Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting information

for

Deep Eutectic Solvent Assisted Synthesis of Dihydropyrimidinones/thiones via Biginelli Reaction: Theoretical Investigations on their Electronic and Global Reactivity Descriptors

M. Shaibuna,[a] Muhammed Jeneesh Kariyottu Kuniyil[b] and K. Sreekumar[a]*

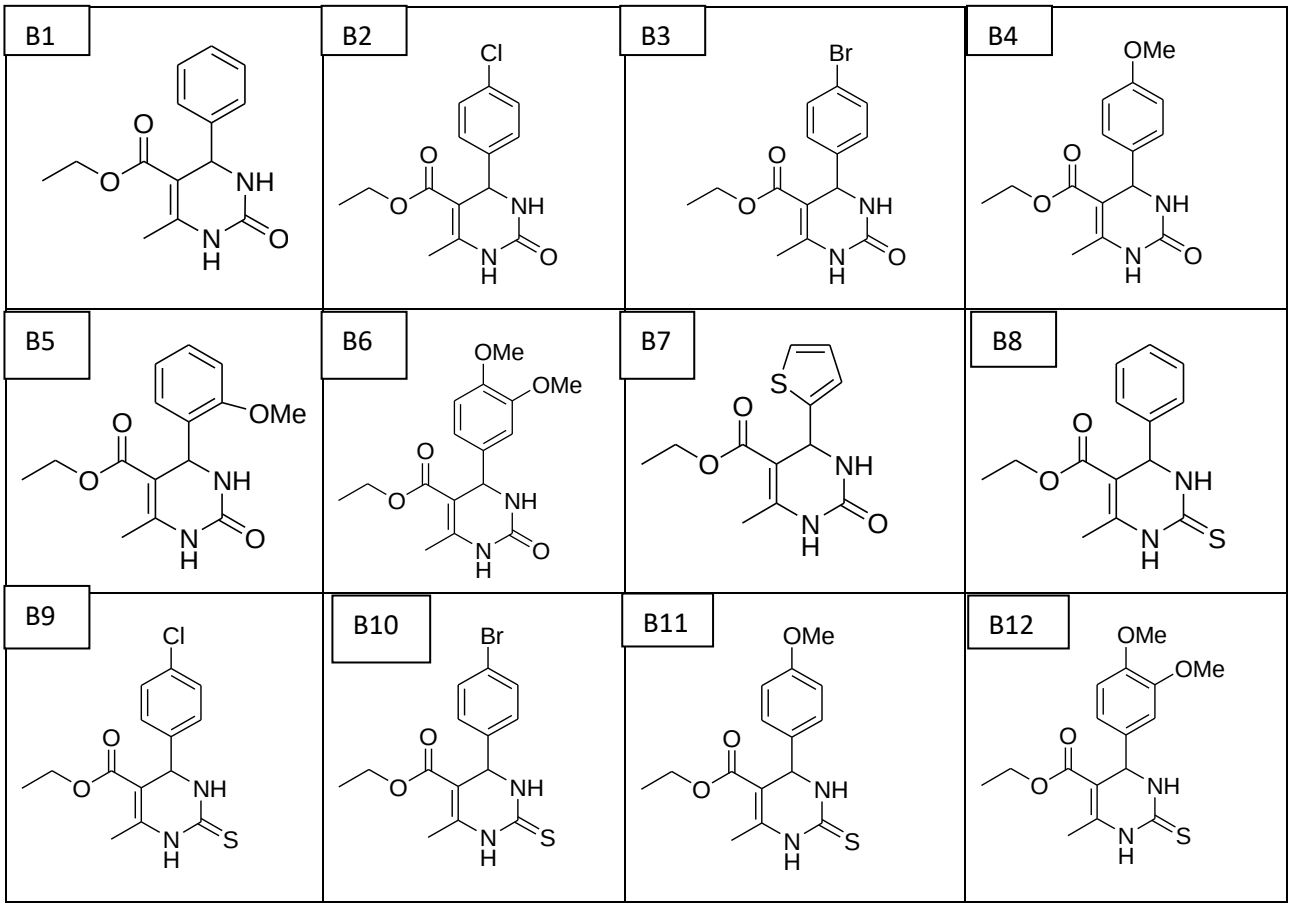
[a]Department of Applied Chemistry, Cochin University of Science and Technology, Cochin 682022, India.

[b]Department of Chemistry, Pondicherry University, R V Nagar, Kalapet, Puducherry 605 014, India

E-mail: K. Sreekumar- kskpolymer.cusat@gmail.com

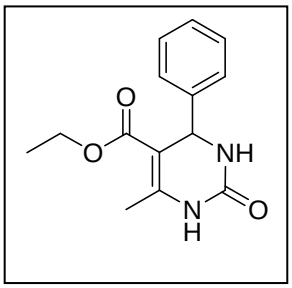
Entry	Content	Page no.
1	Structures of synthesized products	1
2	Spectral data of the synthesized products	2-4
3	GC- MS, ^{1}H and ^{13}C NMR spectra of the synthesized products	5-21
4	References	22

Structures of the synthesised products



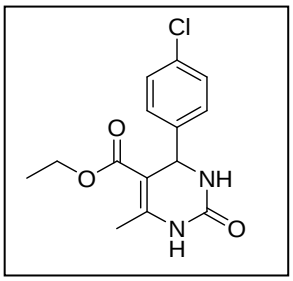
Spectral data of the synthesized products

1. 5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (B1)



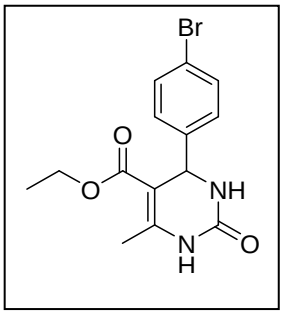
White solid, m. p. 203 ℃ (202–204 ℃)[1], GC-MS (M^+): 260; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.16 (s, 1H), 7.66(d, 5H), 7.29 (s, 1H), 5.38 (d, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 2.33 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.7, 153.4, 146.3, 128.7, 128.0, 126.6, 101.4, 60.1, 55.8, 18.7, 14.2.

2. 5-(Ethoxycarbonyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (B2)



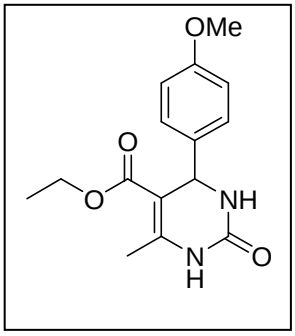
White solid, m. p. 213 ℃ (212–214 ℃)[1], GC-MS (M^+): 294; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.95 (s, 1H), 7.24-7.25(m, 4H), 5.36 (s, 1H), 4.05 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.5, 153.1, 146.4, 142.2, 133.8, 128.9, 128.1, 101.2, 60.2, 55.2, 18.8, 14.2.

3. 5-(Ethoxycarbonyl)-4-(4-bromophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (B3)



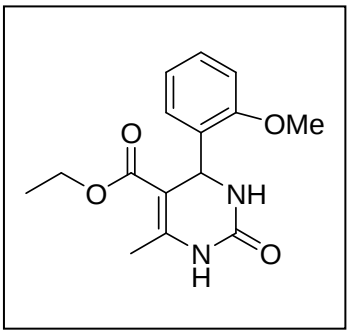
White solid, m. p. 152 ℃ (150–151 ℃)[2], GC-MS (M^+): 338; ^{1}H NMR (DMSO-*d6*, 400 MHz) δ: 9.28 (s, 1H), 7.82 (s, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 5.15 (s, 1H), 3.98 (q, *J* = 7.0 Hz, 2H), 2.26 (s, 3H), 1.09 (t, *J* =7.0 Hz, 3H); ^{13}C NMR (DMSO-*d6*, 100 MHz) δ: 166.6, 153.1, 149.9, 145.3, 132.7, 129.7, 121.5, 99.9, 60.5, 54.6, 18.9, 15.2.

4. 5-(Ethoxycarbonyl)-6-methyl-4-(4-methoxylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (B4)



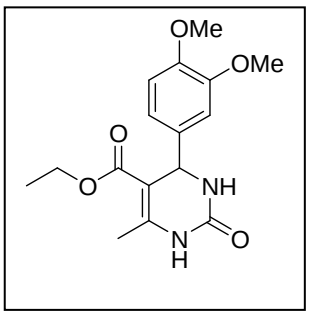
White solid, m. p. 204 °C (202-204 °C),[1] GC-MS (M^+): 290; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.14 (s, 1H), 7.66 (s, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 5.07 (s, 1H), 3.96 (q, *J* = 7.1 Hz, 2H), 3.70 (s, 3H), 2.23 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 166.2, 159.2, 152.9, 148.8, 137.8, 128.1, 114.5, 100.3, 59.9, 55.8, 54.1, 18.5, 14.9.

5. 5-(Ethoxycarbonyl)-6-methyl-4-(2-methoxylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (B5)



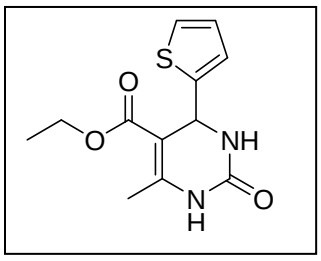
White solid, m. p. 145 °C (145- 146 °C)[2], GC-MS (M^+): 290; ^{1}H NMR (DMSO-*d6*, 400 MHz) δ: 7.52 (d, *J* = 3.29, 1H), 7.25- 7.21 (m, *J* = 8.42, 1H), 7.04 (dd, *J* = 1.65, *J* = 7.51, 1H), 6.96 (d, *J* = 8.06, 1H), 6.86 (t, *J* = 7.32, 1H), 5.46 (d, *J*= 3.29, 1H), 3.99-3.94 (m, 2H), 3.77 (s, 3H), 3.10 (s, 3H,, 2.49 (s, 3H), 1.05 (t, *J* = 7.14, 3H); ^{13}C NMR (DMSO-*d6*, 100 MHz) δ 165.6, 156.6, 153.1, 150.4, 130.8, 128.7, 126.9, 120.1, 111.1, 101.1, 59.3, 55.4, 47.9, 29.6, 15.9, 13.9.

6. 5-(Ethoxycarbonyl)-6-methyl-4-(3,4-dimethoxylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (B6)



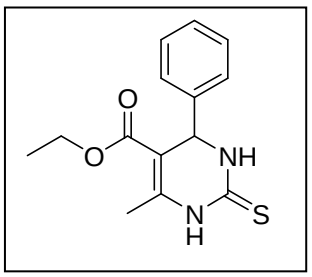
White solid, m. p. 176 °C (176- 177 °C)[3], GC-MS (M^+): 320; ^{1}H NMR (DMSO-*d6*, 400 MHz) δ: 8.95 (s,1H), 7.25 (s, 1H), 6.85 (m, 1H), 6.80 (m, 2H), 5.25 (s, 1H), 4.05 (q, 2H, *J* = 7.0 Hz), 3.80 (s, 6H), 2.30 (s, 3H), 1.15 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (DMSO-*d6*, 100 MHz) δ: 165.6, 153.8, 148.9, 148.6, 146.1, 136.4, 118.5, 111.1, 109.9, 101.3, 59.9, 55.8, 55.1, 18.4, 8 14.1.

7. 5-(Ethoxycarbonyl)-6-methyl-4-(2-thienyl)-3,4-dihydropyrimidin-2(1*H*)-one (B7)



Brown solid, m. p. 216 °C (215-217 °C)[1] , GC-MS (M^+): 266; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.68 (s, 1H), 7.16 (d, 1H), 7.14 – 6.71 (m, 2H), 5.68 (s, 1H), 4.15 (q, 2H), 2.32 (s, 3H), 1.23 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ:165.3, 153.1, 147.2, 146.4, 126.7, 124.9, 124.0, 101.8, 60.2, 50.8, 18.7, 14.2.

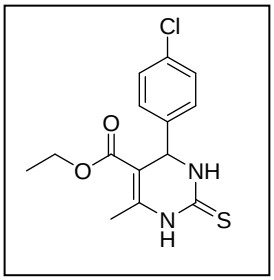
8. 5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(*1H*)-thione (B8)



White solid, m. p. 209 °C (208-210 °C)[1] , GC-MS (M^+): 276; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.15 (s, 1H), 7.18-7.24 (m, 5H), 5.31 (s, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 2.28 (s, 3H), 1.06 (t, *J* =

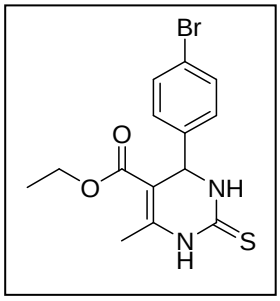
7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 174.5, 165.2, 142.7, 142.3, 128.8, 128.3, 126.8, 102.9, 60.4, 56.2, 18.3, 14.0.

9. 5-(Ethoxycarbonyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (B9)



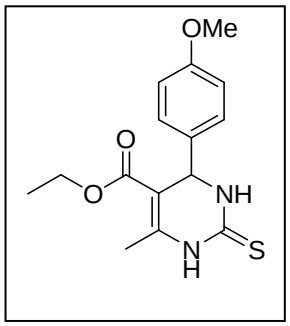
White solid, m. p. 193 °C (192-194 °C)[1] , GC-MS (M^+): 310; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.34 (s, 1H), 7.89 (s, 1H), 7.13-7.22 (m, 5H), 5.29 (s, 1H), 4.02 (q, *J* = 7.0, 2.6 Hz, 2H), 2.28 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 174.3, 165.1, 143.1, 140.9, 129.0, 128.2, 102.6, 60.5, 55.4, 18.2, 14.1.

10. 5-(Ethoxycarbonyl)-4-(4-bromophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (B10)



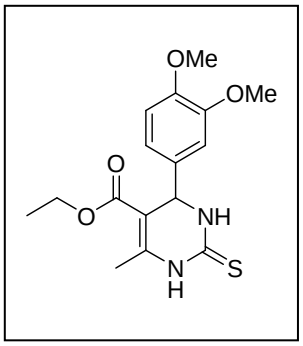
White solid, m. p. 183 °C (182 - 183 °C)[2], GC-MS (M^+): 336; ^{1}HNMR (DMSO-*d*6, 400 MHz) δ 10.38 (s, 1H), 9.66 (s, 1H), 7.56 (d, *J* = 8.42, 2H), 7.17 (d, *J* = 8.42, 2H), 5.15 (d, *J* = 3.66, 1H), 4.00 (q, *J* = 6.96, *J* = 13.51, 2H), 2.29 (s, 3H), 1.09 (t, *J* = 7.14, 3H); ^{13}C NMR (DMSO-*d*6, 100 MHz) δ: 174.2, 164.9, 145.3, 142.7, 131.4, 128.6, 120.7, 100.2, 59.6, 53.5, 17.1.

11. 5-(Ethoxycarbonyl)-6-methyl-4-(4-methoxylphenyl)-3,4-dihydropyrimidin-2(1*H*)-thione (B11)



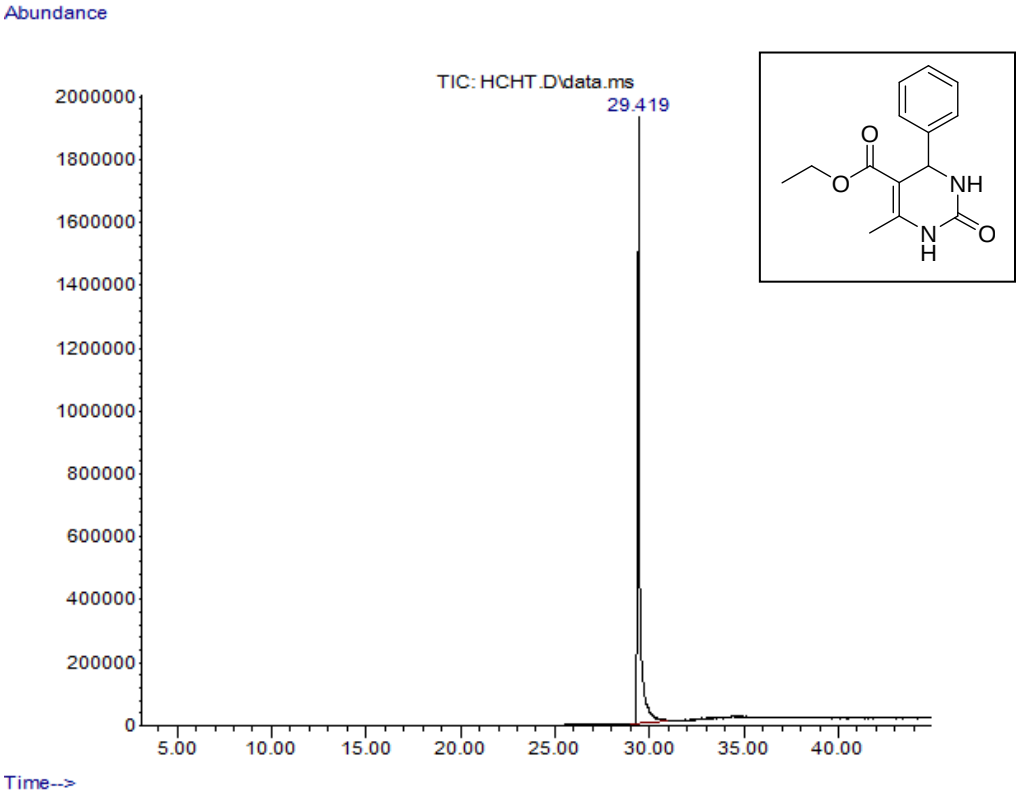
White solid, m. p. 151 °C (150-152 °C)[1], GC-MS (M^+): 306; ^{1}H NMR (DMSO-*d6*, 400 MHz) δ: 10.29 (s, 1H), 9.59 (s, 1H), 7.14-6.87 (m, 4H), 5.10 (s, 1H), 3.99 (q, *J* = 7.0 Hz, 2H), 3.71 (s, 3H), 2.27 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (DMSO-*d6*, 100 MHz) δ: 174.0, 165.2, 158.8, 144.7, 135.8, 127.7,113.9, 101.1, 59.6, 55.1, 53.5, 17.2, 14.1.

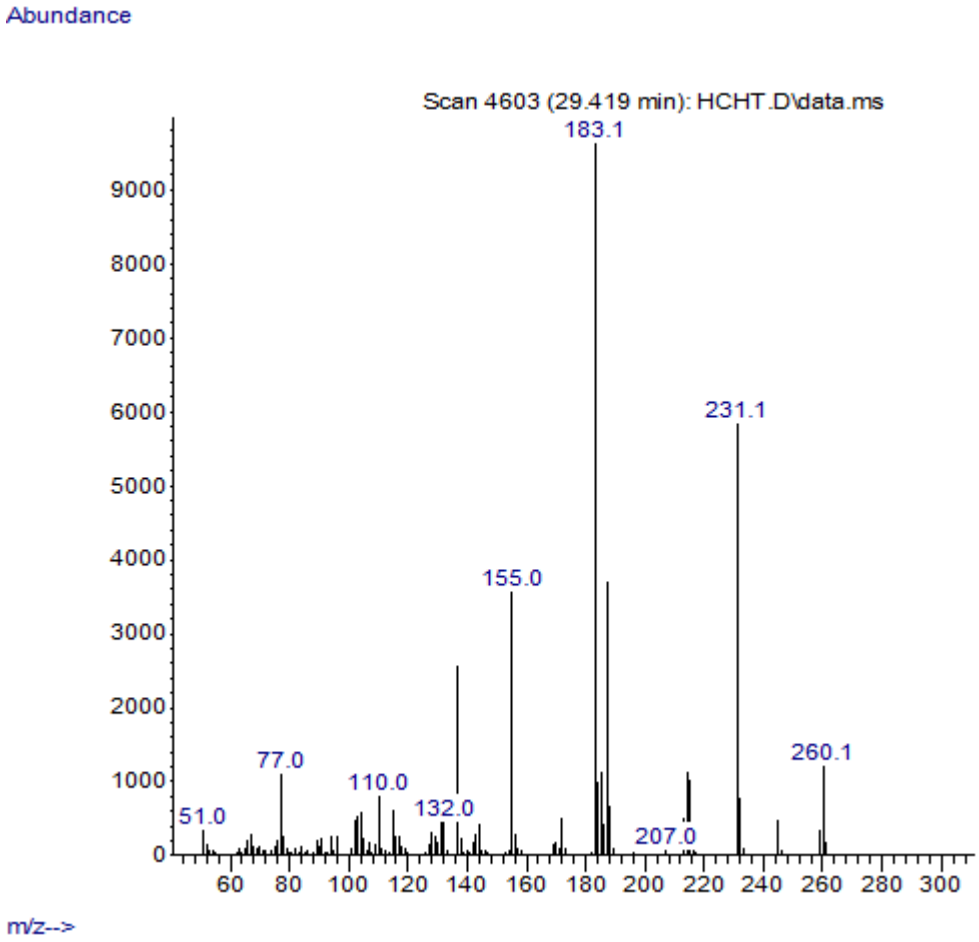
12. 5-(Ethoxycarbonyl)-6-methyl-4-(3,4-dimethoxylphenyl)-3,4-dihydropyrimidin-2(1H)-thione (B12)

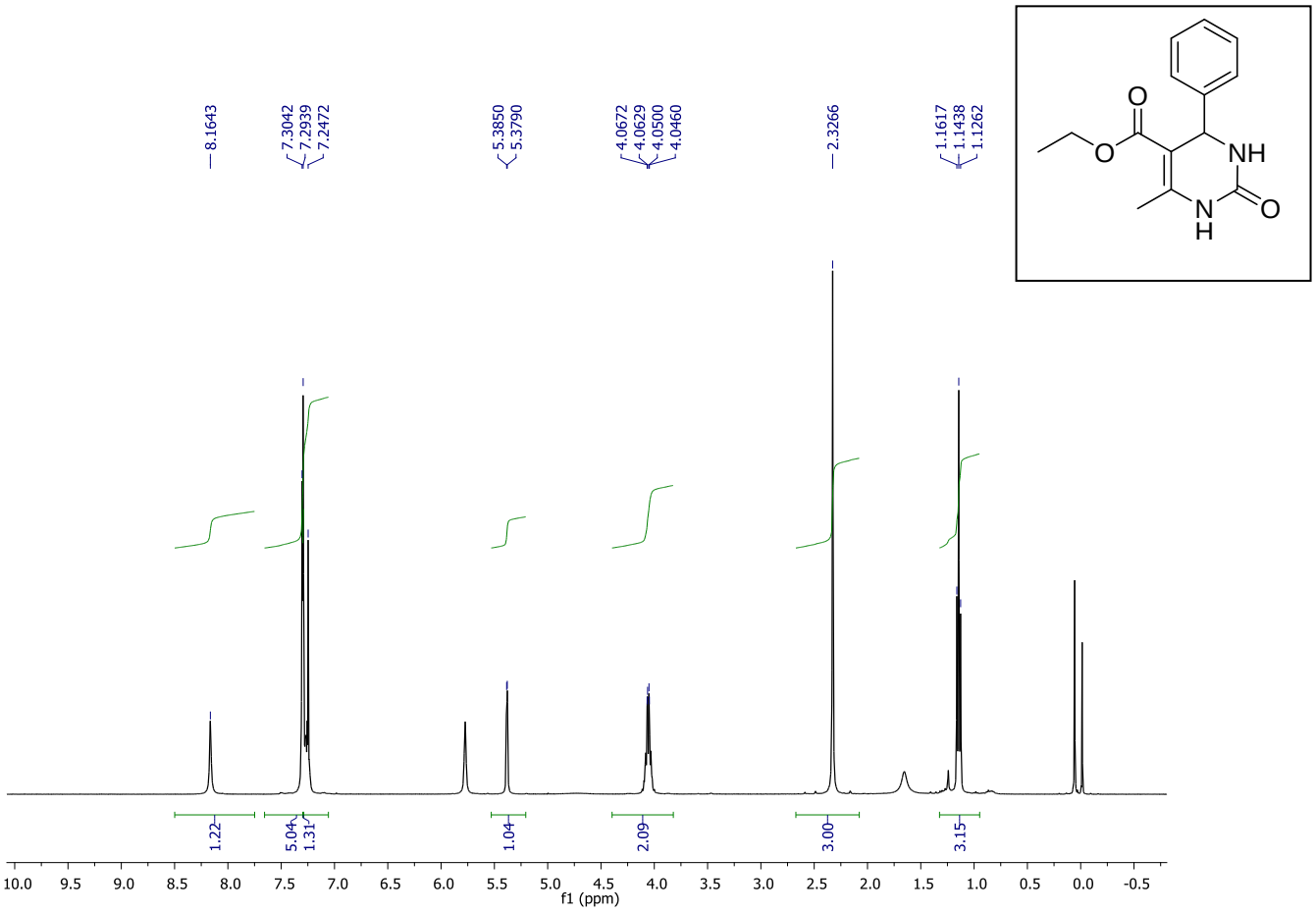


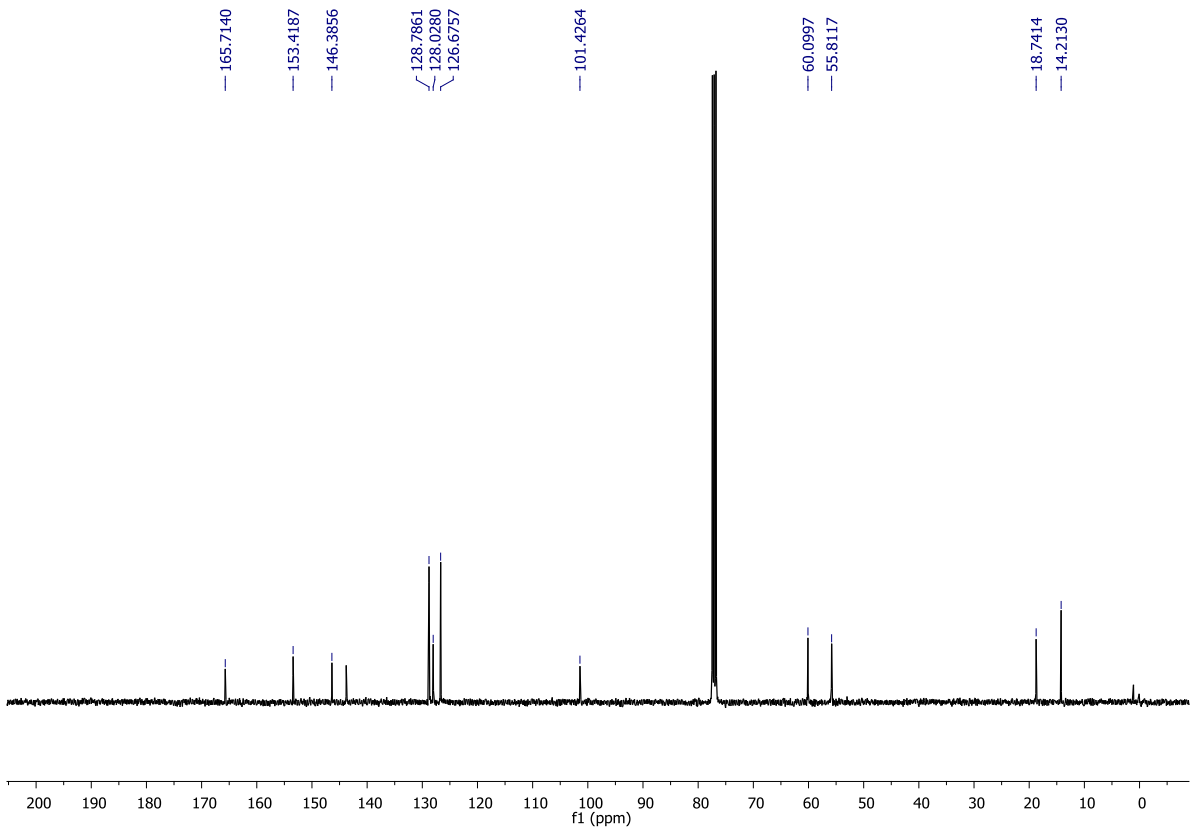
White solid, m. p. 177 °C (178 °C)[4], GC-MS (M^+): 336; ^{1}H NMR (DMSO-*d6*, 400 MHz) δ: 10.29 (s, 1H), 9.59 (s, 1H), 6.91(d, *J* =8.2, 1H), 6.84 (s, 1H), 6.70 (d, *J* =8.2, 1H), 5.13 (s, 1H), 4.03 (q, *J*=7.1, 2H), 3.73 (s, 6H), 2.30 (s, 3H), 1.13 (t, *J*=7.1, 3H); ^{13}C NMR (DMSO-*d6*, 100 MHz) δ: 173.9, 164.9, 148.3, 148.1, 144.5, 135.7, 117.9, 111.6, , 110.2, 100.6, 59.3, , 55.2, 53.3, 16.9, 13.8.

Gas chromatogram and mass spectrum of B1 (MW: 260)

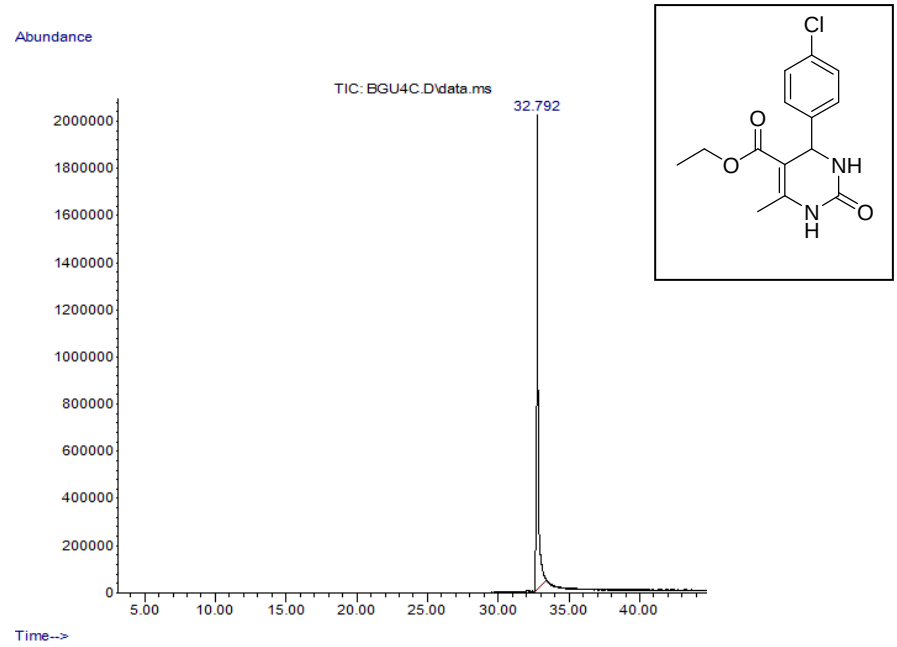


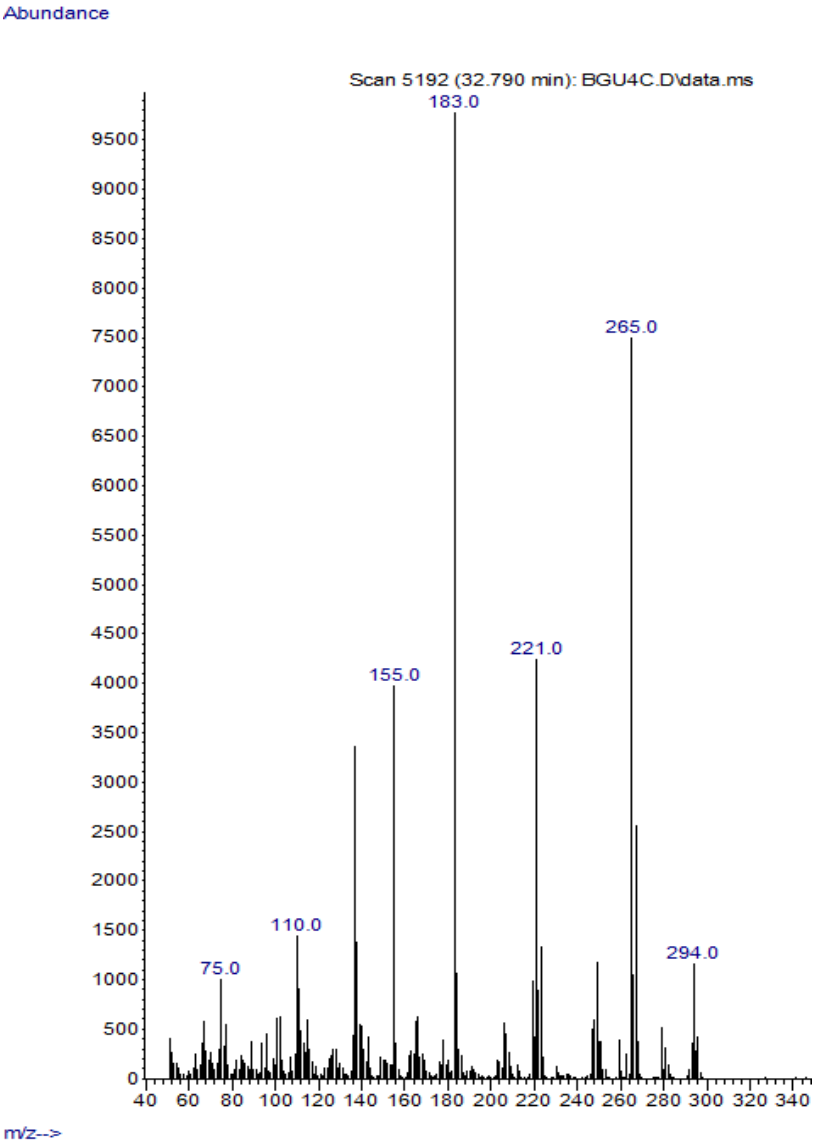


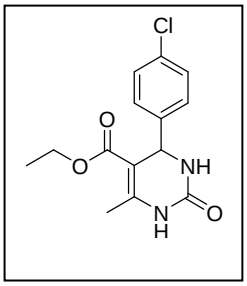

8.1643
7.3042
7.2939
7.2472
5.3850
5.3790
4.0672
4.0629
4.0500
4.0460
2.3266
1.1617
1.1438
1.1262
1.22
5.04
1.31
1.04
2.09
3.00
3.15
f1 (ppm)


165.7140
153.4187
146.3856
128.7861
128.0280
126.6757
101.4264
60.0997
55.8117
18.7414
14.2130
f1 (ppm)

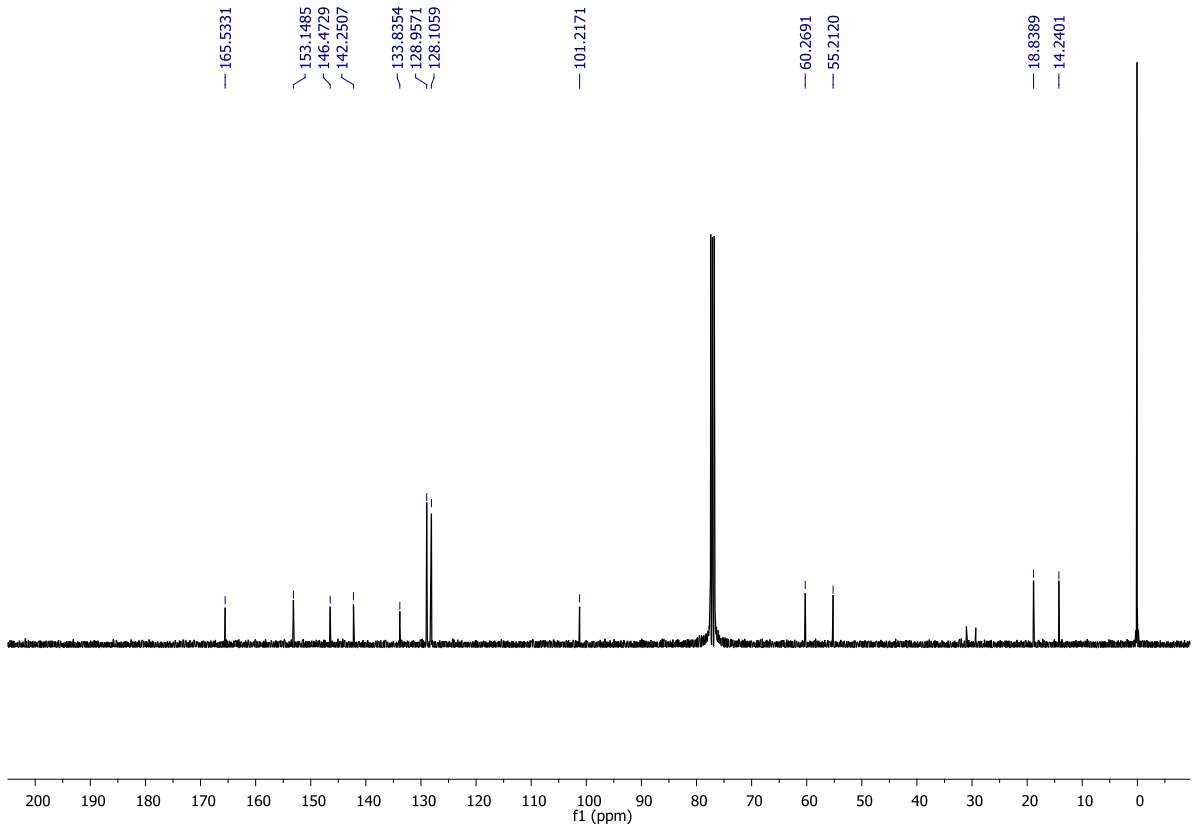
Gas chromatogram and mass spectrum of B2 (MW: 294)



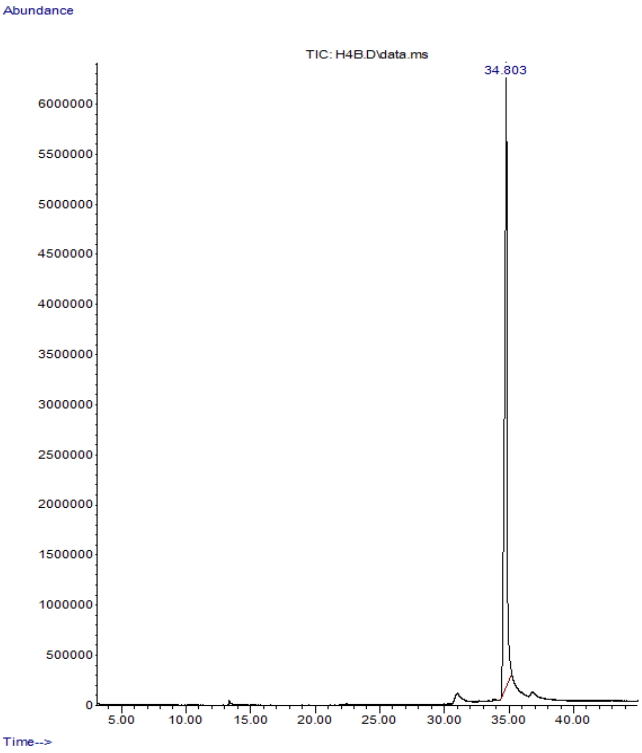


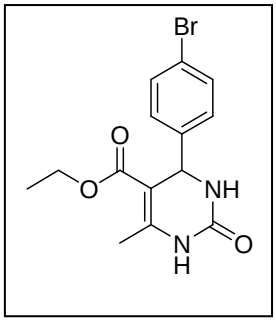

Cl
O
O
NH
N
H
O

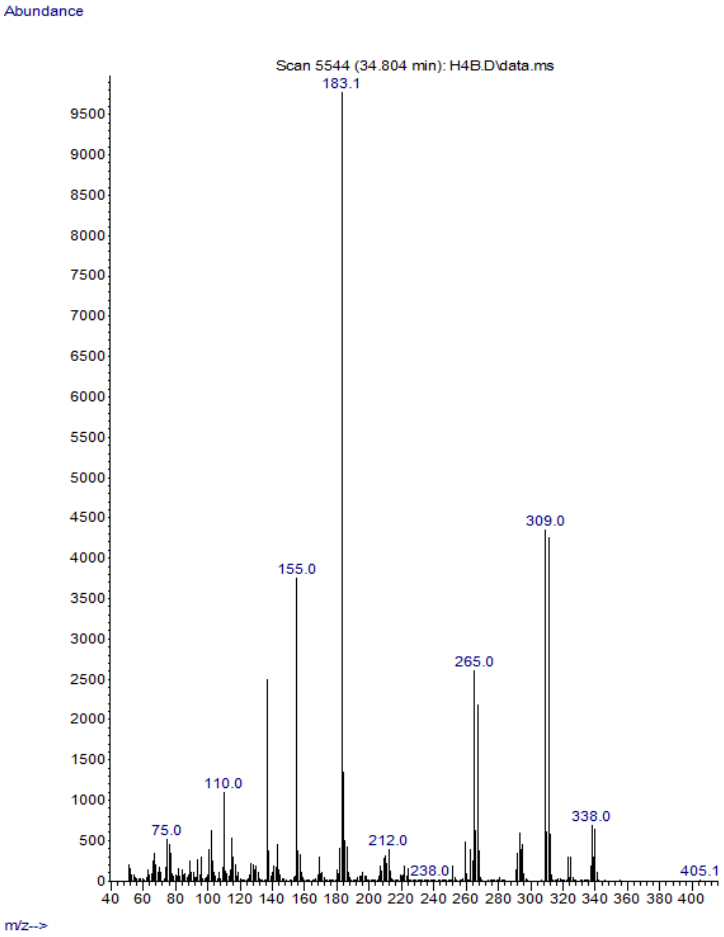
7.95
7.25
7.25
7.24
7.24
5.36
4.07
4.07
4.05
4.05
2.32
1.17
1.15
1.14
0.95
4.29
0.69
2.03
3.31
3.33
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


165.5331
153.1485
146.4729
142.2507
133.8354
128.9571
128.1059
101.2171
60.2691
55.2120
18.8389
14.2401
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

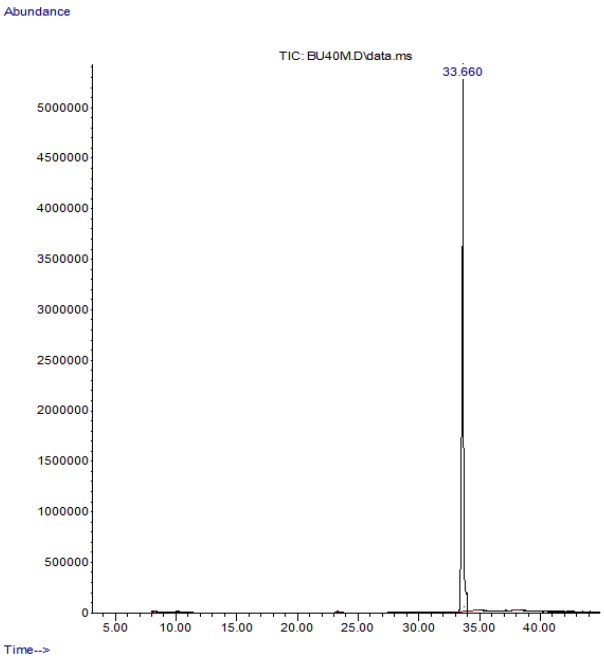
Gas chromatogram and mass spectrum of B3 (MW: 339)

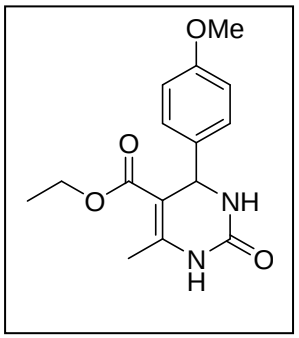


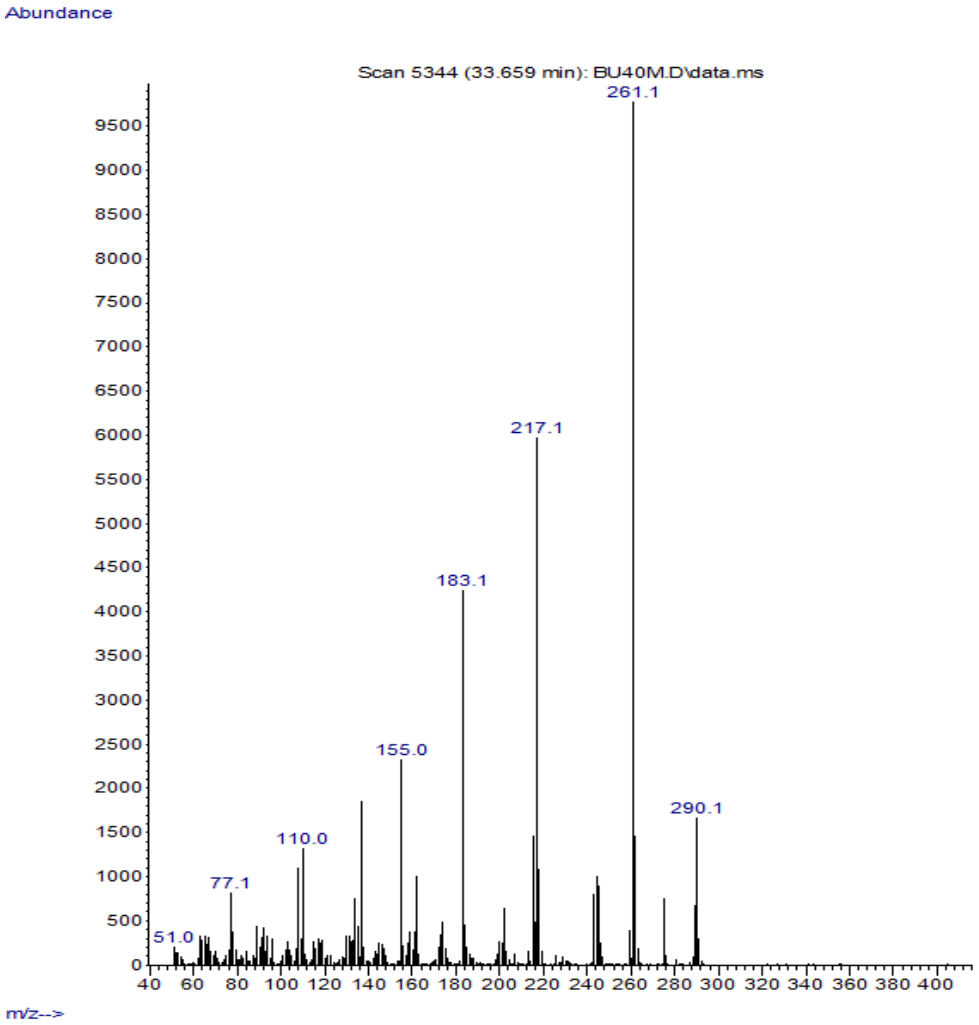




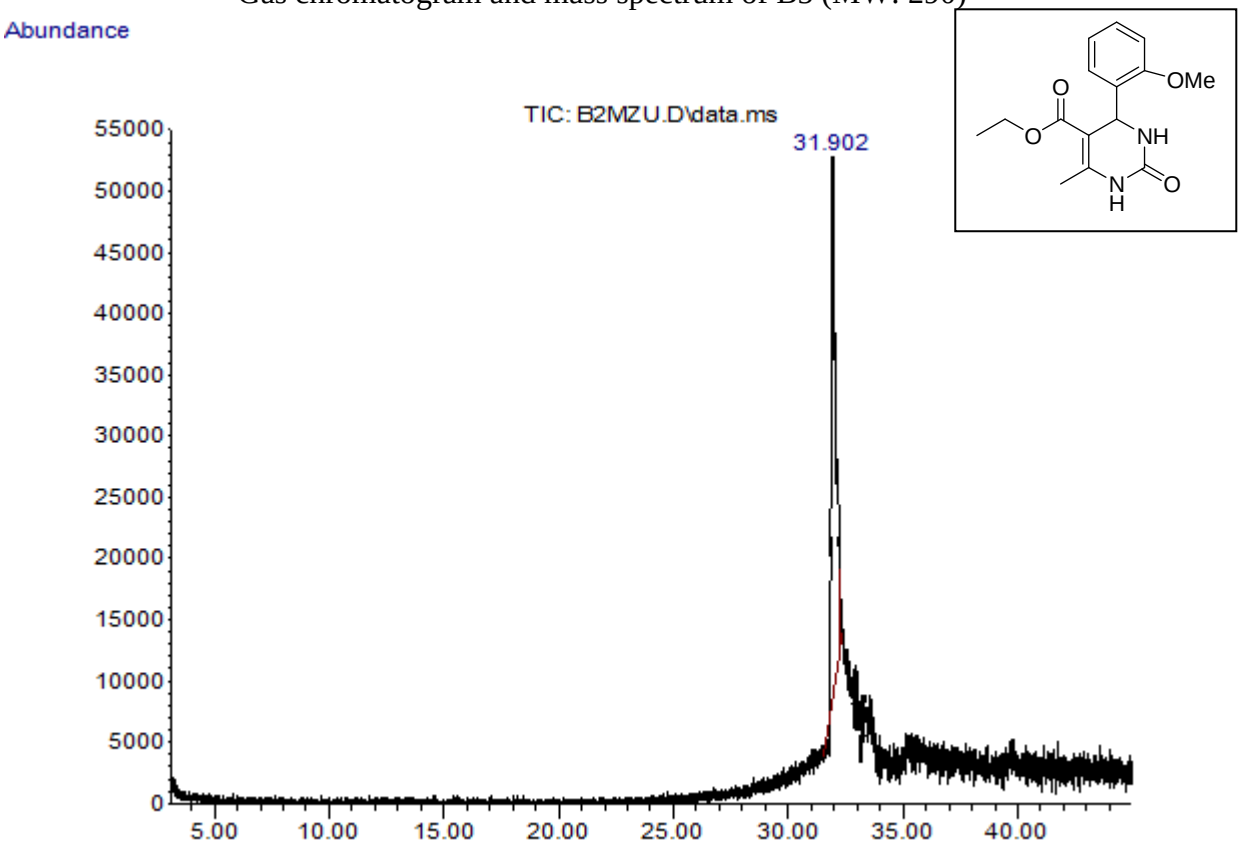
Gas chromatogram and mass spectrum of B4 (MW: 290)

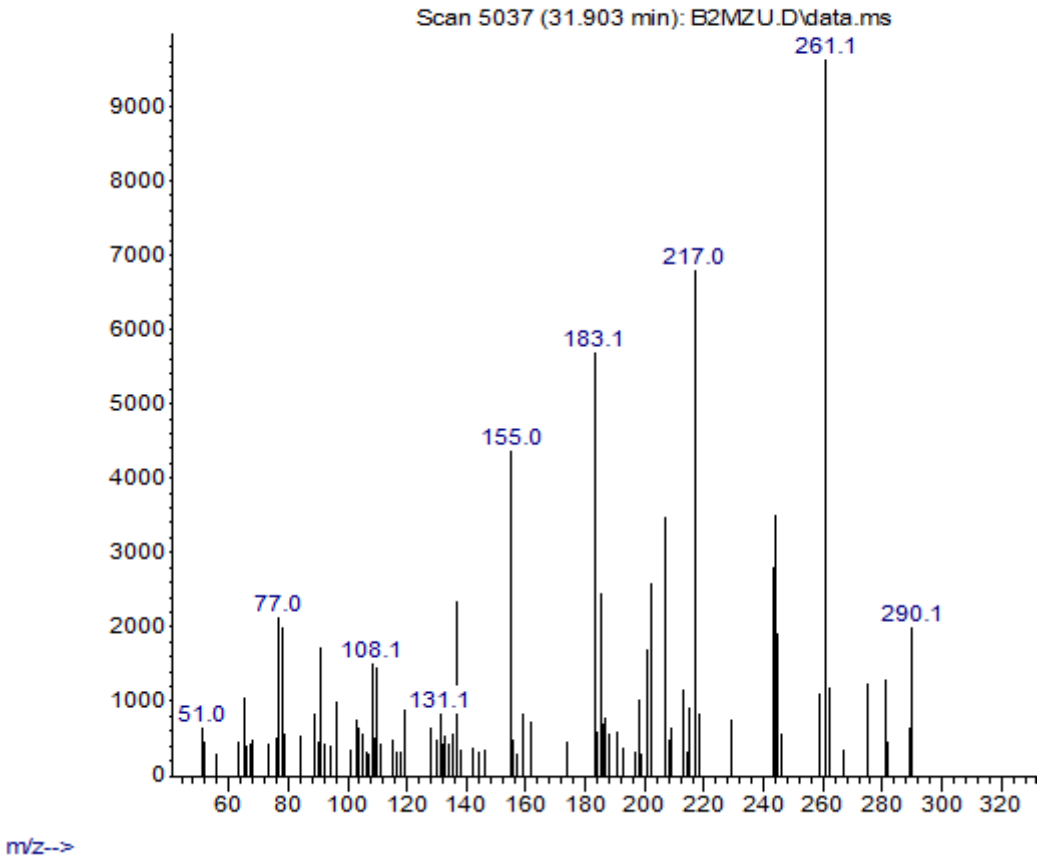




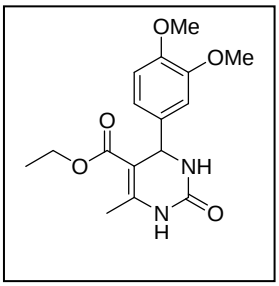


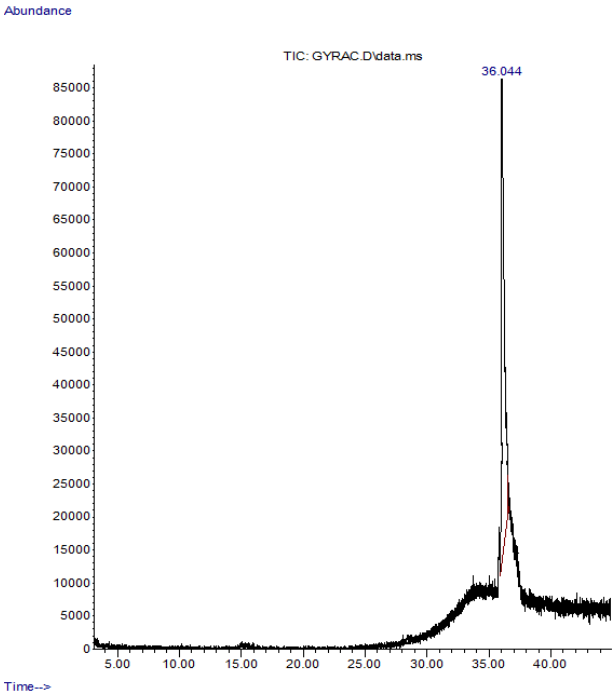
Gas chromatogram and mass spectrum of B5 (MW: 290)

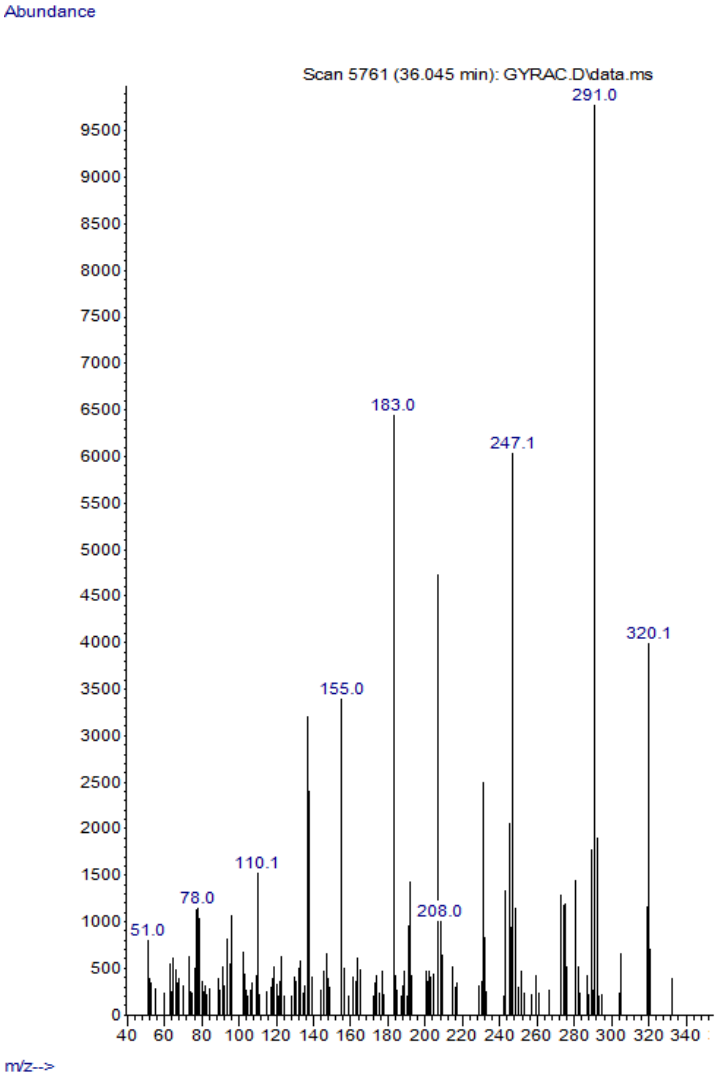




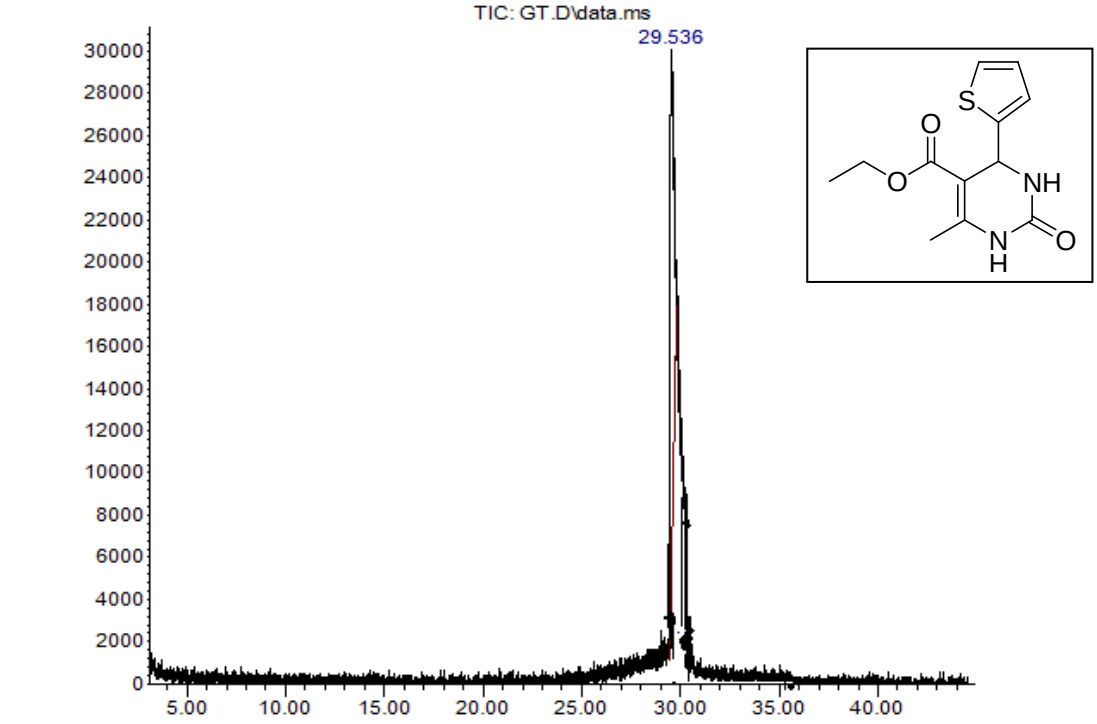
Gas chromatogram and mass spectrum of B6 (MW: 320)

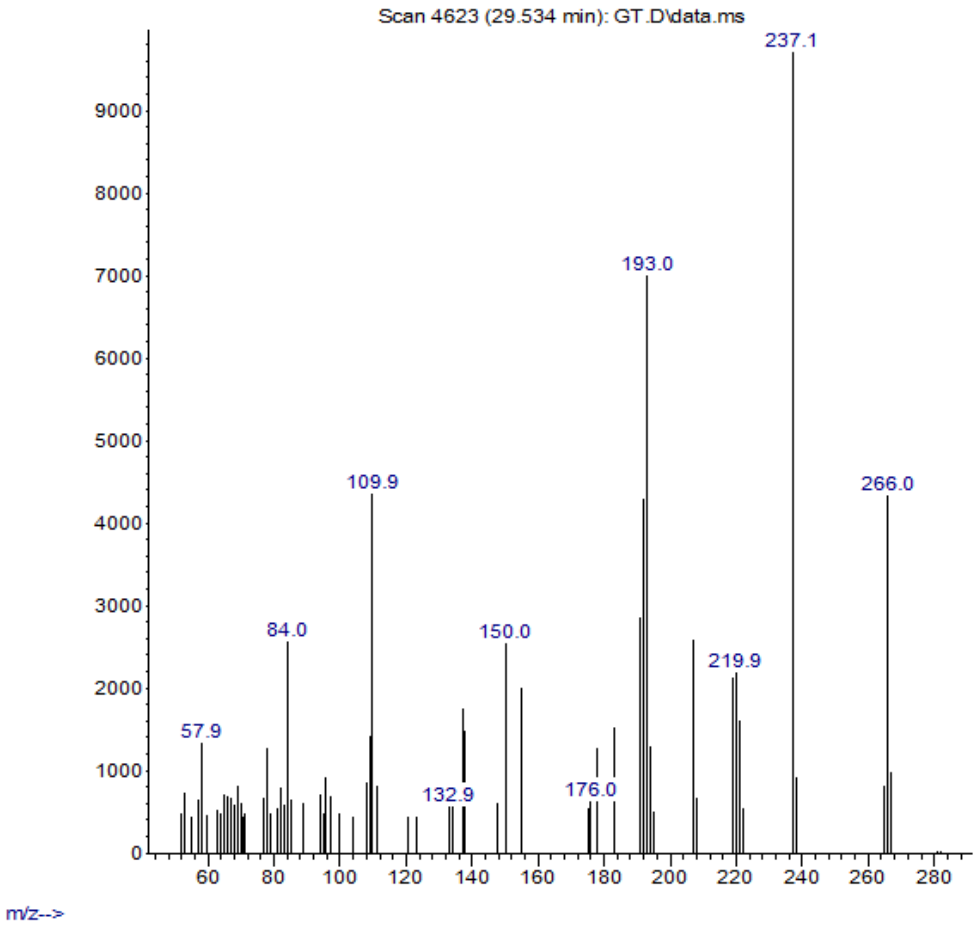


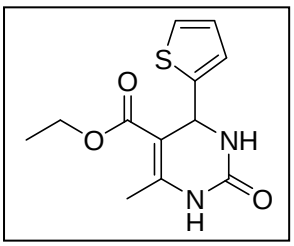


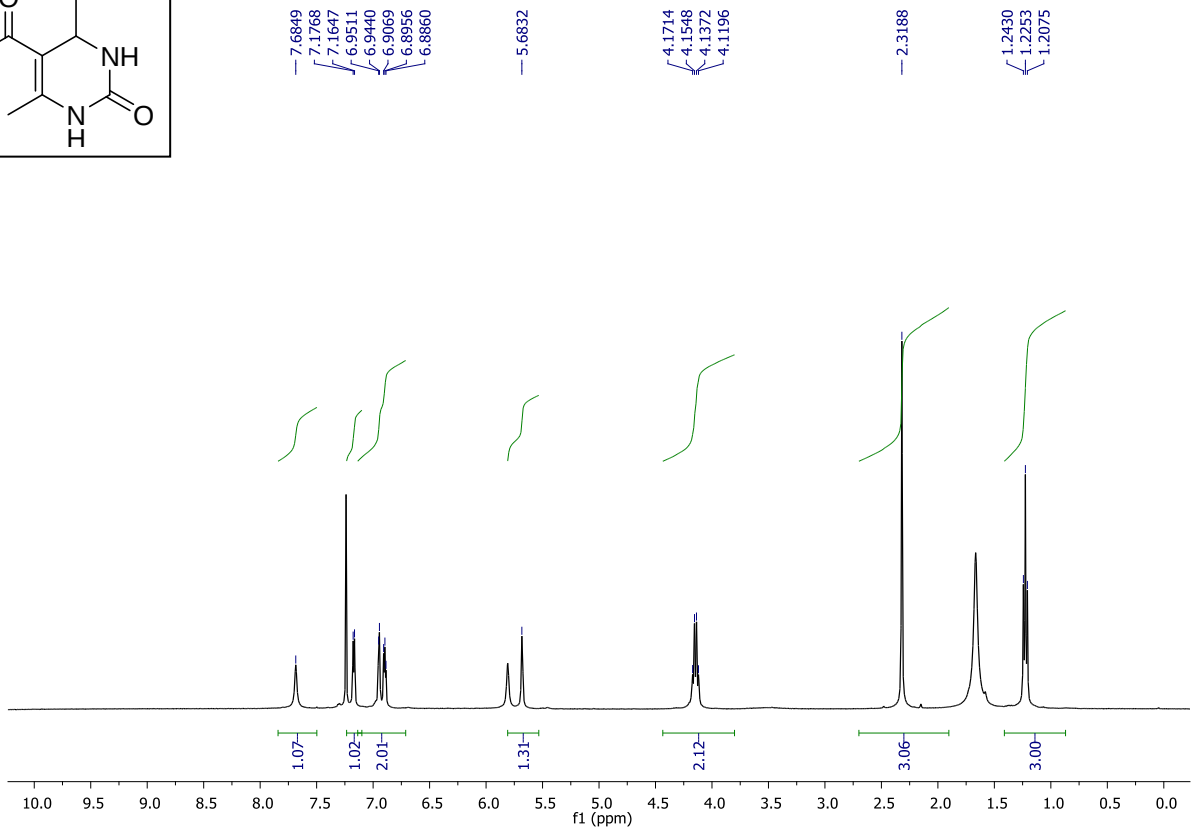


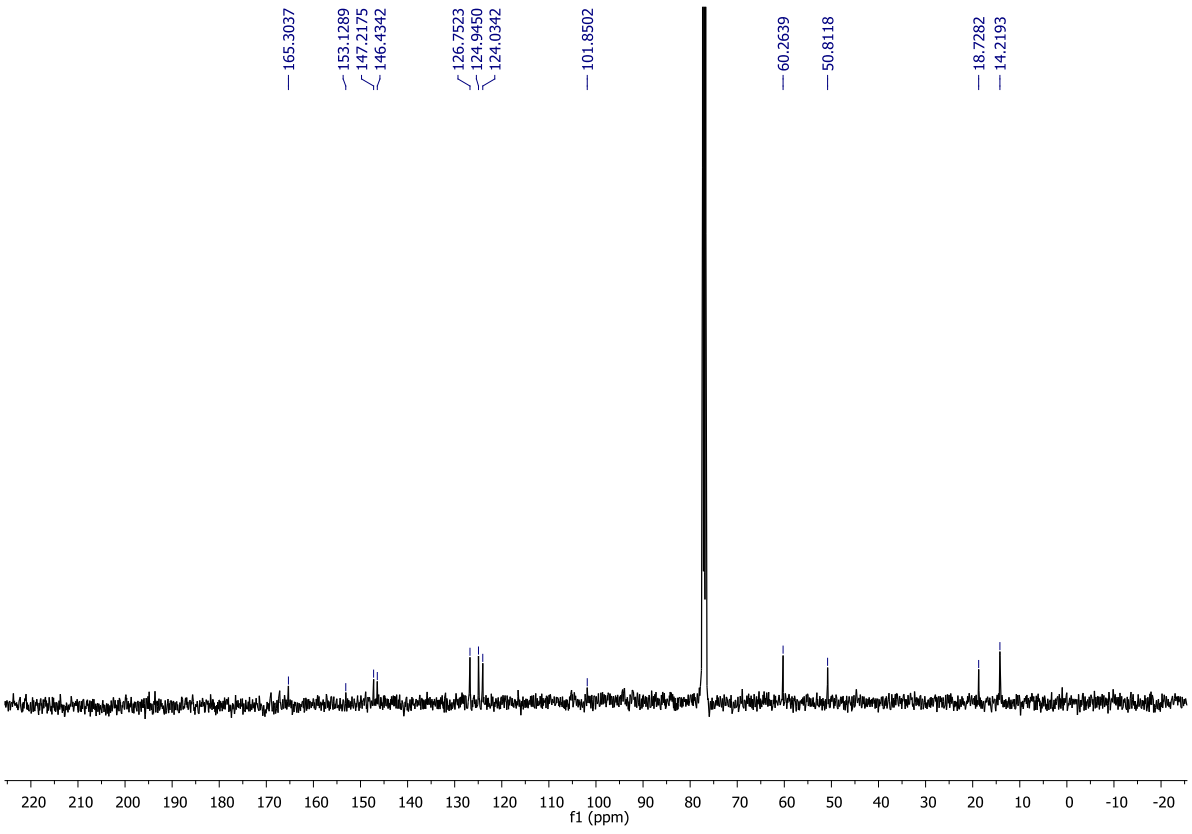
Gas chromatogram and mass spectrum of B7 (MW: 266)



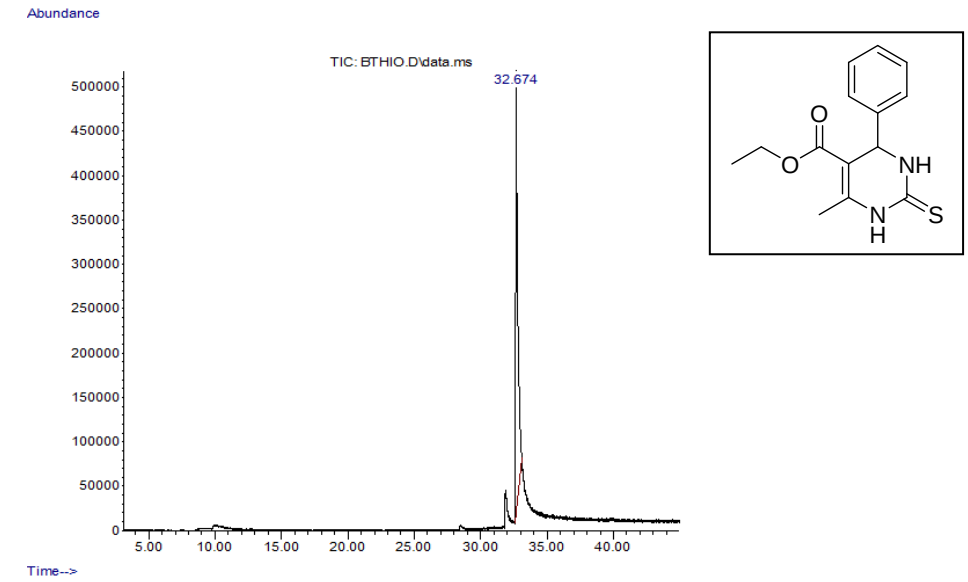


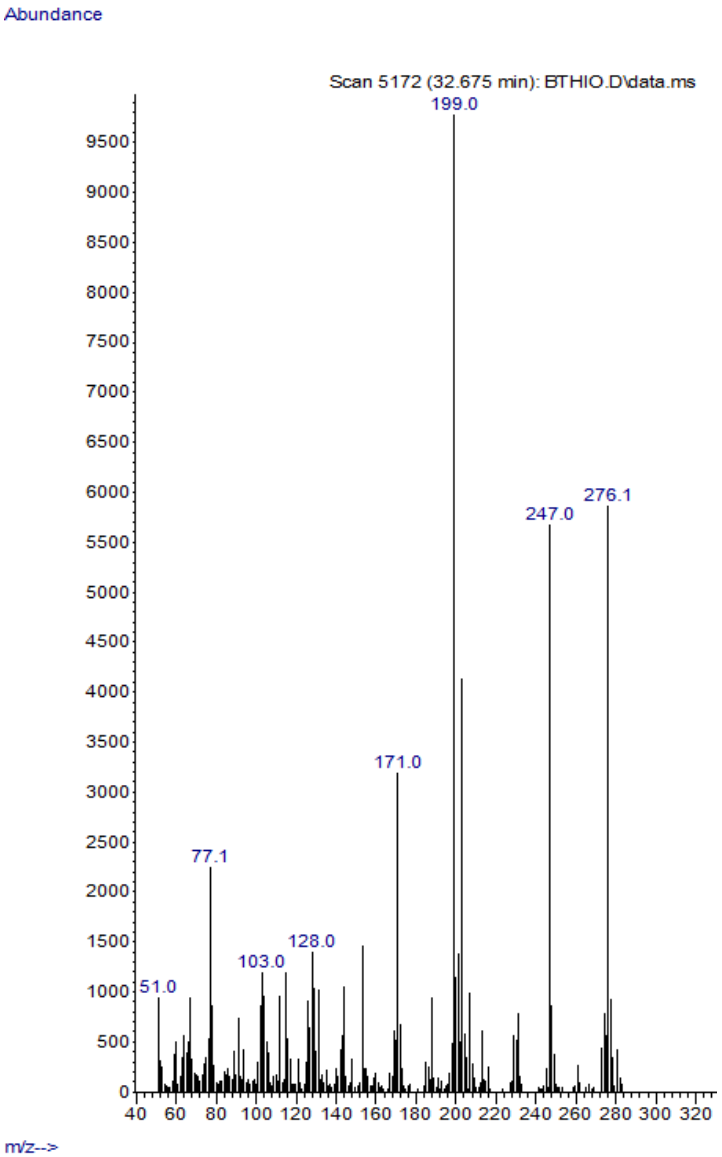

S
O
O
NH
N
H
O

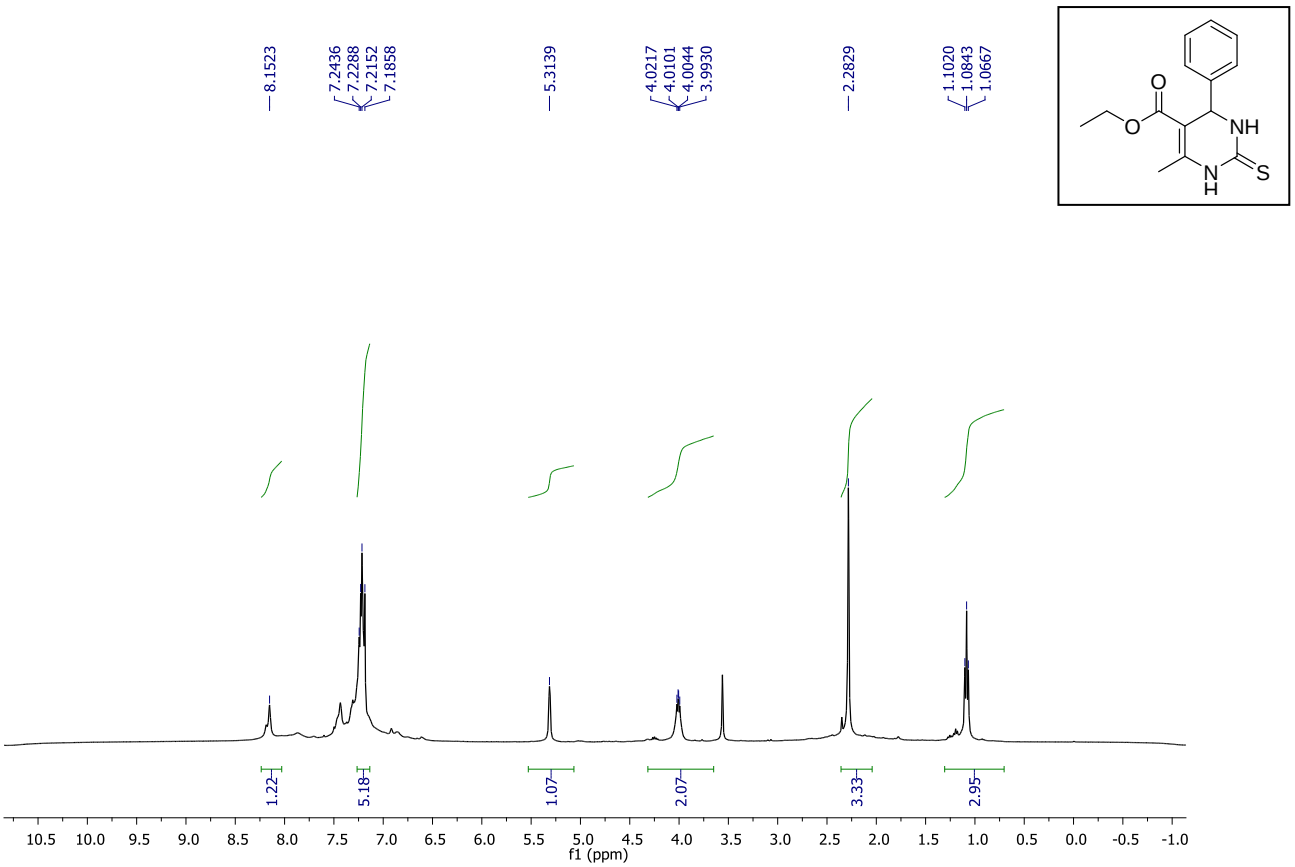

7.6849
7.1768
7.1647
6.9511
6.9440
6.9069
6.8956
6.8860
5.6832
4.1714
4.1548
4.1372
4.1196
2.3188
1.2430
1.2253
1.2075
1.07
1.02
2.01
1.31
2.12
3.06
3.00
f1 (ppm)

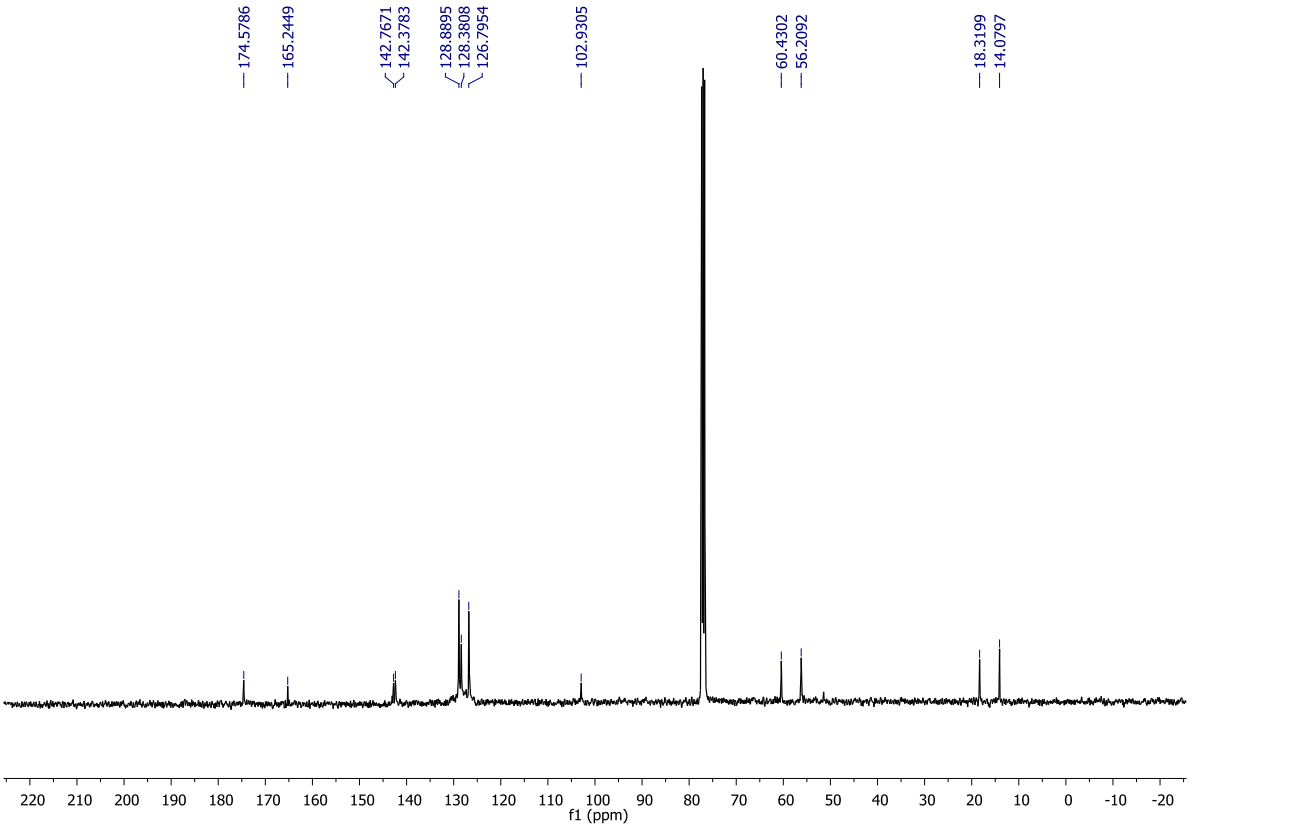

165.3037
153.1289
147.2175
146.4342
126.7523
124.9450
124.0342
101.8502
60.2639
50.8118
18.7282
14.2193
f1 (ppm)

Gas chromatogram and mass spectrum of B8 (MW: 276)

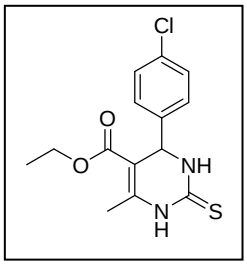


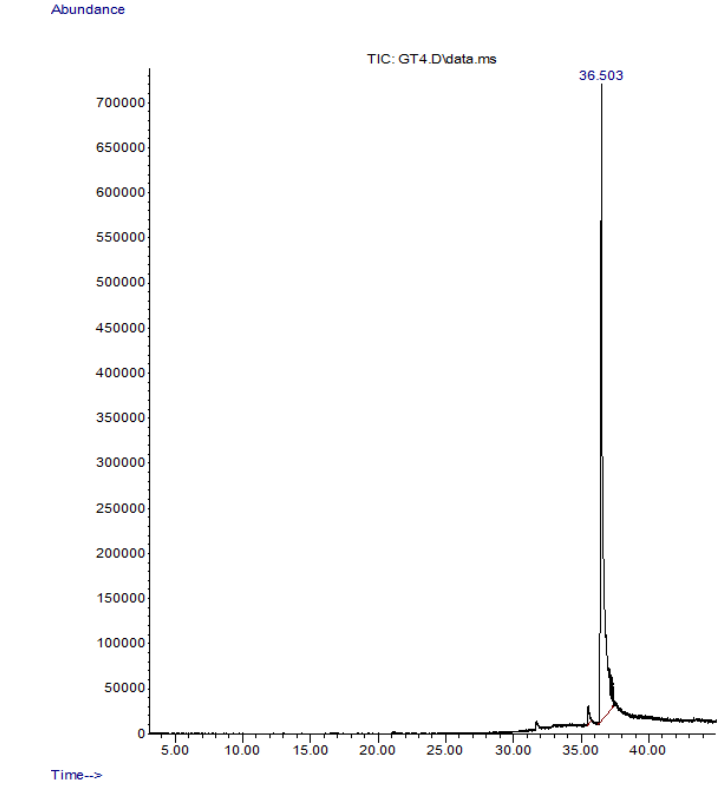


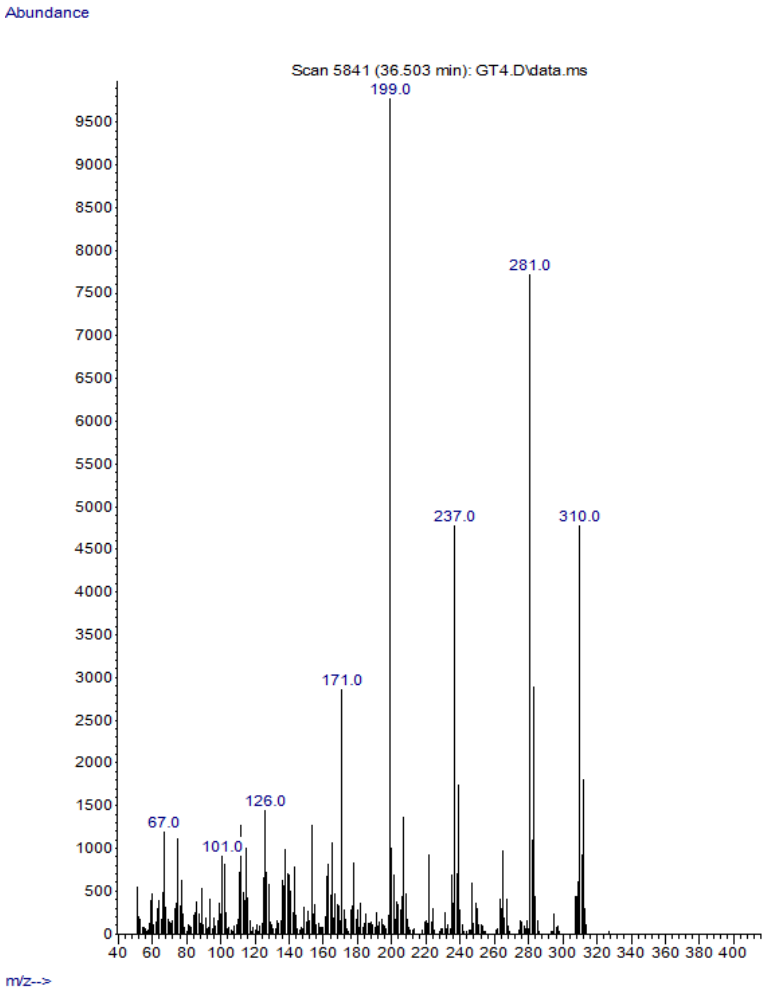

8.1523
7.2436
7.2288
7.2152
7.1858
5.3139
4.0217
4.0101
4.0044
3.9930
2.2829
1.1020
1.0843
1.0667
O
O
NH
N
H
S
1.22
5.18
1.07
2.07
3.33
2.95
f1 (ppm)

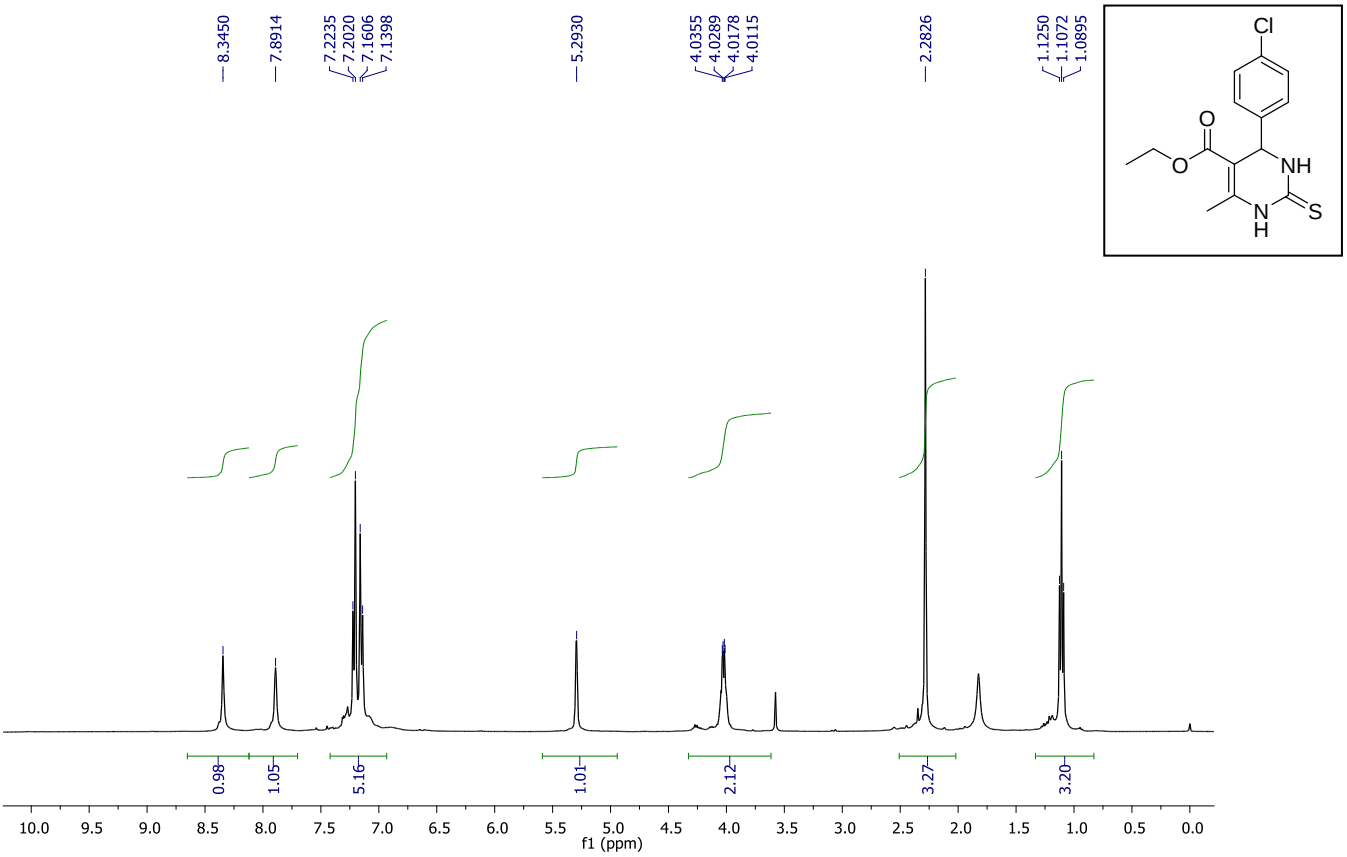

174.5786
165.2449
142.7671
142.3783
128.8895
128.3808
126.7954
102.9305
60.4302
56.2092
18.3199
14.0797
f1 (ppm)

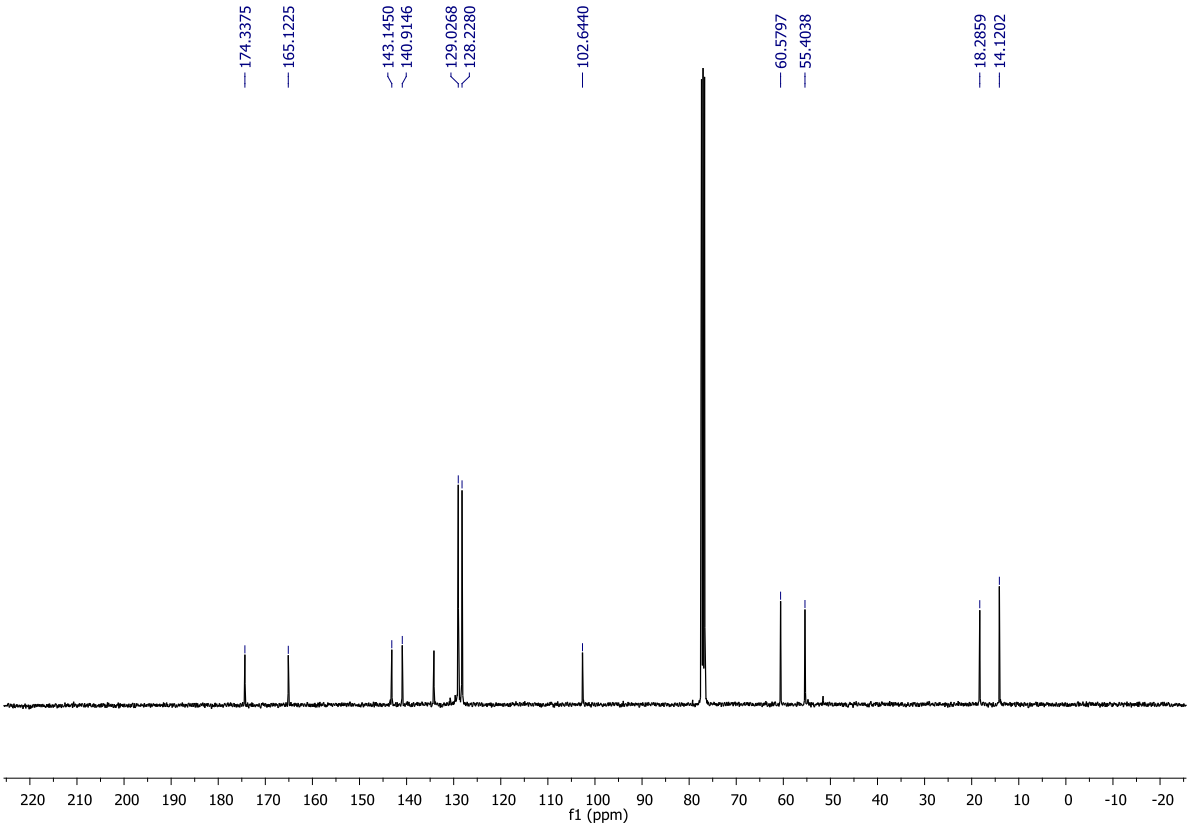
Gas chromatogram and mass spectrum of B9 (MW: 310)



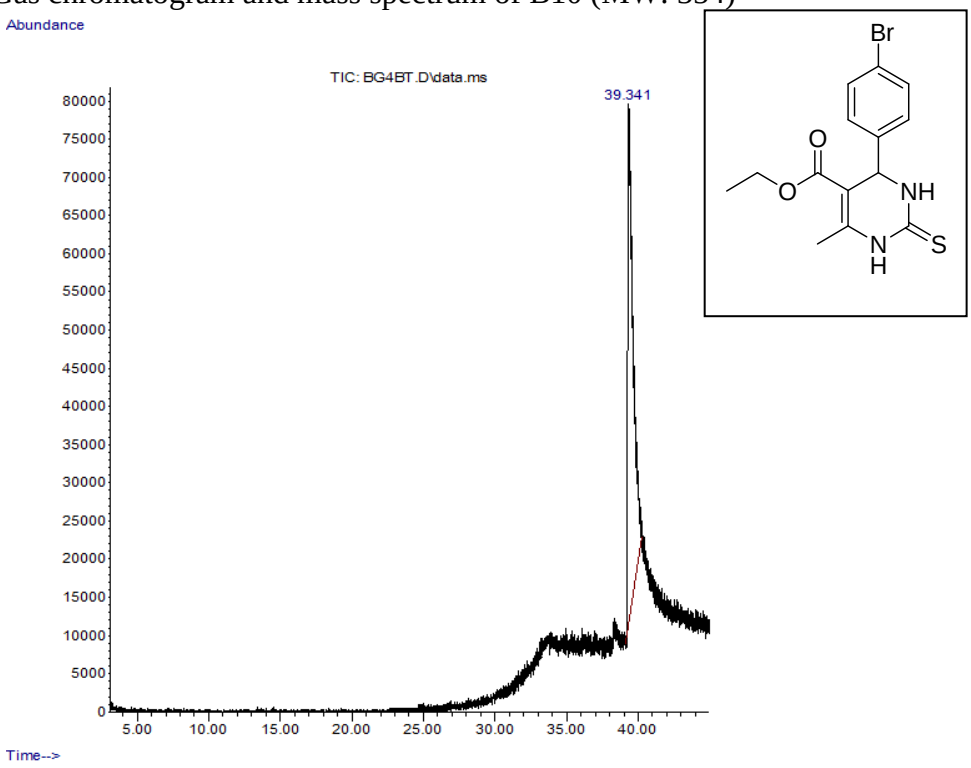


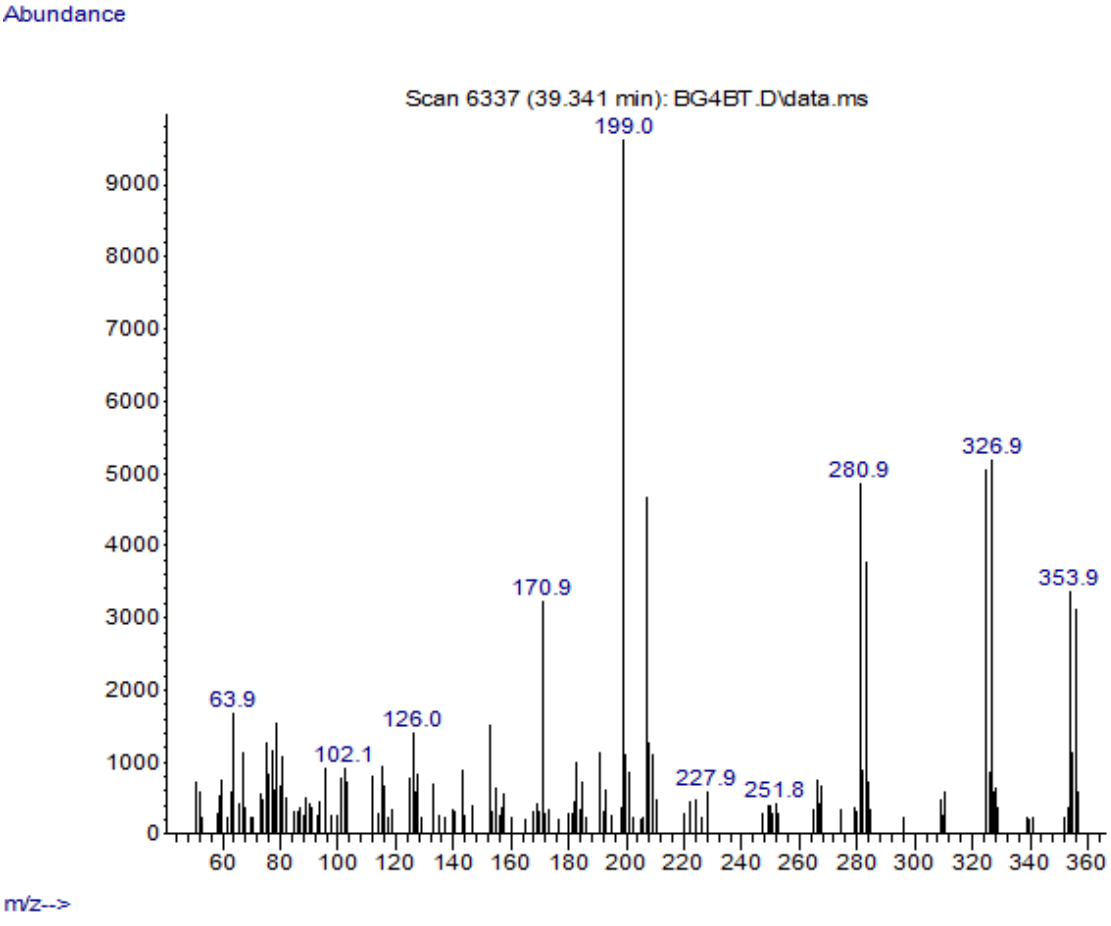



8.3450
7.8914
7.2235
7.2020
7.1606
7.1398
5.2930
4.0355
4.0289
4.0178
4.0115
2.2826
1.1250
1.1072
1.0895
Cl
O
O
NH
N
H
S
0.98
1.05
5.16
1.01
2.12
3.27
3.20
f1 (ppm)

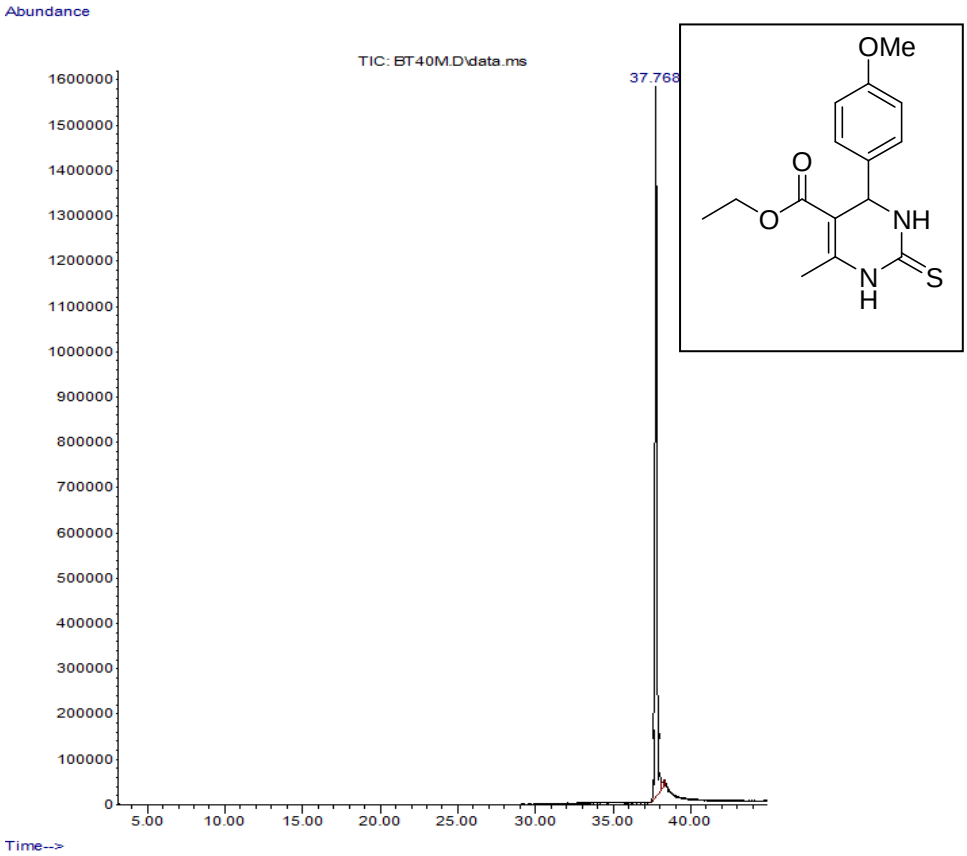

174.3375
165.1225
143.1450
140.9146
129.0268
128.2280
102.6440
60.5797
55.4038
18.2859
14.1202
f1 (ppm)

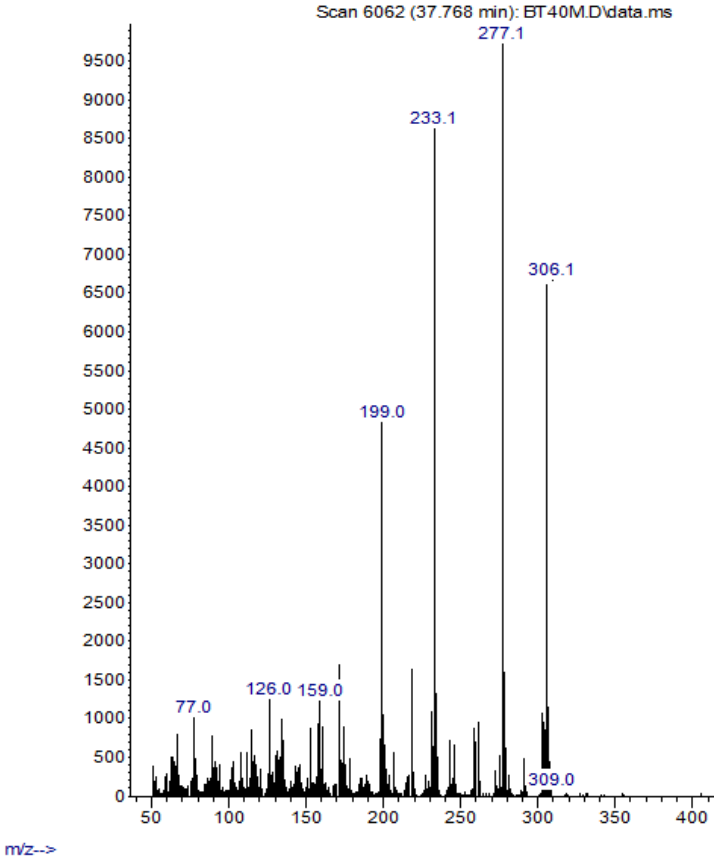
Gas chromatogram and mass spectrum of B10 (MW: 354)



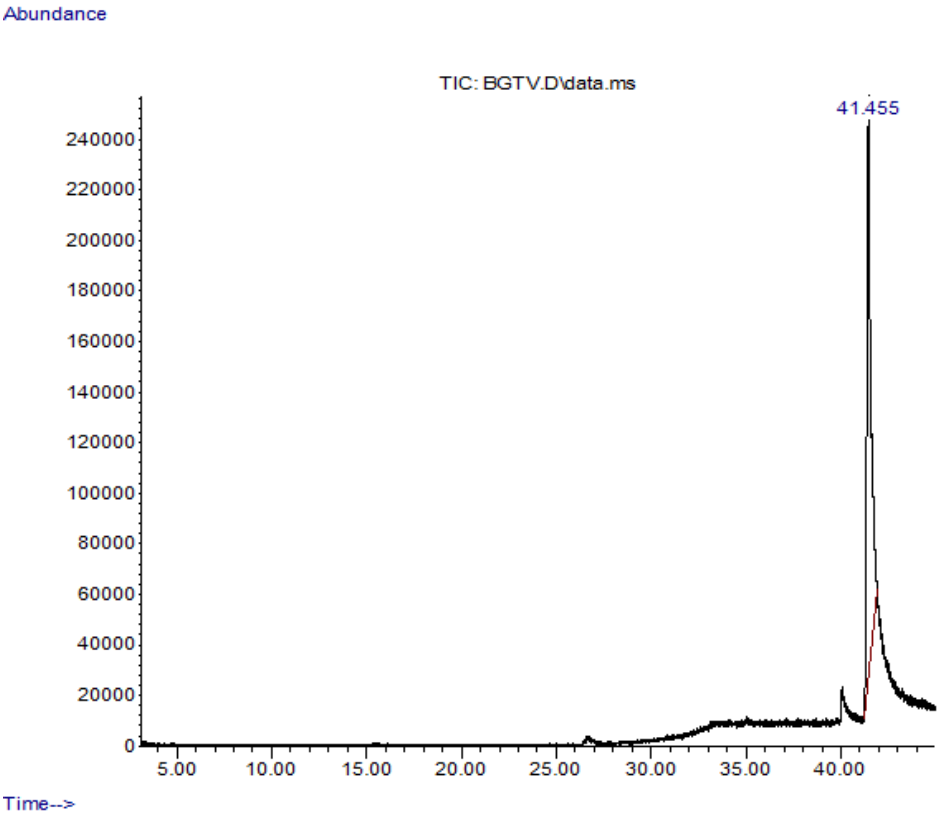


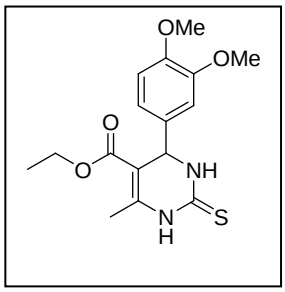
Gas chromatogram and mass spectrum of B6 (MW: 306)

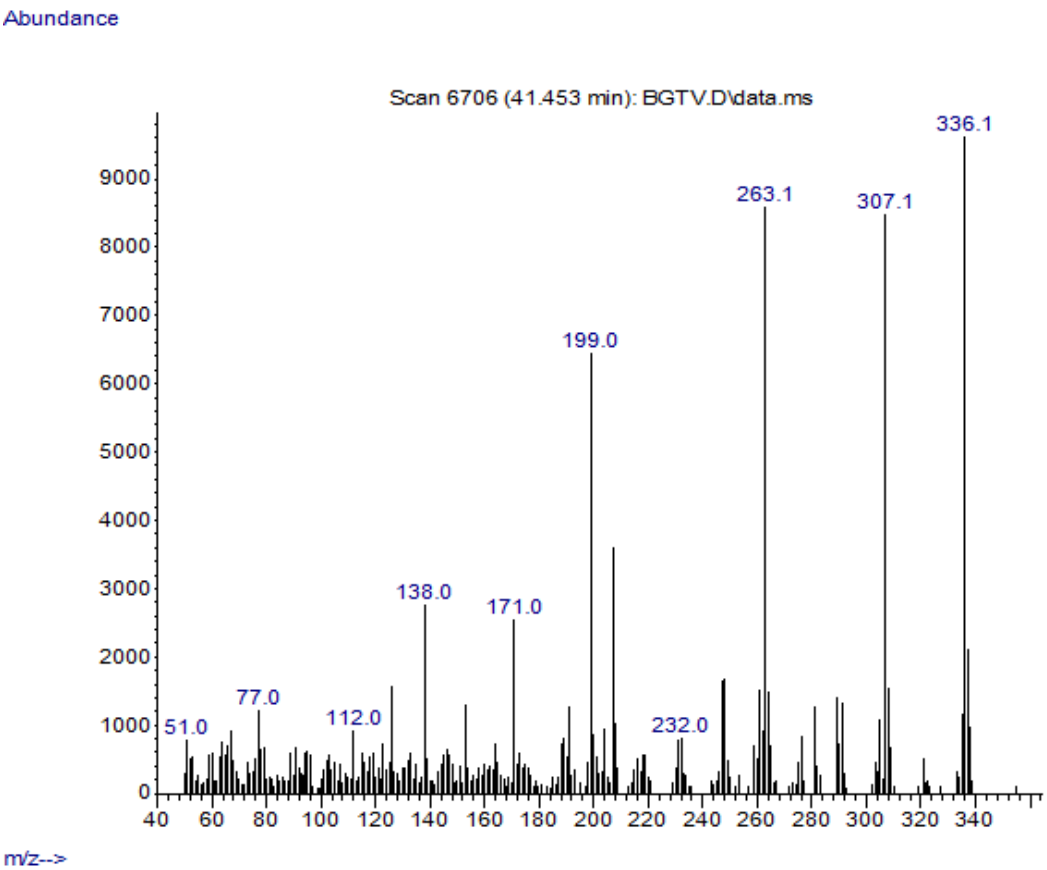




Gas chromatogram and mass spectrum of B6 (MW: 336)







References

1. N. Fu, Y. Yuan, Z. Cao, S. Wang, J. Wang, and C. Peppe, *Tetrahedron*, 2002, **58**, 4801-4807.
2. G. Aridoss and Y. T. Jeong, *Bull. Korean Chem. Soc.* 2010, **31**, 863-868.
3. J. S. Yadav, B. V. S. Reddy, K. B. Reddy, K. S. Raj and A. R. Prasad, *J. Chem. Soc., Perkin Trans.*, 2001, **1**, 1939-1941.
4. S. Kolb, O. Mondesert, M. Goddard, D. Jullien, B. O. Villoutreix, B. Ducommun, C. Garbay and E. Braud, *ChemMedChem*, 2009, **4**, 633-648.