Hydrogenation in Flow: Homogeneous and Heterogeneous Catalysis Using Teflon AF-2400 to Effect Gas-Liquid Contact at Elevated Pressure.

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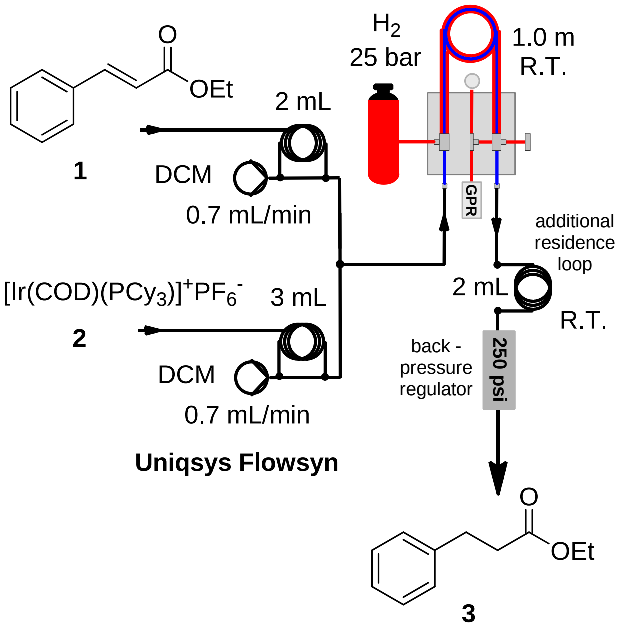
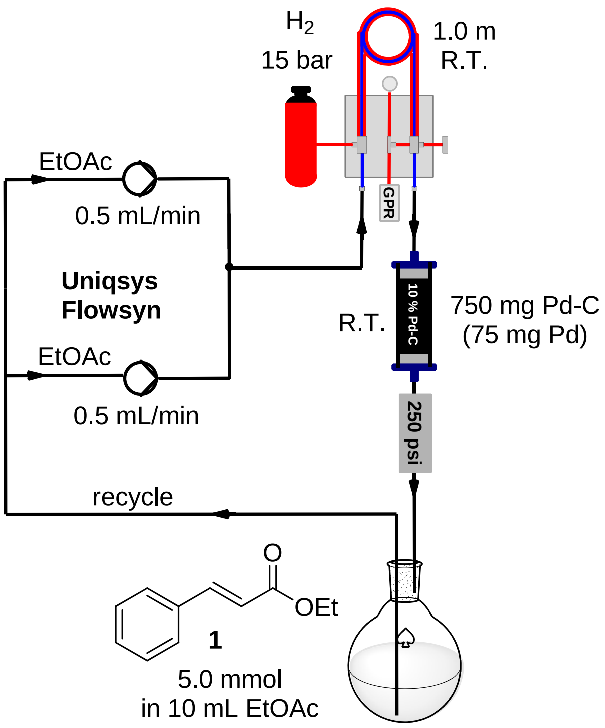
Supporting Information

Homogeneous Hydrogenation – Representative Preparative Procedure for Table 1:



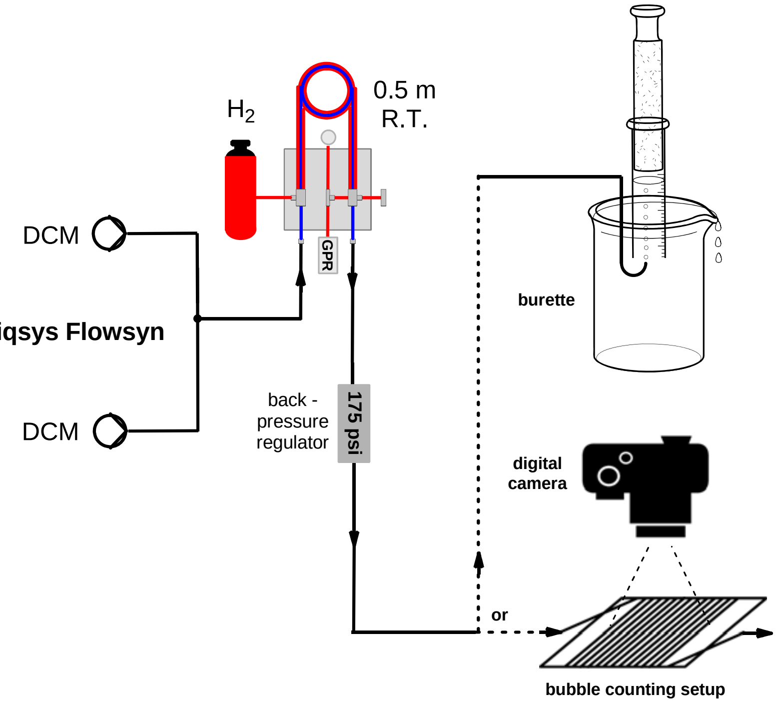
Dichloromethane (freshly distilled from calcium hydride under nitrogen, then deoxygenated by sparging for 1 hour with argon) was set pumping through both pumps of a Uniqsys Flowsyn apparatus (2 × 0.7 mL/min) and onto the reactor as shown above. A pressure of 25 bar of hydrogen was applied to the reactor. The substrate injection loop (2.0 mL, PEEK) was loaded with a solution of substrate **1** (2.0 mL of a 0.5 M solution in DCM, 1.0 mmol). The catalyst injection loop (3.0 mL, PTFE) was loaded with a solution of the catalyst **2** (3.0 mL of a 0.001 M solution in DCM, 0.003 mmol). The catalyst solution was injected into the flow stream. 15 seconds later the substrate solution was injected into the flow stream. The solution was collected from the outlet for 20 minutes. The solvent was removed by evaporation under reduced pressure to afford the product **3** as a clear pale-yellow oil (179 mg, 100%). The spectroscopic data (see spectra in accompanying document) were in agreement with those reported in the literature for this compound (references compiled at bottom of this document).

Heterogeneous Hydrogenation – Representative Preparative Procedure for Table 2:



5 mL of ethyl acetate (used as purchased from Fisher Scientific) was pumped from a 10 mL round bottomed flask through both pumps of a Uniqsis Flowsyn apparatus at a rate of 2 × 0.5 mL/min (1.0 mL min combined flow rate) into the reactor/injector and through the cartridge of Pd-C catalyst (10 % Pd-C, 750 mg) as shown in the above diagram. The pump inlets were placed in the same round bottomed flask so that the same solvent was recycled through the system. A pressure of 15 bar of hydrogen was applied to the reactor. A solution of the substrate **1** in ethyl acetate (5 mL, 1.0 M, 5 mmol) was then added to the round bottomed flask. Outgassing of hydrogen downstream of the back-pressure regulator stopped after 10 minutes. Outgassing returned after 2 hours. After an additional 30 minutes, the pump inlet lines were placed in a reservoir of fresh ethyl acetate and solution was collected from the outlet for 20 minutes. The collected product solutions were combined and solvent was removed by evaporation at reduced pressure to afford the product **3** as a clear, colourless oil (891 mg, 100%). The spectroscopic data for this compound (see spectra in accompanying document) were in agreement with those reported in the literature (references compiled at bottom of this document).

Apparatus for measurement of outgassing



DCM was pumped into the reactor/injector using both pumps (equal flow rate for each one) of a Uniqsis Flowsyn device. The outlet of the reactor/injector was passed through a back pressure regulator (100 or 175 psi) before passing either to a burette or the bubble-counting apparatus. The burette was constructed from a syringe so that it could easily be refilled by simply pushing the plunger in and out and was held firmly in place. The inflowing DCM was able to run out of the beaker via the spout and was thus always at the same level. The burette reading was always taken with the liquids on the inside and outside at the same height. Volumes measured were 1.5 mL or 2.0 mL.

The bubble counting apparatus was constructed by wrapping PFA tubing (1.54 metres) around a rectangular support and gluing it in place. A small quantity of sudan red 7B was added (1.0 mM conc.) to the DCM for the bubble-counting experiments. The camera was a Canon EOS 350D 8 megapixel digital SLR. Both the camera and the wrapped tubing device were held very firmly in place during the course of the bubble counting measurements. Prior to taking each photograph, the pumps were stopped and the liquid/gas in the wrapped tubing was allowed to reach standstill in order to allow any residual internal pressure to relax, this took about six seconds. Any liquid/gas in the system was allowed to clear the entire system before taking the next photograph. The Python script used to process the images is given below. The script was run on a PC in Python 2.6, Windows 7 operating system.

Python Script for Processing of Digital Bubble Counting Images

```
# this program applies a red pixel count for each .jpg file in
# a folder. it creates a report txt file and appends the pixel count
# for each file to it as well as the average and standard deviation
# also writes a new bmp file of pure red or white pixels for checking
# requires python image library http://www.pythonware.com/products/pil/
# images were first resaved as jpegs using renaming program
# camera used was a canon eos-350-D 8 megapixel digital SLR


import os
from PIL import Image

def redpix(filename, foldername):
   realname = foldername + '\\' + filename
   im = Image.open(realname)
   l = im.getdata()

   newdata = []

   reds = 0
   for pixel in l:
       r,g,b = pixel
       rf = float(r)
       gf = float(g)
       bf = float(b)
       rf +=1
       gf +=1
       bf +=1
       if rf/gf>3.5 and rf/bf>3.5:
           reds = reds+1
           newdata.append((255,0,0))
       else:
           newdata.append((255,255,255))
   im.putdata(newdata)
   spli = os.path.splitext(realname)
   im.save(spli[0] +'conv' + '.bmp', 'BMP')

   return reds

def SD(vals):
    fvals = [float(x) for x in vals]
    s = 0
    for i in fvals:
        s += i
    l = len(fvals)
    mean = s/l
    sqdiffs = []
    for i in fvals:
        sqdiff = (i-mean)**2
        sqdiffs.append(sqdiff)
    sumsqdiffs = 0
    for i in sqdiffs:
        sumsqdiffs += i
    sd = (sumsqdiffs/l)**0.5

    return sd


folder = r'C:\Users\m\Documents\computing\pythonstuff\gasflow\xxx'

# this is the path of the folder containing the digital images

reportname = folder + '\\' + 'report.txt'
fi = open(reportname, 'a')
```

```
values = []

for f in os.listdir(folder):
   if f.endswith('jpg'):
       print f
       a =  redpix (f, folder)
       print a
       values.append(a)
       fi.write('\n' + str(f) + '\n' + str(a))

   else:
       pass

print values
sum = sum(values)
fsum = float(sum)
ave = fsum/len(values)
print ave
m = SD(values)
print 'sd = ' + str(m)

fi.write('\n' + 'average = ' + str(ave) + '\n' + 'sd = ' + str(m))

fi.close()
```

Renaming script (run first on each folder of images prior to running pixel counter):

```
#converts each image in folder to jpeg
#jpegs straight from canon camera did not load into processing script
#adds '_J' and '.jpg' to filename

import os
from PIL import Image

def rename(filename, folder):
    realname = folder + '\\' + filename
    im = Image.open(realname)
    spli = os.path.splitext(realname)
    im.save(spli[0] + '_J' +'.jpg')

folder = r'C:\Users\m\Documents\computing\pythonstuff\gasflow\xxx'

# this is the path for the folder to be processed

for f in os.listdir(folder):
    rename(f, folder)
```

Photographs of Apparatus

Figure S1. Bubble Counting Camera Setup

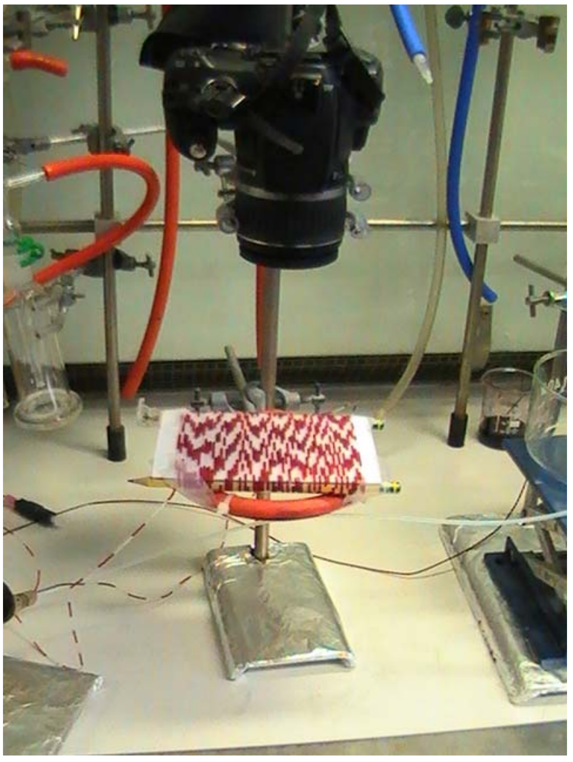
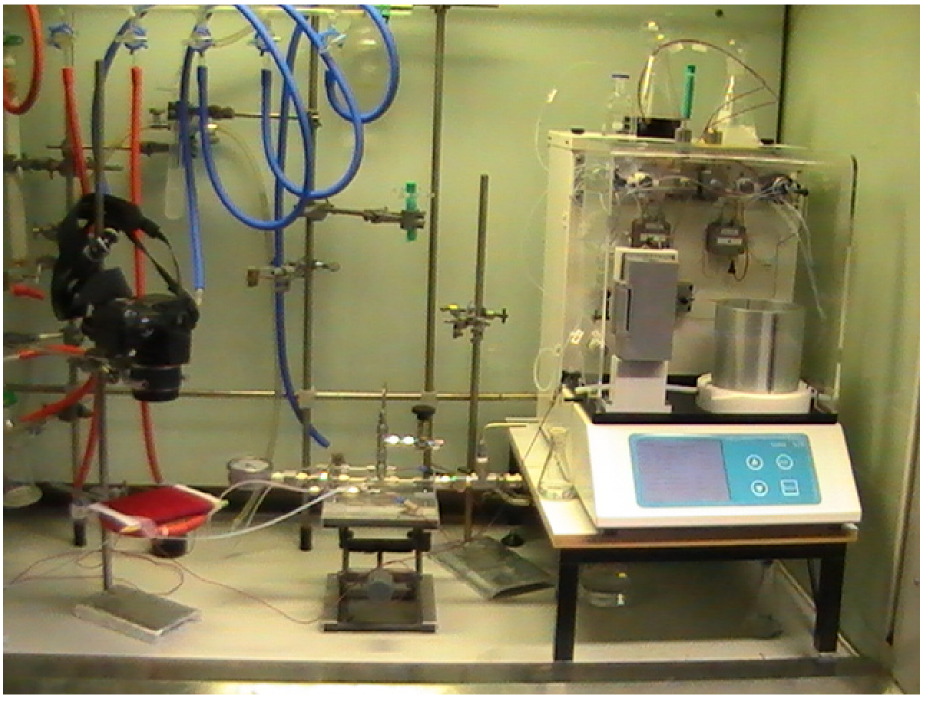


Figure S2. Bubble counting apparatus, Gas reactor and Uniqsis Flowsyn (left to right)



Literature references for spectroscopic data of products:

Compound 3: M. Amatore, C. Gosmini and J. Périchon, *J. Org. Chem.*, 2006, **71**, 6130-6134.

Compound 5: J. A. Murphy, F. Schoenebeck, N. J. Findlay, D. W. Thomson, S.-z. Zhou and J. Garnier, *J. Am. Chem. Soc.*, 2009, **131**, 6475-6479

Compound 7: C. Stueckler, N. J. Mueller, C. K. Winkler, S. M. Glueck, K. Gruber, G. Steinkellner and K. Faber, *Dalton Trans.*, 2010, **39**, 8472-8476

Compound 9: P. J. Black, M. G. Edwards and J. M. J. Williams, *Eur. J. Org. Chem.*, 2006, 4367-4378.

Compound 11: C. Pourbaix, F. Carreaux and B. Carboni, *Org. Lett.*, 2001, **3**, 803-805.

Compound 13: D. J. Fox, D. S. Pedersen and S. Warren, *Org. Biomol. Chem.*, 2006, **4**, 3102-3107.

Compound 15: The Aldrich library of ^{13}C and ^{1}H FT-NMR spectra, edition I, volume II and online at the Sigma-Aldrich catalogue (www.sigmaaldrich.com)

Compound 17: H. C. Maytum, J. Francos, D. J. Whatrup and J. M. J. Williams, *Chem. Asian J.*, 2010, **5**, 538-542.

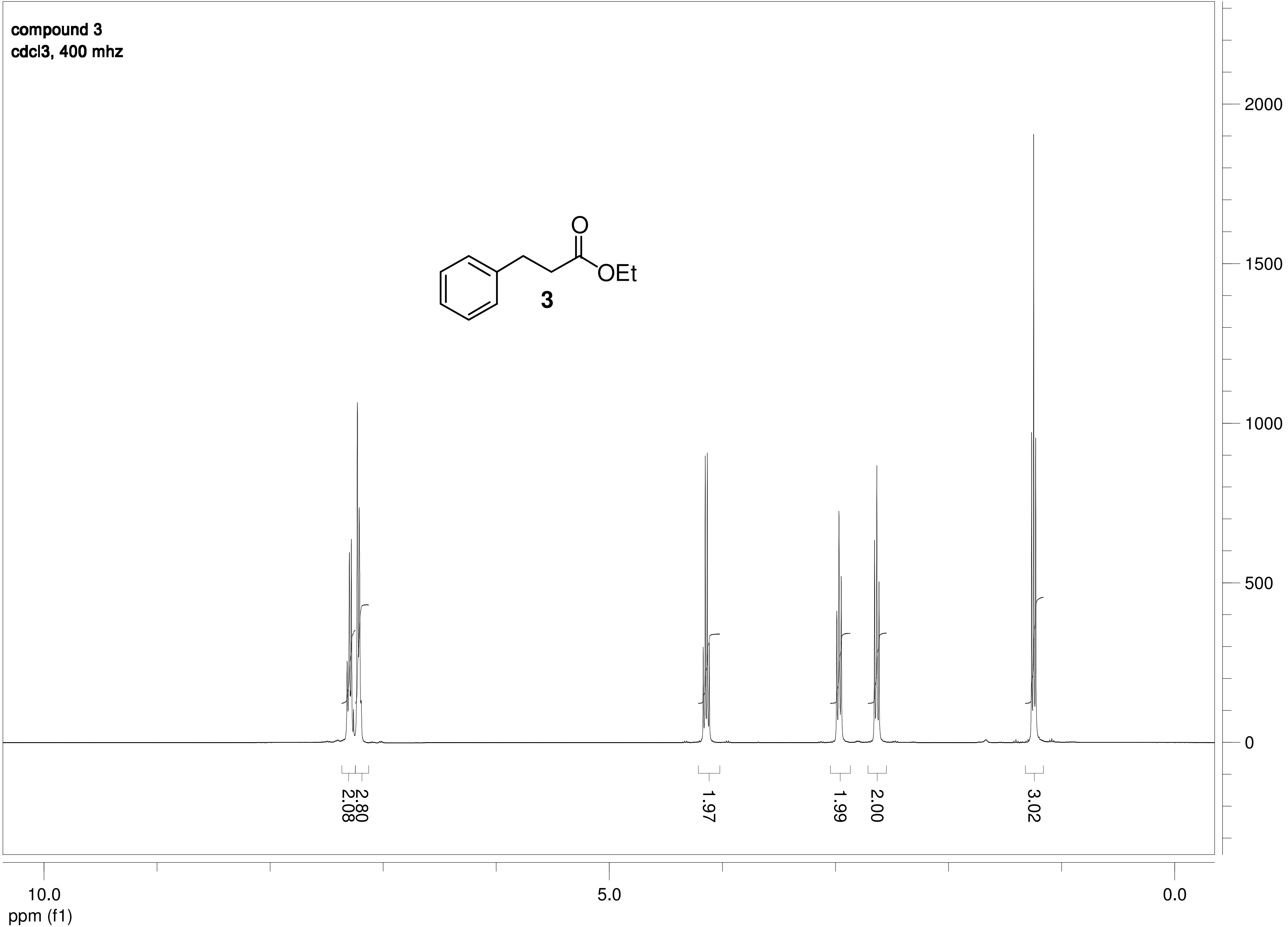
Compound 19: O. Vechorkin and X. Hu, *Angew. Chem. Int. Ed.*, 2009, **48**, 2937-2940.

Compound 21: K. Zeitler and C. A. Rose, *J. Org. Chem.*, 2009, **74**, 1759-1762.

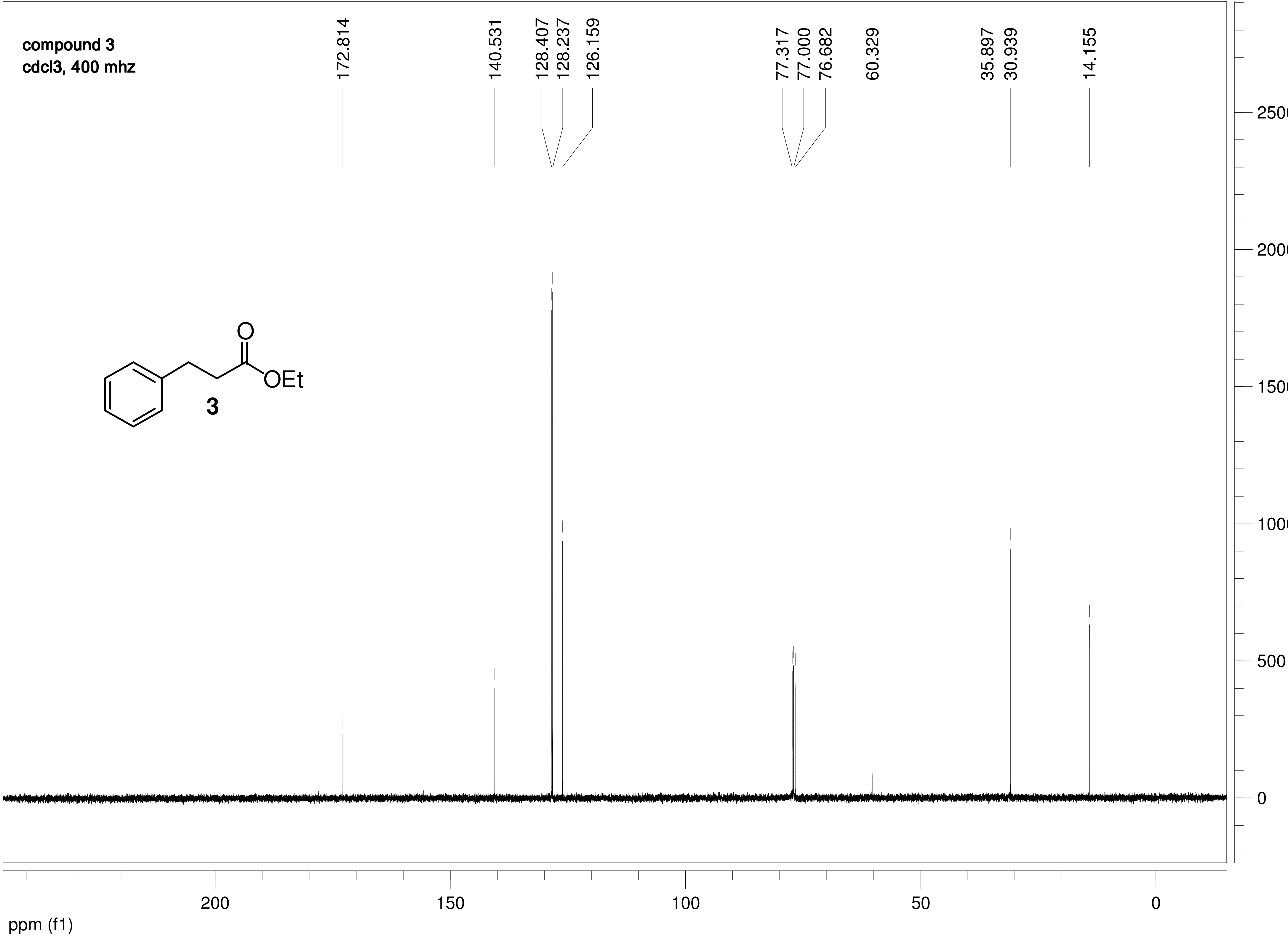
Compound 23: C. Smit, M. W. Fraaije and A. J. Minnaard, *J. Org. Chem.*, 2008, **73**, 9482-9485.

Compound 26: T. O. Vieira, M. J. Green and H. Alper, *Org. Lett.*, 2006, **8**, 6143-6145.

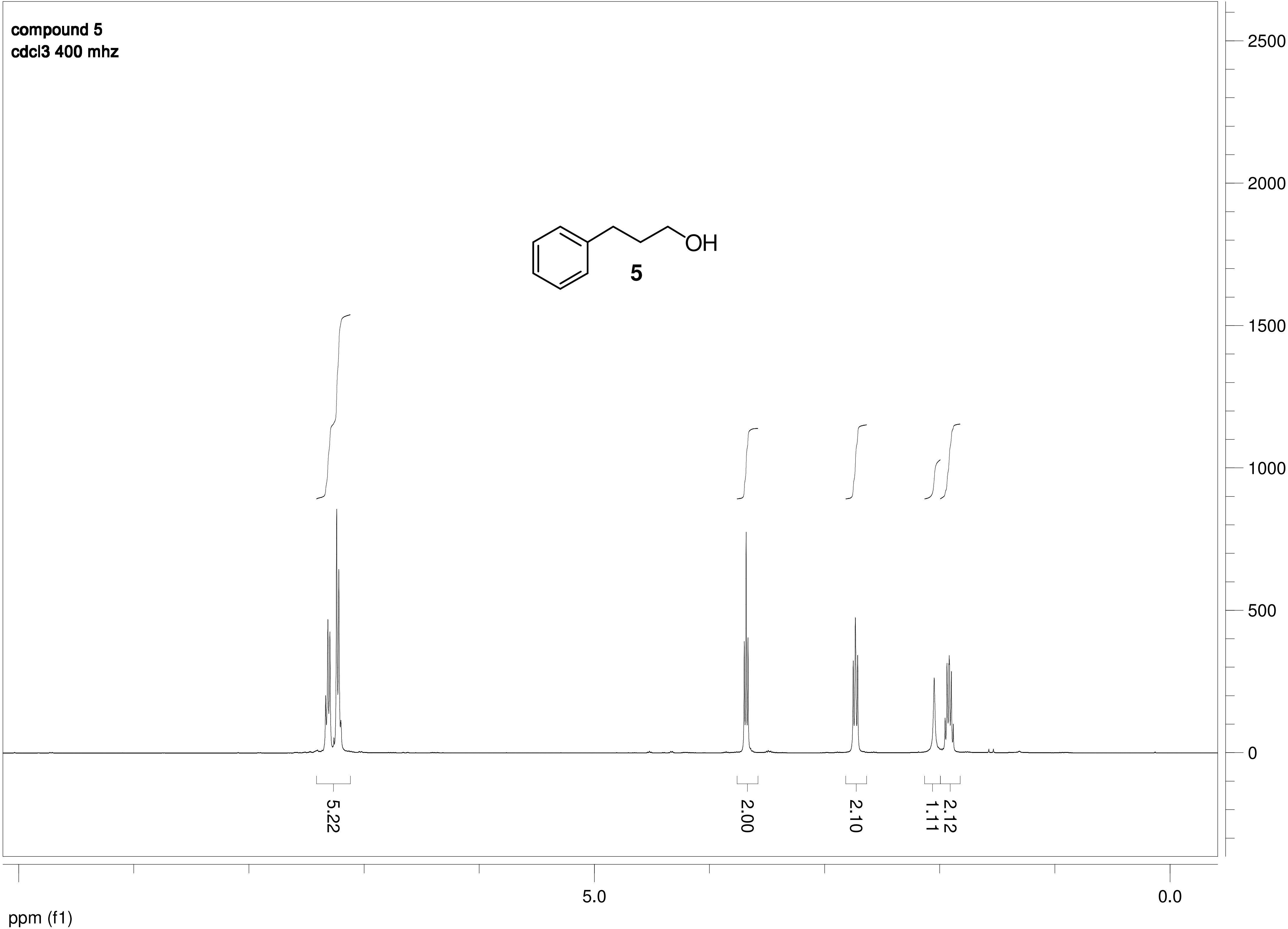
Compound 28: K. Okamoto, R. Akiyama and S. Kobayashi, *J. Org. Chem.*, 2004, **69**, 2871-2873.



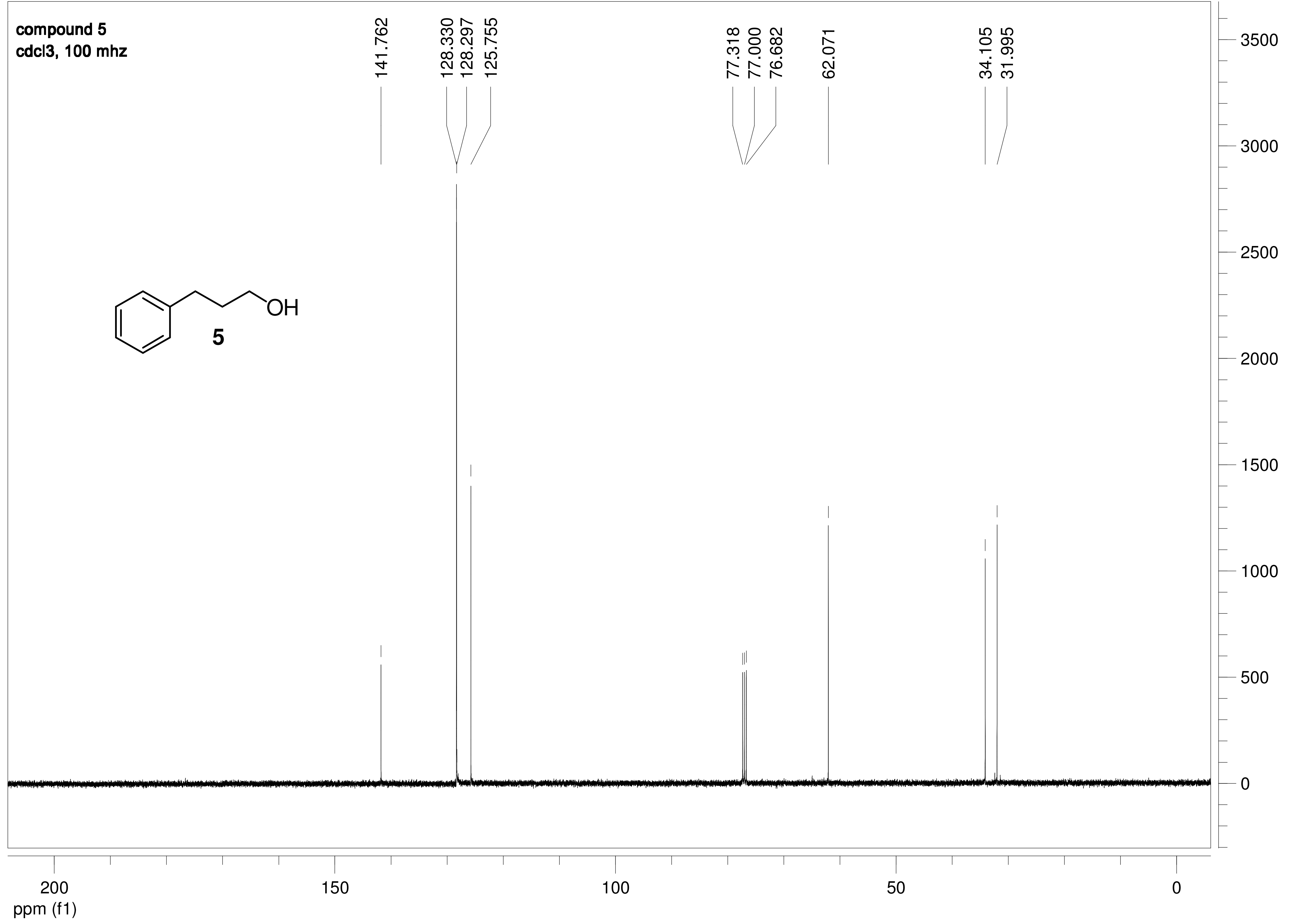
compound 3
cdcl3, 400 mhz
O
OEt
3
2.08
2.80
1.97
1.99
2.00
3.02
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)



compound 3
cdcl3, 400 mhz
172.814
140.531
128.407
128.237
126.159
77.317
77.000
76.682
60.329
35.897
30.939
14.155
O
OEt
3
2500
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)



compound 5
cdcl3 400 mhz
OH
5
2500
2000
1500
1000
500
0
5.22
2.00
2.10
1.11
2.12
5.0
0.0
ppm (f1)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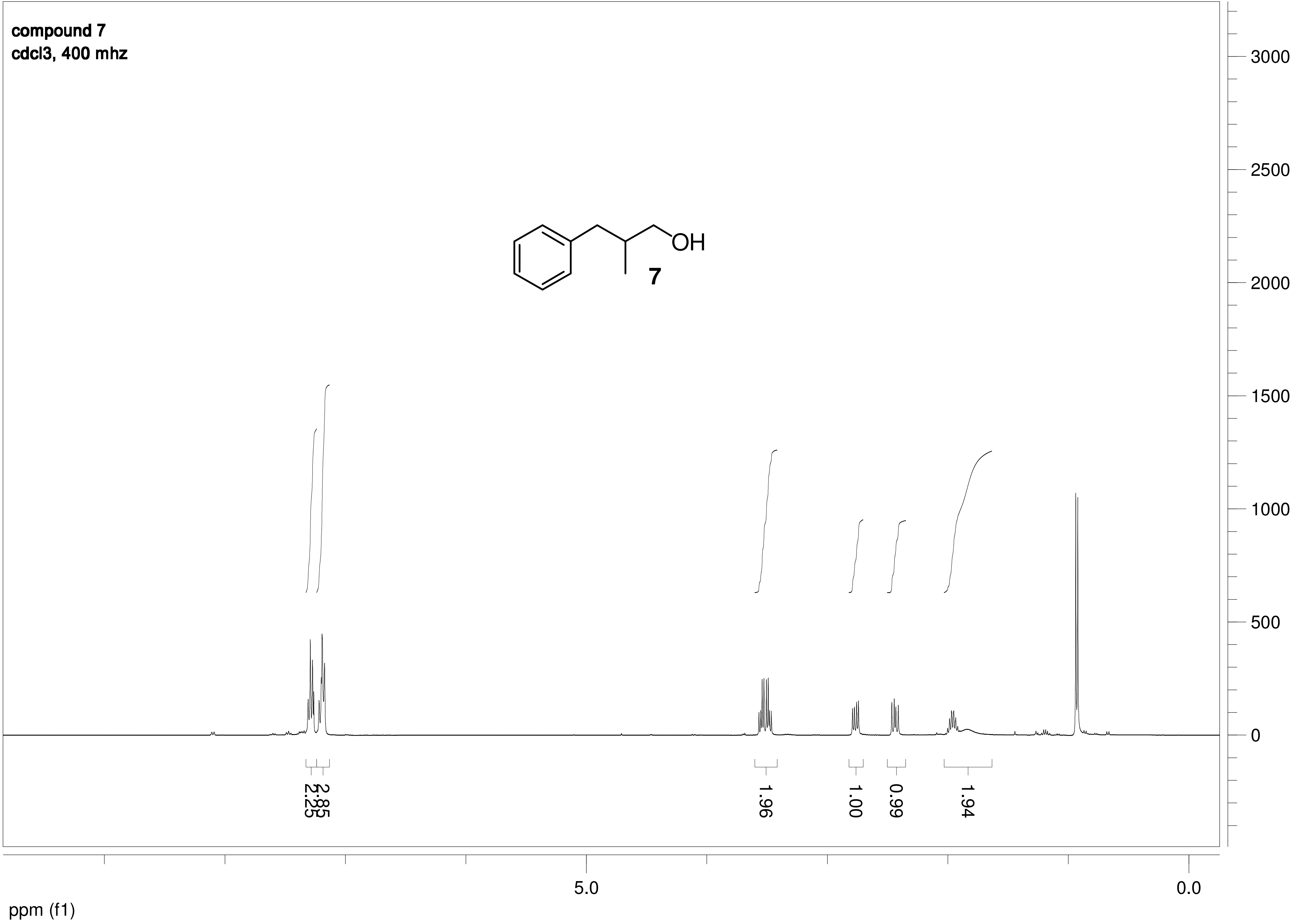
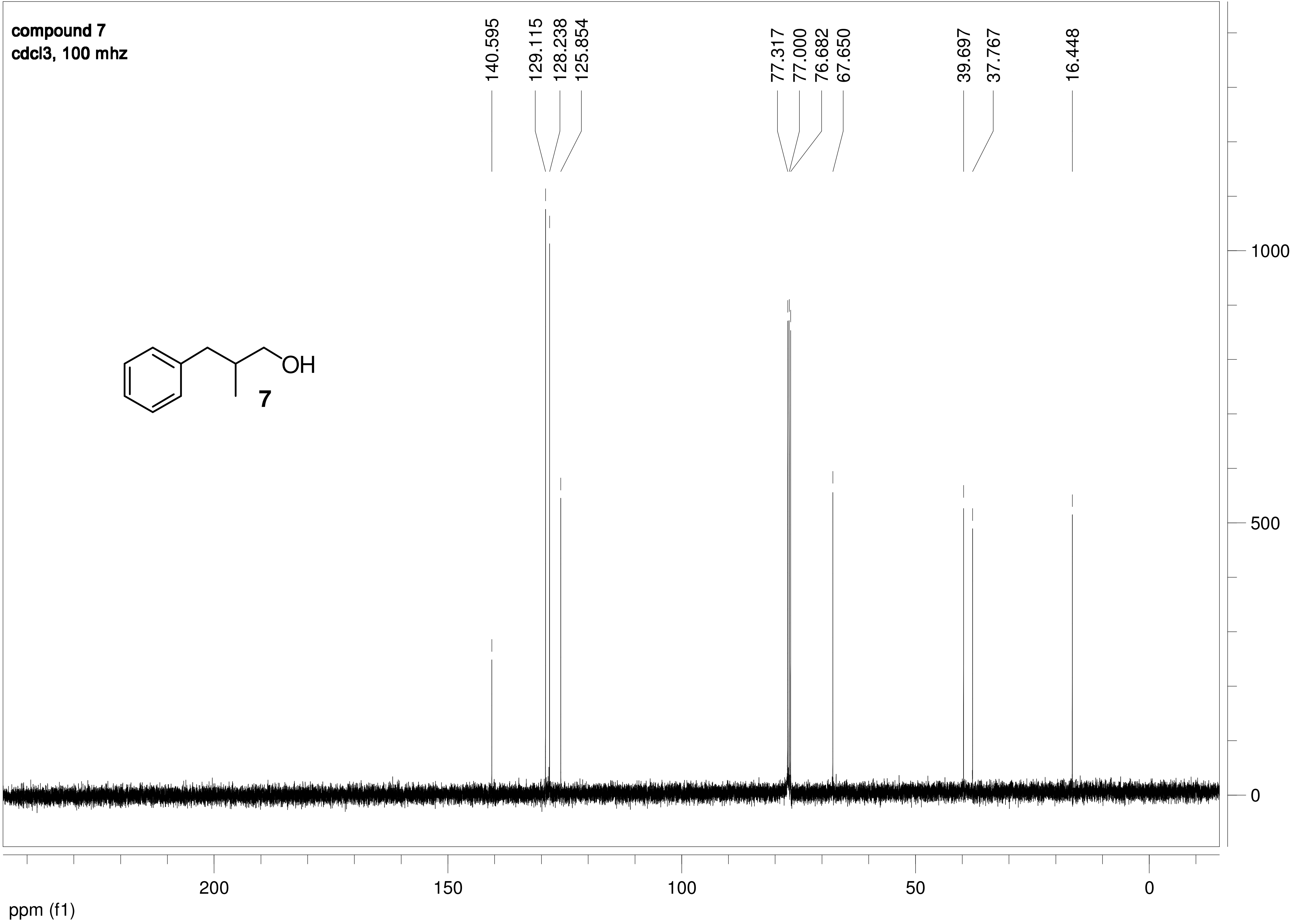
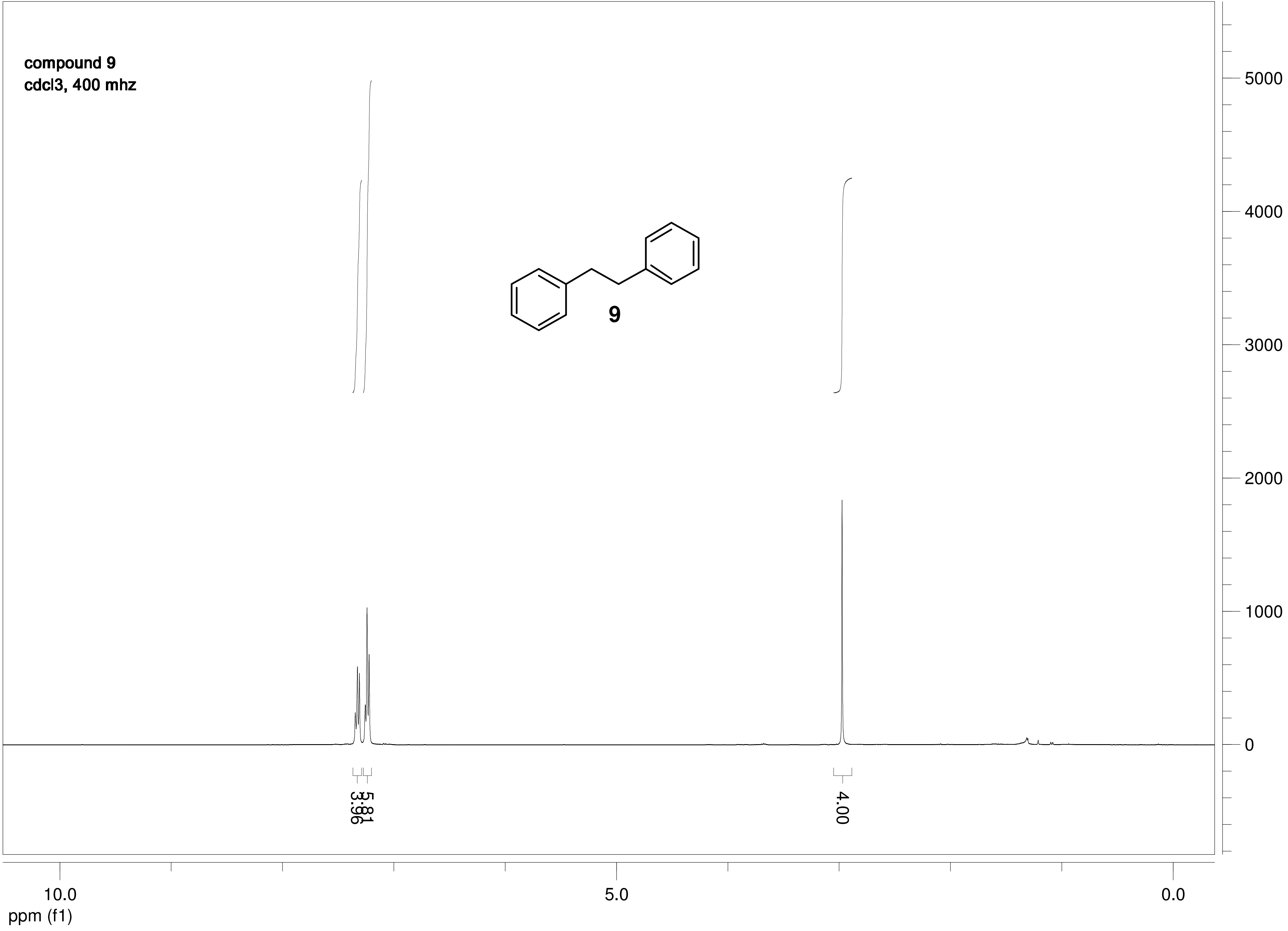
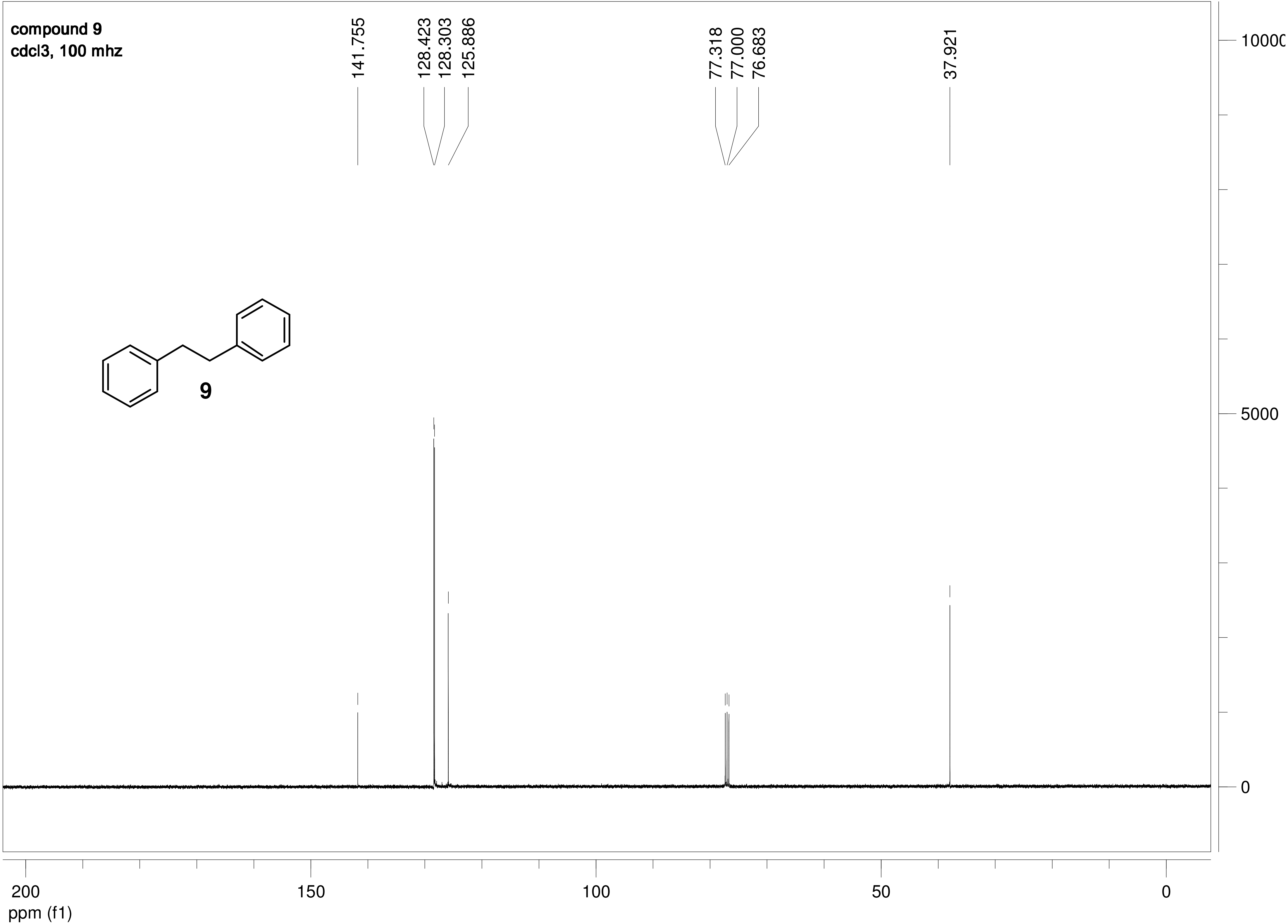
cdcl3, 100 mhz
141.762
128.330
128.297
125.755
77.318
77.000
76.682
62.071
34.105
31.995
OH
5
3500
3000
2500
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)


compound 7
cdcl3, 400 mhz
OH
7
3000
2500
2000
1500
1000
500
0
2.25
2.85
1.96
1.00
0.99
1.94
5.0
0.0
ppm (f1)


compound 7
cdcl3, 100 mhz
140.595
129.115
128.238
125.854
77.317
77.000
76.682
67.650
39.697
37.767
16.448
OH
7
1000
500
0
200
150
100
50
0
ppm (f1)


compound 9
cdcl3, 400 mhz
9
5000
4000
3000
2000
1000
0
3.96
5.81
4.00
10.0
5.0
0.0
ppm (f1)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cdcl3, 100 mhz
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128.423
128.303
125.886
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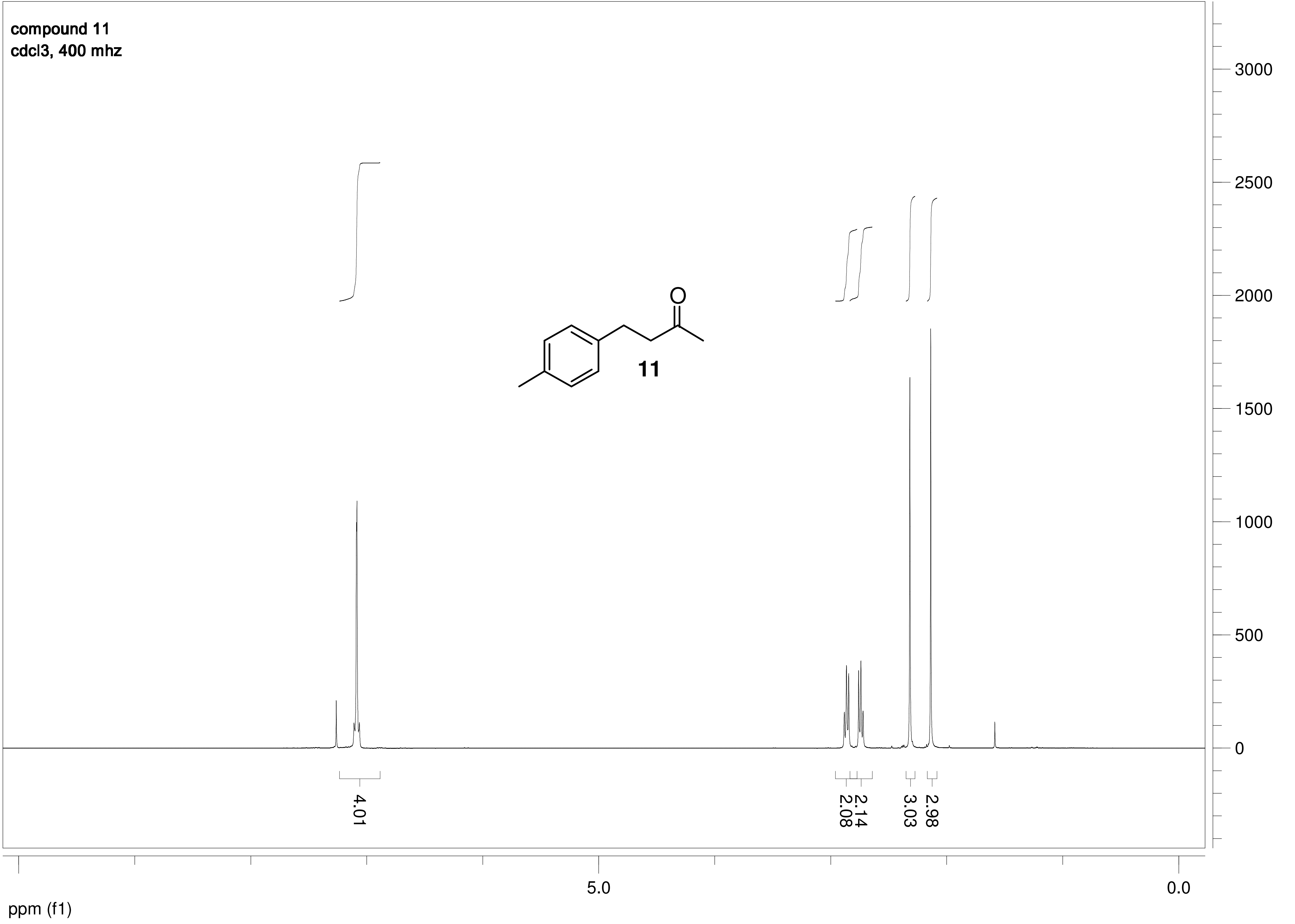
76.683
37.921
9
10000
5000
0
200
150
100
50
0
ppm (f1)


compound 11
cdcl3, 400 mhz
11
4.01
2.08
2.14
3.03
2.98
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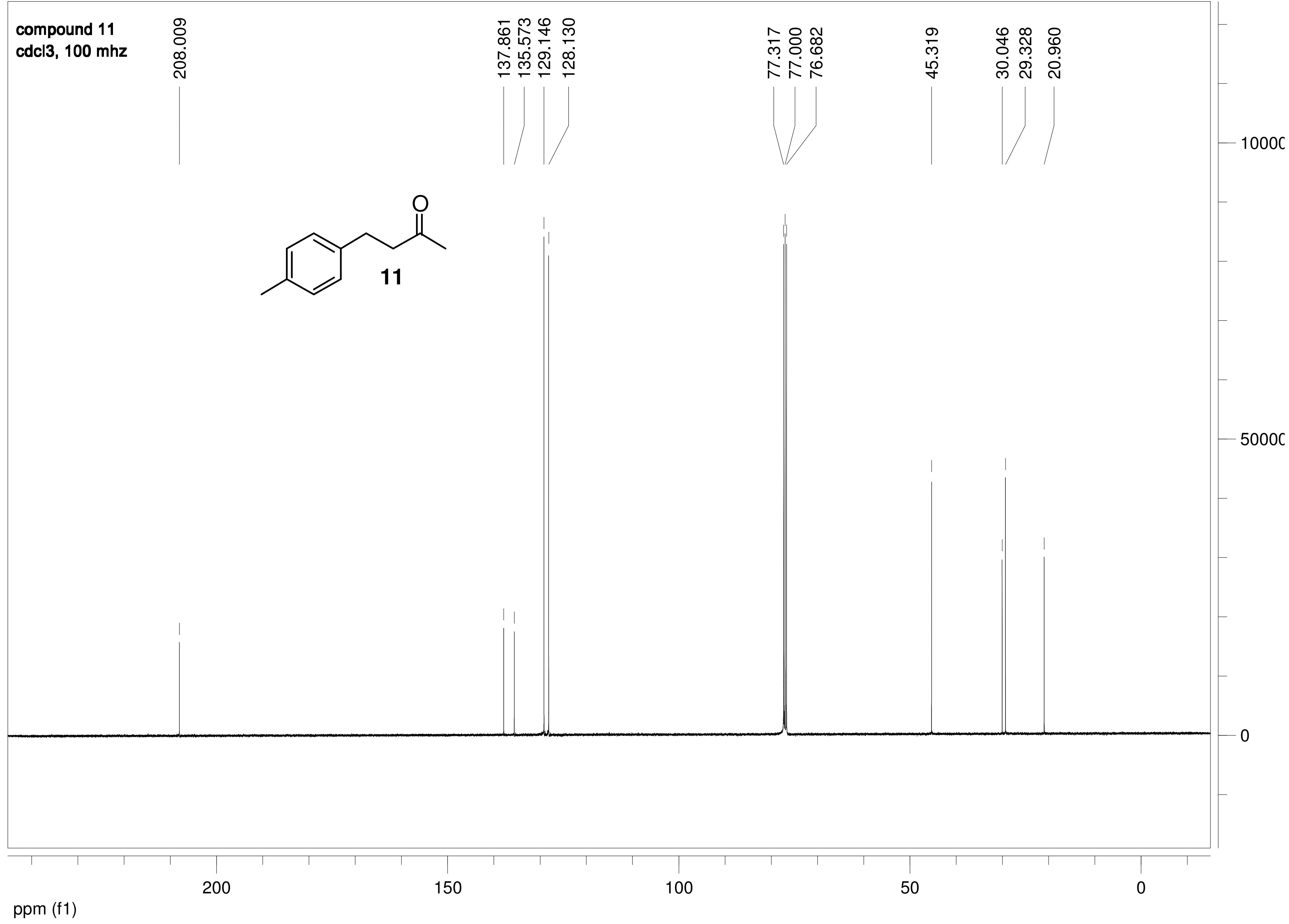
2500
2000
1500
1000
500
0
5.0
0.0
ppm (f1)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cdcl3, 100 mhz
208.009
137.861
135.573
129.146
128.130
77.317
77.000
76.682
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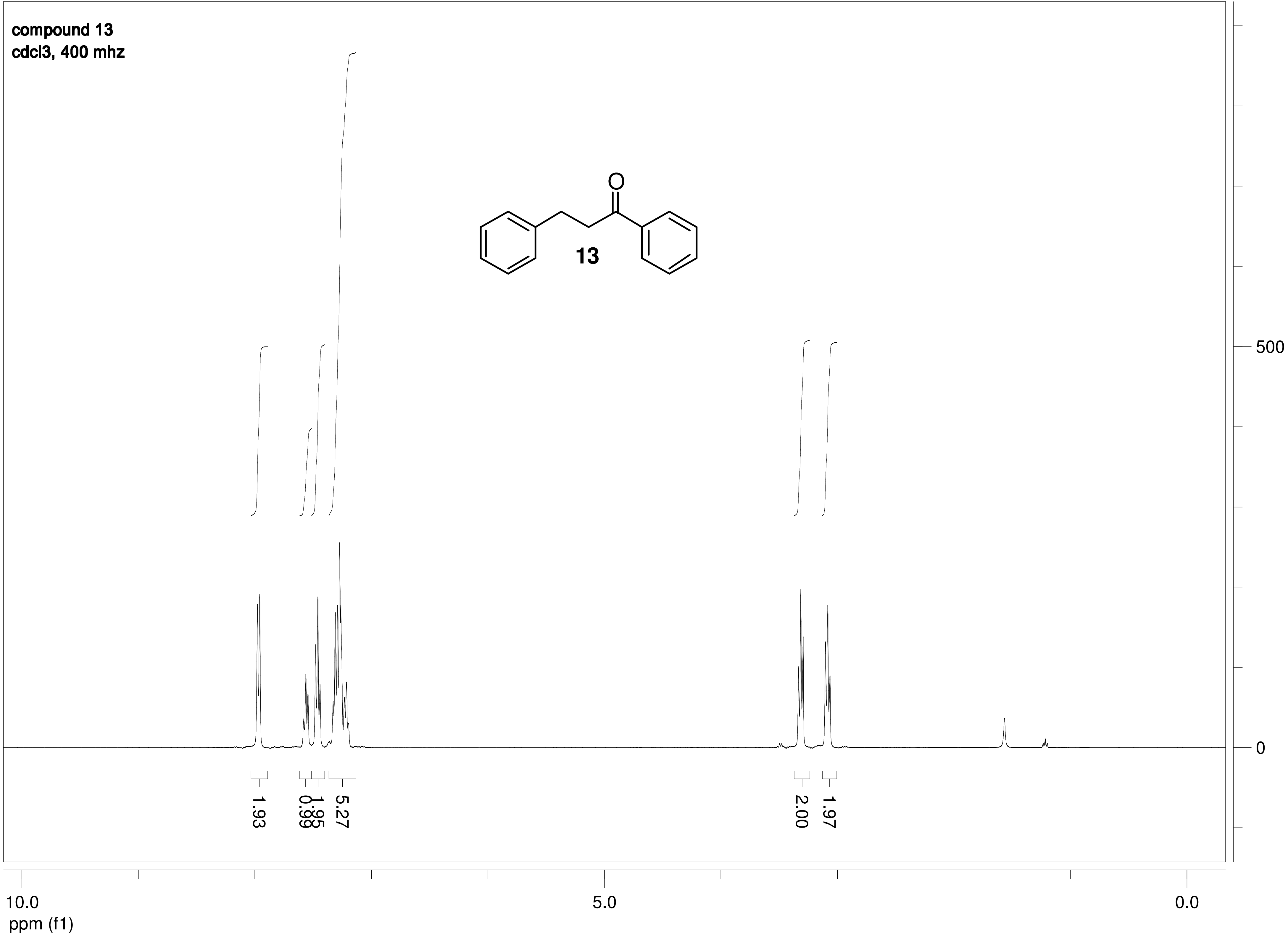
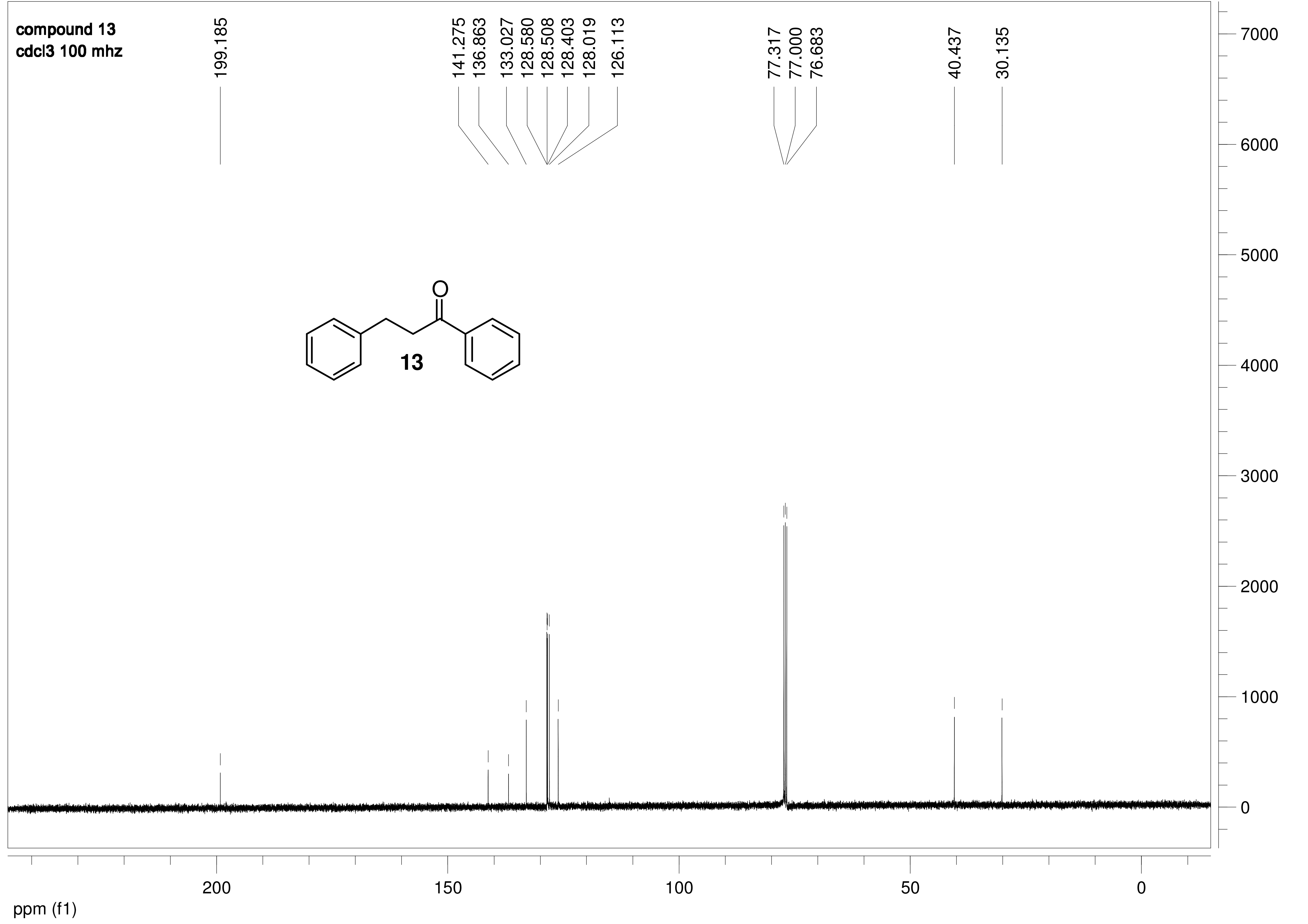
29.328
20.960
O
11
10000
50000
0
200
150
100
50
0
ppm (f1)


compound 13
cdcl3, 400 mhz
O
13
500
0
1.93
0.99
1.95
5.27
2.00
1.97
10.0
5.0
0.0
ppm (f1)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cdcl3 100 mhz
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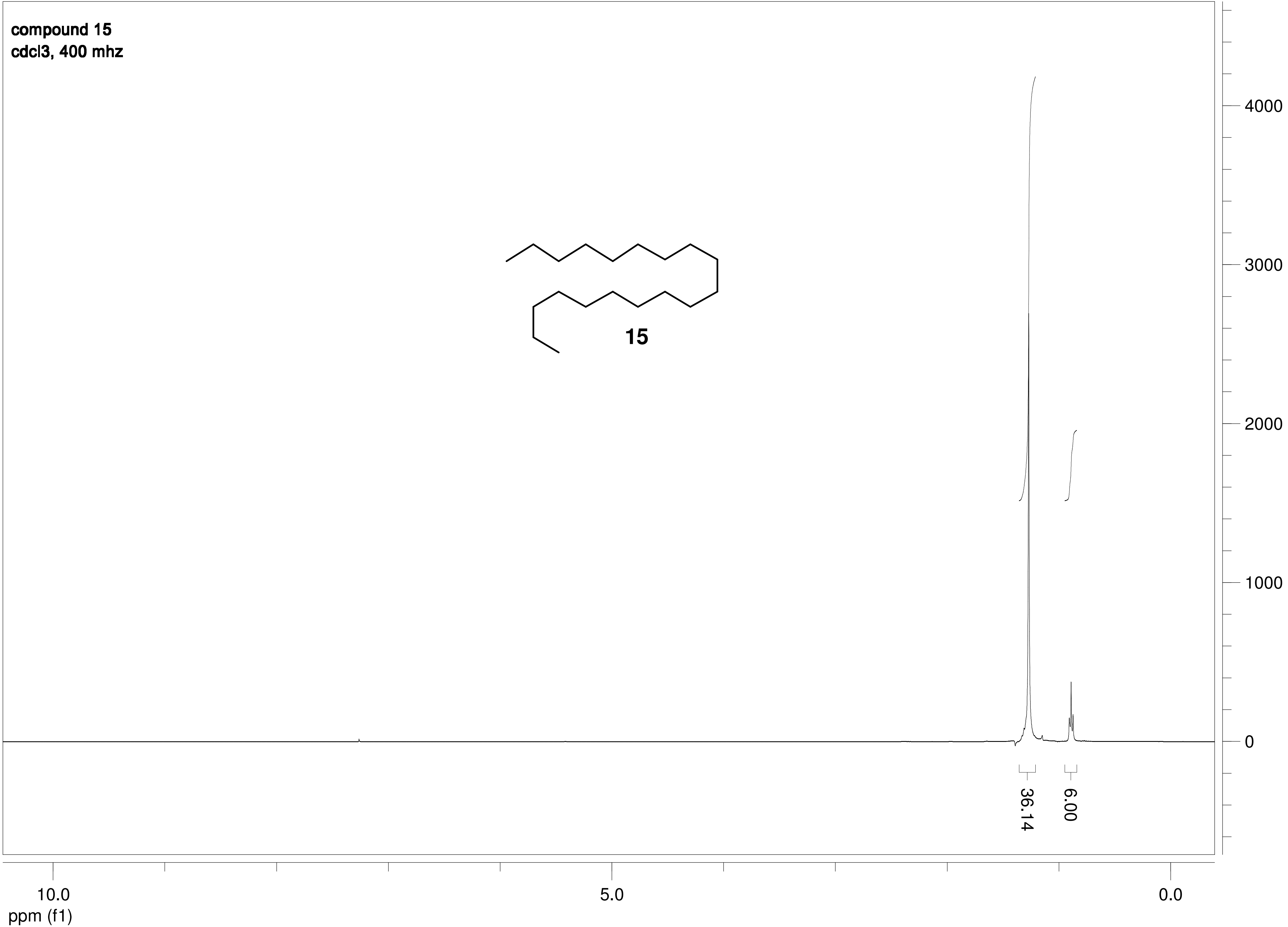
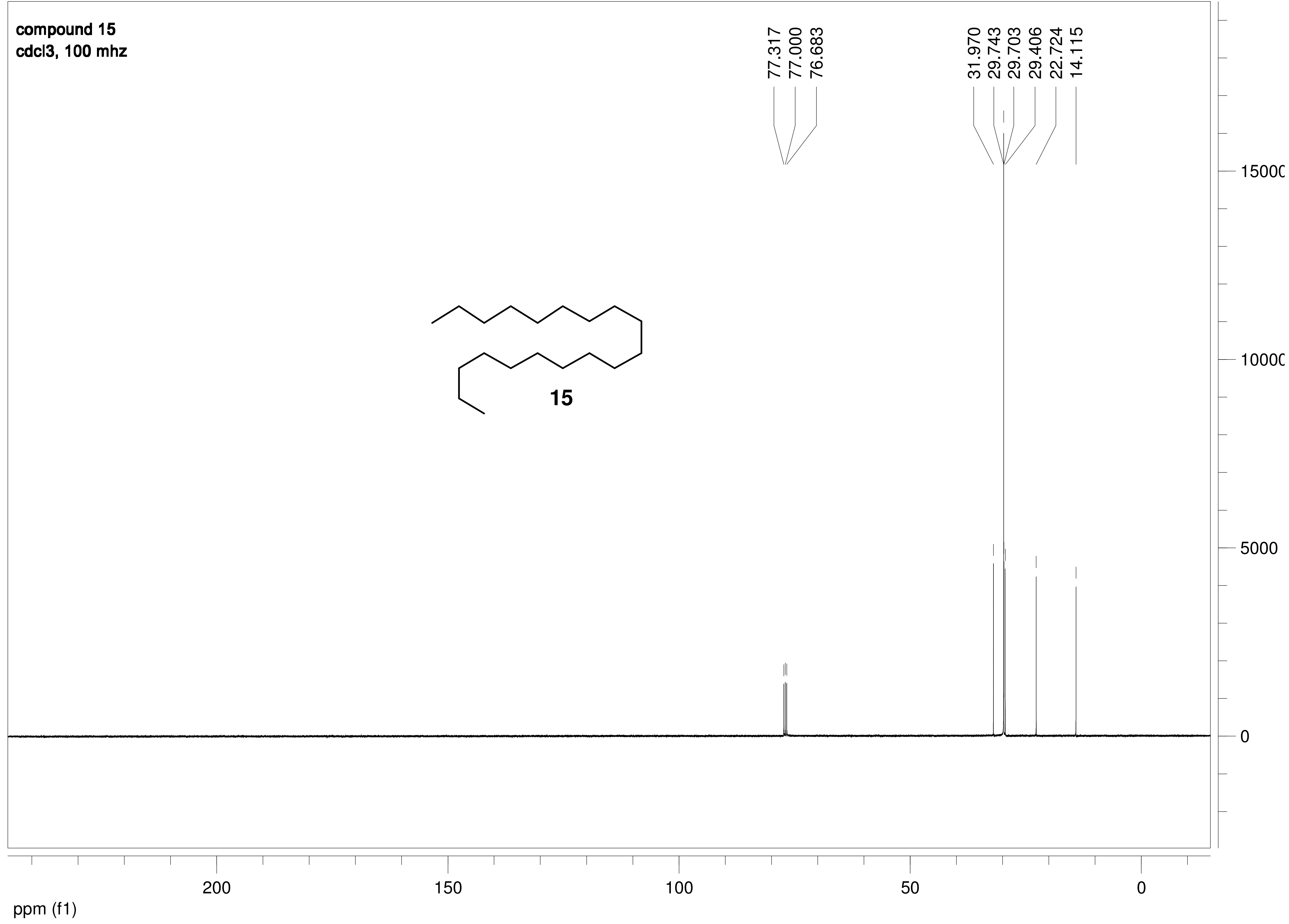
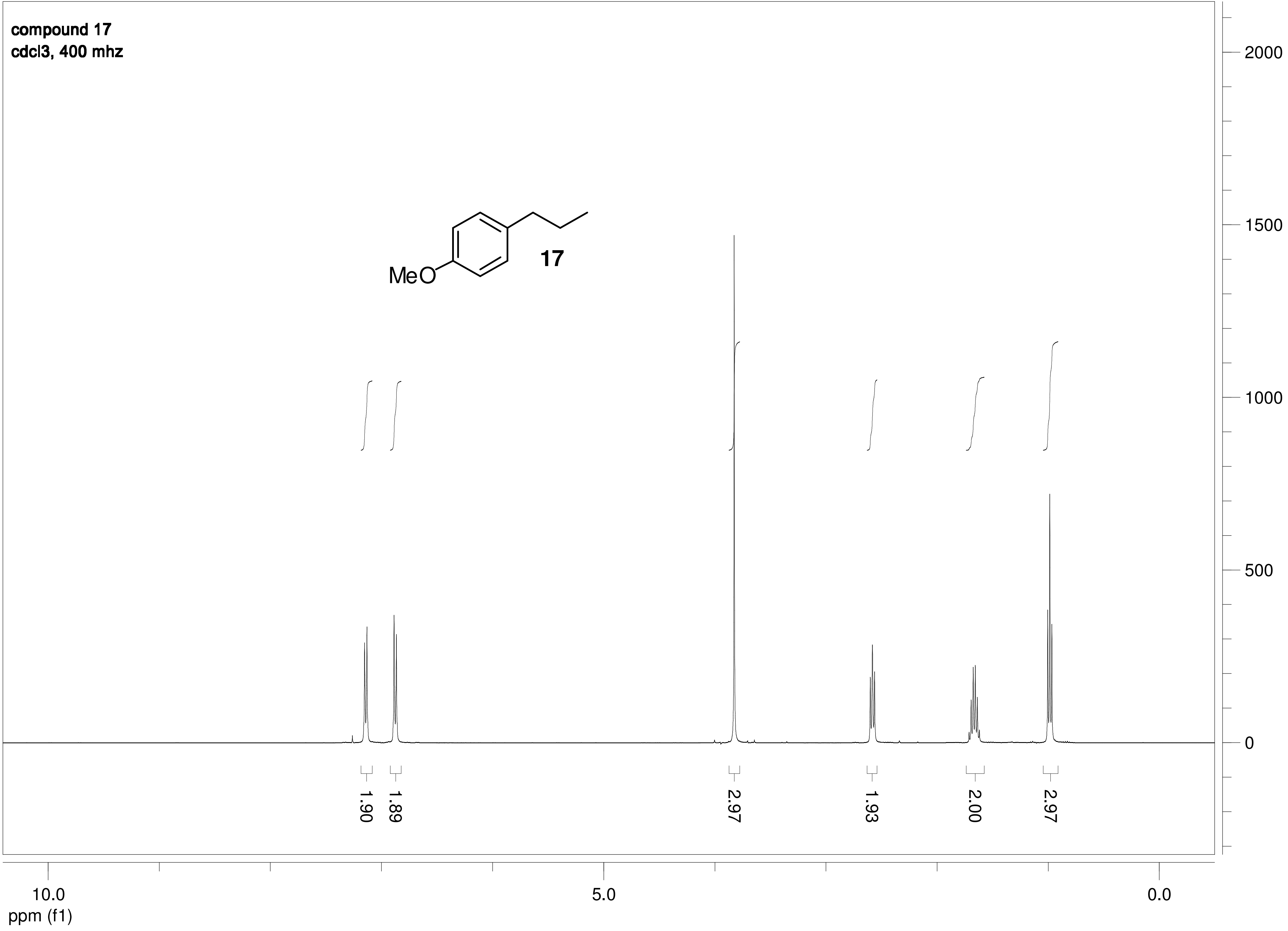
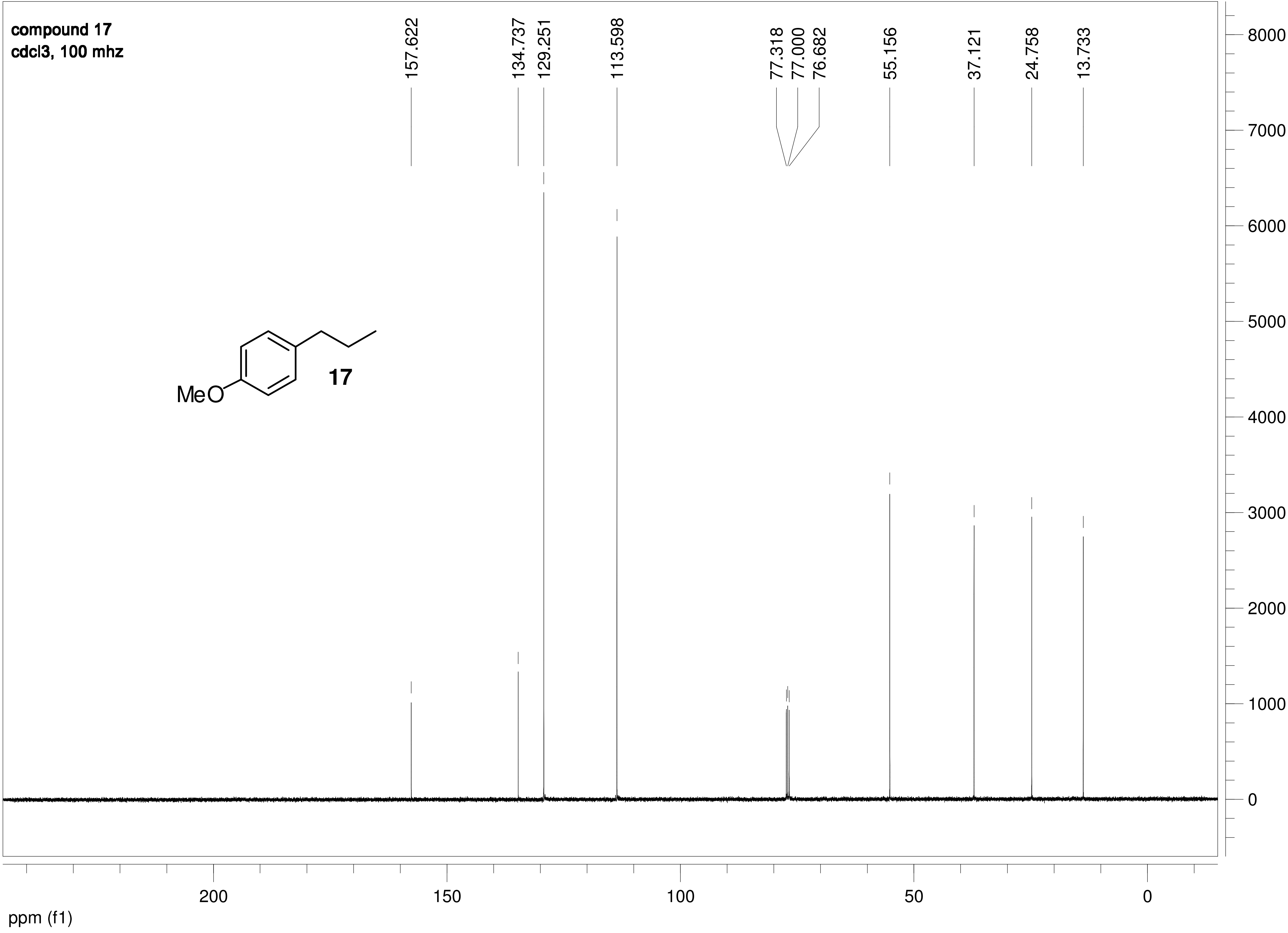
141.275
136.863
133.027
128.580
128.508
128.403
128.019
126.113
77.317
77.000
76.683
40.437
30.135
13
7000
6000
5000
4000
3000
2000
1000
0
200
150
100
50
0
ppm (f1)


compound 15
cdcl3, 400 mhz
15
36.14
6.00
4000
3000
2000
1000
0
10.0
5.0
0.0
ppm (f1)

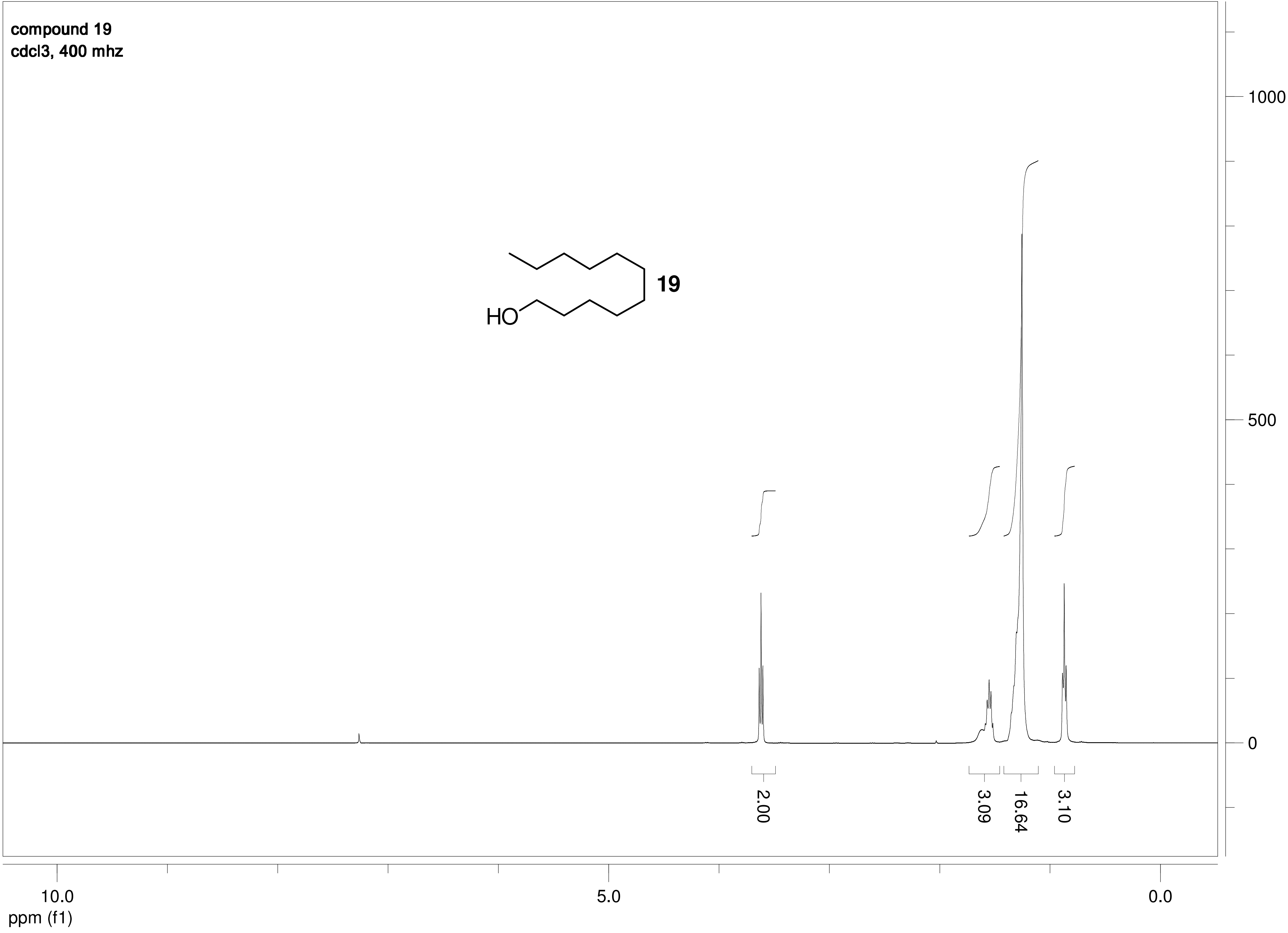

compound 15
cdcl3, 100 mhz
77.317
77.000
76.683
31.970
29.743
29.703
29.406
22.724
14.115
15
15000
10000
5000
0
200
150
100
50
0
ppm (f1)



compound 17
cdcl3, 400 mhz
MeO
17
1.90
1.89
2.97
1.93
2.00
2.97
10.0
5.0
0.0
ppm (f1)
2000
1500
1000
500
0



compound 17
cdcl3, 100 mhz
157.622
134.737
129.251
113.598
77.318
77.000
76.682
55.156
37.121
24.758
13.733
MeO
17
8000
7000
6000
5000
4000
3000
2000
1000
0
200
150
100
50
0
ppm (f1)



compound 19
cdcl3, 400 mhz
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19
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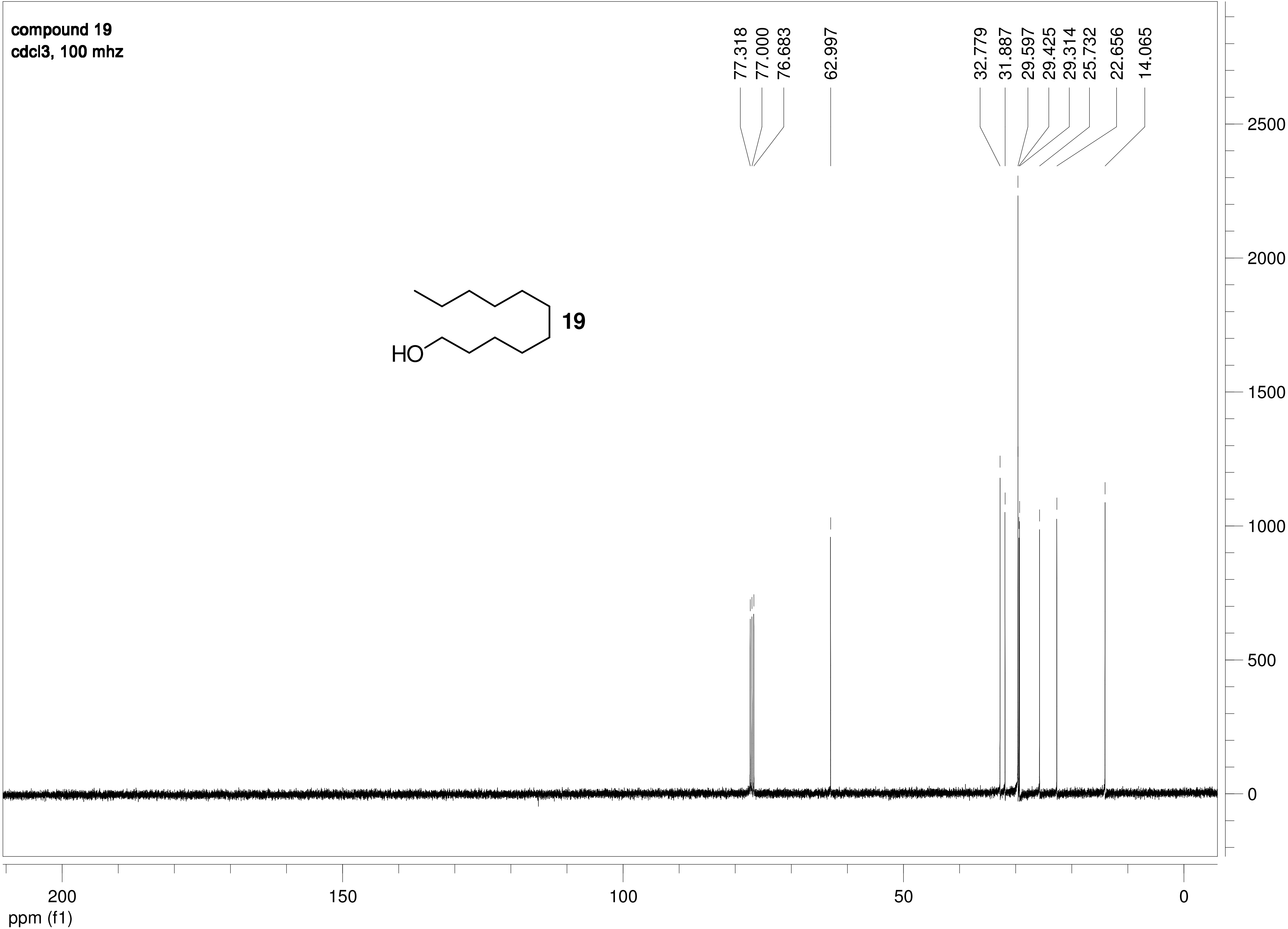
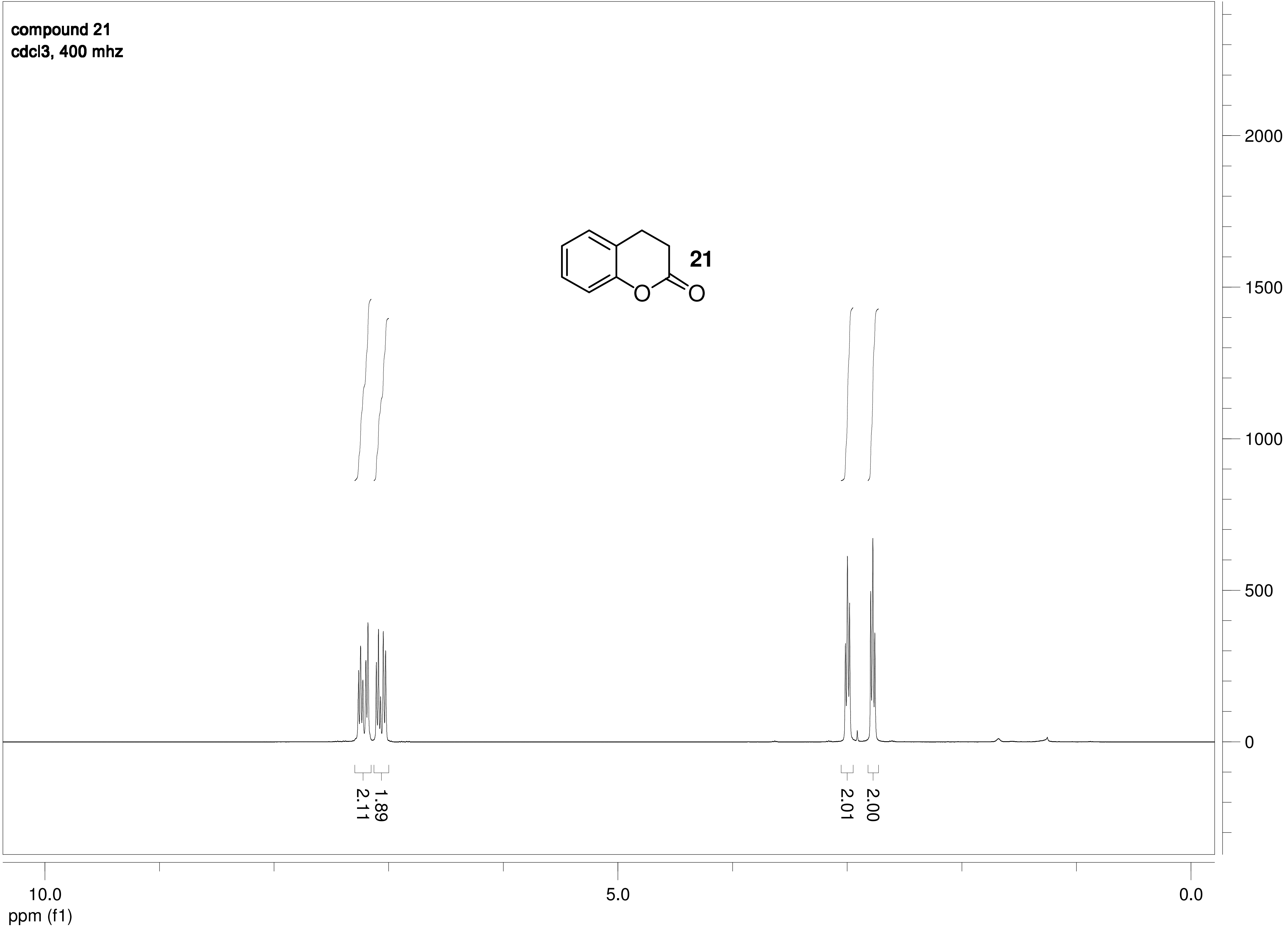
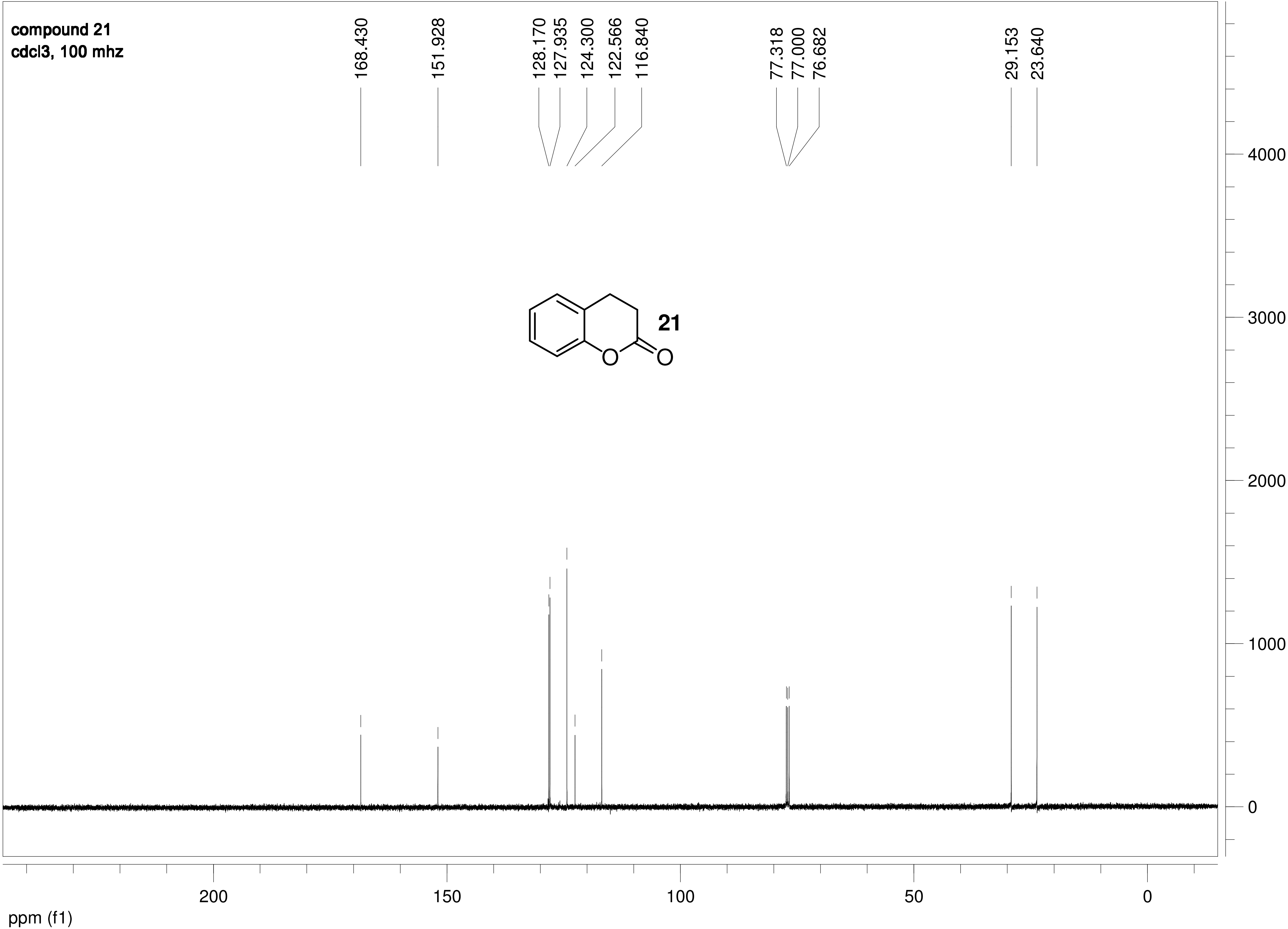
3.09
16.64
3.10
1000
500
0
10.0
5.0
0.0
ppm (f1)

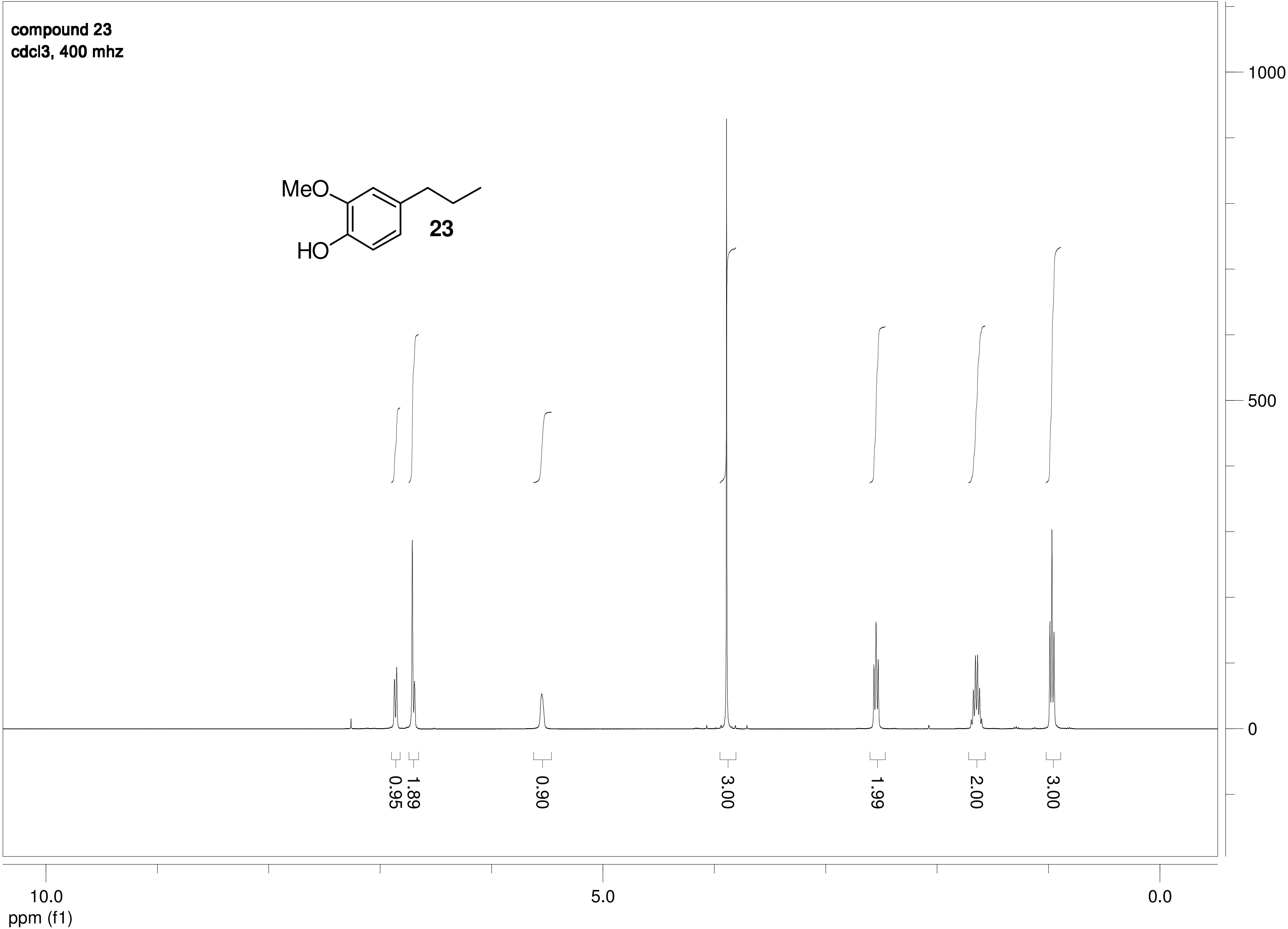

compound 19
cdcl3, 100 mhz
77.318
77.000
76.683
62.997
32.779
31.887
29.597
29.425
29.314
25.732
22.656
14.065
HO
19
2500
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)

compound 21
cdcl3, 400 mhz

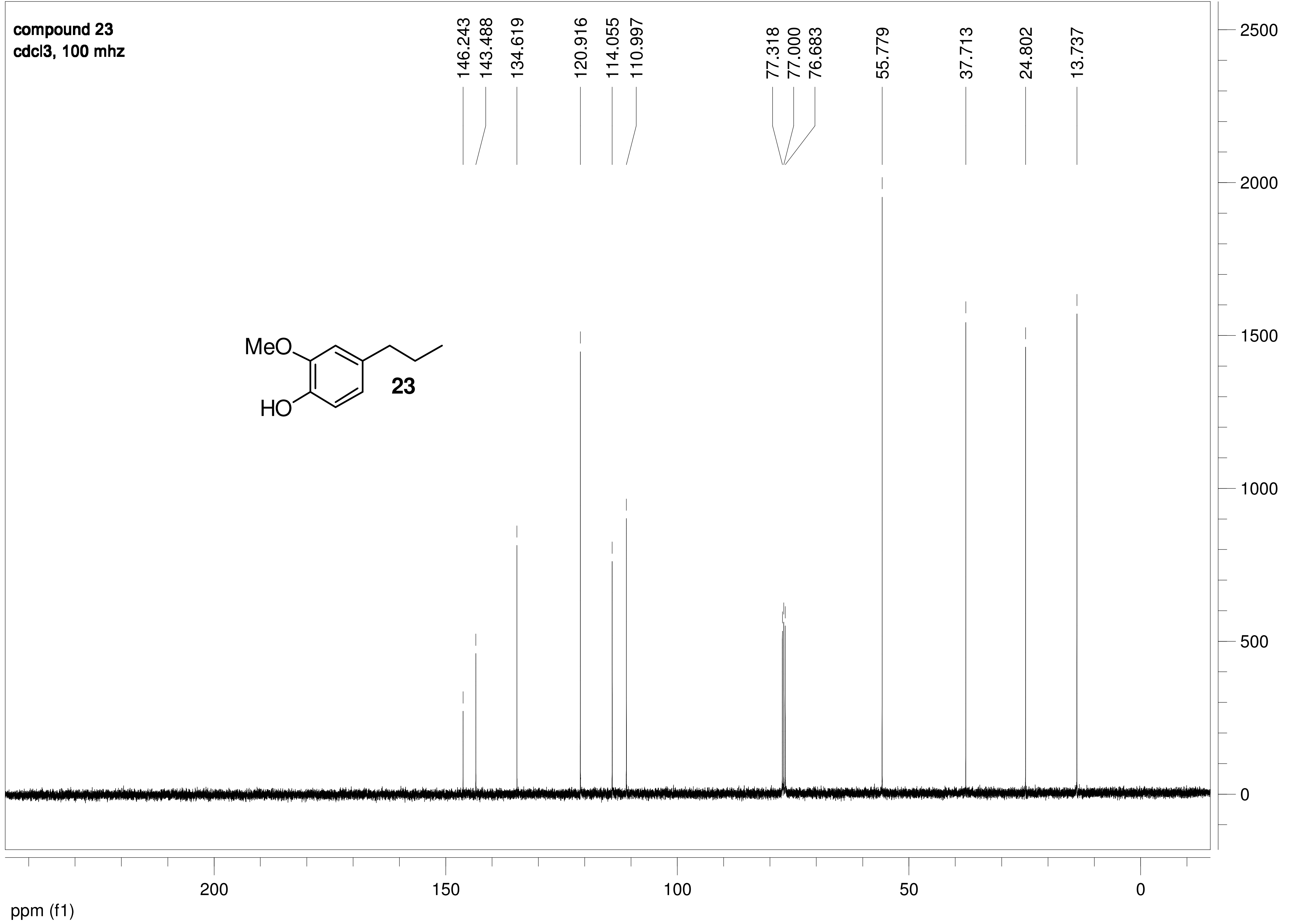




compound 21
cdcl3, 100 mhz
168.430
151.928
128.170
127.935
124.300
122.566
116.840
77.318
77.000
76.682
29.153
23.640
21
O
O
4000
3000
2000
1000
0
200
150
100
50
0
ppm (f1)



compound 23
cdcl3, 400 mhz
MeO
HO
23
1000
500
0
0.95
1.89
0.90
3.00
1.99
2.00
3.00
10.0
5.0
0.0
ppm (f1)


compound 23
cdcl3, 100 mhz
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114.055
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77.000
76.683
55.779
37.713
24.802
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HO
23
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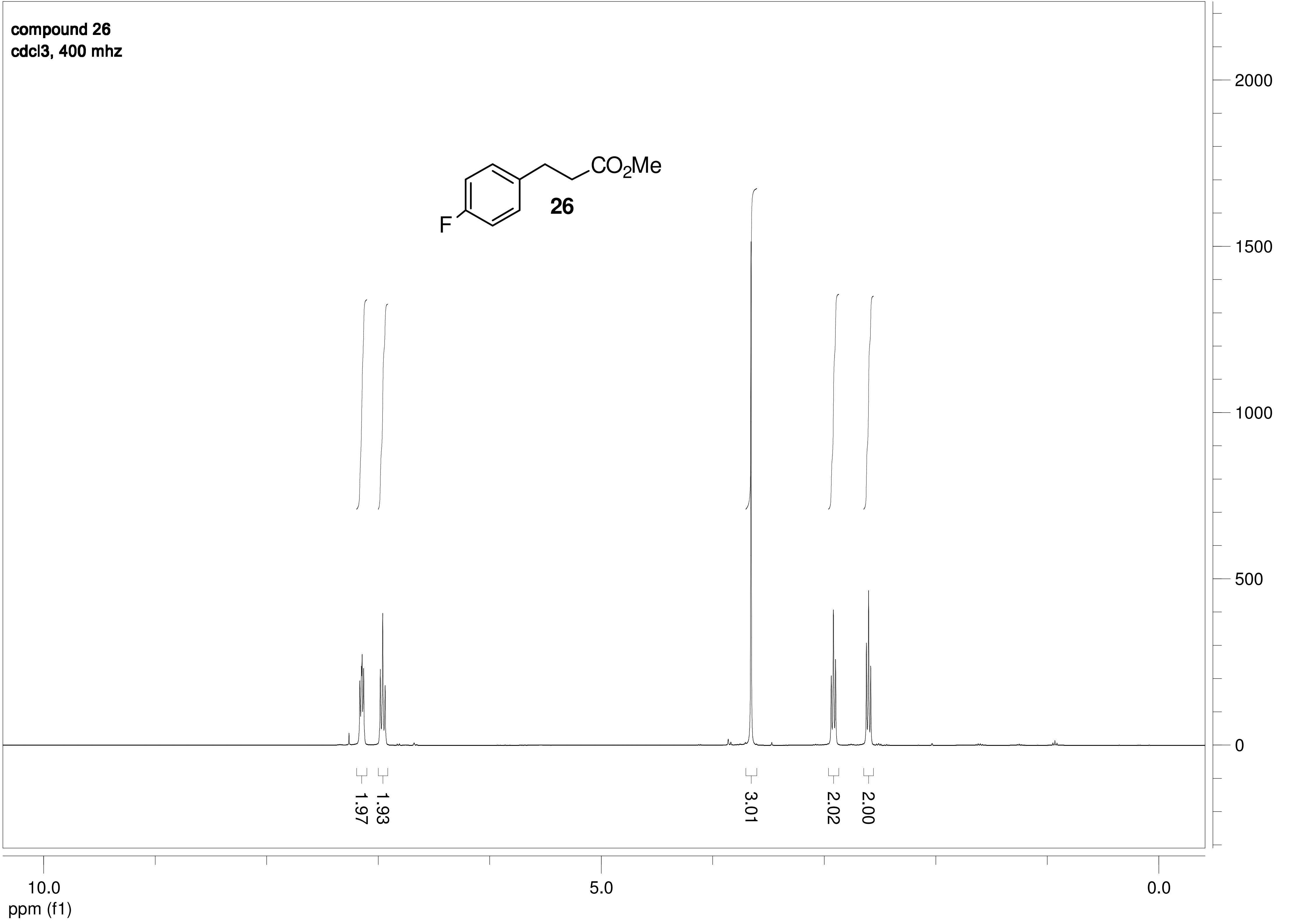
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)


compound 26
cdcl3, 400 mhz
CO2Me
F
26
2000
1500
1000
500
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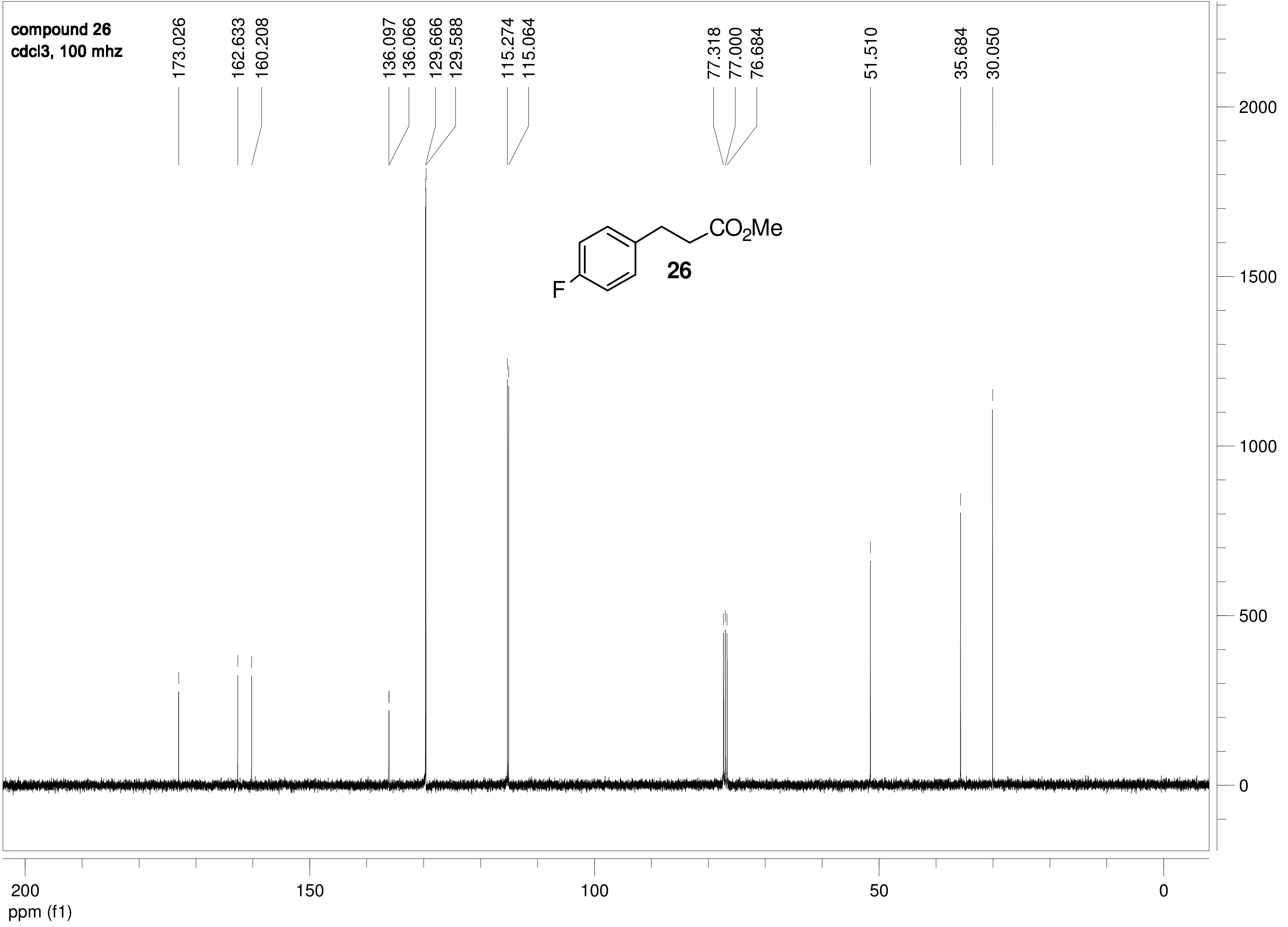
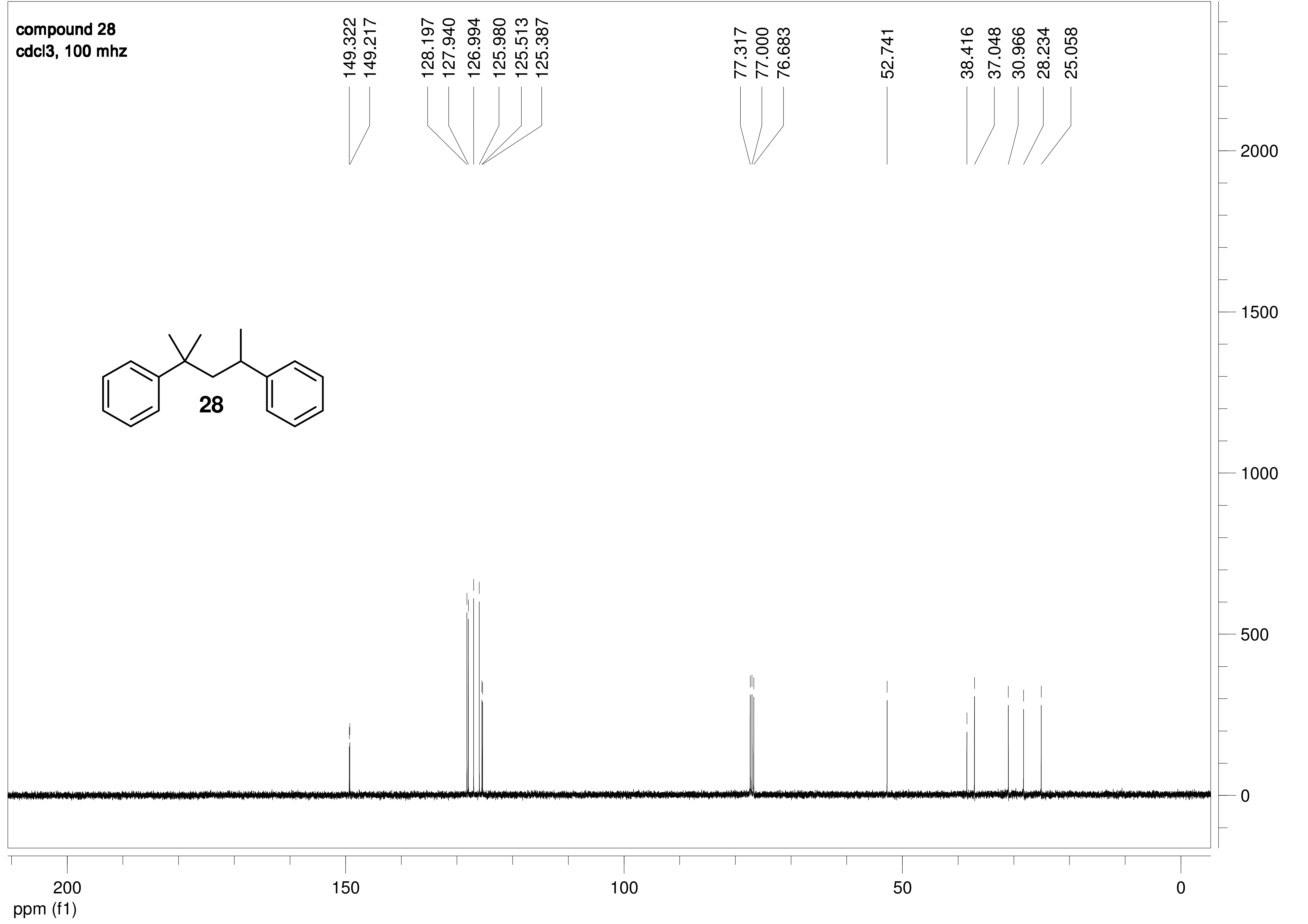
1.97
1.93
3.01
2.02
2.00
10.0
5.0
0.0
ppm (f1)


compound 26
cdcl3, 100 mhz
173.026
162.633
160.208
136.097
136.066
129.666
129.588
115.274
115.064
77.318
77.000
76.684
51.510
35.684
30.050
CO2Me
F
26
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)

compound 28
cdcl3, 400 mhz
28
4.19
4.18
2.02
1.03
1.09
1.07
3.36
3.27
3.27
10.0
5.0
0.0
ppm (f1)
400
300
200
100
0



compound 28
cdcl3, 100 mhz
149.322
149.217
128.197
127.940
126.994
125.980
125.513
125.387
77.317
77.000
76.683
52.741
38.416
37.048
30.966
28.234
25.058
28
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)