Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

Multicomponent Diversity-Oriented Synthesis of Symmetrical and Unsymmetrical 1,4-dihydropyridines in Recyclable Glycine Nitrate Ionic ($GlyNO_3$) Liquid: A Mechanistic Insight Using Q-TOF, ESI-MS/MS

Rajesh Kumar[1][2] *Nitin H. Andhare,* [2] *Amit Shard,* [1] *Richa*[1] *and Arun K. Sinha*[*1][2][3]

[1] Natural Plant Products Division,
CSIR-Institute of Himalayan Bioresource Technology,
Palampur (H.P.)-176061, India
[2] Academy of Scientific and Innovative Research (AcSIR), New Delhi, India
[3] Medicinal and Process Chemistry Division, C.S.I.R.-Central Drug Research Institute Lucknow- 226031(U.P.), India, E Mail*: aksinha8@rediffmail.com

[*]Corresponding author. (A. K. Sinha)
E-mail addresses: aksinha08@rediffmail.com

Experimental Section:

Materials and instrumentation:

All reagents were obtained from commercial sources (Merck or Acros or HiMedia). The solvents used for isolation/purification of compounds were obtained from Merck and used without further purification. Melting points were determined using digital Barnstead Electrothermal 9100 apparatus and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75.4 MHz) NMR spectra were recorded on a Bruker Avance-300 spectrometer. TMS was used as internal reference for NMR. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. HRMS and ESI-MS/MS spectra were determined using Micromass Q-TOF Ultima spectrometer.

CEM Discover© focused microwave (2450 MHz, 300W) was used wherever mentioned. The temperature of reactions in microwave experiments was measured by an inbuilt infrared temperature probe that determined the temperature on the surface of reaction flask. The sensor is attached in a feedback loop with an on-board microprocessor to control the temperature rise rate. In the case of conventional heating, the temperature of reaction mixture was monitored by thermometer.

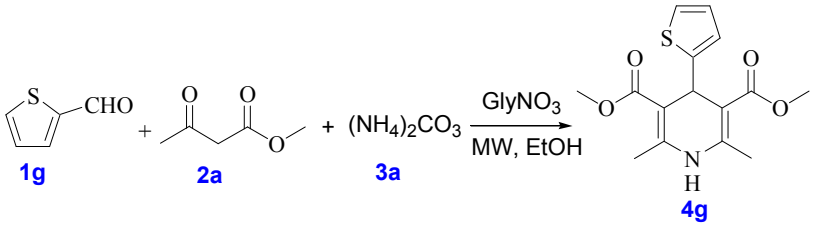
All amino acid based ionic liquids were synthesized according to reported method.[1]

---

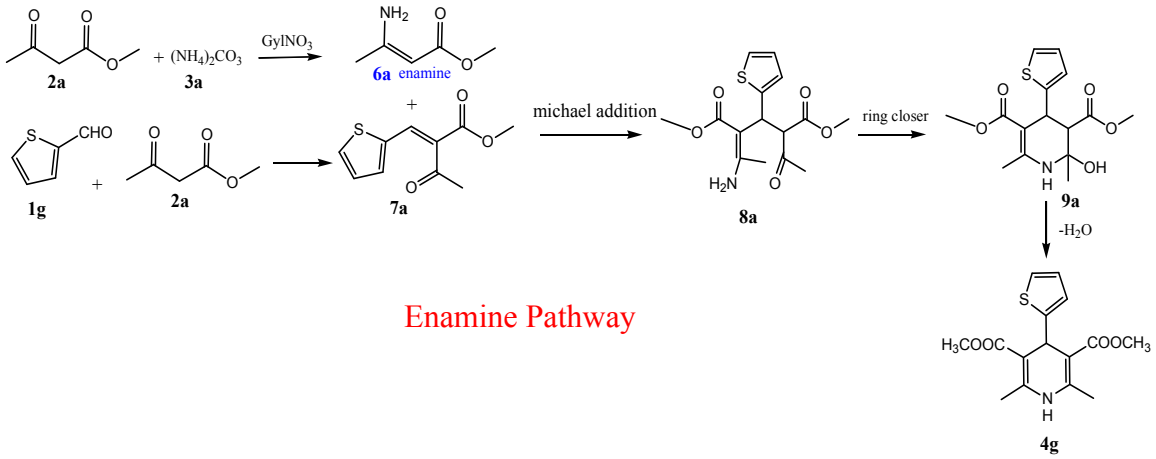
[1] G. H. Tao, L. He, N. Sun and Y. Kou, *Chem. Commun*., 2005, 3562-3564.

Plausible mechanism for the synthesis of symmetrical 1,4 DHPs:-

There are four plausible pathways i.e. i) enamine ii) diketone iii) dienamine and iv) imine for the synthesis of symmetrical 1,4-DHPs (scheme S1) as discuss below in scheme S2-S5.

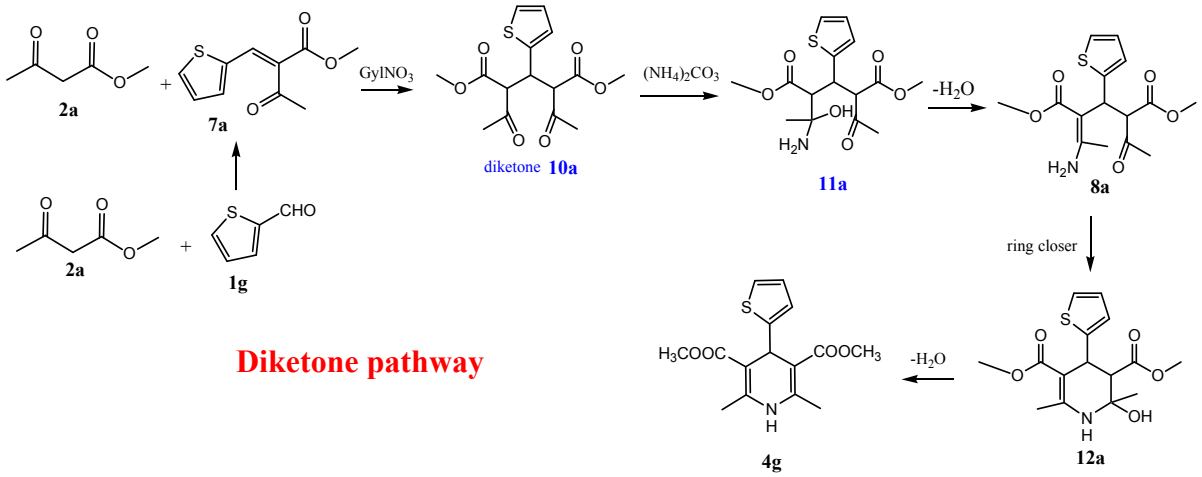


SchemeS1 The one-pot three component Hantzsch reaction.



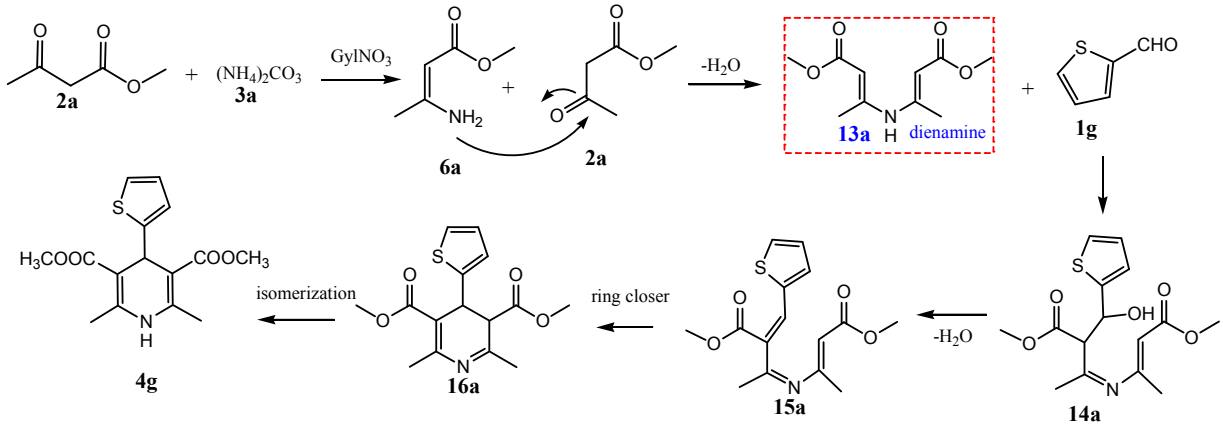
Scheme S2: Enamine pathway for the synthesis of 1,4 DHPs

In enamine pathway first one mole of methylacetoacetate (**2a**) react with ammonium carbonate (**3a**) to form enamine (**6a**) which is further react with *in situ* generated Knoevenagel product (**7a**) by the condensation of thiophene-2-carboxyaldehyde (**1g**) and second mole of methylacetoacetate (**2a**) to form adduct (**8a**) which further undergoes ring closer to form (**9a**) followed by dehydration to form 1,4-DHPs as a desired product (**4g**) as shown in scheme S2.



Scheme S3: Diketone pathway for the synthesis of 1, 4 DHPs

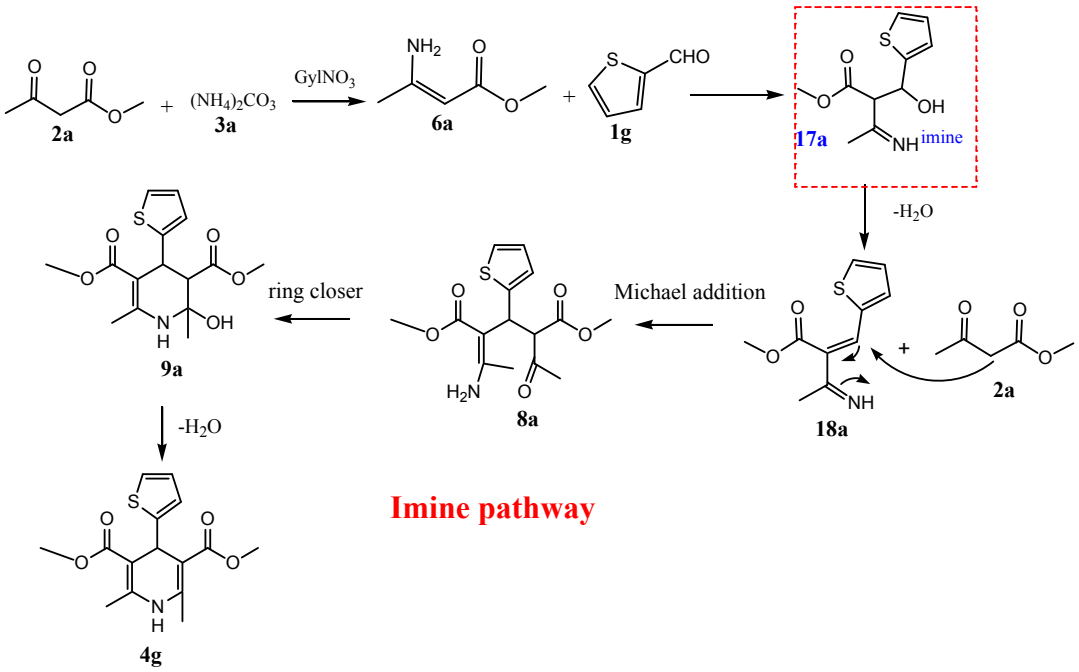
In diketone pathway *in situ* generated Knoevenagel adduct (**7a**) formed by the condensation of thiophene-2-carboxyaldehyde (**1g**) and one mole of methylacetoacetate (**2a**) react with second mole of methylacetoacetate (**2a**) to formed diketone intermediate (**10a**) (Scheme S3) which is further react with ammonium carbonate (**3a**) to formed adduct (**11a**). This adduct then under goes dehydration and ring closer process via intermediate (**8a**) and (**12a**) to form desired product (**4g**).



Scheme S4: Dienamine pathway for the synthesis of 1,4 DHPs

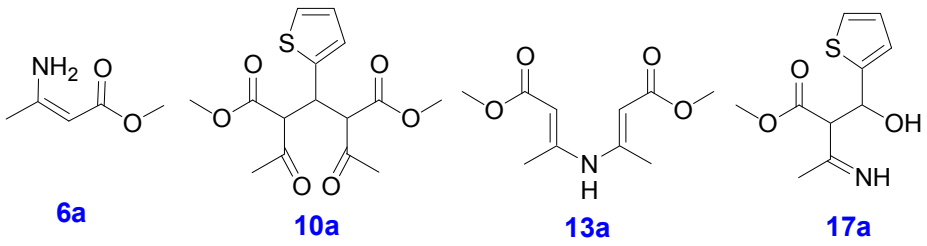
In dienamine pathway first one mole of methylacetoacetate (**2a**) react with ammonium carbonate (**3a**) to form enamine (**6a**) which is further react with second molecules of methylacetoacetate (**2a**) to formed dienamine intermediate (**13a**) (Scheme S4) then it react with thiophene-2-carboxyaldehyde (**1g**) to formed adduct (1**4a**). The adduct (**14a**)

then under goes dehydration, ring closer, isomerization process *via* intermediate (**15a**) and (**16a**) to form desired product (**4g**).



Scheme 5: Imine pathway for the synthesis of 1,4 DHPs.

In imine pathway first one mole of methylacetoacetate (**2a**) react with ammonium carbonate (**3a**) to form enamine (**6a**) which is further react with thiophene-2-carboxyaldehyde (**1g**) to form imine intermediate (**17a**) (Scheme S5). This intermediate further react with second mole of methylacetoacetate (**2a**) via Michael addition to form adduct (**8a**) which further under goes ring closer and dehydrative process via intermediate (**9a**) to form 1,4 –DHPs as desired product.



Scheme S6. Key intermediates of four plausible pathways.

Therefore in order to prove the exact mechanistic pathway among four plausible pathways we preferably used Q-TOF electrospray ionization mass spectrometry (ESI-MS) technique for studying reaction intermediate because of its ability to "fish" ionic or ionized intermediates directly from reaction solutions into the gas phase, with high speed and sensitivity.

Therefore, we performed Q-TOF ESI (+ve) MS studies on aliquots of samples withdrawn after 10 min from $GlyNO_3$ catalyzed reaction of **1g**, **2a** and **3a** (Scheme 1) at capillary voltage (3100 V), cone voltage (25 V), dissolution temp. (200°C) and source temperature (80 °C).

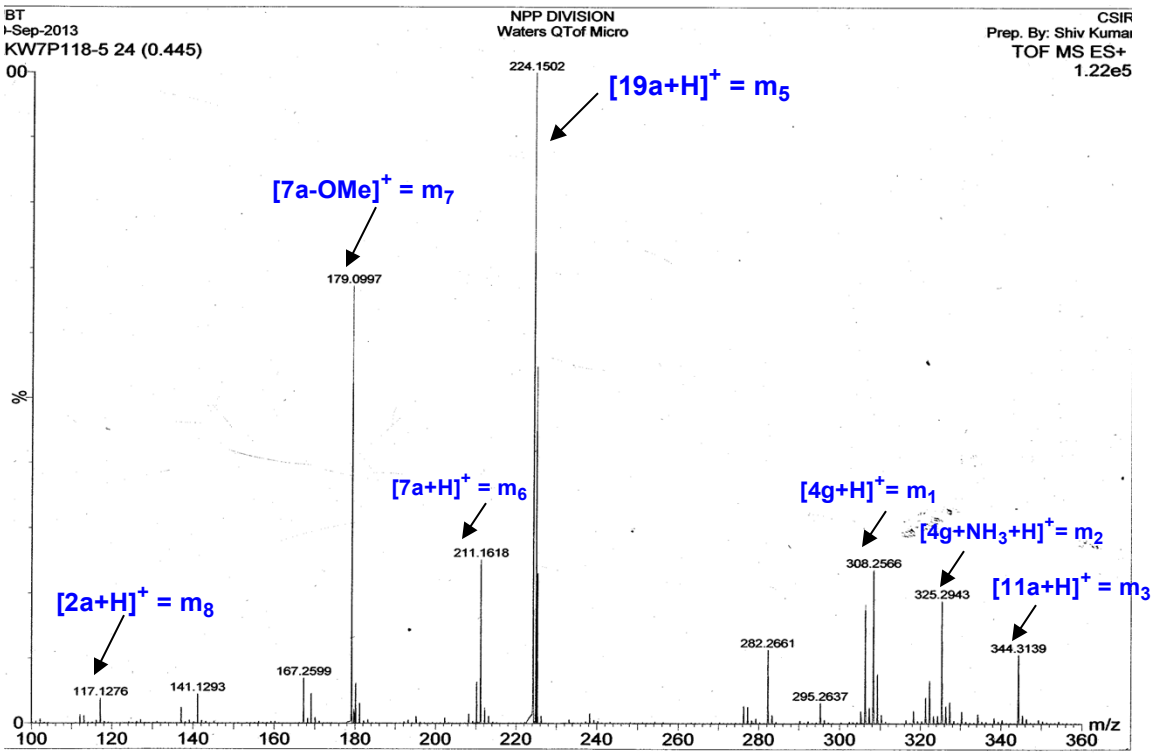


Figure S1: Full scan TIC of Q-TOF, ESI (+) MS of sample withdraws after 10 min for three-component Hantzsch reaction of **1g**, **2a** and **3a** catalyzed by $GlyNO_3$.

The total ion chromatogram (TIC) revealed the presence of ions at m/z 308.26 (m_1), 325.29 (m_2), 344.31 (m_3), 327.31 (m_4),(Figure S2) 224.15 (m_5), 211.16 (m_6), 179.09 (m_7), and 117.13 (m_8) corresponding to $[4g + H]^+$, $[4g + NH_3 + H]^+$, $[11a + H]^+$, $[10a + H]^+$, $[19a + H]^+$, $[7a + H]^+$, $[7a - OMe]^+$ and $[2a + H]^+$ respectively. The presence of characteristic peaks $m_3 = [11a + H]^+$, $m_4 = [10a + H]^+$ and $m_6 = [7a + H]^+$ in figure S1

revealed the possibility of diketone pathway (Scheme S3) and absence of key intermediate **6a**, **13a** and **17a** (Scheme S6) ruled out the possibility of enamine, dienamine and imine pathways.

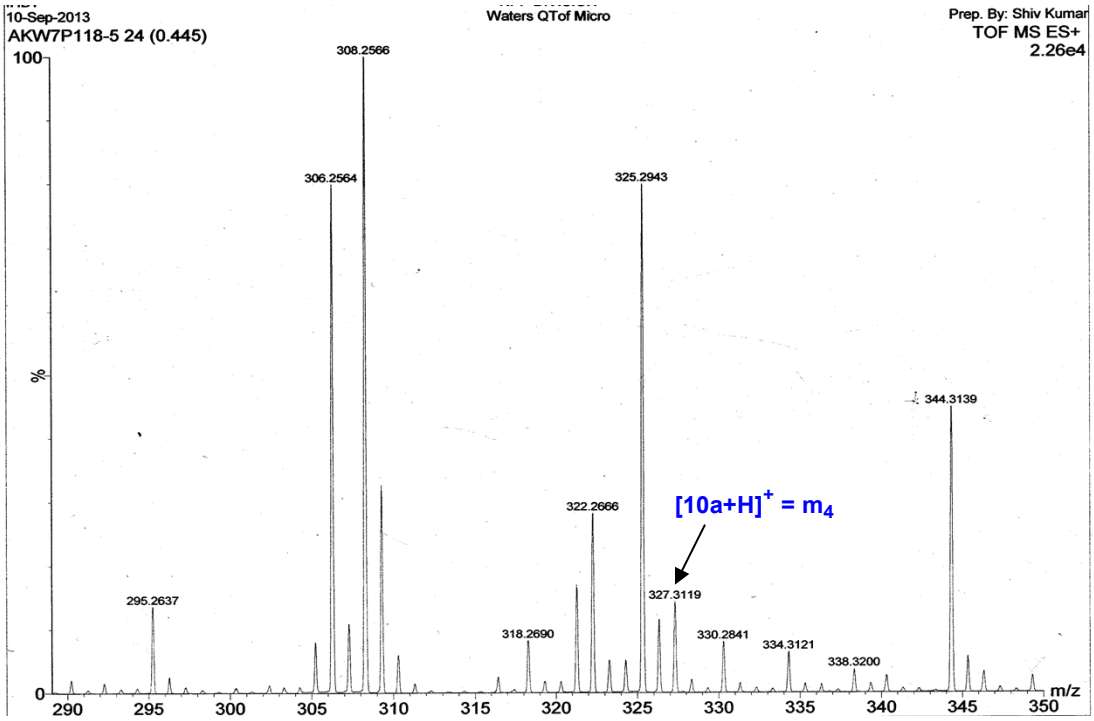


Figure S2: Expansion of figure S1 from m/z 290-350.

For further structure elucidation in context of diketone pathway and product formation, tandem MS/MS experiments were carried out for few selected ions observed in TIC (Figure S1) at *m/z* 308.17 = m_1, 325.39 = m_2, 344.31 = m_3 and 344.31 = m_4. The MS/MS or MS^2 spectra derived from the ion of *m/z* 308.17 = m_1 showed peak at *m/z* 276.14 and 224.15 assigned as $[4g - OCH_3]^+$ and $[4g - C_4H_3S + H]^+$ (Figure S3), confirmed the product formation. In case of m_2, the MS^2 spectra (Figure S4) exhibited the parent ion m_2 = $[4g + NH_3 + H]^+$ and daughter ion with *m/z* 308.17, 224.1464 corresponded to $[4g - NH_3 + H]^+$ and $[4g - C_4H_3S + H]^+$ respectively, confirmed the ammoniated adduct of 4g.

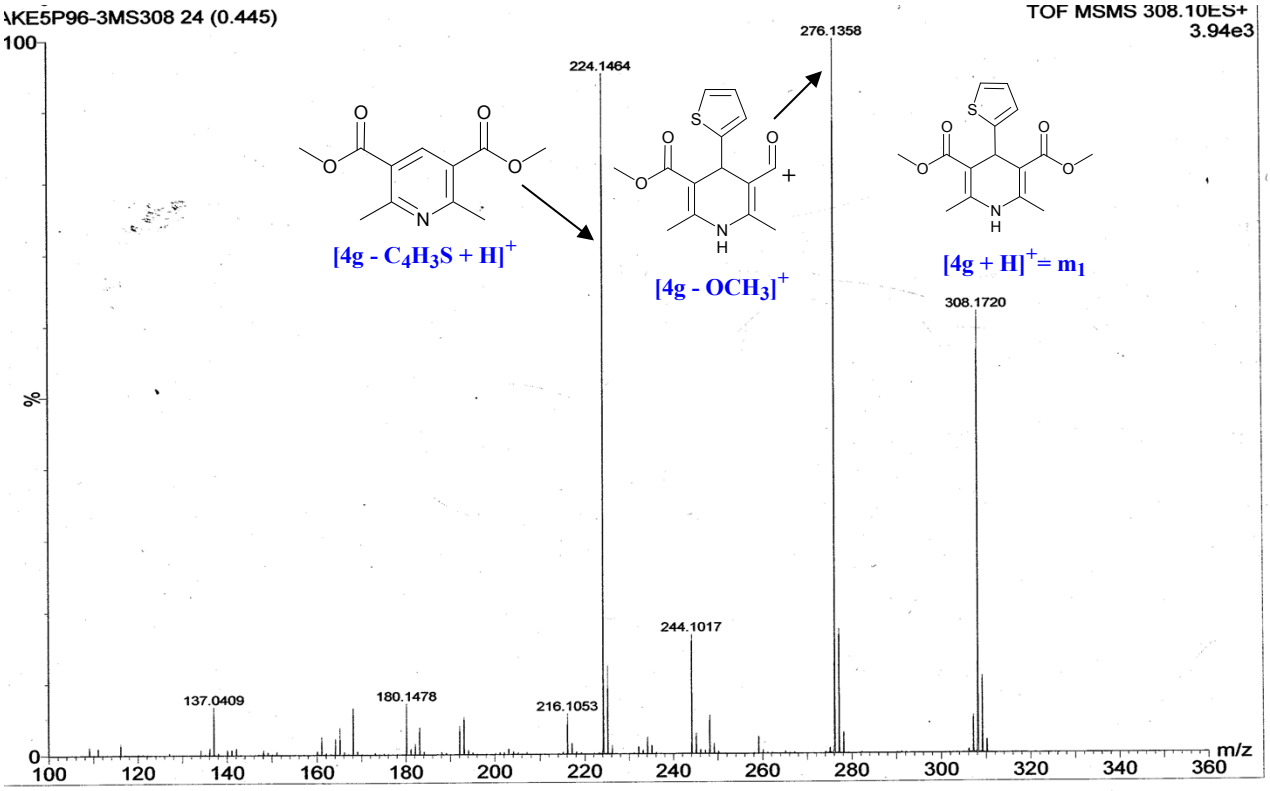


Figure S3: On line Q-TOF, ESI (+) MS/MS of peak (m_1) as shown in figure S1

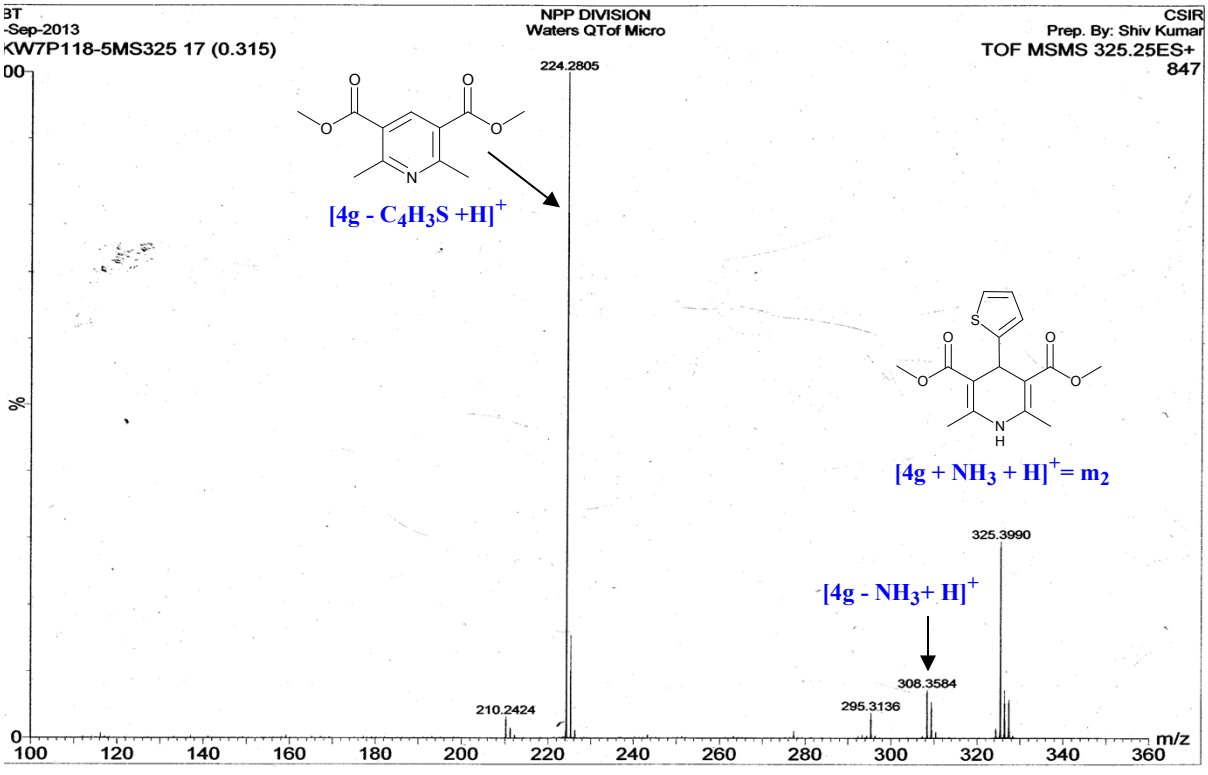


Figure S4: Full scan spectra of figure 4.

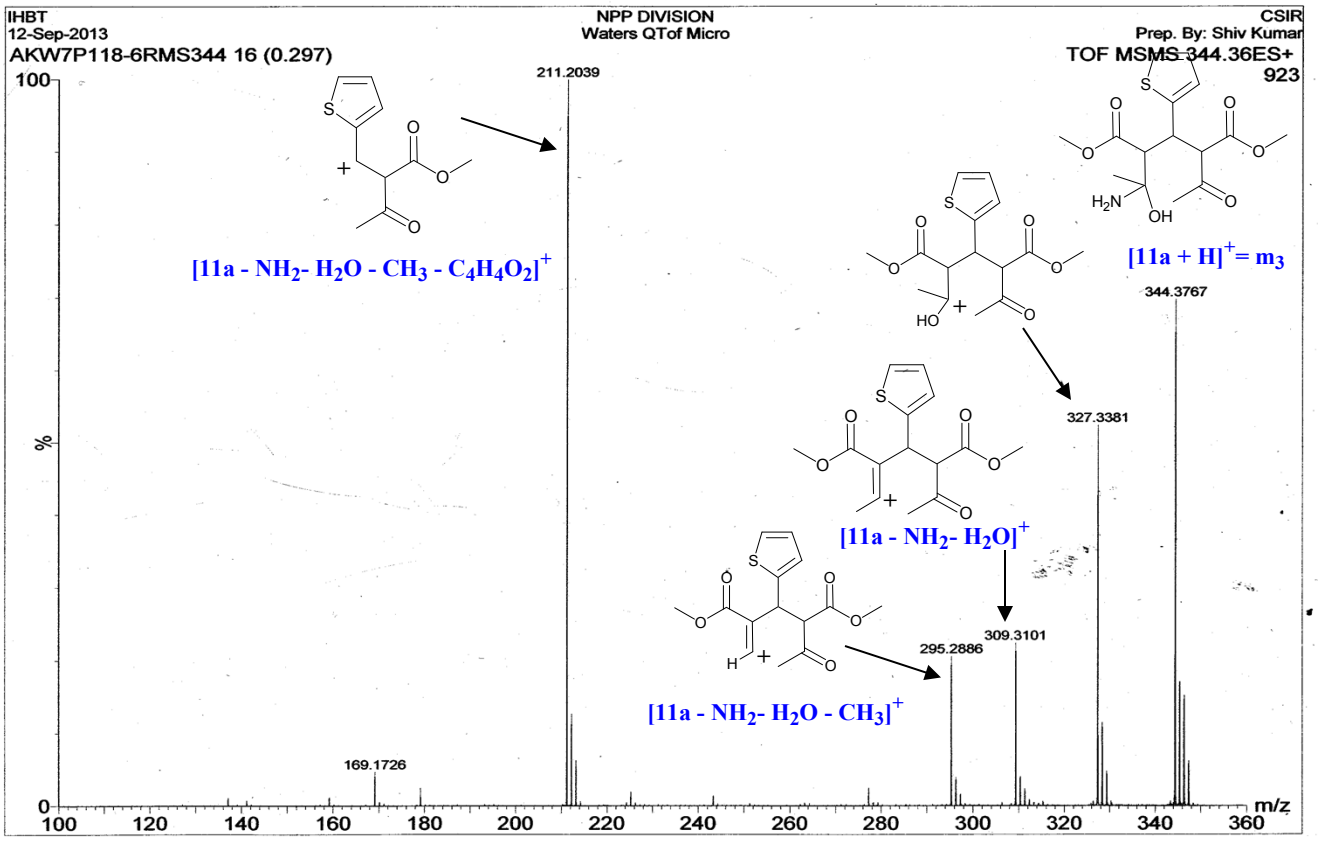


Figure S5: Full scan spectra of figure 5.

To further confirm the presence of intermediate (m_3) involved in diketone pathway, the MS^2 experiment was carried out of $m_3 = [11a + H]^+$ ion (Figure S5). The MS/MS spectra revealed the presence of ion with *m/z* 327.34, 309.31, 295.29 and 211.21 which are diagnose as $[11a - NH_2]^+$, $[11a - NH_2 - H_2O]^+$, $[11a - NH_2 - H_2O - CH_3]^+$ and $[11a - NH_2 - H_2O - CH_3 - C_4H_4O_2]^+$ respectively, confirmed the fragment of m_3 and their involvement in diketone pathway.

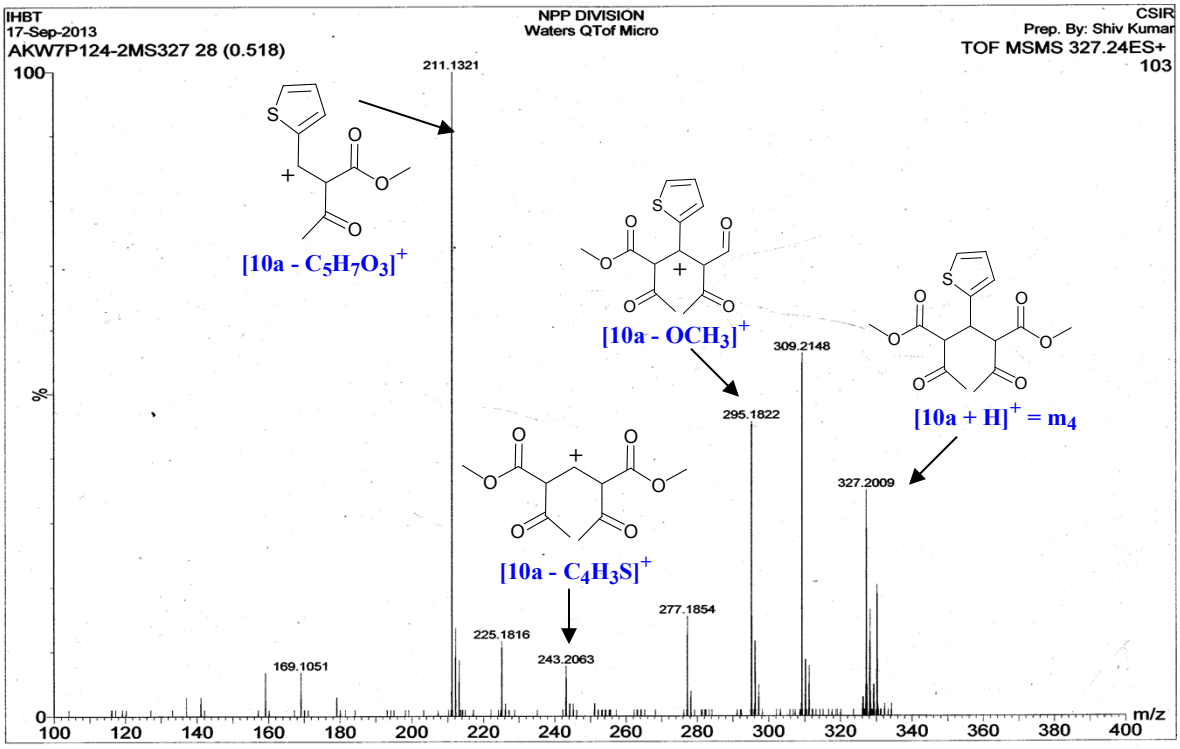


Figure S6: Full scan spectra of figure 6.

Most importantly, the key intermediate of diketone pathway m_4 = $[10a + H]^+$ was also ascertain by MS^2 experiment. The MS^2 spectra (Figure S6) exhibited the parent ion m_4 = $[10a + H]^+$ and daughter ions with *m/z* 295.18, 243.21 and 211.13 correspond to $[10a – OCH_3]^+$, $[10a – C_4H_3S]^+$ and $[10a – C_5H_7O_3]^+$ respectively, confirmed the fragments of ion m_4 and their involvement in diketone pathway.

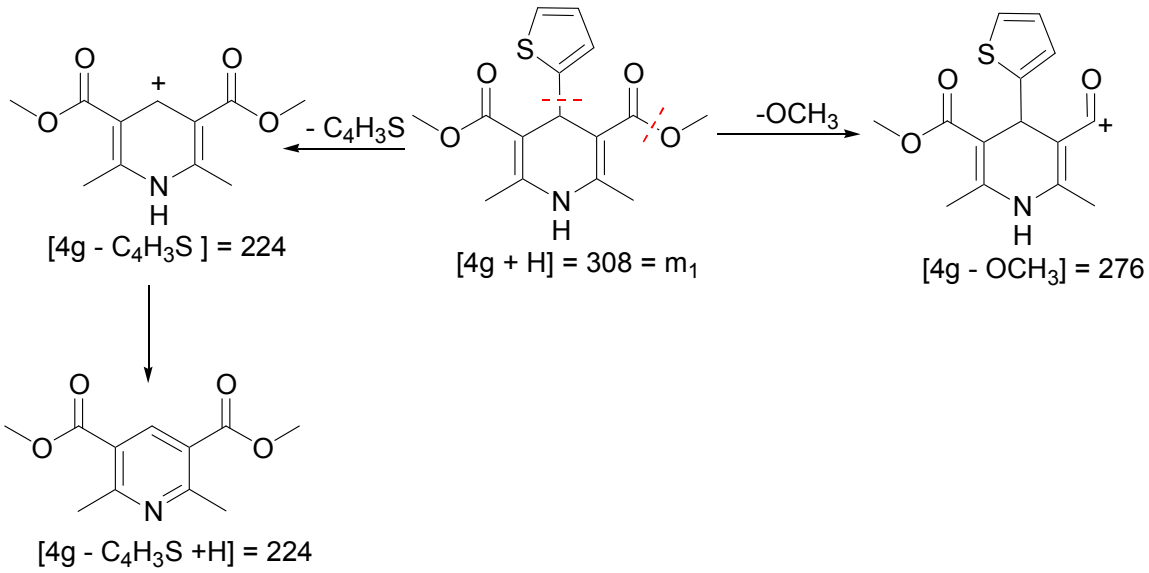


Figure S7 Fragmentation pattern of m/z $[4g + H]^+$ =308 = m_1

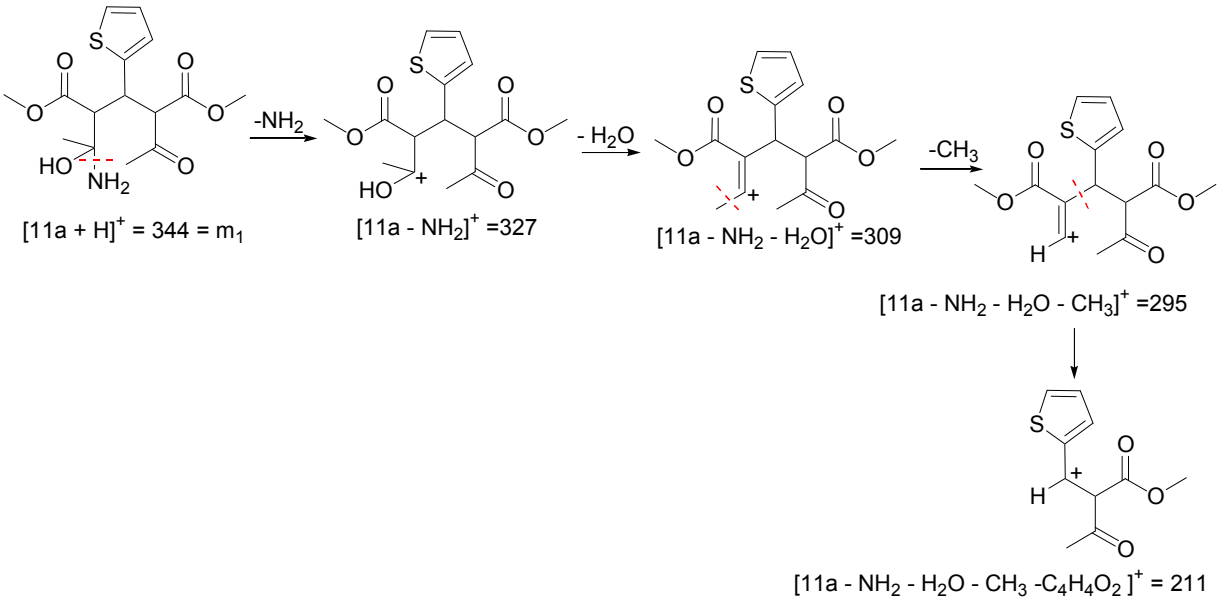


Figure S8 Fragmentation pattern of m/z $[11a + H]^+$ = 344 = m_3

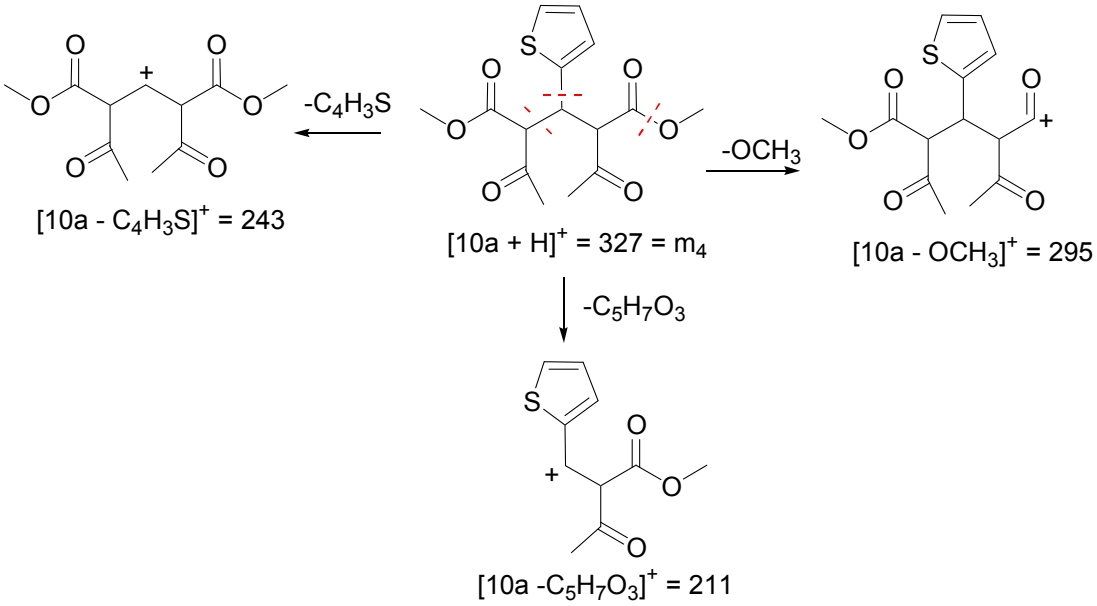
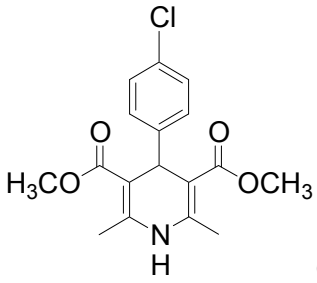


Figure S9 Fragmentation pattern of m/z $[10a + H]^+ = 327 = m_4$

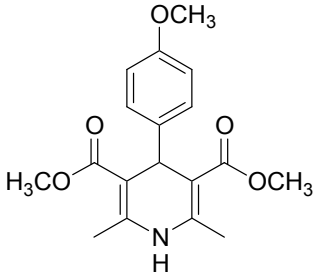
NMR data recorded for compounds:-

3,5-dimethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4a)



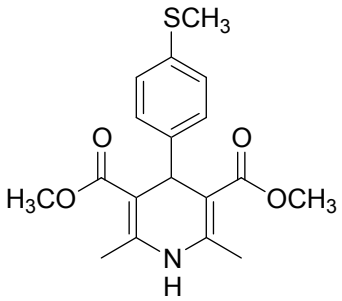
Creamish solid (Yield 87 %) m.p. 131-134^{o}C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27-7.20 (4H, m), 5.74 (1H, s), 4.99 (1H, s), 3.66 (6H, s), 2.35 (6H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz); δ 168.2, 146.4, 144.7, 132.2, 129.5, 128.5, 104.1, 51.4, 39.4, and 20.0; HRMS-ESI: m/z $[M+H]^+$ for $C_{17}H_{18}ClNO_4$ calculated 336.6013; observed 336.6032.

3,5-dimethyl4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4b)



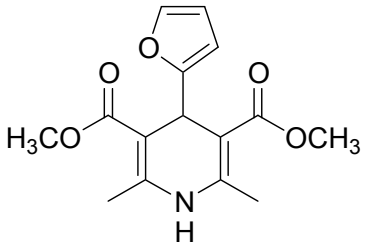
Light yellow solid (Yield 70 %), ^{1}H NMR (Pyr-d_5, 300 MHz): δ 10.38 (1H, s), 7.33-7.32 (2H, m), 6.99-6.93 (2H, m), 6.13 (1H, s), 3.61 (3H, m), 2.37 (3H, s), 2.31 (3H, s), 1.04 (3H, s), 0.98 (3H, s); ^{13}C NMR (Pyr-d_5, 75.4 MHz); δ 195.0, 152.7, 150.4, 127.1, 124.3, 112.7, 51.2, 40.7, 32.6, 29.6 and 27.2; HRMS-ESI: m/z $[M+Na]^+$ for $C_{18}H_{23}NO_5$ calculated 356.1873; observed 356.1800

3,5-dimethyl 2,6-dimethyl-4-[4-(methylsulfanyl)phenyl]-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4c)



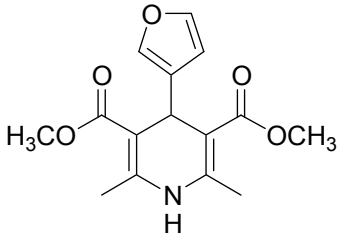
Light yellow solid (Yield 71 %) m.p. 170-173^{o}C, ^{1}H NMR (DMSO, 300 MHz):δ 8.87 (1H, s), 7.11-7.03 (4H, m), 4.81(1H, d), 3.53 (6H, s), 2.39 (3H, s), 2.24 (6H, s); ^{13}CNMR (DMSO,75.4 MHz) 167.4, 145.7, 144.8, 135.3, 127.7, 125.9, 100.5, 50.7, 38.1, 18.2 and 14.8; HRMS-ESI: m/z $[M+H]^{+}$ for $C_{18}H_{21}NO_4S$ calculated 348.2383; observed 348.2302

3,5-dimethyl 4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4d)



Brownish solid (Yield 90 %) m.p.168-170^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz):δ 9.01 (1H, s), 7.39 (1H, s), 6.24 (H, s), 5.82 (1H, s), 5.02 (1H, s), 3.59 (6H, s), 2.05 (6H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz) 167.8, 159.2, 147.5, 141.9, 110.9, 104.6, 98.92, 51.5, 33.3 and 18.8; HRMS-ESI: m/z $[M+H]^{+}$ for $C_{15}H_{17}NO_5$ calculated 292.1405; observed 292.1430.

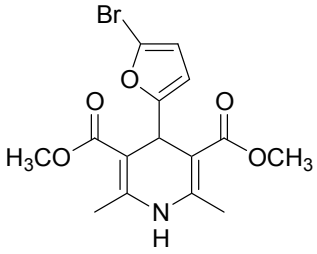
3,5-dimethyl 4-(furan-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4e)



Light yellow solid (Yield 86 %) m.p. 169-174^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz):δ 8.91 (1H, s), 7.42 (1H, s), 7.15 (H, s), 6.16 (1H, s), 4.78 (1H, s),

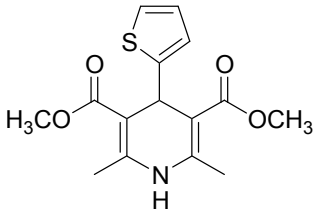
3.59 (6H, s), 2.24 (6H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz) 168.1, 147.2, 143.7, 139.1, 131.6, 110.8, 101.1, 51.6, 30.2 and 18.9; HRMS-ESI: m/z $[M+H]^+$ for $C_{15}H_{17}NO_5$ calculated 292.1405; observed 292.1422.

3,5-dimethyl 4-(5-bromofuran-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4f)



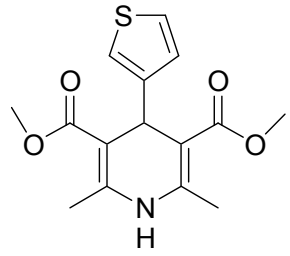
Creamish yellow solid (Yield 71 %) m.p.150-154^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz):δ 9.09 (1H, s), 6.33 (1H, d, J = 3.3 Hz), 5.90 (1H, d, J = 3.3 Hz), 5.02 (1H, s), 3.60 (6H, s), 2.26 (6H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz) 167.8, 161.7, 148.1, 119.5, 113.0, 107.9, 98.5, 51.7, 33.8 and 19.0

3,5-dimethyl 2,6-dimethyl-4-(thiophen-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4g)



Pale yellow solid (Yield 91 %) m.p. 189-192^{o}C, ^{1}H NMR (Pyr-d_5, 300 MHz): δ 9.94 (1H, s), 7.16.-6.83 (3H, m), 5.71(H, s), 3.69 (6H, s), 2.51(6H, s);^{13}C NMR (Pyr-d_5, 75.4 MHz), 167.9, 155.0, 147.5, 130.3, 109.9, 102.2, 51.2, 35.7 and 18.63; HRMS-ESI: m/z $[M+H]^+$ for $C_{15}H_{17}NO_4S$ calculated 308.1987; observed 308.1972.

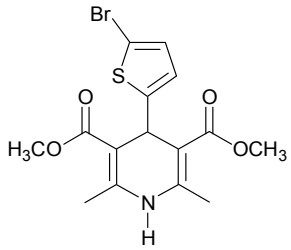
3,5-dimethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4h)



Light yellow solid (Yield 75 %) m.p. 181-183 ^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.93 (1H, s), 7.32-7.29 (1H, m), 6.89-6.84 (2H, m), 4.98 (1H,

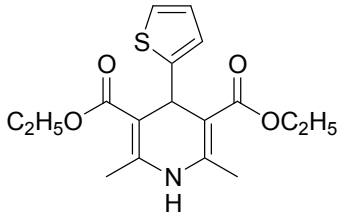
s), 3.58 (6H, s), 2.56 (6H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 168.2, 148.9, 146.9, 127.8, 126.4, 120.6, 101.8, 51.6, 34.6 and 18.9.

3,5-dimethyl 2,6-dimethyl-4-(5-bromothiophen-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4i)



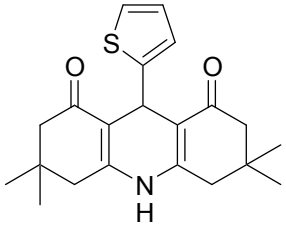
Yellow solid (Yield 93%) m.p. 150-154^{o}C, ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 300 MHz): δ 9.04 (1H, s), 7.16-7.14 (1H, m), 6.83 (1H, dd), 5.16 (1H, s), 3.60 (6H, s), 2.25 (6H, s); ^{13}C NMR (DMSO-d_6 + $CDCl_3$,75.4 MHz) 167.1, 151.8, 146.2, 126.4, 123.3, 122.2, 101.2, 50.7, 48.7, 33.7 and 18. 1. HRMS-ESI: m/z $[M+H]^+$ for $C_{15}H_{16}BrNO_4S$ calculated 386.2015; observed 386.2567.

3,5-diethyl 2,6-dimethyl-4-(thiophen-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate, (Table 2, Compound 4j)



Light yellow solid (Yield 69 %) m.p. 166-168 ^{o}C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.08-7.05 (1H, m), 6.87-6.80 (2H, m), 5.92 (1H, s), 5.36 (1H, s), 4.23-4.13 (4H, m), 2.35 (6H, s), 1.31 (6H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz); δ 167.8, 151.9, 144.9, 126.7, 123.5, 103.9, 60.3, 34.7, 19.9, and 14.7; HRMS-ESI: m/z $[M+H]^+$ for $C_{17}H_{21}NO_4S$ calculated 336.2383; observed 336.2378

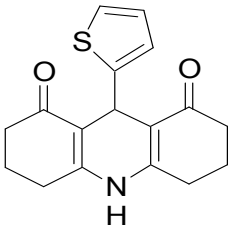
3,3,6,6-tetramethyl-9-(thiophen-2-yl)-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione, (Table 2, Compound 4k)



Brownish solid (Yield 76 %) m.p. 151-154^{o}C, ^{1}H NMR ^{1}H NMR (Pyr-d_5, 300 MHz): δ 10.38 (1H, s), 7.36 (1H, d, J = 3.27 Hz), 6.97-6.95 (2H, m), 6.13

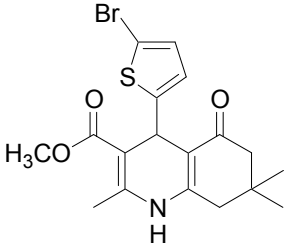
(1H, s), 2.54 (4H, s), 2.38 (4H, s), 1.01 (6H, s), 0.97 (6H, s) ^{13}C NMR (Pyr-d_5, 75.4 MHz); δ 195.0, 152.7, 127.1, 124.3, 112.7, 51.2, 40.7, 32.6, 29.6 and 27.2; HRMS-ESI: m/z $[M+H]^+$ for $C_{21}H_{25}NO_2S$ calculated 356.2707; observed 356.2725.

9-(thiophen-2-yl)-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione, (Table 2, Compound 4l)



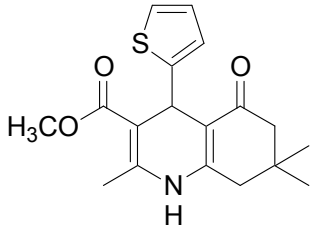
Light brown solid (Yield 52 %), ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.44 (1H, s), 6.98 (1H, d, J = 4.8 Hz), 6.64 (1H, d, J = 3.6 Hz), 6.45 (1H, s), 5.0 (1H, s), 2.11-1.65 (12H, m); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 195.7, 152.4, 127.2, 124.1, 123.5, 112.8, 49.5, 37.5, 27.8, 21.7 and 14.9; HRMS-ESI: m/z $[M+H]^+$ for $C_{17}H_{17}NO_2S$ calculated 300.2005; observed 300.2015.

Methyl 4-(5-bromothiophen-2-yl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate , (Table 3, Compound 5a)



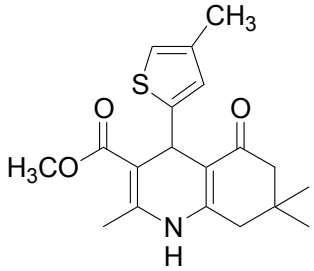
Yellow solid (Yield 83 %) m.p. 197-199 ^{o}C, ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 300 MHz): δ 9.33(1H, s), 6.89(1H, d, J = 3.6 Hz), 6.46(1H, d, J = 3.6 Hz), 5.08 (1H, s), 3.61 (3H, s), 2.44-2.06 (7H, m), 1.02 (3H, s), 0.92 (3H, s); ^{13}C NMR (DMSO-d_6 + $CDCl_3$, 75.4 MHz); δ 195.2, 167.7, 154.0, 150.9, 147.3, 130.5, 124.01, 109.7, 109.2, 102.7, 51.7, 50.9, 33.0, 31.9, 29.7, 27.6 and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{20}BrNO_3S$ calculated 410.2307; observed 410.2925.

Methyl 2,7,7-trimethyl-5-oxo-4-(thiophen-2-yl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5b)



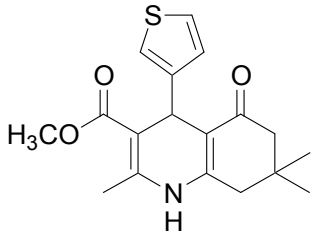
Off white solid (Yield 81%) m.p. 231-234^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.29 (1H, s), 7.17 (1H, s), 6.82 (1H, s), 6.65 (1H, s) 5.16 (1H, s), 3.59 (3H, s), 2.39-2.08 (7H, m), 1.00 (3H, s), 0.92 (3H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 194.4, 167.2, 151.5, 149.9, 145.9, 126.5, 123.4, 122.5, 109.6, 102.8, 50.8, 50.2, 32.1, 30.6, 29.2, 26.6 and 18.3; HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{21}NO_3S$ calculated 332.2311; observed 332.2269

Methyl 4-(4-methythiophen-2-yl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5c)



Light yellow solid (Yield 82 %) m.p. 222-225^{o}C, ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 300 MHz): δ 9.20 (1H, s), 6.67 (1H, s), 6.47 (1H, s), 5.13 (1H, s), 3.65 (3H, s), 2.37-2.18 (7H, m), 2.12 (3H, s), 1.05 (3H, s), 0.98 (3H, s); ^{13}C NMR (DMSO-d_6 + $CDCl_3$, 75.4 MHz); δ 199.8, 172.7, 156.9, 155.3, 151.2, 141.7, 130.2, 123.7, 115.2, 108.4, 56.2, 55.8, 37.7, 36.2, 34.8, 32.4, 23.9 and 21.2;

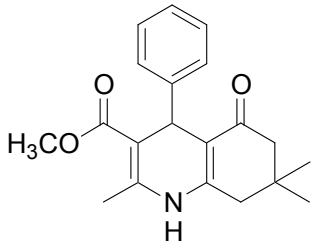
Methyl 2,7,7-trimethyl-5-oxo-4-(thiophen-3-yl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5d)



Off white solid (Yield 89 %) m.p. 233-236 ^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.14 (1H, s), 7.30-7.27 (1H, m), 6.87-6.82 (2H, m), 4.97 (1H, s), 3.57 (3H, s), 2.42-2.03 (7H, m), 1.00 (3H, s), 0.86 (3H, s); ^{13}C NMR (DMSO-d_6, 75.4

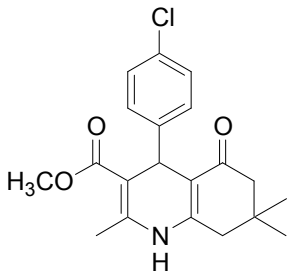
MHz); δ 195.4, 168.2, 150.7, 148.7, 146.6, 128.1, 126.2, 120.5, 110.4, 103.5, 51.6, 51.1, 32.9, 31.5, 29.9, 27.4 and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{21}NO_3S$ calculated 332.2389; observed 332.2341.

Methyl 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5e)



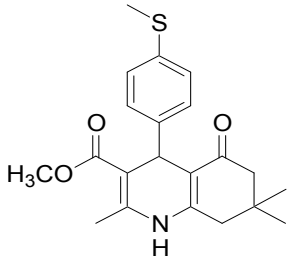
Light yellow solid (Yield 88 %) m.p. 247-250 ^oC, ^1H NMR (DMSO-d_6, 300 MHz): δ 9.11 (1H, s), 7.18-7.06 (5H, m), 4.86 (1H, s), 3.52 (3H, s), 2.50-2.00 (7H, m), 1.00 (3H, s), 0.83 (3H,); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 195.3, 168.2, 150.5, 148.3, 146.1, 128.7, 128.1, 126.6, 110.9, 104.1, 51.5, 51.1, 36.5, 32.9, 29.9, 27.3 and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{20}H_{23}NO_3$ calculated 326.1965; observed 326.1852

Methyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5f)



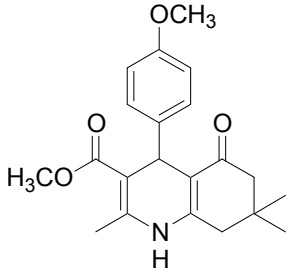
Light yellow solid (Yield 84 %) m.p. 230-235^oC, ^1H NMR (DMSO-d_6, 300 MHz): δ 9.16(1H, s), 7.25 (2H, d, J = 8.7 Hz), 7.16 (2H, d, J = 8.7 Hz), 4.84 1H, s), 3.54 (3H, s), 2.39-1.95 (7H, m), 0.99 (3H, s), 0.82 (3H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 195.3, 168.0, 150.6, 147.2, 146.5, 131.1, 129.9, 128.6, 110.5, 103.7, 51.6, 51.0, 36.2, 32.9, 29.9, 27.2, and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{20}H_{22}ClNO_3$ calculated 360.1288; observed 360.1252.

Methyl 2,7,7-trimethyl-4-[4-(methylsulfanyl)phenyl]-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5g)



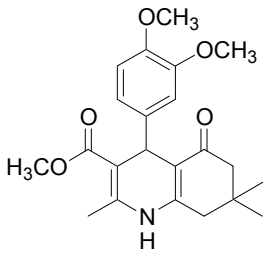
Light yellow solid (Yield 71 %) m.p. 190-193 ^{o}C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.10 (1H, s), 7.08 (4H, s), 4.81 (1H, s), 3.54 (3H, s), (2.39, 3H, s), 2.30-1.95 (7H, m), 1.00 (3H, s), 0.83 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz); δ 195.3, 168.2, 150.4, 146.1, 145.3, 135.7, 128.8, 126.6, 110.7, 104.4, 51.5, 51.1, 36.1, 32.9, 29.9, 27.3, 19.1 and 15.6. HRMS-ESI: m/z $[M+H]^+$ for $C_{21}H_{25}NO_3S$ calculated 372.1555; observed 372.1523.

Methyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5h)



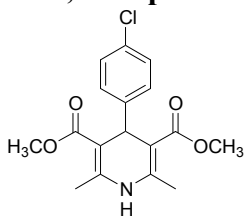
Light yellow solid (Yield 87 %) m.p. 238-240 ^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.06 (1H, s), 7.05-7.03 (2H, d, J = 7.2 Hz), 6.75-6.72 (2H, d, J = 7.2 Hz), 4.79 (1H, s), 3.66 (3H, s), 3.50 (3H, s), 2.37-1.99 (7H, m), 0.99 (3H, s), 0.84 (3H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 195.2, 168.2, 158.2, 150.2, 145.8, 140.7, 129.1, 114.1, 111.1, 104.44, 55.7, 51.5, 51.1, 35.6, 32.9, 29.9, 27.3 and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{21}H_{25}NO_4$ calculated 356.1957; observed 356.1920.

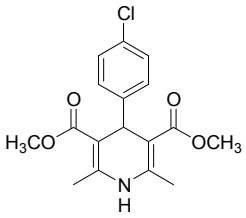
Methyl 4-(3,4-dimethoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, (Table 3, Compound 5i)



Light yellow solid (Yield 93 %) m.p. 197-199^{o}C, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.08 (1H, s), 6.77 (2H, d, J = 8.4 Hz), 6.62 (1H, s), 4.80 (1H, s), 3.66 (3H, s), 3.65 (3H, s), 3.54 (3H, s), 2.50-2.0 (7H, s), 1.01 (3H, s), 0.87 (3H, s); ^{13}C NMR (DMSO-d_6, 75.4 MHz); δ 195.4, 168.3, 150.4, 148.9, 147.8, 145.8, 141.2, 119.9, 112.4, 110.9, 104.4, 56.3, 56.2, 51.5, 35.8, 32.9, 31.5, 30.1, 27.2 and 19.1; HRMS-ESI: m/z $[M+H]^+$ for $C_{22}H_{27}NO_5$ calculated 386.1907; observed 386.1863.

(Table 2, Compound 4a)

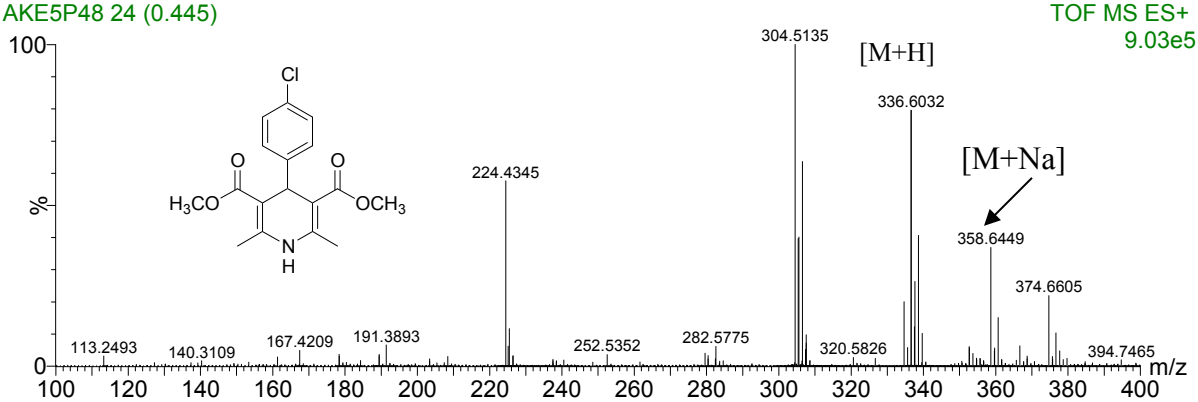




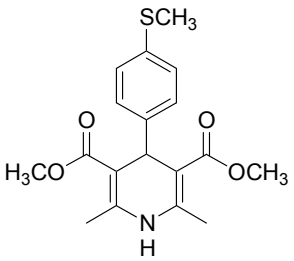
IHBT
20-Aug-2013
AKE5P48 24 (0.445)

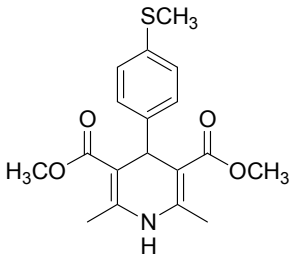
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
TOF MS ES+
9.03e5



(Table 2, Compound 4c)

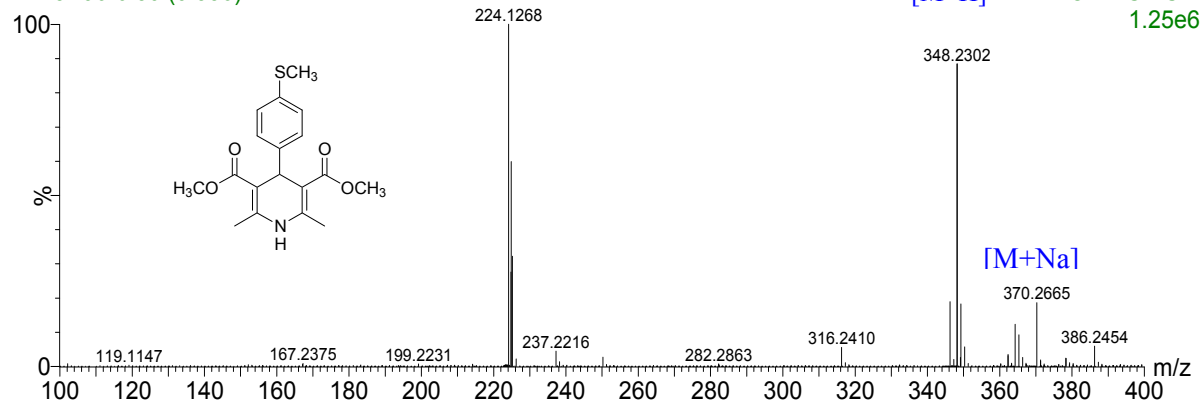




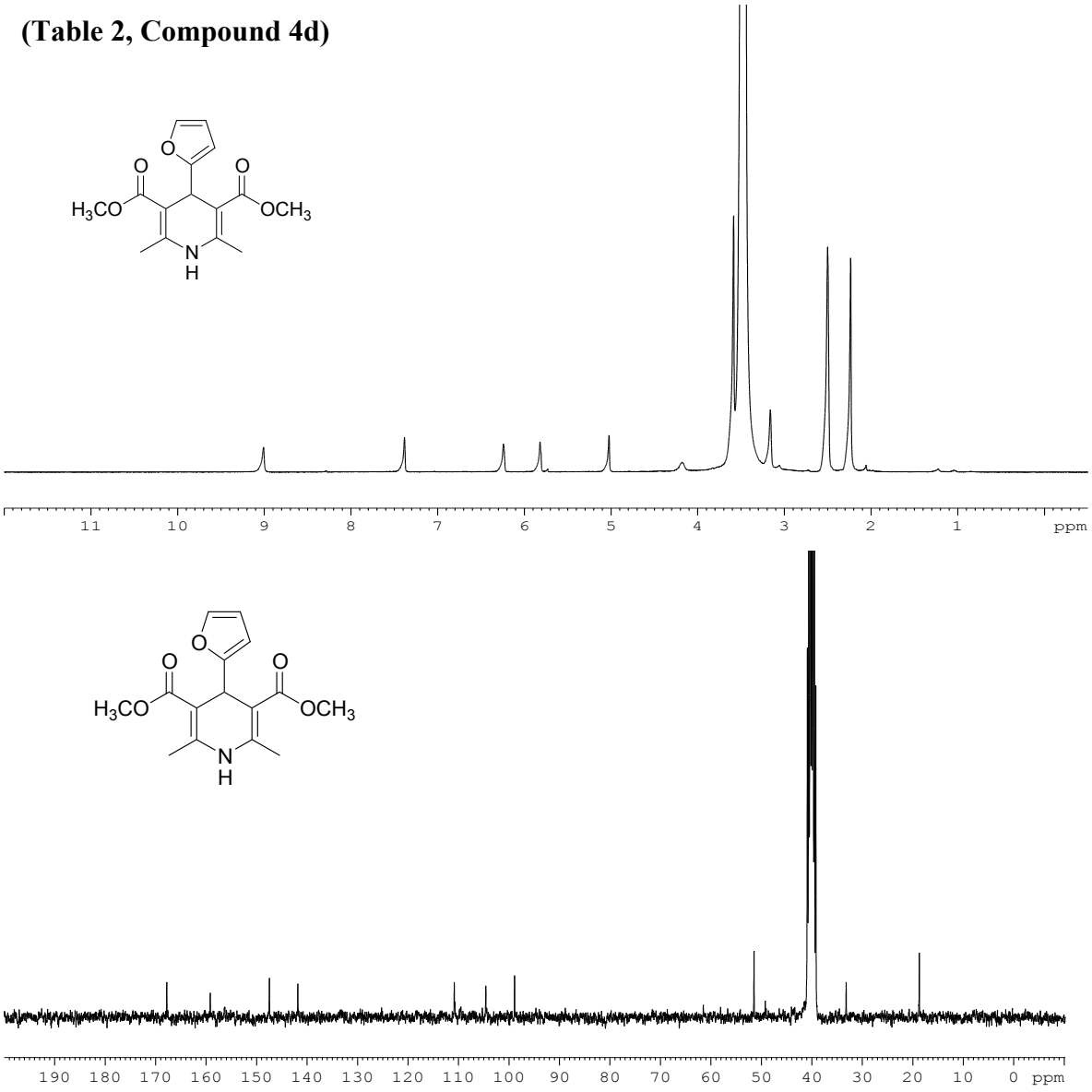
IHBT
30-Aug-2013
AKE5P96-6 30 (0.556)

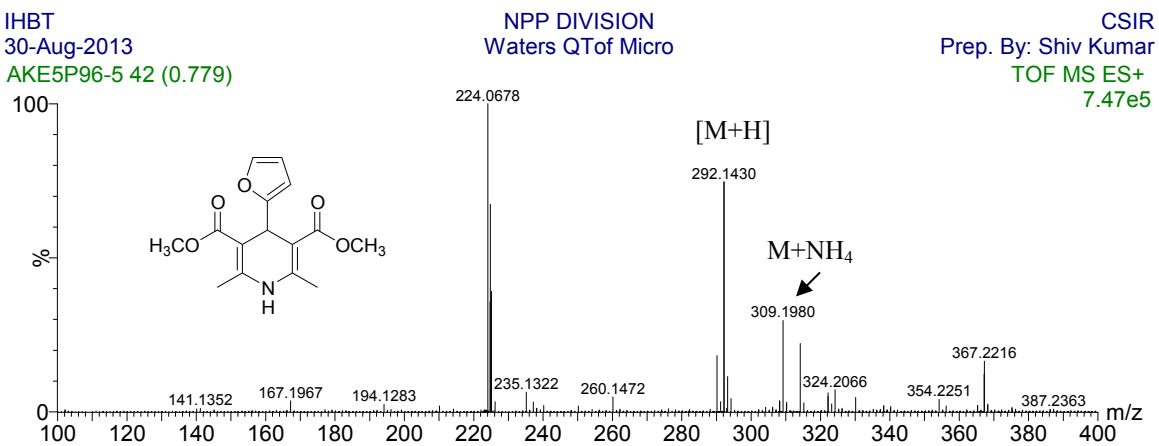
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
[M+H] TOF MS ES+
1.25e6

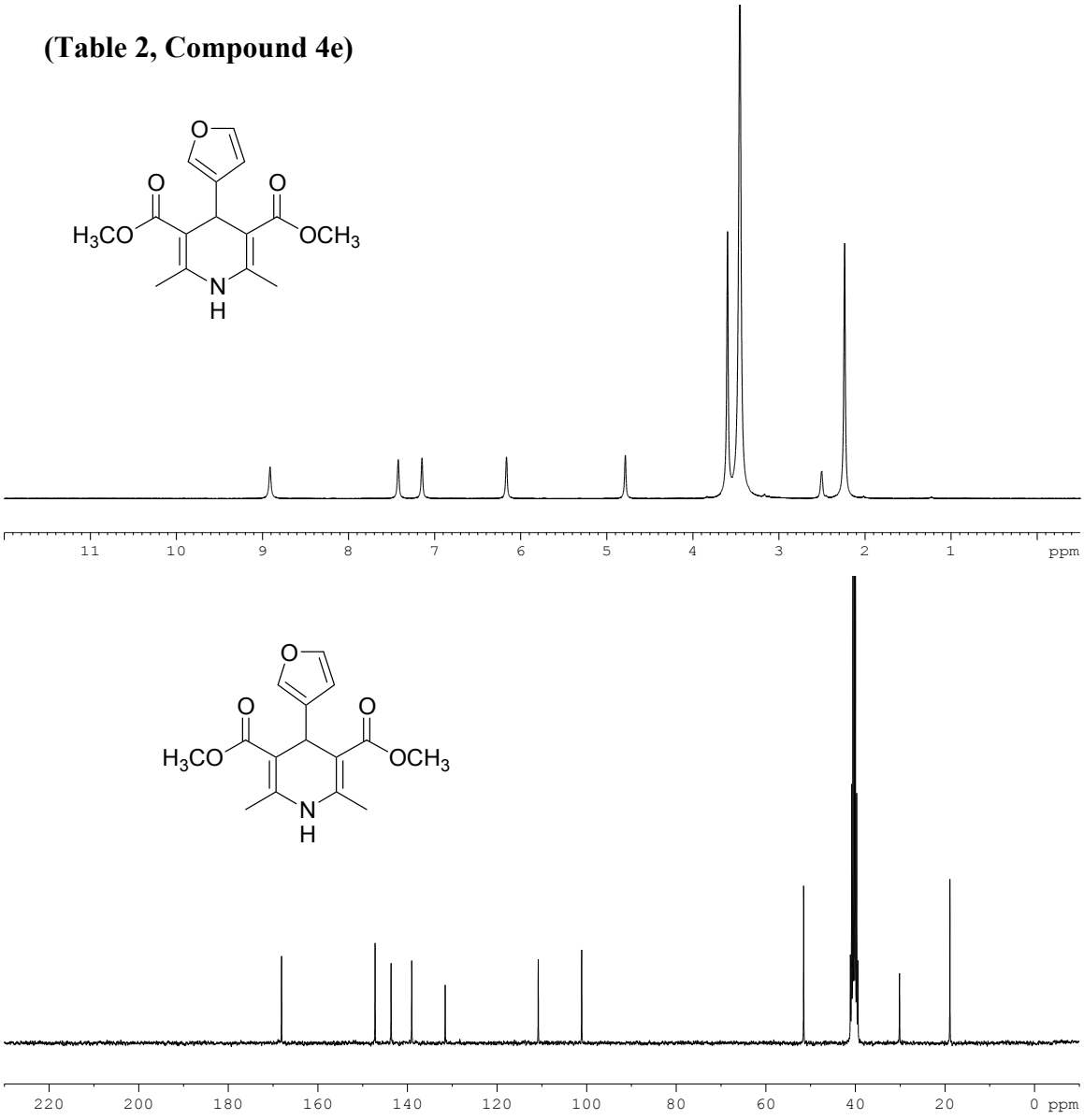


(Table 2, Compound 4d)





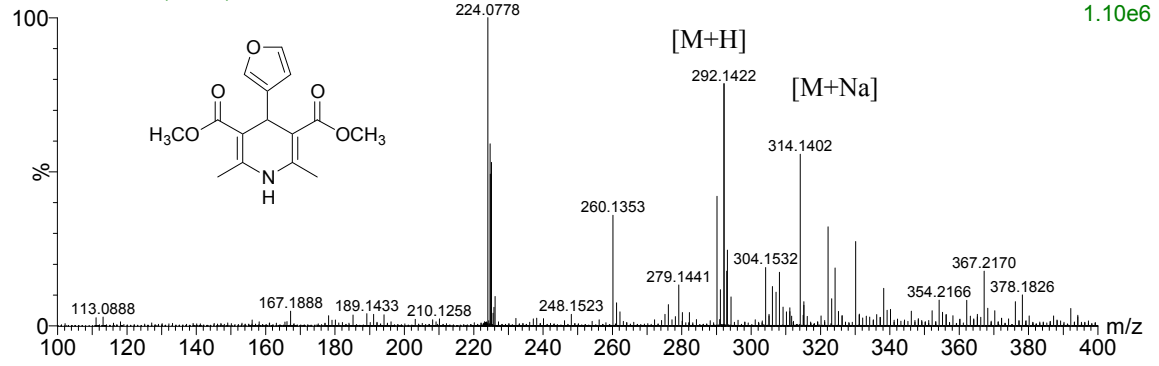
(Table 2, Compound 4e)



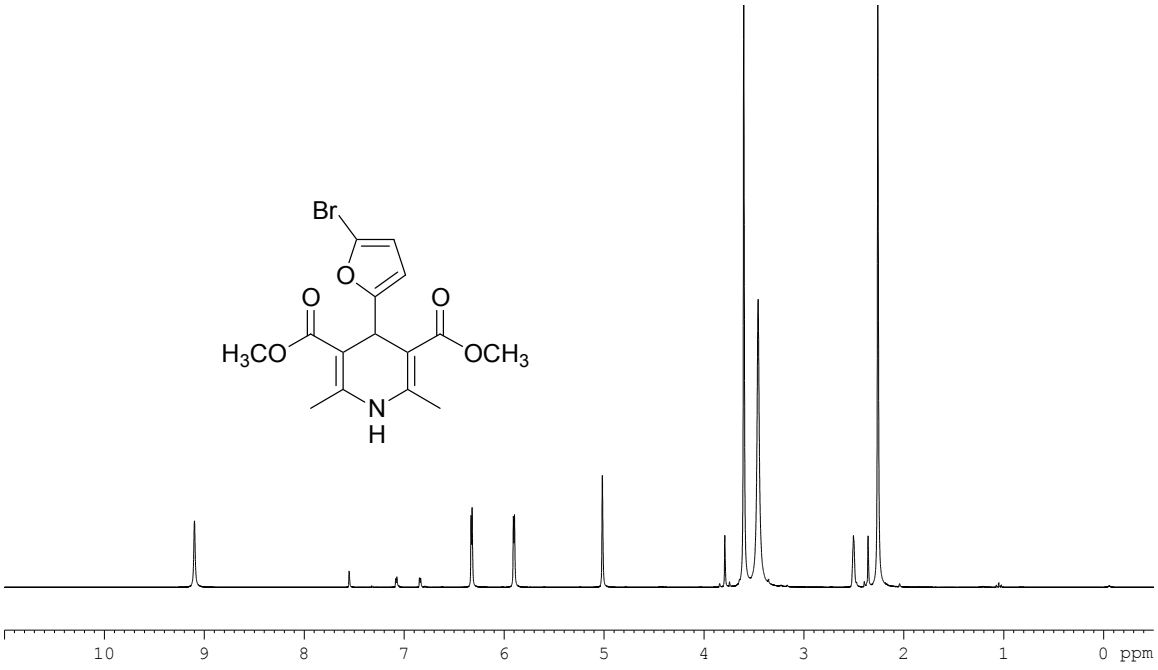
IHBT
20-Aug-2013
AKE5P86-1 16 (0.297)

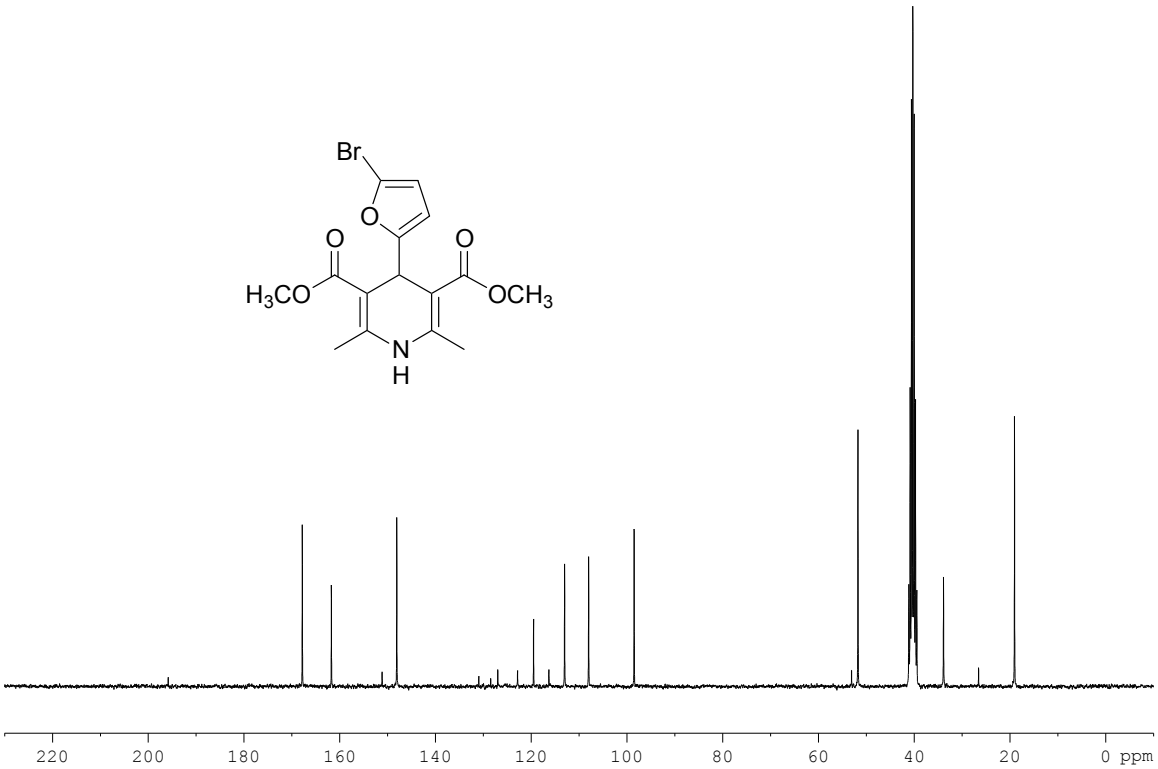
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
TOF MS ES+
1.10e6

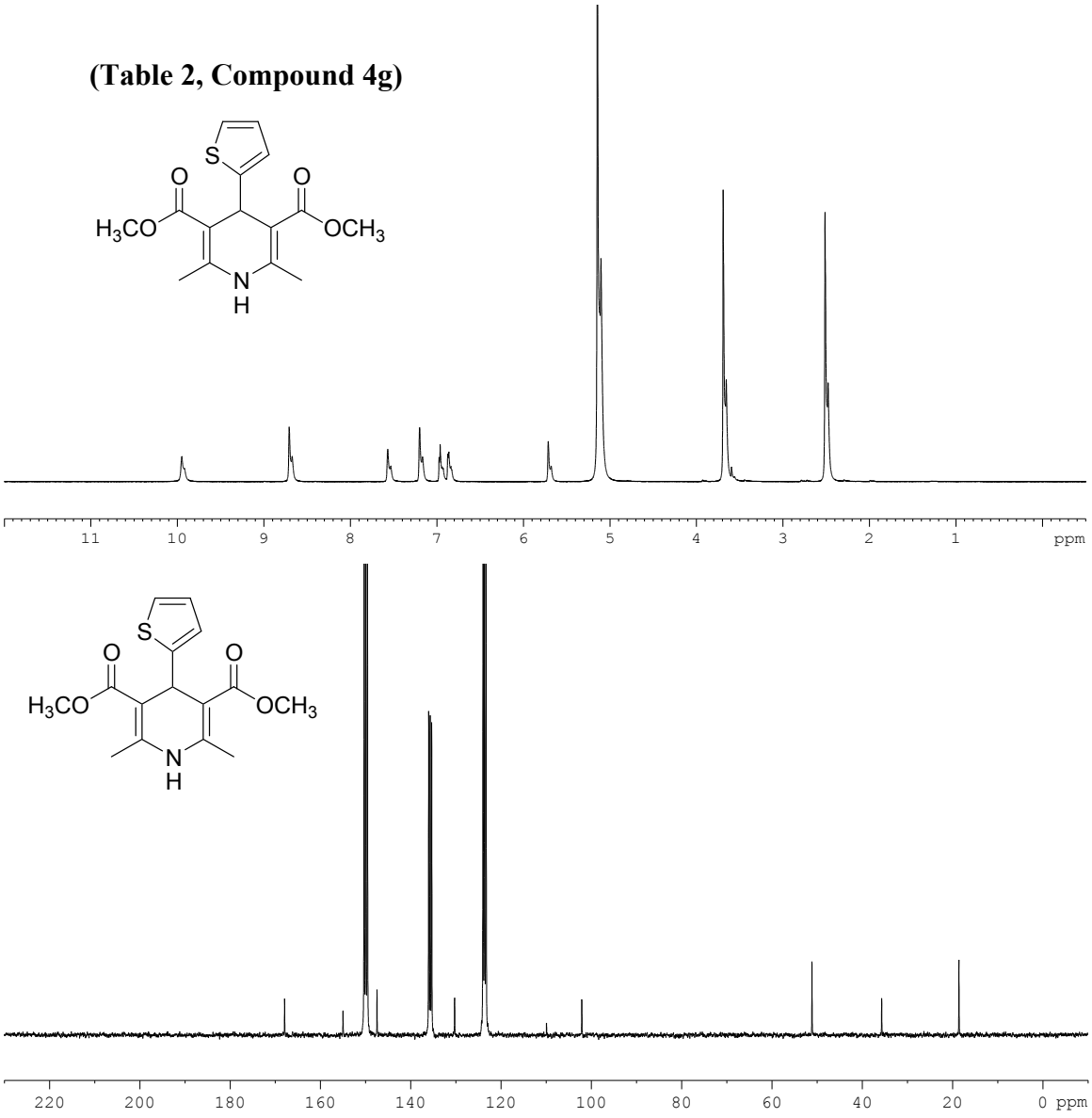


(Table 2, compound 4f)





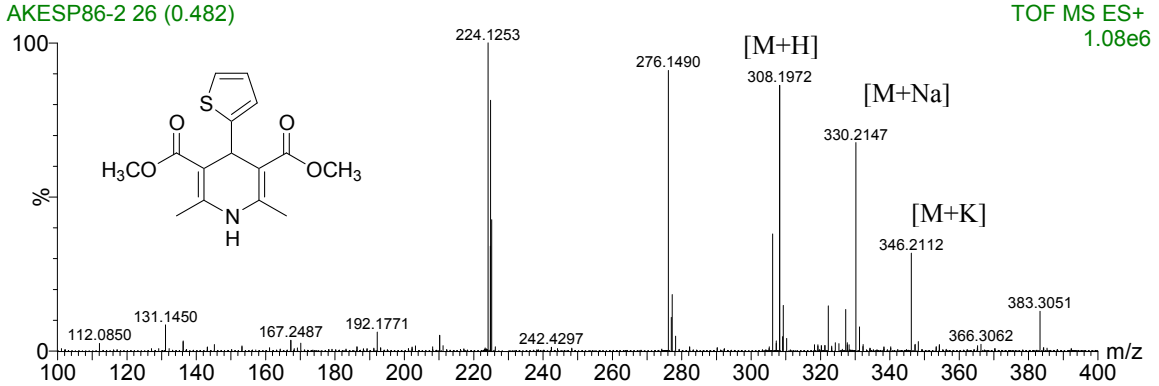
(Table 2, Compound 4g)



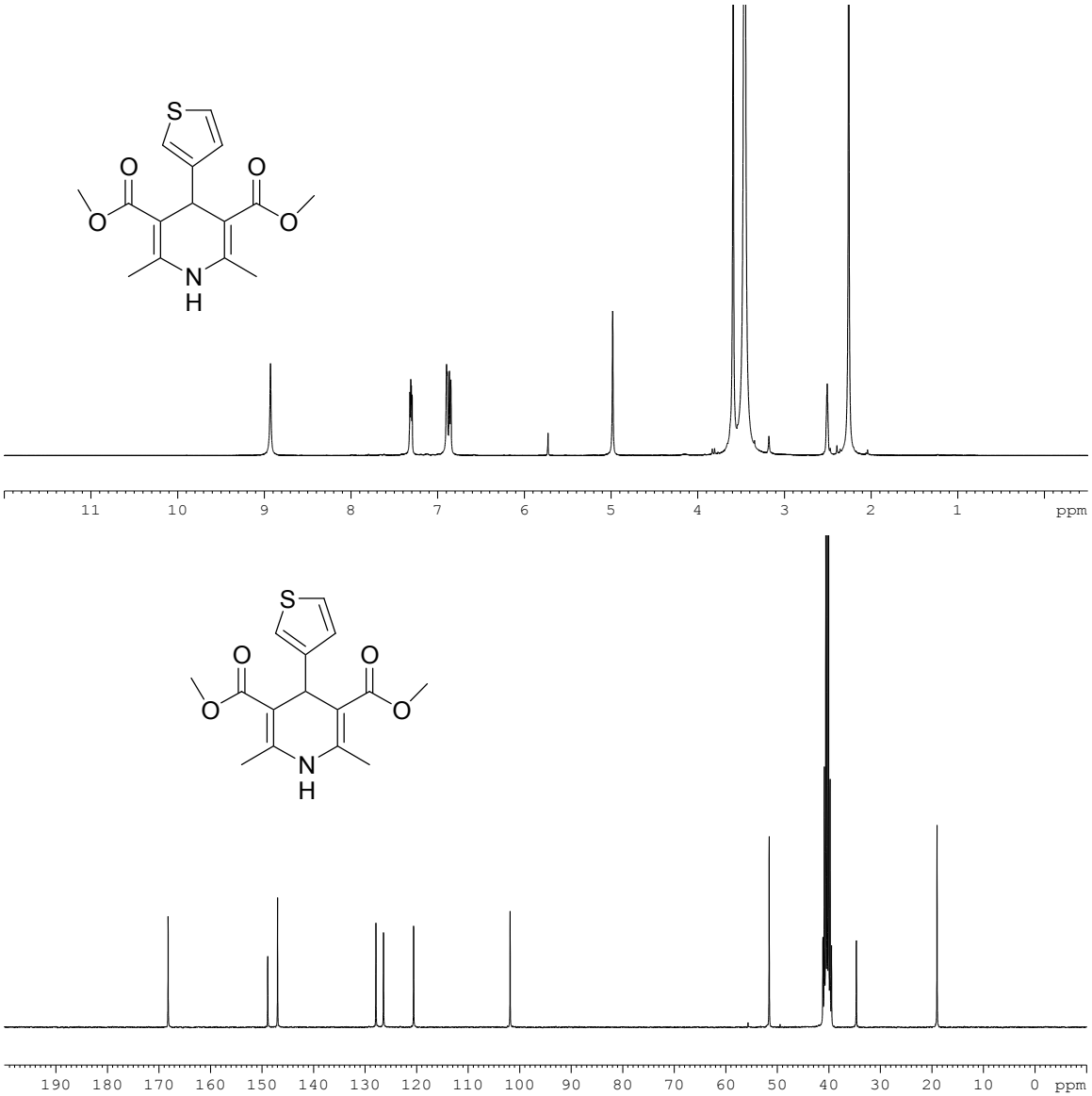
IHBT
21-Aug-2013
AKESP86-2 26 (0.482)

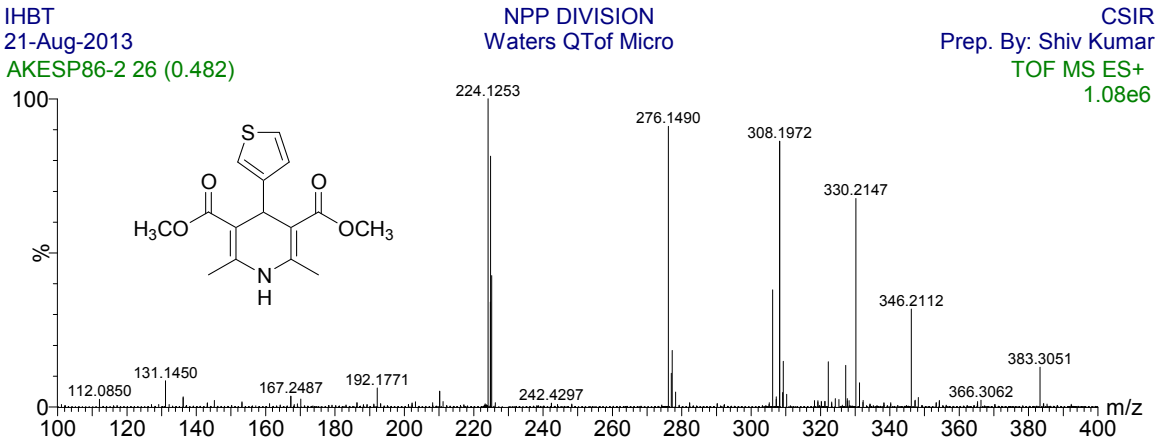
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
TOF MS ES+
1.08e6

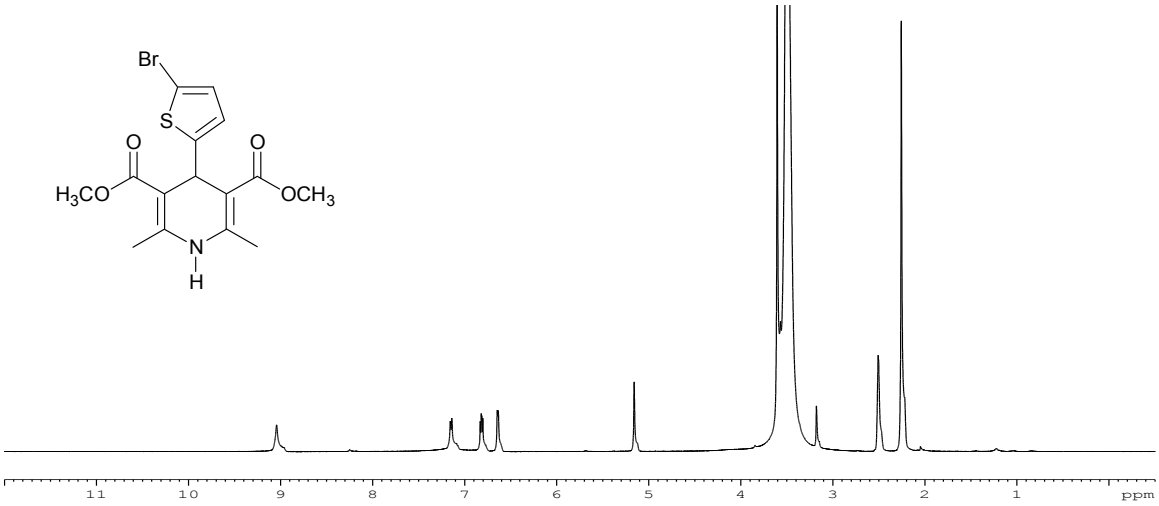


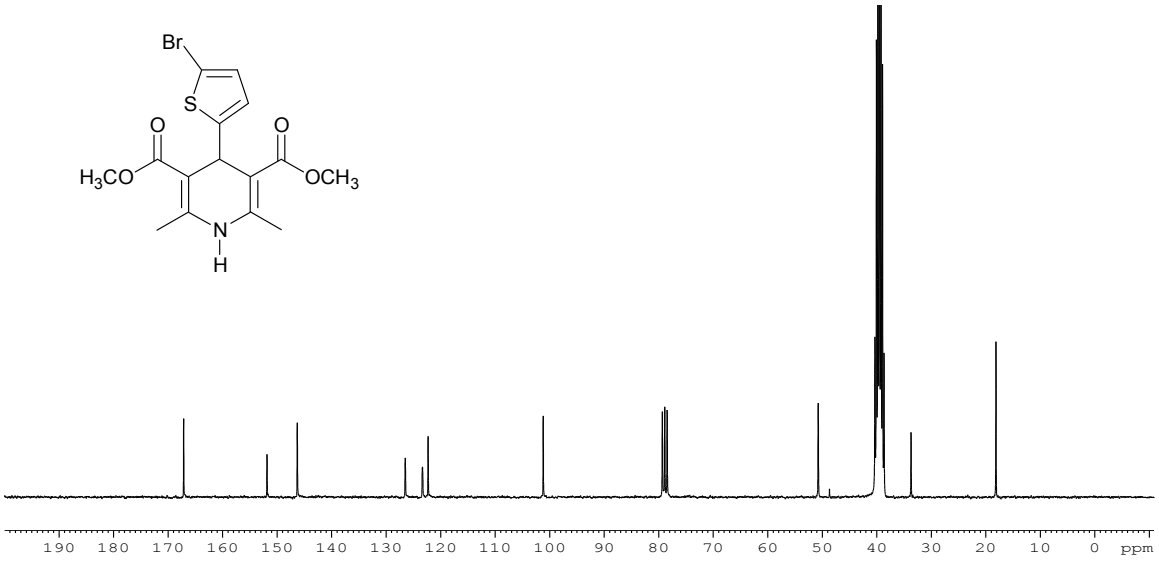
(Table 2, Compound 4h)

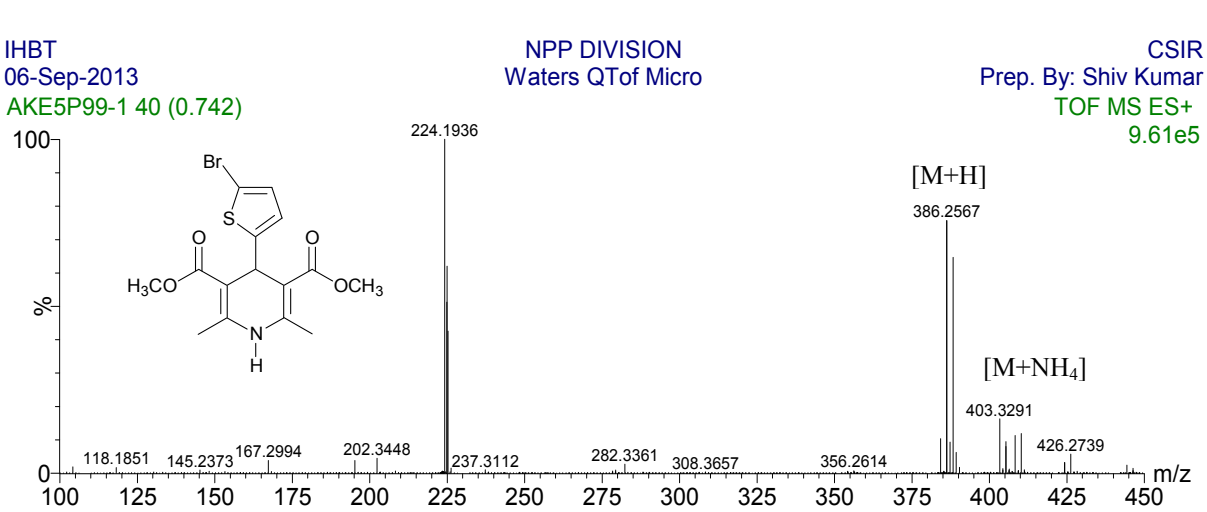




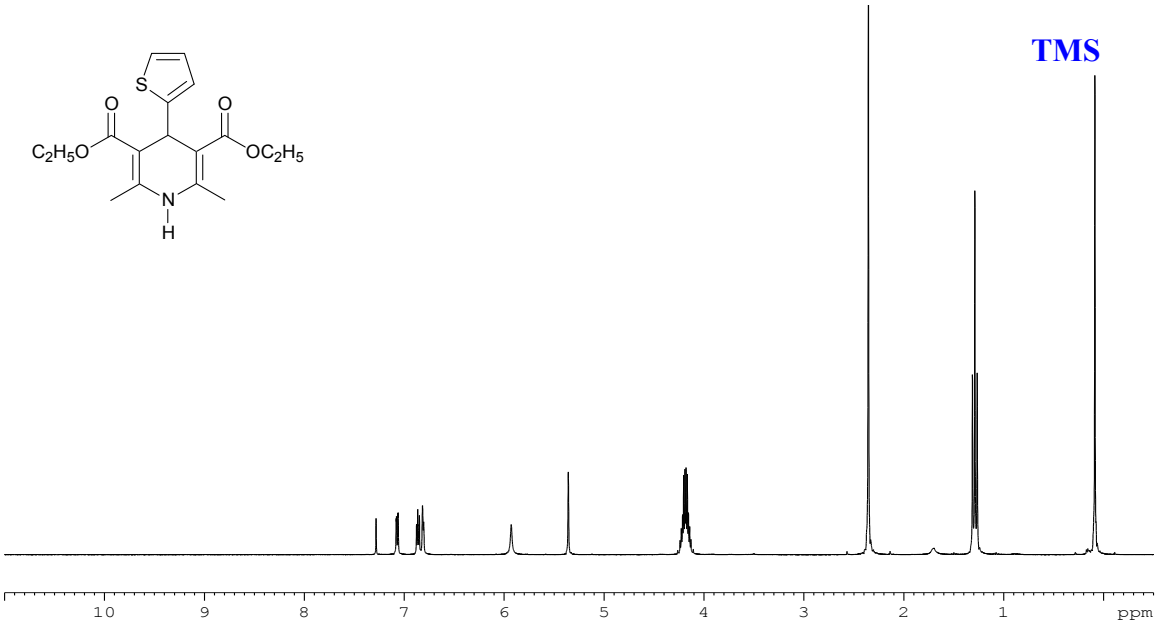
(Table 2, Compound 4i)

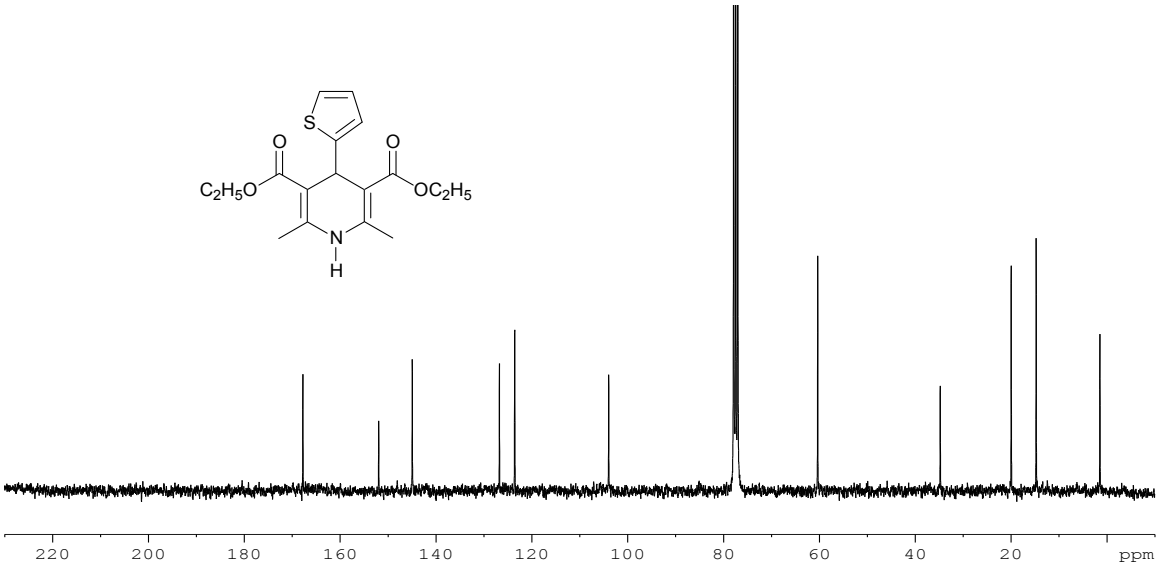


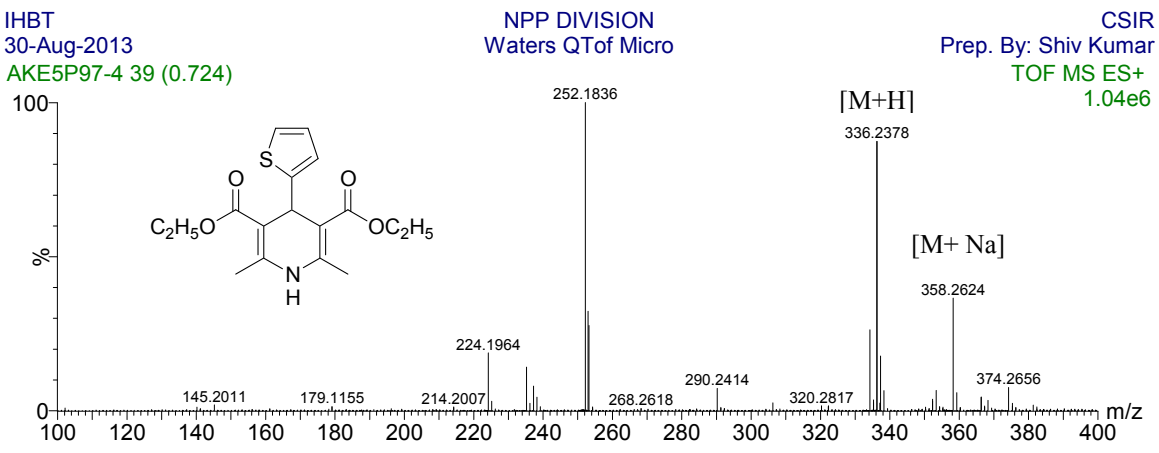




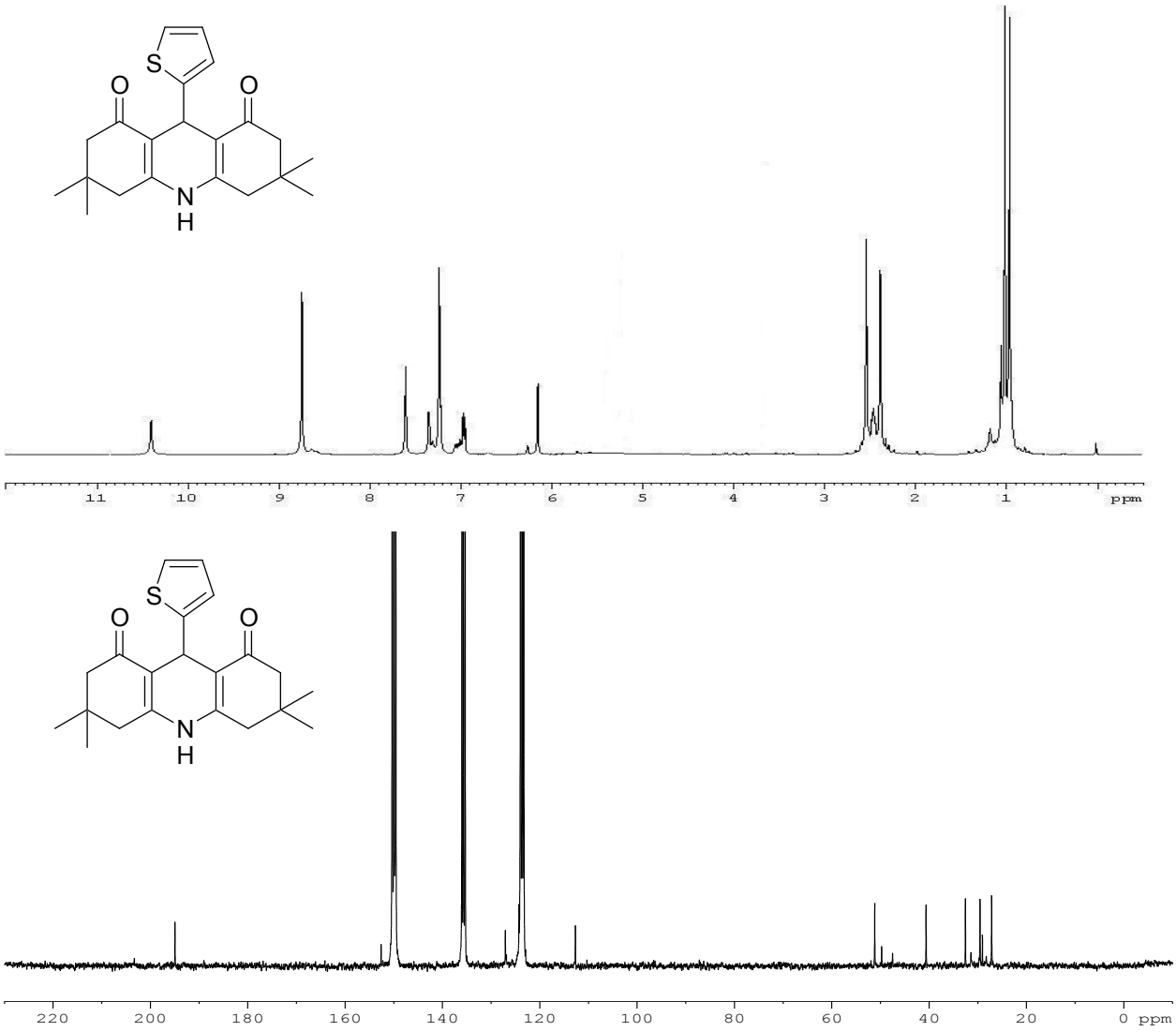
(Table 2, Compound 4j)

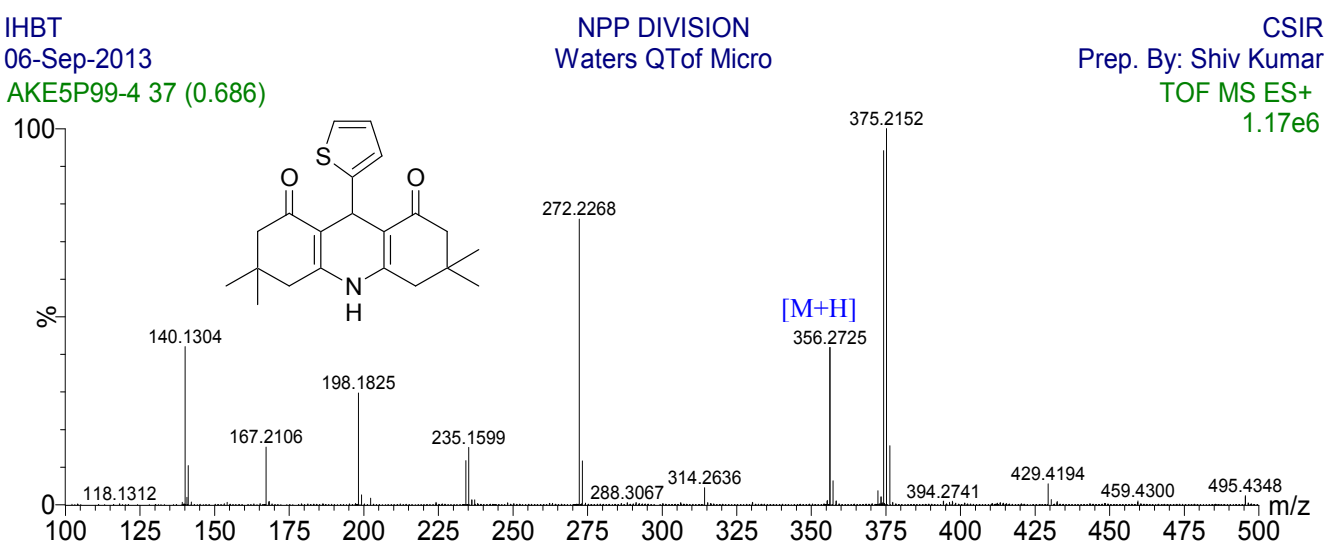




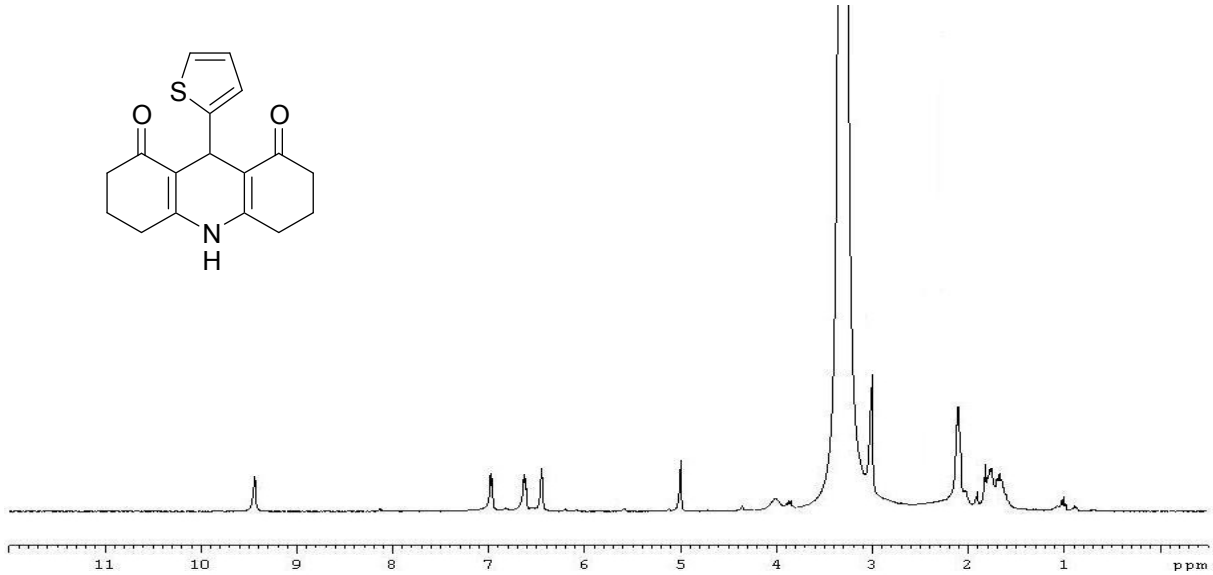


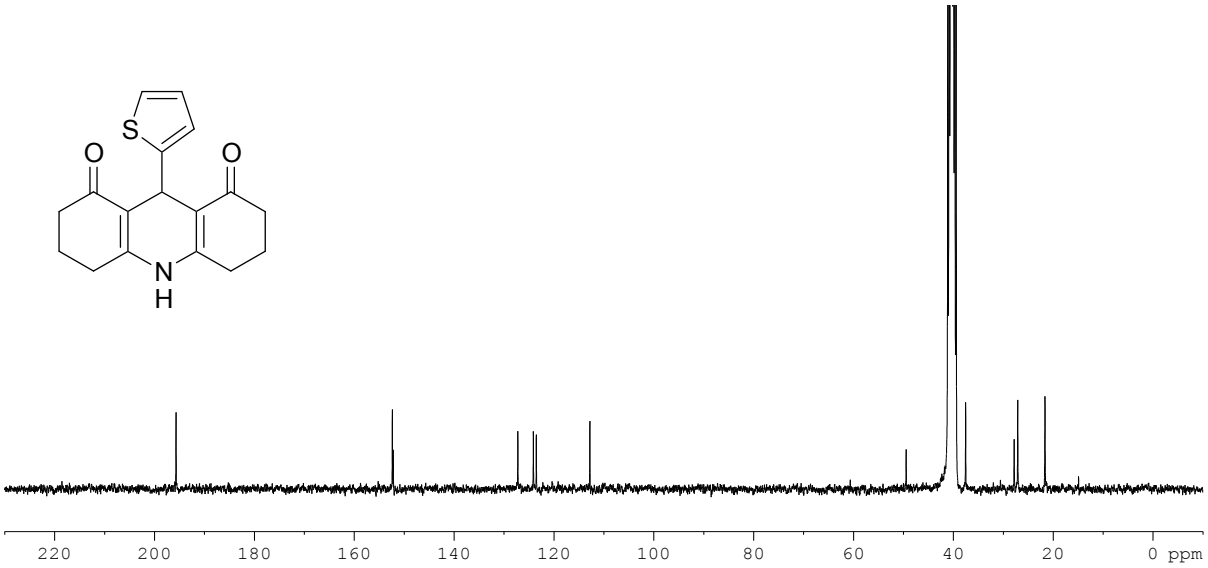
(Table 2, Compound 4k)

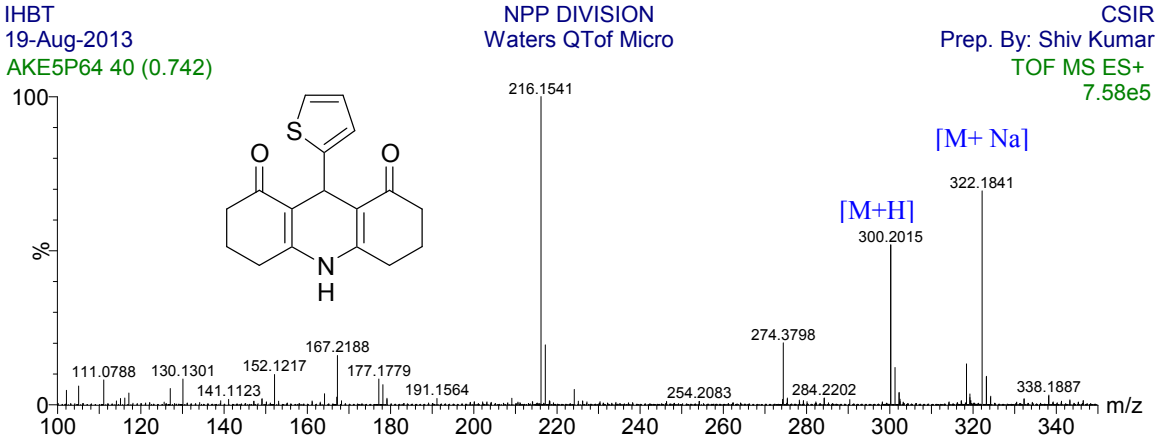




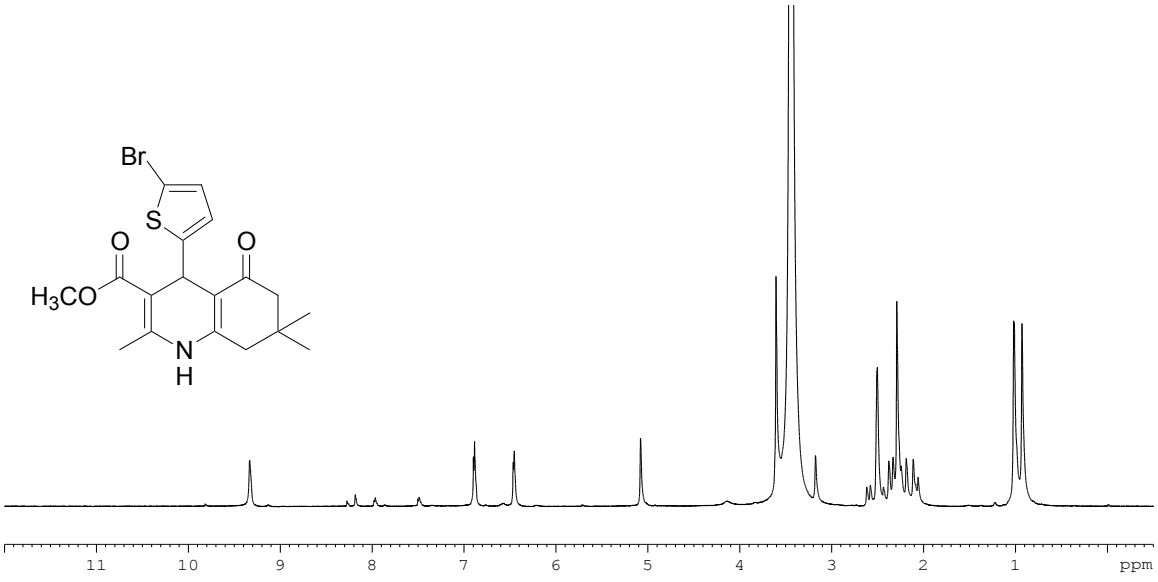
(Table 2, Compound 4l)

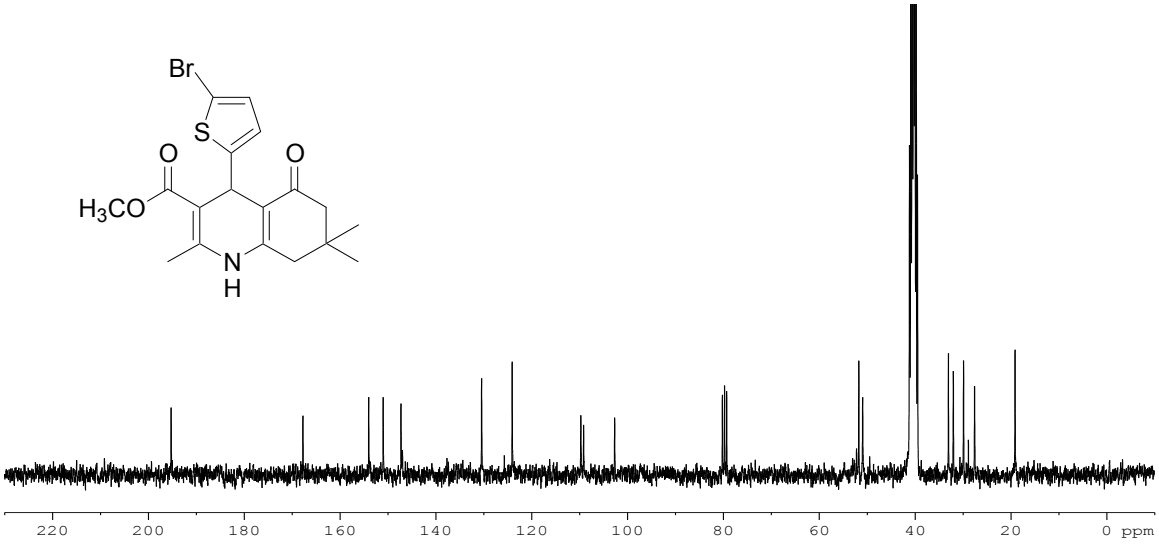






(Table 3, Compound 5a)

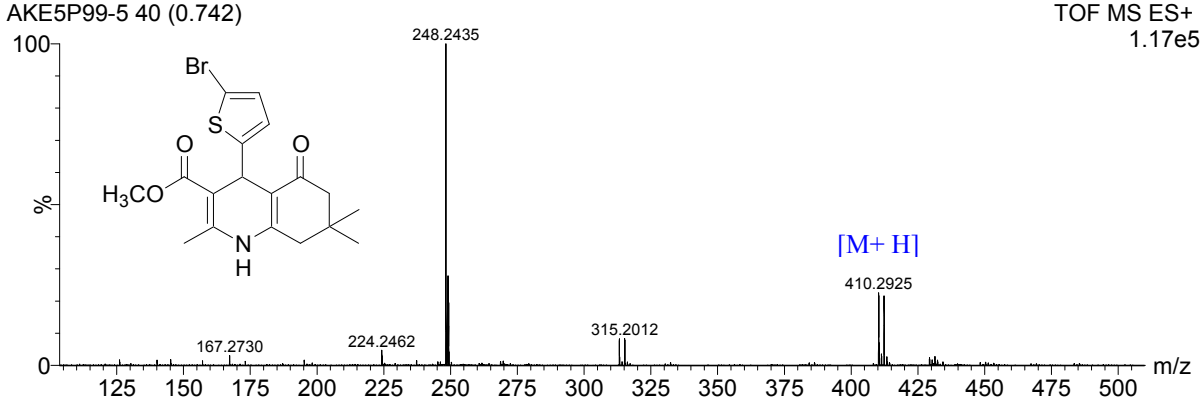




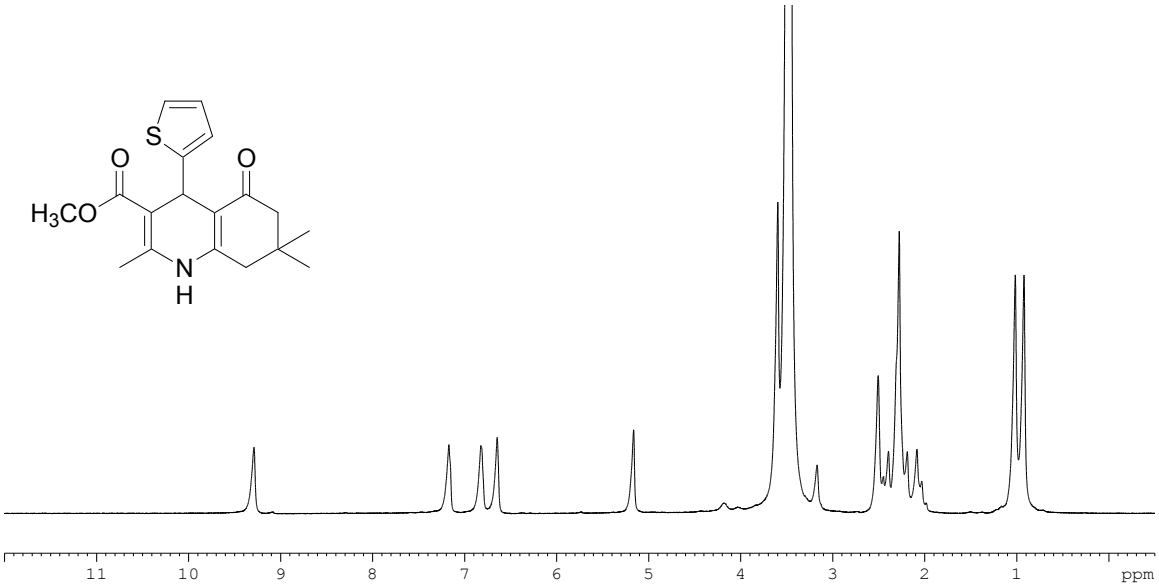
IHBT
06-Sep-2013
AKE5P99-5 40 (0.742)

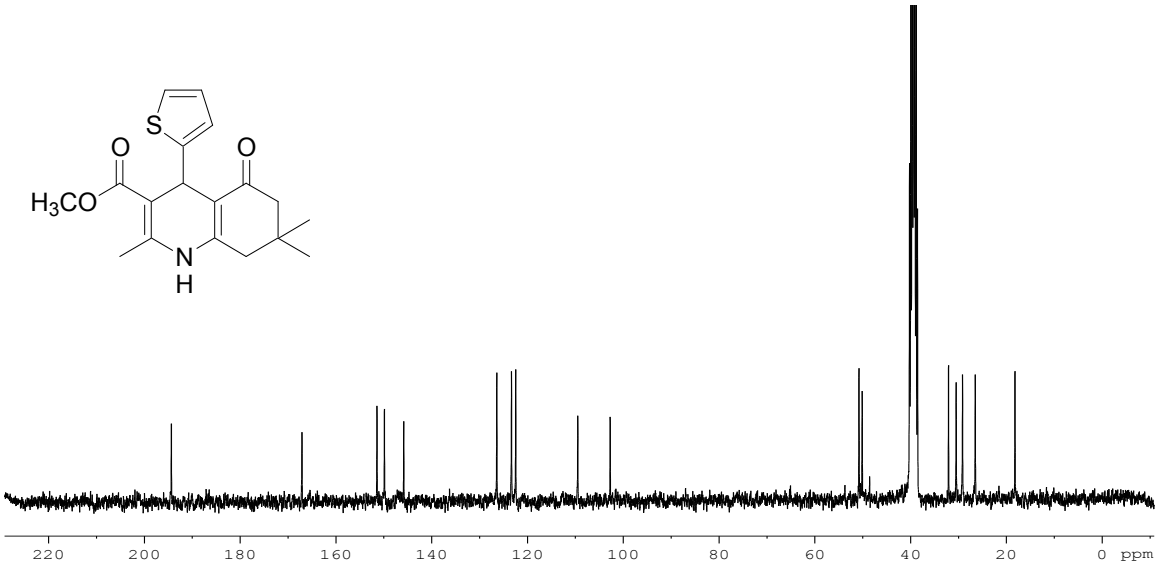
NPP DIVISION
Waters QTof Micro

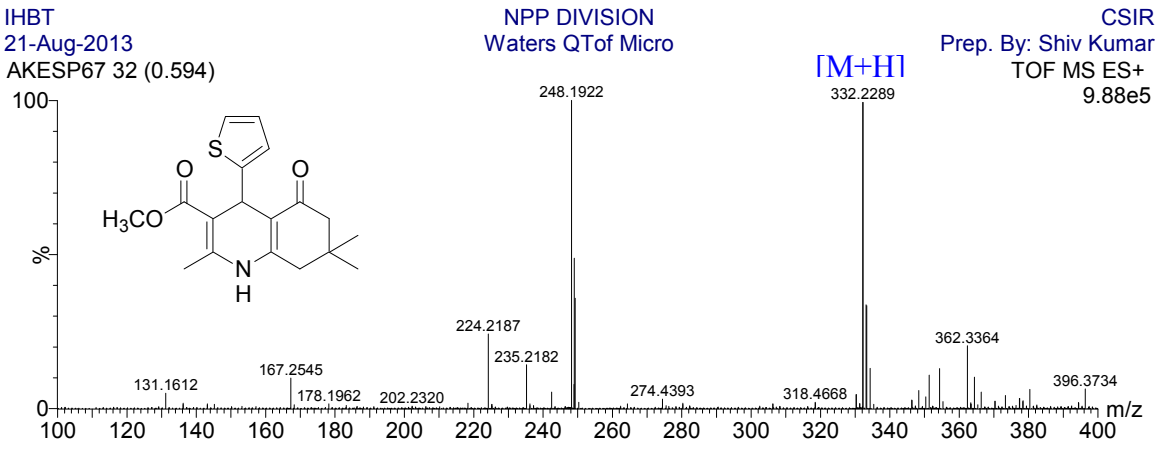
CSIR
Prep. By: Shiv Kumar
TOF MS ES+
1.17e5



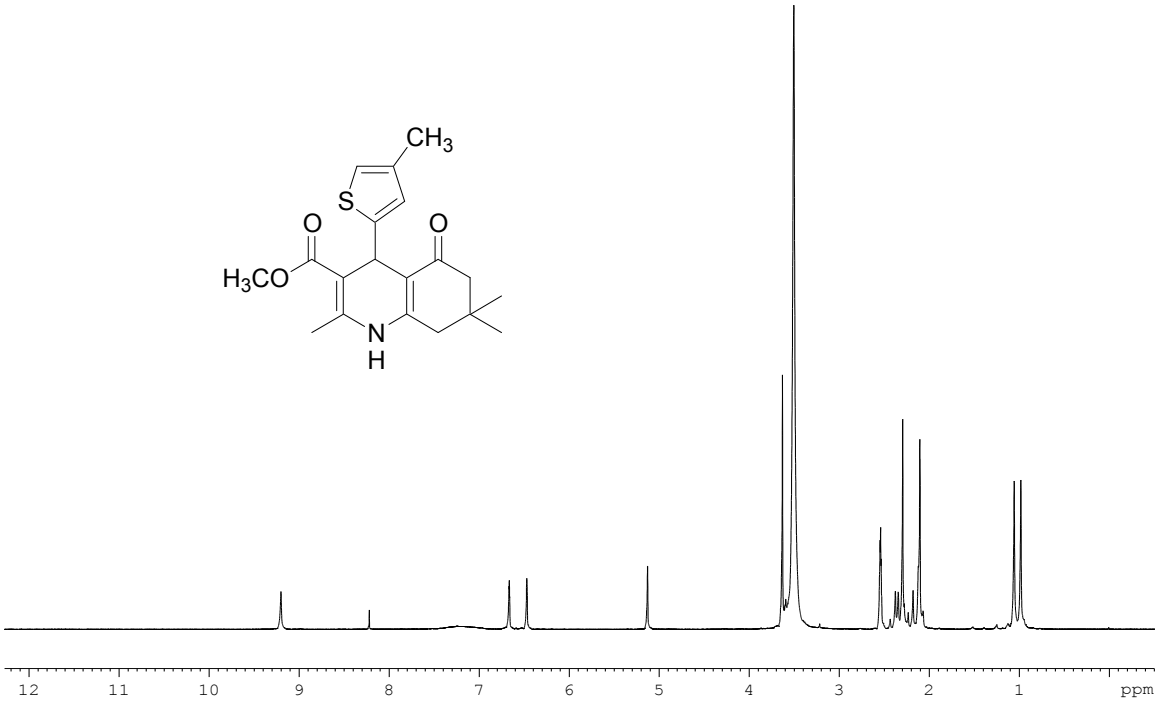
(Table 3, Compound 5b)

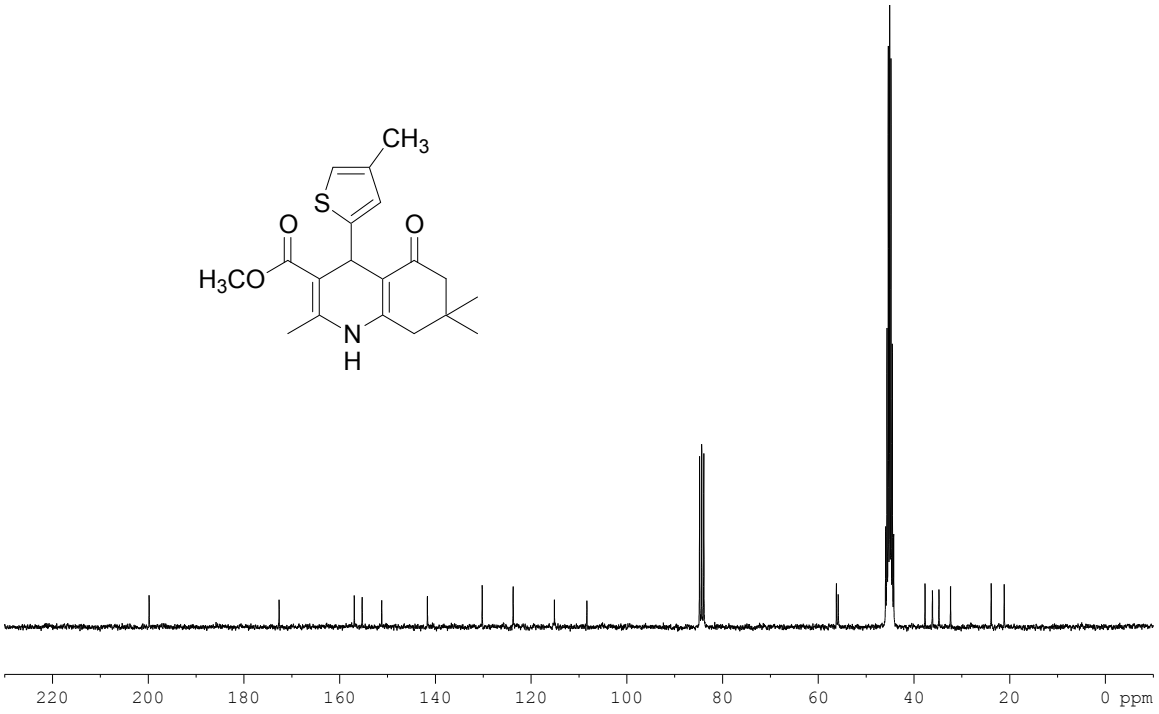




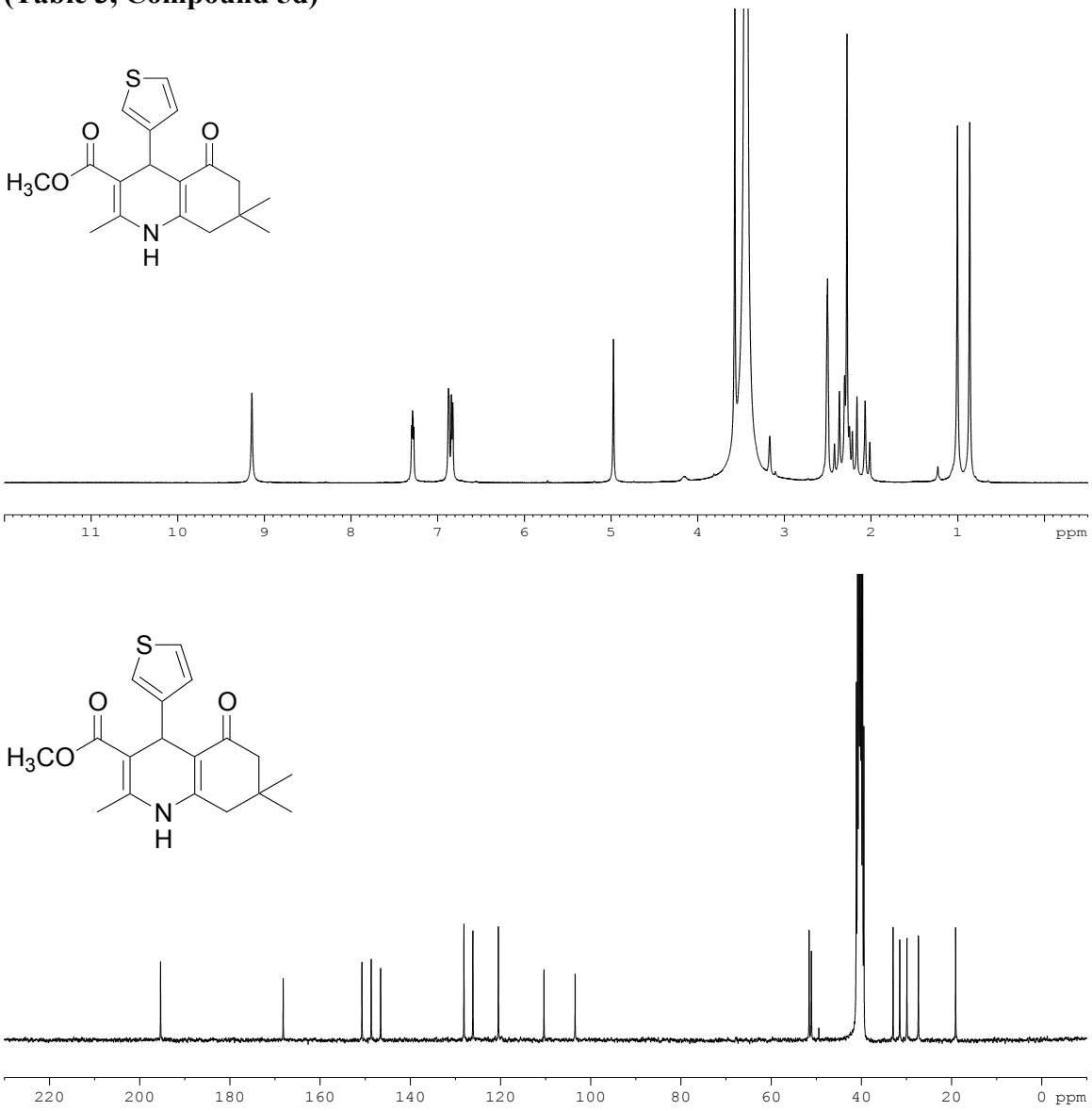


(Table 3, Compound 5c)





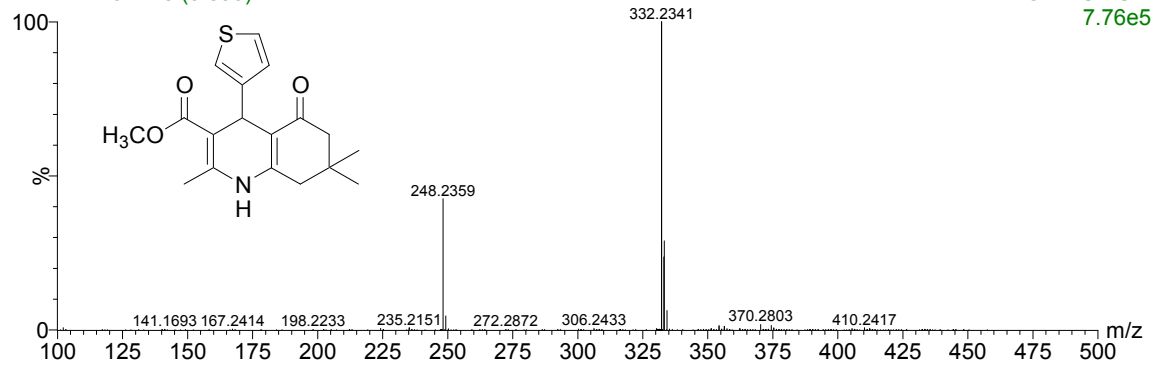
(Table 3, Compound 5d)



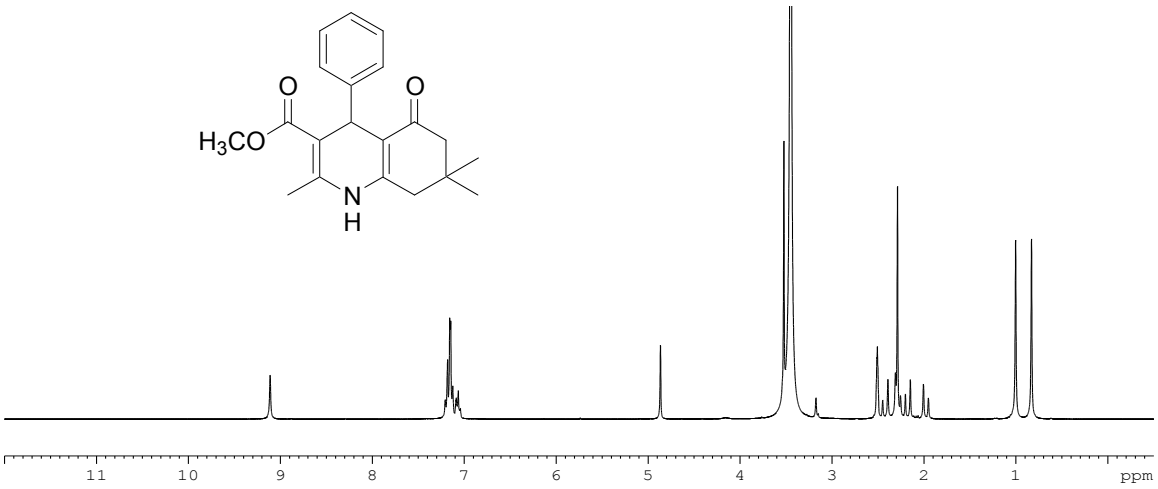
IHBT
22-Nov-2013
AKW7P143-1 48 (0.890)

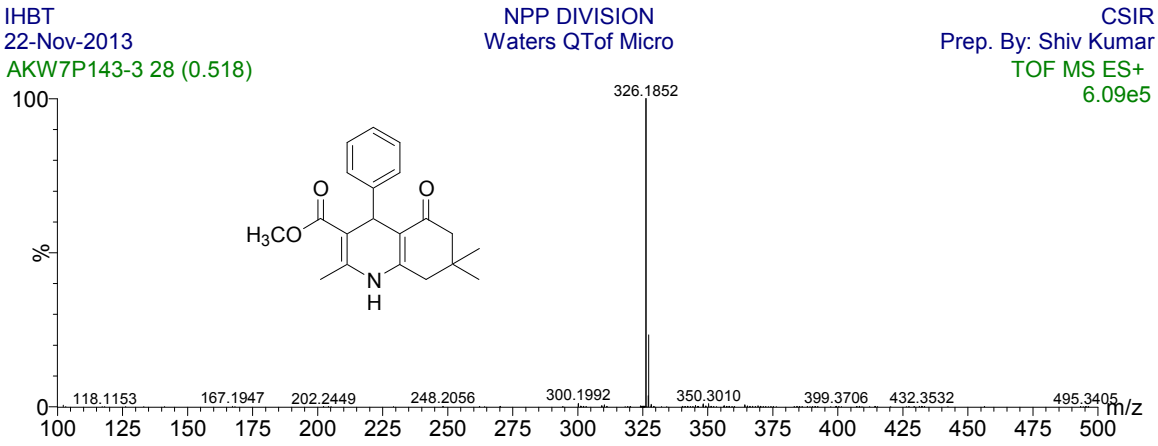
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
TOF MS ES+
7.76e5

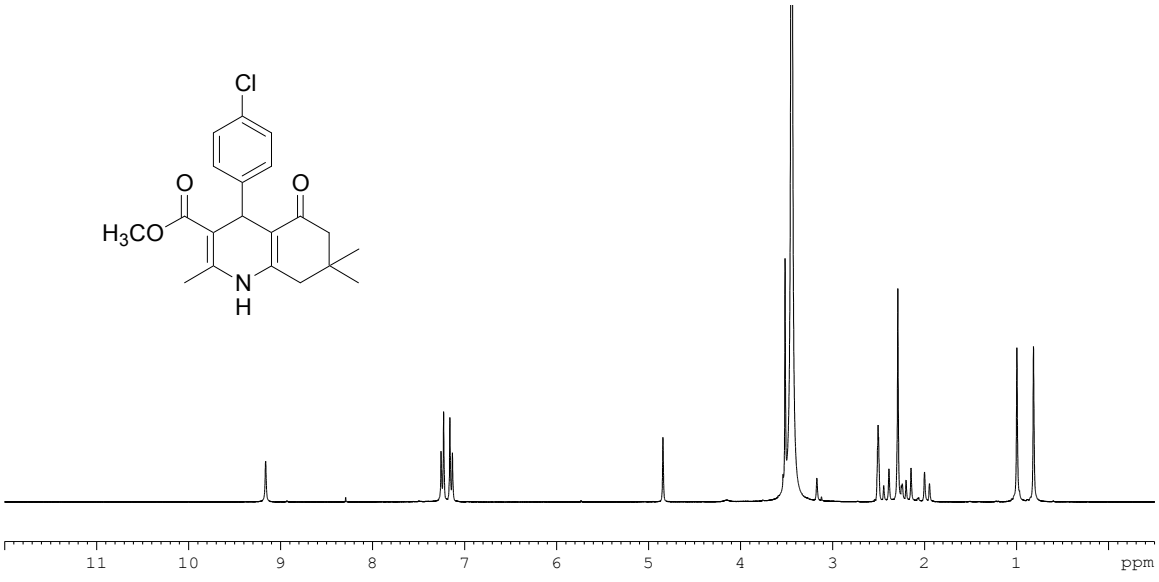


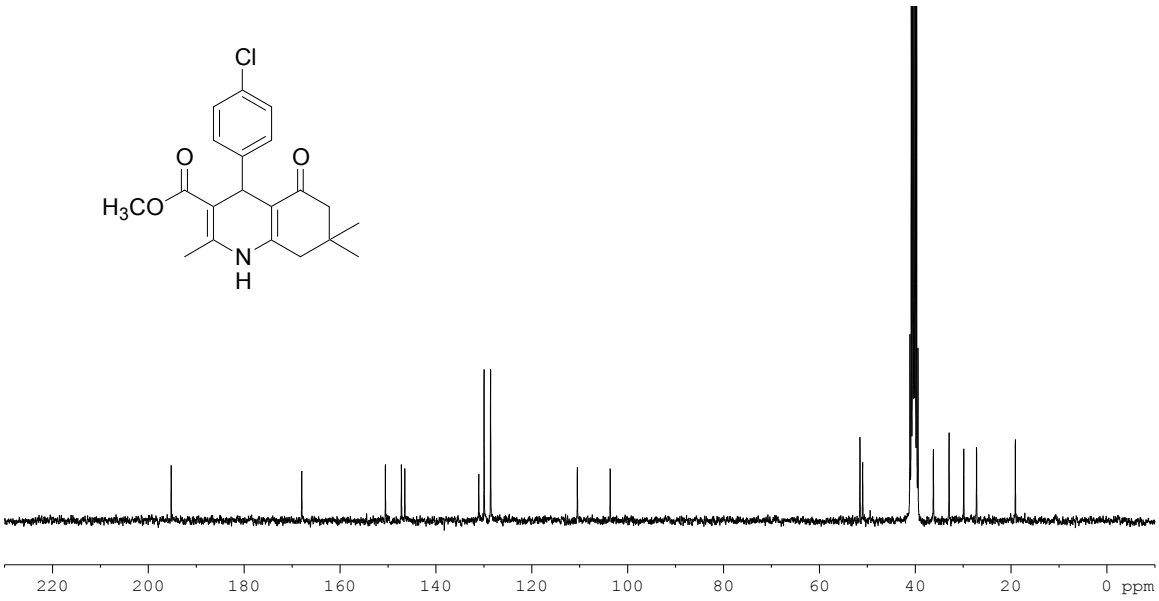
(Table 3, Compound 5e)





(Table 3, Compound 5f)

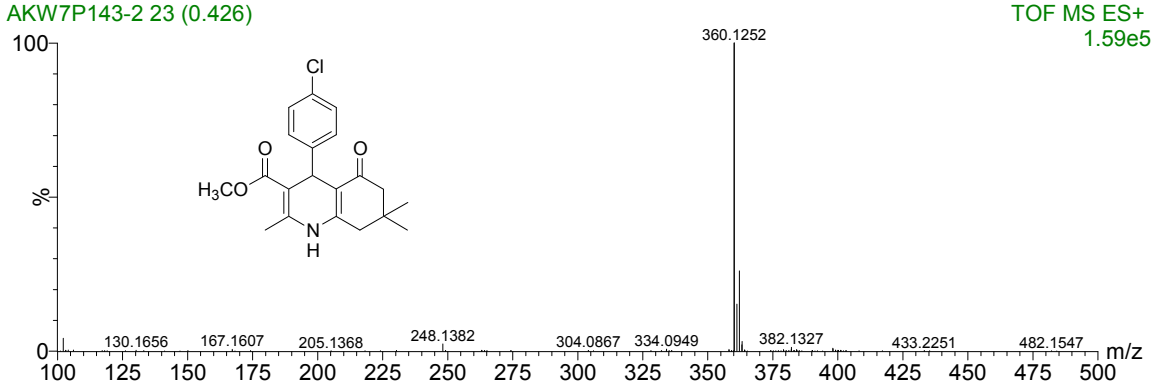




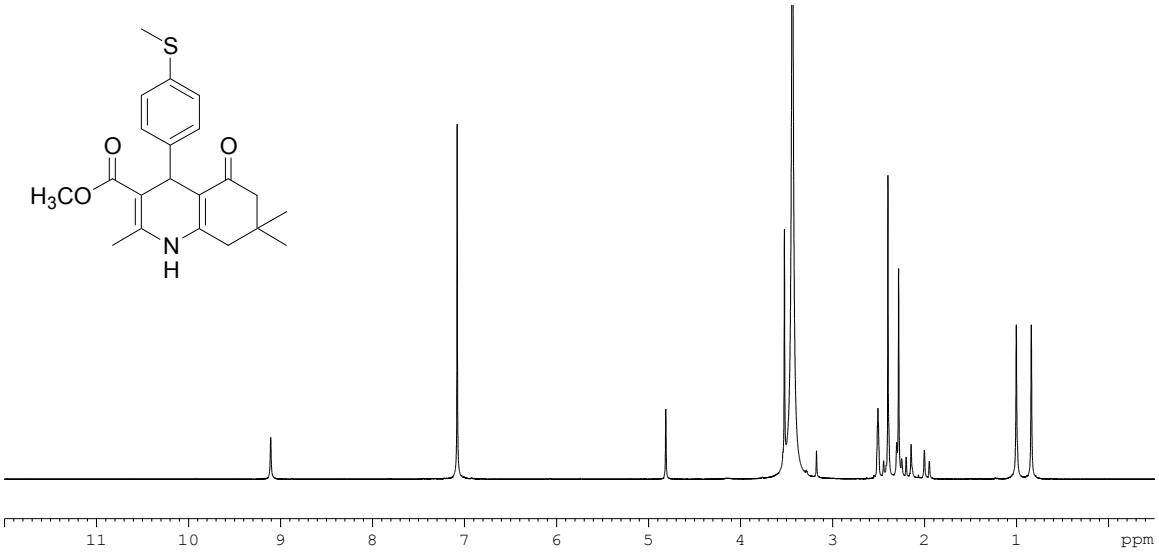
IHBT
22-Nov-2013
AKW7P143-2 23 (0.426)

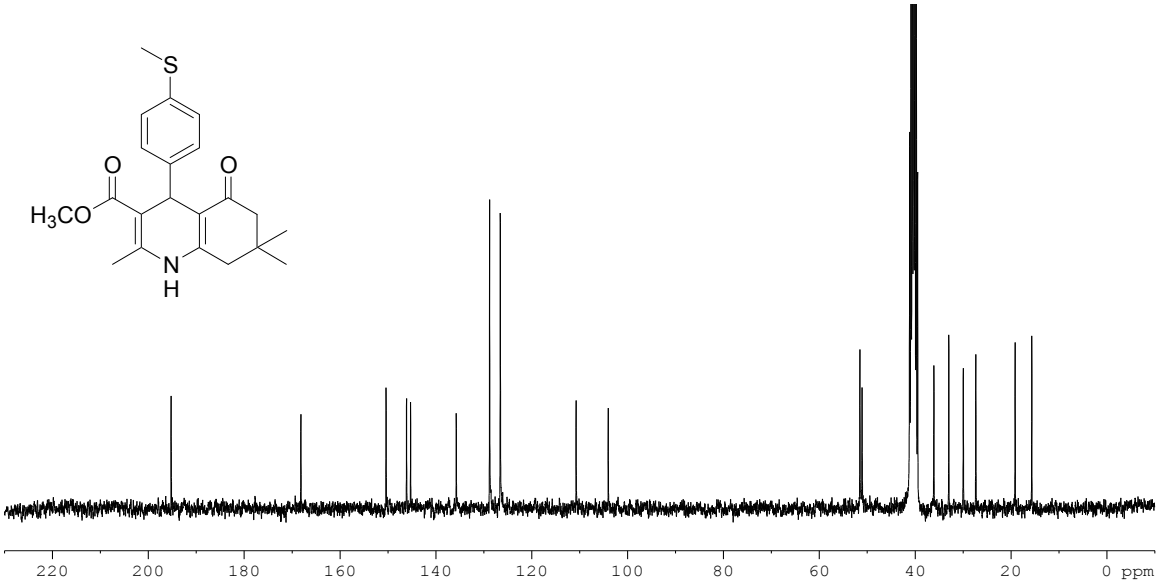
NPP DIVISION
Waters QTof Micro

CSIR
Prep. By: Shiv Kumar
TOF MS ES+
1.59e5



(Table 3, Compound 5g)

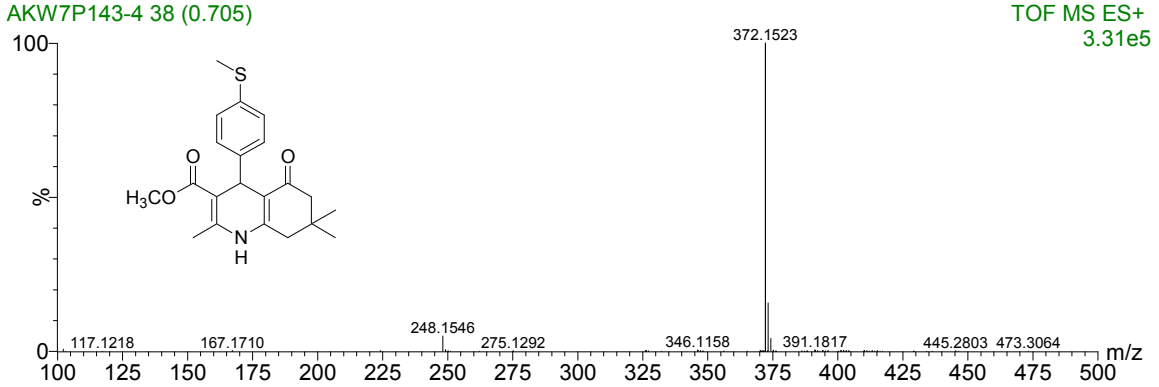




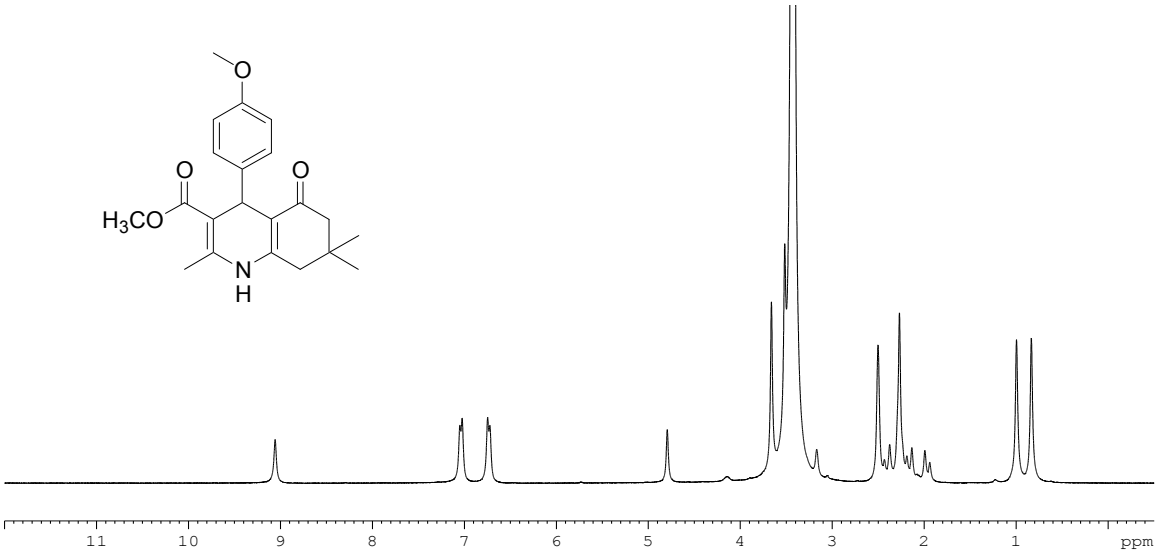
IHBT
22-Nov-2013
AKW7P143-4 38 (0.705)

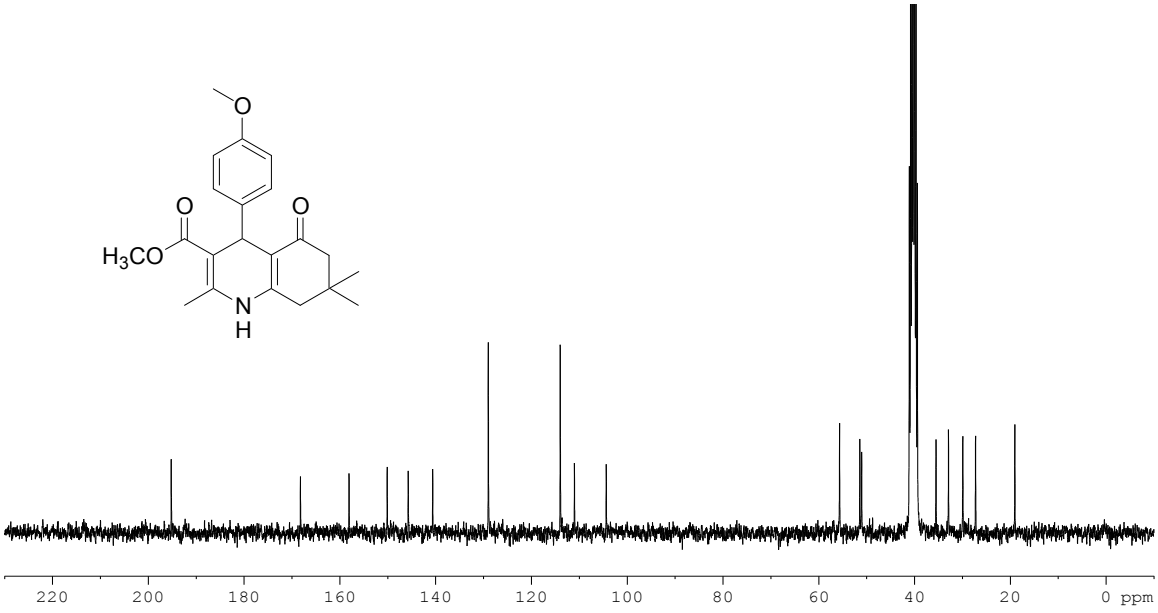
NPP DIVISION
Waters QTof Micro

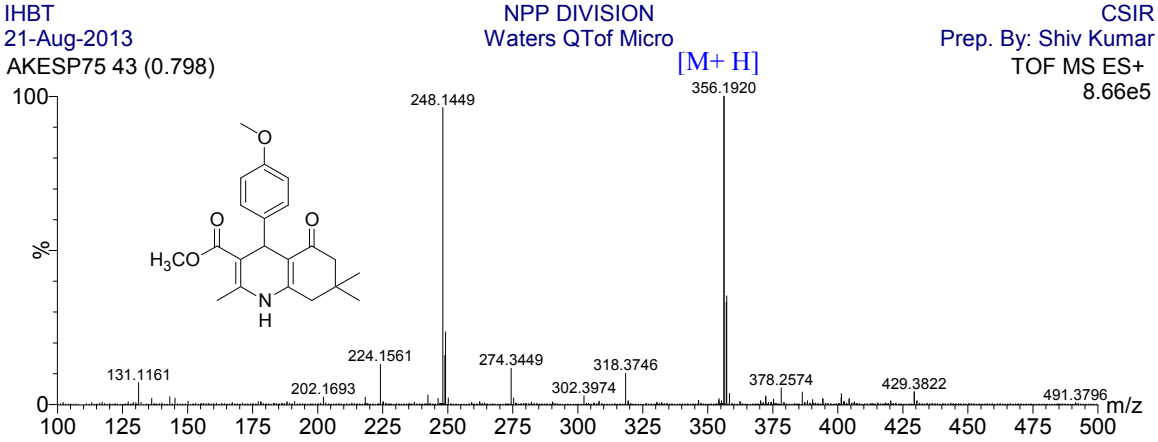
CSIR
Prep. By: Shiv Kumar
TOF MS ES+
3.31e5



(Table 3, Compound 5h)







(Table 3, Compound 5i)