Supporting Information

Stereospecific Approach to the Synthesis of Ring-A Oxygenated *Sarpagine* Indole Alkaloids. Total Synthesis of the Dimeric Indole Alkaloid *P*-(+)-Dispegatrine and Six Other Monomeric Indole Alkaloids

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E-mail: capncook@uwm.edu

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General Experimental Considerations

All reactions were carried out under an argon atmosphere with dry solvents using anhydrous conditions unless otherwise stated. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from Na/benzophenone ketyl prior to use. Dichloromethane was distilled from calcium hydride prior to use. Methanol was distilled over magnesium sulfate. Benzene and toluene were distilled over Na. Acetonitrile was distilled over CaH_2 prior to use. Reagents were purchased of the highest commercial quality and used without further purification unless otherwise stated. Thin layer chromatography (TLC) was performed on UV active silica gel, 200 µm, plastic backed and UV active alumina N, 200 µm, F-254 plastic backed. Flash and gravity chromatography were performed using silica gel P60A, 40-63 µm, basic alumina (Act I, 50-200 µm) and neutral alumina (Brockman I, ~150 mesh). TLC plates were visualized by exposure to short wavelength UV light (254 nm). Indoles were visualized with a saturated solution of ceric ammonium sulfate in 50% sulfuric acid. All samples submitted for CHN analyses were first dried under high vacuum for a minimum of six hours using a drying pistol with isopropyl alcohol or benzene as the solvent with potassium hydroxide pellets in the drying bulb. ^1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = doublet of doublet, dt = doublet of triplet, ddd = doublet of doublet of doublets, td = triplet of doublets, qd = quartet of doublets, m = multiplet), integration, and coupling constants (Hz). ^{13}C NMR data are reported in parts per million (ppm) on the δ scale. The low resolution mass spectra (LRMS) were obtained as electron impact (EI, 70eV) using a magnetic sector (EBE) analyzer. HRMS were recorded by electrospray ionization (ESI) using a TOF analyzer, electron impact (EI) using a trisector analyzer and Matrix-assisted laser desorption (MALDI) using an ion trap analyzer.

Table 1. Comparison of the ^{1}H NMR data for Natural and Synthetic (+)-Lochneram (**11**)

Protons[a]	**^{1}H NMR Natural (HDO)**[a,b,c,d]	**^{1}H NMR Synthetic (600 MHz, CD_3OD)**[b]
H-12	7.35 (d, *J* = 9.0 Hz)	7.31 (d, 1H, *J* = 9.0 Hz)
H-9	7.00 (br, s)	7.04 (br, s, 1H)
H-11	6.70 (d, *J* = 9.0 Hz)	6.87 (d, 1H, *J* = 8.4 Hz)
H-19	5.50 (q)	5.68 (q, 1H, *J* = 6.6 Hz)
	nr	4.91 (1H, peak is embedded in CD_3OD peak)
	nr	4.46 (d, 1H, *J* = 15.6 Hz)
	nr	4.25 (d, 1H, *J* = 15.6 Hz)
Ar-OMe	3.77 (s)	3.85 (s, 3H)
	nr	3.58 (d, 3H, *J* = 7.8 Hz)
	nr	3.31 (d, 1H, *J* = 4.8 Hz, part of the peak is embedded in CD_3OD peak)
N_b^{+}—Me	2.82 (s)	3.15 – 3.10 (m, 5H)
	nr	2.55 (t, 1H, *J* = 12.0 Hz)
	nr	2.21 – 2.17 (m, 2H)
3(H-18)	1.55 (d)	1.74 (d, 3H, *J* = 6.6 Hz)

[a] The numbering and the assignment of the protons follows that from the literature.§ [b] Values are in ppm (δ). [c] nr = not reported. [d] NMR frequency not reported.

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§Arnold, W.; Berlage, F.; Bernauer, H.; Schmid, H.; Karrer, P. *Helv. Chim. Acta.* **1958**, *41*, 1505.

Table 2. Comparison of the ^{1}H NMR Data for Natural and Synthetic Lochvinerine (**9**)

Protons^{a,b}	**^{1}H NMR Natural (60 MHz, CDCl$_3$)**^{a,b}	**^{1}H NMR Synthetic (300 MHz, CDCl$_3$)**^{b}
NH	8.06 (s)	10.2 (br, s, 1H)
H-12	7.13 (d, *J* = 8.0 Hz)	7.30 (d, 1H, part of the peak is embedded in CDCl$_3$ peak)
H-9	6.89 (d, *J* = 2.5 Hz)	6.87 (d, 1H, *J* = 2.2 Hz)
H-11	6.75 (dd, *J* = 8.0, 2.5 Hz)	6.80 (dd, 1H, *J* = 8.8, 2.3 Hz)
H-19	5.29 (q)	5.16 (d, 1H, *J* = 6.8 Hz)
	nr	4.43 (d, 1H, *J* = 5.8 Hz)
	nr	3.88 – 3.84 (m, 4H)
	nr	3.71 (d, 1H, *J* = 17.6 Hz)
	nr	3.52 (dd, 1H, J_2 = 7.2 Hz, part of the peak is embedded in MeOH peak)
	nr	3.50 (1H is embedded in MeOH peak)
	nr	3.11 (d, 1H, *J* = 16.6 Hz)
	nr	3.36 – 3.24 (m, 2H)
	nr	2.93 (br, s, 1H)
	nr	2.35 – 2.33 (m, 1H)
OH	2.08 (s)	2.19 (s, 1H)
	nr	2.03 – 1.95 (m, 2H)
3(H-18)	1.57 (d, 3H, J = 7.0 Hz)	1.63 (d, 3H, J = 6.5 Hz)

aThe numbering and the assignment of the protons follows that from the literature.‡ ***b***Values are in ppm (δ). *c*nr = not reported.

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‡Banerji, A.; Chakrabarty, M. *Phytochemistry* **1974**, *13*, 2309.

X-ray Structural Analysis and Methods for 16 and 36a

Single-crystal X-ray diffraction data on compounds **16** and **36a** were collected using MoKα radiation ($\lambda = 0.71073$ Å) and a Bruker APEX 2 CCD area detector. Crystals were prepared for data collection by coating with high viscosity microscope oil (Paratone-N, Hampton Research). The oil-coated crystal was placed on a MicroMesh mount (MiTeGen, Ithaca, NY) and transferred immediately to the diffractometer. Data collection temperature is as indicated in the summary information for each compound. Corrections were applied for Lorentz polarization, and absorption effects.

The structures were solved by direct methods and refined by full-matrix least squares on F^2 values using the programs found in the SHELXTL suite (Bruker, SHELXTL v6.10, 2000, Bruker AXS Inc., Madison, WI). Parameters refined included atomic coordinates and anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms on carbons were included using a riding model [coordinate shifts of C applied to H atoms] with C-H distance set at 0.96 Å.

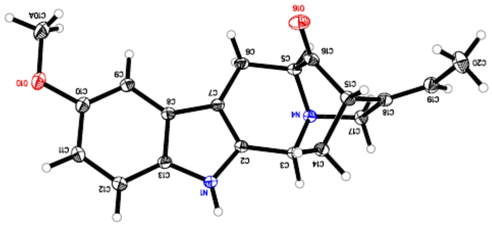


Figure S1: Displacement ellipsoid plot of (6*S*,11a*S*,*E*)-9-ethylidene-2-methoxy-6,8,9,10,11a,12-hexahydro-6,10-methanoindolo-[3,2-*b*]quinolizin-11(5*H*)-one (**16**).

16. The 0.06 x 0.05 x 0.02 mm^3 crystal was monoclininc in space group $P\ 2_1$ with unit cell dimensions a = 13.6533(4) Å, b = 5.9180(2) Å, c = 16.7753(5) Å, and β= 99.732(2)°. Data were 94.3% complete to 58.94° θ (approximately 0.83 Å) with an average redundancy of 2.72.

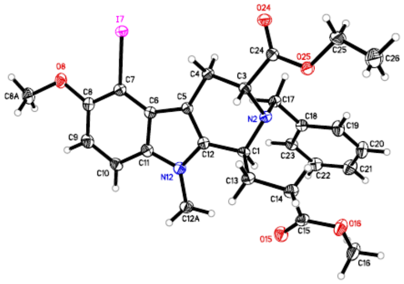
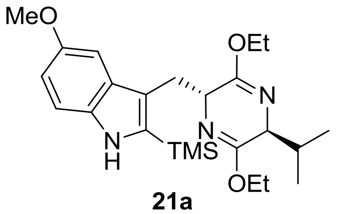


Figure S2: Displacement ellipsoid plot of (6*S*,11a*S*,*E*)-9-ethylidene-2-methoxy-6,8,9,10,11a,12-hexahydro-6,10-methanoindolo-[3,2-*b*]quinolizin-11(5*H*)-one (**36a**).

36a. The 0.586 x 0.456 x 0.055 mm^3 crystal was orthorhombic in space group $P\ 2_12_12_1$ with unit cell dimensions a = 8.2247(4) Å, b = 12.0571(6) Å, and c = 26.6490(10) Å. Data were 99.8% complete to 29.15° θ (approximately 0.73 Å) with an average redundancy of 6.39.

Copies of ^{1}H and ^{13}C NMR Spectra:

Spectra's are in the following order for each compound (^{1}H NMR, ^{13}C NMR, DEPT 135 and DEPT 90) or (^{1}H NMR, ^{13}C NMR, DEPT 90)



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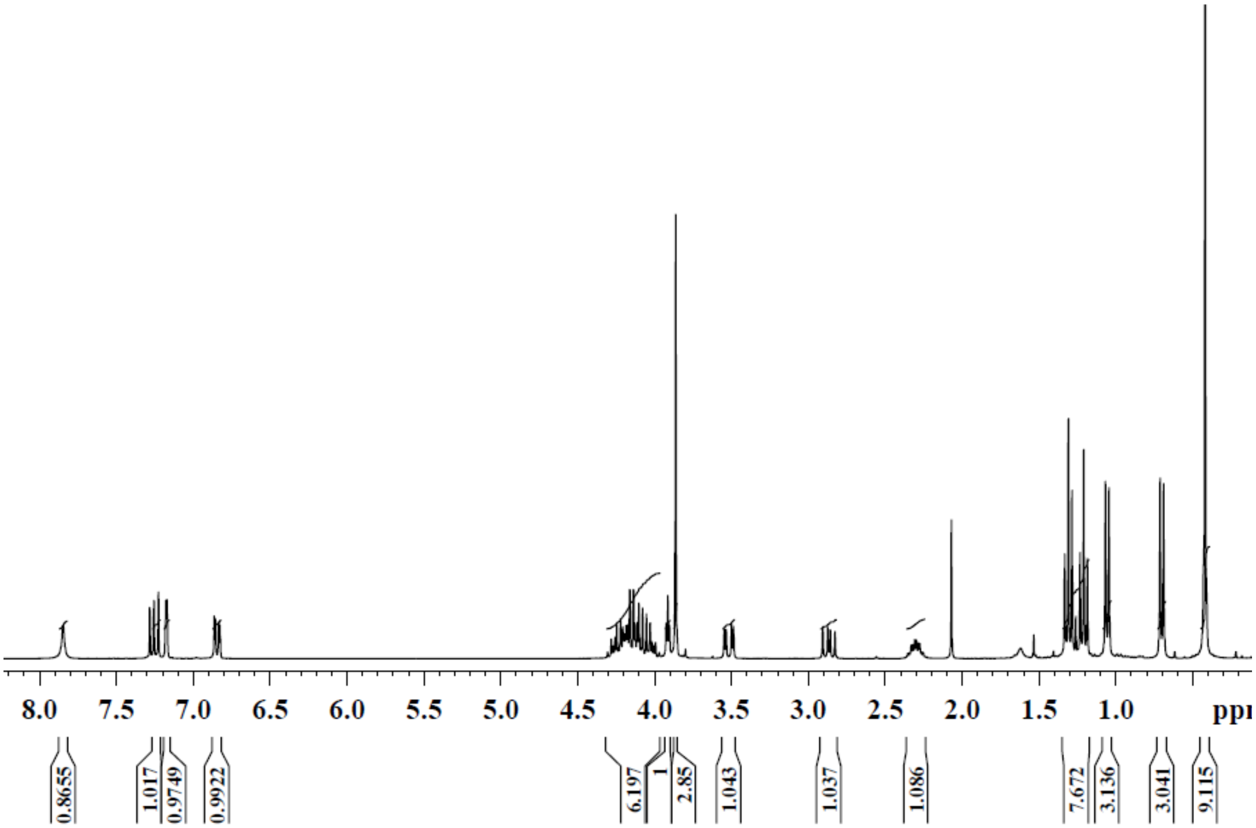

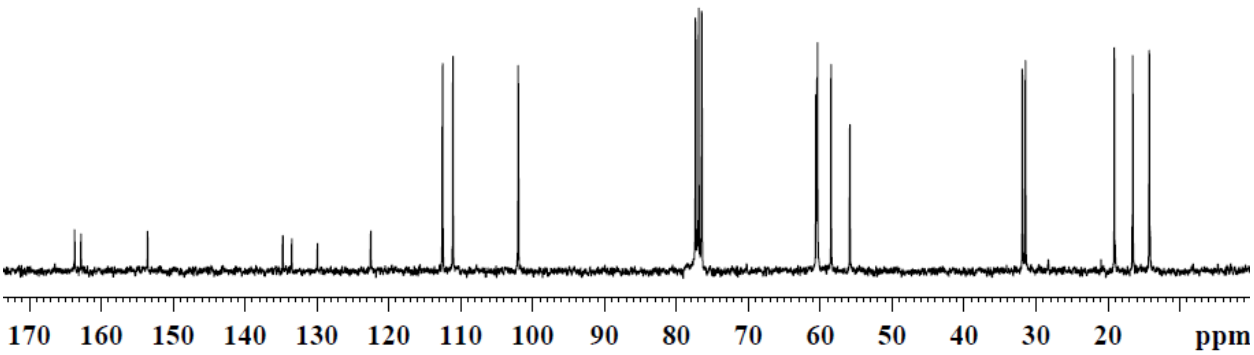
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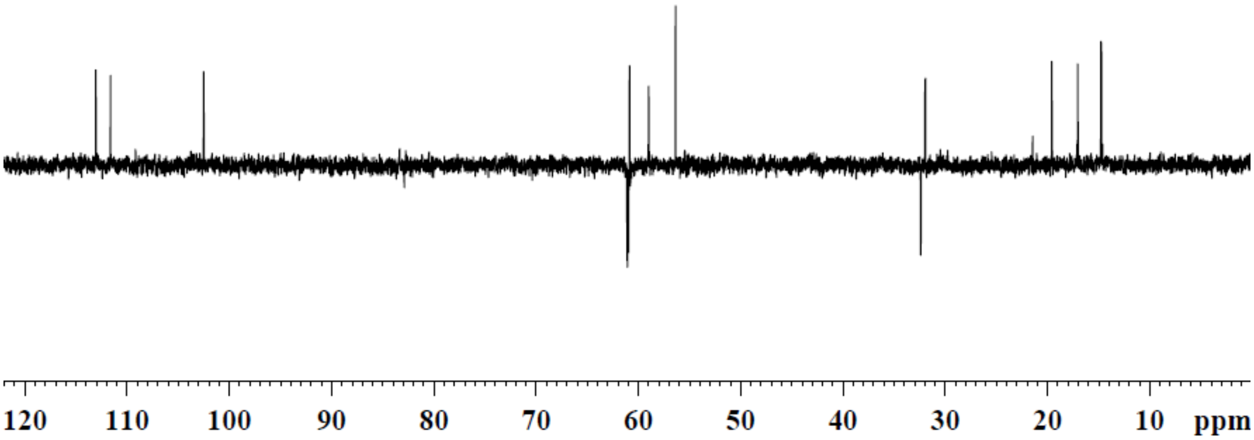
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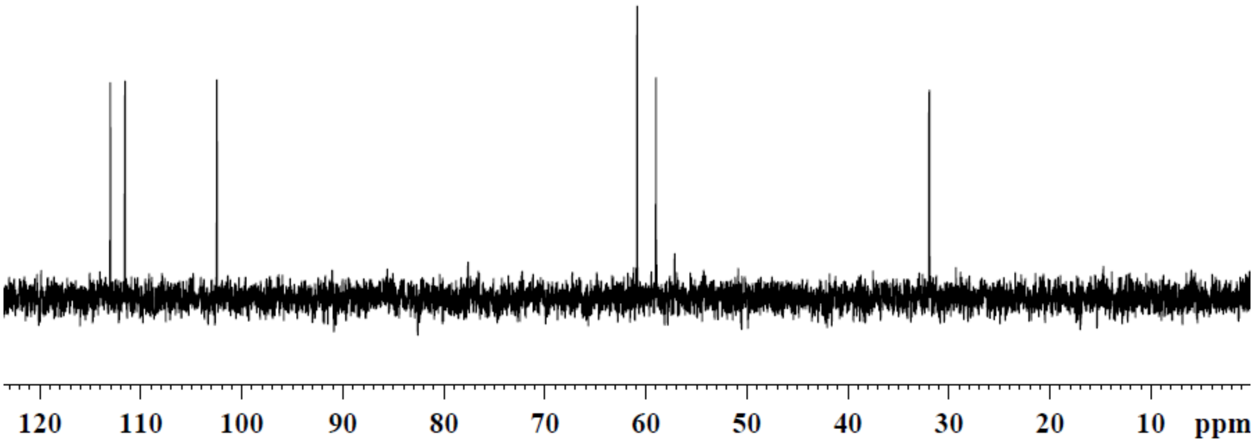
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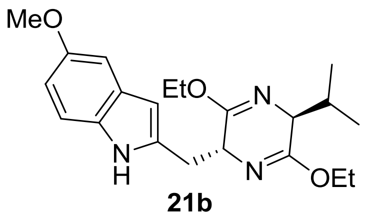
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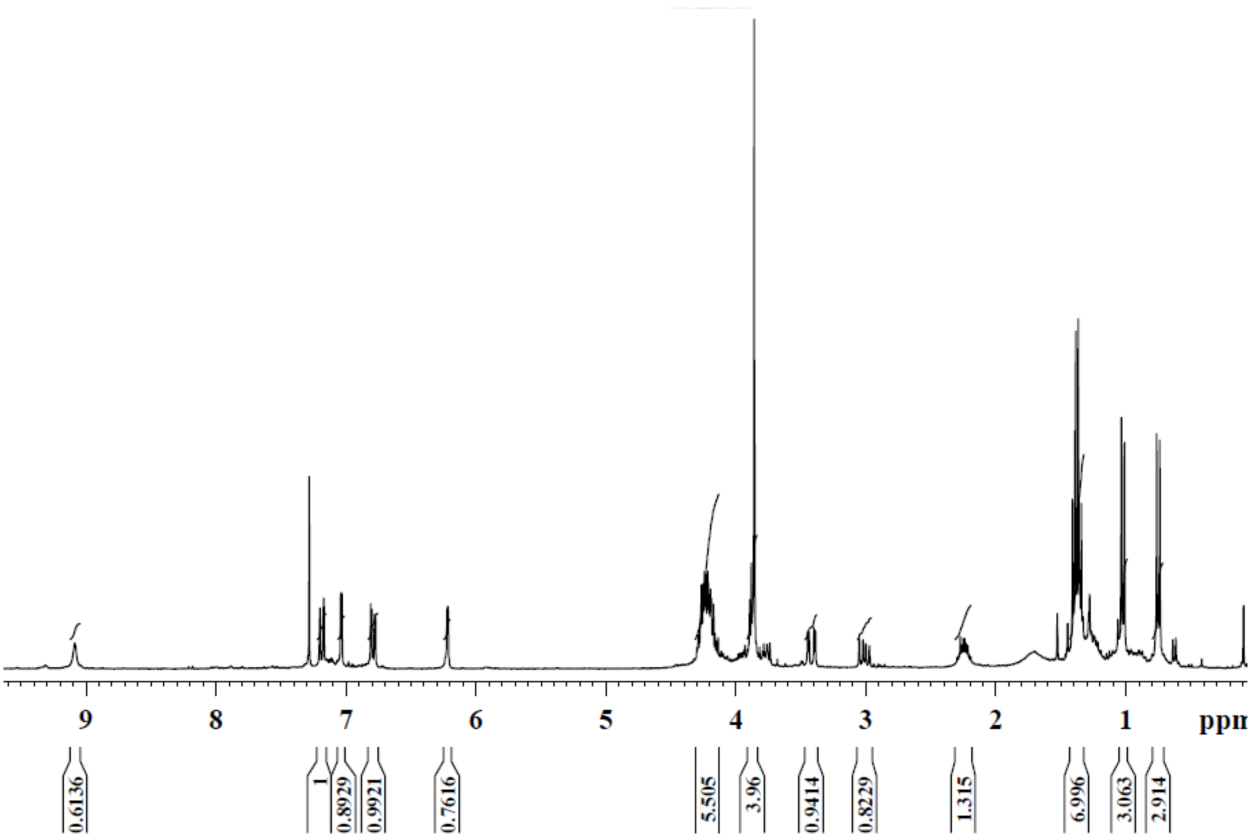
N
OEt
N
H

21b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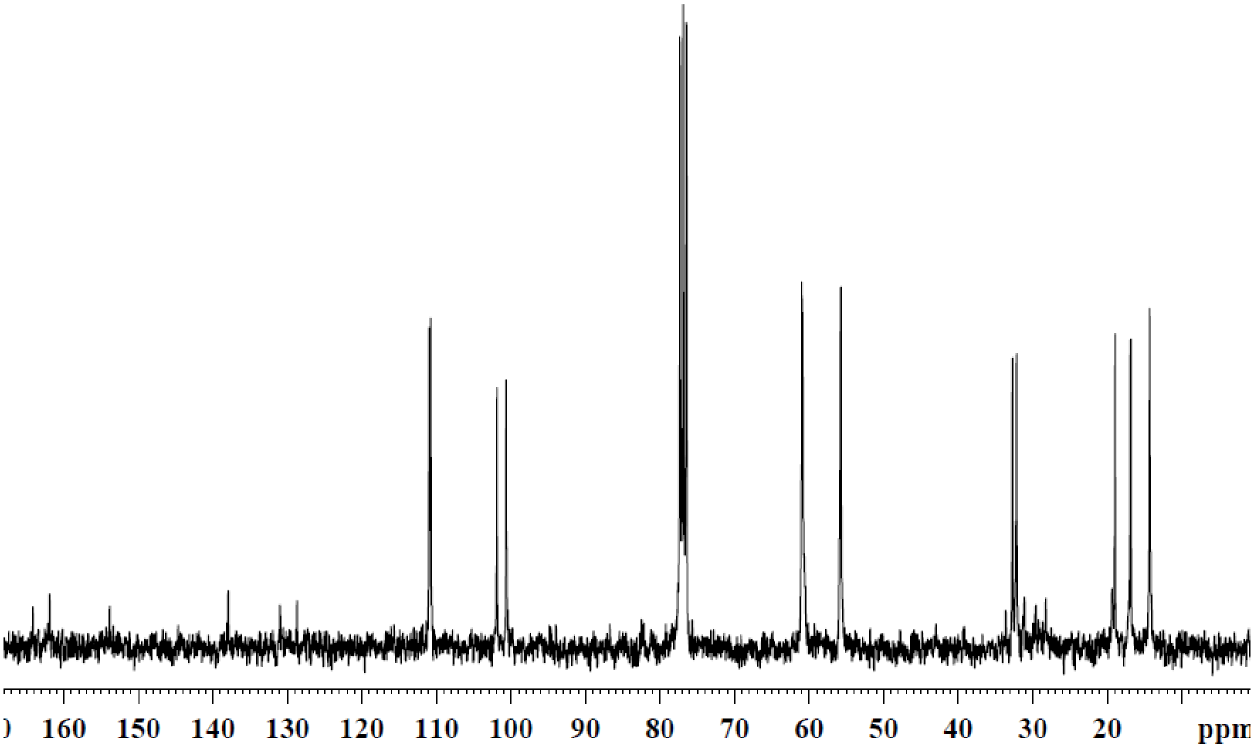
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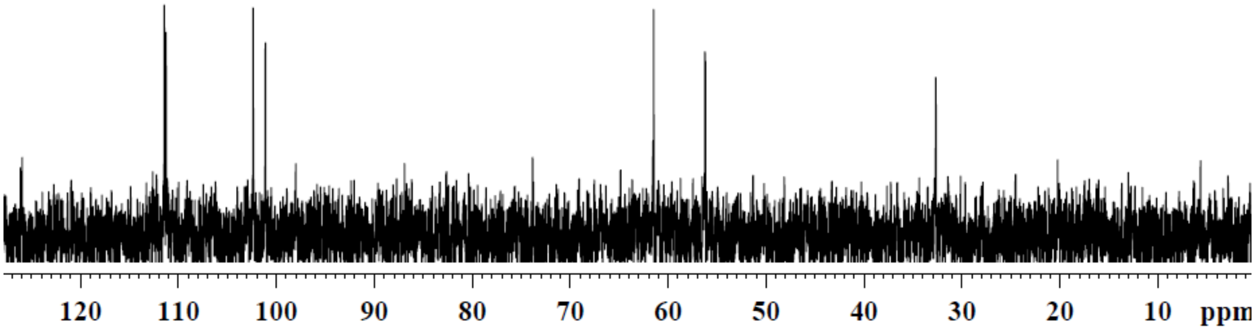
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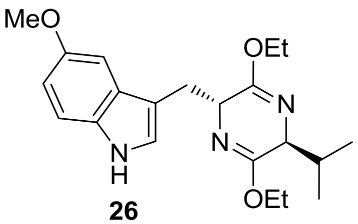
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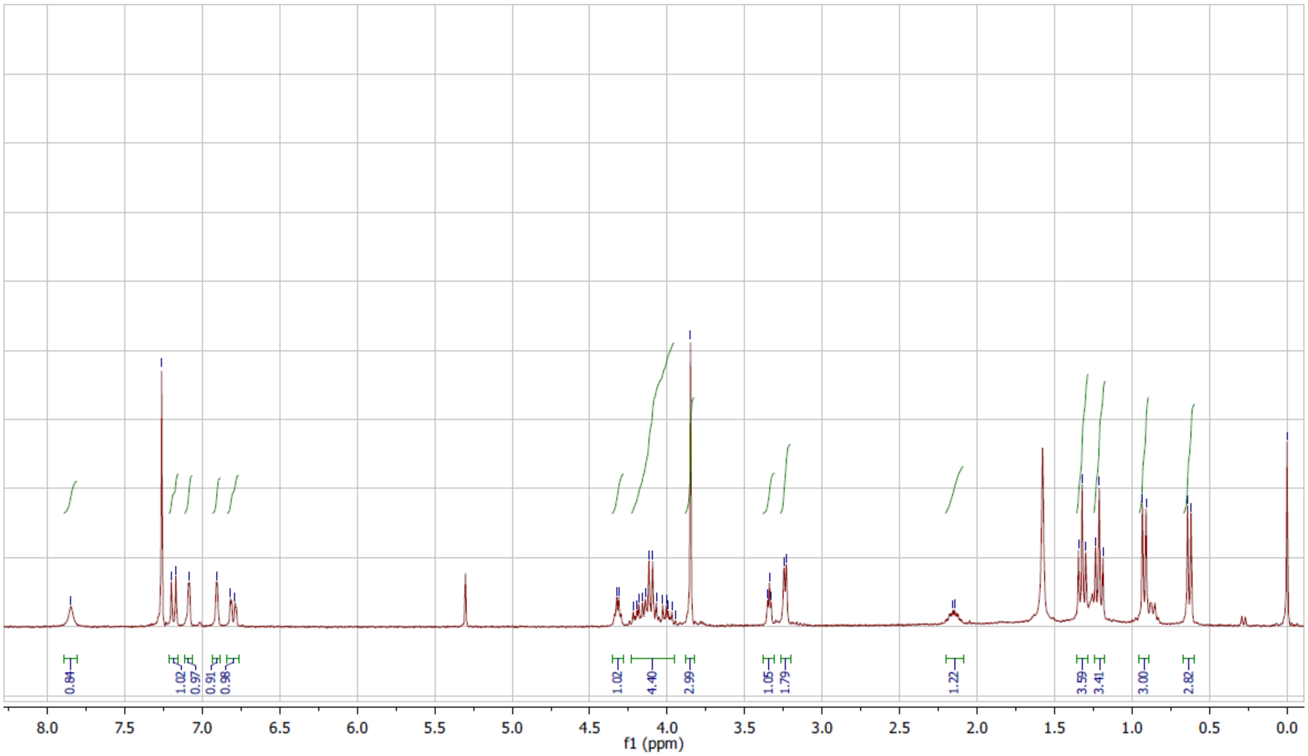
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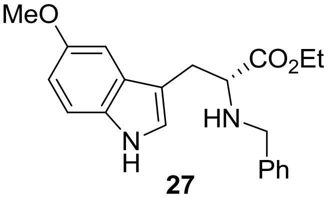
f1 (ppm)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CO2Et
HN
Ph
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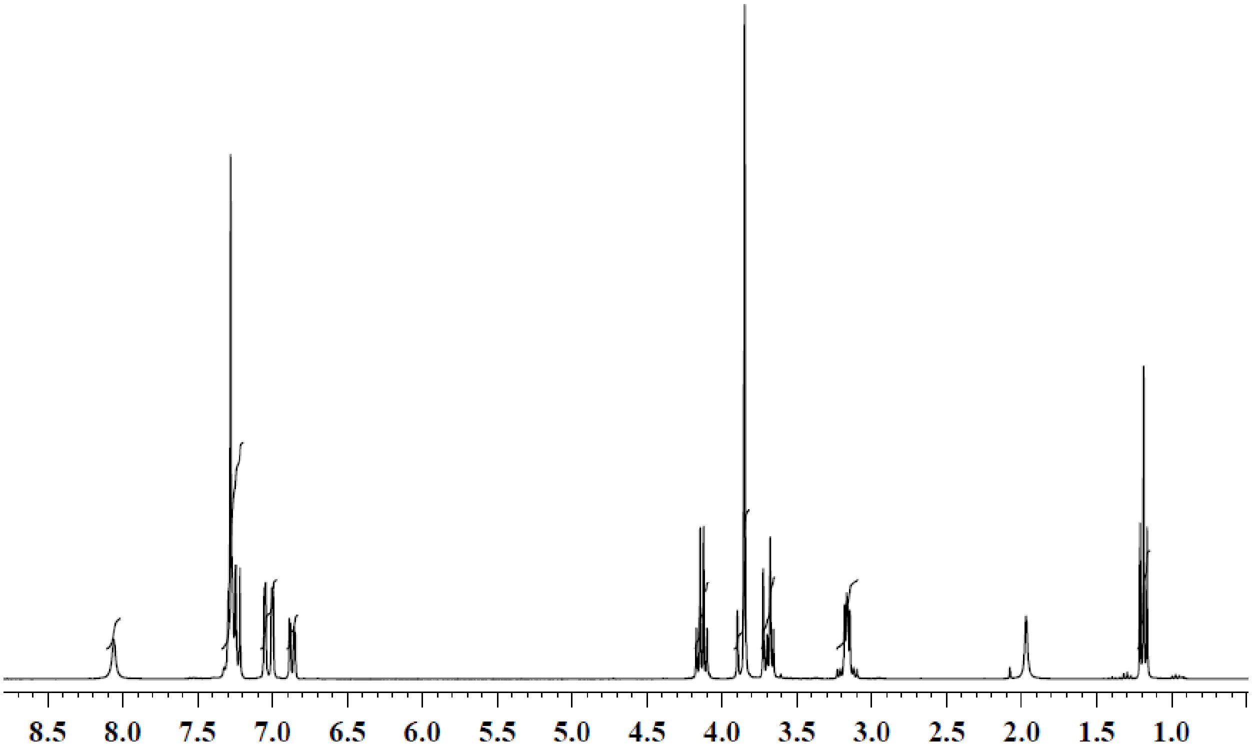
H

27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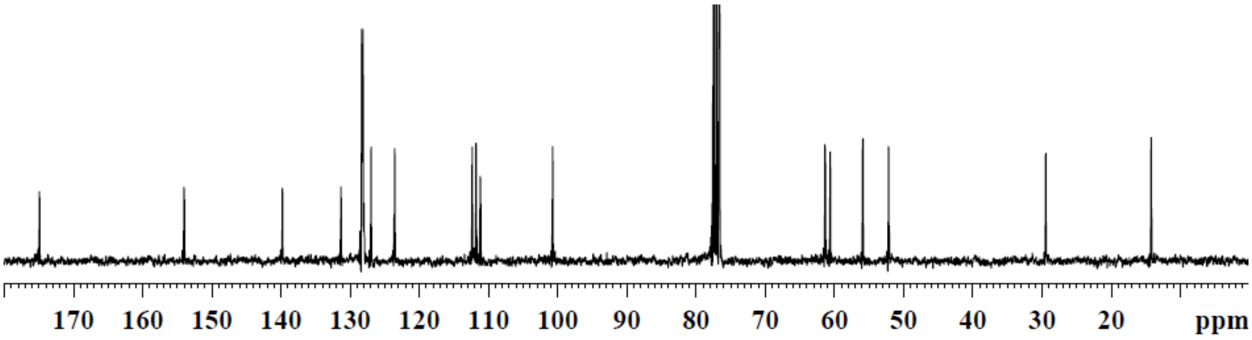
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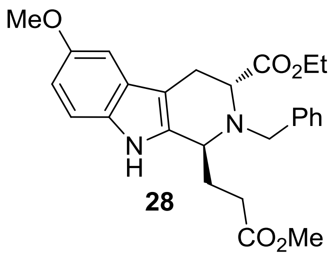
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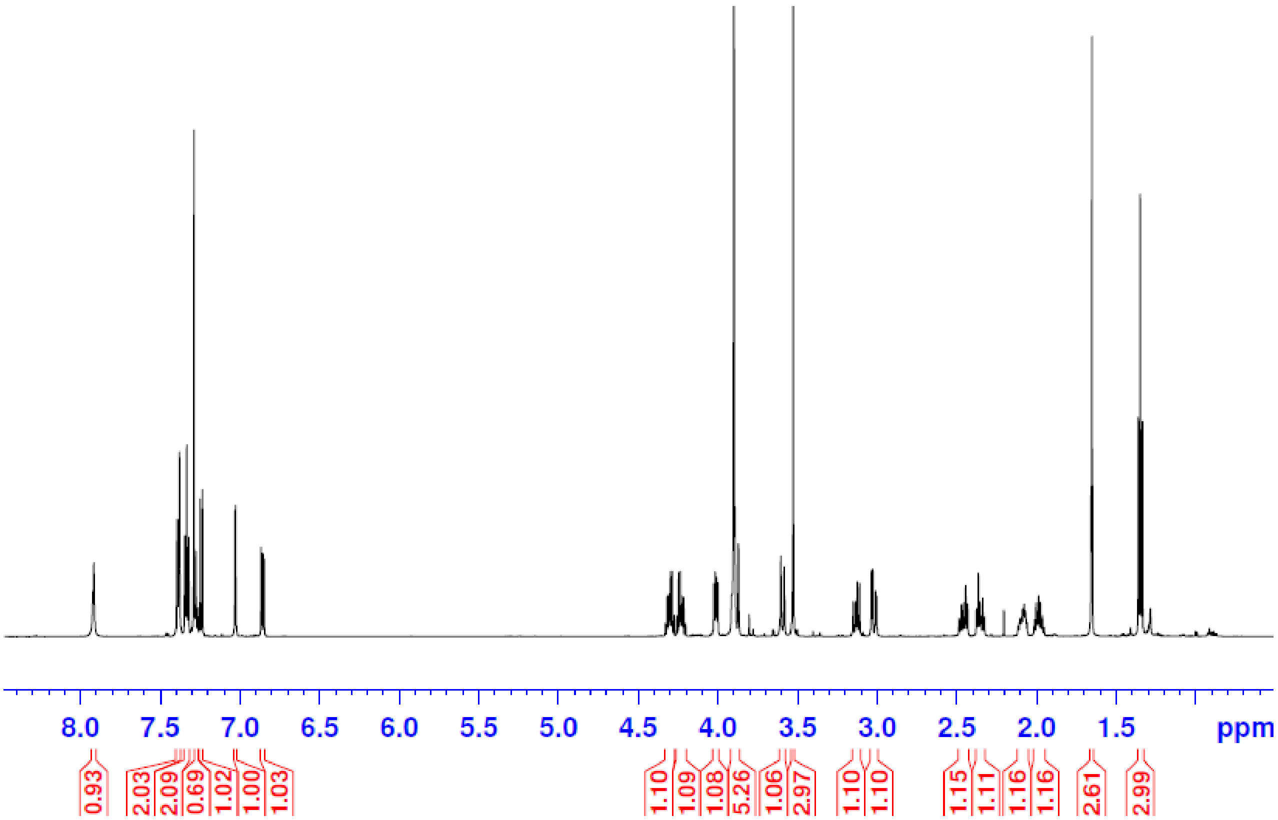
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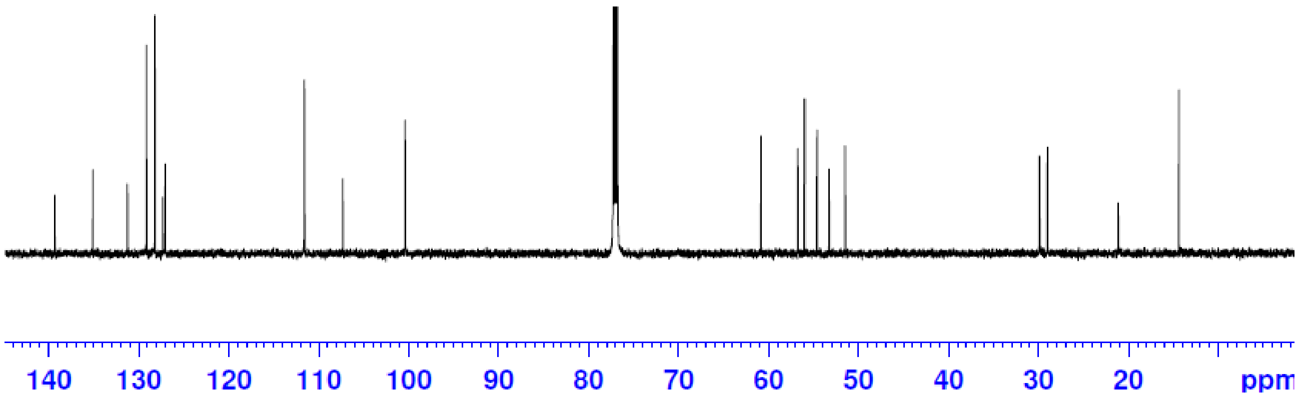
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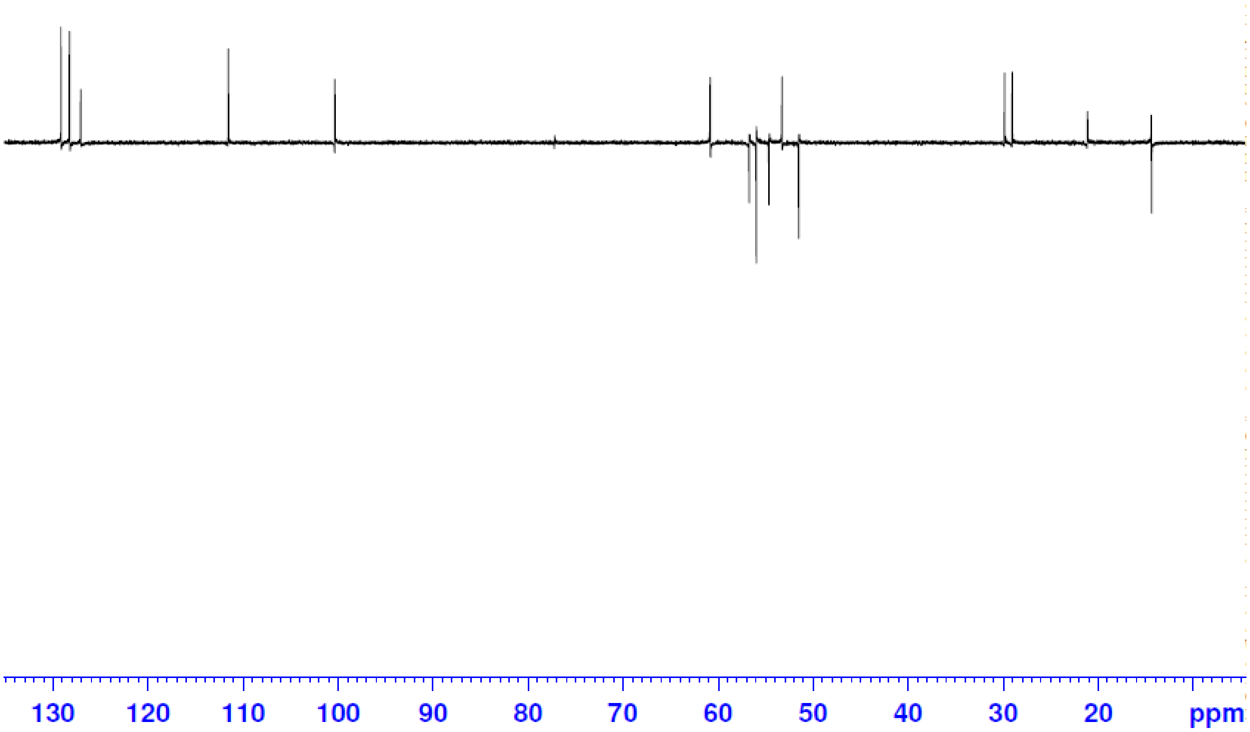
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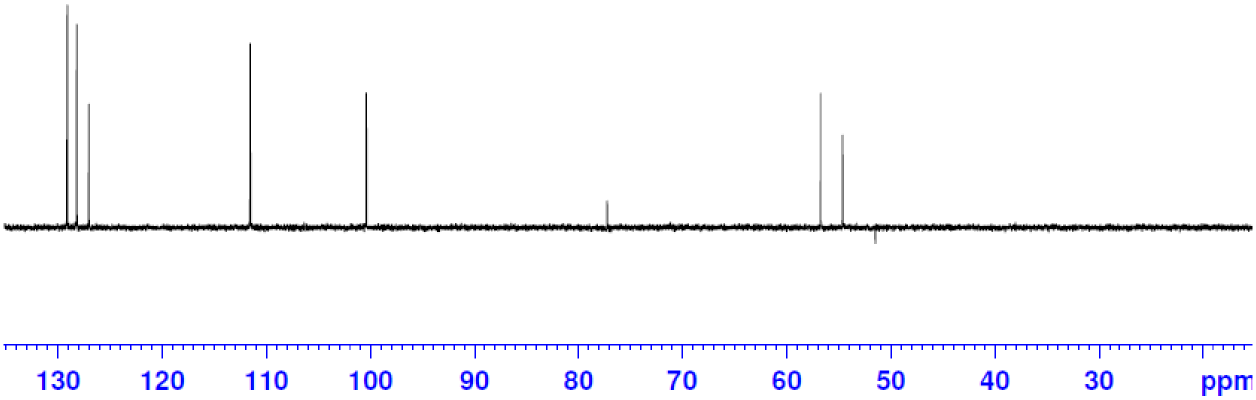
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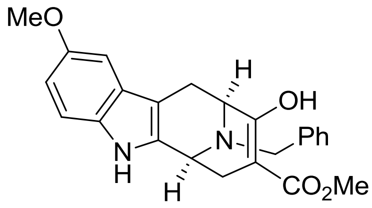
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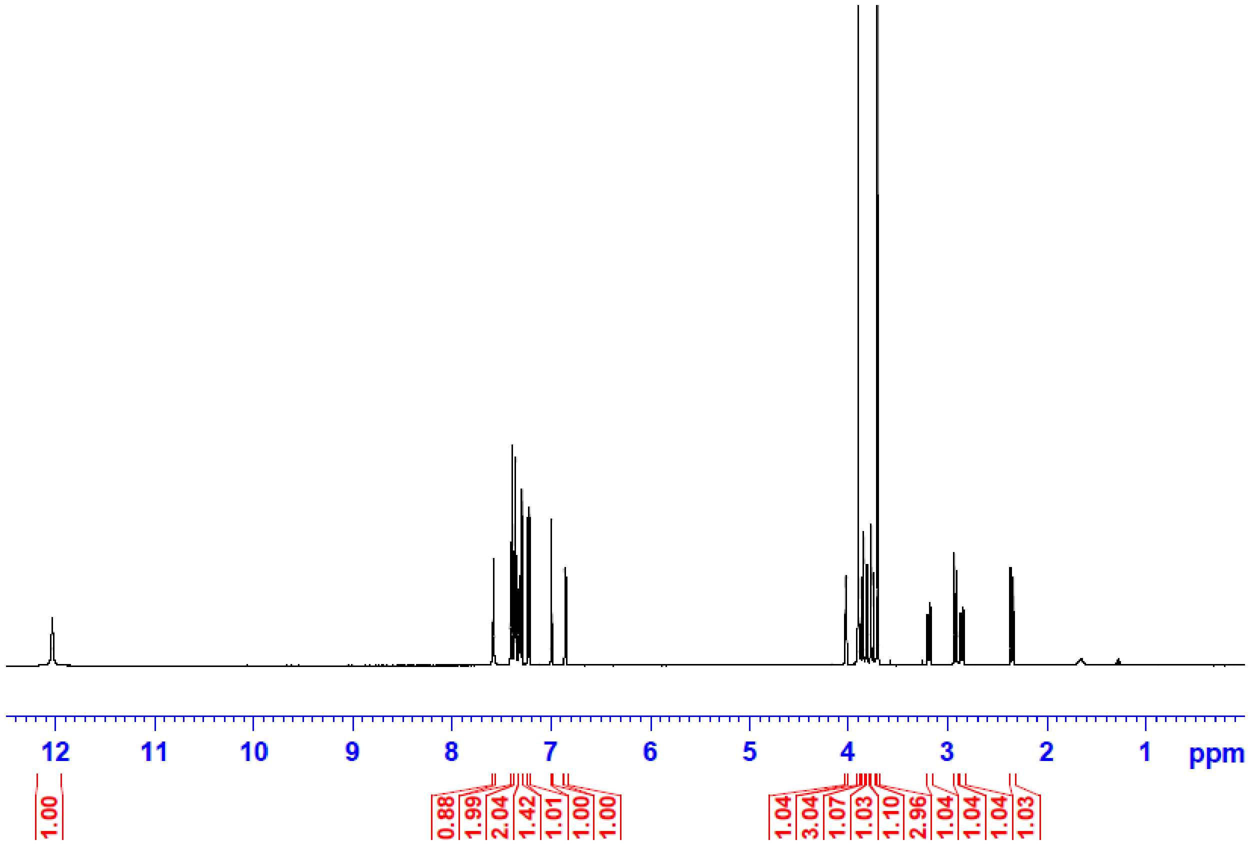
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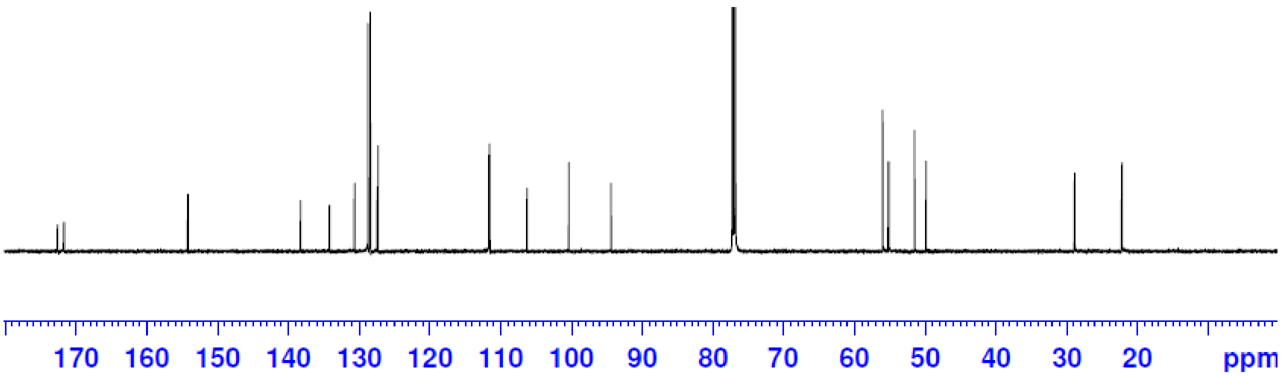
1.03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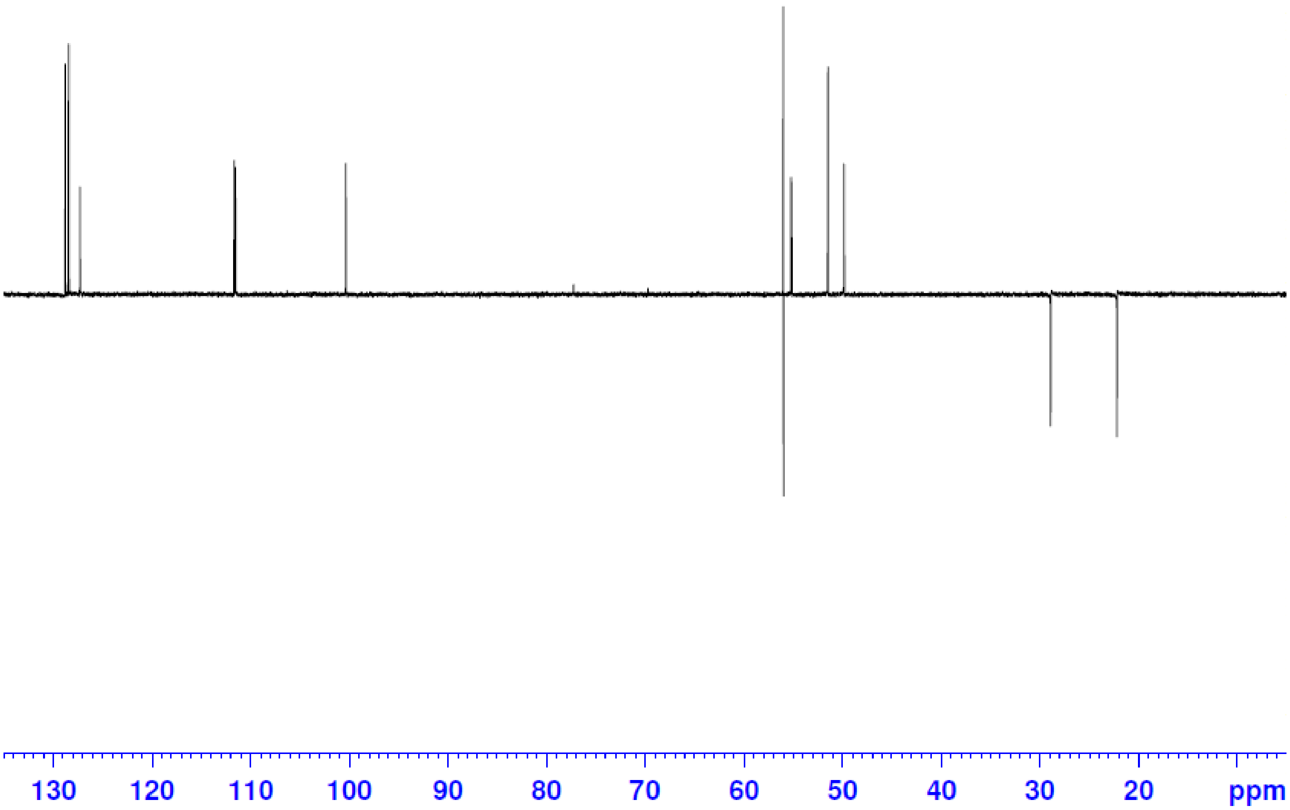
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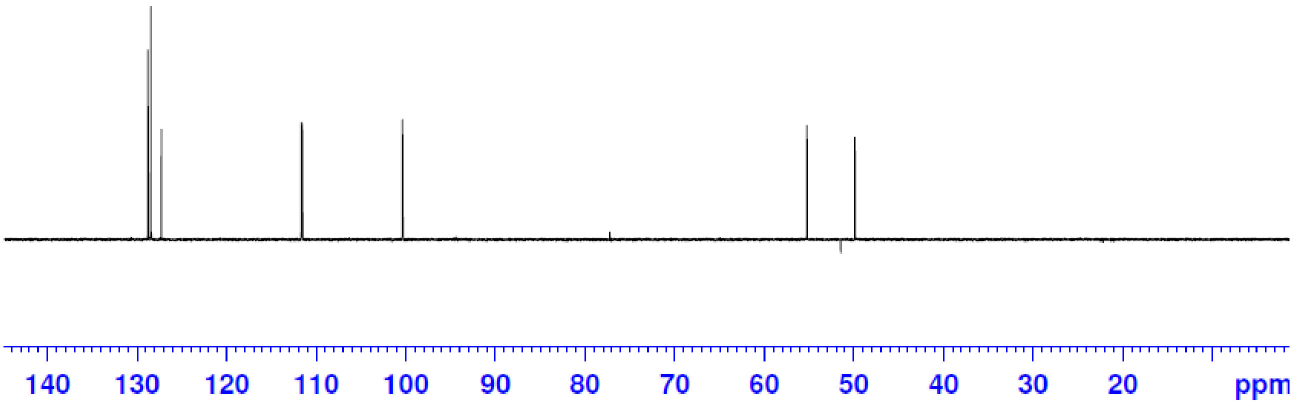
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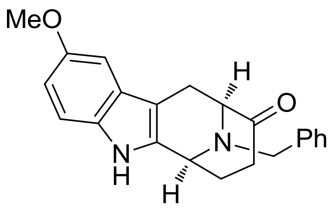
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Ph
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H

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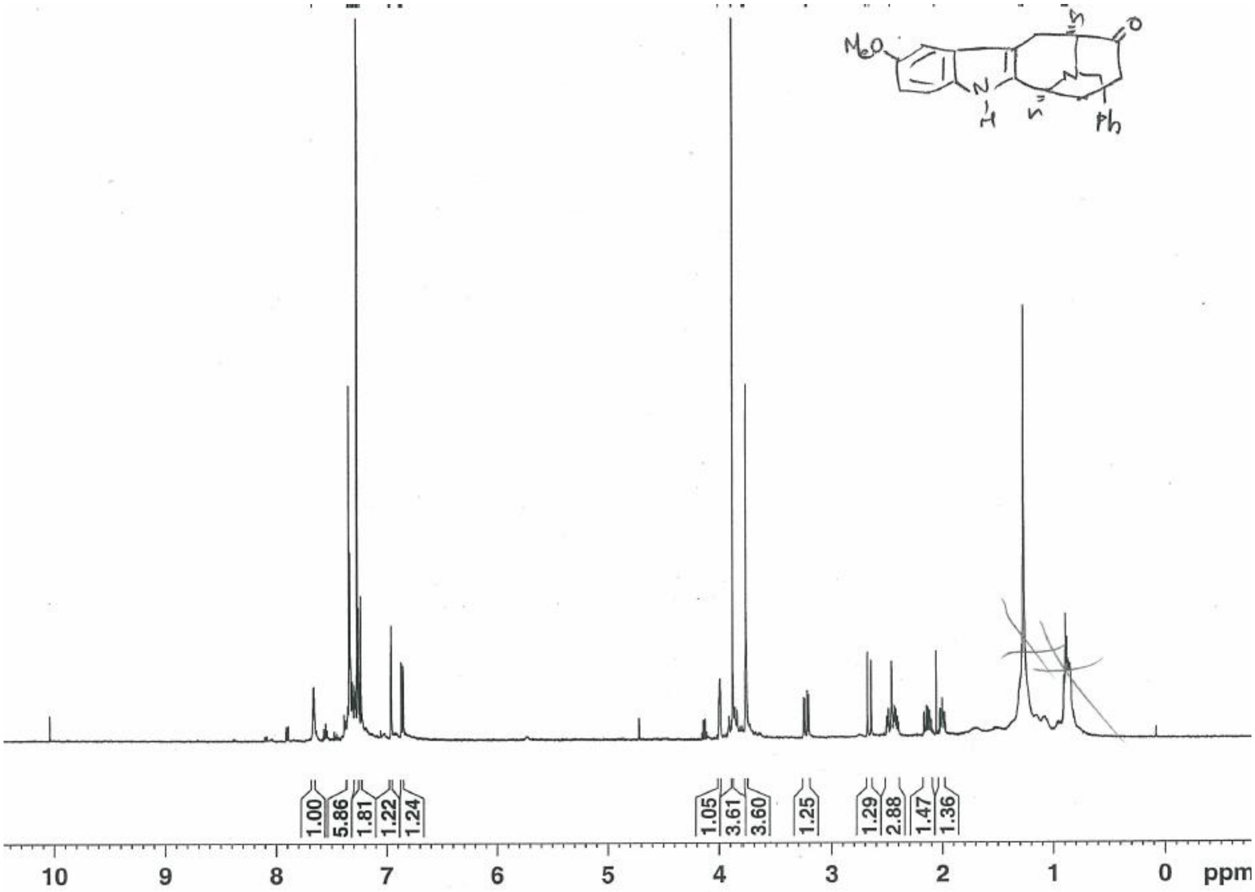
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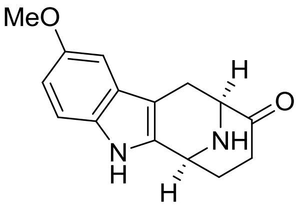

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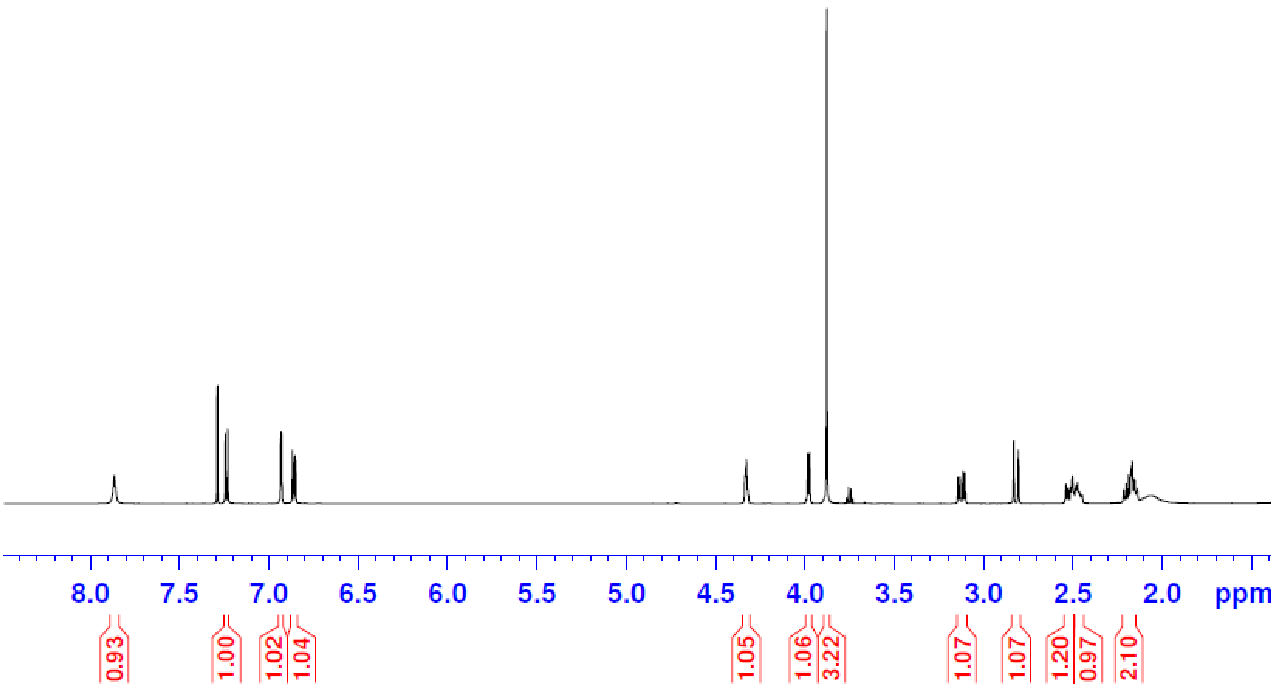

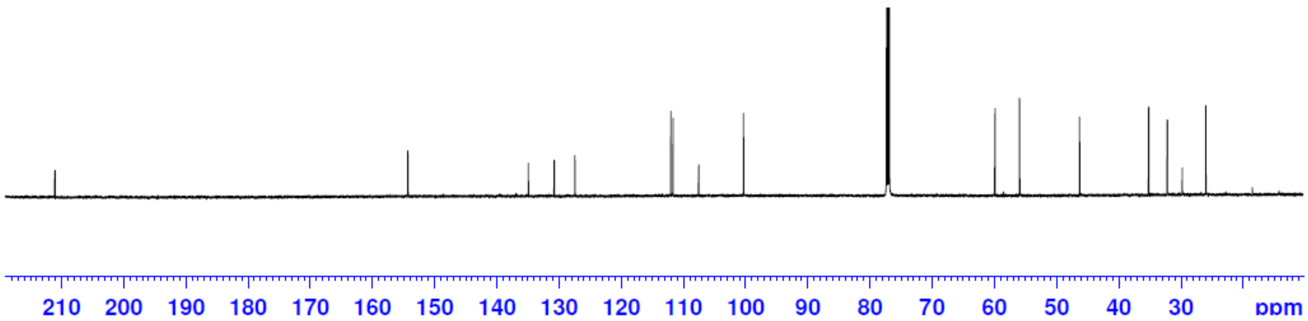

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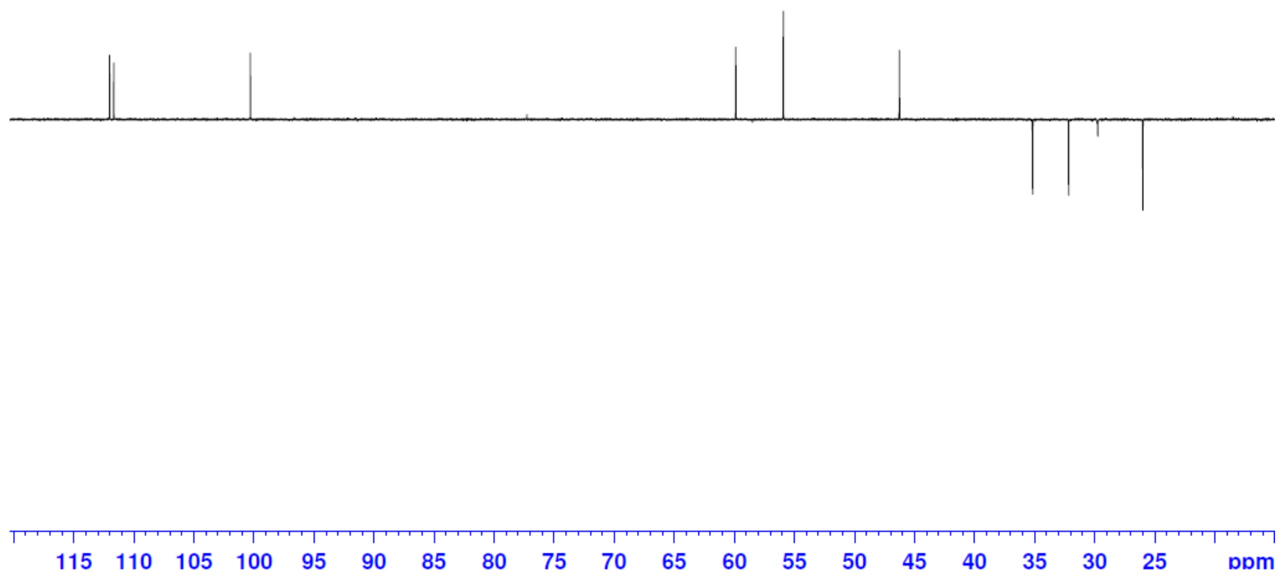
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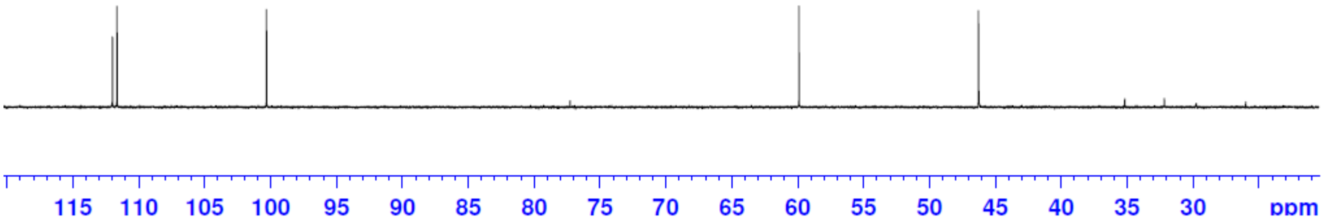
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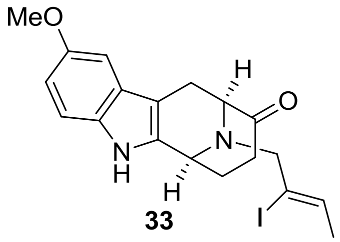
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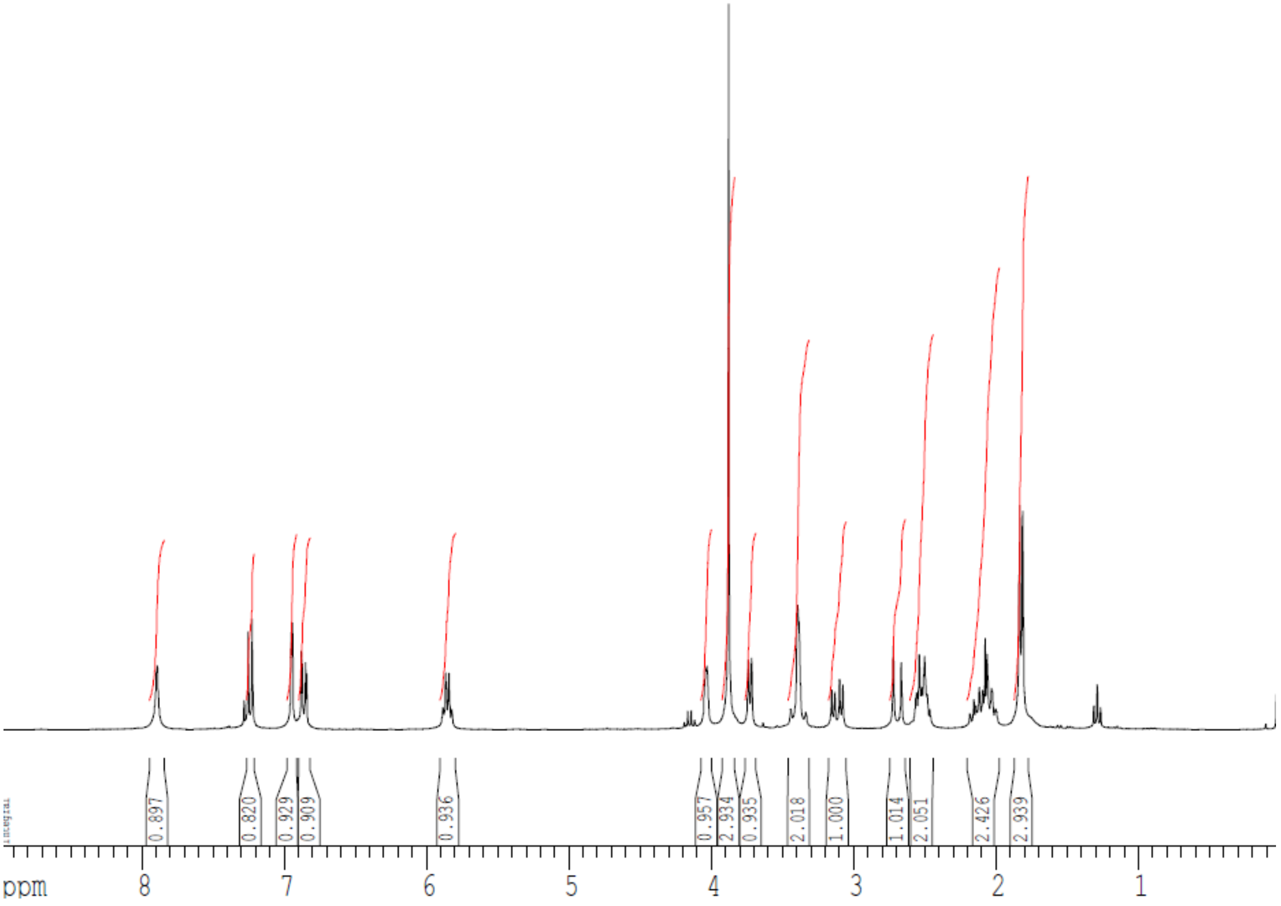
N
H
H
I

33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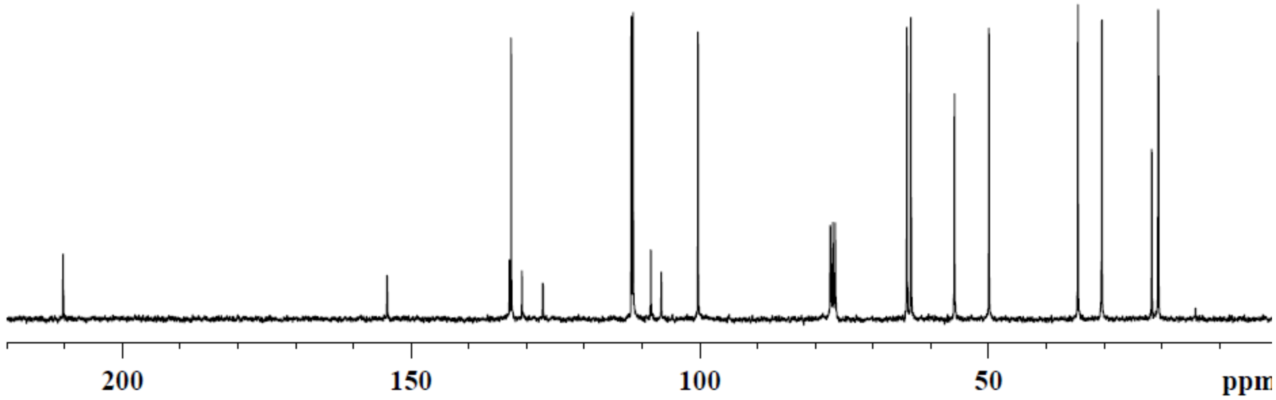
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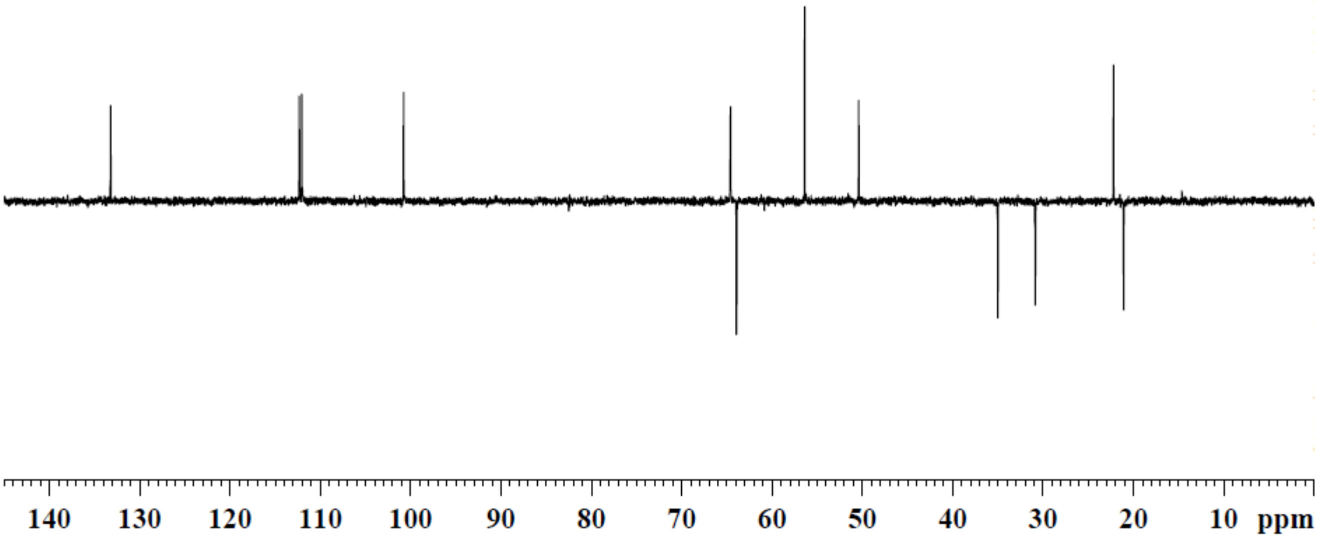
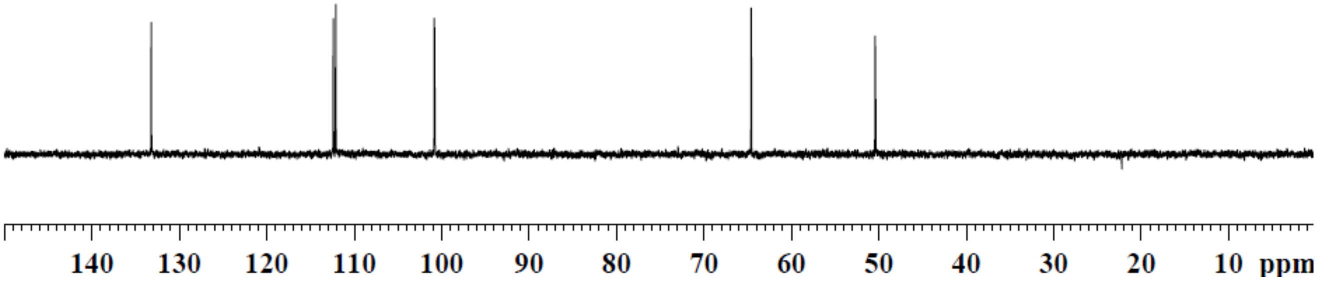
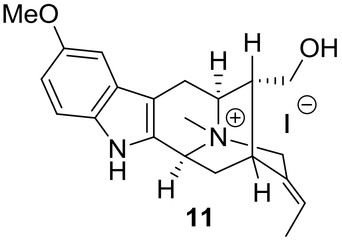
50
ppm

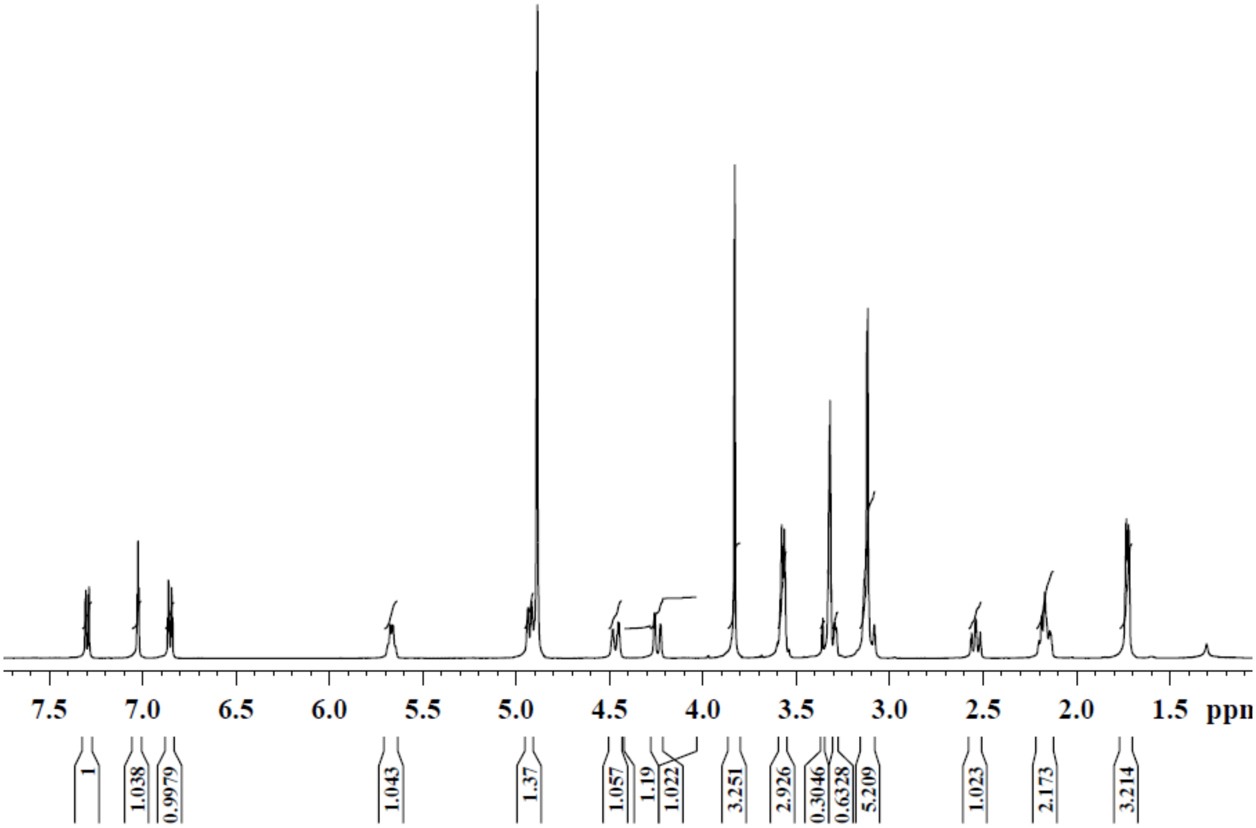

140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

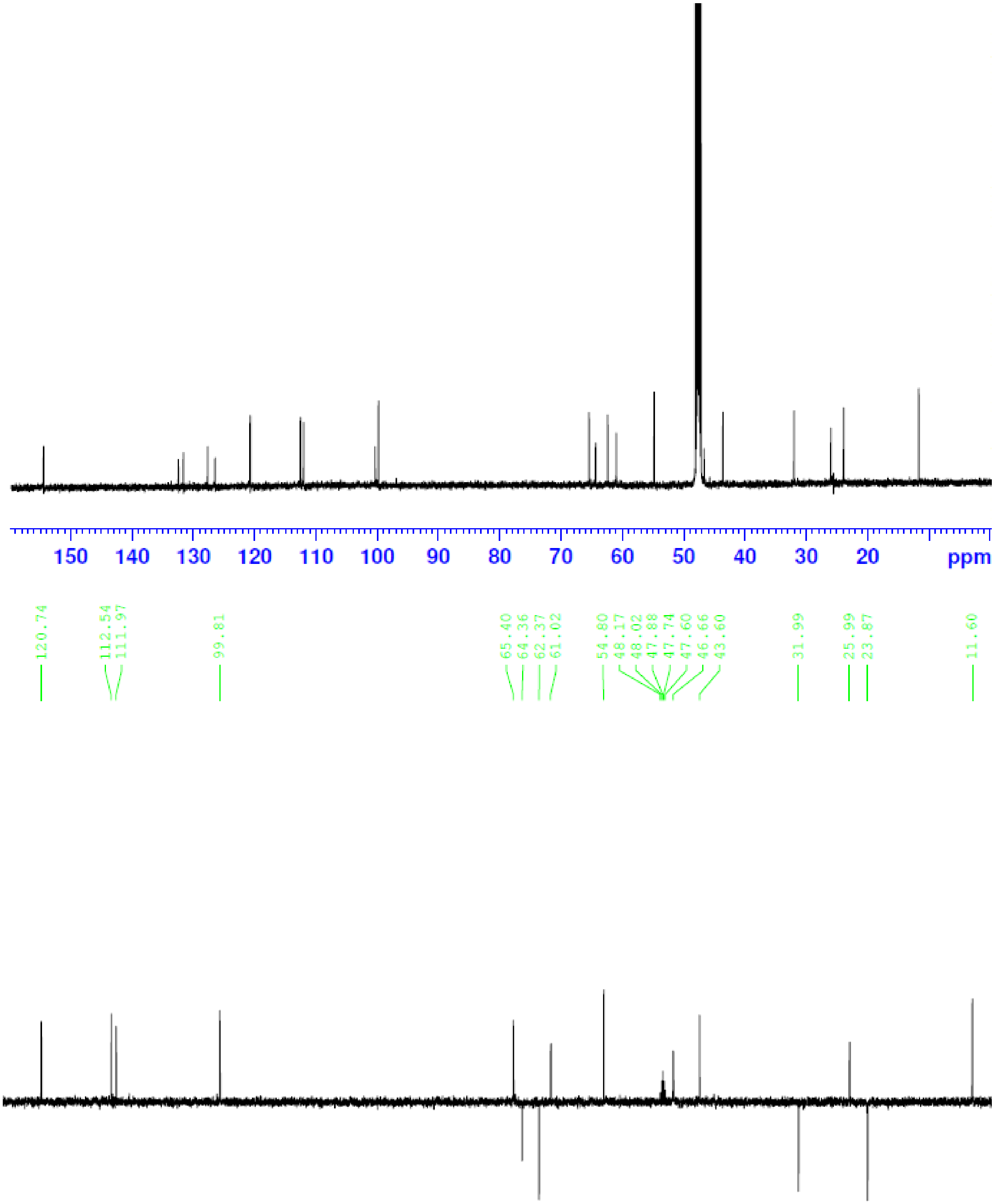

140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

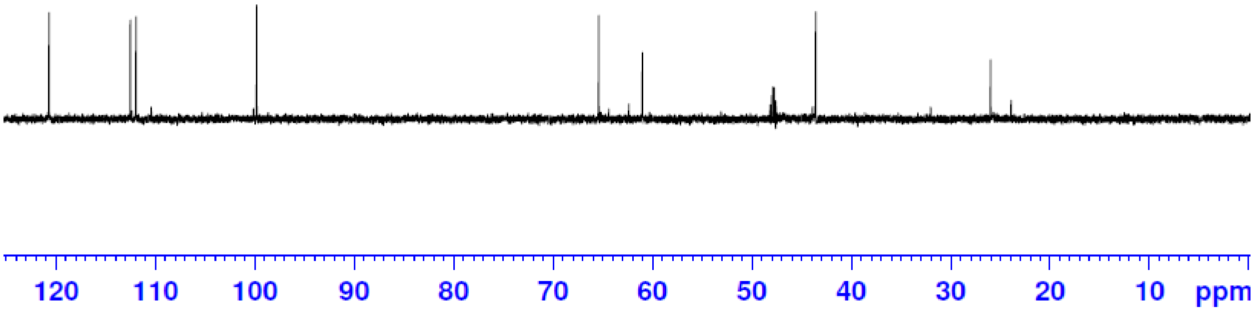


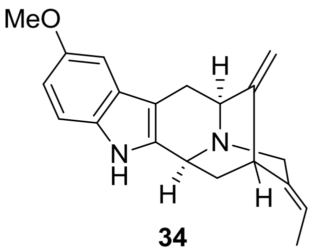
11

(+)-lochneram

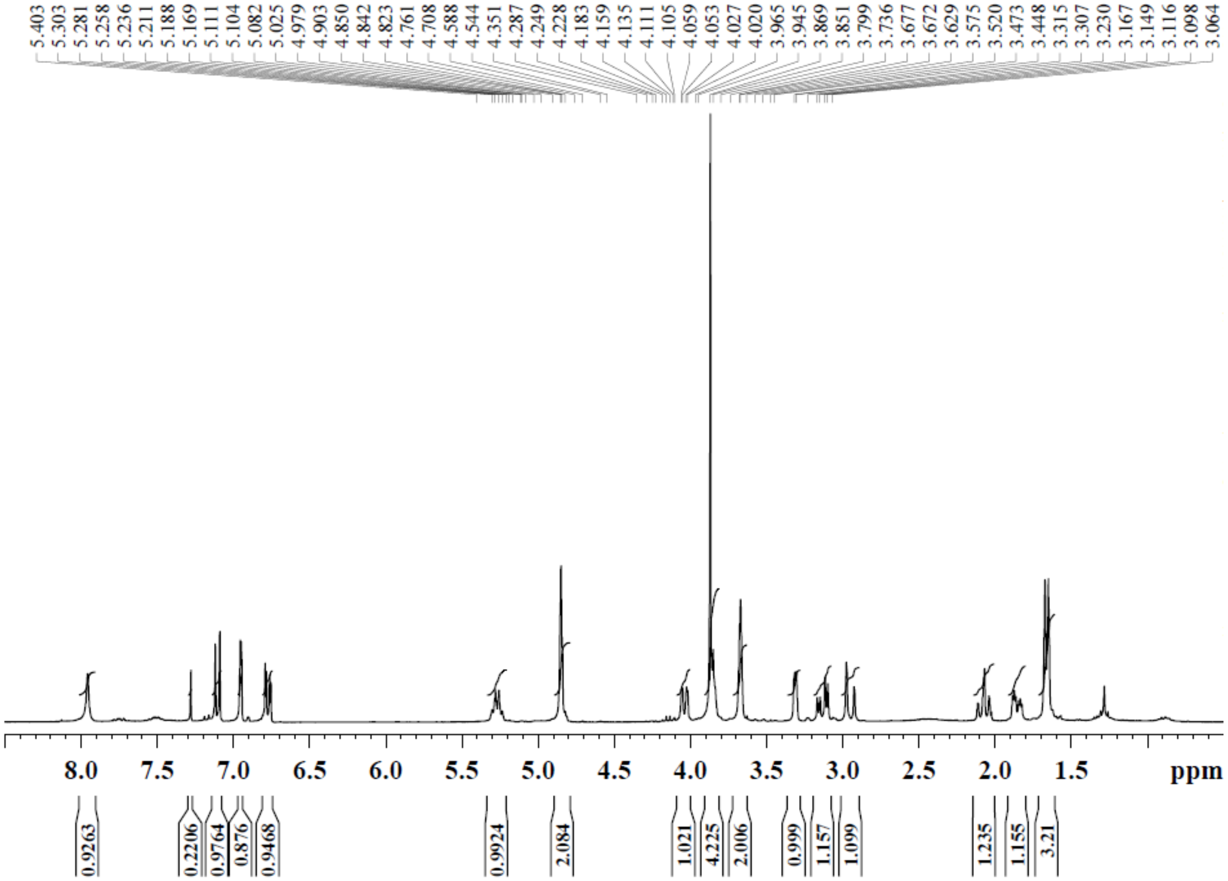


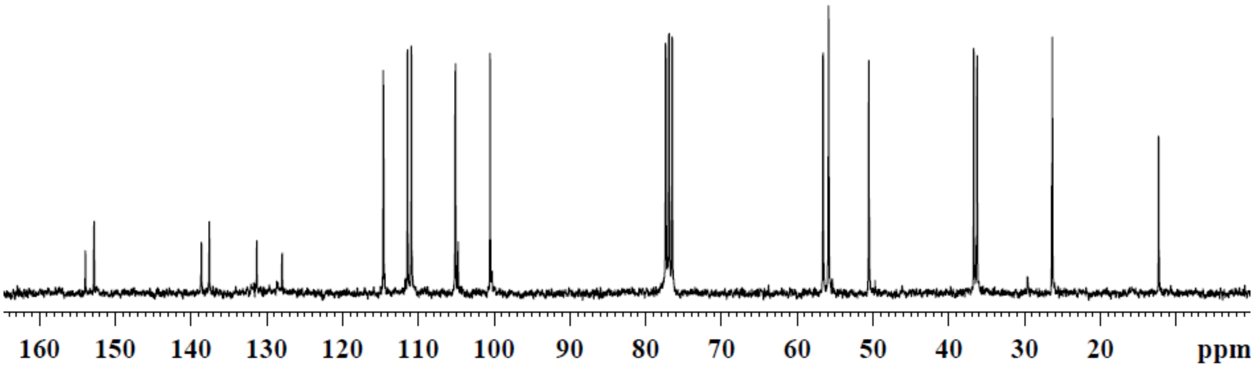

150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
120.74
112.54
111.97
99.81
65.40
64.36
62.37
61.02
54.80
48.17
48.02
47.88
47.74
47.60
46.66
43.60
31.99
25.99
23.87
11.60

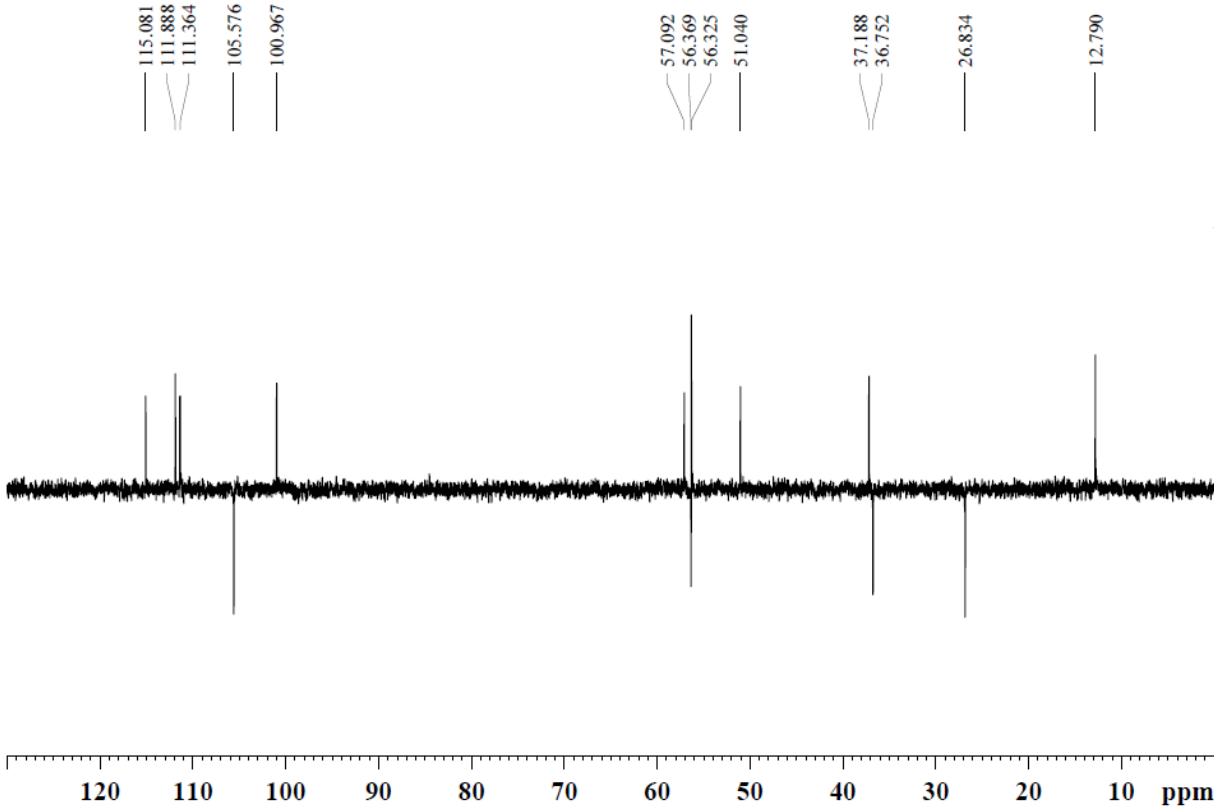

120
110
100
90
80
70
60
50
40
30
20
10
ppm

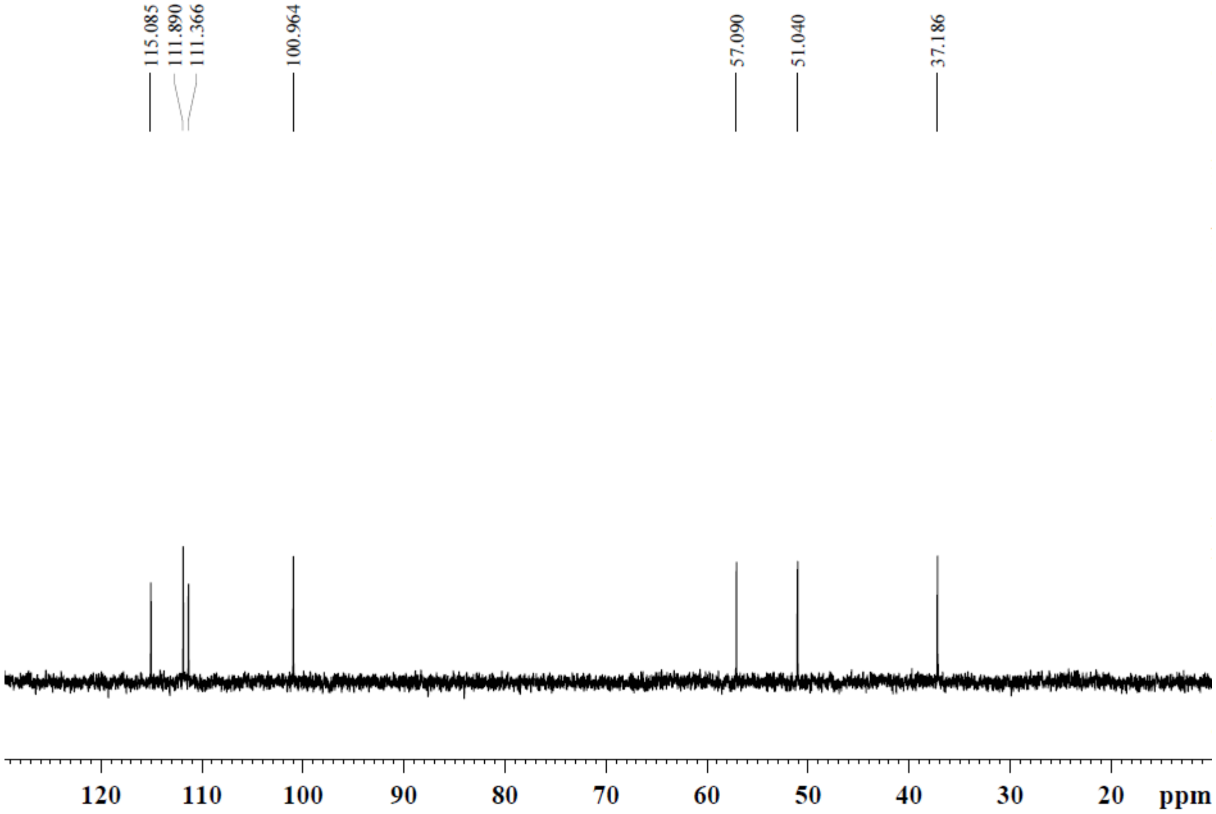

MeO
H
N
NH
H
H

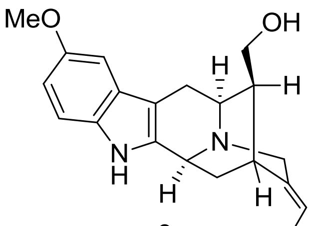
34


5.403
5.303
5.281
5.258
5.236
5.211
5.188
5.169
5.111
5.104
5.082
5.025
4.979
4.903
4.850
4.842
4.823
4.761
4.708
4.588
4.544
4.351
4.287
4.249
4.228
4.183
4.159
4.135
4.111
4.105
4.059
4.053
4.027
4.020
3.965
3.945
3.869
3.851
3.799
3.736
3.677
3.672
3.629
3.575
3.520
3.473
3.448
3.315
3.307
3.230
3.167
3.149
3.116
3.098
3.064
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.9263
0.2206
0.9764
0.876
0.9468
0.9924
2.084
1.021
4.225
2.006
0.999
1.157
1.099
1.235
1.155
3.21


160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

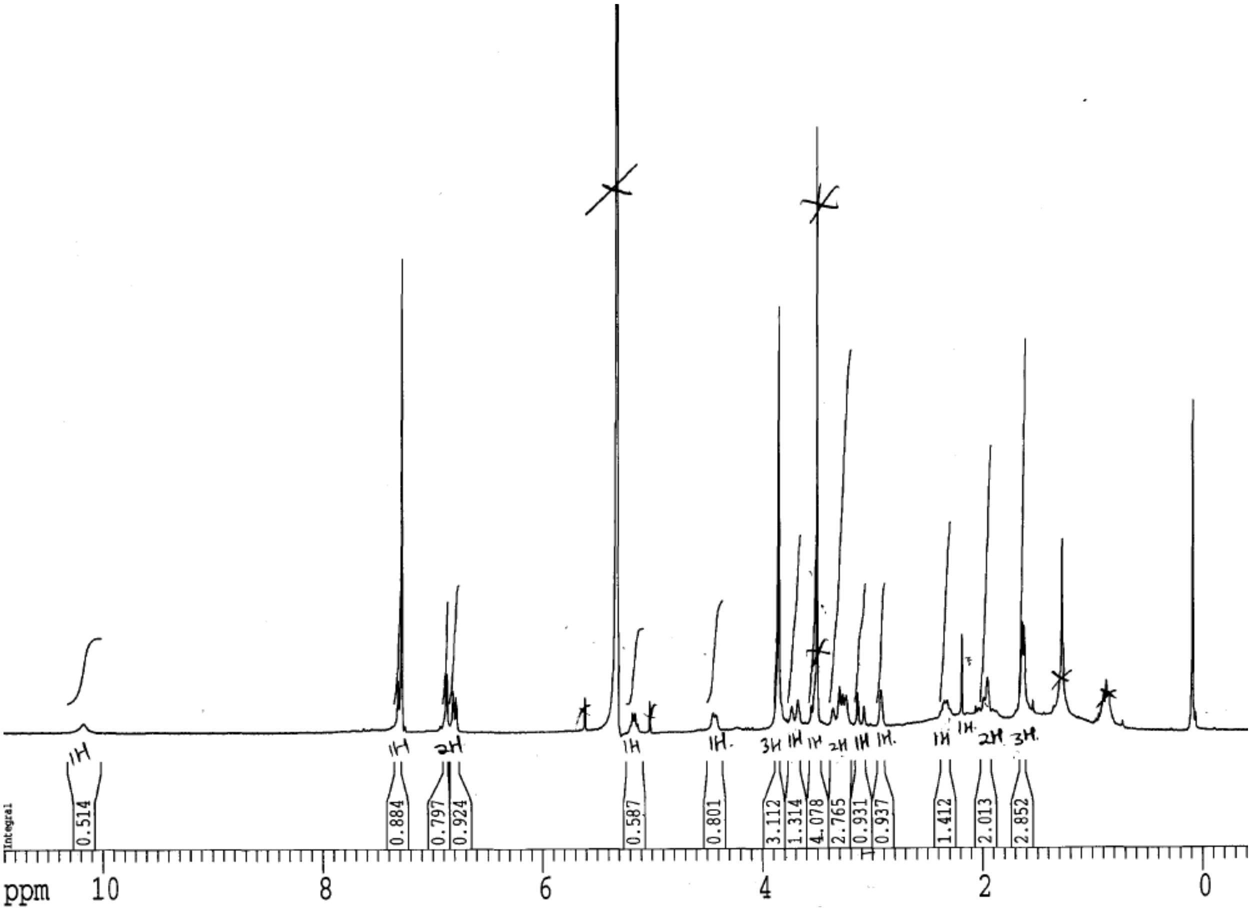

115.081
111.888
111.364
105.576
100.967
57.092
56.369
56.325
51.040
37.188
36.752
26.834
12.790
120
110
100
90
80
70
60
50
40
30
20
10
ppm

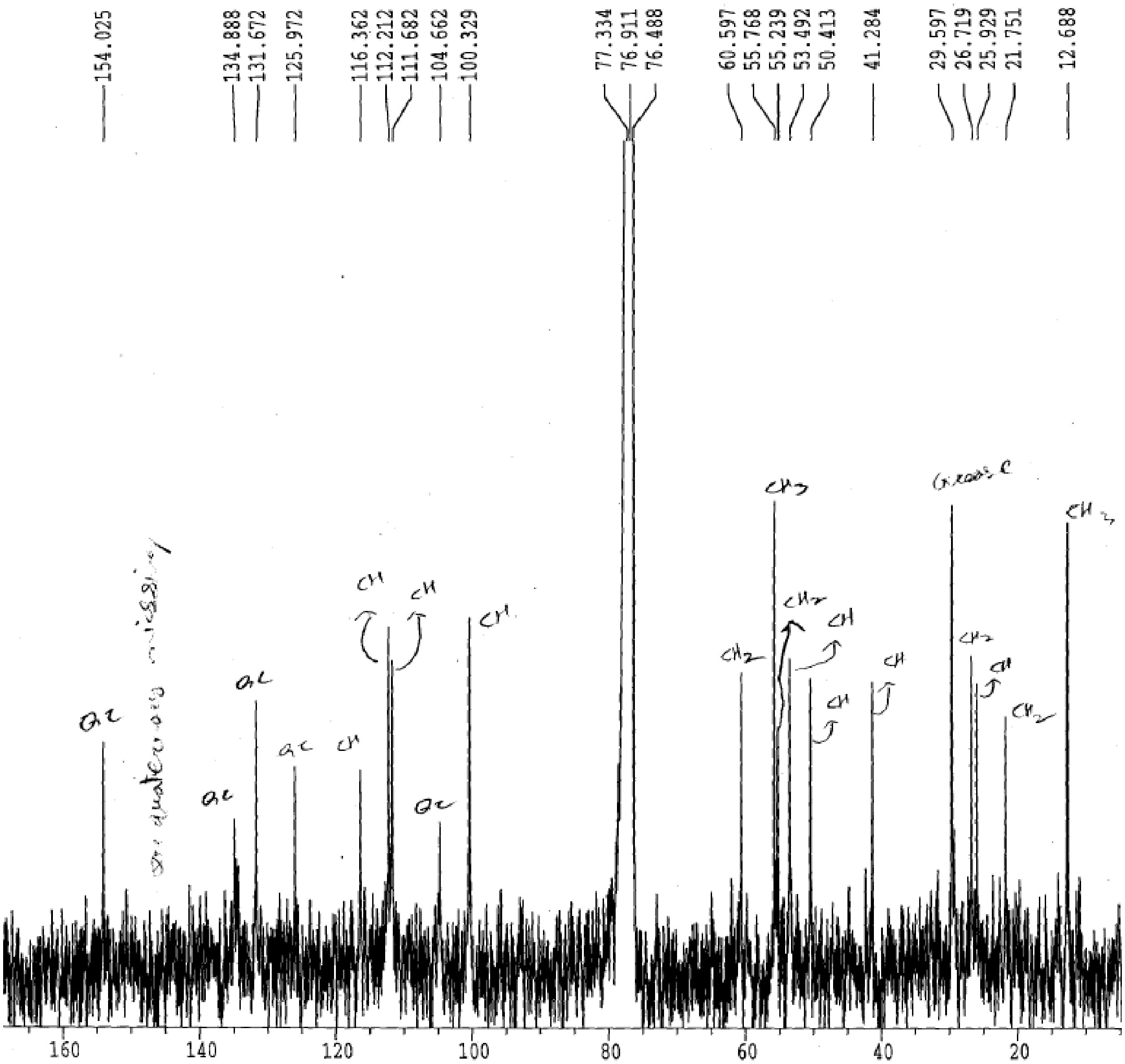

115.085
111.890
111.366
100.964
57.090
51.040
37.186
120
110
100
90
80
70
60
50
40
30
20
ppm

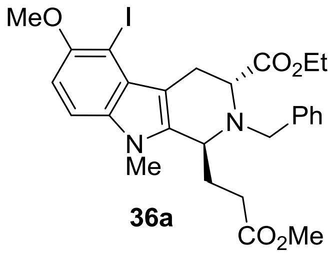


9

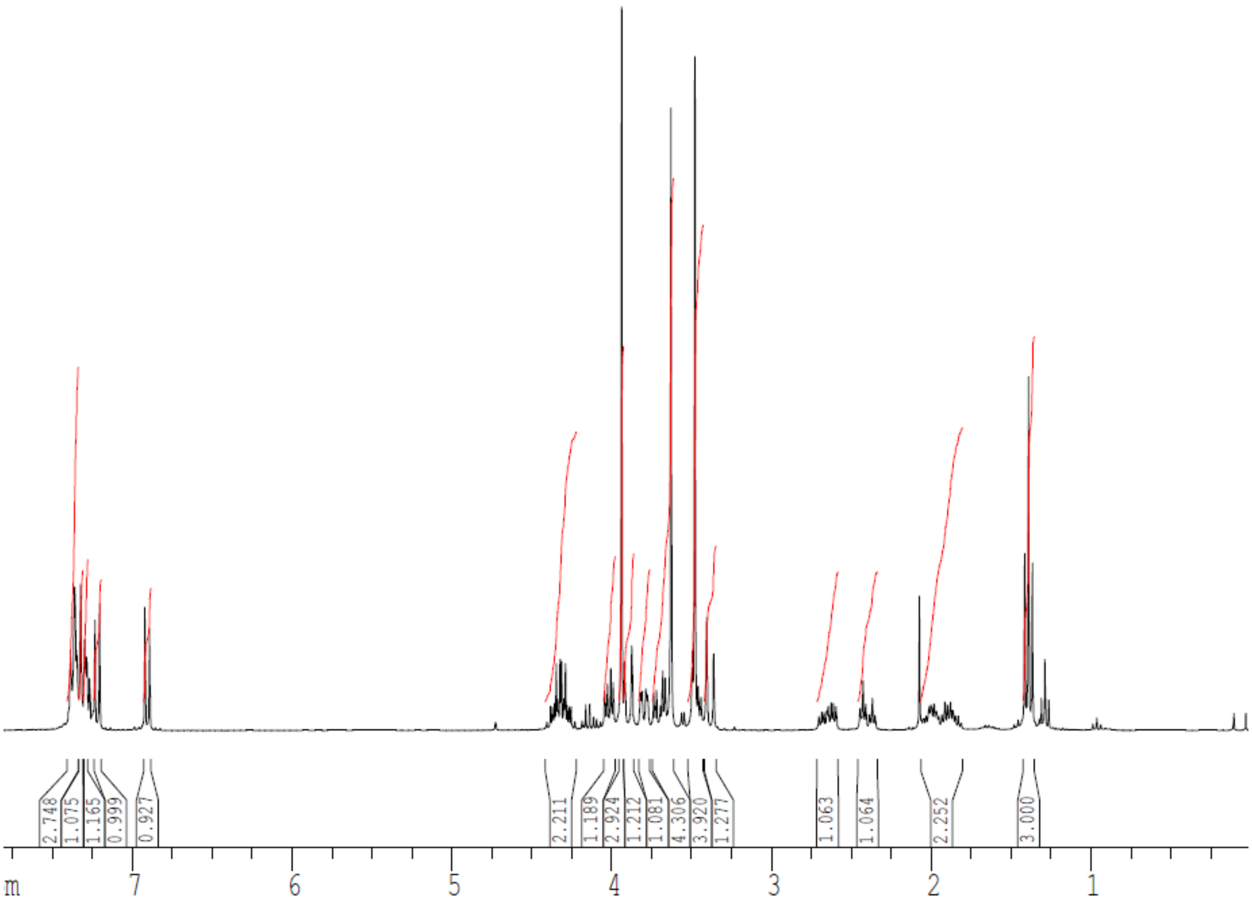
(+)-lochvinerine

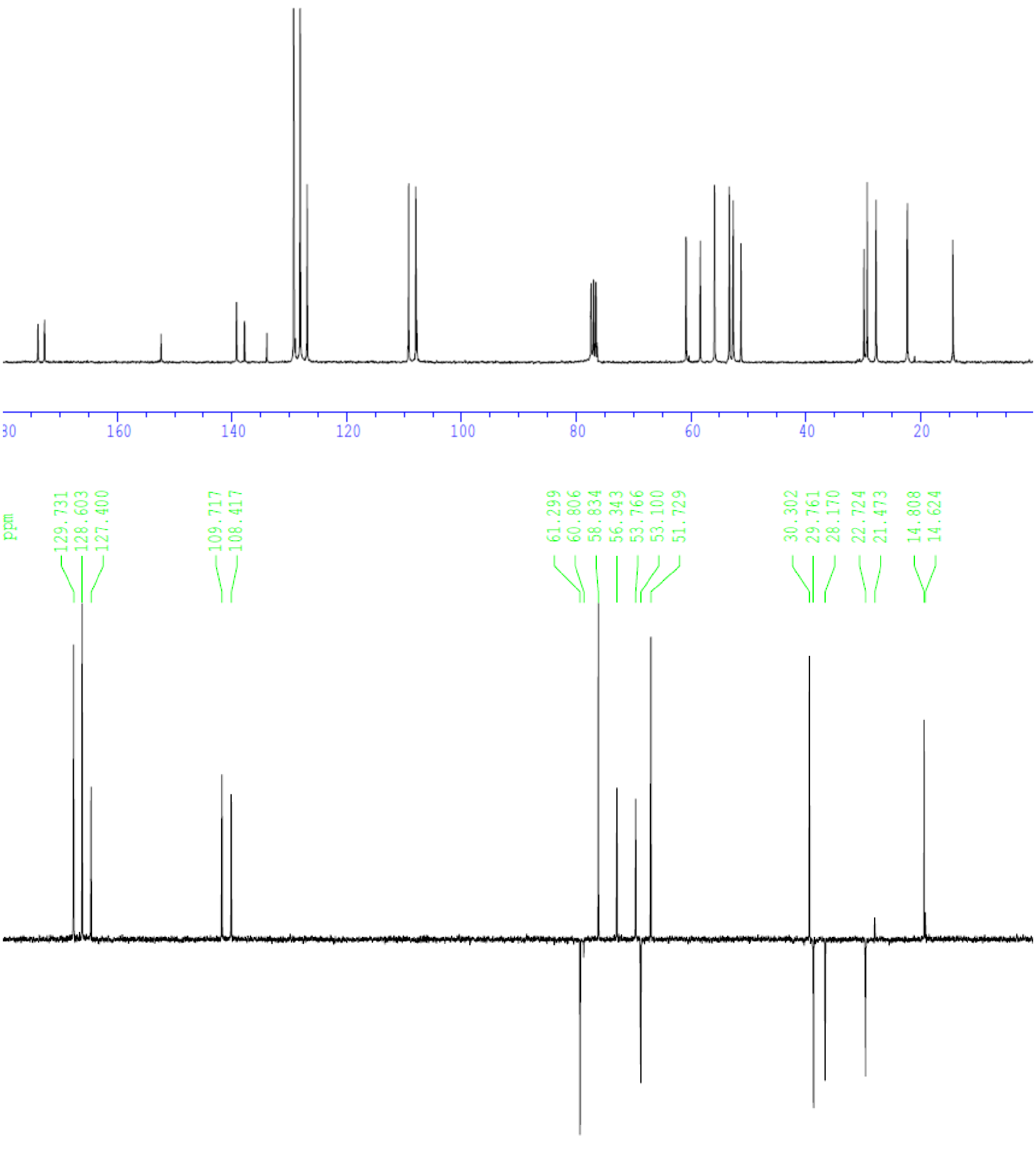


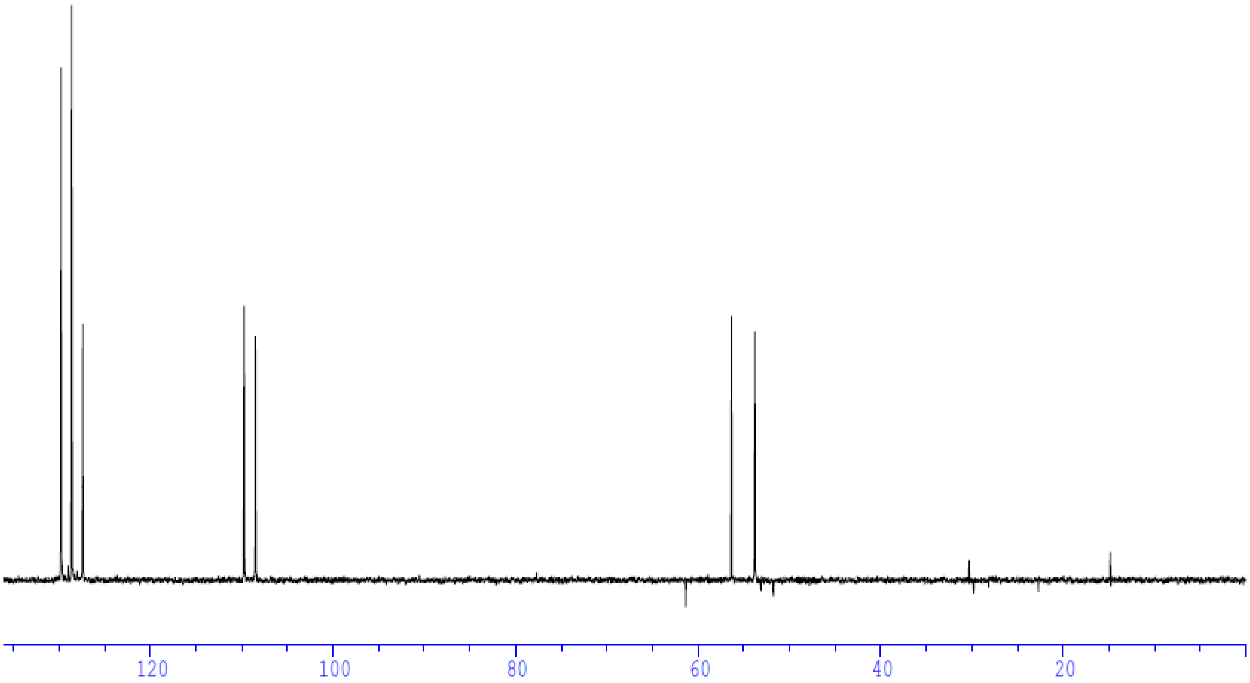

154.025
134.888
131.672
125.972
116.362
112.212
111.682
104.662
100.329
77.334
76.911
76.488
60.597
55.768
55.239
53.492
50.413
41.284
29.597
26.719
25.929
21.751
12.688
QC
QC
QC
QC
QC
CH
CH
CH
CH
CH2
CH3
CH2
CH
CH
CH
CH2
CH
Grease C
CH2
CH3
2x quaternary missing
160
140
120
100
80
60
40
20

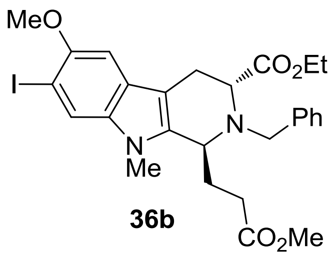

MeO
I
CO2Et
N
Ph
N
Me
CO2Me

36a

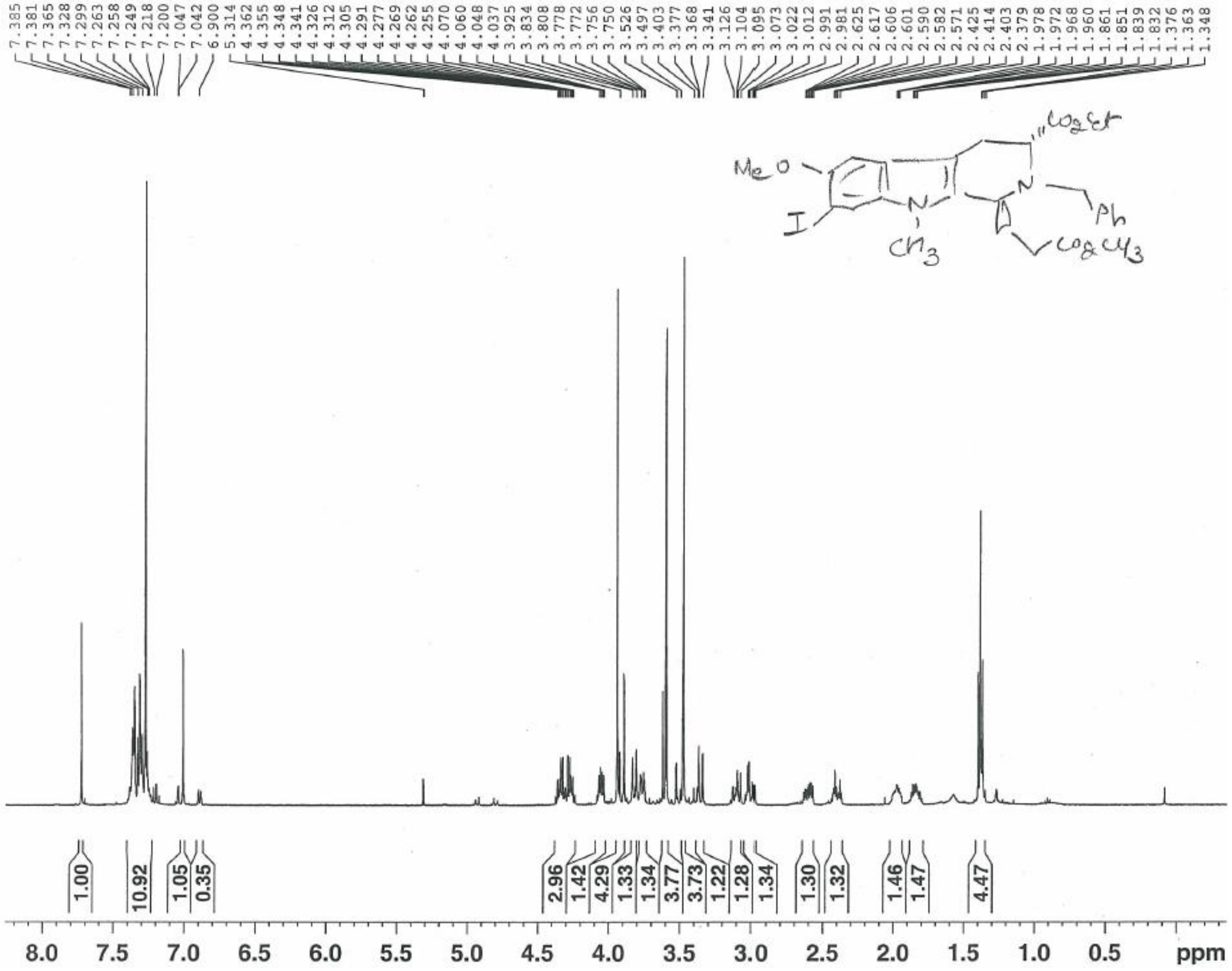

2.748
1.075
1.165
0.999
0.927
2.211
1.189
2.924
1.212
1.081
4.306
3.920
1.277
1.063
1.064
2.252
3.000
m
7
6
5
4
3
2
1

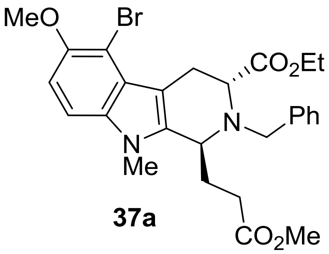

160
140
120
100
80
60
40
20
ppm
129.731
128.603
127.400
109.717
108.417
61.299
60.806
58.834
56.343
53.766
53.100
51.729
30.302
29.761
28.170
22.724
21.473
14.808
14.624


120
100
80
60
40
20

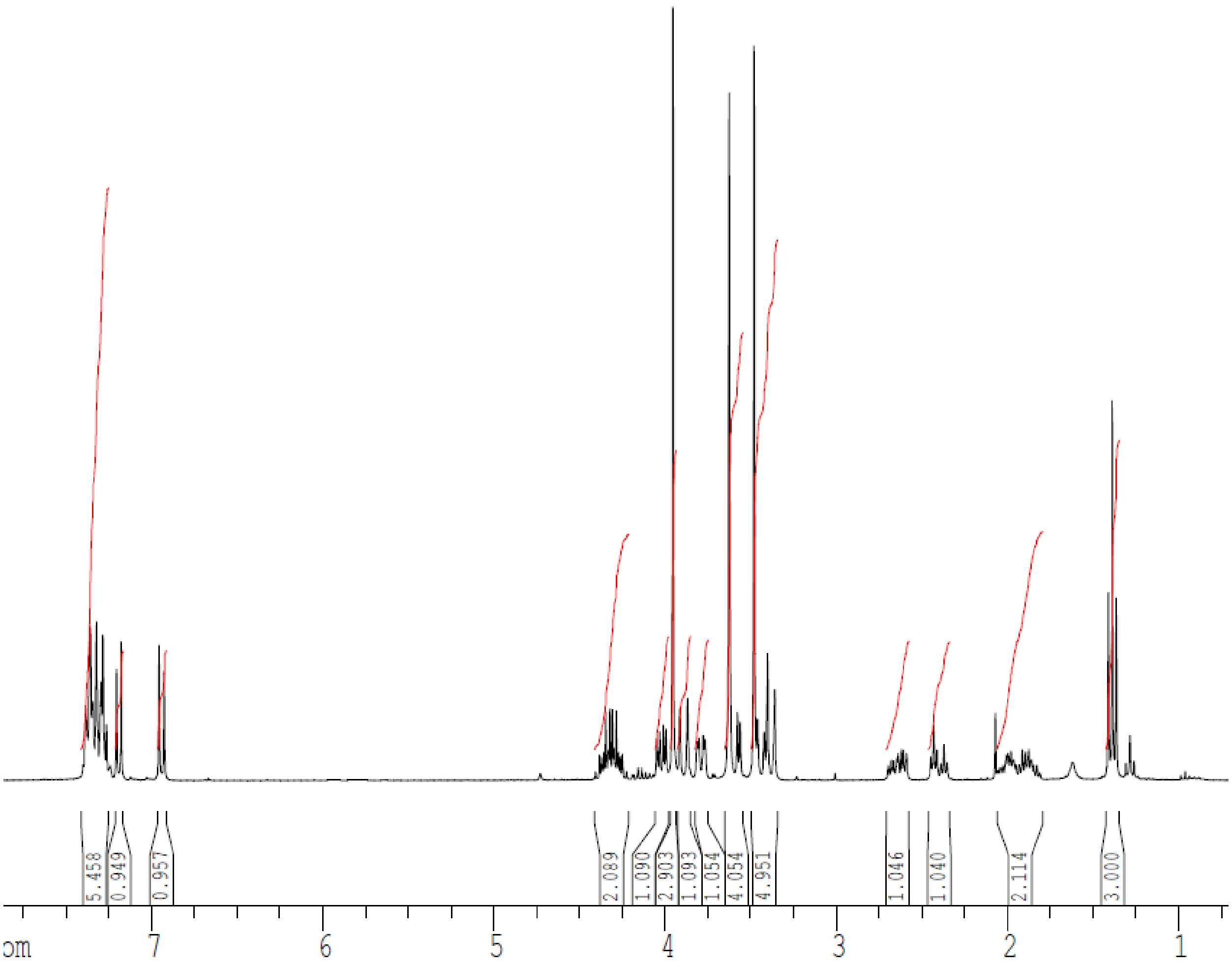

MeO
CO_2Et
I
N
Ph
N
Me
CO_2Me

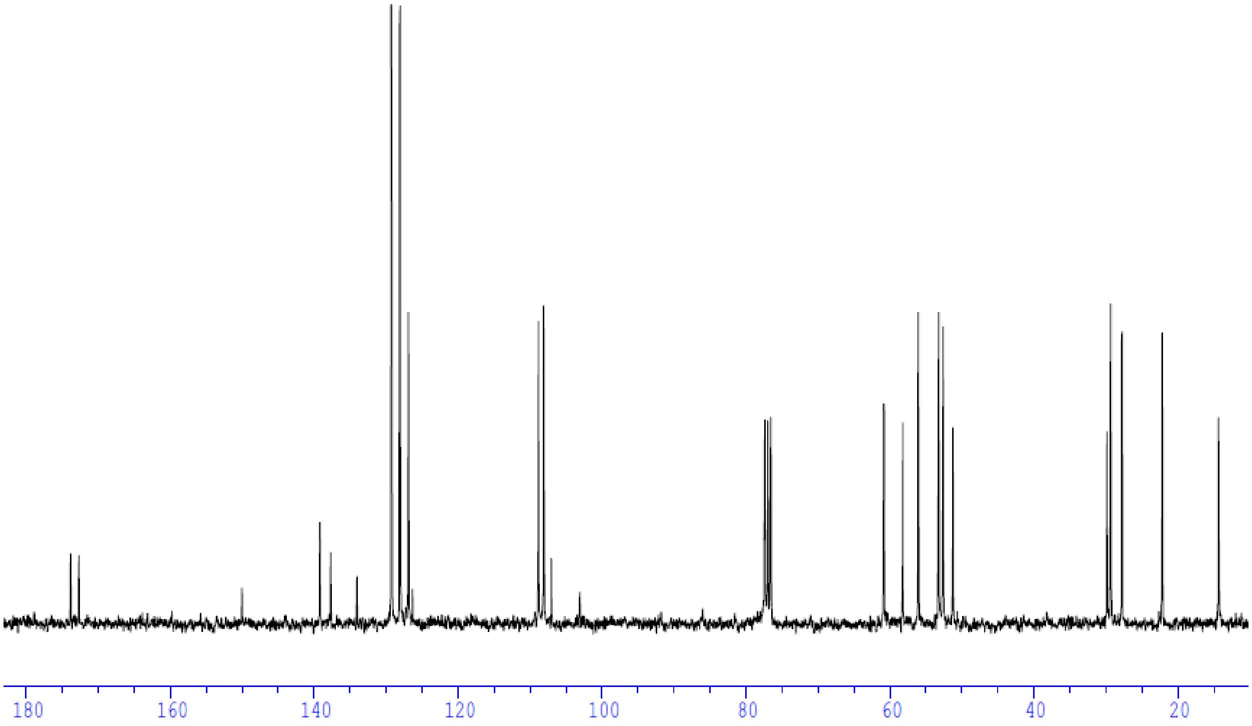
36b

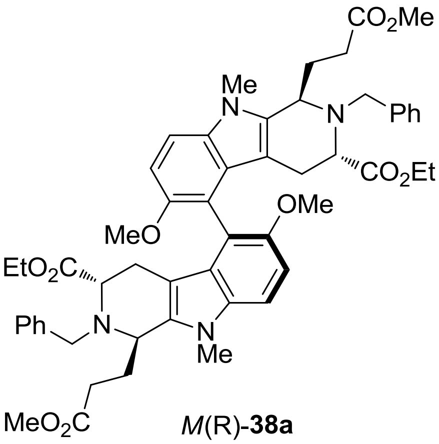

7.385
7.381
7.365
7.328
7.299
7.263
7.258
7.249
7.218
7.200
7.047
7.042
6.900
5.314
4.362
4.355
4.348
4.341
4.326
4.312
4.305
4.291
4.277
4.269
4.262
4.255
4.070
4.060
4.048
4.037
3.925
3.834
3.808
3.778
3.772
3.756
3.750
3.526
3.497
3.403
3.377
3.368
3.341
3.126
3.104
3.095
3.073
3.022
3.012
2.991
2.981
2.625
2.617
2.606
2.601
2.590
2.582
2.571
2.425
2.414
2.403
2.379
1.978
1.972
1.968
1.960
1.861
1.851
1.839
1.832
1.376
1.363
1.348
MeO
CO_2Et
N
Ph
I
N
CH_3
CO_2CH_3
1.00
10.92
1.05
0.35
2.96
1.42
4.29
1.33
1.34
3.77
3.73
1.22
1.28
1.34
1.30
1.32
1.46
1.47
4.47
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


MeO
Br
CO2Et
N
Ph
N
Me
CO2Me

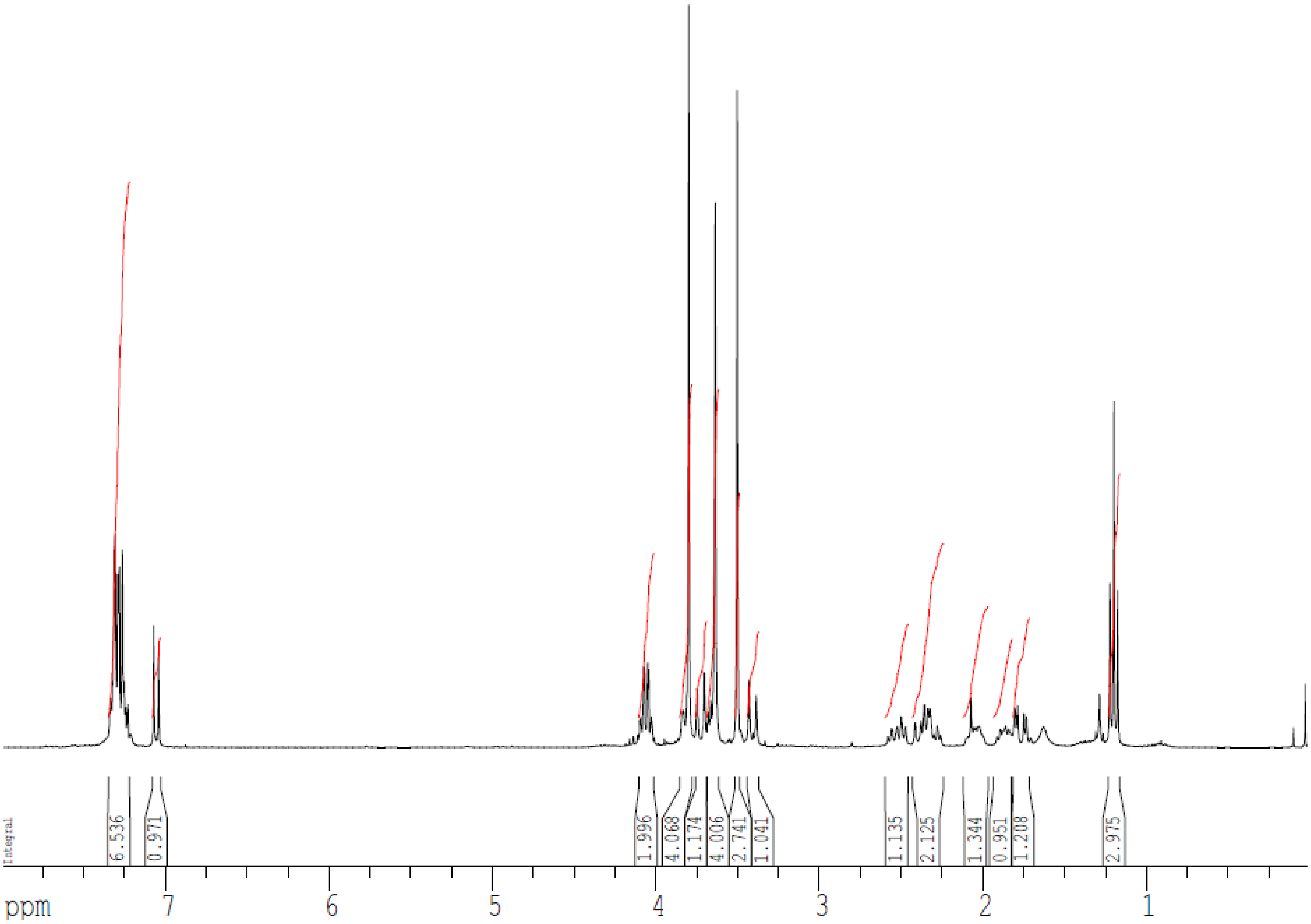
37a

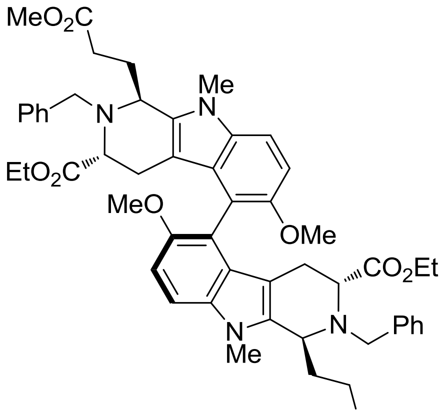

5.458
0.949
0.957
2.089
1.090
2.903
1.093
1.054
4.054
4.951
1.046
1.040
2.114
3.000
om
7
6
5
4
3
2
1


180
160
140
120
100
80
60
40
20

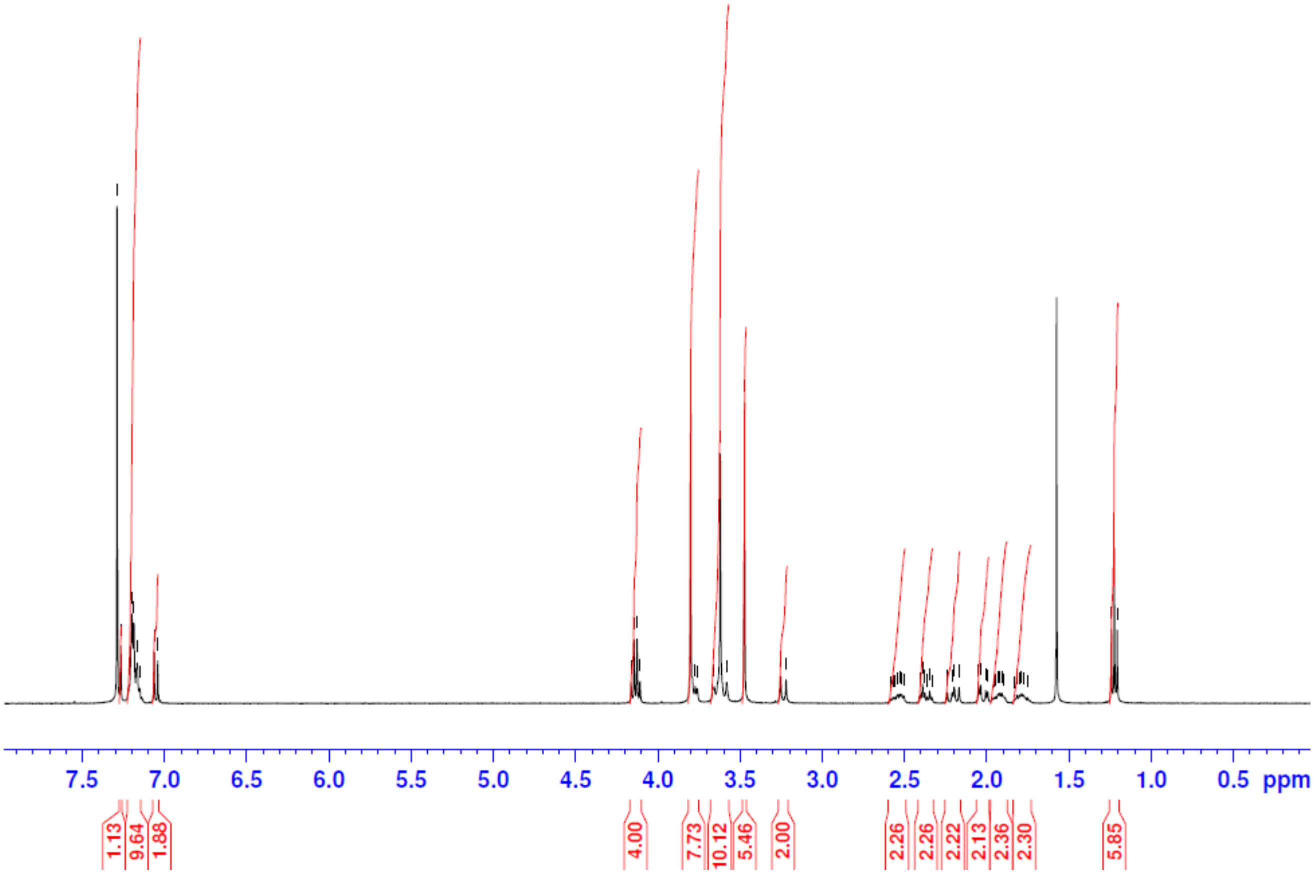


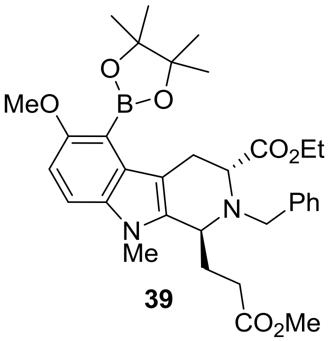
M(R)-**38a**


Integral
6.536
0.971
1.996
4.068
1.174
4.006
2.741
1.041
1.135
2.125
1.344
0.951
1.208
2.975
ppm
7
6
5
4
3
2
1

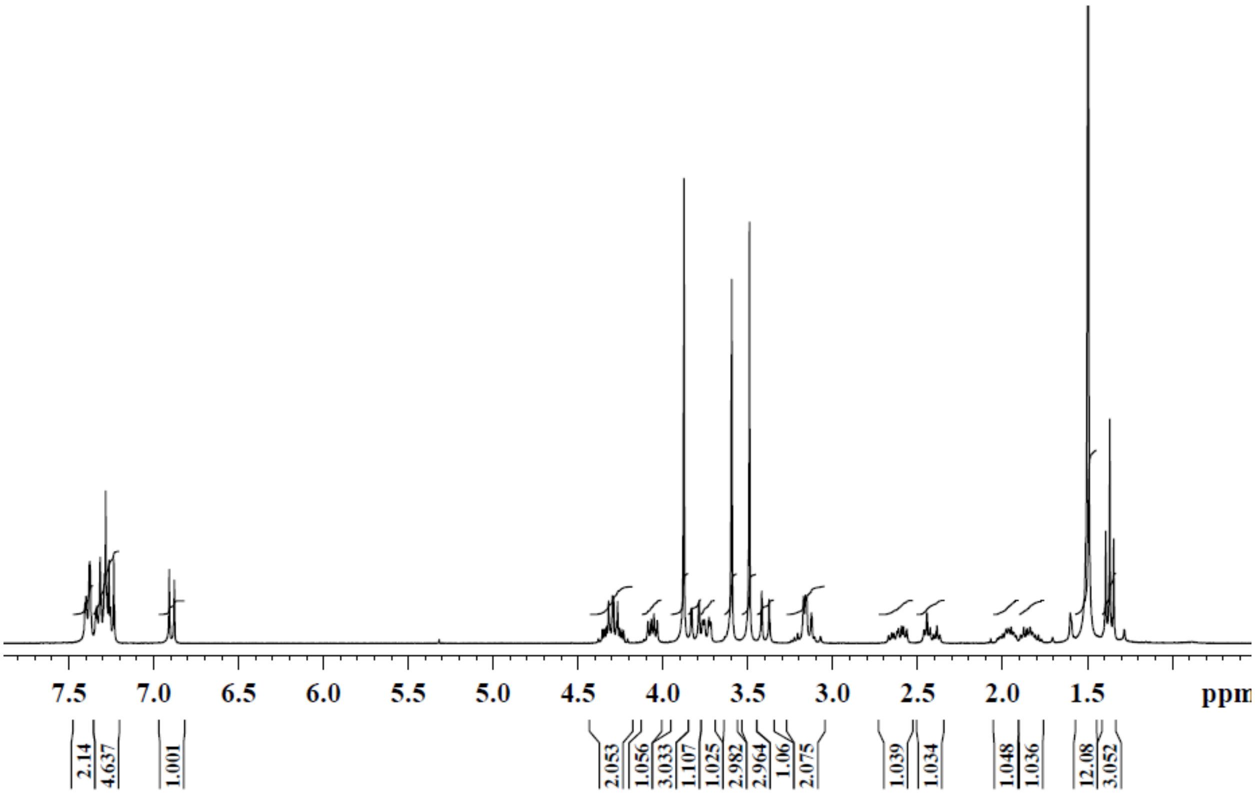

MeO2C
Ph
N
Me
N
EtO2C
MeO
OMe
CO2Et
N
Ph
N
Me
CO2Me

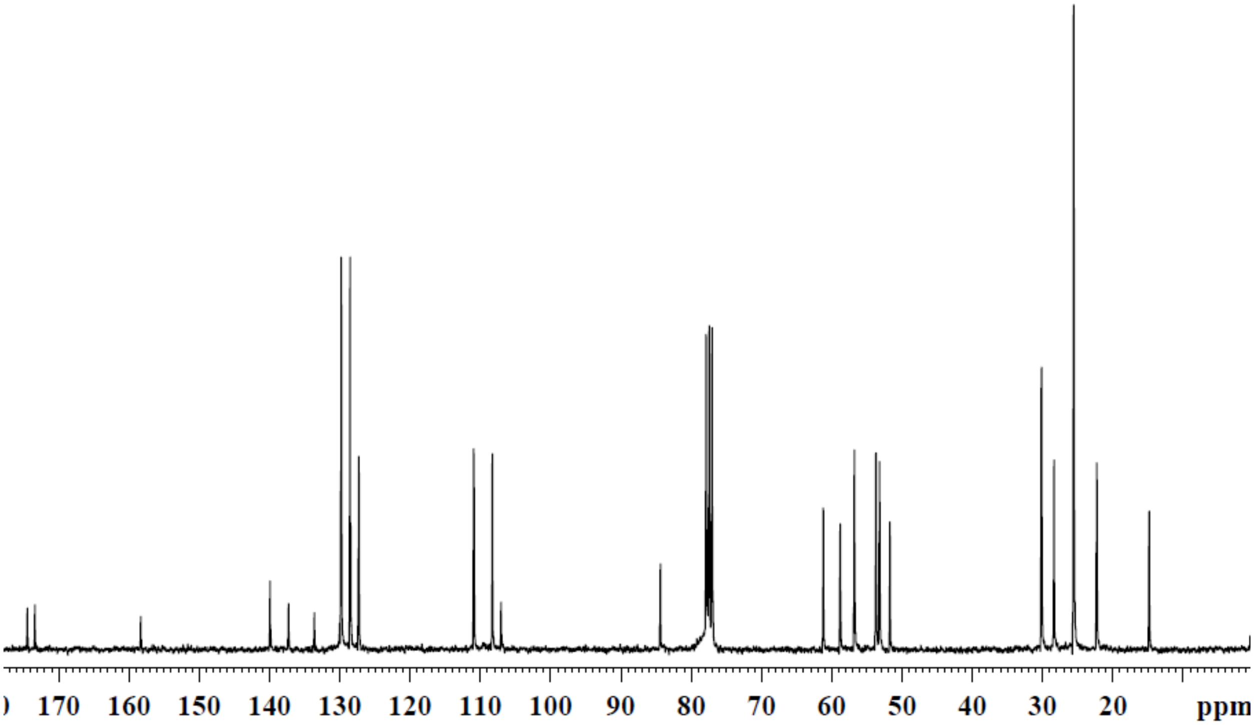
P(*S*)-**38b**

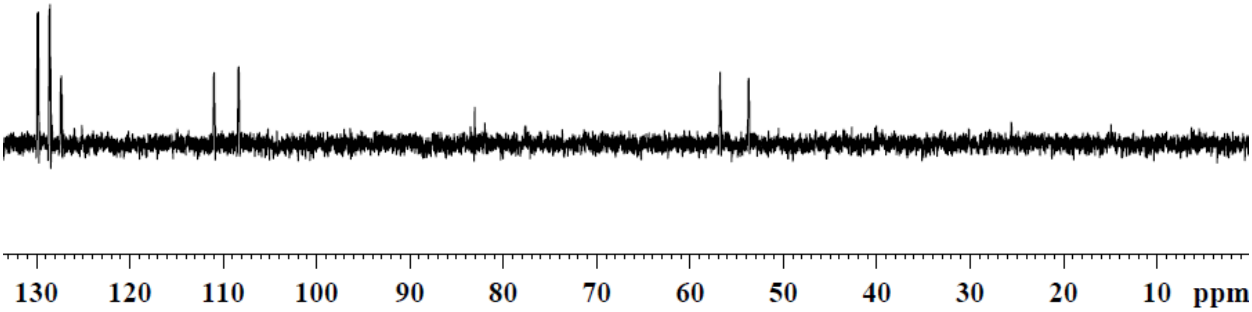

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.13
9.64
1.88
4.00
7.73
10.12
5.46
2.00
2.26
2.26
2.22
2.13
2.36
2.30
5.85


MeO
O
B
O
CO2Et
N
Ph
N
Me
CO2Me

39


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
2.14
4.637
1.001
2.053
1.056
3.033
1.107
1.025
2.982
2.964
1.06
2.075
1.039
1.034
1.048
1.036
12.08
3.052


170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


130
120
110
100
90
80
70
60
50
40
30
20
10
ppm