CHEMISTRY
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Supporting Information

A General Approach to Aza-Heterocycles *via* Domino Sequences Driven by Hydroformylation

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Supporting Information

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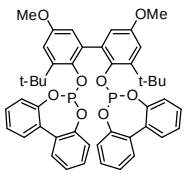
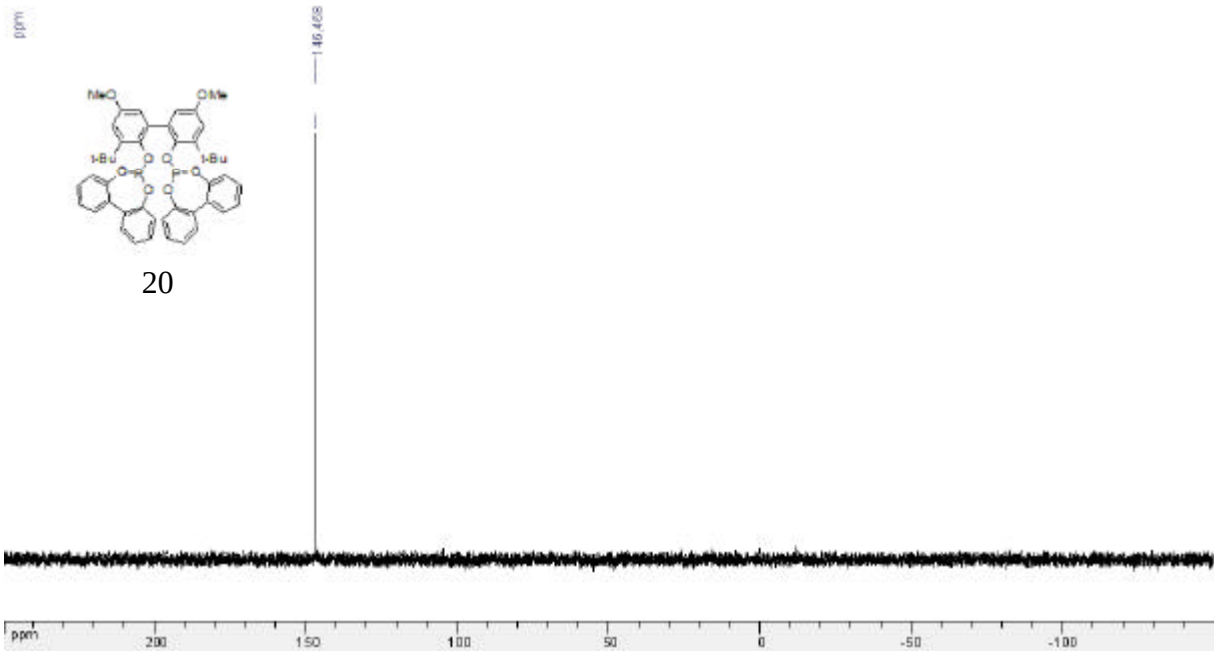
Stability of biphephos (20) in acidic media

As stability of biphephos was questionable in our reaction conditions, some experiments were conducted. Analyses were made by ^{31}P NMR of the crude reaction mixture.



$C_{46}H_{44}O_8P_2$
Exact Mass: 786,2511
Mol. Wt.: 786,7843

Biphephos 20. ^{31}P NMR ($CDCl_3$, 81 MHz) δ 146.5.



20

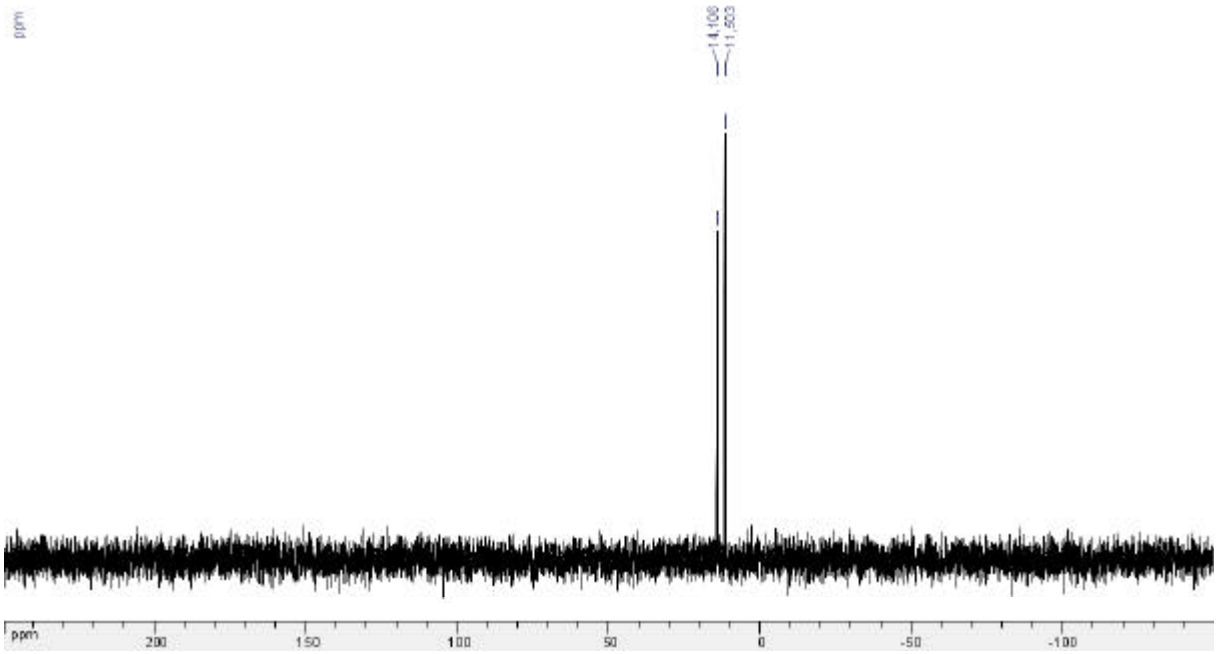
Table 1. Stability of biphephos.[a]

Entry	Solvent	$Rh(CO)_2acac$ (eq.)	Acid (eq.)	Conditions	^{31}P NMR picks observed (ppm)	Spectrum (see below)
1	CH_2Cl_2	-	TFA (25)	reflux, 12 h	14.1; 11.5	1
2	CH_2Cl_2	1	TFA (25)	reflux, 12 h	145.5; 142.7	2
3	THF	-	*p*TSA (5)	70 °C, 12 h	146.5, 146.2, 1.6, -3.0	3
4	THF	1	*p*TSA (5)	70 °C, 12 h	146.5, 146.2, 11.0, -3.0, -3.5	4

[a] biphephos **20** (5 mg, 0.006 mmol), [**20**] = 0.01 M.

Entry 1 showed that biphephos was hydrolysed after heating for 12 h in presence of 25 eq. of TFA (Spectrum 1). But when $Rh(CO)_2acac$ was added to the reaction mixture (entry 2), biphephos remained intact (Spectrum 2). In THF with 5 eq. of *p*TSA without (entry 3) or with Rh catalyst (entry 4) in the reaction mixture, some biphephos remained after 12 h.

In conclusion, these results showed that the complex rhodium-biphephos is stable under strong acidic conditions. Indeed we can observed by ^{31}P NMR some biphephos after heating for 12 h in acidic media. Thus, hydroformylation could be done with acids additives and allows us to make domino reactions.



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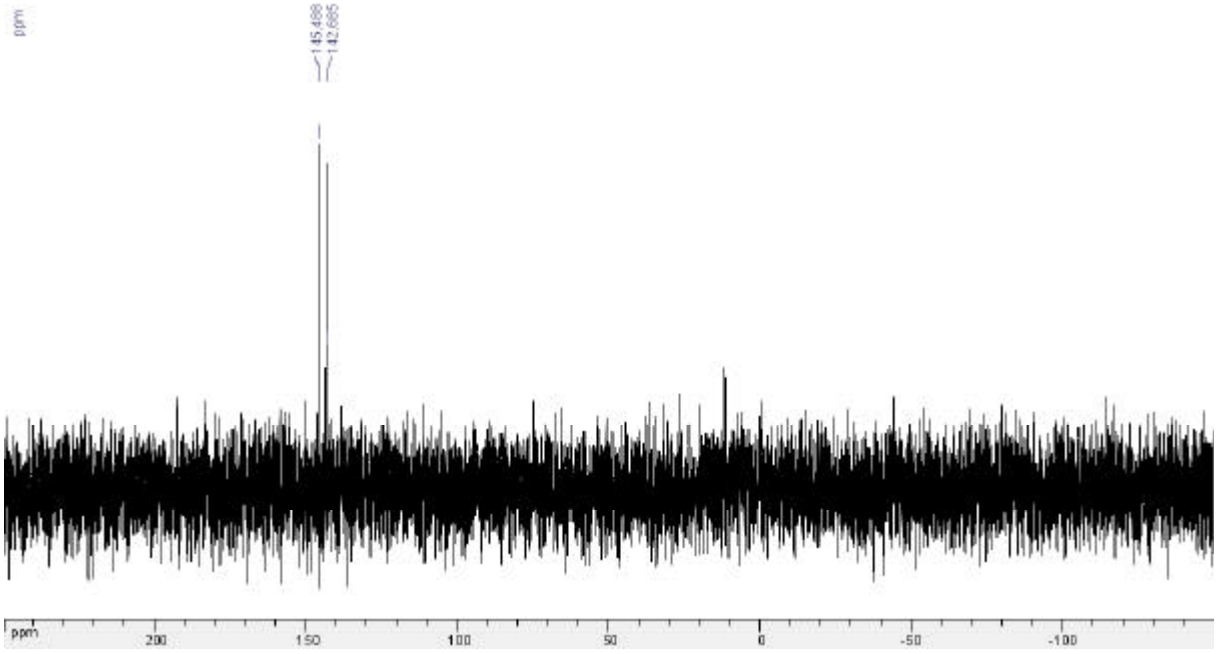

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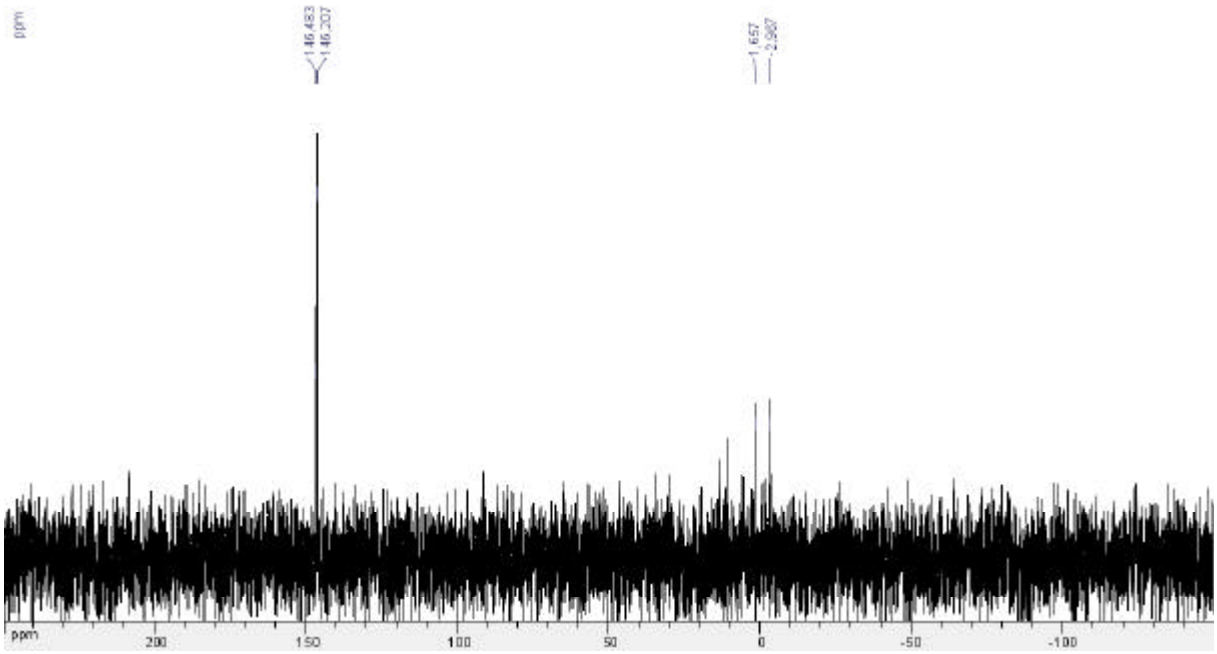

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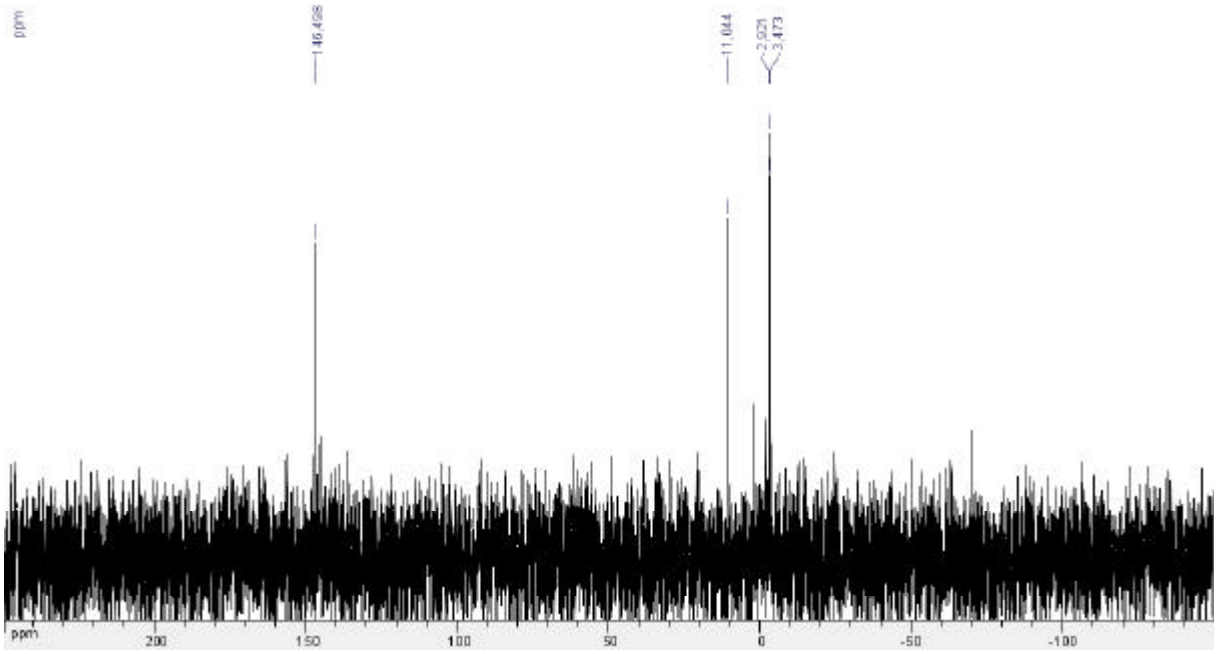
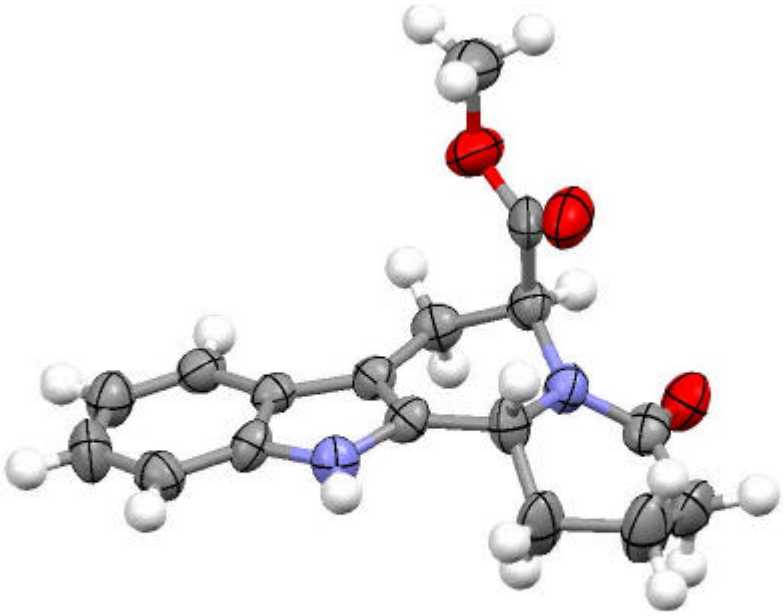


Spectrum 4

Crystal data for 27: CCDC 696805



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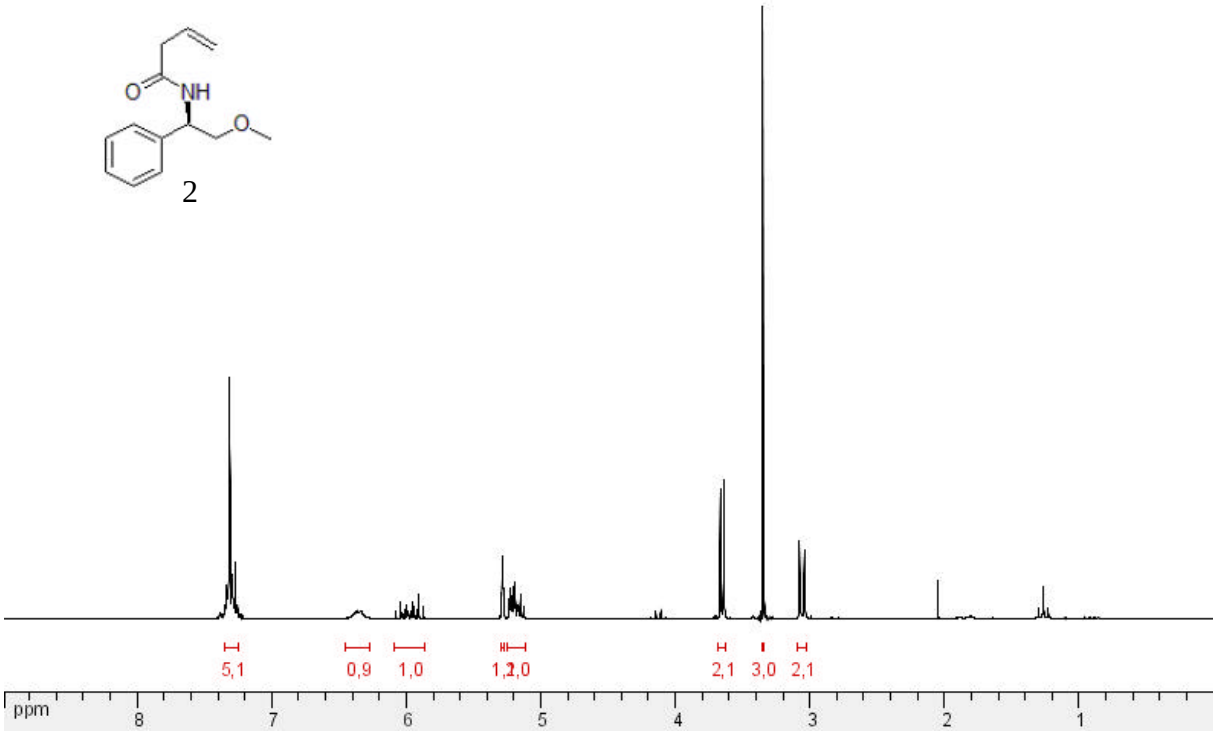
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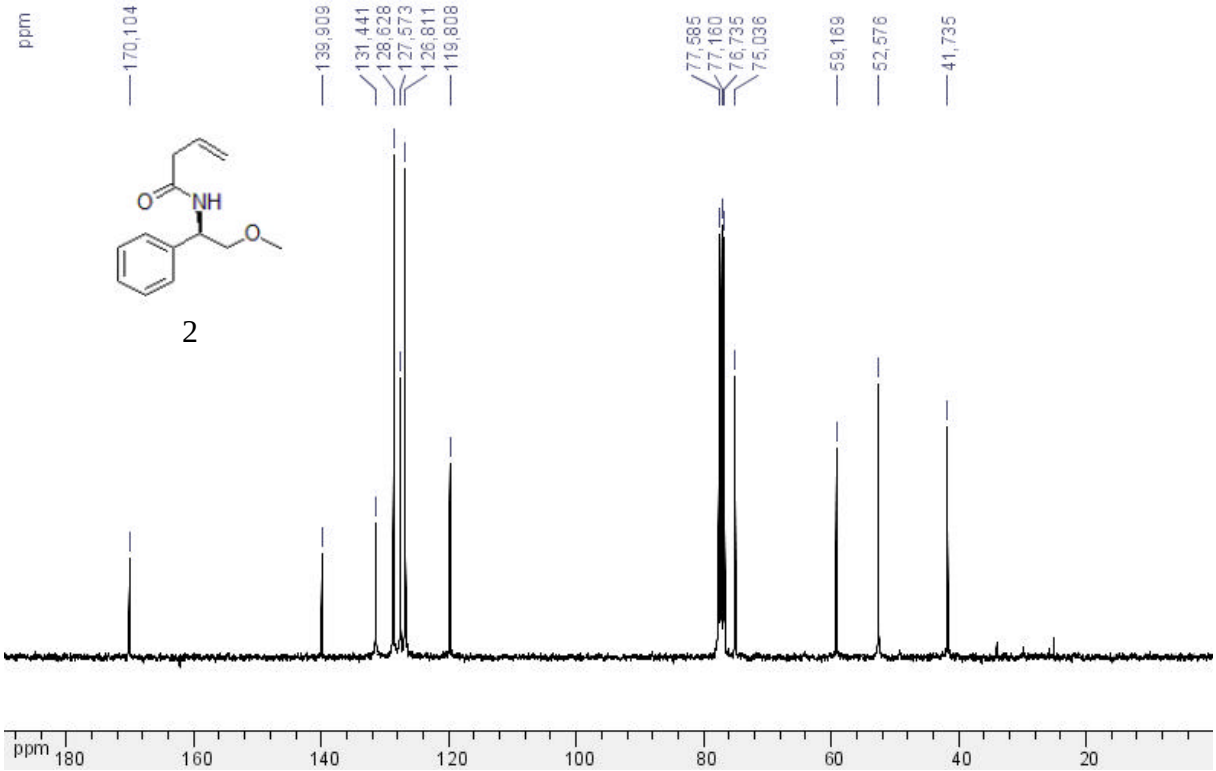
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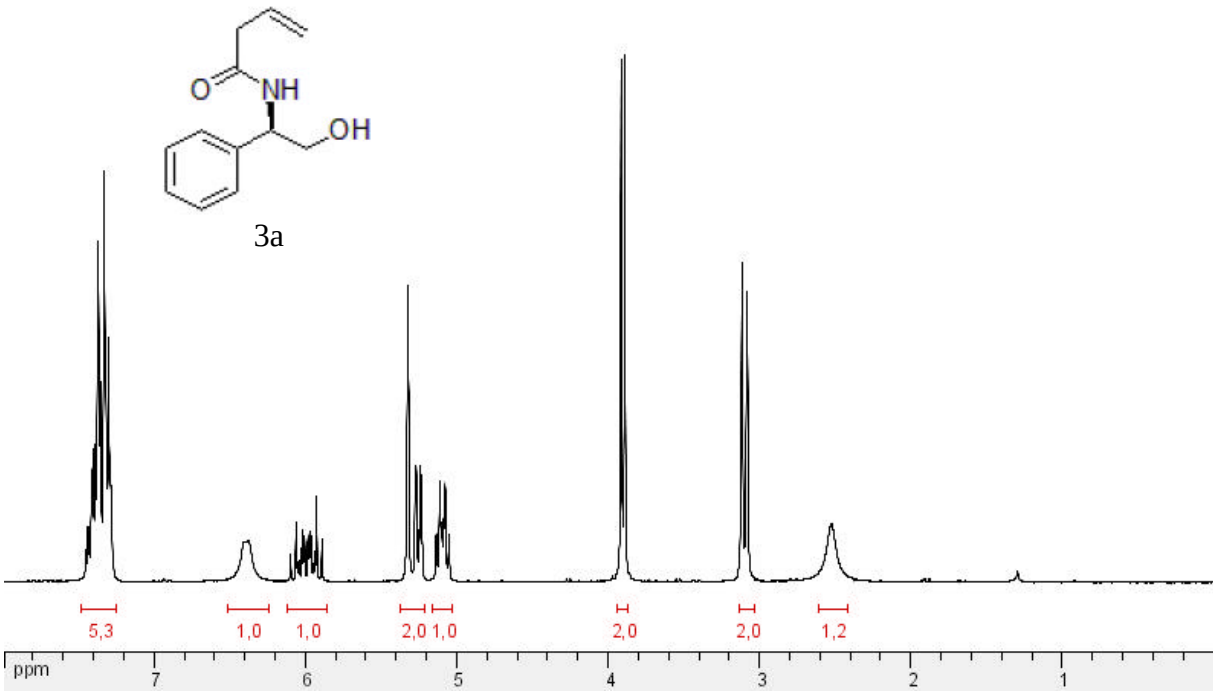
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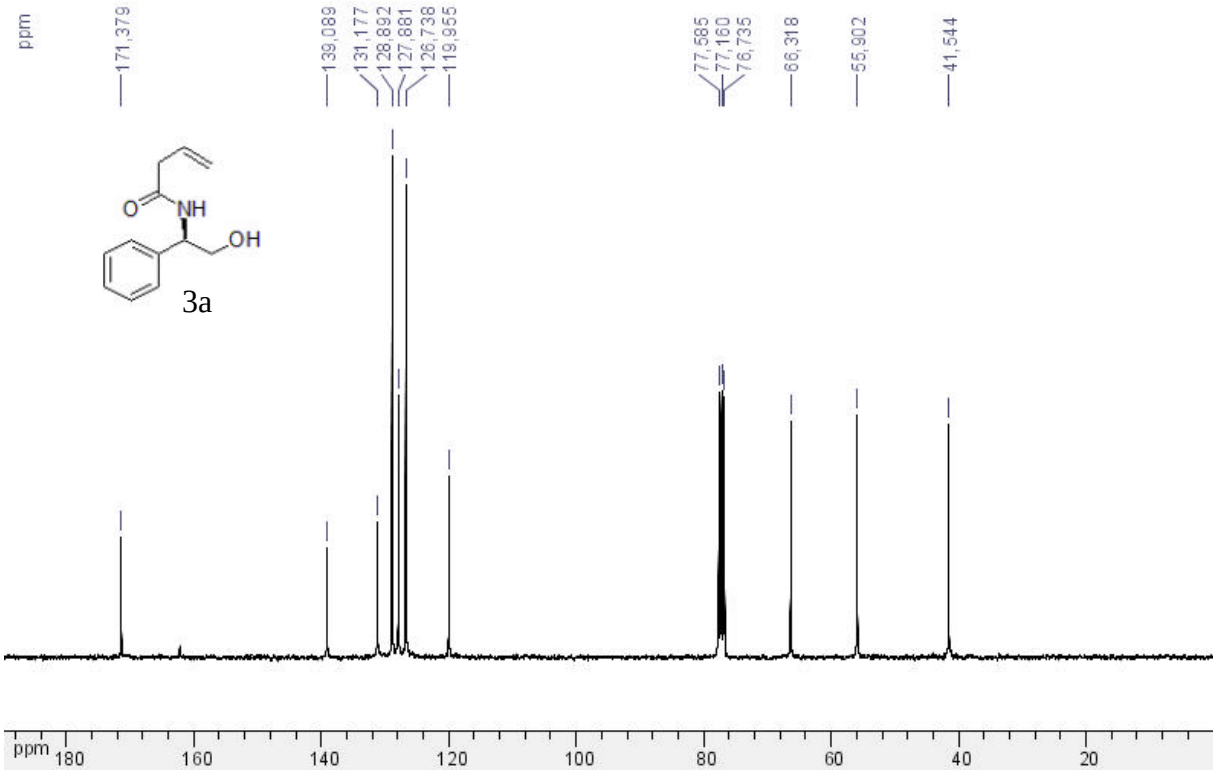
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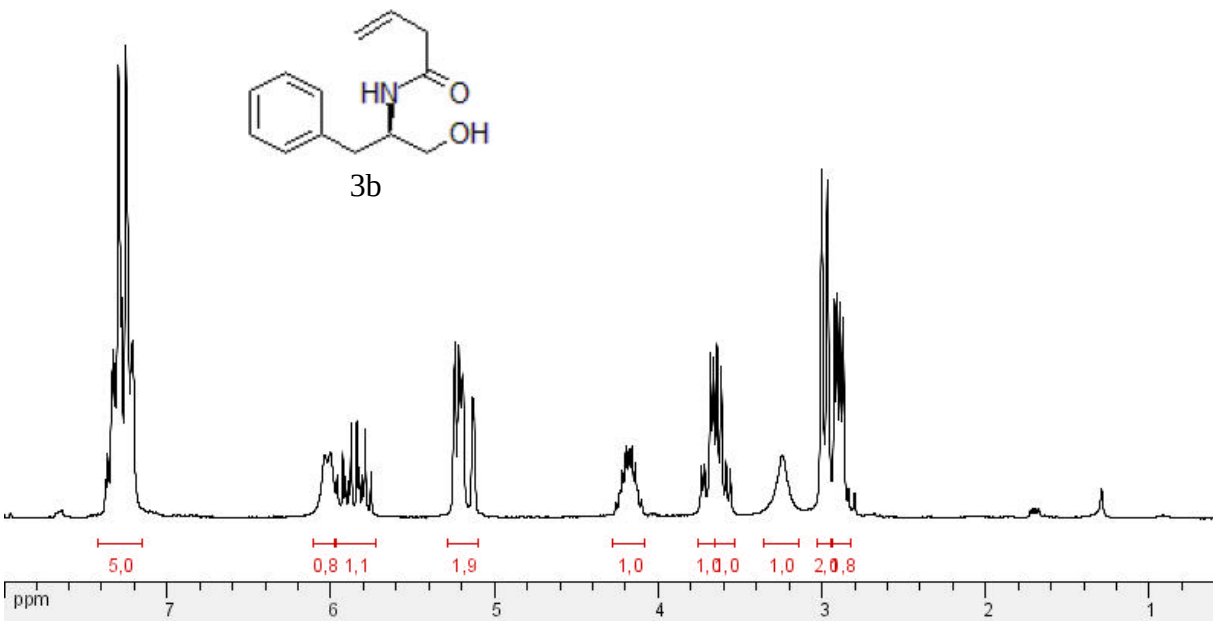
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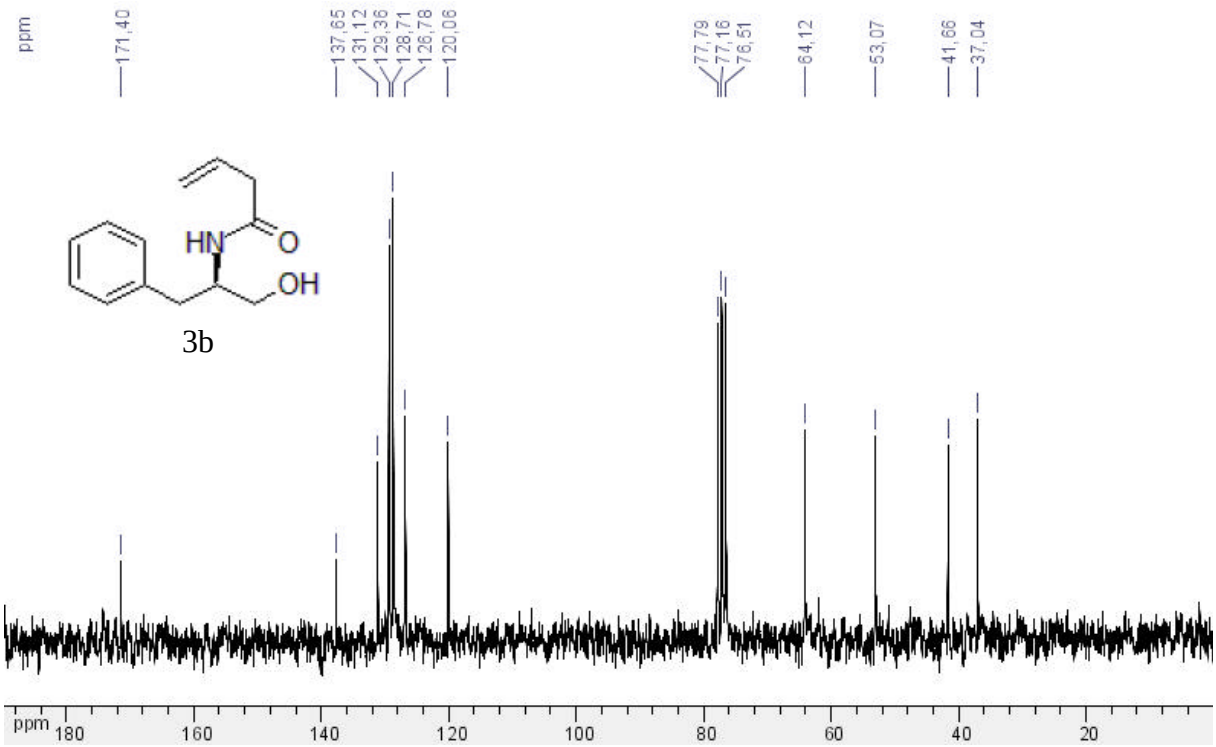
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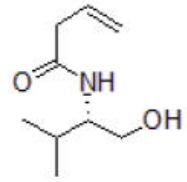
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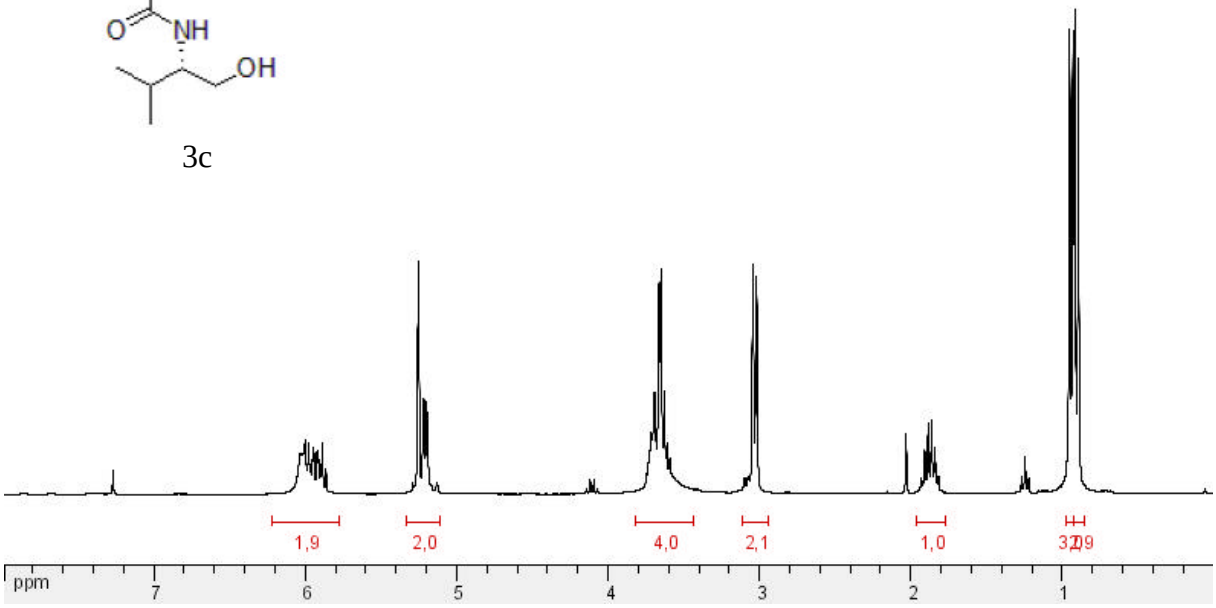
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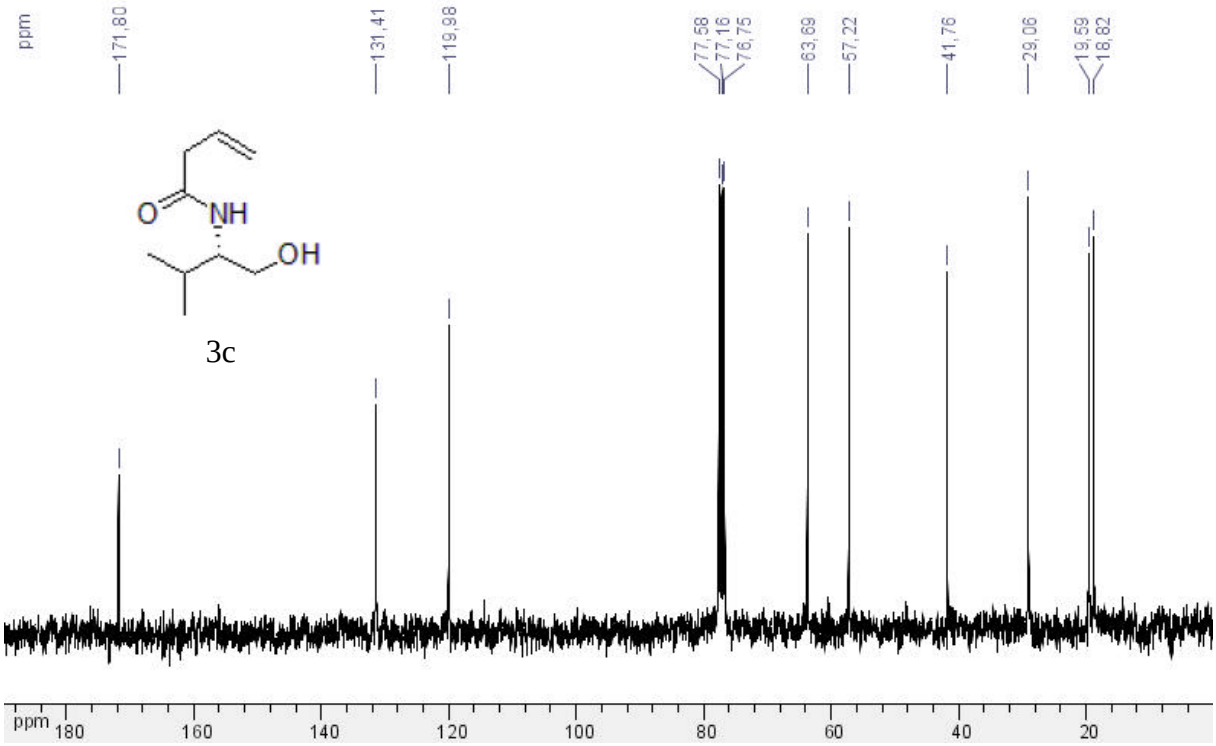
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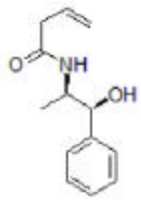
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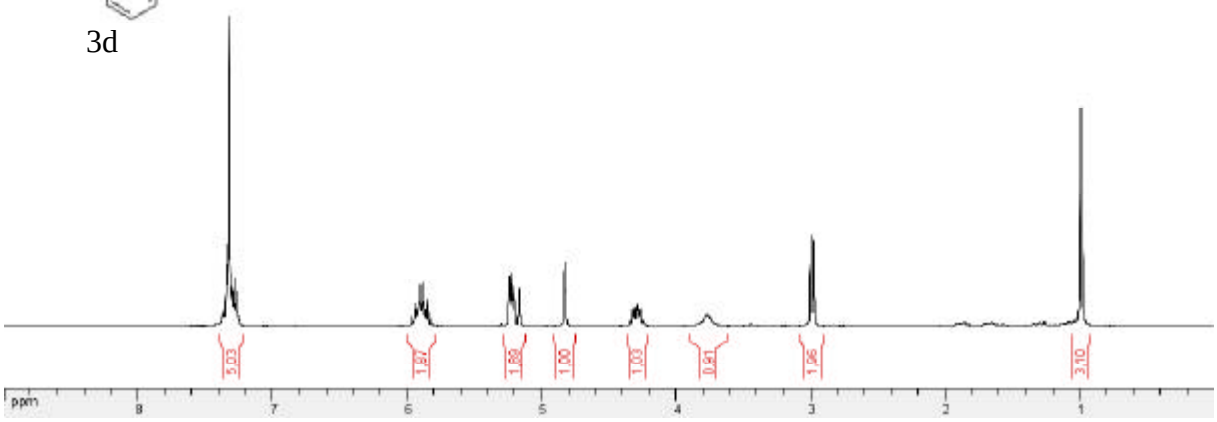
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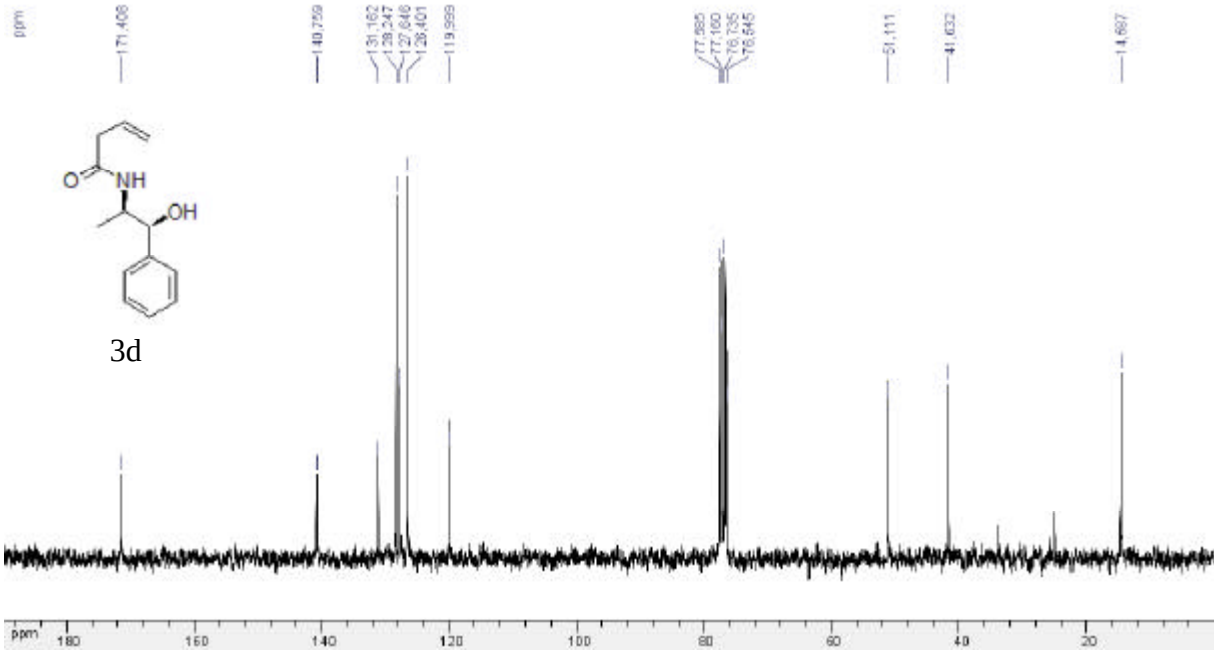
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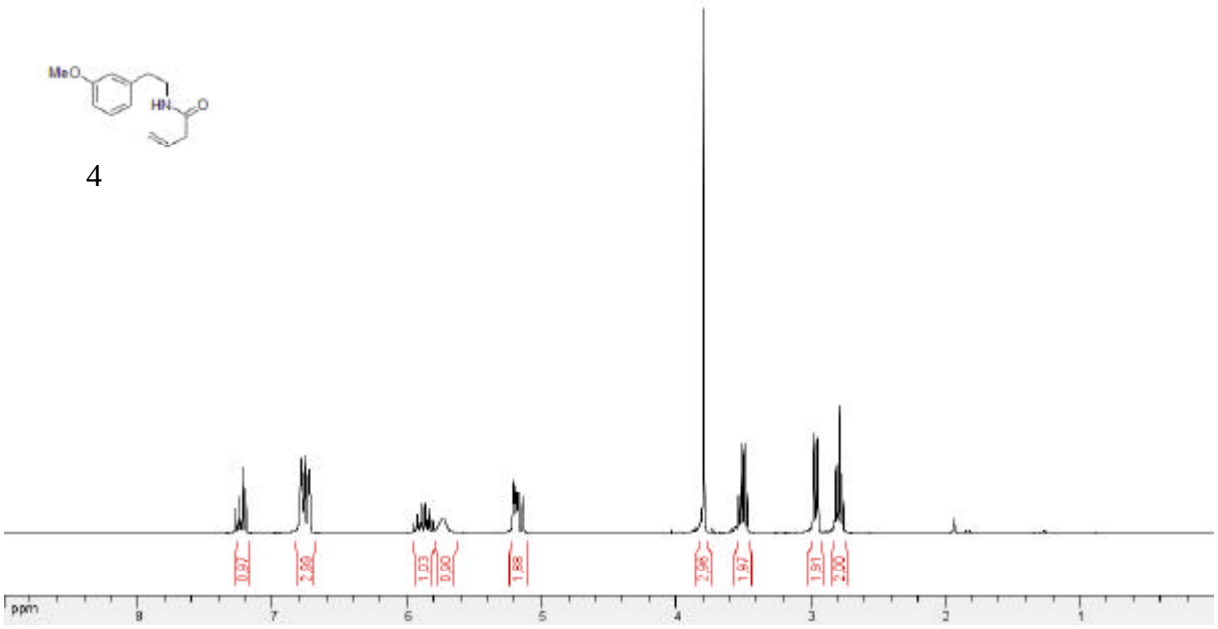
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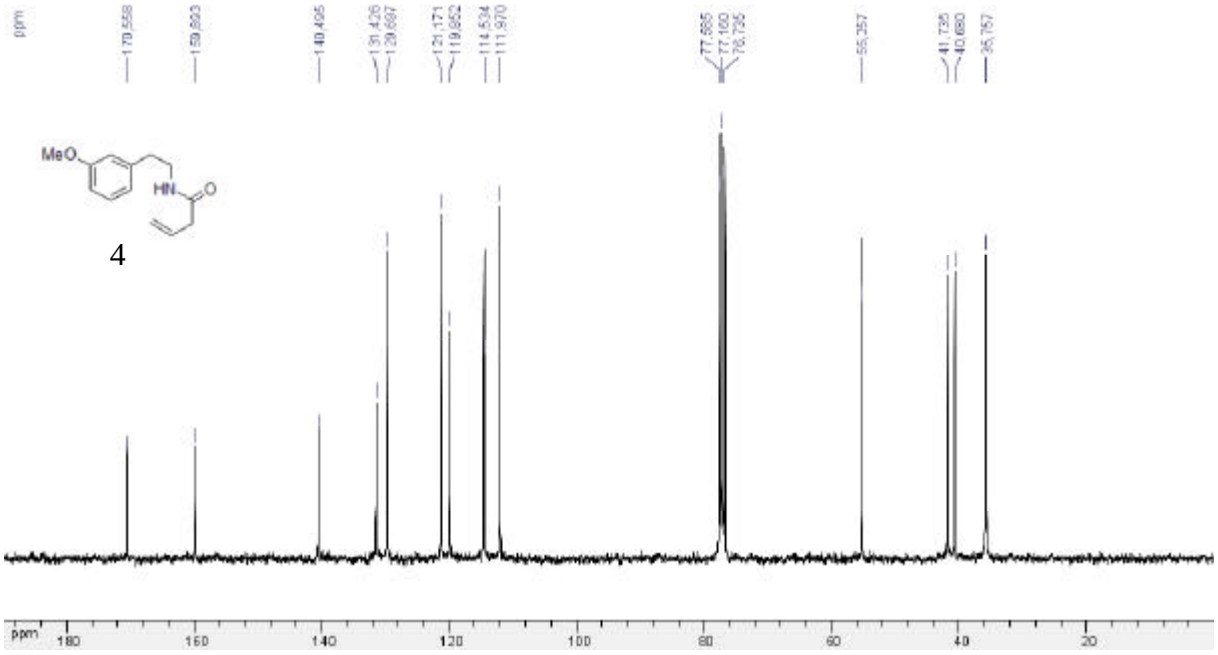
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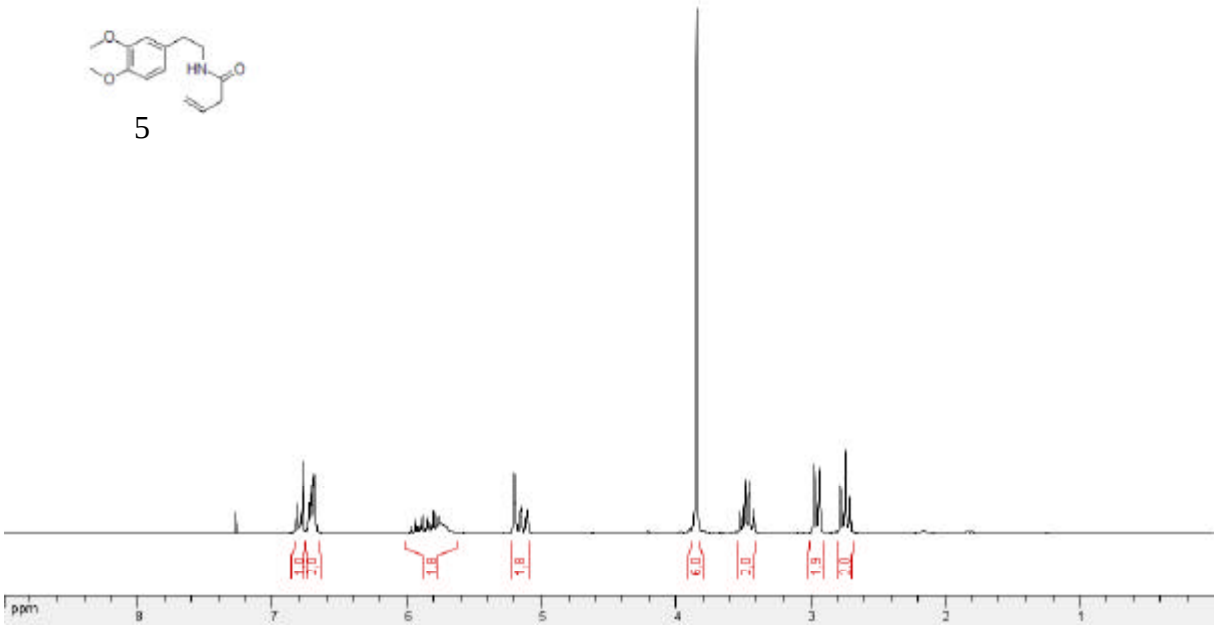
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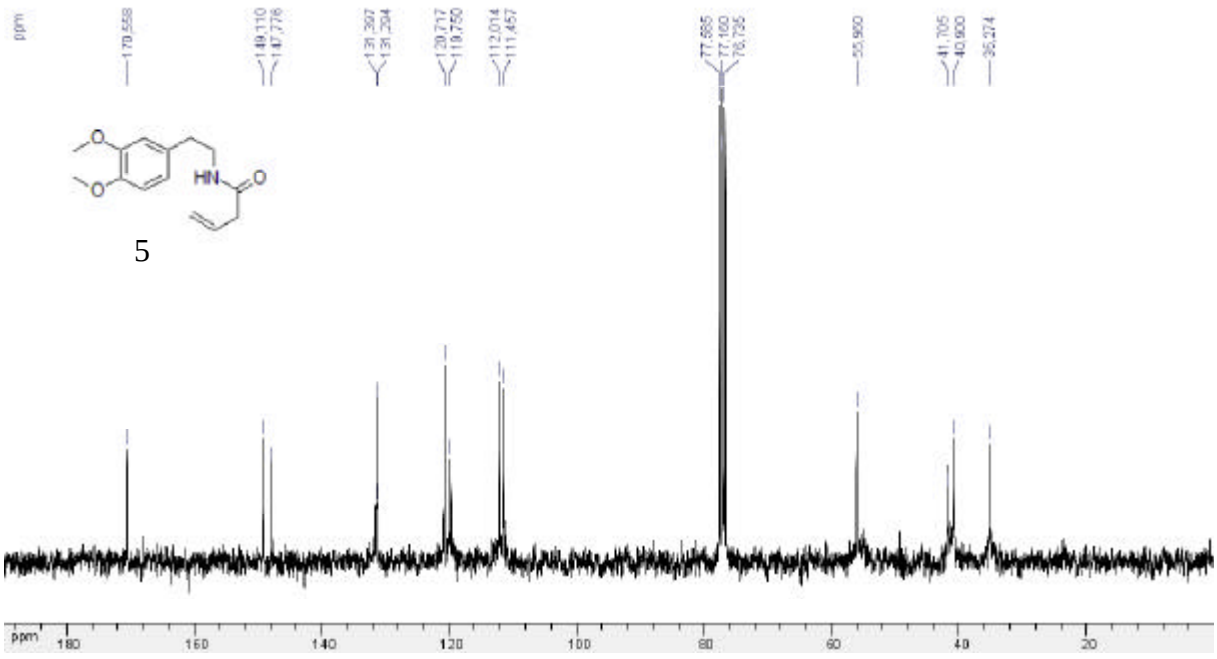
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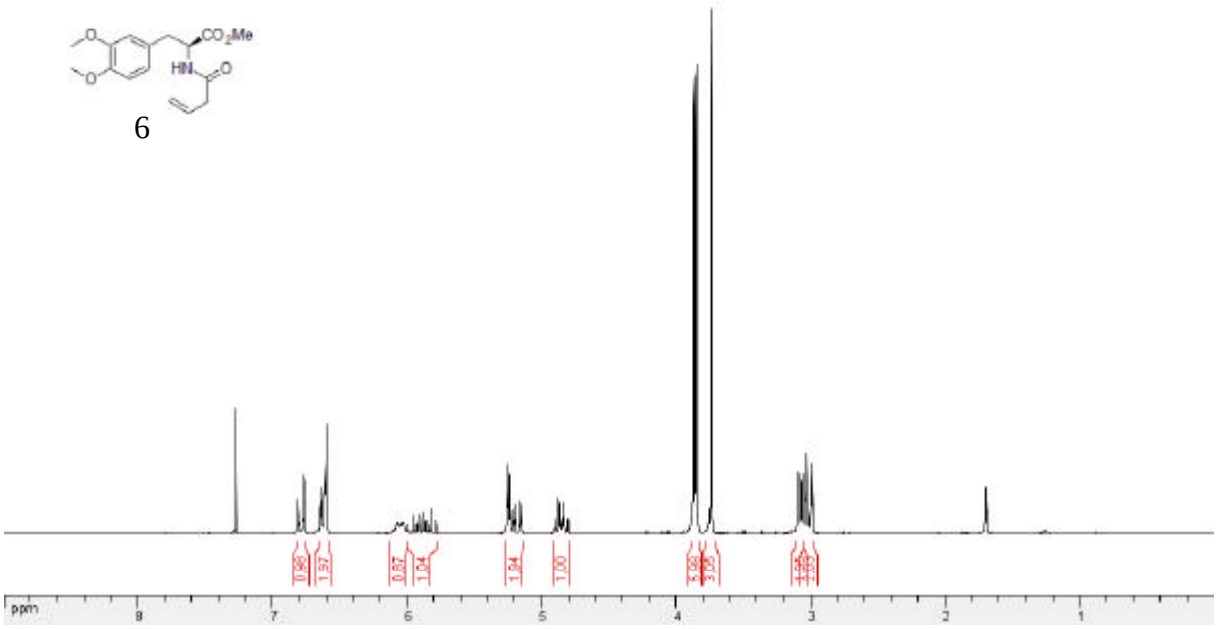
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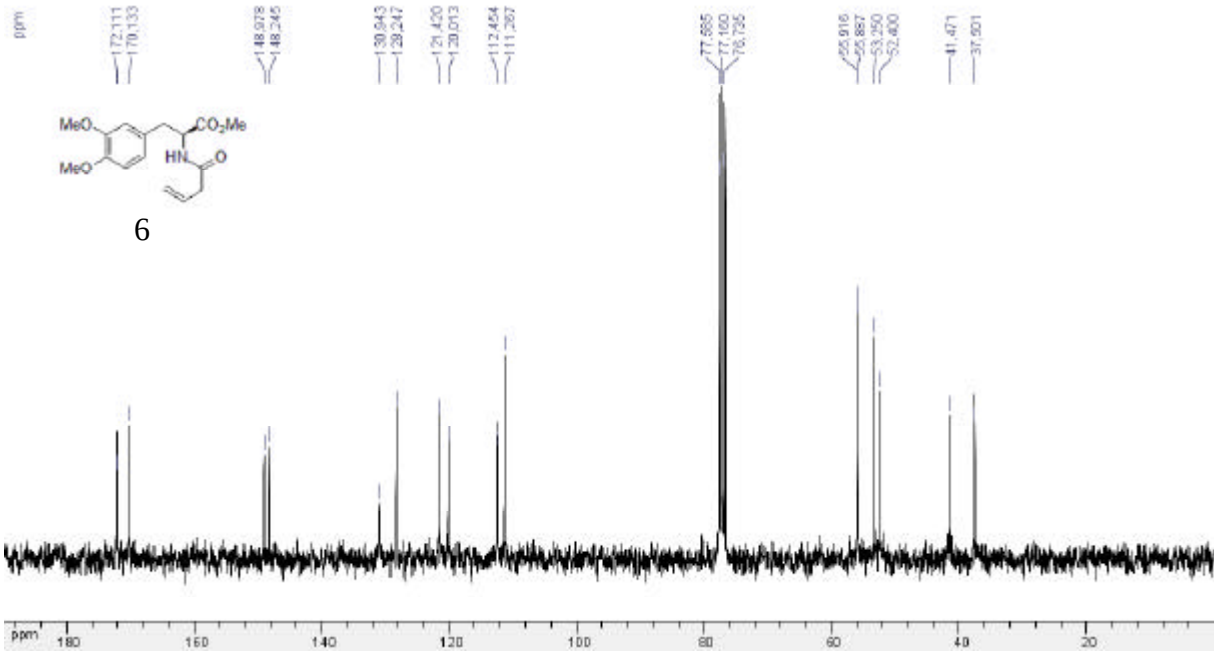
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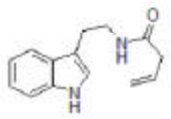

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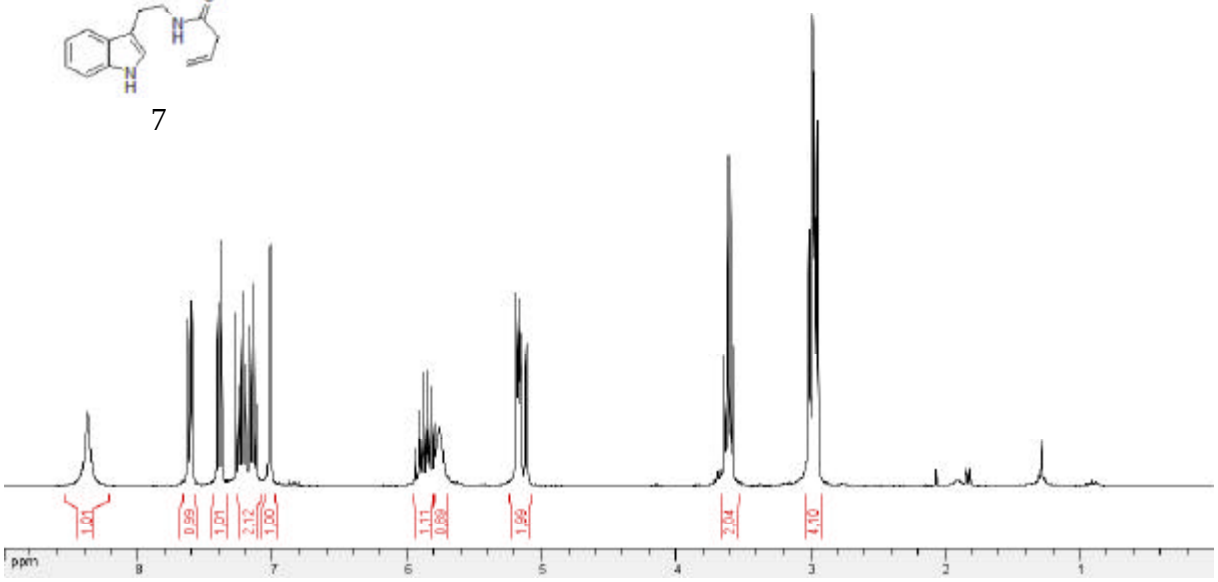
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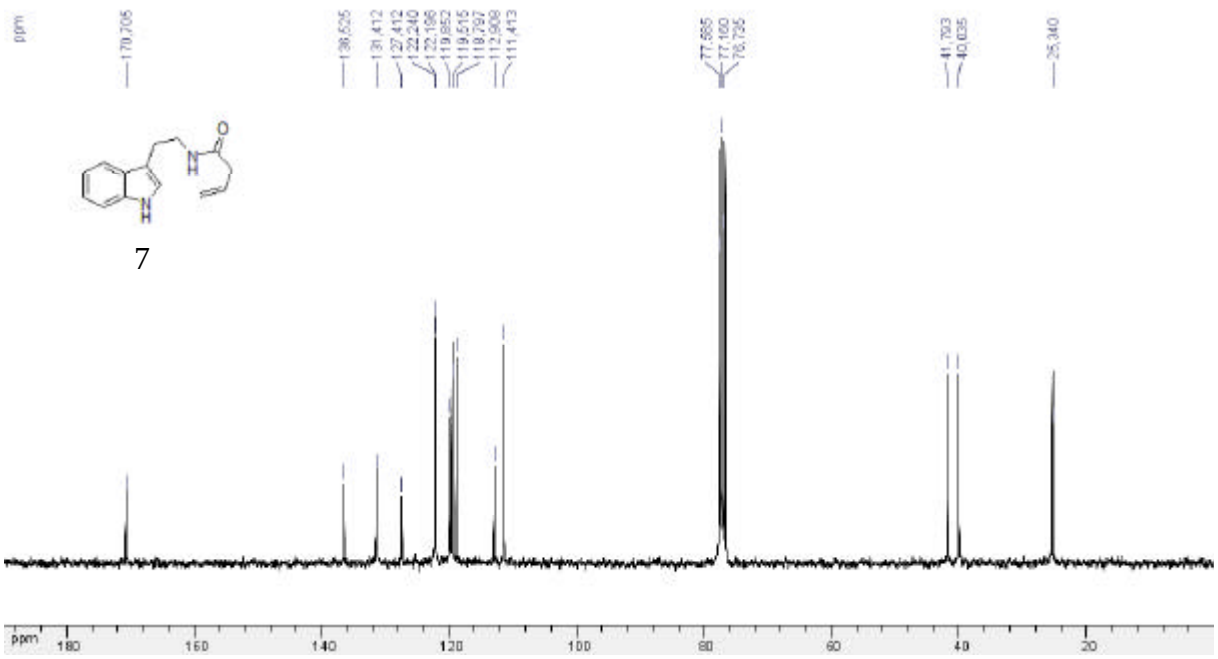
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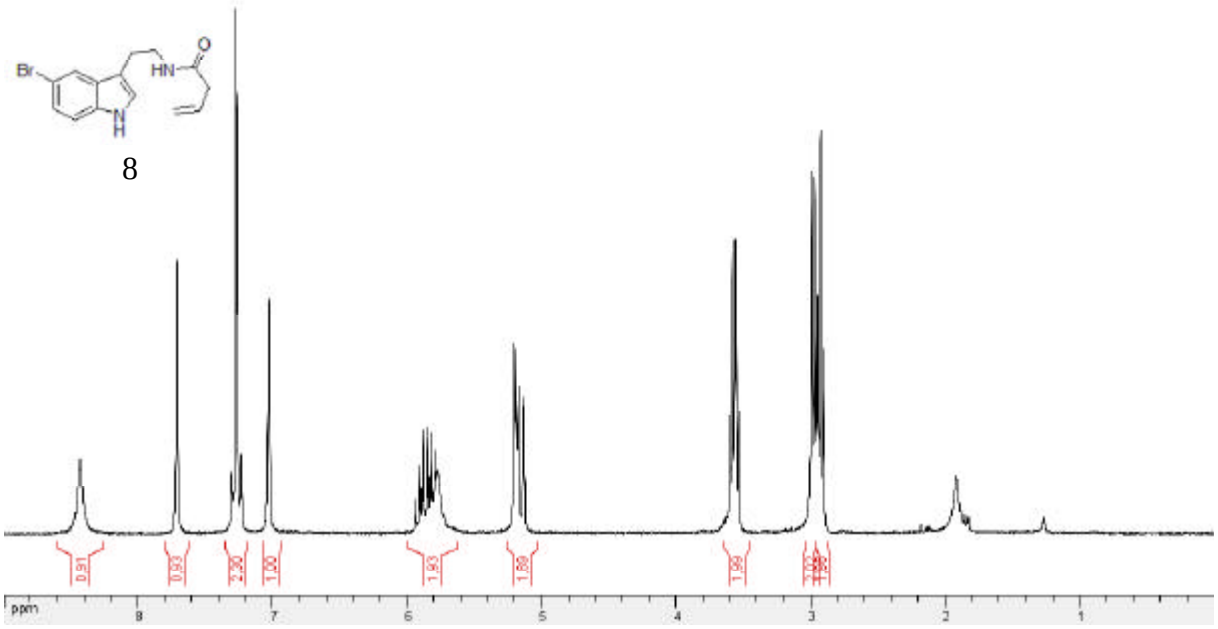
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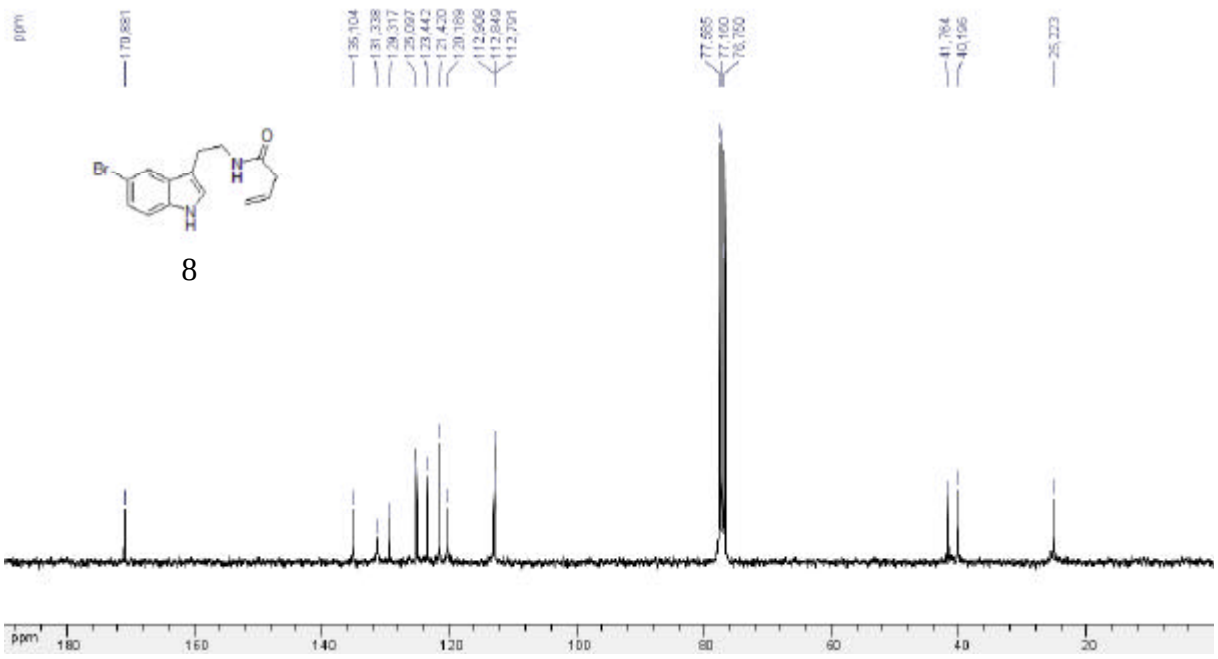
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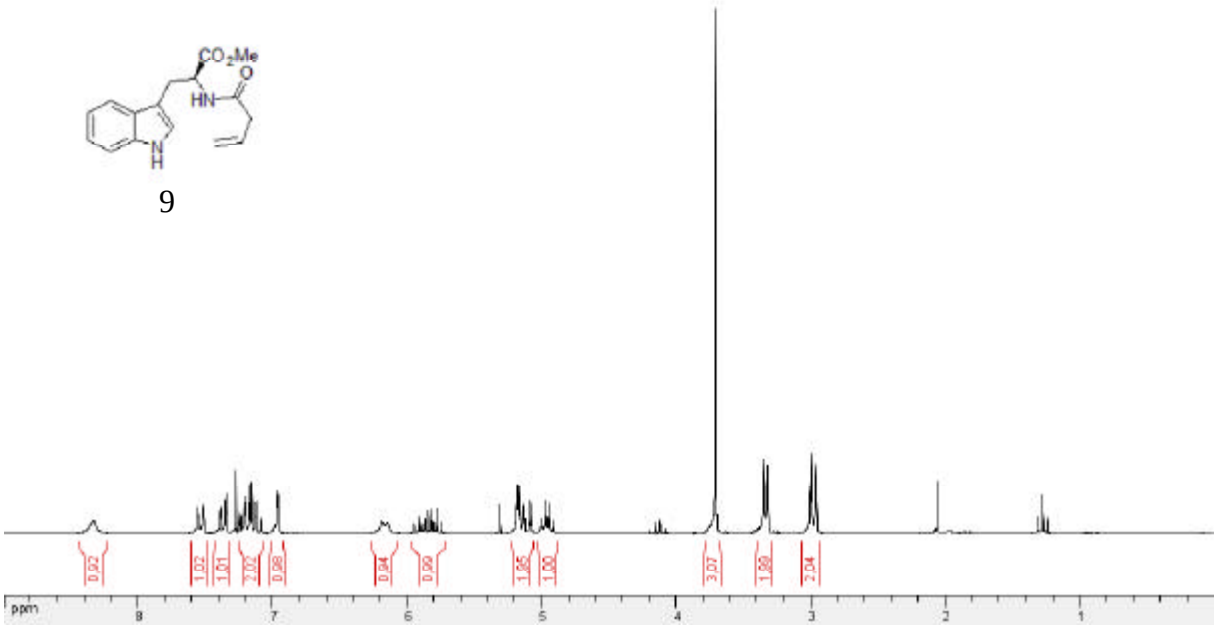
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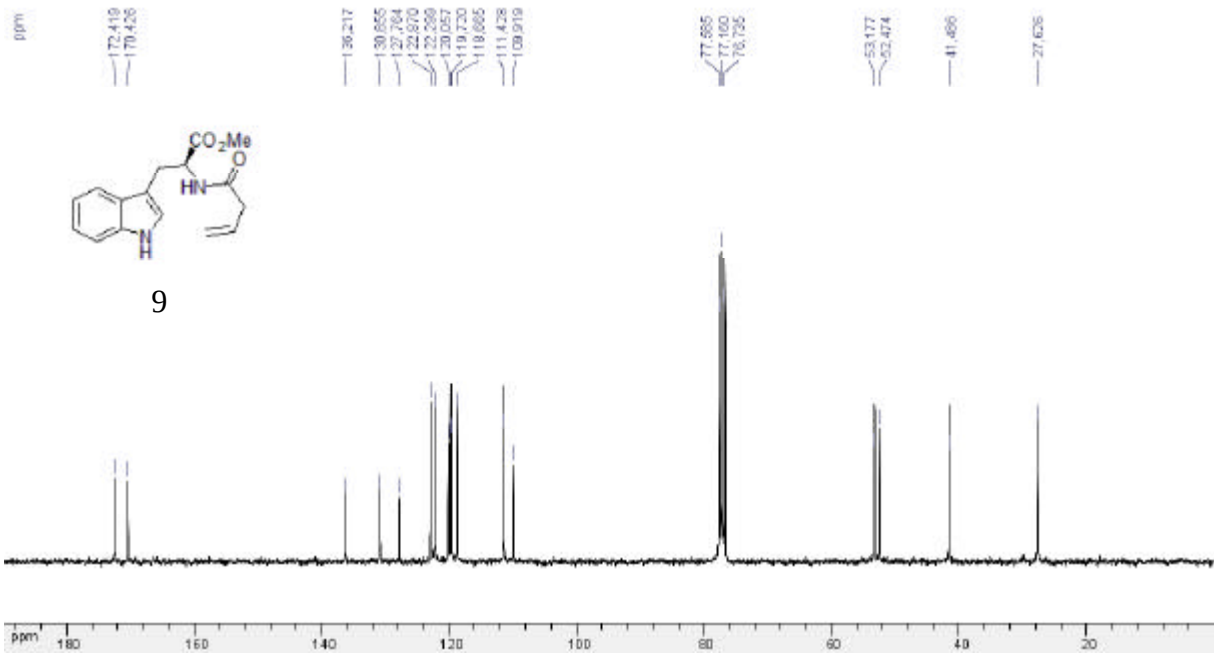
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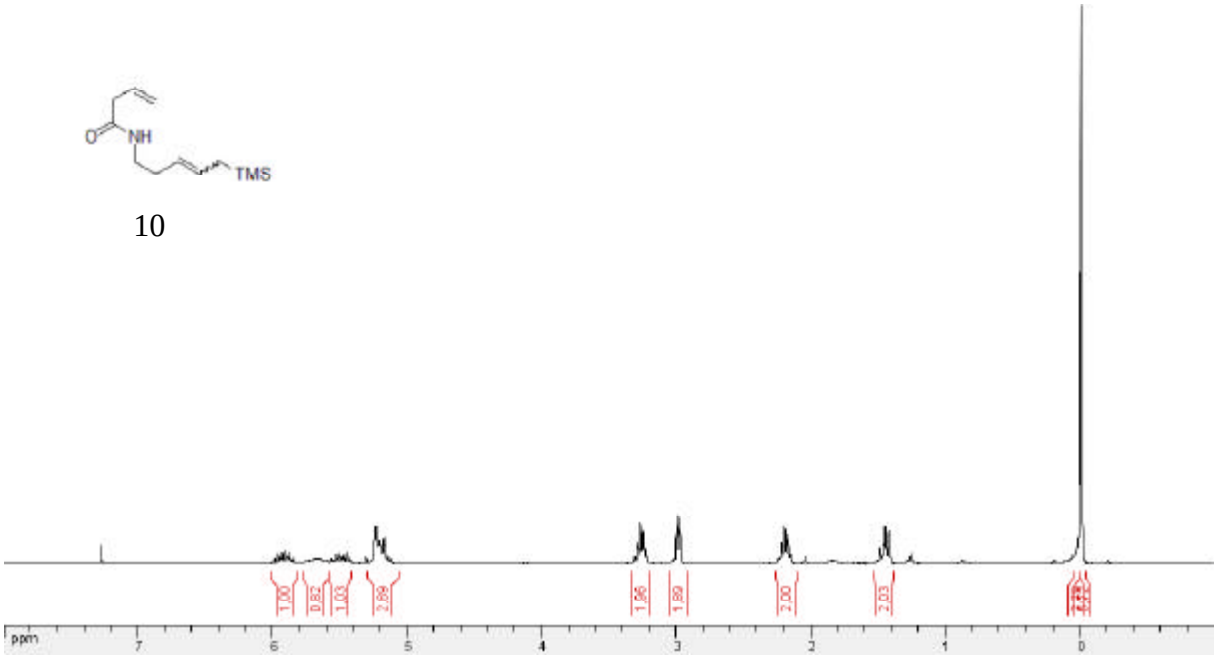
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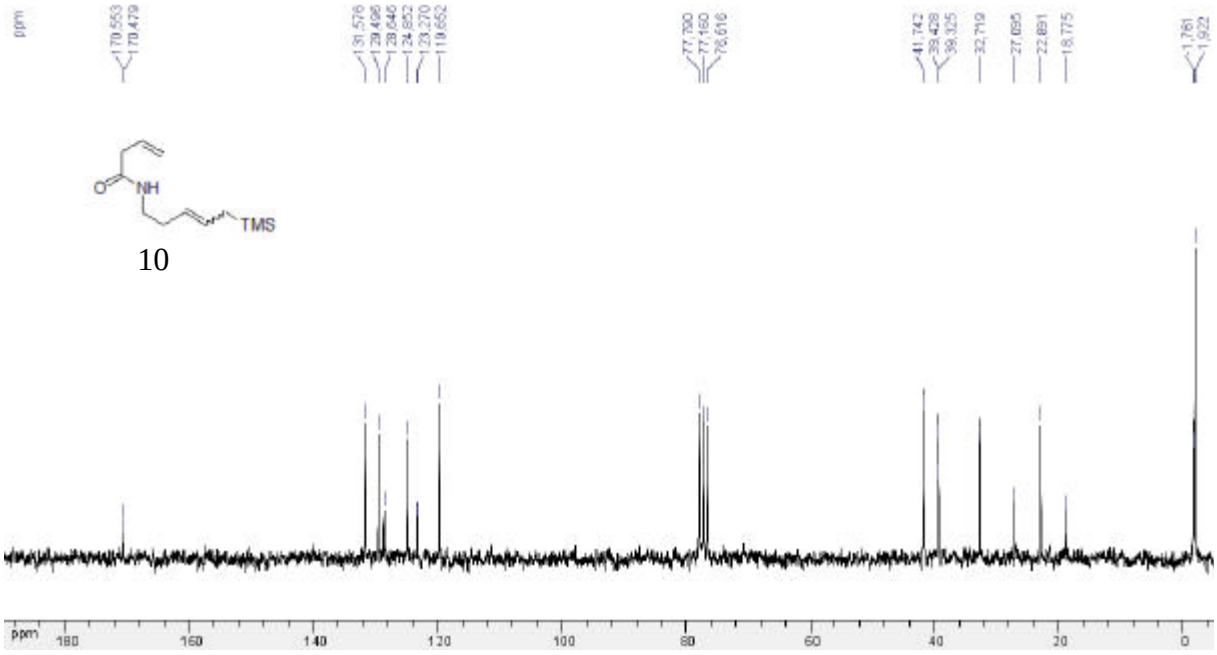
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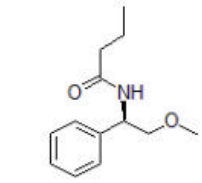
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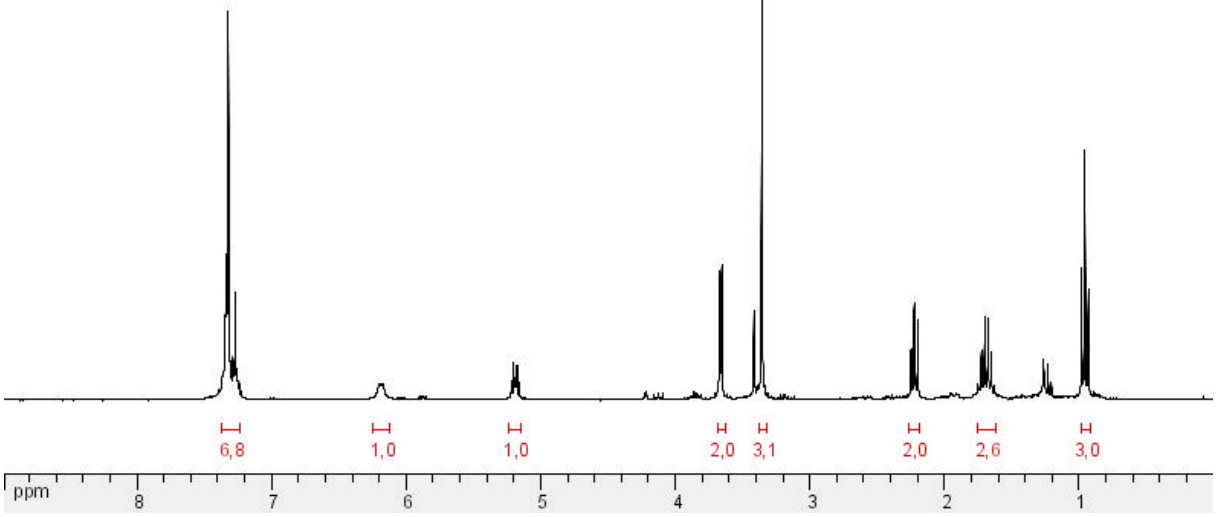
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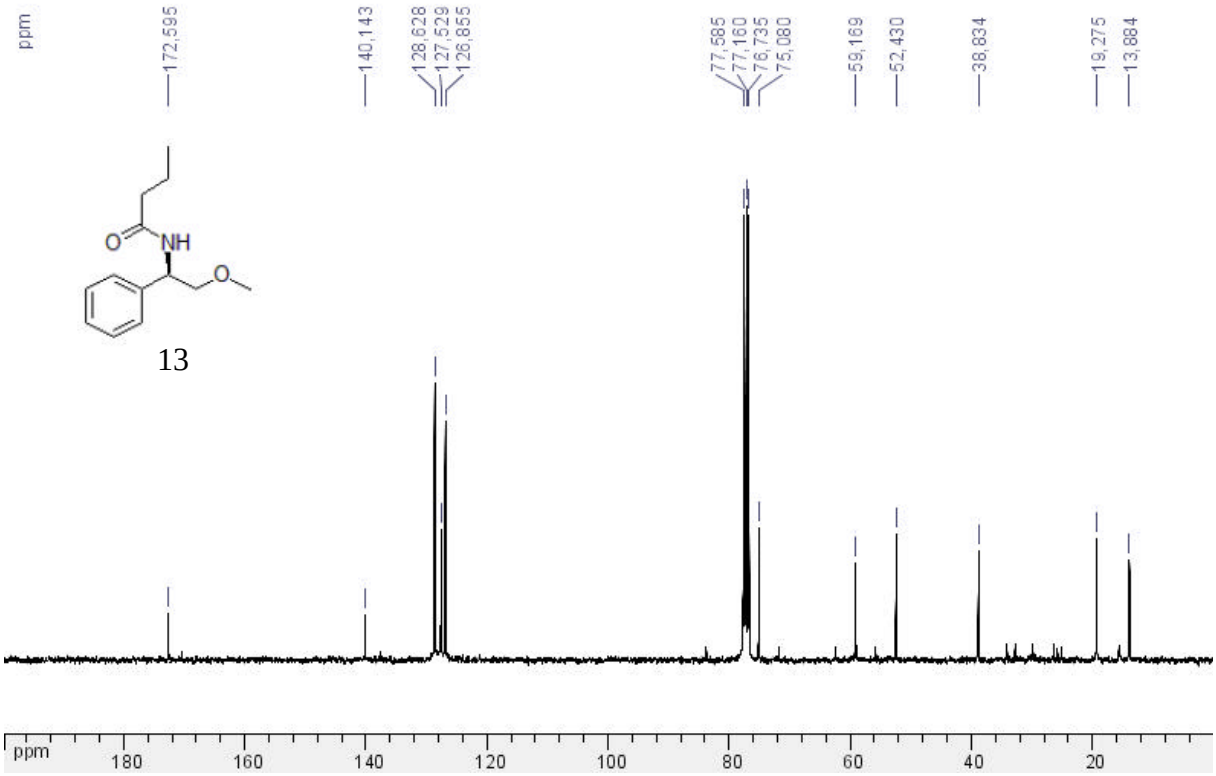
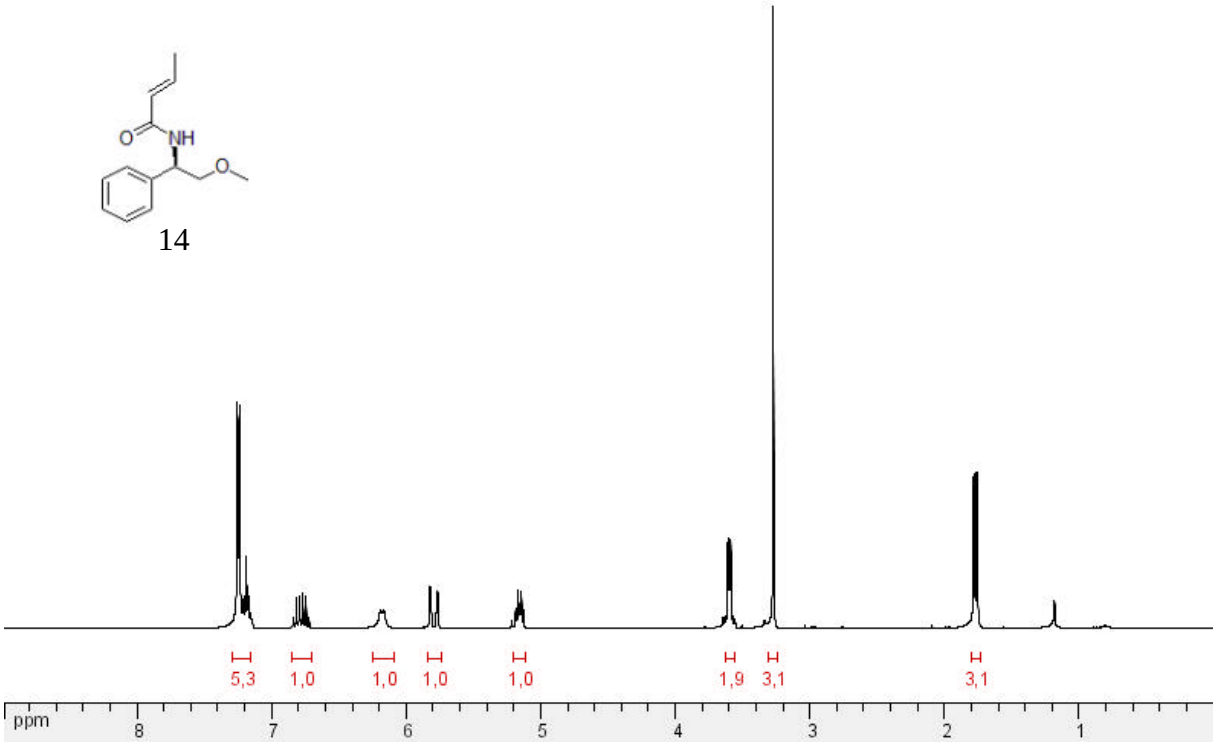
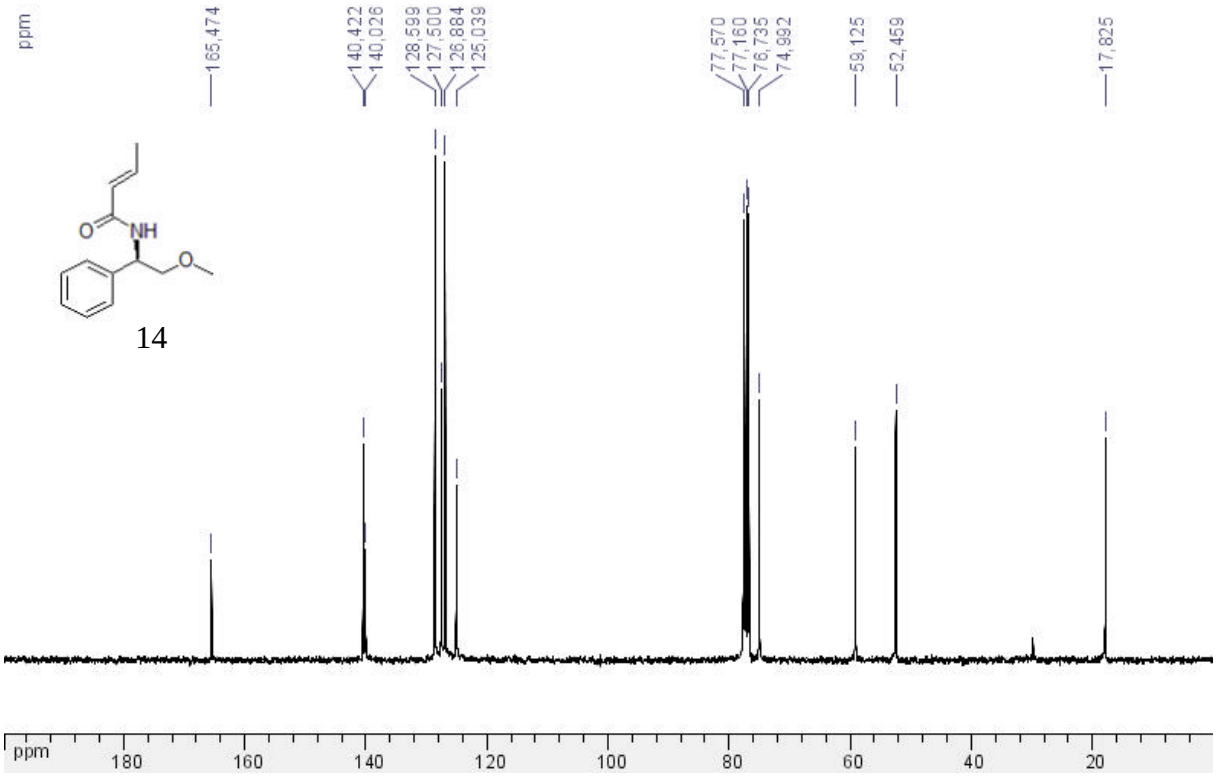
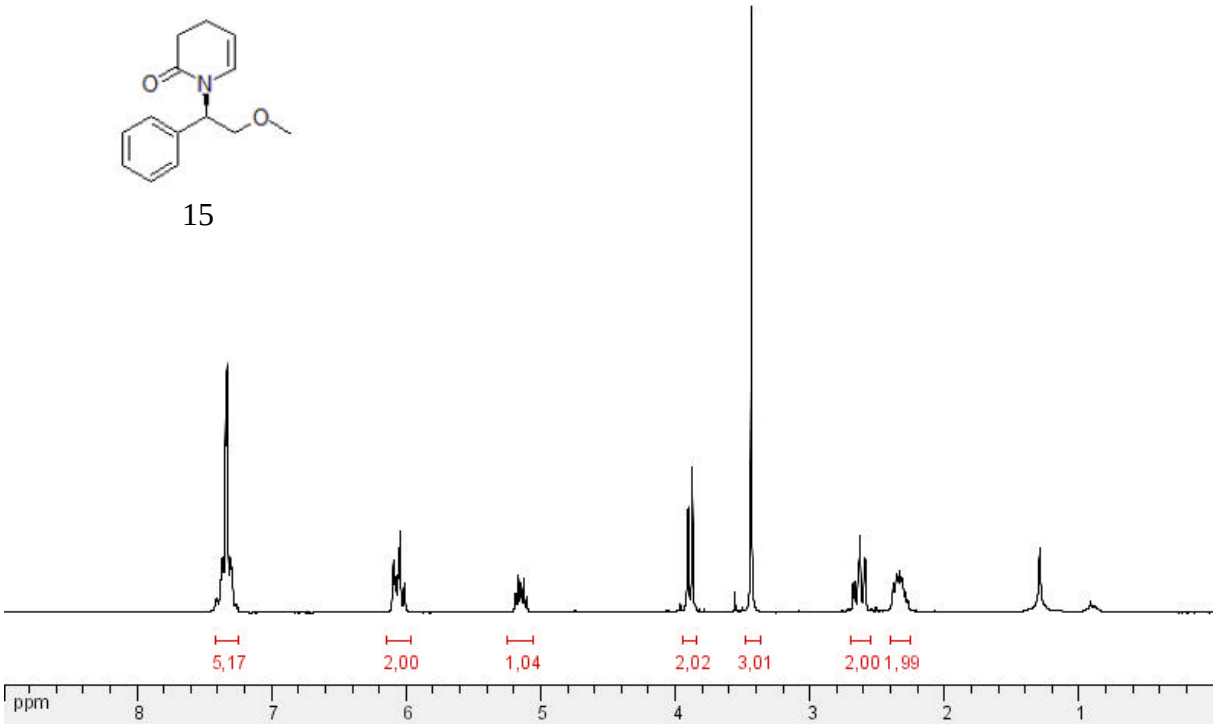

ppm
172,595
140,143
128,628
127,529
126,855
77,585
77,160
76,735
75,080
59,169
52,430
38,834
19,275
13,884
O
NH
O
ppm
180
160
140
120
100
80
60
40
20

13

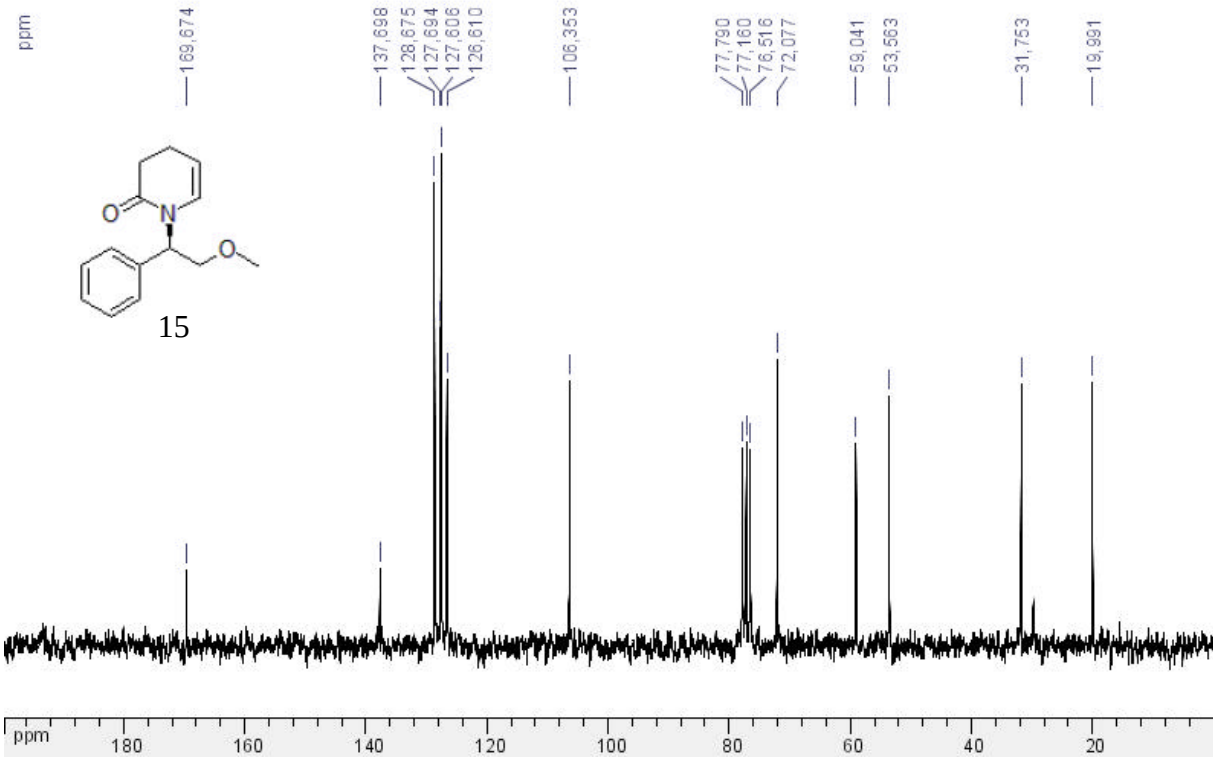

NH
O
O
14
5,3
1,0
1,0
1,0
1,0
1,9
3,1
3,1
ppm
8
7
6
5
4
3
2
1

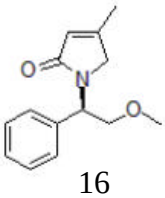

ppm
165,474
140,422
140,026
128,599
127,500
126,884
125,039
77,570
77,160
76,735
74,992
59,125
52,459
17,825
NH
O
O
14
ppm
180
160
140
120
100
80
60
40
20

15

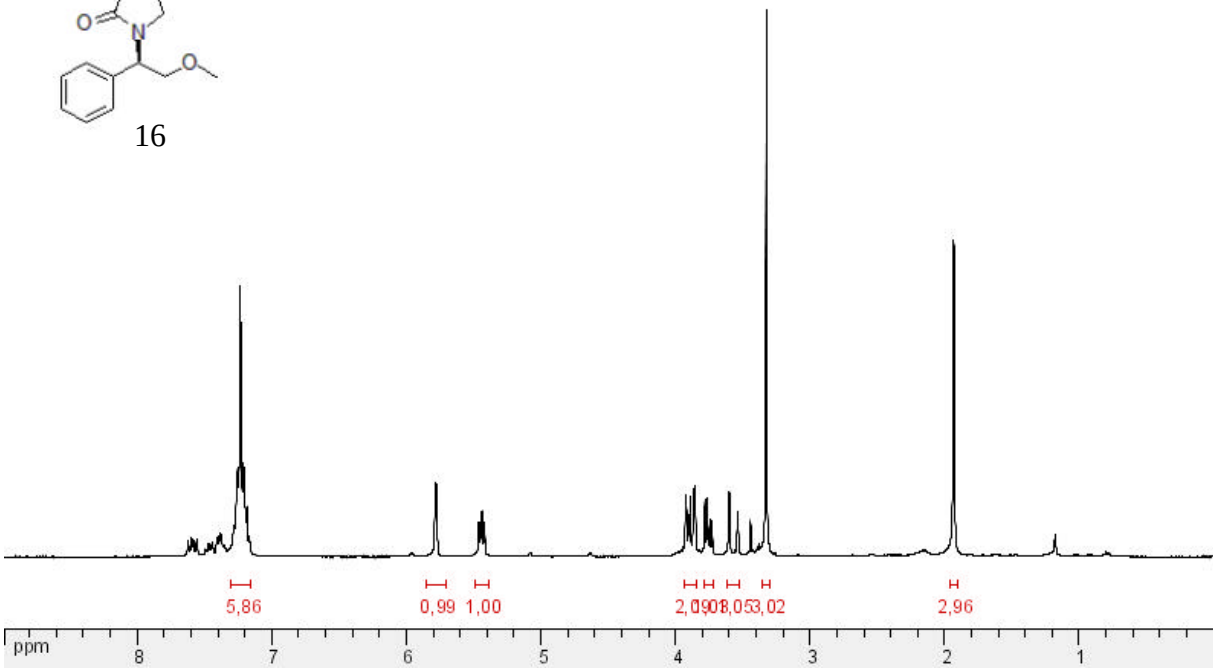

5,17
2,00
1,04
2,02
3,01
2,00
1,99
ppm
8
7
6
5
4
3
2
1

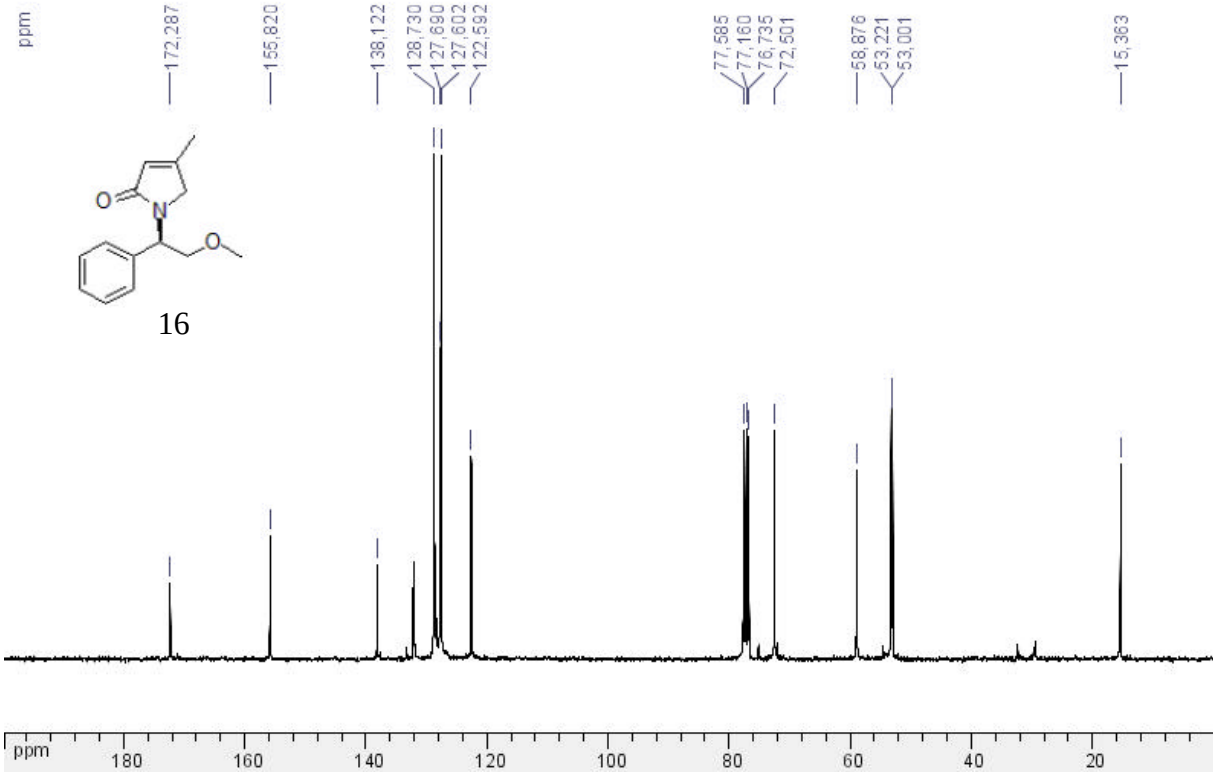
15


ppm
169,674
137,698
128,675
127,694
127,606
126,610
106,353
77,790
77,160
76,516
72,077
59,041
53,563
31,753
19,991
ppm
180
160
140
120
100
80
60
40
20

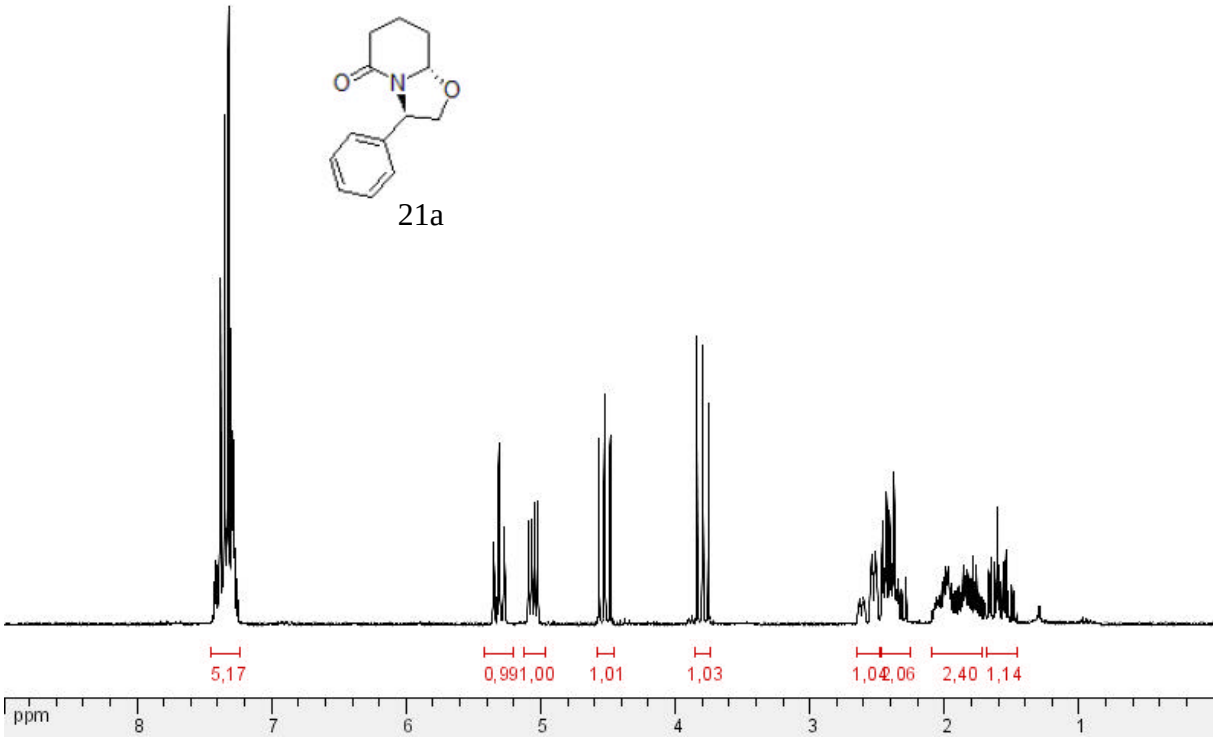


16

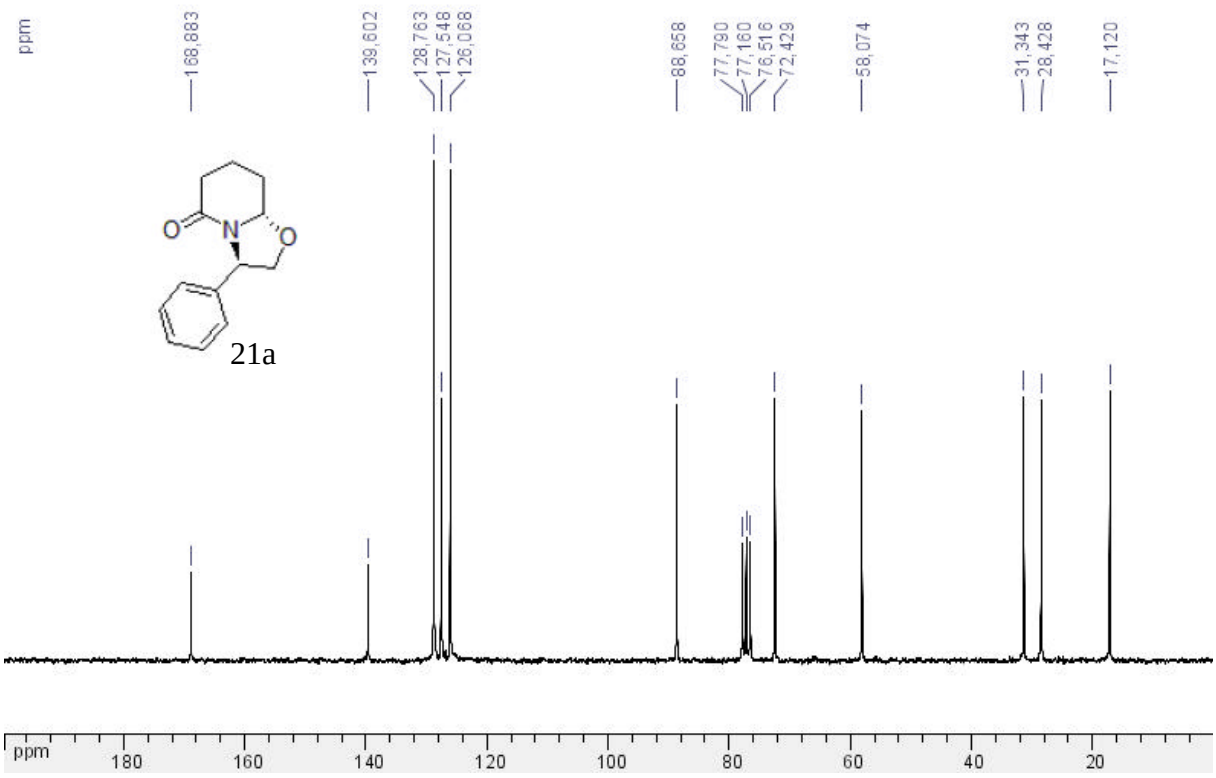

5,86
0,99
1,00
2,96
ppm
8
7
6
5
4
3
2
1


ppm
172,287
155,820
138,122
128,730
127,690
127,602
122,592
77,585
77,160
76,735
72,501
58,876
53,221
53,001
15,363
ppm
180
160
140
120
100
80
60
40
20

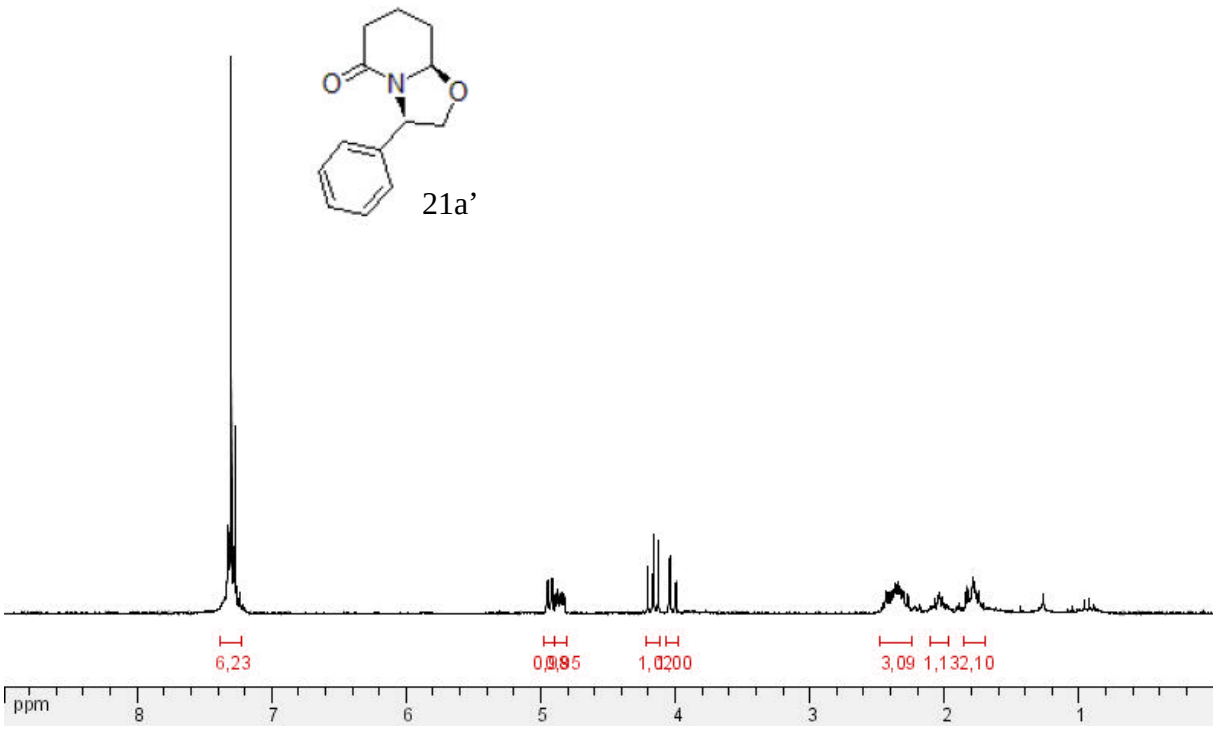
16


O
N
O
5,17
0,99
1,00
1,01
1,03
1,04
2,06
2,40
1,14
ppm
8
7
6
5
4
3
2
1

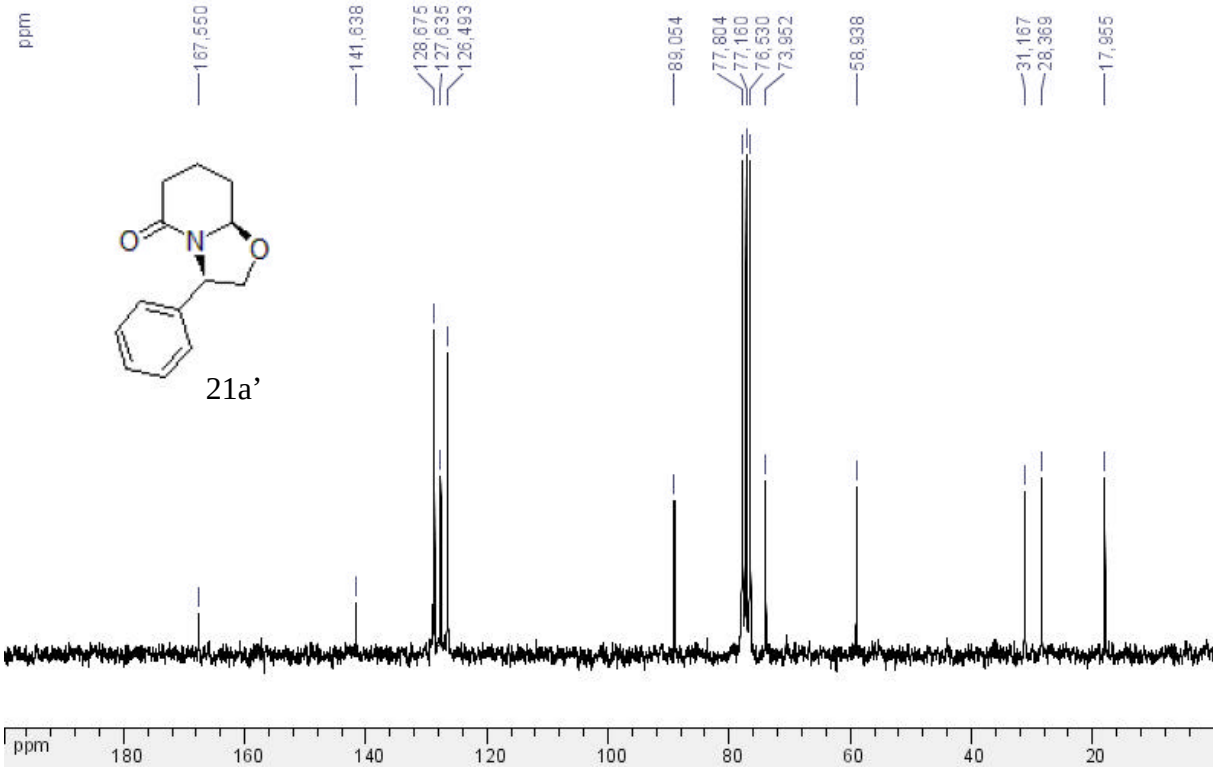
21a


ppm
168,883
139,602
128,763
127,548
126,068
88,658
77,790
77,160
76,516
72,429
58,074
31,343
28,428
17,120
O
N
O
ppm
180
160
140
120
100
80
60
40
20

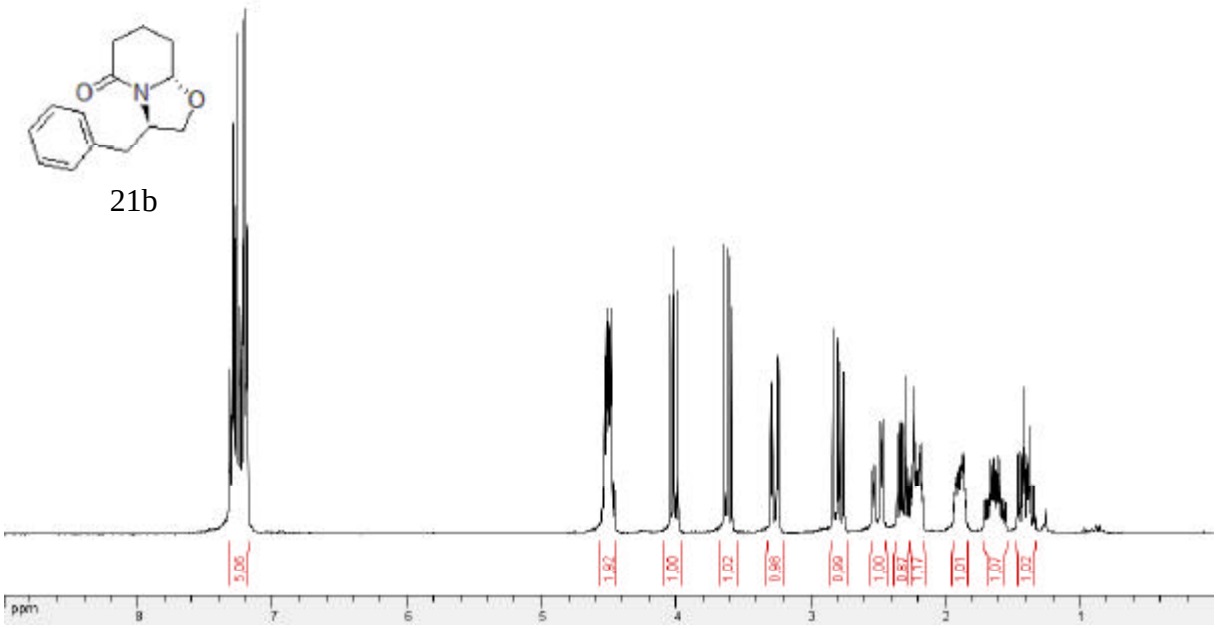
21a


O
N
O
6,23
3,09
1,13
2,10
ppm
8
7
6
5
4
3
2
1

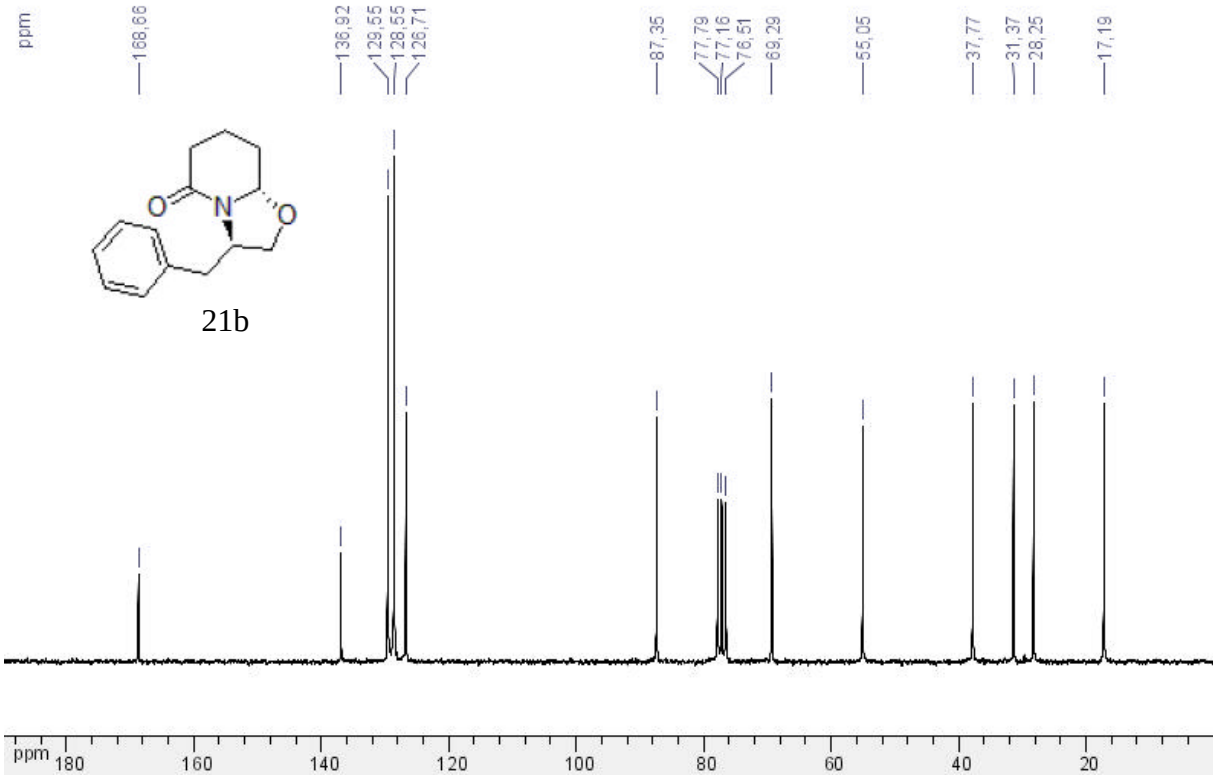
21a’


ppm
167,550
141,638
128,675
127,635
126,493
89,054
77,804
77,160
76,530
73,952
58,938
31,167
28,369
17,955
O
N
O
ppm
180
160
140
120
100
80
60
40
20

21a’

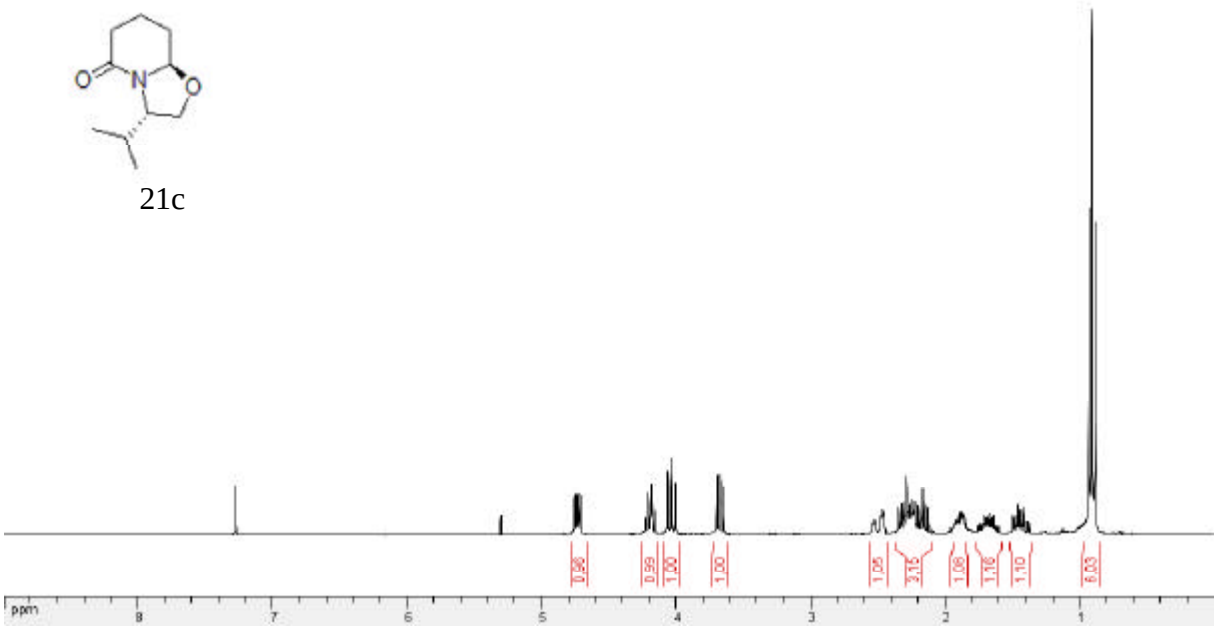


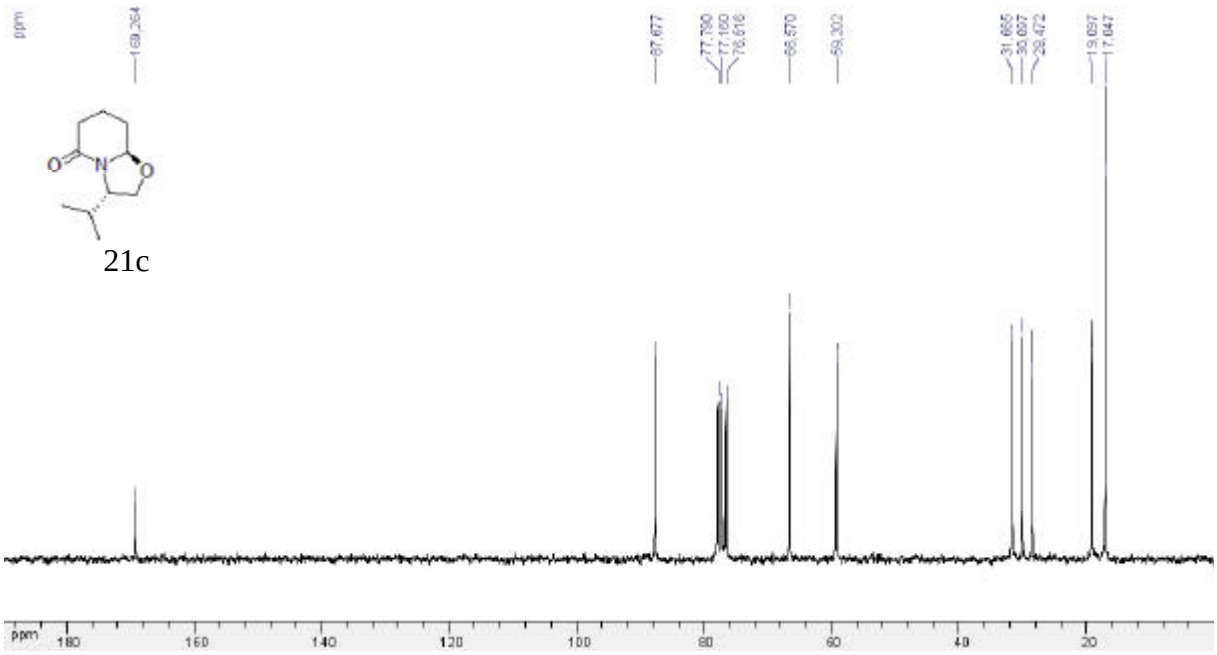
21b



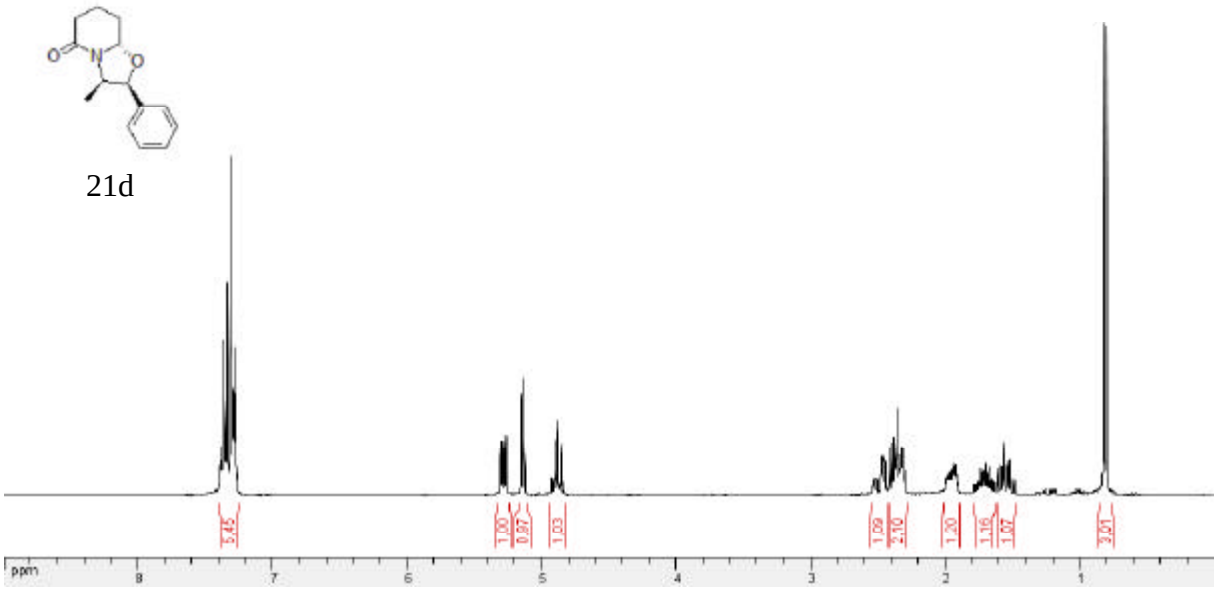
21b

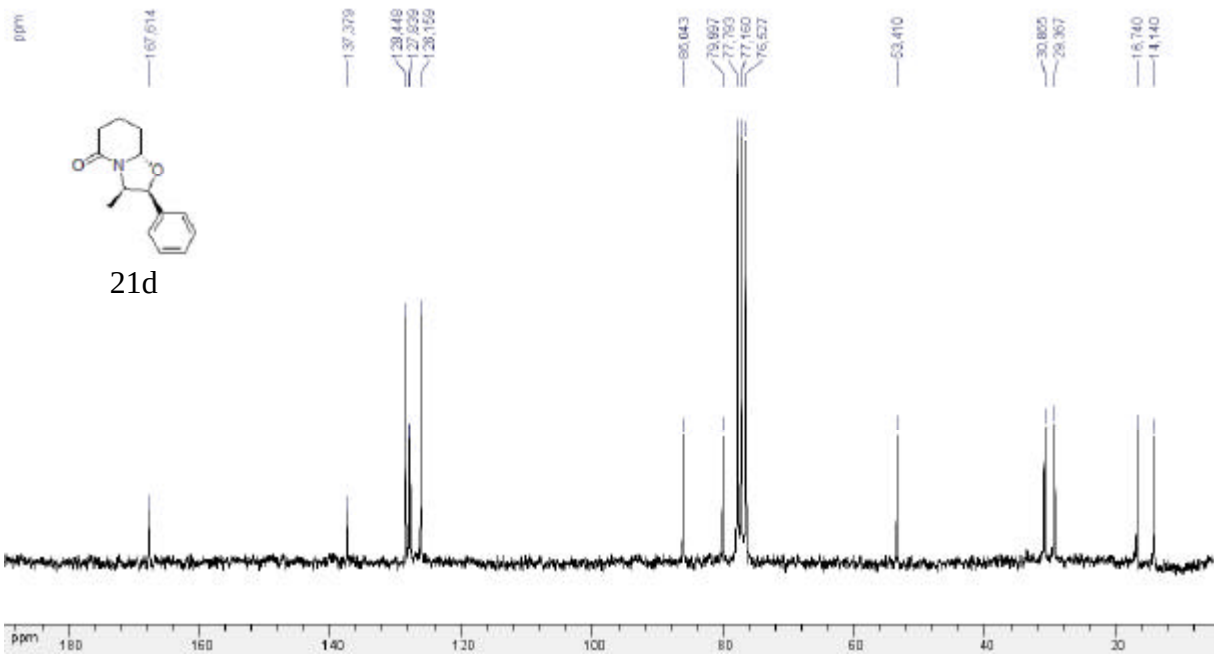
21c

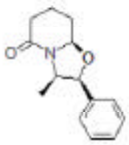

0.86
0.99
1.00
1.00
1.05
3.15
1.06
1.16
1.10
6.03
ppm
8
7
6
5
4
3
2
1


ppm
169.364
87.677
77.790
77.160
76.616
66.570
59.302
31.665
30.697
28.472
19.697
17.647
ppm
180
160
140
120
100
80
60
40
20

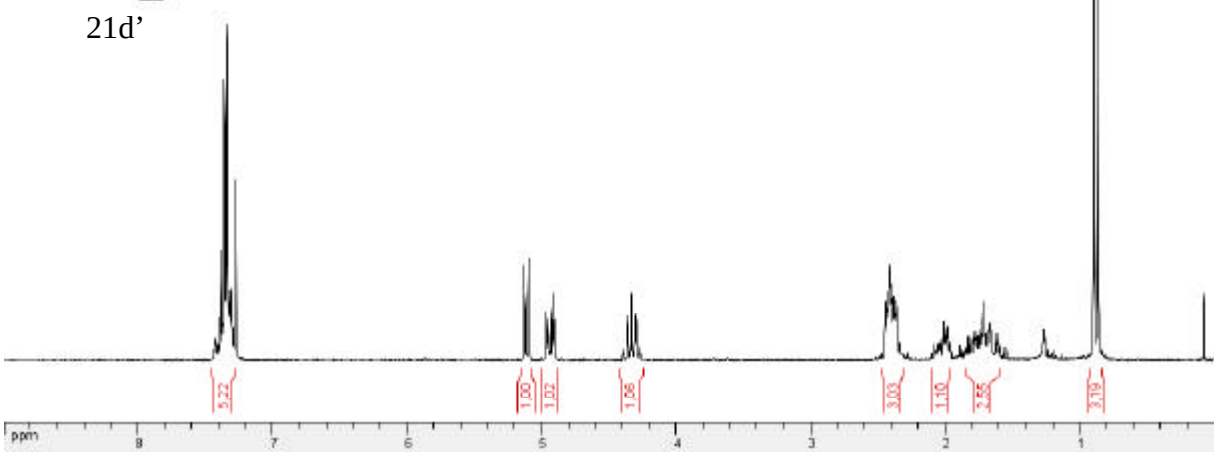
21c

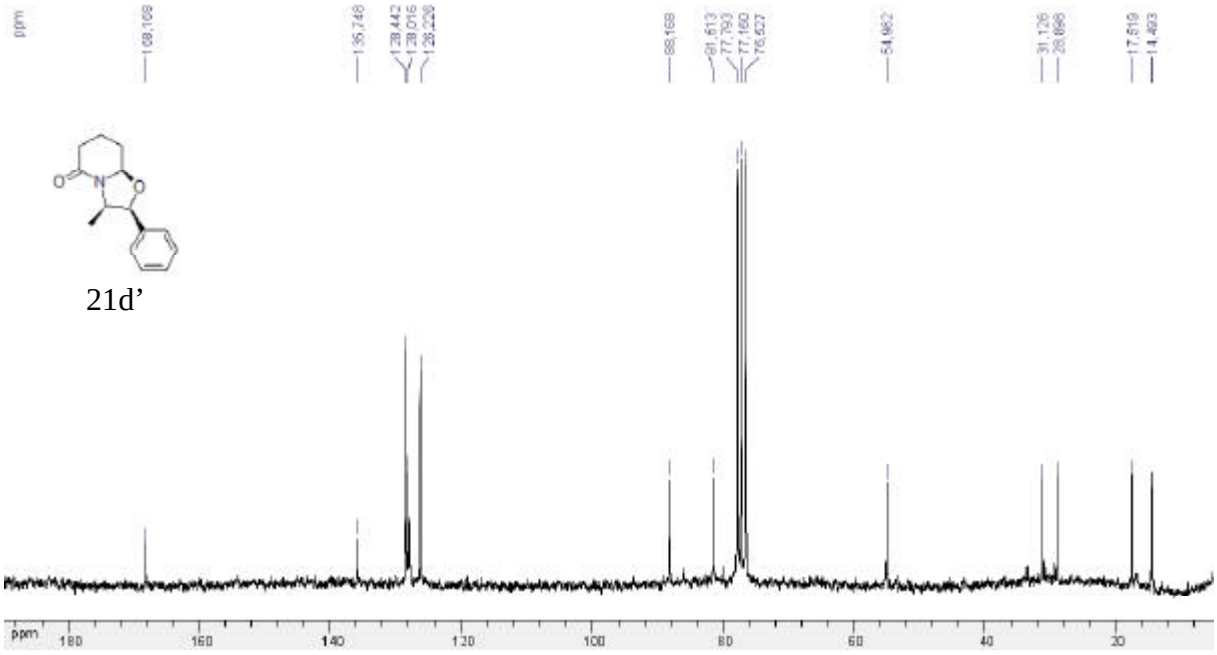

21d
5.45
1.00
0.97
1.03
1.09
2.10
1.20
1.16
1.02
3.01
ppm


ppm
167.614
137.379
129.446
127.899
126.159
86.643
79.997
77.760
77.160
76.527
53.410
30.865
29.367
16.740
14.140
21d



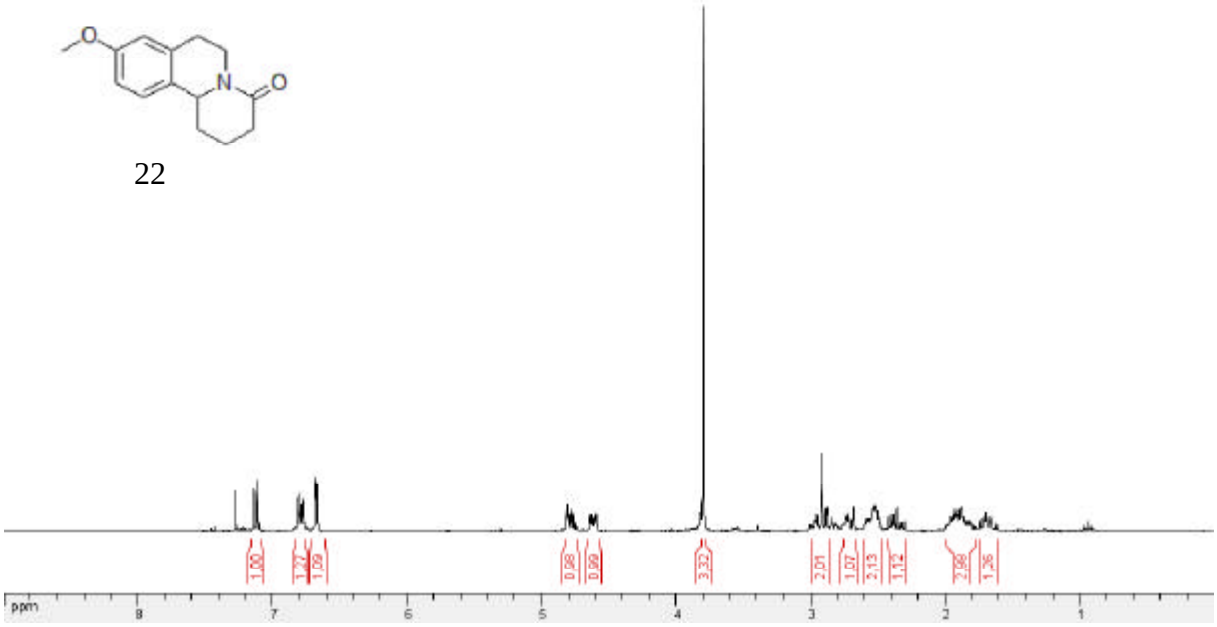
21d’

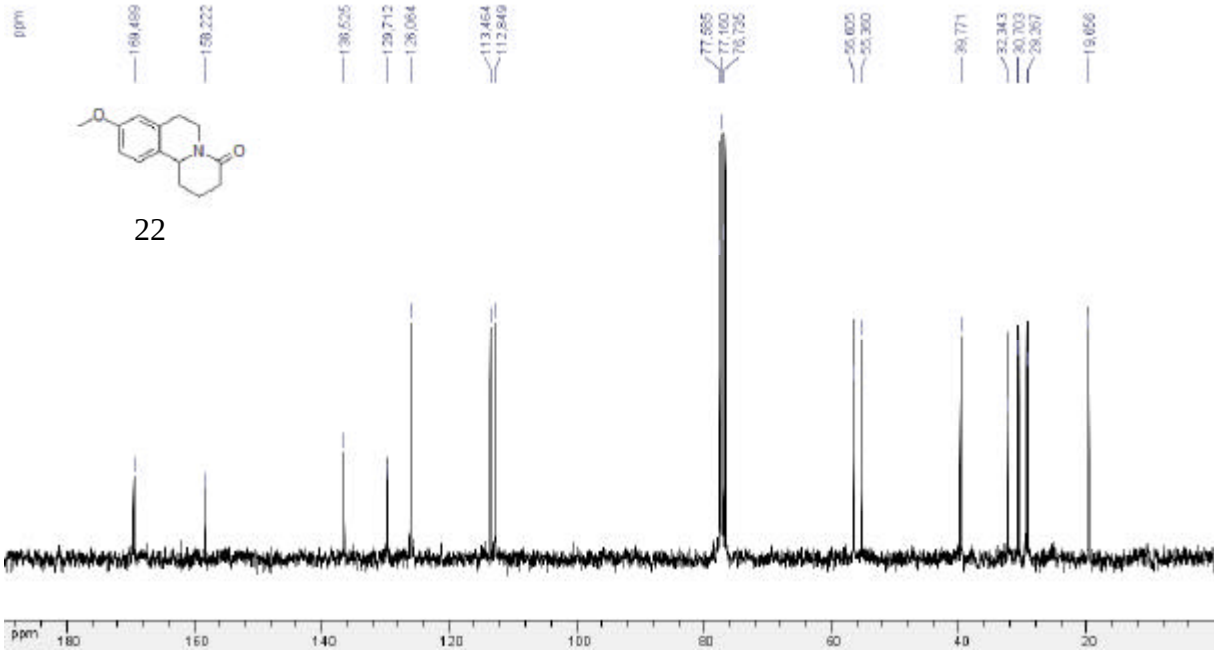

5.22
1.00
1.02
1.06
3.03
1.10
2.65
3.19
ppm
8
7
6
5
4
3
2
1


ppm
169.169
135.748
128.442
128.016
126.226
88.168
81.613
77.793
77.160
76.527
54.962
31.126
28.886
17.619
14.483
ppm
180
160
140
120
100
80
60
40
20

21d’

22

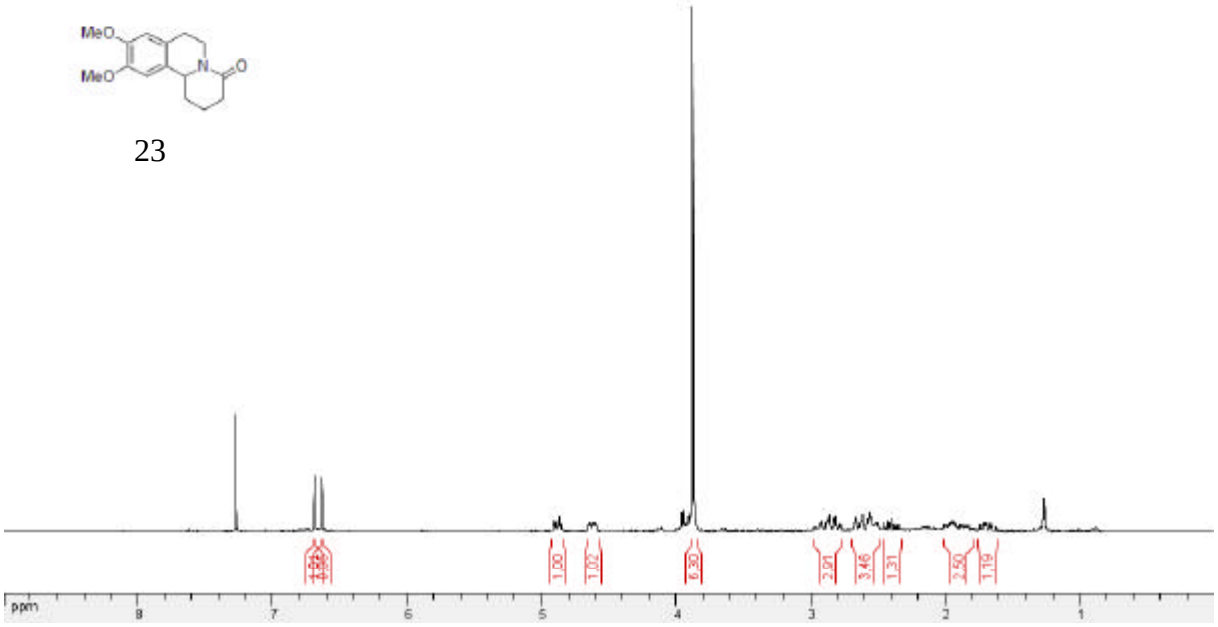

1.00
1.07
1.09
0.98
0.98
3.32
2.01
1.07
2.15
1.12
2.96
1.26
ppm
8
7
6
5
4
3
2
1

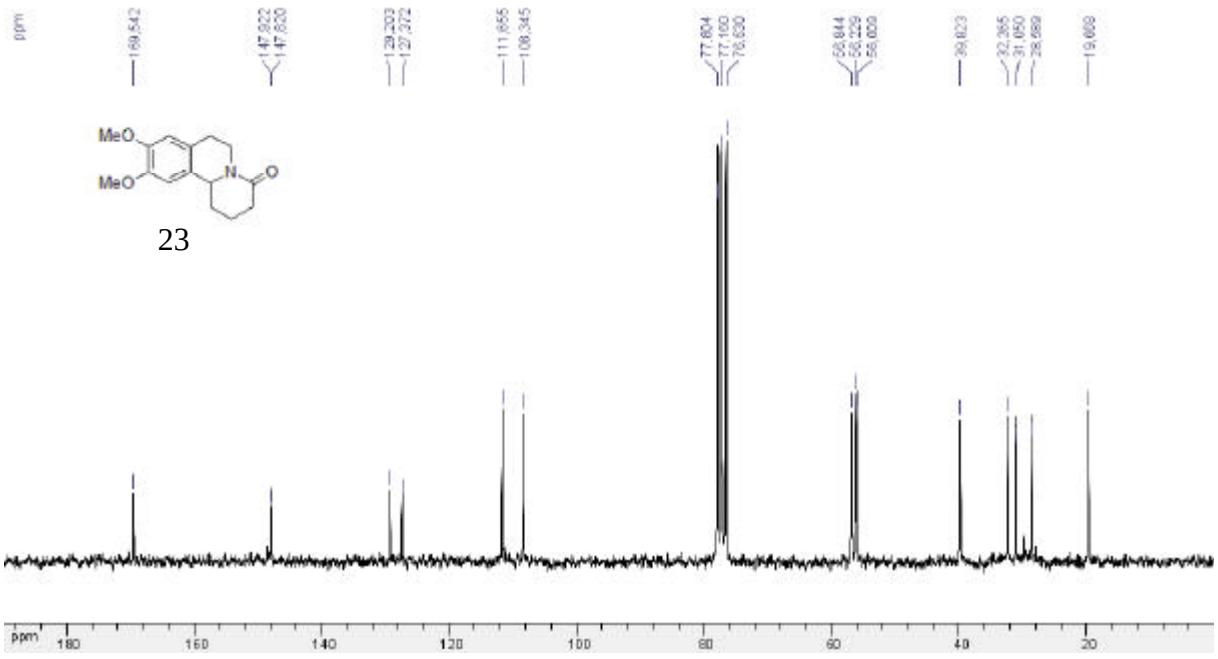

ppm
169.489
158.222
136.525
129.712
126.064
113.464
112.849
77.585
77.160
76.735
56.605
55.360
39.771
32.343
30.703
29.357
19.656
ppm
180
160
140
120
100
80
60
40
20

22

MeO
MeO
N
O

23

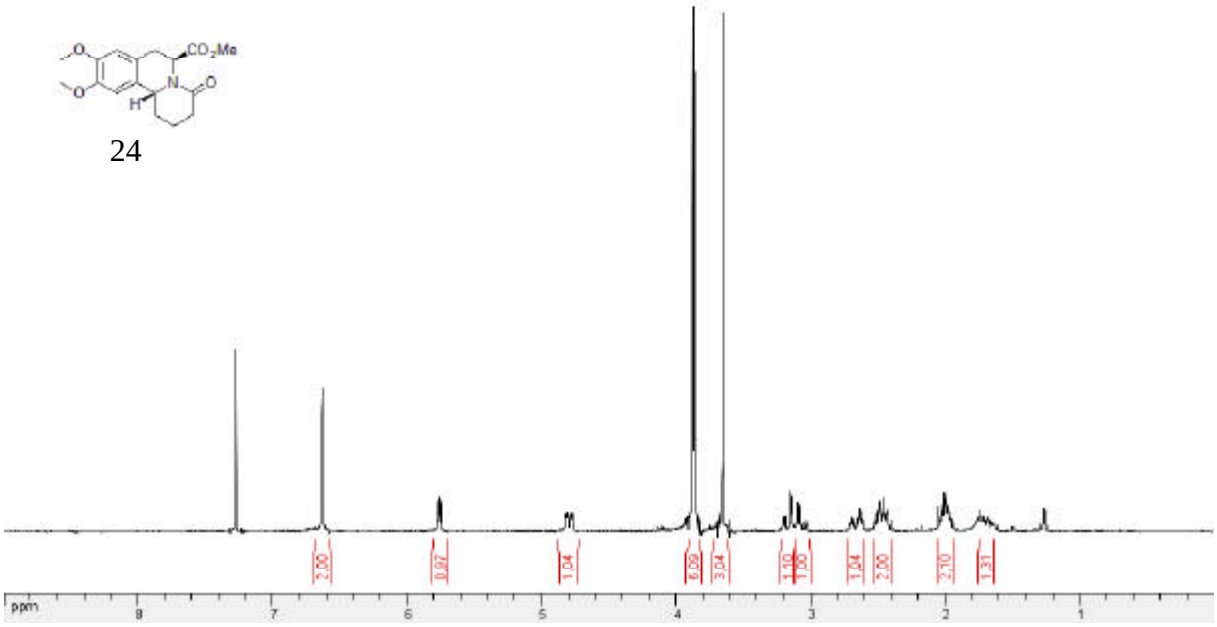

1.00
1.02
6.30
2.91
3.46
1.31
2.50
1.19
ppm
8
7
6
5
4
3
2
1

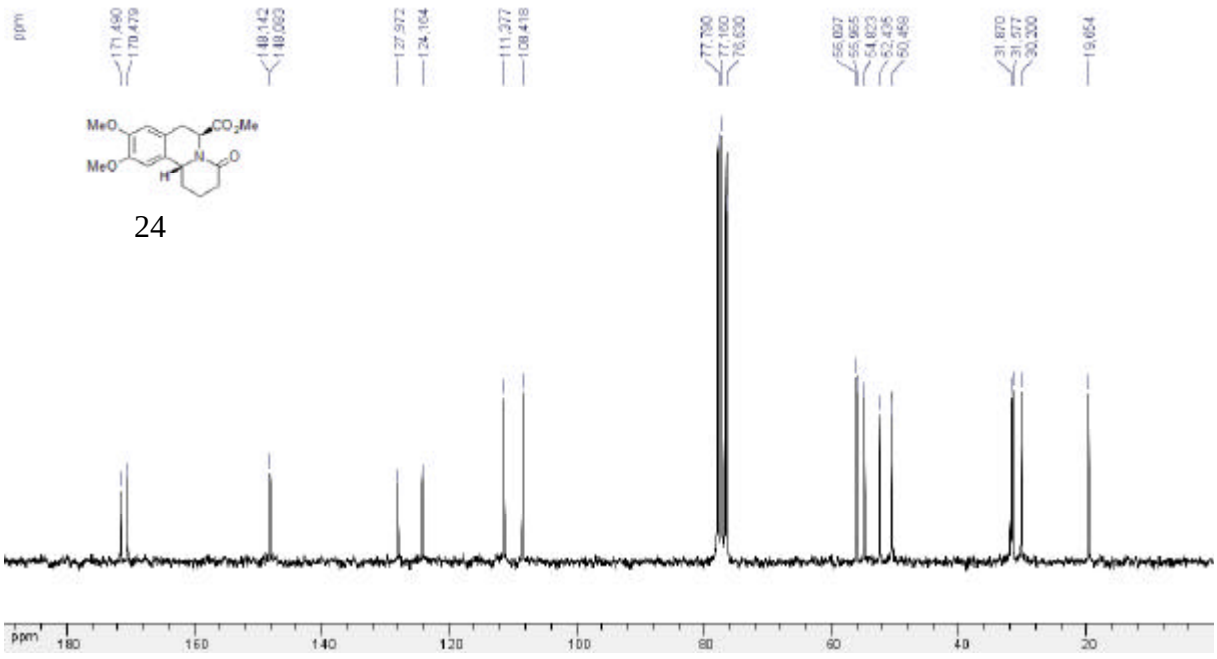

ppm
169.542
147.822
147.820
129.203
127.372
111.855
108.345
77.604
77.160
76.630
56.844
56.229
56.609
39.823
32.365
31.050
28.589
19.669
ppm
180
160
140
120
100
80
60
40
20

MeO
MeO
N
O

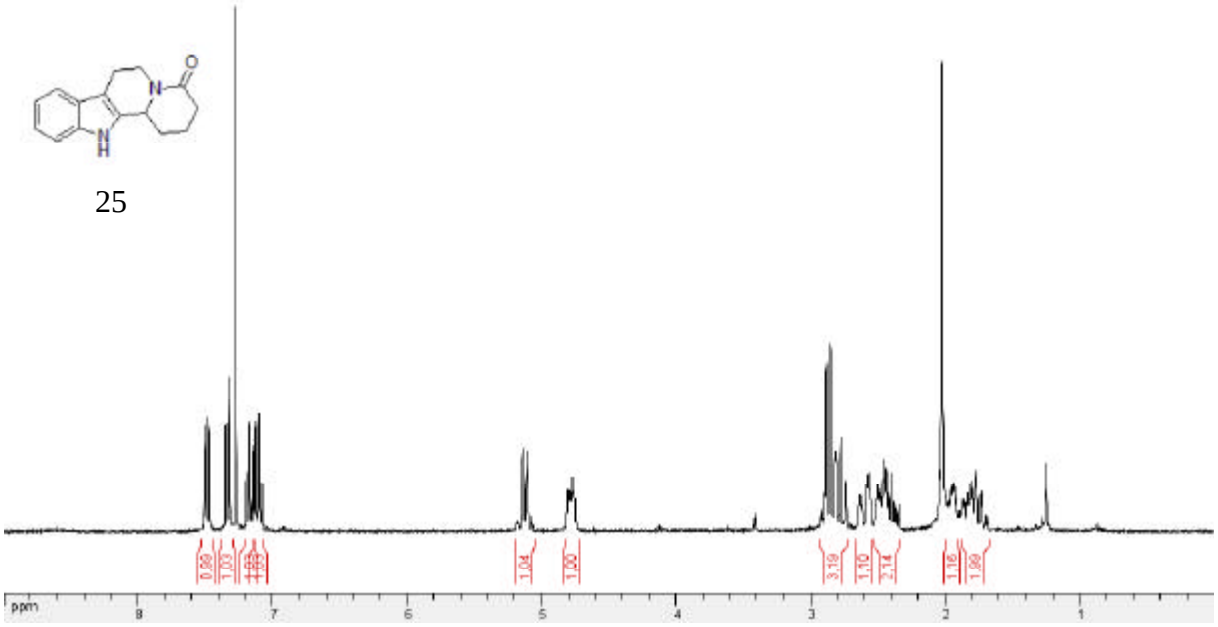
23

24

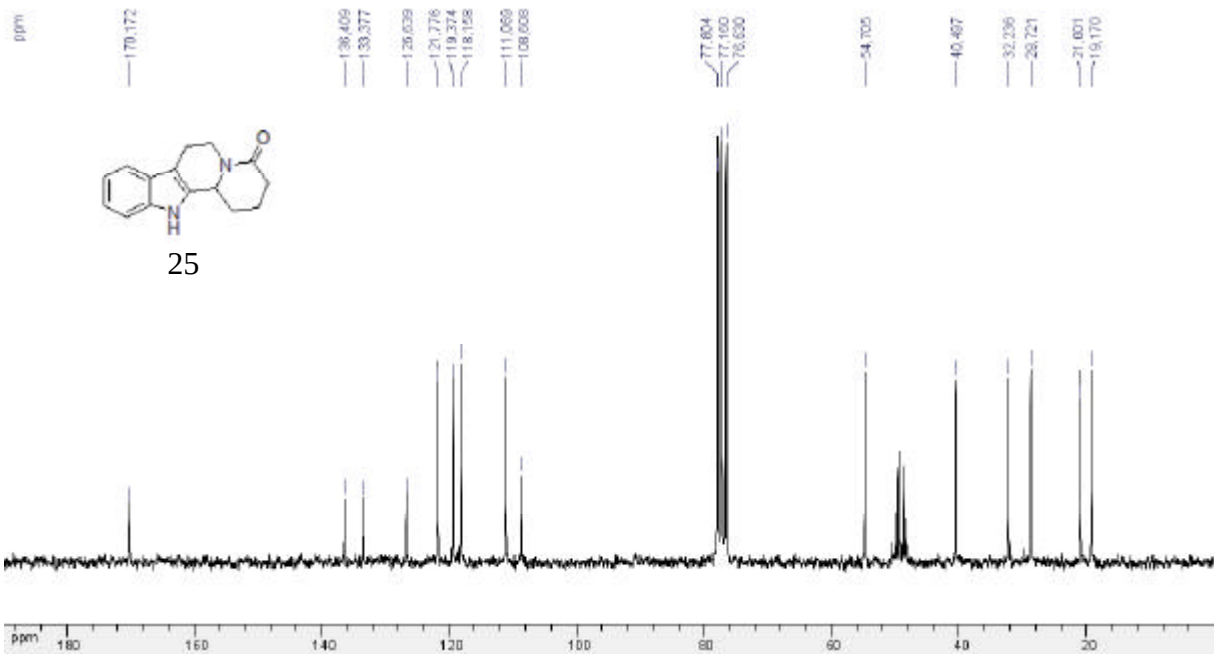

2.00
0.87
1.04
6.09
3.04
1.48
1.00
1.04
2.00
2.10
1.31
ppm
8
7
6
5
4
3
2
1


ppm
171.490
170.479
148.142
148.093
127.972
124.164
111.377
108.418
77.790
77.160
76.530
56.697
56.565
54.823
52.435
50.468
31.870
31.577
30.200
19.664
180
160
140
120
100
80
60
40
20

24



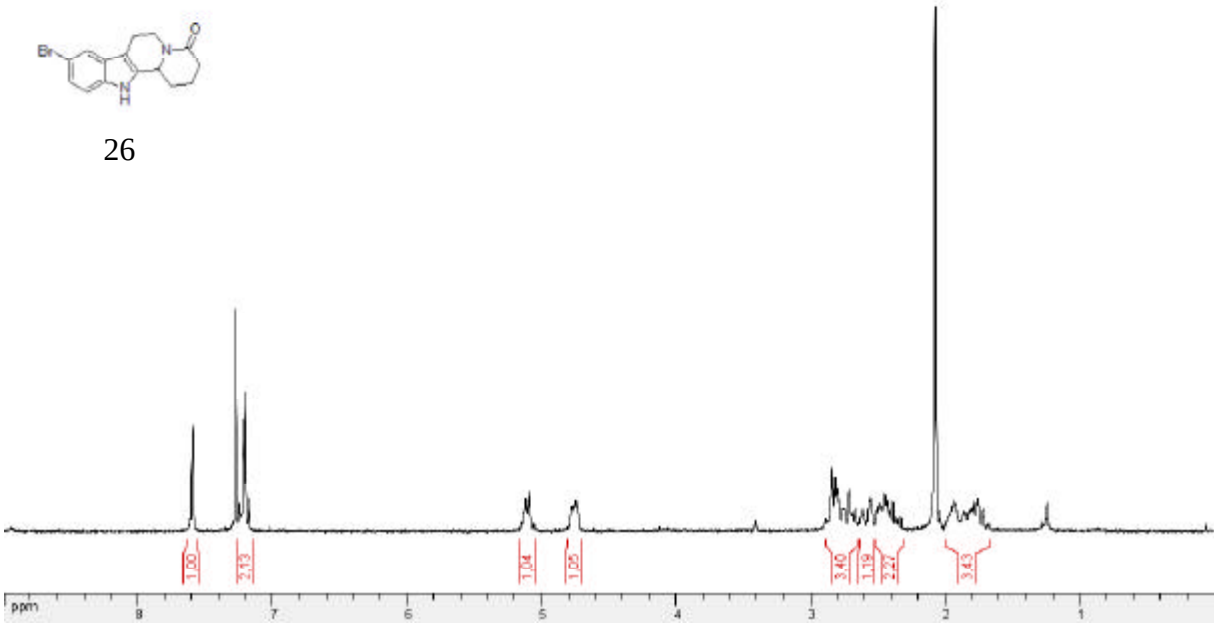
25

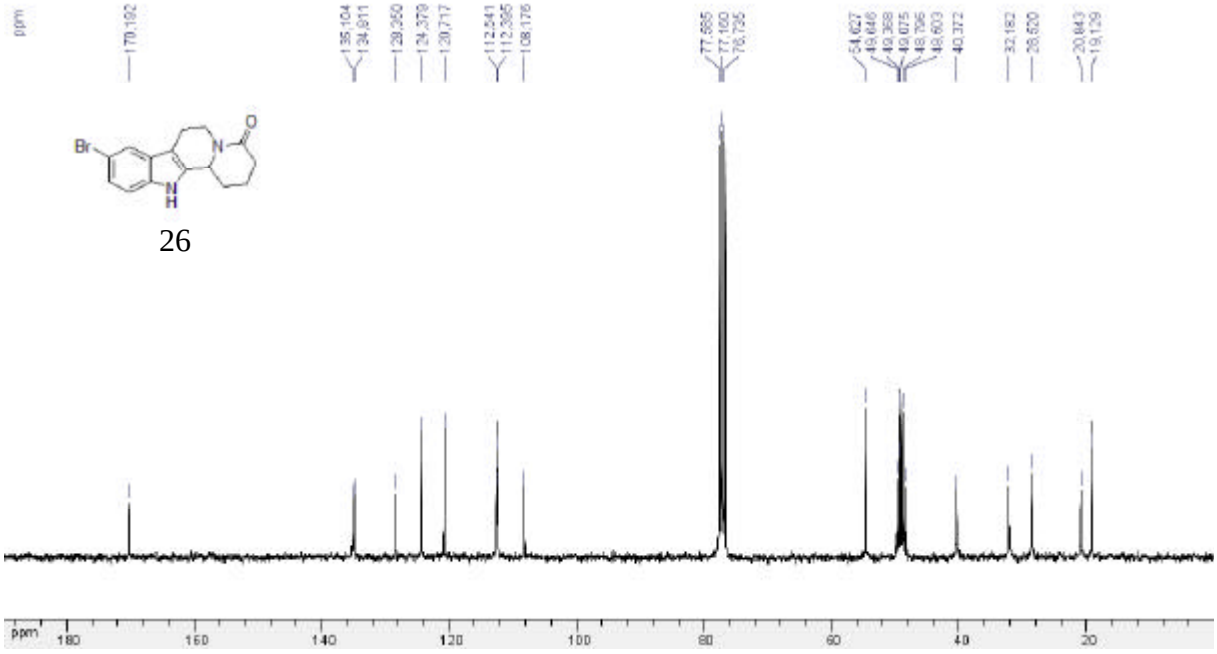


25

Br
O
N
H

26


1.00
2.13
1.04
1.05
3.40
1.19
2.27
3.43
ppm
8
7
6
5
4
3
2
1

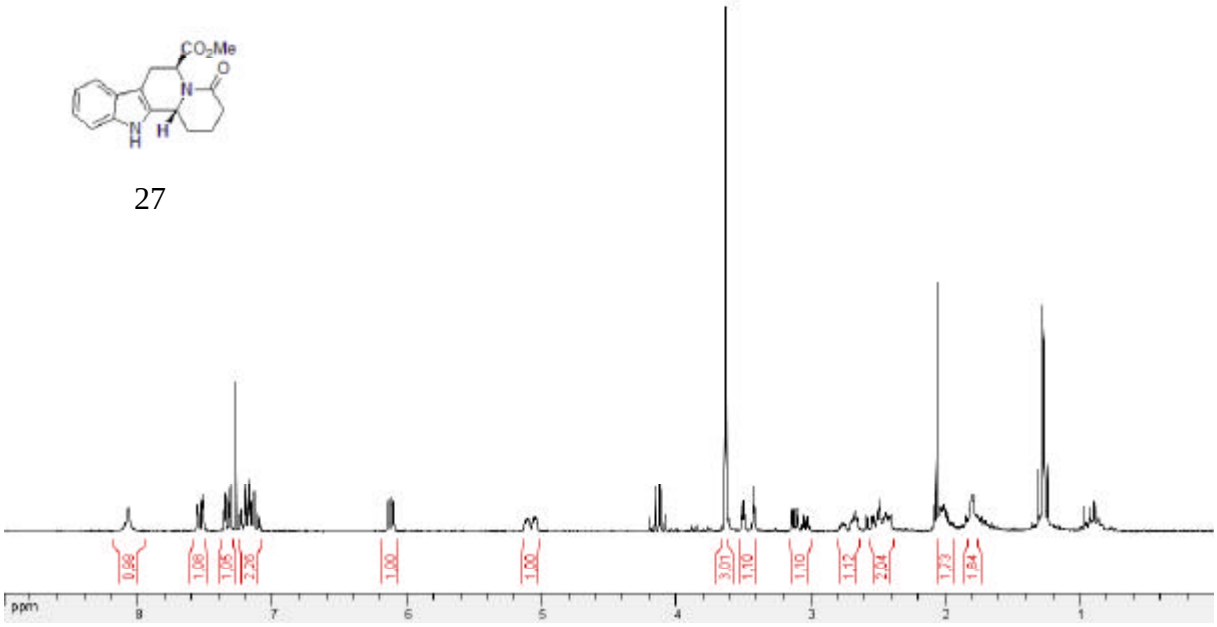

ppm
170.192
135.104
134.911
129.950
124.379
120.717
112.541
112.395
108.176
77.585
77.160
76.735
54.627
49.646
49.388
49.075
48.796
48.603
40.372
32.182
28.620
20.843
19.179
ppm
180
160
140
120
100
80
60
40
20

Br
O
N
H

26

CO2Me
O
N
H
N
H

27


0.99
1.06
1.05
2.20
1.00
1.00
3.01
1.10
1.10
1.12
2.04
1.73
1.84
ppm
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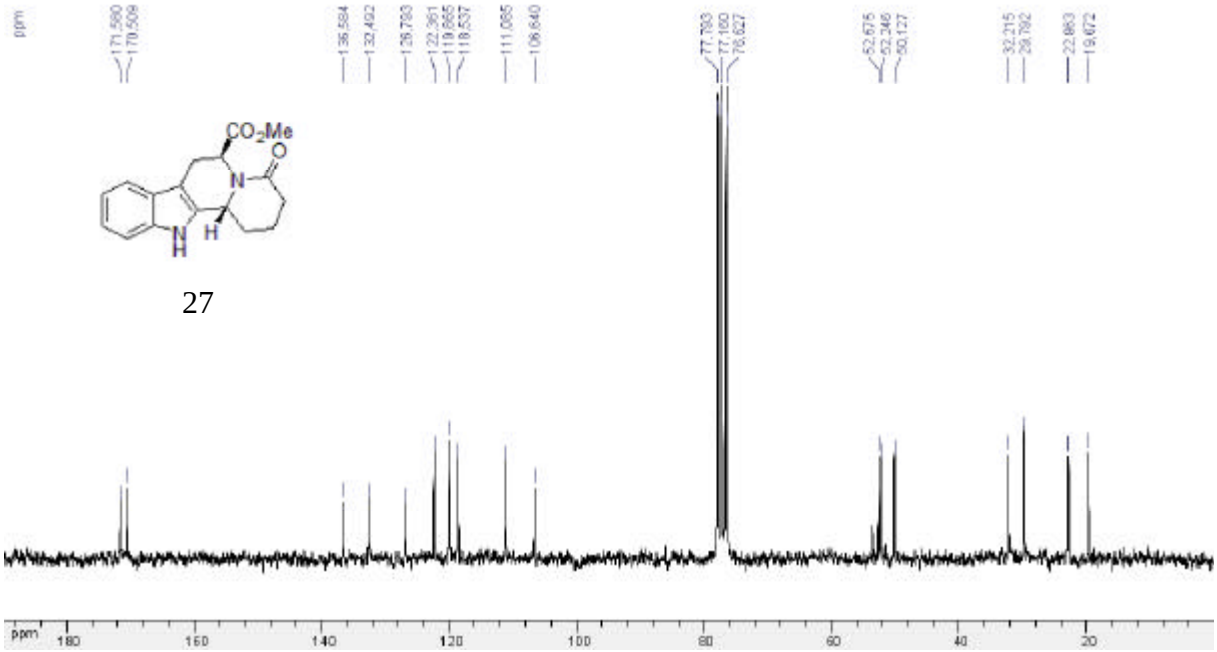
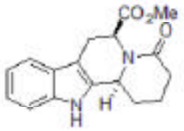
6
5
4
3
2
1

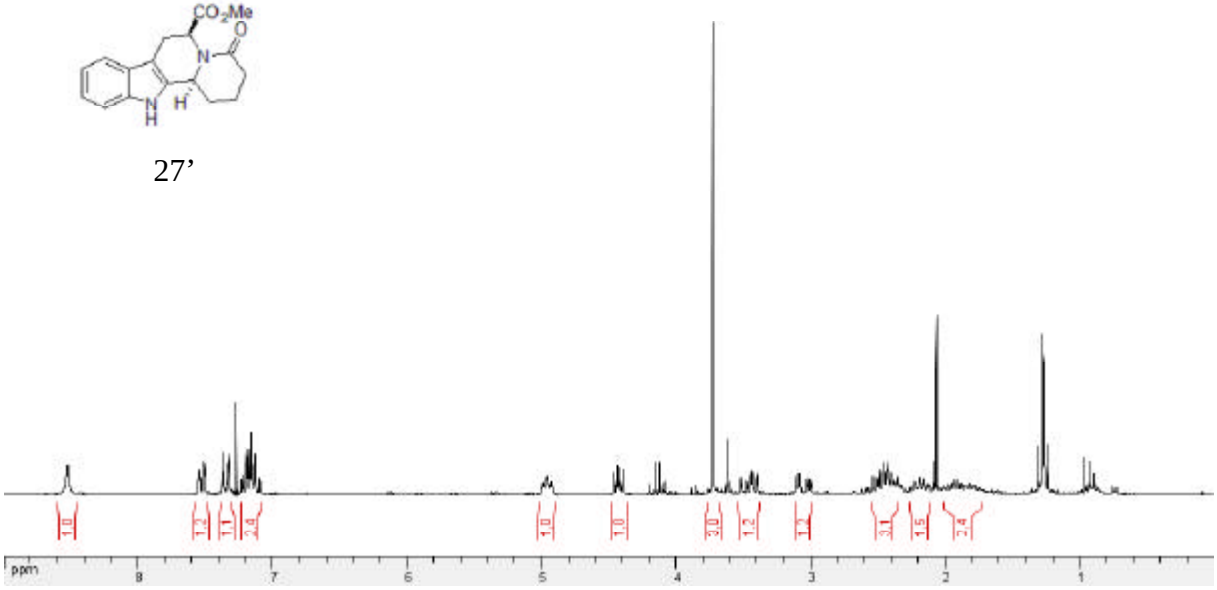

ppm
171.590
170.509
136.584
132.492
126.783
122.361
119.865
118.537
111.085
106.640
77.783
77.160
76.627
52.675
52.246
50.127
33.215
28.792
22.863
19.672
ppm
180
160
140
120
100
80
60
40
20

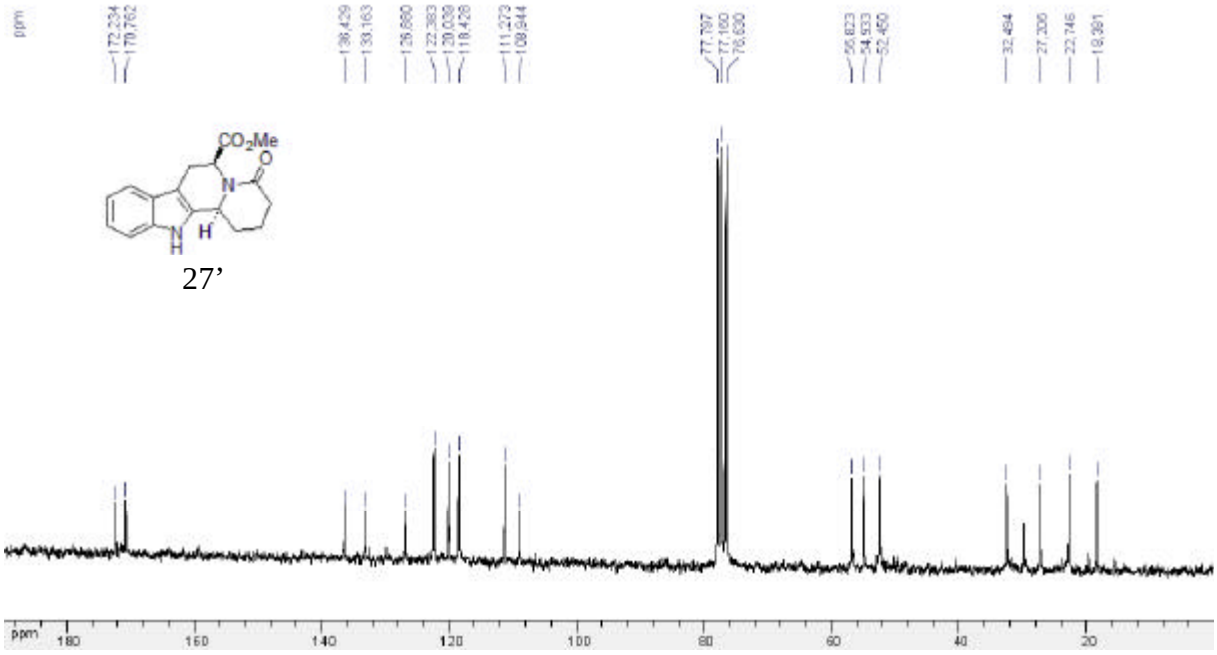
CO2Me
O
N
H
N
H

27


CO2Me
O
N
H
N
H

27’


1.0
1.2
1.1
2.4
1.0
1.0
3.0
1.2
1.0
3.1
1.5
2.4
ppm
8
7
6
5
4
3
2
1

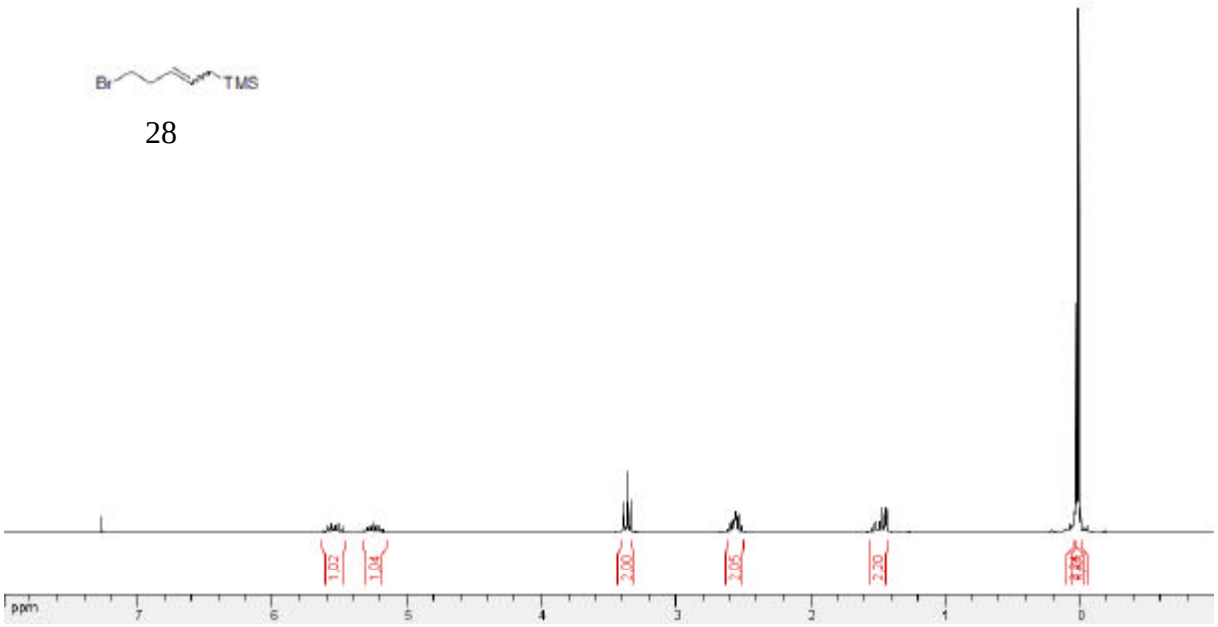

ppm
172.234
170.762
136.429
133.163
126.880
122.383
120.039
118.428
111.273
108.944
77.797
77.160
76.630
56.823
54.933
52.460
32.494
27.206
22.746
18.361
ppm
180
160
140
120
100
80
60
40
20

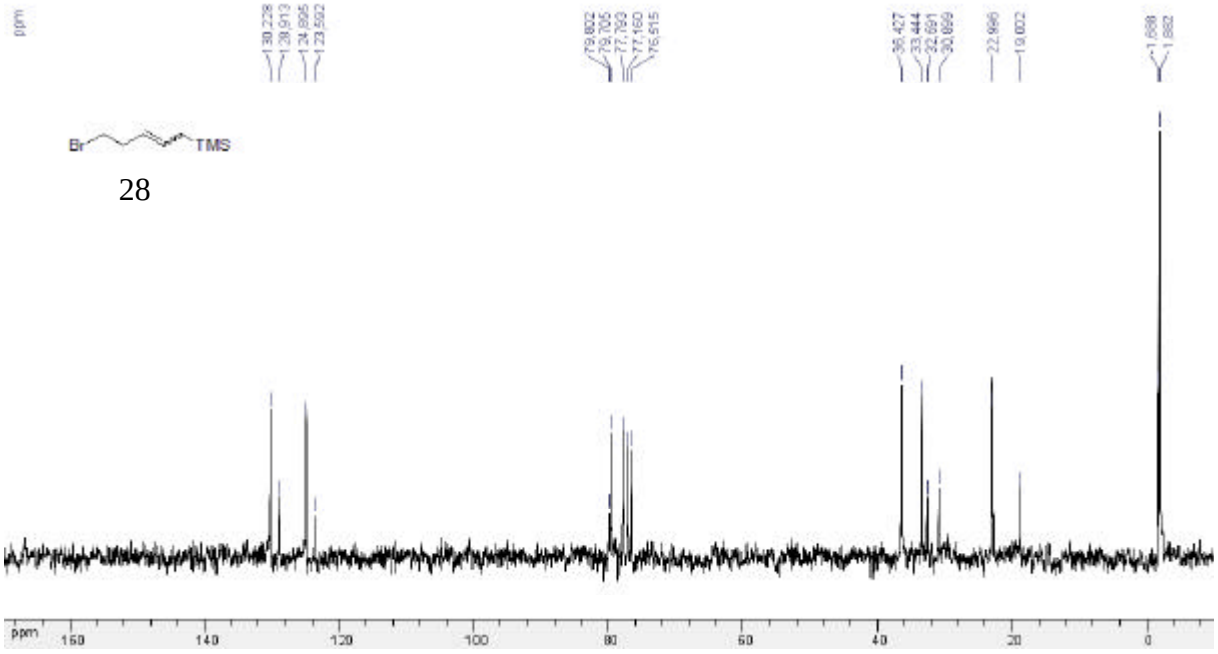
CO2Me
O
N
H
N
H

27’

Br
TMS

28


1.03
1.04
2.00
2.05
2.20
ppm
7
6
5
4
3
2
1
0

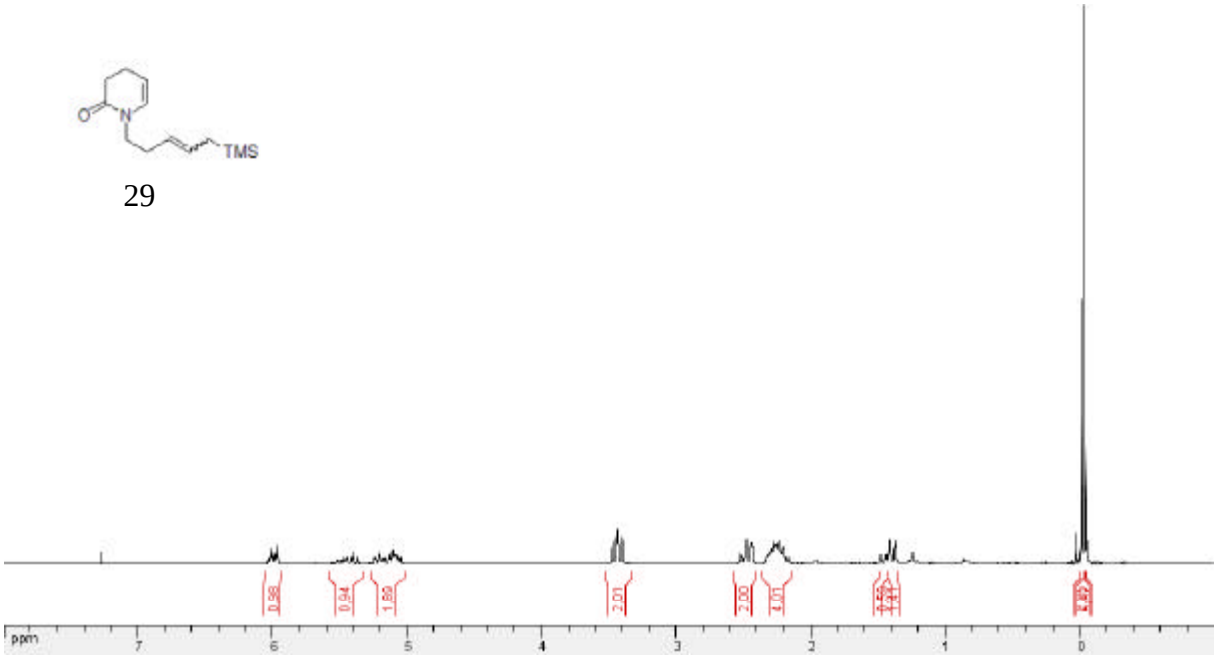

ppm
139.228
138.913
124.895
123.592
79.802
79.705
77.789
77.160
76.515
36.427
33.444
32.691
30.899
22.996
19.602
1.698
1.882
ppm
160
140
120
100
80
60
40
20
0

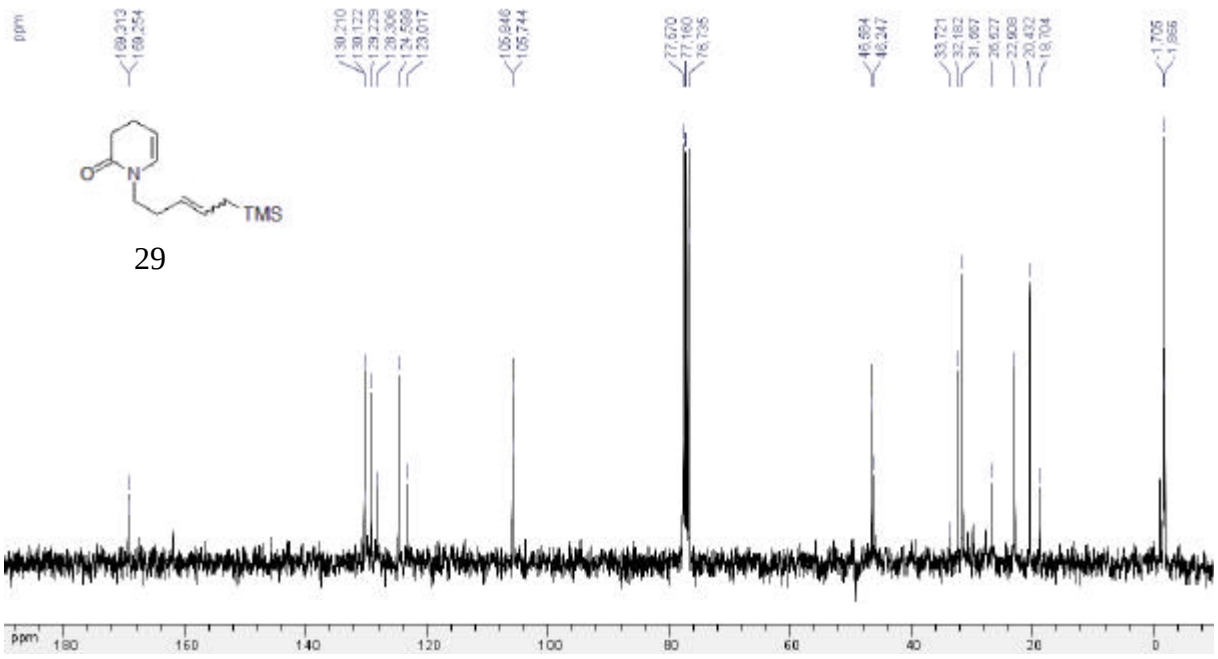
Br
TMS

28

O
N
TMS

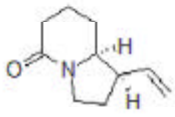
29


0.88
0.94
1.88
2.01
2.00
1.01
ppm
7
6
5
4
3
2
1
0

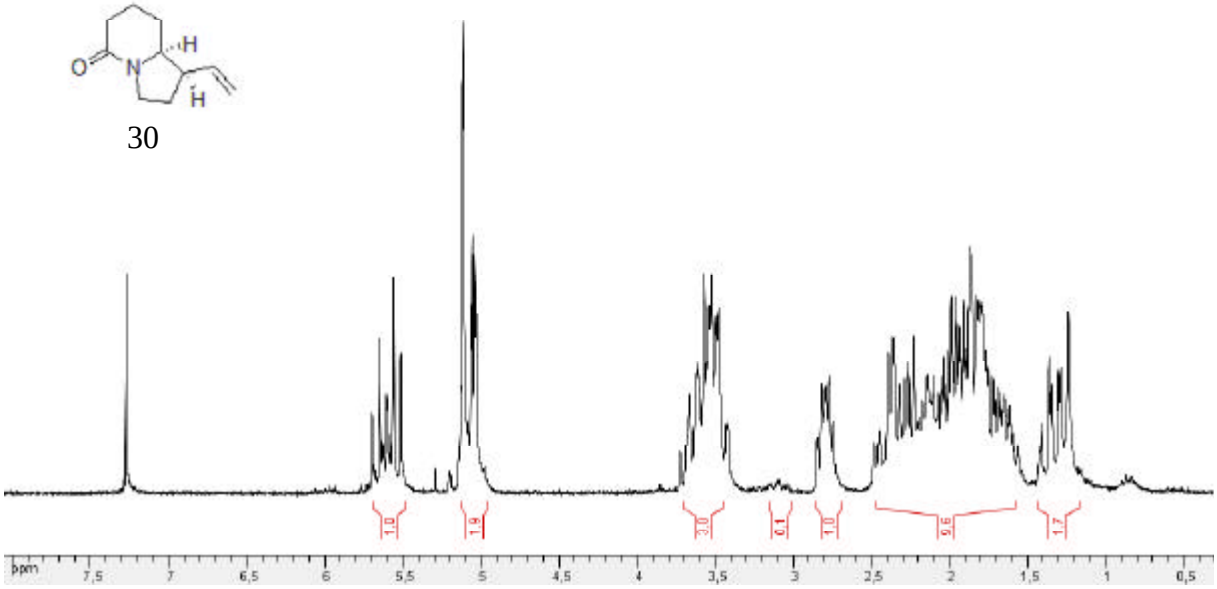

ppm
169.313
169.254
130.210
130.122
129.229
128.306
124.599
123.017
105.846
105.744
77.670
77.160
76.735
46.694
46.247
33.721
32.182
31.667
26.527
23.908
20.432
18.704
-1.705
-1.856
180
160
140
120
100
80
60
40
20
0

O
N
TMS

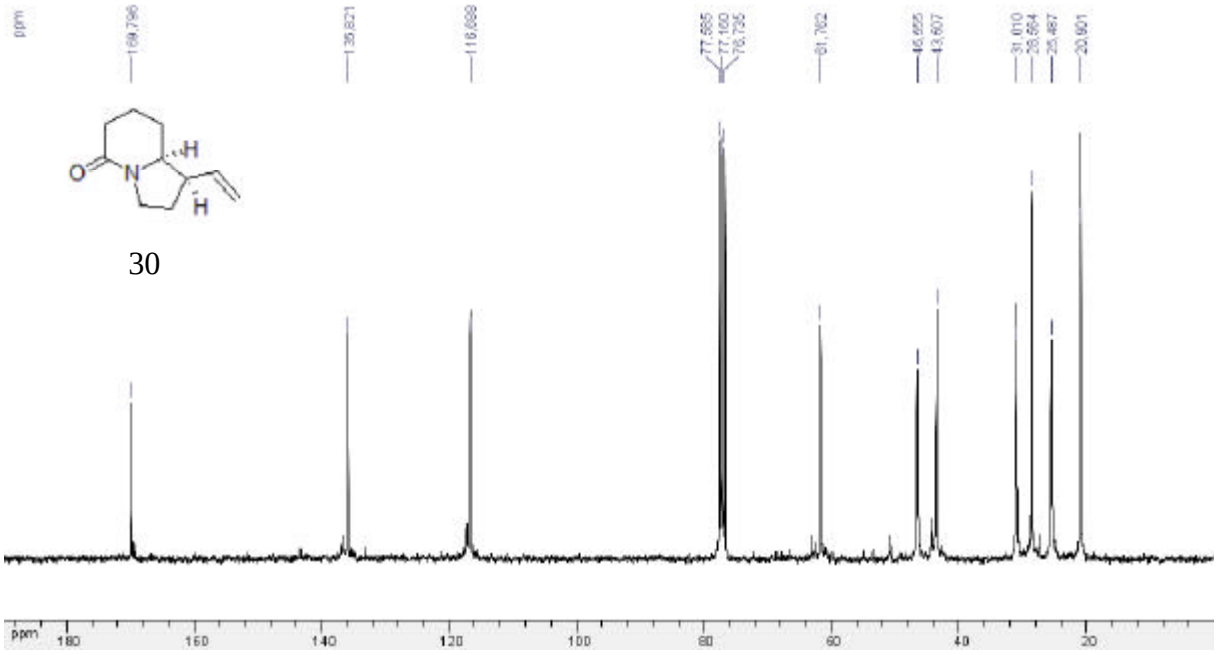
29

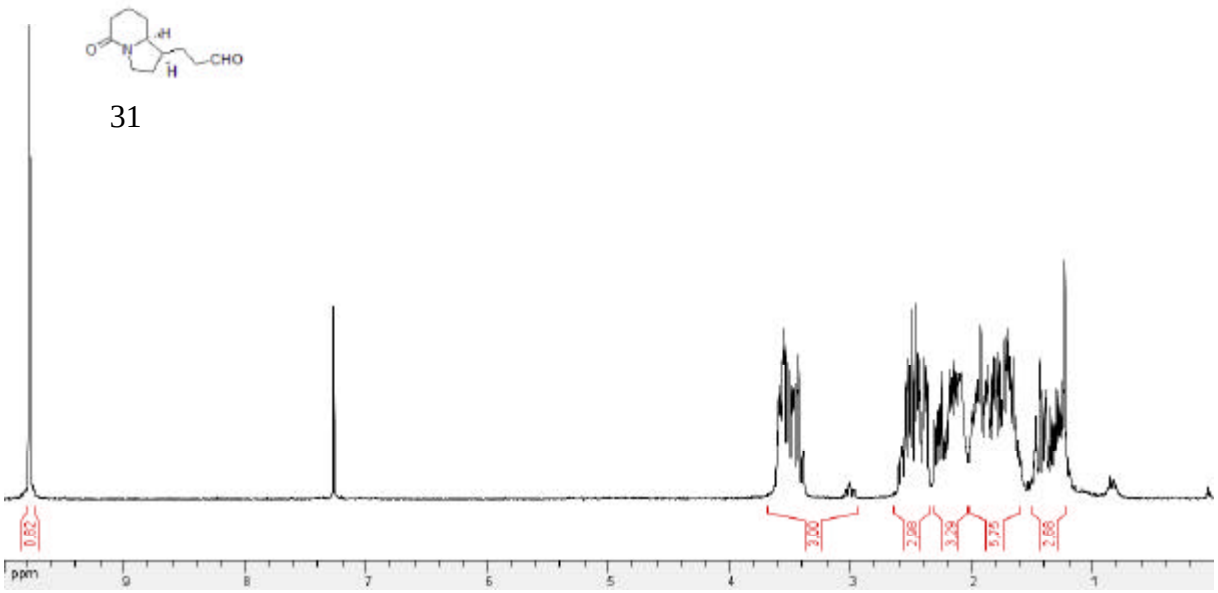


30

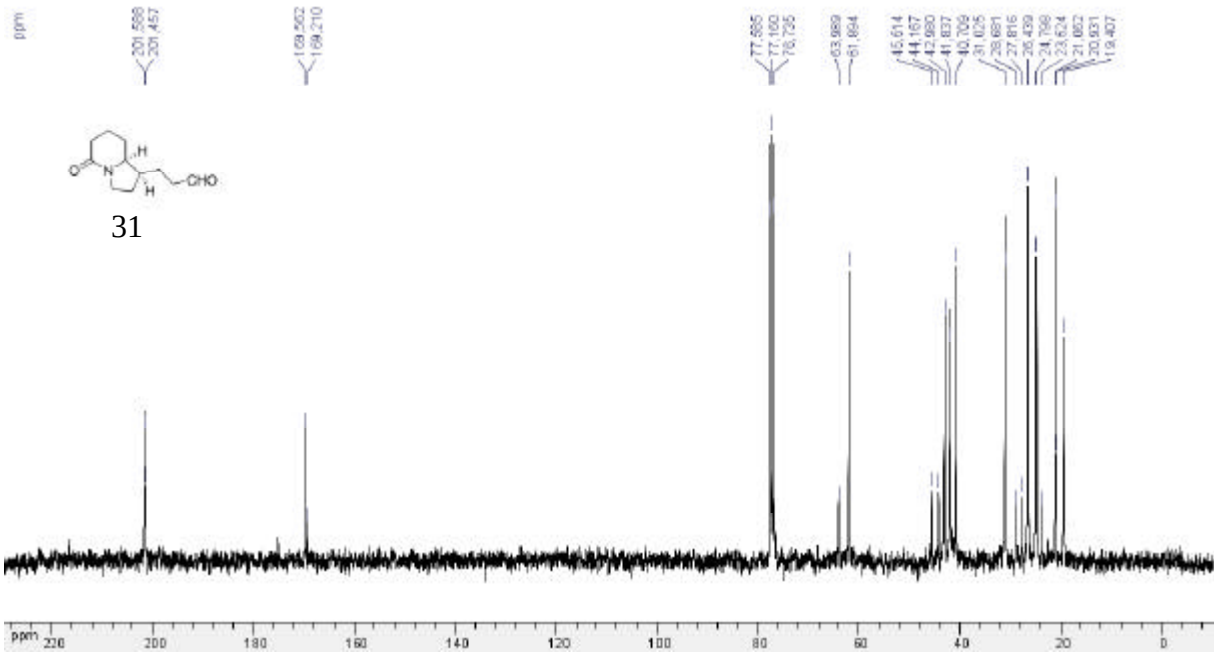

1.0
1.9
3.0
0.1
1.0
9.6
1.7
ppm
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

30

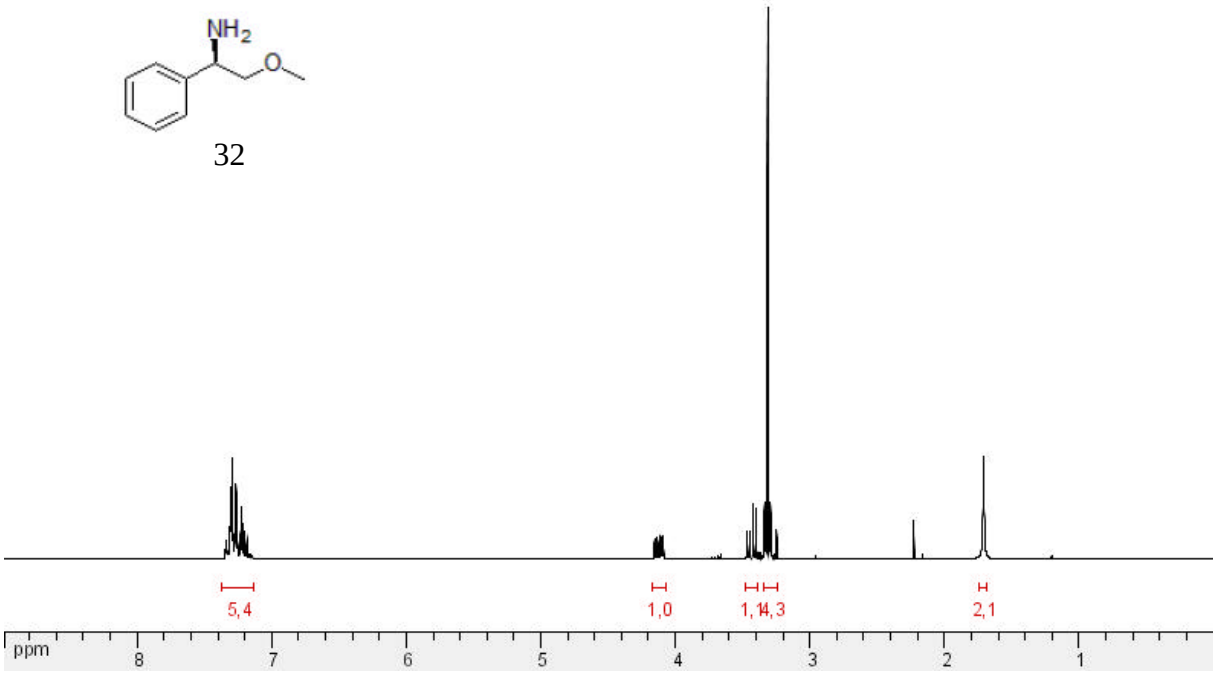

ppm
169.796
135.821
116.699
77.585
77.160
76.735
61.762
46.655
43.607
31.610
28.664
25.467
20.901
ppm
180
160
140
120
100
80
60
40
20


CHO
0.82
3.00
2.08
3.29
3.75
2.66
ppm

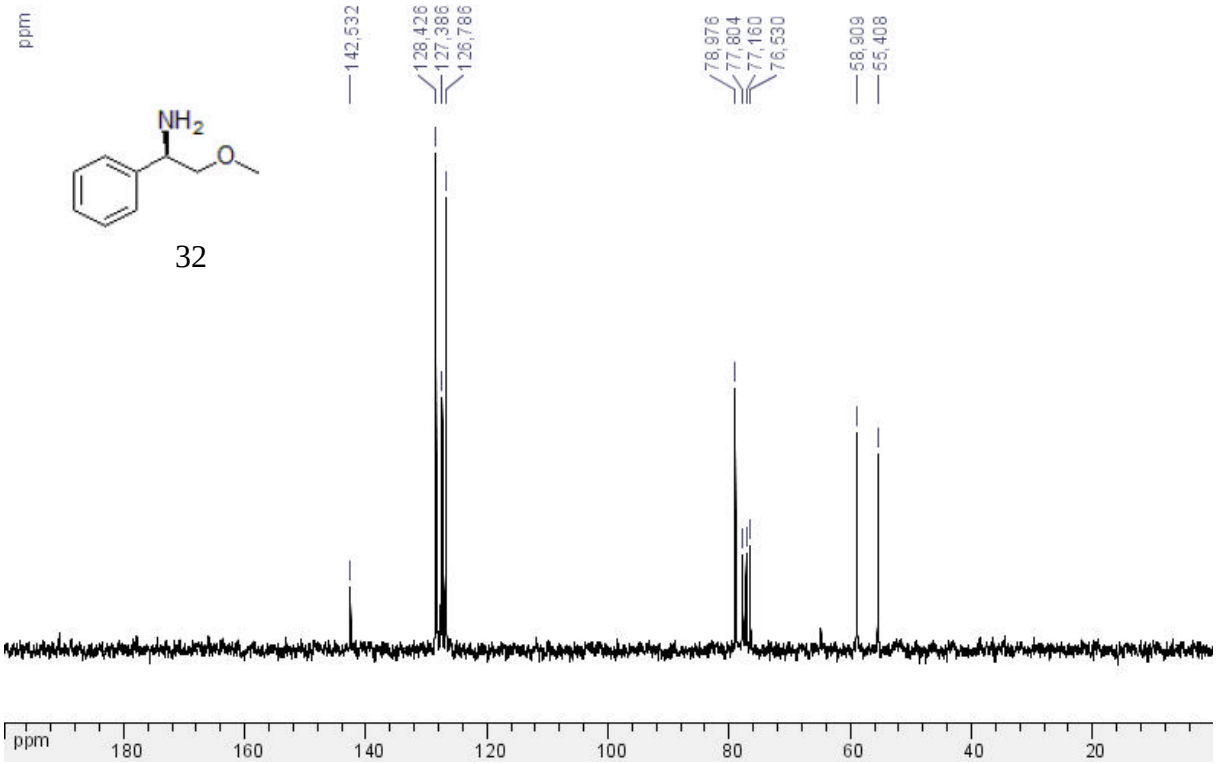
31


ppm
201.586
201.457
169.562
169.210
77.685
77.160
76.735
63.969
61.884
45.614
44.167
42.990
41.837
40.709
31.025
28.691
27.816
26.439
24.799
23.624
21.662
20.931
19.407
CHO
ppm

31

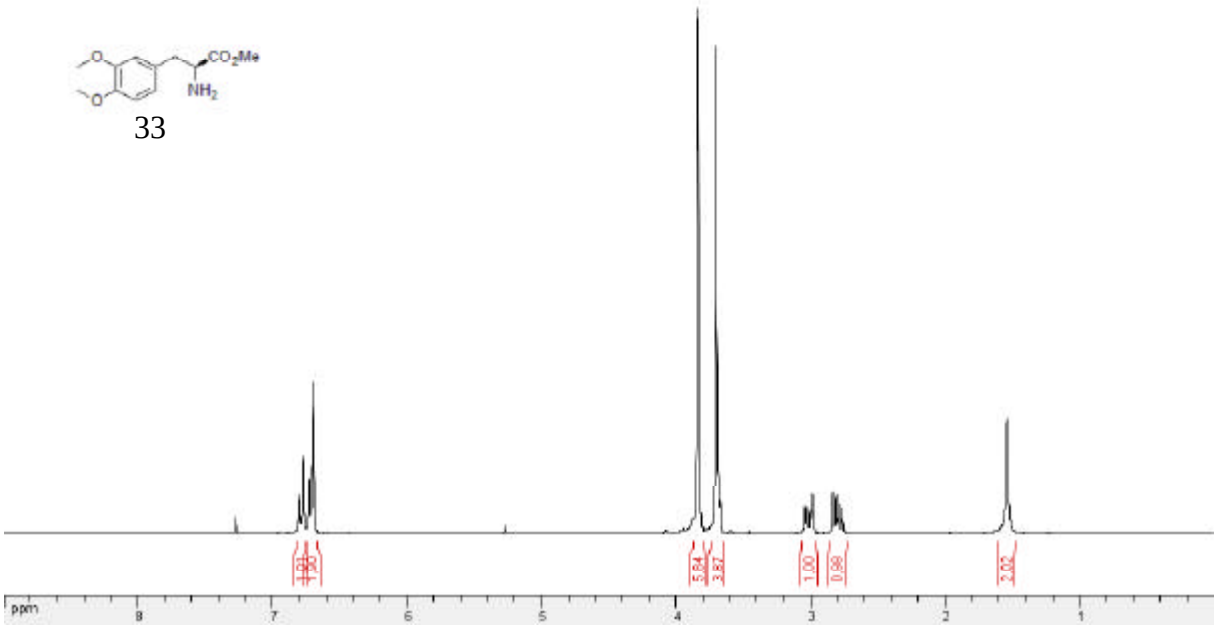

NH2
O
5,4
1,0
1,14,3
2,1
ppm
8
7
6
5
4
3
2
1

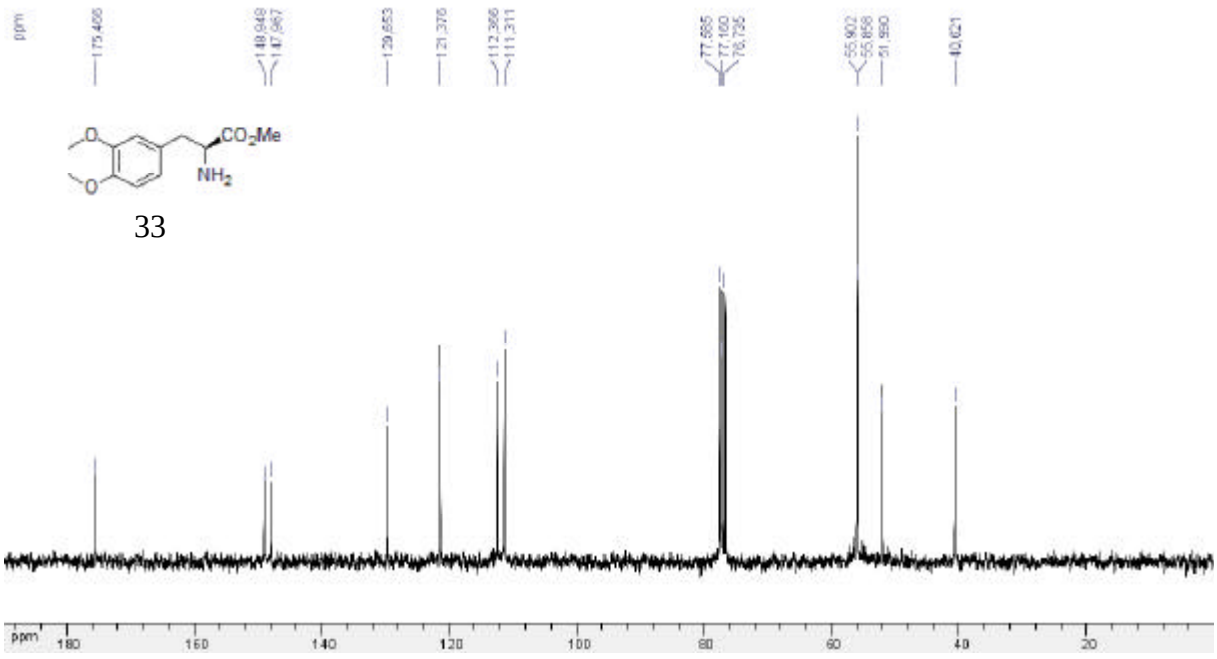
32


ppm
142,532
128,426
127,386
126,786
78,976
77,804
77,160
76,530
58,909
55,408
NH2
O
ppm
180
160
140
120
100
80
60
40
20

32

33

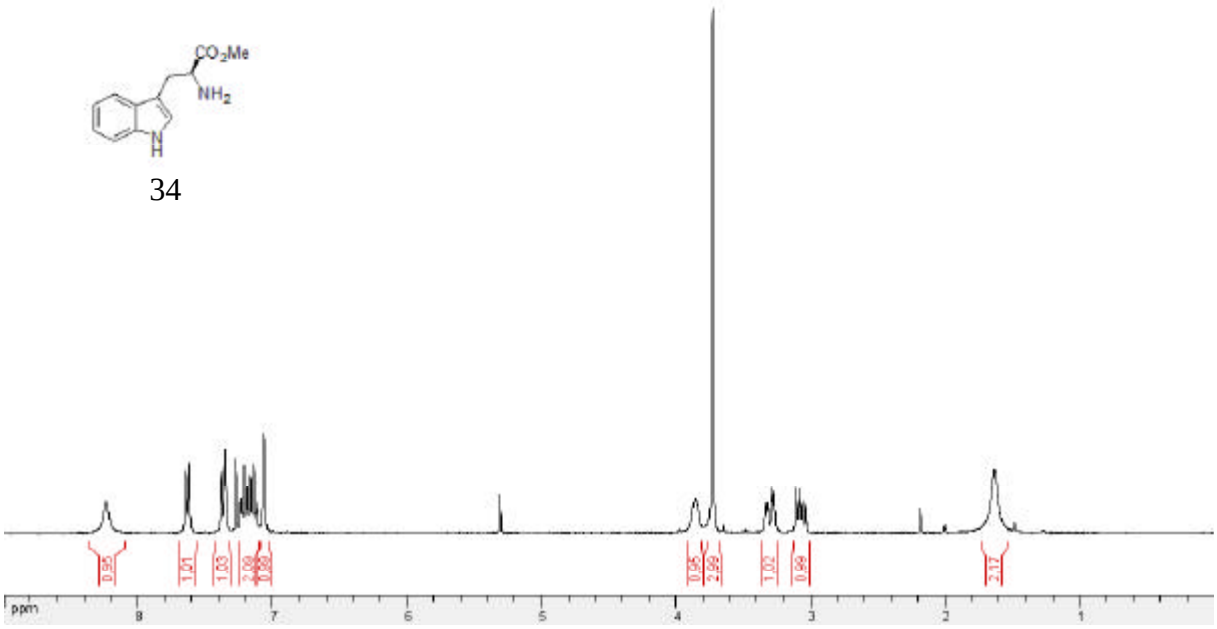

1.93
1.90
5.64
3.87
1.00
0.88
2.05
ppm
8
7
6
5
4
3
2
1

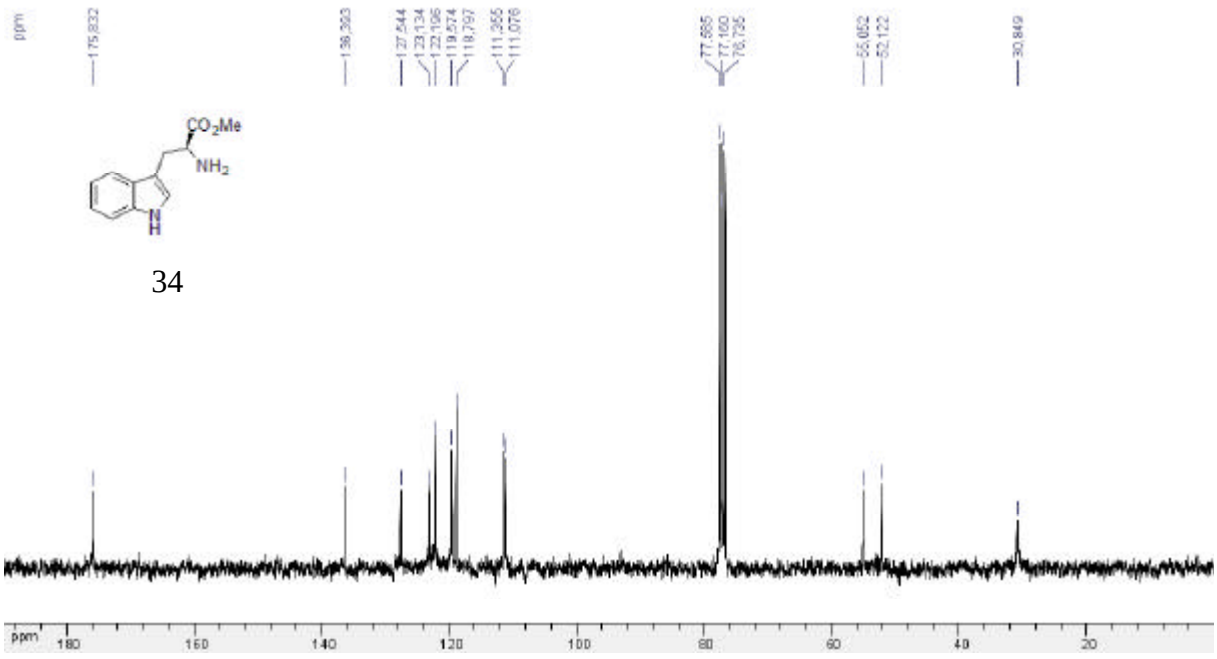

ppm
175.406
148.948
147.967
129.653
121.376
112.366
111.311
77.585
77.160
76.735
55.902
55.856
51.990
40.621
ppm
180
160
140
120
100
80
60
40
20

33

CO2Me
NH2

34


0.95
1.01
1.03
2.09
0.88
0.85
2.99
1.02
0.99
2.17
ppm
8
7
6
5
4
3
2
1

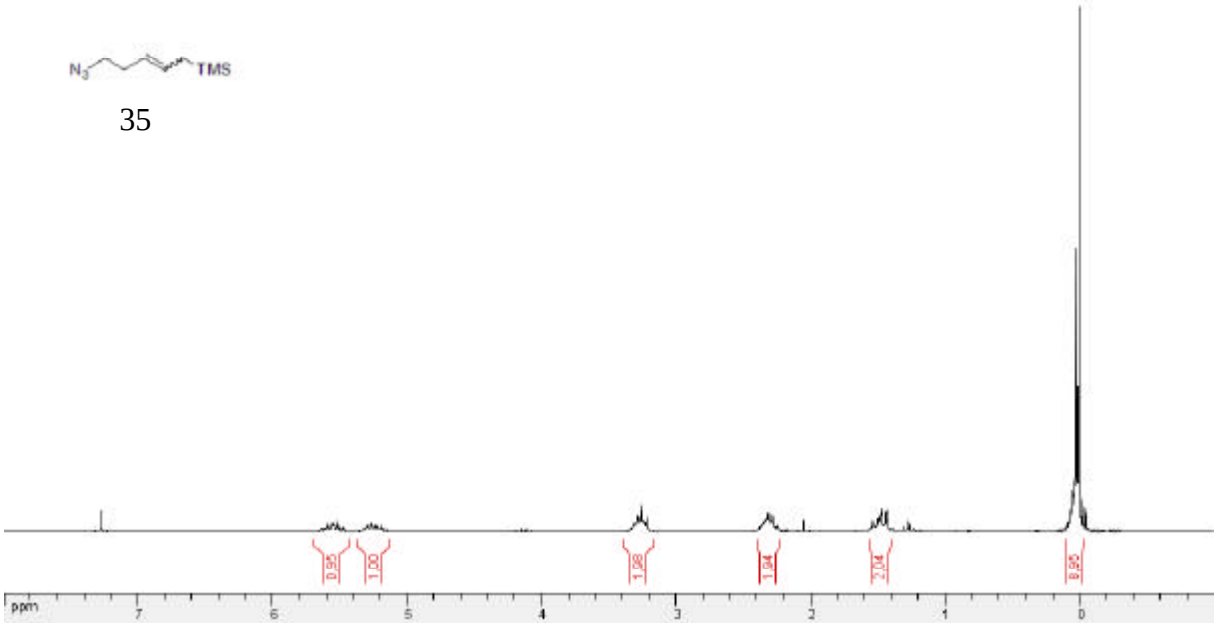

ppm
175.832
136.393
127.544
123.134
122.196
119.574
118.797
111.365
111.076
77.585
77.160
76.736
56.062
52.122
30.849
ppm
180
160
140
120
100
80
60
40
20

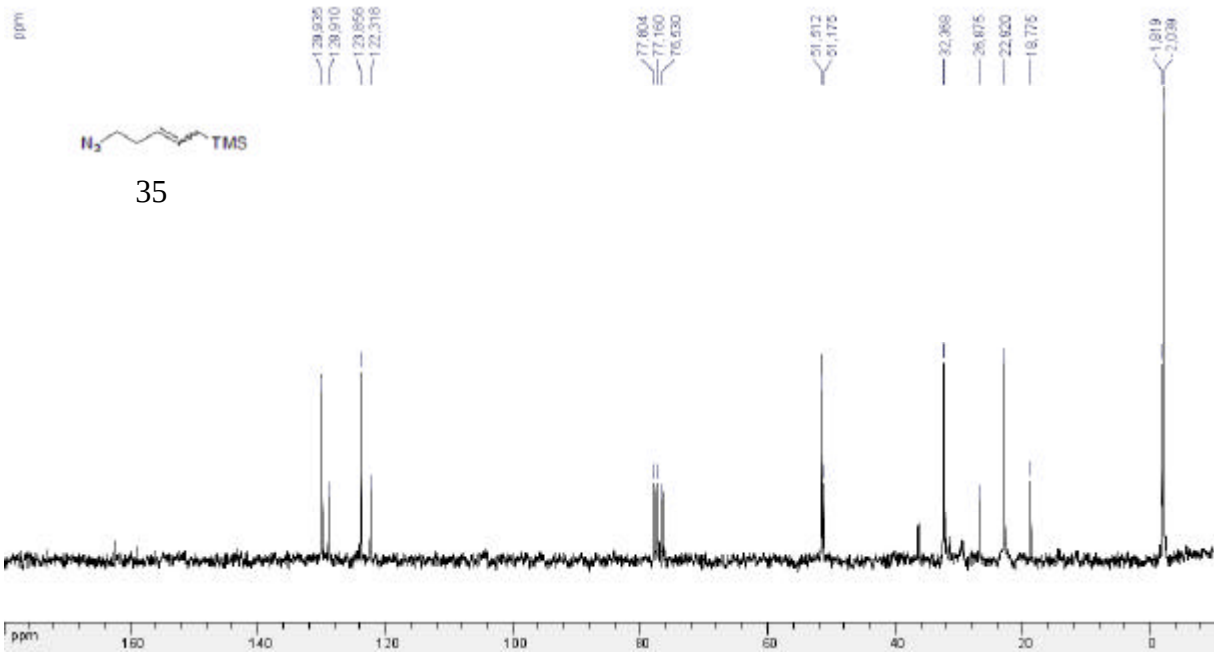
CO2Me
NH2

34

N3
TMS

35


0.95
1.00
1.98
1.94
7.04
8.95
ppm
7
6
5
4
3
2
1
0

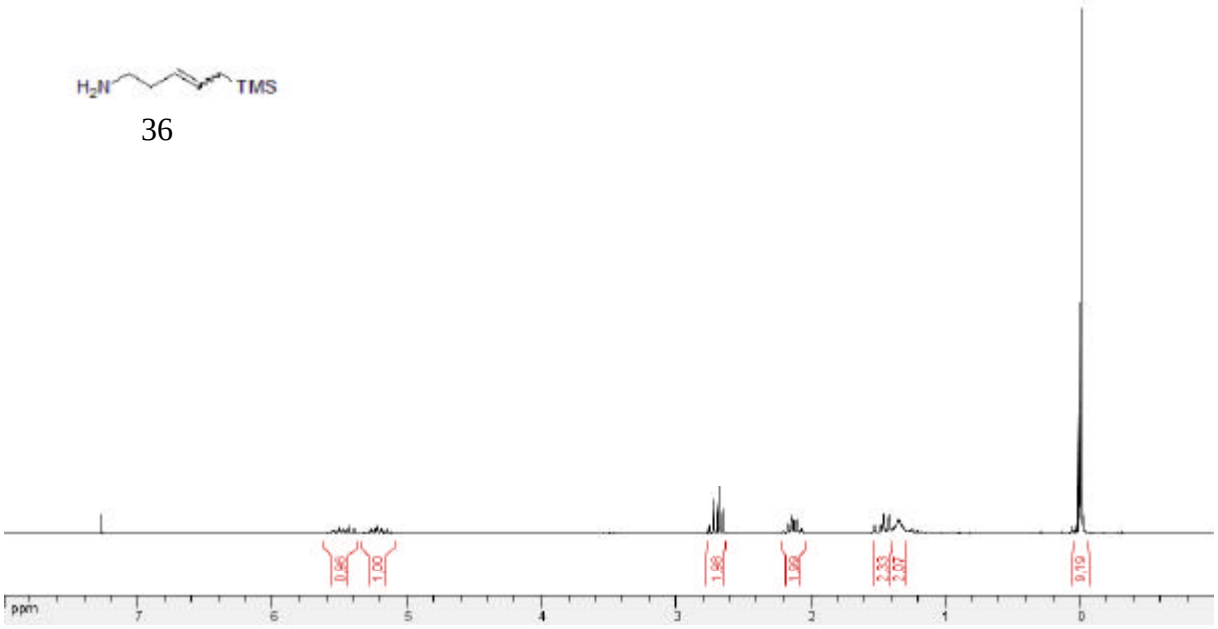

ppm
139.935
139.910
123.856
122.316
77.604
77.160
76.530
51.512
51.175
32.368
26.875
22.920
18.775
1.819
2.039
ppm
160
140
120
100
80
60
40
20
0

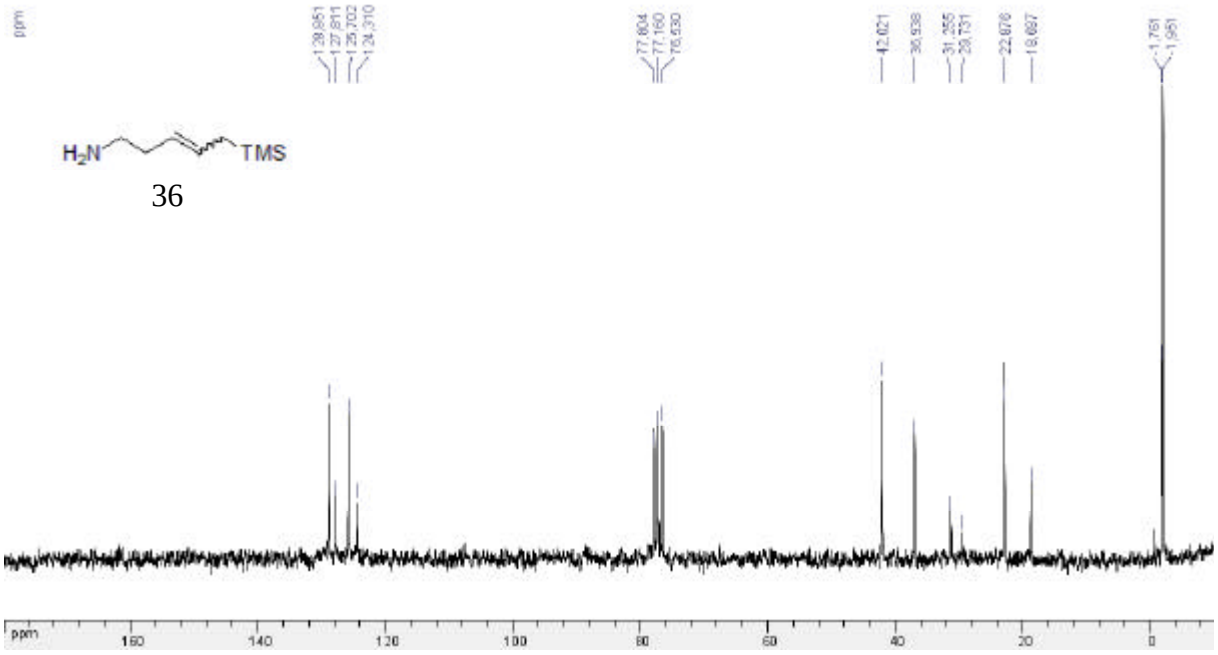
N3
TMS

35

H2N
TMS

36


0.96
1.00
1.96
1.99
2.33
2.07
9.19
ppm
7
6
5
4
3
2
1
0


ppm
138.851
127.811
125.702
124.310
77.604
77.160
76.630
42.021
36.938
31.255
28.751
22.876
18.667
-1.751
-1.951
ppm
160
140
120
100
80
60
40
20
0

H2N
TMS

36