

## Molybdate Sulfuric acid (MSA): an efficient reusable catalyst for the synthesis of tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-ones under solvent-free conditions and evaluation for their *in vitro* bioassay

MudumalaVeeranarayana Reddy,<sup>a</sup> Gangireddy Chandra SekharReddy,<sup>b</sup> Yeon Tae Jeong<sup>a</sup>

<sup>a</sup>Department of Image Science and Engineering, Pukyong National University, Busan 608-737, Korea, Tel.: +82-51-629-6411; fax: +82-51-629- 6408; E-mail: [ytjeong@pknu.ac.kr](mailto:ytjeong@pknu.ac.kr).

<sup>b</sup>Department of Chemistry, Sri Venkateswara College of Engineering, Tirupati – 517 507, India.

Supporting information (<sup>1</sup>H and <sup>13</sup>C NMR spectra of isolated compounds (4a-y) (4z and 4a' reported compounds))

**3,3-dimethyl-12-(pyridin-2-yl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4a).** Yield 92%; White solid; mp 340-342 °C. IR (KBr):  $\nu = 3385, 2990, 2877, 1663, 1610, 1583, 1560 \text{ cm}^{-1}$ . <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  11.05 (s, 1H), 8.31 (d, *J* = 4.7 Hz, 1H), 7.73-7.70 (m, 2H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.16-7.13 (q, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.49 (s, 1H), 2.61 (d, *J* = 16.8 Hz, 1H), 2.47 (d, *J* = 16.1 Hz, 1H), 2.25 (d, *J* = 16.1 Hz, 1H), 2.02 (d, *J* = 16.1 Hz, 1H), 1.04 (s, 3H), 0.90 (s, 3H); <sup>13</sup>C NMR (100. MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 192.5, 158.5, 151.1, 149.3, 145.7, 141.9, 136.2, 132.1, 122.8, 122.6, 121.6, 120.3, 116.8, 109.6, 105.0, 49.8, 40.1, 32.3, 28.7, 26.4; HRMS (ESI, *m/z*): calcd for C<sub>21</sub>H<sub>20</sub>N<sub>4</sub>O (M+H<sup>+</sup>) 344.164, found: 344.160.

**12-(2,3-dihydroxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4b).** Yield 94%; White solid; mp 282-284 °C. IR (KBr):  $\nu = 3400, 2983, 2850, 1640, 1608, 15850, 1575 \text{ cm}^{-1}$ . <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  11.00 (s, 1H), 9.31 (s, 1H), 8.74 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 7.94 (t, *J* = 7.6 Hz, 1H), 6.60 (s, 1H), 6.55 (t, *J* = 7.6 Hz, 2H), 6.48 (d, *J* = 7.6 Hz, 1H), 2.61 (d, *J* = 16.2 Hz, 1H), 2.47 (d, *J* = 16.1 Hz, 1H), 2.25 (d, *J* = 16.1 Hz, 1H), 2.04 (d, *J* = 16.1 Hz, 1H), 1.06 (s, 3H), 0.98 (s, 3H); <sup>13</sup>C NMR (100. MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 192.7, 150.7, 145.5, 145.1, 142.8, 141.7, 132.2, 127.9, 121.5, 120.2, 118.8, 114.3, 109.6, 105.8, 50.0, 39.3, 32.2, 28.8, 26.6; HRMS (ESI, *m/z*): calcd for C<sub>22</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub> (M+H<sup>+</sup>) 375.158, found: 375.155.

**12-(2,4-dihydroxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4c).** Yield 90%; White solid; mp 270-272 °C. IR (KBr):  $\nu = 3400, 2986, 2863, 1662, 1613, 1591, 1563 \text{ cm}^{-1}$ . <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  10.96 (s, 1H), 9.71 (s, 1H), 7.33 (d, *J* = 6.9 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 5.8 Hz, 1H), 7.05 (d, *J* = 6.2 Hz, 1H), 6.94 (d, *J* = 6.2 Hz, 1H), 6.47 (s, 1H), 6.27 (d, *J* = 7.3 Hz, 1H), 6.22 (s, 1H), 2.60 (d, *J* = 16.8 Hz, 1H), 2.47 (d, *J* = 16.1 Hz, 1H), 2.24 (d, *J* = 16.1 Hz, 1H), 2.02 (d, *J* = 16.1 Hz, 1H), 1.06 (s, 3H), 0.98 (s, 3H); <sup>13</sup>C NMR (100. MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 192.5, 159.4, 155.6, 150.3, 145.8, 141.9, 132.2, 121.3, 120.0, 116.6, 109.6, 105.4, 104.4, 101.0, 50.0, 38.2, 32.1, 28.9, 26.5; HRMS (ESI, *m/z*): calcd for C<sub>22</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub> (M+H<sup>+</sup>) 375.158, found: 375.160.

**12-(2-hydroxy-3-methoxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4d).** Yield 91%; White solid; mp 301-303 °C. IR (KBr):  $\nu = 3398,$

2996, 2865, 1650, 1617, 1587, 1565  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.00 (s, 1H), 8.99 (s, 1H), 7.33 (d,  $J = 7.3$  Hz, 2H), 7.02 (t,  $J = 7.6$  Hz, 2H), 7.93 (t,  $J = 7.3$  Hz, 1H), 6.72 (d,  $J = 7.3$  Hz, 1H), 6.64 (s, 1H), 6.61 (s, 1H), 3.71 (s, 3H), 2.62 (d,  $J = 16.2$  Hz, 1H), 2.48 (d,  $J = 16.1$  Hz, 1H), 2.24 (d,  $J = 16.1$  Hz, 1H), 2.02 (d,  $J = 16.1$  Hz, 1H), 1.05 (s, 3H), 0.97 (s, 3H);  $^{13}\text{C}$  NMR (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.5, 150.6, 147.4, 145.7, 143.7, 141.8, 132.2, 127.5, 121.5, 120.1, 118.6, 116.7, 110.6, 109.5, 105.5, 55.5, 50.0, 40.1, 32.1, 28.8, 26.6; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_3$  ( $\text{M}+\text{H}^+$ ) 389.174, found: 389.170.

**12-(2-hydroxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4e).** Yield 92%; White solid; mp 296-298  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3382, 2994, 2871, 1664, 1610, 1595, 1571$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.01 (s, 1H), 9.68 (s, 1H), 7.34-7.23 (m, 3H), 7.03-6.92 (m, 3H), 6.67 (d,  $J = 6.9$  Hz, 2H), 6.54 (s, 1H), 2.61 (d,  $J = 16.1$  Hz, 1H), 2.47 (d,  $J = 16.1$  Hz, 1H), 2.24 (d,  $J = 16.1$  Hz, 1H), 2.03 (d,  $J = 16.1$  Hz, 1H), 1.06 (s, 3H), 0.98 (s, 3H);  $^{13}\text{C}$  NMR (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.5, 154.6, 150.6, 145.7, 141.8, 132.8, 129.4, 128.6, 127.3, 121.4, 120.1, 118.7, 116.6, 115.6, 190.6, 105.2, 50.0, 38.2, 32.6, 29.3, 26.0; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_2$  ( $\text{M}+\text{H}^+$ ) 359.163, found: 359.158.

**3,3-dimethyl-12-(thiophen-2-yl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4f).** Yield 89%; White solid; mp 310-312  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3401, 2990, 2871, 1640, 1611, 1592, 1562$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.17 (s, 1H), 7.50 (d,  $J = 7.3$  Hz, 1H), 7.38 (d,  $J = 7.3$  Hz, 1H), 7.28 (d,  $J = 6.0$  Hz, 1H), 7.18 (d,  $J = 6.0$  Hz, 1H), 7.10-7.01 (m, 2H), 6.85 (dd,  $J = 2.3, 10.2$  Hz, 1H), 6.81 (s, 1H), 2.64 (d,  $J = 16.1$  Hz, 1H), 2.47 (d,  $J = 16.1$  Hz, 1H), 2.31 (d,  $J = 16.1$  Hz, 1H), 2.11 (d,  $J = 15.9$  Hz, 1H), 1.07 (s, 3H), 1.02 (s, 3H);  $^{13}\text{C}$  NMR (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.4, 150.6, 145.0, 144.5, 141.9, 131.6, 126.4, 126.0, 125.4, 121.9, 120.5, 116.9, 110.2, 105.9, 48.7, 38.7, 32.1, 28.9, 26.5; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{20}\text{H}_{19}\text{N}_3\text{OS}$  ( $\text{M}+\text{H}^+$ ) 349.125, found: 349.120.

**3,3-dimethyl-12-propyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4g).** Yield 92%; White solid; mp 240-242  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3395, 2983, 2880, 1643, 1615, 1608, 1561$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.80 (s, 1H), 7.48 (dd,  $J = 2.2, 10.2$  Hz, 1H), 7.40 (dd,  $J = 2.2, 10.2$  Hz, 1H), 7.11-7.08 (m, 2H), 5.58 (t,  $J = 6.6$  Hz, 1H), 2.54 (d,  $J = 16.1$  Hz, 1H), 2.43 (d,  $J = 16.1$  Hz, 1H), 2.28 (d,  $J = 15.9$  Hz, 1H), 1.99-1.93 (m, 1H), 1.74-1.69 (m, 1H), 1.16-1.10 (m, 1H), 1.05 (s, 6H), 0.64-0.63 (q, 4H);  $^{13}\text{C}$  NMR (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :193.1, 151.7, 146.2, 141.9, 131.8, 121.6, 120.4, 117.0, 109.6, 104.1, 50.0, 38.7, 34.5, 32.0, 28.7, 26.7, 16.0, 13.6; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 309.184, found: 309.181.

**12-ethyl-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4h).** Yield 91%; White solid; mp 271-273  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3412, 3045, 2855, 1645, 1613, 1595, 1560$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 10.79 (s, 1H), 7.48 (d,  $J = 6.9$  Hz, 1H), 7.41-7.39 (q, 1H), 7.13-7.05 (m, 2H), 5.61 (t,  $J = 2.9$  Hz, 1H), 2.54 (d,  $J = 16.1$  Hz, 1H), 2.44 (d,  $J = 16.1$  Hz, 1H), 2.29 (d,  $J = 16.1$  Hz, 1H), 2.19 (d,  $J = 16.1$  Hz, 1H), 2.06-2.01 (m, 1H), 1.78-1.72 (m, 1H), 1.07 (s, 6H) 0.45 (t,  $J = 7.3$  Hz, 1H 3H);  $^{13}\text{C}$  NMR (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :193.1, 152.0, 146.4, 142.0, 131.7, 121.6, 120.4, 117.0, 109.6, 103.4, 50.7, 50.0, 32.0, 28.7, 26.8, 24.7, 6.8; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 295.168, found: 295.164.

**12-(2,4-difluorophenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4i).** Yield 89%; White solid; mp 288-290 °C. IR (KBr):  $\nu$ = 3410, 2955, 2845, 1664, 1620, 1589, 1542  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 10.19 (s, 1H), 7.40-7.32 (m, 2H), 7.23 (d,  $J$  = 7.6 Hz, 1H), 7.12-6.92 (m, 3H), 6.57-6.50 (m, 1H), 6.51 (s, 1H), 2.62 (d,  $J$  = 16.1 Hz, 1H), 2.47 (d,  $J$  = 16.1 Hz, 1H), 2.25 (d,  $J$  = 16.1 Hz, 1H), 2.05 (d,  $J$  = 16.1 Hz, 1H), 1.06 (s, 3H), 0.95 (s, 3H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.5, 161.8 (d,  $J$  = 240.0 Hz), 156.3, 150.7, 145.8, 141.9, 132.1, 121.5, 120.1, 1416.7, 109.8, 104.8, 102.5, 50.0, 38.2, 32.1, 28.8, 26.5; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{22}\text{H}_{19}\text{F}_2\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 379.150, found: 379.142.

**12-(2,3-difluorophenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4j).** Yield 88%; White solid; mp 308-310 °C. IR (KBr):  $\nu$ = 3423, 3045, 2905, 1652, 1612, 1590, 1562  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.19(s, 1H), 7.41-7.23 (m, 3H), 7.12-6.95 (m, 4H), 6.61 (s, 1H), 2.63 (d,  $J$  = 16.1 Hz, 1H), 2.54 (d,  $J$  = 16.1 Hz, 1H), 2.25 (d,  $J$  = 16.1 Hz, 1H), 2.05 (d,  $J$  = 16.1 Hz, 1H), 1.06 (s, 3H), 0.95 (s, 3H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.6, 152.5, 150.6, 145.0, 141.8, 133.4, 131.6, 121.9, 121.2, 120.6, 117-116.2, 111.3, 109.9, 105.5, 53.1, 38.2, 32.3, 28.3, 26.6; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{22}\text{H}_{19}\text{F}_2\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 379.150, found: 379.144..

**12-isopropyl-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4k).** Yield 89%; White solid; mp 221-223 °C. IR (KBr):  $\nu$ = 3395, 2987, 2893, 1644, 1612, 1575, 1545  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  10.25 (s, 1H), 7.10-7.08 (m, 2H), 6.87-6.84 (m, 2H), 5.46 (br, s, 1H), 2.22 (br, s, 4H), 2.09-2.03 (m, 1H), 1.72 (br, s, 3H), 1.40 (br, s, 3H), 0.99 (s, 6H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.6, 154.9, 138.1, 134.2, 124.8, 119.2, 116.5, 117.7, 111.9, 104.3, 46.7, 38.7, 31.3, 27.9, 25.4, 20.3; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 309.184, found: 309.180.

**12-(2-chloro-6-fluorophenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4l).** Yield 88%; White solid; mp 278-280 °C. IR (KBr):  $\nu$ = 3323, 3040, 2949, 1646, 1621, 1585, 1515  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.03 (s, 1H), 7.34 (d,  $J$  = 7.7 Hz, 1H), 7.12-6.86 (m, 6H), 6.82 (s, 1H), 2.59 (d,  $J$  = 16.1 Hz, 1H), 2.39 (d,  $J$  = 17.2 Hz, 1H), 2.22 (d,  $J$  = 16.1 Hz, 1H), 2.00 (d,  $J$  = 16.1 Hz, 1H), 1.05 (s, 3H), 0.96 (s, 3H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.4, 157.5, 151.1, 146.3, 141.8, 134.3, 132.3, 129.1, 122.7, 121.3, 120.1, 119.5, 116.7, 114.9, 108.8, 103.3, 50.2, 39.5, 32.0, 28.9, 26.3; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{22}\text{H}_{19}\text{ClFN}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 395.120, found: 395.115.

**12-(5-chloro-2-hydroxyphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4m).** Yield 92%; White solid; mp 305-307 °C. IR (KBr):  $\nu$ = 3410, 2955, 2875, 1641, 1613, 1589, 1565  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.06 (s, 1H), 9.94 (s, 1H), 7.33 (t,  $J$  = 7.6 Hz, 2H), 7.22 (d,  $J$  = 7.3 Hz, 1H), 7.02 (t,  $J$  = 8.0 Hz, 2H), 6.94 (t,  $J$  = 7.6 Hz, 1H), 6.64 (d,  $J$  = 8.4 Hz, 1H), 6.50 (s, 1H), 2.67 (br, s, 2H), 2.32-2.24 (m, 2H), 1.97-1.95 (m, 1H), 1.88-1.86 (m, 1H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.8, 154.0, 152.9, 145.4, 141.8, 132.1, 129.1, 128.6, 128.3, 122.1, 121.5, 120.2, 117.2, 116.7, 109.5, 105.6, 55.8, 36.4, 26.5, 20.8; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{20}\text{H}_{16}\text{ClN}_3\text{O}_2$  ( $\text{M}+\text{H}^+$ ) 365.093, found: 365.090.

**12-(2-hydroxy-3-methoxyphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4n).** Yield 90%; White solid; mp 298-300 °C. IR (KBr):  $\nu$ = 3415, 2978, 2890, 1658,

1620, 1589, 1560  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.02 (s, 1H), 8.97 (s, 1H), 7.33 (t,  $J = 8.0$  Hz, 2H), 7.03 (d,  $J = 7.6$  Hz, 1H), 6.94 (t,  $J = 7.7$  Hz, 1H), 6.74 (t,  $J = 7.6$  Hz, 2H), 6.64 (d,  $J = 8.0$  Hz, 1H), 6.61 (s, 1H), 3.72 (s, 3H), 2.68 (br, s, 2H), 2.33-2.18 (m, 2H), 2.01-1.96 (m, 1H), 1.89-1.83 (m, 1H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.9, 152.6, 147.4, 145.3, 143.6, 141.7, 132.2, 127.5, 121.4, 120.5, 118.7, 116.6, 110.6, 109.5, 106.7, 55.5, 49.2, 36.4, 26.5, 20.8; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}_3$  ( $\text{M}+\text{H}^+$ ) 361.143, found: 361.138.

**12-(2-hydroxyphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4o).** Yield 91%; White solid; mp 311-313  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3395, 22985, 2890, 1660, 1612, 1589, 1561$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.01 (s, 1H), 9.67 (s, 1H), 7.32 (d,  $J = 7.7$  Hz, 1H), 7.27 (d,  $J = 7.6$  Hz, 1H), 7.20 (d,  $J = 7.6$  Hz, 1H), 7.03-6.92 (m, 3H), 6.66 (t,  $J = 7.7$  Hz, 2H), 6.55 (s, 1H), 2.67 (br, s, 2H), 2.33-2.18 (m, 2H), 2.02-1.96 (m, 1H), 1.87-1.82 (m, 1H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.8, 154.5, 152.5, 145.6, 141.9, 132.2, 129.3, 128.5, 127.1, 121.4, 120.0, 118.8, 116.6, 115.6, 109.5, 106.5, 49.9, 36.4, 26.5, 20.8 ; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2$  ( $\text{M}+\text{H}^+$ ) 331.132, found: 331.128.

**12-(pyridin-2-yl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4p).** Yield 93%; White solid; mp 309-311  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3380, 2991, 2874, 1664, 1615, 1590, 1571$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.08 (s, 1H), 8.31 (d,  $J = 4.4$  Hz, 1H), 7.72 (d,  $J = 8.0$  Hz, 2H), 7.35 (d,  $J = 8.0$  Hz, 1H), 7.24 (t,  $J = 7.6$  Hz, 1H), 7.16-7.12 (q, 1H), 7.02 (t,  $J = 6.9$  Hz, 1H), 6.92 (t,  $J = 7.6$  Hz, 1H), 6.50 (s, 1H), 2.67 (t,  $J = 5.8$  Hz, 2H), 2.35-2.27 (m, 1H), 2.24-2.17 (m, 1H), 1.99-1.93 (m, 1H), 1.86-1.81 (m, 1H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.8, 158.7, 153.0, 149.4, 145.6, 141.9, 136.2, 132.1, 122.8, 122.6, 121.6, 120.2, 116.8, 109.6, 106.1, 55.3, 36.2, 26.5, 20.7; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}$  ( $\text{M}+\text{H}^+$ ) 316.132, found: 316.128.

**12-(4-isopropylphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4q).** Yield 92%; White solid; mp 353-355  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3440, 2955, 2854, 1652, 1617, 1590, 1564$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.06 (s, 1H), 7.36 (d,  $J = 7.6$  Hz, 1H), 7.27 (d,  $J = 7.6$  Hz, 1H), 7.23 (d,  $J = 8.0$  Hz, 2H), 7.08 (d,  $J = 8.0$  Hz, 2H), 7.04 (t,  $J = 7.6$  Hz, 1H), 6.95 (t,  $J = 7.6$  Hz, 1H), 6.38 (s, 1H), 2.81-2.75 (m, 1H), 2.70-2.68 (m, 2H), 2.32-2.20 (m, 2H), 2.00-1.94 (m, 1H), 1.87-1.80 (m, 1H), 1.09 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.8, 147.5, 145.3, 139.0, 131.7, 126.8, 121.6, 120.3, 116.8, 109.9, 107.5, 53.5, 36.3, 32.9, 26.4, 23.6, 20.7; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 357.184, found: 357.180.

**12-(4-ethoxyphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4r).** Yield 93%; White solid; mp 378-380  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3402, 2983, 2864, 1661, 1608, 1590, 1570$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.08 (s, 1H), 7.36 (d,  $J = 7.7$  Hz, 1H), 7.23 (d,  $J = 8.0$  Hz, 3H), 7.04 (t,  $J = 7.3$  Hz, 1H), 6.95 (t,  $J = 7.6$  Hz, 1H), 6.75 (d,  $J = 8.4$  Hz, 2H), 6.36 (s, 1H), 3.92-3.87 (q, 2H), 2.72-2.67 (m, 2H), 2.30-2.19 (m, 2H), 2.00-1.94 (m, 1H), 1.86-1.80 (m, 1H), 1.23 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (100. MHz,  $\text{DMSO-}d_6$ )  $\delta$ :192.8, 157.7, 151.9, 145.2, 141.9, 133.6, 131.8, 128.1, 121.6, 120.2, 116.8, 113.9, 109.9, 107.6, 62.8, 53.3, 36.3, 26.4, 20.7, 14.5; HRMS (ESI,  $m/z$ ): calcd for  $\text{C}_{22}\text{H}_{21}\text{N}_3\text{O}_2$  ( $\text{M}+\text{H}^+$ ) 359.163, found: 359.159.

**12-(3,4,5-trimethoxyphenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4s).** Yield 91%; White solid; mp 312-314  $^{\circ}\text{C}$ . IR (KBr):  $\nu = 3430, 2998, 2890, 1641, 1612, 1589, 1555$   $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$ 11.08 (s, 1H), 7.45 (d,  $J = 7.6$  Hz, 1H), 7.37

(d,  $J = 7.6$  Hz, 1H), 7.01-6.97 (m, 2H), 6.63 (s, 2H), 6.39 (s, 1H), 3.68 (s, 6H), 3.55 (s, 3H), 2.77-2.63(m, 2H), 2.34-2.23 (m, 2H), 2.01-1.89 (m, 2H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :192.9, 152.6, 145.1, 141.8, 137.1, 136.8, 132.0, 121.7, 120.4, 116.8, 110.2, 107.2, 104.5, 59.8, 55.8, 53.9, 36.4, 26.5, 20.7; HRMS (ESI, m/z): calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_4$  ( $\text{M}+\text{H}^+$ ) 405.169, found: 405.165.

**12-(2,4-difluorophenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4t).** Yield 88%; White solid; mp 375-377 °C. IR (KBr):  $\nu = 33985, 2955, 2885, 1644, 1610, 1579, 1545$   $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ):  $\delta$ 11.23 (s, 1H), 7.63-7.57 (m, 1H), 7.37 (d,  $J = 7.6$  Hz, 1H), 7.13-6.97 (m, 5H), 6.55 (s, 1H), 2.70-2.67 (m, 2H), 2.30-2.19 (m, 2H), 1.99-1.95 (m, 1H), 1.88-1.84 (m, 1H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :192.8, 152.8, 144.9, 141.8, 131.7, 121.9, 120.5, 117.0, 111.3, 109.0, 105.3, 103.8, 49.2, 36.3, 26.5, 20.7; HRMS (ESI, m/z): calcd for  $\text{C}_{20}\text{H}_{15}\text{F}_2\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 351.118, found: 351.112.

**12-(2,3-difluorophenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4u).** Yield 89%; White solid; mp 304-306 °C. IR (KBr):  $\nu = 3380, 2986, 2860, 1662, 1618, 1587, 1561$   $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ):  $\delta$ 11.19 (s, 1H), 7.40-7.32 (m, 2H), 7.08-7.84 (m, 5H), 6.82 (s, 1H), 2.66-2.56 (m, 2H), 2.30-2.17 (m, 2H), 1.99-1.94 (m, 1H), 1.88-1.82 (m, 1H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :192.7, 157.5, 152.9, 146.3, 141.7, 134.3, 132.3, 129.1, 122.9, 121.3, 120.6, 120.1, 119.5, 117.1, 116.7, 115.0, 108.8, 104.5, 50.3, 36.4, 26.5, 20.8; HRMS (ESI, m/z): calcd for  $\text{C}_{20}\text{H}_{15}\text{F}_2\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 351.118, found: 351.113.

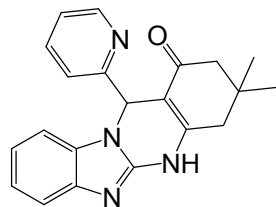
**12-(3,4-difluorophenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4v).** Yield 85%; White solid; mp 378-380°C. IR (KBr):  $\nu = 3400, 2990, 2850, 1654, 1610, 1594, 1565$   $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ):  $\delta$ 11.26 (s, 1H), 7.49 (d,  $J = 7.6$  Hz, 1H), 7.38 (d,  $J = 8.0$  Hz, 1H), 7.27 (d,  $J = 7.6$  Hz, 1H), 7.20-7.17 (m, 1H), 7.09-6.95 (m, 3H), 6.46 (s, 1H), 2.74-2.62 (m, 2H), 2.31-2.20 (m, 2H), 1.98-1.86 (m, 2H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :192.9, 152.6, 144.9, 141.8, 139.2, 131.7, 123.6, 121.9, 120.6, 120.5, 117.4, 117.0, 116.5, 111.4, 109.9, 106.7, 106.7, 53.1, 36.2, 26.5, 20.6; HRMS (ESI, m/z): calcd  $\text{C}_{20}\text{H}_{15}\text{F}_2\text{N}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 351.118, found: 351.110.

**12-(2-chloro-6-fluorophenyl)-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4w).** Yield 85%; White solid; mp 365-367 °C. IR (KBr):  $\nu = 3390, 2987, 2893, 1651, 1612, 1575, 1540$   $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ):  $\delta$ 11.26 (s, 1H), 7.39 (d,  $J = 7.6$  Hz, 1H), 7.32 (d,  $J = 6.6$  Hz, 1H), 7.25 (d,  $J = 8.8$  Hz, 1H), 7.10-7.05 (m, 3H), 6.99 (t,  $J = 7.6$  Hz, 1H), 6.61 (s, 1H), 2.70 (br, s, 2H), 2.34-2.20 (m, 2H), 1.99-1.94 (m, 1H), 1.90-1.84 (m, 1H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :192.8, 153.0, 144.8, 141.8, 131.7, 130.4, 125.2, 124.6, 122.0, 120.7, 117.1, 116.7, 108.9, 105.2, 49.1, 36.2, 26.5, 20.7; HRMS (ESI, m/z): calcd for  $\text{C}_{20}\text{H}_{15}\text{ClFN}_3\text{O}$  ( $\text{M}+\text{H}^+$ ) 367.089, found: 367.085.

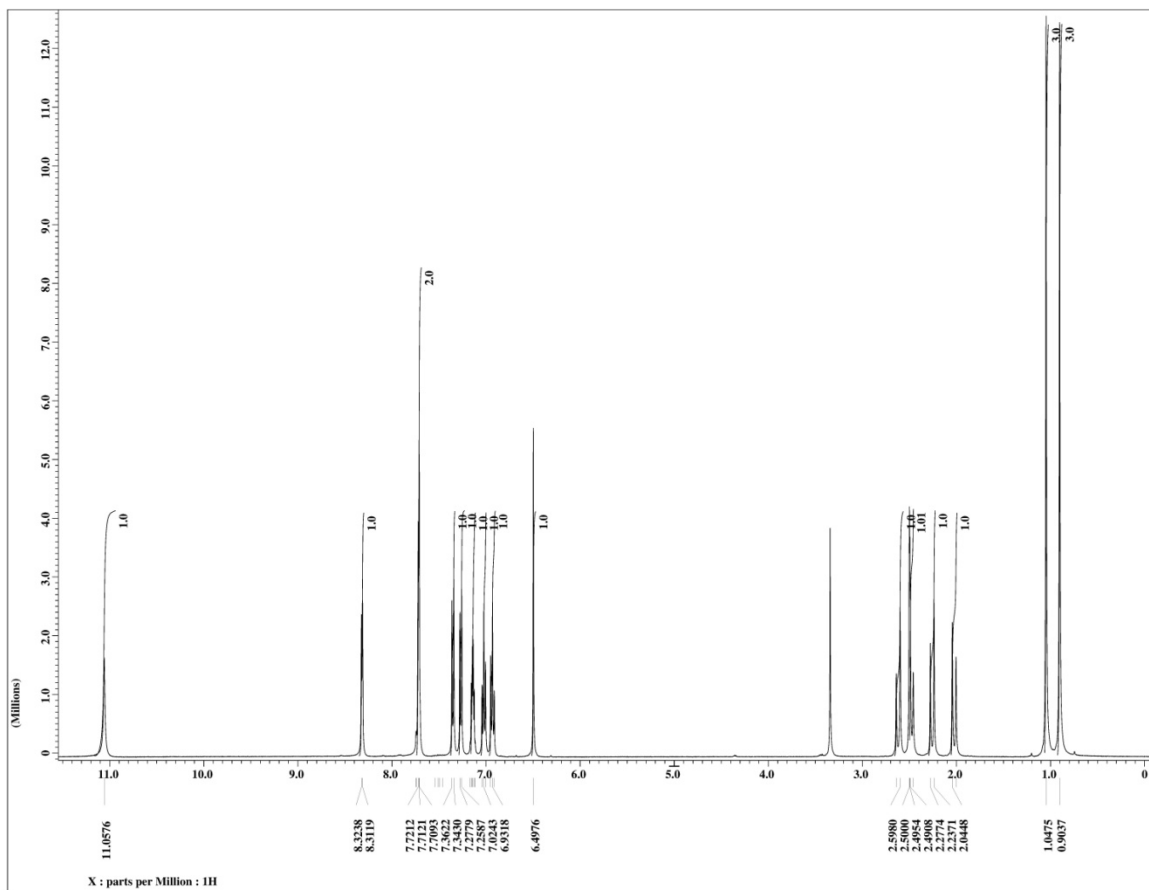
**12-propyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4x).** Yield 90%; White solid; mp 310-312 °C. IR (KBr):  $\nu = 3323, 3040, 2950, 1646, 1620, 1585, 1520$   $\text{cm}^{-1}$ .  $^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ):  $\delta$ 10.81 (s, 1H), 7.47 (d,  $J = 6.9$  Hz, 1H), 7.39 (d,  $J = 6.9$  Hz, 1H), 7.12-7.06 (m, 2H), 5.58 (t,  $J = 3.3$  Hz, 1H), 2.60 (br, s, 2H), 2.38-2.28 (m, 2H), 1.96-1.89 (m, 3H), 1.71-1.65 (m, 1H), 1.16-1.10 (m, 1H), 0.64 (t,  $J = 6.1$  Hz, 4H);  $^{13}\text{C}$  NMR (100. MHz, DMSO- $d_6$ )  $\delta$ :193.4, 153.6, 146.1, 141.9, 131.8, 121.6, 120.4, 116.9, 109.5, 105.1, 49.9, 36.4,

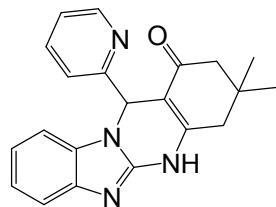
34.5, 26.4, 20.8, 15.8, 13.6; HRMS (ESI, m/z): calcd for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O (M+H<sup>+</sup>) 281.153, found: 281.150.

12-ethyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1(2H)-one (4y). Yield 89%; White solid; mp 258-260 °C. IR (KBr):  $\nu$ =3411, 2951, 2875, 1641, 1625, 1589, 1560 cm<sup>-1</sup>. <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$ 10.80 (s, 1H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.11-7.07 (m, 2H), 5.61 (s, 1H), 2.61 (br, s, 2H), 2.34-2.27 (m, 2H), 2.02-1.93 (m, 3H), 1.73-1.70 (m, 1H), 0.44 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (100. MHz, DMSO-*d*<sub>6</sub>)  $\delta$ :193.4, 153.9, 146.2, 142.0, 131.7, 121.6, 120.4, 117.0, 109.5, 104.4, 50.6, 39.0, 26.4, 24.7, 20.9, 6.7; HRMS (ESI, m/z): calcd for C<sub>16</sub>H<sub>17</sub>N<sub>3</sub>O (M+H<sup>+</sup>) 267.137, found: 267.134.

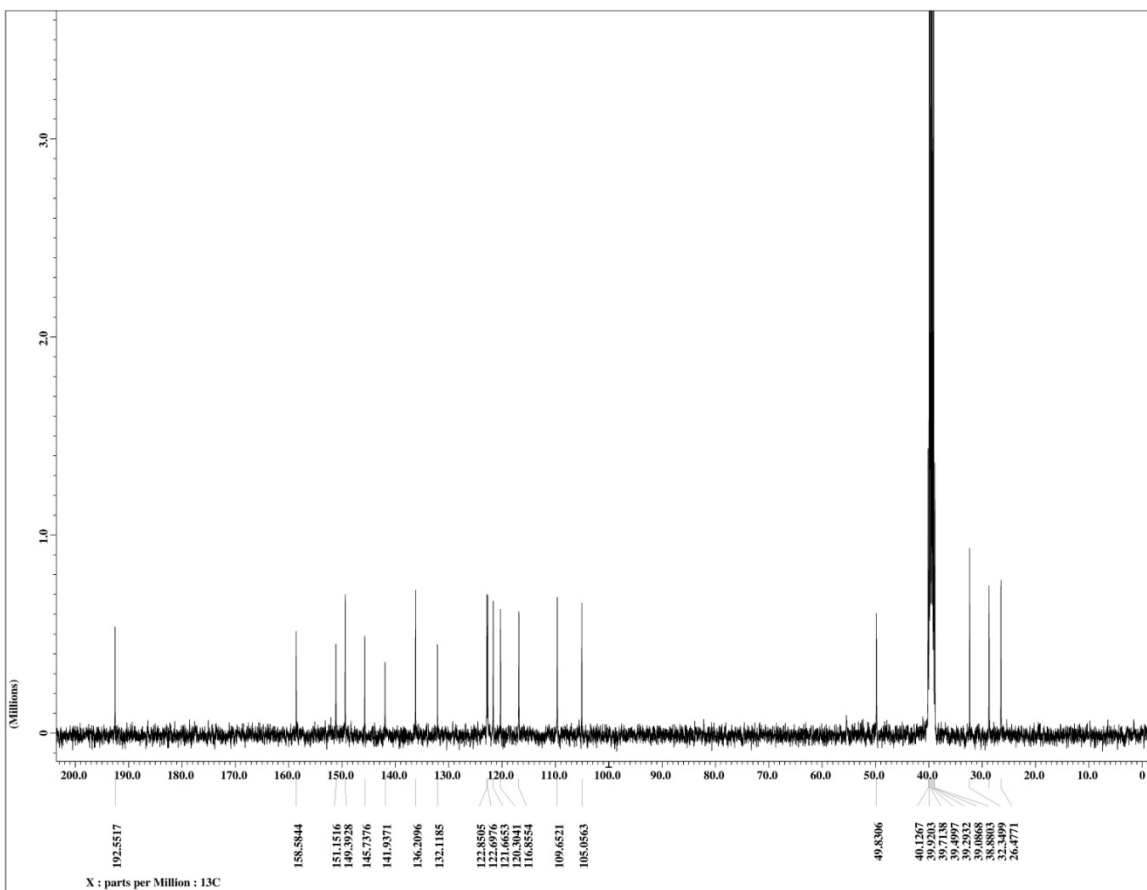


4a-<sup>1</sup>H-NMR

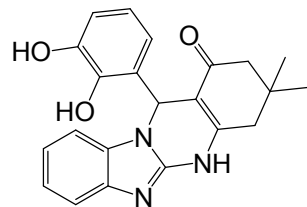




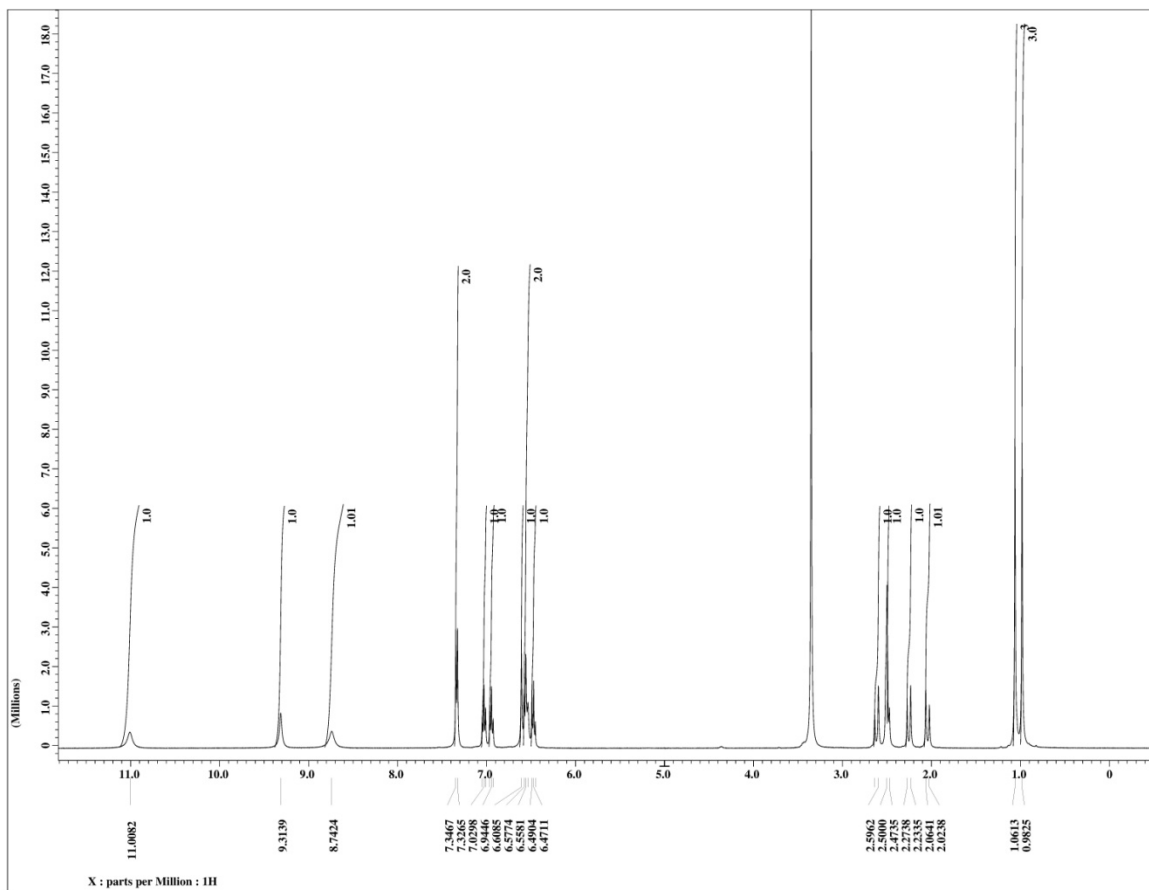
4a-<sup>13</sup>C-NMR

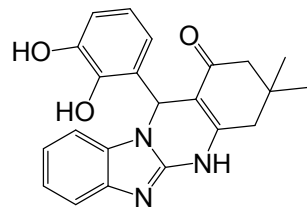




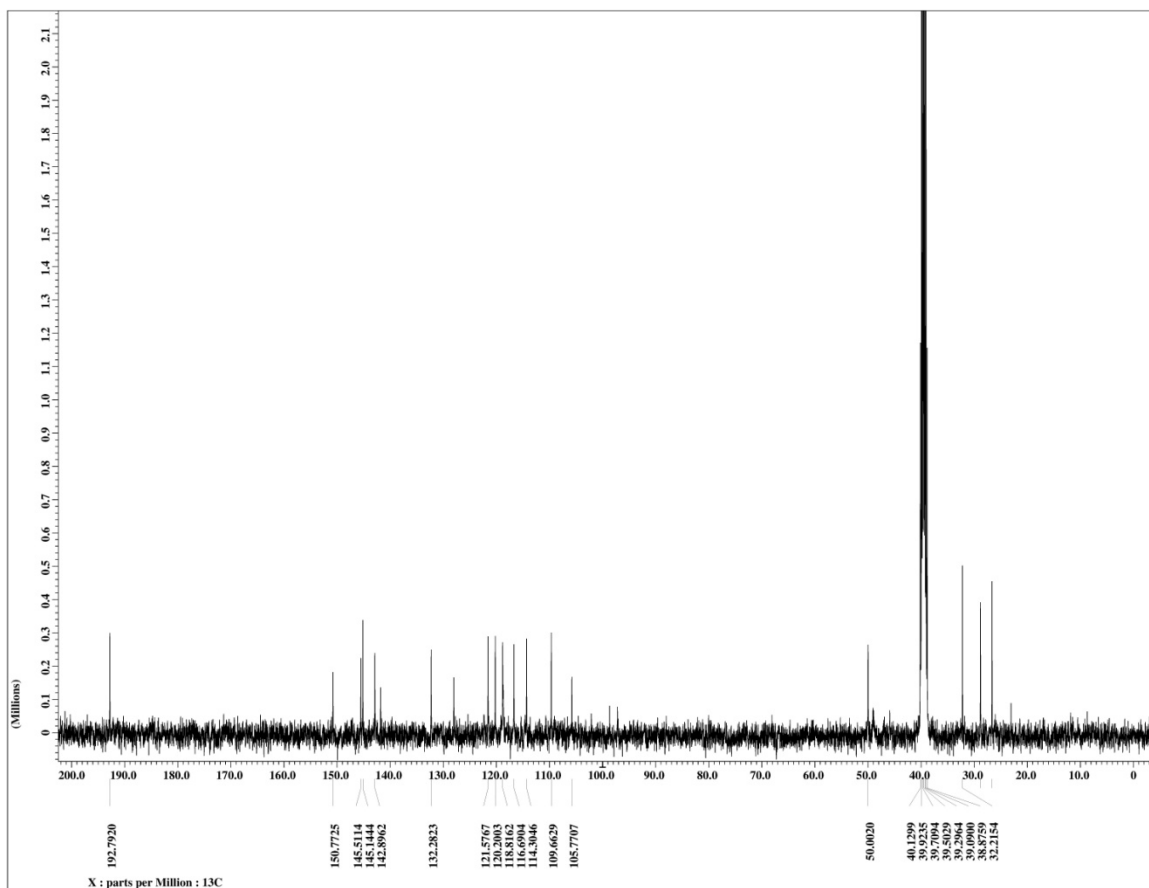


4b-<sup>1</sup>H-NMR

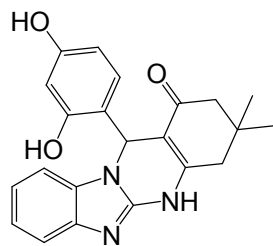




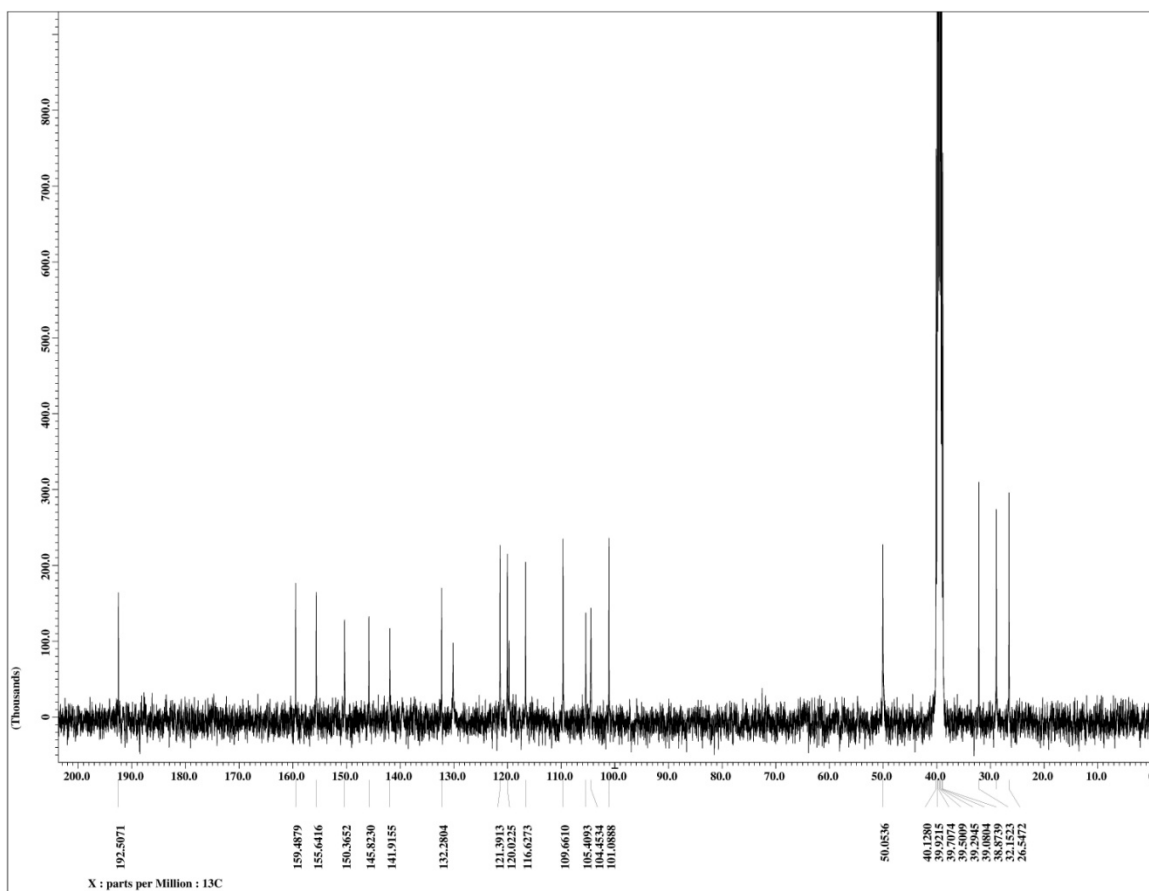
4b-<sup>13</sup>C-NMR

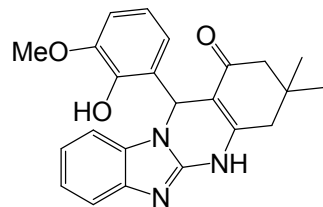




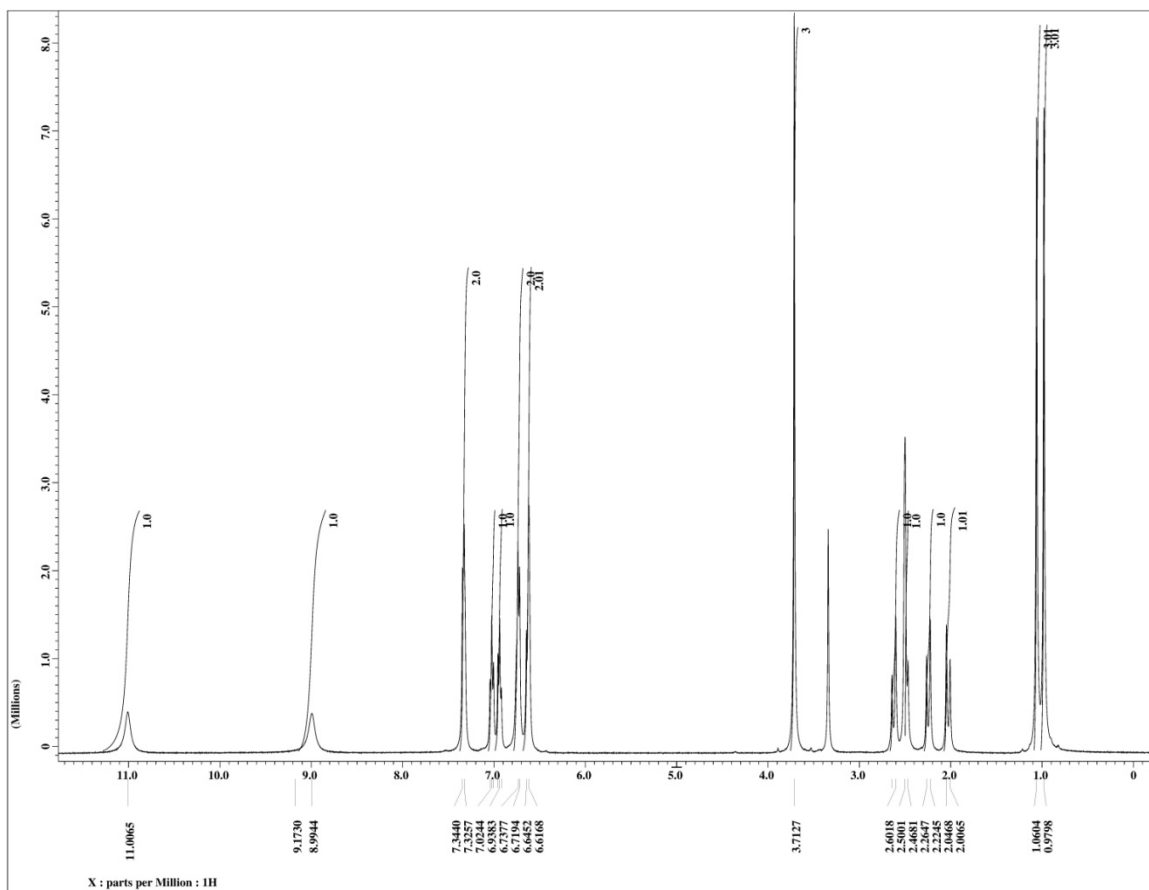


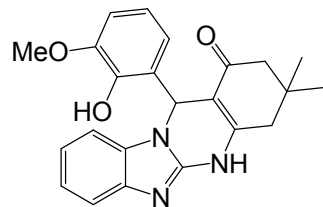
4c-<sup>13</sup>C-NMR



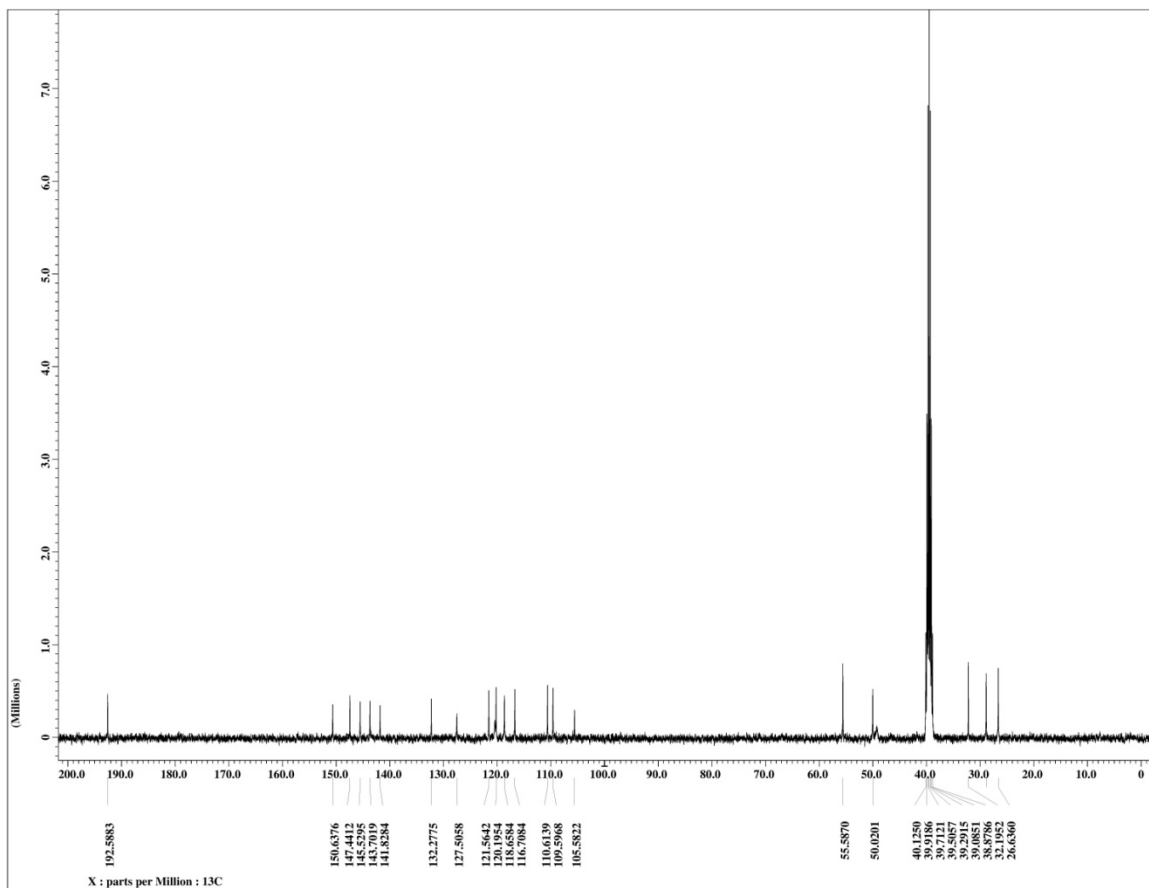


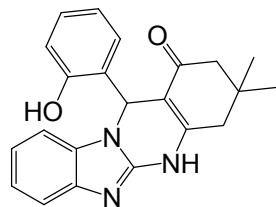
4d -<sup>1</sup>H-NMR



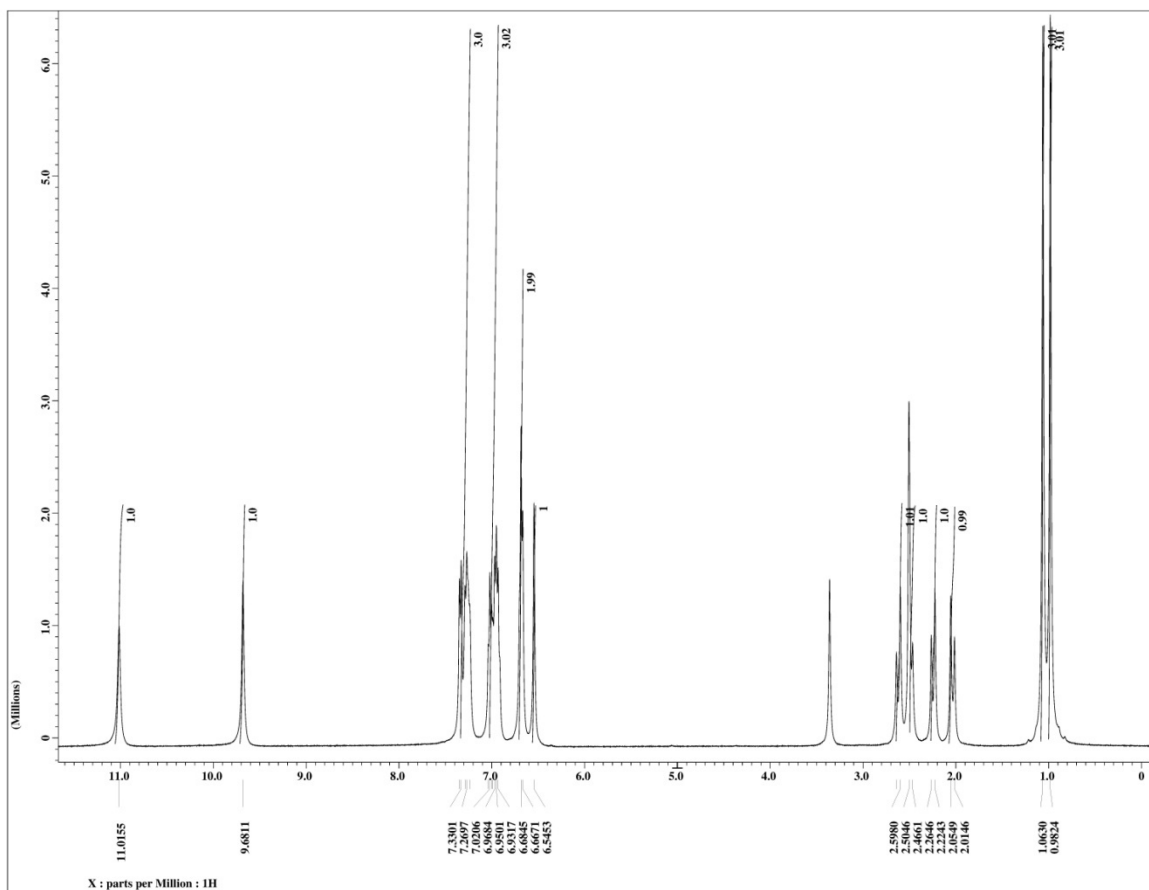


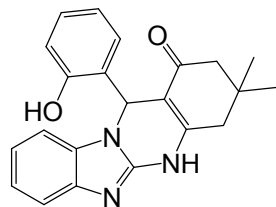
4d -  $^{13}\text{C}$ -NMR



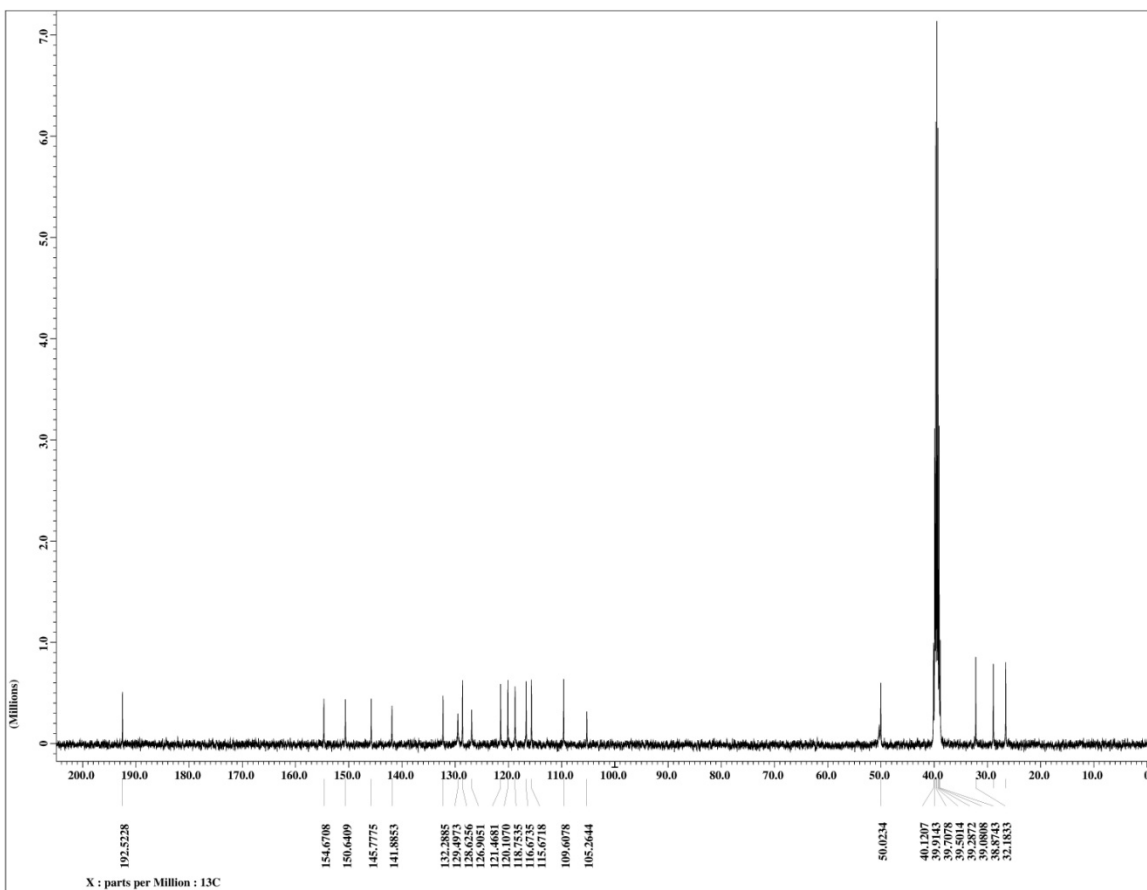


4e-<sup>1</sup>H-NMR

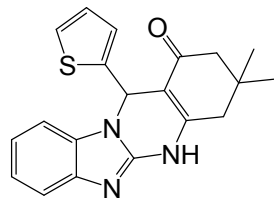




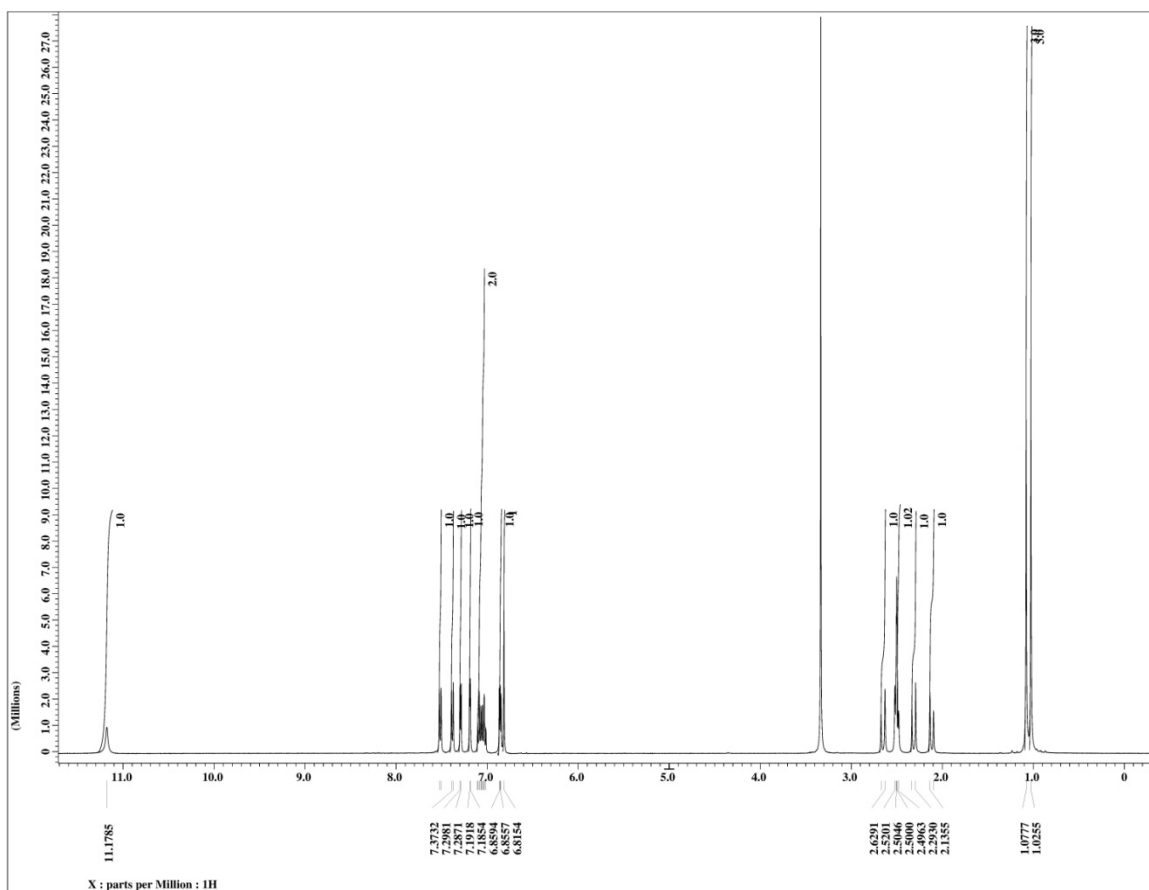
4e-<sup>13</sup>C-NMR

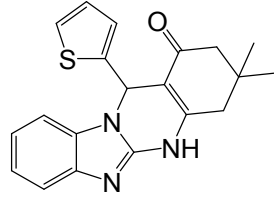




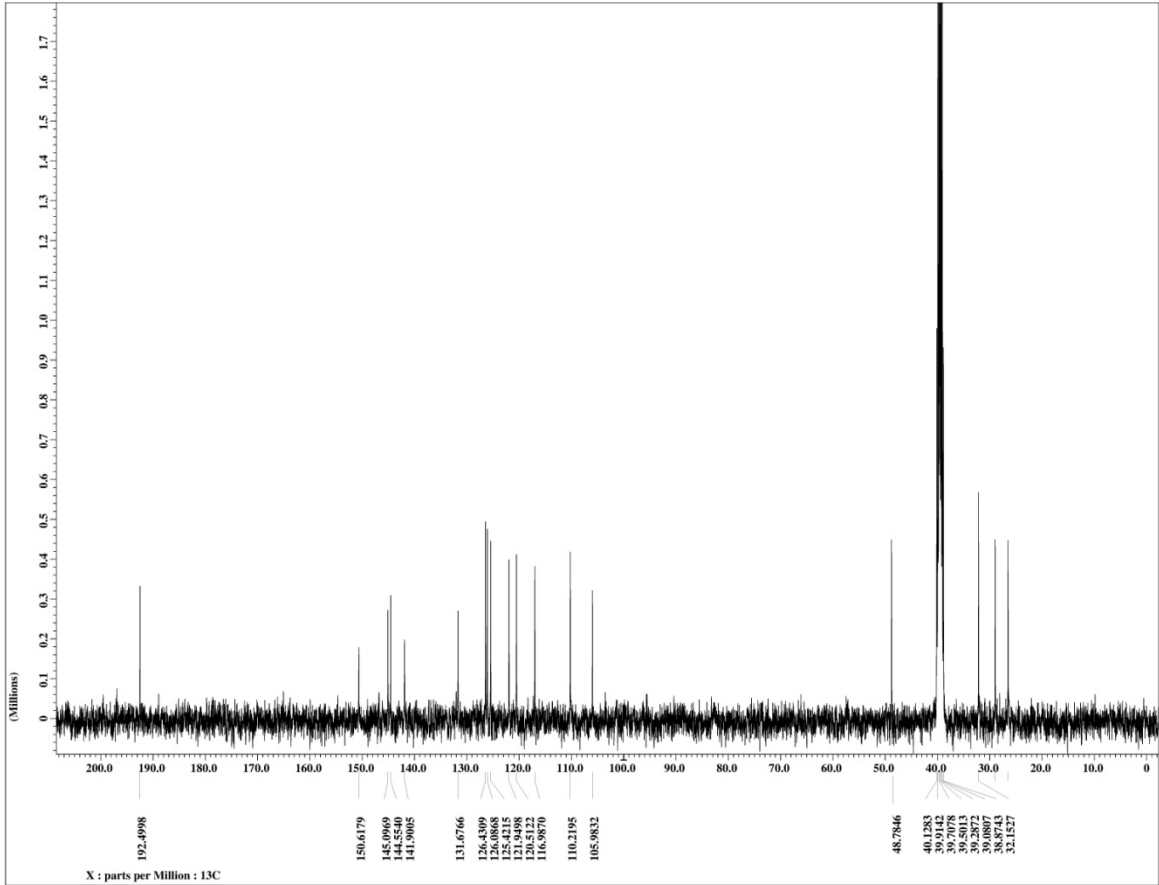


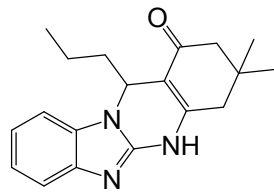
4f-<sup>1</sup>H-NMR



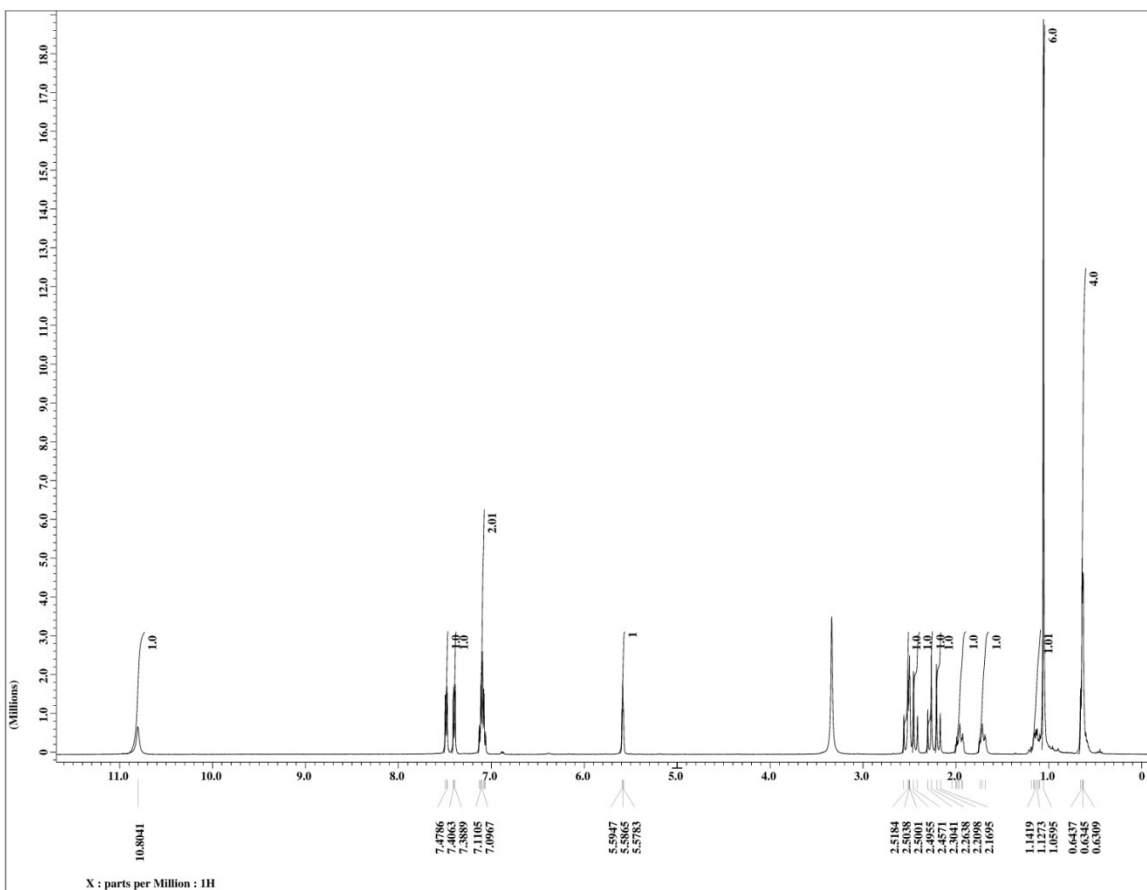


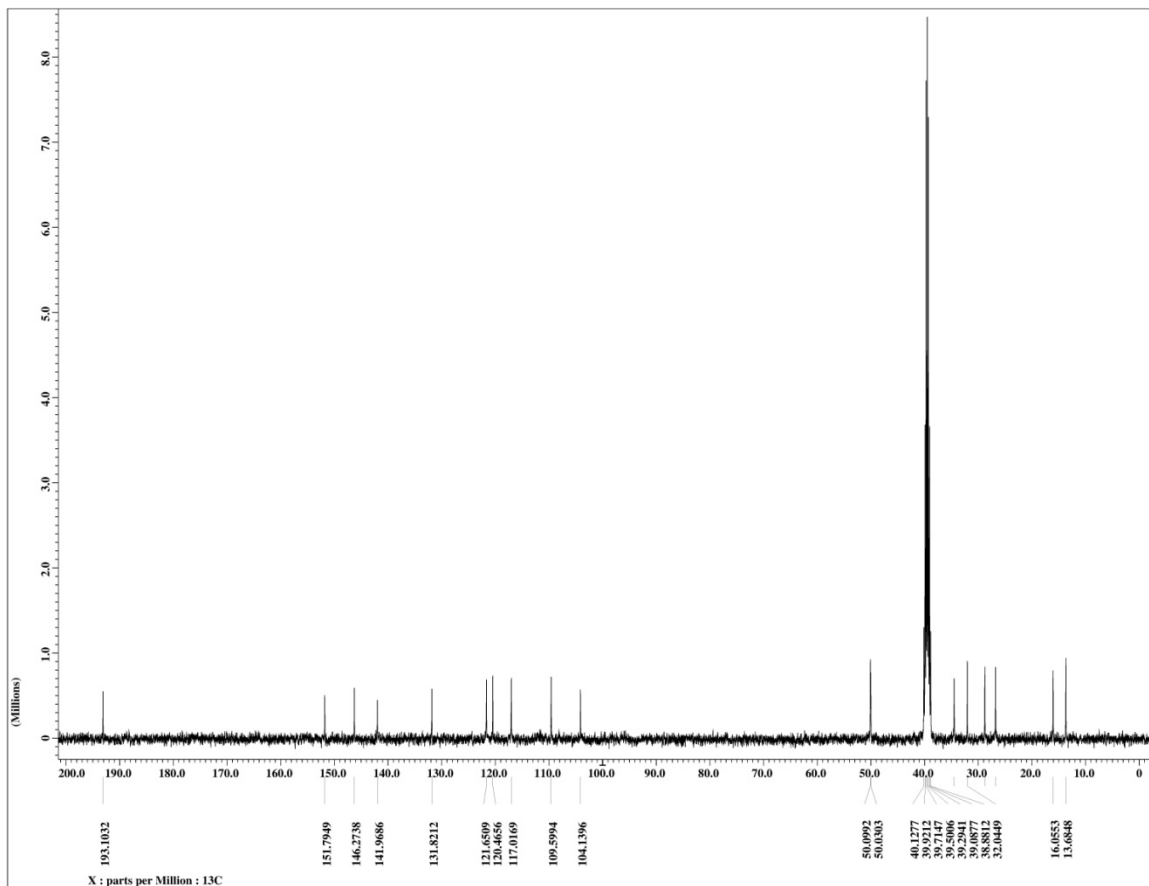
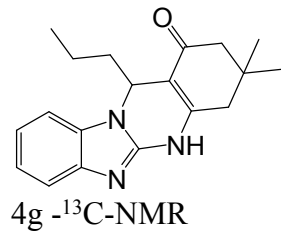
4f-<sup>13</sup>C-NMR

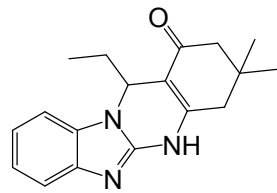




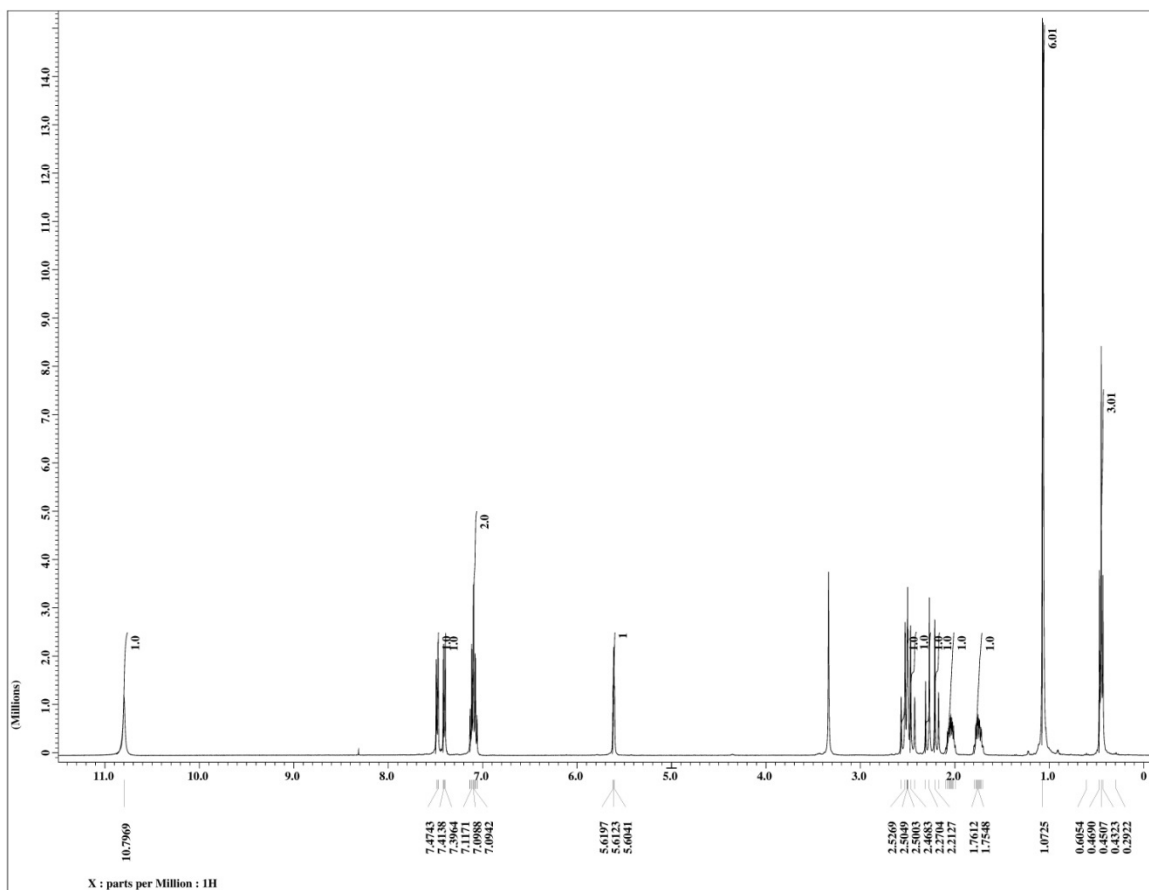
4g -<sup>1</sup>H-NMR

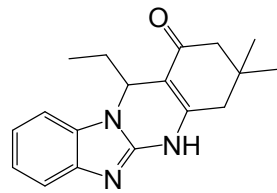




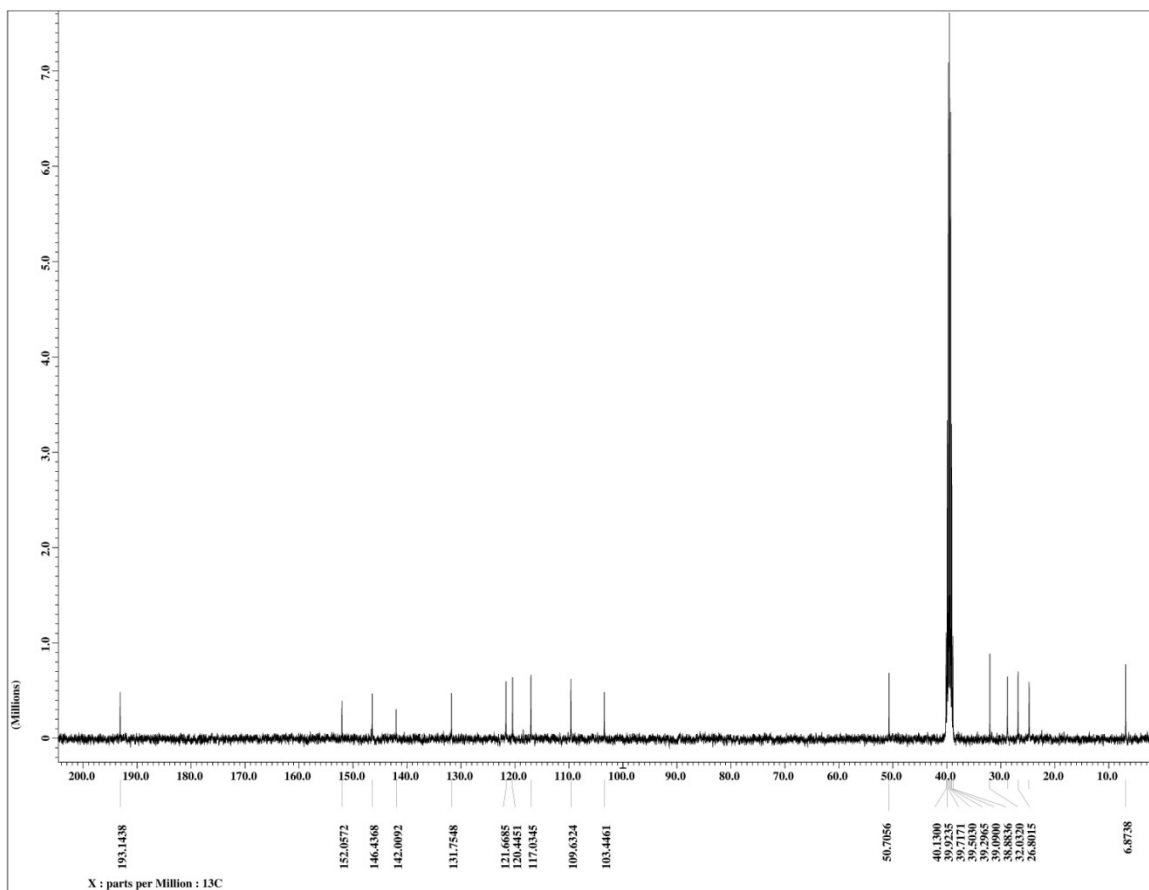


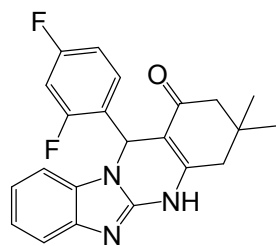
4h- <sup>1</sup>H-NMR



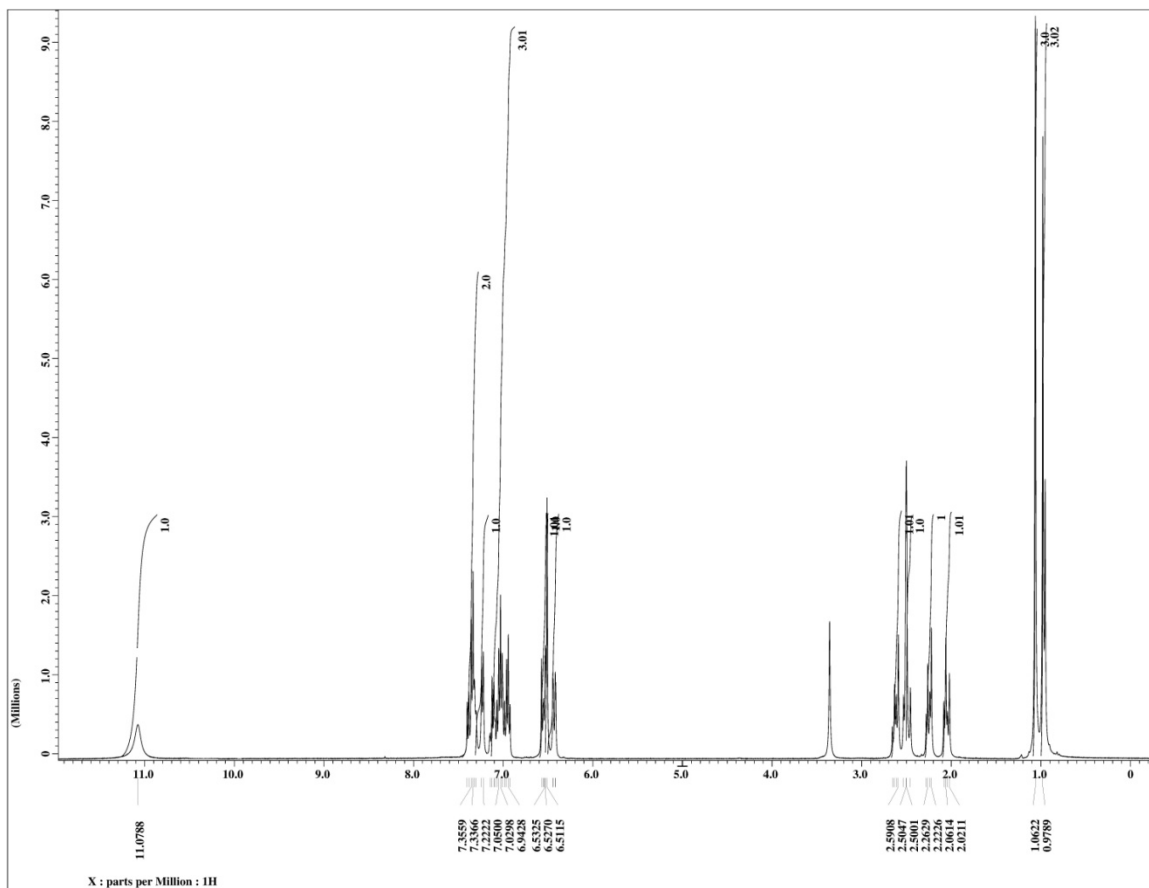


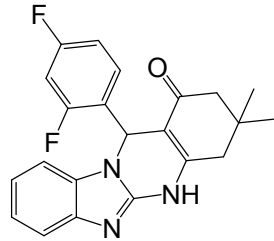
4h-  $^{13}\text{C}$ -NMR



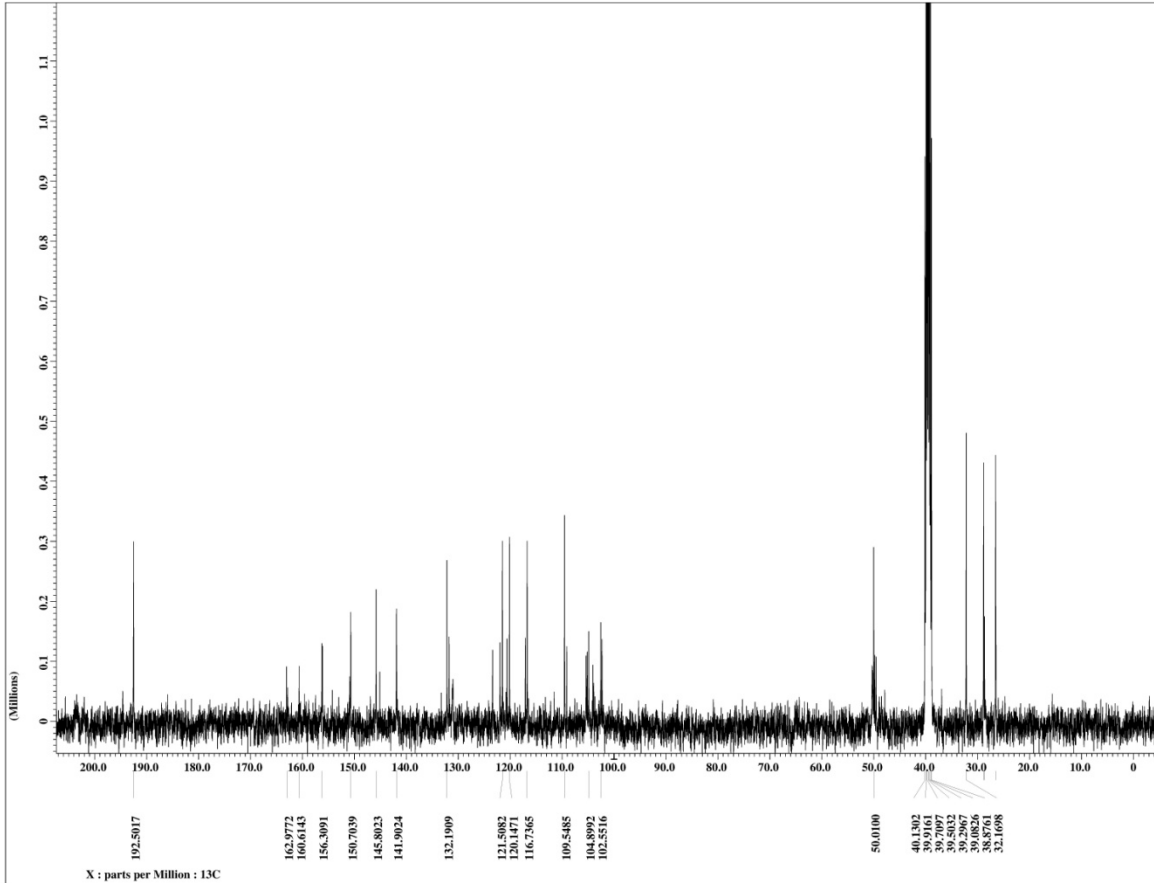


4i-<sup>1</sup>H-NMR

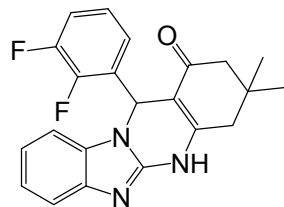




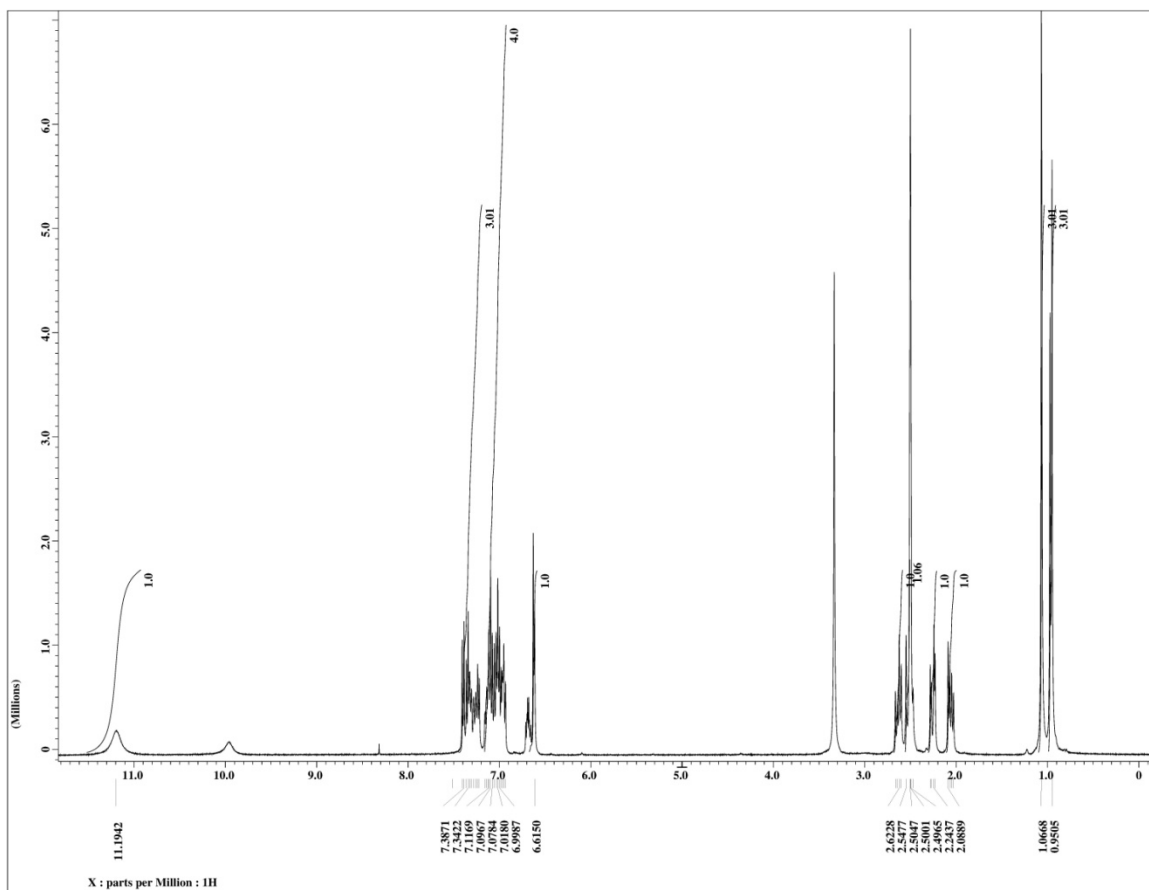
4i-<sup>13</sup>C-NMR

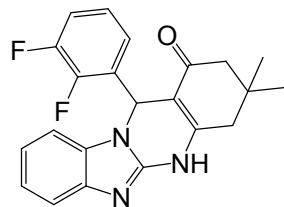




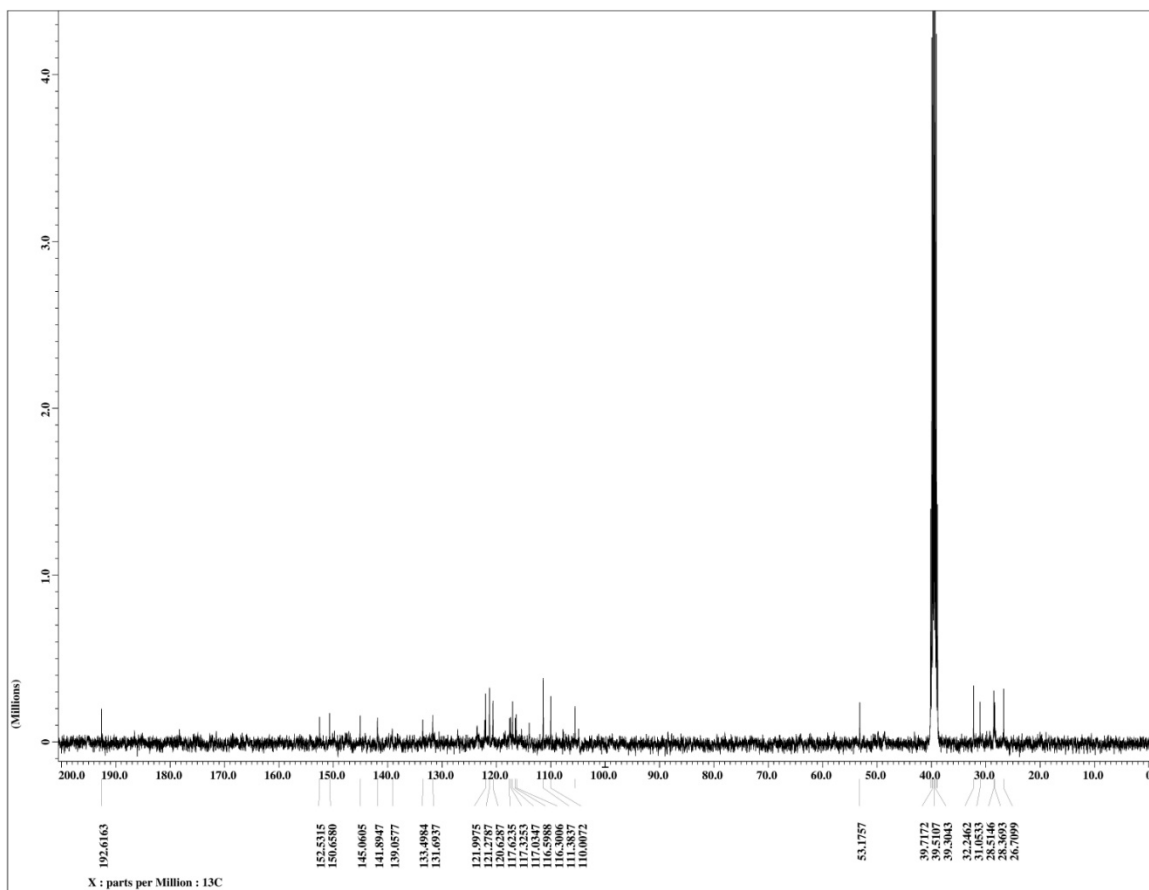


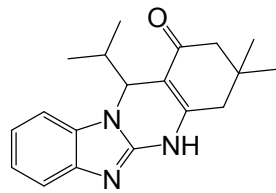
4j-<sup>1</sup>H-NMR



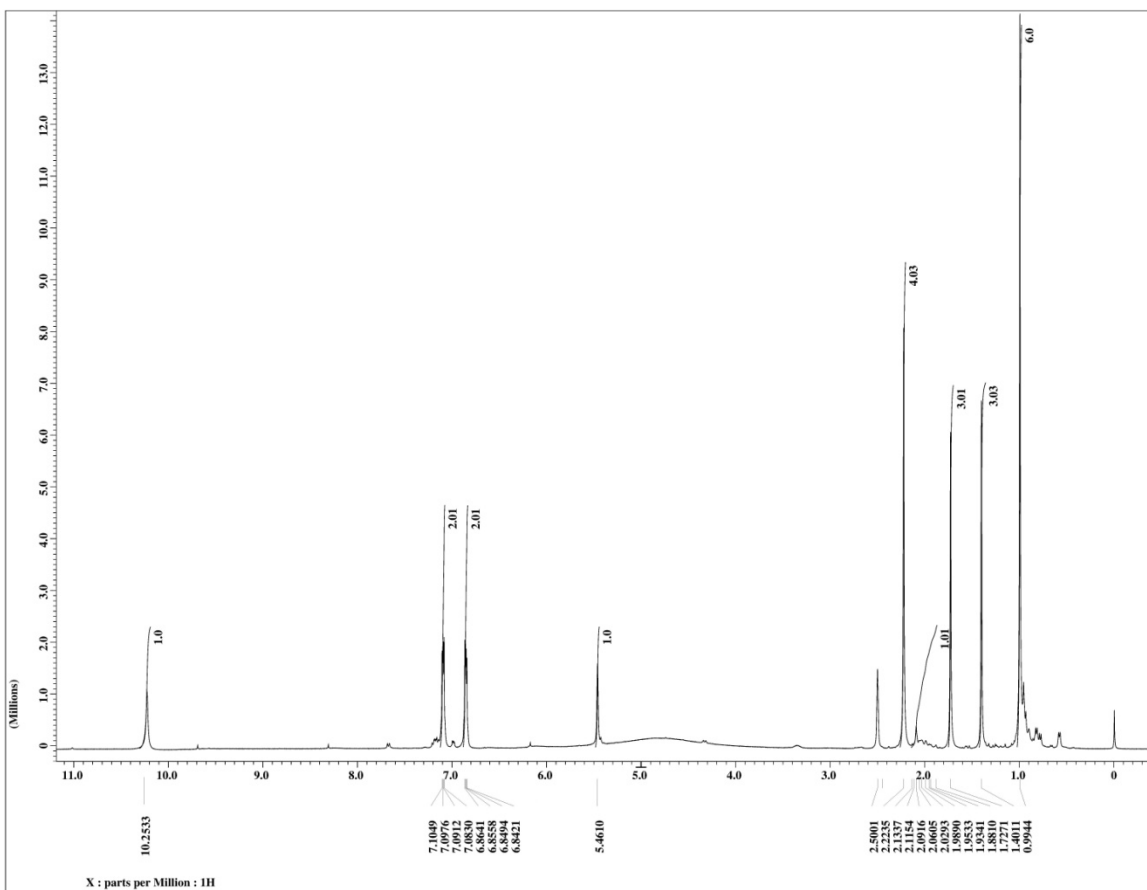


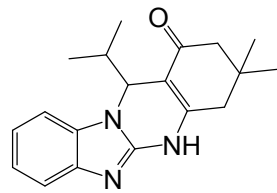
4j-<sup>13</sup>C-NMR



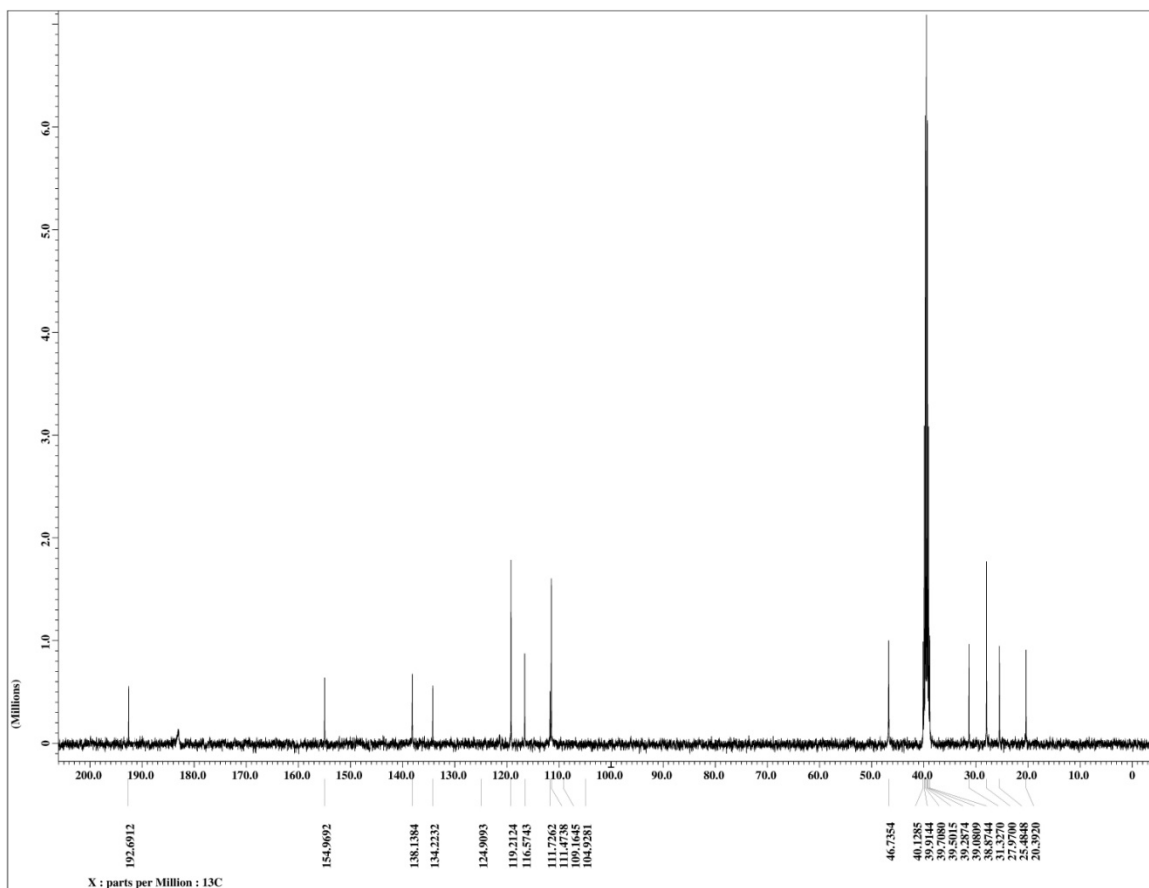


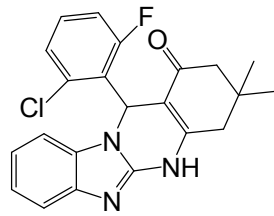
4k- <sup>1</sup>H-NMR



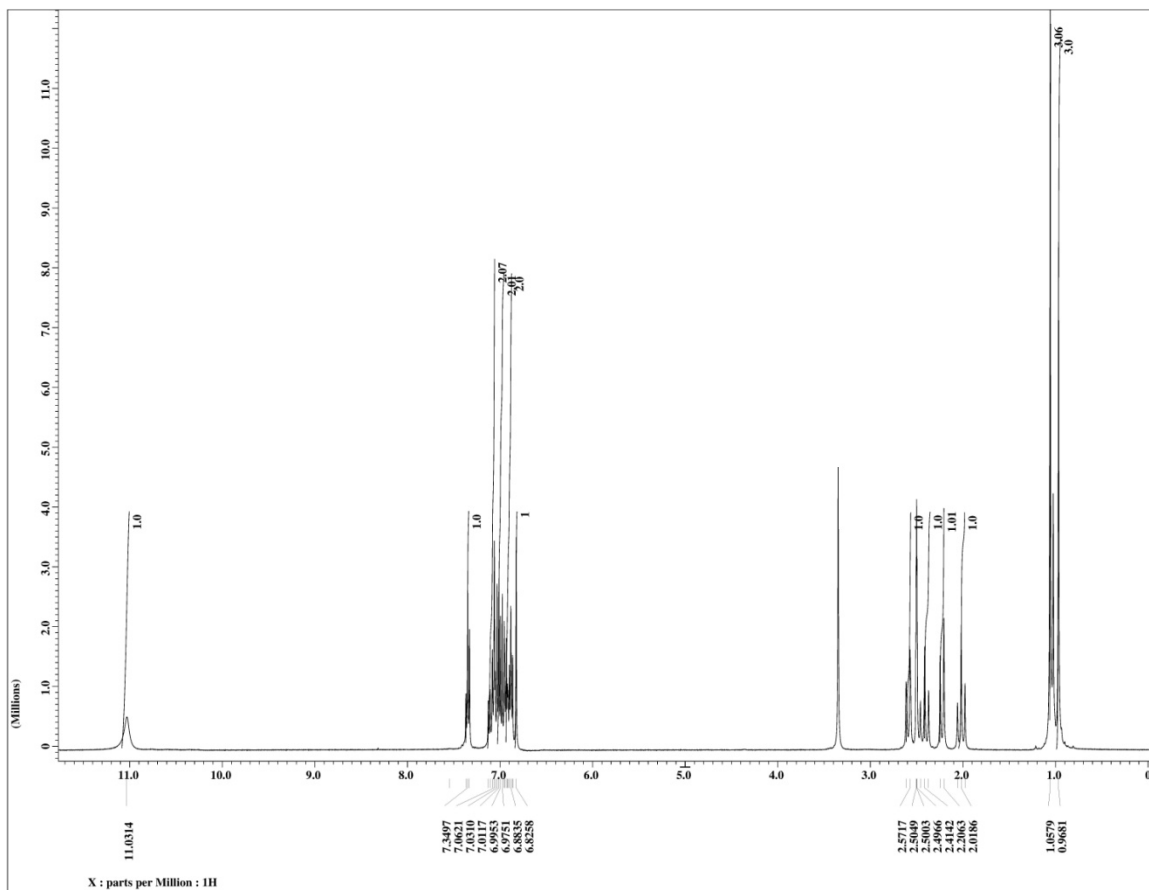


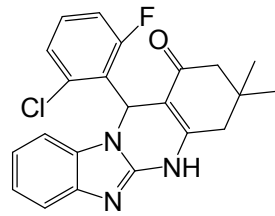
4k-  $^{13}\text{C}$ -NMR



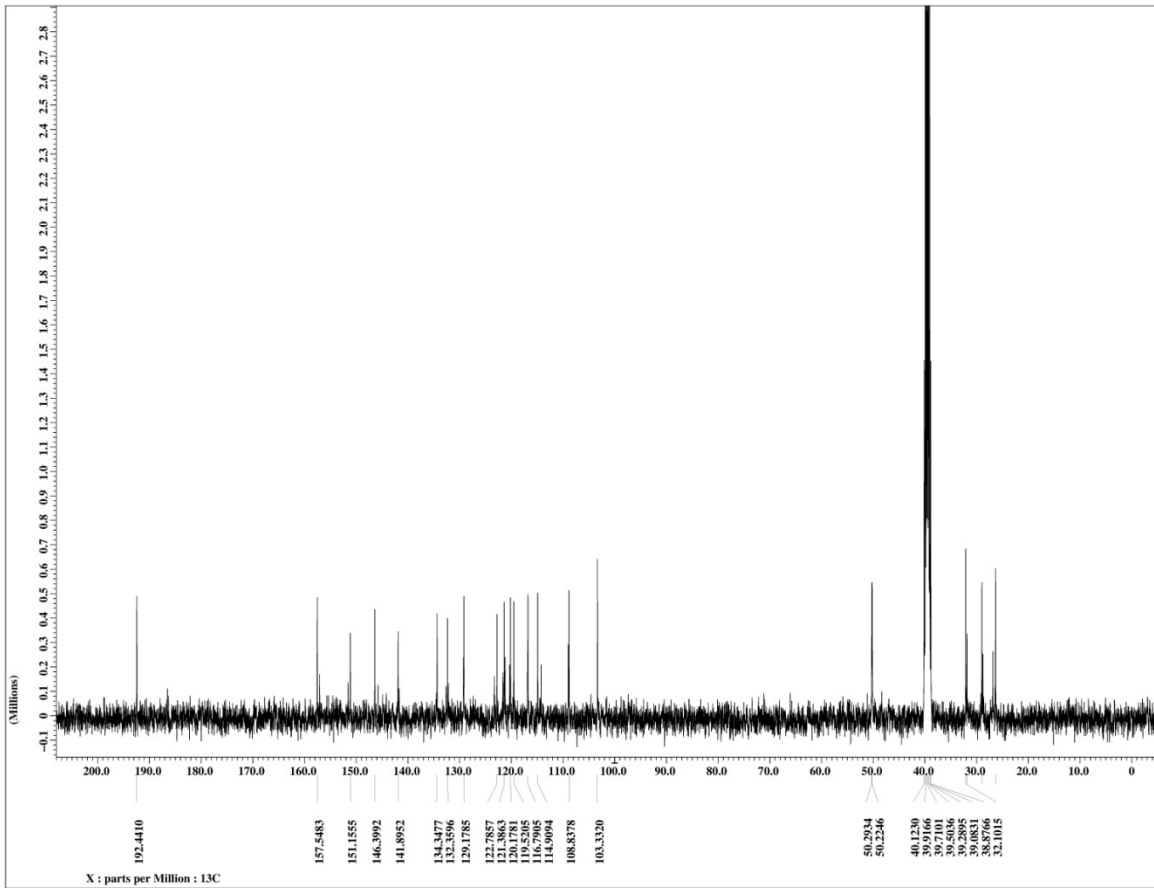


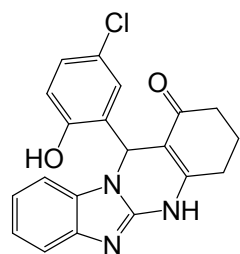
41-<sup>1</sup>H-NMR



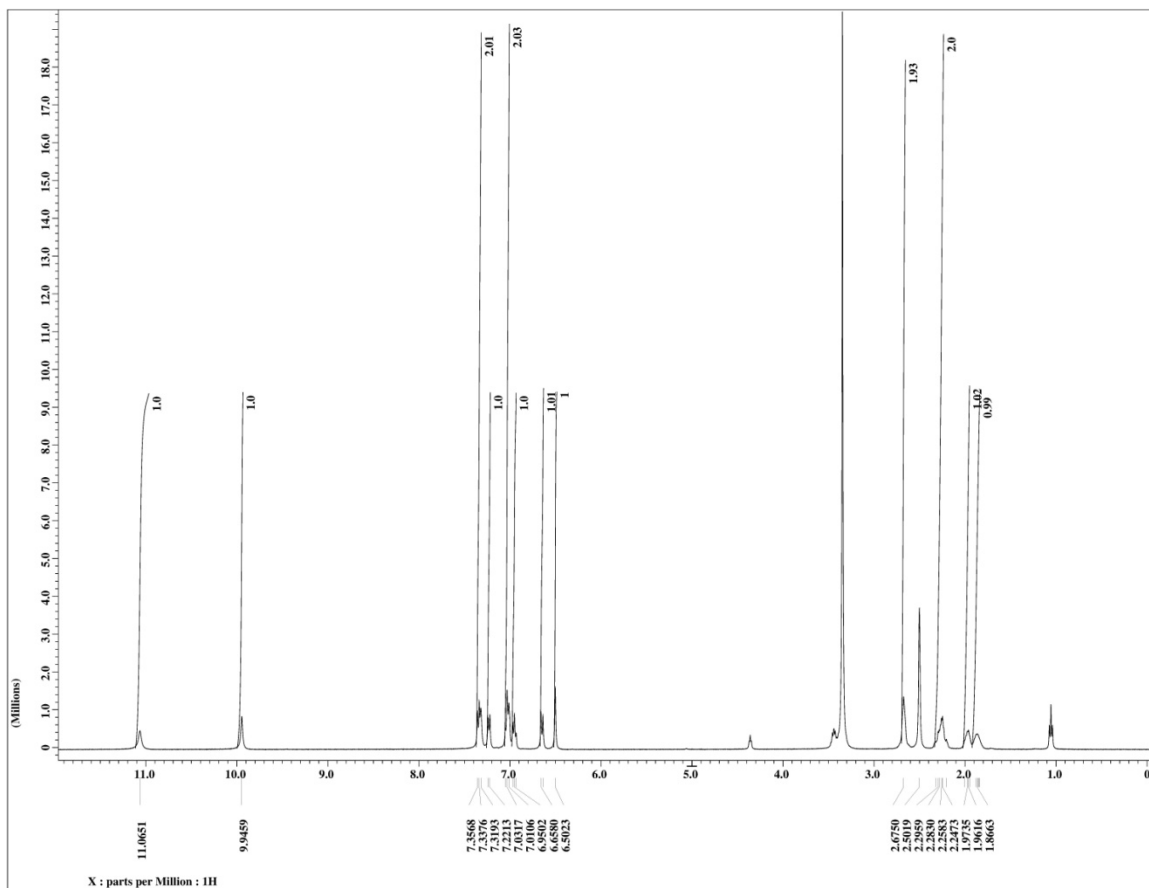


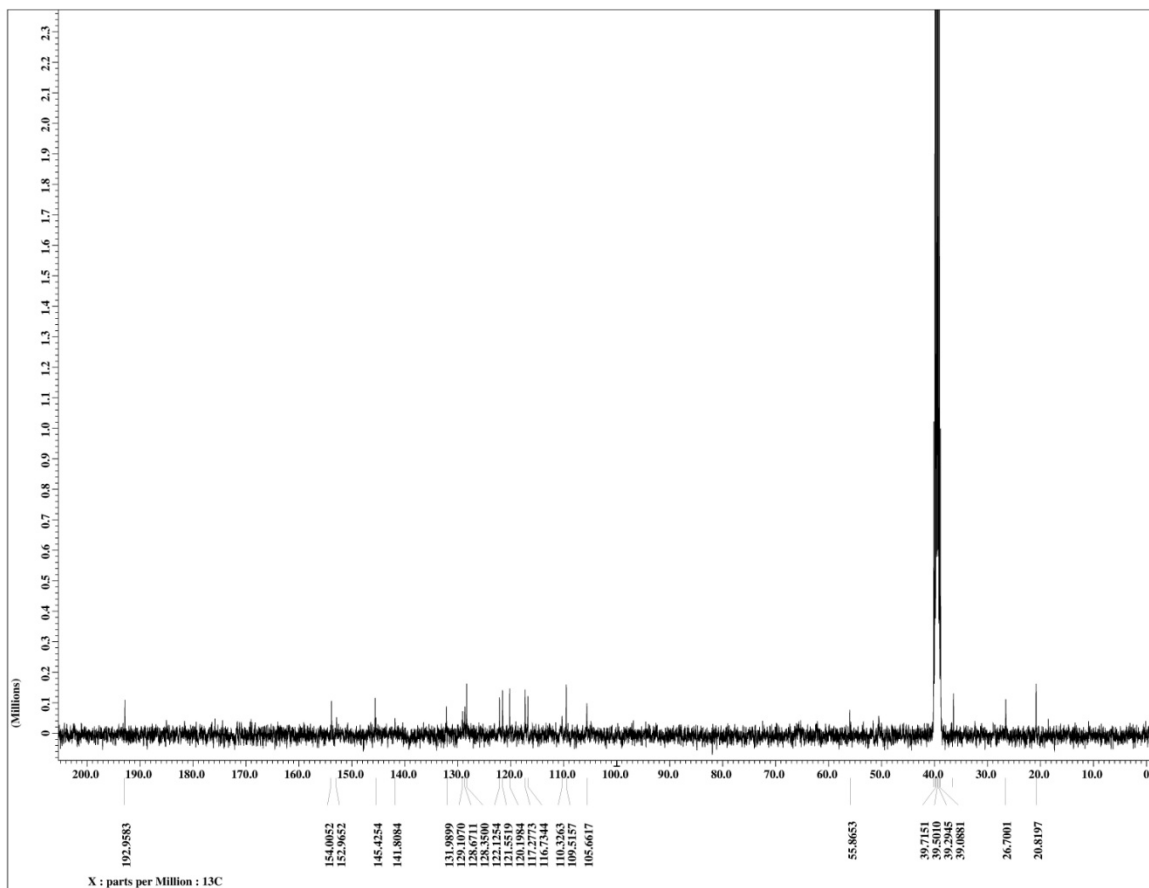
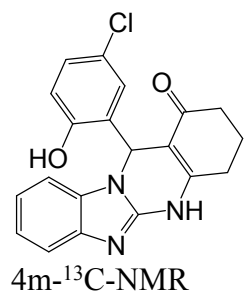
4f-<sup>13</sup>C-NMR



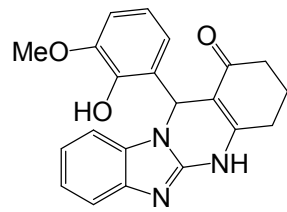


4m-<sup>1</sup>H-NMR

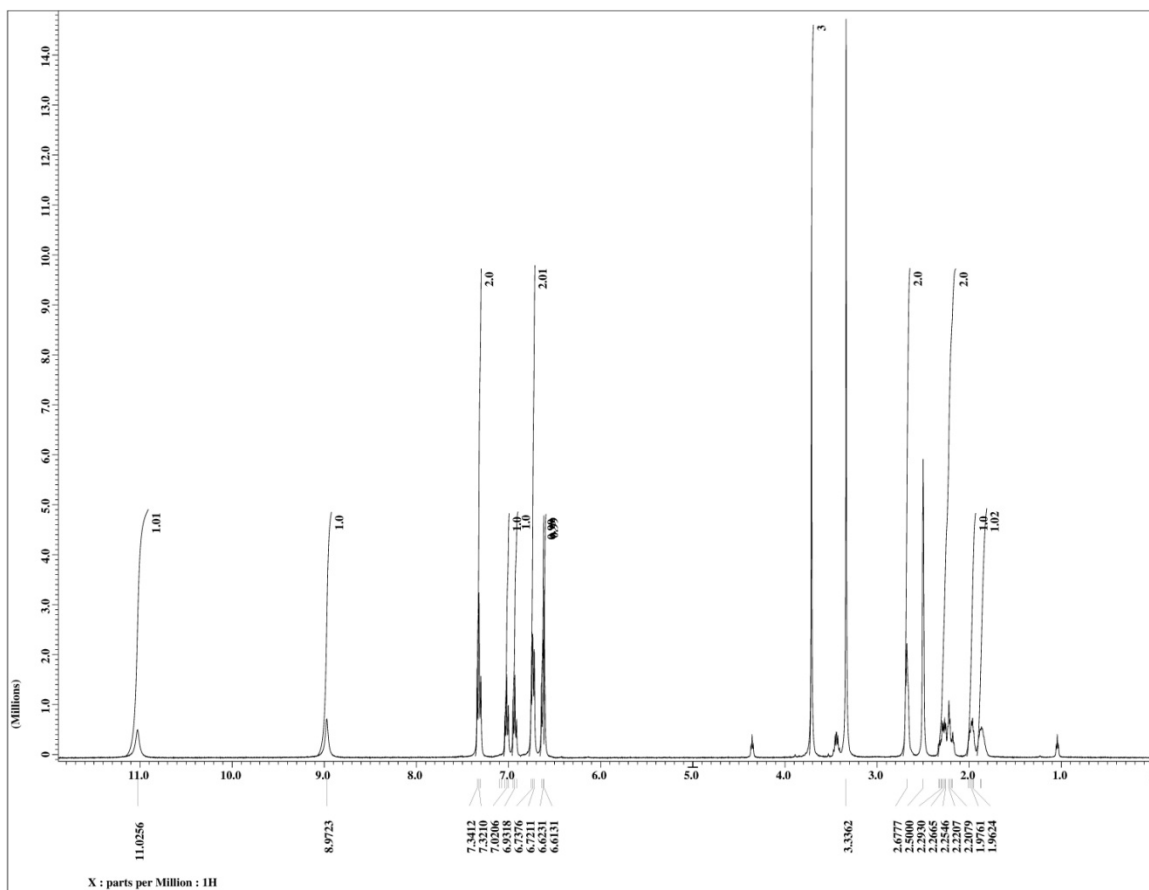


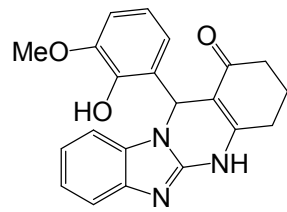




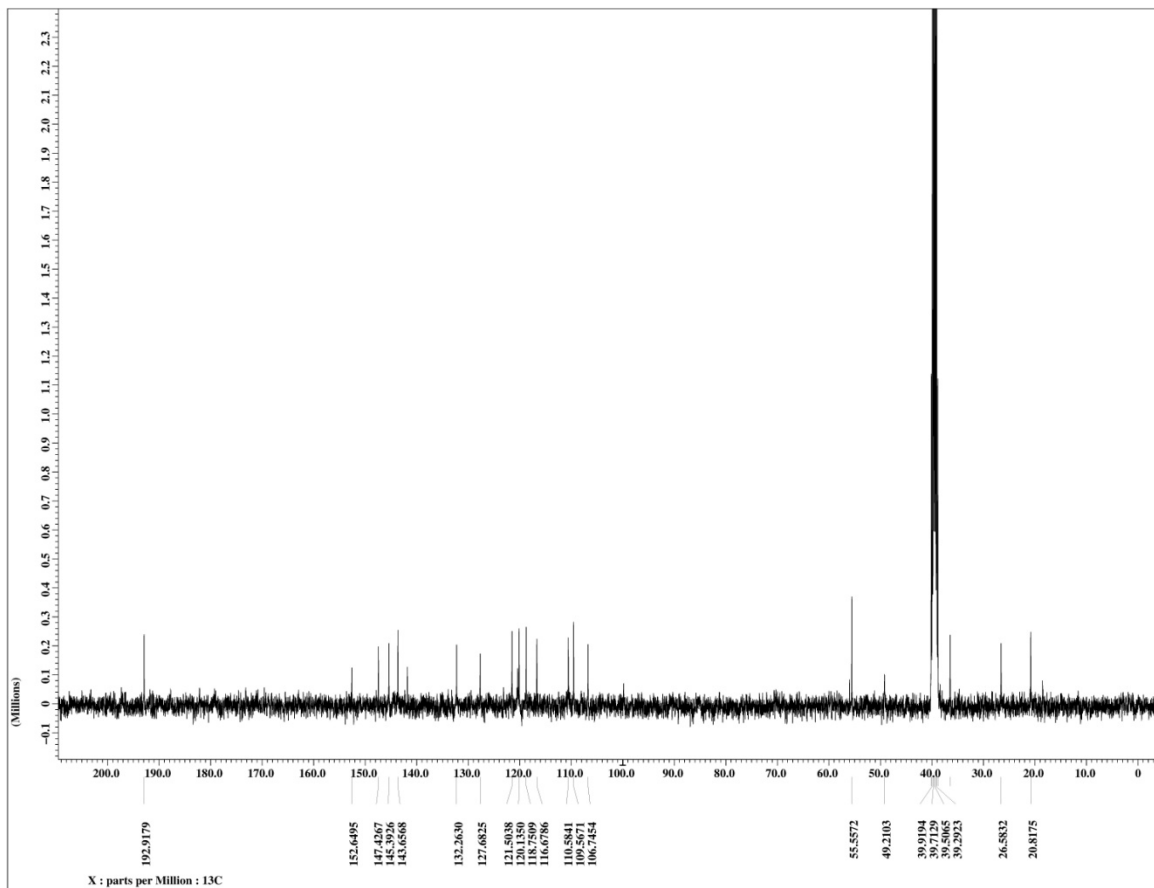


4n-<sup>1</sup>H-NMR

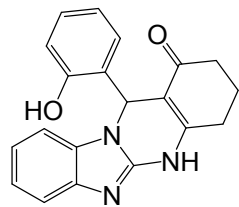




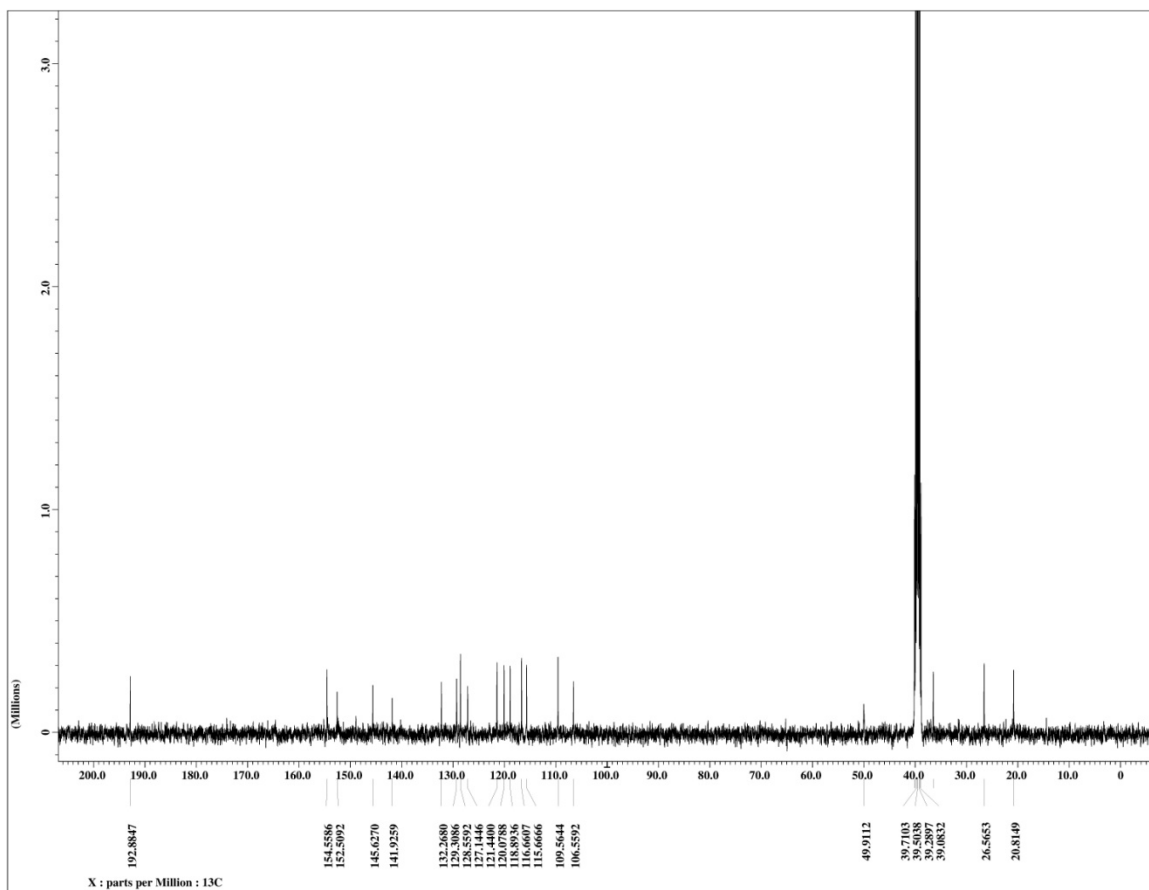
4n-<sup>13</sup>C-NMR

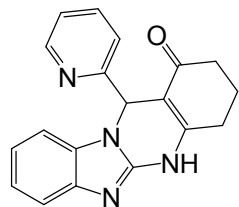




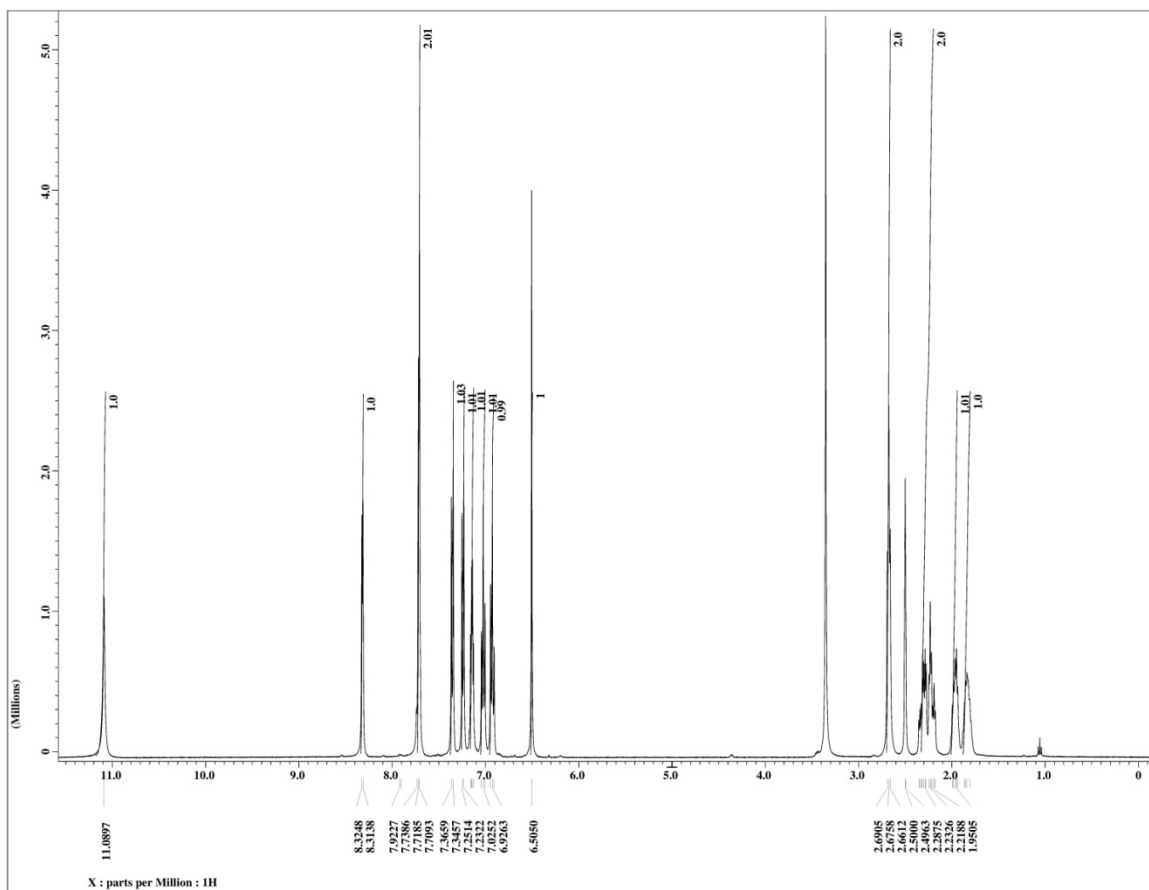


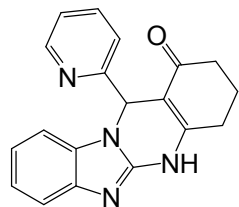
4o-<sup>13</sup>C-NMR



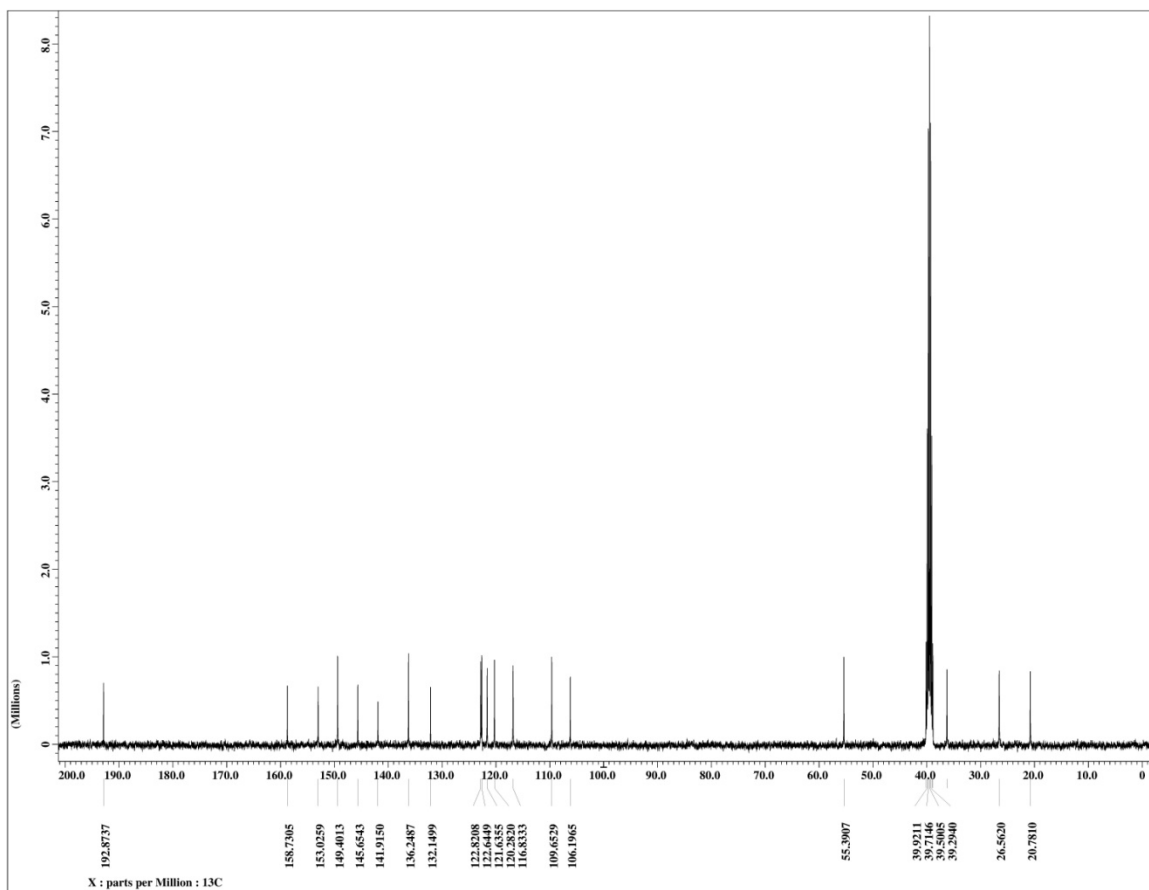


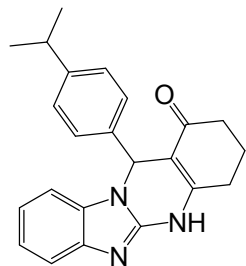
4p-<sup>1</sup>H-NMR



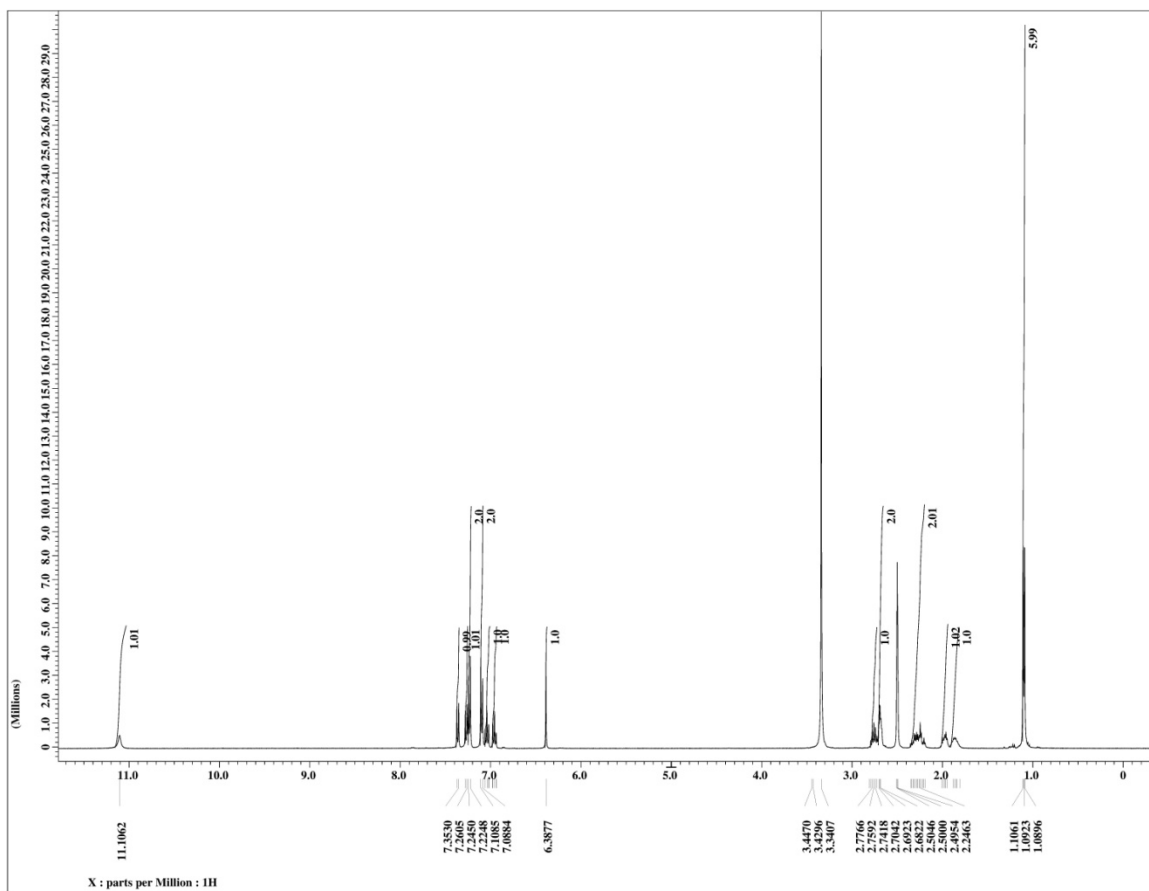


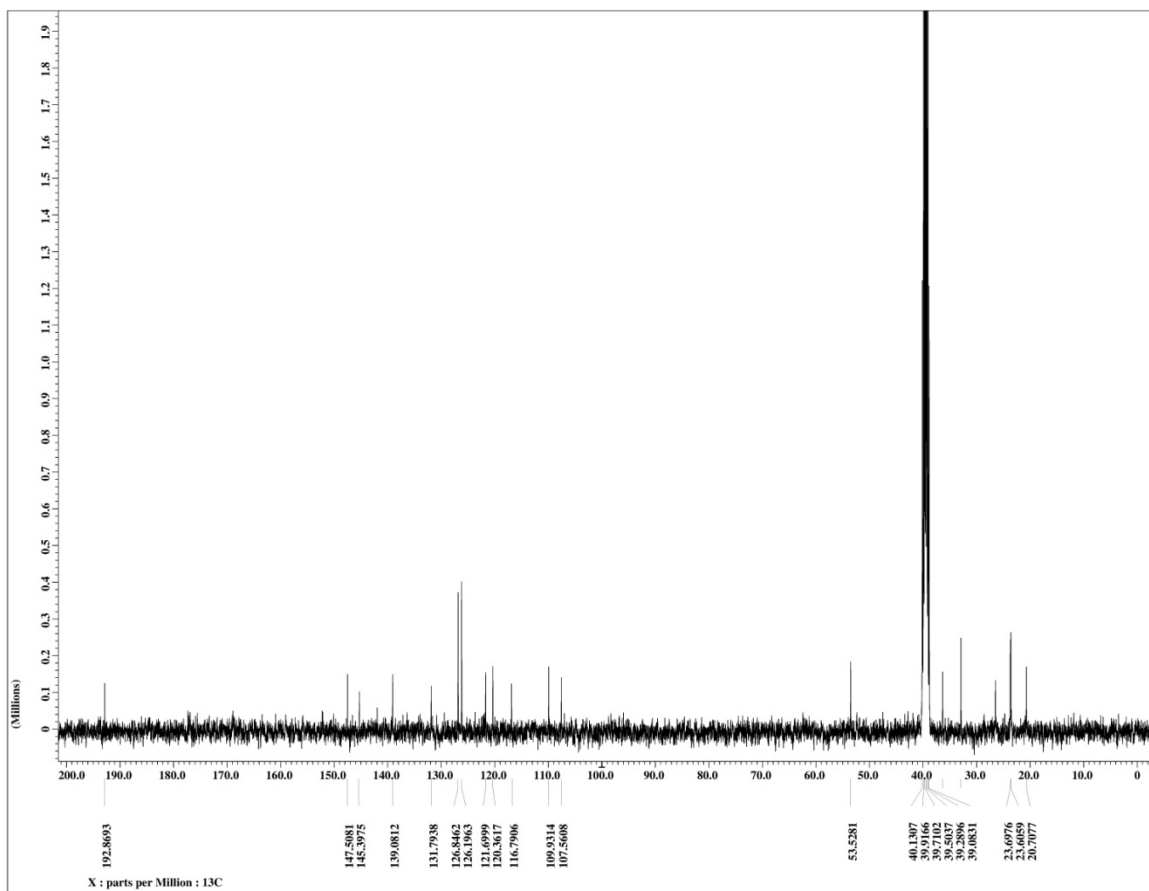
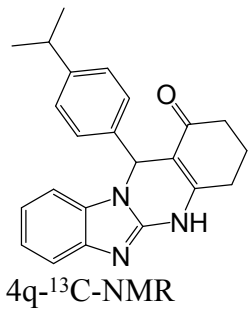
4p-<sup>13</sup>C-NMR



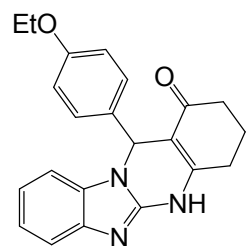


4q-<sup>1</sup>H-NMR

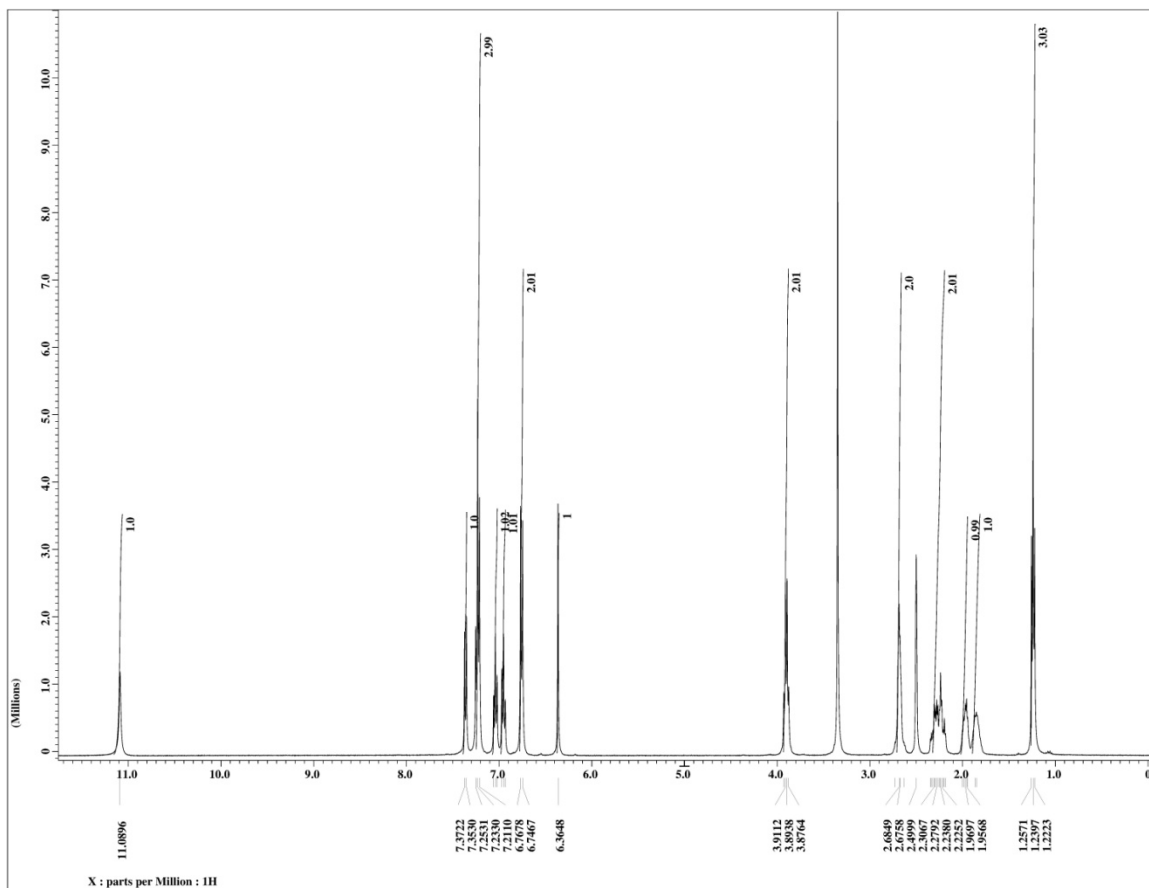


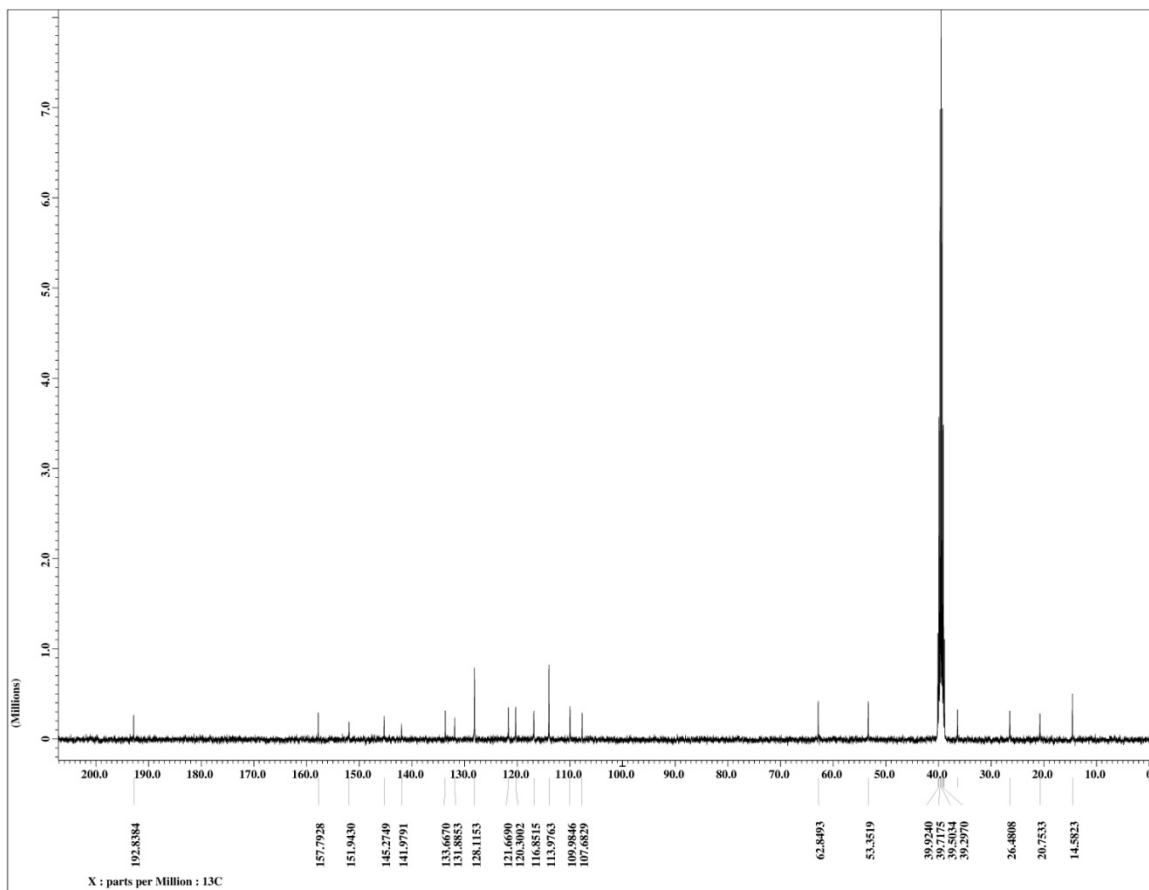
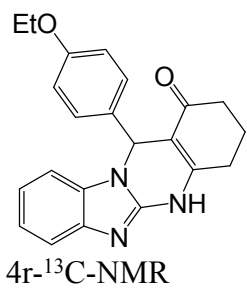


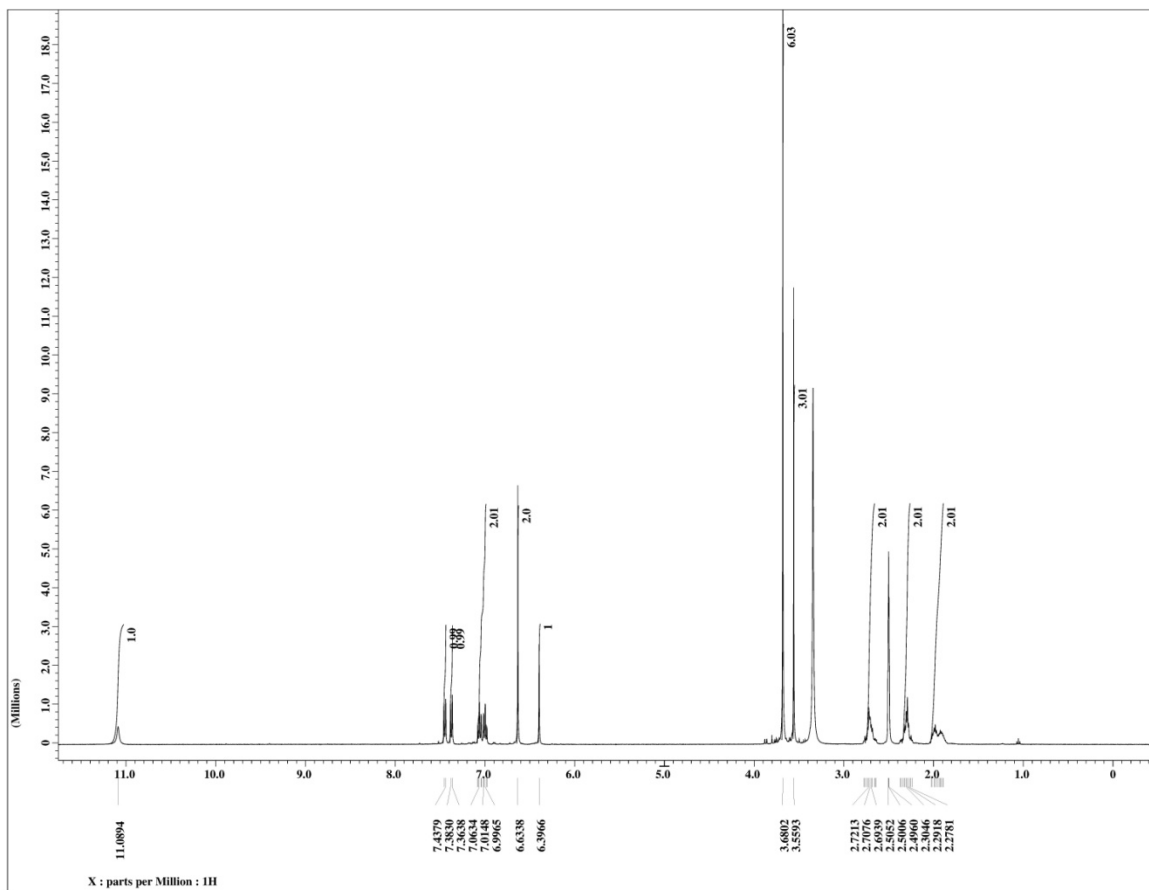
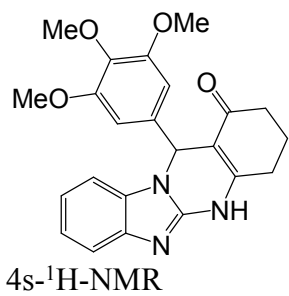


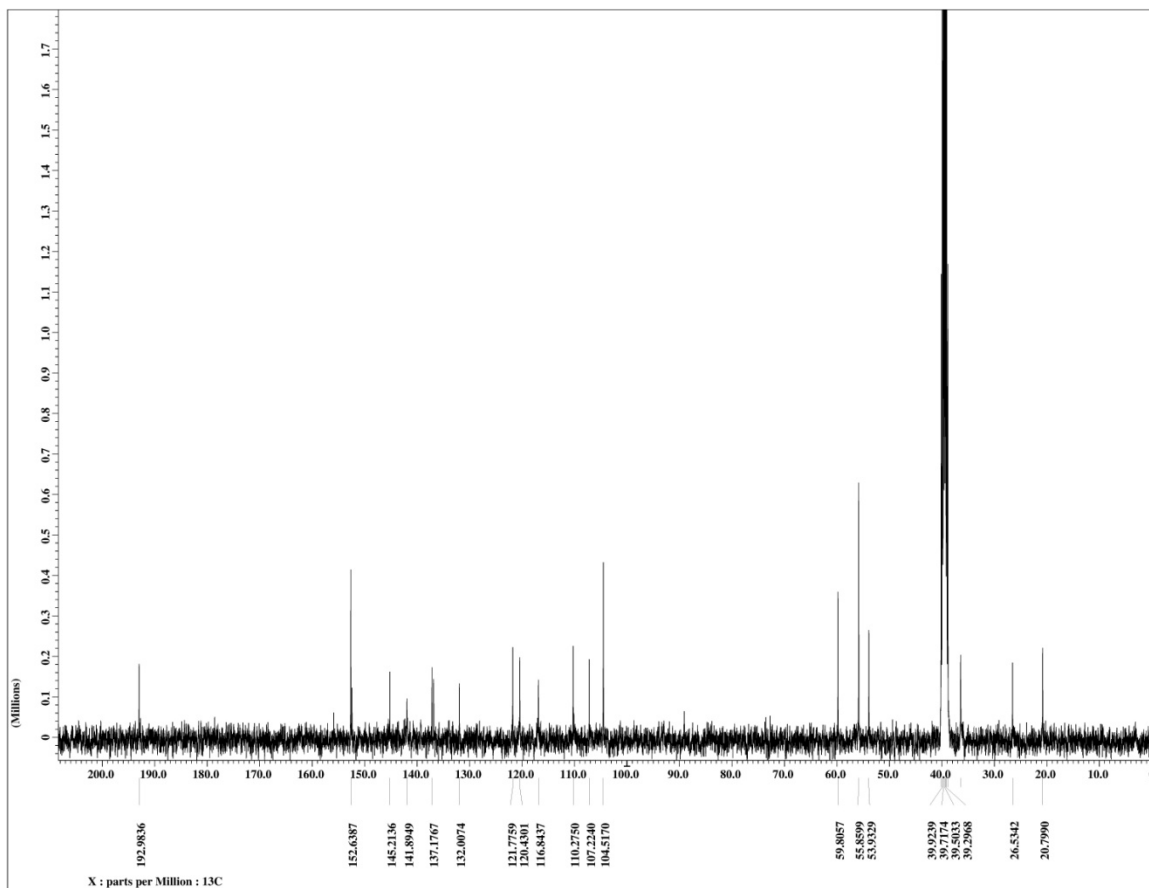
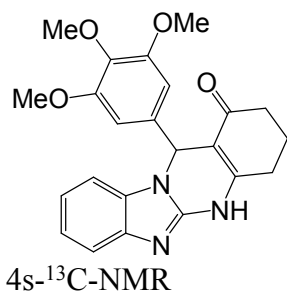


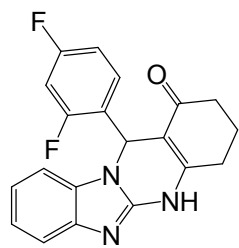
4r-<sup>1</sup>H-NMR



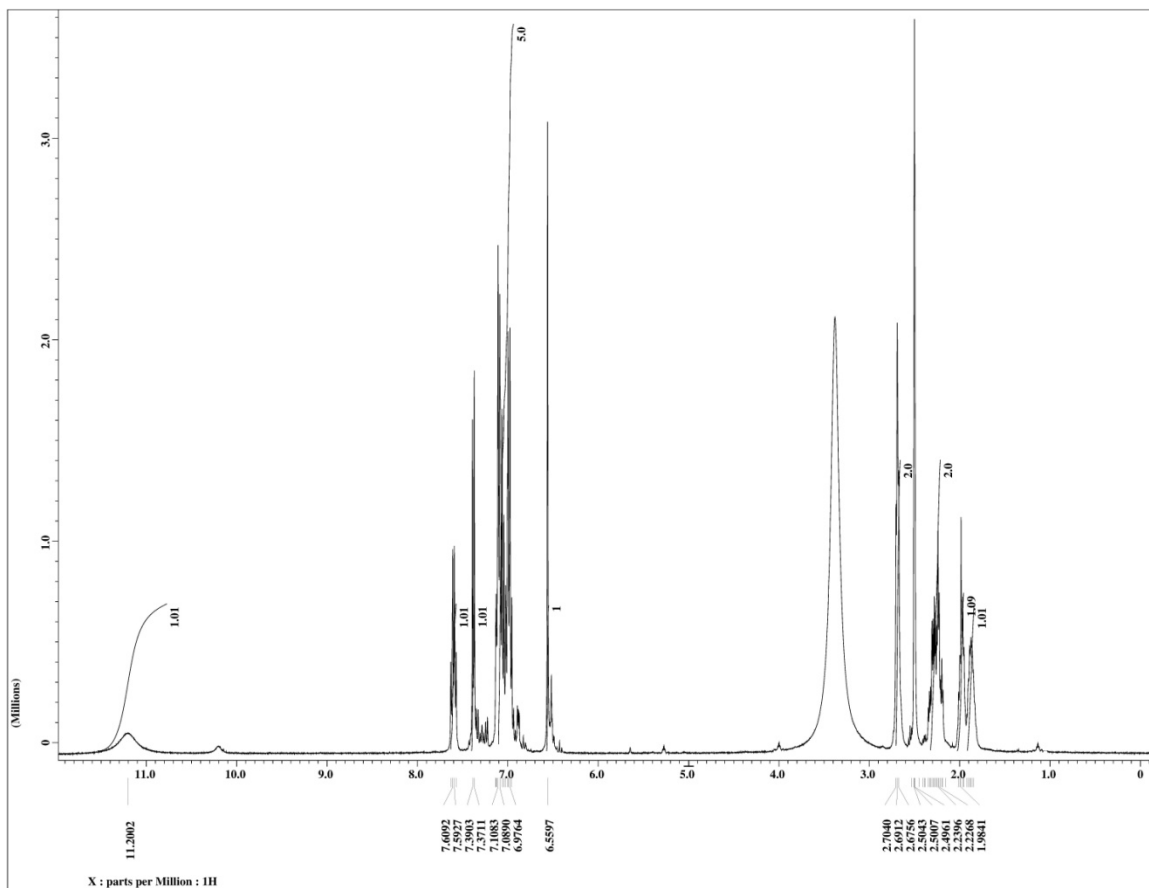


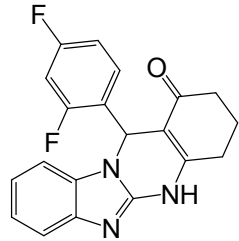




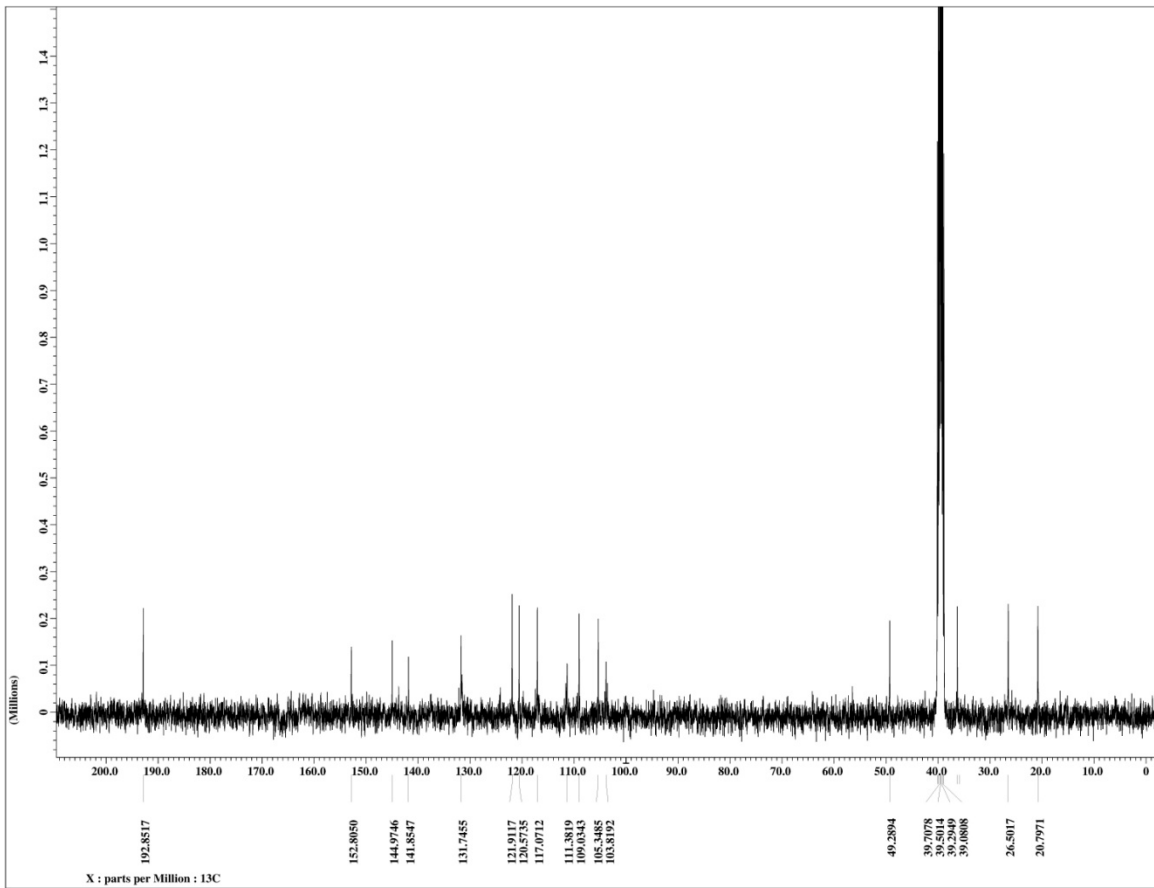


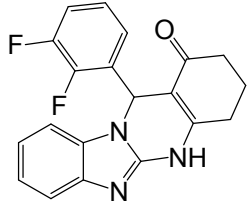
4t-<sup>1</sup>H-NMR



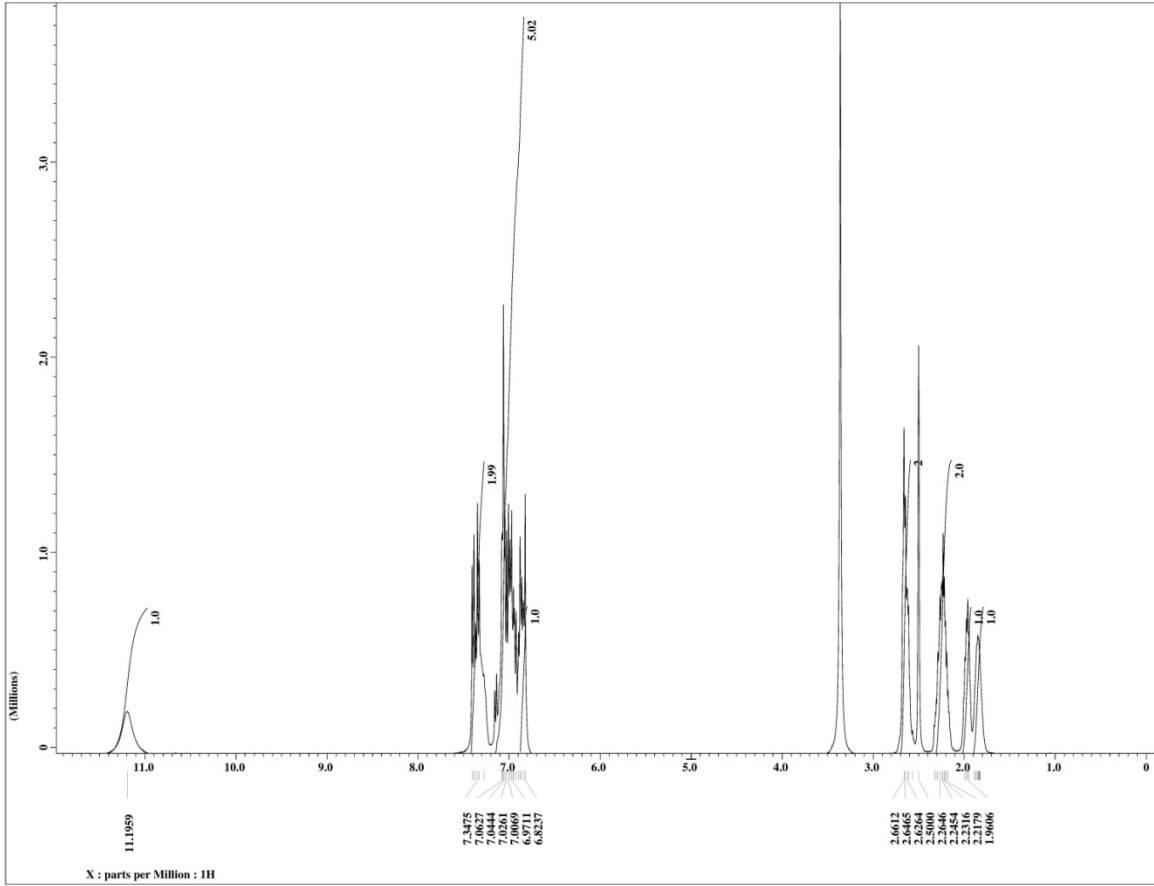


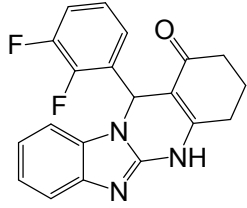
4t-<sup>13</sup>C-NMR



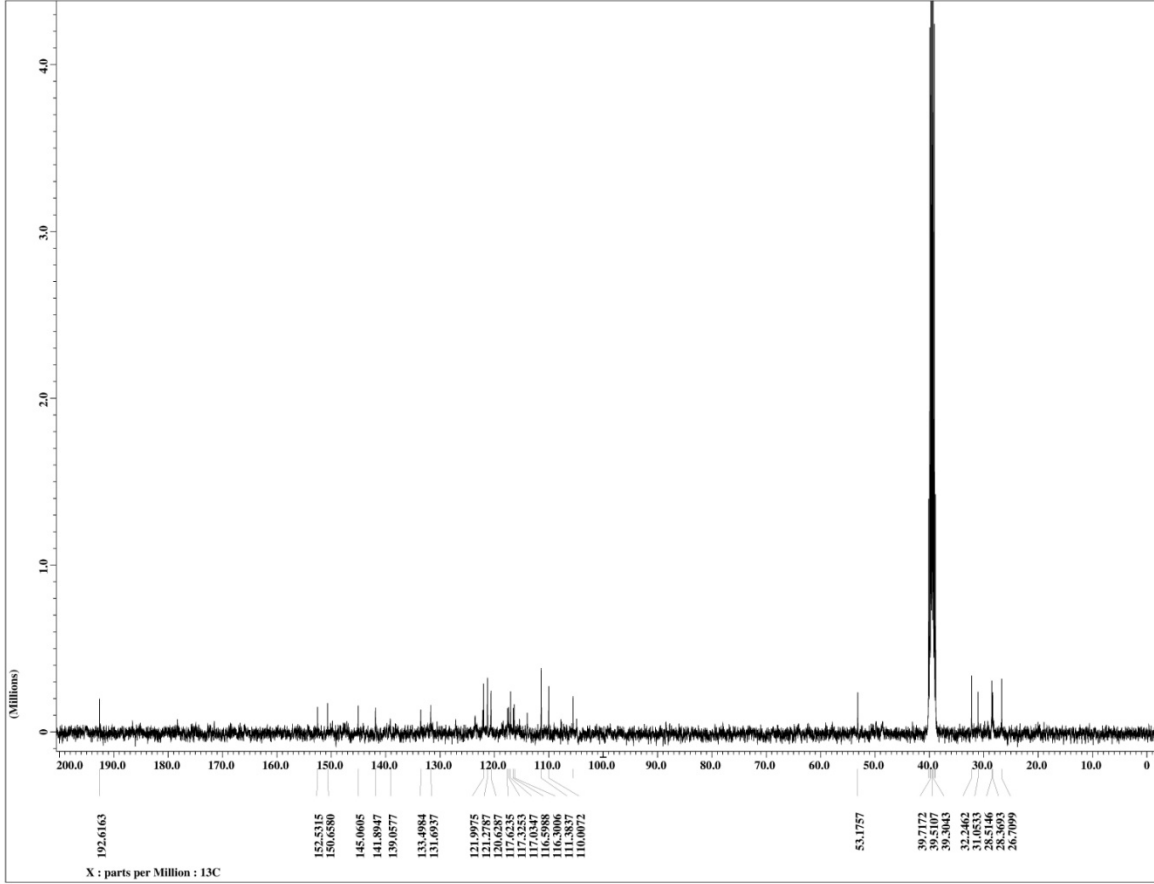


4u-<sup>1</sup>H-NMR

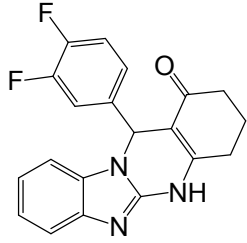




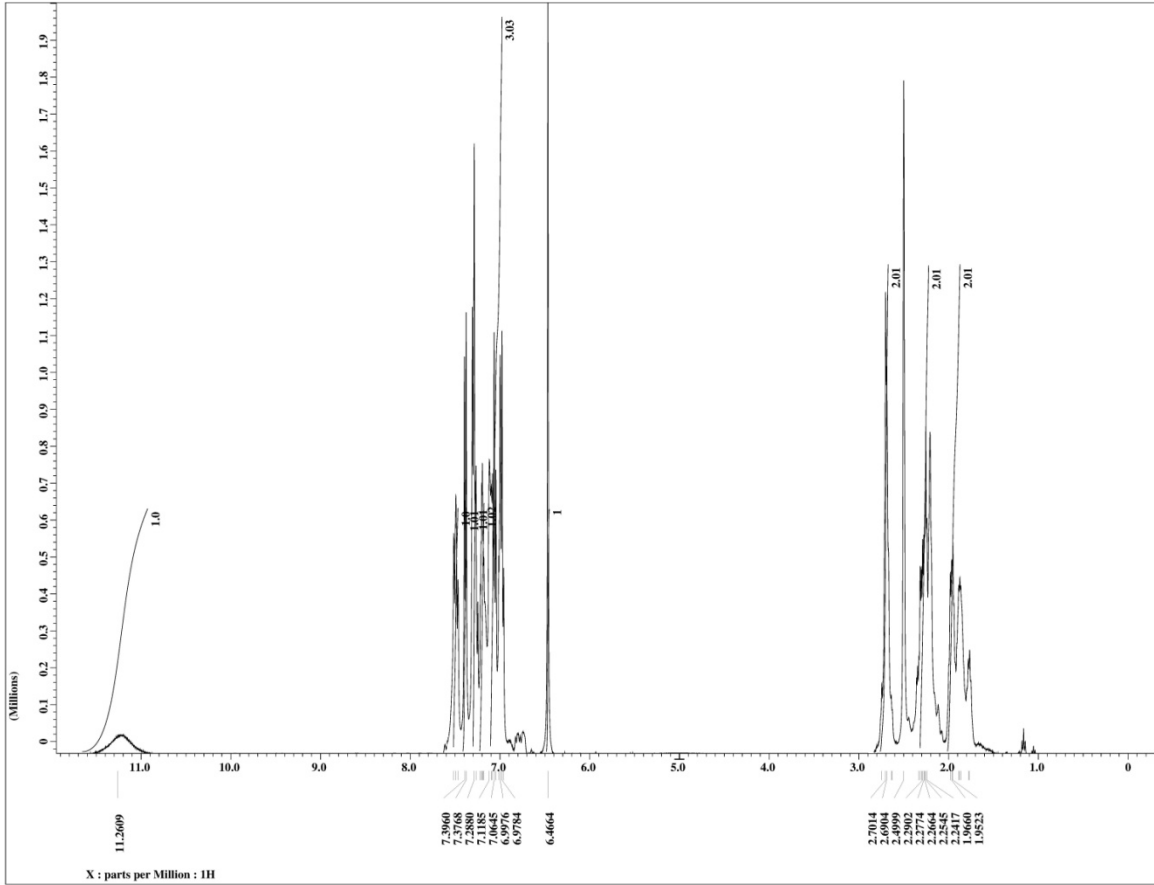
4u-<sup>13</sup>C-NMR

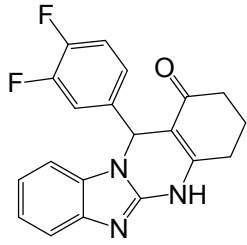




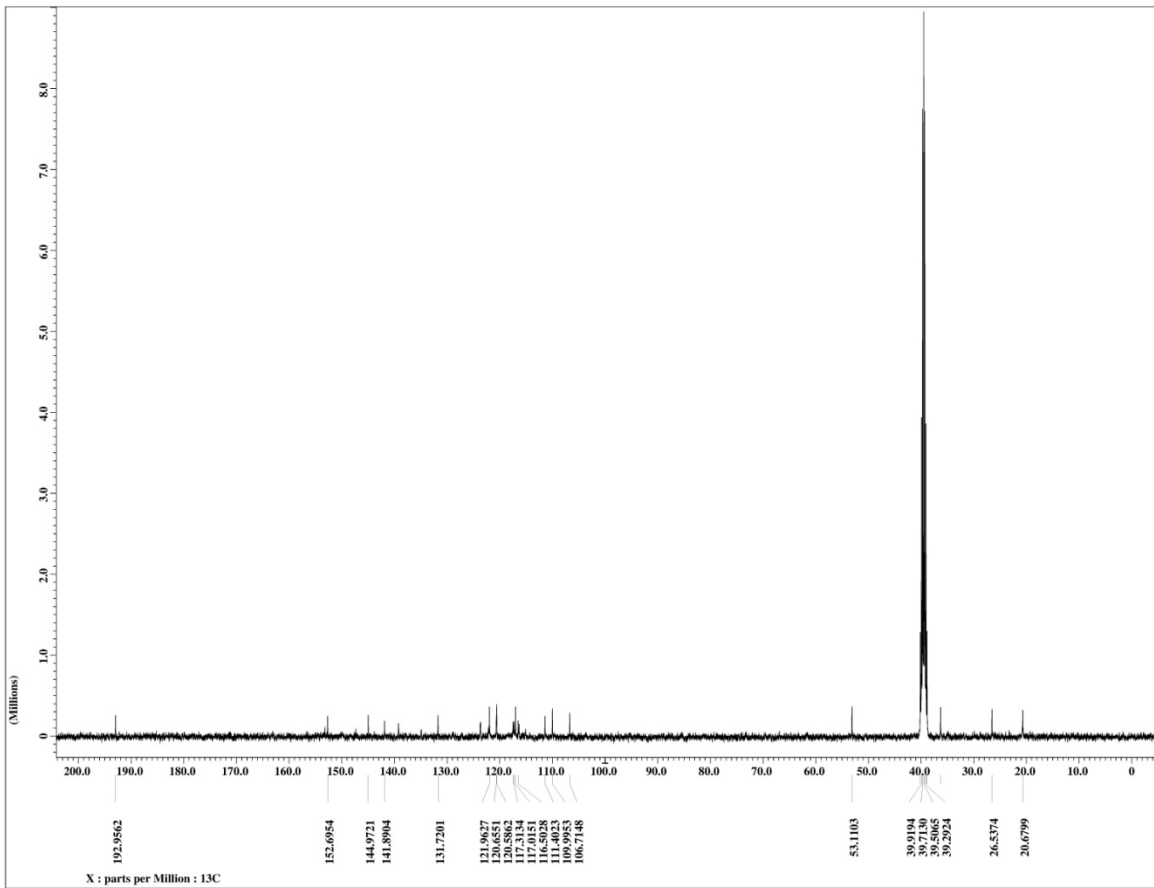


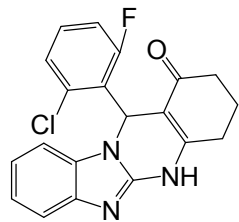
4v-<sup>1</sup>H-NMR



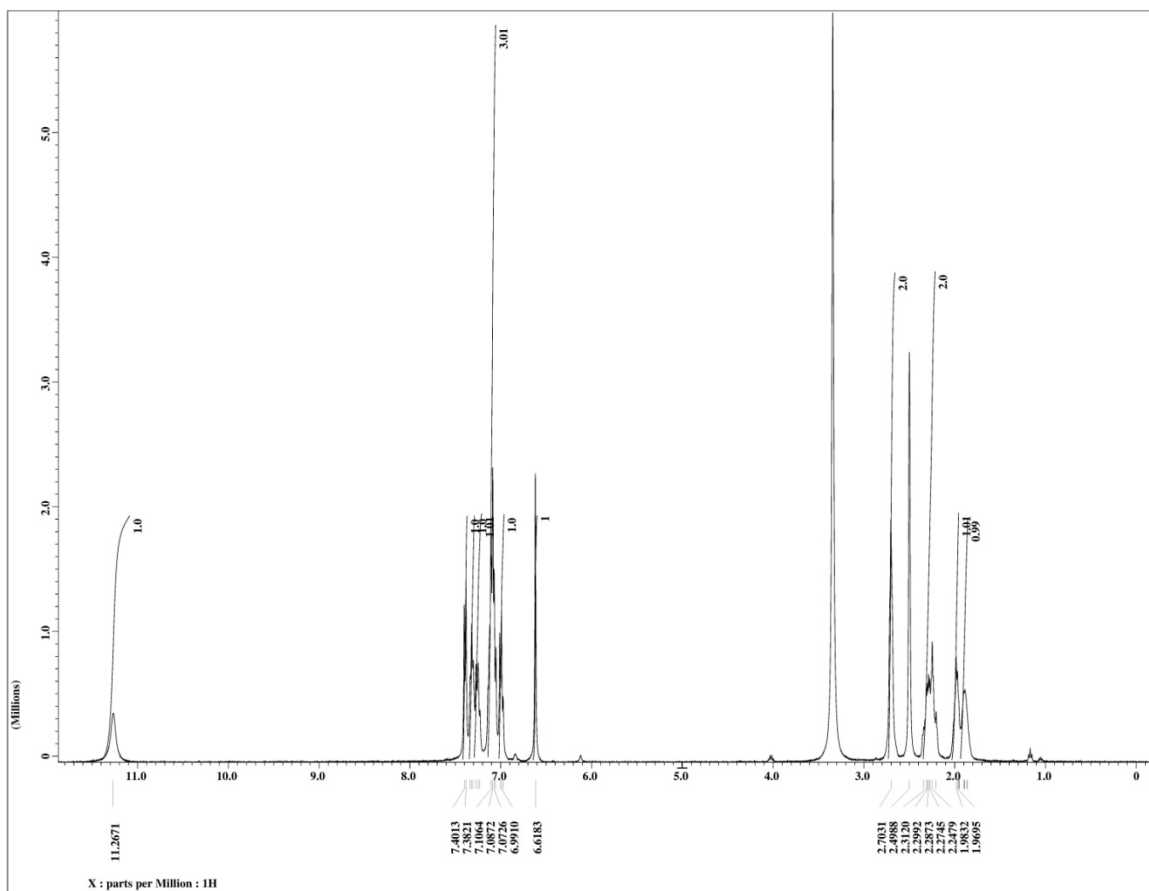


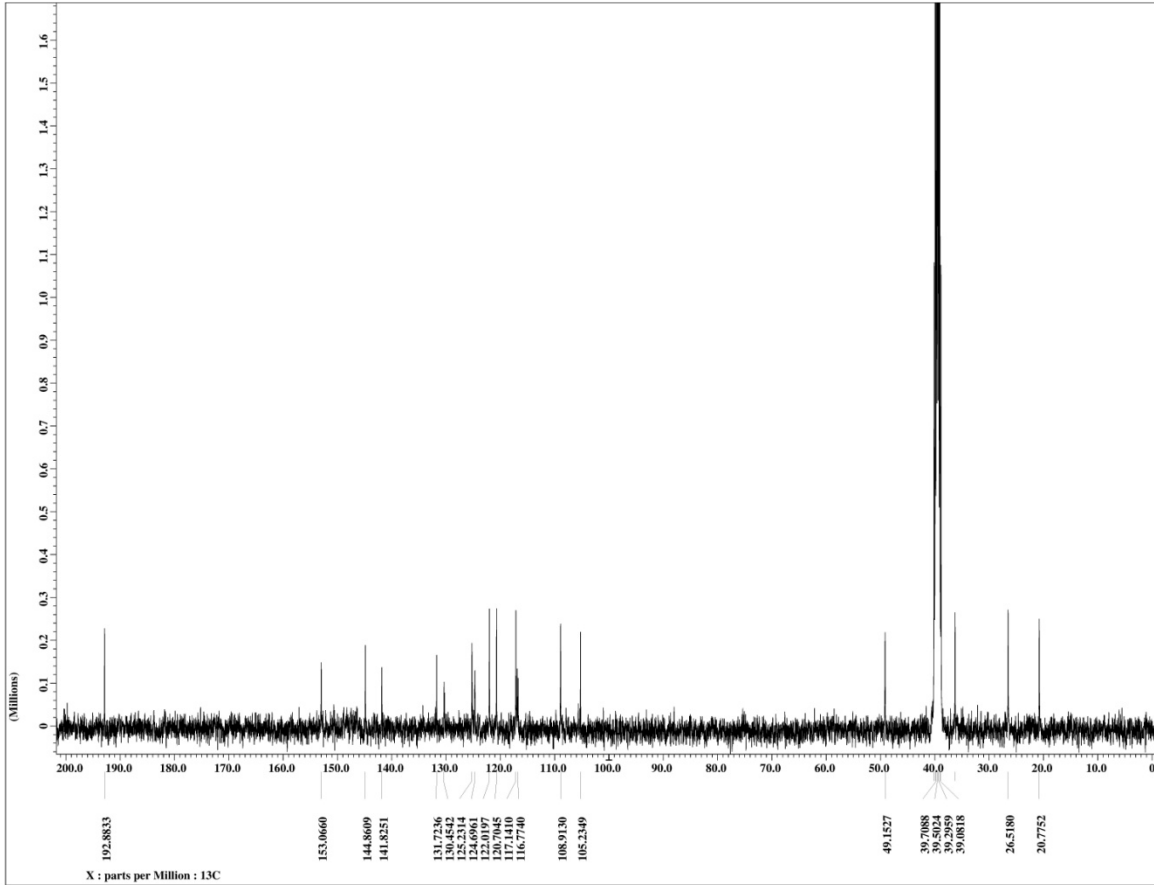
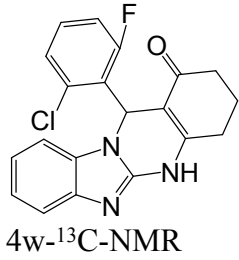
4v-<sup>13</sup>C-NMR

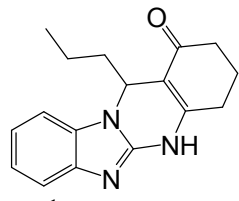




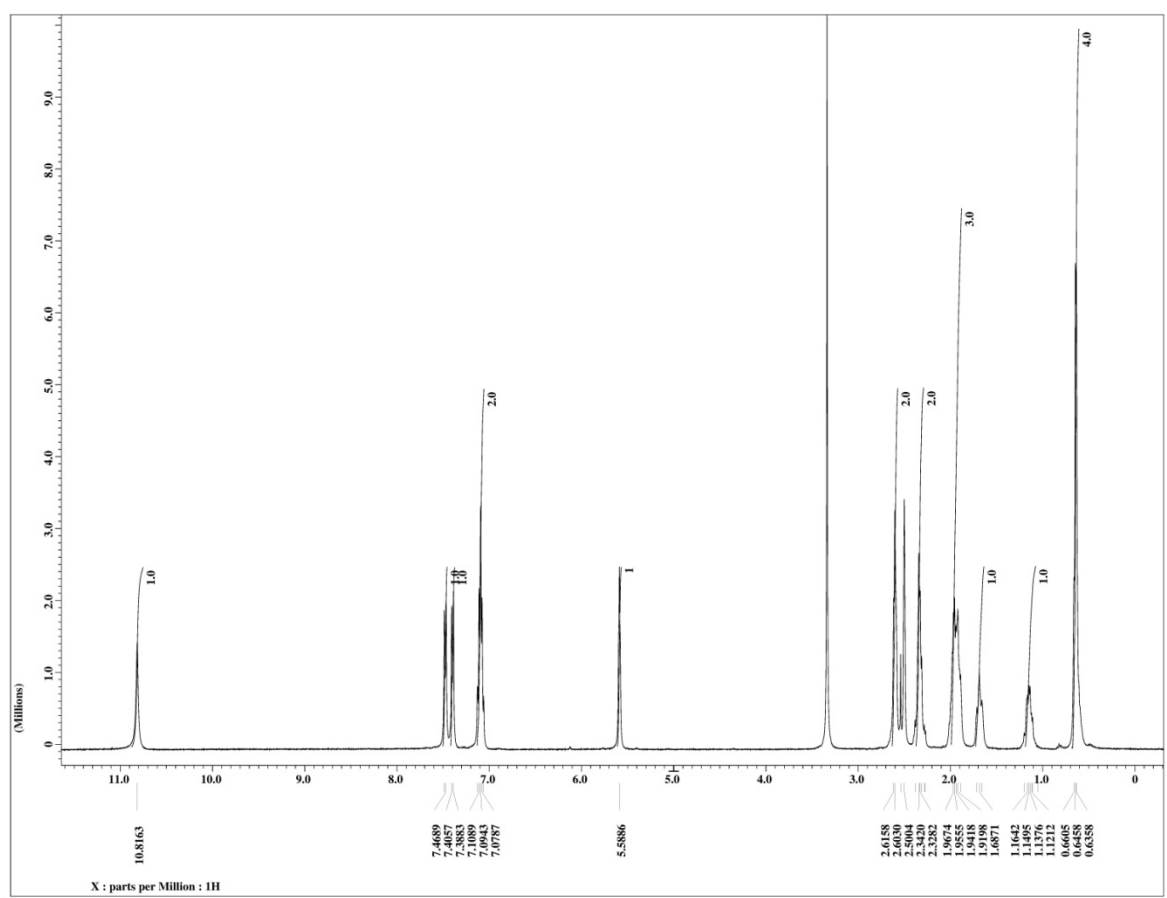
4w-<sup>1</sup>H-NMR

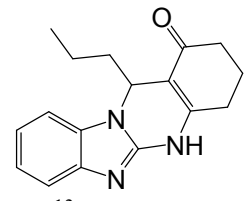




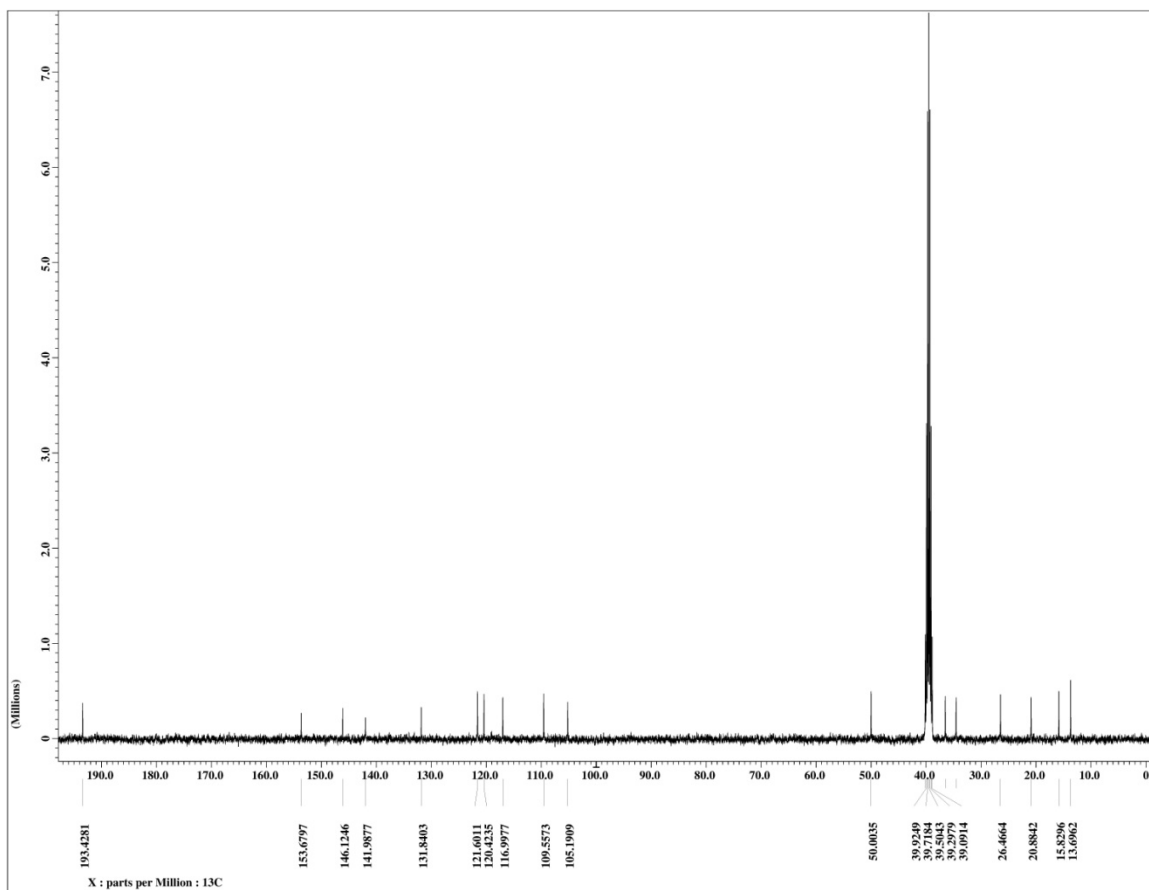


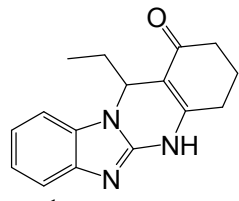
4x-<sup>1</sup>H-NMR





4x-<sup>13</sup>C-NMR





4y-<sup>1</sup>H-NMR

