Electronic Supplementary Material (ESI) for RSC Advances.

Assigning Regioisomeric or Diastereoisomeric Relations of Problematic Trisubstituted Double-Bonds through Heteronuclear 2D Selective J-Resolved NMR Spectroscopy

Supporting Information

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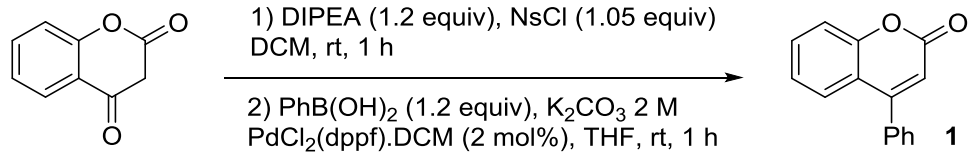
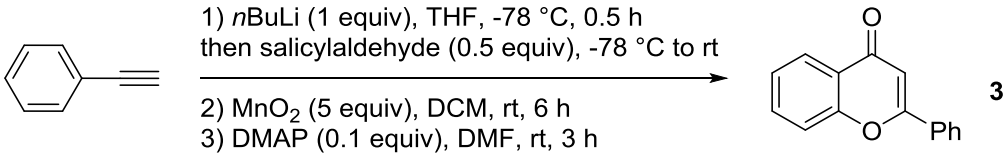
General pathways for the synthesis of different compounds:

Scheme A. Synthesis of **1** by nosylation and palladium cross-coupling from chromane-2,4-dione.[1]

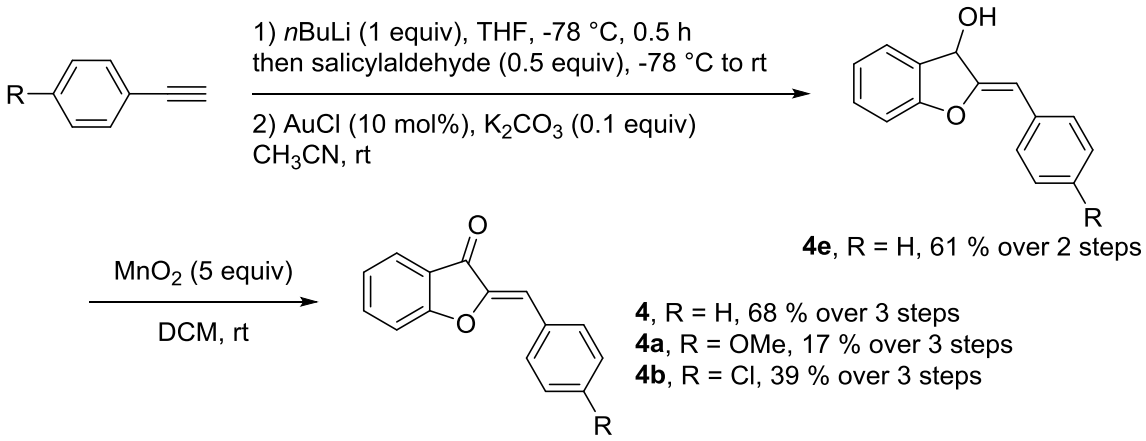


Scheme B. Synthesis of **3** by alkynylation, oxidation and cyclization from phenylacetylene and salicylaldehyde.[2]



41 % over 3 steps

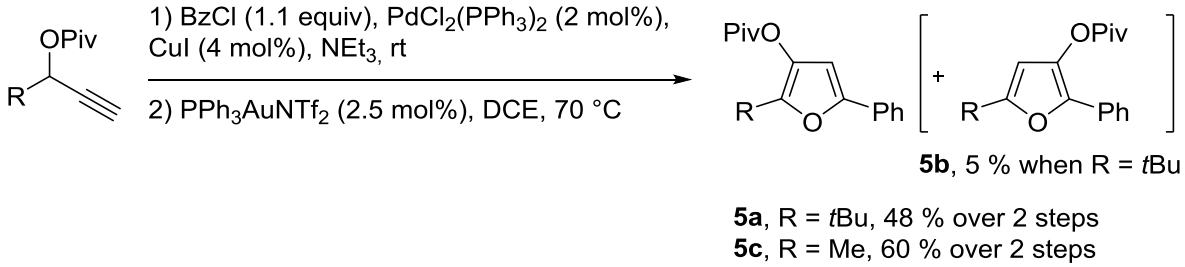
Scheme C. Synthesis of **4**, **4a**, **4b** and **4e** by alkynylation, gold(I) cyclisation and oxidation.[2b]



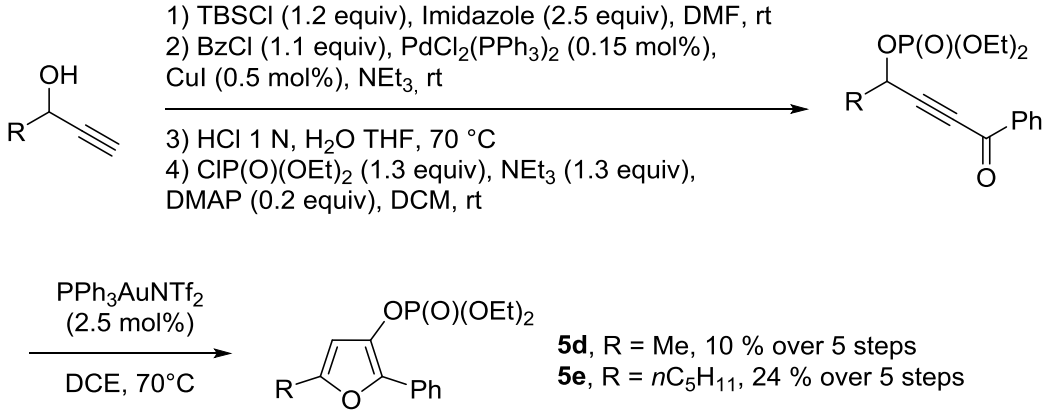
4e, R = H, 61 % over 2 steps

4, R = H, 68 % over 3 steps
4a, R = OMe, 17 % over 3 steps
4b, R = Cl, 39 % over 3 steps

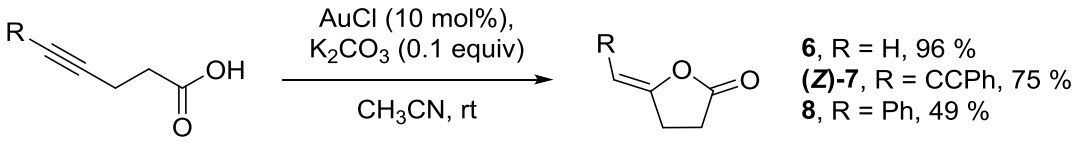
Scheme D. Synthesis of **5a**, **5b** and **5c** by Sonogashira reaction and gold(I) rearrangement.[3]



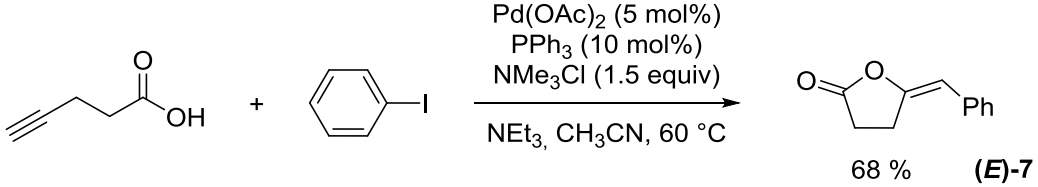
Scheme E. Synthesis of **5d** and **5e** by propargylic alcohol silylation, Sonogashira reaction, desilylation, phosphorylation and gold(I)-catalysis.[3,4]



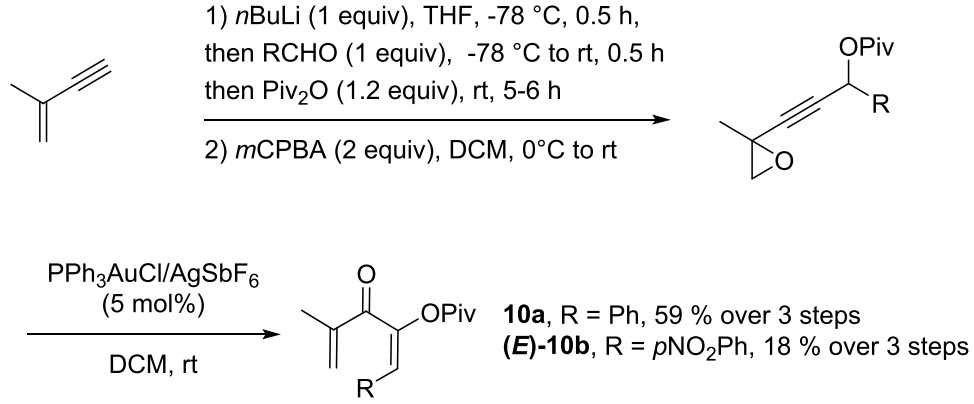
Scheme F. Synthesis of **6**, **(*Z*)-7** and **8** by gold(I)-cyclisation.[5]



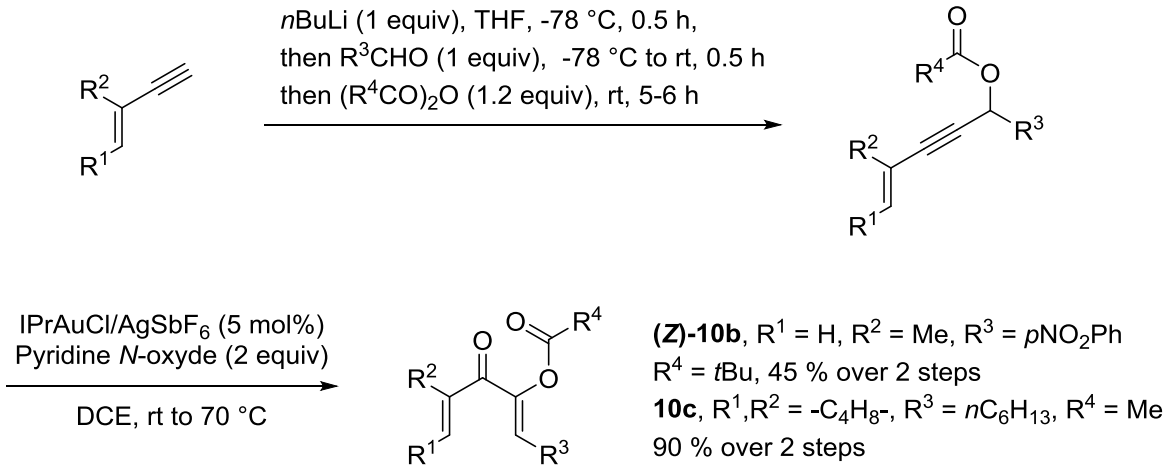
Scheme G. Synthesis of **(*E*)-7** by tandem cross coupling reaction and cyclisation from pent-4-ynoic acid.[6]



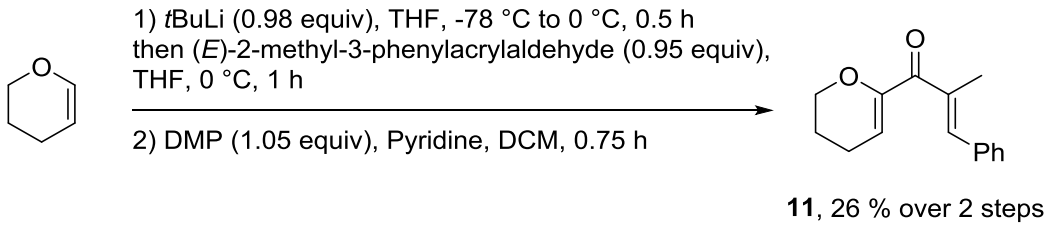
Scheme H. Synthesis of **10a** and **(*E*)-10b** by *one-pot* alkynylation-esterification, epoxydation and gold rearrangement.[7]



Scheme I. Synthesis of **(*Z*)-10b** and **10c** by *one-pot* alkynylation-esterification and gold-catalyzed oxidative rearrangement.[7,8]

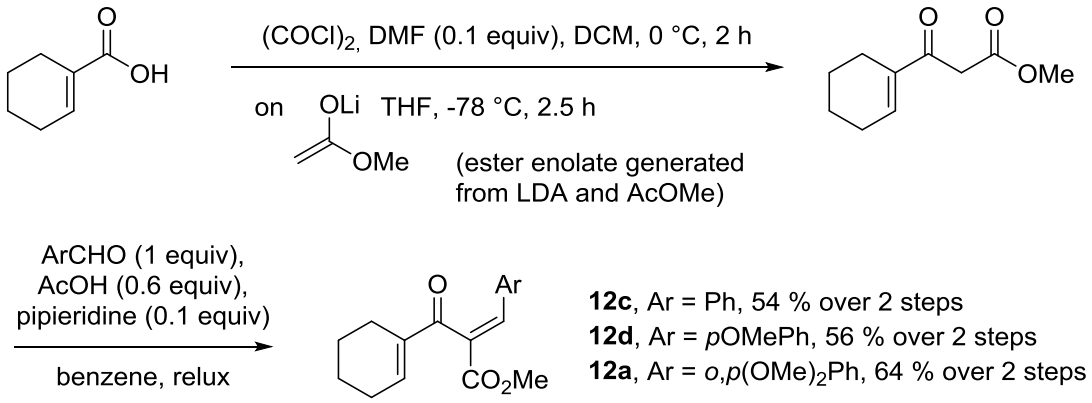


Scheme J. Synthesis of **11** by alkenylation and oxydation from dihydropyrane.[7]



11, 26 % over 2 steps

Scheme K. Synthesis of **12a**, **12c** and **12d** by ketoester synthesis and Knoevenagel condensation.[9]



[1] Cheval, N. P.; Dikova, A.; Blanc, A.; Weibel, J.-M.; Pale, P. *Chem. Eur. J.* **2013**, *19*, 8765.

[2] (a) Yoshida, M.; Fujino, Y.; Saito, K.; Doi, T. *Tetrahedron* **2011**, *67*, 9993. (b) Harkat, H.; Blanc, A.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2008**, *73*, 1620.

[3] Hoffmann, M.; Miaskiewicz, S.; Weibel, J.-M.; Pale, P.; Blanc, A. *Beilstein J. Org. Chem.* **2013**, *9*, 1774.

[4] Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868.

[5] Harkat, H.; Dembelé, A. Y.; Weibel, J.-M.; Blanc, A.; Pale, P. *Tetrahedron* **2009**, *65*, 1871.

[6] Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. R. *J. Org. Chem.* **1992**, *57*, 976.

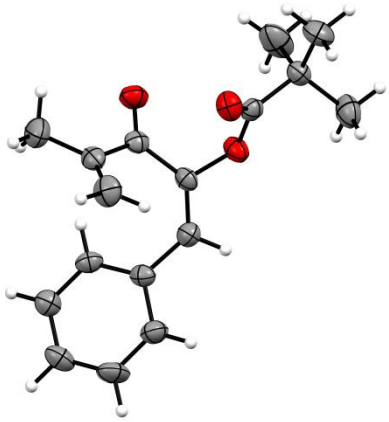
[7] Hoffmann, M.; Weibel, J.-M.; de Frémont, P.; Pale, P.; Blanc, A. *Org. Lett.* **2014**, *16*, 908.

[8] Ji, K.; Nelson, J.; Zhang, L. *Beilstein J. Org. Chem.* **2013**, *9*, 1925.

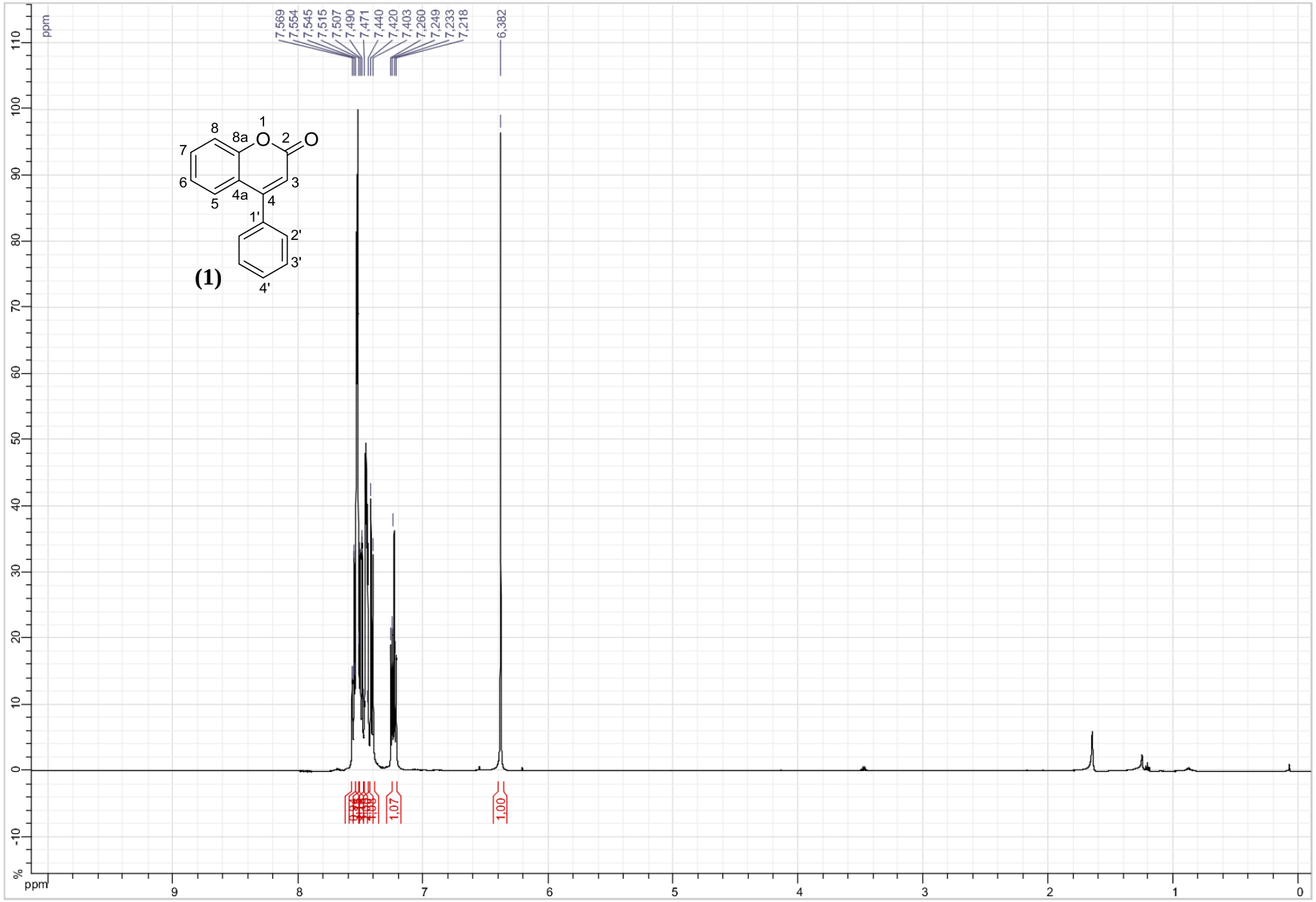
[9] (a) Bee, C.; Leclerc, E.; Tius, M. A. *Org. Lett.* **2003**, *5*, 4927. (b) He, W.; Herrick, I. R.; Atesin, T. A.; Caruana, P. A.; Kellenberger, C. A.; Frontier, A. J. *J. Am. Chem. Soc.* **2008**, *130*, 1003.

Image of XRD for 10a and table of crystal data and refinement details: CCDC 1047510

(hydrogens were omitted for clarity)



Identification Code	ppmh140130 **(10a)**
Formula	$C_{17}H_{20}O_3$
Formula weight	272.33
Crystal system	Monoclinic
Space group	P 21/c
a (Å)	9.3092(6)
b (Å)	17.6398(16)
c (Å)	9.9340(8)
α (°)	90
β (°)	106.889(4)
γ (°)	90
V ($Å^3$)	1560.9(2)
Z	4
Density (g cm^{-3})	1.159
mu (MoKα) (mm^{-1})	0.078
F(000)	584
Data collection	
Temperature (K)	173(2)
Radiation (Å)	MoKα – 0.71073
Theta min - max	0.998 – 27.485
Dataset[h, k, l]	-11/12, -20/22, -12/12
Tot., Uniq. Data, R(int)	10436, 3509, 0.1019
Observed data (>2σ(I))	2046
Refinement	
Nreflections, Nparameters	3509, 185
R2, R1, wR2, wR1, Goof	0.1594, 0.0846, 0.1971, 0.1697, 1.127
Max. and Av. Shift/Error	0.000, 0.000
Min, Max. Resd Dens. (e-/$Å^3$)	-0.261, 0.199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7,490
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7,260
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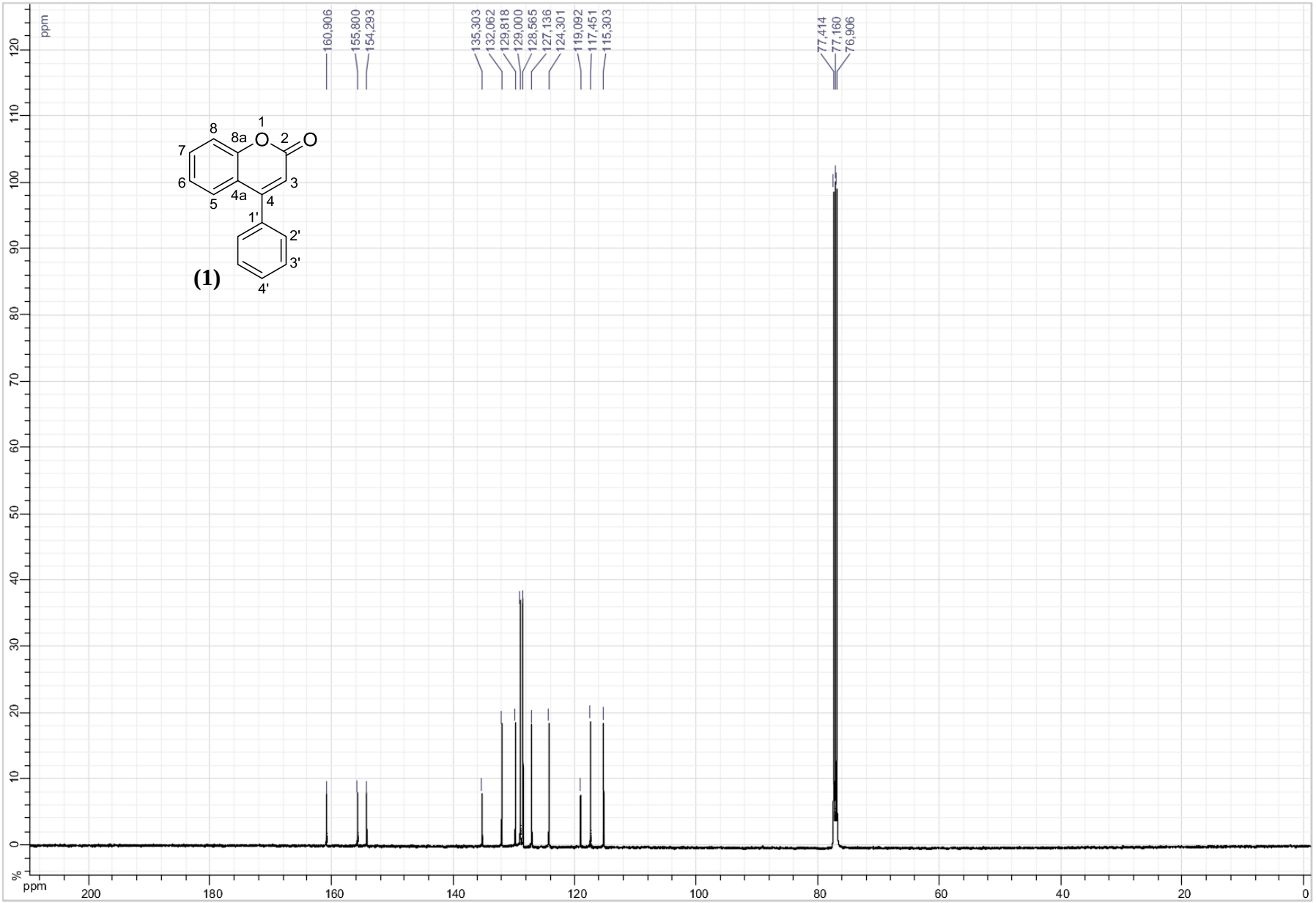
7,233
7,218
6,382
1,07
1,00
ppm

(1)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77,414
77,160
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(1)
ppm
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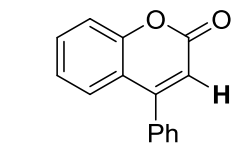
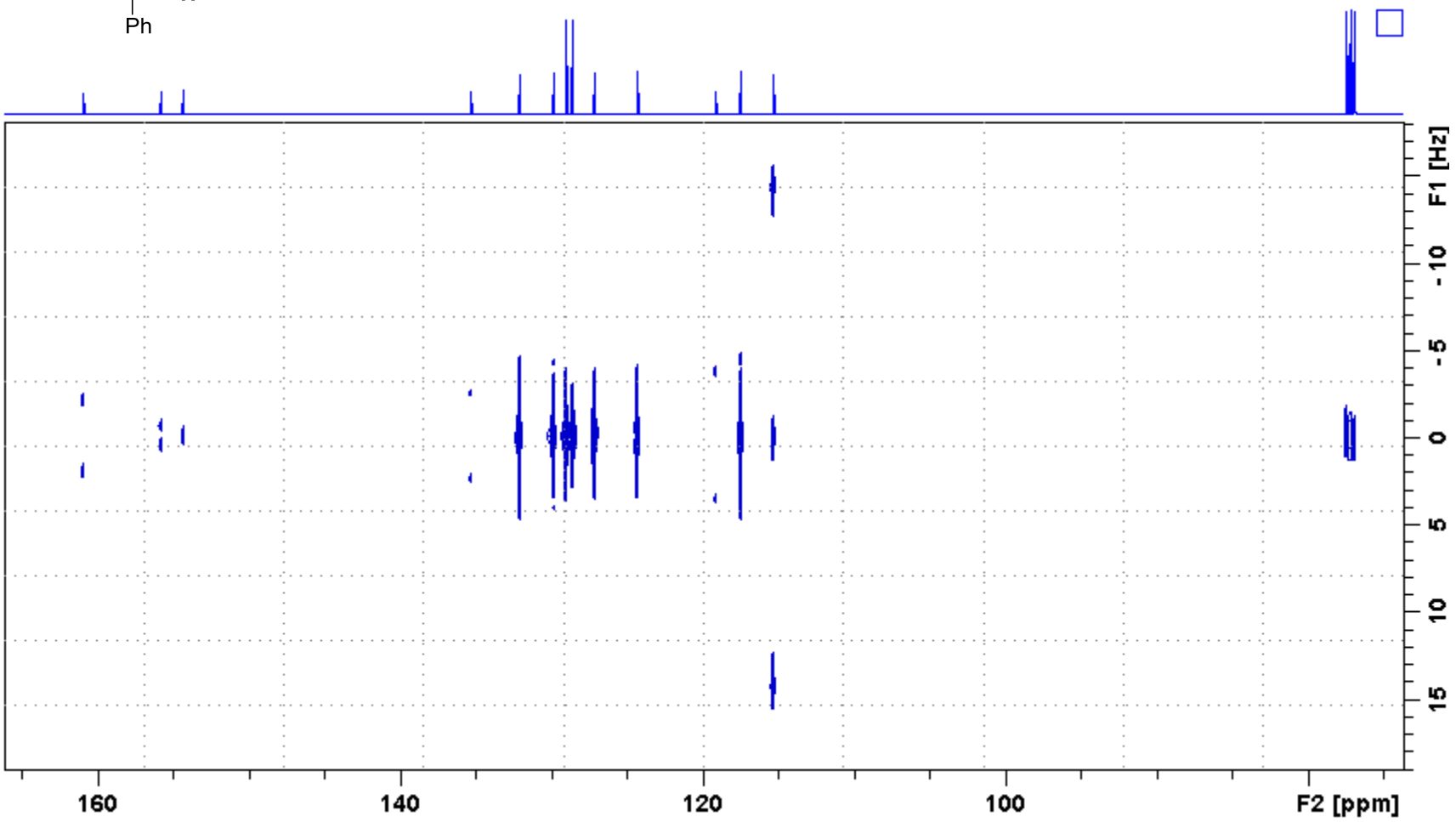
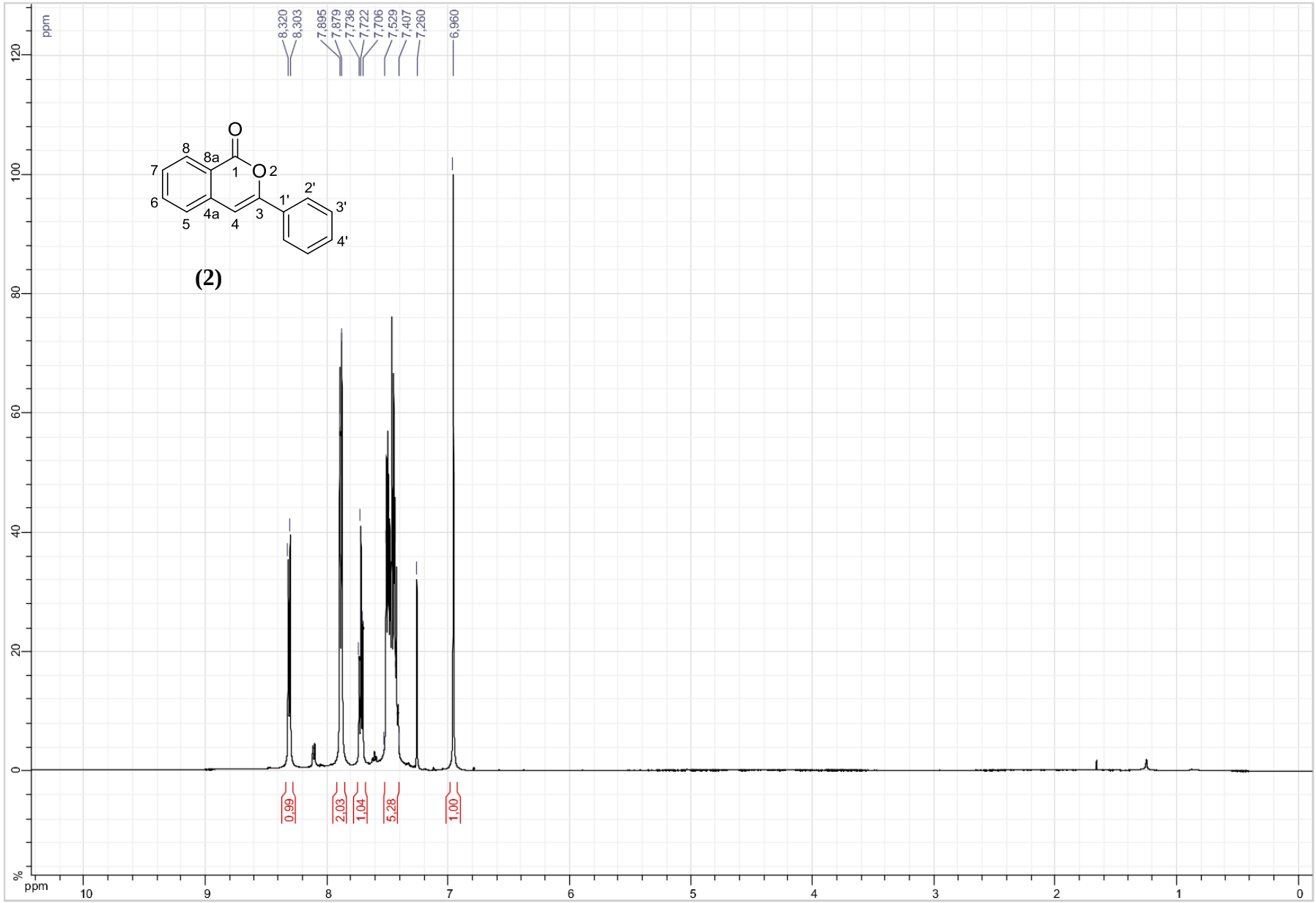
180
160
140
120
100
80
60
40
20
0
%

(1)



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7,736
7,722
7,706
7,529
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7,260
6,960
O
8
8a
1
O
2
7
6
5
4a
4
3
2'
1'
3'
4'
(2)
0,99
2,03
1,04
5,28
1,00
%
ppm
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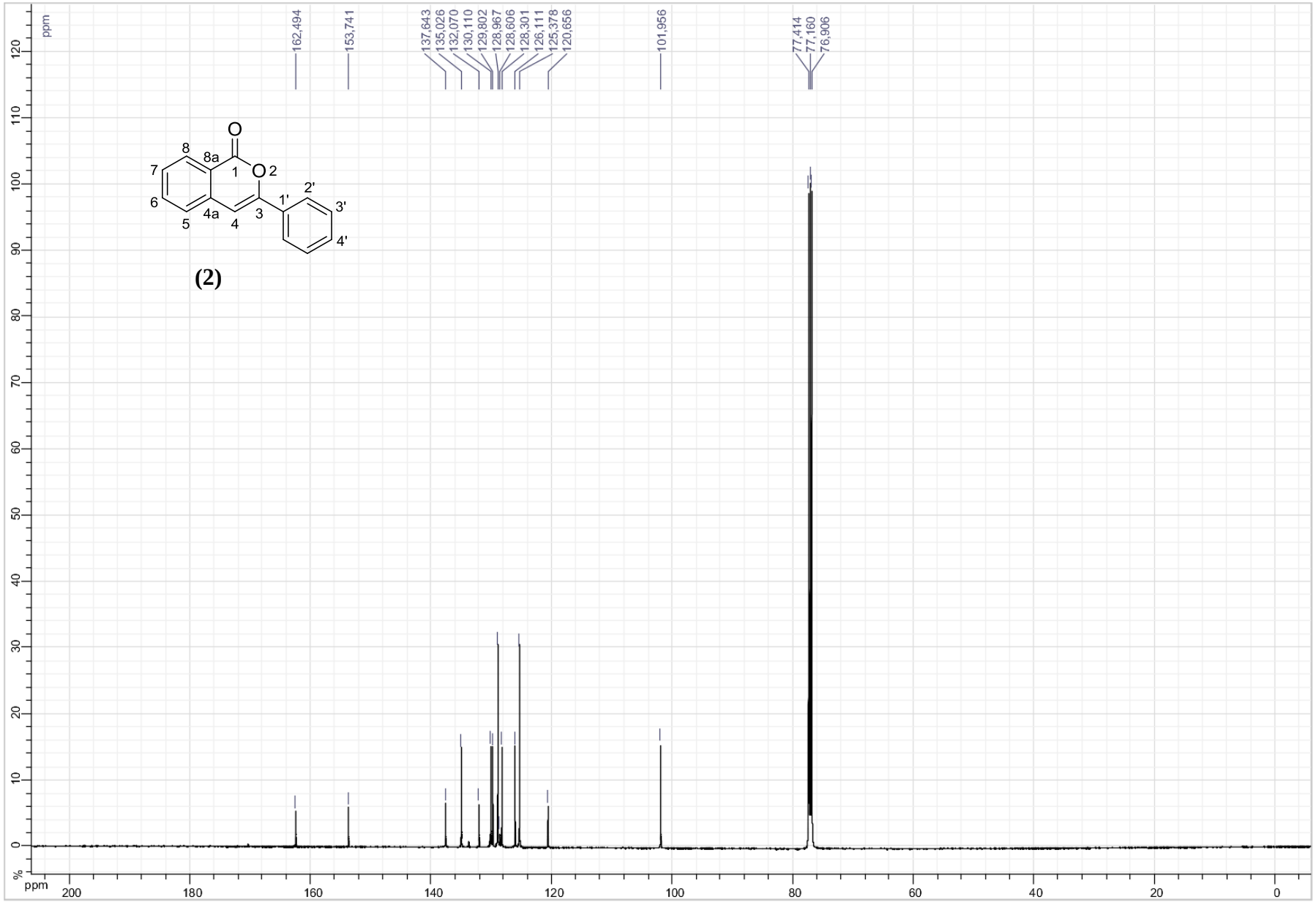
9
8
7
6
5
4
3
2
1
0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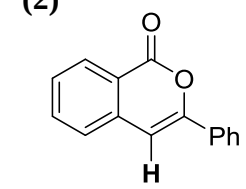
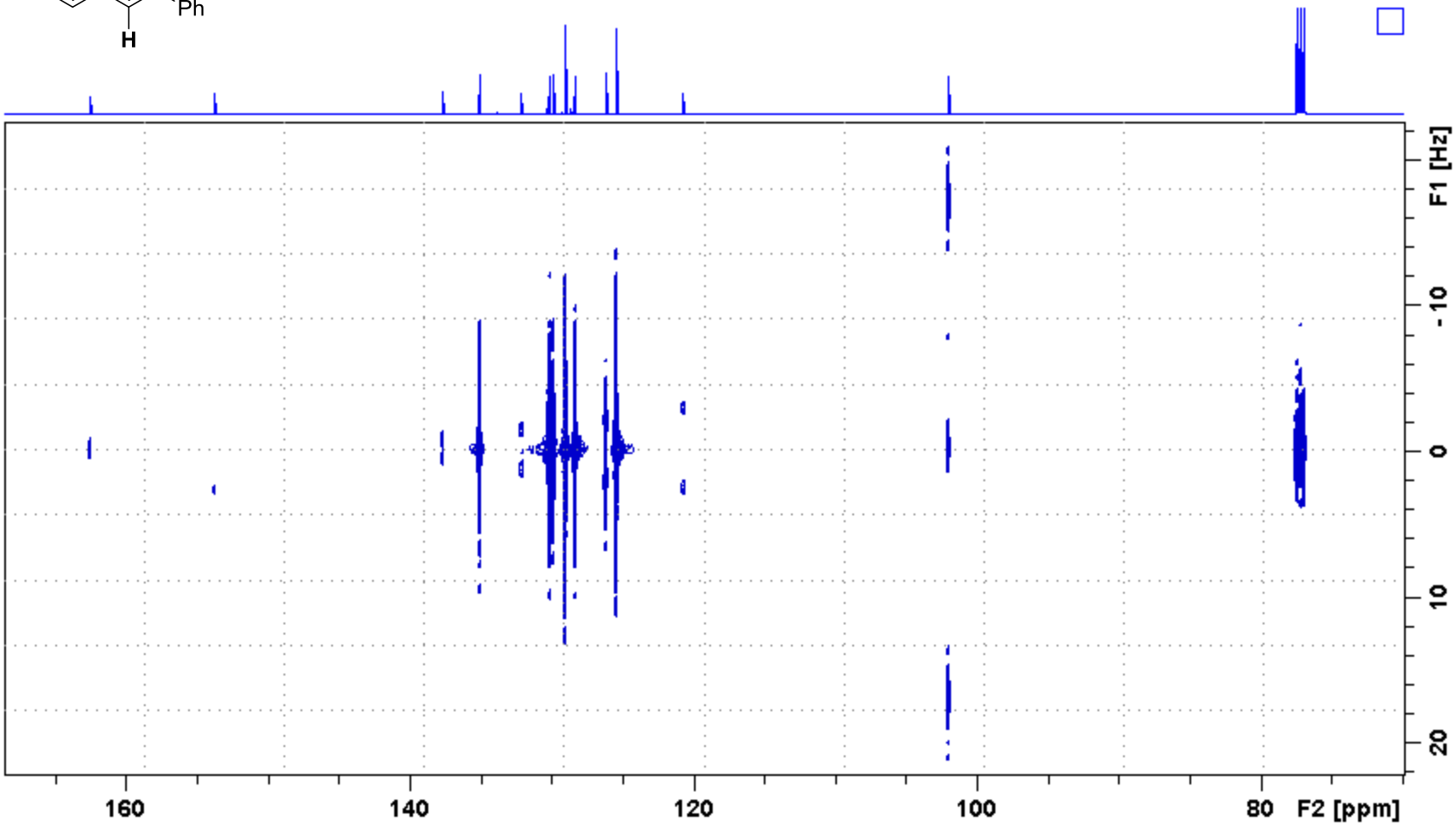
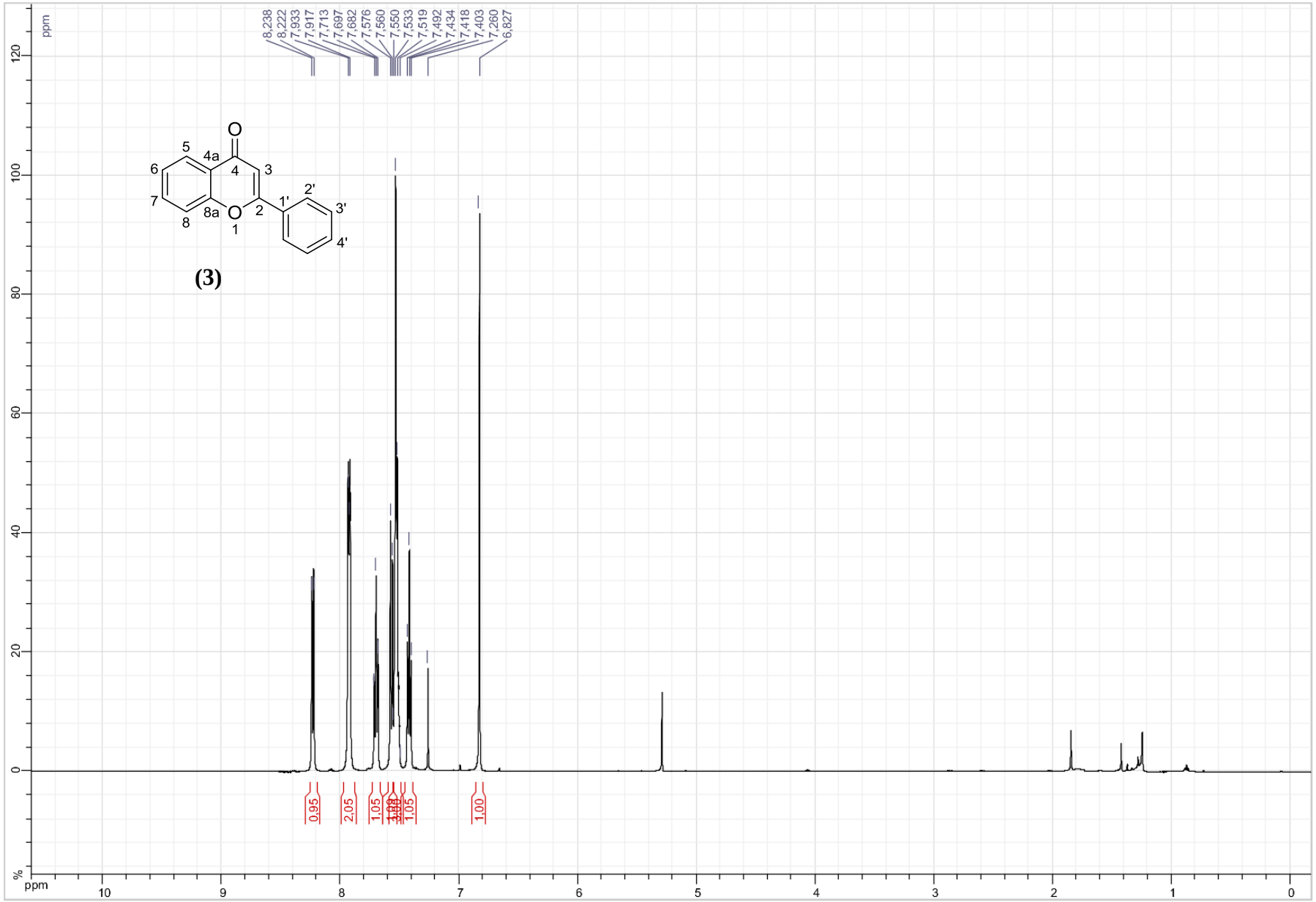
128,606
128,301
126,111
125,378
120,656
101,956
77,414
77,160
76,906
O
8
8a
1
O
2
7
2'
6
1'
3'
4a
3
5
4
4'
(2)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(2)



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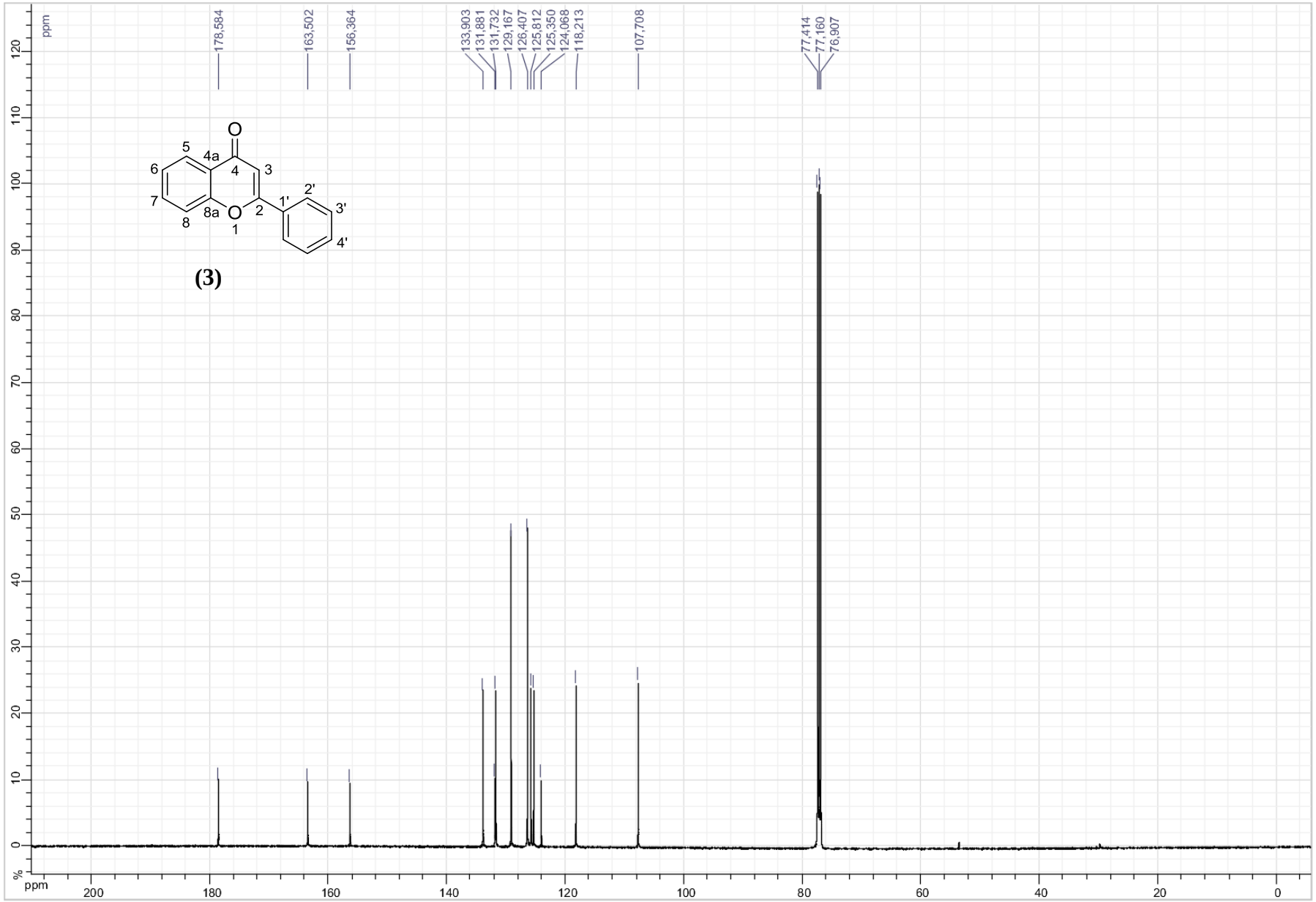
7,713
7,697
7,682
7,576
7,560
7,550
7,533
7,519
7,492
7,434
7,418
7,403
7,260
6,827
O
5
4a
4
3
6
2'
7
1'
3'
8a
2
8
O
1
4'
(3)
0,95
2,05
1,05
1,05
1,00
ppm
%
120
100
80
60
40
20
0
10
9
8
7
6
5
4
3
2
1
0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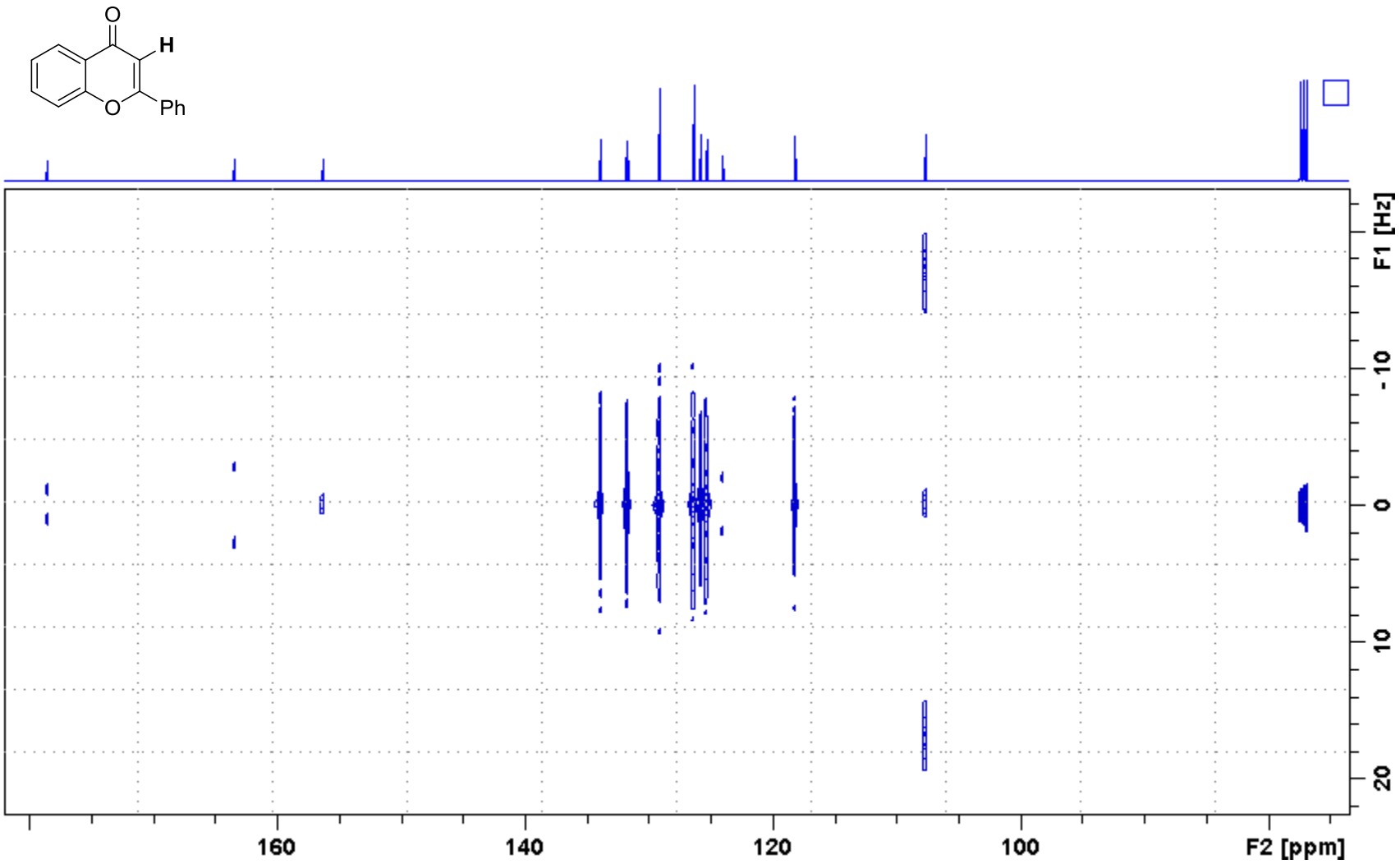
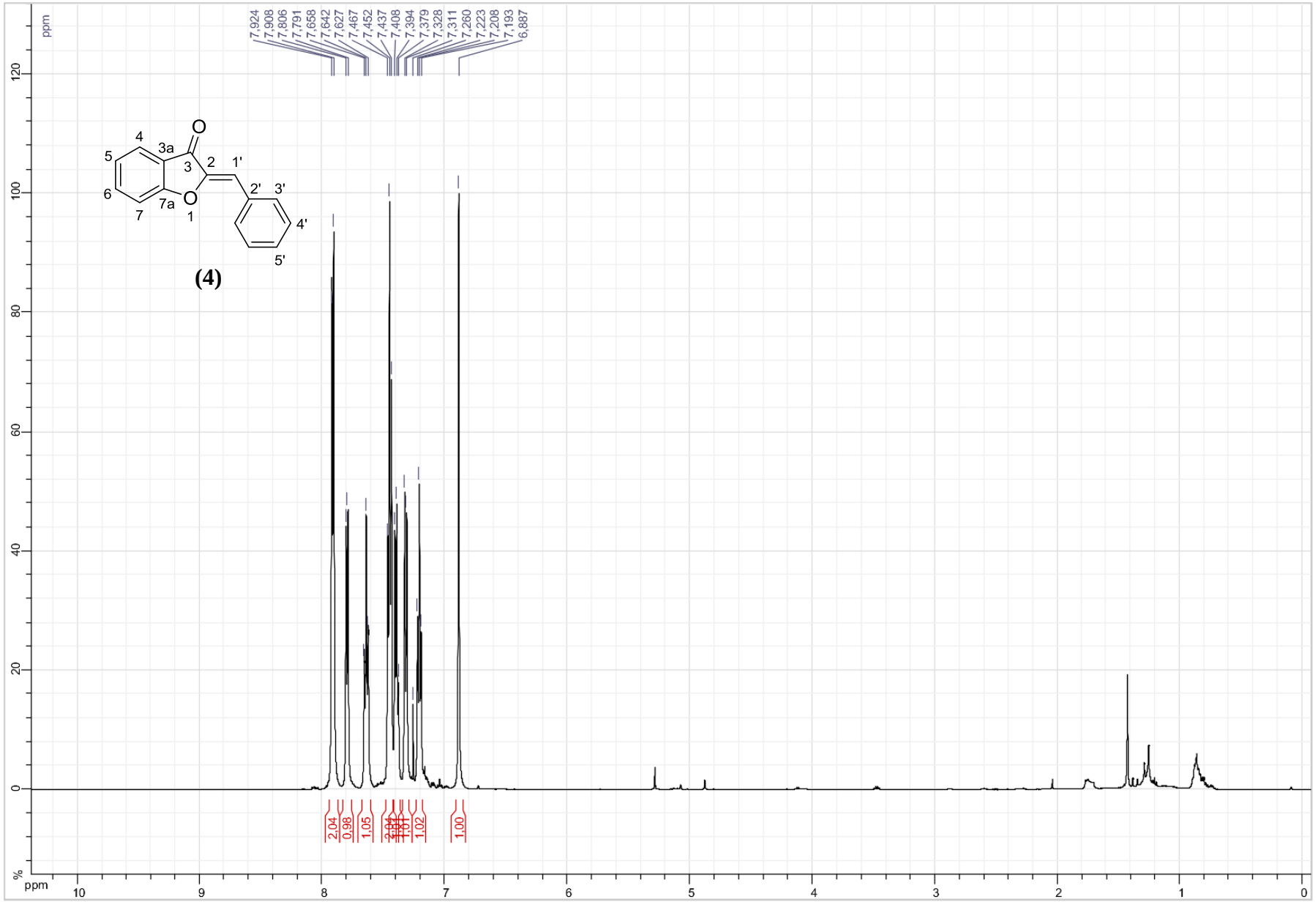
125,350
124,068
118,213
107,708
77,414
77,160
76,907
O
5
4a
4
3
6
2'
7
1'
3'
8a
2
8
O
1
4'
(3)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(3)

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7,806
7,791
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7,642
7,627
7,467
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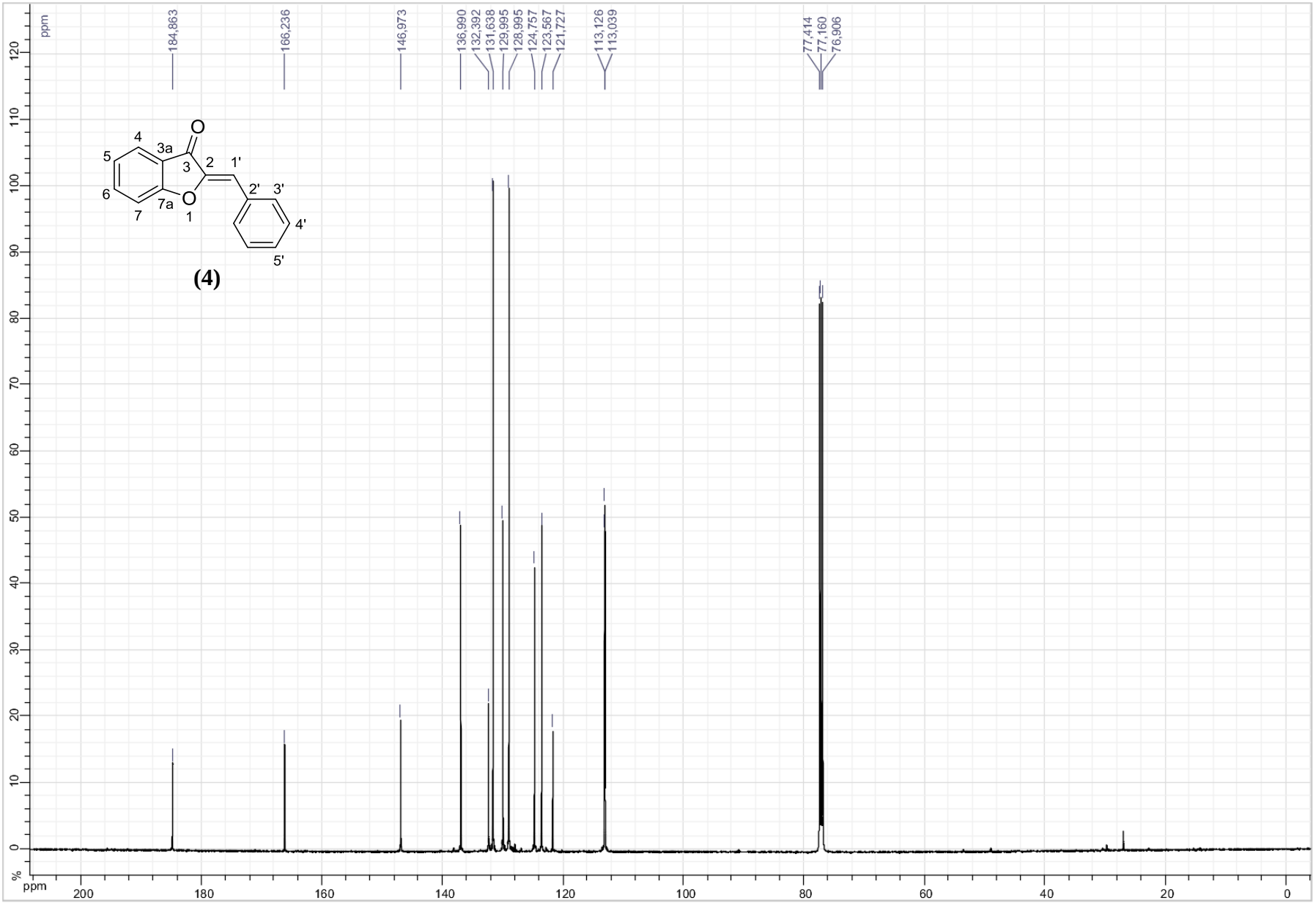
7,437
7,408
7,394
7,379
7,328
7,311
7,260
7,223
7,208
7,193
6,887
ppm
O
4
3a
5
3
2
1'
6
2'
3'
7a
O
7
1
4'
5'
(4)
2,04
0,98
1,05
1,02
1,00
%
ppm
10
9
8
7
6
5
4
3
2
1
0
120
100
80
60
40
20
0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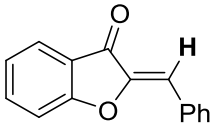
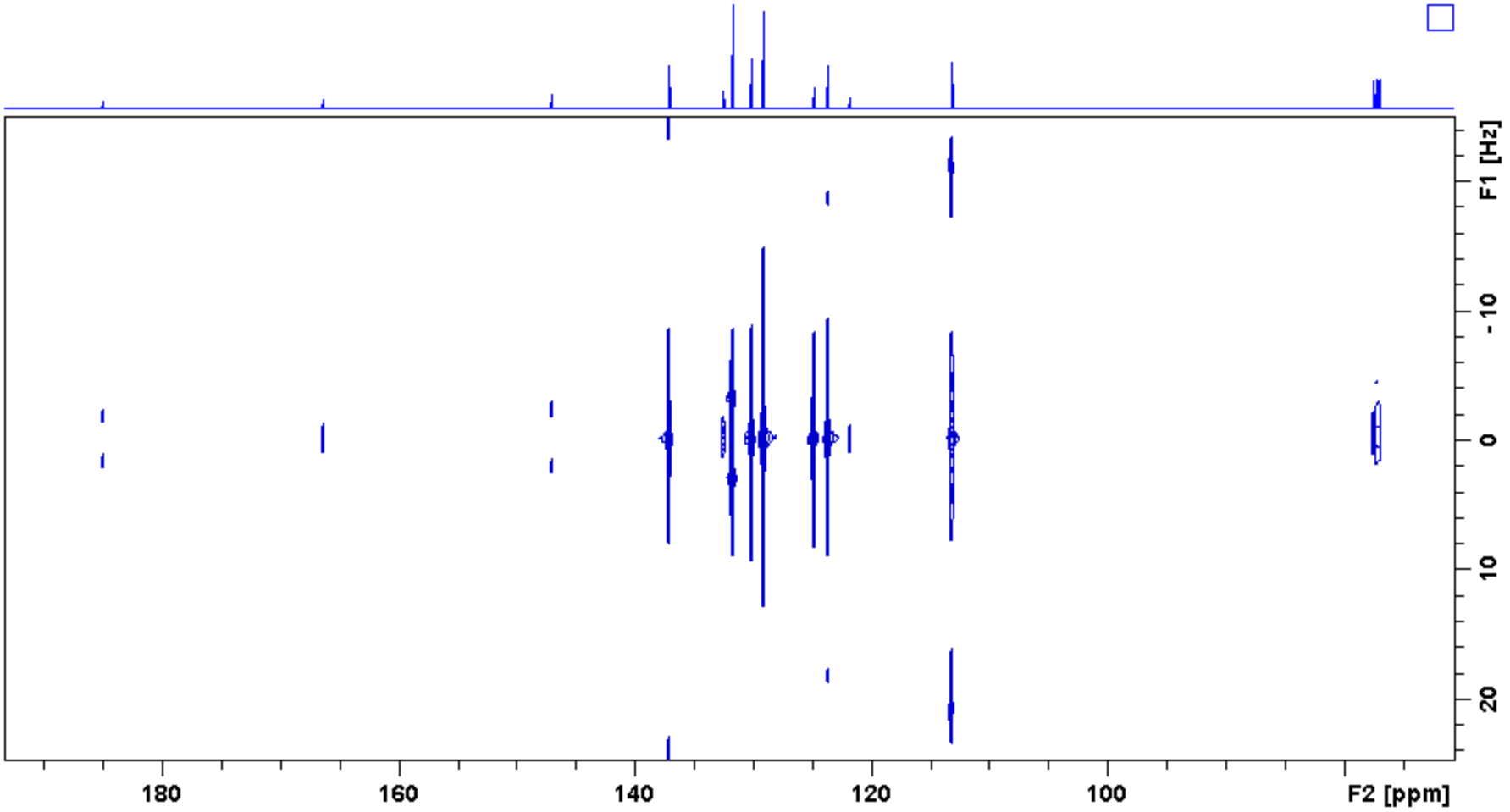
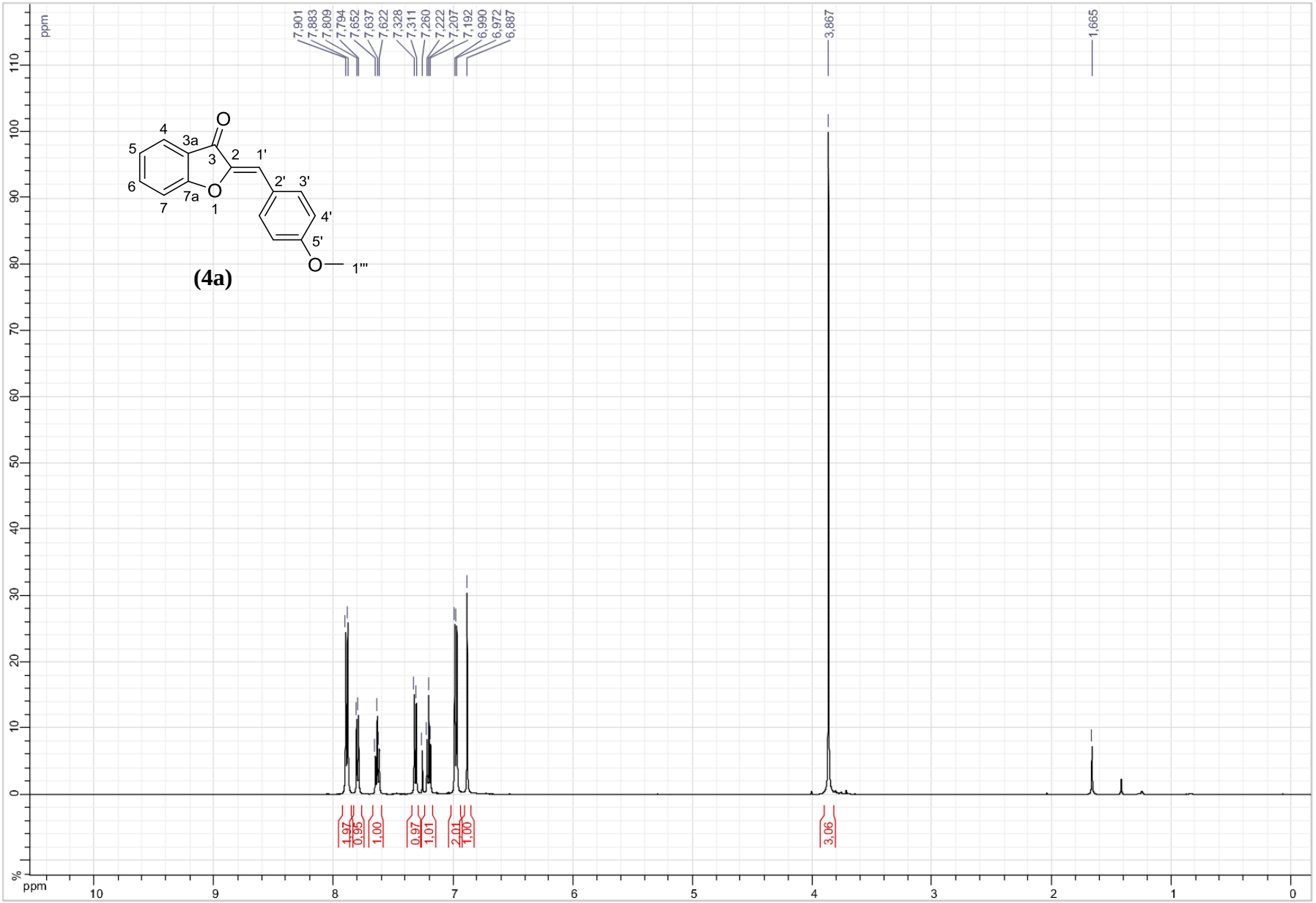
124,757
123,567
121,727
113,126
113,039
77,414
77,160
76,906
O
4
3a
5
3
2
1'
6
2'
3'
7a
O
7
1
4'
5'
(4)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(4)



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7,311
7,260
7,222
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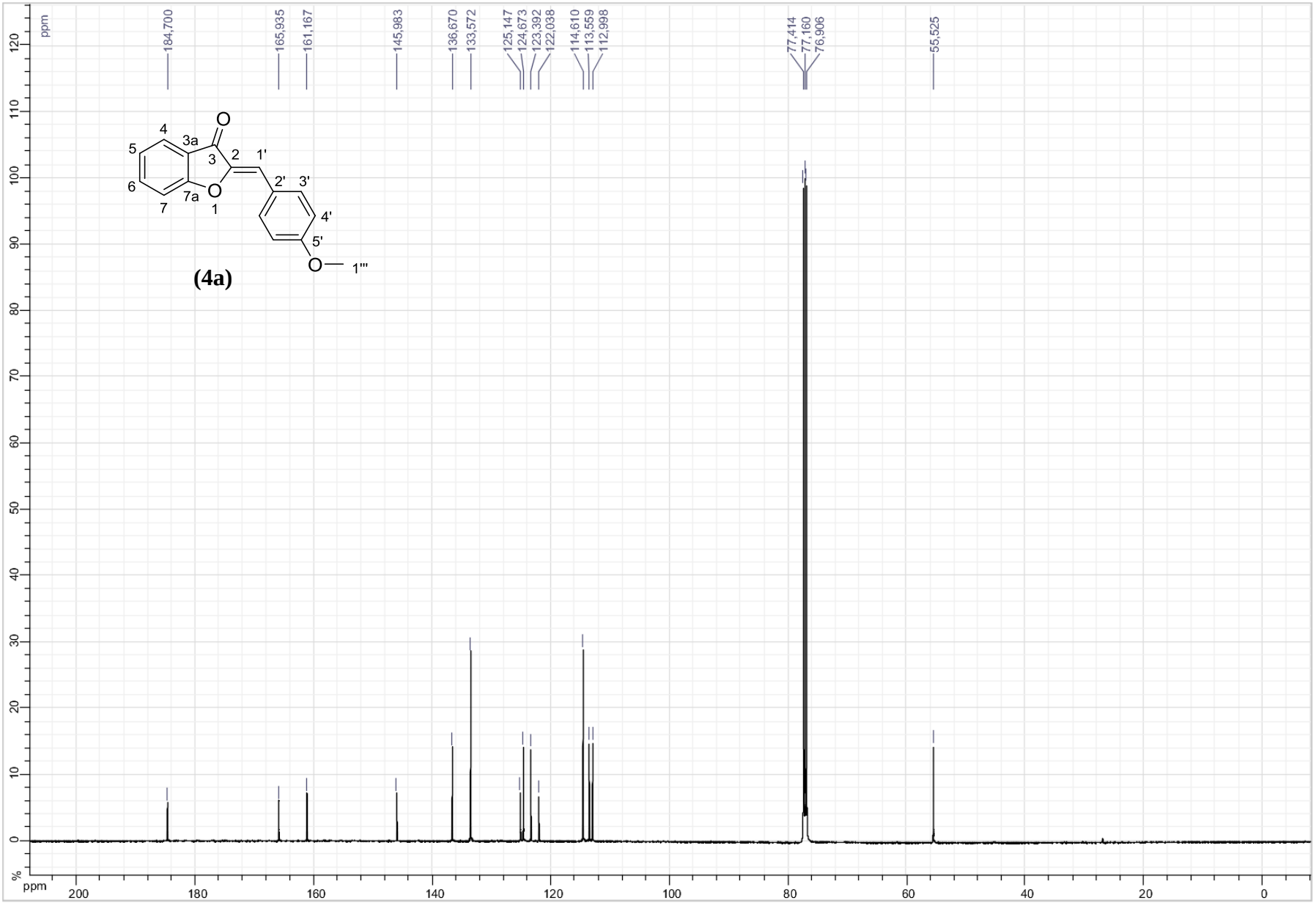
6,972
6,887
3,867
1,665
O
4
3a
5
3
2
1'
6
2'
3'
7a
O
7
1
4'
5'
O
1'''
(4a)
1,97
0,95
1,00
0,97
1,01
2,01
1,00
3,06
%
ppm
10
9
8
7
6
5
4
3
2
1
0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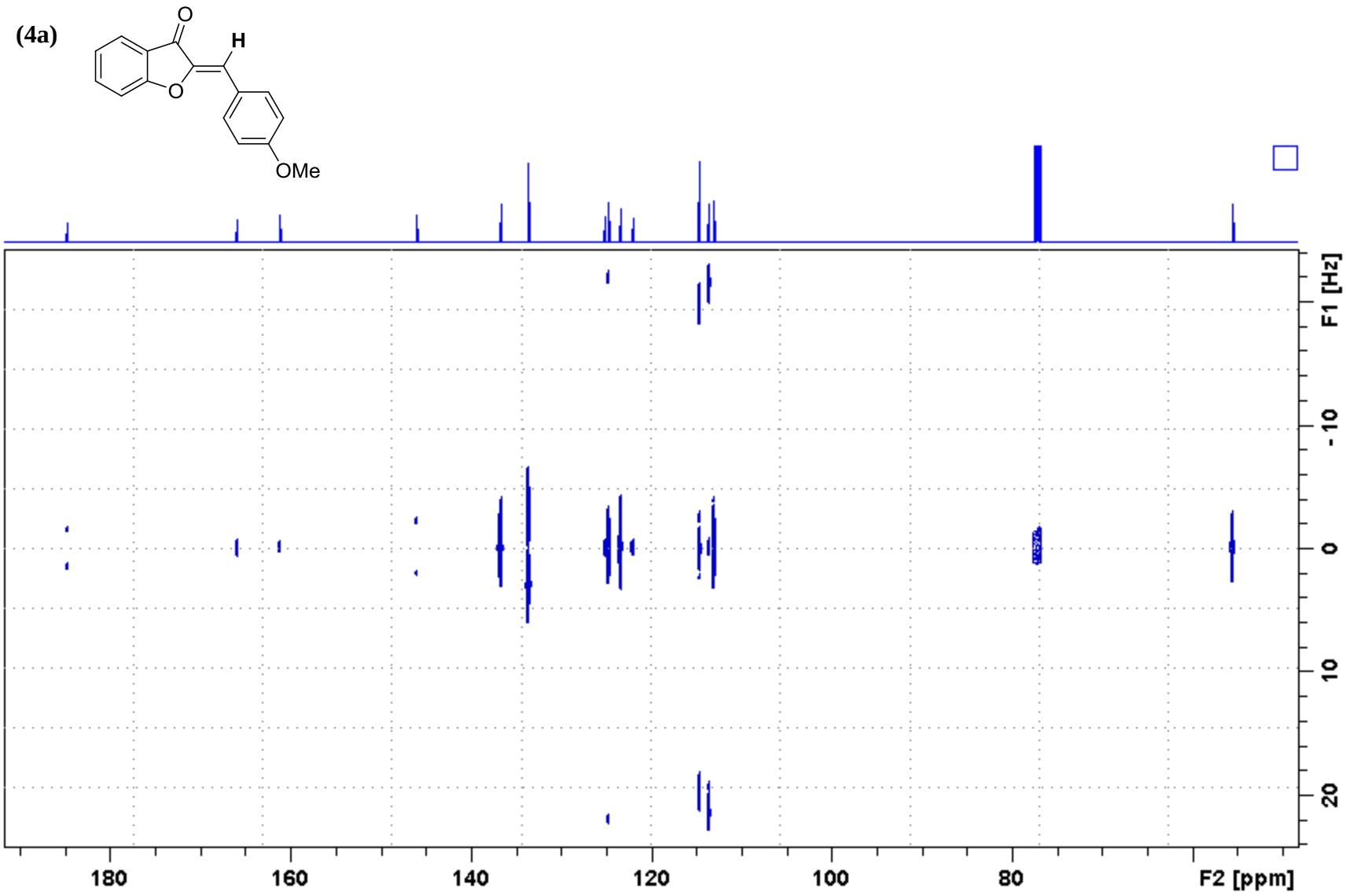
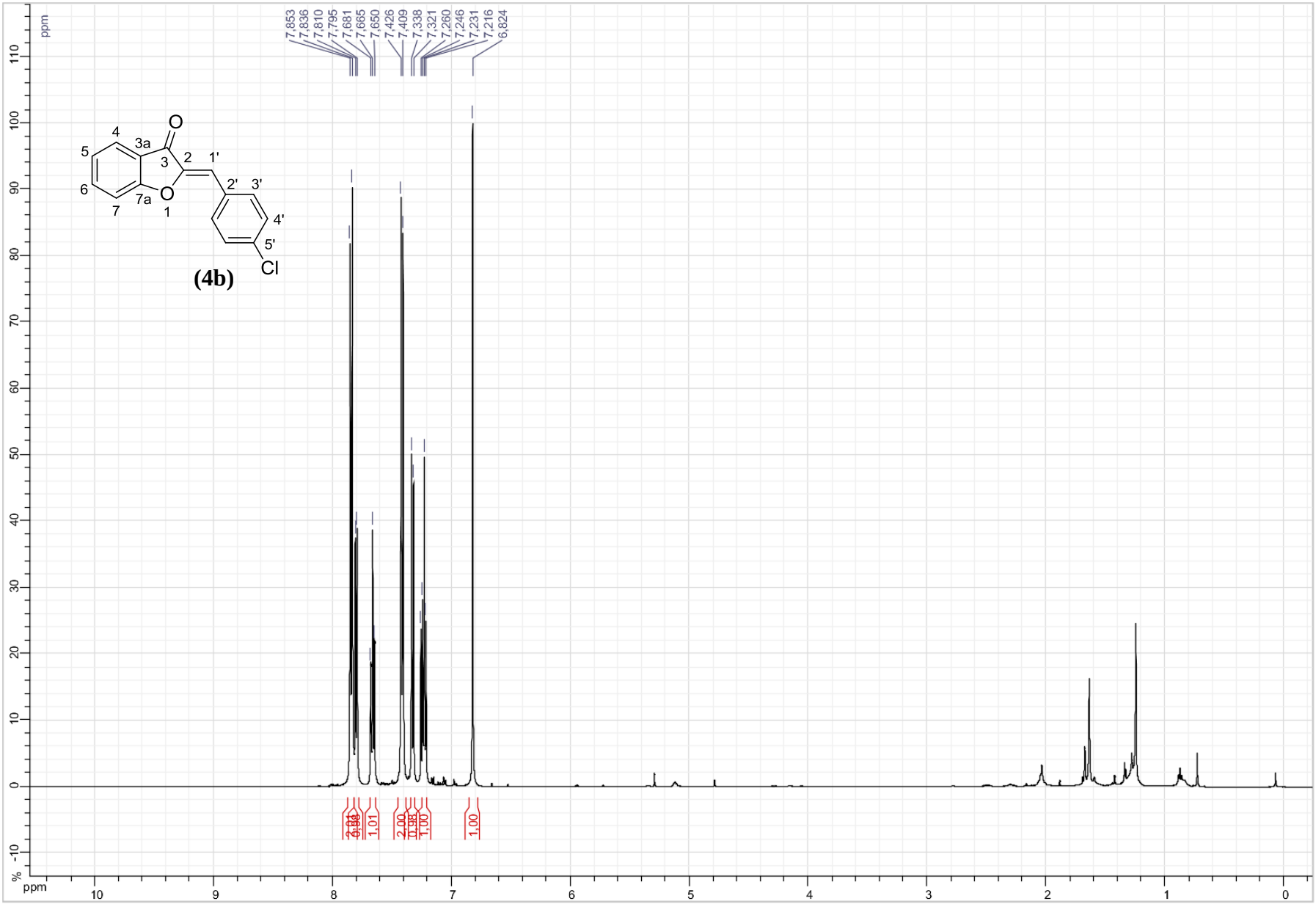
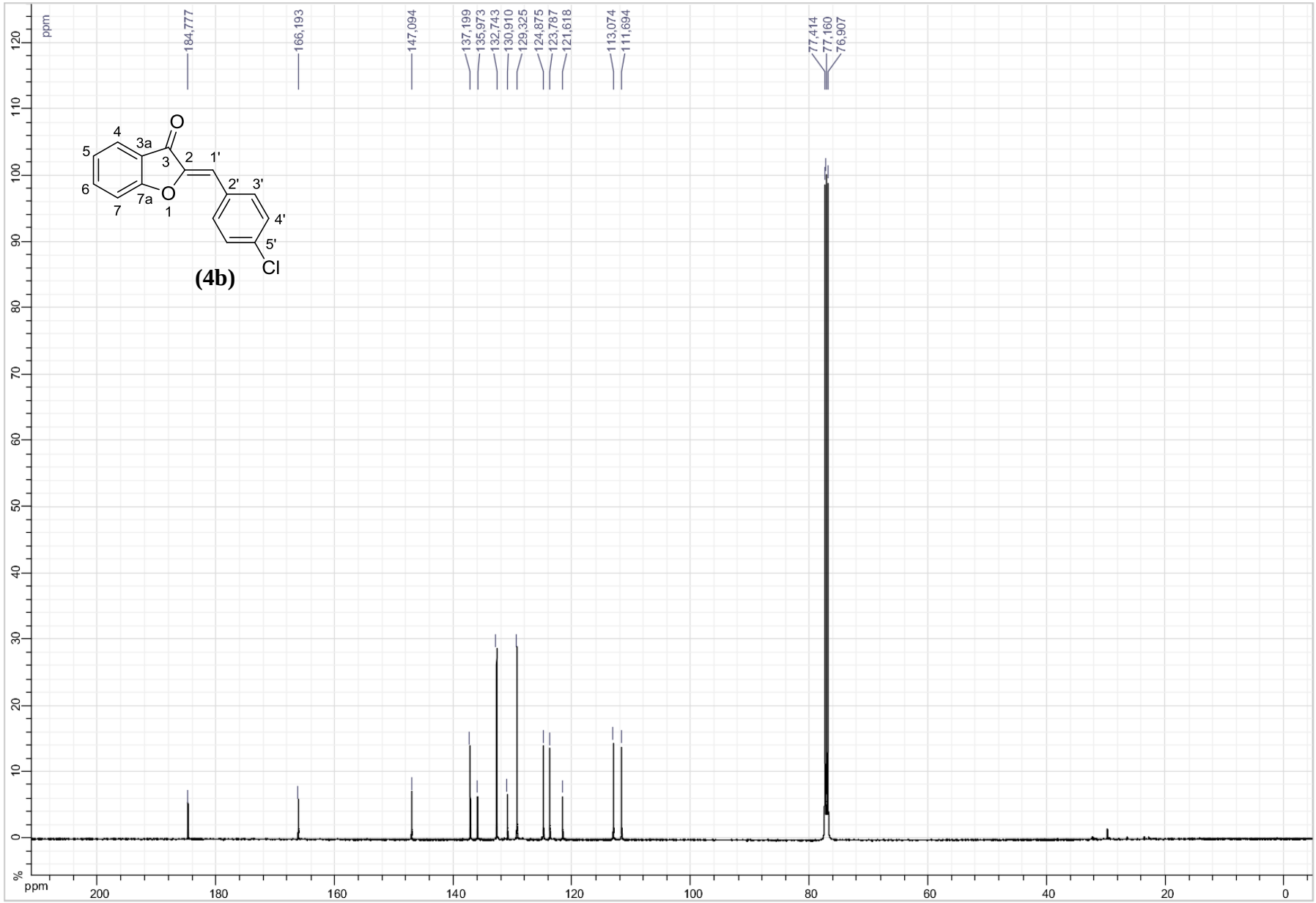
125,147
124,673
123,392
122,038
114,610
113,559
112,998
77,414
77,160
76,906
55,525
O
4
3a
3
2
1'
5
6
7
7a
O
1
2'
3'
4'
5'
O
1'''
(4a)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(4a)




7,853
7,836
7,810
7,795
7,681
7,665
7,650
7,426
7,409
7,338
7,321
7,260
7,246
7,231
7,216
6,824
O
4
3a
3
2
1'
5
6
7
7a
O
1
2'
3'
4'
5'
Cl
(4b)
ppm
1.01
2.00
0.98
1.00
1.00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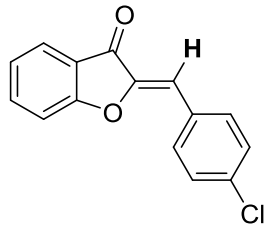
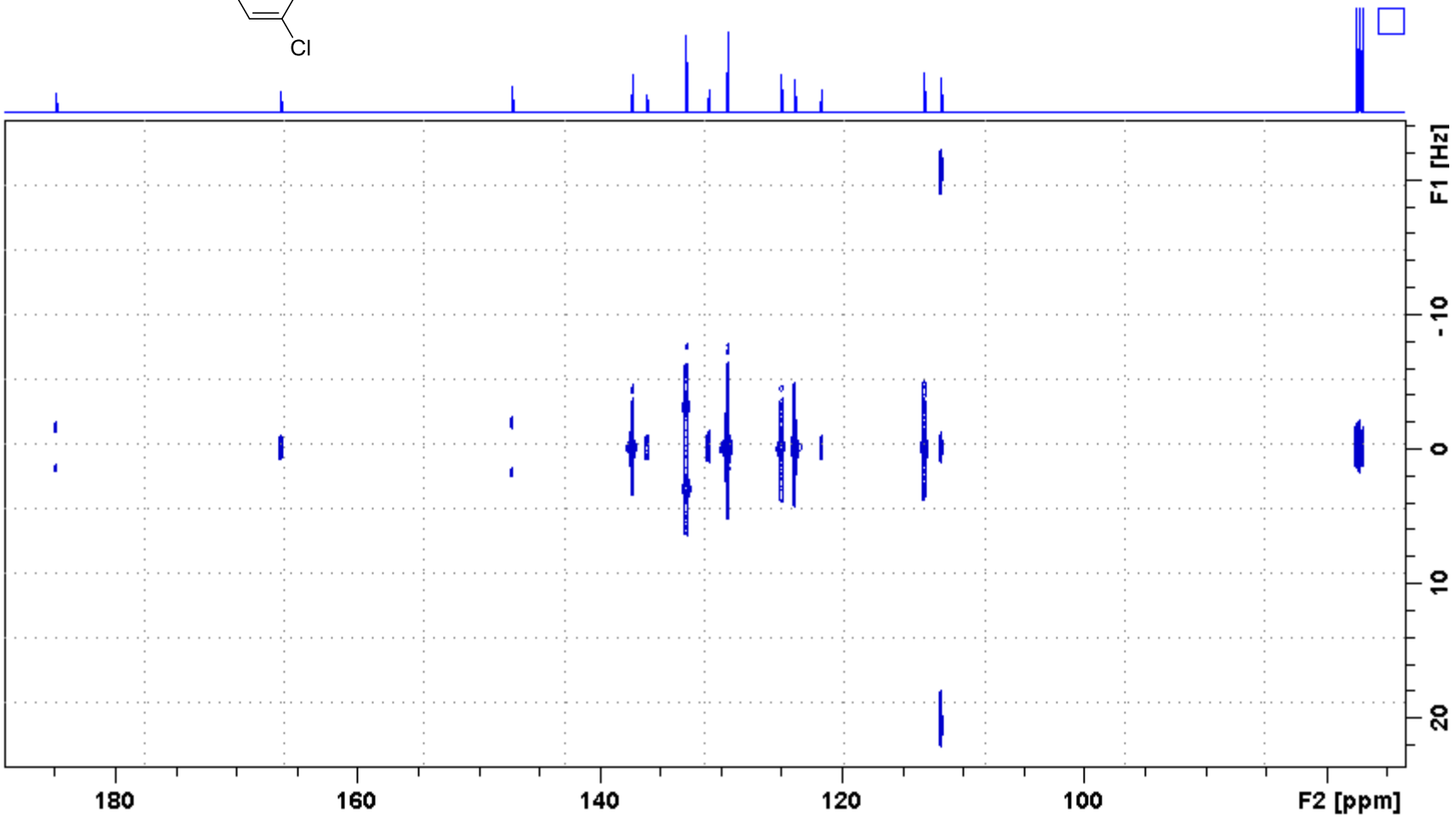
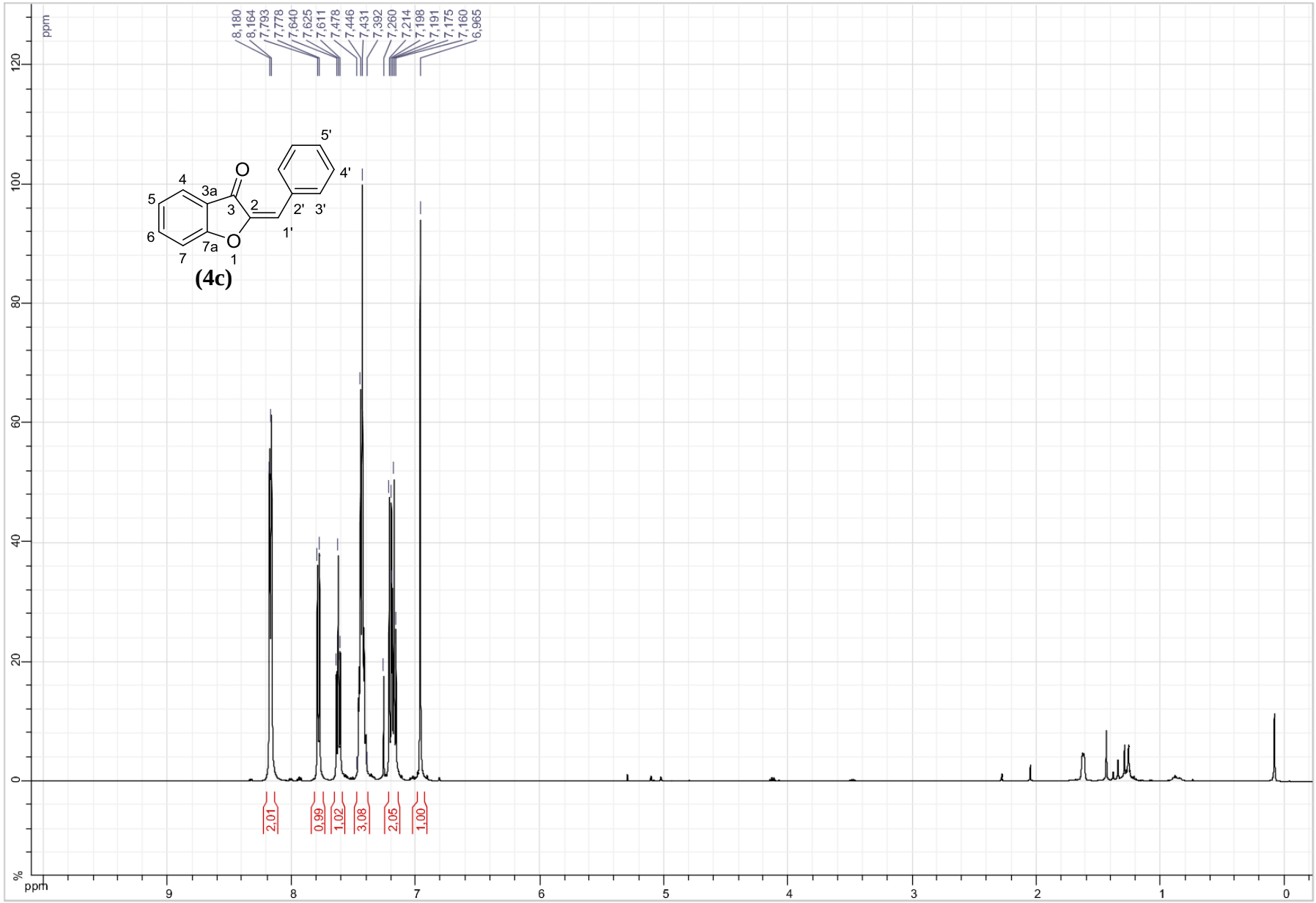
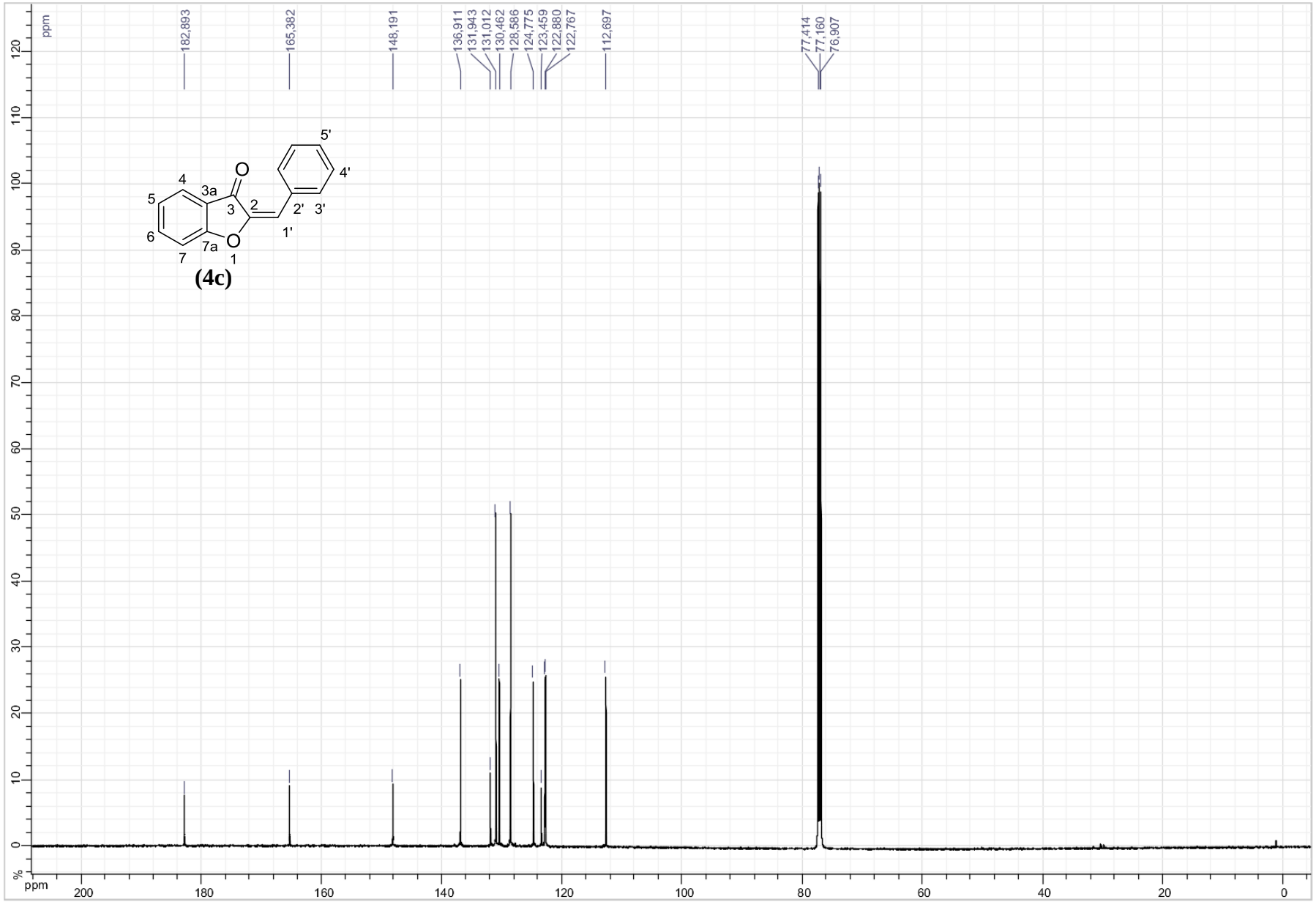
137,199
135,973
132,743
130,910
129,325
124,875
123,787
121,618
113,074
111,694
77,414
77,160
76,907
O
4
3a
3
2
1'
5
6
7
7a
O
1
2'
3'
4'
5'
Cl
(4b)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(4b)

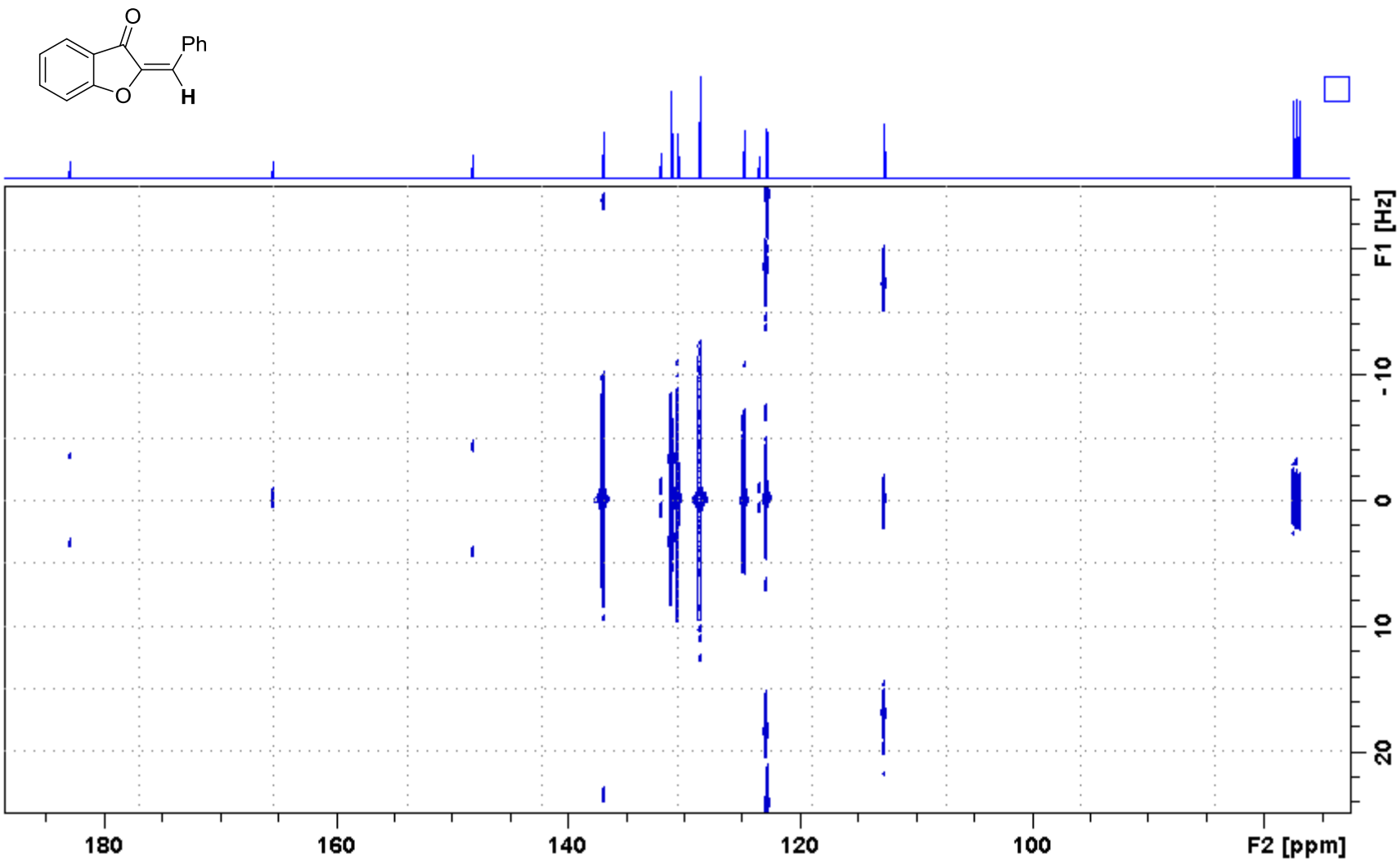


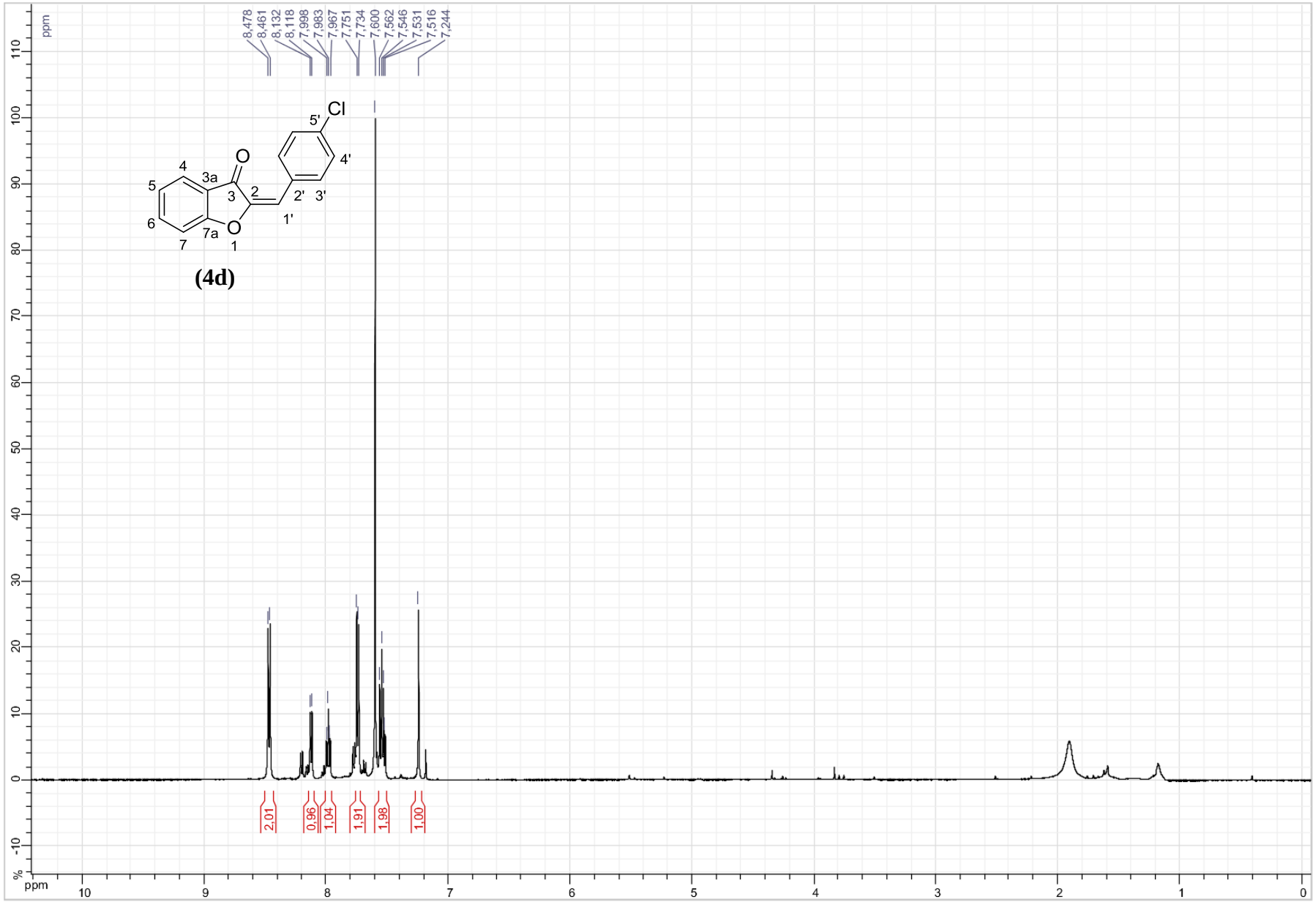


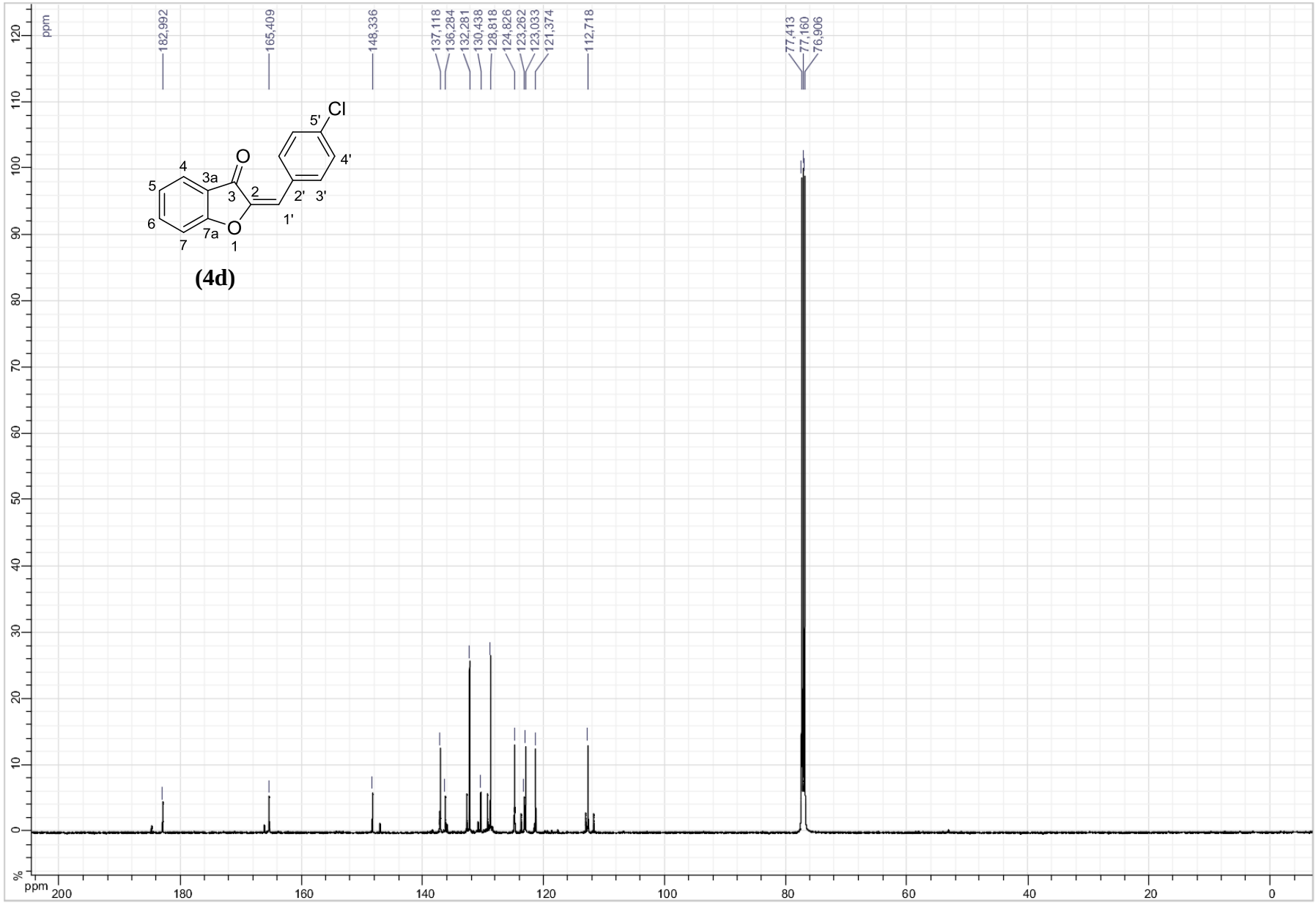

8.180
8.164
7.793
7.778
7.640
7.625
7.611
7.478
7.446
7.431
7.392
7.260
7.214
7.198
7.191
7.175
7.160
6.965
ppm
120
100
80
60
40
20
0
%
ppm
9
8
7
6
5
4
3
2
1
0
2.01
0.99
1.02
3.08
2.05
1.00
O
4
3a
5
3
2
2'
3'
5'
4'
6
7a
1'
7
O
1
(4c)


ppm
182,893
165,382
148,191
136,911
131,943
131,012
130,462
128,586
124,775
123,459
122,880
122,767
112,697
77,414
77,160
76,907
O
4
3a
5
3
2
5'
4'
2'
3'
6
7a
1'
7
O
1
(4c)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

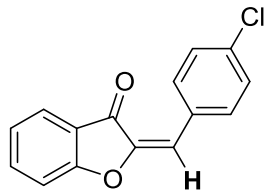
(4c)

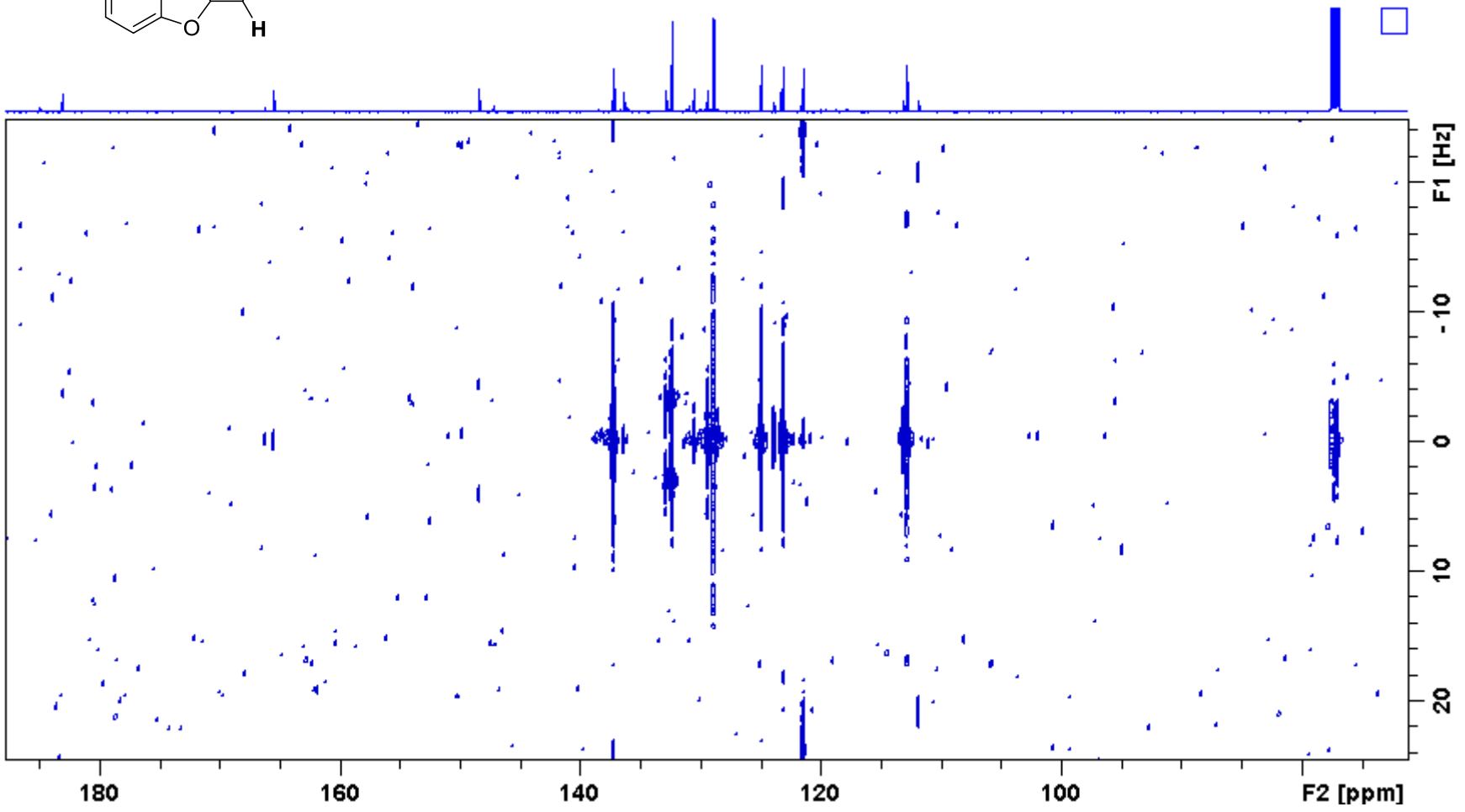


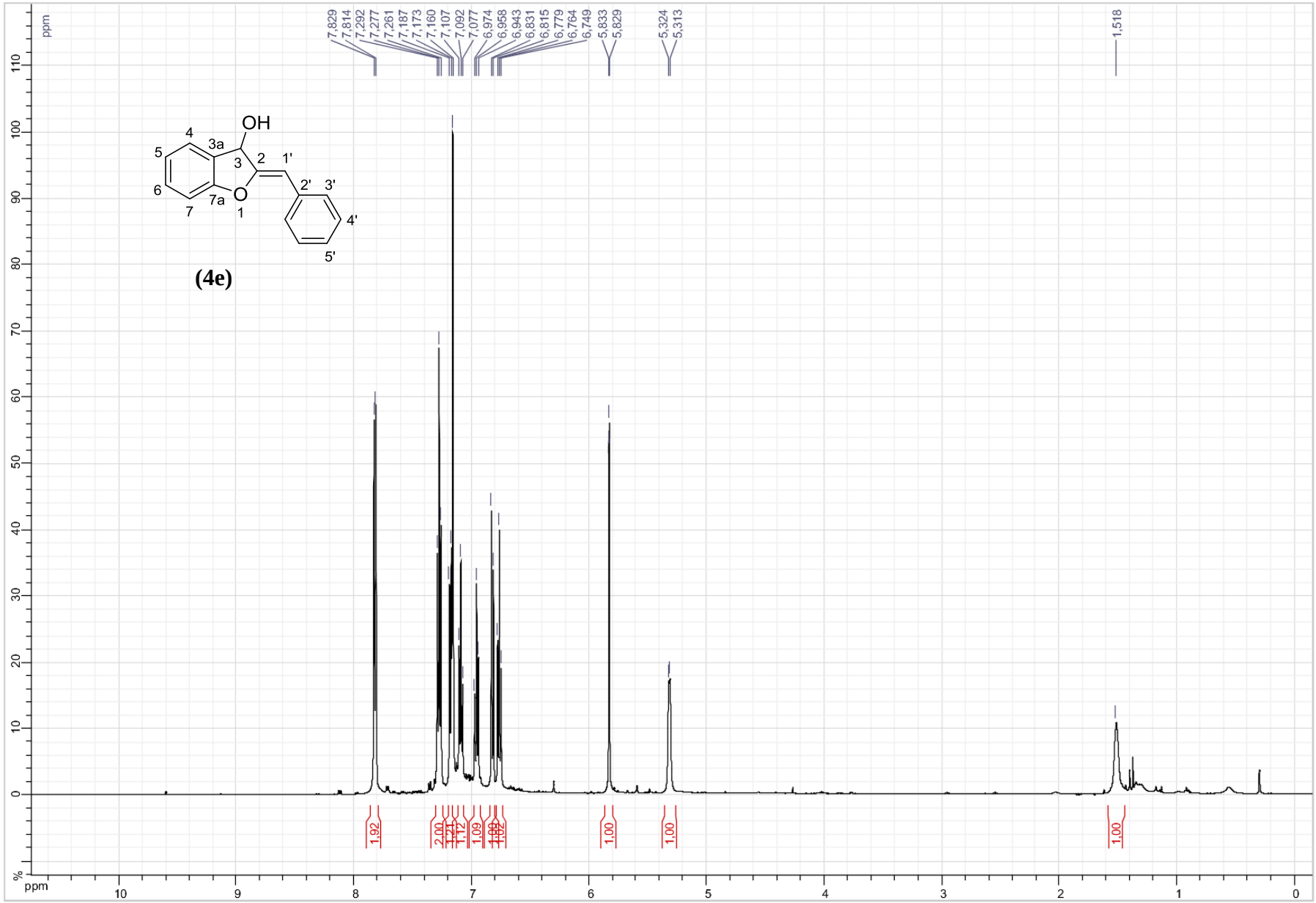

8,478
8,461
8,132
8,118
7,998
7,983
7,967
7,751
7,734
7,600
7,562
7,546
7,531
7,516
7,244
Cl
5'
4'
O
4
3a
5
3
2
2'
3'
6
1'
7a
O
7
1
(4d)
2,01
0,96
1,04
1,91
1,98
1,00
ppm
%

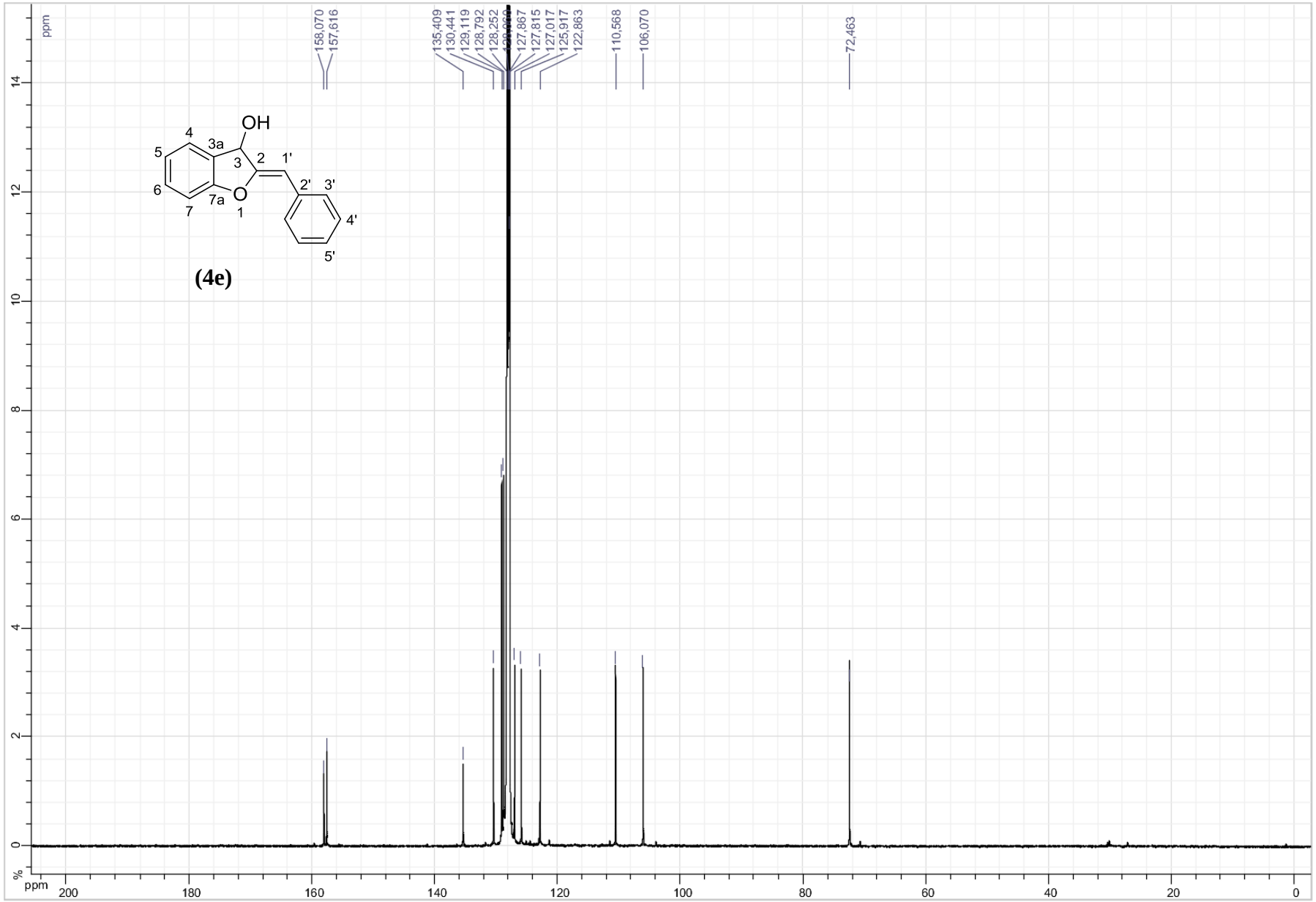

ppm
182,992
165,409
148,336
137,118
136,284
132,281
130,438
128,818
124,826
123,262
123,033
121,374
112,718
77,413
77,160
76,906
Cl
5'
4'
O
4
3a
5
3
2
2'
3'
6
1'
7
7a
O
1
(4d)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(4d)

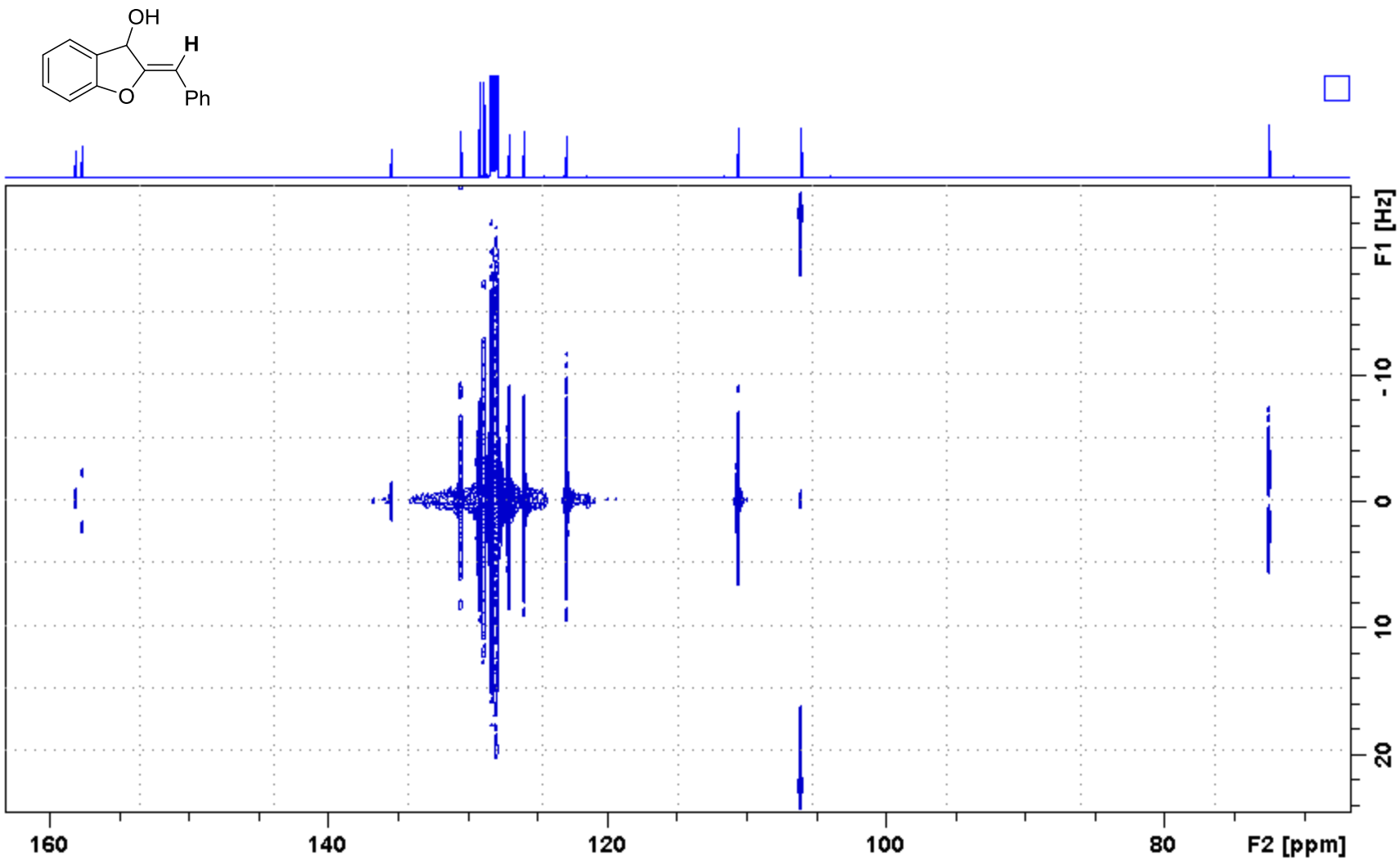


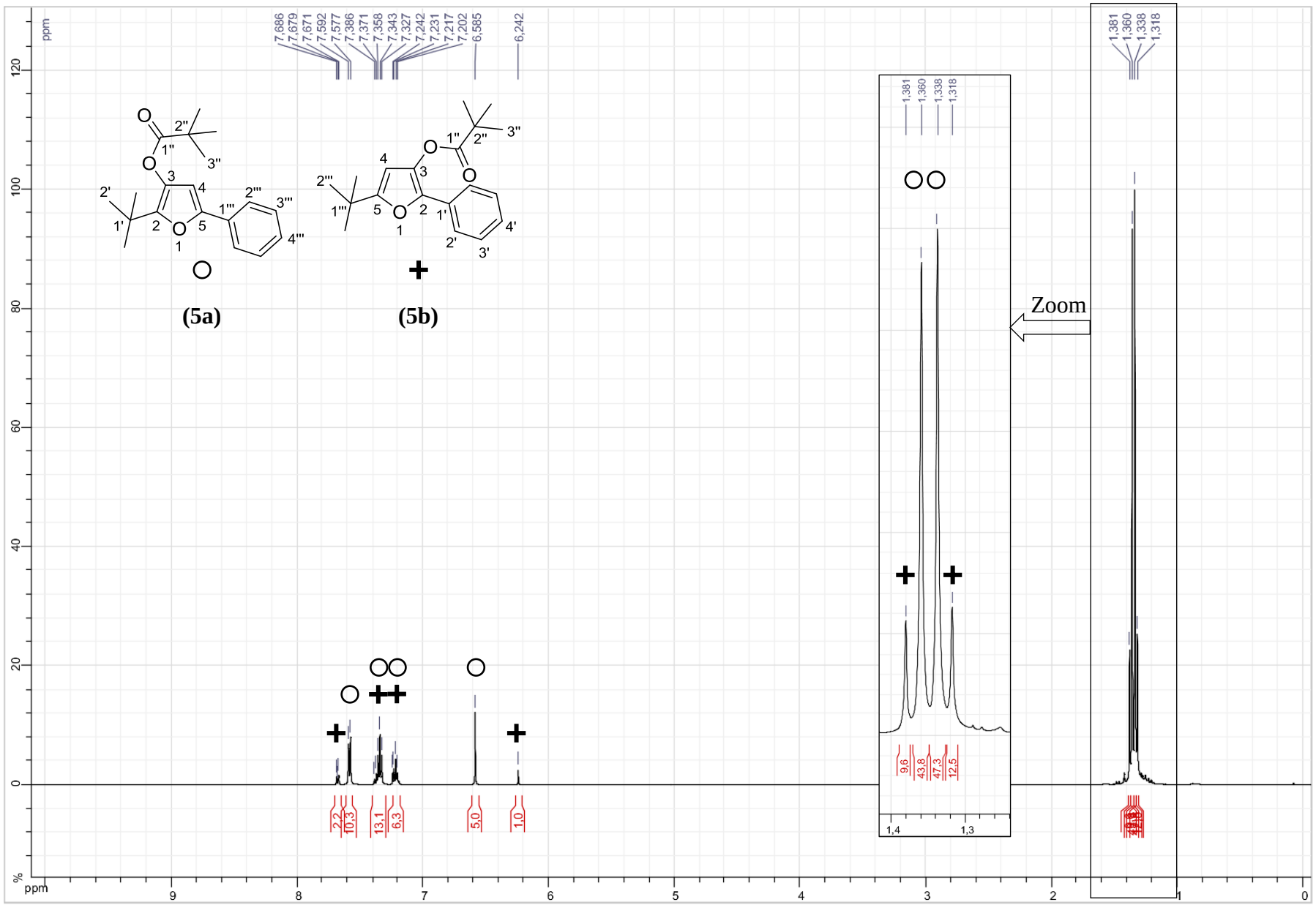


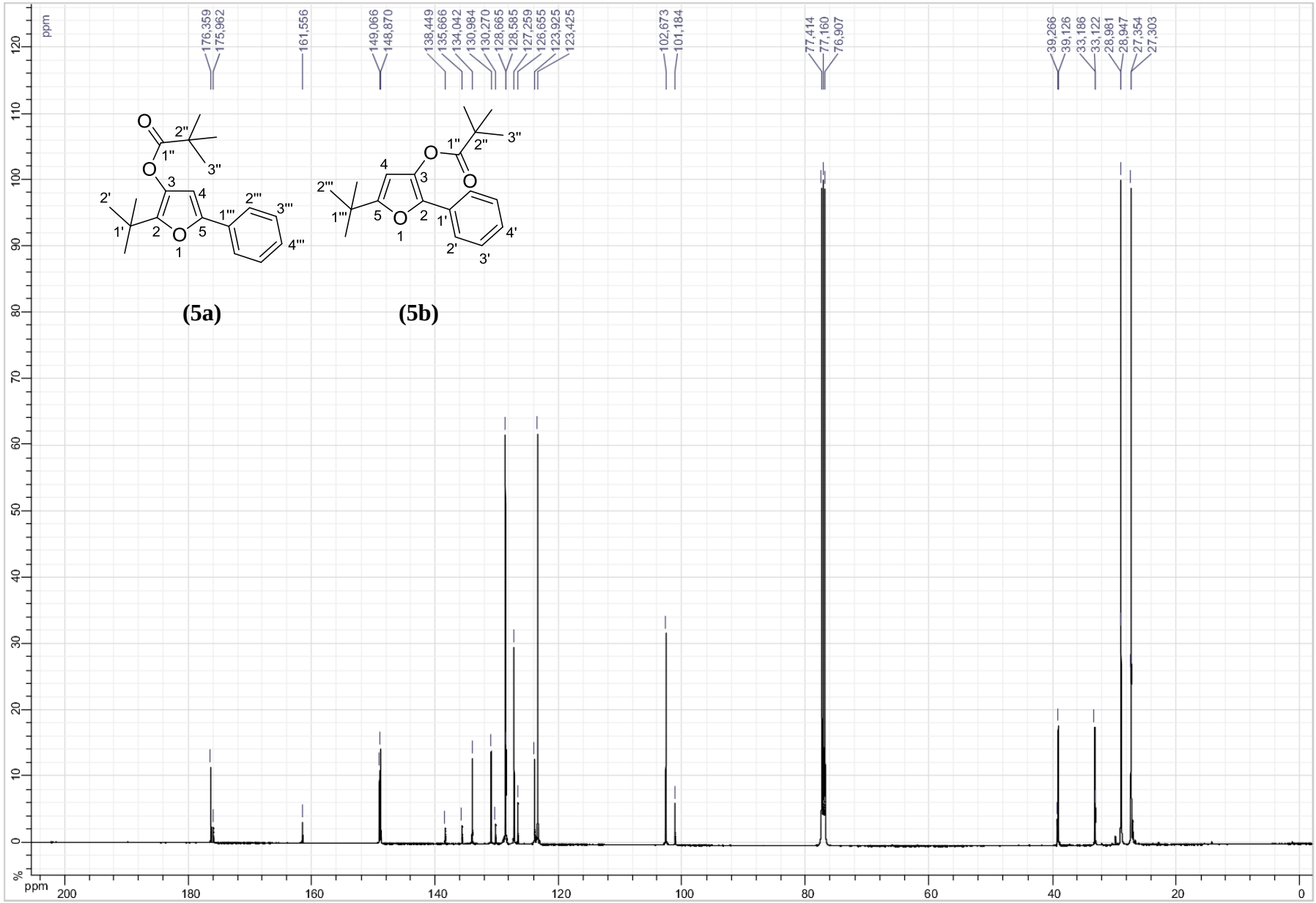

7,829
7,814
7,292
7,277
7,261
7,187
7,173
7,160
7,107
7,092
7,077
6,974
6,958
6,943
6,831
6,815
6,779
6,764
6,749
5,833
5,829
5,324
5,313
1,518
OH
4
3a
5
3
2
1'
6
2'
3'
7
7a
O
1
4'
5'
(4e)
1,92
2,00
1,12
1,09
1,00
1,00
1,00
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
158,070
157,616
135,409
130,441
129,119
128,792
128,252
127,867
127,815
127,017
125,917
122,863
110,568
106,070
72,463
OH
4
3a
5
3
2
1'
6
2'
3'
7
7a
O
1
4'
5'
(4e)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

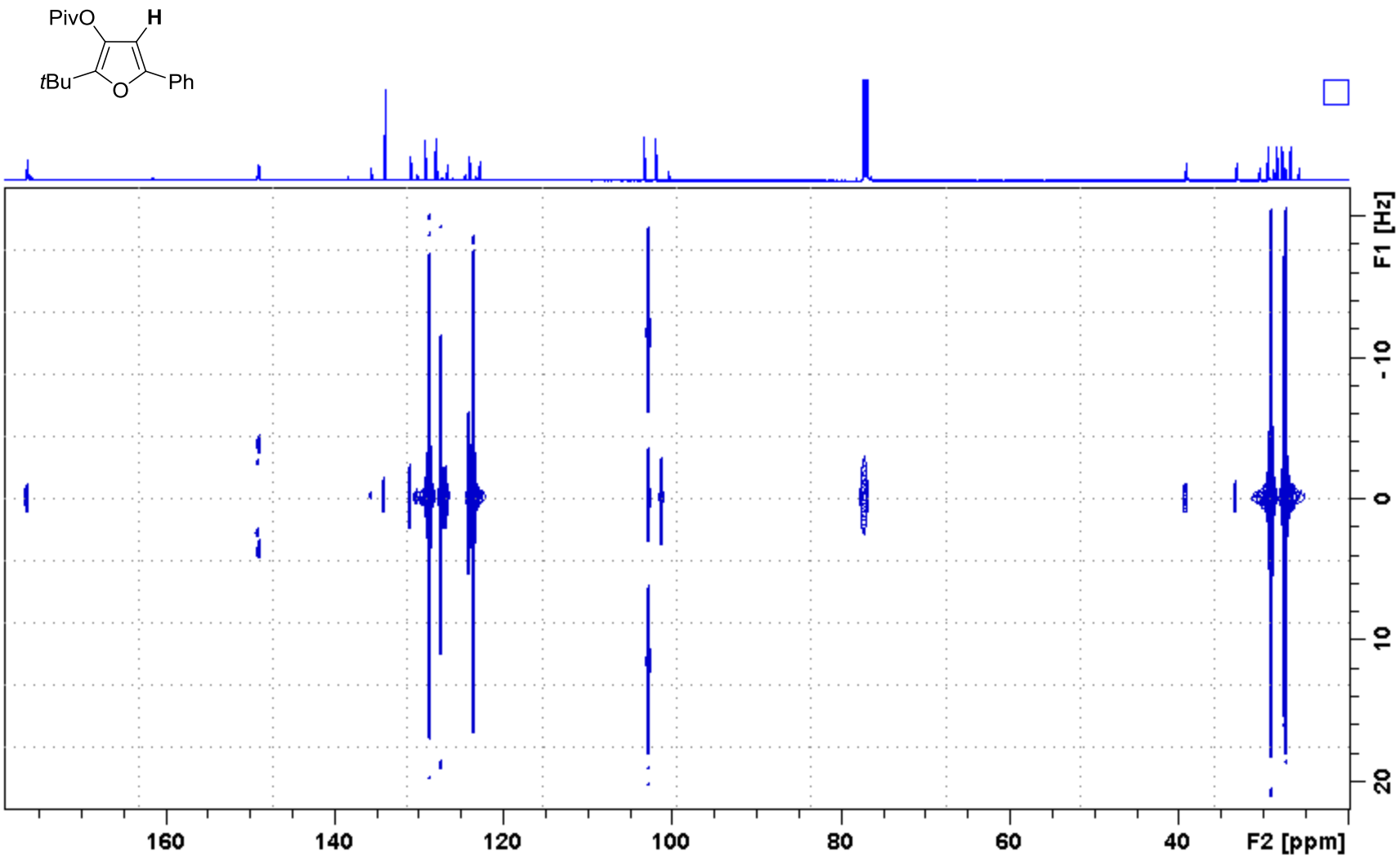
(4e)



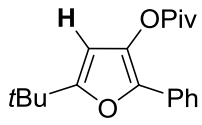

(5a)
(5b)
Zoom
ppm

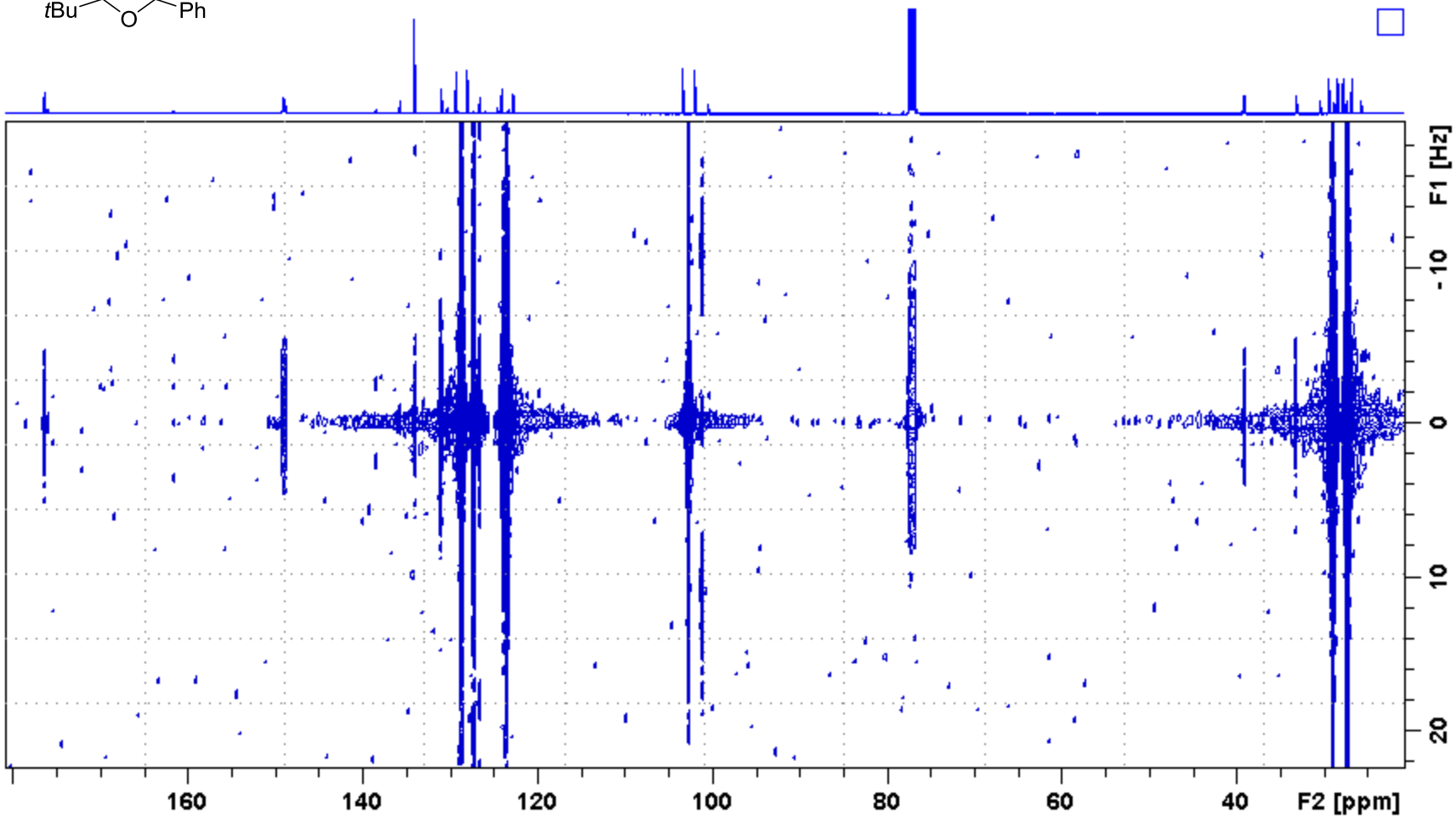

ppm
176,359
175,962
161,556
149,066
148,870
138,449
135,666
134,042
130,984
130,270
128,665
128,585
127,259
126,655
123,925
123,425
102,673
101,184
77,414
77,160
76,907
39,266
39,126
33,186
33,122
28,981
28,947
27,354
27,303
(5a)
(5b)

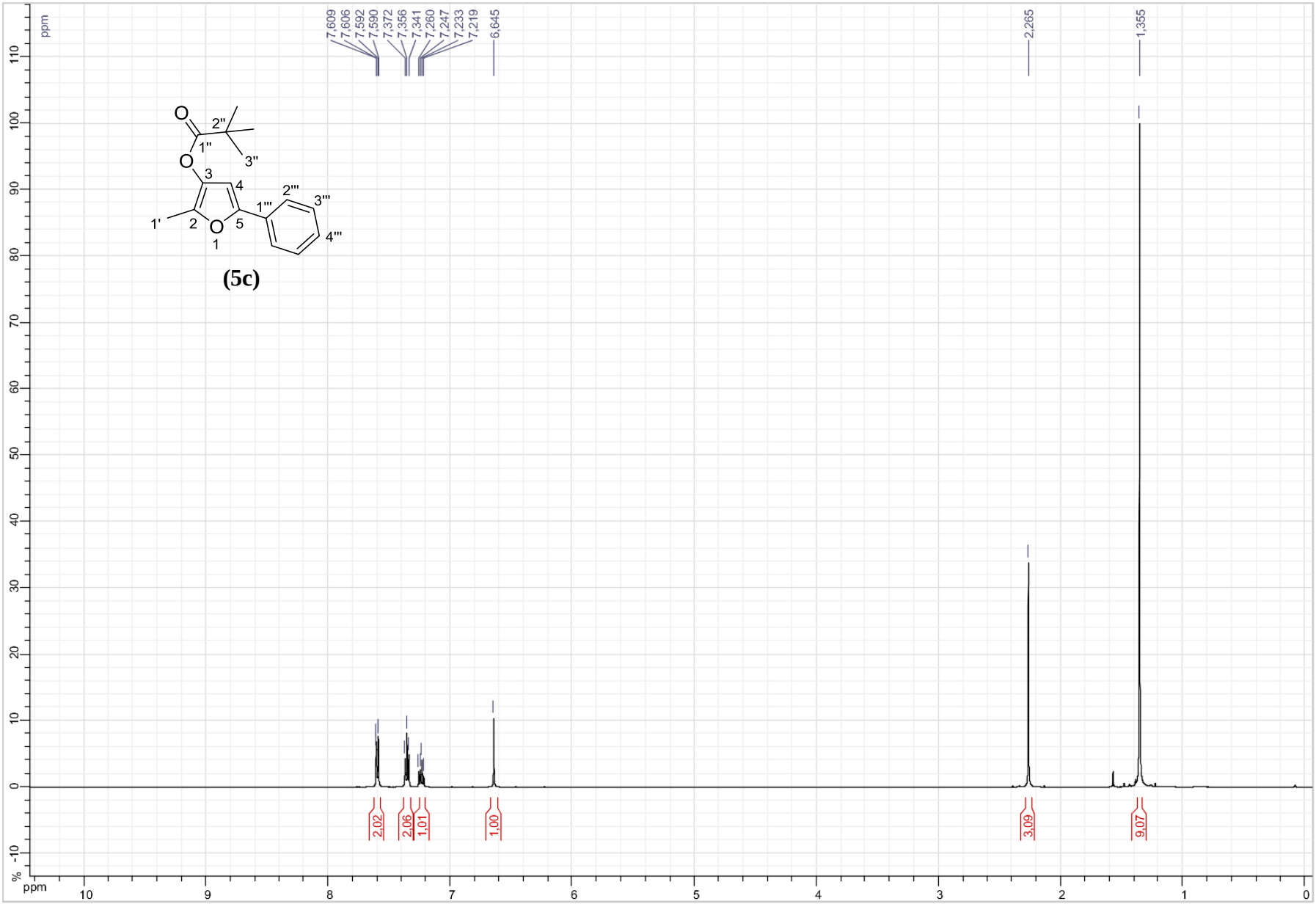
(5a)



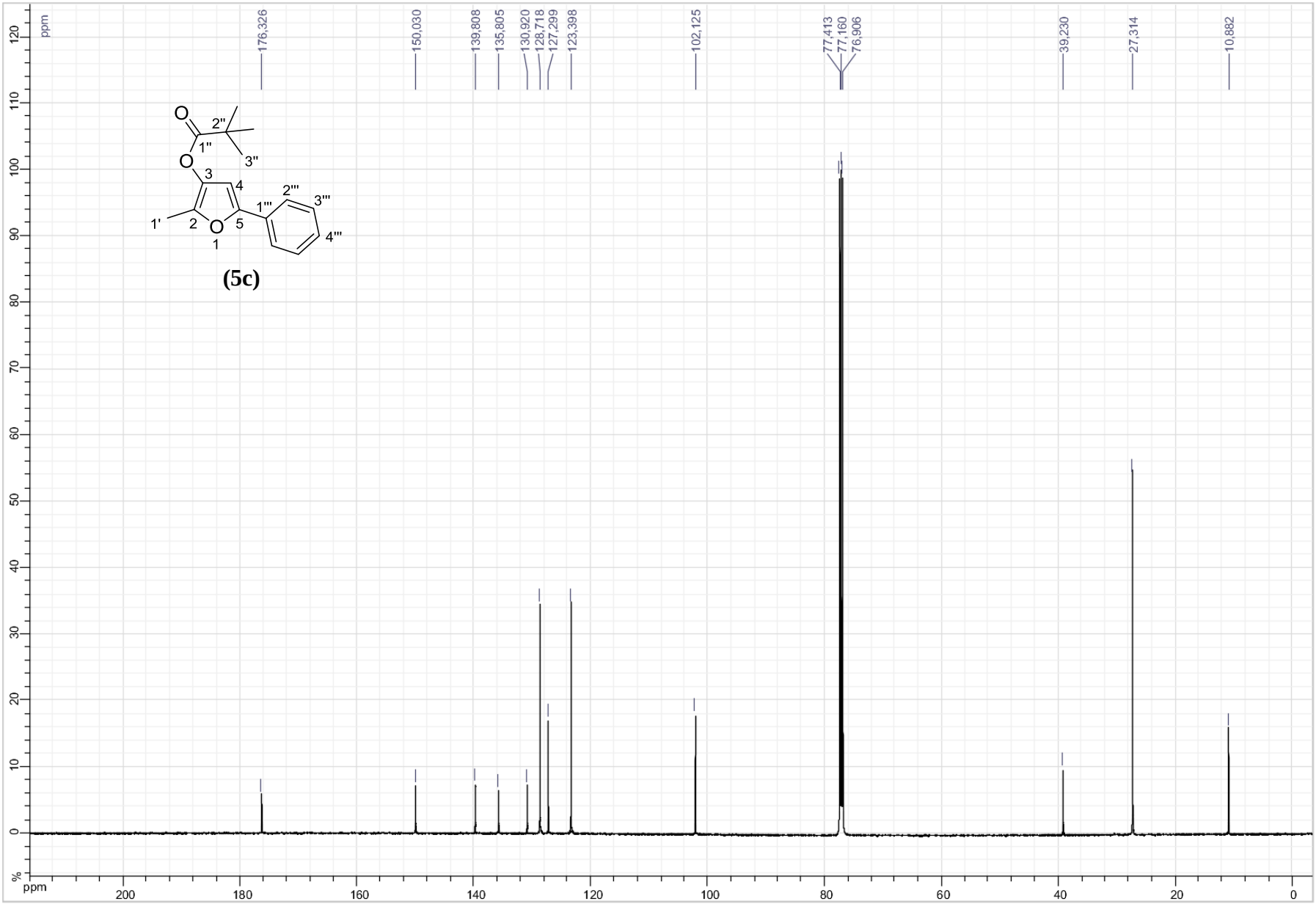
(5b)



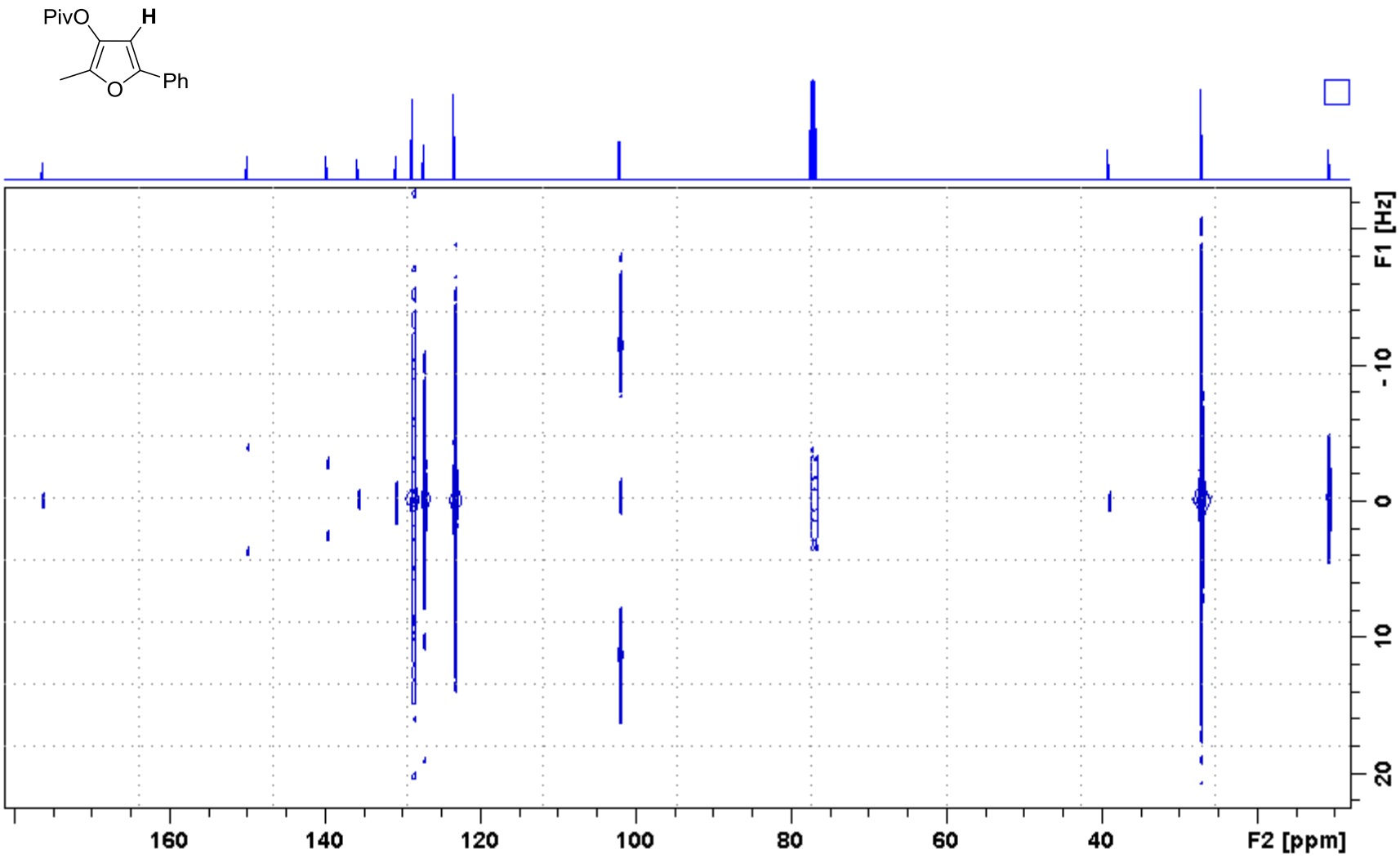


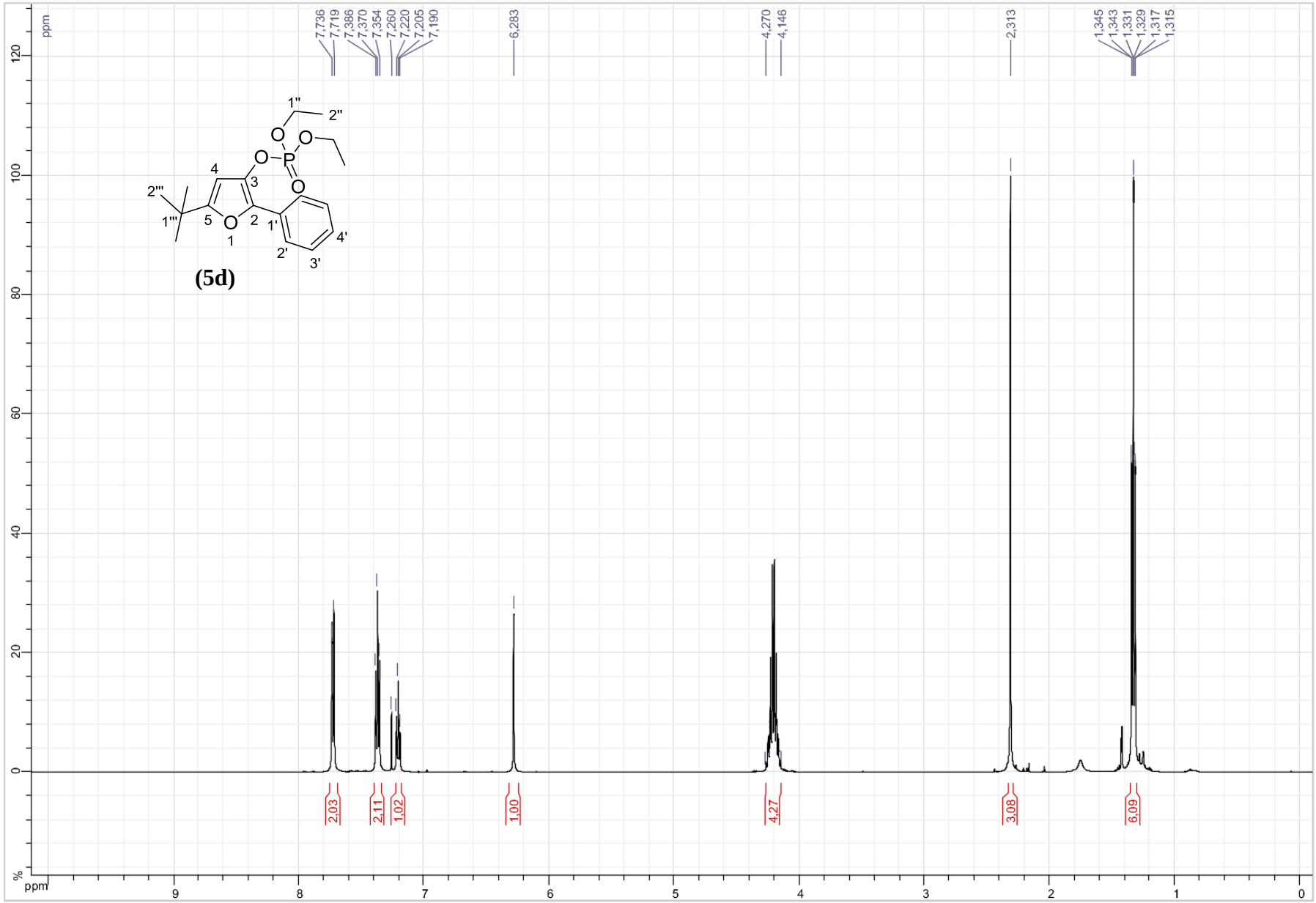

7,609
7,606
7,592
7,590
7,372
7,356
7,341
7,260
7,247
7,233
7,219
6,645
2,265
1,355
2,02
2,06
1,01
1,00
3,09
9,07
ppm
10
9
8
7
6
5
4
3
2
1
0

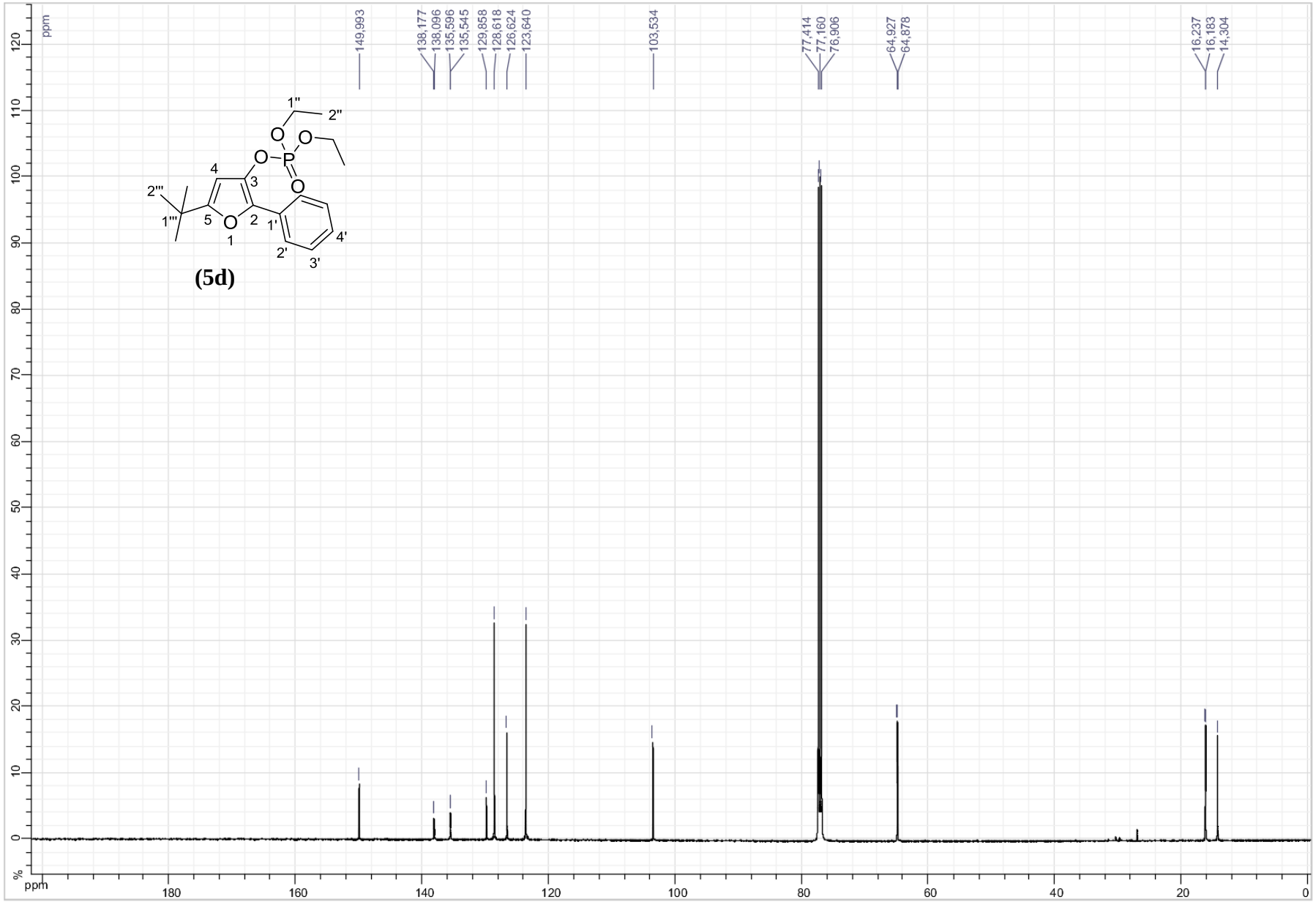
(5c)


ppm
176,326
150,030
139,808
135,805
130,920
128,718
127,299
123,398
102,125
77,413
77,160
76,906
39,230
27,314
10,882
O
2"
1"
3"
O
3
4
2'''
3'''
1'''
1'
2
O
5
1
4'''
(5c)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

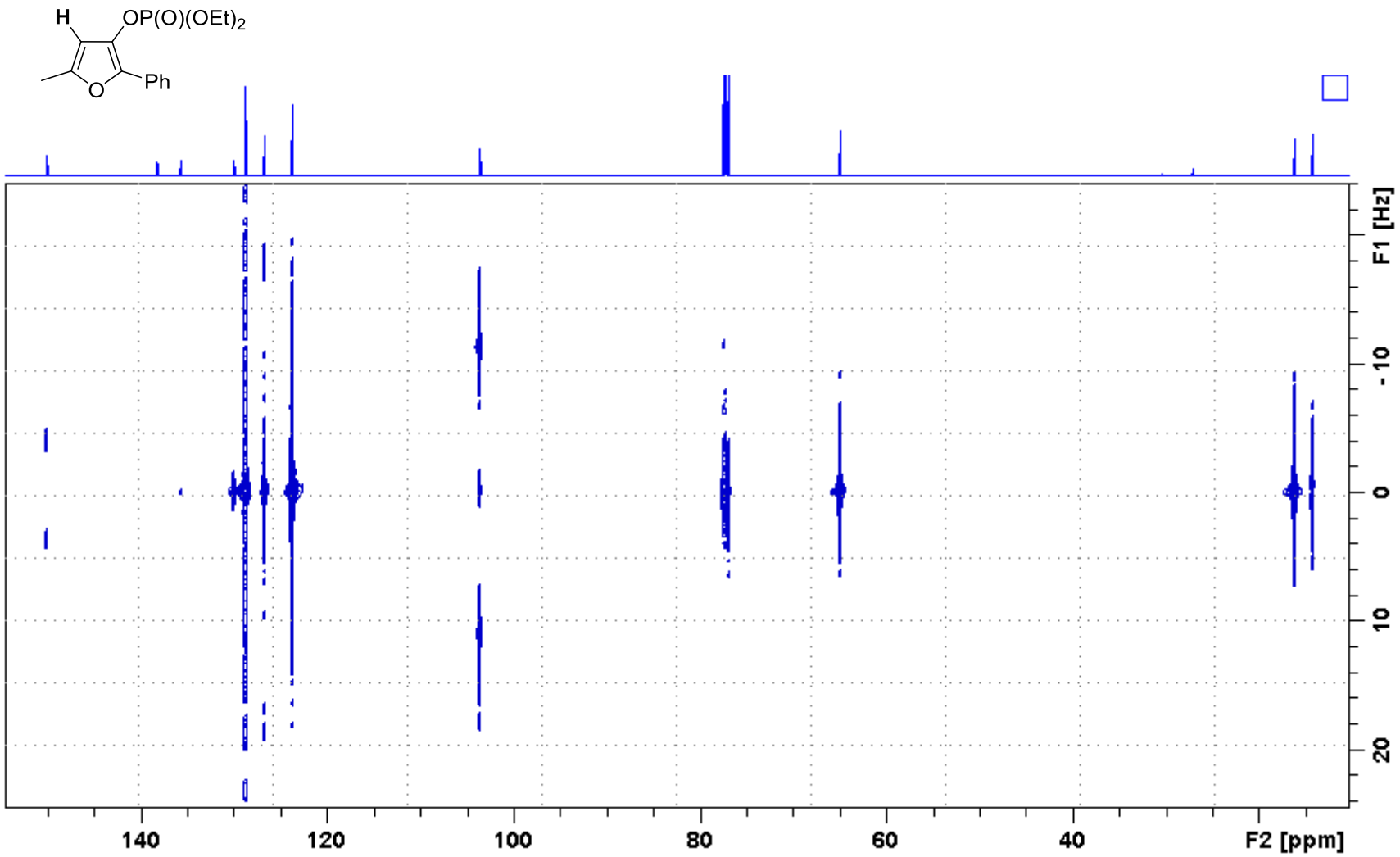
(5c)

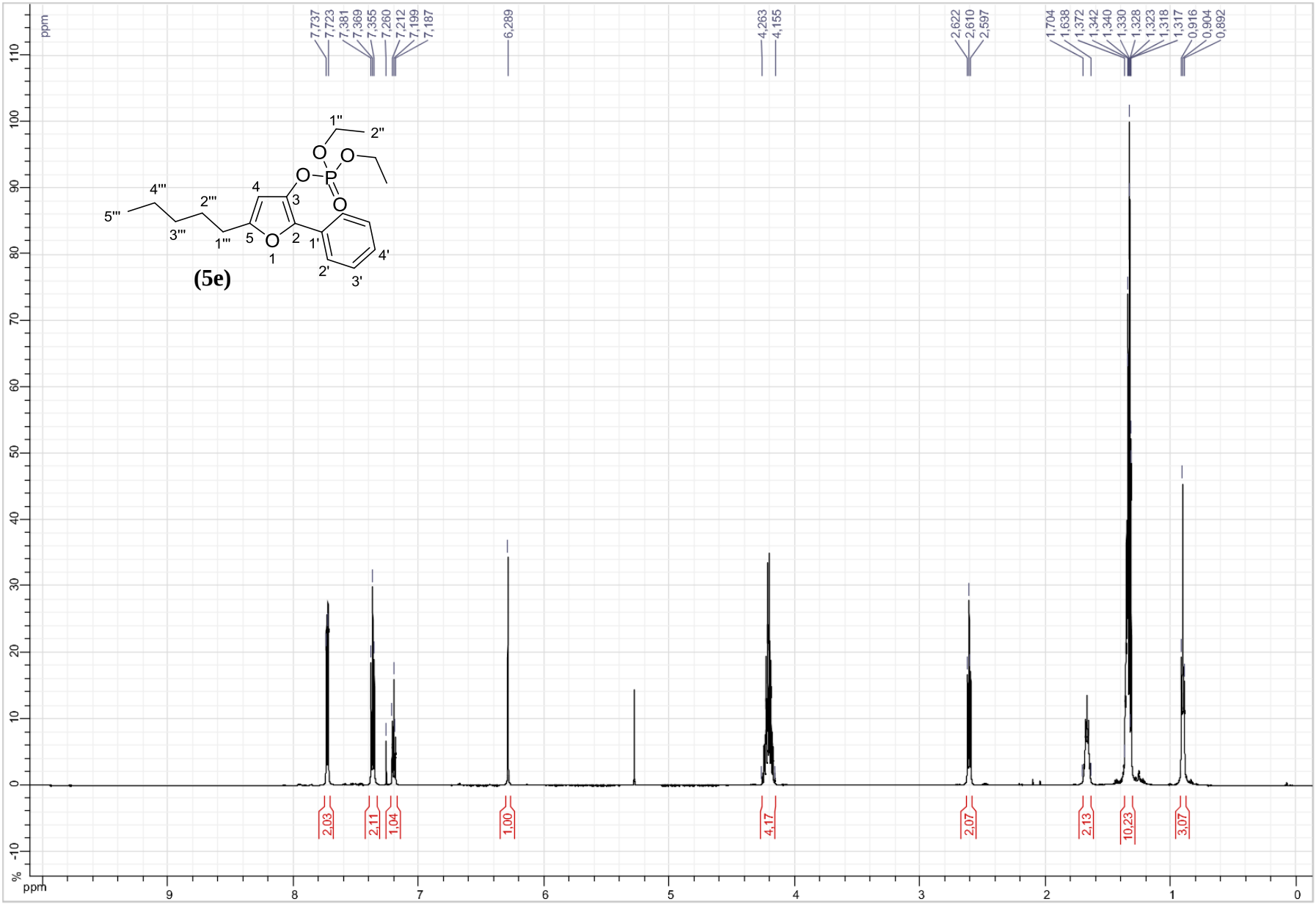


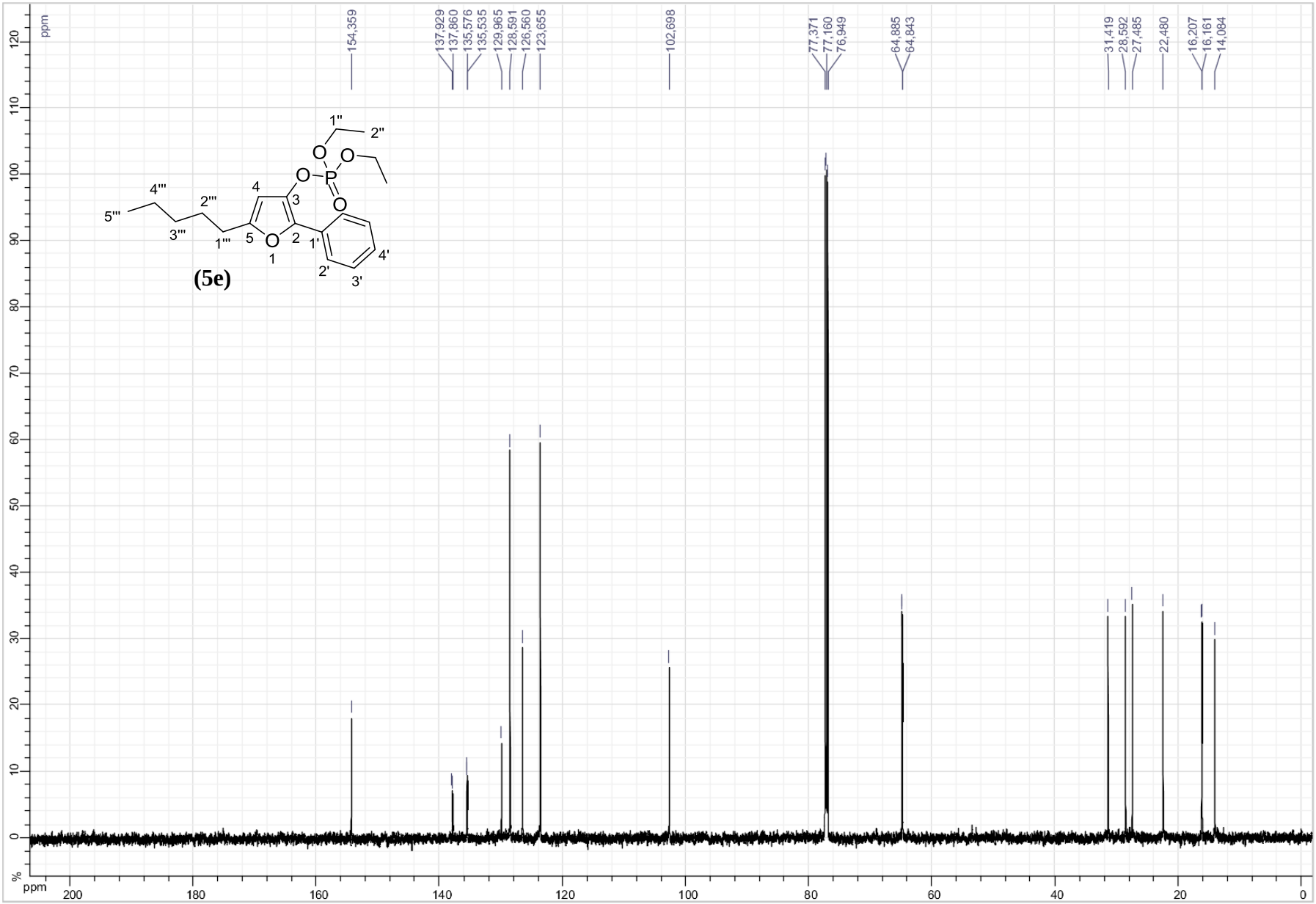

ppm
7,736
7,719
7,386
7,370
7,354
7,260
7,220
7,205
7,190
6,283
4,270
4,146
2,313
1,345
1,343
1,331
1,329
1,317
1,315
1"
2"
O
O
O
P
O
4
3
2'''
1'''
5
O
2
1'
1
2'
3'
4'
(5d)
2,03
2,11
1,02
1,00
4,27
3,08
6,09
%
ppm
9
8
7
6
5
4
3
2
1
0


ppm
149,993
138,177
138,096
135,596
135,545
129,858
128,618
126,624
123,640
103,534
77,414
77,160
76,906
64,927
64,878
16,237
16,183
14,304
(5d)
ppm
180
160
140
120
100
80
60
40
20
0

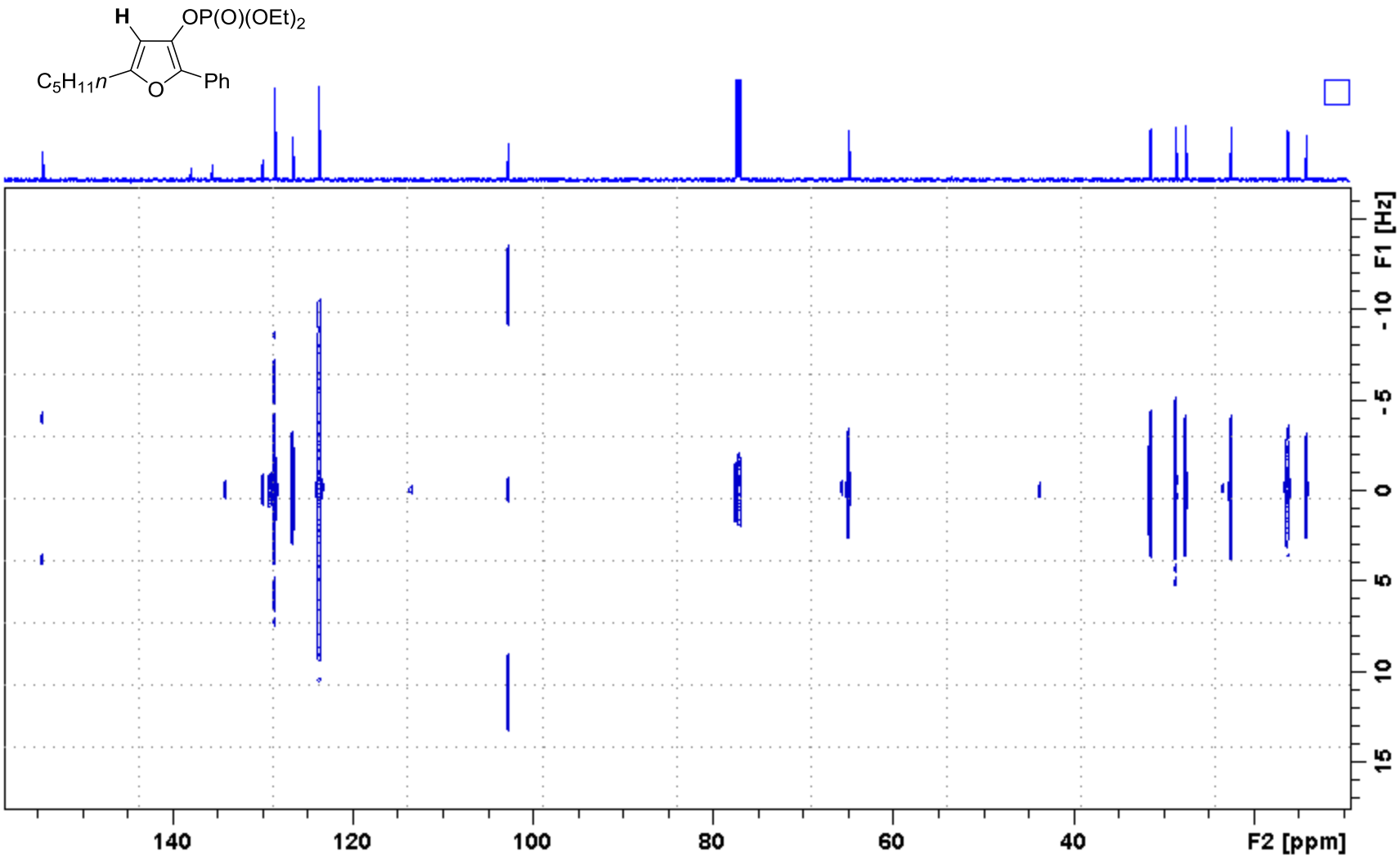
(5d)

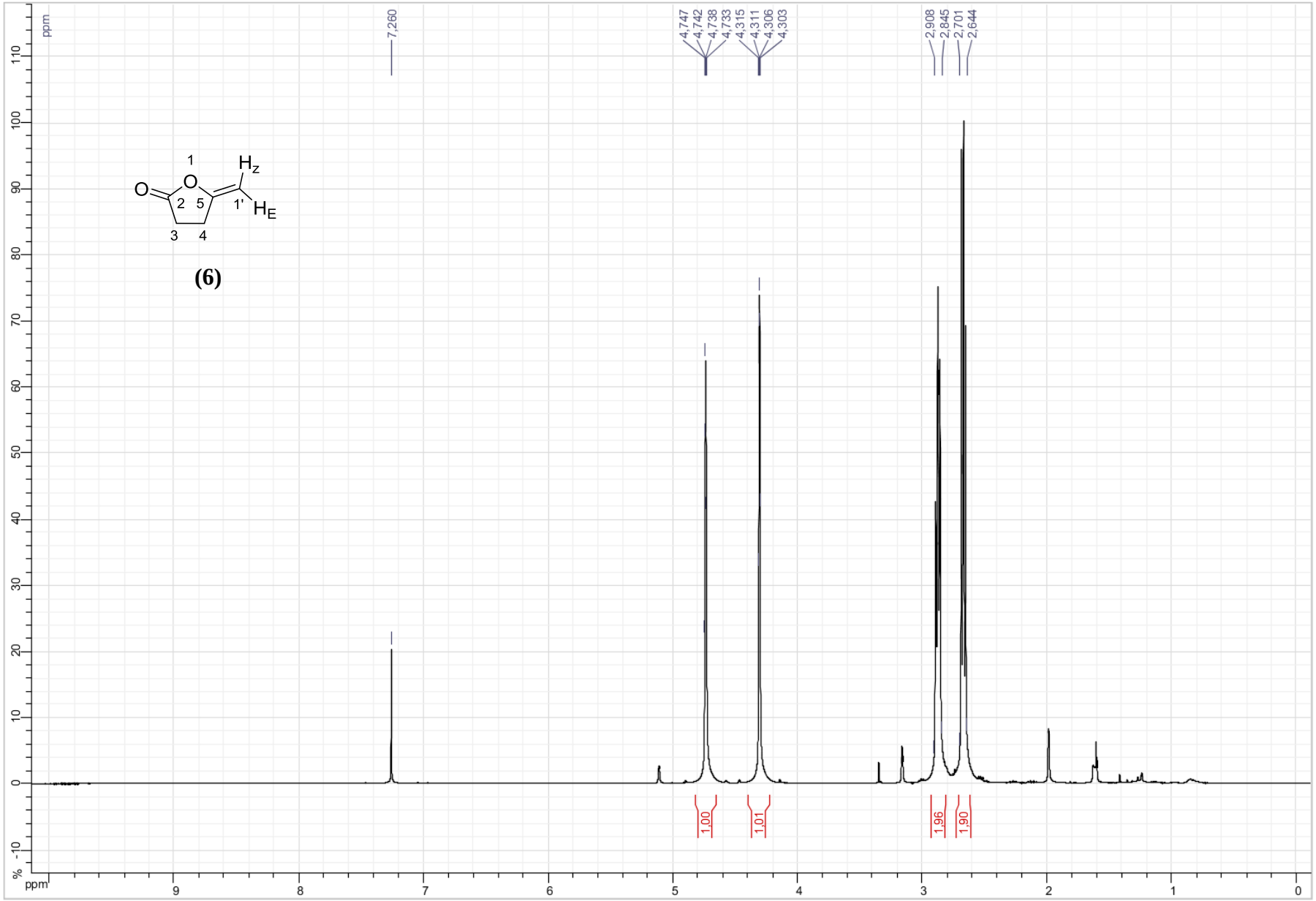



ppm
7,737
7,723
7,381
7,369
7,355
7,260
7,212
7,199
7,187
6,289
4,263
4,155
2,622
2,610
2,597
1,704
1,638
1,372
1,342
1,340
1,330
1,328
1,323
1,318
1,317
0,916
0,904
0,892
(5e)
2,03
2,11
1,04
1,00
4,17
2,07
2,13
10,23
3,07

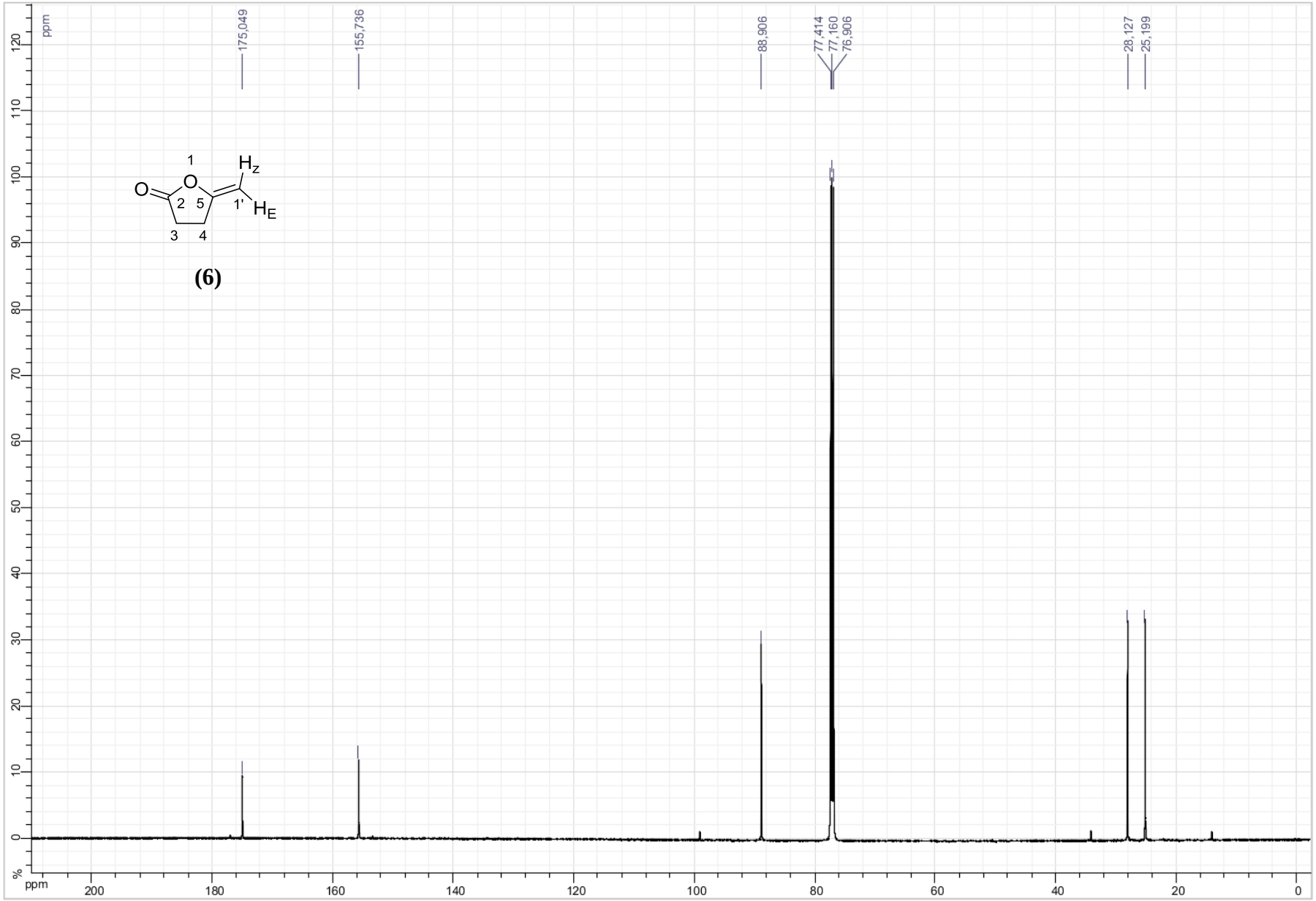

ppm
154,359
137,929
137,860
135,576
135,535
129,965
128,591
126,560
123,655
102,698
77,371
77,160
76,949
64,885
64,843
31,419
28,592
27,485
22,480
16,207
16,161
14,084
1"
2"
O
O
O
P
O
4
3
4'''
2'''
5'''
3'''
1'''
5
O
2
1'
1
2'
3'
4'
(5e)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(5e)

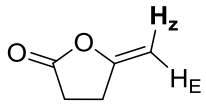

H
OP(O)(OEt)2
C5H11n
O
Ph
F1 [Hz]
-10
-5
0
5
10
15
140
120
100
80
60
40
F2 [ppm]


ppm
7,260
4,747
4,742
4,738
4,733
4,315
4,311
4,306
4,303
2,908
2,845
2,701
2,644
1,00
1,01
1,96
1,90
1
O
O
2
5
3
4
1'
H_Z
H_E

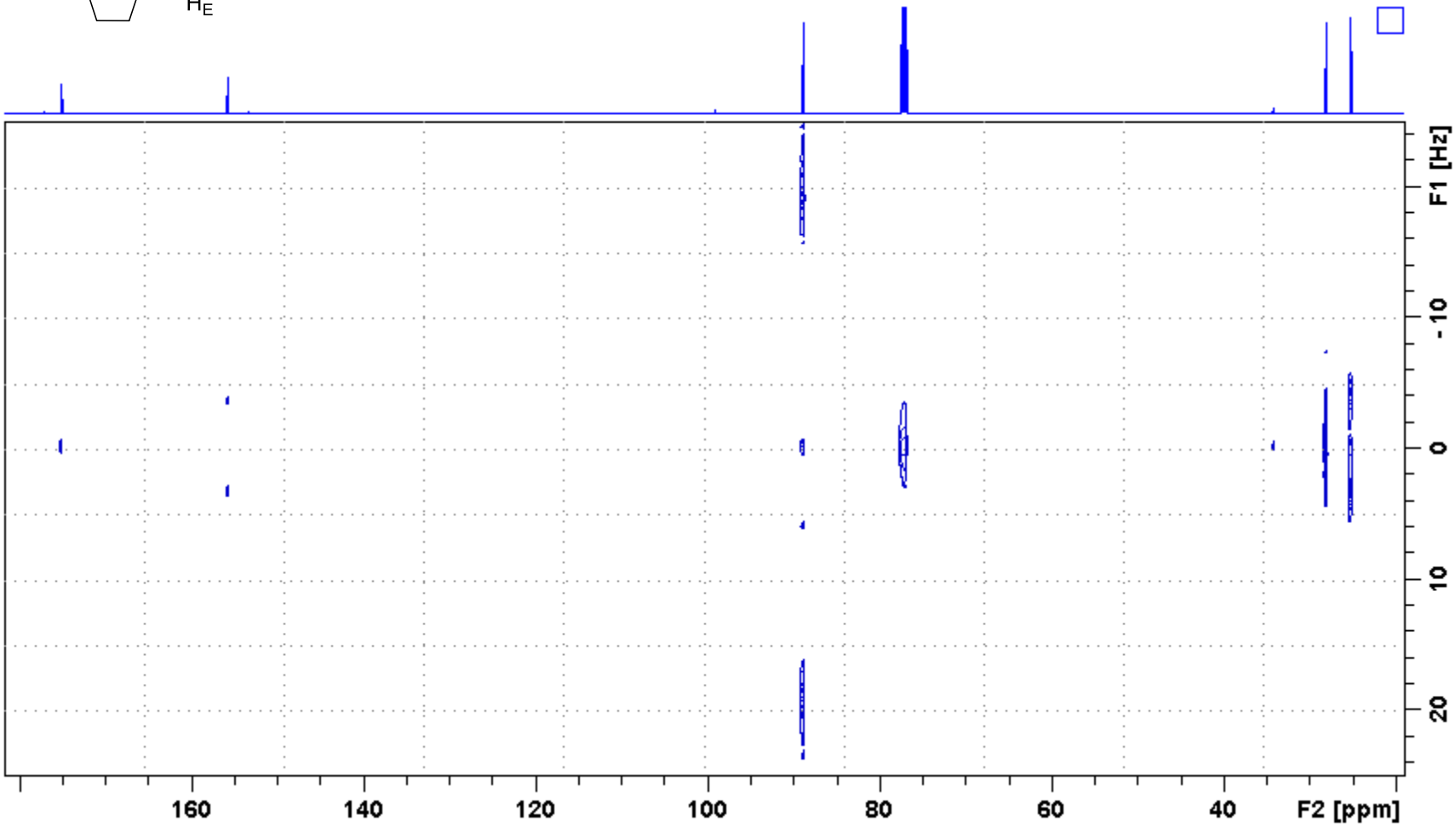
(6)


ppm
175,049
155,736
88,906
77,414
77,160
76,906
28,127
25,199
1
O
O
2
5
1'
H_Z
H_E
3
4
(6)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

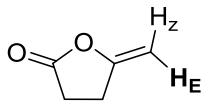
(6)



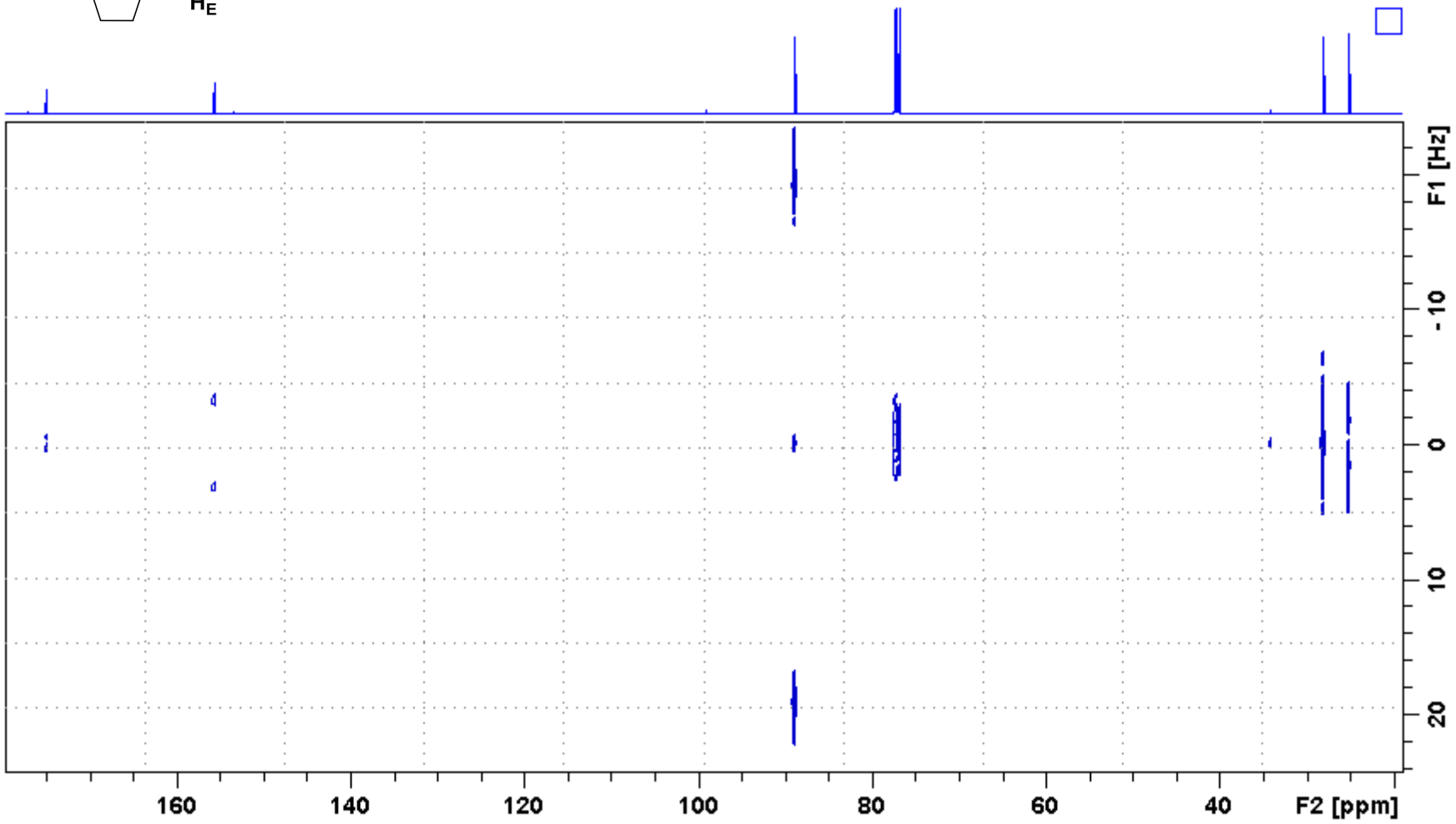
Selelected hydrogen:
$\mathbf{H_Z}$ 4.75ppm

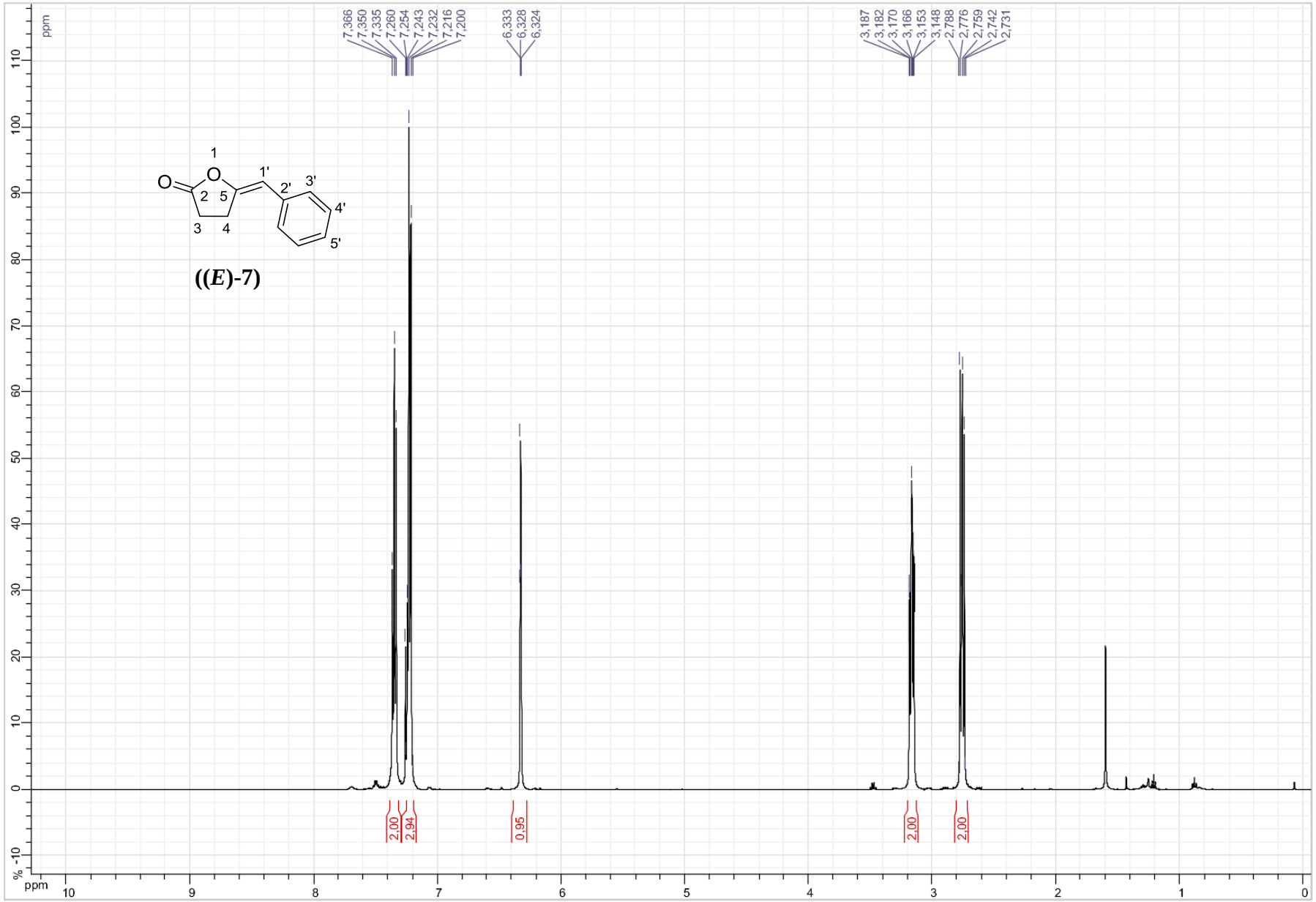


(6)

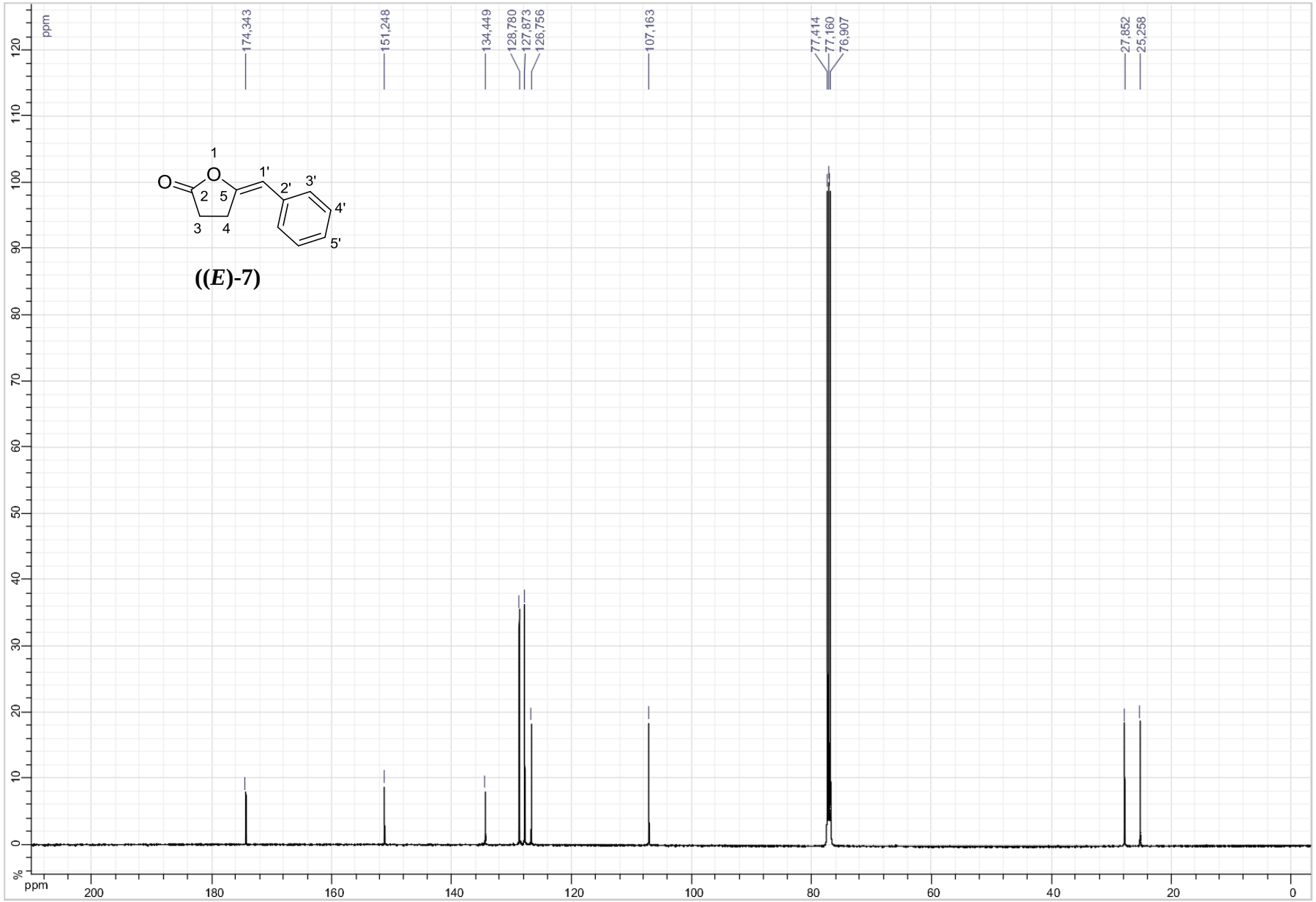


Selelected hydrogen:
H$_E$ 4.31 ppm

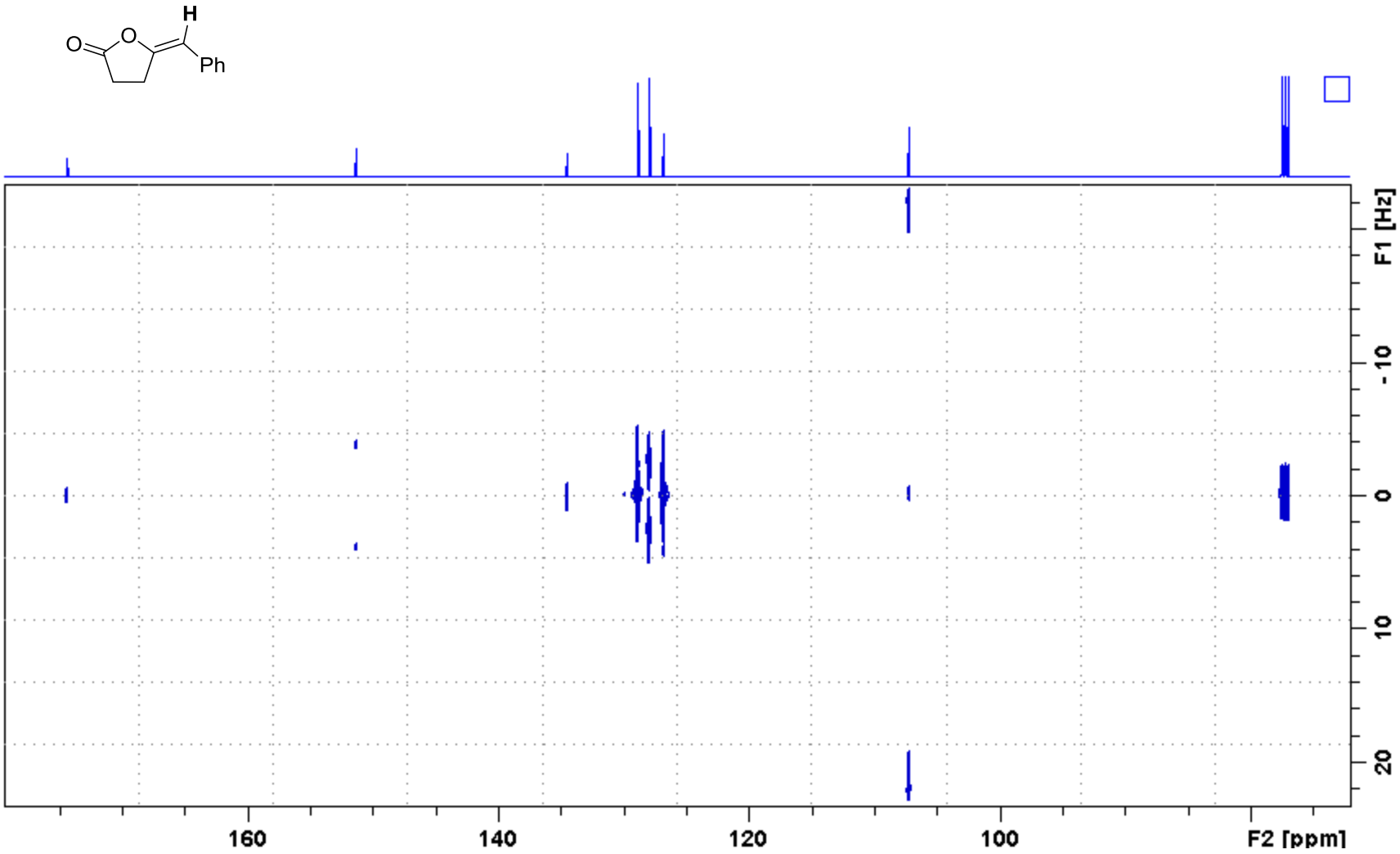


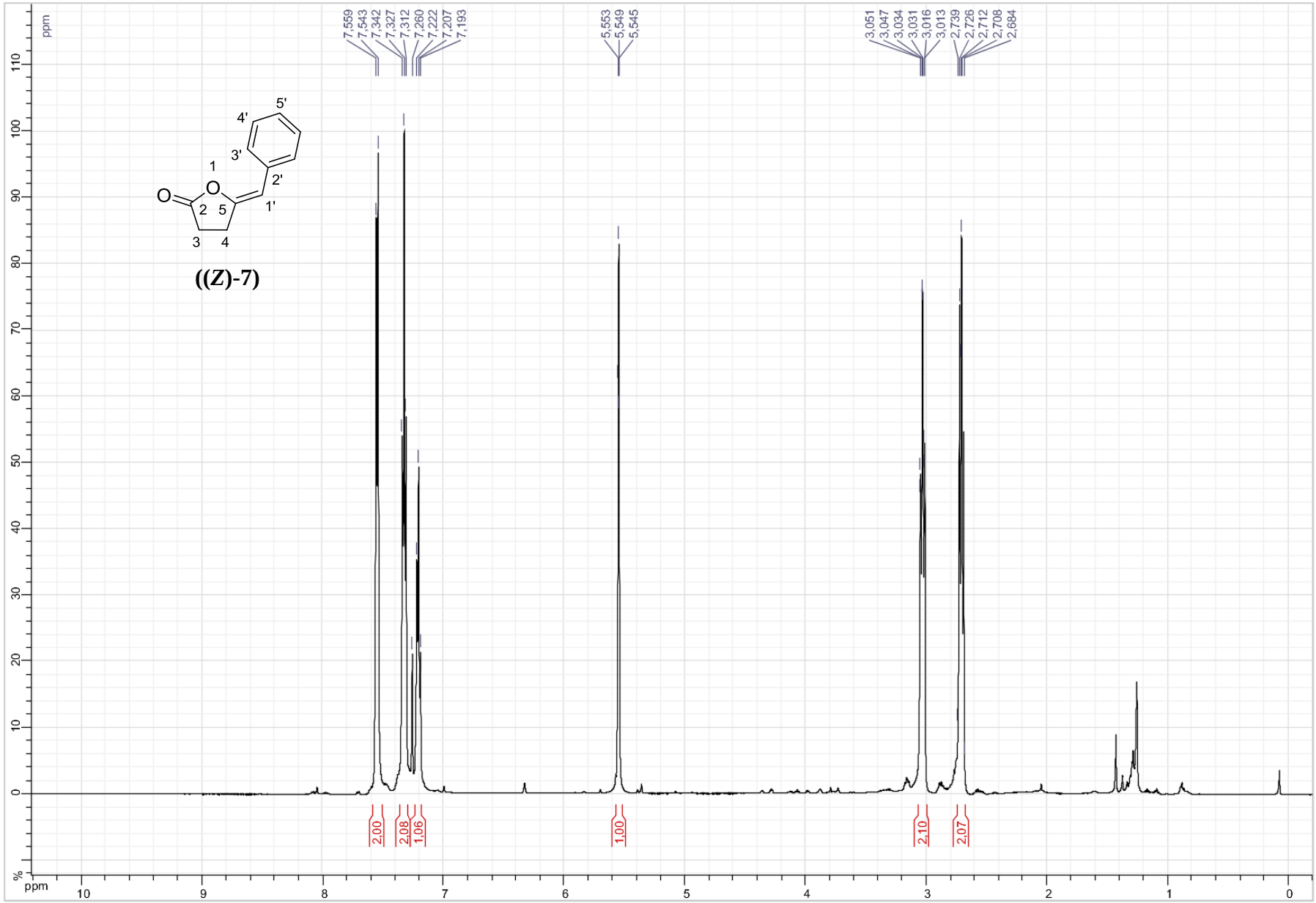

7,366
7,350
7,335
7,260
7,254
7,243
7,232
7,216
7,200
6,333
6,328
6,324
3,187
3,182
3,170
3,166
3,153
3,148
2,788
2,776
2,759
2,742
2,731
2,00
2,94
0,95
2,00
2,00
ppm
10
9
8
7
6
5
4
3
2
1
0
1
O
O
2
5
3
4
1'
2'
3'
4'
5'

((*E*)-7)

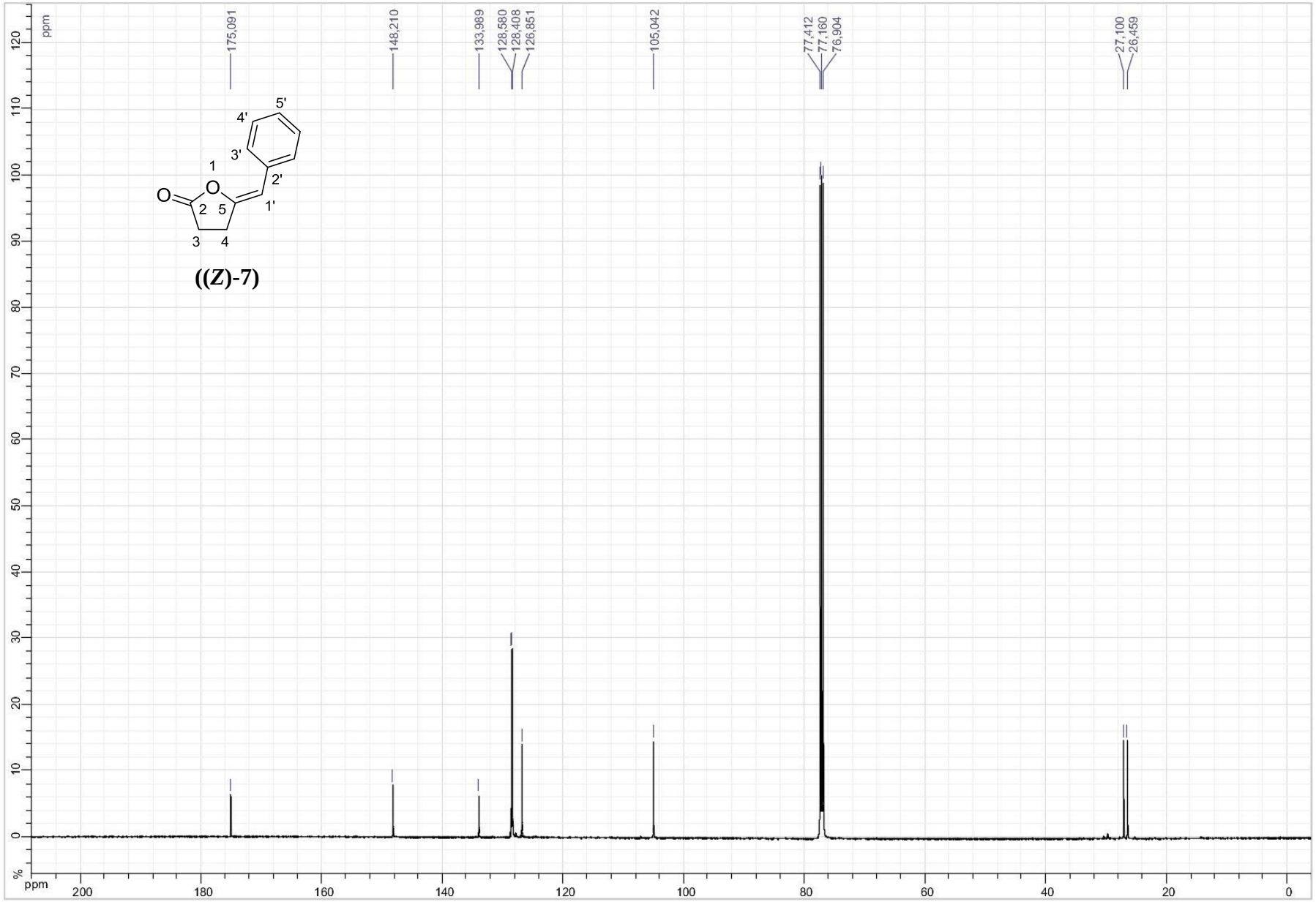

ppm
174,343
151,248
134,449
128,780
127,873
126,756
107,163
77,414
77,160
76,907
27,852
25,258
1
O
O
2
5
1'
2'
3'
4'
5'
3
4
((E)-7)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

((*E*)-7)

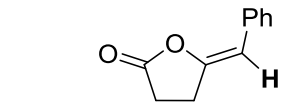


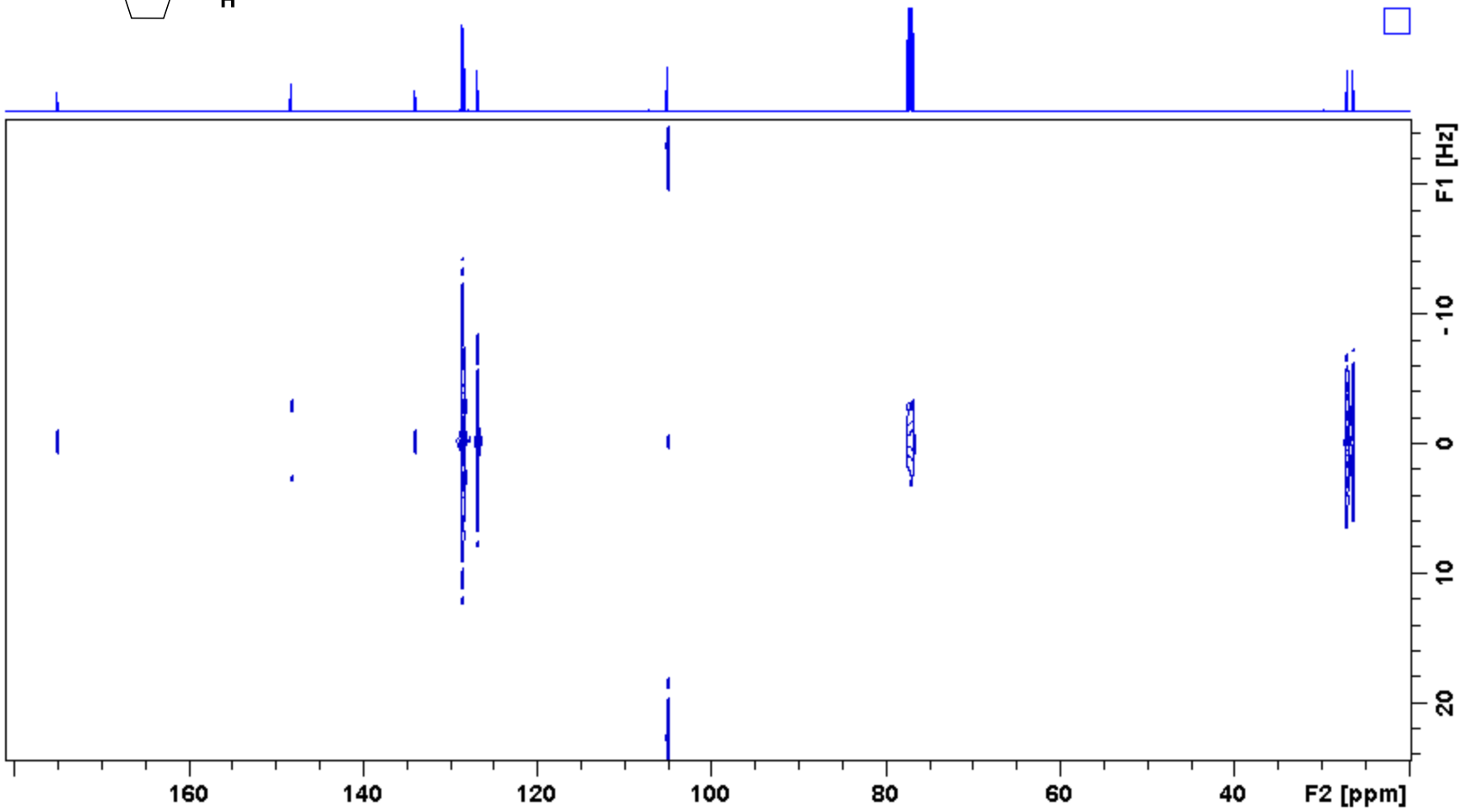

7,559
7,543
7,342
7,327
7,312
7,260
7,222
7,207
7,193
5,553
5,549
5,545
3,051
3,047
3,034
3,031
3,016
3,013
2,739
2,726
2,712
2,708
2,684
ppm
2,00
2,08
1,06
1,00
2,10
2,07

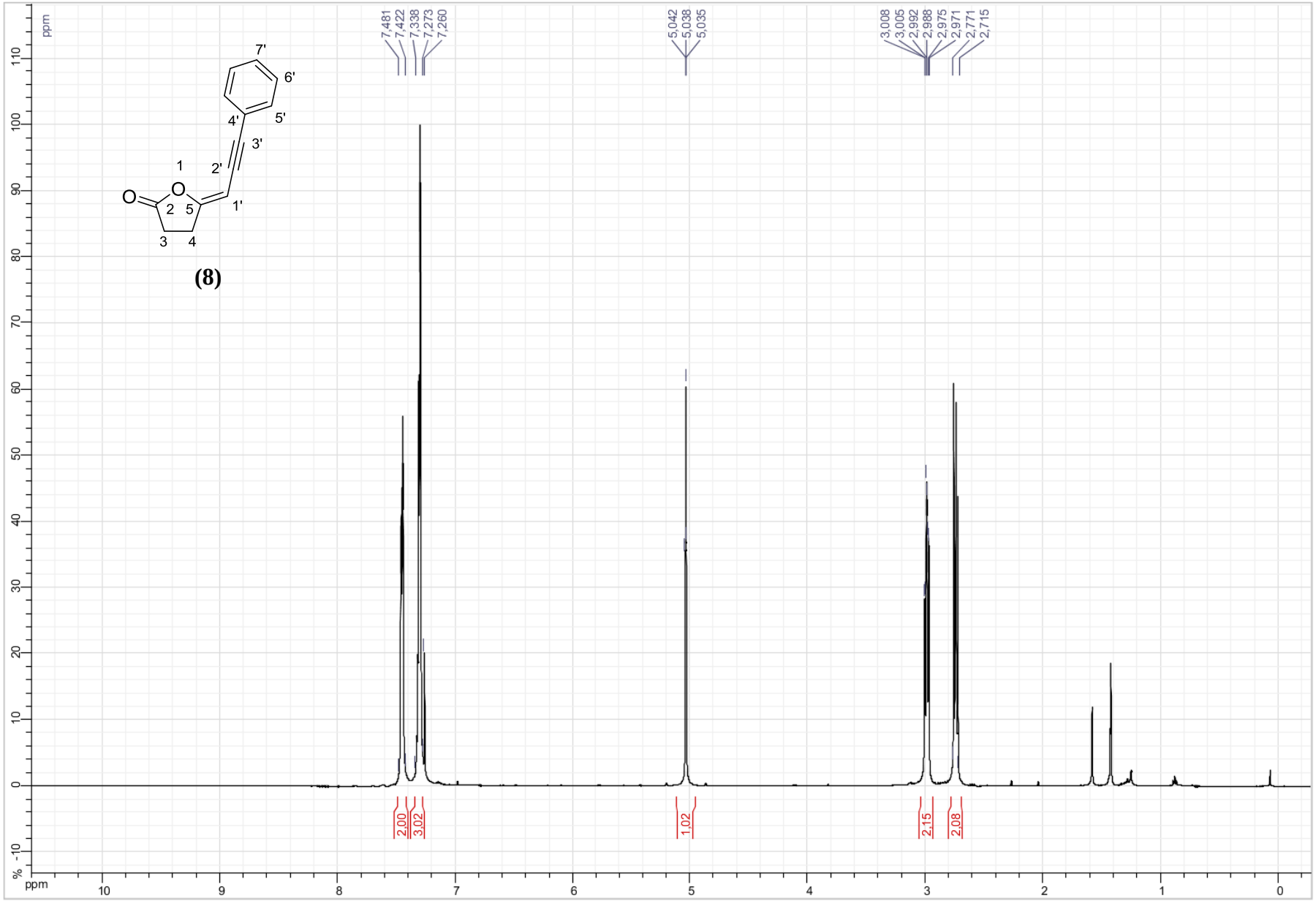
((Z)-7)

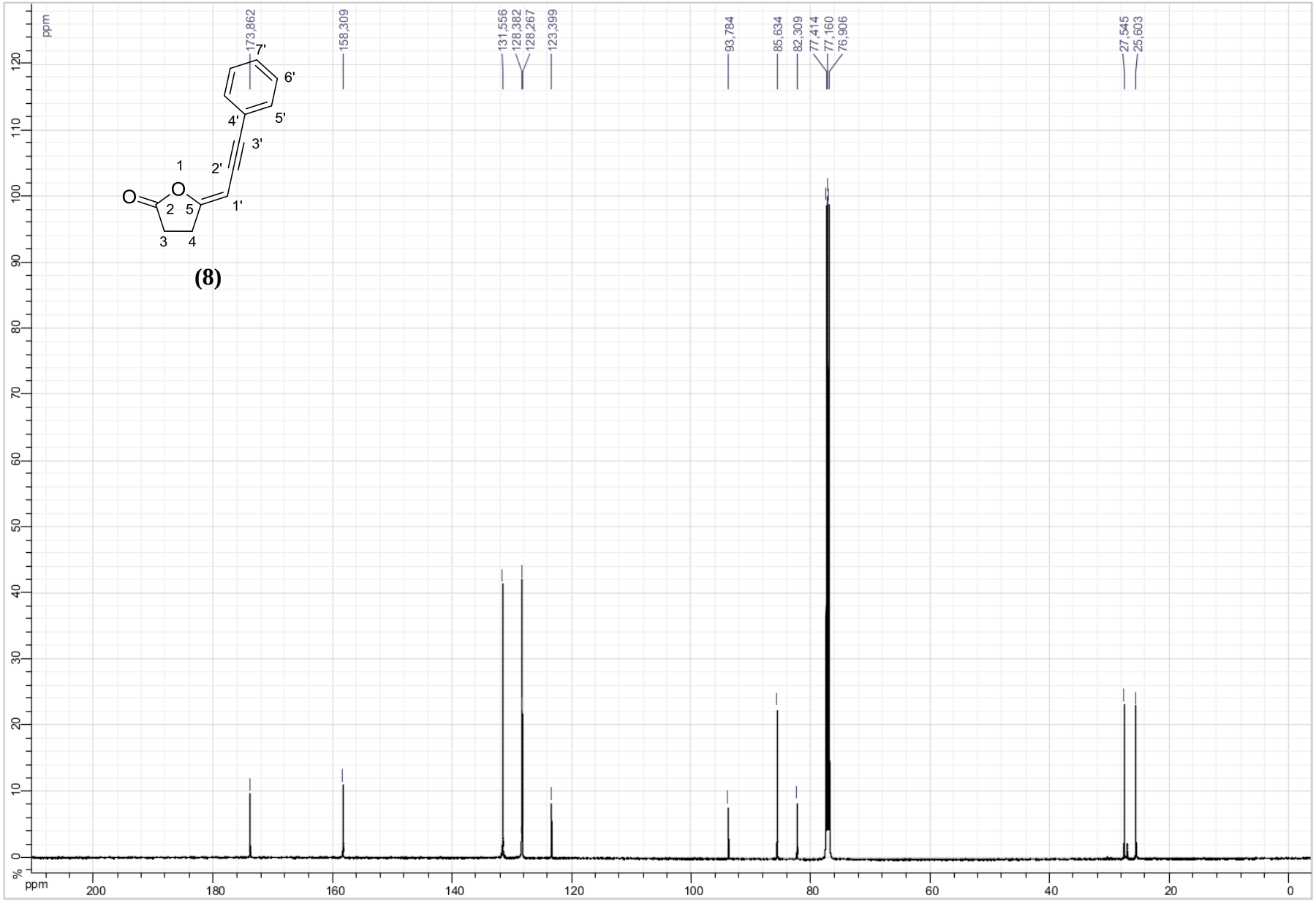

ppm
175,091
148,210
133,989
128,580
128,408
126,851
105,042
77,412
77,160
76,904
27,100
26,459
5'
4'
3'
1
2'
O
O
2
5
1'
3
4
((Z)-7)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

((*Z*)-7)

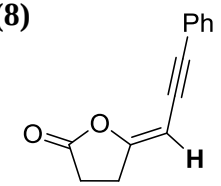


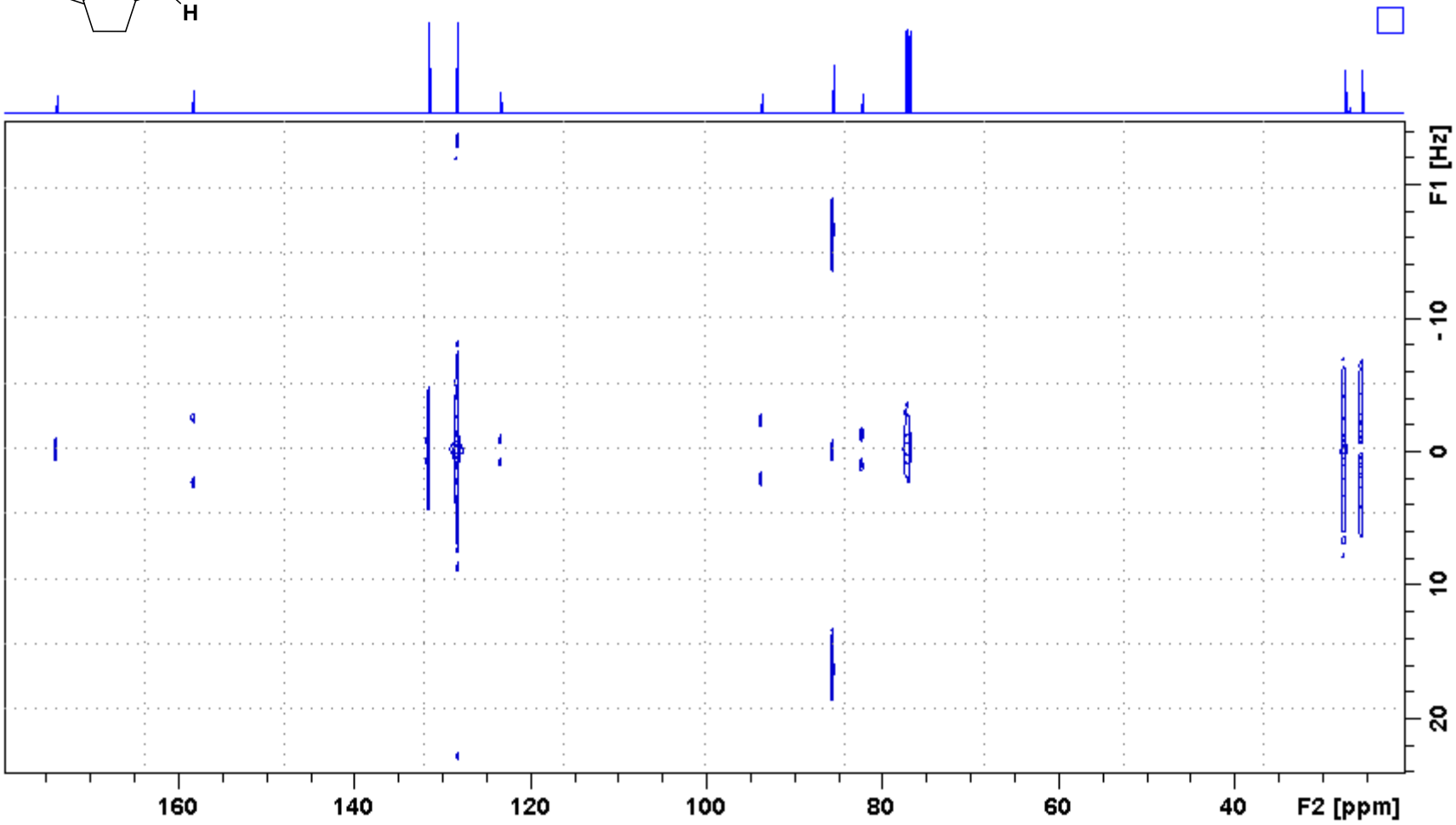


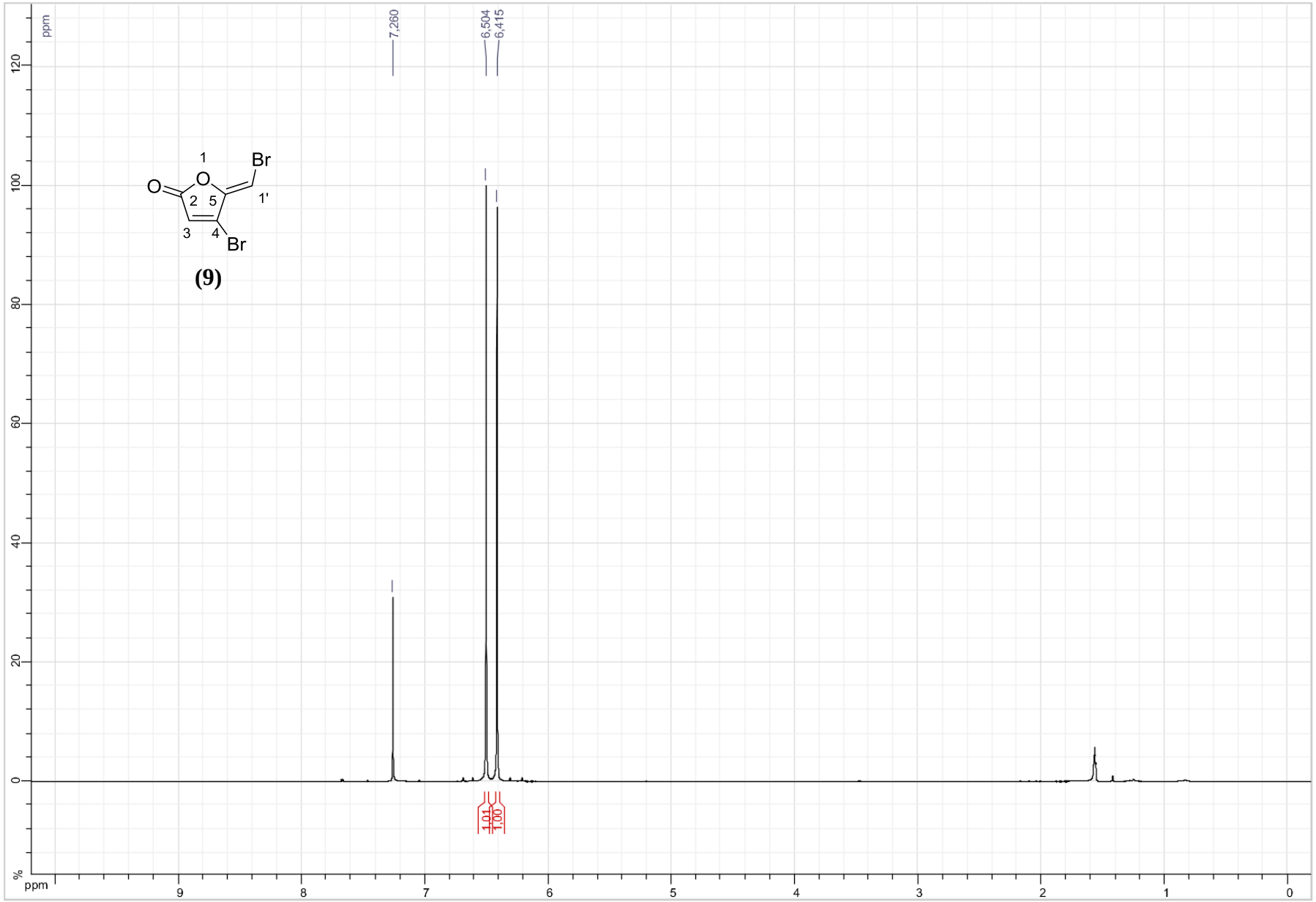

ppm
7,481
7,422
7,338
7,273
7,260
5,042
5,038
5,035
3,008
3,005
2,992
2,988
2,975
2,971
2,771
2,715
2,00
3,02
1,02
2,15
2,08
7'
6'
5'
4'
3'
2'
1'
1
2
3
4
5
O
O
(8)

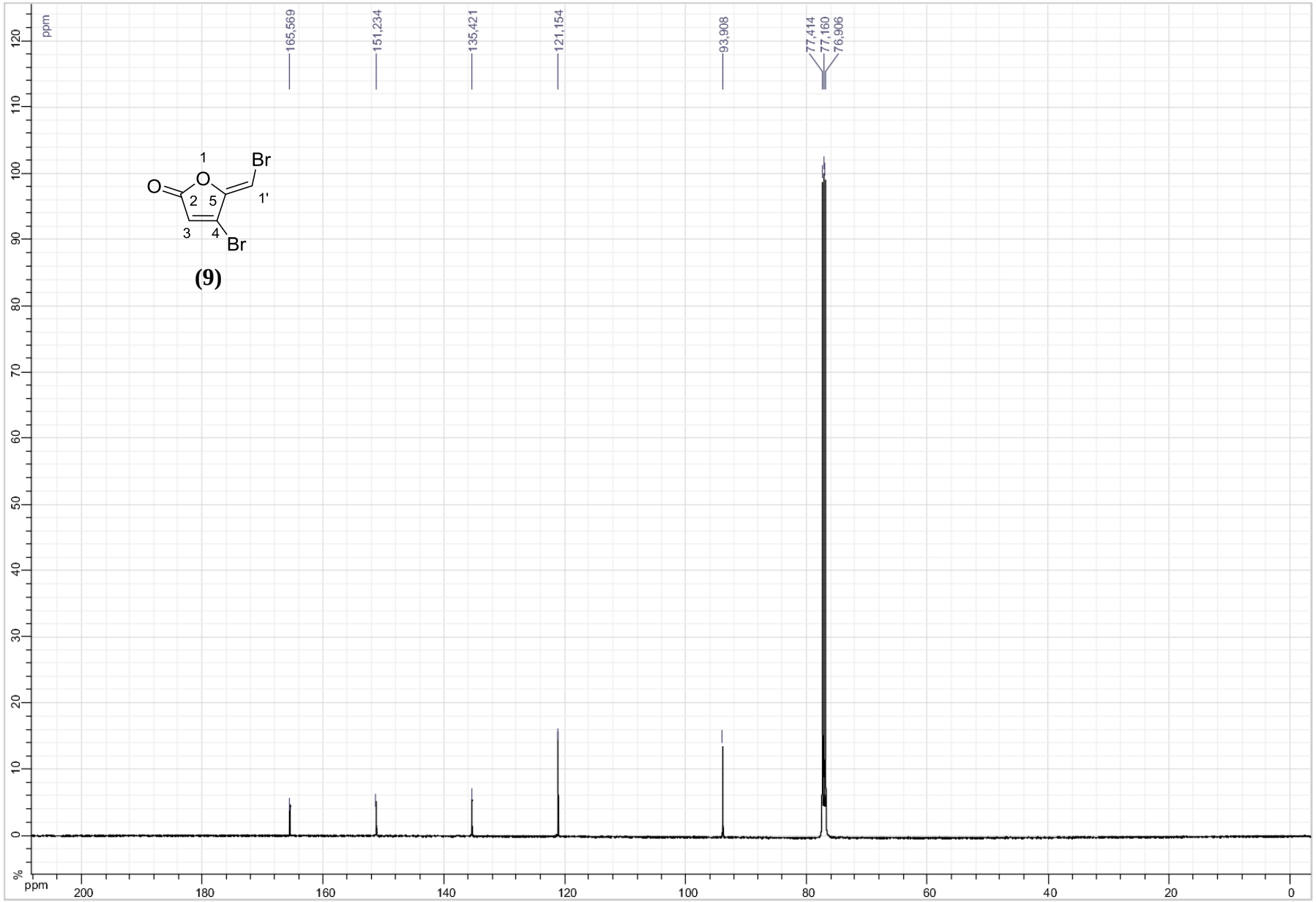

ppm
173,862
158,309
131,556
128,382
128,267
123,399
93,784
85,634
82,309
77,414
77,160
76,906
27,545
25,603
7'
6'
5'
4'
3'
2'
1'
1
2
3
4
5
O
O
(8)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(8)

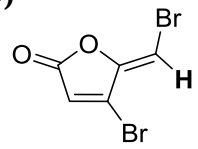


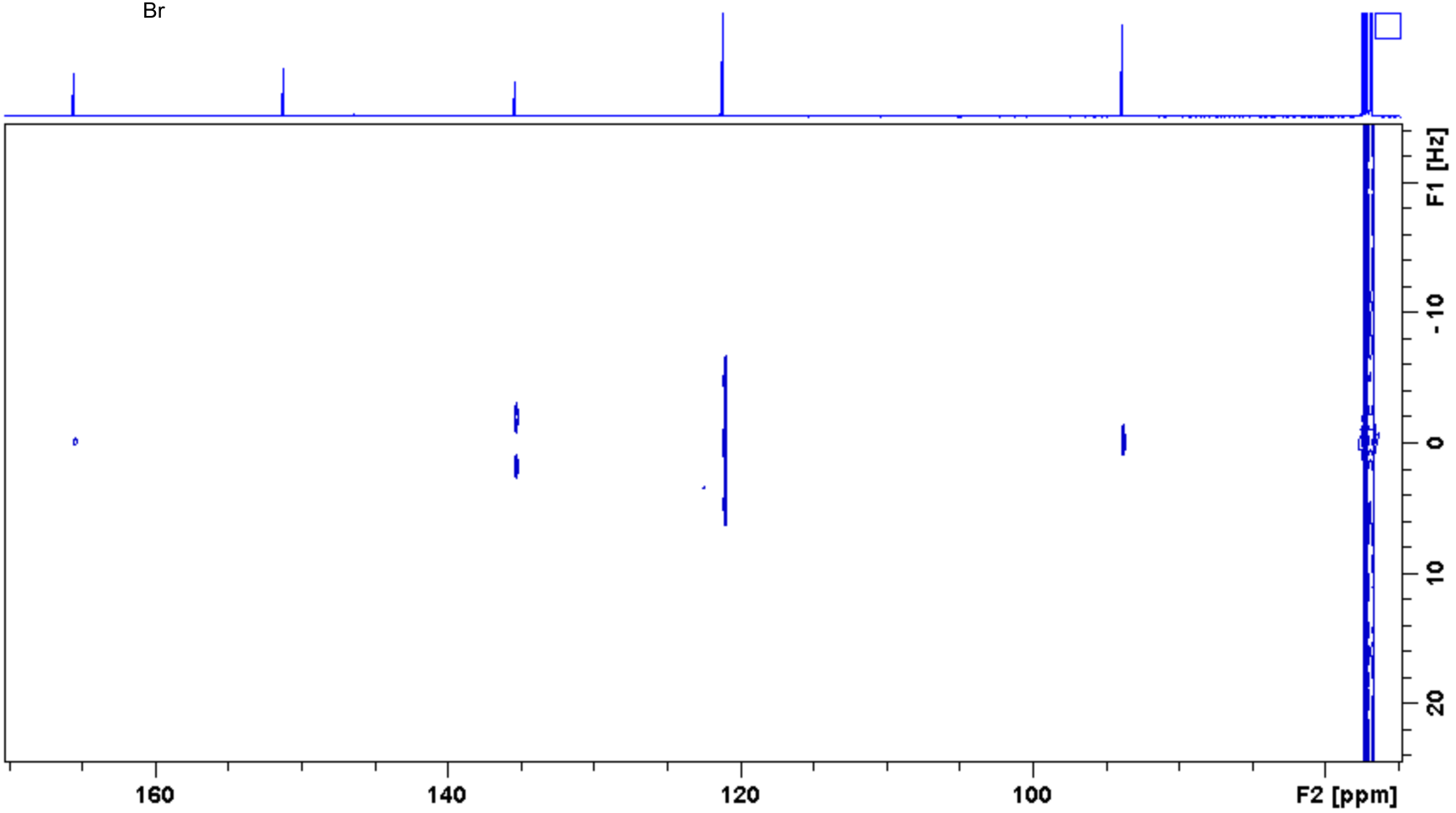


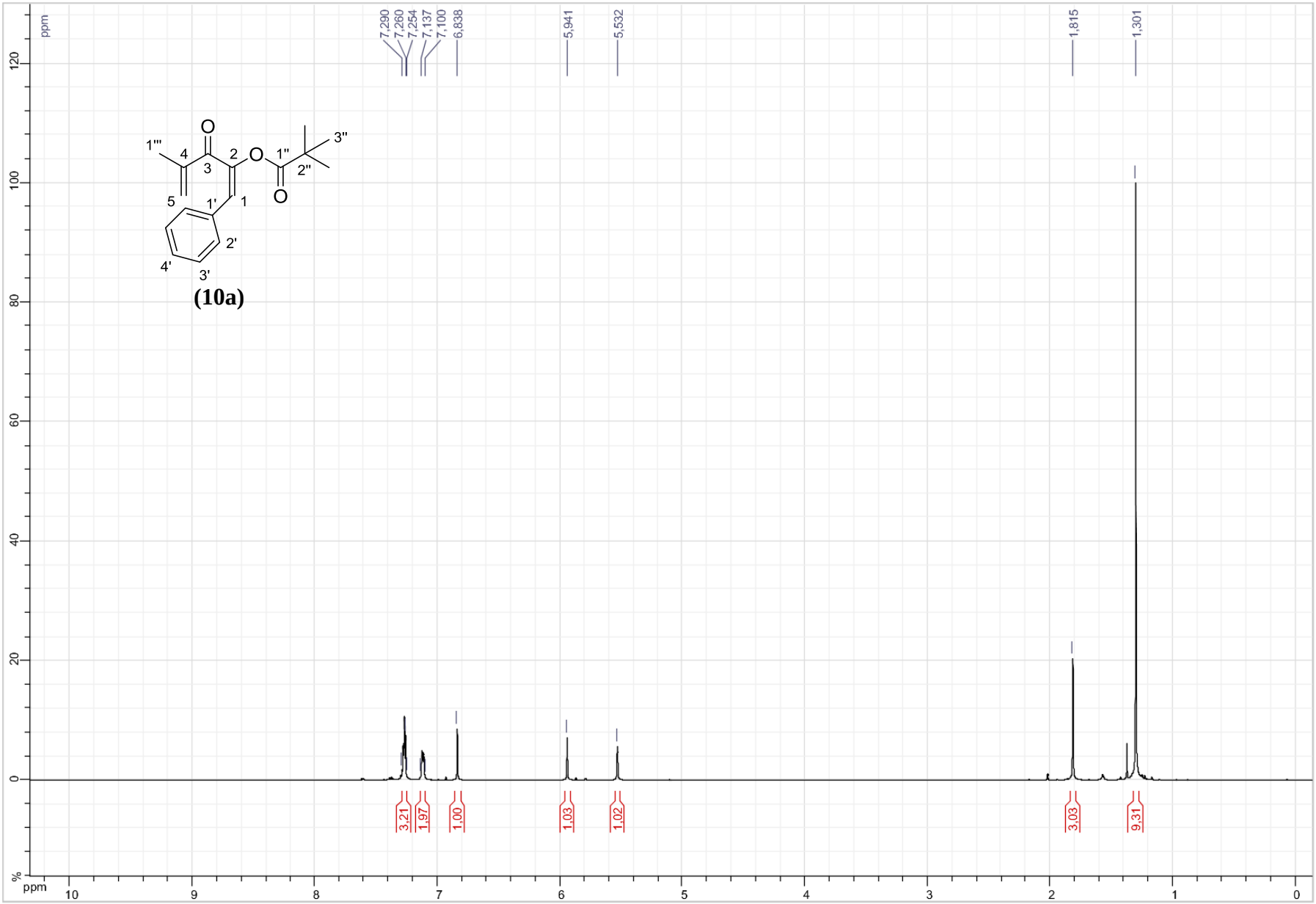

ppm
7,260
6,504
6,415
1
Br
O
O
2
5
1'
3
4
Br
(9)
120
100
80
60
40
20
0
%
ppm
9
8
7
6
5
4
3
2
1
0
1,01
1,00


ppm
165,569
151,234
135,421
121,154
93,908
77,414
77,160
76,906
1
Br
O
O
2
5
1'
3
4
Br
(9)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

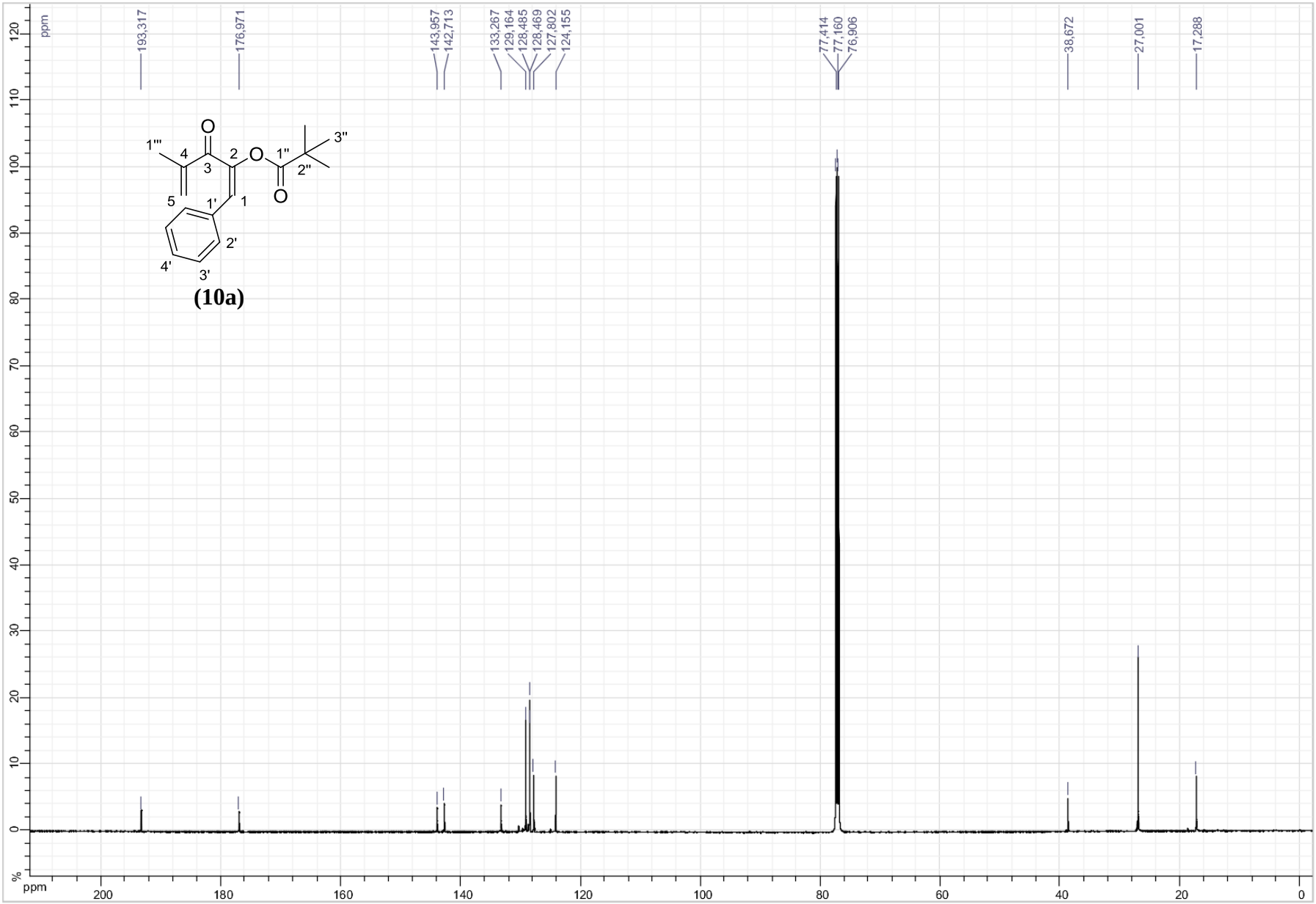
(9)



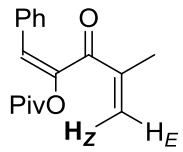



ppm
7,290
7,260
7,254
7,137
7,100
6,838
5,941
5,532
1,815
1,301
3,21
1,97
1,00
1,03
1,02
3,03
9,31
%
ppm

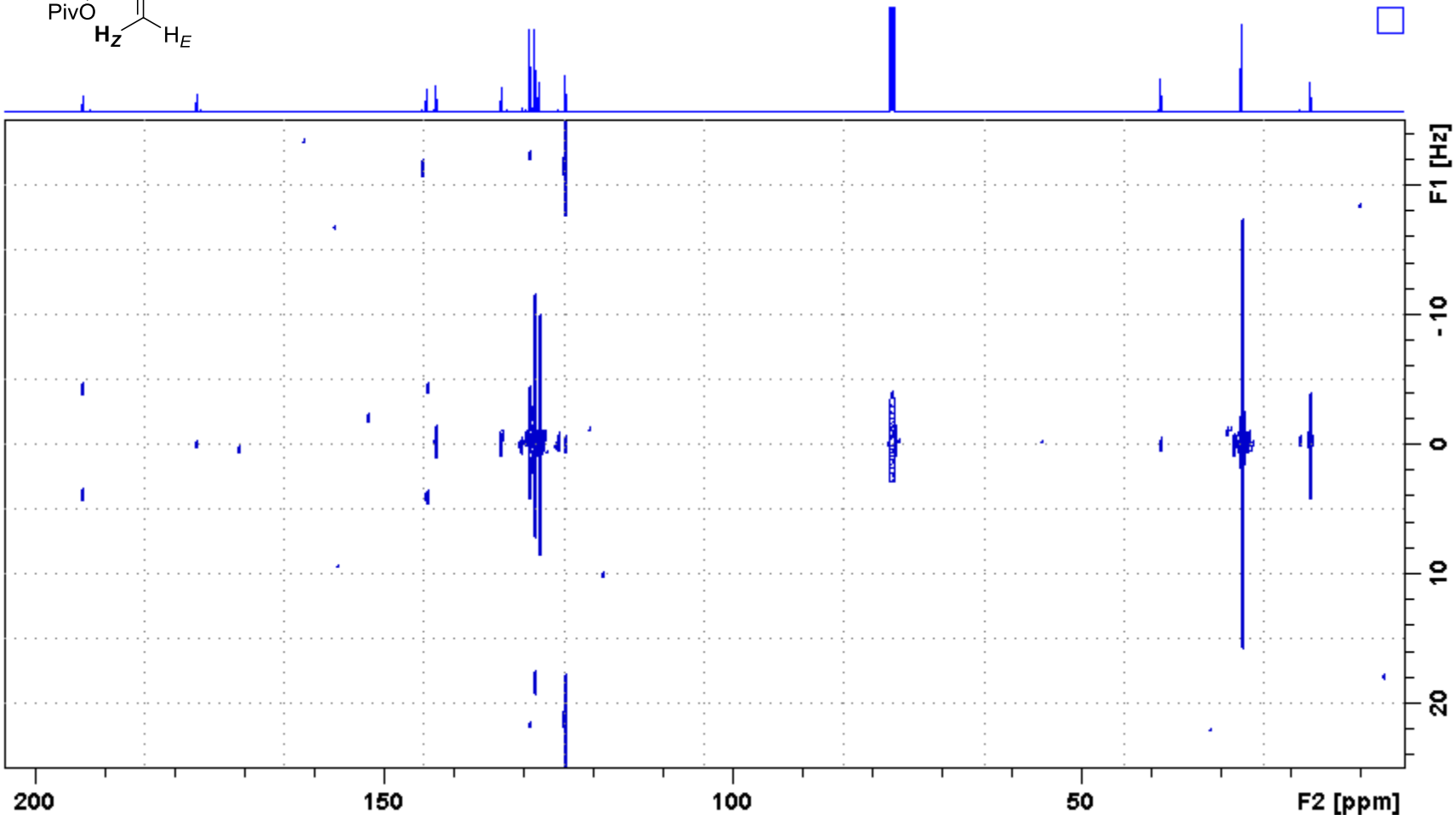
(10a)


ppm
193,317
176,971
143,957
142,713
133,267
129,164
128,485
128,469
127,802
124,155
77,414
77,160
76,906
38,672
27,001
17,288
O
O
O
1'''
4
3
2
1''
3''
2''
5
1'
1
2'
4'
3'
(10a)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

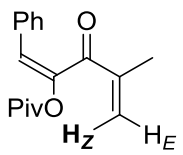
(10a)



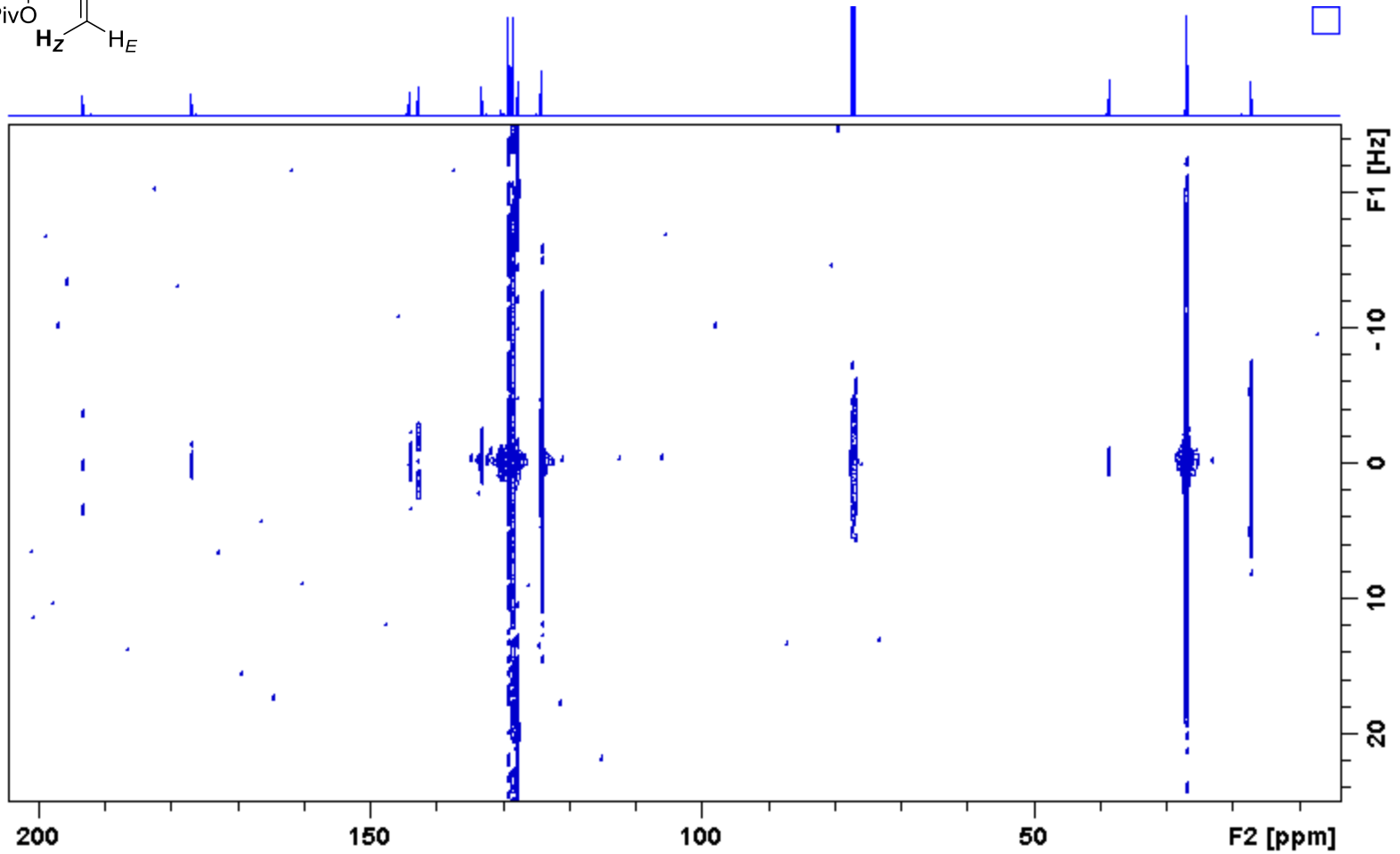
Selelected hydrogen:
C**H**Ph 6.84 ppm



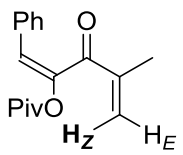
(10a)



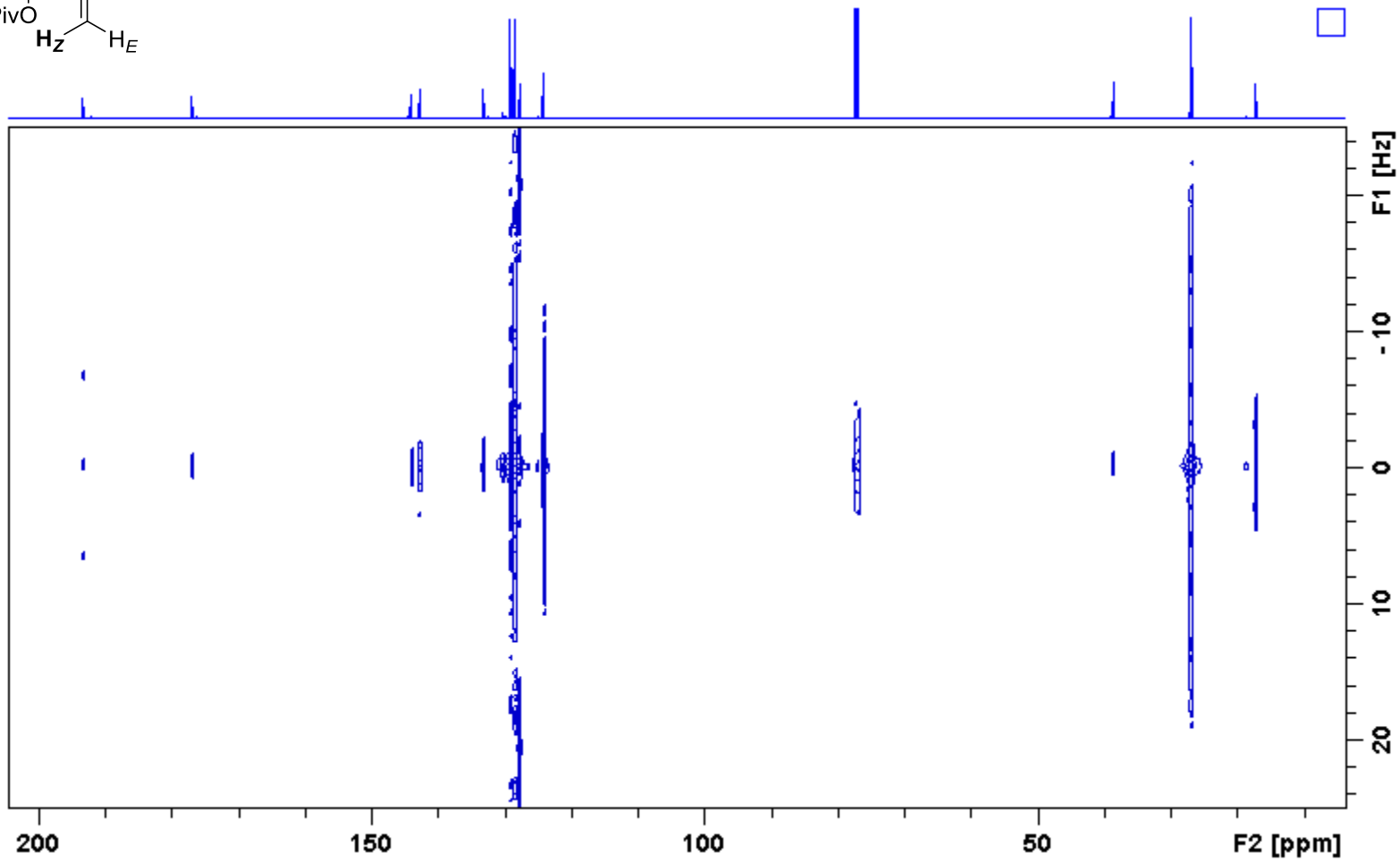
Selelected hydrogen:
$\mathbf{H_Z}$ 5.94 ppm

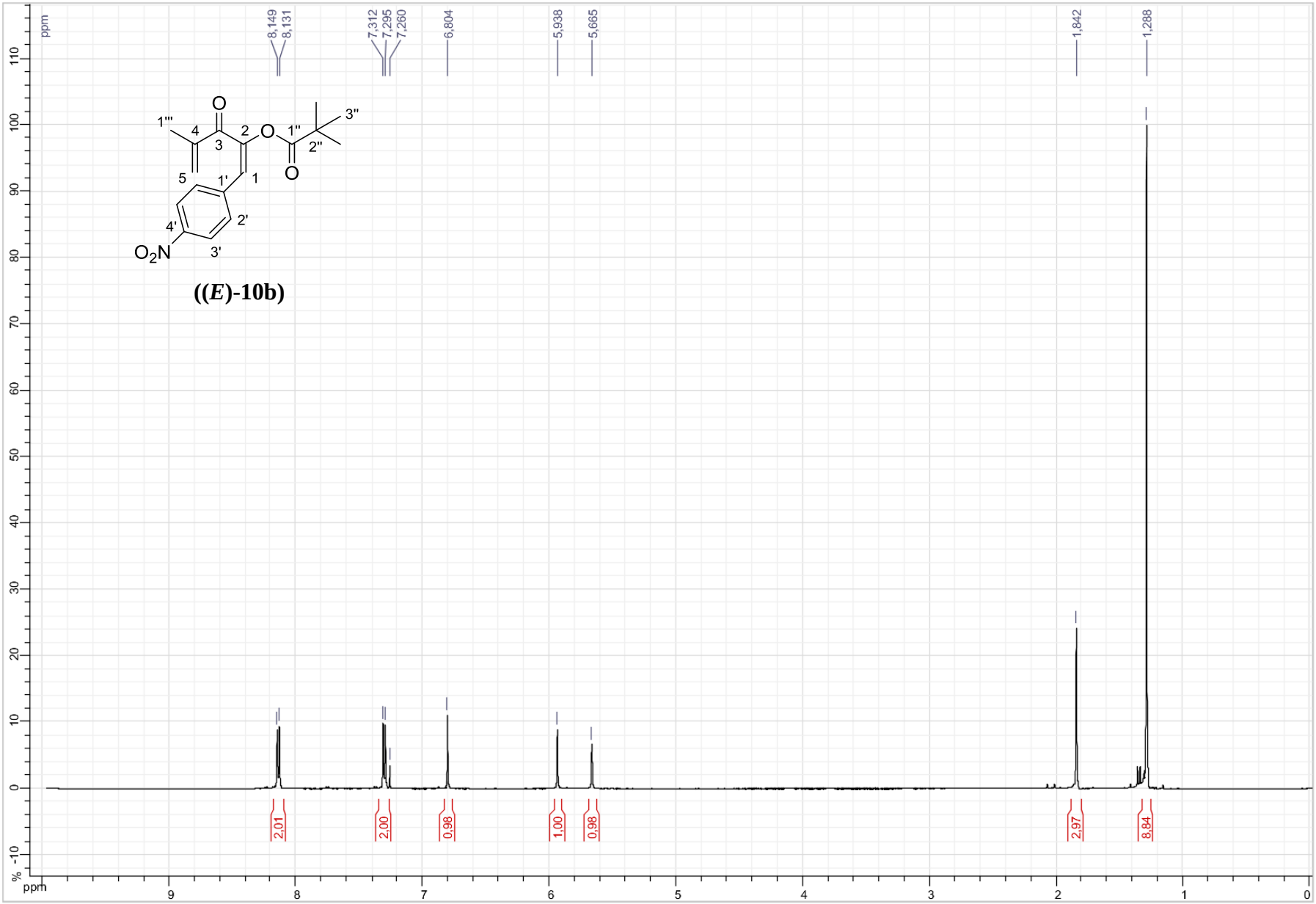


(10a)

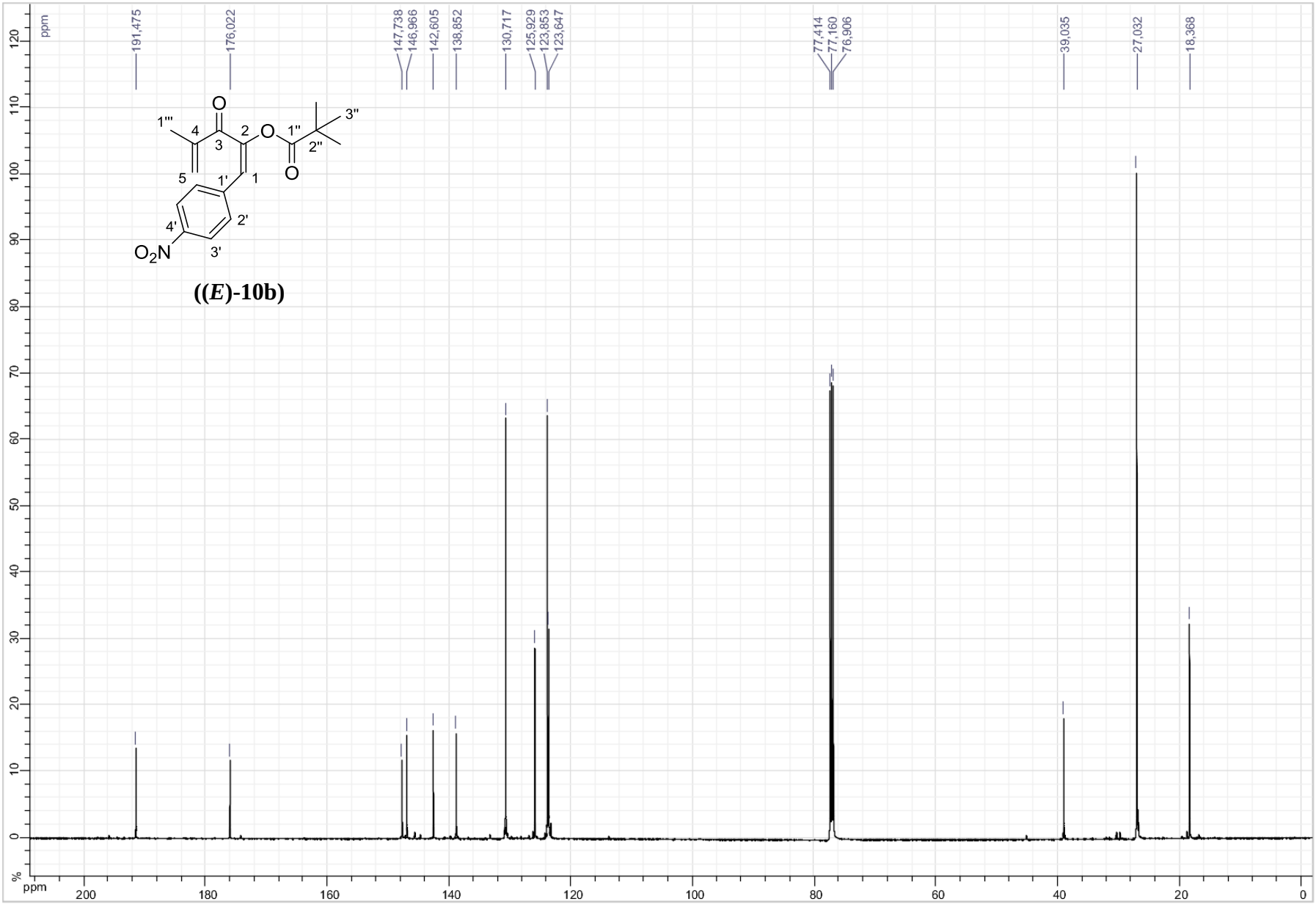


Selelected hydrogen:
$\mathbf{H_E}$ 5.53 ppm



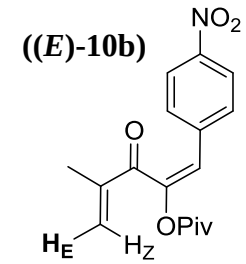

ppm
8,149
8,131
7,312
7,295
7,260
6,804
5,938
5,665
1,842
1,288
O
1'''
4
3
2
O
1''
3''
2''
O
5
1'
1
4'
2'
O2N
3'
2,01
2,00
0,98
1,00
0,98
2,97
8,84
ppm
9
8
7
6
5
4
3
2
1
0
%
110
100
90
80
70
60
50
40
30
20
10
0
-10

((*E*)-10b)

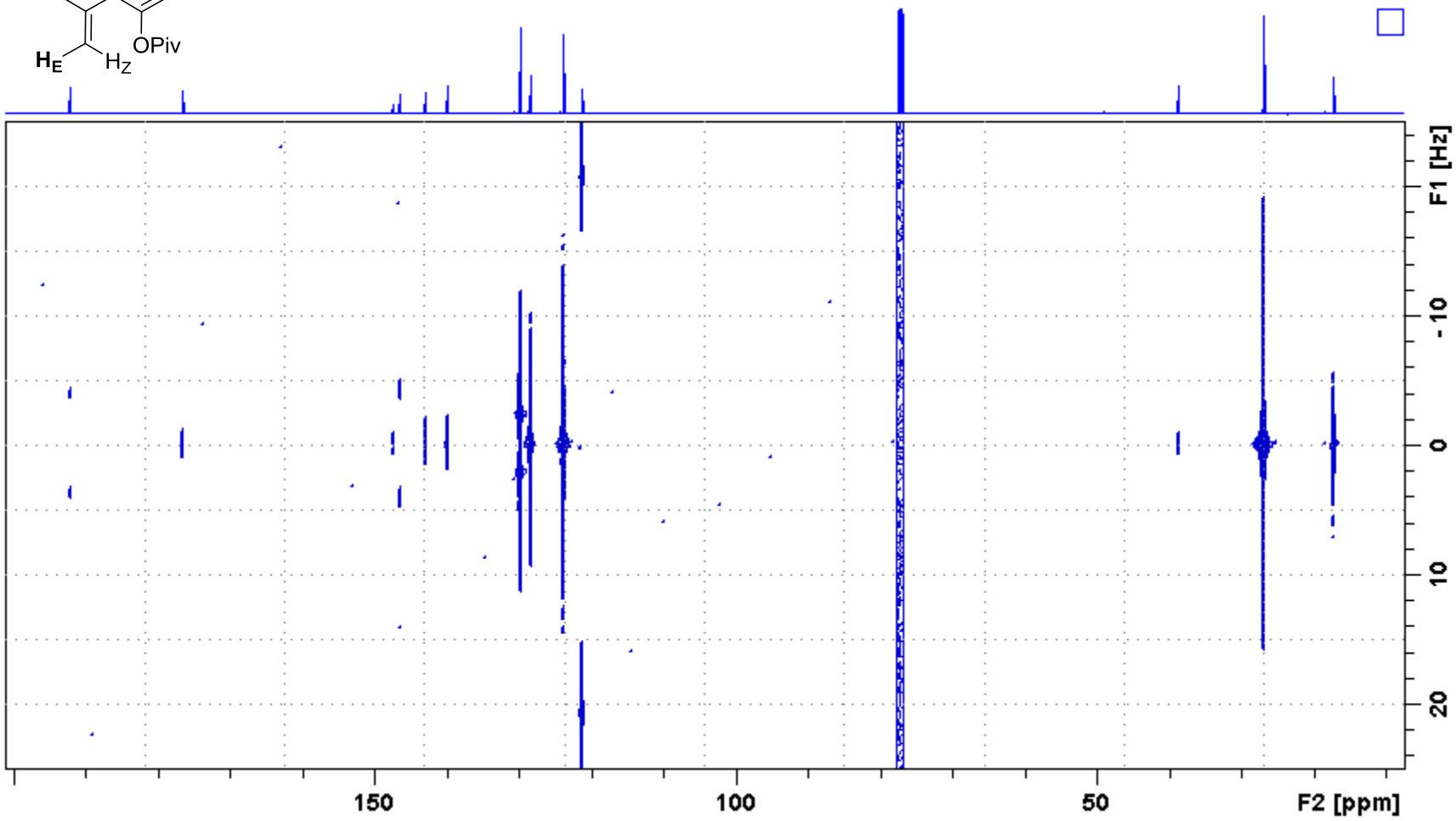

191,475
176,022
147,738
146,966
142,605
138,852
130,717
125,929
123,853
123,647
77,414
77,160
76,906
39,035
27,032
18,368
ppm
O
O
O
1'''
4
3
2
1''
3''
2''
5
1'
1
4'
2'
3'
O_2N

((*E*)-10b)

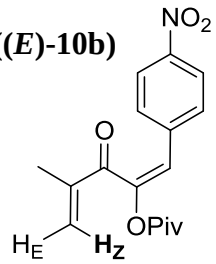
((*E*)-10b)



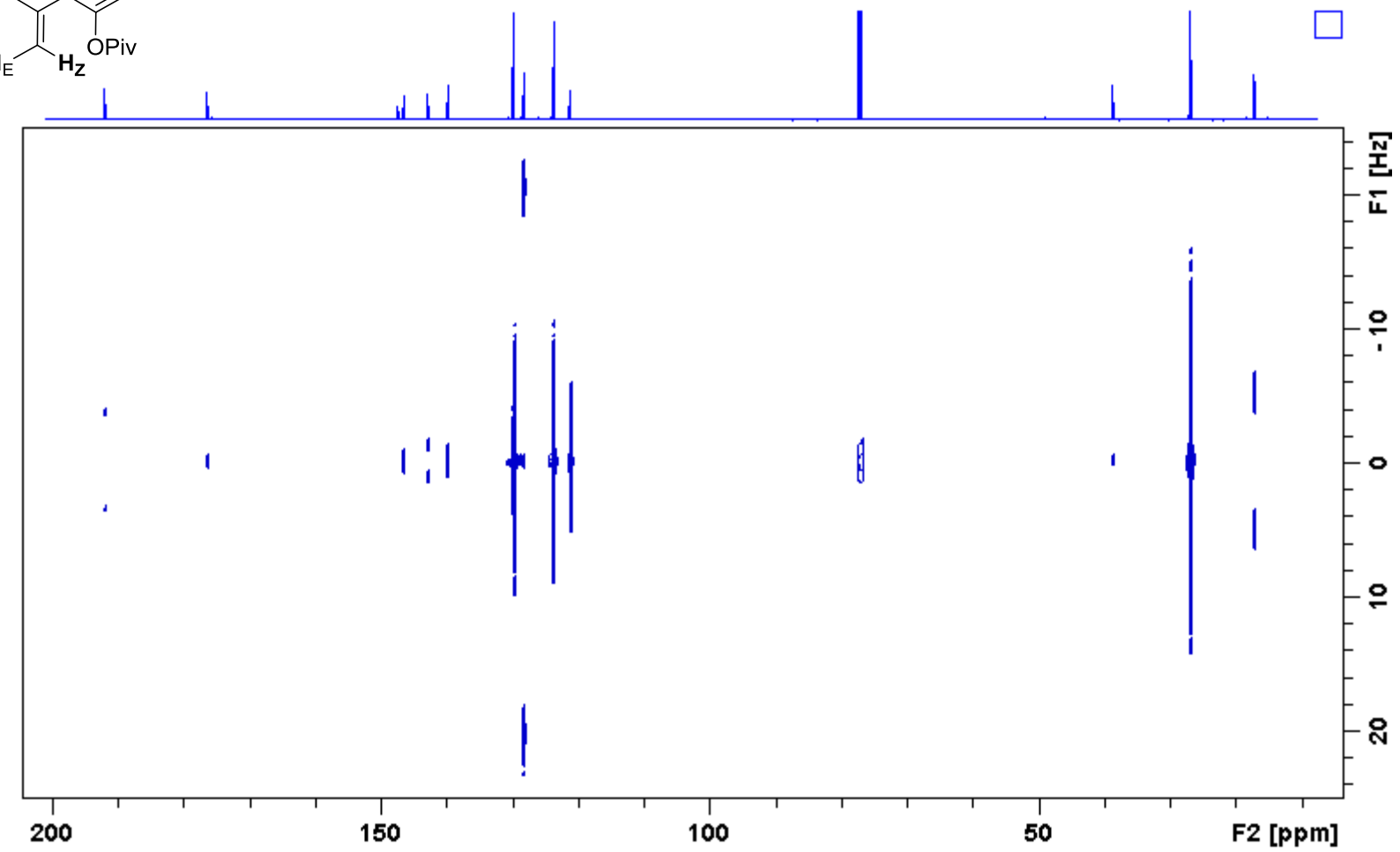
Selelected hydrogen:
C**H**Ar 6.80 ppm



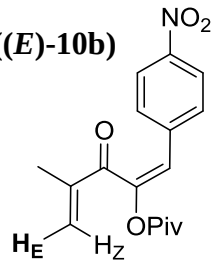
((*E*)-10b)



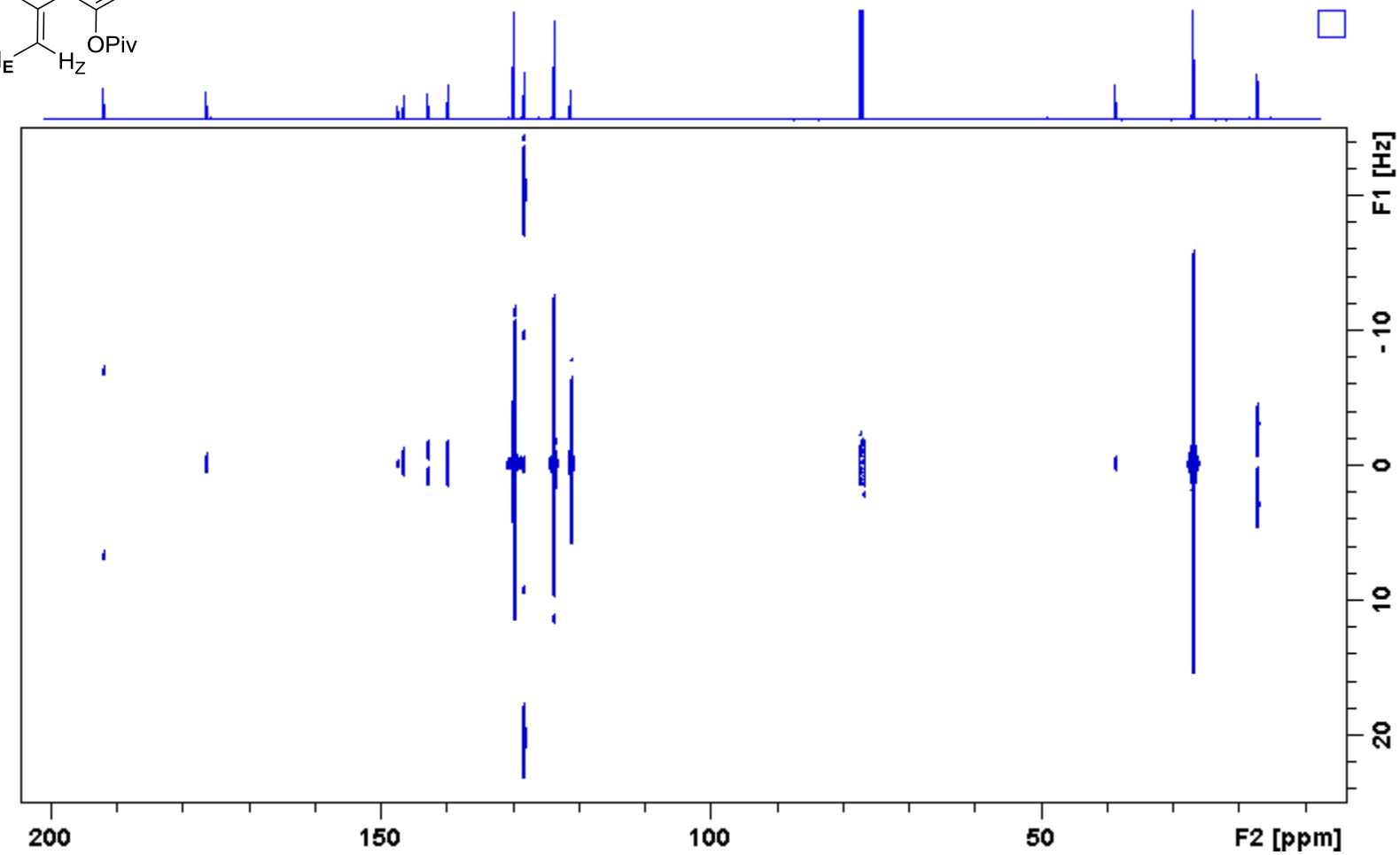
Selelected hydrogen:
$\mathbf{H_Z}$ 5.94 ppm

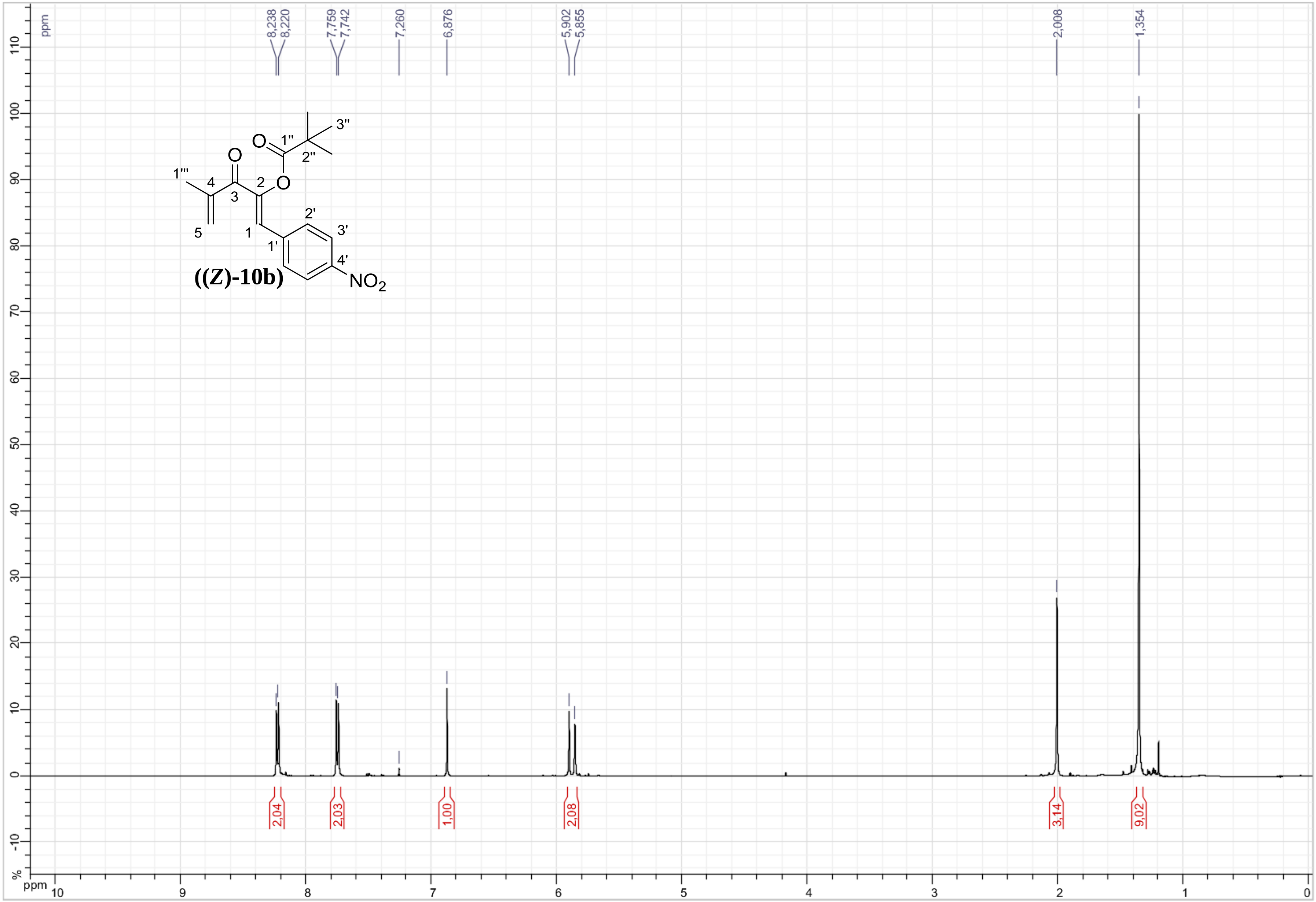


((*E*)-10b)

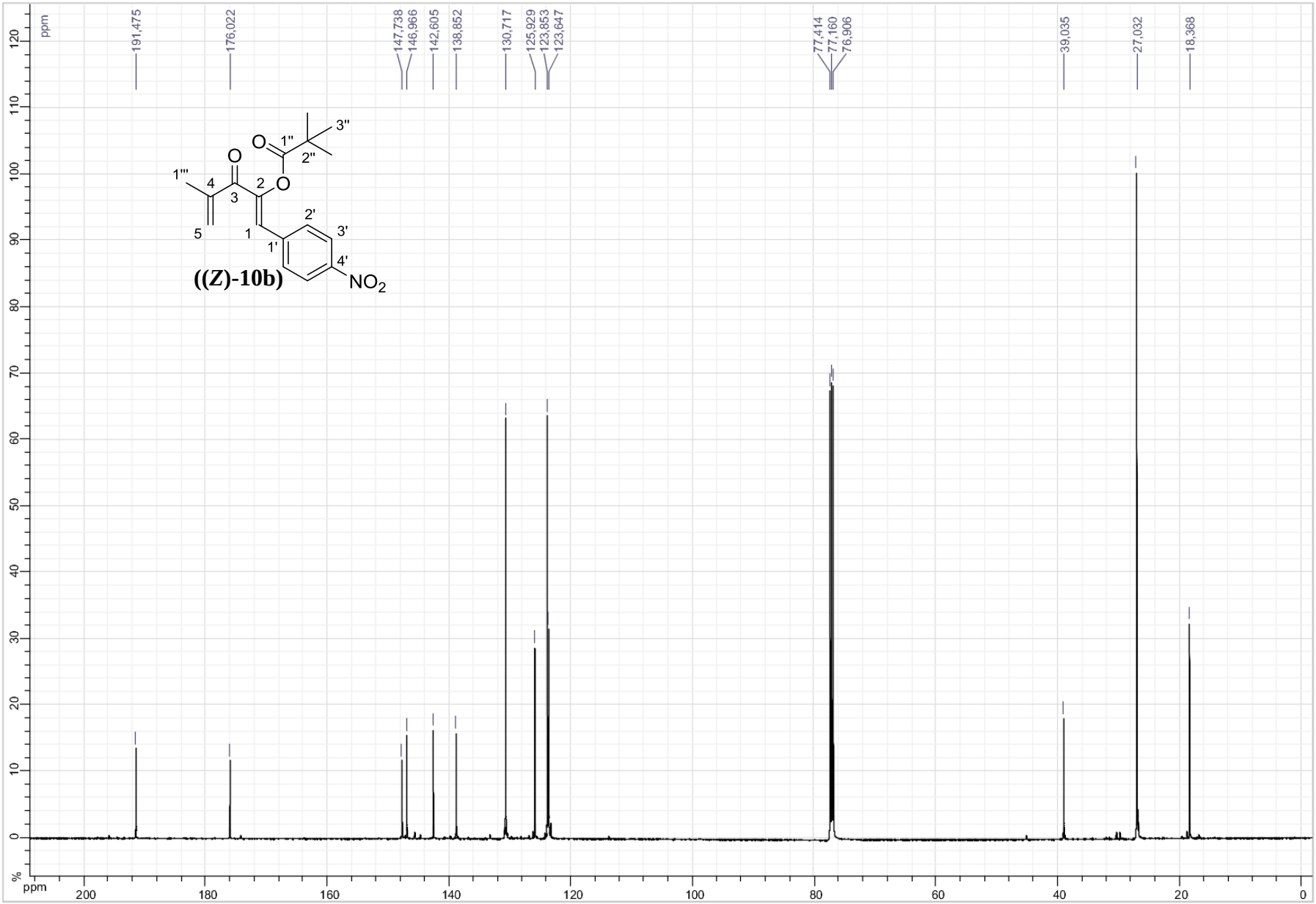


Selelected hydrogen:
$\mathbf{H_E}$ 5.67 ppm

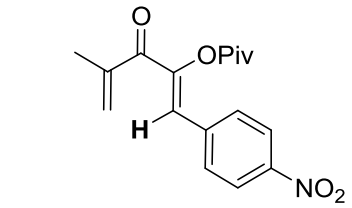


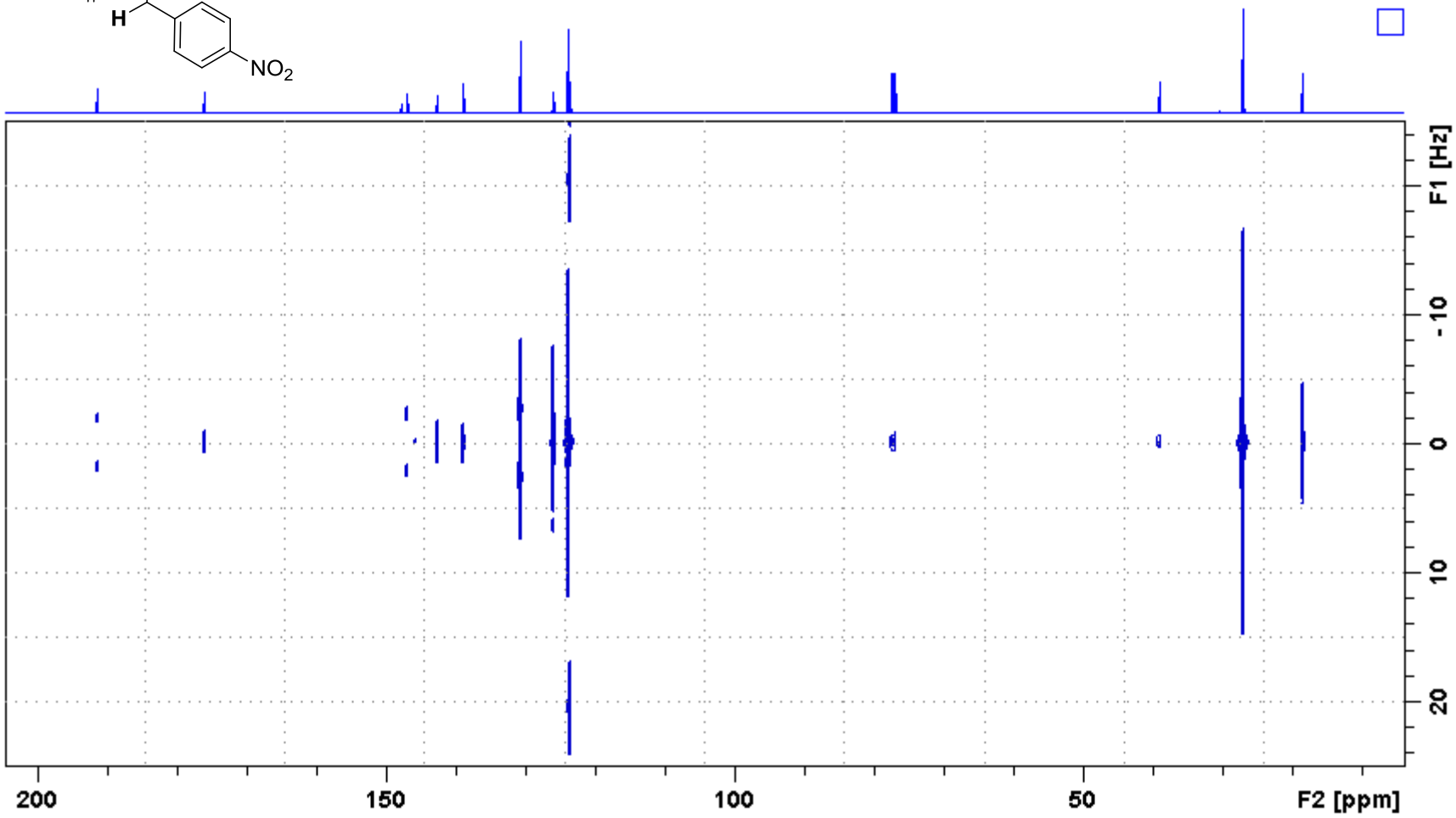


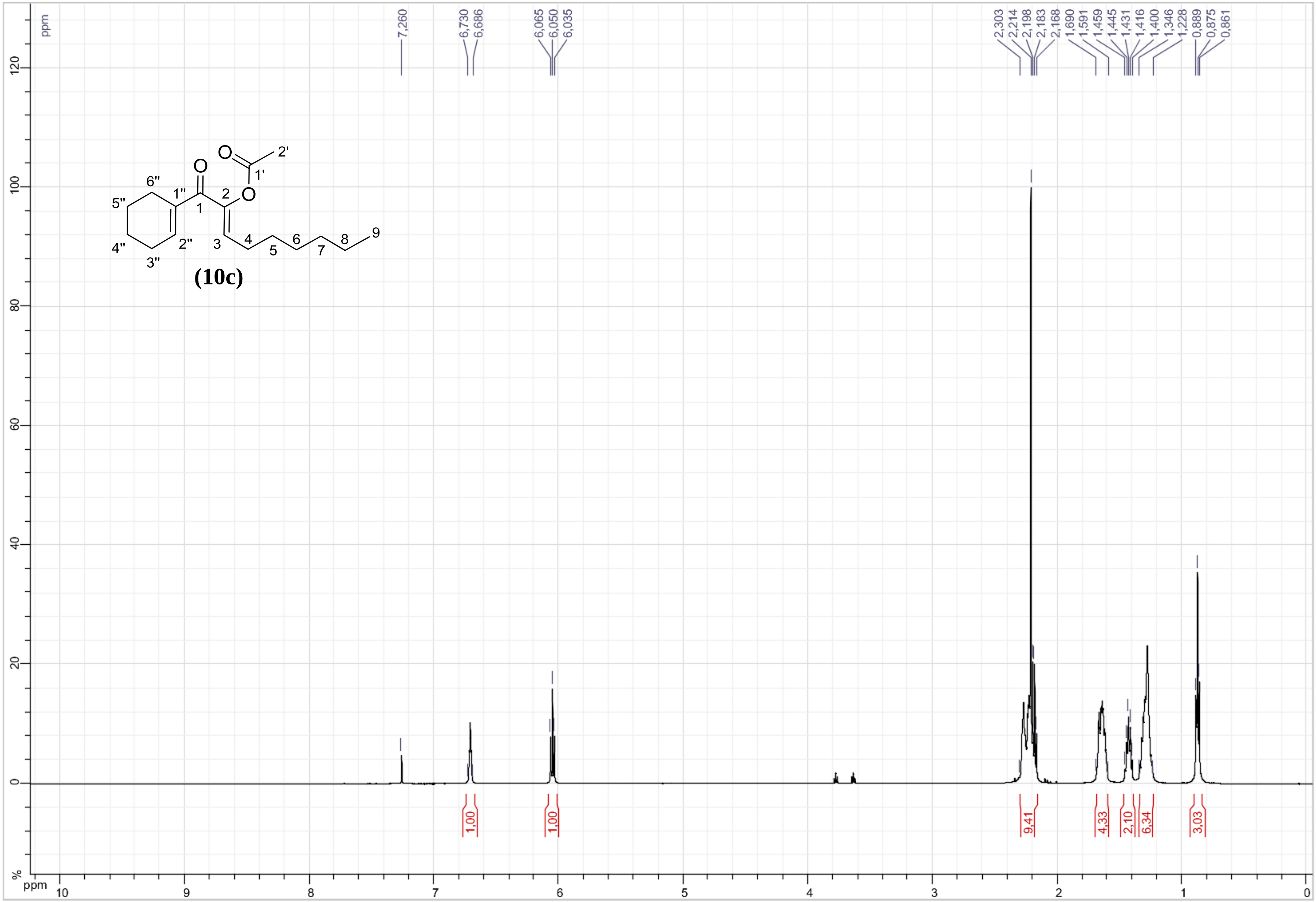
8,238
8,220
7,759
7,742
7,260
6,876
5,902
5,855
2,008
1,354
((Z)-10b)
NO2
2,04
2,03
1,00
2,08
3,14
9,02
ppm
%

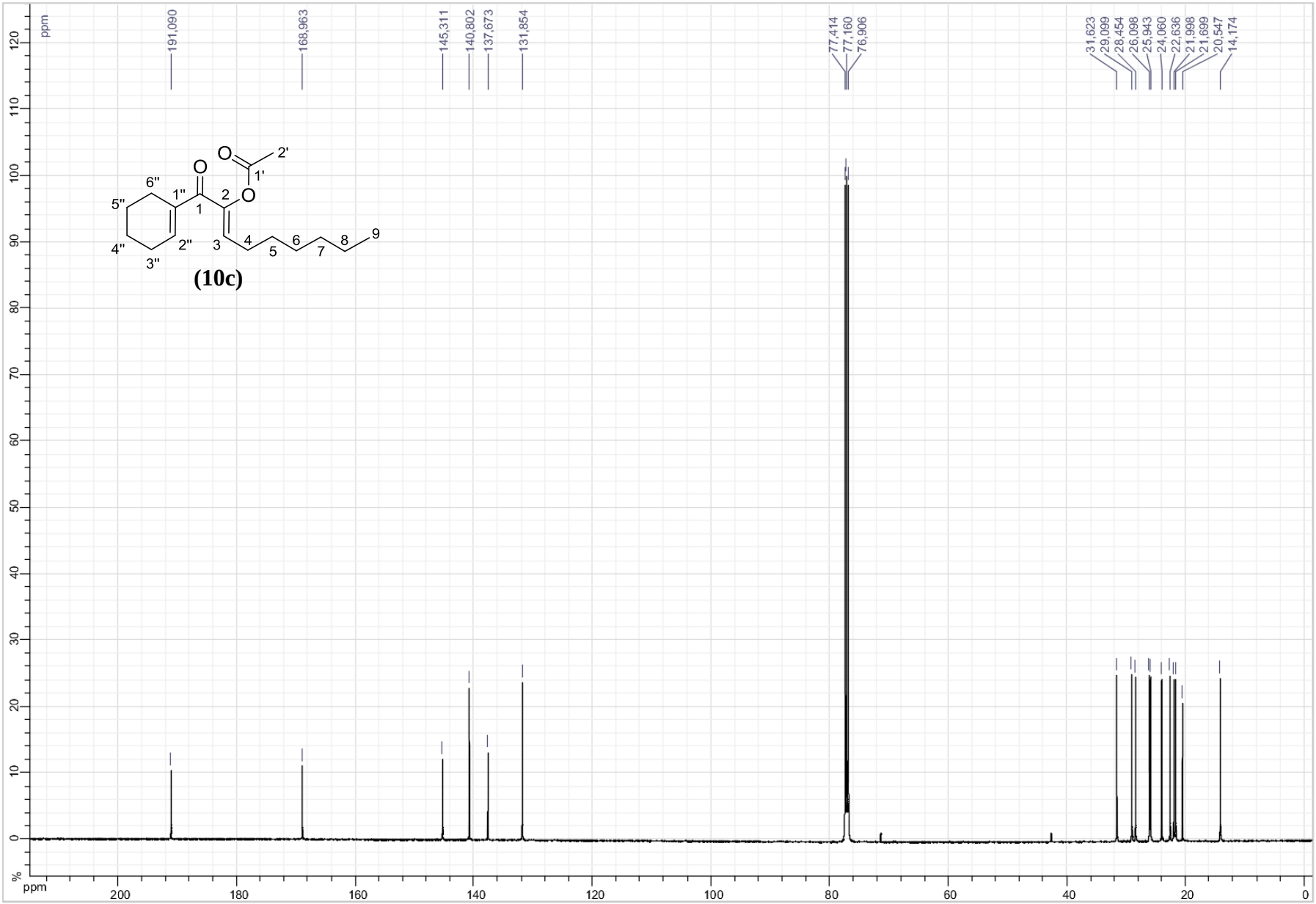

191,475
176,022
147,738
146,966
142,605
138,852
130,717
125,929
123,853
123,647
77,414
77,160
76,906
39,035
27,032
18,368
ppm
((Z)-10b)
NO2

((*Z*)-10b)

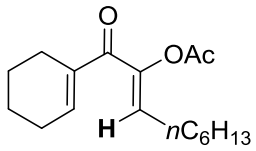




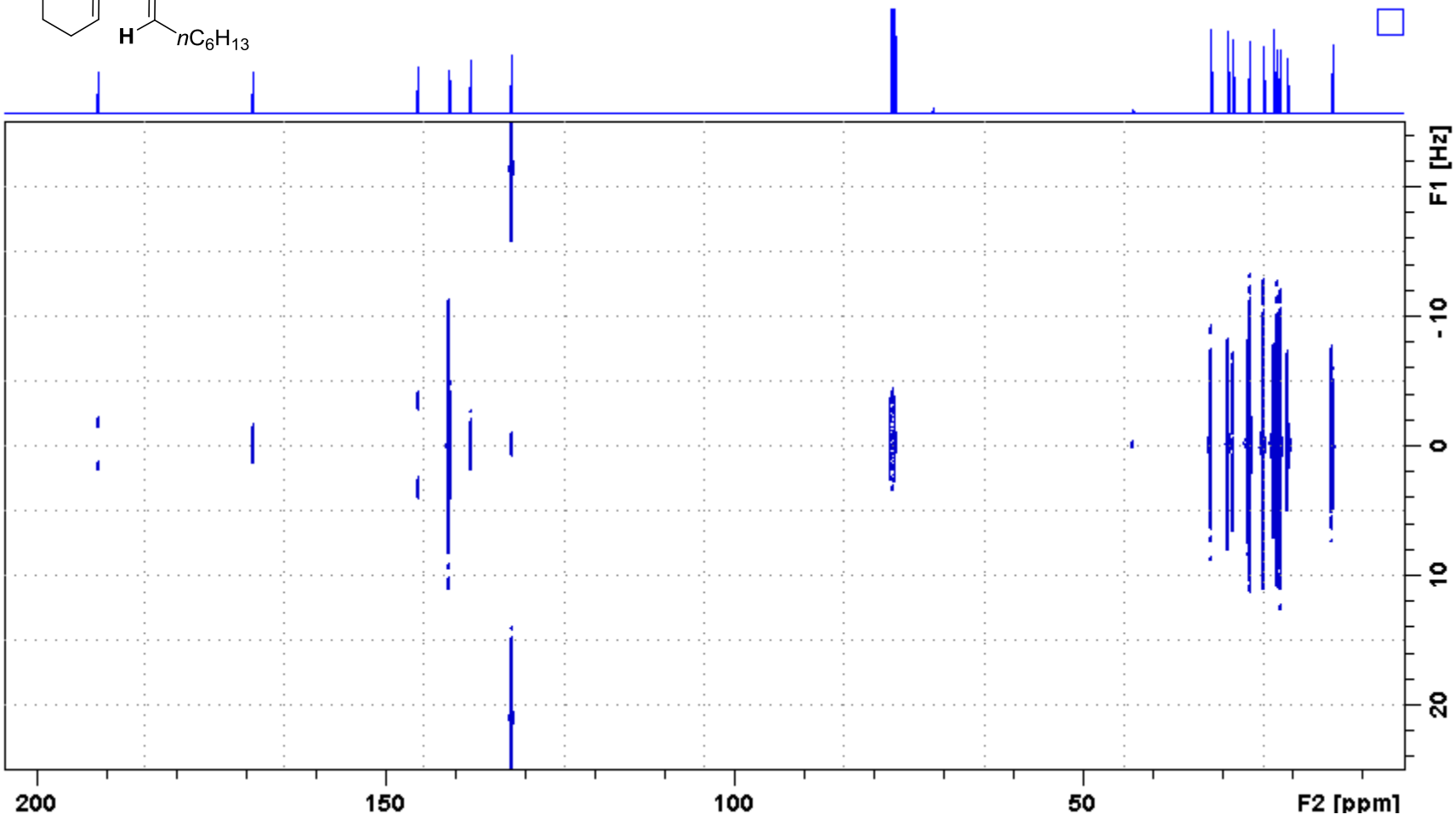

ppm
7,260
6,730
6,686
6,065
6,050
6,035
2,303
2,214
2,198
2,183
2,168
1,690
1,591
1,459
1,445
1,431
1,416
1,400
1,346
1,228
0,889
0,875
0,861
(10c)
1,00
1,00
9,41
4,33
2,10
6,34
3,03
%
ppm


ppm
191,090
168,963
145,311
140,802
137,673
131,854
77,414
77,160
76,906
31,623
29,099
28,454
26,098
25,943
24,060
22,636
21,998
21,699
20,547
14,174
O
O
O
1
2
1'
2'
1"
2"
3"
4"
5"
6"
3
4
5
6
7
8
9
(10c)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

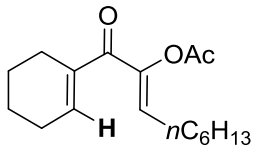
(10c)



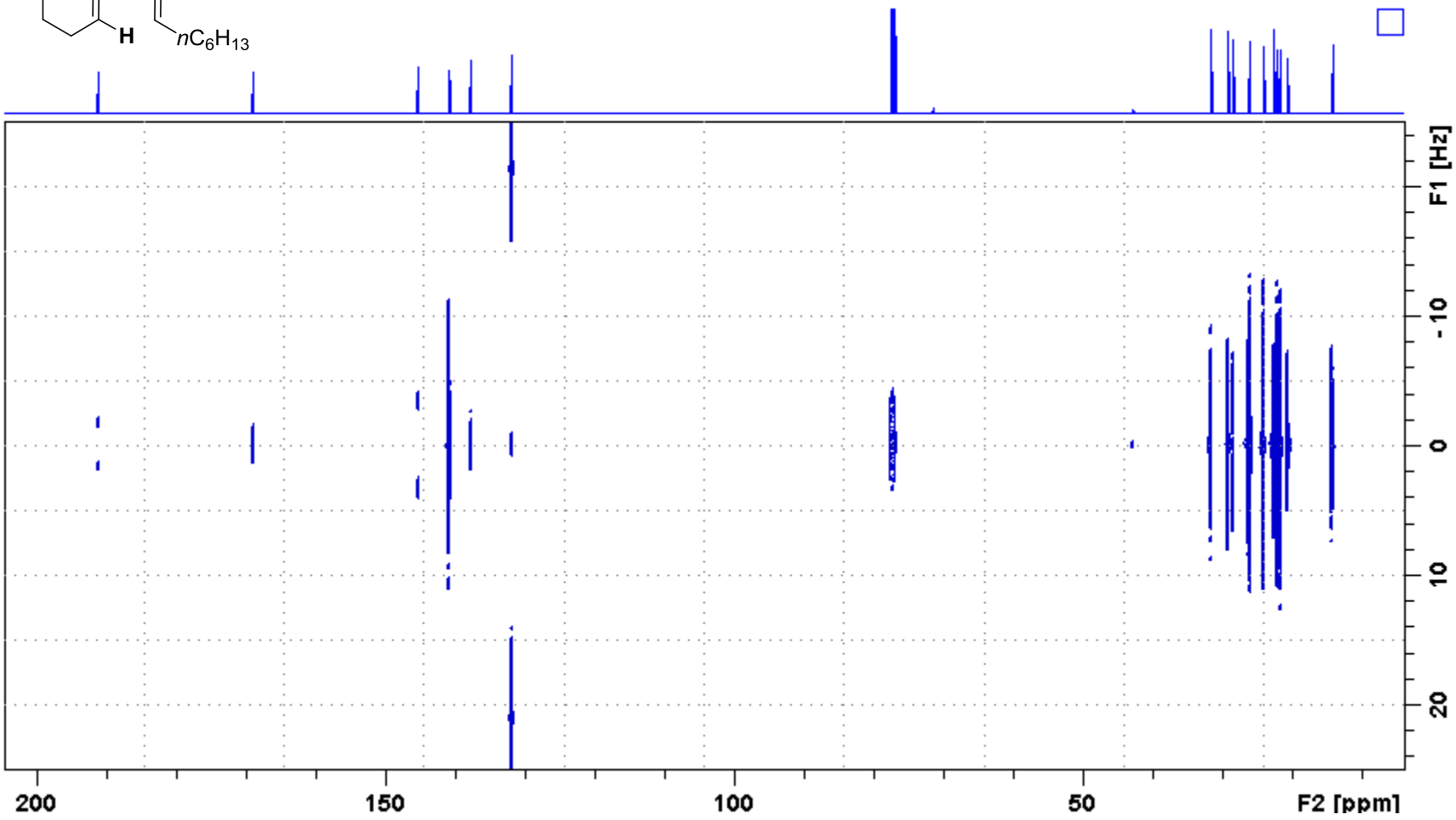
Selelected hydrogen:
C**H**$(CH_2)_5CH_3$ 6.05 ppm

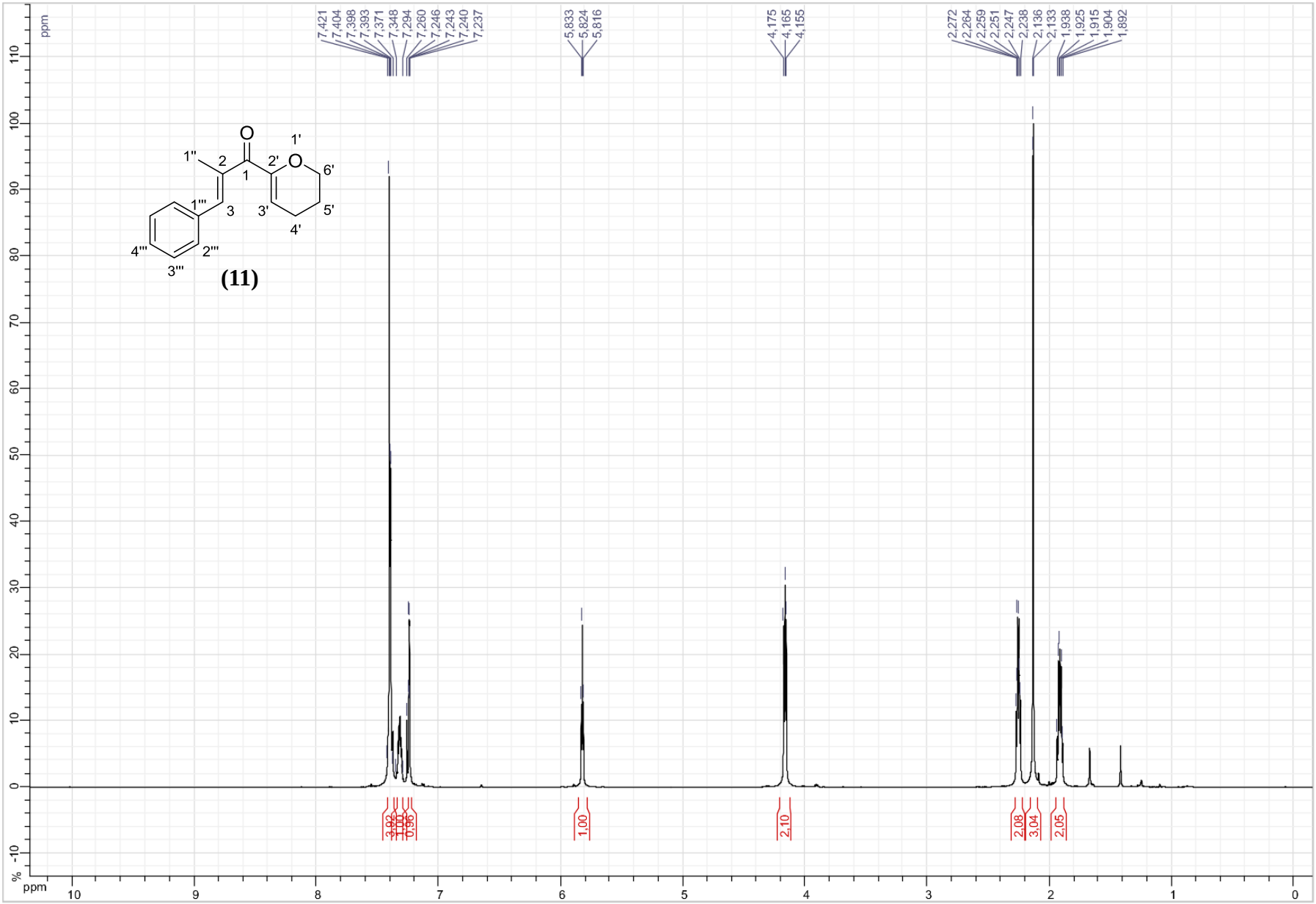


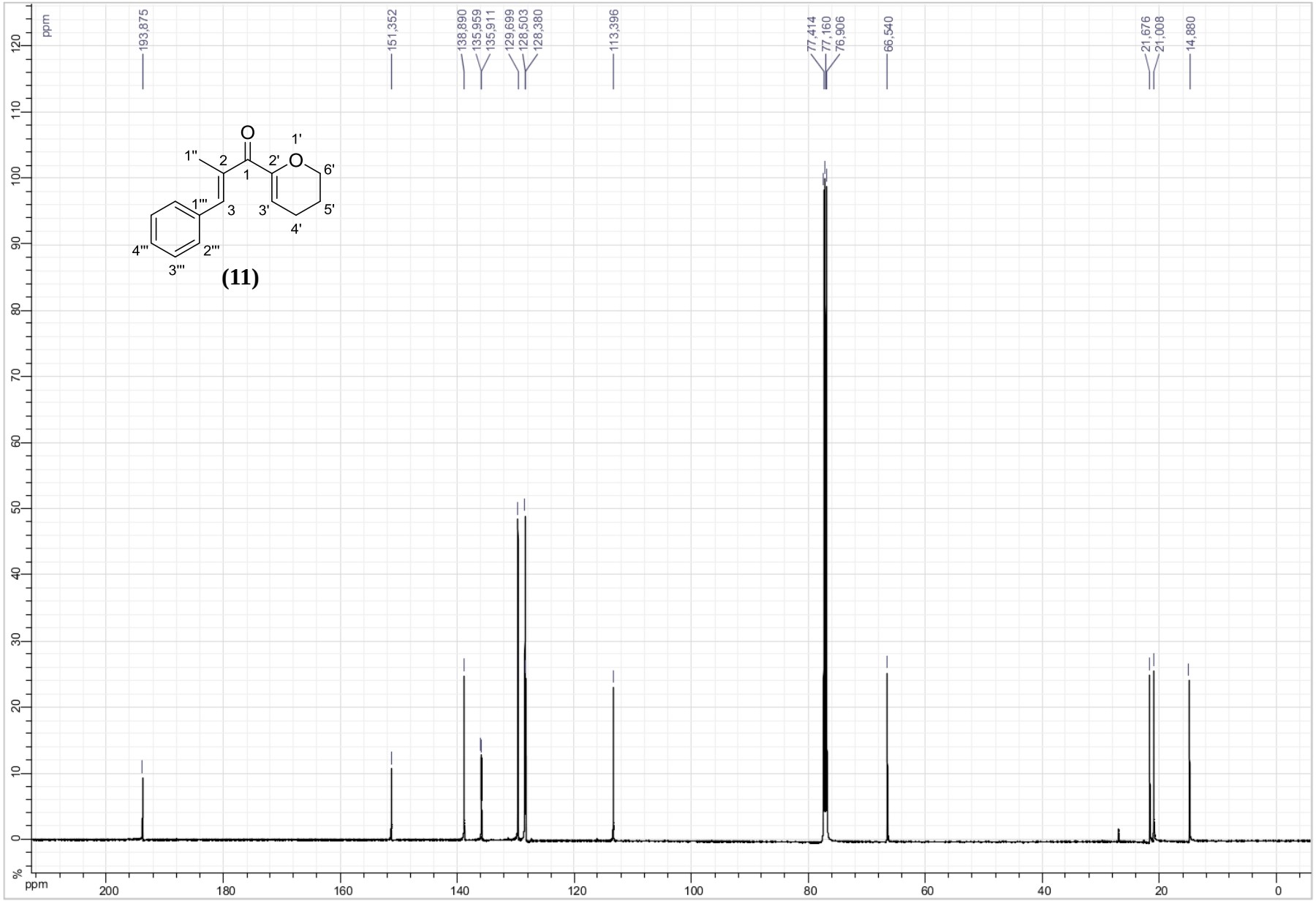
(10c)



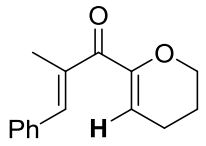
Selelected hydrogen:
C**H**$(CH_2)_4$CC(O) 6.69–6.73 ppm



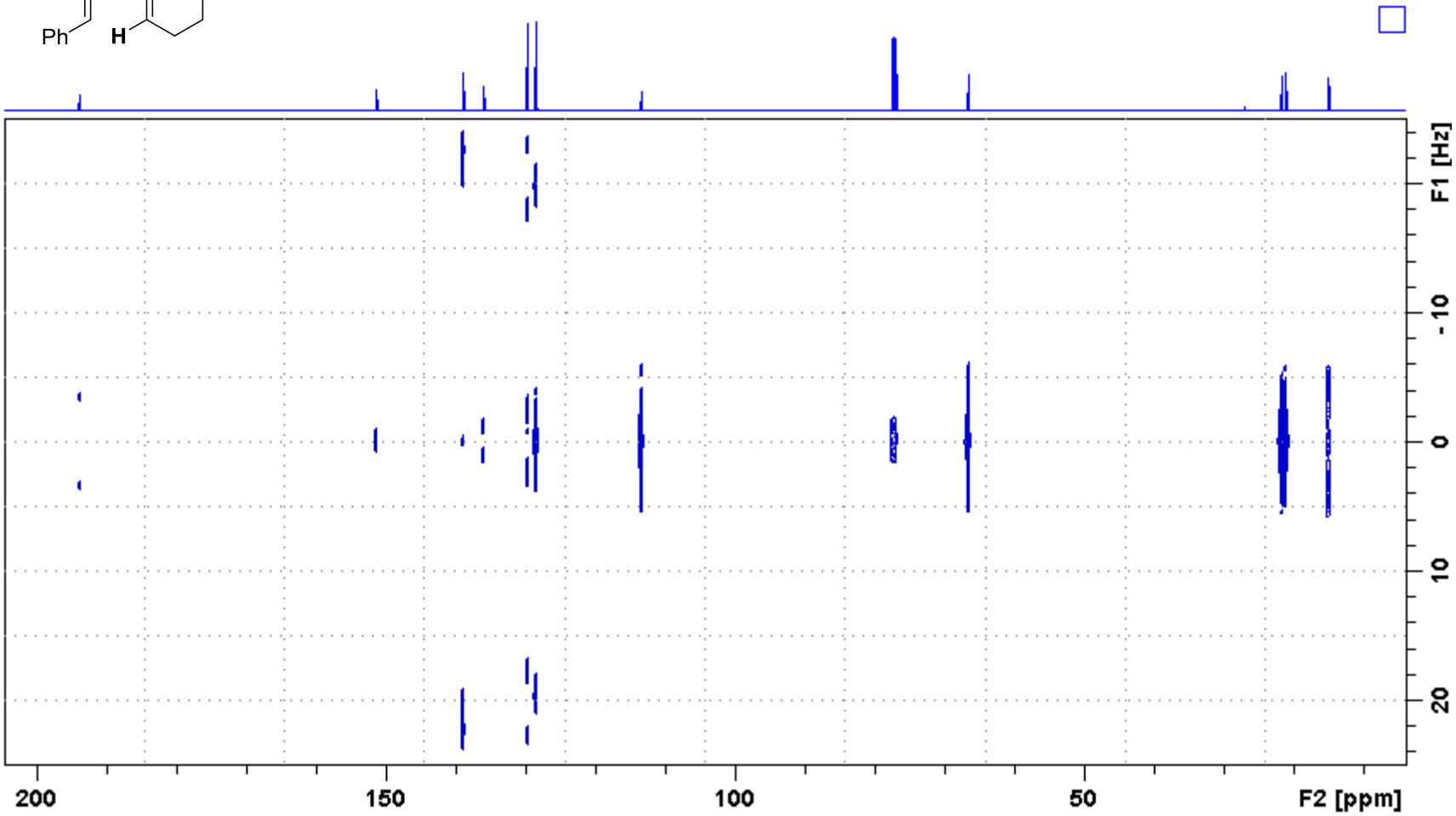

7,421
7,404
7,398
7,393
7,371
7,348
7,294
7,260
7,246
7,243
7,240
7,237
5,833
5,824
5,816
4,175
4,165
4,155
2,272
2,264
2,259
2,251
2,247
2,238
2,136
2,133
1,938
1,925
1,915
1,904
1,892
3,06
1,00
0,96
1,00
2,10
2,08
3,04
2,05
ppm
(11)


ppm
193,875
151,352
138,890
135,959
135,911
129,699
128,503
128,380
113,396
77,414
77,160
76,906
66,540
21,676
21,008
14,880
O
1'
1''
2
2'
O
6'
1
1'''
3
3'
5'
4'
4'''
2'''
3'''
(11)
%
ppm
200
180
160
140
120
100
80
60
40
20
0

(11)

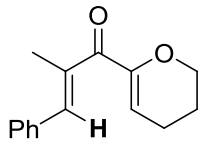


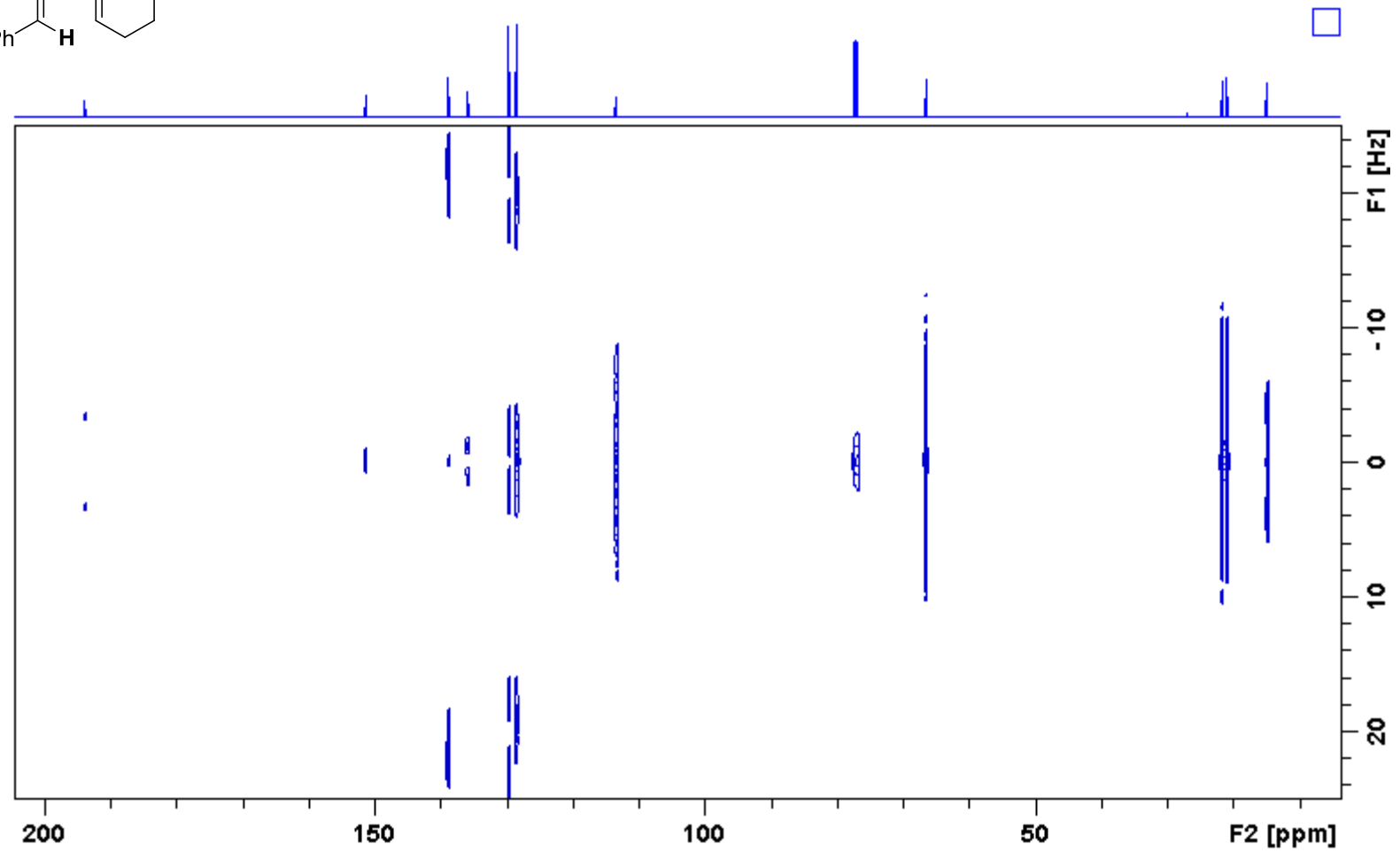
Selelected hydrogen:
C**H**CO 5.82 ppm

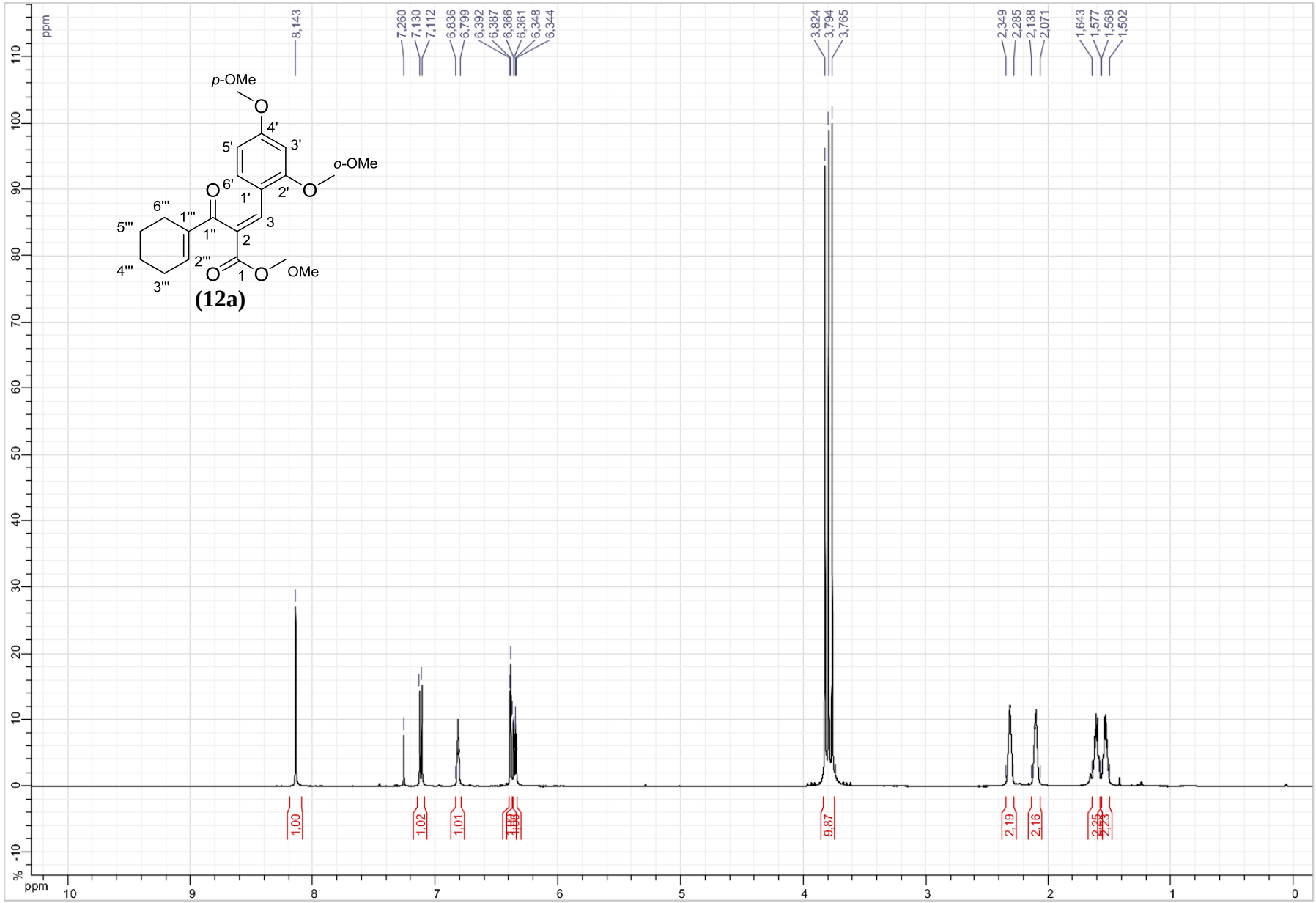


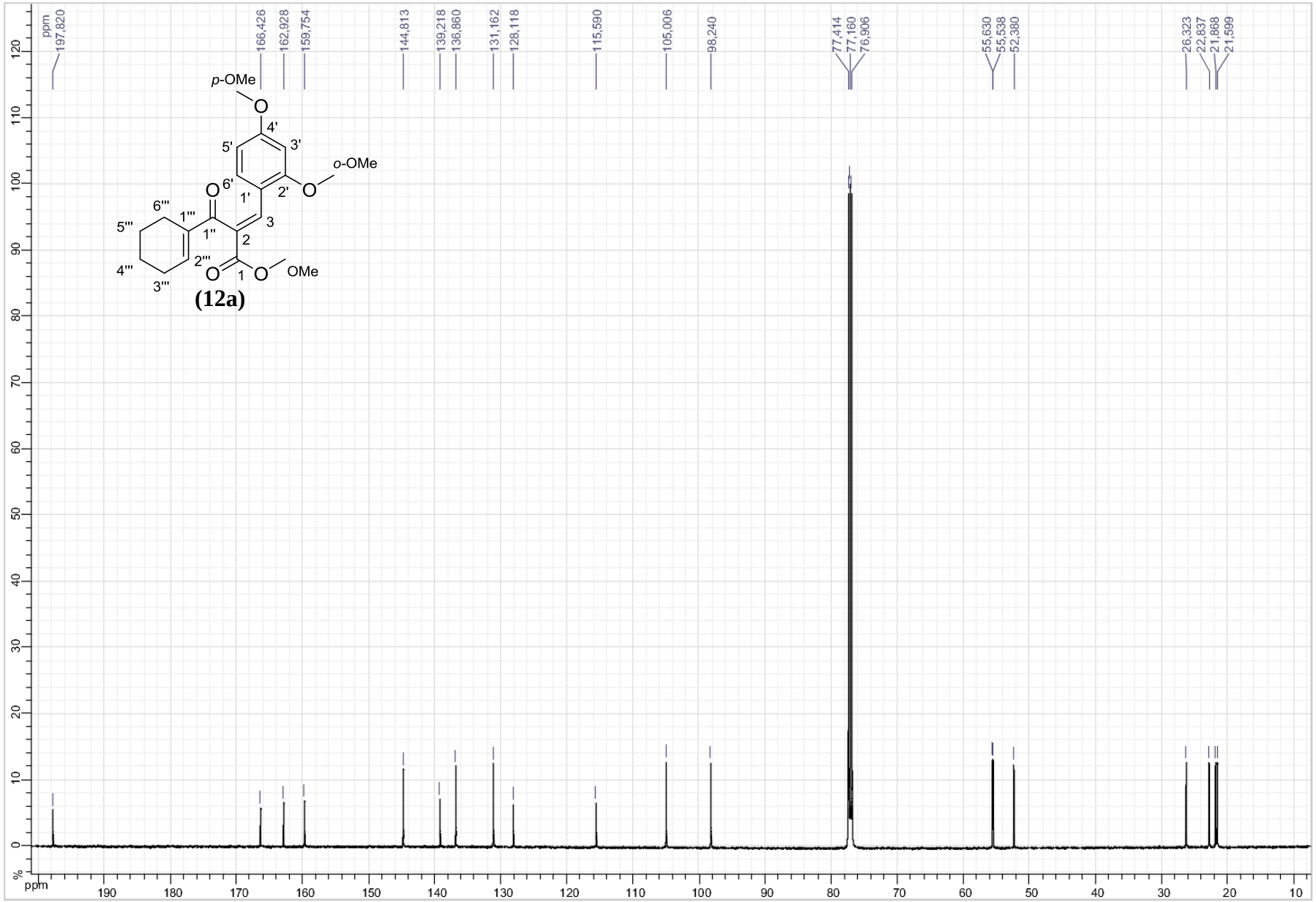
(11)

Selelected hydrogen:
C**H**Ph 7.24 ppm

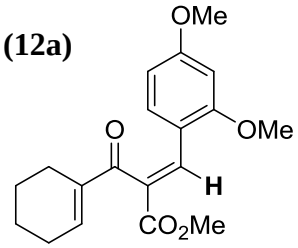




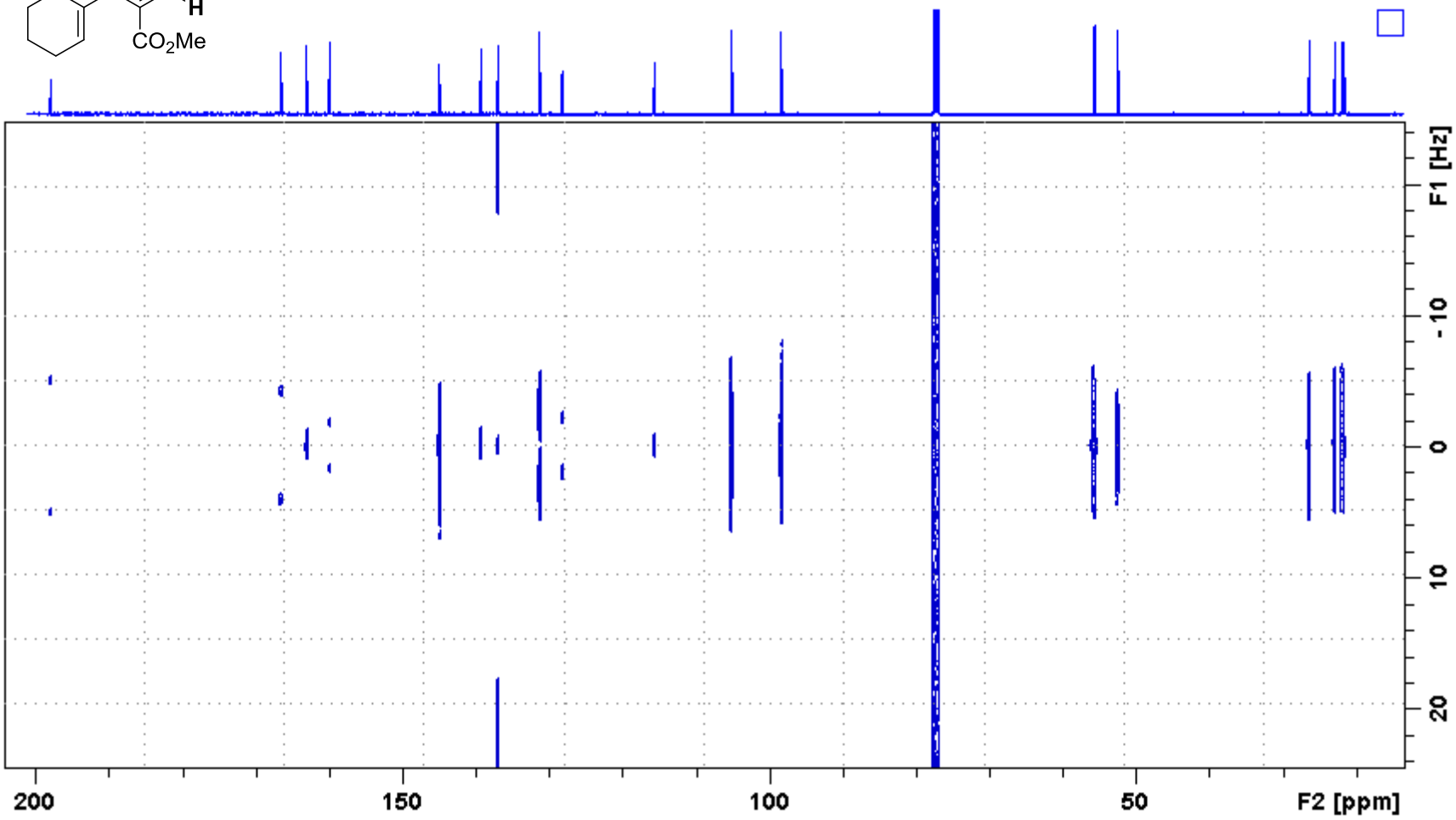

p-OMe
o-OMe
OMe
(12a)
8,143
7,260
7,130
7,112
6,836
6,799
6,392
6,387
6,366
6,361
6,348
6,344
3,824
3,794
3,765
2,349
2,285
2,138
2,071
1,643
1,577
1,568
1,502
1,00
1,02
1,01
9,87
2,19
2,16
ppm


ppm
197,820
166,426
162,928
159,754
144,813
139,218
136,860
131,162
128,118
115,590
105,006
98,240
77,414
77,160
76,906
55,630
55,538
52,380
26,323
22,837
21,868
21,599
p-OMe
o-OMe
OMe
(12a)

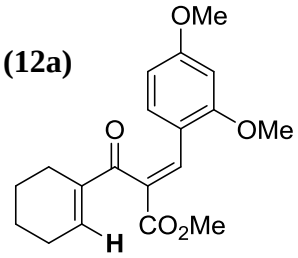
(12a)



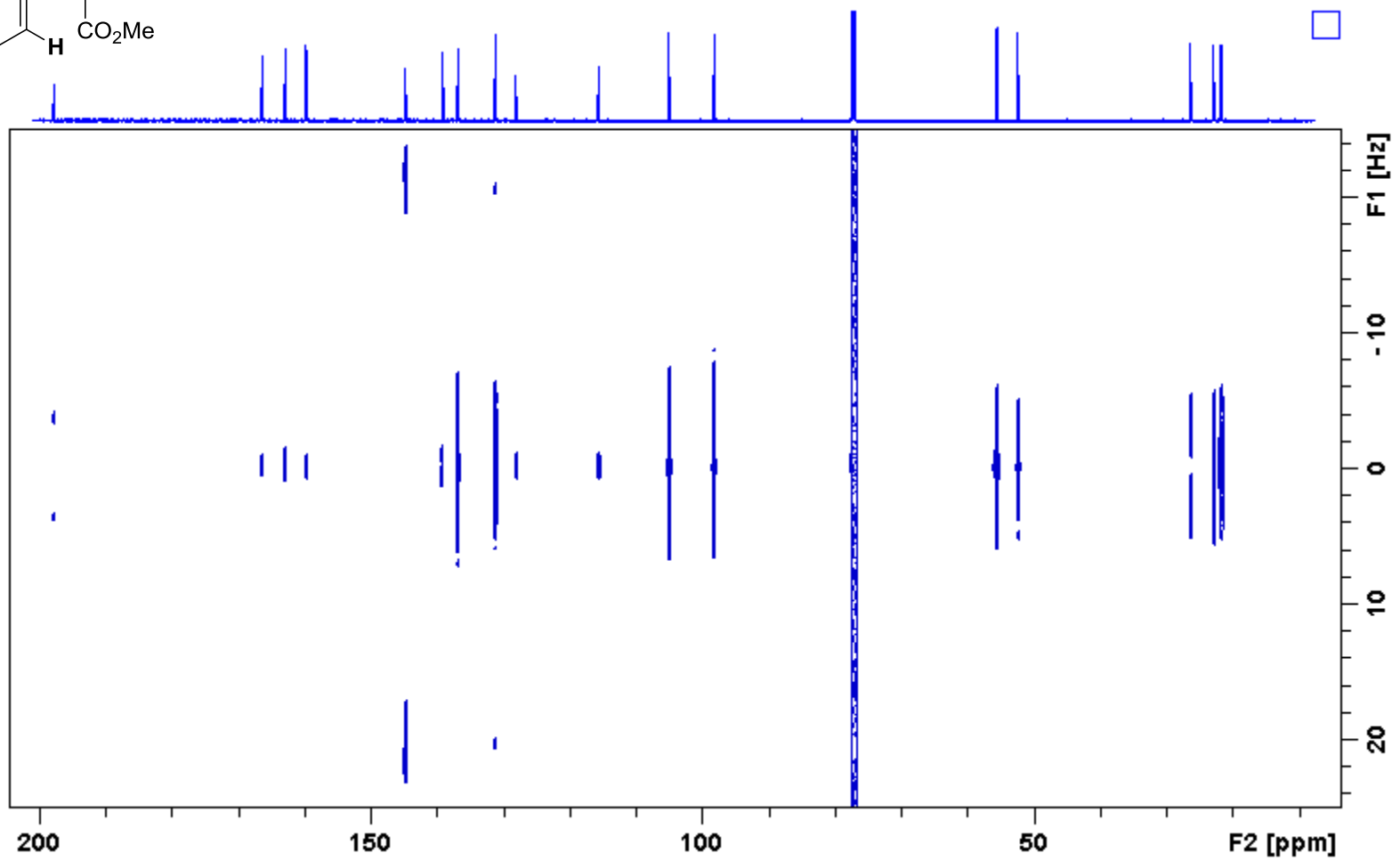
Selelected hydrogen:
C**H**Ar 8.14 ppm

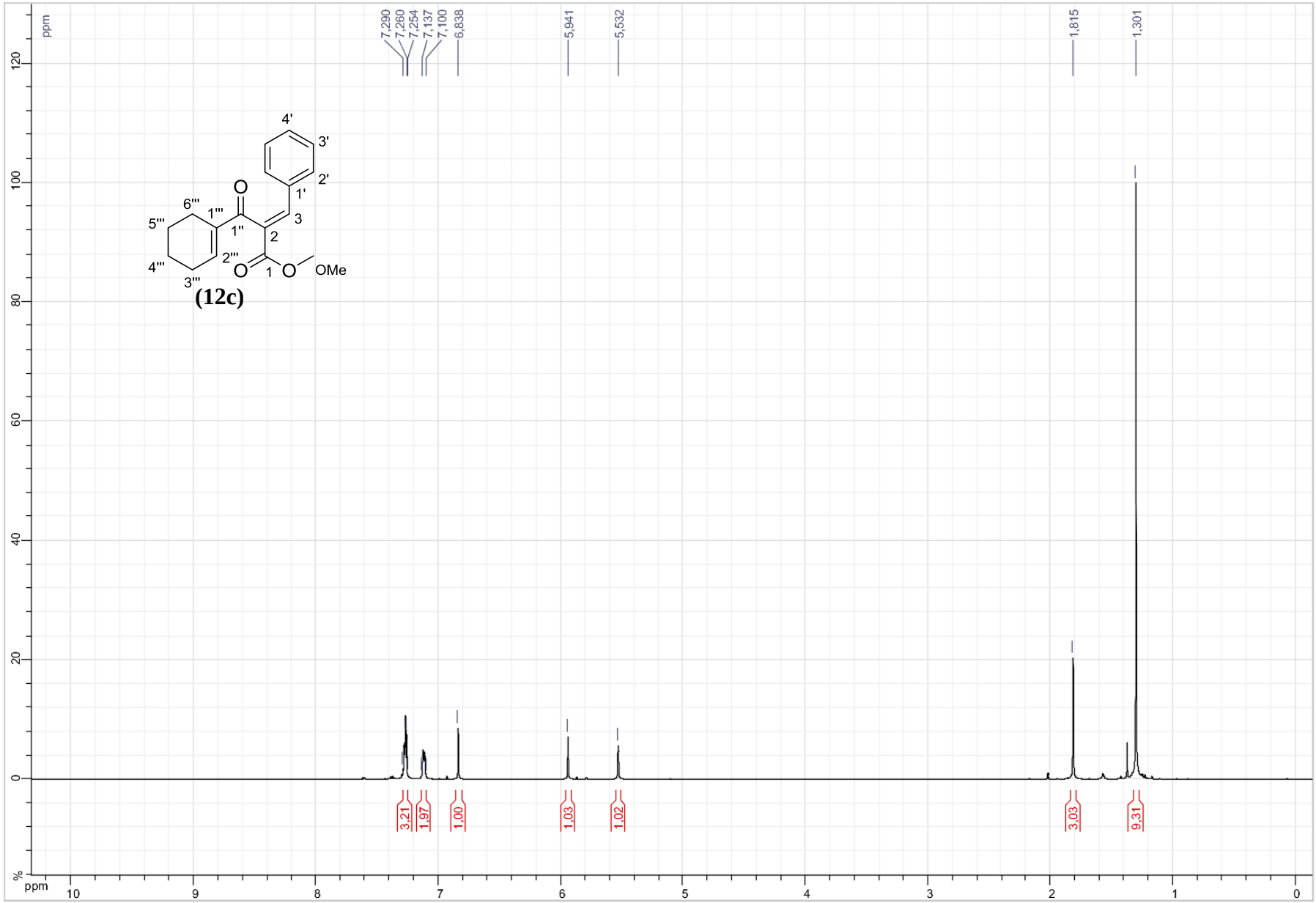


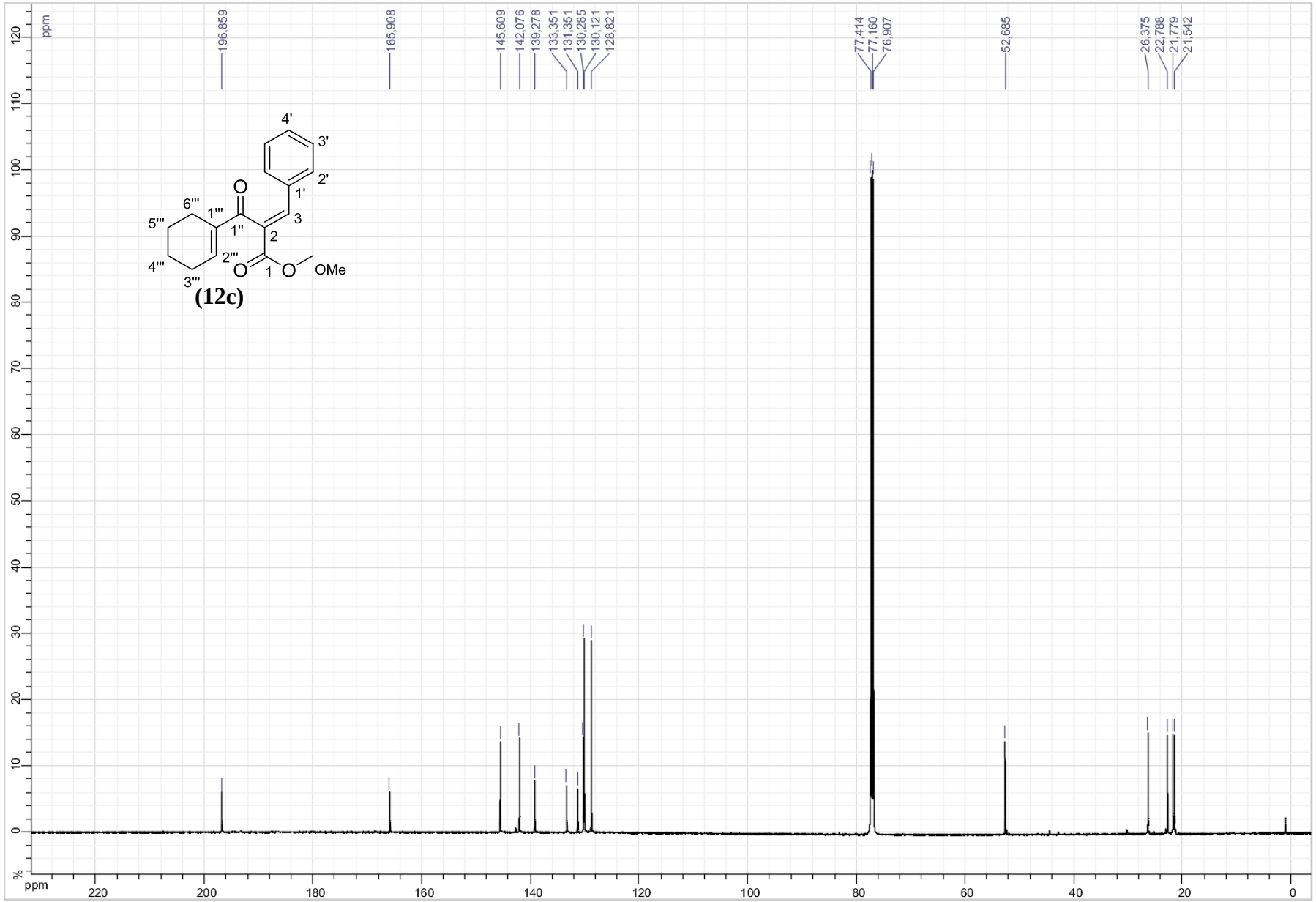
(12a)



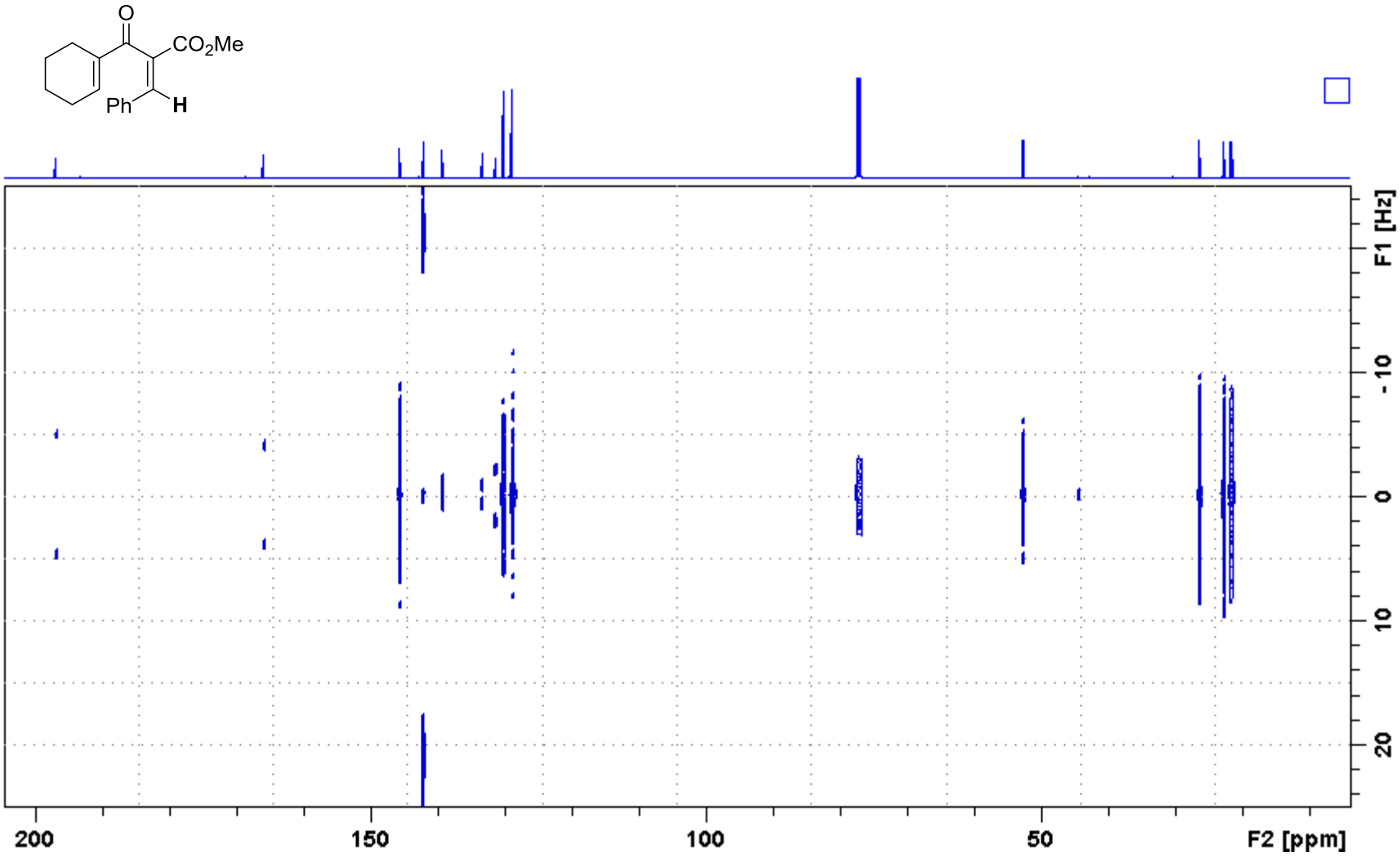
Selelected hydrogen:
C**H**$(CH_2)_4$ 6.80–6.84 ppm

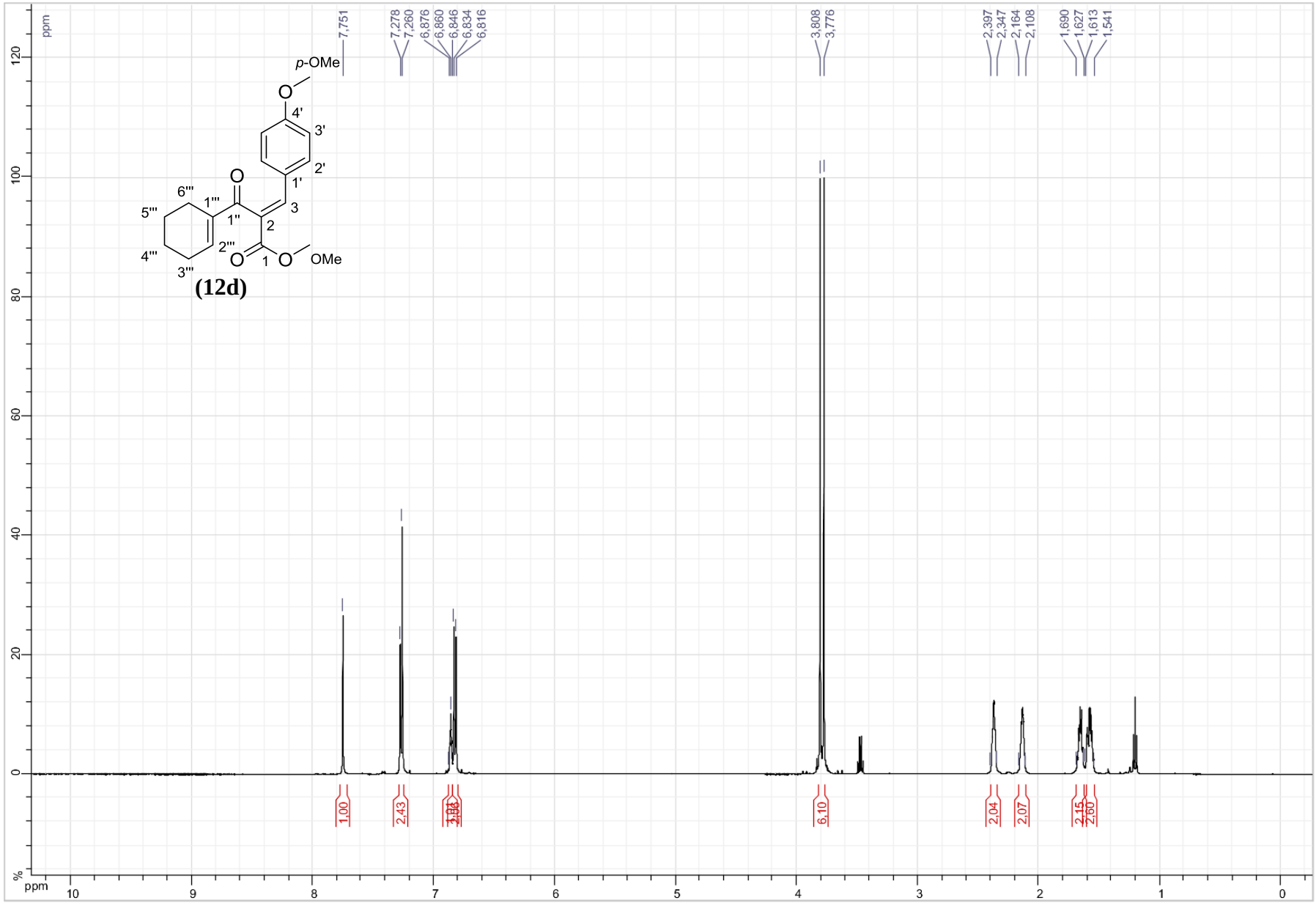


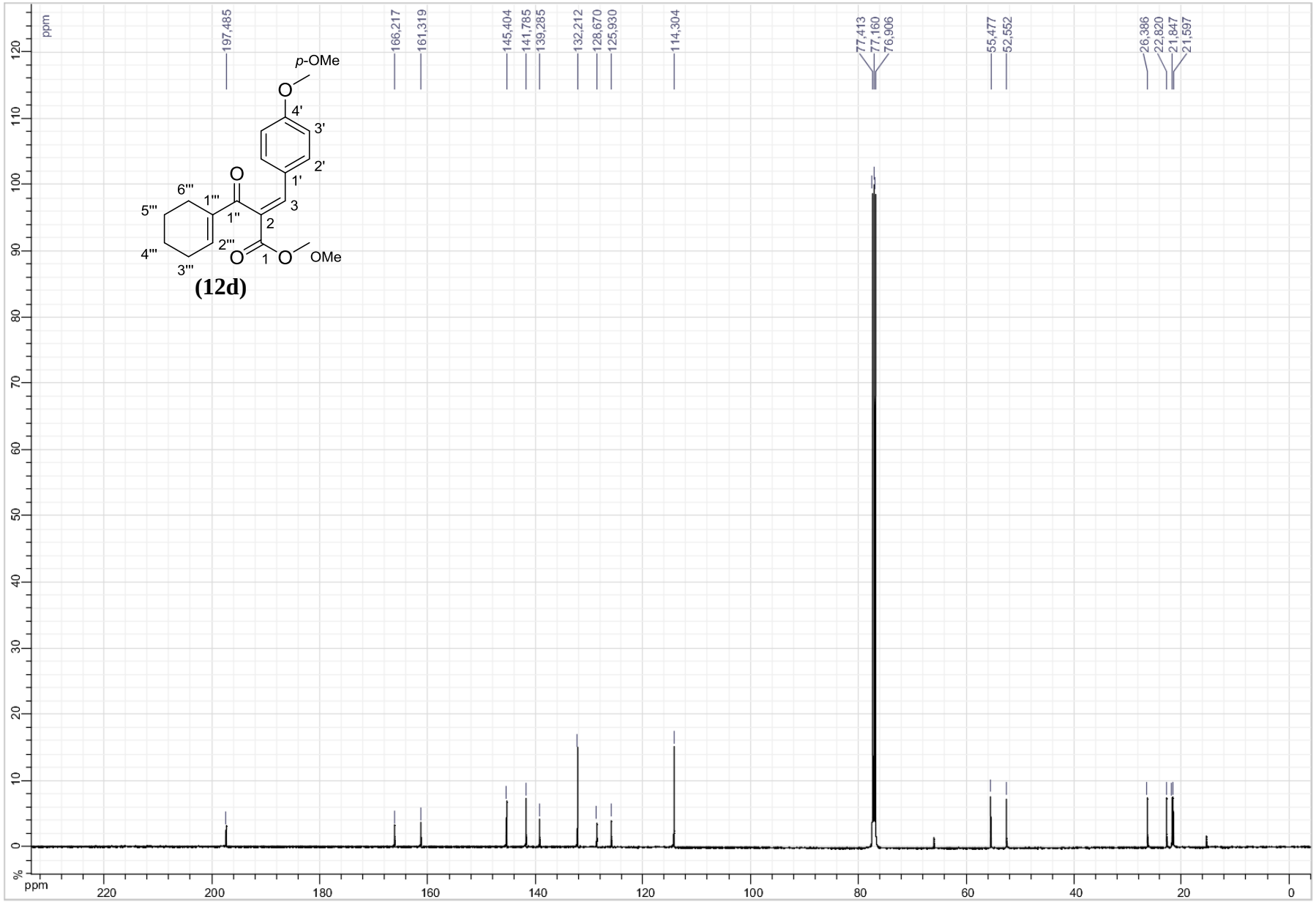

ppm
7,290
7,260
7,254
7,137
7,100
6,838
5,941
5,532
1,815
1,301
4'
3'
2'
1'
3
2
1
O
6'''
1'''
5'''
1''
2'''
4'''
3'''
O
1
O
OMe
(12c)
3,21
1,97
1,00
1,03
1,02
3,03
9,31
%
ppm


ppm
196,859
165,908
145,609
142,076
139,278
133,351
131,351
130,285
130,121
128,821
77,414
77,160
76,907
52,685
26,375
22,788
21,779
21,542
4'
3'
2'
1'
3
2
1
O
1"
1'''
2'''
3'''
4'''
5'''
6'''
OMe
(12c)
%
ppm
220
200
180
160
140
120
100
80
60
40
20
0

(12c)




ppm
7,751
7,278
7,260
6,876
6,860
6,846
6,834
6,816
3,808
3,776
2,397
2,347
2,164
2,108
1,690
1,627
1,613
1,541
p-OMe
4'
3'
2'
1'
3
2
1
1''
2''
3''
4''
5''
6''
1'''
2'''
3'''
4'''
5'''
6'''
OMe
(12d)
1,00
2,43
6,10
2,04
2,07
2,15
2,60


ppm
197,485
166,217
161,319
145,404
141,785
139,285
132,212
128,670
125,930
114,304
77,413
77,160
76,906
55,477
52,552
26,386
22,820
21,847
21,597
p-OMe
O
4'
3'
2'
1'
3
2
1
O
OMe
6'''
1'''
5'''
1''
2'''
4'''
3'''
(12d)
%
ppm
220
200
180
160
140
120
100
80
60
40
20
0

(12d)