Electronic Supplementary Information (ESI)

Mild and convenient one-pot synthesis of 2-amino-1,3,4-oxadiazoles promoted by trimethylsilyl isothiocyanate (TMSNCS)

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1. General Information

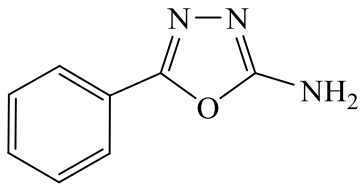
Melting points were determined in open capillaries on a Stuart apparatus and are uncorrected. Reagents and solvents were obtained in the highest available purity and used without further purification unless indicated. The purity of the compounds was checked by TLC

(silica gel, ethyl acetate/hexane (1:3)). The IR spectra were recorded in KBr pellets on a Perkin Elmer Spectrum One FT-IR Spectrometer and the wave numbers were given in cm^{-1}. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AMX 400 NMR spectrometer in DMSO. Mass spectra were recorded on a low-resolution (Agilent Technologies GC/MS: 6890N, 5973N mass selective detector) EI mass spectrometer. All products **2** were known compounds.

2. Experimental Section

Typical experimental procedure for synthesis of 2-Amino-5-aryl-1,3,4-oxadiazole: A mixture of acid hydrazide (1.0 mmol) and trimethylsilyl isothiocyanate (1.0 mmol) and ethanol (10 ml) was refluxed for 2-4 h and then 1 ml of 5N NaOH was added, resulting in the formation of clear solution. To this 5% iodine in potassium iodide solution was added drop wise with stirring till the colour of iodine persisted at room temperature. The reaction mixture was refluxed for additional 1-2 h, cooled and poured into ice-cold water. Resultant solid was filtered on a Buchner funnel and dried. Recrystallization of the solid from ethanol afforded pure products **2a-m**.

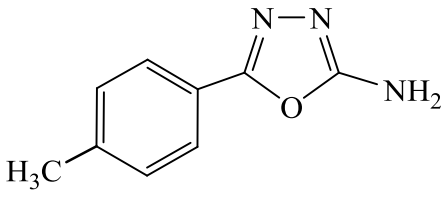
2-Amino-5-phenyl-1,3,4-oxadiazole (2a) [S1]



2a

Compound **2a,** Yield: 94%, white solid; m.p. 241-243 °C (lit.[S1] m.p. 241-242 °C). IR: (KBr, cm^{-1}) 1022, 1282, 1490, 1597, 1652, 3109, 3266; ^{1}H NMR (400 MHz, DMSO): δ 7.14 (bs, 2H, NH_2) 7.46 (t, 3H, Ph-H), 7.79 (t, 2H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 124.88, 125.43, 129.40, 130.57 (Aromatic carbons), 157.83 (C-5), 164.30 (C-2). GC/MS: m/z (%), 161 (M^{+}, 42), 118 (58), 105 (58), 89 (45), 77 (100), 63 (38), 51 (50).

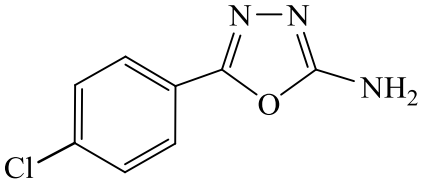
2-Amino-5-(*p*-methylphenyl)-1,3,4-oxadiazole (2b) [S1]



2b

Compound **2b,** Yield: 91%, white solid; m.p. 261-263 °C (lit.[S1] m.p. 260-261 °C). IR: (KBr, cm^{-1}) 1031, 1289, 1487, 1593, 1657, 2951, 3092, 3273; ^{1}H NMR (400 MHz, DMSO): δ 2.32 (s, 3H Ph-CH_3), δ 6.82 (bs, 2H, NH_2), 7.20 (d, 2H, Ph-H), 7.65 (d, 2H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 21.51 (CH_3), 122.09, 125.42, 129.71, 140.43 (Aromatic carbons), 158.18 (C-5), 164.00 (C-2). GC/MS: m/z (%), 175 (M^+, 100), 132 (43), 119 (58), 91 (53), 77 (11), 65 (17).

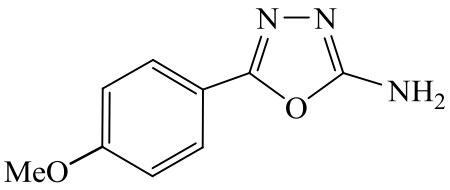
2-Amino-5-(*p*-chlorophenyl)-1,3,4-oxadiazole (2c)[S1]



2c

Compound **2c,** Yield: 92 %, white solid; m.p. 264-265 °C (lit.[S1] m.p. 260-264 °C). IR: (KBr, cm^{-1}) 1023, 1272, 1481, 1594, 1643, 3081, 3285; ^{1}H NMR (400 MHz, DMSO): δ 7.30 (bs, 2H, NH_2), δ 7.56 (d, 2H, Ph-H), 7.79 (d, 2H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 123.61, 129.21, 129.85, 131.61 (Aromatic carbons), 157.07 (C-5), 167.00 (C-2). GC/MS: m/z (%), 195 (M^+, 85), 152 (60), 139 (96), 111 (82), 75 (100), 50 (38).

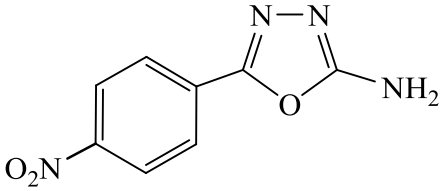
2-Amino-5-(*p*-methoxyphenyl)- 1,3,4-oxadiazole (2d) [S1]



2d

Compound **2d,** Yield: 91 %, brown solid; m.p. 251-252 °C (lit.[S1] m.p. 250- 252 °C). IR: (KBr, cm-[1]) 1036, 1293, 1498, 1581, 1655, 2981, 3102, 3262; ^{1}H NMR (400 MHz, DMSO): δ 3.81 (s, 3H, OCH_3) 7.07 (d, 2H, Ph-H), 7.14 (bs, 2H, NH_2), 7.72 (d, 2H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 55.83 (OCH_3), 115.13, 117.39, 127.25, 157.76 (Aromatic carbons), 161.28 (C-5), 163.95 (C-2). GC/MS: m/z (%), 191 (M^+, 100), 148 (17), 135 (62), 105 (16), 77 (14), 63 (7).

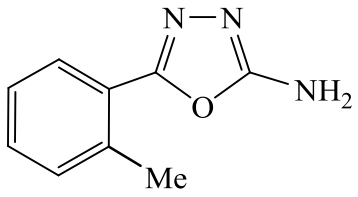
2-Amino-5-(*p*-nitrophenyl) -1,3,4-oxadiazole (2e) [S1]



2e

Compound **2e,** Yield 88 %, brown solid; m.p. 249-250 °C (lit.[S1] m.p. 250-251 °C). IR: (KBr, cm-[1]) 1036, 1290, 1346, 1479, 1524, 1597, 1655, 3142, 3273; ^{1}H NMR (400 MHz, DMSO): δ 7.44 (bs, 2H, NH_2), 8.01 (d, 2H, Ph-H), 8.13 (d, 2H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 124.84, 126.34, 148.33, 149.67 (Aromatic carbons), 156.47 (C-5), 165.06 (C-2). GC/MS: m/z (%), 206 (M^+, 100), 163 (93), 133 (13), 104 (23), 90 (17), 76 (25), 50 (14).

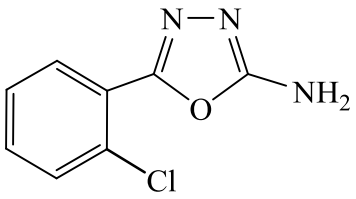
2-Amino-5-(*o*-methylphenyl)-1,3,4-oxadiazole (2f) [S2]



2f

Compound **2f,** Yield: 86 %, white solid; IR: (KBr, cm^{-1}) 1042, 1279, 1481, 1593, 1658, 2964, 3108, 3283; ^{1}H NMR (400 MHz, DMSO): δ 2.32 (s, 3H, Ph-CH_3), 6.73 (bs, 2H, NH_2), 7.26-7.52 (m, 4H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 21.24 (CH_3) 124.92, 125.62, 128.89, 131.02, 132.21, 137.41 (Aromatic carbons), 157.09 (C-5), 165.41 (C-2).

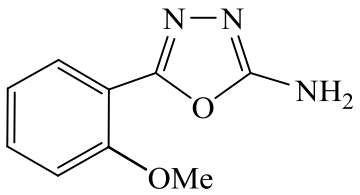
2-Amino-5-(*o*-chlorophenyl)-1,3,4-oxadiazole (2g)[S3]



2g

Compound **2g,** Yield: 87 %, white solid; IR: (KBr, cm^{-1}) 1051, 1283, 1478, 1596, 1641, 3082, 3267; ^{1}H NMR (400 MHz, DMSO): δ 6.89 (bs, 2H, NH_2), 7.32-7.45 (m, 4H, Ph-H), ^{13}C NMR (100 MHz, DMSO): δ 123.93, 127.25, 130.21, 131.06, 131.41, 131.79 (Aromatic carbons), 156.11 (C-5), 164.44 (C-2). GC/MS: m/z (%), 195 (M^{+}, 52), 151 (60), 138 (52), 111 (51), 75 (100), 51 (16).

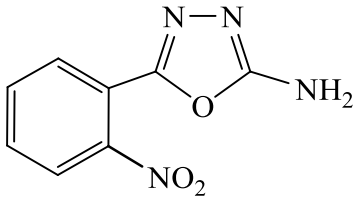
2-Amino-5-(*o*-methoxyphenyl)-1,3,4-oxadiazole (2h) [S4]



2h

Compound **2h,** Yield: 84 %, white solid; m.p. 174 -176°C. IR: (KBr, cm^{-1}) 1048, 1291, 1461, 1581, 1648, 3091, 3257; ^{1}H NMR (400 MHz, DMSO): δ 3.86 (s, 3H, OCH_3), 6.72 (bs, 2H, NH_2), 7.11-7.31 (m, 4H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 54.01 (OCH_3), 116.39, 118.81, 121.83, 128.31, 131.14, 152.11 (Aromatic carbons), 159.88 (C-2), 164.10 (C-2).

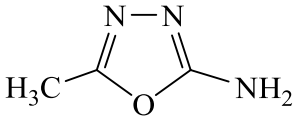
2-Amino-5-(*o*-nitrophenyl)-1,3,4-oxadiazole (2i)[S5]



2i

Compound **2i,** Yield: 83 %, red solid; IR: (KBr, cm^{-1}) 1046, 1270, 1348, 1469, 1532, 1591, 1642, 3123, 3281; ^{1}H NMR (400 MHz, DMSO): δ 6.94 (bs, 2H, NH_2), 7.29-738 (m, 4H, Ph-H). ^{13}C NMR (100 MHz, DMSO): δ 123.91, 125.98, 129.11, 130.12, 132.98, 142.41 (Aromatic carbons), 157.12 (C-5), 164.21 (C-2).

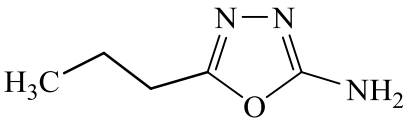
2-Amino-5-methyl-1,3,4-oxadiazole (2j) [S6]



2j

Compound **2j,** Yield: 79 %, white solid; m.p. 232-234 °C (lit.[S6] m.p. 233-235 °C). IR: (KBr, cm^{-1}) 1041, 1289, 1468, 1581, 1657, 2984, 3257; ^{1}H NMR (400 MHz, DMSO): δ 2.15 (s, 3H, CH_3). 6.67 (bs, 2H, NH_2) ^{13}C NMR (100 MHz, DMSO): δ 10.81 (CH_3), 148.82 (C-5), 165.85 (C-2).

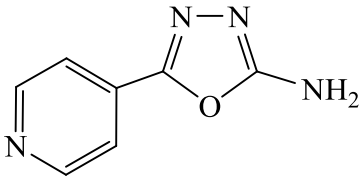
2-Amino-5-propyl-1,3,4-oxadiazole (2k)[S7]



2k

Compound **2k,** Yield: 81 %, white solid; IR: (KBr, cm^{-1}) 1091, 1267, 1360, 1461, 1588, 1644, 2949, 3266; ^{1}H NMR (400 MHz, DMSO): δ 0.82 (t, 3H, CH_3), 1.52-1.58 (q, 2H, CH_2) 2.42 (t, 2H, CH_2), 6.56 (bs, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO): δ 12.71 (CH_3), 20.61 (CH_2), 26.31 (CH_2), 151.81 (C-5), 165.31 (C-2).

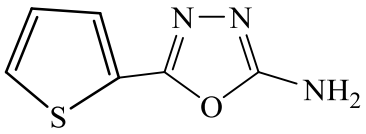
2-Amino-5-(pyridin-4-yl)-1,3,4-oxadiazole (2l)[S5]



2l

Compound **2l,** Yield: 86 %, yellow solid; IR: (KBr, cm^{-1}) 1037, 1298, 1425, 1590, 1665, 3040, 3284; ^{1}H NMR (400 MHz, DMSO): δ 7.41 (bs, 2H, NH_2), 7.67 (d, 2H, Py-H), 8.69 (s, 2H, Py-H). ^{13}C NMR (100 MHz, DMSO): δ 119.14, 131.96, 150.61 (Pyridine carbons), 156.07 (C-5), 165.00 (C-2).

2-Amino-5-(thiophen-2-yl)- 1,3,4-oxadiazole (2m)[S8]



2m

Compound **2m,** Yield: 88 %, pale yellow solid; IR: (KBr, cm^{-1}) 1053, 1251, 1442, 1582, 1651 3028, 3290; ^{1}H NMR (400 MHz, DMSO): δ 7.09 (bs, 2H, NH_2), 7.10 (t, 1H, Th-H), 7.45 (d, 1H, Th-H), 7.55 (d, 1H, Th-H). ^{13}C NMR (100 MHz, DMSO): δ 125.50, 127.09, 127.89, 128.33 (Thiophene carbons), 153.87 (C-5), 163.24 (C-2). GC/MS: m/z (%), 167 (M^{+}, 100), 124 (57), 111 (34), 97 (26), 69 (17), 57 (5).

References

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S2. K. Sanjeev, *Turk. J. Chem.*, 2011, **35**, 99.

S3. M. Mitsuhiko, S. Takuji, M. Toshimi and I. Kin-Ichi, *Chem. Pharm. Bull.*, 1976, **24(11)**, 2871.

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S5. (a) S. Kumar and D. P. Srivastava, *Indian J. Pharm. Sci.*, 2010, **72(4)**, 458;
(b) S. Laxmi Kath, S. Susma and R. K. P. Singh, *Indian J. Chem*., 2011, **50B**, 110.

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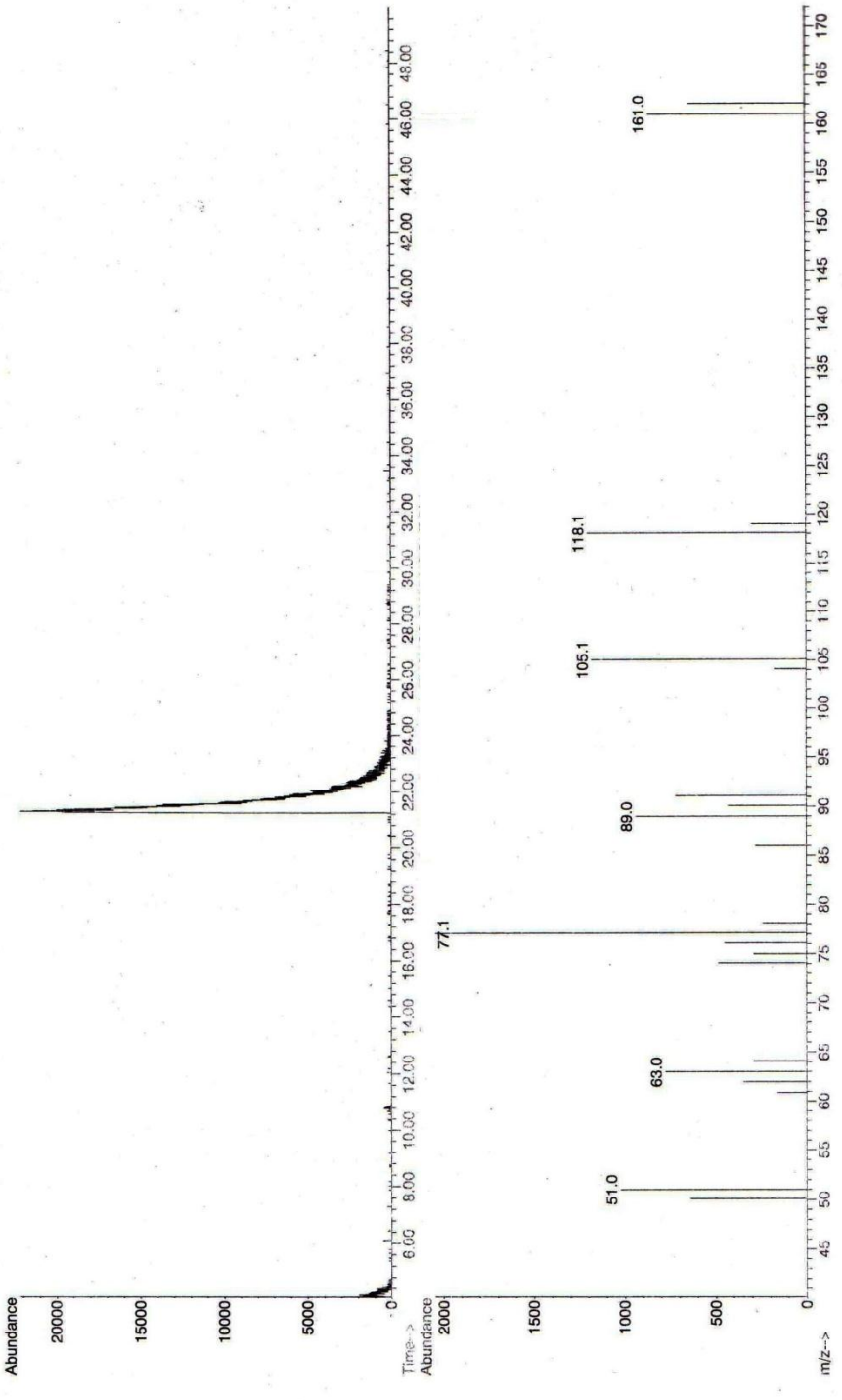
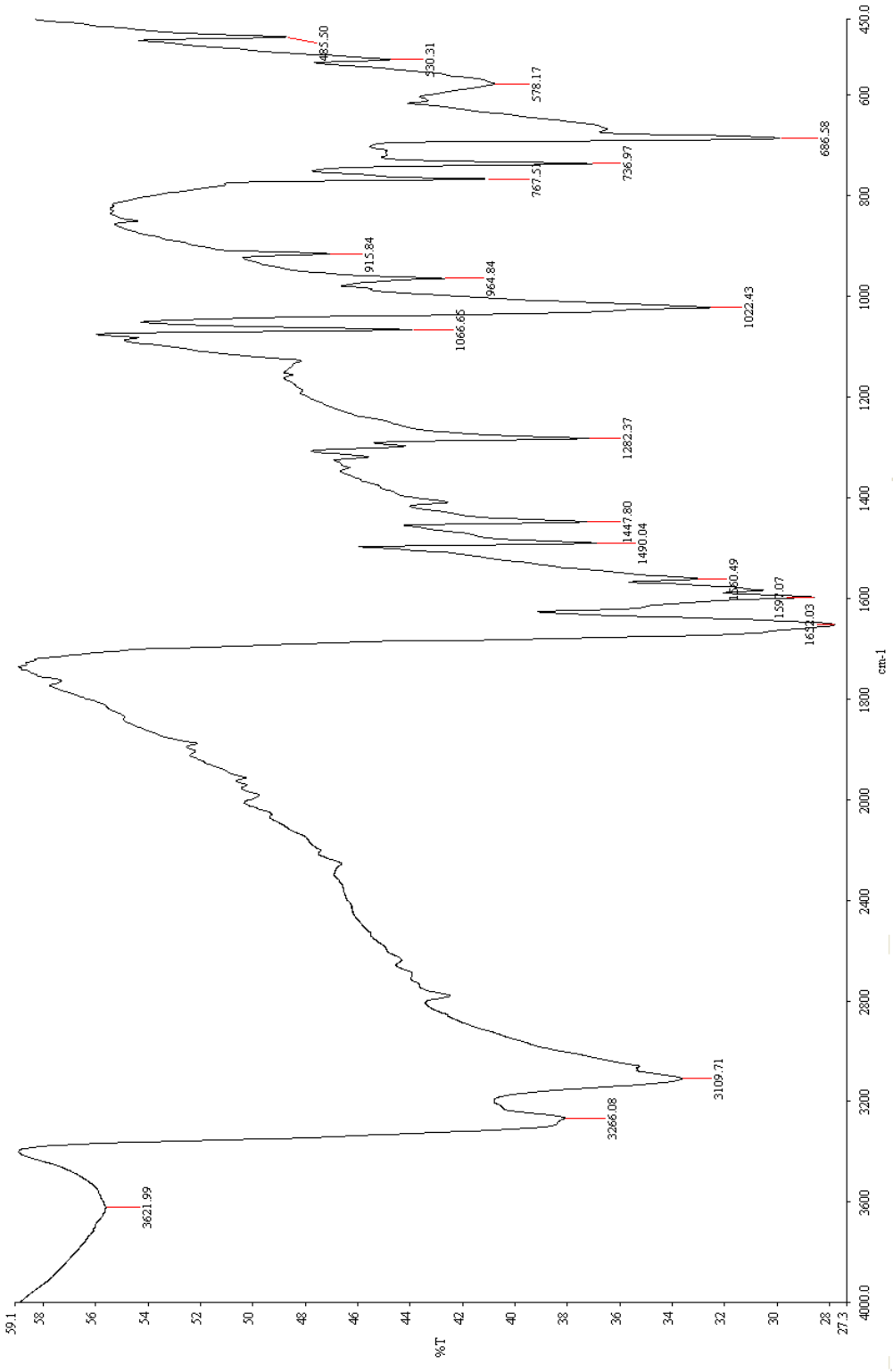
S7. S.Kumar, *J. Korean Chem. Soc.*, 2009, **53(2)**, 159.

S8. G. D. Fallon, C. L. Francis, K. Johansson, A. J. Liepa and R. C. J. Woodgate, *Australian J. Chem*., 2005, **58(12)**, 891.

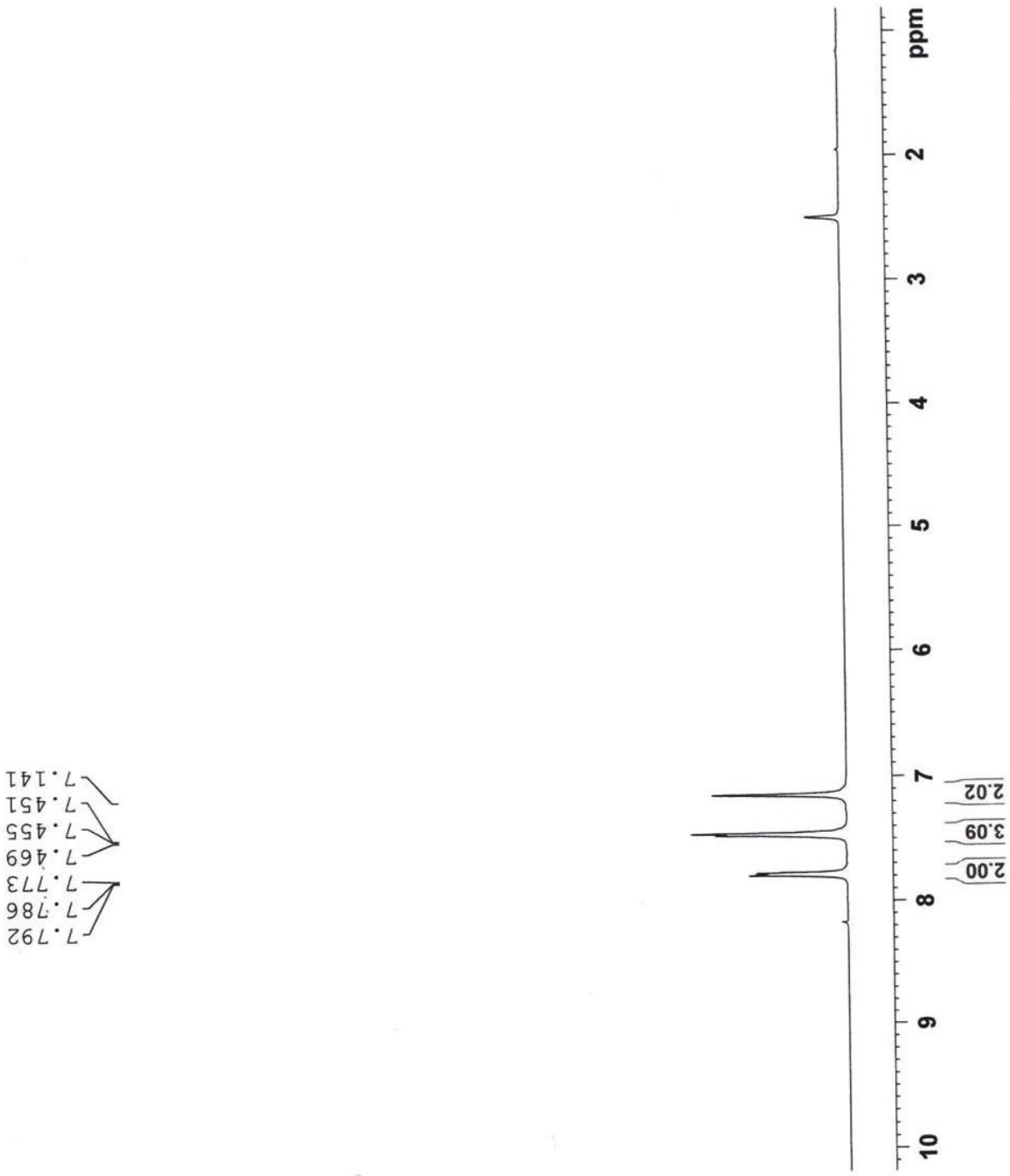
Spectra of Compound 2a-m



GC / MS of **2a**



IR of **2a**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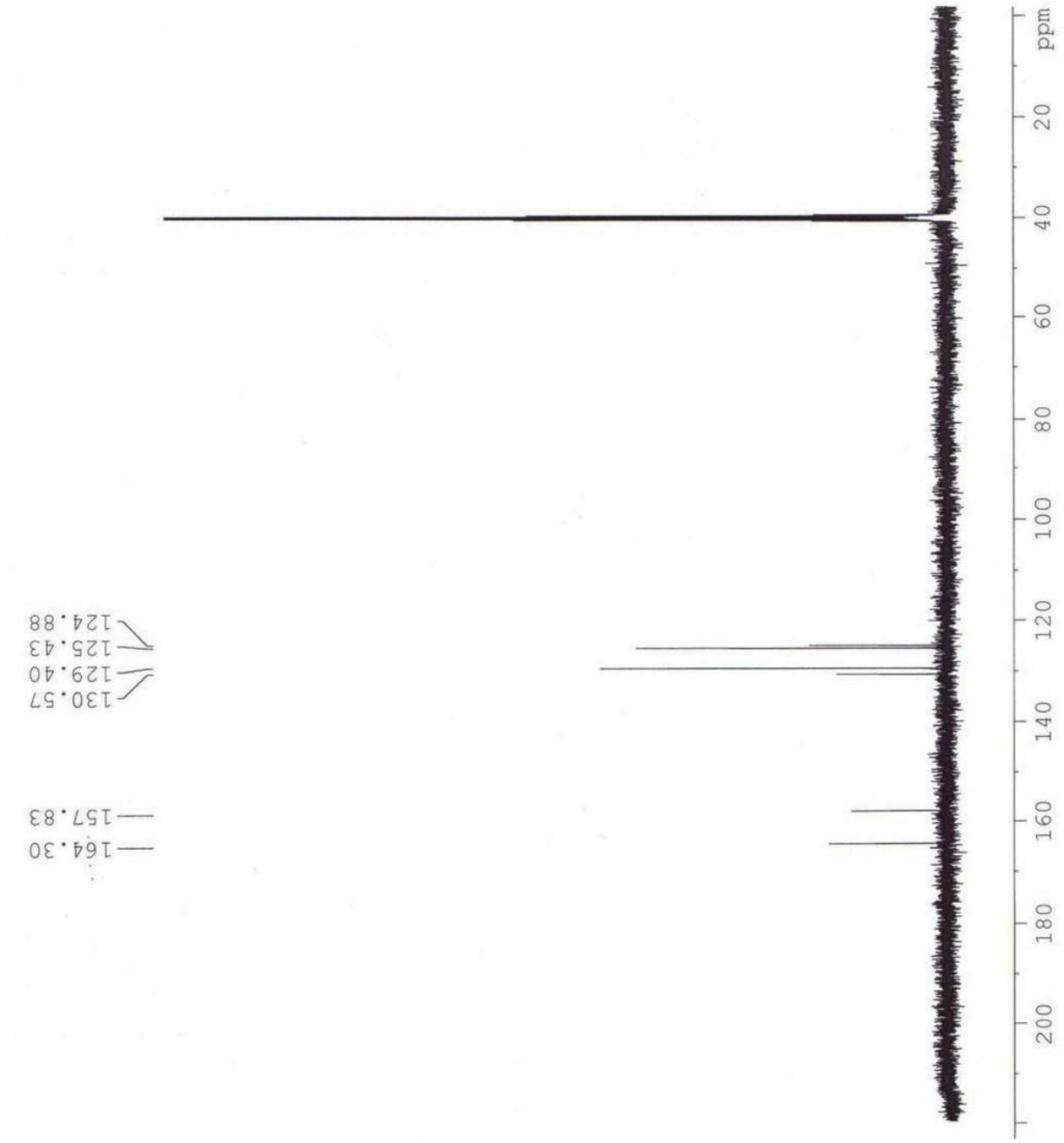
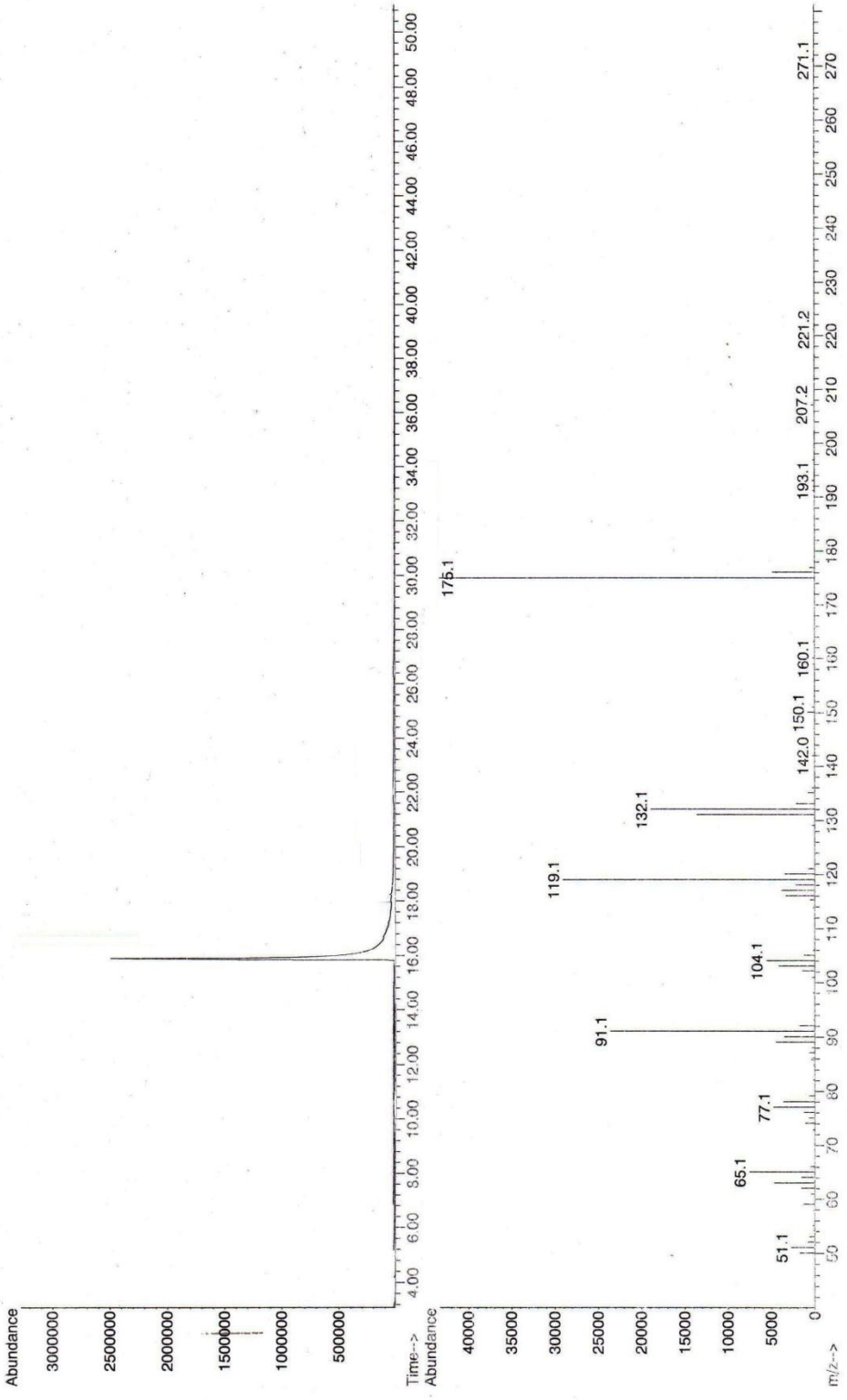
7.469
7.455
7.451
7.141
ppm
2
3
4
5
6
7
8
9
10
2.02
3.09
2.00

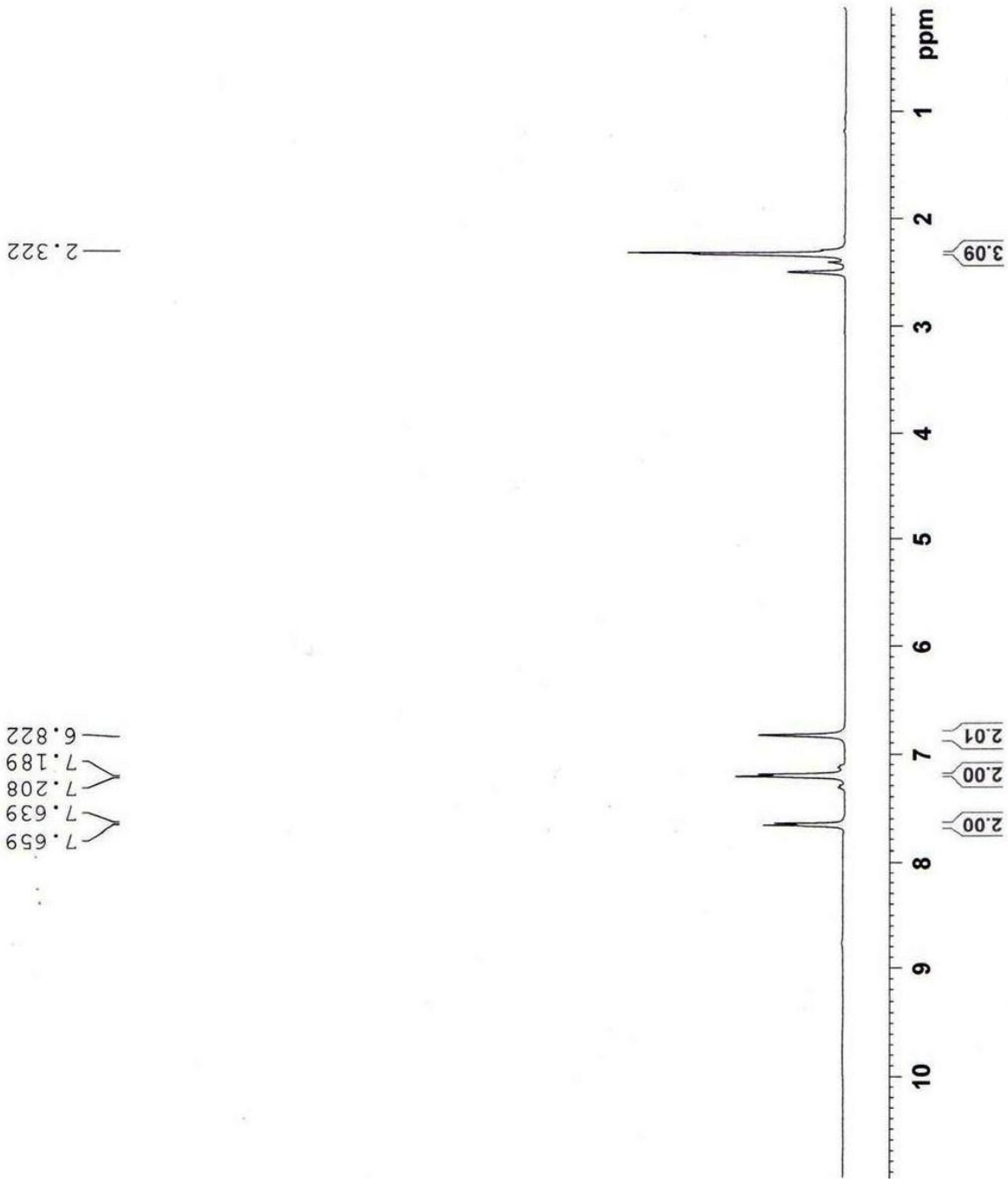
^{1}H NMR of **2a**



^{13}C NMR of **2a**



GC / MS of **2b**



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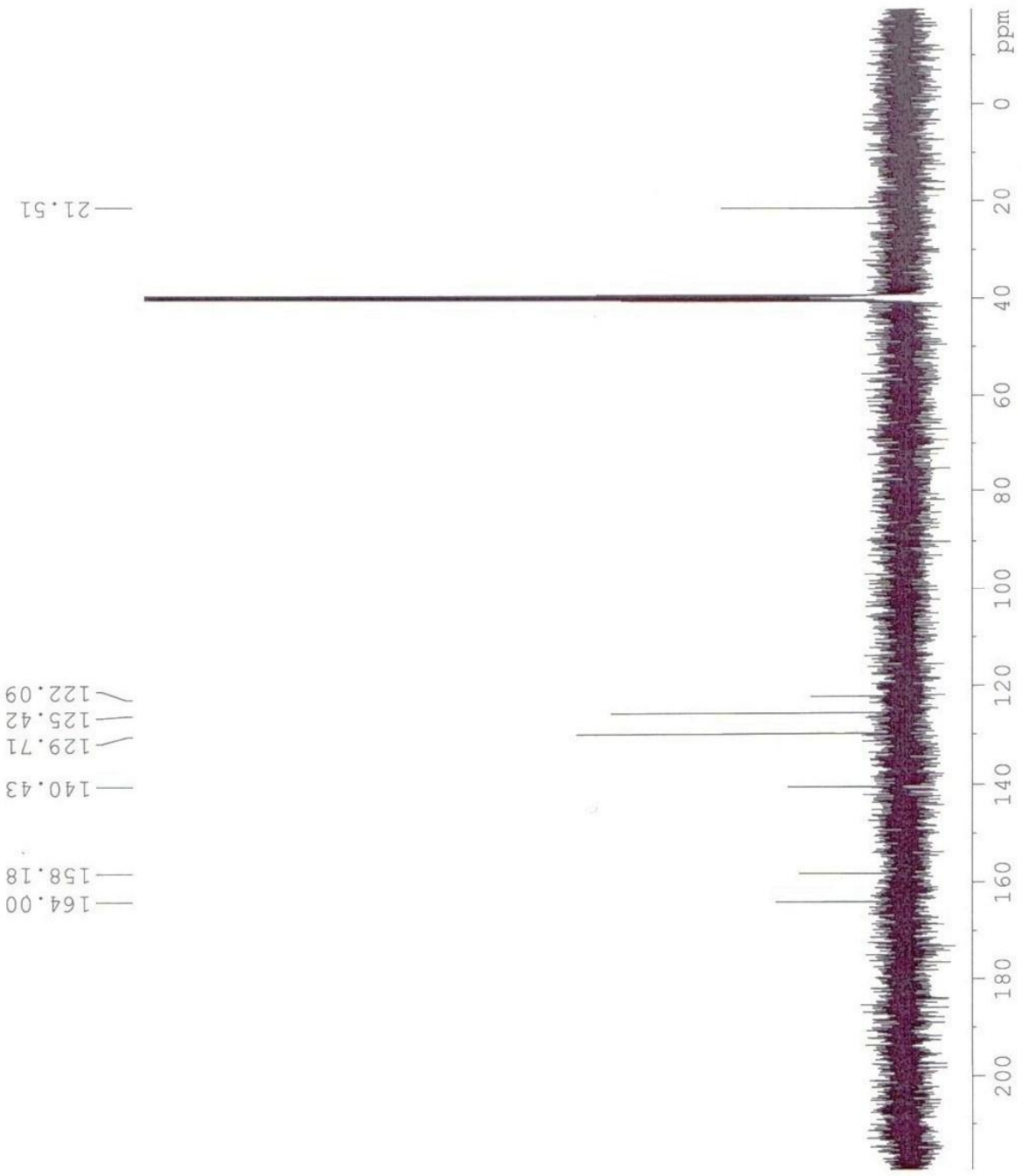
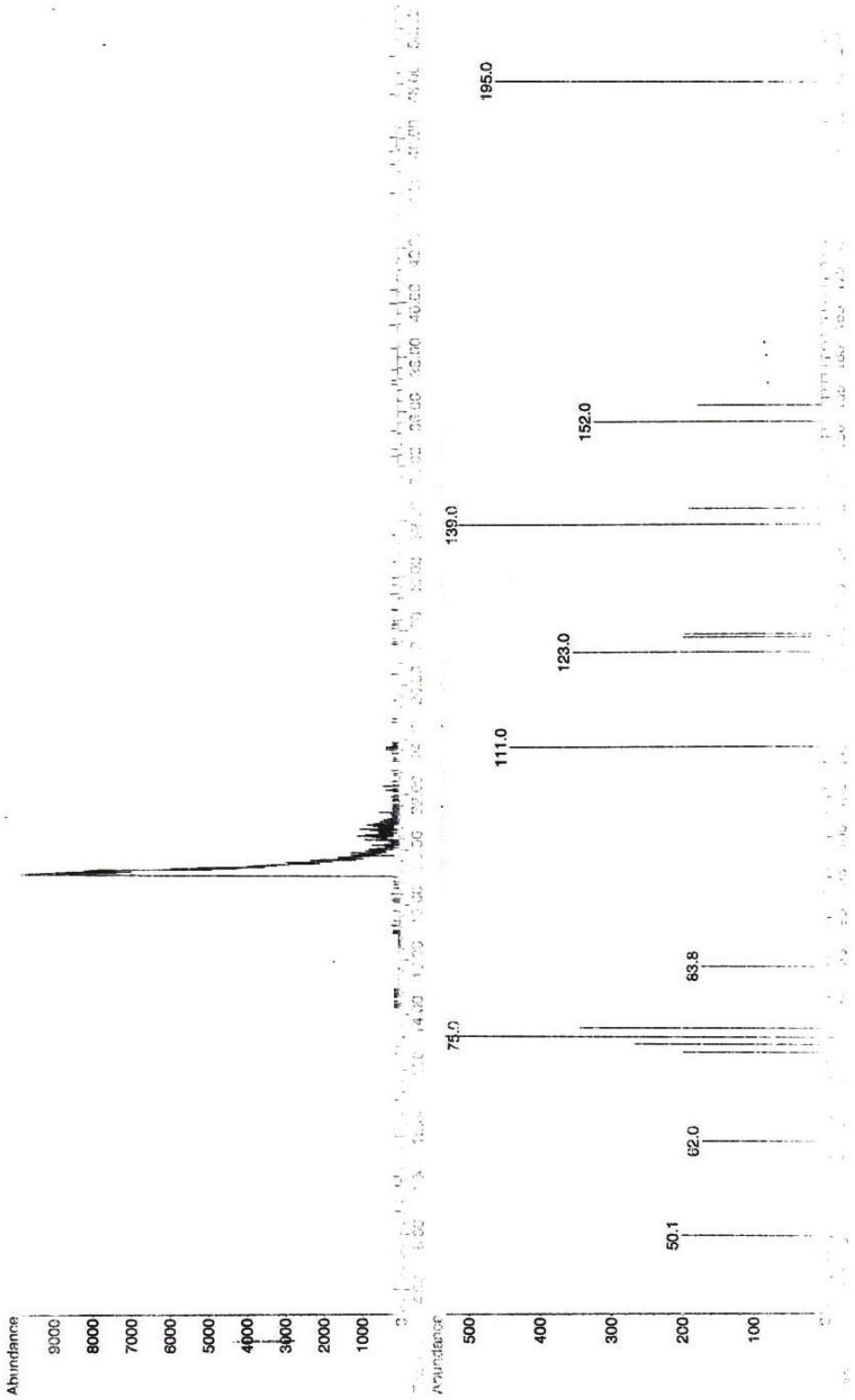
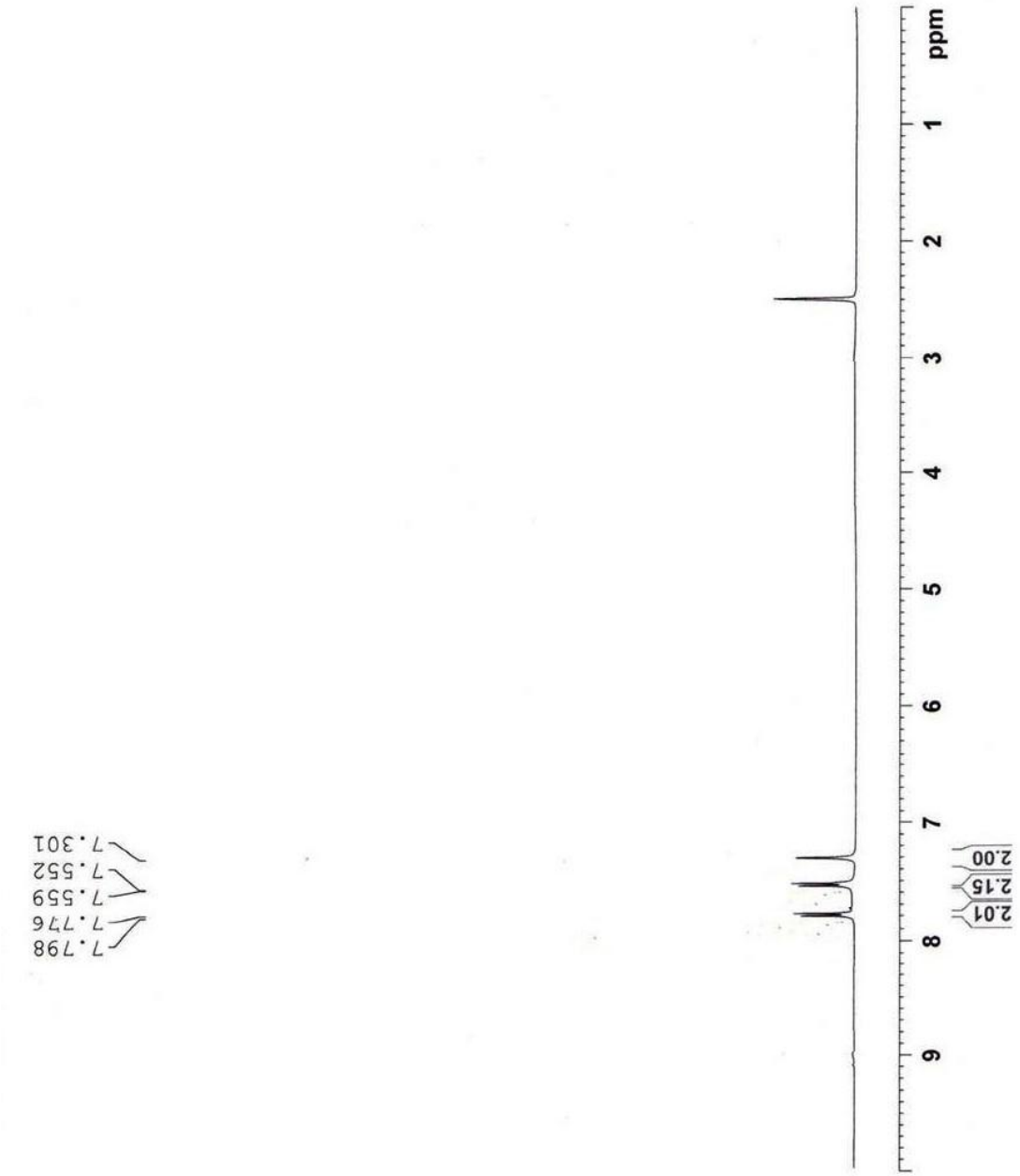


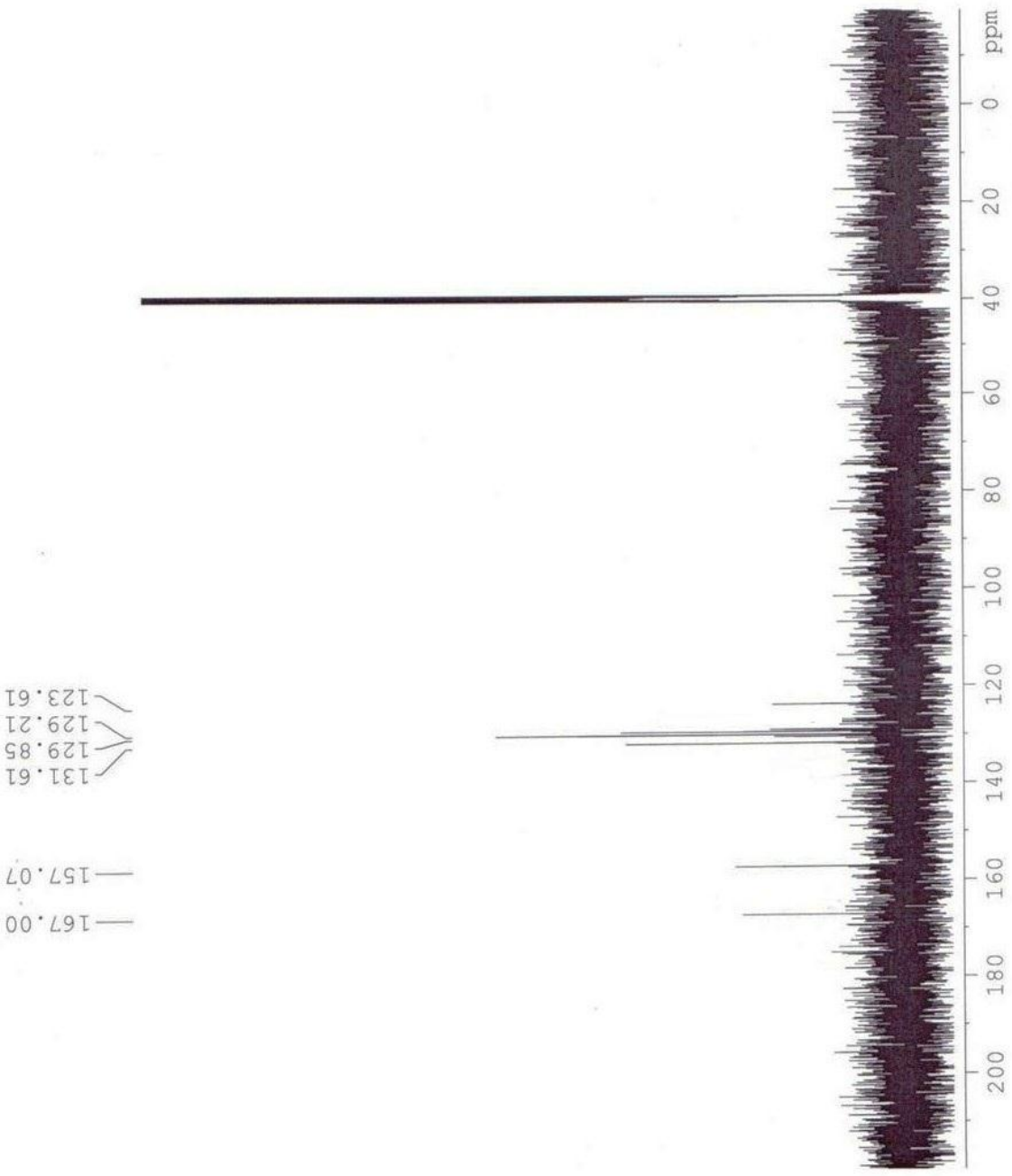
^{13}C NMR of **2b**



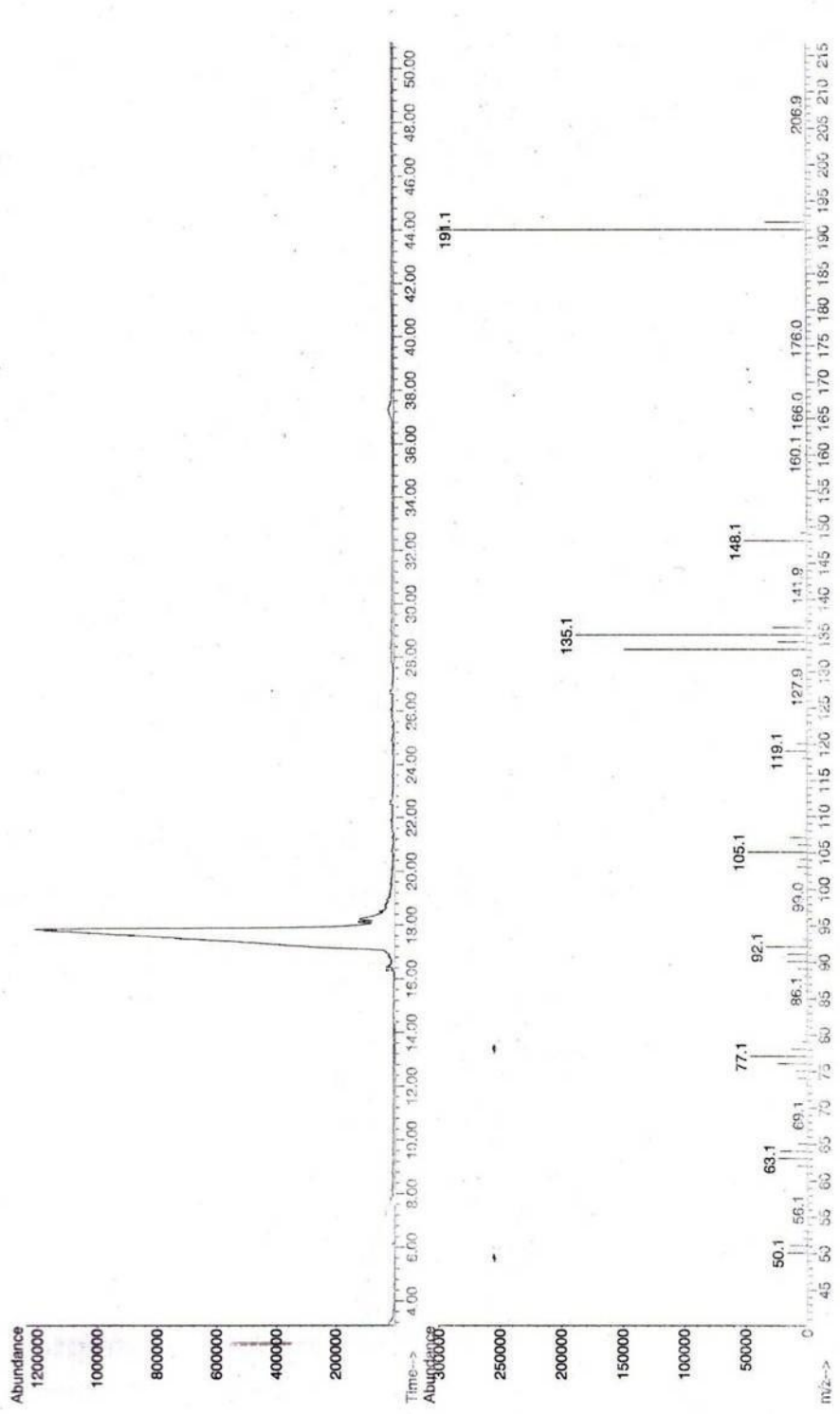
GC / MS of **2c**



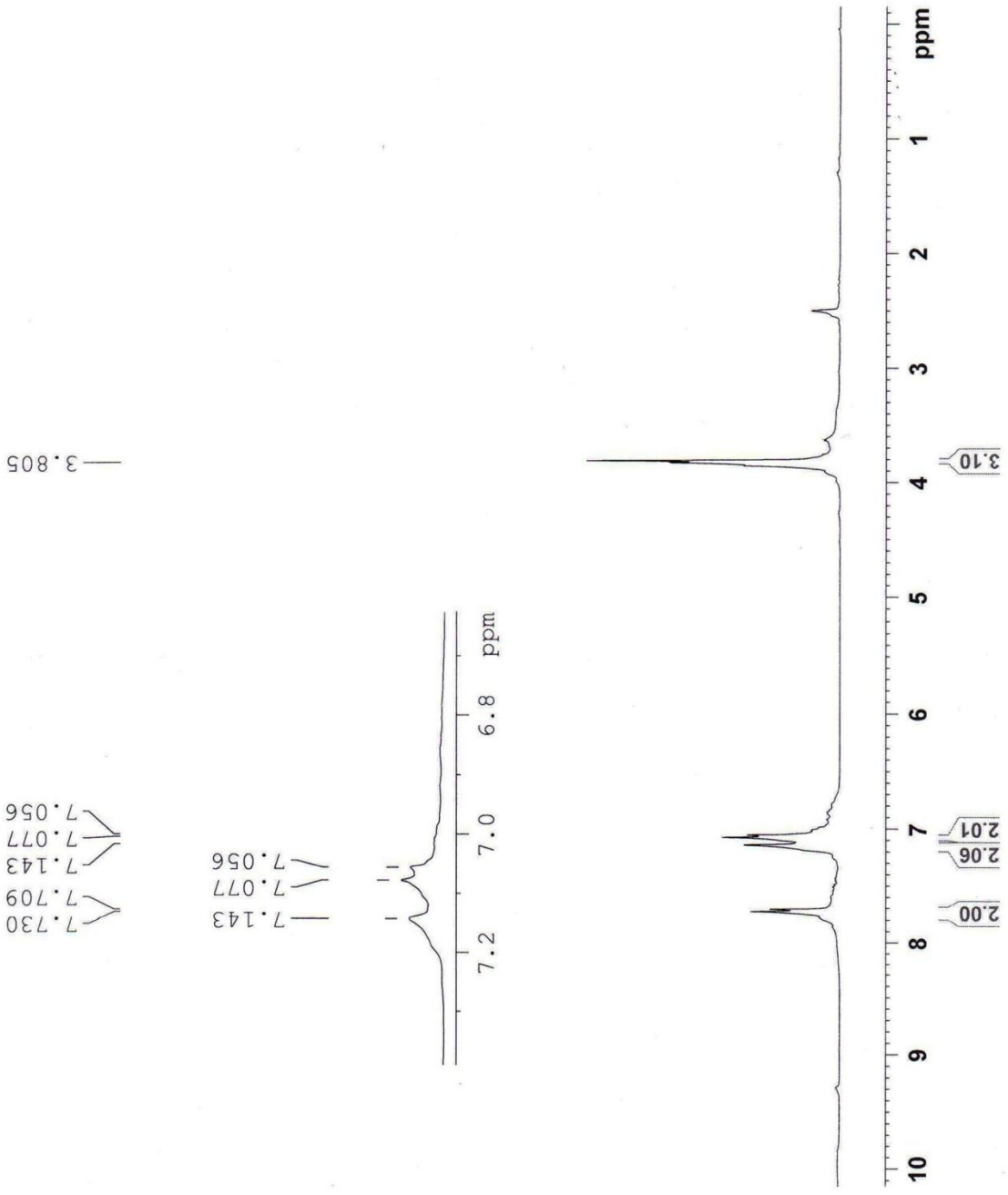
^{1}H NMR of **2c**



^{13}C NMR of **2c**



GC/MS of **2d**



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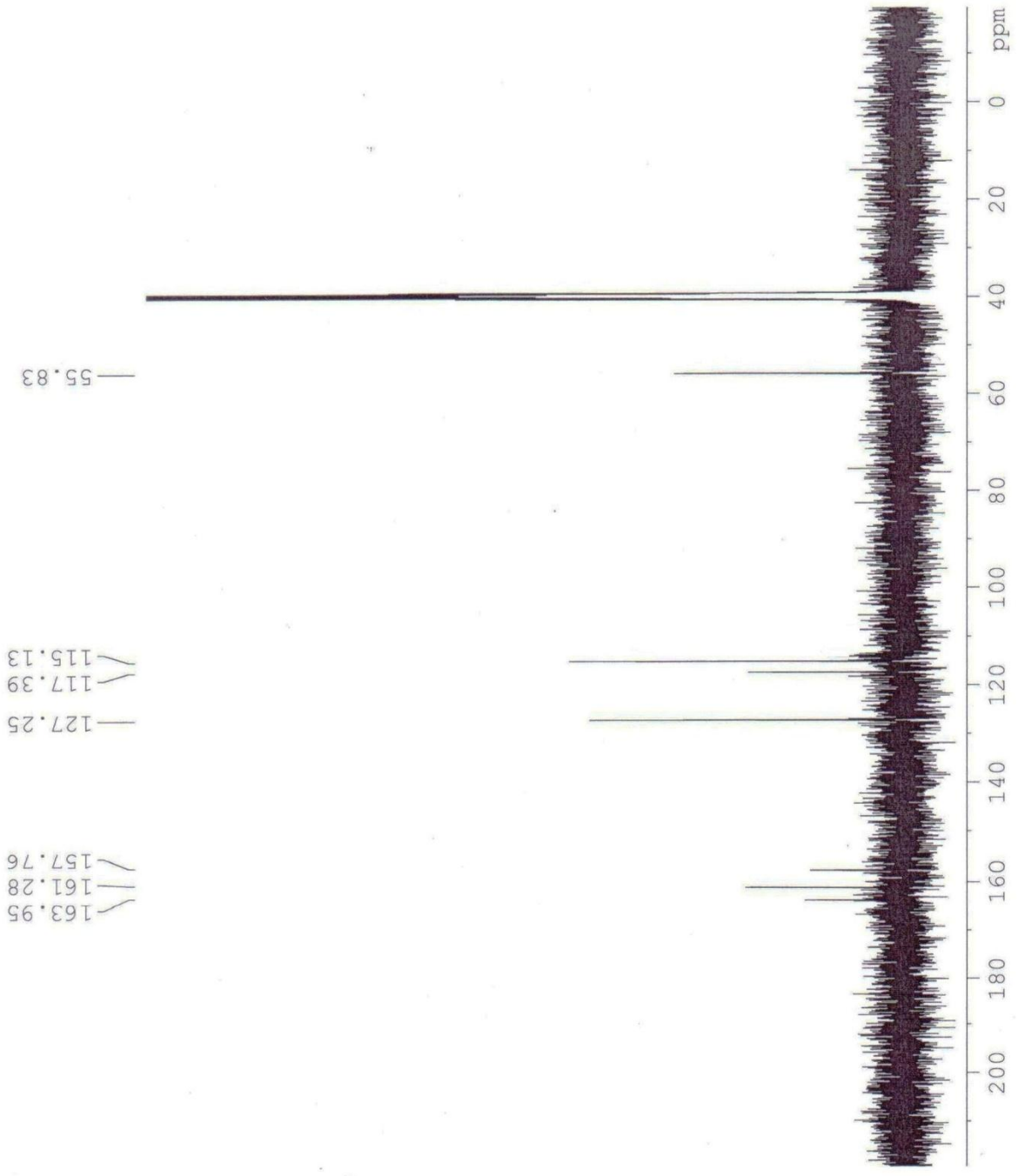

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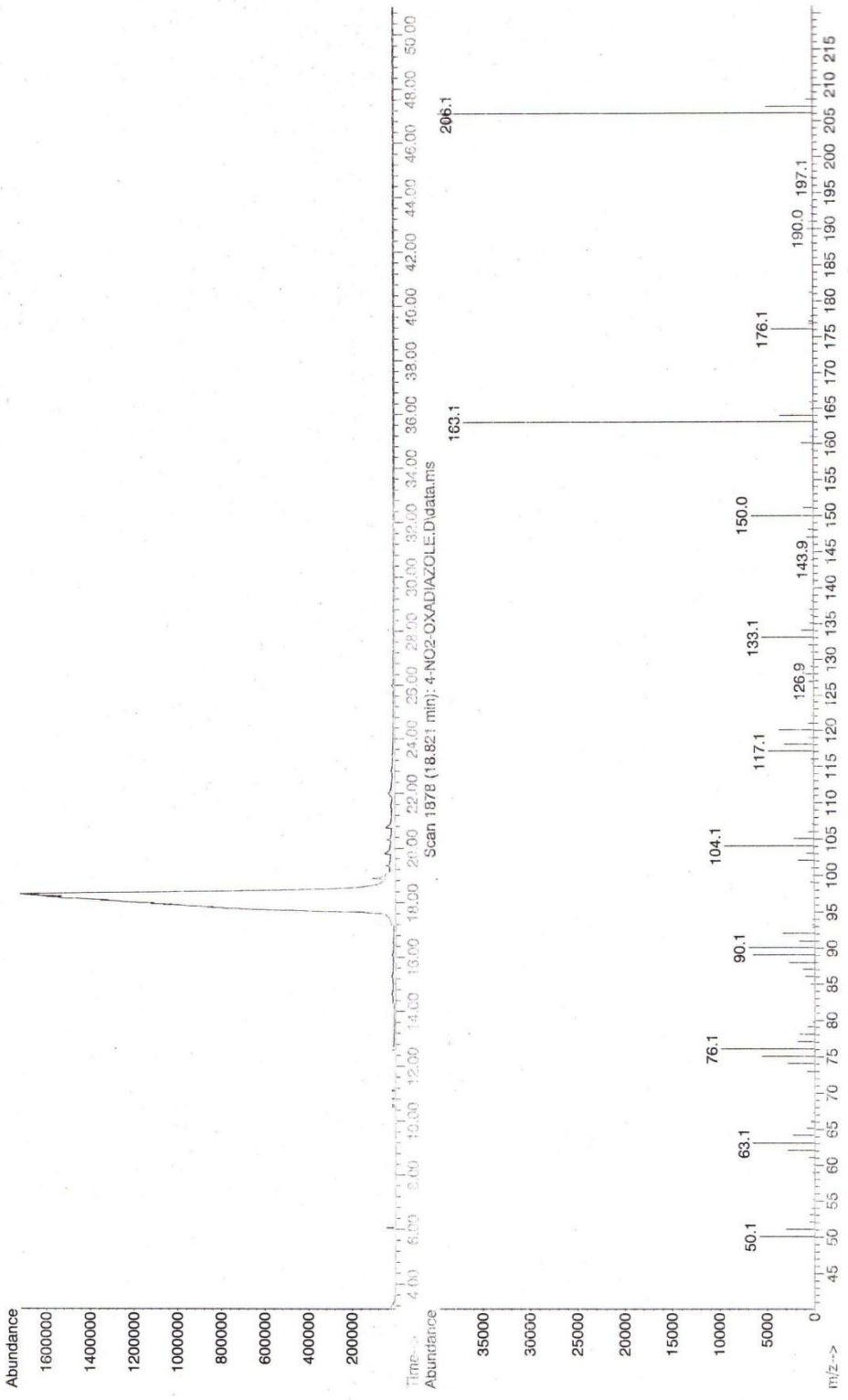
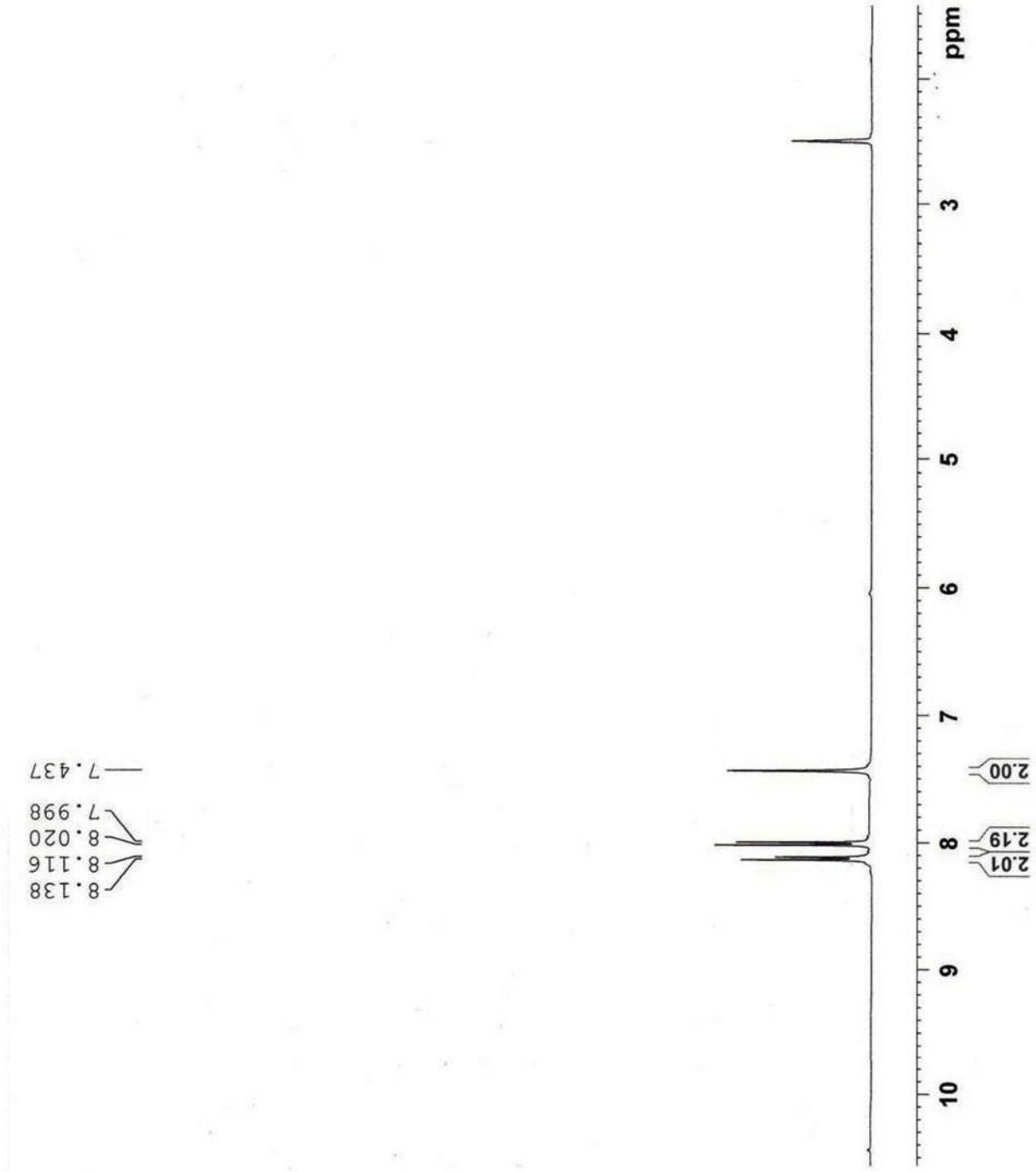
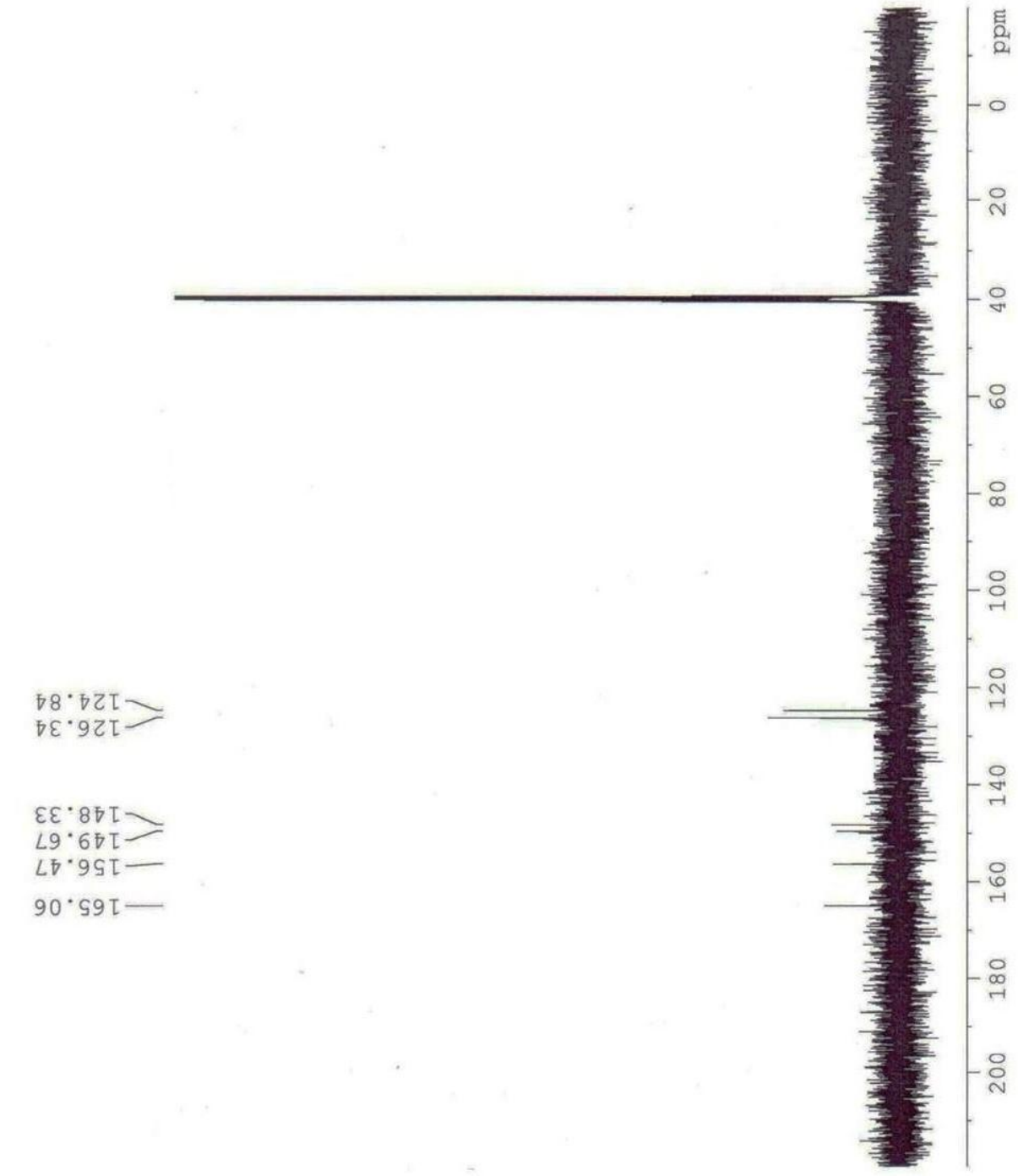


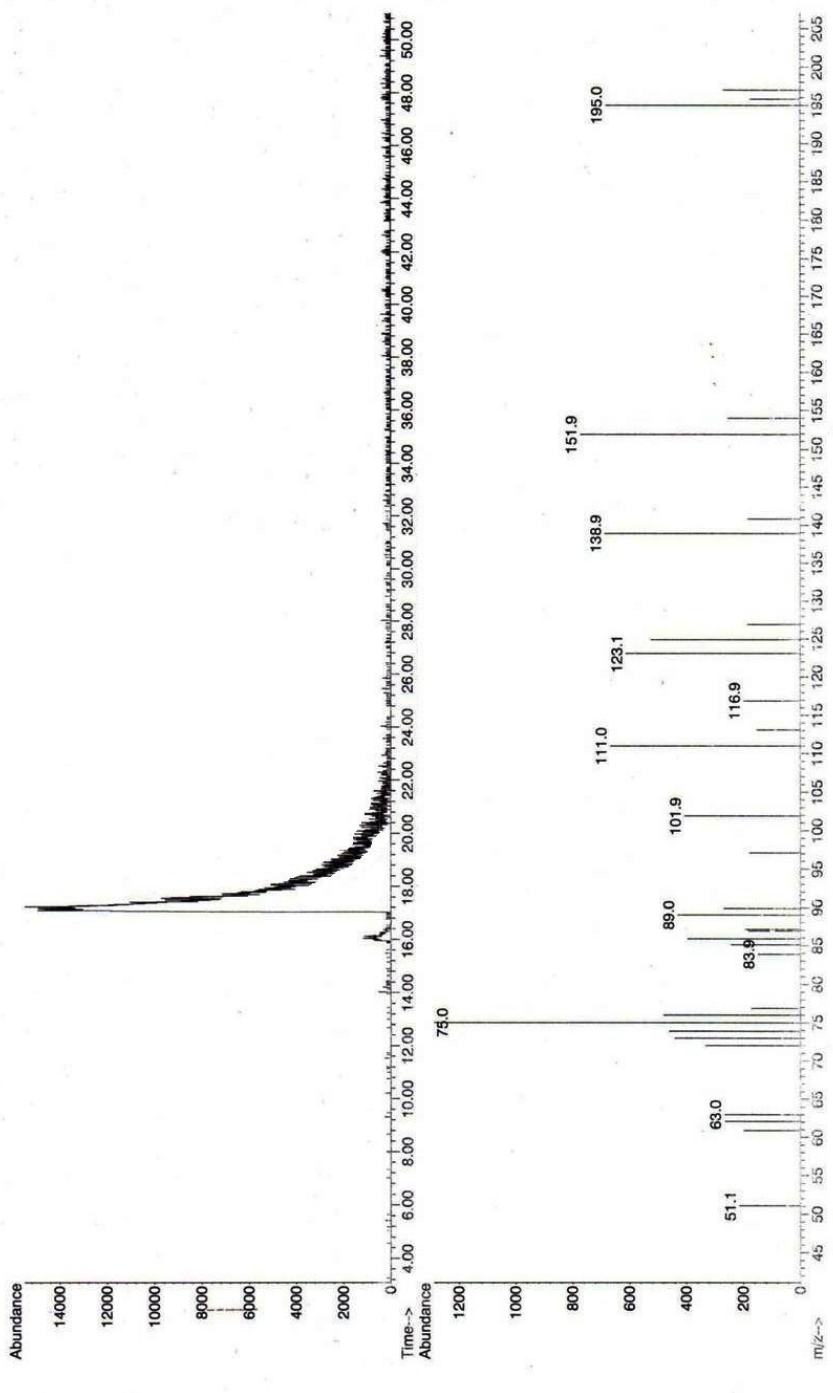
GC-MS of **2e**



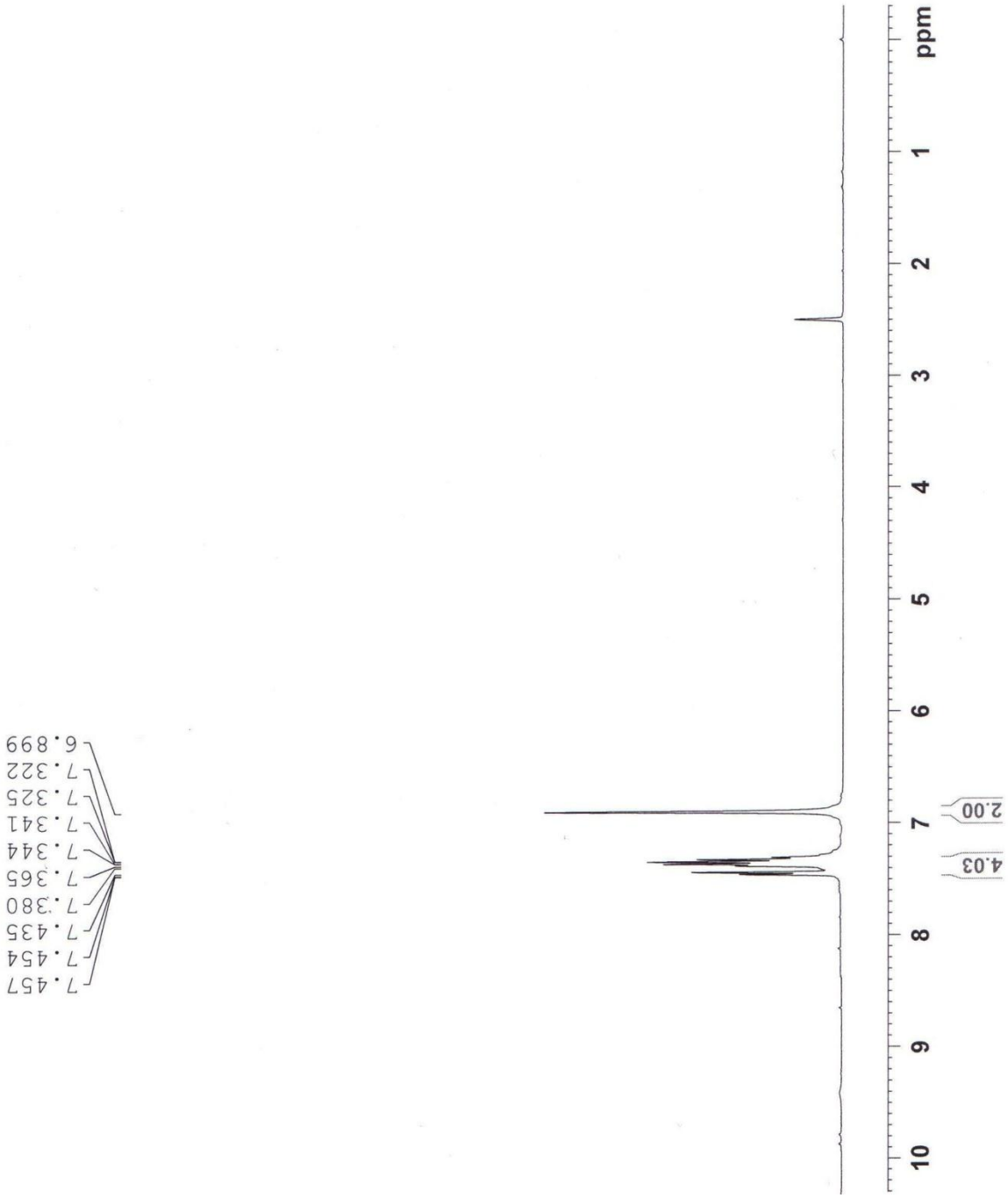
^{1}H NMR of **2e**



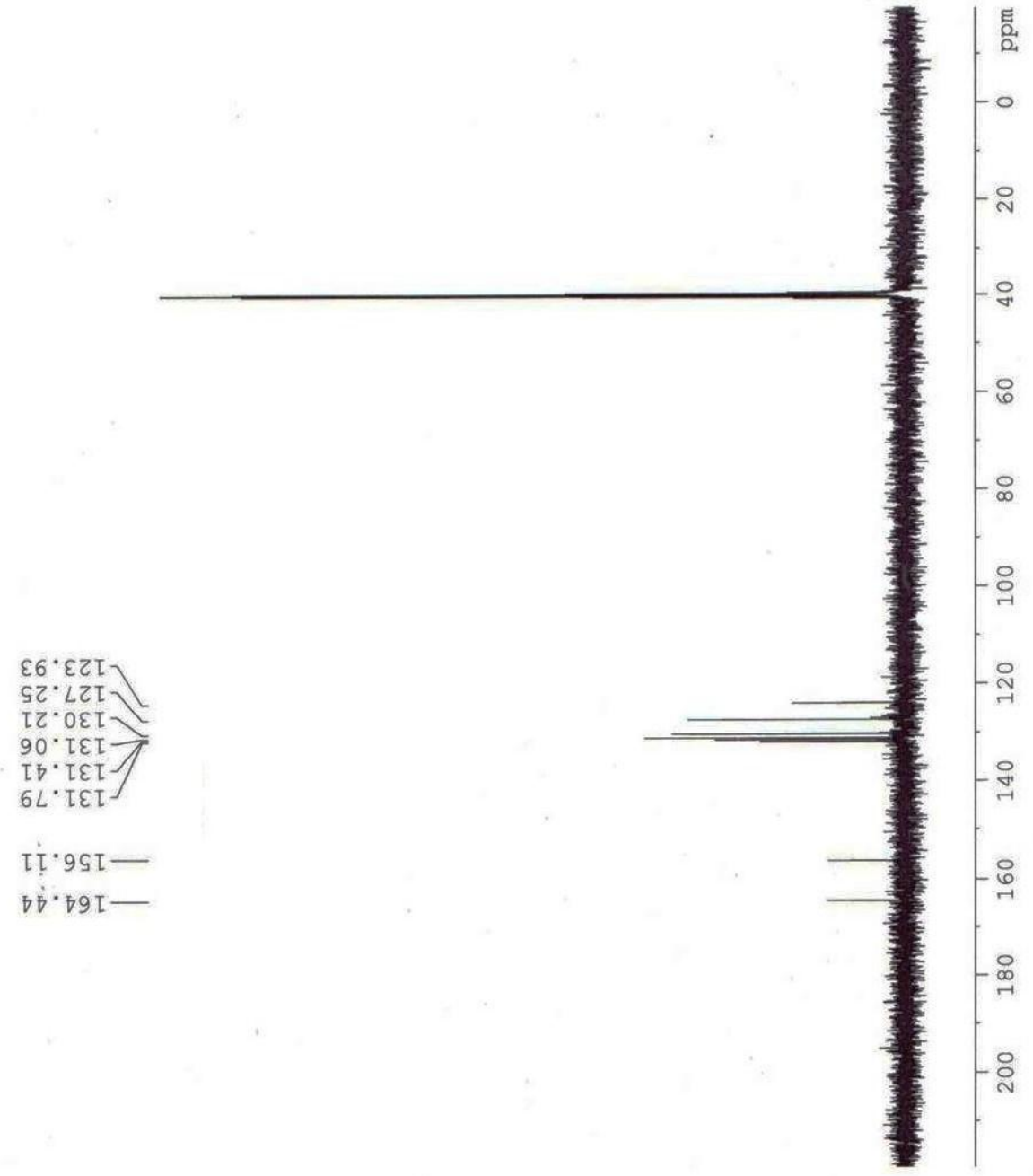
^{13}C NMR of **2e**



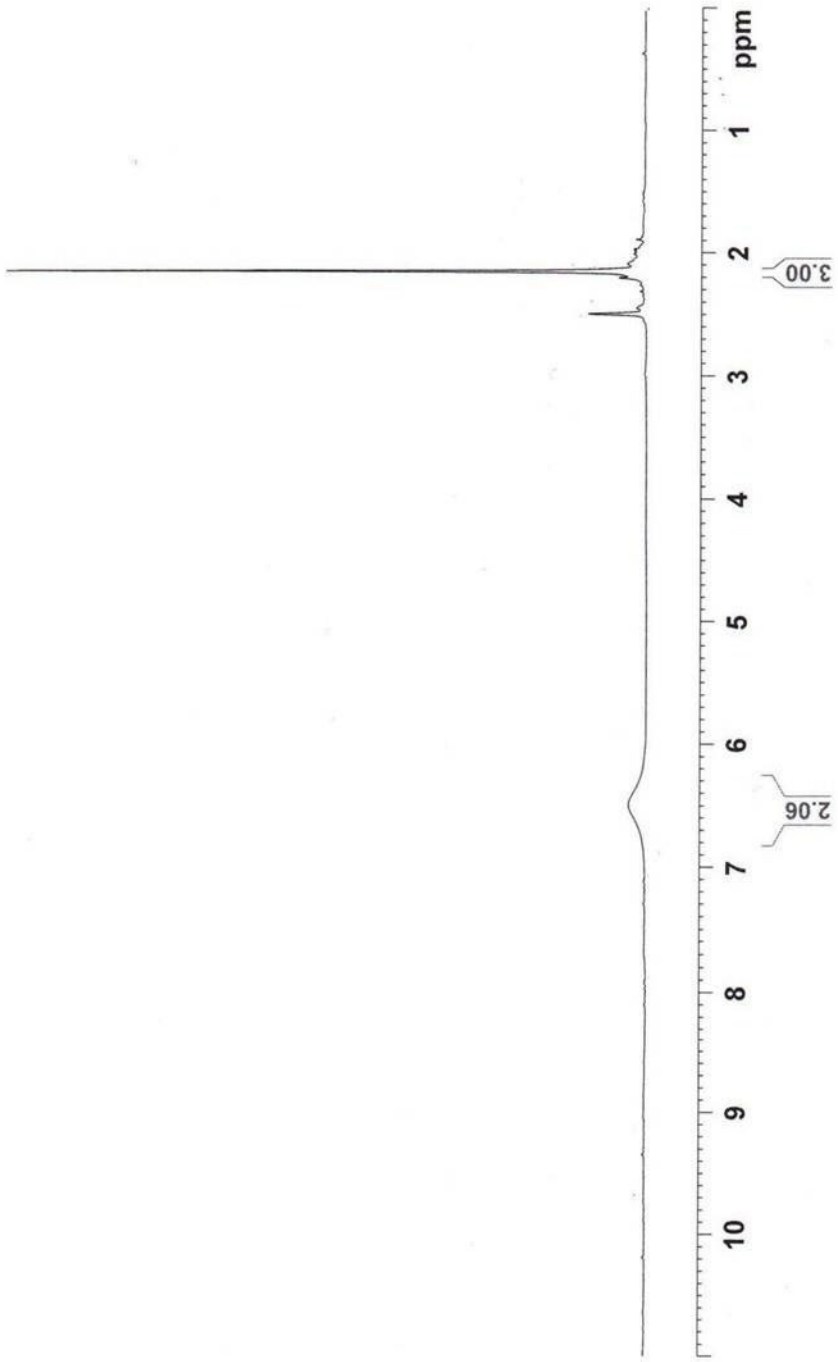
GC-MS of **2g**



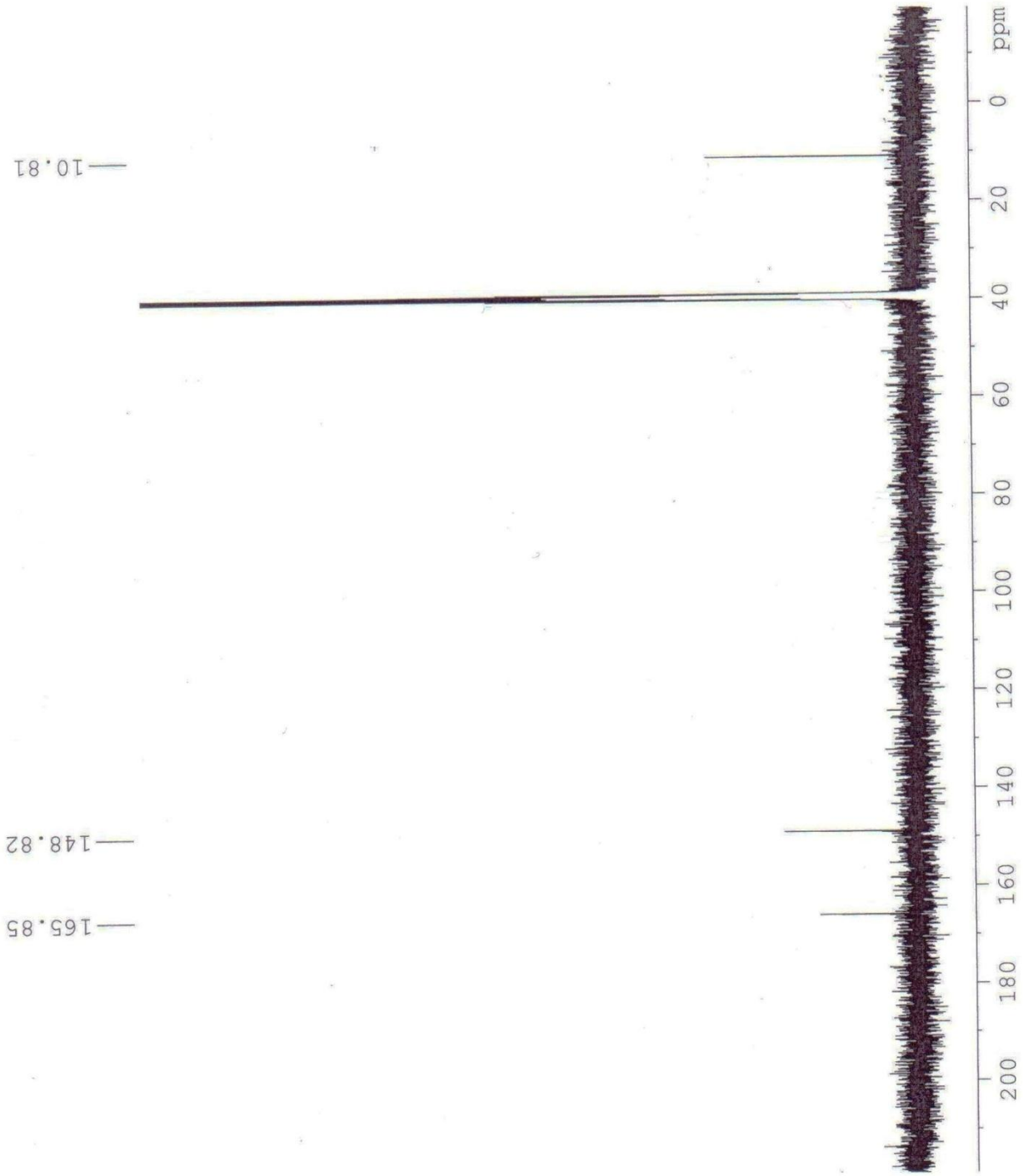
^{1}H NMR of **2g**


ppm
0
20
40
60
80
100
120
140
160
180
200
123.93
127.25
130.21
131.06
131.41
131.79
156.11
164.44

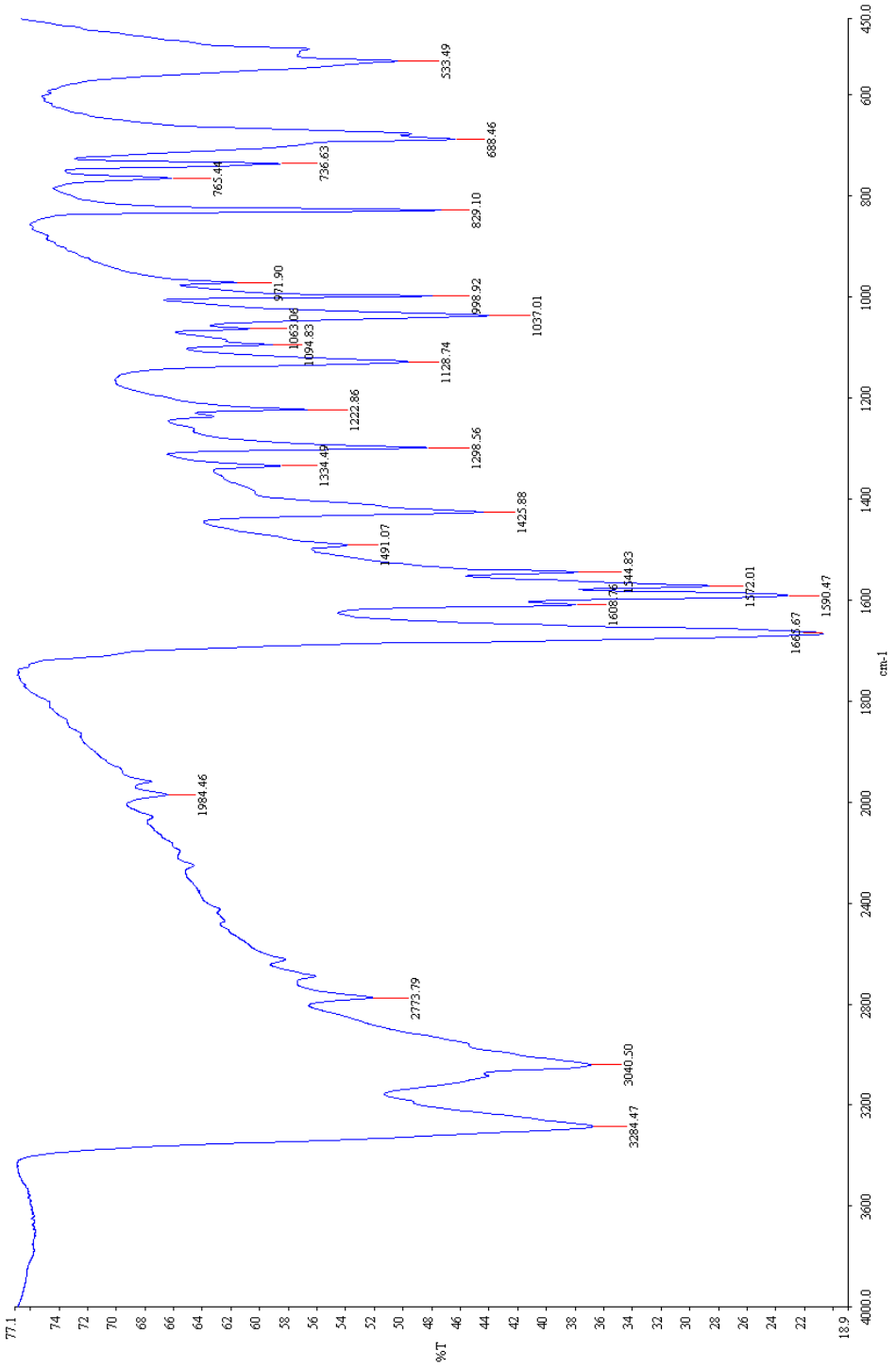
^{13}C NMR of **2g**



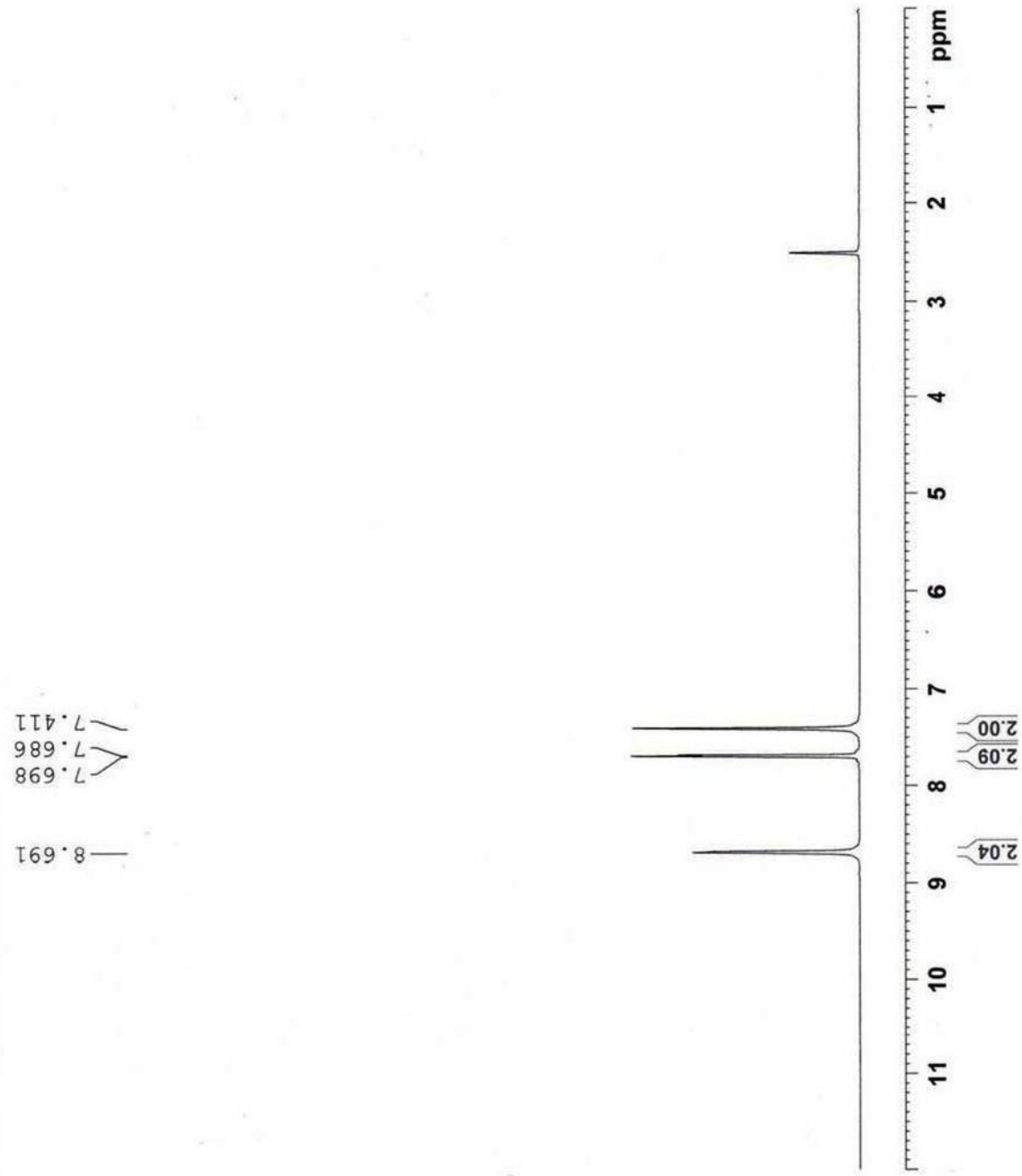
^{1}H NMR of **2j**



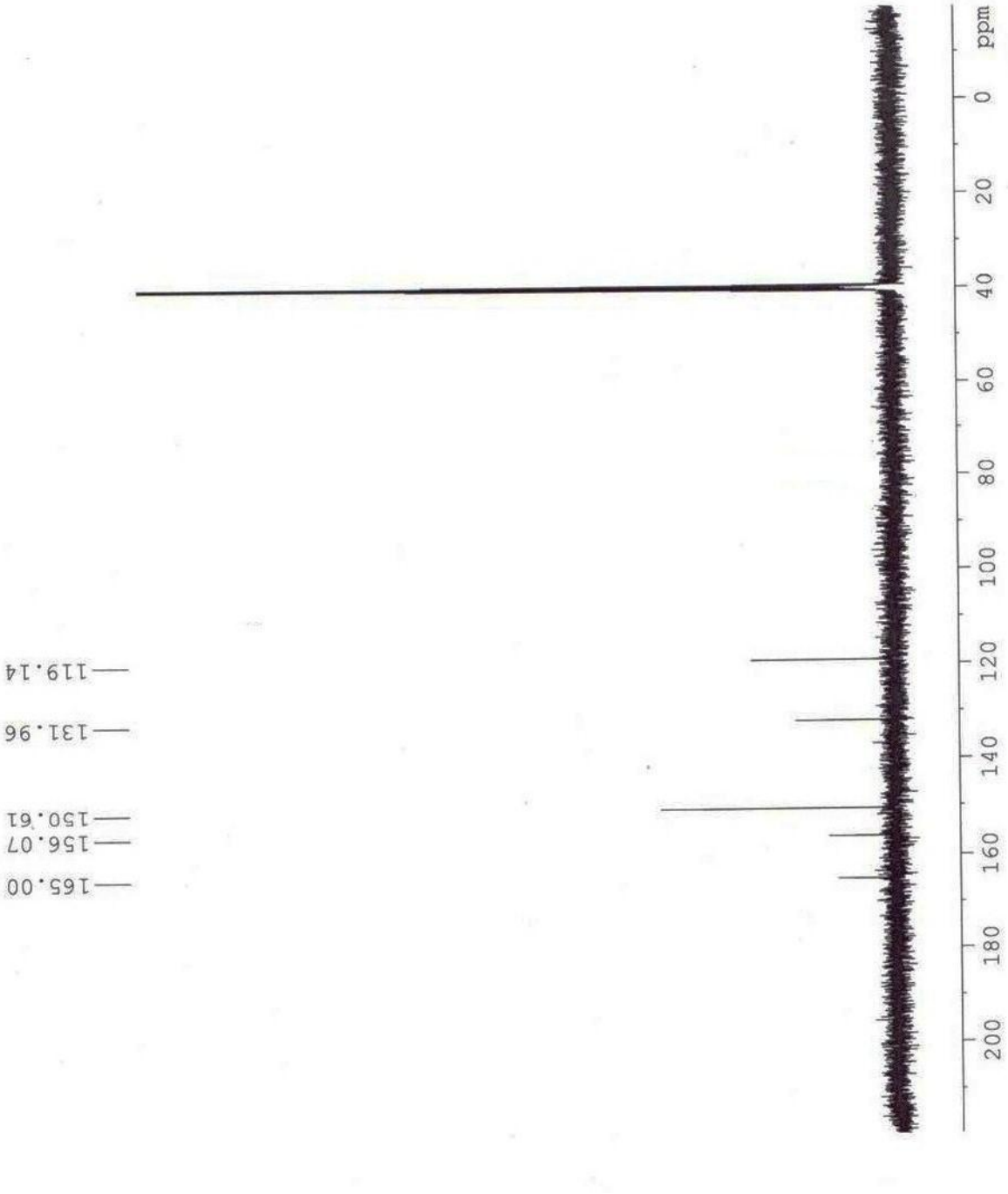
^{13}C NMR of **2j**


533.49
688.46
736.63
765.44
829.10
971.90
998.92
1037.01
1063.06
1094.83
1128.74
1222.86
1298.56
1334.49
1425.88
1491.07
1544.83
1572.01
1590.47
1608.76
1665.67
1984.46
2773.79
3040.50
3284.47
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
450.0
cm-1
77.1
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
28
26
24
22
18.9
%T

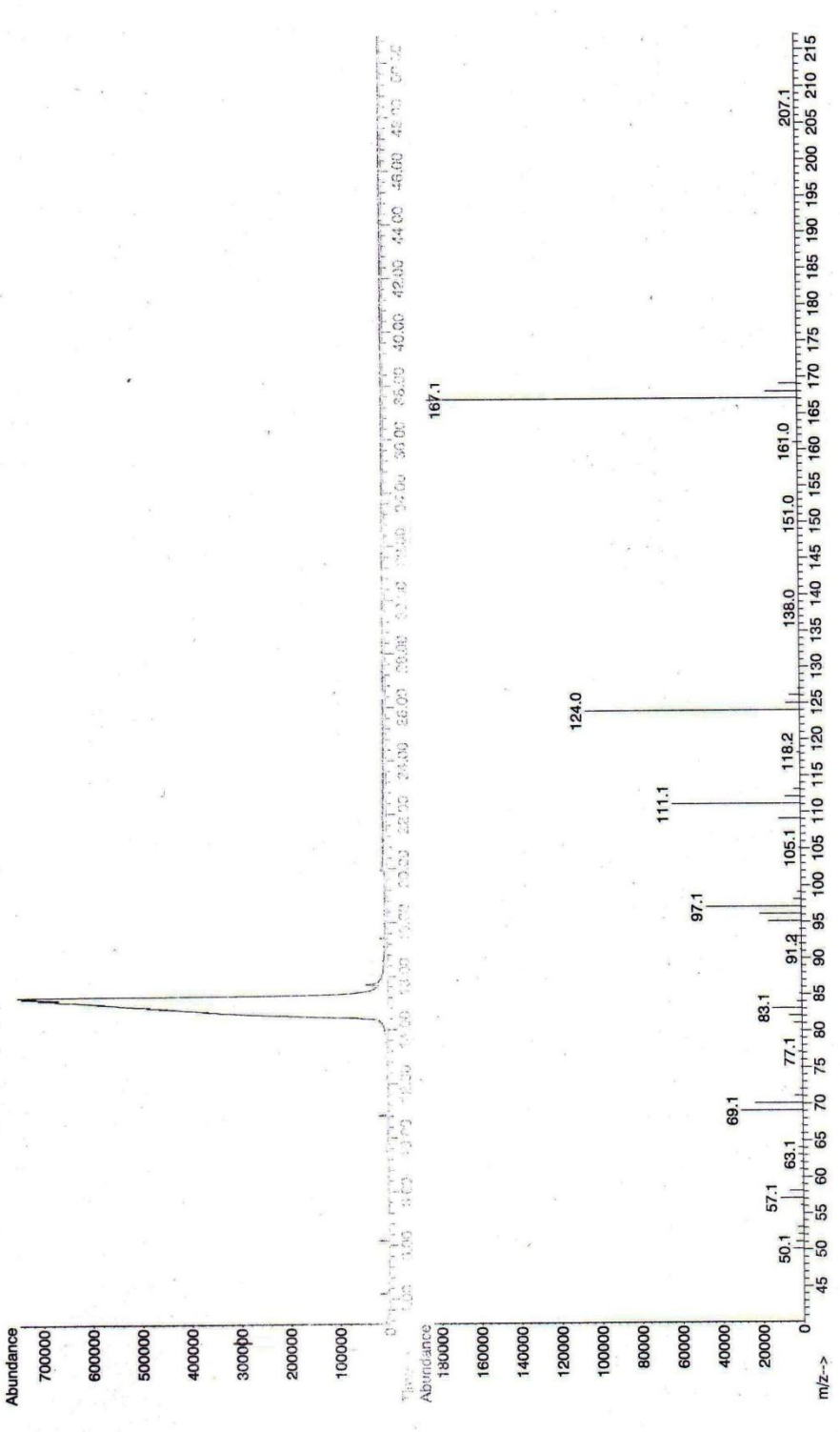
IR of **2l**



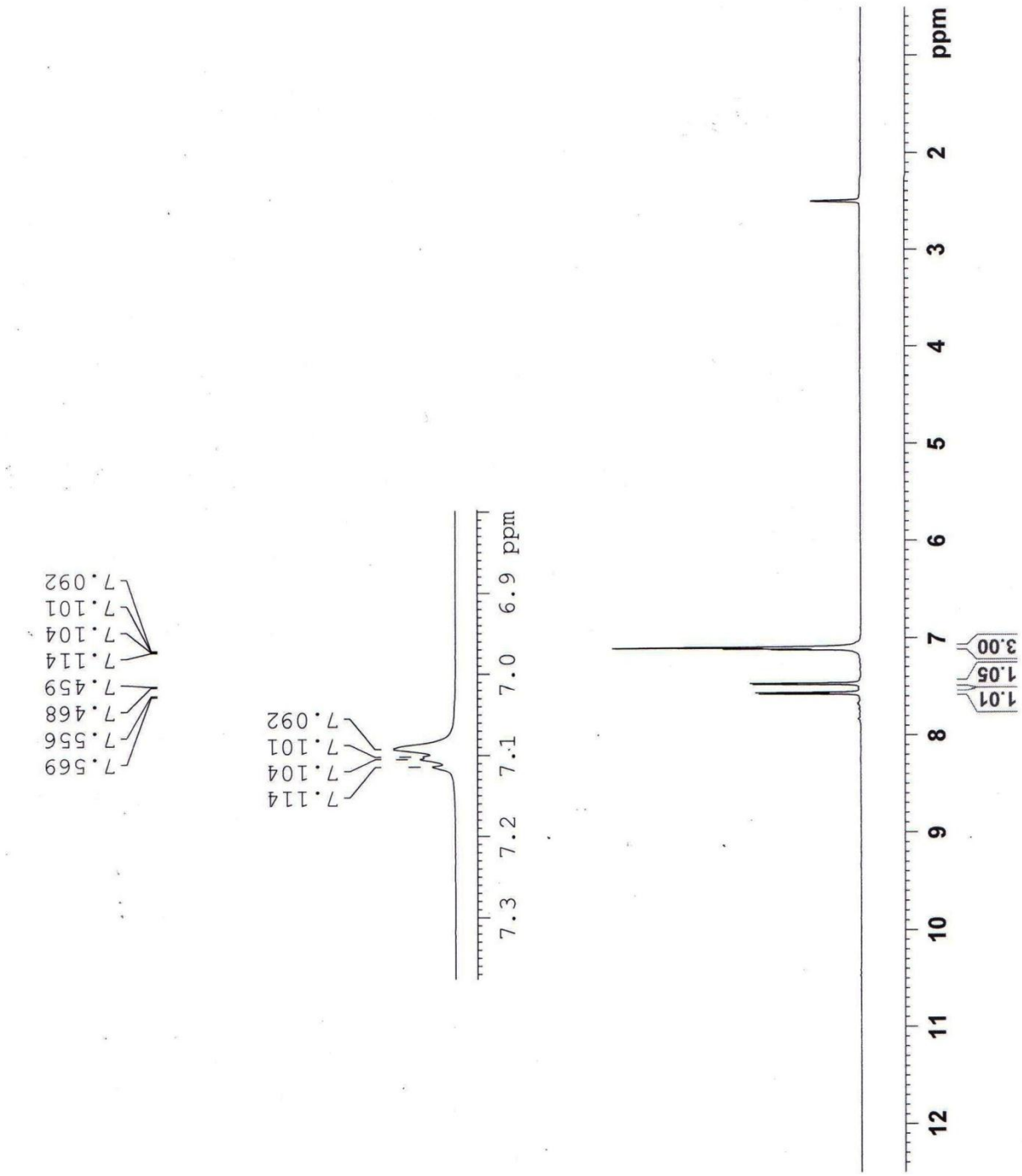
^{1}H NMR of **2l**



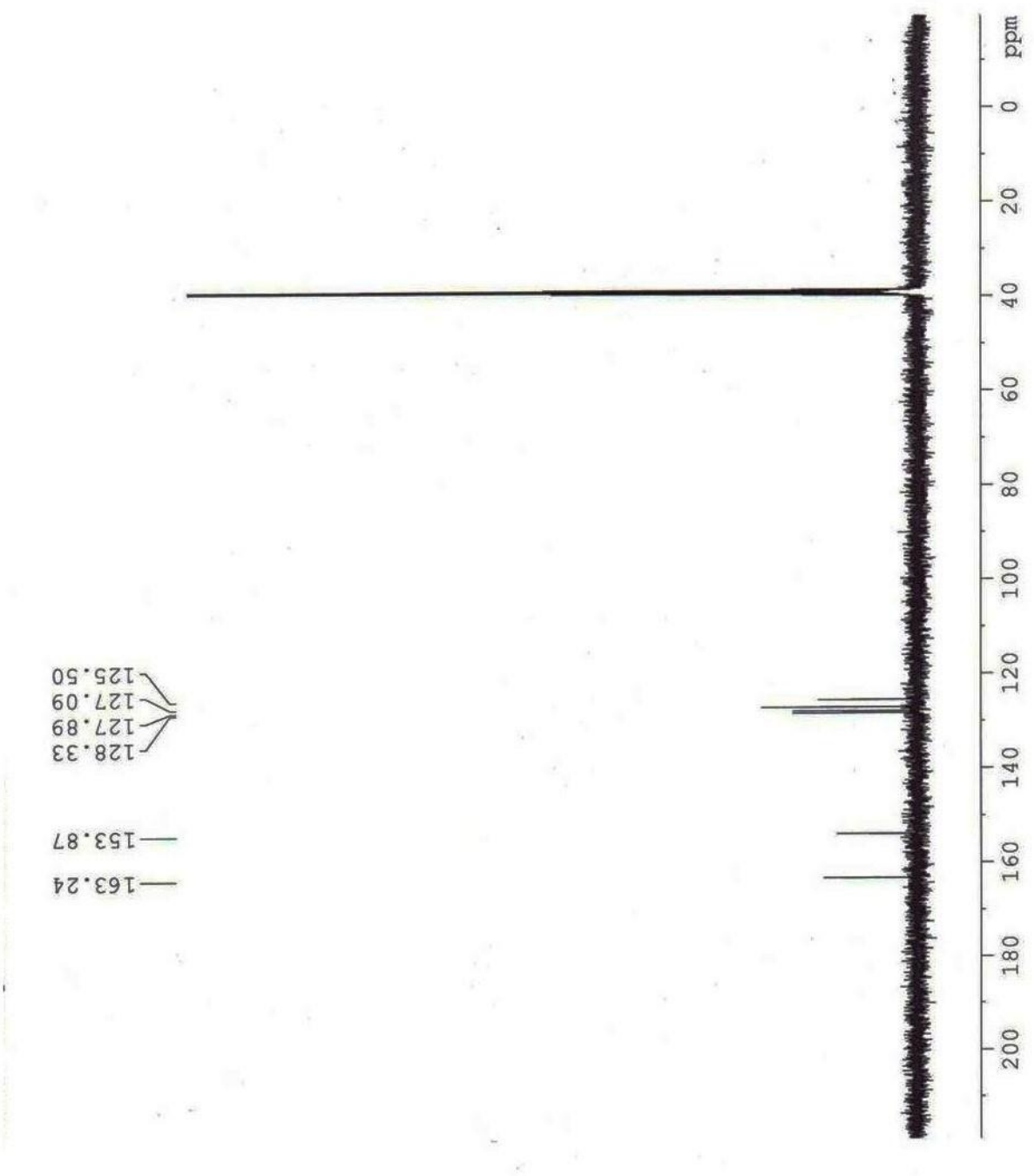
^{13}C NMR of **2l**



GC-MS of **2m**



^{1}H NMR of **2m**



^{13}C NMR of **2m**