Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Palladium-Catalyzed Diazine N-Oxide Cross Coupling Reactions with Aryl Chlorides, Bromides and Iodides

*Jean-Philippe Leclerc and Keith Fagnou**

Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, ON, K1N 6N5, Canada.
e-mail: keith.fagnou@uottawa.ca

General Methods

All experiments were carried out under an atmosphere of nitrogen. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$ (with Me_4Si as an internal standard) or $(CD_3)_2CO$ or $(CD_3)_2SO$ solutions using a Bruker AVANCE 300 or a Bruker AVANCE 400 or a Varian 500 spectrometer. High-resolution mass spectra were obtained on a Kratos Concept IIH. Infra-Red analysis was performed with a Bruker EQUINOX 55. HPLC analysis was performed on Waters apparatus using photodiode array detector. HPLC Grade THF, Et_2O, Benzene, Toluene and CH_2Cl_2 are dried and purified via MBraun SP Series solvent purification system. Triethylamine was freshly distilled from NaOH before every use. Dimethylacetamide was degassed with N_2 before every use. Palladium and Copper complexes were stored in a dessicator and were weighed out to air unless otherwise specified. All other reagents and solvents were used without further purification from commercial sources. Unless noted below, all other compounds have been reported in the literature or are commercially available.

General Procedure 1: Diazine oxidation

The appropriate diazine (1 equiv.) and mCPBA (1 equiv.) were dissolved in DCM (0.2 M). The reaction was allowed to stir for 16 hours. PPh_3 (0.5 equiv.) was then added to reduce any unreacted peracid and the mixture was stirred for an additional 4 h. The volatiles were evaporated under reduce pressure and the residue was purified via silica gel column chromatography.

General Procedure 2: Palladium catalyzed direct arylation with aryl chlorides and bromides.

To a dried flask was added the diazine *N*-oxide (1.0 to 3.0 equiv.), K_2CO_3 (2.0 equiv.), $Pd(OAc)_2$ (5 mol %) and $HP(t\text{-}Bu)_3BF_4$ (15 mol %). If the arylhalide is a solid, it is added at this point (1.0 equiv.). The flask and its contents were then purged under nitrogen for 10 minutes. If the aryl halide is a liquid, it is added via syringe after purging, followed by the addition of degassed dioxane (to produce a reaction concentration of 0.3 M relative to the halide). The reaction mixture was then heated at 110 °C until the reaction was complete, after which the volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography.

General Procedure 3: Palladium catalyzed direct arylation with with aryl iodides.

To a dried flask was added the diazine *N*-oxide (1.0 to 3.0 equiv.), K_2CO_3 (2.0 equiv.), $Pd(OAc)_2$ (5 mol %), $HP(t\text{-}Bu)_3BF_4$ (15 mol %) and Ag_2CO_3 (0.5 eq.). If the arylhalide is a solid, it is added at this point (1.0 equiv.). The flask and its contents were then purged under nitrogen for 10 minutes. If the aryl halide is a liquid, it is added via syringe after purging, followed by the addition of degassed dioxane (to produce a reaction concentration of 0.3 M relative to the halide). The reaction mixture was then heated at 110 °C until the reaction was complete, after which the volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography.

General Procedure 4: Intermolecular palladium catalysed direct Arylation with pyrimidine *N*-oxides.

To a dried flask was added the diazine *N*-oxide (1.0 to 3.0 equiv.), K_2CO_3 (2.0 equiv.), $Pd(OAc)_2$ (5 mol %), $HP(t\text{-}Bu)_3BF_4$ (15 mol %) CuCN (10 mol%). If the arylhalide is a solid, it is added at this point (1.0 equiv.). The flask and its contents were then purged under nitrogen for 10 minutes. If the aryl halide is a liquid, it is added via syringe after purging, followed by the addition of degassed dioxane (to produce a reaction concentration of 0.3 M relative to the halide). The reaction mixture was then heated at 110 °C until the reaction was complete, after which the volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography.

General Procedure 5: Reduction of the *N*-Oxide moiety (Method 1)

Ammonium formate (~10 equiv.) or H_2 was added to a stirring methanol (0.3M) solution of the *N*-oxide (1.0 eq.) and Pd/C (0.1 eq.) in a round bottom flask. When the reaction was deemed complete by TLC analysis, the reaction was filtered through celite

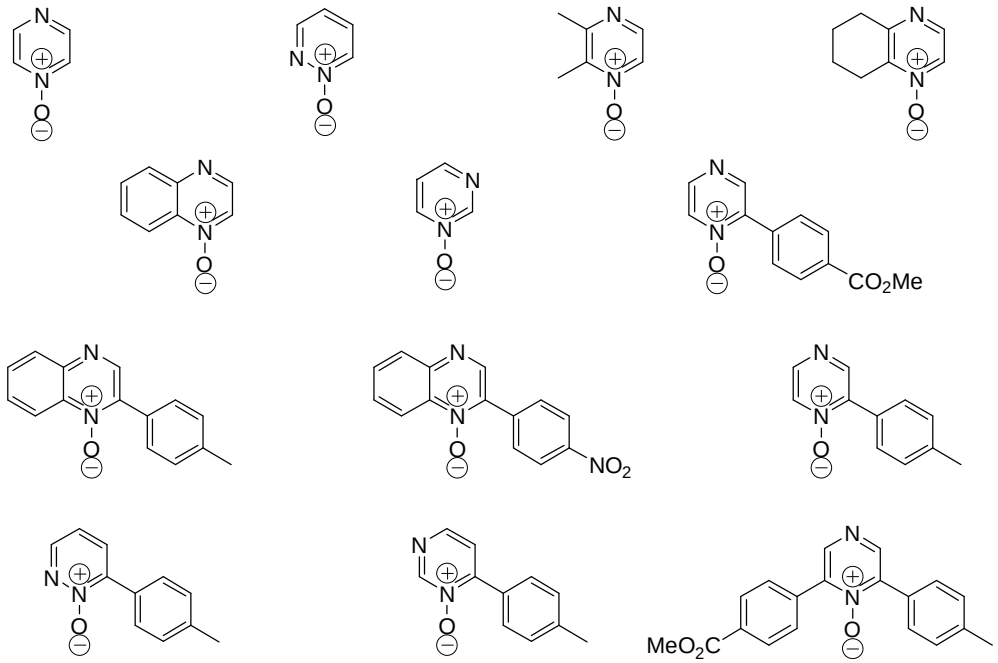
and evaporated under reduced pressure. The residue was then purified via silica gel chromatography.

General Procedure 6: Reduction of the *N*-Oxide moiety (Method 2)

A solution of *N*-oxide (1.0 eq.), Pd/C (0.1 eq.) in NH_4OH (0.2M) was reacted under an atmosphere of H_2 in a round bottom flask. When the reaction was deemed complete by TLC analysis, the reaction was filtered through celite and evaporated under reduced pressure. The residue was then purified via silica gel chromatography.

Calorimetry

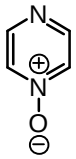
All of the following compounds have been analyzed by differential scanning calorimetry up to 250 °C and showed no sign of exothermic decomposition.



Compound Characterization

Oxidized Diazines

Pyrazine *N*-oxide (1)

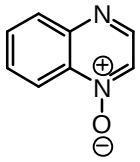


Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 20 % MeOH/EtOAc gave a white solid (88 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.50 (2H, d, *J*= 3.9 Hz), 8.14 (2H, d, *J*= 4.8 Hz).

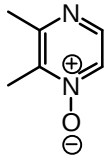
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 147.8, 134.0.
HRMS calculated for $C_4H_4N_2O_1$ (M+) 96.0324; Found: 96.0295.
Melting point °C: 103.2-104.5
IR (ν_{max}/cm^{-1}): 3120, 3088, 1595, 861, 847, 838.
Rf (20 % MeOH/EtOAc**):** 0.3

Quinoxaline *N*-oxide (7)



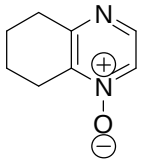
Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc gave a yellow solid (70 %). Spectral data is identical to previous reports[1]

2, 3-dimethylpyrazine *N*-oxide (table 3, entry 8 and 9)



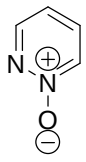
Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 10 %MeOH/EtOAc gave a white solid (88 %). Spectral data is identical to previous reports[2].

5, 6, 7, 8-tetrahydroquinoxaline *N*-oxide (table 3, entry 10 and 11)



Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 5 % MeOH/EtOAc gave a white solid (77 %).
^{1}H NMR (500 MHz, $CDCl_3$, 293K, TMS): d 8.26 (1H, d, *J*= 3.5 Hz), 8.03 (1H, d, *J*= 4 Hz), 2.93 (4H, dt, *J*= 6 and 19 Hz), 1.93-1.89 (4H, m).
^{13}C NMR (125 MHz, $CDCl_3$, 293K, TMS): 157.3, 143.5, 143.2, 131.2, 31.7, 23.5, 21.6, 21.2.
HRMS calculated for $C_8H_{10}N_2O_1$ (M+) 150.0793; Found: 150.0789.
Melting point °C: 74.1-75.0
IR (ν_{max}/cm^{-1}): 3114, 2939, 2879, 1584, 1453, 1296, 975, 830.
Rf (5 % MeOH/EtOAc**):** 0.4

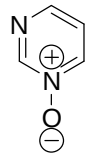
Pyridazine *N*-oxide (3)



Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 20 % MeOH/EtOAc gave a brownish oil (quant.).
1H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.59 (1H, s), 8.33 (1H, d, *J*= 6.6 Hz), 7.92 – 7.87 (1H, m), 7.29 (1H, dd, *J*= 5.7 and 6.6 Hz).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 149.8, 133.9, 133.6, 115.9.
HRMS calculated for $C_4H_4N_2O_1$ (M+) 96.0324; Found: 96.0318.
IR (ν_{max}/cm^{-1}): 3109, 1583, 1416, 982, 847.
Rf (20 % MeOH/EtOAc**):** 0.3

[1] Arthur F. Kluge, Michael L. Maddox, Graham S. Lewis *J. Org. Chem.*, **1980**, 45(10), 1909-1914.
[2] A. Ohta *et. al. J. Heterocycl. Chem.*, **1982**, 19, 465-473.

Pyrimidine *N*-oxide (2)



Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 15 % MeOH/EtOAc gave a white solid (92 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.03 (1H, s), 8.47 (1H, d, *J*= 6.6 Hz), 8.30 (1H, d, *J*= 4.2 Hz), 7.39 (1H, t, *J*= 5.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 149.6, 144.1, 143.5, 121.0.

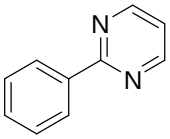
HRMS calculated for $C_4H_4N_2O_1$ (M+) 96.0324; Found: 96.0304.

Melting point °C : 92.0-92.5

IR (ν_{max}/cm^{-1}): 3083, 1653, 1541, 1414, 1251, 843.

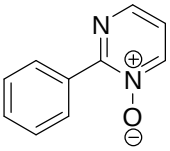
Rf (15 % MeOH/EtOAc**):** 0.3

2-Phenylpyrimidine (supporting information)



To a dried flask was added the 2-chloropyrimidine (0.50 g, 4.37 mmol), phenylboronic acid (0.69 g, 5,68 mmol), Na_2CO_3 (0.92 g, 8.70 mmol), $PdCl_2$ (38,7 mg, 0.22 mmol) and dppb (92.9 mg, 0.22 mmol). The mixture was then purged under nitrogen for 10 minutes, followed by the addition of a degassed mixture of toluene (12 mL), water (6 mL), ethanol (2 mL). The reaction mixture was allowed to stir at 100 °C. After 20 h, the mixture was filtered on a celite pad, then the volatiles were removed under reduced pressure. Purification via silica gel column chromatography using a mixture of 10 % Et_2O/DCM gave a white solid (65 %). Spectral data is identical to previous reports[3].

2-Phenylpyrimidine *N*-oxide (supporting information)



Synthesized according to general procedure **1**. Purification via silica gel column chromatography using 100 % EtOAc then a mixture of 10 % MeOH/EtOAc gave a beige solide.

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.50-8.45 (3H, m), 8.32 (1H, dd, *J*= 1.2 and 3.0 Hz), 7.51-7.49 (3H, m), 7.18 (1H, dd, *J*= 3.0 and 4.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 156.4, 146.6, 143.5, 131.3, 131.1, 129.7, 127.9, 119.2.

HRMS calculated for $C_{10}H_8N_2O$ (M+) 172.0637; Found: 172.0647.

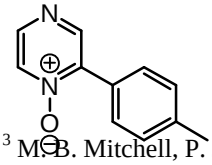
Melting point °C : 89.7-91.2.

IR (ν_{max}/cm^{-1}): 3097, 2933, 1534, 1400, 1249, 722.

Rf (10 % MeOH/EtOAc**):** 0.1

2-Arylpyrazine *N*-Oxides

2-*p*-Tolylpyrazine *N*-oxide (4)

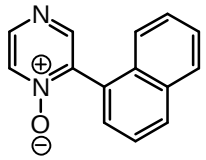


Synthesized according to general procedure **2** employing the corresponding aryl bromide and chloride or **3** with the corresponding aryl iodide. Purification via silica gel column chromatography using

[3] M. B. Mitchell, P. J. Wallbank *Tet. Lett.*, **1991**, *32*(20), 2273.

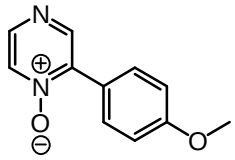
100 % DCM then a mixture of 20 % Acetone/DCM gave a white solid, 72 % (from the bromide), 75 % (from the chloride) and 77 % (from the iodide).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.63 (1H, s), 8.37 (1H, s), 8.20 (1H, s), 7.72 (2H, d, *J*= 8.1 Hz), 7.33 (2H, d, *J*= 7.8 Hz), 2.43 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 148.2, 145.2, 144.6, 140.8, 134.2, 129.8, 129.0, 125.9, 21.5.
HRMS calculated for $C_{11}H_{10}N_2O_1$ (M+) 186.0793; Found: 186.0790.
Melting point °C : 136.1-137.0
IR (ν_{max}/cm^{-1}): 3110, 3038, 2925, 2850, 1590, 1301, 869, 821.
Rf (10 % Acetone/DCM**):** 0.25

2-(Naphthalen-1-yl)pyrazine *N*-oxide (table 2, entry 2, 13 and 14)



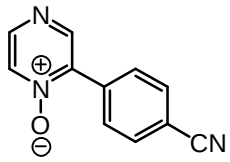
Synthesized according to general procedure **2** employing the corresponding aryl bromide and chloride. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a brown oil, 89 % from the bromide and 60 % from the chloride.
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.61 (1H, s), 8.48 (1H, d, *J*= 3.9 Hz), 8.26 (1H, d, *J*= 4.2 Hz), 8.00 (1H, d, *J*= 7.8 Hz), 7.93-7.87 (1H, m), 7.59-7.37 (5H, m).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 150.1, 147.1, 145.7, 134.8, 133.9, 131.5, 131.3, 129.2, 128.9, 127.6, 127.0, 125.7, 125.3.
HRMS calculated for $C_{14}H_{10}N_2O_1$ (M+) 222.0793; Found: 222.0775.
IR (ν_{max}/cm^{-1}): 3057, 3010, 2923, 2853, 1578, 1301, 873, 801, 776.
Rf (10 % Acetone/DCM**):** 0.5

2-(4-Methoxyphenyl)pyrazine *N*-oxide (table 2, entry 3)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a beige solid (82 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.62 (1H, s), 8.32 (1H, s), 8.18 (1H, s), 7.82 (2H, d, *J*= 8.4 Hz), 7.04 (2H, d, *J*= 8.7 Hz), 3.87 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 161.0, 147.9, 144.7, 144.1, 134.3, 130.6, 120.9, 113.9, 55.3.
HRMS calculated for $C_{11}H_{10}N_2O_2$ (M+) 202.0742; Found: 202.0755.
Melting point °C : 145.0-146.2
IR (ν_{max}/cm^{-1}): 3164, 3082, 2965, 2840, 1456, 1294, 861, 838, 820, 803.
Rf (10 % Acetone/DCM**):** 0.2

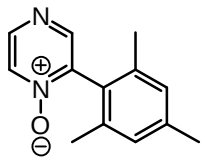
4-(Pyrazin-2-yl)benzonitrile *N*-oxide (table 2, entry 4)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a white solid (53 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.66 (1H, s), 8.48 (1H, d, *J*= 3.9 Hz), 8.24 (1H, d, *J*= 4.2 Hz), 7.97 (2H, d, *J*= 8.1 Hz), 7.82 (2H, d, *J*= 8.1 Hz).

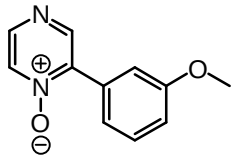
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 148.1, 146.6, 142.8, 134.5, 133.2, 132.2, 129.8, 118.0, 113.9.
HRMS calculated for $C_{11}H_7N_3O_1$ (M+) 197.0589; Found: 197.0565.
Melting point °C : 194.7-196.5.
IR (ν_{max}/cm^{-1}): 3098, 3067, 3046, 2240, 1589, 1389, 870, 836.
Rf (15 % Acetone/DCM**):** 0.3

2-Mesitylpyrazine *N*-oxide (table 2, entry 5)



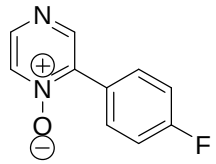
Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a beige solid 70 % yield with 2 eq. of the *N*-oxide and 76 % yield with 3 eq. of the *N*-oxide.
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.45 (1H, d, *J*= 3.9 Hz) 8.42 (1H, s), 8.26 (1H, d, *J*= 4.2 Hz), 7.00 (2H, s), 2.34 (3H, s), 2.07 (6H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 149.4, 146.2, 145.3, 140.0, 137.2, 134.3, 128.5, 125.7, 21.1, 19.4.
HRMS calculated for $C_{13}H_{14}N_2O_1$ (M+) 214.1106; Found: 214.1091.
Melting point °C : 118.0-119.3.
IR (ν_{max}/cm^{-1}): 3106, 2971, 2913, 2855, 1582, 1389, 1007, 862, 843.
Rf (10 % Acetone/DCM**):** 0.3

2-(3-Methoxyphenyl)pyrazine *N*-oxide (table 2, entry 6 and 7)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a white solid, 72 % with 2 eq. of the *N*-oxide and 84 % yield with 3 eq. of the *N*-oxide).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.63 (1H, s), 8.38 (1H, d, *J*= 3.9 Hz), 8.20 (1H, d, *J*= 4.2 Hz), 7.46-7.29 (3H, m), 7.05 (1H, dd, *J*= 1.8 and 8.4 Hz), 3.85 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 159.4, 148.3, 145.5, 144.3, 134.4, 130.0, 129.6, 121.3, 116.2, 114.4, 55.3.
HRMS calculated for $C_{11}H_{10}N_2O_2$ (M+) 202.0742; Found: 202.0770.
Melting point °C : 89.6-90.4.
IR (ν_{max}/cm^{-1}): 3117, 3011, 2976, 2930, 2843, 1591, 1302, 886, 858, 848.
Rf (15 % Acetone/DCM**):** 0.2

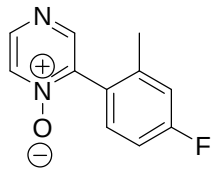
2-(4-Fluorophenyl)pyrazine *N*-oxide (table 2, entry 8)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM, then a mixture of 15 % Acetone/DCM gave a white solid (70 %).
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): d 8.62 (1H, s), 8.39 (1H, d, *J*= 3.0 Hz), 8.21 (1H, d, *J*= 3.0 Hz), 7.84 (2H, dd, *J*= 4.2 and 6.0 Hz), 7.22 (2H, t, *J*= 6.3 Hz).

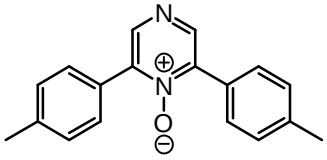
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): 163.7 (d, *J*= 250.1 Hz), 148.1, 145.6, 143.6, 134.4, 131.3 (d, *J*= 8.6 Hz), 124.9 (d, *J*= 3.5 Hz), 115.8 (d, 21.8 Hz).
HRMS calculated for $C_{10}H_7N_2OF$ (M+) 190.0542; Found: 190.0531.
Melting point °C : 169.5-170.1.
IR (ν_{max}/cm^{-1}): 3109, 3073, 3017, 1584, 1458, 1297, 832.
Rf (10 % Acetone/DCM**):** 0.3

2-(4-Fluoro-2-methylphenyl)pyrazine *N*-oxide (table 2, entry 9 and 10)



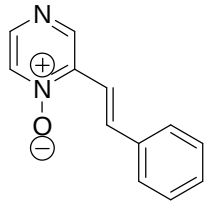
Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM, then a mixture of 10 % Acetone/DCM gave a white solid, 50 % yield with 2 eq. of the *N*-oxide and 96 % yield with 4 eq. of the *N*-oxide.
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): d 8.49 (1H, s), 8.46 (1H, d, *J*= 4.0 Hz), 8.22 (1H, d, *J*= 4.0 Hz), 7.27-7.22 (1H, m), 7.08-7.00 (2H, m), 2.23 (3H, s).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): 163.7 (d, *J*= 248.3 Hz), 149.0, 146.4, 145.4, 141.5 (d, *J*= 8.4 Hz), 134.1, 131.6 (d, *J*= 9.0 Hz), 125.0 (d, *J*= 3.2 Hz), 117.3 (d, *J*= 21.6 Hz), 113.1 (d, *J*= 21.8 Hz), 19.5 (d, *J*= 1.4 Hz)
HRMS calculated for $C_{11}H_9N_2OF$ (M+) 204.0699; Found: 204.0755.
Melting point °C : 75.0-75.4
IR (ν_{max}/cm^{-1}): 3083, 3025, 2925, 1582, 1455, 1297, 866.
Rf (10 % Acetone/DCM**):** 0.45

2,6-dip-tolylpyrazine *N*-oxide (table 2, entry 11)



Synthesized according to general procedure **2** and using 0.3 eq. of pyrazine ***N***-Oxide. Purification via silica gel column chromatography using 100 % DCM gave a beige solid (50 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.53 (2H, s), 7.74 (4H, d, *J*= 8.1 Hz), 7.32 (4H, d, *J*= 7.8 Hz), 2.43 (6H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 145.9, 144.6, 140.4, 129.3, 129.1, 126.5, 21.4.
HRMS calculated for $C_{18}H_{16}N_2O$ (M+) 276.1263; Found: 276.1279.
Melting point °C : 146.0-147.6
IR (ν_{max}/cm^{-1}): 3026, 2922, 2862, 1500, 1297, 865, 826.
Rf (100 % DCM**):** 0.7

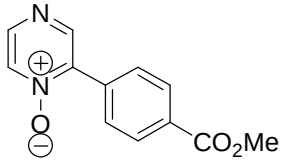
2-Styrylpyrazine *N*-oxide (table 2, entry 12)



Synthesized according to general procedure **2.** Purification via silica gel column chromatography using 100 % DCM, then a mixture of 10 % Acetone/DCM gave a brownish solid, 32 % yield with 2 eq. of the *N*-oxide and 40 % yield with 3 eq. of the *N*-oxide).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.82 (1H, s), 8.31-8.22 (1H, m), 8.14-8.11 (1H, m), 7.72 (1H, d, *J*= 16.5 Hz), 7.62 (2H, dd, *J*= 3.0 and 7.8 Hz), 7.53 (1H, d, *J*= 16.5 Hz), 7.45-7.34 (3H, m)

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 145.8, 143.9, 136.7, 135.7, 133.9, 129.5, 128.9, 128.4, 127.5, 115.6.
HRMS calculated for $C_{12}H_{10}N_2O$ (M+) 198.0793; Found: 198.0786.
Melting point °C : 152.0-153.3
IR (ν_{max}/cm^{-1}): 3112, 3061, 3024, 1589, 1410, 1273, 981.
Rf (10 % Acetone/DCM**):** 0.35

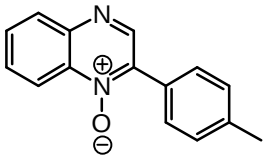
Methyl 4-(pyrazin-2-yl)benzoate *N*-oxide (table 2, entry 16)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a beige solid (82 %).
^{1}H NMR (300 MHz, DMSO, 383K): d 8.77 (1H, s), 8.50 (1H, d, *J*= 4.2 Hz), 8.38 (1H, d, *J*= 4.5 Hz), 8.08 (2H, d, *J*= 8.7 Hz), 8.01 (2H, d, *J*= 8.7 Hz), 3.92 (3H, s).
^{13}C NMR (75 MHz, DMSO, 383K): 165.1, 147.5, 146.0, 142.0, 133.9, 133.2, 130.4, 128.8, 128.2, 51.4.
HRMS calculated for $C_{12}H_{10}N_2O_3$ (M+) 230.0691; Found: 230.0686.
Melting point °C : 215.9-217.1.
IR (ν_{max}/cm^{-1}): 3074, 2917, 2854, 1722, 1384, 1278, 856.
Rf (10 % Acetone/DCM**):** 0.2

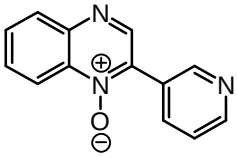
Substituted Arylpyrazine *N*-Oxides

2-*p*-Tolylquinoxaline *N*-oxide (table 3, entry 1)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM gave a yellow solid (68 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.89 (1H, s), 8.69-8.65 (1H, m), 8.13-8.10 (1H, m), 7.91 (2H, d, *J*= 8.1 Hz), 7.81-7.73 (2H, m), 7.37 (2H, d, *J*= 8.1 Hz), 2.44 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 147.3, 144.2, 140.6, 139.2, 137.3, 130.9, 130.3, 129.8, 129.3, 129.2, 126.9, 119.2, 21.5.
HRMS calculated for $C_{15}H_{12}N_2O_1$ (M+) 236.0871; Found: 236.0958.
Melting point °C : 149.1-150.5
IR (ν_{max}/cm^{-1}): 3127, 3034, 2920, 2856, 1578, 1488, 1351, 818, 763, 749.
Rf (5 % Acetone/DCM**):** 0.4

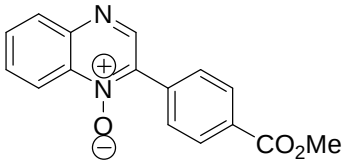
2-(Pyridin-3-yl)quinoxaline *N*-oxide (table 3, entry 2 and 3)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 10 % Acetone/DCM, then a mixture of 40 % Acetone/DCM gave a white solid 50 % with 1 eq. of the *N*-oxide and 80 % yield with 2 eq. of the *N*-oxide).
^{1}H NMR (300 MHz, DMSO, 293K): d 9.18 (2H, d, *J*= 16.8 Hz),

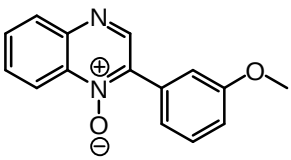
8.72 (1H, s), 8.55-8.47 (2H, m), 8.17 (1H, d, *J*= 7.8 Hz), 8.00-7.78 (2H, m), 7.62 (1H, m).
^{13}C NMR (75 MHz, DMSO, 293K): 150.5, 149.9, 147.6, 144.2, 137.1, 136.4, 136.4, 131.7, 130.7, 129.7, 126.2, 123.2, 118.6.
HRMS calculated for $C_{13}H_9N_3O_1$ (M+) 223.0746; Found: 223.0726.
Melting point °C : 181.9-183.0
IR (ν_{max}/cm^{-1}): 3103, 3063, 3025, 2920, 1491, 1327, 902, 782, 770, 753.
Rf (10 % Acetone/DCM**):** 0.1

Methyl 4-(quinoxalin-2-yl)benzoate *N*-oxide (table 3, entry 4)



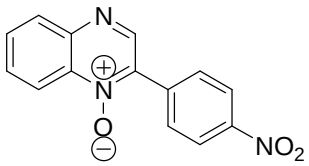
Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 2.5 % Acetone/DCM, then a mixture of 5 % Acetone/DCM gave a beige solid (84 %).
^{1}H NMR (300 MHz, CDCl$_3$, 293K, TMS): d 8.92 (1H, s), 8.68 (1H, dd, *J*= 1.5 and 9 Hz), 8.23 (2H, d, *J*= 8.7 Hz), 8.16 (1H, d, *J*= 7.8 Hz), 8.08 (2H, d, *J*= 8.7 Hz), 7.82 (2 H, m), 3.98 (3H, s).
^{13}C NMR (75 MHz, CDCl$_3$, 293K): 166.3, 147.0, 144.7, 138.4, 137.4, 134.2, 131.5, 131.4, 130.7, 130.1, 129.7, 129.4, 119.3, 52.4.
HRMS calculated for $C_{16}H_{12}N_2O_3$ (M+) 280.0848; Found: 280.0824.
Melting point °C : 219.3-220.0
IR (ν_{max}/cm^{-1}): 3116, 3061, 2987, 1715, 1491, 1349, 901, 766.
Rf (5 % Acetone/DCM**):** 0.35

2-(3-Methoxyphenyl)quinoxaline *N*-oxide (table 3, entry 5)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 2 % Acetone/DCM gave a yellow solid (57 %).
^{1}H NMR (300 MHz, CDCl$_3$, 293K, TMS): d 8.90 (1H, s), 8.67 (1H, d, *J*= 7.8 Hz), 8.12 (1H, d, *J*= 7.5 Hz), 7.83-7.74 (2H, m), 7.61 (1H, s), 7.48 (1H, m), 7.07 (1H, d, *J*= 6.3 Hz), 3.88 (3H, s).
^{13}C NMR (75 MHz, CDCl$_3$, 293K, TMS): 159.4, 147.3, 144.3, 139.0, 137.3, 131.1, 131.0, 130.3, 129.9, 129.6, 121.6, 119.2, 116.3, 114.5, 55.3.
HRMS calculated for $C_{15}H_{12}N_2O_2$ (M+) 252.0899; Found: 252.0911.
Melting point °C : 132.0-133.6
IR (ν_{max}/cm^{-1}): 3066, 3013, 2970, 2930, 1491, 1354, 1033, 760, 755.
Rf (2 % Acetone/DCM**):** 0.3

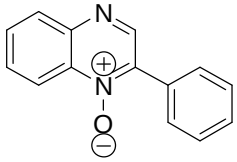
2-(4-Nitrophenyl)quinoxaline *N*-oxide (table 3, entry 6)



Synthesized according to general procedure **3**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 3 % Acetone/DCM, then a mixture of 5 % Acetone/DCM gave a yellow solid (70 %).
^{1}H NMR (300 MHz, DMSO, 368 K): d 9.09 (1H, s), 8.58 (1H, d, *J*= 8.7 Hz), 8.42-8.28 (4H, m), 8.18 (1H, d, *J*= 9 Hz), 8.02-7.84 (2H, m).

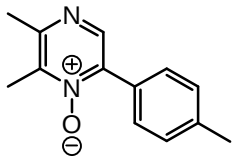
^{13}C NMR (75 MHz, DMSO, 368K): 149.1, 148.3, 145.5, 138.0, 137.8, 137.2, 132.8, 131.8, 131.6, 130.7, 124.1, 119.7.
HRMS calculated for $C_{14}H_9N_3O_3$ (M+) 267.0644; Found: 267.0645.
Melting point °C : 255 (decomp.)
IR (ν_{max}/cm^{-1}): 3108, 2955, 2921, 1519, 1338, 842, 763.
Rf (5 % Acetone/DCM**):** 0.4

2-Phenylquinoxaline *N*-oxide (table 3, entry 7)



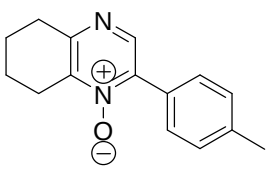
Synthesized according to general procedure **3**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 3 % Acetone/DCM gave a beige solid (84 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.90 (1H, s), 8.69 (1H, d, *J*= 7.8 Hz), 8.13 (1H, d, *J*= 9.3 Hz), 7.99 (2H, d, *J*= 7.8 Hz), 7.79 (2H, m), 7.62-7.48 (3H, m).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 147.4, 144.4, 139.2, 137.3, 131.1, 130.4, 130.2, 129.9, 129.8, 129.3, 128.6, 119.3.
HRMS calculated for $C_{14}H_{10}N_2O$ (M+) 222.0793; Found: 222.0791.
Melting point °C : 153.4-155.0.
IR (ν_{max}/cm^{-1}): 3049, 3006, 1485, 1317, 893, 766.
Rf (3 % Acetone/DCM**):** 0.3

2,3-dimethyl-5-*p*-tolylpyrazine *N*-oxide (table 3, entry 8 and 9)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a white solid, 40 % yield with 0.5 eq. of the *N*-oxide, 18 % yield with 1 eq. of the *N*-oxide, 48 % yield with 2 eq. of the *N*-oxide and 56 % with 3 eq. of the *N*-oxide
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.36 (1H, s), 7.67 (1H, d, *J*= 3.9 Hz), 7.30 (1H, d, *J*= 4.2 Hz), 2.62 (3H, s), 2.54 (3H, s), 2.42 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 153.5, 143.3, 142.7, 141.8, 139.9, 129.0, 129.0, 127.0, 22.5, 21.4, 13.3.
HRMS calculated for $C_{13}H_{14}N_2O_1$ (M+) 214.1106; Found: 214.1117.
Melting point °C : 135.1-136.8.
IR (ν_{max}/cm^{-1}): 3028, 2996, 2918, 1585, 1464, 1300, 879, 817.
Rf (10 % Acetone/DCM**):** 0.3

5,6,7,8-tetrahydro-2-*p*-tolylquinoxaline *N*-oxide (table 3, entry 10 and 11)

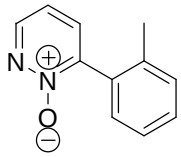


Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM, then a mixture of 5 % Acetone/DCM gave a white solid, 34 % yield with 1 eq. of the *N*-oxide, 52 % yield with 2 eq. of the *N*-oxide and 56 % yield with 3 eq. of the *N*-oxide.
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.41 (1H, s), 7.68 (2H, d, *J*= 8.1 Hz), 7.30 (2H, d, *J*= 8.1 Hz), 3.03-2.90 (4 H, m), 2.01-1.84 (4H, m).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 154.8, 143.7, 143.4, 141.7, 139.9, 129.1, 126.9, 31.8, 24.1, 21.7, 21.5, 21.4.
HRMS calculated for $C_{15}H_{16}N_2O_1$ (M+) 240.1263; Found: 240.9852.
Melting point °C : 149.0-151.6.
IR (ν_{max}/cm^{-1}): 3031, 2950, 2871, 1584, 1459, 1300, 819.
Rf (10 % Acetone/DCM**):** 0.45

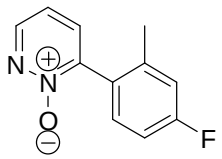
2-Arylpyridazine *N*-Oxides

3-*o*-Tolylpyridazine *N*-oxide (5)



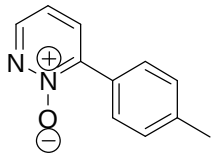
Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a brownish oil (72 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.48 (1H, d, *J*= 7.2 Hz), 7.63 (1H, dd, *J*= 2.4 and 6 Hz), 7.41-7.20 (4H, m), 7.13 (1H, dd, *J*= 5.4 and 6 Hz), 2.23 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 149.6, 145.7, 137.6, 135.4, 131.6, 130.2, 129.8, 129.1, 125.9, 115.7, 19.2.
HRMS calculated for $C_{11}H_{10}N_2O_1$ (M+) 186.0793; Found: 186.0790.
IR (ν_{max}/cm^{-1}): 3058, 2955, 2866, 1539, 1369, 768.
Rf (10 % Acetone/DCM**):** 0.35

3-(4-Fluoro-2-methylphenyl)pyridazine *N*-oxide (table 3, entry 13)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM, then a mixture of 15 % Acetone/DCM gave a brownish oil (74 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.54-8.44 (1H, m), 7.64 (1H, dd, *J*= 2.4 and 9.0 Hz), 7.23-7.13 (2H, m), 7.04-6.95 (2H, m), 2.23 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 163.3 (d, *J*= 247.7 Hz), 149.8, 144.9, 140.6 (d, *J*= 8.5 Hz), 135.5, 131.0 (d, *J*= 9 Hz), 127.6 (d, *J*= 3.2 Hz), 117.2 (d, *J*= 21.6 Hz), 115.7, 113.0 (d, 21.8 Hz), 19.4.
HRMS calculated for $C_{11}H_9N_2OF$ (M+) 204.0699; Found: 204.0717.
IR (ν_{max}/cm^{-1}): 3073, 3033, 2932, 1572, 1449, 1303, 871.
Rf (10 % Acetone/DCM**):** 0.25

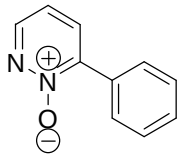
3-*p*-Tolylpyridazine *N*-oxide (table 3, entry 14)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM gave white solid (73 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.40 (1H, m), 7.75 (1H, dd, *J*= 2.1 and 6.0 Hz), 7.71 (2H, d, *J*= 8.1 Hz), 7.28 (2H, d, *J*= 7.8 Hz), 7.13 (1H, dd, *J*= 5.1 and 6.0 Hz), 2.40 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 148.7, 144.3, 140.3, 134.4, 129.0, 128.7, 128.3, 116.3, 21.3.

HRMS calculated for $C_{11}H_{10}N_2O$ (M+) 186.0793; Found: 186.0768.
Melting point °C : 160.1-161.6.
IR (ν_{max}/cm^{-1}): 3031, 2918, 1451, 1359, 1291, 828, 783.
Rf (10 % Acetone/DCM**):** 0.4

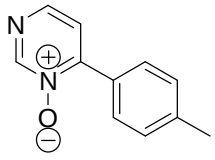
3-Phenylpyridazine *N*-oxide (table 3, entry 15)



Synthesized according to general procedure **3**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a white solid (91 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.47-8.38 (1H, m), 7.86-7.74 (3H, m), 7.50-7.43 (3H, m), 7.15 (1H, dd, *J*= 5.1 and 9 Hz).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 149.1, 144.3, 134.6, 131.3, 130.0, 128.8, 128.4, 116.3.
HRMS calculated for $C_{10}H_8N_2O$ (M+) 172.0637; Found: 172.0612.
Melting point °C : 124.3-126.1.
IR (ν_{max}/cm^{-1}): 3078, 2920, 1542, 1375, 871, 685.
Rf (10 % Acetone/DCM**):** 0.3

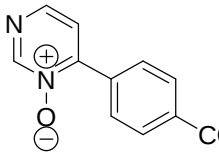
2-Arylpyrimidine *N*-Oxides

4-*p*-Tolylpyrimidine *N*-oxide (table 3, entry 16)



Synthesized according to general procedure **4**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a beige-orange solid (61 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.07 (1H, s), 8.21 (1H, d, *J*= 3 Hz), 7.91 (2H, d, *J*= 4.8 Hz), 7.45 (1H, d, *J*= 3 Hz), 7.34 (2H, d, *J*= 5.1 Hz), 2.44 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 153.6, 151.2, 143.0, 141.9, 129.3, 128.9, 126.9, 120.8, 21.6.
HRMS calculated for $C_{11}H_{10}N_2O$ (M+) 186.0793; Found: 186.0780.
Melting point °C : 121.8-123.1.
IR (ν_{max}/cm^{-1}): 3076, 3035, 2922, 1371, 1255, 1038, 849, 808.
Rf (10 % Acetone/DCM**):** 0.3

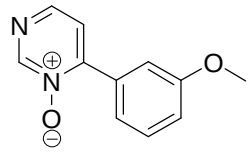
Methyl 4-(pyrimidin-4-yl)benzoate *N*-oxide (table 3, entry 19)



Synthesized according to general procedure **4**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 20 % Acetone/DCM gave a beige solid (50 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.11 (1H, s), 8.28 (1H, d, *J*= 5.1 Hz), 8.19 (2H, d, *J*= 8.4 Hz), 8.06 (2H, d, *J*= 8.1 Hz), 7.49 (1H, d, *J*= 4.8 Hz), 3.97 (3H, s).

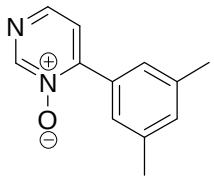
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 151.2, 143.3, 133.9, 132.3, 129.9, 129.7, 129.1, 121.2, 99.4, 52.5.
HRMS calculated for $C_{12}H_{10}N_2O_3$ (M+) 230.2194; Found: 230.0671.
IR (ν_{max}/cm^{-1}): 3029, 2920, 2857, 1733, 1652, 1254, 739.
Rf (20 % Acetone/DCM**):** 0.3

2-(3-Methoxyphenyl)pyrimidine *N*-oxide (table 3, entry 18)



Synthesized according to general procedure **4**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 20 % Acetone/DCM gave an orange oil (62 %).
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): d 9.08 (1H, s), 8.23 (1H, d, *J*= 4.8 Hz), 7.61 (1H, m), 7.46-7.41 (3H, m), 7.08 (1H, dt, *J*= 2.4 and 9.6 Hz), 3.86 (3H, s).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): 159.4, 153.4, 151.1, 143.3, 130.9, 129.6, 121.2, 121.2, 117.2, 114.2, 55.4.
HRMS calculated for $C_{11}H_{10}N_2O_2$ (M+) 202.0742; Found: 202.0762.
IR (ν_{max}/cm^{-1}): 3080, 2962, 2837, 1696, 1585, 1477, 1258, 1028.
Rf (20 % Acetone/DCM**):** 0.25

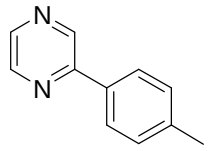
2-(3,5-dimethylphenyl)pyrimidine *N*-oxide (table 3, entry 17)



Synthesized according to general procedure **4**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a orange oil (55 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.08 (1H, s), 8.22 (1H, d, *J*= 4.8 Hz), 7.55 (2H, s), 7.42 (1H, d, *J*= 5.1 Hz), 7.17 (1H, s), 2.39 (6H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 151.0, 143.2, 138.2, 132.9, 129.6, 126.6, 121.2, 21.3. 2 peaks are overlaping.
HRMS calculated for $C_{11}H_{12}N_2O$ (M+) 200.0950; Found: 200.0970.
IR (ν_{max}/cm^{-1}): 3090, 2920, 2860, 1698, 1579, 1373, 1254, 834.
Rf (15 % Acetone/DCM**):** 0.3

Deoxygenated Aryldiazines

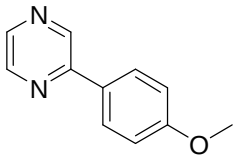
2-*p*-*T*olylpyrazine (table 4, entry 1)



Synthesized according to general procedure **5**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 2.5 % Acetone/DCM gave a white solid (86 %).
Exhibited identical spectral data according to previous reports[4].

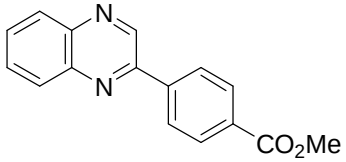
[4] D. H. Huh, H. Ryu and Y. G. Kim *Tetrahedron*, **2004,** 60, 9857-9862.

2-(4-Methoxyphenyl)pyrazine (table 4, entry 2)



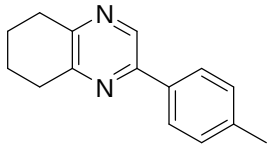
Synthesized according to general procedure **5**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM gave a white solid (82 %).
Exhibited identical spectral data according to previous reports[4].

Methyl 4-(quinoxalin-2-yl)benzoate (table 4, entry 3)



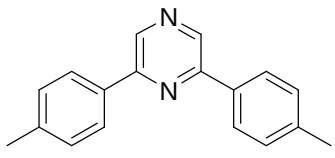
Synthesized according to general procedure **5**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a yellow solid (98 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.35 (1H, s), 8.29-8.11 (6H, m), 7.84-7.72 (2H, m), 3.97 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 166.5, 150.5, 143.1, 142.1, 141.7, 140.7, 131.3, 130.5, 130.2, 130.0, 129.7, 129.1, 127.4, 52.3.
HRMS calculated for $C_{16}H_{12}N_2O_2$ (M+) 264.0899; Found: 264.0883.
Melting point °C : 141.0-142.6.
IR (ν_{max}/cm^{-1}): 2952, 2924, 2853, 1733, 1605, 1285, 772, 755.
Rf (10 % Acetone/DCM**):** 0.6

5,6,7,8-tetrahydro-2-*p*-Tolylquinoxaline (table 4, entry 4)



Synthesized according to general procedure **5**. Purification via silica gel column chromatography using 100 % DCM then a mixture of 3 % Acetone/DCM gave a white solid (84 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.71 (1H, s), 7.87 (2H, d, *J*= 8.1 Hz), 7.29 (2H, d, *J*= 8.1 Hz), 3.06-2.93 (4H, m), 2.41 (3H, s), 2.00-1.90 (4H, m).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 152.1, 150.7, 149.7, 139.2, 138.6, 134.1, 129.6, 126.6, 32.2, 31.7, 22.7, 21.3. 2 peaks are overlaping.
HRMS calculated for $C_{15}H_{16}N_2$ (M+) 224.1313; Found: 224.1326.
Melting point °C : 80.0-81.2.
IR (ν_{max}/cm^{-1}): 3067, 3017, 2943, 2862, 1451, 1143, 826.
Rf (3 % Acetone/DCM**):** 0.45

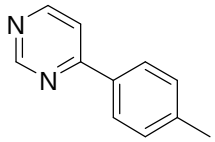
2,6-di*p*-tolylpyrazine (table 4, entry 5)



Synthesized according to general procedure **5**. Purification via silica gel column chromatography using 100 % DCM gave a white solid (76 %).
Exhibited identical spectral data according to previous reports[5].

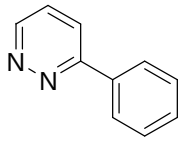
[5] G. Jia, Z. Lim and Y. Zhang *Heteroatom Chemistry*, **1998**, 9(3), 3341-345.

4-*p*-Tolylpyrimidine (table 4, entry 10)



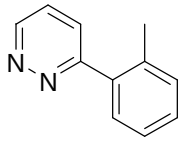
Synthesized according to general procedure **6**. Purification via silica gel column chromatography using a mixture of 5 % Acetone/DCM gave a beige solid (81 %).
Exhibited identical spectral data according to previous reports[6].

3-Phenylpyridazine (table 4, entry 6 and 7)



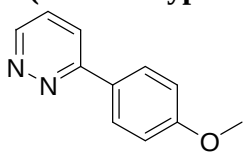
Synthesized according to general procedure **6**. The product was obtained pure without purification (87 %).
Exhibited identical spectral data according to previous reports[7].

3-*o*-*T*olylpyridazine (table 4, entry 8)



Synthesized according to general procedure **6**. Purification via silica gel column chromatography using a mixture of 30 % EtOAc /Benzene, then a mixture of 45 % EtOAc /Benzene gave brown oil (70 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.20 (1H, dd, *J*= 1.8 and 6.0 Hz), 7.61-7.53 (2H, m), 7.46-7.31 (4H, m), 2.40 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 162.2, 149.6, 137.2, 136.1, 130.9, 129.8, 129.2, 127.2, 126.1, 126.1, 20.3.
HRMS calculated for $C_{11}H_{10}N_2$ (M+) 170.0844; Found: 170.0838.
IR (ν_{max}/cm^{-1}): 3065, 2963, 2928, 1580, 1435, 765.
Rf (30 % EtOAc/Benzene**):** 0.3

3-(4-Methoxyphenyl)pyridazine (table 4, entry 9)



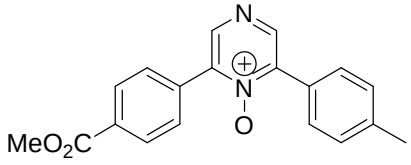
Synthesized according to general procedure **6**. Purification via silica gel column chromatography using a mixture of 35 % EtOAc /Benzene, then a mixture of 50 % EtOAc /Benzene gave brown oil (70 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 9.10 (1H, d, *J*= 4.5 Hz), 8.06 (2H, d, *J*= 9.0 Hz), 7.80 (1H, d, *J*= 9.6 Hz), 7.49 (1H, dd, *J*= 4.8 and 9.0 Hz), 7.05 (2H, d, *J*= 8.7 Hz), 3.88 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 161.3, 158.9, 149.4, 128.7, 128.4, 126.6, 123.1, 114.4, 55.3.
HRMS calculated for $C_{11}H_{10}N_2O$ (M+) 186.0793; Found: 186.0794.
Melting point °C : 110.4-111.1.
IR (ν_{max}/cm^{-1}): 3054, 2929, 2847, 1612, 1436, 1249, 1025, 811.
Rf (30 % EtOAc/benzene**):** 0.2

---

[6] S. N. Balasubrahmanyam, B. Jeyashri and I. N. N. Namboothiri *Tetrahedron*, **1994,** 50(27), 8127-8142.
[7] M. S. South, T. L. Jakuboski, M. D. Westmeyer and D. R. Dukesherer *J. Org. Chem.*, **1996,** 61(25), 8921-8934.

Functionalized Diazine *N*-Oxides

Methyl 4-(6-*p*-tolylpyrazin-2-yl)benzoate (9)



Synthesized according to general procedure **2**. Purification via silica gel column chromatography using 15 % Acetone/DCM then a mixture of 25 % Acetone/DCM gave a beige solid (74 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.58 (2H, d, *J*= 10.8 Hz), 8.18 (2H, d, *J*= 8.4 Hz), 7.93 (2H, d, *J*= 8.4 Hz), 7.74 (2H, d, *J*= 8.1 Hz), 7.33 (2H, d, *J*= 8.1 Hz), 3.96 (3H,s), 2.43 (3H,s).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 166.3, 146.9, 146.0, 144.8, 143.7, 140.7, 133.9, 131.4, 129.5, 129.4, 129.2, 129.2, 126.2, 52.3, 21.5.

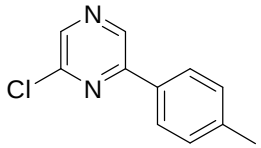
HRMS calculated for $C_{19}H_{16}N_2O_3$ (M+) 320.1161; Found: 320.1141.

Melting point °C : 178.5-180.5.

IR (ν_{max}/cm^{-1}): 2964, 2921, 2854, 1727, 1612, 1291, 1105, 815.

Rf (10 % Acetone/DCM**):** 0.15

2-Chloro-6-*p*-tolylpyrazine (10)



To a solution of toluene (1.0 mL) and DMF (1.0 mL) was added $POCl_3$ (0.049 mL, 0.54 mmol). The mixture was stirred for 10 minutes at 0 ^{o}C, then 2-*p*-tolylpyrazine ***N***-oxide (50 mg, 0.27 mmol) in DMF (0.5 mL) was added. After 10 minutes, the reaction mixture was allowed to warm to room temperature and stirred over night. The solvent was then evaporated via Kugelrohr distillation. The residue was cooled in a ice bath and a saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted 3 times with DCM. The combined organic phases was dried over MgSO4, filtered and concentrated under vacuum to give a pure pale yellow solid (54 mg, 98 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.89 (1H, s), 8.47 (1H, s), 7.92 (2H, d, *J*= 7.8 Hz), 7.31 (2H, d, *J*= 7.8 Hz), 2.42 (3H, s).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 152.5, 148.8, 141.9, 140.9, 139.1, 131.9, 129.8, 126.9, 21.4.

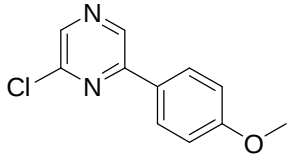
HRMS calculated for $C_{11}H_9N_2Cl$ (M+) 204.0454; Found: 204.0447.

Melting point °C : 72.5-73.7.

IR (ν_{max}/cm^{-1}): 3029, 2919, 2855, 1507, 1158, 1005, 821.

Rf (10 % Acetone/DCM**):** 0.5

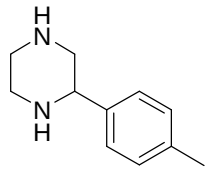
2-Chloro-6-(4-methoxyphenyl)pyrazine (supporting information)



To a solution of toluene (1.0 mL) and DMF (1.0 mL) was added $POCl_3$ (0.045 mL, 0.49 mmol). The mixture was stirred for 10 minutes at 0 ^{o}C, then 2-(4-methoxyphenyl)pyrazine ***N***-oxide (50 mg, 0.25 mmol) in DMF (0.5 mL) was added. After 10 minutes, the reaction mixture was allowed to warm to room temperature and stirred over night. The solvent was then evaporated via Kugelrohr distillation. The residue was cooled in a ice bath and a saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted 3 times with DCM. The combined organic

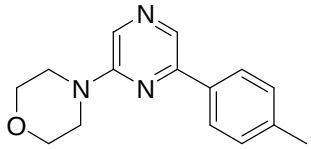
phases was dried over MgSO4, filtered and concentrated under vacuum to give a pure pale yellow solid (47.3 mg, 87 %).
Exhibited identical spectral data according to previous reports[8].

2-*p*-Tolylpiperazine (13)



To a round bottom flask was added Pt_2O (8 mg, 0.03 mmol) and 2-*p*-tolylpyrazine ***N***-oxide (50 mg, 0.27 mmol). The mixture was then purged under nitrogen for 10 minutes. Addition of the acetic acid (3 mL) was followed by the addition of hydrogen via a balloon. When complete, the reaction mixture was filtered trought a pad of celite, and the solvent was evaporated via Kugelrohr distillation. A 10 % solution of NaOH was added and the aqueous layer was extracted 3 times with DCM. The combined organic phases was dried over MgSO4, filtered and concentrated under vacuum to give a pure beige solid (32 mg, 68 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 7.27 (2H, d, *J*= 7.8 Hz), 7.13 (2H, *J*= 7.8 Hz), 3.71 (1H, dd, *J*= 2.4 and 9 Hz), 3.13-2.82 (5H, m), 2.70 (1H, dd, *J*= 10.2 and 12 Hz), 2.33 (3H, s), 1.84 (2H,s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 139.7, 137.0, 129.0, 126.7, 61.7, 54.3, 47.8, 46.0, 21.0.
HRMS calculated for $C_{11}H_6N_2$ (M+) 176.1313; Found: 176.1319.
Melting point °C : 88.7-90.3.
IR (ν_{max}/cm^{-1}): 3274, 3018, 2940, 2826, 1514, 813.
Rf (10 % Acetone/DCM**):** 0.05

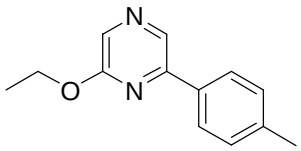
2-Morpholino-6-*p*-tolylpyrazine (11)



To a dry Schlenck tube was added 2-chloro-6-*p*-tolylpyrazine (60 mg, 0.29 mmol), sodium *tert*-butoxide (40 mg, 0.41 mmol), $Pd(OAc)_2$ (2 mg, 0.01 mmol) and 2-(dicyclohexylphosphino) biphenyl (6 mg, 0.02). The mixture was then purged under nitrogen for 10 minutes. Addition of morpholine (0.031 mL, 0.35 mmol) was followed by the addition of degassed toluene (1.0 mL). The reaction mixture was heated at 100 ^{o}C over night. The reaction was filtered trought a pad of celite, and the solvent was evaporated under reduce pressure. Purification of the residue via silica gel column chromatography using 100 % DCM, then a mixture of 5 %Acetone/DCM gave a pale yellow solid (70 %).
^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.37 (1H, s), 8.03 (1H, s), 7.90 (2H, d, *J*= 8.1 Hz), 7.27 (2H, d, *J*= 8.1 Hz), 3.86 (4H, t, *J*= 4.5 Hz), 3.65 (4H, t, *J*= 5.1 Hz), 2.40 (3H,s).
^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 154.1, 149.3, 139.5, 134.1, 130.2, 129.4, 128.3, 126.6, 66.6, 44.7, 21.3.
HRMS calculated for $C_{15}H_{17}N_3O$ (M+) 255.1372; Found: 255.1362.
Melting point °C : 88.9-90.1.
IR (ν_{max}/cm^{-1}): 3058, 2963, 2854, 1525, 1253, 820.
Rf (5 % Acetone/DCM**):** 0.3

[8] F. Buron, N. Ple, A. Turck and G. Queguiner *J. Org. Chem.*, **2005**, 70(7), 2616.

2-Ethoxy-6-*p*-tolylpyrazine (12)



To a round bottom flask was added 2-chloro-6-*p*-tolylpyrazine (60 mg, 0.29 mmol), sodium ethoxide (60 mg, 0.88 mmol) and EtOH (3 mL). The reaction mixture was heated at 90 ^{o}C for 2 days. The solvent was evaporated under reduce pressure and the residue was extracted 3 times using water/brine and DCM. The combined organic phases was dried over MgSO4, filtered and concentrated under vacuum. Purification of the residue via silica gel column chromatography using 100 % DCM, then a mixture of 2 %Acetone/DCM gave a pale yellow solid (85 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.55 (1H, s), 8.10 (1H, s), 7.92 (2H, d, *J*= 7.8 Hz), 7.28 (2H, d, *J*= 7.8 Hz), 4.50 (2H, q, *J*= 6.9 Hz), 2.41 (3H, s), 1.45 (3H, t, *J*= 6.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 159.4, 148.9, 139.7, 133.5, 133.2, 132.6, 129.5, 126.6, 61.9, 21.3, 14.4.

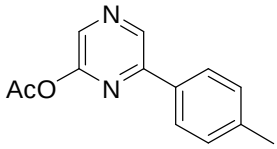
HRMS calculated for $C_{13}H_{14}N_2O$ (M+) 214.1106; Found: 214.1115.

Melting point °C : 61.5-62.8.

IR (ν_{max}/cm^{-1}): 3070, 2981, 2920, 1538, 1424, 826.

Rf (2 % Acetone/DCM**):** 0.3

6-*p*-Tolylpyrazin-2-yl acetate (8)



To a round bottom flask was added 2-*p*-tolylpyrazine ***N***-Oxide and acetic anhydride (0.65 mL). The solvent was evaporated via Kugelrohr distillation and the residue was stirred over night at 50 ^{o}C in a acetone / silica gel mixture . The solvent was removed under vacum purified via silica gel column chromatography using a mixture of 20 %Acetone/DCM. A yellow oil was obtained (71 %).

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): d 8.92 (1H, s), 8.39 (1H, s), 7.90 (2H, d, *J*= 8.1 Hz), 7.30 (2H, d, *J*= 8.1 Hz), 2.41 (6H, s).

^{13}C NMR (75 MHz, $CDCl_3$, 293K, TMS): 168.5, 153.8, 151.4, 140.6, 139.0, 136.2, 132.2, 129.8, 127.0, 21.4, 21.1.

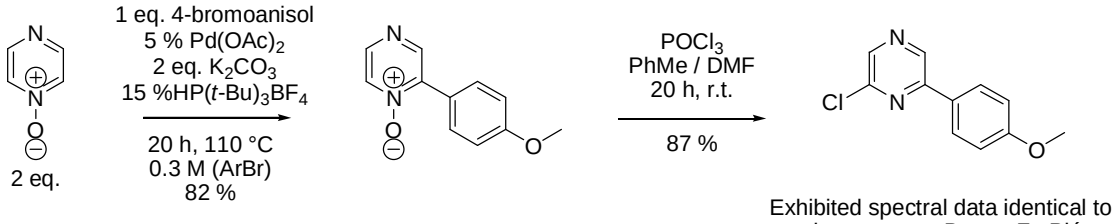
HRMS calculated for $C_{13}H_{12}N_2O_2$ (M+) 228.0899; Found: 228.0880.

IR (ν_{max}/cm^{-1}): 3062, 2924, 2855, 1773, 1531, 1185, 822.

Rf (20 % Acetone/DCM**):** 0.3

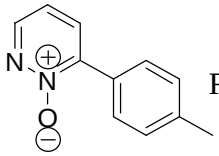
Structural Proof (Arylation Regiochemistry)

Pyrazine *N*-oxides



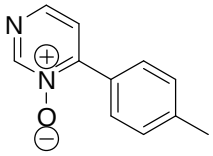
Exhibited spectral data identical to previous reports: Buron, F., Plé, N., Turck, A., Queguigner, G.; *J. Org. Chem*., **2005**, 70, 2616-2621.

Pyridazine *N*-oxide



Regiochemistry was proven via X-ray crystallographic analysis. See crystallographic data ; registry number : CCDC 612951

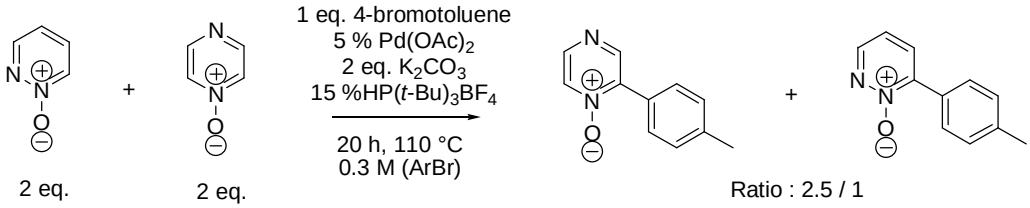
Pyrimidine *N*-oxide



Regiochemistry was proven via X-ray crystallographic analysis. See crystallographic data ; registry number : CCDC 612952

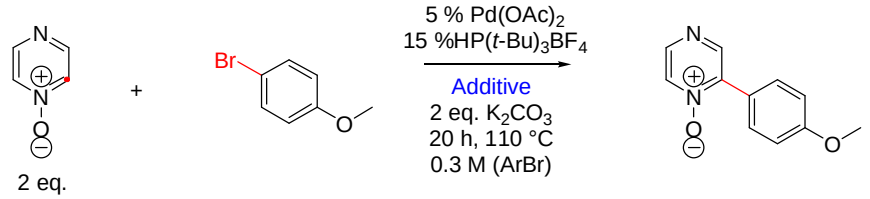
Competition Experiments

Pyrazine *N*-Oxide Vs Pyridazine *N*-Oxide



To a dried flask was added both *N*-oxide (2.0 eq. each), K_2CO_3 (2.0 eq.), $Pd(OAc)_2$ (5 mol %) and $HP(t\text{-}Bu)_3BF_4$ (15 mol %). The mixture was then purged under nitrogen for 10 minutes. Addition of the 4-brotoluene (1.0 eq.) was followed by the addition of degassed dioxane (0.3 M). The reaction mixture was allowed to stir at 110 °C. After 20 h, the volatiles were removed under reduce pressure using MeOH as a co solvent and the residue was purified via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM to give the products in a 92 % yield. The product ratio of the solid mixture was determined by NMR ^{1}H analysis.

Pyrazine *N*-Oxide Vs Pyrimidine *N*-Oxide

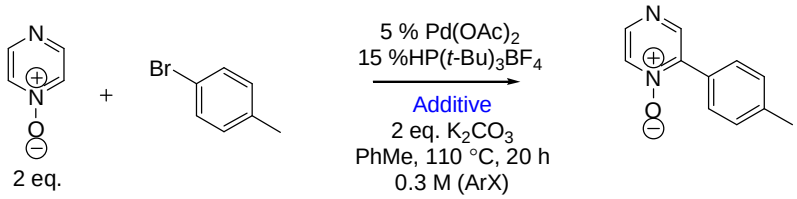


Additives

None			
82 %	0.5 eq. = 53 % 1.0 eq. = 39 %	0.5 eq. = No reaction 1.0 eq. = No reaction	0.5 eq. = trace

To a dried flask was added *N*-oxide (2.0 eq.), K_2CO_3 (2.0 eq.), $Pd(OAc)_2$ (5 mol %), $HP(t\text{-}Bu)_3BF_4$ (15 mol %) and the corresponding pyrimidine ***N***-oxide (0.5 eq. to 1.0 eq.) The mixture was then purged under nitrogen for 10 minutes. Addition of the 4-bromoanisol (1.0 eq.) was followed by the addition of degassed dioxane (0.3 M). The reaction mixture was allowed to stir at 110 °C. After 20 h, the volatiles were removed under reduce pressure using MeOH as a co solvent and the residue was purified via silica gel column chromatography using 100 % DCM then a mixture of 15 % Acetone/DCM gave a beige solid.

Pyrazine *N*-Oxide Vs Pyridine and Vs Pyrimidine N-Oxide

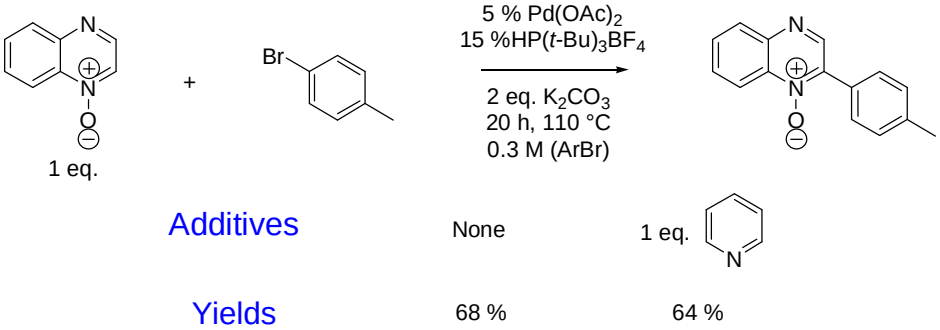


Additives	None	2 eq.	2 eq.
Yields	75 %	69 %	8 %

To a dried flask was added the pyrazine *N*-oxide (2.0 eq.), K_2CO_3 (2.0 eq.), $Pd(OAc)_2$ (5 mol %) and $HP(t\text{-}Bu)_3BF_4$ (15 mol %). The mixture was then purged under nitrogen for 10 minutes. Addition of the 4-bromotoluene (1.0 eq.) and the additive (2.0 eq.) was followed by the addition of degassed dioxane (0.3 M). The reaction mixture was allowed to stir at 110 °C. After 20 h, the volatiles were removed under reduce pressure using MeOH as a co solvent and the residue was purified via silica gel column

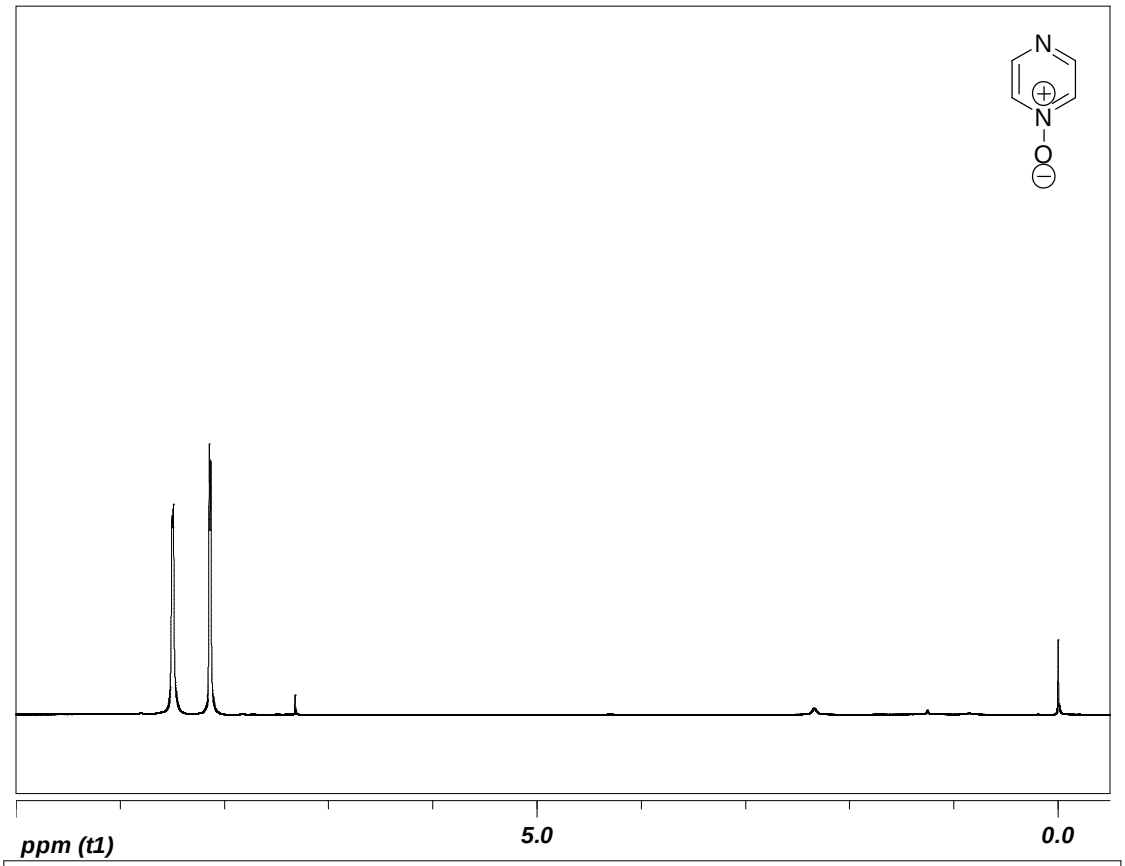
chromatography using 100 % DCM then a mixture of 10 % Acetone/DCM gave a beige solid.

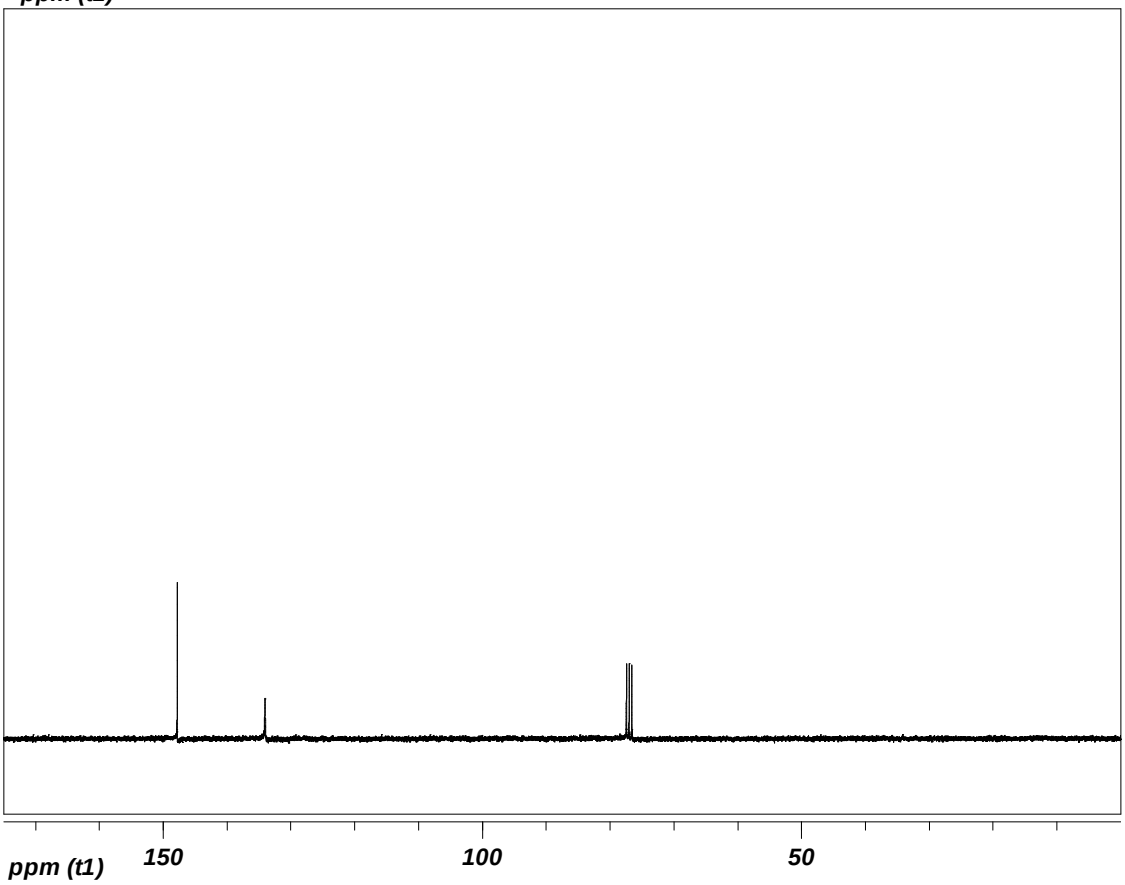
Quinoxaline *N*-oxide Vs Pyridine

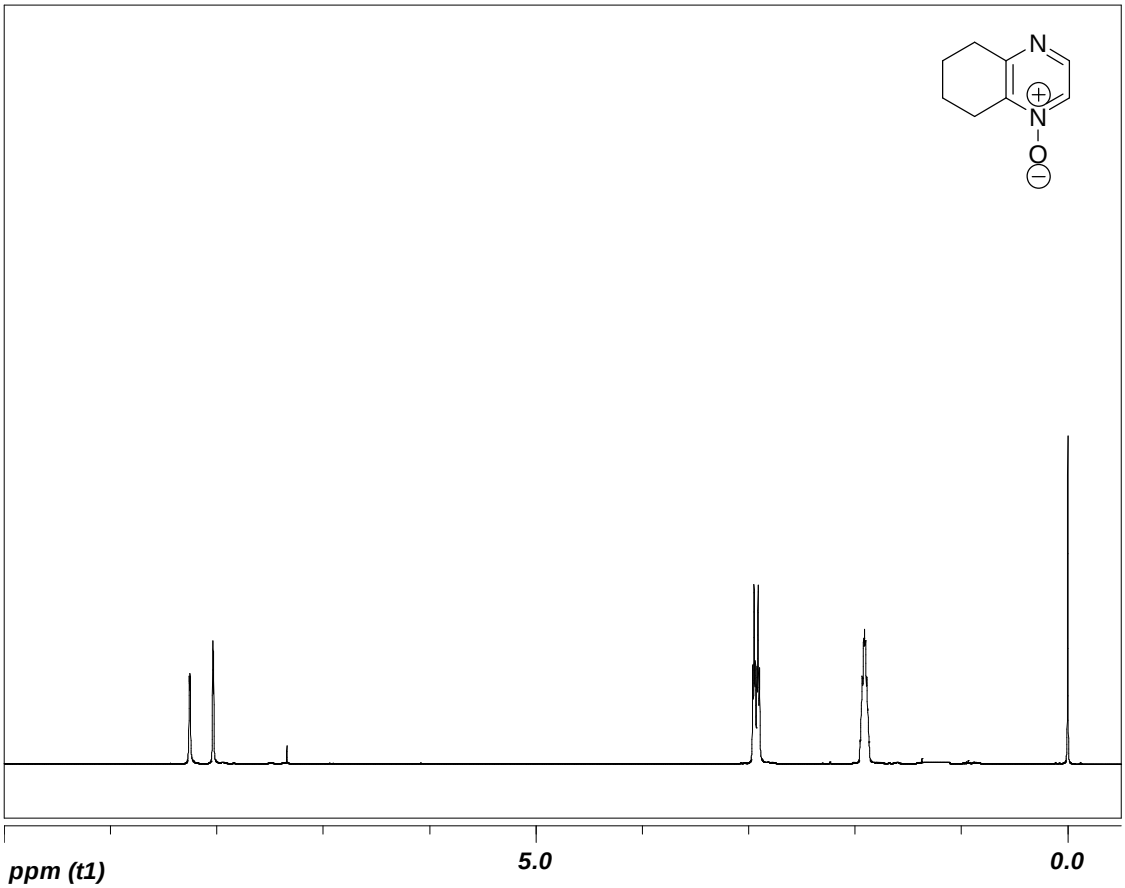


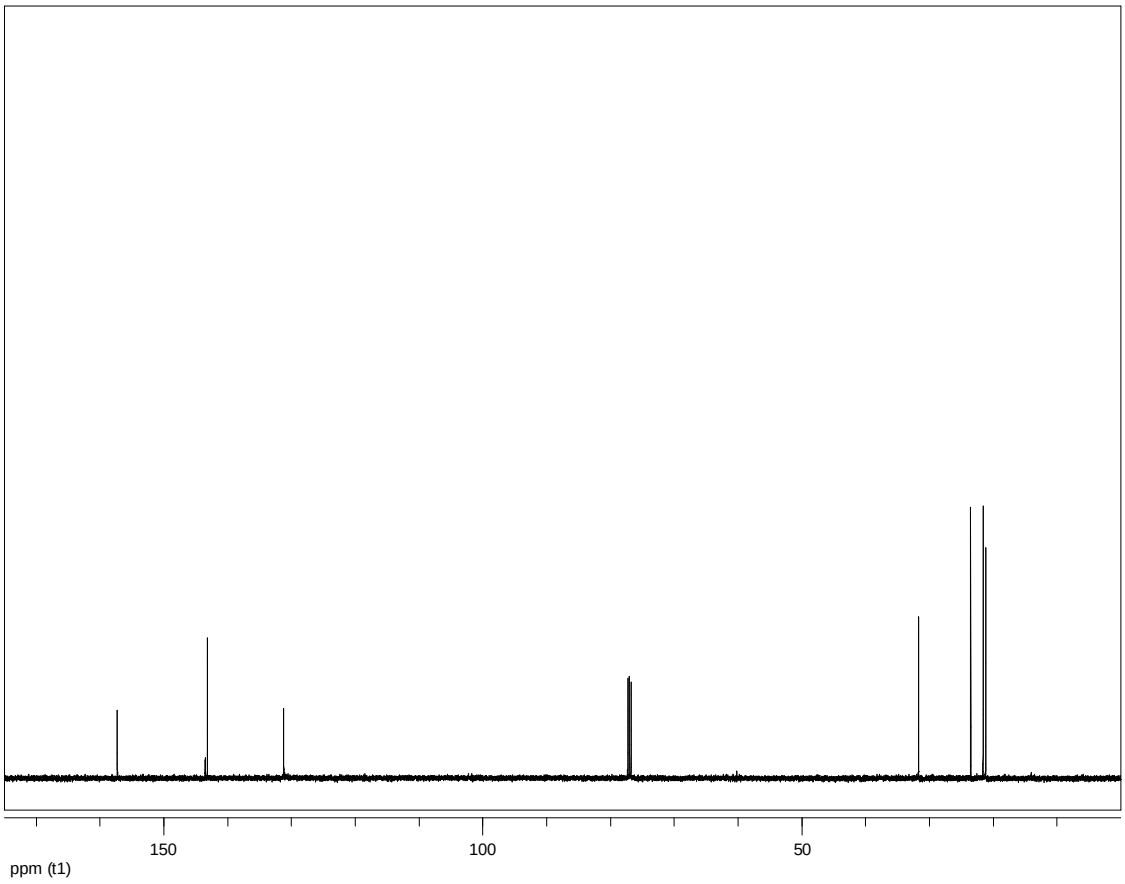
To a dried flask was added the quinoxaline *N*-oxide (1.0 eq.), K_2CO_3 (2.0 eq.), $Pd(OAc)_2$ (5 mol %), and $HP(t\text{-}Bu)_3BF_4$ (15 mol %). The mixture was then purged under nitrogen for 10 minutes. Addition of the 4-bromotoluene (1.0 eq.) and pyridine (1.0 eq.) was followed by the addition of degassed dioxane (0.3 M). The reaction mixture was allowed to stir at 110 °C. After 20 h, the volatiles were removed under reduce pressure using MeOH as a co solvent and the residue was purified via silica gel column chromatography using 100 % DCM then a mixture of 5 % Acetone/DCM gave a beige solid (64 %).

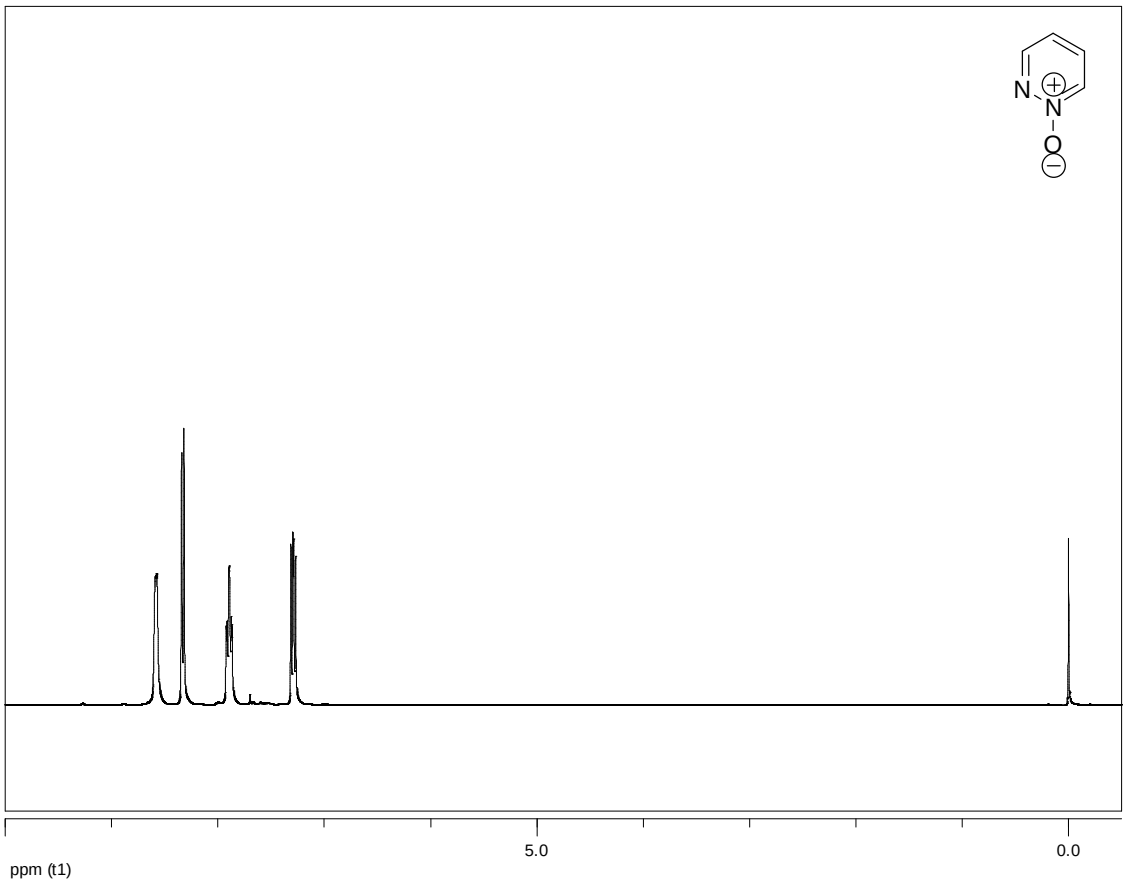
1H and 13C NMR Spectrums

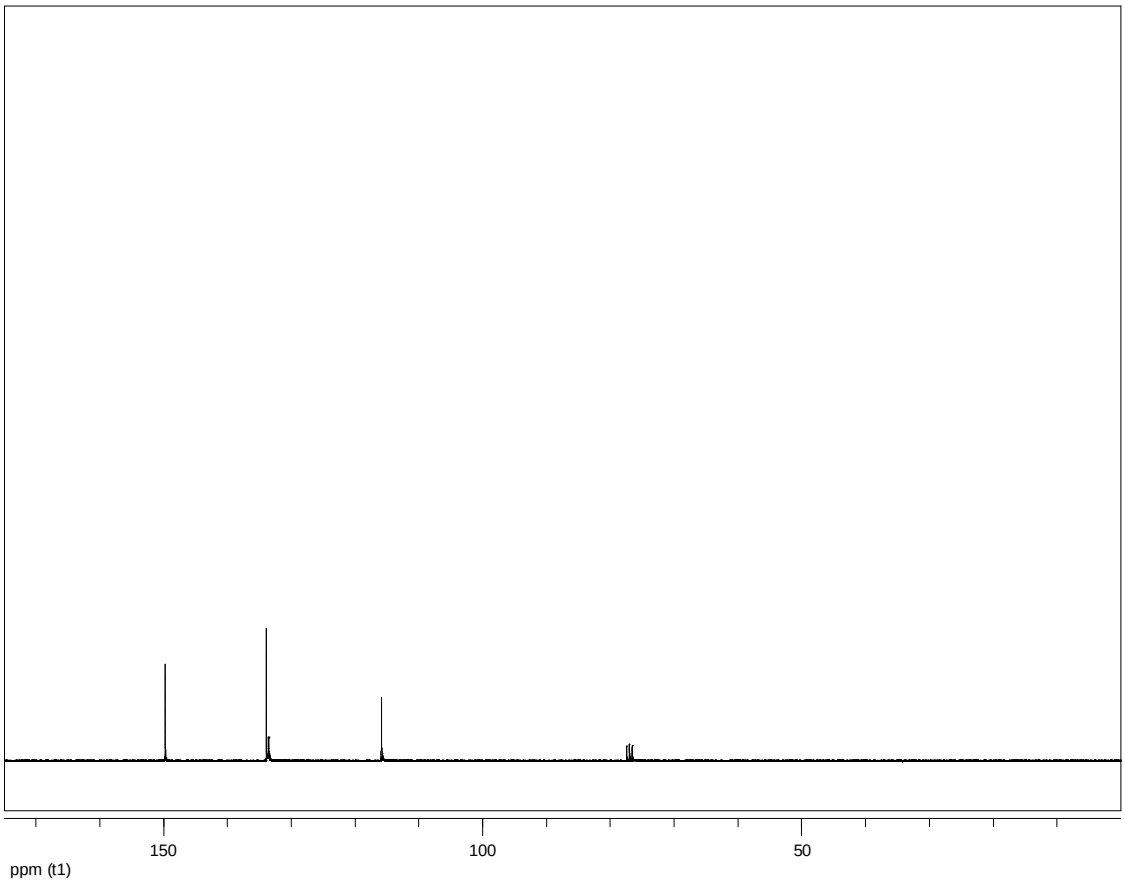


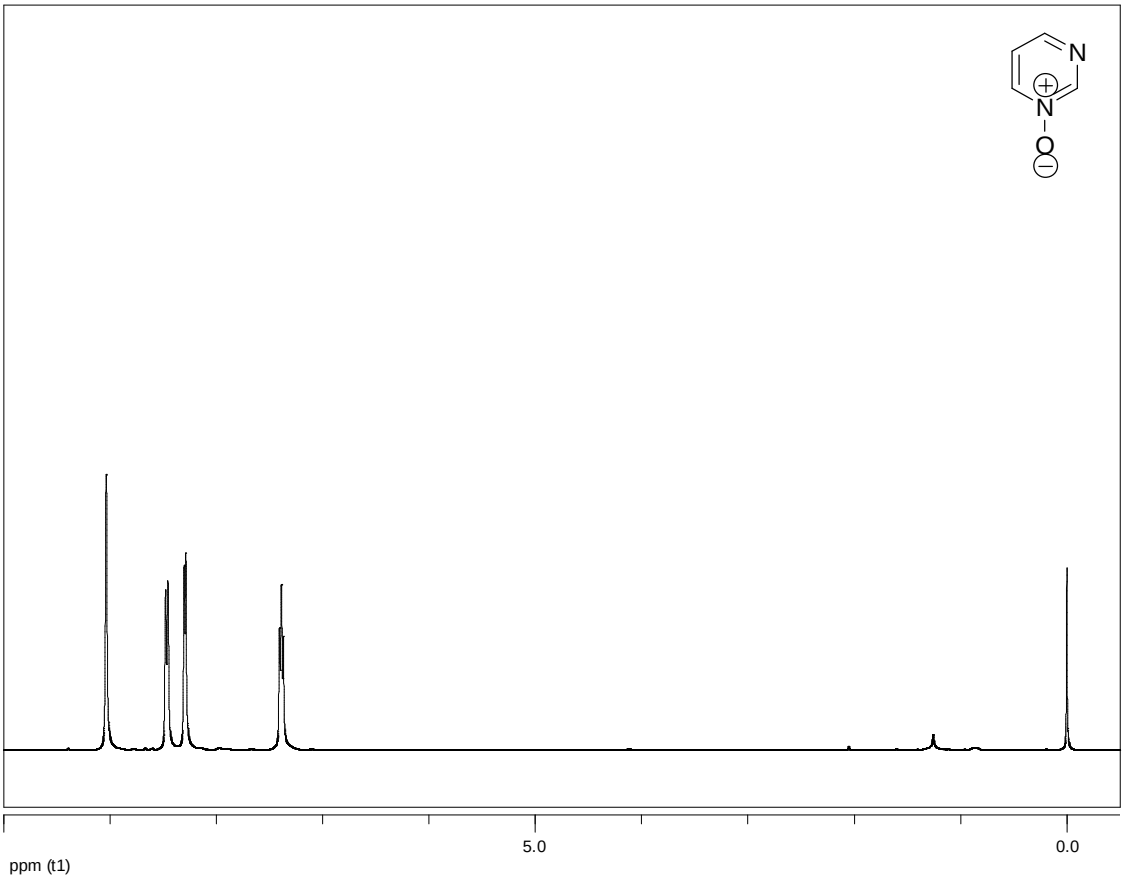


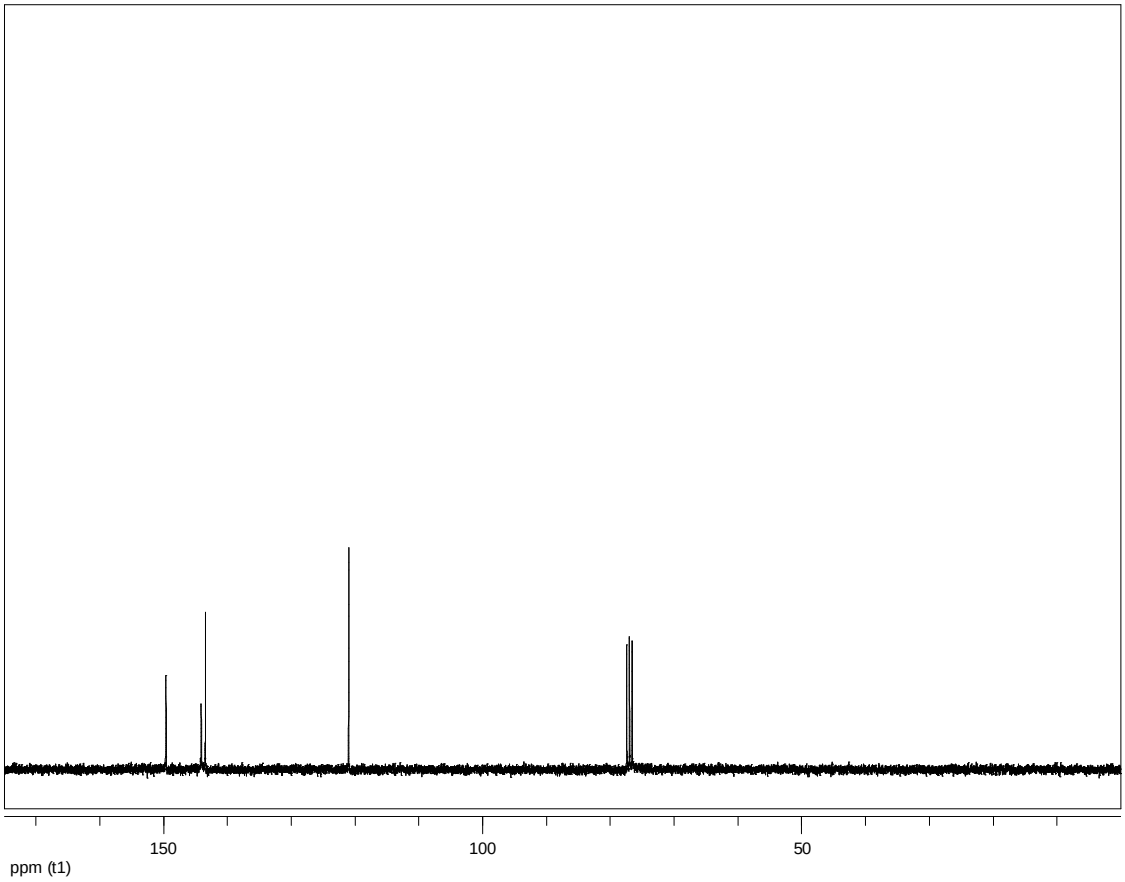

N
N
O
5.0
0.0
ppm (t1)

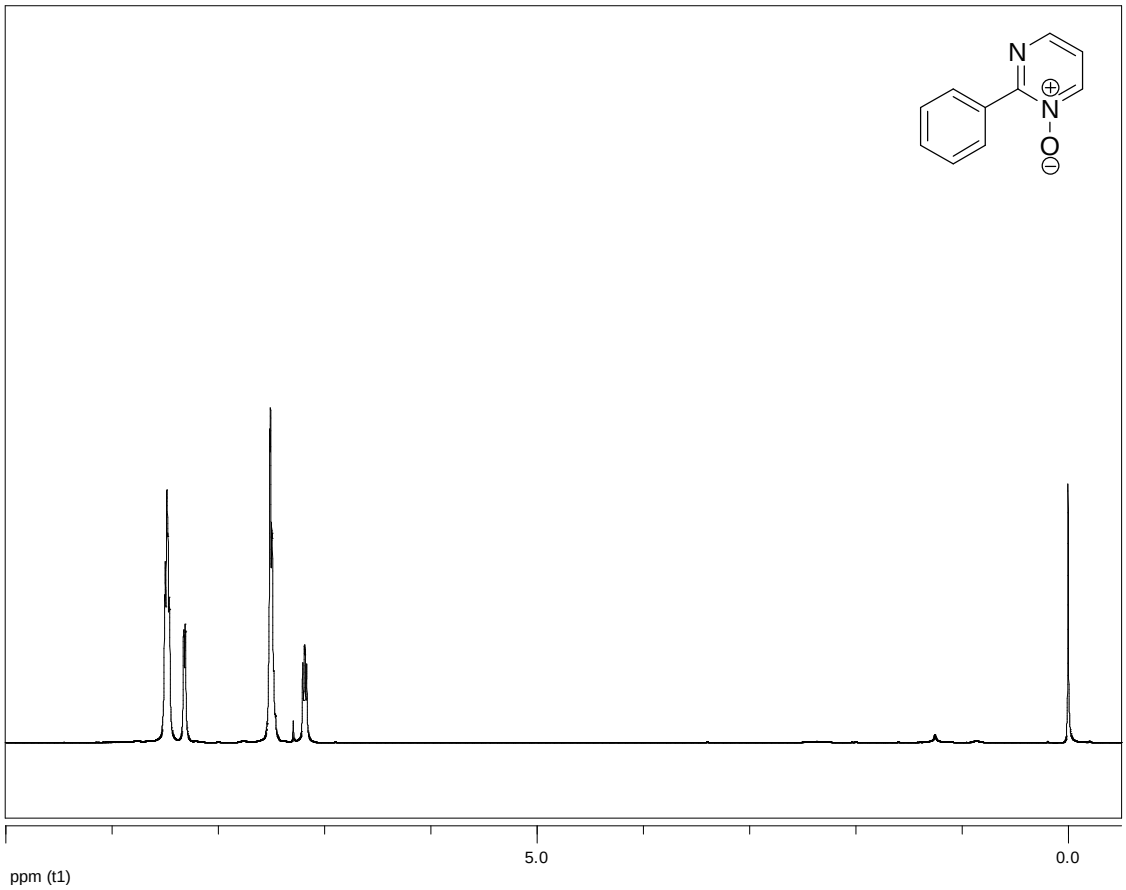

150
100
50
ppm (t1)

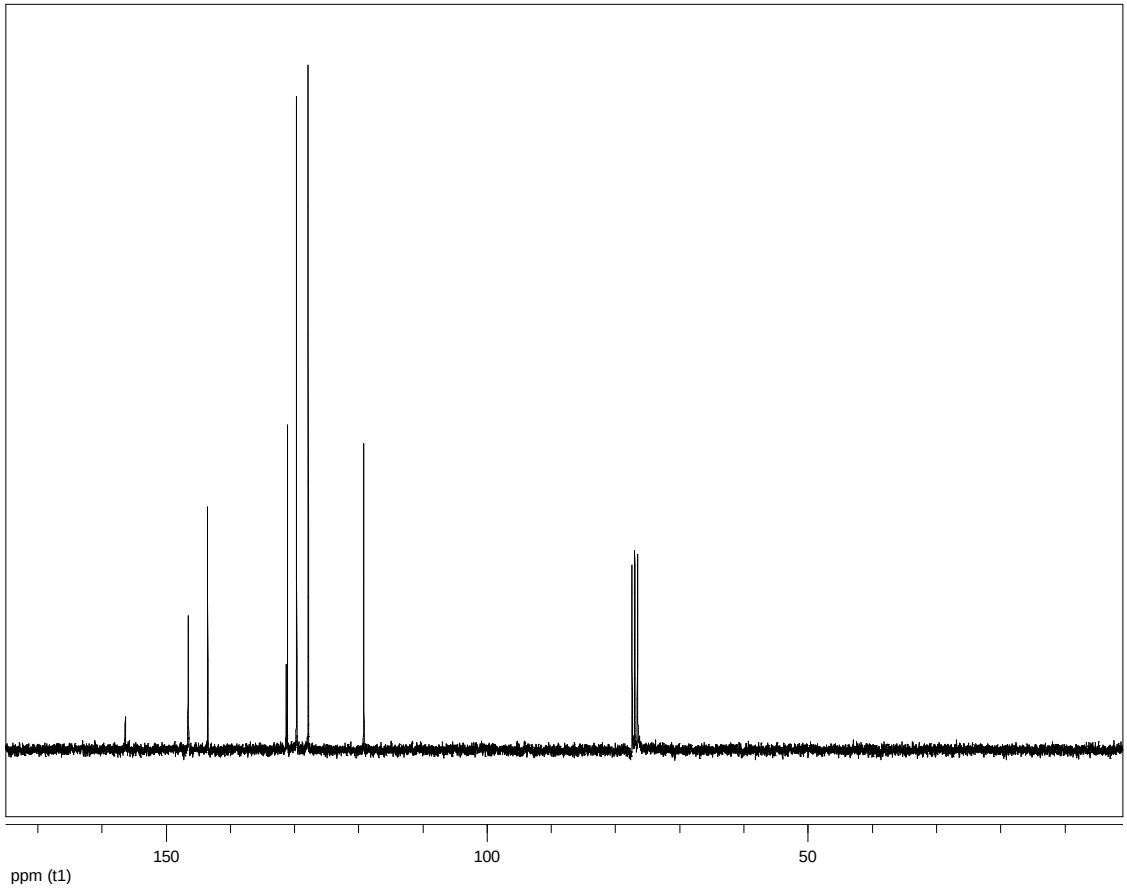

5.0
0.0
ppm (t1)

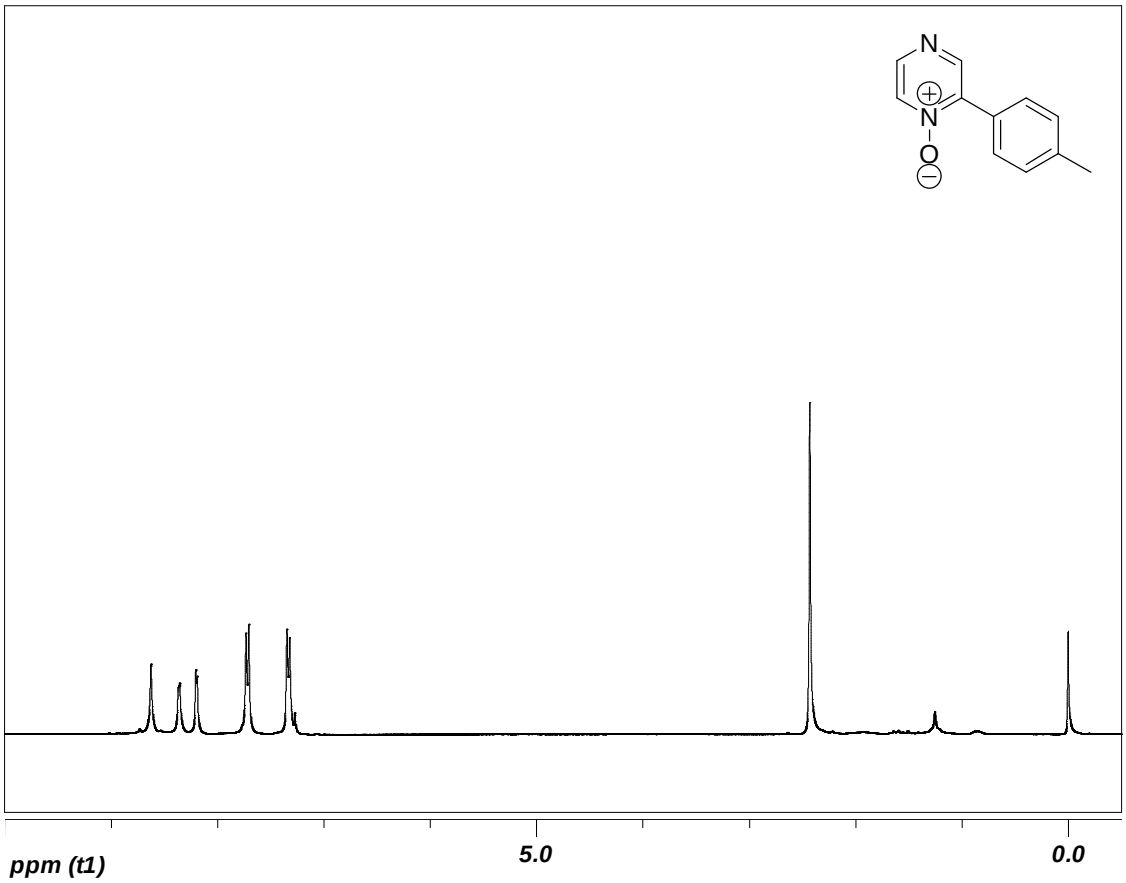

150
100
50
ppm (t1)

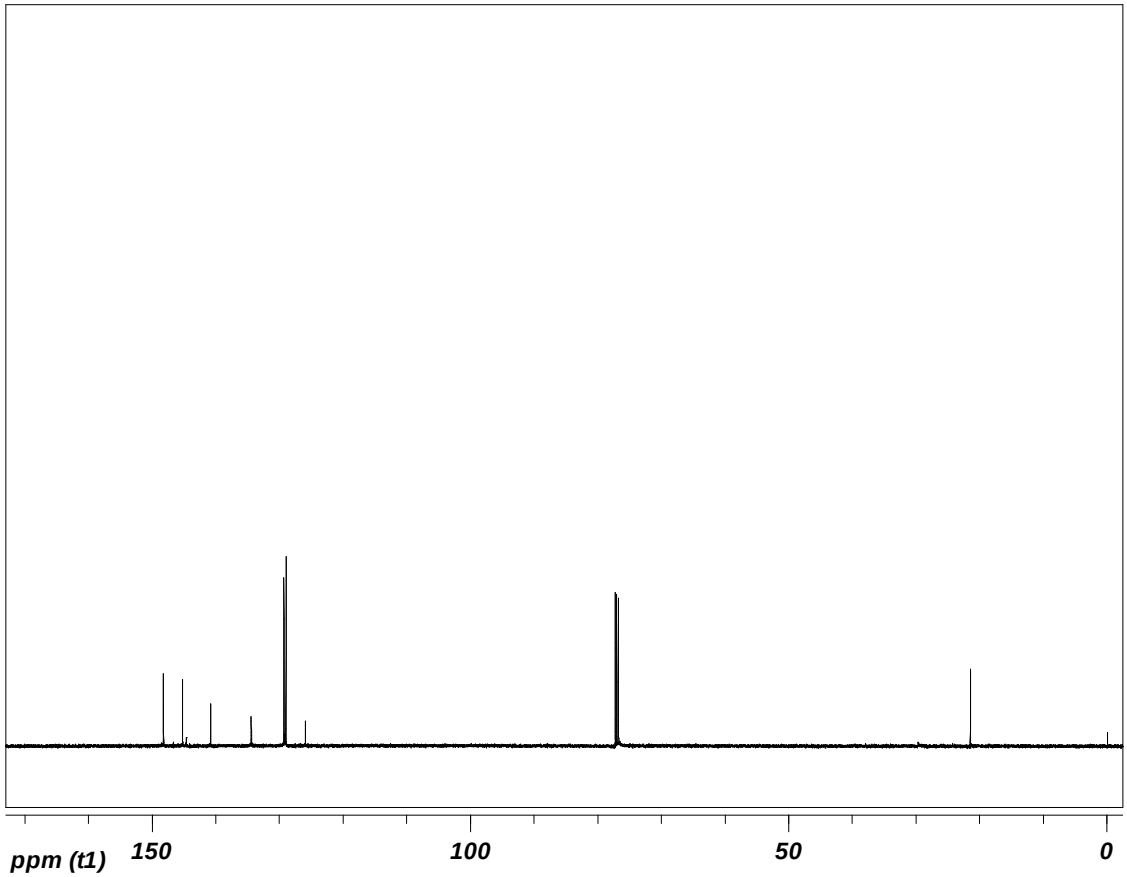

N
N
O
5.0
0.0
ppm (t1)

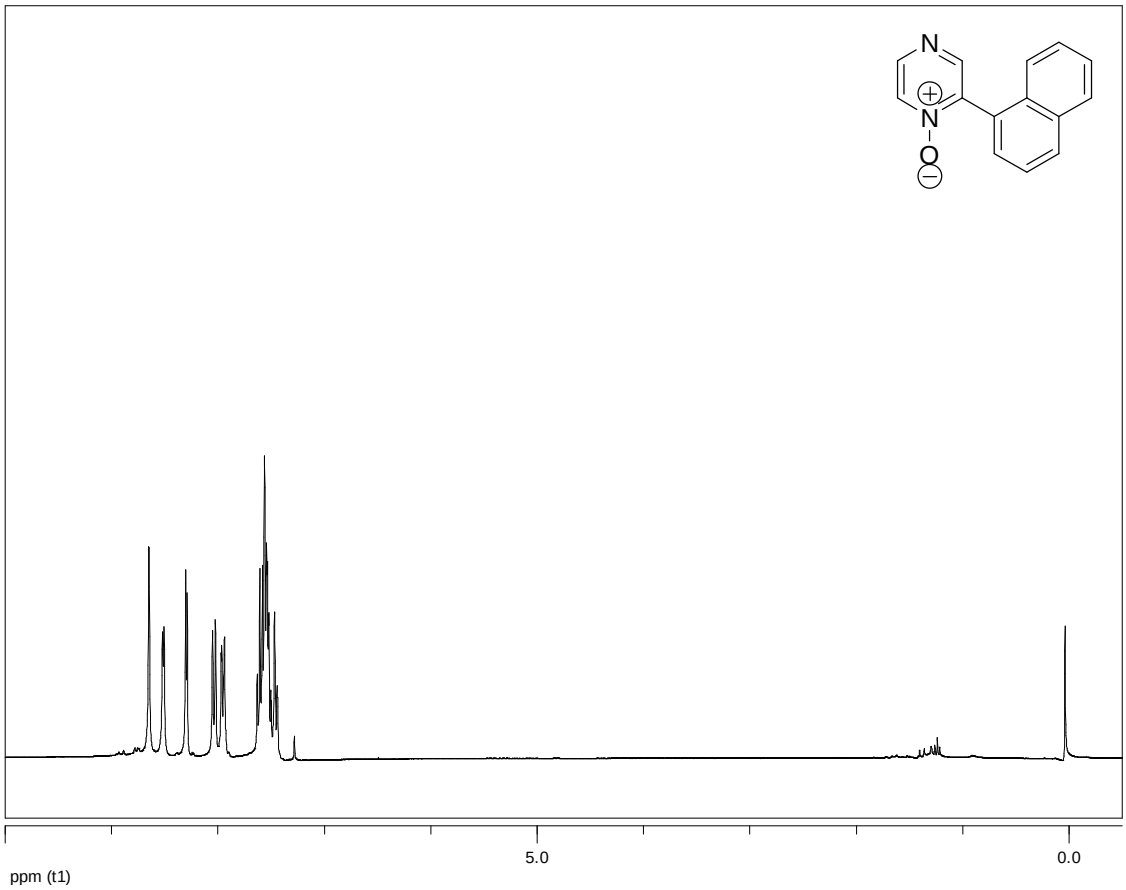

150
100
50
ppm (t1)

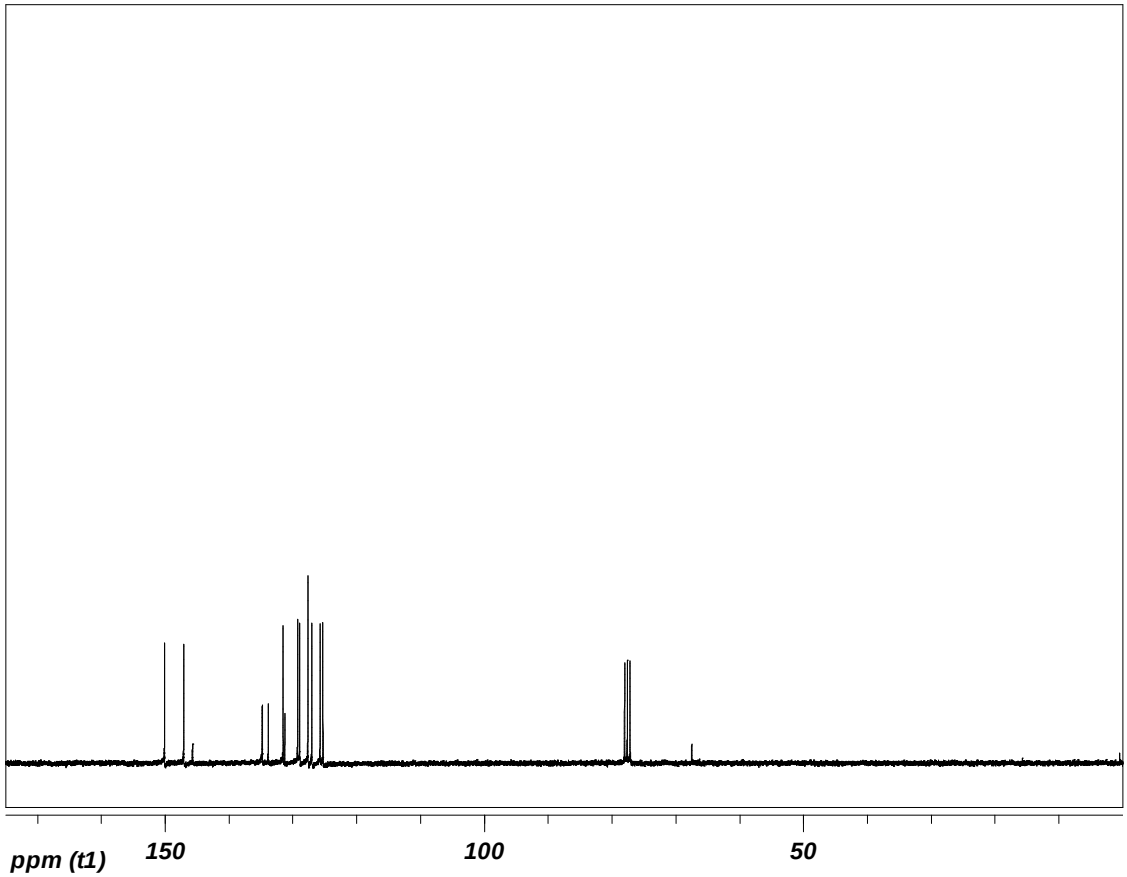

N
N
O
5.0
0.0
ppm (t1)

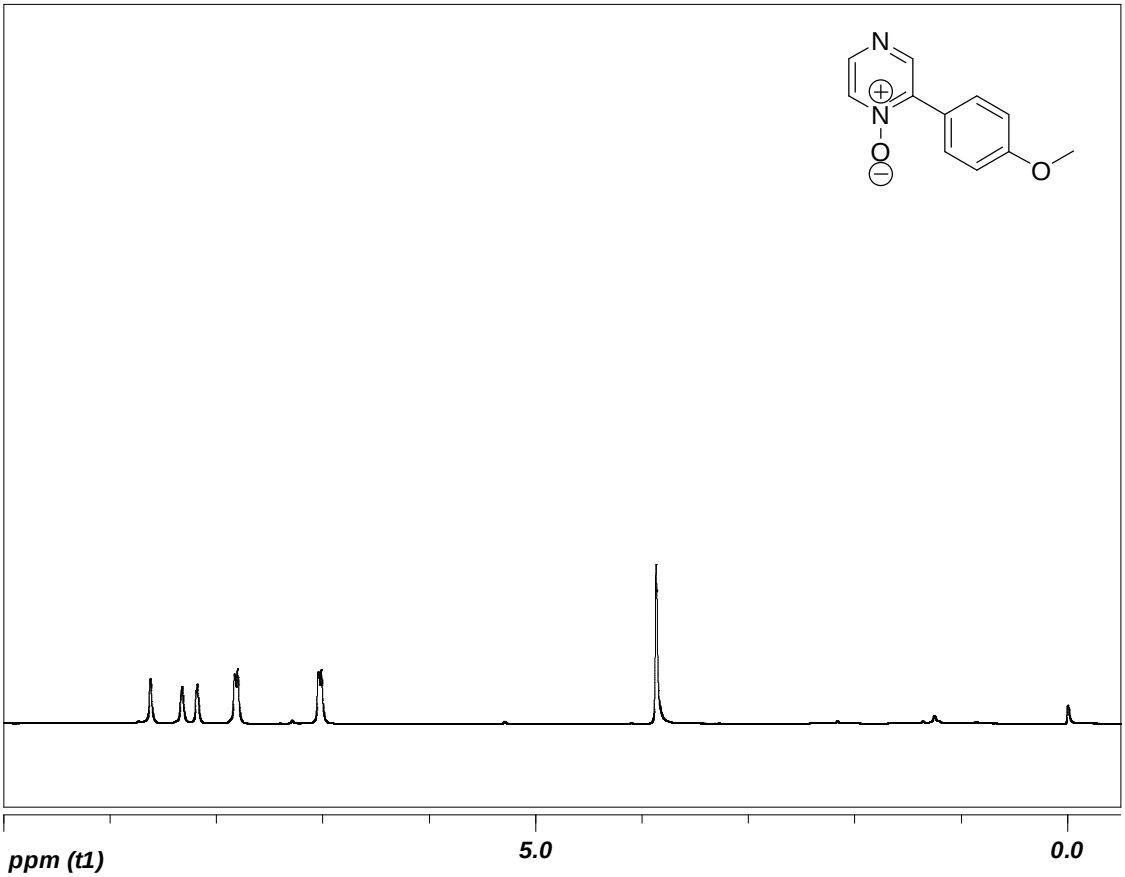

150
100
50
ppm (t1)

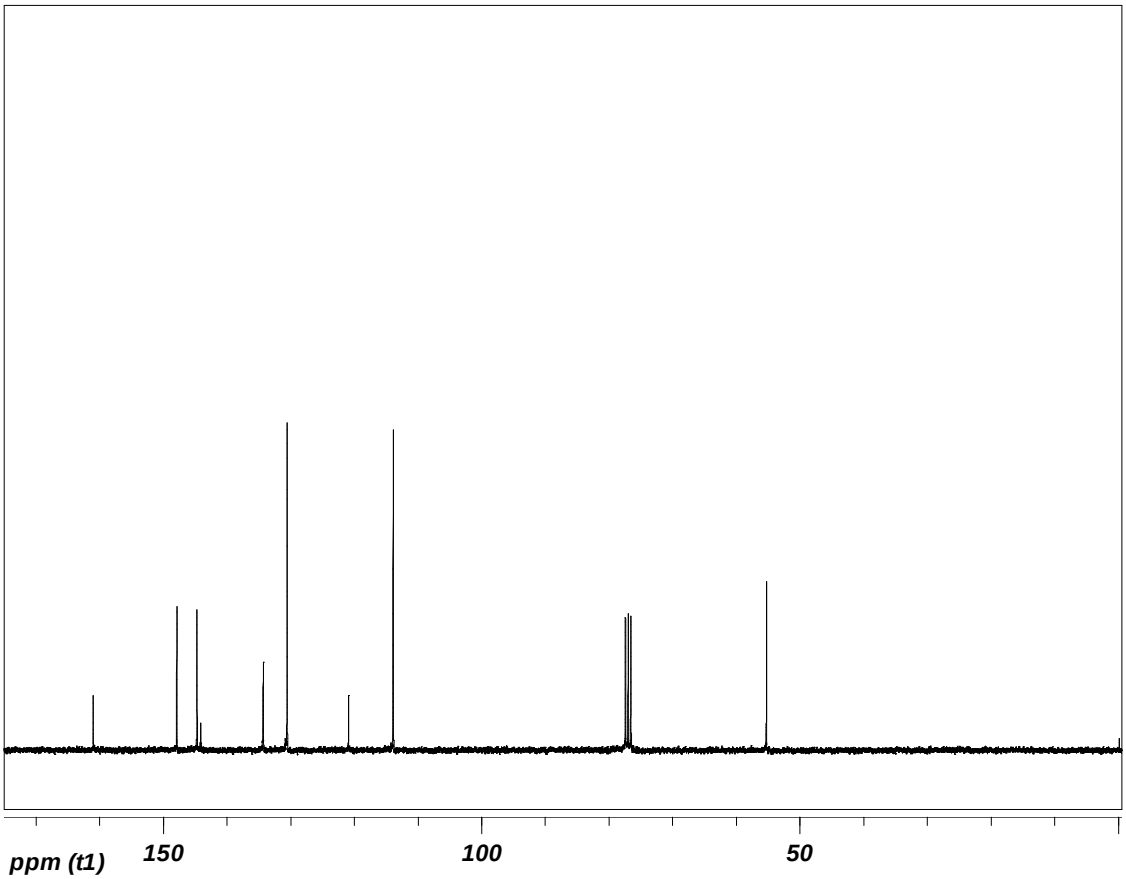

N
N
O
ppm (t1)
5.0
0.0

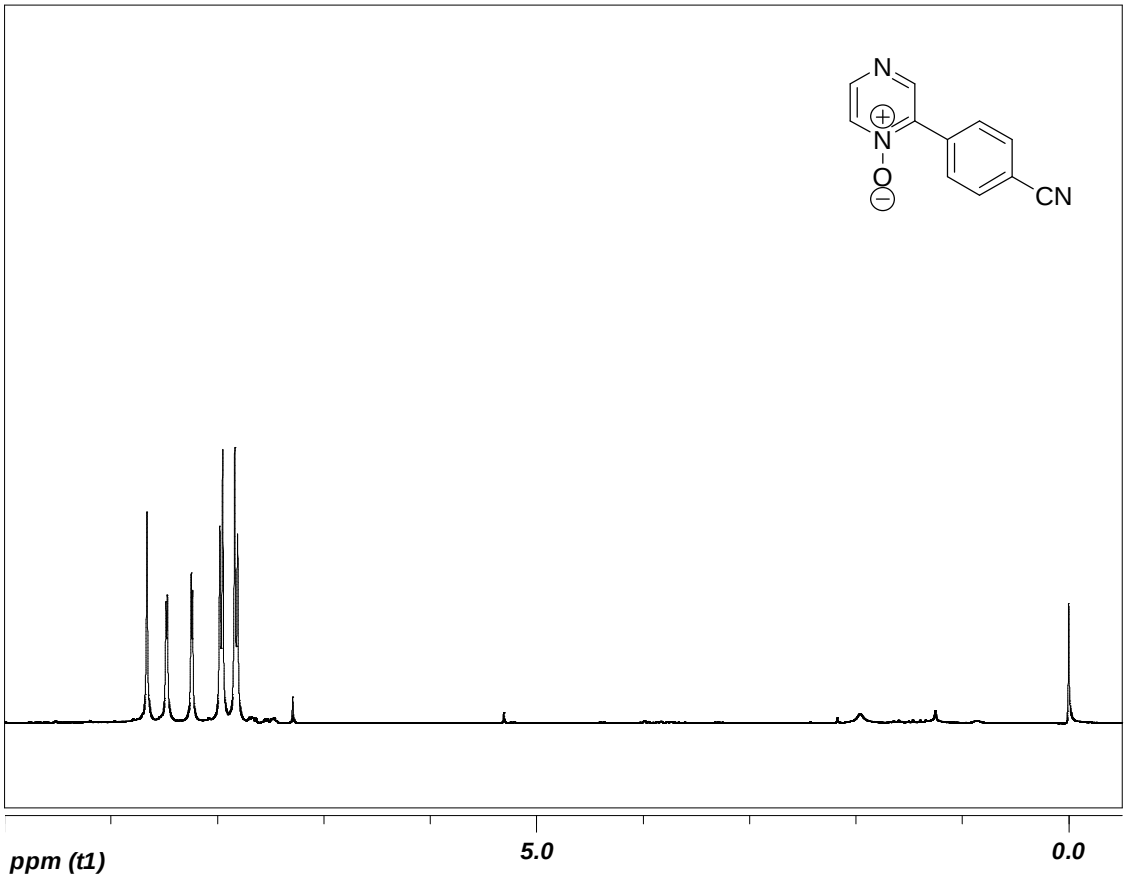

ppm (t1)
150
100
50
0

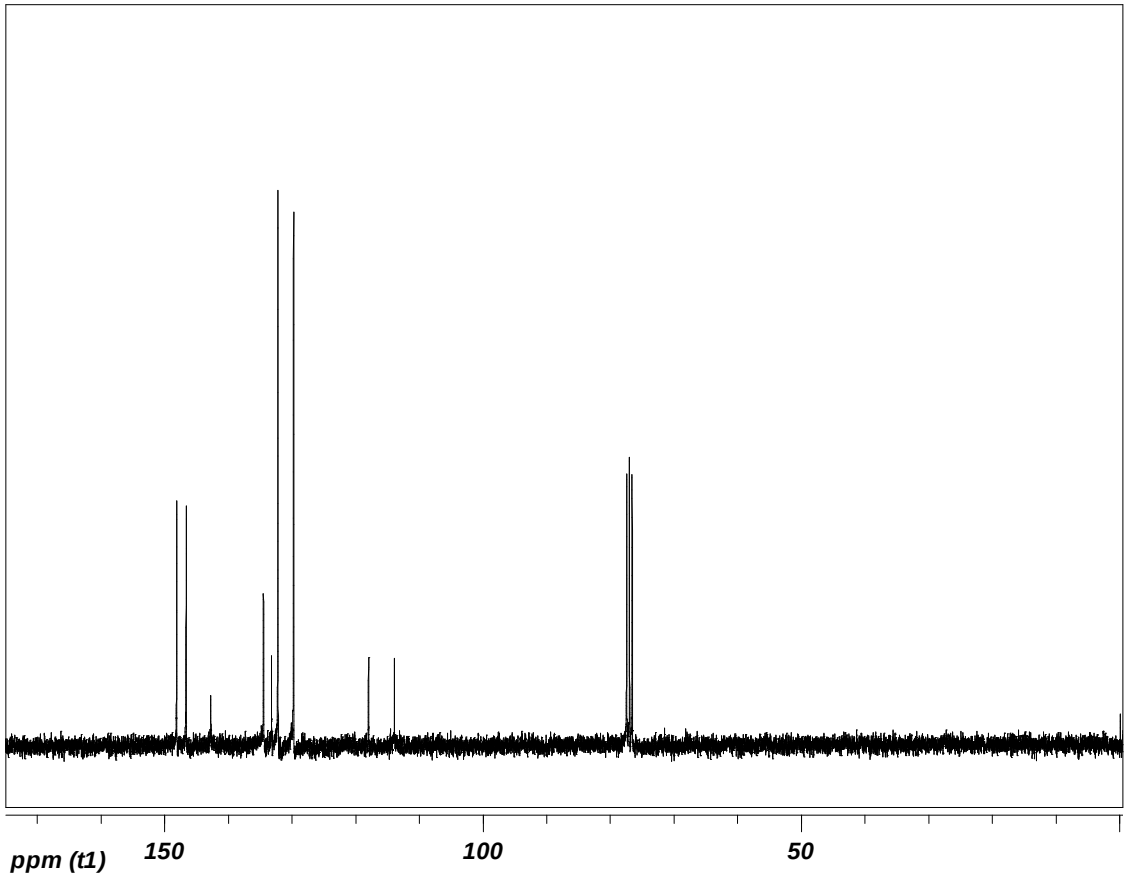

N
N
O
5.0
0.0
ppm (t1)

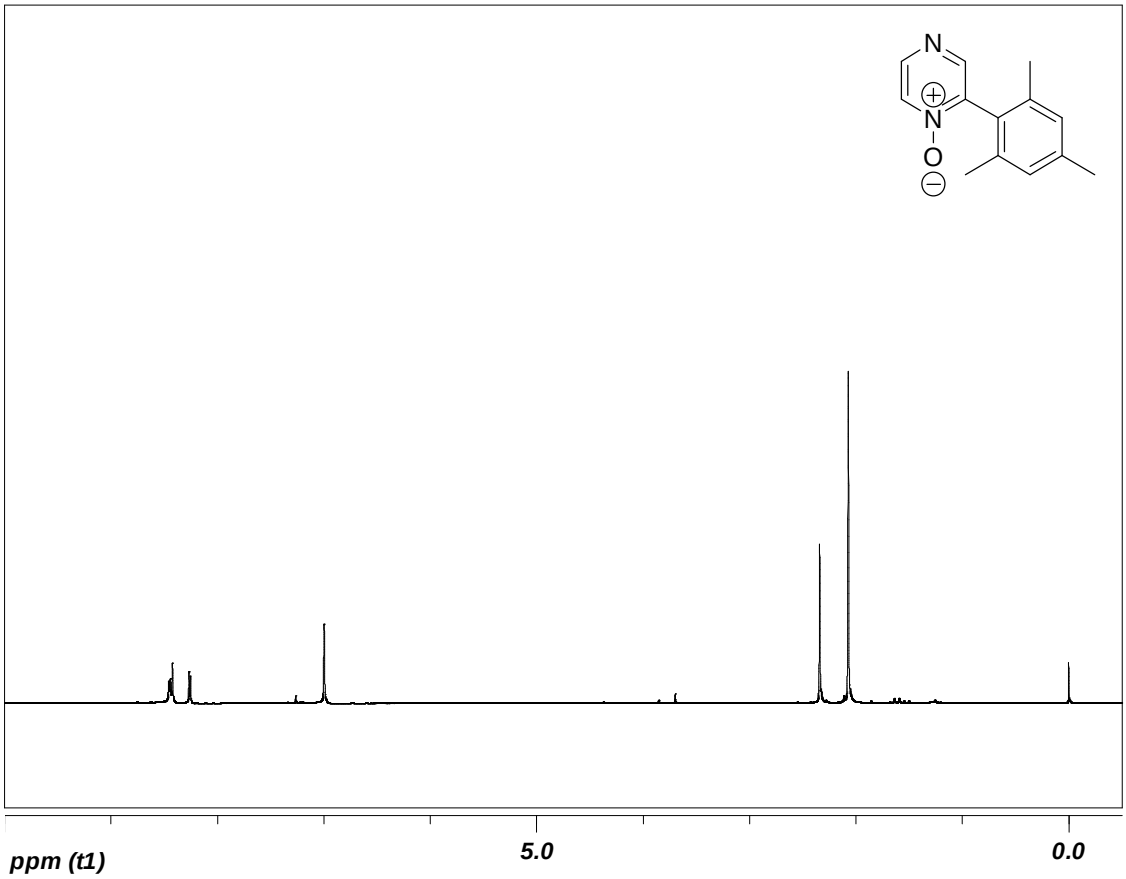

150
100
50
ppm (t1)

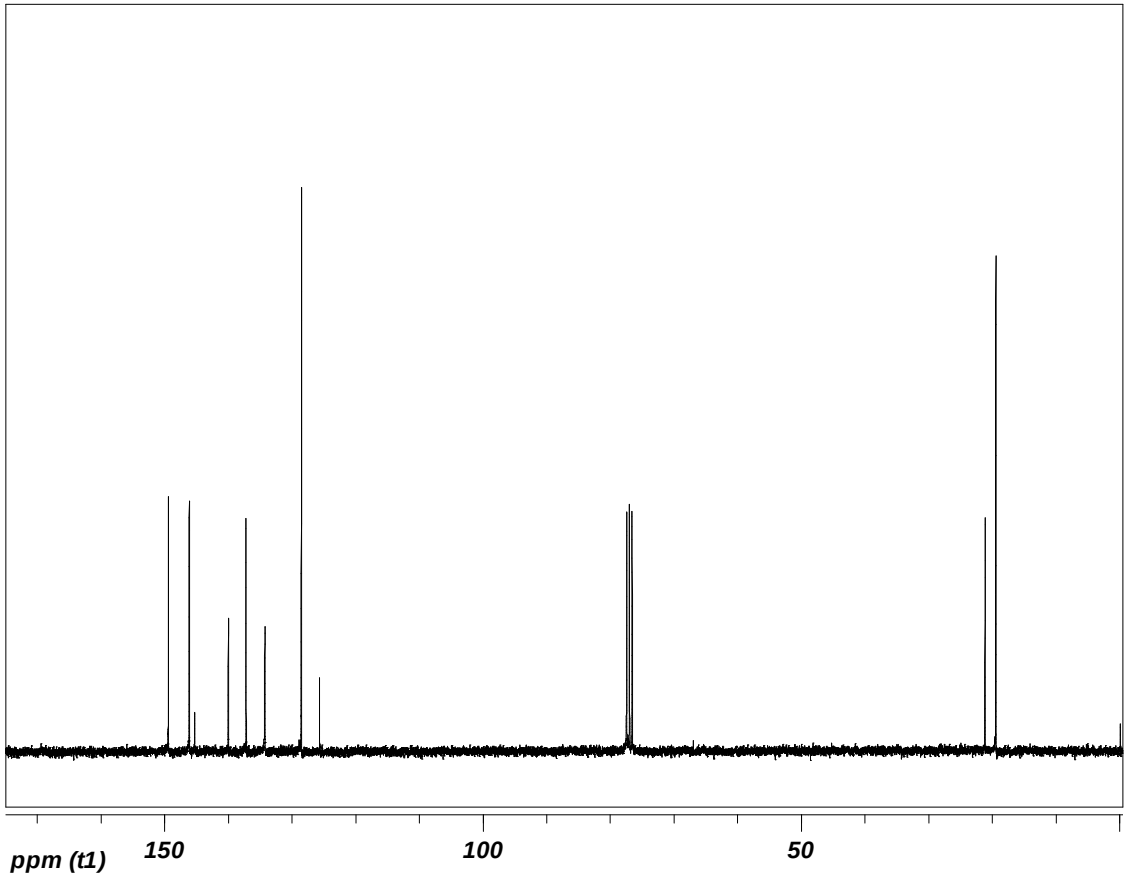

N
N
O
O
ppm (t1)
5.0
0.0

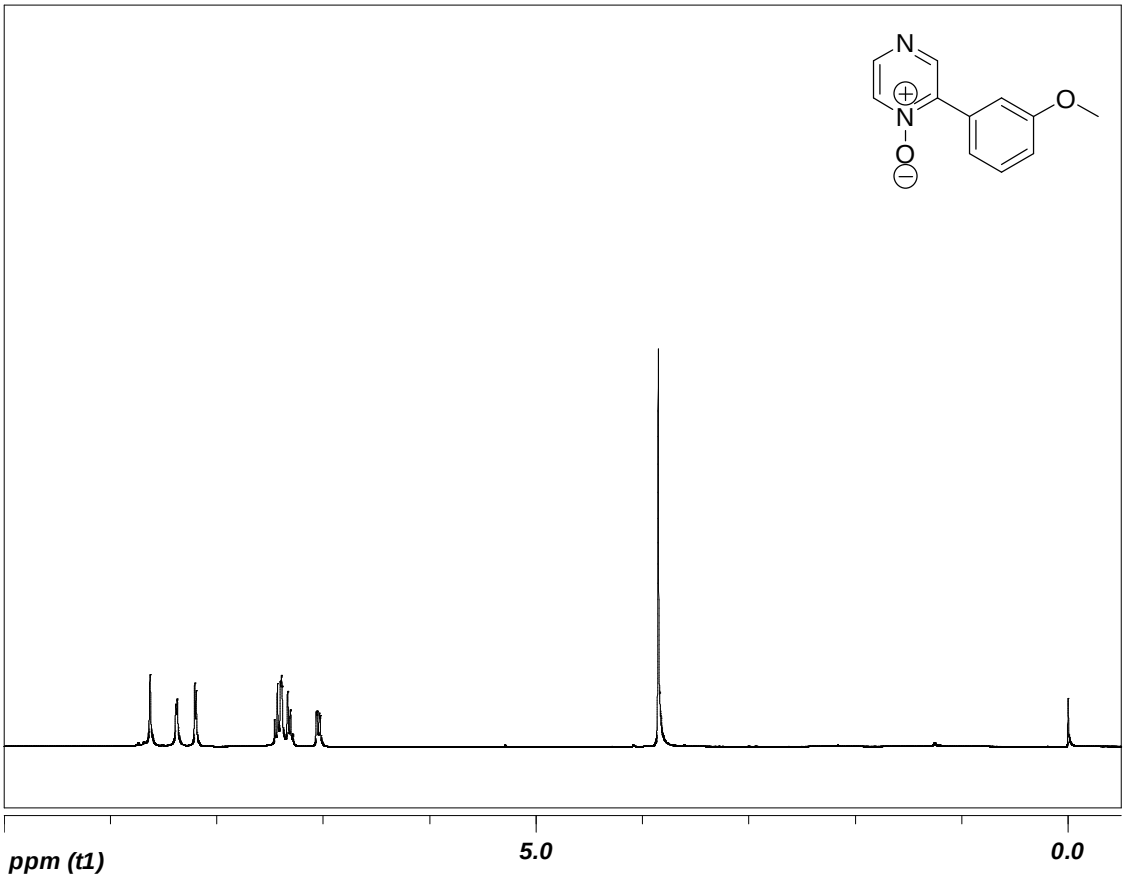

ppm (t1)
150
100
50

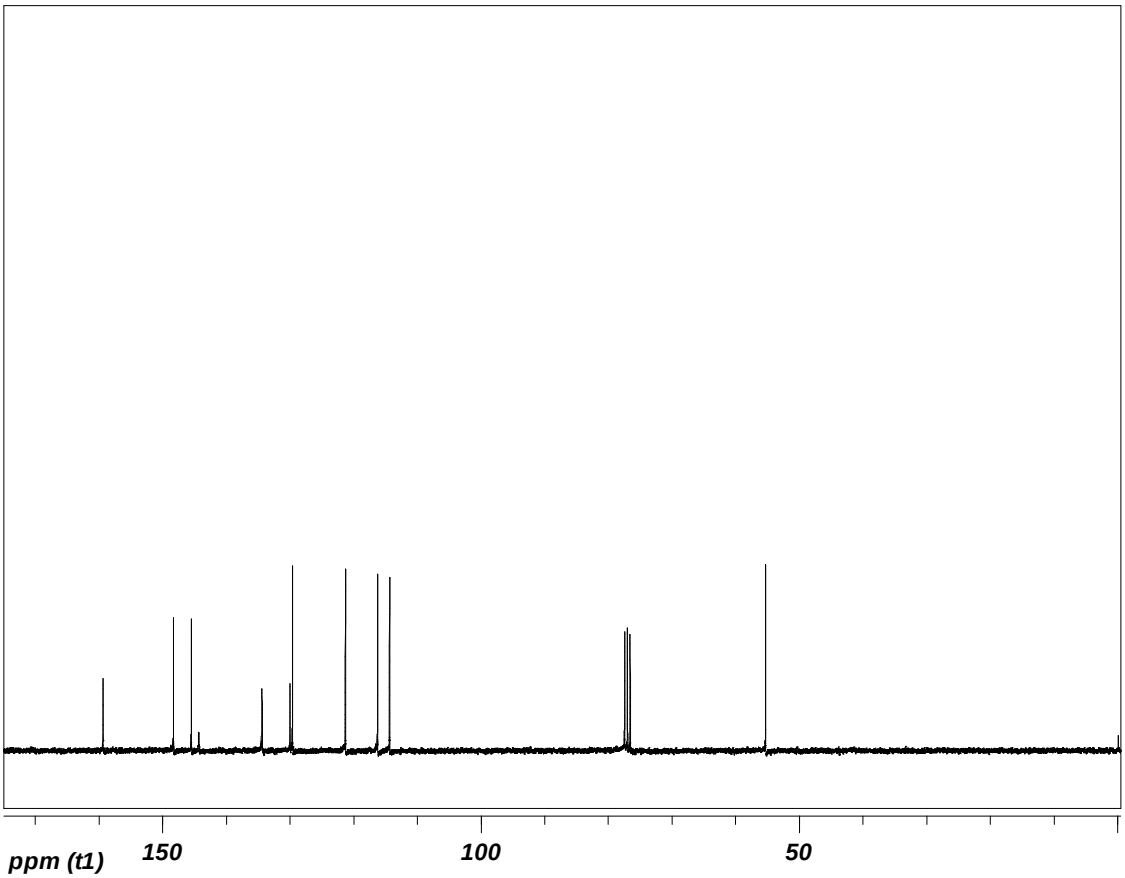

N
N
O
CN
ppm (t1)
5.0
0.0

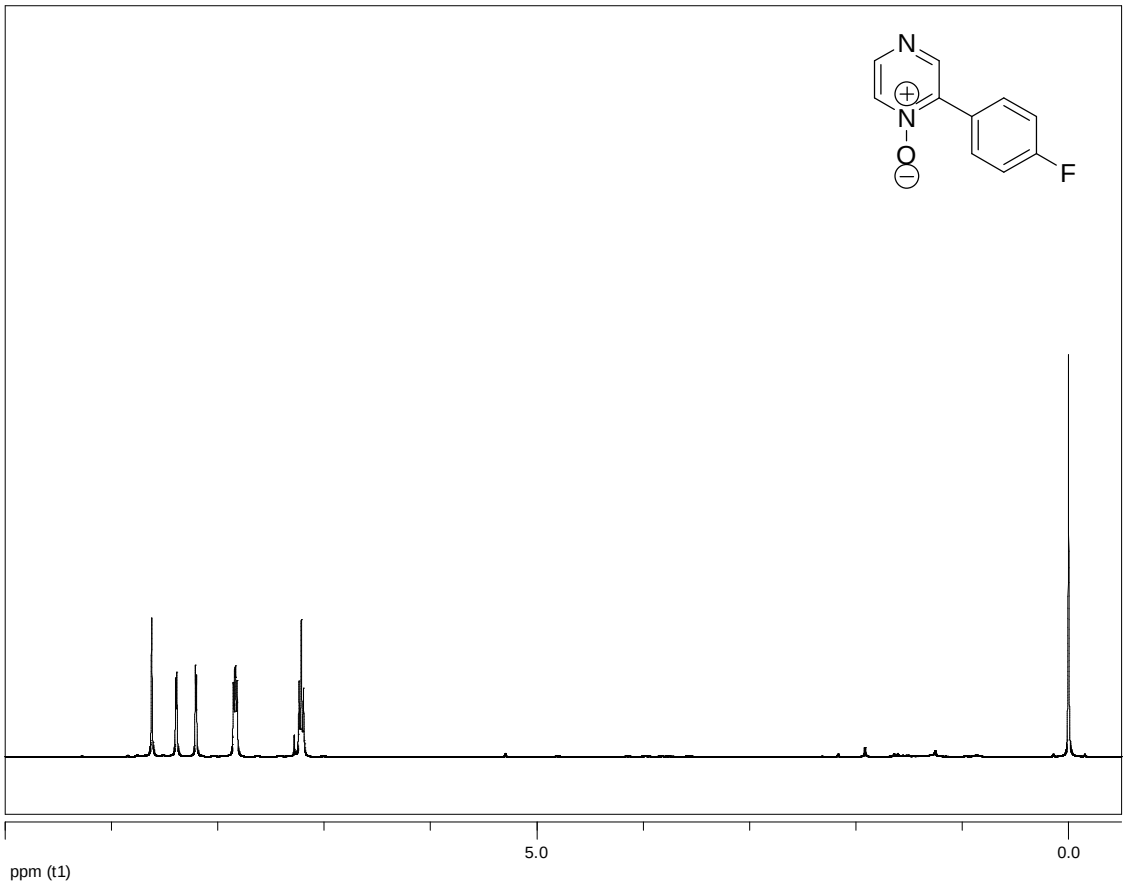

ppm (t1)
150
100
50

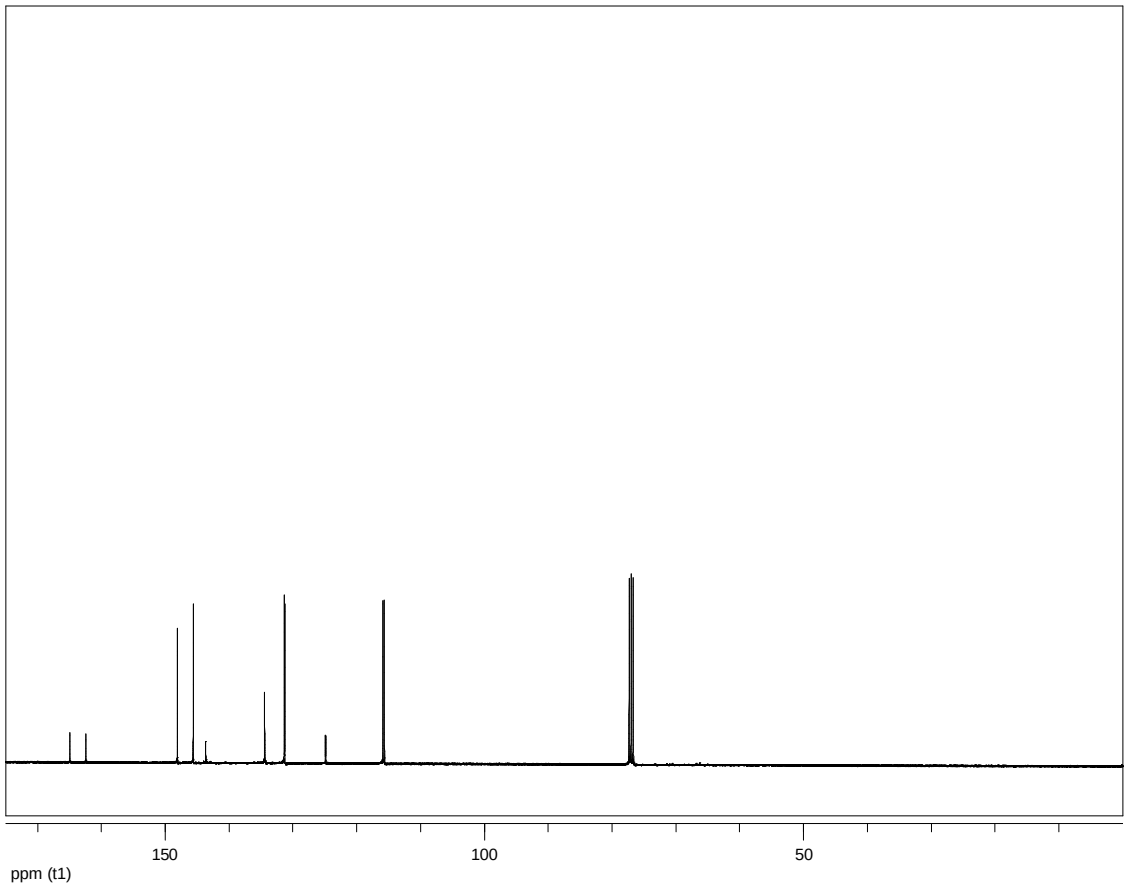

N
N
O
ppm (t1)
5.0
0.0

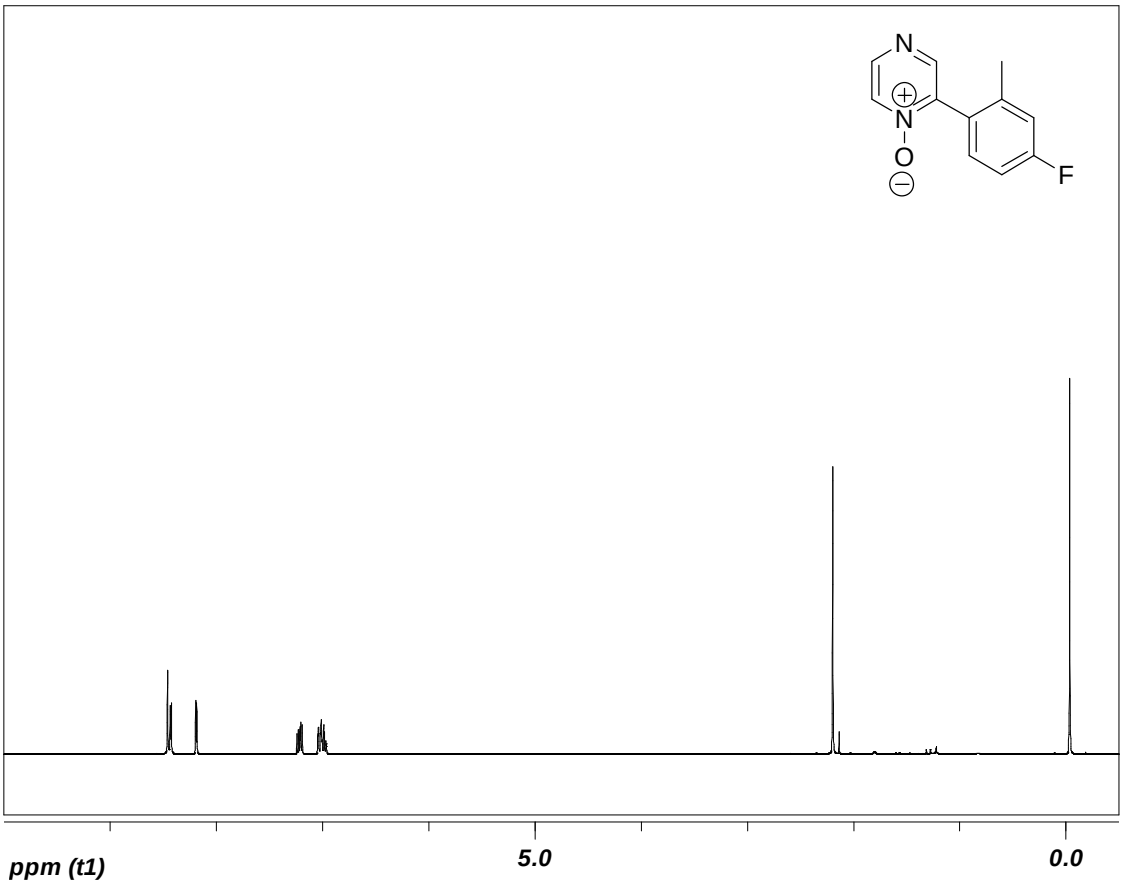

ppm (t1)
150
100
50

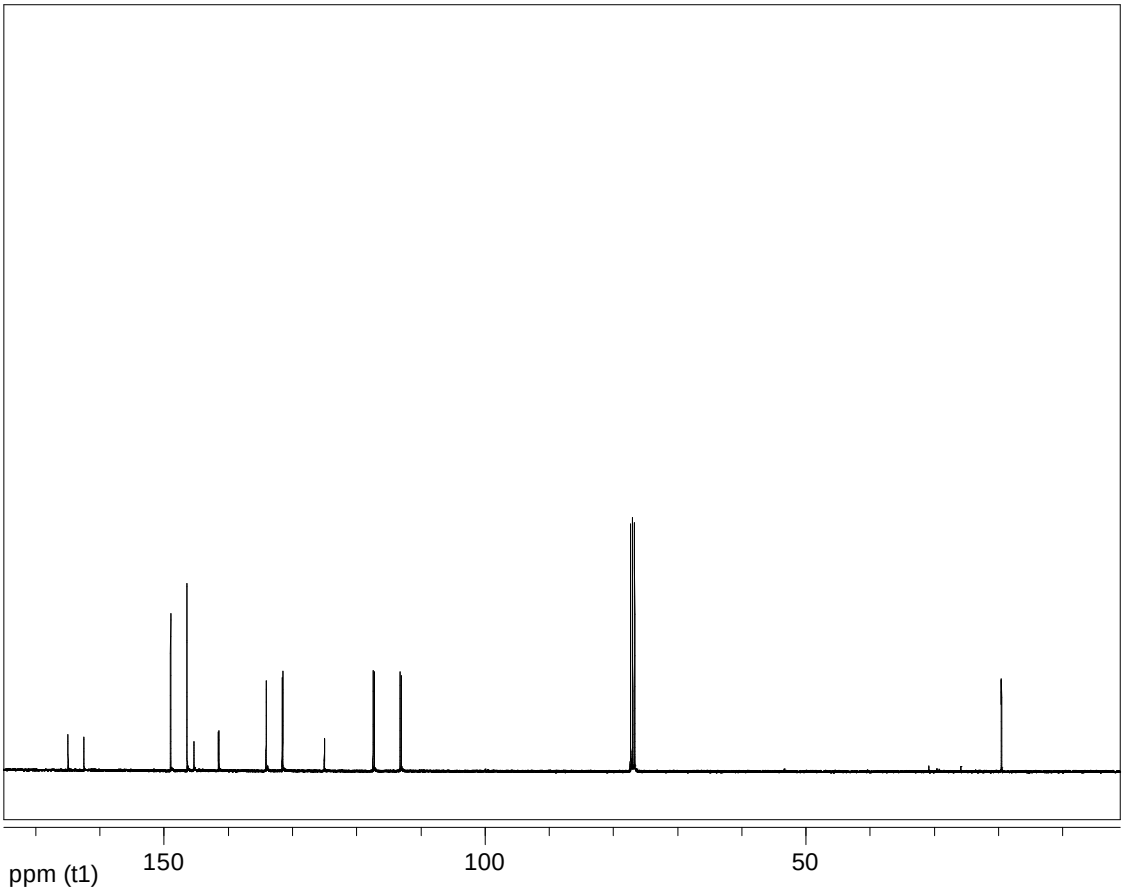

N
N
O
O
ppm (t1)
5.0
0.0

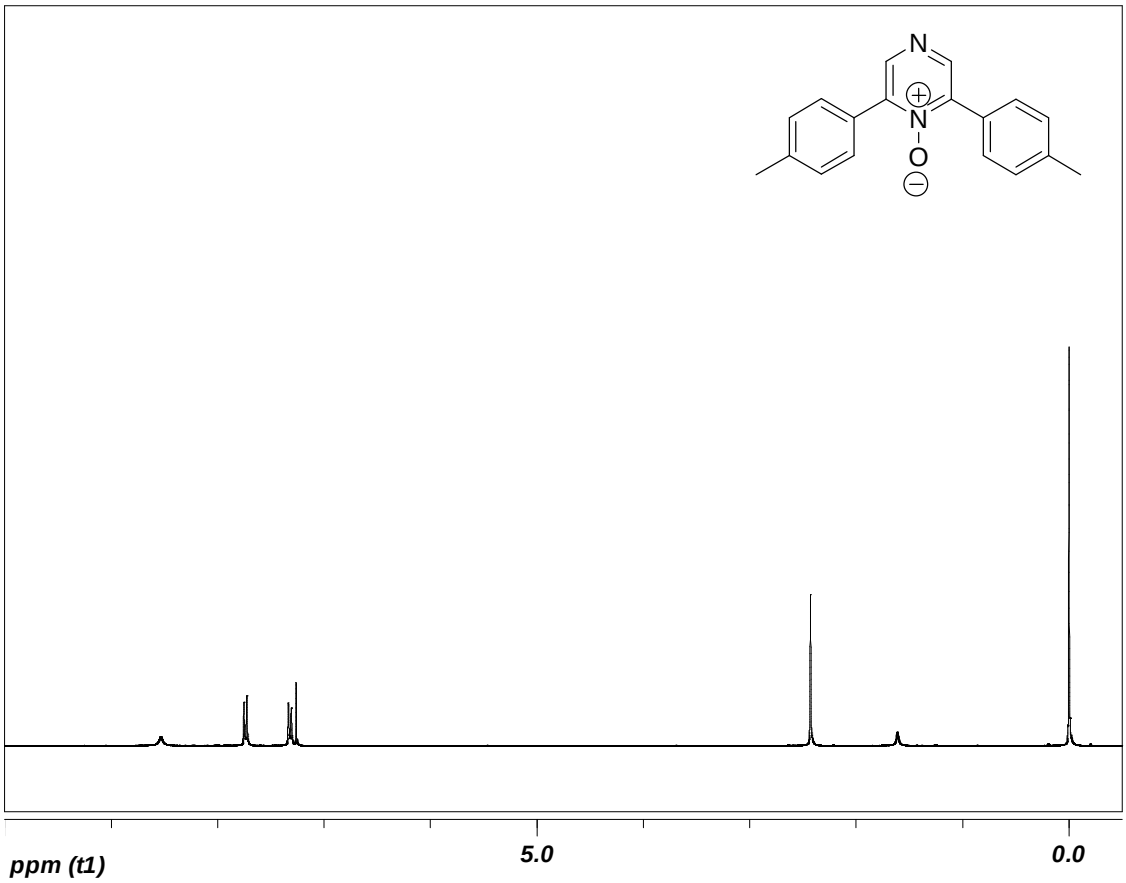

ppm (t1)
150
100
50

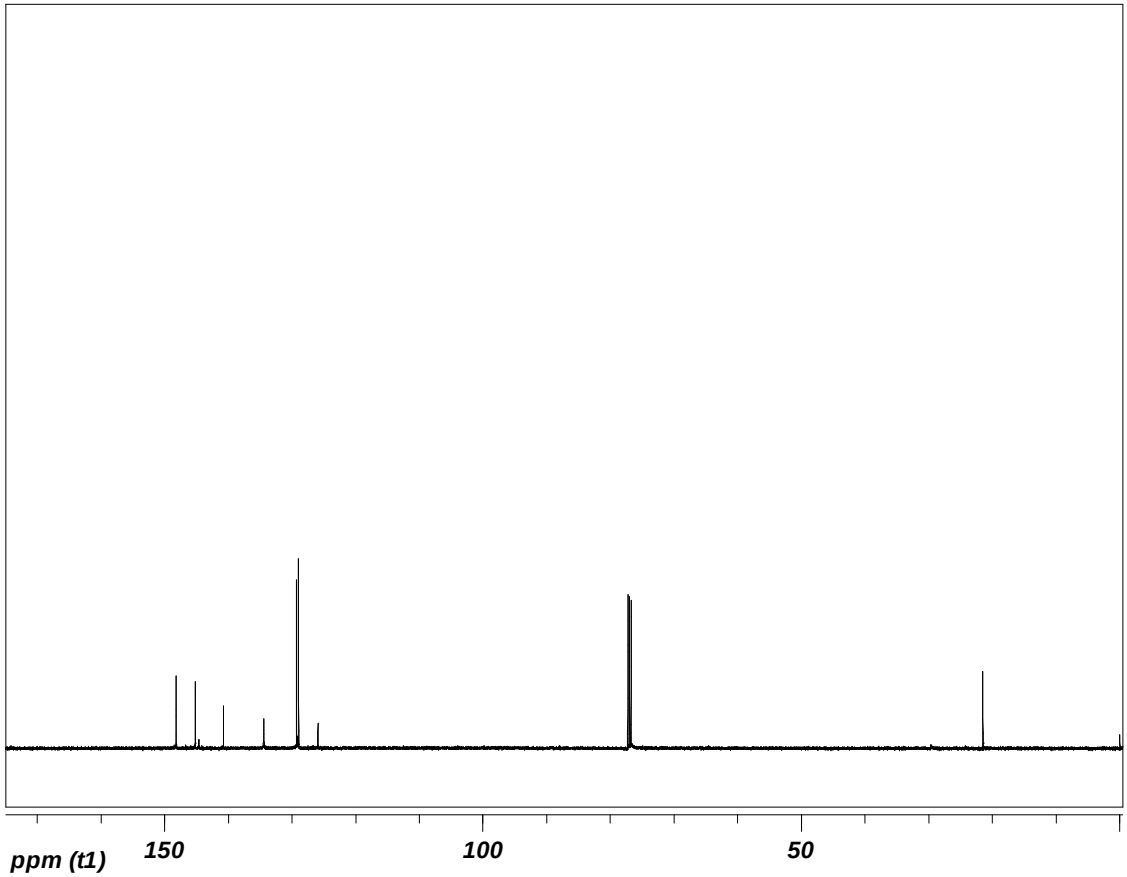

N
N
O
F
5.0
0.0
ppm (t1)

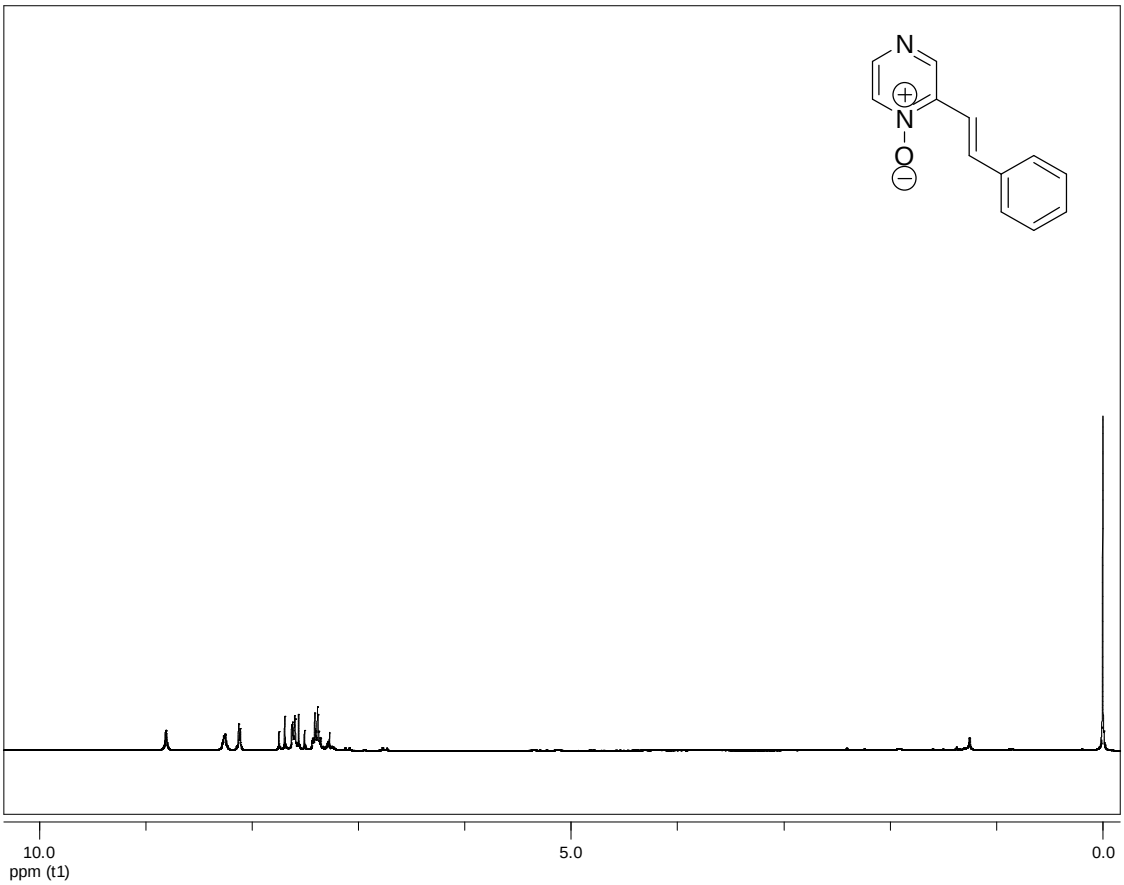

150
100
50
ppm (t1)

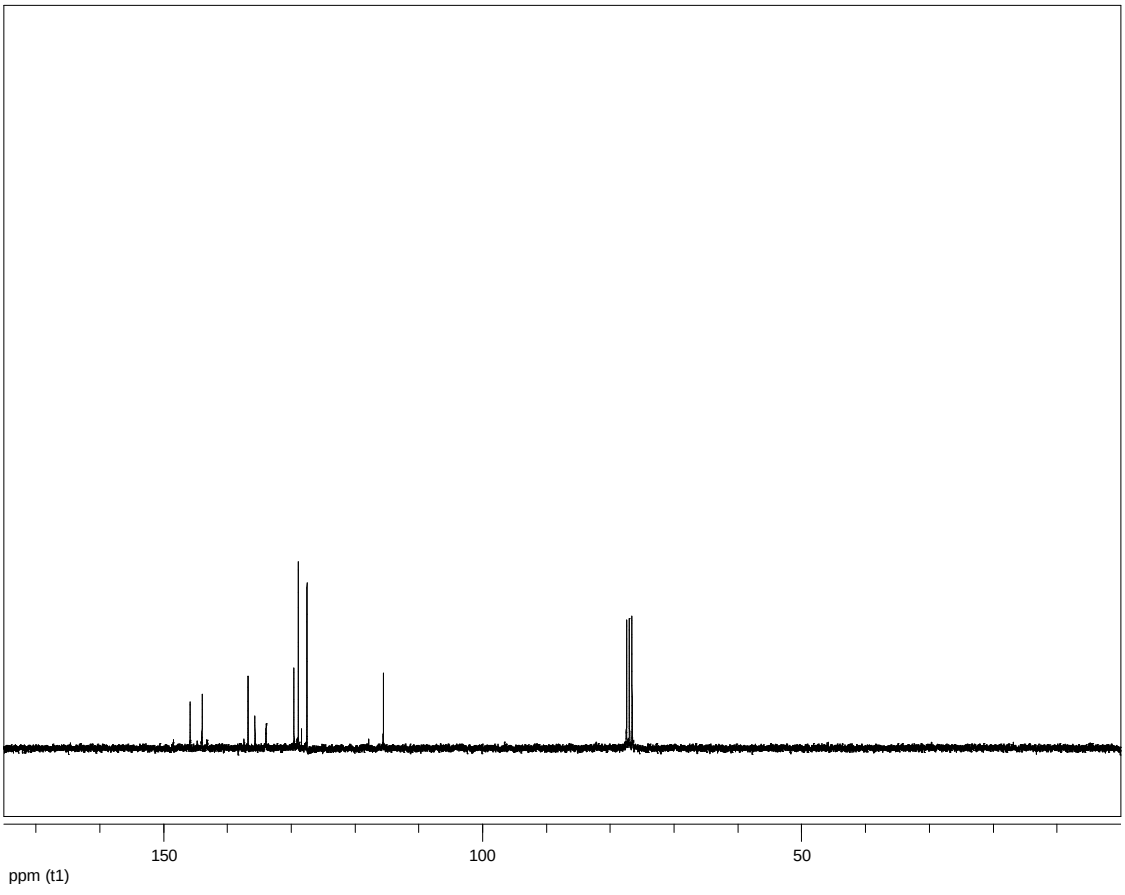

N
N
O
F
ppm (t1)
5.0
0.0

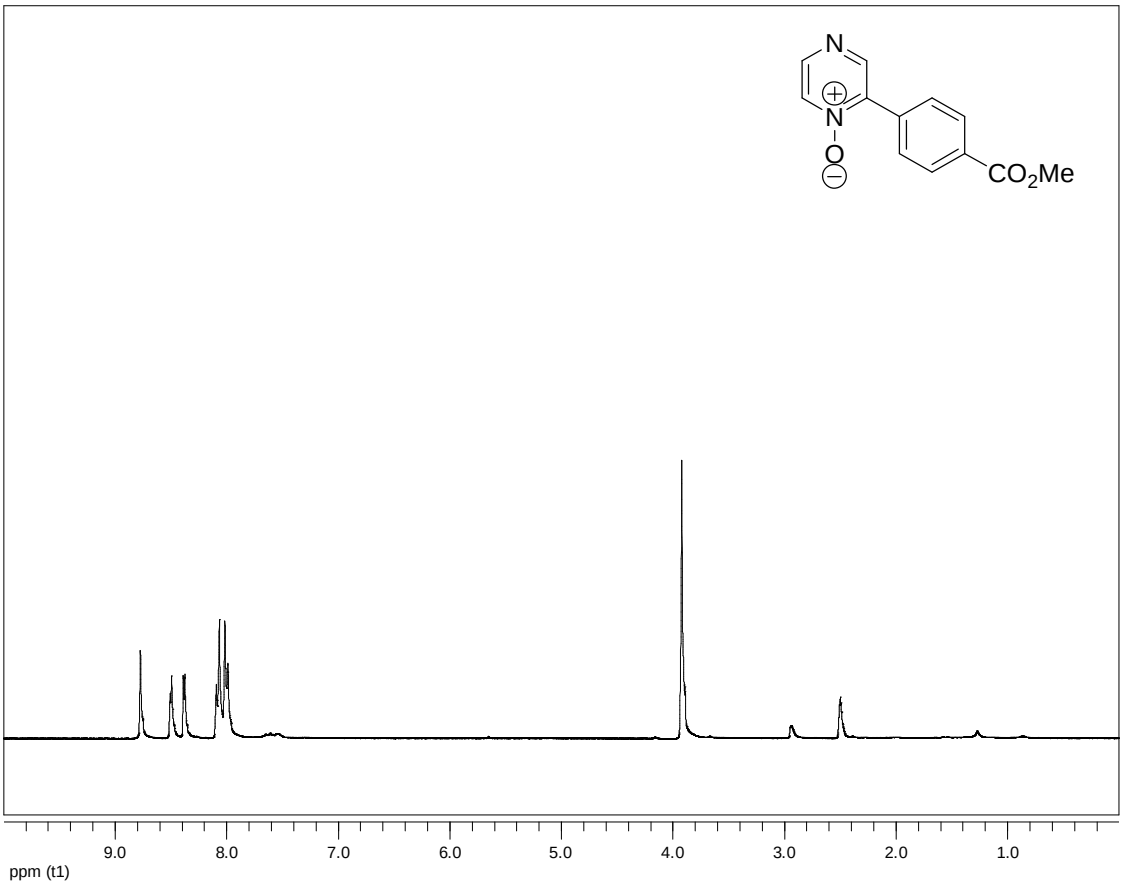

ppm (t1)
150
100
50

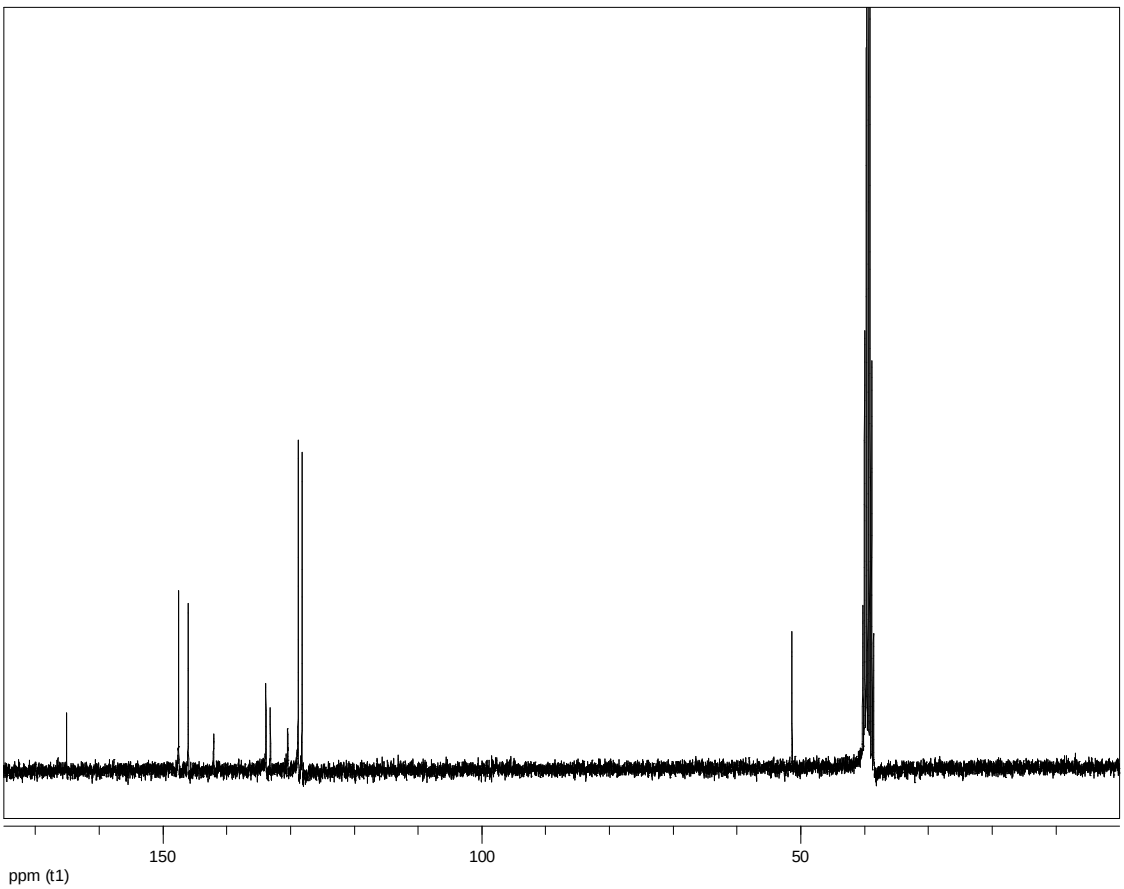

N
N
O
ppm (t1)
5.0
0.0

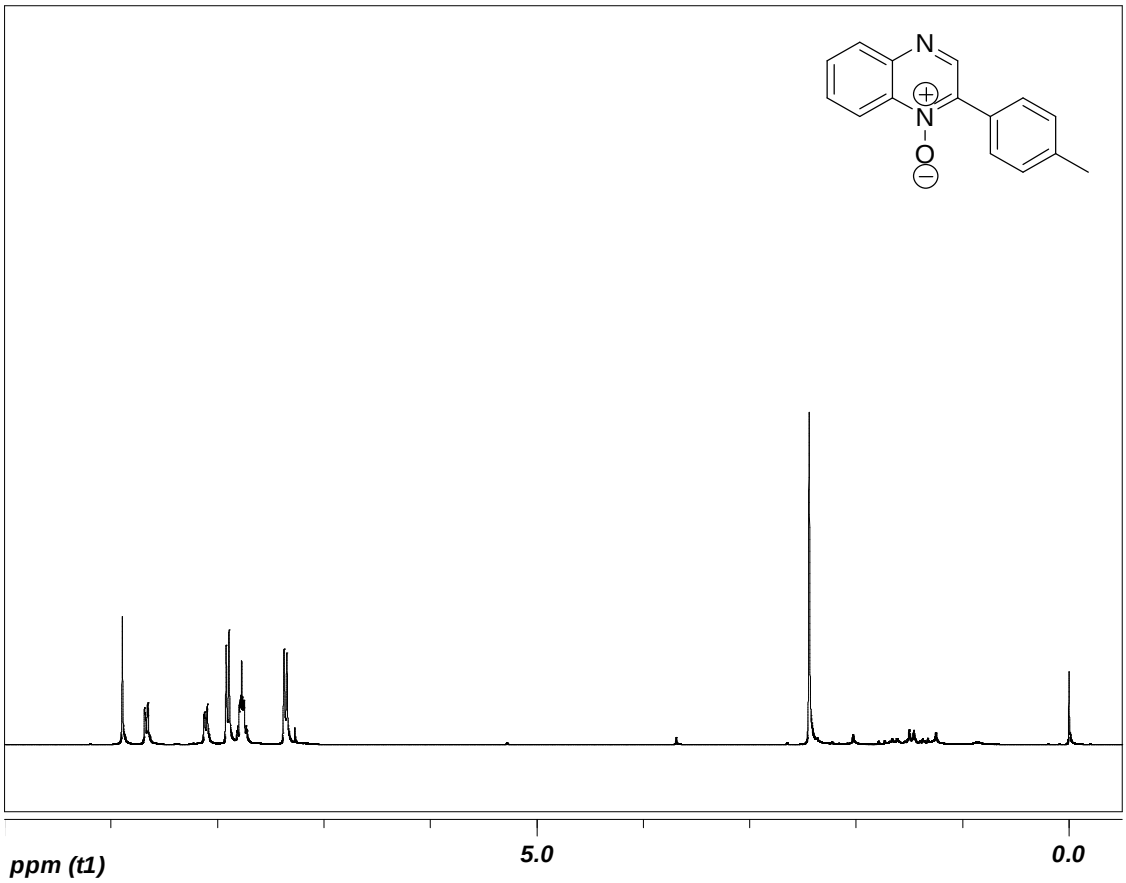

ppm (t1)
150
100
50

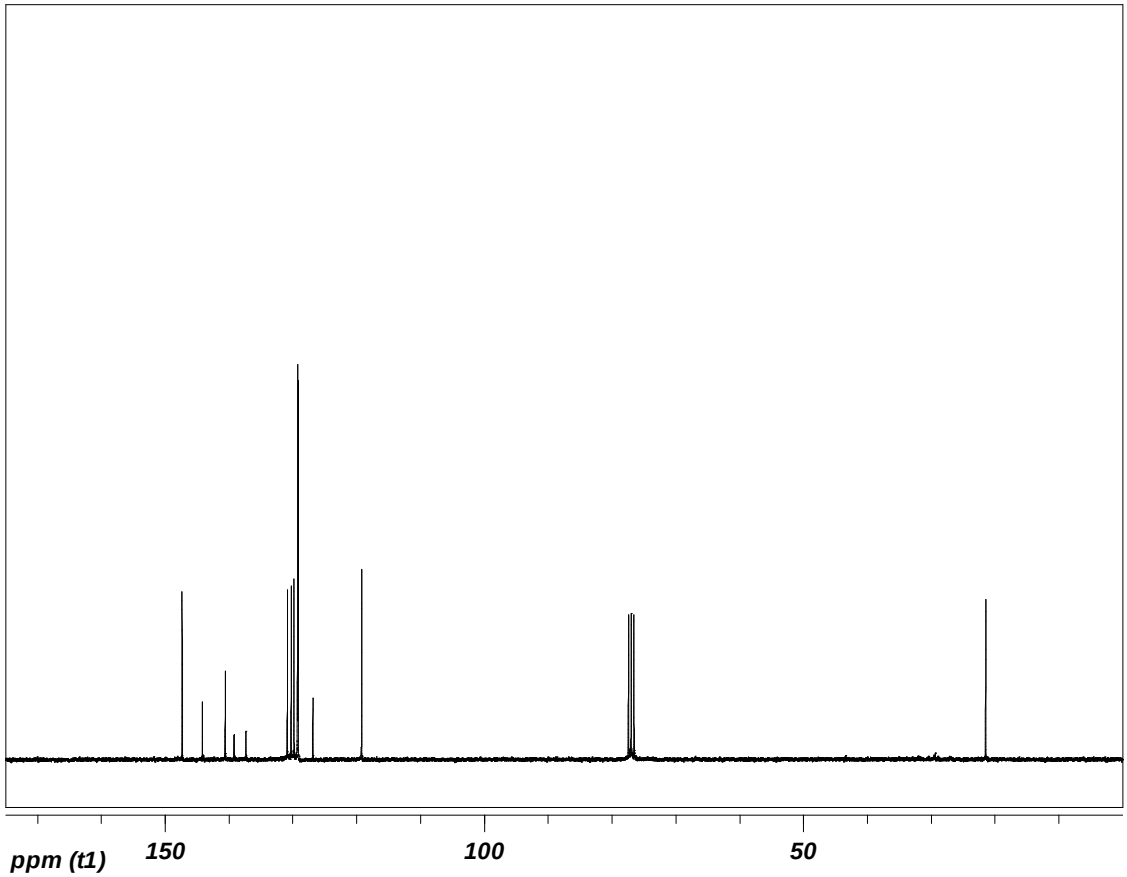

N
N
O
10.0
ppm (t1)
5.0
0.0

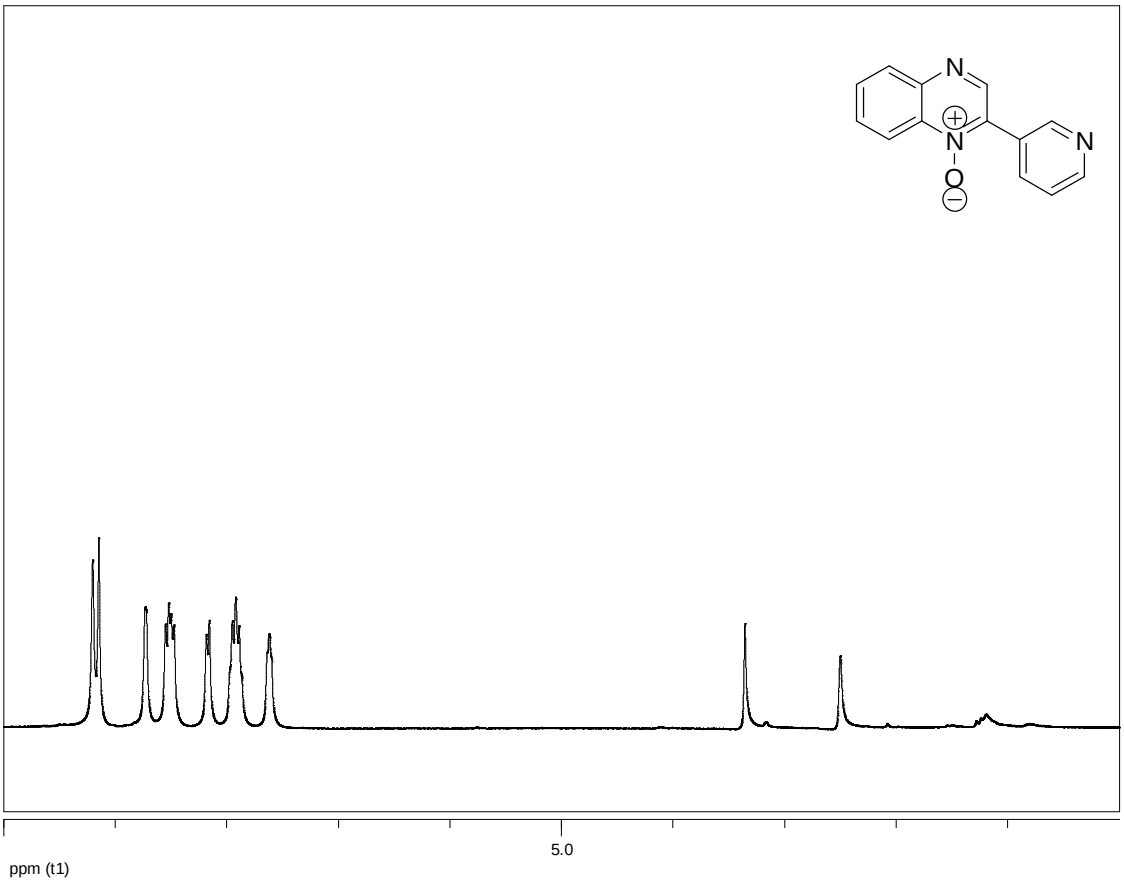

150
100
50
ppm (t1)

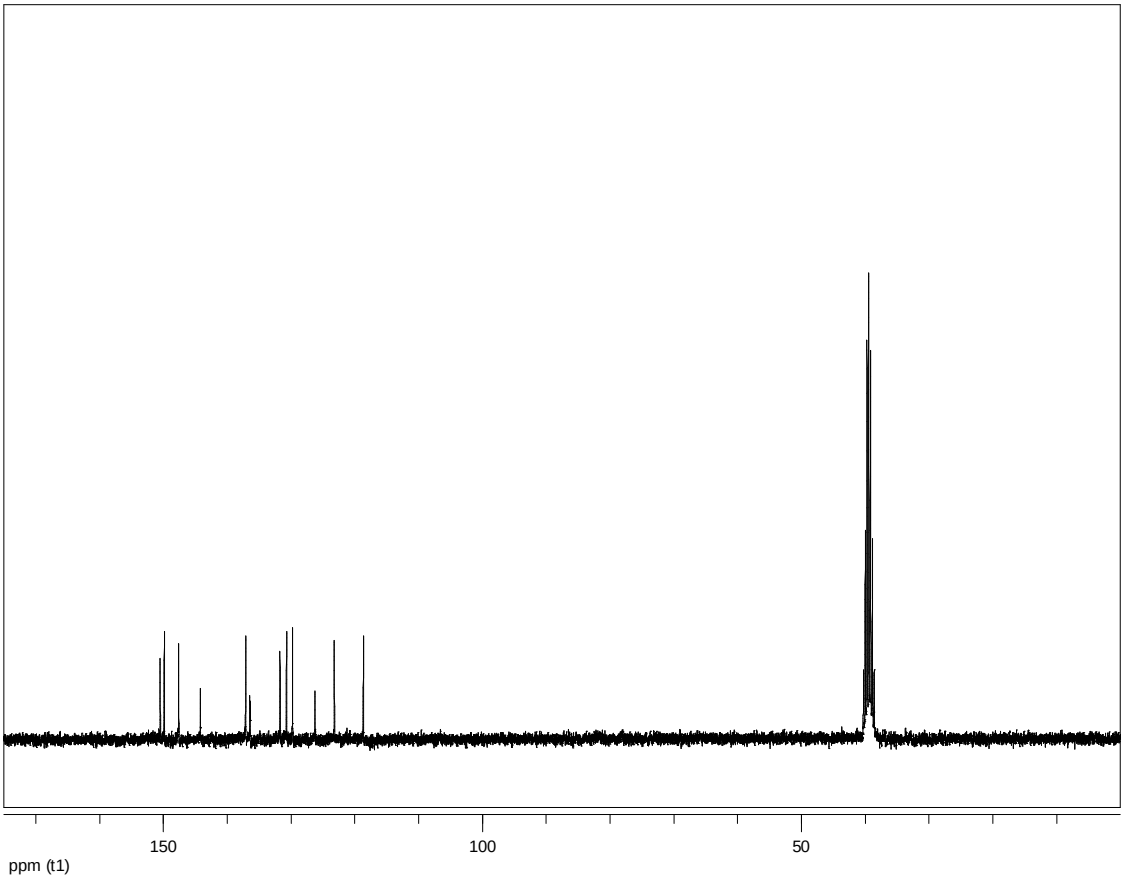

N
N
O
CO2Me
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

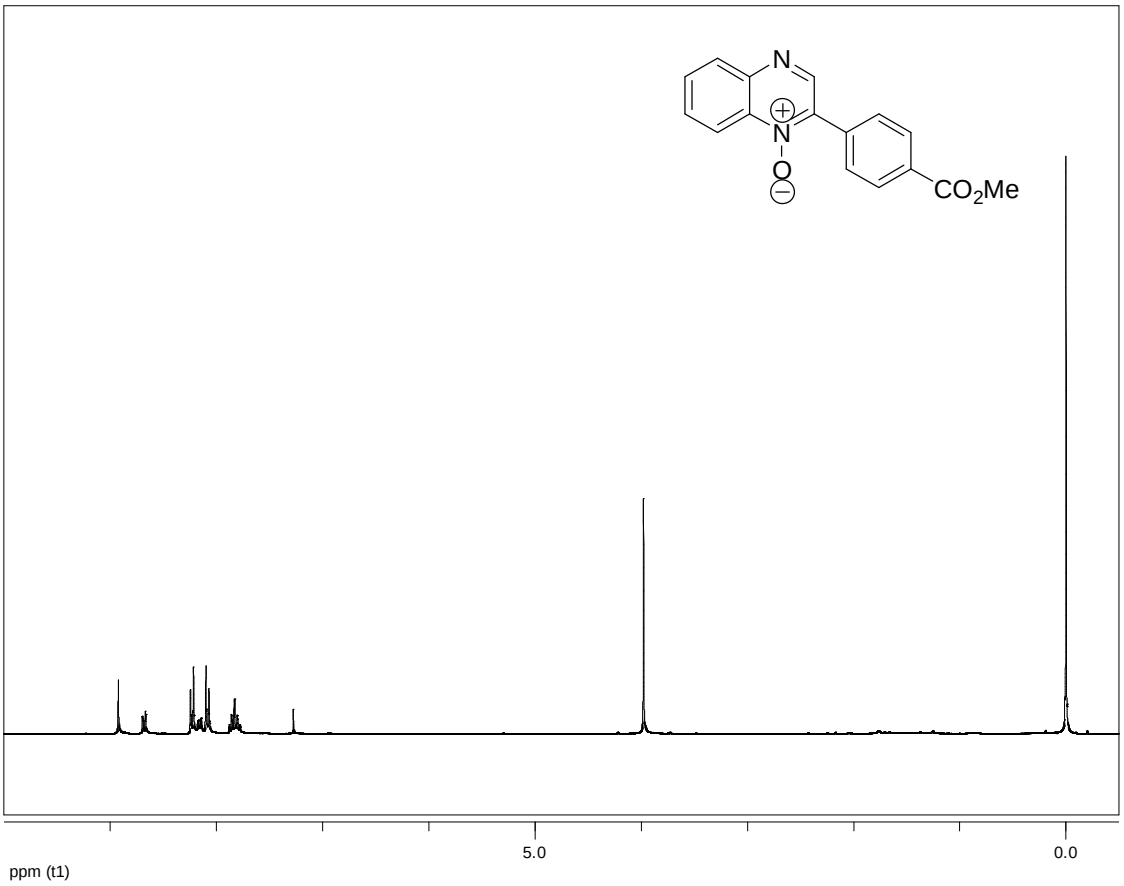

150
100
50
ppm (t1)

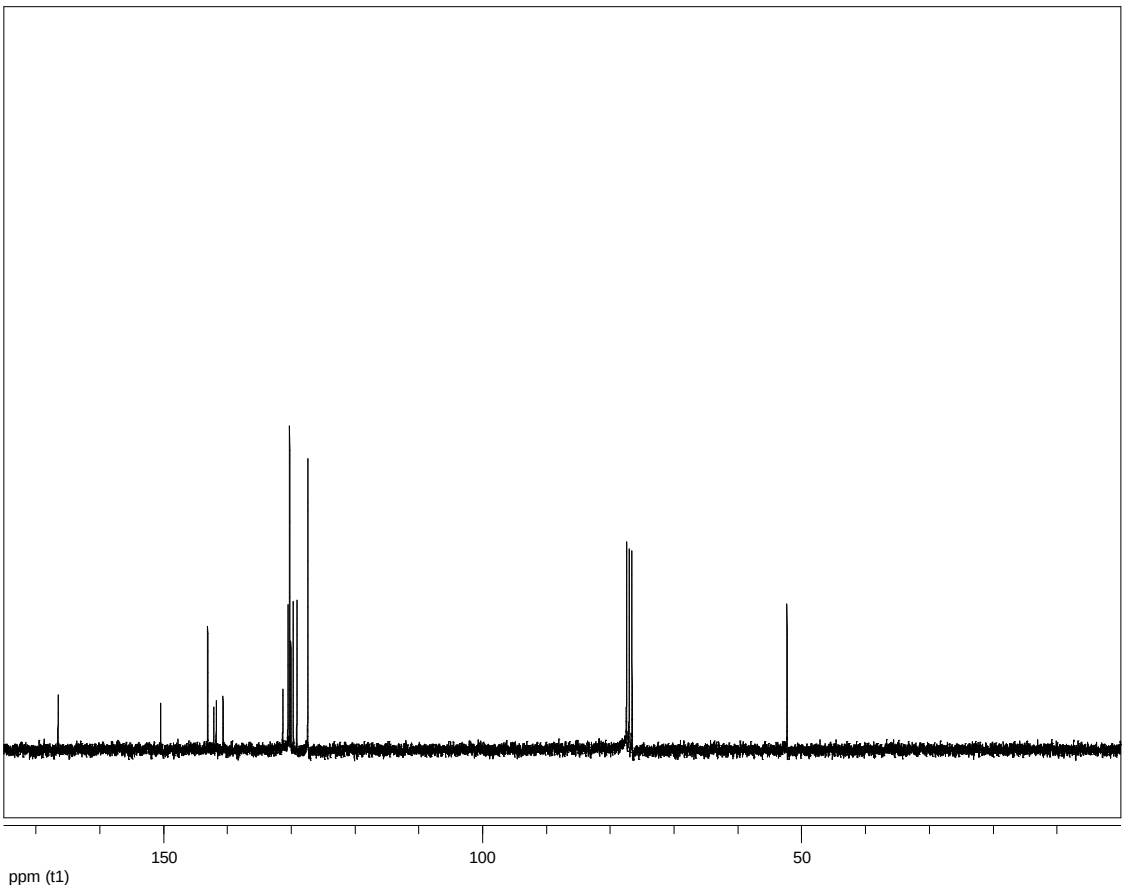

N
N
O
5.0
0.0
ppm (t1)

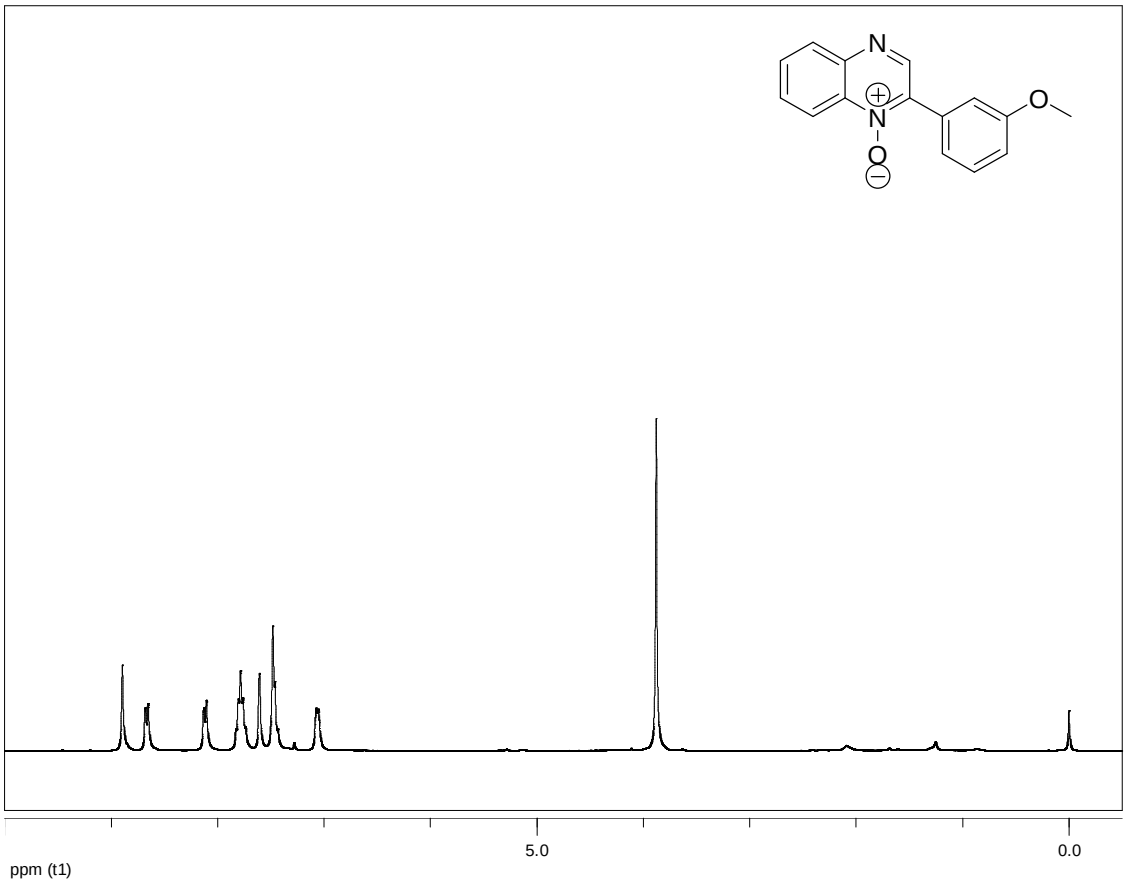

150
100
50
ppm (t1)

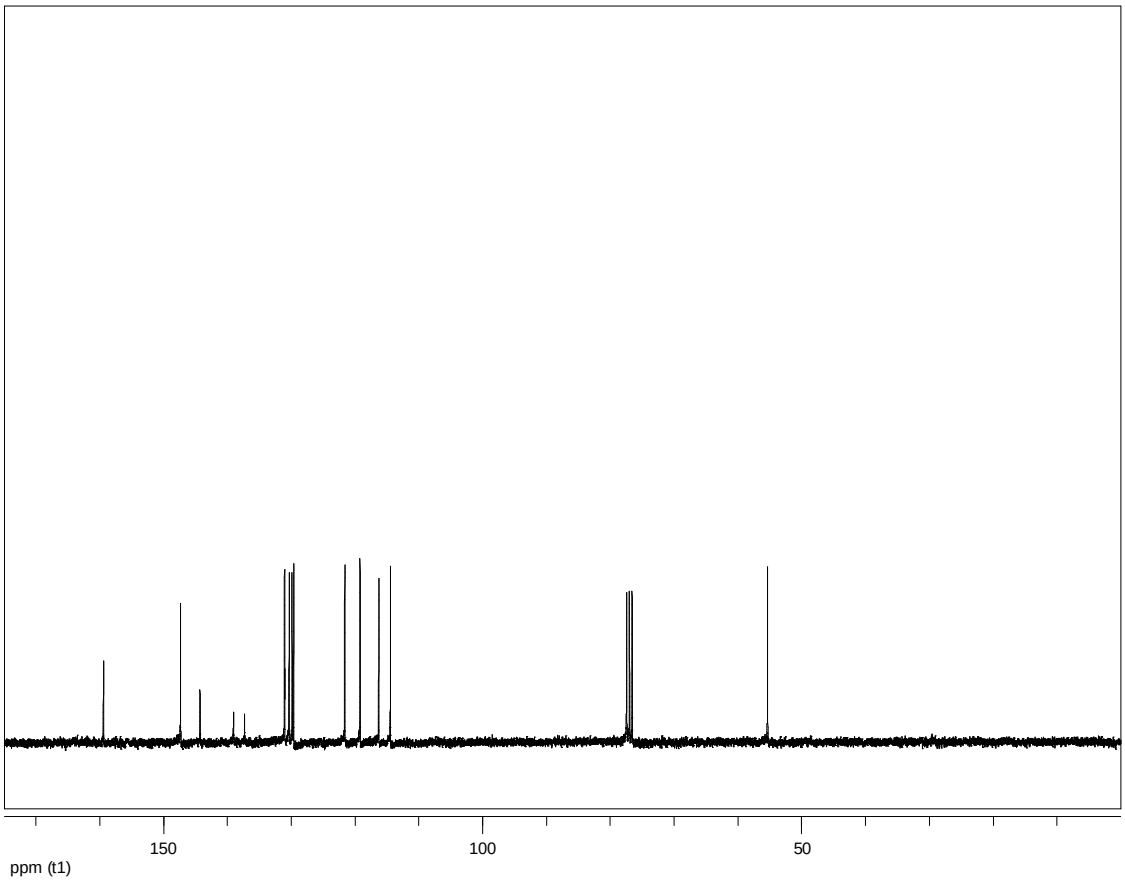

N
N
O
N
5.0
ppm (t1)

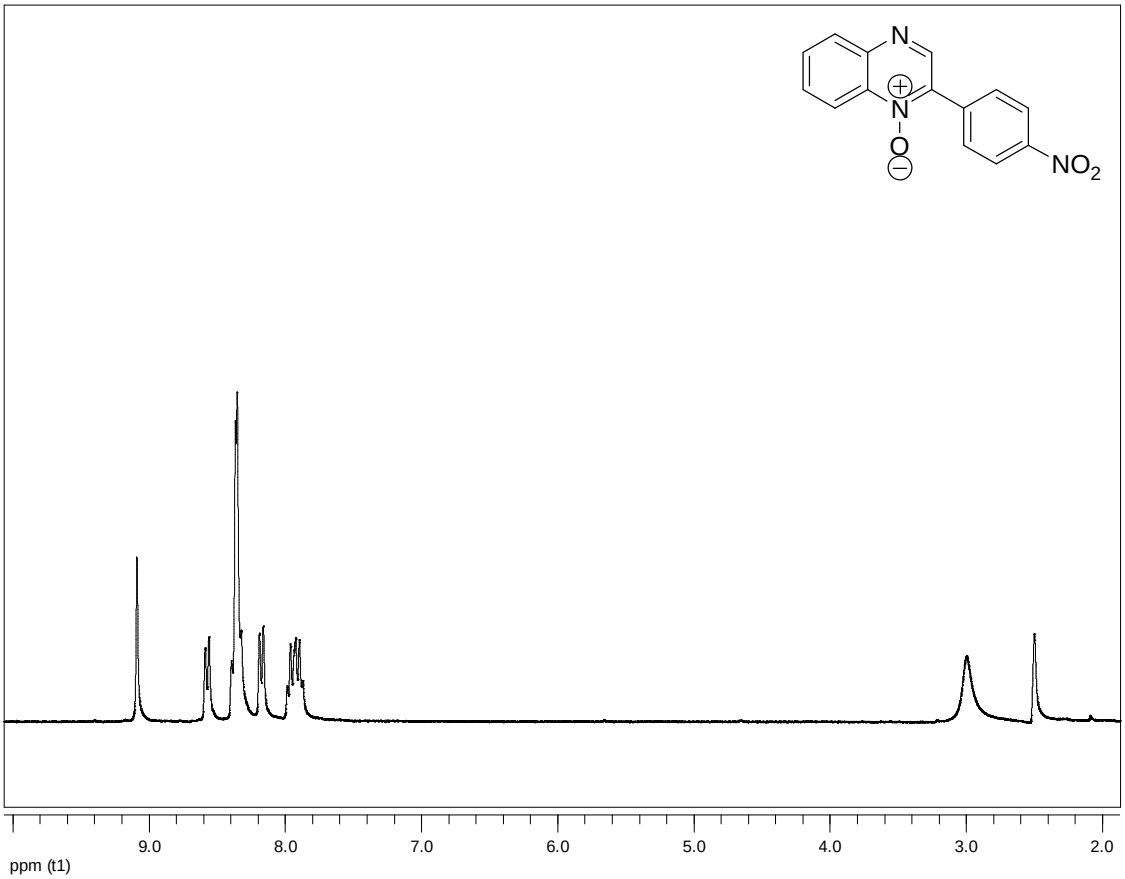

150
100
50
ppm (t1)

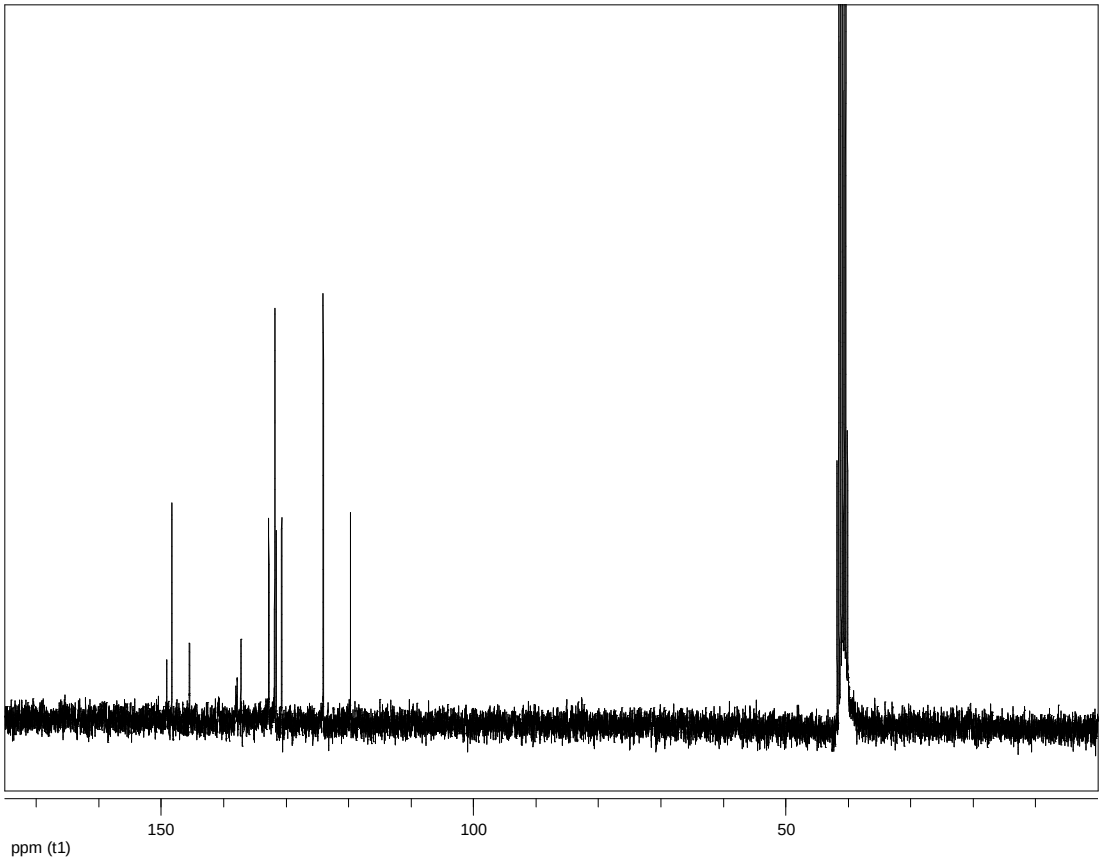

N
N
O
CO2Me
5.0
0.0
ppm (t1)

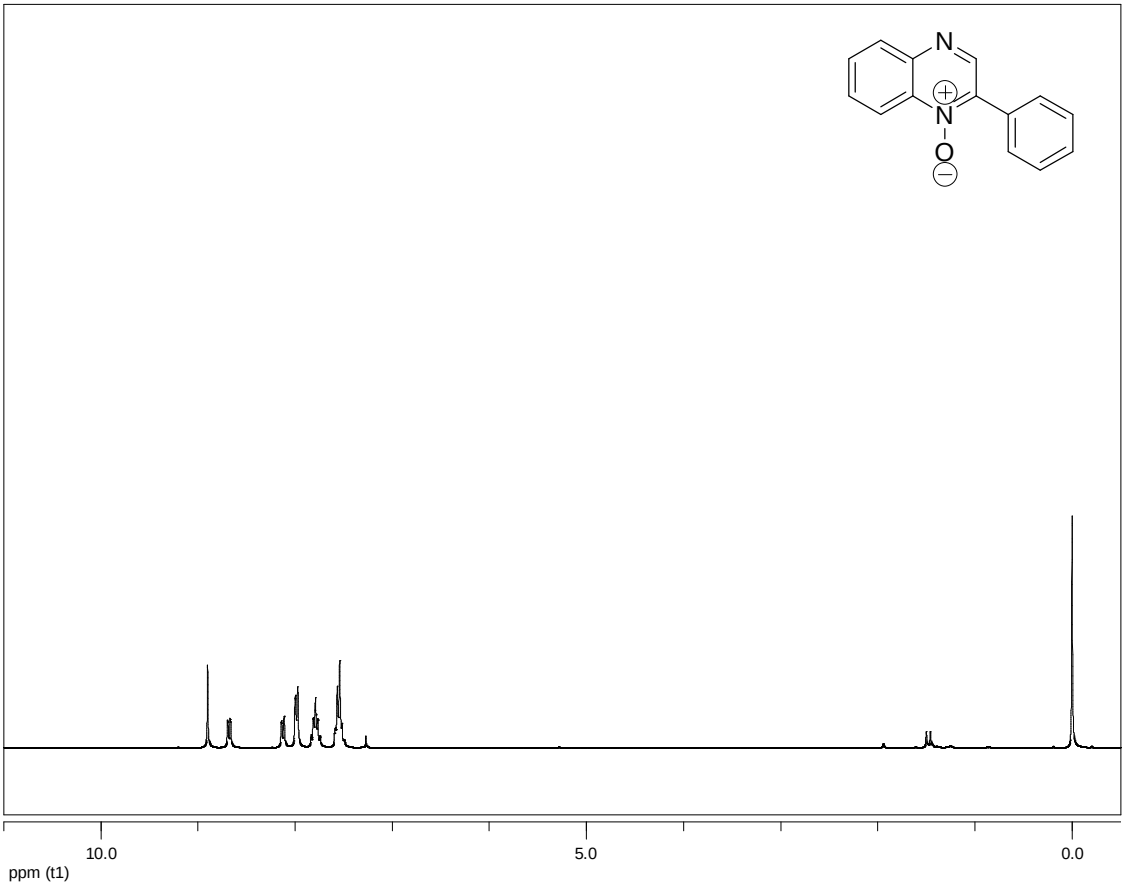

150
100
50
ppm (t1)

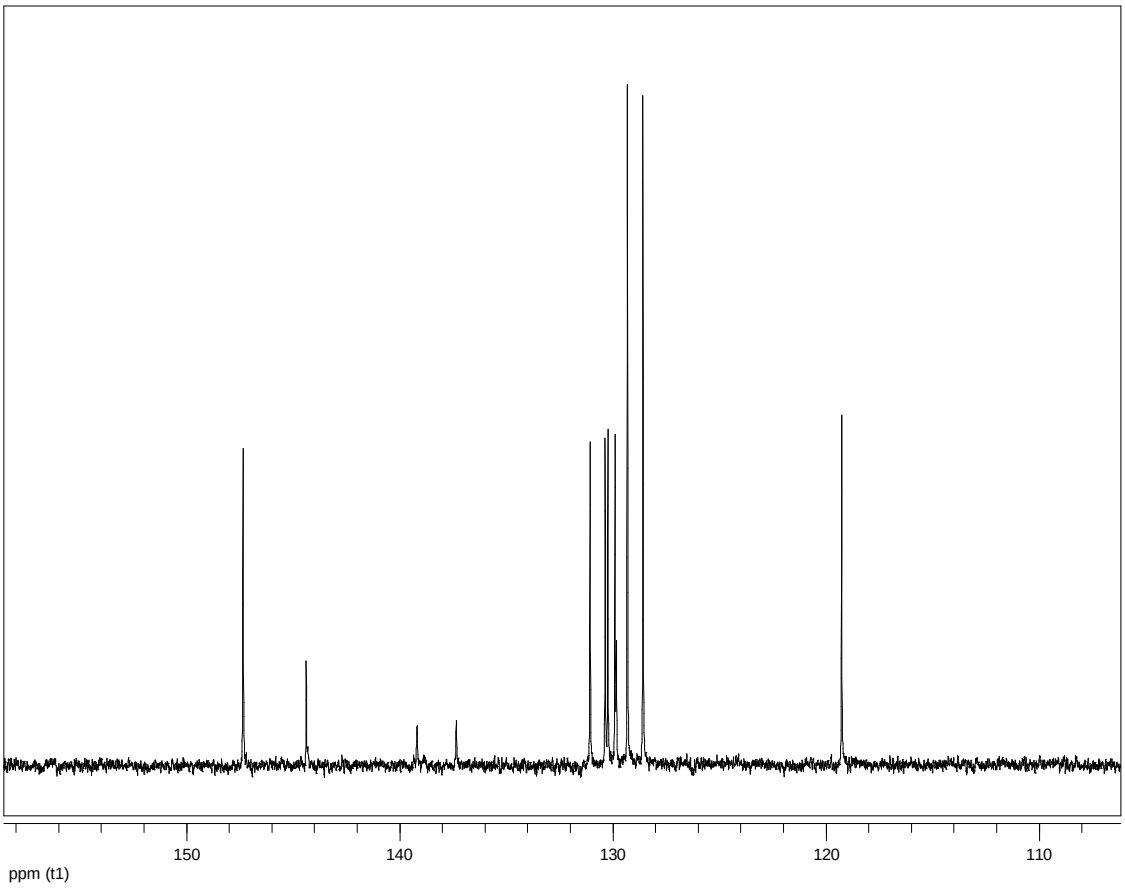

N
N
O
O
5.0
0.0
ppm (t1)

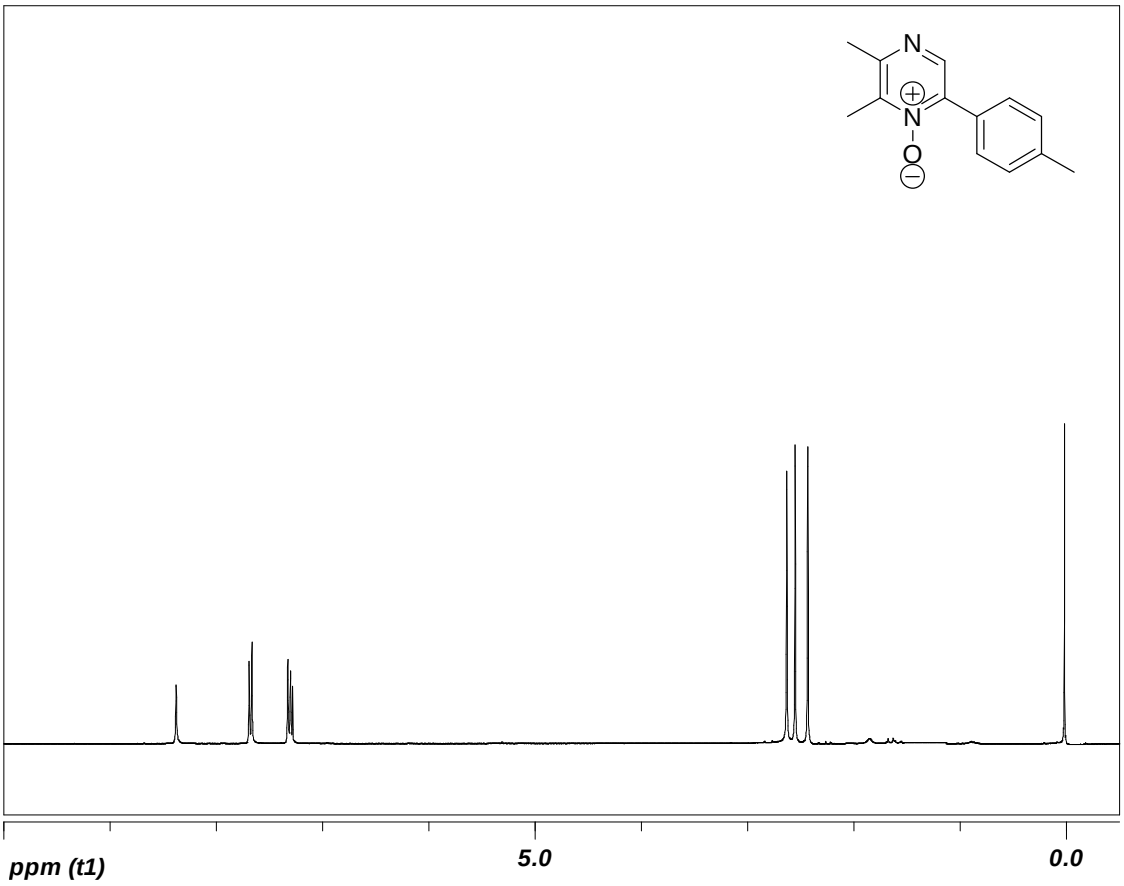

150
100
50
ppm (t1)

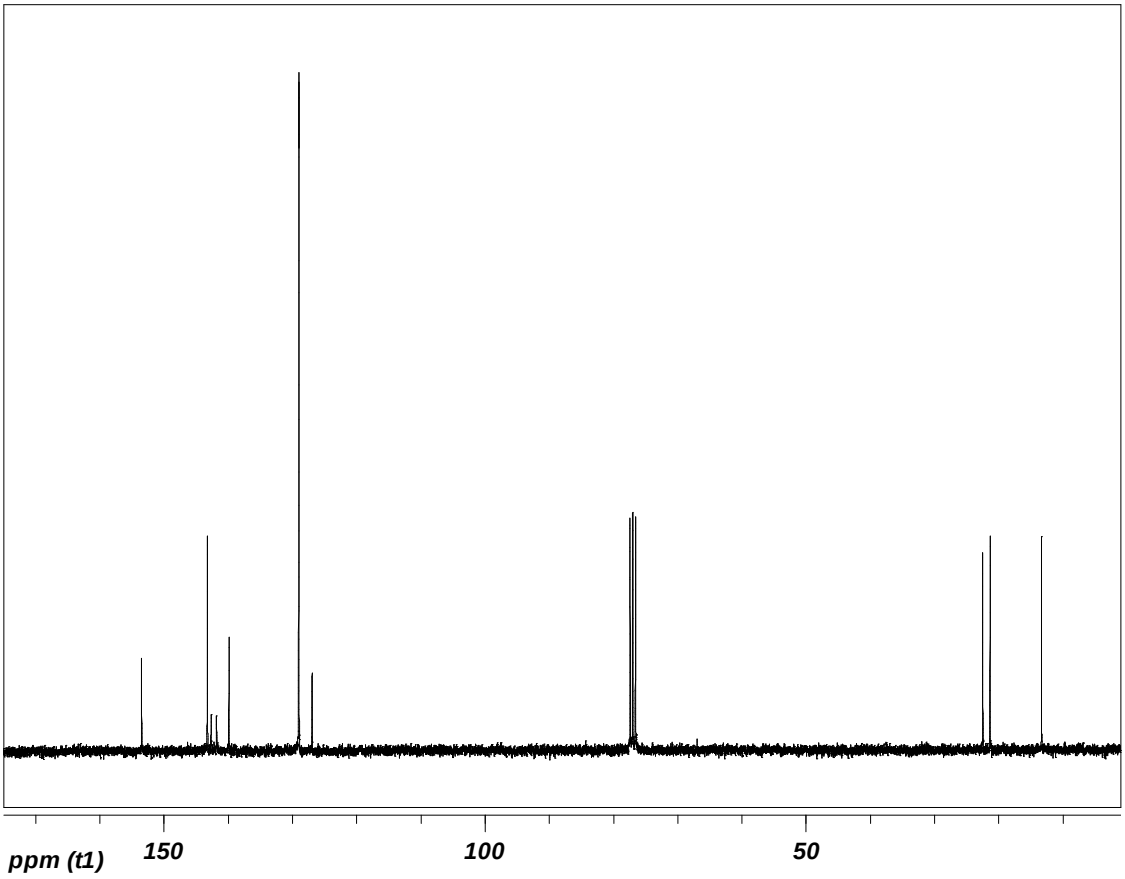

N
N
O
NO2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

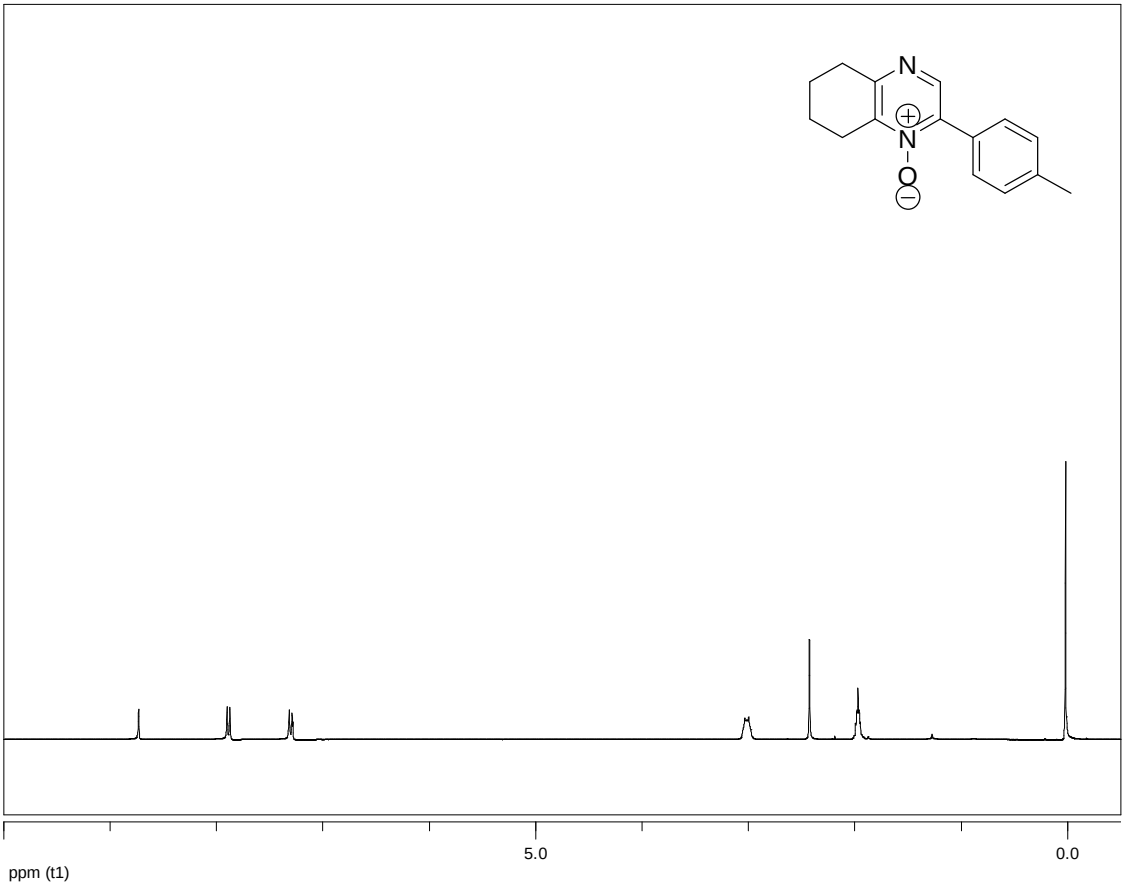

150
100
50
ppm (t1)

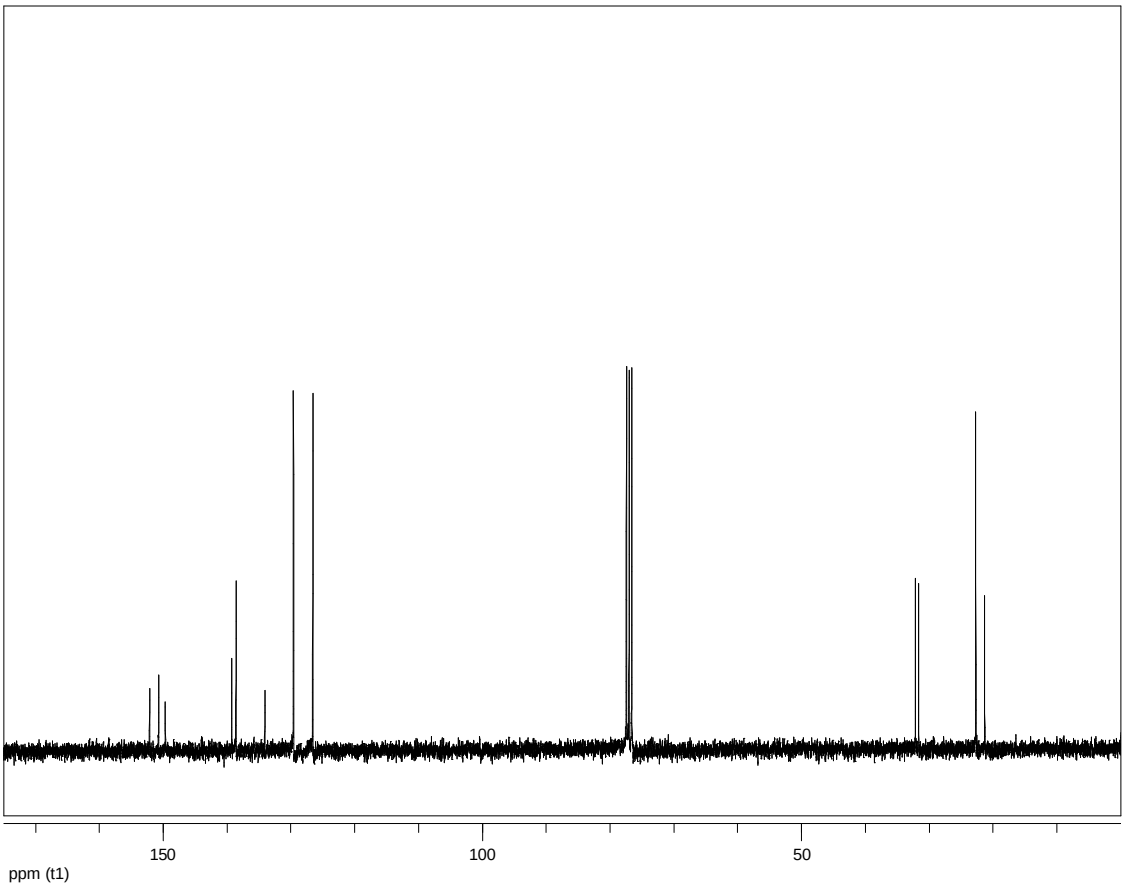

N
N
O
10.0
5.0
0.0
ppm (t1)

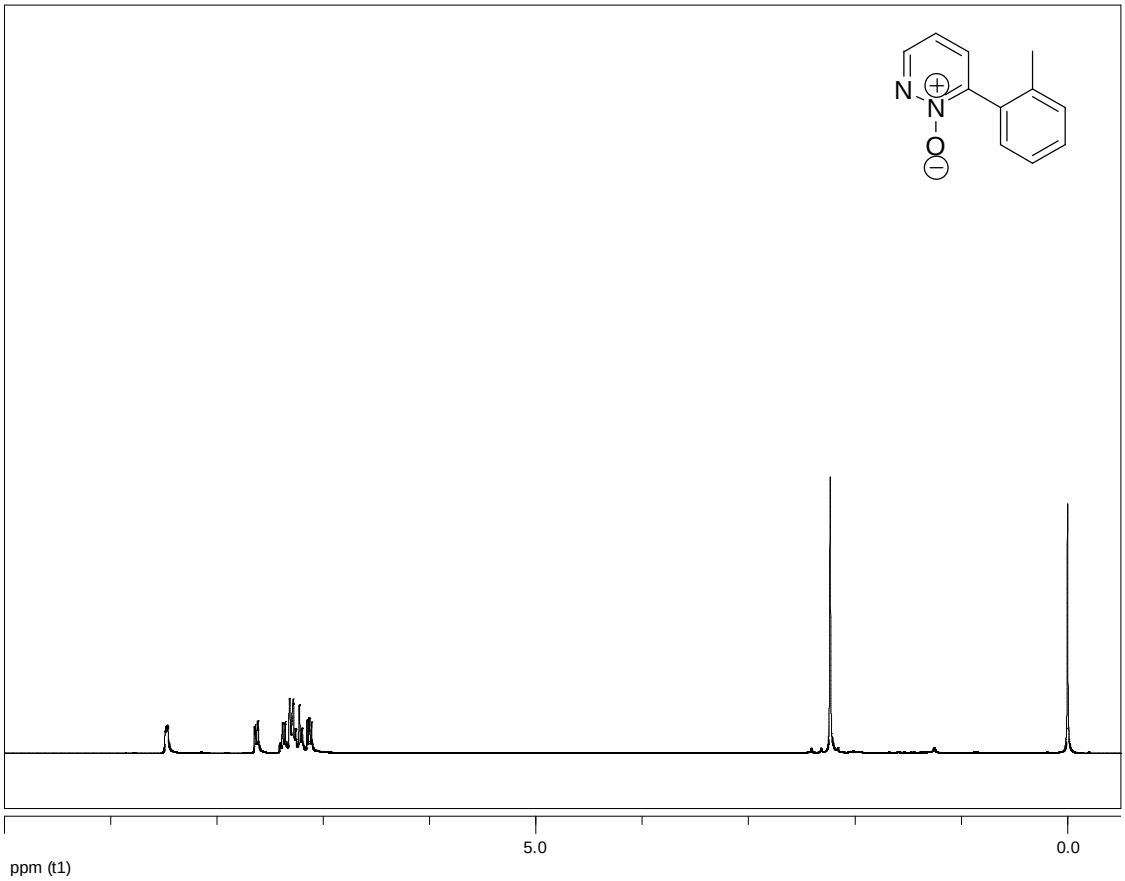

150
140
130
120
110
ppm (t1)

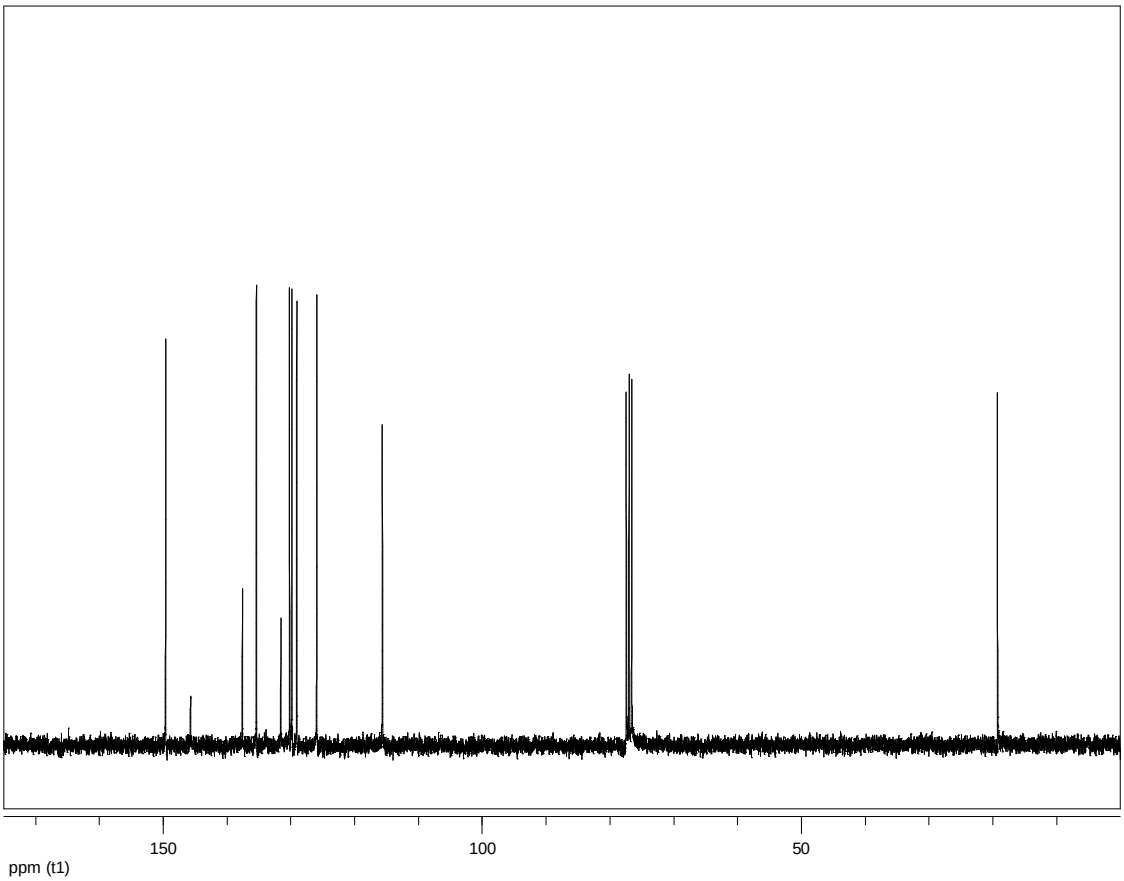

N
N
O
ppm (t1)
5.0
0.0

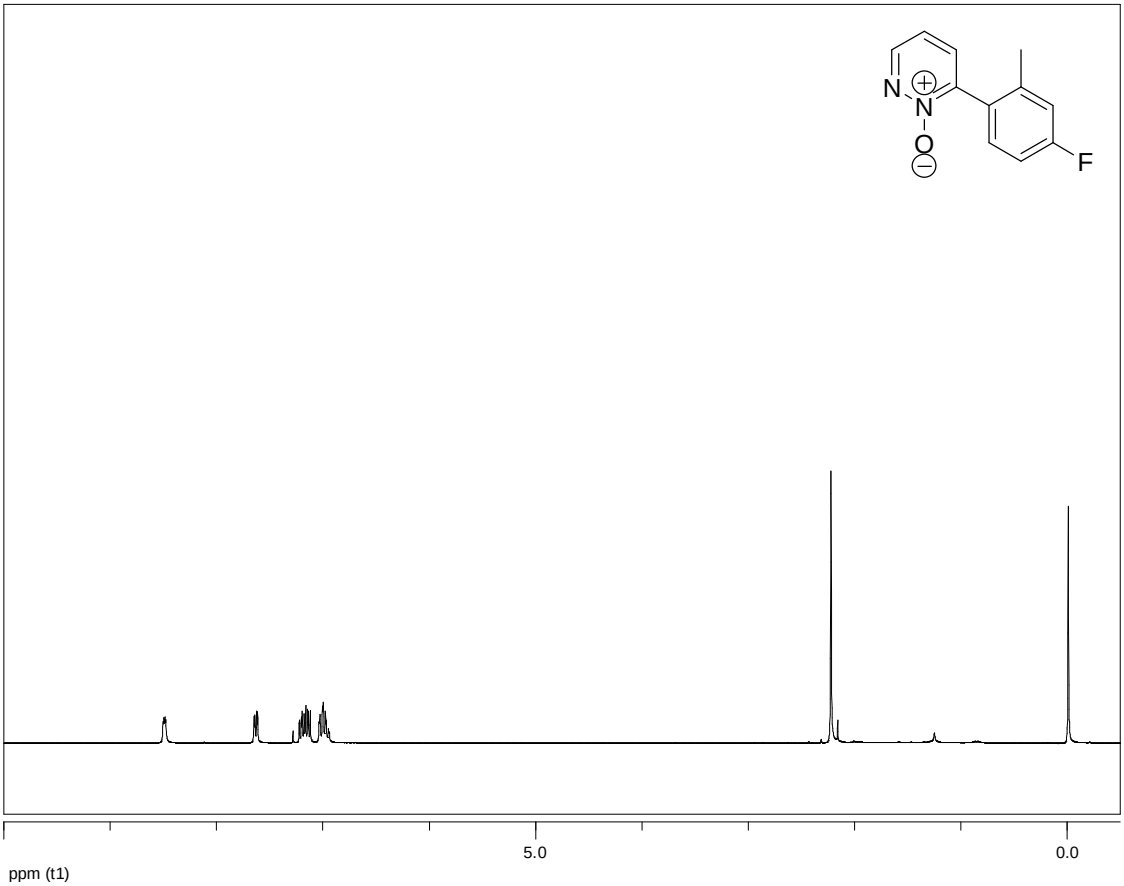

ppm (t1)
150
100
50

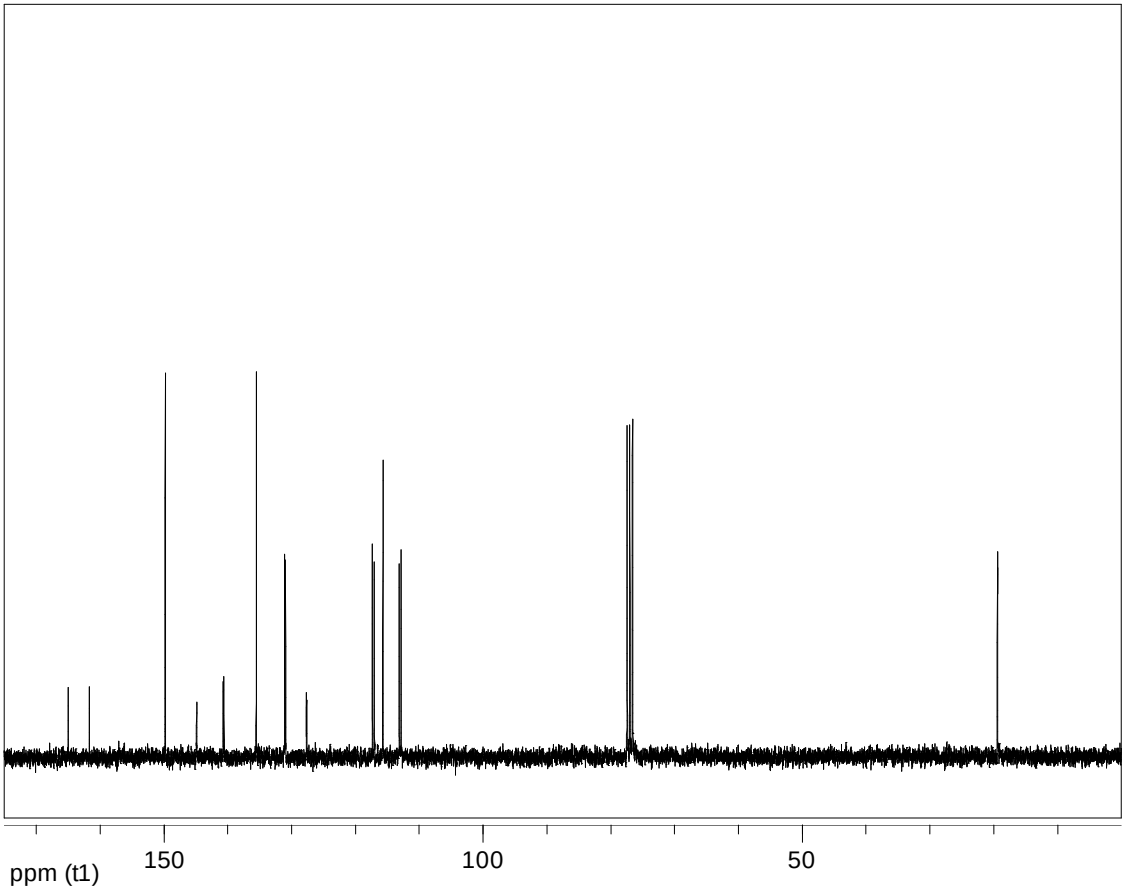

N
N
O
5.0
0.0
ppm (t1)

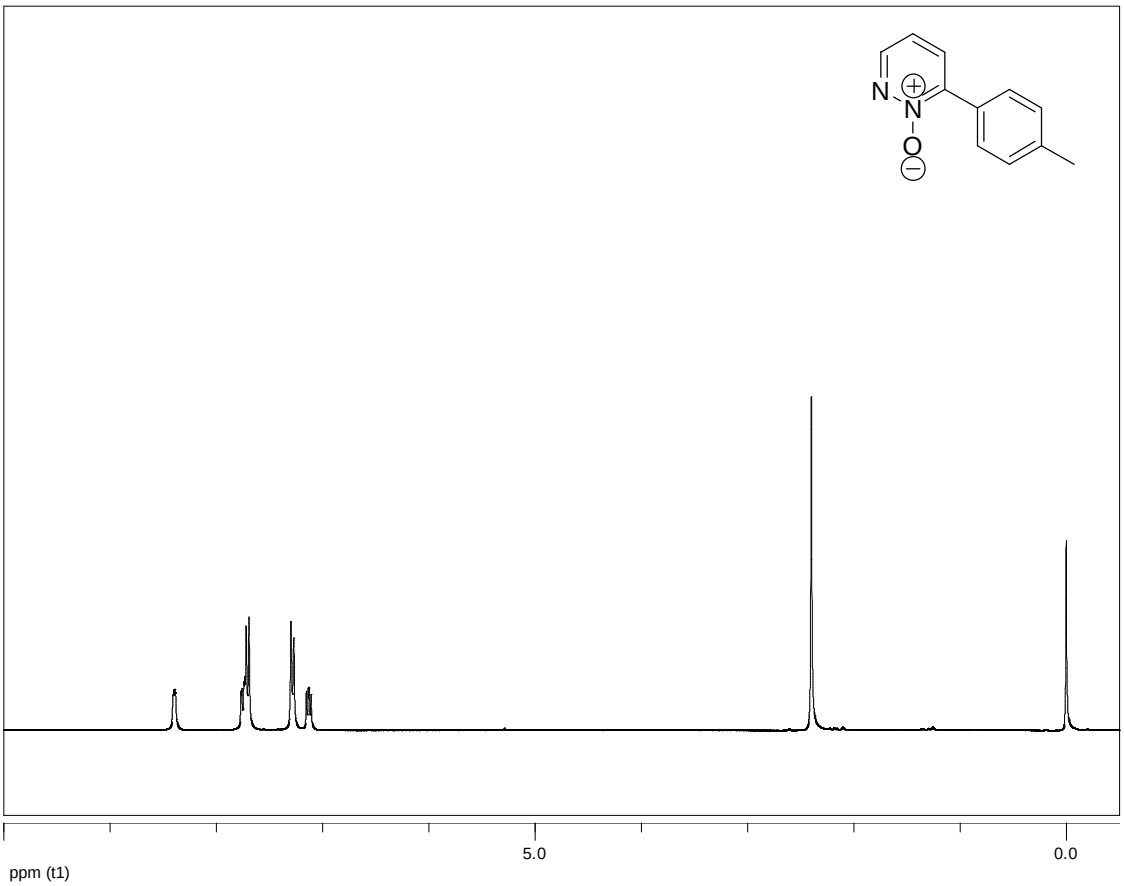

150
100
50
ppm (t1)

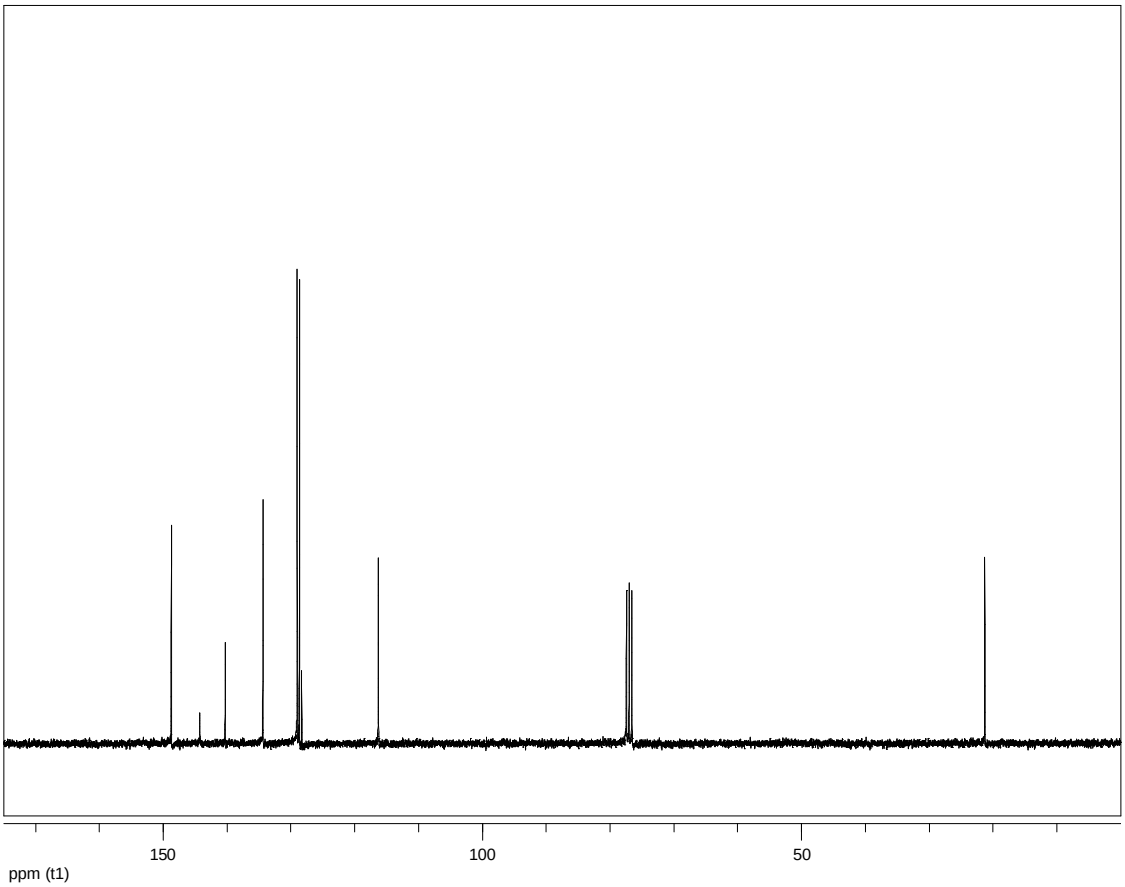

5.0
0.0
ppm (t1)

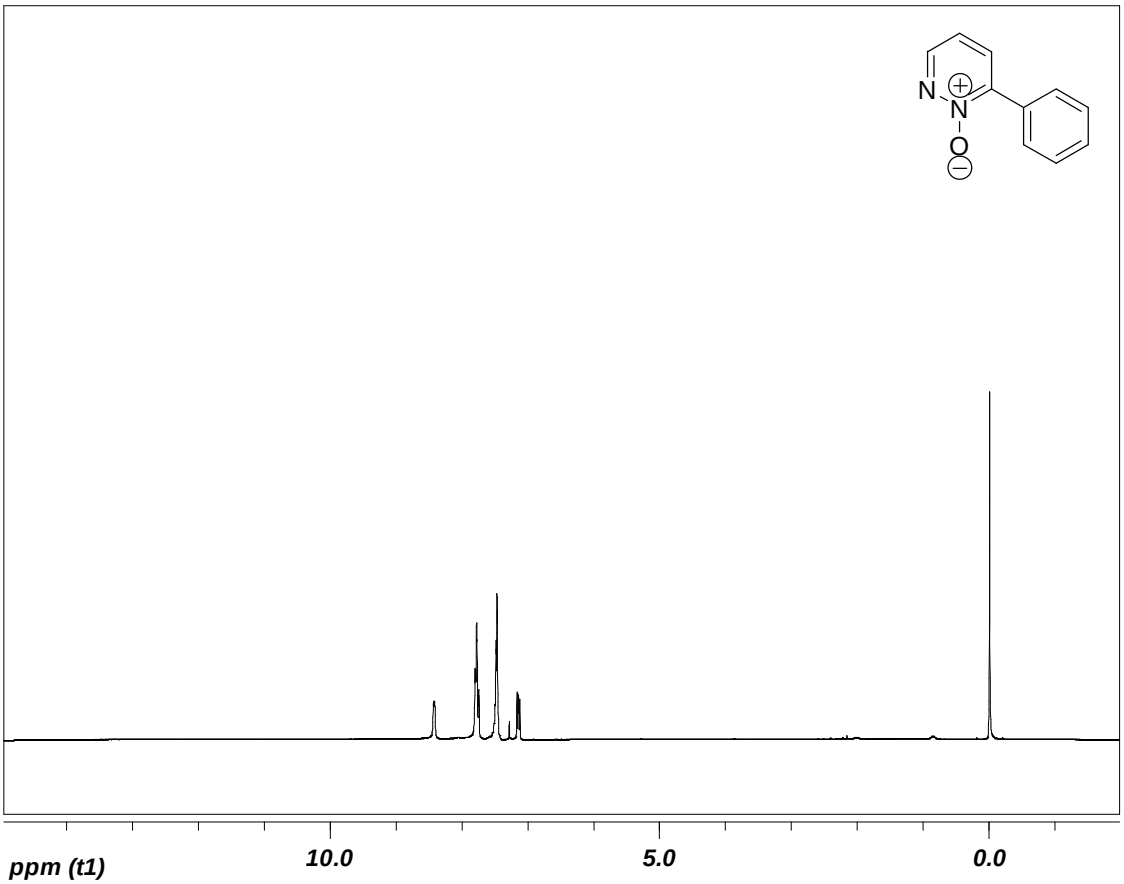

150
100
50
ppm (t1)

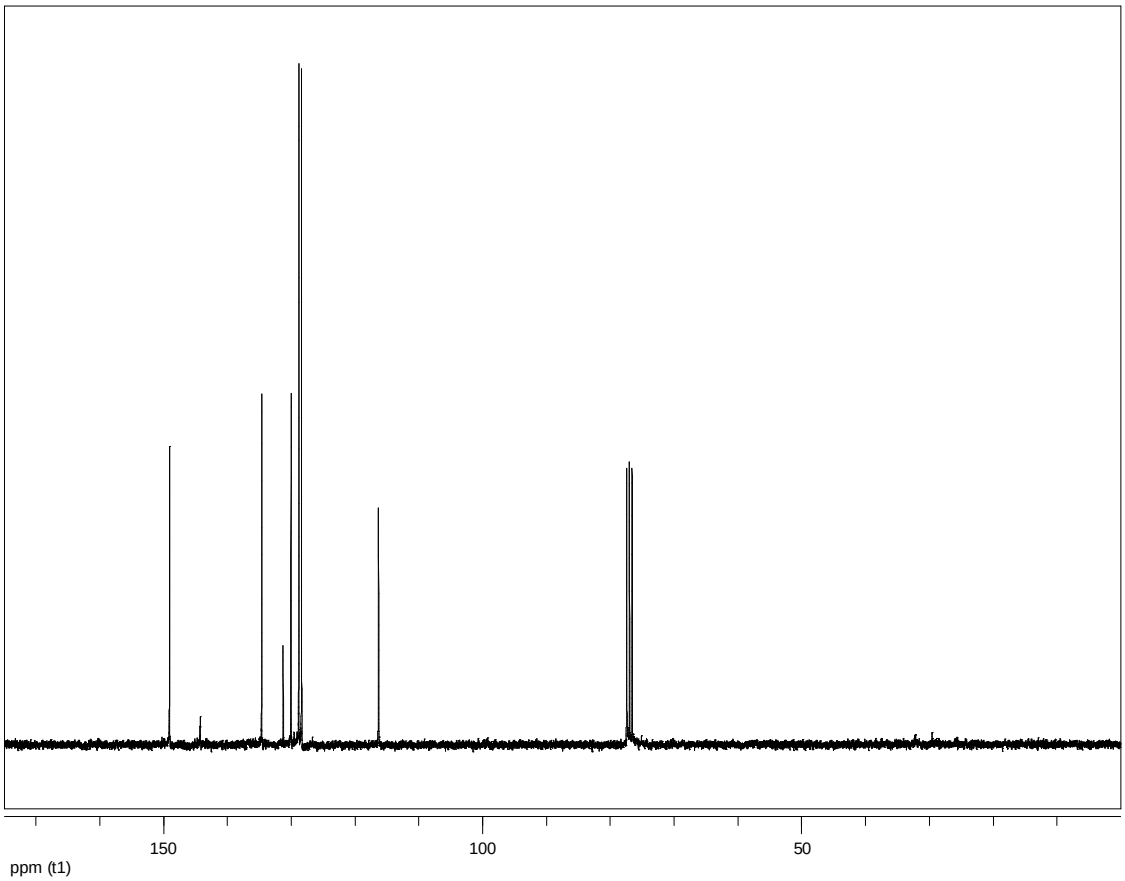

N
N
O
F
5.0
0.0
ppm (t1)

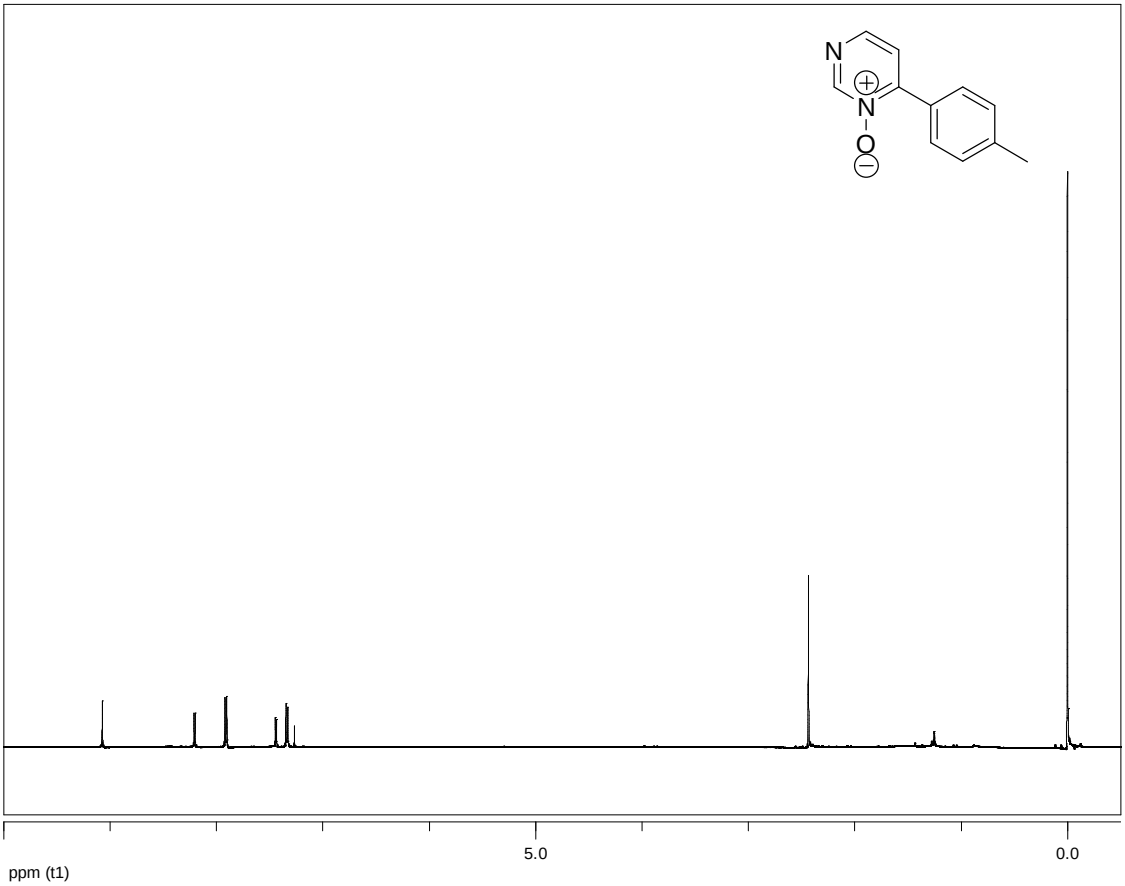

150
100
50
ppm (t1)

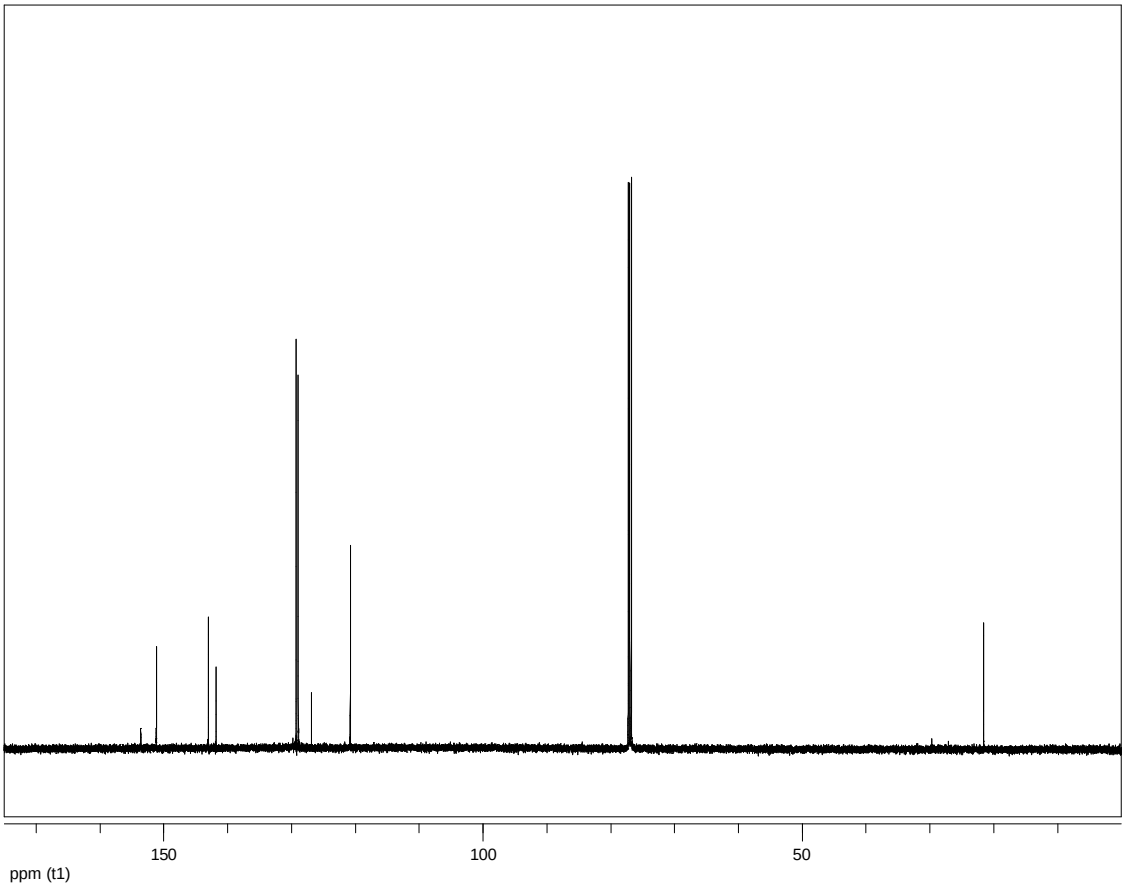

N
N
O
5.0
0.0
ppm (t1)

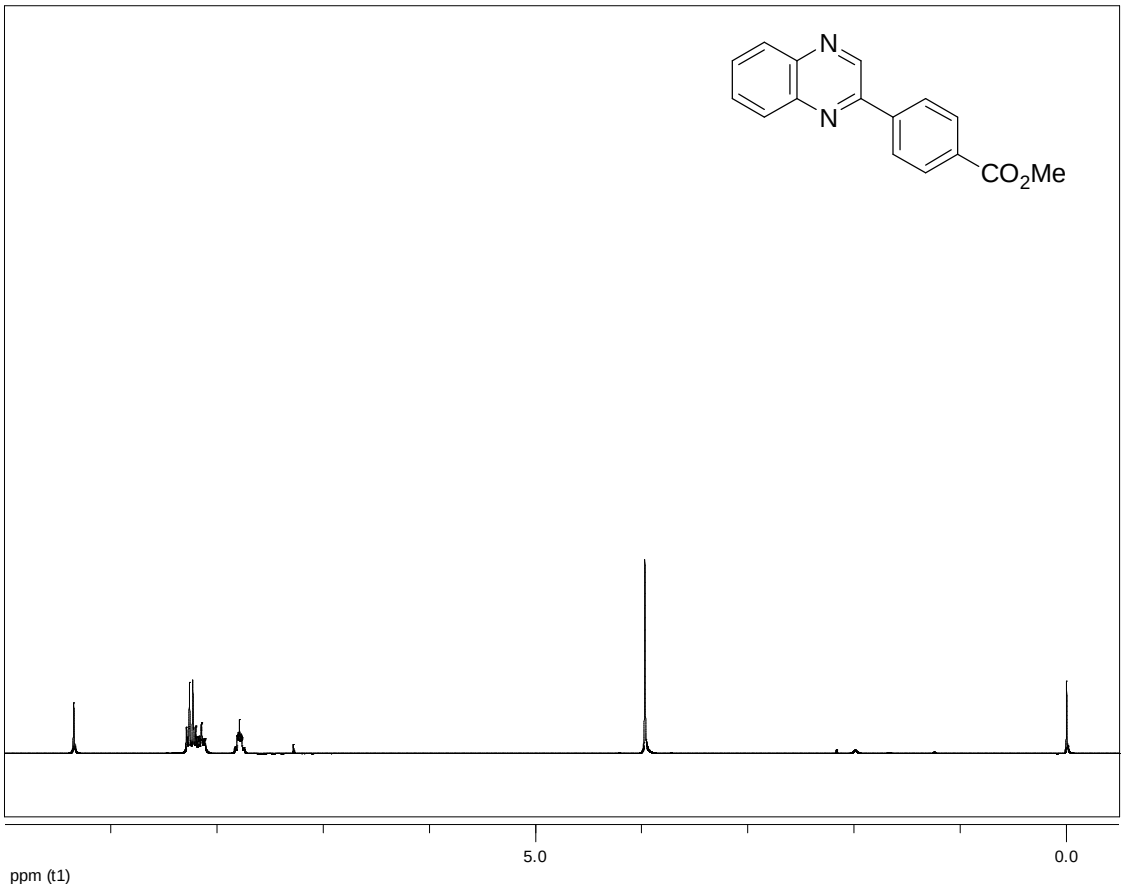

150
100
50
ppm (t1)

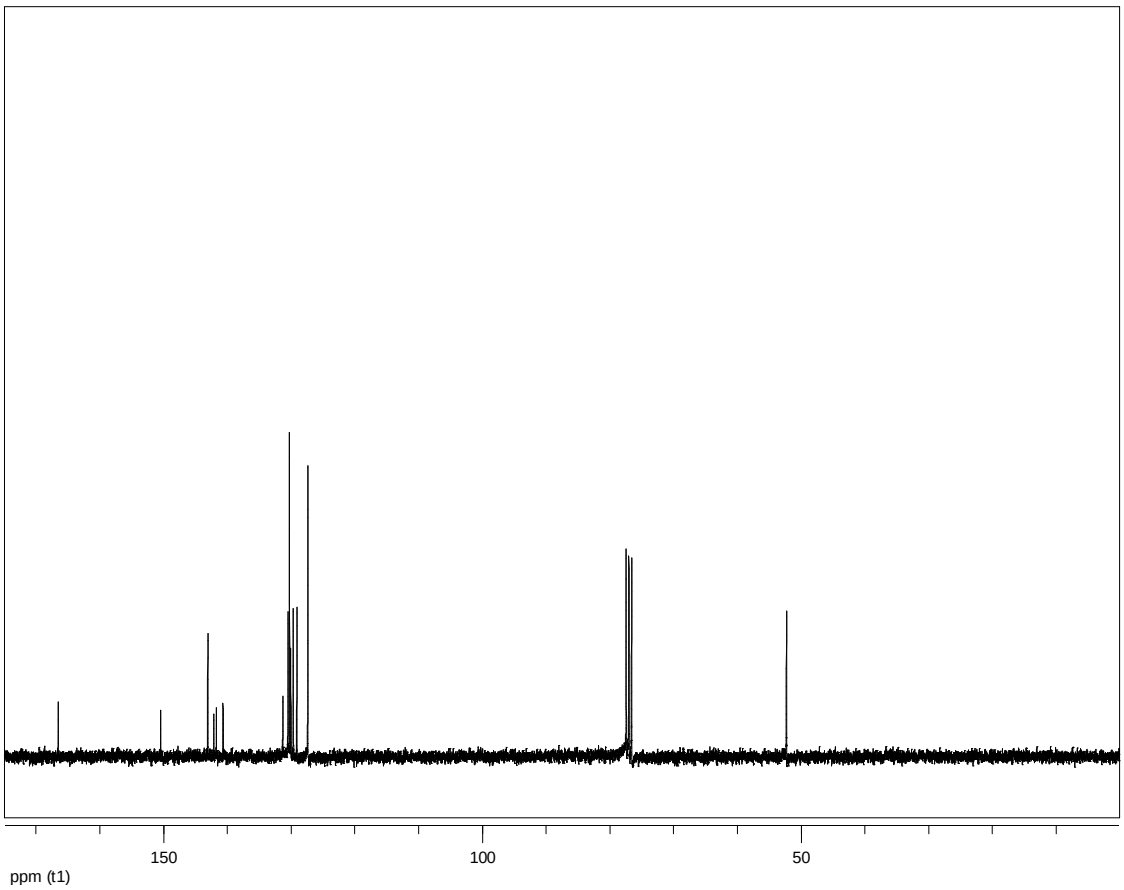

ppm (t1)
10.0
5.0
0.0

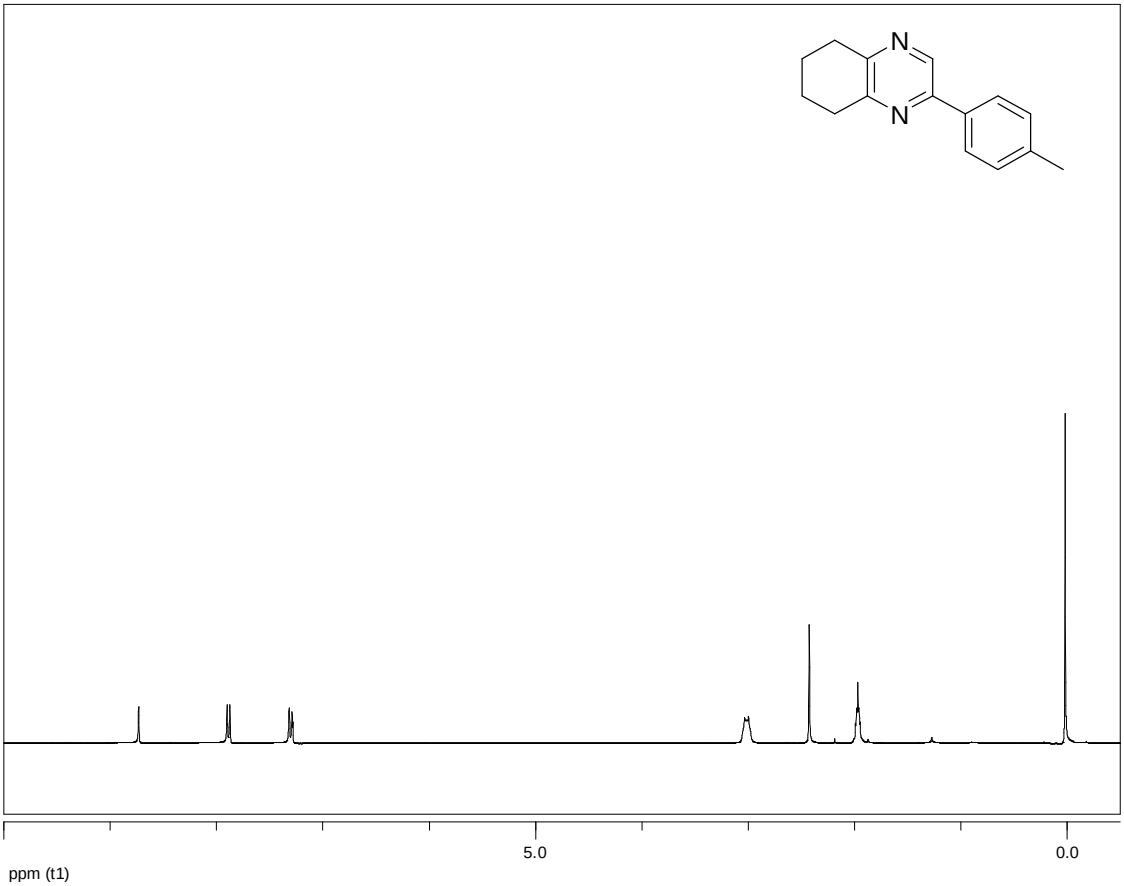

150
100
50
ppm (t1)

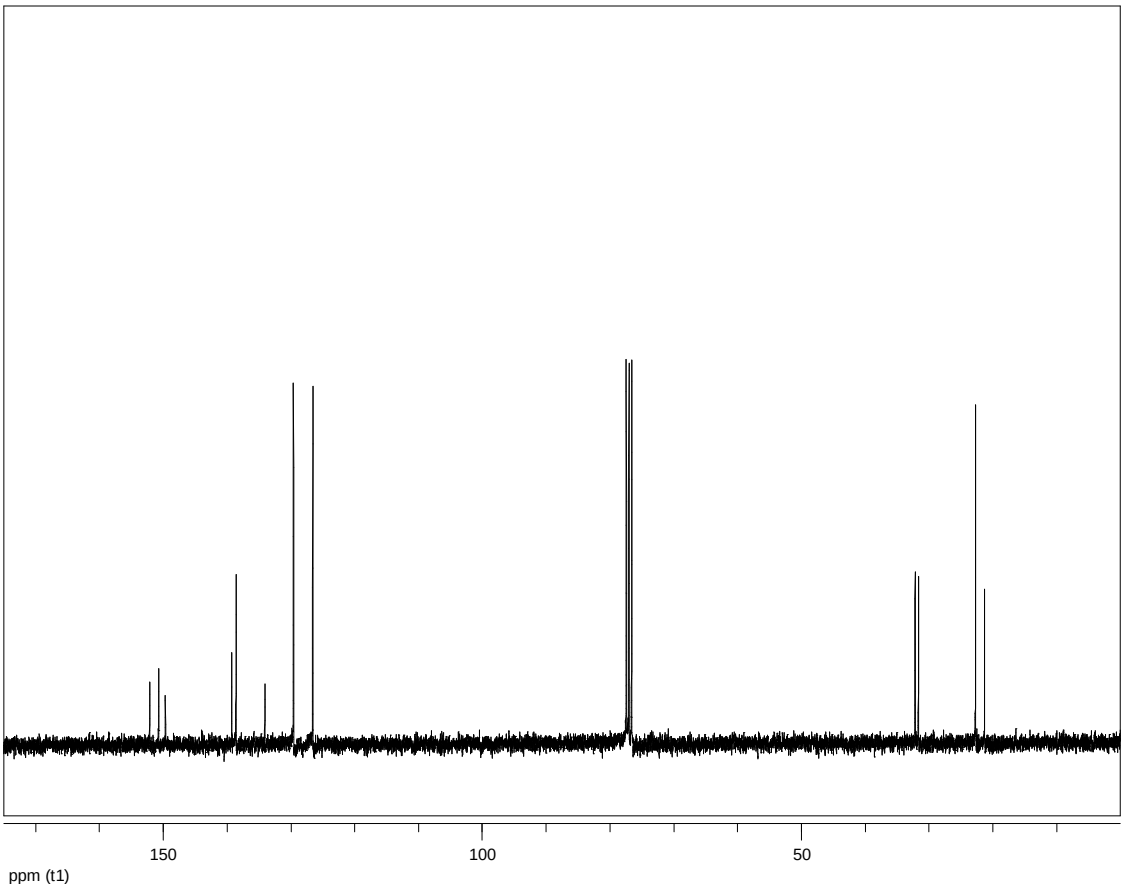

N
N
O
5.0
0.0
ppm (t1)

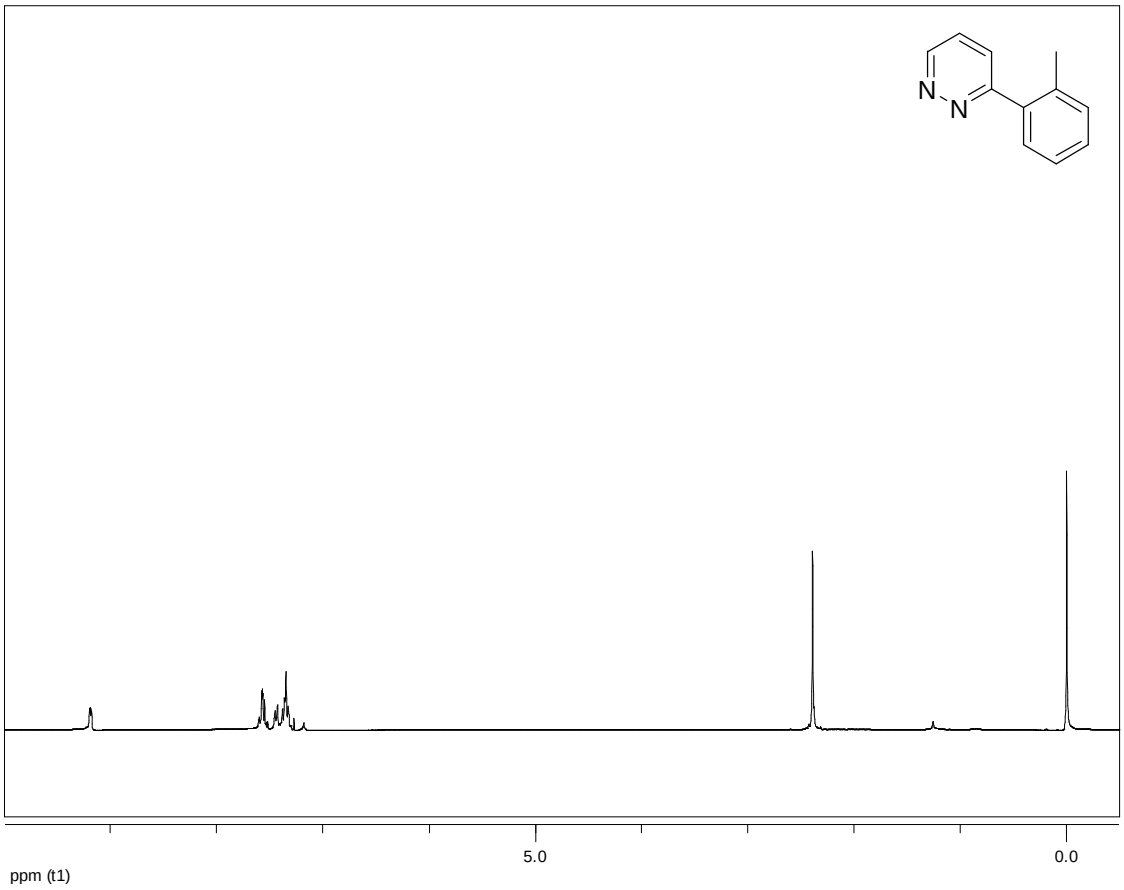

150
100
50
ppm (t1)

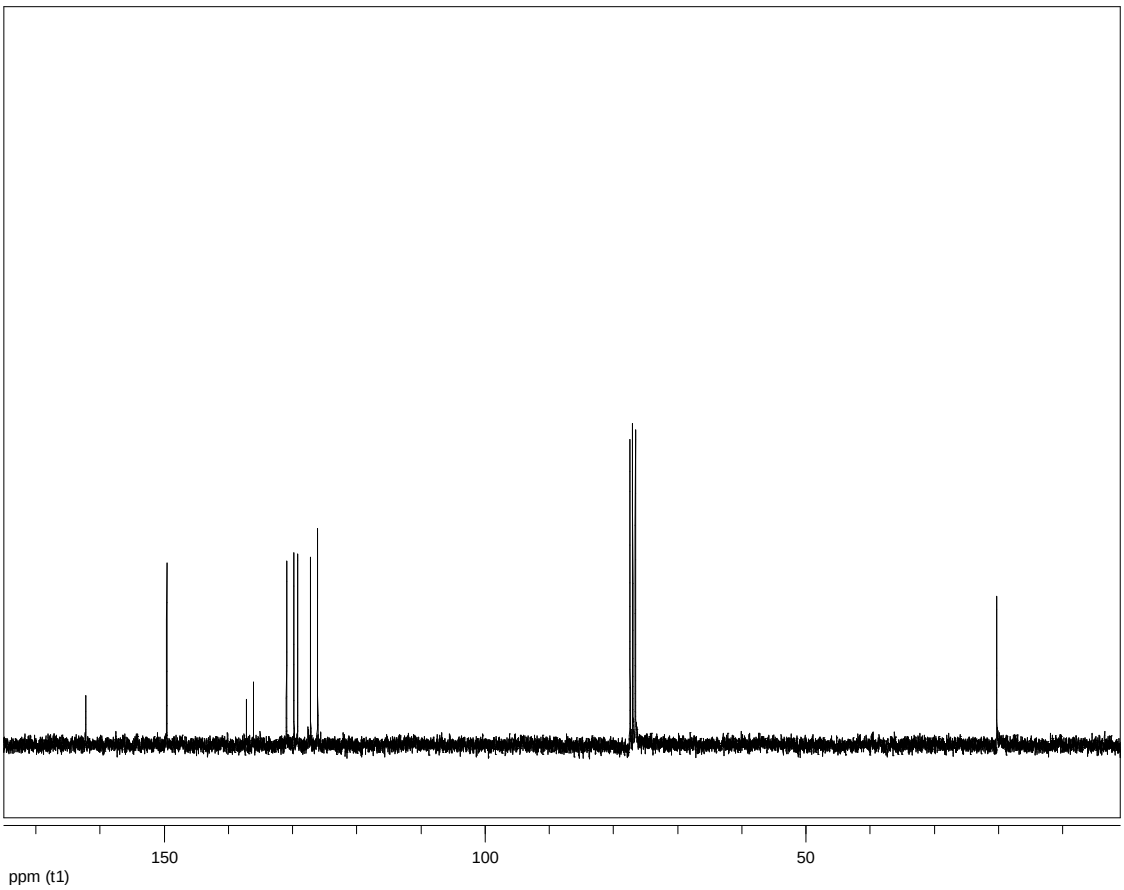

N
N
CO2Me
5.0
0.0
ppm (t1)

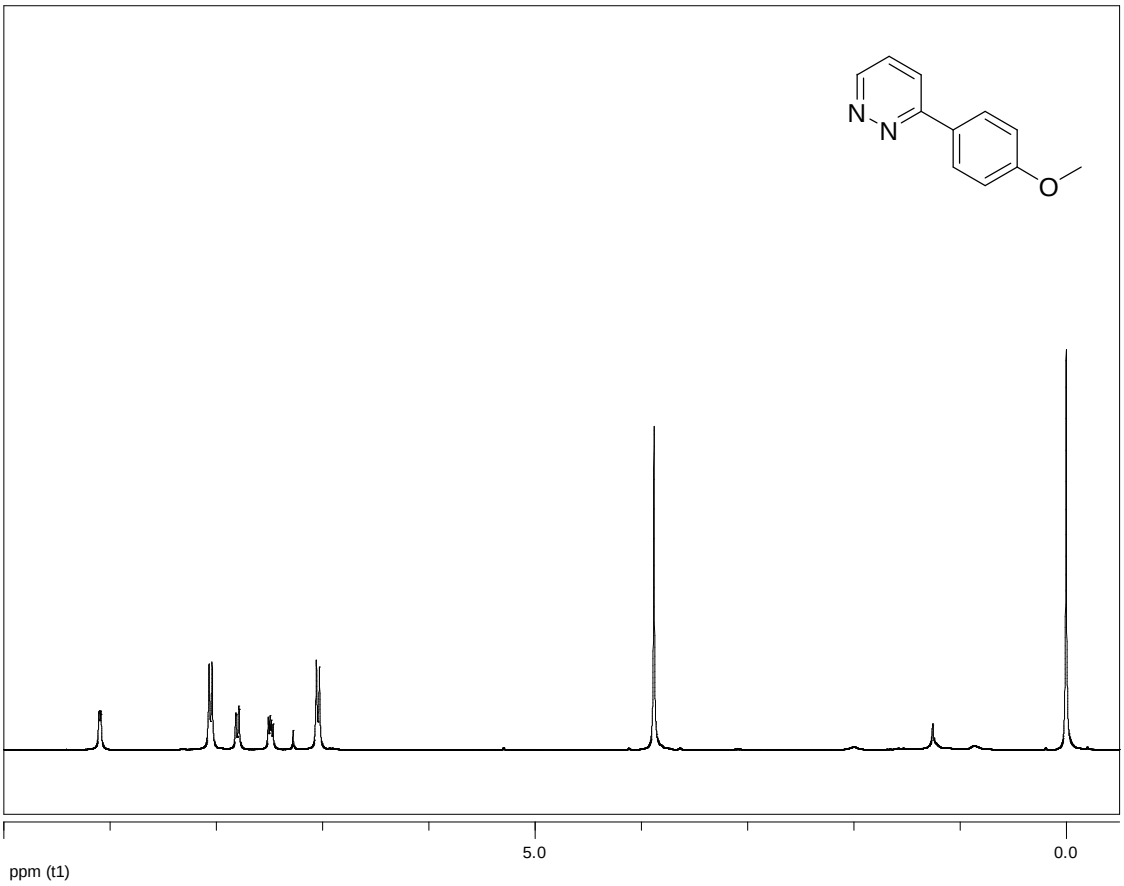

150
100
50
ppm (t1)

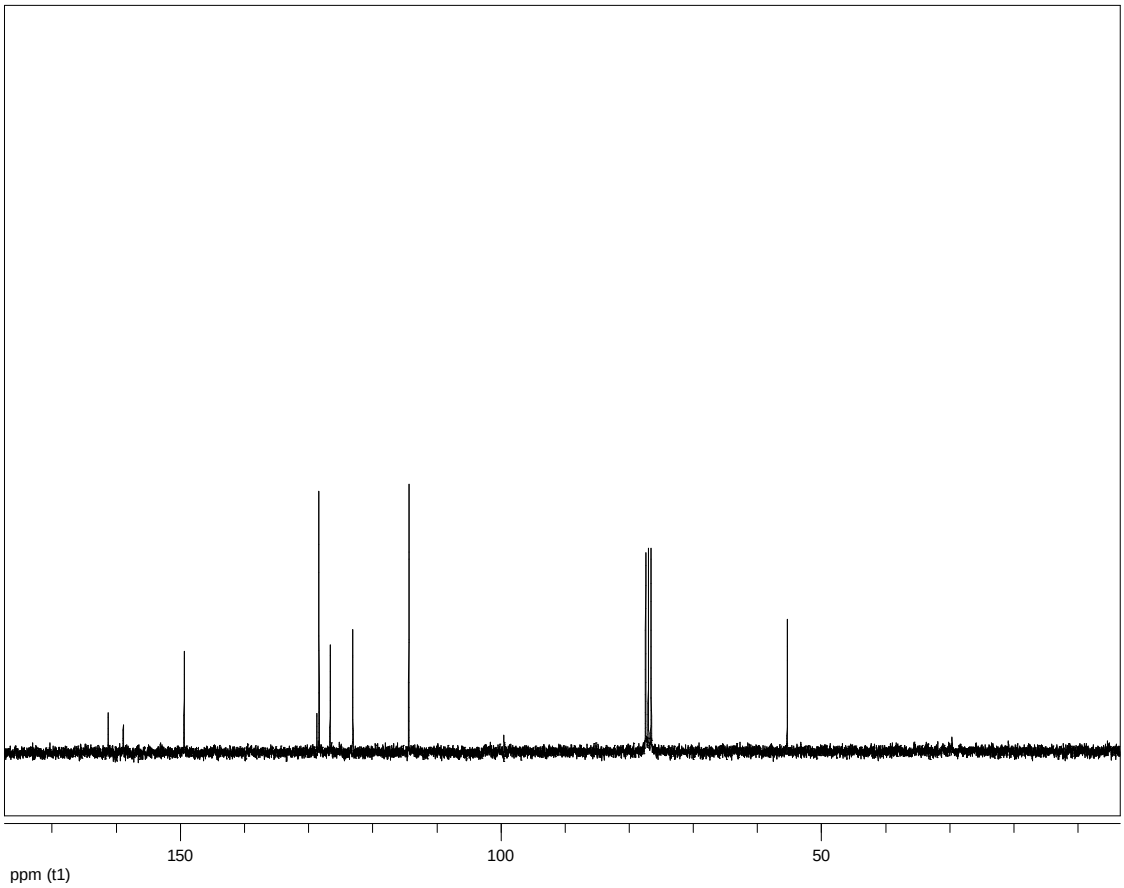

N
N
5.0
0.0
ppm (t1)

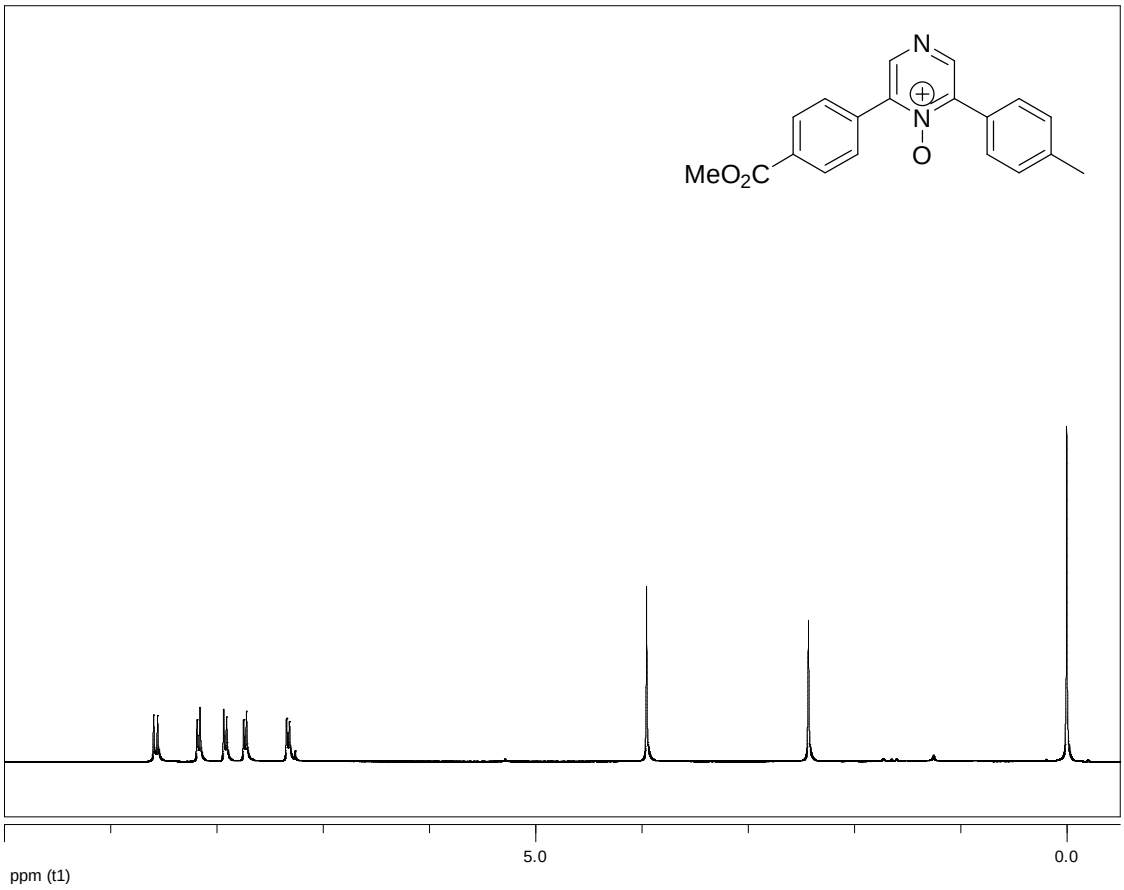

150
100
50
ppm (t1)

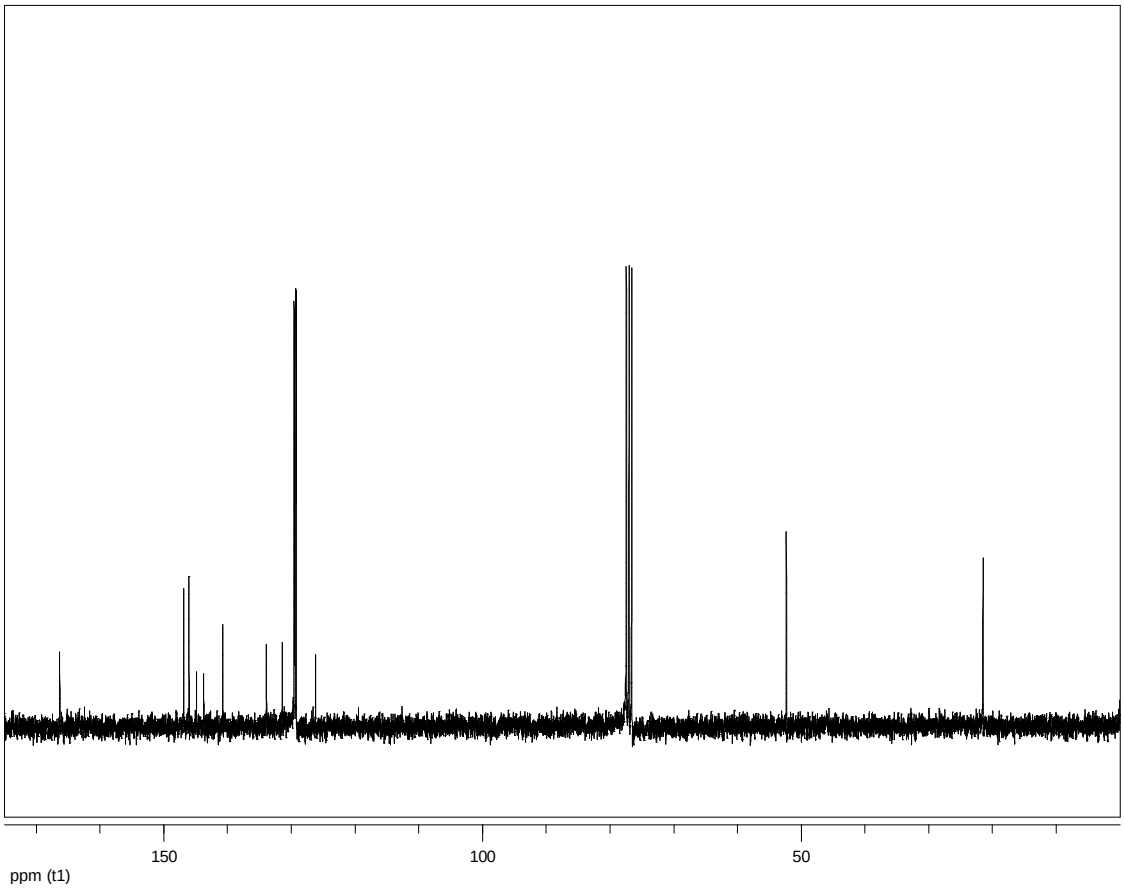

N
N
5.0
0.0
ppm (t1)

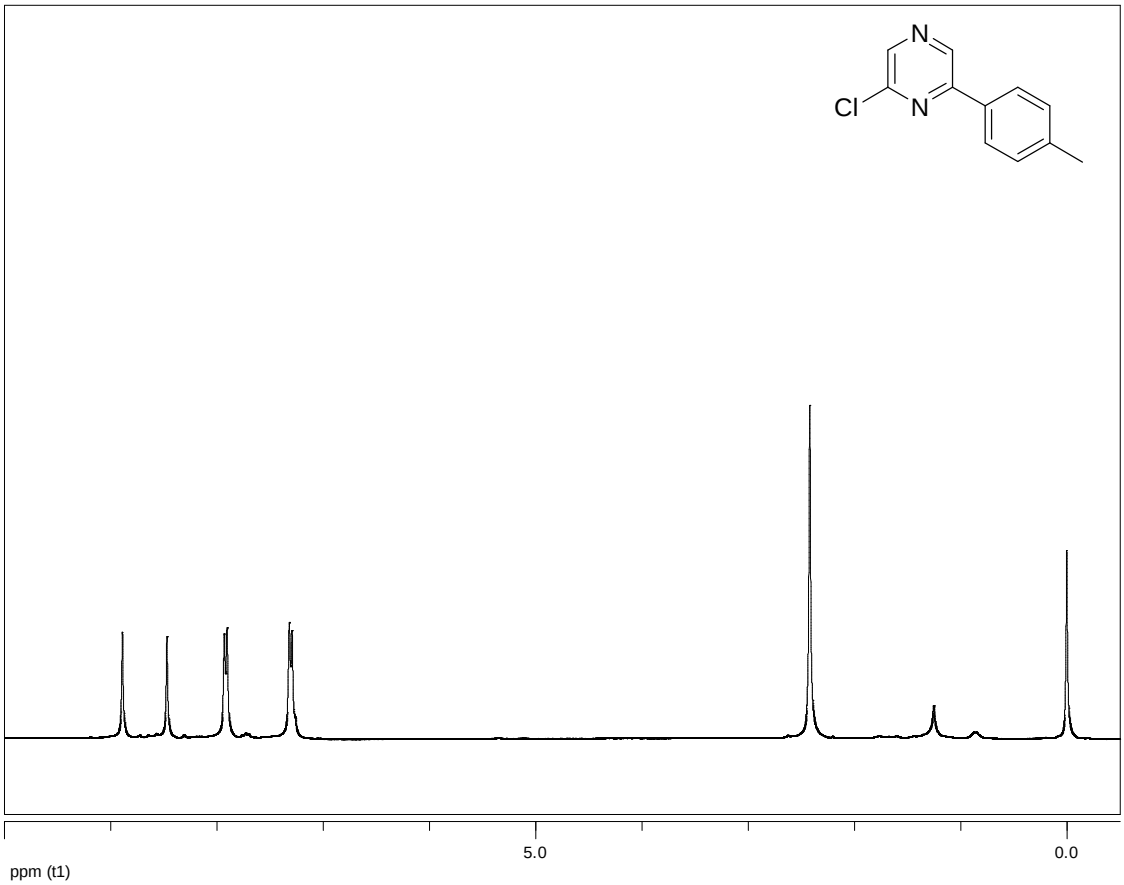

150
100
50
ppm (t1)

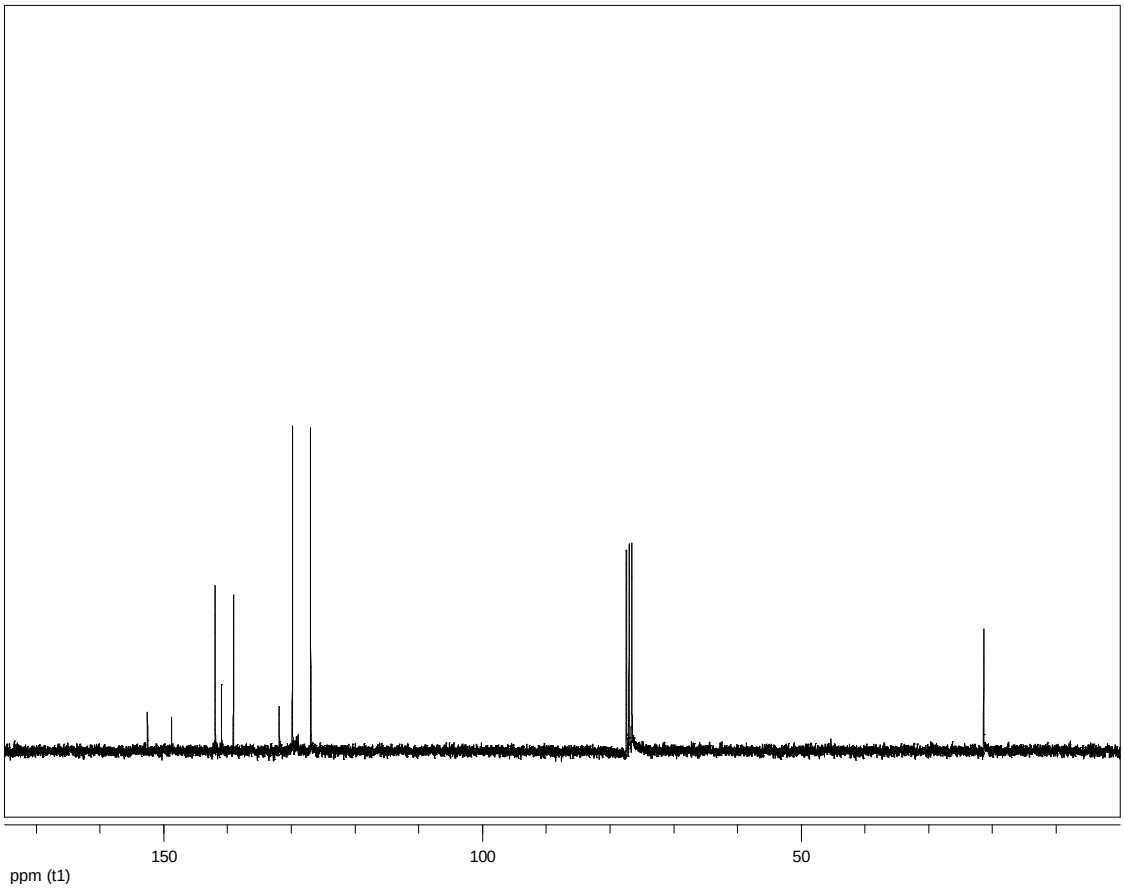

N
N
O
5.0
0.0
ppm (t1)

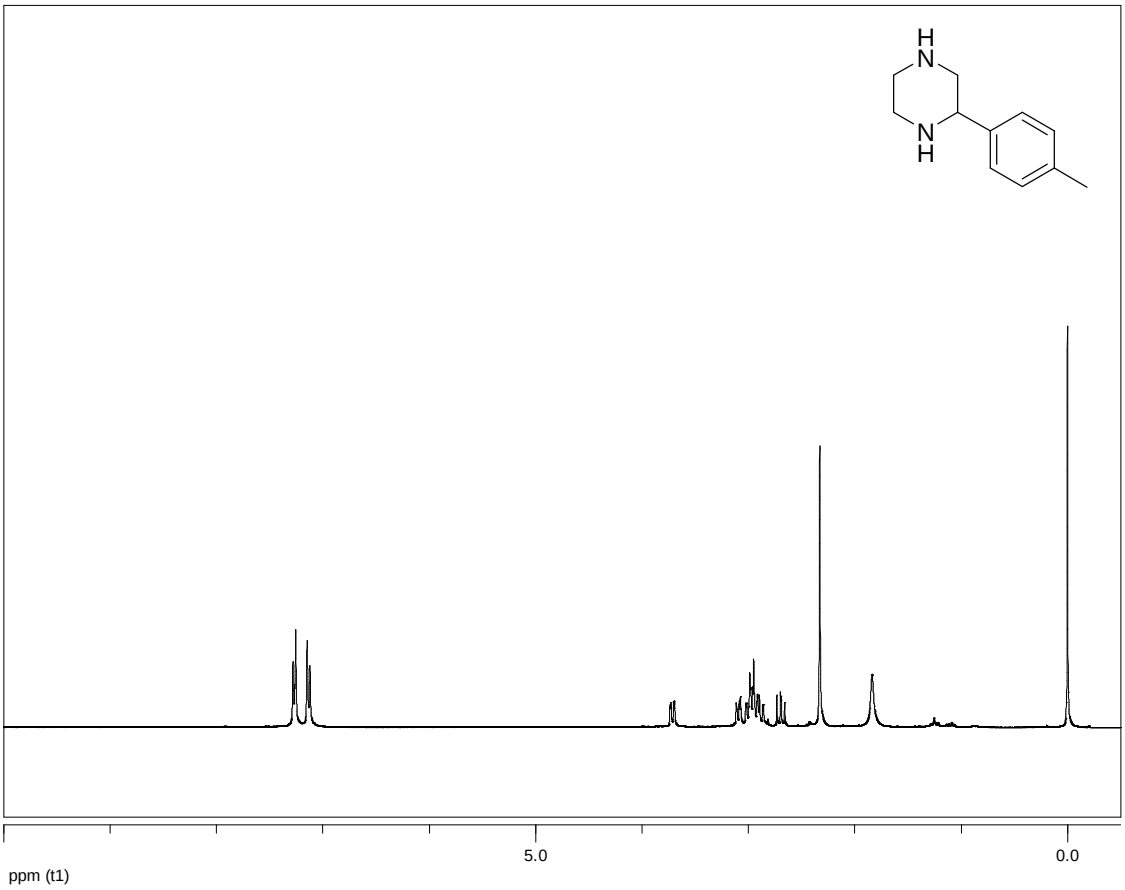

150
100
50
ppm (t1)

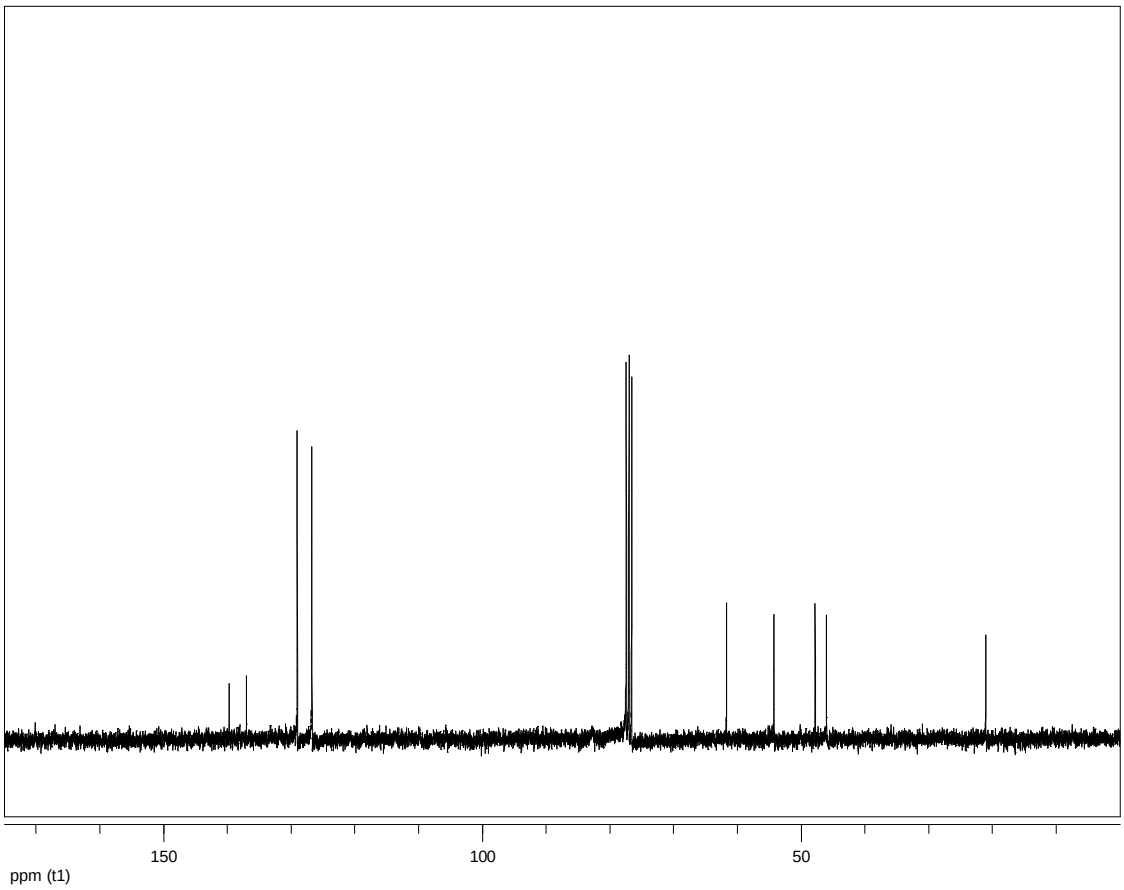

N
N
O
MeO2C
5.0
0.0
ppm (t1)

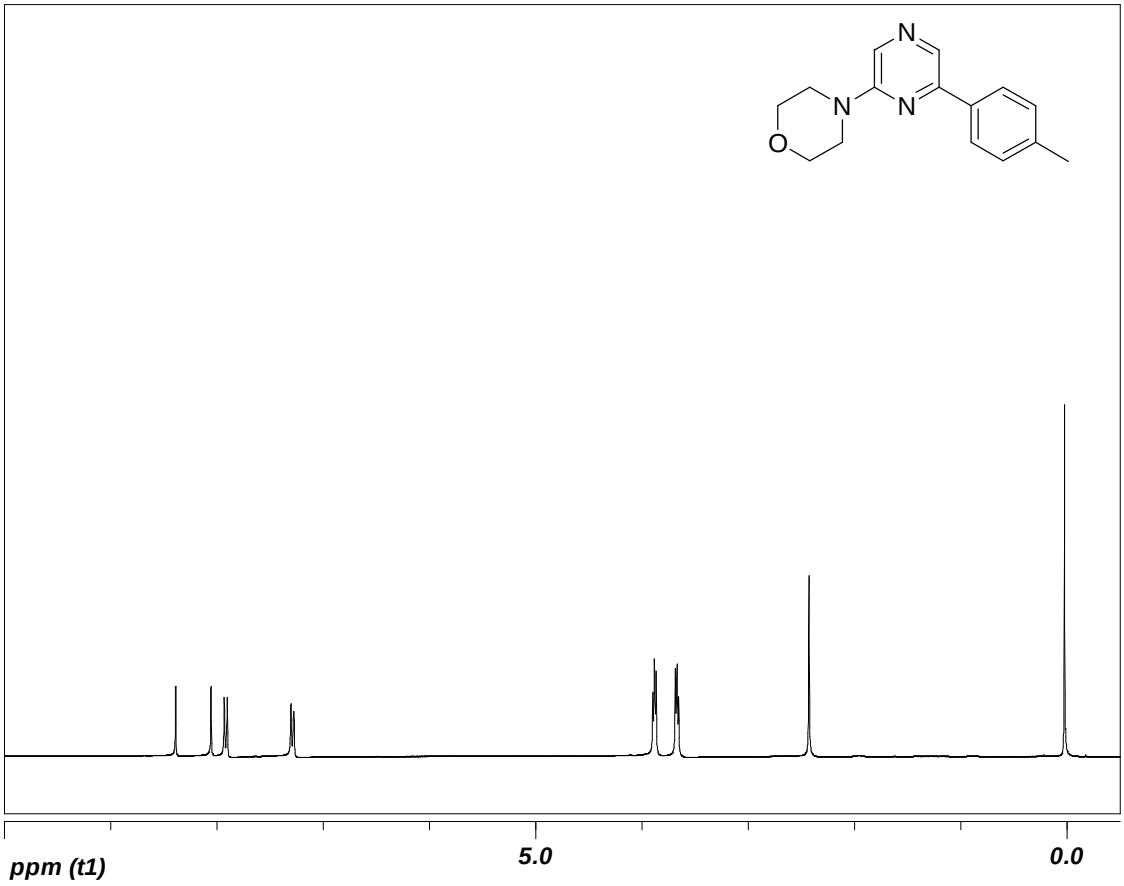

150
100
50
ppm (t1)

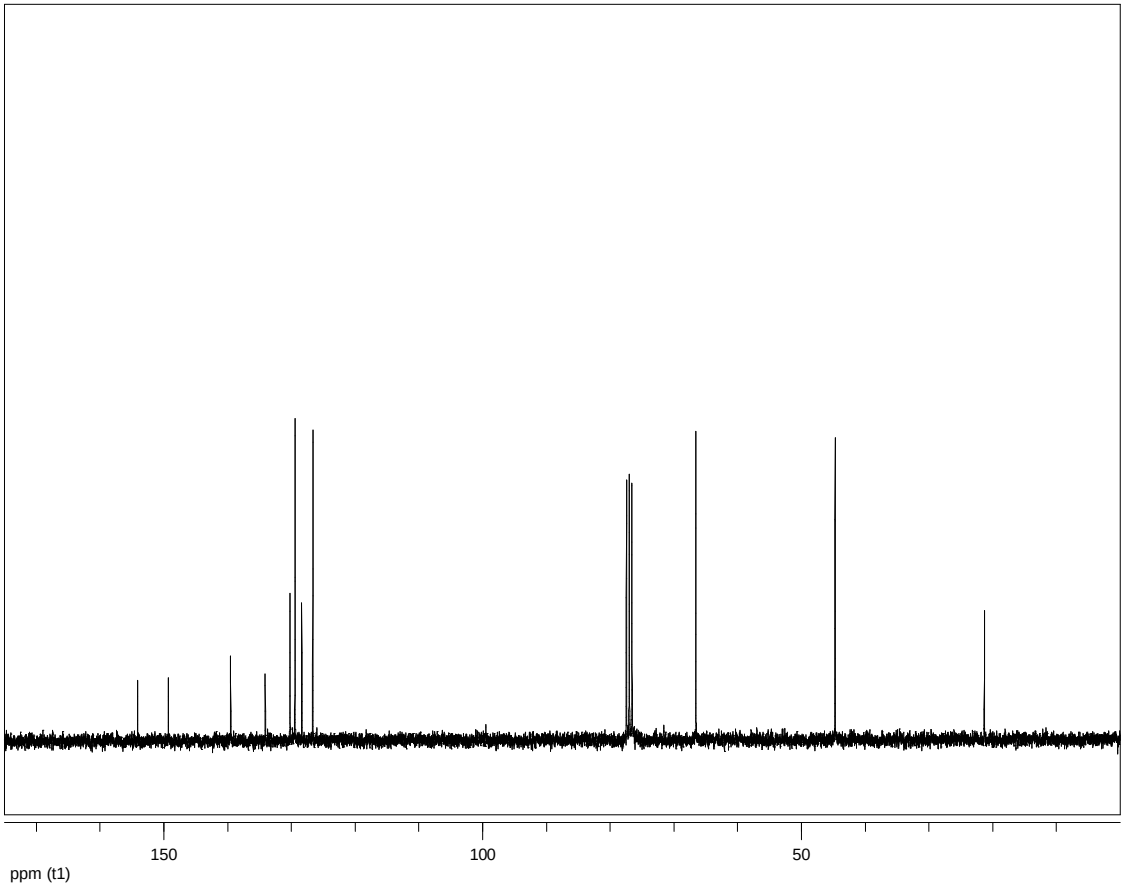

N
Cl
N
5.0
0.0
ppm (t1)

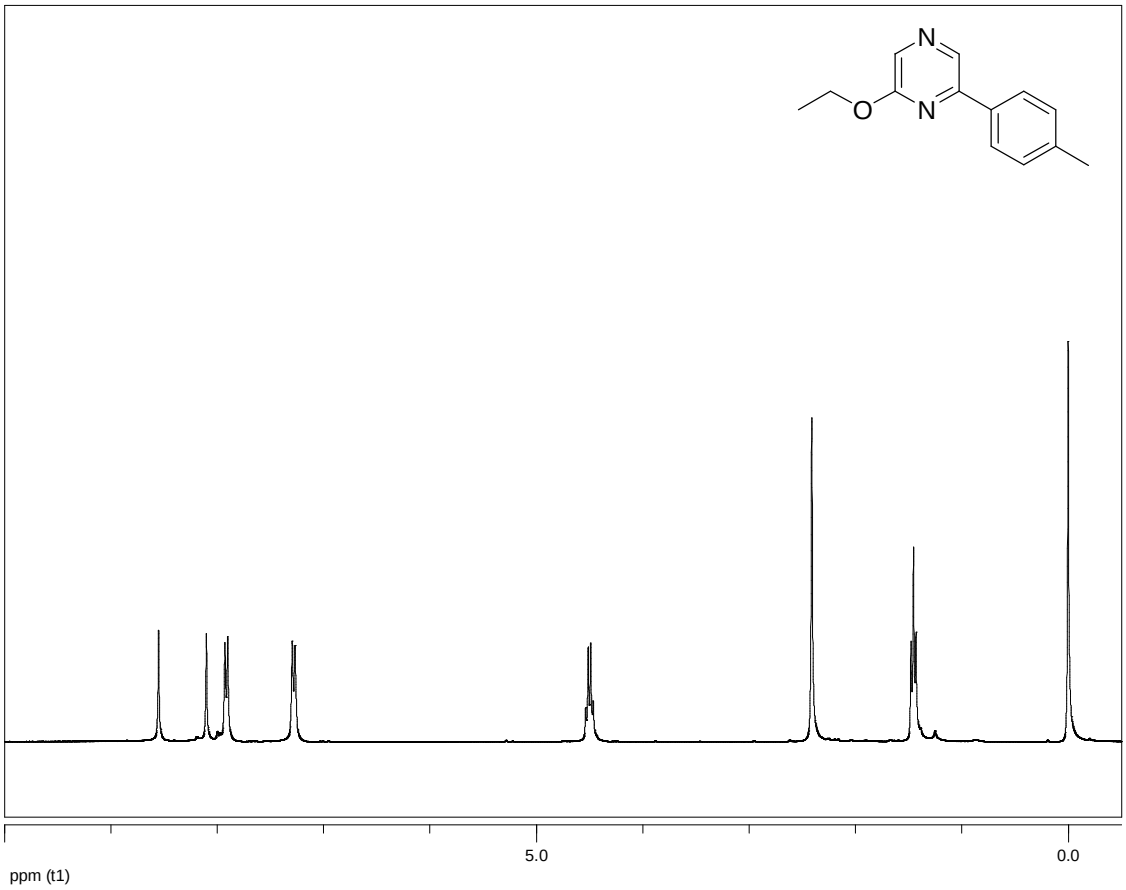

150
100
50
ppm (t1)

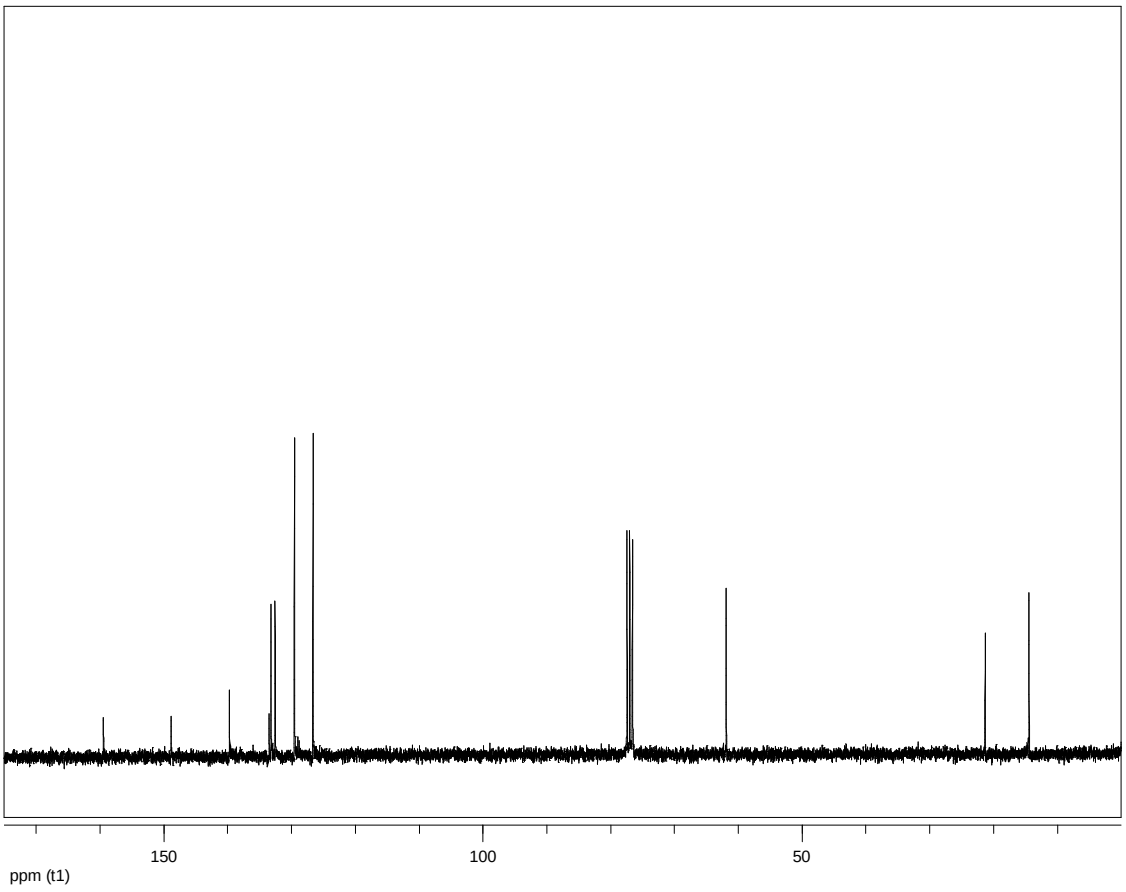

H
N
N
H
5.0
0.0
ppm (t1)

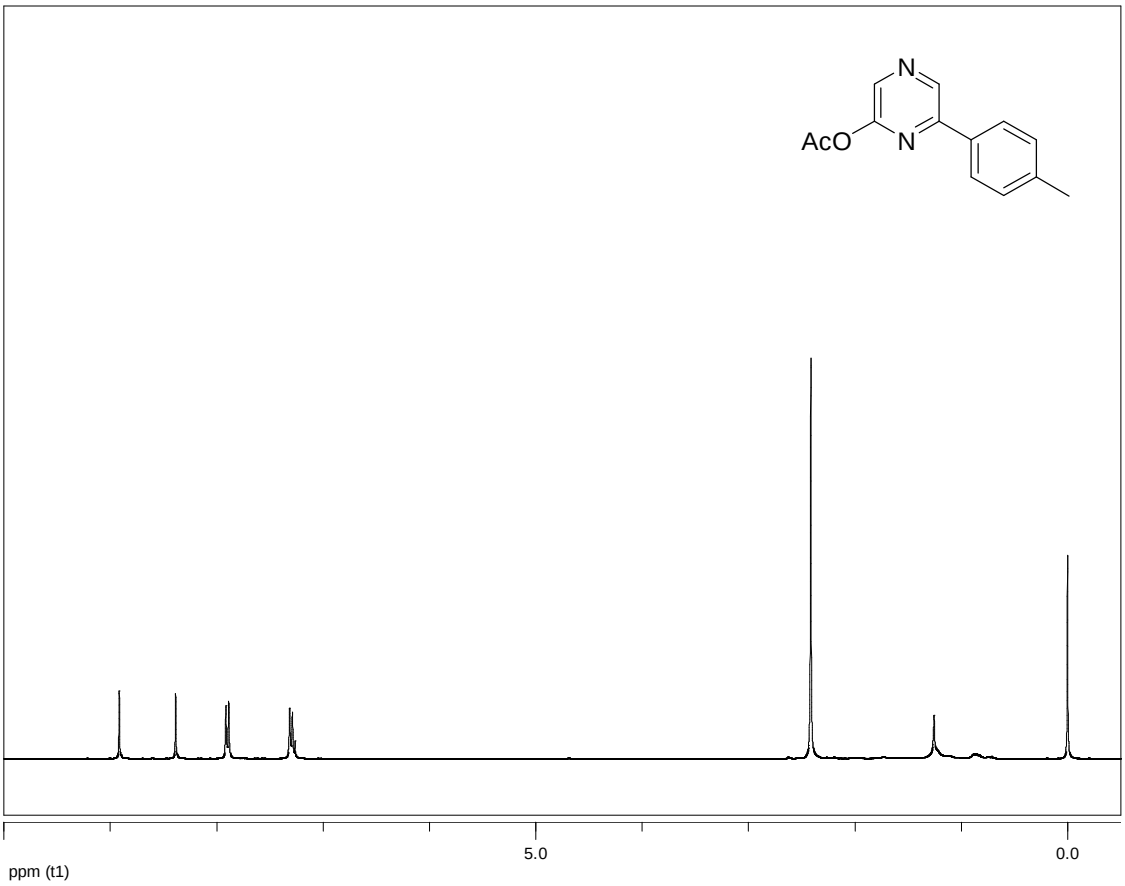

150
100
50
ppm (t1)

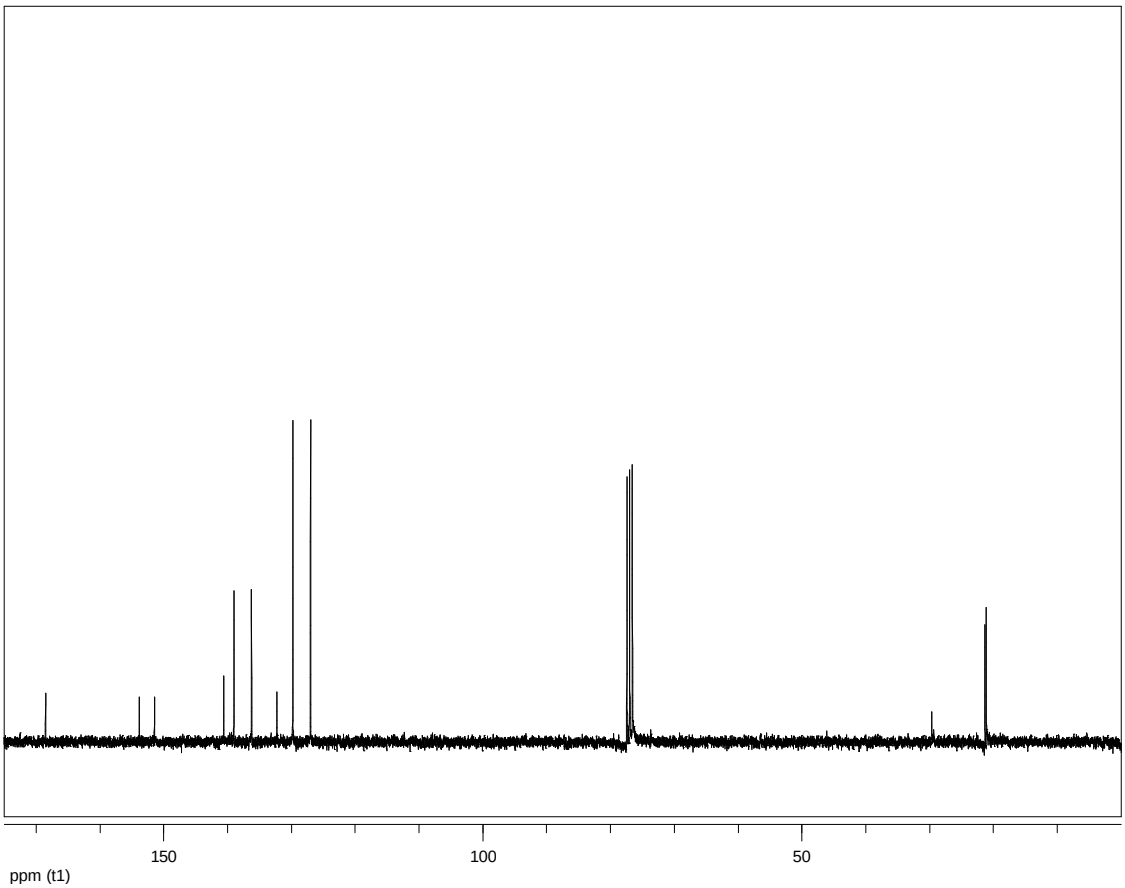

N
N
N
O
ppm (t1)
5.0
0.0

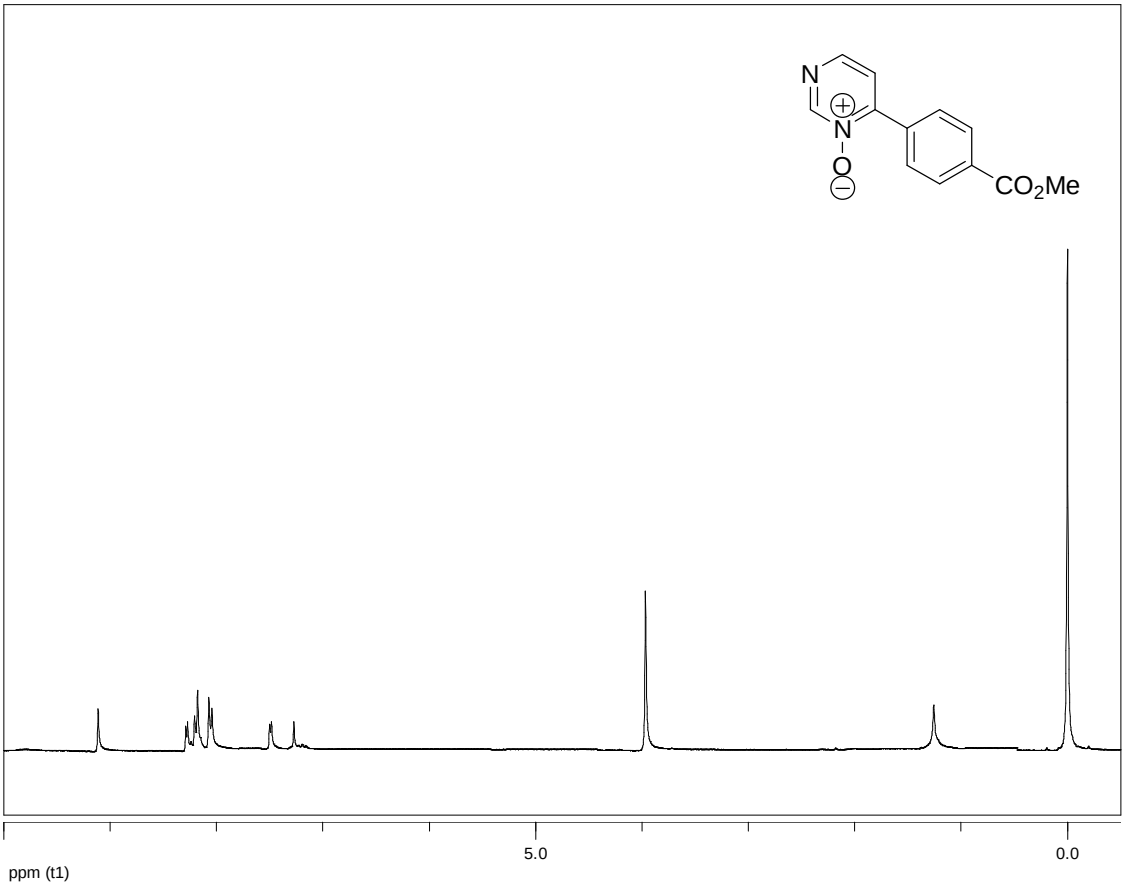

150
100
50
ppm (t1)

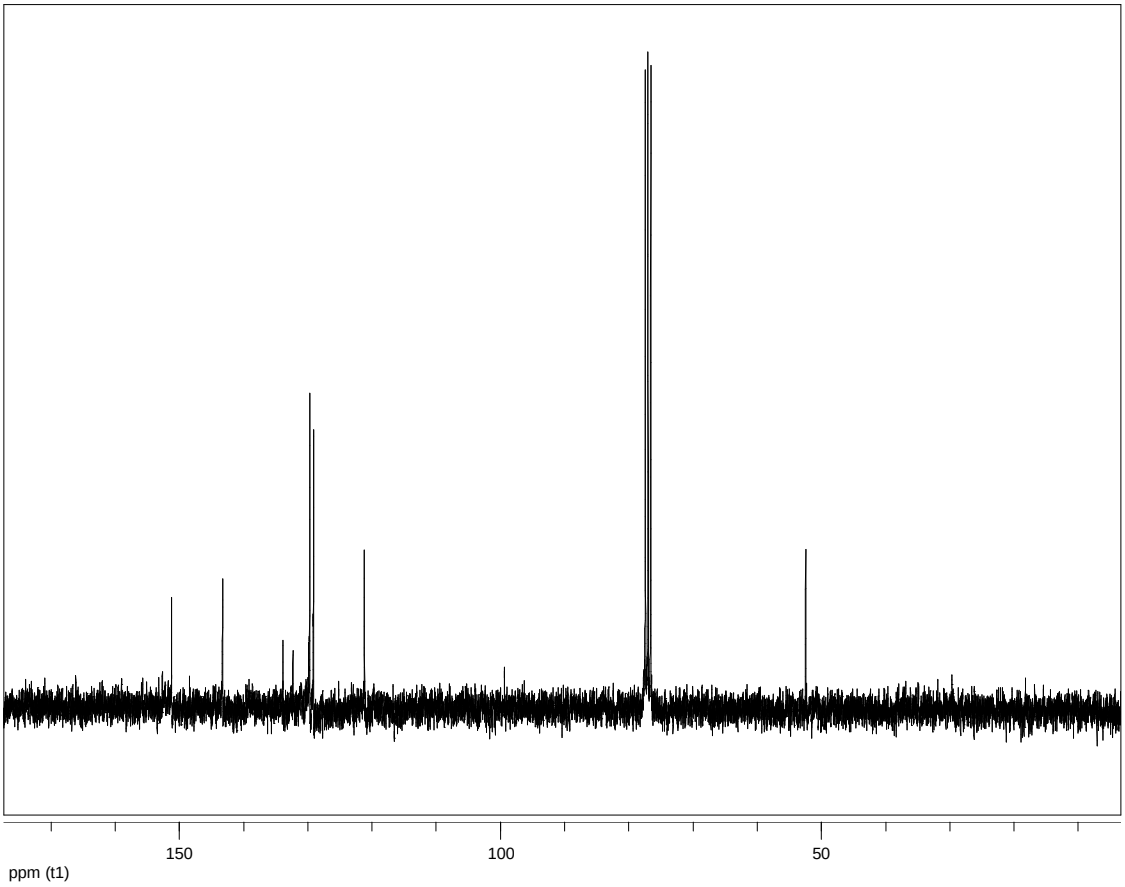

N
O
N
5.0
0.0
ppm (t1)

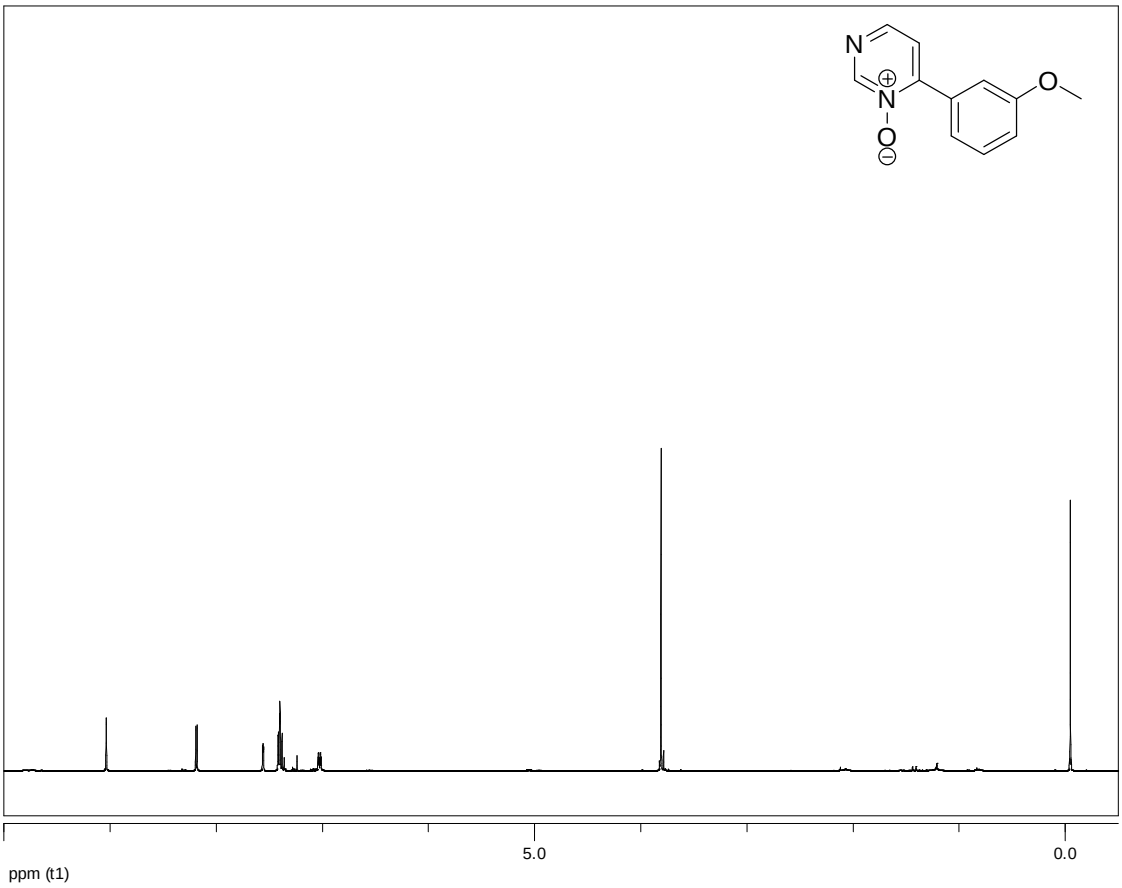

150
100
50
ppm (t1)

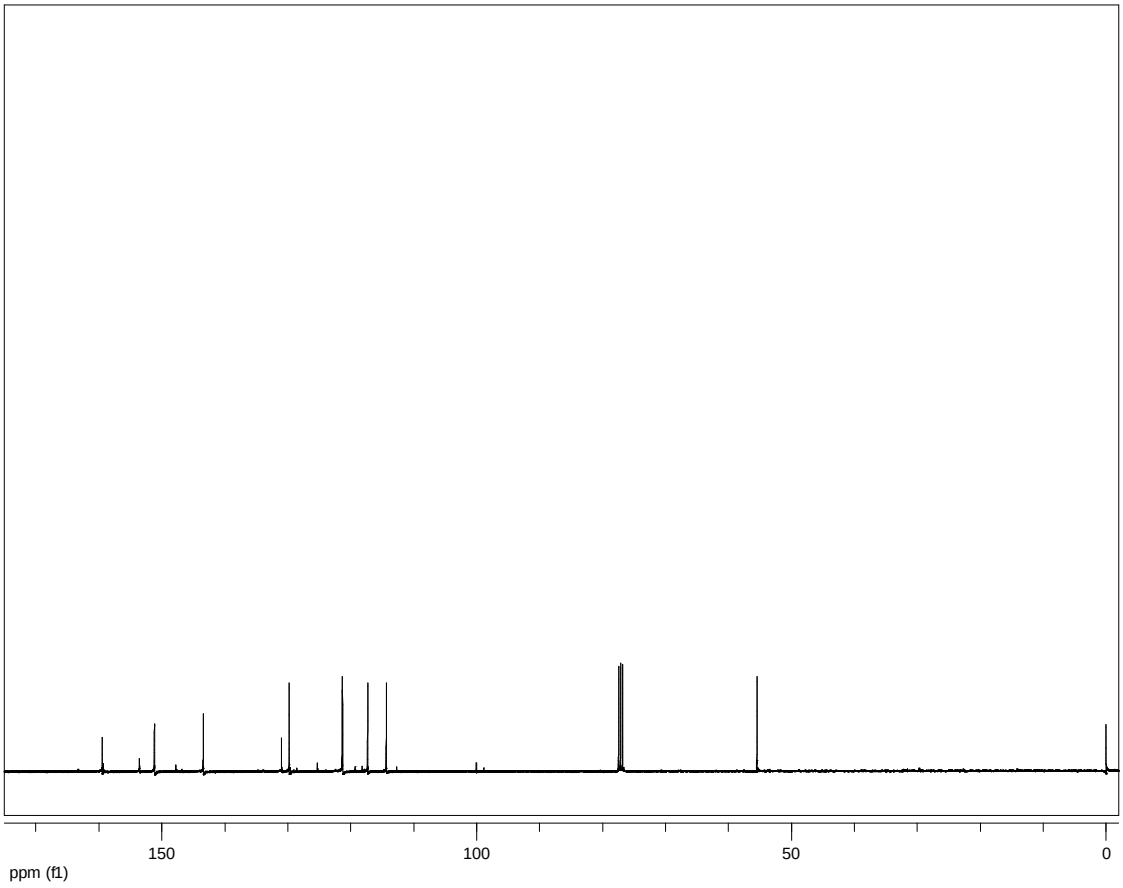

N
AcO
N
5.0
0.0
ppm (t1)

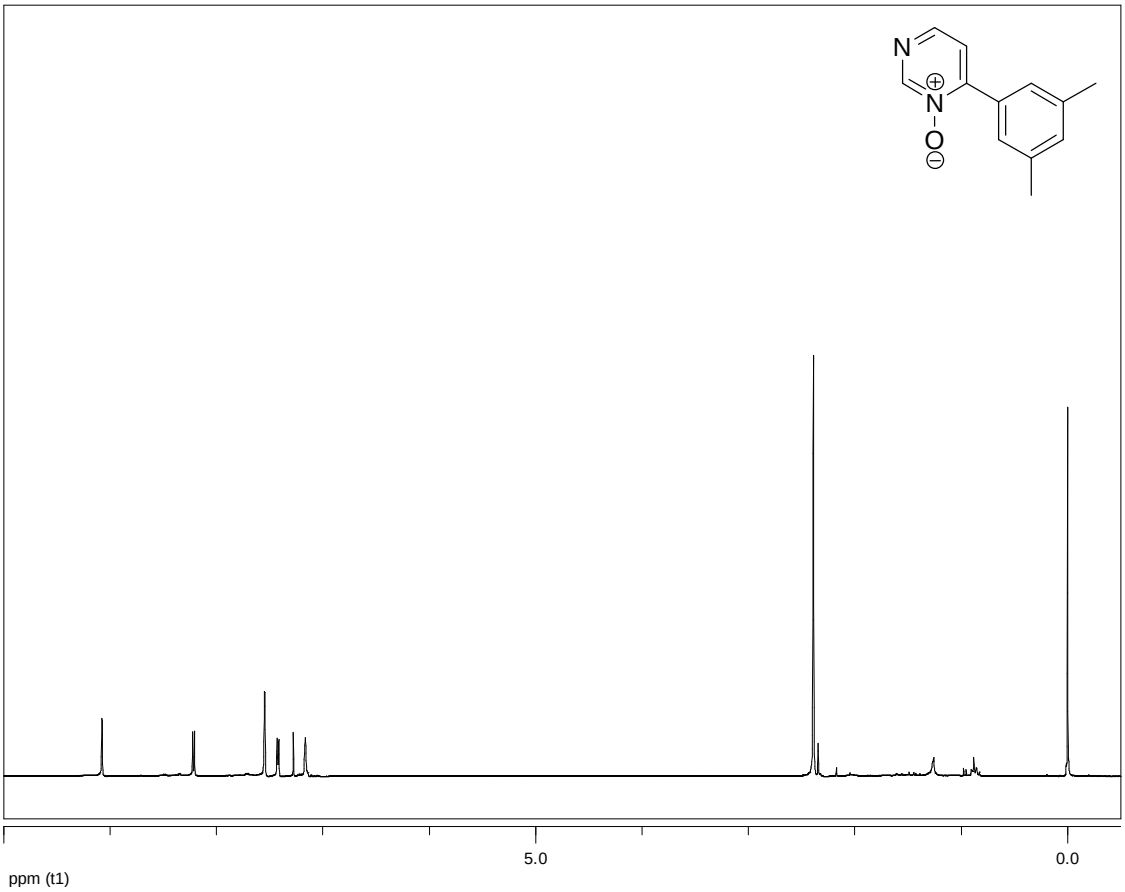

150
100
50
ppm (t1)

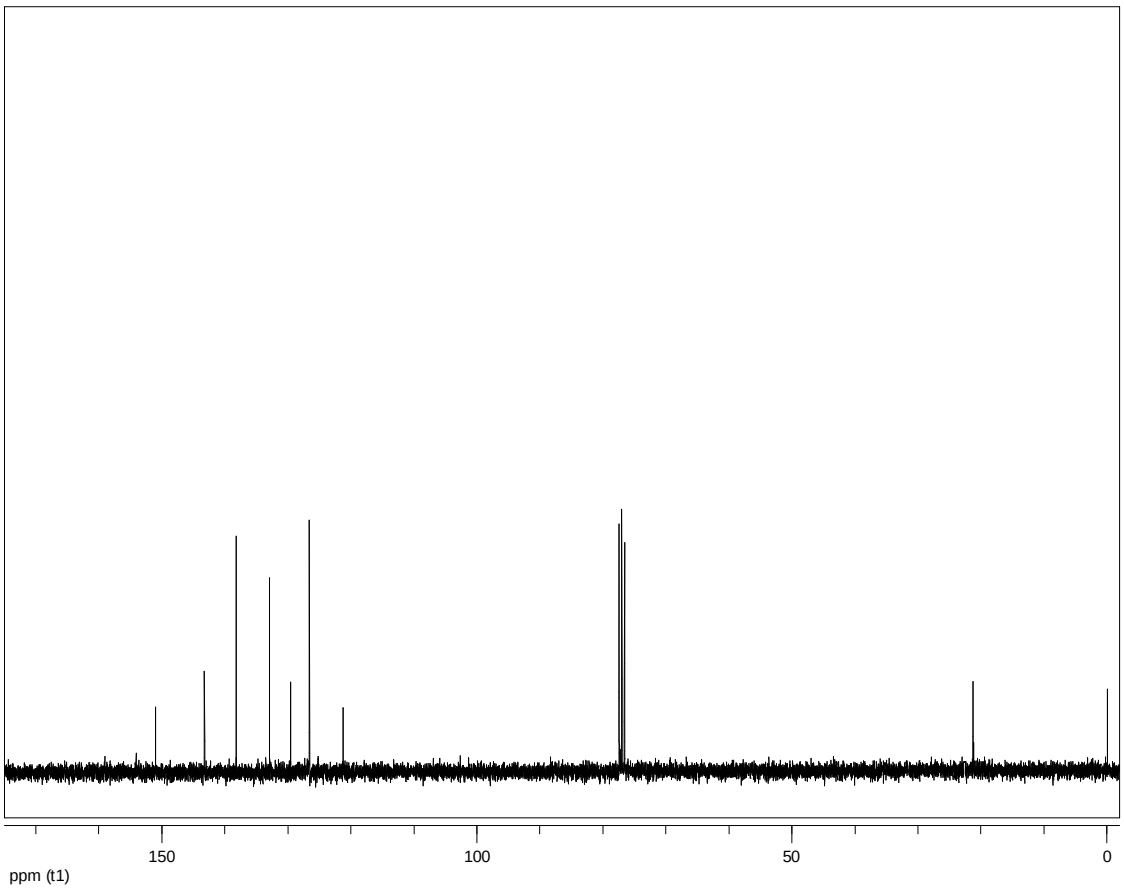

N
N
O
CO2Me
5.0
0.0
ppm (t1)


150
100
50
ppm (t1)


N
N
O
O
5.0
0.0
ppm (t1)


150
100
50
0
ppm (f1)


N
N
O
5.0
0.0
ppm (t1)


150
100
50
0
ppm (t1)