Desulfonative Photoredox Alkylation of N-Heteroaryl Sulfones – An Acid-free Approach for Substituted Heteroarene Synthesis

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Contents

1. General Considerations

Unless otherwise noted, all reactions were carried out under an inert atmosphere of argon or nitrogen via standard Schlenk techniques or in a glovebox. Reactions were monitored by HPLC, ^{1}H NMR, and/or by TLC on 254 nm silica gel plates. Thin layer chromatography was performed using hexanes/EtOAc as the eluents and visualized using $KMnO_4$ stain and/or UV light. Reactions were purified by flash chromatography accompanied with an automated system (visualized at 254 nm, monitored with all-wavelength and ELS detector) with silica cartridges (60 Å porosity, 20-40 μm). Unless otherwise mentioned, all sulfones were purchased from commercial sources and used as received. Eosin Y and Rodamin 6G were purchased from commercial sources and used as received, $[Ru(bpy)_3][PF_6]_2$,[1] $[Ir\{dF(CF_3)_2ppy\}_2(bpy)][PF_6]$,[2] and 4CzIPN[3] were synthesized according to literature procedures. Acetonee and DMF (extra dry, 99.8%) were purchased and used as received. Other solvents were purified either by distillation over Na or CaH_2 or by passing through alumina cartridges in a solvent purification system. Diisopropylammounium alkylbis(catecholato)silicates[4] and alkyl 1,4-dihydropyridines[5] were synthesized according to the literature. Sulfone substrates were either purchased or synthesized according to literature[6] and matched with reported data. Irradiation of reaction vessels was accomplished using 5W 455 nm blue LEDs (light emitting diodes) about 3 cm from the reaction vessel with a fan above to maintain room temperature. The photoredox reaction equipment was constructed according to a previous report.[7] Reaction optimization was carried out via high throughput experimentation and verified on the benchtop. Factors affecting reaction performance, such as solvents, photoredox catalysts, additives (e.g., transition metal, base, etc.), substrate loadings, as well as temperature have been thoroughly examined.

Melting points (°C) are uncorrected. NMR Spectra (^{1}H, ^{13}C {^{1}H}, ^{19}F) were recorded on a 500 MHz spectrometer at 298 K. All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signal for $CHCl_3$ (7.26 ppm). All ^{13}C NMR spectra were reported in ppm relative to residual $CHCl_3$ (77.2 ppm) and were obtained with ^{1}H decoupling. Coupling constants (*J*) are reported in Hertz (Hz). HRMS was obtained by either ESI or EI with a TOF spectrometer in CH_3CN or $CHCl_3$. IR spectra were obtained with neat samples.

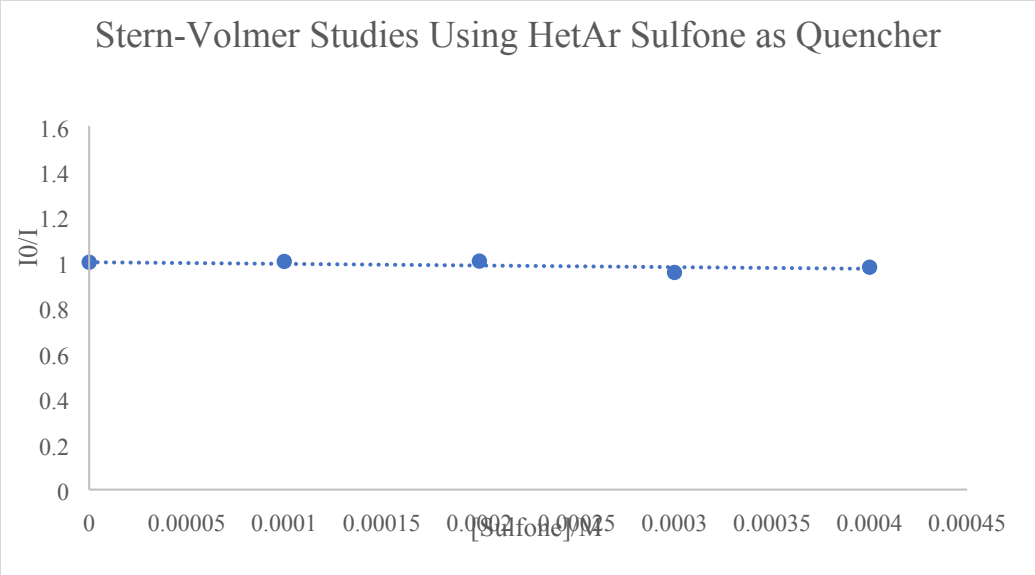
2. Mechanistic Study

2.1 Stern-Volmer Fluorescence Quenching Studies

Stern-Volmer experiments were conducted on a spectrofluorometer. Stock solutions of substrates, photocatalyst, and base were prepared with dry acetone. The solutions were mixed and purged with argon for 30 seconds accordingly right before measurement. The samples were excited at 435 nm, and emission data were recorded at 531 nm. I_0/I value of each sample were calculated from the average of three scans per data point. Linear regression of I_0/I against concentration was carried out to yield K_{sv}.

2.1.1 Quenching with Variable Amounts of Heteroaryl Sulfone

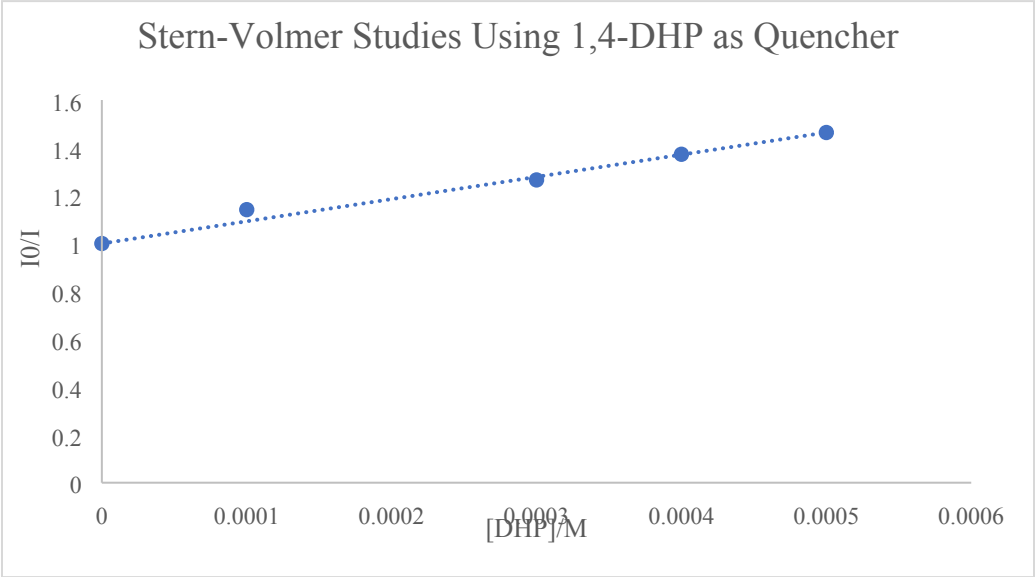
Species	Concentration (10^{-6} M)
4CzIPN	1.0
4,6-dichloropyrimidyl methylsulfone	100 to 400



As is shown in the chart, the trendline is parallel to X-axis, therefore the fluorescence of 4CzIPN is not quenched by 4,6-dichloropyrimidyl methylsulfone.

2.1.2 Quenching with Variable Amounts of Heteroaryl Sulfone

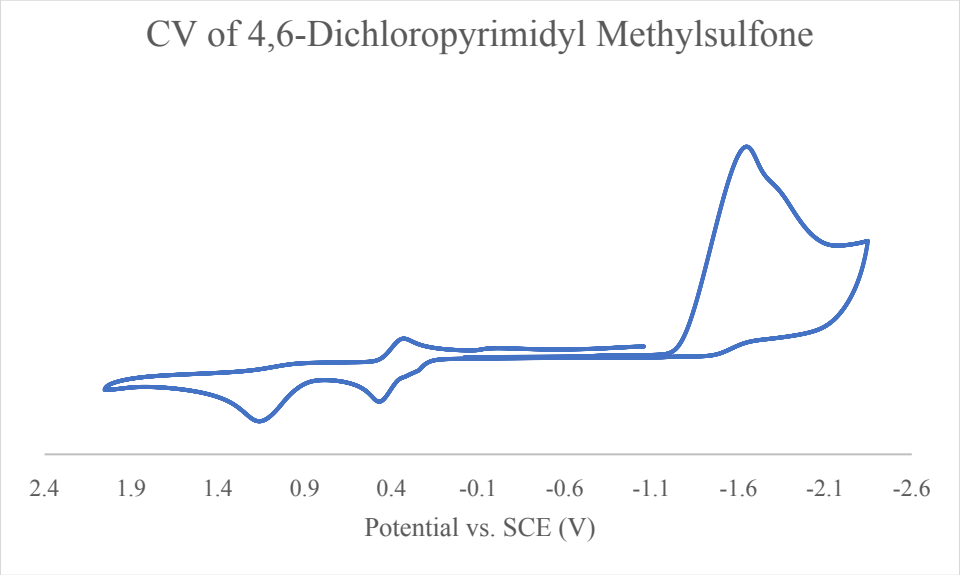
Species	Concentration (10^{-6} M)
4CzIPN	1.0
Tetrahydropyranyl 1,4-DHP	100 to 500



Linear relationship was observed with the K_{SV} = (9.3 ± 0.6) x 10^2 M^{-1}, when tetrahydropyranyl 1,4-DHP was applied. This suggested dynamic quenching of the photocatalyst 4CzIPN, which is in line with the proposed mechanism

2.2 Cyclic Voltammetry of 4,6-Dichloropyrimidyl Methylsulfone

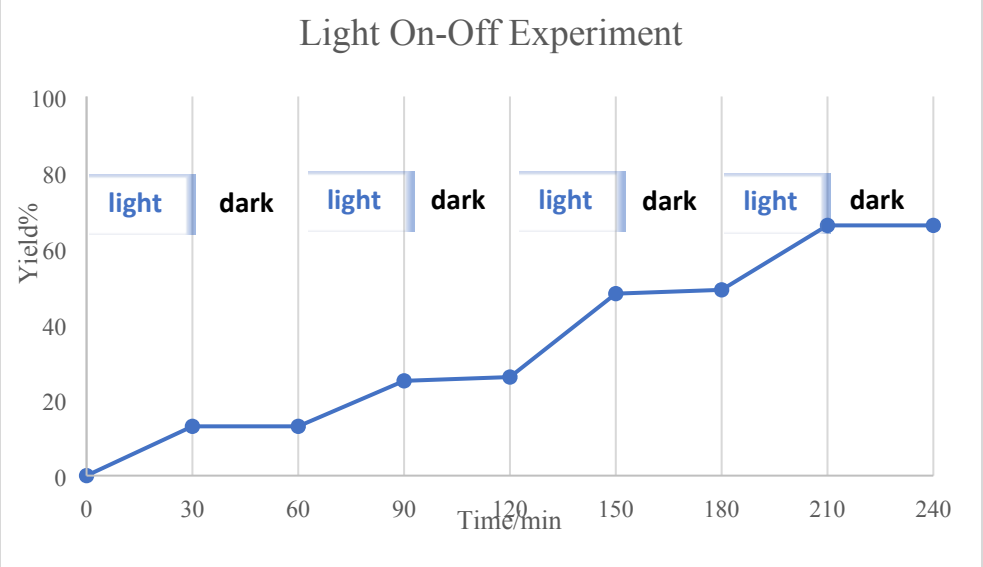
Cyclovoltammetry experiment was carried out on a CHI electrochemical workstation using glassy carbon working electrode, Ag/AgCl reference electrode and Pt wire counter electrode. The measurements were taken at room temperature in MeCN containing 0.1 M Bu_4NPF_6 as electrolyte. 0.05 mmol of the designated substrate was dissolved in 10 mL of such solution, and 1.9 mg of ferrocene was added as reference. A scan rate of 200mV/s was used for the reported voltagrams, although the measurements were taken at three different scan rates.



$E^{red}_{(sulfone^{\cdot -}/sulfone)}$ = -1.68 V (vs. SCE), which has exceeded the range of reduced photocatalysts used in this project.

2.3 Light Switch On-Off Experiment

time/min	0	30	60	90	120	150	180	210	240
yield%	0	13	13	25	26	48	49	66	66



Light switch on-off experiment was carried out under standard reaction condition, using 4,6-dichloro-2-(methylsulfonyl)pyrimidine and cyclohexyl DHP as substrates and 1,3,5-trimethoxybenzene as internal standard. Light was switched on and off on 30-minute intervals, and reaction was monitored by NMR after each period. As is shown on the chart, during light-off periods of the reaction, formation of desired product was completely halted, which favors the photocatalysis or short radical chain propagation pathway.

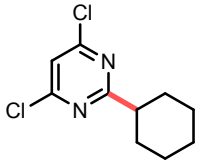
3. Acid-free Photoredox Alkylation of *N*-Heteroaromatic Sulfones

3.1 Alkylation using Diisopropylammonium Alkylbis(catecholato)silicates

3.1.1 General Procedure Using Alkylsilicates (GP1)

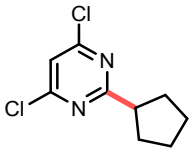
To an 8-mL reaction vial equipped with a stir bar and septa screw-cap were added organosilicates (0.6 mmol, 1.2 equiv), heteroaryl methyl sulfones (0.5 mmol, 1 equiv), $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 2.5 mmol %). The vial was subsequently closed, and three vacuum/argon cycles were performed, followed by addition of 5 mL of dry DMF (0.1 M). After stirring under a blue LED for 16 h, the reaction was diluted with 40 mL of EtOAc and washed three times with 30 mL of saturated Na_2CO_3 and subsequently three times with 30 mL of brine. The organic phase was dried ($MgSO_4$), and the solvent was removed by rotvap. The product was purified by flash column chromatography, using hexanes and EtOAc as eluent.

3.1.2 Characterization Data



4,6-Dichloro-2-cyclohexylpyrimidine (3a)

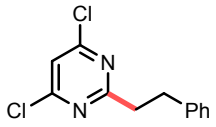
Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium cyclohexyl bis(catecholato) silicate (257.5 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (95.9. mg, 83%). mp = 85 – 87 ℃. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.57 (s, 1H), 3.38 (t, *J* = 12.4 Hz, 1H), 2.21 (tt, *J* = 12.5, 12,5 Hz, 2H), 1.89 (d, *J* = 13.0 Hz, 2H), 1.77 (d, *J* = 12.9 Hz, 1H), 1.65 (d, *J* = 12.8 Hz, 2H), 1.37 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 155.1, 136.4, 41.1, 28.1, 26.8, 25.7. IR (neat, cm^{-1}): 2959, 2937, 2851, 1720, 1533, 1511, 1446, 1414,1370, 1350, 1331, 1284, 1215, 1128, 1086, 1044, 1018, 843, 818, 782. HRMS (EI+) calcd for ($C_{10}H_{12}Cl_2N_2$) $[M]^+$ 230.0378 found 230.0369.



4,6-Dichloro-2-cyclopentylpyrimidine (3b)

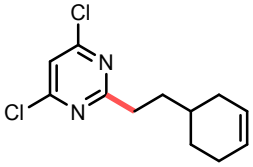
Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium cyclopentyl bis(catecholato) silicate (249.4 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred

under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (72.7 mg, 67%). mp = 79 – 81 °C. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.57 (s, 1H), 3.77 (p, *J* = 9.3 Hz, 1H), 2.12 – 2.05 (m, 2H), 1.97 – 1.91 (m, 4H), 1.75 – 1.69 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7, 155.0, 135.8, 39.9, 29.8, 27.1. IR (neat, cm^{-1}): 3205, 2953, 2872, 1530, 1510, 1455, 1413, 1359, 1345, 1327, 1133, 828. HRMS (EI+) calcd for ($C_9H_{10}Cl_2N_2$) $[M]^+$ 216.0221, found 216.0226.



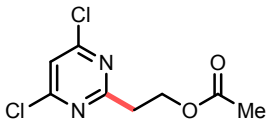
4,6-Dichloro-2-phenethylpyrimidine (3c)

Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium benzyl bis(catecholato) silicate (262.6 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (96.8 mg, 81%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 3H), 3.20 – 3.16 (m, 2H), 2.93 – 2.89 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.0, 155.8, 140.0, 132.7, 128.8, 128.5, 126.8, 33.5, 32.5. IR (neat, cm^{-1}): 3027, 1544, 1528, 1516, 1496, 1454, 1413, 1355, 1336, 1134, 993.8. HRMS (EI+) calcd for ($C_{12}H_{10}Cl_2N_2$) $[M]^+$ 252.0221, found 252.0207.



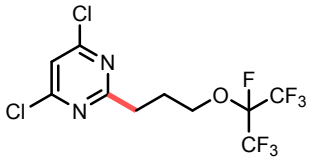
4,6-Dichloro-2-(2-(cyclohex-3-en-1-yl)ethyl)pyrimidine (3d)

Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 2-(cyclohex-3-en-1-yl)ethyl bis(catecholato)silicate (273.4 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (57.9 mg, 45%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.62 (s, 1H), 5.71 – 5.64 (m, 2H), 2.97 – 2.90 (m, 2H), 2.21 (d, *J* = 17.2 Hz, 1H), 2.15 – 2.03 (m, 3H), 1.83 (d, *J* = 16.1 Hz, 1H), 1.70 – 1.66 (m, 1H), 1.61 – 1.56 (m, 2H), 1.39 – 1.31 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7, 155.5, 134.0, 127.3, 126.2, 34.0, 33.9, 31.6, 28.6, 28.1, 25.2. IR (neat, cm^{-1}): 2916, 2874, 1543, 1514, 1409, 1138, 845, 789. HRMS (EI+) calcd for ($C_{12}H_{14}Cl_2N_2$) $[M]^+$ 256.0534, found 256.0533.



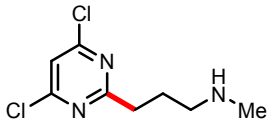
2-(4,6-Dichloropyrimidin-2-yl)ethyl acetate (3e)

Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium acetoxyethyl bis(catecholato)silicate (259.9 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (54.1 mg, 46%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.68 (s, 1H), 4.38 (t, *J* = 6.5 Hz, 2H), 3.28 (t, *J* = 6.5 Hz, 2H), 2.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 162.6, 156.4, 129.8, 61.0, 29.8, 21.0. IR (neat, cm^{-1}): 2926, 1742, 1516, 1411, 1362, 1229, 1040, 805, 787. HRMS (ES+) calcd for ($C_8H_9Cl_2N_2O_2$) $[M+H]^+$ 235.0041, found 235.0056.



4,6-Dichloro-2-(4,5,5,5-tetrafluoro-4-(trifluoromethyl)pentyl)pyrimidine (3f)

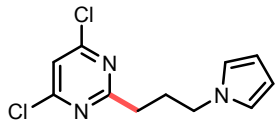
Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 2-(4,5,5,5-tetrafluoro-4-(trifluoromethyl)pentyl bis(catecholato)silicate (334.6 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (111.3 mg, 62%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.66 (s, 1H), 4.13 (t, *J* = 5.8 Hz, 2H), 3.12 – 3.00 (m, 2H), 2.03 (tt, *J* = 8.0, 5.8 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 162.0, 156.1, 132.2, 27.2, 26.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -78.99 (s, 6F), -142.25 (s, 1F). IR (neat, cm^{-1}): 1543, 1516, 1454, 1411, 1353, 1224, 1168, 1076. HRMS (EI+) calcd for ($C_{10}H_7Cl_2F_7N_2O$) $[M^+]$ 373.9824; found 373.9818. Although perfluoroisopropyl peaks are missing, both ^{19}F NMR and HRMS indicate its presence.



3-(4,6-Dichloropyrimidin-2-yl)-N-methylpropan-1-amine (3g)

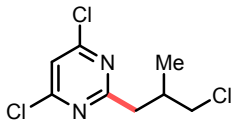
Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium N-Methylpropylamino bis(catecholato)silicate (251.2 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (61.4 mg, 45%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.21 (s, 1H), 6.40 – 6.04 (br, 1H), 3.46 – 3.38 (m, 2H), 3.17 (s, 3H), 2.77 (t, *J* = 6.5 Hz, 2H), 1.98 (m, 2H). ^{13}C NMR (126

MHz, $CDCl_3$) δ 155.4, 120.8, 115.2, 49.3, 36.4, 23.7, 20.0. IR (neat, cm^{-1}): 2950, 1580, 1549, 1354, 1192, 1060, 770. HRMS (EI+) calcd for ($C_8H_{11}Cl_2N_3$) $[M]^+$ 219.0330, found 219.0329.



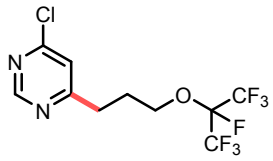
2-(3-(1*H*-Pyrrol-1-yl)propyl)-4,6-dichloropyrimidine (3h)

Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 3-(N-pyrrole)propyl bis(catecholato)silicate (251.2 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (61.4 mg, 45%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.64 (s, 1H), 6.70 (t, *J* = 4.0 Hz, 2H), 6.18 (t, *J* = 4.5 Hz, 2H), 4.04 (t, *J* = 13.5 Hz, 2H), 2.88 – 2.85 (m, 2H), 2.14 – 2.08 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 155.9, 132.5, 120.6, 108.6, 49.2, 29.0, 27.7. IR (neat, cm^{-1}): 2981, 2254, 1710, 1416, 1362, 1223, 1091, 906, 725, 648, 531. HRMS (EI+) calcd for ($C_8H_{11}Cl_2N_3$) $[M]^+$ 255.0330, found 255.0329



4,6-Dichloro-2-(3-chloro-2-methylpropyl)pyrimidine (3i)

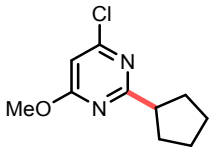
Following general procedure GP1 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 3-chloro-2-methylpropyl bis(catecholato)silicate (262.9 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (34.7 mg, 62%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.66 (s, 1H), 3.61 – 3.49 (m, 2H), 3.09 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.90 (dd, *J* = 13.8, 8.6 Hz, 1H), 2.41 (dt, *J* = 8.2, 6.0 Hz, 1H), 1.08 (d, *J* = 6.8 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5, 156.0, 131.8, 50.4, 35.3, 34.5, 17.7. IR (neat, cm^{-1}): 2927, 1541, 1514, 1458, 1407, 1355, 1295, 1066, 882. HRMS (ES+) calcd for ($C_8H_{10}Cl_3N_2$) $[M+H]^+$ 238.9910, found 238.9933.



4-Chloro-6-(3-((perfluoropropan-2-yl)oxy)propyl)pyrimidine(3j):

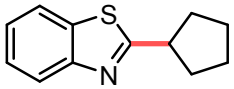
Following general procedure GP1 using 4-chloro-6-(methylsulfonyl)pyrimidine (96.3 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 3-(heptafluoroisopropoxy)propylbis(catecholato)silicate (344.2 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (27.3 mg, 16%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.25 (s, 1H), 4.07 (t, *J* = 5.9 Hz, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 2.22 – 2.15 (m, 2H). ^{13}C NMR

(126 MHz, $CDCl_3$) δ 171.0, 161.6, 158.9, 121.1, 66.3, 33.3, 27.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -79.01 (6F, d, J = 7.4 Hz), -142.34 (1F, s). IR (neat, cm^{-1}): 2924, 1568, 1531, 1455, 1326, 1173, 1102, 922, 857, 745. HRMS (ES+) calcd for ($C_{10}H_8ClF_7N_2O$) $[M+H]^+$ 341.0292, found 341.0305. Although perfluoroisopropyl peaks are missing, both ^{19}F NMR and HRMS indicate its presence.



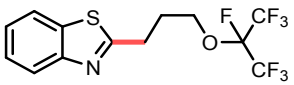
4-Chloro-2-cyclopentyl-6-methoxypyrimidine (3k)

Following general procedure GP1 using 4-chloro-6-methoxy-2-(methylsulfonyl)pyrimidine (111.3 mg, 0.5 mmol, 1.0 equiv), cyclopentyl l bis(catecholato)silicate (249.4 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a sticky light-yellow oil (25.6 mg, 24%). ^1H NMR (500MHz, $CDCl_3$) δ 8.37 (s, 1H), 4.00 (s, 3H), 3.51 (tt, J = 8.6, 8.6 Hz, 1H), 1.94 – 1.78 (m, 6H), 1.73 – 1.58 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 159.0, 154.6, 123.6, 54.6, 37.9, 30.1, 26.9. IR (neat, cm^{-1}): 2952, 2870, 1541, 1464 1410, 1374, 1297, 1152, 1026, 873. HRMS (EI+) calcd for ($C_{10}H_{13}ClN_2O$) $[M^+]$ 212.0716, found 212.0718.



2-Cyclopentylbenzo[d]thiazole (3l):

Following general procedure GP1 using 2-(methylsulfonyl)benzo[d]thiazole (106.6 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium cyclopentylbis(catecholato)silicate (249.4 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a white solid (36.7 mg, 36%). mp = 91 - 94 ℃. ^1H NMR (500MHz, $CDCl_3$) δ 7.96 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 7.7 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 3.55 (tt, J = 8.2, 8.2 Hz, 1H), 2.26 (dtd, J = 14.0, 7.6, 2.7 Hz, 2H), 2.03 – 1.91 (m, 2H), 1.88 (tt, J = 6.7, 2.4 Hz, 2H), 1.74 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 153.4, 135.0, 125.9, 124.6, 122.6, 121.6, 44.9, 34.2, 25.7. IR (neat, cm^{-1}):2952, 2868, 1516, 1436, 1412, 1241, 1199, 1105, 1014, 898, 757. HRMS (EI+) calcd for ($C_{12}H_{13}NS$) $[M]^+$ 203.0769, found 203.0776.



2-(4,5,5,5-Tetrafluoro-4-(trifluoromethyl)pentyl)benzo[d]thiazole (3m)

Following general procedure GP1 using 2-(methylsulfonyl)benzo[d]thiazole (106.6 mg, 0.5 mmol, 1.0 equiv), diisopropylammonium 2-(4,5,5,5-tetrafluoro-4-(trifluoromethyl)pentyl bis(catecholato)silicate (334.6 mg, 0.6 mmol, 1.2 equiv) and $[Ru(bpy)_3][PF_6]_2$ (10.7 mg, 0.0125 mmol, 2.5 mol%) in DMF (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a light-yellow oil (43.2 mg, 25%).^1H NMR (500MHz, $CDCl_3$) δ 7.97 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.52 – 7.42 (m, 1H), 7.42 – 7.32 (m, 1H), 4.15 (t, J = 6.0 Hz, 2H), 3.24 (t, J = 7.5 Hz, 2H), 2.32 (tt, J = 7.6, 6.1 Hz, 2H). ^{13}C NMR (126 MHz,

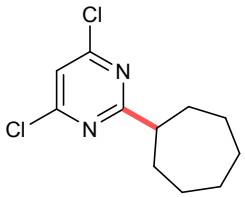
$CDCl_3$) δ 169.9, 153.4, 135.2, 126.2, 125.1, 122.8, 121.7, 66.2, 30.1, 28.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -78.96 (d, *J* = 2.8 Hz, 6F), -142.18 – -142.29 (m, 1F). IR (neat, cm^{-1}): 2926, 1522, 1437, 1228, 1181, 1098, 1013, 989, 731. HRMS (EI+) calcd for ($C_{13}H_{10}F_7NOS$) $[M]^+$ 361.0371, found 361.0358. Although perfluoroisopropyl peaks are missing, both ^{19}F NMR and HRMS indicate its presence.

3.2 Alkylation Using Alkyl 1,4-Dihydropyridines

3.2.1 General Procedure (GP2)

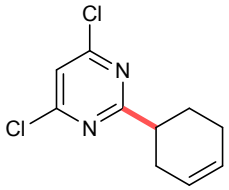
To an 8-mL reaction vial equippaed with a stir bar and septa screw-cap were added alkyl 1,4-dihydropyridines (1.0 mmol, 2.0 equiv), heteroaryl methyl sulfones (0.5 mmol, 1 equiv), and 4-CzIPN (9.8 mg, 2.5 mmol %). The vial was subsequently closed, and three vacuum/argon cycles were performed, followed by addition of 5 mL of dry acetone (0.1 M). After stirring under a blue LED for 16 h, the reaction was stopped and concentrated by rotovap. Final product was purified by flash column chromatography, using hexanes and EtOAc as eluent.

3.2.2 Characterization Data



4,6-Dichloro-2-cycloheptylpyrimidine (5b)

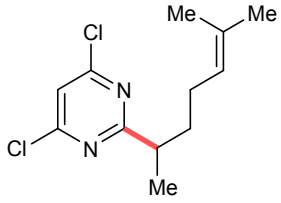
Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-cycloheptyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (349.5 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (96.9 mg, 79%). ^1H NMR (500MHz, $CDCl_3$) δ 8.57 (s, 1H), 3.55-3.49 (m, 1H), 2.20-2.13 (m, 2H), 1.88-18.2 (m, 2H), 1.75-1.68 (m, 4H), 1.63-1.57 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.8, 154.7, 138.2, 41.7, 30.8, 28.5, 27.9. IR (neat, cm^{-1}): 2992, 2854, 1530, 1509, 1447, 1411, 1368, 1349, 1324, 1222, 923, 825, 785, 788,763. HRMS (EI+) calcd for ($C_{11}H_{14}Cl_2N_2$) $[M]^+$ 244.0534, found 244.0523.



4,6-Dichloro-2-(cyclohex-3-en-1-yl) pyrimidine (5c)

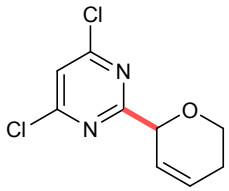
Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(cyclohex-3-en-1-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (333.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (77.2mg, 67%). ^1H NMR (500MHz, $CDCl_3$) δ 8.60 (s, 1H), 5.76 (m, 2H), 3.66 (s, 1H), 2.76 (t, *J* =37.5 Hz, 1H) 2.55-2.47 (m, 1H), 2.21 (m, 2H), 2.10 (d, *J* =21.89 Hz, 1H), 1.74 (d, *J* = 16.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.3, 154.4, 135.9, 127.1, 125.7,

37.0, 27.2, 25.9, 24.7. IR (neat, cm^{-1}): 3021, 2921, 1529, 1512,1436,1414, 1369, 1349, 1330, 1316, 1255, 1238, 1196, 1185, 1146, 1128, 916, 812, 781, 672. HRMS (ES+) calcd for ($C_{10}H_{10}Cl_2N_2$) $[M+H]^+$ 229.0299, found 229.0302.



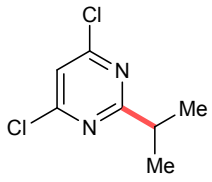
4,6-Dichloro-2-(6-methylhept-5-en-2-yl)pyrimidine (5d)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 2,6-dimethyl-4-(6-methylhept-5-en-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate (363.5mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (75.4mg, 58%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.58 (s, 1H), 5.04-5.03 (m, 1H), 3.63-3.59 (m, 1H), 2.10 – 2,03 (m, 1H), 1.96-1.86 (m, 2H), 1.82-1.78 (m, 1H), 1.64 (s, 3H), 1.47 (s, 3H), 1.37 (d, J = 8.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.2, 136.4, 132.7, 124.0, 123.6, 35.1, 33.4, 26.4, 25.8, 17.7, 17.34. IR (neat, cm^{-1}): 2969, 2930, 1530, 1511, 1454, 1411, 1377, 1357, 1328, 1273, 1236, 1216, 1140, 1110, 1076, 1048, 971, 815, 783, 583. HRMS (ES+) calcd for $C_{12}H_{16}Cl_2N_2$ $[M+H]^+$ 259.0769, found 259.0759.



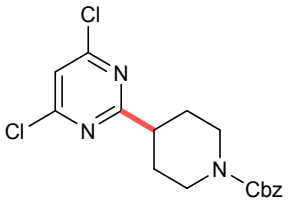
4,6-Dichloro-2-(5,6-dihydro-2H-pyran-2-yl) pyrimidine (5e)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(5,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (335.4mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (75.4mg, 58%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.70 (s, 1H), 6.47 (d, J = 8.1 Hz, 1H), 5.46-5.43 (m, 1H), 4.85 (t, J = 15.0 Hz, 1 H), 2.54-2.45 (m, 1H), 2.34-2.27 (m, 1H), 2.15-2.10 (m, 1H) 1.91-1.87 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 162.2, 143.3, 120.0, 101.0, 72.6, 27.3, 19.4. IR (neat, cm^{-1}): 3056, 2934, 2848, 1651, 1529, 1415, 1386, 1372, 1343, 1325, 1229, 1108, 1059, 959, 841, 779, 726, 557. HRMS (EI+) calcd for ($C_{12}H_{16}Cl_2N_2$) $[M]^+$ 230.0014, found 230.0019.



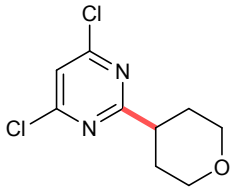
4,6-Dichloro-2-isopropylpyrimidine (5f)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-isopropyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (295.4mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (64.2mg, 67%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.57 (s, 1H), 3.77-3.72 (m, 1H), 1.40 (d, J = 8.1 Hz, 6H)· ^{13}C NMR (126 MHz, $CDCl_3$) δ (126 MHz, $CDCl_3$) δ 161.5, 155.2, 137.2, 30.1, 18.9. IR (neat, cm^{-1}): 2970, 2935, 2878, 1532, 1468, 1411, 1387, 1350, 1232, 1182, 1156, 1106, 954, 889, 799, 783, 571. HRMS (ES+) calcd for ($C_7H_9Cl_2N_2$) $[M+H]^+$ 191.0143, found 191.0144.



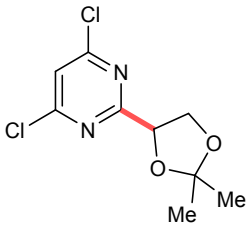
Benzyl 4-(4,6-dichloropyrimidin-2-yl)piperidine-1-carboxylate (5g)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(1-((benzyloxy)carbonyl)piperidin-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (470.6 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (109.9 mg, 60%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.39-7.37 (m, 4H). 7.33 (s, 1H), 5.15 (s, 2H), 4.31 (s, 2H), 3.04 (t, J = 12.0 Hz, 1H), 2.94 (s, 2H), 2.01 (s, 2H), 1.89-1.81(m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ (126 MHz, $CDCl_3$) δ 174.2, 161.8, 155.1, 136.7, 128.4, 127.9, 127.8, 118.9, 67.0, 44.7, 43.6, 30.1. IR (neat, cm^{-1}): 3072, 2965, 2853, 1694, 1544, 1469, 1366, 1348, 1284, 1246, 1128, 1092, 1027, 931, 941, 763. HRMS (EI+) calcd for ($C_{17}H_{17}Cl_2N_3O_2$) $[M]^+$ 365.0698, found 365.0688.



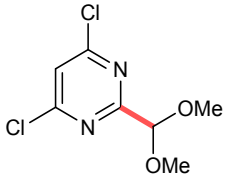
4,6-Dichloro-2-(tetrahydro-2H-pyran-4-yl)pyrimidine (5h)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 2,6-dimethyl-4-(tetrahydro-2H-pyran-4-yl)-1,4-dihydropyridine-3,5-dicarboxylate (337.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a white solid (52 mg, 44%). mp = 113 - 115 ℃. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.62 (s, 1H), 4.12 (dd, J =11.5, 4.5 Hz, 2H), 3.67-3.63 (m, 1H), 3.53-3.50 (m, 2H) 2.66-2.57 (m, 2H), 1.53 (d, J =13.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 155.6, 134.3, 68.4, 38.3, 27.8. IR (neat, cm^{-1}): 3022, 2921, 2898, 2831, 1530, 1512, 1415, 1370, 1349, 1331, 1316, 1238, 1196, 1185, 1146, 812, 784, 672, 560. HRMS (EI+) calcd for ($C_9H_{10}Cl_2N_2O$) $[M]^+$ 232.0170, found 232.0179.



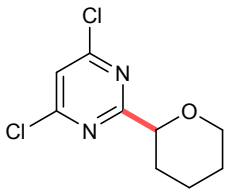
4,6-Dichloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl) pyrimidine (5i)

Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (353.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a white solid (52 mg, 44%). mp = 65 – 67 ℃. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.33 (s, 1H), 5.19 (t, J =16.3 Hz, 1H), 4.44-4.41 (m, 1H), 4.21-4.19 (m, 1H), 1.57 (s, 3H), 1.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 162.2, 120.1, 111.5, 77.5, 69.0, 26.1, 25.7. IR (neat, cm^{-1}): 1526.4, 1276.3, 1368.8, 1317.3, 1250.3, 1221.1, 1207.2, 1150.8, 1110.7, 1098.7, 1056.9, 869.5, 851.9, 936.1, 823.1, 810.6, 783.9, 755.1, 623.6, 512.1. HRMS (ES+) calcd for ($C_9H_{11}Cl_2N_2O_2$) $[M+H]^+$ 249.0198, found 249.0192.



4,6-Dichloro-2-(dimethoxymethyl)pyrimidine (5j)

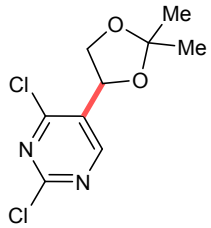
Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(dimethoxymethyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (327.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (78.6 mg, 70%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.73 (s, 1H), 5.76 (s, 1H), 3.52 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.3, 157.2, 128.3, 102.7, 56.2. IR (neat, cm^{-1}): 2934, 2833, 1721, 1538, 1518, 1444, 1418, 1372, 1332, 1243, 1208, 1192, 1138, 1096, 1070, 989, 875, 798, 723, 572. HRMS (EI+) calcd for ($C_7H_8Cl_2N_2O_2$) $[M-H]^+$ 220.9885, found 220.9884.



4,6-Dichloro-2-(tetrahydro-2H-pyran-2-yl) pyrimidine (5k)

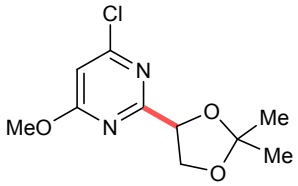
Following general procedure GP2 using 4,6-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 2,6-dimethyl-4-(tetrahydro-2H-pyran-2-yl)-1,4-dihydropyridine-3,5-dicarboxylate

(337.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (46.5 mg, 40%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.65 (s, 1H), 5.01 (dd, *J* = 15.0, 3.1 Hz, 1H), 4.18-4.14 (m, 1H), 3.61-3.56 (m, 1H), 2.22-2.17 (m, 1H), 2.04-2.00 (m, 1H), 1.79-1.68 (m, 2H), 1.66-1.61 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 161.2, 156.4, 75.9, 69.1, 27.5, 25.3, 23.6. IR (neat, cm^{-1}): 2925, 2854, 1724, 1540, 1515, 1441, 1415, 1374, 1346, 1330, 1262, 1228, 1207, 1087, 1046, 1002, 911,810, 792, 779. HRMS (EI+) calcd for ($C_9H_{10}Cl_2N_2O$) $[M]^+$ 232.0170, found 232.0167.



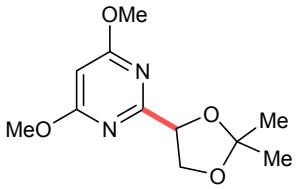
2,4-Dichloro-5-(2,2-dimethyl-1,3-dioxolan-4-yl)pyrimidine (5l)

Following general procedure GP2 using 2,4-dichloro-5-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (353.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (90.9 mg, 73%). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.55 (s, 1H), 5.08 (t, *J* = 15.6 Hz, 1H), 4.49 (t, *J* = 20.0 Hz, 1H), 4.01 (dd, *J* = 18.1, 11.2 Hz, 1H), 1.54 (s, 3H), 1.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ174.6, 163.5, 160.4, 116.4, 111.5, 76.6, 69.5, 26.5, 25.3. IR (neat, cm^{-1}): 2987, 2935, 1712, 1615, 1514, 1456, 1375, 1331, 1216, 1155, 1074, 1017, 972, 912, 858, 737. HRMS (EI+) calcd for ($C_8H_{10}Cl_2N_2$) $[M]^+$ 248.0119, found 248.0121.



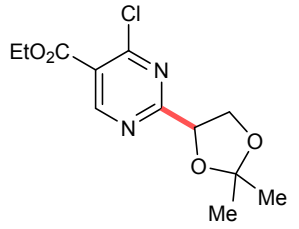
4-Chloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-6-methoxypyrimidine (5m)

Following general procedure GP2 using 4-chloro-6-methoxy-2-(methylsulfonyl)pyrimidine (111.3 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (353.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (46.5 mg, 40%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.49 (s, 1H), 5.57 (t, *J* = 18.8 Hz, 1H) 4.20-4.12 (m, 2H), 1.58 (s, 3H), 1.55 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 160.0, 156.9, 115.3, 110.3, 71.2, 66.7, 54.7, 25.9, 25.3. IR (neat, cm^{-1}): 2984, 2914, 1564, 1544, 1421, 1384, 1370, 1363, 1315, 1302, 1246, 1217, 1154, 1061, 1022, 957, 943, 893, 846, 822, 784. HRMS (ES+) calcd for ($C_{10}H_{14}ClN_2O_3$) $[M+H]^+$ 245.0693, found 245.0692.



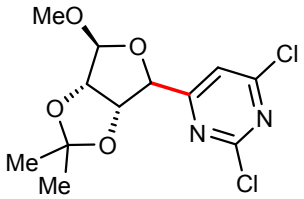
2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4,6-dimethoxypyrimidine (5n)

Following general procedure GP2 using 4,6-dimethoxy-2-(methylsulfonyl)pyrimidine (109.1 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (353.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (71.4 mg, 58%). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.37 (s, 1H), 5.50-5.47 (m, 1H),4.20-4.16 (m, 1H), 4.07 (t, J = 17.5 Hz, 1H), 3.98 (s, 6H), 1.53 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 156.5, 109.4, 100.0, 77.2, 68.6, 66.6, 54.1, 26.2, 25.8. IR (neat, cm^{-1}): 2985, 1721, 1574, 1466, 1380, 1301, 1244, 1214, 1157, 1120, 1059, 967, 948, 858, 808, 791, 669, 510, 500. HRMS (EI+) calcd for ($C_{11}H_{16}N_2O_4$) $[M]^+$ 240.1110, *found* 240.1111.



Ethyl 4-chloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl) pyrimidine-5-carboxylate (5o)

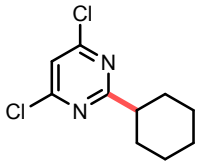
Following general procedure GP2 using 4-chloro-6-ethoxy-2-(methylsulfonyl)pyrimidine (118.3 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (353.4 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (71.7 mg, 49%). ^{1}H NMR (500MHz, $CDCl_3$) δ 9.13 (s, 1H), 5.28 (t, J = 13.0 Hz, 1H) 4.50-4.44 (m, 3H), 4.23-4.20 (m, 1H), 1.58 (s, 3H), 1.51 (s, 3H), 1.43 (d, J = 14.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 162.4, 160.5, 160.2, 123.0, 111.5, 77.6, 69.1, 62.4, 26.1, 25.7, 14.0. IR (neat, cm^{-1}): 2925, 1733, 1559, 1445, 1372, 1295, 1174, 1070, 803. HRMS (ES+) calcd for ($C_{12}H_{16}ClN_2O_4$) $[M+H]^+$ 287.0812, found 287.0810.



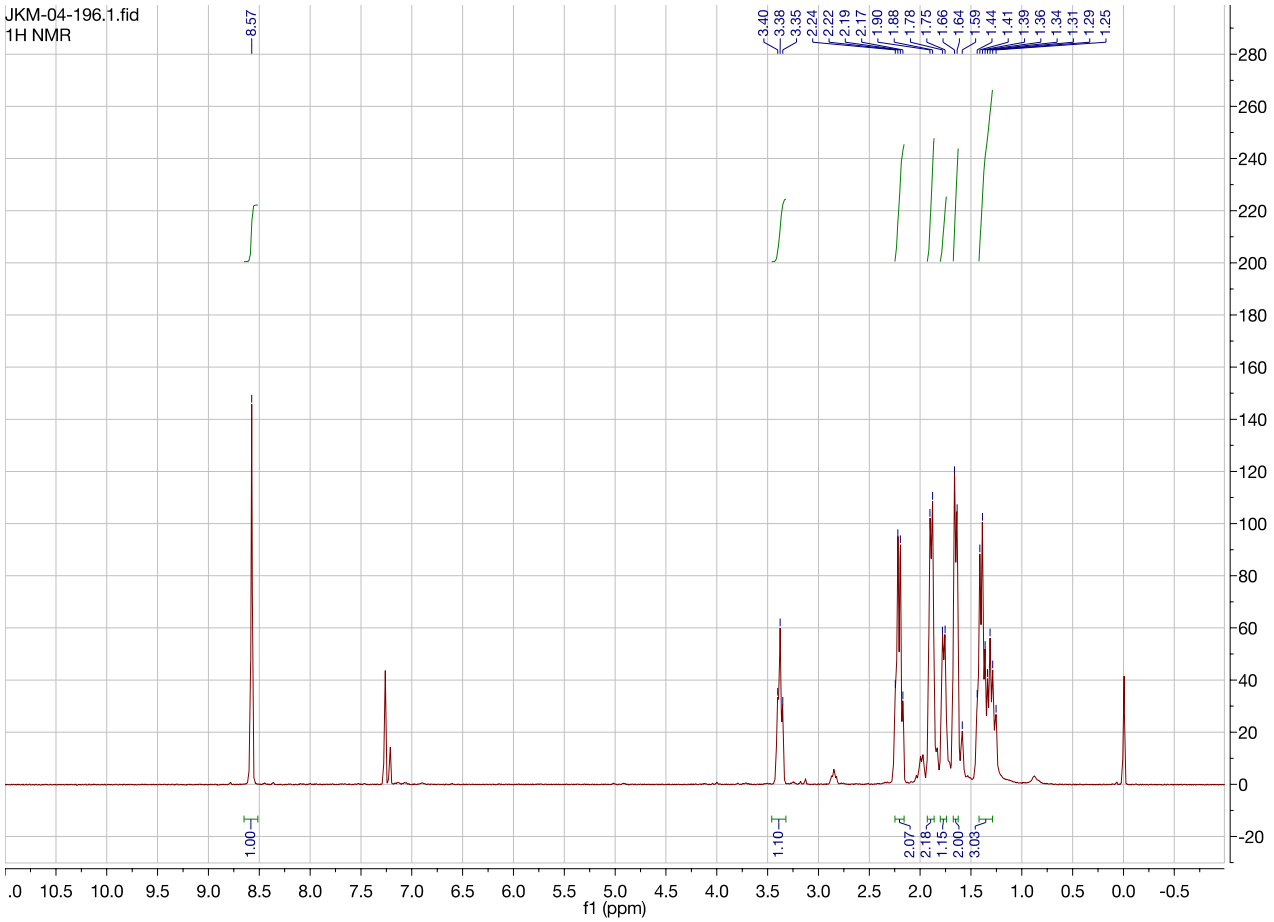
2,4-Dichloro-6-((3aS,6S,6aS)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)pyrimidine (5p)

Following general procedure GP2 2,4-dichloro-2-(methylsulfonyl)pyrimidine (113.5 mg, 0.5 mmol, 1.0 equiv), diethyl 4-(6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (425.5 mg, 1.0 mmol, 2.0 equiv) and 4-CzIPN (9.8 mg, 2.5 mmol %) in acetone (5 mL, 0.1 M). The reaction was stirred under blue LED at rt for 16 h. Silica gel purification using an automated system (hexanes/EtOAc, 0 to 20%) gave the product as a colorless oil (86.4 mg, 54%). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.52 (d, *J* = 0.9 Hz, 1H), 5.28 (dd, *J* = 5.9, 1.5 Hz, 1H), 5.17 (s, 1H), 5.15 (s, 1H), 4.56 (d, *J* = 5.9 Hz, 1H), 1.54 (s, 3H), 1.36 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 162.9, 160.3, 117.2, 113.3, 111.2, 87.4, 84.7, 83.9, 56.1, 26.7, 25.2. IR (neat, cm^{-1}): 2937, 1558, 1528, 1456, 1374, 1303, 1274, 1243, 1213, 1196, 1160. 1105, 1091, 1060, 1047, 980, 966, 944, 866, 831. HRMS (EI+) calcd for ($C_{12}H_{14}Cl_2N_2O_4$) $[M]^+$ 320.0331, *found* 320.0391.

5. Spectral Data



^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-cyclohexylpyrimidine (3a)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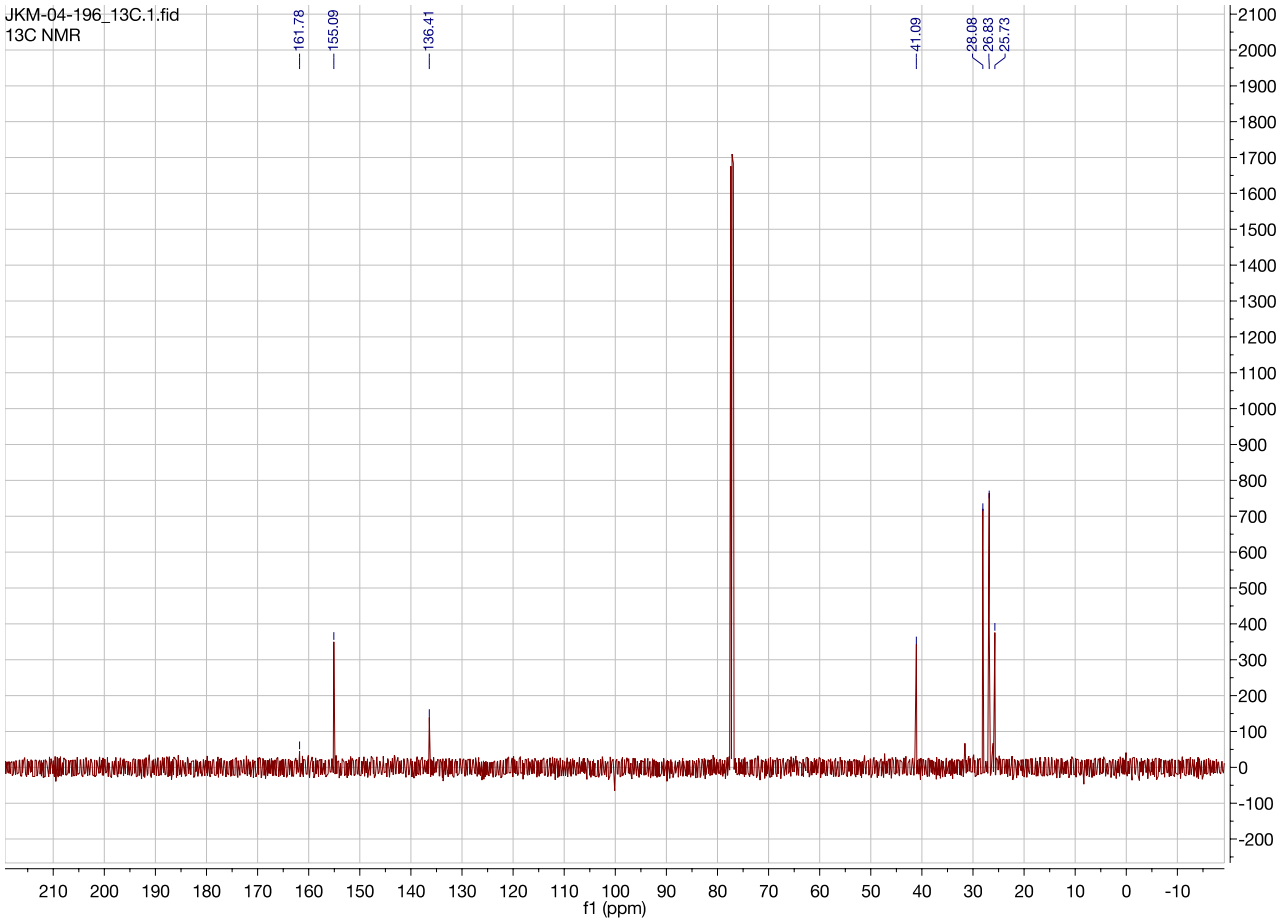
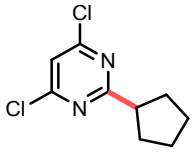
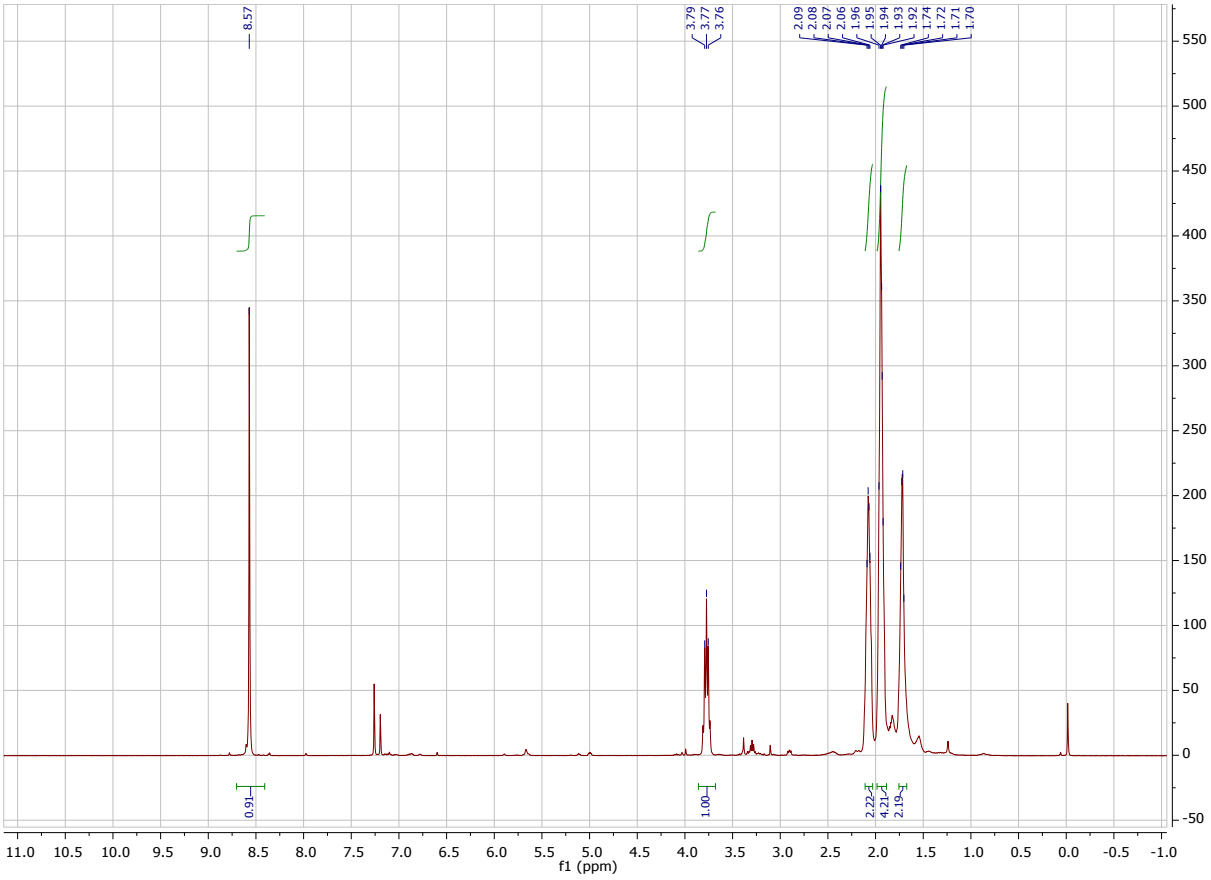
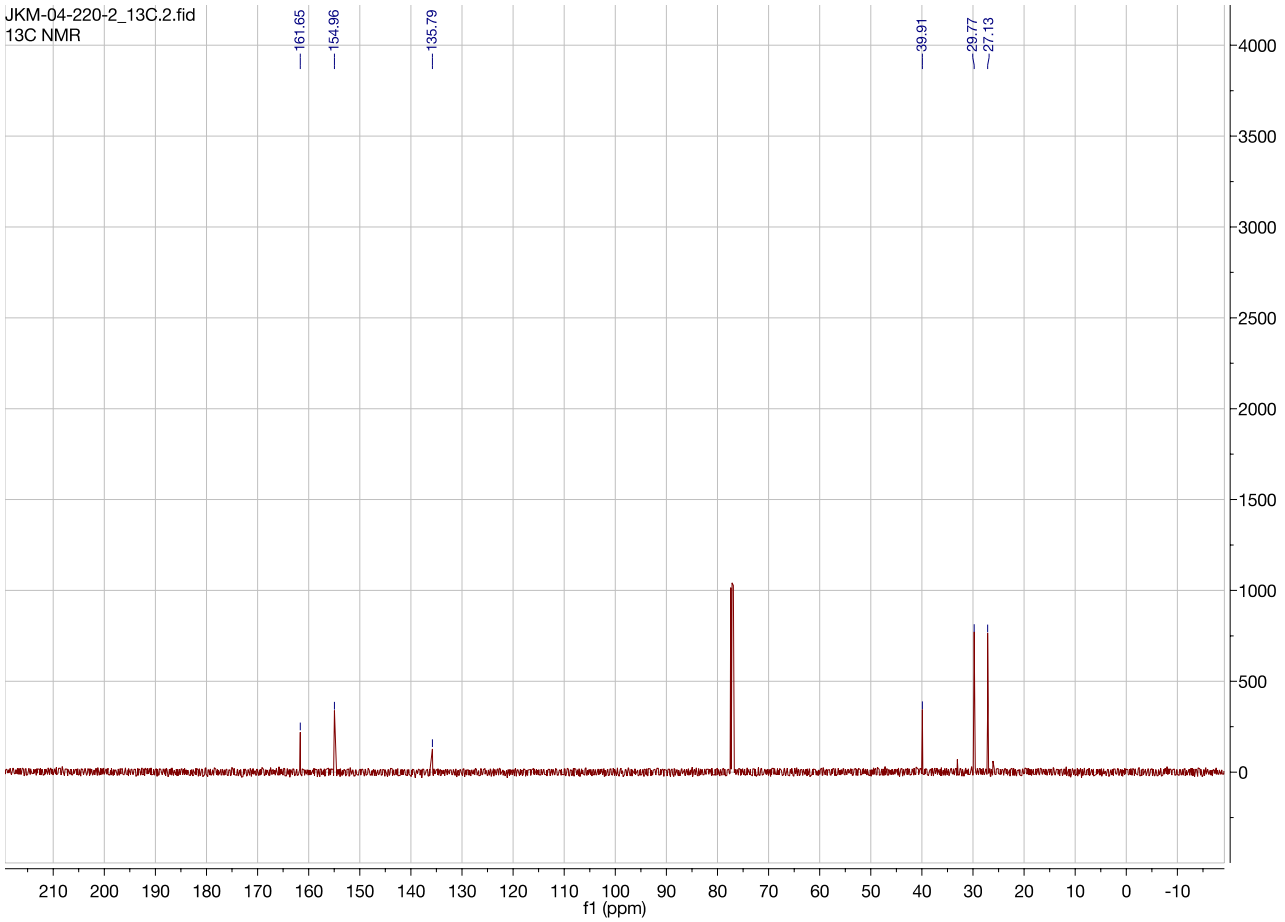
1H NMR
8.57
3.40
3.38
3.35
2.24
2.22
2.19
2.17
1.90
1.88
1.78
1.75
1.66
1.64
1.59
1.44
1.41
1.39
1.36
1.34
1.31
1.29
1.25
1.00
1.10
2.07
2.18
1.15
2.00
3.03
f1 (ppm)

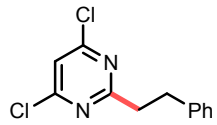

JKM-04-196_13C.1.fid
13C NMR
161.78
155.09
136.41
41.09
28.08
26.83
25.73
f1 (ppm)


Cl
N
Cl
N

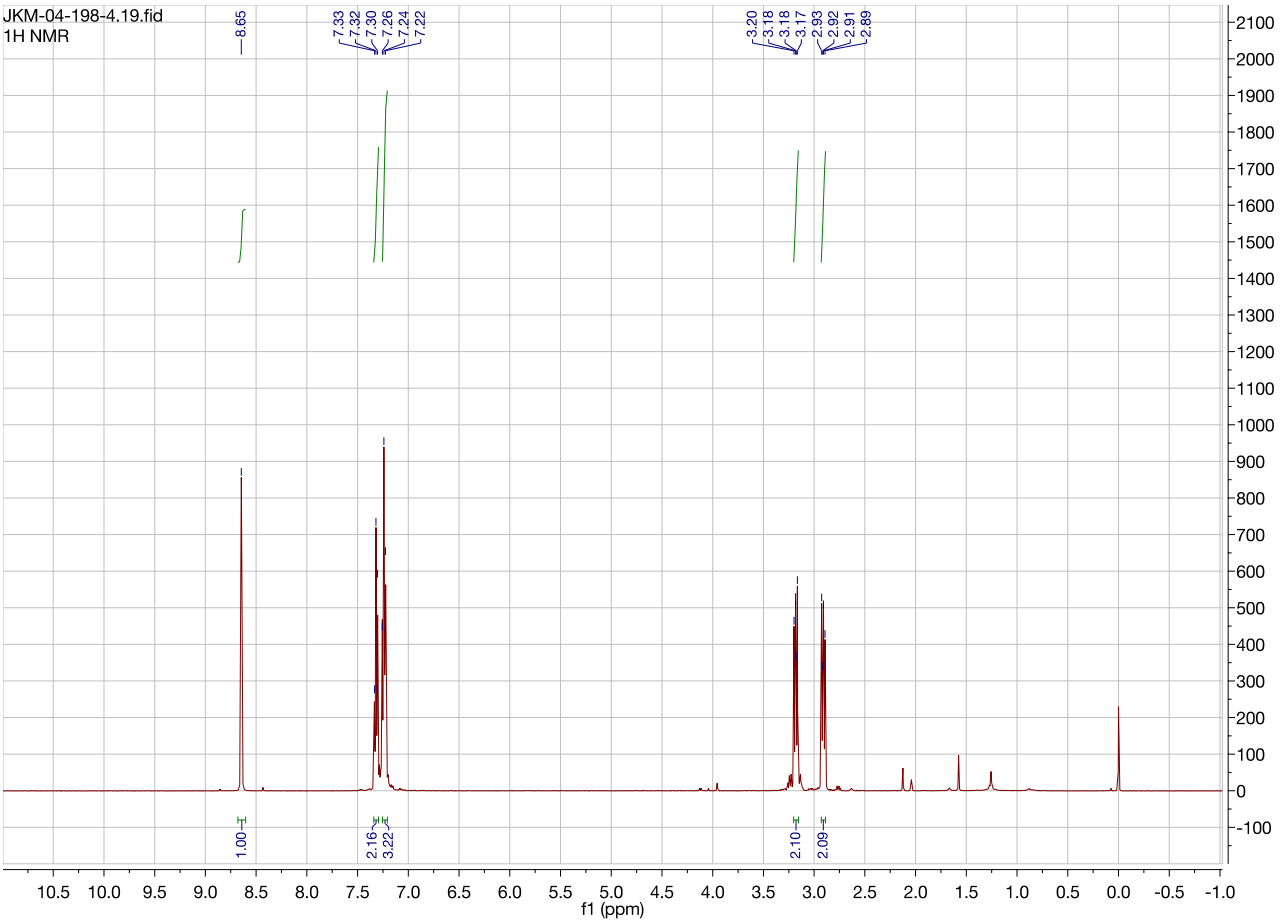
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-cyclopentylpyrimidine (3b)

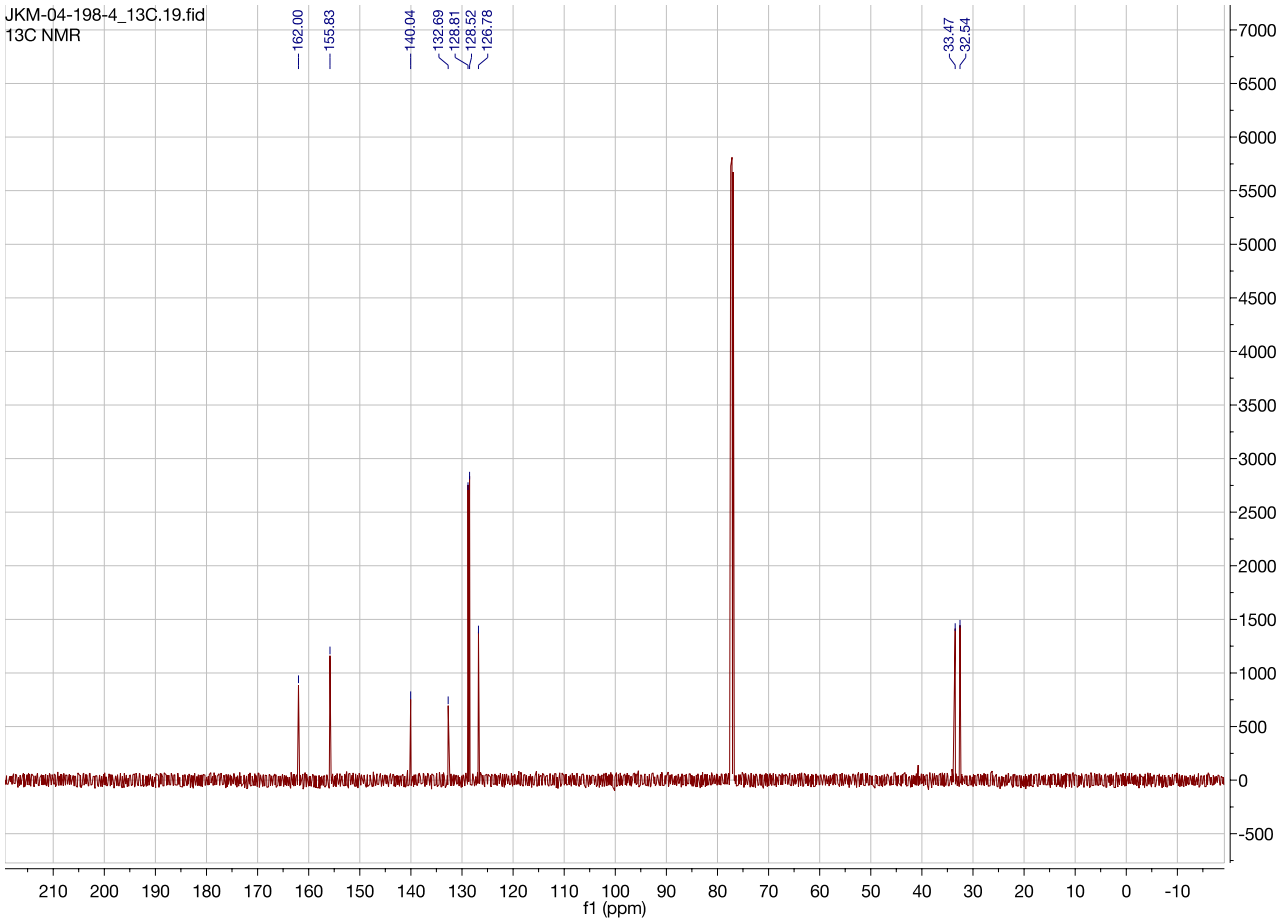


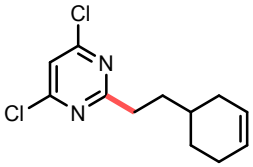

JKM-04-220-2_13C.2.fid
13C NMR
161.65
154.96
135.79
39.91
29.77
27.13
4000
3500
3000
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



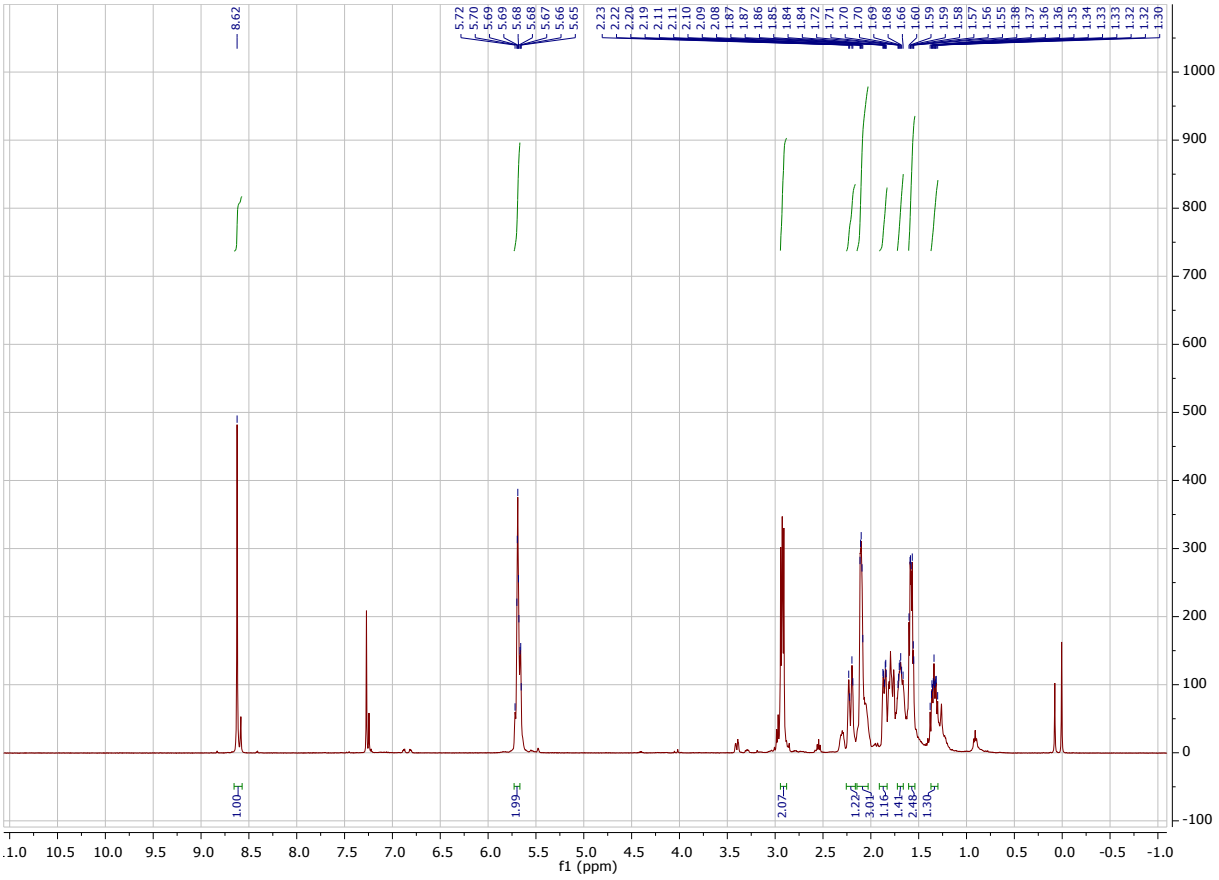
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-phenethylpyrimidine (3c)

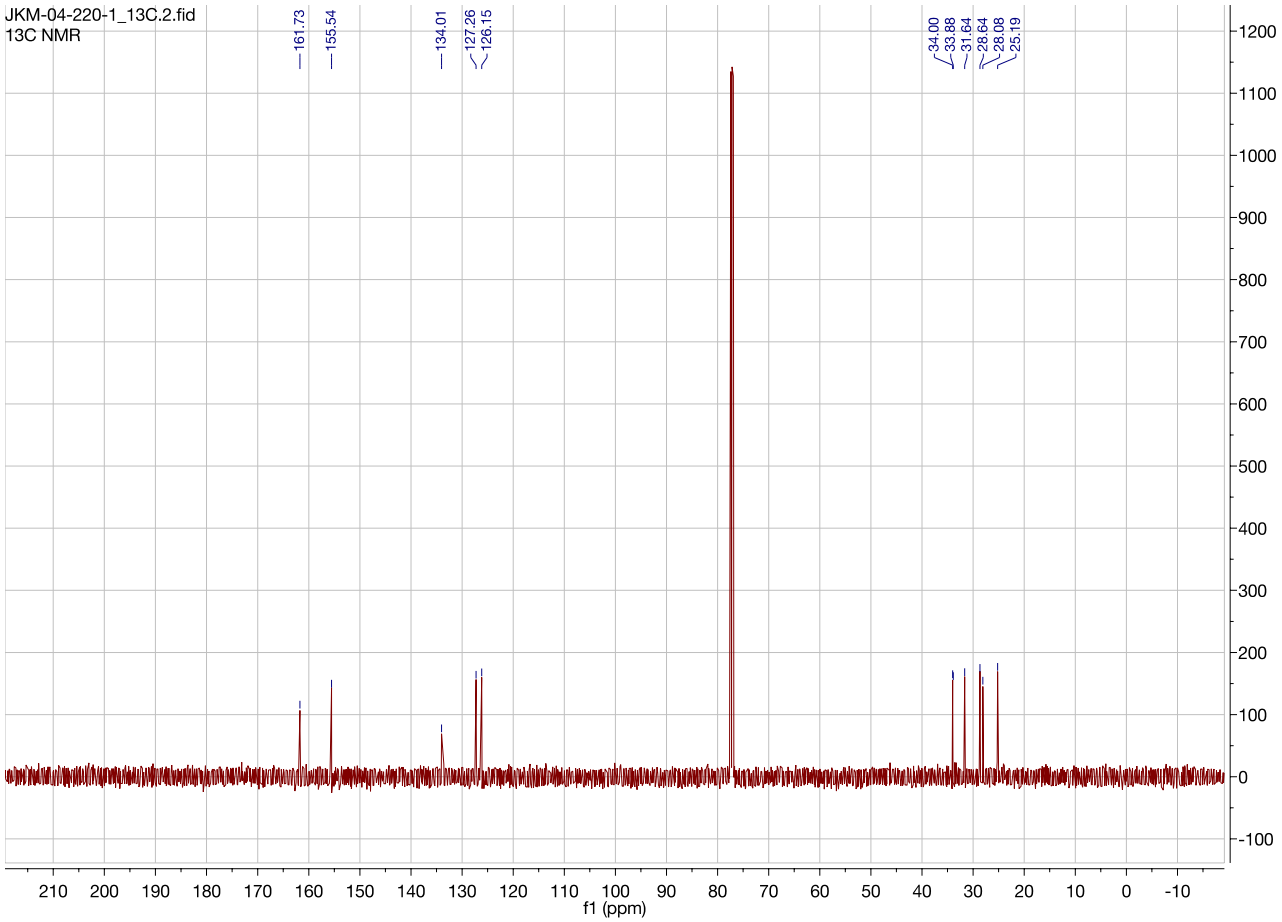


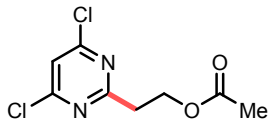

JKM-04-198-4_13C.19.fid
13C NMR
162.00
155.83
140.04
132.69
128.81
128.52
126.78
33.47
32.54
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



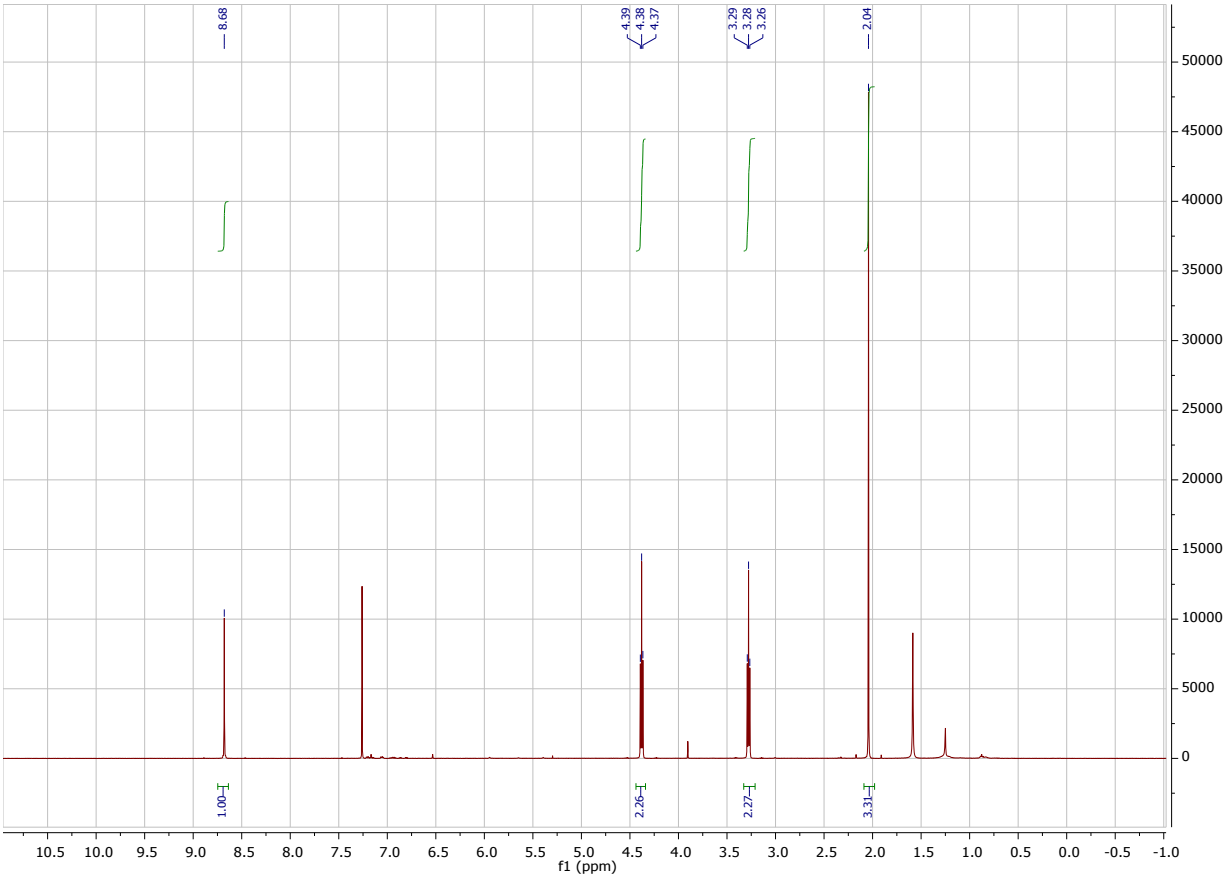
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(2-(cyclohex-3-en-1-yl)ethyl)pyrimidine (3d)

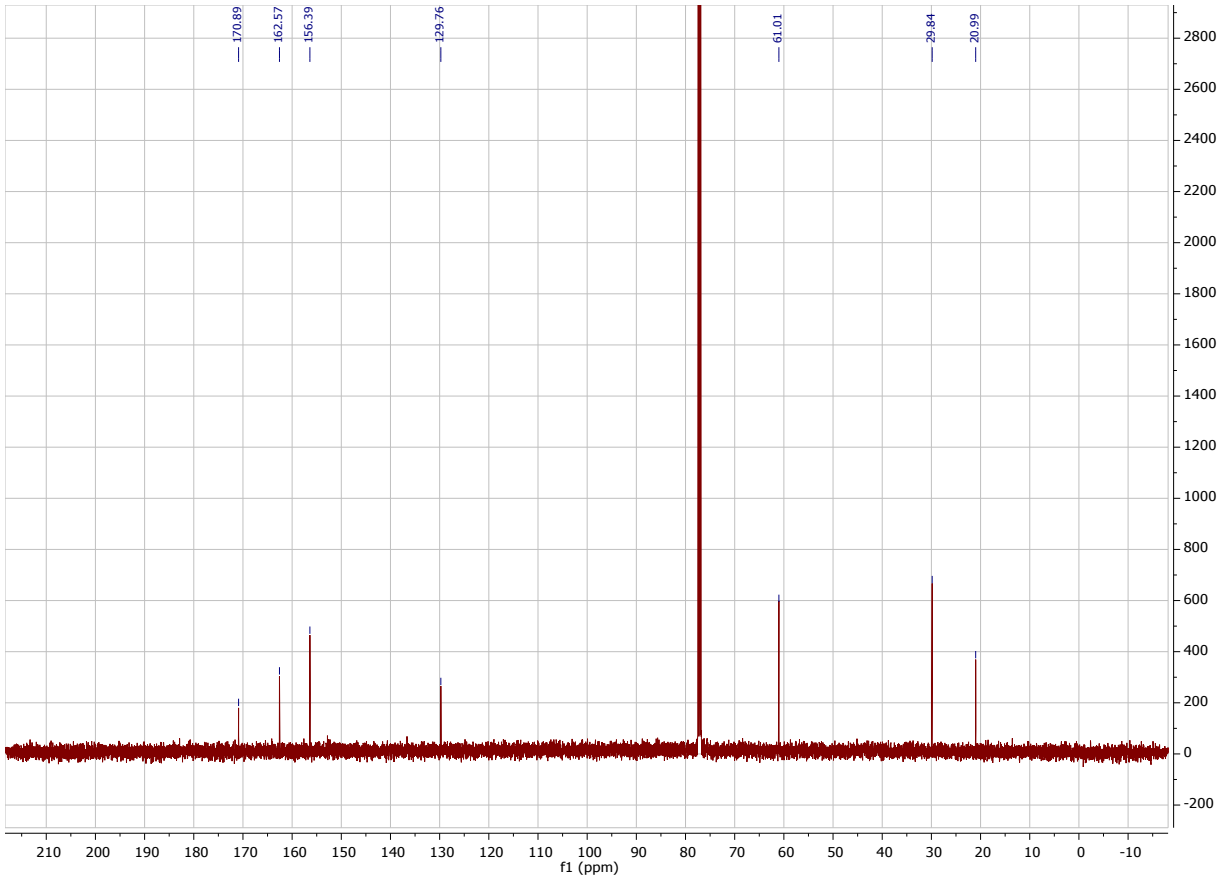


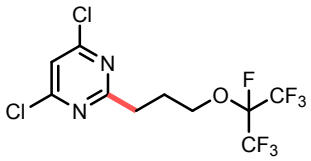

JKM-04-220-1_13C.2.fid
13C NMR
161.73
155.54
134.01
127.26
126.15
34.00
33.88
31.64
28.64
28.08
25.19
f1 (ppm)



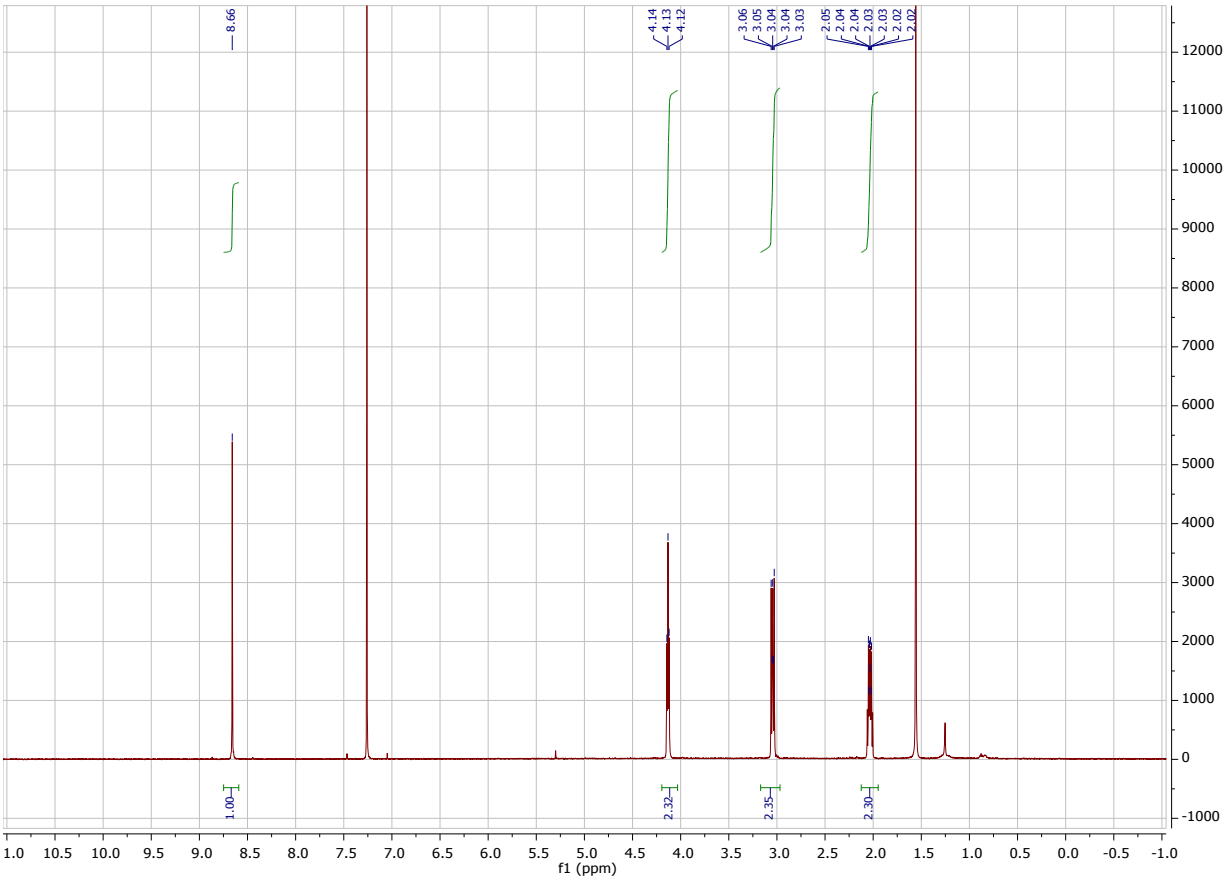
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2-(4,6-Dichloropyrimidin-2-yl)ethyl acetate (3e)

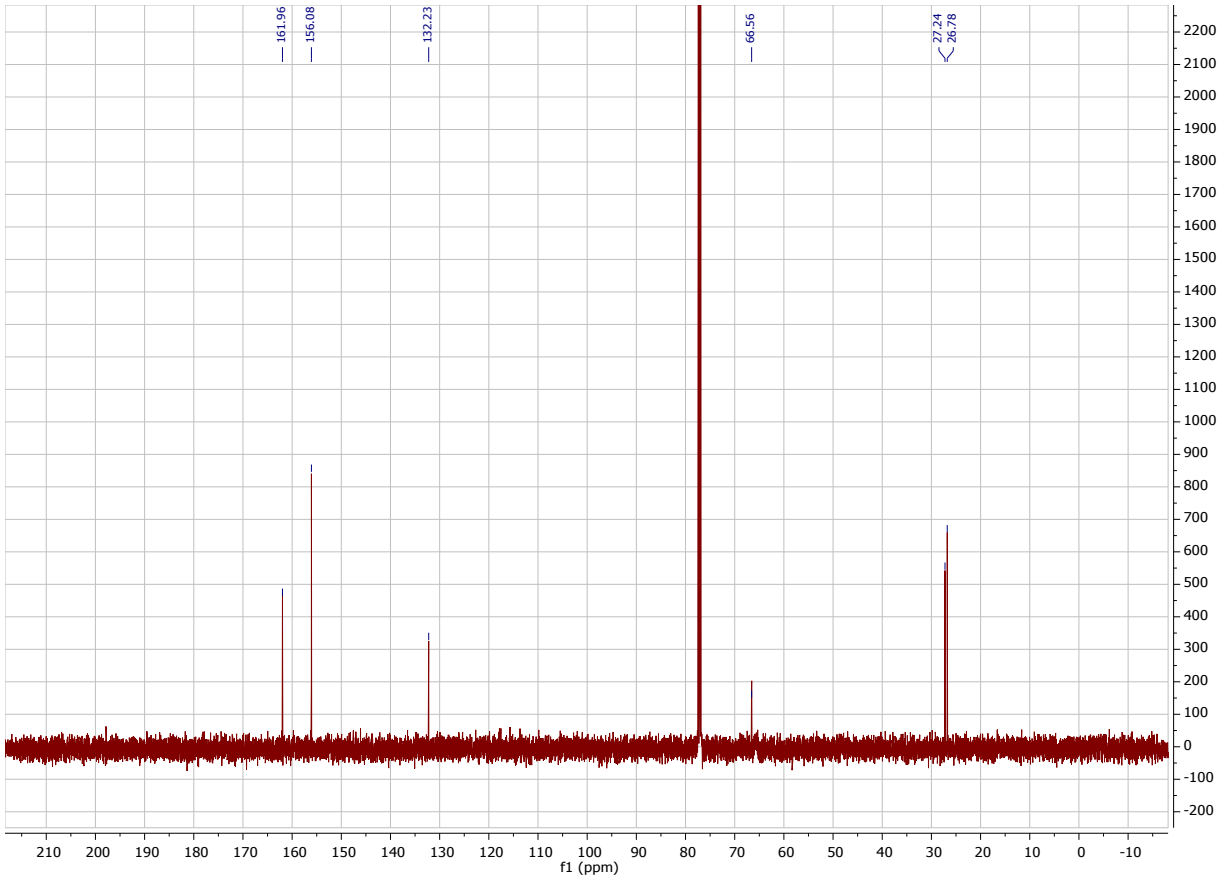


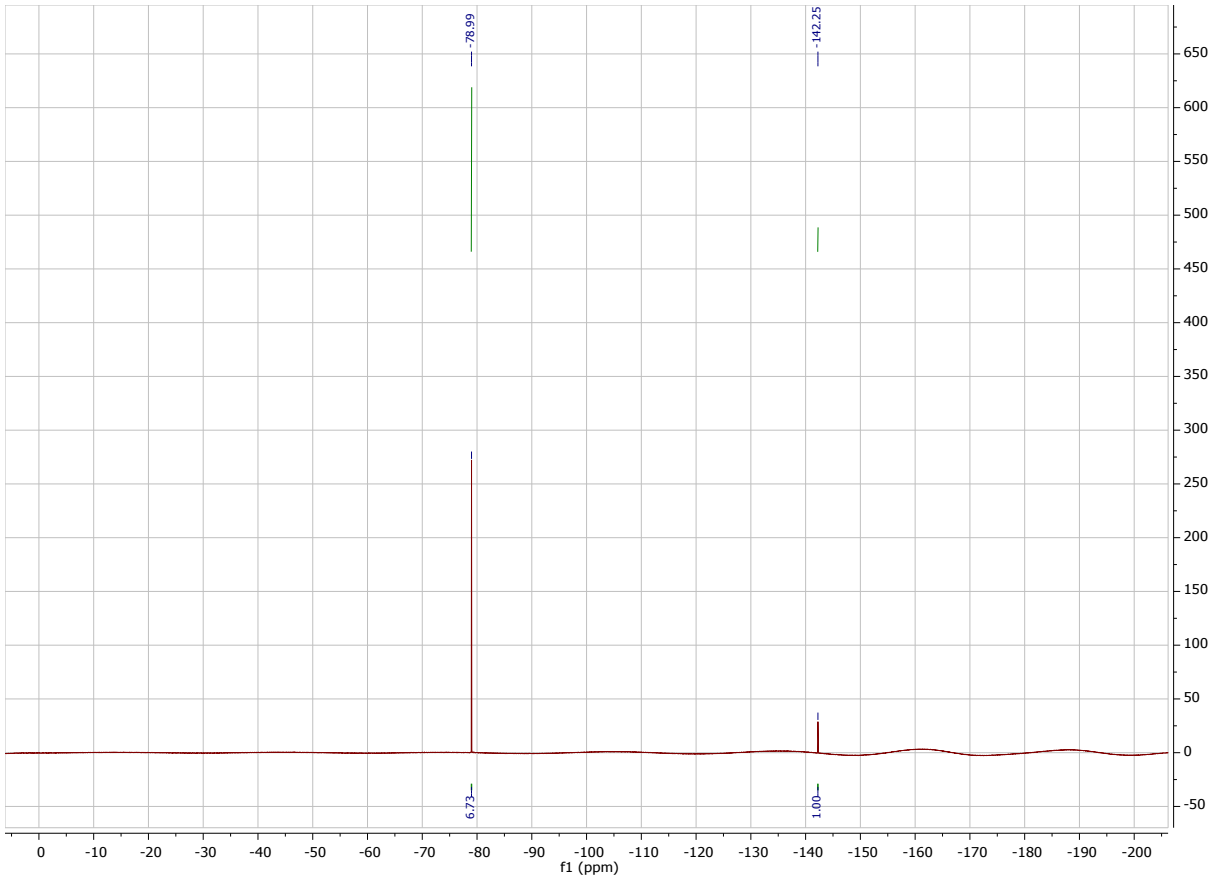

170.89
162.57
156.39
129.76
61.01
29.84
20.99
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

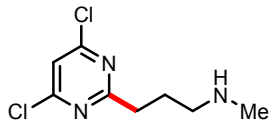


^{1}H NMR ($CDCl_3$, 500 MHz), ^{13}C NMR ($CDCl_3$, 126 MHz) and ^{19}F NMR (471 MHz, $CDCl_3$) of 4,6-Dichloro-2-(4,5,5,5-tetrafluoro-4-(trifluoromethyl)pentyl)pyrimidine (3f)

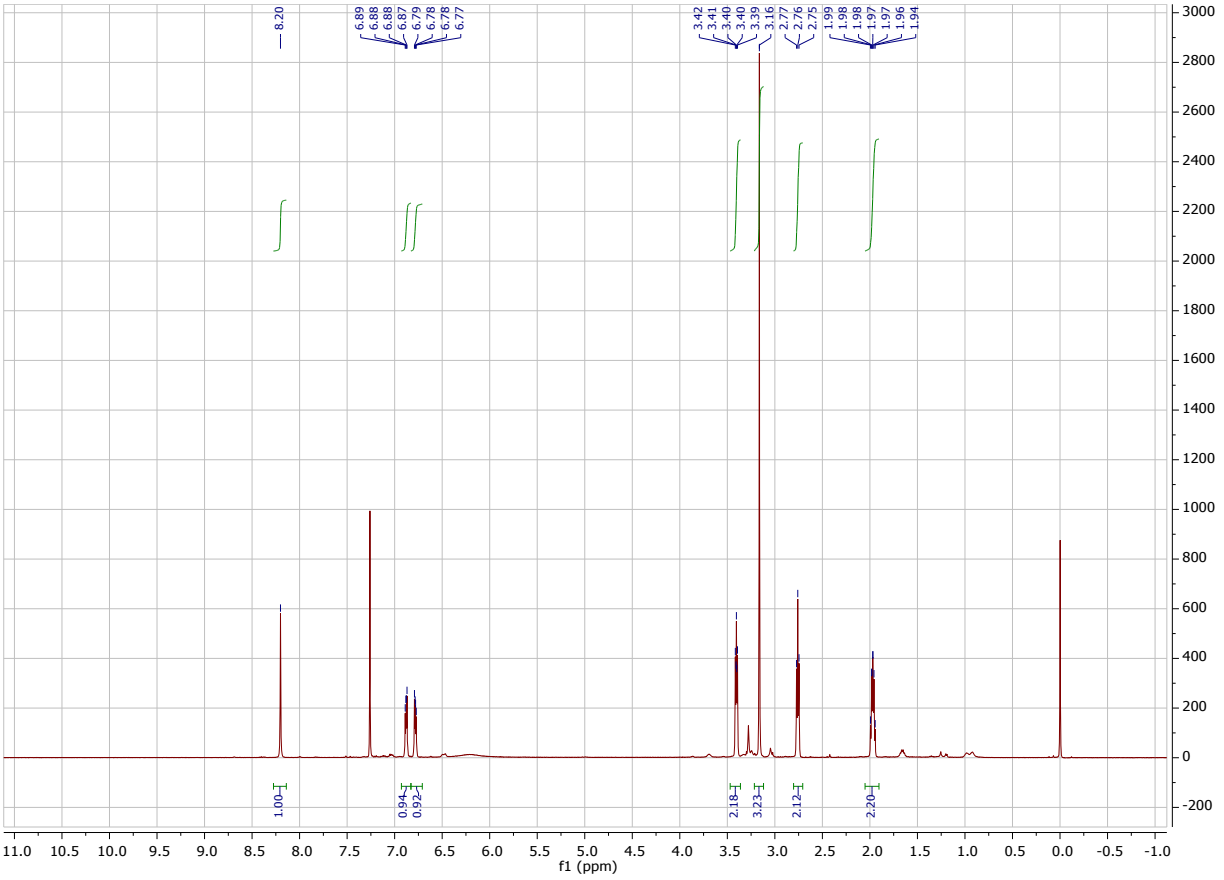


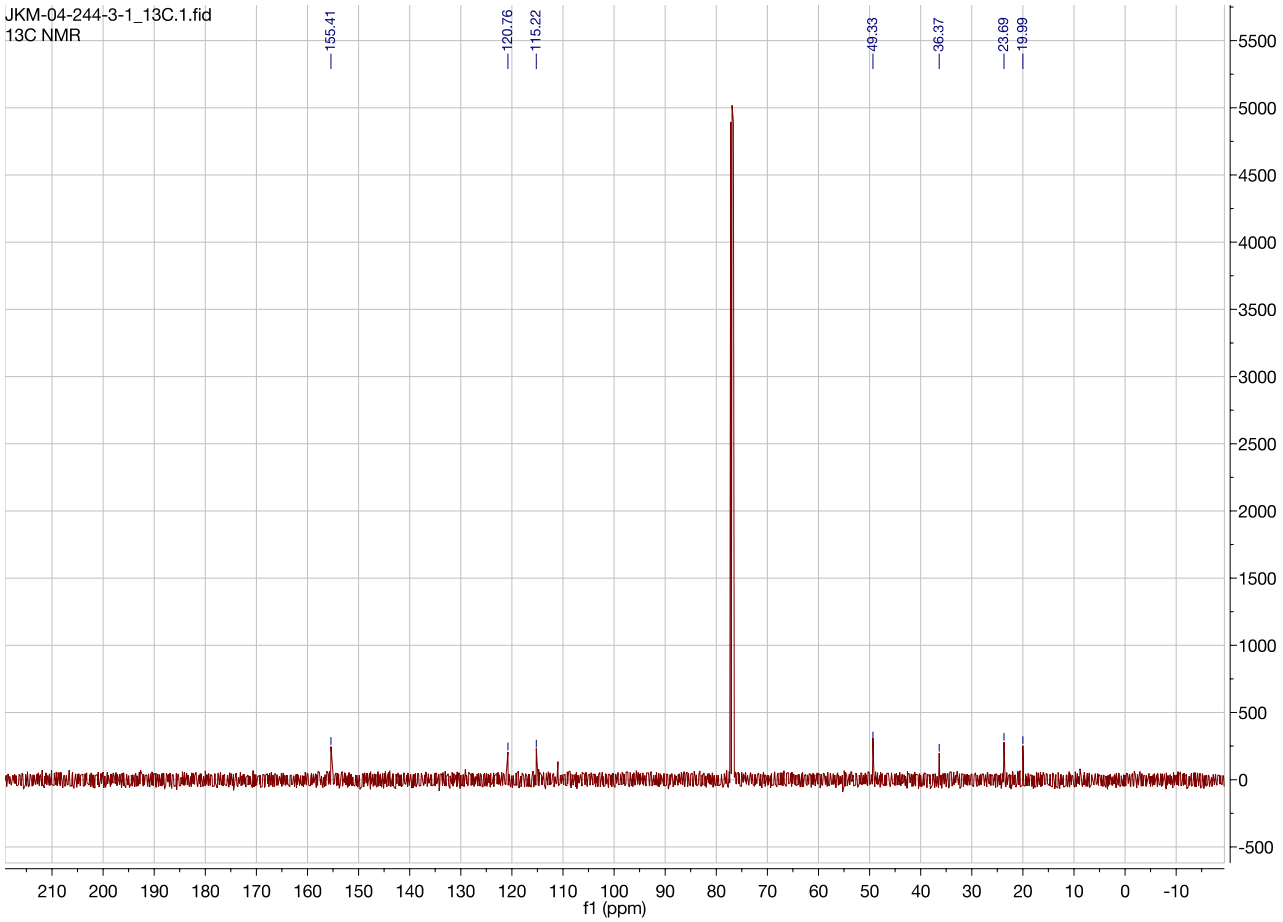

161.96
156.08
132.23
66.56
27.24
26.78
f1 (ppm)

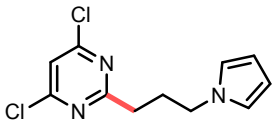

-78.99
-142.25
6.73
1.00
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



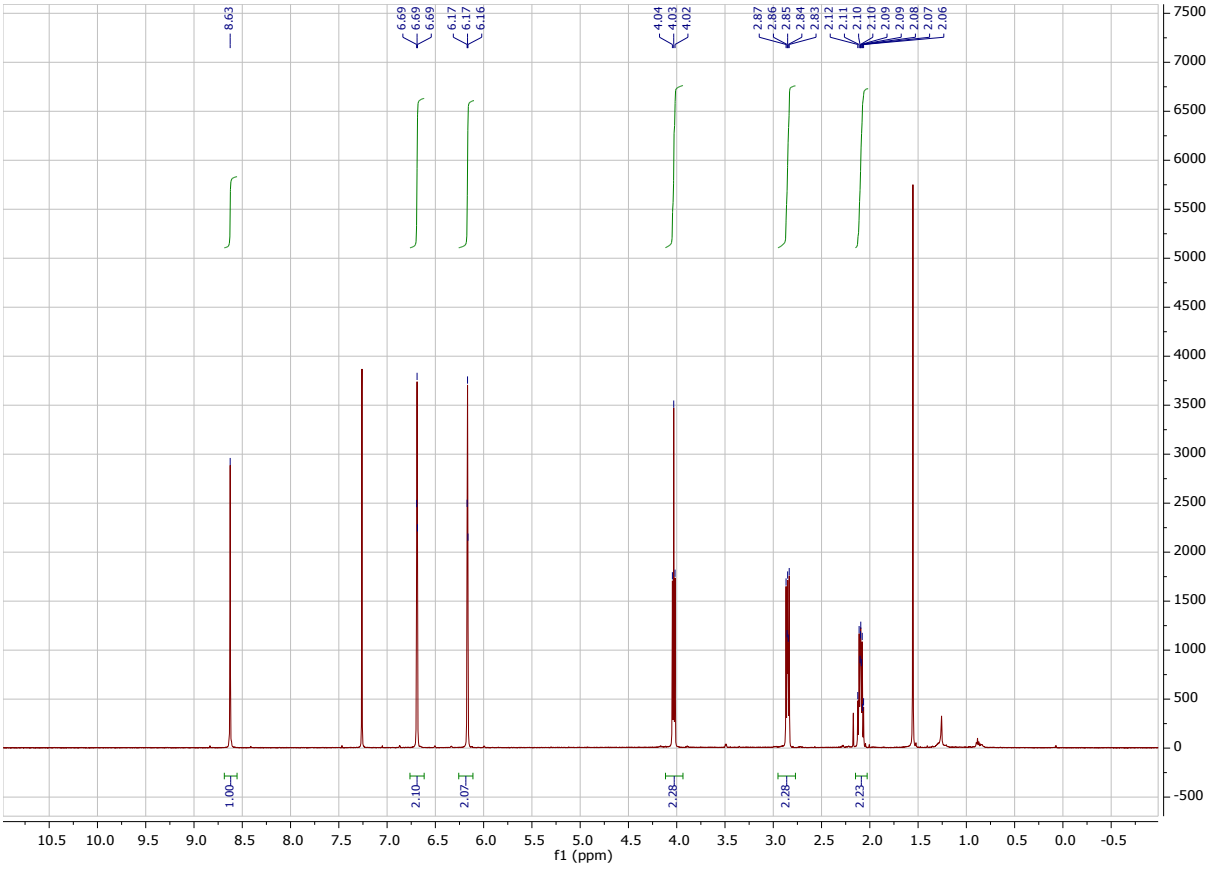
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 3-(4,6-Dichloropyrimidin-2-yl)-N-methylpropan-1-amine (3g)

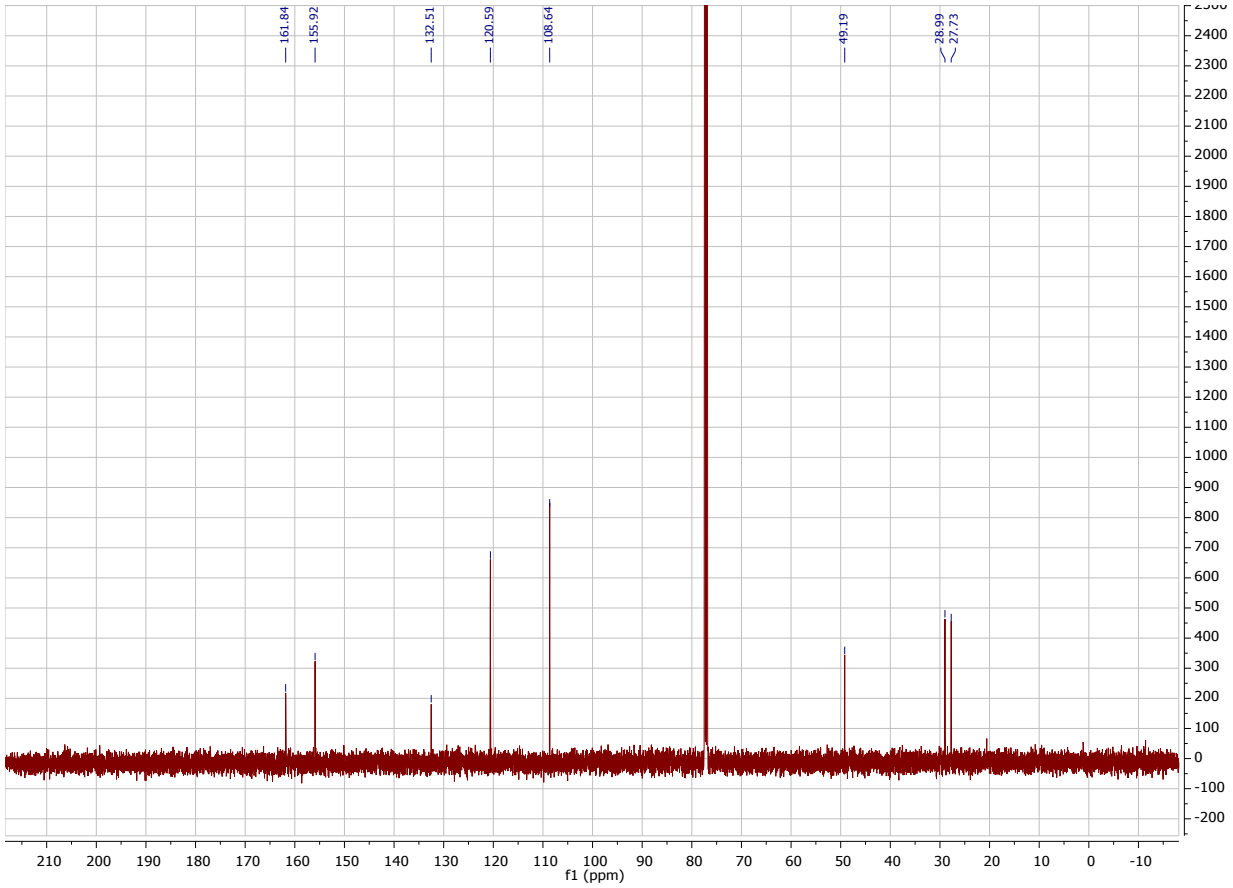


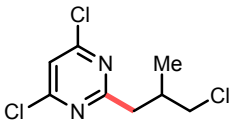

JKM-04-244-3-1_13C.1.fid
13C NMR
155.41
120.76
115.22
49.33
36.37
23.69
19.99
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



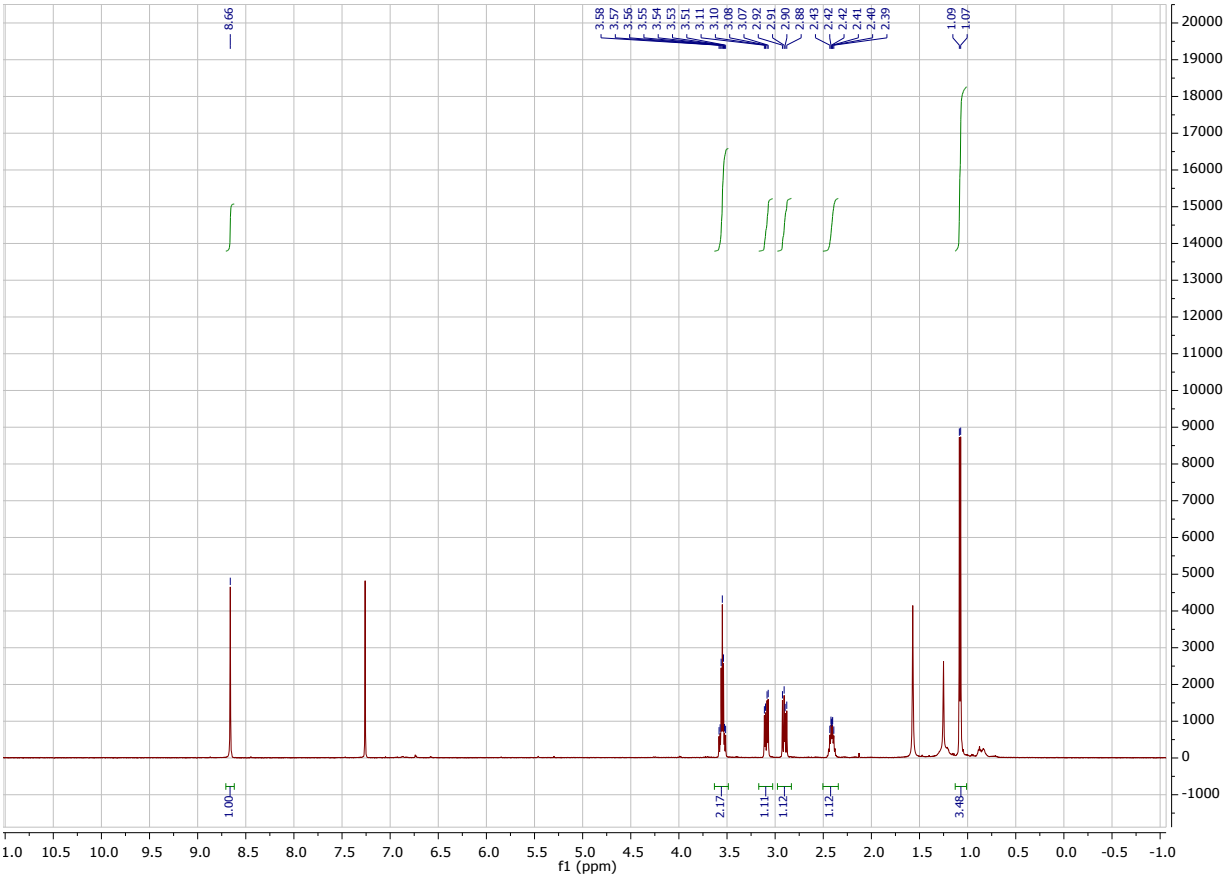
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2-(3-(1*H*-Pyrrol-1-yl)propyl)-4,6-dichloropyrimidine (3h)

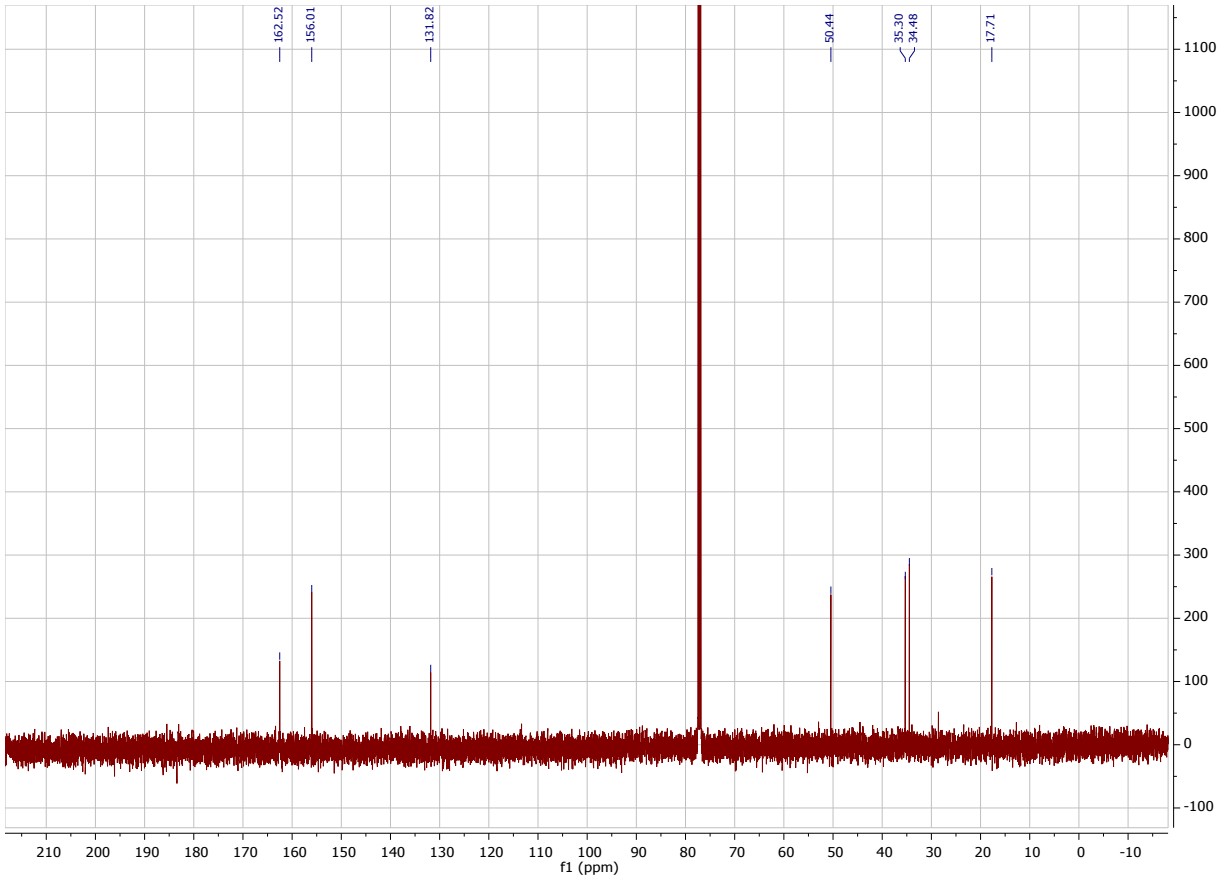


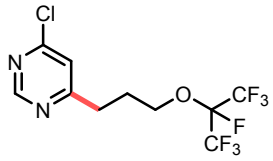

161.84
155.92
132.51
120.59
108.64
49.19
28.99
27.73
f1 (ppm)



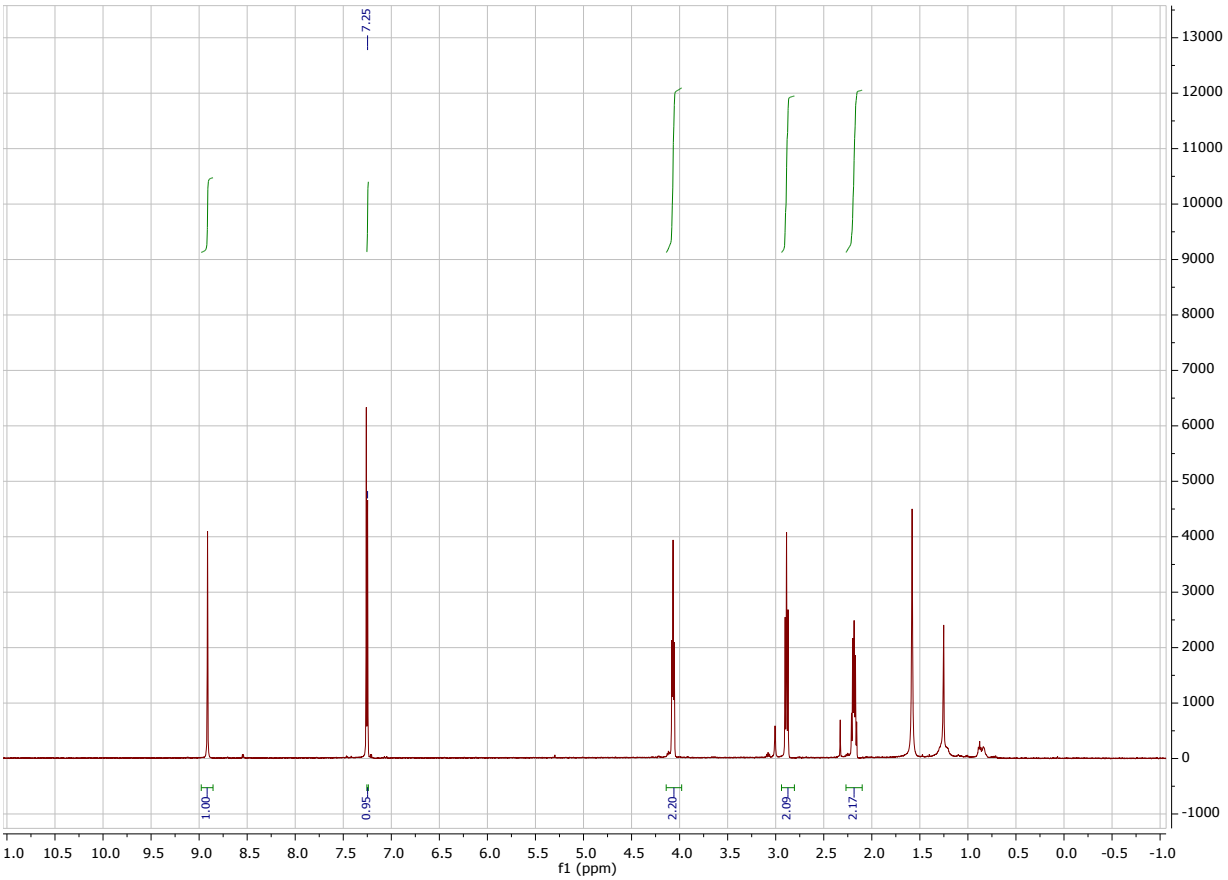
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(3-chloro-2-methylpropyl)pyrimidine (3i)

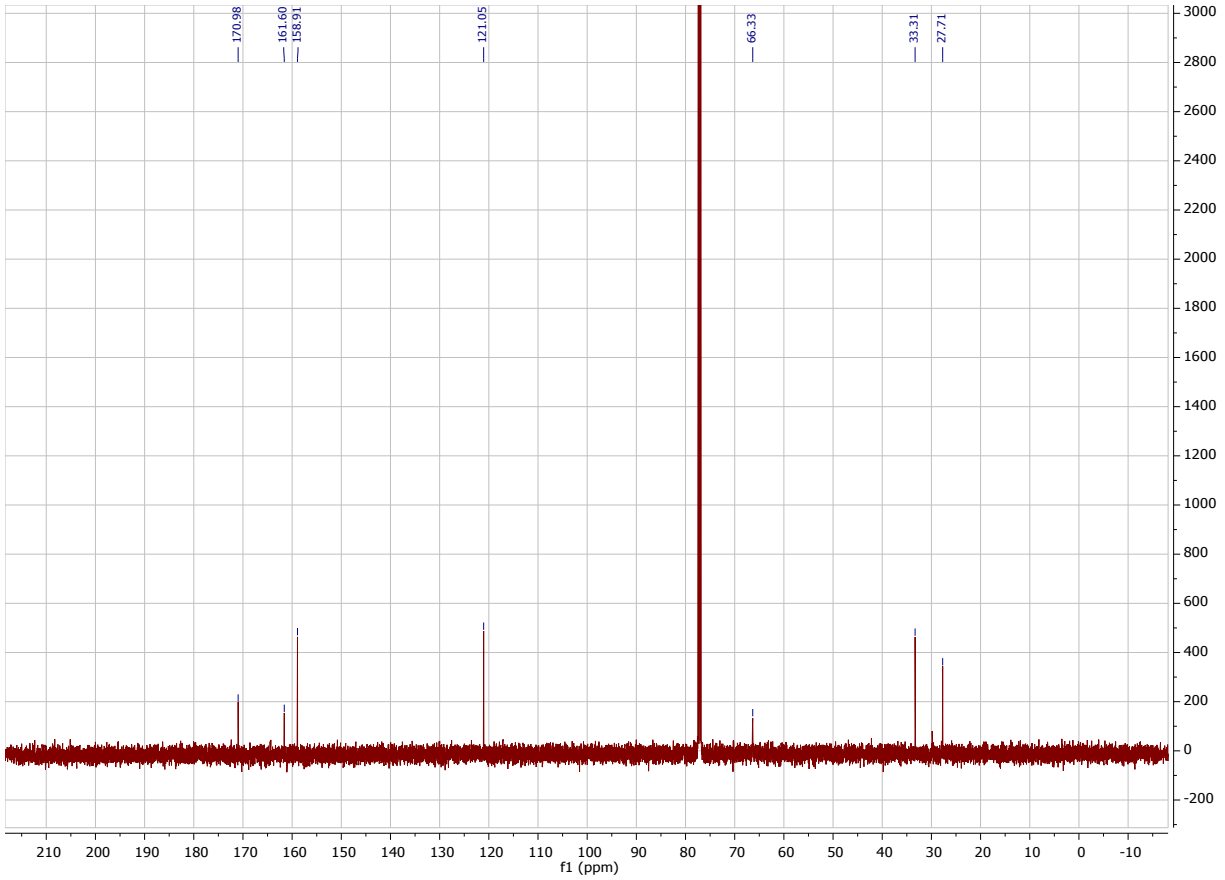


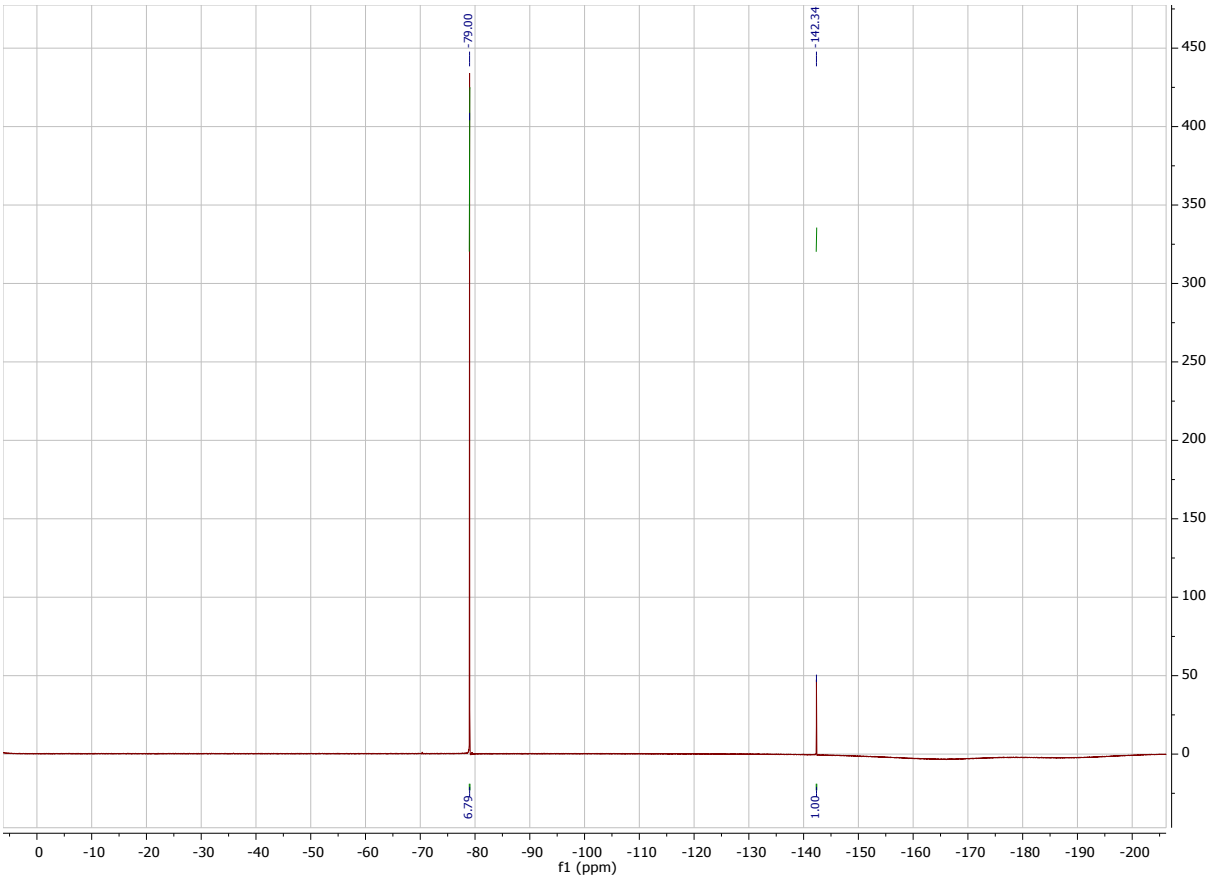

162.52
156.01
131.82
50.44
35.30
34.48
17.71
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

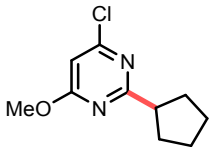


^{1}H NMR ($CDCl_3$, 500 MHz), ^{13}C NMR ($CDCl_3$, 126 MHz) and ^{19}F NMR (471 MHz, $CDCl_3$) of 4-Chloro-6-(3-((perfluoropropan-2-yl)oxy)propyl)pyrimidine(3j):

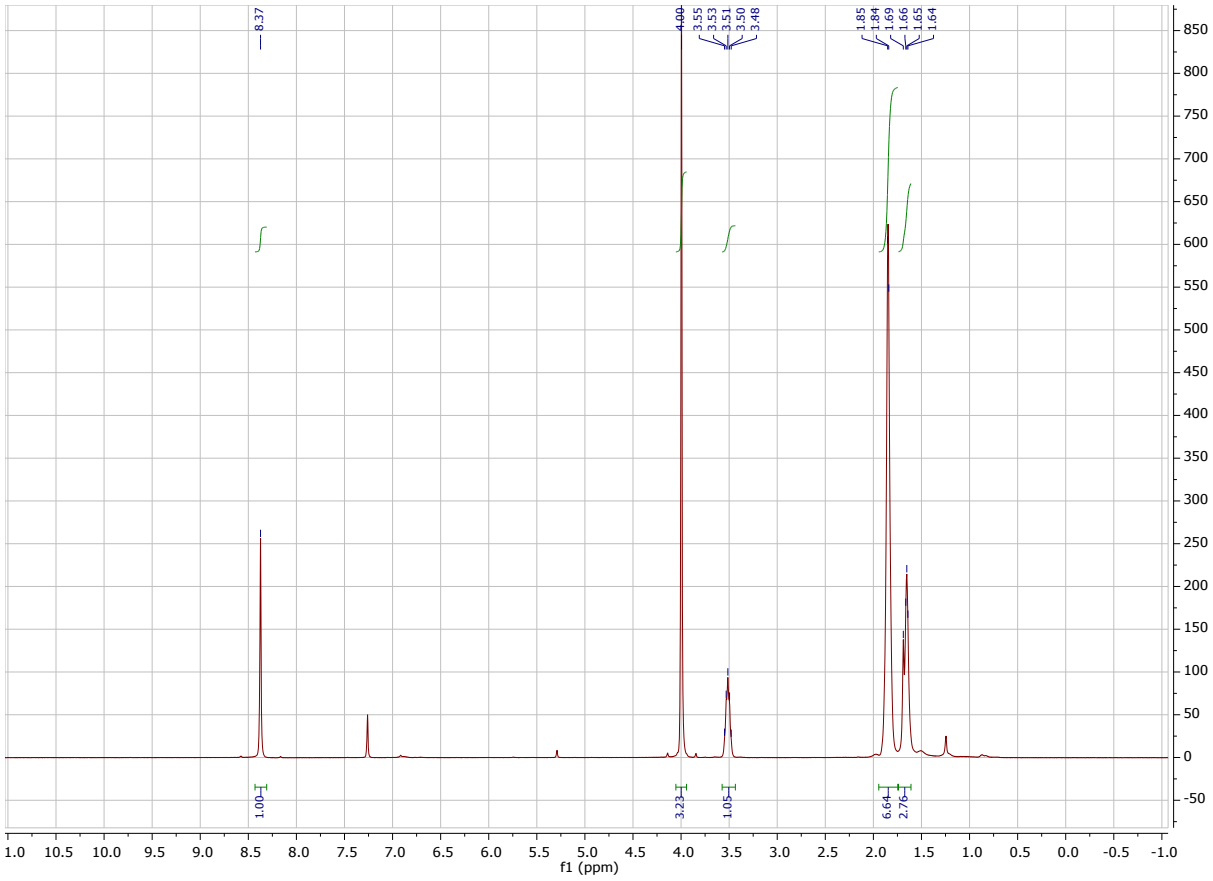


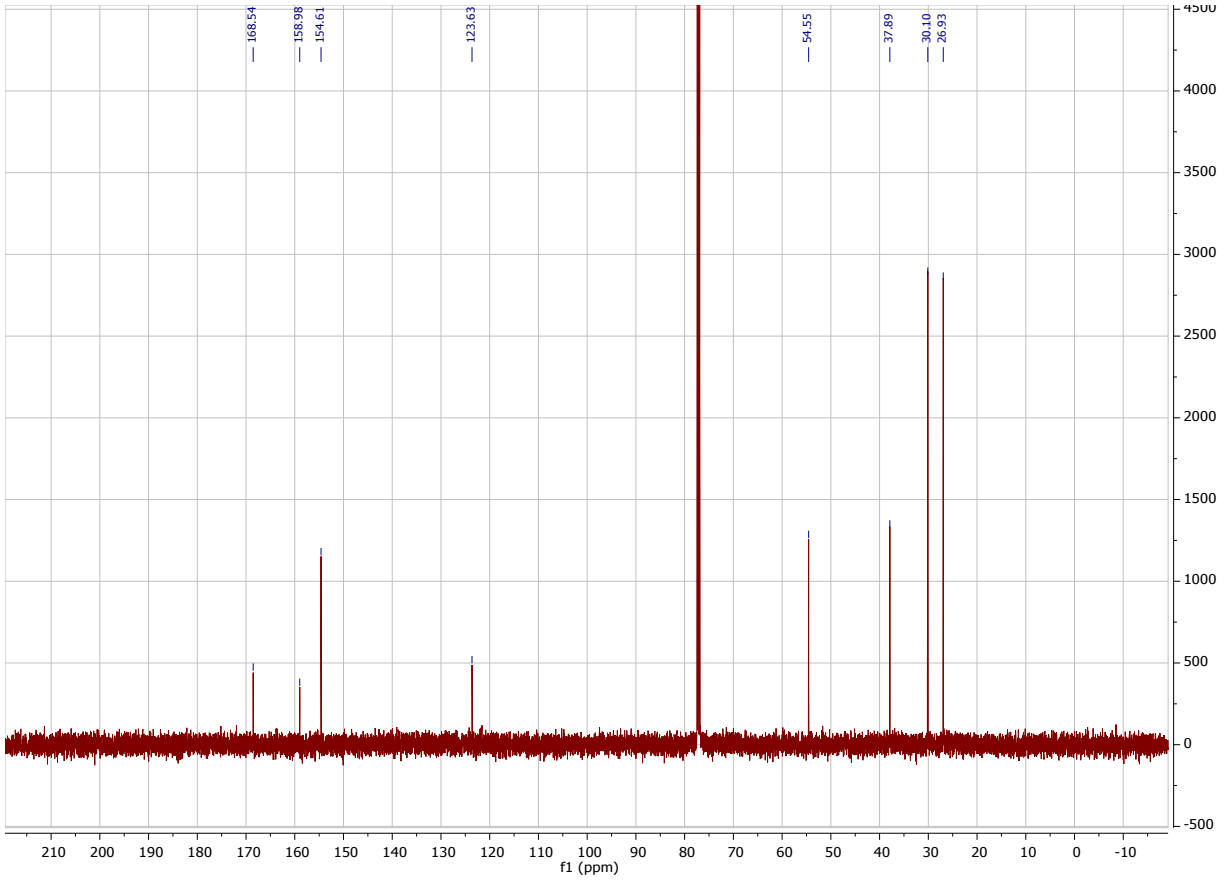

170.98
161.60
158.91
121.05
66.33
33.31
27.71
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

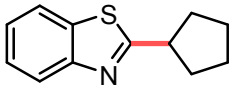

-79.00
-142.34
6.79
1.00
f1 (ppm)



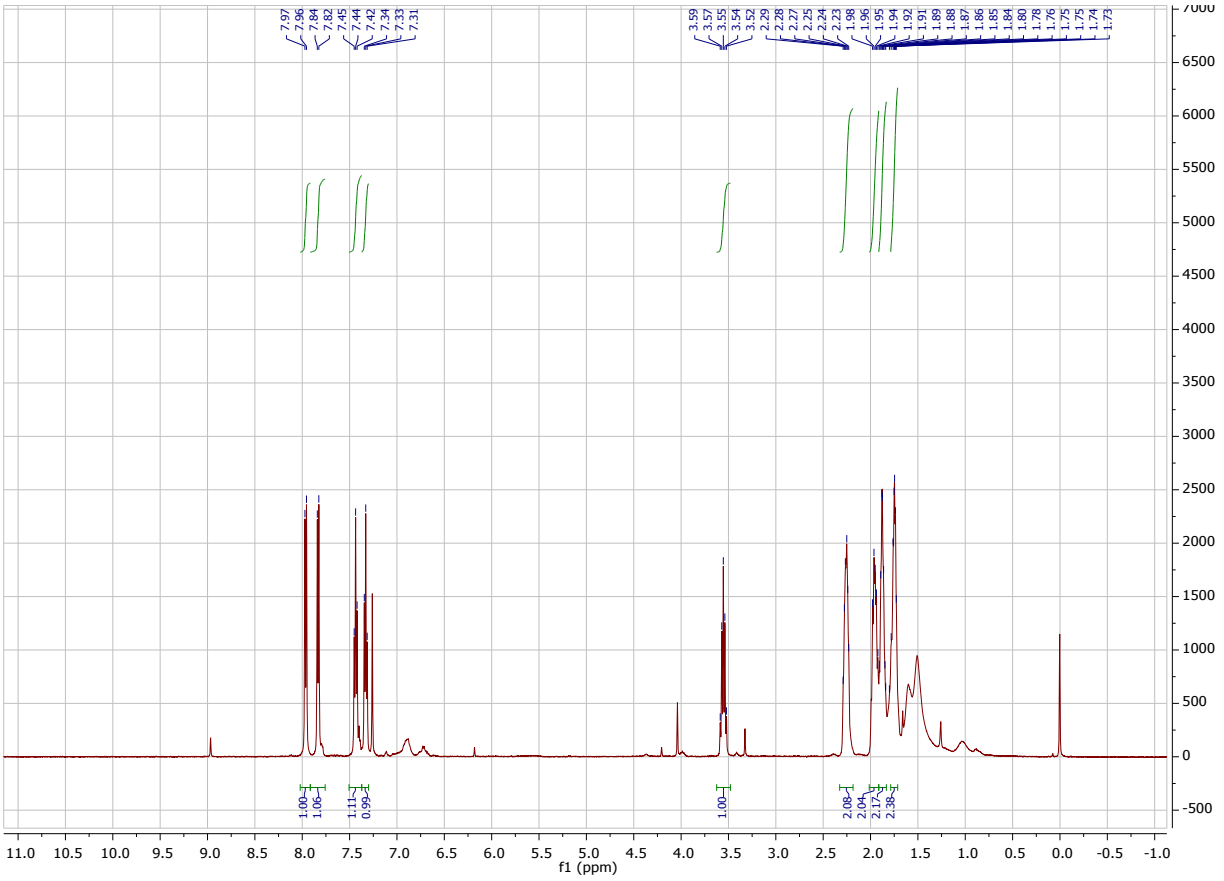
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4-Chloro-2-cyclopentyl-6-methoxypyrimidine (3k)

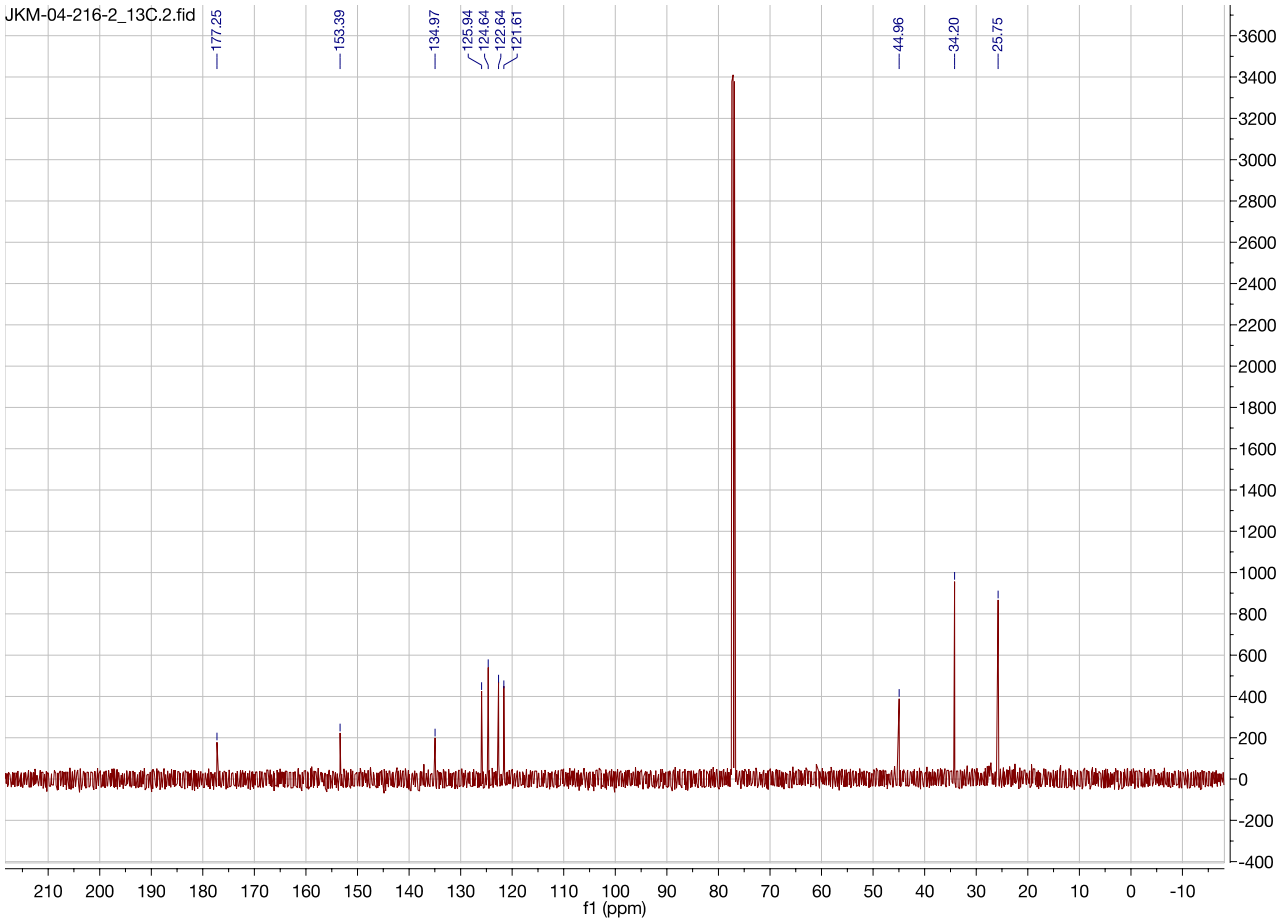


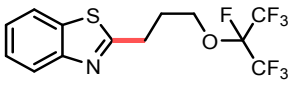

168.54
158.98
154.61
123.63
54.55
37.89
30.10
26.93
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



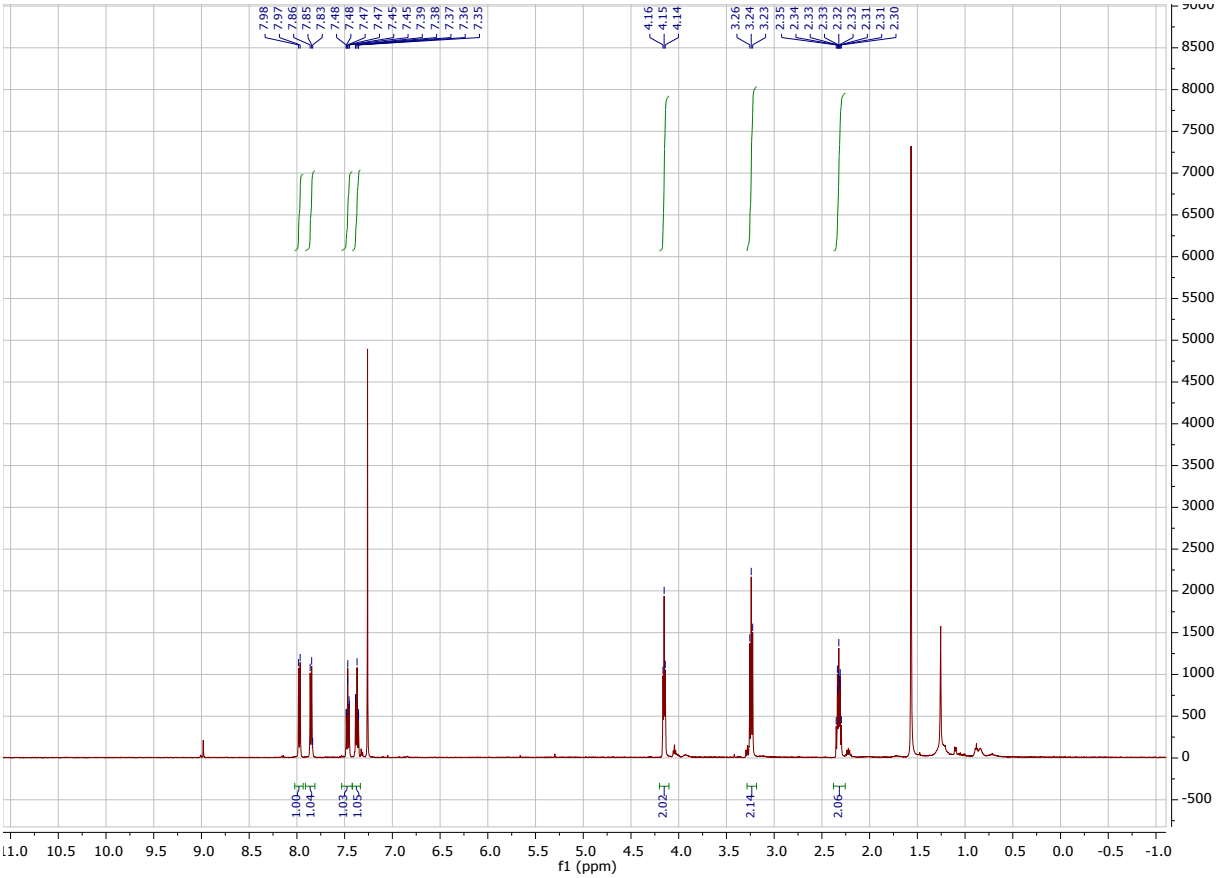
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2-Cyclopentylbenzo[d]thiazole (3l):

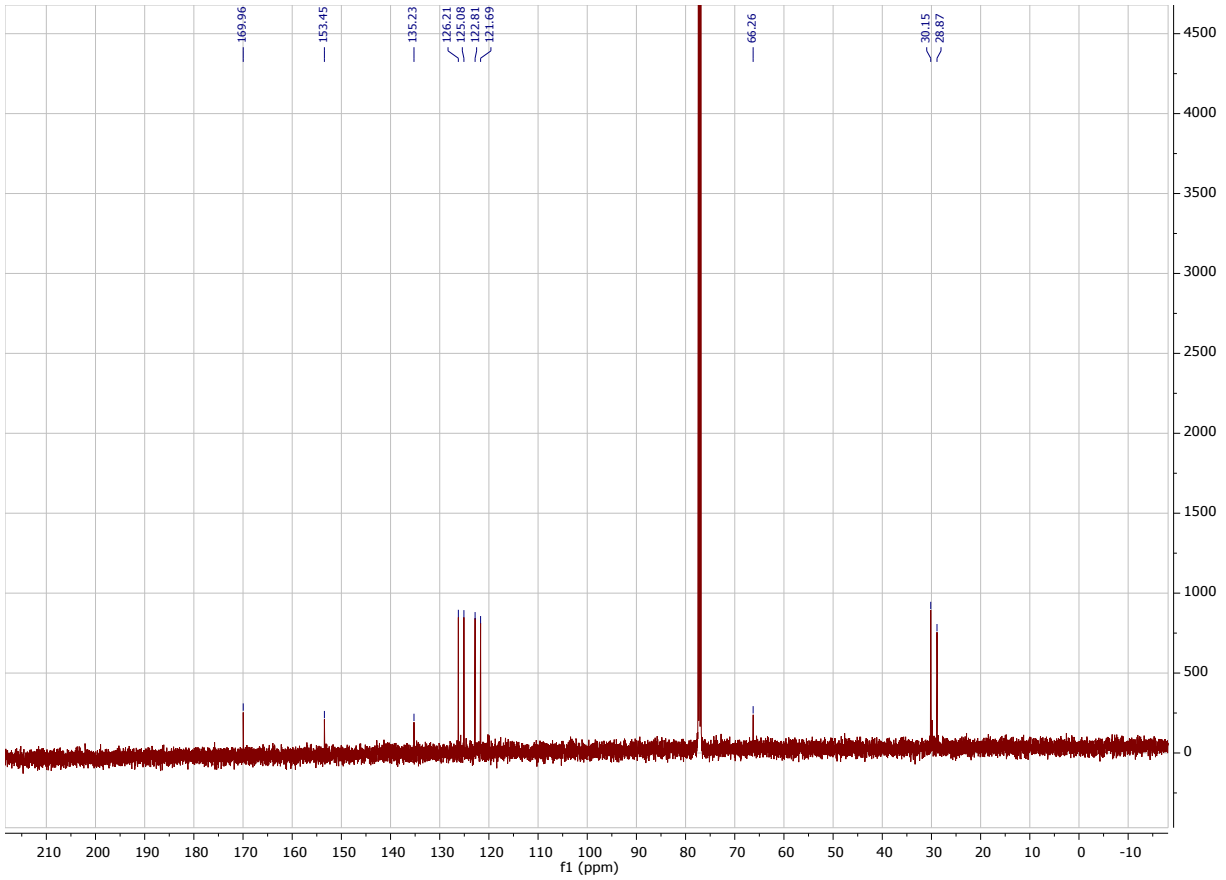


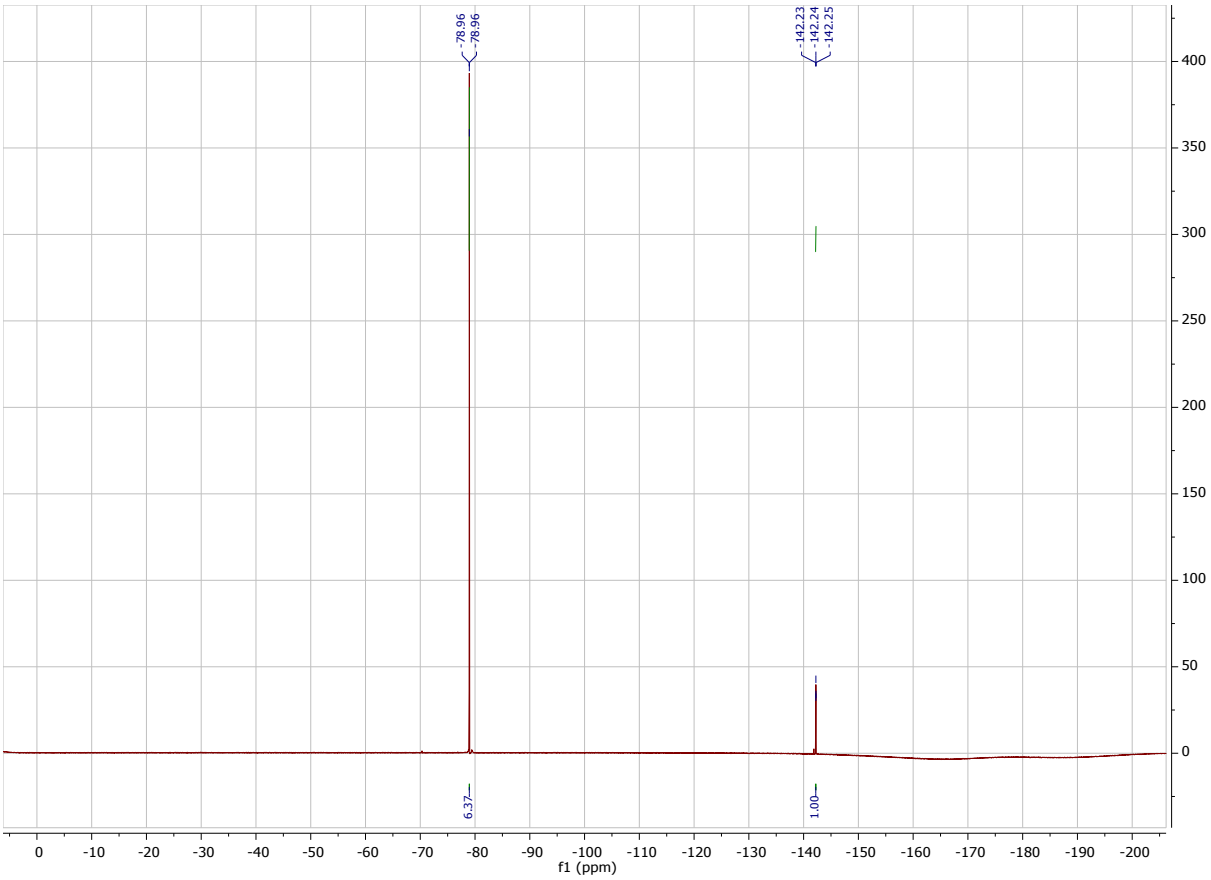

JKM-04-216-2_13C.2.fid
177.25
153.39
134.97
125.94
124.64
122.64
121.61
44.96
34.20
25.75
f1 (ppm)

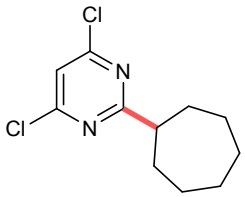


^{1}H NMR ($CDCl_3$, 500 MHz), ^{13}C NMR ($CDCl_3$, 126 MHz) and ^{19}F NMR (471 MHz, $CDCl_3$) of 2-(4,5,5,5-Tetrafluoro-4-(trifluoromethyl)pentyl)benzo[d]thiazole (3m)

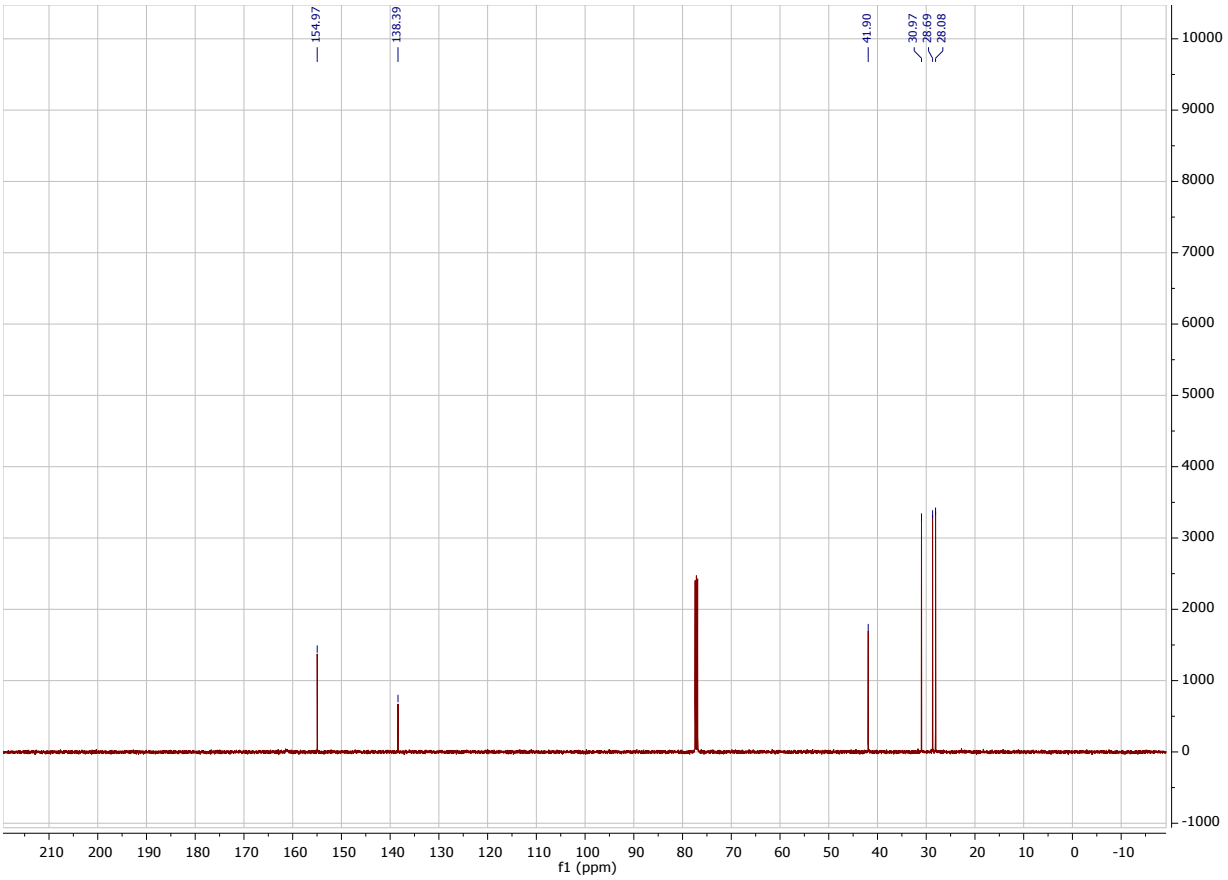


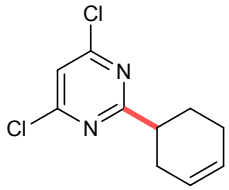

169.96
153.45
135.23
126.21
125.08
122.81
121.69
66.26
30.15
28.87
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-78.96
-78.96
-142.23
-142.24
-142.25
400
350
300
250
200
150
100
50
0
6.37
1.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

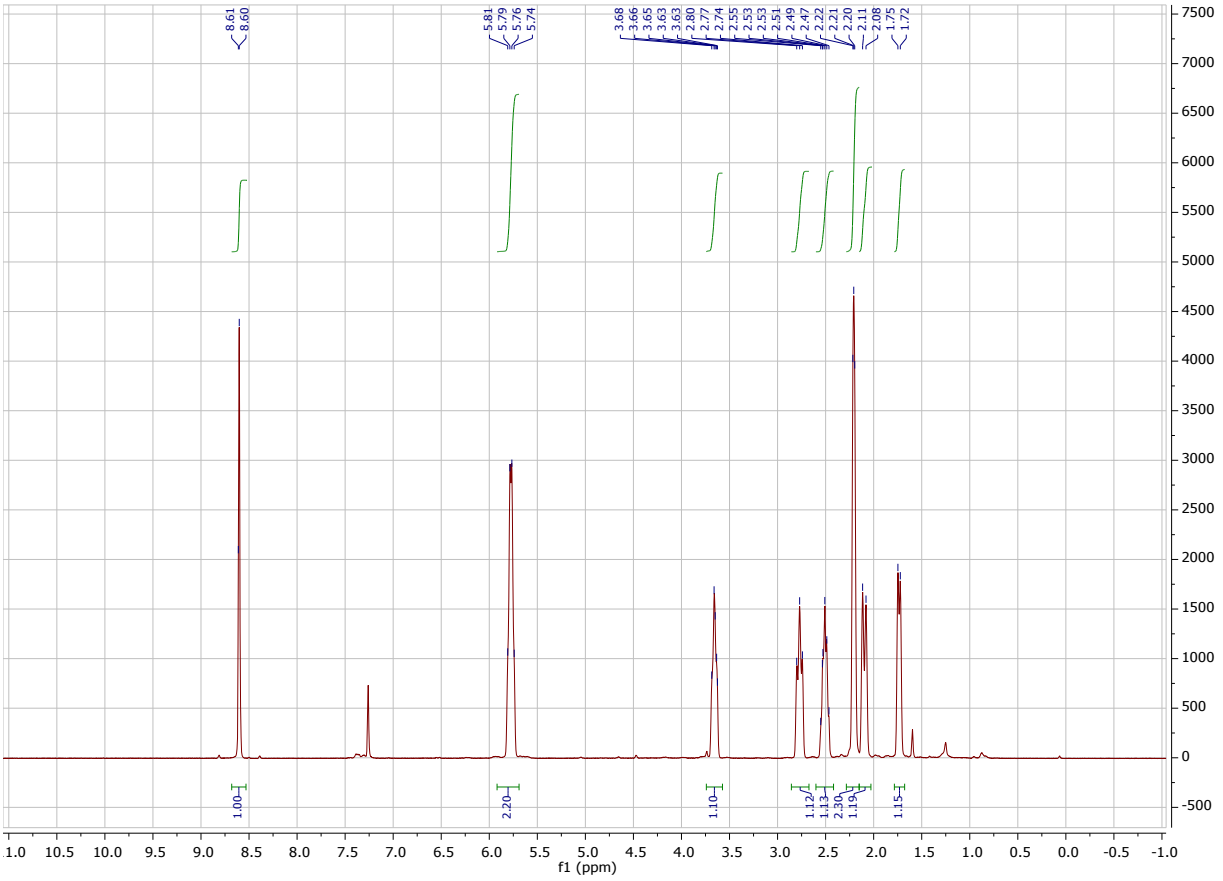


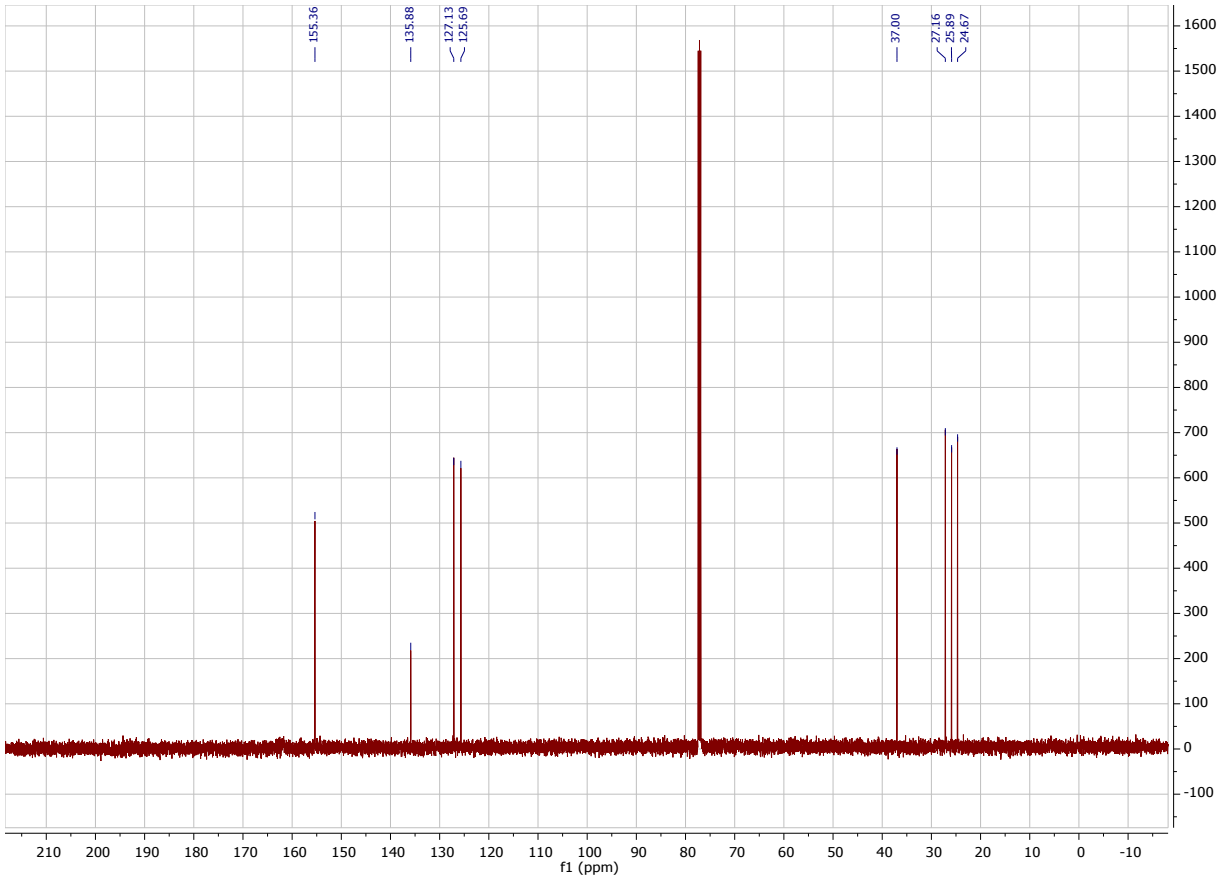
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-cycloheptylpyrimidine (5b)

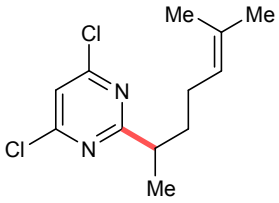

154.97
138.39
41.90
30.97
28.69
28.08
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



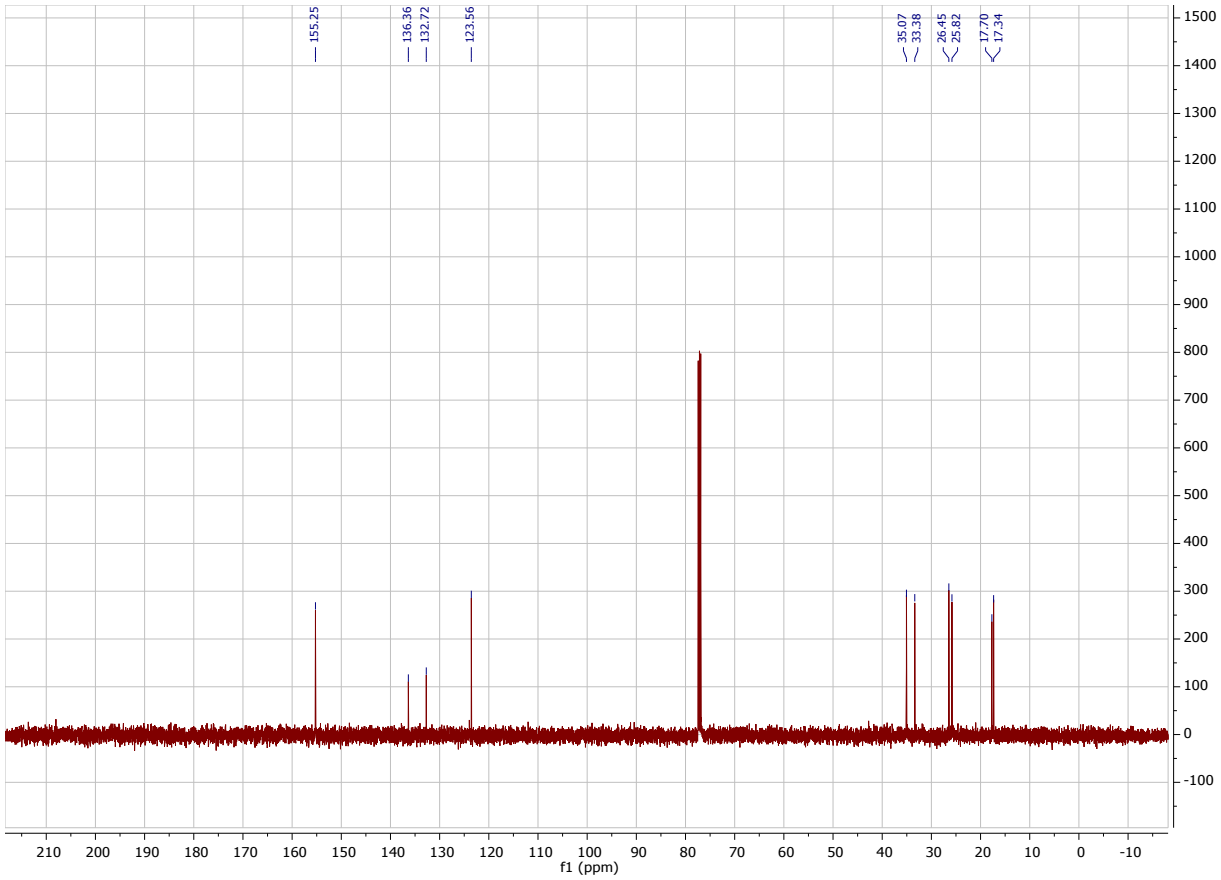
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(cyclohex-3-en-1-yl) pyrimidine (5c)

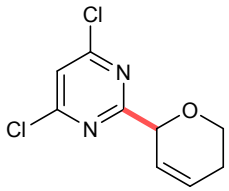



155.36
135.88
127.13
125.69
37.00
27.16
25.89
24.67
f1 (ppm)

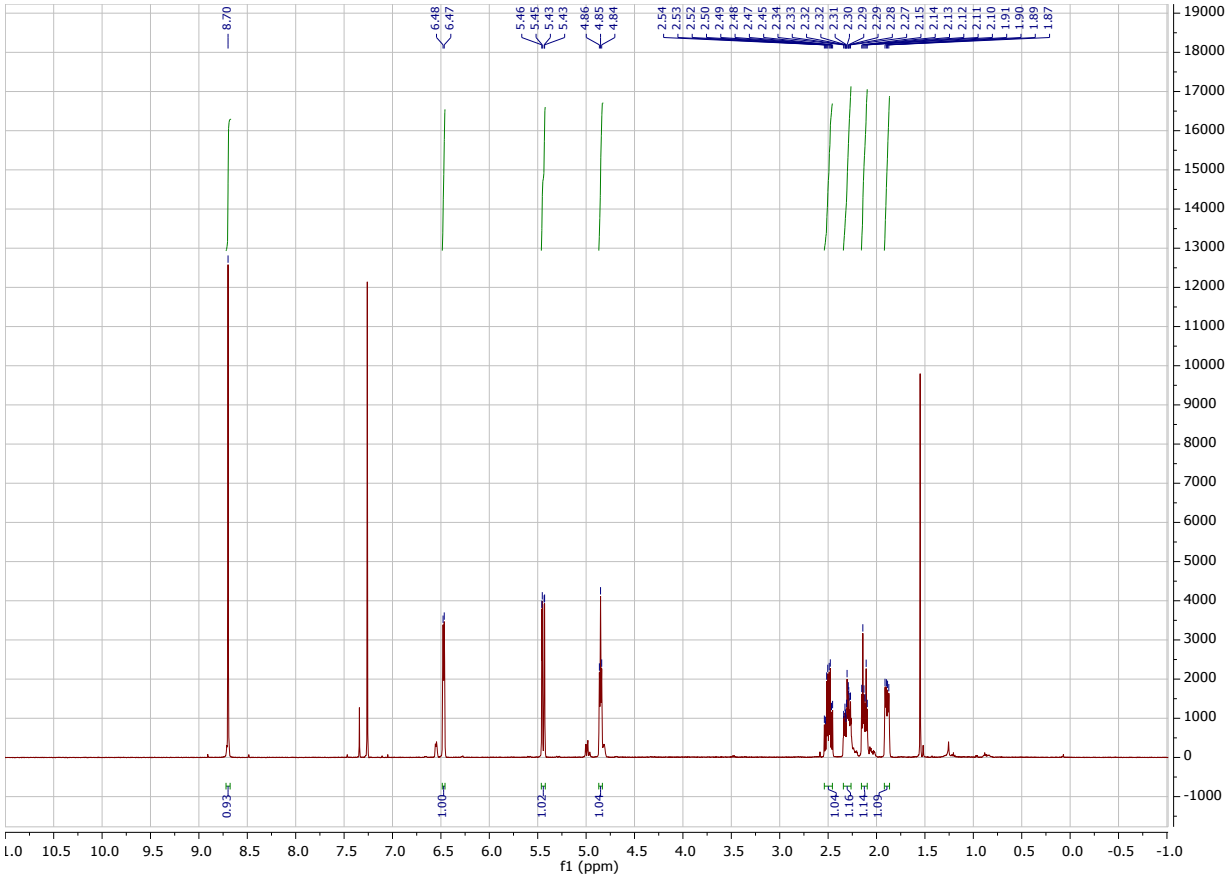


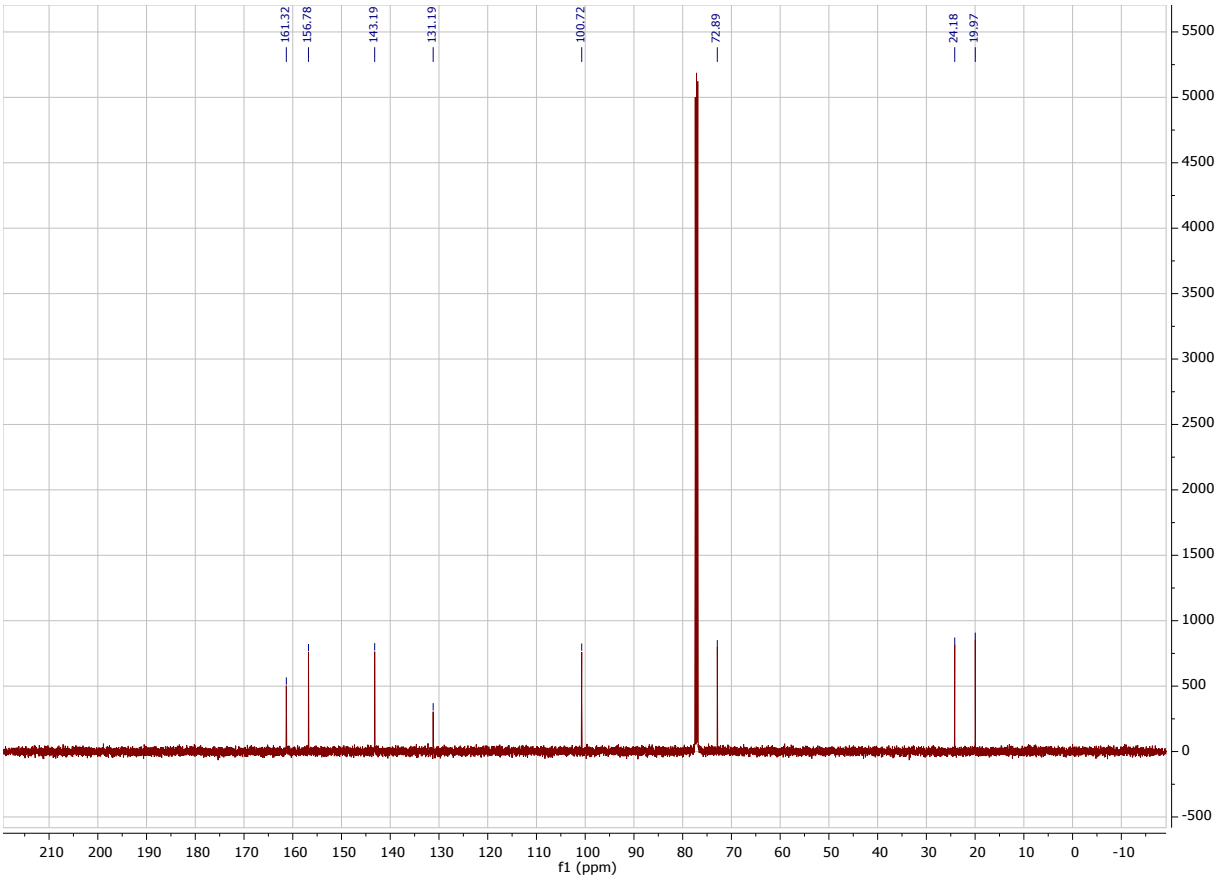
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(6-methylhept-5-en-2-yl)pyrimidine (5d)

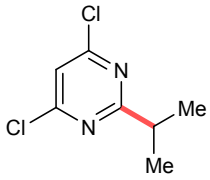

155.25
136.36
132.72
123.56
35.07
33.38
26.45
25.82
17.70
17.34
f1 (ppm)



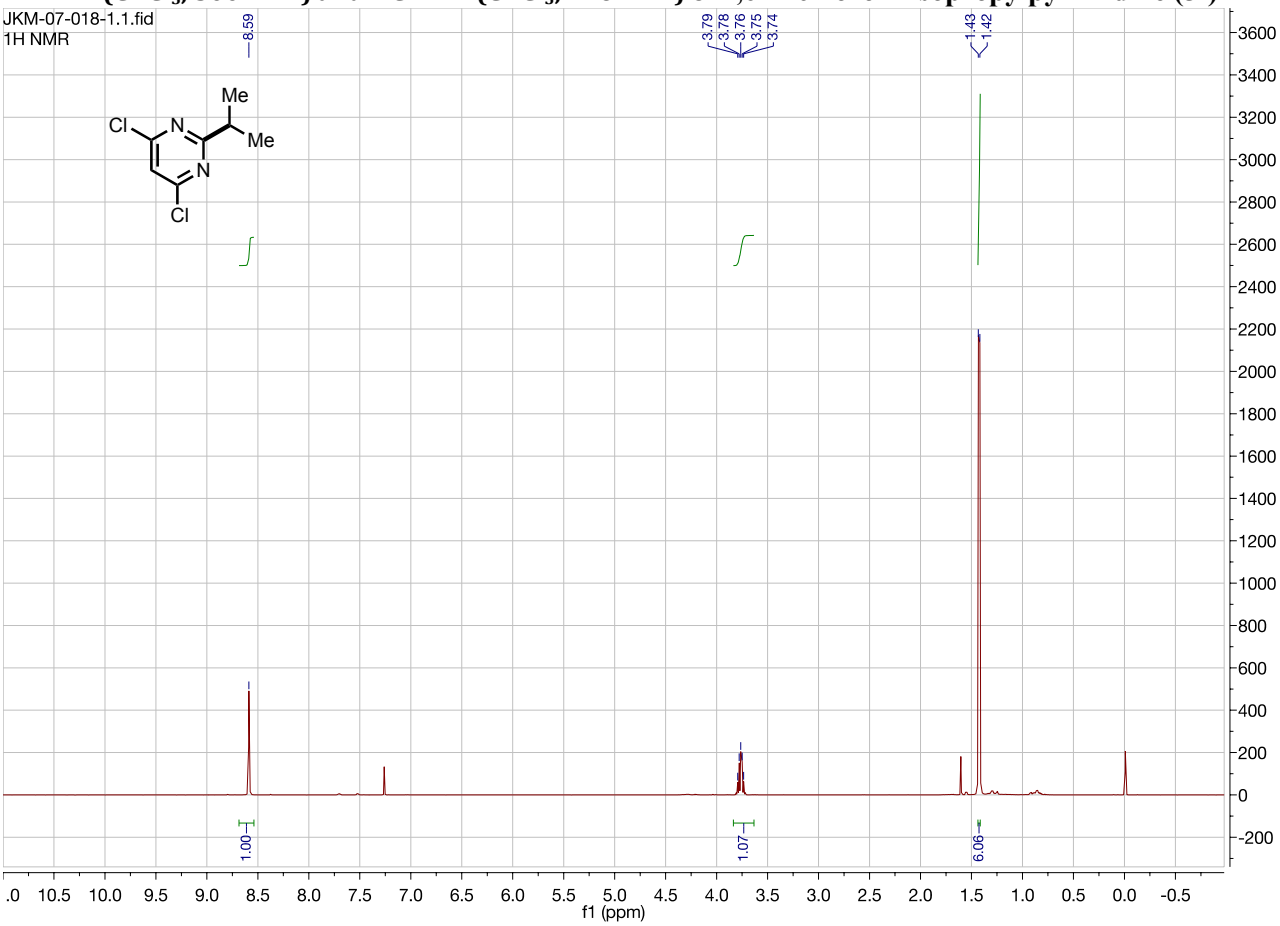
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(5,6-dihydro-2H-pyran-2-yl) pyrimidine (5e)

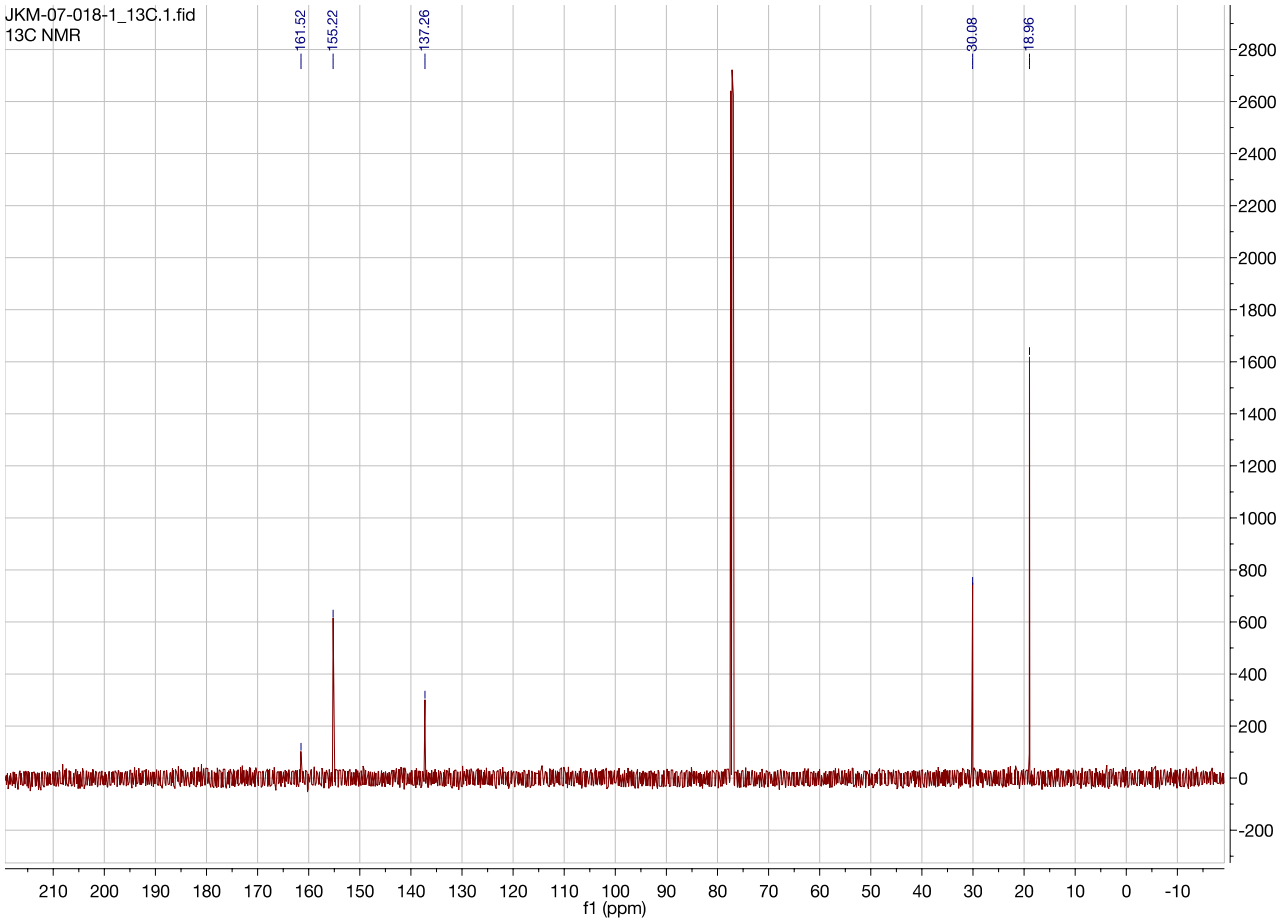


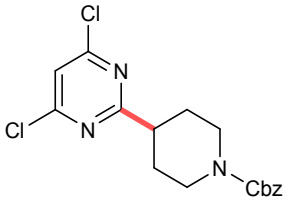

161.32
156.78
143.19
131.19
100.72
72.89
24.18
19.97
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



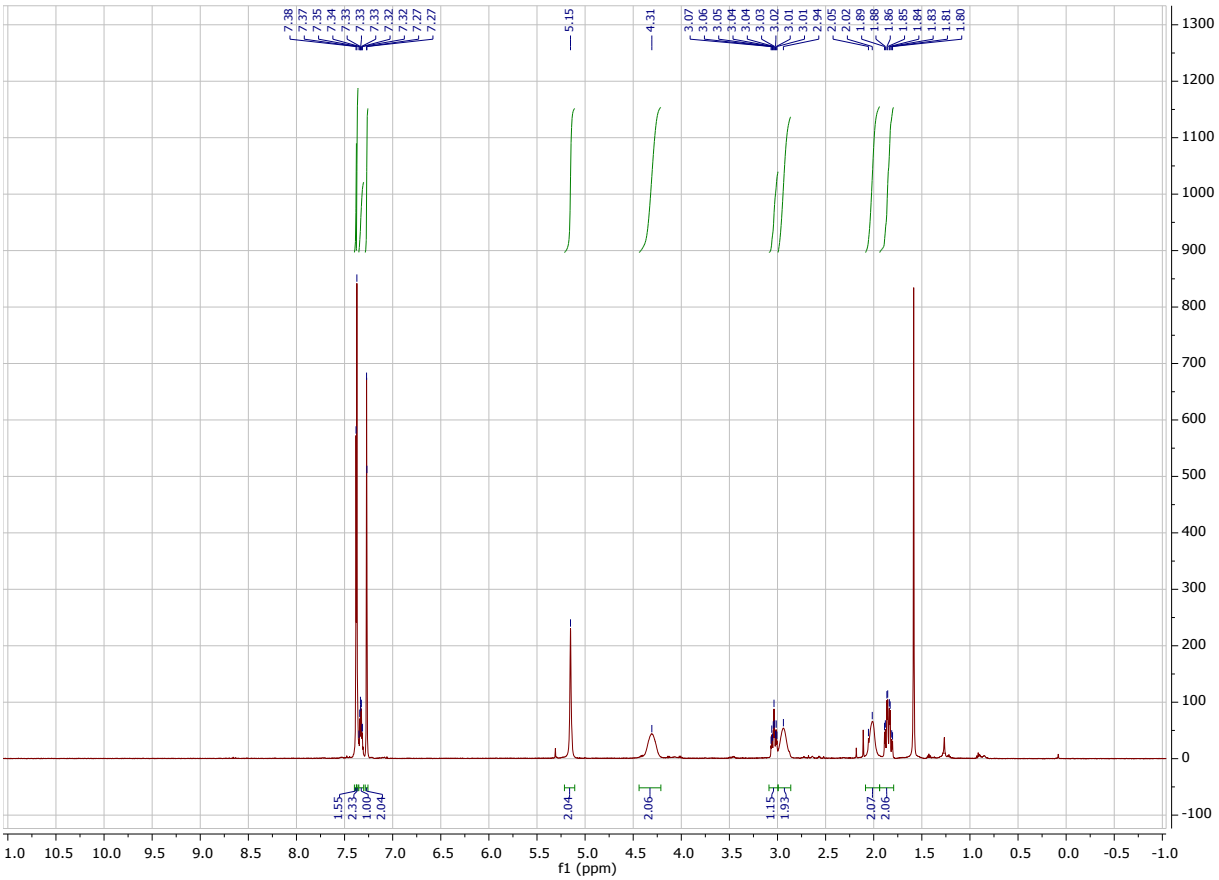
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-isopropylpyrimidine (5f)

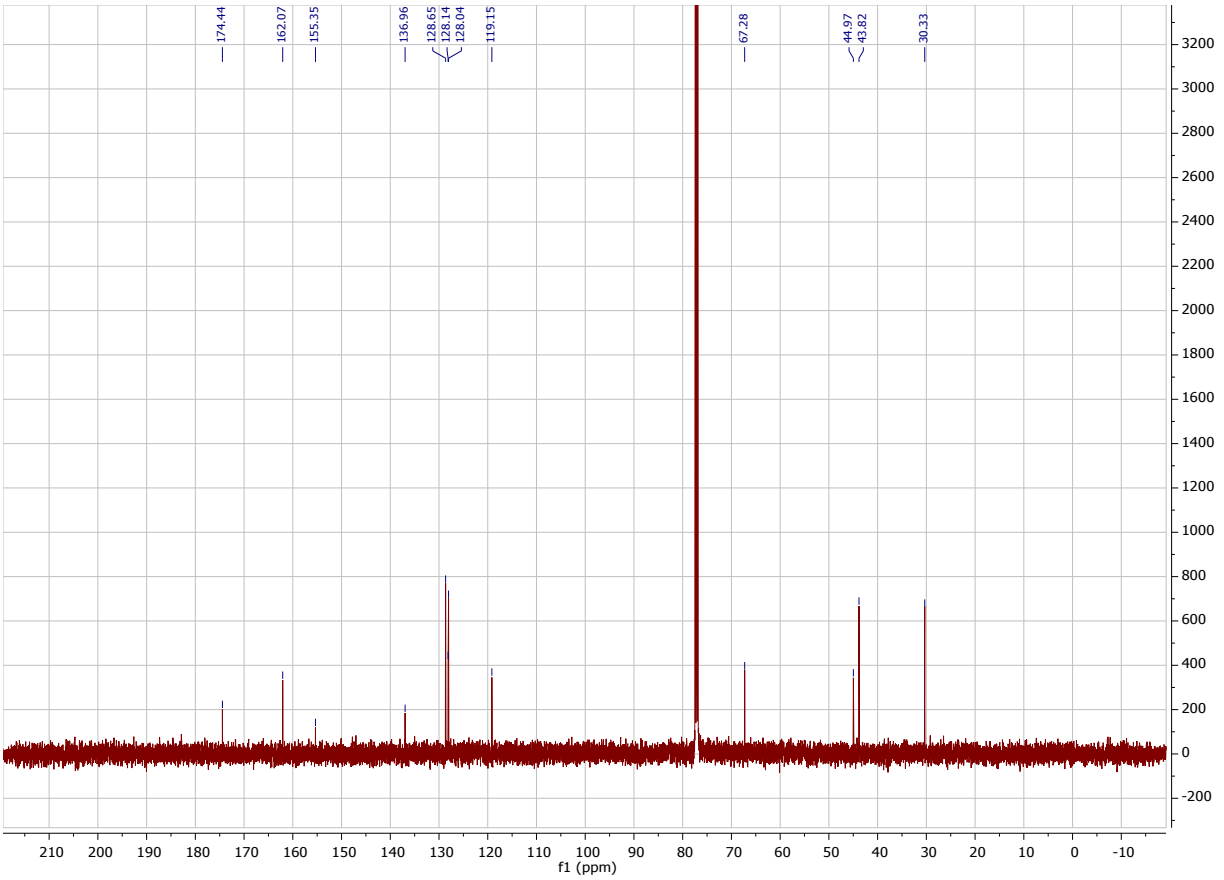


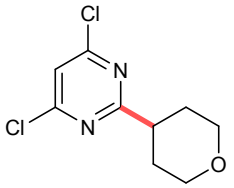

JKM-07-018-1_13C.1.fid
13C NMR
161.52
155.22
137.26
30.08
18.96
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



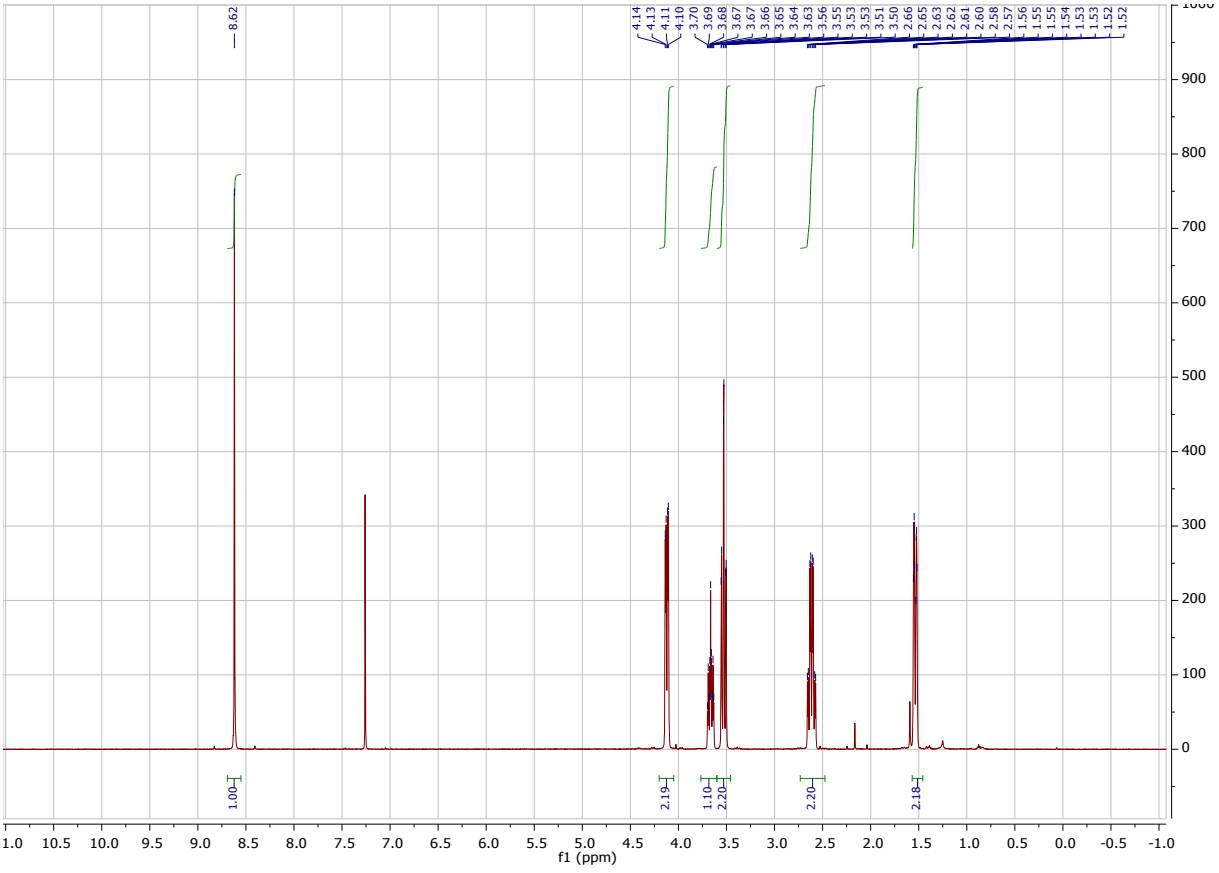
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of Benzyl 4-(4,6-dichloropyrimidin-2-yl)piperidine-1-carboxylate (5g)

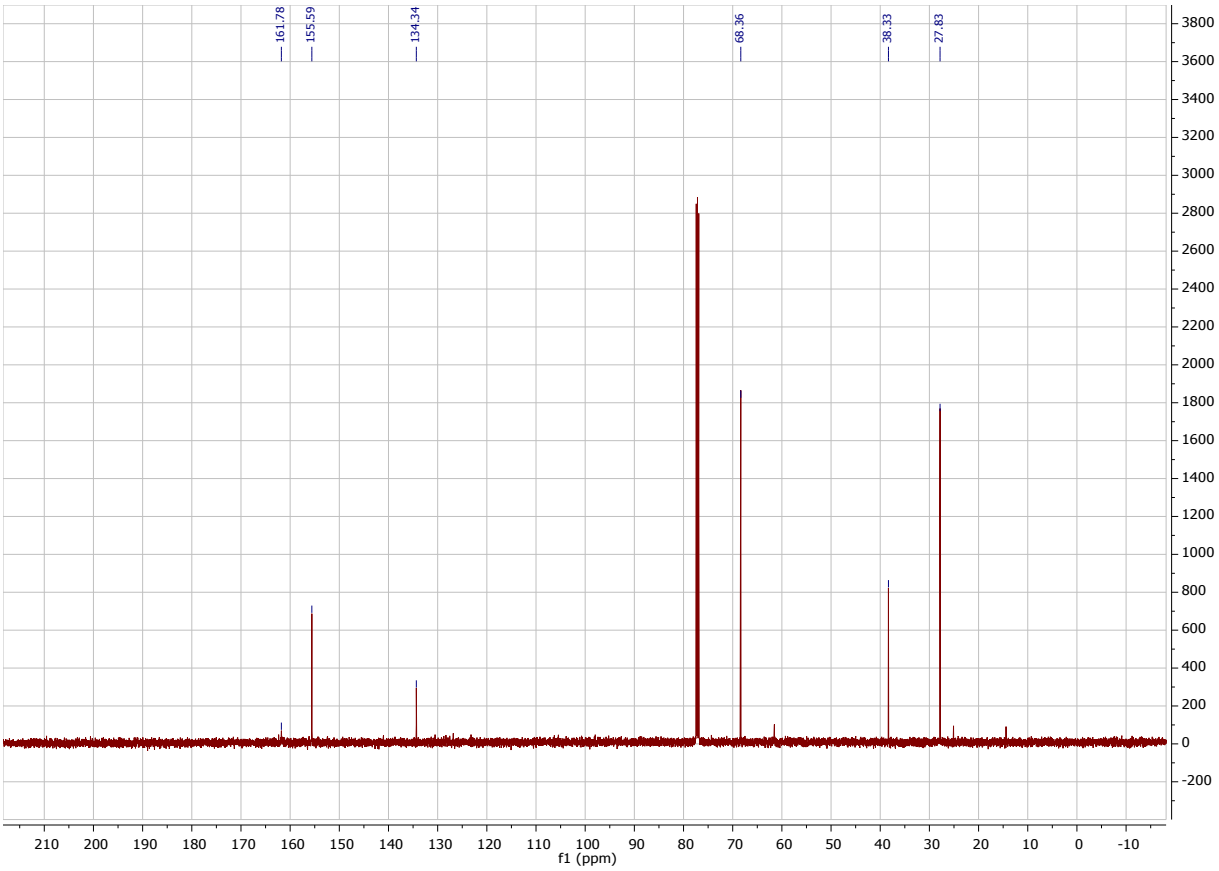


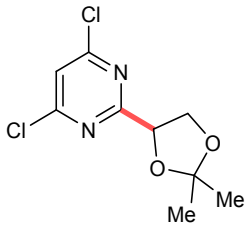

174.44
162.07
155.35
136.96
128.65
128.14
128.04
119.15
67.28
44.97
43.82
30.33
f1 (ppm)



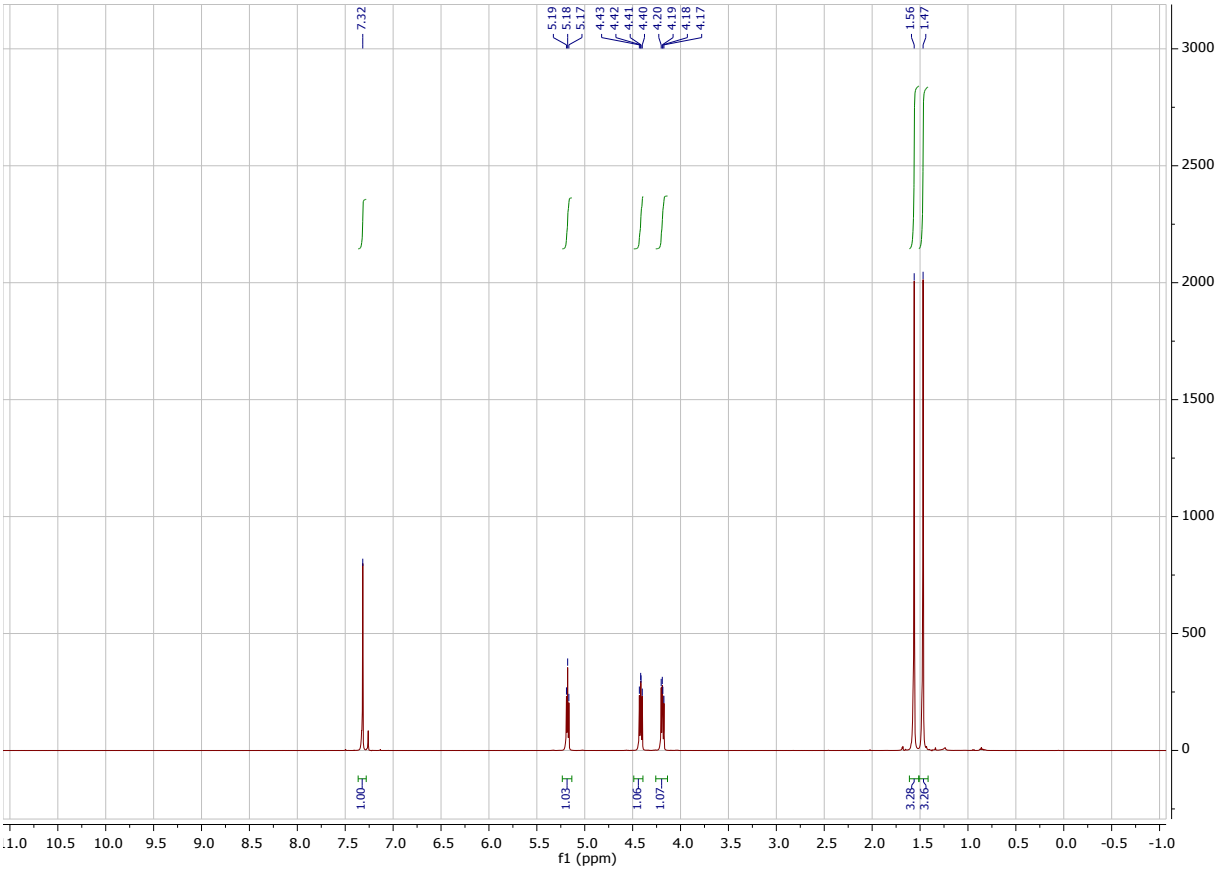
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(tetrahydro-2H-pyran-4-yl)pyrimidine (5h)

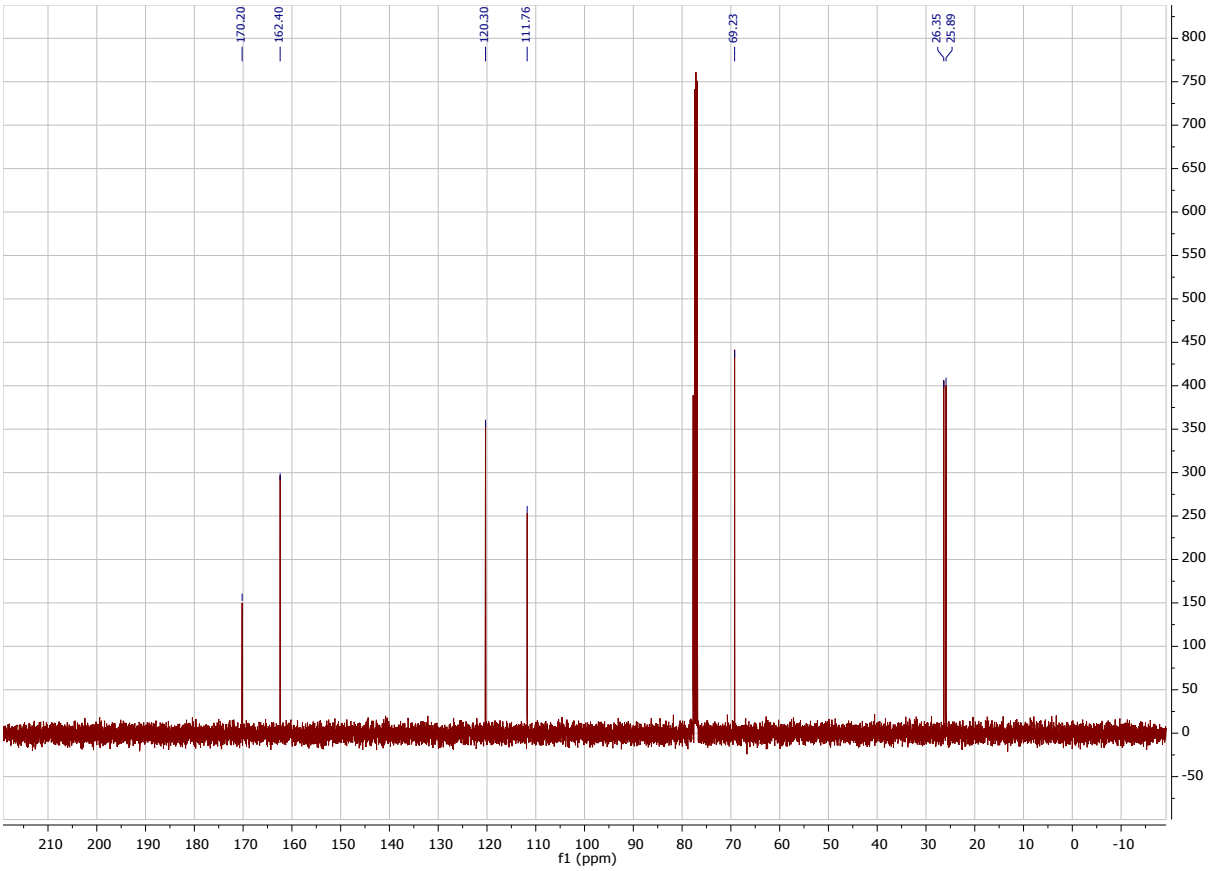


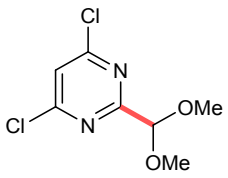

161.78
155.59
134.34
68.36
38.33
27.83
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



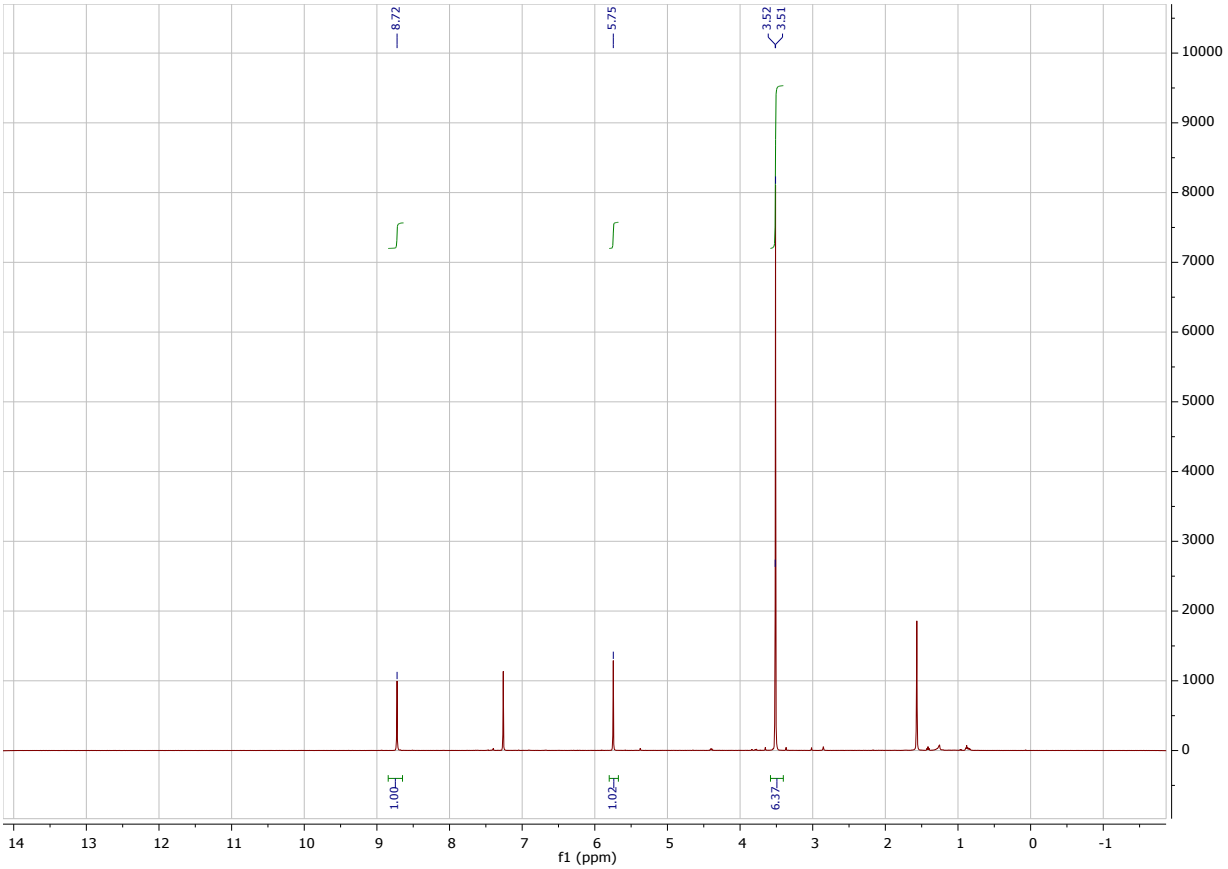
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl) pyrimidine (5i)

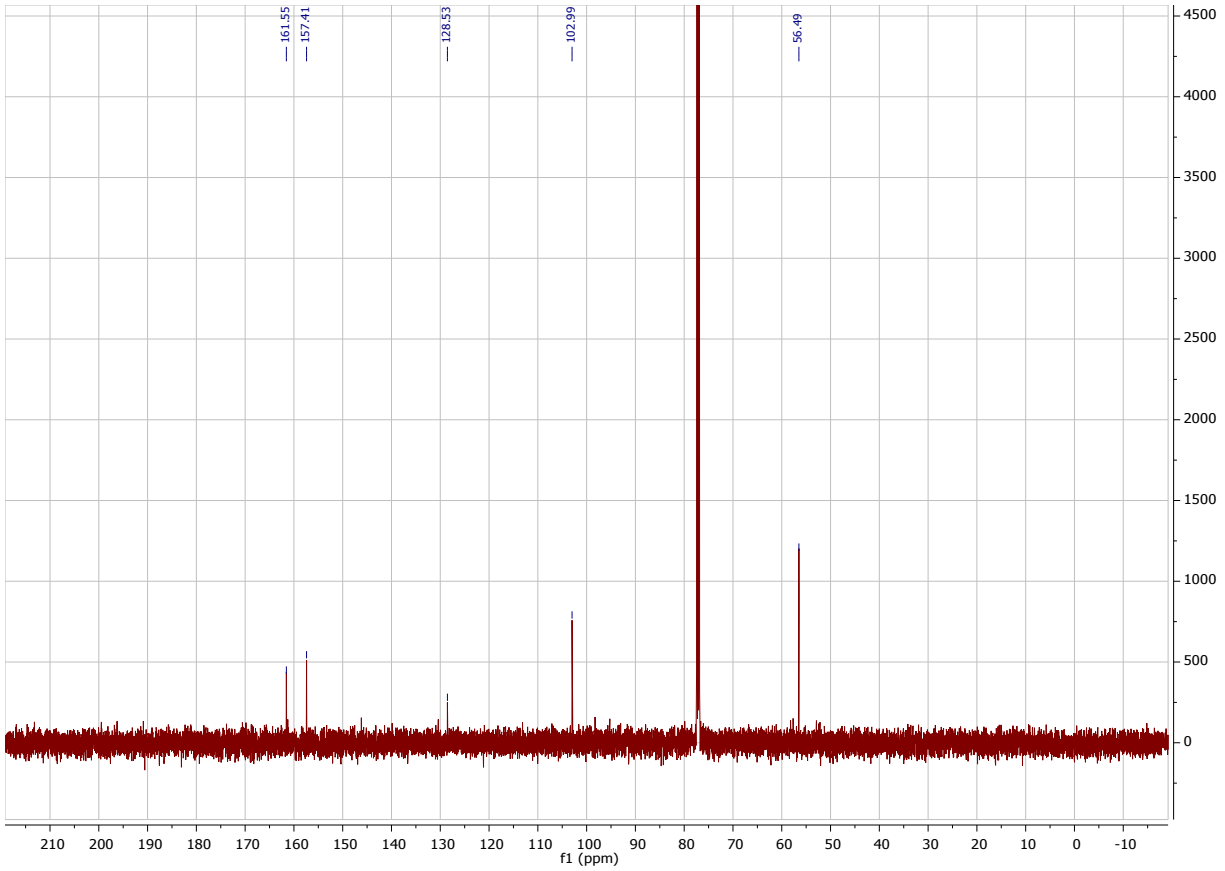


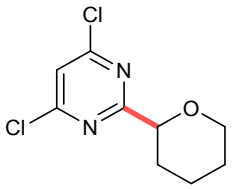

170.20
162.40
120.30
111.76
69.23
26.35
25.89
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Cl
N
OMe
Cl
N
OMe

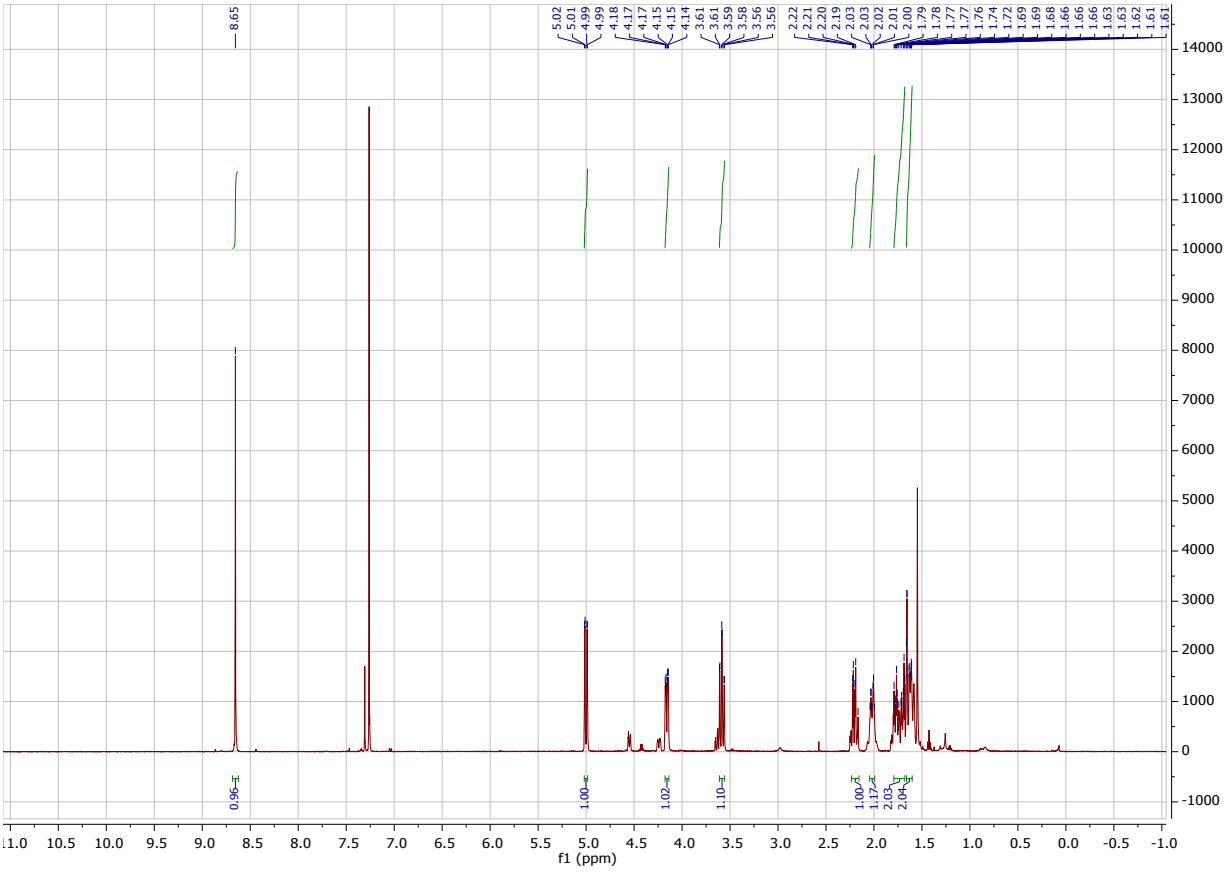
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(dimethoxymethyl)pyrimidine (5j)

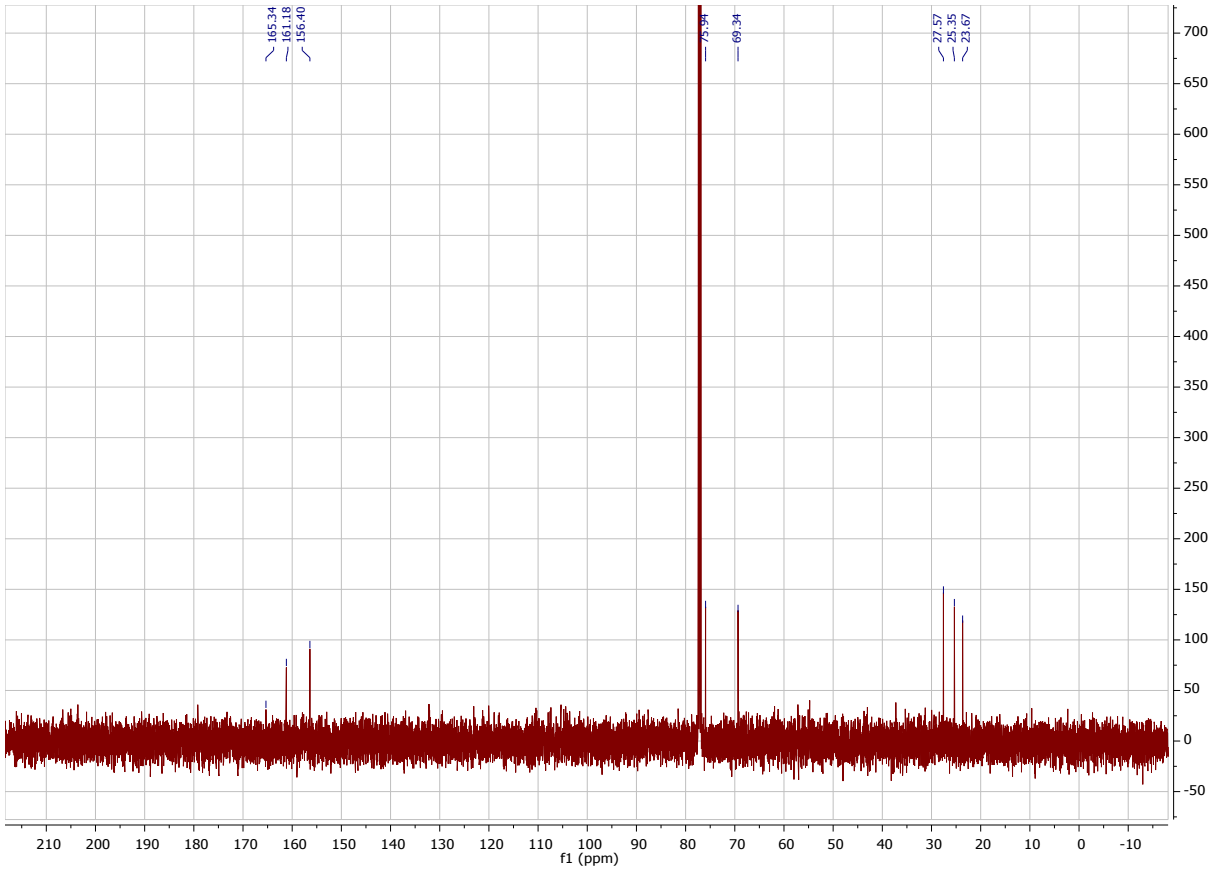


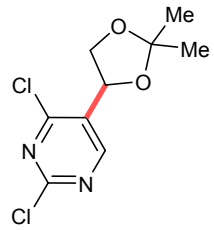

161.55
157.41
128.53
102.99
56.49
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



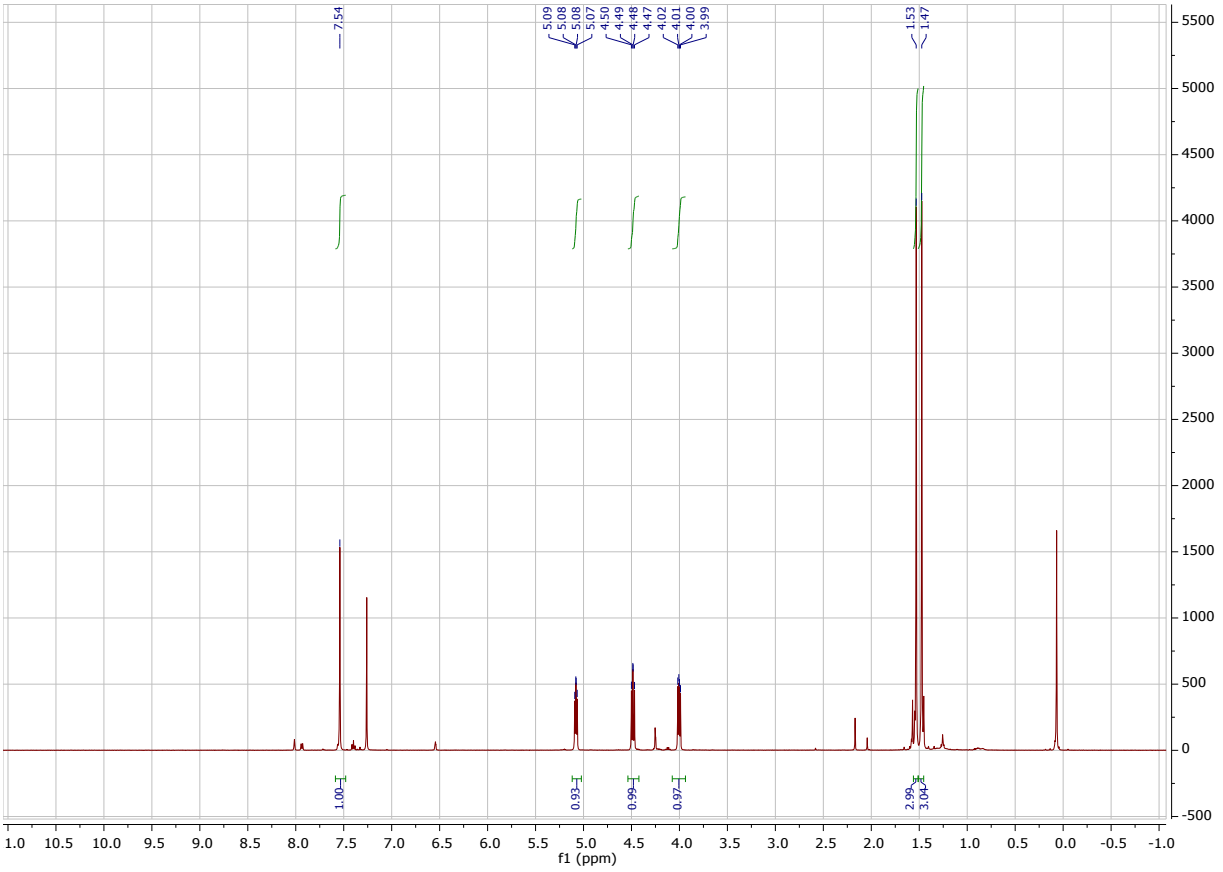
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4,6-Dichloro-2-(tetrahydro-2H-pyran-2-yl) pyrimidine (5k)

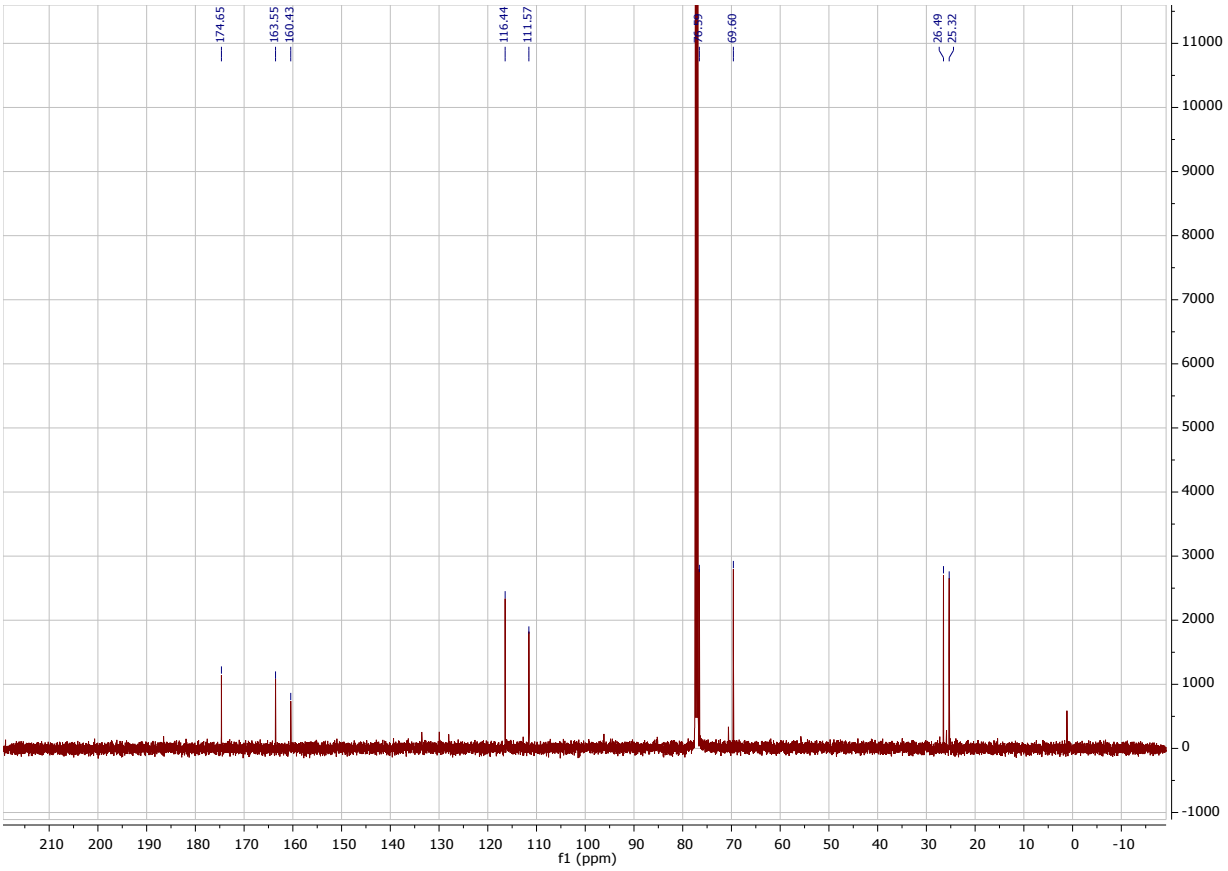


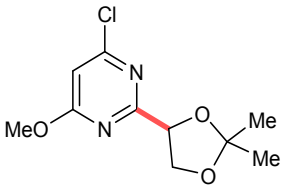

165.34
161.18
156.40
79.94
69.34
27.57
25.35
23.67
f1 (ppm)



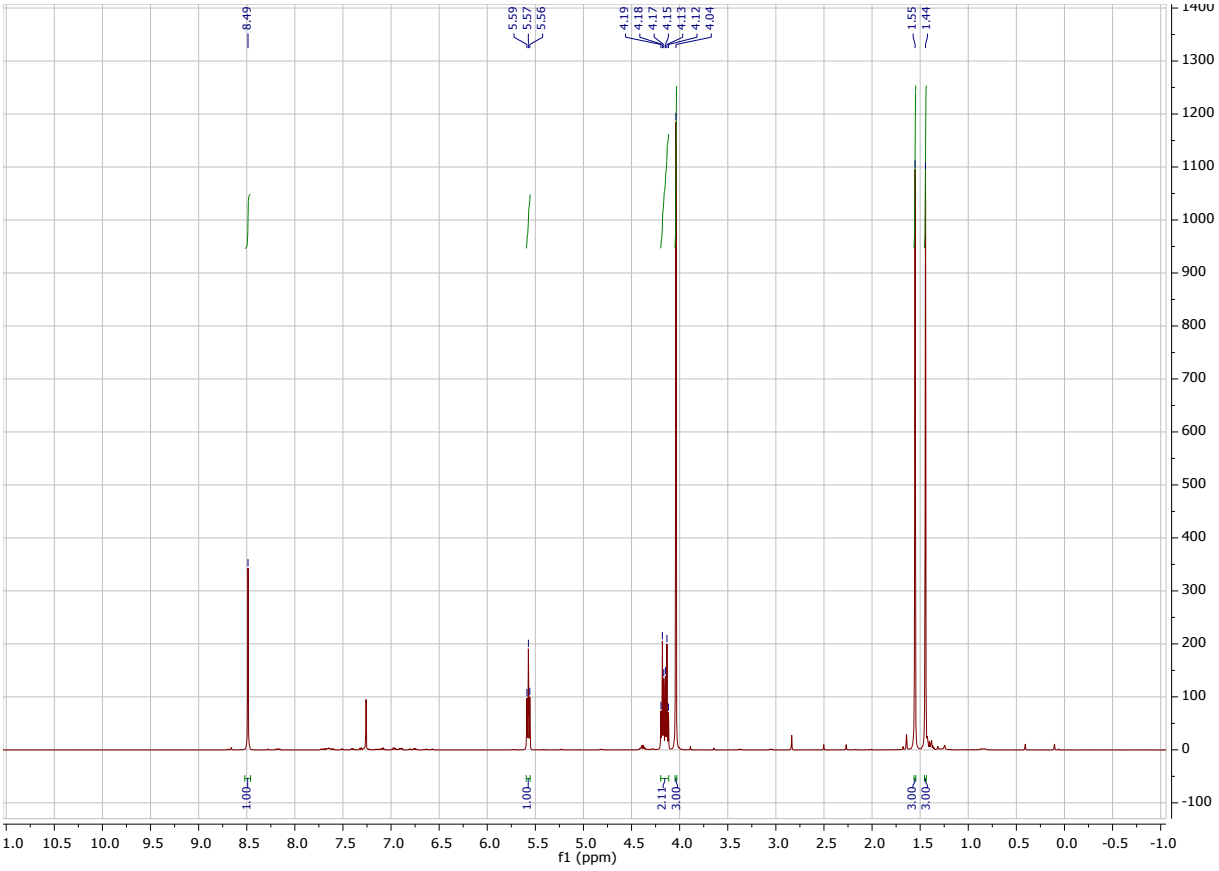
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2,4-Dichloro-5-(2,2-dimethyl-1,3-dioxolan-4-yl)pyrimidine (5l)

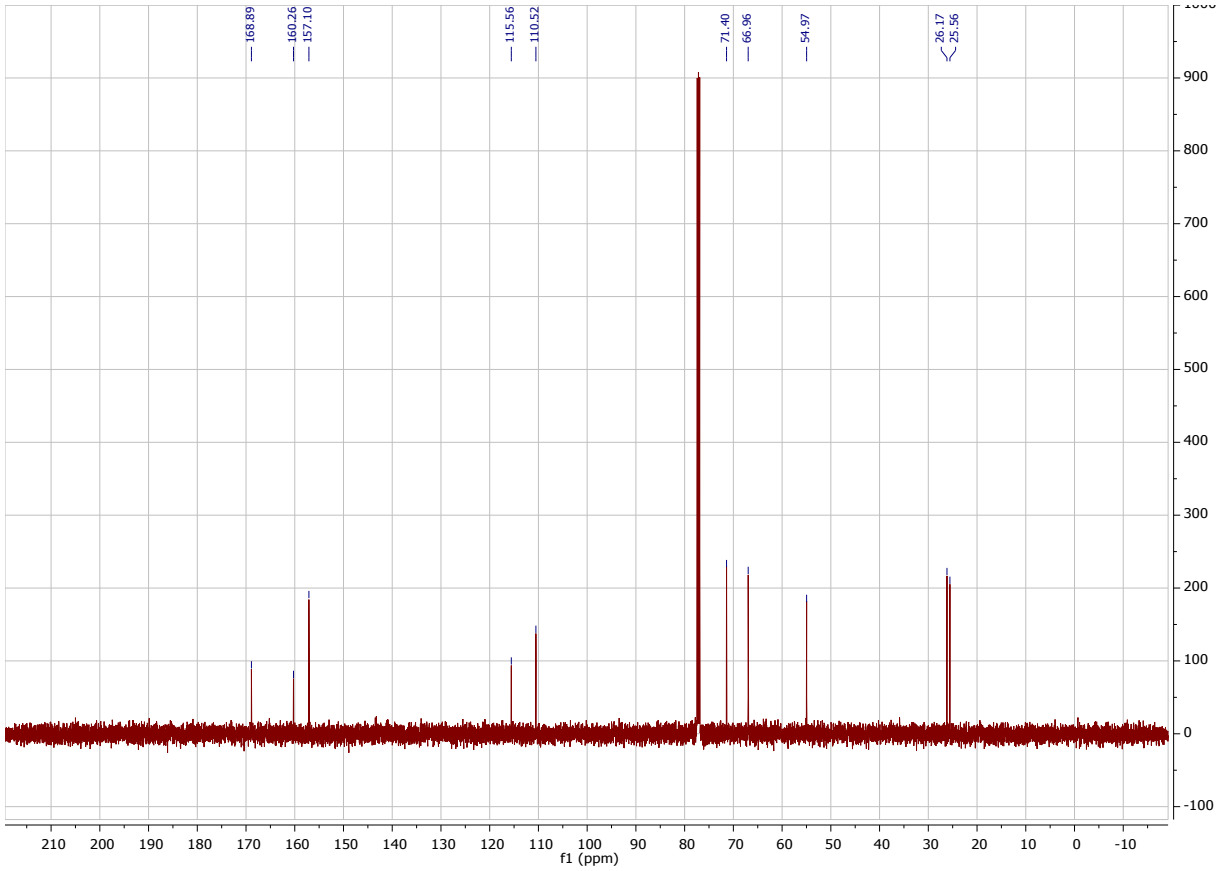


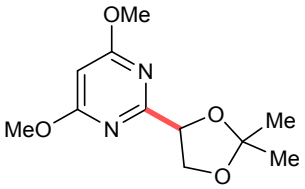

174.65
163.55
160.43
116.44
111.57
70.99
69.60
26.49
25.32
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



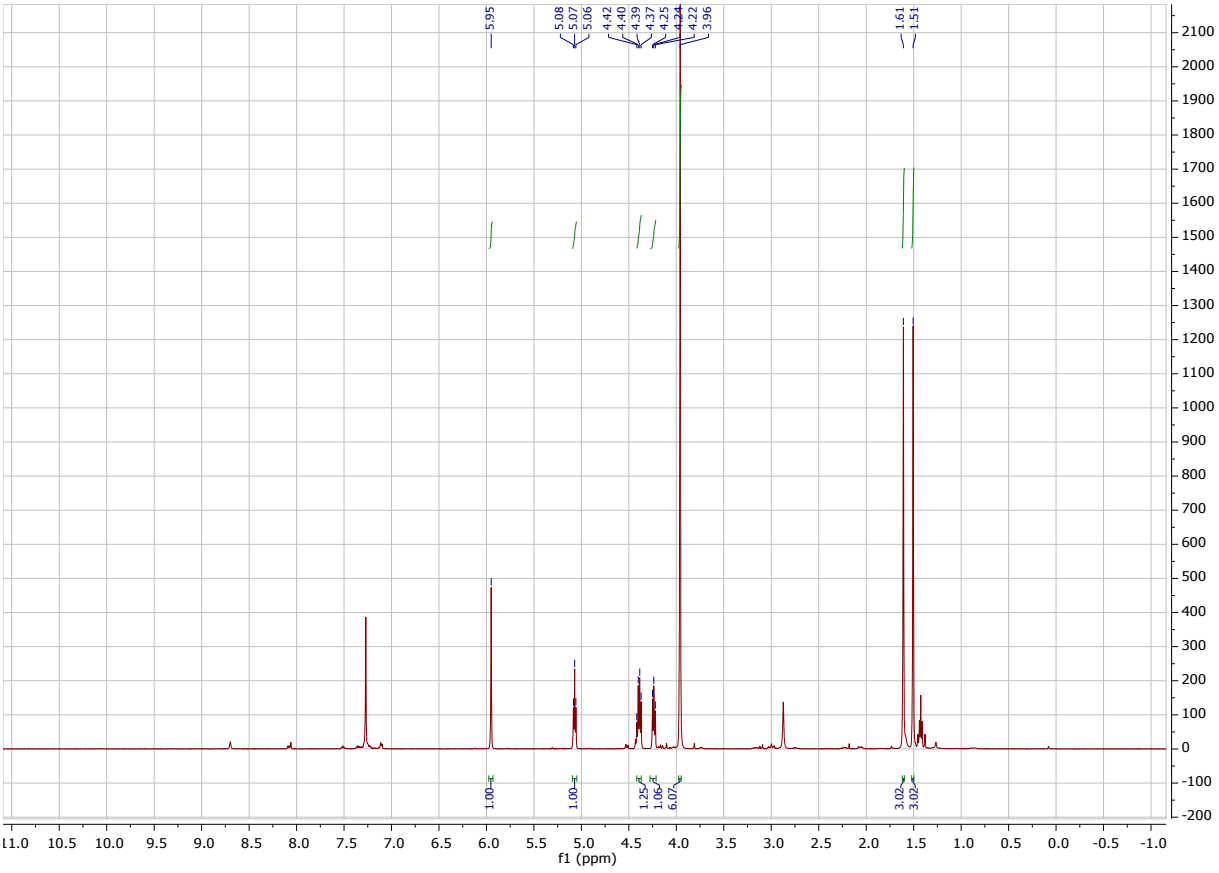
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 4-Chloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-6-methoxypyrimidine (5m)

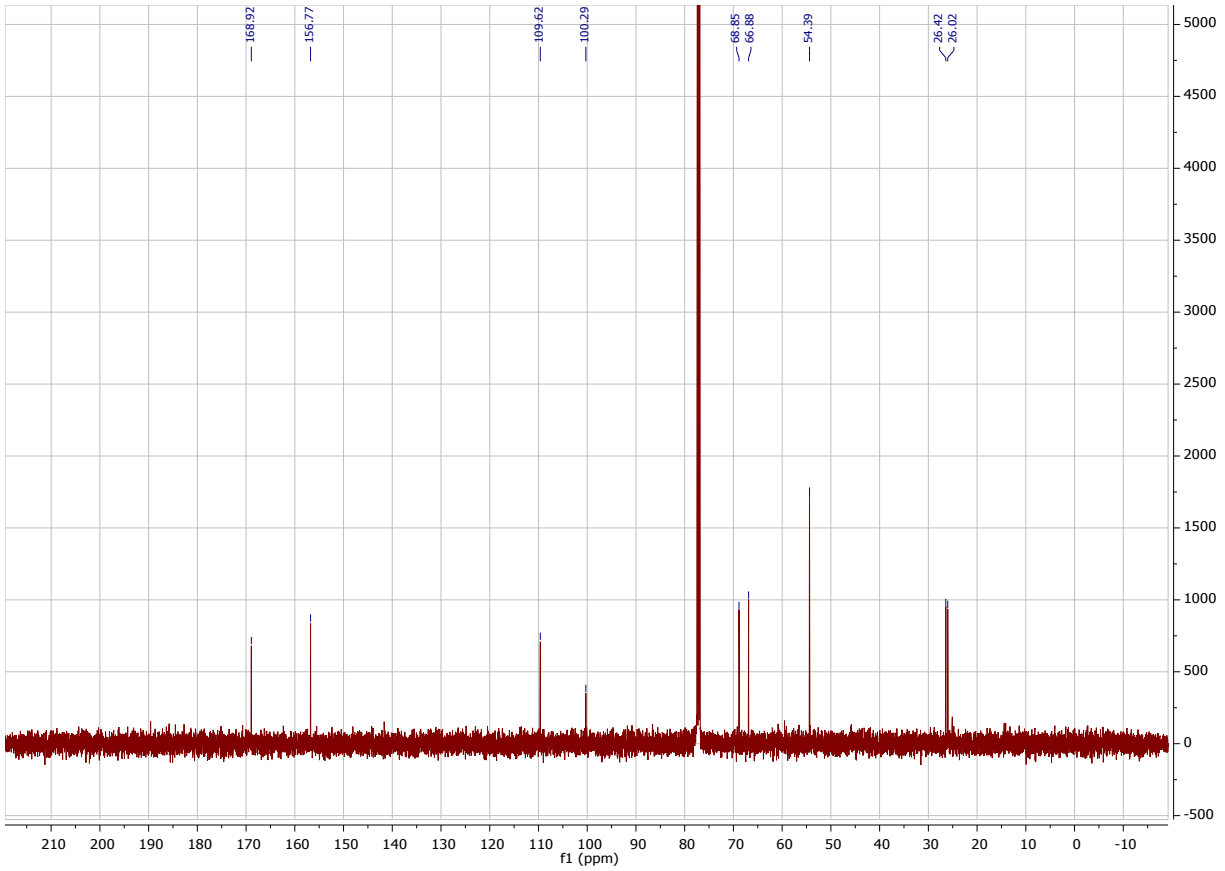


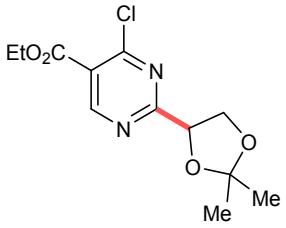

168.89
160.26
157.10
115.56
110.52
71.40
66.96
54.97
26.17
25.56
f1 (ppm)



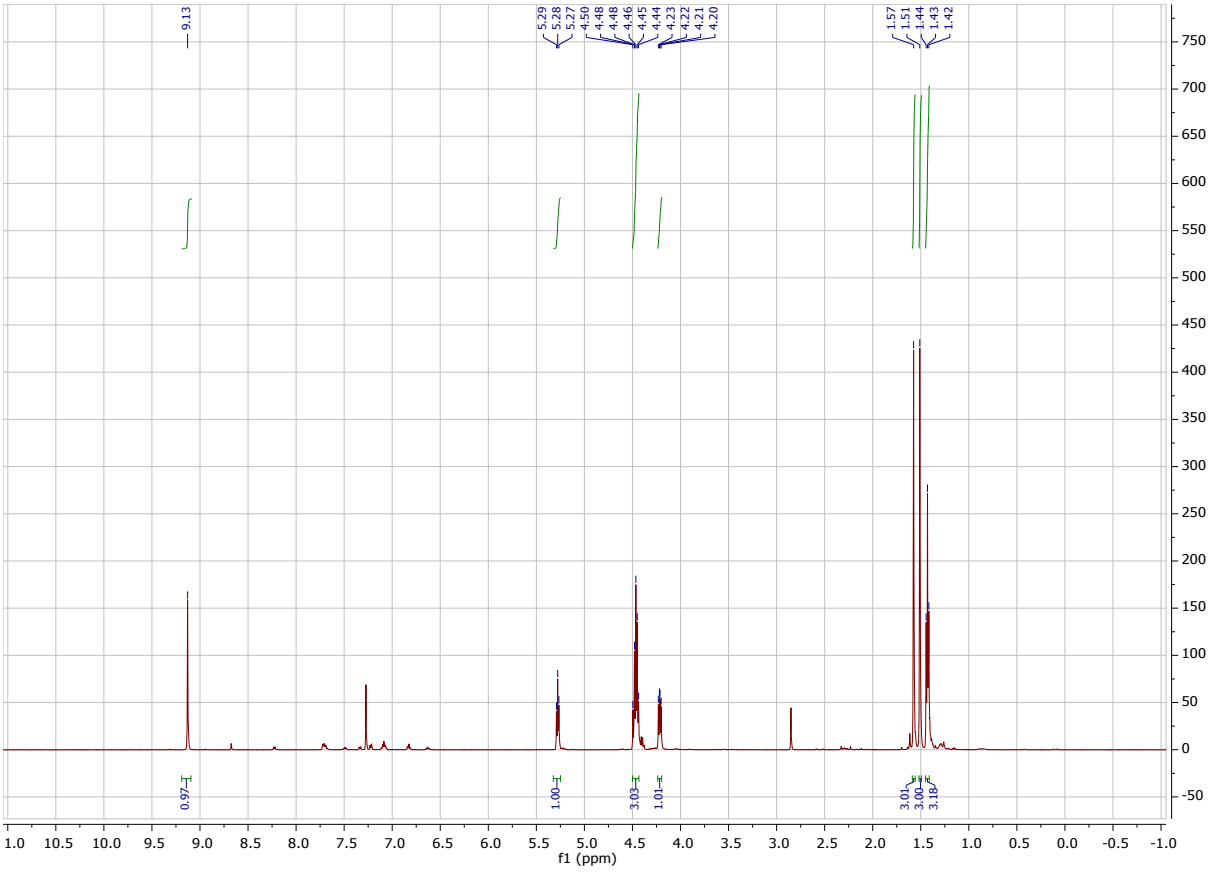
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4,6-dimethoxypyrimidine (5n)

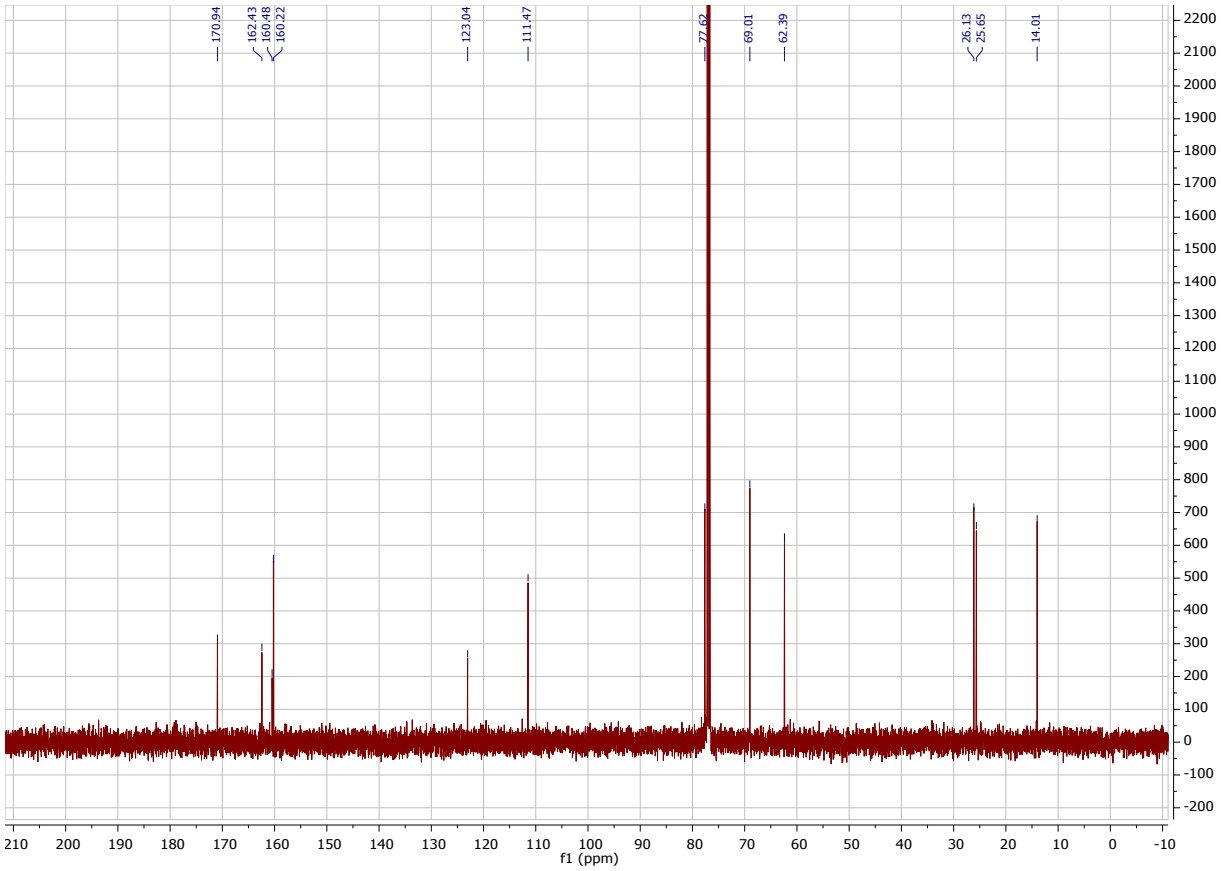


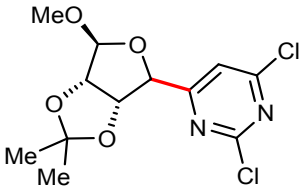

168.92
156.77
109.62
100.29
68.85
66.88
54.39
26.42
26.02
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



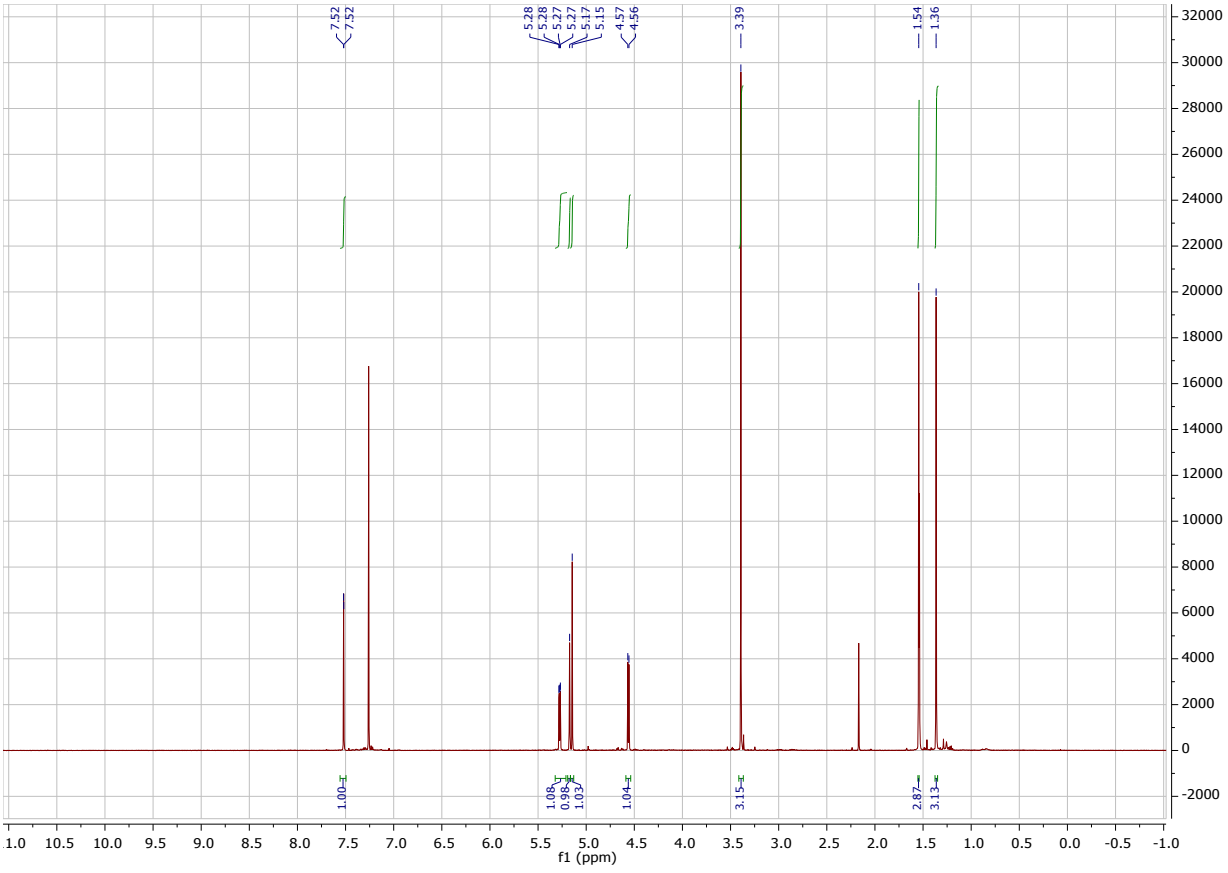
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of Ethyl 4-chloro-2-(2,2-dimethyl-1,3-dioxolan-4-yl) pyrimidine-5-carboxylate (5o)

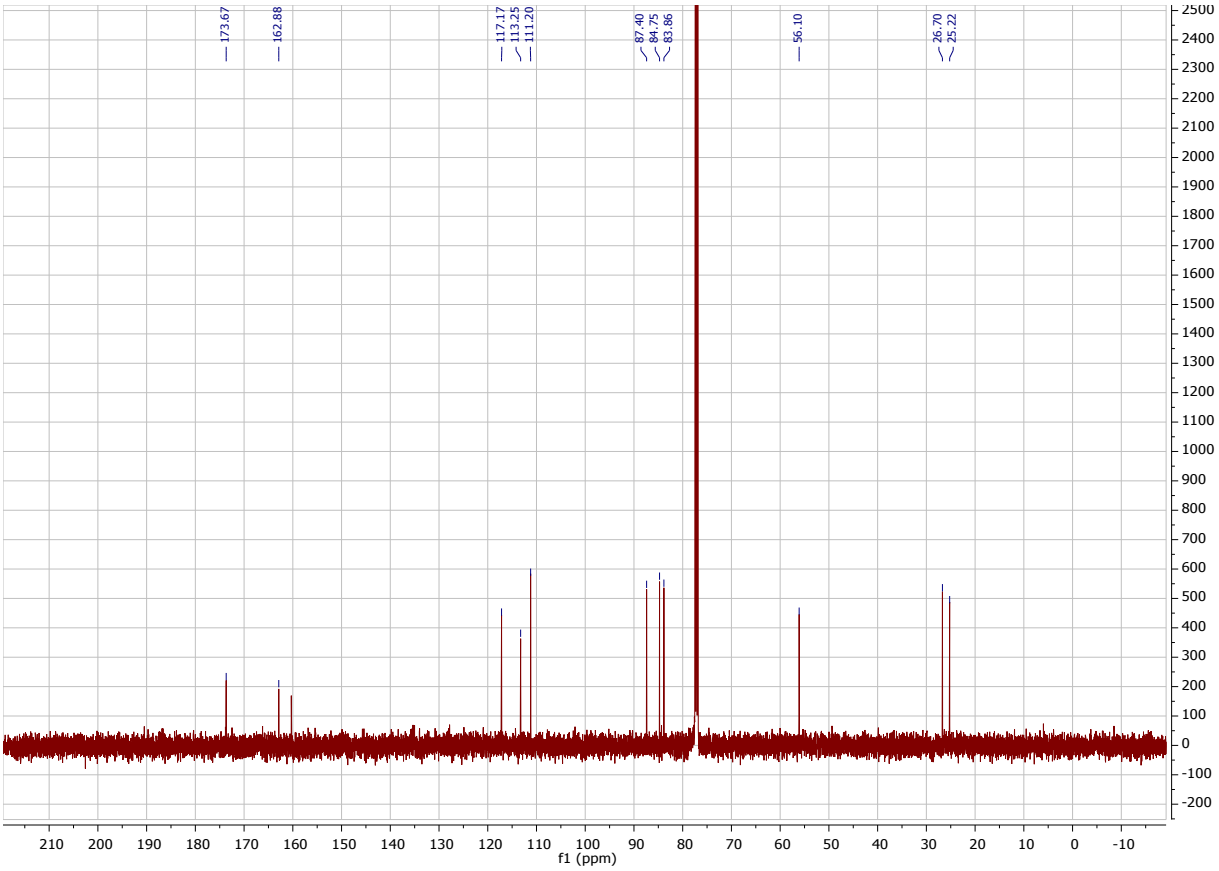



170.94
162.43
160.48
160.22
123.04
111.47
77.62
69.01
62.39
26.13
25.65
14.01
f1 (ppm)



^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 126 MHz) of 2,4-Dichloro-6-((3aS,6S,6aS)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)pyrimidine (5p)





6. References

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4. M. Jouffroy, D. N. Primer and G. A. Molander, *J. Am. Chem. Soc.*, 2016, **138**, 475-478.
5. Á. Gutiérrez-Bonet, J. C. Tellis, J. K. Matsui, B. A. Vara and G. A. Molander, *ACS Catal.*, 2016, **6**, 8004-8008.
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7. N. R. Patel, C. B. Kelly, M. Jouffroy and G. A. Molander, *Org. Lett.*, 2016, **18**, 764-767.