

Supporting Information

An efficient, mild and metal free L-Proline catalyzed construction of fused pyrimidines under microwave conditions in water

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Table of Contents

Contents	Page No.
Methods and Material	S2
Characterization Data	S3-S7
Scanned NMR Spectra	S8-S25

Materials and methods

Experimental

All reagents such as L-proline, 4-hydroxy coumarin, aldehydes etc. were analytical grade and have more than 98% purity. ^1H and ^{13}C NMR spectra were recorded on BRUKER AVANCE II 500 NMR spectrometer using CDCl_3 and DMSO-d_6 as solvent. Purity of the compound was checked by TLC. MS 1927 microwave starter kit was used for microwave reactions. Reaction was carried out under microwave conditions at 300 W in open to air conditions. E-Merck precoated TLC plates, RANKEM silica gel G for preparative thin-layer chromatography were used. Melting points were determined in open capillary and are uncorrected.

Typical Procedure for Synthesis

In a 50 mL, 3 necks round bottom flask, charged appropriate aldehydes (5 mmol), 4-hydroxy coumarin (5 mmol) and urea/thiourea (5 mmol), water (10 mL) and L-proline (10 mol%). Stir the reaction mass and reflux at 70 °C. Reaction completion has monitored by TLC analysis. After reaction completion (monitoring by TLC), filtered the solid mass under vacuum then suck dried the solid and solid was recrystallized in ethanol.

Characterization Data

4-Phenyl-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4a**)

Off white powder, mp 160-162 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3450 (-NH), 1730 (C=O), 1610 (C=); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.36 (s, 1H, -CH), 7.09-7.39 (m, 9H, Ar-H), 7.60 (s, 1H, NH), 7.90 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO d_6): 36 (C-1), 103 (C-2), 115 (C-13), 116 (C-17), 121 (C-14), 122 (C-15), 124 (C-16), 125 (C-6 and 10), 126 (C-8), 126 (C-7), 128 (C-9), 131 (C-5), 140 (C-12), 152 (C-3), 164 (C-4), 165 (C-11); ESI-MS: m/z Calculated for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_3$ 292.29 Found $[\text{M}]^+$ 292.3; C, H and N analyses Calculated for C 69.86, H 4.14, N 9.58, Found C 70.02, H 4.18, N 9.69.

4-(2-Hydroxyphenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4b**)

Off white powder, mp 240-242 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3440 (-NH), 1745 (C=O), 1625 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.25 (s, 1H, -CH), 6.49-6.56 (m, 2H, Ar-H), 6.79 (d, 2H, $J = 8.0$ Hz, Ar-H), 6.98 (t, 1H, $J = 7.5$ Hz, Ar-H), 7.28-7.34 (m, 2H, Ar-H), 7.56 (t, 1H, $J = 7.0$ Hz, Ar-H), 7.67 (1, 1H, -NH), 7.88 (s, 1H, -NH), 9.66 (s, 1H, OH); ^{13}C NMR (125 MHz, DMSO d_6): 35 (C-1), 104 (C-2), 111 (C-13), 112 (C-17), 113 (C-14), 115 (C-15), 117 (C-16), 117 (C-7), 123 (C-8), 129 (C-9), 131 (C-10), 141 (C-5), 152 (C-6), 154 (C-12), 157 (C-3), 164 (C-4), 165 (C-11); ESI-MS: m/z Calculated for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_4$ 308.29 Found $[\text{M}]^+$ 309; C, H and N analyses Calculated for C 66.23, H 3.92, N 9.09, Found C 66.32, H 3.99, N 9.15.

4-(4-Chlorophenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4c**)

Off white powder, mp 195-197 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3430 (-NH), 1735 (C=O), 1655 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.28 (s, 1H, CH), 7.13 (d, 2H, $J = 8.5$ Hz, Ar-H), 7.54-7.34 (m, 6H, Ar-H), 7.56 (s, 1H, NH), 7.87 (s, 1H, -NH); ^{13}C NMR (125 MHz, DMSO d_6): 35 (C-1),

104 (C-2), 116 (C-13), 118 (C-17), 123 (C-14), 128 (C-15), 128 (C-16), 129 (C-7), 130 (C-9), 131 (C-10), 132 (C-5), 137 (C-8), 139 (C-12), 152 (C-3), 164 (C-4), 165 (C-11); ESI-MS: m/z Calculated for $C_{17}H_{11}ClN_2O_3$ 326.73 Found $[M]^+$ 326.7; C, H and N analyses Calculated for C 62.49, H 3.39, N 8.57, Found C 62.32, H 3.49, N 8.65.

4-(4-Dimethylamino phenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4d**)

Off white powder, mp 235-237 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3432 (-NH), 1725 (C=O), 1651 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 3.11 (s, 6H, $\text{N}(\text{CH}_3)_2$), 6.27 (s, 1H, -CH), 7.21-7.28 (m, 8H, Ar-H), 7.51 (s 1H, -NH), 7.79 (s, 1H, -NH); ^{13}C NMR (125 MHz, DMSO d_6): 35 (C-1), 45 ($\text{N}(\text{CH}_3)_2$), 103 (C-2), 111 (C-13), 115 (C-17), 119 (C-14), 122 (C-15 and 16), 124 (C-8 and 5), 128 (C-7 and 9), 131 (C-6 and 10), 131 (C-12), 152 (C-3), 164 (C-4), 167 (C-11); ESI-MS: m/z Calculated for $C_{19}H_{17}N_3O_3$ 335.36 Found $[M]^+$ 336; C, H and N analyses Calculated for C 68.05, H 5.11, N 12.53, Found C 68.12, H 5.22, N 12.61.

4-(3-Nitrophenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4e**)

Off white powder, mp 172-174 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3445 (-NH), 1755 (C=O), 1615 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.37 (s, 1H, -CH), 7.27- 7.33 (m, 4H, Ar-H), 7.38 (d, 2H, $J = 8.5$ Hz, Ar-H), 7.56 (t, 2H, $J = 8.0$ Hz, Ar-H), 7.84 (s, 1H, -NH), 8.09 (s, 1H, -NH); ^{13}C NMR (125 MHz, DMSO d_6): 36 (C-1), 103 (C-2), 115 (C-13), 118 (C-17), 123 (C-14), 123 (C-15), 124 (C-16), 124 (C-5), 128 (C-6), 130 (C-10), 131 (C-7 and 9), 145 (C-8), 150 (C-12), 152 (C-3), 164 (C-4), 166 (C-11); ESI-MS: m/z Calculated for $C_{17}H_{11}N_3O_5$ 337.29 Found $[M]^+$ 337.3; C, H and N analyses Calculated for C 60.54, H 3.29, N 12.46, Found C 60.70, H 3.41, N 12.29.

4-(4-Hydroxy-3-methoxyphenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4f**)

Off white powder, mp 208-210 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3437 (-NH), 1730 (C=O), 1627 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 3.72 (s, 3H, OCH₃), 6.39 (s, 1H, -CH), 7.16-7.39 (m, 7H, Ar-H), 7.60 (s, 1H, -NH), 7.93 (s, 1H, -NH), 10.20 (br, 1H, OH); ^{13}C NMR (125 MHz, DMSO d_6): 35 (C-1), 56 (OCH₃), 104 (C-2), 116 (C-13), 117 (C-17), 123 (C-14), 123 (C-15), 124 (C-16), 125 (C-8), 126 (C-9), 128 (C-7), 129 (C-10), 130 (C-6), 132 (C-5), 139 (C-12), 152 (C-3), 164 (C-4), 166 (C-11); ESI-MS: m/z Calculated for C₁₈H₁₄N₂O₅ 338.31 Found [M]⁺ 338.3; C, H and N analyses Calculated for C 63.90, H 4.17, N 8.28, Found C 63.76, H 4.31, N 8.11.

4-(2-chlorophenyl)-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidine-2,5-dione (**4g**)

Pale yellow, mp 198-200 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3445 (-NH), 1755 (C=O), 1632 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.28 (s, 1H, -CH), 7.13 (d, 1H, Ar-H, $J = 8.5$ Hz), 7.15-7.34 (m, 7H, Ar-H), 7.56 (t, 2H, Ar-H, $J = 1.5$ Hz), 7.85 (d, 1H, Ar-H, $J = 8.0$ Hz), 9.66 (br, 1H, -NH), 9.81 (br, 1H, -NH); ^{13}C NMR (125 MHz, DMSO d_6): 36 (C-1), 103 (C-2), 116 (C-13), 117 (C-17), 123 (C-14), 123 (C-15), 127 (C-16), 128 (C-5), 130 (C-6 and 10), 131 (C-7 and 9), 139 (C-8), 152 (C-12), 164 (C-3), 165 (C-4), 166 (C-11); C, H and N analyses Calculated for C, 62.49, H, 3.39, N, 8.57, Found C 62.68, H 3.08, N 8.81.

4-Phenyl-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4h**)

Off white powder, mp 185-187 °C; IR (KBr) ($\nu_{\max}$, cm^{-1}): 3448 (-NH), 1715 (C=O), 1625 (C=C); ^1H NMR (500 MHz, DMSO d_6): δ_{H} 6.34 (s, 1H, -CH), 7.24-7.39 (m, 9H, Ar-H), 7.82 (s, 1H, -NH), 8.09 (s, 1H, -NH); ^{13}C NMR (125 MHz, DMSO d_6): 36 (C-1), 103 (C-2), 115 (C-13), 119 (C-17), 123 (C-14), 123 (C-15), 124 (C-16), 127 (C-5), 131 (C-6 and 10), 132 (C-7 and 9), 145 (C-8), 150 (C-12), 152 (C-3), 164 (C-4), 166 (C-11); ESIMS: m/z Calculated for C₁₇H₁₂N₂O₂S

308.35 Found [M]⁺ 308.3; C, H and N analyses Calculated for C₁₇H₁₂N₂O₃S 308.35 Found [M]⁺ 308.3; C 66.22, H 3.92, N 9.08, Found C 66.46, H 4.01, N 9.18.

4-(2-Hydroxyphenyl)-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4i**)

Off white powder, mp 170-172 °C; IR (KBr) ($\nu_{\max}$, cm⁻¹): 3435 (-NH), 1725 (C=O), 1635 (C=C); ¹H NMR (500 MHz, DMSO *d*₆): δ_{H} 5.38 (s, 1H, -CH), 7.05-7.69 (m, 8H, Ar-H), 8.02 (s, 1H, -NH), 8.15 (s, 1H, -NH), 11.74 (s, 1H, OH); ¹³C NMR (125 MHz, DMSO *d*₆): 35 (C-1), 102 (C-2), 109 (C-13), 110 (C-17), 111 (C-14), 113 (C-15), 115 (C-16), 115 (C-5), 121 (C-6), 127 (C-10), 129 (C-7), 139 (C-9), 150 (C-8), 152 (C-12), 155 (C-3), 162 (C-4), 163 (C-11); ESI-MS: *m/z* Calculated for C₁₇H₁₂N₂O₃S 324.35 Found [M]⁺ 324.4; C, H and N analyses Calculated for C 62.95, H 3.73, N 8.64, Found C 62.88, H 3.81, N 8.72.

4-(4-Chlorophenyl)-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4j**)

Off white powder, mp 187-189 °C; IR (KBr) ($\nu_{\max}$, cm⁻¹): 3440 (-NH), 1732 (C=O), 1625 (C=C); ¹H NMR (500 MHz, DMSO *d*₆): δ_{H} 6.29 (s, 1H, -CH), 7.14 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.24-7.35 (m, 5H, Ar-H), 7.55-7.59 (m, 2H, Ar-H), 7.88 (s, 1H, -NH), 7.93 (s, 1H, -NH); ¹³C NMR (125 MHz, DMSO *d*₆): 35 (C-1), 104 (C-2), 116 (C-13), 117 (C-17), 123 (C-14), 128 (C-15), 129 (C-16), 130 (C-5), 131 (C-6 and 10), 132 (C-7 and 9), 137 (C-8), 138 (C-12), 152 (C-3), 164 (C-4), 166 (C-11); ESI-MS: *m/z* Calculated for C₁₇H₁₁ClN₂O₂S 342.80 Found [M]⁺ 343; C, H and N analyses Calculated for C 59.56, H 3.23, N 8.17, Found C 60.78, H 3.31, N 8.22.

4-(4-Dimethylaminophenyl)-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4k**)

Off white powder, mp 238-240 °C; IR (KBr) ($\nu_{\max}$, cm⁻¹): 3435 (-NH), 1725 (C=O), 1622 (C=C); ¹H NMR (500 MHz, DMSO *d*₆): δ_{H} 3.11 (s, 6H, N(CH₃)₂), 6.26 (s, 1H, -CH), 7.17-7.28 (m, 4H, Ar-H), 7.49-7.56 (m, 4H, Ar-H), 7.69 (s, 1H, NH), 7.80 (s, 1H, NH); ¹³C NMR (125 MHz,

DMSO d_6): 36 (C-1), 45 (N(CH₃)₂), 103 (C-2), 111 (C-13), 115 (C-17), 119 (C-14), 123 (C-15), 123 (C-16), 124 (C-7 and 9), 124 (C-6 and 10), 128 (C-5 and 8), 131 (C-12), 153 (C-3), 164 (C-4), 167 (C-11); ESI-MS: m/z Calculated for C₁₉H₁₇N₃O₂S 351.42 Found [M]⁺ 351.2; C, H and N analyses Calculated for C 64.94, H 4.88, N 11.96, Found C 64.78, H 4.01, N 12.10.

4-(3-Nitrophenyl)-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4l**)

Off white powder, mp 182-184 °C; IR (KBr) ($\nu_{\max}$, cm⁻¹): 3430 (-NH), 1725 (C=O), 1615 (C=C); ¹H NMR (500 MHz, DMSO d_6): δ_H 6.34 (s, 1H, -CH), 7.23-7.30 (m, 4H, Ar-H), 7.35 (d, 2H, J = 9.0 Hz, Ar-H), 7.53 (t, 2H, Ar-H, J = 7.5 Hz), 7.80 (s, 1H, NH), 8.07 (s, 1H, NH); ¹³C NMR (125 MHz, DMSO d_6): 37 (C-1), 103 (C-2), 115 (C-13), 118 (C-17), 123 (C-14), 123 (C-15), 123 (C-16), 124 (C-7) 124 (C-9), 128 (C-6) 130 (C-10), 131 (C-5) 145 (C-8), 150 (C-12), 152 (C-3), 164 (C-4), 166 (C-11); C, H and N analyses Calculated for C 57.78, H 3.14, N 11.89, Found C 57.43, H 3.33, N 12.06.

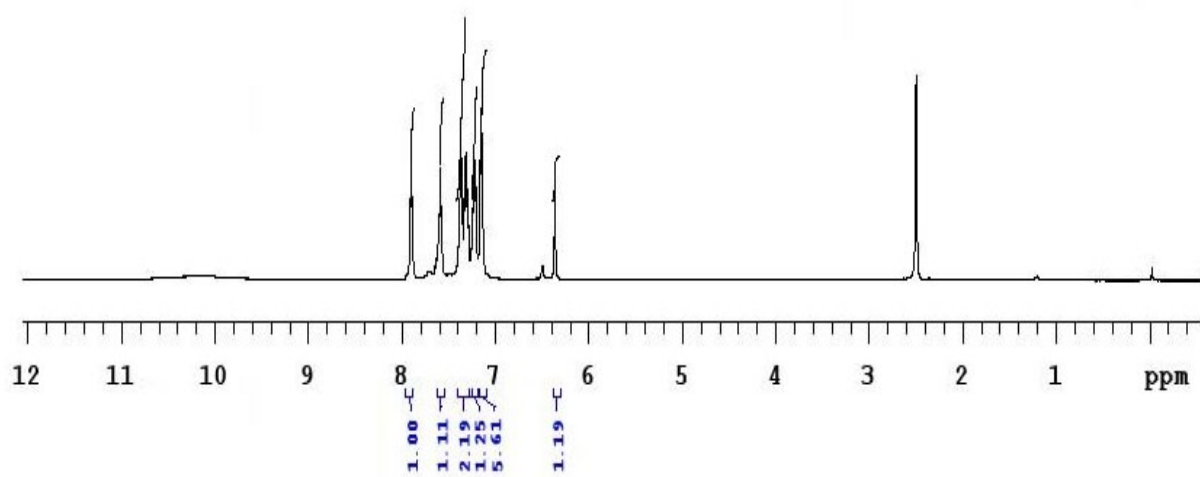
4-(4-Methoxyphenyl)-2-thioxo-3,4-dihydro-1*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4m**)

Off white powder, mp 262-264 °C; IR (KBr) ($\nu_{\max}$, cm⁻¹): 3430 (-NH), 1725 (C=O), 1612 (C=C); ¹H NMR (500 MHz, DMSO d_6): δ_H 3.58 (s, 3H, OCH₃) 6.24 (s, 1H, -CH), 6.53 (d, 1H, J = 7.5 Hz, Ar-H), 6.66 (dd, 2H, J = 7.0 Hz, Ar-H), 7.36 (m, 4H, Ar-H), 7.89 (s, 1H, NH), 8.20 (s, 1H, NH); ¹³C NMR (125 MHz, DMSO d_6): 35 (C-1), 56 (OCH₃) 105 (C-2), 115 (C-13), 116 (C-17), 118 (C-14), 119 (C-15), 124 (C-16), 124 (C-7) 128 (C-9), 132 (C-6) 134 (C-10), 144 (C-5) 144 (C-8), 145 (C-12), 152 (C-3), 164 (C-4), 164 (C-11); C, H and N analyses Calculated for C 63.89, H 4.17, N 8.28, Found C 64.14, H 4.38, N 8.41.

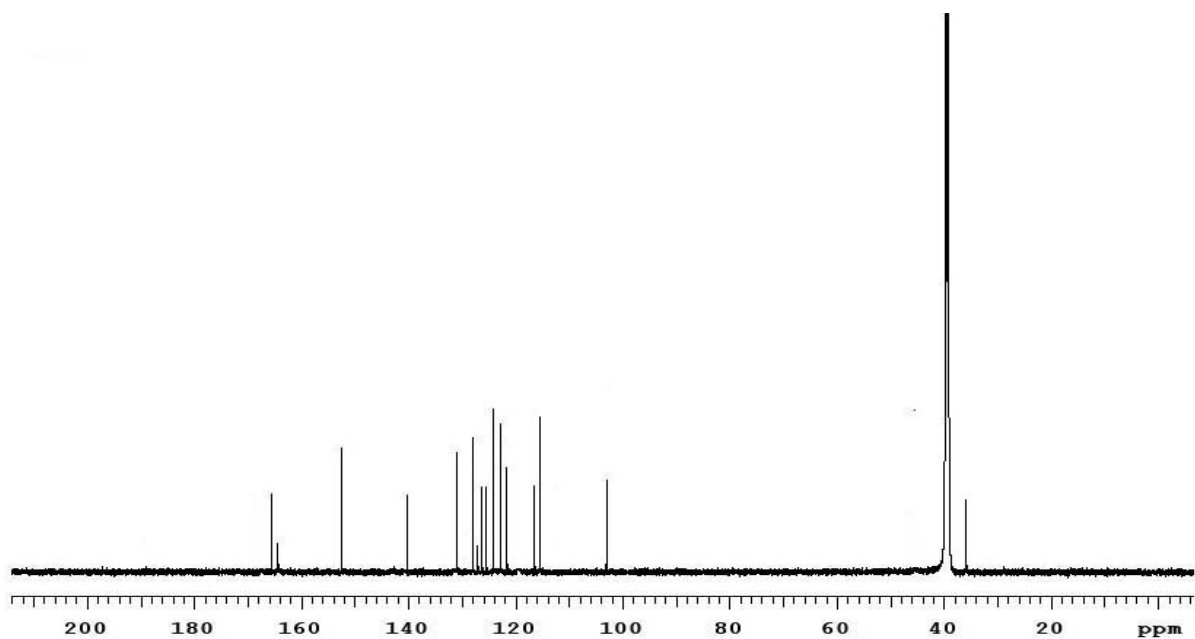
Scanned NMR Spectra

Compound 4a

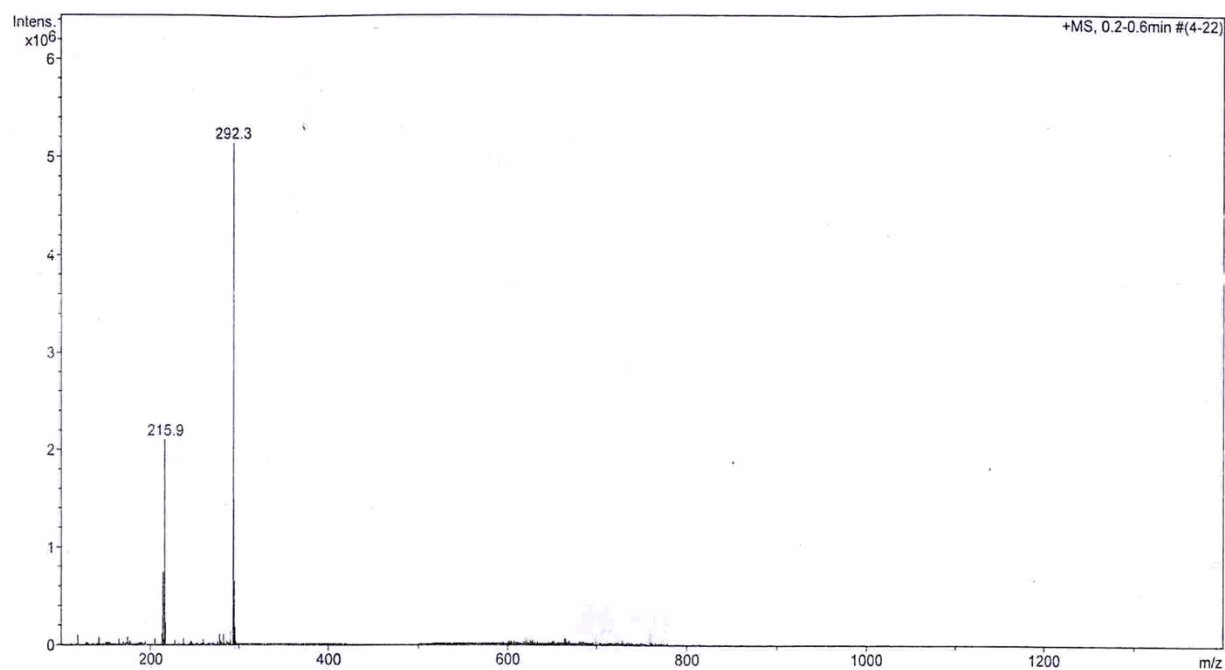
¹H NMR



¹³C NMR

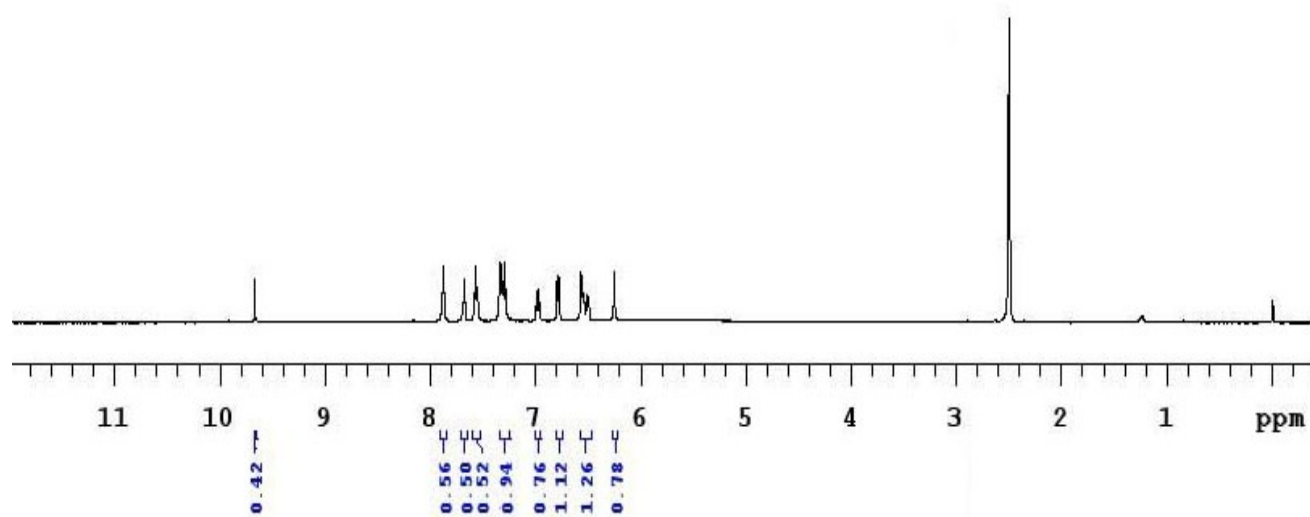


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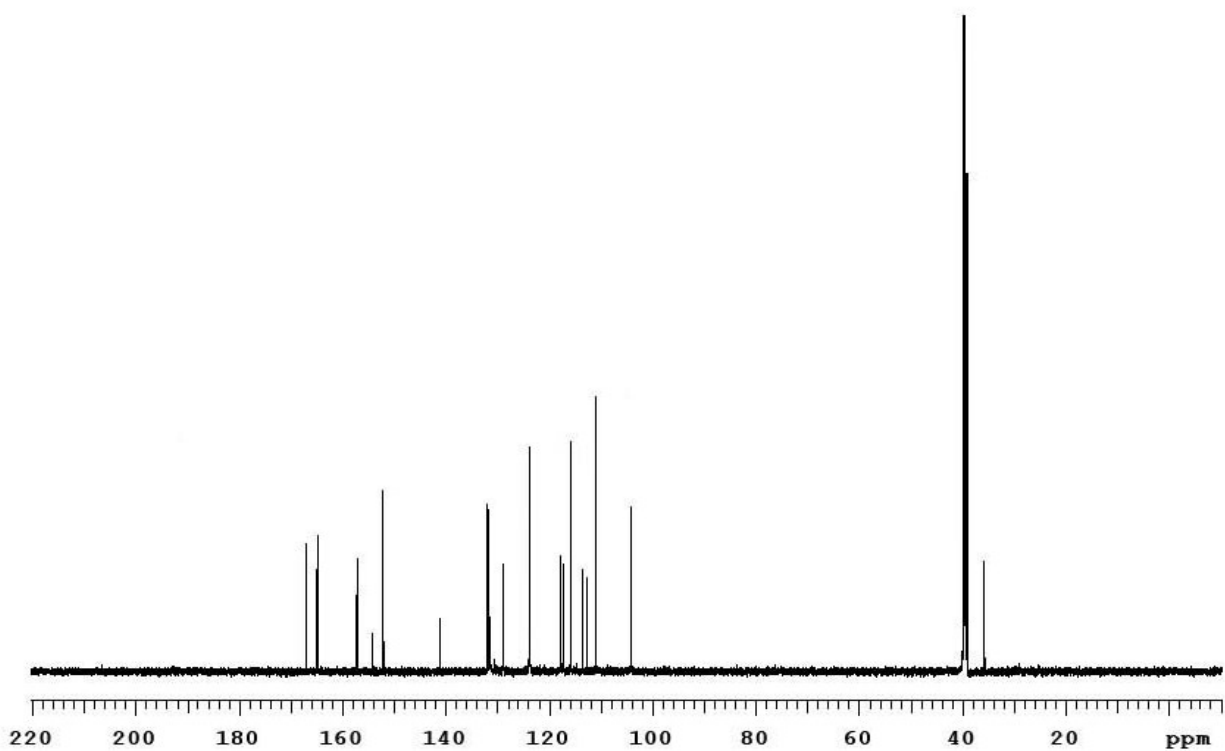


Compound 4b

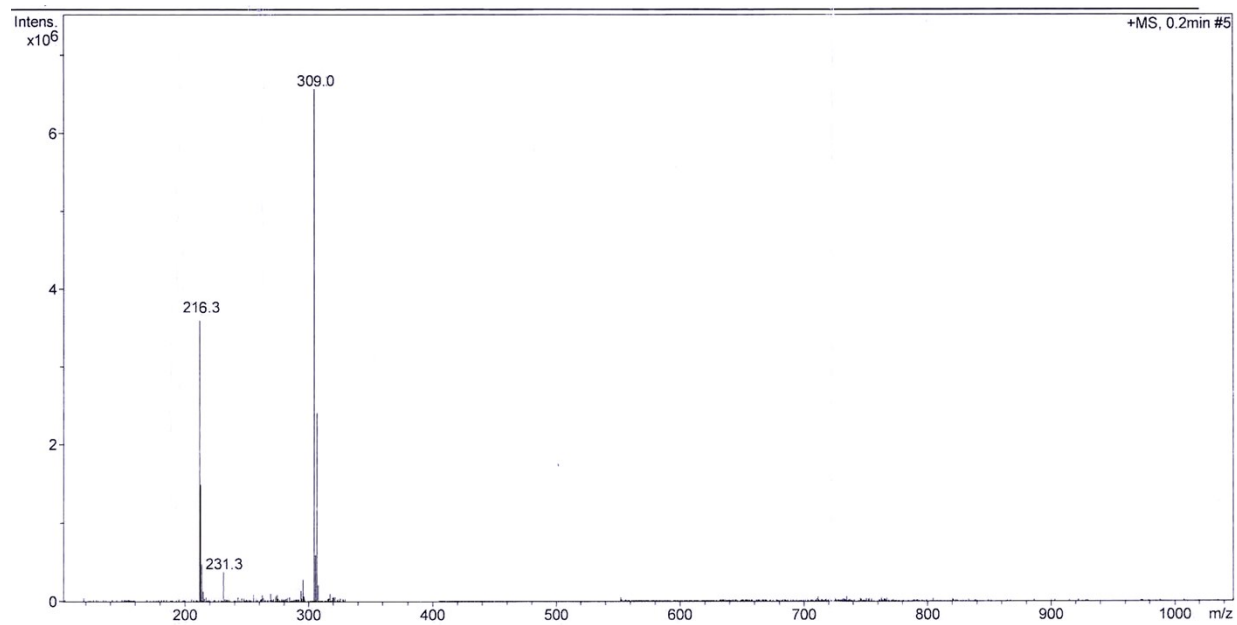
¹H NMR



¹³C NMR

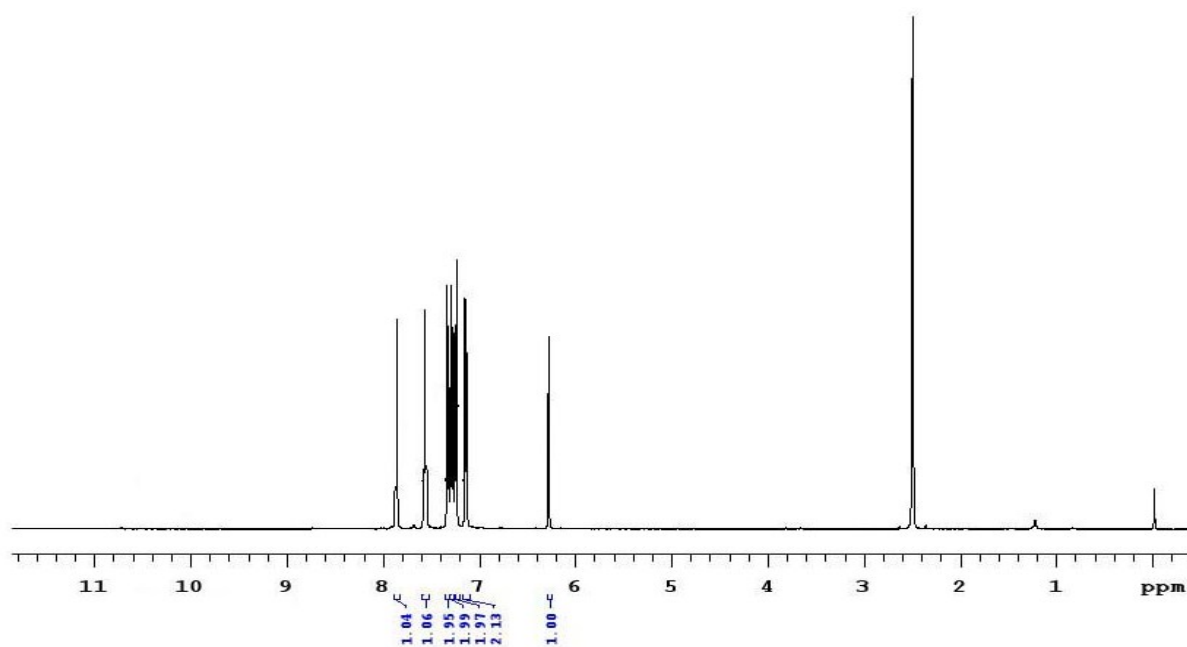


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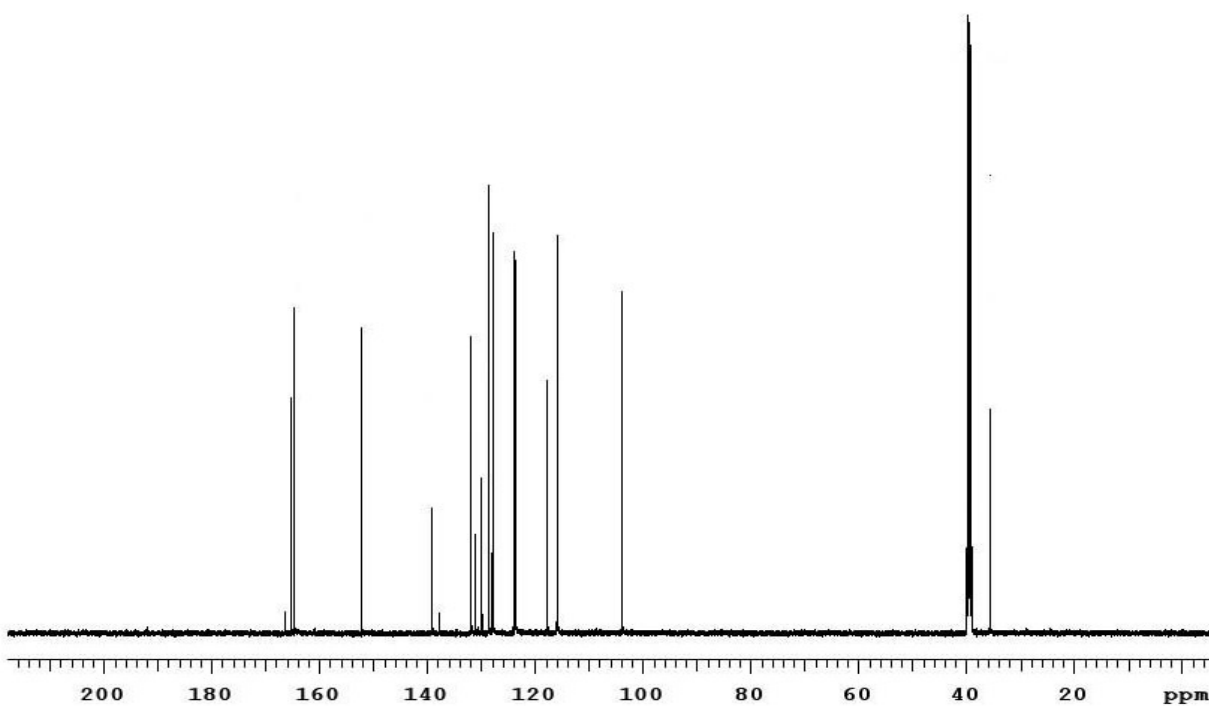


Compound 4c

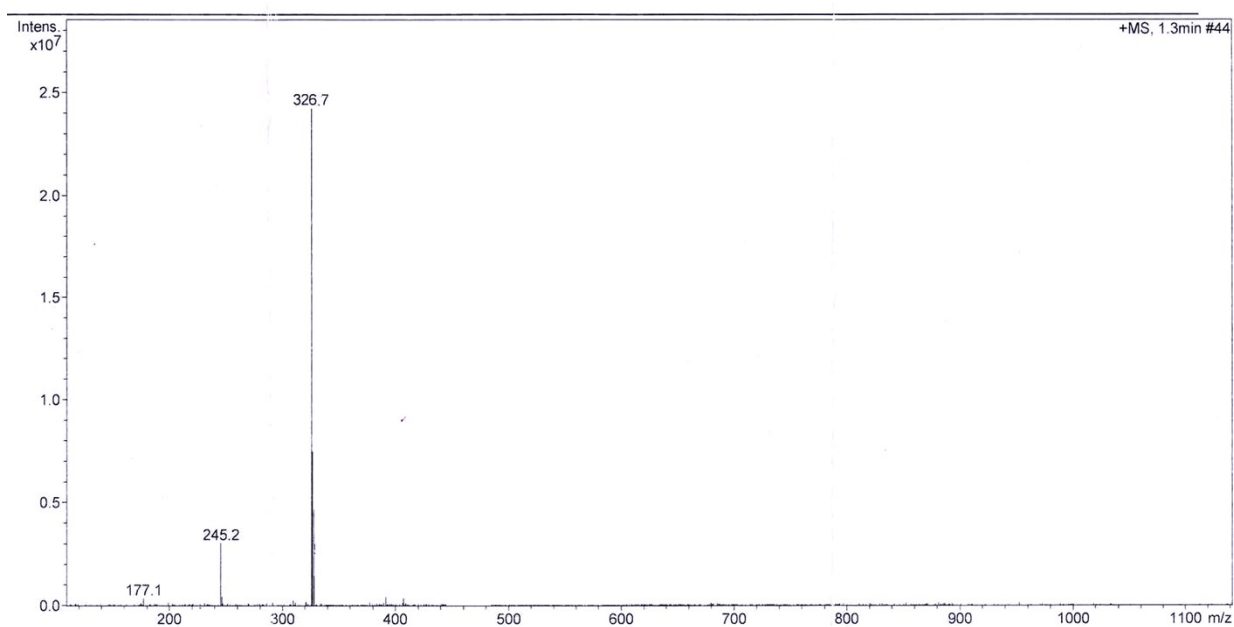
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¹³C NMR

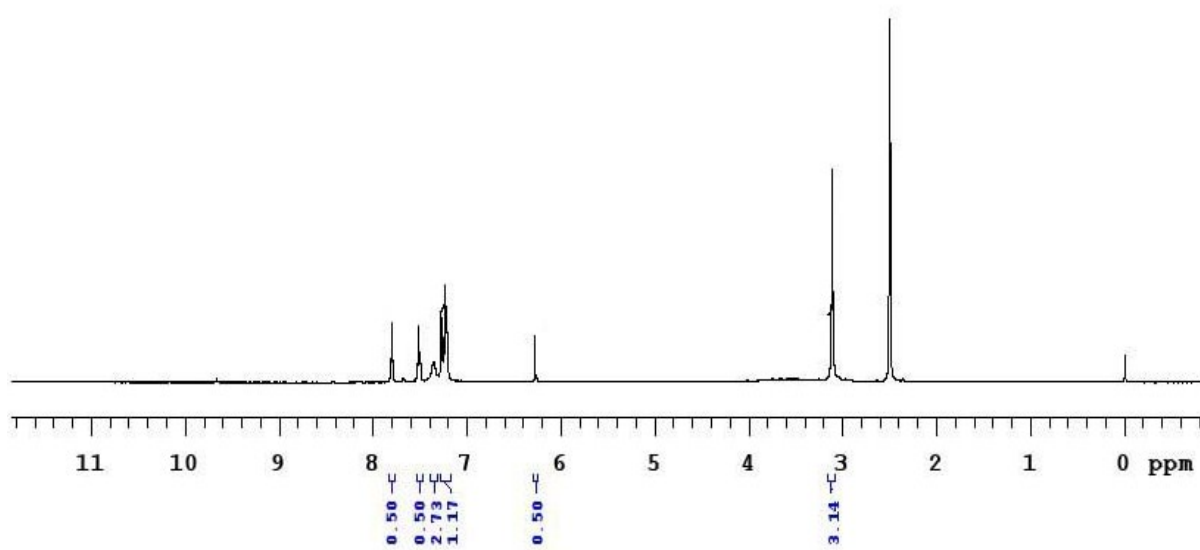


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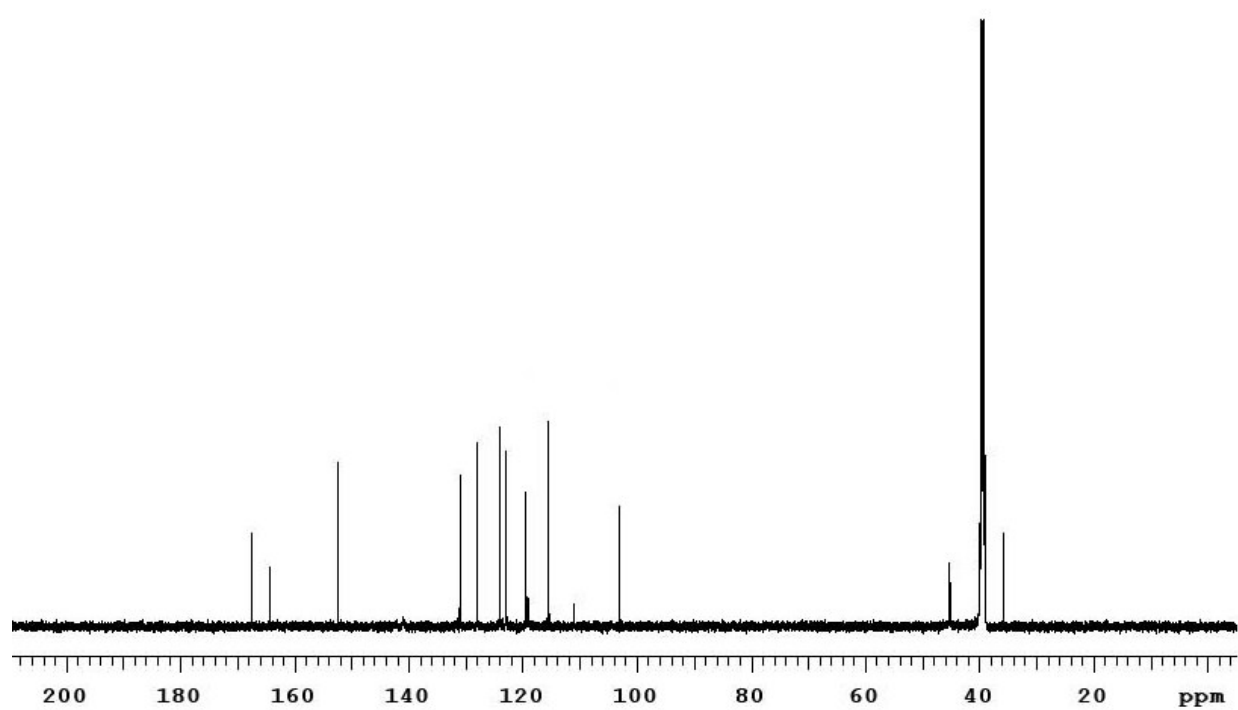


Compound 4d

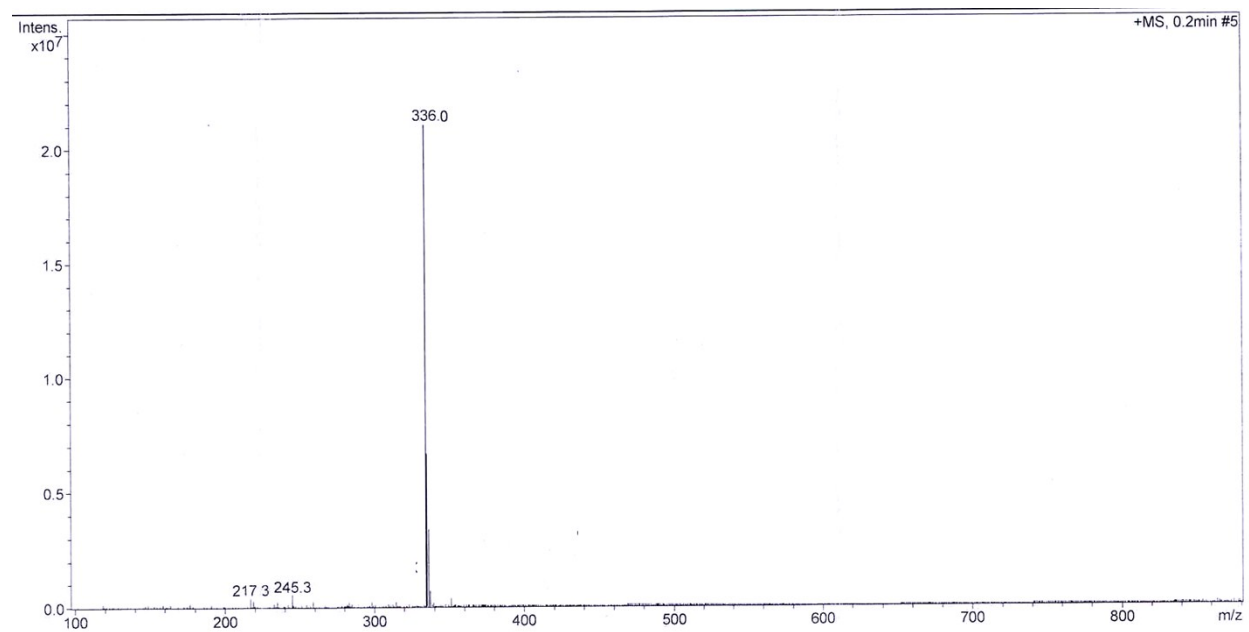
^1H NMR



^{13}C NMR

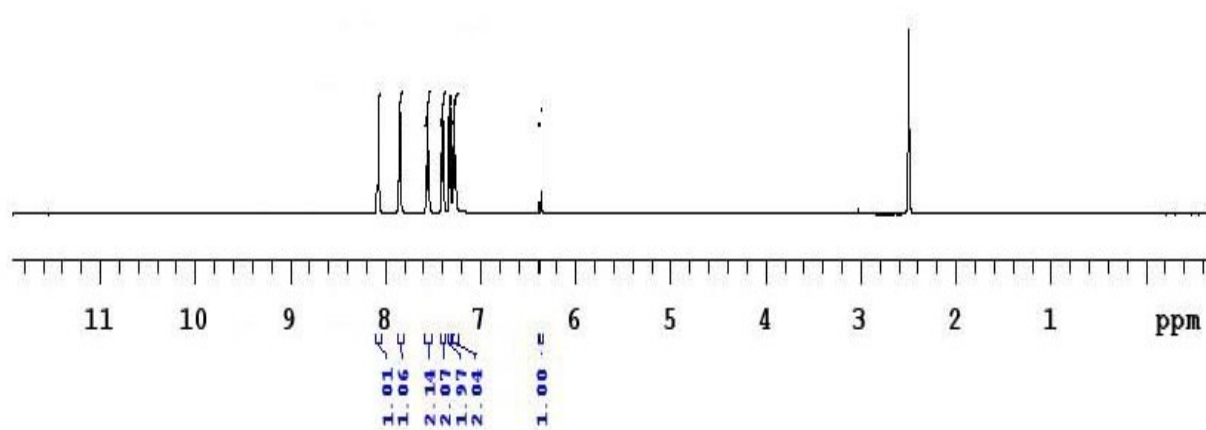


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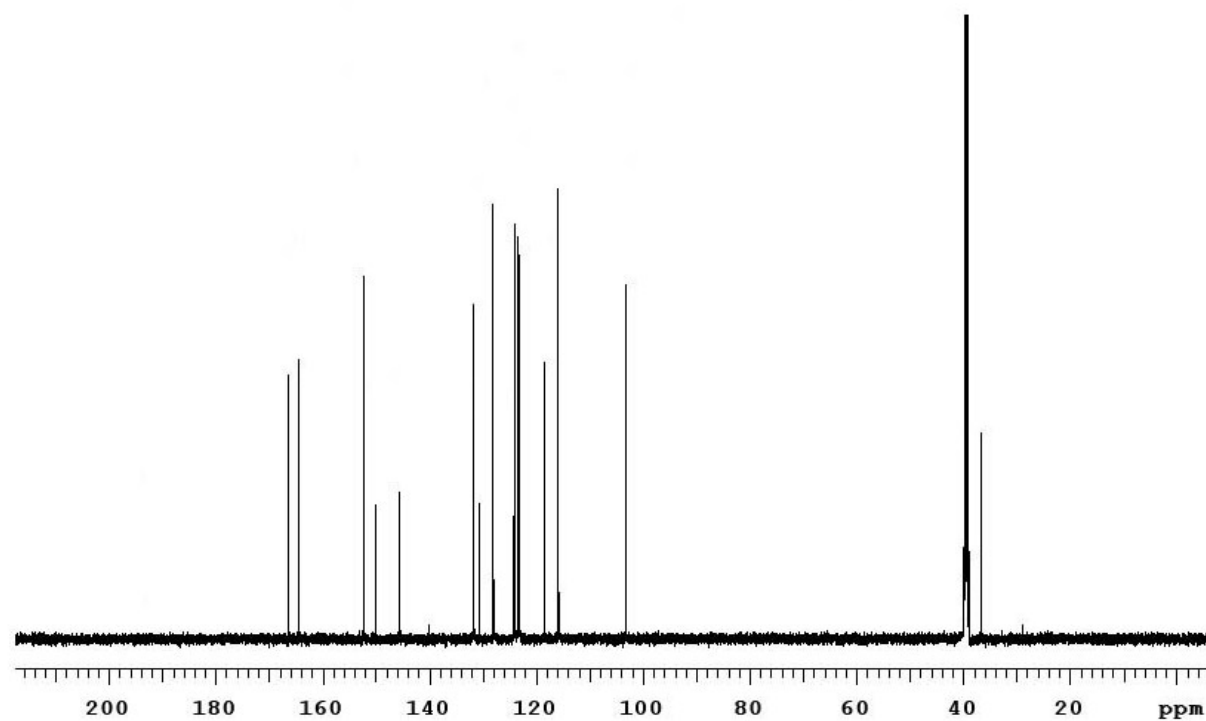


Compound 4e

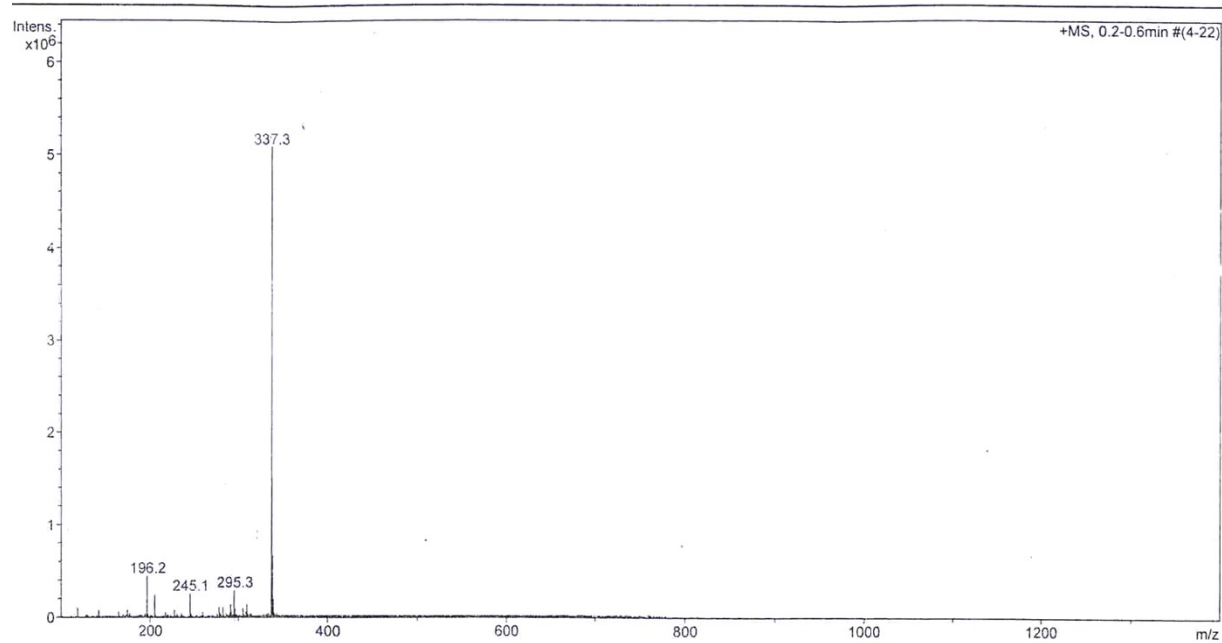
¹H NMR



¹³C NMR

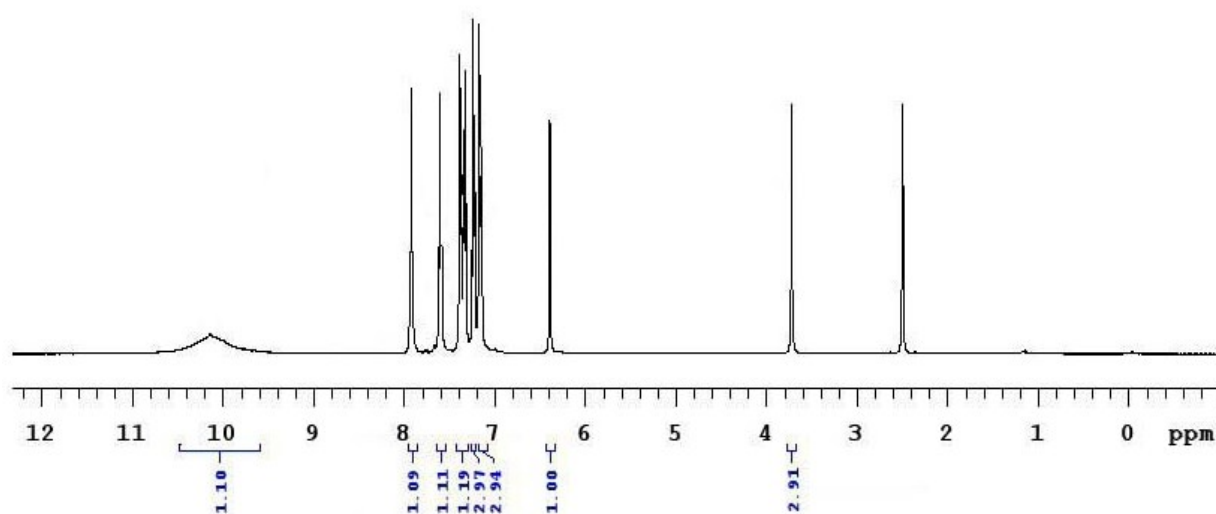


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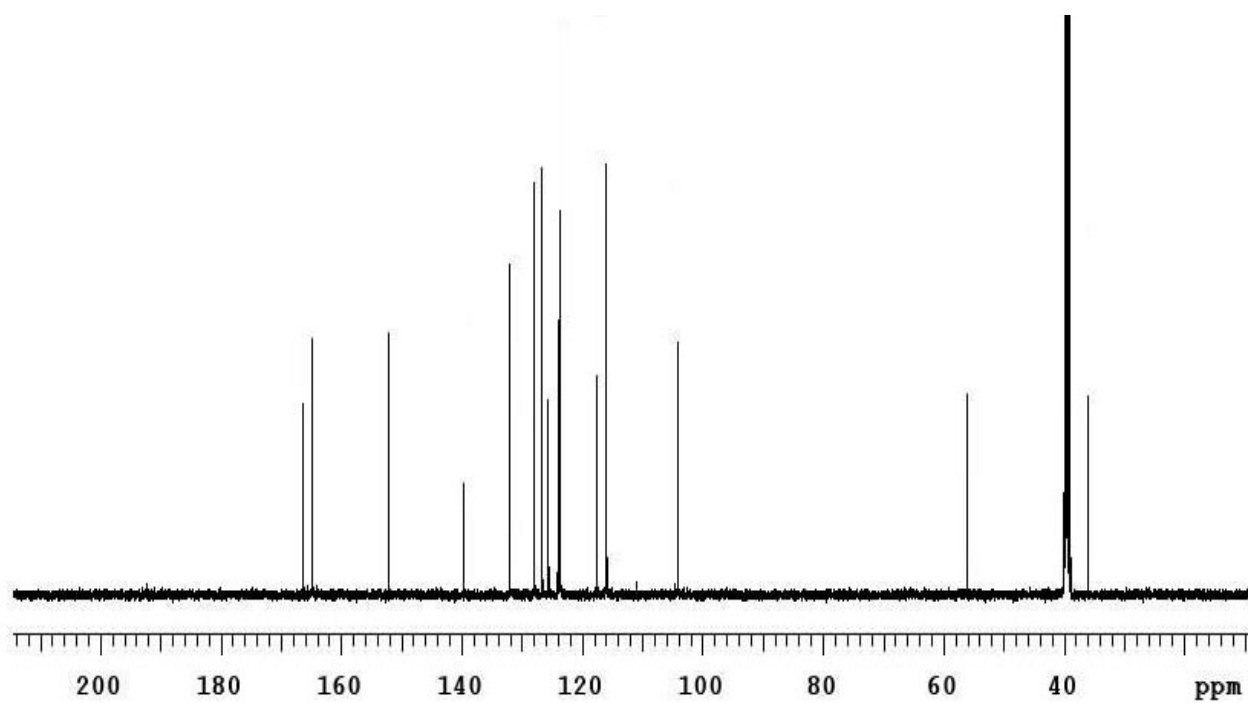


Compound 4f

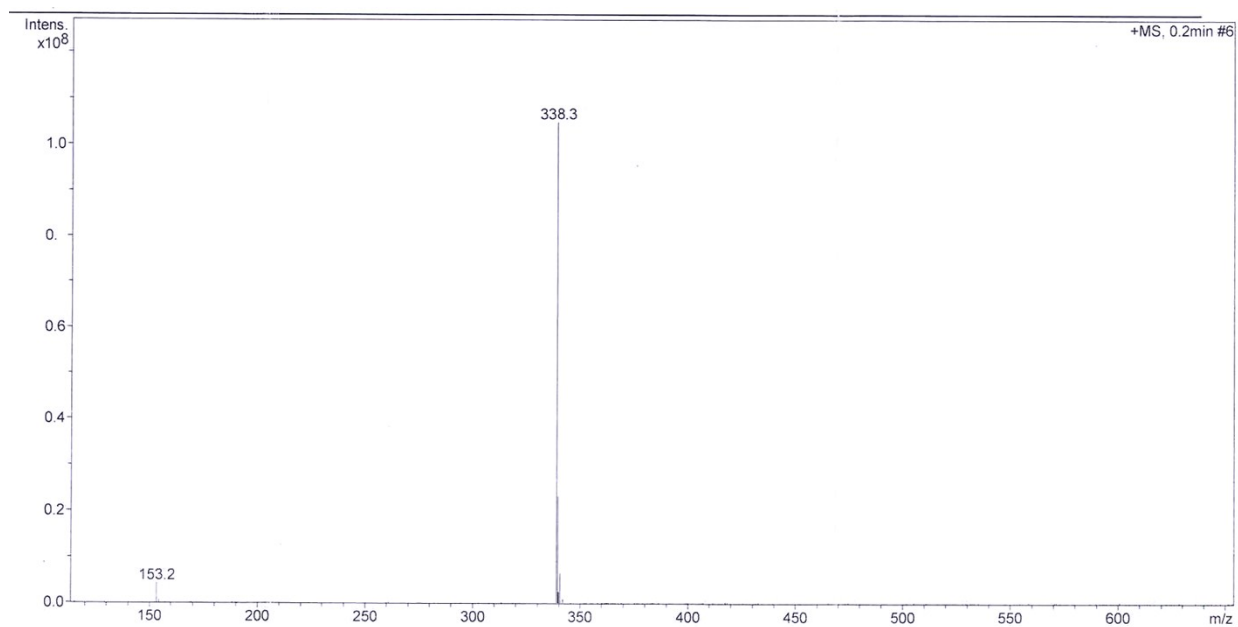
^1H NMR



^{13}C NMR

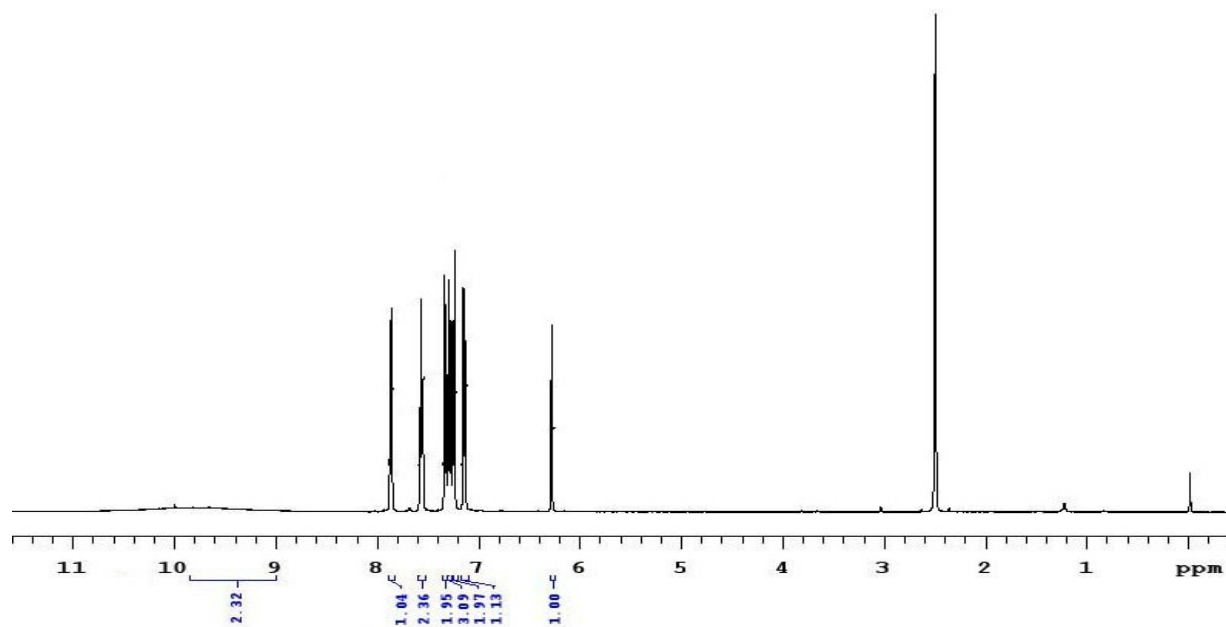


Mass

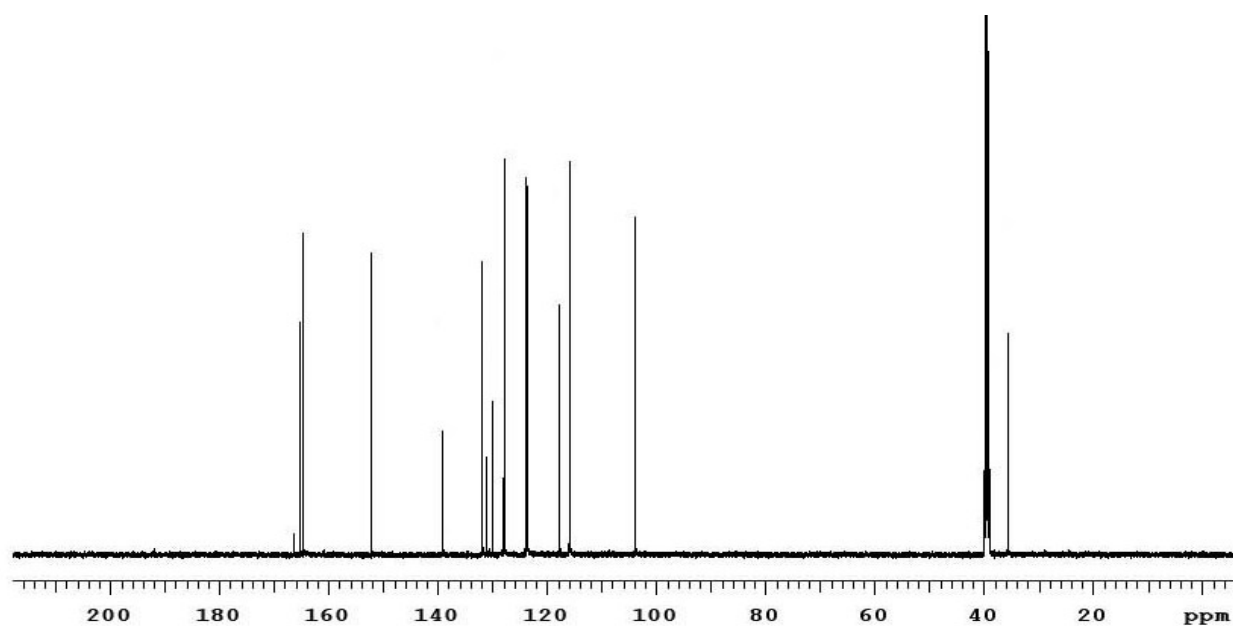


Compound 4g

¹H NMR

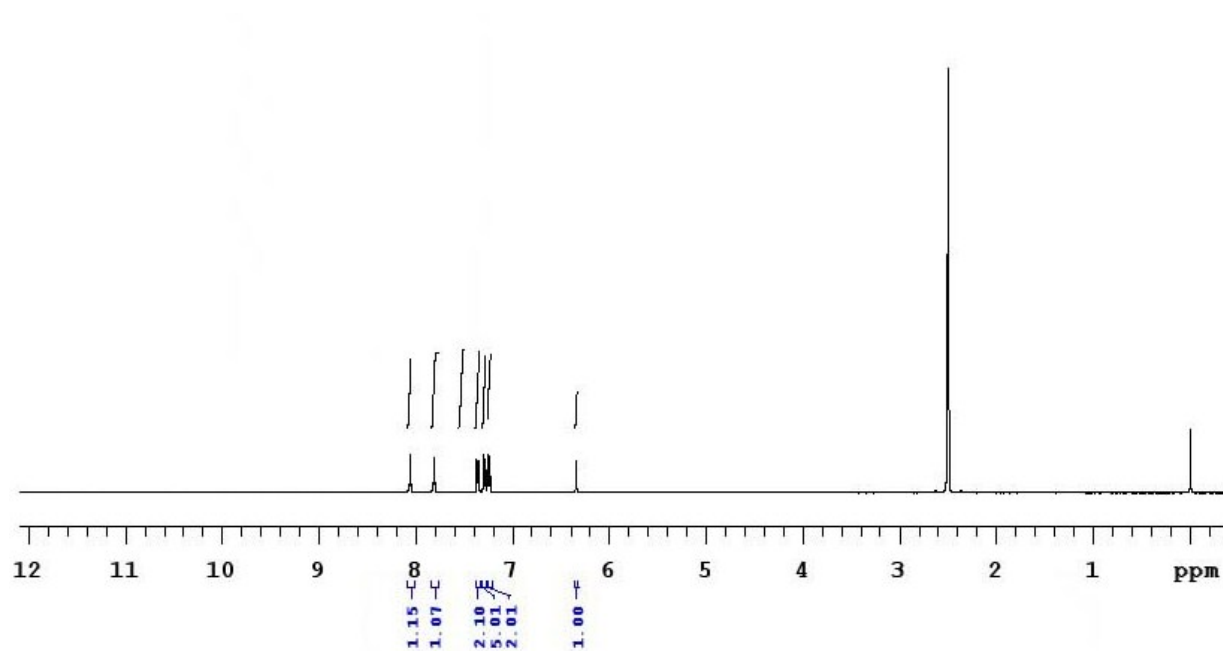


¹³C NMR

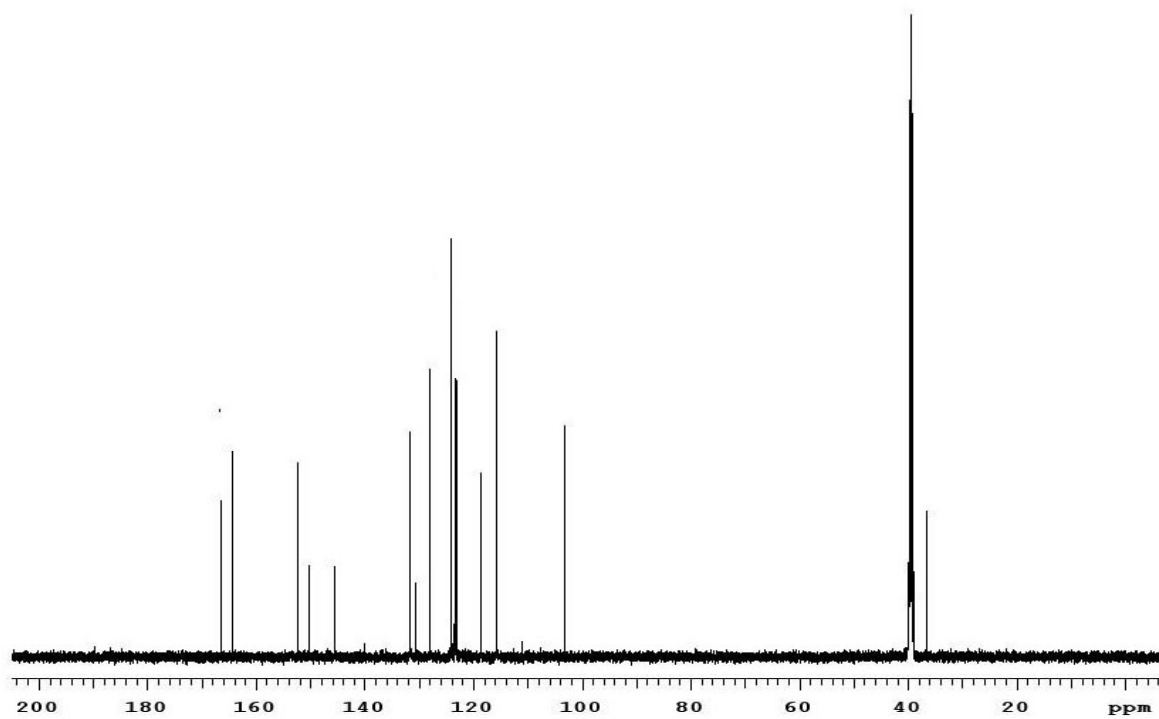


Compound 4h

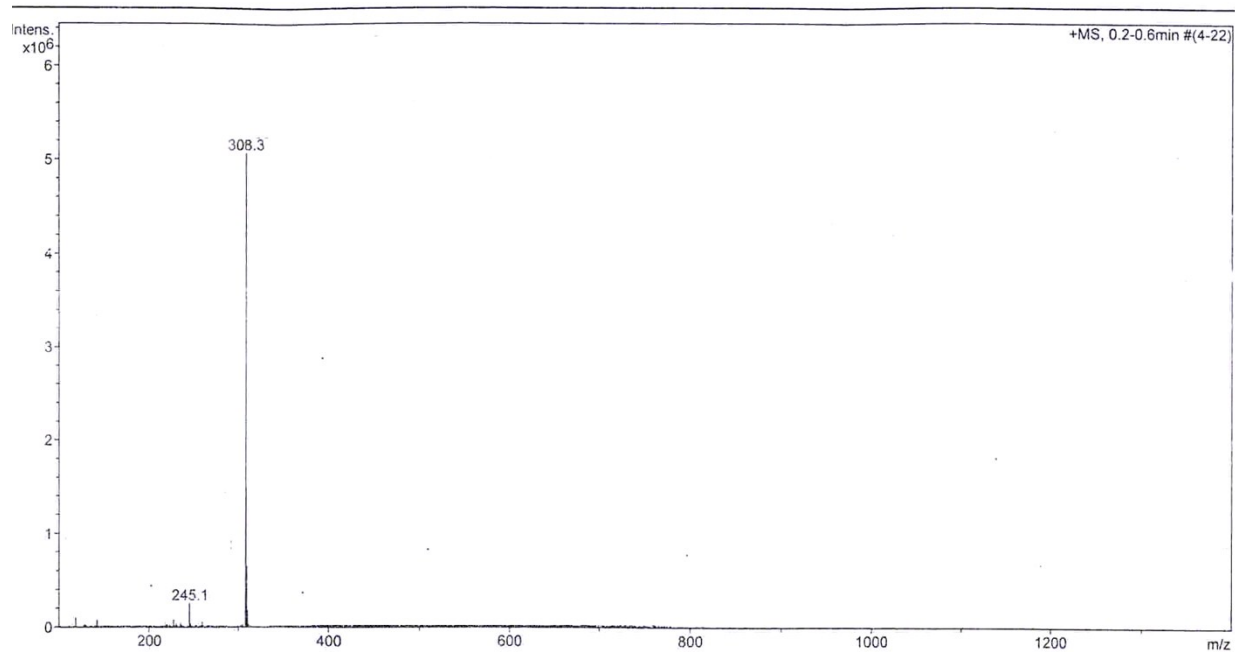
¹H NMR



¹³C NMR

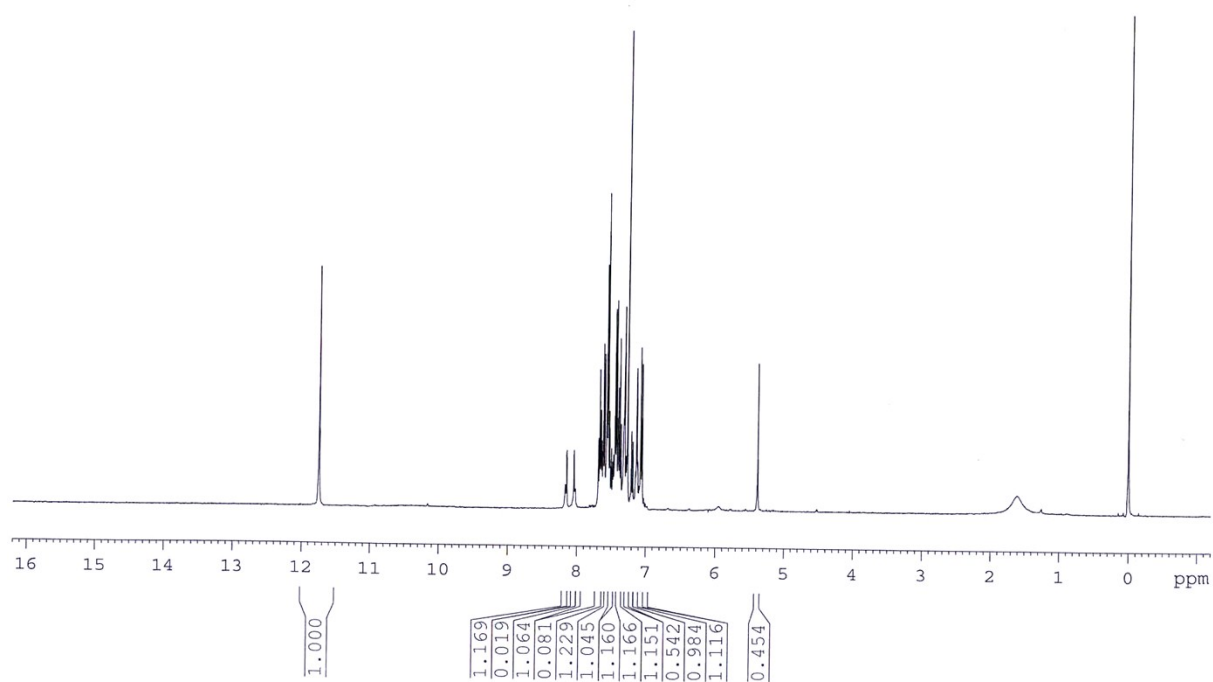


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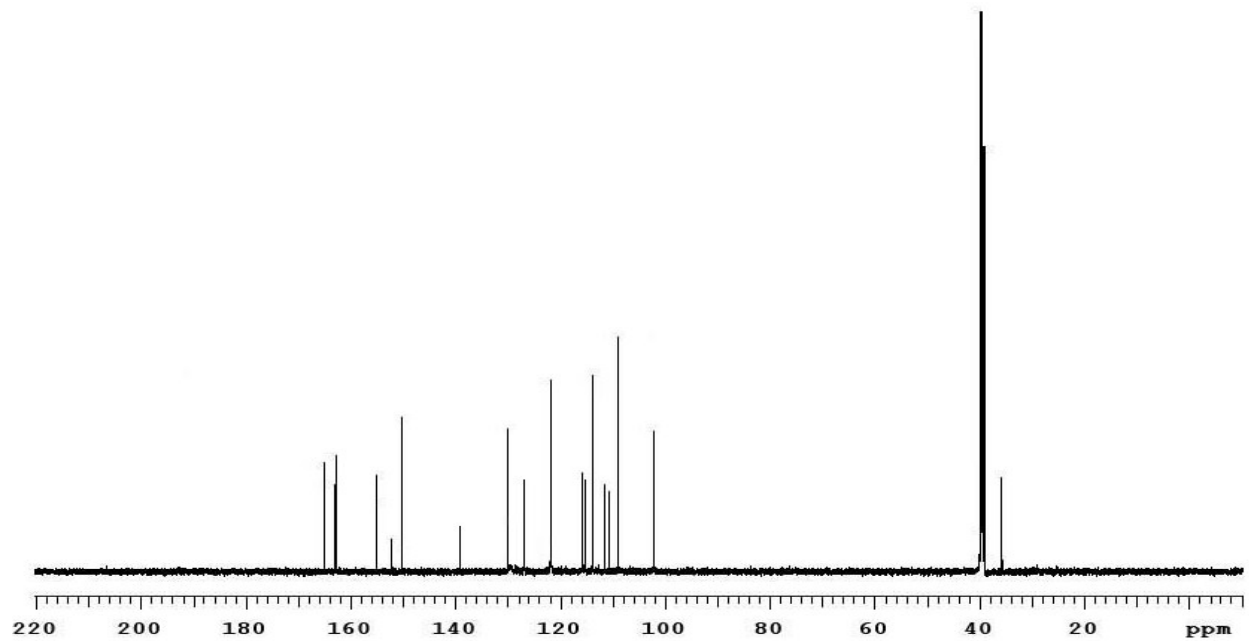


Compound 4i

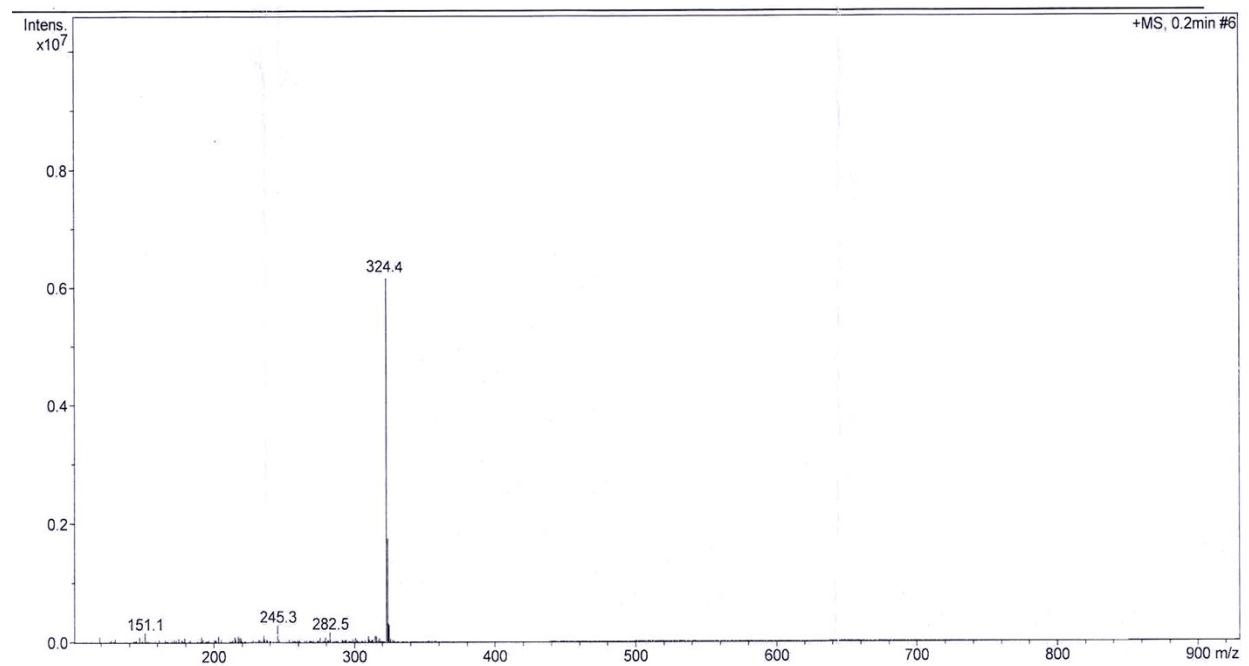
¹H NMR



¹³C NMR

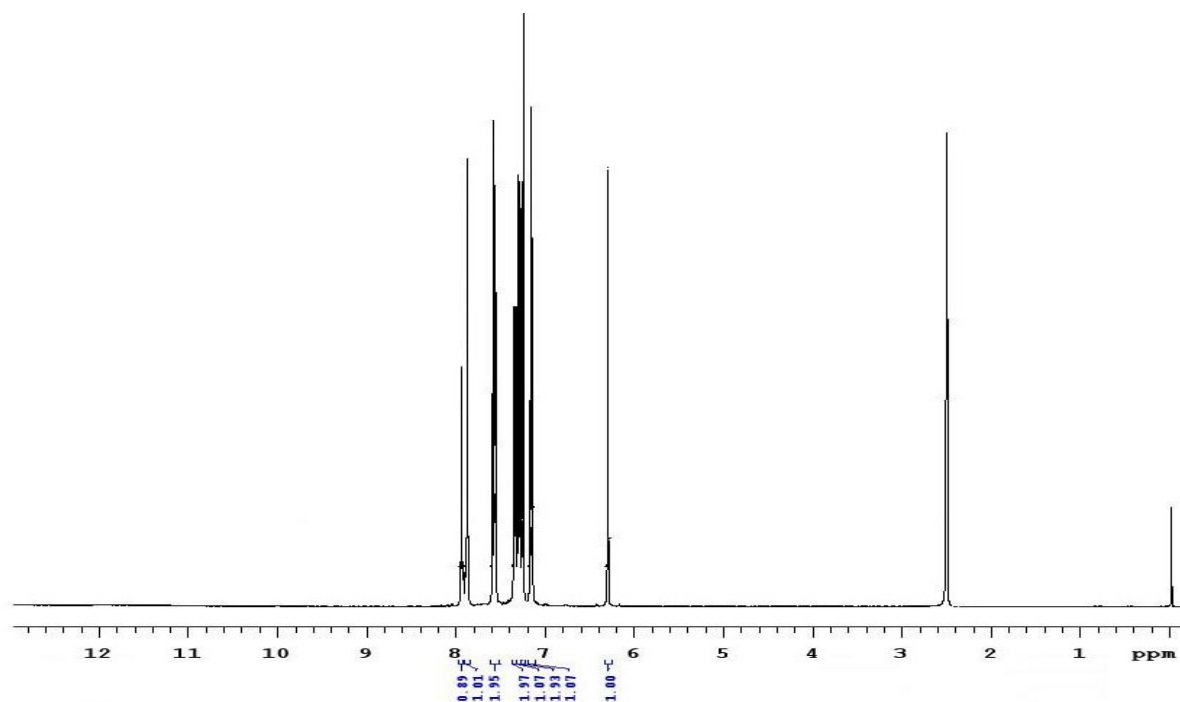


Mass

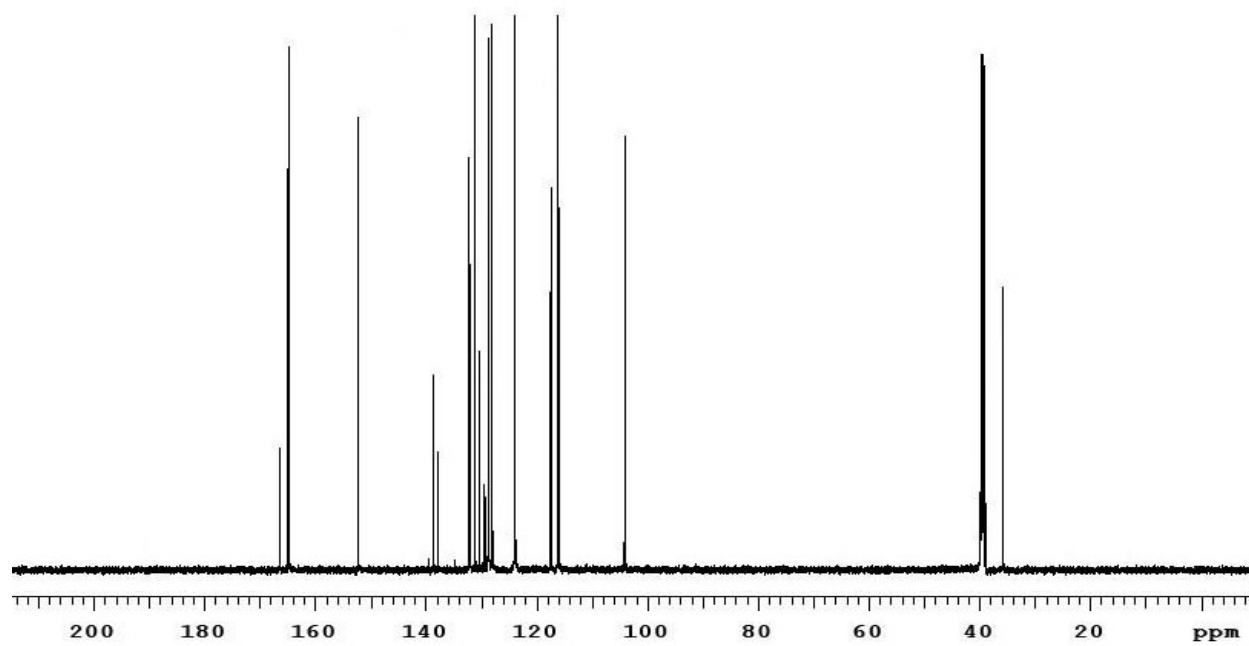


Compound 4j

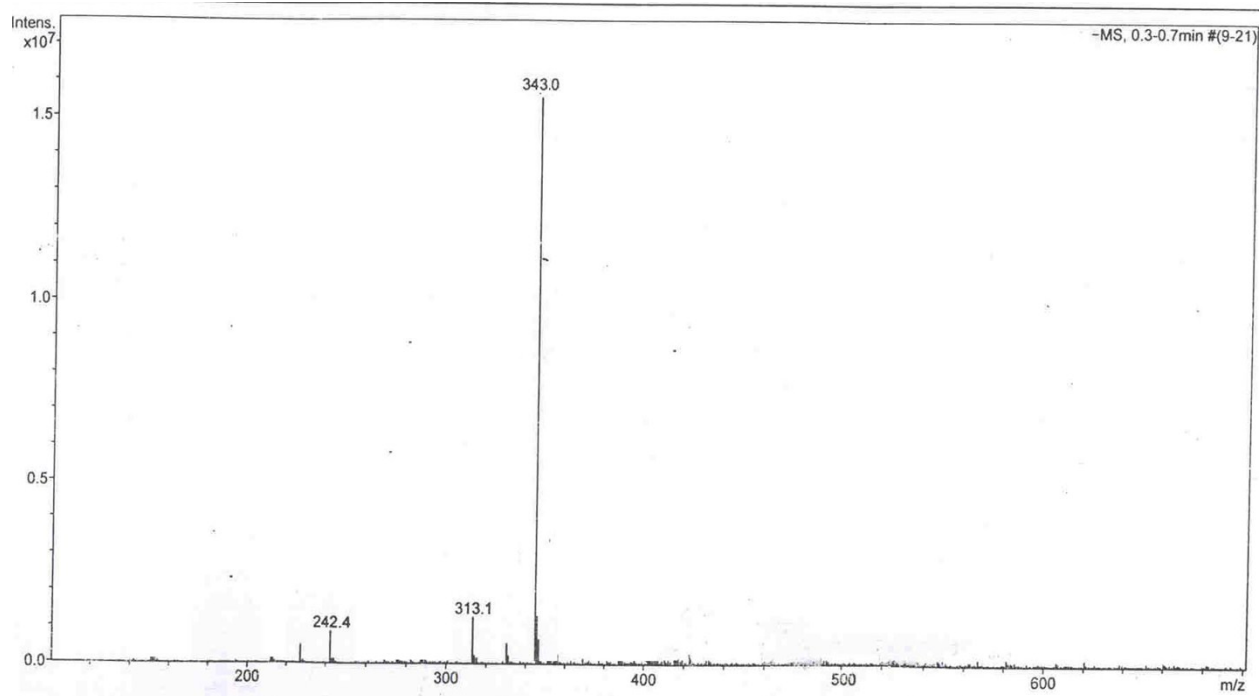
¹H NMR



¹³C NMR

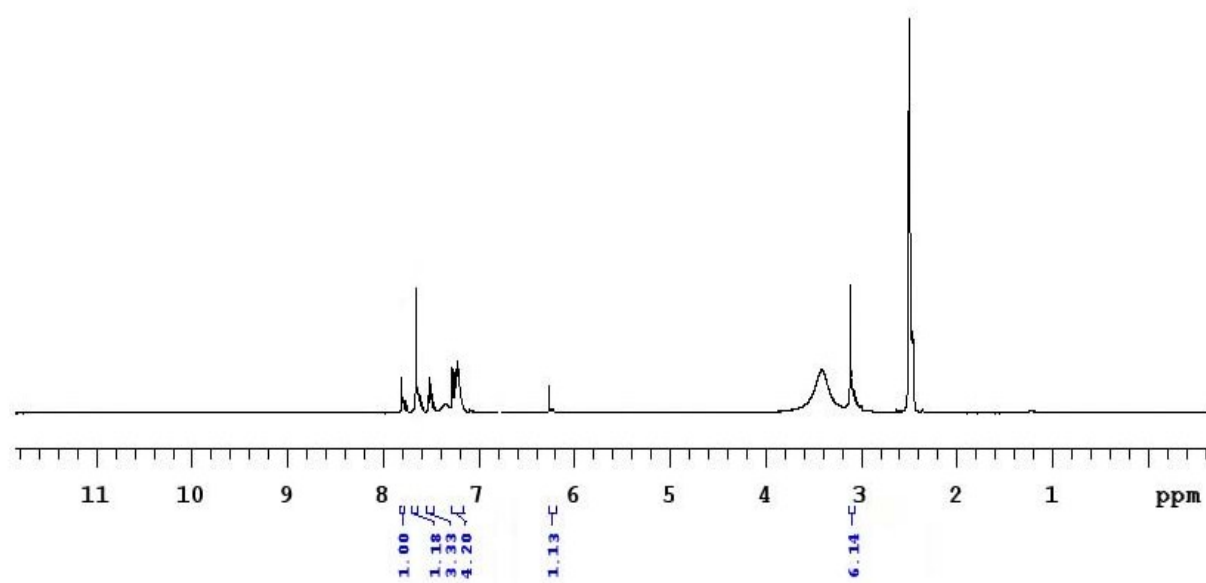


Mass

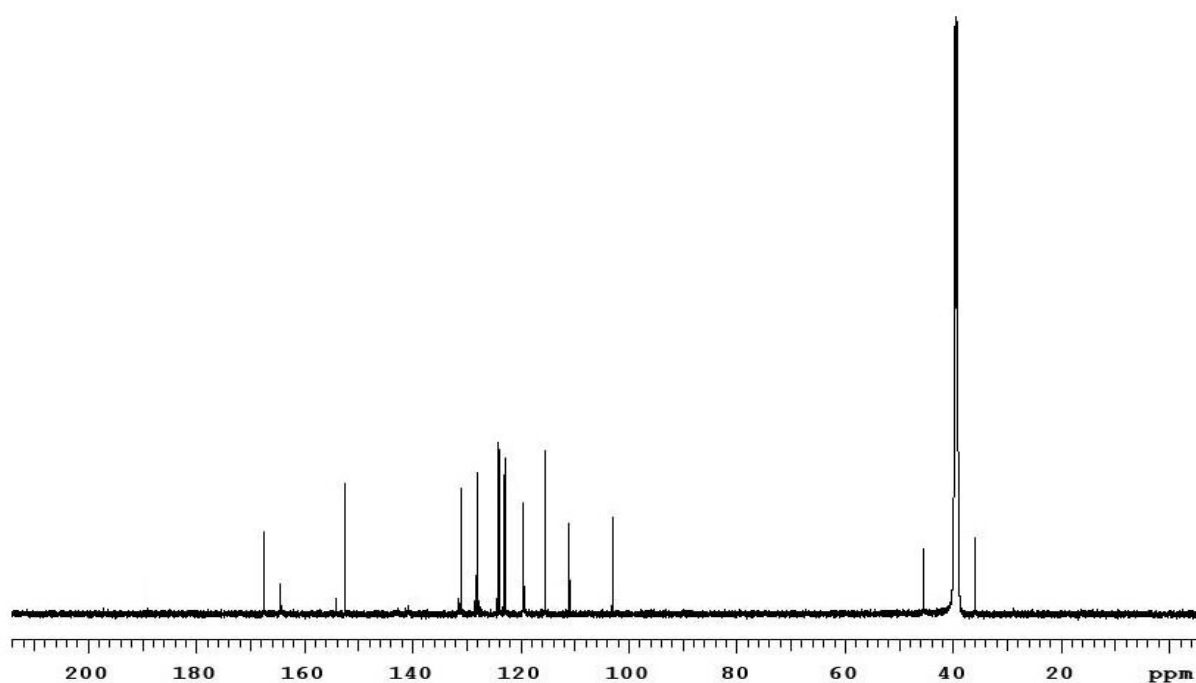


Compound 4k

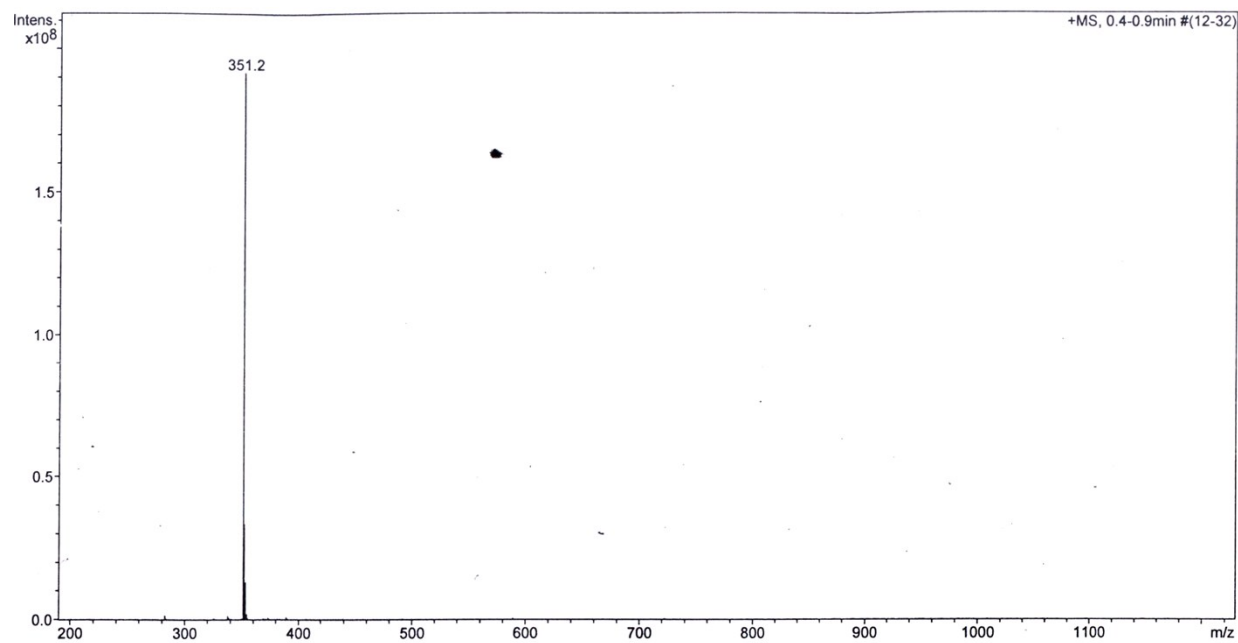
^1H NMR



¹³C NMR

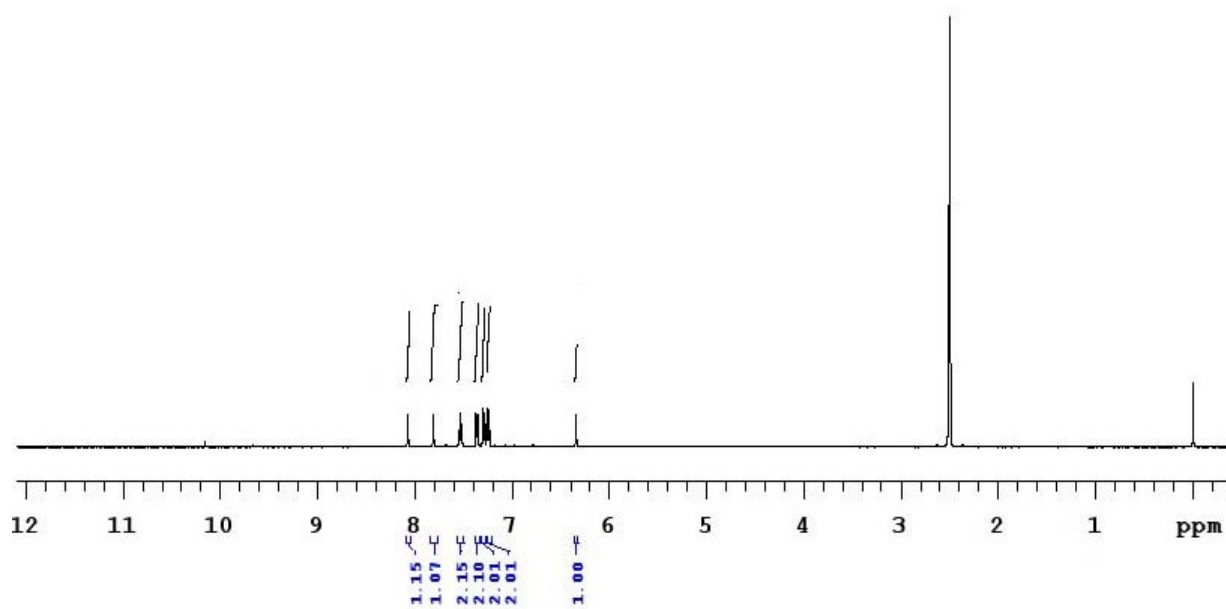


Mass

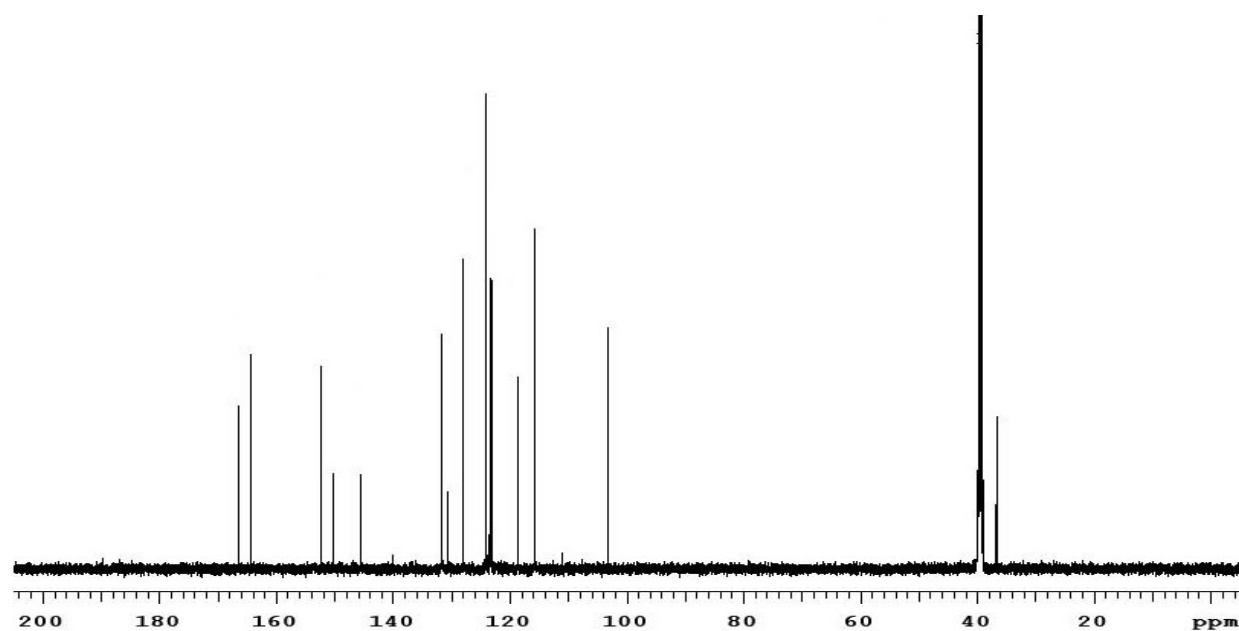


Compound 4l

¹H NMR

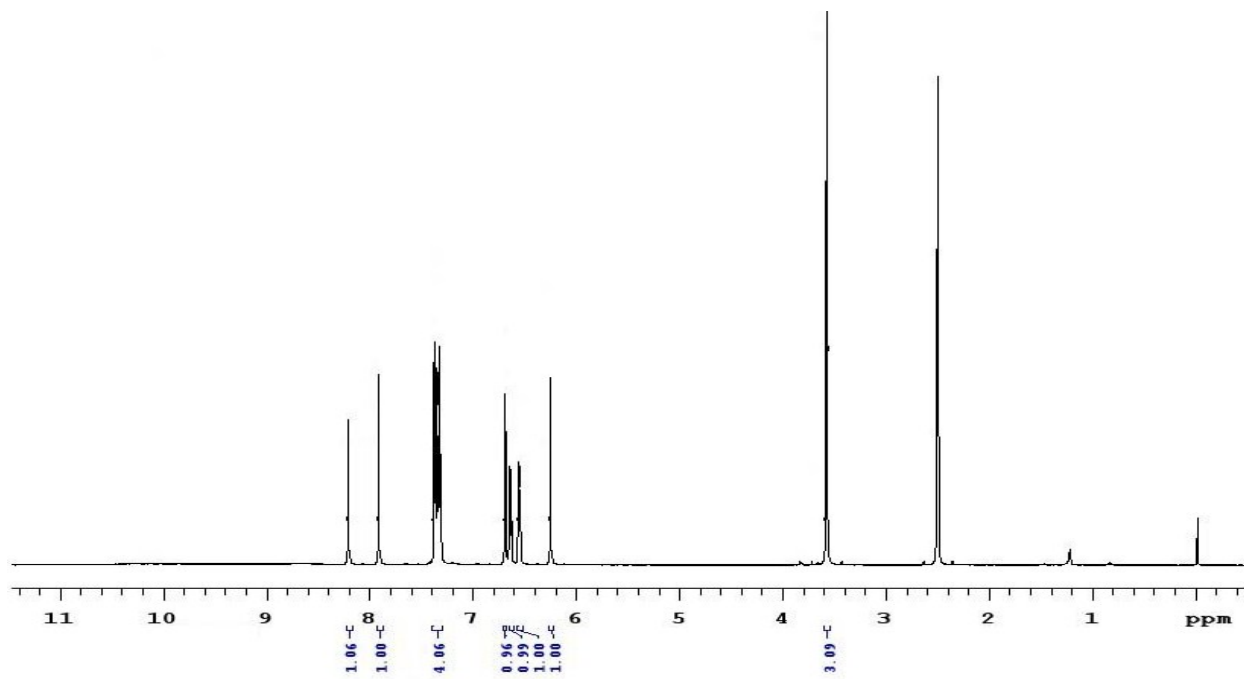


¹³C NMR



Compound 4m

¹H NMR



¹³C NMR

