

Supporting Information

Acid catalyzed synthesis of 2-(2-aminophenyl)quinazoline-4-amine and reaction with aromatic aldehydes

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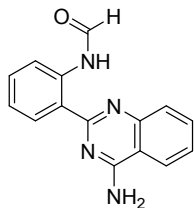
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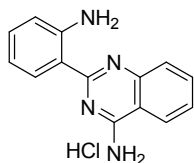
1. General Information

All compounds were fully characterized by elemental analysis and spectroscopic data. The NMR spectra were recorded at room temperature, on a Varian Unity Plus (^1H : 300 MHz, ^{13}C : 75 MHz), or Bruker Avance II⁺ 400 (^1H : 400 MHz, ^{13}C : 100 MHz, ^{15}N : 40.6 MHz) including the ^1H - ^{13}C and ^1H - ^{15}N correlation spectra (HMQC and HMBC). Deuterated DMSO was used as solvent. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet and br, broad. The coupling constants, J , are reported in Hertz (Hz). IR spectra were recorded on a FT-IR Bomem MB 104 using Nujol mulls and NaCl cells. The reactions under microwave irradiation were performed on a CEM microwave reactor, model Mars 5, using a quartz open vessel. All reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F₂₅₄ (Merck). The melting points were determined on a Stuart SMP3 melting point apparatus and are uncorrected. Elemental analyses were performed on a LECO CHNS-932 instrument. High resolution mass spectra (HRMS) were obtained from the C.A.C.T.I.-Universidade de Vigo.

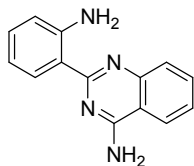
2. Synthesis and Characterization data of the Products



Synthesis of [2-(4-aminoquinazolin-2-yl)phenyl]formamide (2a) A mixture of the nitrate salt of 13*H*-quinazolino[3,4-*a*]quinazolin-13-imine nitrate **1a** (0.08 g, 0.26 mmol) in 3M NaOH (1 mL) was stirred at room temperature for 18 h, leading to a yellow solid suspension. The solid was filtered, washed with water and identified as 2-(4-aminoquinazolin-2-yl)phenyl]formamide **2a** (0.07 g, 0.25 mmol, 96%); mp 187-189 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 13.45 (s, 1H, NH), 8.63 (s, 1H), 8.61 (d, *J* = 8.0, 2H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.14 (brs, 2H, NH), 7.87 (d, *J* = 8.0 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.52 (td, *J* = 1.2, 8.0 Hz, 1H), 7.44 (td, *J* = 1.2, 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.48, 160.36, 160.21, 148.90, 138.86, 133.46, 130.81, 130.38, 127.41, 125.87, 123.60, 123.33, 122.74, 120.55, 112.63; IR (Nujol mull) 3450, 3335, 3217, 1641, 1624, 1603, 1588, 1580, 1545, 1502 cm⁻¹; Anal. Calcd for C₁₅H₁₂N₄O: C, 68.16; H, 4.59; N, 21.20. Found: C, 68.08; H, 4.66; N, 21.18.



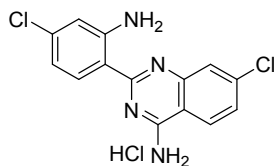
Synthesis of the hydrochloride salt of 2-(2-aminophenyl) quinazolin-4-amine (3a) Concentrated HCl (5 μL) was added to a pale yellow suspension of the nitrate salt of 13*H*-quinazolino[3,4-*a*]quinazolin-13-imine **1a** (0.05 g, 0.16 mmol) in methanol (2 mL). The reaction mixture was stirred at room temperature leading to a homogeneous yellow solution after 5 minutes. A yellow solid started to precipitate after 25 minutes and the suspension was stirred for a further 4 hours. The yellow solid was filtered, washed with diethyl ether and identified as the hydrochloride salt of 2-(2-aminophenyl)quinazolin-4-amine **3a** (0.04 g, 0.15 mmol, 93%), mp 283-285 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 10.06 (brs, 1H, NH), 9.96 (brs, 1H, NH), 8.53 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.12 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.00 (td, *J* = 1.2, 7.2 Hz, 1H), 7.68 (td, *J* = 1.2, 7.2 Hz, 1H), 7.42 (td, *J* = 1.2, 8.4 Hz, 1H), 7.12 (dd, *J* = 1.2, 8.4 Hz, 1H), 6.74 (t, *J* = 8.0 Hz, 1H), 4.86 (brs, NH₂+H₂O); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 162.48, 157.49, 146.32, 139.84, 136.31, 134.04, 130.35, 127.49, 125.07, 119.77, 119.52, 118.61, 113.81, 110.79; IR (Nujol mull) 3332, 3239, 1650, 1629, 1607, 1563, 1541, 1506 cm⁻¹; Anal. Calcd for C₁₄H₁₃N₄Cl·0.2H₂O: C, 60.84; H, 4.80; N, 20.28. Found: C, 60.76; H, 4.93; N, 20.38.



Neutralization of the hydrochloride salt of 2-(2-aminophenyl) quinazolin-4-amine (3a)

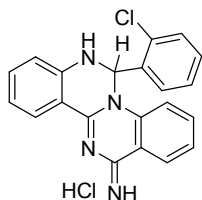
A suspension of the hydrochloride salt of 2-(2-aminophenyl) quinazolin-4-amine **3a** (0.11 g, 0.39 mmol) in acetone (0.5 mL) was combined with a 3M NaOH aqueous solution (0.2 mL) and the mixture was stirred at room temperature. A homogeneous yellow solution was immediately formed. Addition of water (1 mL) and cooling in an ice bath for a few minutes led to a beige solid that started to precipitate from solution. The solid was filtered, washed with water and identified as 2-(2-aminophenyl) quinazolin-4-amine **3a** (0.07 g, 0.30 mmol, 77%), mp 152-154 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 8.38 (dd, *J* = 1.6, 8.0 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.73 (brs, 2H, NH₂), 7.71 (td, *J* = 1.2, 8.4 Hz,

1H), 7.68 (dd, $J = 1.2, 8.4$ Hz, 1H), 7.41 (td, $J = 1.2, 8.4$ Hz, 1H), 7.33 (brs, 2H, NH₂), 7.09 (td, $J = 1.2, 8.4$ Hz, 1H), 6.72 (dd, $J = 1.2, 8.4$ Hz, 1H), 6.54 (t, $J = 8.0$ Hz, 1H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.98, 161.06, 149.90, 149.53, 132.92, 130.62, 130.55, 127.10, 124.68, 123.48, 117.96, 116.40, 114.39, 112.44; IR (Nujol mull) 3458, 3391, 3313, 3196, 1613, 1572, 1543 cm⁻¹; Anal. Calcd for C₁₄H₁₂N₄: C, 71.16; H, 5.13; N, 23.72. Found: C, 71.23; H, 5.11; N, 23.79.

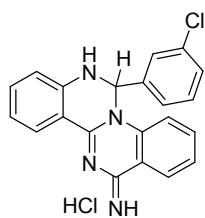


Synthesis of the hydrochloride salt of 2-(2-amino-4-chlorophenyl)-7-chloroquinazolin-4-amine (3b) Concentrated HCl (5 μL) was added to a pale yellow suspension of the nitrate salt of 3,9-dichloro-13*H*-quinazolino[3,4-*a*]quinazolin-13-imine **1b** (0.05 g, 0.14 mmol) in methanol (2 mL). The reaction mixture was stirred at room temperature leading to a homogeneous yellow solution after 15 min. A yellow solid started to precipitate after 45 minutes and the suspension was kept stirring for a further 15 hours. The yellow solid was filtered, washed with diethyl ether and identified as the hydrochloride salt of 2-(2-amino-4-chlorophenyl)-7-chloroquinazolin-4-amine **3b** (0.04 g, 0.13 mmol, 93%), mp >300 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 10.10 (brs, 1H, NH), 10.07 (brs, 1H, NH), 8.52 (d, $J = 8.8$ Hz, 1H), 8.38 (d, $J = 2.0$ Hz, 1H), 8.22 (d, $J = 8.8$ Hz, 1H), 7.73 (dd, $J = 2.0, 8.8$ Hz, 1H), 6.97 (d, $J = 2.0$ Hz, 1H), 6.66 (dd, $J = 2.0, 8.8$ Hz, 1H), 4.65 (brs, NH₂+H₂O); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.82, 157.60, 152.16, 141.01, 140.49, 138.83, 132.00, 127.37, 127.13, 118.75, 116.31, 115.08, 109.51, 108.38; IR (Nujol mull) 3313, 1656, 1630, 1605, 1570, 1537, 1503 cm⁻¹; Anal. Calcd for C₁₄H₁₁N₄Cl₃·0.5H₂O: C, 47.95; H, 3.46; N, 15.98. Found: C, 47.93; H, 3.47; N, 16.01.

General procedure for the synthesis of the hydrochloride salt of 6-Aryl-6,7-dihydro-13*H*-quinazolino[3,4-*a*]quinazolin-13-imine (5) The aldehyde **4** (1.1-1.2 equiv) was added to a yellow suspension of the hydrochloride salt of 2-(2-aminophenyl)quinazolin-4-amine **2a** in ethanol (2-3 mL). The yellow suspension was refluxed for 15 min-12.5 hours (method A) or irradiated at a constant power of 400 W for 5 minutes (method B). The solid was filtered and washed with diethyl ether, leading to the pure product **5**.

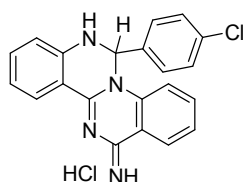


6-(2-Chlorophenyl)-6,7-dihydro-13*H*-quinazolino[3,4-*a*]quinazolin-13-imine hydrochloride (5a). Isolated as a yellow solid; mp 242-244 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 9.99 (s, 1H, NH), 9.98 (s, 1H, NH), 8.54 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.40 (d, $J = 4.0$ Hz, 1H, NH), 8.22 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.02 (td, $J = 1.2, 8.4$ Hz, 1H), 7.76 (t, $J = 8.4$ Hz, 1H), 7.72 (d, $J = 4.0$ Hz, 1H), 7.63 (d, $J = 8.4$ Hz, 1H), 7.60 (td, $J = 1.2, 8.4$ Hz, 1H), 7.46 (td, $J = 1.2, 8.4$ Hz, 1H), 7.34 (td, $J = 1.2, 8.4$ Hz, 1H), 7.11 (t, $J = 8.4$ Hz, 1H), 6.89-6.95 (m, 3H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.97, 153.01, 144.31, 137.18, 136.89, 136.59, 133.90, 131.24, 130.75, 130.82, 128.23, 127.92, 127.87, 126.52, 126.00, 119.33, 116.45, 116.17, 113.07, 112.70, 65.34; IR (Nujol mull) 3324, 1667, 1613, 1598, 1573, 1523 cm⁻¹; Anal. Calcd for C₂₁H₁₆N₄Cl₂: C, 63.80; H, 4.09; N, 14.18. Found: C, 63.77; H, 4.07; N, 14.22.



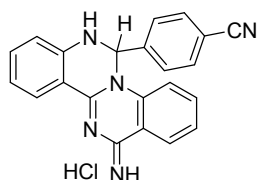
6-(3-Chlorophenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5b). Isolated as a yellow solid; mp 241-243 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 9.91 (s, 1H, NH), 9.89 (s, 1H, NH), 8.67 (d, *J* = 4.0 Hz, 1H, NH), 8.54 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.14 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.06 (td, *J* = 1.2, 8.4 Hz, 1H), 7.80 (t, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.49 (td, *J* = 1.2, 8.4 Hz, 1H), 7.45 (s, 1H), 7.35 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.25 (t, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.92 (t, *J* = 8.4 Hz, 1H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.98, 152.57, 145.44, 139.95, 137.95, 136.92, 136.56, 133.62, 130.67, 128.99, 128.22, 127.94, 126.11, 126.00, 124.26, 119.44, 116.77, 116.04, 113.73, 112.67, 66.03; IR (Nujol mull) 3377, 3340, 3141, 1667, 1613, 1598, 1516 cm⁻¹; Anal. Calcd for C₂₁H₁₆N₄Cl₂: C, 63.80; H, 4.09; N, 14.18. Found: C, 63.83; H, 4.11; N, 13.96.



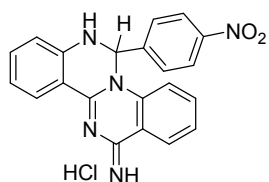
6-(4-Chlorophenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5c). Isolated as a yellow solid; mp 240-242 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 9.95 (s, 1H, NH), 9.89 (s, 1H, NH), 8.74 (d, *J* = 4.0 Hz, 1H, NH), 8.57 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.13 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.05 (td, *J* = 1.2, 8.4 Hz, 1H), 7.79 (t, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 4.0 Hz, 1H), 7.48 (td, *J* = 1.2, 8.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.90 (t, *J* = 8.0 Hz, 1H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.89, 152.57, 145.55, 137.97, 136.90, 136.50, 133.62, 131.15, 128.77, 128.19, 127.91, 127.82, 126.04, 119.31, 116.84, 116.08, 113.69, 112.60, 66.04; IR (Nujol mull) 3099, 1661, 1612, 1596, 1520 cm⁻¹; Anal. Calcd for C₂₁H₁₆N₄Cl₂: C, 63.80; H, 4.09; N, 14.18. Found: C, 63.85; H, 4.18; N, 13.89.



4-(13-Imino-7,13-dihydro-6H-quinazolino[3,4-a]quinazolin-6-yl)benzonitrile

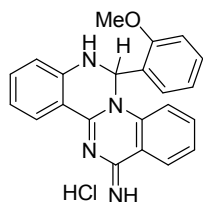
hydrochloride (5d). Isolated as a yellow solid; mp 253-255 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 9.92 (s, 1H, NH), 9.91 (s, 1H, NH), 8.76 (d, *J* = 4.0 Hz, 1H, NH), 8.54 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.12 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.06 (td, *J* = 1.2, 8.0 Hz, 1H), 7.83 (d, *J* = 4.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.49 (td, *J* = 1.2, 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.92 (td, *J* = 1.2, 8.0 Hz, 1H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 161.99, 152.52, 145.37, 142.77, 137.97, 136.94, 136.57, 132.73, 128.24, 127.99, 126.98, 126.02, 119.56, 118.16, 116.71, 116.13, 113.80, 112.69, 111.80, 66.03; IR (Nujol mull) 3344, 2239, 1663, 1614, 1602, 1518 cm⁻¹; HRMS-FAB (*m/z*): [M+H]⁺ calcd for C₂₂H₁₆N₅Cl 350.14078, found: 350.14122.



6-(4-Nitrophenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

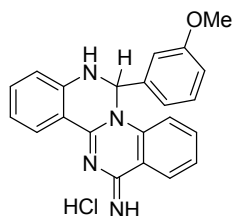
hydrochloride (5e). Isolated as a yellow solid; mp 210-212 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 10.02 (s, 1H, NH), 9.94 (s, 1H, NH), 8.88 (d, *J* = 4.0 Hz, 1H, NH), 8.60 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.20 (d, *J* =

8.4 Hz, 1H), 8.13 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.11 (d, $J = 8.4$ Hz, 2H), 8.06 (td, $J = 1.2, 8.4$ Hz, 1H), 7.90 (d, $J = 4.0$ Hz, 1H), 7.81 (t, $J = 8.4$ Hz, 1H), 7.51-7.46 (m, 3H), 7.02 (d, $J = 8.4$ Hz, 1H), 6.92 (td, $J = 1.2, 8.4$ Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO- d_6) δ 161.93, 152.52, 147.74, 145.34, 144.57, 137.93, 136.93, 136.53, 128.21, 127.97, 127.45, 126.12, 123.83, 119.54, 116.70, 116.14, 113.75, 112.67, 65.96; IR (Nujol mull) 1668, 1612, 1596, 1519 cm^{-1} ; Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{N}_5\text{O}_2\text{Cl}\cdot 0.1\text{H}_2\text{O}$: C, 61.86; H, 4.01; N, 17.18. Found: C, 61.81; H, 4.26; N, 17.13.



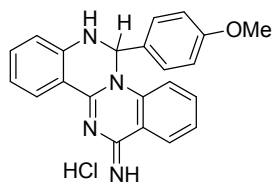
6-(2-methoxyphenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5f). Isolated as a yellow solid; mp 244-247 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (400 MHz, DMSO- d_6) δ 9.95 (s, 1H, NH), 9.87 (s, 1H, NH), 8.55 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.18 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.18 (d, $J = 4.0$ Hz, 1H, NH), 7.99 (td, $J = 1.2, 8.4$ Hz, 1H), 7.79 (d, $J = 8.8$ Hz, 1H), 7.74 (t, $J = 8.0$ Hz, 1H), 7.65 (d, $J = 4.0$ Hz, 1H), 7.43 (td, $J = 1.2, 8.4$ Hz, 1H), 7.28 (td, $J = 1.2, 8.4$ Hz, 1H), 7.11 (d, $J = 7.6$ Hz, 1H), 6.93 (d, $J = 8.0$ Hz, 1H), 6.88 (t, $J = 8.0$ Hz, 1H), 6.78 (dd, $J = 1.2, 8.0$ Hz, 1H), 6.71 (t, $J = 8.4$ Hz, 1H), 3.88 (s, 3H, CH_3); $^{13}\text{C-NMR}$ (100 MHz, DMSO- d_6) δ 161.80, 155.96, 153.13, 145.50, 137.51, 136.62, 136.36, 130.79, 128.05, 127.65, 125.86, 125.83, 124.63, 120.33, 118.65, 116.75, 115.60, 112.68, 112.59, 111.97, 63.93, 55.87; IR (Nujol mull) 1665, 1622, 1601, 1523 cm^{-1} ; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_4\text{OCl}$: C, 67.59; H, 4.65; N, 14.34. Found: C, 67.64; H, 4.62; N, 14.30.



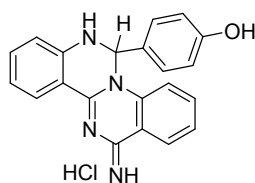
6-(3-Methoxyphenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5g). Isolated as a yellow solid; mp 214-216 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6) δ 9.93 (s, 1H, NH), 9.87 (s, 1H, NH), 8.69 (d, $J = 4.0$ Hz, 1H, NH), 8.56 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.19 (d, $J = 8.4$ Hz, 1H), 8.13 (dd, $J = 1.2, 8.4$ Hz, 1H), 8.06 (td, $J = 1.2, 8.4$ Hz, 1H), 7.79 (t, $J = 8.4$ Hz, 1H), 7.69 (d, $J = 4.0$ Hz, 1H), 7.47 (td, $J = 1.2, 8.4$ Hz, 1H), 7.15 (t, $J = 8.4$ Hz, 1H), 6.99 (d, $J = 8.4$ Hz, 1H), 6.83-6.92 (m, 3H), 6.56 (d, $J = 8.4$ Hz, 1H), 3.66 (s, 3H, CH_3); $^{13}\text{C-NMR}$ (75 MHz, DMSO- d_6) δ 161.84, 159.43, 152.71, 145.84, 139.12, 138.07, 136.86, 136.46, 129.97, 128.13, 127.86, 125.99, 119.14, 117.61, 116.98, 115.94, 113.66, 113.59, 112.49, 112.41, 66.50, 55.08; IR (Nujol mull) 3200, 1661, 1613, 1597, 1524 cm^{-1} ; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_4\text{OCl}$: C, 67.59; H, 4.65; N, 14.34. Found: C, 67.53; H, 4.70; N, 14.23.



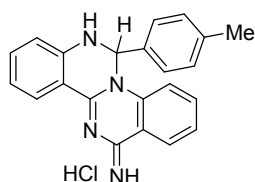
6-(4-Methoxyphenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5h). Isolated as a yellow solid; mp 235-237 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (400 MHz, DMSO- d_6) δ 9.85 (s, 1H, NH), 9.83 (s, 1H, NH), 8.60 (sl, 1H, NH), 8.51 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.17 (d, $J = 8.0$ Hz, 1H), 8.13 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.06 (td, $J = 1.2$ Hz, 8.0 Hz, 1H), 7.78 (t, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 4.0$ Hz, 1H), 7.47 (td, $J = 1.2, 8.0$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 2H), 6.96 (d, $J = 8.0$ Hz, 1H), 6.90 (t, $J = 8.0$ Hz, 1H), 6.82 (d, $J = 8.0$ Hz, 2H), 3.64 (s, 3H, CH_3); $^{13}\text{C-NMR}$ (100 MHz, DMSO- d_6) δ 161.83, 159.53, 152.69, 145.78, 138.00, 136.82, 136.41, 129.37, 128.15, 127.83, 127.12, 125.88, 119.06, 117.04, 115.99, 114.12, 113.61, 112.52, 66.41, 55.08; IR (Nujol mull) 3119, 1648, 1622, 1566, 1530 cm^{-1} ; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_4\text{OCl}$: C, 67.59; H, 4.65; N, 14.34. Found: C, 67.50; H, 4.73; N, 14.40.



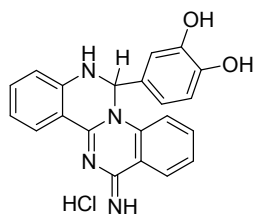
4-(13-Imino-7,13-dihydro-6H-quinazolino[3,4-a]quinazolin-6-yl)phenol

hydrochloride (5i). Isolated as a yellow solid; mp 228-230°C; $^1\text{H-NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 9.86 (s, 1H, NH), 9.81 (s, 1H, NH), 9.62 (s, 1H, OH), 8.59 (sl, 1H, NH), 8.53 (d, $J = 8.0$ Hz, 1H), 8.16 (d, $J = 8.0$ Hz, 1H), 8.14 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.06 (t, $J = 8.0$ Hz, 1H), 7.74 (t, $J = 8.0$ Hz, 1H), 7.61 (d, $J = 4.0$ Hz, 1H), 7.47 (td, $J = 1.2, 8.0$ Hz), 6.98 (d, $J = 8.0$ Hz, 2H), 6.96 (d, $J = 8.0$ Hz, 1H), 6.91 (t, $J = 8.0$ Hz, 1H), 6.63 (d, $J = 8.0$ Hz, 2H); $^{13}\text{C-NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 161.77, 157.90, 152.69, 145.85, 138.01, 136.76, 136.35, 132.06, 128.12, 127.69, 127.11, 125.88, 118.96, 117.08, 115.82, 115.39, 113.57, 112.51, 66.60; IR (Nujol mull) 3390, 3256, 1652, 1613, 1597, 1530 cm^{-1} ; Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{OCl}\cdot 0.2\text{H}_2\text{O}$: C, 66.29; H, 4.62; N, 14.73. Found: C, 66.24; H, 4.35; N, 14.80.



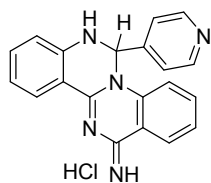
6-(4-Methylphenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

hydrochloride (5j). Isolated as a yellow solid; mp 227-230 °C; $^1\text{H-NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 9.88 (s, 1H, NH), 9.84 (s, 1H, NH), 8.63 (d, $J = 4.0$ Hz, 1H, NH), 8.54 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.16 (d, $J = 8.0$ Hz, 1H), 8.12 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.04 (td, $J = 1.2, 8.0$ Hz, 1H), 7.77 (t, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 4.0$ Hz, 1H), 7.46 (td, $J = 1.2, 8.0$ Hz, 1H), 7.09-7.02 (m, 4H), 6.97 (d, $J = 8.0$ Hz, 1H), 6.88 (t, $J = 8.0$ Hz, 1H), 2.16 (s, 3H, CH_3); $^{13}\text{C-NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 161.86, 152.74, 145.82, 129.33, 138.07, 136.86, 136.43, 134.57, 138.44, 128.11, 127.87, 125.70, 125.95, 119.11, 117.01, 116.02, 113.68, 112.51, 66.57; IR (Nujol mull) 1660, 1611, 1595, 1518 cm^{-1} ; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_4\text{Cl}$: C, 70.48; H, 5.12; N, 14.95. Found: C, 70.53; H, 5.22; N, 14.87.



4-(13-Imino-7,13-dihydro-6H-quinazolino[3,4-a]quinazolin-6-yl)benzene-1,2-diol hydrochloride (5k).

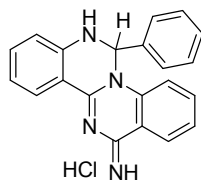
Isolated as a yellow solid; mp 256-258 °C; $^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) δ 9.83 (s, 1H, NH), 9.81 (s, 1H, NH), 9.13 (s, 1H, OH), 8.97 (s, 1H, OH), 8.53-8.50 (m, $\text{ArH}+\text{NH}$, 2H), 8.18 (d, $J = 7.8$ Hz, 1H), 8.13 (dd, $J = 1.2, 7.8$ Hz, 1H), 8.06 (t, $J = 7.8$ Hz, 1H), 7.78 (t, $J = 7.8$ Hz, 1H), 7.55 (d, $J = 4.0$ Hz, 1H), 7.45 (td, $J = 1.2, 7.8$ Hz, 1H), 6.96 (d, $J = 7.8$ Hz, 1H), 6.89 (t, $J = 7.8$ Hz, 1H), 6.58 (d, $J = 7.8$ Hz, 1H), 6.54 (s, 1H), 6.40 (dd, $J = 1.2, 7.8$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ 161.73, 152.76, 146.01, 145.90, 145.89, 138.10, 136.81, 136.40, 128.36, 128.14, 127.81, 125.86, 118.90, 117.21, 116.95, 115.95, 115.33, 113.46, 113.19, 112.43, 66.87; IR (Nujol mull) 3379, 1651, 1610, 1598, 1526 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{O}_2\text{Cl}$: C, 64.20; H, 4.37; N, 14.26. Found: C, 64.19; H, 4.50; N, 14.35.



6-Pyridin-4-yl-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine

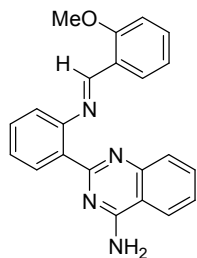
hydrochloride (5l). Isolated as a yellow solid; mp 183-185°C; $^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) δ 9.98

(s, 1H, NH), 9.93 (s, 1H, NH), 8.85 (d, $J = 4.0$ Hz, 1H, NH), 8.58 (dd, $J = 1.2, 8.1$ Hz, 1H), 8.48 (d, $J = 8.1$ Hz, 2H), 8.20 (d, $J = 8.1$ Hz, 1H), 8.12 (dd, $J = 1.2, 8.1$ Hz, 1H), 8.07 (td, $J = 1.2, 8.1$ Hz, 1H), 7.80 (d, $J = 4.0$ Hz, 1H), 7.78 (t, $J = 8.1$ Hz, 1H), 7.49 (td, $J = 1.2, 8.1$ Hz, 1H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.04 (d, $J = 8.1$ Hz, 1H), 6.92 (t, $J = 8.1$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ 162.03, 152.54, 150.07, 146.39, 145.58, 138.08, 137.01, 136.57, 128.29, 128.02, 126.14, 121.04, 119.65, 116.70, 116.23, 113.92, 112.69, 65.59; IR (Nujol mull) 1661, 1610, 1595, 1521 cm^{-1} ; HRMS-FAB (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{16}\text{N}_5\text{Cl}$ 326.14078, found: 326.13977.



6-Phenyl-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine hydrochloride

(5m). Isolated as a yellow solid; mp 253-255°C; $^1\text{H-NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 9.92 (s, 1H, NH), 9.86 (s, 1H, NH), 8.71 (d, $J = 4.0$ Hz, 1H, NH), 8.56 (d, $J = 8.0$ Hz, 1H), 8.19 (d, $J = 8.0$ Hz, 1H), 8.13 (dd, $J = 1.2, 8.0$ Hz, 1H), 8.05 (t, $J = 8.0$ Hz, 1H), 7.78 (t, $J = 8.0$ Hz, 1H), 7.74 (d, $J = 4.0$ Hz, 1H), 7.47 (td, $J = 1.2, 8.0$ Hz, 1H), 7.29-7.26 (m, 3H), 7.17 (d, $J = 8.0$ Hz, 2H), 6.99 (d, $J = 8.0$ Hz, 1H), 6.88 (t, $J = 8.0$ Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 161.86, 152.72, 138.10, 145.79, 137.51, 136.45, 136.18, 128.87, 128.80, 128.18, 127.87, 126.01, 125.78, 119.14, 116.96, 116.02, 113.66, 112.55, 66.56; IR (Nujol mull) 3164, 1658, 1611, 1598, 1526 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{Cl}$: C, 69.89; H, 4.76; N, 15.53. Found: C, 70.01; H, 4.84; N, 15.59.



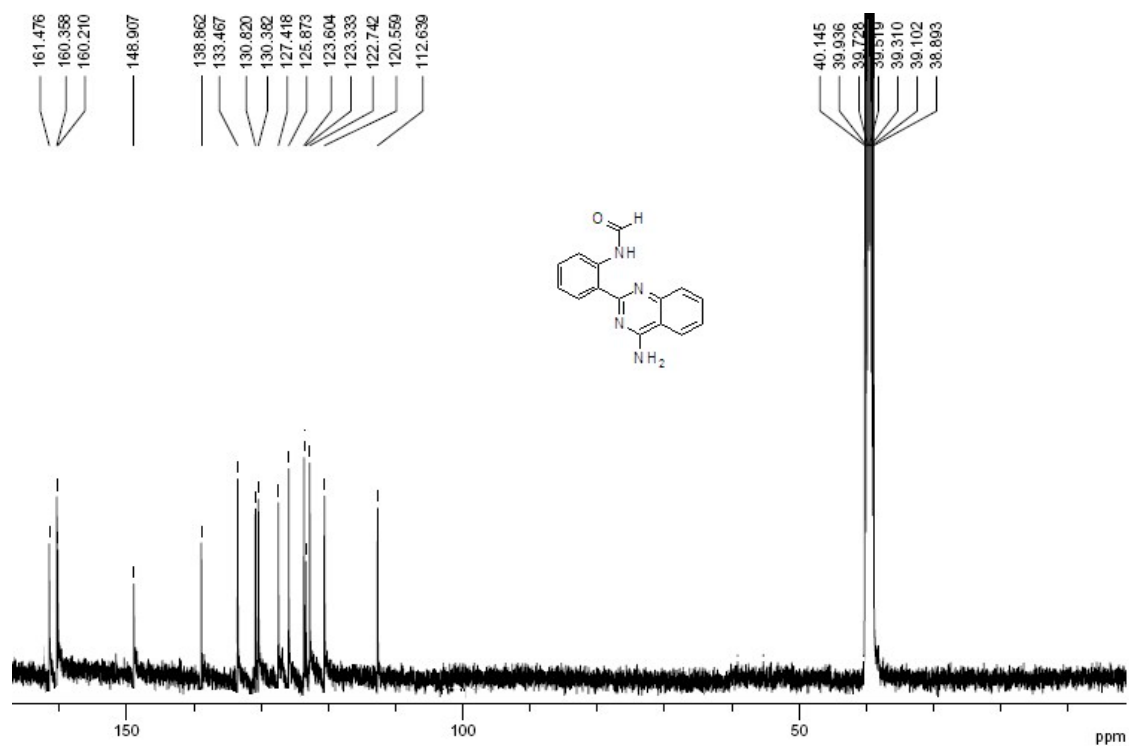
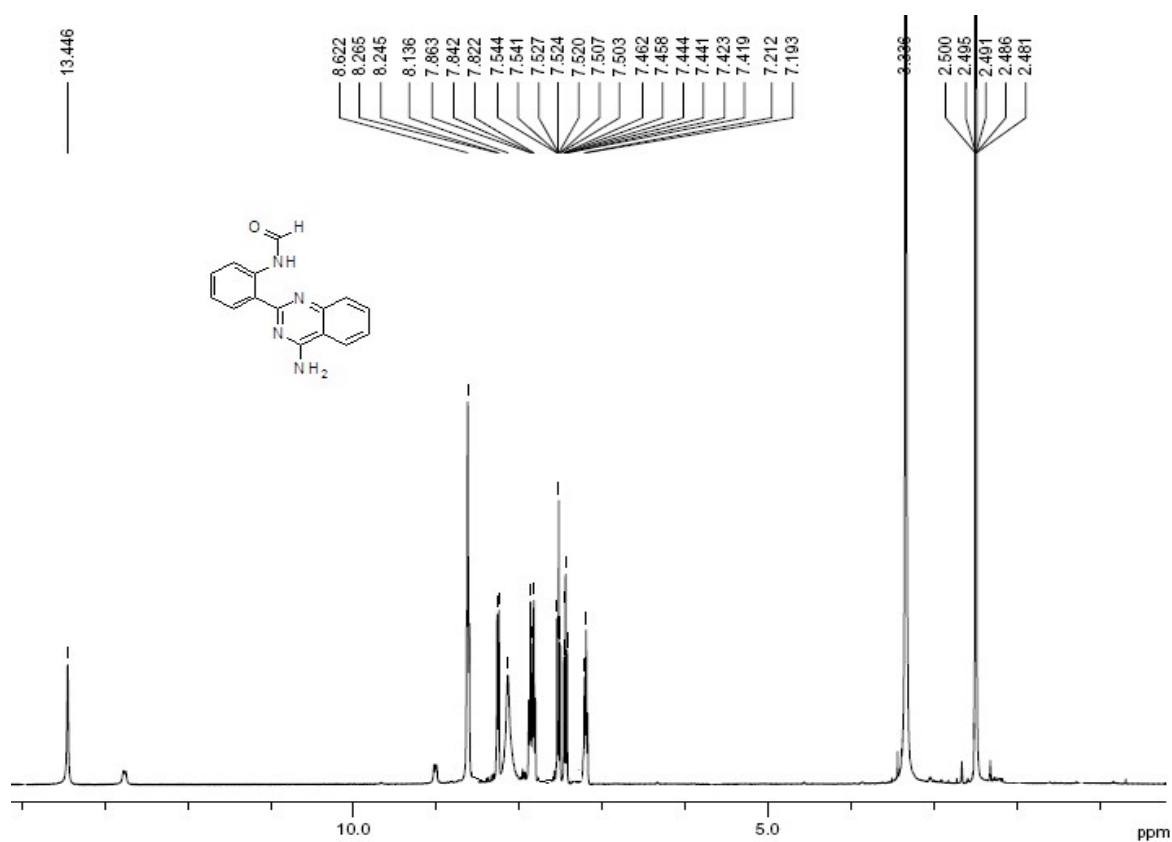
Neutralization of the hydrochloride salt of 6-(2-methoxyphenyl)-6,7-dihydro-13H-quinazolino[3,4-a]quinazolin-13-imine hydrochloride (5f)

DBU (22 μL) was added, at room temperature, to an orange suspension of compound **5f** (0.06 g, 0.15 mmol) in acetonitrile (1 mL) leading immediately to a white suspension. The white solid was filtered and washed with acetonitrile leading to a product identified as 2-(2-(2-methoxybenzylideneamino)phenyl)quinazolin-4-amine **6f** contaminated with the hydrochloride salt of DBU (0.04 g) by ^1H and ^{13}C NMR, including HMBC and HMQC correlation techniques. Traces of the neutral form of **5f** were also detected by NMR.

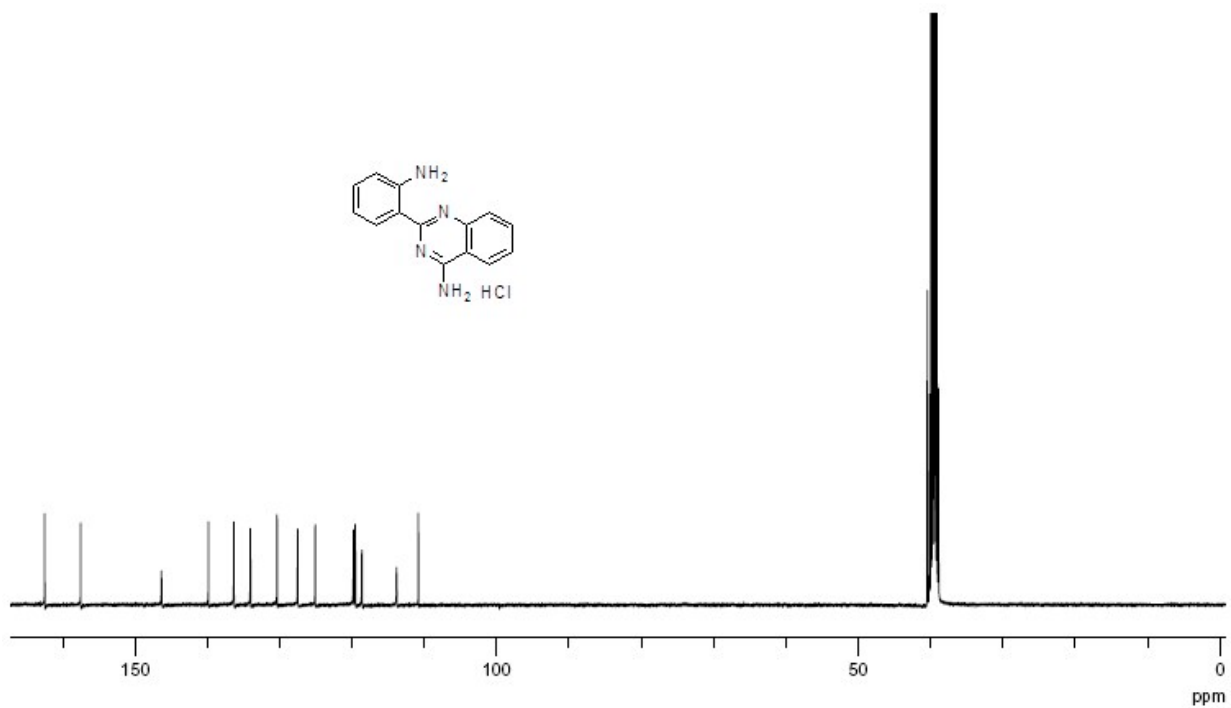
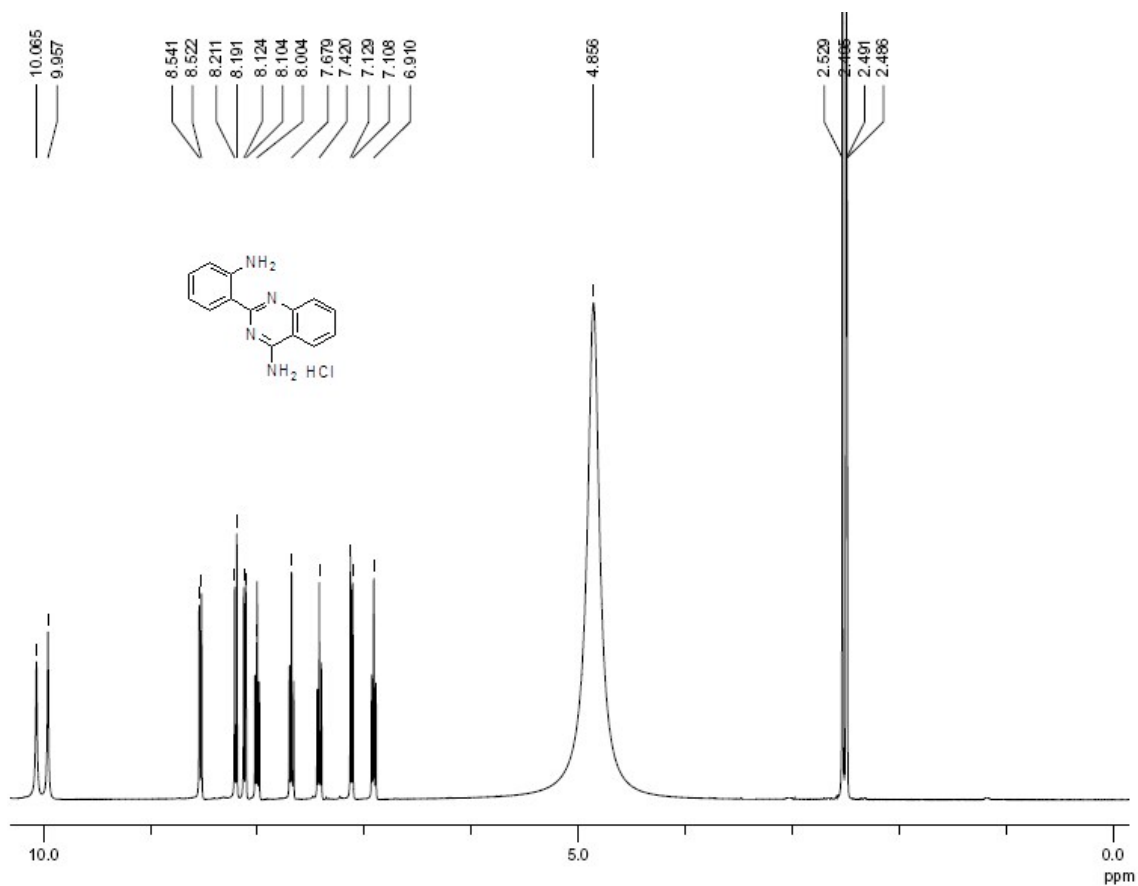
$^1\text{H-NMR}$ signals for product **6f** (400 MHz, $\text{DMSO-}d_6$) δ 8.68 (s, 1H, CH), 8.20 (d, $J = 8.0$ Hz, 1H), 7.78 (dd, $J = 1.6, 8.0$ Hz, 1H), 7.73-7.66 (m, 4H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.45-7.41 (m, 3H), 7.26 (td, $J = 1.2, 8.0$ Hz, 1H), 7.07 (d, $J = 8.4$ Hz, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 6.93 (t, $J = 8.0$ Hz, 1H); $^{13}\text{C-NMR}$ signals for product **6f** (100 MHz, $\text{DMSO-}d_6$) δ 162.23, 161.49, 158.93, 155.59, 151.47, 150.01, 133.44, 132.65(2C), 130.11, 129.35, 127.37, 127.05, 125.05, 124.38, 124.27, 123.43, 120.49, 119.87, 112.53, 111.74, 55.58.

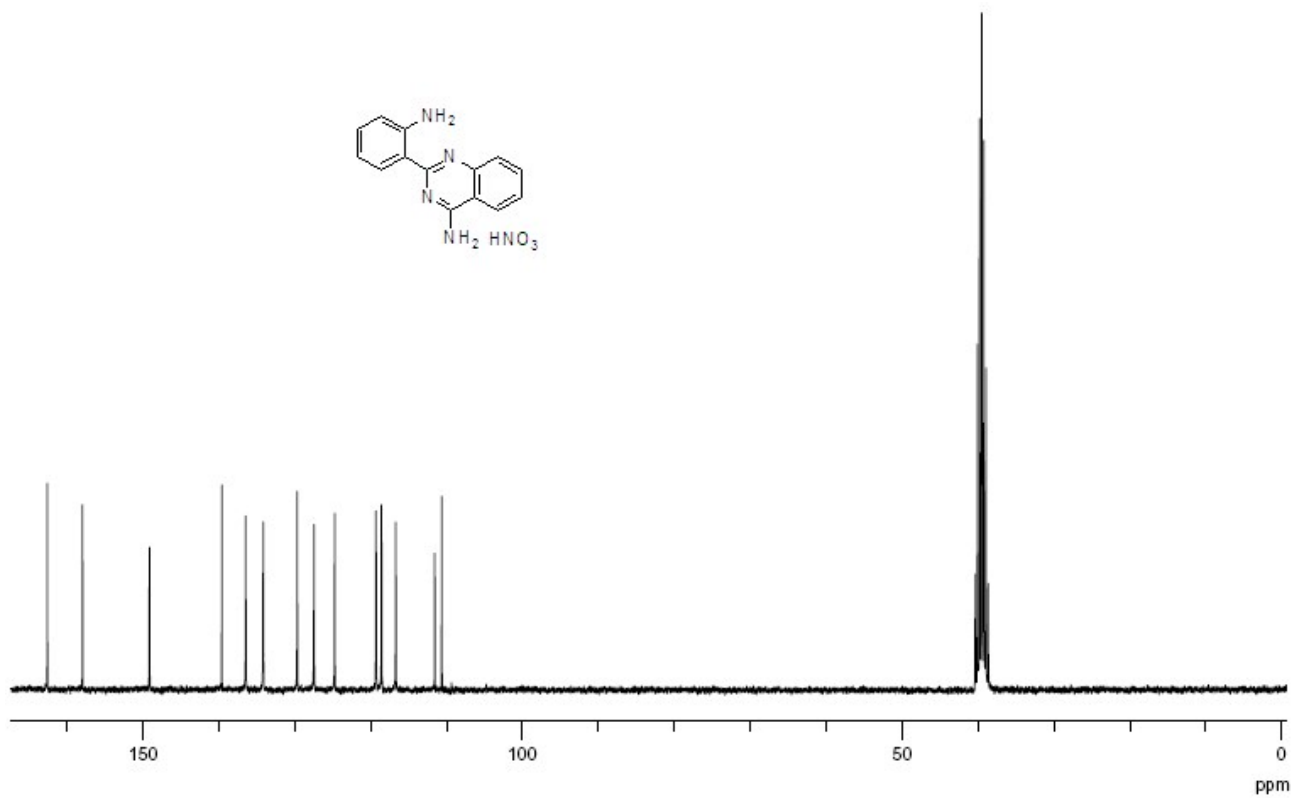
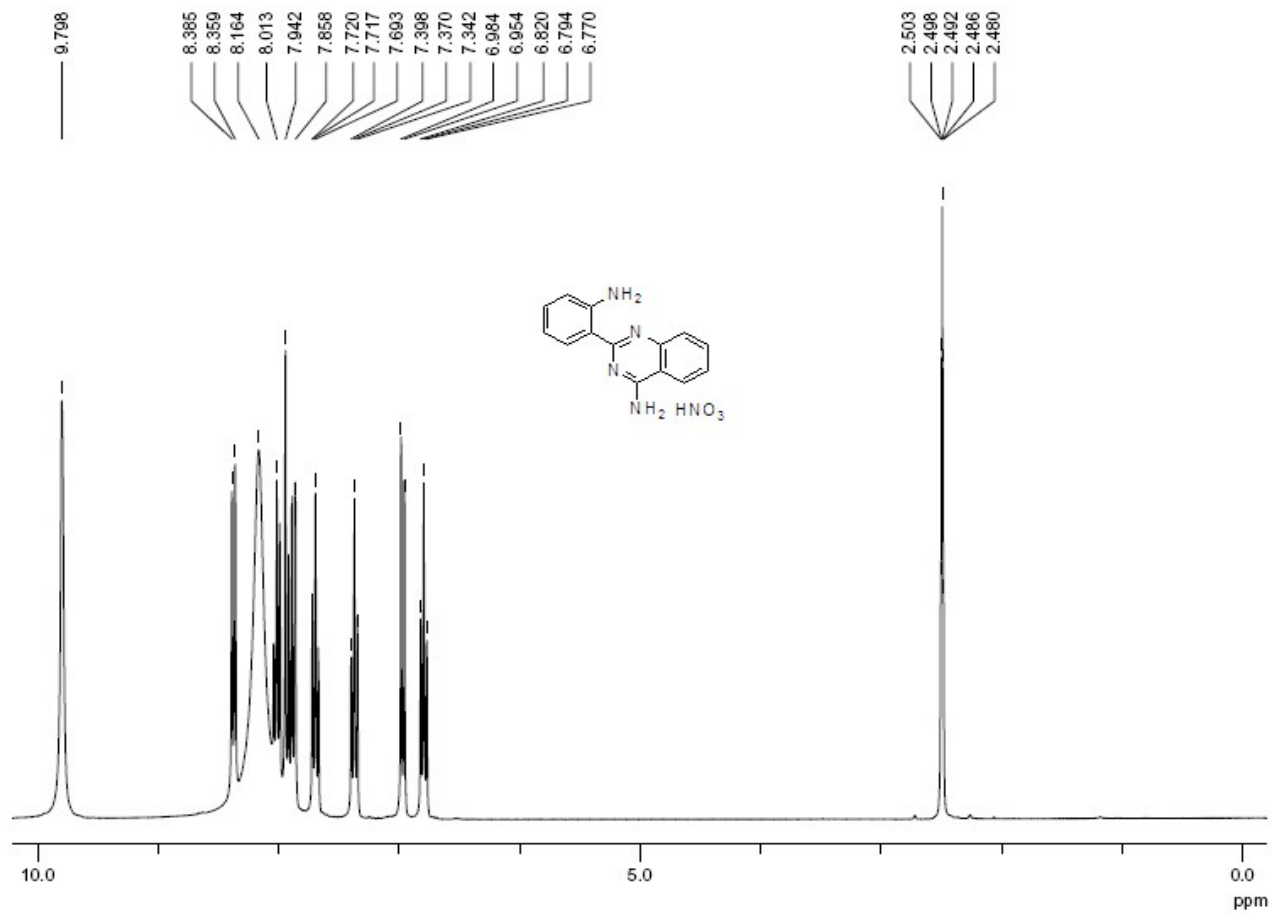
3. NMR Spectra of the Products

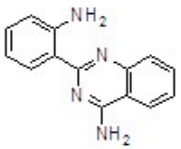
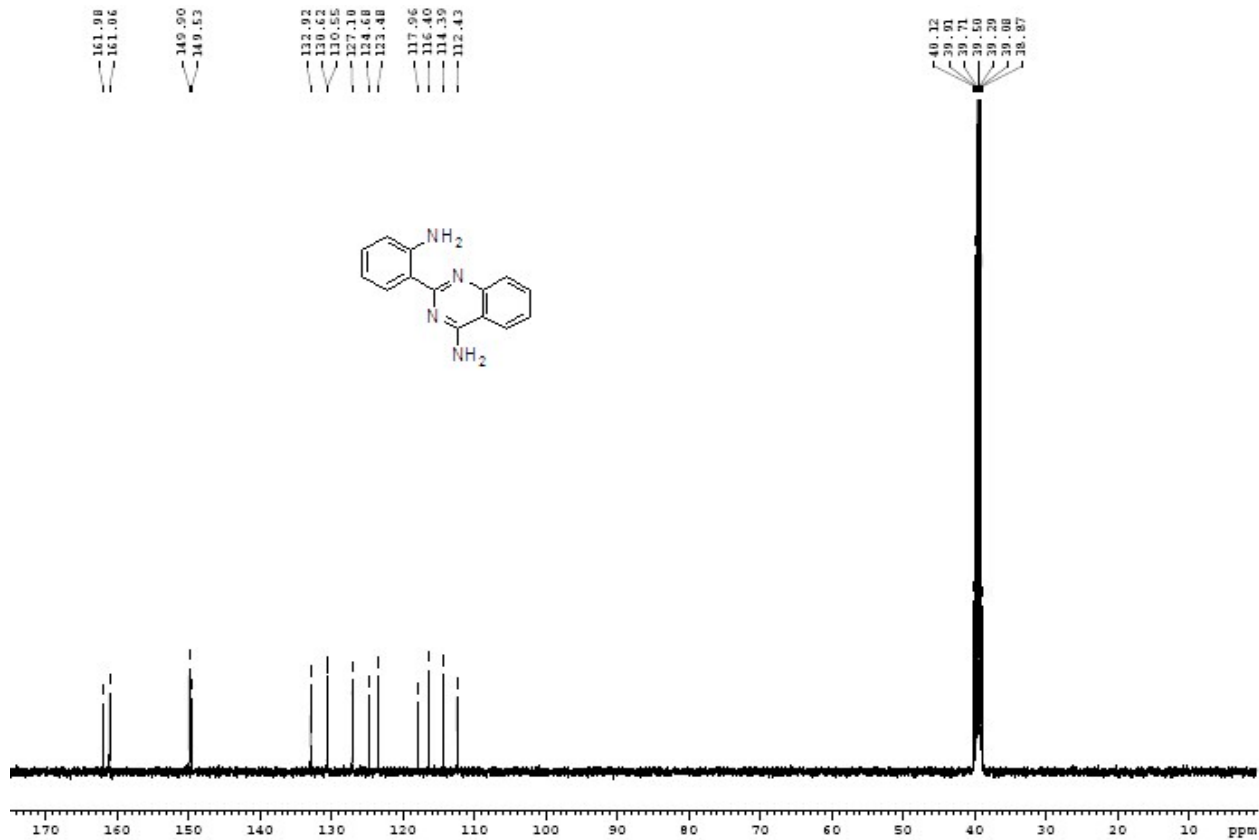
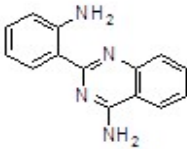
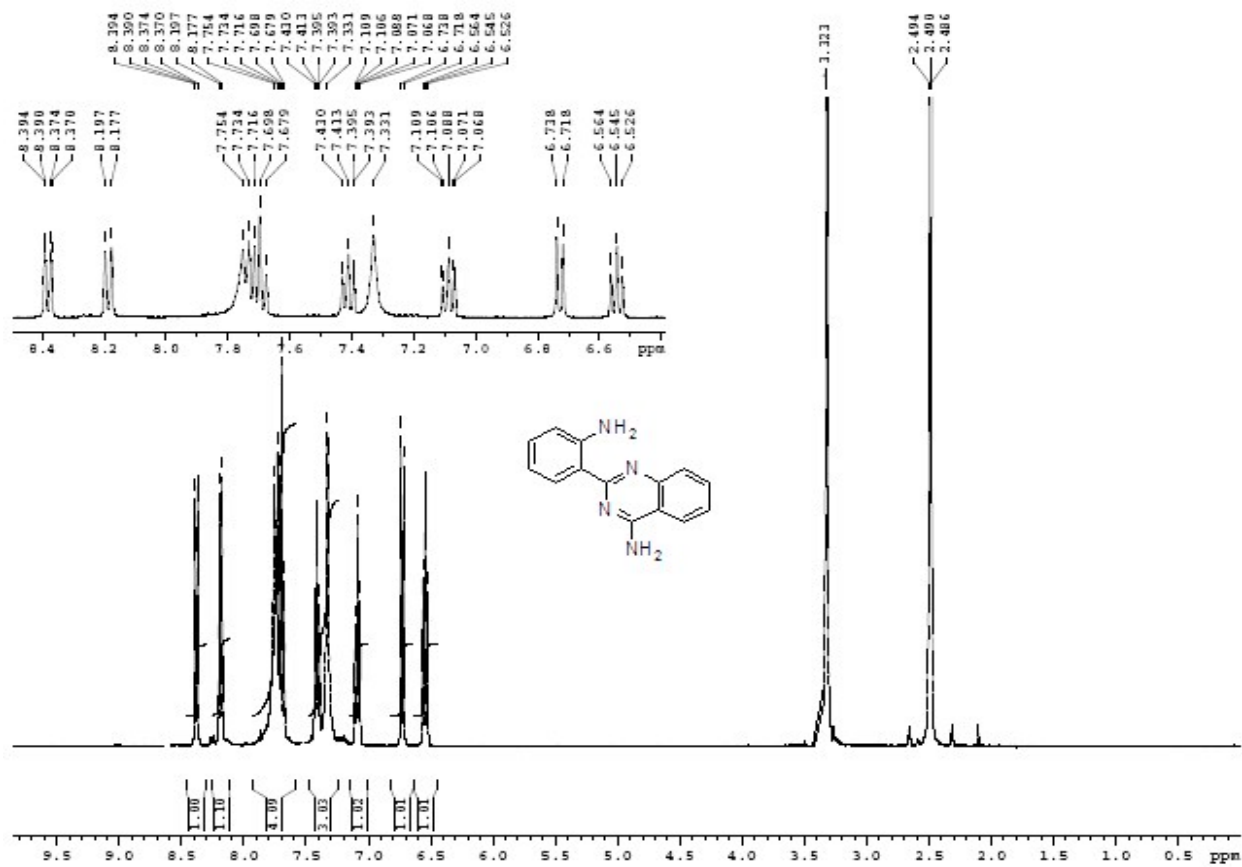
^1H and ^{13}C NMR for compound **2a**

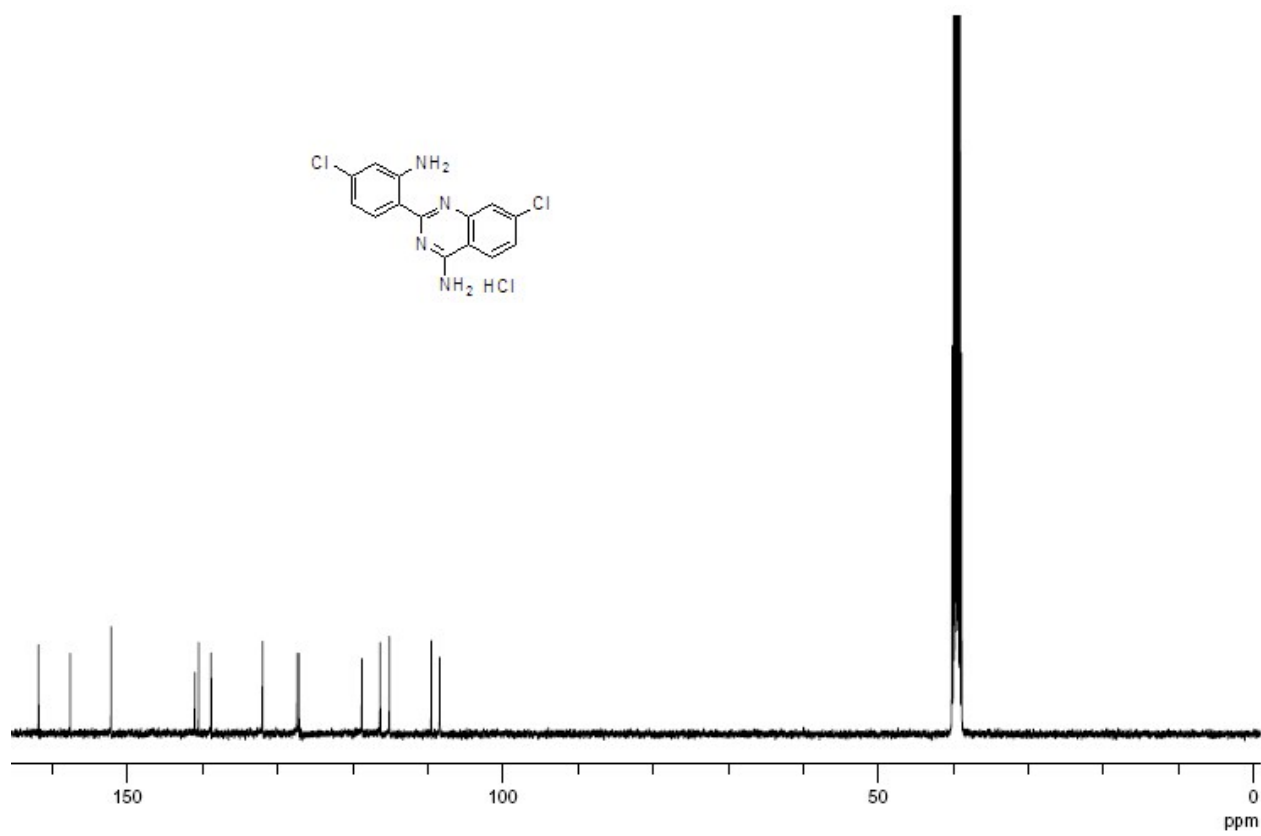
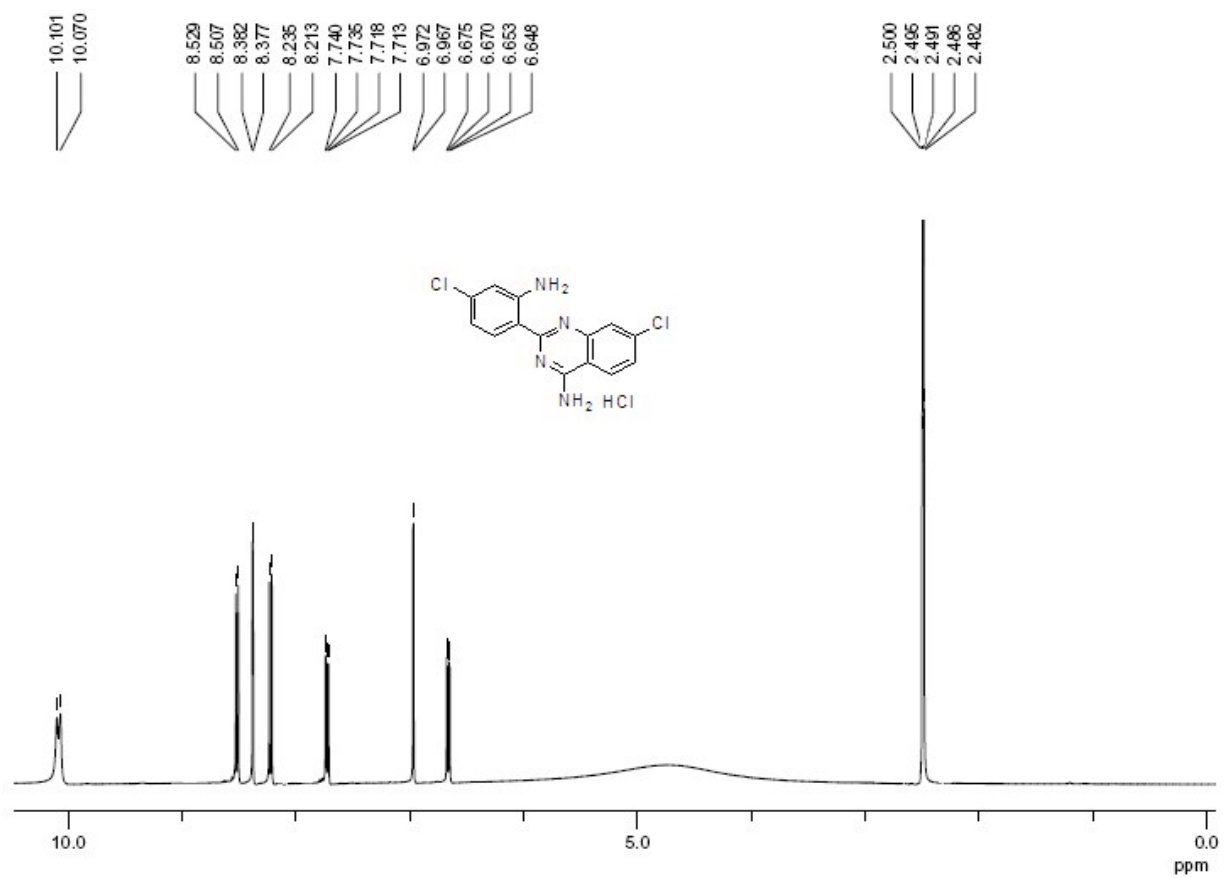


^1H and ^{13}C NMR for compounds **3a-b**

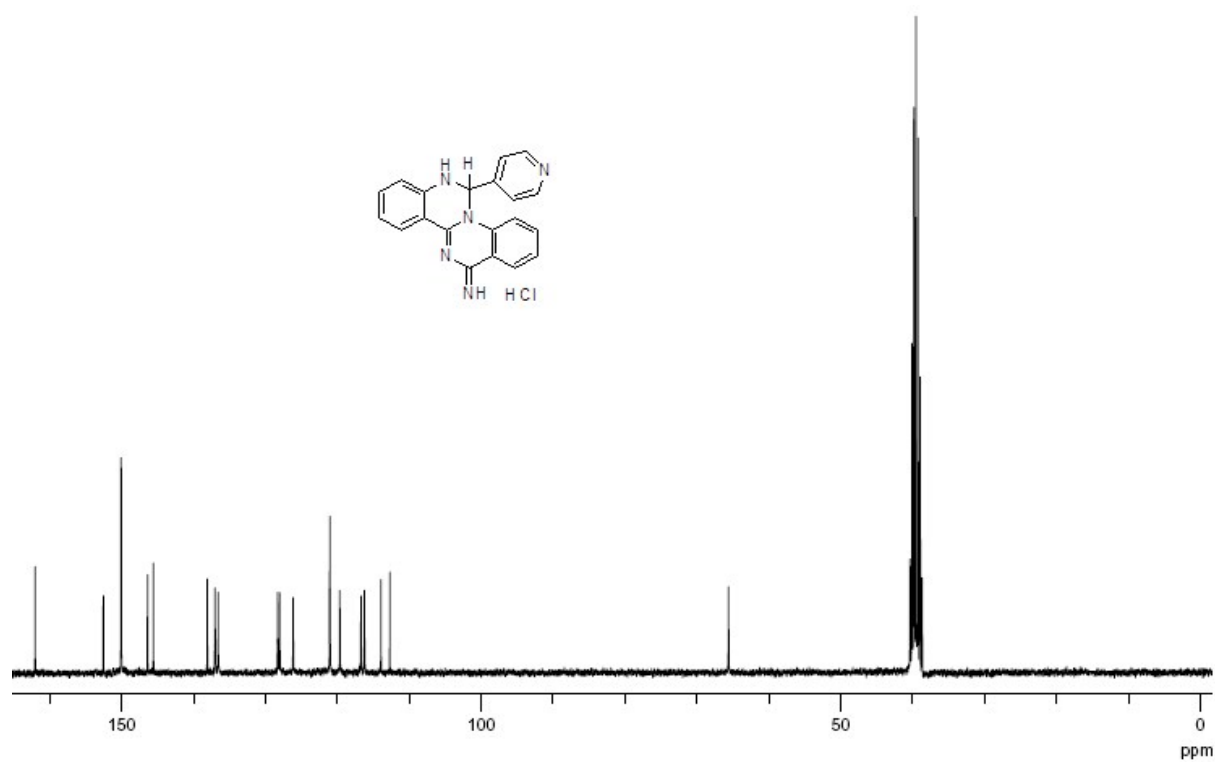
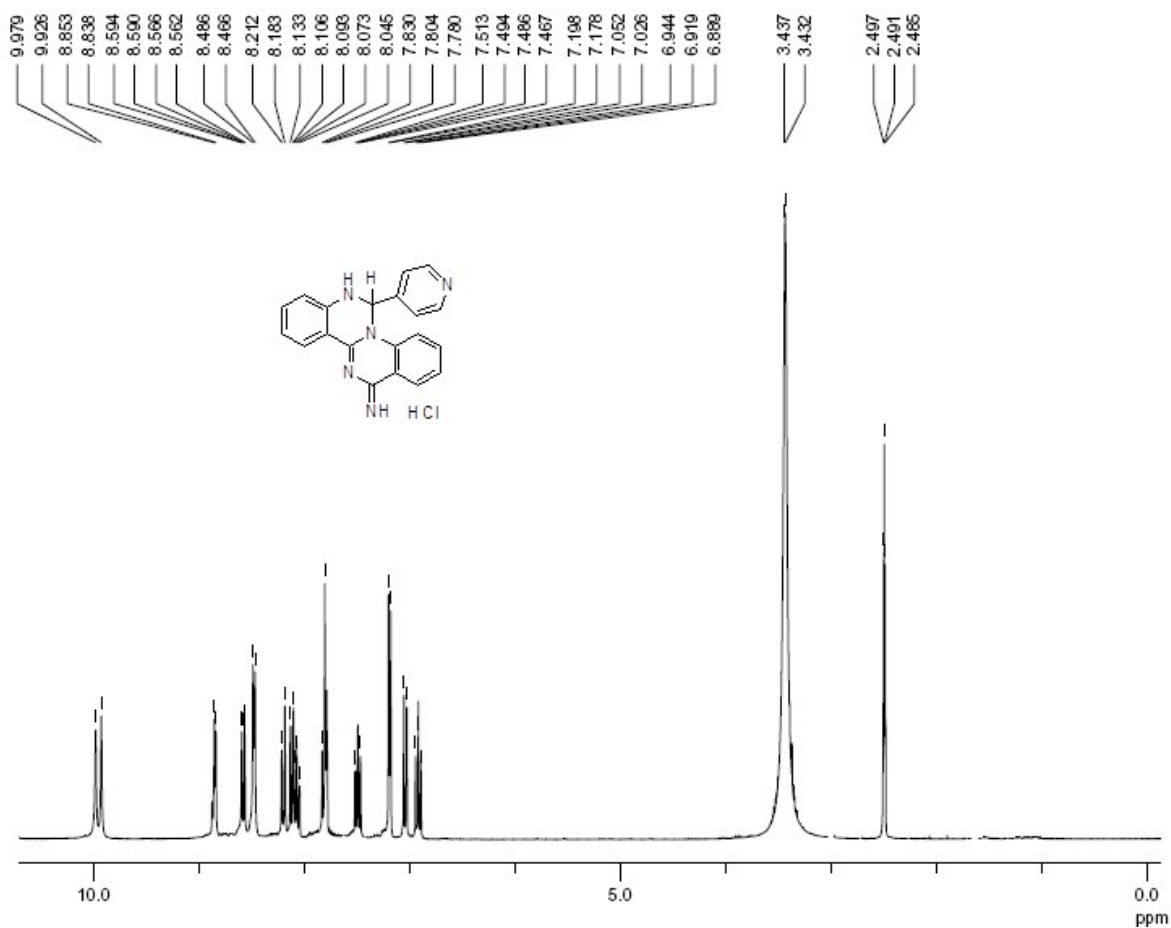


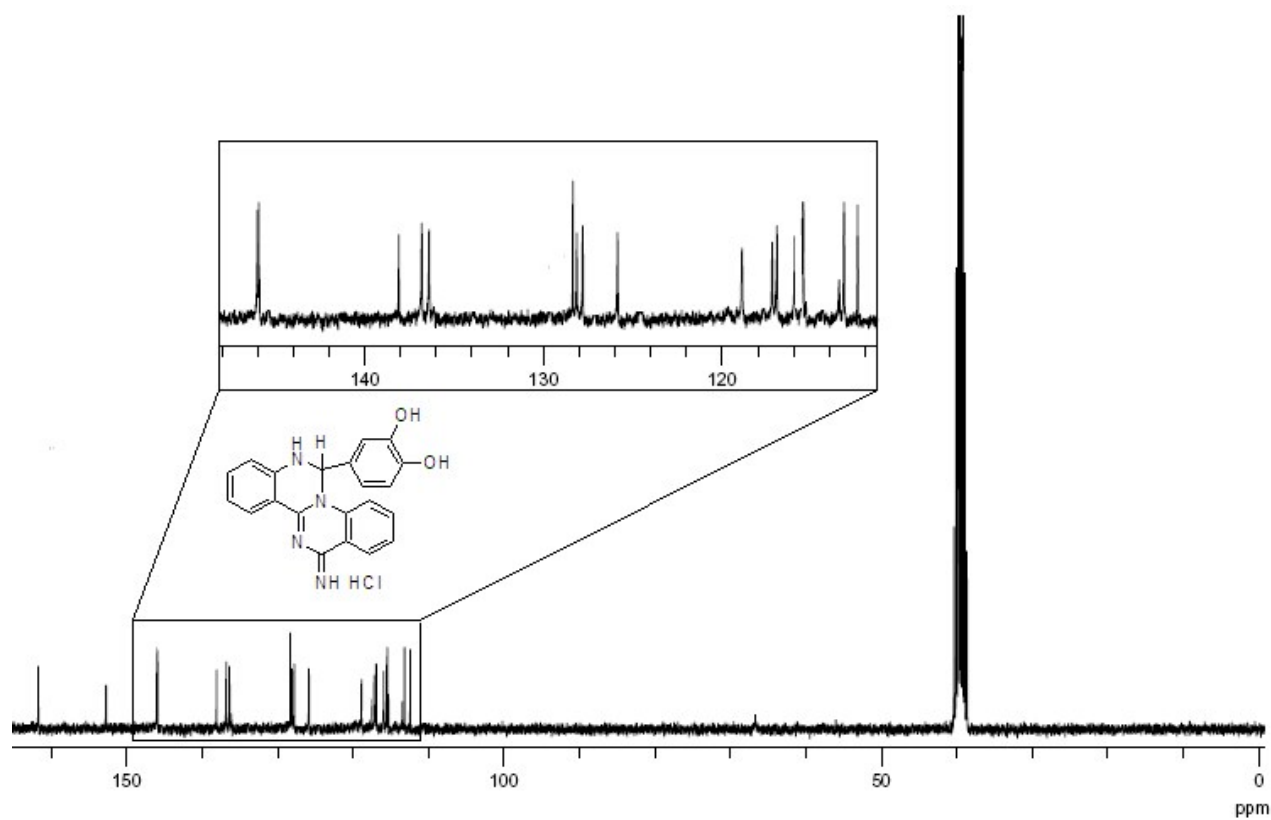
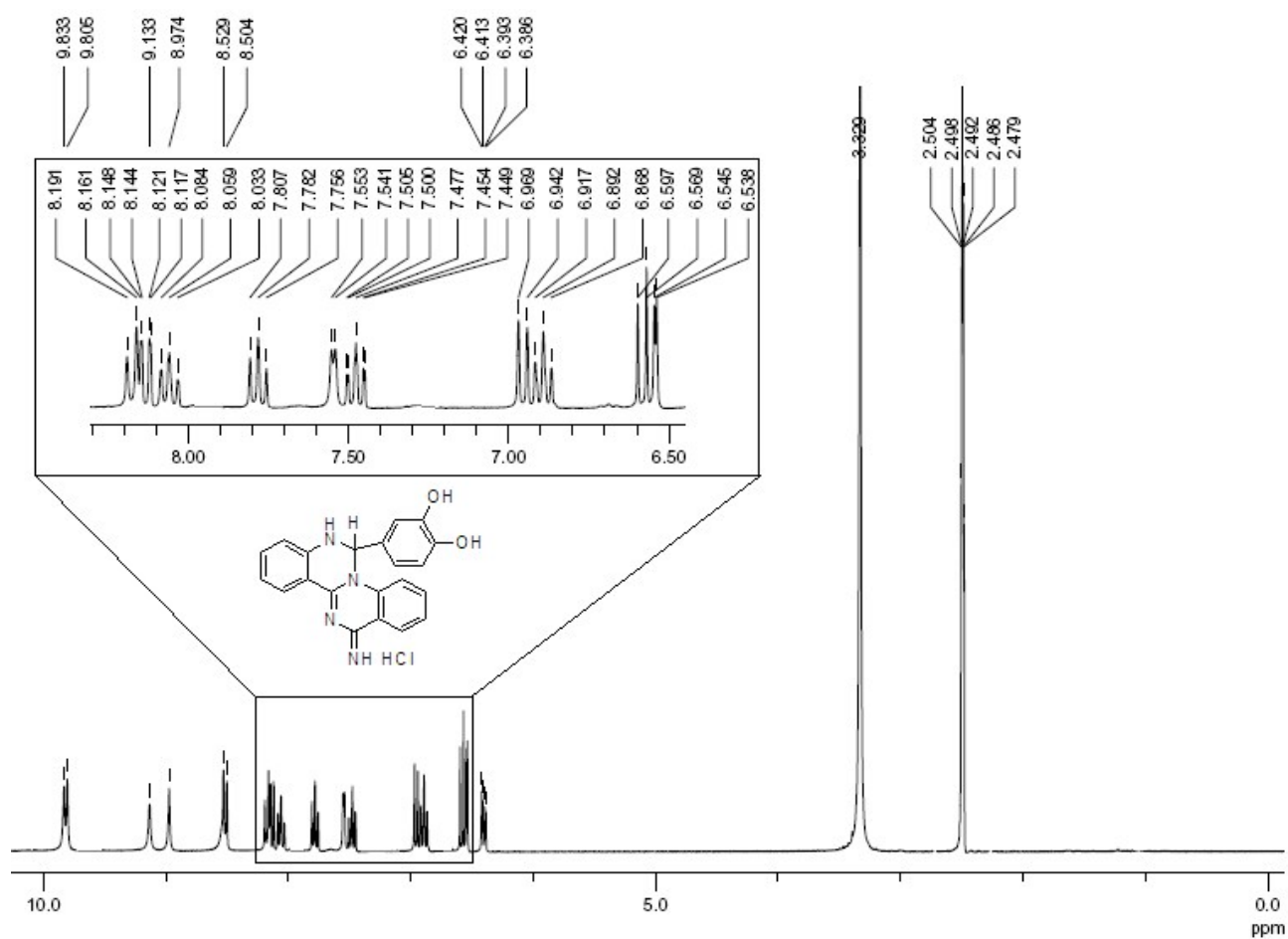


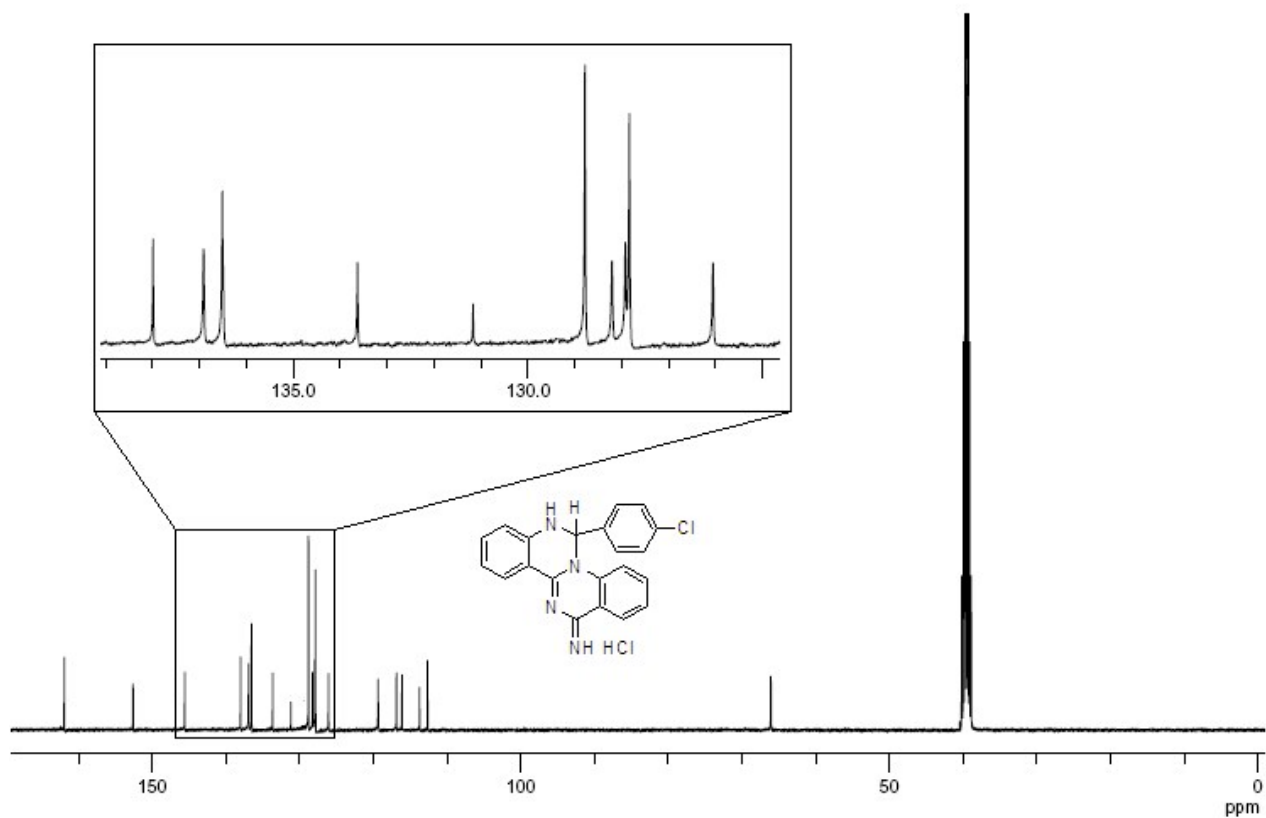
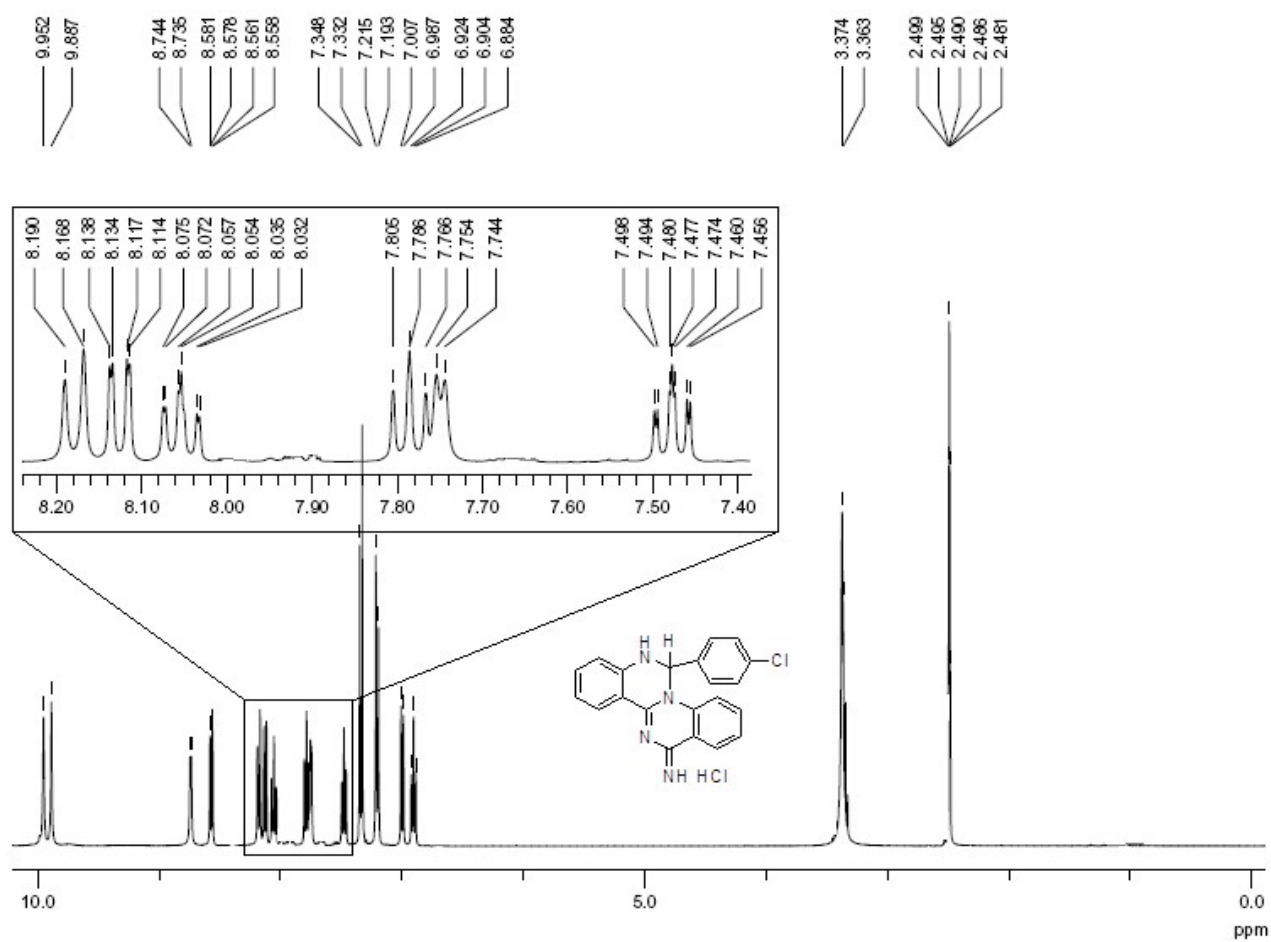


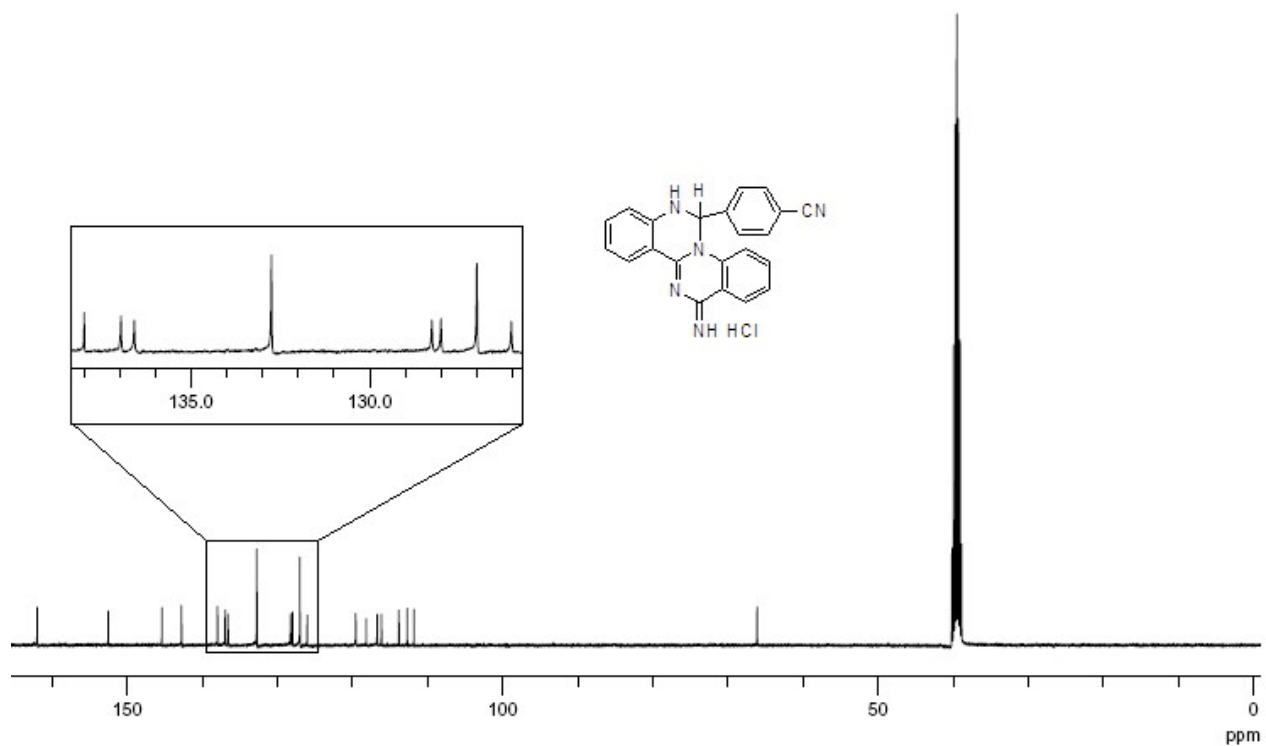
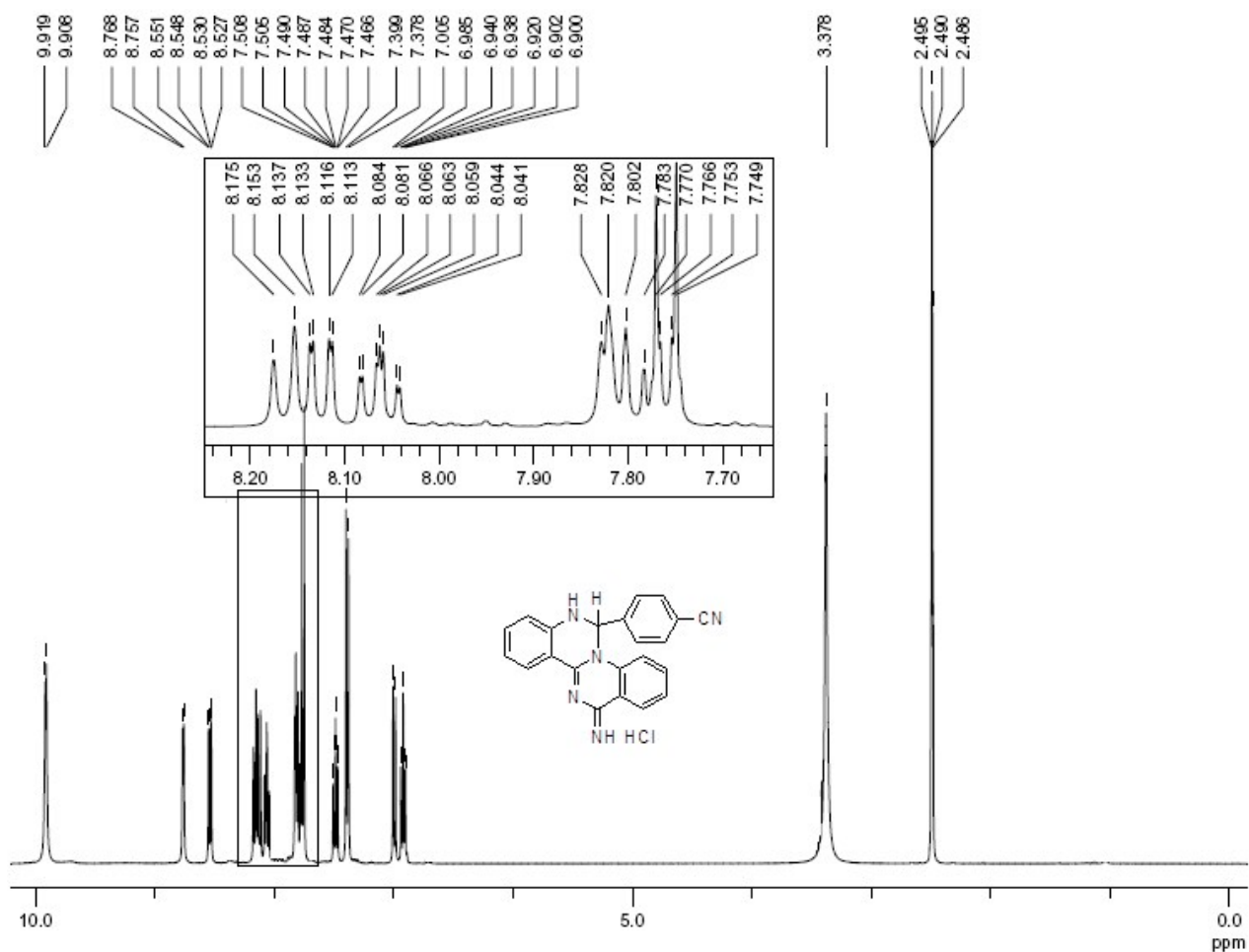


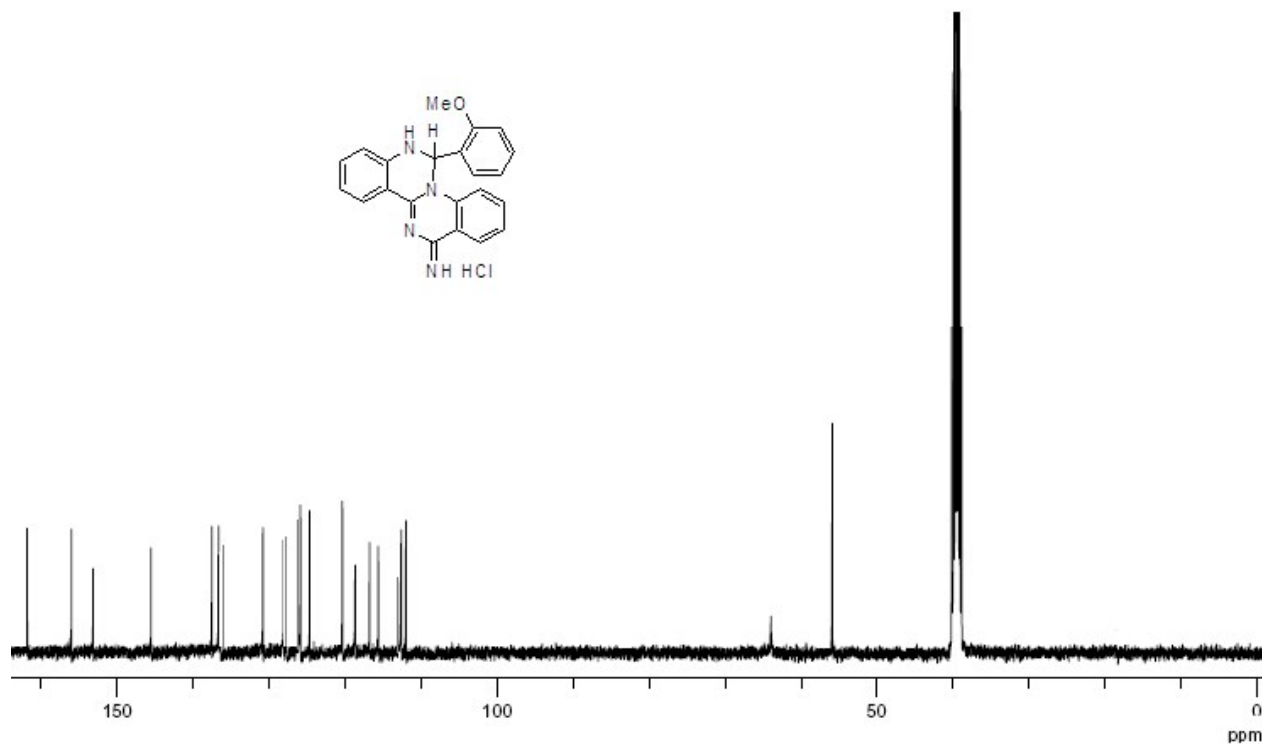
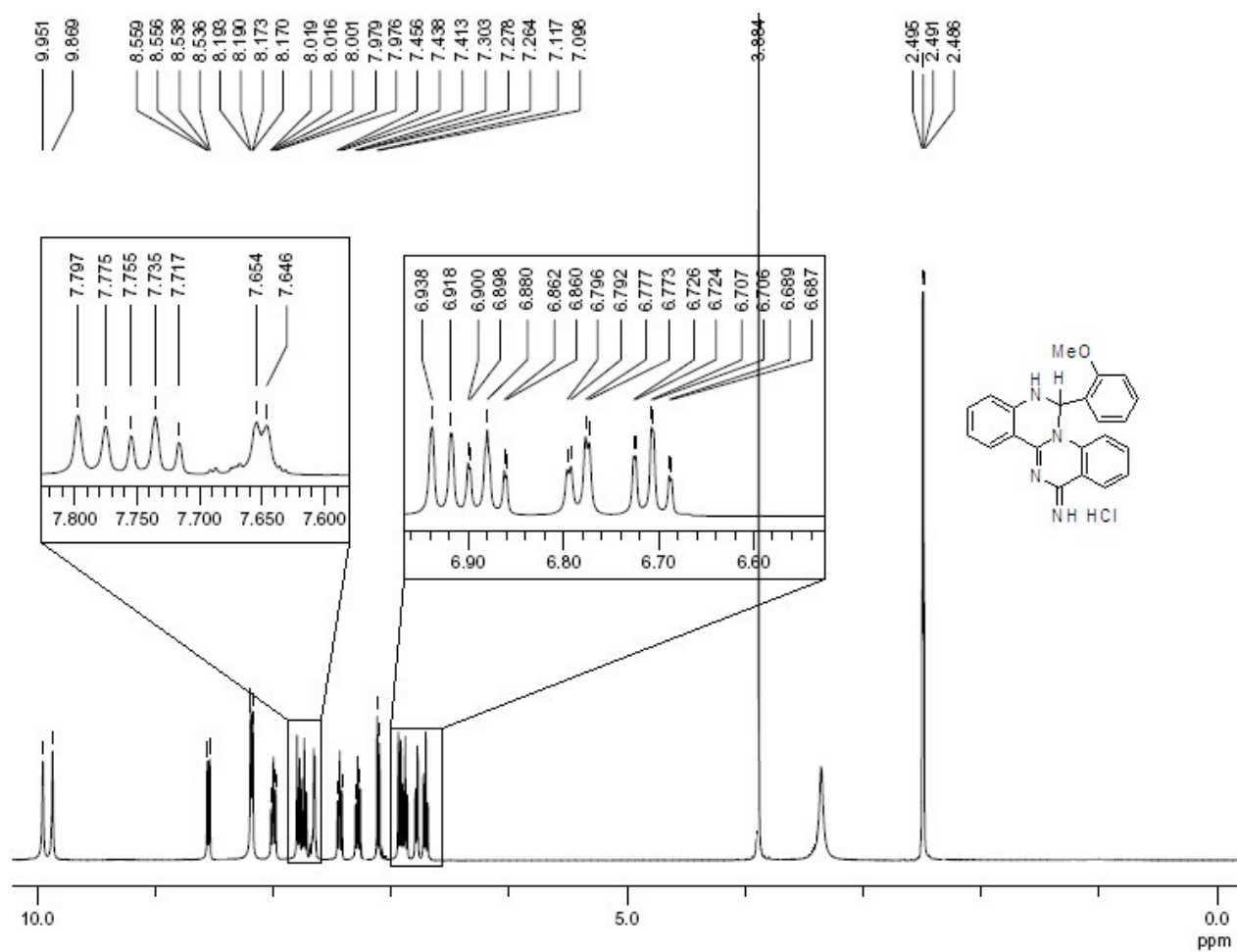
^1H and ^{13}C NMR for compounds **5a-m**

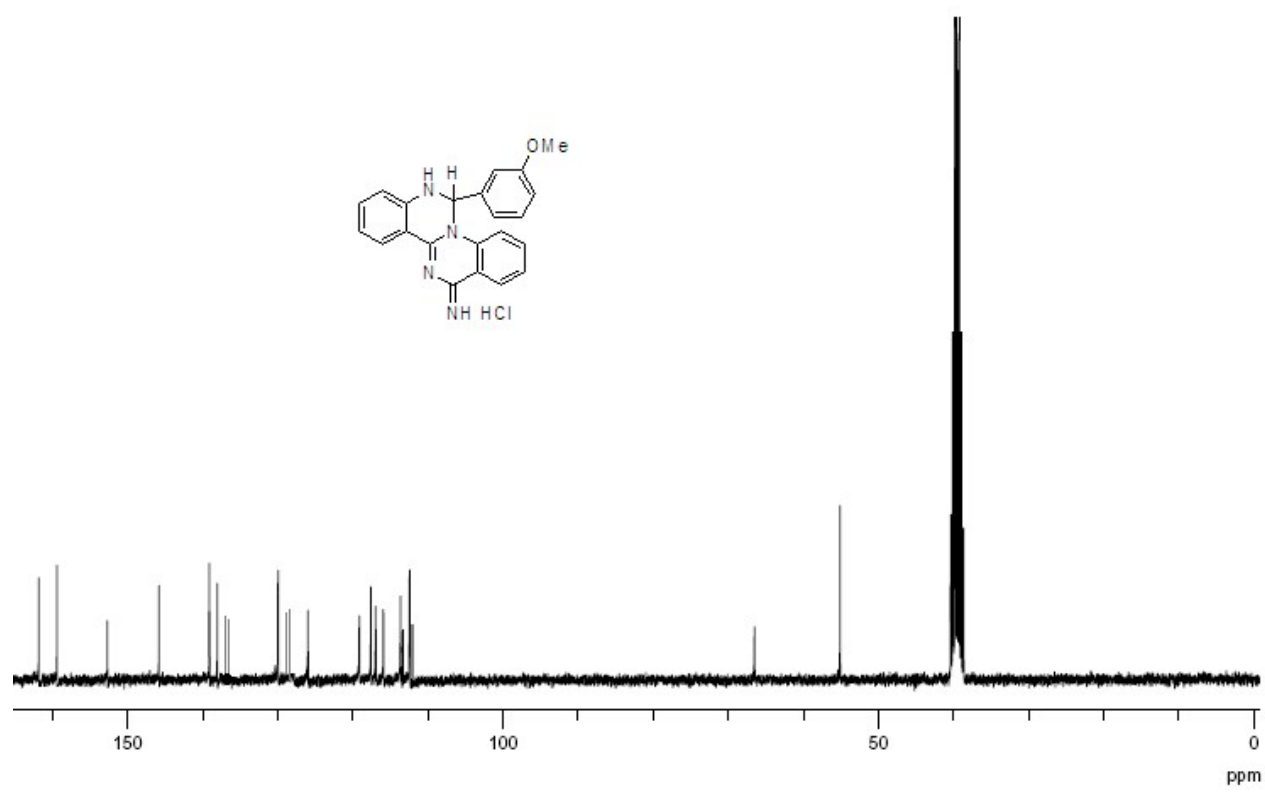
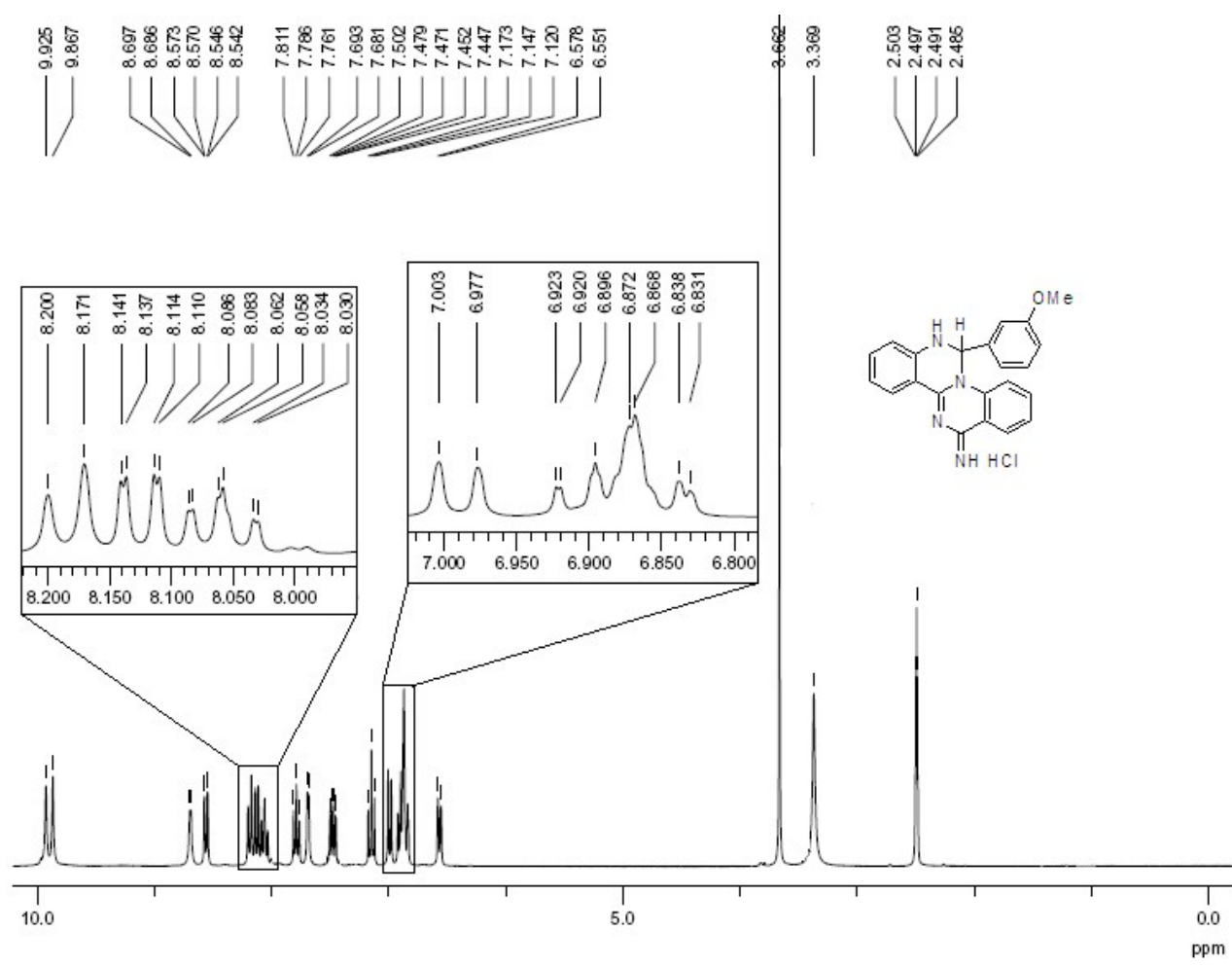


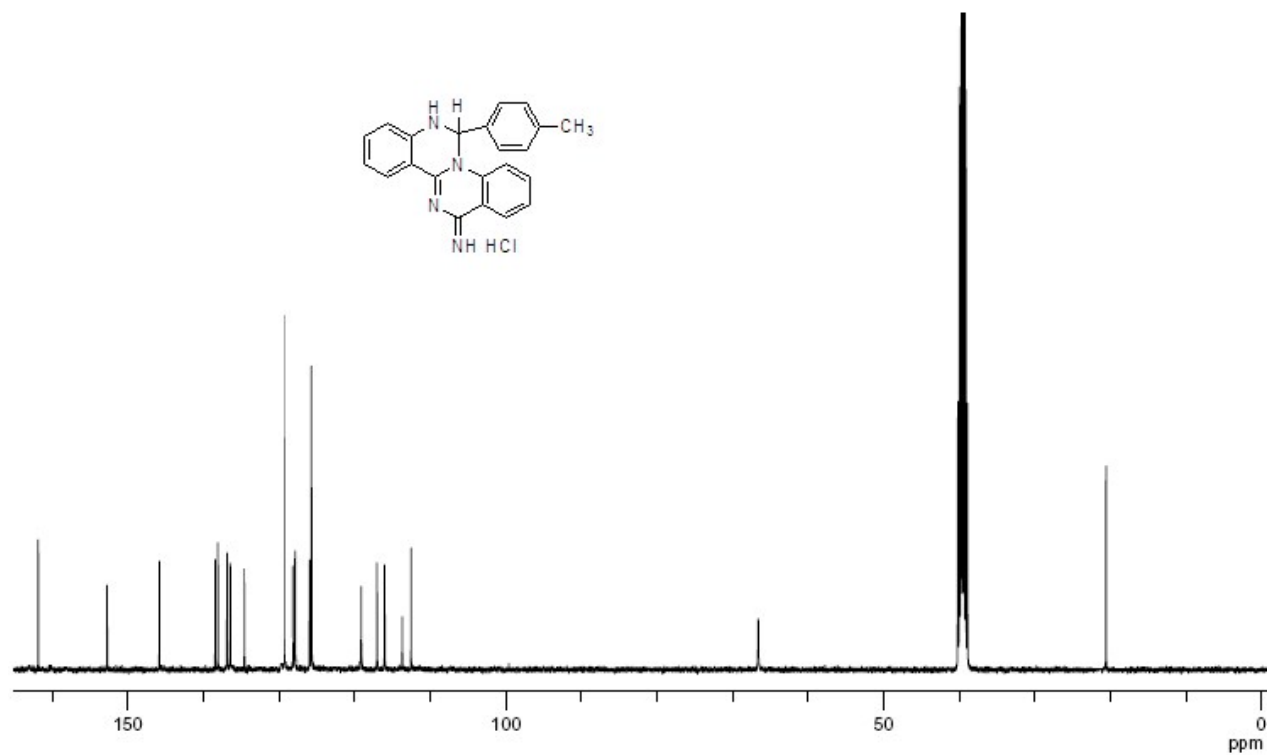
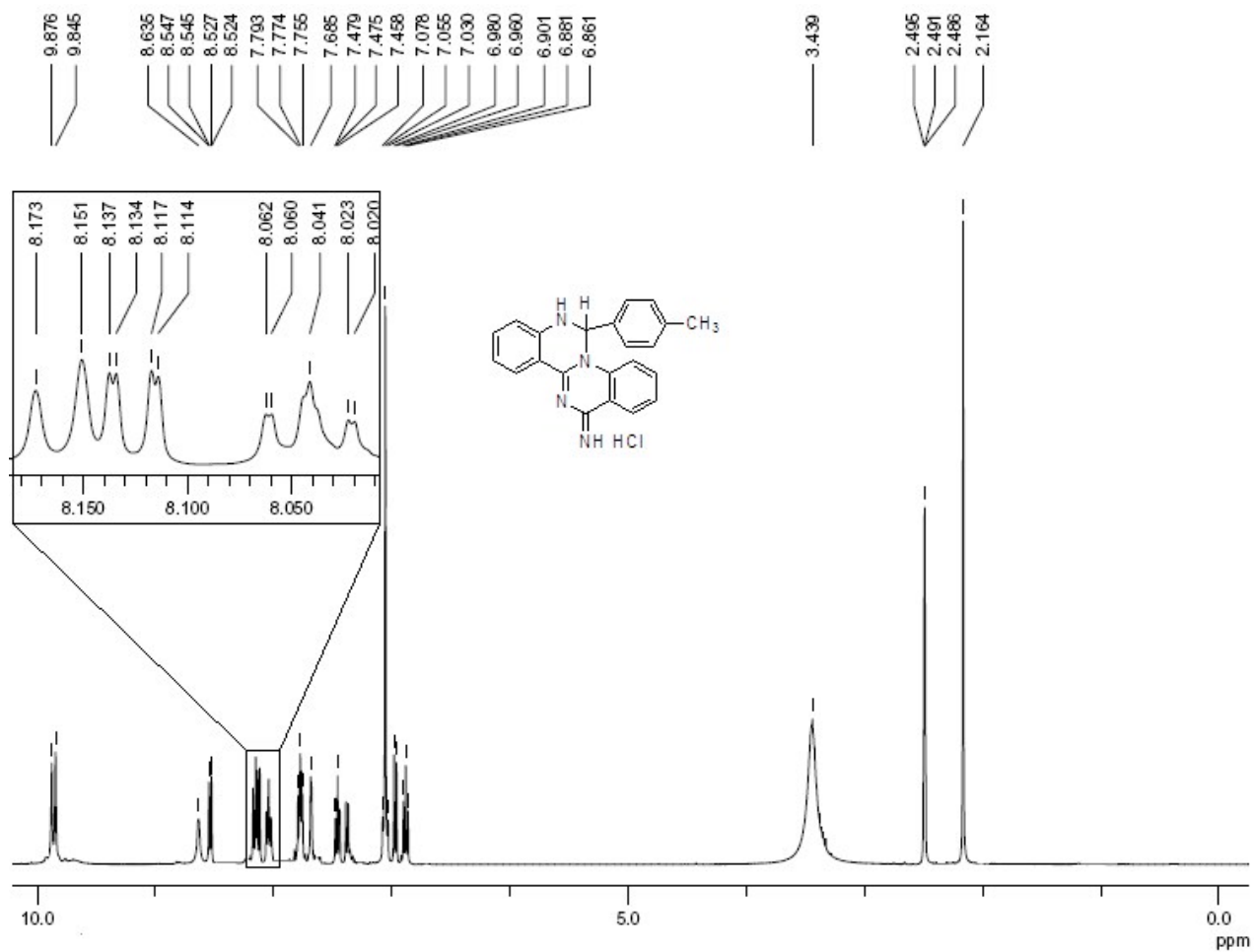


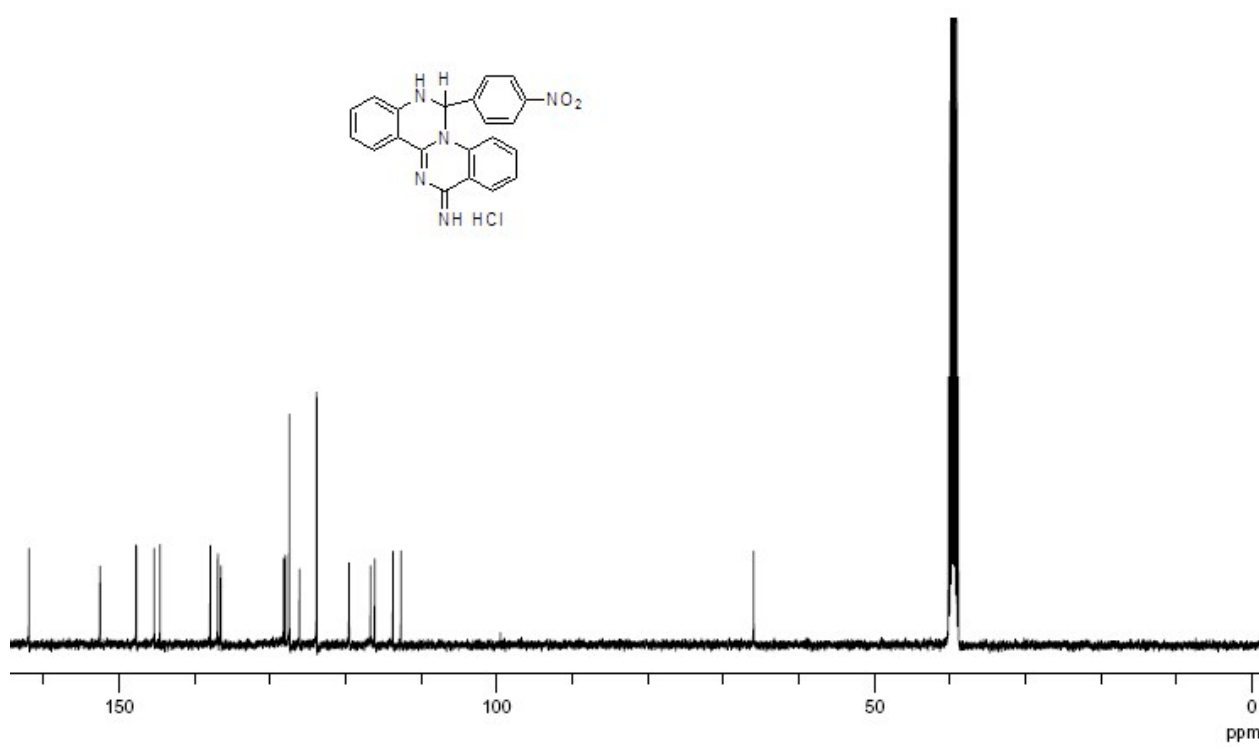
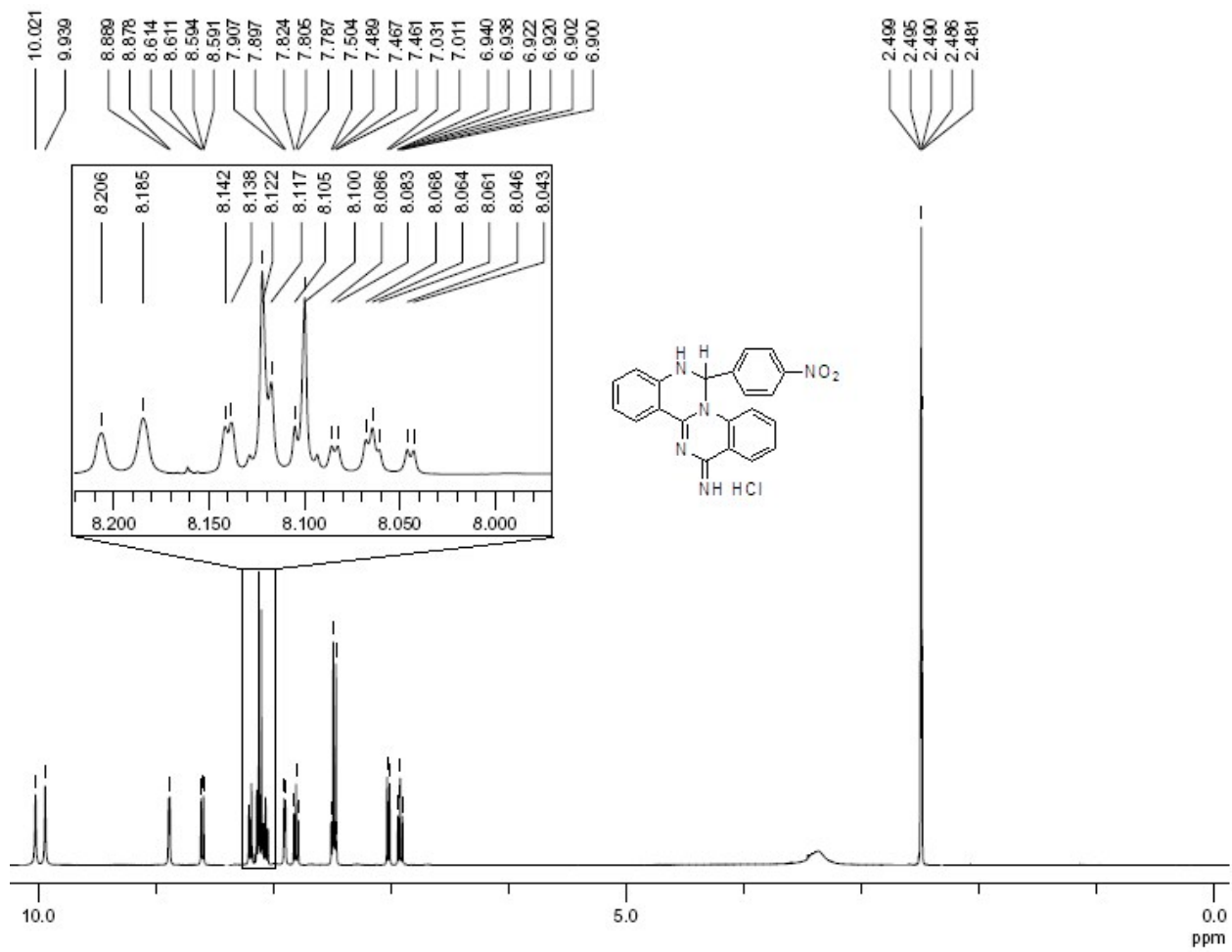


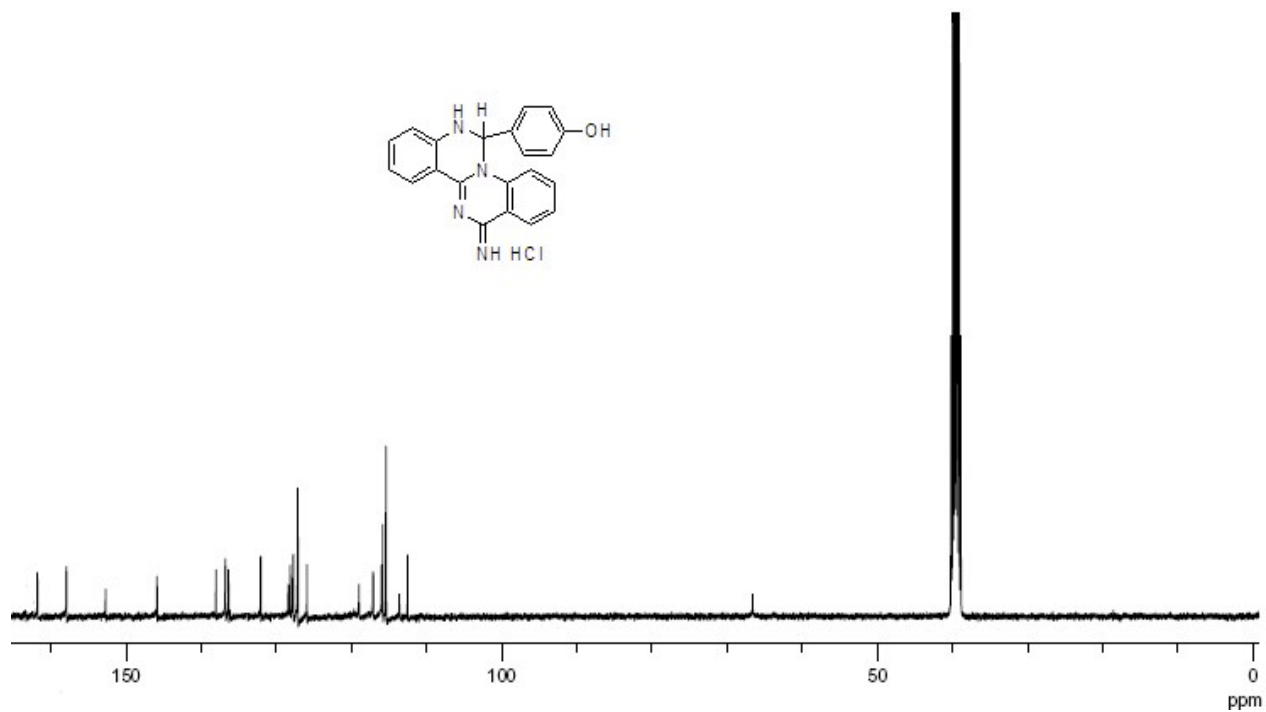
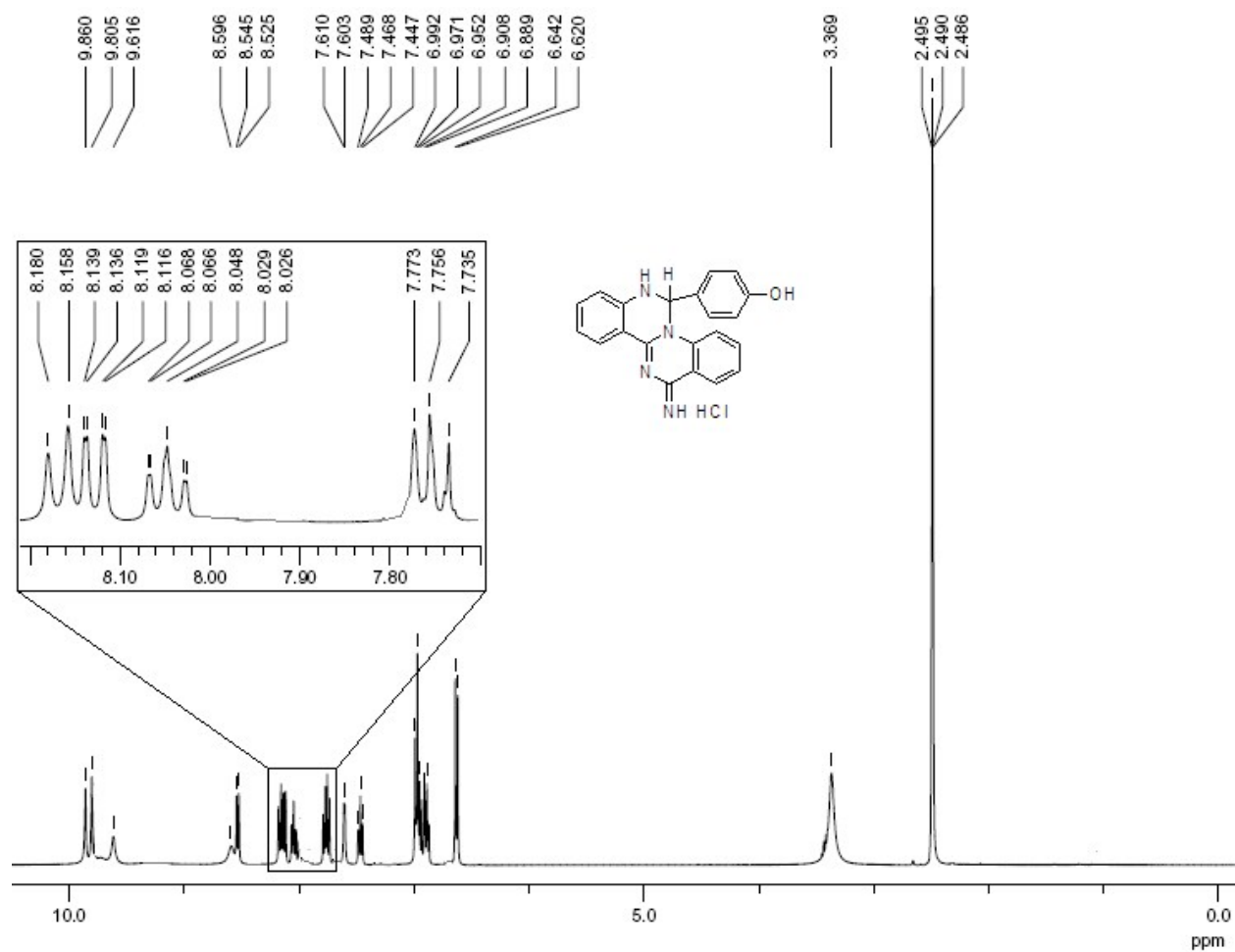


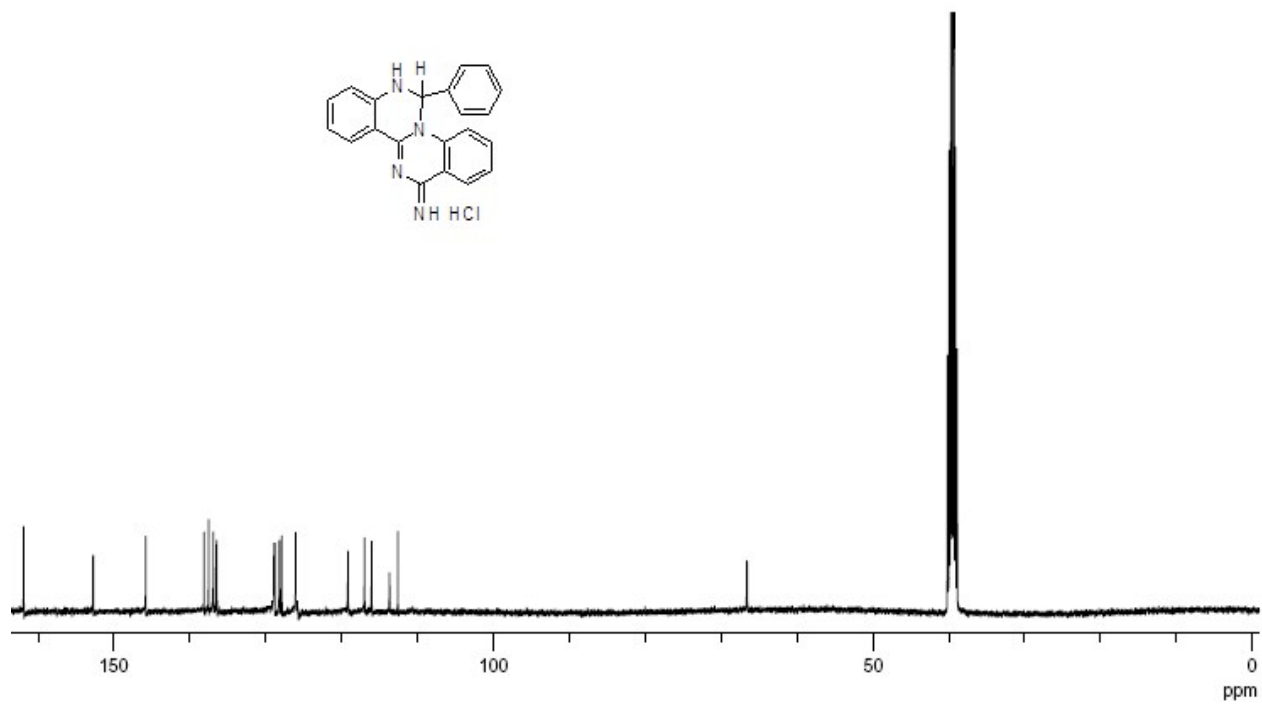
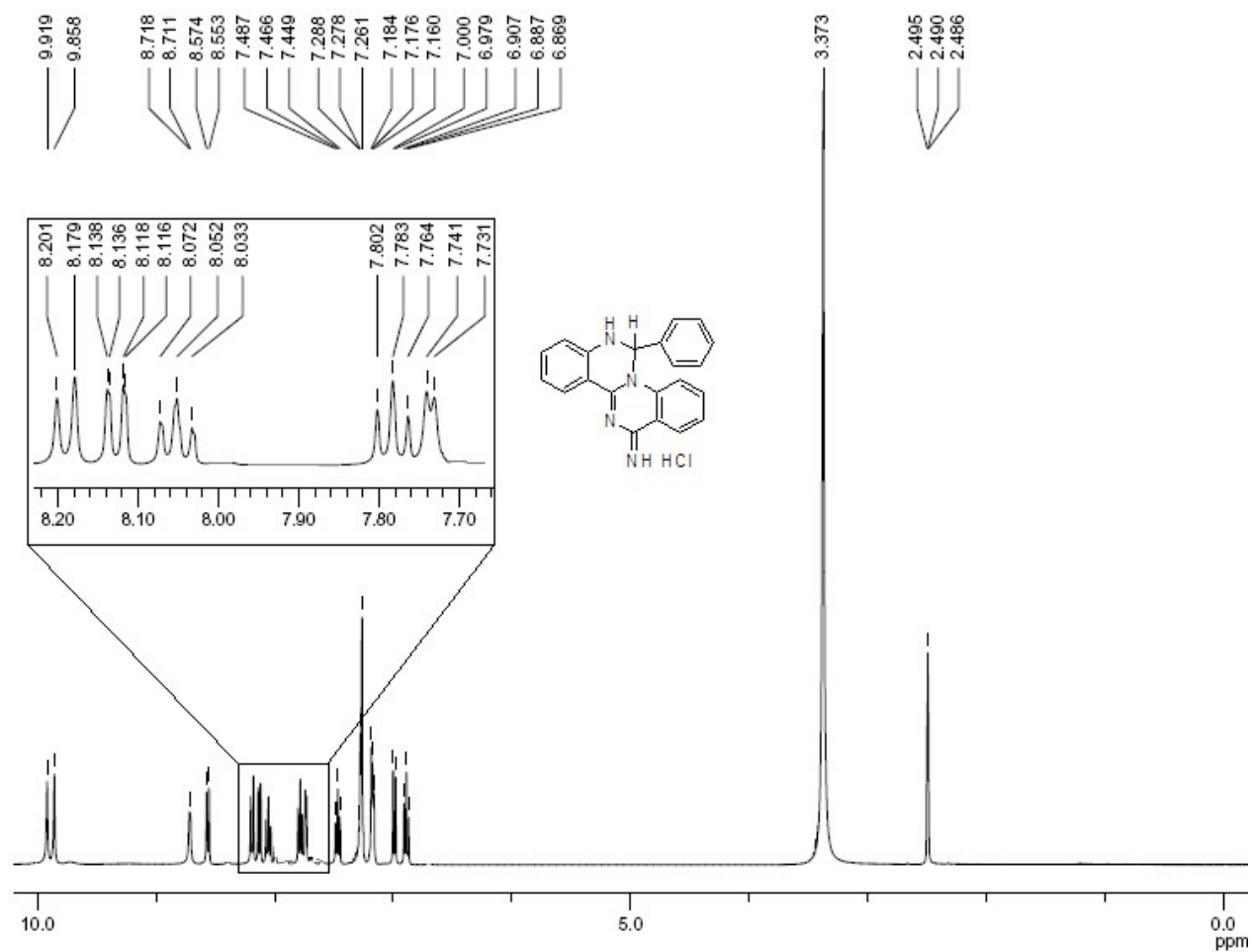


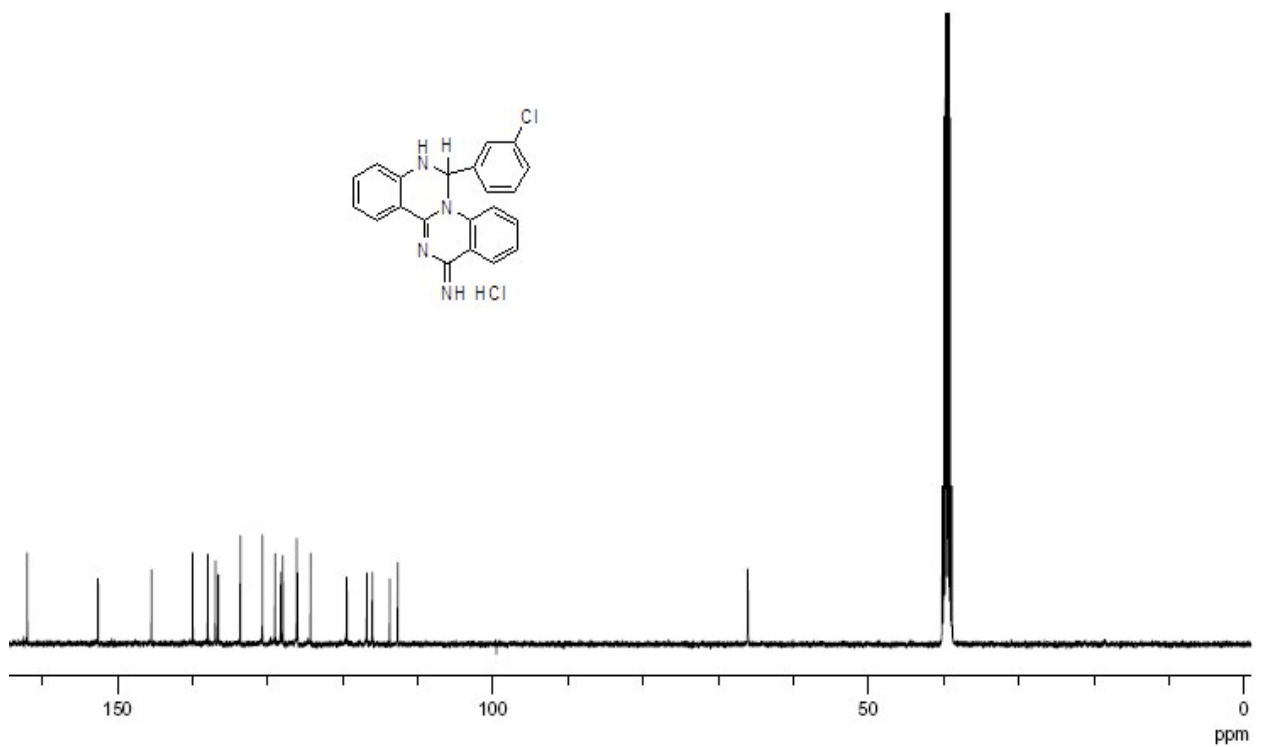
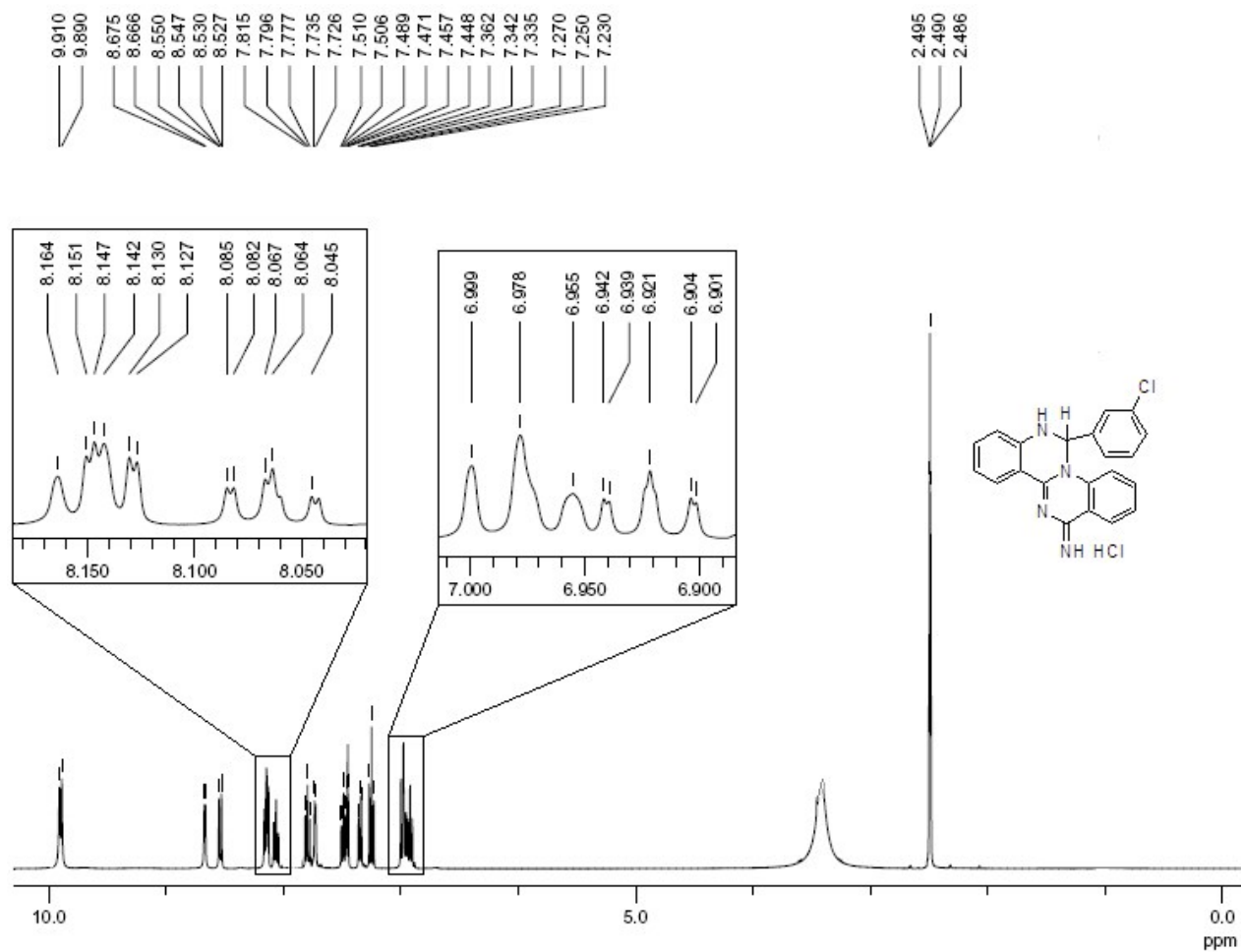


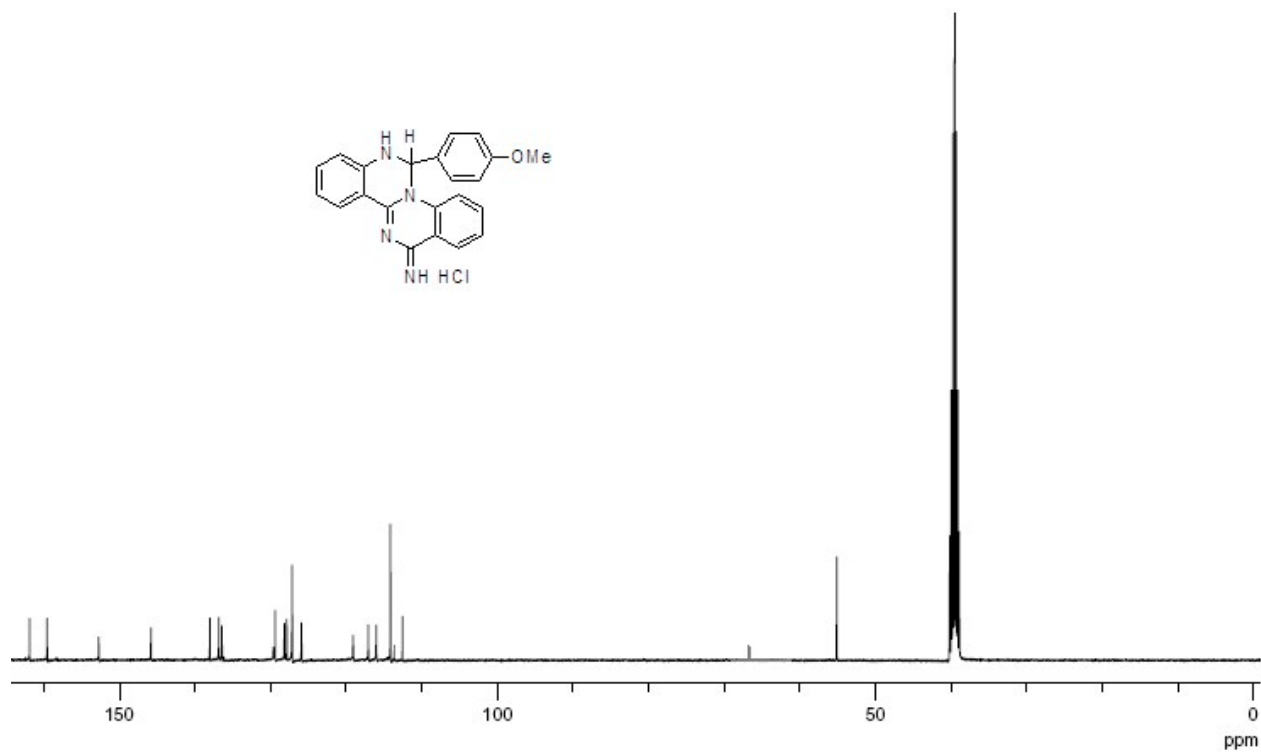
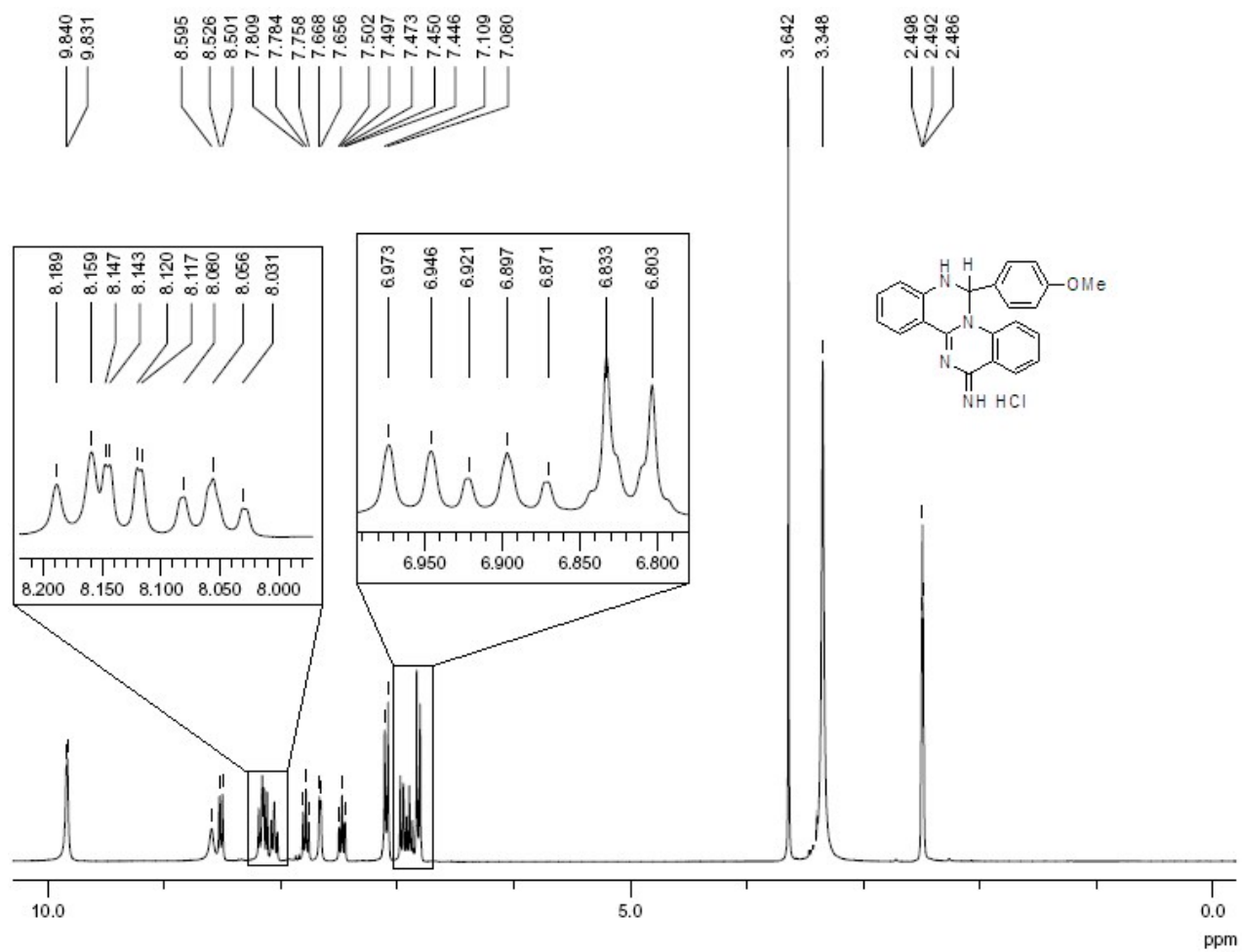


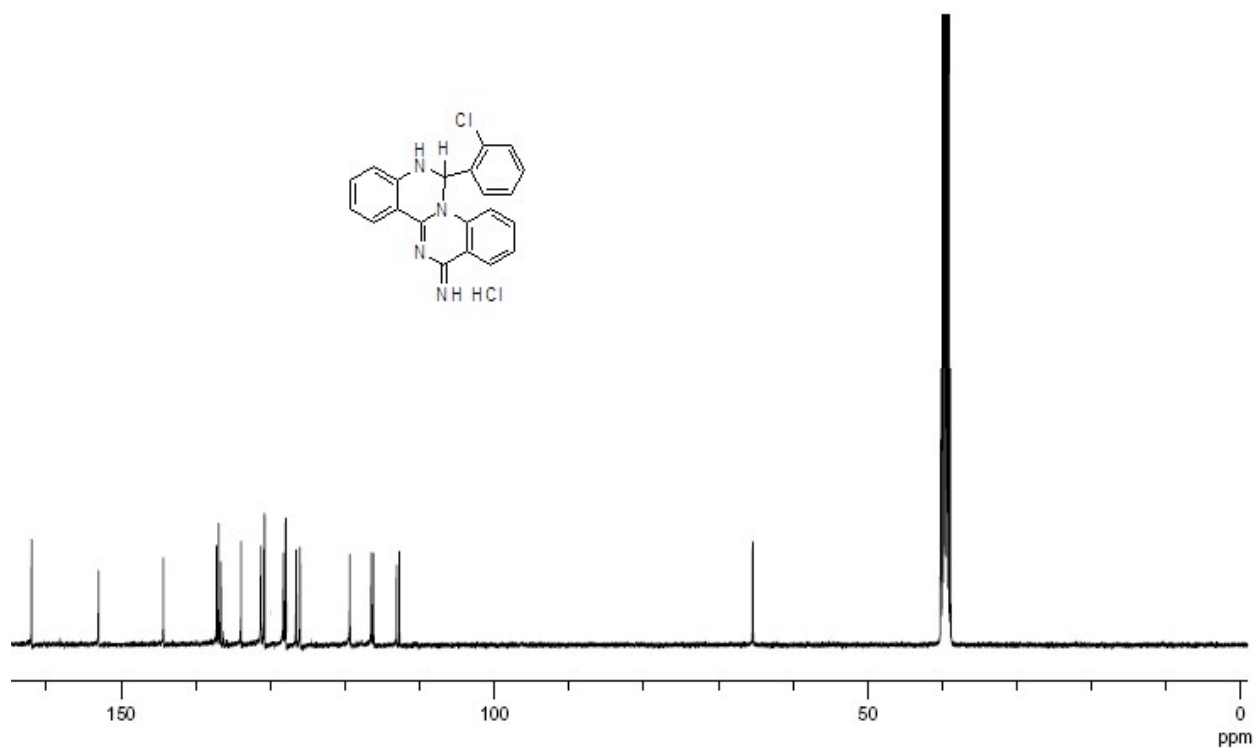
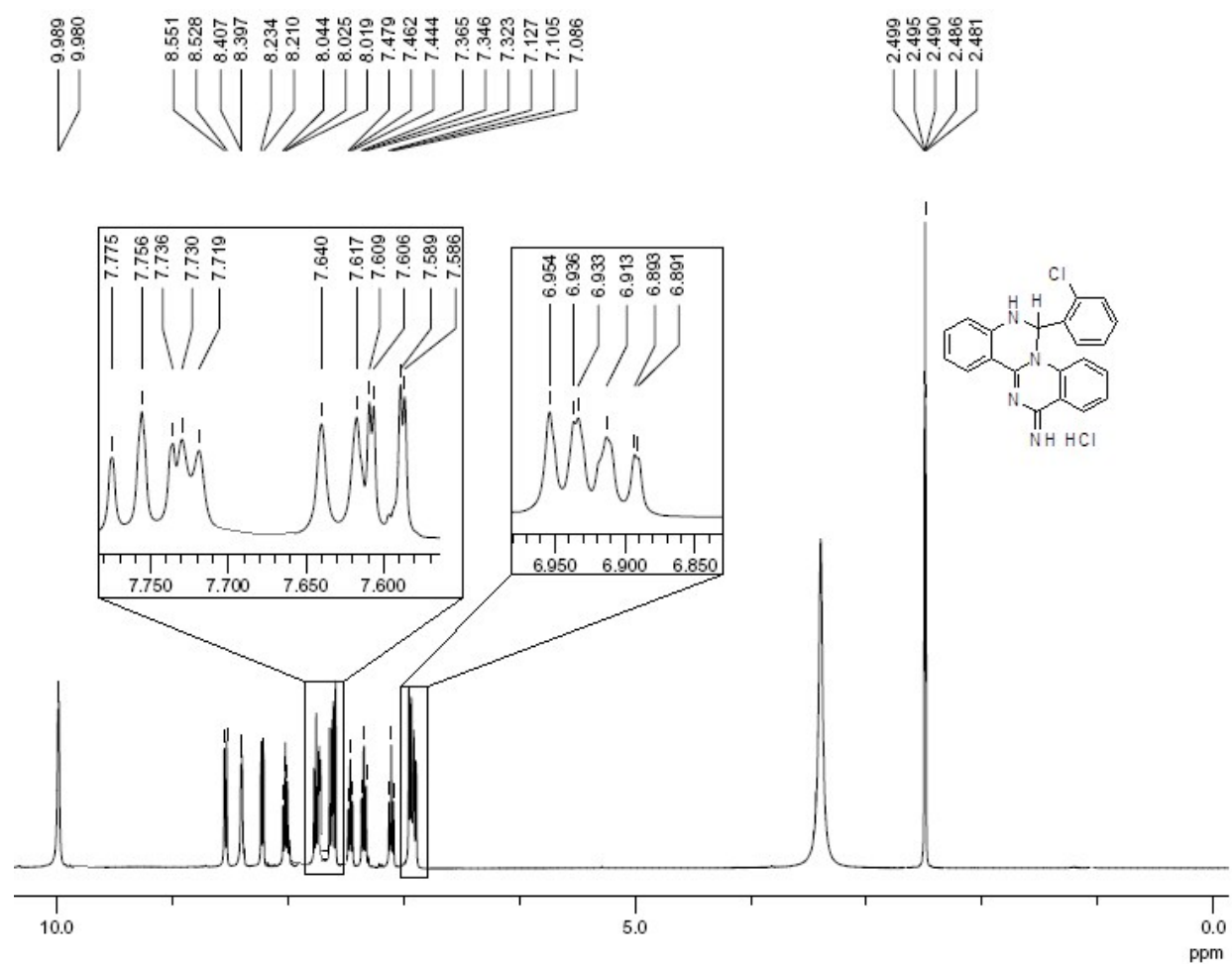












^1H and ^{13}C NMR for compounds **6f**

