

One-pot Friedel-Crafts/Robinson-Gabriel synthesis of oxazoles using oxazolone templates

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Supplemental Material

Table of contents

Table of contents of supplemental material.....	S1
General experimental prologue.....	S2
Characterization data of oxazoles 1-14.....	S2-S4
Spectral data of oxazoles 1-14.....	S5-S18

Reactions were carried out in flame-dried glassware under nitrogen or argon atmosphere, unless otherwise noted. Commercial solvents and reagents were used as received. Anhydrous solvents were dispensed from a delivery system, which passes the solvents through packed columns (tetrahydrofuran, methylene chloride: dry neutral alumina). All reactions were magnetically stirred and monitored by TLC with 0.25 μm pre-coated silica gel plates and column chromatography was carried out on Silica Gel 60 (230–400 mesh). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Melting points were determined on a hot-stage melting point apparatus with a microscope attachment. Infrared spectra were recorded on a single beam IR spectrometer. Chemical shifts are reported relative to the residue peaks of the solvent CDCl_3 (7.24 ppm for ^1H and 77.0 ppm for ^{13}C). HRMS were obtained at the Mass Spectrometry Facility of the Michigan State University with a high/low resolution magnetic sector mass spectrometer. Combustion analysis was carried out in house on a CHNS/O analyzer.

Oxazole 1: 2,5-diphenyl-oxazole.

^1H NMR (500 MHz) (CDCl_3) δ 8.06 (2H, d, $J = 7.4$ Hz), 7.66 (2H, d, $J = 7.6$ Hz), 7.36–7.44 (6H, m), 7.28 (1H, t, $J = 7.4$ Hz); ^{13}C NMR (125 MHz) (CDCl_3) δ 160.8, 145.7, 135.9, 129.1, 129.0, 128.7, 128.3, 127.7, 125.4, 126.5, 123.7. MS (EI) m/e 221.0 (100.0) (M^+). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{NO}$: C, 81.45; H, 4.98; N, 6.33. Found: C, 81.23; H, 4.41; N, 6.25. IR (cm^{-1}) 2924.46, 1491.16, 1444.87, 1134.29. Melting Point 70–71°C.

Oxazole 2: 2-benzyl-5-phenyl-oxazole.

^1H NMR (500 MHz) (CDCl_3) δ 8.02 (2H, d, $J = 7.4$ Hz), 7.57 (1H, $J = 7.2$ Hz), 7.47 (2H, t, $J = 7.2$ Hz), 7.34 (2H, t, $J = 7.0$ Hz), 7.26–7.30 (4H, m), 4.30 (2H, s); ^{13}C NMR (125 MHz) (CDCl_3) δ 188.9, 136.6, 134.5, 133.1, 129.4, 128.7, 128.6, 128.5, 126.9, 45.4. MS (EI) m/e 235.0 (89.6) (M^+). Anal. Calcd for $\text{C}_{16}\text{H}_{13}\text{NO}$: C, 81.70; H, 5.53; N, 5.96. Found: C, 81.02; H, 5.58; N, 5.82. IR (cm^{-1}) 2920.61, 1686.30, 1448.80, 1337.23, 1075.23. Melting point 50–52°C.

Oxazole 3: 2-methyl-5-phenyl-oxazole.

^1H NMR (500 MHz) (CDCl_3) δ 7.58 (2H, d, $J = 7.4$ Hz), 7.38 (2H, t, $J = 7.4$ Hz), 7.28 (1H, t, $J = 7.4$ Hz), 7.18 (1H, s), 2.50 (3H, s); ^{13}C NMR (125 MHz) (CDCl_3) δ 161.2, 151.3, 129.1, 128.5, 128.3, 124.2, 122.1, 14.3. MS (EI) m/e 159.0 (100.0) (M^+). Anal. Calcd for $\text{C}_{10}\text{H}_9\text{ON}$: C, 75.47; H, 5.66; N, 8.81. Found: C, 71.56; H, 4.02; N, 10.31. IR (cm^{-1}) 2924.90, 1653.52, 1559.26, 1485.45, 1130.73. Melting Point 57–59°C.

Oxazole 4: 4-methyl-2,5-diphenyl-oxazole.

^1H NMR (500 MHz) (CDCl_3) δ 8.09 (2H, d, $J = 7.4$ Hz), 7.69 (2H, d, $J = 7.7$ Hz), 7.42–7.49 (5H, m), 7.33 (1H, t, $J = 7.4$ Hz), 2.49 (3H, s); ^{13}C NMR (125 MHz) (CDCl_3) δ 159.8, 145.6, 133.9, 131.0, 129.3, 128.9, 128.8, 127.7, 127.5, 126.3, 125.4, 33.9. MS (EI) m/e 235.1 (100.0) (M^+). Anal. Calcd for $\text{C}_{16}\text{H}_{13}\text{NO}$: C, 81.70;

H, 5.53; N, 5.95. Found: C, 81.41; H, 5.20; N, 5.95. IR (cm⁻¹) 2930.00, 1597.26, 1485.38, 1448.73, 1075.00. Melting Point 78 -80°C.

Oxazole 5: 4-benzyl-2,5-diphenyl-oxazole.

¹H NMR (300 MHz) (CDCl₃) δ 8.11 (2H, d, *J* = 7 Hz), 7.66 (2H, d, *J* = 7.2 Hz), 7.40-7.48 (5H, m), 7.28-7.36 (5H, m), 7.21 (1H, s), 4.21 (2H, s); ¹³C NMR (75 MHz) (CDCl₃) δ 160.1, 146.8, 138.8, 136.0, 132.5, 130.5, 129.1, 129.0, 128.9, 128.7, 128.3, 127.7, 126.7, 126.6, 125.9, 33.4. MS (EI) *m/e* 310.8 (100.0) (M⁺). Anal. Calcd for C₂₂H₁₇NO: C, 84.89; H, 5.47; N, 4.50. Found: C, 84.83; H, 5.66; N, 4.20. IR (cm⁻¹) 2924.64, 1599.82, 1493.79, 1447.76, 1069.98, 1026.89. Melting Point 53 -56°C.

Oxazole 6 : 4-isopropyl-2,5-diphenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.10 (2H, d, *J* = 7.7 Hz), 7.65 (2H, d, *J* = 7.6 Hz), 7.39-7.47 (5H, m), 7.32 (1H, t, *J* = 7.7 Hz), 3.29 (1H, hept, *J* = 6 Hz), 1.38 (6H, d, *J* = 6 Hz); ¹³C NMR (125 MHz) (CDCl₃) δ 159.7, 144.0, 143.3, 129.9, 129.4, 128.8, 128.6, 127.8, 127.6, 126.3, 125.9, 26.0, 22.0. MS (EI) *m/e* 263.0 (78.7) (M⁺). Anal. Calcd for C₁₈H₁₇NO: C, 82.13; H, 6.46; N, 5.32. Found: C, 81.83; H, 6.54; N, 5.10. IR (cm⁻¹) 2959.33, 1607.17, 1485.52, 1444.37, 1113.79, 1052.06. Melting Point 95 -98°C.

Oxazole 7: 2,4,5-triphenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.15 (2H, d, *J* = 7.2 Hz), 7.72 (2H, d, *J* = 7.4 Hz), 7.67 (2H, d, *J* = 7.2 Hz), 7.45-7.51 (3H, m), 7.31-7.42 (6H, m); ¹³C NMR (125 MHz) (CDCl₃) δ 160.1, 145.5, 136.7, 132.5, 130.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 127.3, 126.5, 126.4. MS (EI) *m/e* 297.1 (35.3) (M⁺). Anal. Calcd for C₂₁H₁₅NO: C, 84.85; H, 5.05; N, 4.71. Found: C, 84.35; H, 5.15; N, 4.72. IR (cm⁻¹) 1596.71, 1583.10, 1514.21, 1456.10, 1399.91, 1245.81, 1025.81. Melting Point 112 -113°C.

Oxazole 8: 4-methyl-2-phenyl-5-p-tolyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.08 (2H, d, *J* = 7.2 Hz), 7.58 (2H, d, *J* = 7.4 Hz), 7.37-7.42 (3H, m), 7.28 (2H, d, *J* = 7.2 Hz), 2.48 (3H, s), 2.40 (3H, s); ¹³C NMR (125 MHz) (CDCl₃) δ 159.5, 146.0, 137.9, 135.9, 130.5, 129.8, 129.0, 127.8, 126.7, 126.2, 125.5, 21.5, 13.5. MS (EI) *m/e* 249.1 (100.0) (M⁺). Anal. Calcd for C₁₇H₁₅NO: C, 81.03; H, 6.02; N, 5.62. Found: C, 81.02; H, 6.07; N, 5.46. IR (cm⁻¹) 2920.97, 1603.96, 1478.32, 1444.83, 1244.72, 1092.74. Melting Point 80 - 82°C.

Oxazole 9: 5-(4-methoxy-phenyl)-4-methyl-2-phenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.05 (2H, d, *J* = 7.2 Hz), 7.59 (2H, d, *J* = 7.4 Hz), 7.46-7.39 (3H, m), 6.98 (2H, d, *J* = 7.4 Hz), 3.83 (3H, s), 2.44 (3H, s); ¹³C NMR (125 MHz) (CDCl₃) δ 159.1, 158.8, 145.4, 131.7, 129.9, 128.7, 127.5, 126.8, 126.0, 121.9, 114.2, 55.3, 13.3. MS (EI) *m/e* 265.1 (100.0) (M⁺). Anal. Calcd for C₁₇H₁₅NO₂: C, 76.98; H, 5.66; N, 5.28. Found: C, 76.93; H, 5.64; N, 5.27. IR (cm⁻¹)

1604.98, 1549.04, 1489.24, 1286.68, 1248.10, 1174.80, 1014.69. Melting Point 88 -90°C.

Oxazole 10: 5-(4-methoxy-phenyl)-2-phenyl-oxazole.

¹H NMR (300 MHz) (CDCl₃) δ 8.07 (2H, d, *J* = 7.4 Hz), 7.63 (2H, d, *J* = 7.4 Hz), 7.45-7.44 (3H, m), 7.30 (1H, s), 6.95 (2H, d, *J* = 7.2 Hz), 3.82 (3H, s); ¹³C NMR (75 MHz) (CDCl₃) δ 160.0, 155.8, 130.2, 129.0, 128.8, 127.6, 126.3, 125.8, 120.9, 117.3, 110.9, 55.5. MS (EI) *m/e* 251.1 (100.0) (M⁺). Anal. Calcd for C₁₆H₁₃NO₂: C, 76.49; H, 5.18; N, 5.58. Found: C, 76.38; H, 5.45; N, 5.52. IR (cm⁻¹) 2920.11, 1585.70, 1566.63, 1495.12, 1446.93, 1341.64, 1253.48, 1128.55, 1023.47. Melting Point 118 -120°C.

Oxazole 11: 5-biphenyl-4-yl-2-phenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.12 (2H, d, *J* = 7.4 Hz), 7.78 (2H, d, *J* = 7.2 Hz), 7.67 (2H, d, *J* = 7.2 Hz), 7.62 (2H, d, *J* = 7.4), 7.51-7.44 (6H, m), 7.36 (1H, t, *J* = 7.2); ¹³C NMR (125 MHz) (CDCl₃) δ 161.2, 151.1, 141.2, 140.3, 130.4, 128.9, 128.8, 127.7, 127.6, 127.4, 126.9, 126.8, 126.3, 124.6, 123.5. MS (EI) *m/e* 297.2 (100.0) (M⁺). Anal. Calcd for C₁₇H₁₅NO₂: C, 84.85; H, 5.05; N, 4.71. Found: C, 84.35; H, 4.88; N, 4.44. IR (cm⁻¹) 2919.71, 1652.70, 1558.21, 1540.85, 1477.21, 1409.71, 1139.73, 1060.66. Melting Point 152 -154°C.

Oxazole 12: 5-(4-bromo-phenyl)-2-phenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.07 (2H, m), 7.53 (4H, s), 7.45 (3H, m), 7.41 (1H, s); ¹³C NMR (125 MHz) (CDCl₃) δ 161.3, 150.2, 132.0, 130.4, 128.8, 127.1, 126.8, 126.2, 125.5, 123.9, 122.2. MS (EI) *m/e* 299.0 (81.5) (M⁺). Anal. Calcd for C₁₇H₁₅NO₂: C, 59.80; H, 3.32; N, 4.65. Found: C, 59.79; H, 3.04; N, 4.14. IR (cm⁻¹) 3059.49, 2924.46, 1684.07, 543.25, 1479.59, 1448.73, 1136.22, 1074.49. Melting Point 93 -95°C.

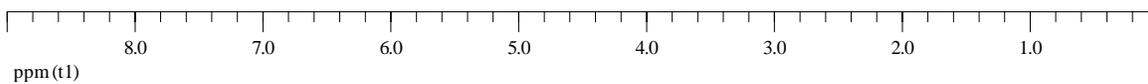
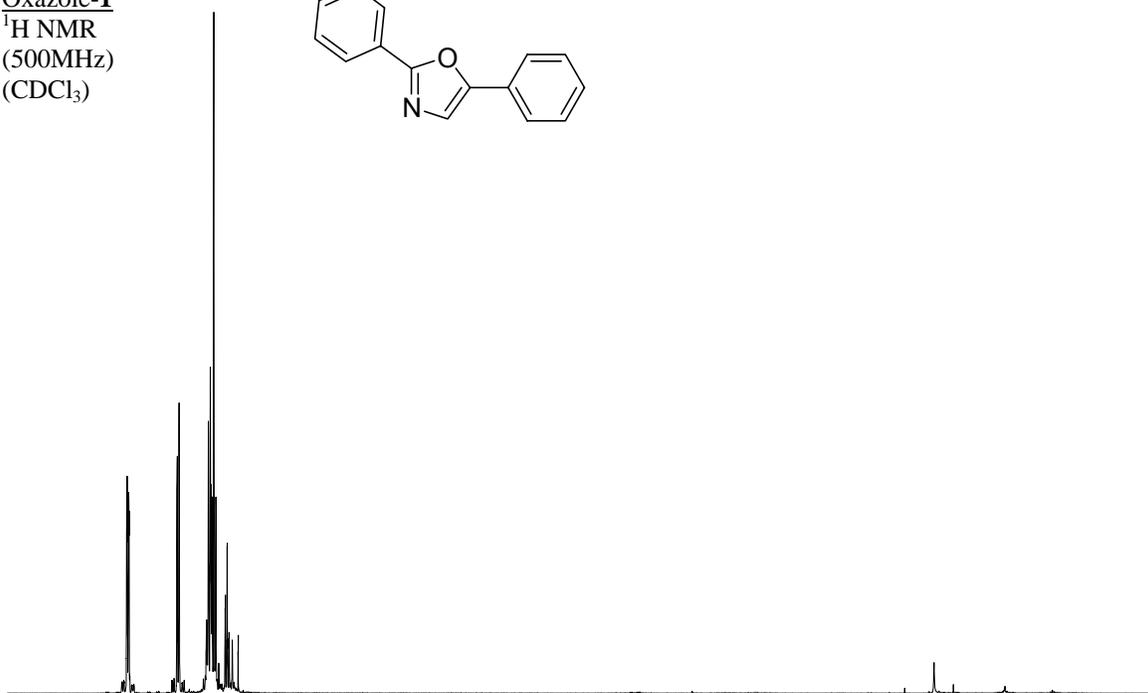
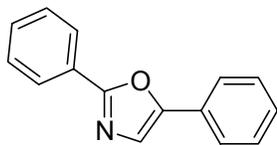
Oxazole 14: 5-naphthalen-1-yl-2-phenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.36 (1H, d, *J* = 7.2 Hz), 8.15 (2H, d, *J* = 7.3 Hz), 7.90 (2H, t, *J* = 7.2 Hz), 7.81 (1H, d, *J* = 7.0 Hz), 7.61-7.47 (7H, m); ¹³C NMR (125 MHz) (CDCl₃) δ 161.5, 150.5, 133.9, 130.4, 130.1, 129.6, 128.8, 128.7, 127.5, 127.1, 126.8, 126.4, 126.3, 126.2, 125.3, 125.2, 124.8. MS (EI) *m/e* 271.2 (100.0) (M⁺). Anal. Calcd for C₁₇H₁₅NO₂: C, 84.13; H, 4.79; N, 5.17. Found: C, 84.53; H, 4.43; N, 5.56. IR (cm⁻¹) 3055.35, 2923.57, 1658.49, 1589.06, 1481.07, 1448.28, 1133.94, 1072.23, 1024.02. Melting Point 103 -106°C.

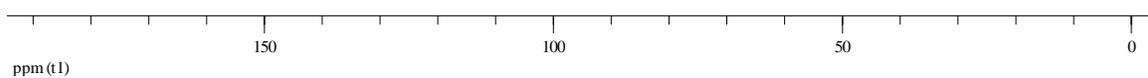
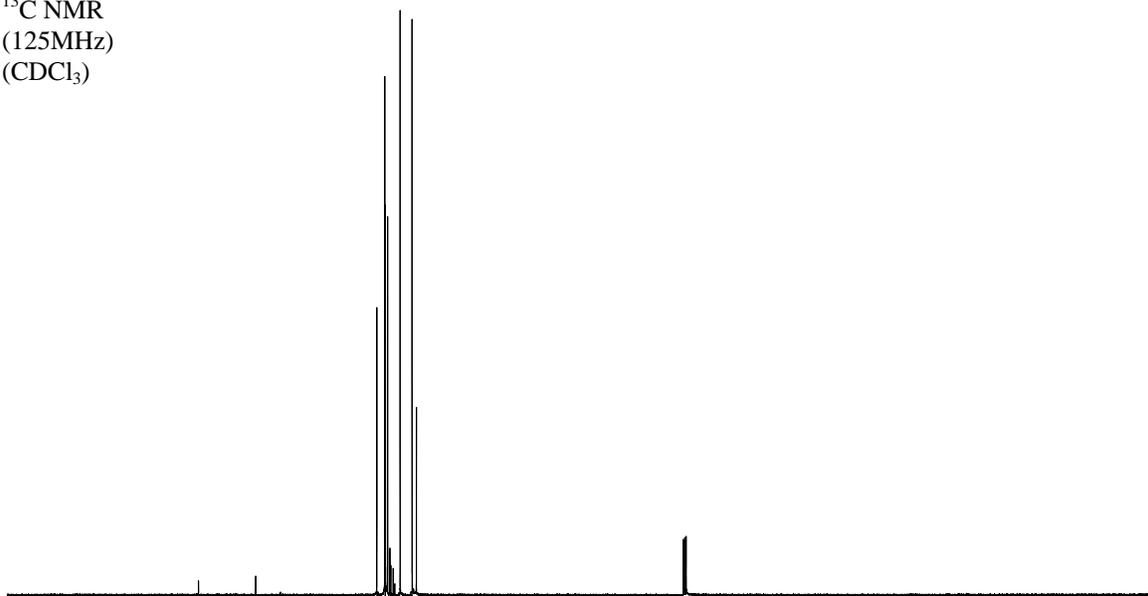
Oxazole 15: 5-naphthalen-2-yl-2-phenyl-oxazole.

¹H NMR (500 MHz) (CDCl₃) δ 8.19 (1H, s), 8.16 (2H, d, *J* = 7.2 Hz), 7.90-7.88 (2H, m), 7.83 (1H, d, *J* = 7.1 Hz), 7.77 (1H, d, *J* = 7.2 Hz), 7.55 (1H, s), 7.53-7.47 (5H, m); ¹³C NMR (125 MHz) (CDCl₃) δ 161.4, 151.4, 133.4, 133.1, 130.4, 128.8, 128.7, 128.2, 127.9, 127.4, 126.8, 126.5, 126.4, 125.3, 123.9, 122.9, 122.1. MS (EI) *m/e* 271.2 (100.0) (M⁺). Anal. Calcd for C₁₇H₁₅NO₂: C, 84.13; H, 4.79; N, 5.17. Found: C, 83.42; H, 4.25; N, 5.43. IR (cm⁻¹) 2921.64, 1698.99, 1683.56, 1652.7, 1558.21, 1540.85, 1456.00, 1128.16. Melting Point 98 -100°C.

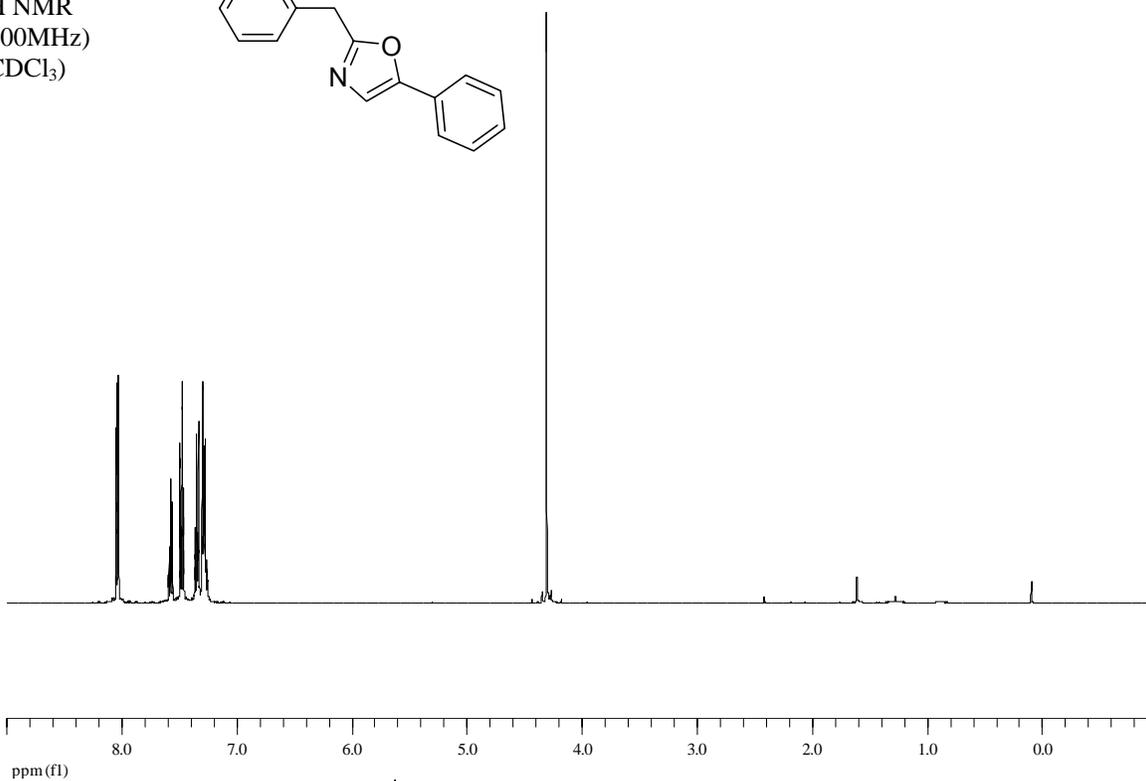
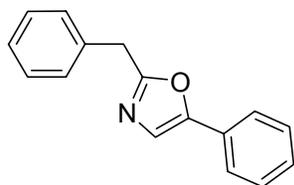
Oxazole-1
¹H NMR
(500MHz)
(CDCl₃)



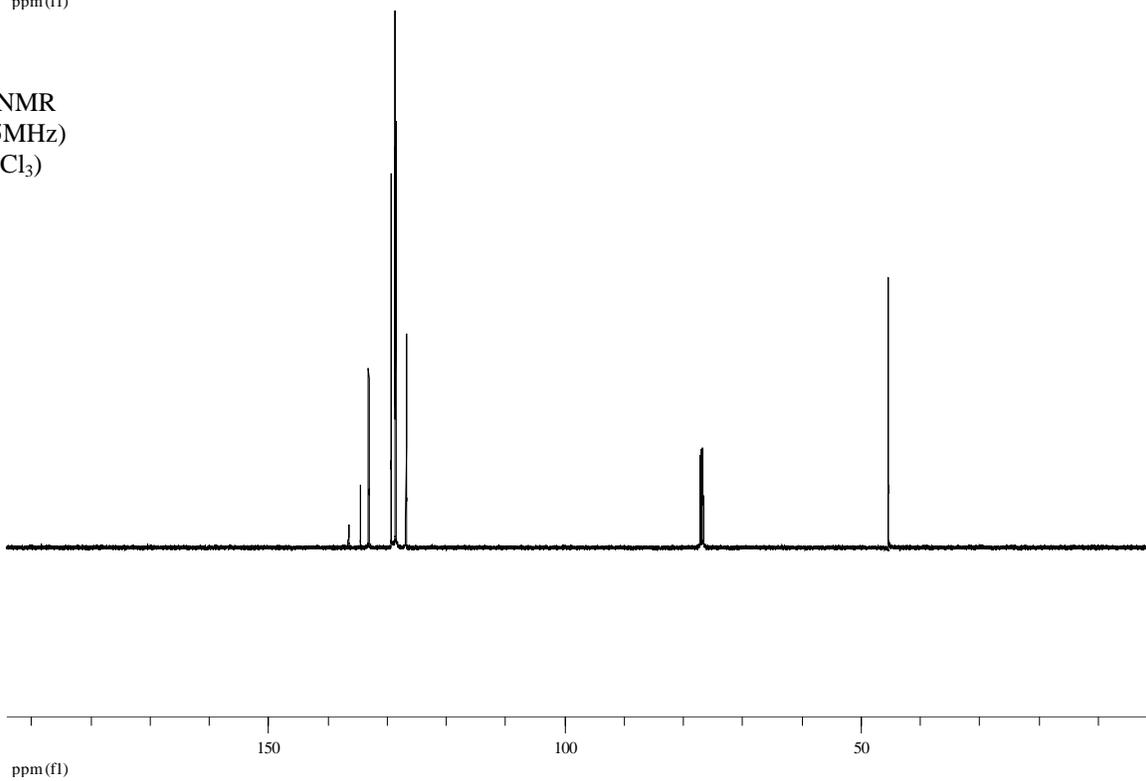
¹³C NMR
(125MHz)
(CDCl₃)



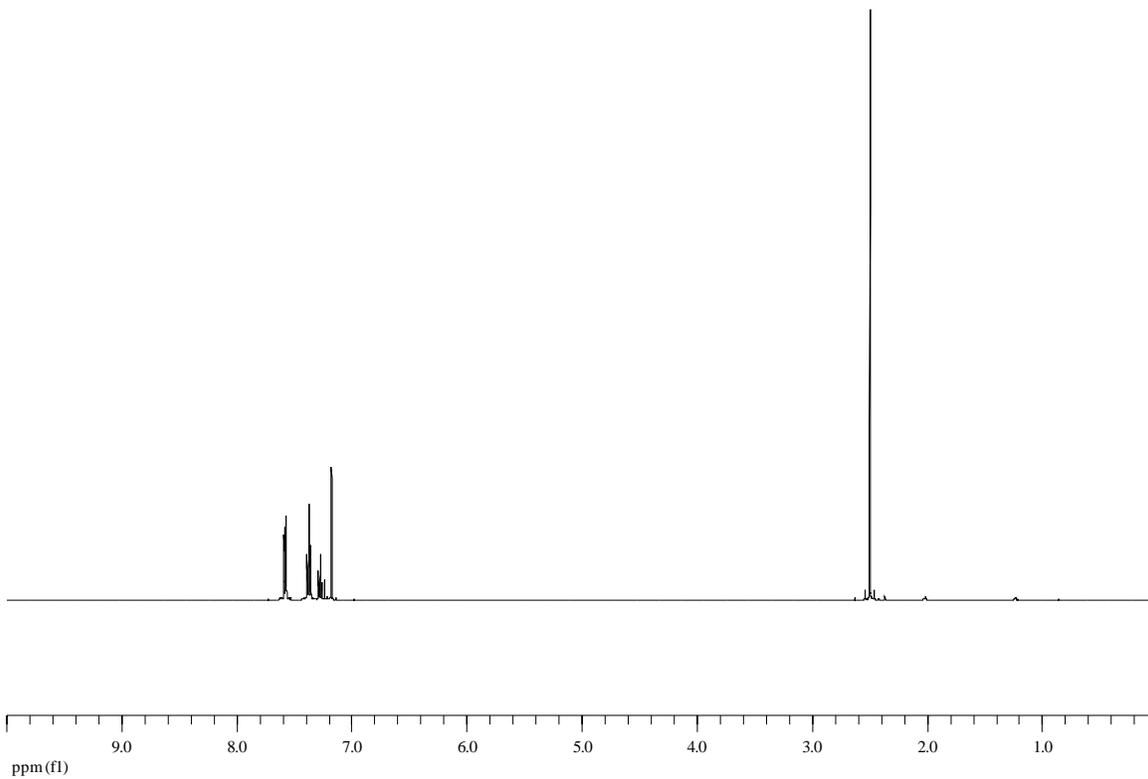
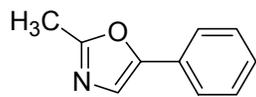
Oxazole-2
¹H NMR
(500MHz)
(CDCl₃)



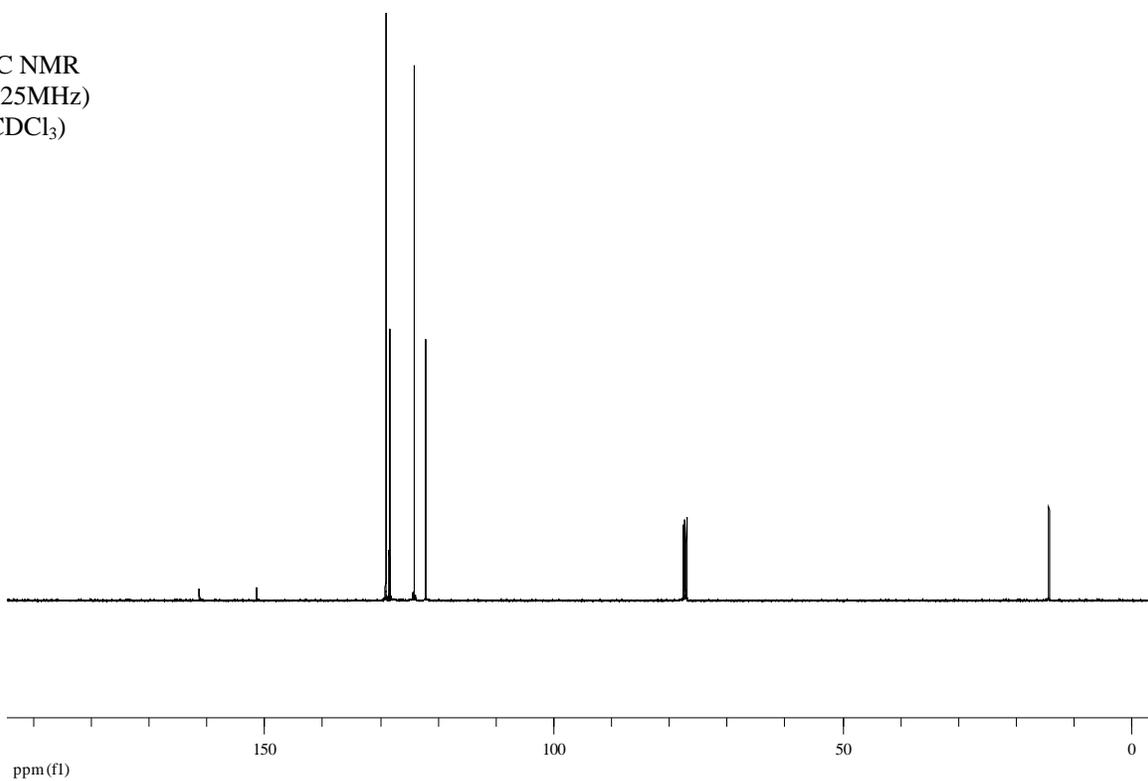
¹³C NMR
(125MHz)
(CDCl₃)



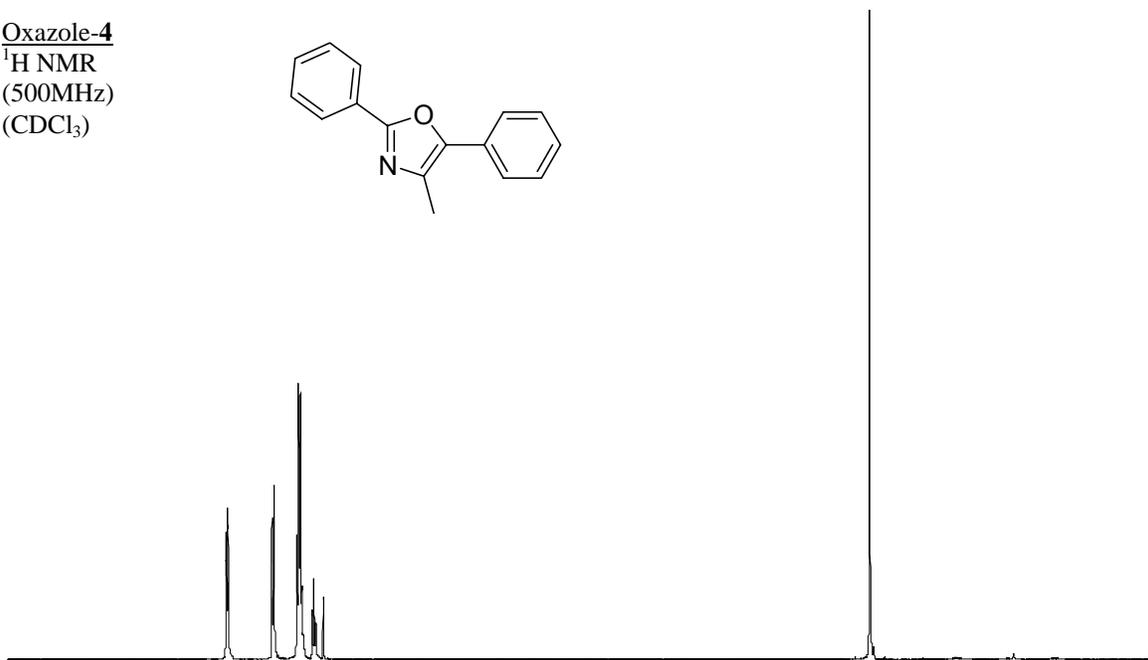
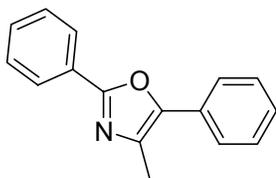
Oxazole-3
¹H NMR
(500MHz)
(CDCl₃)



¹³C NMR
(125MHz)
(CDCl₃)

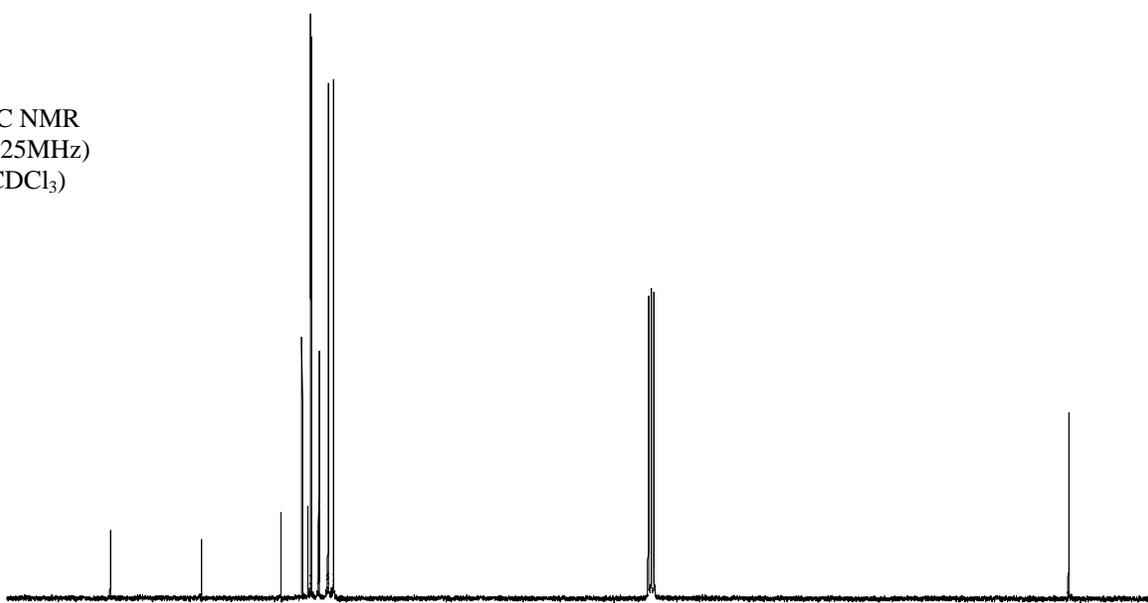


Oxazole-4
¹H NMR
(500MHz)
(CDCl₃)



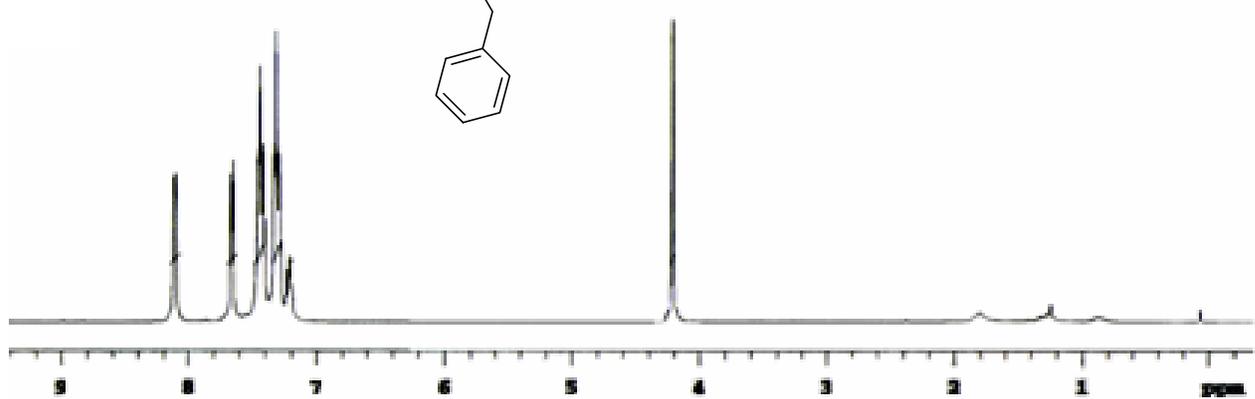
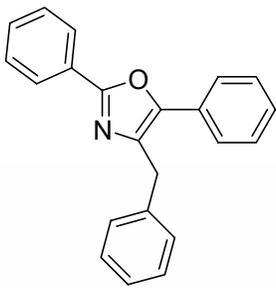
ppm (t1)

¹³C NMR
(125MHz)
(CDCl₃)

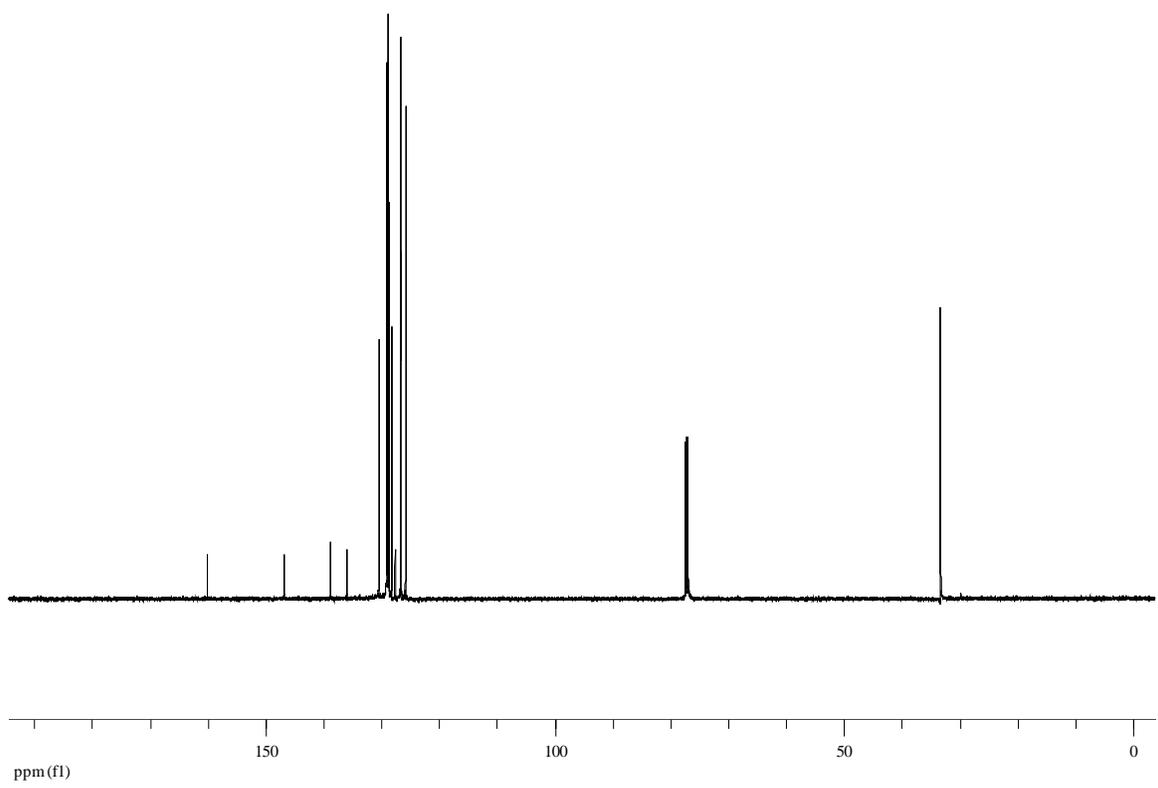


ppm (f1)

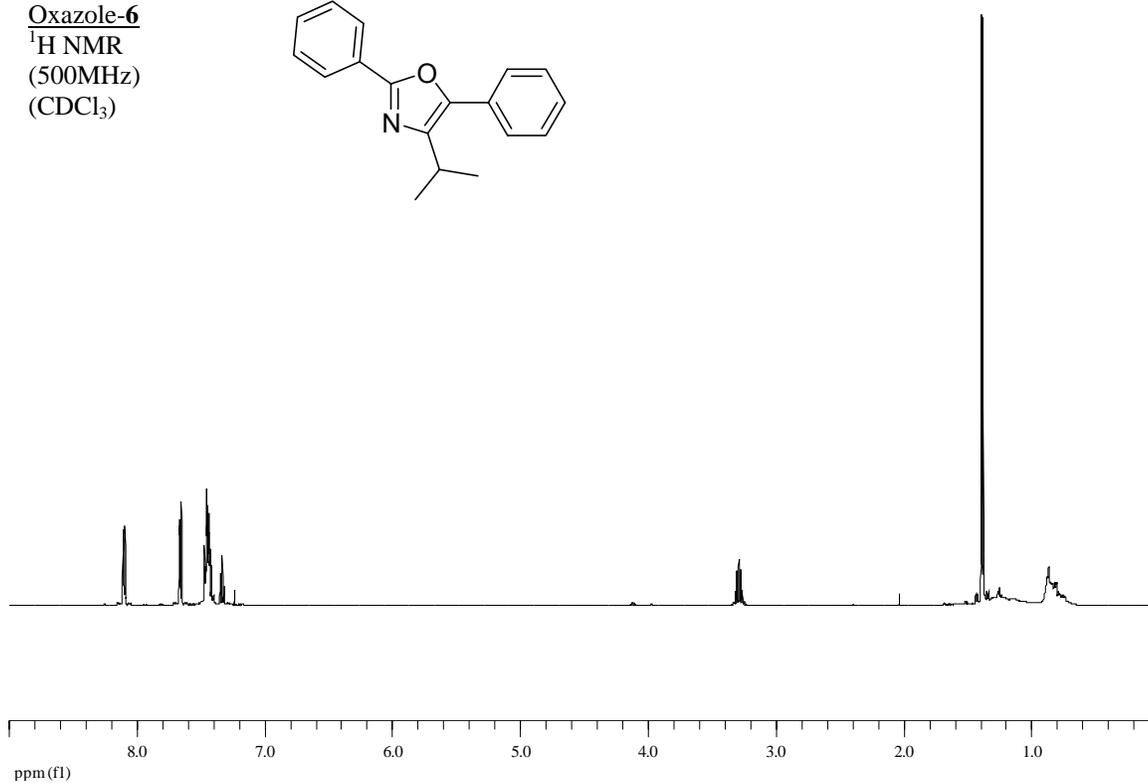
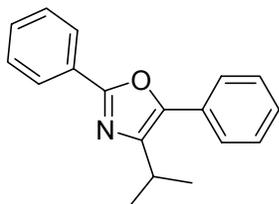
Oxazole-5
¹H NMR
(300MHz)
(CDCl₃)



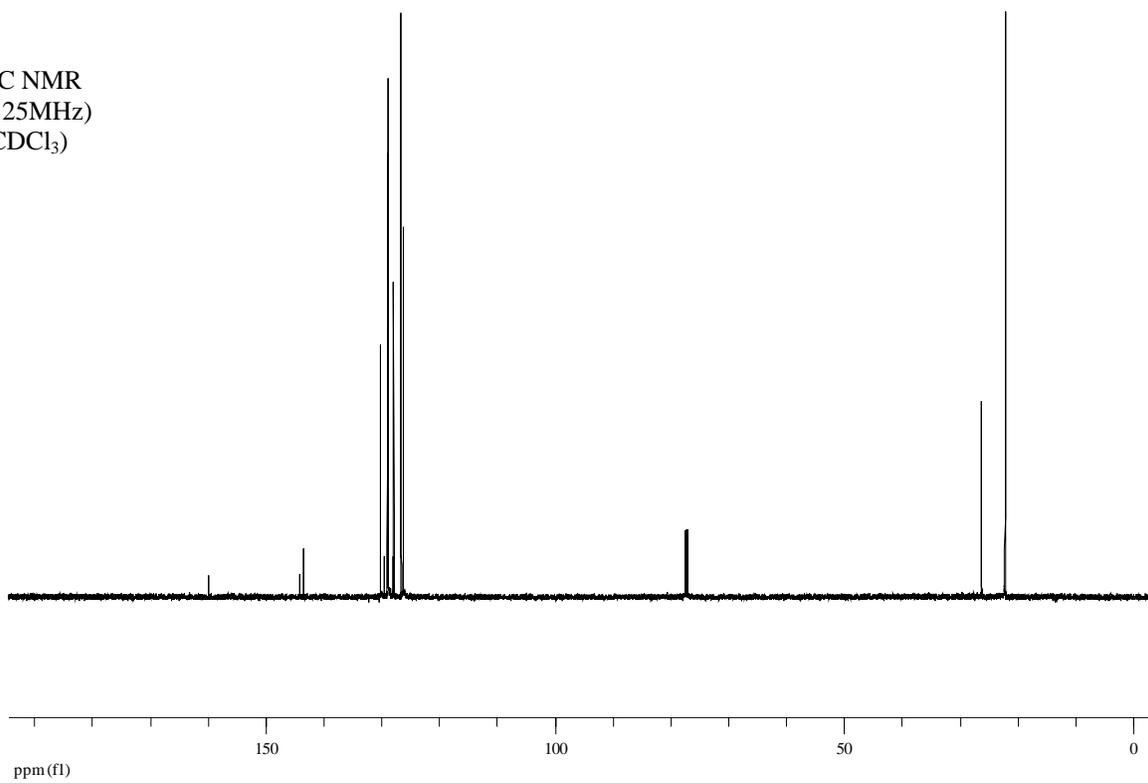
¹³C NMR
(75MHz)
(CDCl₃)



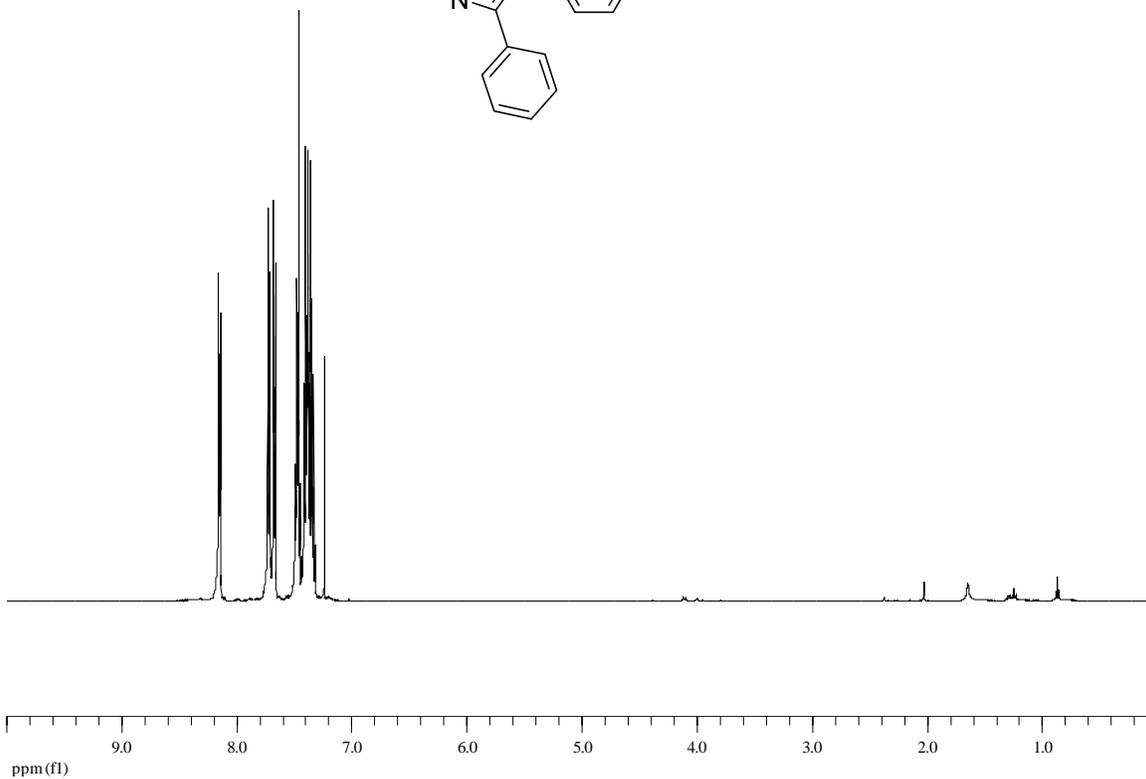
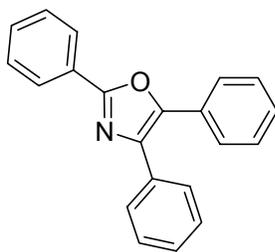
Oxazole-6
 ^1H NMR
(500MHz)
(CDCl_3)



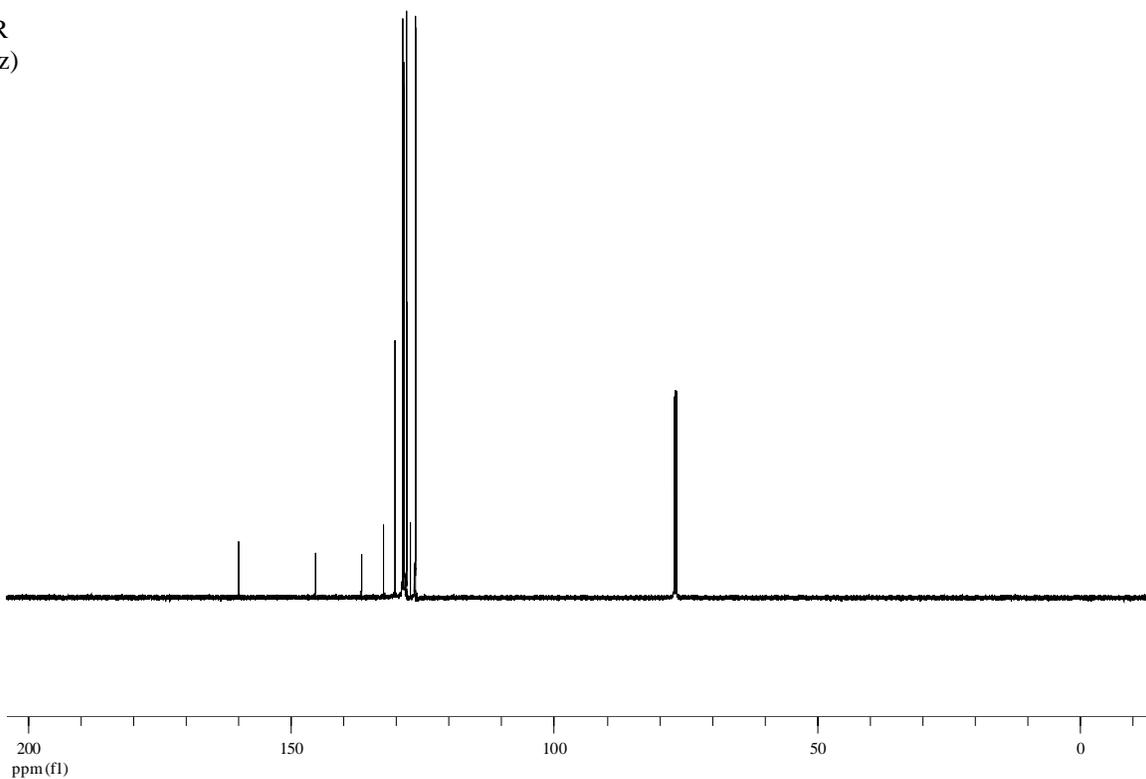
^{13}C NMR
(125MHz)
(CDCl_3)



Oxazole-7
¹H NMR
(500MHz)
(CDCl₃)

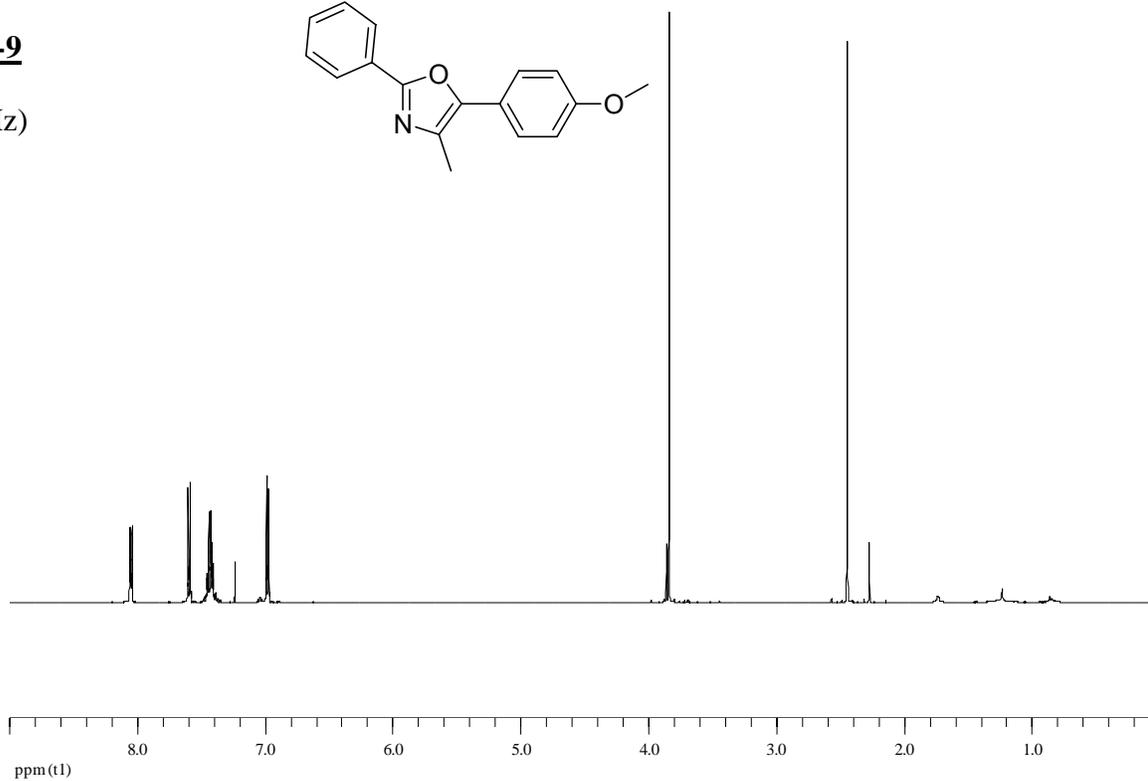
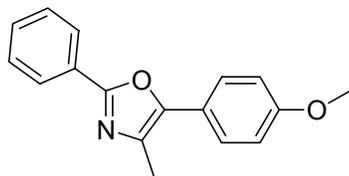


¹³C NMR
(125MHz)
(CDCl₃)

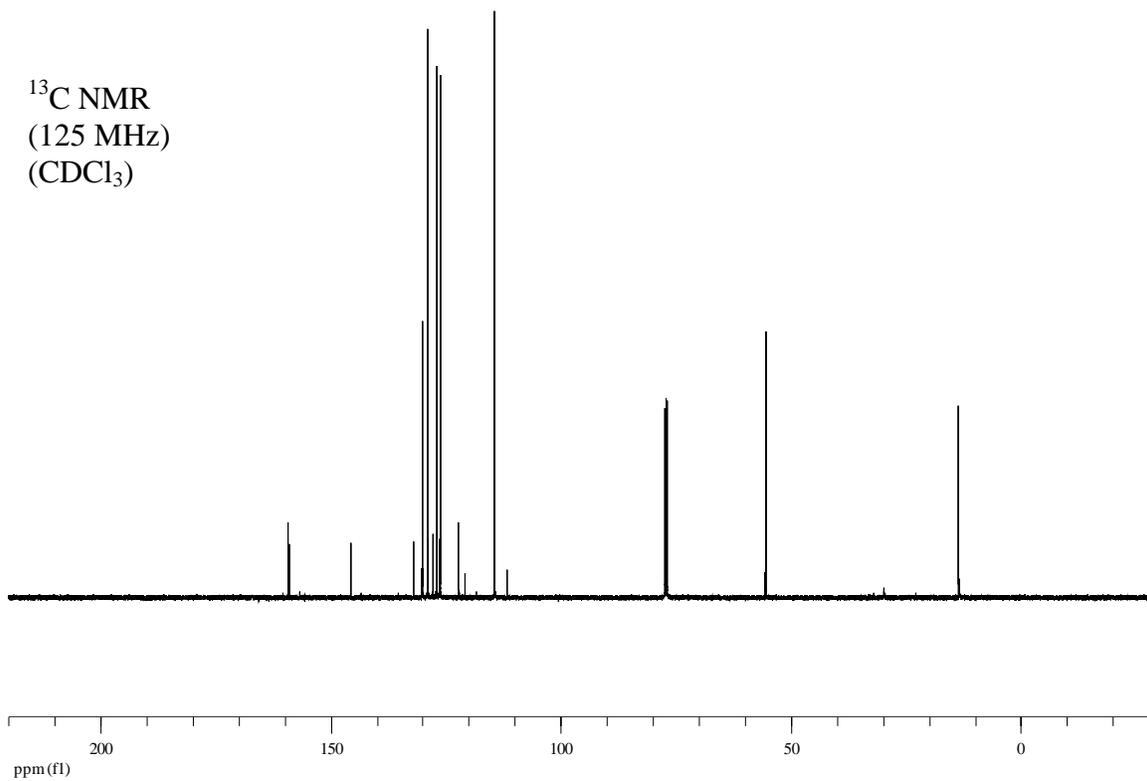


Oxazole-9

¹H NMR
(500 MHz)
(CDCl₃)

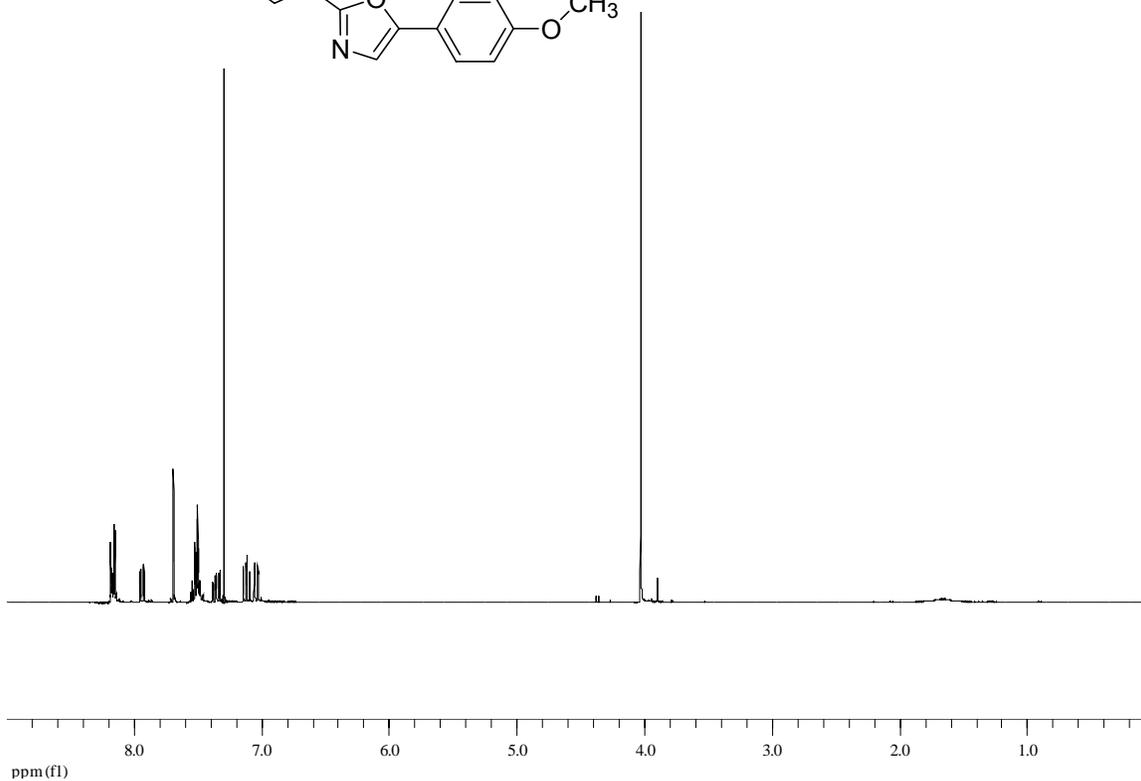
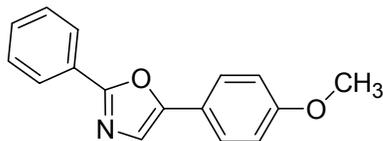


¹³C NMR
(125 MHz)
(CDCl₃)

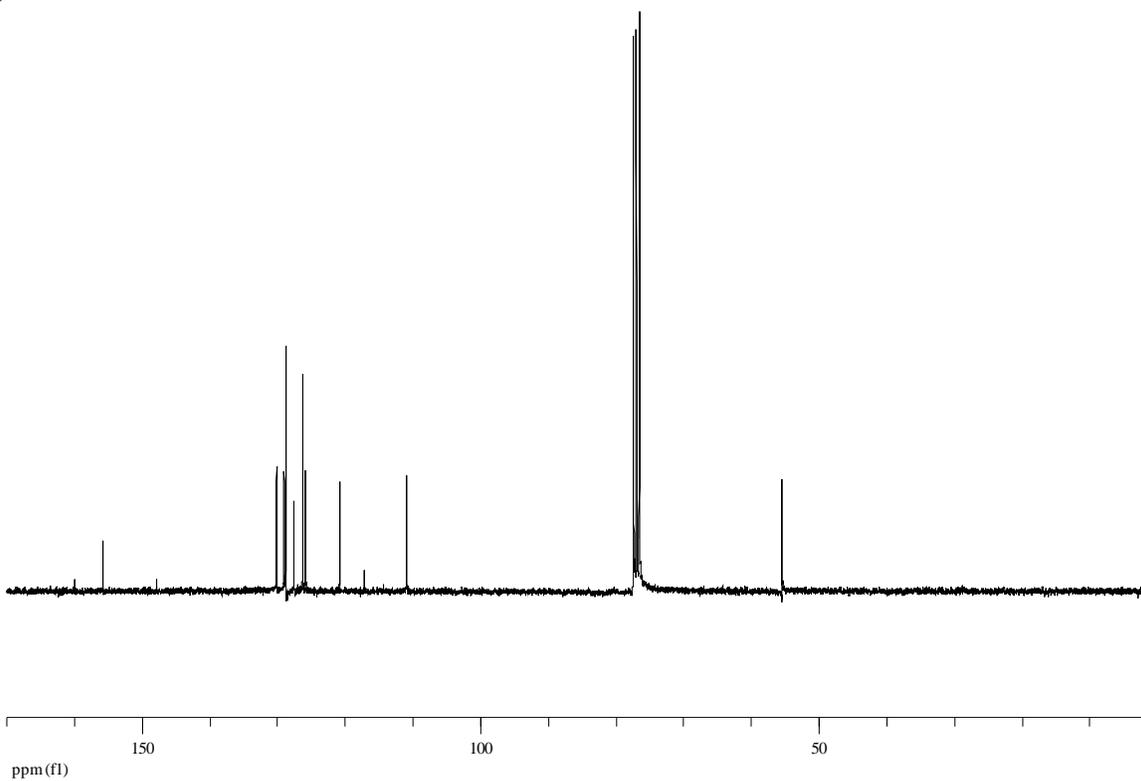


Oxazole-10

¹H NMR
(300 MHz)
(CDCl₃)

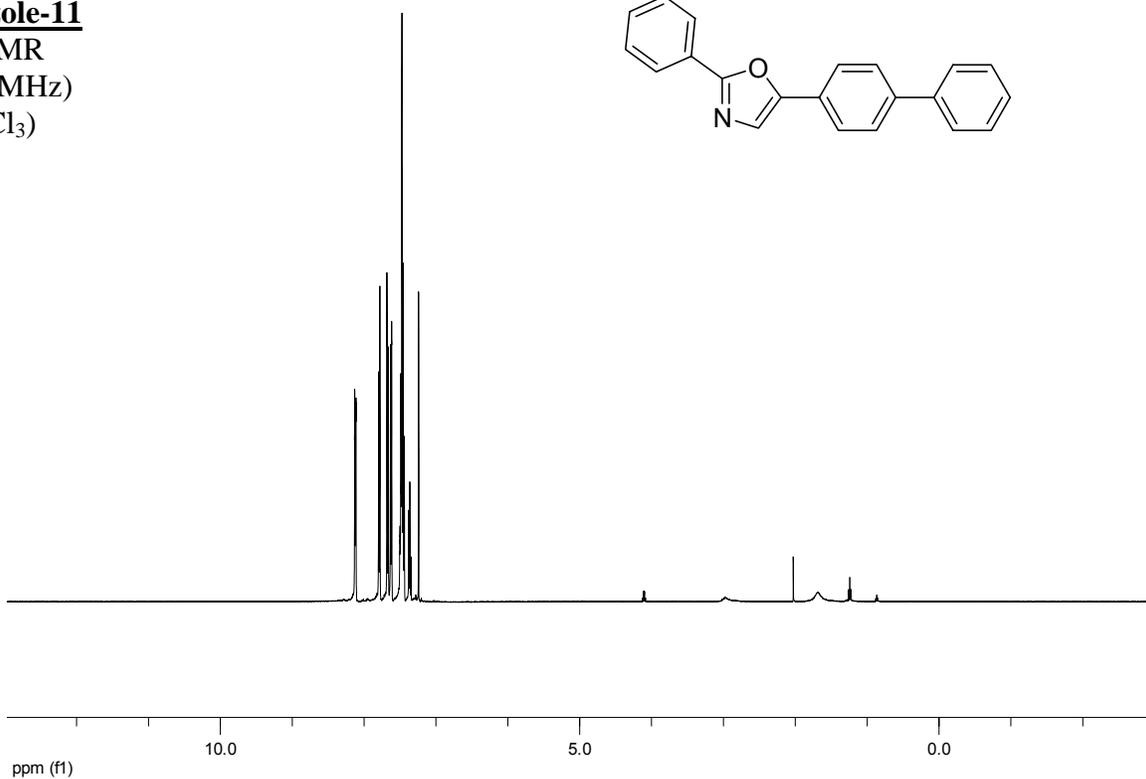
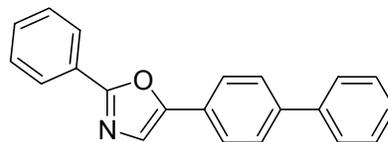


¹³C NMR
(75 MHz)
(CDCl₃)

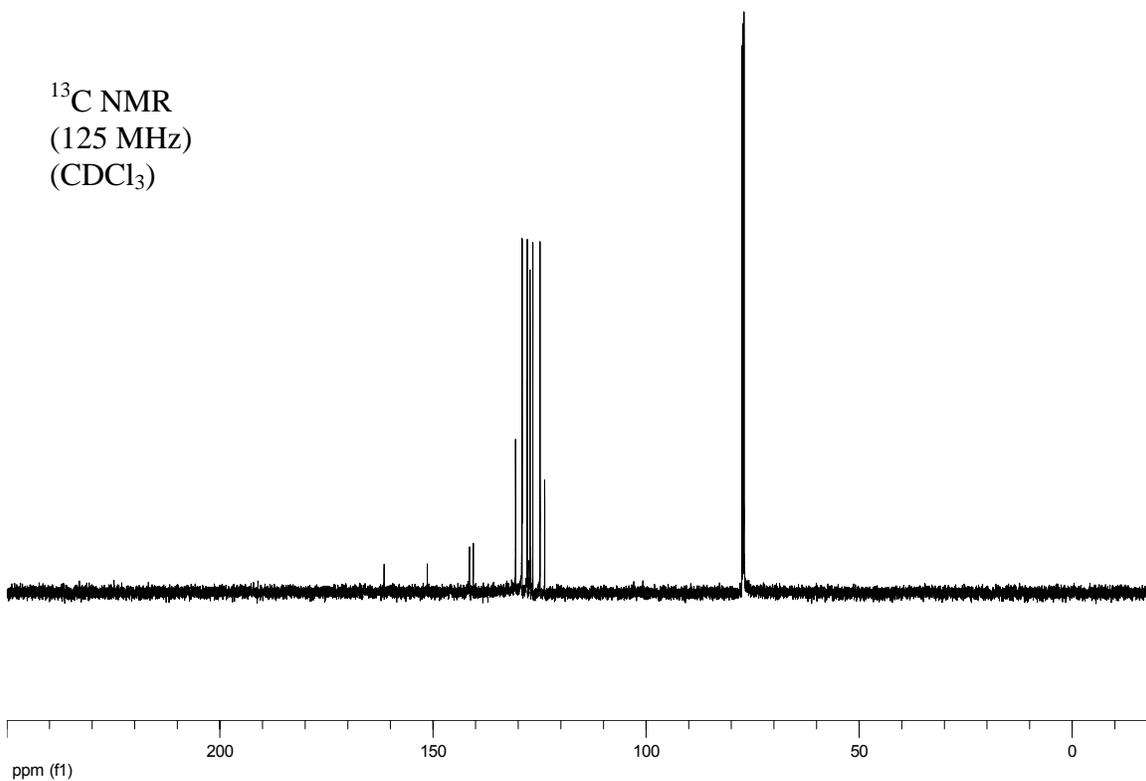


Oxazole-11

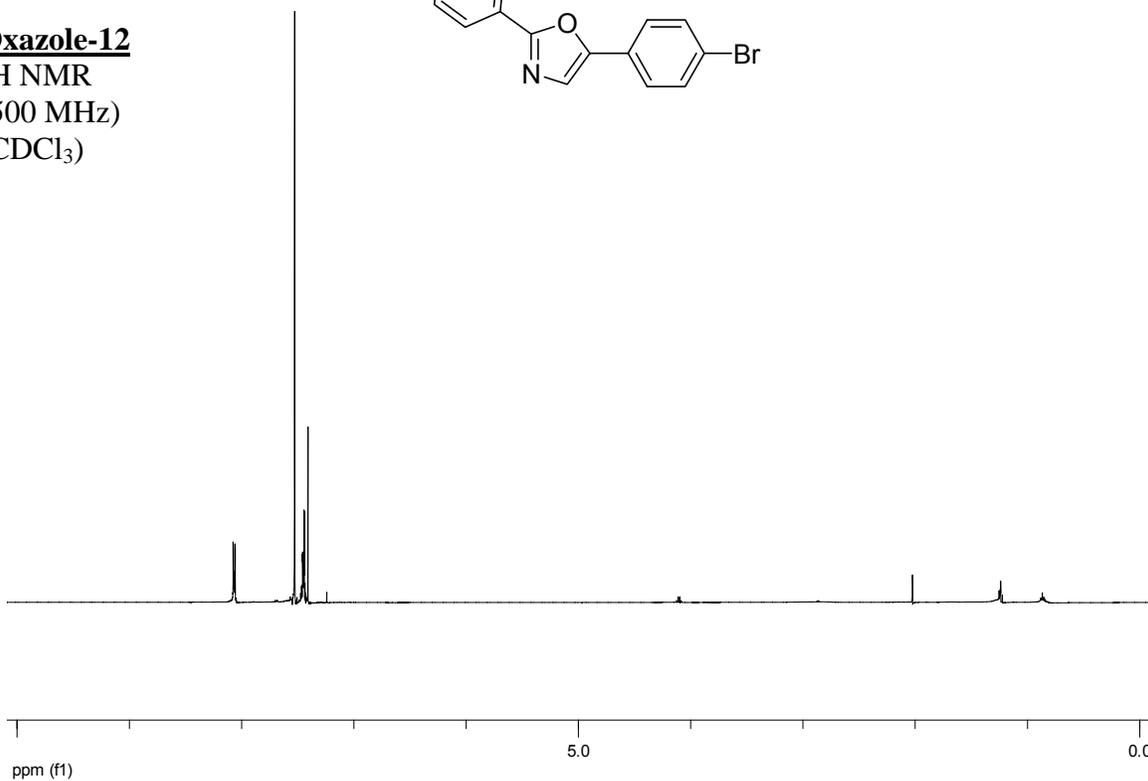
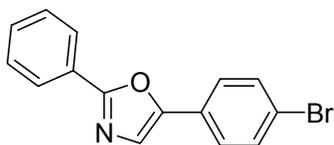
¹H NMR
(500 MHz)
(CDCl₃)



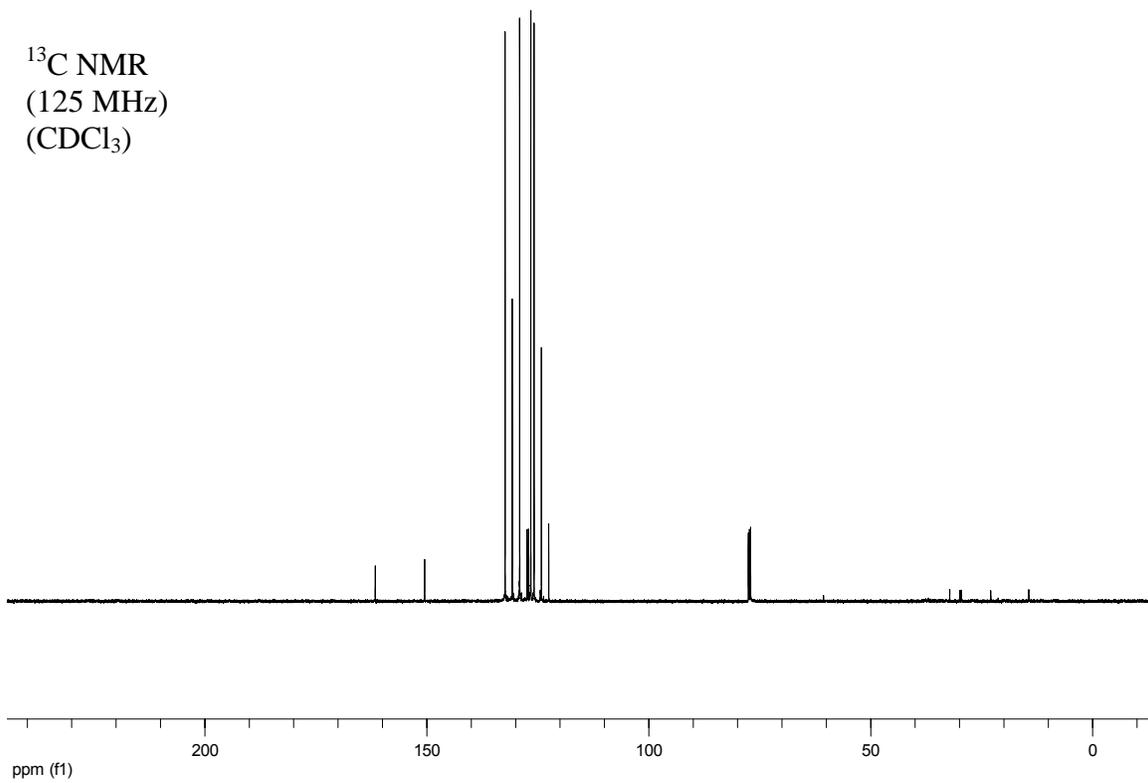
¹³C NMR
(125 MHz)
(CDCl₃)



Oxazole-12
¹H NMR
(500 MHz)
(CDCl₃)

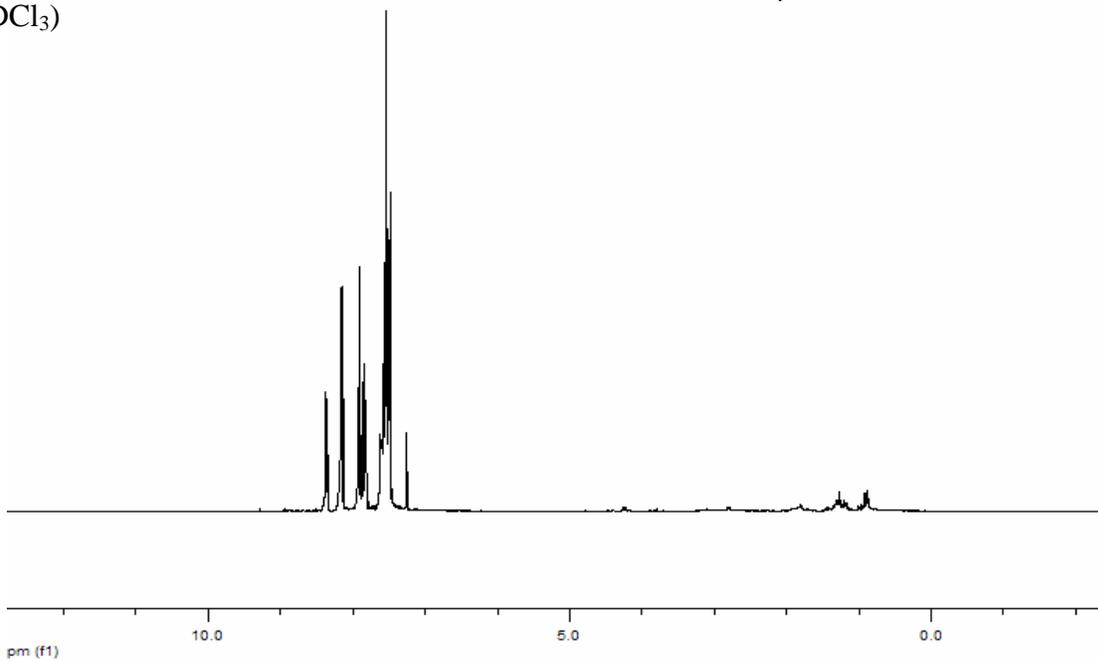
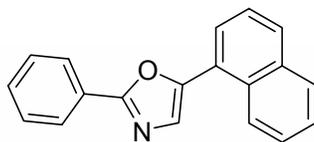


¹³C NMR
(125 MHz)
(CDCl₃)

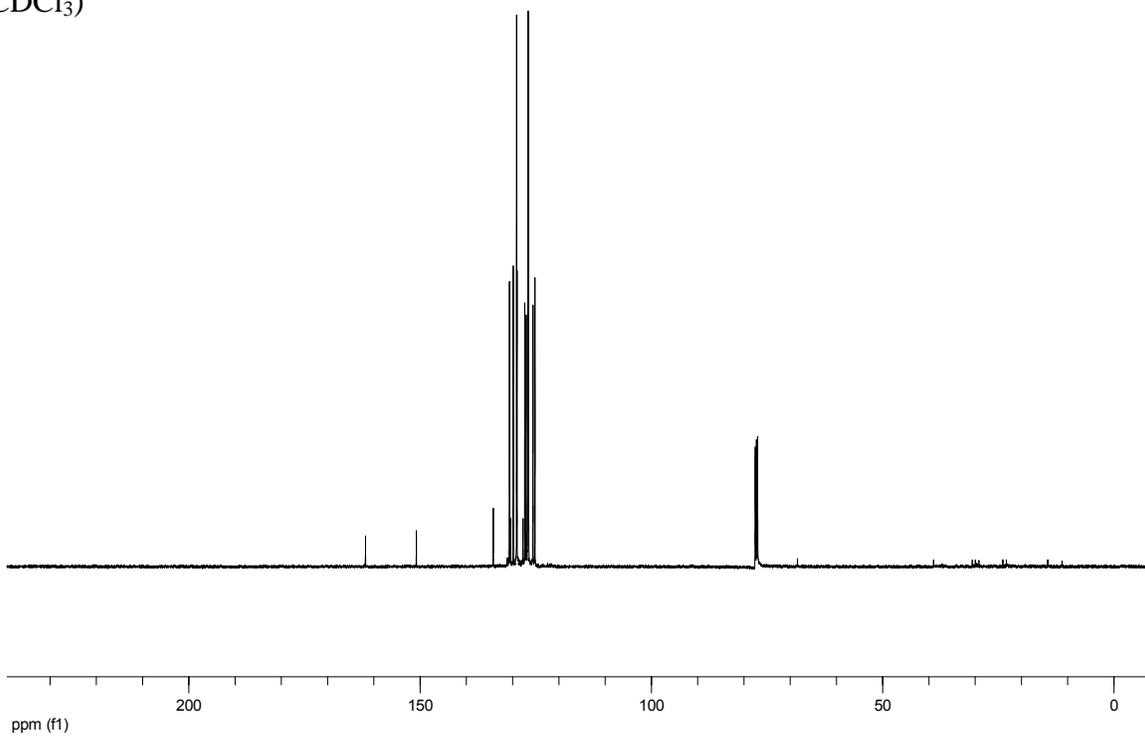


Oxazole-15

¹H NMR
(500 MHz)
(CDCl₃)

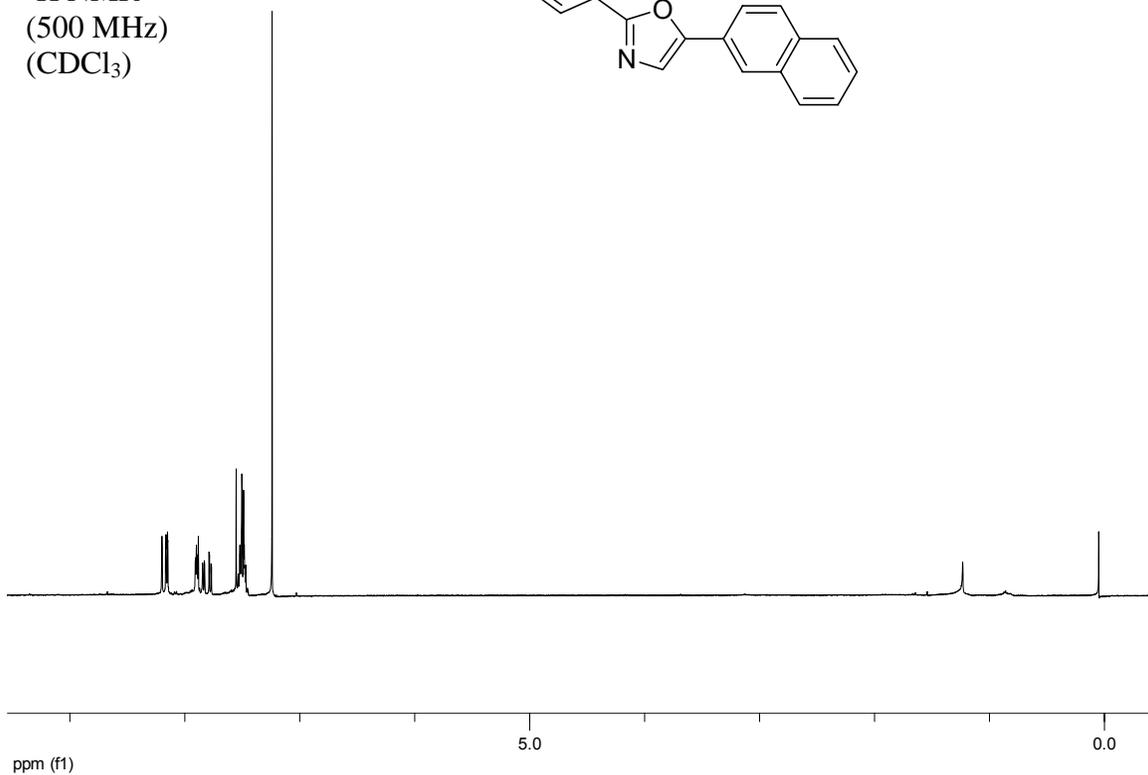
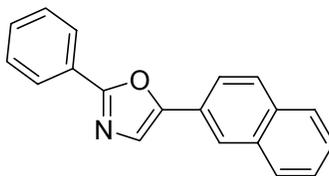


¹³C NMR
(125 MHz)
(CDCl₃)



Oxazole-15

^1H NMR
(500 MHz)
(CDCl_3)



^{13}C NMR
(125 MHz)
(CDCl_3)

