

Supporting Information

Water-mediated selective synthesis of pyrazolo[1,5-*a*]quinazolin-5(4*H*)-ones and [1,2,4]triazolo[1,5-*a*]quinazolin-5(4*H*)-one *via* copper-catalyzed cascade reactions

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I. General Experimental Information

All the starting materials were commercially available agents and used without further purification. Melting points were recorded with a micro melting point apparatus and uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were reported in ppm from tetramethylsilane (TMS) as internal standard in $\text{DMSO}-d_6$ or CDCl_3 solution. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), td (triplet of doublets), br s (broad singlet), etc., and coupling constants were given in Hz. High-resolution mass spectra (HRMS) were obtained *via* ESI mode by using a MicrOTOF mass spectrometer. All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm).

II. Synthetic procedures and spectroscopic data

(I) Typical procedure for the preparation of pyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (**3a**)

To a solution of Cs₂CO₃ (2 mmol) in H₂O (5 mL) were added methyl 2-bromobenzoate (**1a**, 1 mmol), 1*H*-pyrazol-5-amine (**2a**, 1.2 mmol), and CuI (0.2 mmol). The mixture was stirred at 100 °C under nitrogen atomosphere until a complete conversion as indicated by TLC. It was cooled to room temperature and then extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na₂SO₄, and concentrated under vacuum. The crude product was purified by column chromatography eluting with petroleum ether/ethyl acetate (3:1) to give **3a**. Products **3b-3t** and **6** were obtained in a similar manner.

pyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3a): white solid, mp 284-286 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 5.89 (d, *J* = 2.0 Hz, 1H), □ 7.46 (t, *J* = 7.2 Hz, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.84-7.88 (m, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 8.12 (dd, *J*₁ = 8.0 Hz, *J*₂ = 1.2 Hz, 1H), 12.21(s,1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 88.9, 114.8, 116.5, 125.7, 128.6, 135.5, 137.8, 139.0, 142.6, 158.9. HRMS calcd for C₁₀H₈N₃O: 186.0667 [M+H]⁺, found: 186.0674.

7-chloropyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3b): white solid, mp 275-277 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 5.91 (d, *J* = 1.6 Hz, 1H), 7.80 (d, *J* = 2.0 Hz, 1H), 7.89-7.92 (m, 1H), 8.03-8.08 (m, 2H), 12.35 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 89.3, 117.1, 118.2, 127.7, 130.0, 135.3, 136.6, 139.0, 143.0, 157.9. HRMS calcd for C₁₀H₇ClN₃O: 220.0278 [M+H]⁺, found: 220.0285.

7-methoxypyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3c): pale yellow solid, mp 292-294 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 3.86 (d, *J*= 2.4 Hz, 3H), 5.88 (t, *J*= 2.8 Hz, 1H), 7.47 (dd, *J*₁ = 9.2 Hz, *J*₂ = 2.8 Hz, 1H), 7.55 (t, *J*= 2.4 Hz, 1H), 7.72 (d, *J*=2.4 Hz, 1H), 8.02 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.8 Hz, 1H), 12.22 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 56.2, 88.7, 110.2, 116.6, 117.6, 123.7, 132.3, 138.2, 141.9, 157.2, 158.8. HRMS calcd for C₁₁H₁₀N₃O₂: 216.0773 [M+H]⁺, found: 216.0764.

7-nitropyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3d): pale yellow solid, mp 289-291 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 5.92 (d, *J* =2.0 Hz, 1H), 7.85 (d, *J* =2.0 Hz, 1H), 8.11 (d, *J* =8.8 Hz, 1H), 8.56 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.4 Hz, 1H), 8.68 (d, *J*=2.4 Hz, 1H), 12.47 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 89.9, 116.4, 117.0, 124.4, 129.9, 139.9, 141.3, 144.3, 144.7, 157.7. HRMS calcd for C₁₀H₇N₄O₃: 231.0518 [M+H]⁺, found: 231.0527.

8-nitropyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3e): pale yellow solid, mp 282-284 °C; ¹H NMR

(400MHz, DMSO-*d*₆) δ: 5.95 (d, *J* = 1.6 Hz, 1H), 7.86 (d, *J* = 1.6 Hz, 1H), 8.19 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.6 Hz, 1H), □ 8.33 (d, *J* = 8.8 Hz, 1H), 8.63 (d, *J* = 2.4 Hz, 1H), 12.47 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 89.7, 110.0, 119.6, 121.2, 131.0, 138.2, 139.6, 143.7, 151.5, 157.8. HRMS calcd for C₁₀H₇N₄O₃: 231.0518 [M+H]⁺, found: 231.0511.

2-methylpyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3f)^[1]: pale yellow solid, mp 288-290 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 2.25 (s, 3H), 5.73 (s, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 12.09 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 14.4, 88.9, 114.5, 116.2, 125.2, 128.6, 135.5, 137.8, 139.4, 151.7, 158.9.

2-cyclopropylpyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3g): yellow solid, mp 285-287 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 0.74-0.78 (m, 2H), 0.91-0.95 (m, 2H), 1.94-1.98 (m, 1H), 5.59 (s, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.78-7.83 (m, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 12.07 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 8.8, 10.1, 85.5, 114.5, 116.1, 125.0, 128.6, 135.4, 137.8, 139.4, 158.1, 158.9. HRMS calcd for C₁₃H₁₂N₃O: 226.0980 [M+H]⁺, found: 226.0986.

2-phenylpyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3h): red solid, mp 301-303 °C (Lit. ^[2]>300 °C); ¹H NMR (400MHz, DMSO-*d*₆) δ: 6.37 (s, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.44-7.51 (m, 3H), 7.87-7.92 (m, 1H), 7.95-7.97 (m, 2H), 8.13-8.15 (m, 2H), 12.34 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 86.3, 114.8, 116.8, 125.8, 126.3, 128.7, 129.2, 129.3, 132.8, 135.6, 137.8, 140.2, 152.9, 158.9.

2-(thiophen-2-yl)pyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3i)^[1]: red solid, mp 281-283 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 6.29 (s, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 5.2 Hz, 1H), 7.62 (d, *J* = 3.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 12.31 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 86.2, 114.8, 116.7, 125.7, 126.5, 126.9, 128.3, 128.6, 135.6, 135.8, 137.6, 140.2, 148.7, 158.9.

5-oxo-4,5-dihydropyrazolo[1,5-*a*]quinazoline-3-carbonitrile (3j): white solid, mp 301-303 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 7.56 (t, *J* = 8.0 Hz, 1H), 7.92 (t, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.30 (s, 1H), 13.29 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 73.3, 113.5, 117.3, 123.8, 128.0, 128.2, 131.1, 135.9, 146.3, 146.4, 155.6. HRMS calcd for C₁₁H₇N₄O: 211.0620 [M+H]⁺, found: 211.0628.

7-chloro-2-methylpyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3k)^[3]: white solid, mp 281-283 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 2.25 (s, 3H), 5.73 (s, 1H), 7.83 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.4Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 12.21 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 14.4,

89.2, 116.9, 117.7, 127.7, 129.3, 135.3, 136.6, 139.4, 152.1, 157.9.

7-chloro-2-phenylpyrazolo[1,5-a]quinazolin-5(4H)-one (3l): yellow solid, mp 289-291 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 6.38 (s, 1H), 7.38-7.47 (m, 3H), 7.90-7.95 (m, 3H), 8.03 (d, *J* = 2.4 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 12.47 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 86.6, 117.2, 118.4, 126.3, 127.7, 129.2, 129.3, 129.9, 132.6, 135.4, 136.6, 140.2, 153.2, 157.9. HRMS calcd for C₁₆H₁₁ClN₃O: 296.0591 [M+H]⁺, found: 296.0599.

7-methoxy-2-methylpyrazolo[1,5-a]quinazolin-5(4H)-one (3m): pale yellow solid, mp 295-297 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 2.25 (s, 3H), 3.84 (s, 3H), 5.70 (s, 1H), 7.43 (dd, *J*₁ = 9.6 Hz, *J*₂ = 2.4 Hz, 1H), 7.51 (d, *J* = 2.8 Hz, 1H), 7.92 (d, *J* = 9.6 Hz, 1H), 12.10 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 14.4, 56.1, 88.6, 110.1, 116.3, 117.1, 123.6, 132.3, 138.6, 150.8, 156.7, 158.7. HRMS calcd for C₁₂H₁₂N₃O₂: 230.0930 [M+H]⁺, found: 230.0922.

2-cyclopropyl-7-methoxypyrazolo[1,5-a]quinazolin-5(4H)-one (3n): red solid, mp 294-296 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 0.71-0.75 (m, 2H), 0.88-0.93 (m, 2H), 1.92-1.96 (m, 1H), 3.82 (s, 3H), 5.56 (s, 1H), 7.39 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.8 Hz, 1H), 7.48 (d, *J* = 2.8 Hz, 1H), 7.87 (d, *J* = 9.6 Hz, 1H), 12.11 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 8.8, 10.0, 56.0, 85.1, 110.0, 116.3, 117.0, 123.6, 132.2, 138.5, 156.6, 157.3, 158.8. HRMS calcd for C₁₄H₁₄N₃O₂: 256.1086 [M+H]⁺, found: 256.1082.

7-methoxy-2-phenylpyrazolo[1,5-a]quinazolin-5(4H)-one (3o): red solid, mp 287-289 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 3.85 (s, 3H), 6.33 (s, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.42-7.48 (m, 3H), 7.54 (d, *J* = 3.2 Hz, 1H), 7.91-7.93 (m, 2H), 8.06 (d, *J* = 8.8 Hz, 1H), 12.34 (s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 56.1, 86.0, 110.1, 116.6, 117.7, 123.6, 126.1, 129.0, 129.2, 132.1, 132.9, 139.3, 152.2, 157.1, 158.7. HRMS calcd for C₁₇H₁₄N₃O₂: 292.1086 [M+H]⁺, found: 292.1094.

2-methyl-7-nitropyrazolo[1,5-a]quinazolin-5(4H)-one (3p): yellow solid, mp 269-271 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 2.23 (s, 3H), 5.72 (s, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 8.46-8.49 (m, 1H), 8.62 (s, 1H), 12.28 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 14.4, 90.0, 116.0, 116.4, 124.4, 129.8, 140.2, 141.1, 143.8, 154.0, 157.6. HRMS calcd for C₁₁H₉N₄O₃: 245.0675 [M+H]⁺, found: 245.0664.

7-nitro-2-phenylpyrazolo[1,5-a]quinazolin-5(4H)-one (3q): pale yellow solid, mp 292-294 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 6.44 (s, 1H), 7.43-7.50 (m, 3H), 7.95-7.98 (m, 2H), 8.28 (d, *J* = 9.2 Hz, 1H), 8.65 (d, *J* = 9.2 Hz, 1H), 8.78 (s, 1H), 12.63 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 87.4, 116.5, 117.3, 124.5, 126.5, 129.3, 129.7, 130.1, 132.1, 141.2, 144.3, 154.8, 157.8, 162.8. HRMS

calcd for C₁₆H₁₁N₄O₃: 307.0831 [M+H]⁺, found: 307.0838.

2-methyl-8-nitropyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3r): yellow solid, mp 290-292 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 2.26 (s, 3H), 5.75 (s, 1H), 8.10 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.4 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 8.47 (d, *J* = 2.0 Hz, 1H), 12.33 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 14.4, 89.8, 109.7, 119.0, 120.8, 131.0, 138.2, 140.1, 151.6, 153.0, 157.9. HRMS calcd for C₁₁H₉N₄O₃: 245.0675 [M+H]⁺, found: 245.0684.

8-nitro-2-(thiophen-2-yl)pyrazolo[1,5-*a*]quinazolin-5(4*H*)-one (3s): yellow solid, mp 279-281 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 6.39 (s, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 7.64 (d, *J* = 5.2 Hz, 1H), 7.71 (d, *J* = 3.6 Hz, 1H), 8.22 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.0 Hz, 1H), 8.36 (d, *J* = 8.8 Hz, 1H), 8.63 (d, *J* = 2.0 Hz, 1H), 12.64 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 87.0, 109.9, 119.5, 121.3, 127.3, 127.6, 128.5, 131.0, 135.3, 138.0, 140.9, 149.7, 151.6, 157.9. HRMS calcd for C₁₄H₉N₄O₃S: 313.0395 [M+H]⁺, found: 313.0384.

8-nitro-5-oxo-4,5-dihydropyrazolo[1,5-*a*]quinazoline-3-carbonitrile (3t): white solid, mp 296-298 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 8.30 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.44 (s, 1H), 8.66 (s, 1H), 13.63 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 76.0, 110.6, 112.7, 121.0, 122.0, 131.0, 137.6, 145.6, 151.6, 158.3. HRMS calcd for C₁₁H₆N₅O₃: 256.0471 [M+H]⁺, found: 256.0479.

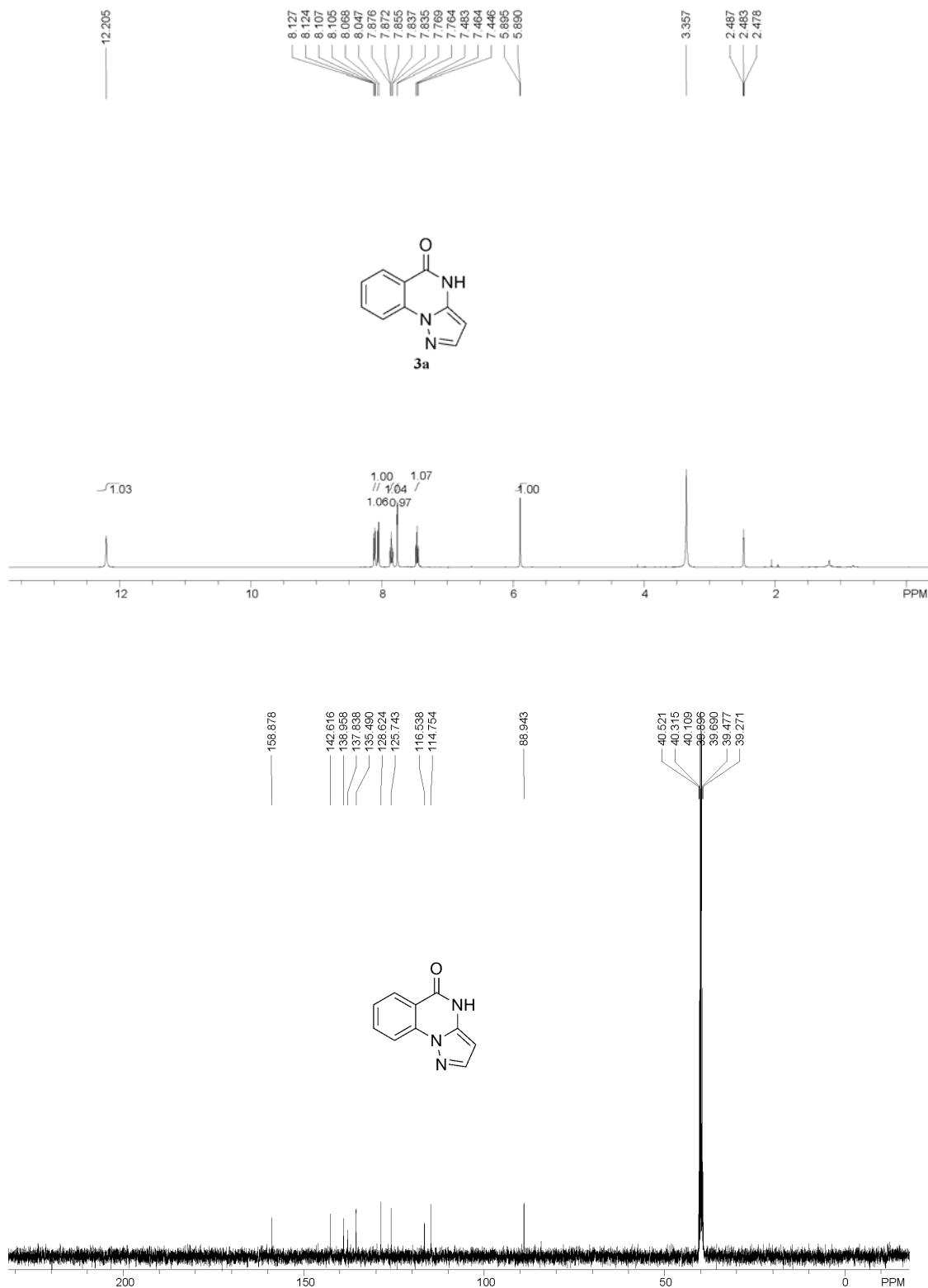
[1,2,4]triazolo[1,5-*a*]quinazolin-5(4*H*)-one (6): white solid, mp 231-233 °C; ¹H NMR (400MHz, DMSO-*d*₆) δ: 7.57 (t, *J* = 7.6 Hz, 1H), 7.94 (t, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 8.17 (s, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 13.05 (br s, 1H); ¹³C NMR (100MHz, DMSO-*d*₆) δ: 115.1, 117.4, 126.7, 128.8, 135.9, 136.2, 148.6, 152.2, 160.3. HRMS calcd for C₉H₇N₄O: 187.0620 [M+H]⁺, found: 187.0624.

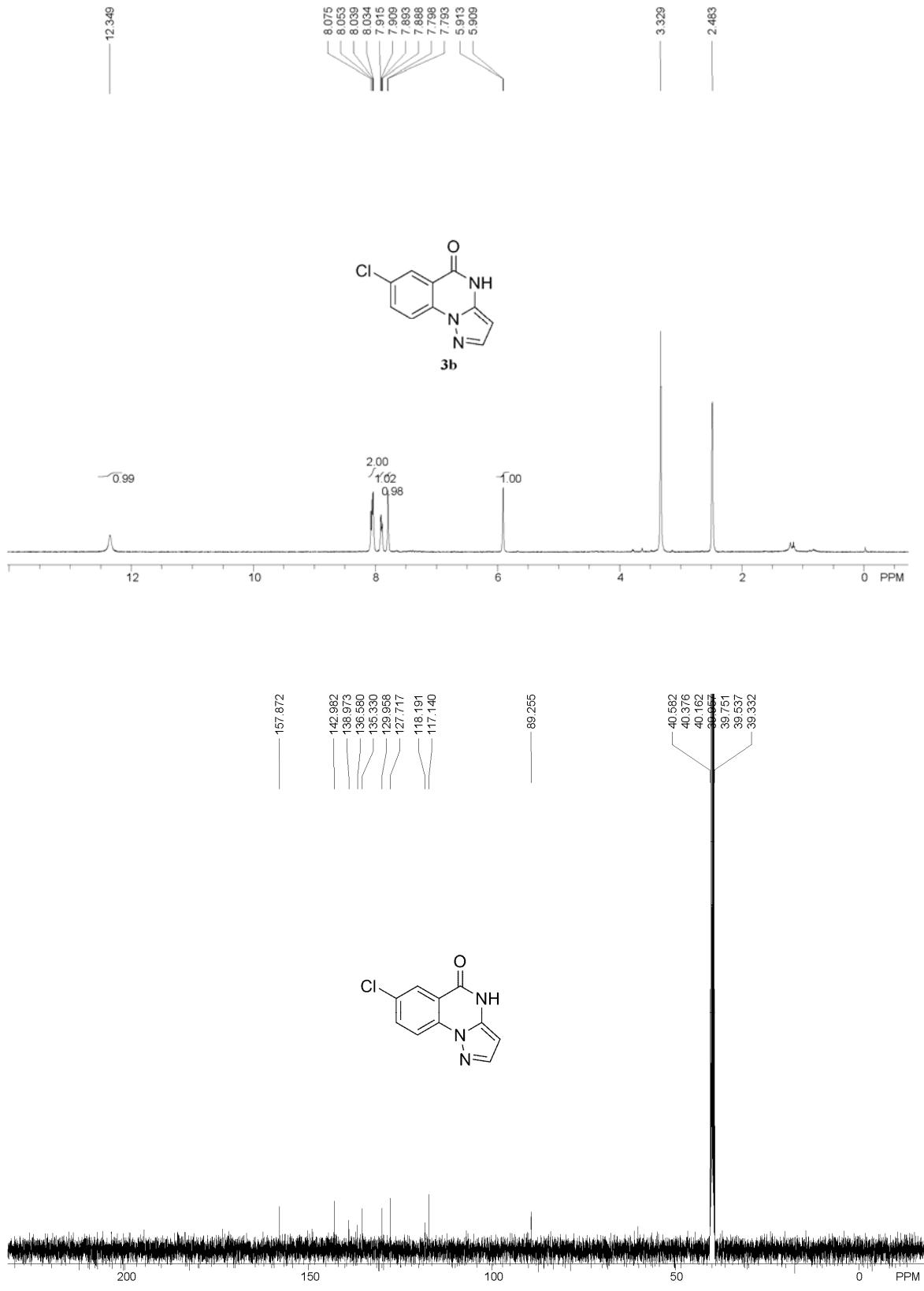
(II) Procedure for the preparation of 2-bromo-N-(1*H*-pyrazol-5-yl)benzamide (C)

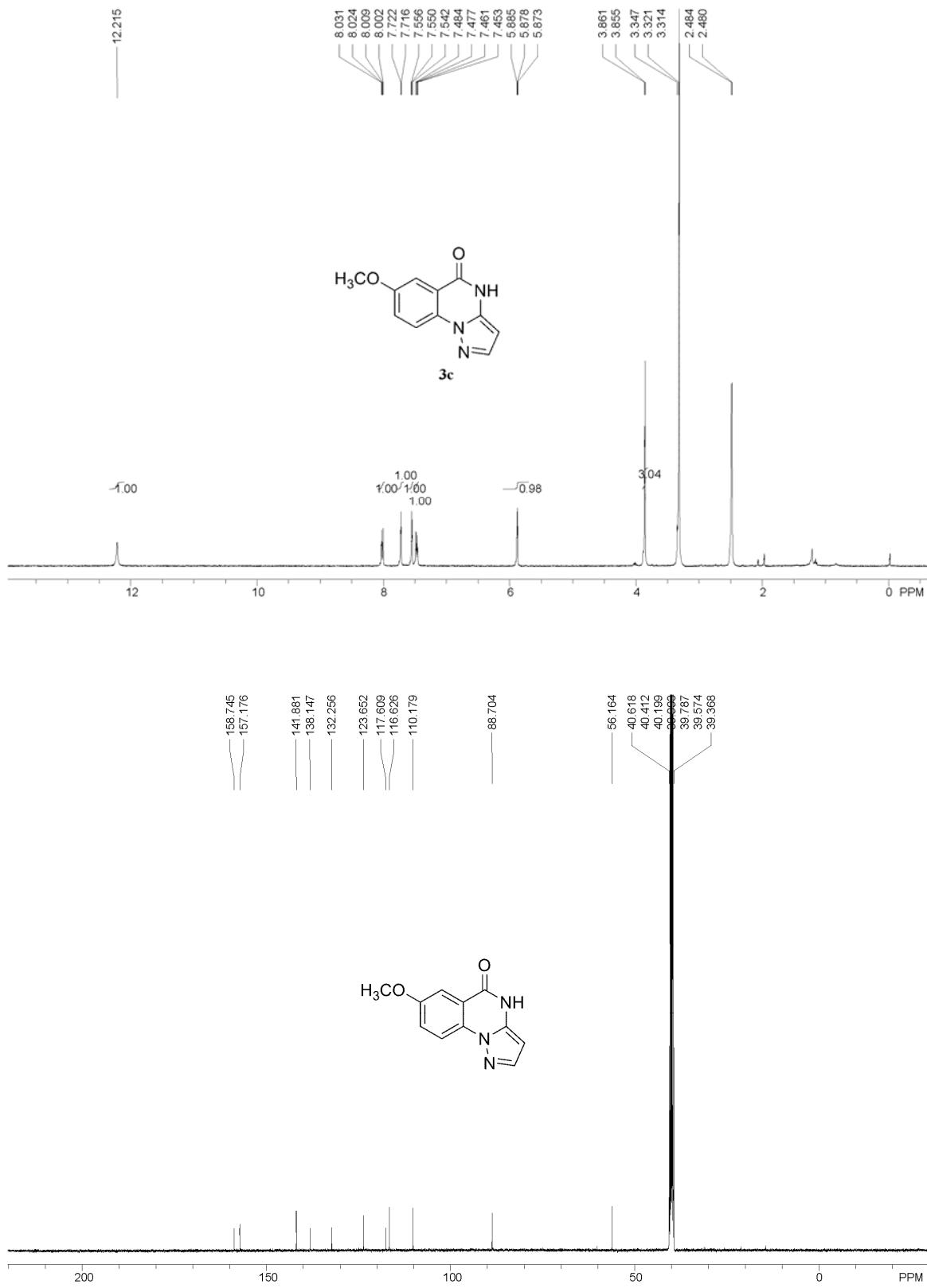
To a solution of Cs₂CO₃ (2 mmol) in H₂O (5 mL) were added methyl 2-bromobenzoate (**1a**, 1 mmol), and 1*H*-pyrazol-5-amine (**2a**, 1.2 mmol). The mixture was stirred at 100 °C for 4 h. The mixture was then cooled to room temperature and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na₂SO₄, and concentrated under vacuum. The crude product was purified by column chromatography eluting with petroleum ether/ethyl acetate (1:2) to give **C**.

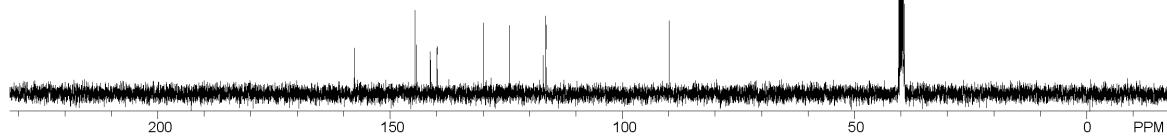
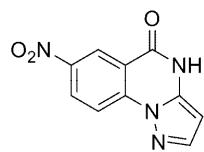
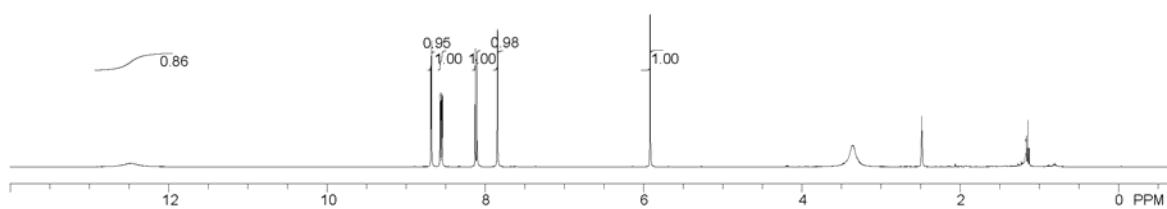
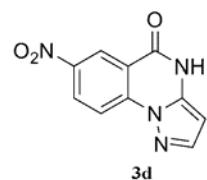
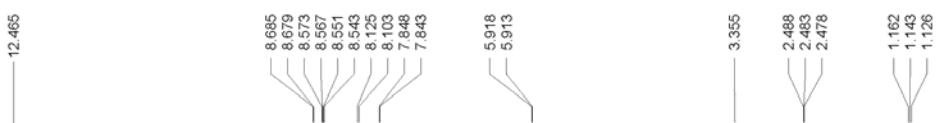
2-bromo-N-(1*H*-pyrazol-5-yl)benzamide (C): ^1H NMR (400MHz, CDCl_3) δ : 6.85 (d, $J_1 = 2.4$ Hz, 1H), 7.18 (td, $J_1 = 8.0$ Hz, $J_2 = 1.6$ Hz, 1H), 7.34 (td, $J_1 = 8.0$ Hz, $J_2 = 1.2$ Hz, 1H), 7.43 (d, $J = 2.8$ Hz, 1H), 7.53 (dd, $J_1 = 7.6$ Hz, $J_2 = 1.6$ Hz, 1H), 7.57-7.59 (m, 1H), 9.82 (br s, 1H); ^{13}C NMR (100MHz, CDCl_3) δ : 97.2, 119.9, 127.4, 129.4, 130.0, 131.5, 133.4, 137.9, 146.7, 165.2. HRMS calcd for $\text{C}_{10}\text{H}_9\text{BrN}_3\text{O}$: 265.9924 [$\text{M}+\text{H}]^+$, found: 265.9926.

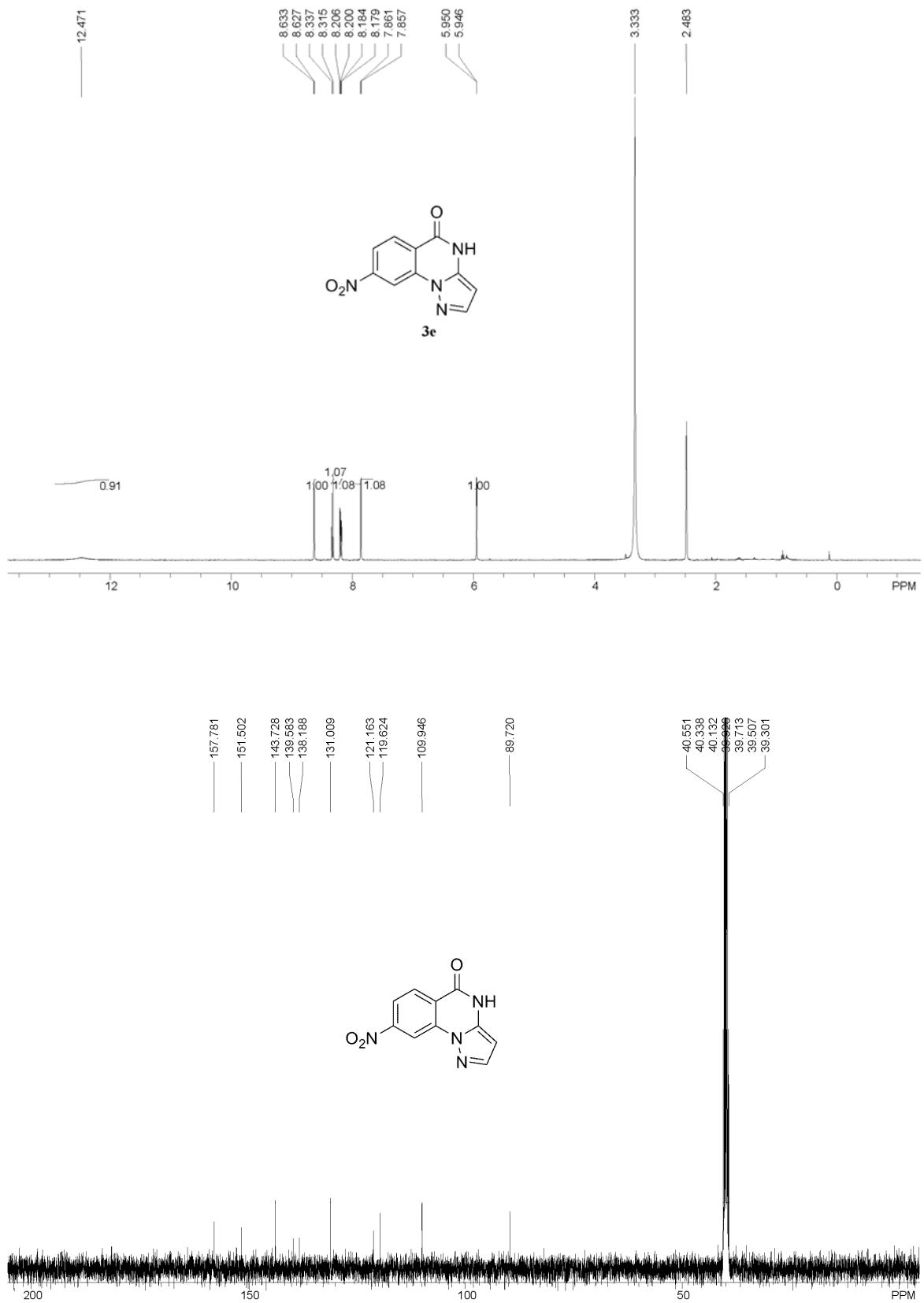
III. Copies of ^1H and ^{13}C NMR spectra of 3a-3t, 6, and C

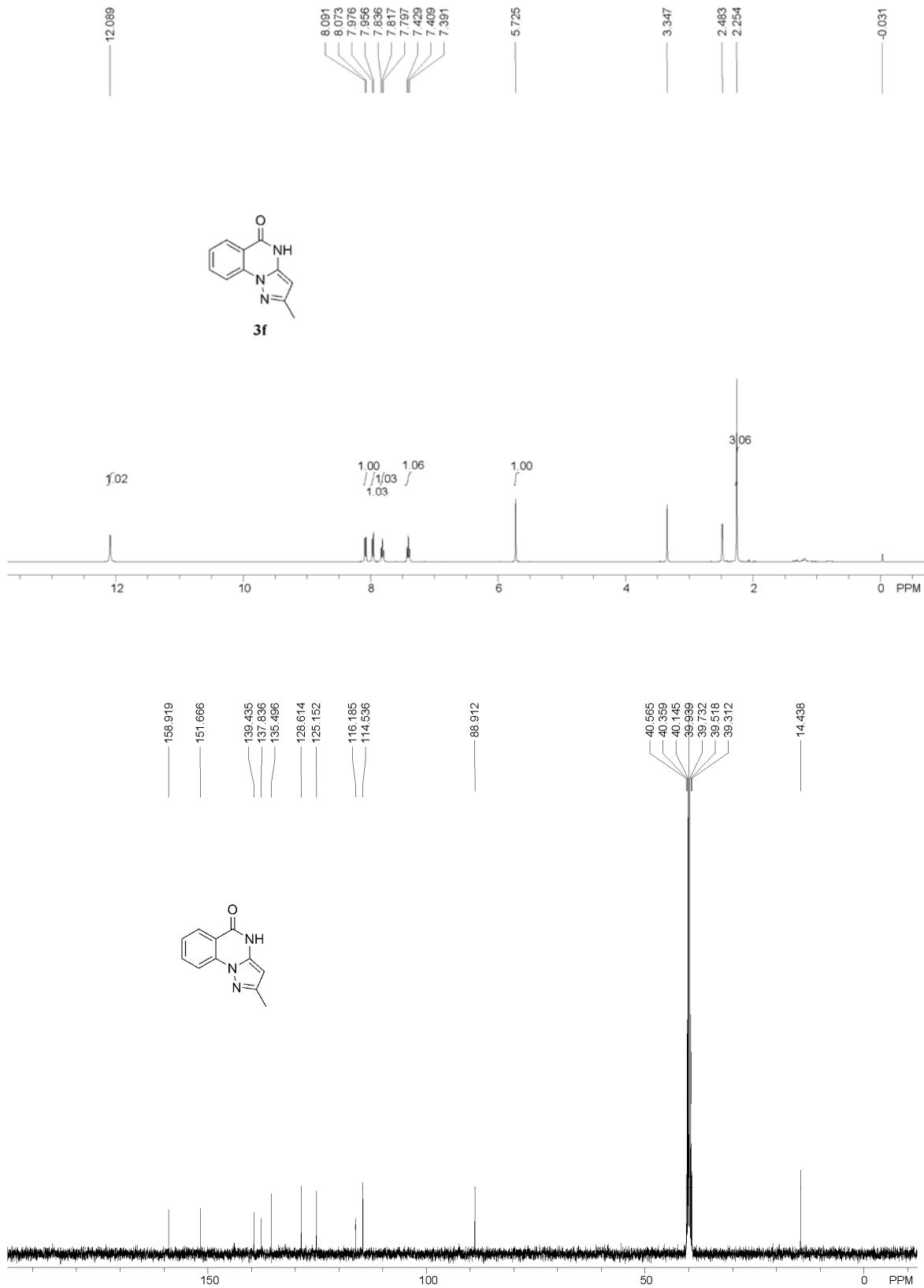


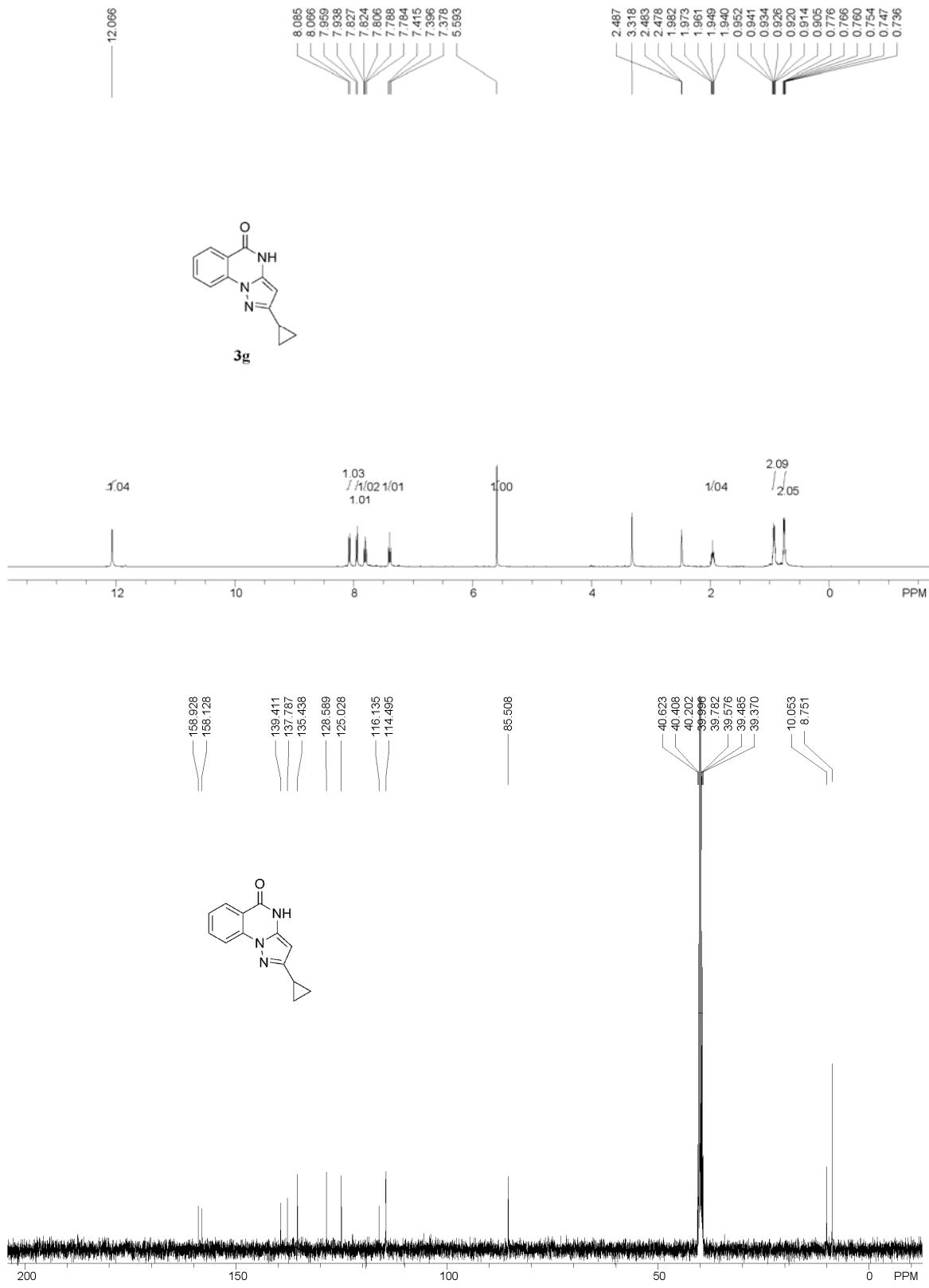


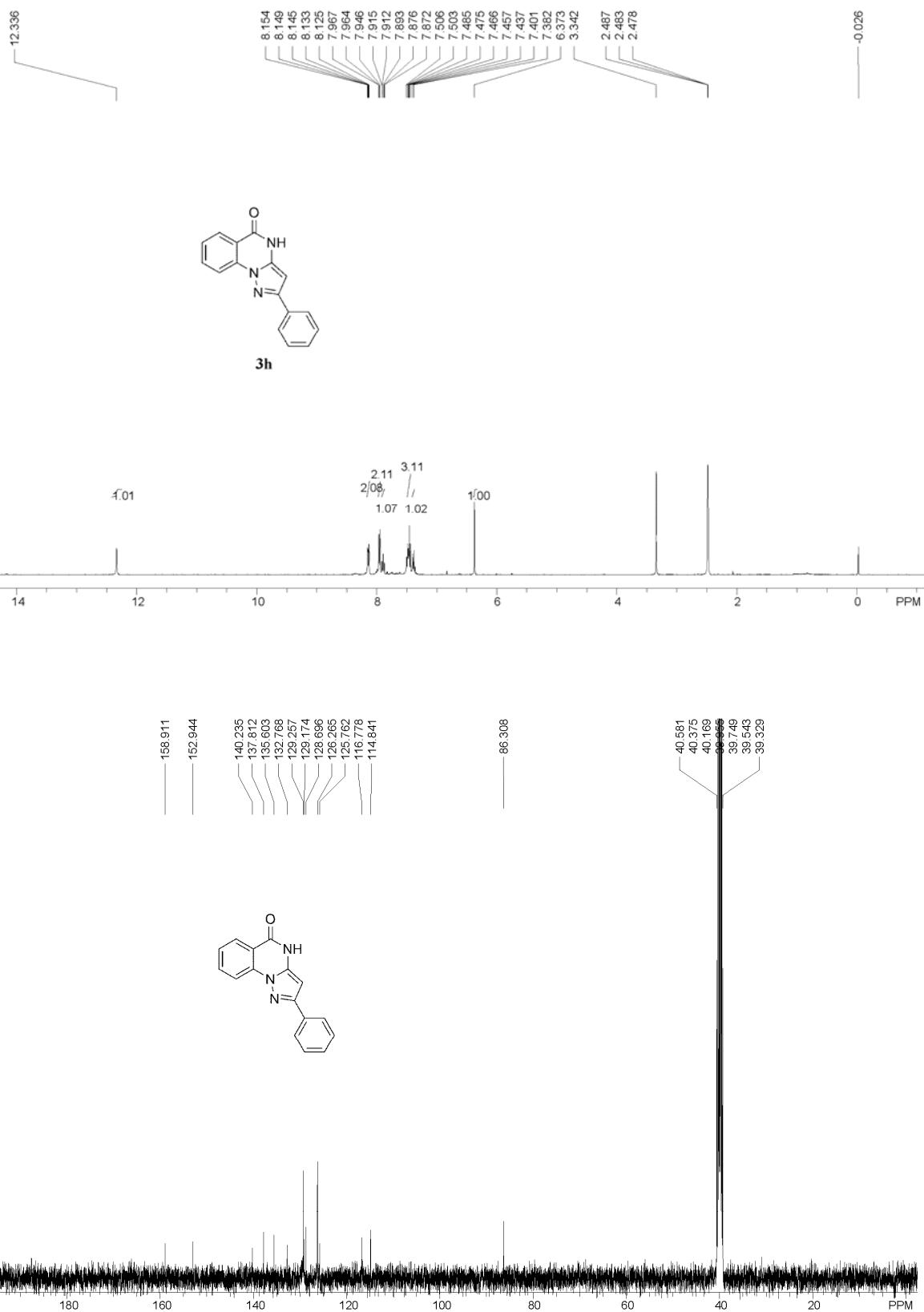


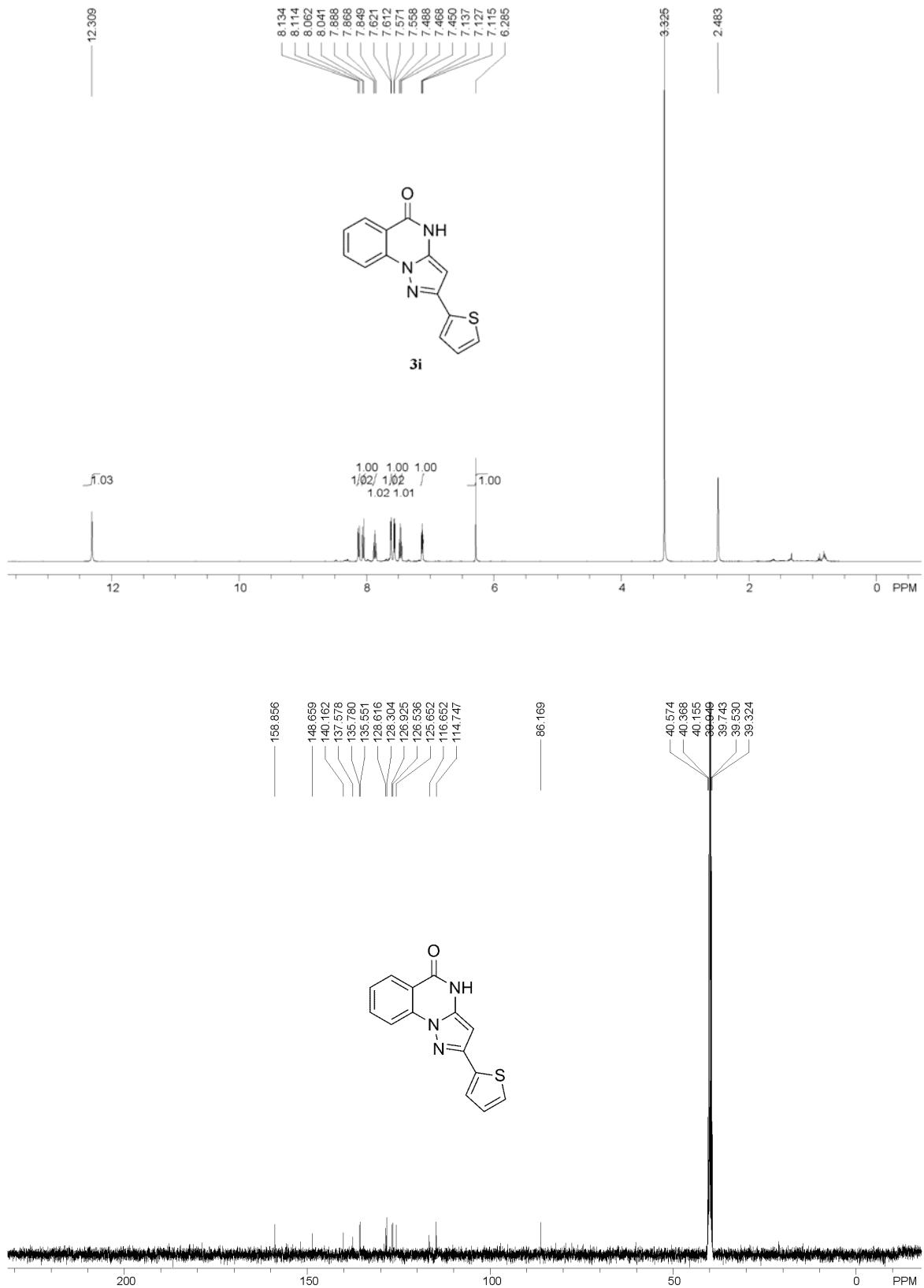


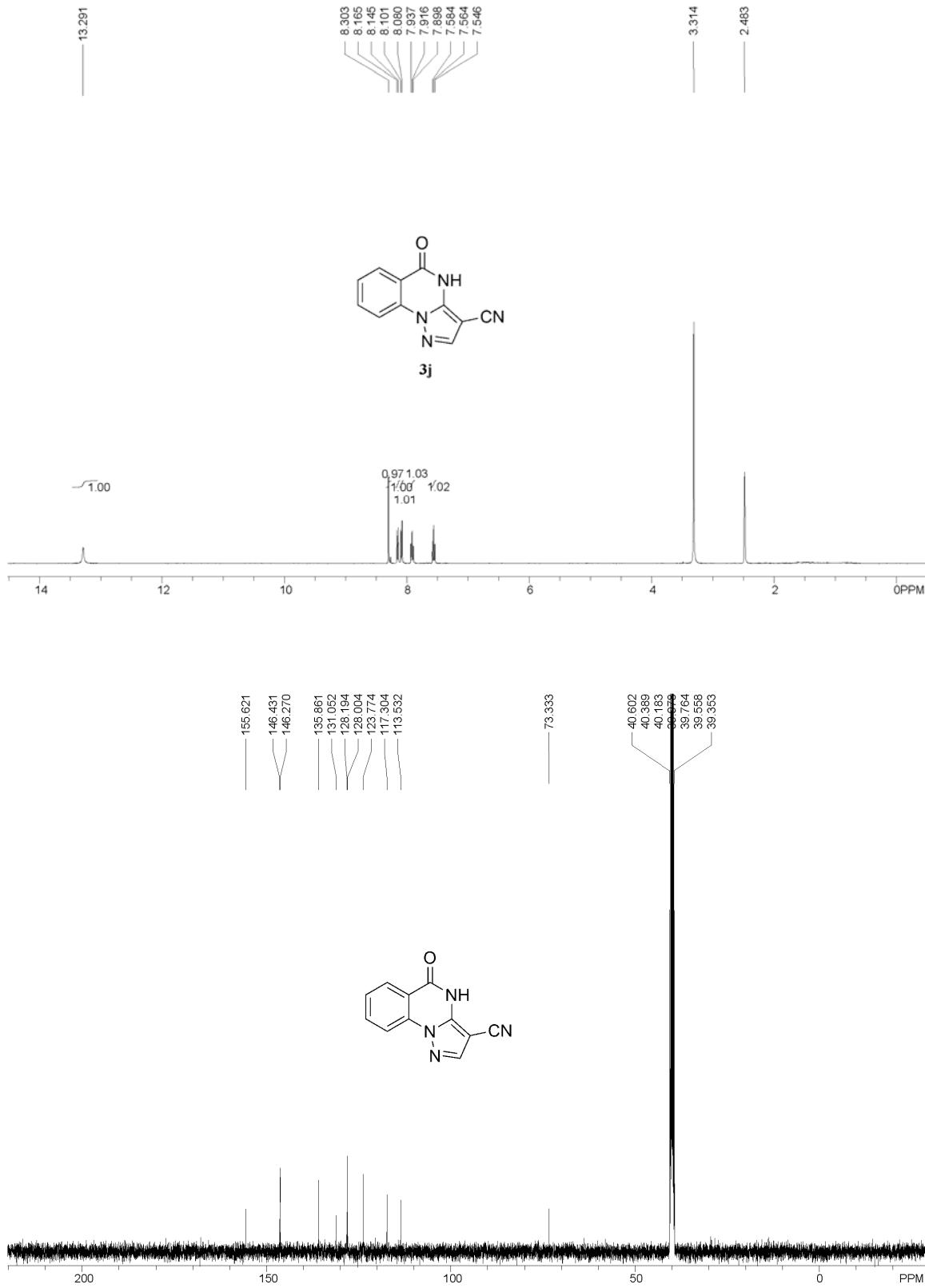


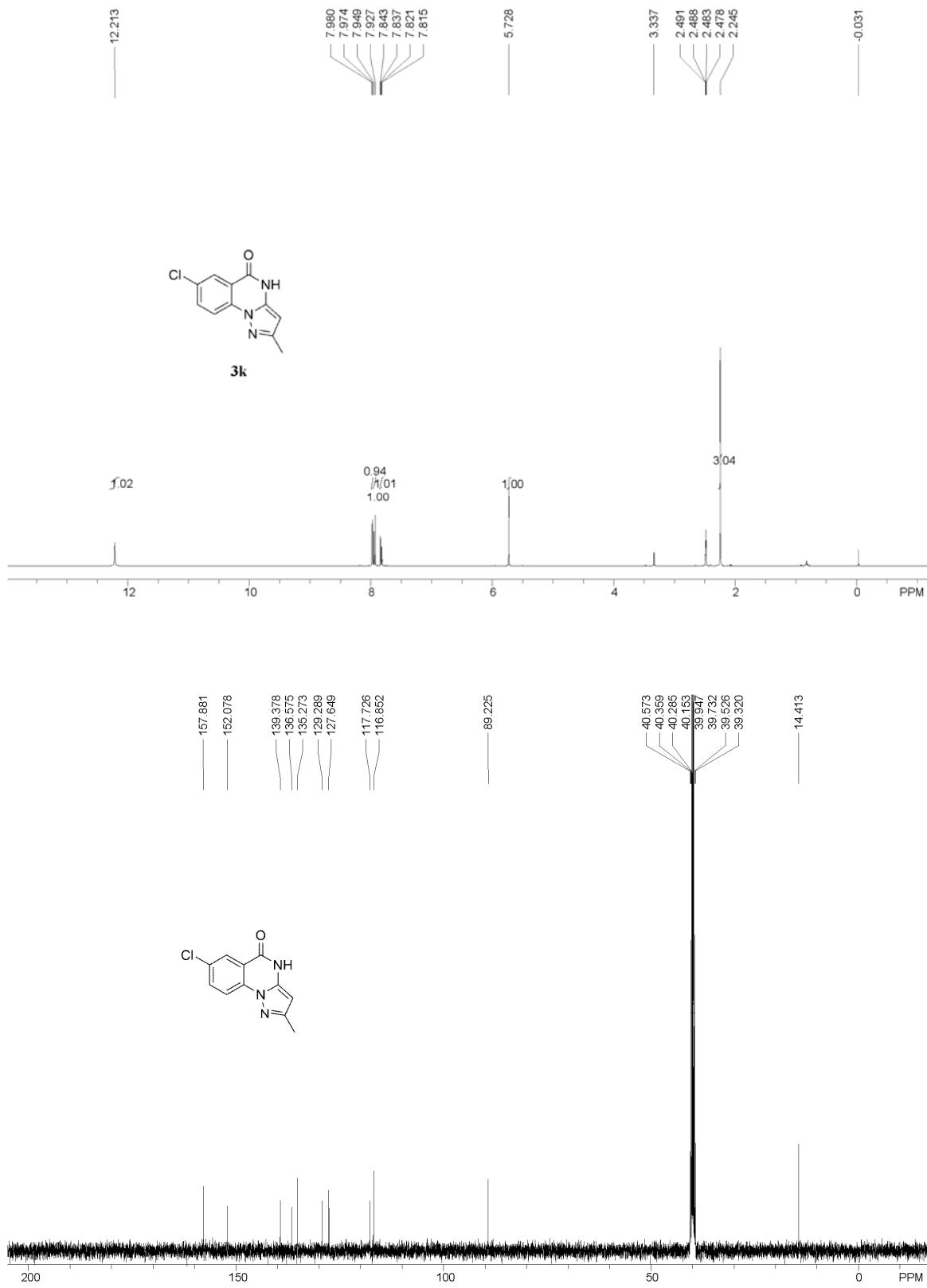


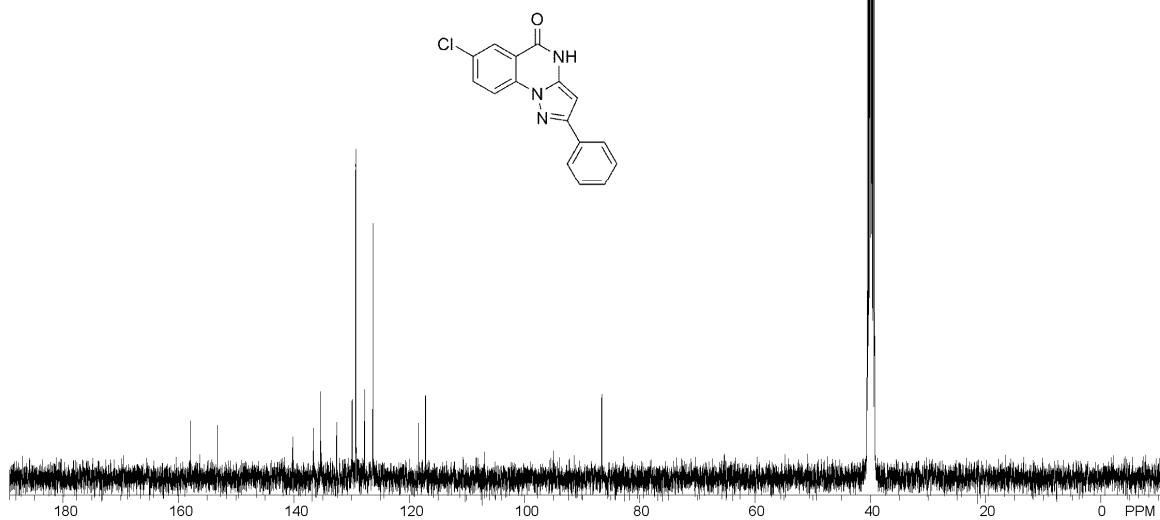
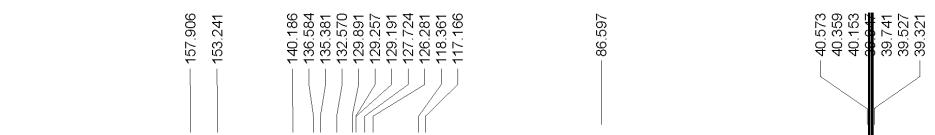
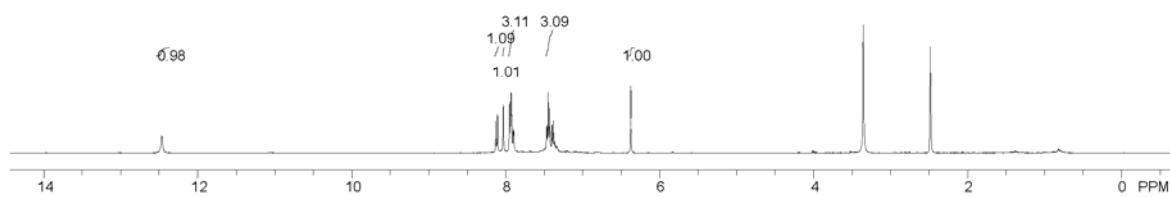
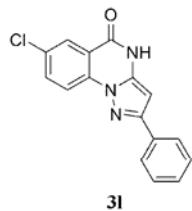
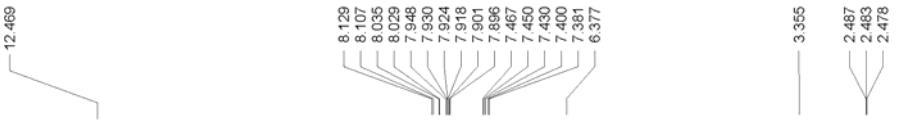


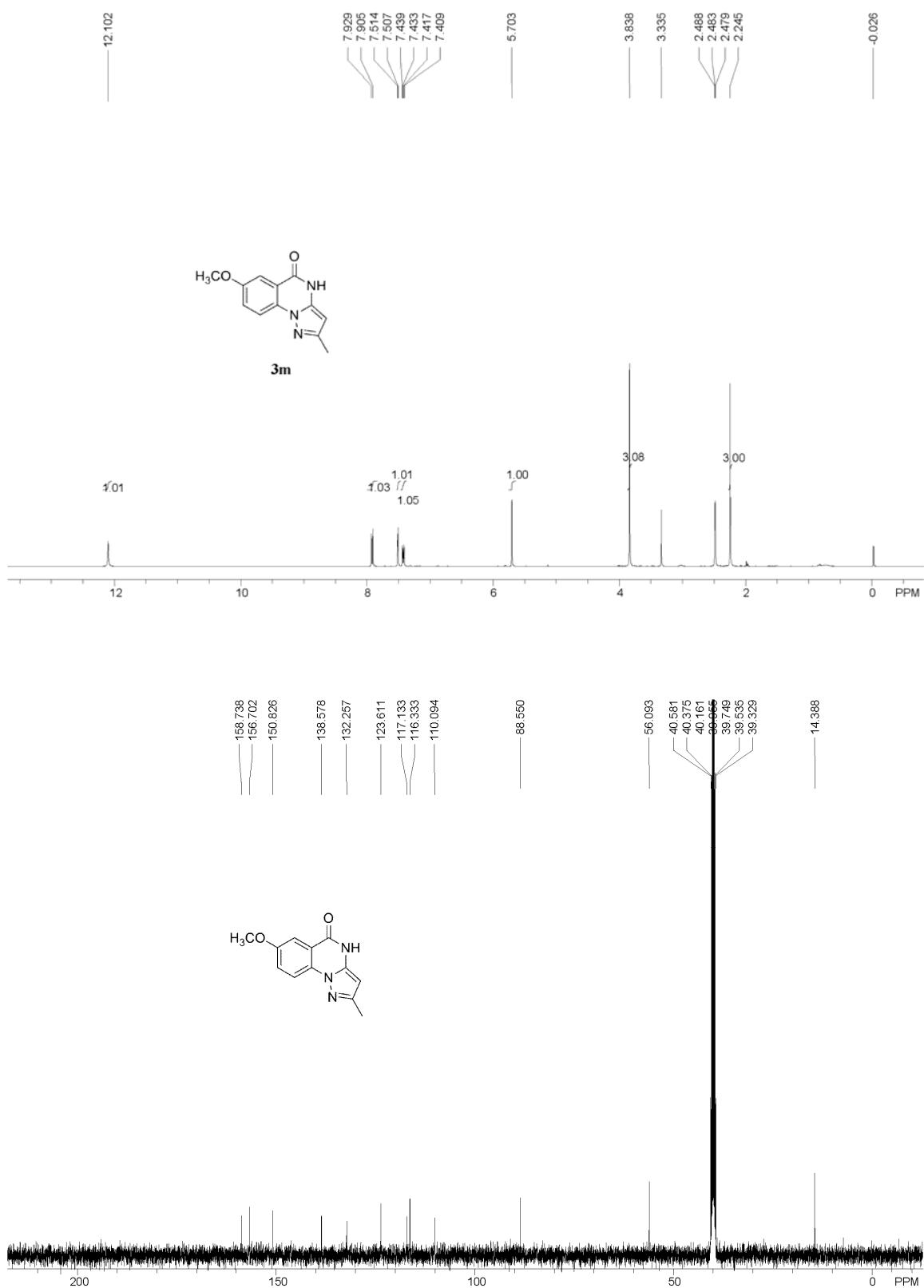


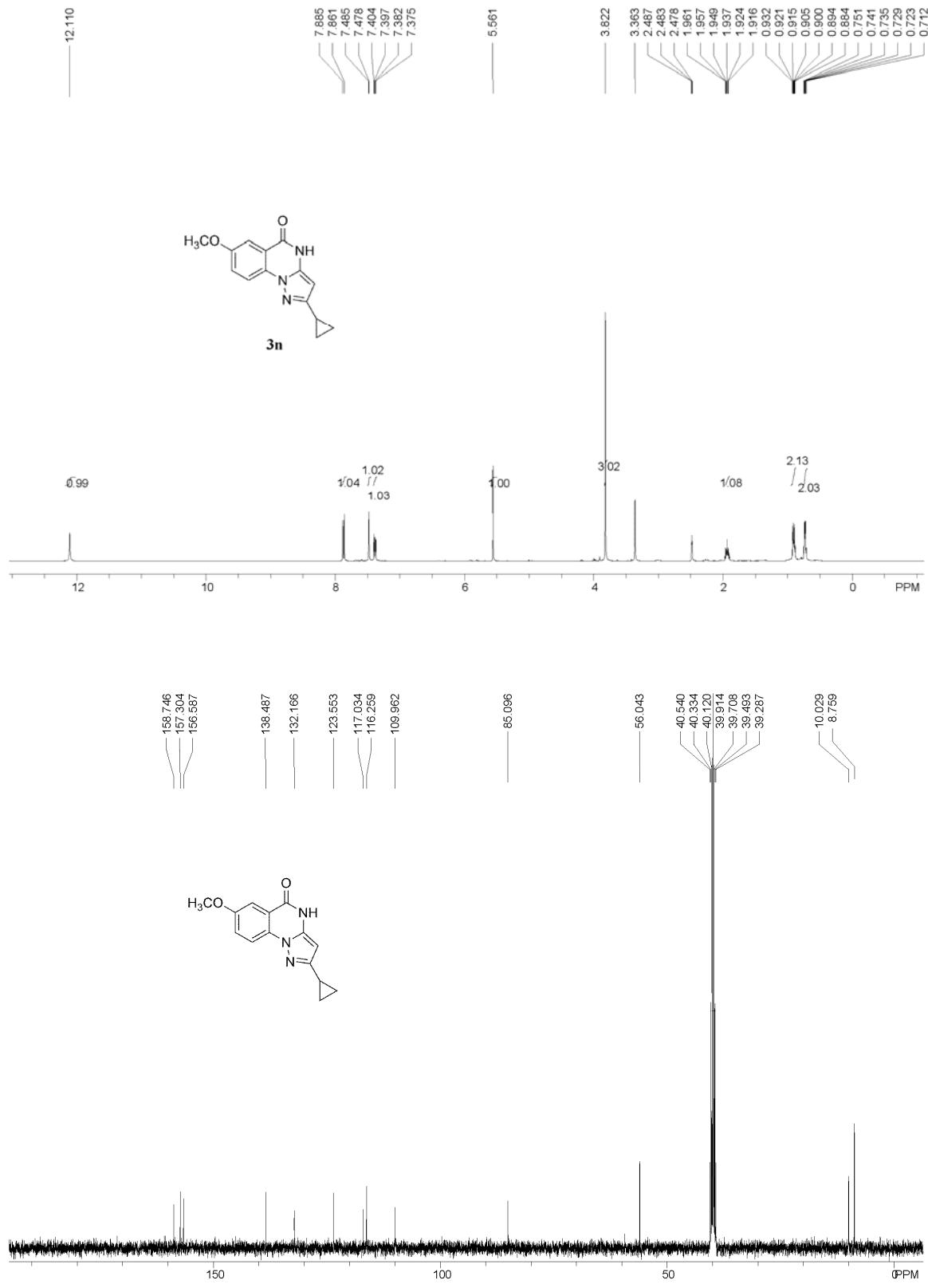


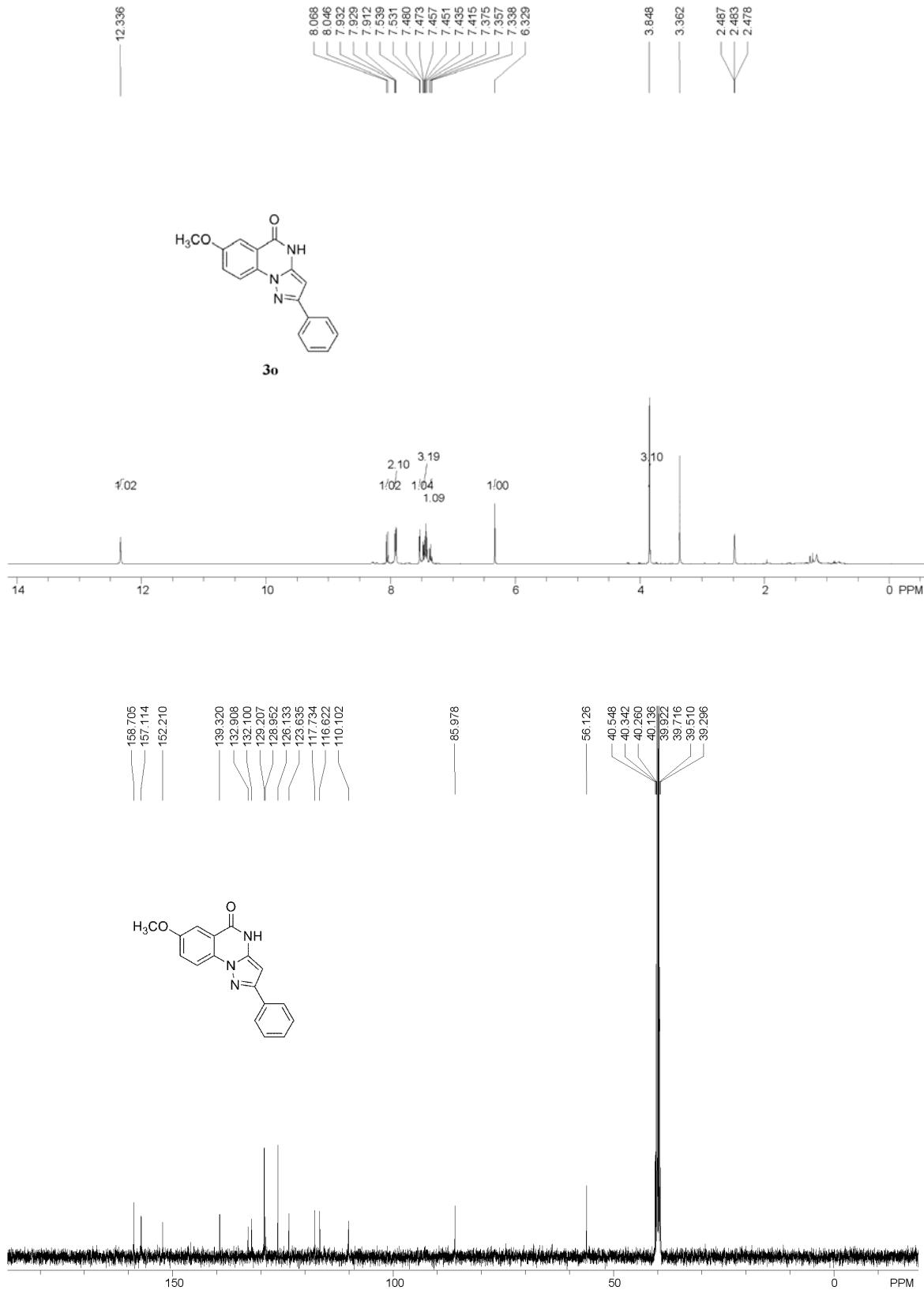


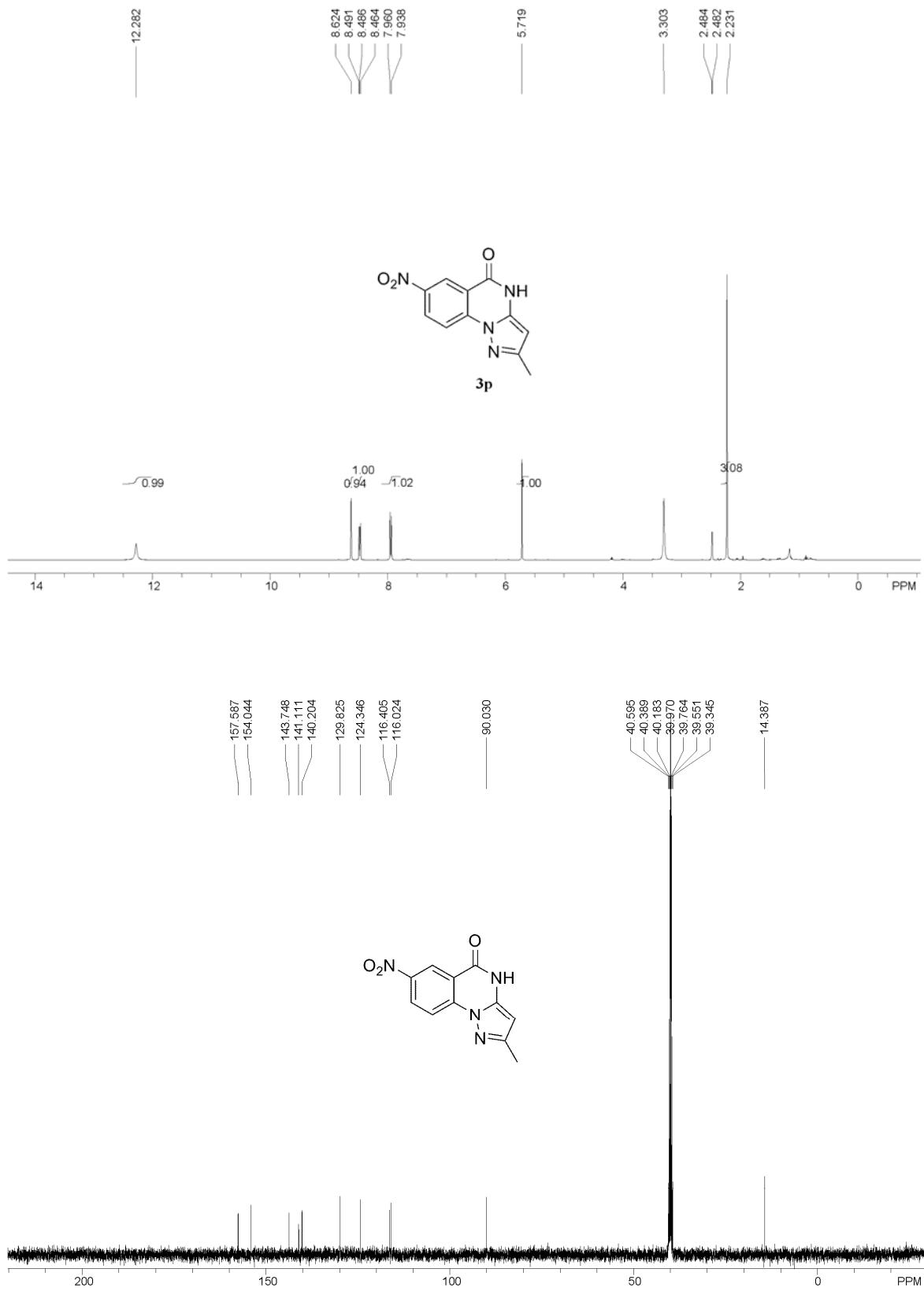


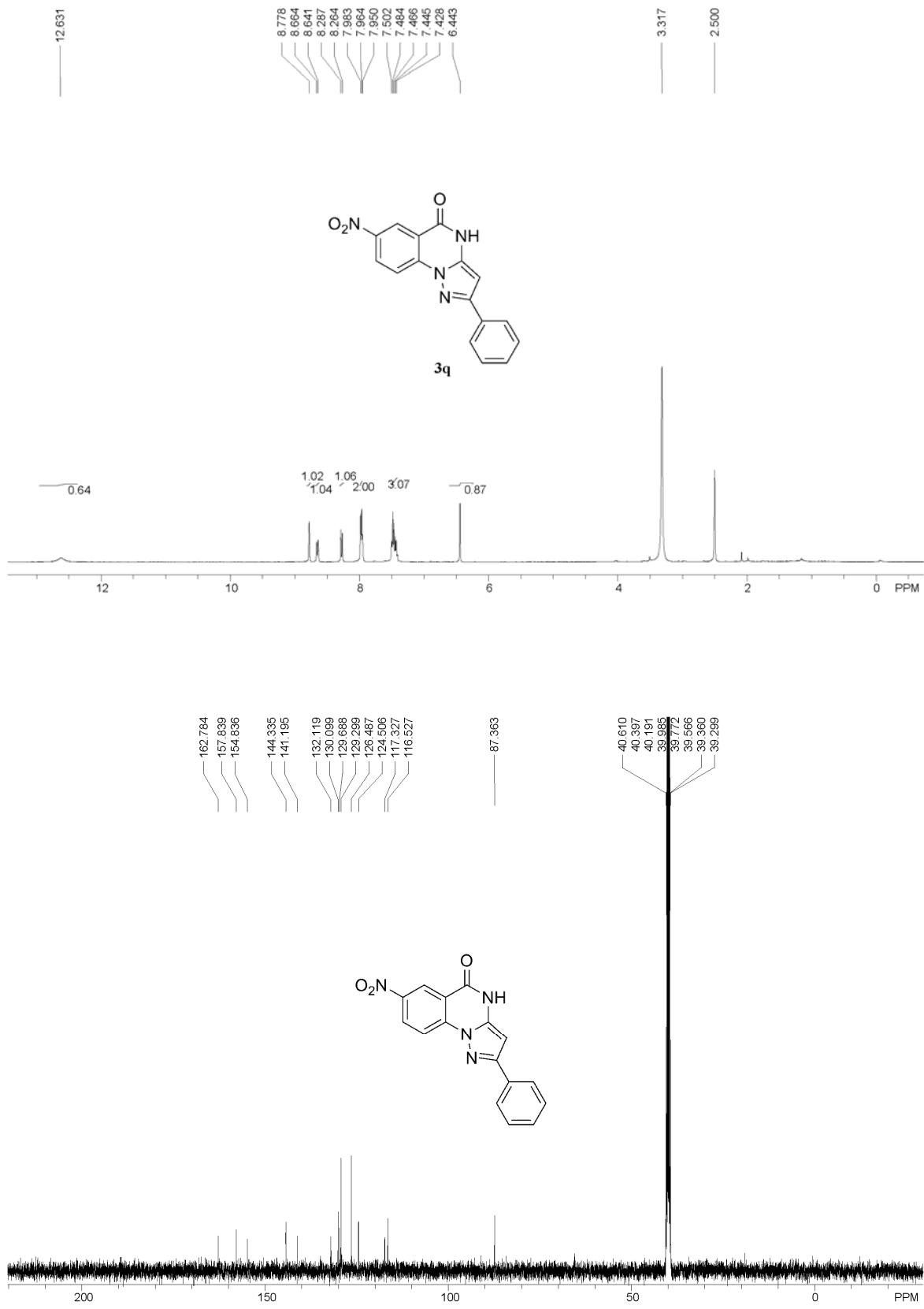


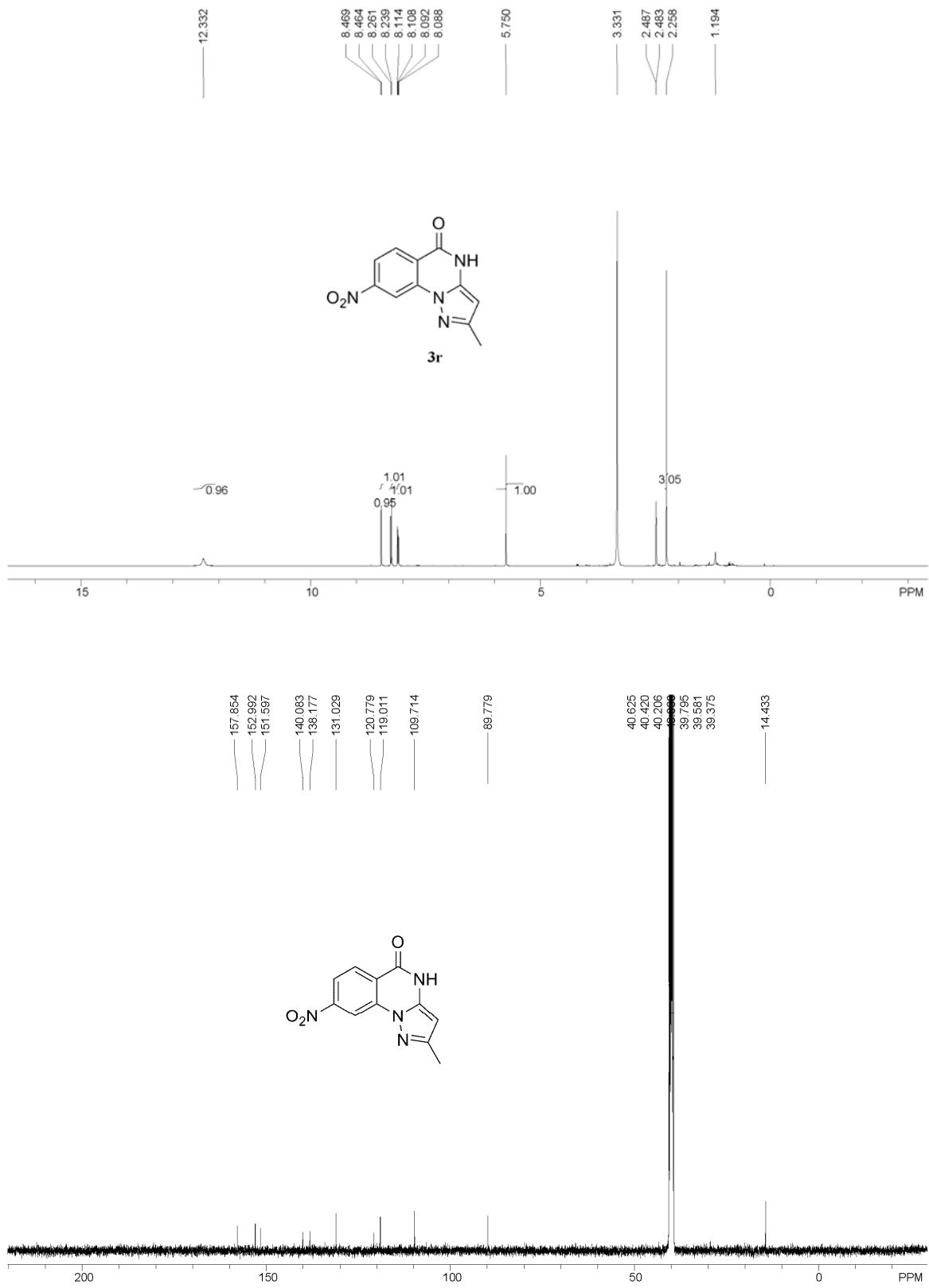


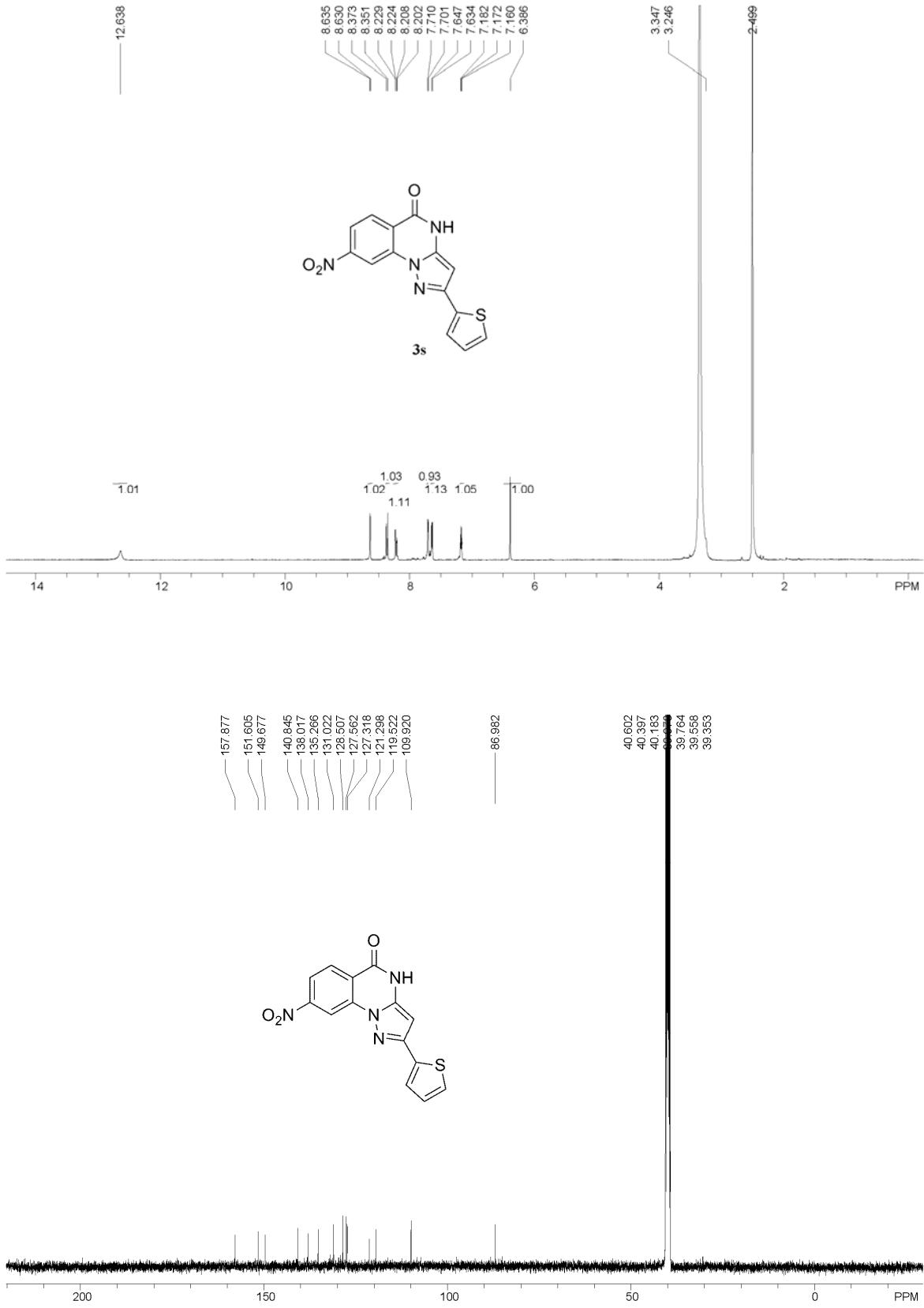


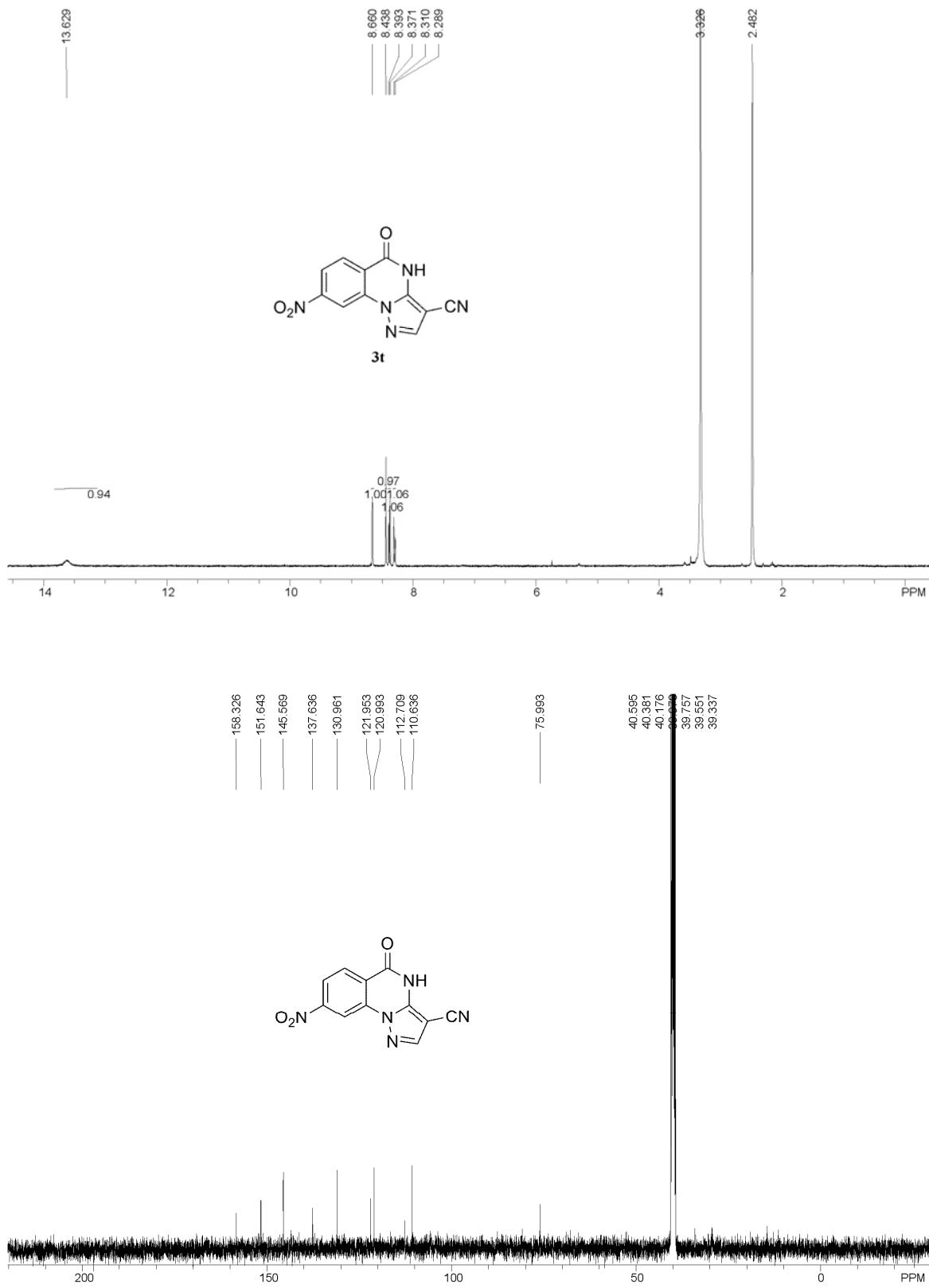


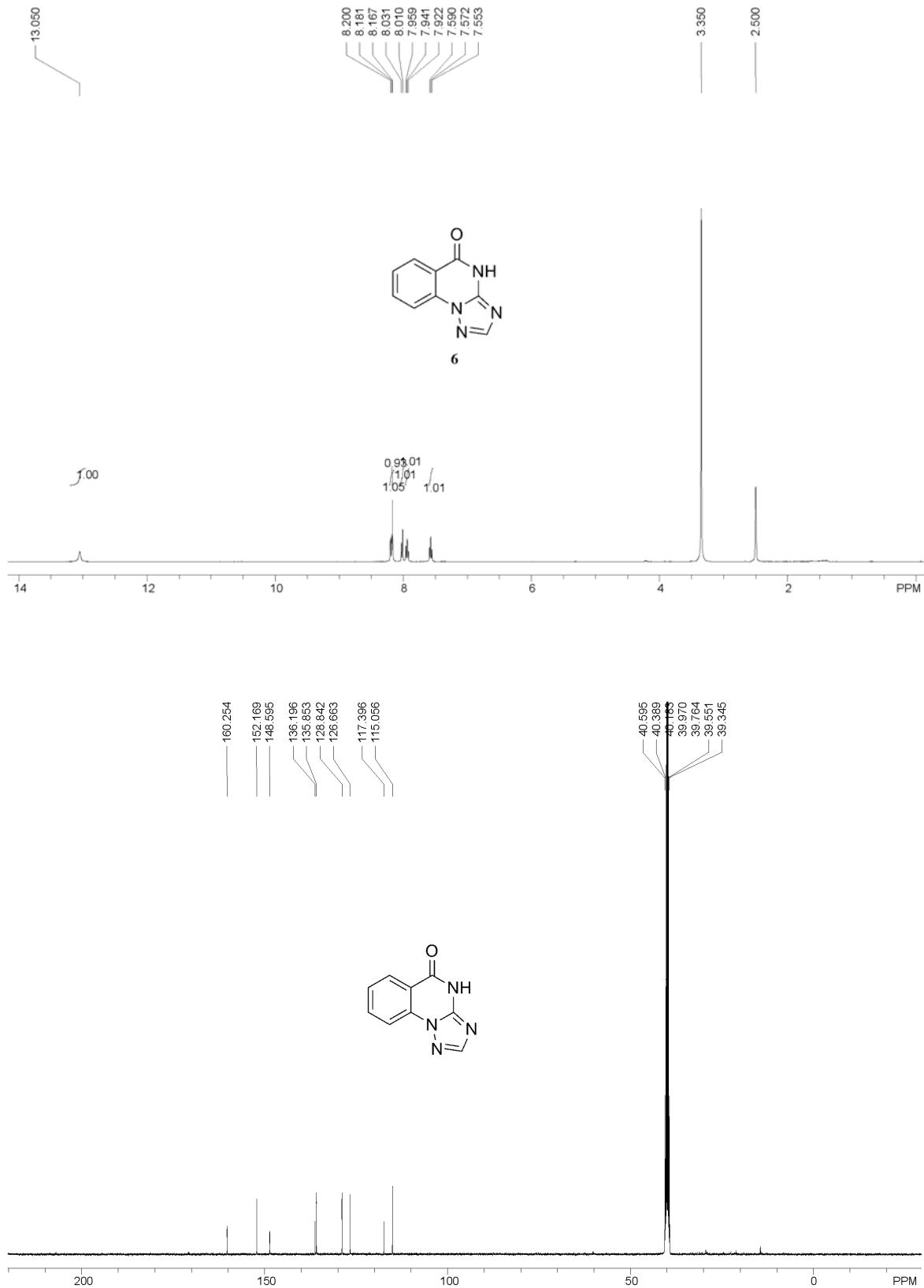


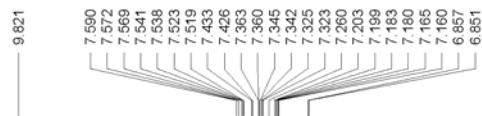




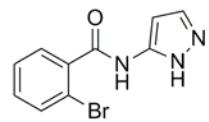
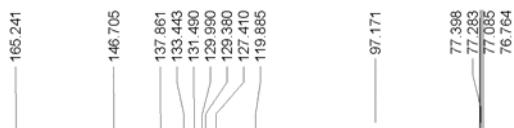
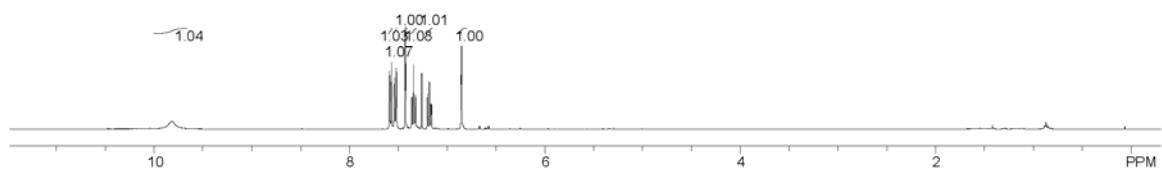




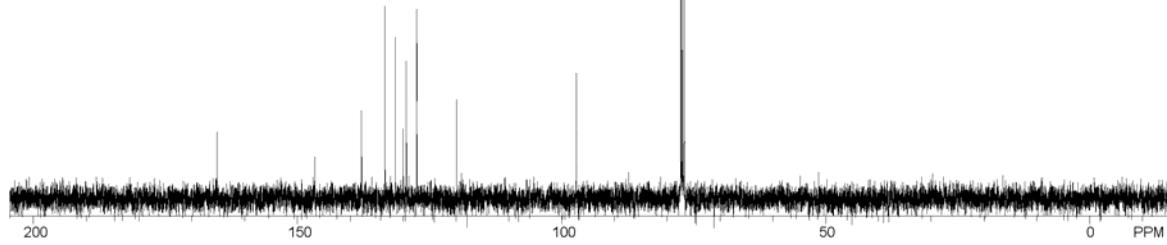




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IV. References

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