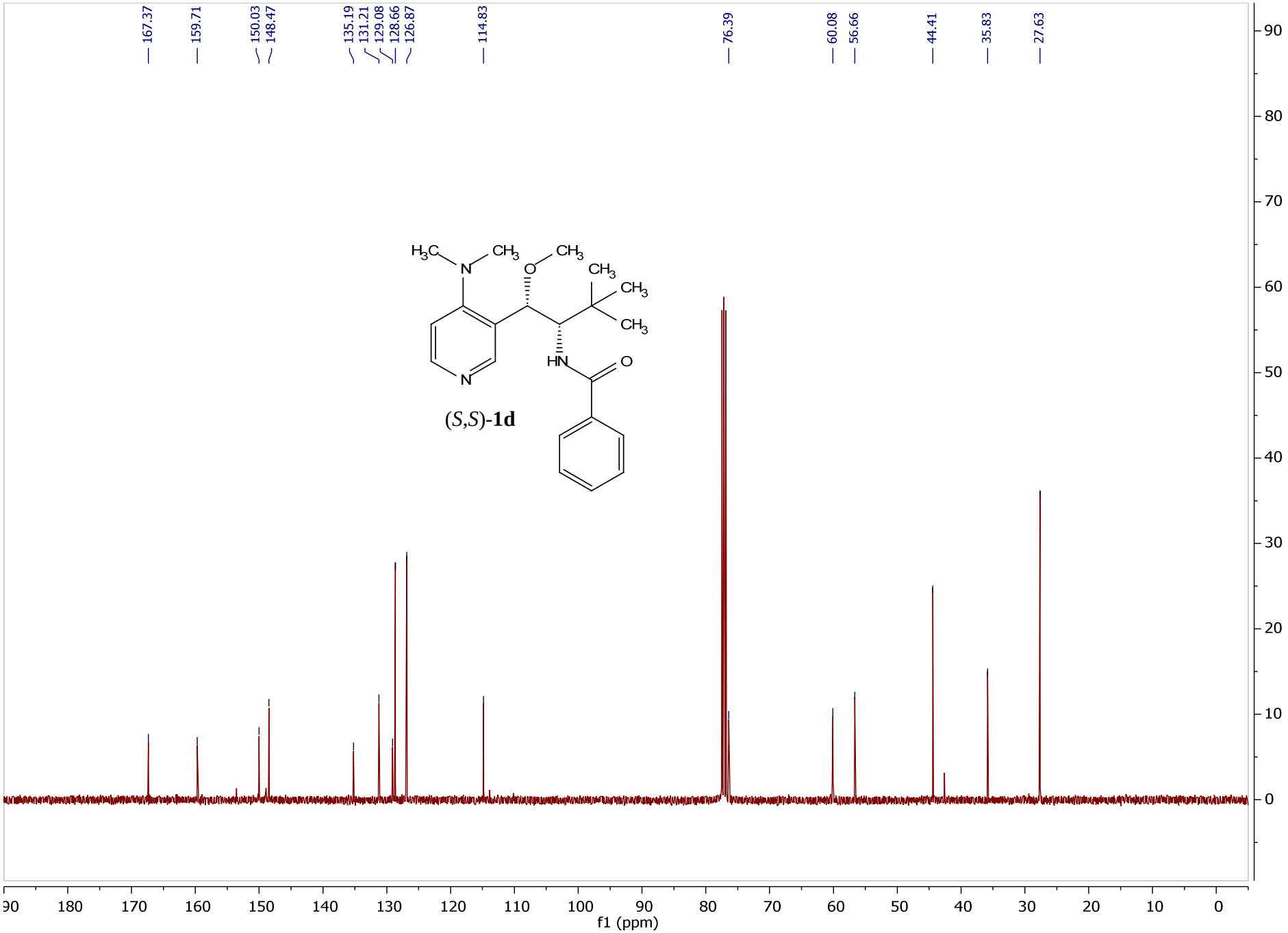

176.76
168.28
159.97
139.50
138.84
133.31
132.24
129.21
126.80
124.11
111.75
77.16 Chloroform-d
69.35
57.84
43.51
35.67
33.87
27.59
18.96
18.82
DCM
f1 (ppm)

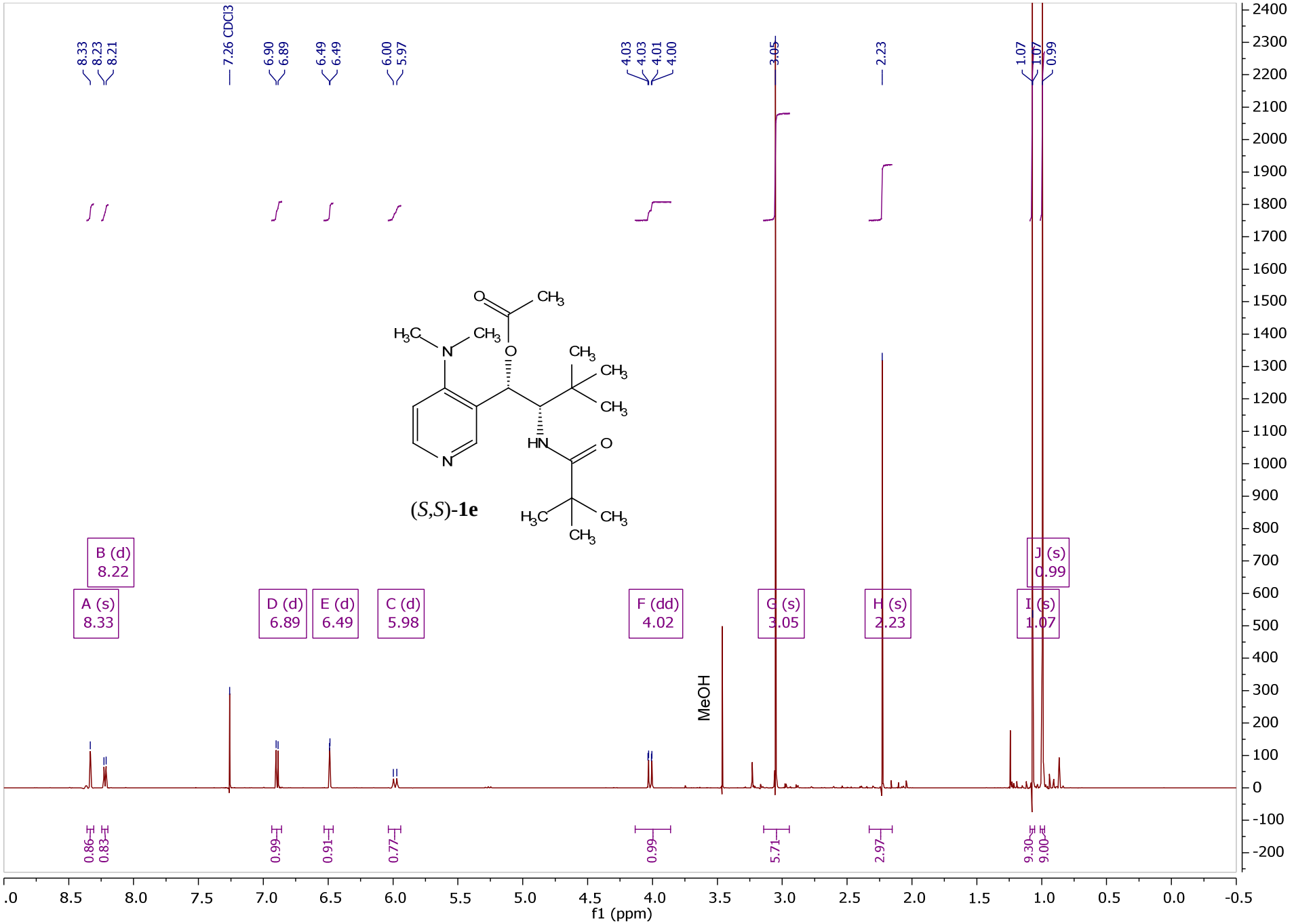
(*S*,*S*)-**1b**

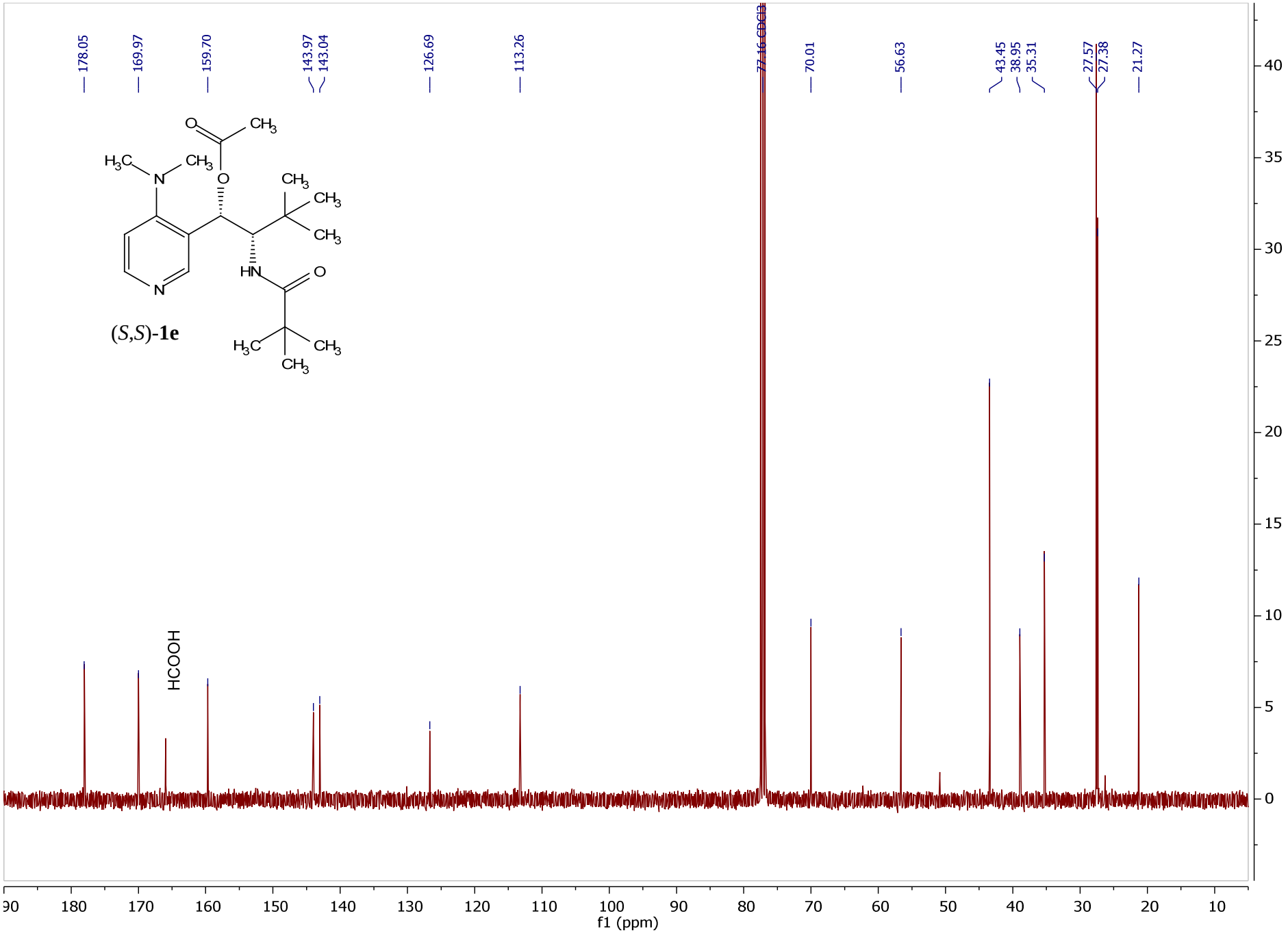

8.22
8.09
7.70
7.68
7.60
7.58
7.48
7.46
7.44
7.43
7.42
7.40
7.38
7.36
7.35
7.32
7.26 Chloroform-d
6.82
6.81
6.66
6.63
6.60
4.10
4.08
3.30
1.08
(S,S)-1c
L (s) 8.09
H (d) 7.59
E (s) 6.66
J (s) 8.22
G (m) 7.40
D (d) 6.61
A (d) 4.09
B (s) 3.30
C (s) 1.08
I (d) 7.69
F (d) 6.81
0.98
1.00
0.96
2.10
3.41
0.96
0.96
0.97
1.00
6.15
9.04
f1 (ppm)

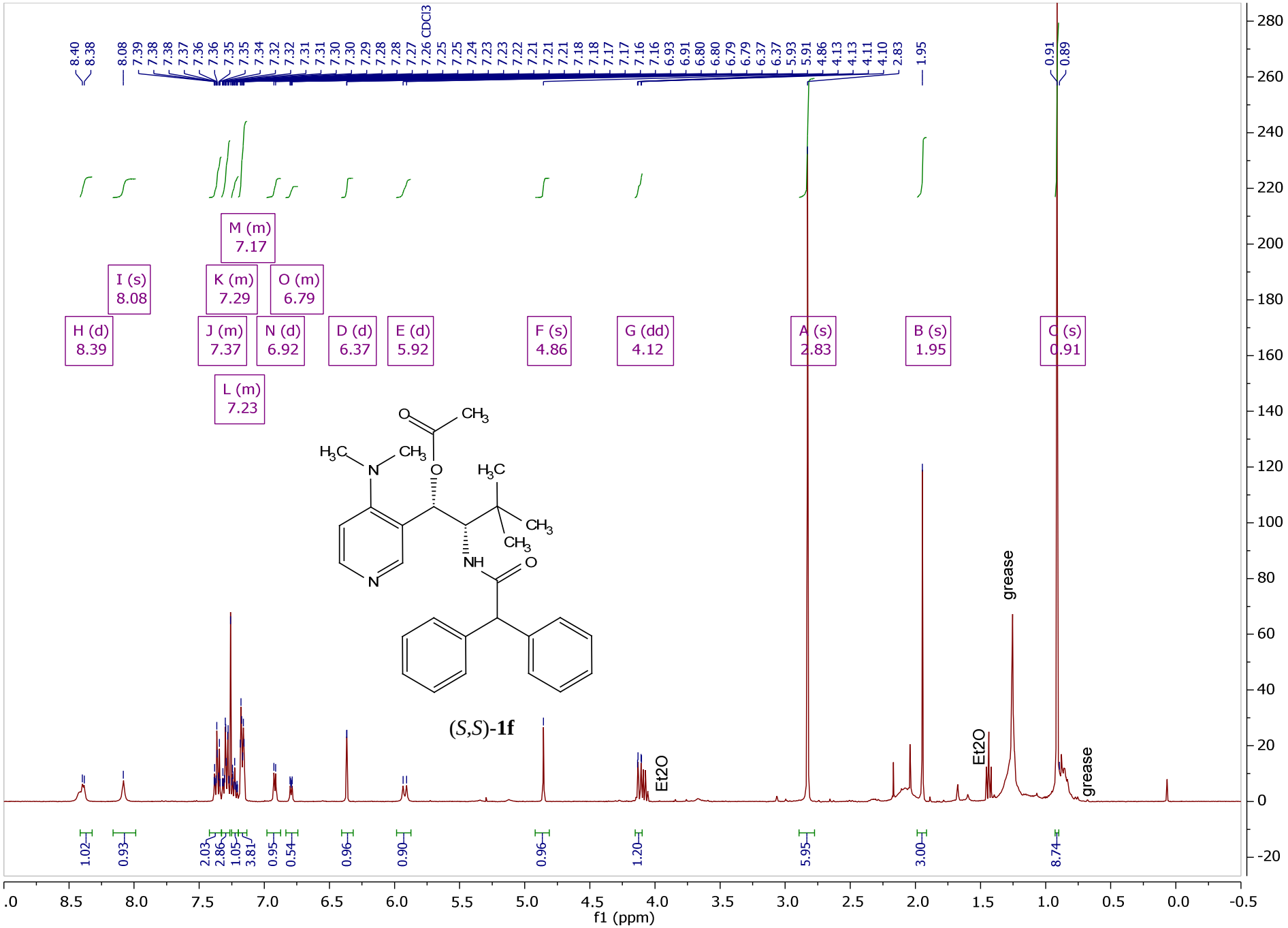

168.52
160.63
159.92
139.08
138.36
133.07
132.24
129.11
126.93
122.68
111.63
77.16 Chloroform-d
68.65
57.82
43.44
35.76
27.52
(S,S)-1c
f1 (ppm)

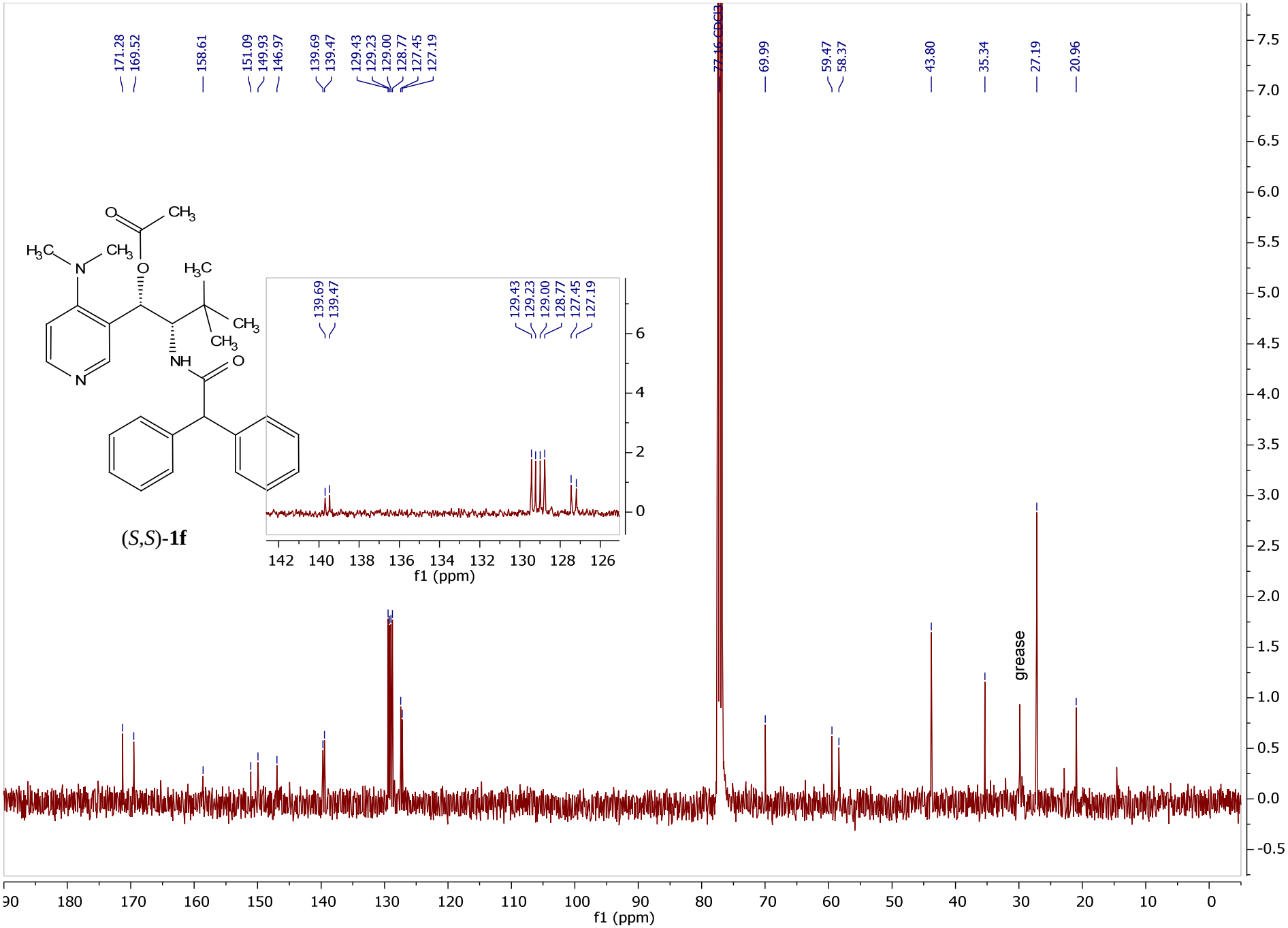

8.37
8.32
8.31
7.67
7.66
7.66
7.66
7.65
7.64
7.64
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.41
7.41
7.41
7.40
7.39
7.39
7.38
7.37
7.37
7.37
7.36
7.26 CDCl3
6.94
6.93
6.64
6.61
5.03
4.08
4.06
3.33
2.78
1.10
B (d) 8.32
D (m) 7.41
F (d) 6.62
A (s) 8.37
C (m) 7.65
E (d) 6.93
G (s) 5.03
H (d) 4.07
I (s) 3.33
J (s) 2.78
K (s) 1.10
(S,S)-1d
0.87
0.94
1.85
2.76
0.93
0.89
0.99
0.61
3.02
6.37
8.92
f1 (ppm)

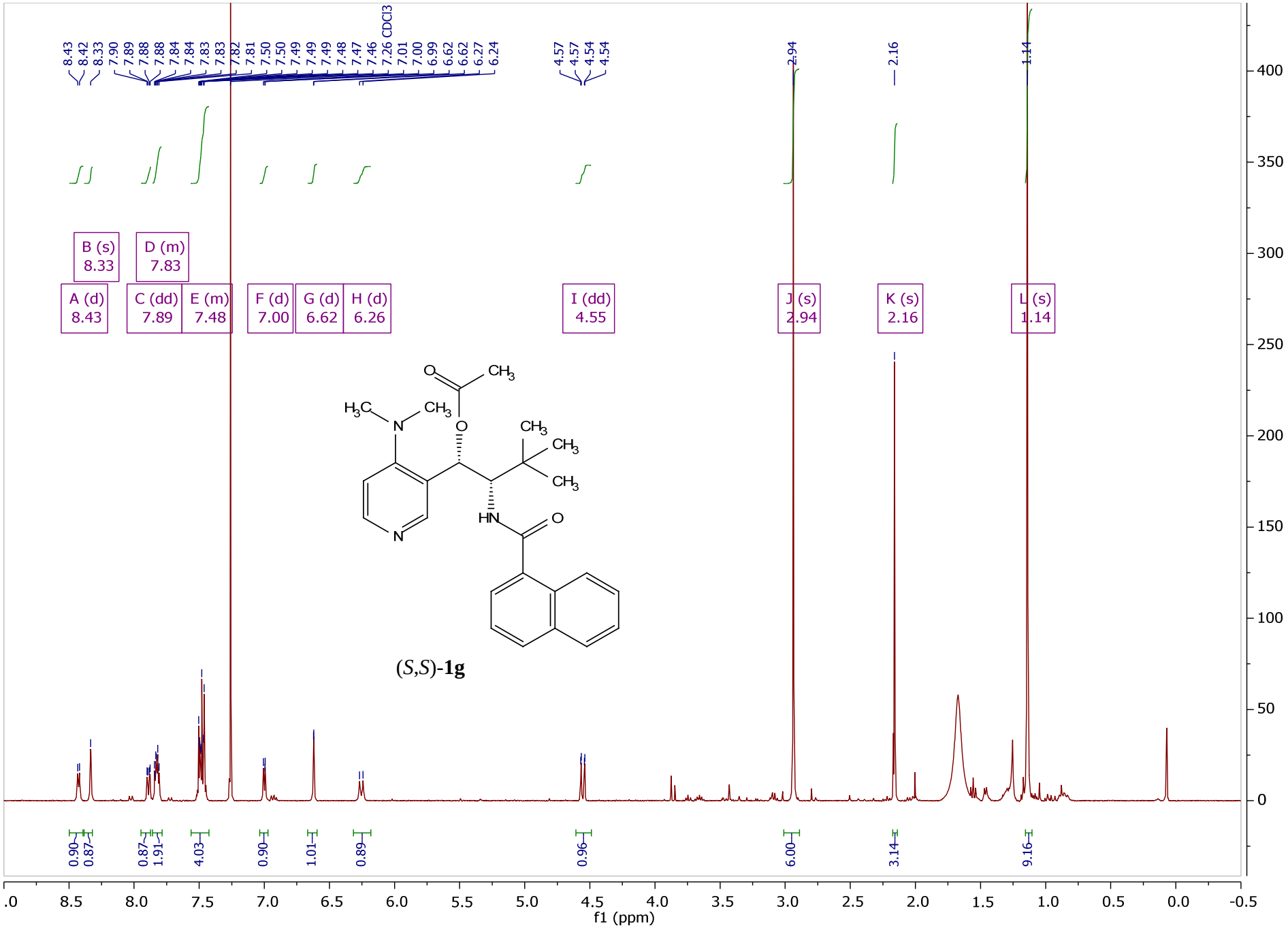

167.37
159.71
150.03
148.47
135.19
131.21
129.08
128.66
126.87
114.83
76.39
60.08
56.66
44.41
35.83
27.63
H3C
CH3
N
CH3
O
CH3
CH3
CH3
HN
O
N
(S,S)-1d
f1 (ppm)


8.33
8.23
8.21
7.26 CDCl3
6.90
6.89
6.49
6.49
6.00
5.97
4.03
4.03
4.01
4.00
3.95
2.23
1.07
1.07
0.99
(S,S)-1e
B (d) 8.22
A (s) 8.33
D (d) 6.89
E (d) 6.49
C (d) 5.98
F (dd) 4.02
G (s) 3.05
H (s) 2.23
J (s) 0.99
I (s) 1.07
MeOH
0.86
0.83
0.99
0.91
0.77
0.99
5.71
2.97
9.30
9.00
f1 (ppm)

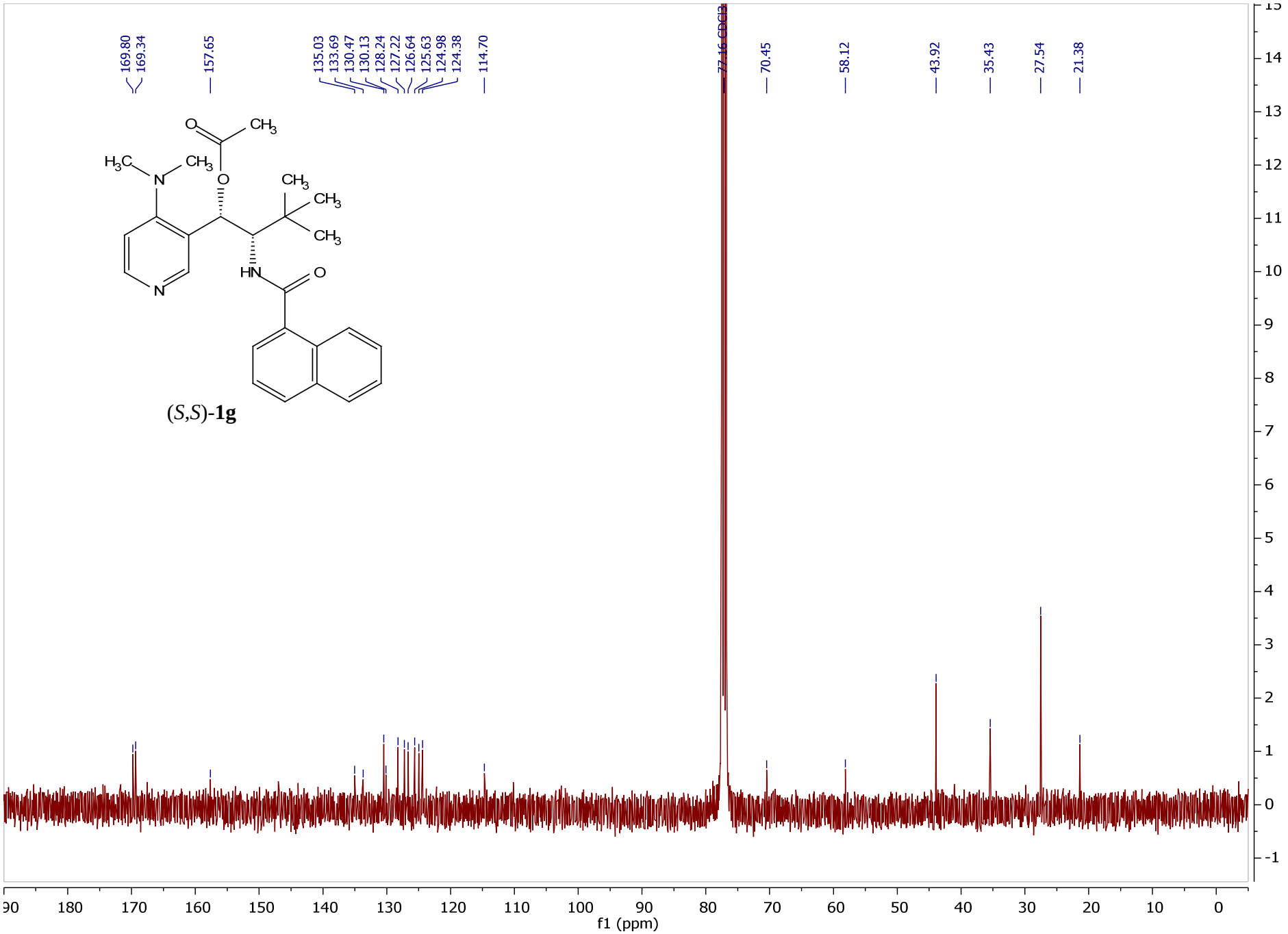

178.05
169.97
159.70
143.97
143.04
126.69
113.26
77.16 CDCl3
70.01
56.63
43.45
38.95
35.31
27.57
27.38
21.27
HCOOH
(S,S)-1e
f1 (ppm)

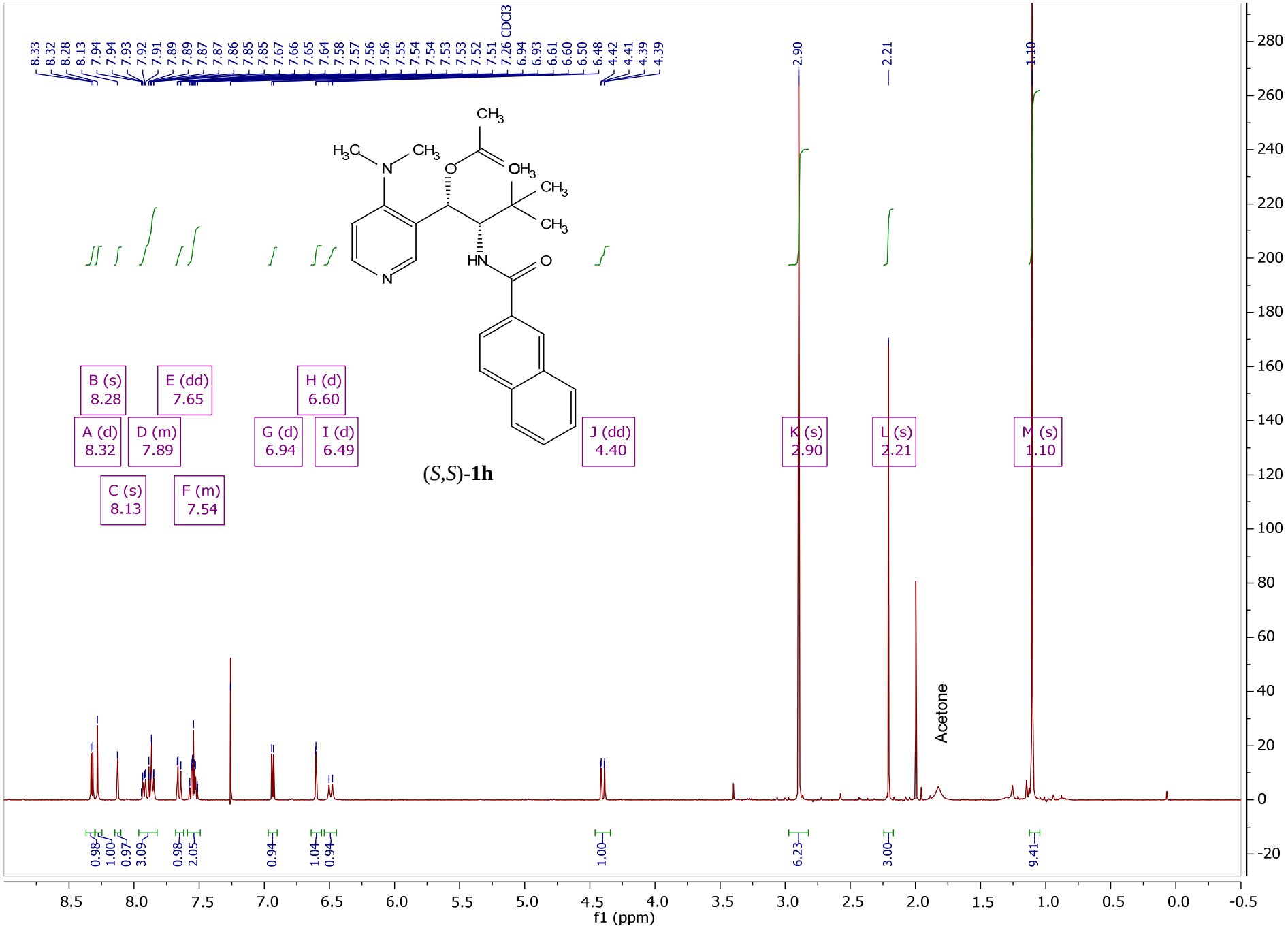

M (m) 7.17
I (s) 8.08
K (m) 7.29
O (m) 6.79
H (d) 8.39
J (m) 7.37
N (d) 6.92
D (d) 6.37
E (d) 5.92
F (s) 4.86
G (dd) 4.12
A (s) 2.83
B (s) 1.95
C (s) 0.91
L (m) 7.23
(S,S)-1f
Et2O
grease
Et2O
grease
f1 (ppm)

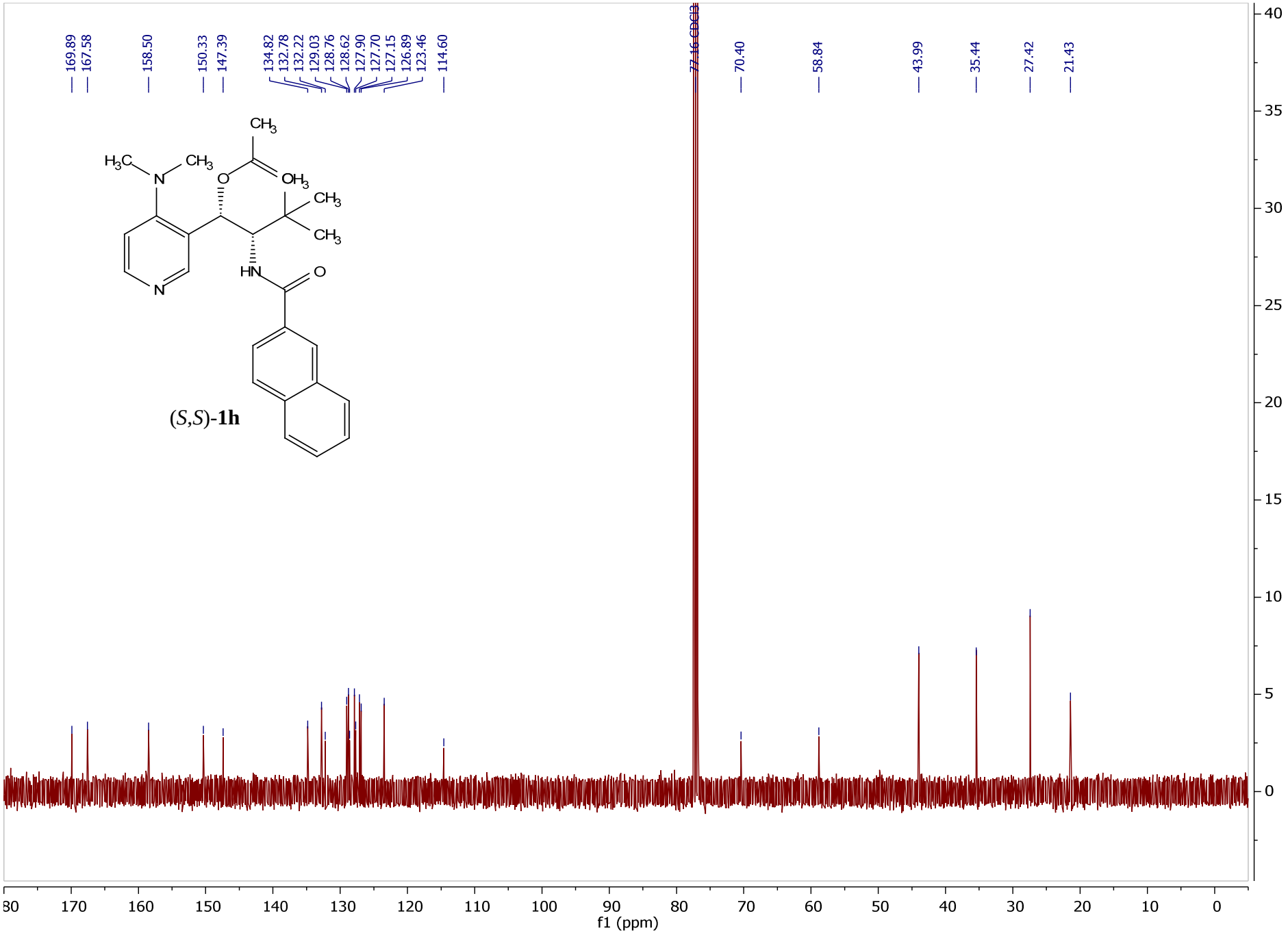

171.28
169.52
158.61
151.09
149.93
146.97
139.69
139.47
129.43
129.23
129.00
128.77
127.45
127.19
77.16 CDCl3
69.99
59.47
58.37
43.80
35.34
27.19
20.96
grease
(S,S)-1f
f1 (ppm)

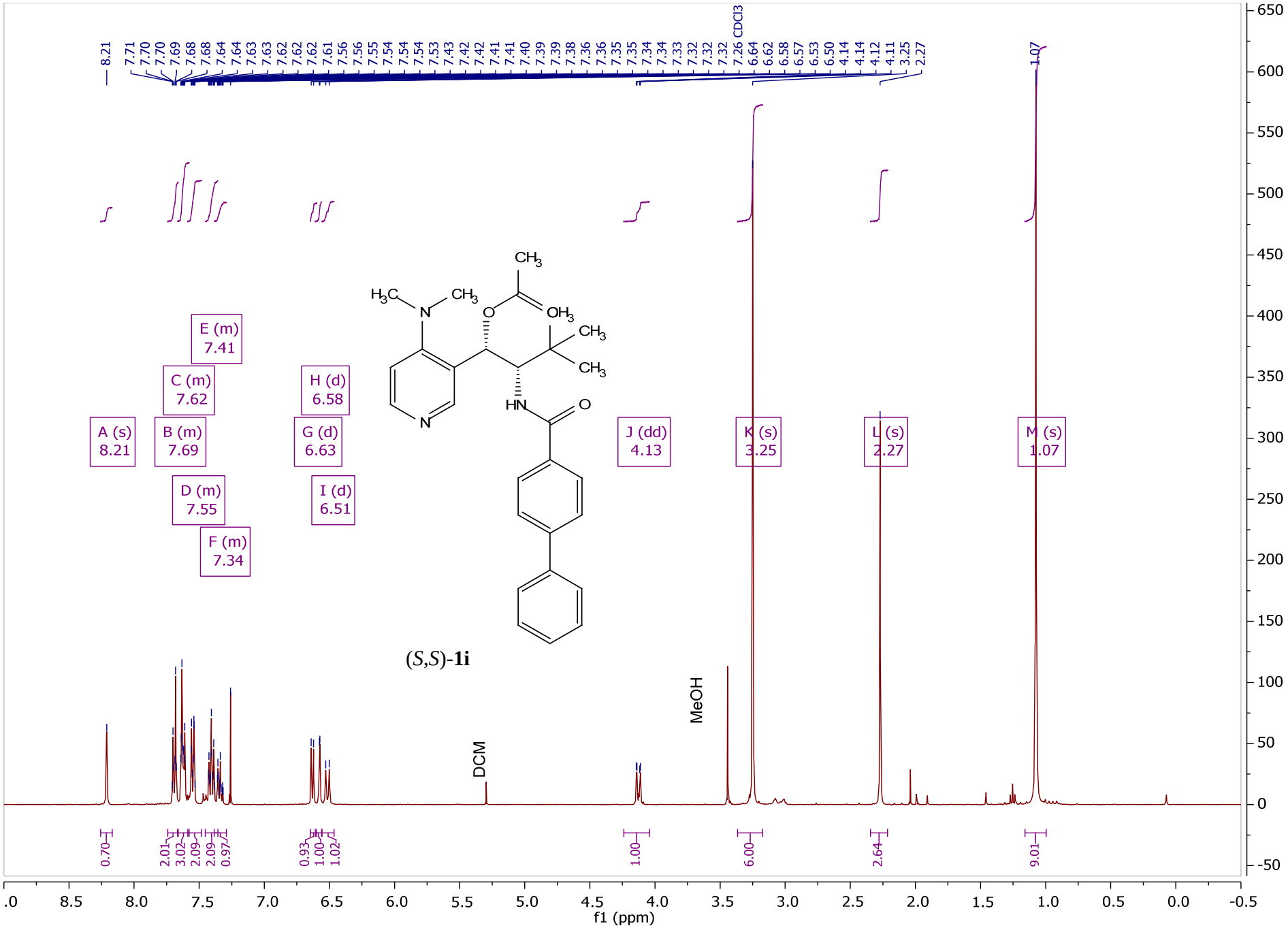

8.43
8.42
8.33
7.90
7.89
7.88
7.88
7.84
7.84
7.83
7.83
7.82
7.81
7.50
7.50
7.49
7.49
7.49
7.48
7.47
7.46
7.26 CDCl3
7.01
7.00
6.99
6.62
6.62
6.27
6.24
4.57
4.57
4.54
4.54
2.94
2.16
1.14
B (s) 8.33
D (m) 7.83
A (d) 8.43
C (dd) 7.89
E (m) 7.48
F (d) 7.00
G (d) 6.62
H (d) 6.26
I (dd) 4.55
J (s) 2.94
K (s) 2.16
L (s) 1.14
0.90
0.87
0.87
1.91
4.03
0.90
1.01
0.89
0.96
6.00
3.14
9.16
f1 (ppm)

(*S*,*S*)-**1g**

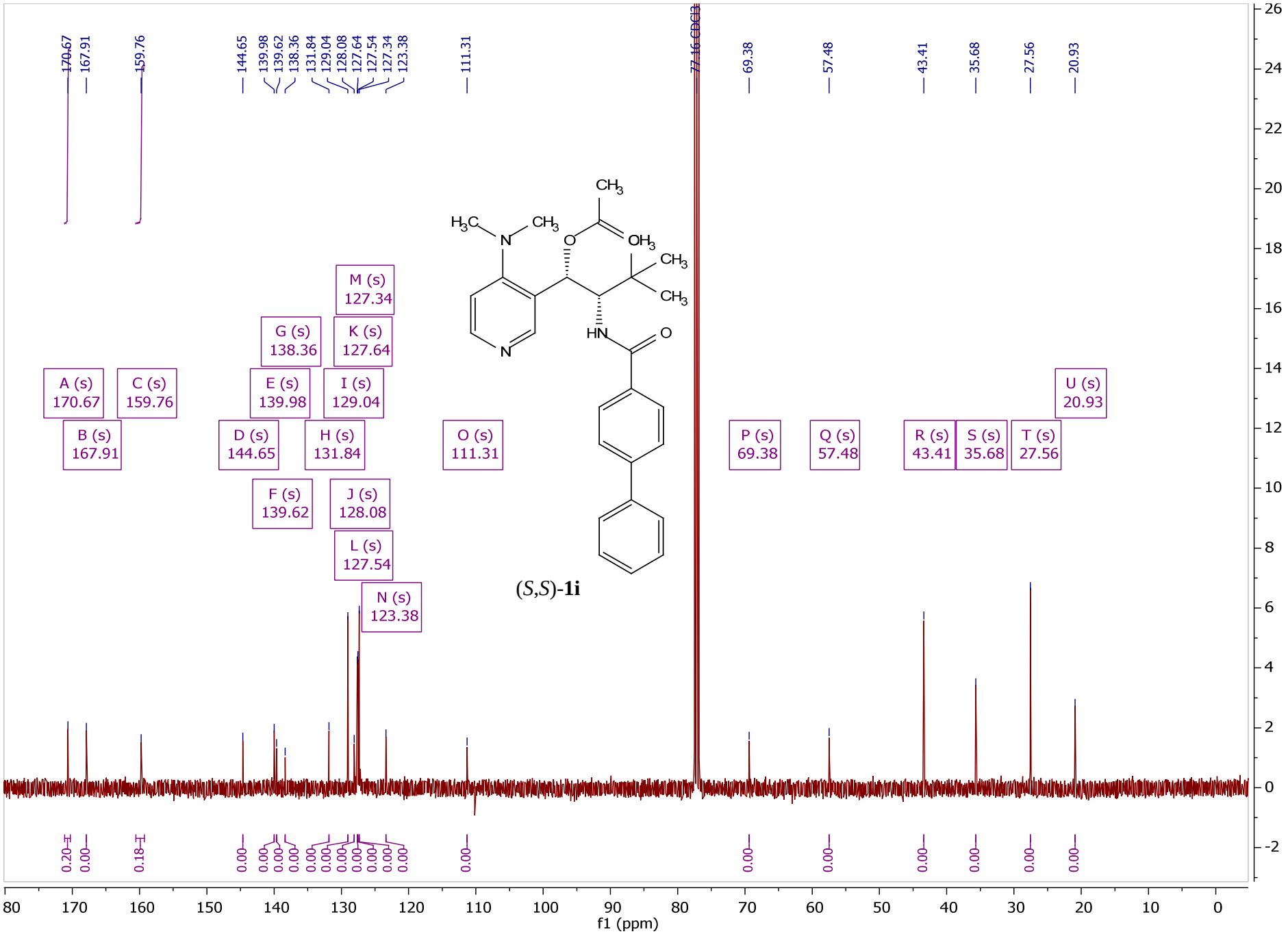

169.80
169.34
157.65
135.03
133.69
130.47
130.13
128.24
127.22
126.64
125.63
124.98
124.38
114.70
77.46 CDCl3
70.45
58.12
43.92
35.43
27.54
21.38
(S,S)-1g
f1 (ppm)

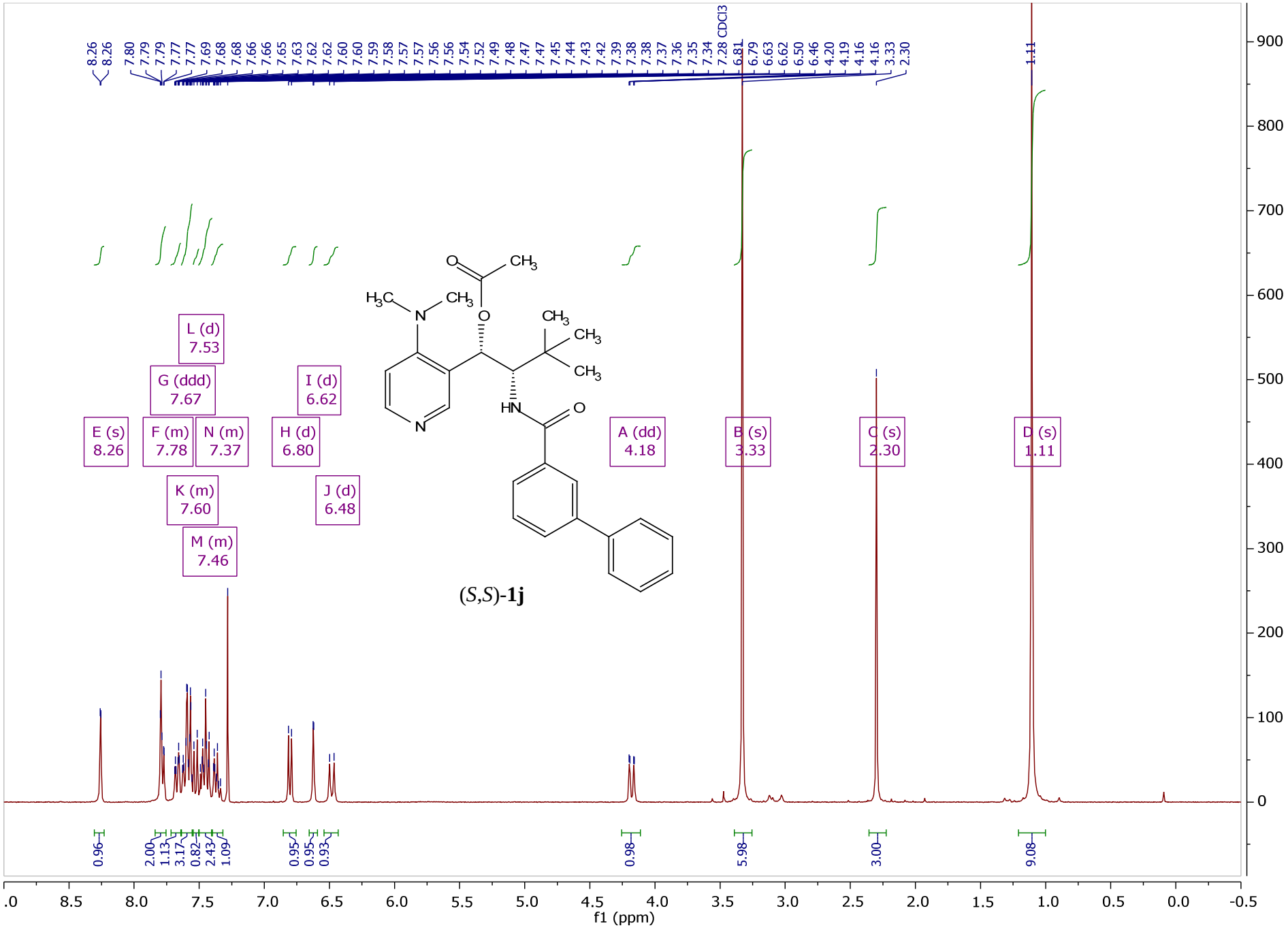

8.33 8.32 8.28 8.13 7.94 7.94 7.93 7.92 7.91 7.89 7.89 7.87 7.87 7.86 7.85 7.85 7.67 7.66 7.65 7.64 7.58 7.57 7.56 7.56 7.55 7.54 7.54 7.53 7.53 7.52 7.51 7.26 CDCl3 6.94 6.93 6.61 6.60 6.50 6.48 4.42 4.41 4.39 4.39
2.90
2.21
1.10
B (s) 8.28
E (dd) 7.65
H (d) 6.60
A (d) 8.32
D (m) 7.89
G (d) 6.94
I (d) 6.49
J (dd) 4.40
K (s) 2.90
L (s) 2.21
M (s) 1.10
C (s) 8.13
F (m) 7.54
(S,S)-1h
Acetone
0.98 1.00 0.97 3.09 0.98 2.05 0.94 1.04 0.94 1.00 6.23 3.00 9.41
f1 (ppm)

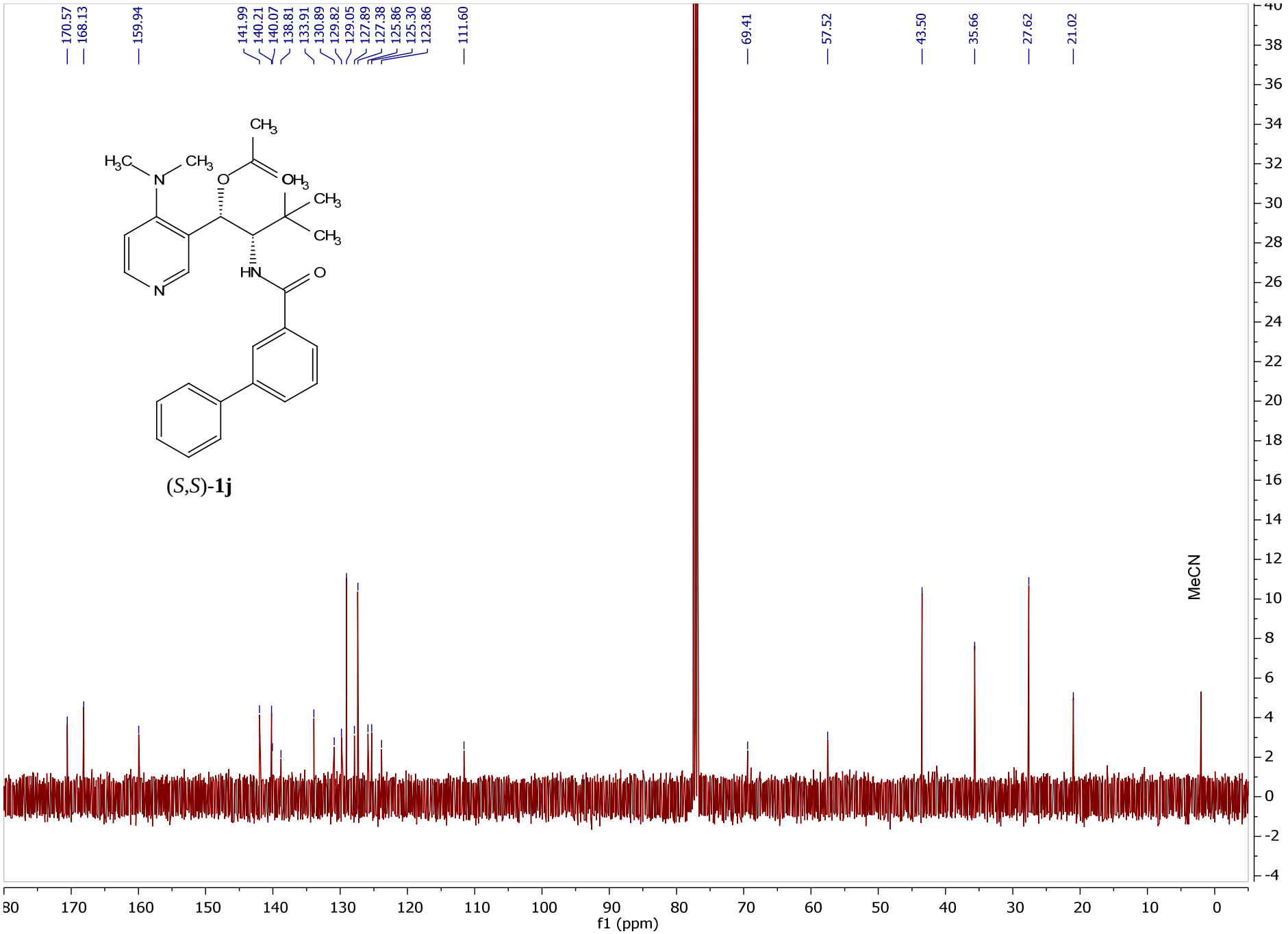

169.89
167.58
158.50
150.33
147.39
134.82
132.78
132.22
129.03
128.76
128.62
127.90
127.70
127.15
126.89
123.46
114.60
77.16 CDCl3
70.40
58.84
43.99
35.44
27.42
21.43
CH3
H3C
CH3
N
O
OH3
CH3
CH3
HN
O
N
(S,S)-1h
40
35
30
25
20
15
10
5
0
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.21
7.71
7.70
7.70
7.69
7.68
7.68
7.64
7.64
7.63
7.63
7.62
7.62
7.62
7.61
7.56
7.56
7.55
7.54
7.54
7.54
7.53
7.43
7.42
7.42
7.41
7.41
7.40
7.39
7.39
7.38
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.32
7.26 CDCl3
6.64
6.62
6.58
6.57
6.53
6.50
4.14
4.12
4.11
3.25
2.27
1.07
A (s) 8.21
B (m) 7.69
C (m) 7.62
D (m) 7.55
E (m) 7.41
F (m) 7.34
G (d) 6.63
H (d) 6.58
I (d) 6.51
J (dd) 4.13
K (s) 3.25
L (s) 2.27
M (s) 1.07
DCM
MeOH
0.70
2.01
3.02
2.09
2.09
0.97
0.93
1.00
1.02
1.00
6.00
2.64
9.01
f1 (ppm)

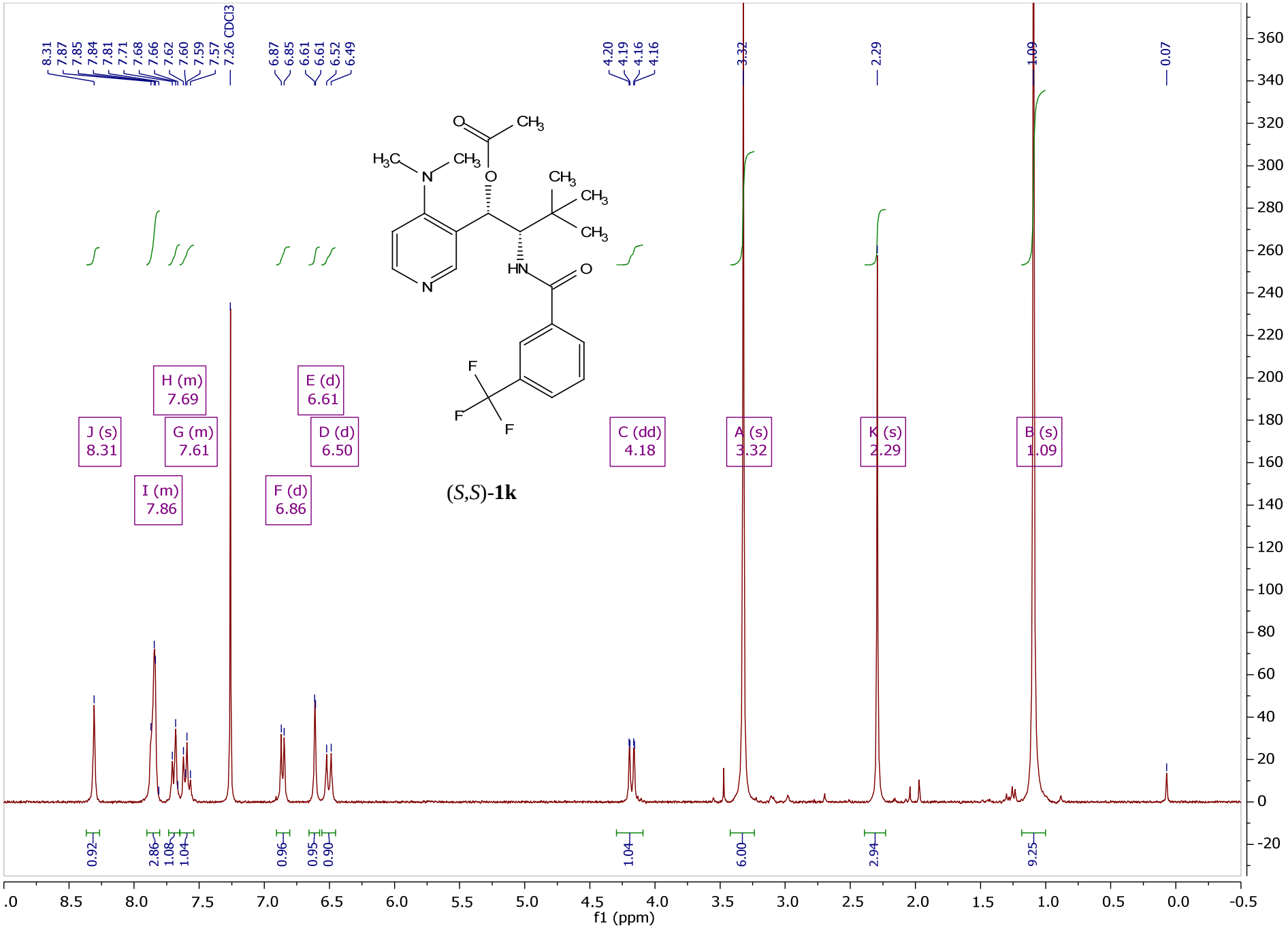
(*S*,*S*)-**1i**


170.67
167.91
159.76
144.65
139.98
139.62
138.36
131.84
129.04
128.08
127.64
127.54
127.34
123.38
111.31
77.16 CDCl3
69.38
57.48
43.41
35.68
27.56
20.93
A (s) 170.67
B (s) 167.91
C (s) 159.76
D (s) 144.65
E (s) 139.98
F (s) 139.62
G (s) 138.36
H (s) 131.84
I (s) 129.04
J (s) 128.08
K (s) 127.64
L (s) 127.54
M (s) 127.34
N (s) 123.38
O (s) 111.31
P (s) 69.38
Q (s) 57.48
R (s) 43.41
S (s) 35.68
T (s) 27.56
U (s) 20.93
(S,S)-1i
f1 (ppm)

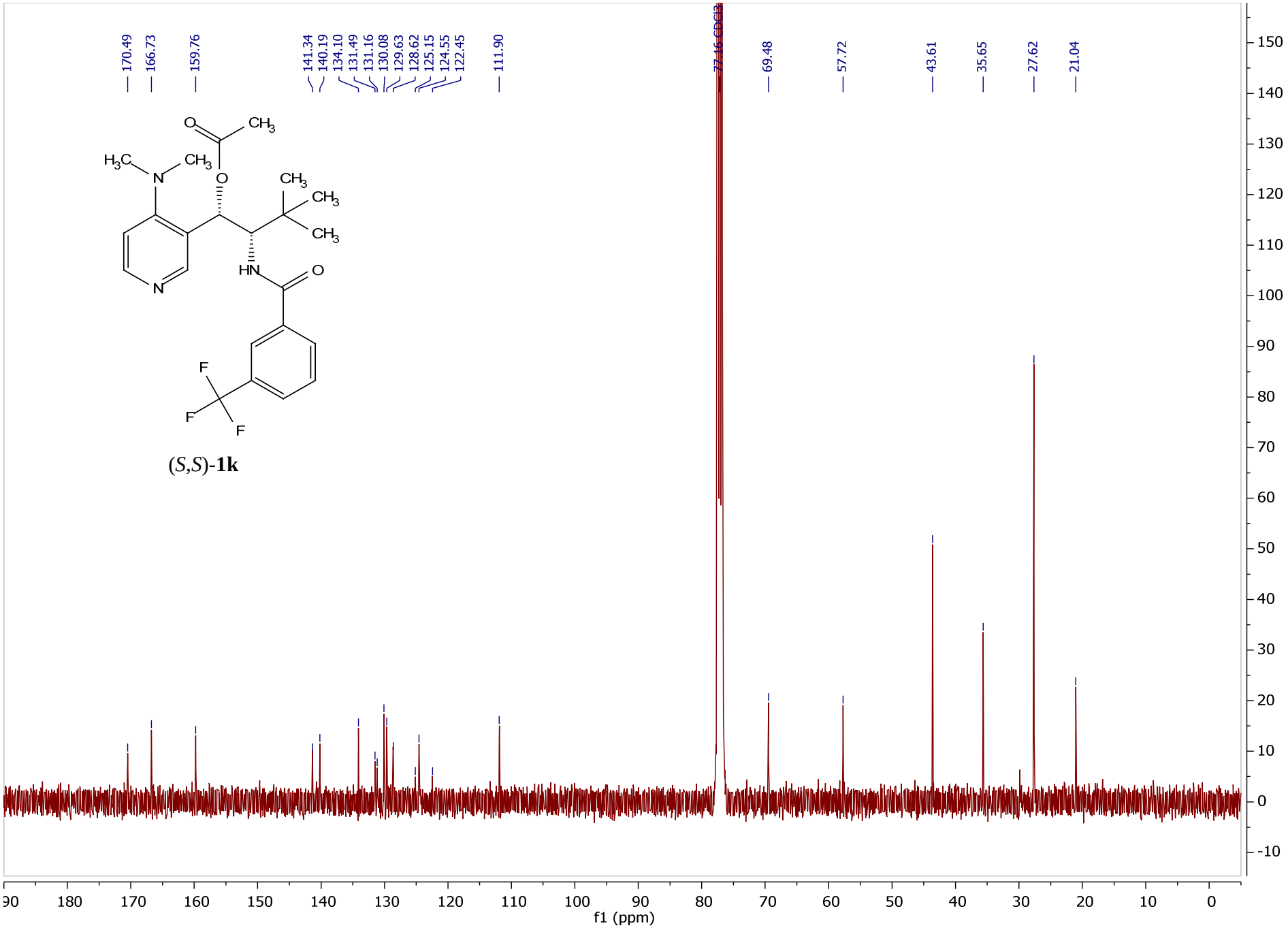

L (d) 7.53
G (ddd) 7.67
I (d) 6.62
E (s) 8.26
F (m) 7.78
N (m) 7.37
H (d) 6.80
A (dd) 4.18
B (s) 3.33
C (s) 2.30
D (s) 1.11
K (m) 7.60
J (d) 6.48
M (m) 7.46
(S,S)-1j
f1 (ppm)


170.57
168.13
159.94
141.99
140.21
140.07
138.81
133.91
130.89
129.82
129.05
127.89
127.38
125.86
125.30
123.86
111.60
69.41
57.52
43.50
35.66
27.62
21.02
MeCN
f1 (ppm)

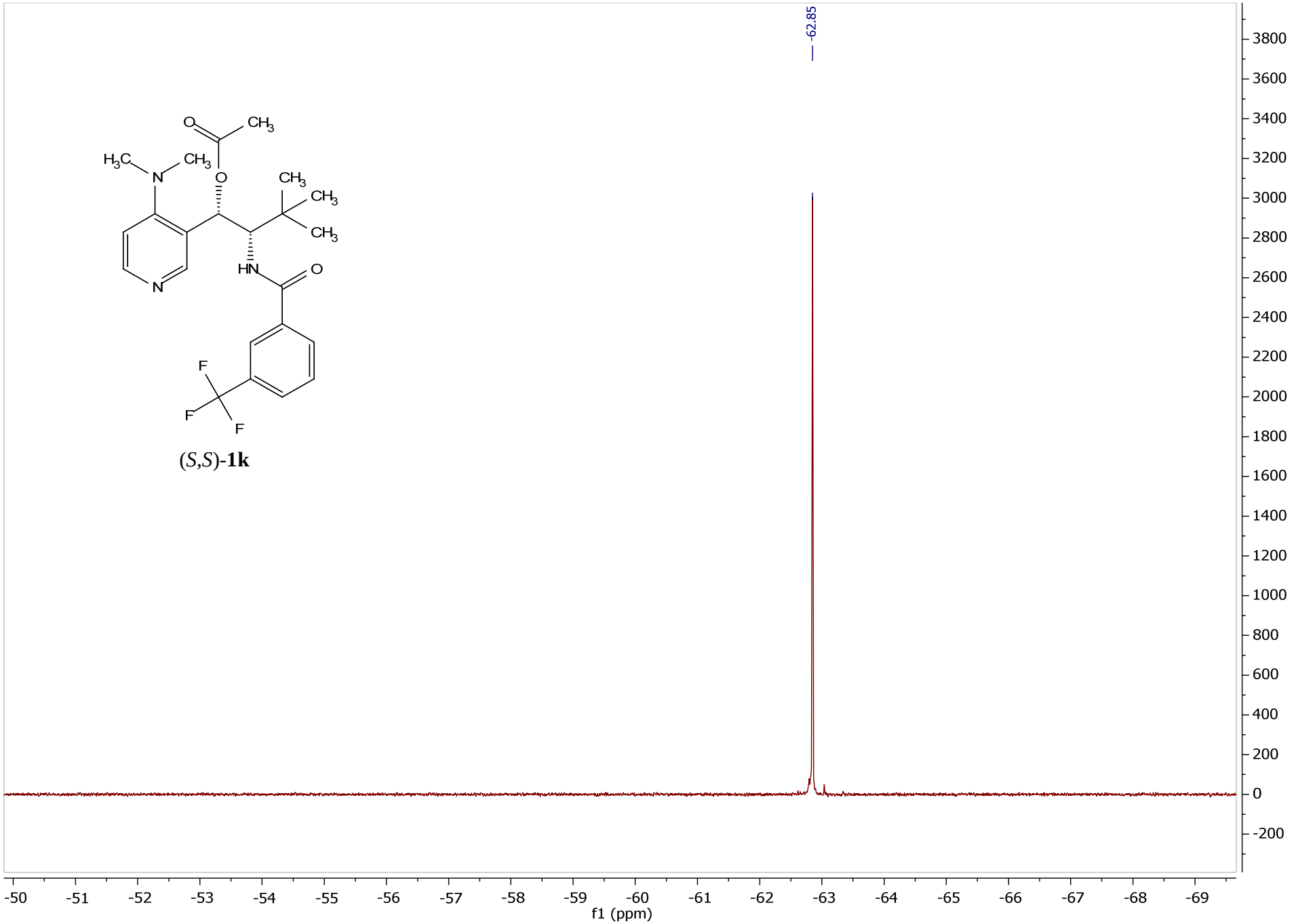
(*S*,*S*)-**1j**


8.31
7.87
7.85
7.84
7.81
7.71
7.68
7.66
7.62
7.60
7.59
7.57
7.26 CDCl3
6.87
6.85
6.61
6.61
6.52
6.49
4.20
4.19
4.16
4.16
3.32
2.29
1.09
0.07
J (s) 8.31
H (m) 7.69
G (m) 7.61
I (m) 7.86
E (d) 6.61
D (d) 6.50
F (d) 6.86
C (dd) 4.18
A (s) 3.32
K (s) 2.29
B (s) 1.09
0.92
2.86
1.08
1.04
0.96
0.95
0.90
1.04
6.00
2.94
9.25
f1 (ppm)

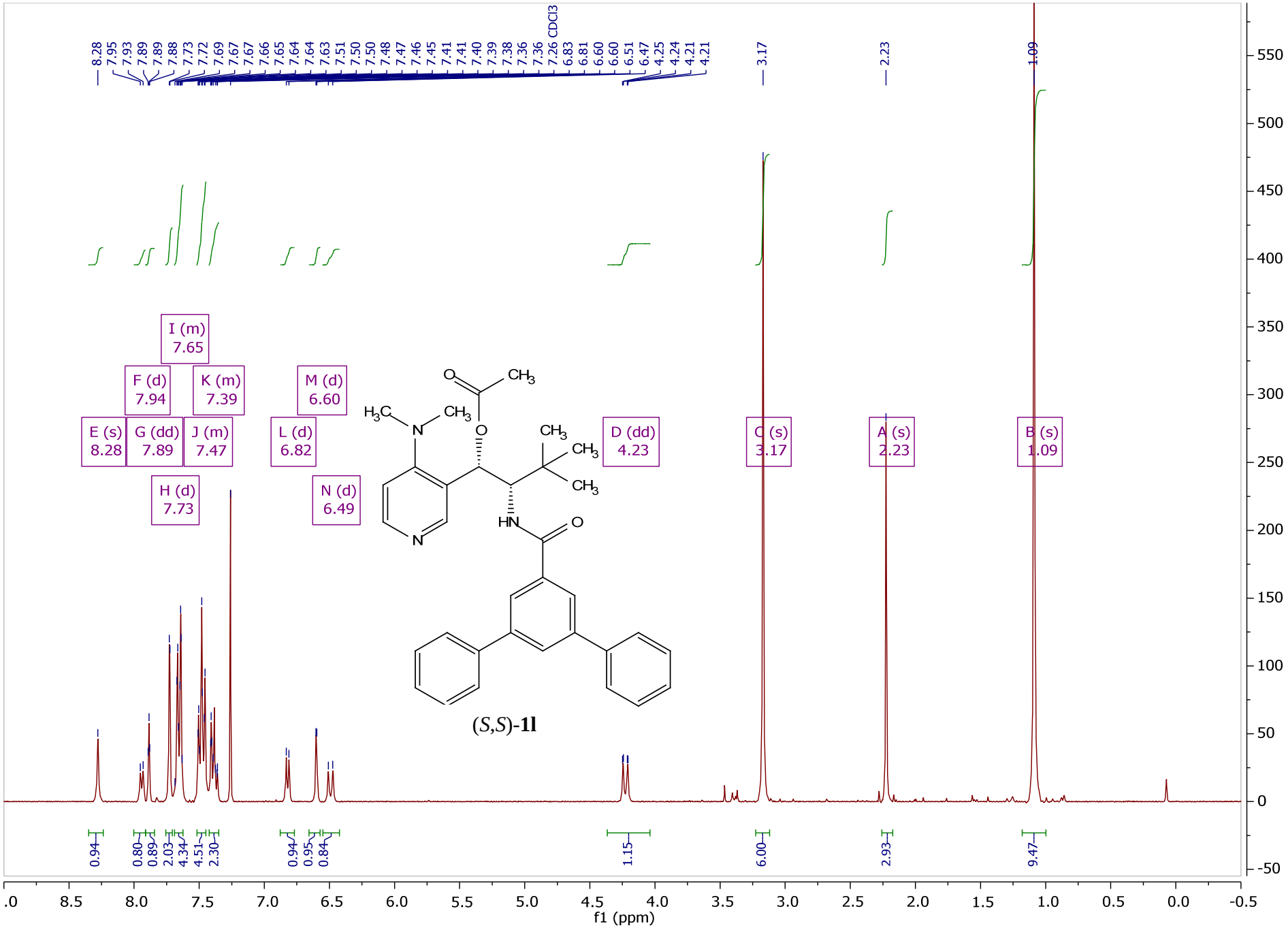
(*S*,*S*)-**1k**


170.49
166.73
159.76
141.34
140.19
134.10
131.49
131.16
130.08
129.63
128.62
125.15
124.55
122.45
111.90
77.46
69.48
57.72
43.61
35.65
27.62
21.04
f1 (ppm)

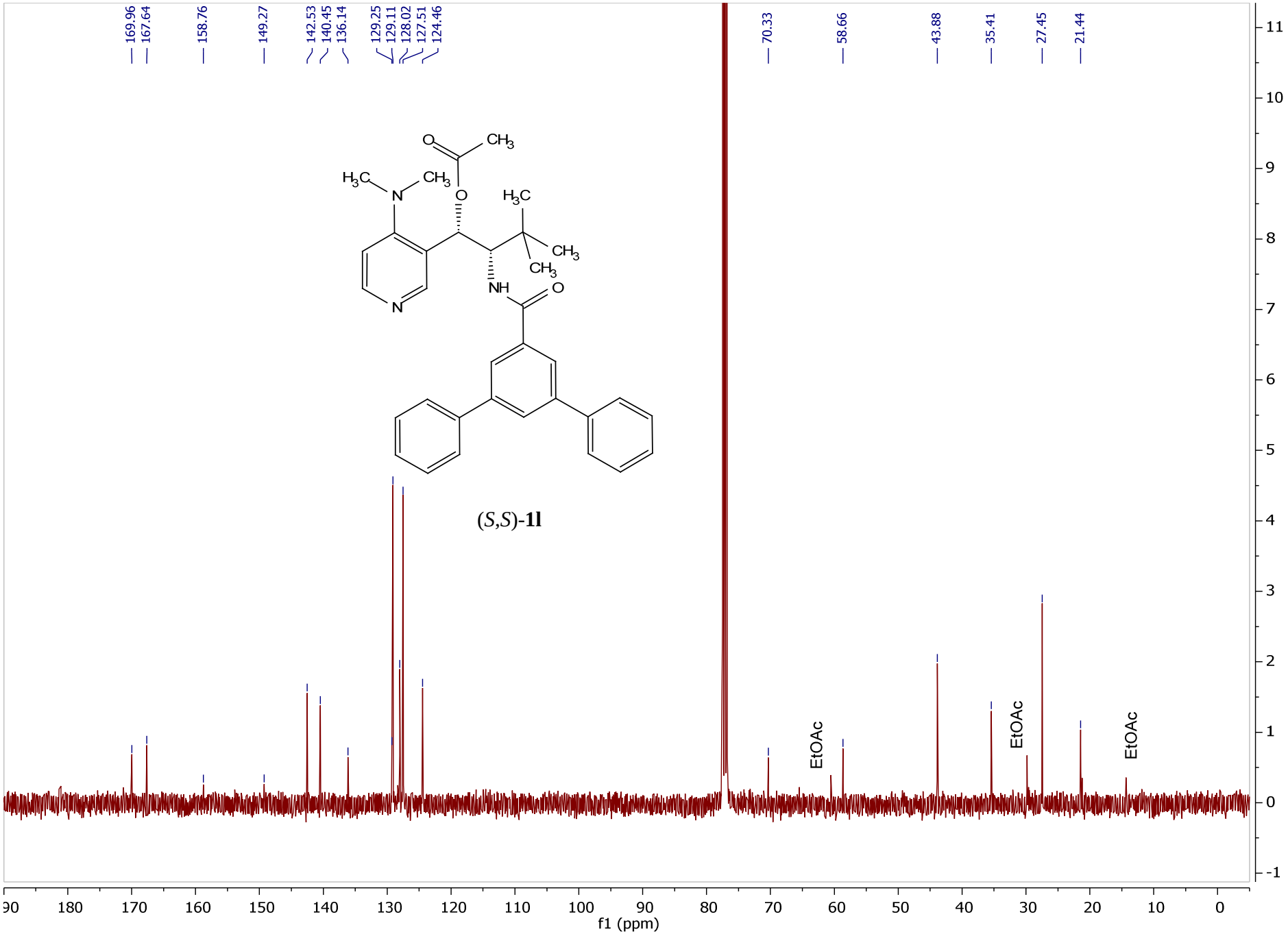
(*S*,*S*)-**1k**


-62.85
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-50
-51
-52
-53
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
f1 (ppm)

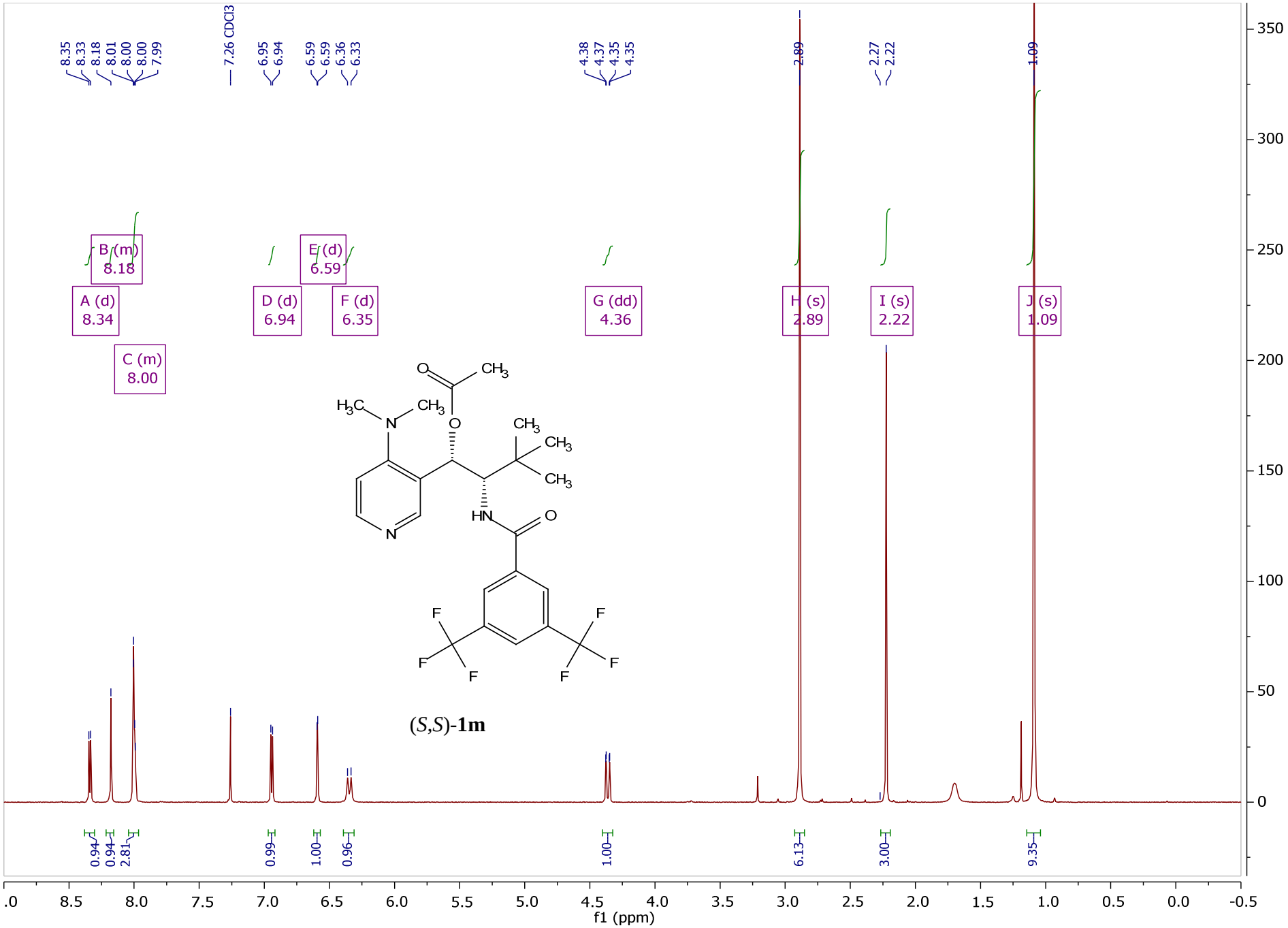
(*S*,*S*)-**1k**


8.28
7.95
7.93
7.89
7.89
7.88
7.73
7.72
7.69
7.67
7.67
7.66
7.65
7.64
7.64
7.63
7.51
7.50
7.50
7.48
7.47
7.46
7.45
7.41
7.41
7.40
7.39
7.38
7.36
7.36
CDCl3
7.26
6.83
6.81
6.60
6.60
6.51
6.47
4.25
4.24
4.21
4.21
3.17
2.23
1.09
I (m) 7.65
F (d) 7.94
K (m) 7.39
M (d) 6.60
E (s) 8.28
G (dd) 7.89
J (m) 7.47
L (d) 6.82
D (dd) 4.23
C (s) 3.17
A (s) 2.23
B (s) 1.09
H (d) 7.73
N (d) 6.49
0.94
0.80
0.89
2.03
4.34
4.51
2.30
0.94
0.95
0.84
1.15
6.00
2.93
9.47
f1 (ppm)

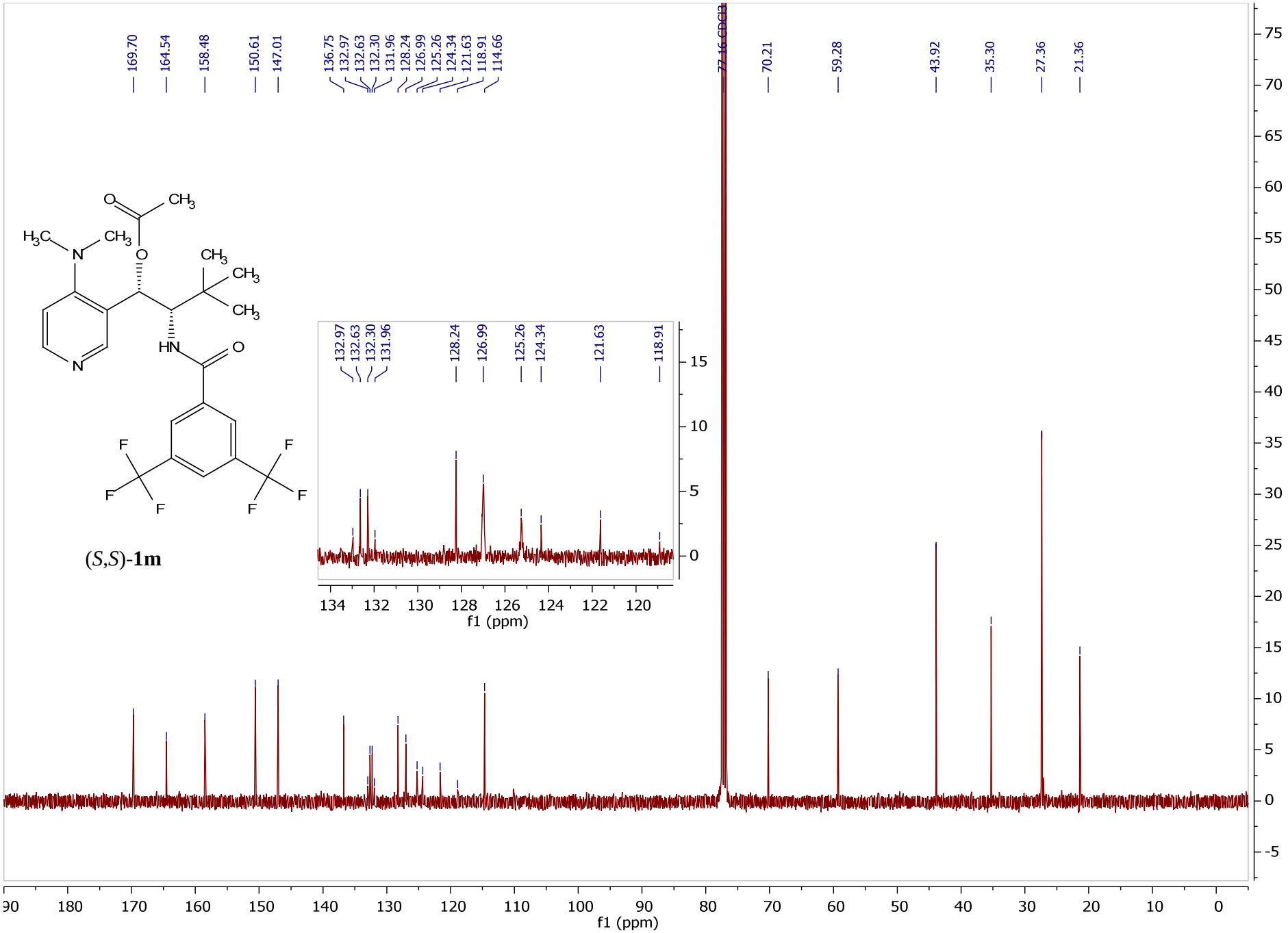
(*S*,*S*)-**1l**

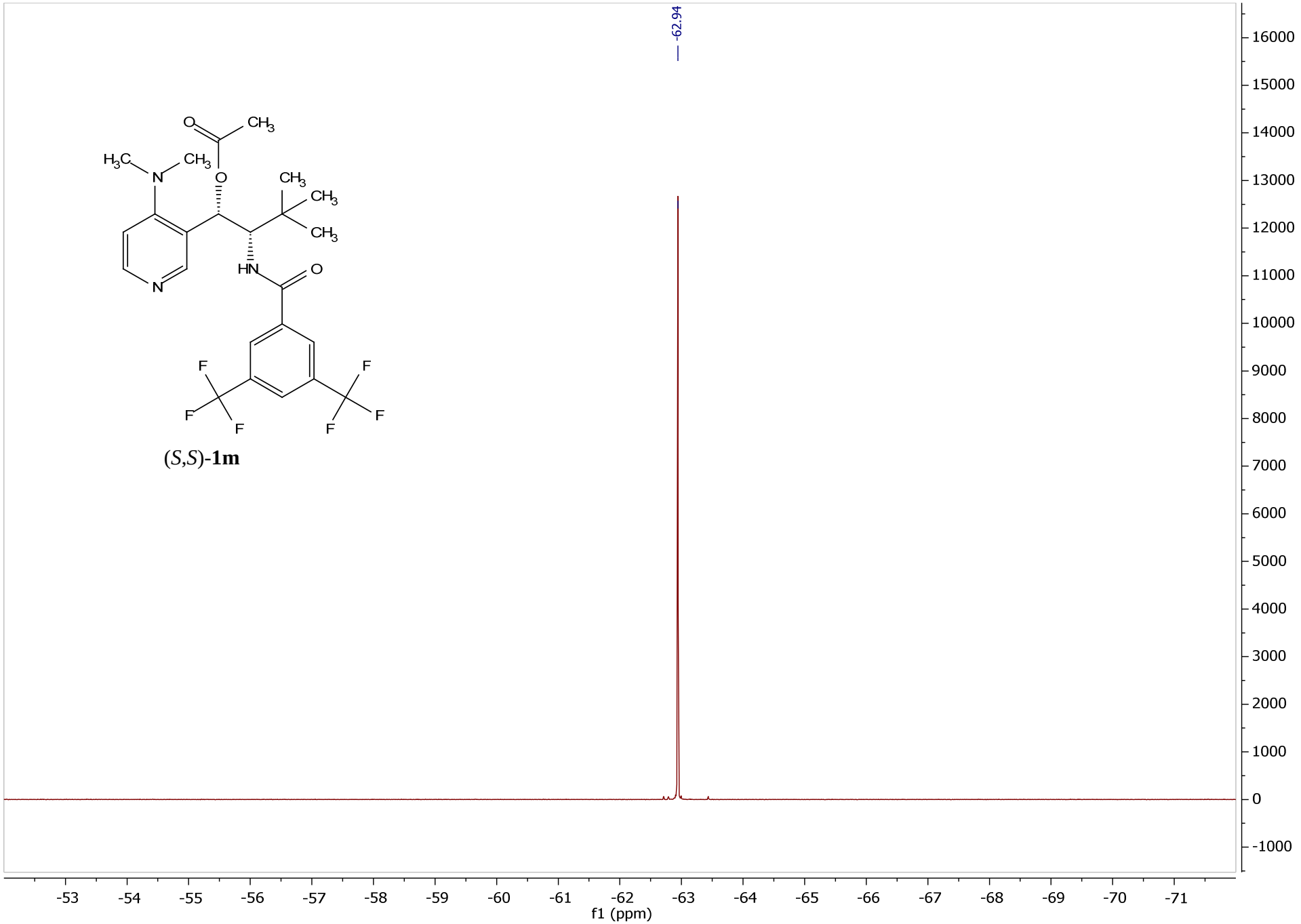

169.96
167.64
158.76
149.27
142.53
140.45
136.14
129.25
129.11
128.02
127.51
124.46
70.33
58.66
43.88
35.41
27.45
21.44
EtOAc
EtOAc
EtOAc
f1 (ppm)

(*S*,*S*)-**1l**

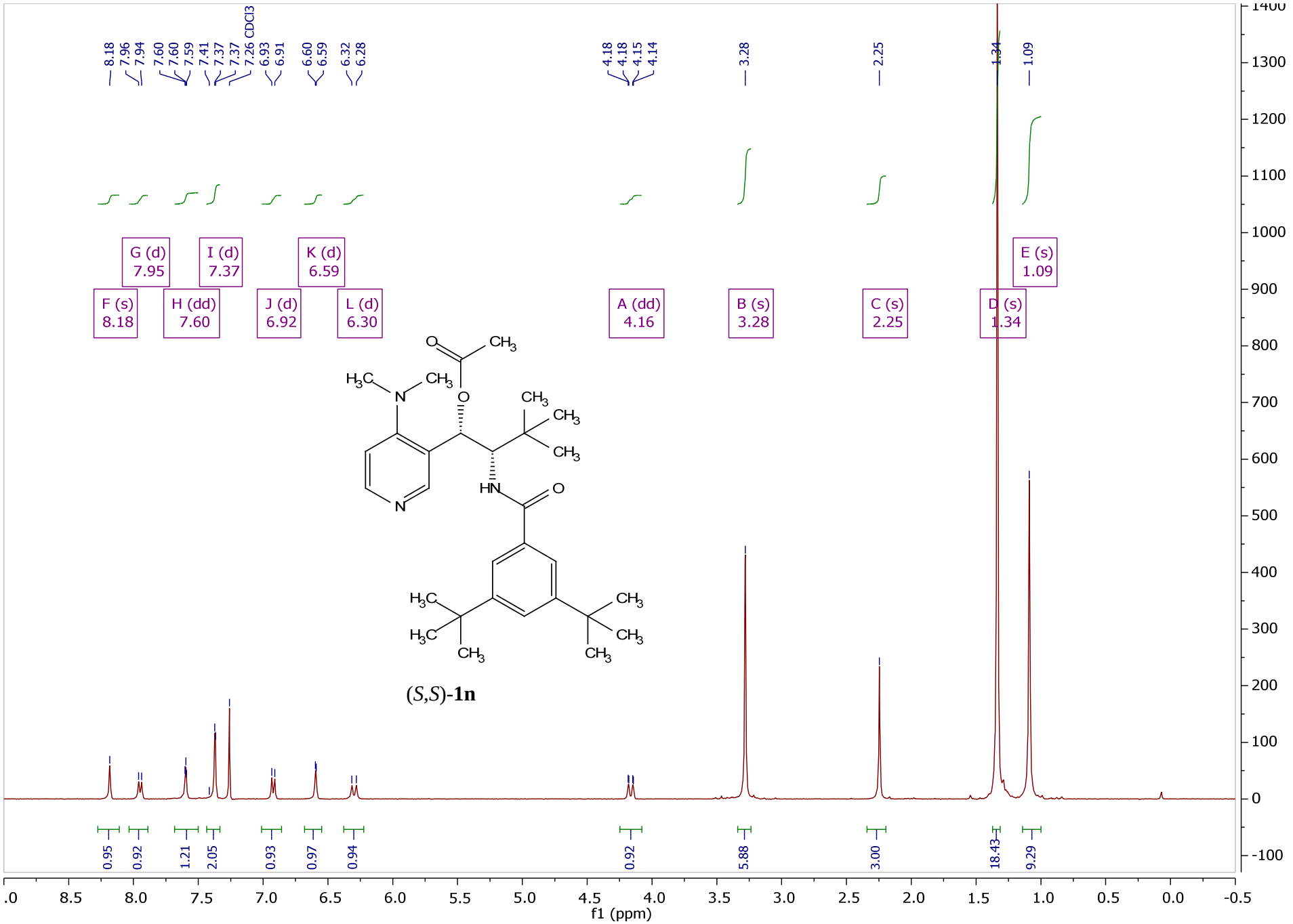

8.35
8.33
8.18
8.01
8.00
8.00
7.99
7.26 CDCl3
6.95
6.94
6.59
6.59
6.36
6.33
4.38
4.37
4.35
4.35
2.89
2.27
2.22
1.09
B (m) 8.18
E (d) 6.59
A (d) 8.34
D (d) 6.94
F (d) 6.35
G (dd) 4.36
H (s) 2.89
I (s) 2.22
J (s) 1.09
C (m) 8.00
0.94
0.94
2.81
0.99
1.00
0.96
1.00
6.13
3.00
9.35
f1 (ppm)

(*S*,*S*)-**1m**

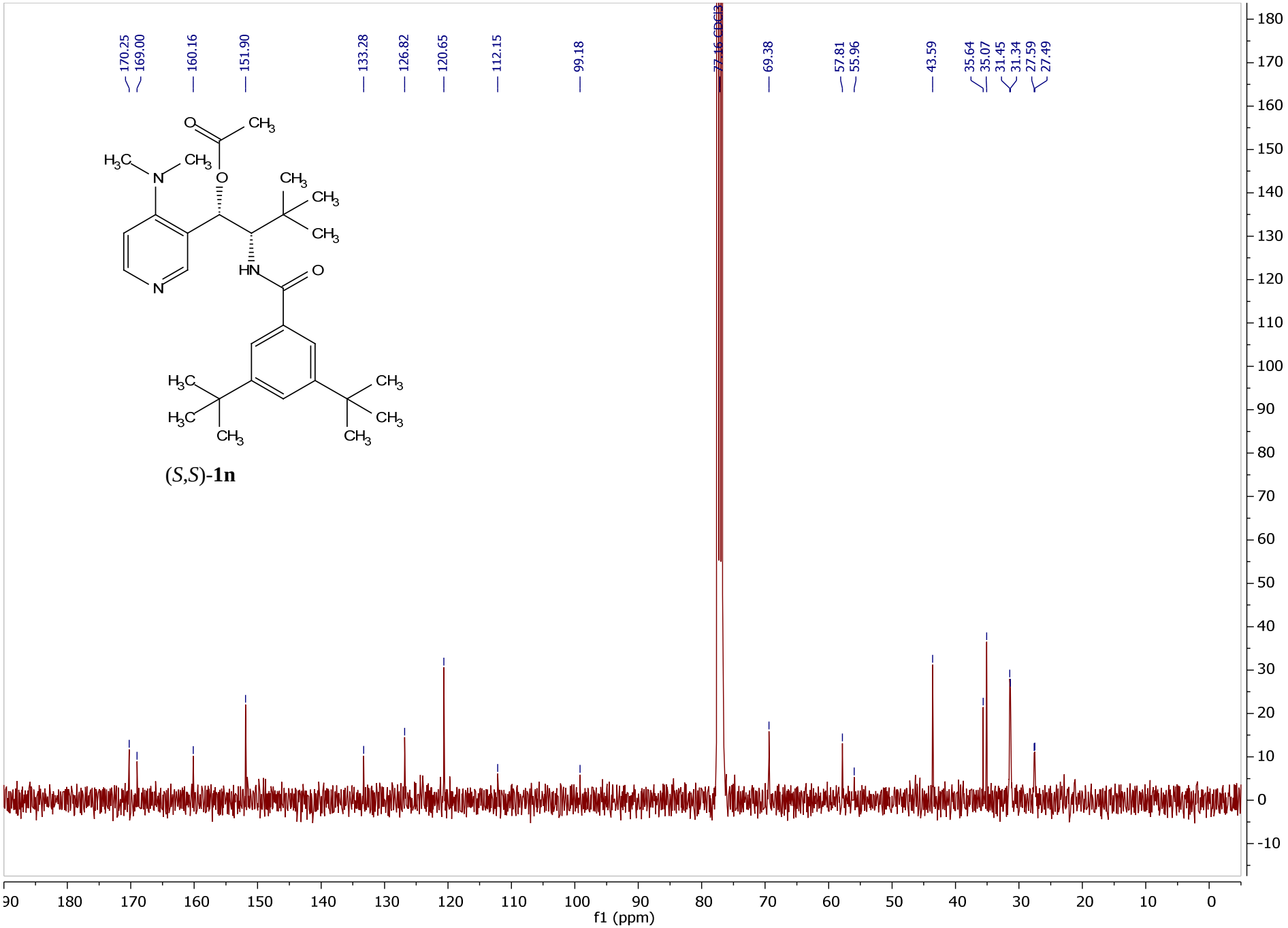

169.70
164.54
158.48
150.61
147.01
136.75
132.97
132.63
132.30
131.96
128.24
126.99
125.26
124.34
121.63
118.91
114.66
77.16 CDCl3
70.21
59.28
43.92
35.30
27.36
21.36
(S,S)-1m
f1 (ppm)
f1 (ppm)


-62.94
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-53
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
-71
f1 (ppm)

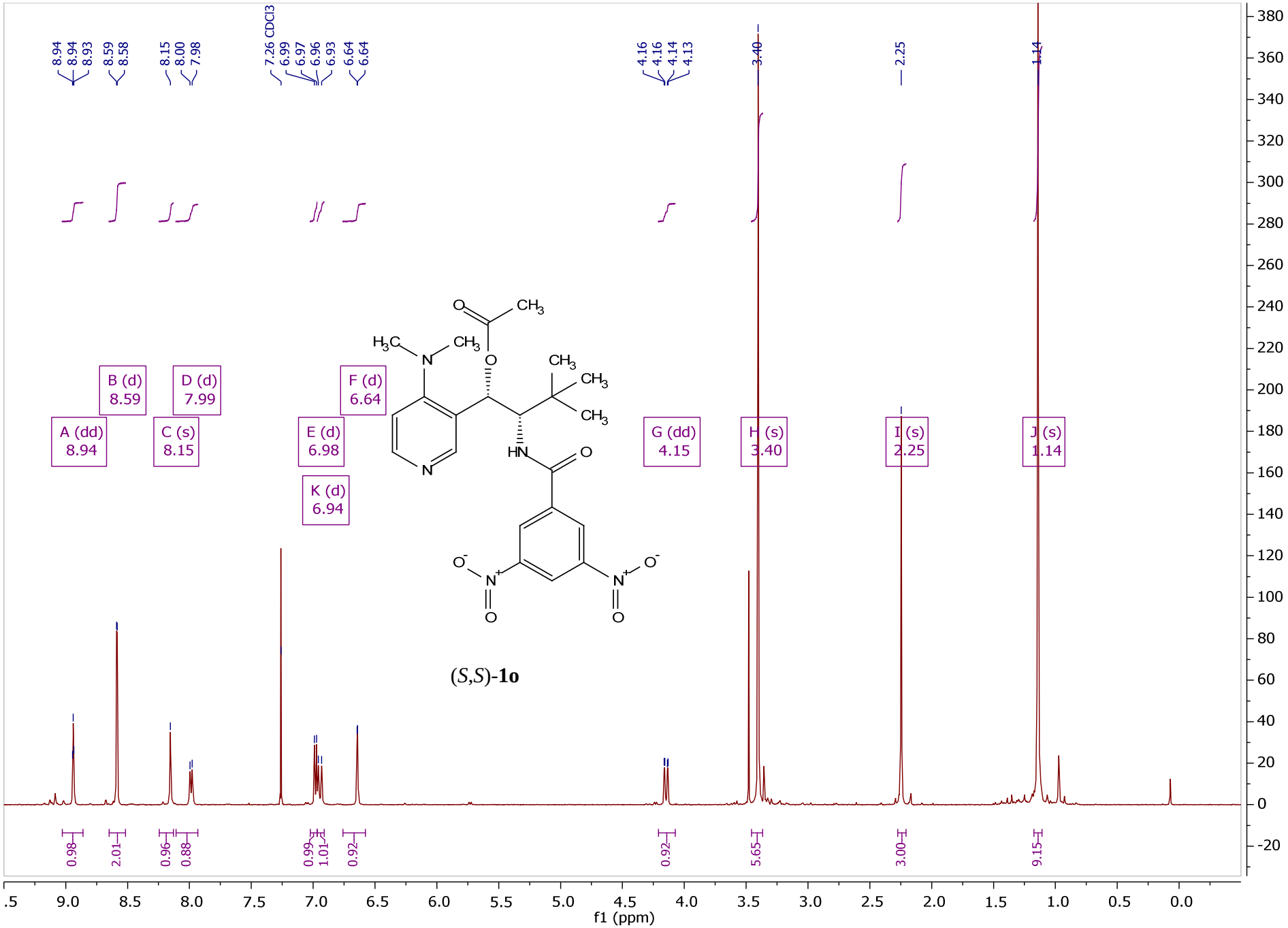
(*S*,*S*)-**1m**


8.18
7.96
7.94
7.60
7.60
7.59
7.41
7.37
7.37
7.26 CDCl3
6.93
6.91
6.60
6.59
6.32
6.28
4.18
4.18
4.15
4.14
3.28
2.25
1.34
1.09
F (s) 8.18
G (d) 7.95
H (dd) 7.60
I (d) 7.37
J (d) 6.92
K (d) 6.59
L (d) 6.30
A (dd) 4.16
B (s) 3.28
C (s) 2.25
D (s) 1.34
E (s) 1.09
0.95
0.92
1.21
2.05
0.93
0.97
0.94
0.92
5.88
3.00
18.43
9.29
f1 (ppm)

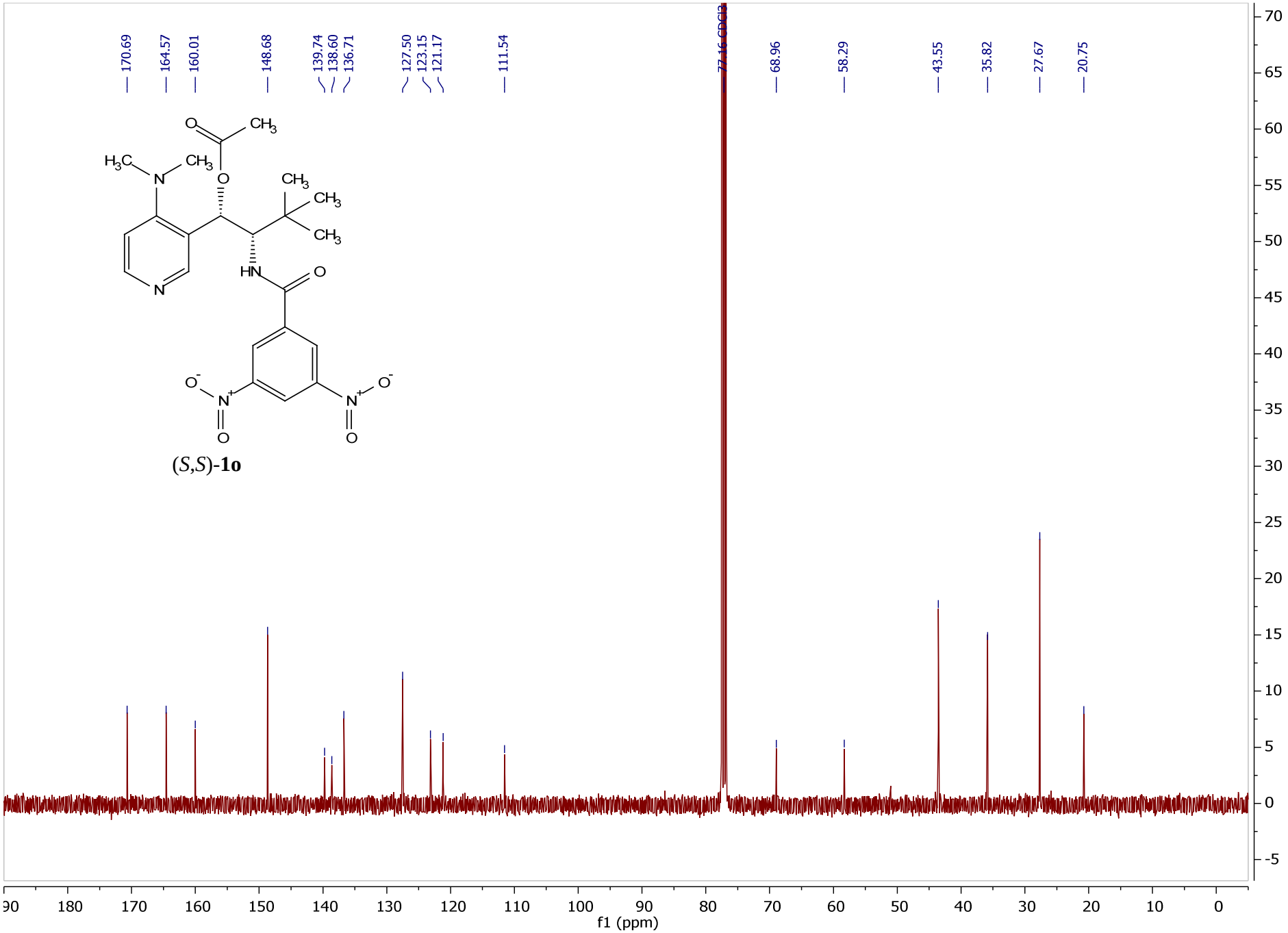
(*S*,*S*)-**1n**


170.25
169.00
160.16
151.90
133.28
126.82
120.65
112.15
99.18
77.16
69.38
57.81
55.96
43.59
35.64
35.07
31.45
31.34
27.59
27.49
f1 (ppm)

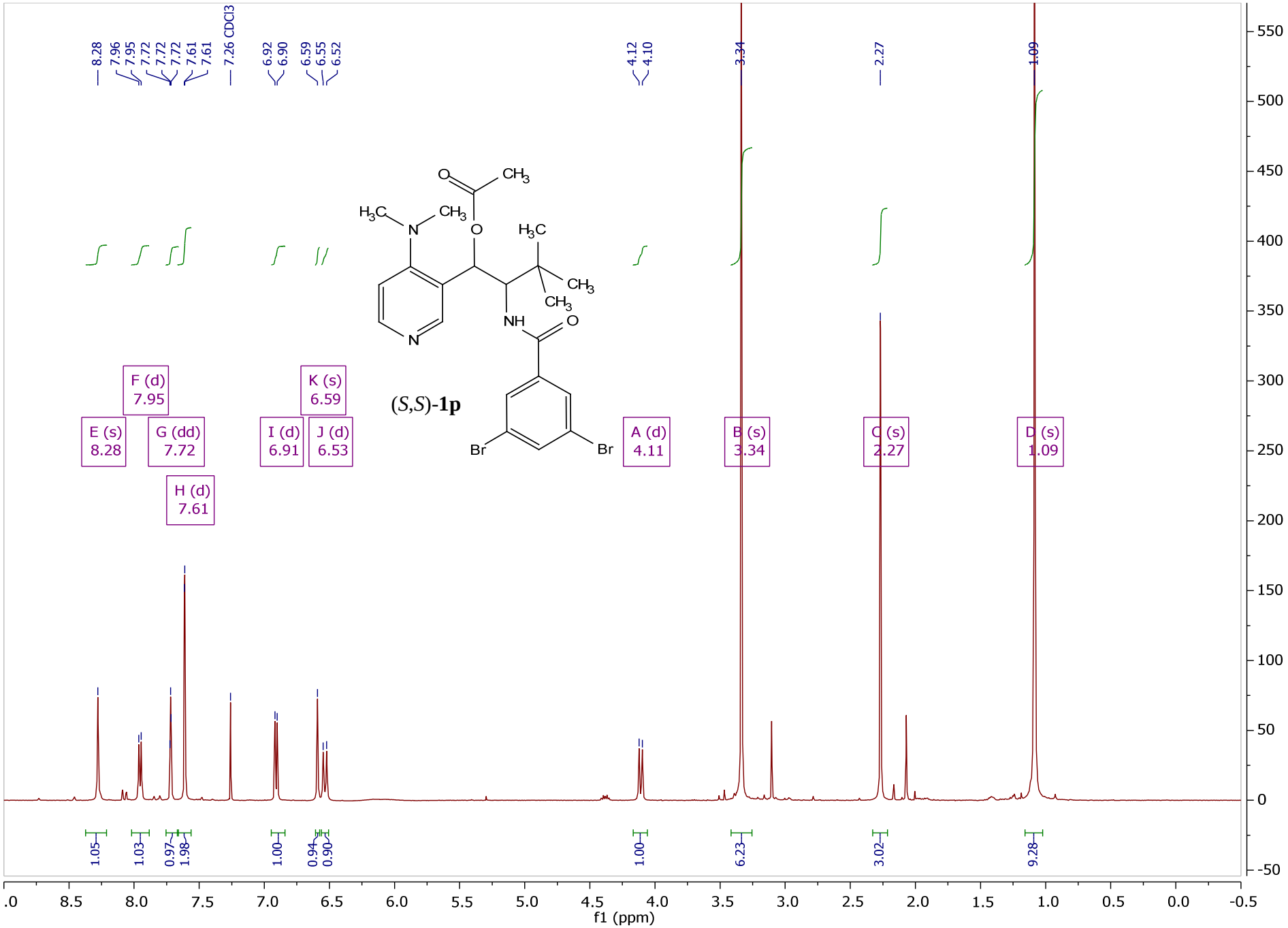
(*S*,*S*)-**1n**

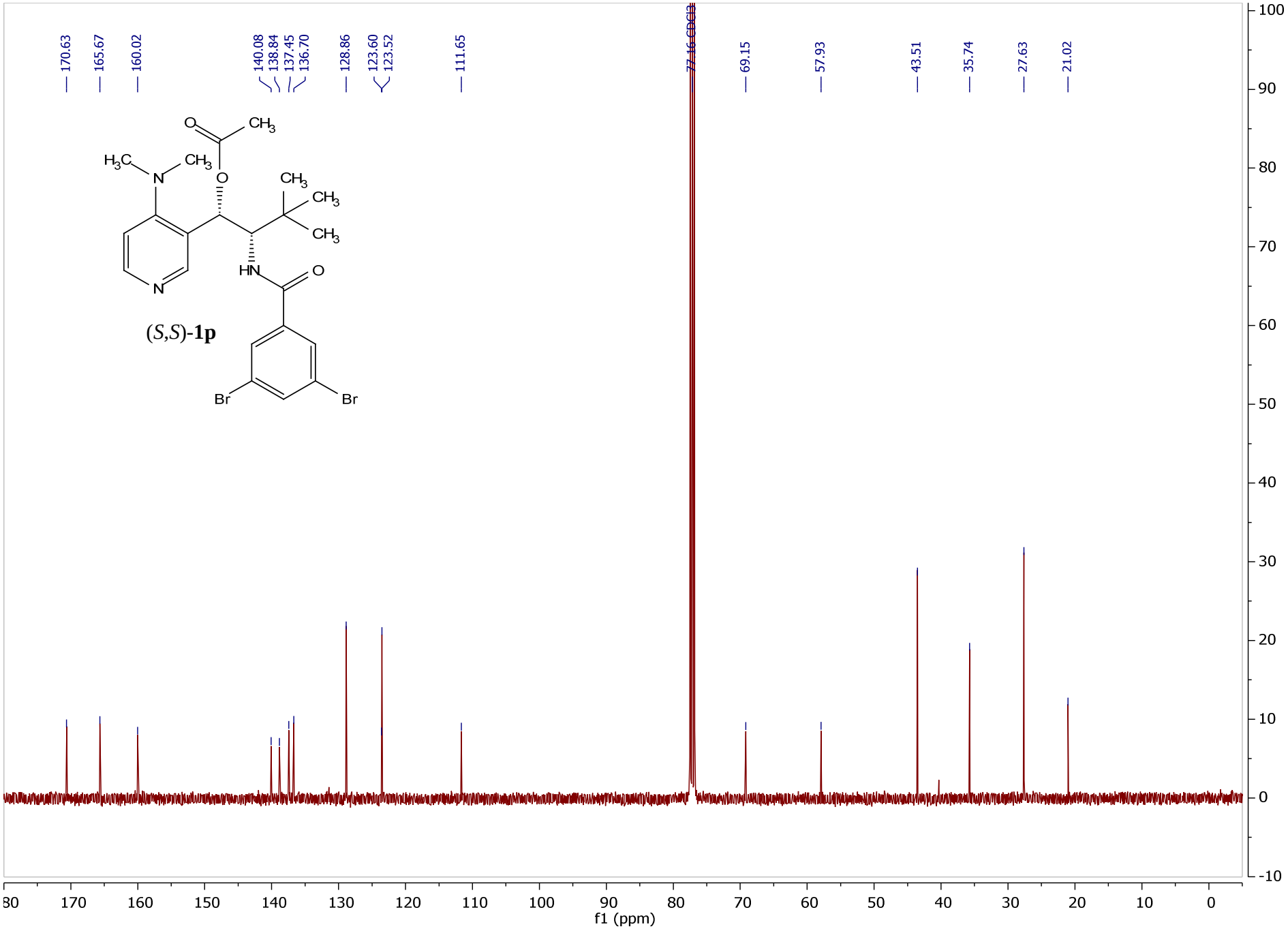

8.94
8.94
8.93
8.59
8.58
8.15
8.00
7.98
7.26 CDCl3
6.99
6.97
6.96
6.93
6.64
6.64
4.16
4.16
4.14
4.13
3.40
2.25
1.14
A (dd) 8.94
B (d) 8.59
C (s) 8.15
D (d) 7.99
E (d) 6.98
F (d) 6.64
G (dd) 4.15
H (s) 3.40
I (s) 2.25
J (s) 1.14
K (d) 6.94
0.98
2.01
0.96
0.88
0.99
1.01
0.92
0.92
5.65
3.00
9.15
f1 (ppm)

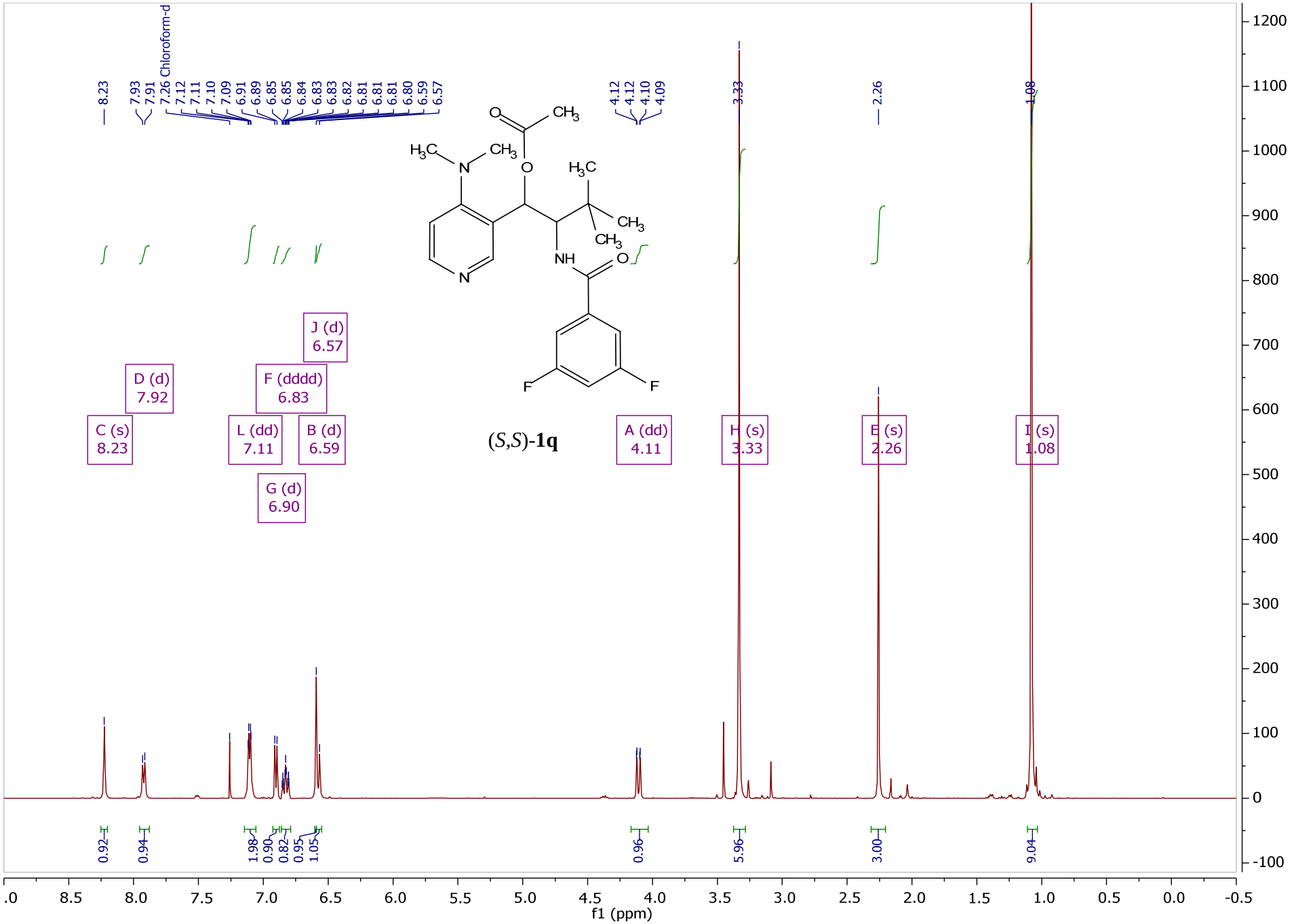
(*S*,*S*)-**1o**

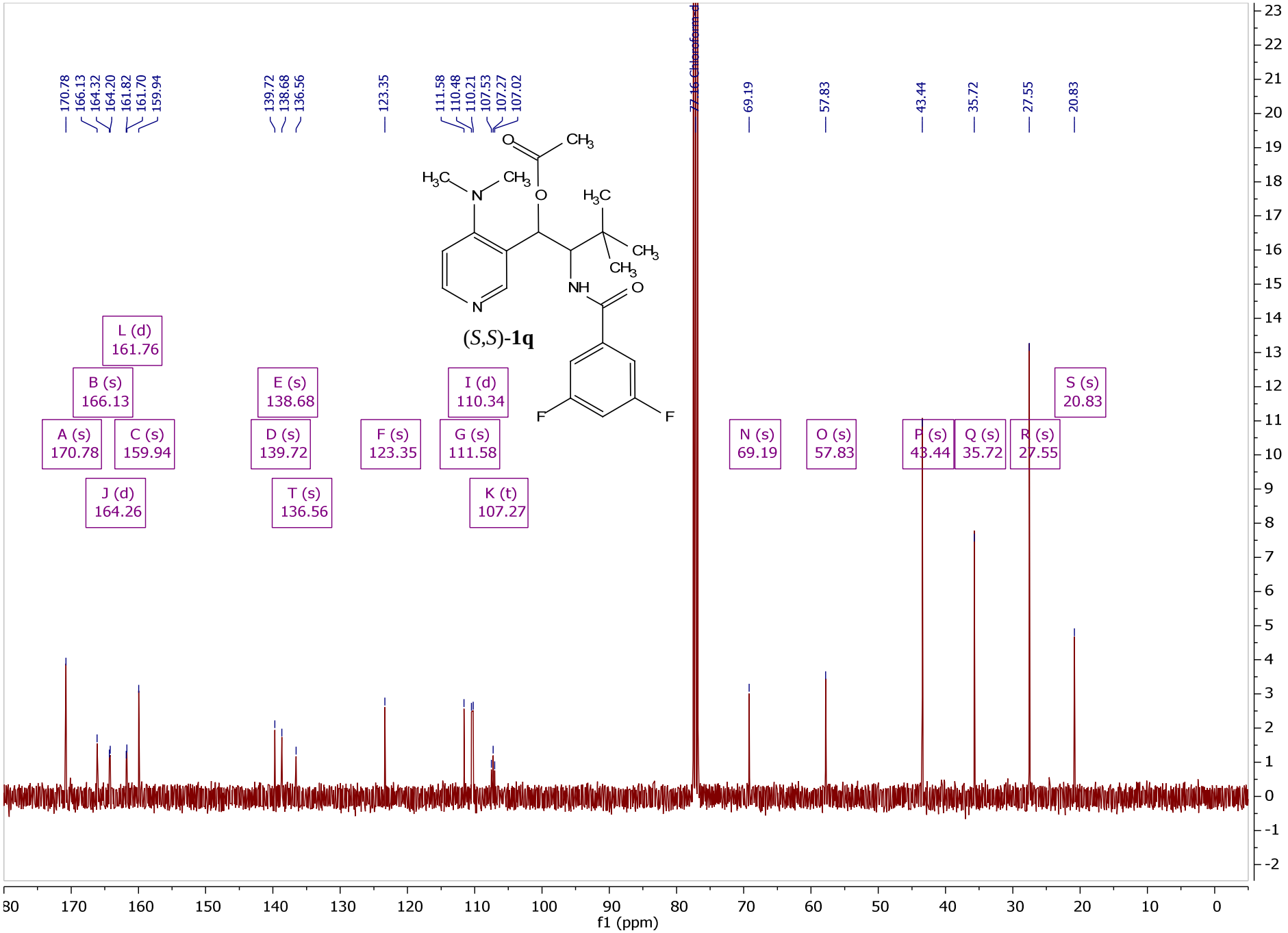

170.69
164.57
160.01
148.68
139.74
138.60
136.71
127.50
123.15
121.17
111.54
77.16
68.96
58.29
43.55
35.82
27.67
20.75
f1 (ppm)

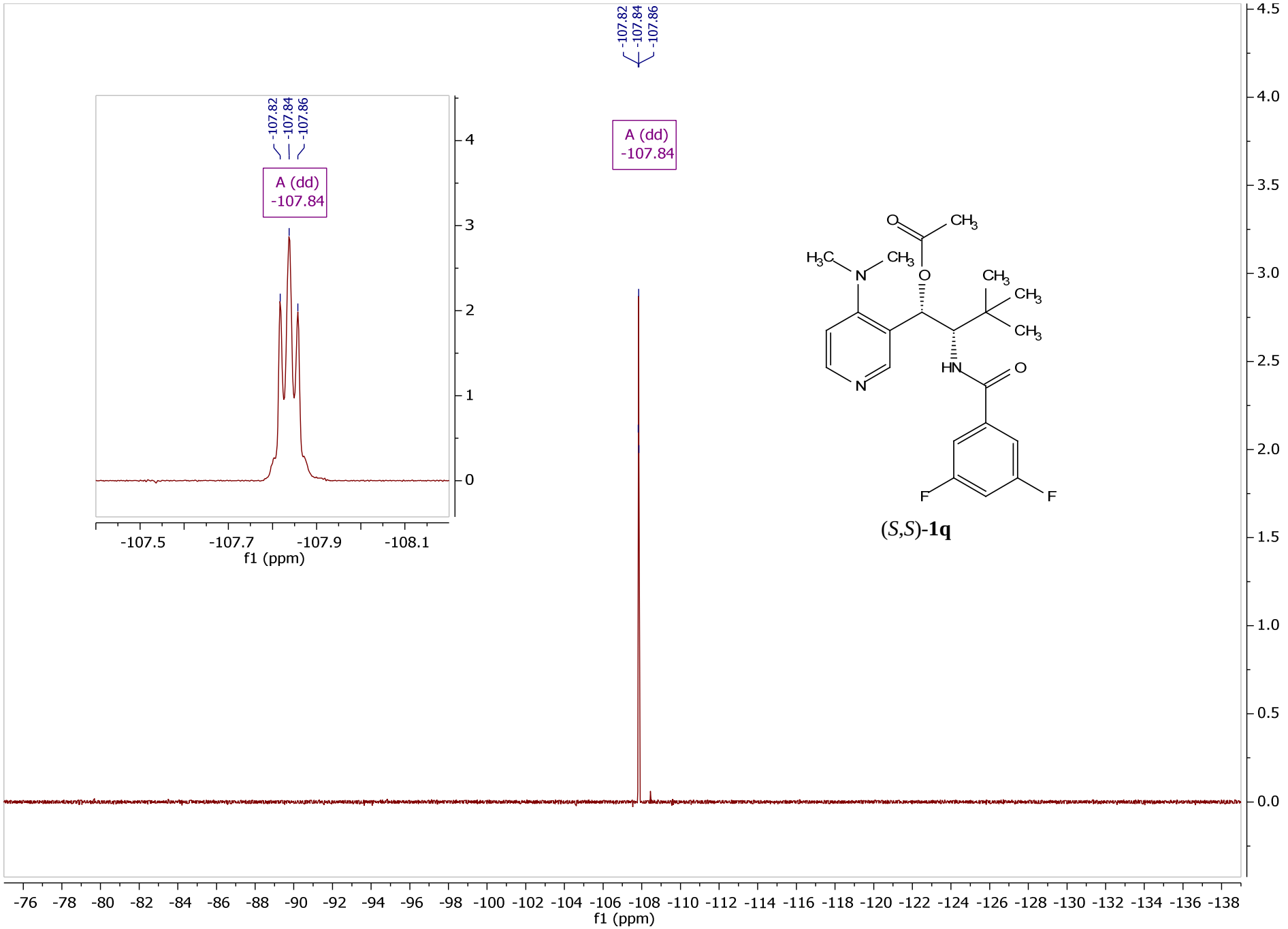
(*S*,*S*)-**1o**


8.28
7.96
7.95
7.72
7.72
7.72
7.61
7.61
7.26 CDCl3
6.92
6.90
6.59
6.55
6.52
4.12
4.10
3.34
2.27
1.09
F (d) 7.95
K (s) 6.59
E (s) 8.28
G (dd) 7.72
I (d) 6.91
J (d) 6.53
H (d) 7.61
A (d) 4.11
B (s) 3.34
C (s) 2.27
D (s) 1.09
(S,S)-1p
1.05
1.03
0.97
1.98
1.00
0.94
0.90
1.00
6.23
3.02
9.28
f1 (ppm)

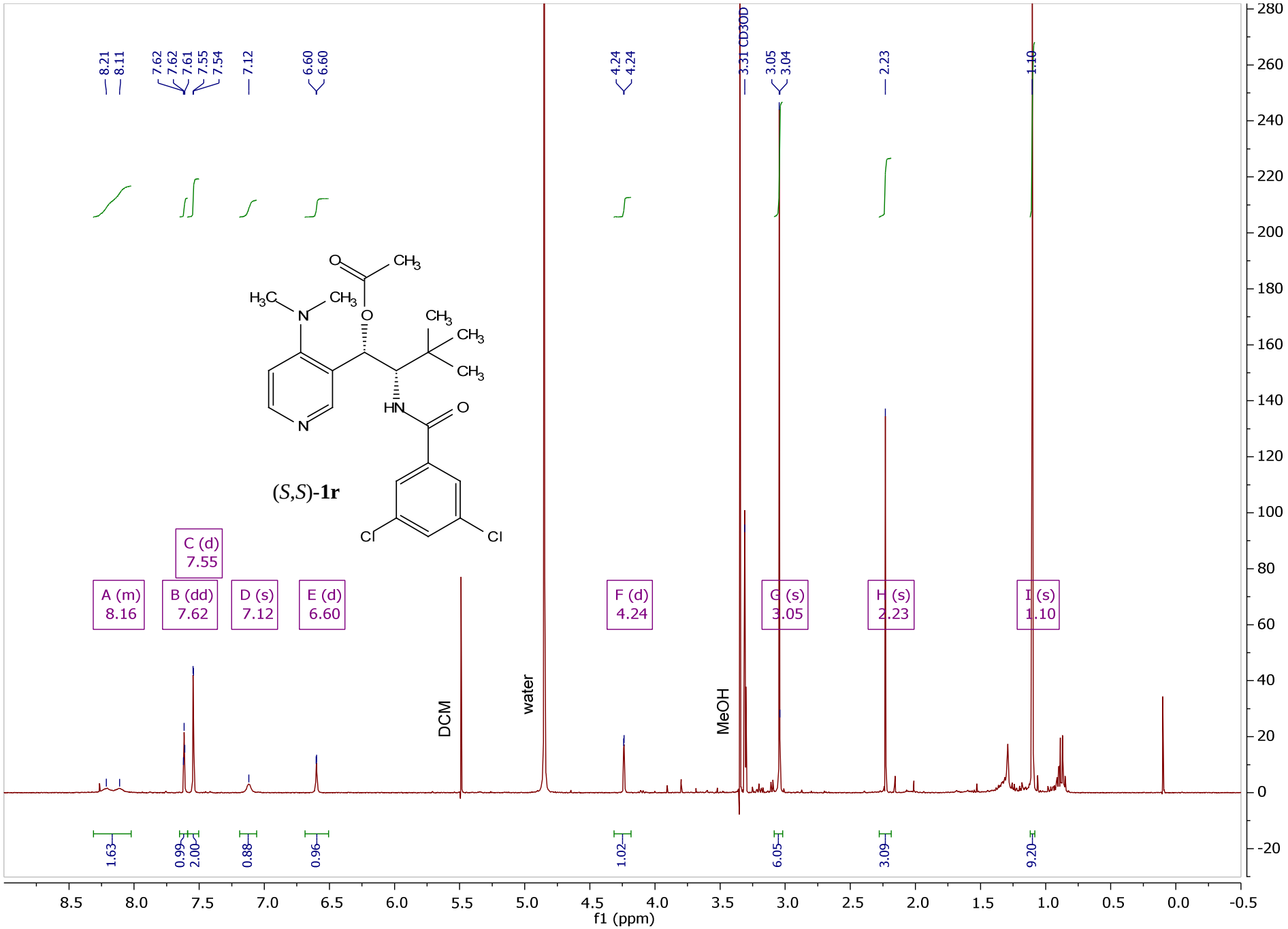

170.63
165.67
160.02
140.08
138.84
137.45
136.70
128.86
123.60
123.52
111.65
77.16 CDCl3
69.15
57.93
43.51
35.74
27.63
21.02
(S,S)-1p
f1 (ppm)

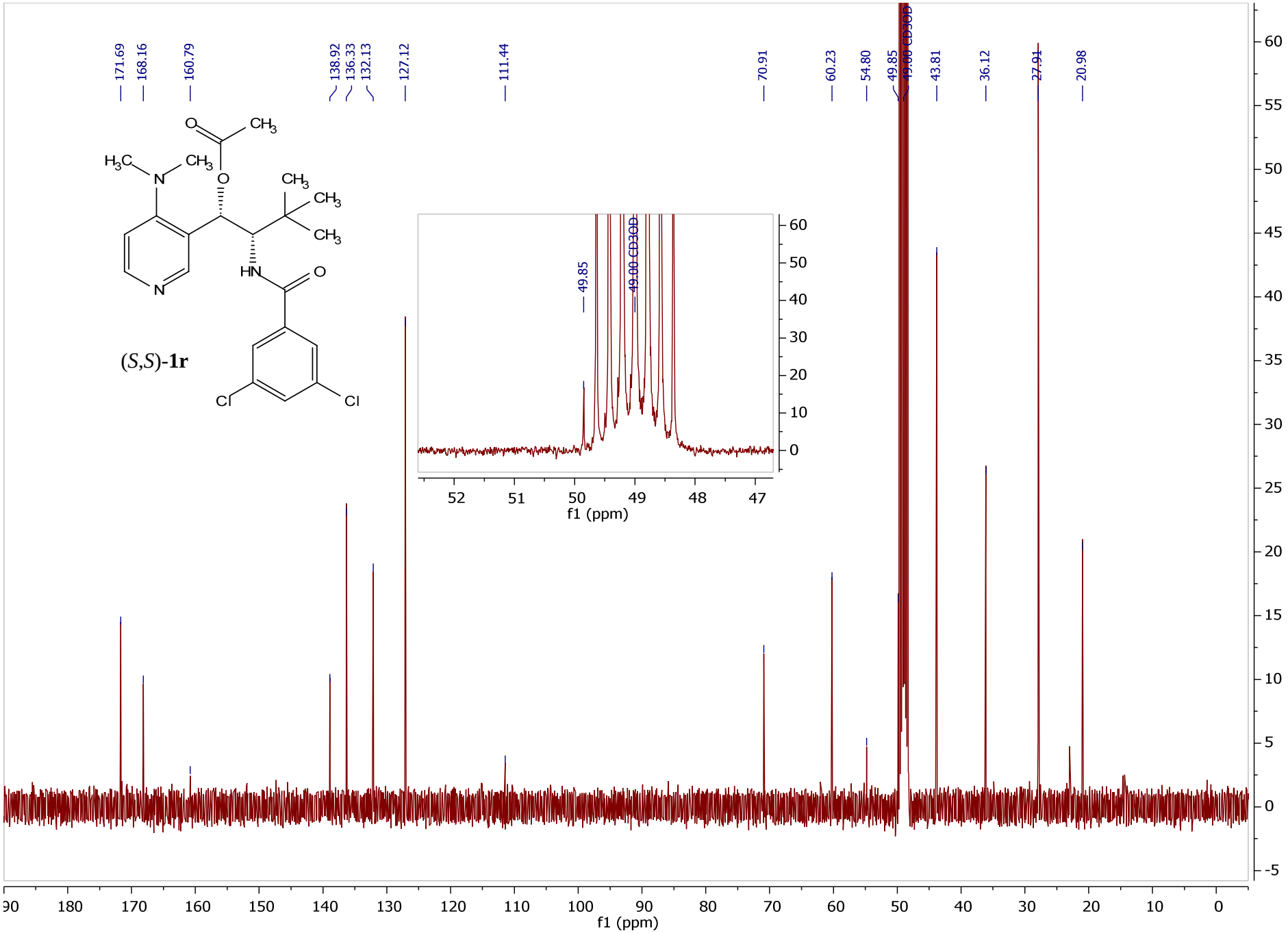

8.23
7.93
7.91
7.26 Chloroform-d
7.12
7.11
7.10
7.09
6.91
6.89
6.85
6.85
6.84
6.83
6.83
6.82
6.81
6.81
6.81
6.80
6.59
6.57
4.12
4.12
4.10
4.09
3.33
2.26
1.08
J (d) 6.57
D (d) 7.92
F (dddd) 6.83
C (s) 8.23
L (dd) 7.11
B (d) 6.59
G (d) 6.90
A (dd) 4.11
H (s) 3.33
E (s) 2.26
I (s) 1.08
(S,S)-1q
0.92
0.94
1.98
0.90
0.82
0.95
1.05
0.96
5.96
3.00
9.04
f1 (ppm)

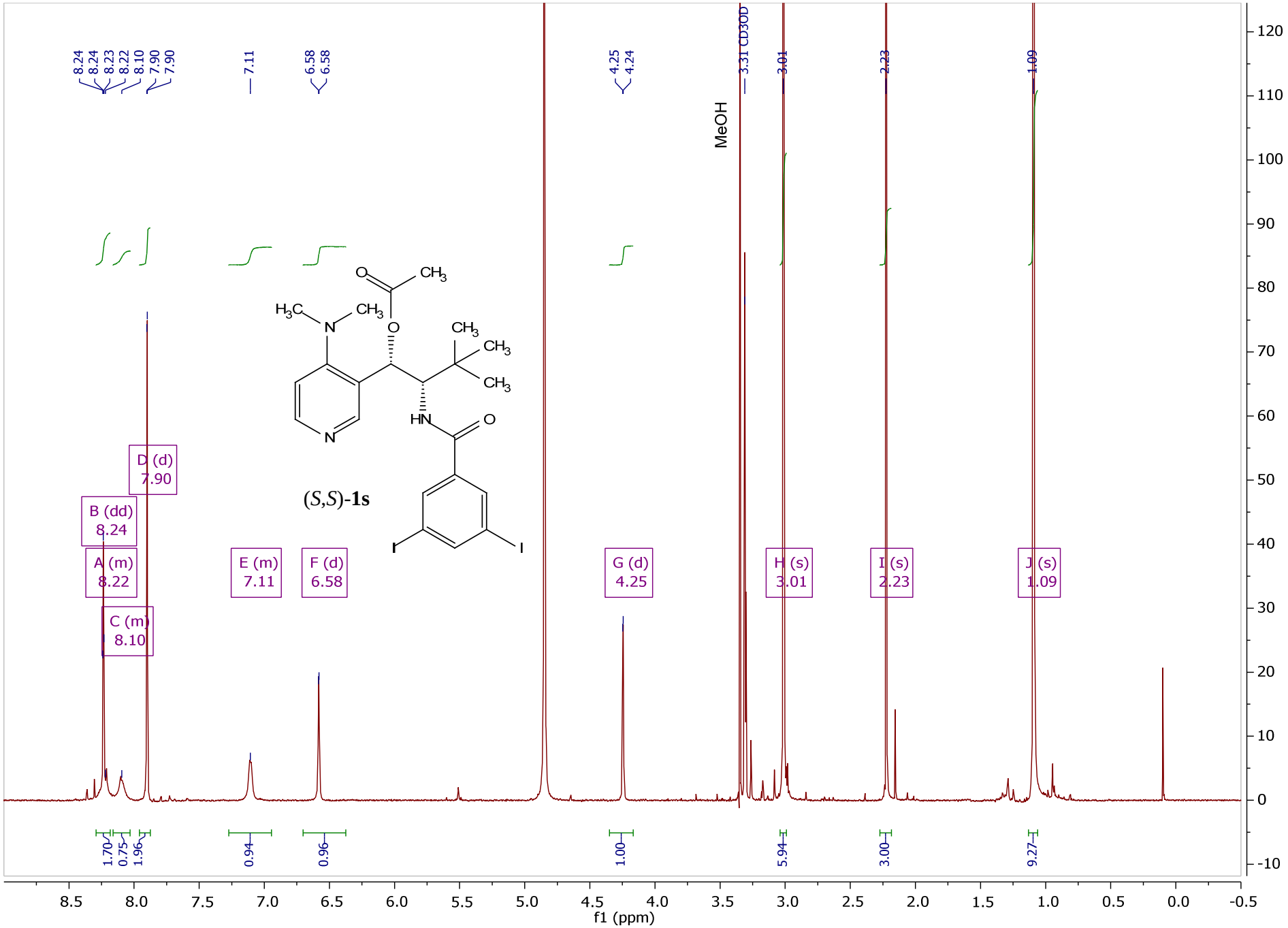

170.78
166.13
164.32
164.20
161.82
161.70
159.94
139.72
138.68
136.56
123.35
111.58
110.48
110.21
107.53
107.27
107.02
77.16 Chloroform-d
69.19
57.83
43.44
35.72
27.55
20.83
(S,S)-1q
L (d) 161.76
B (s) 166.13
A (s) 170.78
C (s) 159.94
J (d) 164.26
E (s) 138.68
D (s) 139.72
T (s) 136.56
F (s) 123.35
I (d) 110.34
G (s) 111.58
K (t) 107.27
N (s) 69.19
O (s) 57.83
P (s) 43.44
Q (s) 35.72
R (s) 27.55
S (s) 20.83
f1 (ppm)

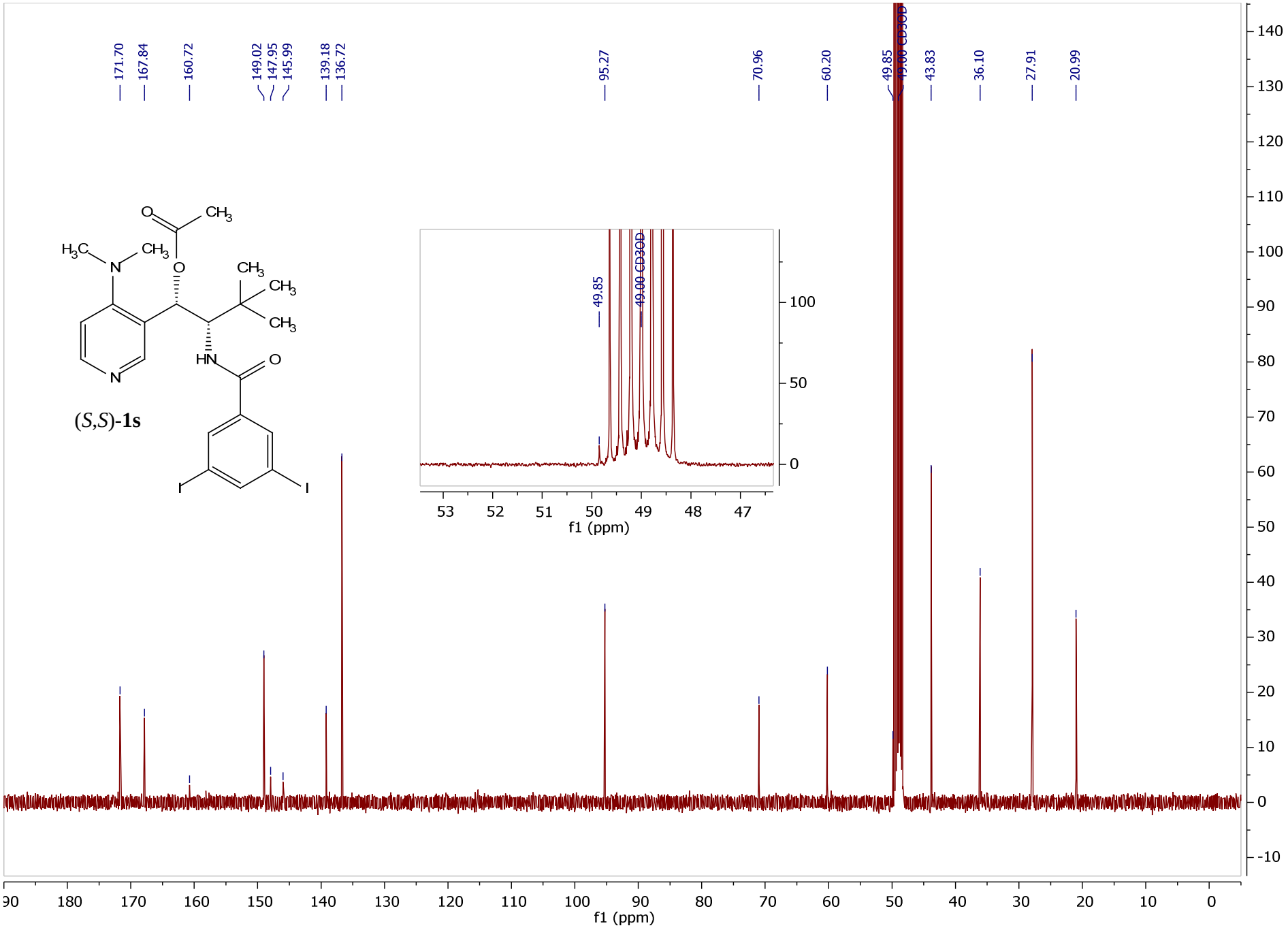

-107.82
-107.84
-107.86
A (dd)
-107.84
-107.5
-107.7
-107.9
-108.1
f1 (ppm)
-76 -78 -80 -82 -84 -86 -88 -90 -92 -94 -96 -98 -100 -102 -104 -106 -108 -110 -112 -114 -116 -118 -120 -122 -124 -126 -128 -130 -132 -134 -136 -138
f1 (ppm)
4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

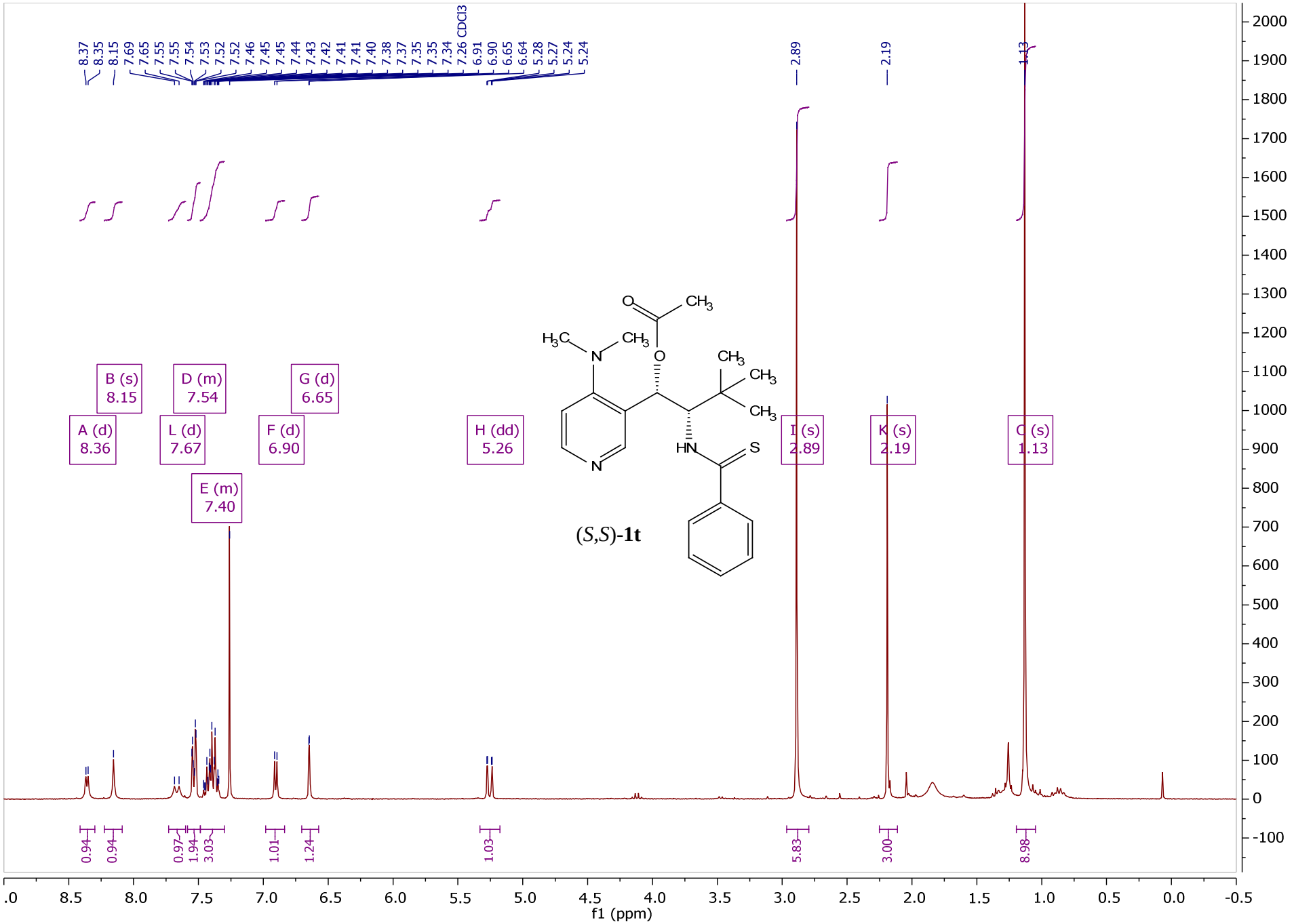
(*S*,*S*)-**1q**

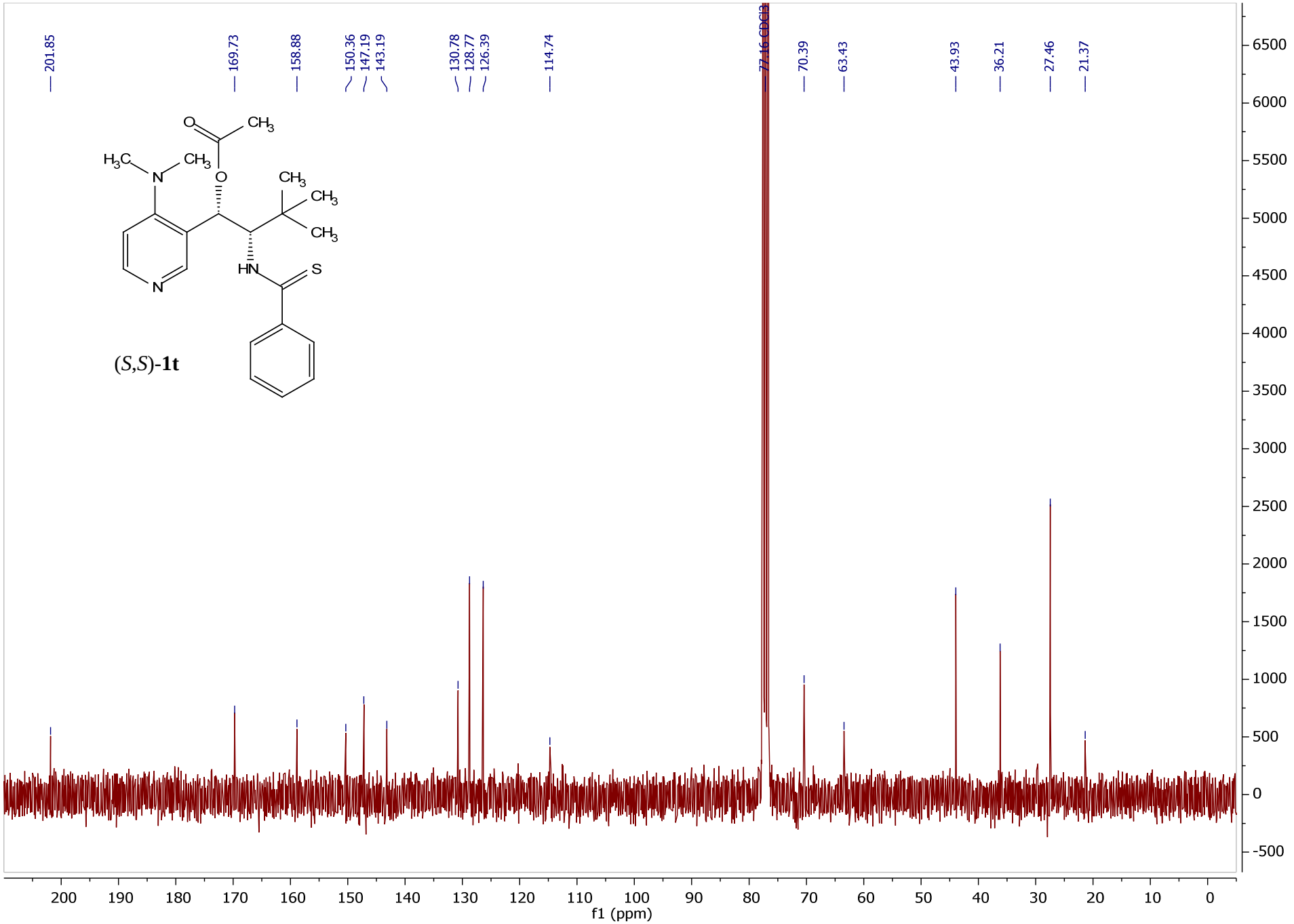

8.21
8.11
7.62
7.62
7.61
7.55
7.54
7.12
6.60
6.60
4.24
4.24
3.31 CD3OD
3.05
3.04
2.23
1.10
(S,S)-1r
A (m) 8.16
B (dd) 7.62
C (d) 7.55
D (s) 7.12
E (d) 6.60
F (d) 4.24
G (s) 3.05
H (s) 2.23
I (s) 1.10
DCM
water
MeOH
1.63
0.99
2.00
0.88
0.96
1.02
6.05
3.09
9.20
f1 (ppm)

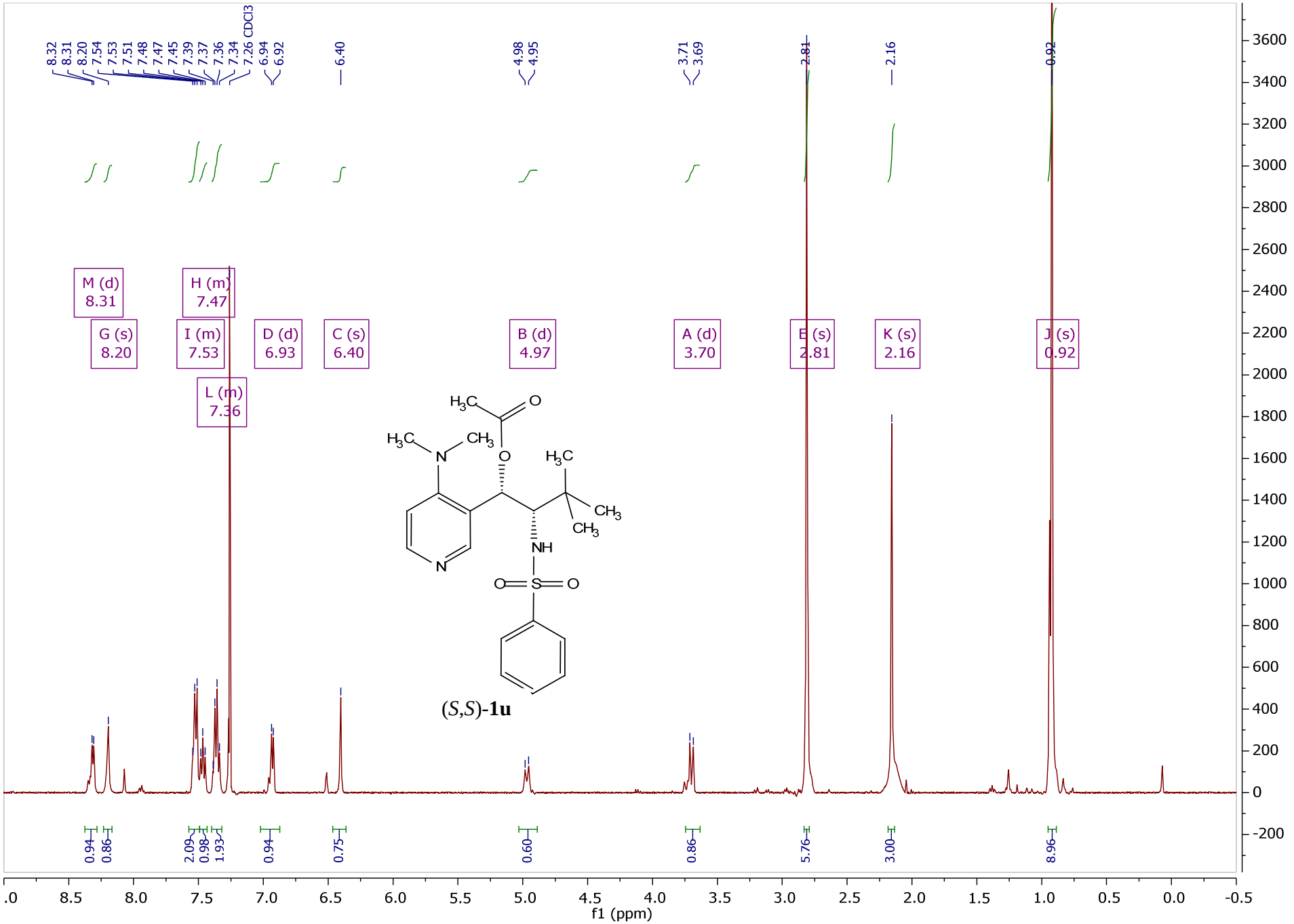

171.69
168.16
160.79
138.92
136.33
132.13
127.12
111.44
70.91
60.23
54.80
49.85
49.00 CD3OD
43.81
36.12
27.91
20.98
(S,S)-1r
f1 (ppm)


8.24
8.24
8.23
8.22
8.10
7.90
7.90
7.11
6.58
6.58
4.25
4.24
3.31 CD3OD
3.01
2.23
1.09
MeOH
(S,S)-1s
D (d) 7.90
B (dd) 8.24
A (m) 8.22
C (m) 8.10
E (m) 7.11
F (d) 6.58
G (d) 4.25
H (s) 3.01
I (s) 2.23
J (s) 1.09
1.70
0.75
1.96
0.94
0.96
1.00
5.94
3.00
9.27
f1 (ppm)

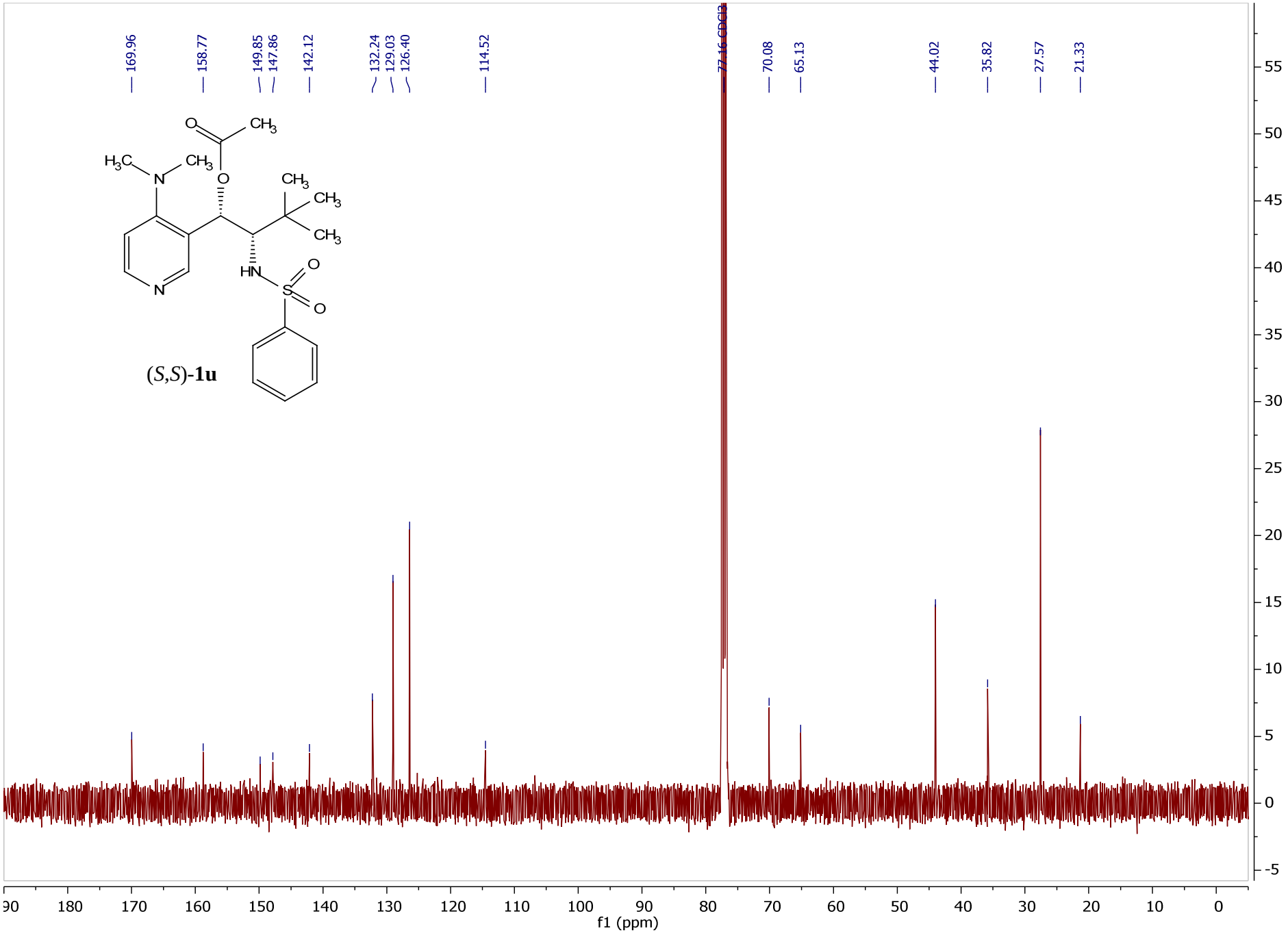

171.70
167.84
160.72
149.02
147.95
145.99
139.18
136.72
95.27
70.96
60.20
49.85
49.00 CD3OD
43.83
36.10
27.91
20.99
(S,S)-1s
49.85
49.00 CD3OD
f1 (ppm)
f1 (ppm)

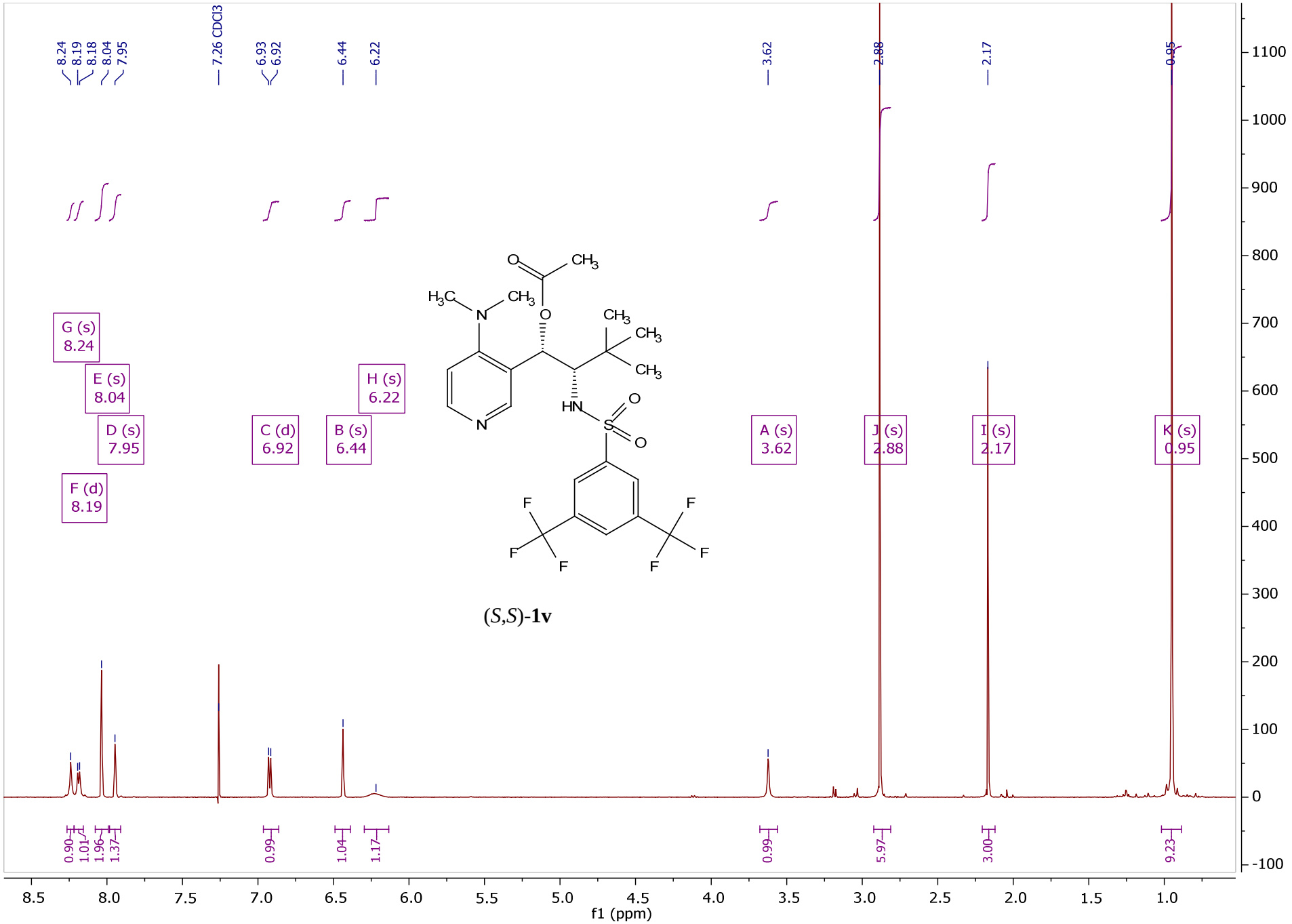

8.37
8.35
8.15
7.69
7.65
7.55
7.55
7.54
7.53
7.52
7.52
7.46
7.45
7.45
7.44
7.43
7.42
7.41
7.41
7.40
7.38
7.37
7.35
7.35
7.34
7.26 CDCl3
6.91
6.90
6.65
6.64
5.28
5.27
5.24
5.24
2.89
2.19
1.13
A (d) 8.36
B (s) 8.15
D (m) 7.54
L (d) 7.67
E (m) 7.40
F (d) 6.90
G (d) 6.65
H (dd) 5.26
I (s) 2.89
K (s) 2.19
C (s) 1.13
(S,S)-1t
0.94
0.94
0.97
1.94
3.03
1.01
1.24
1.03
5.83
3.00
8.98
f1 (ppm)


201.85
169.73
158.88
150.36
147.19
143.19
130.78
128.77
126.39
114.74
77.16 CDCl3
70.39
63.43
43.93
36.21
27.46
21.37
(S,S)-1t
f1 (ppm)

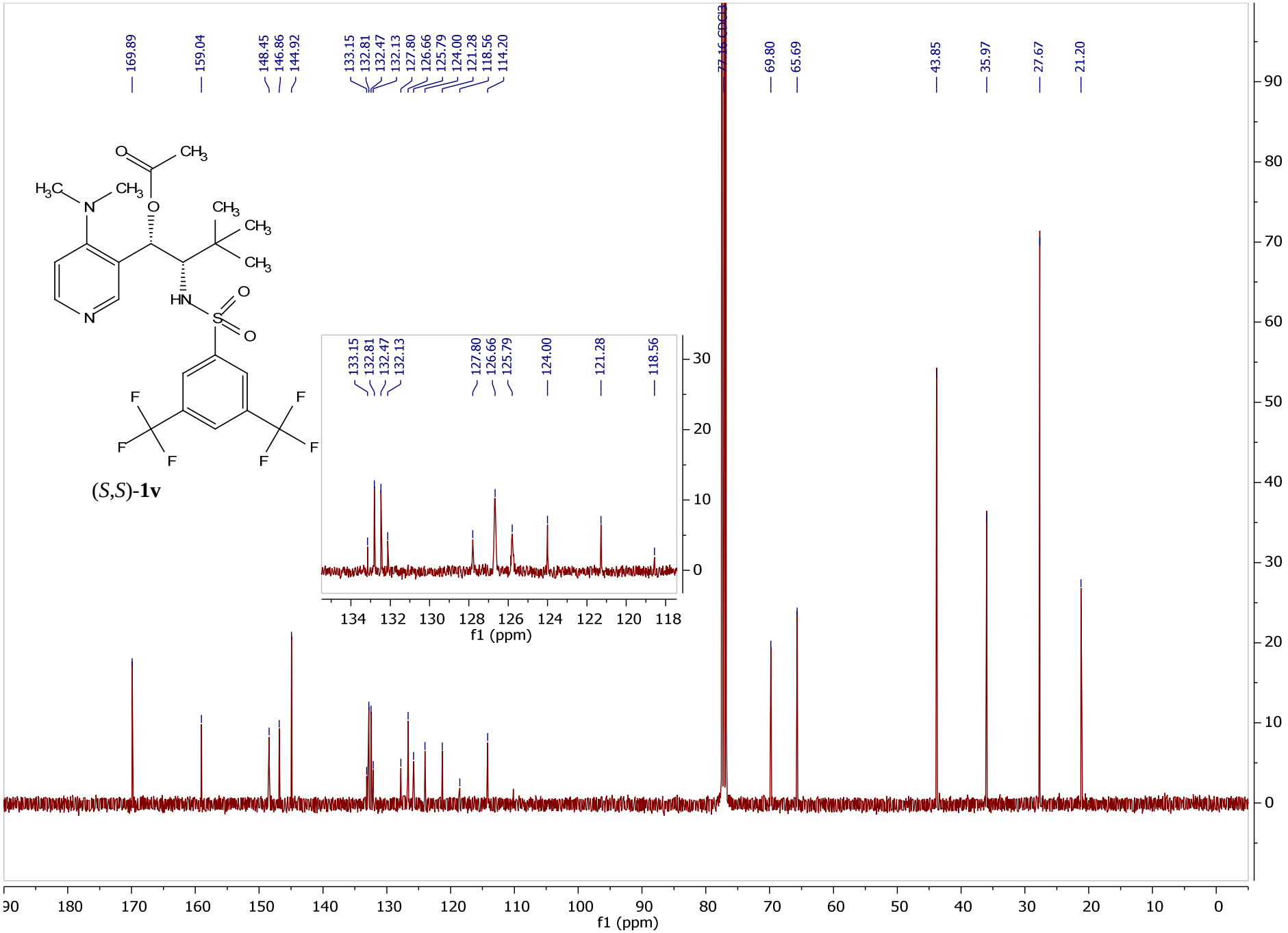

8.32
8.31
8.20
7.54
7.53
7.51
7.48
7.47
7.45
7.39
7.37
7.36
7.34
7.26 CDCl3
6.94
6.92
6.40
4.98
4.95
3.71
3.69
2.81
2.16
0.92
M (d) 8.31
H (m) 7.47
G (s) 8.20
I (m) 7.53
D (d) 6.93
C (s) 6.40
B (d) 4.97
A (d) 3.70
E (s) 2.81
K (s) 2.16
J (s) 0.92
L (m) 7.36
0.94
0.86
2.09
0.98
1.93
0.94
0.75
0.60
0.86
5.76
3.00
8.96
f1 (ppm)

(*S*,*S*)-**1u**

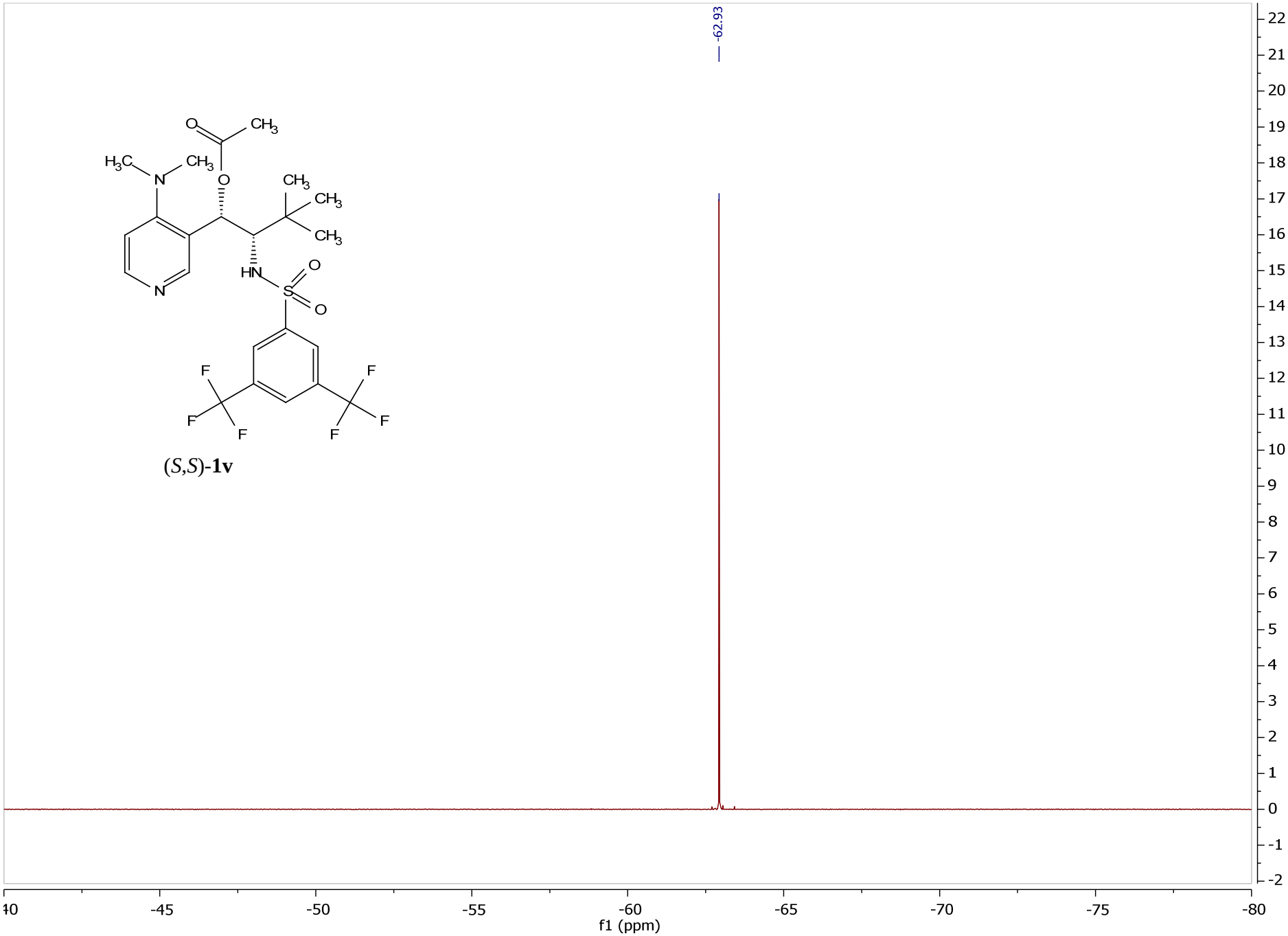

169.96
158.77
149.85
147.86
142.12
132.24
129.03
126.40
114.52
77.16 CDCl3
70.08
65.13
44.02
35.82
27.57
21.33
(S,S)-1u
f1 (ppm)


8.24
8.19
8.18
8.04
7.95
7.26 CDCl3
6.93
6.92
6.44
6.22
3.62
2.88
2.17
0.95
G (s) 8.24
E (s) 8.04
D (s) 7.95
F (d) 8.19
C (d) 6.92
B (s) 6.44
H (s) 6.22
A (s) 3.62
J (s) 2.88
I (s) 2.17
K (s) 0.95
0.90
1.01
1.96
1.37
0.99
1.04
1.17
0.99
5.97
3.00
9.23
f1 (ppm)

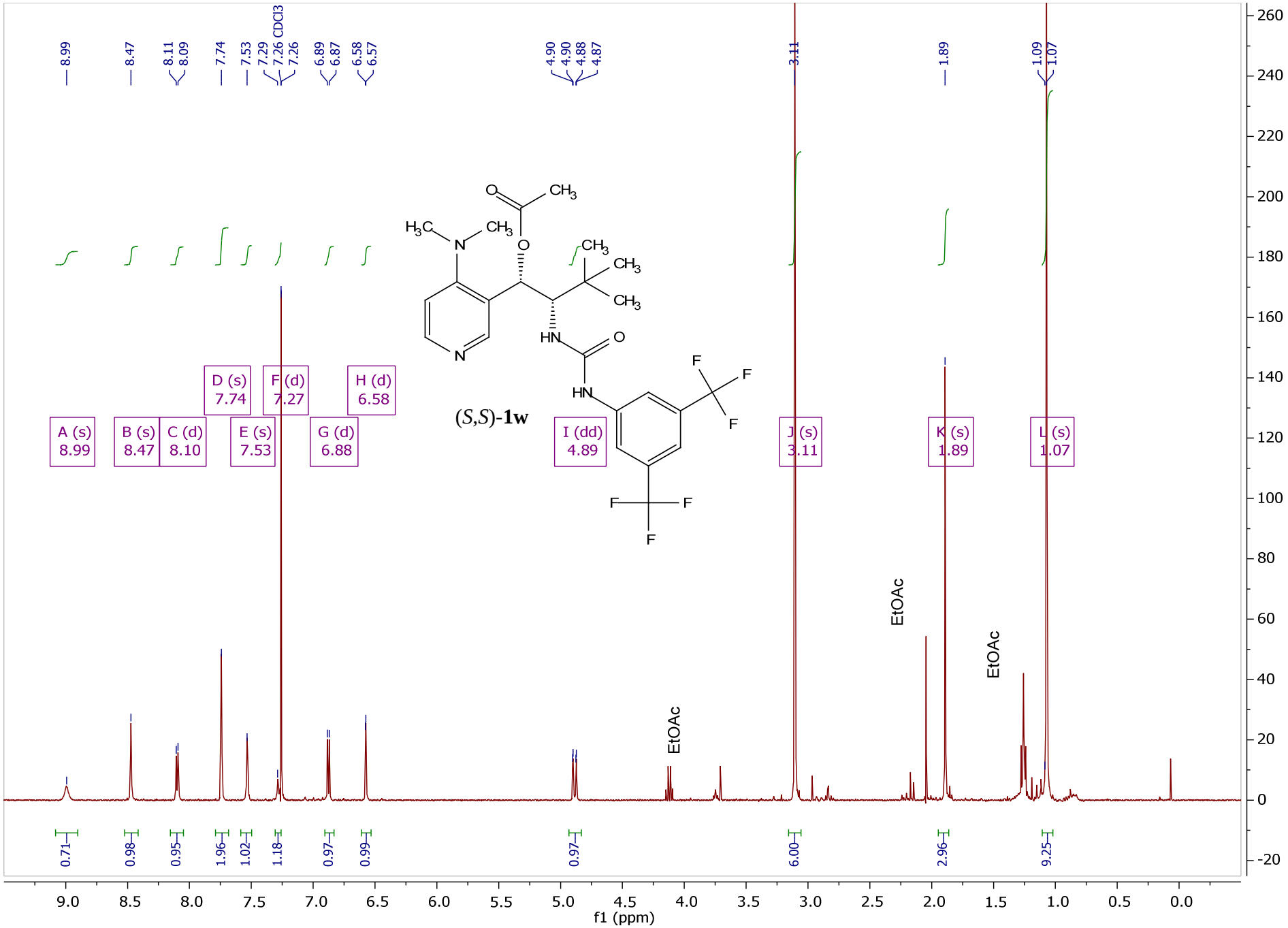
(*S*,*S*)-**1v**

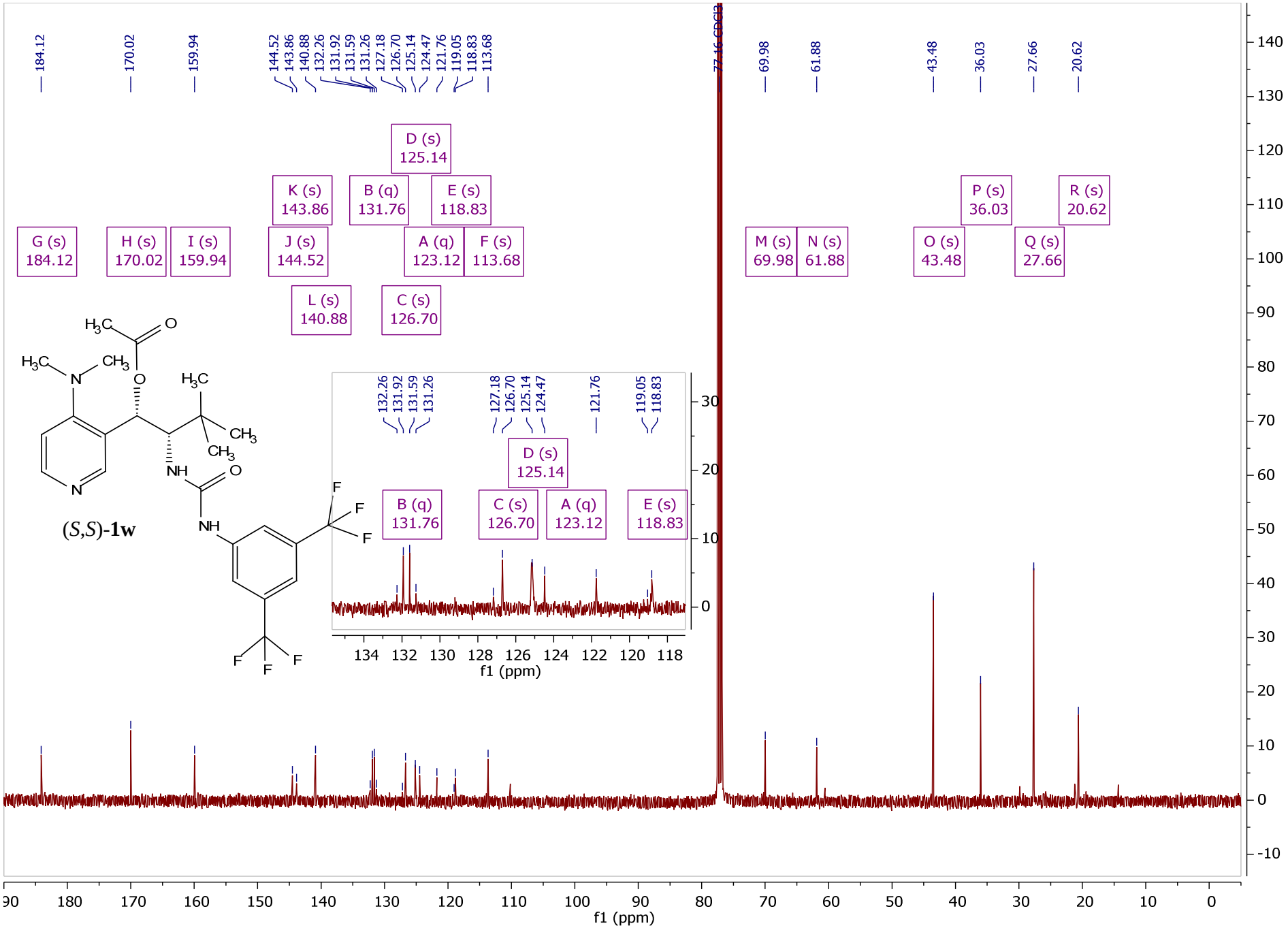

169.89
159.04
148.45
146.86
144.92
133.15
132.81
132.47
132.13
127.80
126.66
125.79
124.00
121.28
118.56
114.20
77.16
69.80
65.69
43.85
35.97
27.67
21.20
f1 (ppm)

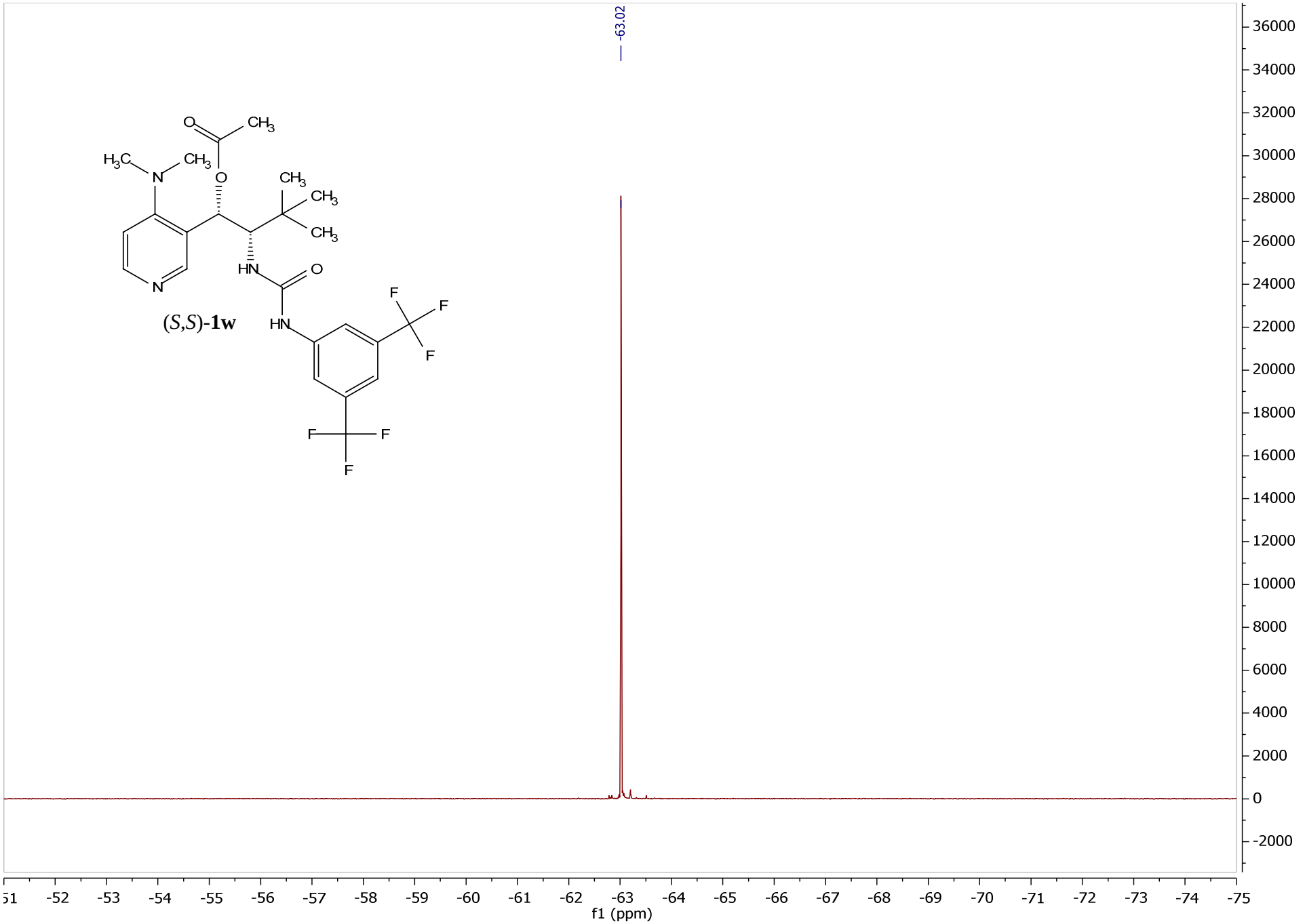
(*S*,*S*)-**1v**

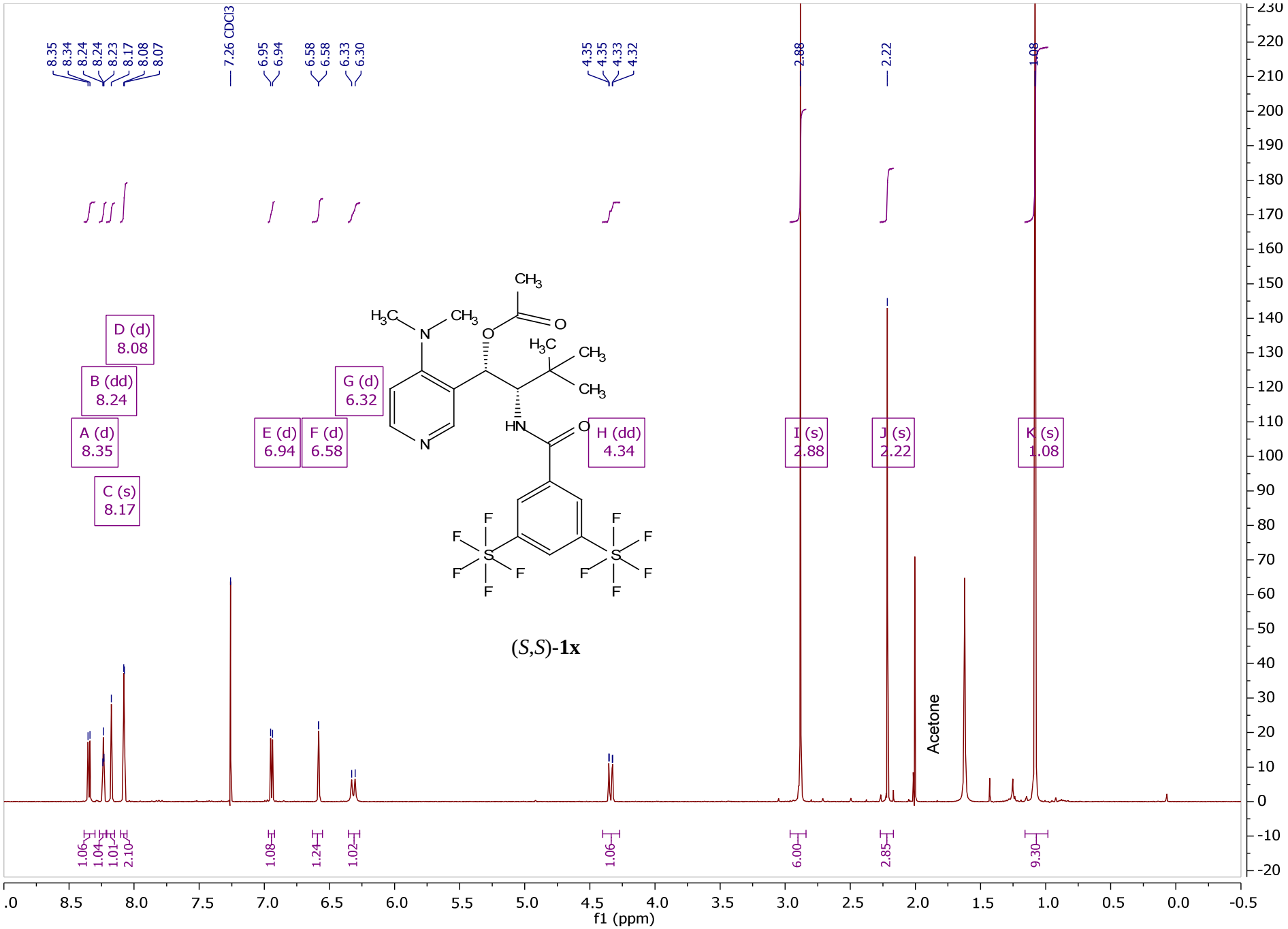


(*S*,*S*)-**1v**

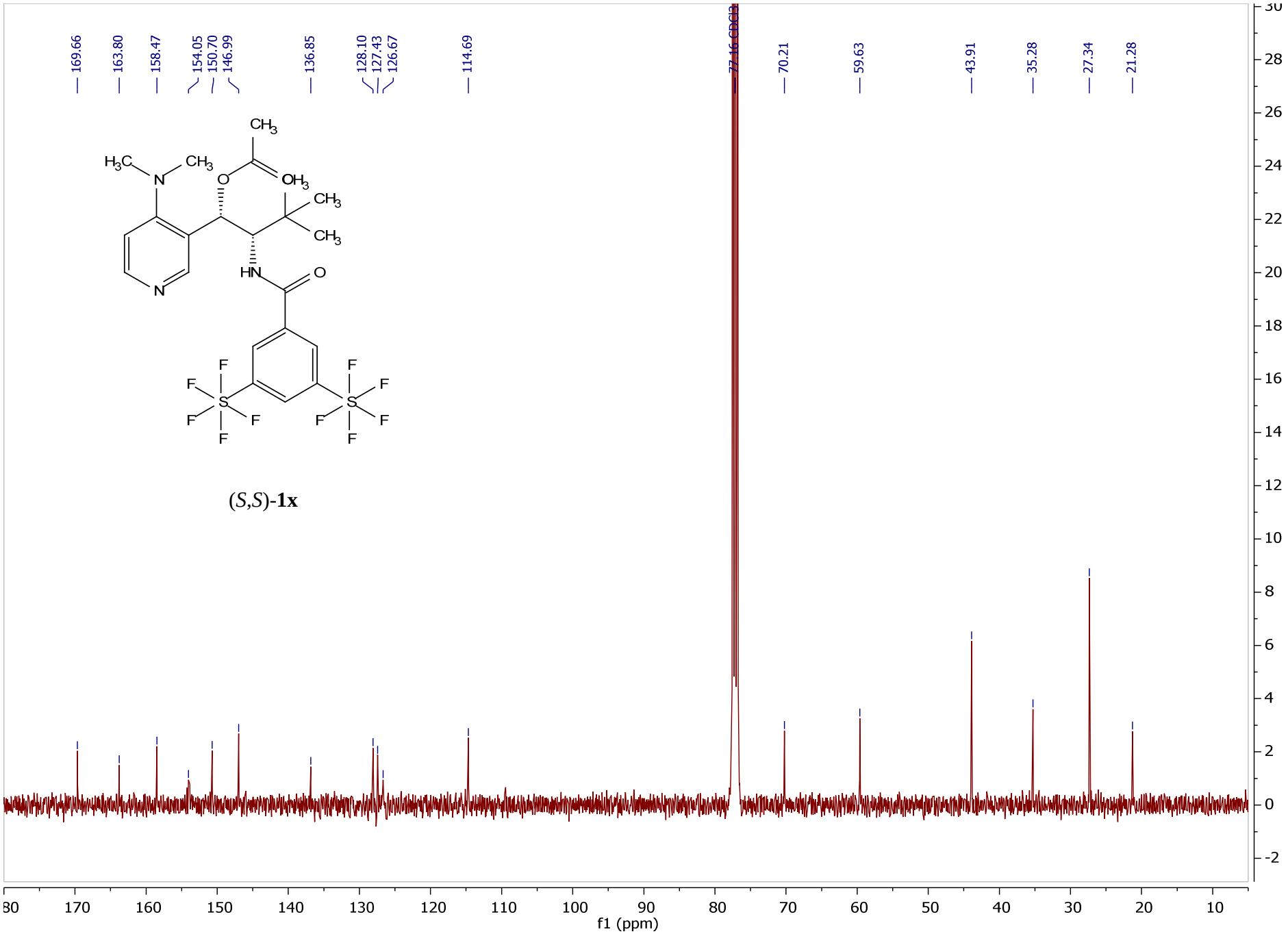

8.99
8.47
8.11
8.09
7.74
7.53
7.29
7.26 CDCl3
7.26
6.89
6.87
6.58
6.57
4.90
4.90
4.88
4.87
3.11
1.89
1.09
1.07
A (s) 8.99
B (s) 8.47
C (d) 8.10
D (s) 7.74
E (s) 7.53
F (d) 7.27
G (d) 6.88
H (d) 6.58
I (dd) 4.89
J (s) 3.11
K (s) 1.89
L (s) 1.07
EtOAc
EtOAc
EtOAc
(S,S)-1w
0.71
0.98
0.95
1.96
1.02
1.18
0.97
0.99
0.97
6.00
2.96
9.25
f1 (ppm)


184.12
170.02
159.94
144.52
143.86
140.88
132.26
131.92
131.59
131.26
127.18
126.70
125.14
124.47
121.76
119.05
118.83
113.68
77.16
69.98
61.88
43.48
36.03
27.66
20.62
D (s) 125.14
K (s) 143.86
B (q) 131.76
E (s) 118.83
P (s) 36.03
R (s) 20.62
G (s) 184.12
H (s) 170.02
I (s) 159.94
J (s) 144.52
A (q) 123.12
F (s) 113.68
M (s) 69.98
N (s) 61.88
O (s) 43.48
Q (s) 27.66
L (s) 140.88
C (s) 126.70
(S,S)-1w
f1 (ppm)

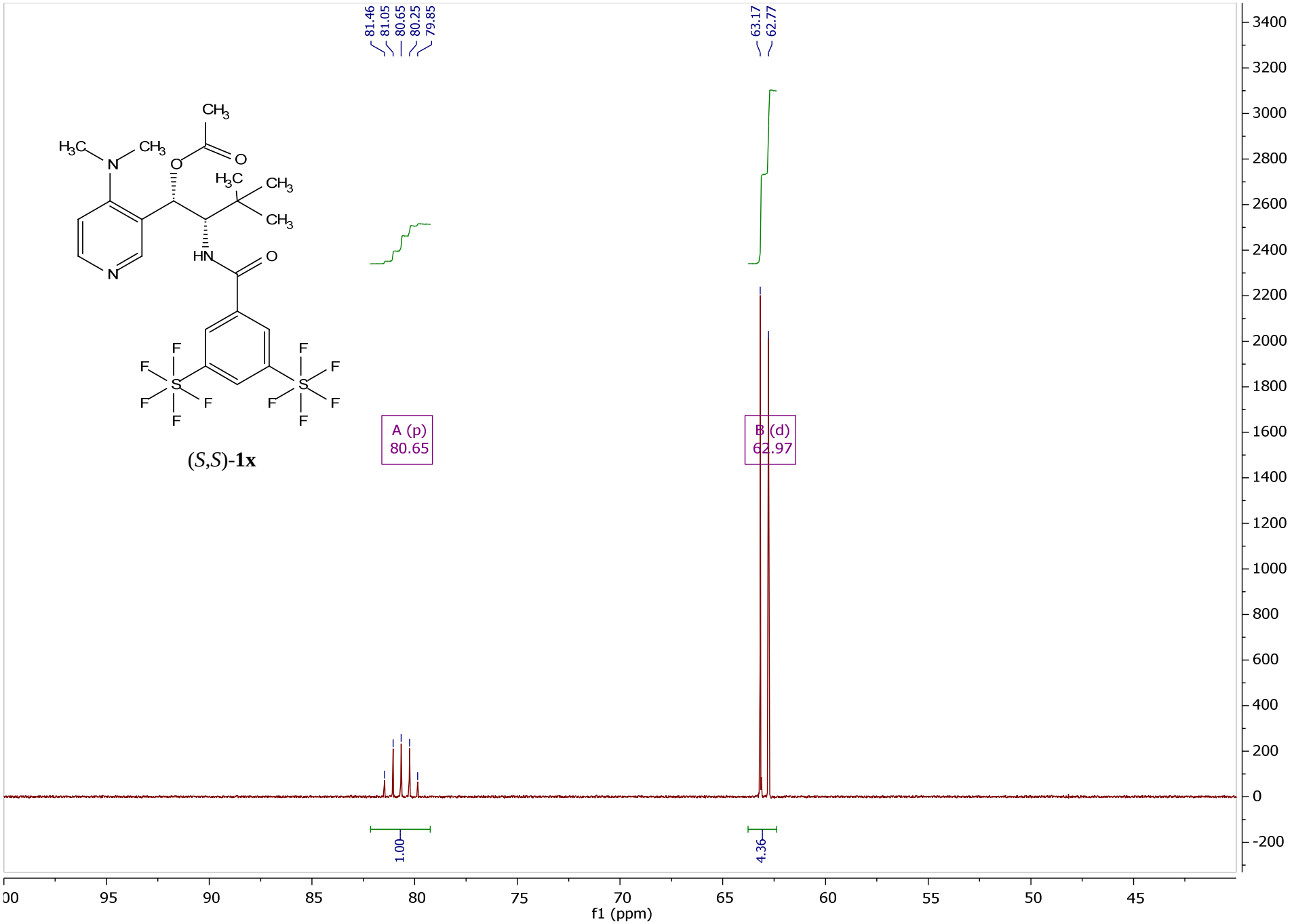

-63.02
(S,S)-1w
f1 (ppm)


8.35
8.34
8.24
8.24
8.23
8.17
8.08
8.07
7.26 CDCl3
6.95
6.94
6.58
6.58
6.33
6.30
4.35
4.35
4.33
4.32
2.88
2.22
1.08
D (d) 8.08
B (dd) 8.24
A (d) 8.35
C (s) 8.17
G (d) 6.32
E (d) 6.94
F (d) 6.58
H (dd) 4.34
I (s) 2.88
J (s) 2.22
K (s) 1.08
Acetone
1.06
1.04
1.01
2.10
1.08
1.24
1.02
1.06
6.00
2.85
9.30
f1 (ppm)

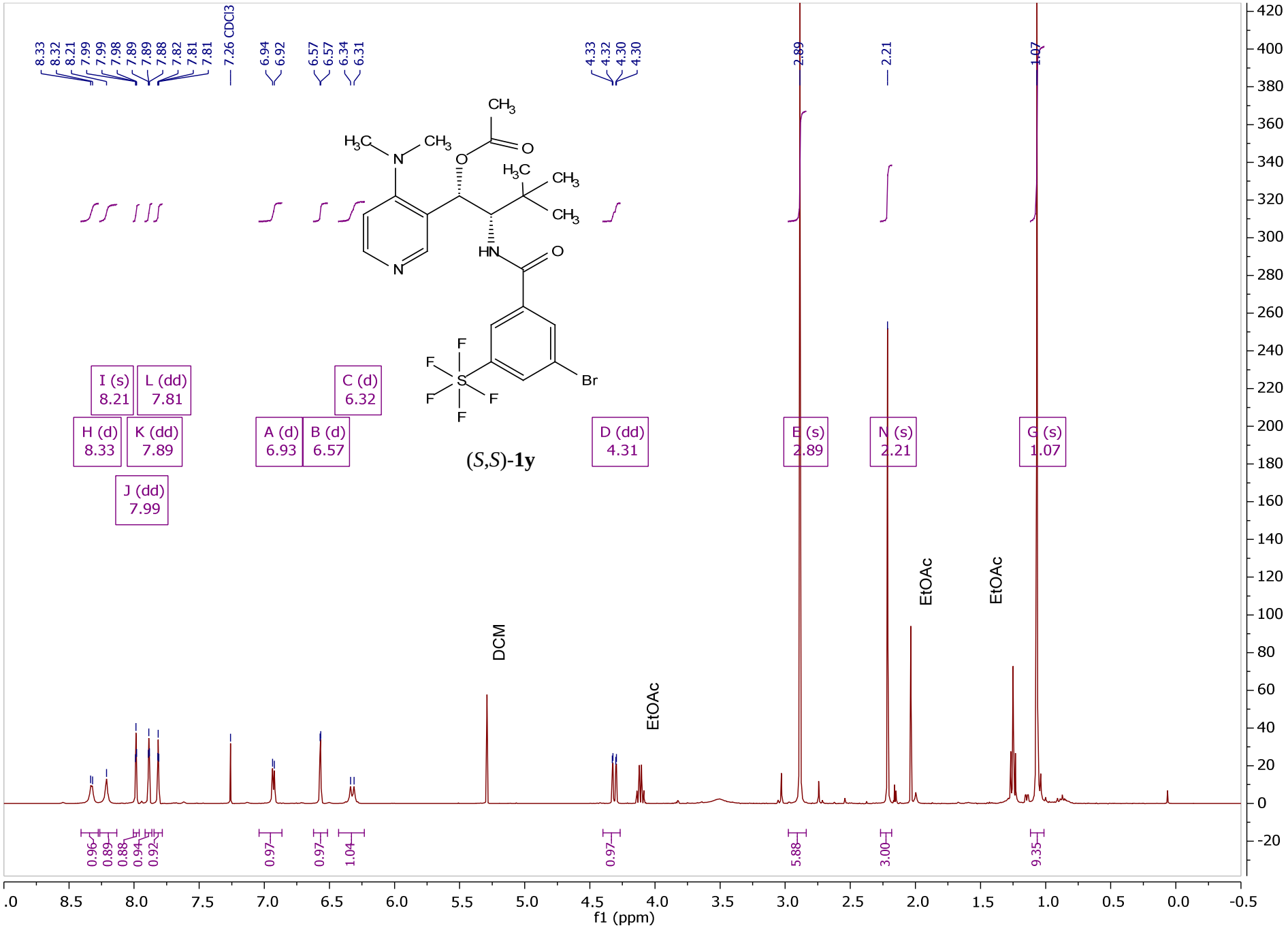
(*S*,*S*)-**1x**

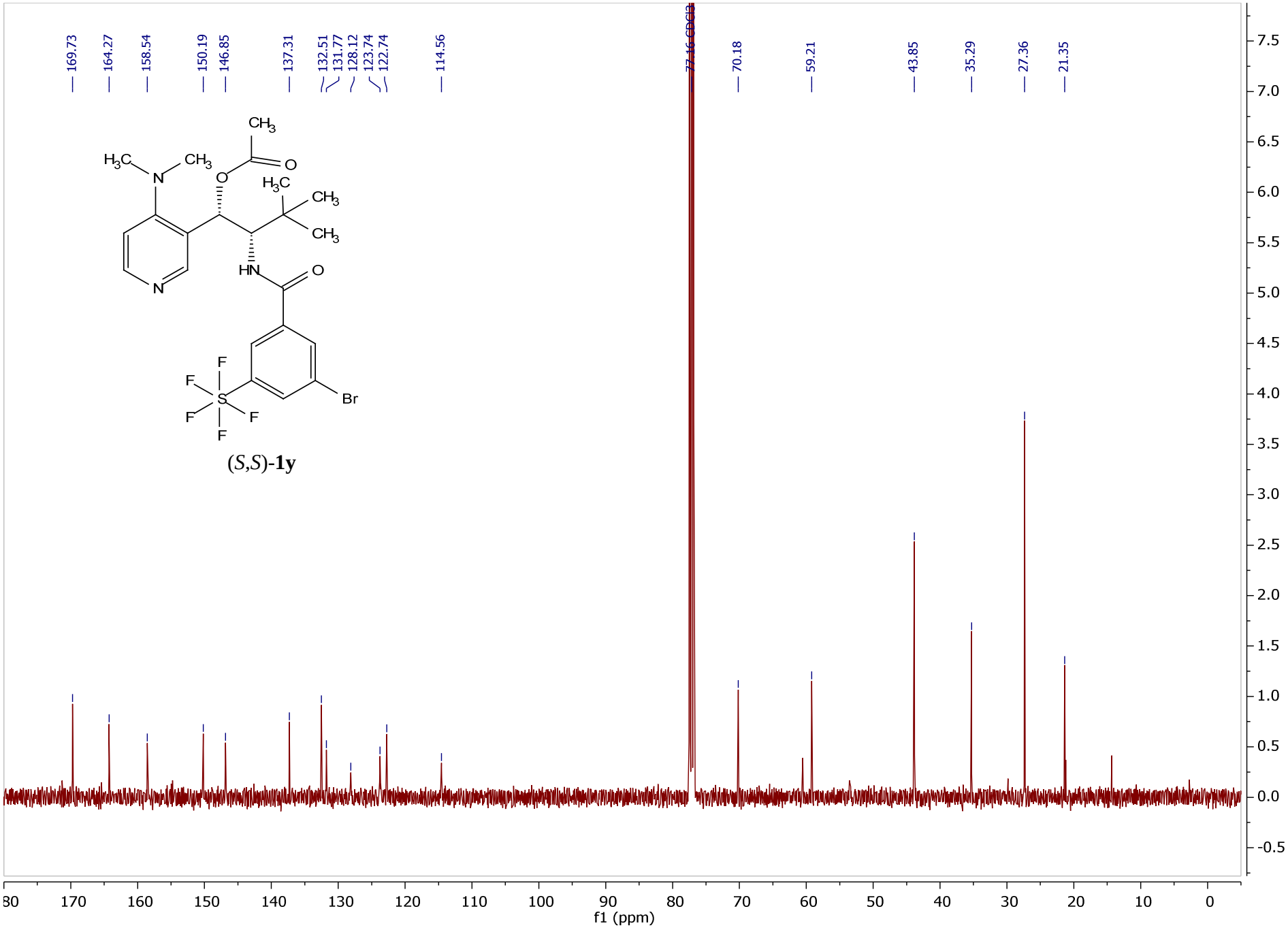

169.66
163.80
158.47
154.05
150.70
146.99
136.85
128.10
127.43
126.67
114.69
77.16 CDCl3
70.21
59.63
43.91
35.28
27.34
21.28
f1 (ppm)

(*S*,*S*)-**1x**

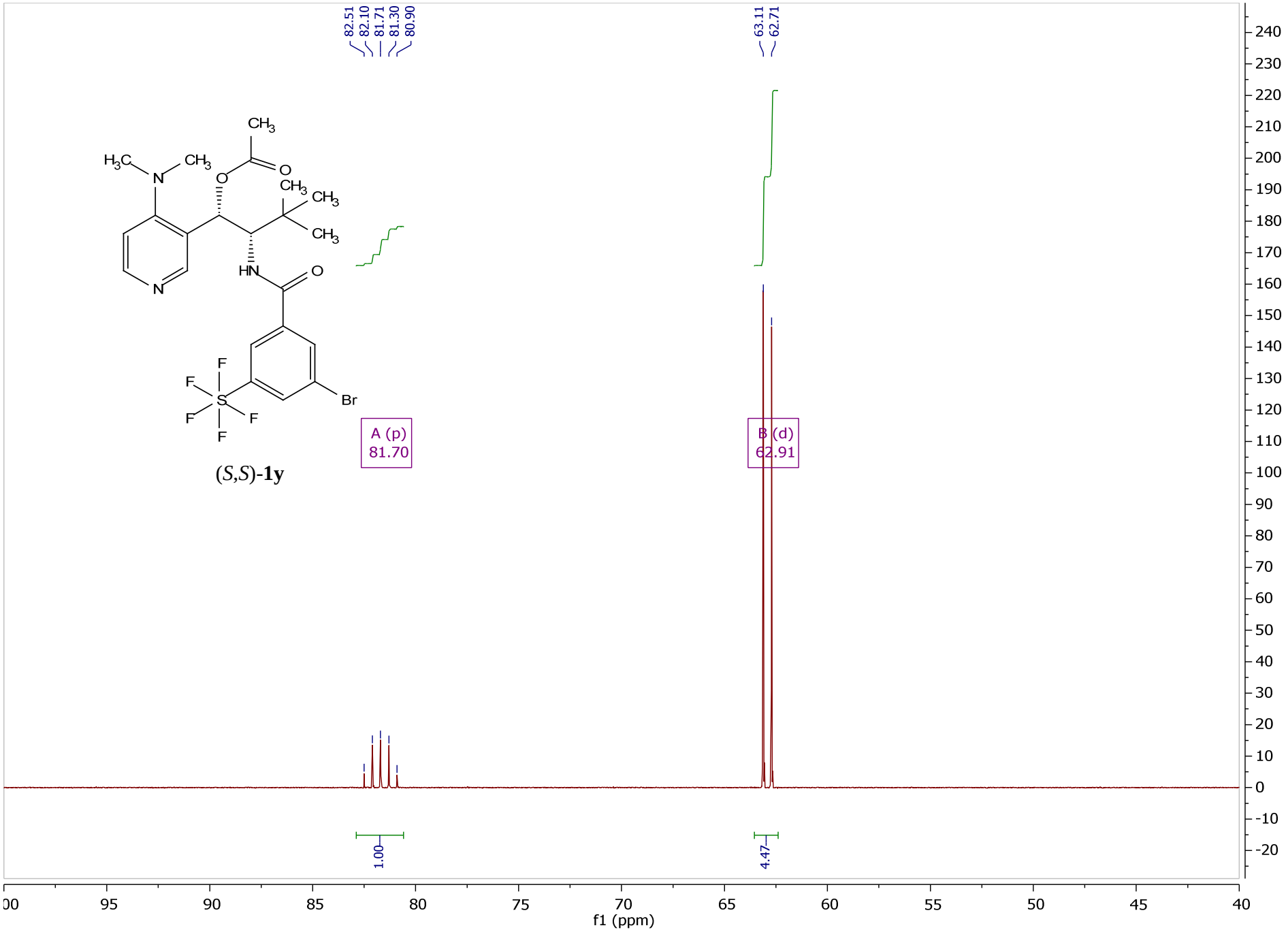

81.46
81.05
80.65
80.25
79.85
63.17
62.77
A (p)
80.65
B (d)
62.97
1.00
4.36
f1 (ppm)

(*S*,*S*)-**1x**

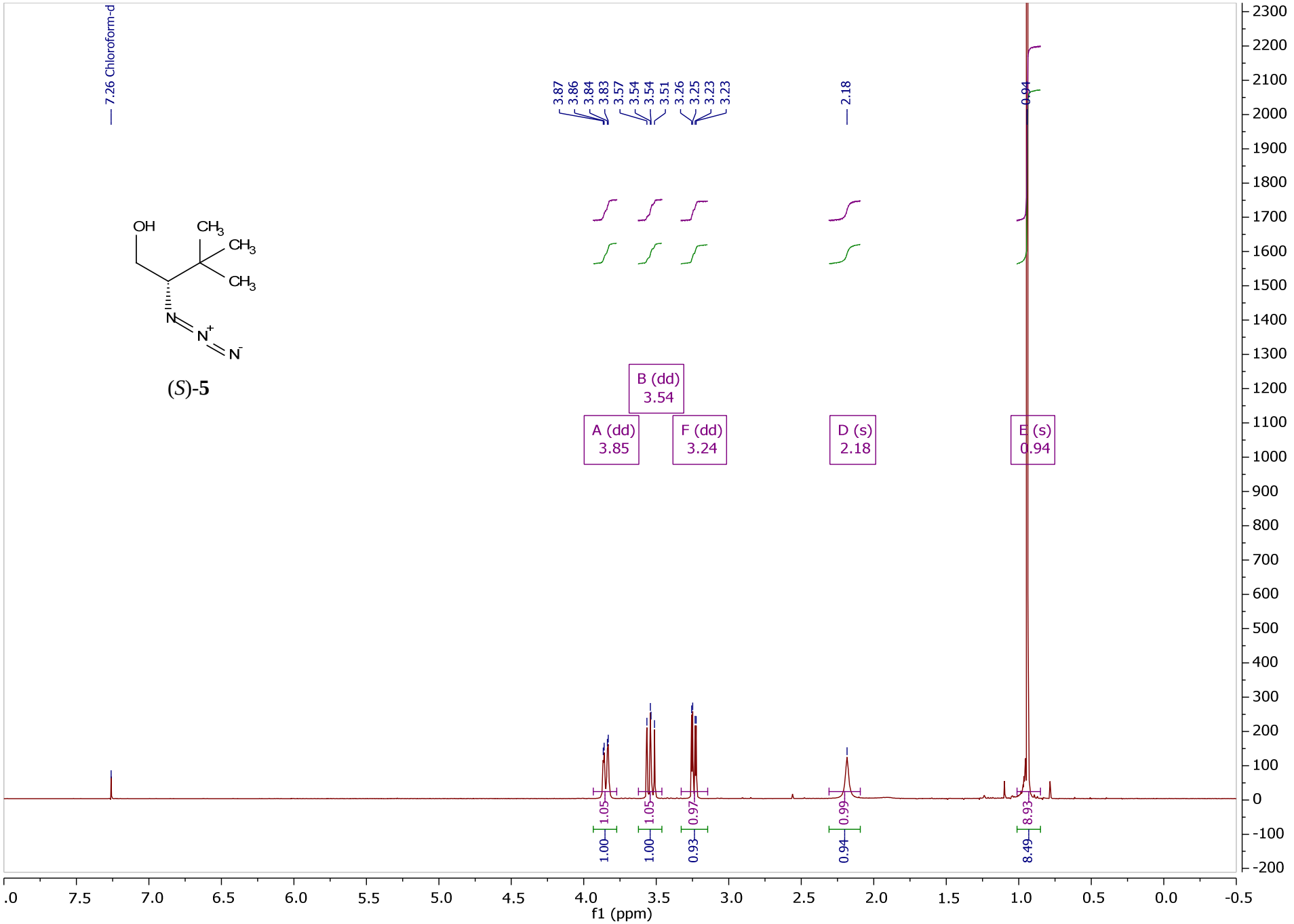

8.33
8.32
8.21
7.99
7.99
7.98
7.89
7.89
7.88
7.82
7.81
7.81
7.26 CDCl3
6.94
6.92
6.57
6.57
6.34
6.31
4.33
4.32
4.30
4.30
2.89
2.21
1.07
I (s) 8.21
L (dd) 7.81
C (d) 6.32
H (d) 8.33
K (dd) 7.89
A (d) 6.93
B (d) 6.57
D (dd) 4.31
E (s) 2.89
N (s) 2.21
G (s) 1.07
J (dd) 7.99
(S,S)-1y
DCM
EtOAc
EtOAc
EtOAc
0.96
0.89
0.88
0.94
0.92
0.97
0.97
1.04
0.97
5.88
3.00
9.35
f1 (ppm)

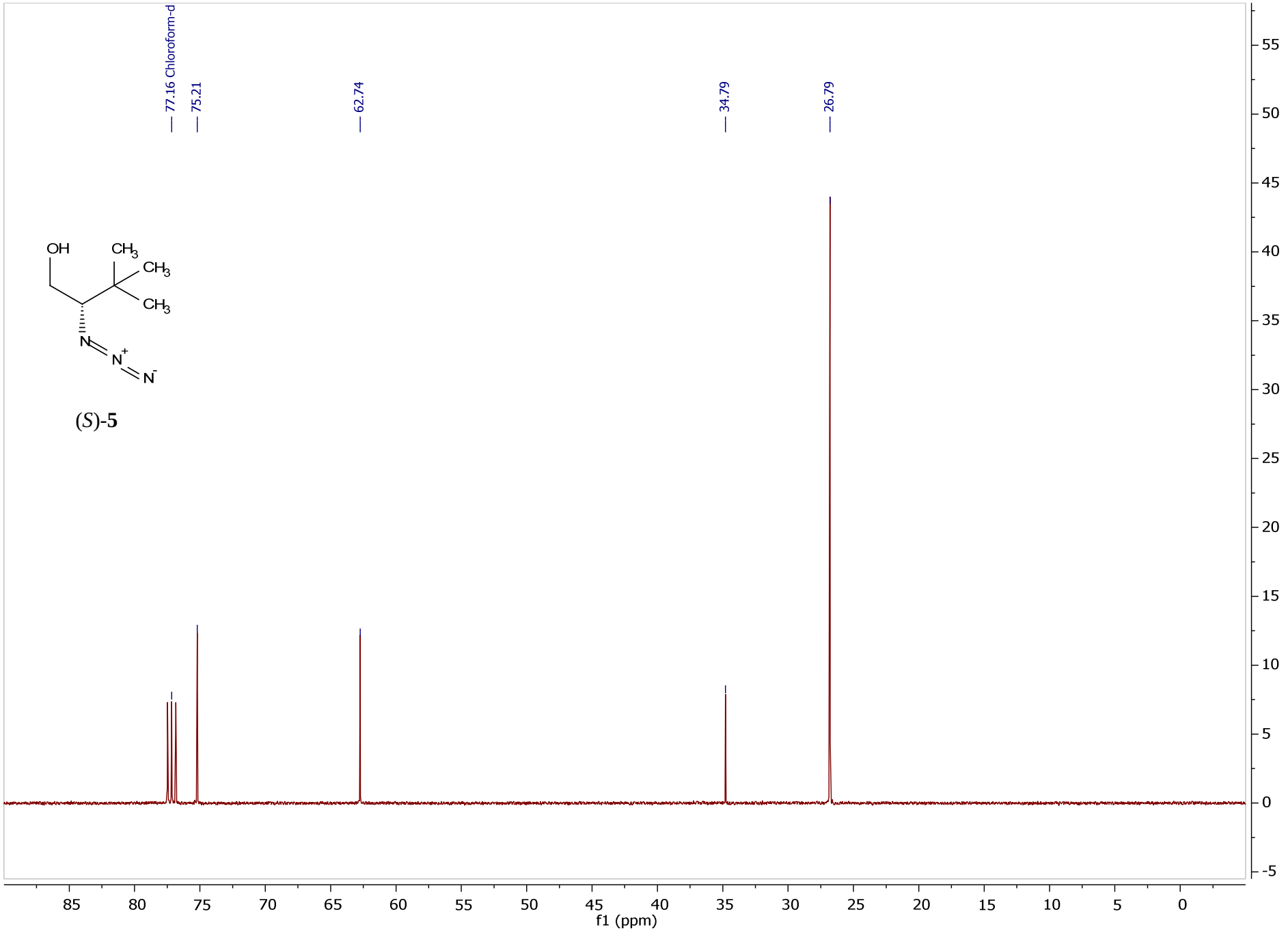

169.73
164.27
158.54
150.19
146.85
137.31
132.51
131.77
128.12
123.74
122.74
114.56
77.16 CDCl3
70.18
59.21
43.85
35.29
27.36
21.35
CH3
H3C
N
CH3
O
O
H3C
CH3
CH3
HN
O
N
F
F
S
F
F
F
Br
f1 (ppm)

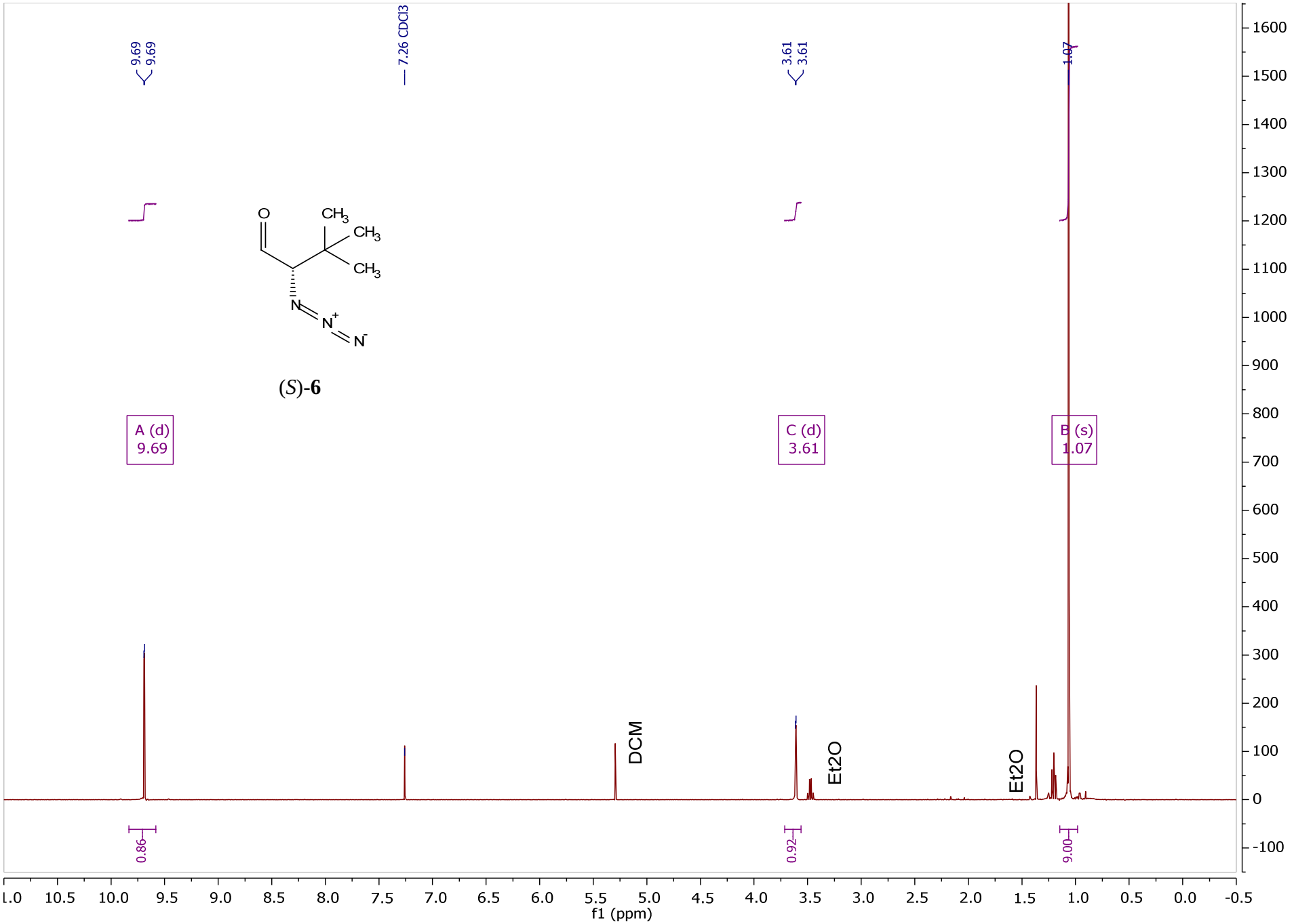
(*S*,*S*)-**1y**

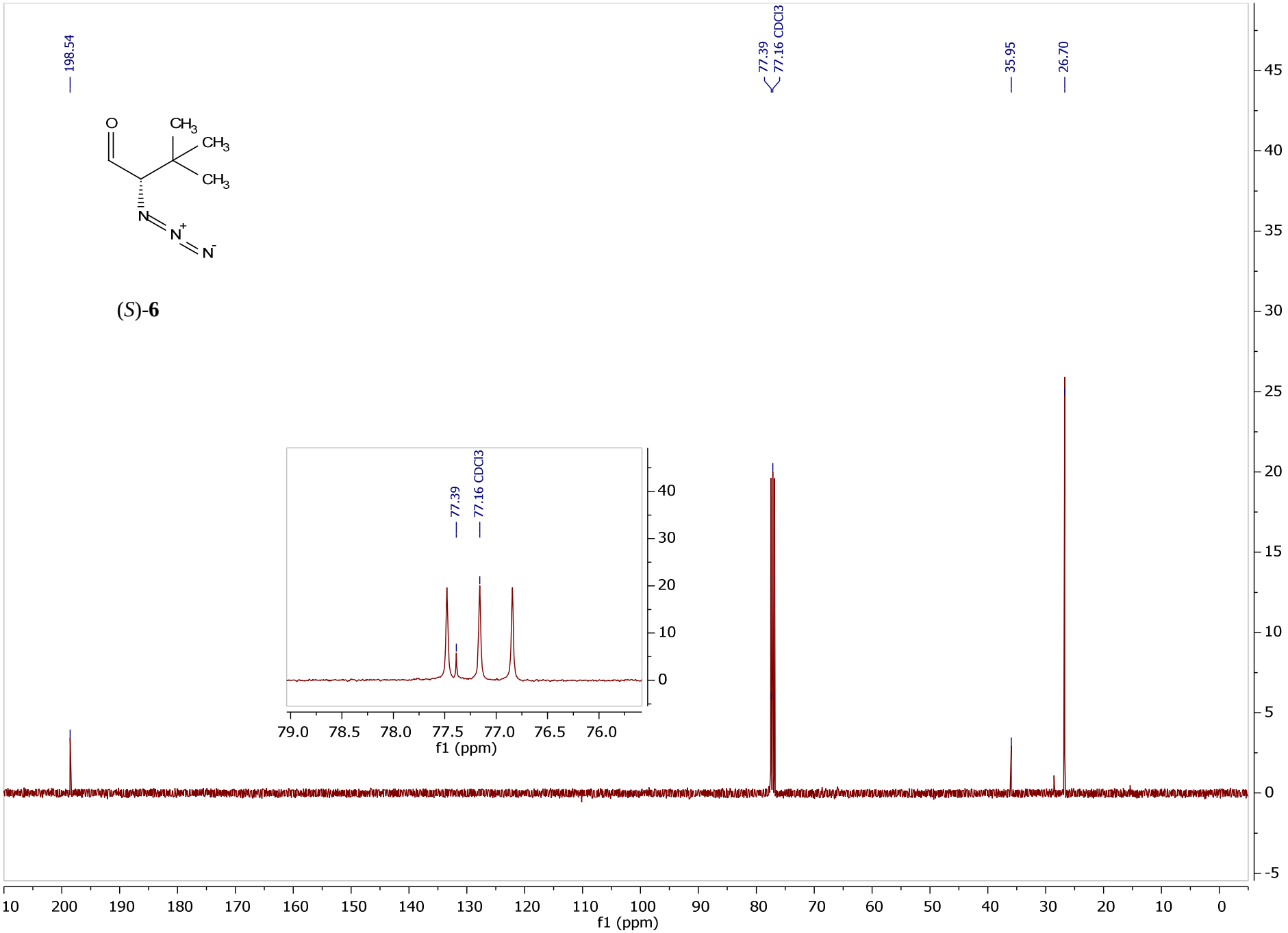

82.51
82.10
81.71
81.30
80.90
63.11
62.71
A (p)
81.70
B (d)
62.91
1.00
4.47
f1 (ppm)

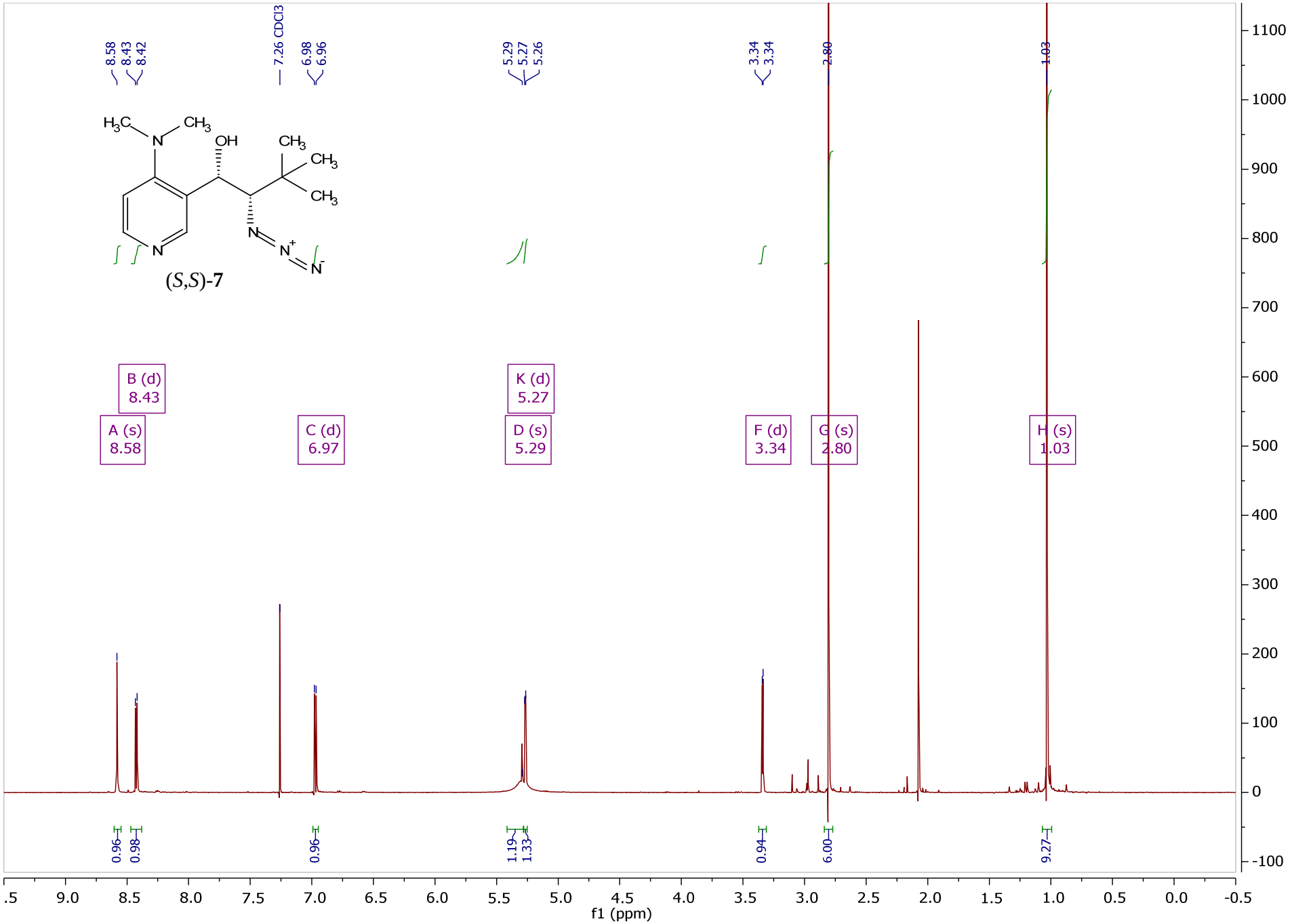
(*S*,*S*)-**1y**

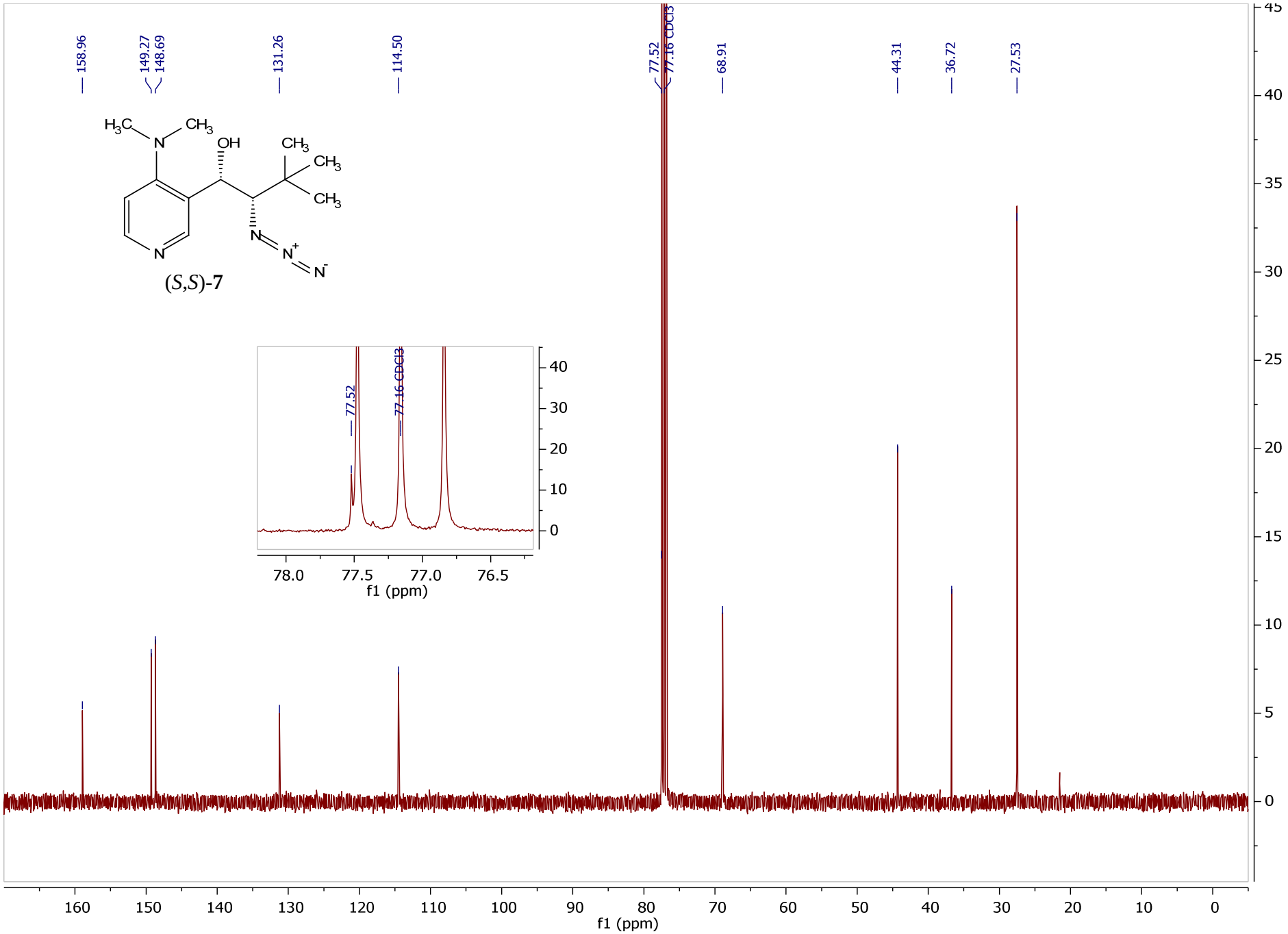

7.26 Chloroform-d
3.87
3.86
3.84
3.83
3.57
3.54
3.54
3.51
3.26
3.25
3.23
3.23
2.18
0.94
OH
CH3
CH3
CH3
N
N+
N-
(S)-5
B (dd)
3.54
A (dd)
3.85
F (dd)
3.24
D (s)
2.18
E (s)
0.94
1.05
1.05
0.97
0.99
8.93
1.00
1.00
0.93
0.94
8.49
f1 (ppm)

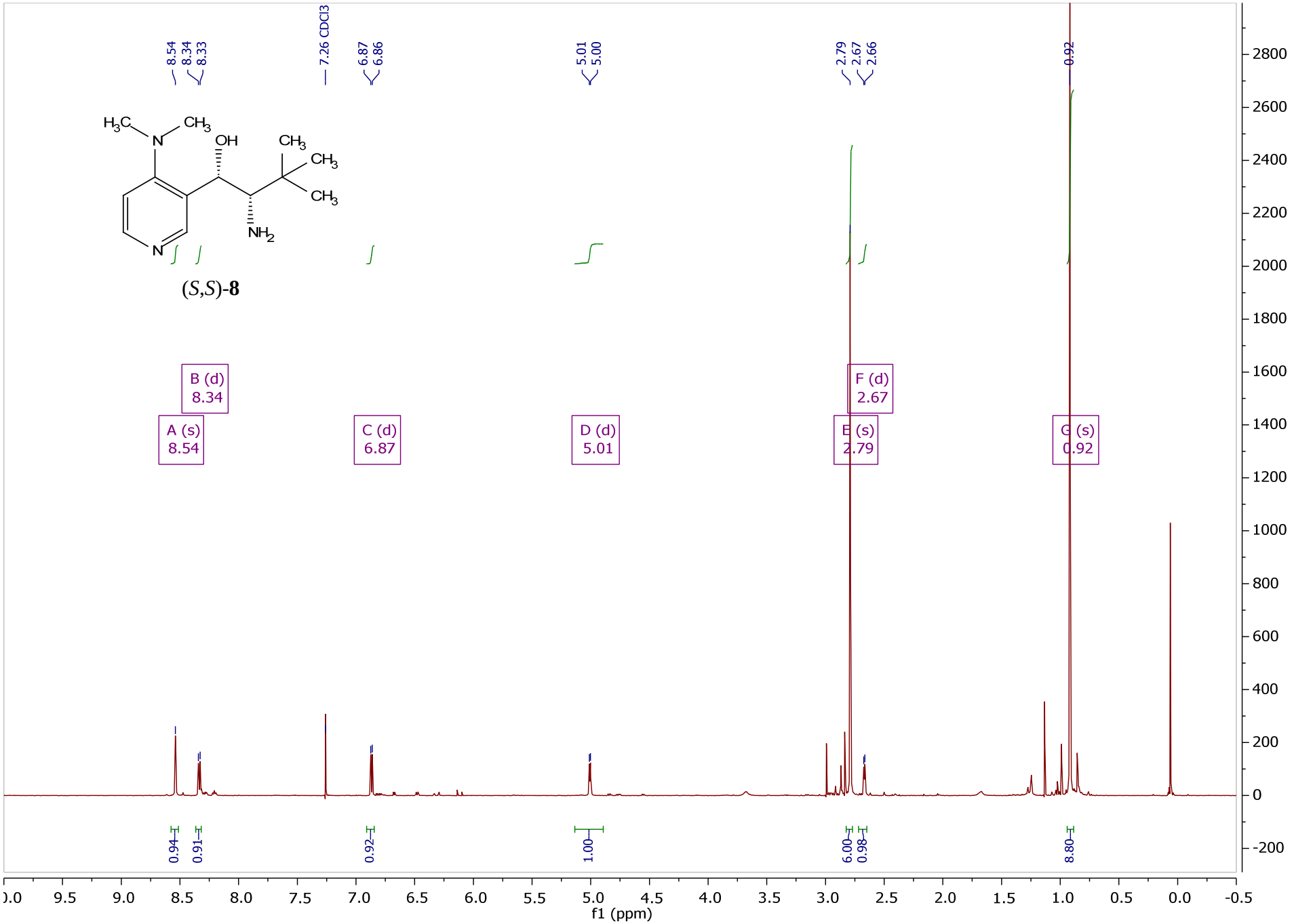

77.16 Chloroform-d
75.21
62.74
34.79
26.79
OH
CH3
CH3
CH3
N
N+
N-
(S)-5
f1 (ppm)


9.69
9.69
7.26 CDCl3
3.61
3.61
1.07
O
CH3
CH3
CH3
N
N+
N-
(S)-6
A (d)
9.69
C (d)
3.61
B (s)
1.07
DCM
Et2O
Et2O
0.86
0.92
9.00
f1 (ppm)

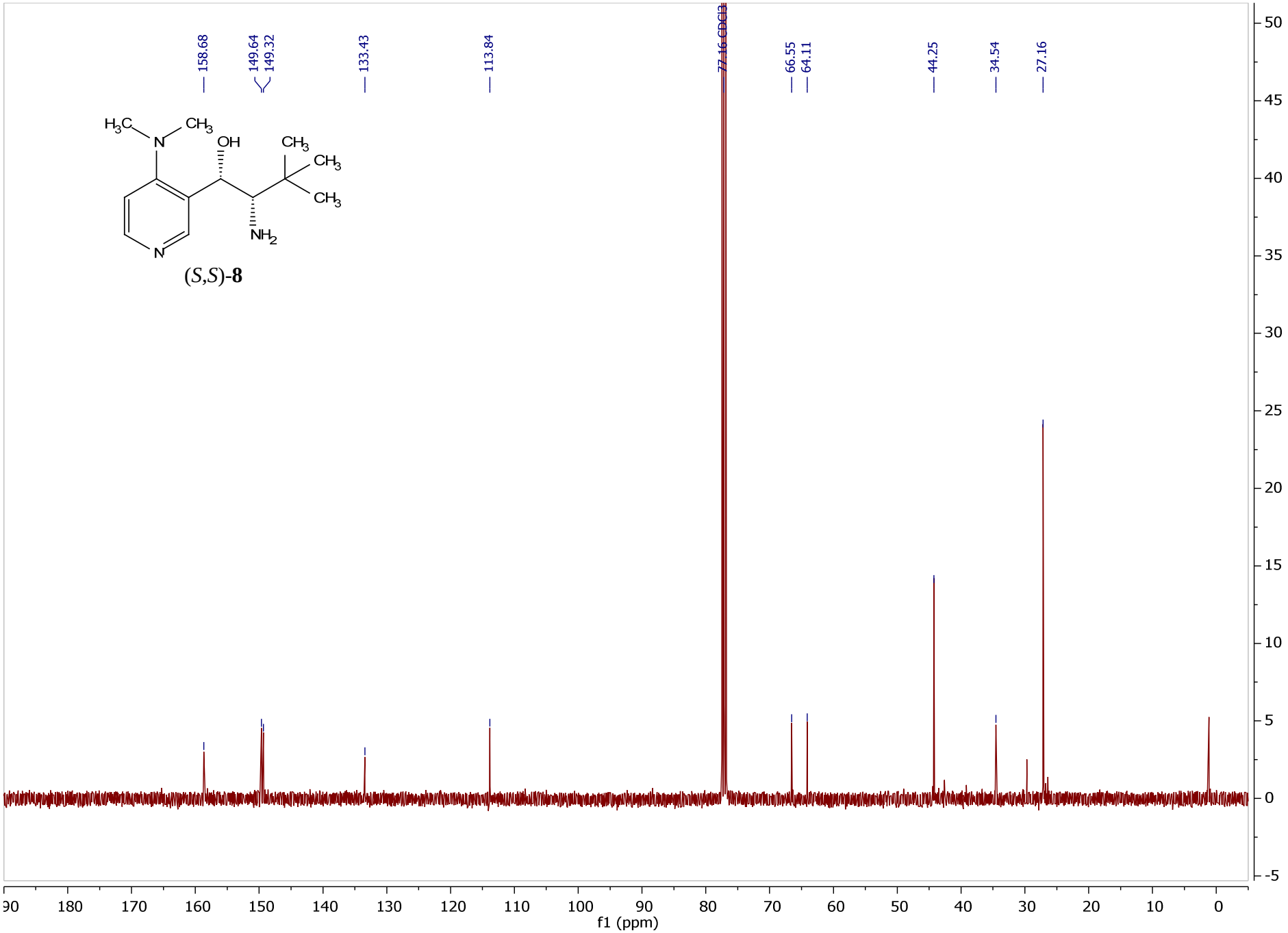

198.54
77.39
77.16 CDCl3
35.95
26.70
O
CH3
CH3
CH3
N
N+
N-
(S)-6
77.39
77.16 CDCl3
f1 (ppm)
f1 (ppm)


8.58
8.43
8.42
7.26 CDCl3
6.98
6.96
5.29
5.27
5.26
3.34
3.34
2.80
1.03
(S,S)-7
B (d) 8.43
A (s) 8.58
C (d) 6.97
K (d) 5.27
D (s) 5.29
F (d) 3.34
G (s) 2.80
H (s) 1.03
0.96
0.98
0.96
1.19
1.33
0.94
6.00
9.27
f1 (ppm)

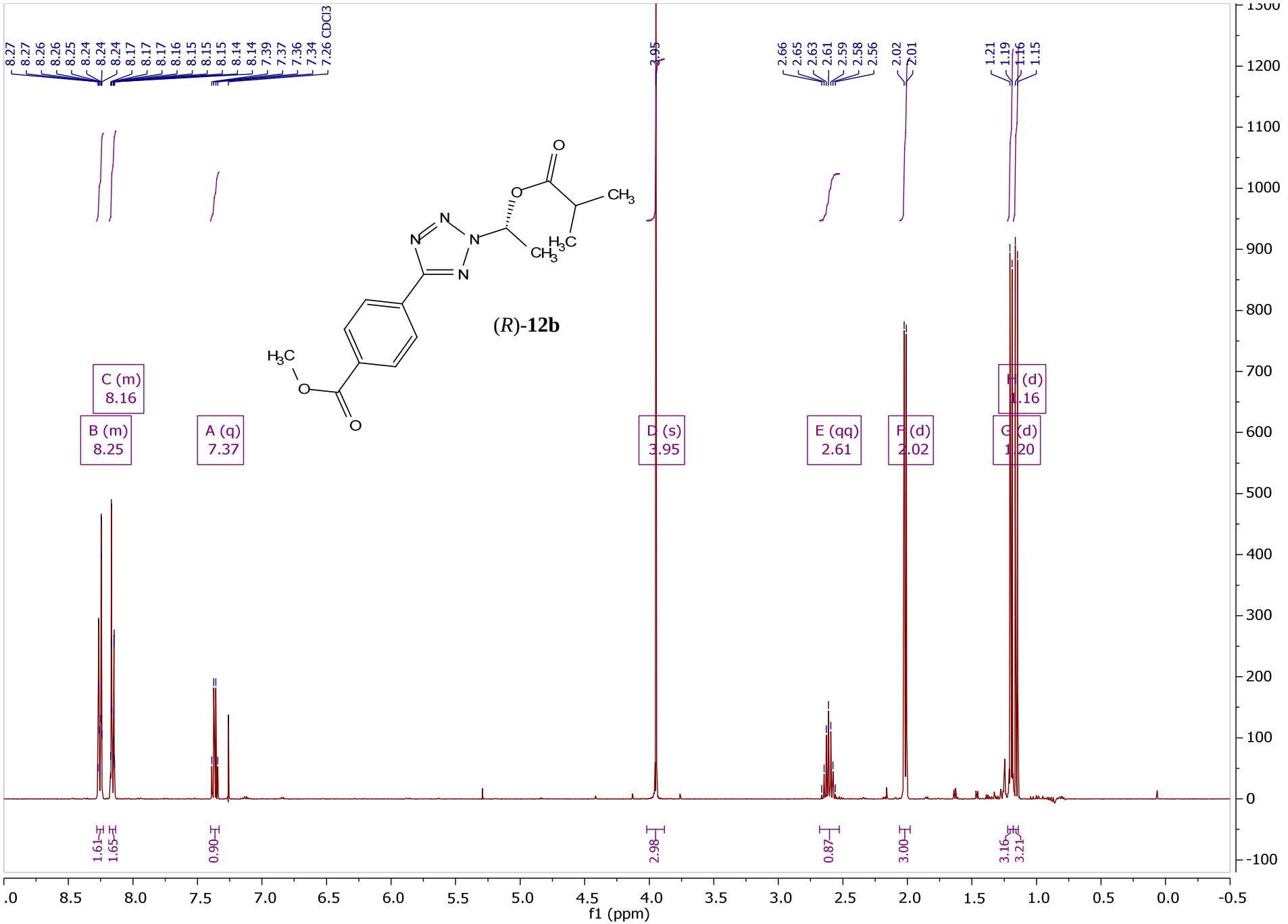

158.96
149.27
148.69
131.26
114.50
77.52
77.16 CDCl3
68.91
44.31
36.72
27.53
(S,S)-7
f1 (ppm)
f1 (ppm)

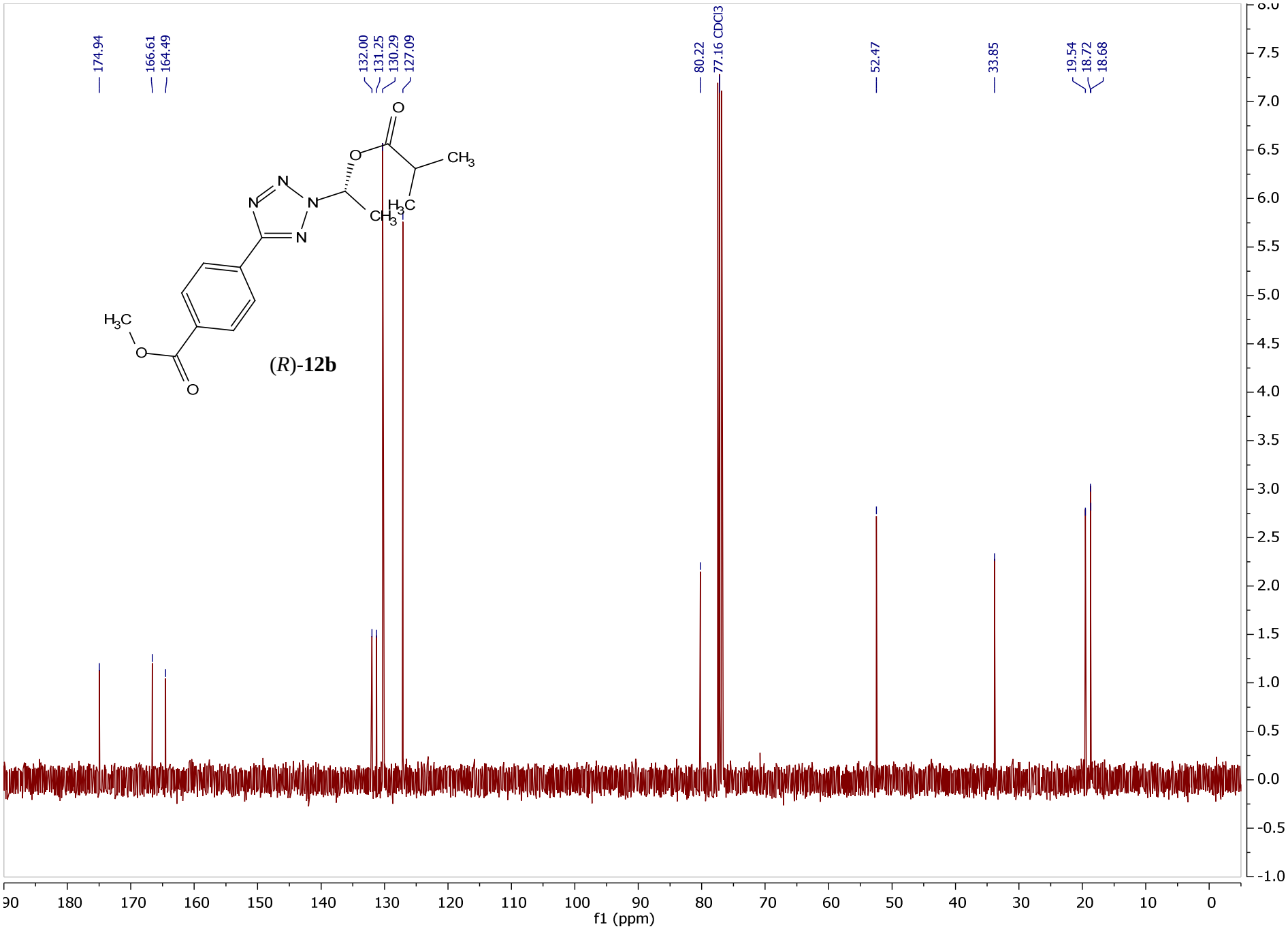

8.54
8.34
8.33
7.26 CDCl3
6.87
6.86
5.01
5.00
2.79
2.67
2.66
0.92
H3C
N
CH3
OH
CH3
CH3
CH3
NH2
N
B (d)
8.34
A (s)
8.54
C (d)
6.87
D (d)
5.01
F (d)
2.67
E (s)
2.79
G (s)
0.92
0.94
0.91
0.92
1.00
6.00
0.98
8.80
f1 (ppm)

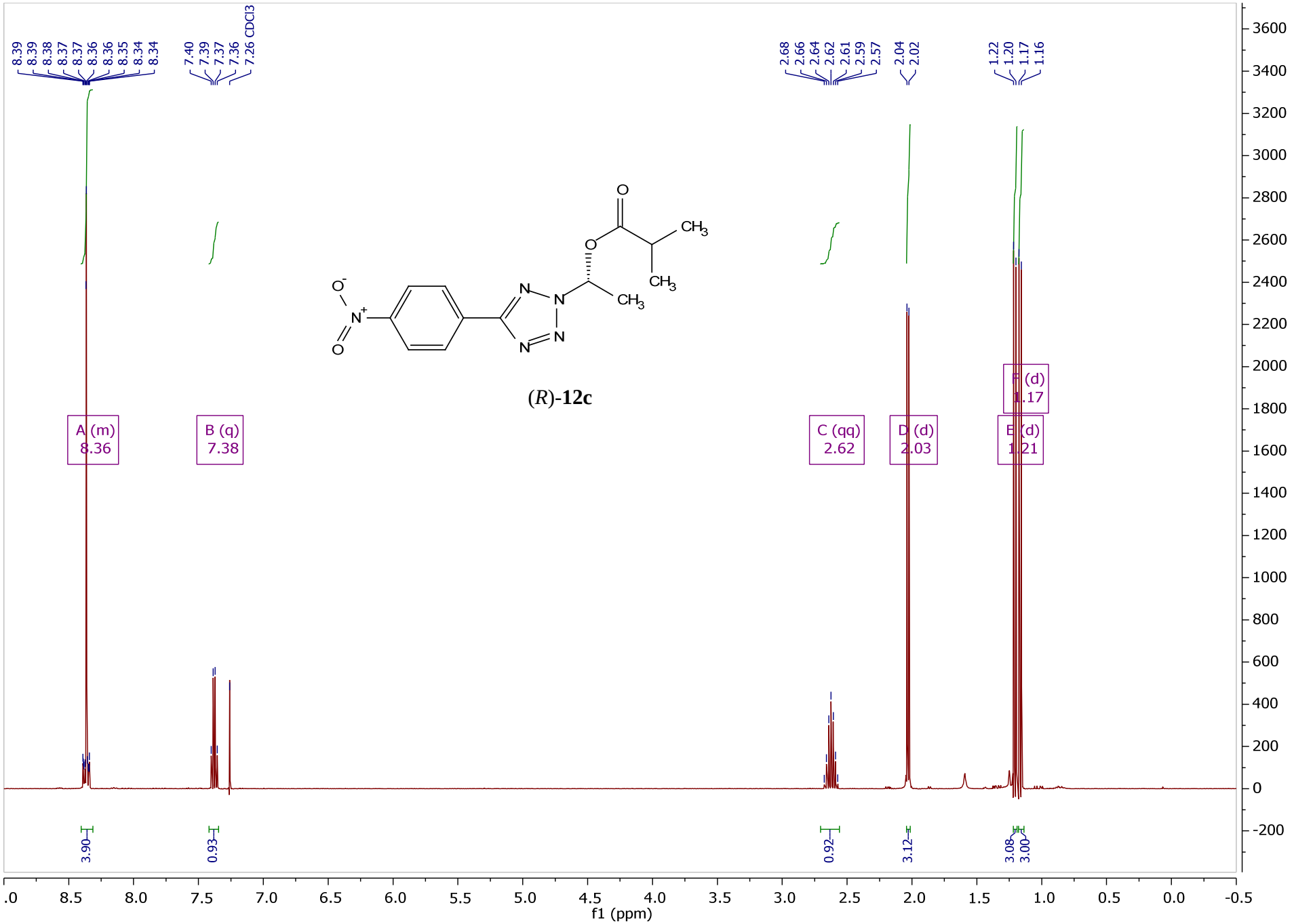
(*S*,*S*)-**8**


158.68
149.64
149.32
133.43
113.84
77.16 CDCl3
66.55
64.11
44.25
34.54
27.16
H3C
CH3
N
OH
CH3
CH3
CH3
NH2
N
f1 (ppm)

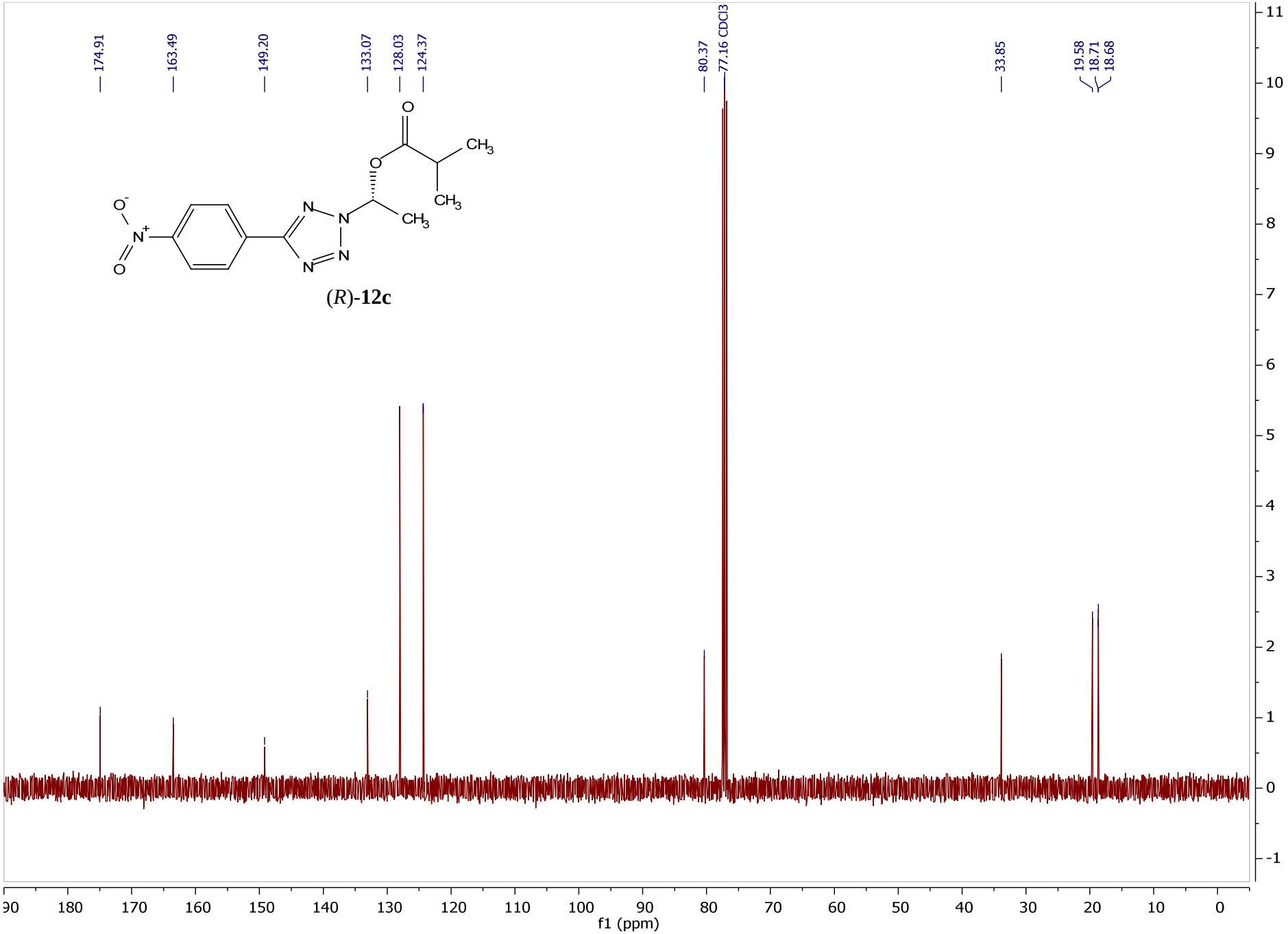
(*S*,*S*)-**8**


8.27 8.27 8.26 8.26 8.25 8.24 8.24 8.24 8.17 8.17 8.17 8.16 8.15 8.15 8.15 8.14 8.14 7.39 7.37 7.36 7.34 7.26 CDCl3
3.95
2.66 2.65 2.63 2.61 2.59 2.58 2.56 2.02 2.01
1.21 1.19 1.16 1.15
(R)-12b
C (m) 8.16
B (m) 8.25
A (q) 7.37
D (s) 3.95
E (qq) 2.61
F (d) 2.02
H (d) 1.16
G (d) 1.20
1.61 1.65 0.90 2.98 0.87 3.00 3.16 3.21
f1 (ppm)

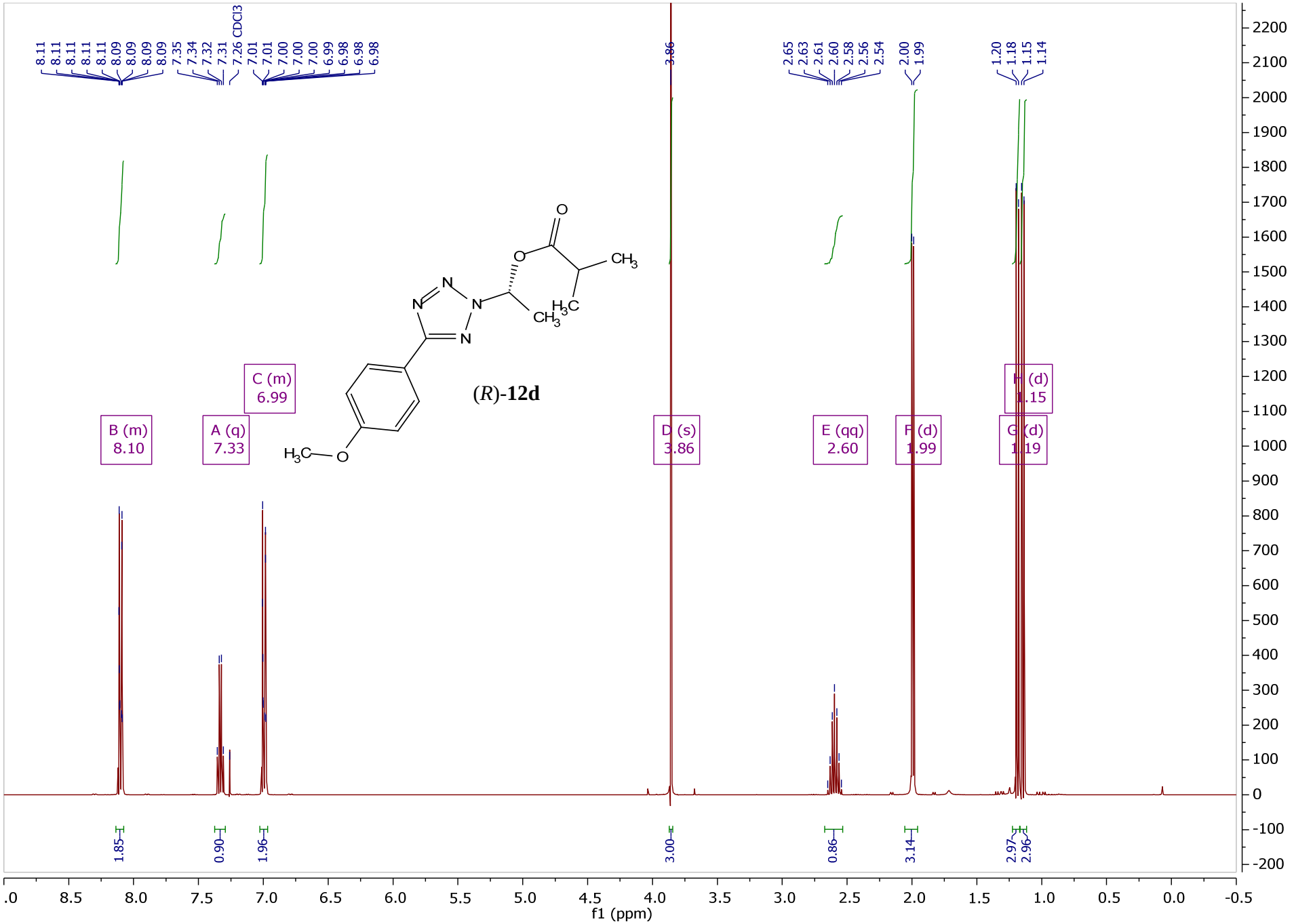

174.94
166.61
164.49
132.00
131.25
130.29
127.09
80.22
77.16 CDCl3
52.47
33.85
19.54
18.72
18.68
(R)-12b
f1 (ppm)

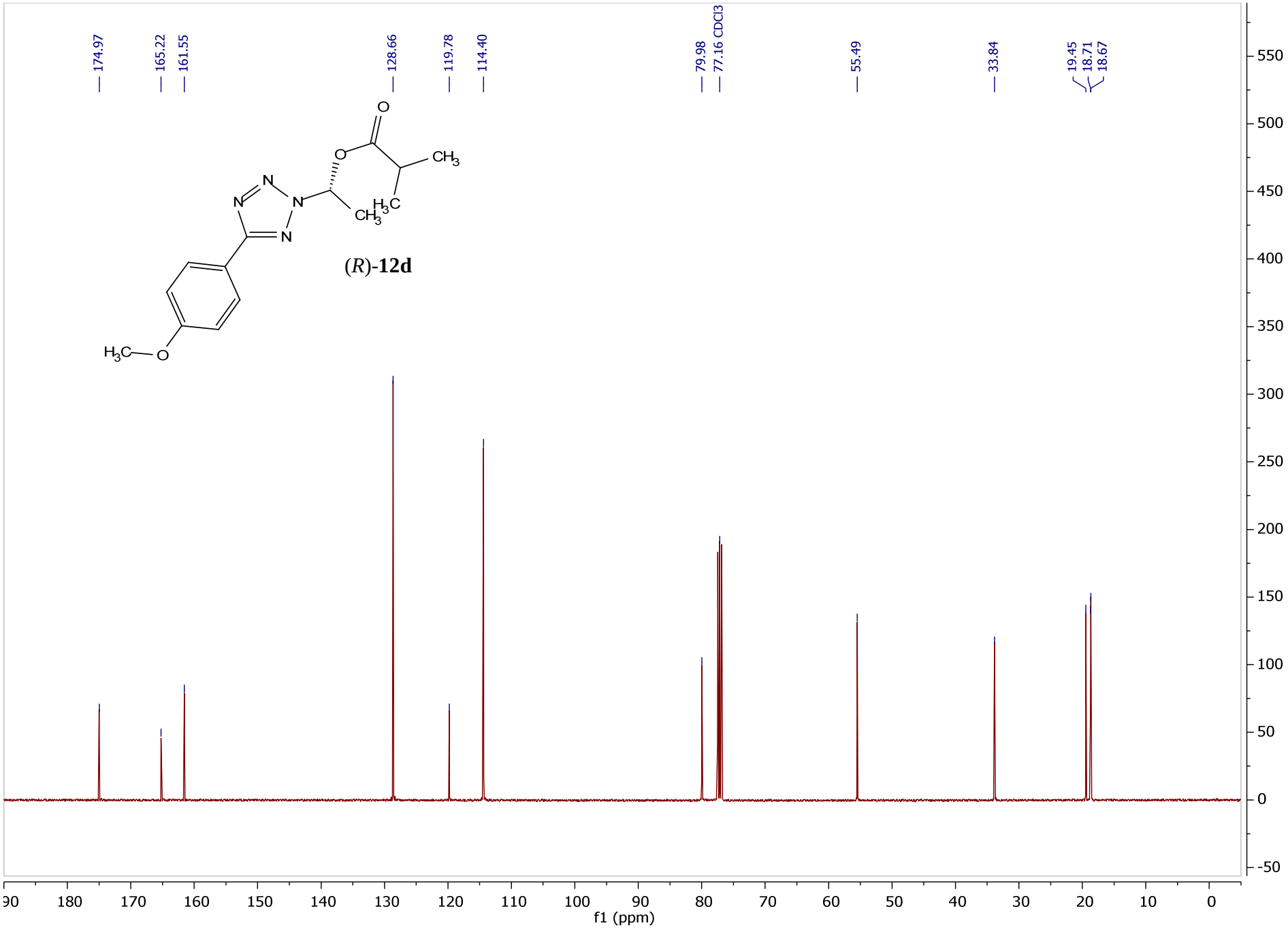

8.39 8.39 8.38 8.37 8.37 8.36 8.36 8.35 8.34 8.34
7.40 7.39 7.37 7.36 7.26 CDCl3
2.68 2.66 2.64 2.62 2.61 2.59 2.57
2.04 2.02
1.22 1.20 1.17 1.16
A (m) 8.36
B (q) 7.38
C (qq) 2.62
D (d) 2.03
E (d) 1.21
F (d) 1.17
3.90
0.93
0.92
3.12
3.08
3.00
f1 (ppm)

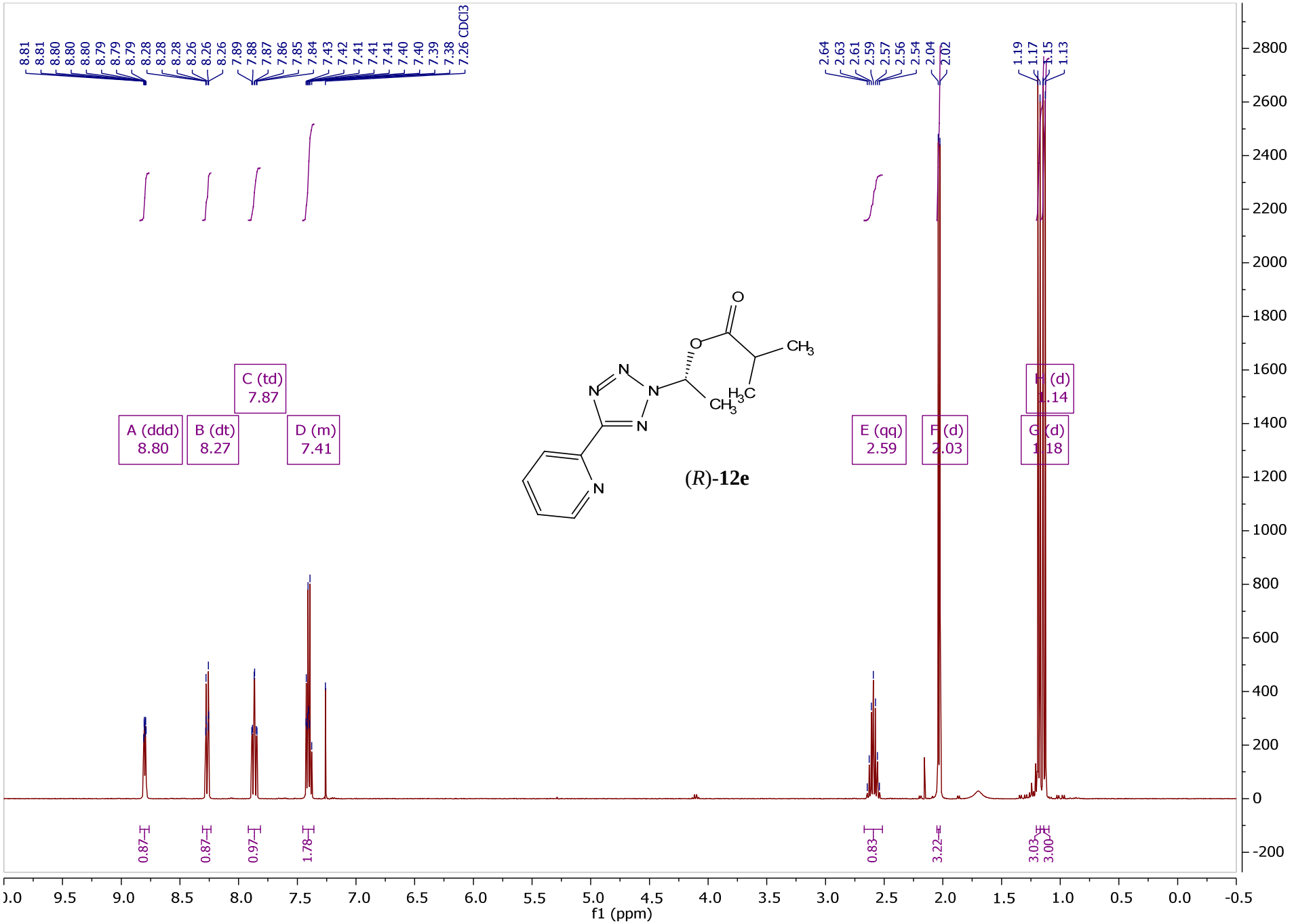
(*R*)-**12c**

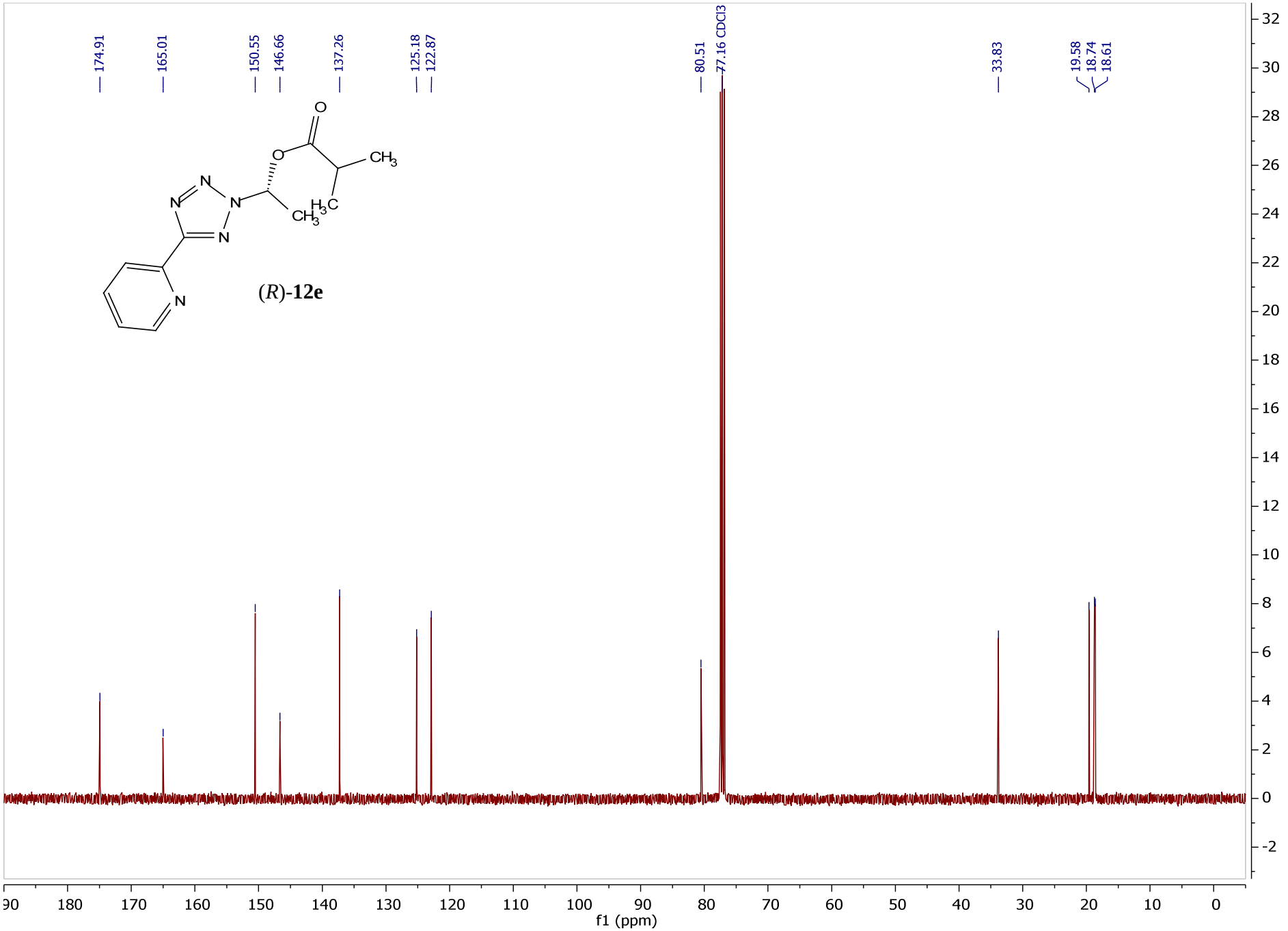

174.91
163.49
149.20
133.07
128.03
124.37
80.37
77.16 CDCl3
33.85
19.58
18.71
18.68
f1 (ppm)

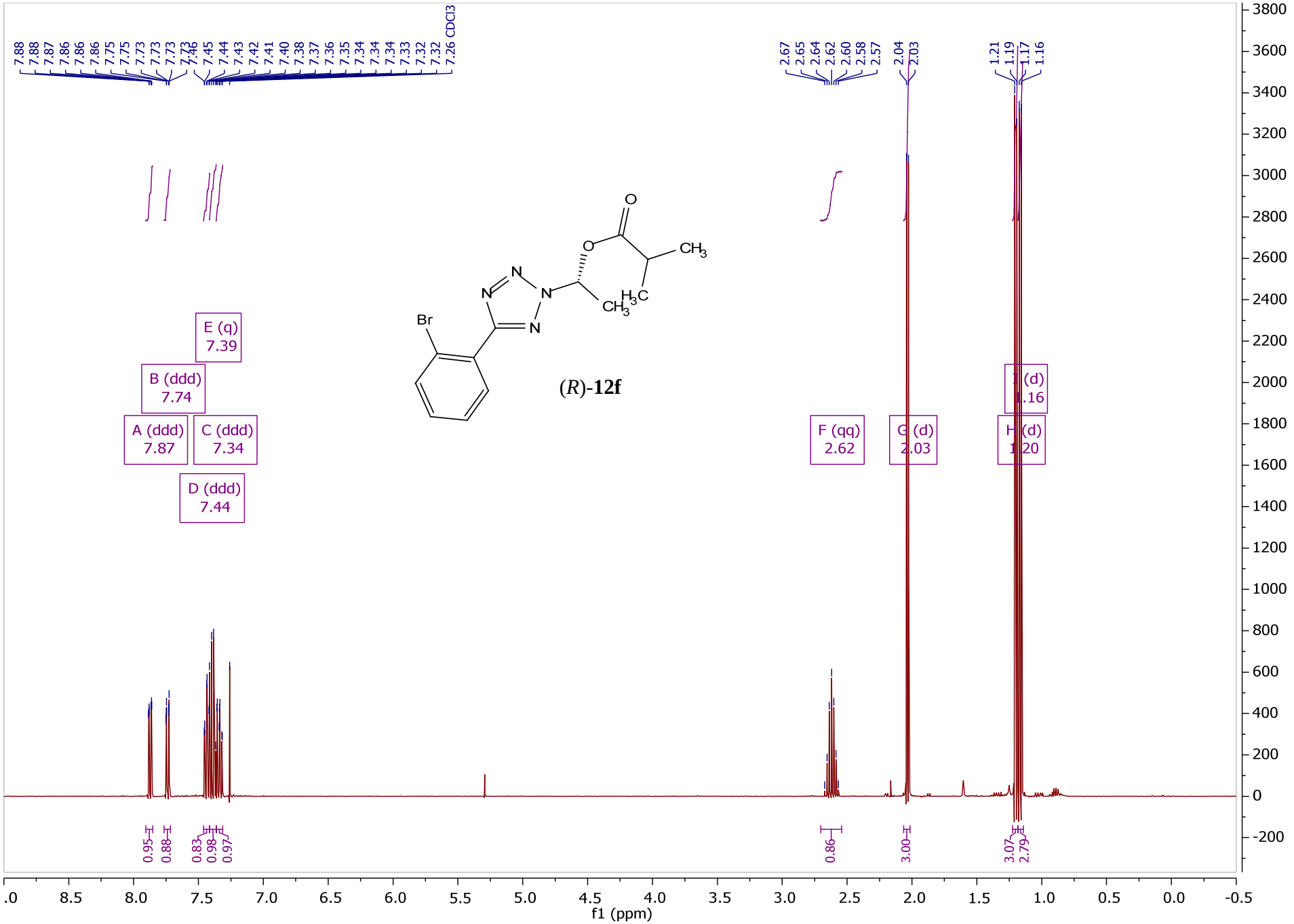
(*R*)-**12c**

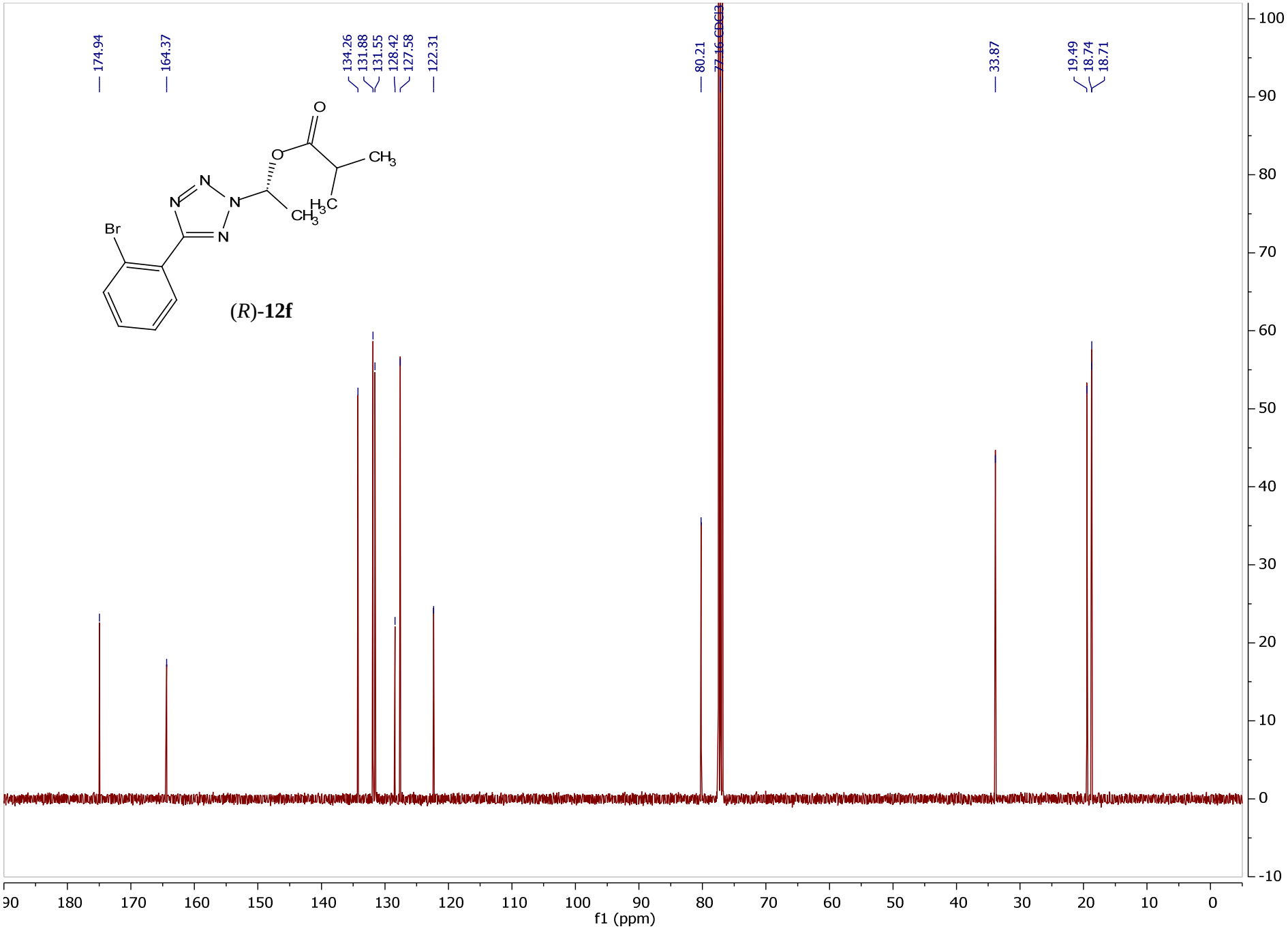

8.11 8.11 8.11 8.11 8.11 8.09 8.09 8.09 8.09 7.35 7.34 7.32 7.31 7.26 CDCl3 7.01 7.01 7.00 7.00 7.00 6.99 6.98 6.98 6.98
3.86
2.65 2.63 2.61 2.60 2.58 2.56 2.54 2.00 1.99
1.20 1.18 1.15 1.14
B (m) 8.10
A (q) 7.33
C (m) 6.99
D (s) 3.86
E (qq) 2.60
F (d) 1.99
G (d) 1.19
H (d) 1.15
(R)-12d
1.85 0.90 1.96 3.00 0.86 3.14 2.97 2.96
f1 (ppm)

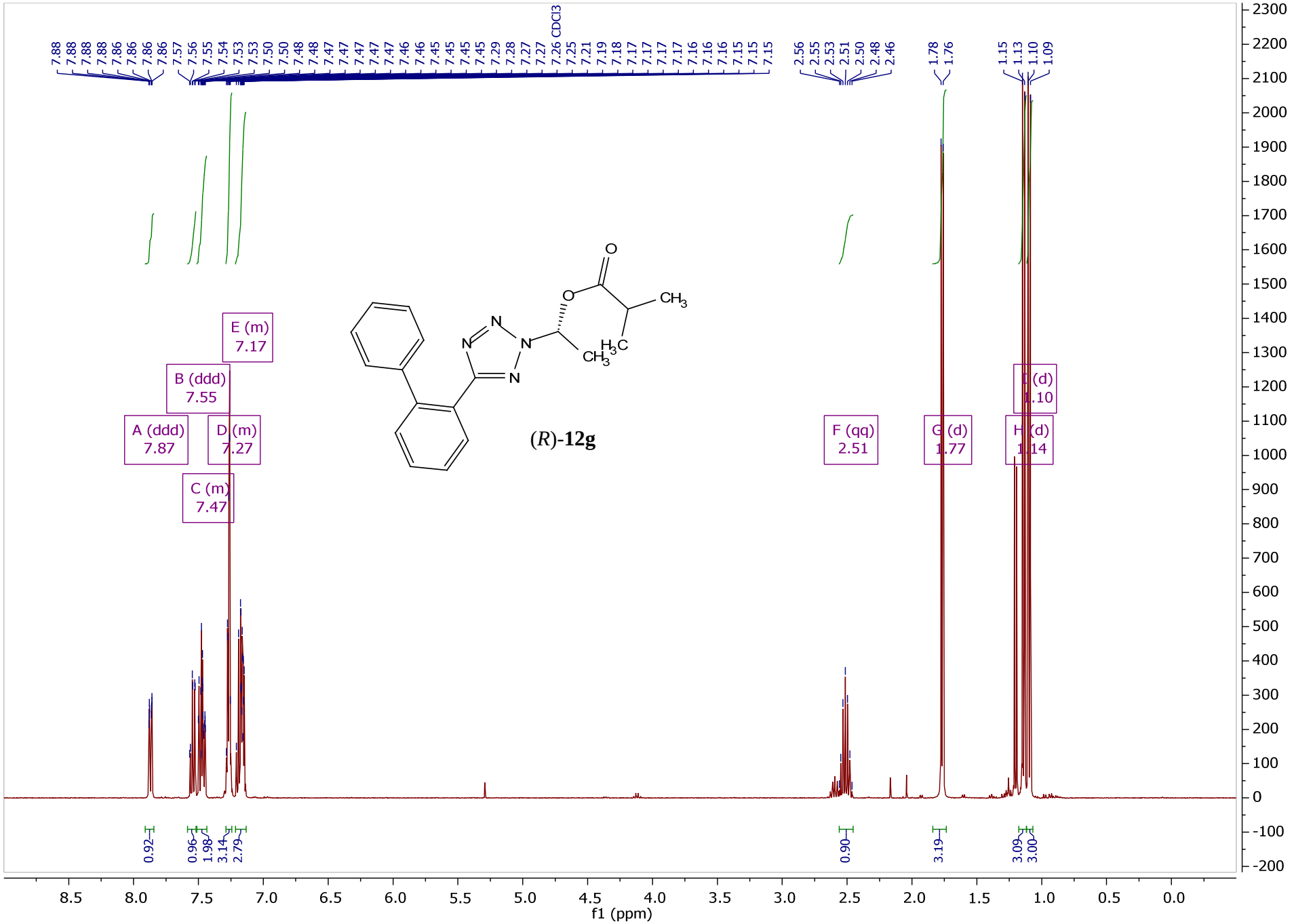

174.97
165.22
161.55
128.66
119.78
114.40
79.98
77.16 CDCl3
55.49
33.84
19.45
18.71
18.67
O
O
CH3
N
N
N
N
H3C
CH3
H3C
O
(R)-12d
f1 (ppm)

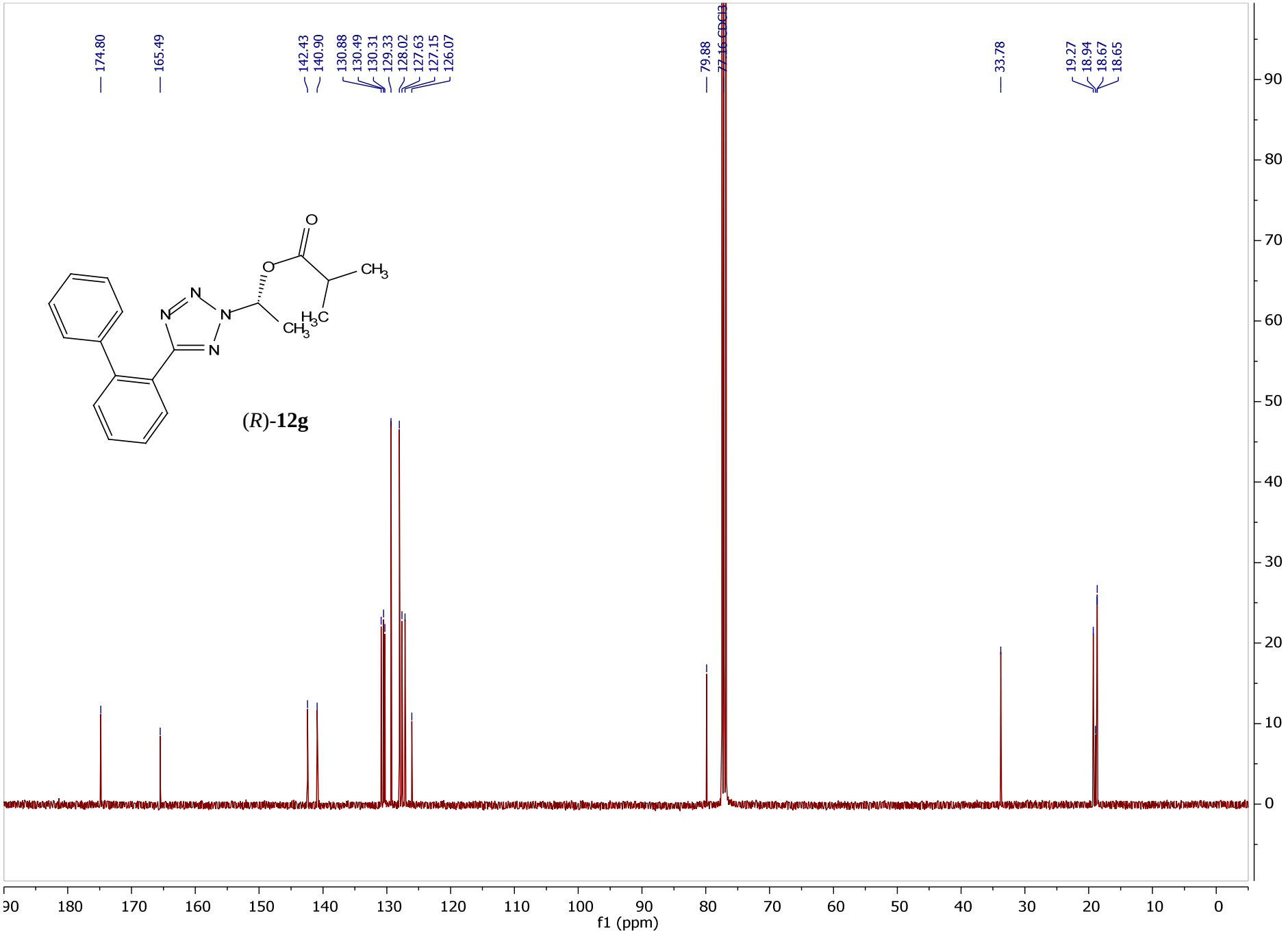

8.81 8.81 8.80 8.80 8.80 8.79 8.79 8.79 8.28 8.28 8.28 8.26 8.26 8.26 7.89 7.88 7.87 7.86 7.85 7.84 7.43 7.42 7.41 7.41 7.41 7.40 7.40 7.39 7.38 7.26 CDCl3
2.64 2.63 2.61 2.59 2.57 2.56 2.54 2.04 2.02
1.19 1.17 1.15 1.13
A (ddd) 8.80
B (dt) 8.27
C (td) 7.87
D (m) 7.41
E (qq) 2.59
F (d) 2.03
G (d) 1.18
H (d) 1.14
(R)-12e
0.87 0.87 0.97 1.78 0.83 3.22 3.03 3.00
f1 (ppm)

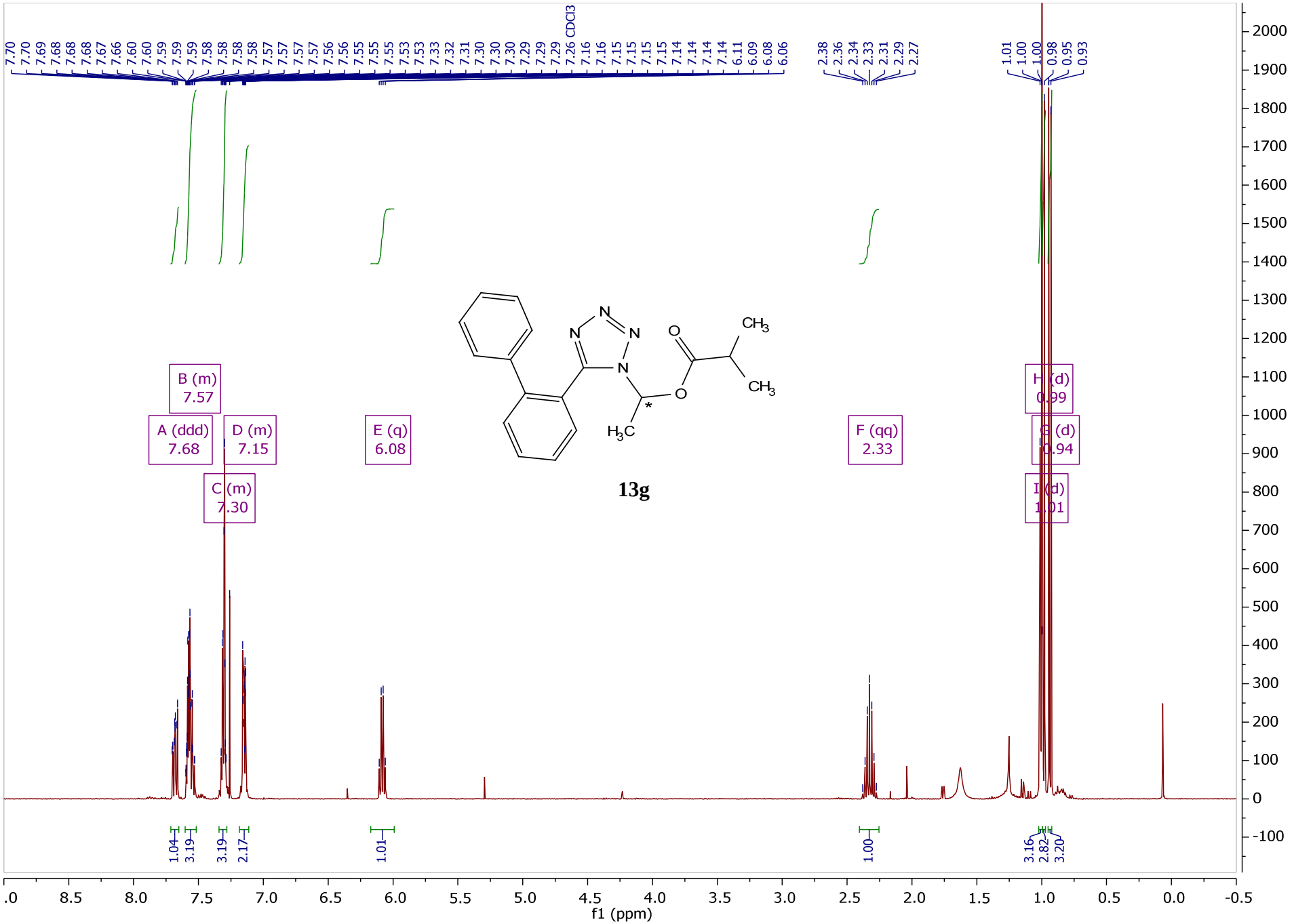

174.91
165.01
150.55
146.66
137.26
125.18
122.87
80.51
77.16 CDCl3
33.83
19.58
18.74
18.61
O
O
CH3
N
N
N
N
H3C
CH3
(R)-12e
f1 (ppm)

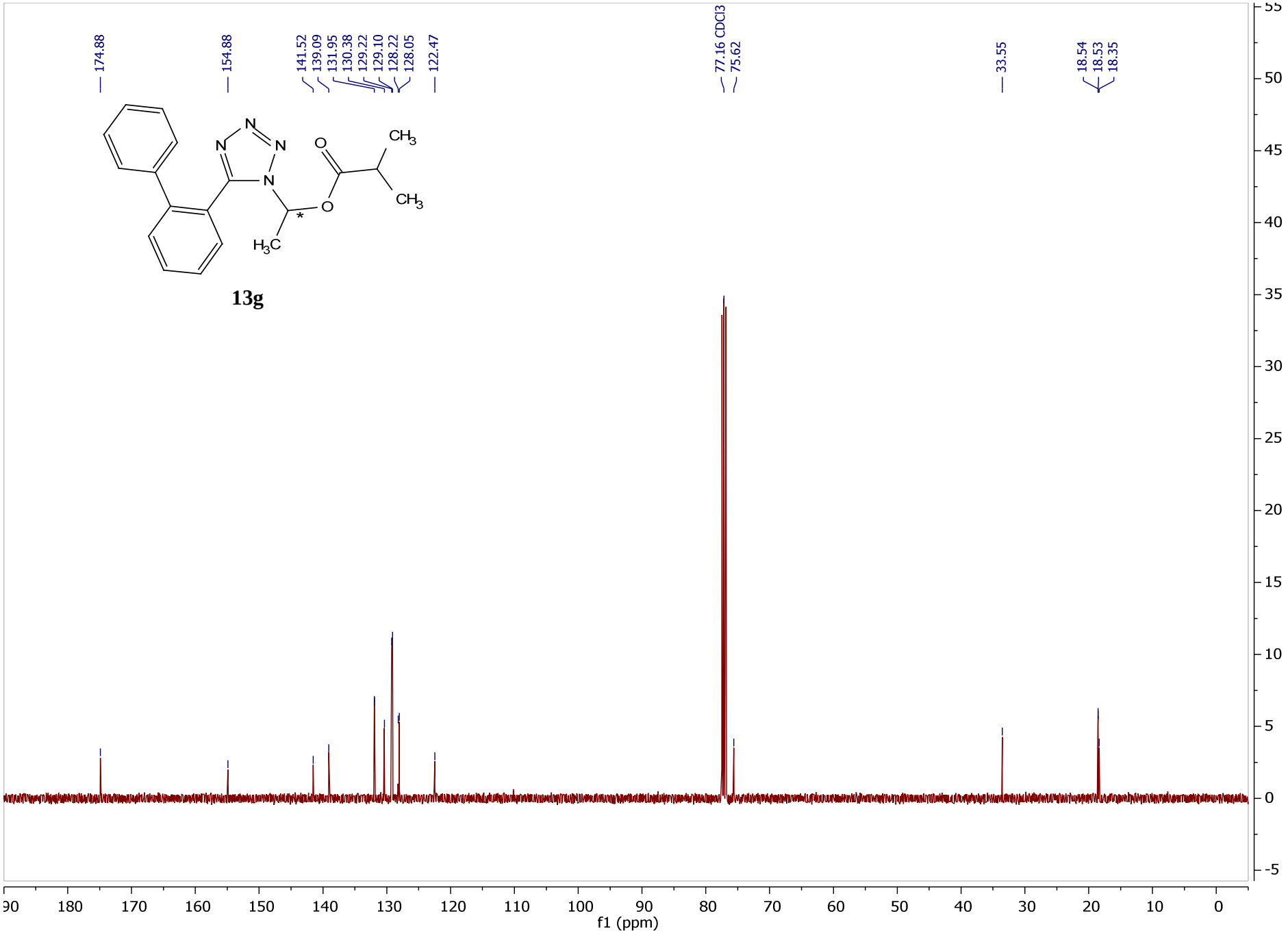

7.88 7.88 7.87 7.86 7.86 7.86 7.75 7.75 7.73 7.73 7.73 7.46 7.45 7.44 7.43 7.42 7.41 7.40 7.38 7.37 7.36 7.35 7.34 7.34 7.34 7.33 7.32 7.32 7.26 CDCl3
2.67 2.65 2.64 2.62 2.60 2.58 2.57 2.04 2.03 1.21 1.19 1.17 1.16
E (q) 7.39
B (ddd) 7.74
A (ddd) 7.87
C (ddd) 7.34
D (ddd) 7.44
F (qq) 2.62
G (d) 2.03
H (d) 1.20
I (d) 1.16
(R)-12f
0.95 0.88 0.83 0.98 0.97 0.86 3.00 3.07 2.79
f1 (ppm)

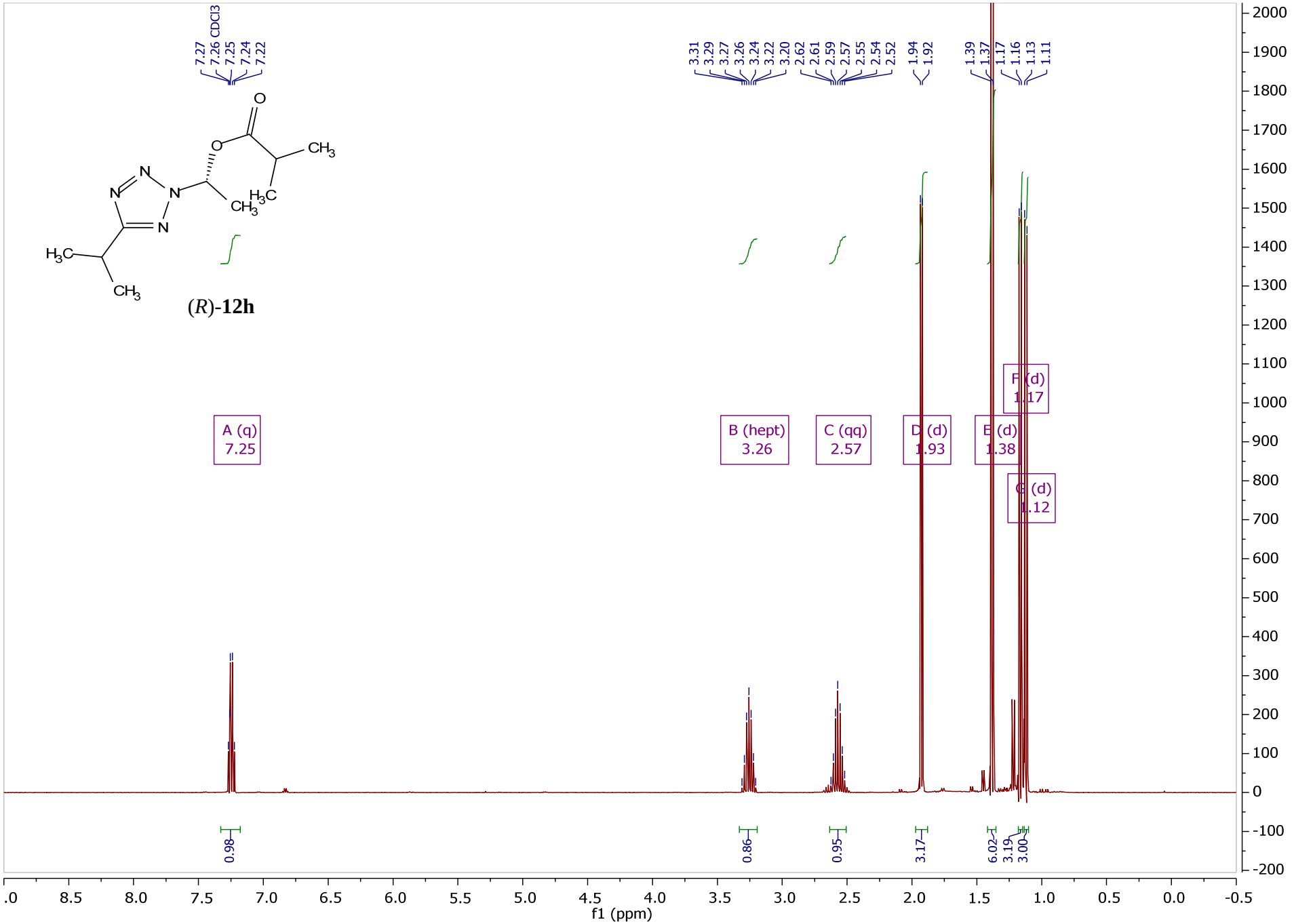

174.94
164.37
134.26
131.88
131.55
128.42
127.58
122.31
80.21
77.16 CDCl3
33.87
19.49
18.74
18.71
Br
N
N
N
O
O
CH3
H3C
CH3
(R)-12f
f1 (ppm)


E (m)
7.17
B (ddd)
7.55
A (ddd)
7.87
D (m)
7.27
C (m)
7.47
F (qq)
2.51
G (d)
1.77
H (d)
1.14
I (d)
1.10
(R)-12g
f1 (ppm)

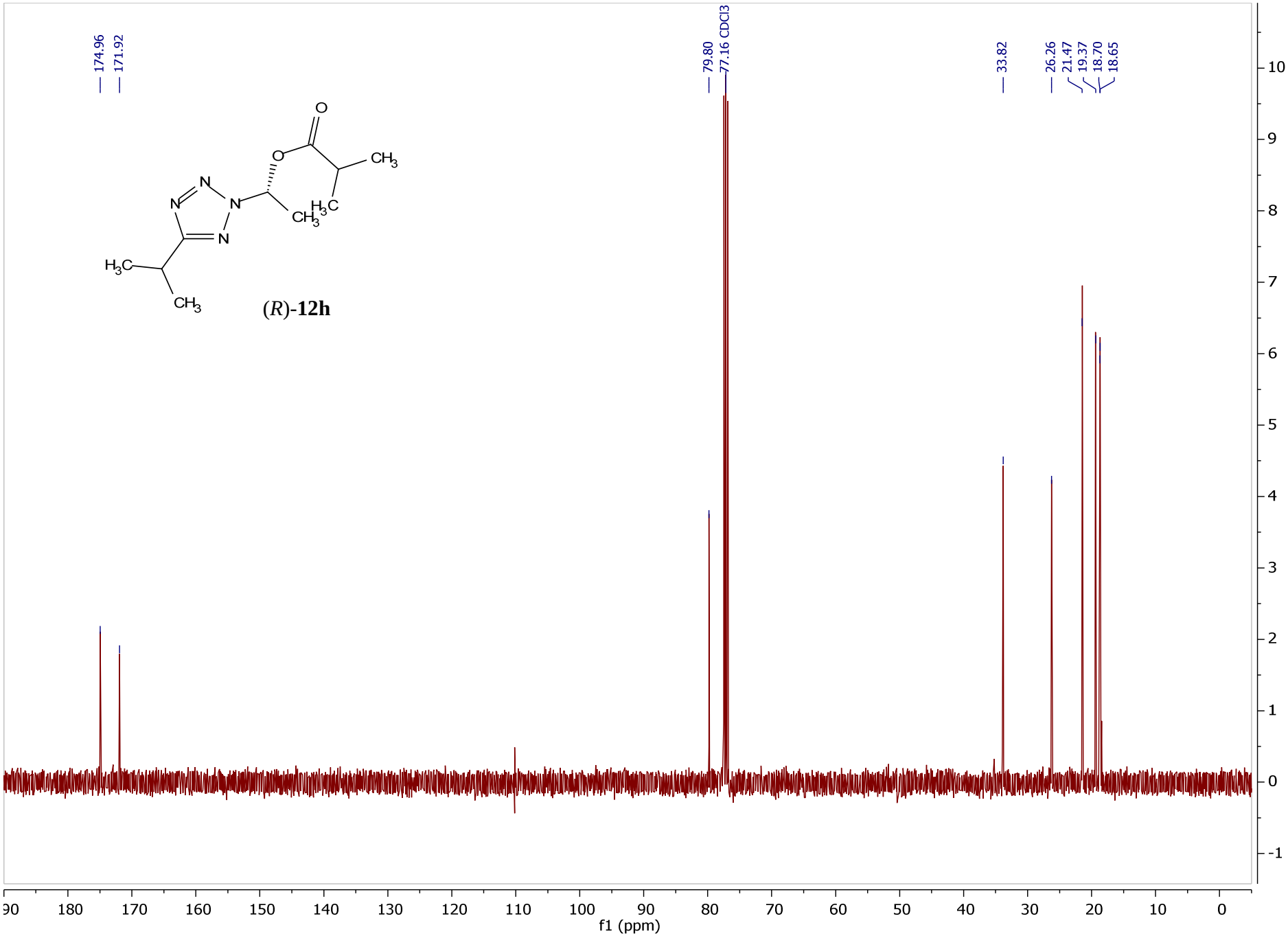

174.80
165.49
142.43
140.90
130.88
130.49
130.31
129.33
128.02
127.63
127.15
126.07
79.88
77.46 CDCl3
33.78
19.27
18.94
18.67
18.65
(R)-12g
f1 (ppm)

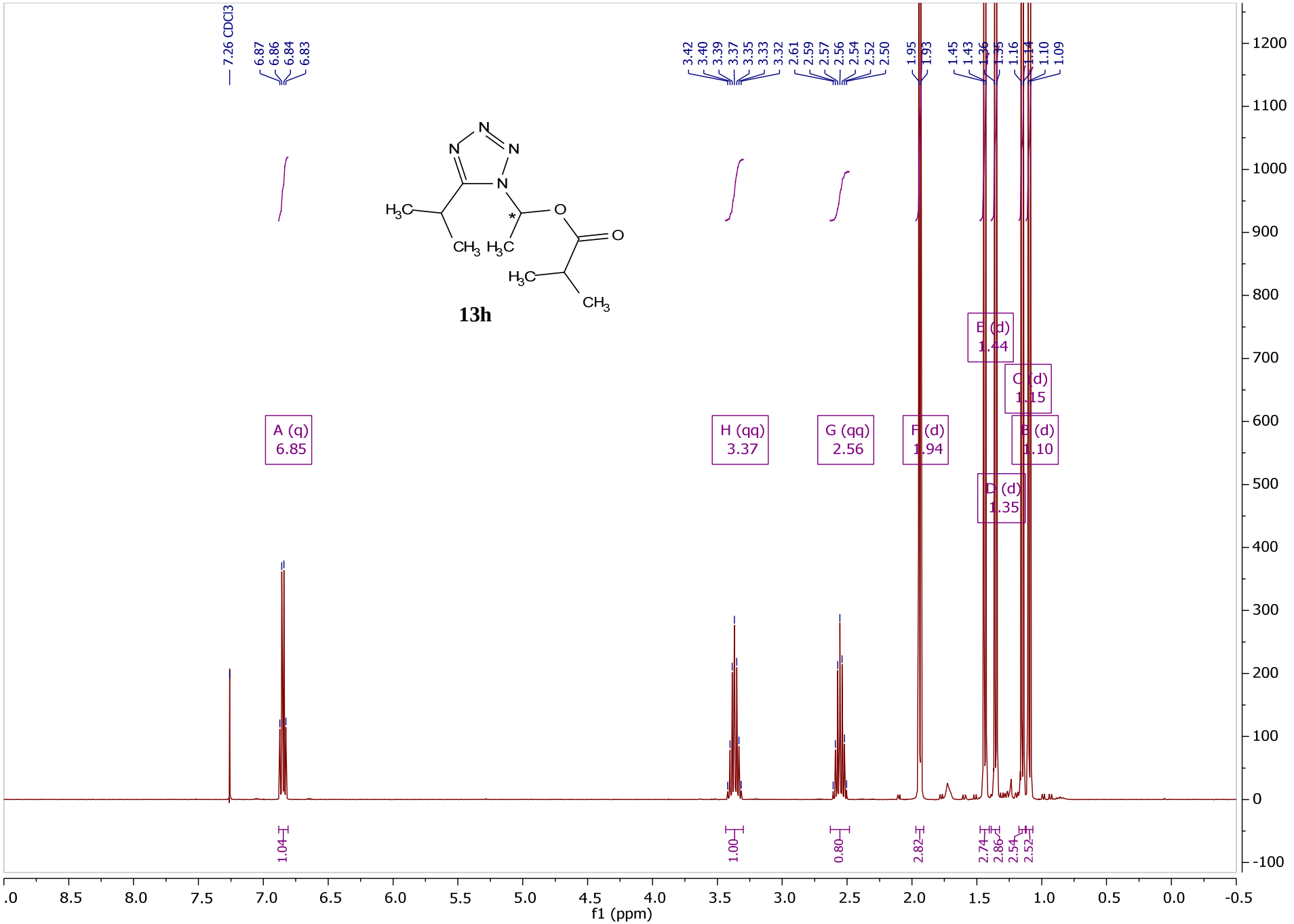

B (m)
7.57
A (ddd)
7.68
D (m)
7.15
C (m)
7.30
E (q)
6.08
F (qq)
2.33
H (d)
0.99
G (d)
0.94
I (d)
1.01
13g
f1 (ppm)


174.88
154.88
141.52
139.09
131.95
130.38
129.22
129.10
128.22
128.05
122.47
77.16 CDCl3
75.62
33.55
18.54
18.53
18.35
N
N
N
N
O
O
CH3
CH3
*
H3C
13g
f1 (ppm)

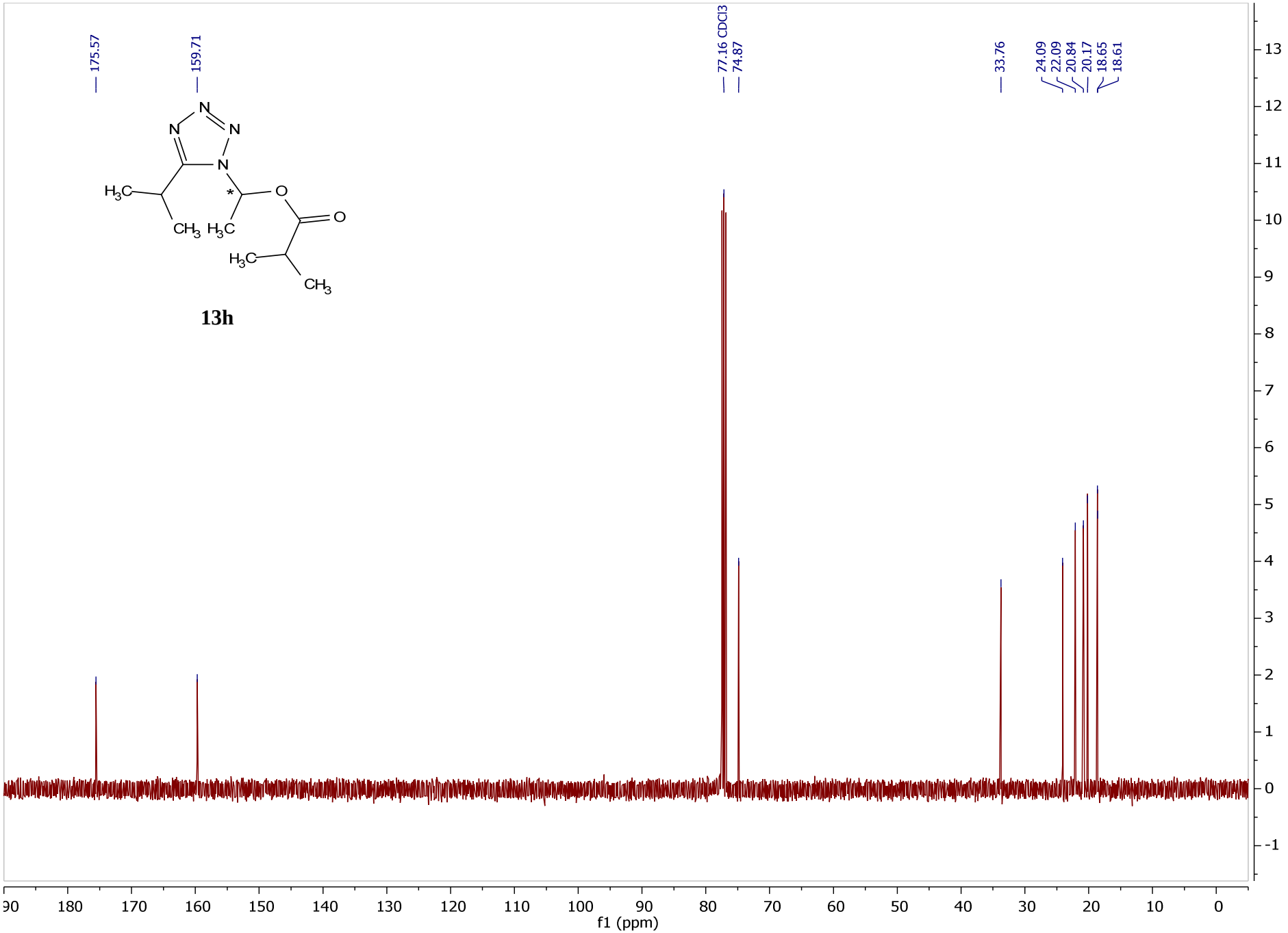

7.27
7.26 CDCl3
7.25
7.24
7.22
3.31
3.29
3.27
3.26
3.24
3.22
3.20
2.62
2.61
2.59
2.57
2.55
2.54
2.52
1.94
1.92
1.39
1.37
1.17
1.16
1.13
1.11
A (q) 7.25
B (hept) 3.26
C (qq) 2.57
D (d) 1.93
E (d) 1.38
F (d) 1.17
G (d) 1.12
0.98
0.86
0.95
3.17
6.02
3.19
3.00
f1 (ppm)

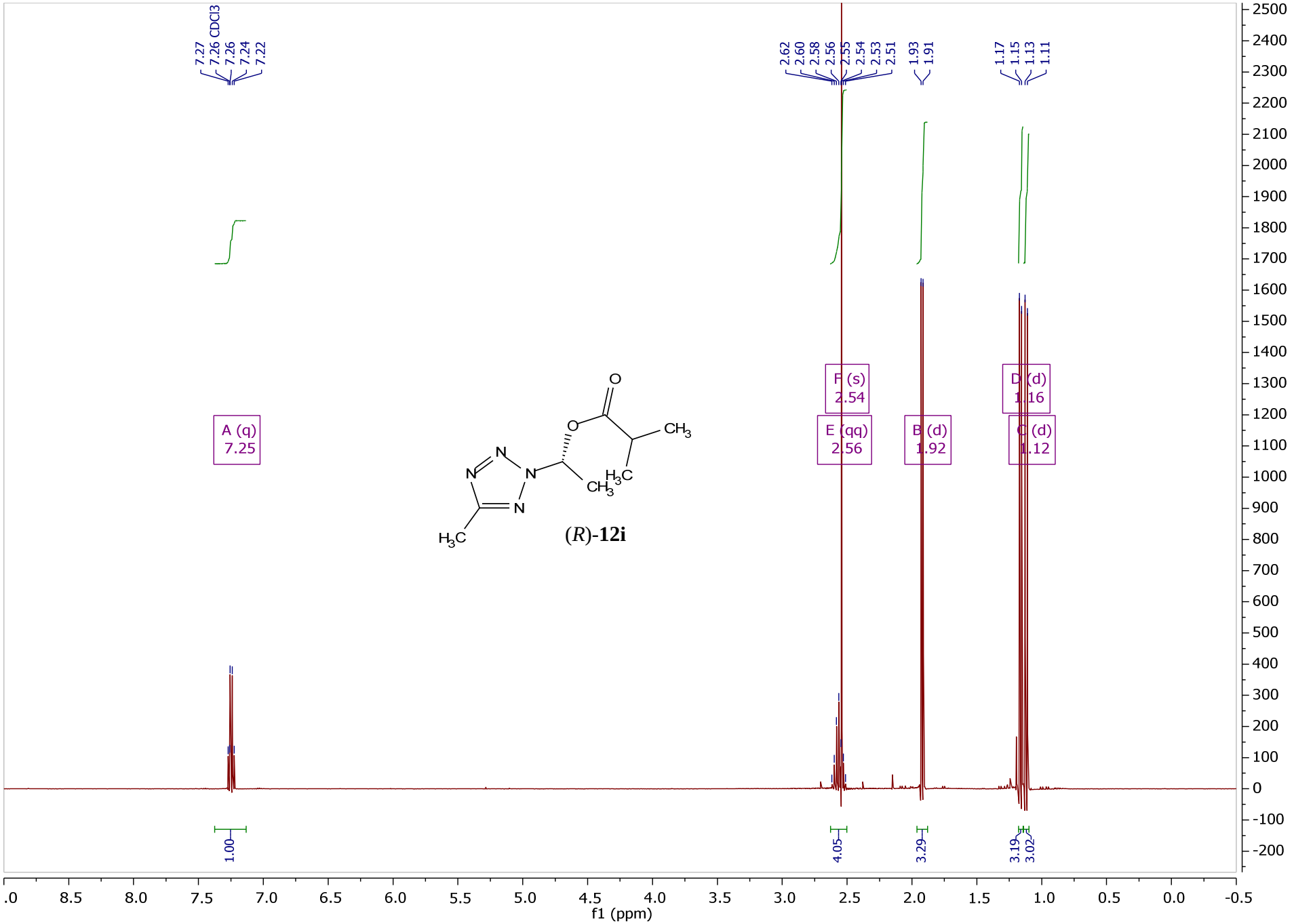
(*R*)-**12h**


174.96
171.92
79.80
77.16 CDCl3
33.82
26.26
21.47
19.37
18.70
18.65
O
O
N
N
N
N
CH3
H3C
CH3
H3C
CH3
(R)-12h
f1 (ppm)

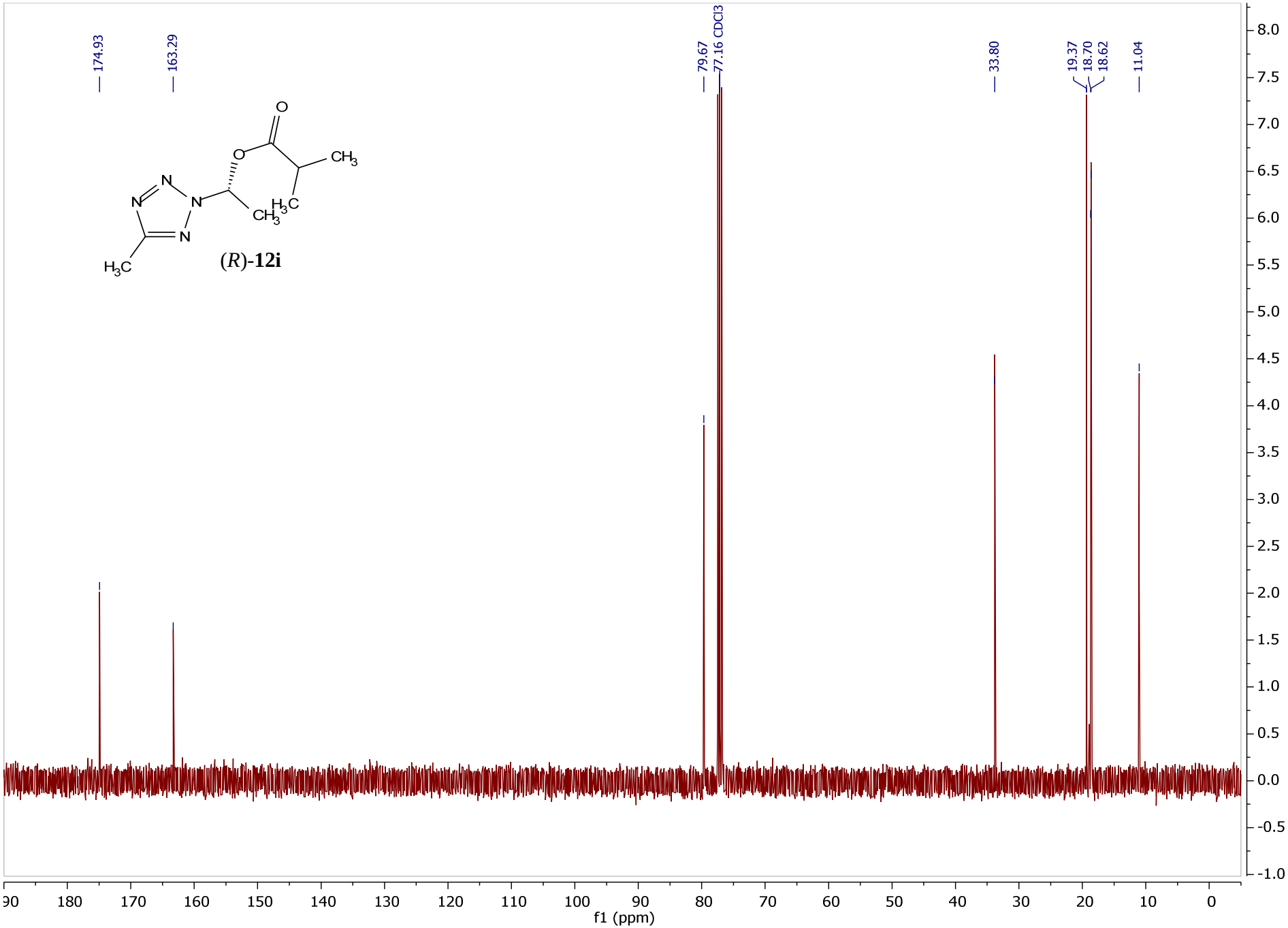

7.26 CDCl3
6.87
6.86
6.84
6.83
3.42
3.40
3.39
3.37
3.35
3.33
3.32
2.61
2.59
2.57
2.56
2.54
2.52
2.50
1.95
1.93
1.45
1.43
1.36
1.35
1.16
1.14
1.10
1.09
A (q) 6.85
H (qq) 3.37
G (qq) 2.56
F (d) 1.94
E (d) 1.44
C (d) 1.15
B (d) 1.10
D (d) 1.35
1.04
1.00
0.80
2.82
2.74
2.86
2.54
2.52
f1 (ppm)

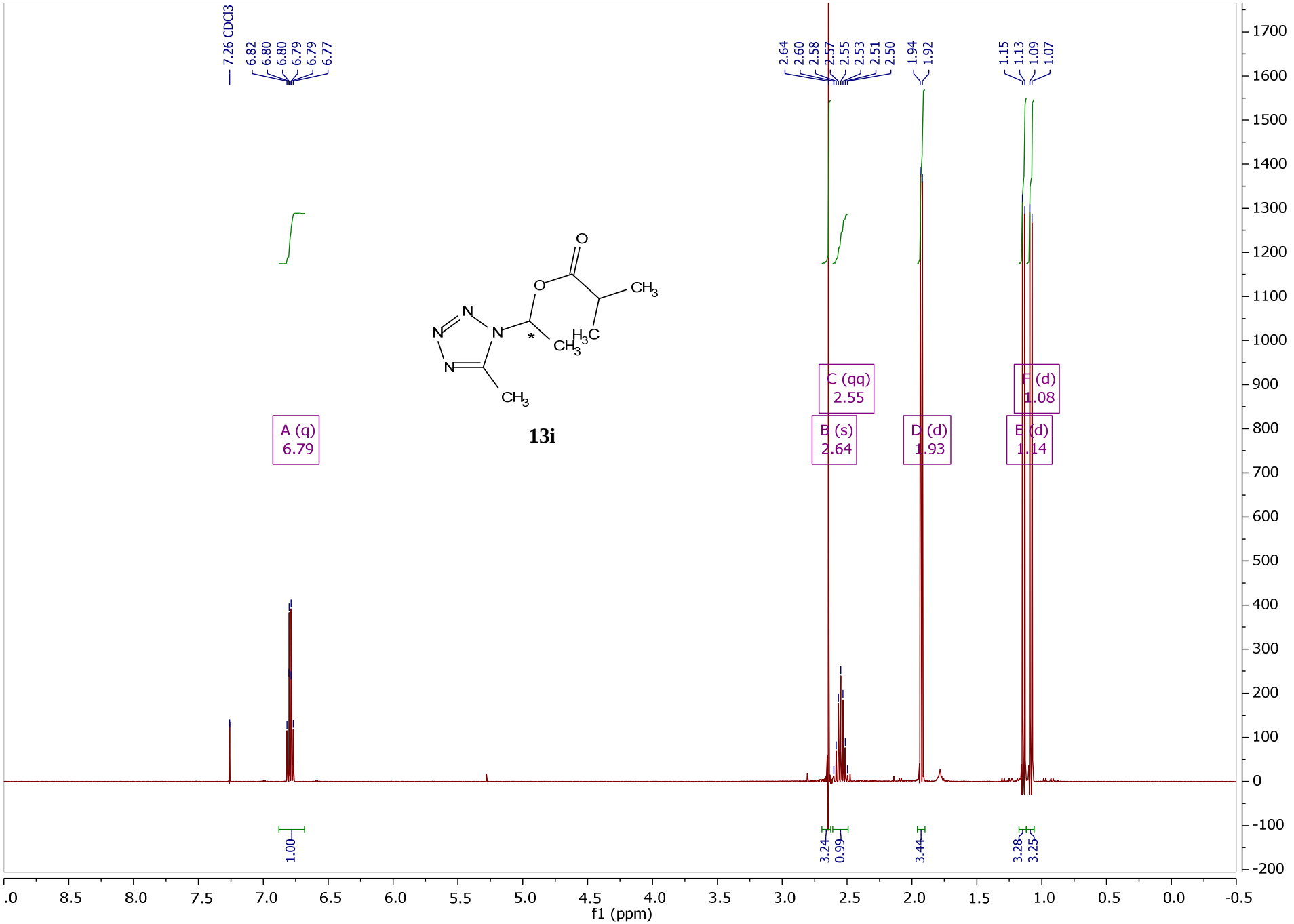
13h


175.57
159.71
77.16 CDCl3
74.87
33.76
24.09
22.09
20.84
20.17
18.65
18.61
N
N
N
N
H3C
CH3
H3C
*
O
O
H3C
CH3
13h
f1 (ppm)

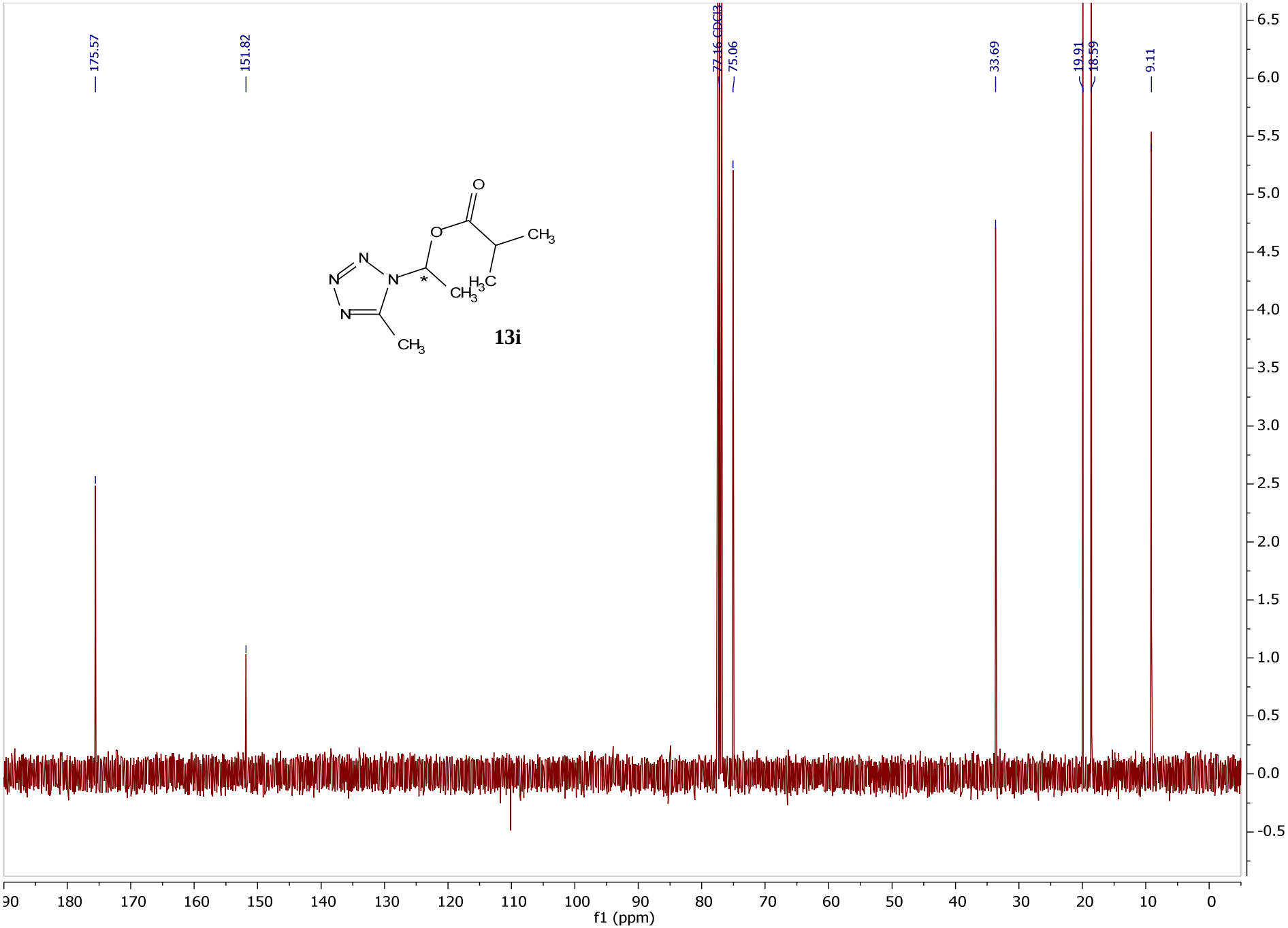

7.27
7.26 CDCl3
7.26
7.24
7.22
2.62
2.60
2.58
2.56
2.55
2.54
2.53
2.51
1.93
1.91
1.17
1.15
1.13
1.11
A (q)
7.25
F (s)
2.54
E (qq)
2.56
B (d)
1.92
D (d)
1.16
C (d)
1.12
1.00
4.05
3.29
3.19
3.02
f1 (ppm)

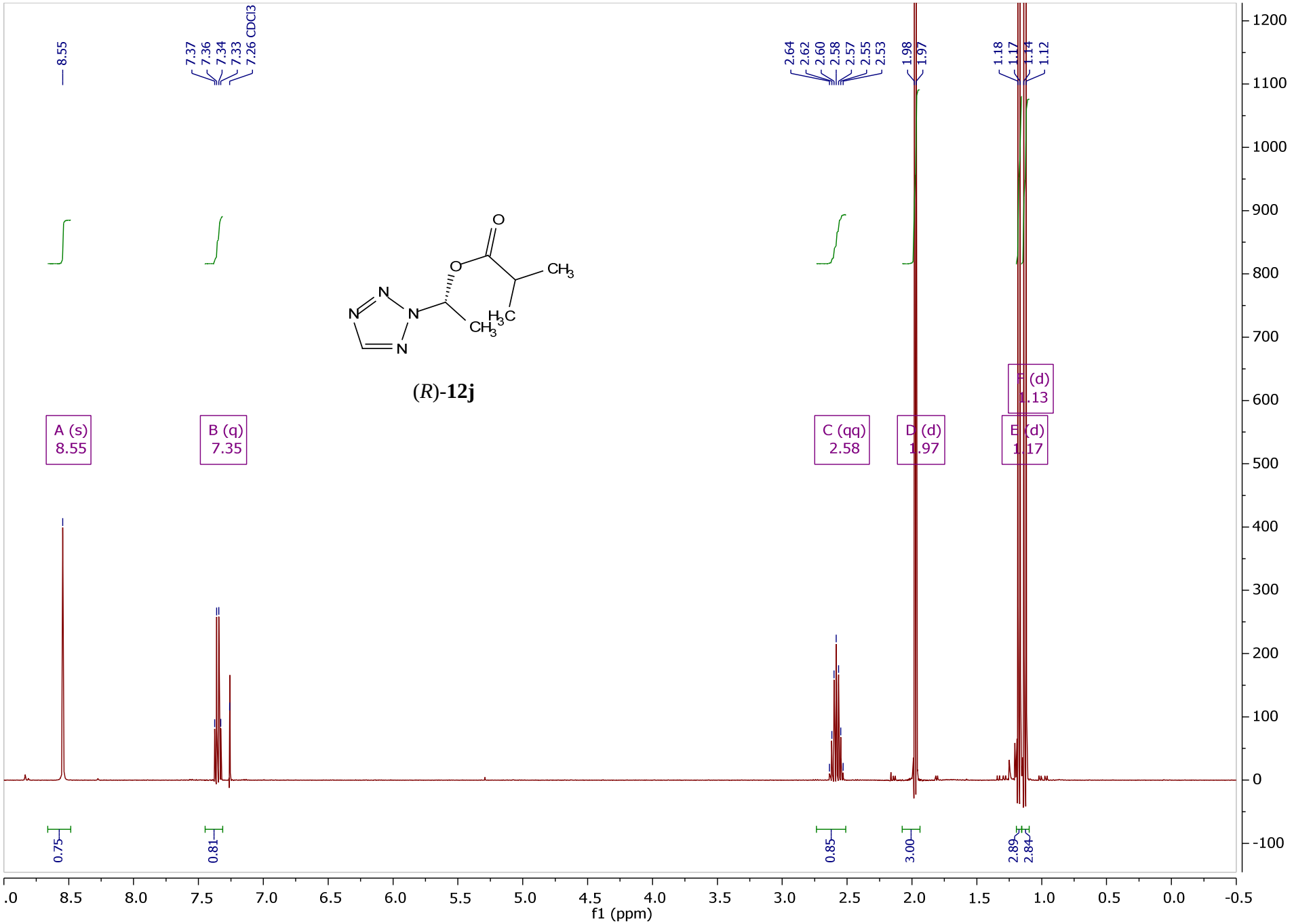
(*R*)-**12i**


174.93
163.29
79.67
77.16 CDCl3
33.80
19.37
18.70
18.62
11.04
O
O
CH3
N
N
N
H3C
CH3
H3C
(R)-12i
f1 (ppm)

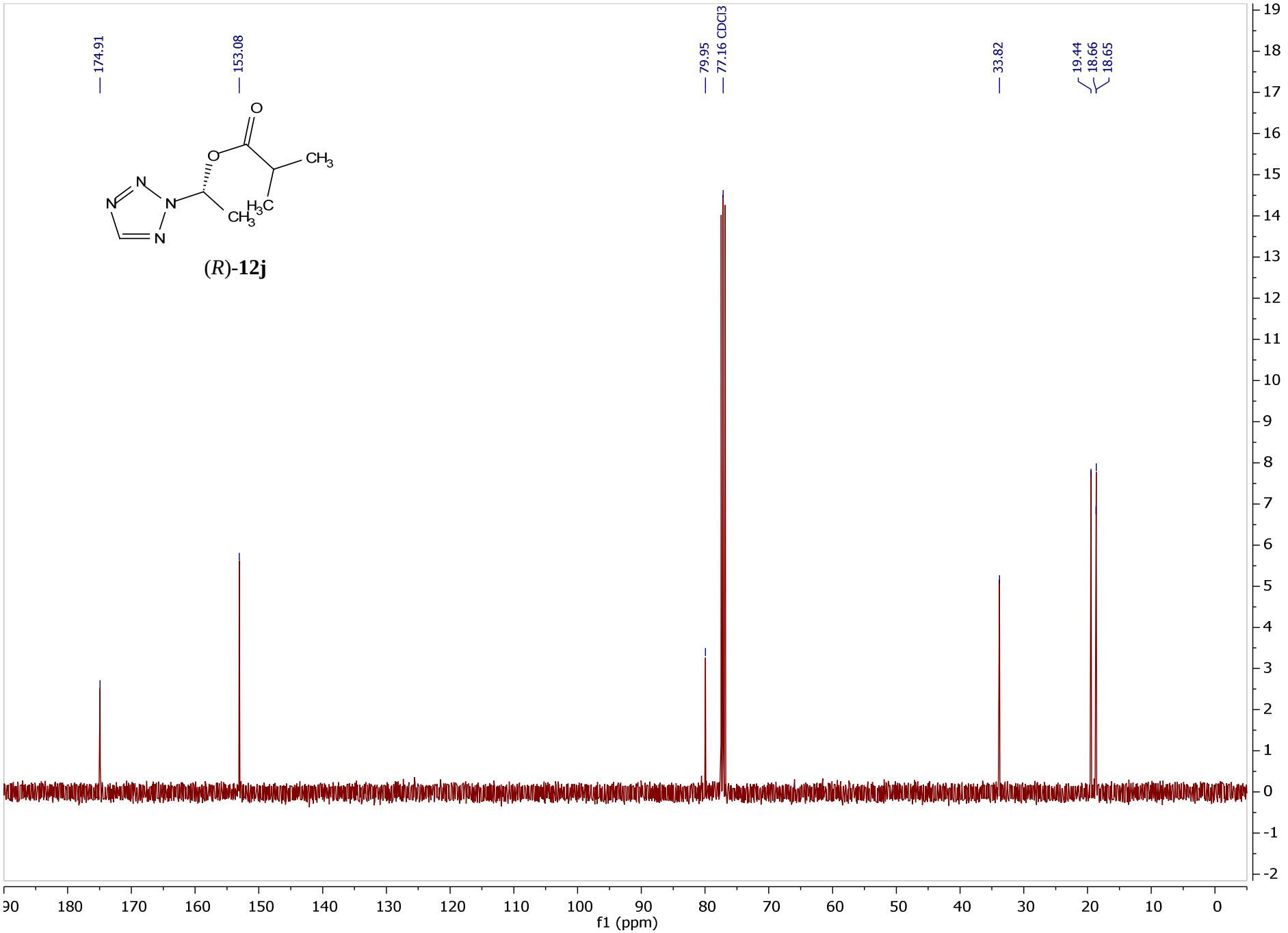

7.26 CDCl3
6.82
6.80
6.80
6.79
6.79
6.77
2.64
2.60
2.58
2.57
2.55
2.53
2.51
2.50
1.94
1.92
1.15
1.13
1.09
1.07
A (q)
6.79
C (qq)
2.55
B (s)
2.64
D (d)
1.93
F (d)
1.08
E (d)
1.14
1.00
3.24
0.99
3.44
3.28
3.25
f1 (ppm)

13i

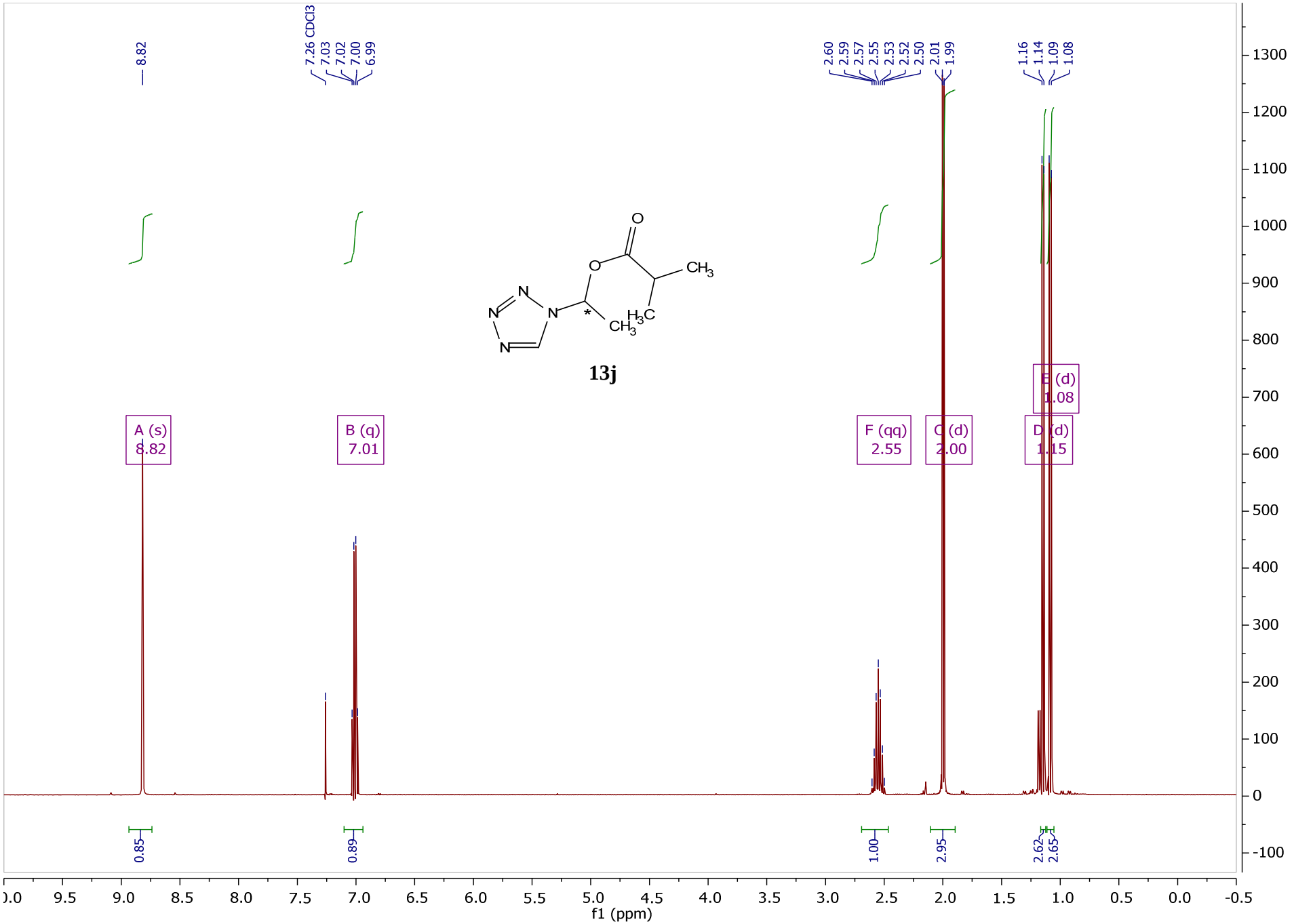

175.57
151.82
77.16 CDCl3
75.06
33.69
19.91
18.59
9.11
O
O
CH3
N
N
N
*
H3C
CH3
CH3
13i
f1 (ppm)


8.55
7.37
7.36
7.34
7.33
7.26 CDCl3
2.64
2.62
2.60
2.58
2.57
2.55
2.53
1.98
1.97
1.18
1.17
1.14
1.12
A (s) 8.55
B (q) 7.35
C (qq) 2.58
D (d) 1.97
E (d) 1.17
F (d) 1.13
0.75
0.81
0.85
3.00
2.89
2.84
f1 (ppm)

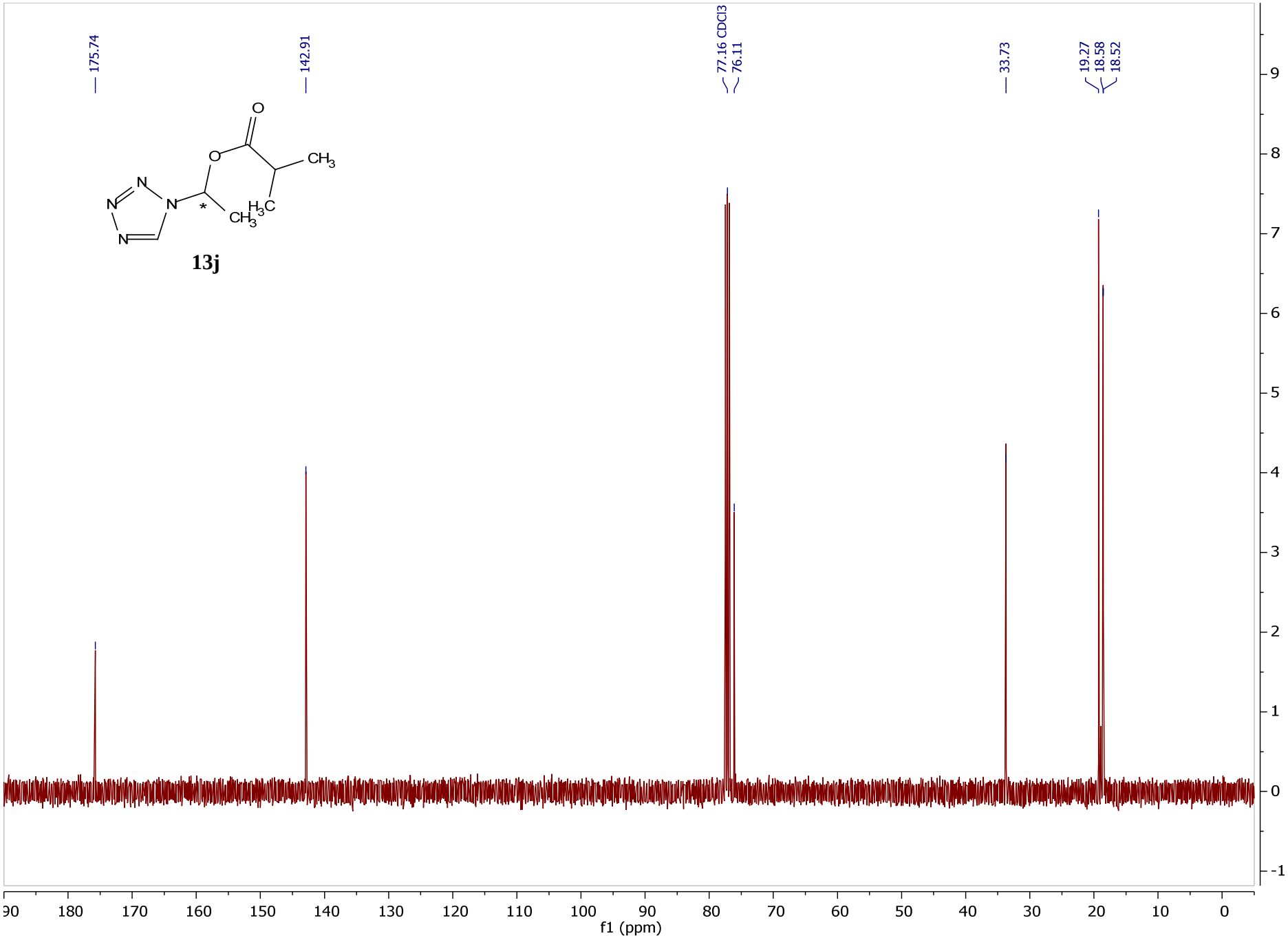
(*R*)-**12j**

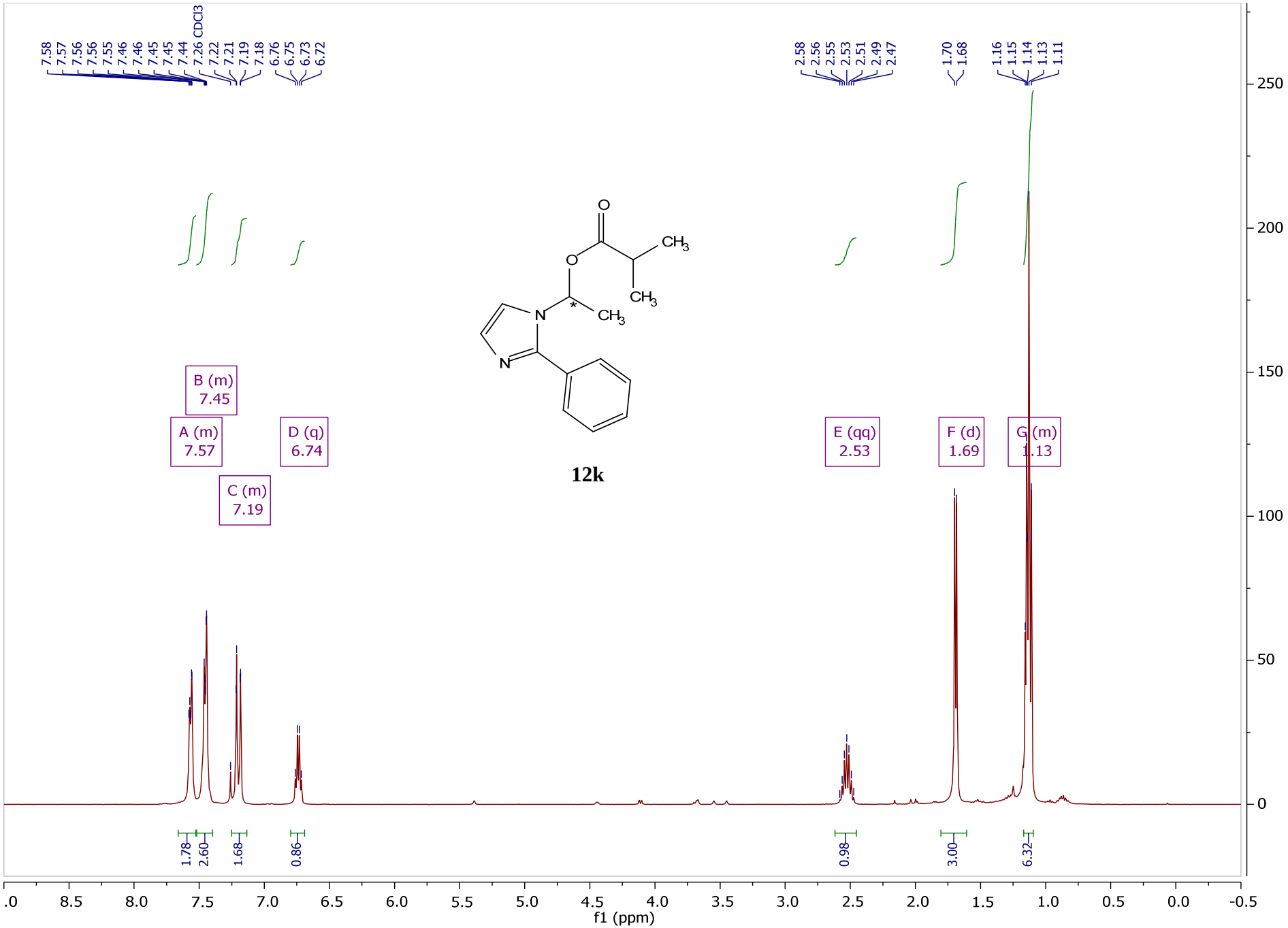

174.91
153.08
79.95
77.16 CDCl3
33.82
19.44
18.66
18.65
O
O
CH3
N
N
N
H3C
CH3
f1 (ppm)

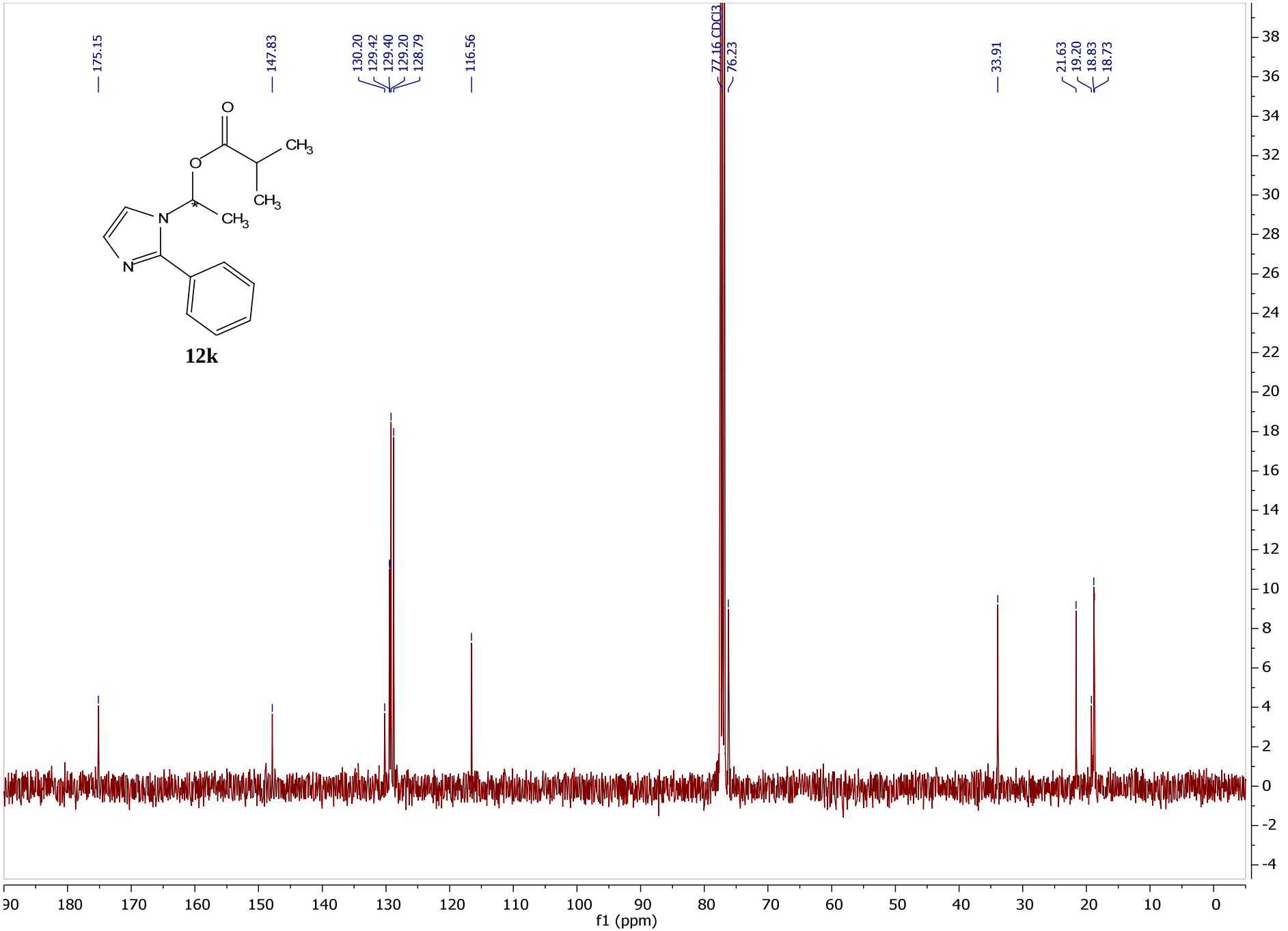
(*R*)-**12j**

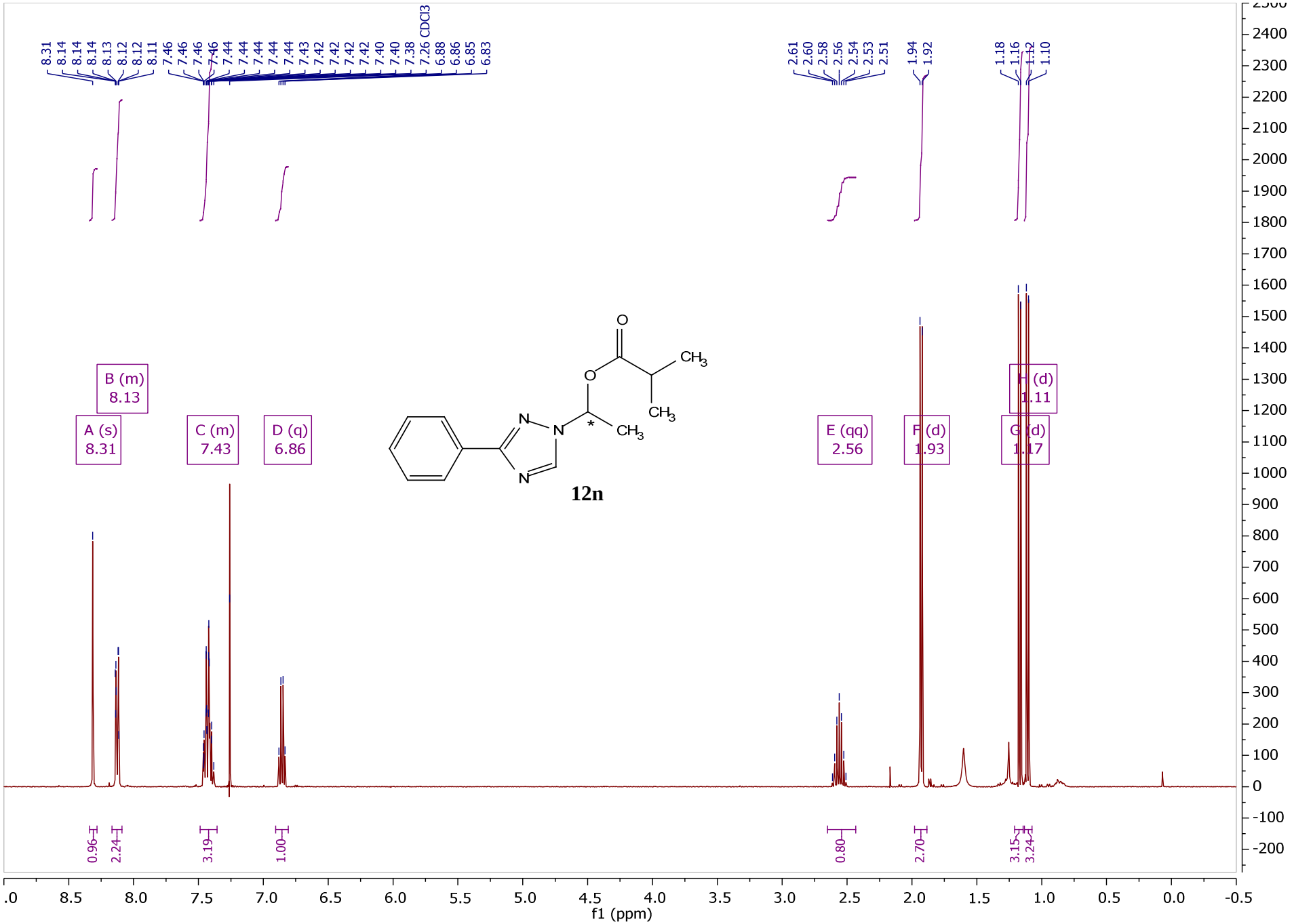

8.82
7.26 CDCl3
7.03
7.02
7.00
6.99
2.60
2.59
2.57
2.55
2.53
2.52
2.50
2.01
1.99
1.16
1.14
1.09
1.08
A (s) 8.82
B (q) 7.01
F (qq) 2.55
C (d) 2.00
D (d) 1.15
E (d) 1.08
0.85
0.89
1.00
2.95
2.62
2.65
f1 (ppm)

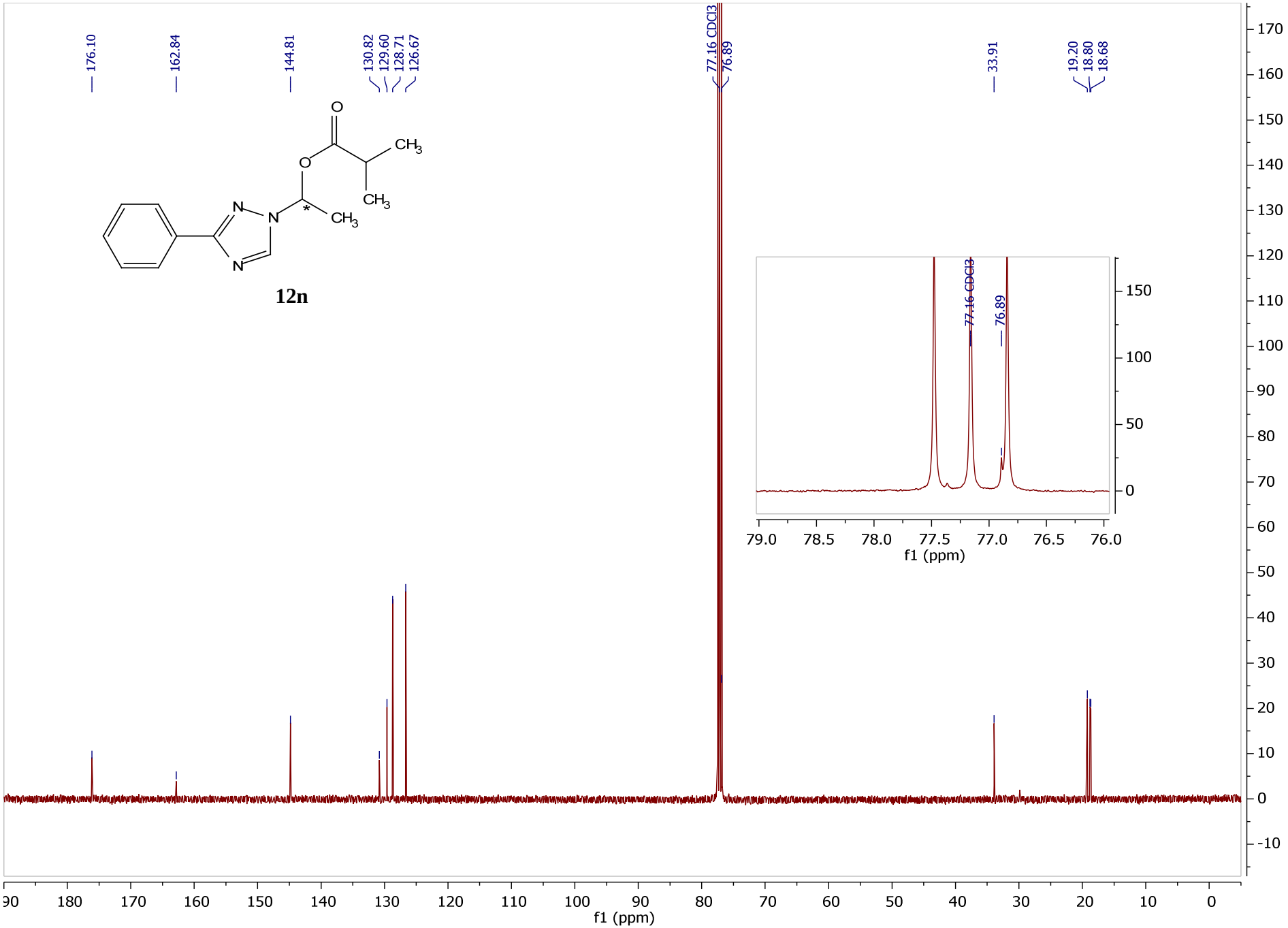
13j

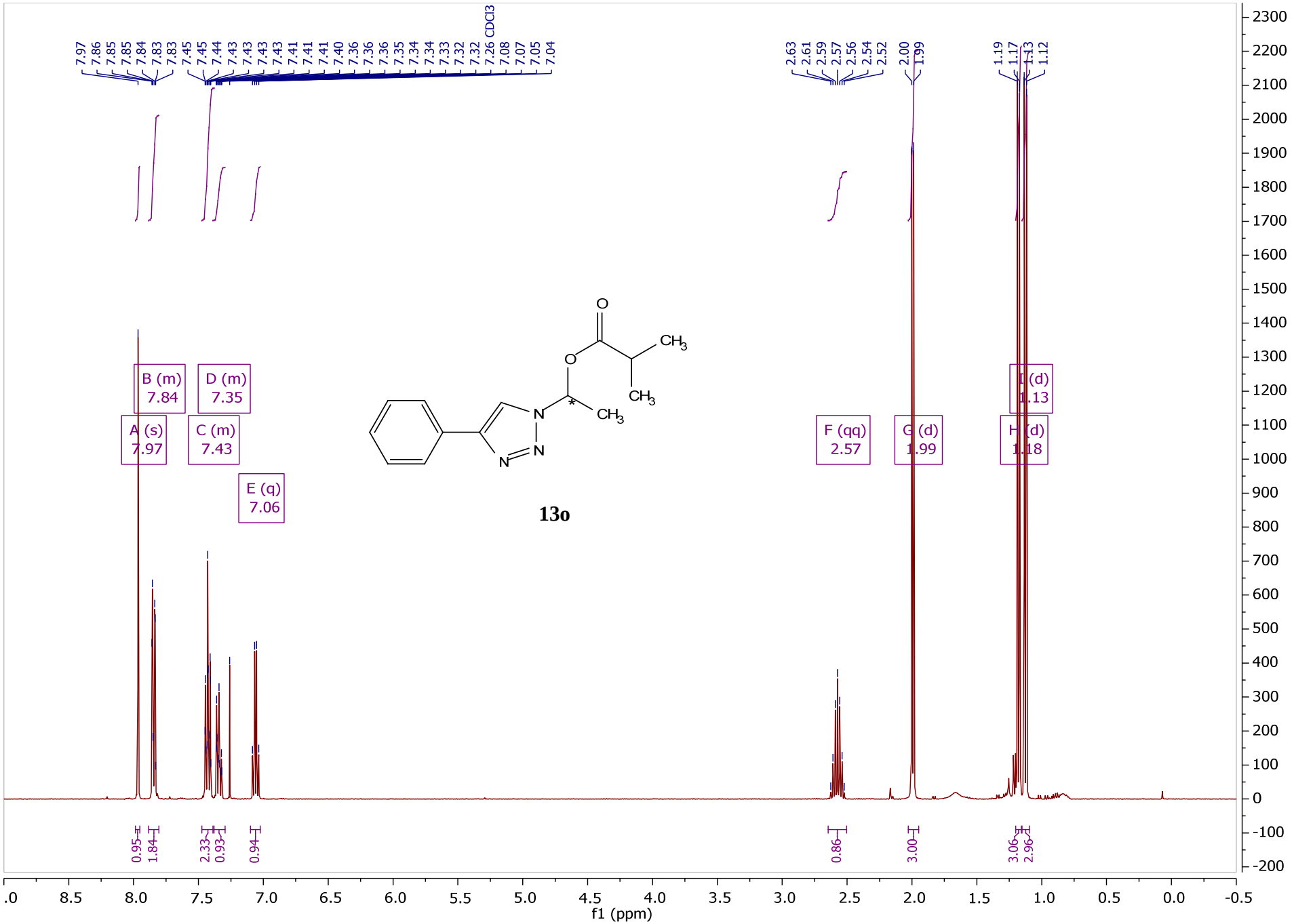

175.74
142.91
77.16 CDCl3
76.11
33.73
19.27
18.58
18.52
O
O
CH3
N
N
N
*
H3C
CH3
13j
f1 (ppm)

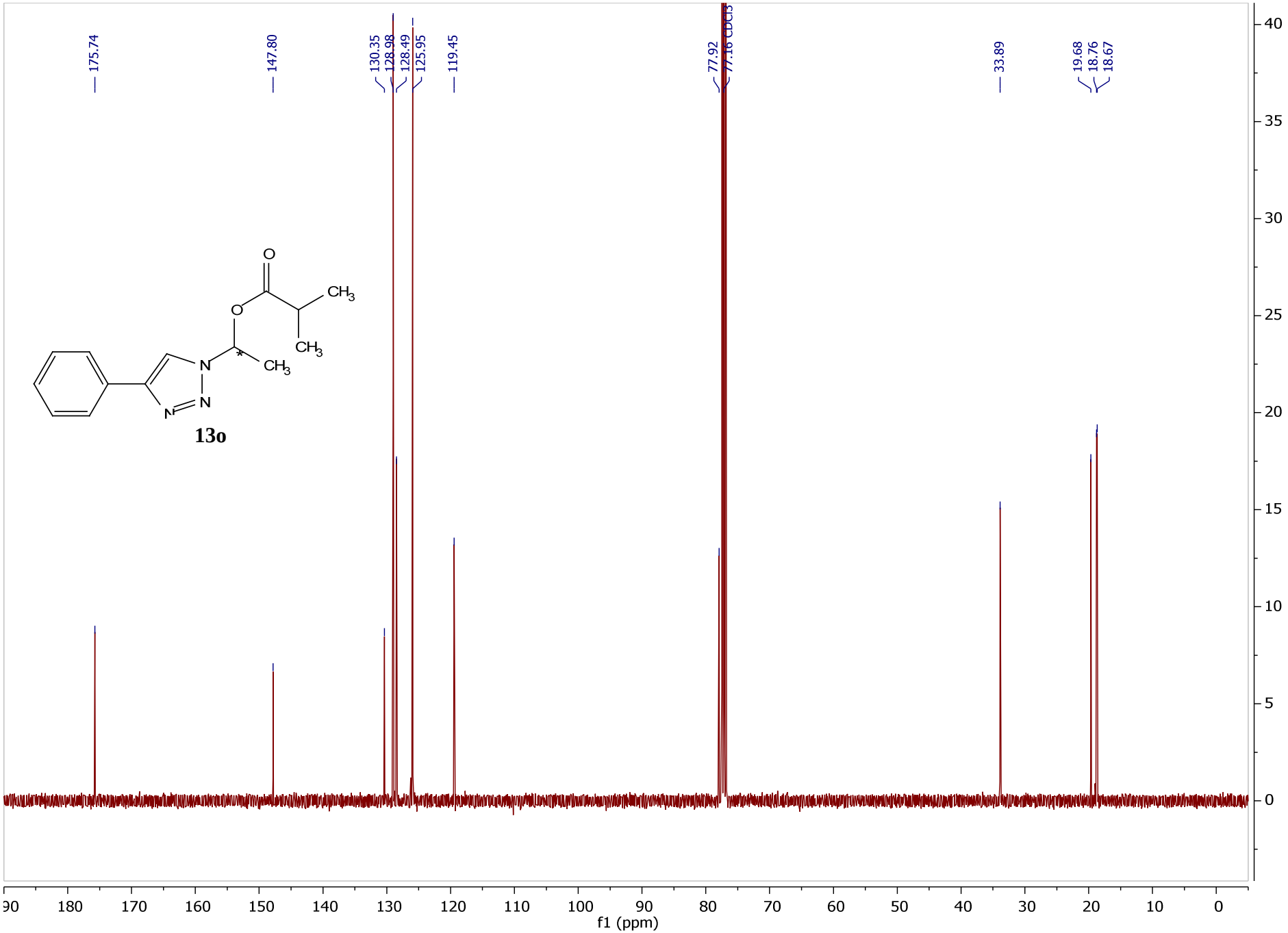

7.58
7.57
7.56
7.56
7.55
7.46
7.46
7.45
7.45
7.44
7.26 CDCl3
7.22
7.21
7.19
7.18
6.76
6.75
6.73
6.72
2.58
2.56
2.55
2.53
2.51
2.49
2.47
1.70
1.68
1.16
1.15
1.14
1.13
1.11
B (m)
7.45
A (m)
7.57
C (m)
7.19
D (q)
6.74
E (qq)
2.53
F (d)
1.69
G (m)
1.13
12k
1.78
2.60
1.68
0.86
0.98
3.00
6.32
f1 (ppm)

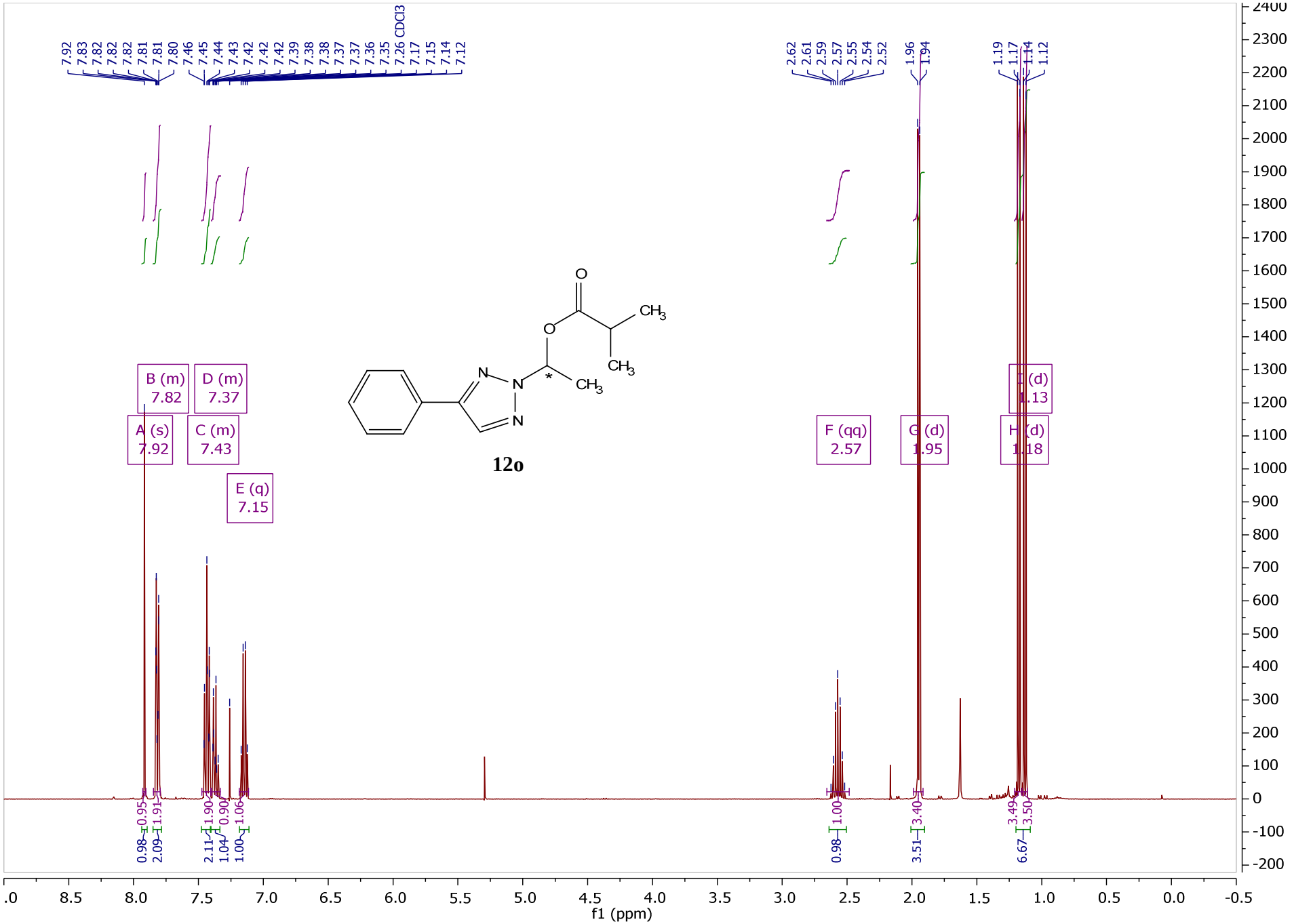

175.15
147.83
130.20
129.42
129.40
129.20
128.79
116.56
77.16 CDCl3
76.23
33.91
21.63
19.20
18.83
18.73
O
O
CH3
CH3
CH3
N
N
*
12k
f1 (ppm)


8.31
8.14
8.14
8.14
8.13
8.12
8.12
8.11
7.46
7.46
7.46
7.46
7.44
7.44
7.44
7.44
7.44
7.43
7.42
7.42
7.42
7.42
7.40
7.40
7.38
CDCl3
7.26
6.88
6.86
6.85
6.83
2.61
2.60
2.58
2.56
2.54
2.53
2.51
1.94
1.92
1.18
1.16
1.12
1.10
B (m)
8.13
A (s)
8.31
C (m)
7.43
D (q)
6.86
E (qq)
2.56
F (d)
1.93
G (d)
1.17
H (d)
1.11
O
O
CH3
CH3
N
N
*
CH3
N
12n
0.96
2.24
3.19
1.00
0.80
2.70
3.15
3.24
f1 (ppm)

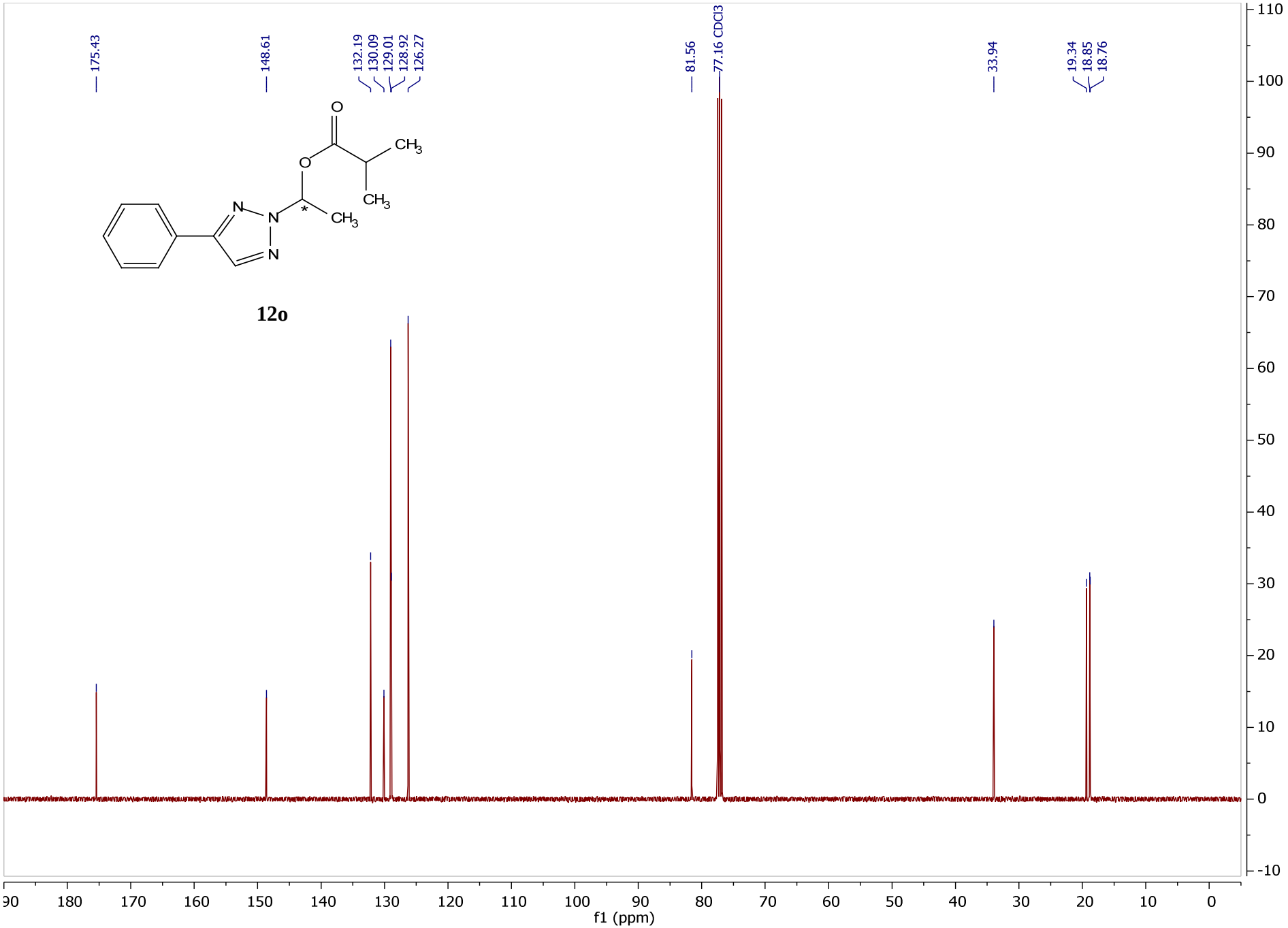

176.10
162.84
144.81
130.82
129.60
128.71
126.67
77.16 CDCl3
76.89
33.91
19.20
18.80
18.68
O
O
CH3
CH3
N
N
*
CH3
N
12n
77.16 CDCl3
76.89
79.0
78.5
78.0
77.5
77.0
76.5
76.0
f1 (ppm)
f1 (ppm)

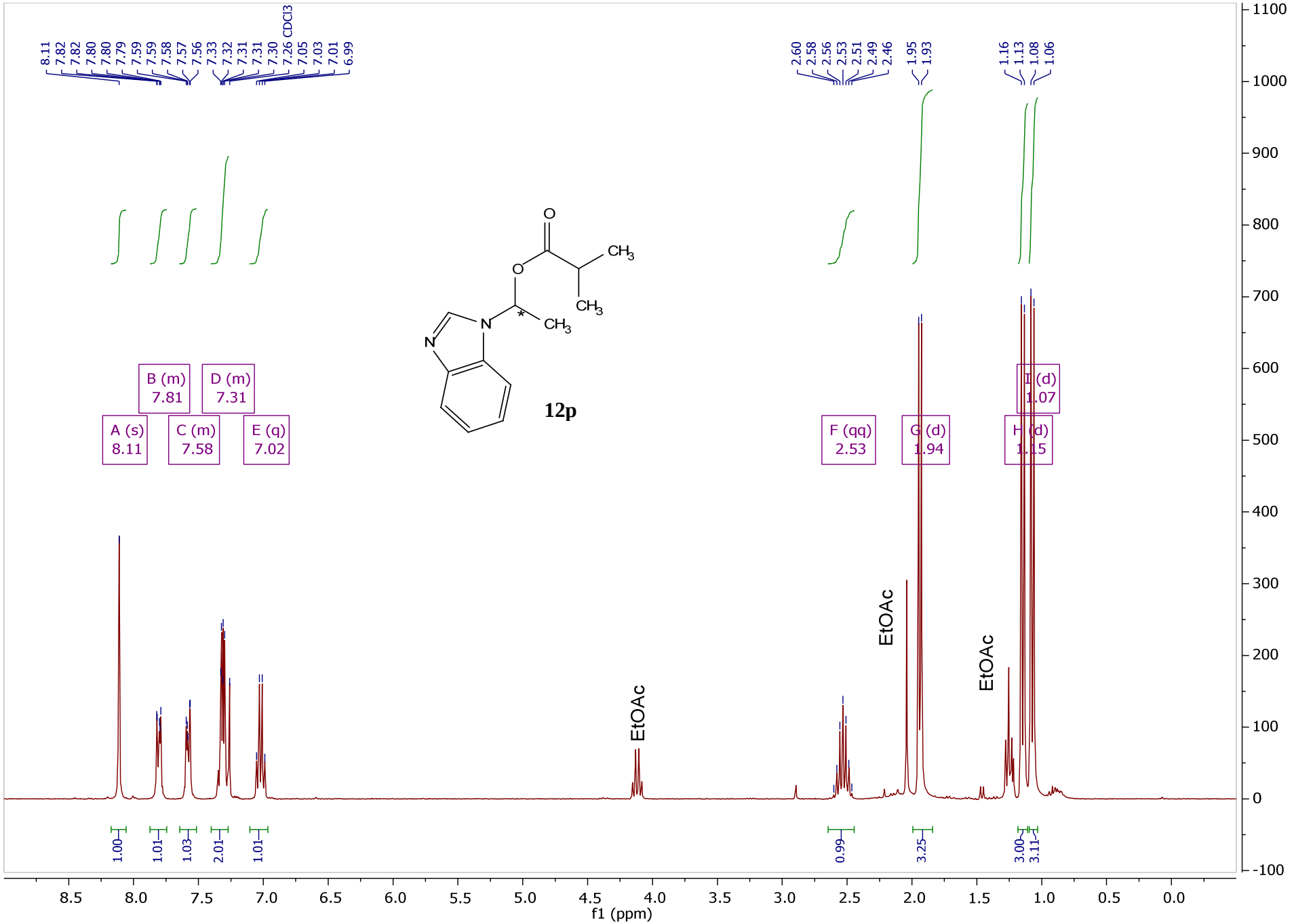

7.97 7.86 7.85 7.85 7.84 7.83 7.83 7.45 7.45 7.44 7.43 7.43 7.43 7.43 7.41 7.41 7.41 7.40 7.36 7.36 7.36 7.35 7.34 7.34 7.33 7.32 7.32 CDCl3 7.08 7.07 7.05 7.04
2.63 2.61 2.59 2.57 2.56 2.54 2.52 2.00 1.99 1.19 1.17 1.13 1.12
B (m) 7.84
D (m) 7.35
A (s) 7.97
C (m) 7.43
E (q) 7.06
F (qq) 2.57
G (d) 1.99
I (d) 1.13
H (d) 1.18
O
O
CH3
CH3
N
*
CH3
N
N
13o
0.95 1.84 2.33 0.93 0.94 0.86 3.00 3.06 2.96
f1 (ppm)

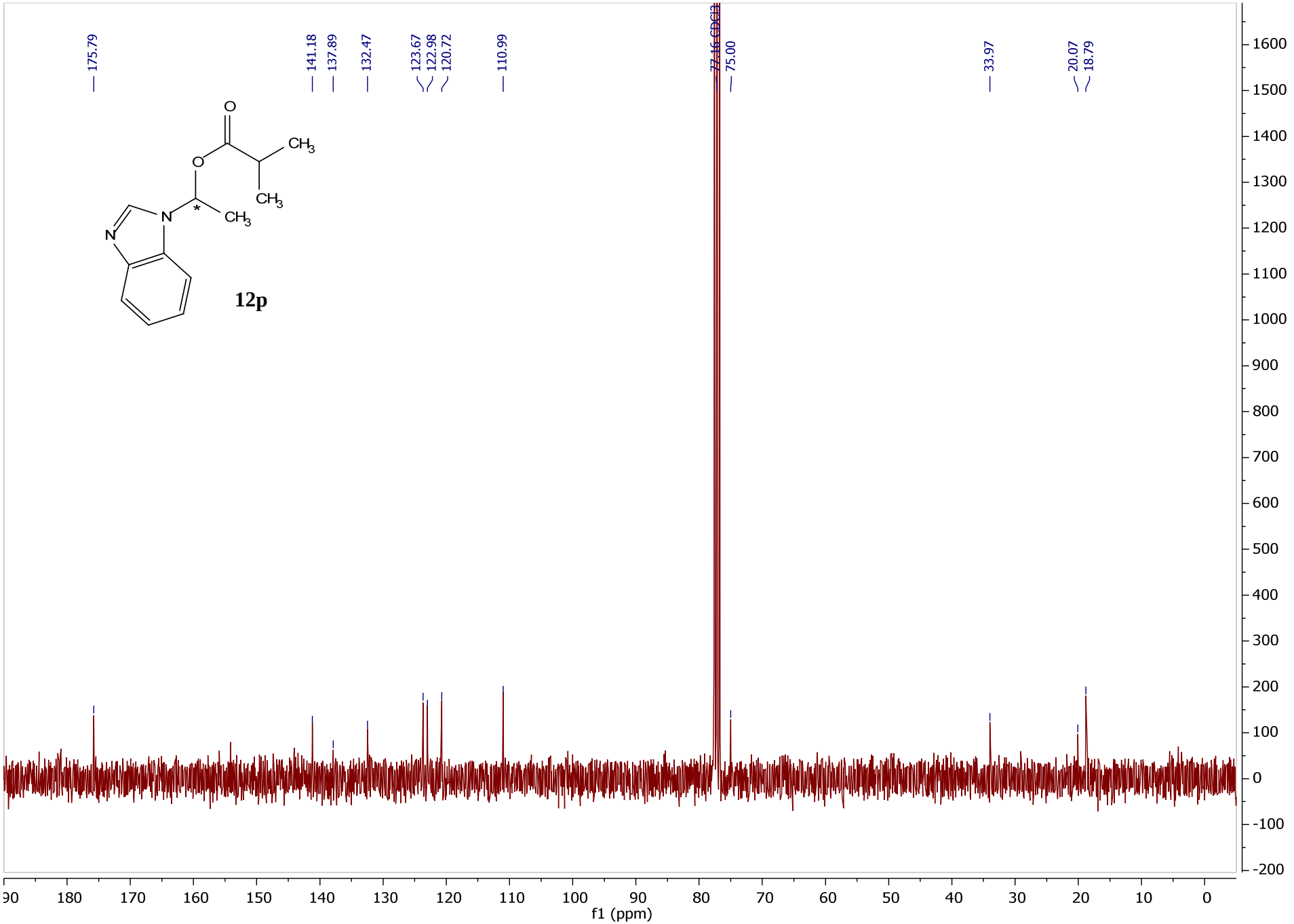

175.74
147.80
130.35
128.98
128.49
125.95
119.45
77.92
77.16 CDCl3
33.89
19.68
18.76
18.67
O
O
CH3
CH3
CH3
N
N
N
*
13o
f1 (ppm)

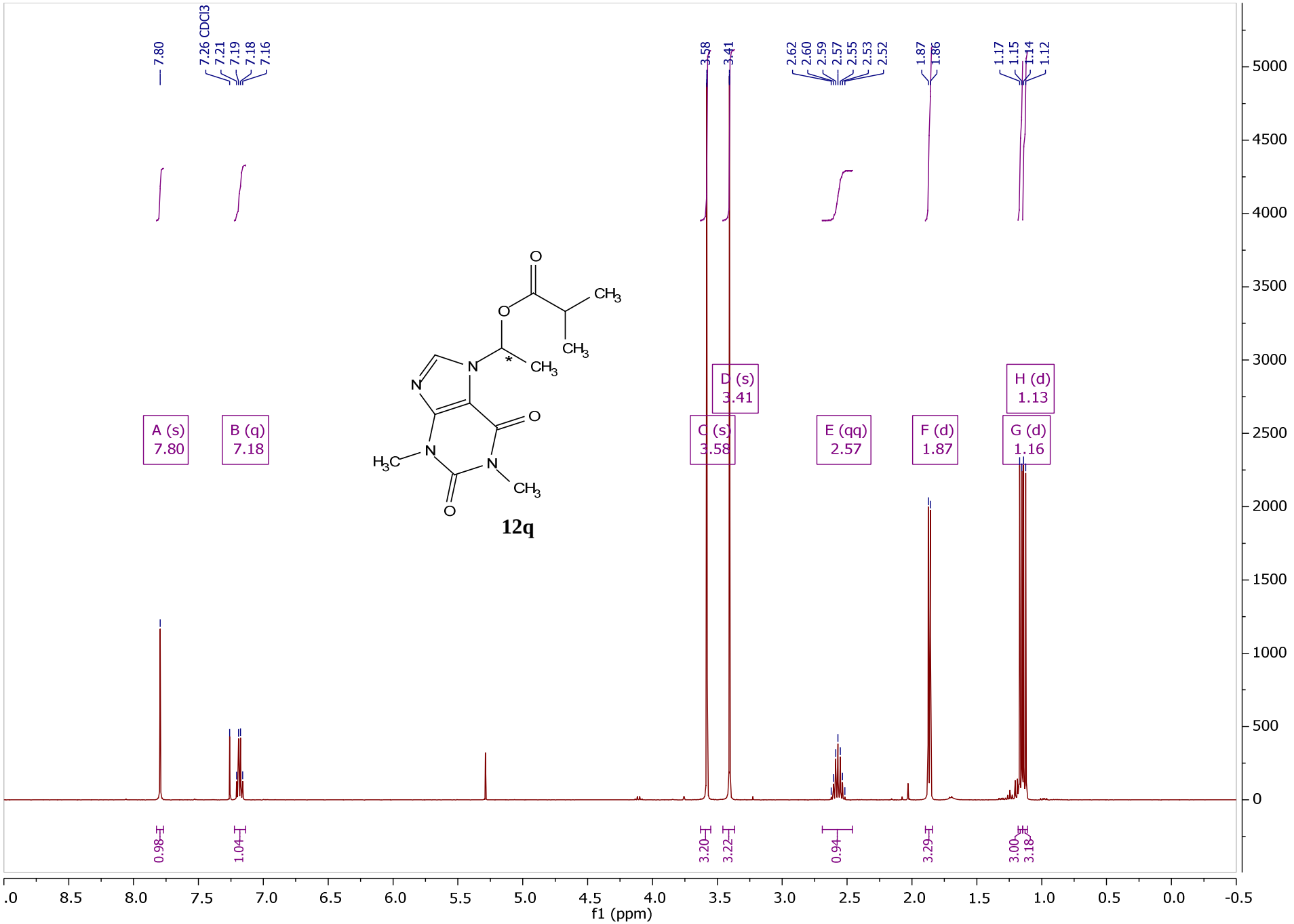

7.92 7.83 7.82 7.82 7.82 7.81 7.81 7.80 7.46 7.45 7.44 7.43 7.42 7.42 7.42 7.39 7.38 7.38 7.37 7.37 7.36 7.35 7.26 CDCl3 7.17 7.15 7.14 7.12
2.62 2.61 2.59 2.57 2.55 2.54 2.52 1.96 1.94 1.19 1.17 1.14 1.12
B (m) 7.82
D (m) 7.37
A (s) 7.92
C (m) 7.43
E (q) 7.15
F (qq) 2.57
G (d) 1.95
H (d) 1.18
I (d) 1.13
0.98 2.09 2.11 1.90 1.04 0.90 1.00 1.06 0.98 3.51 3.49 3.50 6.67
f1 (ppm)

12o

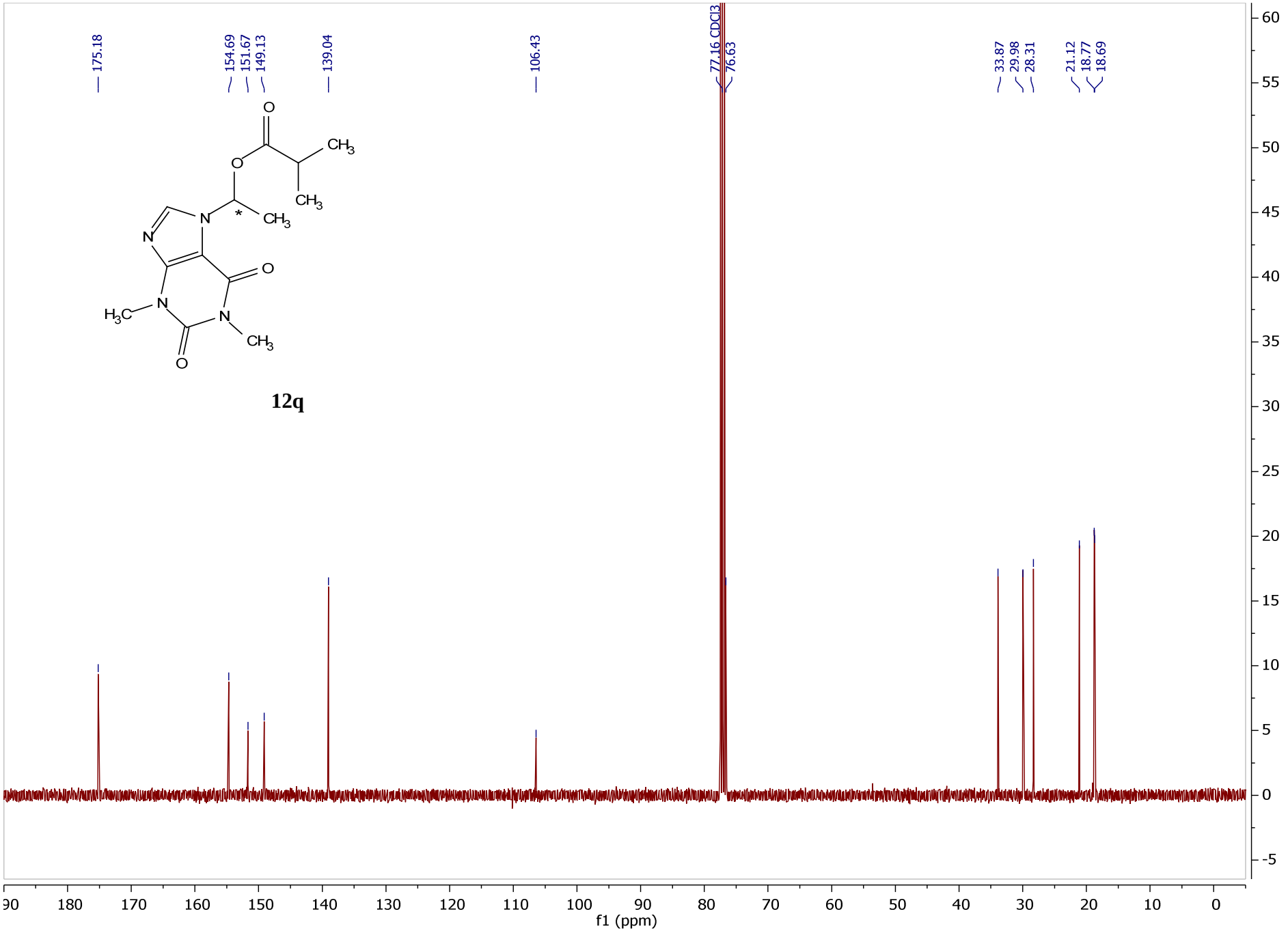

175.43
148.61
132.19
130.09
129.01
128.92
126.27
81.56
77.16 CDCl3
33.94
19.34
18.85
18.76
O
O
CH3
CH3
N
N
*
CH3
N
12o
f1 (ppm)

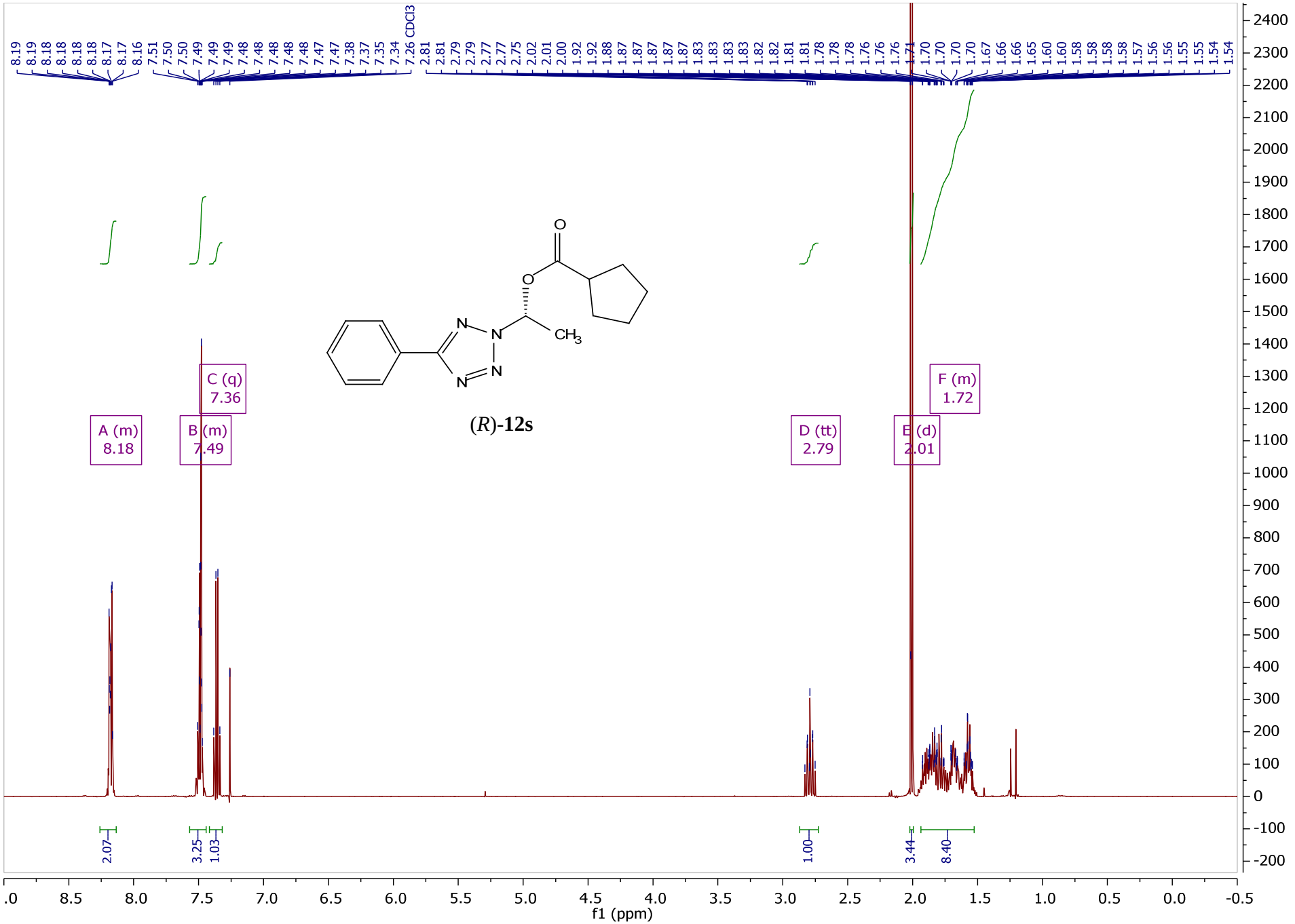

8.11
7.82
7.82
7.80
7.80
7.79
7.59
7.59
7.58
7.57
7.56
7.33
7.32
7.31
7.31
7.30
7.26 CDCl3
7.05
7.03
7.01
6.99
2.60
2.58
2.56
2.53
2.51
2.49
2.46
1.95
1.93
1.16
1.13
1.08
1.06
O
O
CH3
CH3
N
N
*
CH3
12p
B (m) 7.81
D (m) 7.31
A (s) 8.11
C (m) 7.58
E (q) 7.02
F (qq) 2.53
G (d) 1.94
I (d) 1.07
H (d) 1.15
EtOAc
EtOAc
EtOAc
1.00
1.01
1.03
2.01
1.01
0.99
3.25
3.00
3.11
f1 (ppm)


175.79
141.18
137.89
132.47
123.67
122.98
120.72
110.99
77.16 CDCl3
75.00
33.97
20.07
18.79
O
O
CH3
CH3
N
*
CH3
N
12p
f1 (ppm)

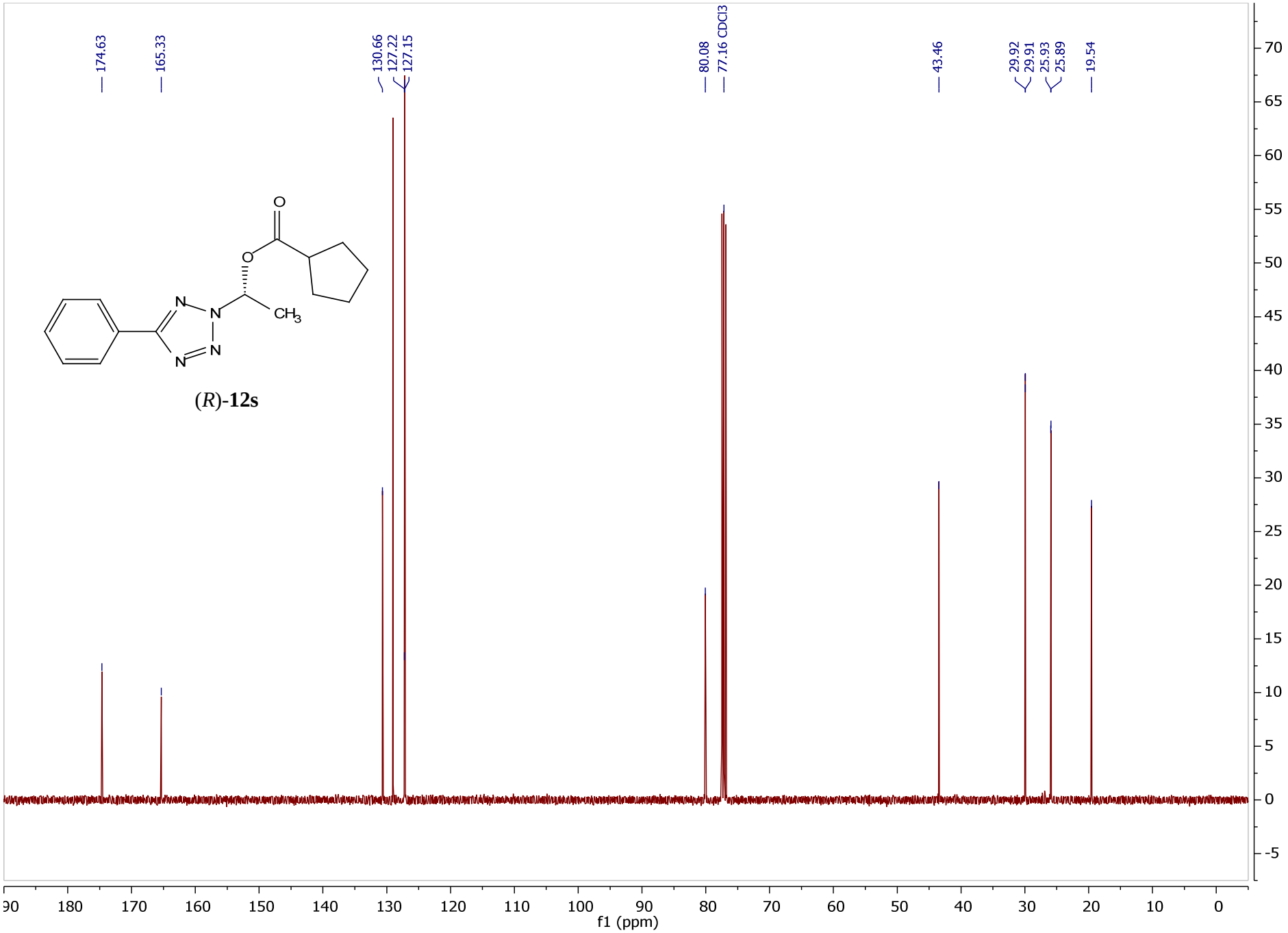

7.80
7.26 CDCl3
7.21
7.19
7.18
7.16
3.58
3.41
2.62
2.60
2.59
2.57
2.55
2.53
2.52
1.87
1.86
1.17
1.15
1.14
1.12
A (s) 7.80
B (q) 7.18
C (s) 3.58
D (s) 3.41
E (qq) 2.57
F (d) 1.87
G (d) 1.16
H (d) 1.13
0.98
1.04
3.20
3.22
0.94
3.29
3.00
3.18
f1 (ppm)

12q

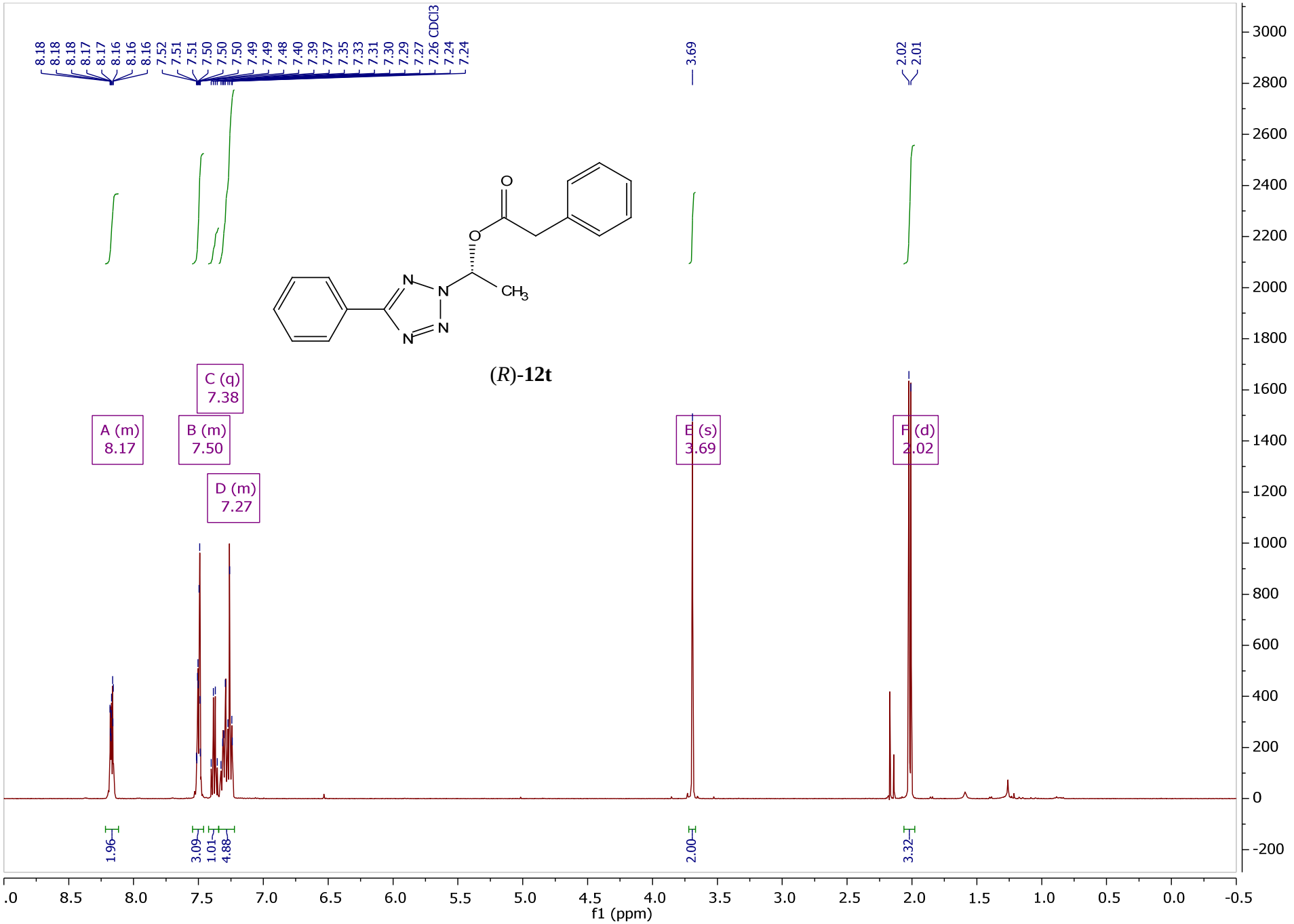

175.18
154.69
151.67
149.13
139.04
106.43
77.16 CDCl3
76.63
33.87
29.98
28.31
21.12
18.77
18.69
O
O
CH3
CH3
N
*
CH3
N
O
N
H3C
N
CH3
O
12q
f1 (ppm)

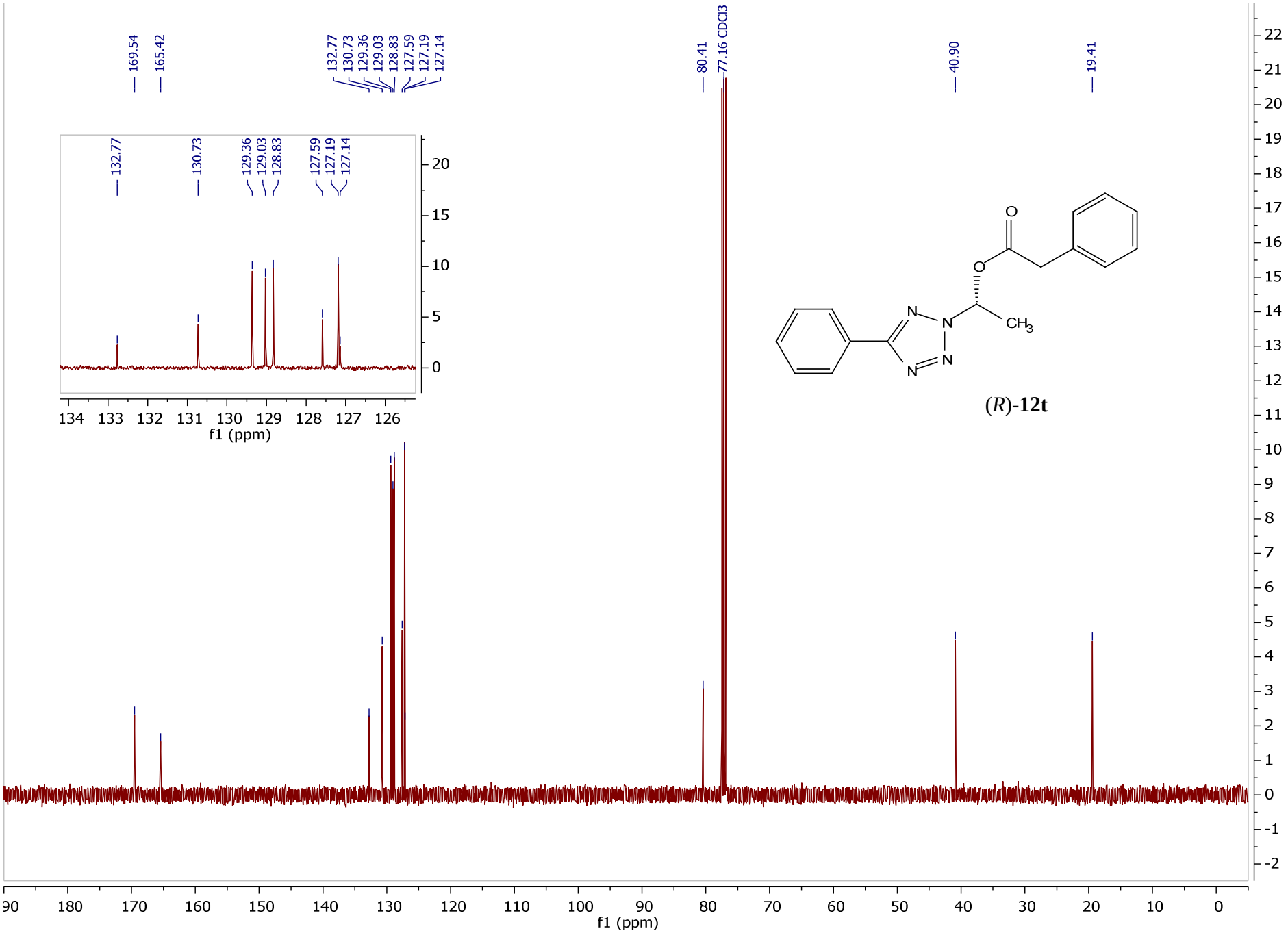

A (m)
8.18
B (m)
7.49
C (q)
7.36
D (tt)
2.79
E (d)
2.01
F (m)
1.72
2.07
3.25
1.03
1.00
3.44
8.40
f1 (ppm)

(*R*)-**12s**

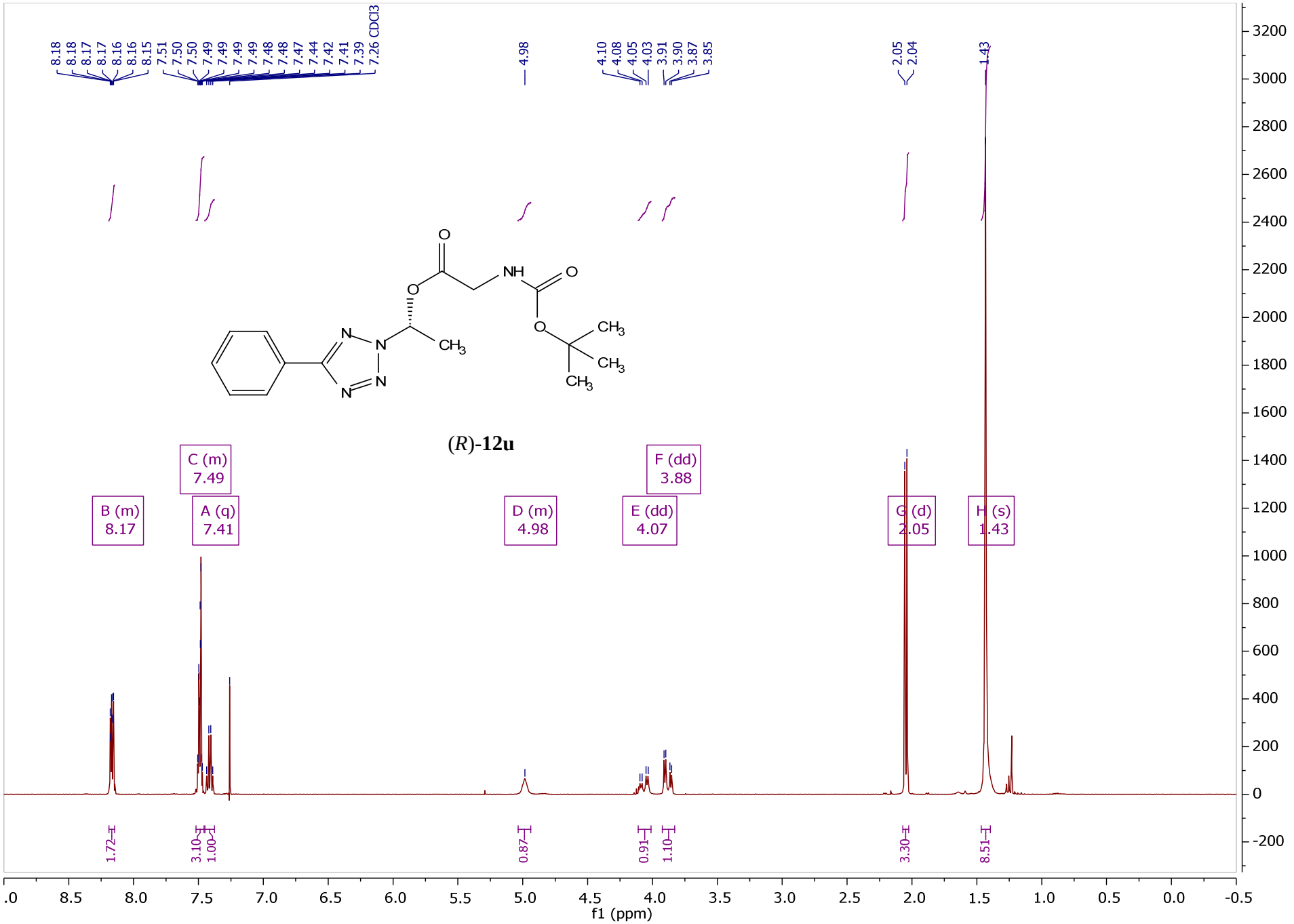

174.63
165.33
130.66
127.22
127.15
80.08
77.16 CDCl3
43.46
29.92
29.91
25.93
25.89
19.54
O
O
N
N
N
N
CH3
f1 (ppm)

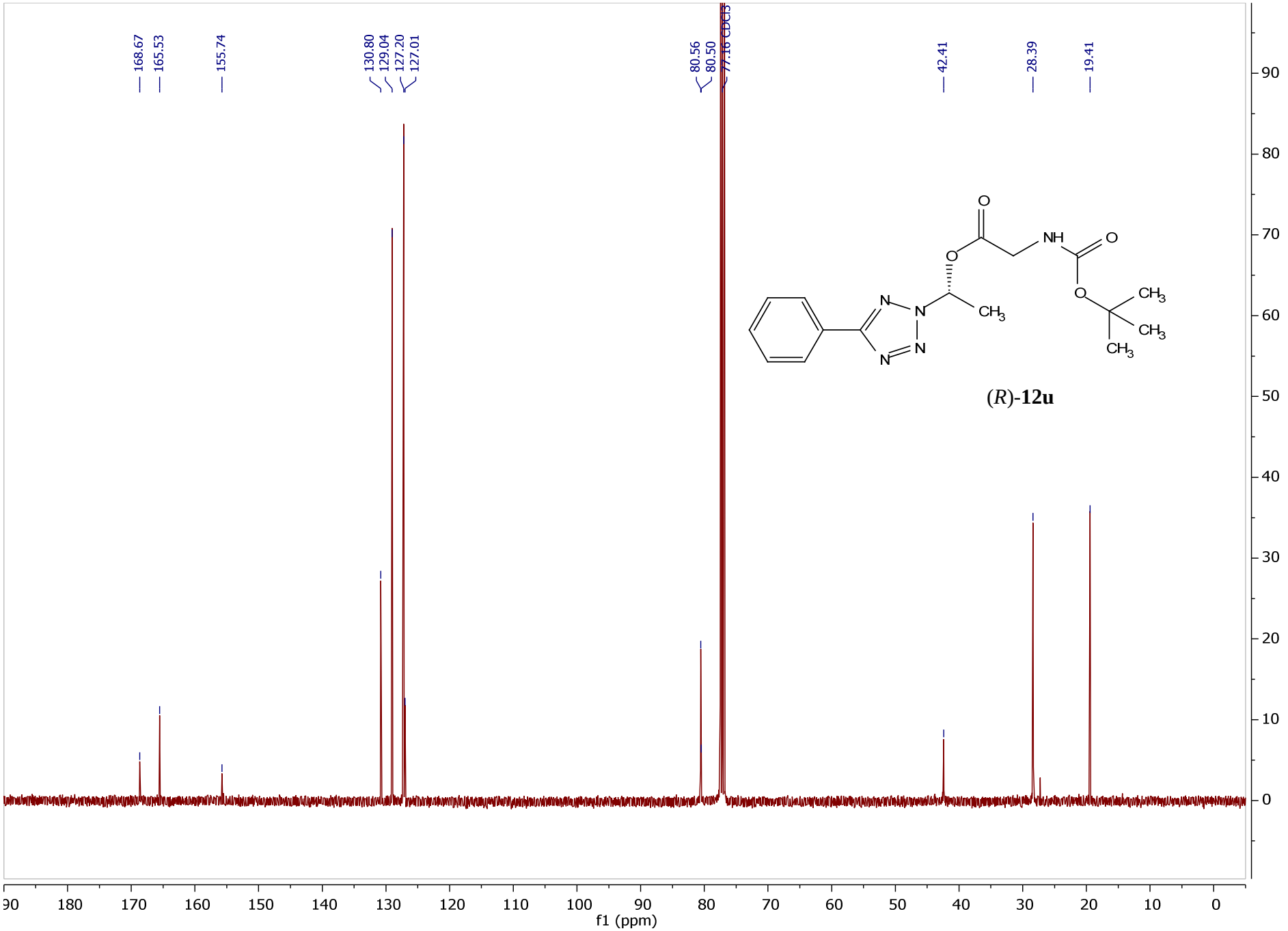
(*R*)-**12s**


8.18
8.18
8.18
8.17
8.17
8.16
8.16
8.16
7.52
7.51
7.51
7.50
7.50
7.50
7.49
7.49
7.48
7.40
7.39
7.37
7.35
7.33
7.31
7.30
7.29
7.27
7.26 CDCl3
7.24
7.24
3.69
2.02
2.01
O
O
N
N
N
N
CH3
(R)-12t
A (m) 8.17
B (m) 7.50
C (q) 7.38
D (m) 7.27
E (s) 3.69
F (d) 2.02
1.96
3.09
1.01
4.88
2.00
3.32
f1 (ppm)

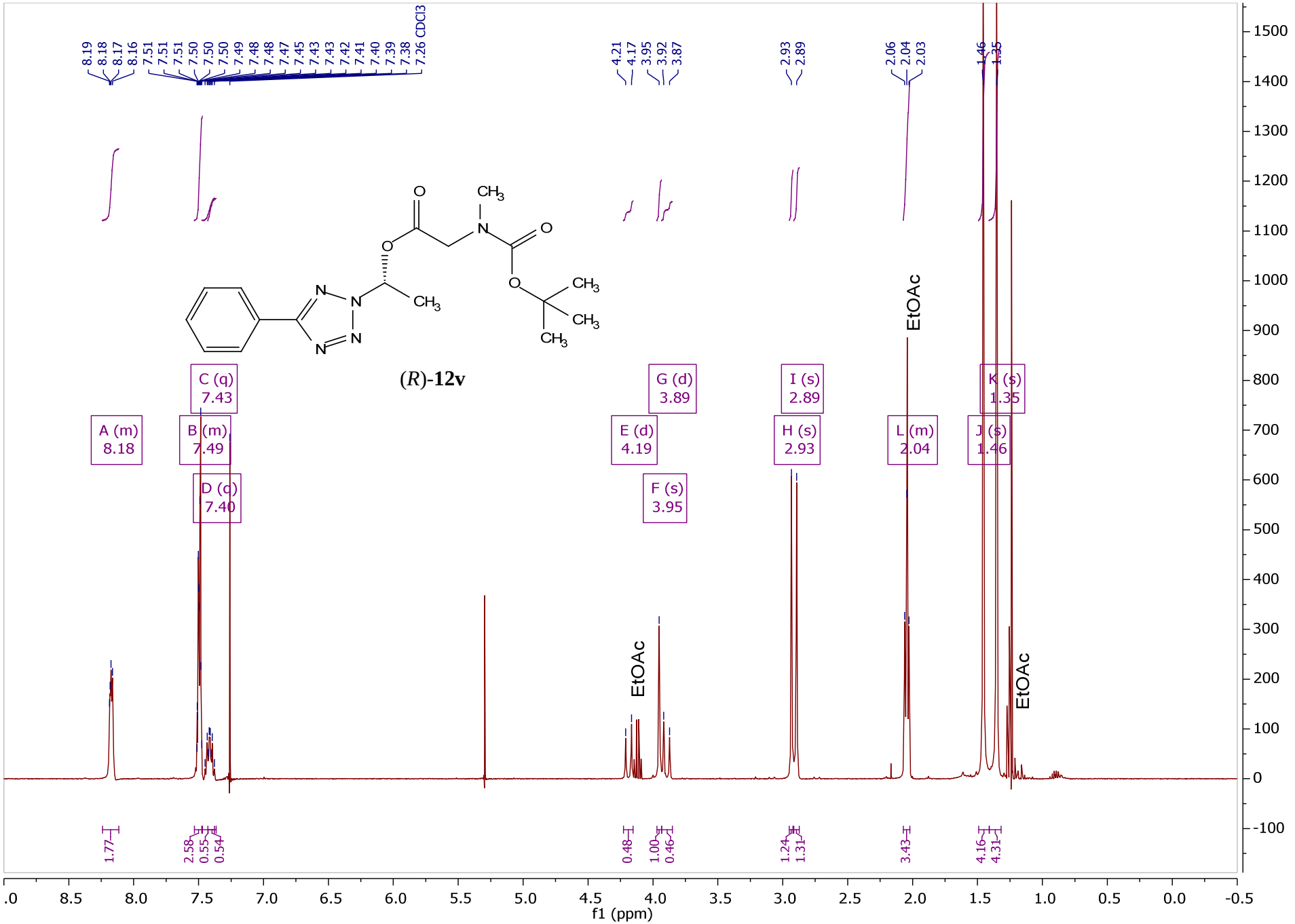

169.54
165.42
132.77
130.73
129.36
129.03
128.83
127.59
127.19
127.14
80.41
77.16 CDCl3
40.90
19.41
f1 (ppm)
O
O
N
N
N
N
CH3

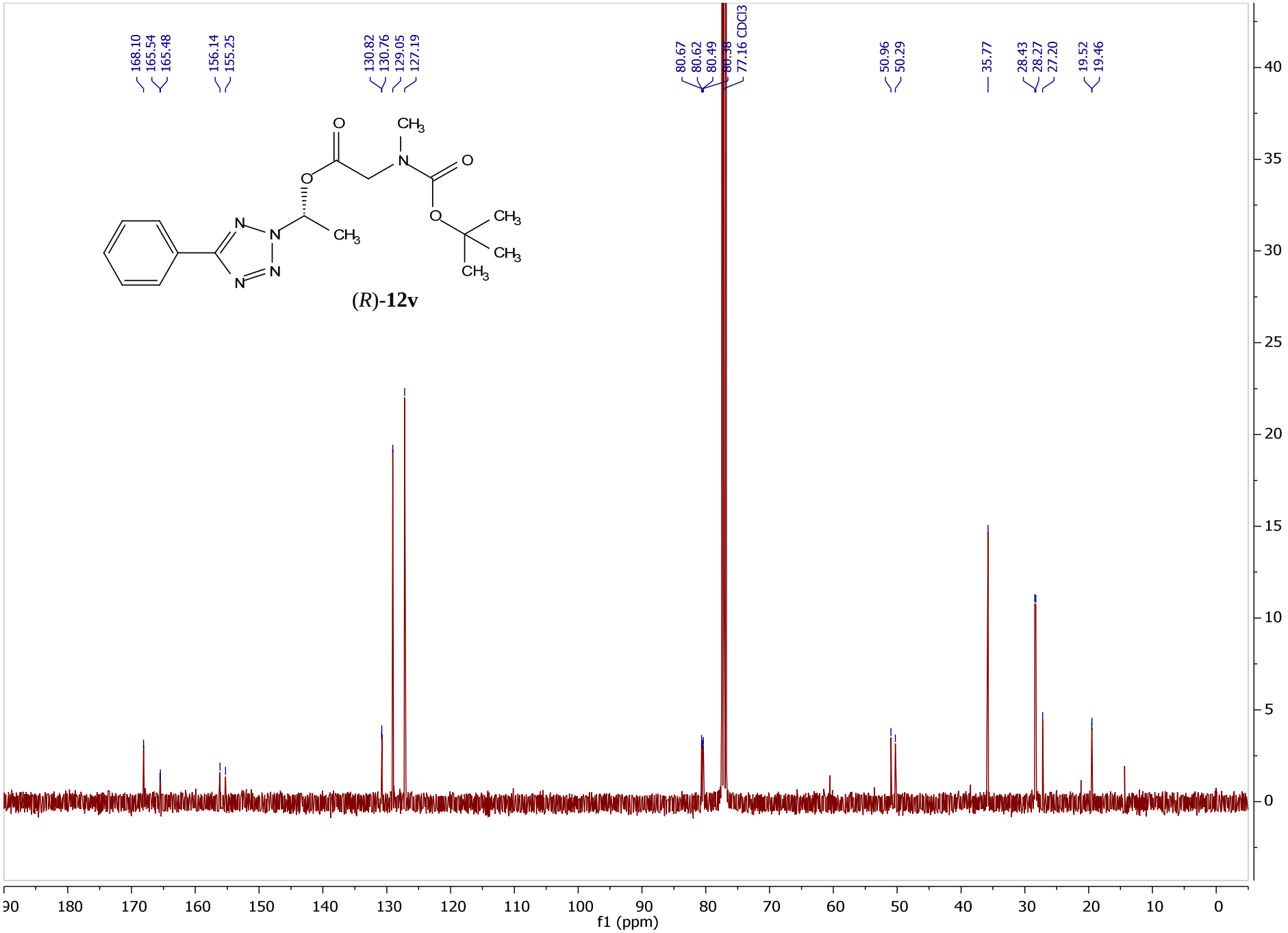
(*R*)-**12t**


8.18
8.18
8.17
8.17
8.16
8.16
8.15
7.51
7.50
7.50
7.49
7.49
7.49
7.49
7.48
7.48
7.47
7.44
7.42
7.41
7.39
7.26 CDCl3
4.98
4.10
4.08
4.05
4.03
3.91
3.90
3.87
3.85
2.05
2.04
1.43
O
NH
O
O
O
CH3
CH3
CH3
N
N
N
N
CH3
(R)-12u
B (m)
8.17
C (m)
7.49
A (q)
7.41
D (m)
4.98
F (dd)
3.88
E (dd)
4.07
G (d)
2.05
H (s)
1.43
1.72
3.10
1.00
0.87
0.91
1.10
3.30
8.51
f1 (ppm)

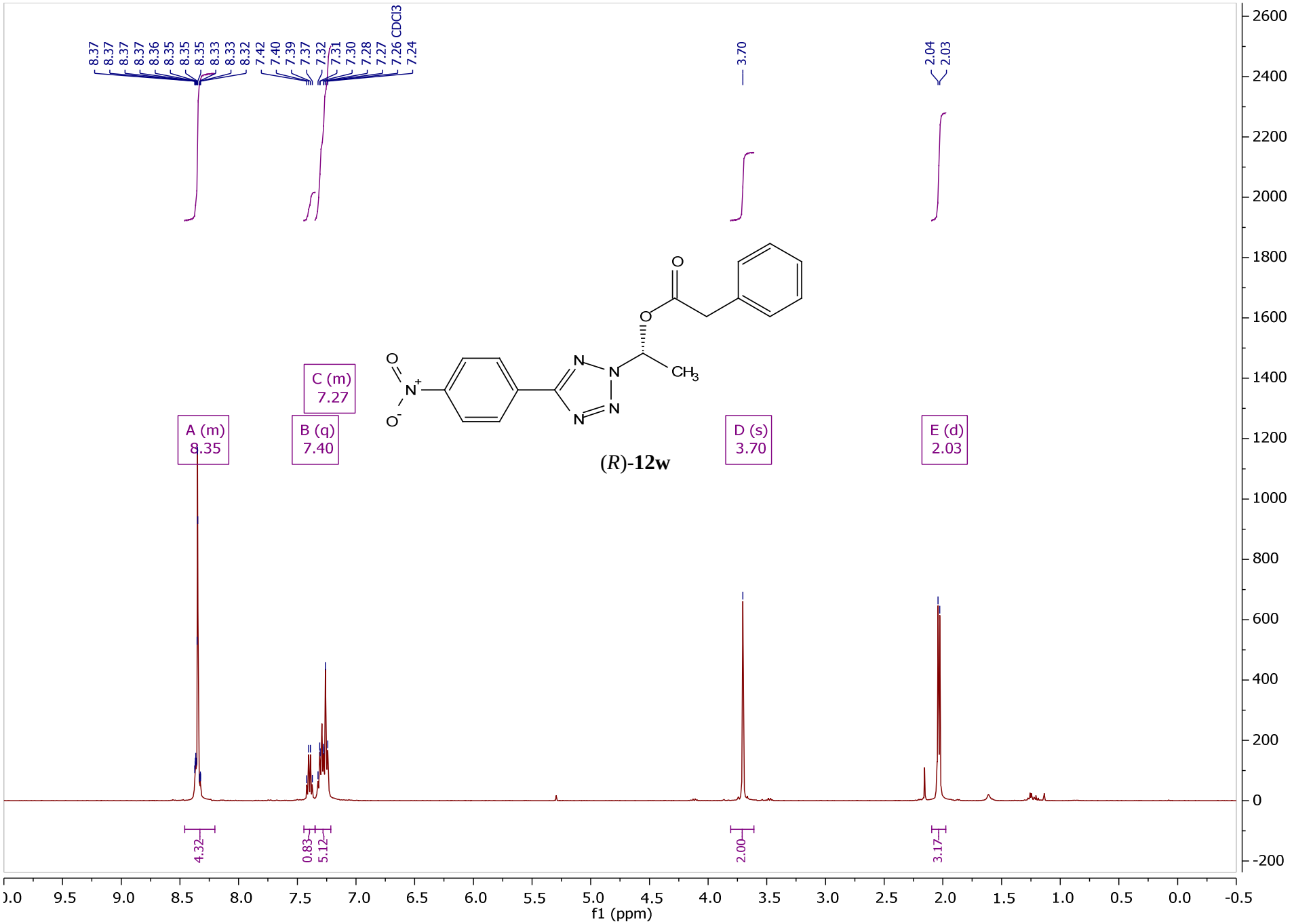

168.67
165.53
155.74
130.80
129.04
127.20
127.01
80.56
80.50
77.16 CDCl3
42.41
28.39
19.41
f1 (ppm)

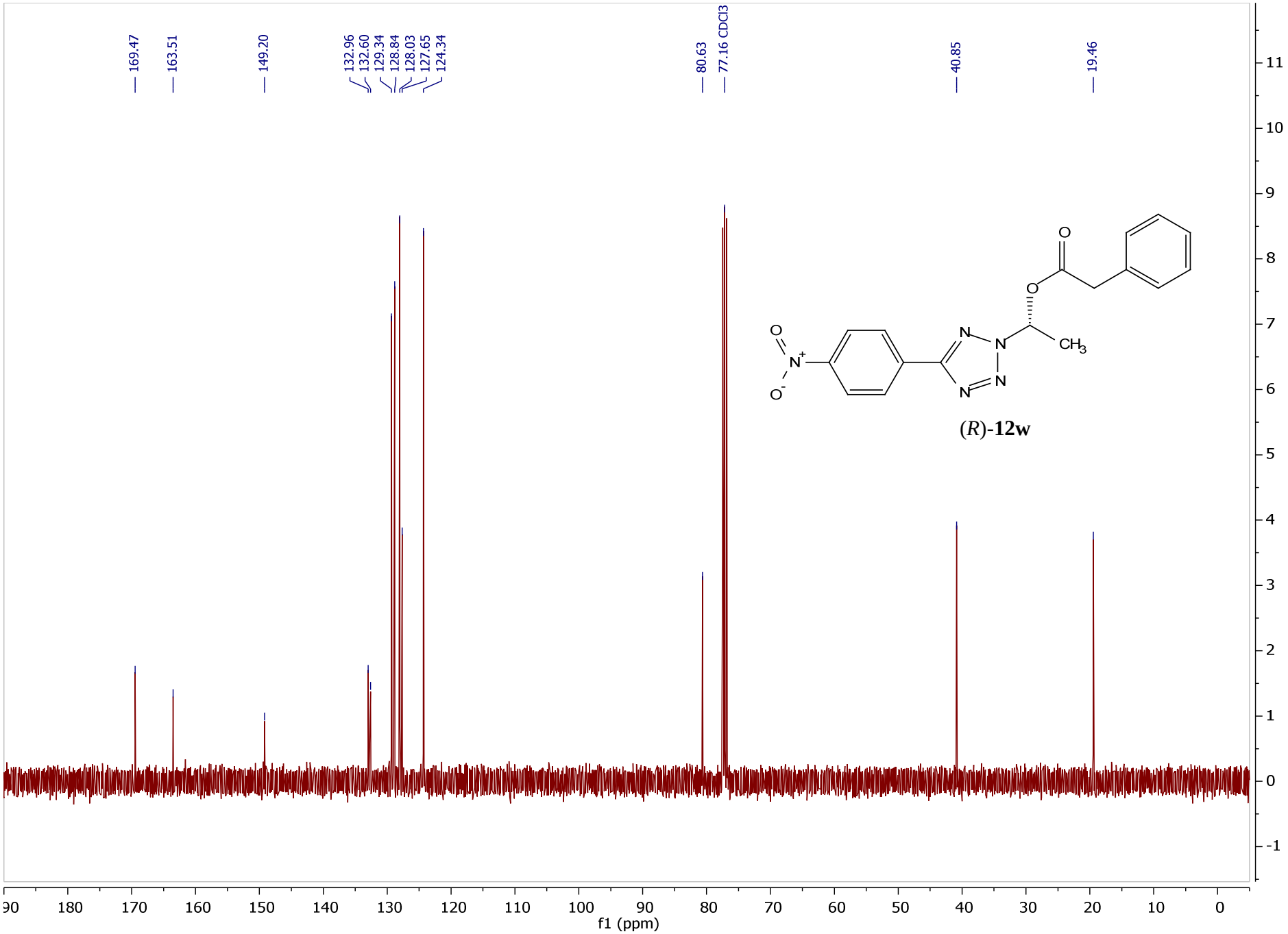
(*R*)-**12u**


8.19 8.18 8.17 8.16 7.51 7.51 7.51 7.50 7.50 7.50 7.49 7.48 7.48 7.47 7.45 7.43 7.43 7.42 7.41 7.40 7.39 7.38 7.26 CDCl3
4.21 4.17 3.95 3.92 3.87
2.93 2.89
2.06 2.04 2.03
1.46 1.35
(R)-12v
A (m) 8.18
B (m) 7.49
C (q) 7.43
D (d) 7.40
E (d) 4.19
F (s) 3.95
G (d) 3.89
H (s) 2.93
I (s) 2.89
L (m) 2.04
J (s) 1.46
K (s) 1.35
EtOAc
EtOAc
EtOAc
1.77 2.58 0.55 0.54 0.48 1.00 0.46 1.24 1.31 3.43 4.16 4.31
f1 (ppm)

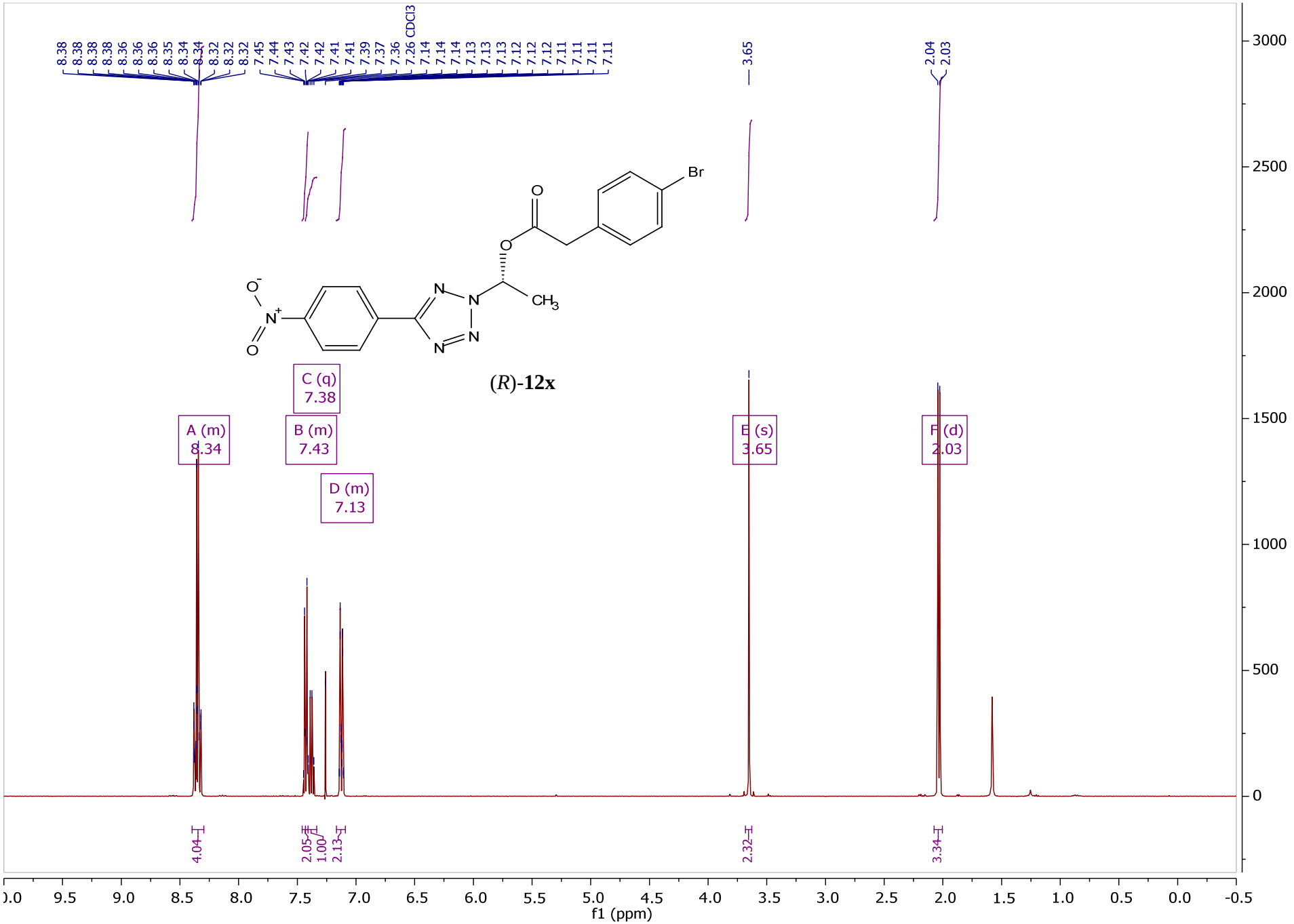

168.10
165.54
165.48
156.14
155.25
130.82
130.76
129.05
127.19
80.67
80.62
80.49
80.38
77.16 CDCl3
50.96
50.29
35.77
28.43
28.27
27.20
19.52
19.46
f1 (ppm)

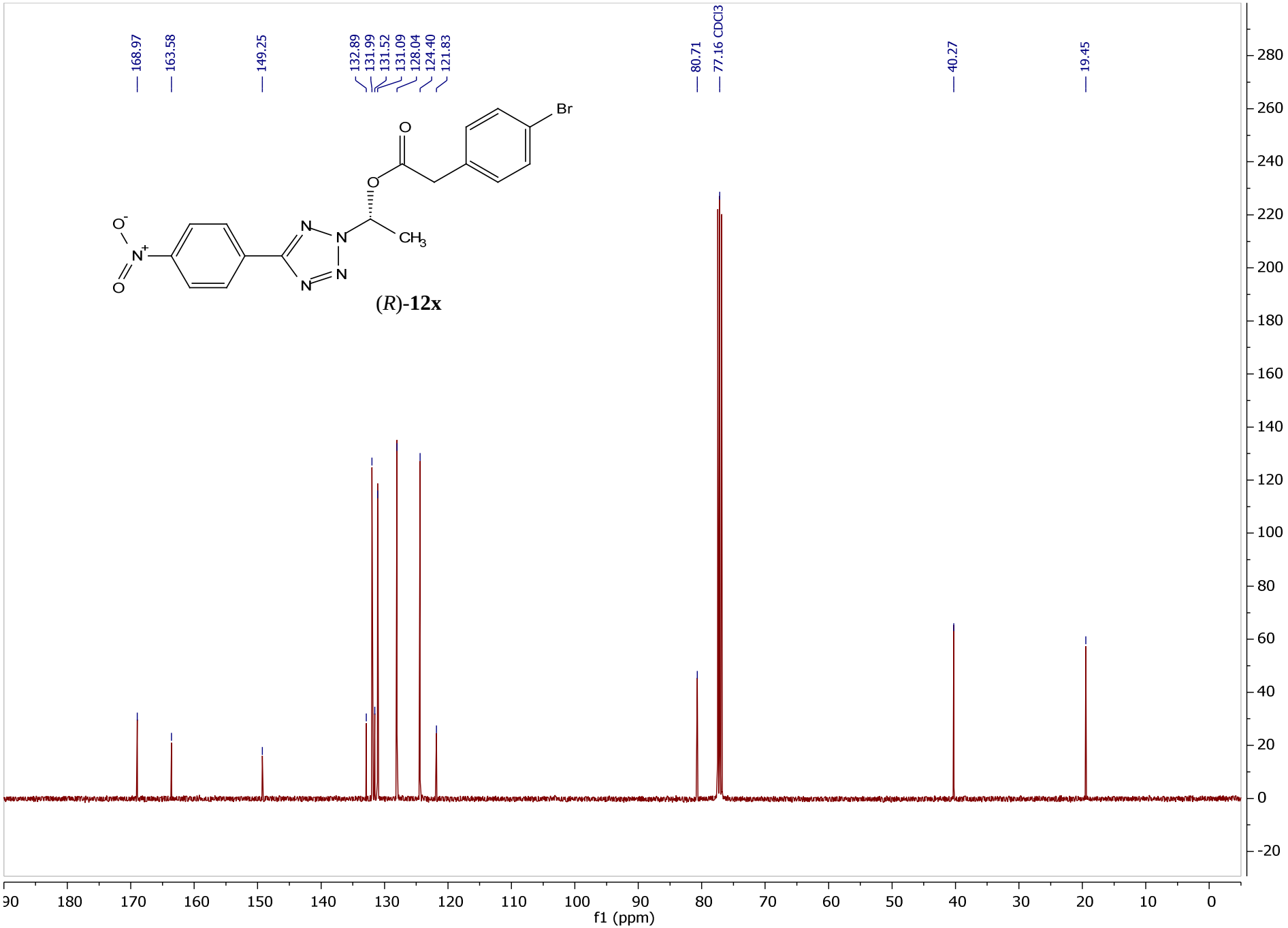
(*R*)-**12v**


8.37
8.37
8.37
8.37
8.36
8.35
8.35
8.35
8.33
8.33
8.32
7.42
7.40
7.39
7.37
7.32
7.31
7.30
7.28
7.27
7.26 CDCl3
7.24
3.70
2.04
2.03
A (m)
8.35
B (q)
7.40
C (m)
7.27
D (s)
3.70
E (d)
2.03
(R)-12w
4.32
0.83
5.12
2.00
3.17
f1 (ppm)

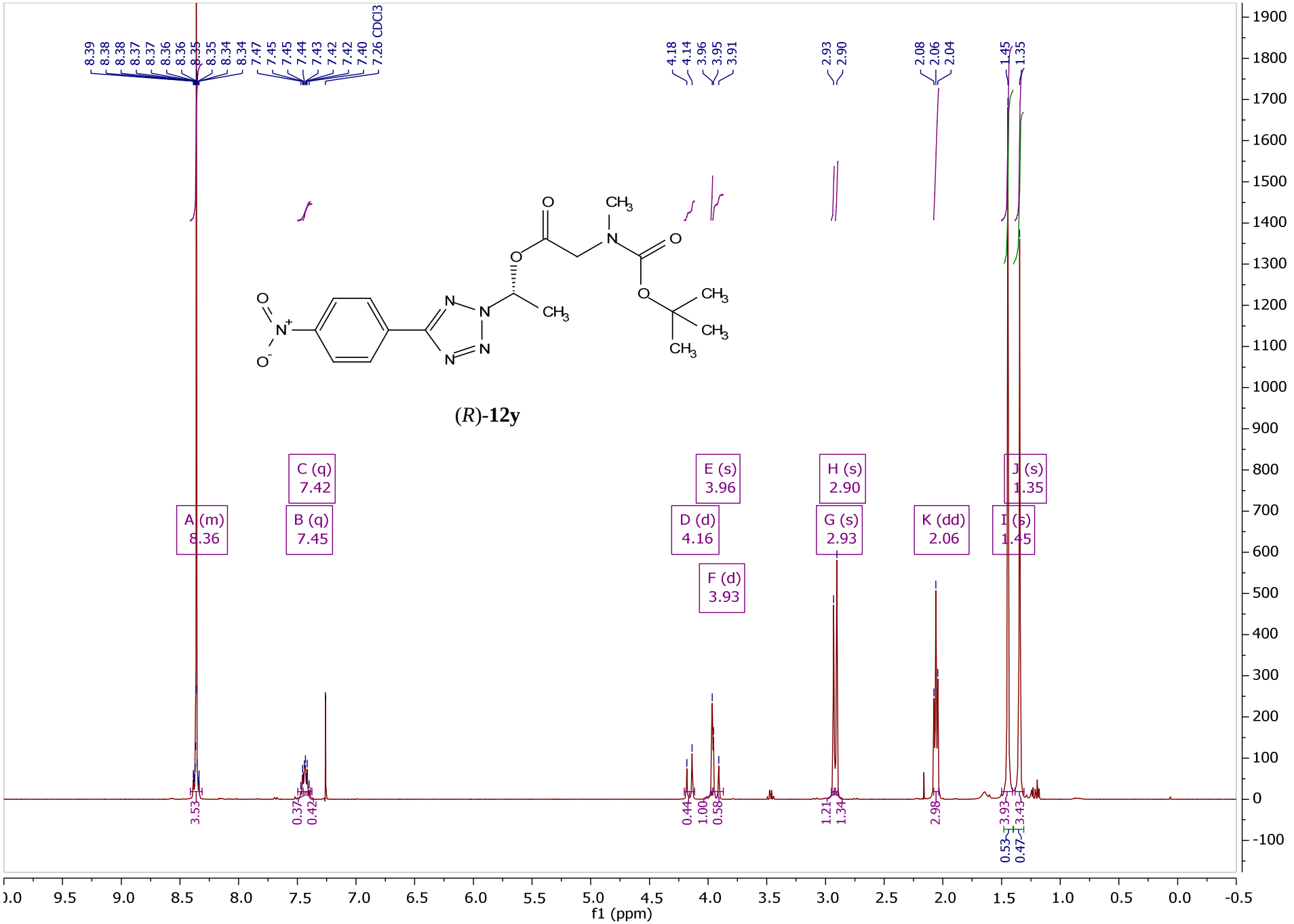

169.47
163.51
149.20
132.96
132.60
129.34
128.84
128.03
127.65
124.34
80.63
77.16 CDCl3
40.85
19.46
f1 (ppm)

(*R*)-**12w**

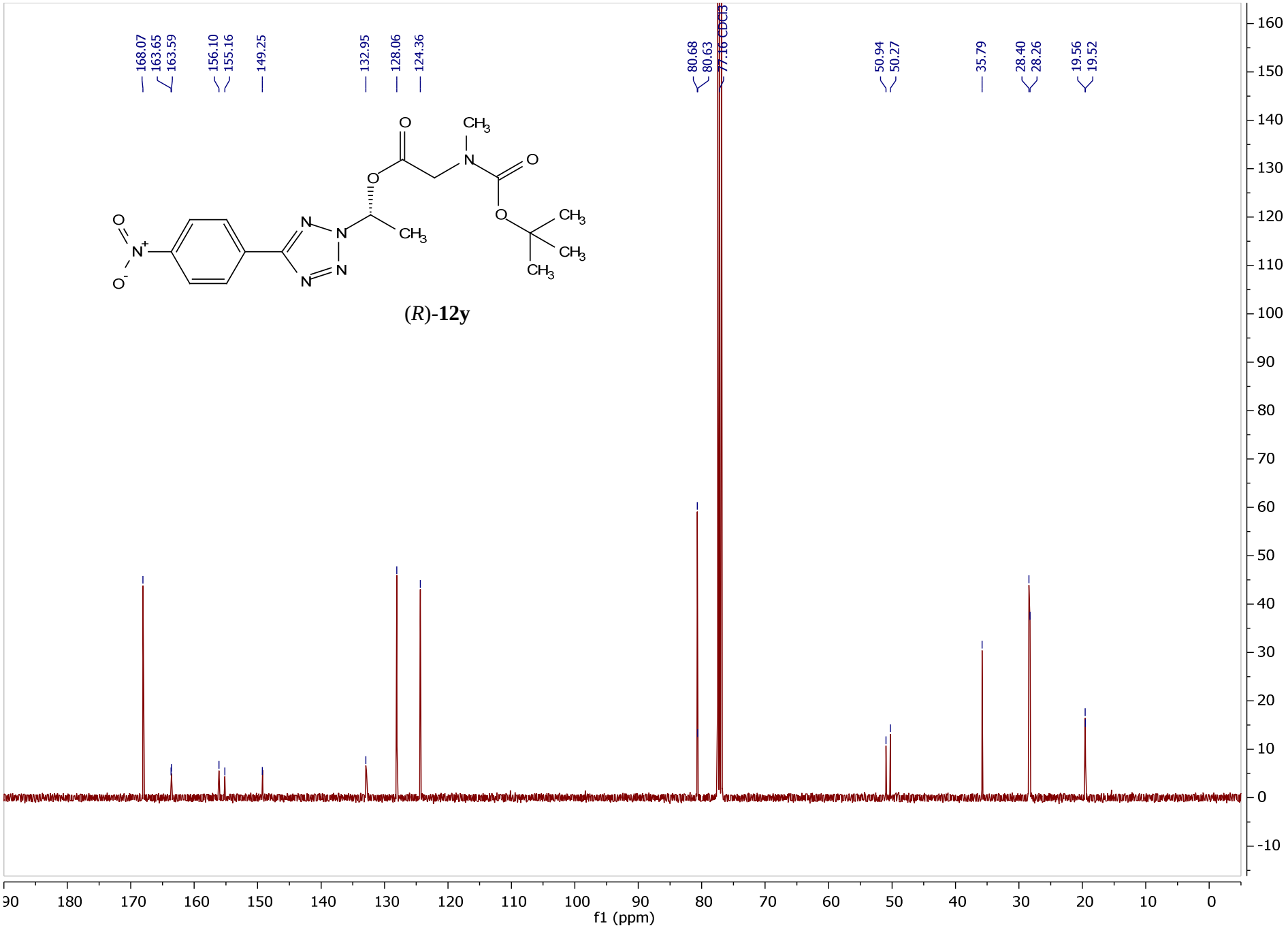

8.38 8.38 8.38 8.38 8.36 8.36 8.36 8.35 8.34 8.34 8.32 8.32 8.32
7.45 7.44 7.43 7.42 7.42 7.41 7.41 7.39 7.37 7.36 7.26 CDCl3 7.14 7.14 7.14 7.13 7.13 7.13 7.12 7.12 7.12 7.11 7.11 7.11 7.11
3.65
2.04 2.03
Br
O
O
O
N+
O-
N
N
N
N
CH3
(R)-12x
A (m) 8.34
B (m) 7.43
C (q) 7.38
D (m) 7.13
E (s) 3.65
F (d) 2.03
4.04
2.05
1.00
2.13
2.32
3.34
3000
2500
2000
1500
1000
500
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 -0.5
f1 (ppm)


168.97
163.58
149.25
132.89
131.99
131.52
131.09
128.04
124.40
121.83
80.71
77.16 CDCl3
40.27
19.45
Br
O
O
N
N
N
N
CH3
O-
N+
O
f1 (ppm)

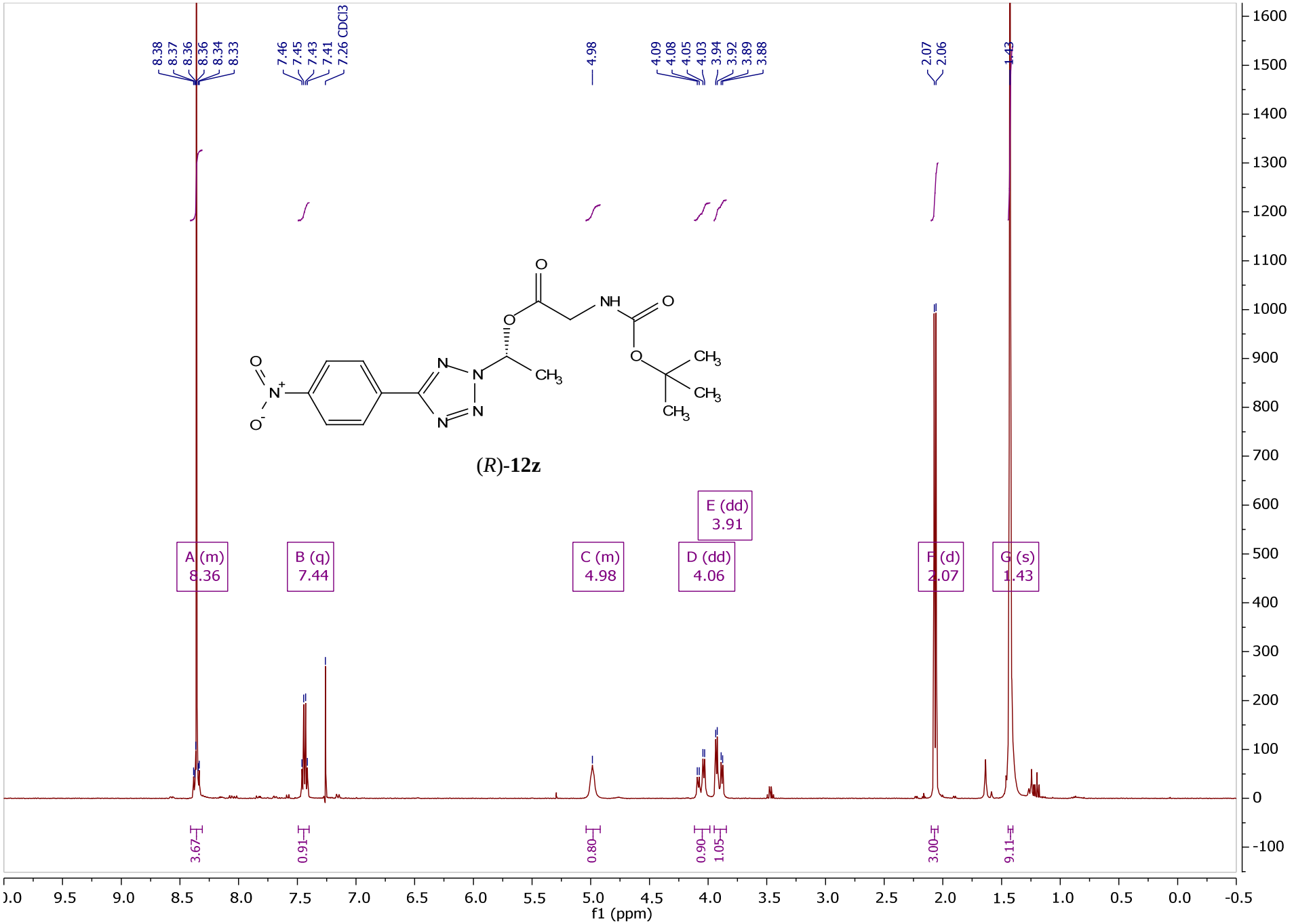
(*R*)-**12x**


8.39 8.38 8.38 8.37 8.37 8.36 8.36 8.35 8.35 8.34 8.34 7.47 7.45 7.45 7.44 7.43 7.42 7.42 7.40 7.26 CDCl3
4.18 4.14 3.96 3.95 3.91
2.93 2.90
2.08 2.06 2.04
1.45 1.35
A (m) 8.36
B (q) 7.45
C (q) 7.42
D (d) 4.16
E (s) 3.96
F (d) 3.93
G (s) 2.93
H (s) 2.90
I (s) 1.45
J (s) 1.35
K (dd) 2.06
3.53
0.37
0.42
0.44
1.00
0.58
1.21
1.34
2.98
0.53
3.93
0.47
3.43
f1 (ppm)

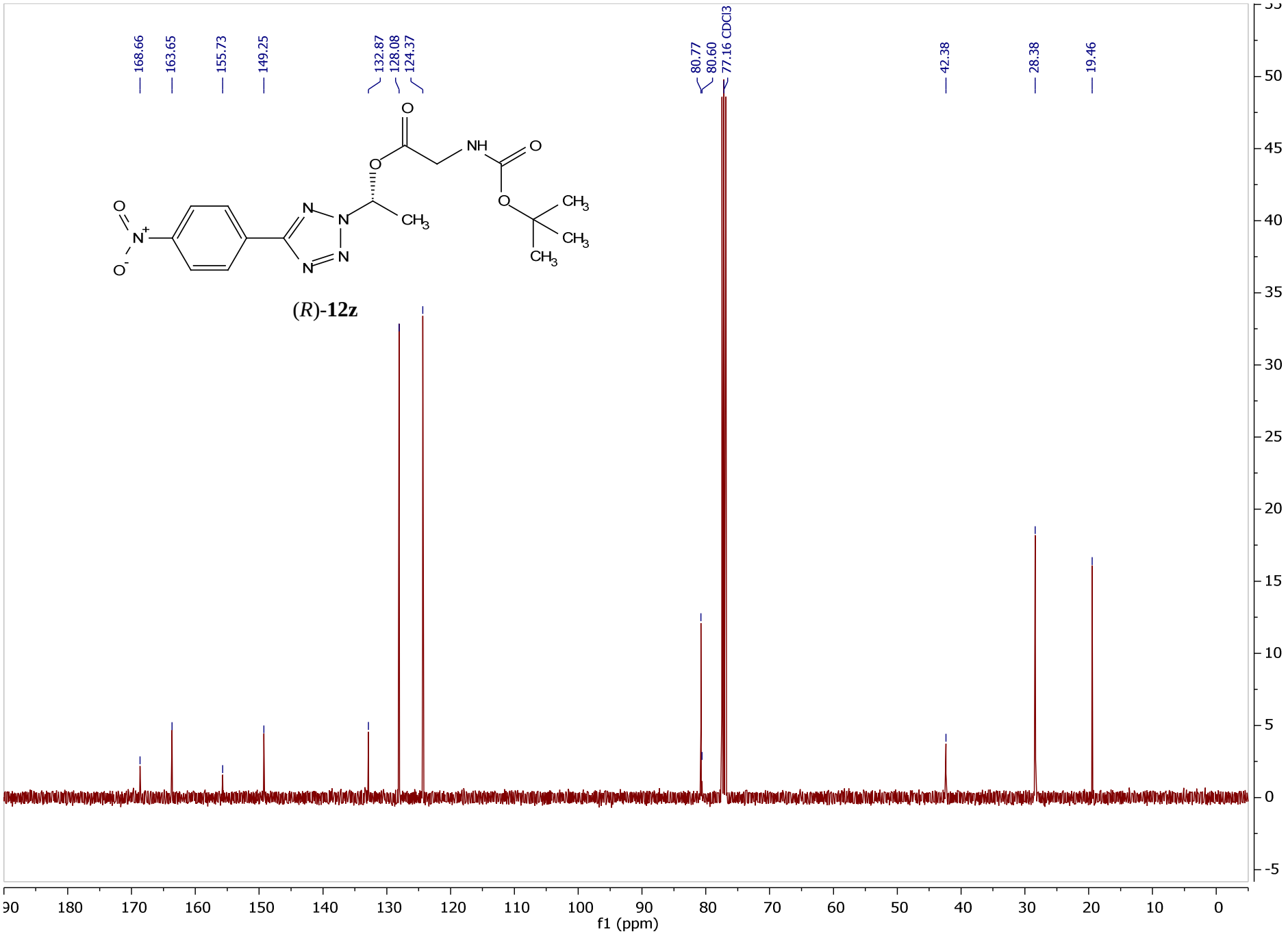
(*R*)-**12y**

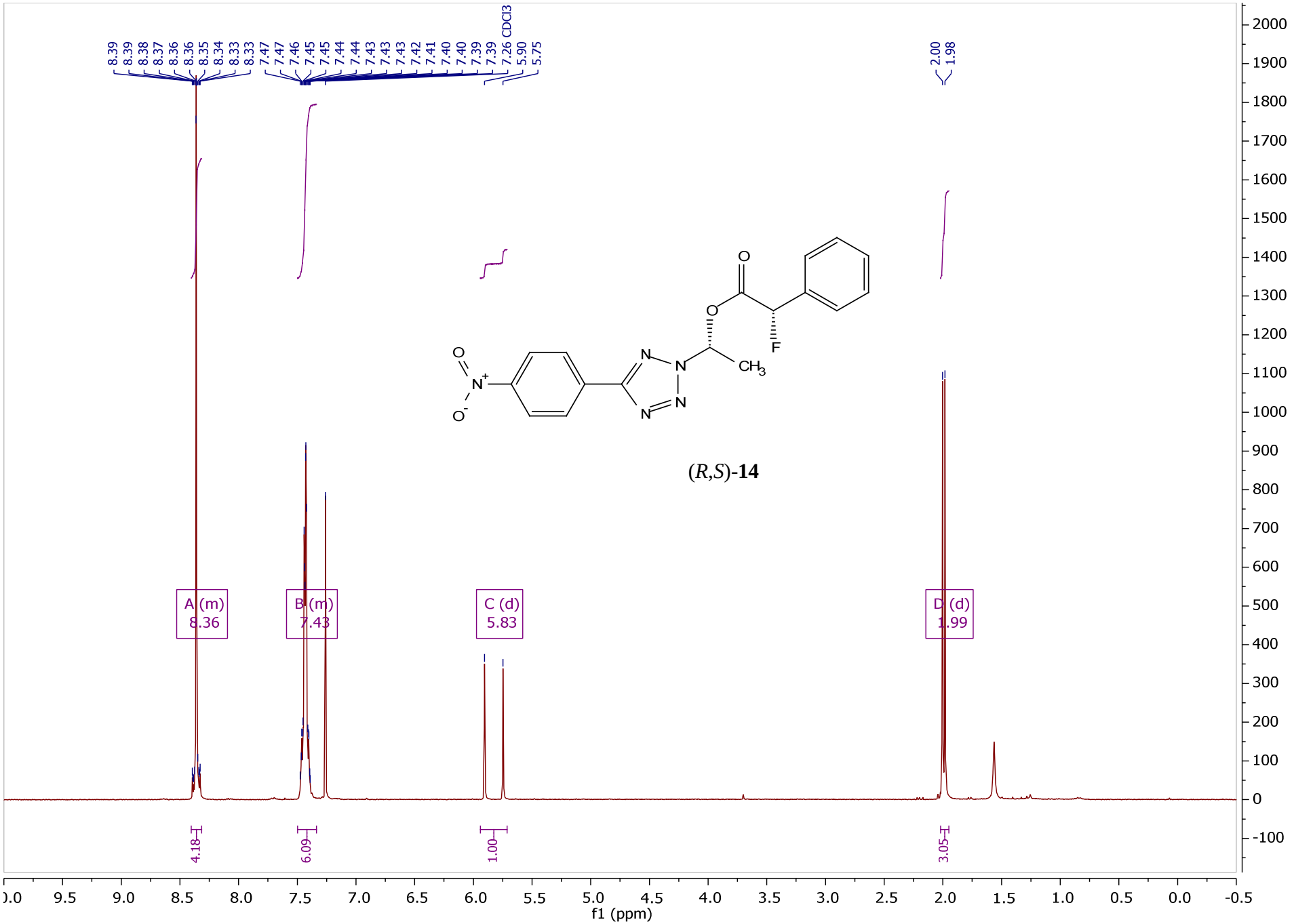

168.07
163.65
163.59
156.10
155.16
149.25
132.95
128.06
124.36
80.68
80.63
77.16 CDCl3
50.94
50.27
35.79
28.40
28.26
19.56
19.52
f1 (ppm)

(*R*)-**12y**

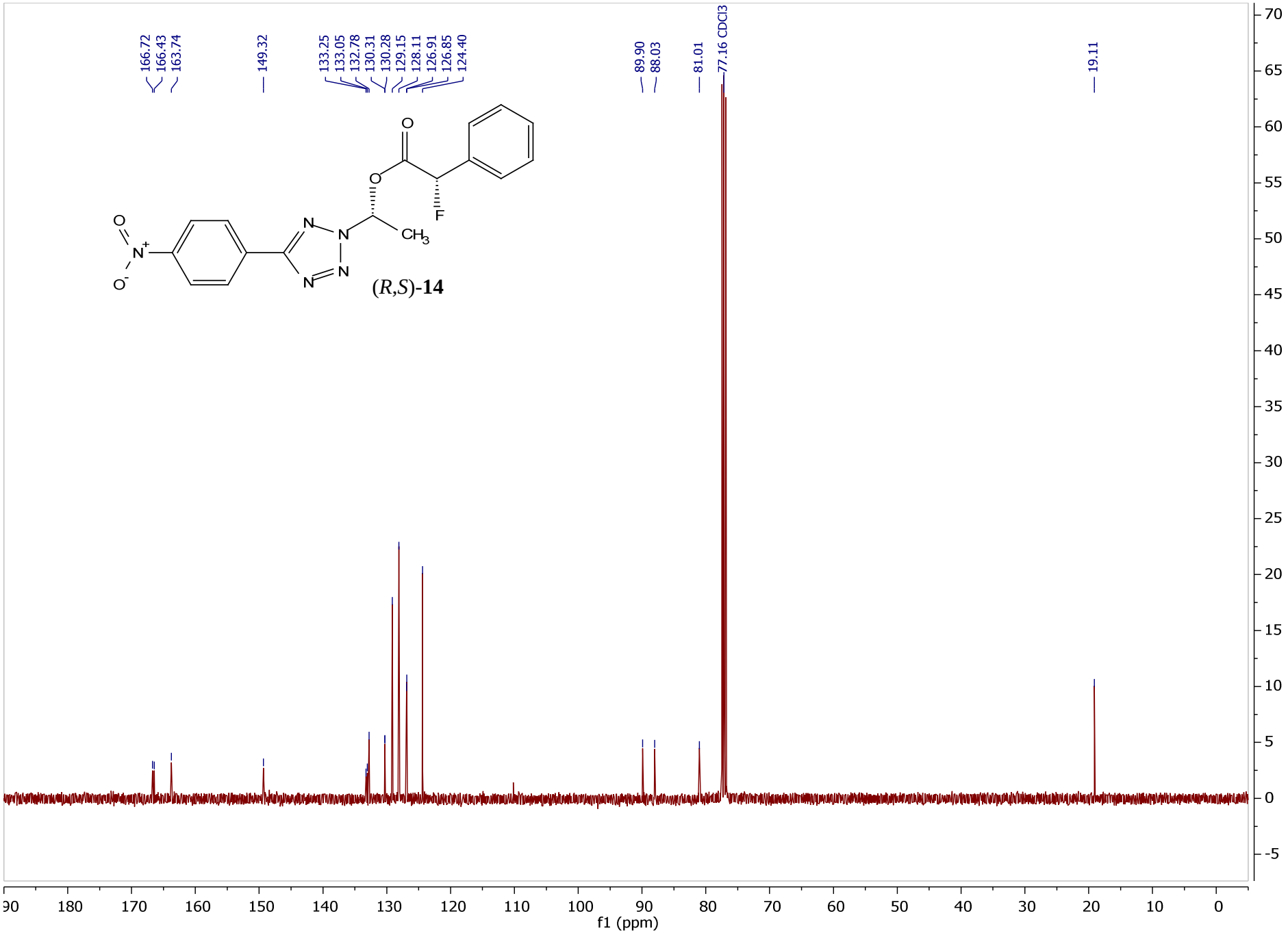

8.38
8.37
8.36
8.36
8.34
8.33
7.46
7.45
7.43
7.41
7.26 CDCl3
4.98
4.09
4.08
4.05
4.03
3.94
3.92
3.89
3.88
2.07
2.06
1.43
A (m)
8.36
B (q)
7.44
C (m)
4.98
E (dd)
3.91
D (dd)
4.06
F (d)
2.07
G (s)
1.43
3.67
0.91
0.80
0.90
1.05
3.00
9.11
f1 (ppm)

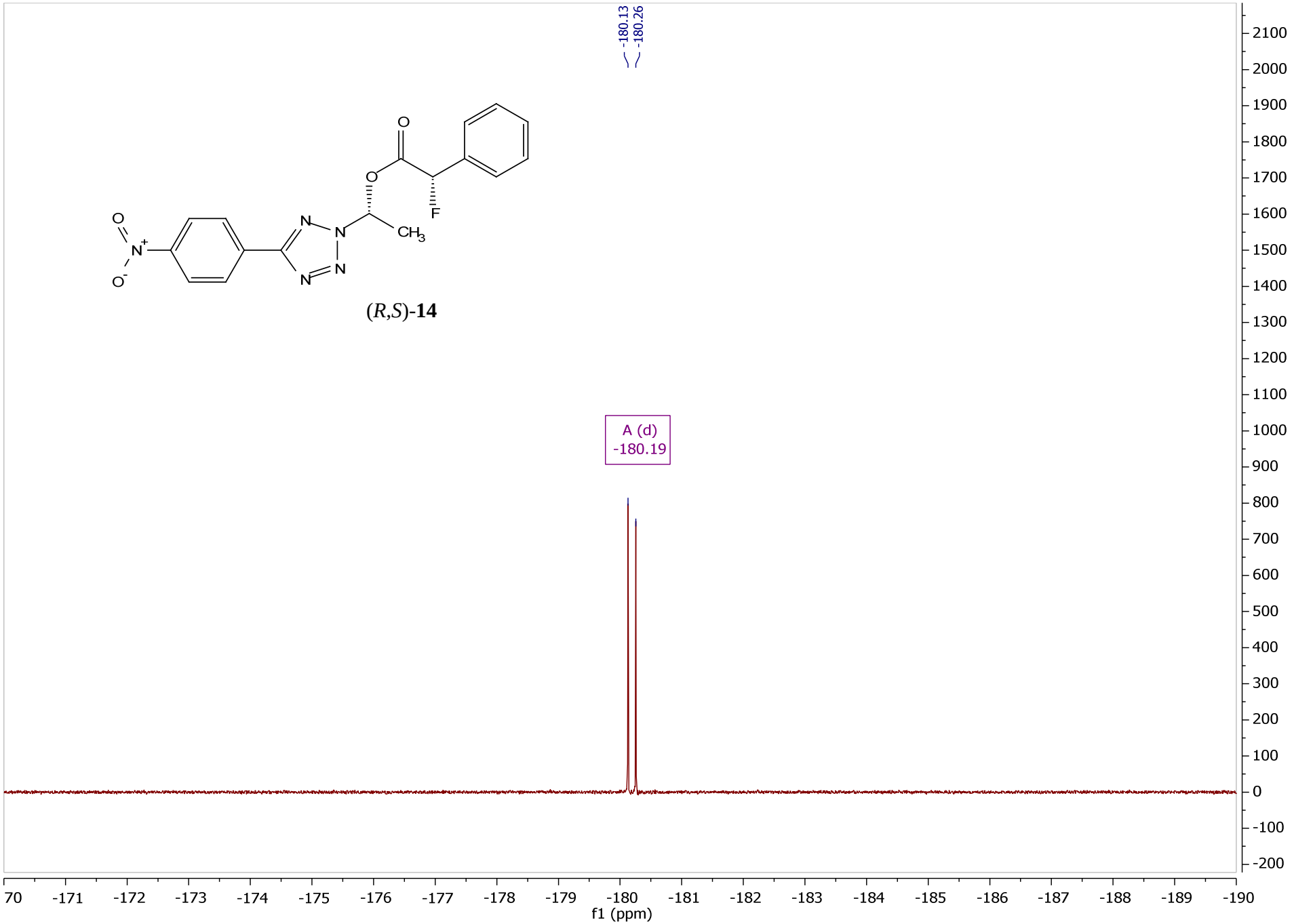
(*R*)-**12z**


168.66
163.65
155.73
149.25
132.87
128.08
124.37
80.77
80.60
77.16 CDCl3
42.38
28.38
19.46
(R)-12z
f1 (ppm)

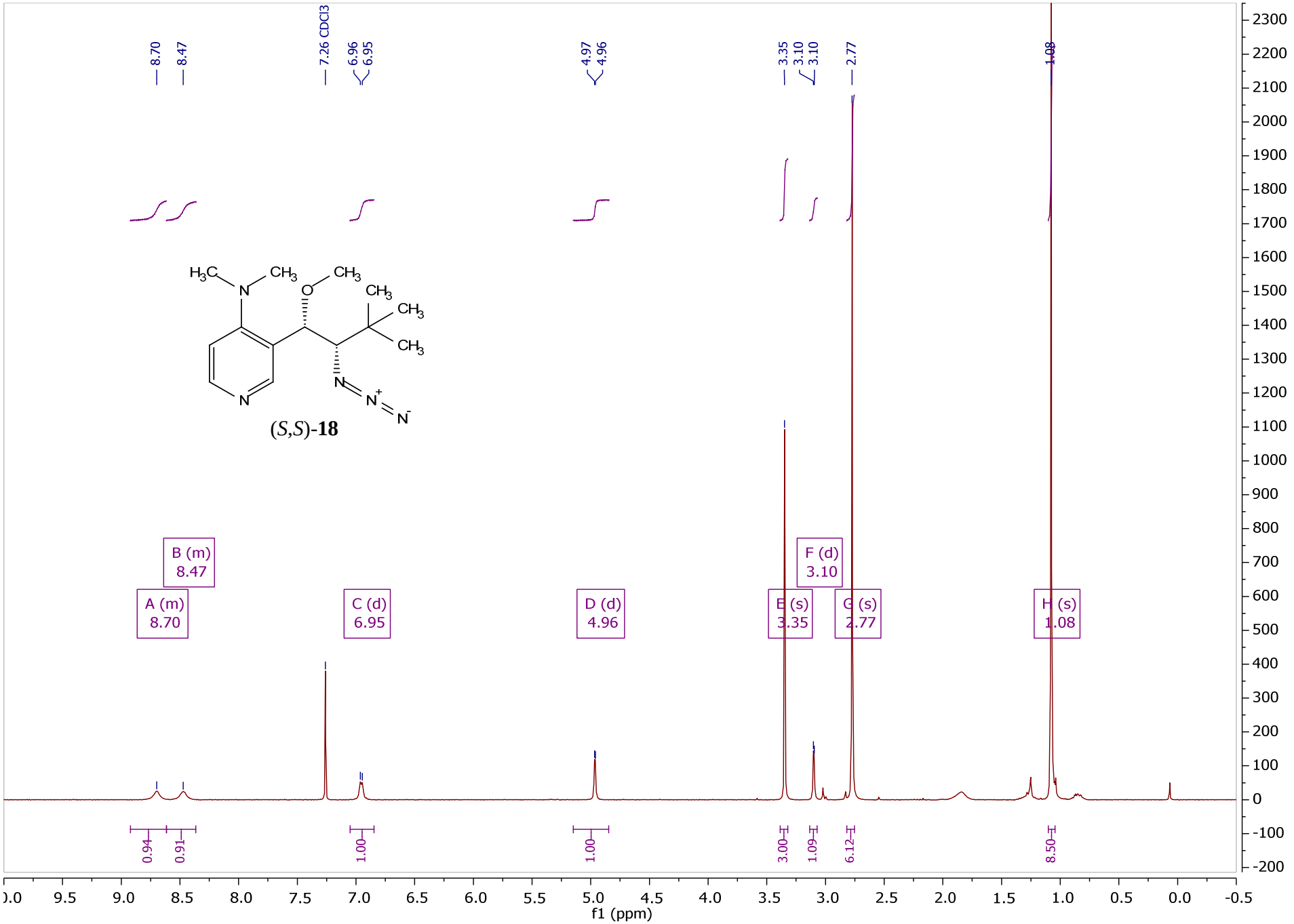

8.39 8.39 8.38 8.37 8.36 8.36 8.35 8.34 8.33 8.33 7.47 7.47 7.46 7.45 7.45 7.44 7.44 7.43 7.43 7.43 7.42 7.41 7.40 7.40 7.39 7.39 7.26 CDCl3 5.90 5.75
2.00 1.98
A (m) 8.36
B (m) 7.43
C (d) 5.83
D (d) 1.99
4.18
6.09
1.00
3.05
f1 (ppm)

(*R*,*S*)-**14**

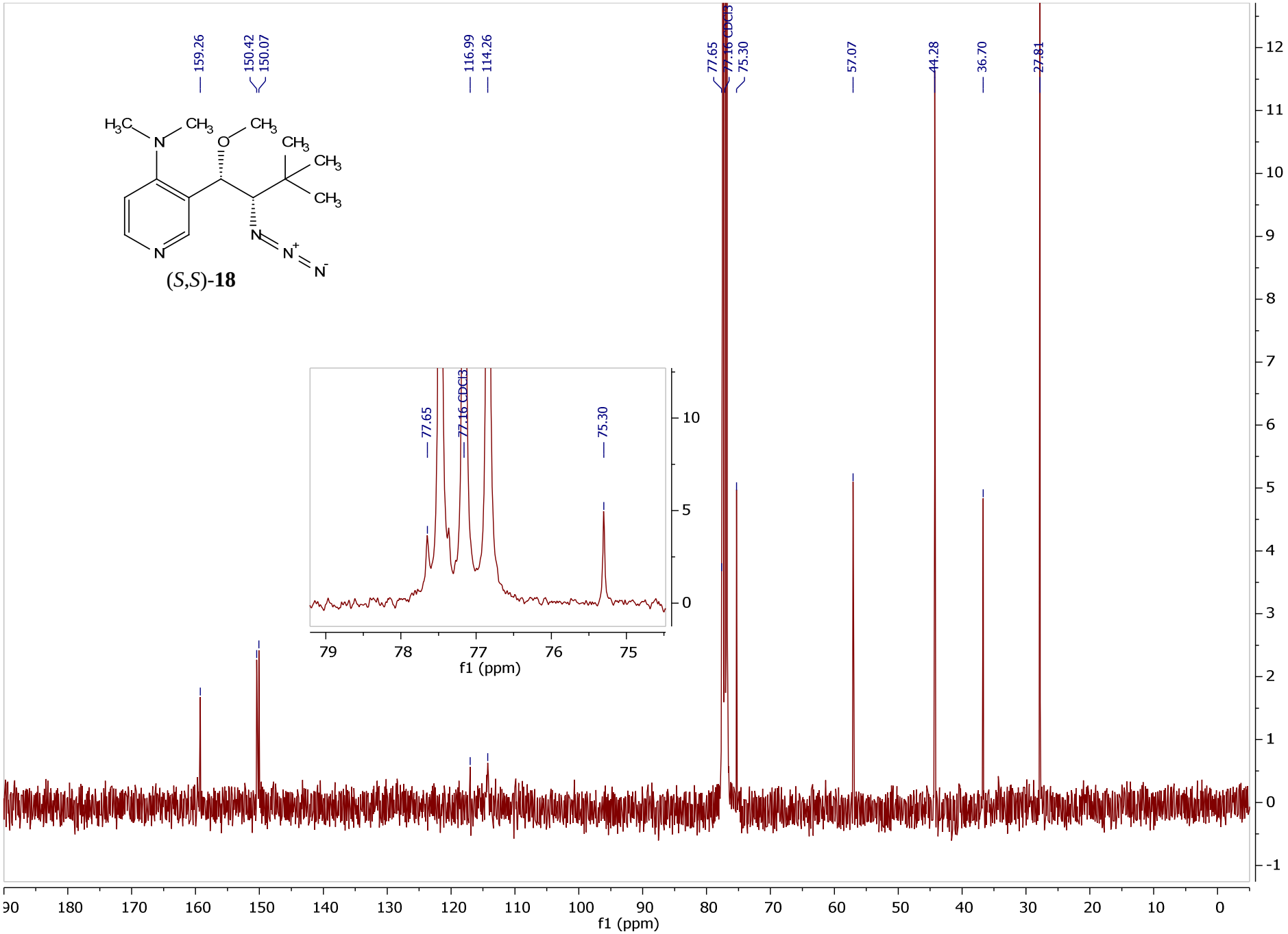

166.72
166.43
163.74
149.32
133.25
133.05
132.78
130.31
130.28
129.15
128.11
126.91
126.85
124.40
89.90
88.03
81.01
77.16 CDCl3
19.11
(R,S)-14
f1 (ppm)

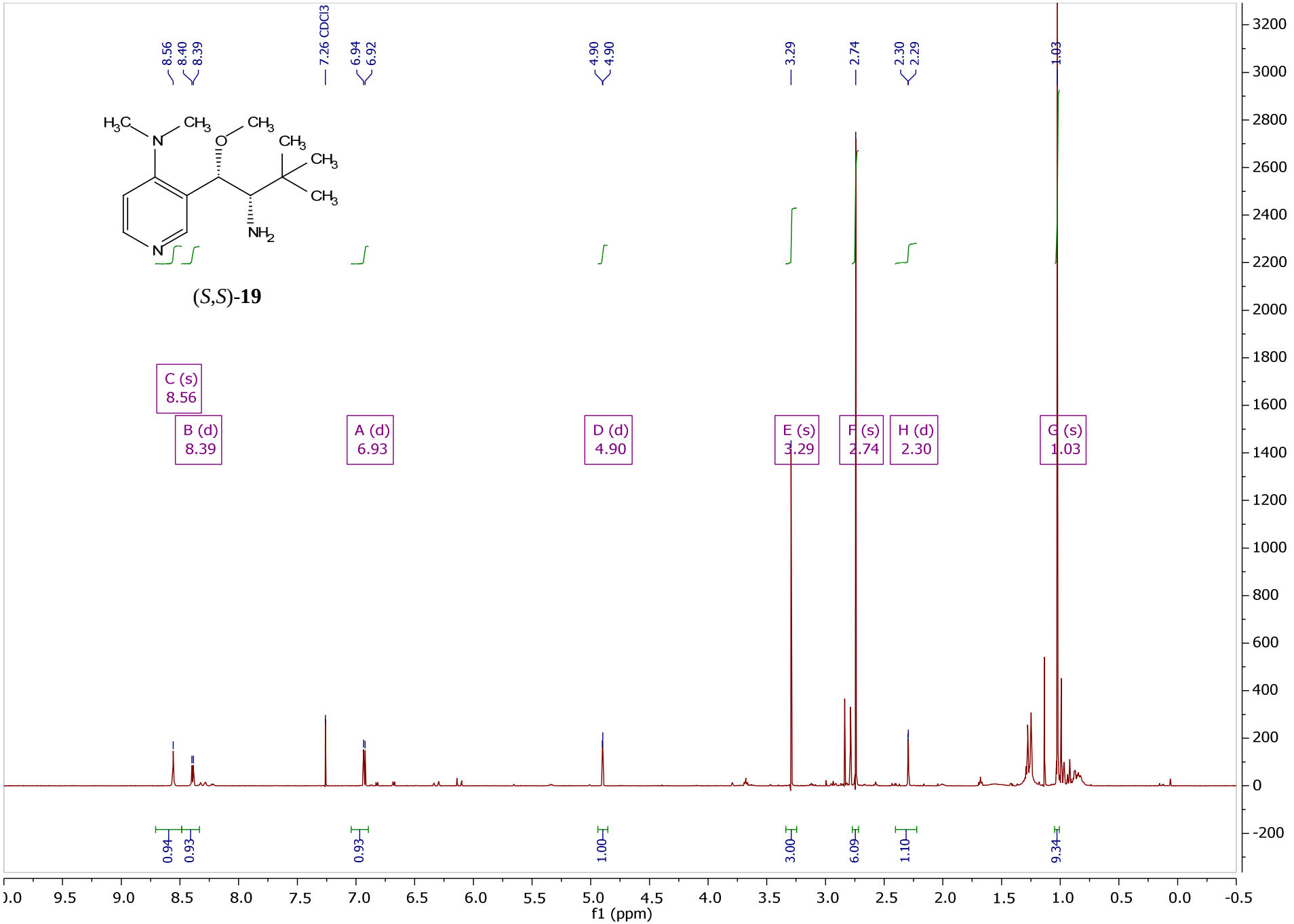


(*R*,*S*)-**14**

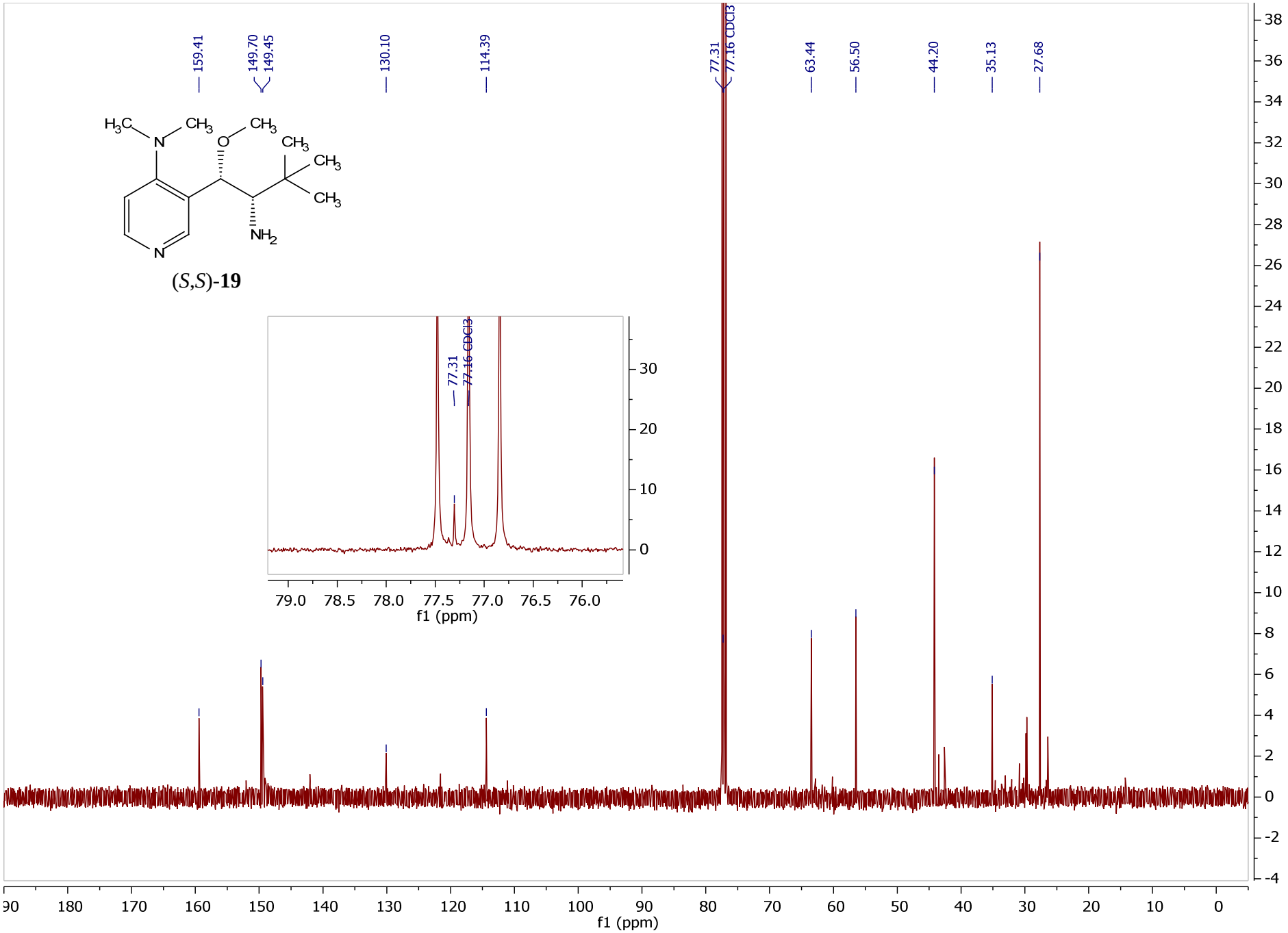

8.70
8.47
7.26 CDCl3
6.96
6.95
4.97
4.96
3.35
3.10
3.10
2.77
1.08
B (m)
8.47
A (m)
8.70
C (d)
6.95
D (d)
4.96
F (d)
3.10
E (s)
3.35
G (s)
2.77
H (s)
1.08
0.94
0.91
1.00
1.00
3.00
1.09
6.12
8.50
f1 (ppm)

(*S*,*S*)-**18**

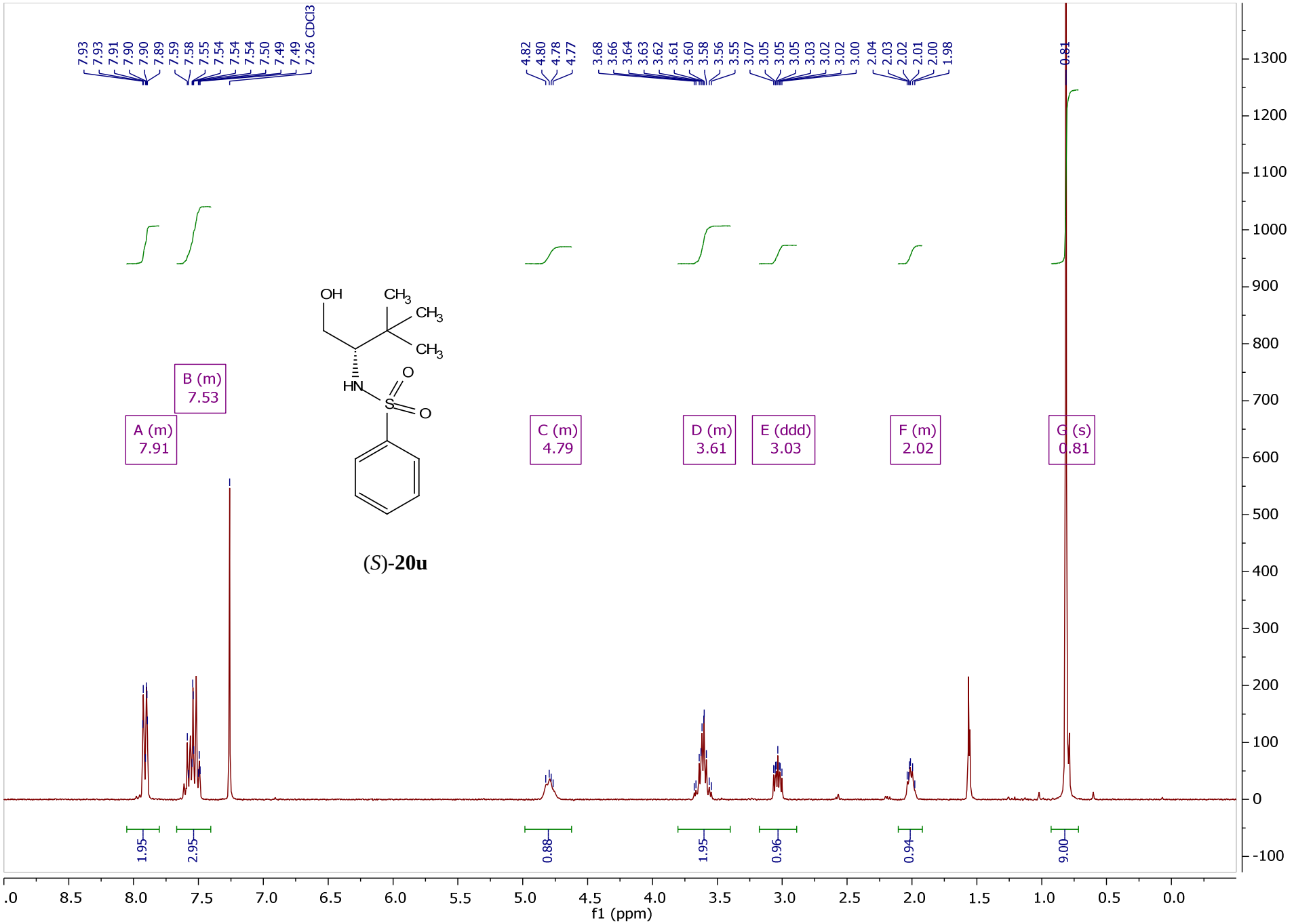

159.26
150.42
150.07
116.99
114.26
77.65
77.16 CDCl3
75.30
57.07
44.28
36.70
27.81
(S,S)-18
f1 (ppm)


8.56
8.40
8.39
7.26 CDCl3
6.94
6.92
4.90
4.90
3.29
2.74
2.30
2.29
1.03
H3C
N
CH3
O
CH3
CH3
CH3
CH3
NH2
N
C (s)
8.56
B (d)
8.39
A (d)
6.93
D (d)
4.90
E (s)
3.29
F (s)
2.74
H (d)
2.30
G (s)
1.03
0.94
0.93
0.93
1.00
3.00
6.09
1.10
9.34
f1 (ppm)

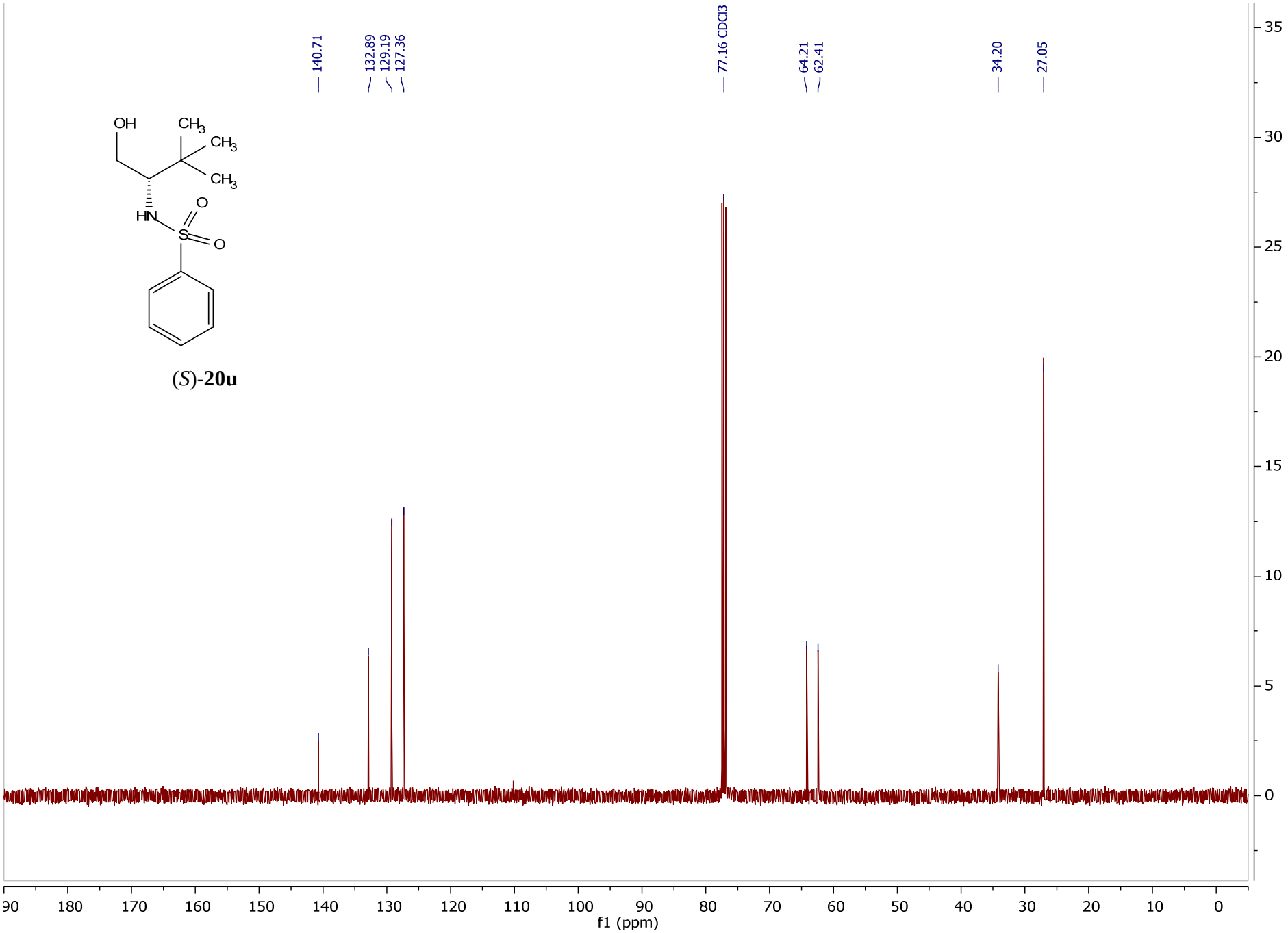
(*S*,*S*)-**19**


159.41
149.70
149.45
130.10
114.39
77.31
77.16 CDCl3
63.44
56.50
44.20
35.13
27.68
f1 (ppm)

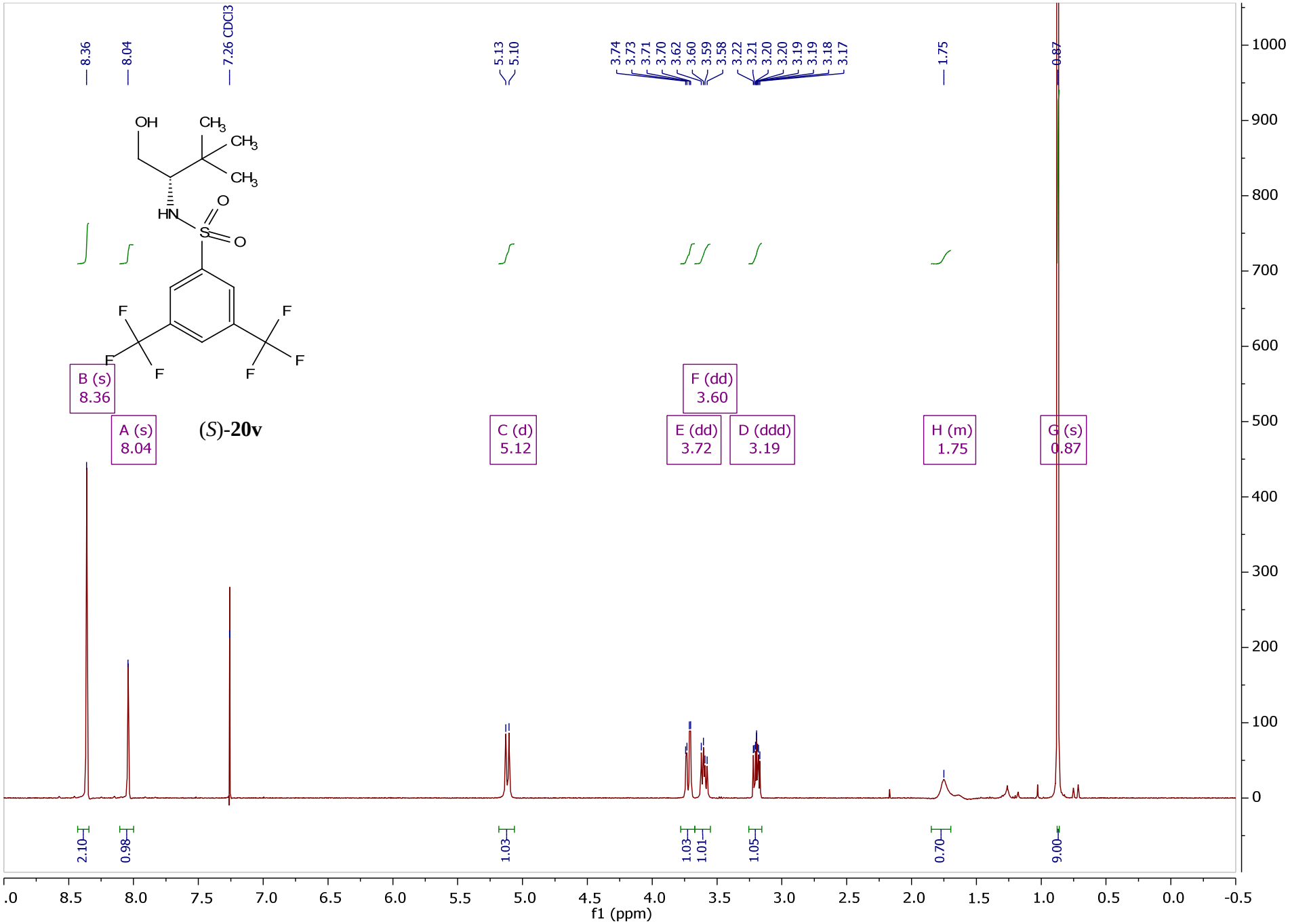
(*S*,*S*)-**19**

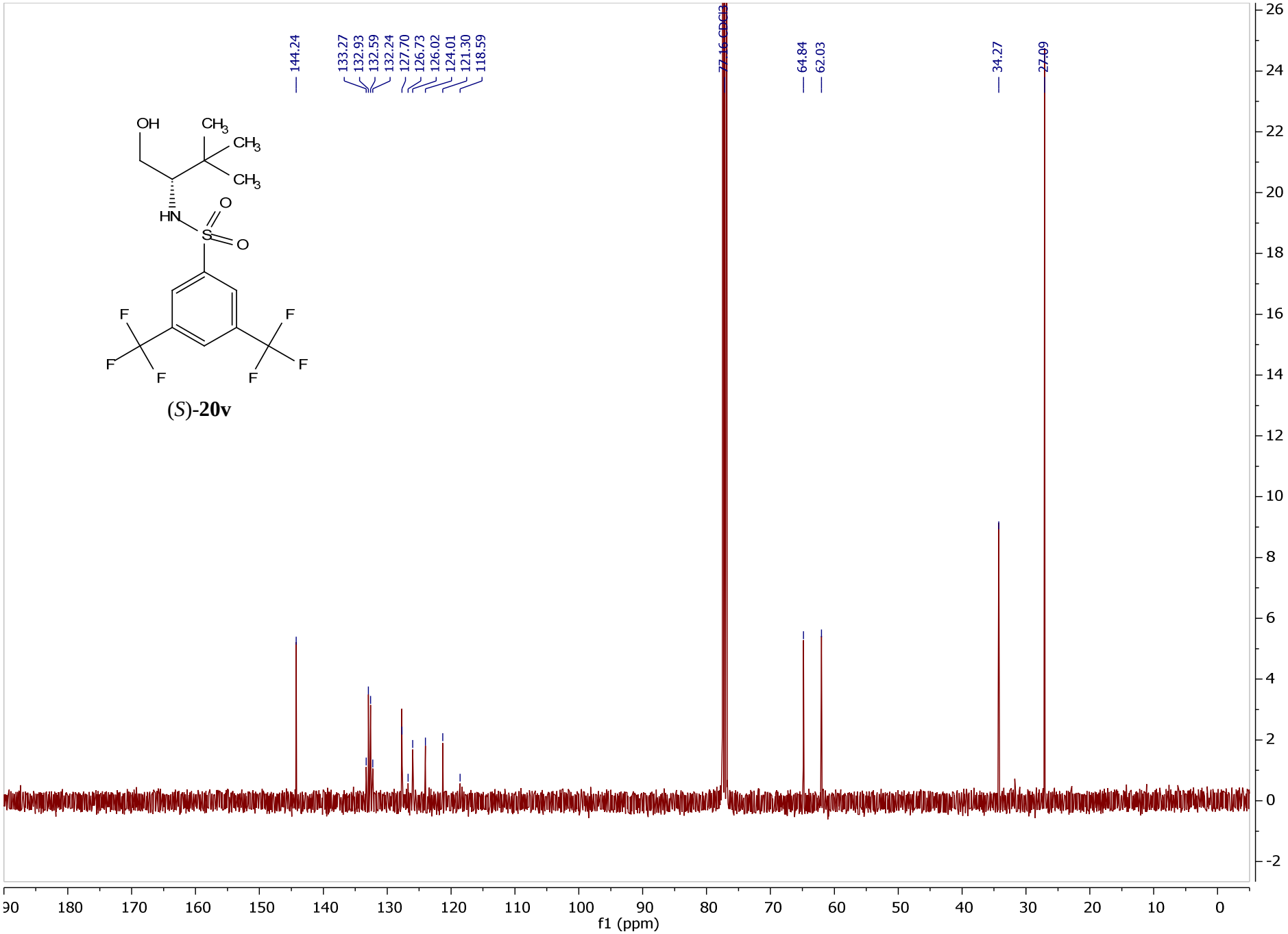

7.93
7.93
7.91
7.90
7.90
7.89
7.59
7.58
7.55
7.54
7.54
7.54
7.50
7.49
7.49
7.26 CDCl3
4.82
4.80
4.78
4.77
3.68
3.66
3.64
3.63
3.62
3.61
3.60
3.58
3.56
3.55
3.07
3.05
3.05
3.05
3.03
3.02
3.02
3.00
2.04
2.03
2.02
2.01
2.00
1.98
0.81
OH
CH3
CH3
CH3
HN
S
O
O
A (m) 7.91
B (m) 7.53
C (m) 4.79
D (m) 3.61
E (ddd) 3.03
F (m) 2.02
G (s) 0.81
1.95
2.95
0.88
1.95
0.96
0.94
9.00
f1 (ppm)

(*S*)-**20u**

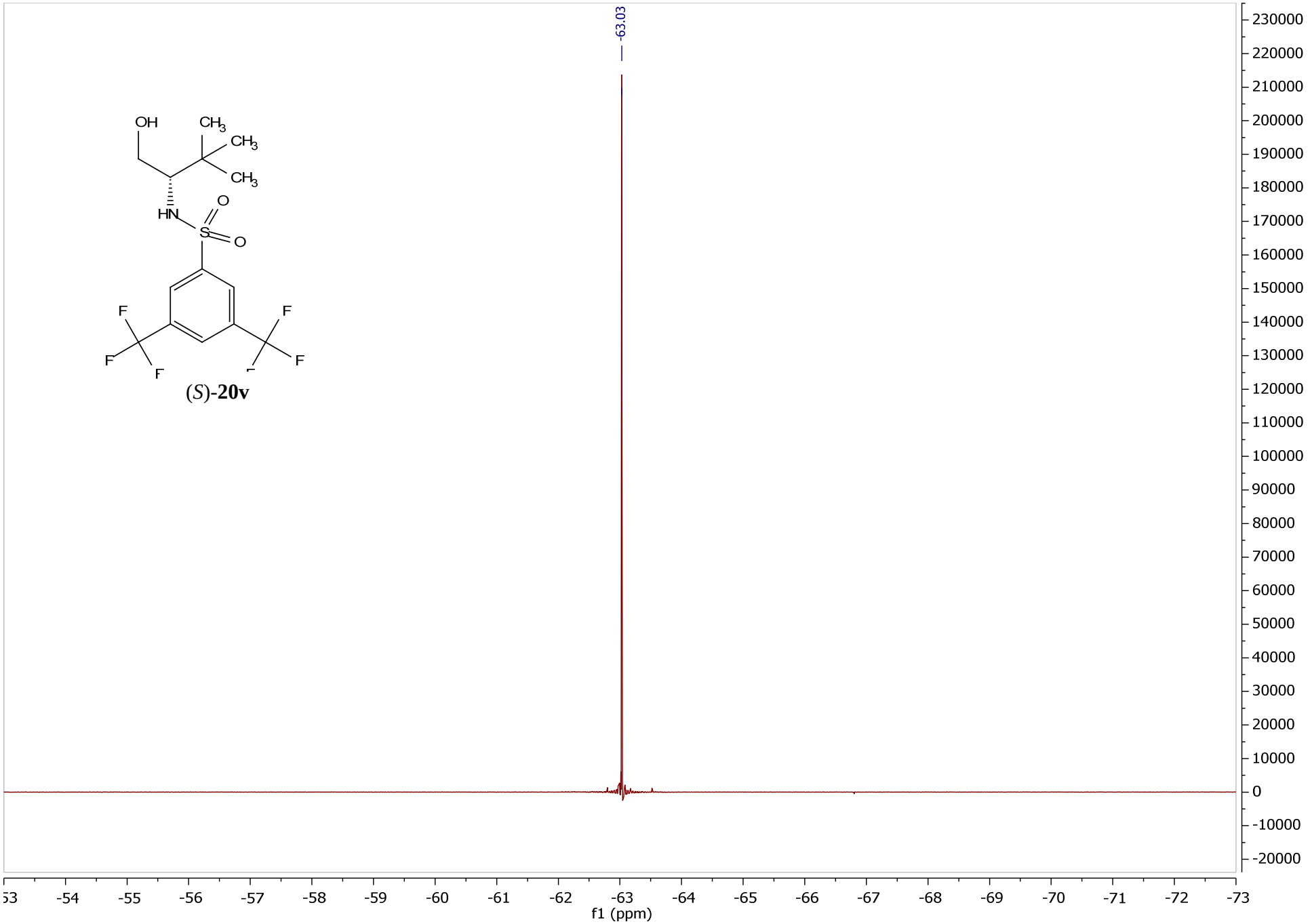

140.71
132.89
129.19
127.36
77.16 CDCl3
64.21
62.41
34.20
27.05
OH
CH3
CH3
CH3
HN
S
O
O
f1 (ppm)

(*S*)-**20u**

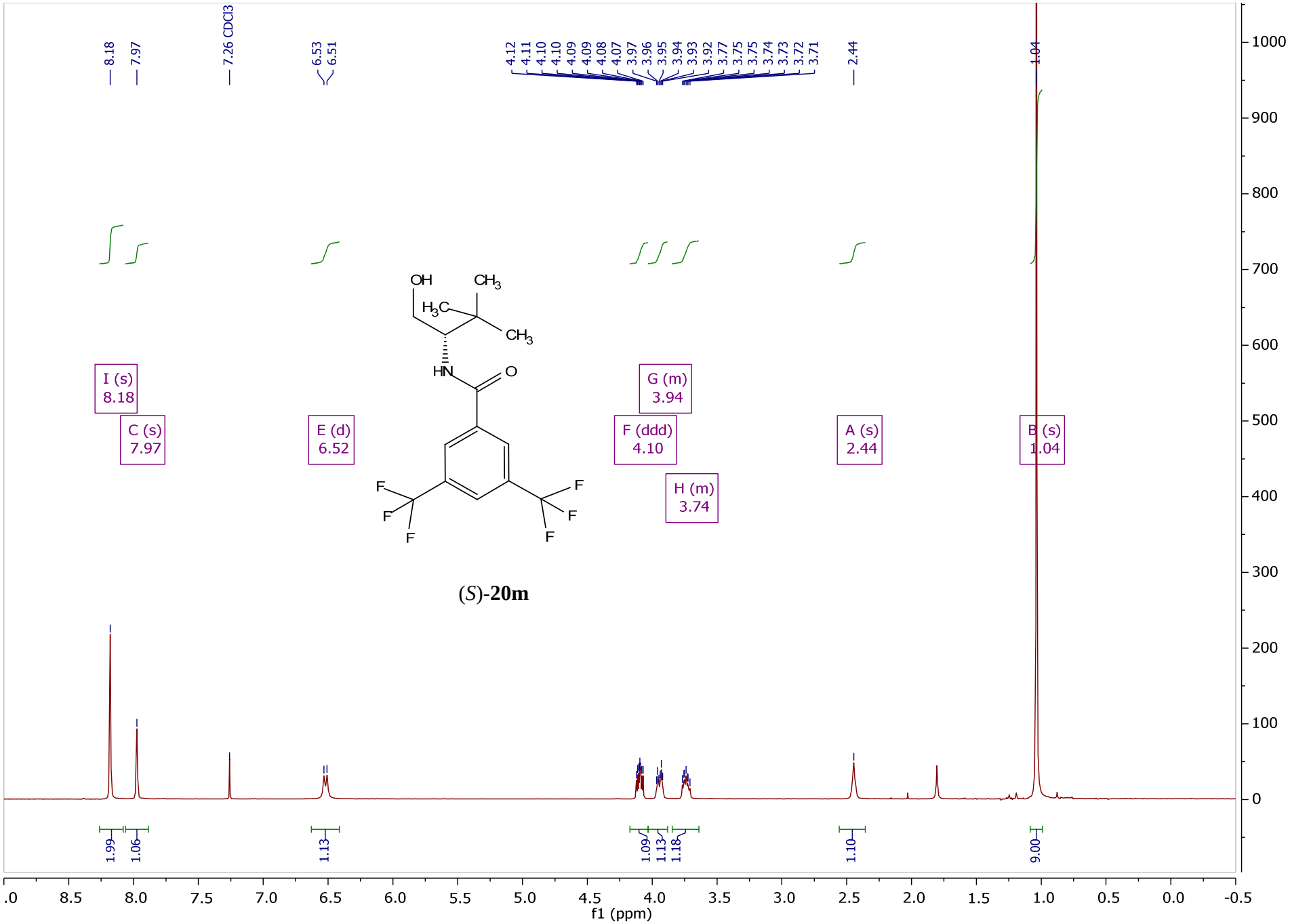

8.36
8.04
7.26 CDCl3
5.13
5.10
3.74
3.73
3.71
3.70
3.62
3.60
3.59
3.58
3.22
3.21
3.20
3.20
3.19
3.19
3.18
3.17
1.75
0.87
OH
CH3
CH3
CH3
HN
S
O
O
F
F
F
F
F
F
B (s) 8.36
A (s) 8.04
(S)-20v
C (d) 5.12
F (dd) 3.60
E (dd) 3.72
D (ddd) 3.19
H (m) 1.75
G (s) 0.87
2.10
0.98
1.03
1.03
1.01
1.05
0.70
9.00
f1 (ppm)


144.24
133.27
132.93
132.59
132.24
127.70
126.73
126.02
124.01
121.30
118.59
77.16 CDCl3
64.84
62.03
34.27
27.09
OH
CH3
CH3
CH3
HN
S
O
O
F
F
F
F
F
F
f1 (ppm)

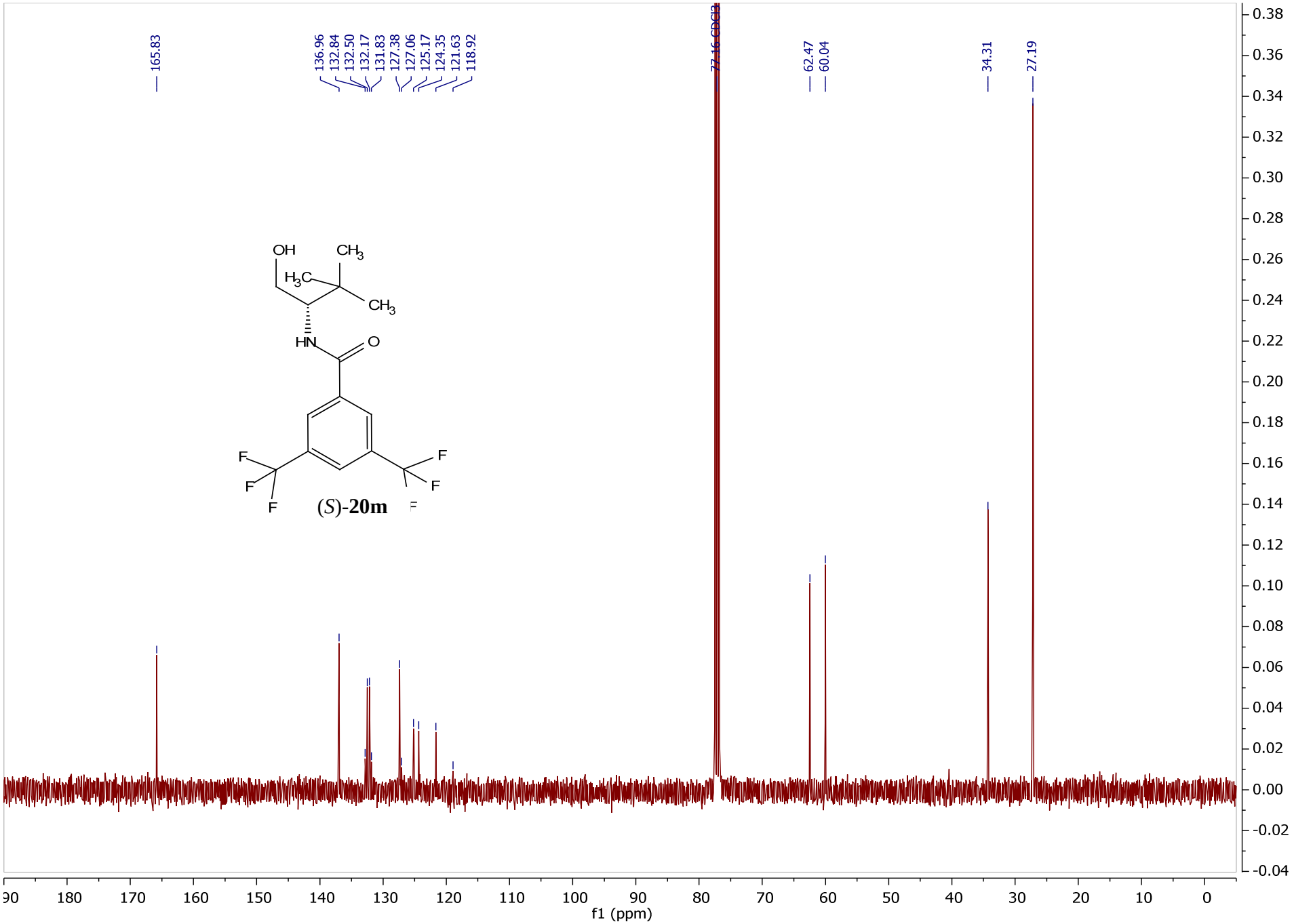
(*S*)-**20v**

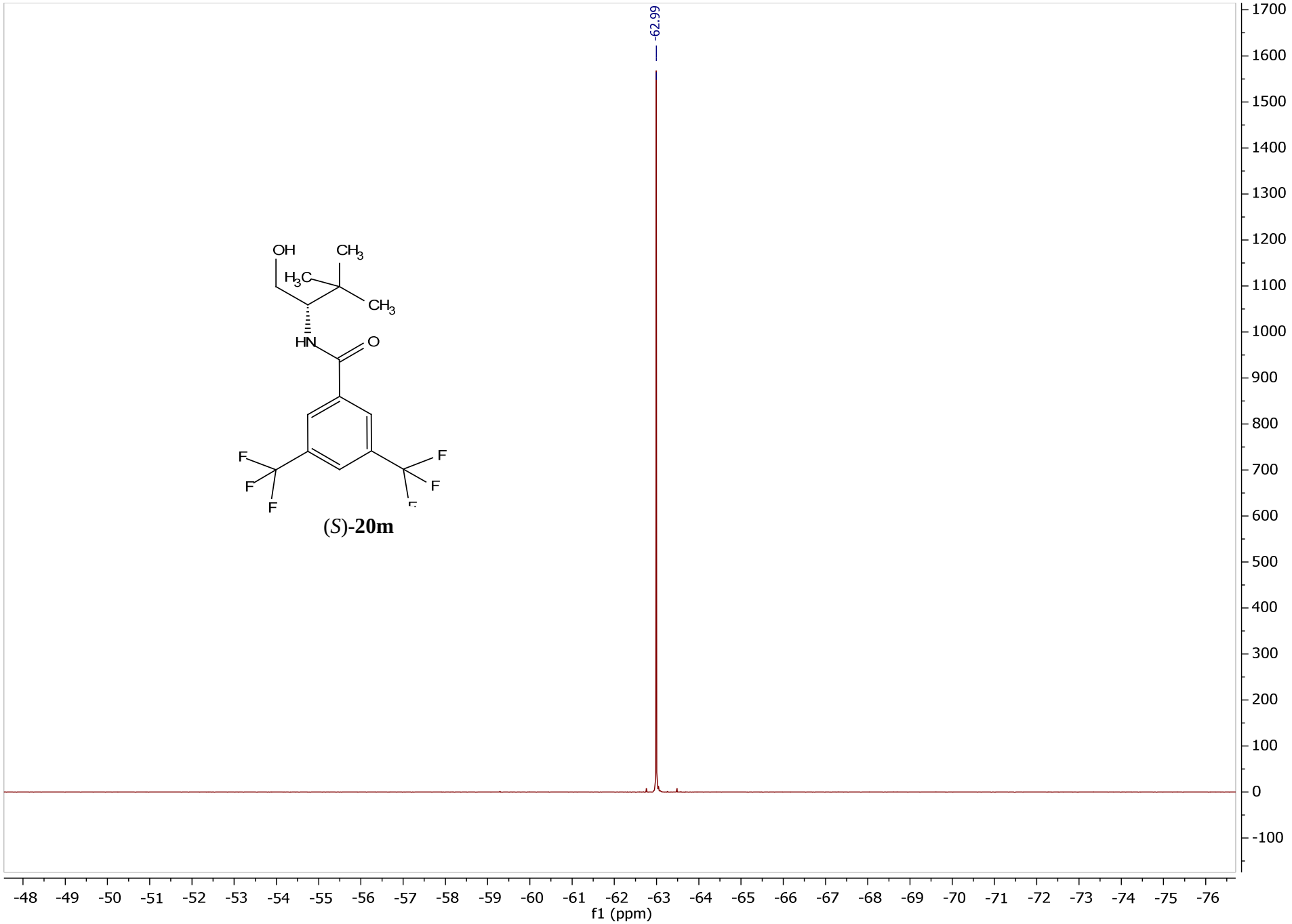

-63.03
OH
CH3
CH3
CH3
HN
S
O
O
F
F
F
F
F
230000
220000
210000
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
-20000
-53
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
-71
-72
-73
f1 (ppm)

(*S*)-**20v**

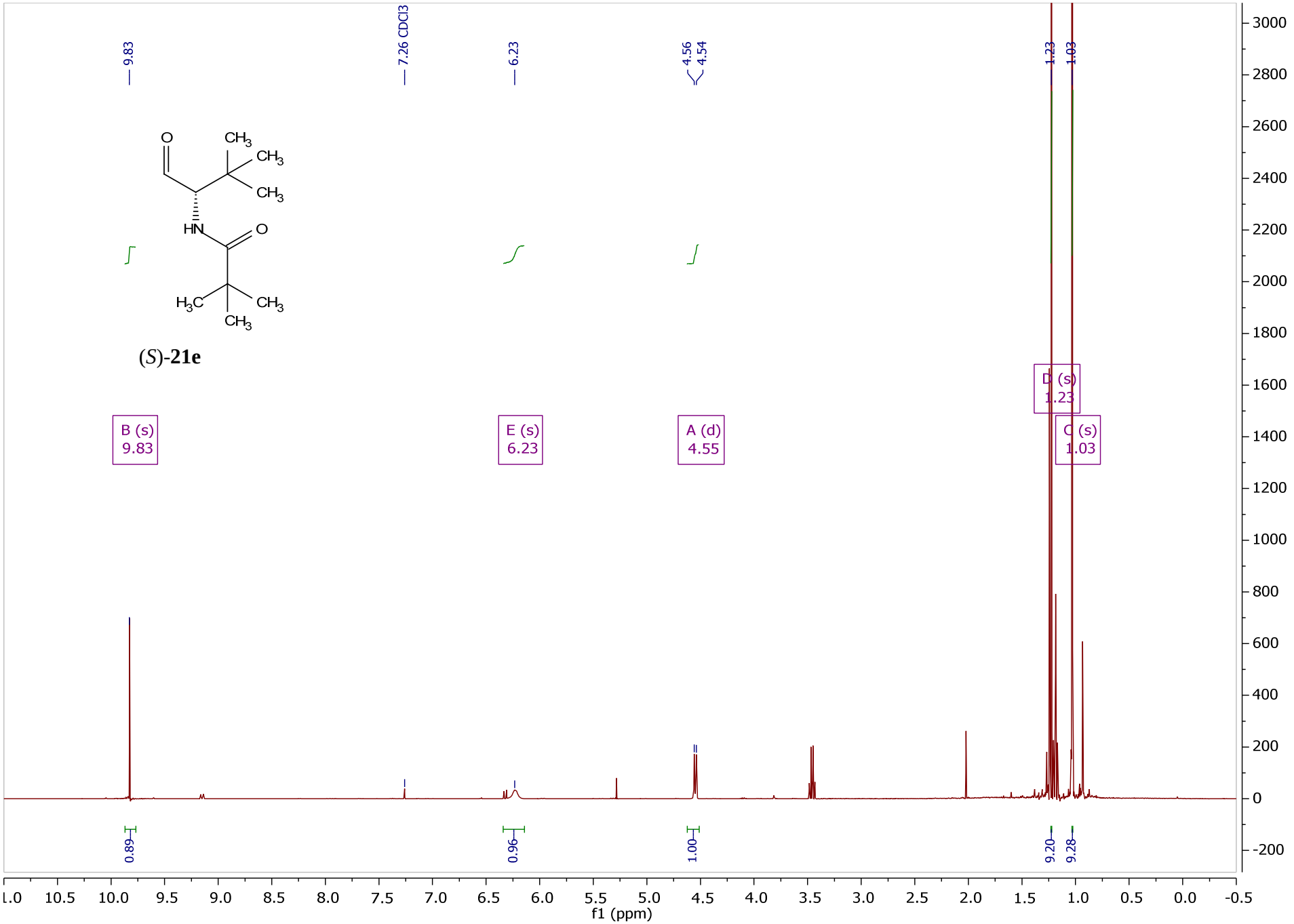

8.18
7.97
7.26 CDCl3
6.53
6.51
4.12
4.11
4.10
4.10
4.09
4.09
4.08
4.07
3.97
3.96
3.95
3.94
3.93
3.92
3.77
3.75
3.75
3.74
3.73
3.72
3.71
2.44
1.04
OH
CH3
H3C
CH3
HN
O
F
F
F
F
F
F
I (s) 8.18
C (s) 7.97
E (d) 6.52
G (m) 3.94
F (ddd) 4.10
H (m) 3.74
A (s) 2.44
B (s) 1.04
1.99
1.06
1.13
1.09
1.13
1.18
1.10
9.00
f1 (ppm)

(*S*)-**20m**

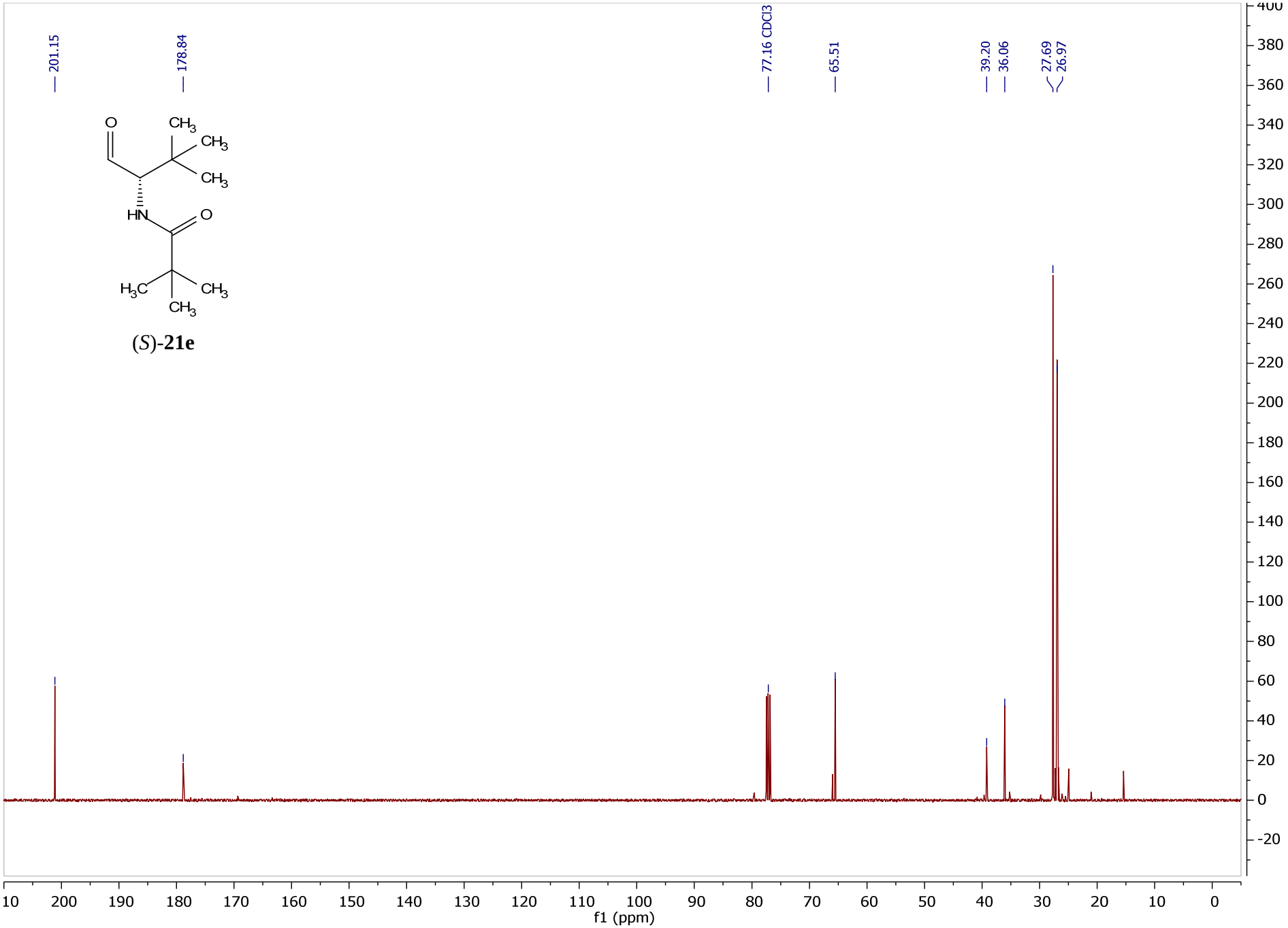

165.83
136.96
132.84
132.50
132.17
131.83
127.38
127.06
125.17
124.35
121.63
118.92
77.16 CDCl3
62.47
60.04
34.31
27.19
OH
CH3
H3C
CH3
HN
O
F
F
F
F
F
F
(S)-20m
0.38
0.36
0.34
0.32
0.30
0.28
0.26
0.24
0.22
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
-0.02
-0.04
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-62.99
OH
CH3
H3C
CH3
HN
O
F
F
F
F
F
F
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-48 -49 -50 -51 -52 -53 -54 -55 -56 -57 -58 -59 -60 -61 -62 -63 -64 -65 -66 -67 -68 -69 -70 -71 -72 -73 -74 -75 -76
f1 (ppm)

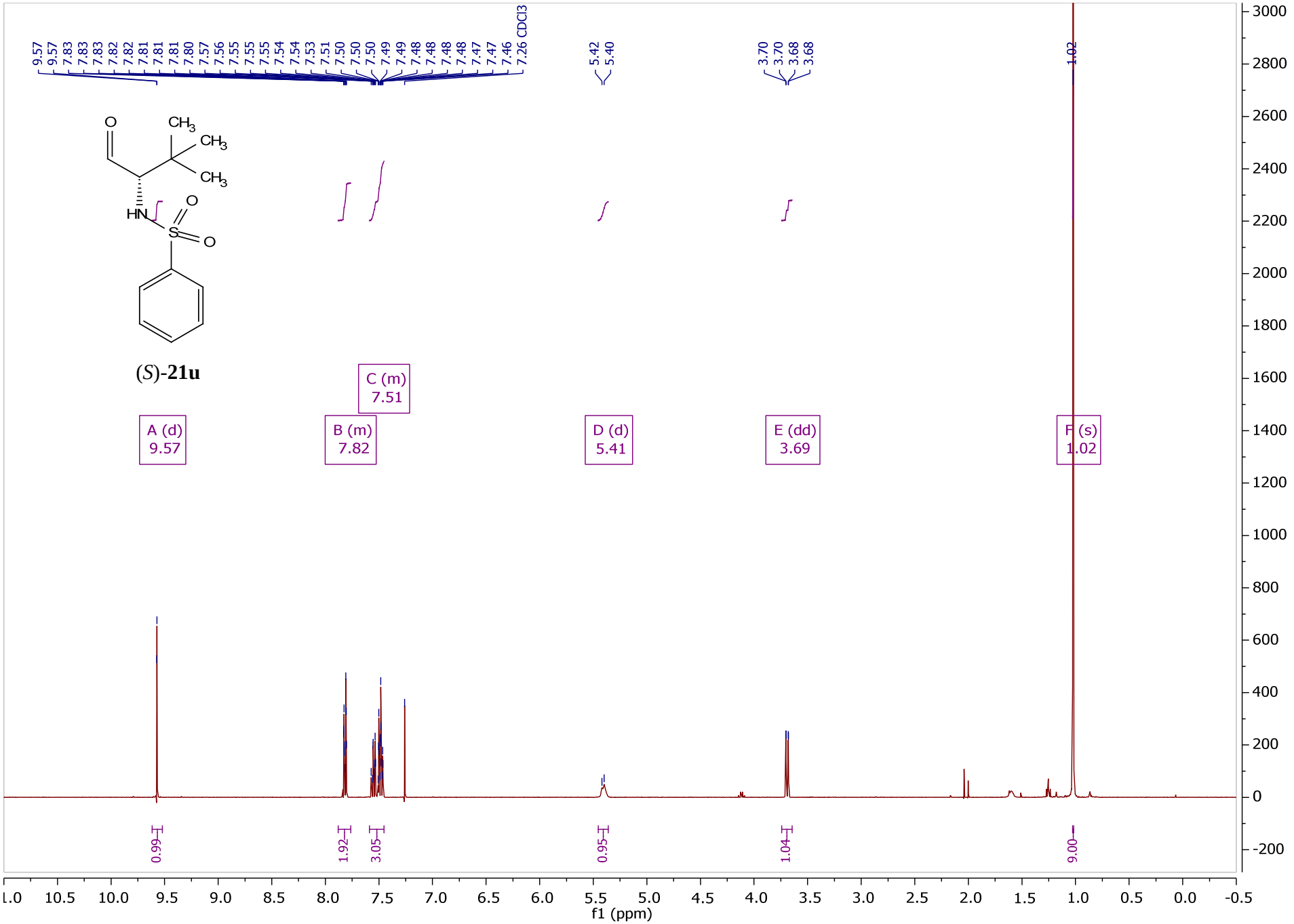
(*S*)-**20m**

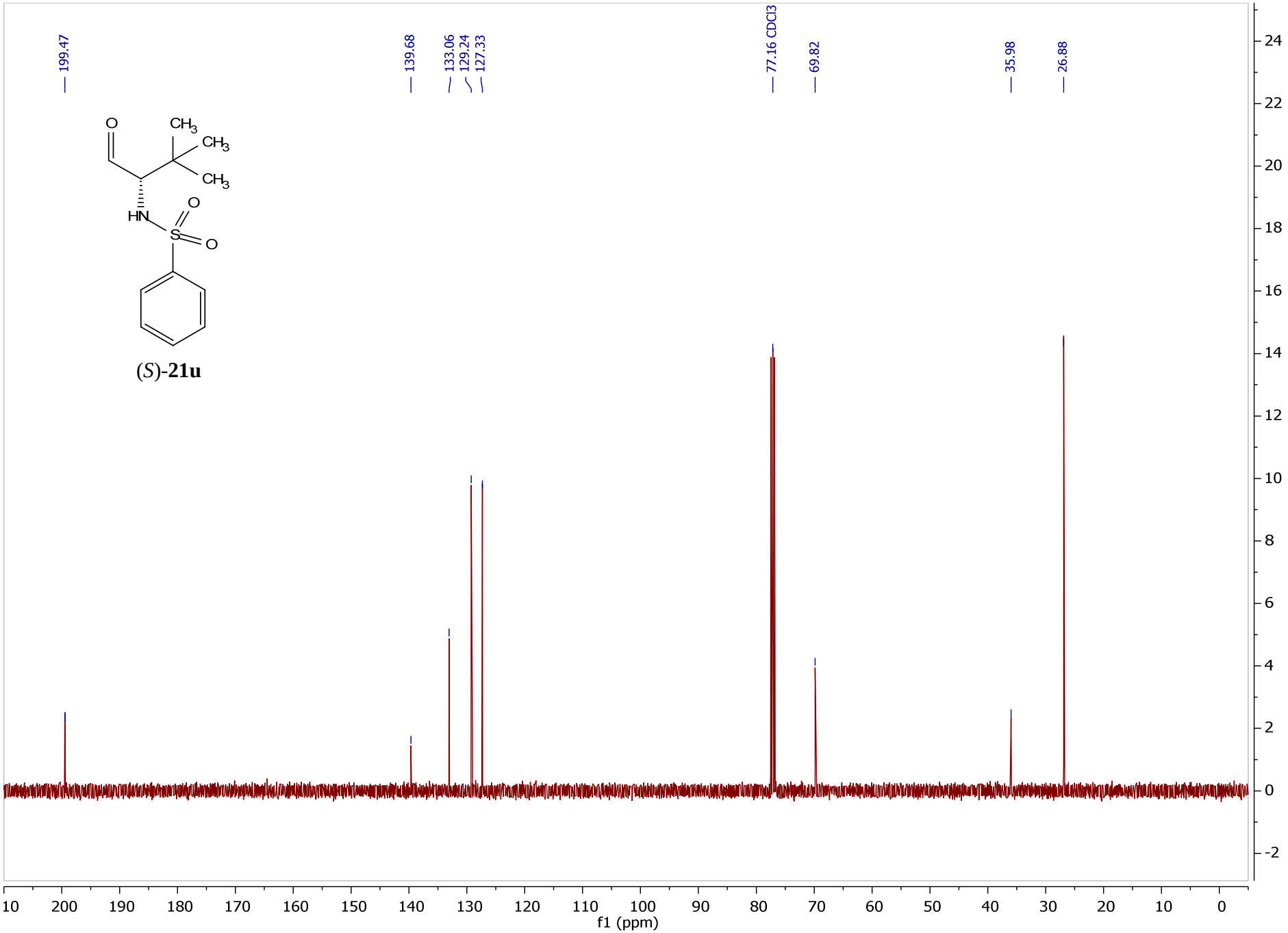

9.83
7.26 CDCl3
6.23
4.56
4.54
1.23
1.03
O
CH3
CH3
CH3
HN
O
H3C
CH3
CH3
B (s)
9.83
E (s)
6.23
A (d)
4.55
D (s)
1.23
C (s)
1.03
0.89
0.96
1.00
9.20
9.28
f1 (ppm)

(*S*)-**21e**

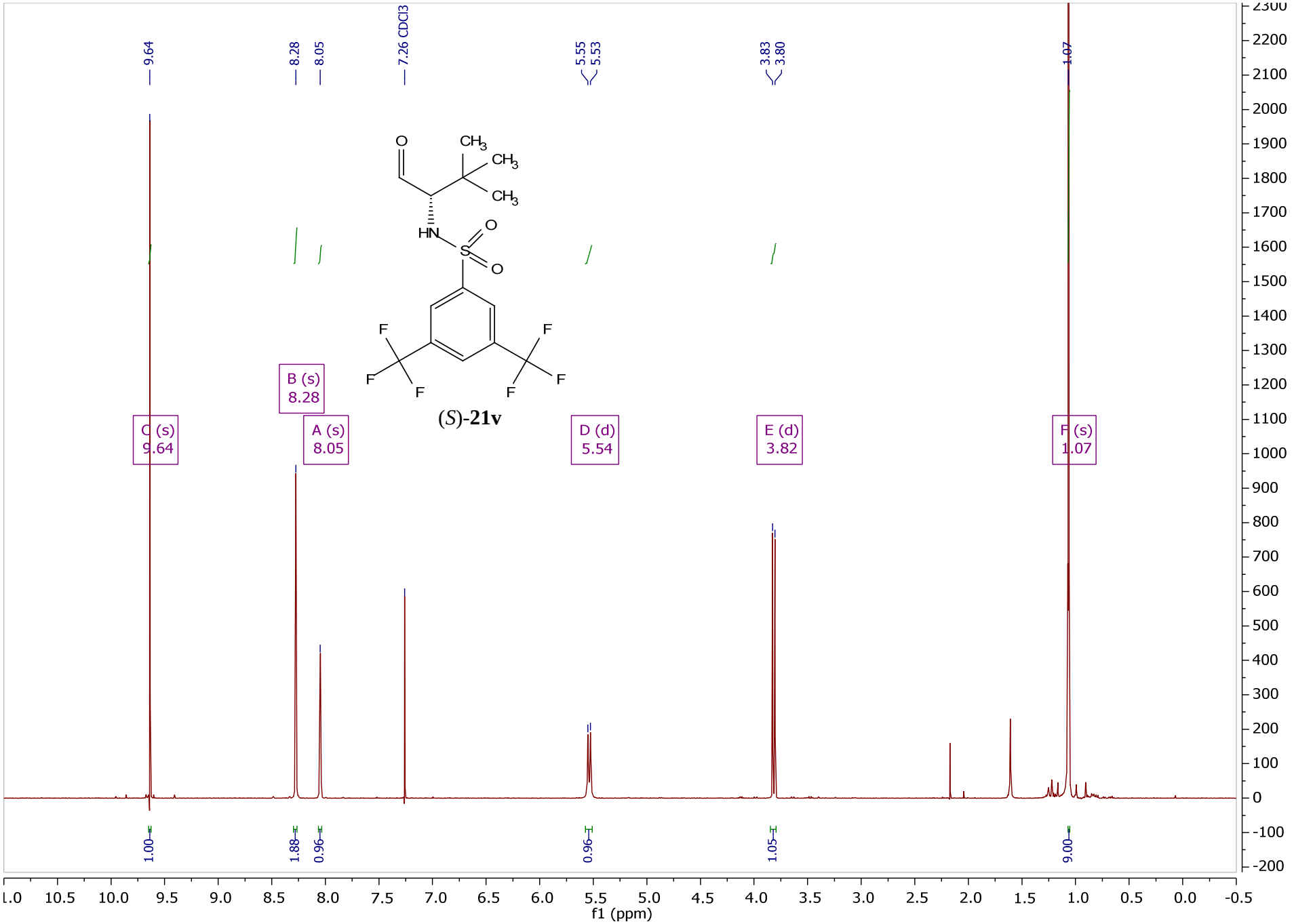

201.15
178.84
77.16 CDCl3
65.51
39.20
36.06
27.69
26.97
O
CH3
CH3
CH3
HN
O
H3C
CH3
CH3
f1 (ppm)

(*S*)-**21e**

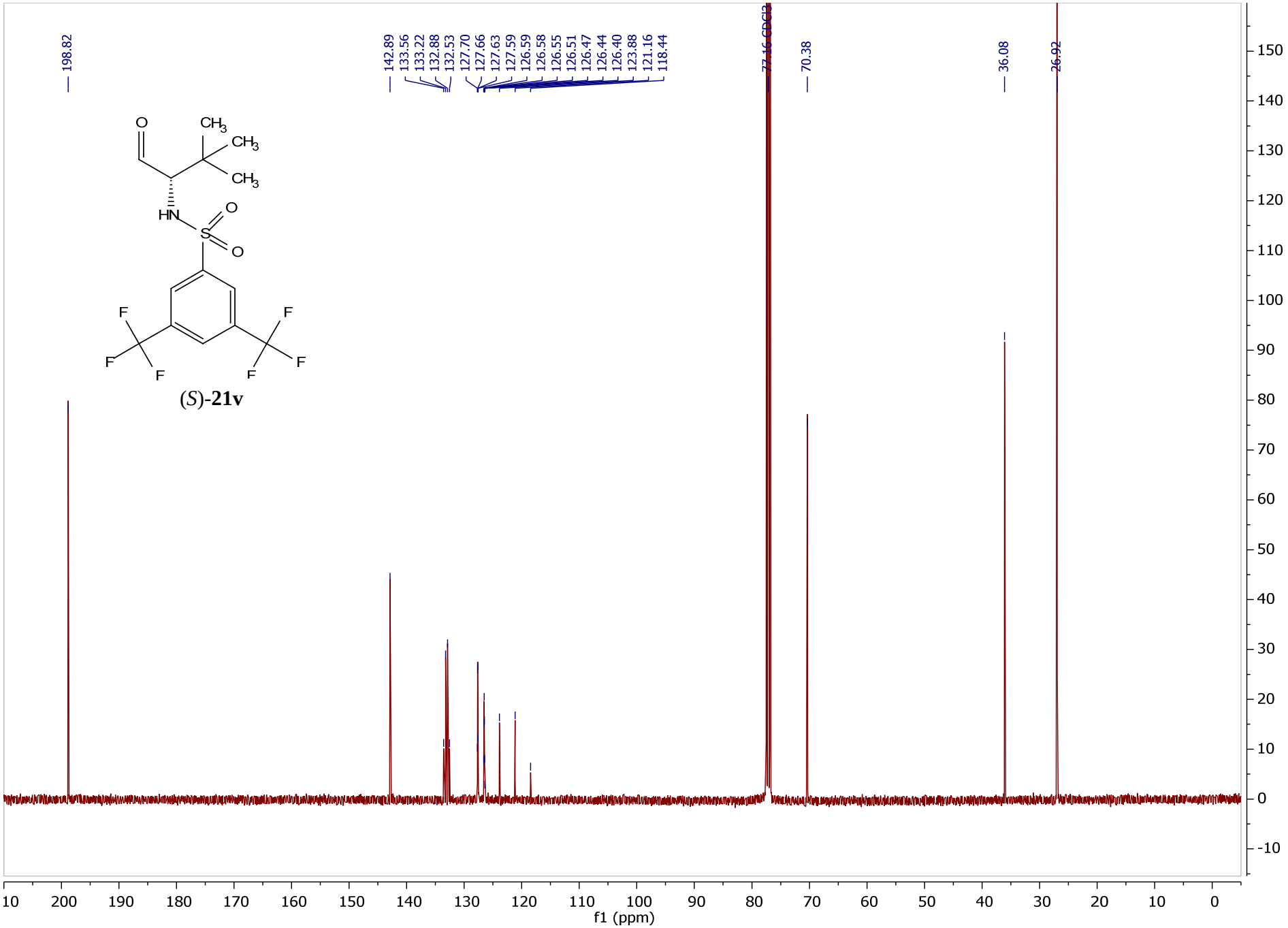

9.57 9.57 7.83 7.83 7.83 7.82 7.82 7.81 7.81 7.81 7.80 7.57 7.56 7.55 7.55 7.54 7.54 7.53 7.51 7.50 7.50 7.50 7.49 7.49 7.48 7.48 7.48 7.48 7.47 7.47 7.46 7.26 CDCl3
5.42 5.40
3.70 3.70 3.68 3.68
1.02
O
CH3
CH3
CH3
HN
S
O
O
(S)-21u
A (d) 9.57
C (m) 7.51
B (m) 7.82
D (d) 5.41
E (dd) 3.69
F (s) 1.02
0.99
1.92
3.05
0.95
1.04
9.00
f1 (ppm)


199.47
139.68
133.06
129.24
127.33
77.16 CDCl3
69.82
35.98
26.88
O
CH3
CH3
CH3
HN
S
O
O
f1 (ppm)

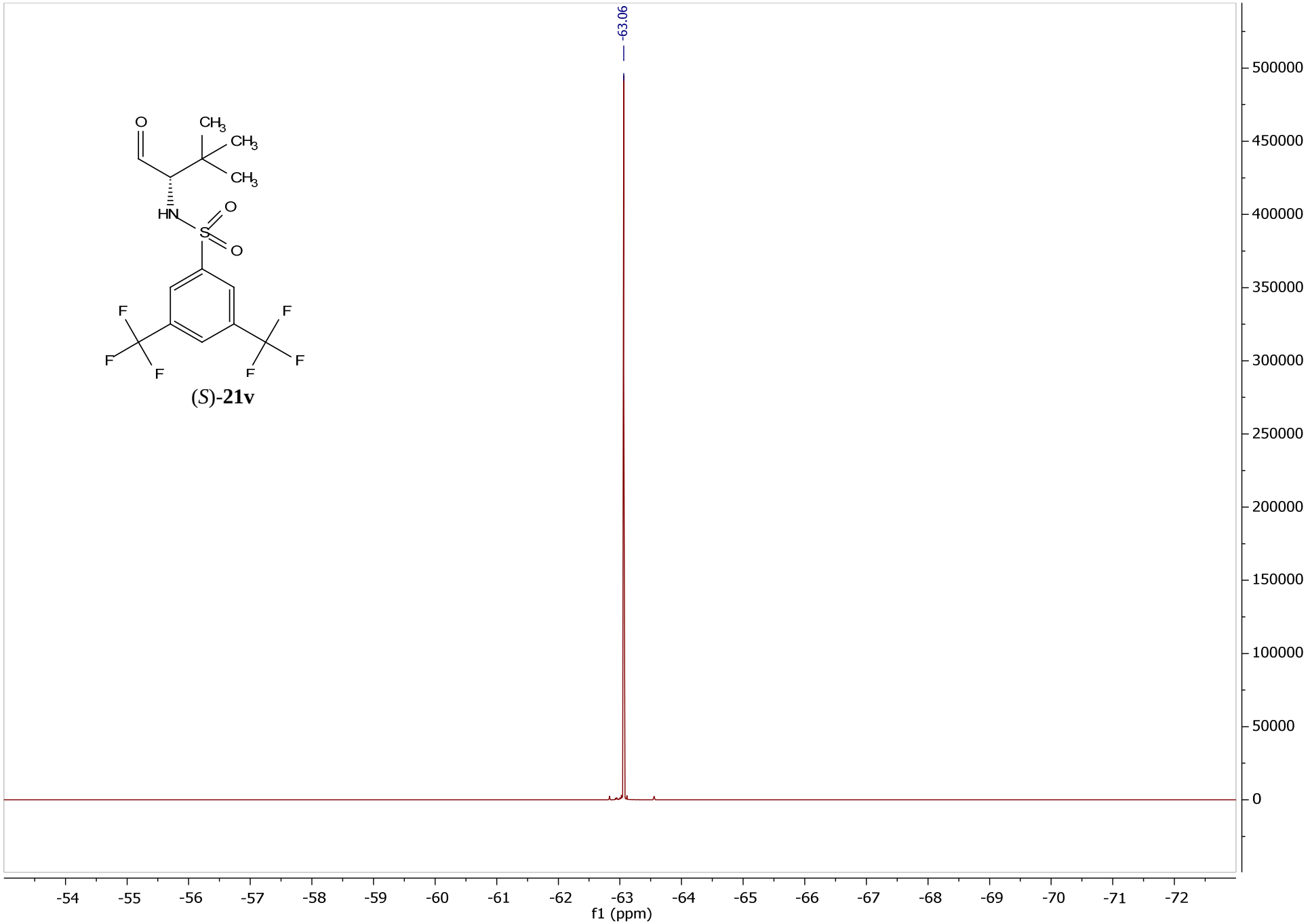
(*S*)-**21u**


9.64
8.28
8.05
7.26 CDCl3
5.55
5.53
3.83
3.80
1.07
B (s)
8.28
C (s)
9.64
A (s)
8.05
D (d)
5.54
E (d)
3.82
F (s)
1.07
1.00
1.88
0.96
0.96
1.05
9.00
f1 (ppm)

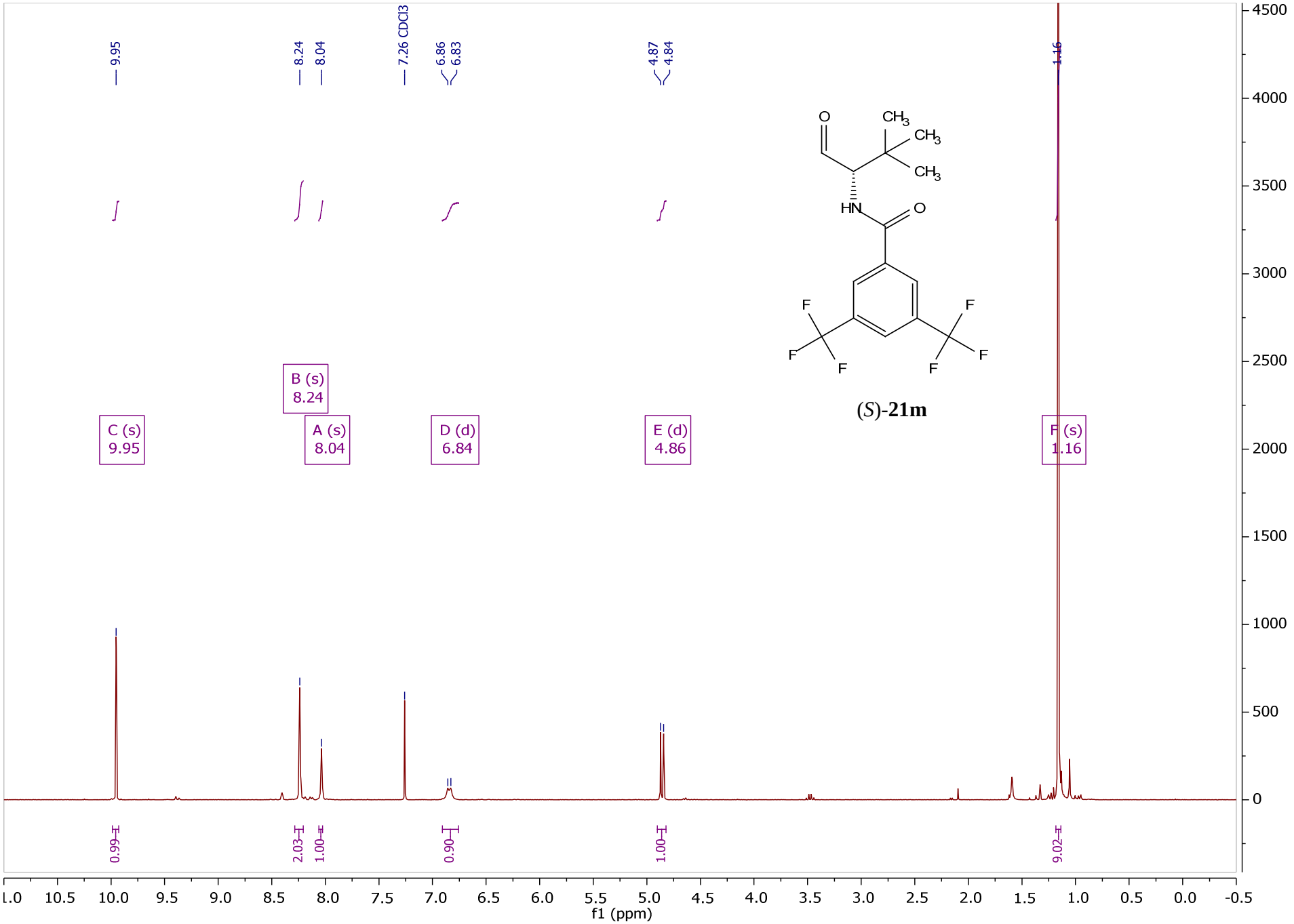
(*S*)-**21v**

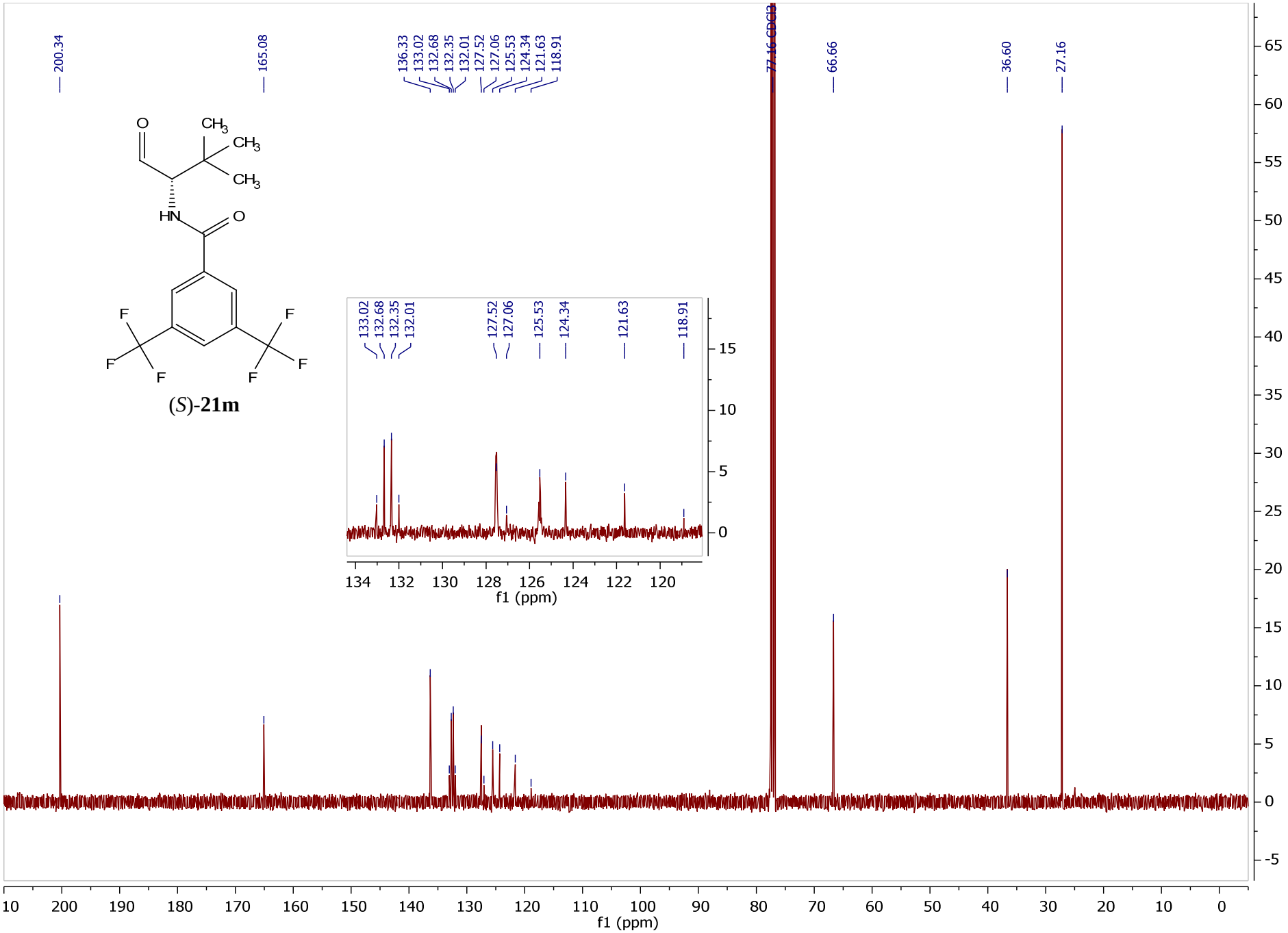

198.82
142.89
133.56
133.22
132.88
132.53
127.70
127.66
127.63
127.59
126.59
126.58
126.55
126.51
126.47
126.44
126.40
123.88
121.16
118.44
77.16 CDCl3
70.38
36.08
26.92
O
CH3
CH3
CH3
HN
S
O
O
F
F
F
F
F
F
f1 (ppm)

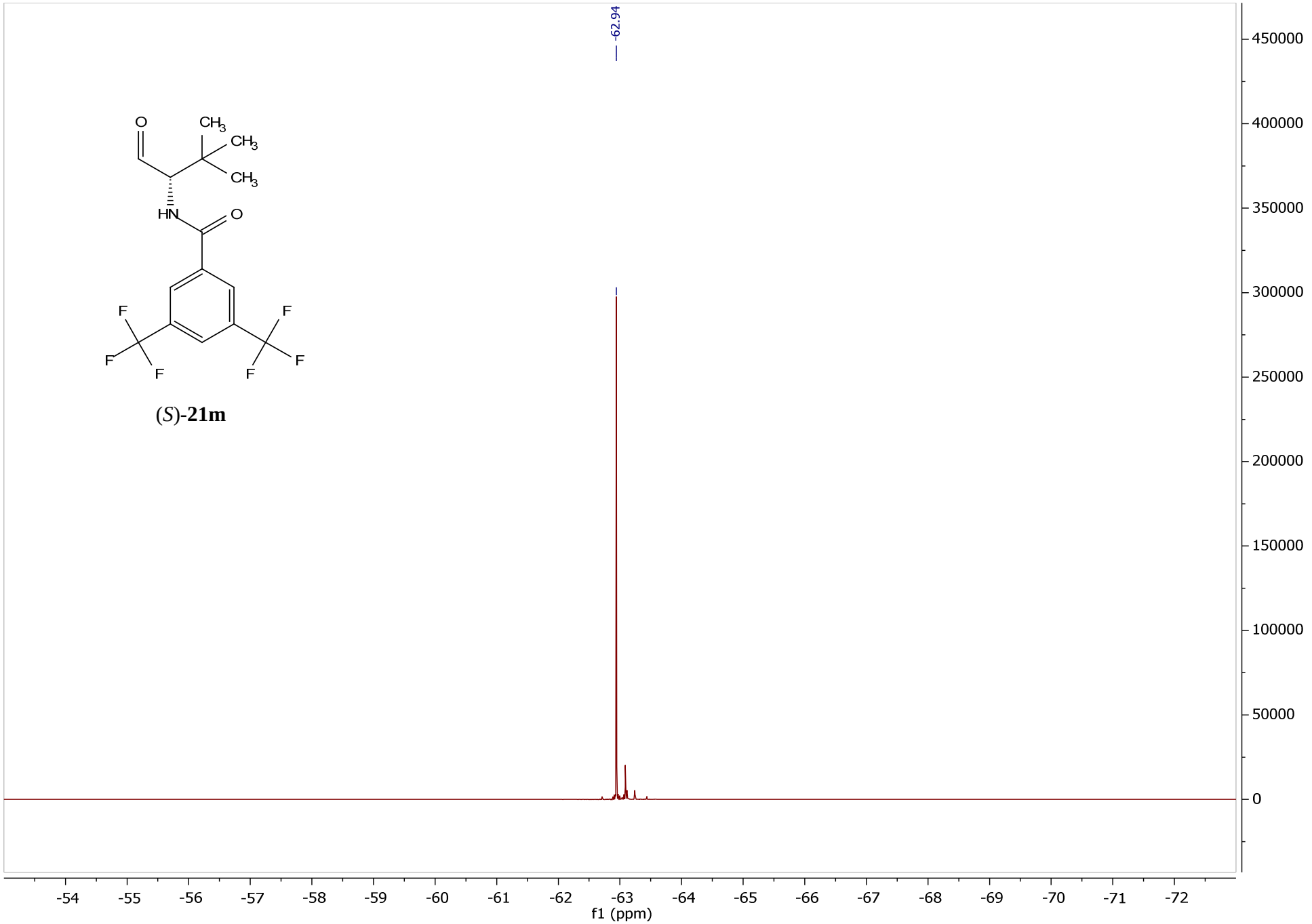
(*S*)-**21v**


-63.06
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
-71
-72
f1 (ppm)

(*S*)-**21v**


9.95
8.24
8.04
7.26 CDCl3
6.86
6.83
4.87
4.84
1.16
O
CH3
CH3
CH3
HN
O
F
F
F
F
F
F
(S)-21m
B (s)
8.24
C (s)
9.95
A (s)
8.04
D (d)
6.84
E (d)
4.86
F (s)
1.16
0.99
2.03
1.00
0.90
1.00
9.02
4500
4000
3500
3000
2500
2000
1500
1000
500
0
10.5
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
-0.5
f1 (ppm)


200.34
165.08
136.33
133.02
132.68
132.35
132.01
127.52
127.06
125.53
124.34
121.63
118.91
77.16 CDCl3
66.66
36.60
27.16
O
CH3
CH3
CH3
HN
O
F
F
F
F
F
F
(S)-21m
f1 (ppm)
f1 (ppm)


-62.94
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-54
-55
-56
-57
-58
-59
-60
-61
-62
-63
-64
-65
-66
-67
-68
-69
-70
-71
-72
f1 (ppm)

O
CH3
CH3
CH3
HN
O
F
F
F
F
F
F

(*S*)-**21m**