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SUPPORTING INFORMATION

Title: Sequential Metal-Catalyzed *N*-Heteroarylation and C–C Cross-Coupling Reactions: An Expedient Route to Tris(hetero)aryl Systems

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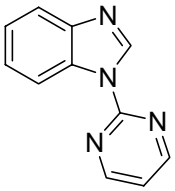
Ref. No.: O200800018

Contents

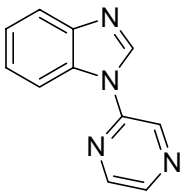
1-(Pyrimidin-2-yl)-1*H*-benzimidazole (10)



Procedure A: Benzimidazole **(1)** (0.284 g, 2.4 mmol), Cs_2CO_3 (1.304 g, 4 mmol), CuI (0.038g, 0.2 mmol), DMF (4 mL), 2-iodopyrimidine **(5a)** (0.412 g, 2 mmol) and 1,10-phenanthroline (0.072 g, 0.4 mmol), were reacted at 110 ^oC for 6 h. Filtration and concentration yielded a white solid which was purified by column chromatography on silica (eluent EtOAc : diethylether 9:1 v/v) yielding **10** as a white powder (0.196 g, 50 %) mp 149.1-150.1 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.03 (s, 1H), 8.66 (d, 2H, *J* = 4.8 Hz), 8.53 (d, 1H, *J* = 6.8 Hz), 7.81 (d, 1H, *J* = 7.3 Hz), 7.39-7.31 (m, 2H), 7.09 (t, 1H, *J* = 4.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 156.5, 145.3, 142.0, 132.1, 124.8, 124.0, 120.6, 118.2, 115.9. MS (EI) *m/z* 196 (M^+, 100 %). $C_{11}H_8N_4$ (196.2) calcd. C 67.34, H 4.11, N 28.55; found: C 67.12, H 4.07, N 28.74. IR (ν_{max}/cm^{-1}): 3127, 3066, 1570, 1463, 1440, 1300, 742.

Procedure B: Benzimidazole **(1)** (0.260 g, 2.2 mmol), Cs_2CO_3 (1.303 g, 4 mmol), Cu_2O (0.014g, 0.1 mmol), acetonitrile (4 mL), 2-bromopyrimidine **(5b)** (0.318 g, 2 mmol) and the ligand chxn-py-al (0.123 g, 0.4 mmol), were reacted at 87 ^oC for 64 h. Work-up as for Procedure A yielded **10** (0.275 g, 78 %) spectroscopically identical to the sample prepared by procedure A.

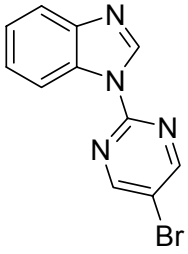
1-(Pyrazin-2-yl)-1*H*-benzimidazole (11)



Benzimidazole **(1)** (0.144 g, 1.22 mmol), Cs_2CO_3 (0.660 g, 2.025 mmol), CuI (0.019 g, 0.10 mmol), DMF (2 mL), 2-iodopyrazine **(6)** (0.309 g, 1.50 mmol) and 1,10-phenanthroline (0.037 g, 0.20 mmol), were reacted at 110 ^oC for 65 h. Filtration and concentration yielded a white solid which was purified by chromatography using a silica column (eluent EtOAc : diethylether 9:1 v/v) yielding **11** as a white powder (0.228 g, 70 %) mp 149.5-150.8 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.03 (d, 1H, *J* = 1.6 Hz), 8.63-8.58 (m, 3H), 8.11 (dd, 1H, *J* = 6.8, 1.6 Hz), 7.90 (dd, 1H, *J* = 5.2, 2.4 Hz), 7.46-7.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.1, 145.1, 143.6, 142.6, 140.9, 136.5,

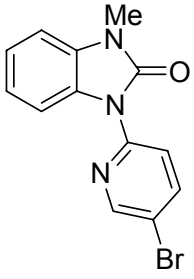
129.6, 125.2, 124.3, 121.4, 113.0. MS (EI) *m/z* 196 (M^+, 100 %). $C_{11}H_8N_4$ (196.2) calcd. C 67.34, H 4.11, N 28.55; found: C 67.11, H 4.13, N 28.33. IR (ν_{max}/cm^{-1}): 3082, 2975, 1501, 1478, 1305, 748.

1-(5-Bromopyrimidin-2yl)-1*H*-benzimidazole (13)



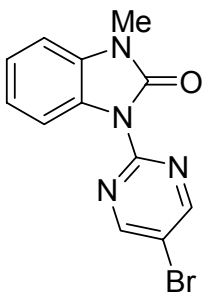
Benzimidazole **(1)** (0.284 g, 2.4 mmol), Cs_2CO_3 (1.304 g, 4.0 mmol), CuI (0.038 g, 0.20 mmol), DMF (4 mL), 5-bromo-2-iodopyrimidine **(7)** (0.570 g, 2.0 mmol) and 1,10-phenanthroline (0.072 g, 0.40 mmol), were reacted at 70 ^oC for 24 h. Filtration and concentration yielded a white solid which was purified by column chromatography on silica (eluent EtOAc : diethylether 9:1 v/v) yielding **13** as a white solid (0.230 g, 57 %) mp 189.1-189.6 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.03 (s, 1H), 8.80 (s, 2H), 8.52 (dd, 1H, *J* = 7.2, 1.6 Hz), 7.85 (dd, 1H, *J* = 6.8, 1.2 Hz), 7.45-7.37 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.4, 154.9, 145.4, 142.1, 132.0, 125.2, 124.4, 120.9, 115.83, 115.77. MS (EI) *m/z* 274 (M^+ [^{79}Br], 100 %), 276 (M^+ [^{81}Br], 97 %). $C_{11}H_7N_4Br$ (275.1) calcd. C 48.02, H 2.56, N 20.37; found: C 47.86, H 2.52, N 20.37. IR (ν_{max}/cm^{-1}): 3124, 3022, 1462, 1439, 1298, 747.

1-(5-Bromopyridin-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (14)



1-Methyl-2-benzimidazolone **(2)** (1.305 g, 8.8 mmol), Cs_2CO_3 (5.213 g, 16 mmol), CuI (0.152g, 0.8 mmol), DMF (20 mL), 2-iodo-5-bromopyrimidine **(7)** (2.271 g, 8.0 mmol) and 1,10-phenanthroline (0.288 g, 1.6 mmol) were reacted at 80 ^oC for 24 h. Filtration and concentration yielded a pale brown solid which was purified by column chromatography on silica (eluent DCM : EtOAc 9:1 v/v) yielding **14** as a white solid (2.27 g, 94 %) mp 148.2-148.6 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.59 (d, 1H, *J* = 2 Hz), 8.16 (d, 1H, *J* = 8.5 Hz), 8.10 (d, 1H, *J* = 8.0 Hz), 7.94 (dd, 1H, *J* = 8.5, 2.5 Hz), 7.23-7.14 (m, 2H), 7.03 (d, 1H, *J* = 8 Hz), 3.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.3, 149.5, 149.1, 141.0, 130.5, 127.6, 123.4, 122.4, 118.7, 116.9, 113.7, 107.8, 27.5. MS (EI) *m/z* 303 (M^+ ^{79}Br], 100 %), 305 (M^+ [^{81}Br], 97 %). $C_{13}H_{10}BrN_3O$ (304.1) calcd. C 51.34, H 3.31, N 13.82; found: C 51.13, H 3.20, N 13.67. IR (ν_{max}/cm^{-1}): 3057, 3013, 1727, 1493, 1472, 1392, 746.

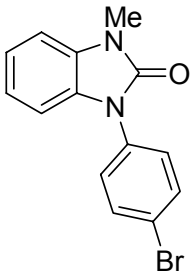
1-(5-Bromopyrimidin-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (15)



1-Methyl-2-benzimidazolone **(2)** (0.652 g, 4.4 mmol), Cs_2CO_3 (2.607 g, 8 mmol), CuI (0.076g, 0.4 mmol), DMF (10 mL), 2-iodo-5-bromopyrimidine **(8)** (1.134 g, 4.0 mmol) and 1,10-phenanthroline (0.144 g, 0.8 mmol) were reacted at 80 ^oC for 18 h. Filtration and concentration yielded a yellow solid which was chromatographed on a silica column (eluent DCM : EtOAc 3:1 v/v) yielding **15** as a white solid (0.92 g, 76 %) mp 175.4-176.7 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ =

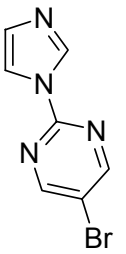
8.87 (s, 2H), 7.93 (d, 1H, J = 9.4 Hz), 7.23-7.11 (m, 2H), 7.01 (d, 1H, J = 7.8 Hz), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.4, 155.1, 152.3, 130.6, 127.2, 123.9, 122.3, 116.2, 113.4, 107.0, 27.6. MS (EI) *m/z* 304 (M^+ [^{79}Br], 100 %), 306 (M^+ [^{81}Br], 97 %). $C_{12}H_9N_4BrO$ (305.1) calcd. C 47.24, H 2.97, N 18.36; found: C 47.27, H 2.98, N 18.43. IR (ν_{max}/cm^{-1}): 3060, 3031, 1735, 1498, 1413, 1384, 745.

1-(4-Bromophen-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (16)



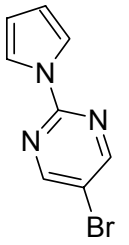
1-Methyl-2-benzimidazolone **(2)** (0.593 g, 4.0 mmol), Cs_2CO_3 (3.37g, 7.3 mmol), CuI (0.076g, 0.40 mmol), DMF (5.5 mL), 1-bromo-4-iodobenzene **(9)** (1.136 g, 3.6 mmol) and 1,10-phenanthroline (0.072 g, 0.4 mmol) were reacted at 80 ^{o}C for 16 h, then at 90 ^{o}C for 6 h and finally at 100 ^{o}C for 2 h. Tlc monitoring showed the reaction was incomplete after heating at 80 ^{o}C and 90 ^{o}C. Filtration and concentration yielded a white solid which was chromatographed on a silica column (eluent DCM : EtOAc 3:1 v/v) yielding **16** as a white solid which was recrystallized from DCM/hexane mixture to give white crystals (0.893 g, 81 %) mp 157.7-158.6 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, 2H, J = 8.8 Hz), 7.44 (d, 2H, J = 8.8 Hz), 7.20-7.04 (m, 4H), 3.49 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.6, 134.2, 133.0, 130.5, 129.2, 127.8, 122.6, 121.9, 121.4, 108.9, 108.2, 27.6. MS (EI) *m/z* 302 (M^+ [^{79}Br], 100 %), 304 (M^+ [^{81}Br], 97 %). $C_{14}H_{11}BrN_2O$ (303.2) calcd. C 55.47, H 3.66, N 9.24; found: C 54.95, H 3.60, N 9.62. HRMS (ES+) calcd. for $C_{14}H_{11}BrN_2O$+H *m/z* 305.01071; found: *m/z* 305.01087. IR (ν_{max}/cm^{-1}): 3056, 2932, 1712, 1501, 1400, 1204, 745.

Compound 17



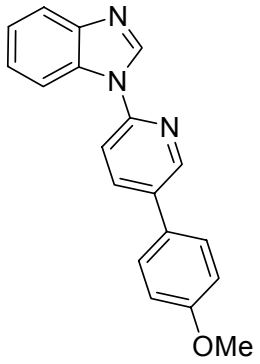
Imidazole **(3)** (0.150 g, 2.2 mmol), Cs_2CO_3 (1.303 g, 4 mmol), CuI (0.038 g, 0.2 mmol), DMF (5 mL), 5-bromo-2-iodopyrimidine **(8)** (0.570 g, 2.2 mmol) and 1,10-phenanthroline (0.072 g, 0.4 mmol) were reacted at 80 ^{o}C for 18 h. Filtration and concentration yielded an off-white solid which was chromatographed on a silica column (eluent EtOAc : Et_2O 9:1 v/v) yielding **17** as a white solid (0.292 g, 65 %) mp ca. 160 ^{o}C (dec.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 2H), 8.56 (s, 1H), 7.83 (t, 1H, J = 1.2 Hz), 7.17 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.6, 153.5, 136.6, 131.4, 116.9, 116.7. MS (EI) *m/z* 223.9 (M^+ [^{79}Br], 100 %), 225.9 (M^+ [^{81}Br], 97 %). $C_7H_5BrN_4$ (225.1) calcd. C 37.36, H 2.24, N 24.90; found: C 36.99, H 2.22, N 24.61. IR (ν_{max}/cm^{-1}): 3134, 1557, 1471, 1446, 754, 648.

Compound 18



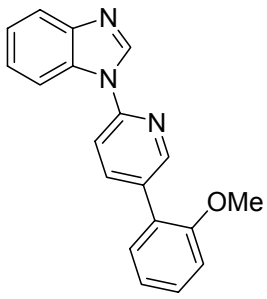
Pyrrole **(4)** (0.295 g, 4.4 mmol), Cs_2CO_3 (2.607 g, 8 mmol), CuI (0.076 g, 0.4 mmol), DMF (10 mL), 5-bromo-2-iodopyrimidine **(8)** (1.140 g, 4.4 mmol) and 1,10-phenanthroline (0.144 g, 0.8 mmol) were reacted at 80 ^oC for 18 h. Filtration and concentration yielded an off-white solid which was chromatographed on a silica column (eluent EtOAc : hexane 1:9 v/v) yielding **18** as a white solid (0.756 g, 84 %) mp ca. 217 ^oC (dec.). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.63 (s, 2H), 7.71 (t, 2H, *J* = 2.0 Hz), 6.35 (t, 2H, *J* = 2.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.6, 153.5, 136.6, 131.4, 116.9, 116.7. $C_8H_6BrN_3$ (224.1) calcd. C 42.88, H 2.70, N 18.75; found: C 42.49, H 2.81, N 18.82. HRMS (ES+) calcd. for $C_8H_6N_3Br$+H *m/z* 223.98178; found: *m/z* 223.98210. IR (ν_{max}/cm^{-1}): 3150, 1555, 1470, 1443, 735, 610.

Compound 22



Compound **12** (0.139 g, 0.505 mmol), 4-methoxybenzeneboronic acid **(19)** (0.085 g, 0.561 mmol), $Pd(PPh_3)_2Cl_2$ (0.020 g, 0.03 mmol), 1,4-dioxane (5 mL) and Na_2CO_3 (1 M, 1.7 mL) were reacted at 80 ^oC for 24 h. Standard work-up and evaporation yielded a white solid which was chromatographed on a silica column (eluent DCM : EtOAc 1:1 v/v) to yield **22** which was recrystallized from hexane as large white crystals (0.112 g, 74 %) mp 155.0-156.2 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.75 (d, 1H, *J* = 2.5 Hz), 8.58 (s, H), 8.07 (dd, 1H, *J* = 7.0, 1.8 Hz), 7.98 (d, 1H, *J* = 8.5, 2.4 Hz), 7.88 (d, 1H, *J* = 7.1), 7.56-7.52 (m, 3H), 7.41-7.33 (m, 2H), 7.02 (d, 1H, *J* = 8.6), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3, 148.6, 147.4, 145.0, 141.6, 136.9, 134.9, 132.5, 129.3, 128.3, 124.5, 123.5, 120.9, 115.0, 114.3, 112.9, 55.7; MS (EI) *m/z* 301 (M^+, 100 %). $C_{19}H_{15}N_3O$ (301.3) calcd. C 75.73, H 5.02, N 13.94; found: C 75.39, H 4.97, N 13.84. IR (ν_{max}/cm^{-1}): 3056, 2933, 2833, 1598, 1487, 1455, 1245, 830, 740. X-ray crystallographic data for **22** have been deposited at the Cambridge Crystallographic Data Centre: CCDC-665603.

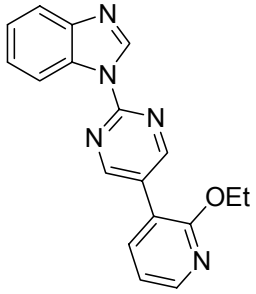
Compound 23



Compound **12** (0.493 g, 1.8 mmol), 2-methoxybenzeneboronic acid **(20)** (0.304 g, 2.0 mmol), $Pd(PPh_3)_2Cl_2$ (0.07 g, 0.1 mmol), 1,4-dioxane (8 mL) and Na_2CO_3 (1 M, 4 mL) were reacted at 80 ^oC for 4 h. Standard work-up and concentration yielded a white solid which was chromatographed on a silica column (eluent EtOAc : DCM 10:1 v/v) yielding **23** as a white solid (0.519 g,

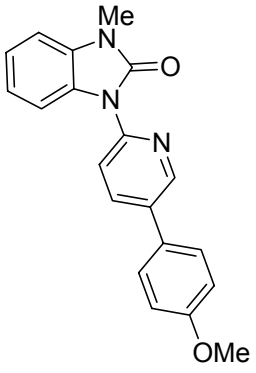
96 %) mp 69.1-72.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (d, 1H, *J* = 2.0 Hz), 8.62 (s, 1H), 8.12-8.09 (m, 2H), 7.89 (d, 1H, *J* = 7.0 Hz), 7.61 (dd, 1H, *J* = 8.5, 0.5 Hz), 7.44-7.36 (m, 4H), 7.12-7.04 (m, 2H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.9, 150.0, 148.6, 145.0, 141.8, 140.1, 133.0, 132.5, 130.8, 130.2, 126.2, 124.5, 123.6, 121.5, 121.0, 113.9, 113.0, 111.7, 55.9. MS (EI) *m/z* 301 (M^+, 100 %). $C_{19}H_{15}N_3O$ (301.3) calcd. C 75.73, H 5.02, N 13.94; found: C 75.45, H 4.98, N 13.95. IR (ν_{max}/cm^{-1}): 3099, 3054, 2833, 1597, 1505, 1480, 1245, 746.

Compound 25



Compound **13** (0.113 g, 0.41 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.076 g, 0.46 mmol), $Pd(PPh_3)_2Cl_2$ (0.016 g, 0.02 mmol), 1,4-dioxane (5 mL) and Na_2CO_3 (1 M, 1.4 mL) were reacted at 80 °C for 18 h. Standard work-up and concentration yielded an white solid which was purified by column chromatography on silica (eluent chloroform : EtOAc 1:1 v/v) followed by recrystallization from hexane to yield **25** as a white solid (0.098 g, 79 %) mp 229.0-230.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.14 (s, 1H), 9.00 (s, 2H), 8.66 (d, 1H, *J* = 7.6 Hz), 8.25 (dd, 1H, *J* = 5.2, 1.6 Hz), 7.87 (d, 1H, *J* = 7.6 Hz), 7.71 (dd, 1H, *J* = 7.2, 2.0 Hz), 7.47-7.37 (m, 2H), 7.05 (dd, 1H, *J* = 4.8, 7.2 Hz), 4.49 (q, 2H, *J* = 7.2 Hz), 1.43 (t, 3H, *J* = 6.8 Hz). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 160.9, 158.5, 155.4, 148.0, 145.4, 142.3, 138.2, 132.2, 127.8, 125.0, 124.2, 120.8, 117.6, 117.5, 116.0, 110.4, 62.7, 30.0, 15.0. MS (EI) *m/z* 317 (M^+, 100 %). $C_{18}H_{15}N_5O$ (317.3) calcd. C 68.13, H 4.76, N 22.07; found: C 68.02, H 4.40, N 22.42. IR (ν_{max}/cm^{-1}): 3128, 2983, 2922, 1587, 1480, 1448, 1300, 735.

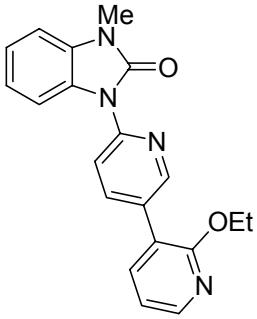
Compound 26



Compound **14** (0.366 g, 1.20 mmol), 4-methoxybenzeneboronic acid **(19)** (0.228 g, 1.50 mmol), $Pd(PPh_3)_2Cl_2$ (0.053 g, 0.08 mmol), degassed 1,4-dioxane (6 mL) and degassed Na_2CO_3 (1 M, 5.7 mL) were reacted at 80 °C for 24 h. Standard work-up and concentration yielded a white solid which was chromatographed on a silica column (eluent DCM : EtOAc 1:1 v/v) yielding **26** as a white solid (0.300 g, 76 %) mp 195.9-196.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 (dd, 1H, *J* = 2.5, 0.5 Hz), 8.17 (dd, 1H, *J* = 8.5, 0.5 Hz), 8.09 (dd, 1H, *J* = 8.0, 1.0 Hz), 8.01 (dd, 1H, *J* = 8.5, 2.5 Hz), 7.57 (d, 2H, *J* = 9.0 Hz), 7.22-7.15 (m, 2H), 7.06-7.02 (m, 3H), 3.88 (s, 3H), 3.50 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 153.5, 149.2, 146.1, 134.1, 130.5, 130.1, 128.4, 128.1, 123.0, 122.2, 117.6, 144.9, 113.3, 107.7, 55.7, 27.4. *m/z* (ES+) 332.2 [$(M+1)^+$, 100 %], 354.2 [$(M+Na)^+$, 72 %],

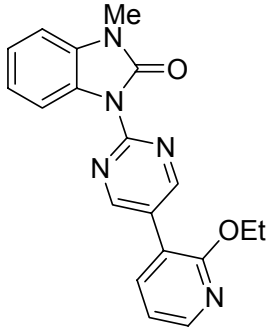
684.9 [(2M+Na]$^+$, 96 %). $C_{20}H_{17}N_3O_2$ (331.4) calcd. C 72.49, H 5.17, N 12.68; found: C 72.26, H 5.14, N 12.62. IR (ν_{max}/cm^{-1}): 3065, 2935, 2837, 1711, 1607, 1483, 1382, 824, 745.

Compound 27



A mixture of **14** (0.401 g, 1.315 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.278 g, 1.46 mmol), $Pd(PPh_3)_4$ (0.085 g, 0.07 mmol), degassed 1,4-dioxane (6 mL) and degassed Na_2CO_3 (1 M, 2.9 mL) were reacted at 80 ^{o}C for 19 h. After cooling to room temperature the solvent was removed in vacuo then EtOAc was added and the organic layer was washed with brine, separated, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was chromatographed on a silica column (eluent DCM : EtOAc 6:1 v/v) yielding **27** as a white solid (0.304 g, 67 %) mp 183.6-184.1 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (dd, 1H, *J* = 1.6 Hz), 8.21-8.19 (m, 2H), 8.09 (dd, 1H, *J* = 7.2, 2.0 Hz), 7.68 (dd, 1H, *J* = 5.6, 1.2 Hz), 7.23-7.16 (m, 2H), 7.05 (d, 1H, *J* = 5.2 Hz), 7.01 (dd, 1H, *J* = 5.6, 4.0 Hz), 4.46 (q, 2H, *J* = 5.6 Hz), 3.51 (s, 3H), 1.41 (t, 3H, *J* = 5.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.0, 153.5, 149.6, 148.3, 147.0, 139.0, 138.7, 130.5, 130.4, 128.0, 123.1, 122.3, 120.9, 117.4, 117.1, 113.4, 107.8, 62.4, 27.5, 15.0. MS (ES+) *m/z* 347.3 [(M+1)$^+$, 100 %]. HRMS (ES+) calcd. for $C_{20}H_{18}N_4O_2$+Na: *m/z* 369.1322; found: *m/z* 324.99488. IR (ν_{max}/cm^{-1}): 3058, 2988, 2932, 1723, 1447, 1400, 739.

Compound 28

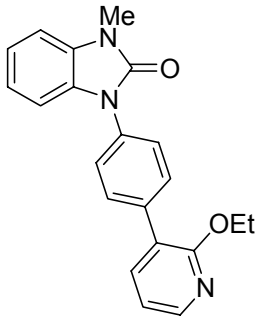


A mixture of **15** (0.458 g, 1.50 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.278 g, 1.67 mmol), $Pd(PPh_3)_4$ (0.0965 g, 0.08 mmol), degassed 1,4-dioxane (10 ml) and degassed Na_2CO_3 (1 M, 3.3 mL) were reacted at 90 ^{o}C for 78 h. Work-up as described for **27** and column chromatography (eluent EtOAc : DCM 10:1 v/v) yielded **28** as a white solid (0.223 g, 43 %) mp 197.1-198.5 ^{o}C (decomp.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 2H), 8.24 (dd, 1H, *J* = 5.2, 2.0 Hz), 8.03 (d, 1H, *J* = 7.2 Hz), 7.70 (dd, 1H, *J* = 7.5, 2.0 Hz), 7.25-7.21 (m, 2H), 7.06-7.02 (m, 2H), 4.48 (q, 2H, *J* = 7.2 Hz), 3.51 (s, 3H), 1.41 (t, 3H, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 158.4, 155.5, 152.6, 148.0, 138.4, 130.7, 127.8, 127.7, 123.6, 122.2, 117.6, 117.5, 113.3, 107.8, 62.7, 27.5, 14.6. MS (ES+) *m/z* 348.2 [(M+H)$^+$, 41

%], 370.2 [(M+Na)$^+$, 33 %), 717.1 [(2M+Na)$^+$, 100 %]. $C_{19}H_{17}N_5O_2$ (347.4) calcd. C 65.69, H 4.93, N 20.16; found: C 65.38, H 4.88, N 20.09. IR (ν_{max}/cm^{-1}): 3060, 2984, 2928, 1723, 1423, 1385, 747.

Compound 28 *One-pot procedure:* To a mixture of 1-methyl-2-benzimidazolone **(2)** (0.163 g, 1.1 mmol), Cs_2CO_3 (0.652 g, 2 mmol) and CuI (0.019 g, 0.1 mmol) in dry degassed DMF (4 mL) was added 5-bromo-2-iodopyrimidine **(7)** (0.284 g, 1.0 mmol) and 1,10-phenanthroline (0.036 g, 0.2 mmol). The mixture was stirred and heated under argon at 80 ^{o}C until tlc monitoring showed the reaction was complete (24 h). To this was added, under argon, 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.129 g, 1.1 mmol), $Pd(PPh_3)_4$ (0.058 g, 0.05 mmol), 1,4-dioxane (5 mL) and Na_2CO_3 (1 M, 2.2 mL) and stirring was continued at 80 ^{o}C for 24 h. Standard workup and column chromatography on silica (eluent DCM : EtOAc 3:1 v/v) yielded **28** as a white solid (0.179 g, 52 %) spectroscopically identical to the sample prepared above by the two-step procedure.

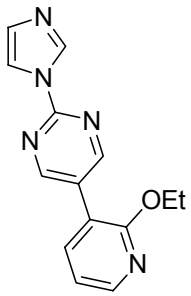
Compound 29



Procedure A: A mixture of **16** (0.294 g, 0.97 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.165 g, 1.08 mmol), $Pd(PPh_3)_2Cl_2$ (0.038 g, 0.05 mmol), 1,4-dioxane (5 mL) and Na_2CO_3 (1 M, 3.2 mL) were reacted at 80 ^{o}C for 40 h. Filtration and concentration yielded a white solid which was chromatographed on a silica column (eluent hexane : EtOAc 1:1 v/v) to yield **29** as a white solid (0.101 g, 30 %) mp 186.6-187.2 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.17 (dd, 1H, *J* = 5.0, 2.0 Hz), 7.74 (d, 2H, *J* = 10.5 Hz), 7.67 (dd, 1H, *J* = 7.5, 2.0 Hz), 7.59 (d, 2H, *J* = 9.0 Hz), 7.19-7.16 (m, 2H), 7.11-7.06 (m, 2H), 6.98 (dd, 1H, *J* = 7.0, 5.0 Hz), 4.47 (q, 2H, *J* = 7.0 Hz), 3.52 (s, 3H), 1.41 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.9, 153.9, 146.3, 139.0, 136.5, 134.3, 130.6, 130.5, 129.6, 125.8, 124.0, 122.4, 121.8, 117.3, 109.2, 109.0, 62.3, 27.6, 15.0. MS (ES+) *m/z* 346.3 [(M+1)$^+$, 50 %], 368.2 [(M+Na)$^+$, 67 %], 712.9 [(2M+Na)$^+$, 100 %]. HRMS (ES+) calcd. for $C_{21}H_{19}N_3O$+Na: *m/z* 368.13695; found: *m/z* 368.13715. IR (ν_{max}/cm^{-1}): 3056, 2989, 2920, 1723, 1450, 1407, 734.

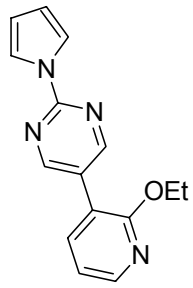
Procedure B: A mixture of **16** (0.294 g, 0.97 mmol), 2-ethoxypyridin-3-yl-boronic acid **21** (0.165 g, 1.08 mmol), $Pd(PPh_3)_4$ (0.062 g, 0.05 mmol), 1,4-dioxane (5 mL) and Na_2CO_3 (1 M, 3.2 mL) were reacted at 80 ^{o}C for 40 h. Work-up as described above gave **29** as a white solid (0.808 g, 83 %) spectroscopically identical to the sample prepared by procedure A.

Compound 30



A mixture of **17** (0.132 g, 0.59 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.109 g, 0.65 mmol), $Pd(PPh_3)_2Cl_2$ (0.023 g, 0.03 mmol), 1,4-dioxane (4 mL) and Na_2CO_3 (1 M, 2.0 mL) were reacted at 80 ^oC for 22 h. Filtration and concentration yielded a white solid which was recrystallized once from hexane and once from toluene as white crystals of **30** (0.091 g, 48 %) mp 155.5-156.6 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.91 (s, 2H), 8.66 (t, 1H, *J* = 1.2 Hz), 8.24 (dd, 1H, *J* = 5.2, 2.0 Hz), 7.93 (t, 1H, *J* = 1.6 Hz), 7.67 (dd, 1H, *J* = 7.6, 2.0 Hz), 7.20-7.19 (m, 1H), 7.04 (dd, 1H, *J* = 7.6, 5.2 Hz), 4.47 (q, 2H, *J* = 7.2 Hz), 1.41 (t, 3H, *J* = 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.9, 158.6, 153.8, 148.1, 138.2, 136.6, 131.1, 128.6, 117.6, 117.2, 116.9, 62.7, 14.9. HRMS (ES+) calcd. for $C_{14}H_{13}N_5O$+H: *m/z* 268.11929; found: *m/z* 268.11953. IR (ν_{max}/cm^{-1}): 3130, 3114, 2974, 1586, 1436, 769.

Compound 31

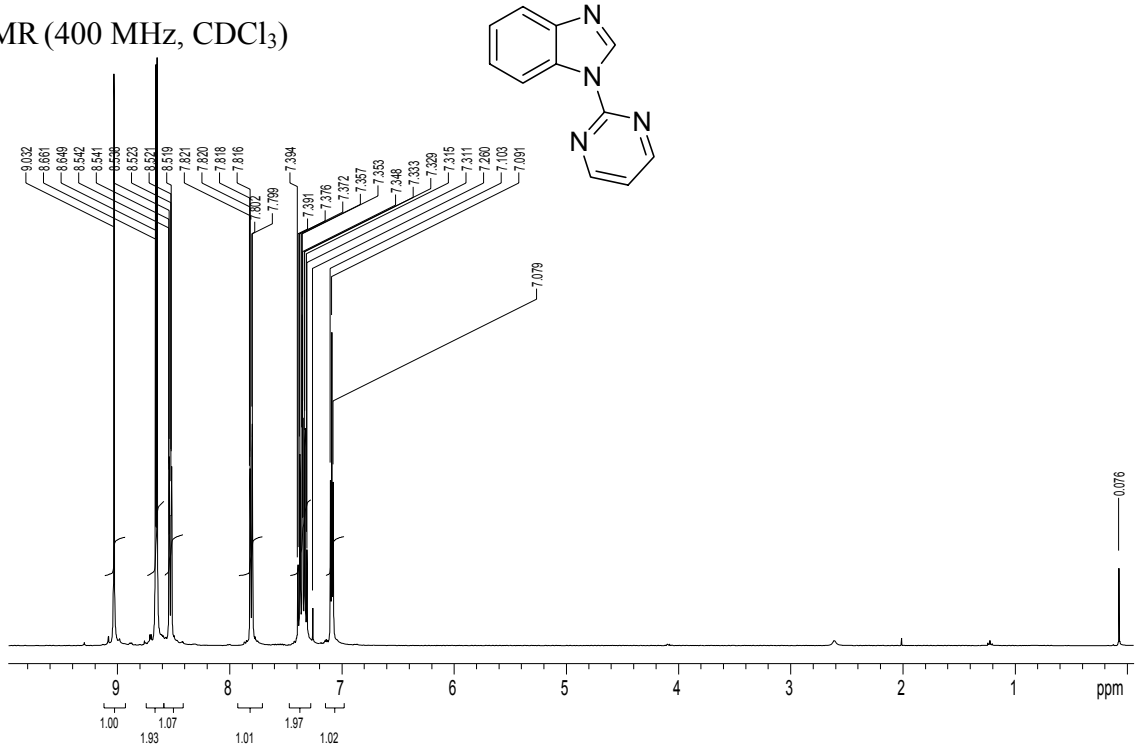


A mixture of **18** (0.132 g, 0.59 mmol), 2-ethoxypyridin-3-yl-boronic acid **(21)** (0.109 g, 0.65 mmol), $Pd(PPh_3)_2Cl_2$ (0.023 g, 0.03 mmol), 1,4-dioxane (4 mL) and Na_2CO_3 (1 M, 2.0 mL) were reacted at 80 ^oC for 22 h. Filtration and concentration yielded a white solid which was chromatographed on a silica column (eluent hexane : EtOAc 4:1 v/v) to yield **31** which was recrystallized once from hexane and once from toluene as crystals (0.122 g, 78 %) mp 109.7-110.1 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.85 (s, 2H), 8.21 (dd, 1H, *J* = 4.8, 2.0 Hz), 7.82 (t, 2H, *J* = 2.0 Hz), 7.66 (t, 1H, *J* = 5.2, 2.0 Hz), 7.02 (dd, 1H, *J* = 4.8, 2.8 Hz), 6.37 (t, 2H, *J* = 2.0 Hz), 4.46 (q, 2H, *J* = 7.2 Hz), 1.41 (t, 3H, *J* = 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.9, 158.4, 147.6, 138.0, 126.7, 119.4, 117.9, 117.5, 112.4, 62.6, 15.0. MS (EI) *m/z* 266.1 (M^+, 100%). $C_{15}H_{14}N_4O$ (266.3) calcd. C 67.65, H 5.30, N 21.04; found: C 67.39, H 5.33, N 20.81. IR (ν_{max}/cm^{-1}): 3100, 1985, 1588, 1479, 1442, 730.

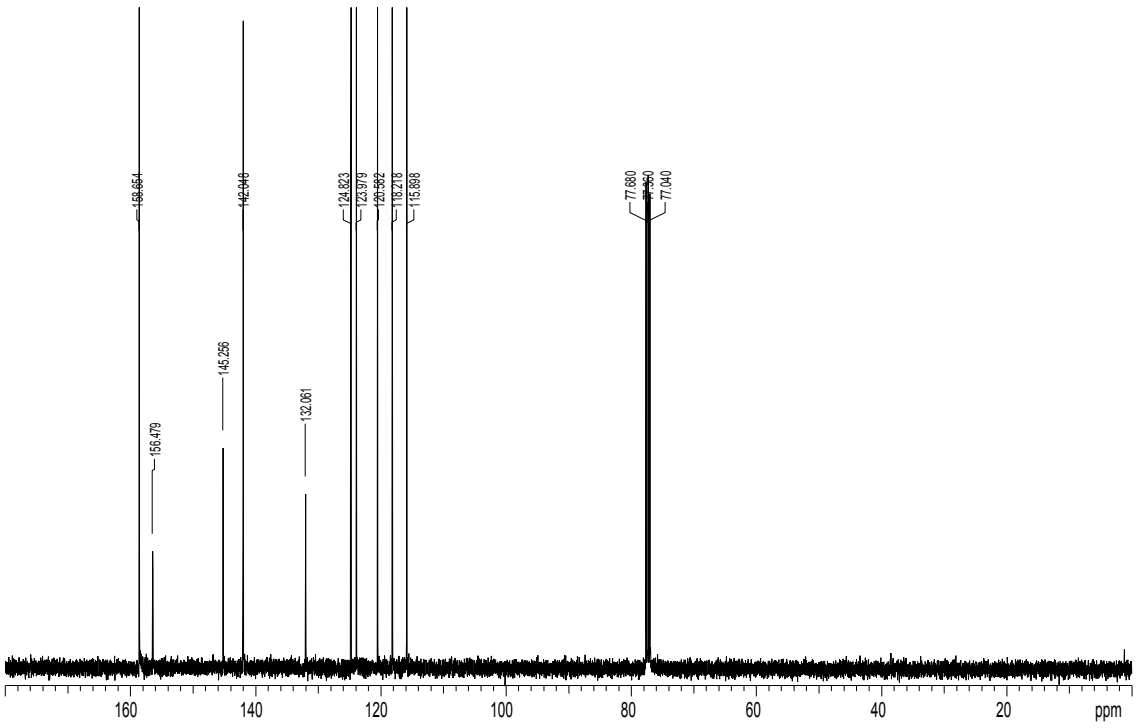
Copies of NMR Spectra

1-(Pyrimidin-2-yl)-1*H*-benzimidazole (10)

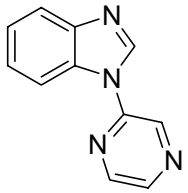
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

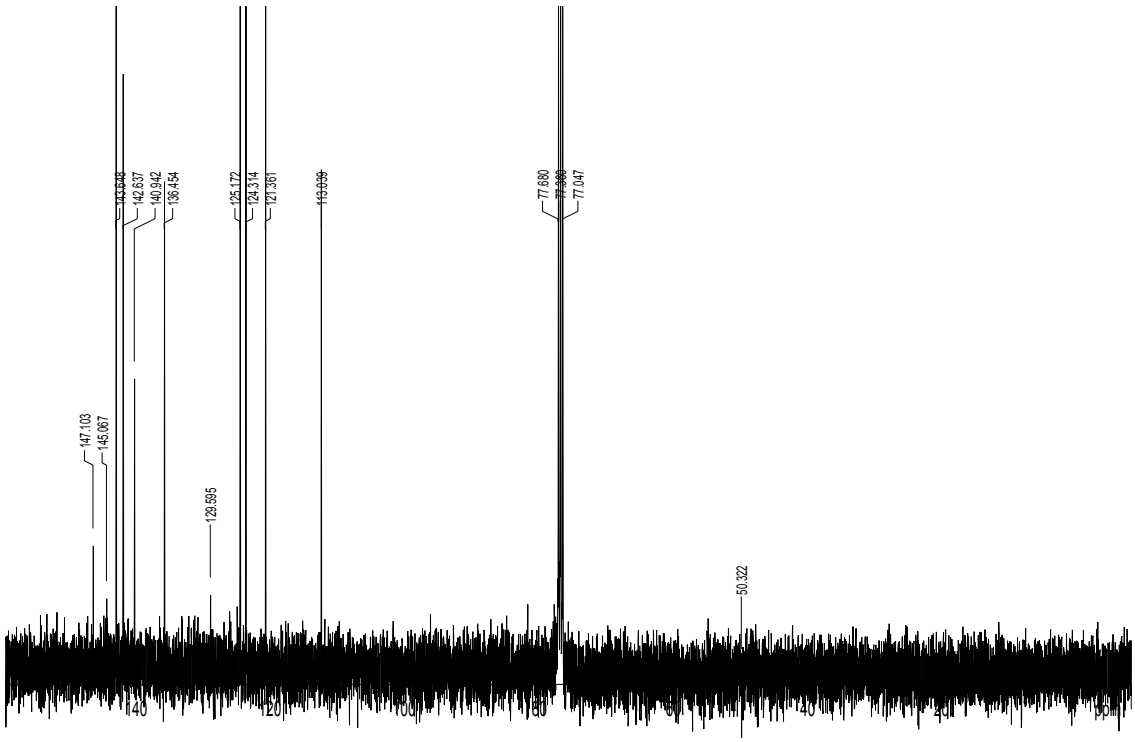


1-(Pyrazin-2-yl)-1*H*-benzimidazole (11)



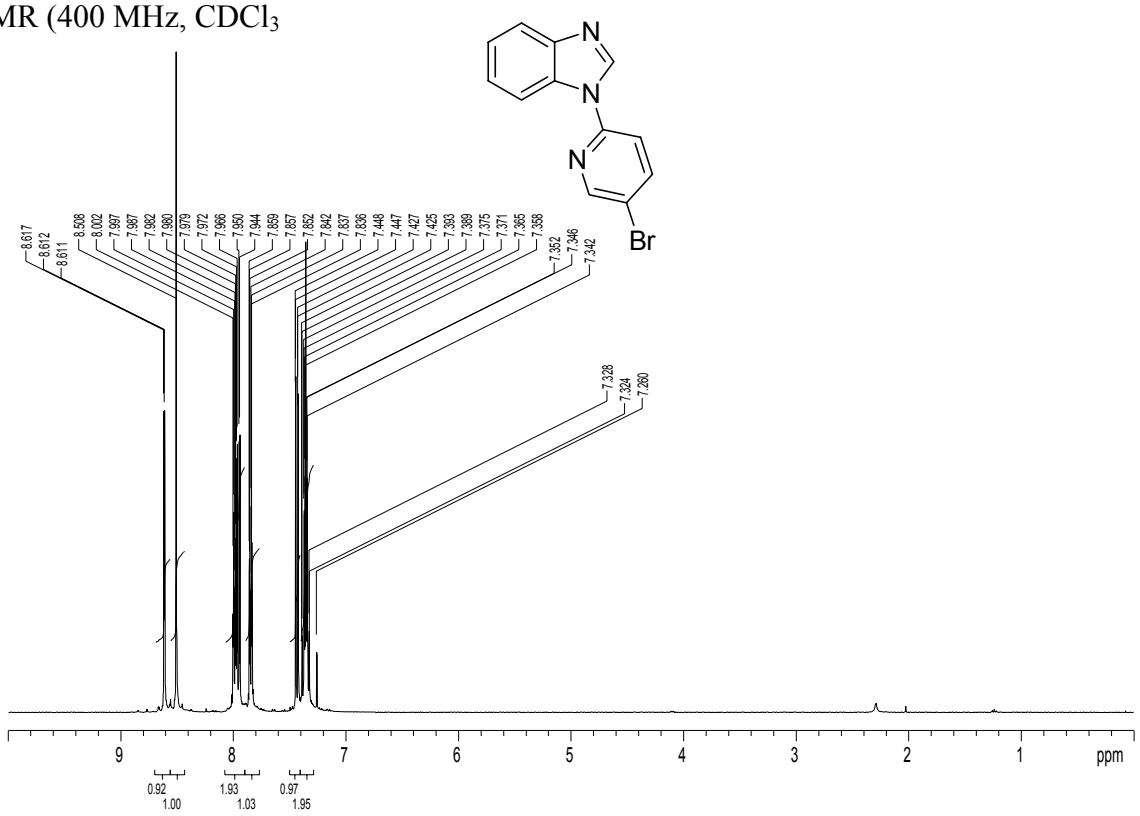
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR (100 MHz, $CDCl_3$)

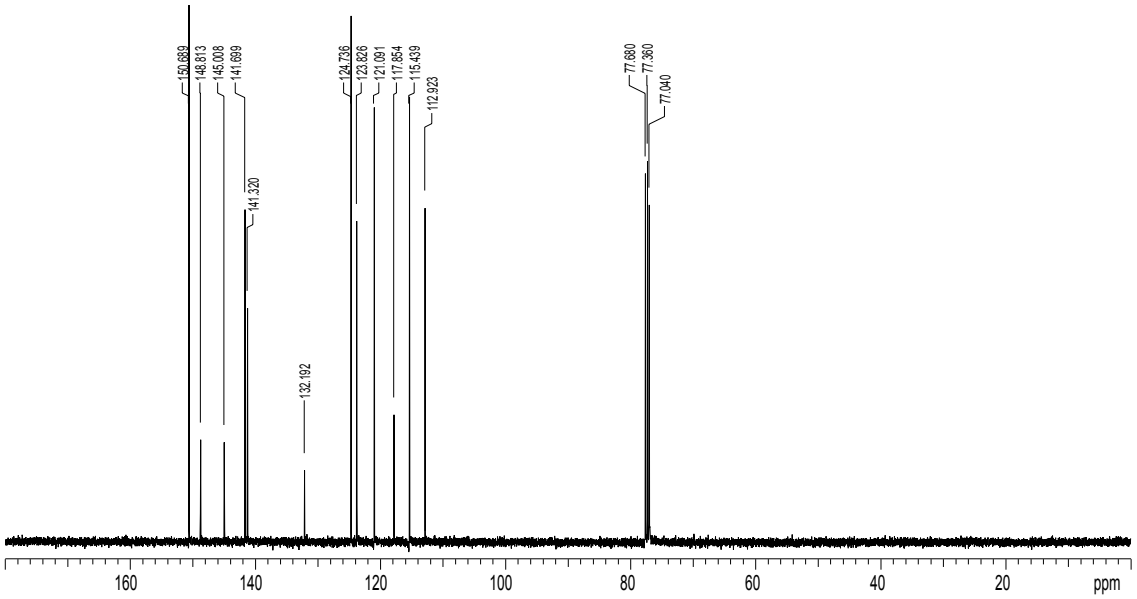


1-(5-Bromopyridin-2yl)-1*H*-benzimidazole (12)

^{1}H NMR (400 MHz, $CDCl_3$

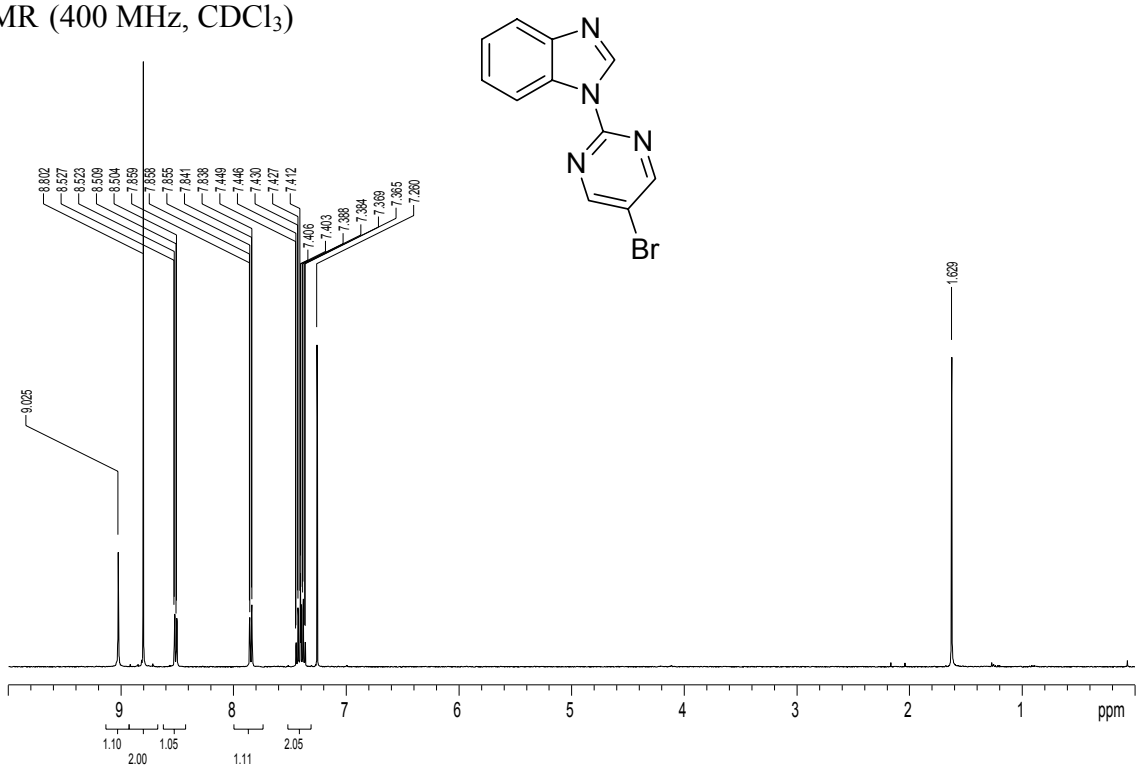


^{13}C NMR (100 MHz, $CDCl_3$)

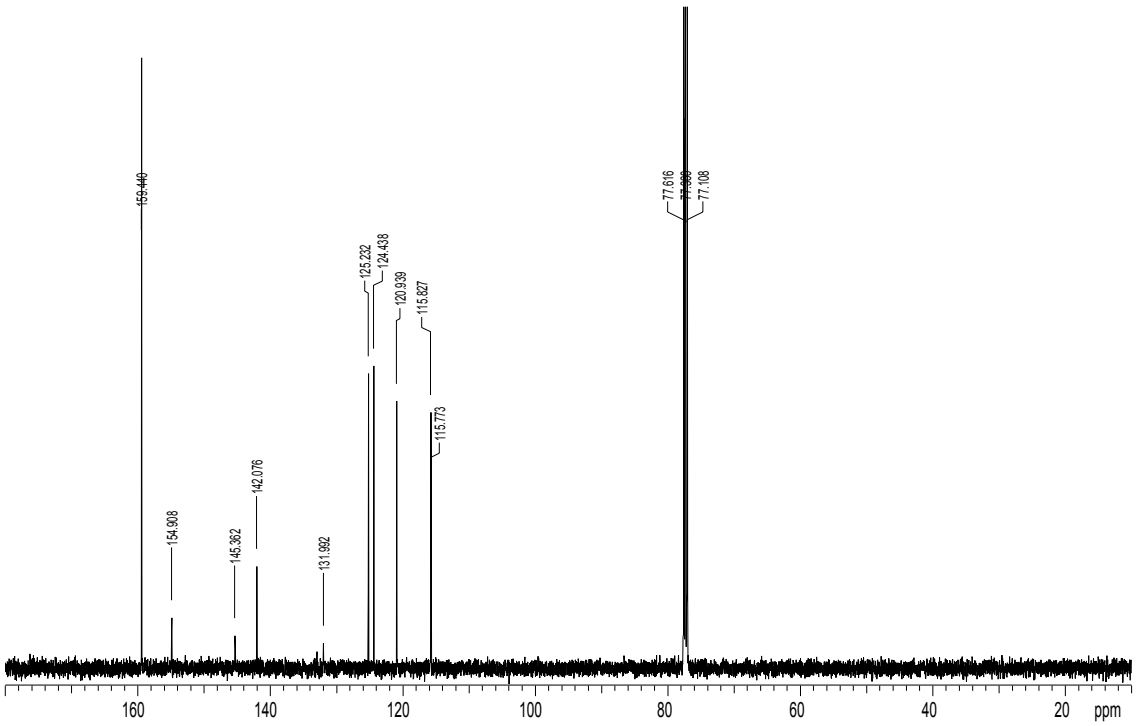


1-(5-Bromopyrimidin-2yl)-1*H*-benzimidazole (13)

^{1}H NMR (400 MHz, $CDCl_3$)

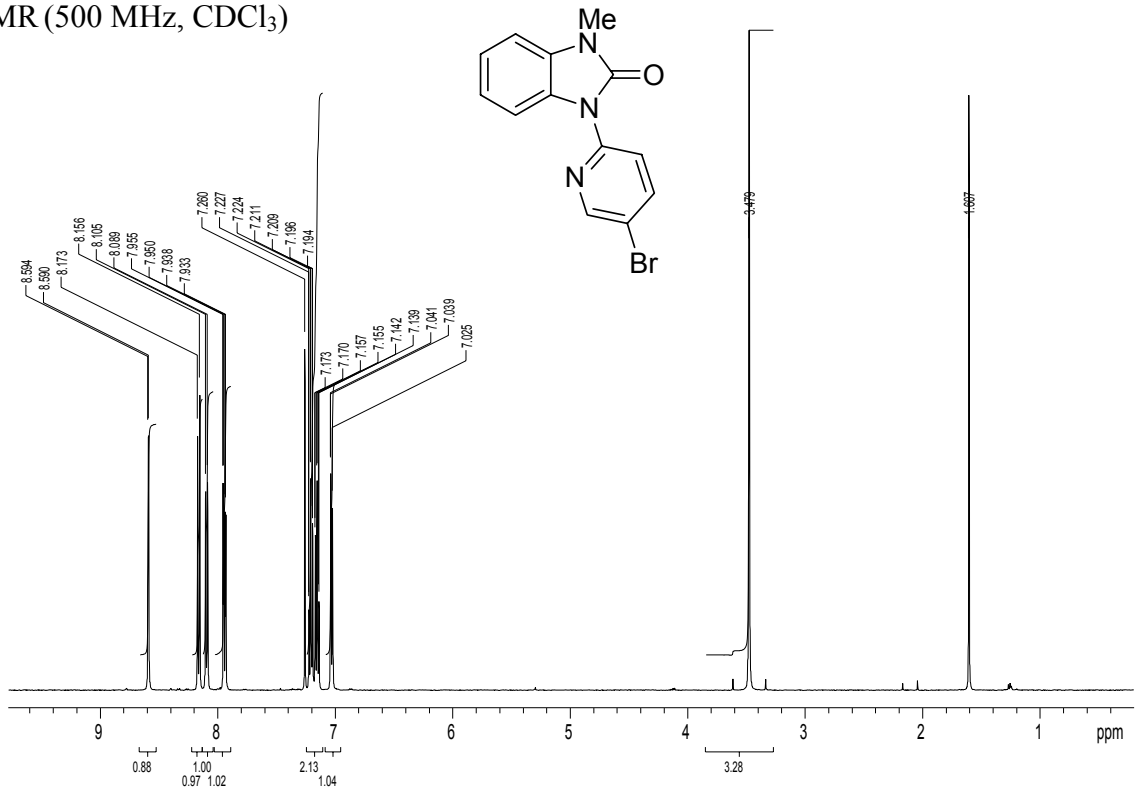


^{13}C NMR (125 MHz, $CDCl_3$)

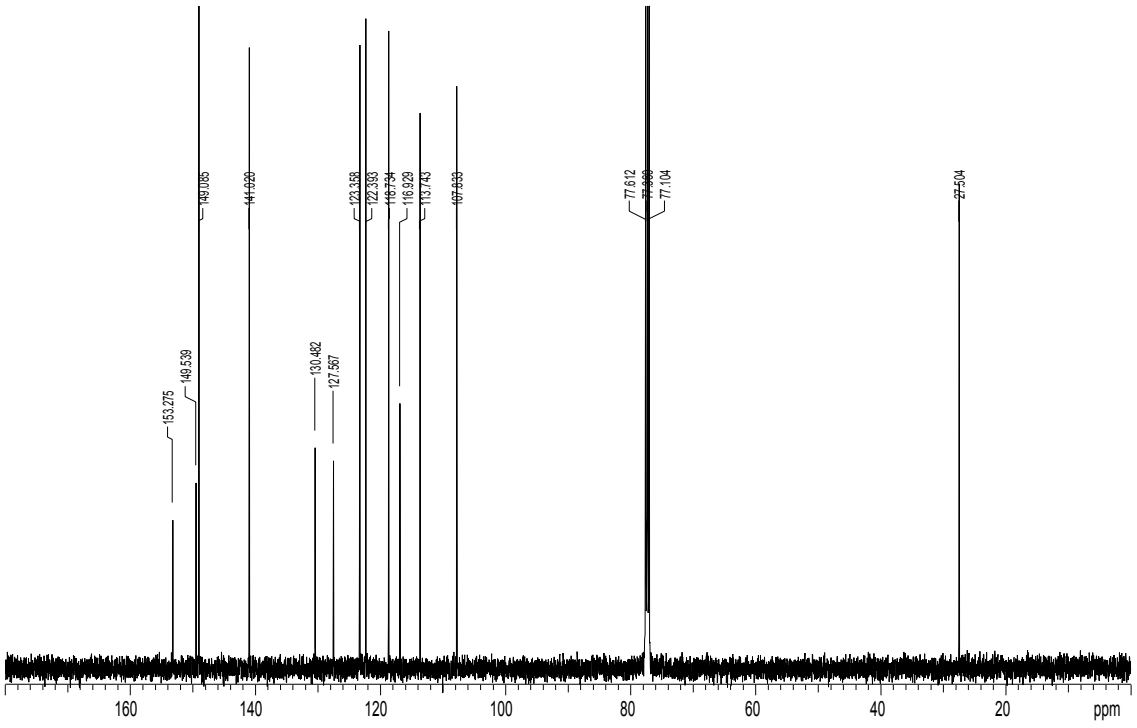


1-(5-Bromopyridin-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (14)

^{1}H NMR (500 MHz, $CDCl_3$)

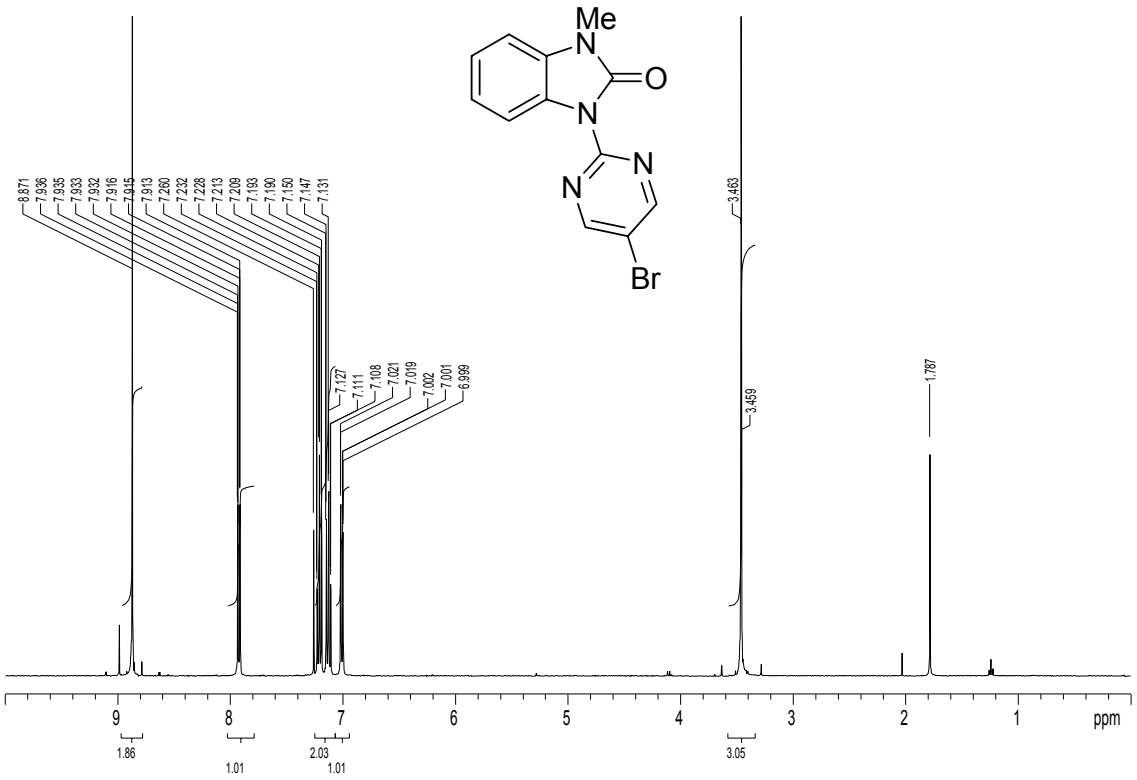


^{13}C NMR (125 MHz, $CDCl_3$)

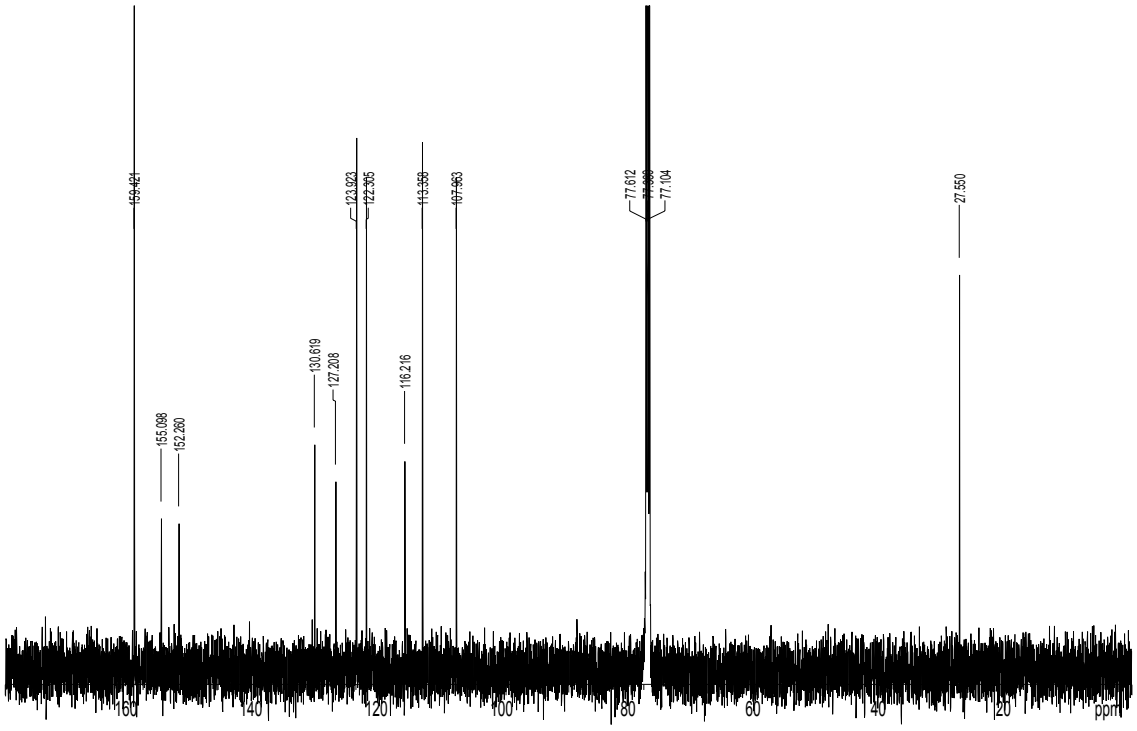


1-(5-Bromopyrimidin-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (15)

^{1}H NMR (400 MHz, $CDCl_3$)

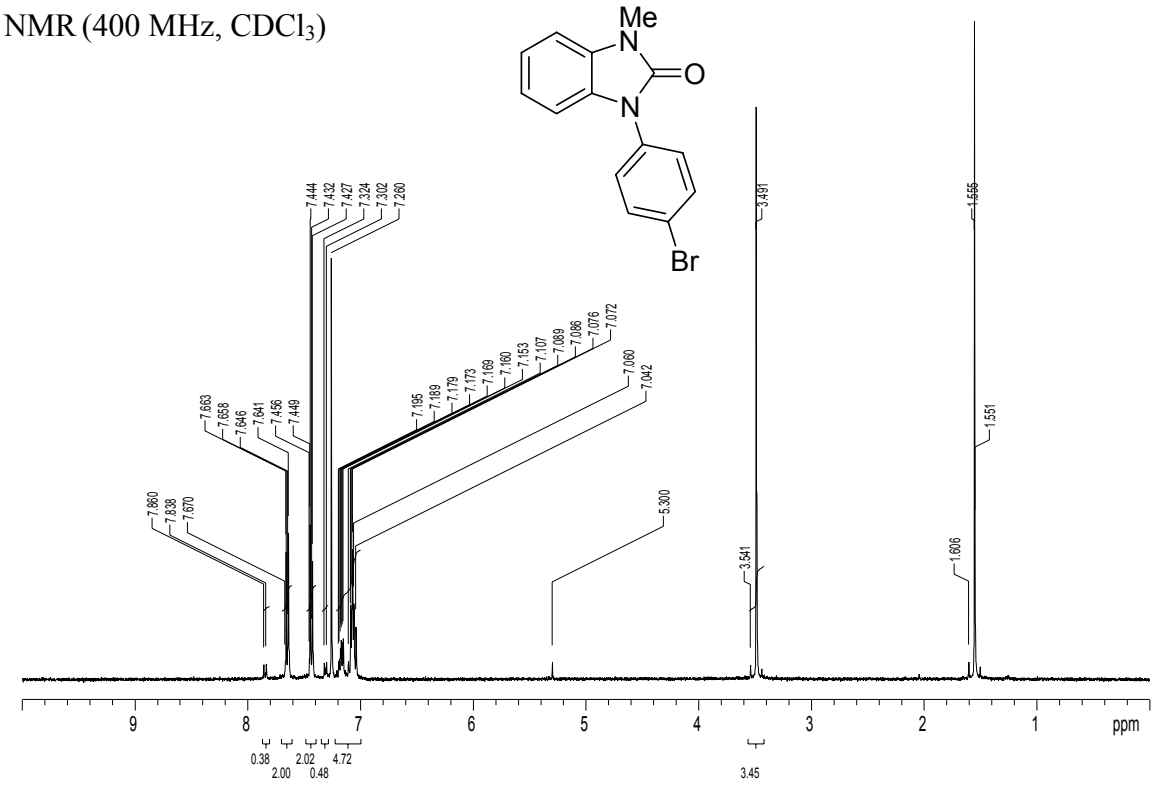


^{13}C NMR (125 MHz, $CDCl_3$)

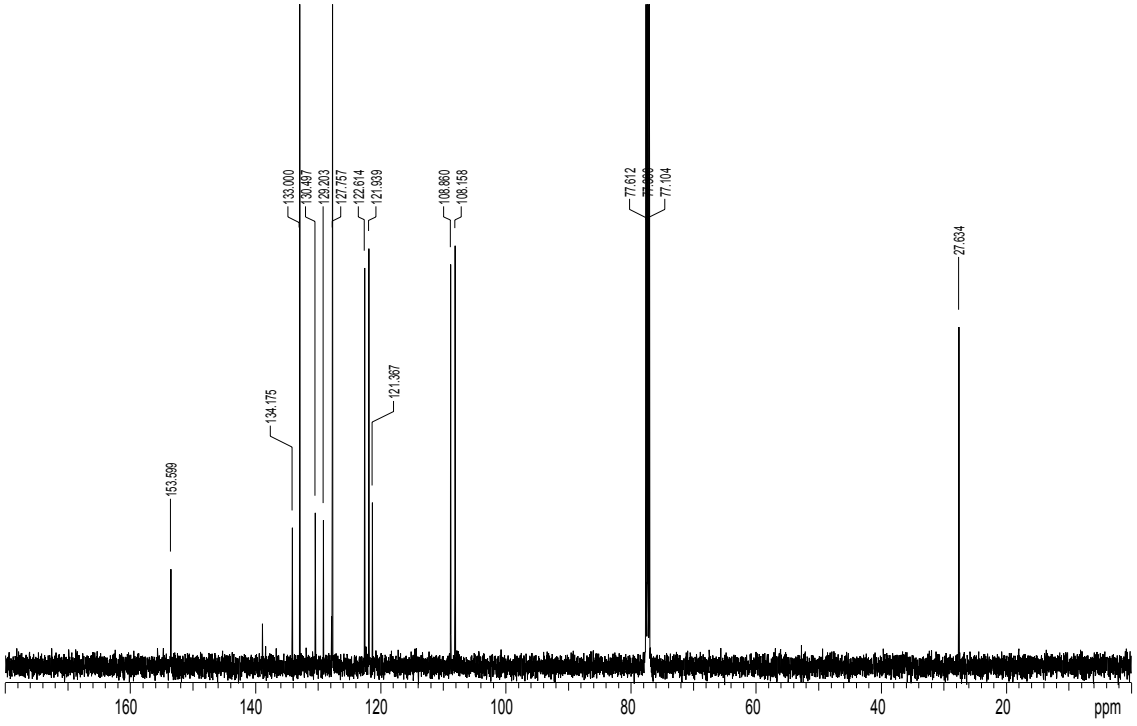


1-(4-Bromophen-2-yl)-3-methyl-1*H*-benzo[d]imidazol-2(3*H*)-one (16)

^{1}H NMR (400 MHz, $CDCl_3$)

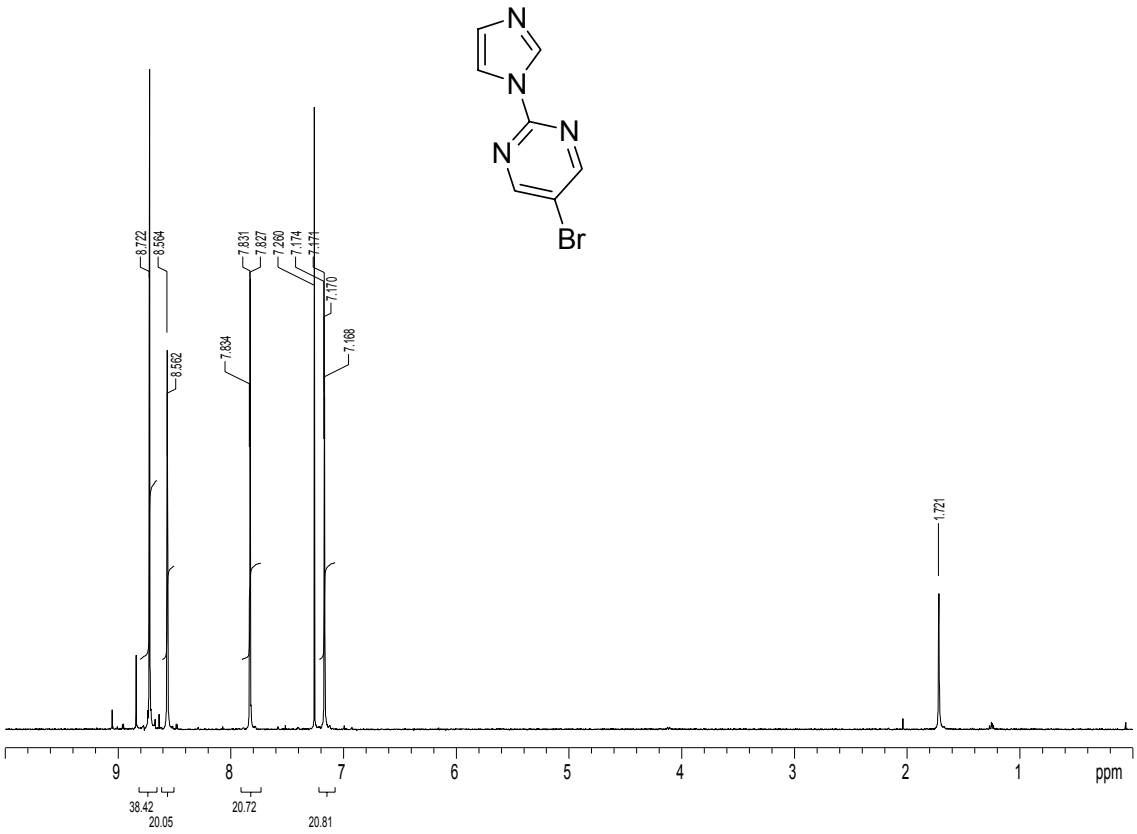


^{13}C NMR (125 MHz, $CDCl_3$)

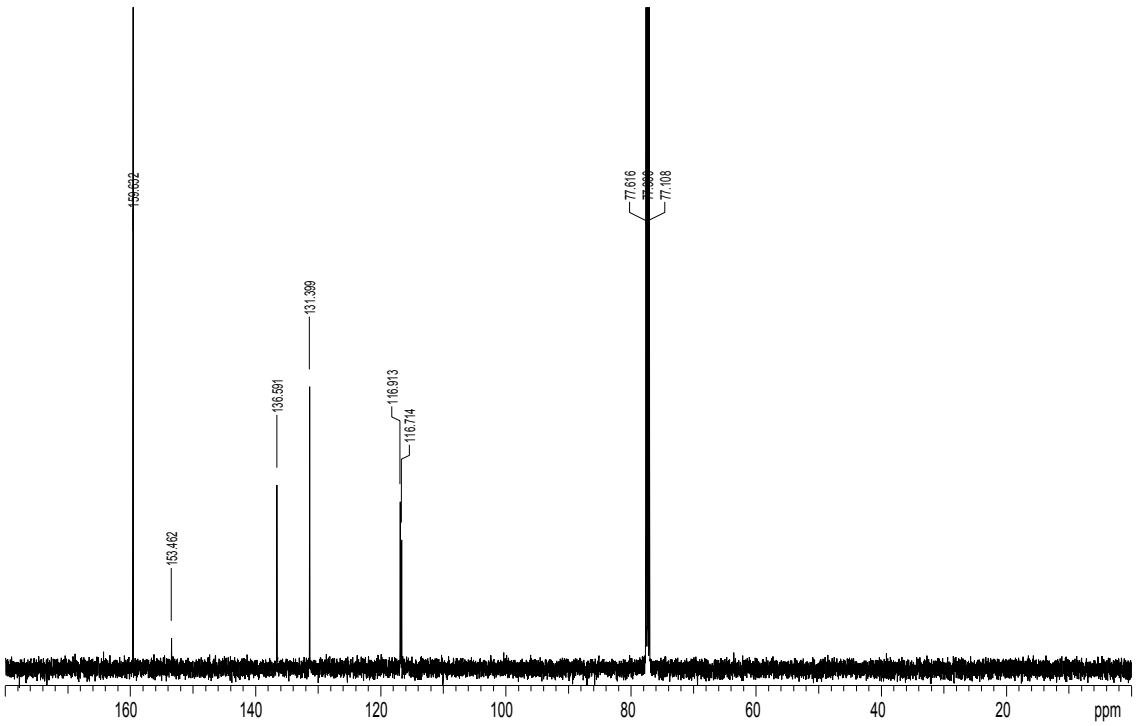


5-Bromo-2-(1H-imidazol-1-yl)pyrimidine (17)

^{1}H NMR (400 MHz, $CDCl_3$)

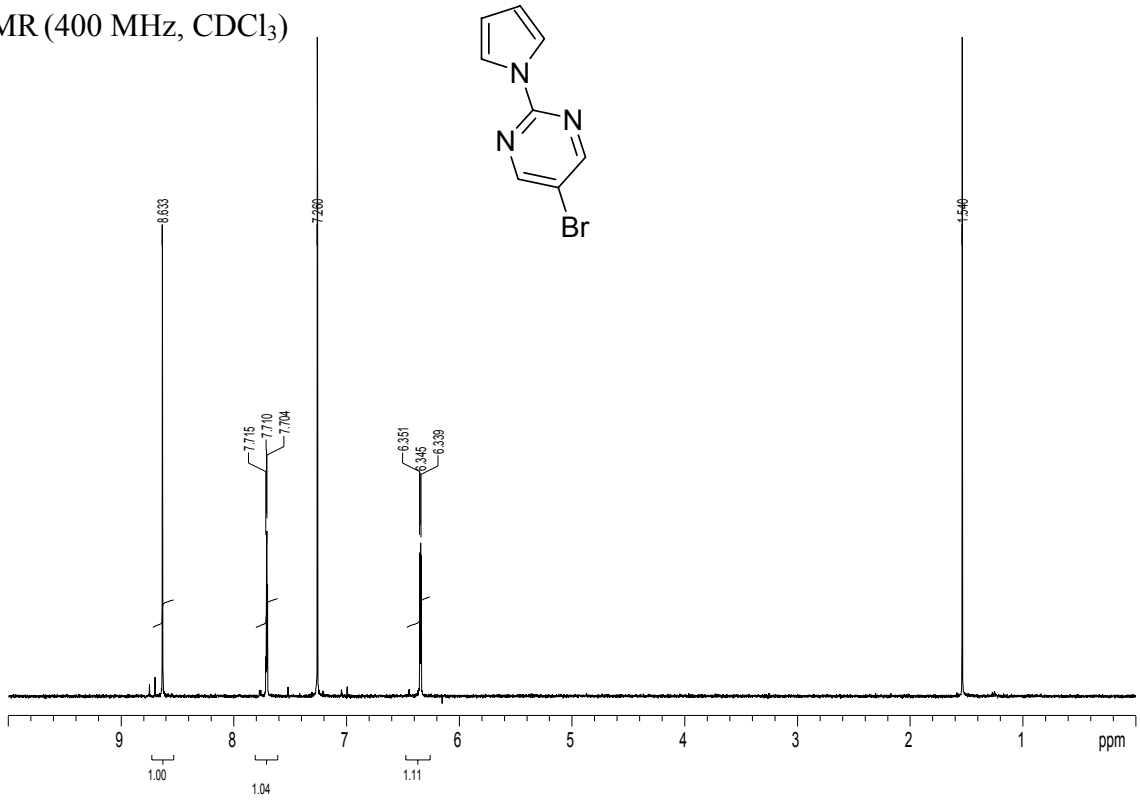


^{13}C NMR (125 MHz, $CDCl_3$)

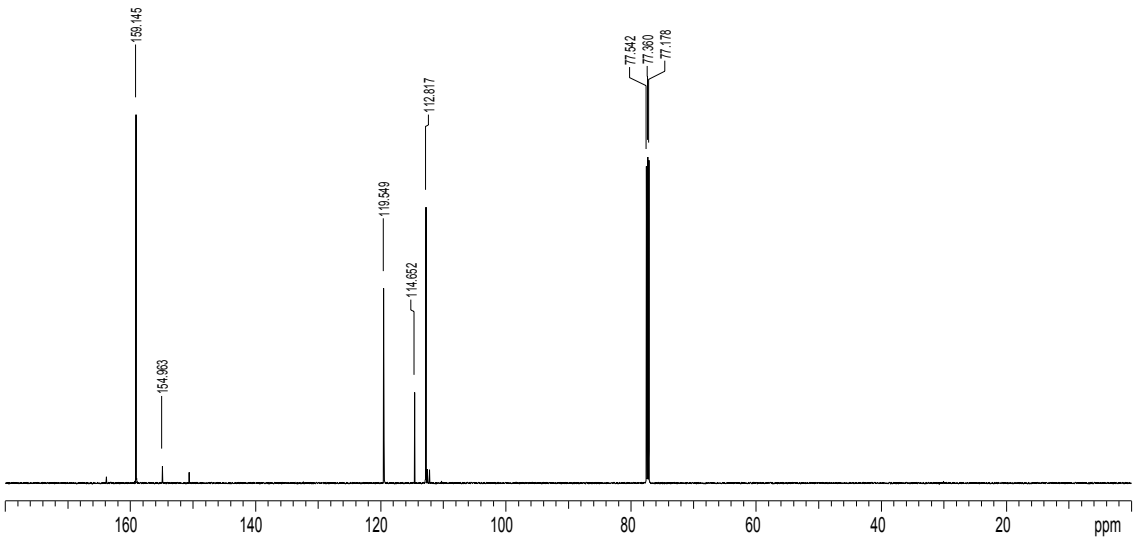


5-Bromo-2-(1H-pyrrol-1-yl)pyrimidine (18)

^{1}H NMR (400 MHz, $CDCl_3$)

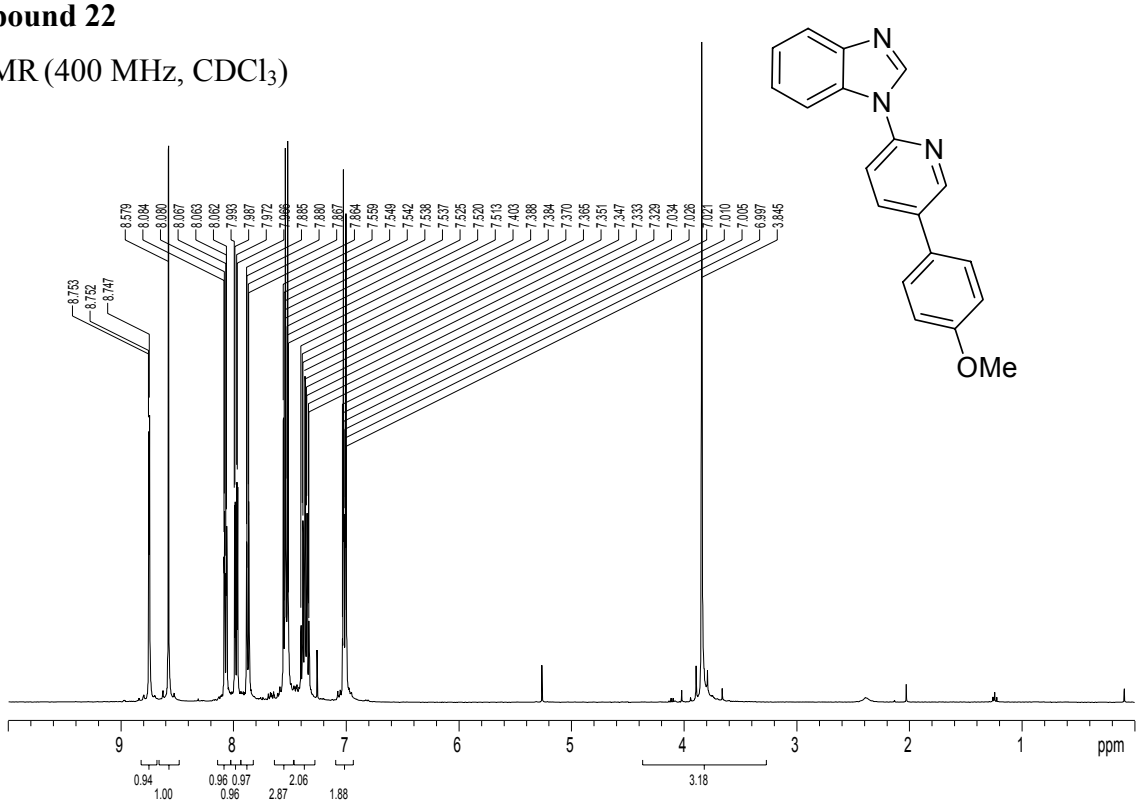


^{13}C NMR (125 MHz, $CDCl_3$)

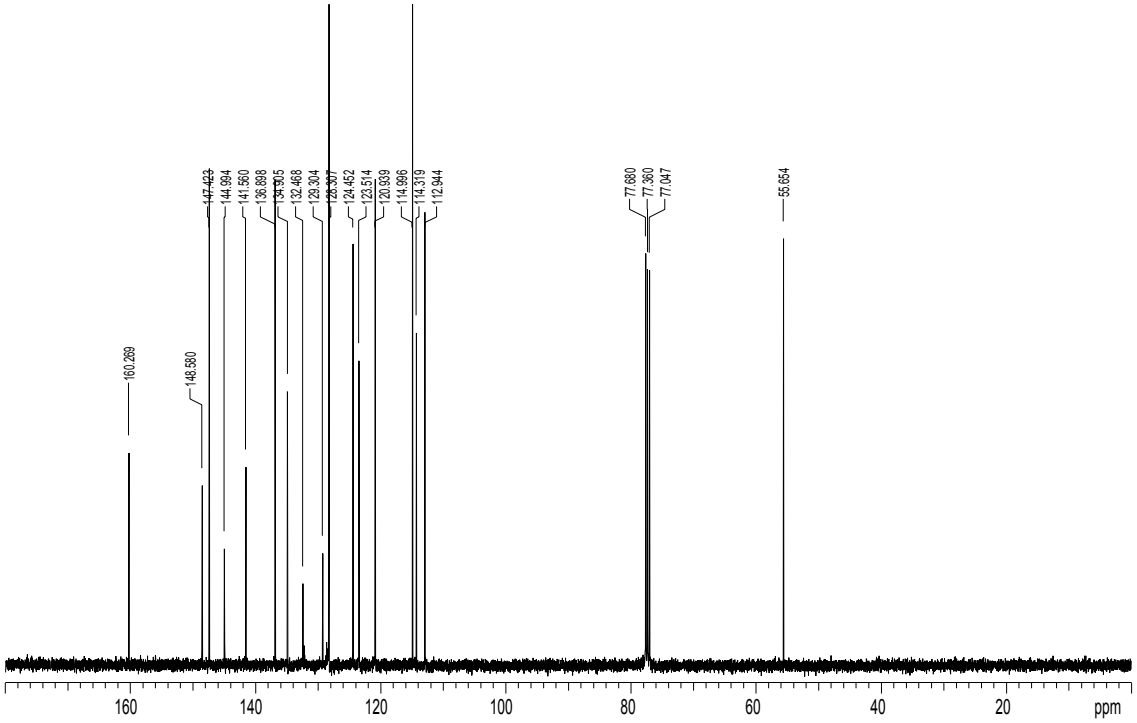


Compound 22

^{1}H NMR (400 MHz, $CDCl_3$)

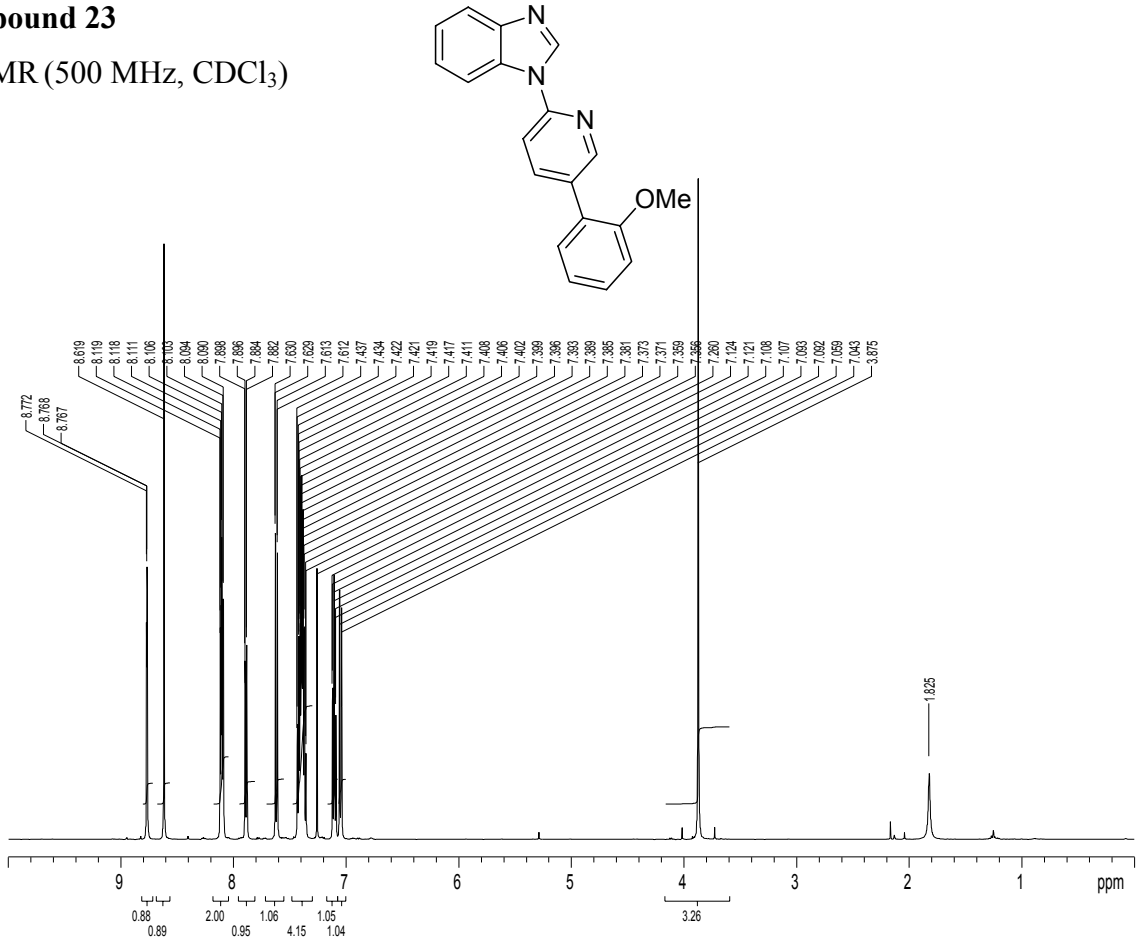


^{13}C NMR (100 MHz , $CDCl_3$)

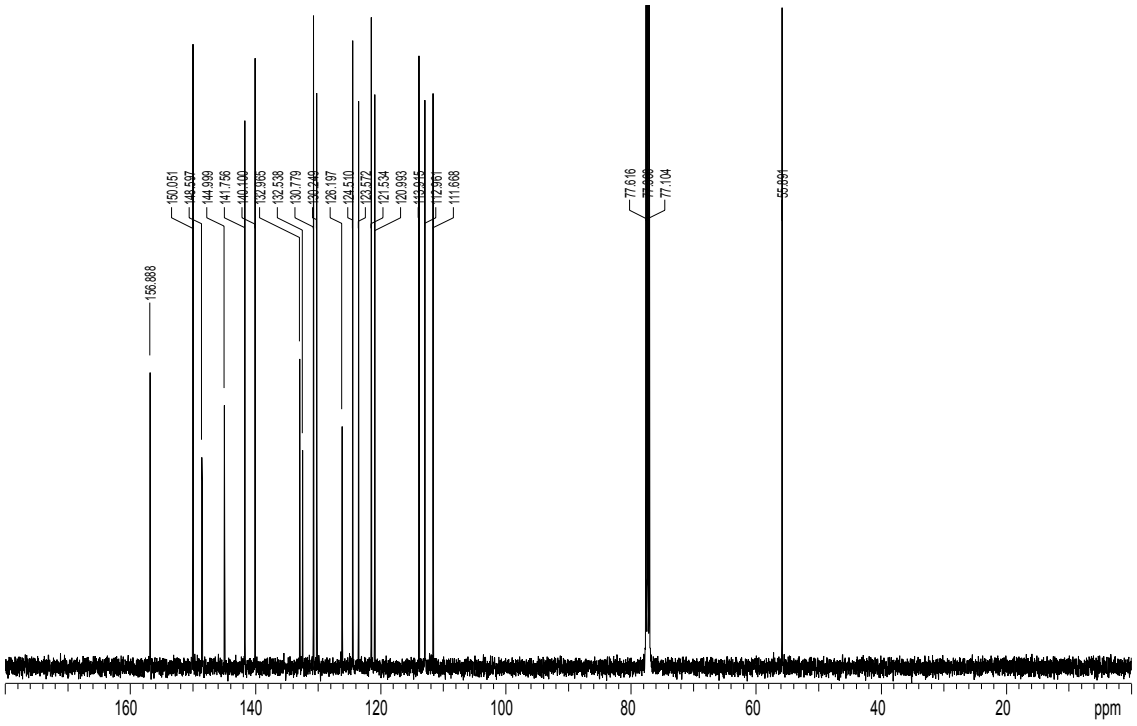


Compound 23

^{1}H NMR (500 MHz, $CDCl_3$)

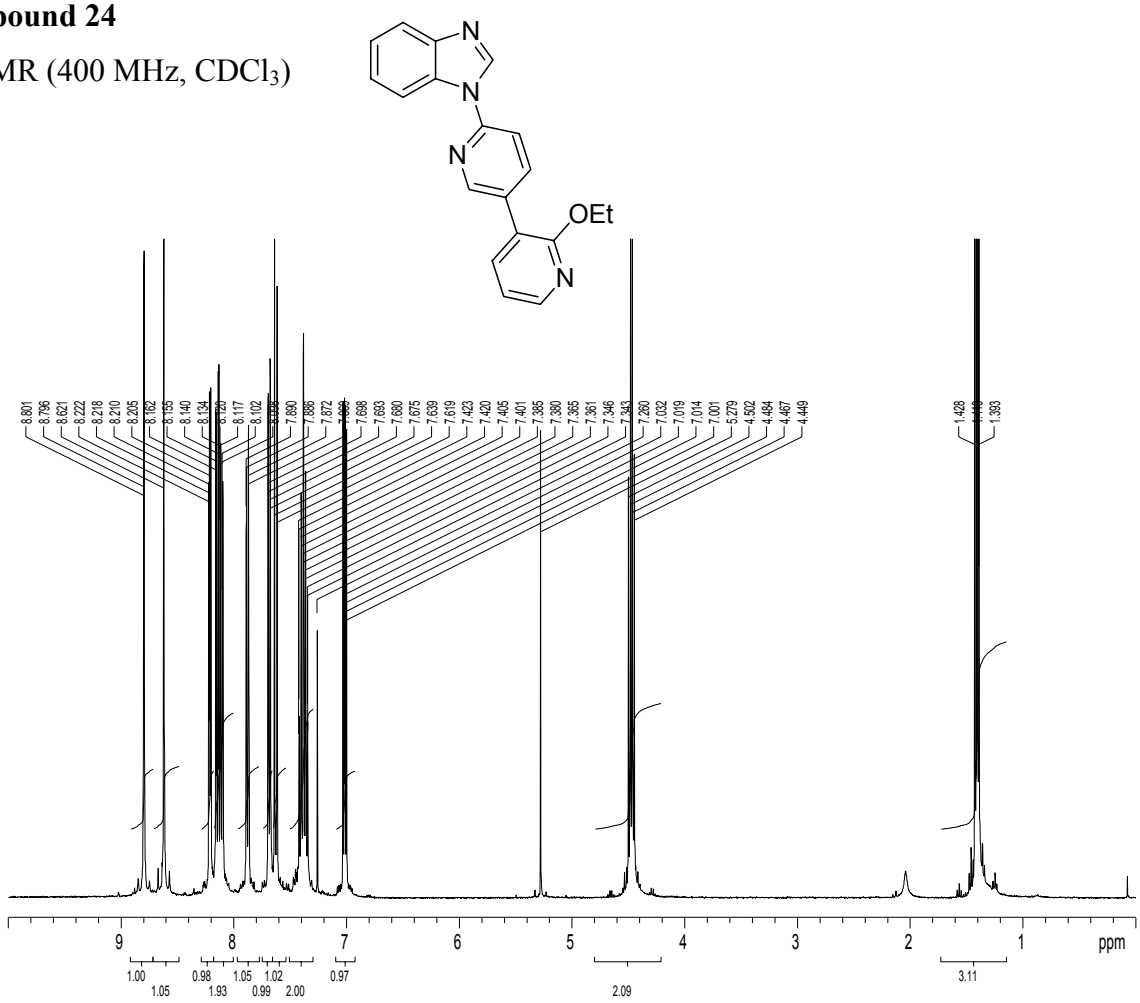


^{13}C NMR (125 MHz , $CDCl_3$)

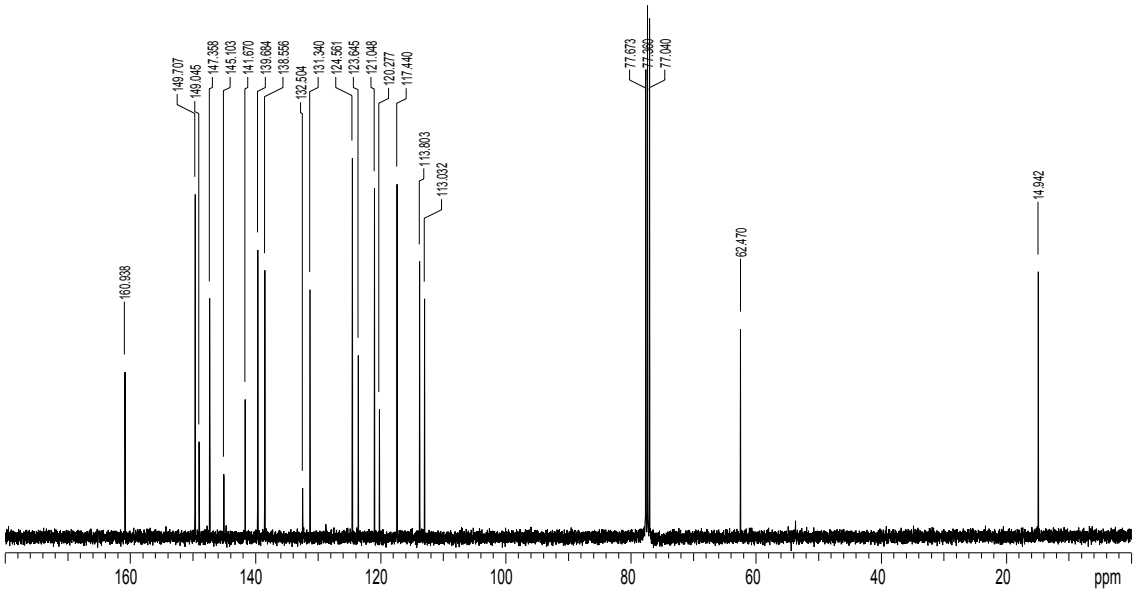


Compound 24

^{1}H NMR (400 MHz, $CDCl_3$)

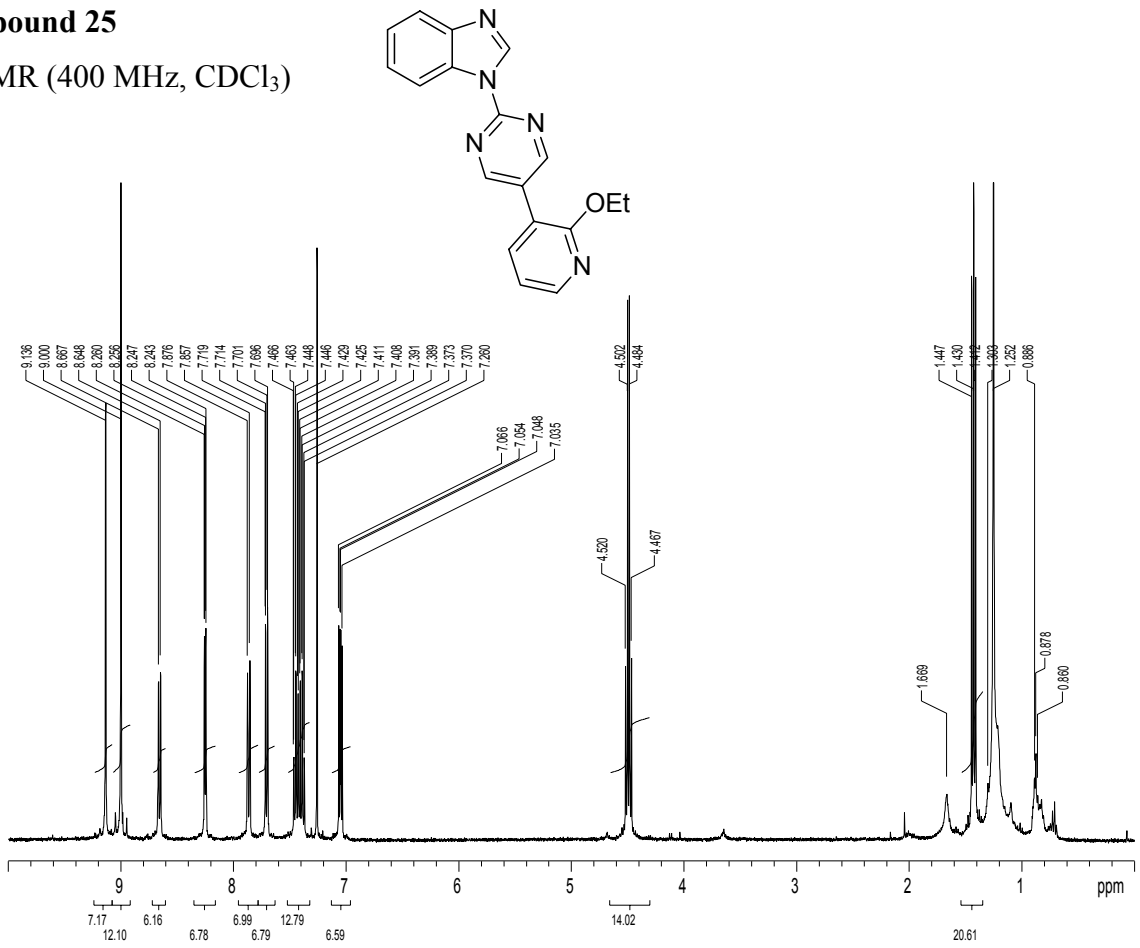


^{13}C NMR (100 MHz, $CDCl_3$)

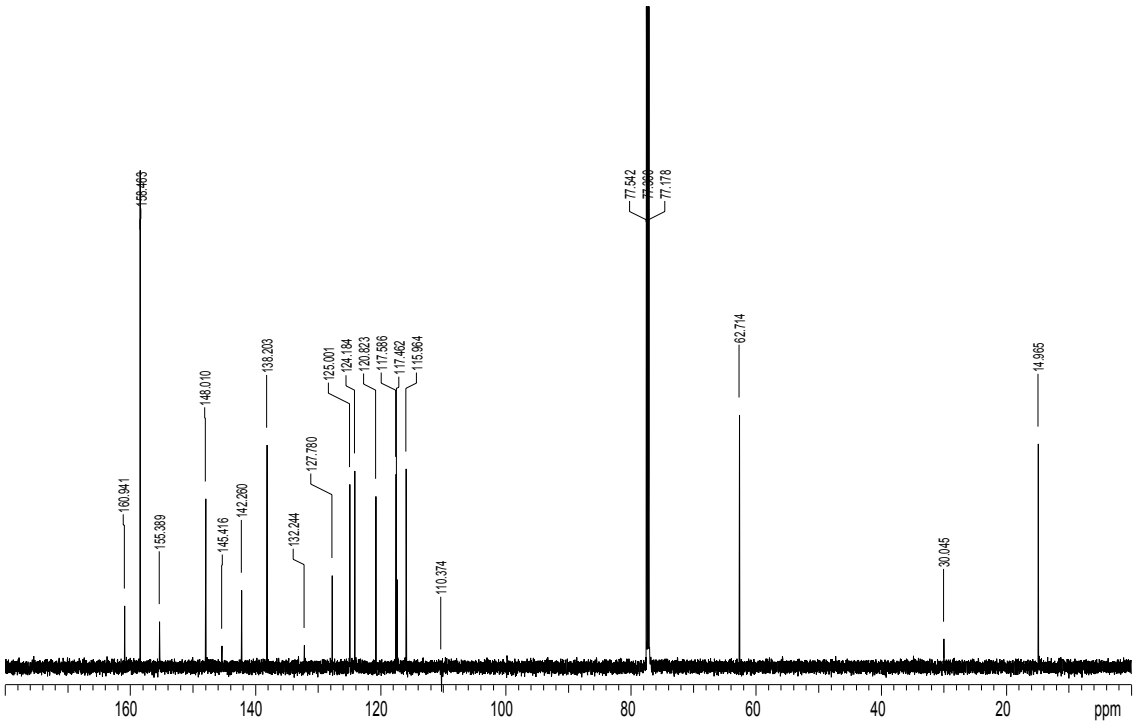


Compound 25

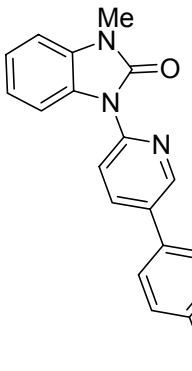
^{1}H NMR (400 MHz, $CDCl_3$)



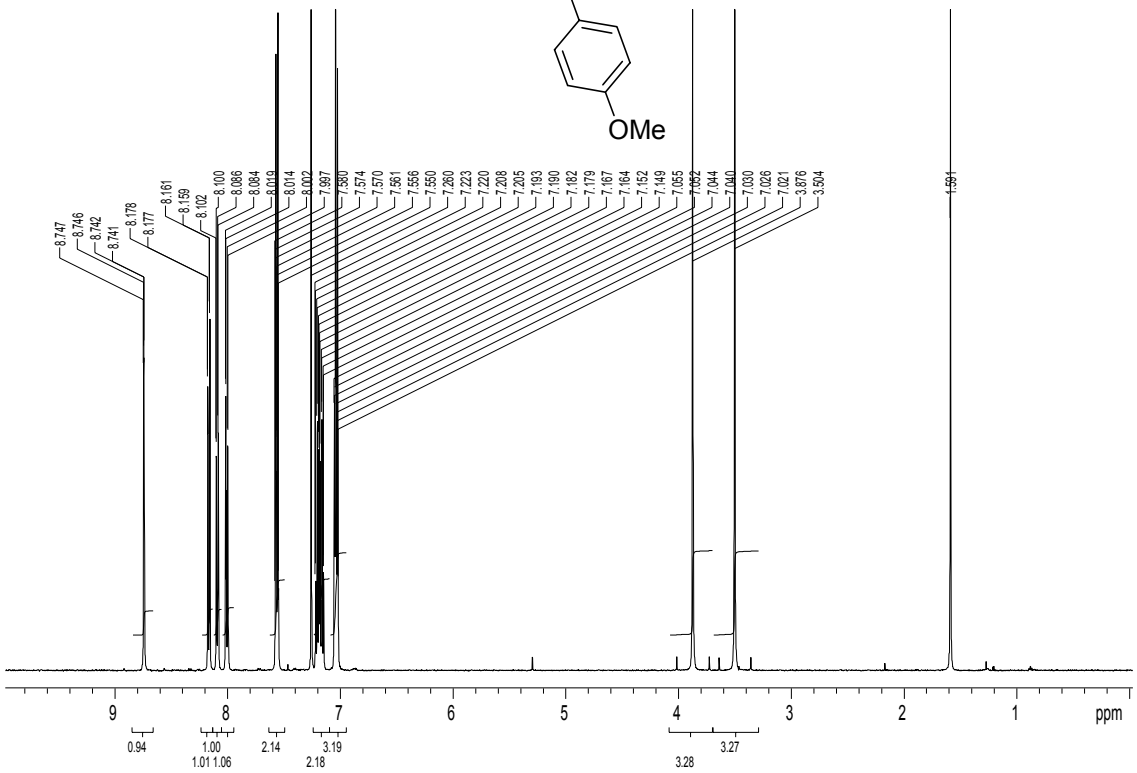
^{13}C NMR (175 MHz, $CDCl_3$)



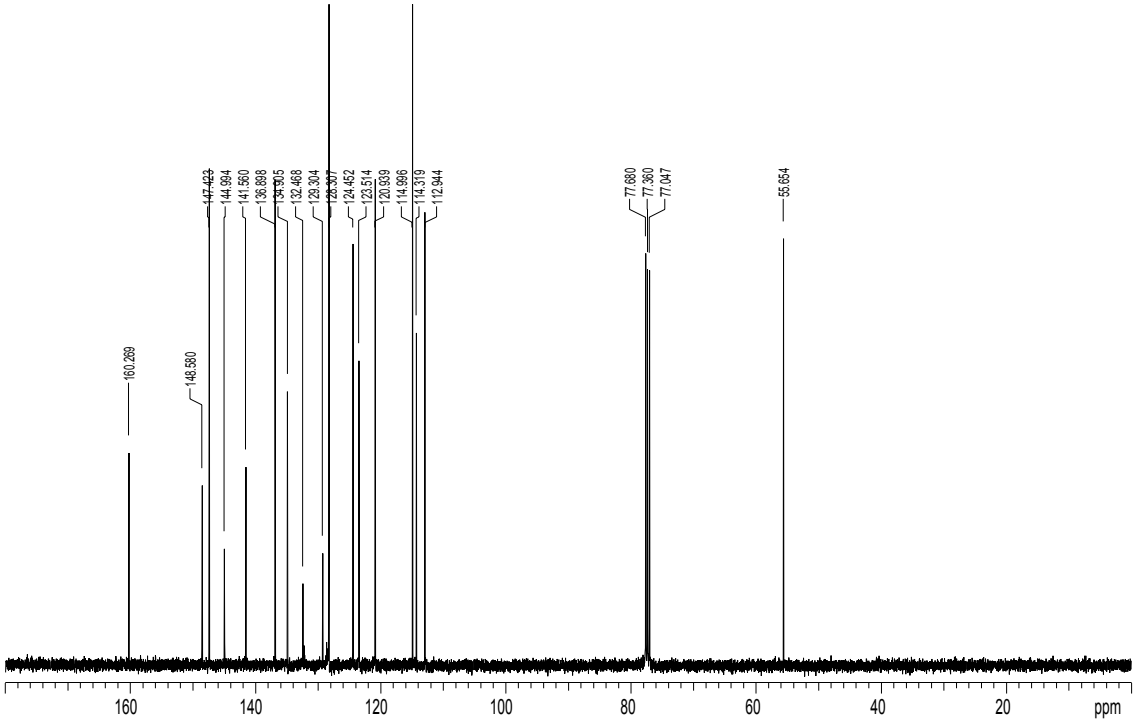
Compound 26



^{1}H NMR (500 MHz, $CDCl_3$)

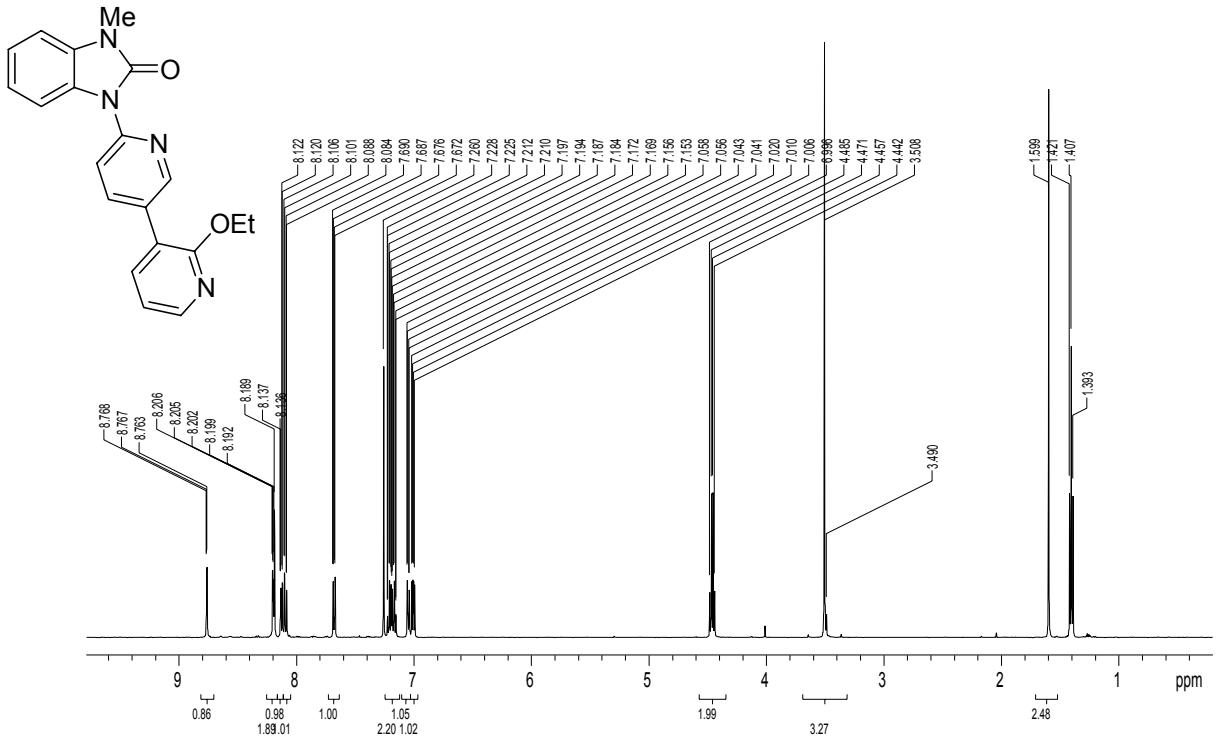


^{13}C NMR (125 MHz, $CDCl_3$)

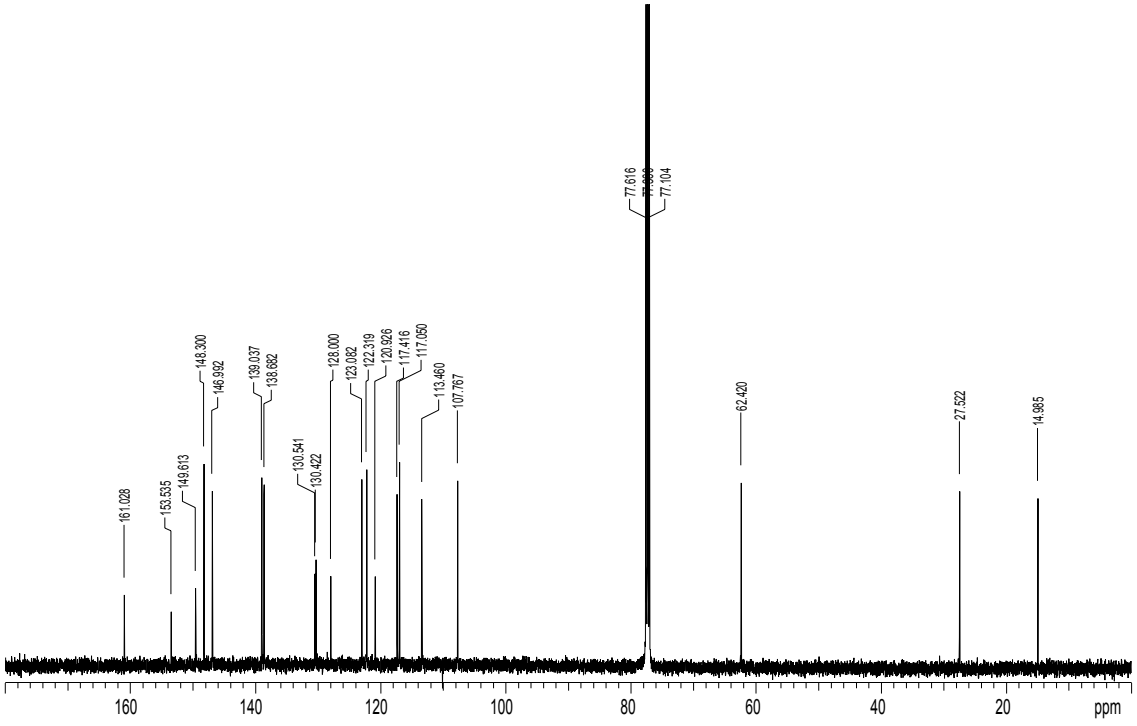


Compound 27

^{1}H NMR (400 MHz, $CDCl_3$

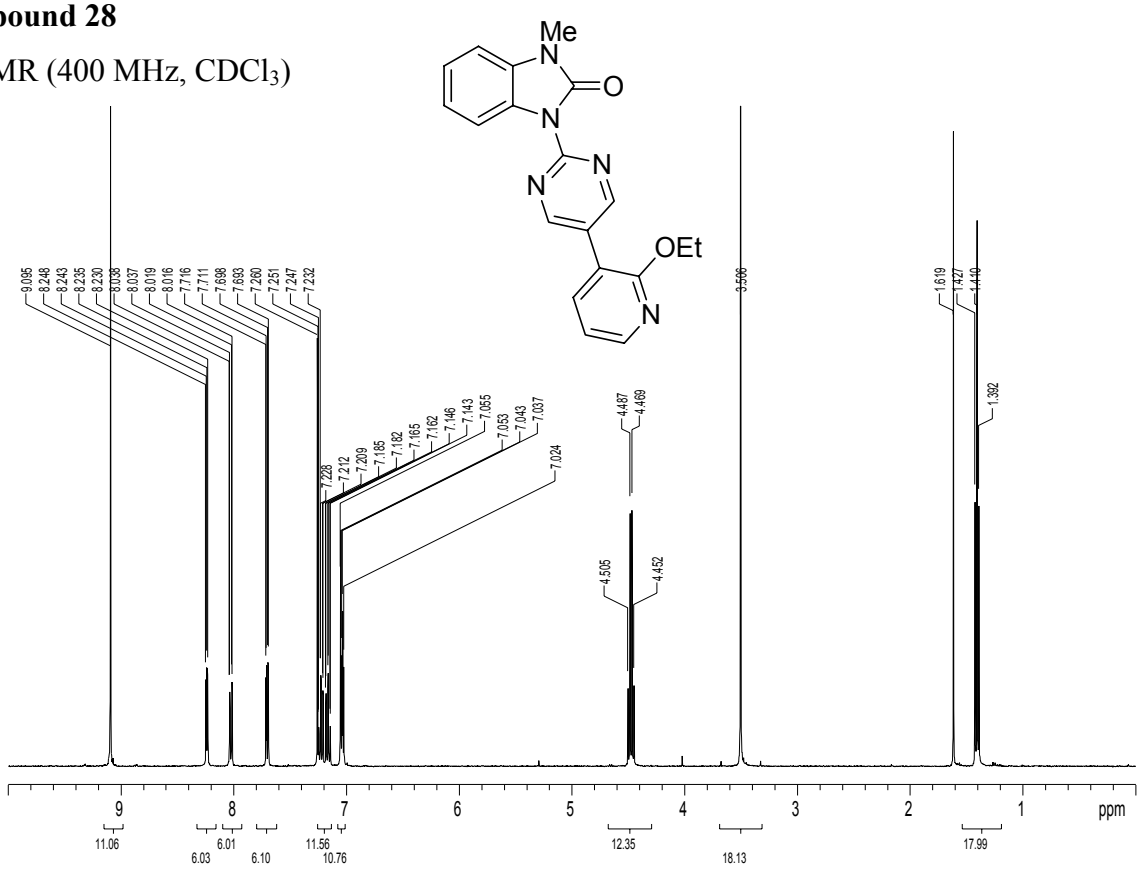


^{13}C NMR (125 MHz, $CDCl_3$)

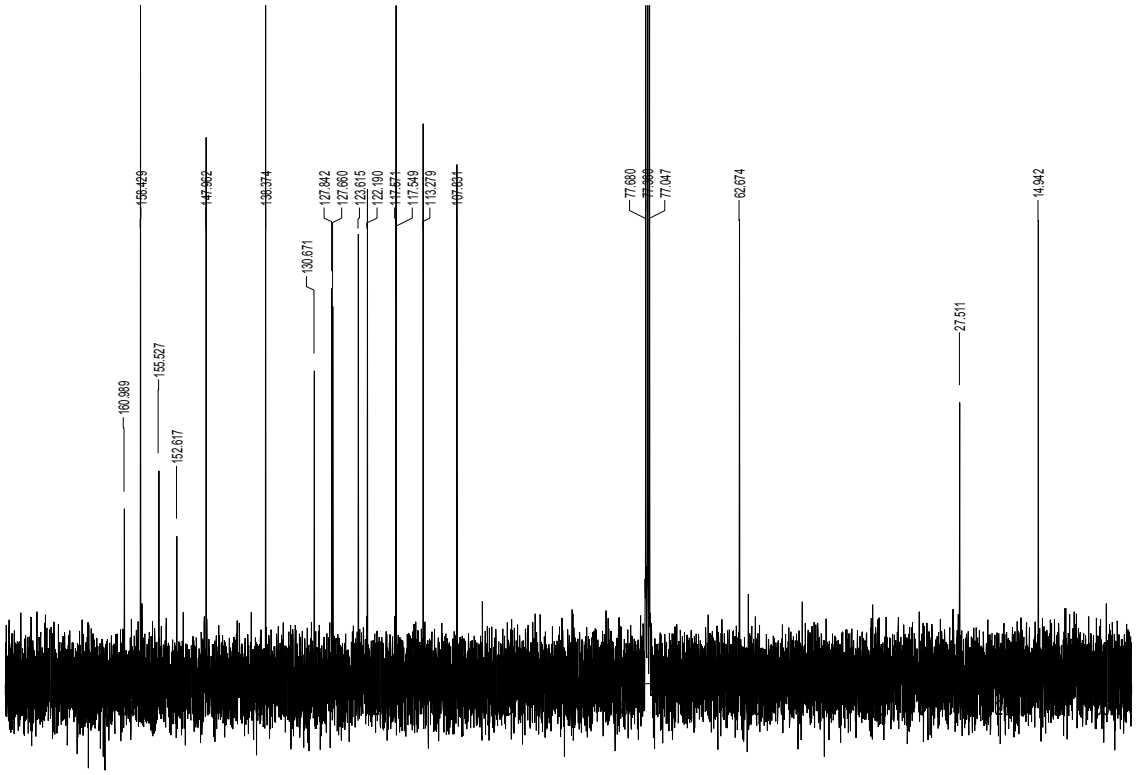


Compound 28

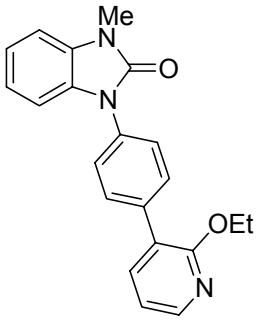
^{1}H NMR (400 MHz, $CDCl_3$)



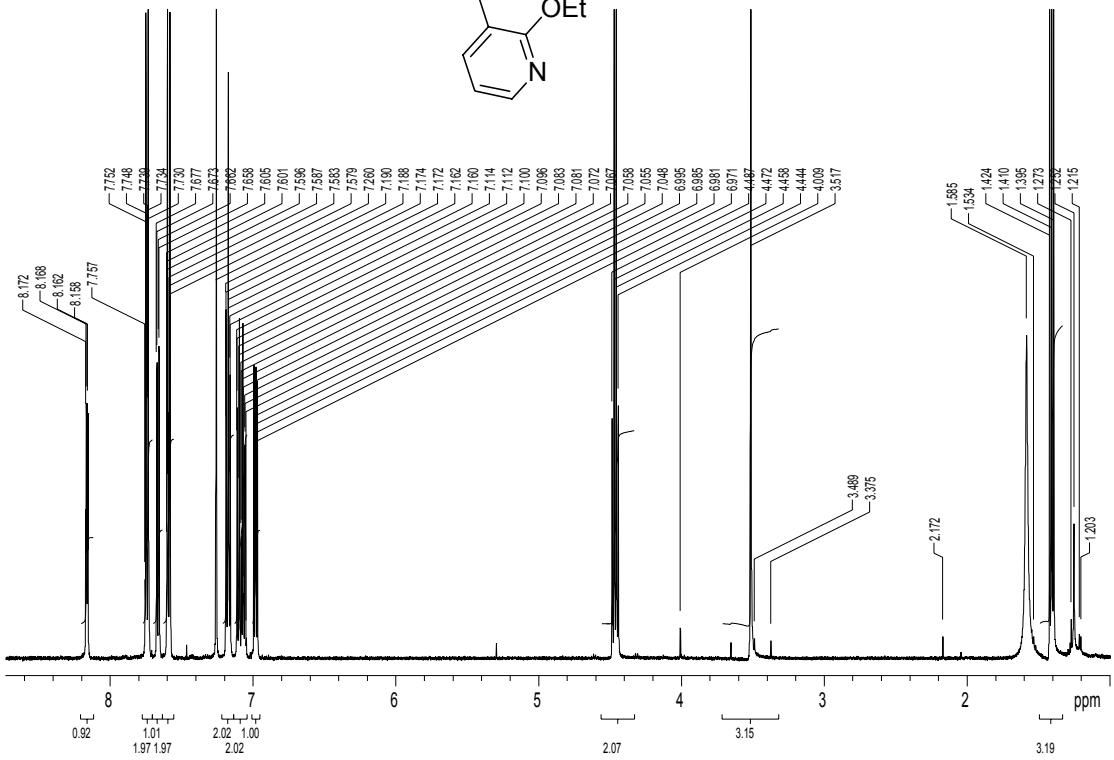
^{13}C NMR (100 MHz, $CDCl_3$)



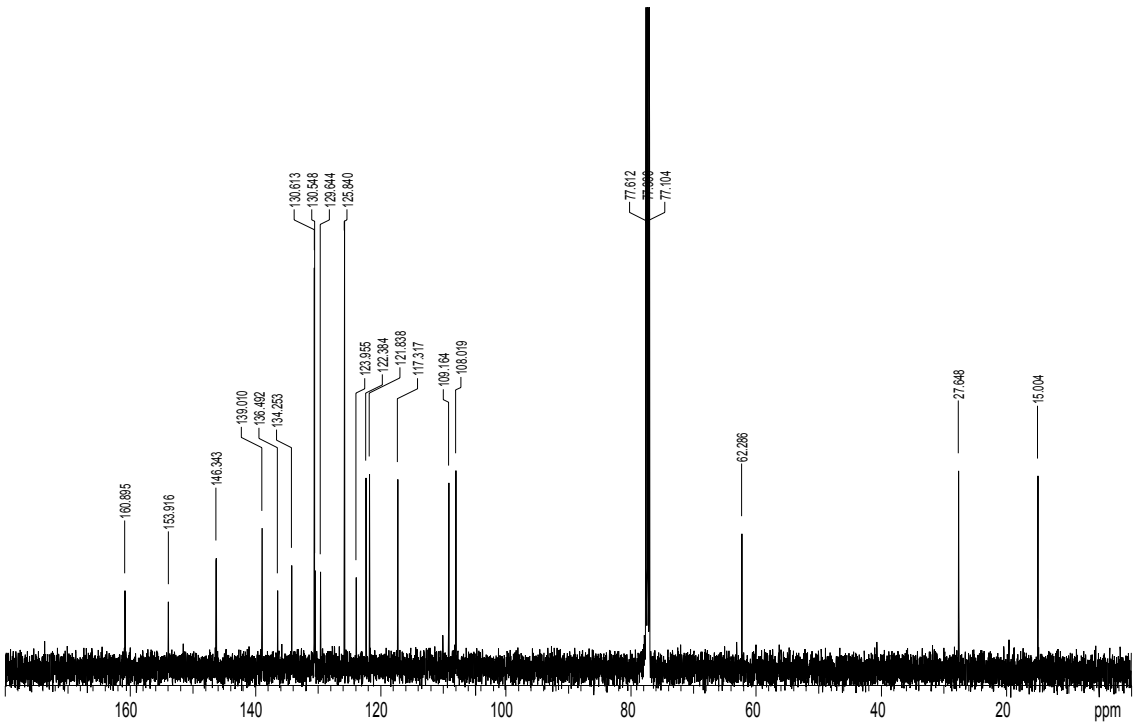
Compound 29



^{1}H NMR (500 MHz, $CDCl_3$)

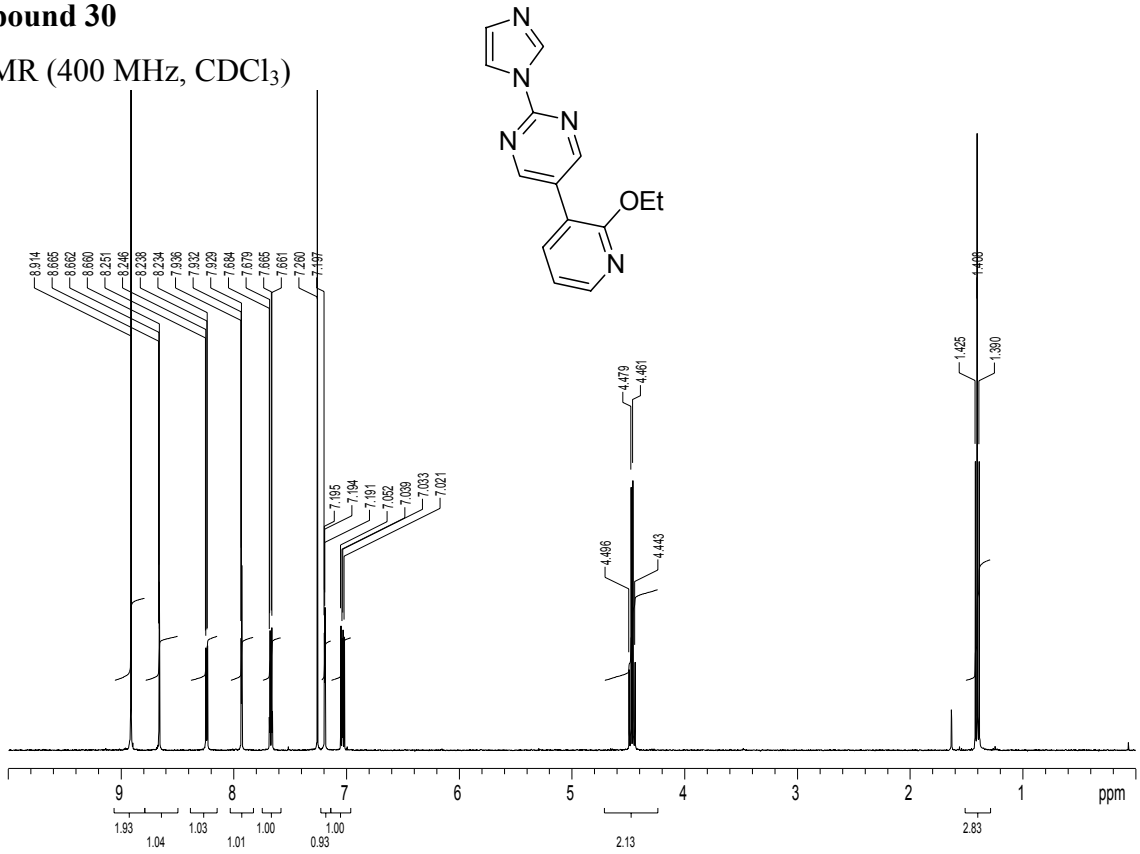


^{13}C NMR (125 MHz, $CDCl_3$)

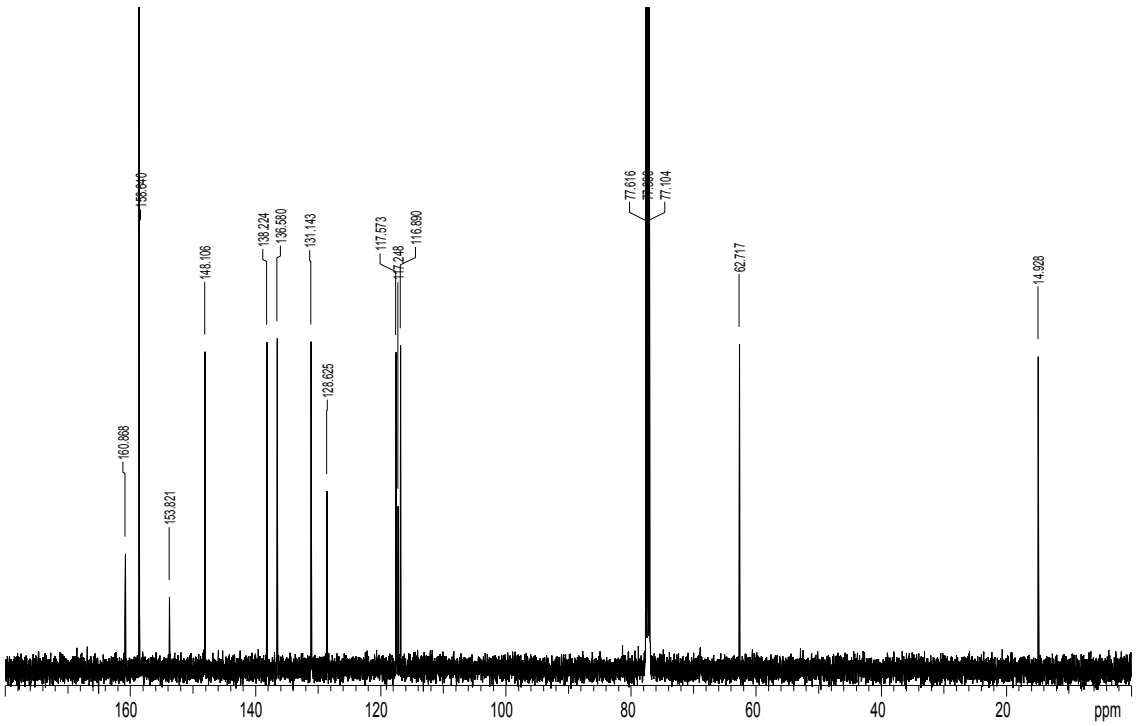


Compound 30

^{1}H NMR (400 MHz, $CDCl_3$)

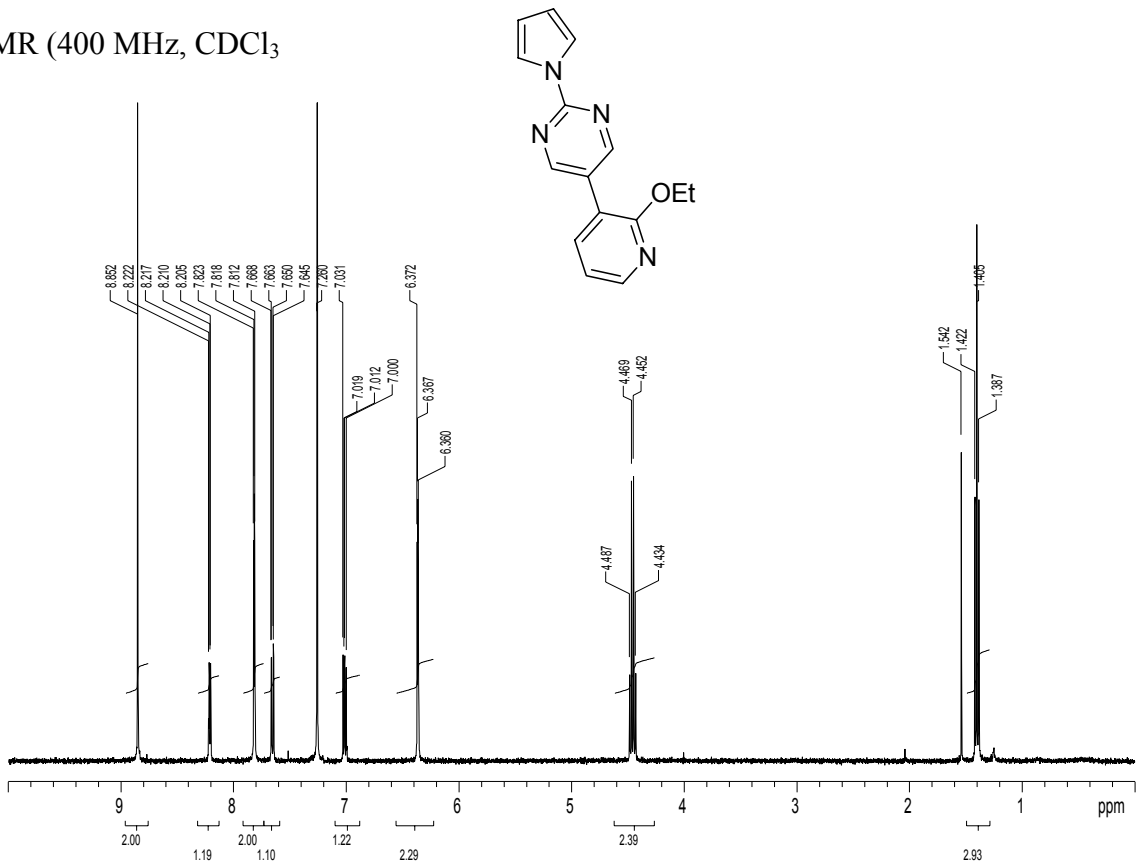


^{13}C NMR (125 MHz, $CDCl_3$)



Compound 31

^{1}H NMR (400 MHz, $CDCl_3$



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