Supporting Information

Direct Dehydrative Cross-Coupling of Tautomerizable Heterocycles with Alkynes via Pd/Cu-Catalyzed Phosphonium Coupling

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I - General Methods

^{1}H NMR spectra were recorded at 400 MHz on a Bruker spectrometer, and were reported in ppm from tetramethylsilane on the scale. Data are reported as follows: chemical shift, multiplicity, coupling constants (Hz), and relative integration. ^{13}C NMR spectra were recorded at 100 MHz on a Bruker spectrometer, and were reported in ppm from TMS using the central deuterated solvent peak as a reference. LCMS was performed on an Agilent 1100 LC/MSD with an Agilent 1100 SL mass spectrometer. Reagents and solvents were purchased from Aldrich.

II - General Procedure for Direct Dehydrative Cross-Coupling

II-1 - Direct Dehydrative Cross-Coupling Condition A in Table 1

To the stirred reaction mixture of 2-quinoxalinone (0.5 mmol), PyBroP (1.2 eq) and Et_3N (6 eq) in 1,4-dioxane (5 mL) under ambient atmosphere in a capped vial were added *p*-tolylacetylene (2 eq) and the base (Et_3N or $NaOBu^t$) (1.5 eq), and it was stirred at room temperature for 18 h. Then, it was diluted with EtOAc, washed with water and brine, and dried over Na_2SO_4. No coupling product was observed by TLC, LCMS and NMR.

II-2 - Direct Dehydrative Cross-Coupling Condition B in Table 1

To the stirred reaction mixture of 2-quinoxalinone (0.5 mmol), PyBroP (1.2 eq) and Et_3N (6 eq) in 1,4-dioxane (5 mL) under ambient atmosphere in a capped vial were added *p*-tolylacetylene (2 eq), Pd catalyst (1 or 5 mol%) and/or CuI (2 or 10 mol%), and it was stirred at room temperature for 18 h. Then, it was diluted with EtOAc, washed with water and brine, and dried over Na_2SO_4. Flash chromatography using a mixture of EtOAc and hexane gave 2-*p*-tolylethynyl-quinoxaline.

II-3 - Direct Dehydrative Cross-Coupling Condition A in Table 2

To the stirred reaction mixture of 2-quinoxalinone (0.5 mmol), PyBroP (1.2 equiv) and Et_3N (6 eq) in 1,4-dioxane (5 mL) under ambient atmosphere in a capped vial was added the alkyne (2 eq), $PdCl_2(PPh_3)_2$ (5mol%), and CuI (10mol%), and it was stirred at room temperature for 18 h. Then, it was diluted with EtOAc, washed with water and brine, and dried over Na_2SO_4. Flash chromatography using a mixture of EtOAc and hexane gave the coupling product.

II-4 - Direct Dehydrative Cross-Coupling Condition B in Table 2

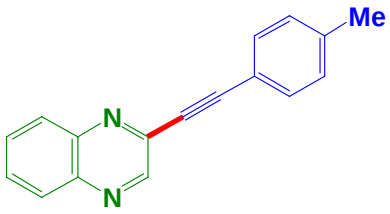
After the reaction mixture of the tautomerizable heterocycle (0.5 mmol), PyBroP (1.2 eq) and Pr^i_2NEt (6 eq) in 1,4-dioxane (5 mL) was stirred at 50°C under ambient atmosphere in a capped vial for 2 h, *p*-tolylacetylene (2 eq), $PdCl_2(PPh_3)_2$ (5mol%), and CuI (10mol%) were added, and it was stirred at 80°C for 18 h. Then, it was diluted with

EtOAc, washed with water and brine, and dried over Na_2SO_4. Flash chromatography using a mixture of EtOAc and hexane gave the coupling product.

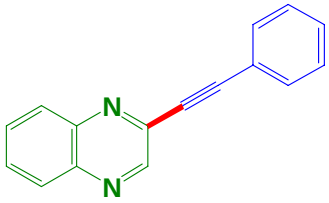
II-5 - Direct Dehydrative Cross-Coupling Condition C in Table 2

To the stirred reaction mixture of 2-quinoxalinone (0.5 mmol), PyBroP (1.2 equiv) and Et_3N (6 eq) in 1,4-dioxane (5 mL) under ambient atmosphere in a capped vial was added the alkyne (2 eq), $PdCl_2(PPh_3)_2$ (5mol%), and it was stirred at 50°C for 18 h. Then, it was diluted with EtOAc, washed with water and brine, and dried over Na_2SO_4. Flash chromatography using a mixture of EtOAc and hexane gave the coupling product.

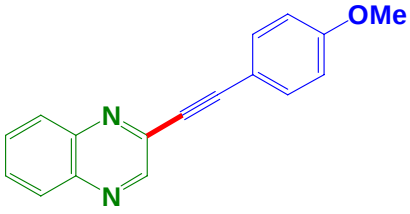
III - Characterization Data



2-*p*-Tolylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 7.18 (d, 2H, *J* = 8.0 Hz), 7.57 (d, 2H, *J* = 8.0 Hz), 7.75 (m, 2H), 8.08 (m, 2H), 8.95 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.7, 86.6, 94.2, 118.3, 129.5, 129.2, 129.3, 130.2, 130.6, 132.3, 139.8, 140.2, 140.8, 142.2, 147.3; MS *m/e* (MH^+) 245.

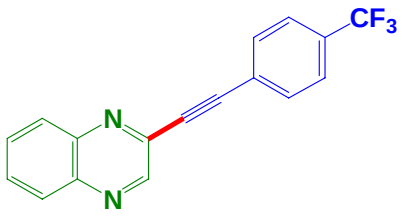


2-Phenylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 7.43 (m, 3H), 7.70 (m, 2H), 7.80 (m, 2H), 8.11 (m, 2H), 8.99 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 86.9, 93.7, 121.4, 128.6, 129.2, 129.3, 129.8, 130.4, 130.7, 132.4, 139.6, 140.9, 142.2, 147.4; MS *m/e* (MH^+) 231.

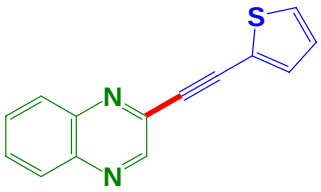


2-*p*-Methoxylphenylethynyl-quinoxaline

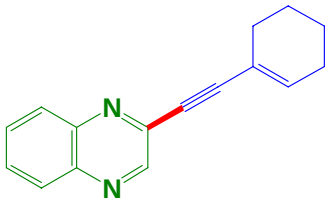
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3H), 6.94 (d, 2H, *J* = 8.0 Hz), 7.64 (d, 2H, *J* = 8.0 Hz), 7.78 (m, 2H), 8.10 (m, 2H), 8.96 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.4, 86.2, 94.3, 113.4, 114.3, 129.1, 129.2, 130.2, 130.6, 134.1, 139.9, 140.8, 142.2, 147.4, 160.8; MS *m/e* (MH^+) 261.



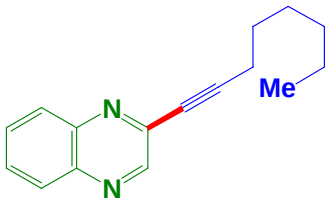
2-*p*-Trifluoromethylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 7.69 (d, 2H, *J* = 8.0 Hz), 7.80 (d, 2H, *J* = 8.0 Hz), 7.82 (m, 2H), 8.13 (m, 2H), 9.01 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 88.8, 91.6, 125.2, 125.5, 129.3, 129.4, 130.8, 130.9, 131.2, 131.5, 132.6, 138.9, 141.2, 142.2, 147.9; MS *m/e* (MH^+) 299.



2-Thiophen-2-ylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 2H), 7.78 (m, 3H), 8.09 (m, 2H), 8.97 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 86.8, 89.0, 120.6, 125.9, 129.2, 129.3, 130.1, 130.4, 130.7, 131.7, 139.6, 140.9, 142.2, 147.2; MS *m/e* (MH^+) 237.

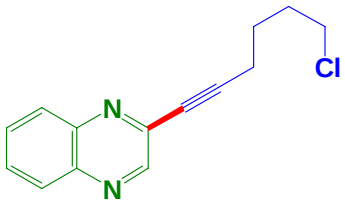


2-1'-Cyclohexenylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 1.68 (m, 4H), 2.20 (m, 2H), 2.32 (m, 2H), 6.49 (m, 1H), 7.75 (m, 2H), 8.06 (d, 2H, *J* = 8.0 Hz), 8.86 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.3, 22.1, 26.0, 28.7, 84.8, 96.1, 119.8, 129.l, 129.2, 130.1, 130.5, 139.5, 140.1, 140.7, 142.2, 147.4; MS *m/e* (MH^+) 235.



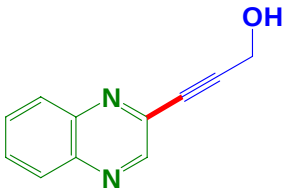
2-Hexylethynyl-quinoxaline

(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, *J* = 8.0 Hz), 1.34 (m, 4H), 1.50 (m, 2H), 1.70 (m, 2H), 2.54 (t, 2H, *J* = 8.0 Hz), 7.75 (m, 2H,), 8.07 (m, 2H), 8.83 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 19.6, 22.6, 28.2, 28.7, 31.3, 78.9, 96.4, 129.1, 129.2, 130.0, 130.5, 140.1, 140.8, 142.1, 147.4; MS *m/e* (MH^+) 239.



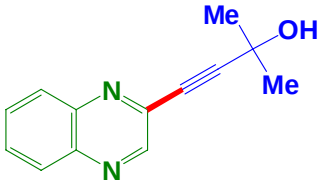
2-4'-Chlorobutylethynyl-quinoxaline

(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 1.87 (m, 2H), 2.00 (m, 2H), 2.60 (t, 2H, *J* = 8.0 Hz), 3.62 (t, 2H, *J* = 8.0 Hz), 7.75 (m, 2H), 8.05 (m, 2H), 8.84 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.9, 25.3, 31.6, 44.4, 79.4, 94.9, 129.0, 129.1, 130.1, 130.5, 139.7, 140.8, 142.0, 147.3; MS *m/e* (MH^+) 245.



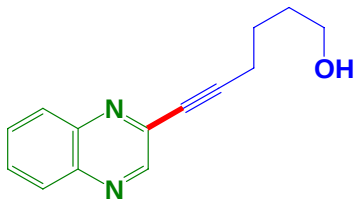
2-Hydroxymethylethynyl-quinoxaline

(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.33 (t, 1H, *J* = 4.0 Hz), 4.64 (d, 2H, *J* = 4.0 Hz), 7.80 (m, 2H), 8.09 (m, 2H), 8.91 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 51.4, 83.1, 91.9, 129.2, 129.3, 130.7, 130.8, 138.8, 141.1, 142.0, 146.9; MS *m/e* (MH^+) 185.

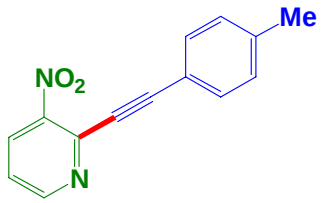


2-2'-Hydroxy-2'-propylethynyl-quinoxaline

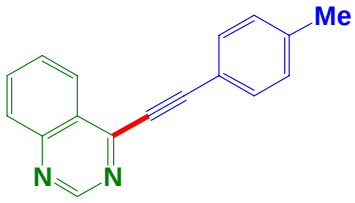
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 1.72 (s, 6H), 3.61 (s, 1H), 7.78 (m, 2H), 8.08 (m, 2H), 8.89 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 31.2, 65.4, 79.8, 98.8, 129.0, 129.1, 130.6, 130.8, 139.1, 140.8, 142.0, 147.0; MS *m/e* (MH^+) 213.



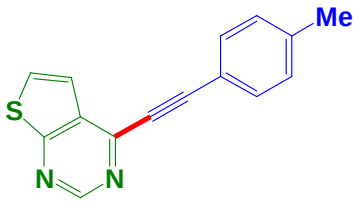
2-4'-Hydroxybutylethynyl-quinoxaline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 1.81 (m, 4H), 1.95 (m, 1H), 2.61 (m, 2H), 3.75 (m, 2H), 7.76 (m, 2H), 8.06 (m, 2H), 8.83 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 19.4, 24.6, 31.9, 62.2, 79.2, 95.8, 129.0, 129.1, 130.1, 130.6, 139.9, 140.8, 142.0, 147.3; MS *m/e* (MH^+) 227; HRMS (ESI) Calcd for $C_{14}H_{15}N_2O$ 227.1184 (MH_+), Found 227.1155.



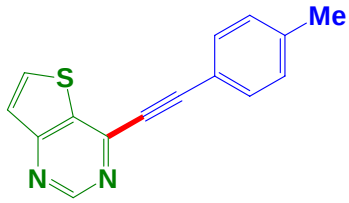
2-*p*-Tolylethynyl-3-nitro-pyridine
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 7.21 (d, 2H, *J* = 8.0 Hz), 7.43 (dd, 1H, *J* = 8.0, 4.0 Hz), 7.58 (d, 2H, *J* = 8.0 Hz), 8.39 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.84 (dd, 1H, *J* = 8.0, 4.0 Hz); ^{13}C NMR ($CDCl_3$) δ 21.8, 84.7, 98.5, 118.3, 122.4, 129.4, 132.5, 132.6, 137.7, 140.7, 146.7, 153.5; MS *m/e* (MH^+) 239.



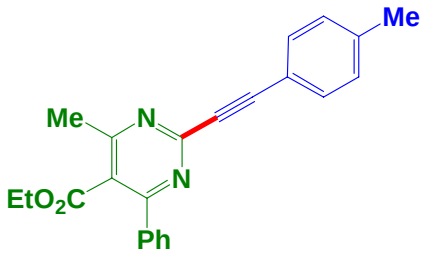
2-*p*-Tolylethynyl-quinazoline
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3H), 7.25 (d, 2H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.0 Hz), 7.72 (t, 1H, *J* = 8.0 Hz), 7.94 (t, 1H, *J* = 8.0 Hz), 8.06 (d, 1H, *J* = 8.0 Hz), 8.41 (d, 1H, *J* = 8.0 Hz), 9.31 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 84.9, 99.4, 118.1, 125.3, 126.6, 128.3, 128.8, 129.5, 132.6, 134.3, 140.9, 150.1, 152.8, 155.0; MS *m/e* (MH^+) 245.



4-*p*-Tolylethynyl-thieno[2,3-d]pyrimidine
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H), 7.23 (d, 2H, *J* = 8.0 Hz), 7.59 (m, 4H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 85.1, 97.8, 118.1, 120.7, 127.8, 129.4, 131.4, 132.5, 140.8, 145.4, 153.4, 168.5; MS *m/e* (MH^+) 251.

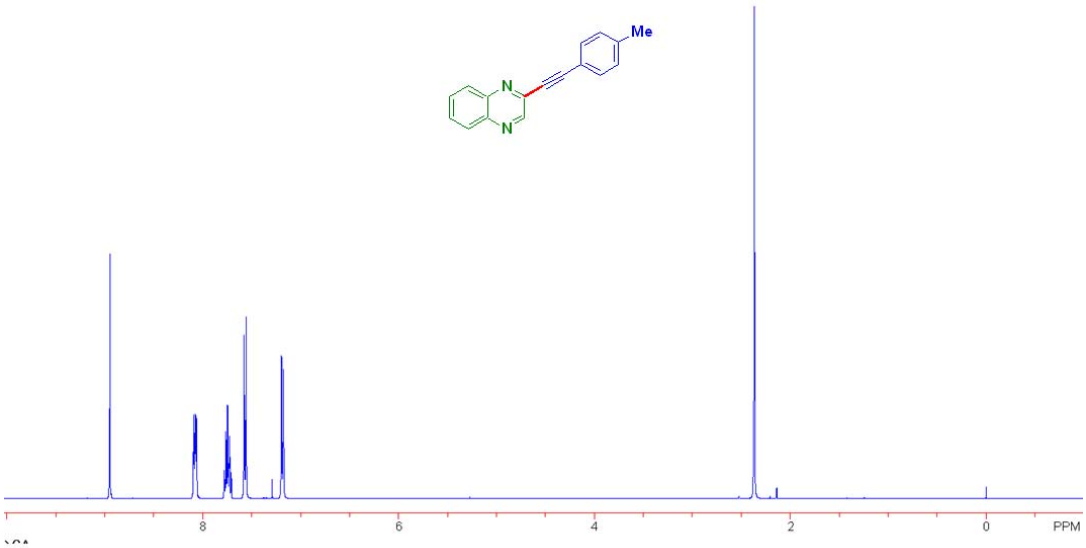


4-*p*-Tolylethynyl-thieno[3,2-d]pyrimidine
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3H), 7.25 (m, 2H), 7.60 (m, 3H), 8.04 (d, 1H, *J* = 4.0 Hz), 9.21 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 84.8, 98.5, 117.8, 124.9, 129.4, 132.6, 133.1, 136.5, 140.9, 145.7, 154.8, 160.6; MS *m/e* (MH^+) 251.



2-*p*-Tolylethynyl-4-methyl-6-phenyl-pyrimidine-5-carboxylic acid ethyl este
(Light yellow solid): ^{1}H NMR ($CDCl_3$) δ 1.07, (t, 3H, *J* = 8.0 Hz), 2.38 (s, 3H), 2.66 (s, 3H), 4.20 (q, 2H, *J* = 8.0 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 7.47 (m, 3H), 7.59 (d, 2H, *J* = 8.0 Hz), 7.67 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.6, 21.7, 22.7, 25.6, 62.0, 68.0, 87.8, 89.1, 118.2, 124.1, 128.4, 128.6, 129.2, 130.2, 132.7, 137.3, 140.2, 152.6, 164.1, 165.6, 167.6; MS *m/e* (MH^+) 357.

IV - NMR Spectra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6
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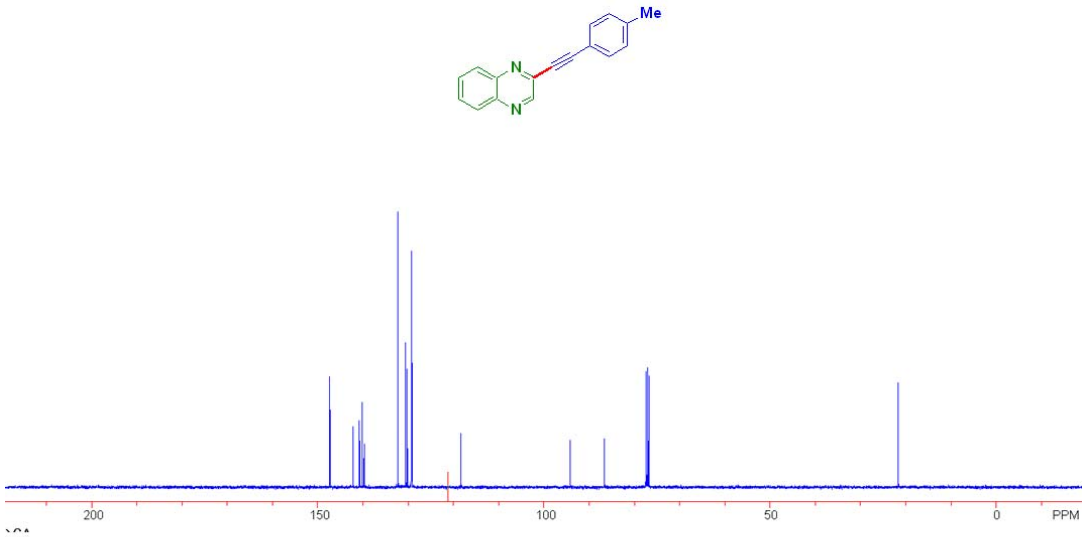
PPM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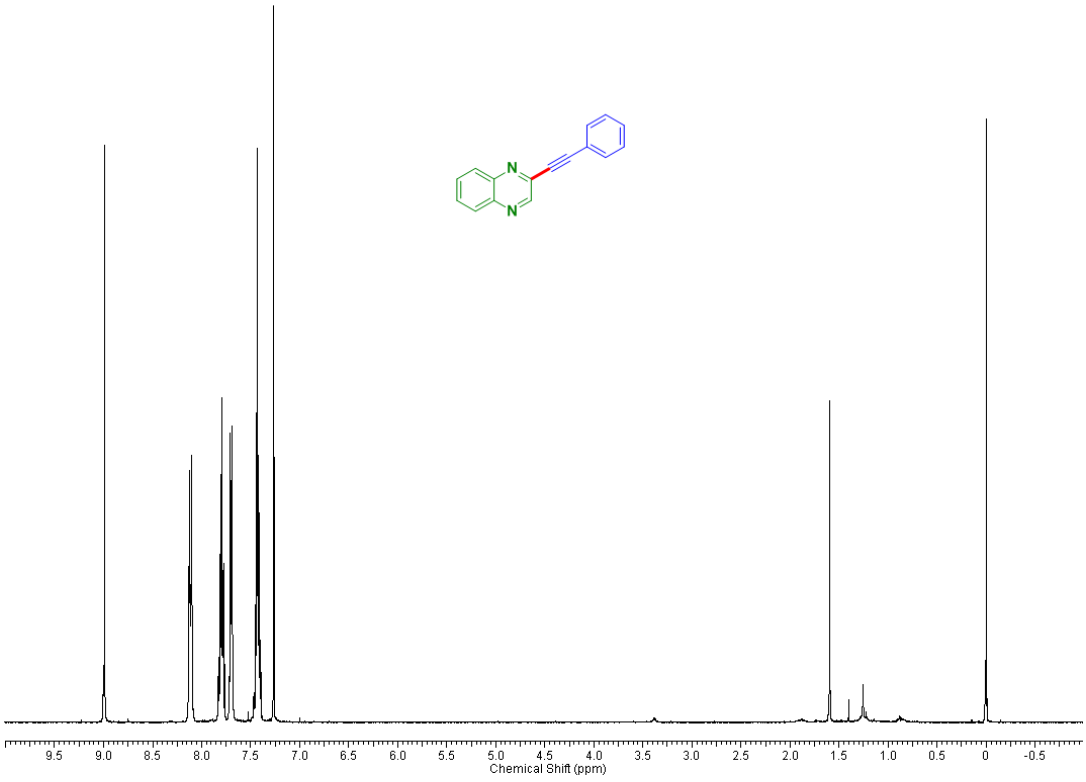
0
PPM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N
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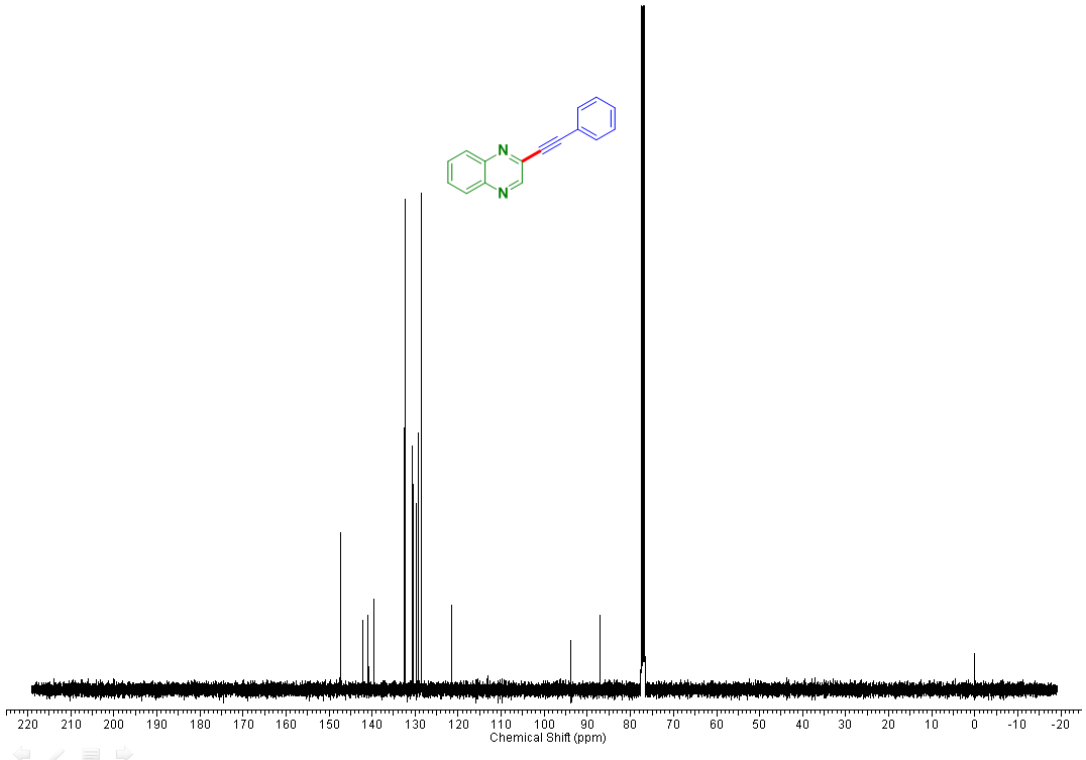
Chemical Shift (ppm)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N
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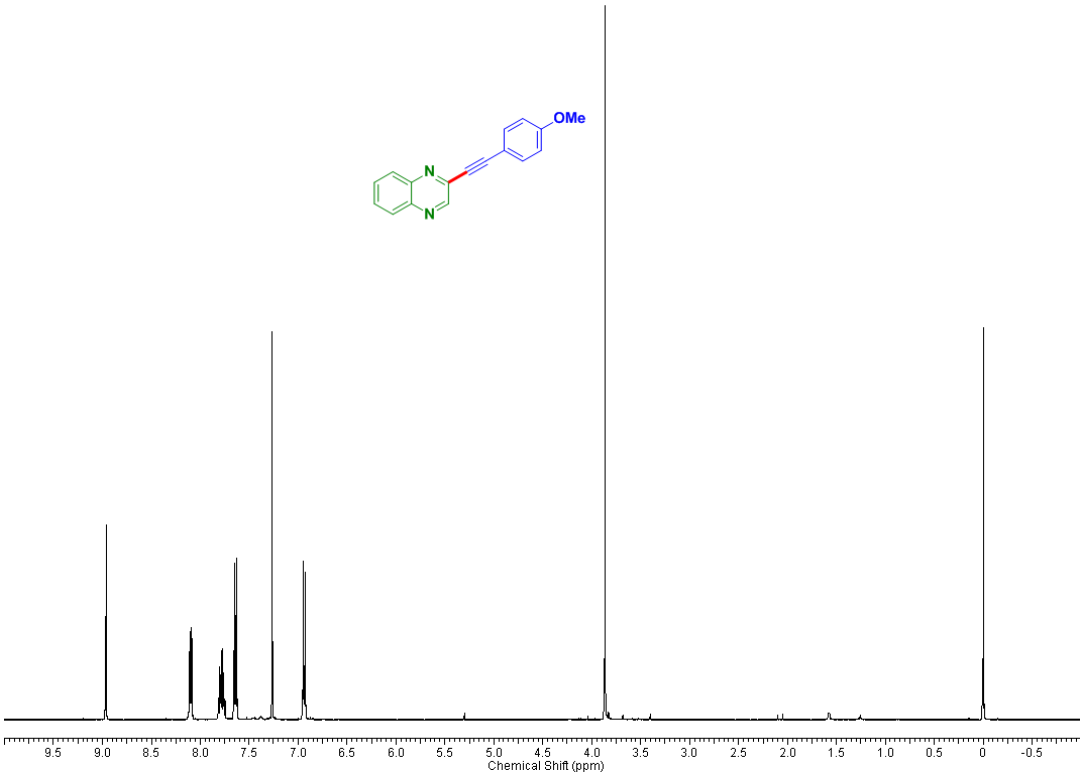
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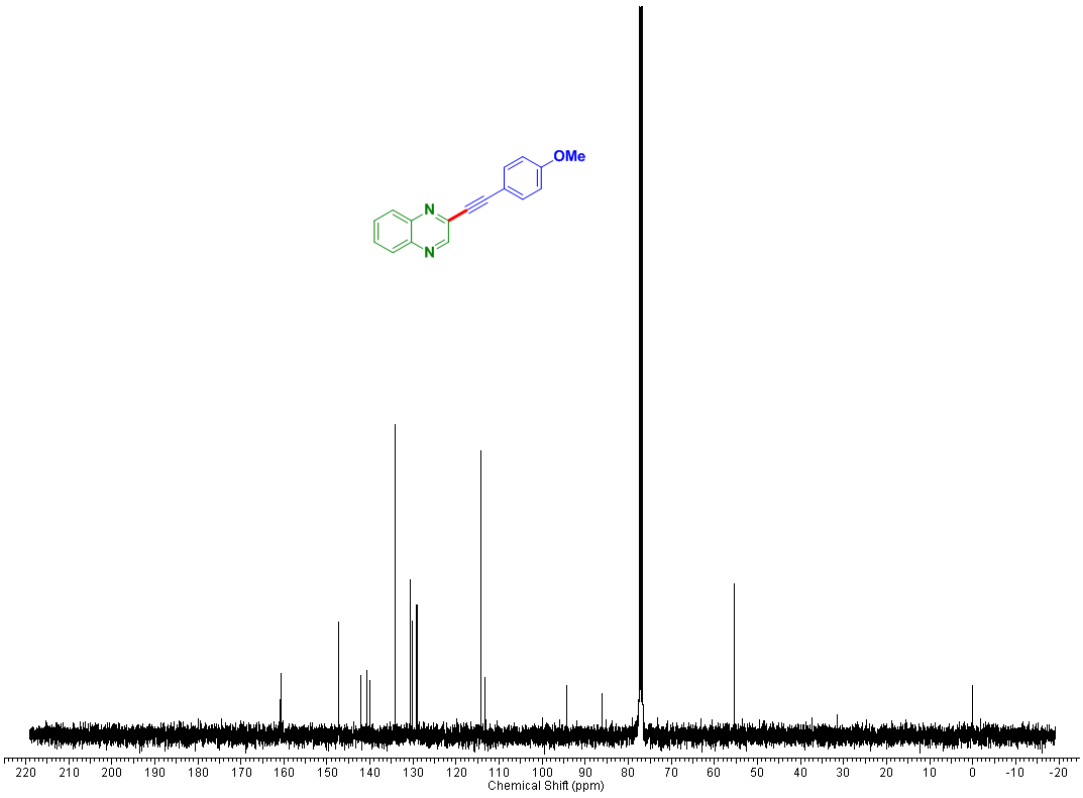
Chemical Shift (ppm)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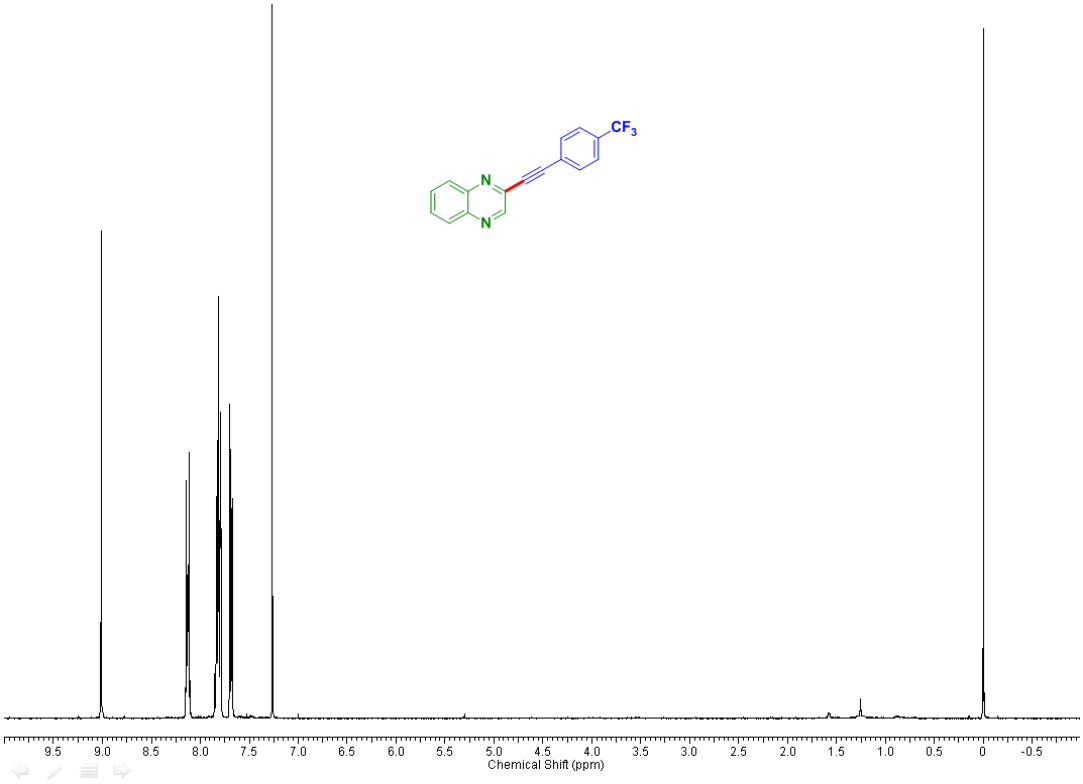
Chemical Shift (ppm)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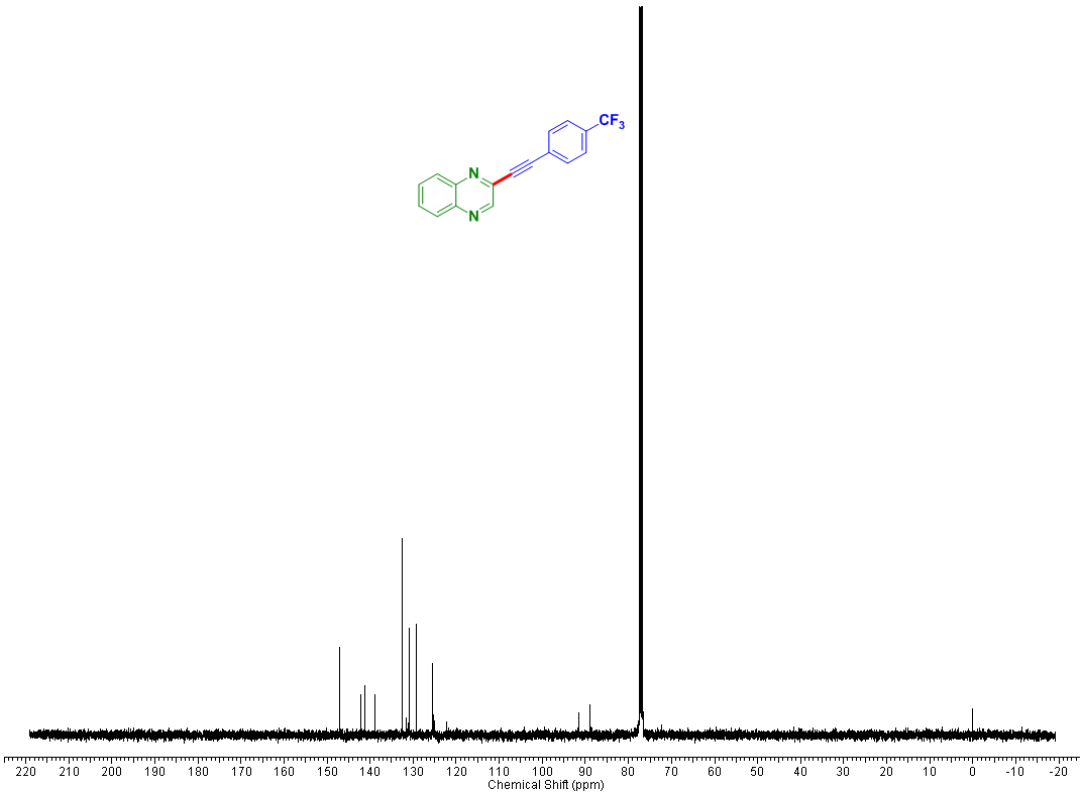
Chemical Shift (ppm)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N
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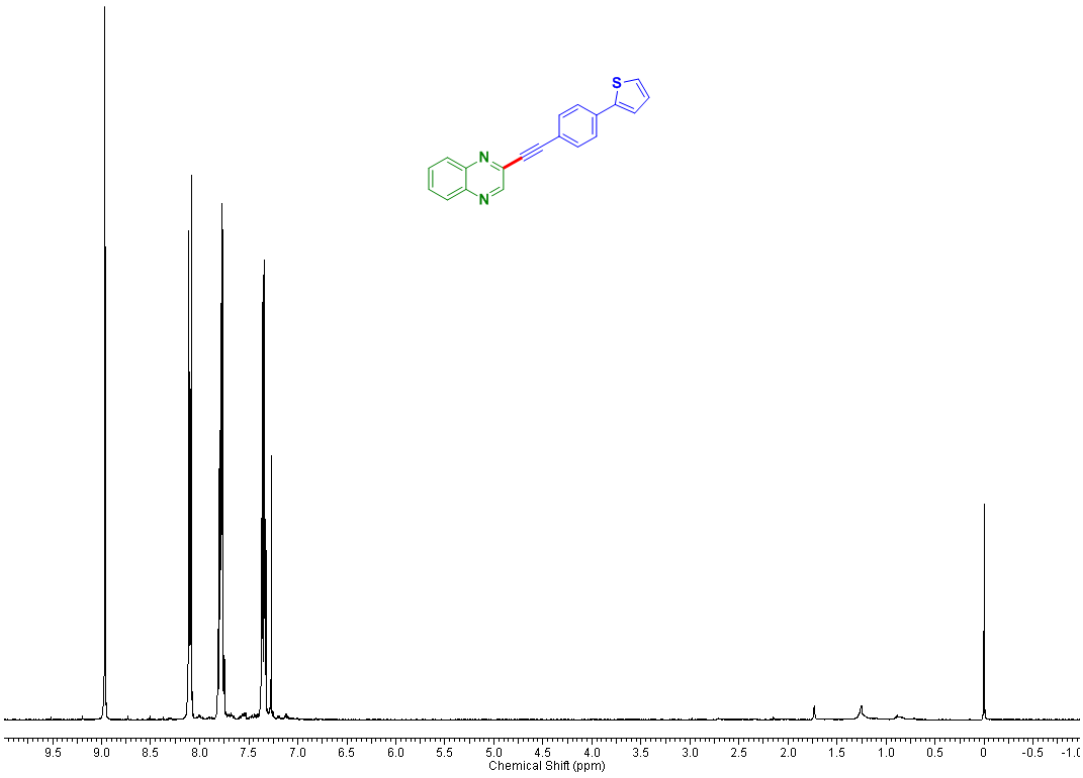
Chemical Shift (ppm)


S
N
N
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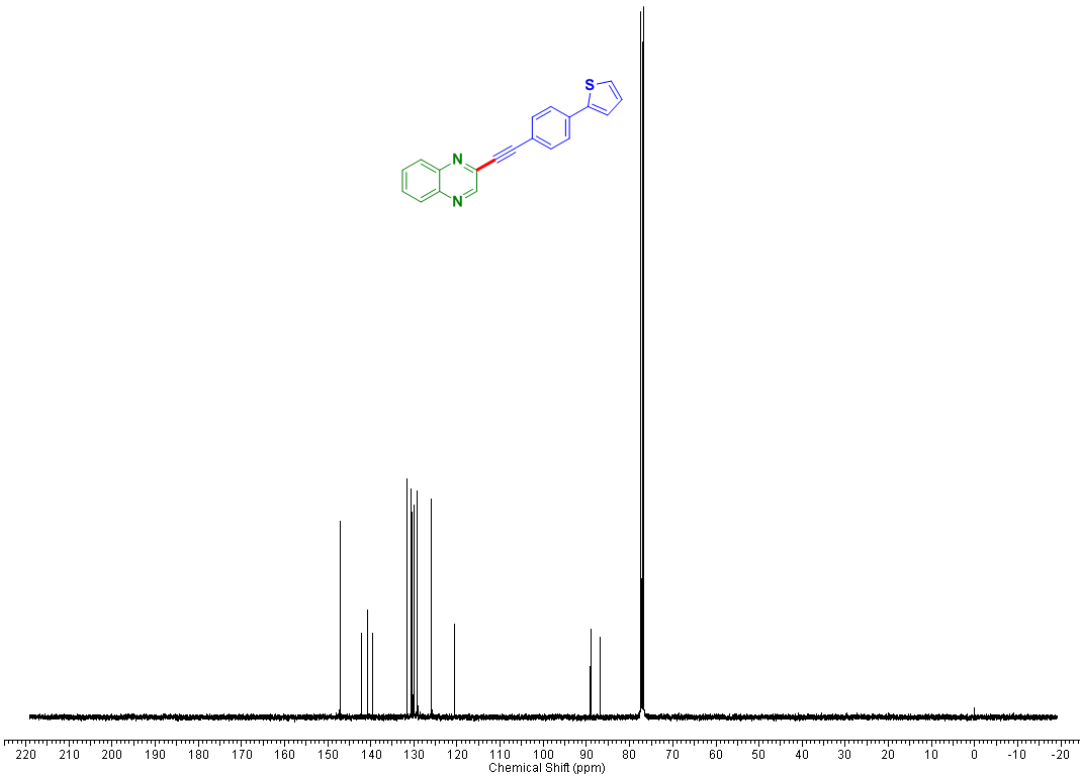
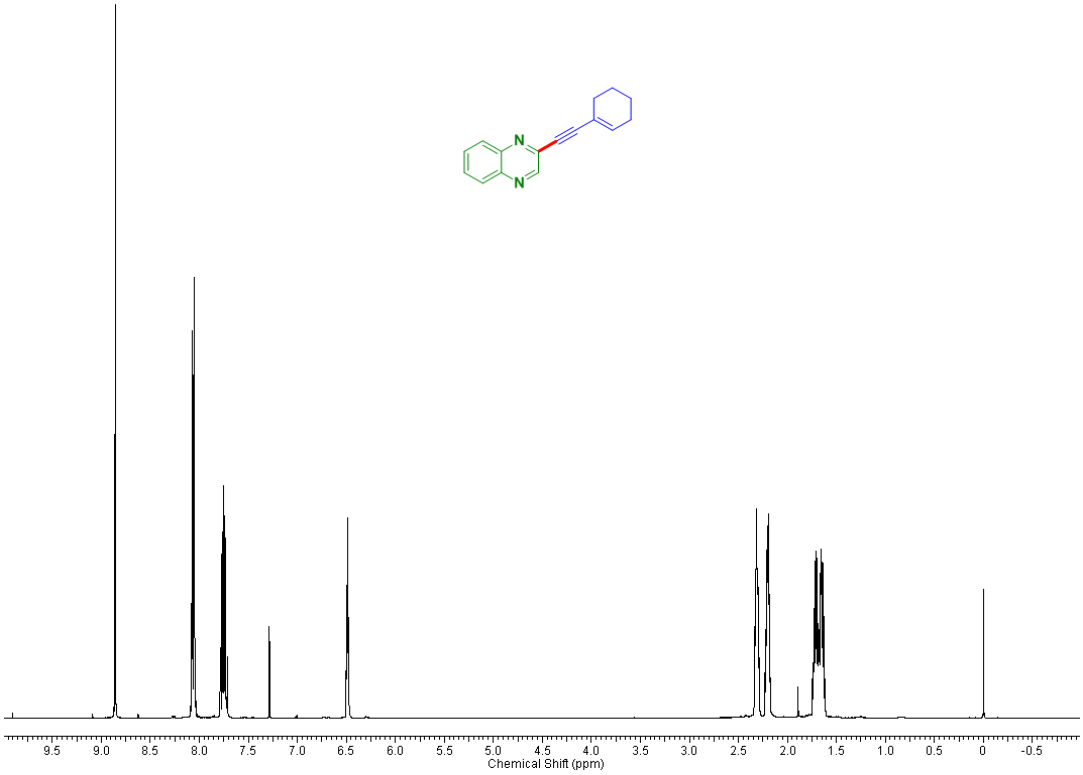
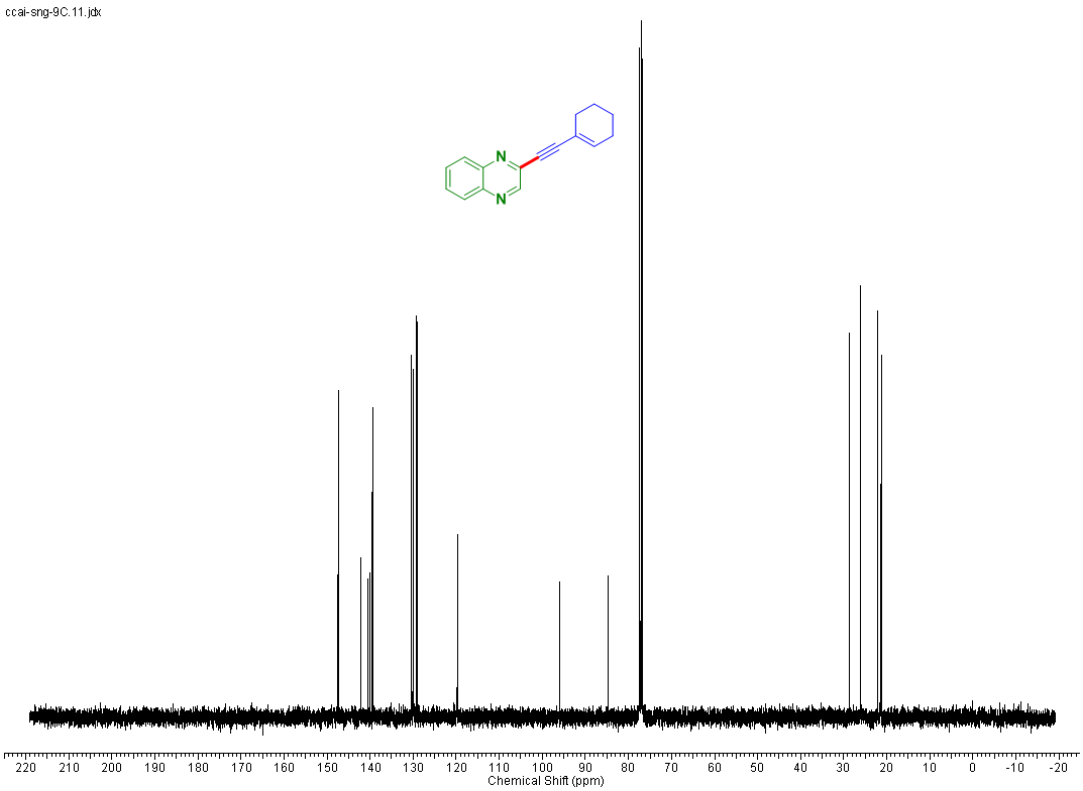
Chemical Shift (ppm)


S
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)


N
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


ccai-sng-9C.11.jdx
N
N
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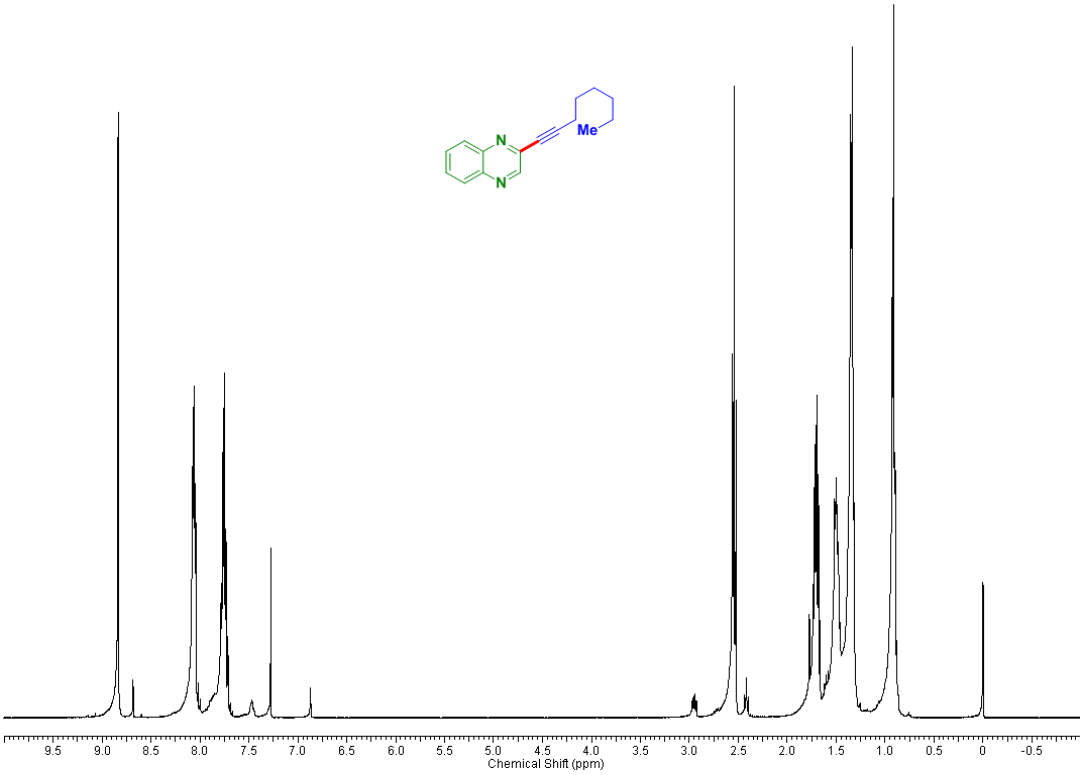
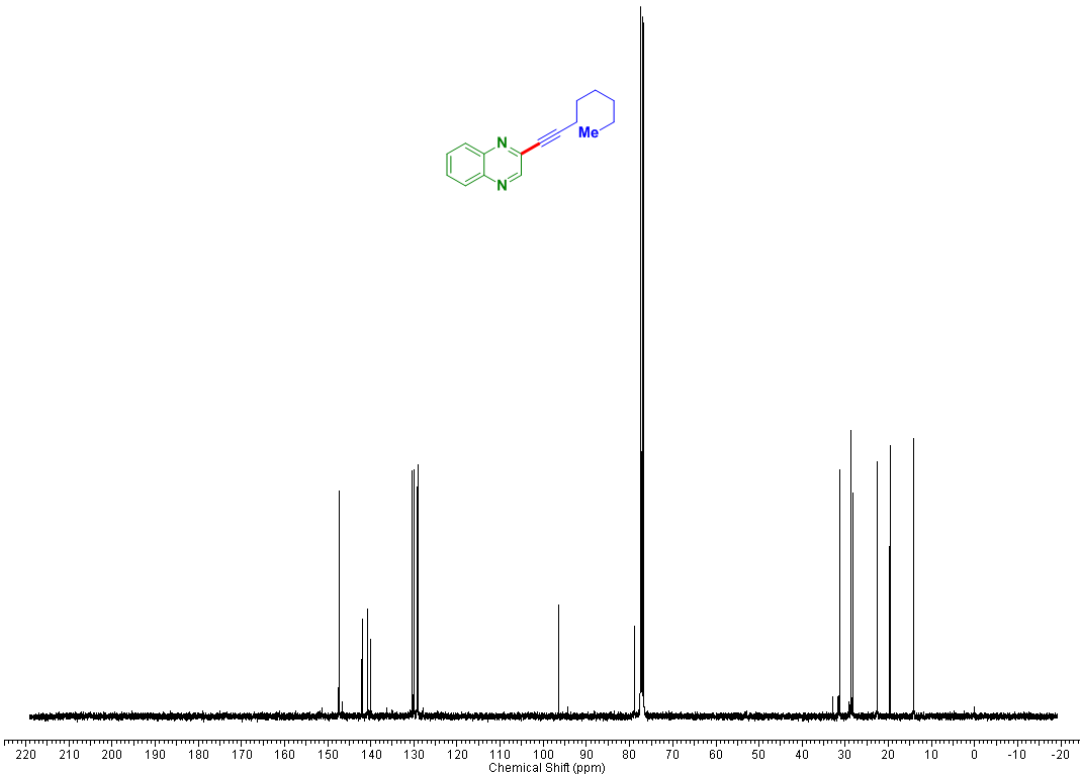
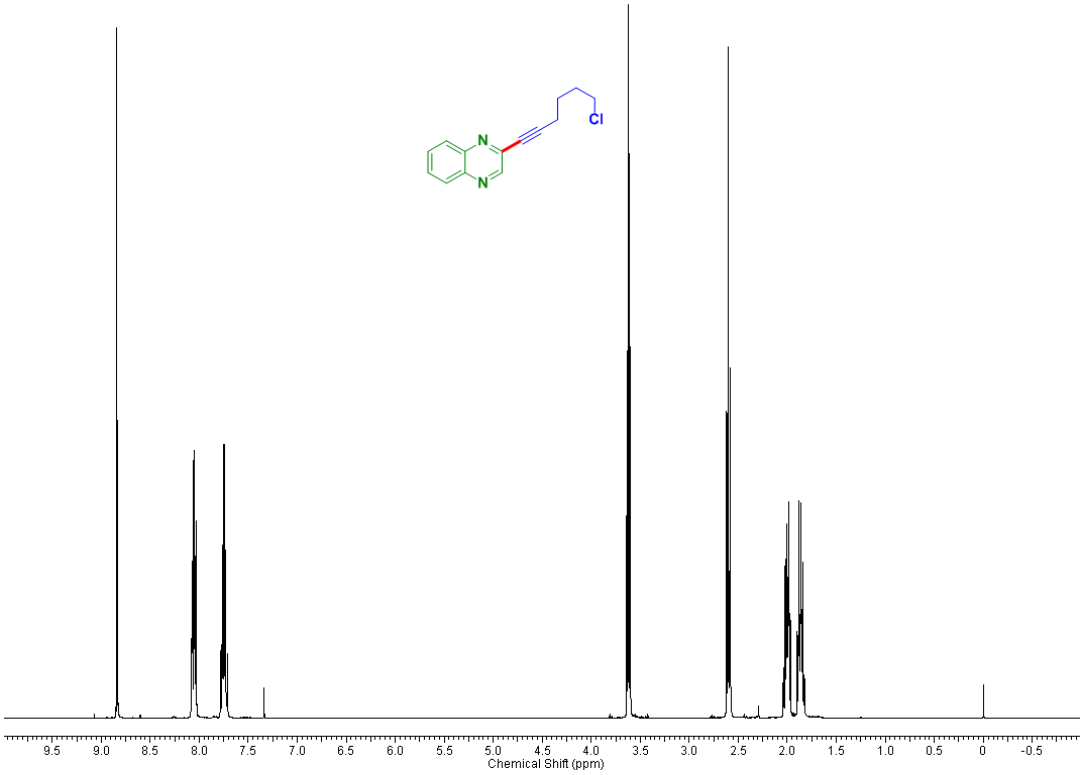
Chemical Shift (ppm)


N
N
Me
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


N
N
Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)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N
Cl
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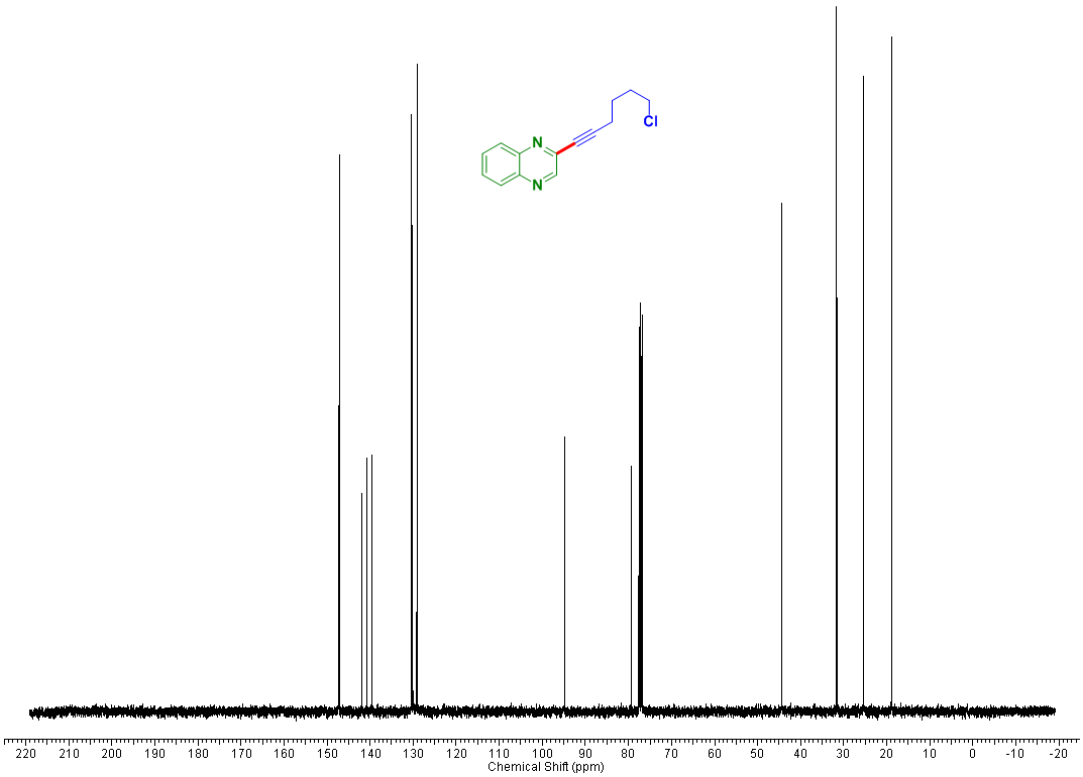
Chemical Shift (ppm)


N
N
Cl
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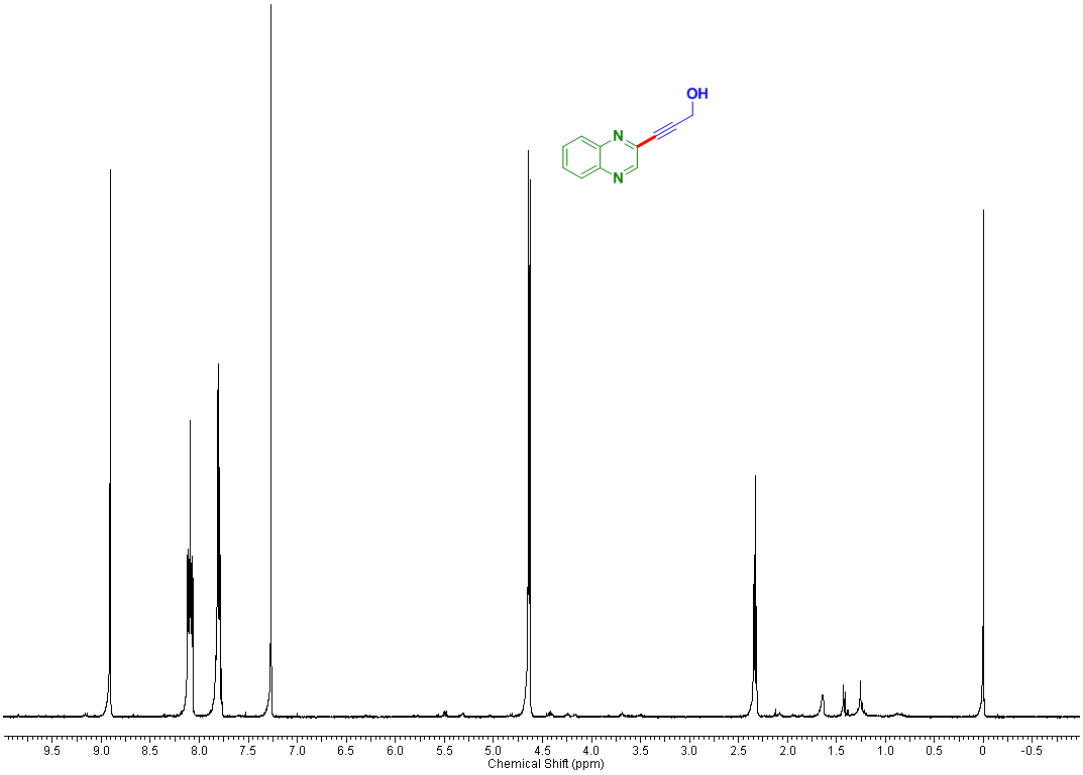
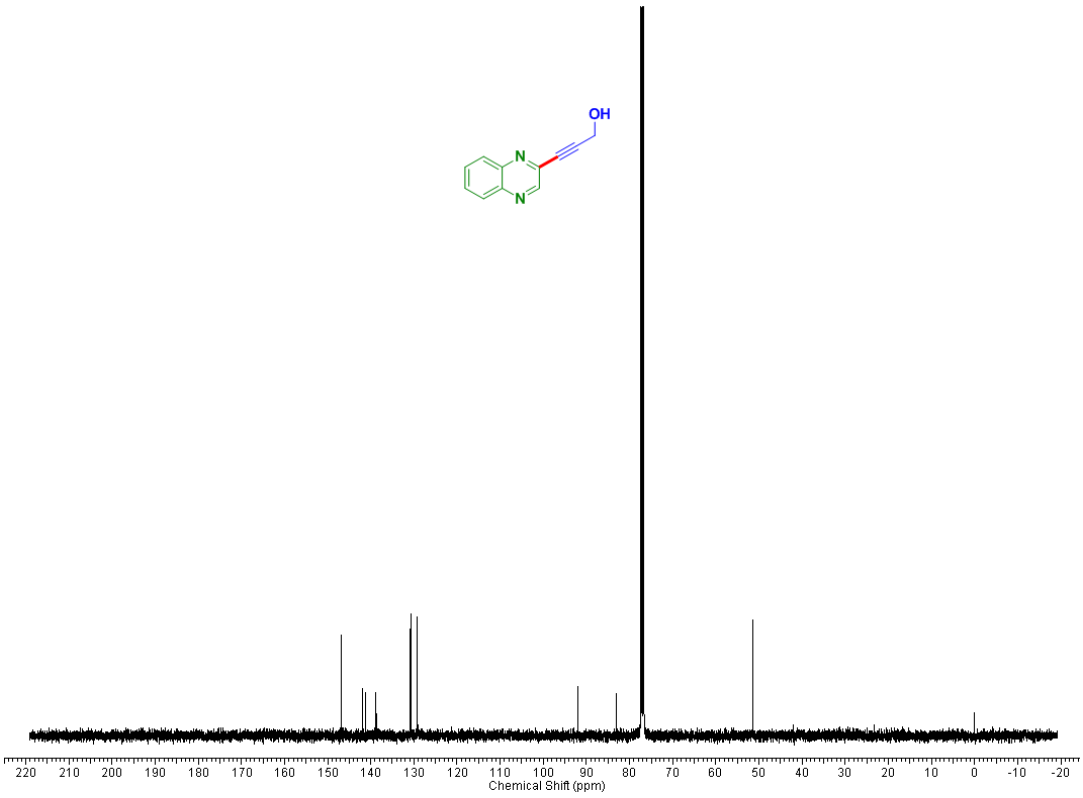
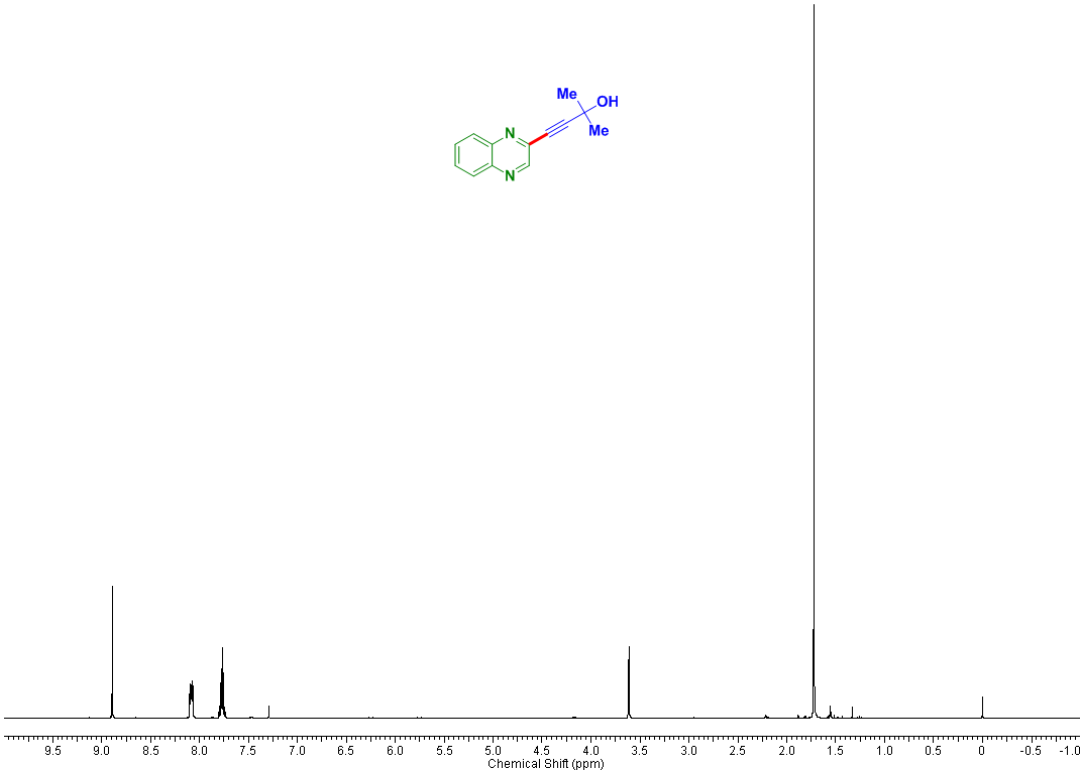
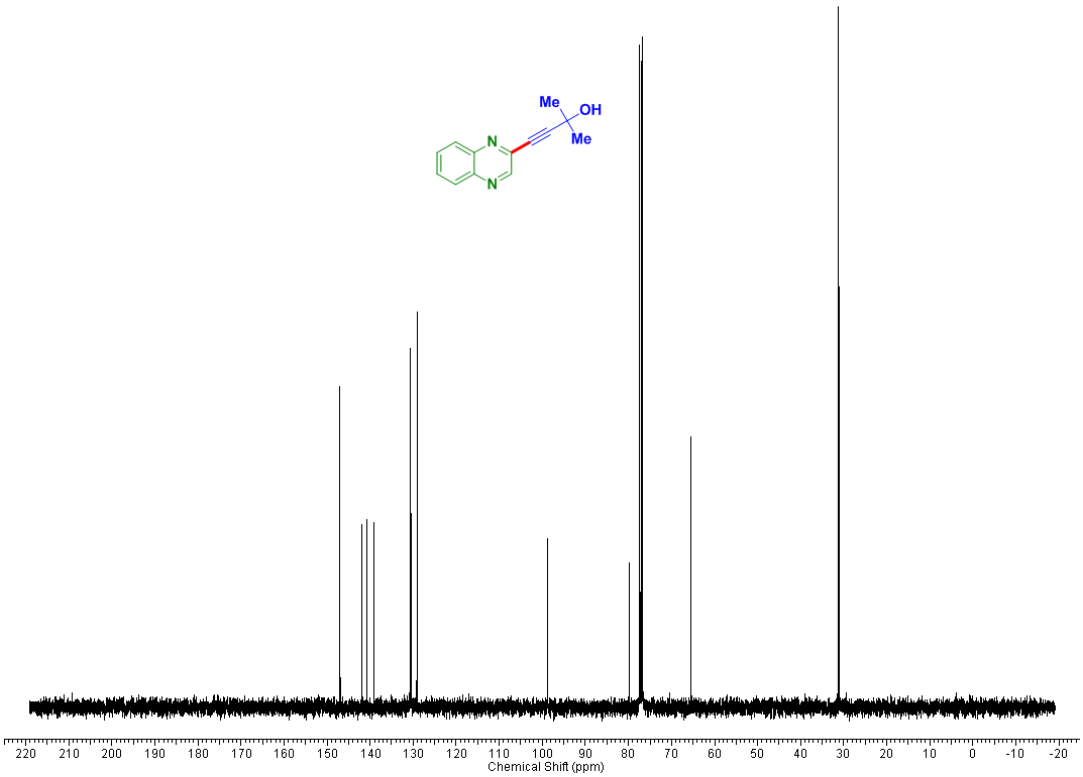
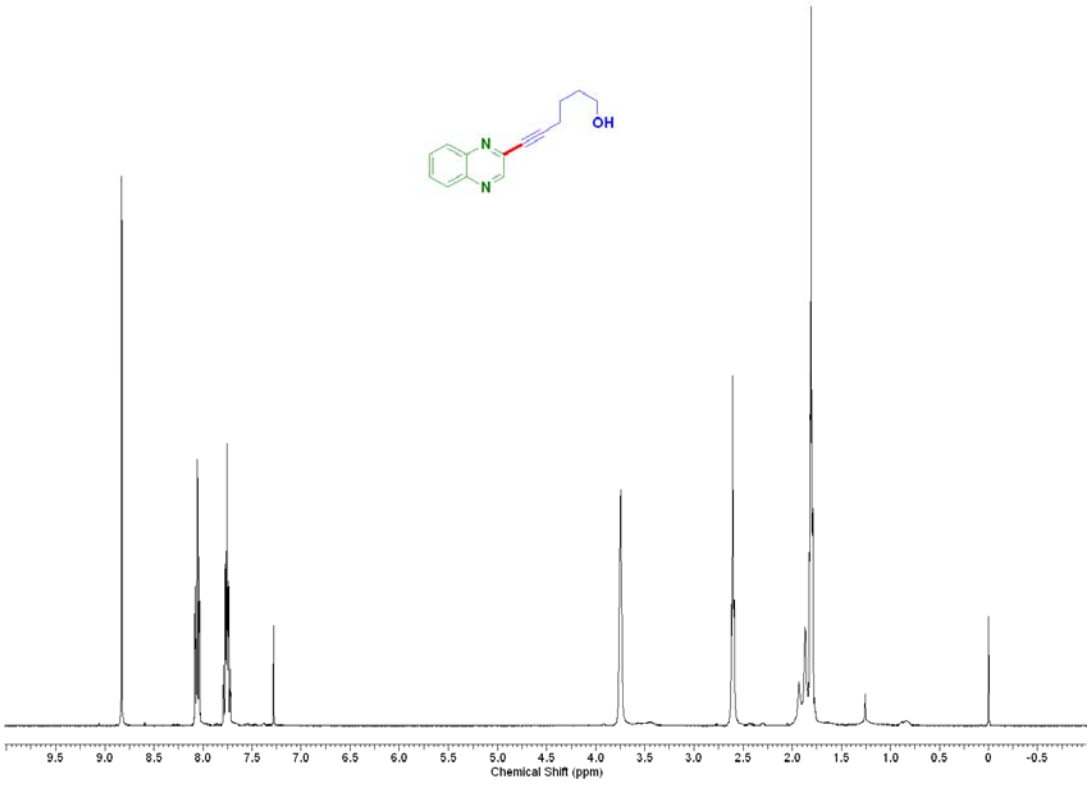
Chemical Shift (ppm)

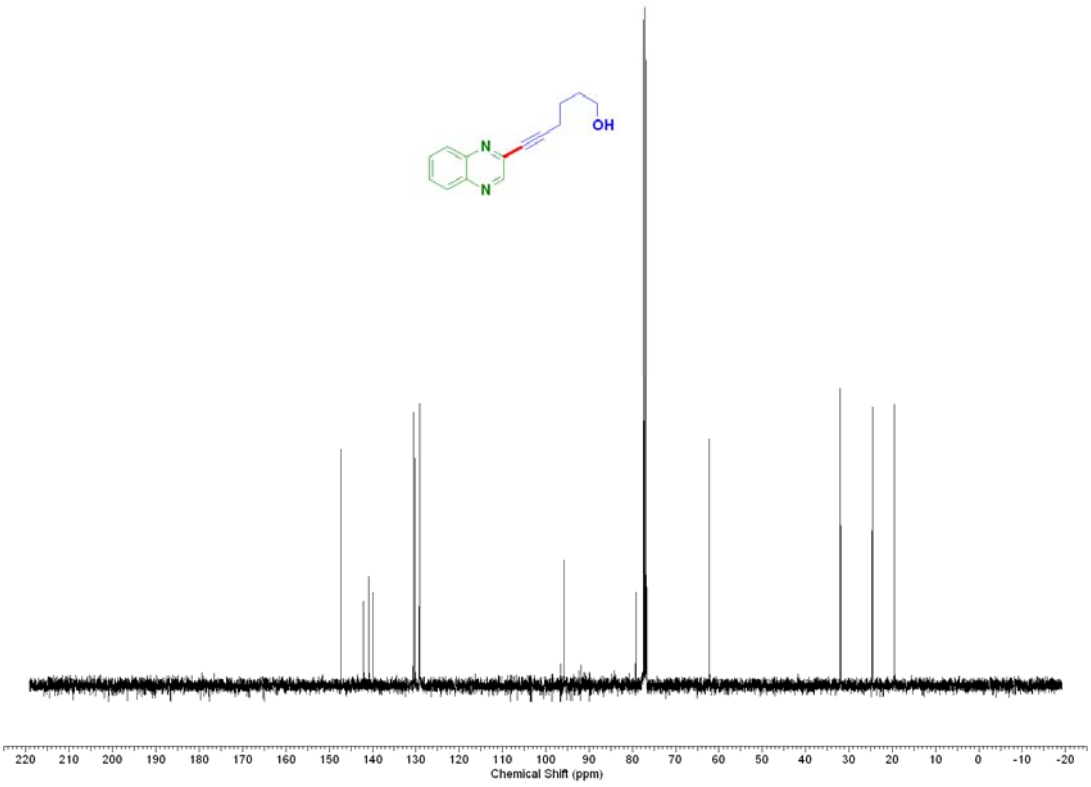

OH
N
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

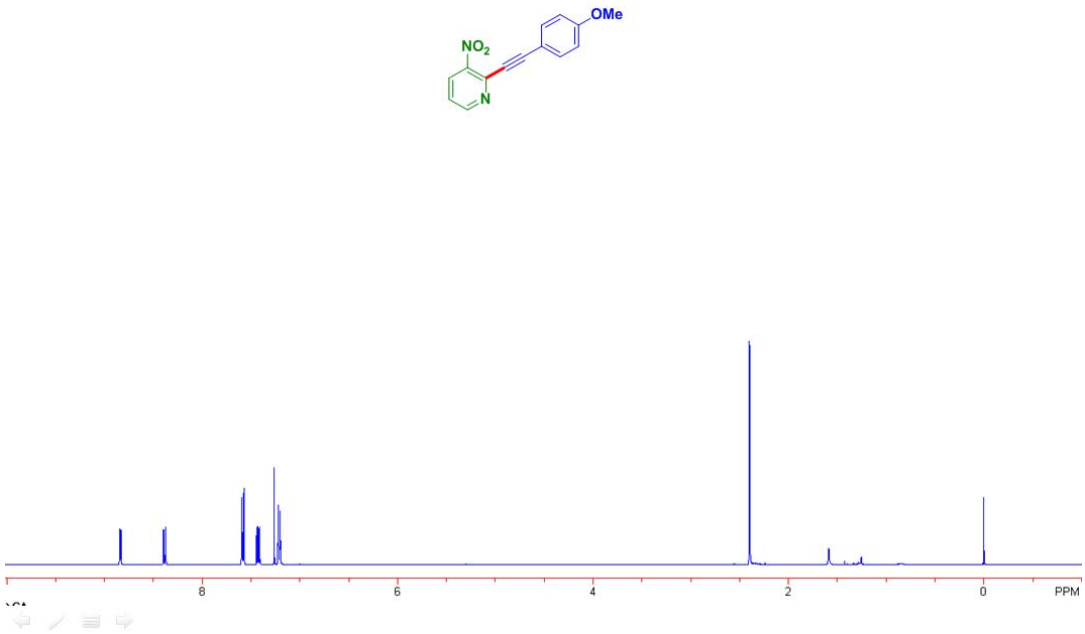

OH
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

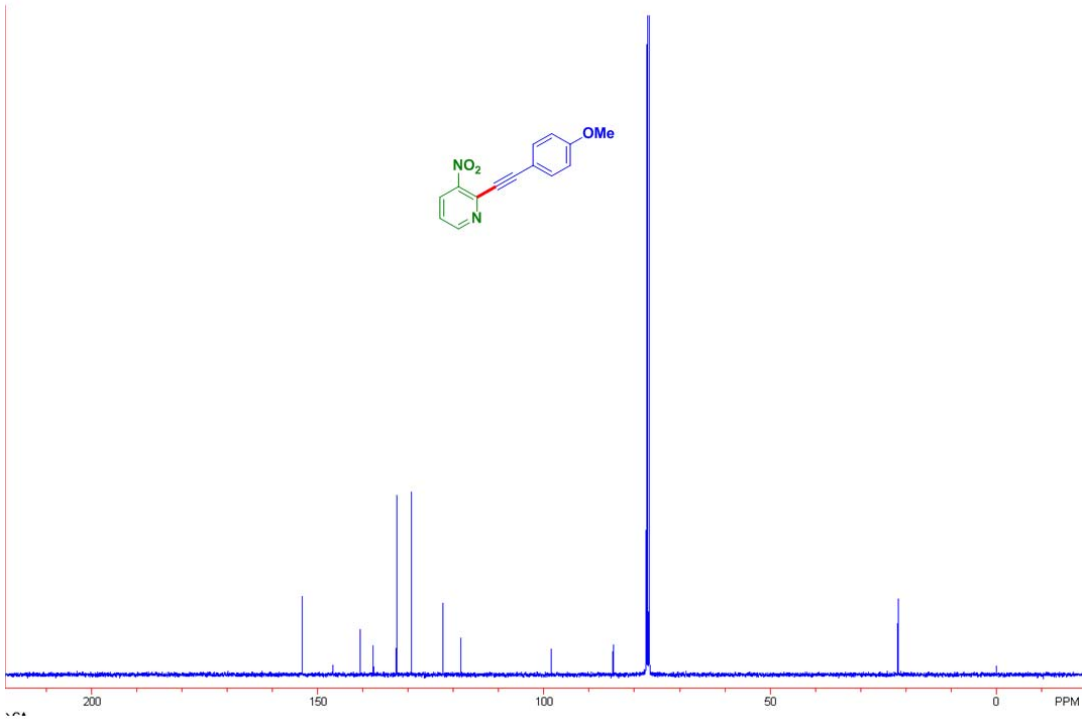

Me
OH
Me
N
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5 -1.0
Chemical Shift (ppm)

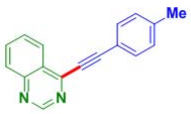

Me
OH
Me
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

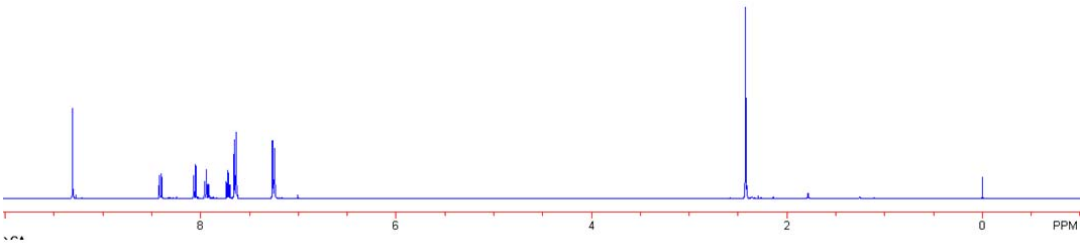

OH
N
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)

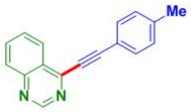

OH
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

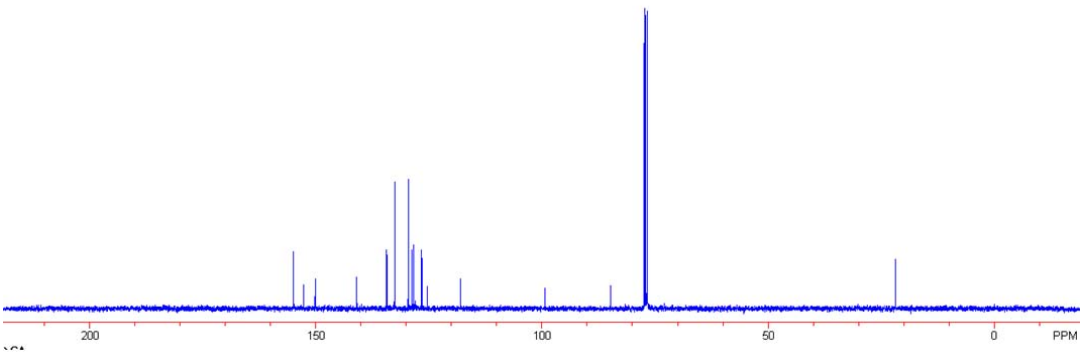

OMe
NO2
N
8
6
4
2
0
PPM

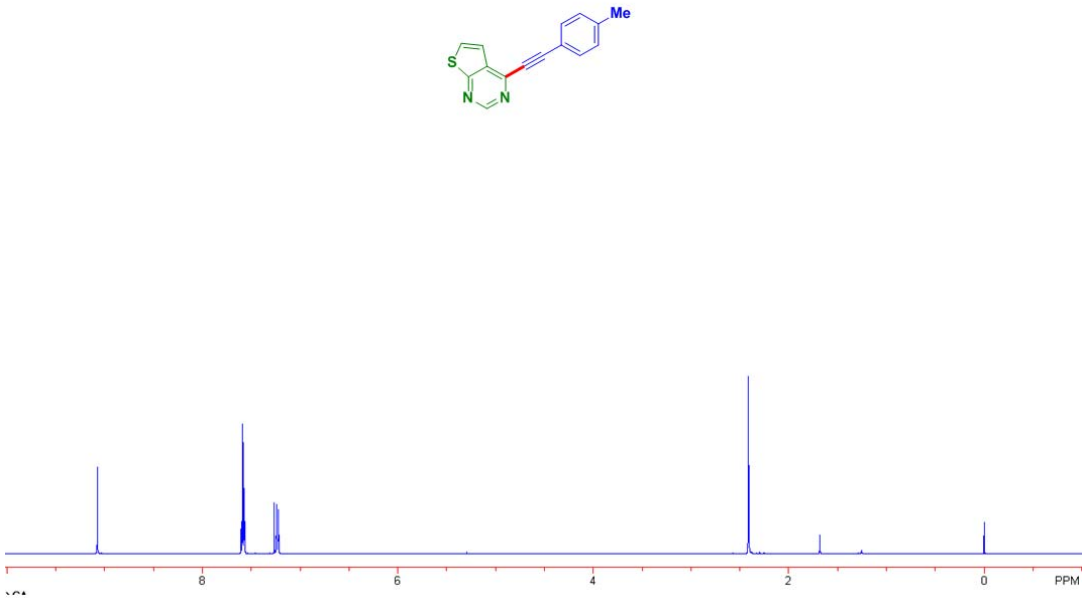

OMe
NO2
N
200
150
100
50
0
PPM

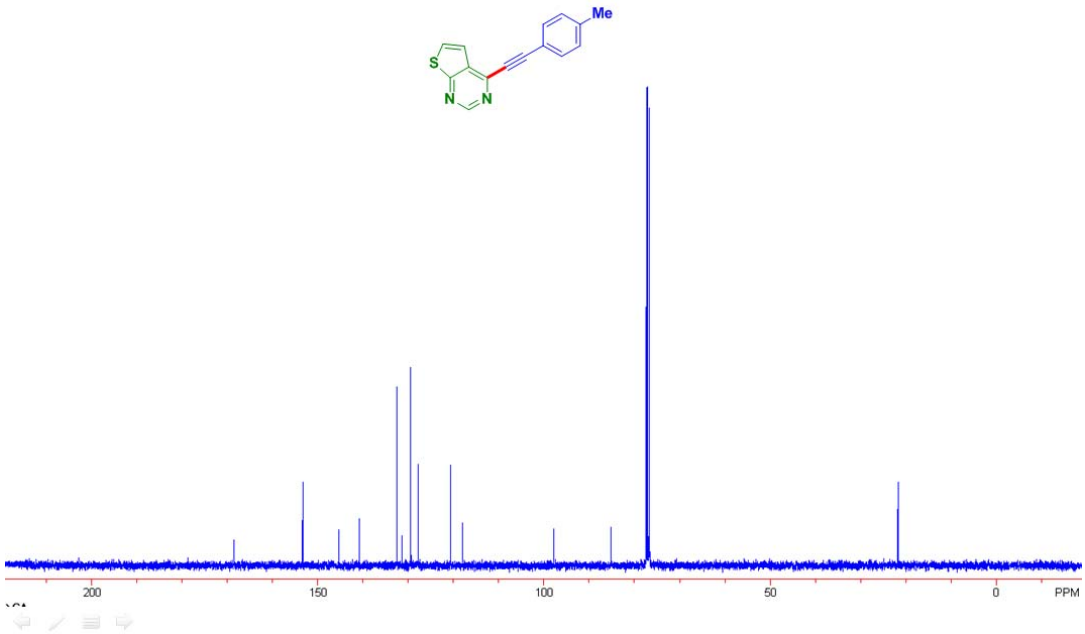

Me
N
N

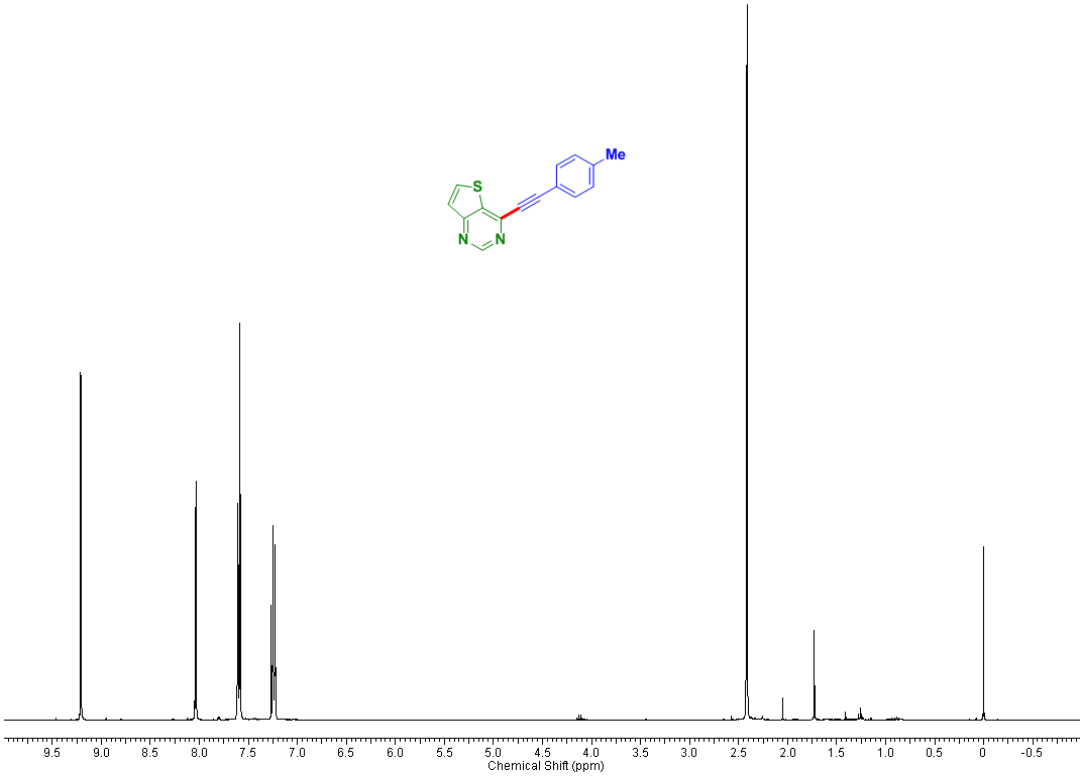

8
6
4
2
0
PPM

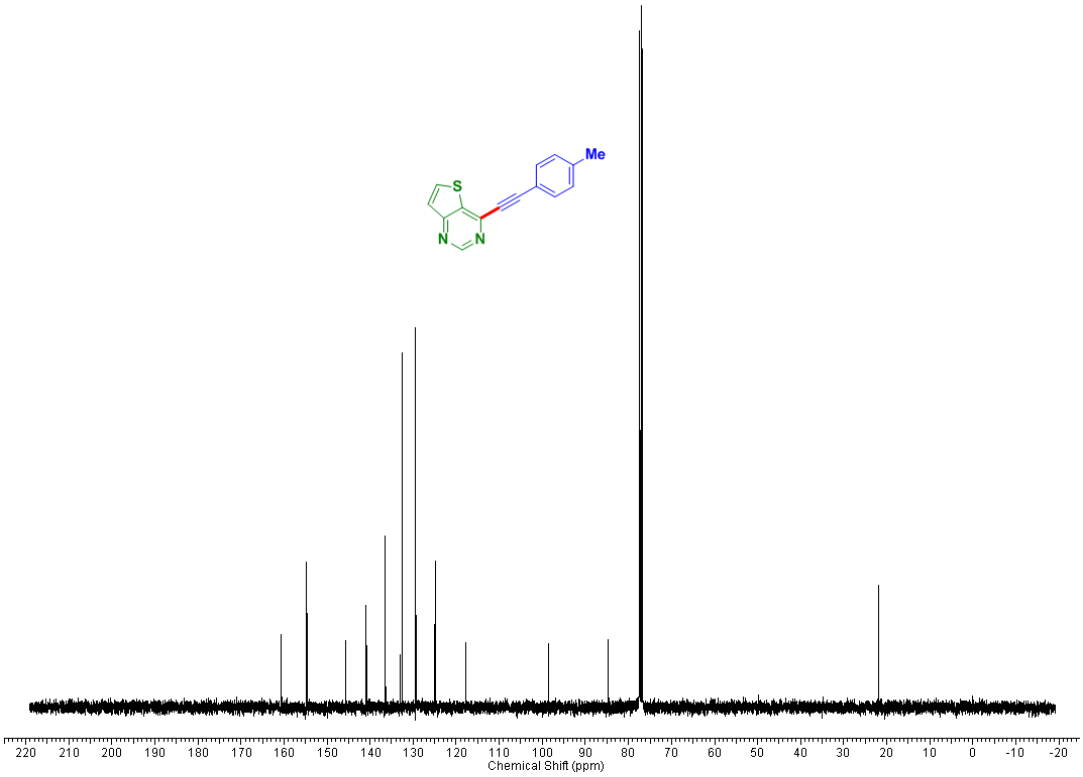

Me
N
N

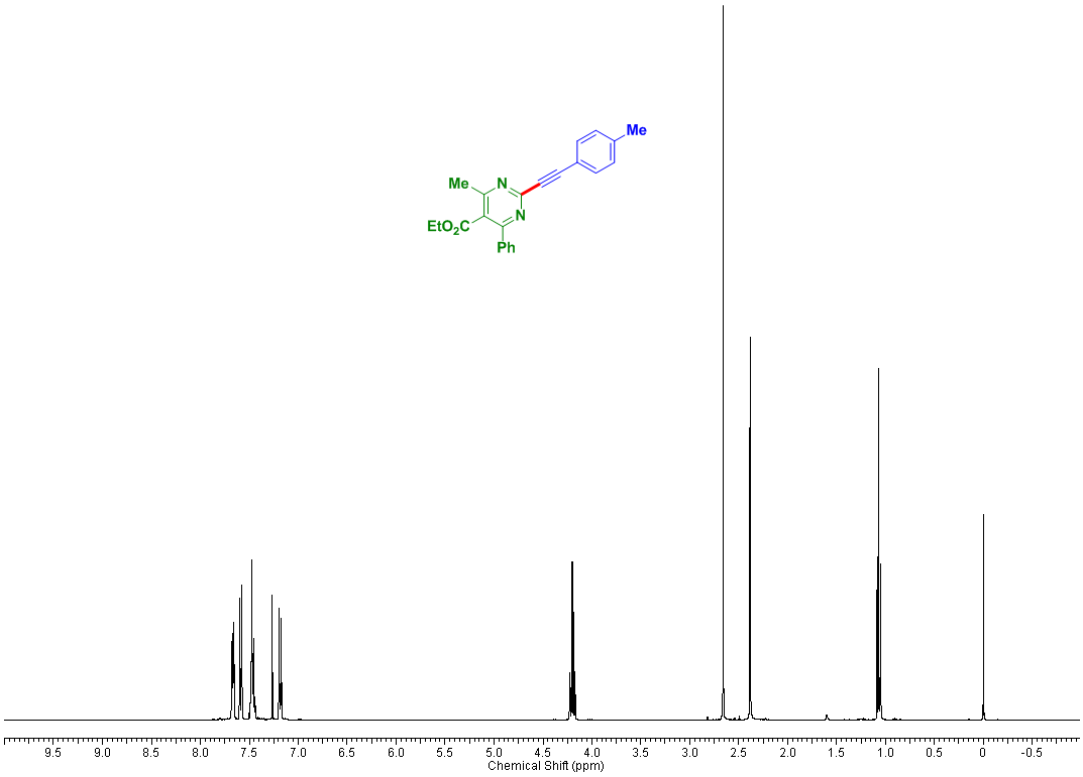

200
150
100
50
0
PPM

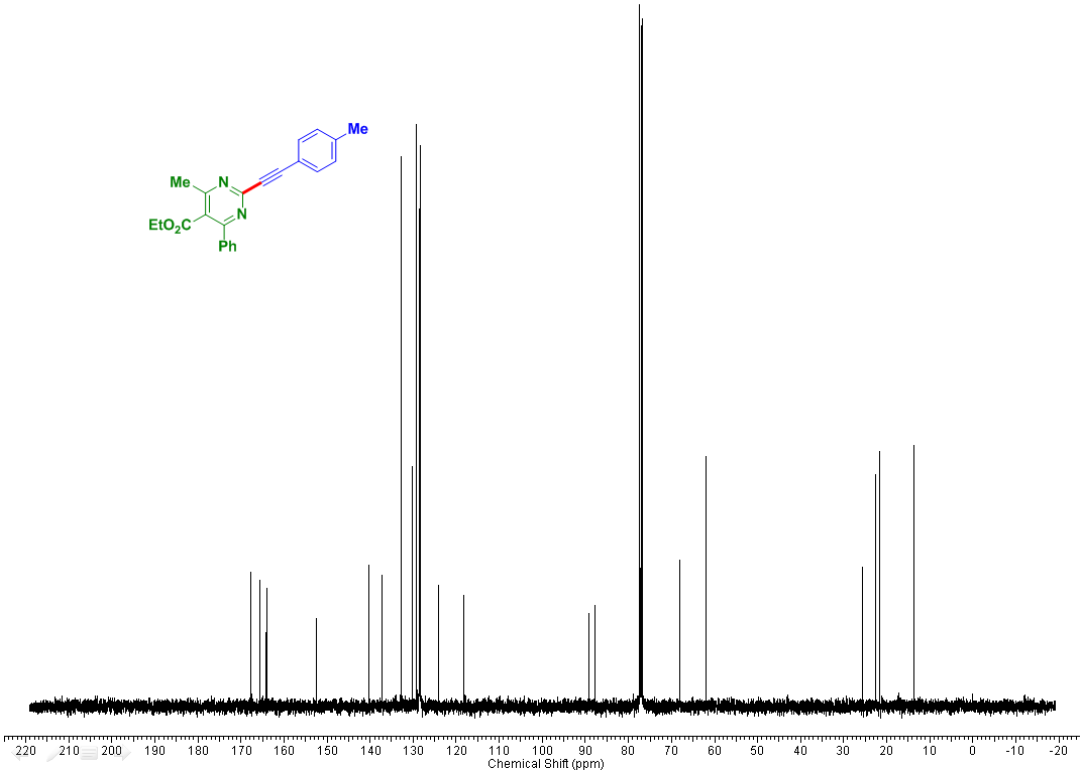

Me
S
N
N
8
6
4
2
0
PPM


Me
S
N
N
200
150
100
50
0
PPM


Me
S
N
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


Me
S
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)


Me
Me
N
N
EtO2C
Ph
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


Me
Me
N
N
EtO2C
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)