Efficient *Mono*- and *Bis*-Functionalization of 3,6-Dichloropyridazine using $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ **

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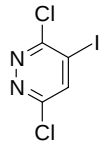
General All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be > 95 % pure as determined by ^{1}H-NMR (25 °C) and capillary GC. NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (δ 7.24 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, br, brought. Column chromatography was performed using silica gel (0.040–0.063 mm, 230–400 mesh ASTM) from Merck if not indicated. TMPH and liquid acid chlorides were distilled prior to use.

Typical Procedure 1: Preparation of the reagent $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (1):
In an argon-flushed Schlenk-flask, $ZnCl_2$ (53.0 mmol, 7.22 g) was dried *in vacuo* at 140 °C for 4 h. After cooling to 25 °C, dry THF (25 mL) and freshly titrated tmpMgCl·LiCl [1] (100 mmol, 1.00 M, 100 mL) was added slowly. The resulting mixture was stirred for 15 h at 25 °C. The freshly prepared $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**1**) solution was titrated prior to use at 0°C with benzoic acid using 4-(phenylazo)diphenylamine as indicator. A concentration of 0.40 M in THF was obtained.

Typical procedure for the preparation of the zincated 3-6-dichloropyridazine (3) using $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$:
A dry and argon flushed 25-mL Schlenck-tube, equipped with a magnetic stirring bar was charged with a solution of 3-6-Dichloropyridazine (**2**, 298 mg, 2.0 mmol) in dry THF (5 mL).

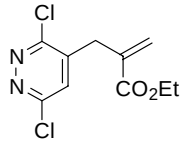
The solution was cooled to -78 °C and $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**1**; 0.4 M in THF, 3.0 mL, 1.2 mmol) was added dropwise. The resulting mixture was stirred for 2 h at -78 °C. The completion of the metalation was checked by GC-analysis of reaction aliquots quenched with a I_2 solution in dry THF. Compound **3** was obtained in >90% yield as determined by titration with I_2.

Synthesis of 3,6-dichloro-4-iodo-pyridazine (4a)



To a solution of the zincated dichloropyridazine **3**, iodine (761 mg, 3.00 mmol) dissolved in THF (6 mL) was added dropwise and stirred for 1 h at -78 °C. The reaction mixture was quenched with a mixture of a sat. aq. NH_4Cl solution (10 mL) and a sat. aq. $Na_2S_2O_3$ solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 5:1) furnished the compound **4a** (451 mg, 82%) as a colourless solid. **m.p.**: 145.1–146.6 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 8.06 (s, 1H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 159.7, 153.9, 139.7, 105.4. **MS** (70 eV, EI) *m/z* (%): 274 (95) [M^+], 127 (23), 123 (10), 121 (70), 119 (100), 86 (15), 84 (43), 49 (8). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3092, 3020, 1796, 1516, 1488, 1464, 1332, 1296, 1276, 1236, 1152, 1136, 1060, 1044, 992, 956, 900, 812, 764, 728, 672, 660, 628, 608, 588, 564. **HRMS (EI)** for **$C_4HCl_2IN_2$** (273.8561): 273.8538.

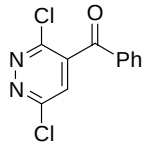
Synthesis of 2-(3,6-dichloro-pyridazin-4-ylmethyl)-acrylic acid ethyl ester (4b)



To a solution of the zincated dichloropyridazine **3**, CuCN·2LiCl (1.0 M solution in THF, 0.5 mL, 0.5 mmol) was added and the reaction mixture was stirred for 5 min. Then, ethyl 2-(bromomethyl)acrylate (483 mg, 2.5 mmol) was added and stirred for 1 h at -78 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was

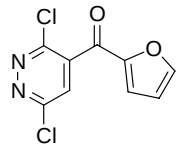
evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 4:1) furnished the compound **4b** (451 mg, 82%) as a pale yellow oil. **^{1}H-NMR ($CDCl_3$, 600 MHz)** δ: 7.39 (s, 1H), 6.45 (s, 1 H), 5.75 (s, 1 H), 4.18 (q, *J*=7.2 Hz, 2 H), 3.72 (s, 2 H), 1.25 (q, *J*=7.2 Hz, 3 H). **^{13}C-NMR ($CDCl_3$, 150 MHz,)** δ: 165.5, 156.8, 155.9, 141.4, 134.7, 129.9, 129.8, 61.5, 34.8, 14.1. **MS** (70 eV, EI) *m/z* (%): 260 (7) [M^+], 227 (22), 225 (77), 217 (10), 215 (16), 199 (34), 198 (9), 197 (100), 189 (8) 187 (11), 123 (9), 63 (9). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 2982, 1709, 1632, 1566, 1476, 1464, 1444, 1406, 1359, 1319, 1294, 1276, 1255, 1206, 1172, 1132, 1100, 1048, 1023, 957, 938, 918, 872, 858, 817, 772, 747, 729, 684, 640, 633, 617, 610, 607, 597, 583, 580, 570, 566. **HRMS (EI)** for **$C_{10}H_{10}Cl_2N_2O_2$** (260.0119): 260.0113.

Synthesis of (3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (4c)



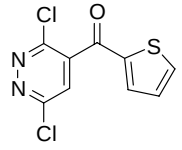
To a solution of the zincated dichloropyridazine **3**, CuCN·2LiCl (1.0 M solution in THF, 2.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for 30 min. Then, benzoyl chloride (353 mg, 2.5 mmol) was added at -78 °C. The reaction mixture was slowly warmed to -20 °C and stirred at this temperature for 16 h. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 3:1) furnished the compound **4c** (368 mg, 73%) as a colourless solid. **m.p.**: 100.2-101.5 °C. **^{1}H-NMR ($CDCl_3$, 600 MHz)** δ: 7.78 (d, *J*=7.2 Hz, 2 H), 7.72 (t, *J*=7.6 Hz, 1 H), 7.56 (t, *J*=7.9 Hz, 2 H), 7.51 (s, 1 H). **^{13}C-NMR ($CDCl_3$, 150 MHz,)** δ: 189.1, 156.2, 151.7, 140.0, 135.5, 134.0, 130.0, 129.3, 127.7. **MS** (70 eV, EI) *m/z* (%): 254 (23), 252 (38) [M^+], 106 (21), 105 (97), 77 (100), 51 (28). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3069, 1665, 1632, 1614, 1590, 1574, 1501, 1487, 1444, 1338, 1324, 1306, 1289, 1257, 1247, 1239, 1222, 1173, 1167, 1155, 1134, 1103, 1070, 1052, 1024, 999, 988, 981, 968, 932, 902, 852, 821, 799, 756, 714, 699, 681, 653, 624, 612, 599, 587, 584, 579, 575, 559. **HRMS (EI)** for **$C_{11}H_6Cl\,N_2O$** (251.9857): 251.9844.

Synthesis of (3,6-dichloro-pyridazin-4-yl)-furan-2-yl-methanone (4d)



To a solution of the zincated dichloropyridazine **3**, CuCN·2LiCl (1.0 M solution in THF, 2.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for 30 min. Then, 2-furoyl chloride (326 mg, 2.5 mmol) was added at -78 °C. The reaction mixture was slowly warmed to -20 °C and stirred at this temperature for 16 h. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 3:1) furnished the compound **4d** (330 mg, 68%) as a colourless solid. **m.p.**: 135.6-136.8 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 7.74 (d, *J*=0.7 Hz, 1 H), 7.56 (s, 1 H), 7.33 (d, *J*=3.2 Hz, 1 H), 6.72 (dd, *J*=3.6, 1.5 Hz, 1 H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 175.8, 156.1, 151.8, 150.5, 149.4, 138.5, 127.9, 122.4, 113.7. **MS** (70 eV, EI) *m/z* (%): 244 (62), 242 (94) [M^+], 96 (18), 95 (100), 84 (13). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3113, 3041, 1657, 1623, 1558, 1505, 1462, 1391, 1353, 1319, 1282, 1243, 1203, 1190, 1183, 1165, 1149, 1119, 1081, 1040, 1034, 981, 931, 927, 911, 883, 872, 864, 802, 789, 778, 768, 740, 692, 683, 644, 641, 630, 620, 591, 570, 552. **HRMS (EI)** for **$C_9H_4Cl_2N_2O_2$** (241.9650): 241.9658.

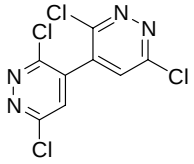
Synthesis of (3,6-dichloro-pyridazin-4-yl)-thiophen-2-yl-methanone (4e)



To a solution of the zincated dichloropyridazine **3**, CuCN·2LiCl (1.0 M solution in THF, 2.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for 30 min. Then, 2-thiophene acid chloride (346 mg, 2.5 mmol) was added at -78 °C. The reaction mixture was slowly warmed to -20 °C and stirred at this temperature for 16 h. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 3:1) furnished the compound **4e** (339 mg, 66%) as a colourless solid. **m.p.**: 158.1-159.8 °C. **^{1}H-NMR ($CDCl_3$, 600 MHz)** δ: 7.94 (d, *J*=6.2 Hz 1 H), 7.55 (s, 1 H), 7.46 (d, *J*=3.8 Hz, 1 H), 7.21-7.24 (m, 1 H). **^{13}C-NMR**

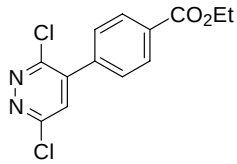
($CDCl_3$, 150 MHz,) δ: 180.6, 156.1; 151.7, 141.1, 139.3, 138.1, 136.8, 129.1, 127.4. **MS** (70 eV, EI) *m/z* (%): 260 (66), 258 (99) [M^+], 113 (23), 112 (28), 111 (100), 84 (12), 83 (25), 57 (9). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3116, 3069, 1630, 1597, 1561, 1507, 1501, 1419, 1402, 1364, 1355, 1343, 1325, 1312, 1270, 1256, 1230, 1206, 1197, 1180, 1142, 1105, 1072, 1054, 1040, 958, 934, 911, 863, 860, 853, 826, 807, 793, 757, 735, 693, 678, 662, 655, 610, 593, 579, 574, 570, 563, 553. **HRMS (EI)** for **$C_9H_4Cl_2N_2OS$** (257.9421): 257.9414.

Synthesis of (3,6,3',6')-tetrachloro-[4,4']bipyridazinyl (4f)



To a solution of the zincated dichloropyridazine **3**, chloranil (290 mg, 1.2 mmol) dissolved in THF (9 mL) was added dropwise and the reaction mixture was stirred for 4 h at -78 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 1:1) furnished the compound **4f** (262 mg, 88%) as a colourless solid. **m.p.**: 164.5–166.5 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 7.56 (s, 2H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 156.1, 153.3, 134.8, 129.6. **MS** (70 eV, EI) *m/z* (%): 296 (100) [M^+], 295 (9), 294 (72), 233 (19), 231 (21), 208 (11), 206 (15), 205 (10), 203 (9), 198 (19), 197 (12), 196 (29), 195 (15), 145 (10), 143 (12), 118 (11), 108 (8), 84 (17). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3031, 1684, 1546, 1434, 1392, 1349, 1327, 1281, 1139, 903, 781, 753, 712, 632, 568. **HRMS (EI)** for **$C_8H_2Cl_2N_4$** (293.9034): 293.9037.

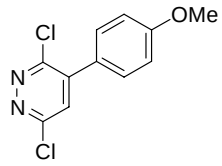
Synthesis of 4-(3,6-dichloro-pyridazin-4-yl)-benzoic acid ethyl ester (4g)



To a solution of the zincated dichloropyridazine **3**, $Pd(dba)_2$ (56 mg, 5 mol%) and P(*o*-furyl)$_3$ (46 mg, 10 mol%) dissolved in THF (4 mL) were then transferred *via* cannula to the reaction

mixture, followed by the addition of ethyl 4-iodobenzoate (607 mg, 2.2 mmol) dissolved in THF (2 mL). The reaction mixture was allowed to warm up within 4 h to -20 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 4:1) furnished the compound **4g** (481 mg, 81%) as a colourless solid. **m.p.**: 81.4-82.0 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 8.18 (ddd, *J*=8.6, 1.9, 1.7 Hz, 2 H), 7.56 (ddd, *J*=8.6, 1.9, 1.7 Hz, 2 H), 7.51 (s, 1 H), 4.42 (q, *J*=7.1 Hz, 2 H), 1.42 (t, *J*=7.0 Hz, 3 H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 165.6, 156.1, 154.5, 141.8, 137.2, 132.2, 130.0, 129.5, 128.9, 61.5, 14.3. **MS** (70 eV, EI) *m/z* (%): 298 (23), 296 (39) [M^+], 270 (34), 268 (53), 255 (11), 254 (12), 253 (62), 252 (17), 251 (100), 188 (10), 153 (17), 126 (11). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3062, 3038, 2984, 2910, 1716, 1612, 1556, 1540, 1482, 1408, 1390, 1364, 1350, 1328, 1314, 1274, 1186, 1136, 1126, 1102, 1060, 1040, 1016, 980, 964, 924, 880, 858, 842, 772, 750, 720, 700, 668, 654, 638, 612, 590, 554. **HRMS (EI)** for **$C_{13}H_{10}Cl_2N_2O_2$** (296.0119): 296.0118.

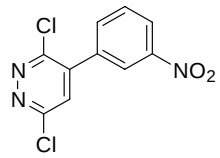
Synthesis of 3,6-dichloro-4-(4-methoxy-phenyl)-pyridazine (4h)



To a solution of the zincated dichloropyridazine **3**, $Pd(dba)_2$ (56 mg, 5 mol%) and P(*o*-furyl)$_3$ (46 mg, 10 mol%) dissolved in THF (4 mL) were then transferred *via* cannula to the reaction mixture, followed by the addition of 1-iodo-4-methoxybenzene (500 mg, 2.2 mmol) dissolved in THF (2 mL). The reaction mixture was allowed to warm up within 4 h to -20 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 6:1) furnished the compound **4h** (366 mg, 76%) as a colourless solid. **m.p.**: 106.5-107.9 °C. **^{1}H-NMR (DMSO, 400 MHz)** δ: 8.06 (s, 1 H), 7.61 (ddd, *J*=9.4, 2.9, 2.5 Hz, 2 H), 7.10 (ddd, *J*=9.4, 2.9, 2.5 Hz, 2 H), 3.83 (s, 3 H). **^{13}C-NMR (DMSO, 100 MHz,)** δ: 160.7, 155.6, 154.5, 142.19, 131.0, 130.2, 124.9, 114.1, 55.34. **MS** (70 eV, EI) *m/z* (%): 256 (58), 255 (12), 254 (100) [M^+], 213 (11), 210 (17), 166 (11), 156 (11) 114 (8). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3016, 2934, 2842, 1604, 1578, 1552, 1510, 1464, 1448, 1440, 1372, 1360, 1332, 1314, 1288, 1258, 1244,

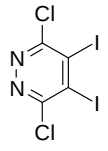
1212, 1190, 1136, 1122, 1058, 1044, 1026, 960, 944, 920, 858, 830, 814, 792, 780, 756, 724, 700, 680, 642, 614, 590, 578. **HRMS (EI)** for **$C_{11}H_8Cl_2N_2O$** (254.0014): 254.0007.

Synthesis of 3,6-dichloro-4-(3-nitro-phenyl)-pyridazine (4i)



To a solution of the zincated dichloropyridazine **3**, $Pd(dba)_2$ (56 mg, 5 mol%) and P(*o*-furyl)$_3$ (46 mg, 10 mol%) dissolved in THF (4 mL) were then transferred *via* cannula to the reaction mixture, followed by the addition of 1-iodo-3-nitrobenzene (510 mg, 2.1 mmol) dissolved in THF (2 mL). The reaction mixture was allowed to warm up within 4 h to -20 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 3:1) furnished the compound **4i** (415 mg, 77%) as a pale yellow solid. **m.p.**: 174.0-175.2 °C. **^{1}H-NMR (DMSO, 400 MHz)** δ: 8.52 (t, *J*=8.2 Hz, 1 H), 8.40 (ddd, *J*=8.4, 2.3, 1.1 Hz, 1 H), 8.27 (s, 1 H), 8.09 (dt, *J*=7.8, 1.4 Hz, 1 H), 7.85 (t, *J*=8.2 Hz, 1 H). **^{13}C-NMR (DMSO, 100 MHz,)** δ: 155.7, 154.2, 147.6, 140.5, 135.9, 134.5, 131.2, 130.2, 124.7, 124.3. **MS** (70 eV, EI) *m/z* (%): 273 (10) 271 (60), 270 (11), 269 (100) [M^+], 241 (11), 195 (14), 160 (35), 153 (16), 126 (11). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3094, 3056, 1614, 1580, 1558, 1522, 1494, 1478, 1348, 1328, 1304, 1280, 1244, 1226, 1190, 1176, 1136, 1112, 1100, 1090, 1066, 1046, 1002, 942, 920, 904, 838, 814, 790, 758, 730, 686, 668, 626, 598, 562. **HRMS (EI)** for **$C_{10}H_5Cl_2N_3O_2$** (268.9759): 269.9763.

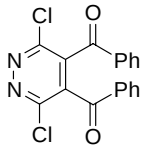
Synthesis of 3,6-dichloro-4,5-iodpyridazin (5a)



A dry and argon flushed 25-mL Schlenck-tube, equipped with a magnetic stirring bar was charged with a solution of 6-dichloro-4-iodo-pyridazine **(4a**, 550 mg, 2.0 mmol) in dry THF (5 mL). The solution was cooled to -78 °C and $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**1**; 0.4 M in THF,

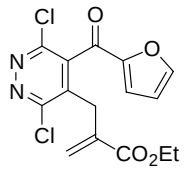
3.00 mL, 1.2 mmol) was added dropwise and the resulting mixture was stirred for 3 h at -78 °C. Iodine (761 mg, 3.00 mmol) dissolved in THF (6 mL) was added dropwise and stirred for 1 h at -78 °C. The reaction mixture was quenched with mixture of a sat. aq. NH_4Cl solution (10 mL) and a sat. aq. $Na_2S_2O_3$ solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Recrystallisation (CH_2Cl_2) furnished the compound **5a** (448 mg, 56%) as a colourless solid. **m.p.**: 193.8 °C (decomposition). **^{1}H-NMR ($CDCl_3$, 400 MHz)** δ: -. **^{13}C-NMR ($CDCl_3$, 100 MHz,)** δ: 157.8, 124.8. **MS** (70 eV, EI) *m/z* (%):400 (100) [M^+], 254 (11), 247 (16), 245 (25), 237 (14), 236 (10), 126 (21), 120 (50), 118 (67), 83 (13). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3092, 1516, 1488, 1464, 1332, 1296, 1276, 1236, 1152, 1136, 1060, 1044, 992, 956, 900, 812, 764, 728, 672, 660, 628, 608, 564. **HRMS (EI)** for **$C_4Cl_2I_2N_2$** (399.7528): 399.7518.

Synthesis of (5-benzoyl-3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (5b)



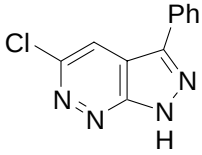
A dry and argon flushed 25-mL Schlenck-tube, equipped with a magnetic stirring bar was charged with a solution of (3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (**4c**; 504 mg, 2.0 mmol) in dry THF (5 mL). The solution was cooled to -78 °C and $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**1**; 0.4 M in THF, 3.00 mL, 1.2 mmol) was added dropwise and the resulting mixture was stirred for 3 h at -78 °C. CuCN·2LiCl (1.0 M solution in THF, 2.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for 30 min. Then, benzoyl chloride (353 mg, 2.5 mmol) was added at -78 °C. The reaction mixture was slowly warmed to -20 °C and stirred at this temperature for 16 h. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 1:1) furnished the compound **5b** (548 mg, 77%) as a pale yellow solid. **m.p.**: 166.8-168.3 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 7.63-7.73 (m, 6 H), 7.46-7.51 (m, 4 H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 188.9, 152.0, 138.1, 135.5, 134.3, 129.9, 129.1. **MS** (70 eV, EI) *m/z* (%): 356 (7) [M^+], 105 (100), 77 (26). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 1668, 1594, 1580, 1450, 1336, 1318, 1258, 1180, 1166, 1150, 1002, 990, 962, 852, 812, 798, 754, 714, 700, 680, 668, 628, 614, 566. **HRMS (EI)** for **$C_{18}H_{10}Cl_2N_2O_2$** (356.0119): 356.0114.

Synthesis of 2-[3,6-dichloro-5-(furan-2-carbonyl)-pyridazin-4-ylmethyl]-acrylic acid ethyl ester (5c)



A dry and argon flushed 25-mL Schlenck-tube, equipped with a magnetic stirring bar was charged with a solution of (3,6-dichloro-pyridazin-4-yl)-furan-2-yl-methanone (**4d**; 486 mg, 2.0 mmol) in dry THF (5 mL). The solution was cooled to -78 °C and $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**1**; 0.4 M in THF, 3.00 mL, 1.2 mmol) was added dropwise and the resulting mixture was stirred for 3 h at -78 °C. CuCN·2LiCl (1.0 M solution in THF, 0.5 mL, 0.5 mmol) was added and the reaction mixture was stirred for 5 min. Then, ethyl 2-(bromomethyl)acrylate (483 mg, 2.5 mmol) was added and stirred for 1 h at -78 °C. The reaction mixture was quenched with a sat. aq. NH_4Cl solution (10 mL), extracted with diethyl ether (5 × 20 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 2:1) furnished the compound **5c** (534 mg, 75%) as a pale yellow solid. **m.p.**: 129.8-131.0 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 7.67 (d, *J*=2.4 Hz, 1 H), 7.28 (d, *J*=3.4 Hz, 1 H), 6.65-6.67 (m, 1 H), 6.22 (t, *J*=1.3 Hz, 1 H), 5.24 (t, *J*=1.7 Hz, 1 H), 4.16 (q, *J*=7.3 Hz, 2 H), 3.58-3.85 (m, 2 H), 1.25 (t, *J*=7.0 Hz, 4 H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 165.3, 158.0, 151.6, 150.9, 149.1, 138.8, 138.2, 134.2, 127.9, 127.8, 113.7, 61.4, 32.0, 14.1. **MS** (70 eV, EI) *m/z* (%): 354 (1) [M^+], 285 (11), 284 (10), 283 (62), 282 (22), 281 (100), 256 (13), 255 (12), 254 (17), 95 (71), 81 (25). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 1668, 1594, 1580, 1450, 1336, 1318, 1258, 1180, 1166, 1150, 1002, 990, 962, 852, 812, 798, 754, 714, 700, 680, 668, 628, 614, 566. **HRMS (EI)** for **$C_{18}H_{10}Cl_2N_2O_2$** (354.0174): 354.0170.

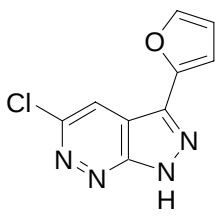
Synthesis of 5-chloro-3-phenyl-1H-pyrazolo[3,4-c]pyridazine (6a)



A 50-mL round bottom flask, equipped with a magnetic stirring bar was charged with a suspension of (3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (**4c**; 504 mg, 2.0 mmol) in EtOH (25 mL). $N_2H_4{\cdot}H_2O$ (0.6 mL, 6 mmol) was added in one portion and the resulting

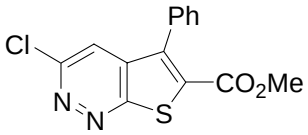
mixture was refluxed for 30 min. After cooling to 25 °C CH_2Cl_2 (100 mL) was added and the organic layer was washed with water (3 x 30 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. The residue was recrystallised from MeOH giving **6a** as a yellow solid (305 mg, 66%). **m.p.**: 255.6-256.6 °C. **^{1}H-NMR (DMSO, 400 MHz)** δ: 8.71 (s, 1 H), 8.04-8.09 (m, 2 H), 7.48, 7.54 (m, 2 H), 7.41-7.47 (m, 1 H). **^{13}C-NMR (DMSO, 100 MHz,)** δ: 155.4, 147.4, 142.5, 131.2, 129.2, 129.1, 126.6, 120.5, 116.0. **MS** (70 eV, EI) *m/z* (%): 232 (26), 231 (11), 230 (100) [M^+], 140 (18), 113 (15), 77 (8).. **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3093, 2993, 2974, 2918, 2893, 2841, 1587, 1510, 1457, 1433, 1394, 1382, 1362, 1287, 1258, 1194, 1177, 1145, 1083, 1068, 1037, 1030, 1004, 992, 932, 910, 879, 865, 832, 801, 786, 776, 756, 688, 676, 620, 604, 593, 584, 579, 575, 571, 559. **HRMS (EI)** for **$C_{11}H_7ClN_4$** (230.0359): 230.0339.

Synthesis of 5-chloro-3-furan-2-yl-1H-pyrazolo[3,4-*c*]pyridazine (6b)



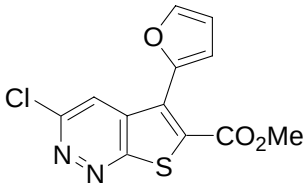
A 50-mL round bottom flask, equipped with a magnetic stirring bar was charged with a suspension (3,6-dichloro-pyridazin-4-yl)-furan-2-yl-methanone (**4d**; 486 mg, 2.0 mmol) in EtOH (25 mL). $N_2H_4 \cdot H_2O$ (0.6 mL, 6 mmol) was added in one portion and the resulting mixture was refluxed for 30 min. After cooling to 25 °C CH_2Cl_2 (100 mL) was added and the organic layer was washed with water (3 x 30 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. The residue was recrystallised from MeOH giving **6b** as a yellow solid (328 mg, 75%). **m.p.**: 256.8-257.5 °C. **^{1}H-NMR (DMSO, 400 MHz)** δ: 8.63 (s, 1 H), 7.86-7.92 (m, 1 H), 7.31 (d, *J*=3.5 Hz, 1 H), 6.72 (dd, *J*=3.2, 1.6 Hz, 1 H). **^{13}C-NMR (DMSO, 100 MHz,)** δ: 154.9, 147.4, 145.9, 143.9, 135.2, 120.0, 115.3, 112.0, 109.2. **MS** (70 eV, EI) *m/z* (%): . **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3132, 3108, 3092, 3000, 2958, 2906, 2852, 1584, 1524, 1512, 1496, 1460, 1416, 1378, 1370, 1330, 1284, 1264, 1224, 1200, 1180, 1164, 1144, 1126, 1102, 1074, 1034, 1010, 968, 936, 900, 882, 844, 820, 798, 774, 738, 688, 668, 648, 624, 592, 570, 558. **HRMS (EI)** for **$C_9H_5ClN_4O$** (220.0152): 220.0139.

Synthesis of 3-chloro-5-phenyl-thieno[2,3-c]pyridazine-6-carboxylic acid methyl ester (7a)



A 50-mL round bottom flask, equipped with a magnetic stirring bar was charged with a suspension of (3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (**4c**; 504 mg, 2.0 mmol) in MeOH (25 mL). $HSCH_2CO_2Me$ (265 mg, 2.5 mmol) and NEt_3 (500 mg, 5 mmol) were added in one portion and the resulting mixture was refluxed for 6 h. After cooling to 25 °C, CH_2Cl_2 (100 mL) was added and the organic layer was washed with water (3 x 30 mL) and NaOH (2 M, 30 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. The residue was recrystallised from MeOH giving **7a** as a pale yellow solid (482 mg, 79%). **m.p**: 160.0-161.1 °C. **^{1}H-NMR ($CDCl_3$, 600 MHz)** δ: 7.62 (s, 1 H), 7.50-7.55 (m, 3 H), 7.36 (dd, *J*=7.4, 2.1 Hz, 2 H), 3.85 (s, 3 H). **^{13}C-NMR ($CDCl_3$, 150 MHz,)** δ: 163.3, 161.5, 152.6, 139.5, 137.4, 135.9, 131.2, 129.4, 129.4, 128.7, 122.1, 53.1. **MS** (70 eV, EI) *m/z* (%): 306 (42), 305 (1), 304 (100) [M^+], 272 (22), 244 (27), 217 (21), 215 (46), 182 (25), 138 (12), 43 (16). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 2950, 1698, 1658, 1554, 1498, 1486, 1448, 1432, 1378, 1330, 1304, 1284, 1244, 1198, 1178, 1140, 1114, 1078, 1054, 1030, 998, 978, 918, 902, 864, 814, 778, 766, 742, 704, 676, 658, 622, 614, 592, 566, 560. **HRMS (EI)** for **$C_{14}H_9ClN_2O_2S$** (304.0073): 304.0060.

Synthesis of 3-chloro-5-furan-2-yl-thieno[2,3-c]pyridazine-6-carboxylic acid methyl ester (7b)



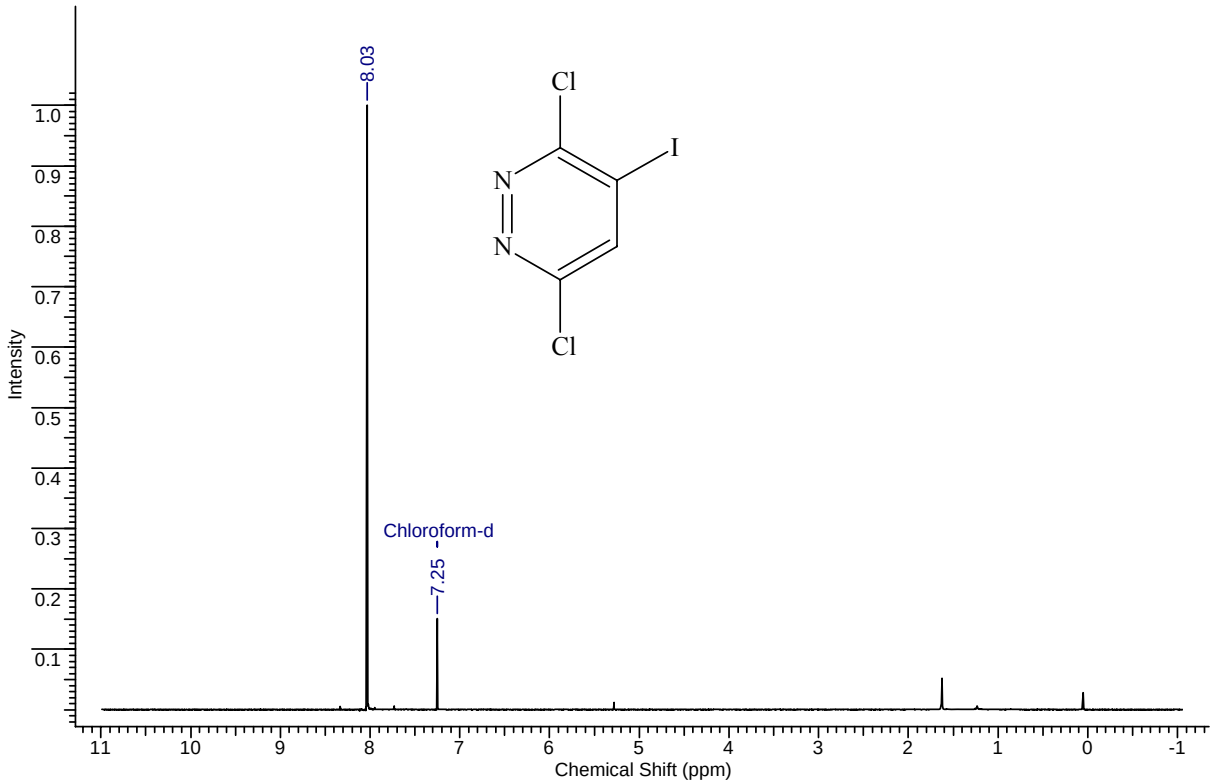
A 50-mL round bottom flask, equipped with a magnetic stirring bar was charged with a suspension (3,6-dichloro-pyridazin-4-yl)-furan-2-yl-methanone (**4d**; 486 mg, 2.0 mmol) in MeOH (25 mL). $HSCH_2CO_2Me$ (265 mg, 2.5 mmol) and NEt_3 (500 mg, 5 mmol) were added in one portion and the resulting mixture was refluxed for 6 h. After cooling to 25 °C, CH_2Cl_2 (100 mL) was added and the organic layer was washed with water (3 x 30 mL) and NaOH (2 M, 30 mL) and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated *in vacuo*. The residue was recrystallised from MeOH giving **7b** as a pale yellow solid (500 mg, 85%). **m.p.**: 159.2-160.3 °C. **^{1}H-NMR ($CDCl_3$, 300 MHz)** δ: 8.40 (s, 1 H), 7.67 (d, *J*=1.5 Hz,

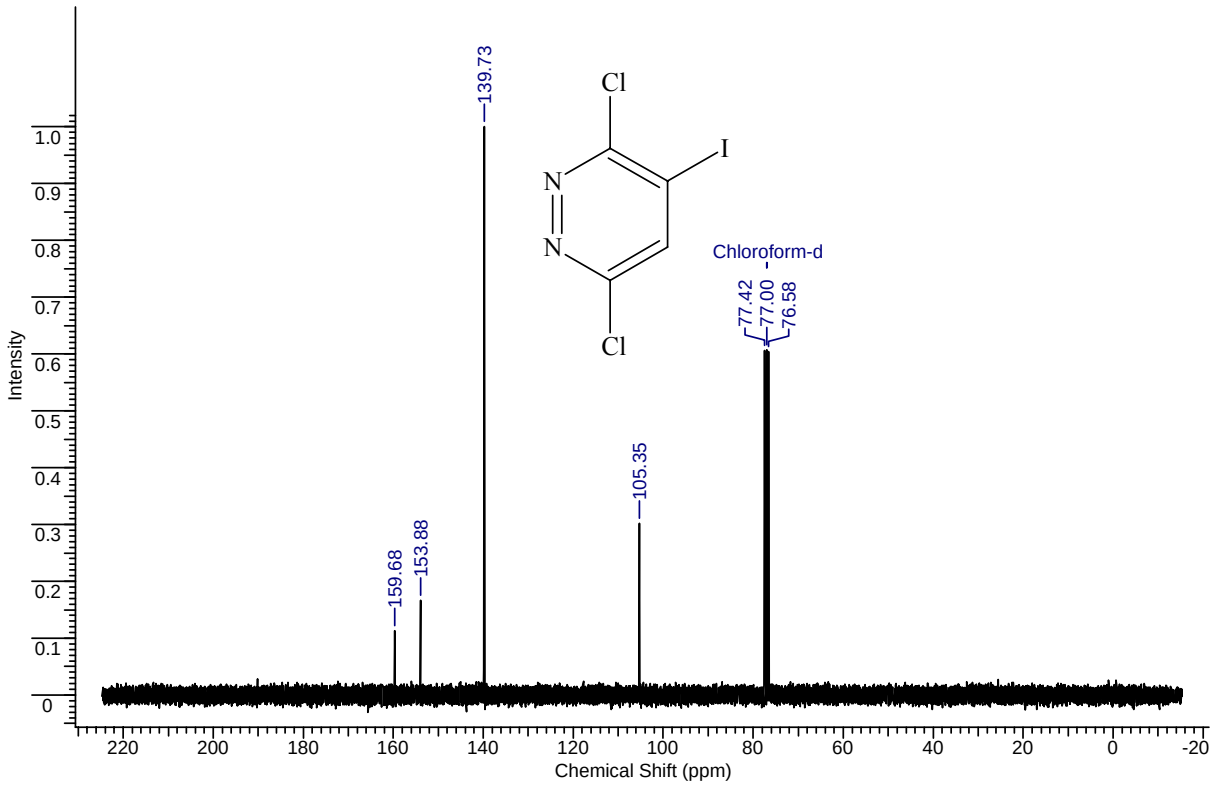
1 H), 7.38 (d, *J*=3.4 Hz, 1 H), 6.64 (dd, *J*=3.5, 1.8 Hz, 1 H), 3.98 (s, 3 H). **^{13}C-NMR ($CDCl_3$, 75 MHz,)** δ: 162.8, 161.4, 152.7, 146.0, 143.7, 135.7, 133.2, 127.5, 123.9, 115.4, 112.1, 53.3. **MS** (70 eV, EI) *m/z* (%): . **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): . **HRMS (EI)** for **$C_{12}H_7ClN_2O_3S$** (293.9866): 293.9873.

Reference:

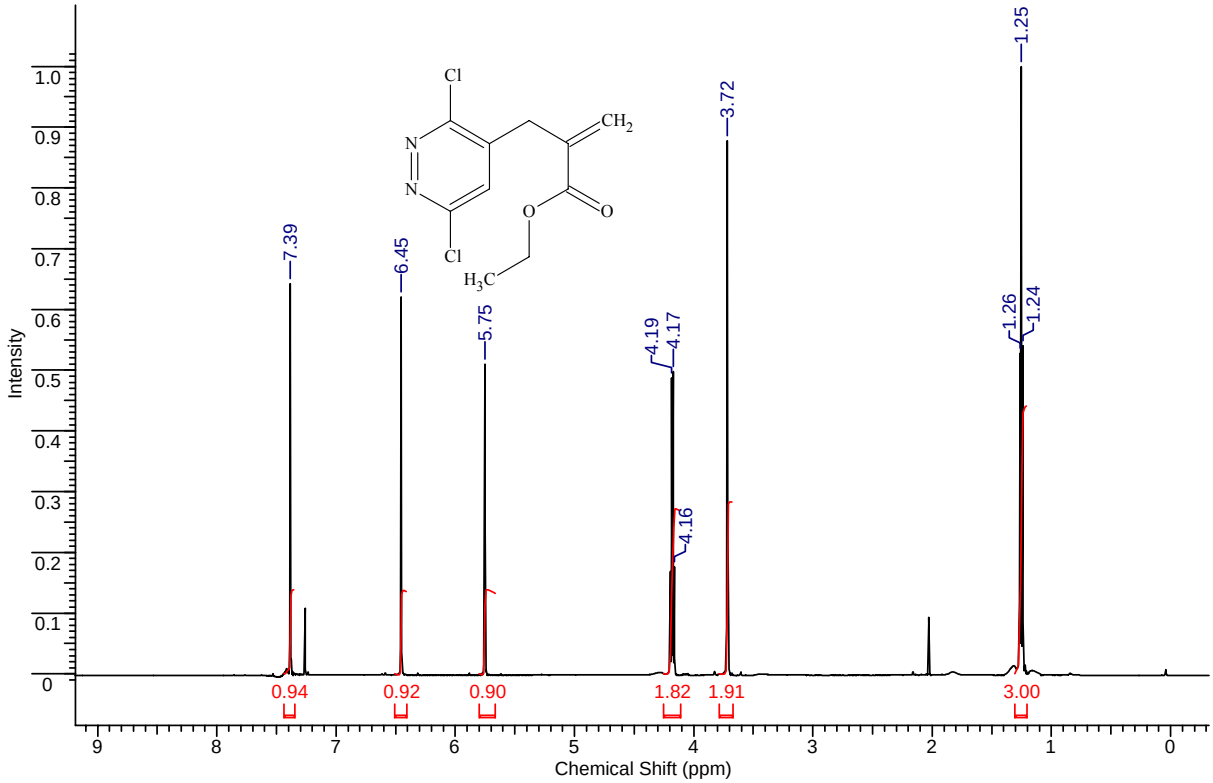
1.) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 2958.

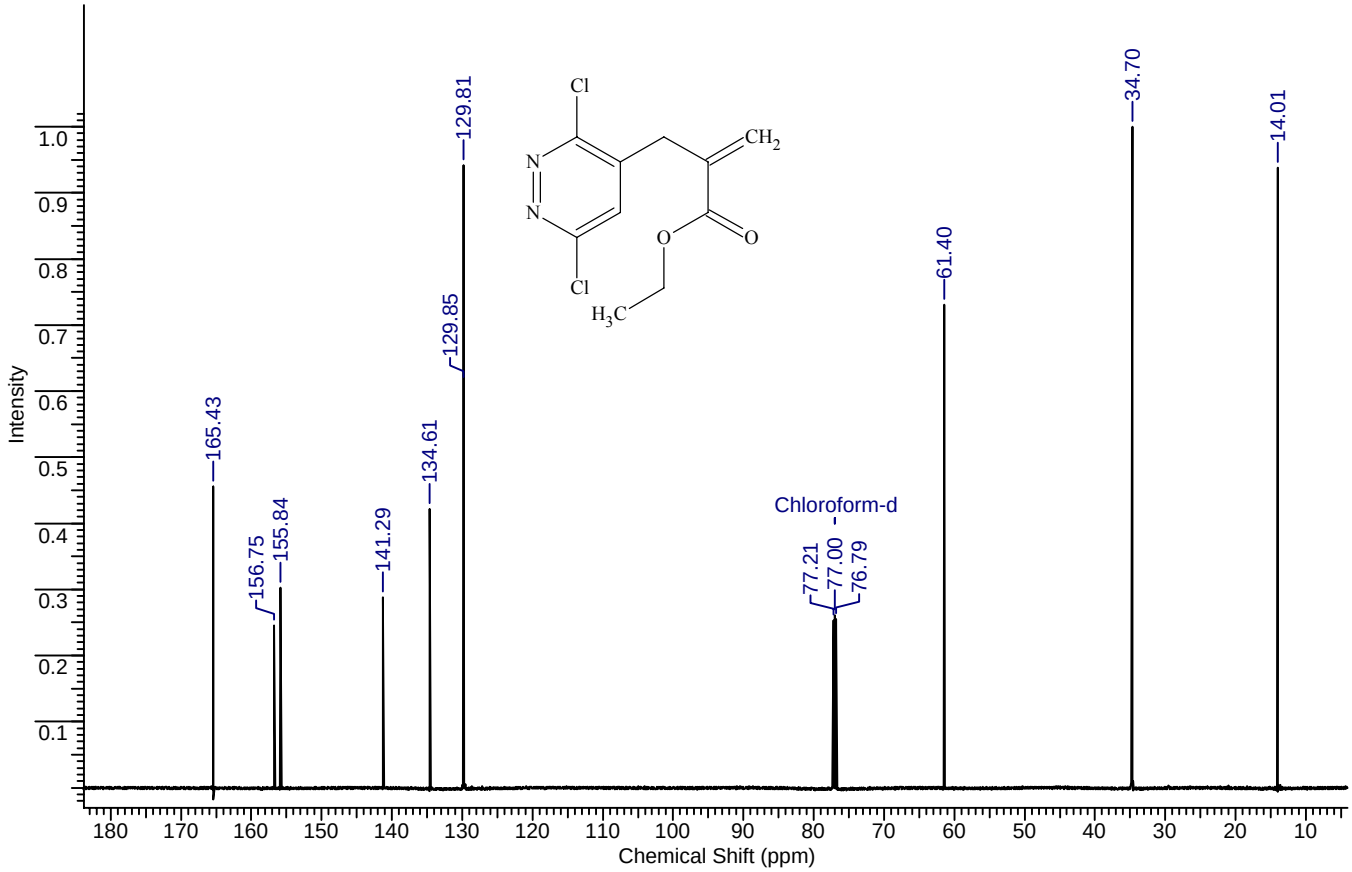
3,6-Dichloro-4-iodo-pyridazine (4a)



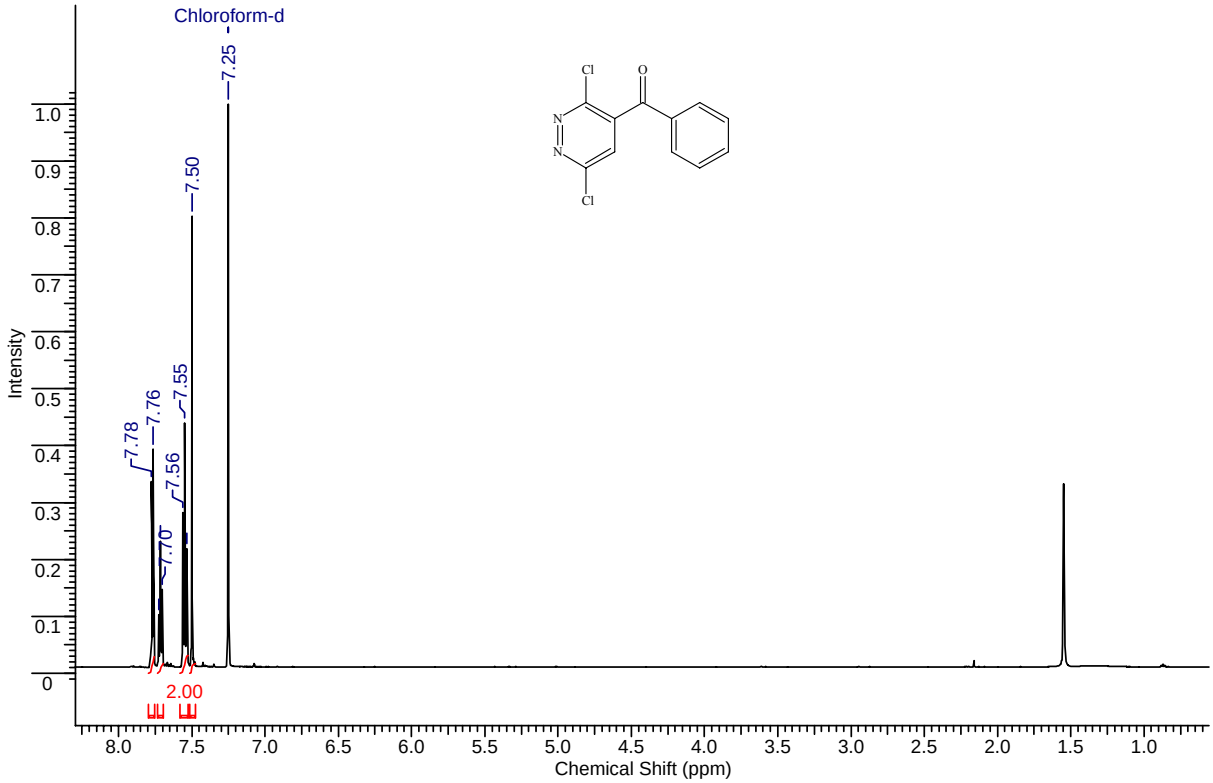


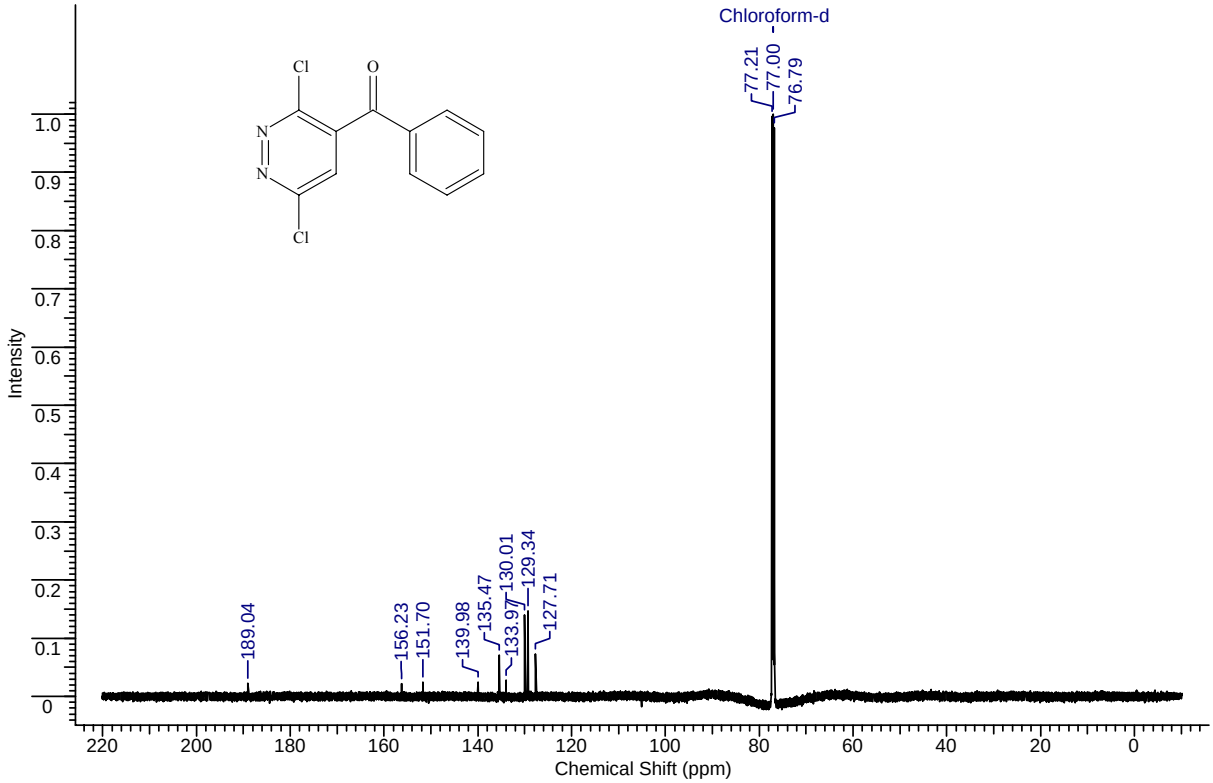
2-(3,6-Dichloro-pyridazin-4-ylmethyl)-acrylic acid ethyl ester (4b)



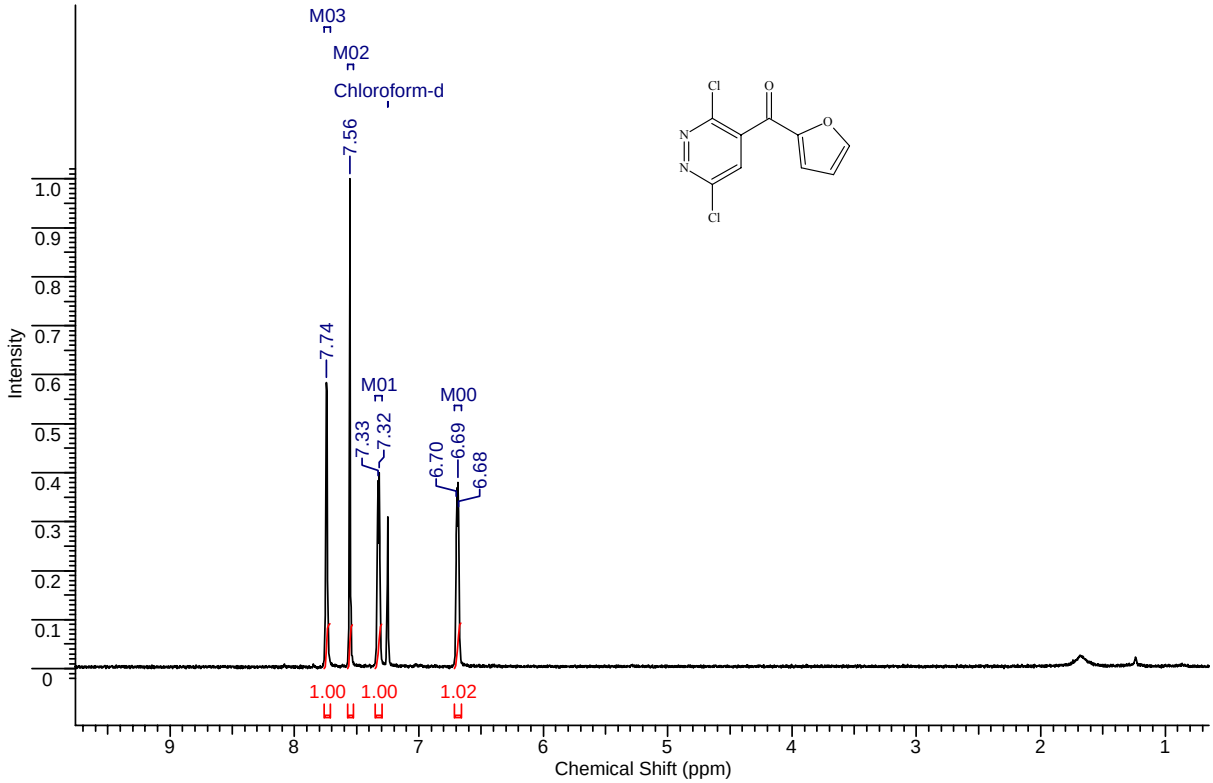


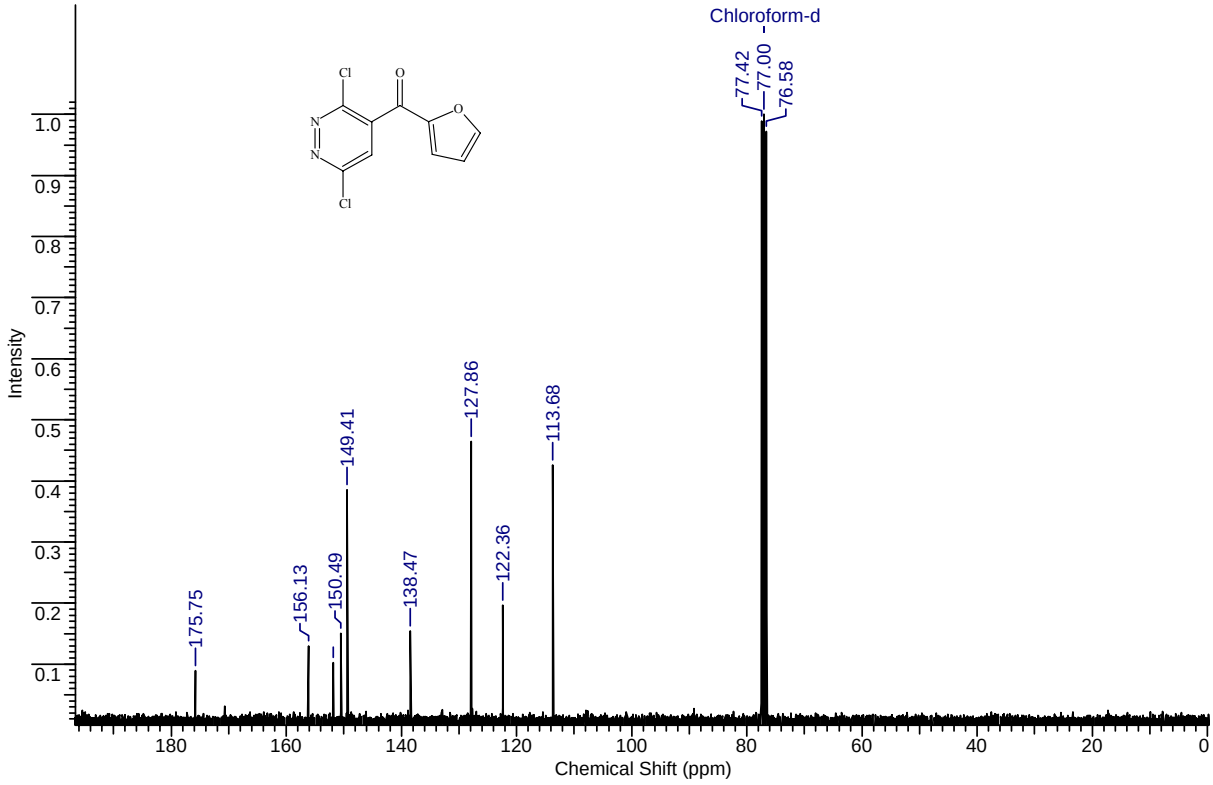
(3,6-Dichloro-pyridazin-4-yl)-phenyl-methanone (4c)



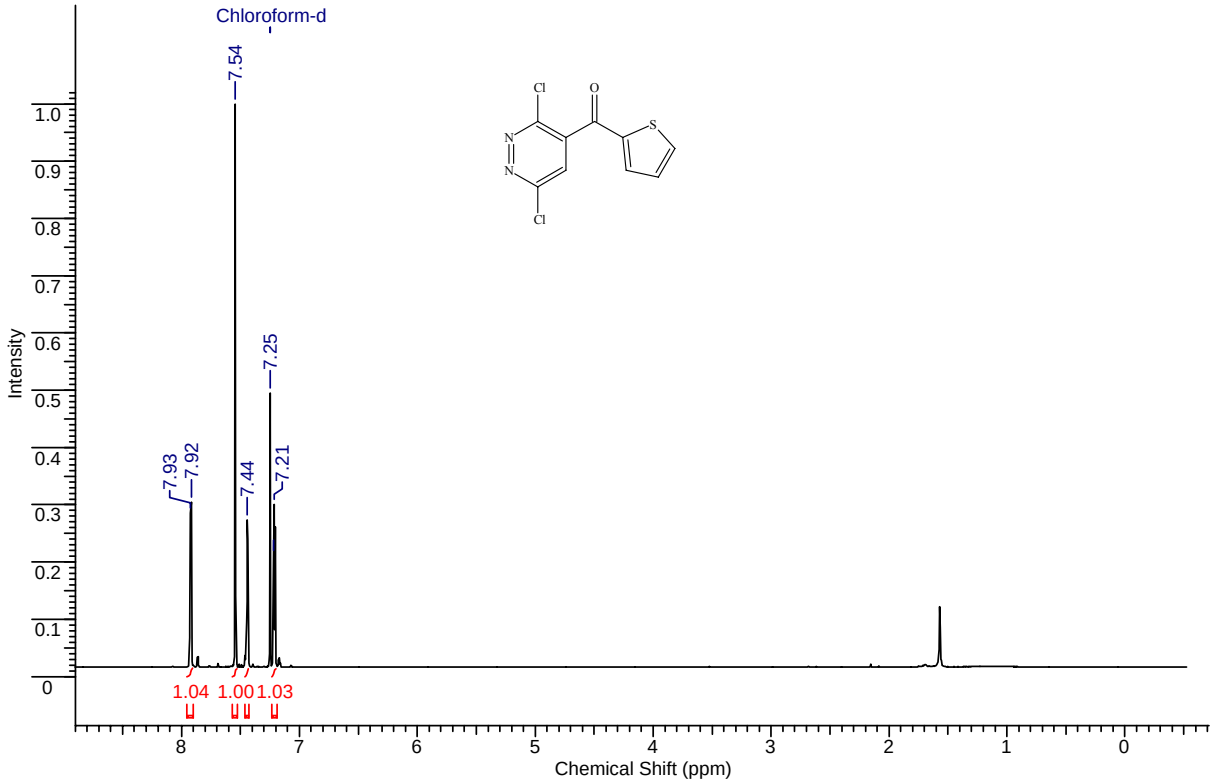


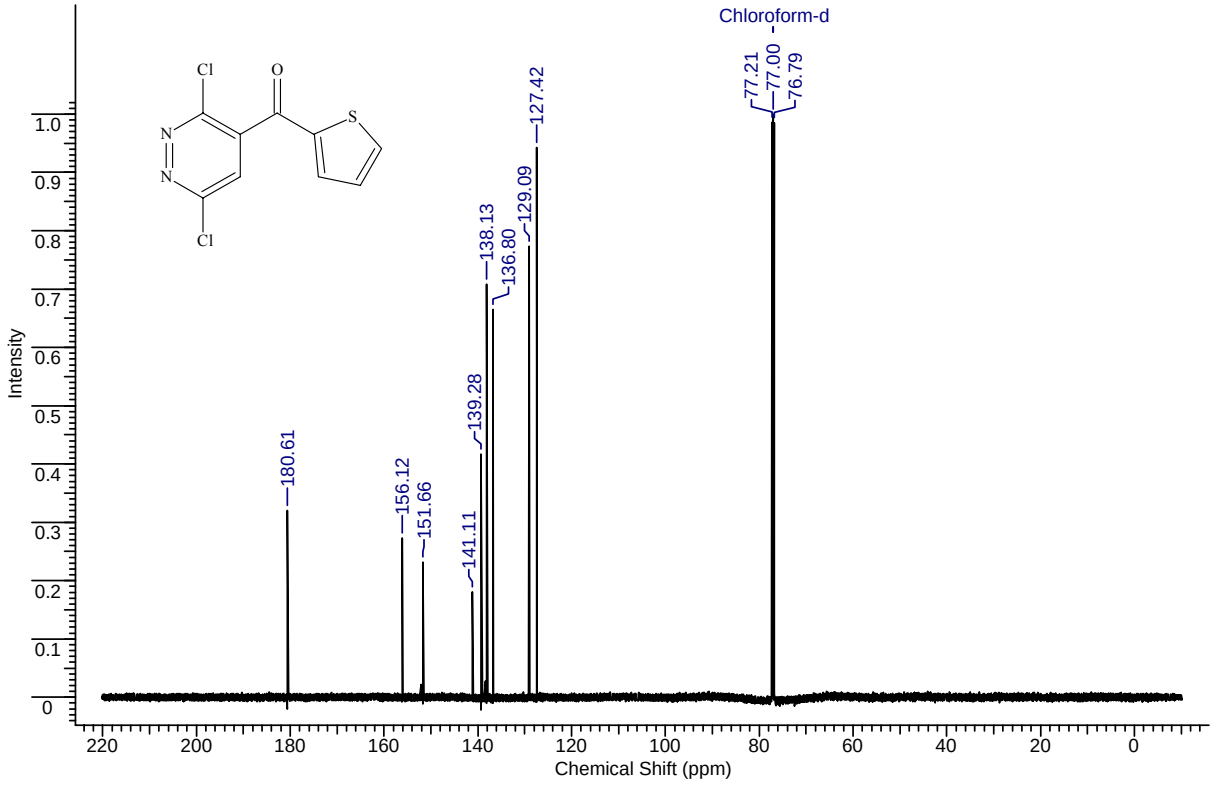
(3,6-Dichloro-pyridazin-4-yl)-furan-2-yl-methanone (4d)



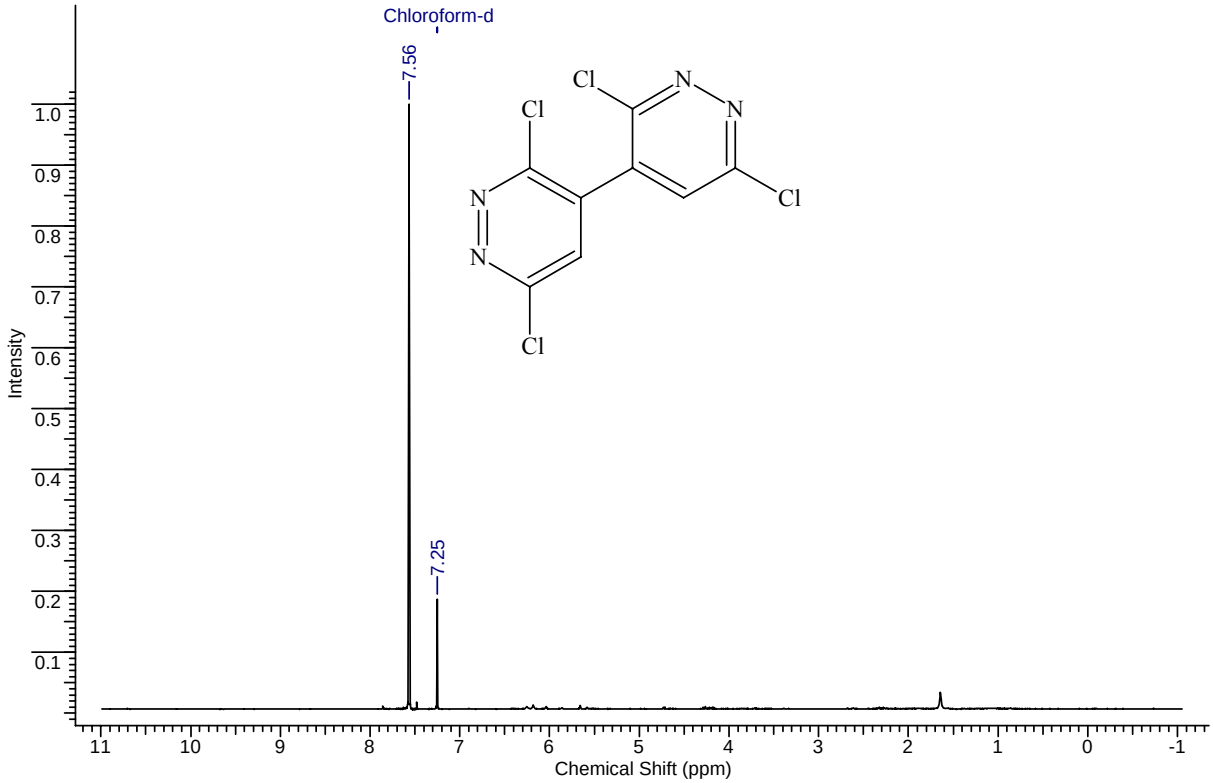


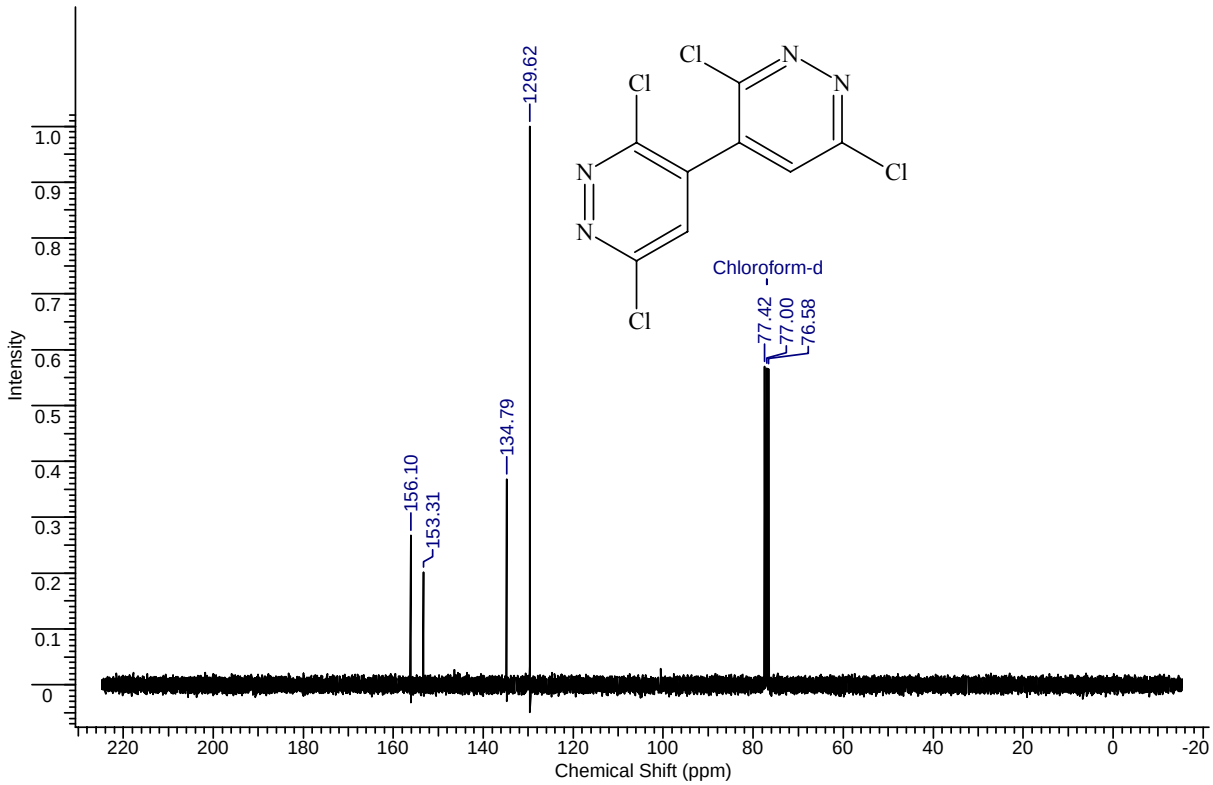
(3,6-Dichloro-pyridazin-4-yl)-thiophen-2-yl-methanone (4e)



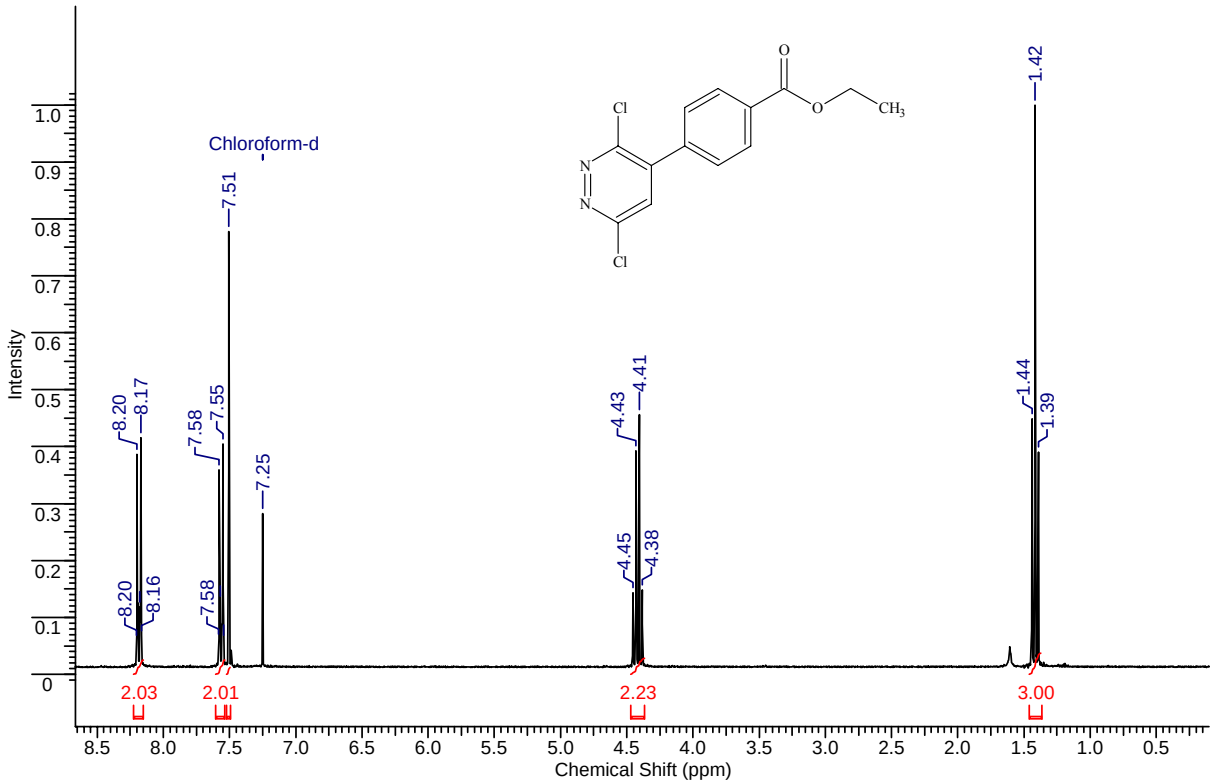


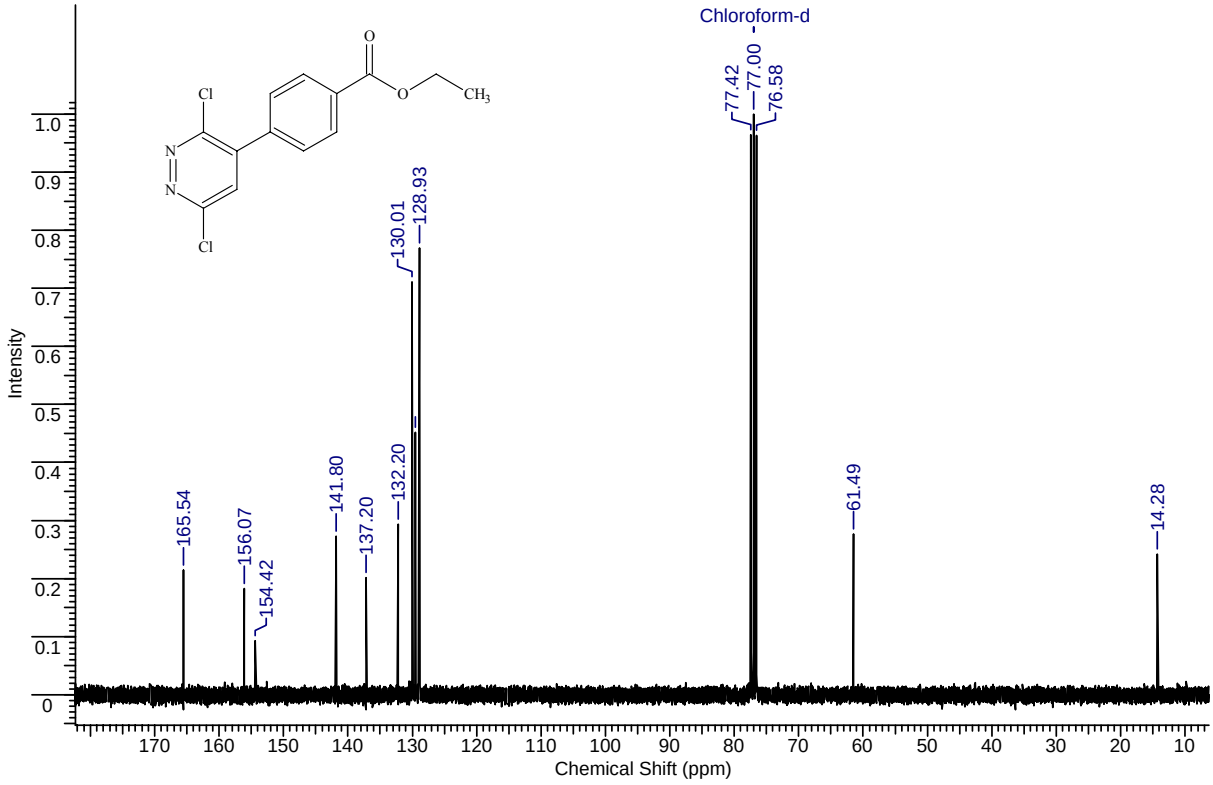
(3,6,3',6')-Tetrachloro-[4,4']bipyridazinyl (4f)



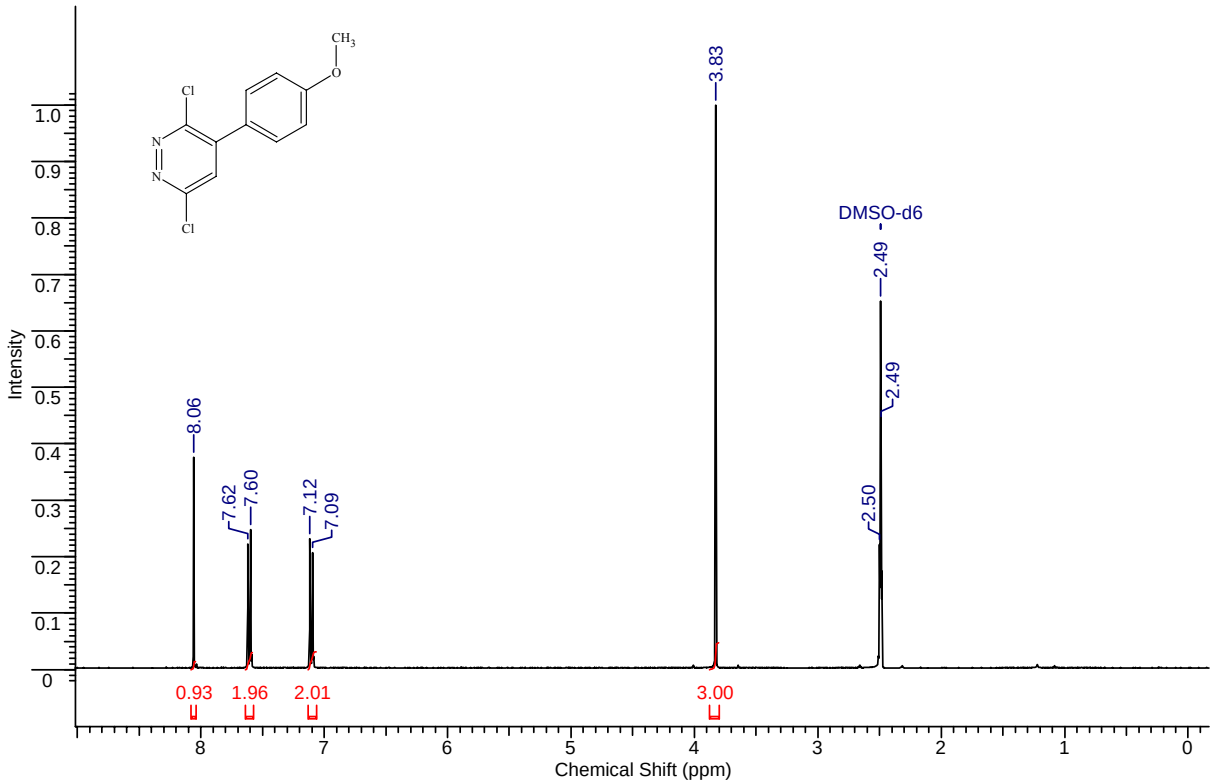


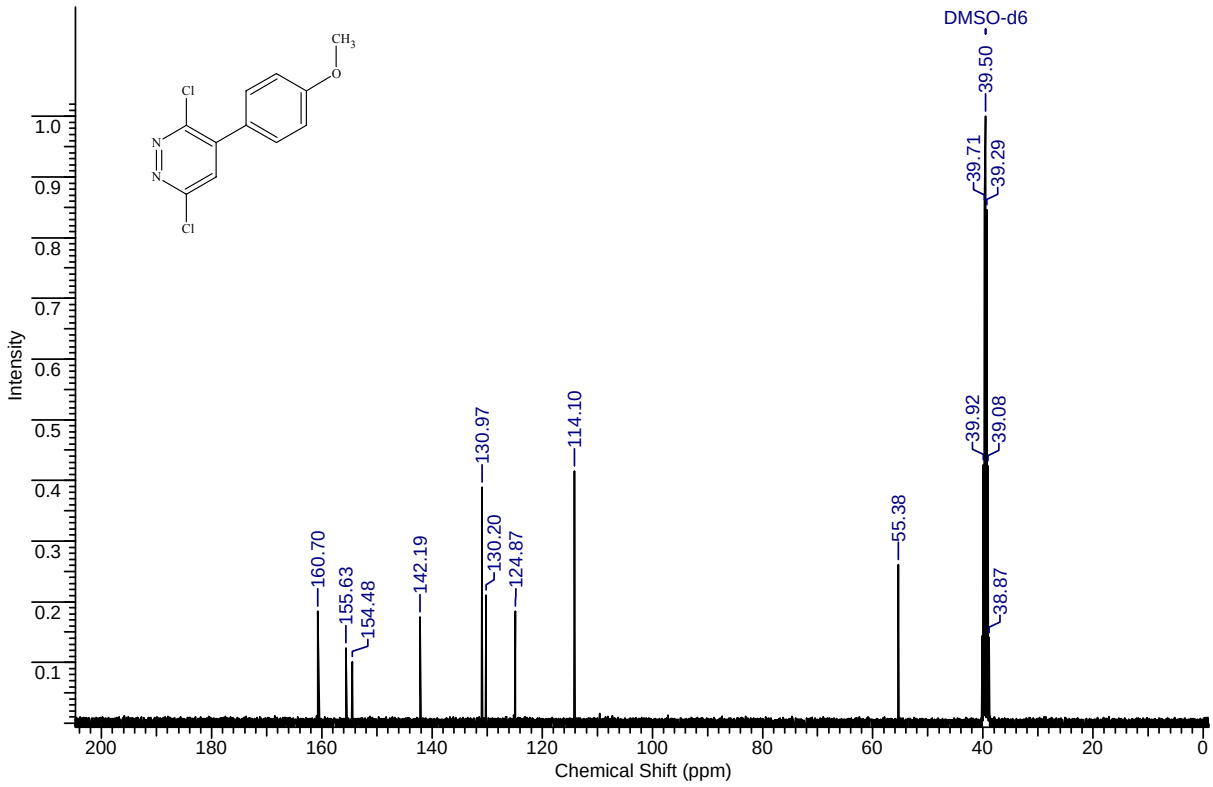
4-(3,6-Dichloro-pyridazin-4-yl)-benzoic acid ethyl ester (4g)



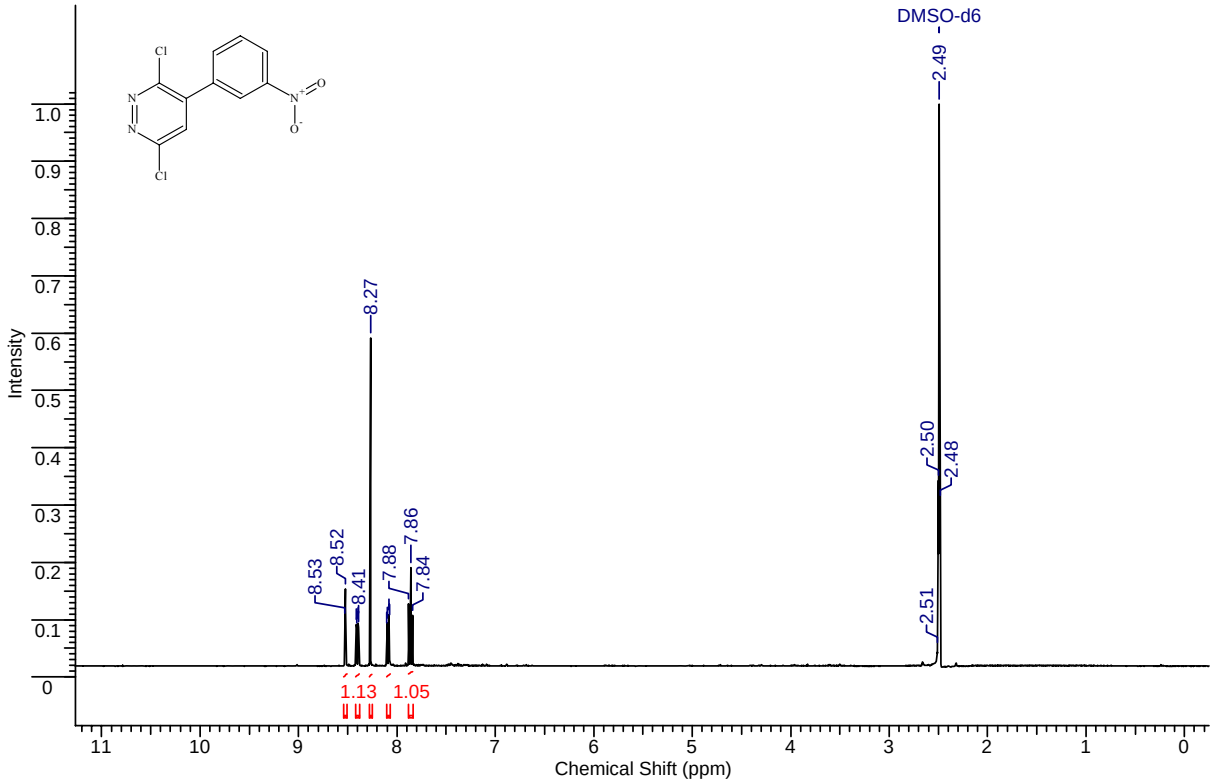


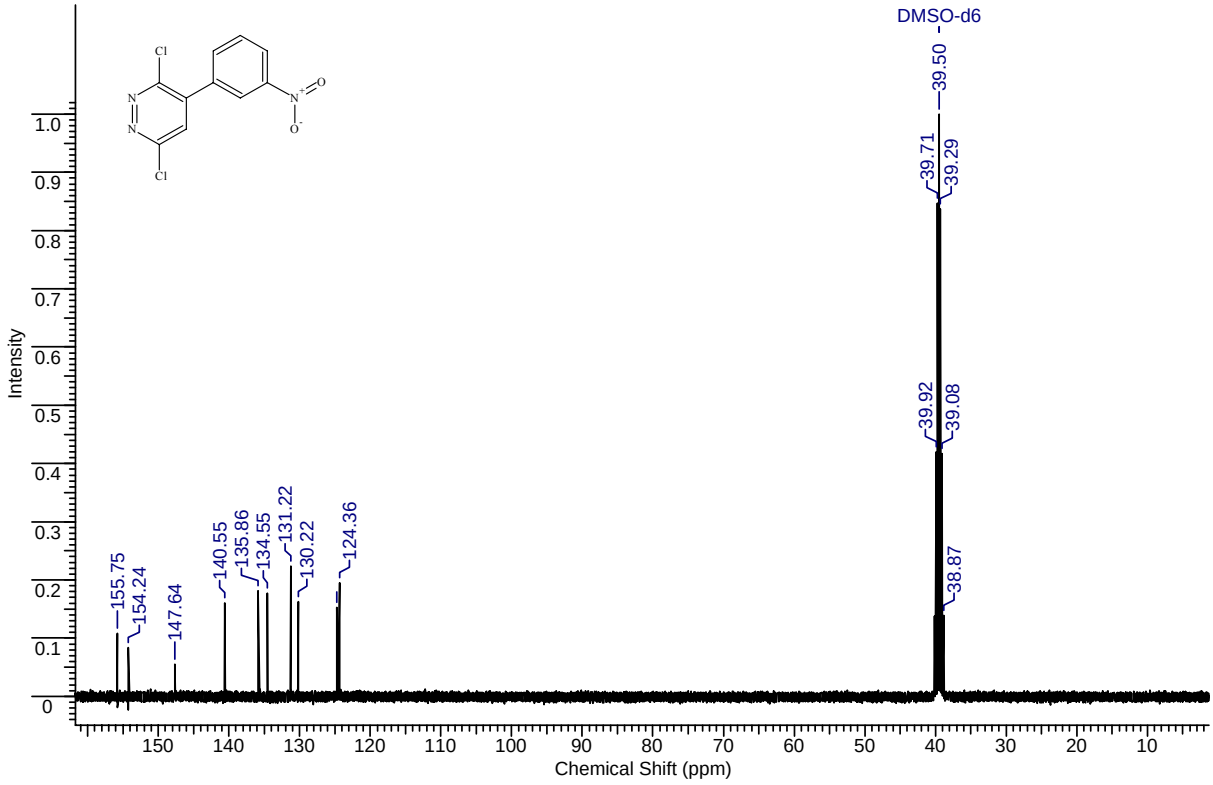
3,6-Dichloro-4-(4-methoxy-phenyl)-pyridazine (4h)



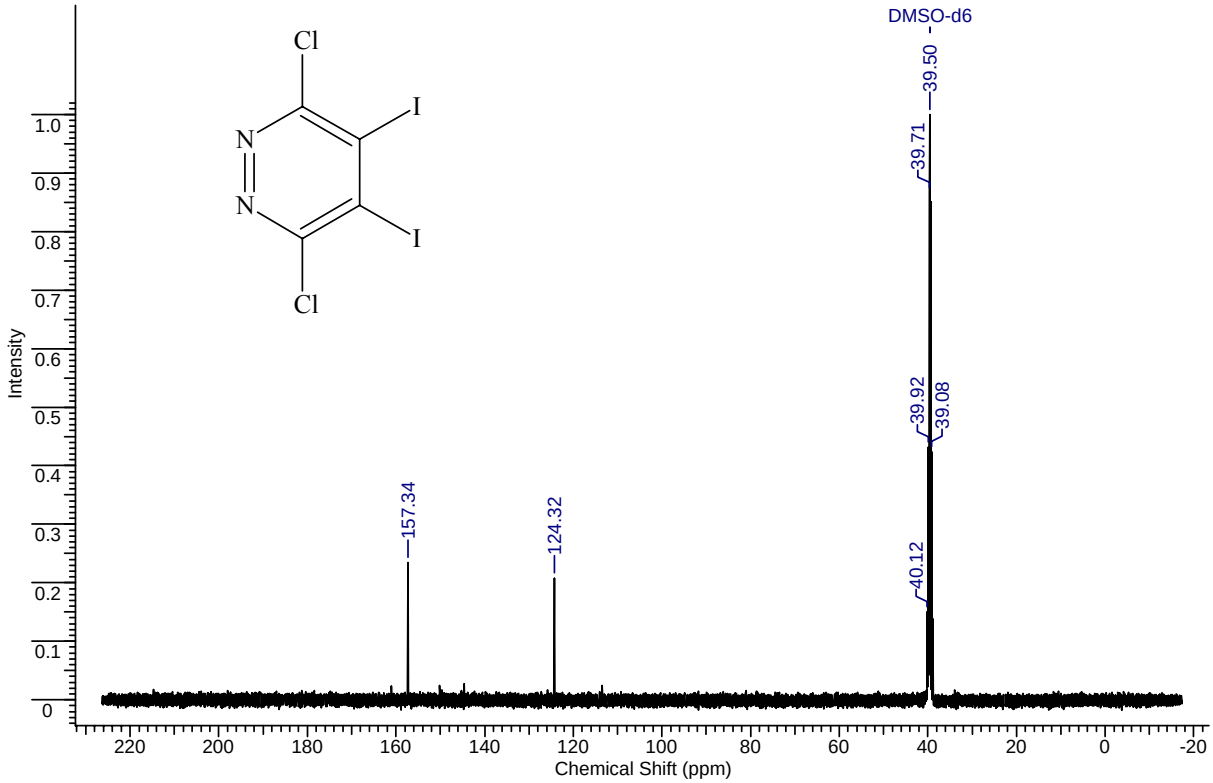


3,6-Dichloro-4-(3-nitro-phenyl)-pyridazine (4i)

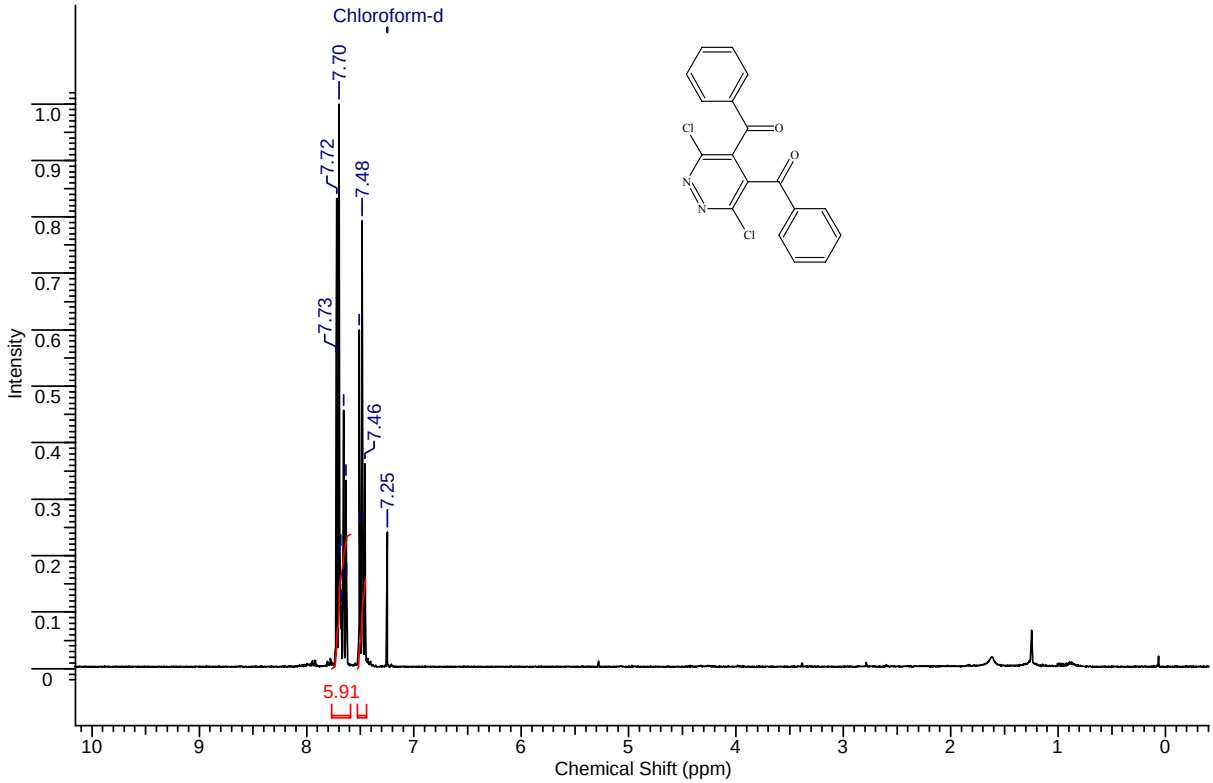


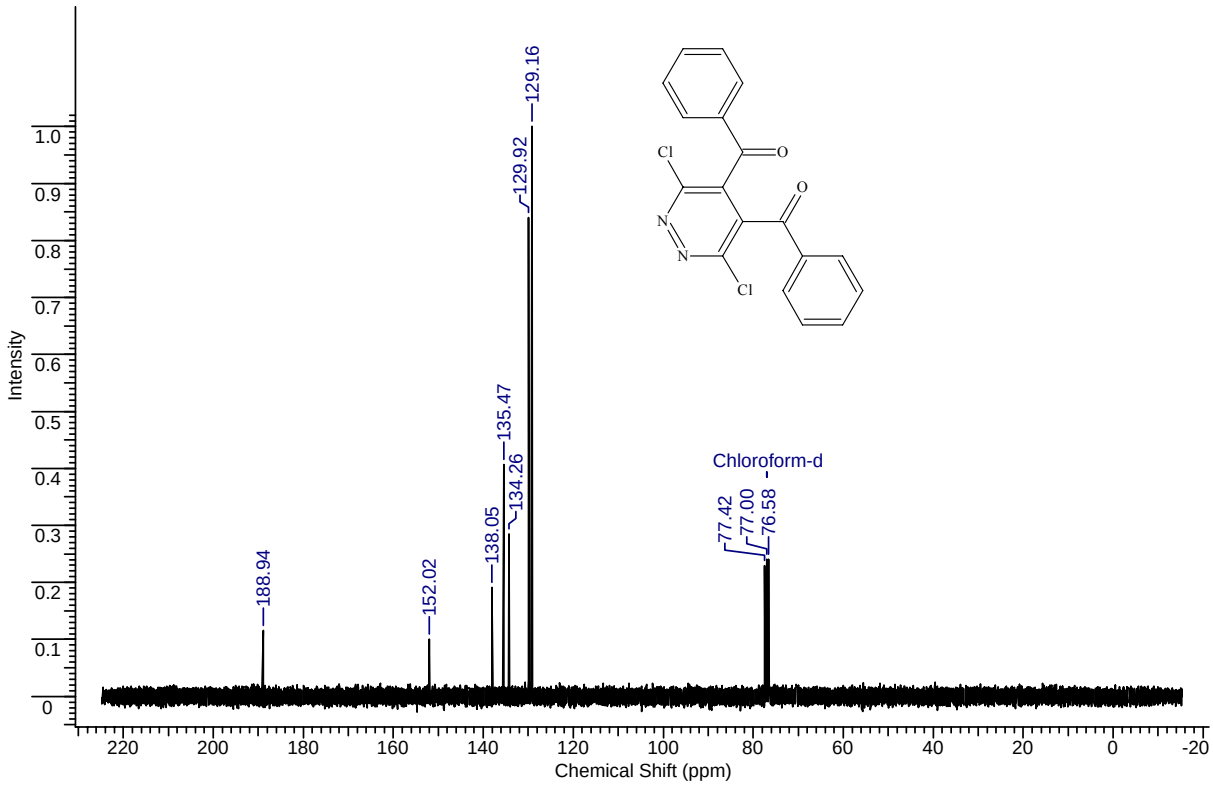


3,6-Dichlor-4,5-iodpyridazin (5a)

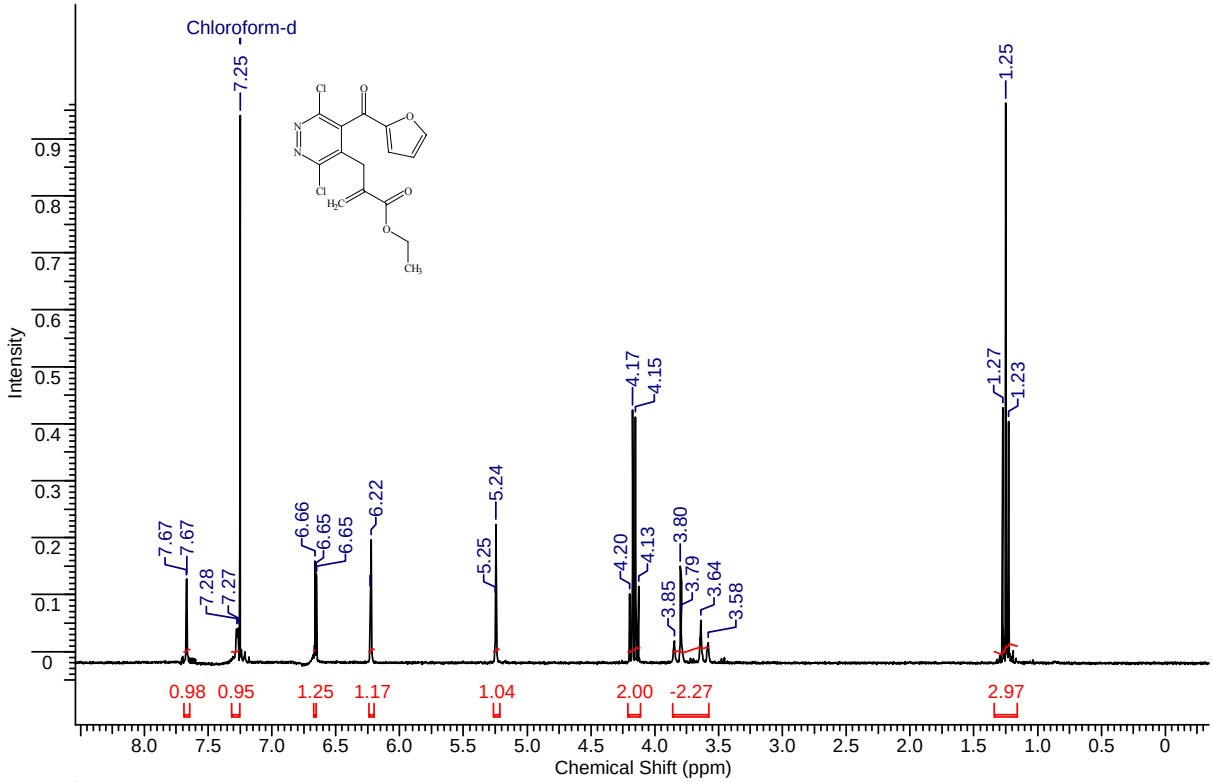


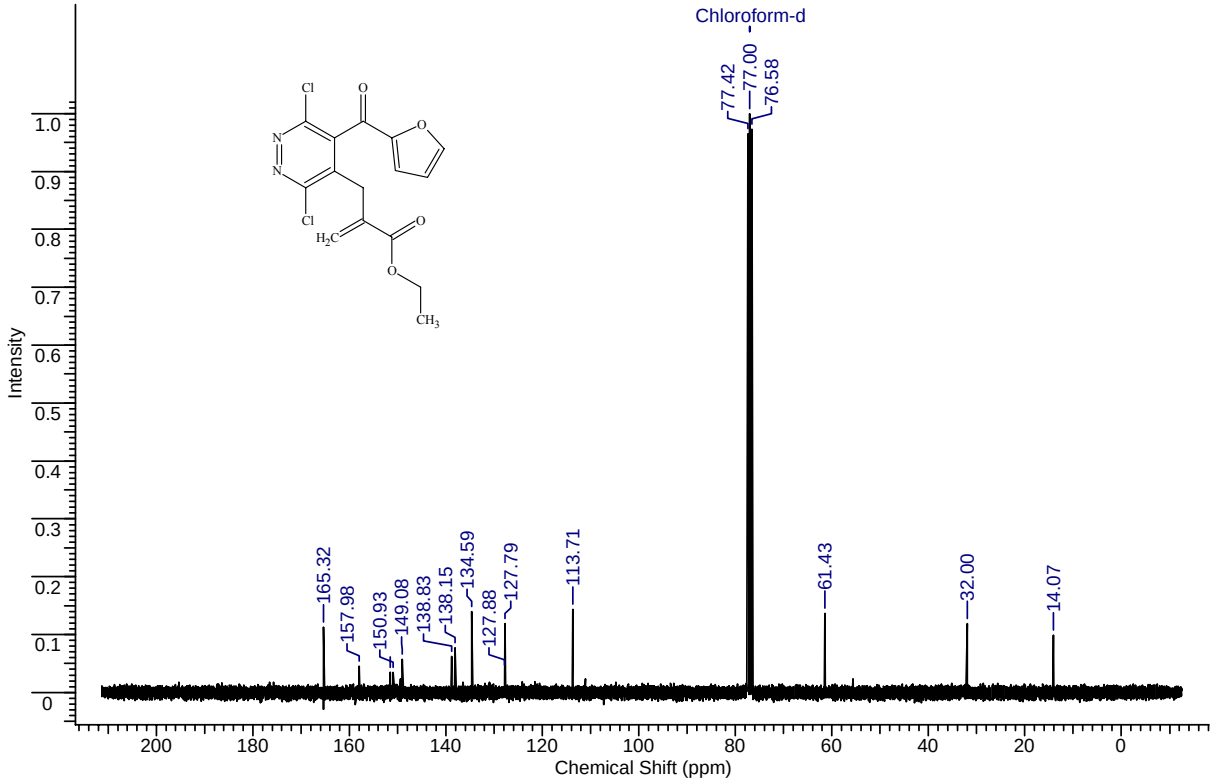
(5-Benzoyl-3,6-dichloro-pyridazin-4-yl)-phenyl-methanone (5b)



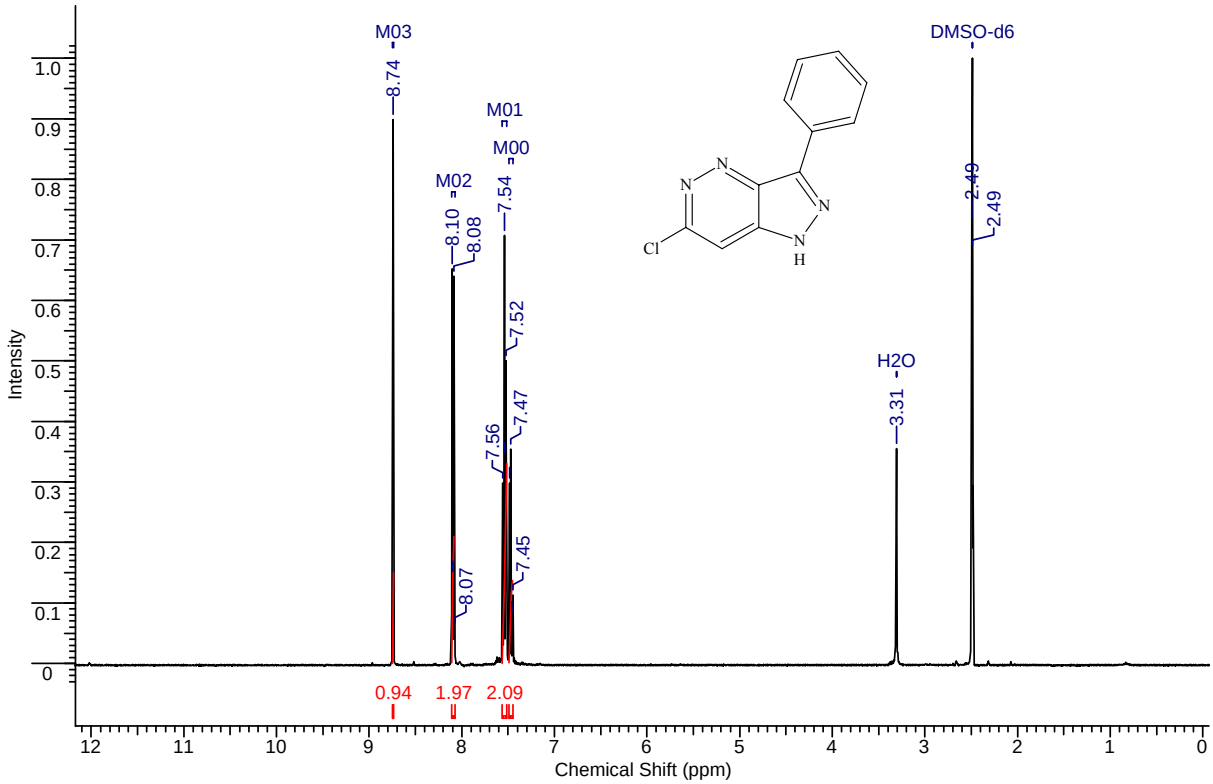


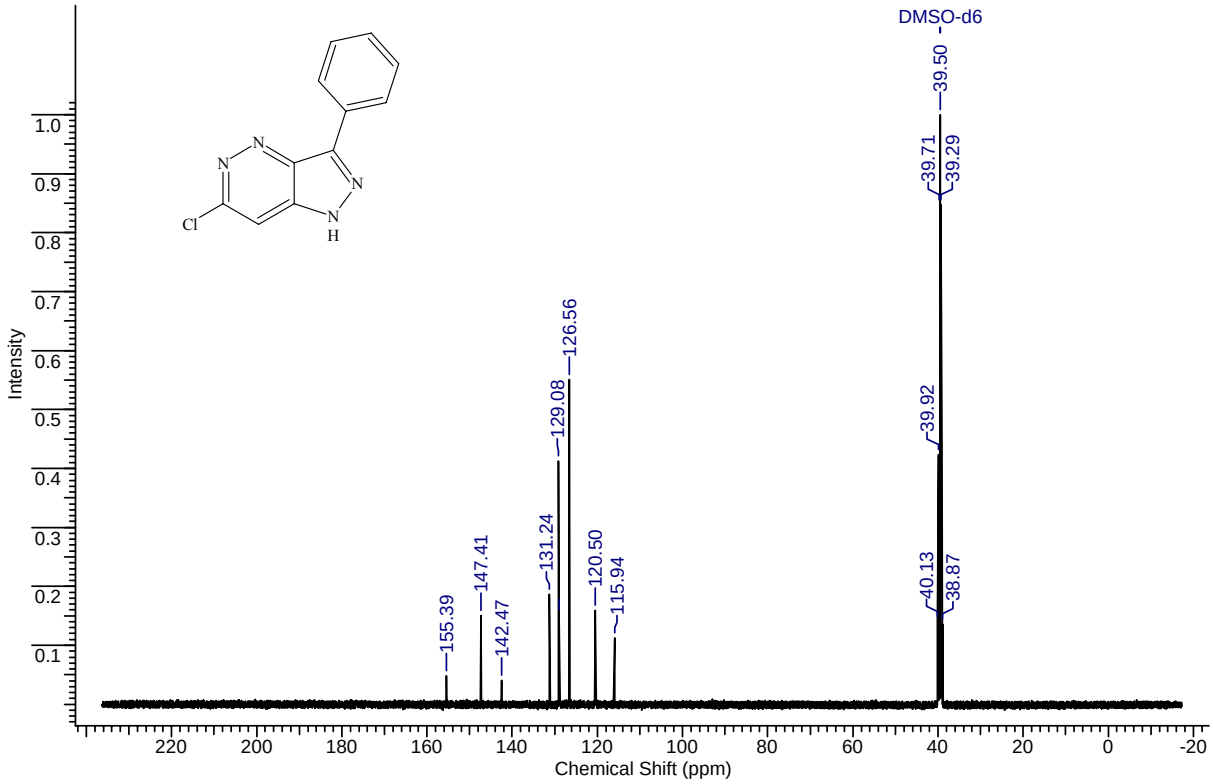
2-[3,6-Dichloro-5-(furan-2-carbonyl)-pyridazin-4-ylmethyl]-acrylic acid ethyl ester (5c)



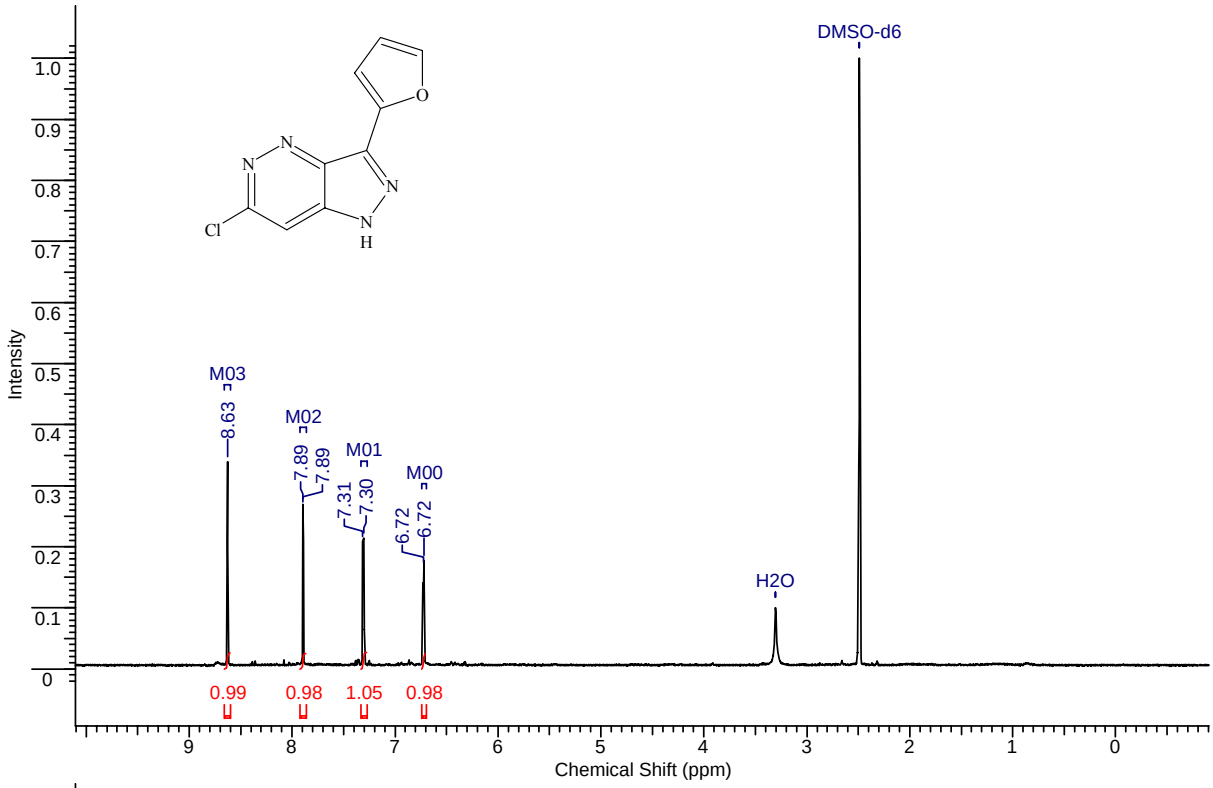


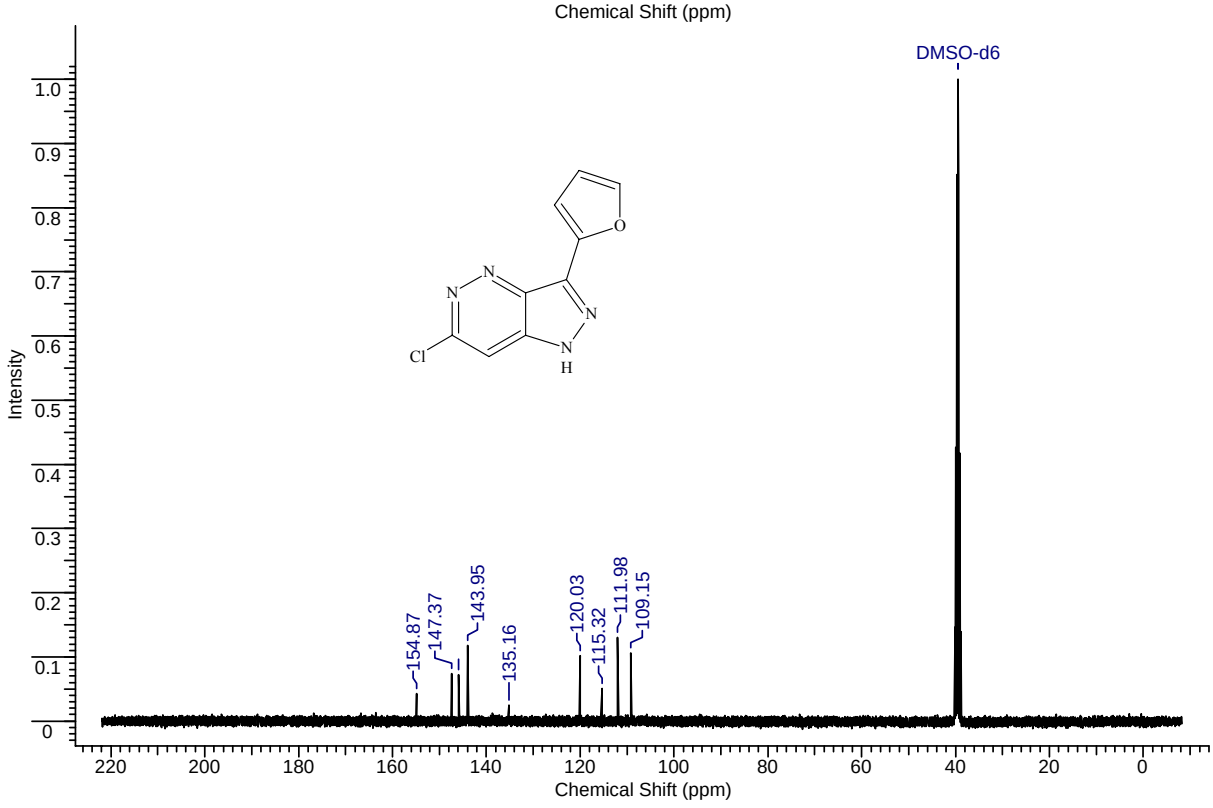
5-Chloro-3-phenyl-1H-pyrazolo[3,4-c]pyridazine (6a)



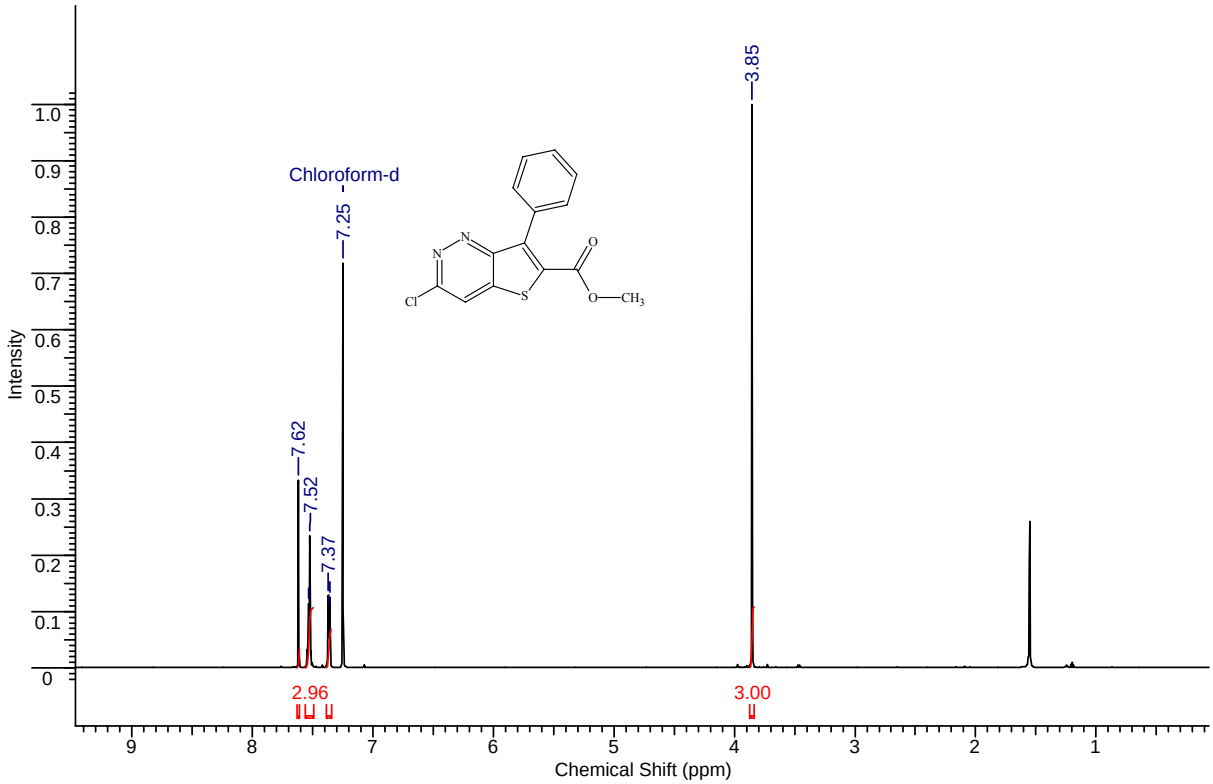


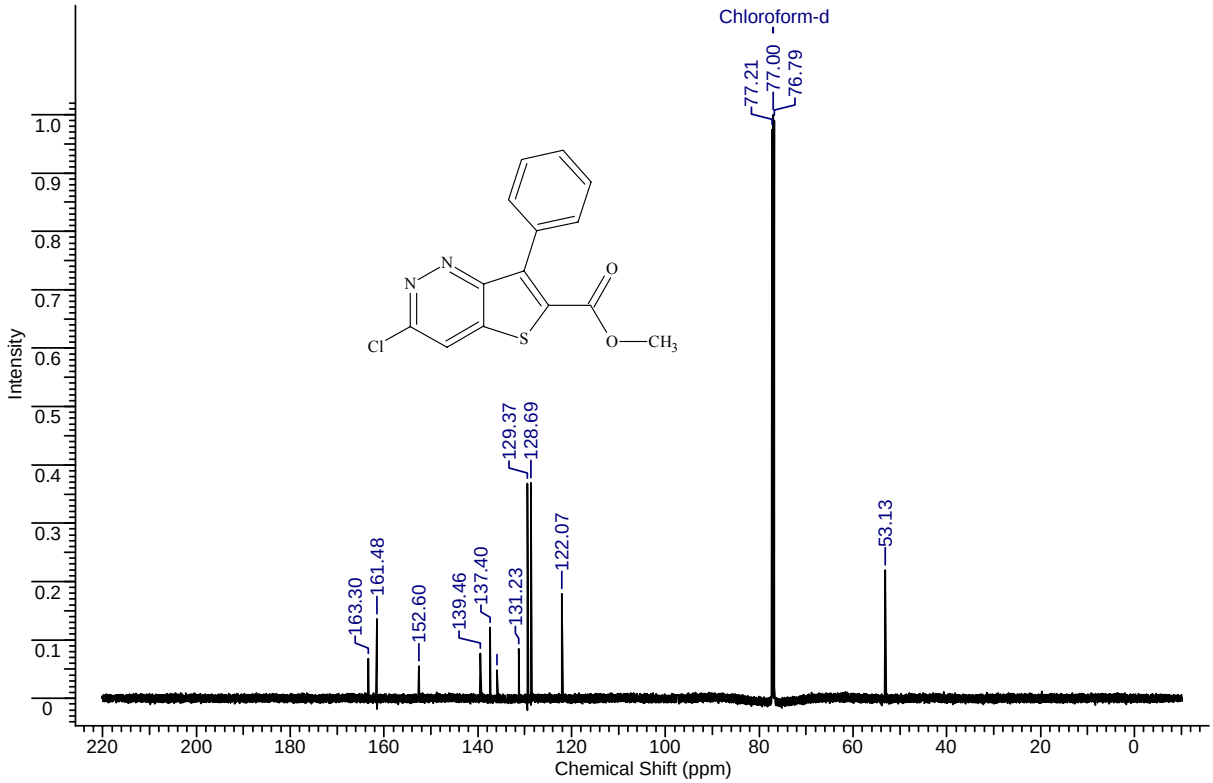
5-Chloro-3-furan-2-yl-1H-pyrazolo[3,4-*c*]pyridazine (6b)





3-Chloro-5-phenyl-thieno[2,3-c]pyridazine-6-carboxylic acid methyl ester (7a)





3-Chloro-5-furan-2-yl-thieno[2,3-c]pyridazine-6-carboxylic acid methyl ester (7b)