Supporting Information

Solvent-free mechanochemical chlorination of pyrazoles with trichloroisocyanuric acid

*Chi-Min Chen, Jia-Xin Chen and Ching Tat To**

Department of Chemistry, Tunghai University, No. 1727, Sec. 4, Taiwan Boulevard, Xitun District, Taichung City 407224, Taiwan, Republic of China

Email: ctto@go.thu.edu.tw

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Experimental Section

Unless otherwise specified, all reagents were purchased from commercial suppliers and directly used without further purification. All reactions were carried out in 10 mL zirconia milling vessel designated for the Retsch MM400 shaker mill. All reactions were repeated once to ensure reproducibility. Silica gel (Merck, 70–230 mesh) was used.

^{1}H, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra were recorded on a Bruker Ascend TM 400MHz (400 MHz for ^{1}H, 100 MHz for ^{13}C and 376.5 MHz for ^{19}F). Chemical shifts (ppm) were referenced internally to the residual solvent proton resonance in $CDCl_3$ (δ = 7.26 ppm) and acetone-d_6 (δ = 2.04 ppm) for ^{1}H NMR, and $CDCl_3$ (δ = 77.2 ppm), acetone-d_6 (δ = 29.8 ppm) for $^{13}C\{^{1}H\}$ NMR, and with reference externally with $C_6H_5CF_3$ (δ -63.7 ppm) for $^{19}F\{^{1}H\}$ NMR. Coupling constants (*J*) are reported in hertz (Hz).

High-resolution mass spectrometry (HRMS) were performed by the Center for Advanced Instrumentation and Department of Applied Chemistry at National Yang Ming Chiao Tung University. Mass spectra of the sample solutions at pH 7.5 were acquired by direct infusion (2 μL). Electrospray ionization (ESI) experiments were carried out using a Bruker Impact HD Q-TOF mass spectrometer equipped with an ESI source operating in positive ion mode. The parameters of ESI(+) included 4.5kV for ion spray voltage, 200 °C for capillary temperature, and 6 L/min for sheath gas flow rate. The mass spectra were collected over the mass range of m/z 50-1500 at a resolving power of 40000. The collected data were analysed using Compass DataAnalysis 4.1.

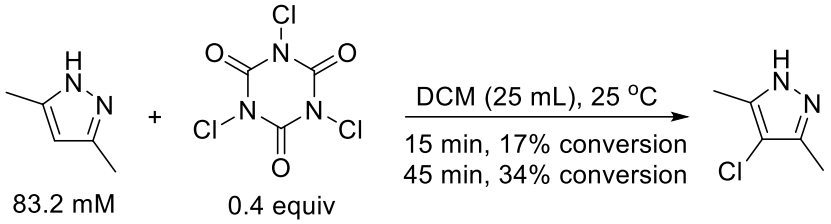
Melting points were determined on a Krüss M3000.

GC-MS analysis was conducted on a Shimadzu QP2010SE system using a Rtx-5MS column (30 m x 0.25 mm). The details of GC program are as follow: the column oven temperature and injection temperature were 100.0 and 230.0 ºC. Helium was used as the carrier gas. Flow control mode was chosen as linear velocity (36.6 cm s^{-1}) with pressure of 68.8 kPa. The total flow, column flow and purge flow were 32.5, 0.95 and 3.0 mL min^{-1}, respectively. Split mode injection with split ratio 30.0 was applied. Sample was injected as solutions in dichloromethane. After injection, the column oven temperature kept at 100.0 ºC for 2 min and then elevated at a rate of 30 ºC min^{-1} until 250.0 ºC. This temperature was kept for 3 min.

X-ray diffraction crystallography was performed on a Bruker D8 Venture diffractometer at National Chung Hsing University.

Compounds **1a-1c**,[1] **1d**,[2] **1e**,[3] **1f-1g**,[4] **1h**,[5] **1i**,[6] **1l**,[7] **1m**,[8] **1n**[9] have been reported.

Procedure for the Chlorination of 3,5-Dimethylpyrazole with TCCA in CH_2Cl_2



In two separate runs, 3,5-dimethylpyrazole (200.0 mg, 2.08 mmol) and TCCA (193.4 mg, 0.83 mmol) were dissolved in CH_2Cl_2 (25 mL) in a 50 mL round bottom flask. The reactions were stirred at r.t for 15 min and 45 min, respectively. The aliquots were then rotary evaporated and the residue was immediately analysed with ^{1}H NMR spectroscopy in $CDCl_3$. The conversions were calculated from the ratio of methyl signals between the starting material and product.

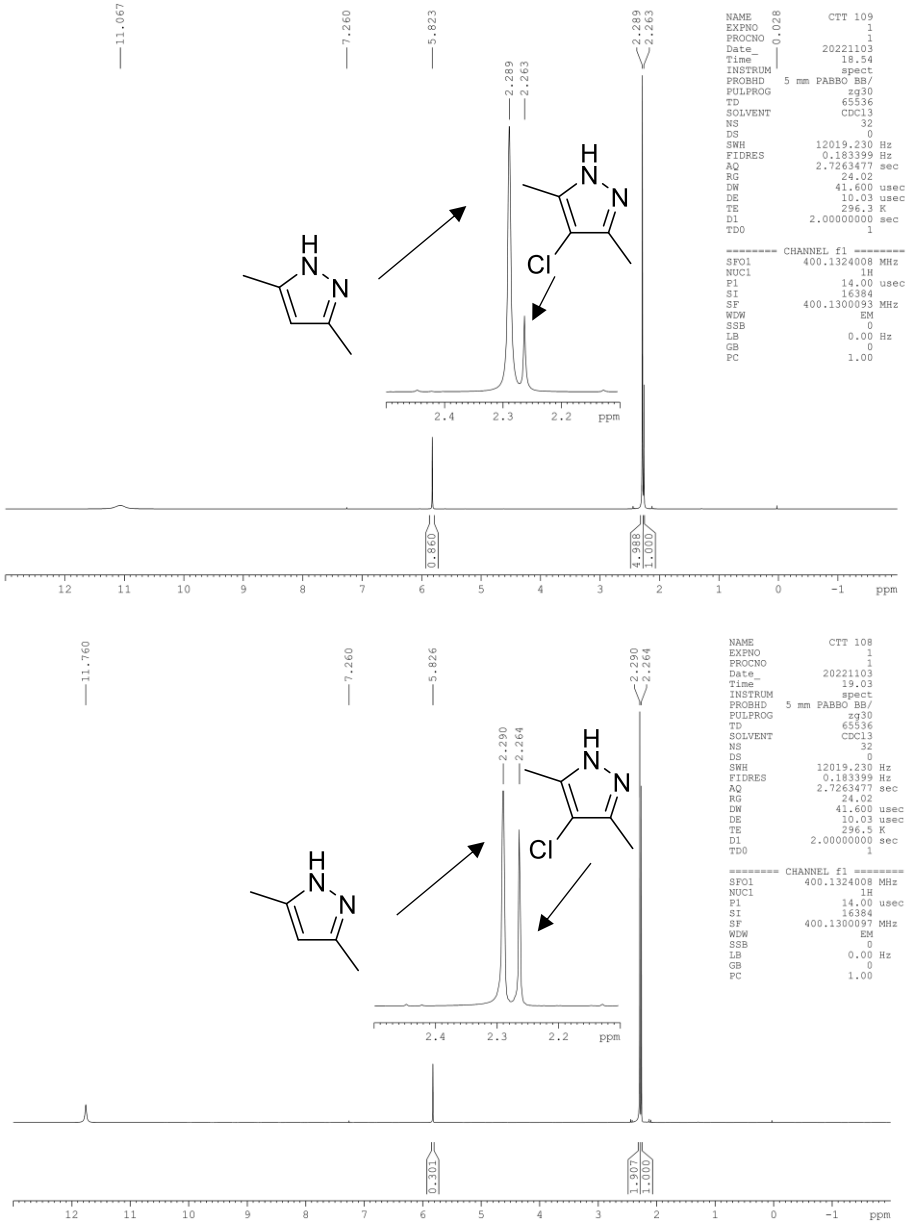


Figure S1. ^{1}H NMR spectrum for 15 min (up) and 45 min (down) reaction time.

General Procedure for the Mechanochemical Chlorination of Pyrazoles with TCCA

In a typical run, pyrazole (2.08 mmol), TCCA (0.83 mmol), silica gel (200.0 mg) and two ZrO_2 milling balls (5.0 mm diameter) were charged into a 10 mL ZrO_2 milling cell. This reaction vessel was then mounted on the shaker mill and oscillated at 30.0 Hz for designated reaction time. The progress of reaction was monitored by temporarily pausing the shaking and analyzed either by TLC or GC-MS until complete consumption of pyrazole. The resultant mixture was extracted with CH_2Cl_2 or MeOH and filtered through a short pad of silica on a frit (2 cm X 1 cm) to remove insoluble solid, followed by washing with 2% NaS_2O_3 solution to quench any remaining active chlorine content. Rotary evaporation of the solvent yielded the corresponding 4-chloropyrazole product.

4-Chloro-3,5-dimethylpyrazole **1a** [CAS 15953-73-8]. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.24 (s, 6 H), 11.25 (br s, 1 H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) 10.5, 107.9, 141.1. HRMS calcd. for $[C_5H_7ClN_2+H]^+$: m/z 131.0371. Found: m/z 131.0371. m.p. Lit. 117-118 ºC. m.p. found 114.7-115.9 ºC.

4-Chloropyrazole **1b** [CAS 15878-00-9]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.57 (s, 2 H), 9.14 (br s, 1 H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) 110.6, 132.1. HRMS calcd. for $[C_3H_3ClN_2+H]^+$: m/z 103.0058. Found: m/z 103.0058. M.p. Lit. 75-79 ºC. M.p. found 76.7-78.1 ºC.

4-Chloro-3,5-diphenylpyrazole **1c** [CAS 71549-28-5]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.40-7.49 (m, 6 H), 7.81 (d, J = 7.2 Hz, 4 H), 10.78 (s, 1 H). HRMS calcd. for $[C_{15}H_{11}ClN_2+H]^+$: m/z 255.0684. Found: m/z 255.0684. mp. Lit. 191-193 ºC. M.p. found 204.8-205.7 ºC.

4-Chloro-3,5-dimethyl-1H-pyrazole-1-carboxamide **1d** [CAS 1174305-03-3]. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.22 (s, 3 H), 2.55 (s, 3 H), 5.27 (br s, 1 H), 7.08 (s, 1 H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) 11.7, 12.1, 113.2, 139.4, 148.2, 151.8. HRMS calcd. for $[C_6H_8ClN_3O+H]^+$: m/z 174.0429. Found: m/z 174.0424. M.p. lit. 141-142 ºC. M.p. found 134.4-135.8 ºC.

4-Chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole **1e** [CAS 1881288-80-7]. ^{1}H NMR ($CDCl_3$, 400 MHz) 1.51-1.57 (m, 3 H), 1.94 (broad s, 3 H), 3.58 (t, J = 10.5 Hz, 1 H), 3.93 (d, J = 11.5 Hz, 1 H), 5.22-5.23 (m, 1 H), 7.38 (s, 1 H), 7.53 (s, 1 H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) 22.1, 24.8, 30.2, 67.6, 87.9, 110.6, 125.7, 137.9. HRMS calcd. for $[C_8H_{11}ClN_2O+H]^+$: m/z 187.0633. Found: m/z 187.0627. (Green Chem. 2016, 18, 6209-6214). Pale yellow oil.

4-Chloro-3,5-dimethyl-1-phenyl-1H-pyrazole **1f** [CAS 861382-34-5]. Purified on silica gel column chromatography with hexane/DCM = 3:1 as the eluent. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.27 (s, 3 H), 2.29 (s, 3 H), 7.32-7.45 (m, 5 H). HRMS calcd. for $[C_{11}H_{11}ClN_2+H]^+$: m/z 207.0684. Found: m/z 207.0686. pale yellow oil.

Di-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-2**. Purified on silica gel column chromatography with hexane/DCM = 3:1 as the eluent. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.32 (s, 3 H), 4.56 (s, 2 H), 7.42-7.57 (m, 5 H). HRMS calcd. for $[C_{11}H_{10}Cl_2N_2+H]^+$: m/z 241.0294. Found: m/z 241.0293.

Tri-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-3**. Purified on silica gel column chromatography with hexane/DCM = 3:1 as the eluent. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.32 (s, 3 H), 6.70 (s, 1 H), 7.45-7.55 (m, 5 H). HRMS calcd. for $[C_{11}H_9Cl_3N_2+H]^+$: m/z 274.9904. Found: m/z 274.9902.

4-Chloro-1-phenylpyrazole **1g** [CAS 6831-92-1]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.31 (t, J = 7.6 Hz, 1 H), 7.45 (t, J = 7.8 Hz, 2 H), 7.63 (d, J = 7.6 Hz, 2 H), 7.65 (s, 1 H), 7.90 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 112.5, 119.1, 125.0, 127.1, 129.7, 139.6, 139.8. HRMS calcd. for $[C_9H_7ClN_2+H]^+$: m/z 179.0371. Found: m/z 179.0371. M.p. Lit. 72.5-74.3 ºC. M.p. found 73.5-74.2 ºC.

4-Chloro-1-(4-methoxyphenyl)-1H-pyrazole **1h** [CAS 1402566-05-5]. ^{1}H NMR ($CDCl_3$, 400 MHz) 3.83 (s, 3 H), 6.96 (d, J = 9.2 Hz, 2 H), 7.52 (d, J = 8.8 Hz, 2 H), 7.60 (s, 1 H), 7.80 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 55.7, 112.0, 114.7, 120.9, 125.1, 133.6, 139.1, 158.7. HRMS calcd. for $[C_{10}H_9ClN_2O+H]^+$: m/z 209.0476. Found: m/z 209.0476. M.p. found 94.5-95.2 ºC.

1-(4-Bromophenyl)-4-chloro-1H-pyrazole **1i** [CAS 1248589-16-3]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.52 (d, J = 9.1 Hz, 2 H), 7.58 (d, J = 8.8 Hz, 2 H), 7.64 (s, 1 H), 7.88 (s, 1 H). ^{1}H NMR (acetone-d_6, 400 MHz) 7.69 (d, J = 8.7 Hz, 2 H), 7.75 (s, 1 H), 7.80 (d, J = 8.7 Hz, 2 H), 8.52 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 112.9, 120.4, 124.8, 132.6, 138.7, 139.9 [one peak is overlapped]. ^{13}C{^{1}H} NMR (acetone-d_6, 100 MHz) 113.1, 120.3, 121.2, 126.5, 133.4, 139.9, 140.3. HRMS calcd. for $[C_9H_6BrClN_2+H]^+$: m/z 256.9476. Found: m/z 256.9473. M.p. found 74.2-75.0 ºC.

4-(4-chloro-1H-pyrazol-1-yl)benzaldehyde **1j** [CAS 1179758-89-4]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.70 (s, 1 H), 7.83 (d, J = 8.6 Hz, 2 H), 7.99 (d, J = 8.7 Hz, 2 H), 8.01 (s, 1 H), 10.02 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 113.9, 118.7, 125.0, 131.5, 134.6, 140.9, 143.8, 190.9. HRMS calcd. for $[C_{10}H_7ClN_2O+H]^+$: m/z 207.0320. Found: m/z 207.0316. M.p. found 122.8-123.3 ºC.

4-(4-chloro-1H-pyrazol-1-yl)benzonitrile **1k** [CAS 1179745-44-8]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.69 (s, 1 H), 7.75 (d, J = 9.0 Hz, 2 H), 7.79 (d, J = 9.0 Hz, 2 H), 7.98 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 110.4, 114.2, 118.3, 118.9, 124.9, 133.9, 141.0, 142.5. HRMS calcd. for $[C_{10}H_6ClN_3+H]^+$: m/z 204.0323. Found: m/z 204.0319. M.p. found 134.5-134.9 ºC.

4-Chloro-1-(4-nitrophenyl)-1*H*-pyrazole **1l** [CAS 65041-53-4]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.72 (s, 1 H), 7.83 (d, J = 9.0 Hz, 2 H), 8.02 (s, 1 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100

MHz) 114.5, 118.6, 125.1, 125.6, 141.4, 143.9, 145.9. HRMS calcd. for $[C_9H_6ClN_3O_2+H]^+$: m/z 224.0221. Found: m/z 224.0220. M.p. Lit. 145.5-146.5 ºC. M.p. found 144.7-146.3 ºC.

2-(4-chloro-1H-pyrazol-1-yl)pyridine **1m** [CAS 77556-33-3]. ^{1}H NMR ($CDCl_3$, 400 MHz) 7.18-7.21 (m, 1 H), 7.64 (s, 1 H), 7.81 (td, *J* = 7.8 Hz, 2.1 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 8.39 (d, *J* = 3.2 Hz, 1 H), 8.54 (s, 1 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 112.0, 113.0, 121.9, 125.1, 138.9, 140.5, 148.2, 151.1. HRMS calcd. for $[C_8H_6ClN_3+H]^+$: m/z 180.0323. Found: m/z 180.0321. mp. Lit. 64-65 ºC. M.p. found 69.6-70.3 ºC.

4-chloro-celecoxib **1n** [2248154-36-9]. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.41 (s, 3 H), 4.89 (br s, 2 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.41 (d, *J* = 8.6 Hz, 2 H), 7.88 (d, *J* = 8.5 Hz, 2 H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) 21.6, 109.9, 120.5 (quartet, $^1J_{CF}$ = 268.5 Hz), 123.4, 125.2, 127.7, 129.8, 130.1, 140.7, 140.8 (quartet, $^2J_{CF}$ = 37.5 Hz), 141.6, 142.0, 142.4. ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz) -63.7 (s). HRMS calcd. for $[C_{17}H_{13}ClF_3N_3O_2S+H]^+$: m/z 416.0442. Found: m/z 416.0440. M.p. Lit. 169-171 ºC. M.p. found 174.5-175.8 ºC. Single crystal suitable for X-ray diffraction was obtained by slow evaporation of CH_2Cl_2/MeOH solution.

Gram-Scale Mechanochemical Chlorination of Pyrazoles with TCCA

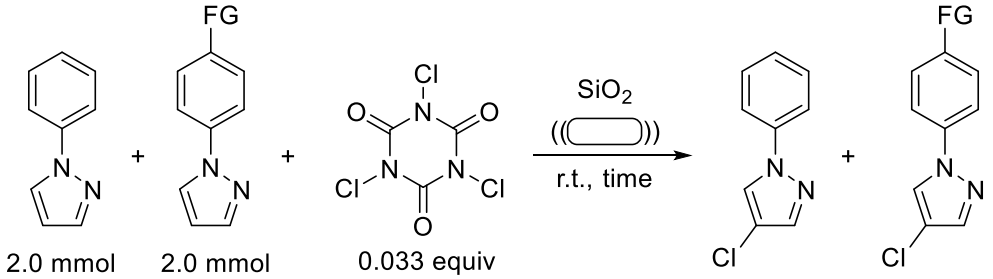
With 3,5-dimethylpyrazole. 3,5-dimethylpyrazole **1** (1.00 g, 10.4 mmol), TCCA (967.0 mg, 4.16 mmol), silica gel (200.0 mg) and one ZrO_2 milling ball (10.0 mm diameter) were charged into a ZrO_2 shaker cell. This reaction vessel was then mounted on the shaker mill and oscillated at 30.0 Hz for 60 min. The resultant mixture was extracted with CH_2Cl_2 and filtered through a short pad of silica on a frit to remove insoluble solid, followed by washing with 5% NaS_2O_3 solution to quench any remaining active chlorine content. Rotary evaporation of the solvent yielded 4-chloro-3,5-dimethylpyrazole **1a** (1.11 g, 8.50 mmol, 82%).

With 1-phenylpyrazole. 1-phenylpyrazole **1** (917 μL, 6.36 mmol), TCCA (591.0 mg, 2.54 mmol), silica gel (200.0 mg) and one ZrO_2 milling ball (10.0 mm diameter) were charged into a ZrO_2 shaker cell. This reaction vessel was then mounted on the shaker mill and oscillated at 30.0 Hz for 45 min. The resultant mixture was extracted with CH_2Cl_2 and filtered through a short pad of silica on a frit to remove insoluble solid, followed by washing with 5% NaS_2O_3 solution to quench any remaining active chlorine content. Rotary evaporation of the solvent yielded 4-chloro-1-phenylpyrazole **1g** (1.06 g, 5.93 mmol, 93%).

Competition Experiments between 1-Phenylpyrazole and 1-Arylpyrazoles

1-phenylpyrazole (2.0 mmol), 1-arylpyrazole (2.0 mmol), TCCA (0.066 mmol), silica gel (200.0 mg) and two ZrO_2 milling balls (5.0 mm diameter) were charged into a 10 mL ZrO_2 milling cell. This reaction vessel was then mounted on the shaker mill and oscillated at 30.0 Hz for designated reaction time. The resultant mixture was extracted with CH_2Cl_2 and filtered through a short pad of silica on a frit to remove insoluble solid, followed by washing with 5% NaS_2O_3 solution to quench any remaining active chlorine content. The ratio between 4-chloro-1-phenylpyrazole **1a** and 4-chloro-1-arylpyrazole was determined by analyzing the mixture with GC-MS.

Table S1. Competition Experiments



2.0 mmol 2.0 mmol 0.033 equiv

entry	FG	time / min	yield / %			$\log(k_{FG}/k_H)^a$
			FG	H	total yield	
1	OMe	30	62	20	82	0.49
2	OMe	45	64	23	89	0.44
3	Br	45	9	70	79	-0.89
4	Br	45	8	73	81	-0.96
5	CHO	30	4	86	91	-1.33
6	CHO	45	3	95	98	-1.50
7	CN	30	2	91	93	-1.66
8	CN	30	2	84	86	-1.62
9	NO_2	30	1	91	91	-3.26
10	NO_2	45	1	85	85	-3.23

Table S2. Hammett Plot of Mechanochemical Chlorination of 1-Arylpyrazoles with TCCA using the Hammett Constant σ_p.

entry	FG	σ_p [a]	$\log(k_{FG}/k_H)$
1	OMe	-0.27	0.49
2	OMe	-0.27	0.44
3	Br	0.23	-0.89
4	Br	0.23	-0.96
5	CHO	0.42	-1.33
6	CHO	0.42	-1.50
7	CN	0.66	-1.66
8	CN	0.66	-1.62
9	NO_2	0.78	-3.26
10	NO_2	0.78	-3.23

[a] Reference 10.

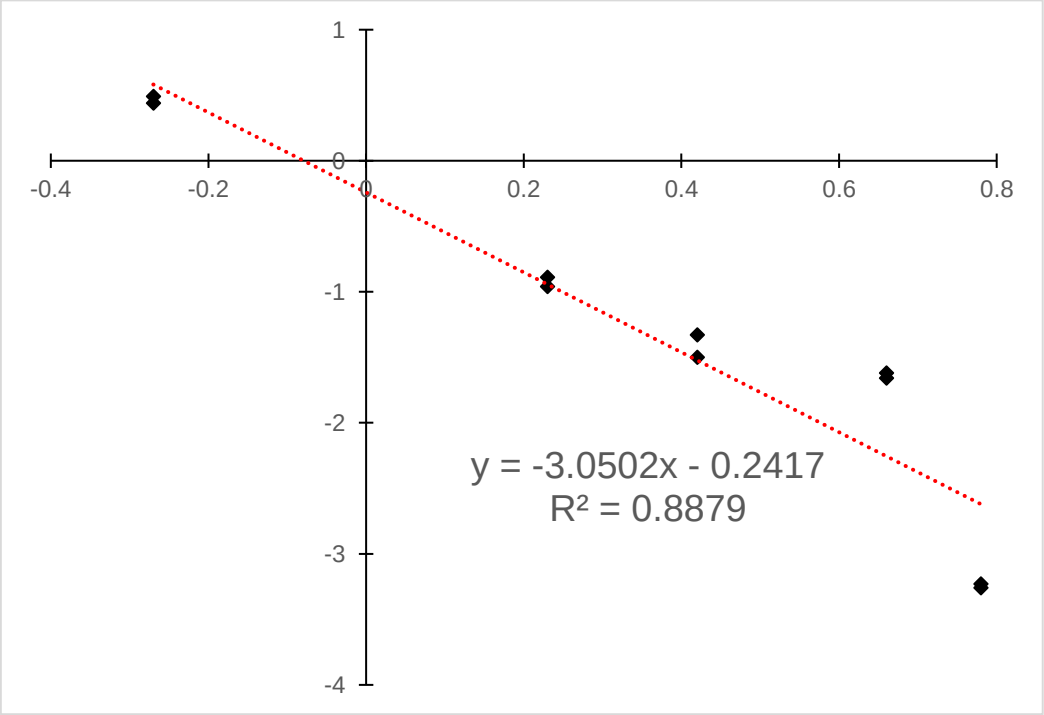
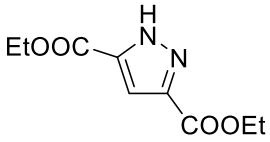
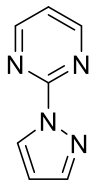
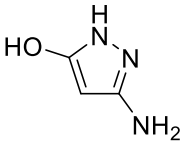
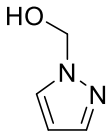
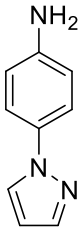
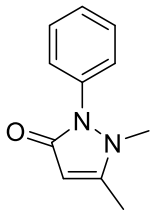
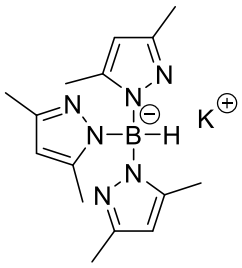
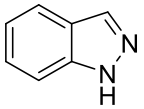
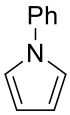
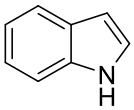
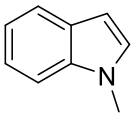
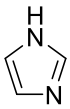
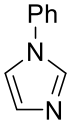
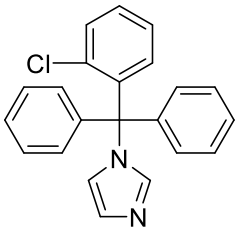


Figure S2. Hammett Plot of Mechanochemical Chlorination of 1-Arylpyrazoles with TCCA using the Hammett Constant σ_p.

Substrates with Unsatisfactory Results[a,b]

entry	substrate	remark
1[c]		expected chlorination product observed but less than 50% conversion in 3 h
2[c]		expected chlorination product observed but less than 50% conversion in 3 h
3		complicated mixture
4		complicated mixture
5		complicated mixture
6		complicated mixture
7		complicated mixture

8		two mono-chlorination products
9[c]		mixture of mono, di, tri, tetra-chlorination products and poly-pyrrolic substances
10[c]		two mono-chlorination products three di-chlorination products one tri-chlorination product one tetra-chlorination product
11[c]		one mono-chlorination product one di-chlorination product
12[c]		one mono-chlorination product one di-chlorination product some chlorinated indolione products
13		unknowns
14[c]		two mono-chlorination products one di-chlorination product one tri-chlorination product
15[c]		three products

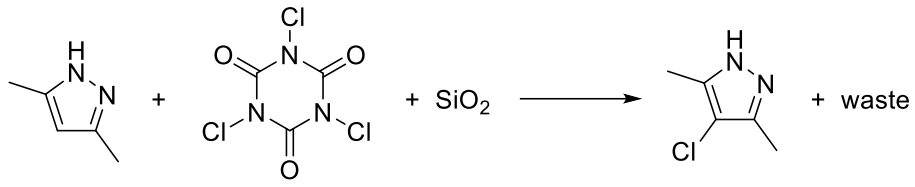
[a] Standard conditions as indicated in the manuscript

[b] Reaction was analyzed after 30 min with TLC, GC-MS or ^{1}H NMR; Regioselectivity not determined

[c] Starting material was remained

Calculation of Green Chemistry Metrics

For mechanochemical chlorination of 3,5-dimethylpyrazole with TCCA



200 mg	193 mg	200 mg	247 mg
MW: 96.13	232.41		130.58

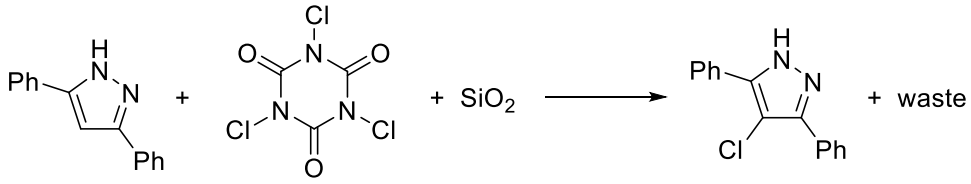
Atom Economy (AE) = 130.58/(96.13 + 232.41/3) x 100% = 75.2%

Reaction Mass Efficiency (RME) = 247/(200 + 193) x 100% = 62.8%

Process Mass Intensity (PMI) = (200 + 193 + 200)/247 = 2.40

E-factor = PMI – 1 = 2.40 – 1 = 1.40

For mechanochemical chlorination of 3,5-diphenylpyrazole with TCCA



458 mg	193 mg	400 mg	445 mg
MW: 220.27	232.41		254.72

Atom Economy (AE) = 254.72/(220.27 + 232.41/3) x 100% = 85.6%

Reaction Mass Efficiency (RME) = 445/(458 + 193) x 100% = 68.4%

Process Mass Intensity (PMI) = (458 + 193 + 400)/445 = 2.36

E-factor = PMI – 1 = 2.36 – 1 = 1.36

For mechanochemical chlorination of 1-phenylpyrazole with TCCA

300 mg	193 mg	200 mg	357 mg
MW: 144.17	232.41		178.62

Atom Economy (AE) = 178.62/(144.17 + 232.41/3) x 100% = 80.6%

Reaction Mass Efficiency (RME) = 357/(300 + 193) x 100% = 72.4%

Process Mass Intensity (PMI) = (300 + 193 + 200)/357 = 1.94

E-factor = PMI – 1 = 1.94 – 1 = 0.94

The green chemistry metrics for the synthesis of 4-chloro-1-phenylpyrazole **1g** using other protocols were calculated according to the published literatures. The results were tabulated below together with this report.

Table S3. Comparison of Green Chemistry Metrics for the Chlorination of 1-phenylpyrazole of various Chlorinating System

Green Chemistry Metrics	this work TCCA	1-Chloro-1,2-benziodoxol-3-one[11]	CBMG[12]	CFBSA[13]	TCCA[14]	NaCl/ Oxone[15]
AE	80.6%	41.9%	50.5%	50.5%	80.6%	35.0%
RME	72.4%	36.7%	45.4%	37.5%	44.1%	10.7%
E-factor	0.94	55.7	47.8	65.3	37.1	13.3
PMI	1.94	56.7	48.8	66.3	38.1	14.3
Purification:	filtration / recrystallization	column chromatography				

X-Ray Diffraction Data

Table S4. Crystal data and structural refinement for **1n**.

Compound	4-chloro-celecoxib **1n**
Empirical formula	$C_{17}H_{13}ClF_3N_3O_2S$
Formula weight	415.81
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P-1
Unit cell dimensions	a = 8.0656(3) Å α = 85.0509(15)° b = 8.5494(3) Å β = 86.9189(14)° c = 13.9078(6) Å γ = 79.3578(14)°
Volume	938.32(6) $Å^3$
Z	2
Density (calculated)	1.472 mg/cm^3
Absorption coefficient	0.361 mm^{-1}
F(000)	424
Crystal size	0.380 x 0.260 x 0.220 mm^3
Theta range for data collection	2.913 to 27.952°
Limiting indices	-10<=h<=10, -11<=k<=11, -18<=l<=18
Reflections collected	18454
Independent reflections	4468 [R(int) = 0.0365]
Completeness to theta = 25.242°	99.2%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6957
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4468 / 0 / 252
Goodness-of fit on F^2	1.070
Final R indices [I>2sigma(I)]	R1 = 0.0394, wR2 = 0.1192
R indices (all data)	R1 = 0.0445, wR2 = 0.1242
Extinction coefficient	n/a
Largest diff. peak and hole	0.367 and -0.528 $e.Å^{-3}$

Table S5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 4-chlorocelecoxib. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl	6202(1)	1128(1)	710(1)	32(1)
S	2686(1)	8964(1)	5370(1)	16(1)
F(1)	1448(2)	210(2)	2608(1)	37(1)
F(2)	3769(2)	-1110(2)	2059(1)	50(1)
F(3)	2113(2)	444(2)	1102(1)	42(1)
O(1)	1144(2)	8800(2)	5900(1)	22(1)
O(2)	4192(2)	8905(2)	5889(1)	22(1)
N(1)	3013(2)	2665(2)	2786(1)	18(1)
N(2)	4066(2)	3740(2)	2700(1)	18(1)
N(3)	2350(2)	10661(2)	4744(1)	19(1)
C(1)	5318(2)	3414(2)	2002(1)	19(1)
C(2)	5041(2)	2051(2)	1631(1)	21(1)
C(3)	3613(2)	1639(2)	2134(1)	19(1)
C(4)	3768(2)	5007(2)	3332(1)	18(1)
C(5)	2113(2)	5542(2)	3662(2)	26(1)
C(6)	1787(2)	6751(3)	4287(2)	26(1)
C(7)	3107(2)	7417(2)	4575(1)	17(1)
C(8)	4755(2)	6882(2)	4243(1)	20(1)
C(9)	5087(2)	5658(2)	3626(1)	21(1)
C(10)	6622(2)	4370(2)	1691(1)	18(1)
C(11)	6200(3)	5820(2)	1150(2)	27(1)
C(12)	7439(3)	6702(2)	843(2)	32(1)
C(13)	9114(3)	6154(3)	1062(2)	28(1)
C(14)	9527(3)	4688(3)	1585(2)	29(1)
C(15)	8298(3)	3796(2)	1903(2)	26(1)
C(16)	10461(3)	7120(3)	742(2)	44(1)
C(17)	2731(3)	293(2)	1985(1)	23(1)

Table S6. Bond lengths [Å] and angles [°] for JXC041.

Bond	Bond Length / Å	Bond	Bond Length / Å
Cl-C(2)	1.7069(18)	C(8)-C(9)	1.389(2)
S-O(1)	1.4346(13)	C(8)-H(8A)	0.9500
S-O(2)	1.4372(13)	C(9)-H(9A)	0.9500
S-N(3)	1.6117(16)	C(10)-C(11)	1.389(3)
S-C(7)	1.7704(18)	C(10)-C(15)	1.388(3)
F(1)-C(17)	1.322(2)	C(11)-C(12)	1.389(3)
F(2)-C(17)	1.330(2)	C(11)-H(11A)	0.9500
F(3)-C(17)	1.337(2)	C(12)-C(13)	1.387(3)
N(1)-C(3)	1.327(2)	C(12)-H(12A)	0.9500
N(1)-N(2)	1.356(2)	C(13)-C(14)	1.388(3)
N(2)-C(1)	1.370(2)	C(13)-C(16)	1.509(3)
N(2)-C(4)	1.431(2)	C(14)-C(15)	1.390(3)
N(3)-H(3A)	0.85(3)	C(14)-H(14A)	0.9500
N(3)-H(3B)	0.85(3)	C(15)-H(15A)	0.9500
C(1)-C(2)	1.374(2)	C(16)-H(16A)	0.9800
C(1)-C(10)	1.473(2)	C(16)-H(16B)	0.9800
C(2)-C(3)	1.400(2)	C(16)-H(16C)	0.9800
C(3)-C(17)	1.494(2)	C(13)-C(16)	1.509(3)
C(4)-C(9)	1.384(2)	C(14)-C(15)	1.390(3)
C(4)-C(5)	1.395(3)	C(14)-H(14A)	0.9500
C(5)-C(6)	1.387(3)	C(15)-H(15A)	0.9500
C(5)-H(5A)	0.9500	C(16)-H(16A)	0.9800
C(6)-C(7)	1.388(3)	C(16)-H(16B)	0.9800
C(6)-H(6A)	0.9500	C(16)-H(16C)	0.9800
C(7)-C(8)	1.391(2)		

Bond	Bond Angle / °	Bond	Bond Angle / °
O(1)-S-O(2)	119.12(8)	C(9)-C(8)-H(8A)	120.1
O(1)-S-N(3)	107.22(8)	C(7)-C(8)-H(8A)	120.1
O(2)-S-N(3)	106.96(8)	C(4)-C(9)-C(8)	119.53(16)
O(1)-S-C(7)	106.97(8)	C(4)-C(9)-H(9A)	120.2
O(2)-S-C(7)	107.29(8)	C(8)-C(9)-H(9A)	120.2
N(3)-S-C(7)	109.01(8)	C(11)-C(10)-C(15)	119.39(17)
C(3)-N(1)-N(2)	104.47(14)	C(11)-C(10)-C(1)	120.40(17)
N(1)-N(2)-C(1)	112.83(14)	C(15)-C(10)-C(1)	120.15(16)
N(1)-N(2)-C(4)	118.15(14)	C(12)-C(11)-C(10)	120.21(18)

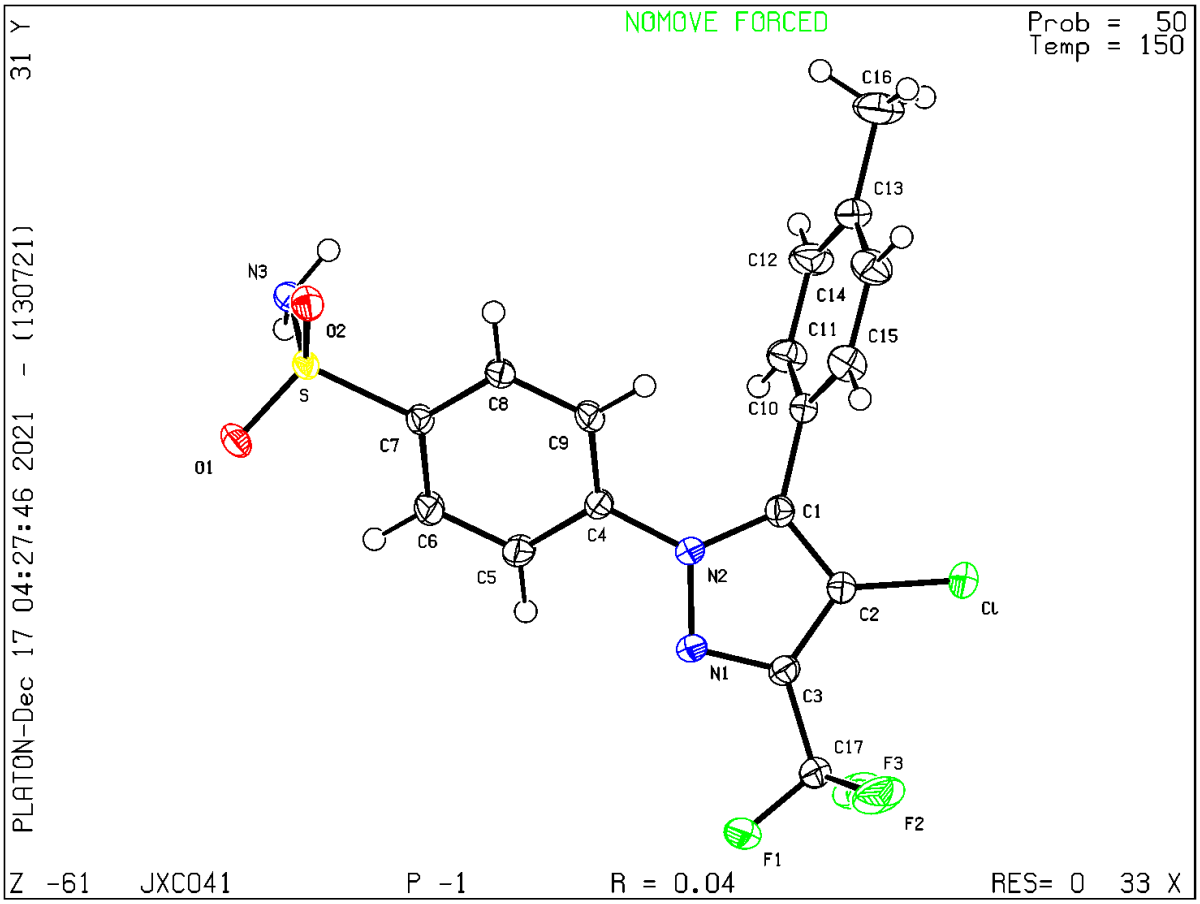
C(1)-N(2)-C(4)	129.01(15)	C(12)-C(11)-H(11A)	119.9
S-N(3)-H(3A)	112.2(17)	C(10)-C(11)-H(11A)	119.9
S-N(3)-H(3B)	110.6(18)	C(11)-C(12)-C(13)	120.95(19)
H(3A)-N(3)-H(3B)	117(2)	C(11)-C(12)-H(12A)	119.5
N(2)-C(1)-C(2)	105.00(15)	C(13)-C(12)-H(12A)	119.5
N(2)-C(1)-C(10)	127.07(16)	C(12)-C(13)-C(14)	118.33(18)
C(2)-C(1)-C(10)	127.88(16)	C(12)-C(13)-C(16)	121.1(2)
C(1)-C(2)-C(3)	106.27(16)	C(14)-C(13)-C(16)	120.5(2)
C(1)-C(2)-Cl	125.33(15)	C(13)-C(14)-C(15)	121.34(19)
C(3)-C(2)-Cl	128.37(14)	C(13)-C(14)-H(14A)	119.3
N(1)-C(3)-C(2)	111.43(16)	C(15)-C(14)-H(14A)	119.3
N(1)-C(3)-C(17)	120.28(16)	C(10)-C(15)-C(14)	119.76(18)
C(2)-C(3)-C(17)	128.23(17)	C(10)-C(15)-H(15A)	120.1
C(9)-C(4)-C(5)	120.85(16)	C(14)-C(15)-H(15A)	120.1
C(9)-C(4)-N(2)	121.00(15)	C(13)-C(16)-H(16A)	109.5
C(5)-C(4)-N(2)	118.14(15)	C(13)-C(16)-H(16B)	109.5
C(6)-C(5)-C(4)	119.50(17)	H(16A)-C(16)-H(16B)	109.5
C(6)-C(5)-H(5A)	120.2	C(13)-C(16)-H(16C)	109.5
C(4)-C(5)-H(5A)	120.2	H(16A)-C(16)-H(16C)	109.5
C(5)-C(6)-C(7)	119.74(17)	H(16B)-C(16)-H(16C)	109.5
C(5)-C(6)-H(6A)	120.1	F(1)-C(17)-F(2)	107.60(16)
C(7)-C(6)-H(6A)	120.1	F(1)-C(17)-F(3)	106.91(17)
C(6)-C(7)-C(8)	120.60(16)	F(2)-C(17)-F(3)	106.27(17)
C(6)-C(7)-S	119.62(13)	F(1)-C(17)-C(3)	112.68(15)
C(8)-C(7)-S	119.78(13)	F(2)-C(17)-C(3)	111.89(17)
C(9)-C(8)-C(7)	119.78(16)	F(3)-C(17)-C(3)	111.13(15)

Table S7. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for JXC041. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl	37(1)	28(1)	32(1)	-14(1)	14(1)	-11(1)
S	12(1)	20(1)	16(1)	-5(1)	0(1)	-3(1)
F(1)	41(1)	43(1)	33(1)	-14(1)	15(1)	-26(1)
F(2)	41(1)	16(1)	91(1)	-7(1)	1(1)	-6(1)
F(3)	65(1)	48(1)	25(1)	-5(1)	-5(1)	-35(1)
O(1)	15(1)	30(1)	20(1)	-4(1)	3(1)	-5(1)
O(2)	15(1)	30(1)	21(1)	-6(1)	-3(1)	-4(1)
N(1)	19(1)	16(1)	20(1)	-2(1)	0(1)	-5(1)
N(2)	18(1)	16(1)	20(1)	-3(1)	1(1)	-5(1)
N(3)	14(1)	21(1)	23(1)	-3(1)	-1(1)	-3(1)
C(1)	19(1)	18(1)	18(1)	-1(1)	1(1)	-2(1)
C(2)	23(1)	19(1)	20(1)	-4(1)	3(1)	-4(1)
C(3)	23(1)	17(1)	19(1)	-2(1)	-1(1)	-5(1)
C(4)	18(1)	16(1)	19(1)	-4(1)	-1(1)	-3(1)
C(5)	16(1)	31(1)	37(1)	-16(1)	0(1)	-7(1)
C(6)	13(1)	32(1)	36(1)	-16(1)	2(1)	-3(1)
C(7)	15(1)	19(1)	18(1)	-4(1)	0(1)	-2(1)
C(8)	15(1)	24(1)	23(1)	-7(1)	1(1)	-5(1)
C(9)	13(1)	25(1)	25(1)	-6(1)	1(1)	-3(1)
C(10)	20(1)	18(1)	19(1)	-4(1)	2(1)	-4(1)
C(11)	22(1)	19(1)	39(1)	3(1)	-1(1)	-2(1)
C(12)	32(1)	20(1)	43(1)	5(1)	2(1)	-9(1)
C(13)	28(1)	29(1)	30(1)	-7(1)	4(1)	-14(1)
C(14)	18(1)	37(1)	34(1)	-2(1)	-4(1)	-7(1)
C(15)	24(1)	26(1)	28(1)	3(1)	-2(1)	-3(1)
C(16)	41(1)	50(2)	50(2)	-5(1)	4(1)	-30(1)
C(17)	27(1)	21(1)	23(1)	-4(1)	4(1)	-8(1)

Table S8. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for JXC041.

	x	y	z	U(eq)
H(3A)	1440(30)	10800(30)	4439(18)	28(6)
H(3B)	3240(40)	10820(30)	4426(19)	30(6)
H(5A)	1217	5082	3460	32
H(6A)	665	7122	4517	32
H(8A)	5650	7352	4437	24
H(9A)	6213	5272	3407	25
H(11A)	5059	6209	990	32
H(12A)	7135	7696	477	38
H(14A)	10672	4287	1730	35
H(15A)	8605	2798	2263	31
H(16A)	11558	6545	961	66
H(16B)	10504	7288	36	66
H(16C)	10196	8155	1021	66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C10
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S
O1
C7
C8
C9
C6
C4
C5
C1
N2
C2
Cl
N1
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F3
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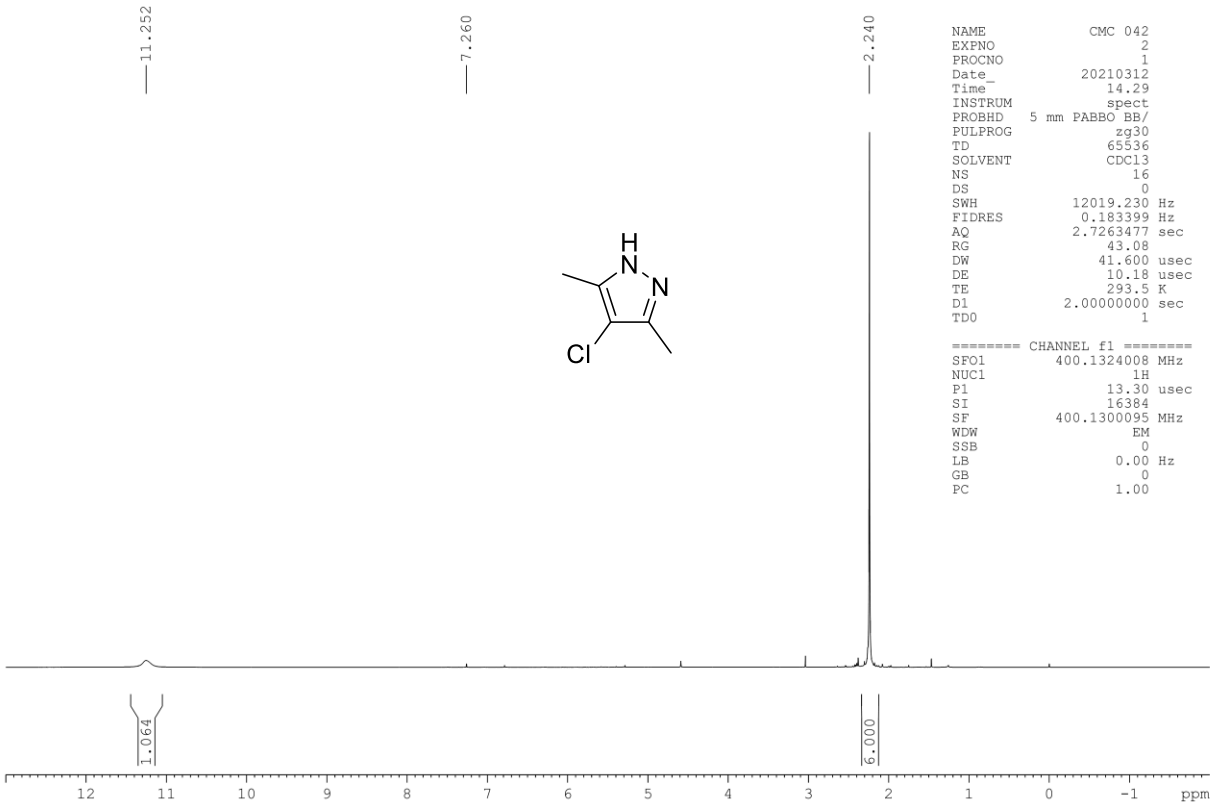
F1

NMR Spectra

4-Chloro-3,5-dimethylpyrazole **1a**

^{1}H, $CDCl_3$

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PROCNO                  1
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TD                  65536
SOLVENT             CDC13
NS                     16
DS                      0
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FIDRES          0.183399 Hz
AQ              2.7263477 sec
RG                  43.08
DW                41.600 usec
DE                10.18 usec
TE                293.5 K
D1             2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
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NUC1                    1H
P1                  13.30 usec
SI                  16384
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PC                   1.00
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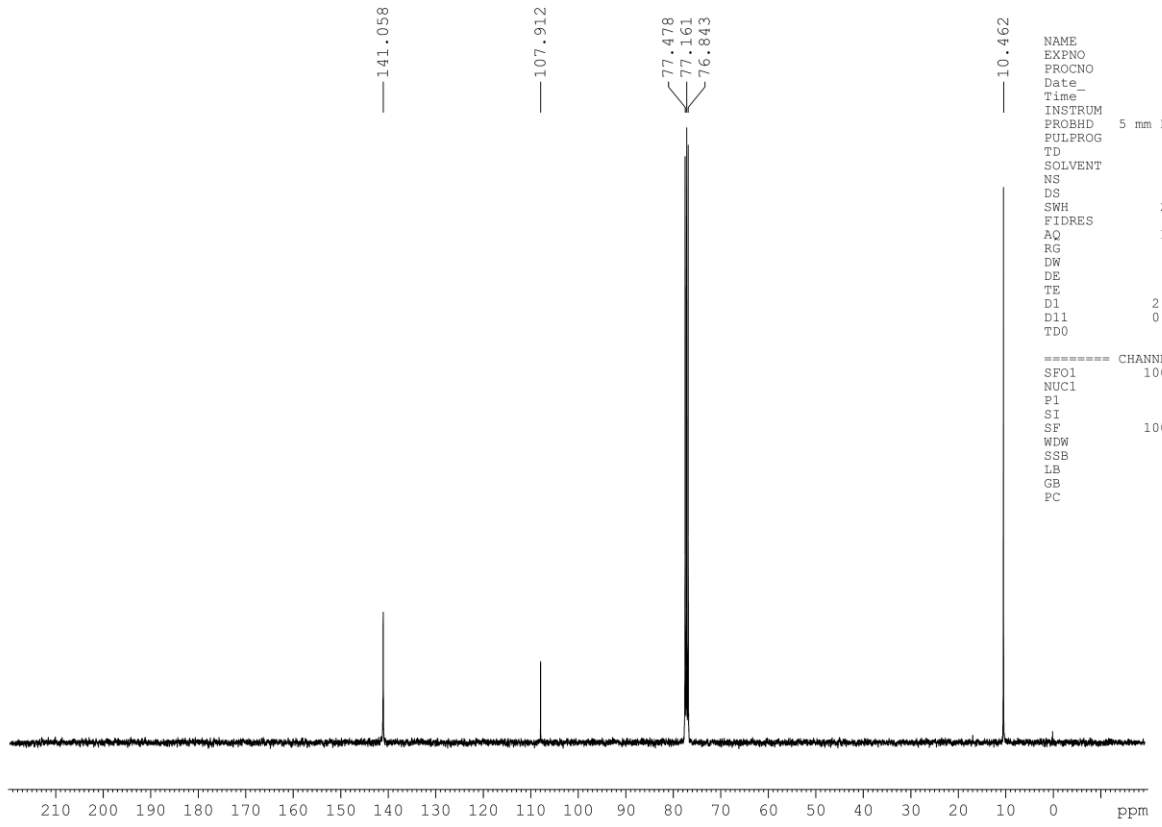
$^{13}C\{^{1}H\}$, $CDCl_3$

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TE                291.9 K
D1             2.00000000 sec
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TD0                     1

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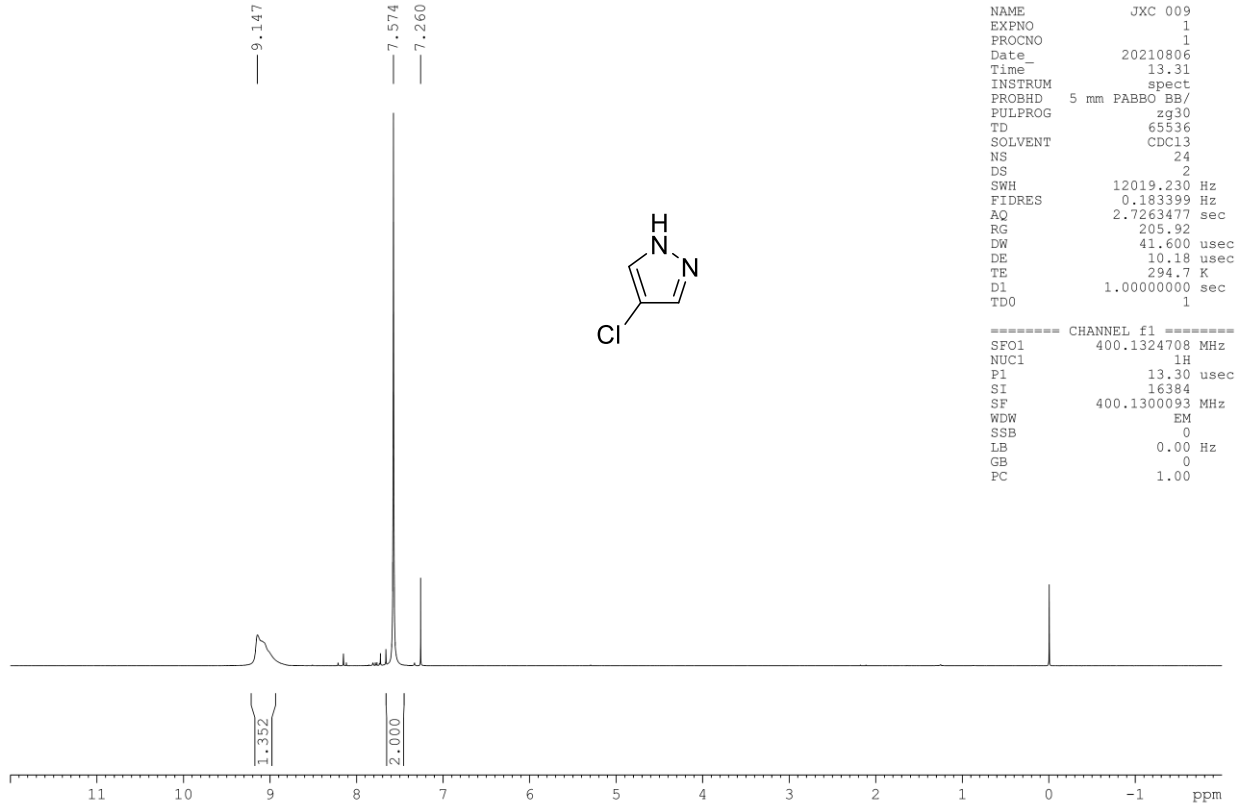
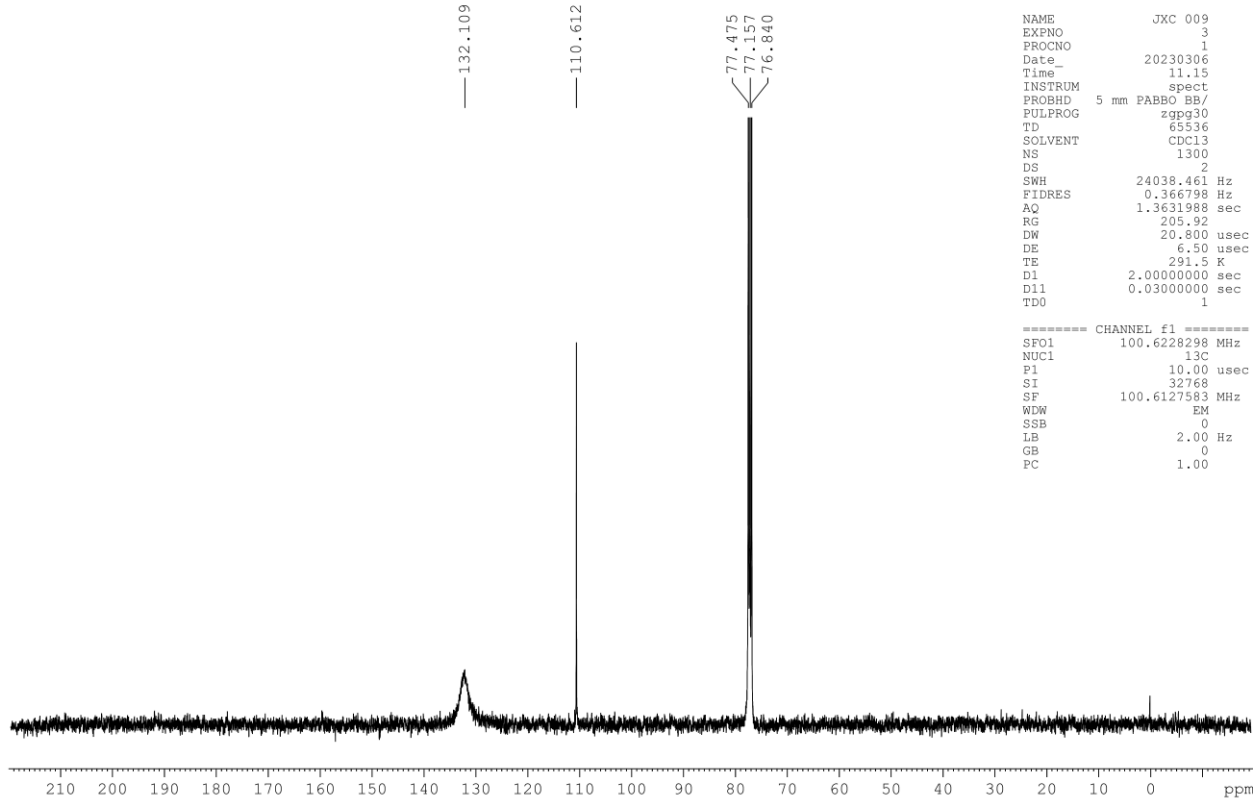
4-Chloropyrazole **1b**

^{1}H, $CDCl_3$

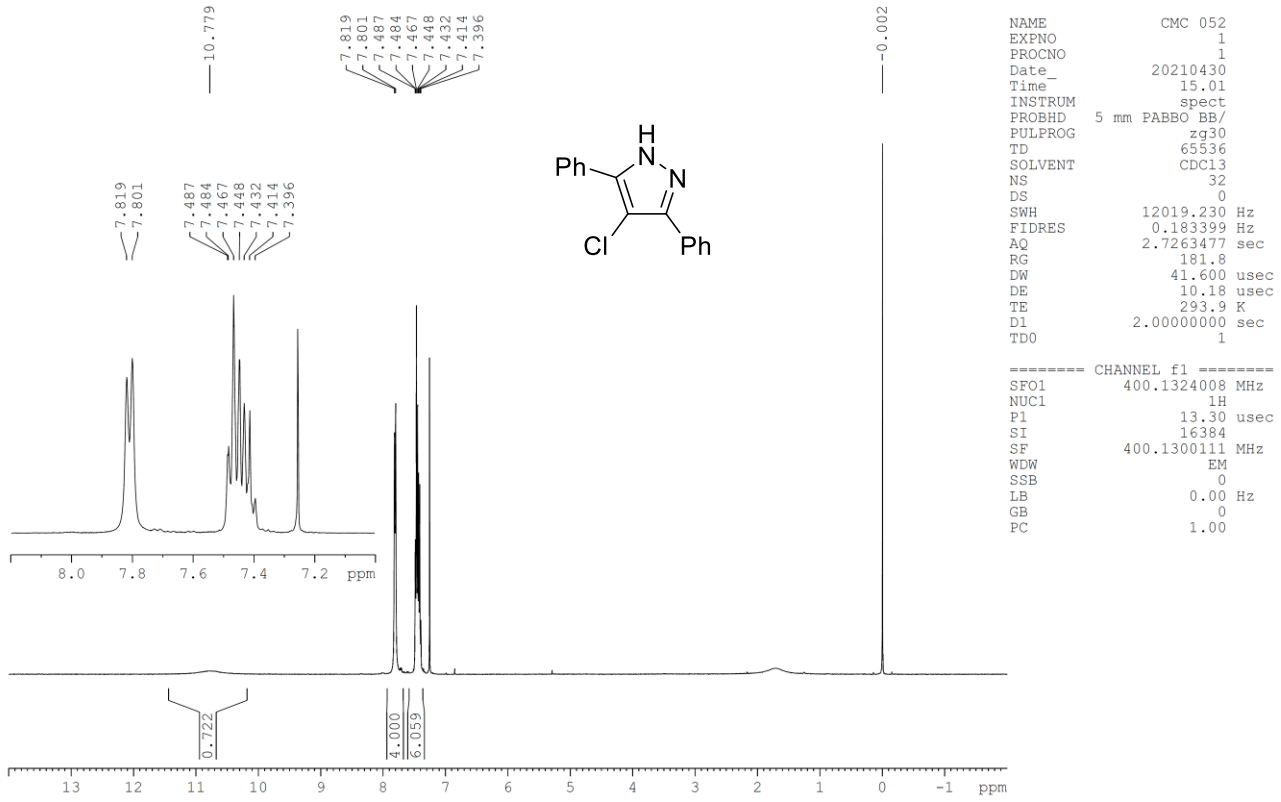


$^{13}C\{^{1}H\}$, $CDCl_3$



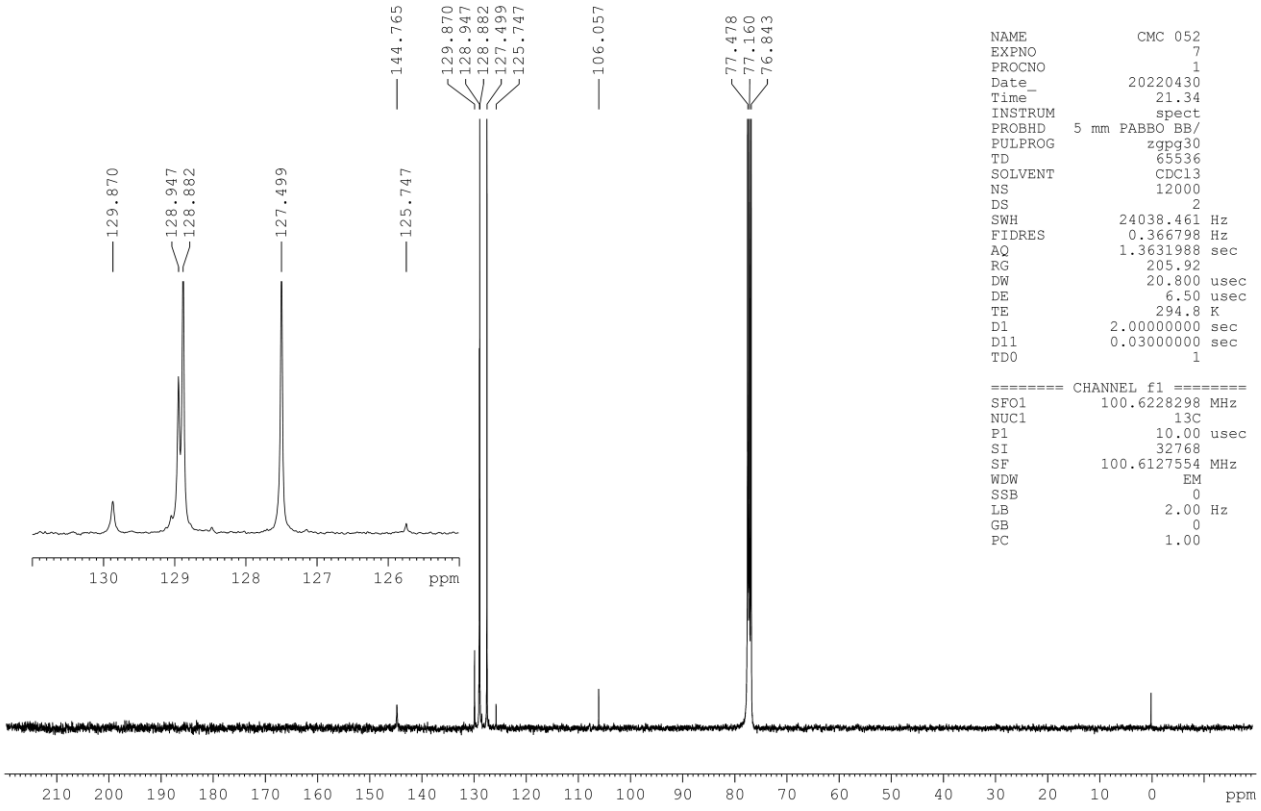
4-Chloro-3,5-diphenylpyrazole **1c**

^{1}H, $CDCl_3$




```
NAME              CMC 052
EXPNO                   1
PROCNO                  1
Date_            20210430
Time                15.01
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     32
DS                      0
SWH             12019.230 Hz
FIDRES          0.183399 Hz
AQ              2.7263477 sec
RG                  181.8
DW                 41.600 usec
DE                 10.18 usec
TE                 293.9 K
D1             2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          400.1324008 MHz
NUC1                   1H
P1                  13.30 usec
SI                  16384
SF            400.1300111 MHz
WDW                    EM
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.00
```

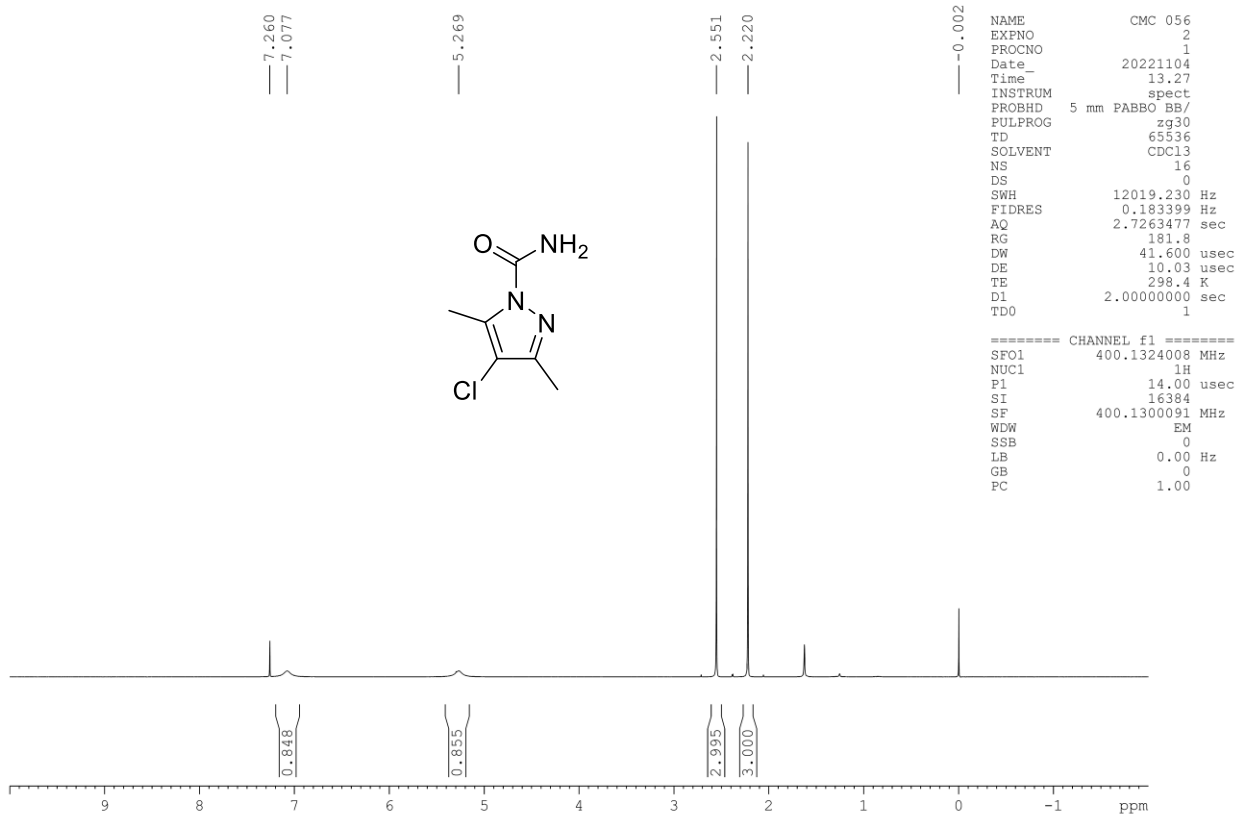
$^{13}C\{^{1}H\}$, $CDCl_3$



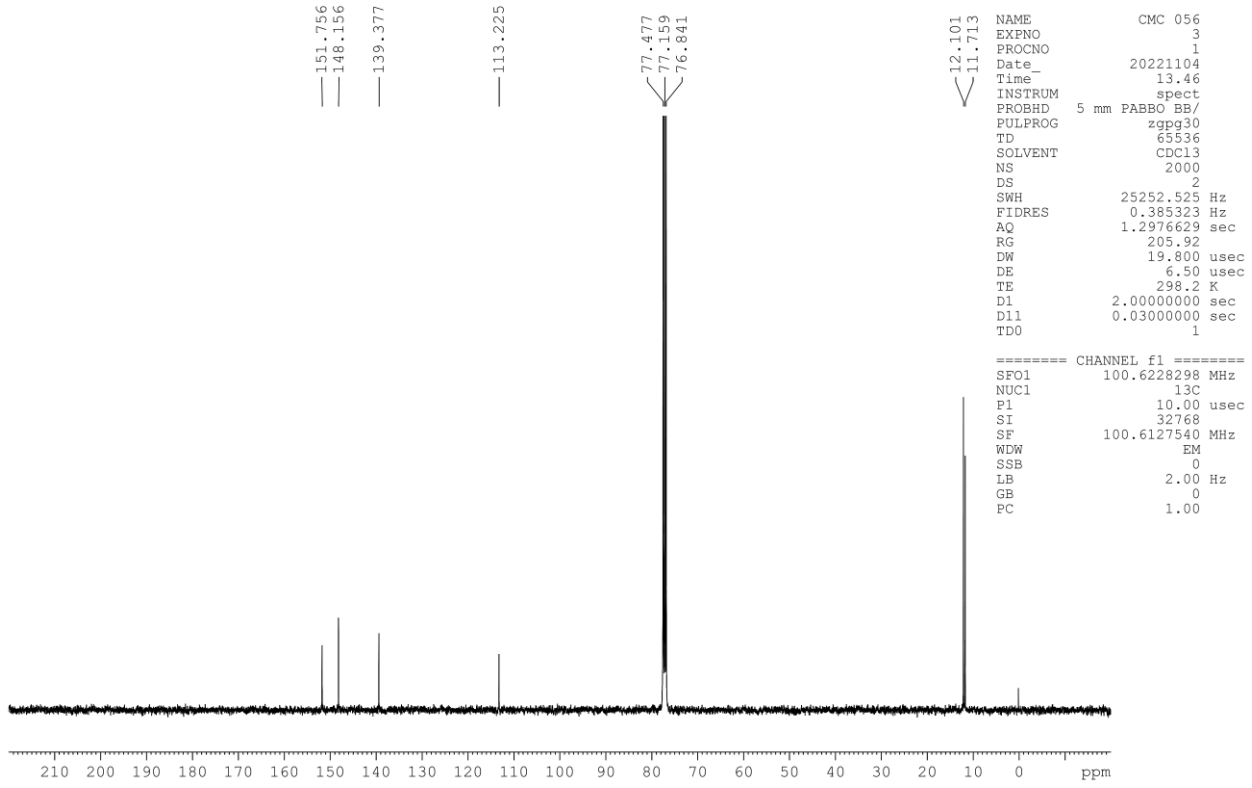

```
NAME              CMC 052
EXPNO                   7
PROCNO                  1
Date_            20220430
Time                21.34
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                  12000
DS                      2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                 205.92
DW                 20.800 usec
DE                  6.50 usec
TE                 294.8 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          100.6228298 MHz
NUC1                   13C
P1                  10.00 usec
SI                  32768
SF            100.6127554 MHz
WDW                    EM
SSB                     0
LB                   2.00 Hz
GB                      0
PC                   1.00
```

4-Chloro-3,5-dimethyl-1H-pyrazole-1-carboxamide **1d**

^{1}H, $CDCl_3$

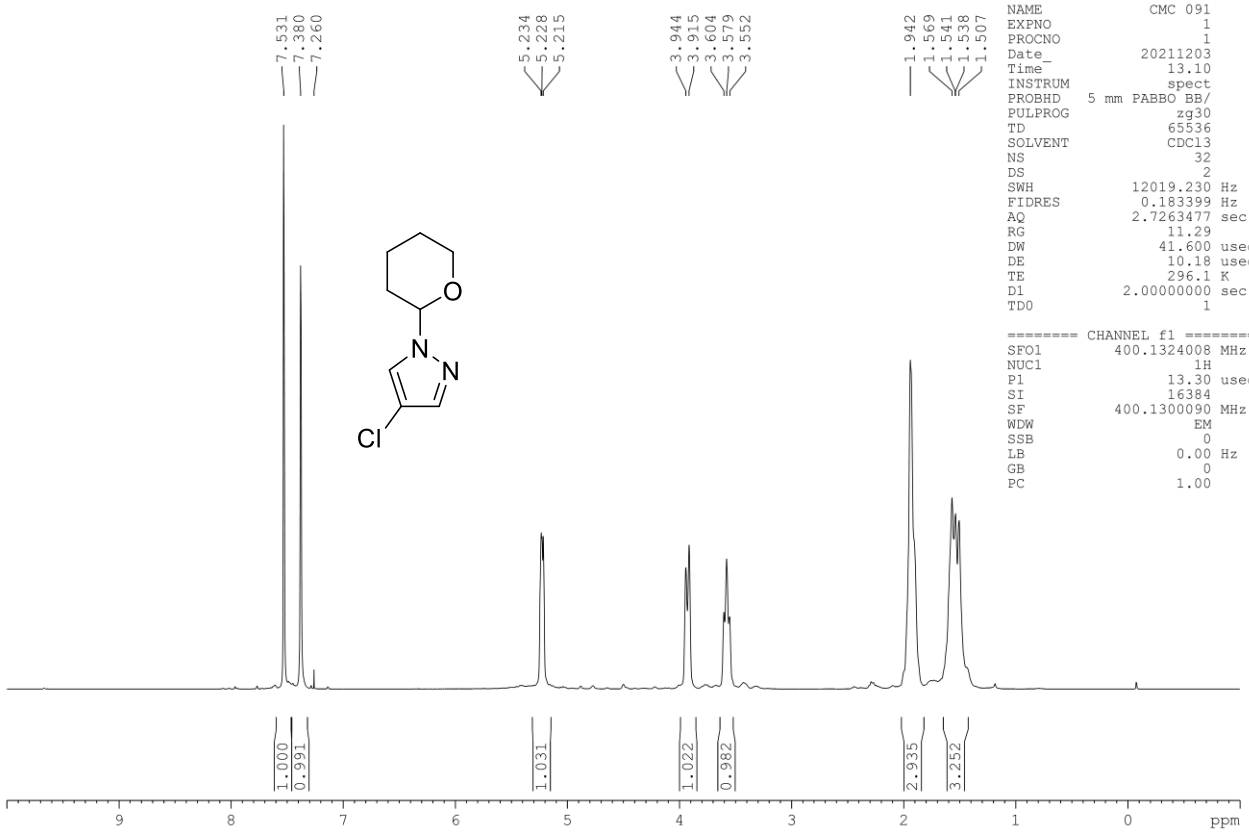


$^{13}C\{^{1}H\}$, $CDCl_3$

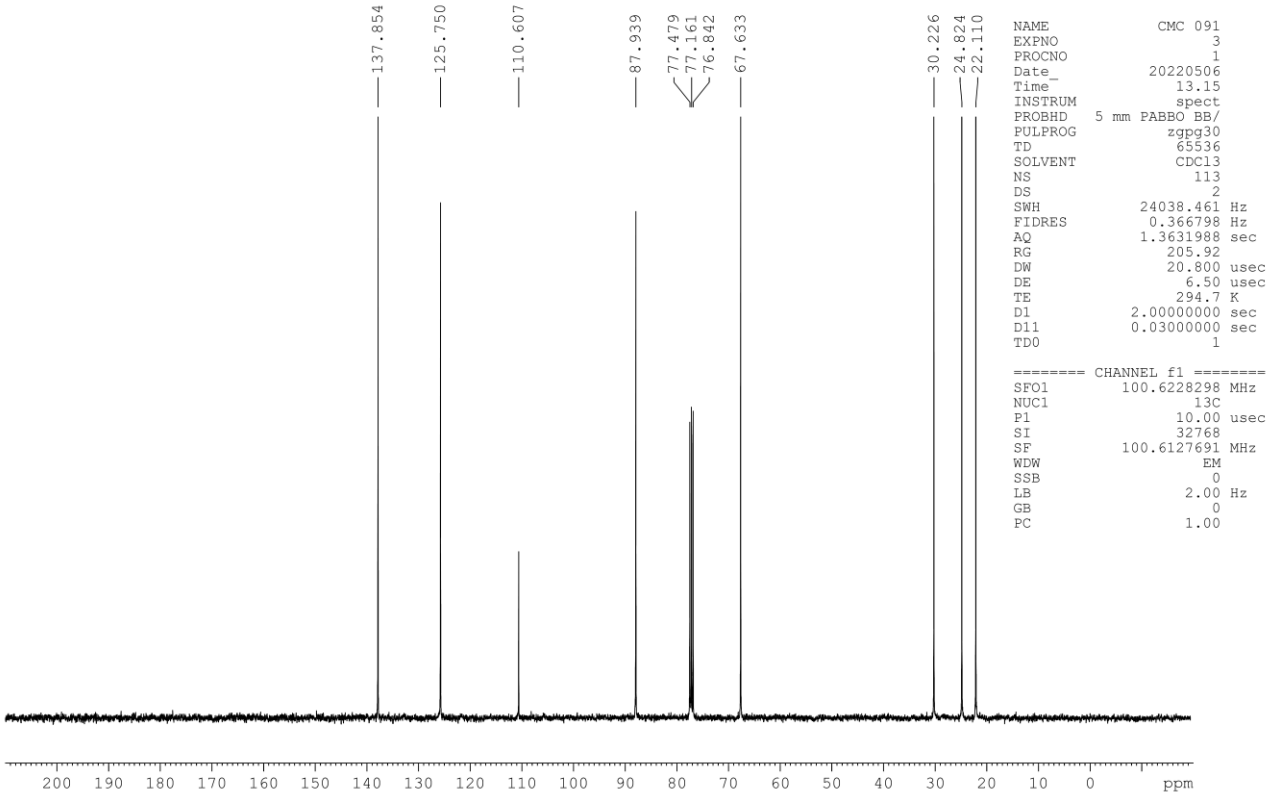


4-Chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole **1e**

^{1}H, $CDCl_3$

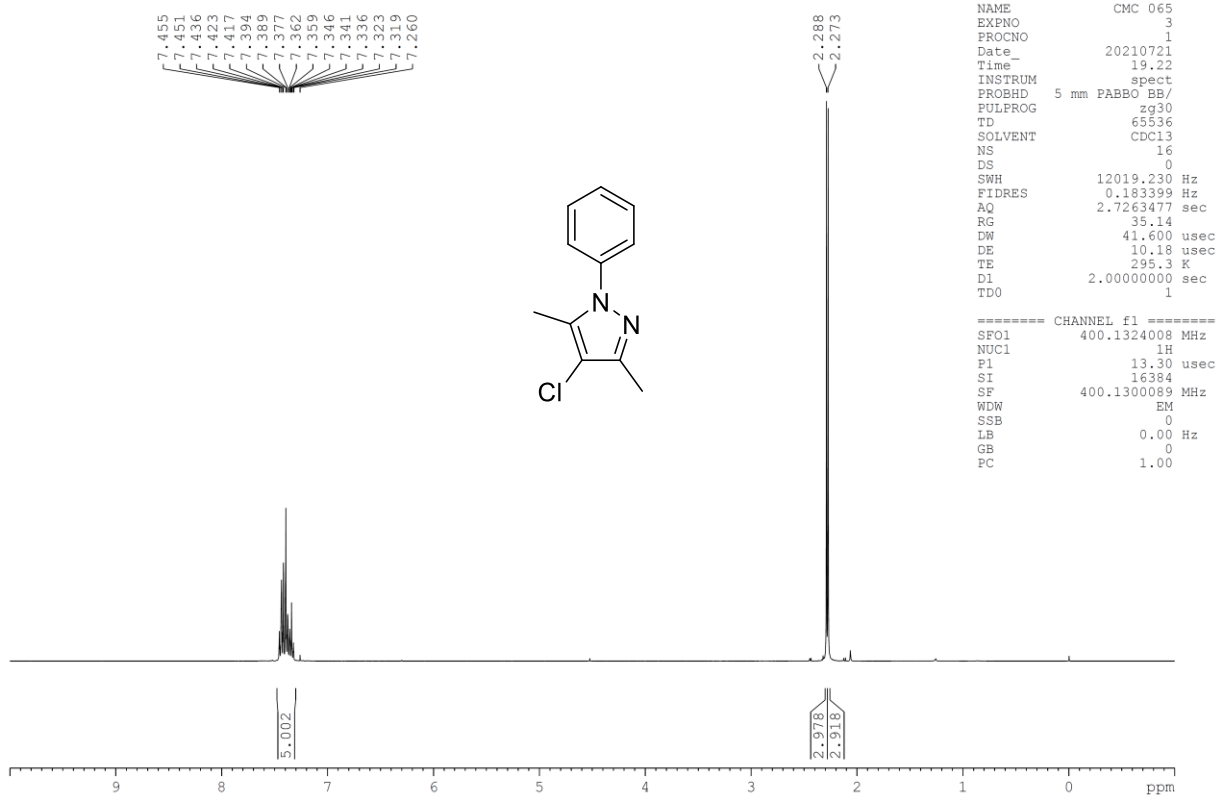


$^{13}C\{^{1}H\}$, $CDCl_3$

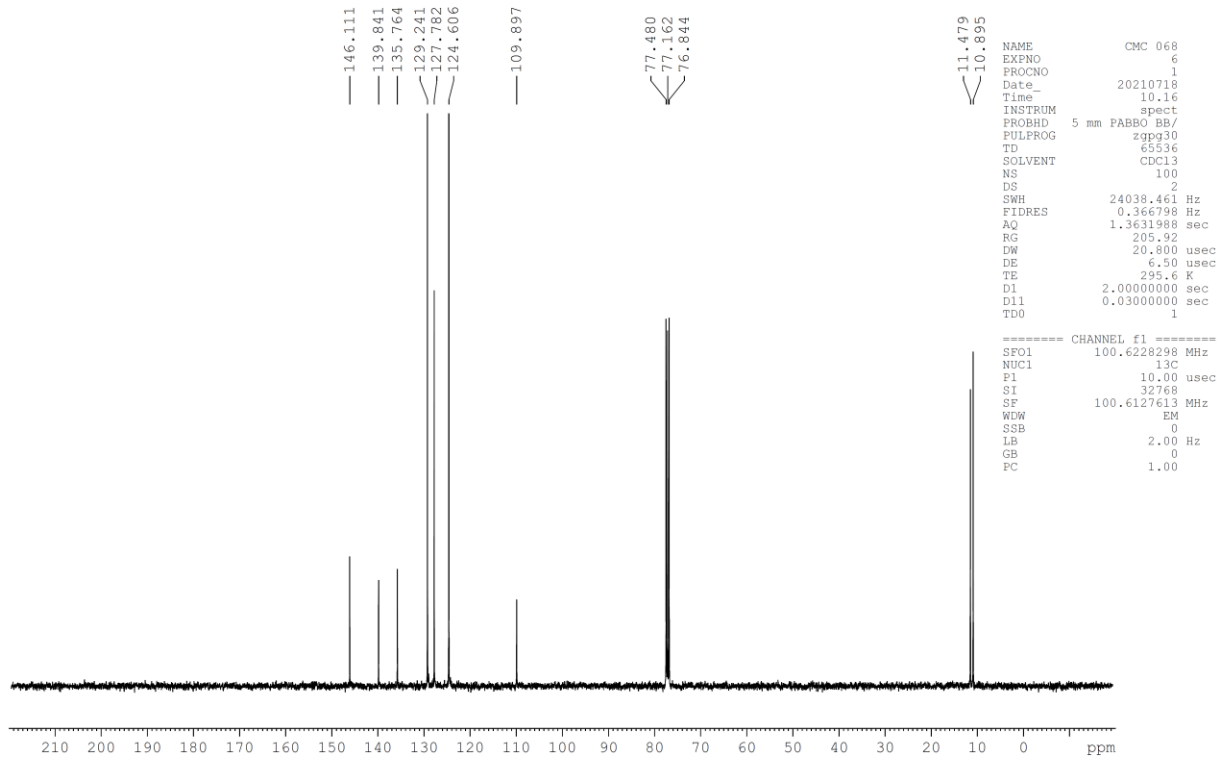


4-Chloro-3,5-dimethyl-1-phenylpyrazole **1f**

^{1}H, $CDCl_3$

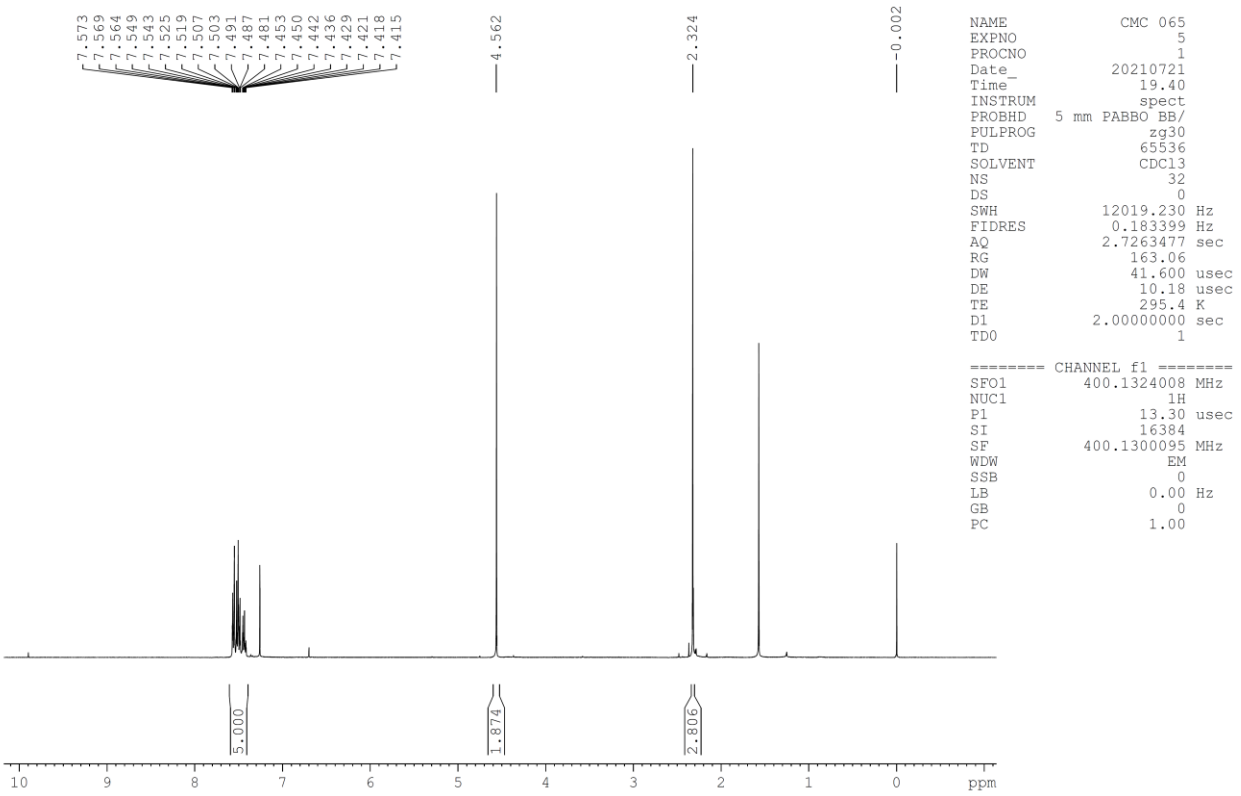


$^{13}C\{^{1}H\}$, $CDCl_3$



di-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-2**

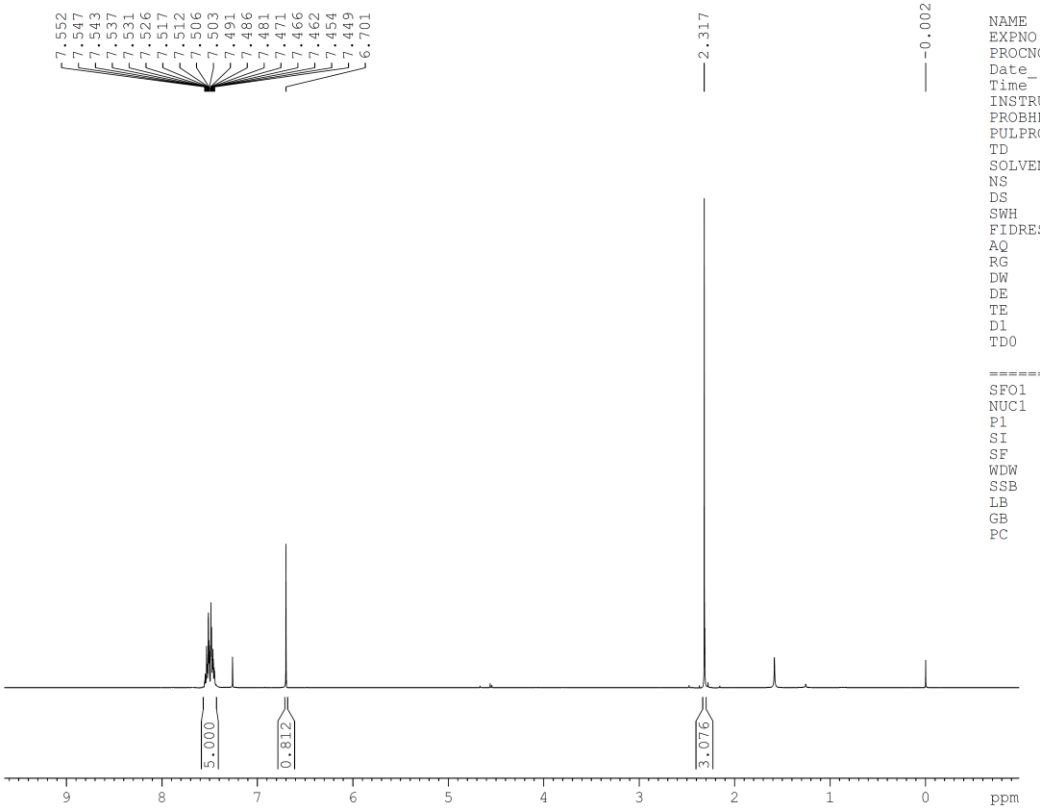
^{1}H, $CDCl_3$




```
NAME            CMC 065
EXPNO                 5
PROCNO                1
Date_          20210721
Time              19.40
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   32
DS                    0
SWH           12019.230 Hz
FIDRES         0.183399 Hz
AQ            2.7263477 sec
RG               163.06
DW               41.600 usec
DE               10.18 usec
TE               295.4 K
D1           2.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        400.1324008 MHz
NUC1                1H
P1                13.30 usec
SI                16384
SF          400.1300095 MHz
WDW                 EM
SSB                  0
LB                0.00 Hz
GB                   0
PC                1.00
```

di-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-3**

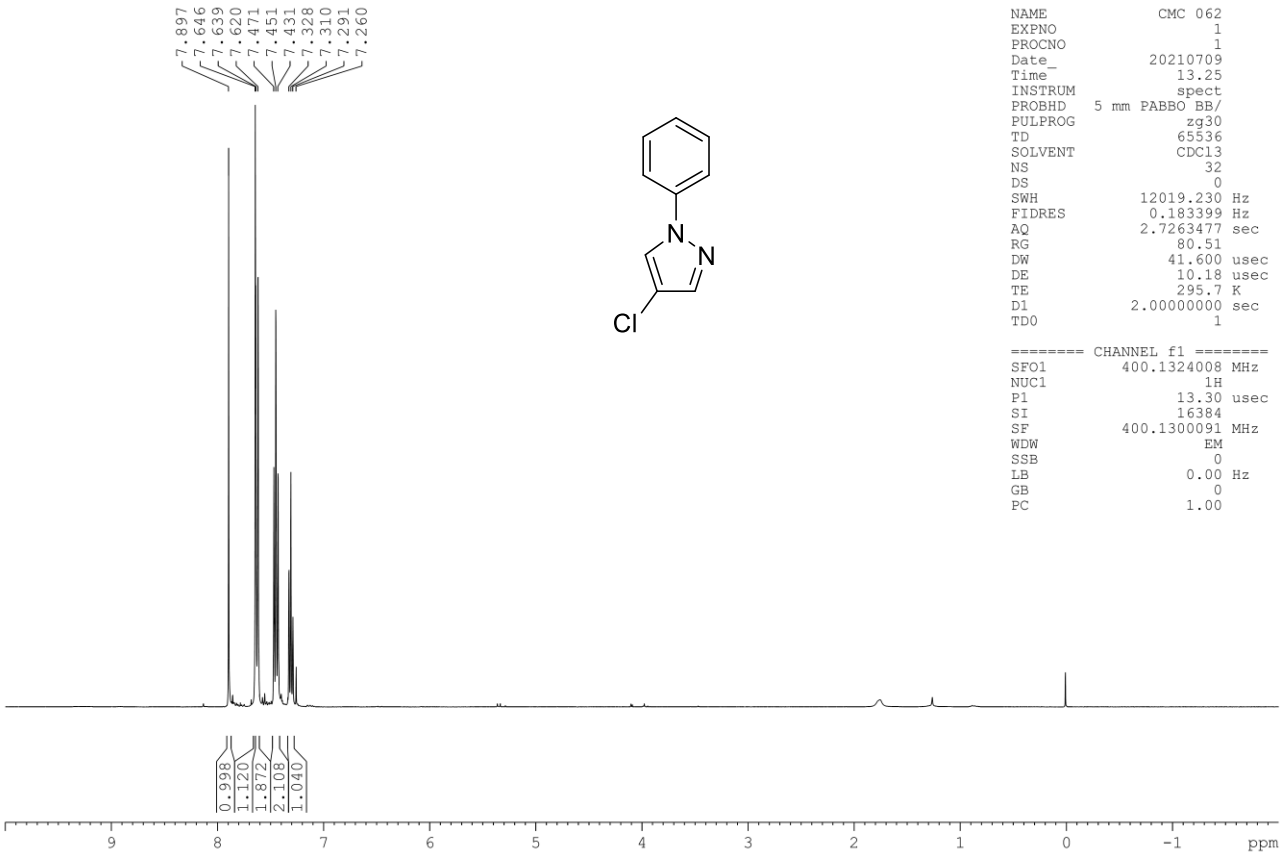
^{1}H, $CDCl_3$




```
NAME            CMC 065
EXPNO                 4
PROCNO                1
Date_          20210721
Time              19.28
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   32
DS                    0
SWH           12019.230 Hz
FIDRES         0.183399 Hz
AQ            2.7263477 sec
RG               163.06
DW               41.600 usec
DE               10.18 usec
TE               295.3 K
D1           2.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        400.1324008 MHz
NUC1                1H
P1                13.30 usec
SI                16384
SF          400.1300096 MHz
WDW                 EM
SSB                  0
LB                0.00 Hz
GB                   0
PC                1.00
```

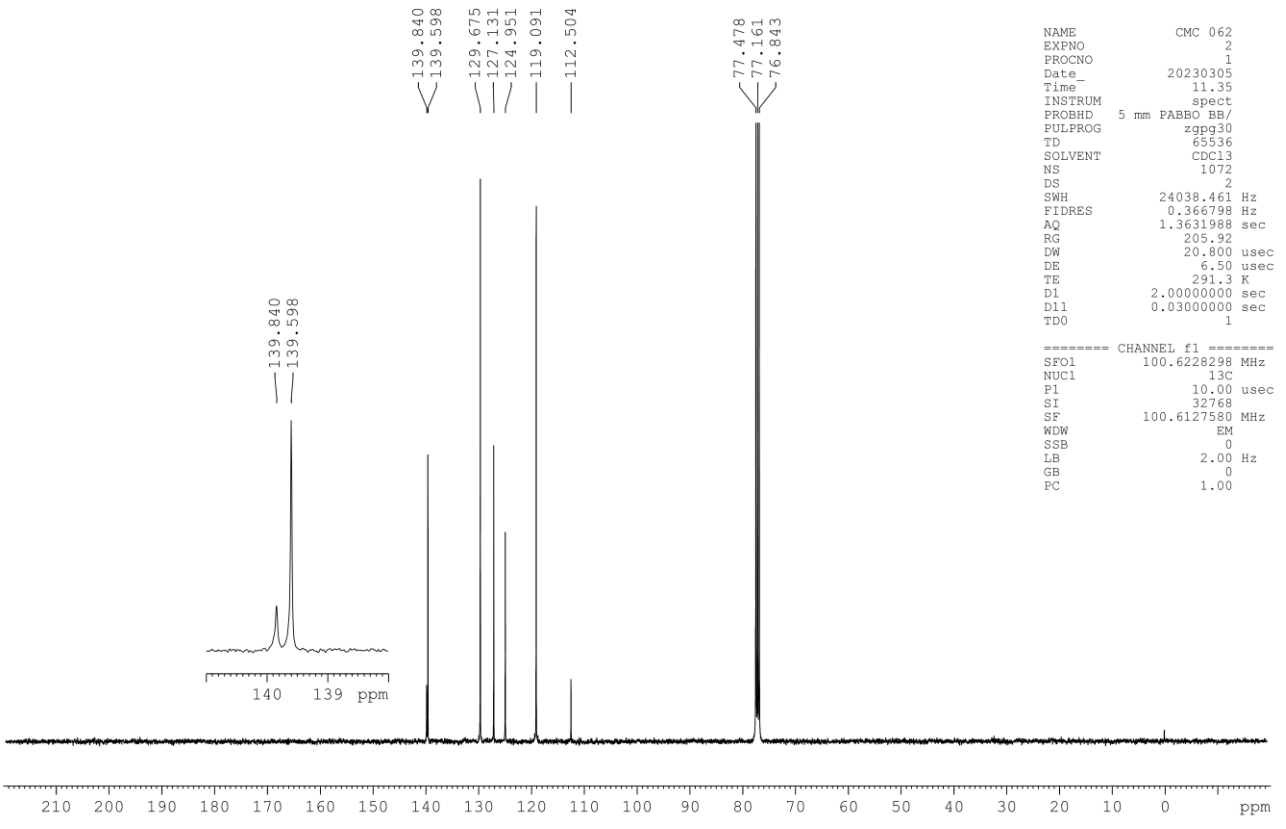
4-Chloro-1-phenylpyrazole **1g**

^{1}H, $CDCl_3$




```
NAME              CMC 062
EXPNO                   1
PROCNO                  1
Date_            20210709
Time                13.25
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     32
DS                      0
SWH             12019.230 Hz
FIDRES          0.183399 Hz
AQ              2.7263477 sec
RG                  80.51
DW                41.600 usec
DE                 10.18 usec
TE                 295.7 K
D1             2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1         400.1324008 MHz
NUC1                   1H
P1                  13.30 usec
SI                  16384
SF           400.1300091 MHz
WDW                    EM
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.00
```

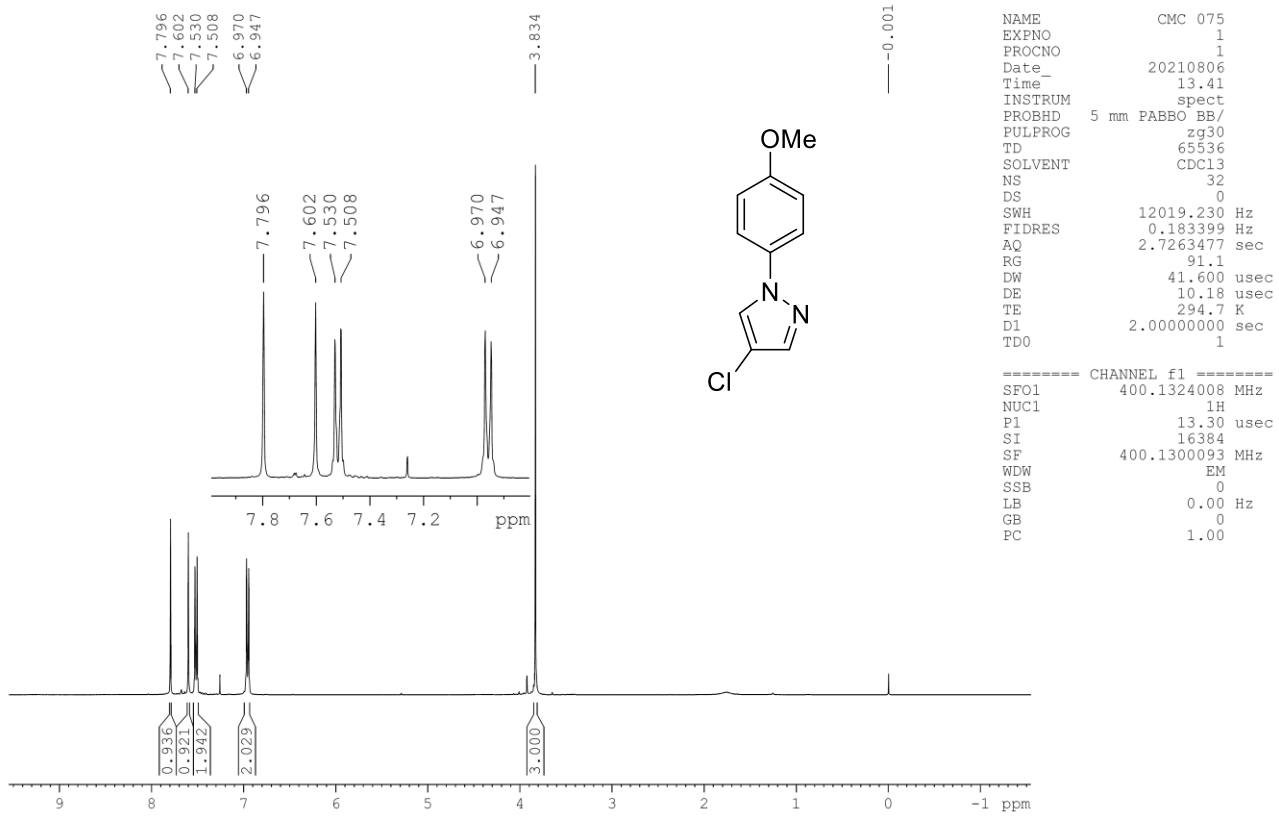
$^{13}C\{^{1}H\}$, $CDCl_3$




```
NAME              CMC 062
EXPNO                   2
PROCNO                  1
Date_            20230305
Time                11.35
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   1072
DS                      2
SWH             24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                 205.92
DW                20.800 usec
DE                 6.50 usec
TE                 291.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1         100.6228298 MHz
NUC1                   13C
P1                  10.00 usec
SI                  32768
SF           100.6127580 MHz
WDW                    EM
SSB                     0
LB                   2.00 Hz
GB                      0
PC                   1.00
```

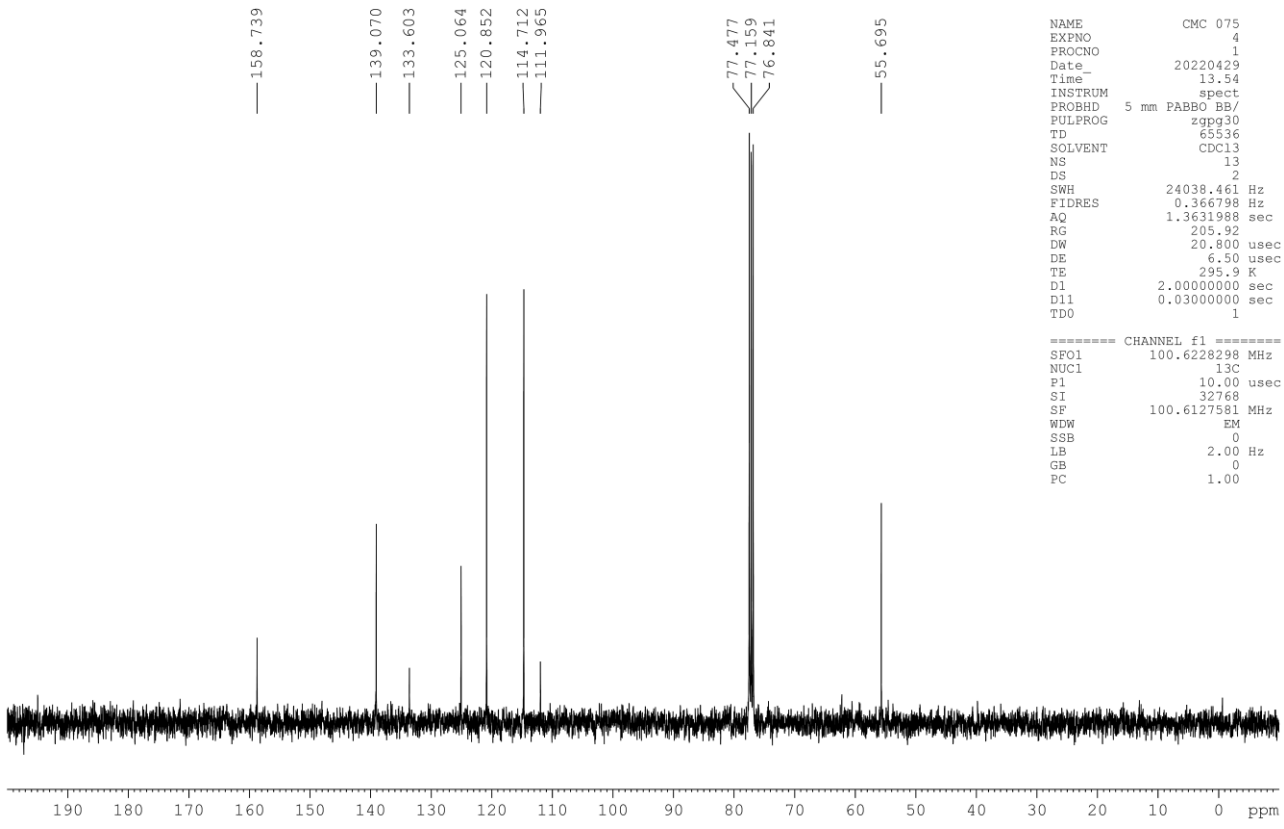
4-chloro-1-(4-methoxyphenyl)pyrazole **1h**

^{1}H, $CDCl_3$



NAME	CMC 075
EXPNO	1
PROCNO	1
Date_	20210806
Time	13.41
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	0
SWH	12019.230 Hz
FIDRES	0.183399 Hz
AQ	2.7263477 sec
RG	91.1
DW	41.600 usec
DE	10.18 usec
TE	294.7 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	400.1324008 MHz
NUC1	1H
P1	13.30 usec
SI	16384
SF	400.1300093 MHz
WDW	EM
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

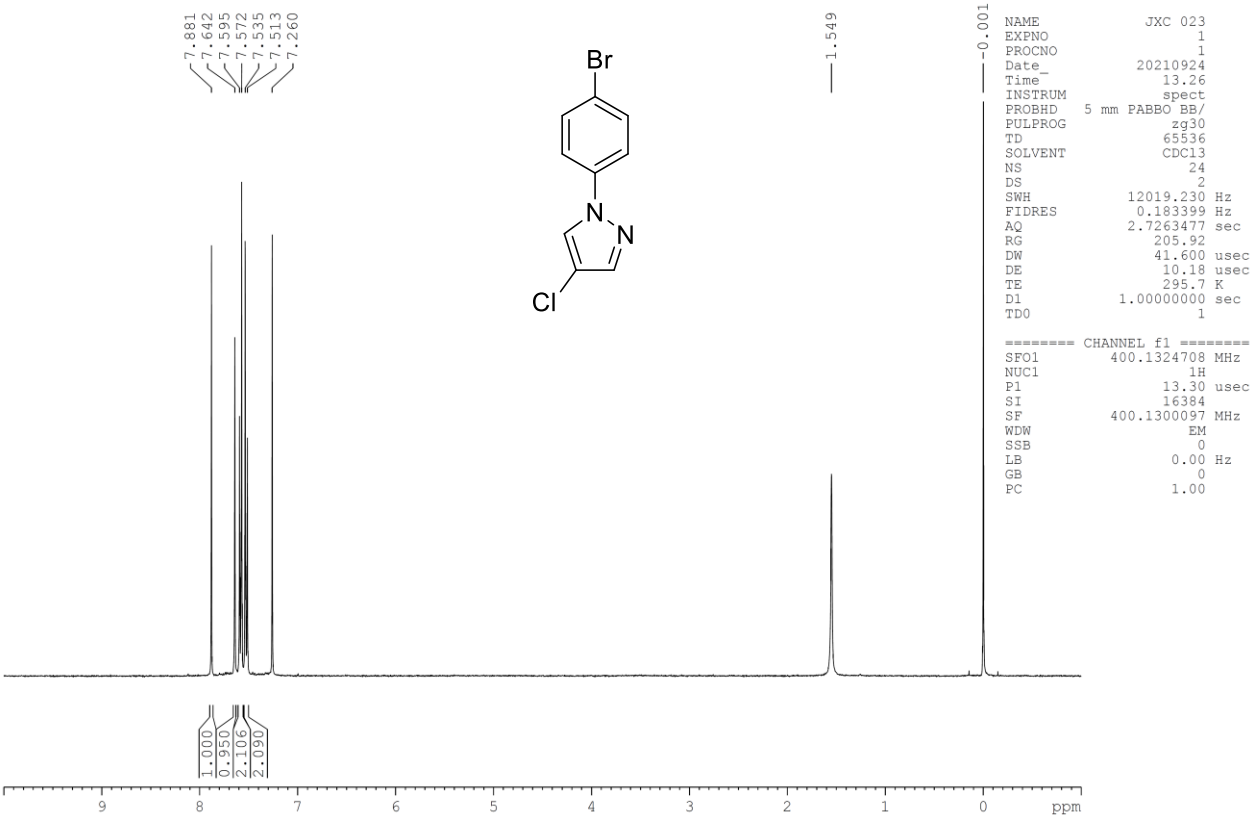
$^{13}C\{^{1}H\}$, $CDCl_3$



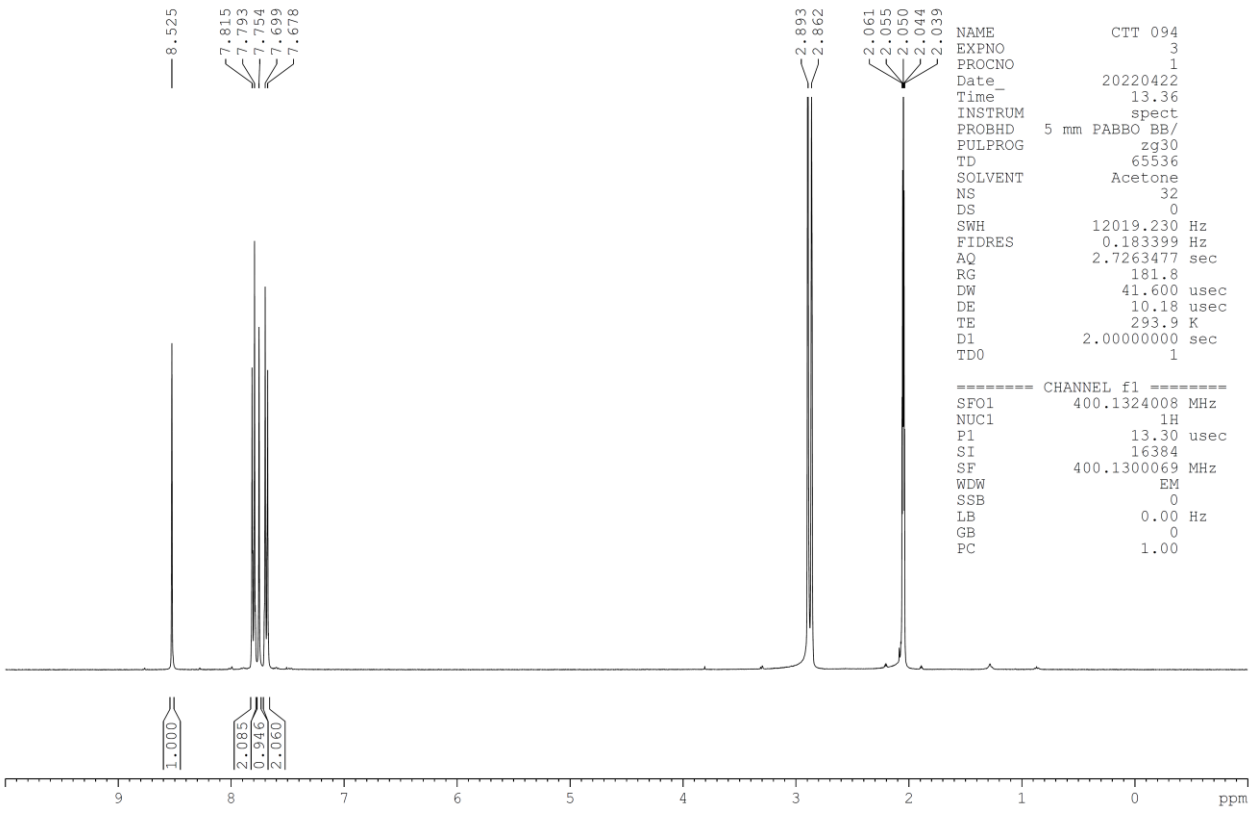
NAME	CMC 075
EXPNO	4
PROCNO	1
Date_	20220429
Time	13.54
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	13
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	205.92
DW	20.800 usec
DE	6.50 usec
TE	295.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	100.6228298 MHz
NUC1	13C
P1	10.00 usec
SI	32768
SF	100.6127581 MHz
WDW	EM
SSB	0
LB	2.00 Hz
GB	0
PC	1.00

4-Chloro-1-(4-bromophenyl)pyrazole **1i**

^{1}H, $CDCl_3$

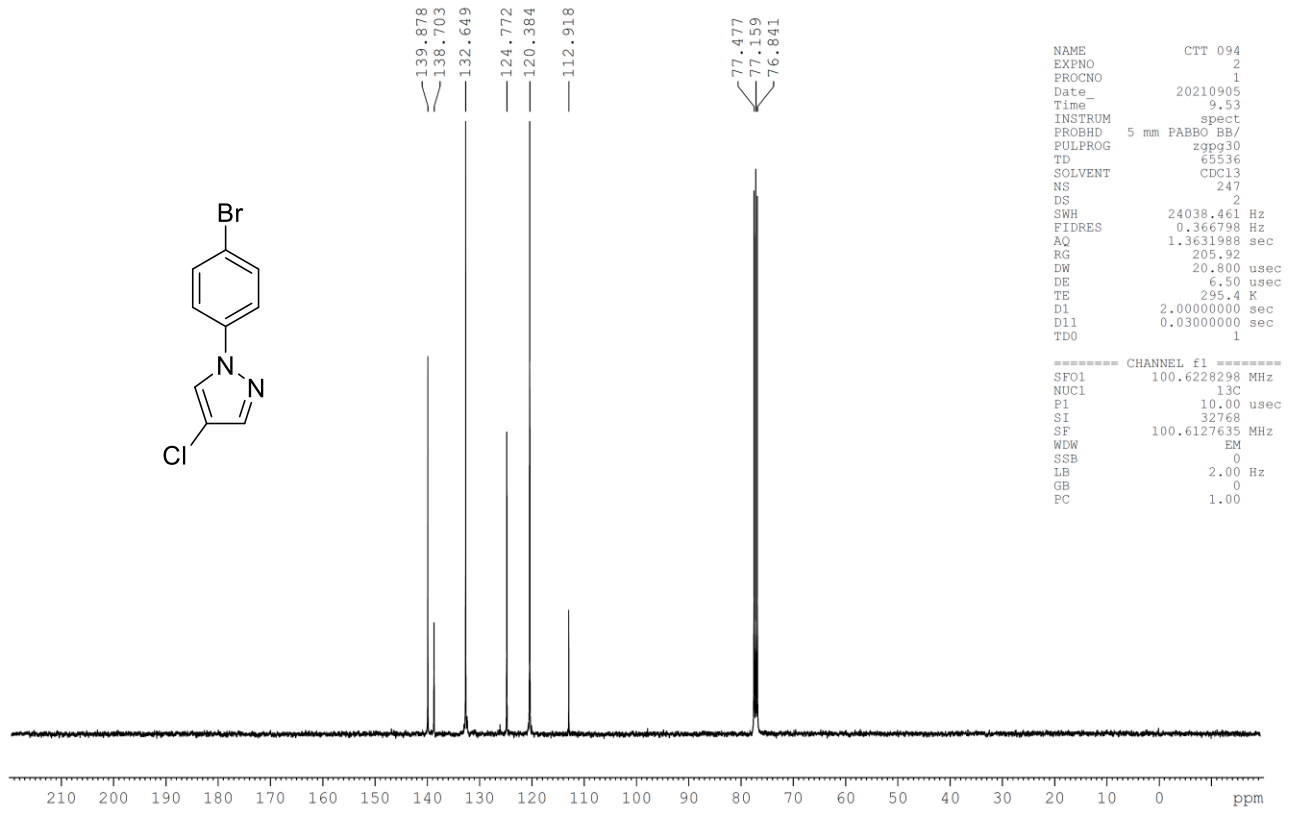


^{1}H, acetone-d_6

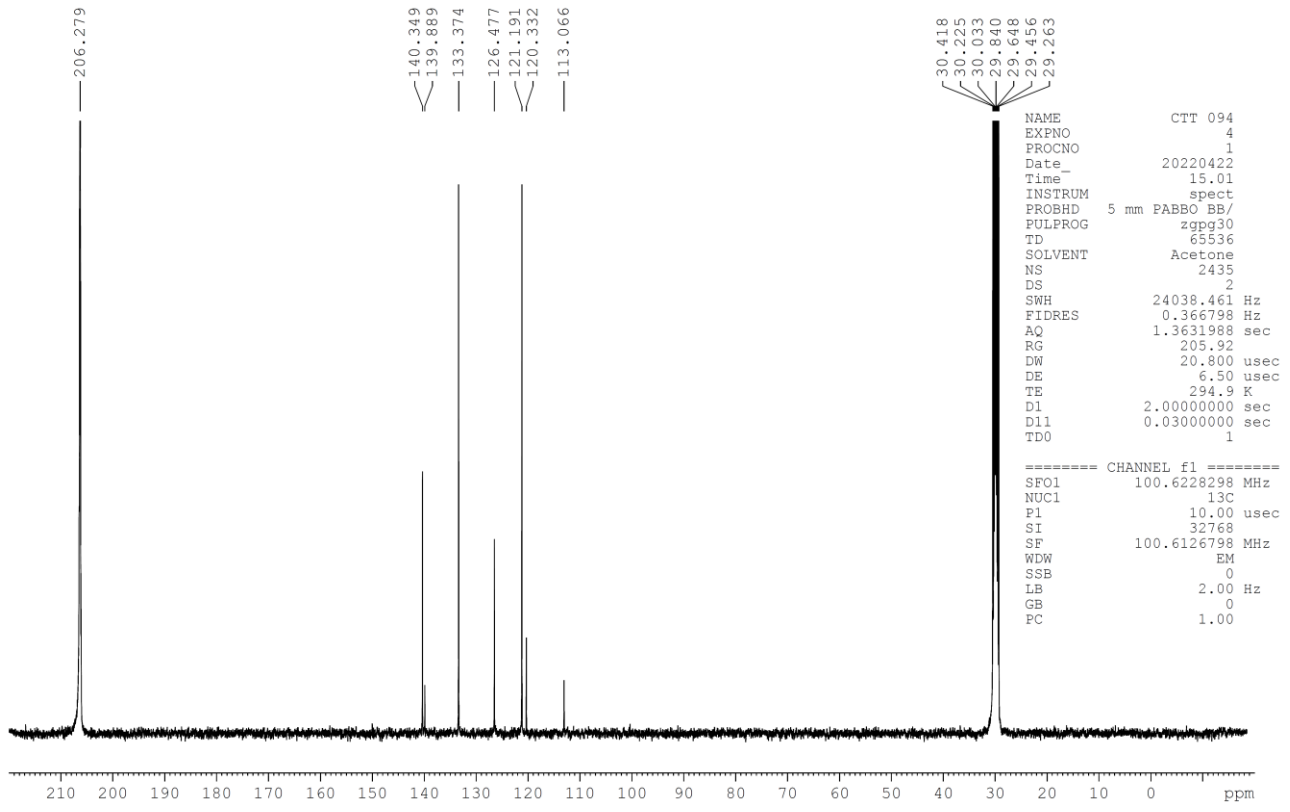


4-Chloro-1-(4-bromophenyl)pyrazole **1i**

$^{13}C\{^{1}H\}$, $CDCl_3$

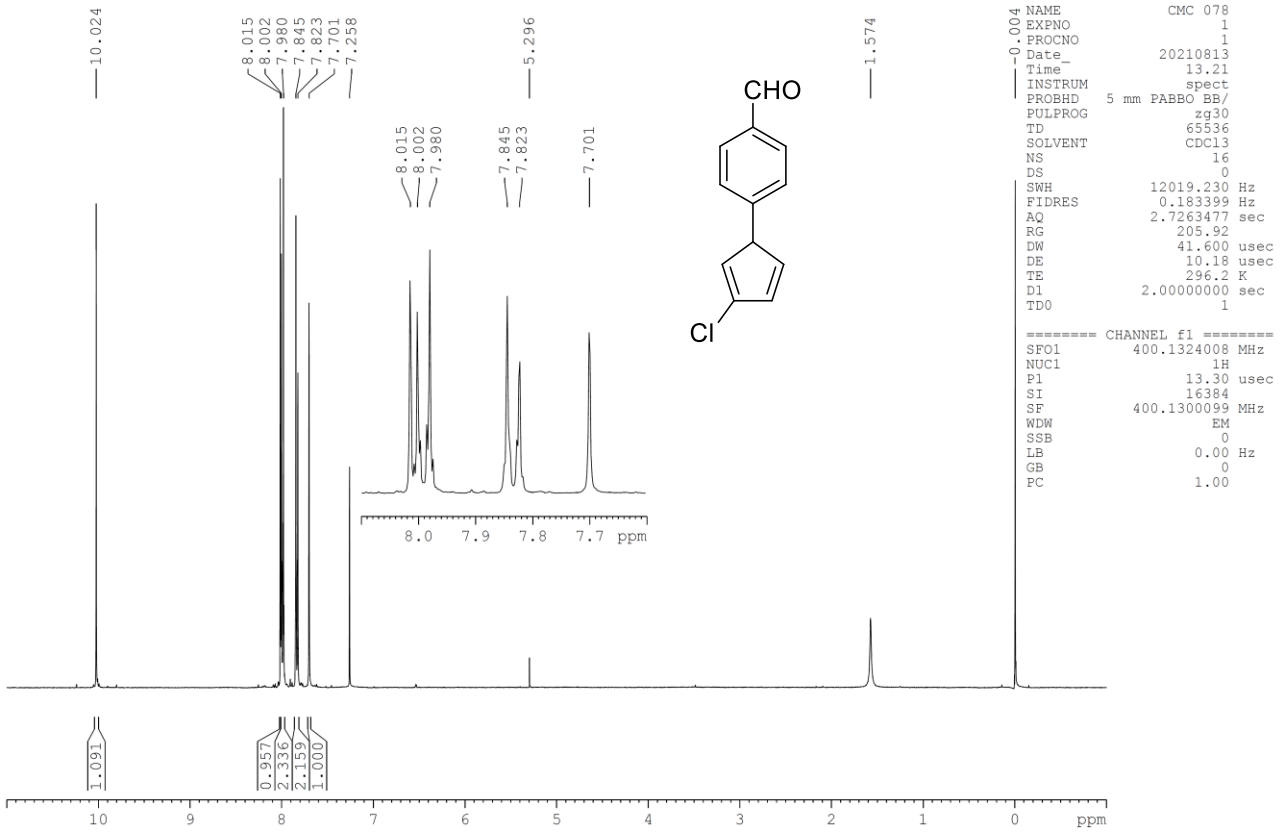


$^{13}C\{^{1}H\}$, acetone-d_6

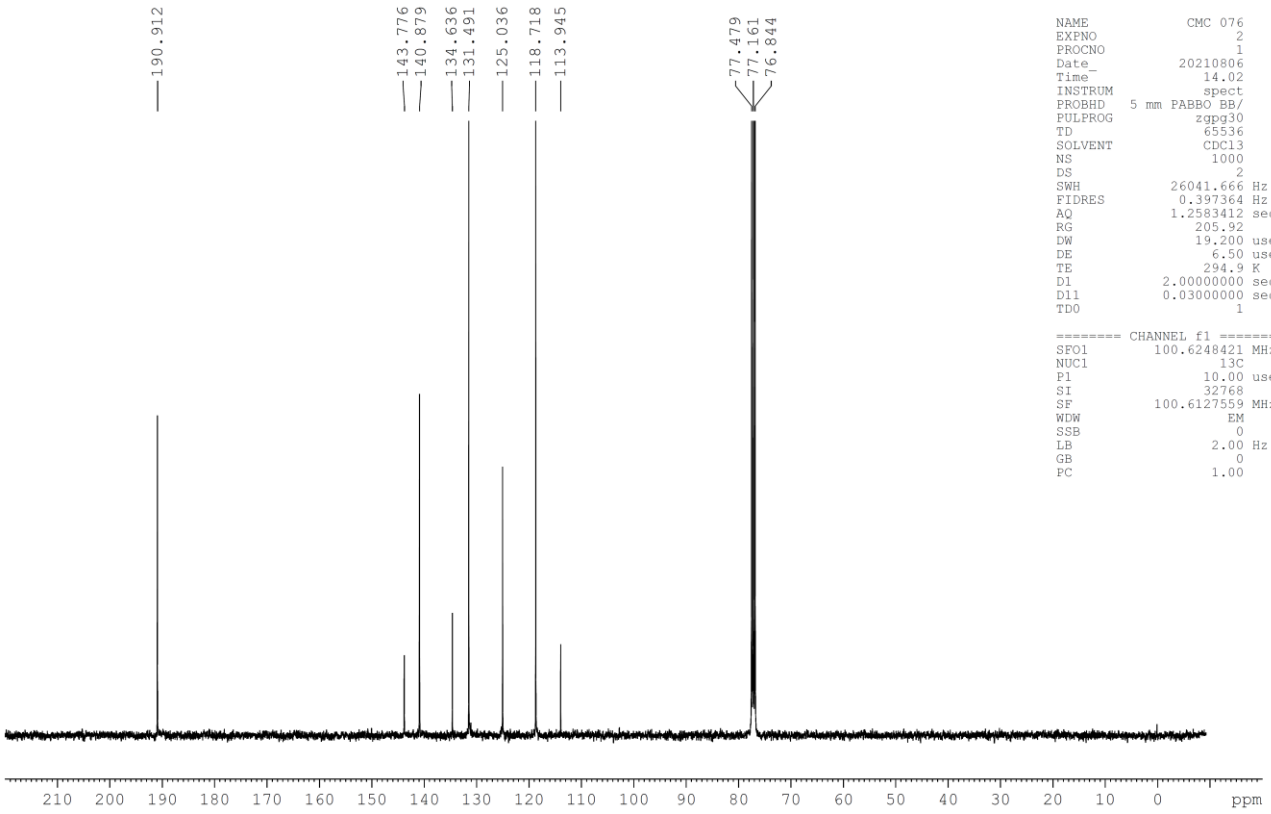


4-(4-chloro-1H-pyrazol-1-yl)benzaldehyde **1j**

^{1}H, $CDCl_3$

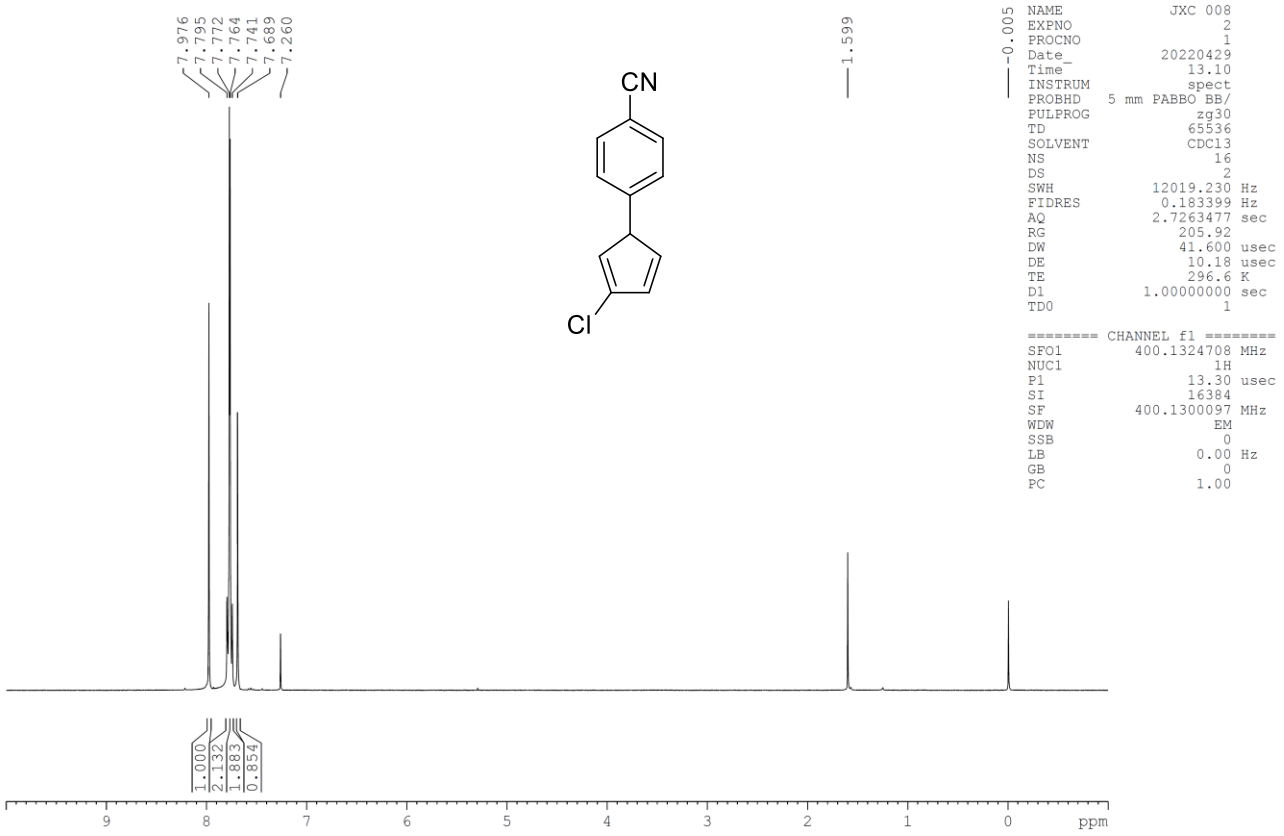


$^{13}C\{^{1}H\}$, $CDCl_3$

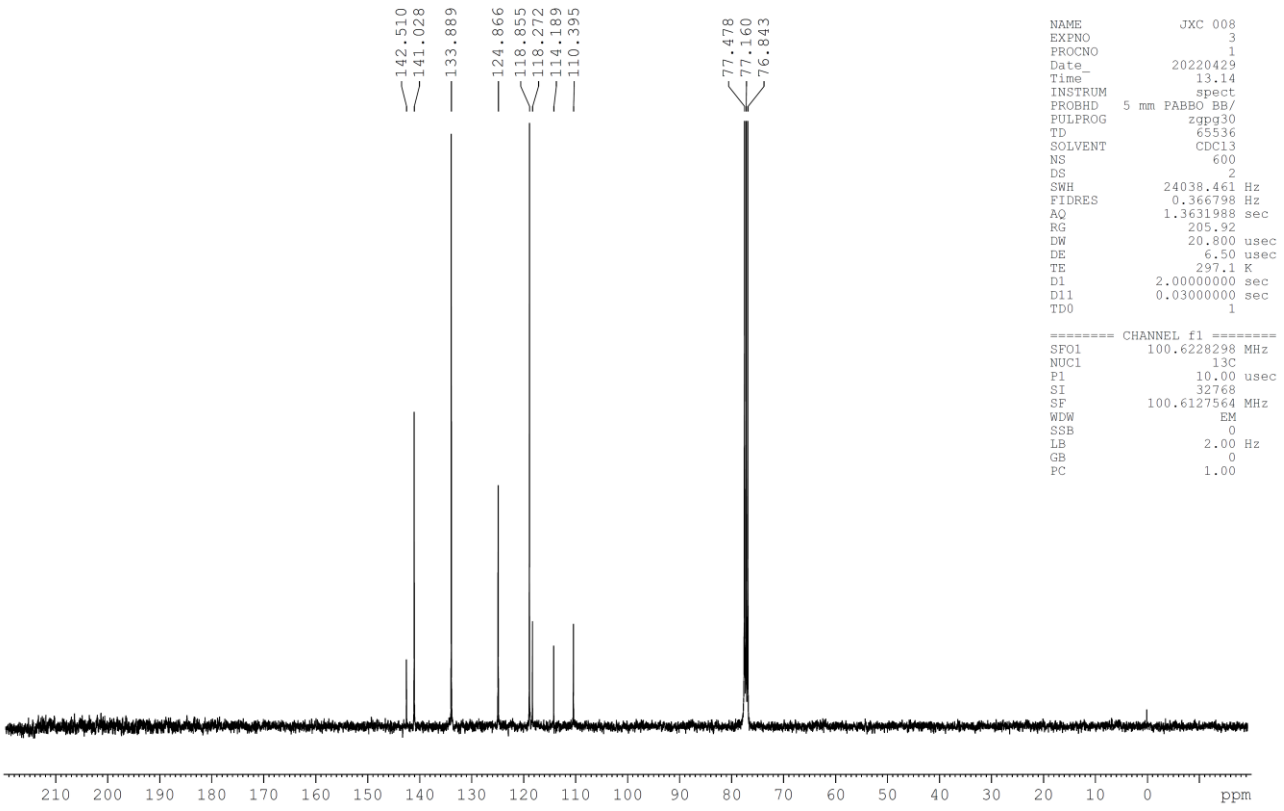


4-(4-chloro-1H-pyrazol-1-yl)benzonitrile **1k**

^{1}H, $CDCl_3$

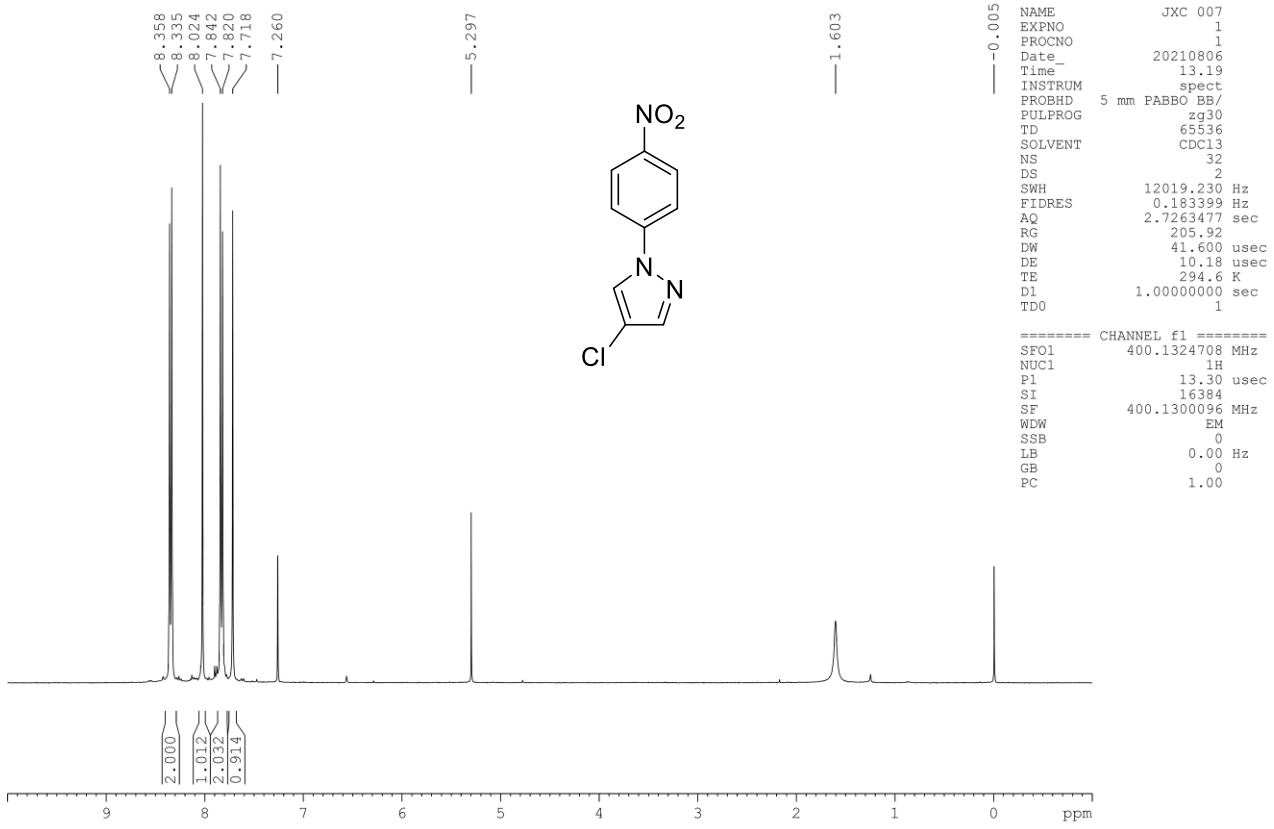


$^{13}C\{^{1}H\}$, $CDCl_3$

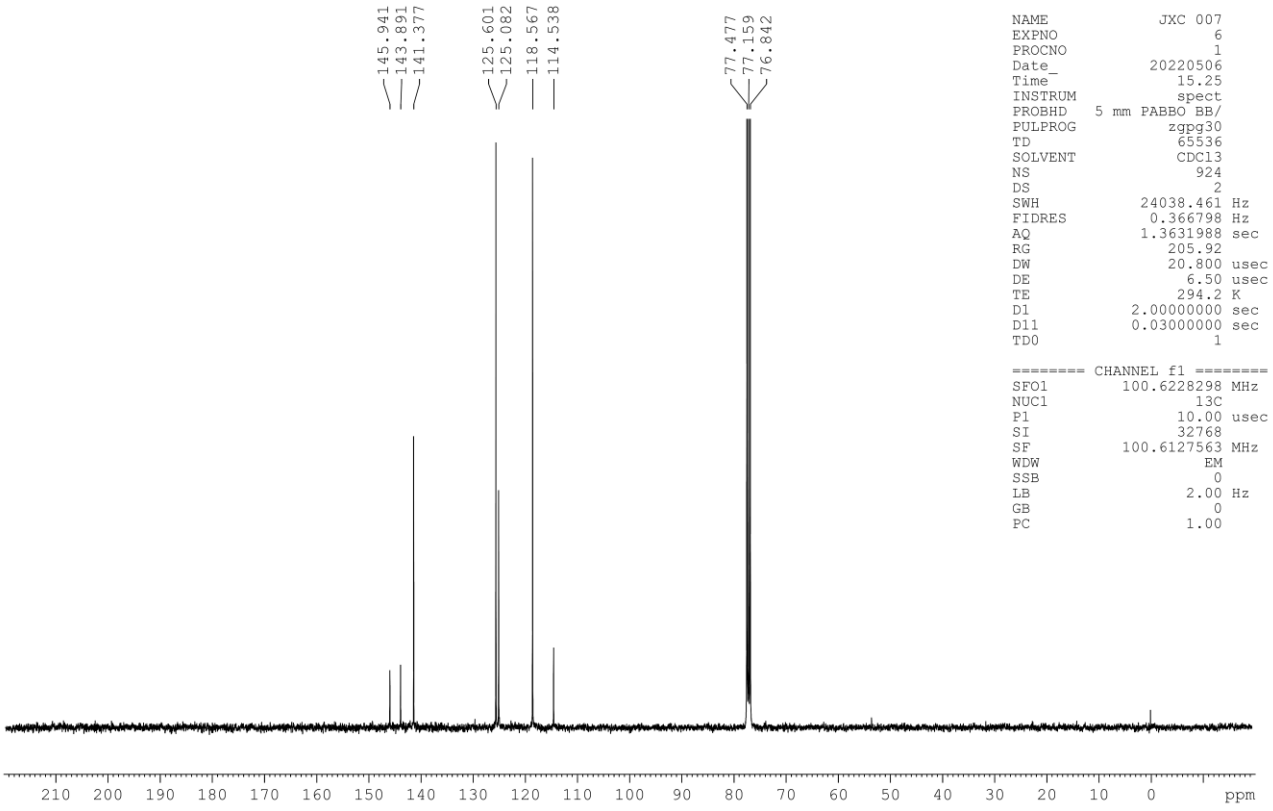


4-chloro-1-(4-nitrophenyl)-1H-pyrazole **1l**

^{1}H, $CDCl_3$

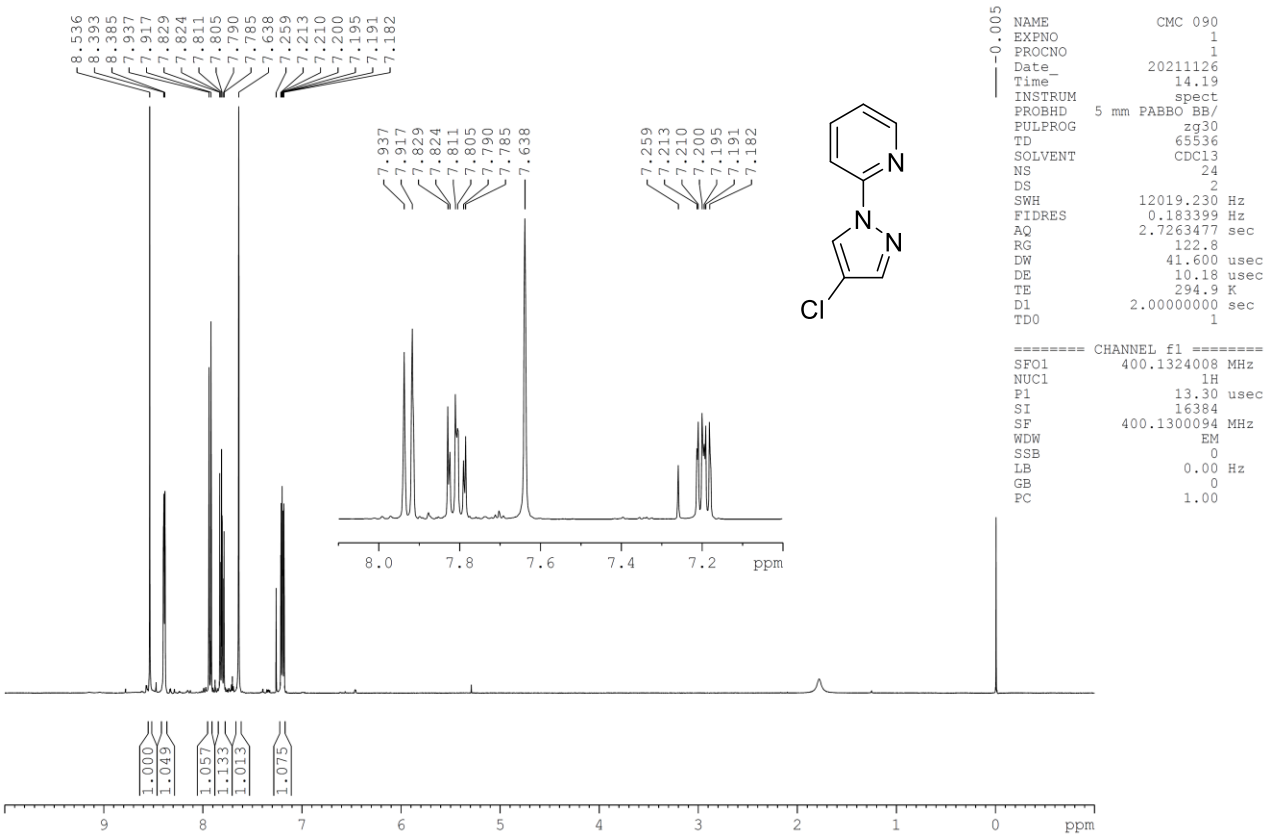


$^{13}C\{^{1}H\}$, $CDCl_3$

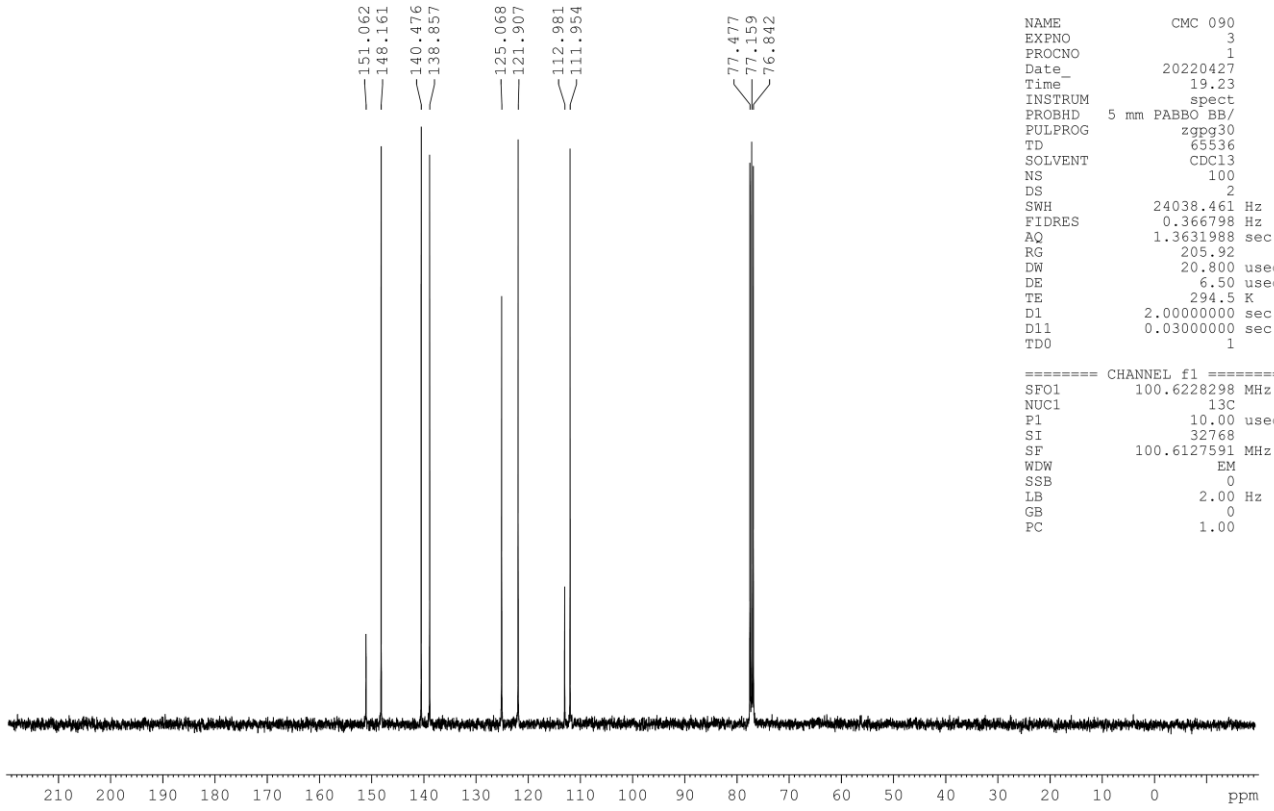


2-(4-chloro-1H-pyrazol-1-yl)pyridine **1m**

^{1}H, $CDCl_3$

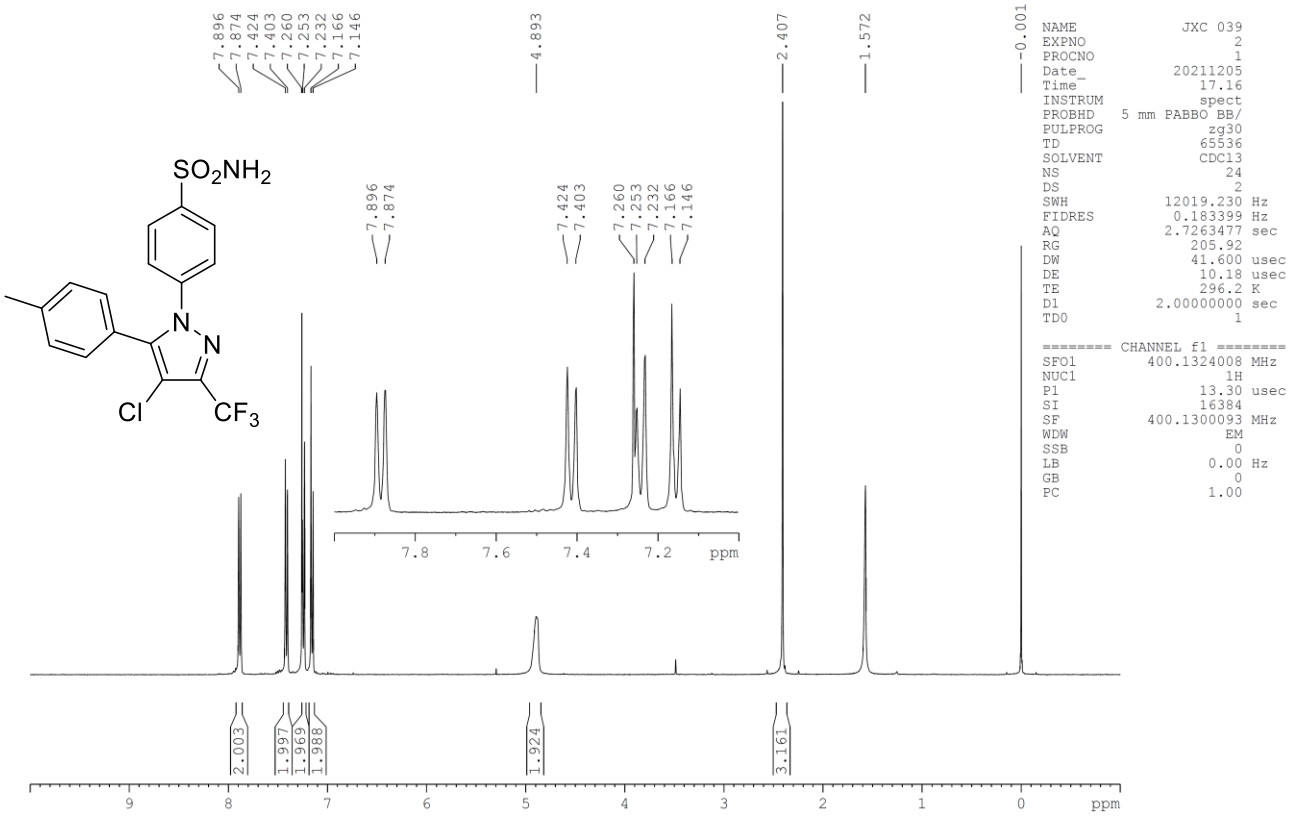


$^{13}C\{^{1}H\}$, $CDCl_3$

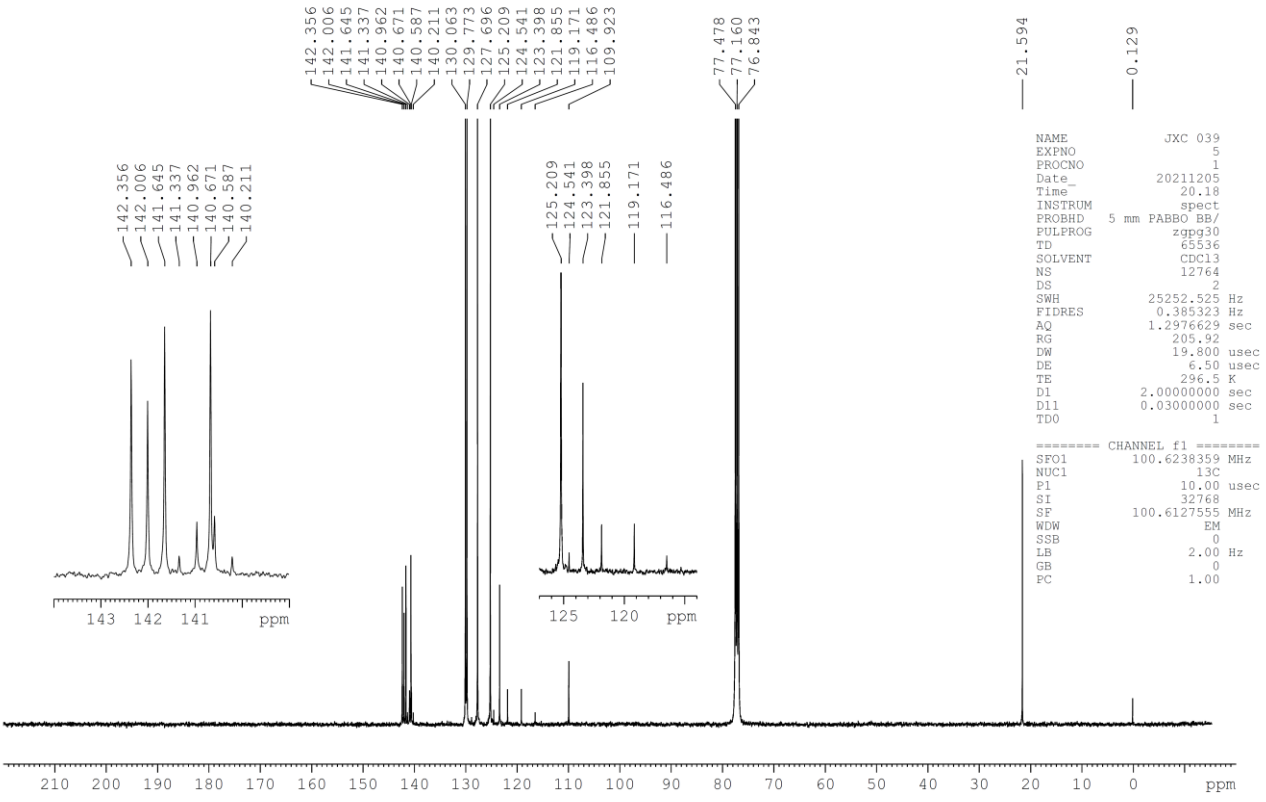


4-chloro-celecoxib **1n**

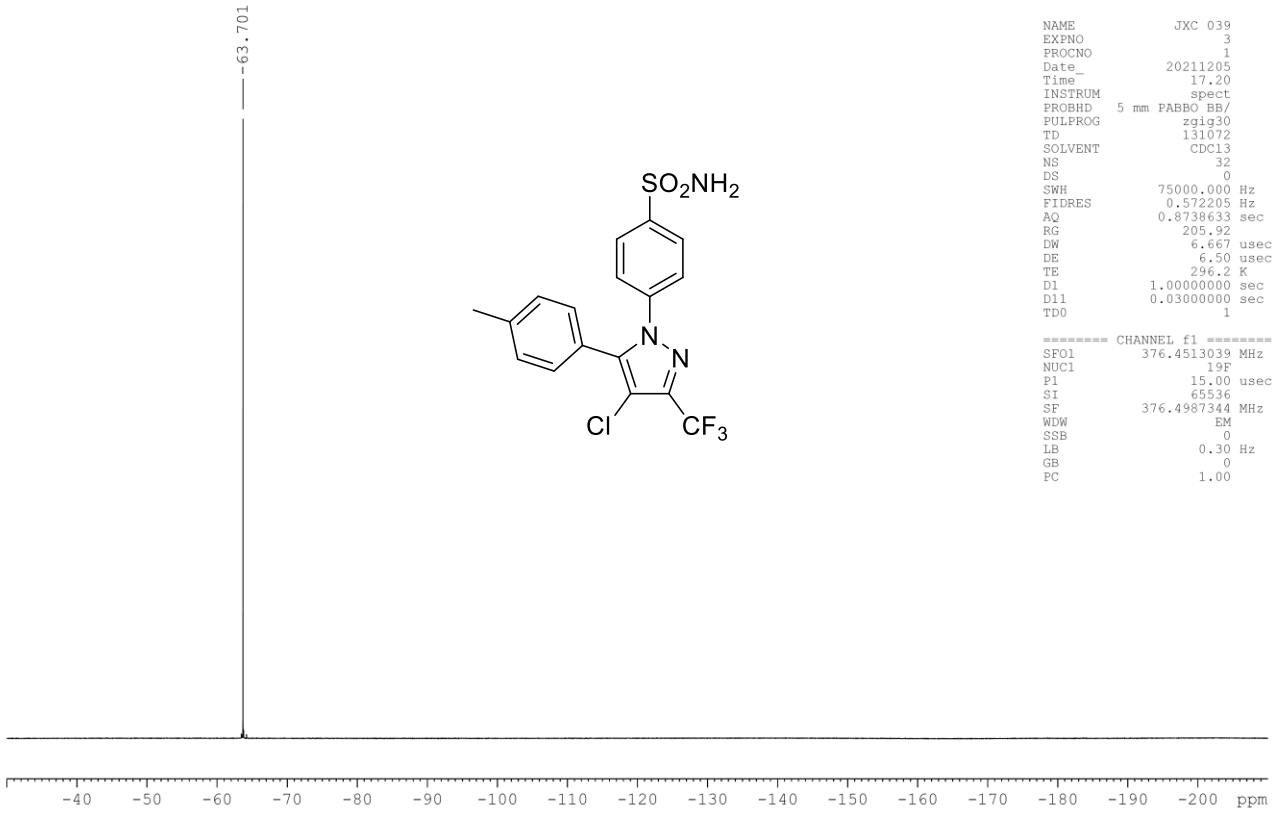
^{1}H, $CDCl_3$



$^{13}C\{^{1}H\}$, $CDCl_3$



$^{19}F\{^{1}H\}$, $CDCl_3$



NAME	JXC 039
EXPNO	3
PROCNO	1
Date_	20211205
Time	17.20
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgig30
TD	131072
SOLVENT	CDCl3
NS	32
DS	0
SWH	75000.000 Hz
FIDRES	0.572205 Hz
AQ	0.8738633 sec
RG	205.92
DW	6.667 usec
DE	6.50 usec
TE	296.2 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	376.4513039 MHz
NUC1	19F
P1	15.00 usec
SI	65536
SF	376.4987344 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

HRMS Spectra

4-Chloro-3,5-dimethylpyrazole **1a**

Display Report

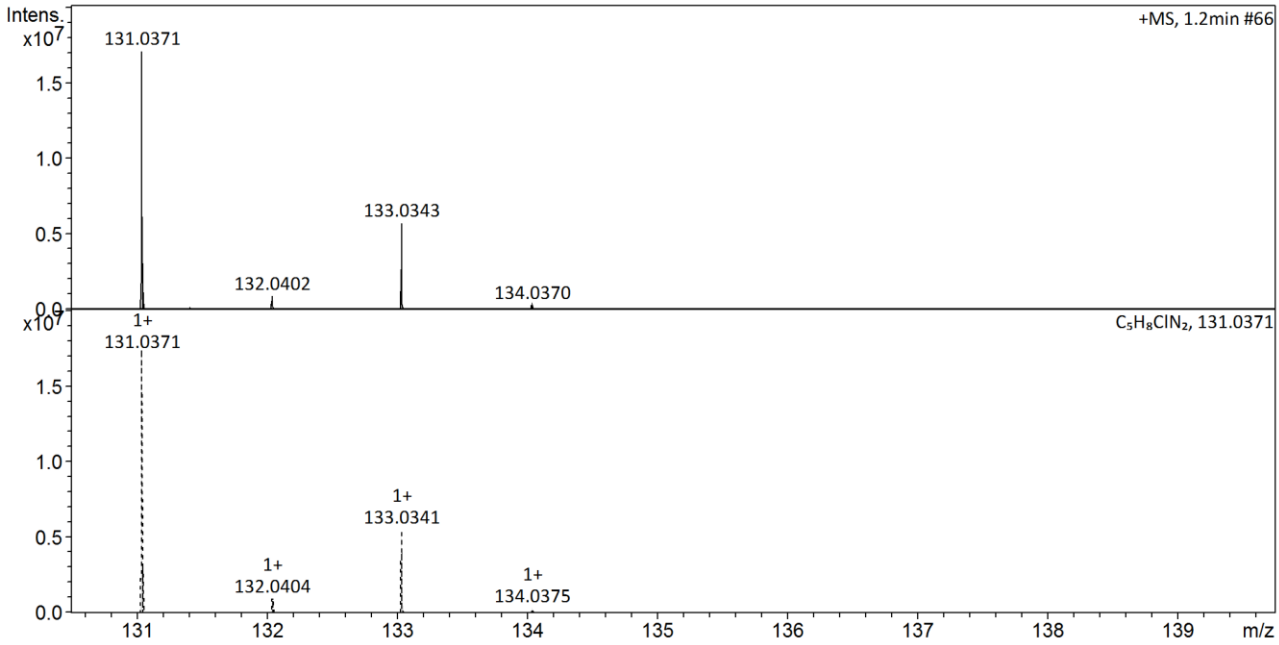
Analysis Info

Acquisition Date	3/4/2022 2:50:53 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC046_GA4_01_28933.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC046	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
131.0371	1	C5H8ClN2	131.0371	0.4	9.2	1	100.00	2.5	even	ok	M+H



4-Chloropyrazole **1b**

Display Report

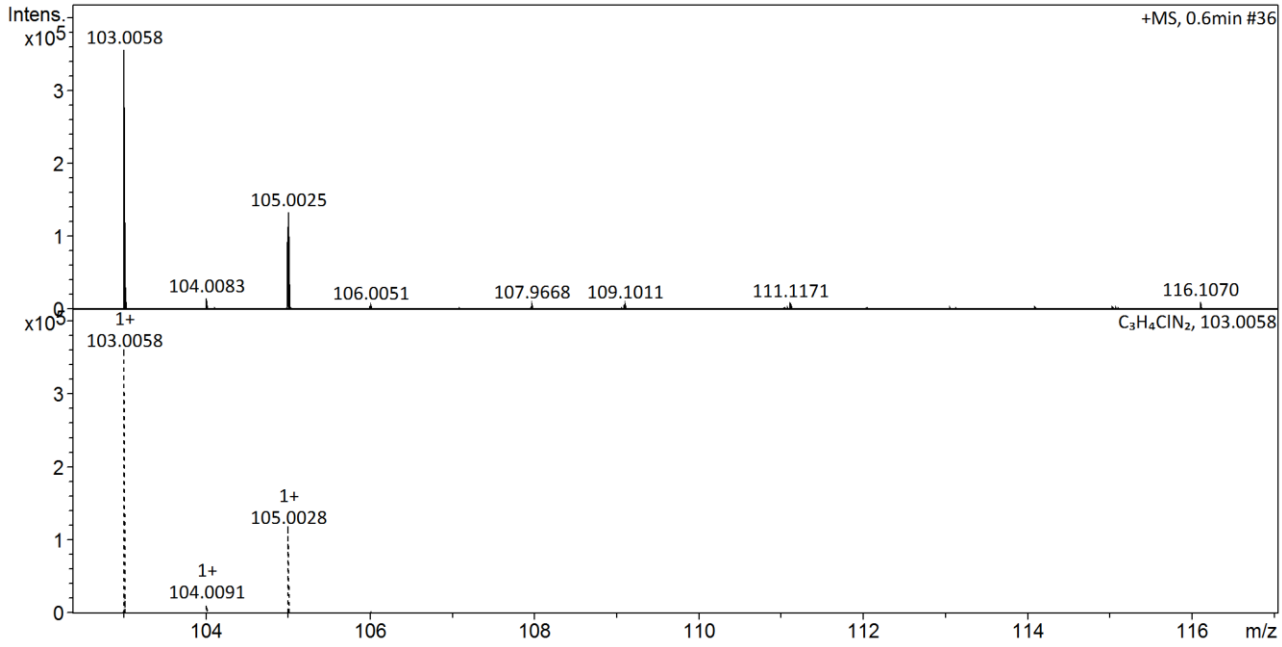
Analysis Info

Acquisition Date	3/4/2022 3:55:31 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\JXC013_GC3_01_28948.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC013	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
103.0058	1	C3H4ClN2	103.0058	-0.5	27.2	1	100.00	2.5	even	ok	M+H



4-Chloro-3,5-diphenylpyrazole **1c**

Display Report

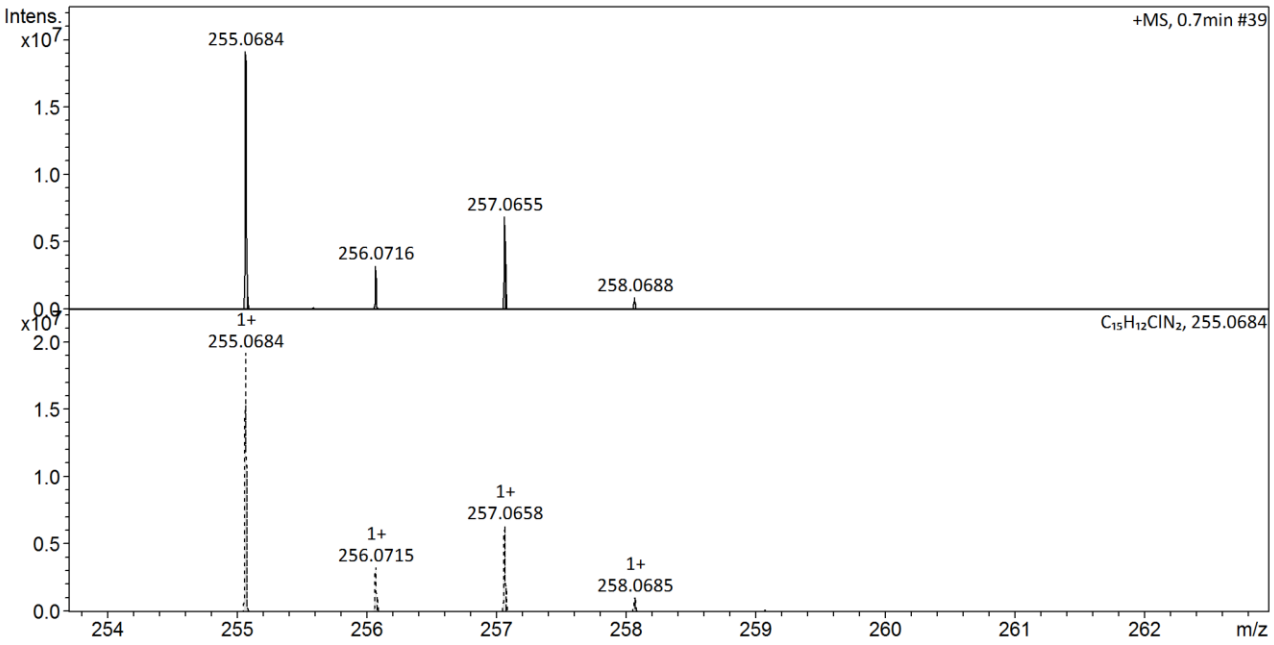
Analysis Info

Acquisition Date	3/4/2022 2:55:15 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC053_GA5_01_28934.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC053	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
255.0684	1	C15H12ClN2	255.0684	0.3	12.1	1	100.00	10.5	even	ok	M+H



4-Chloro-3,5-dimethyl-1H-pyrazole-1-carboxamide **1d**

Display Report

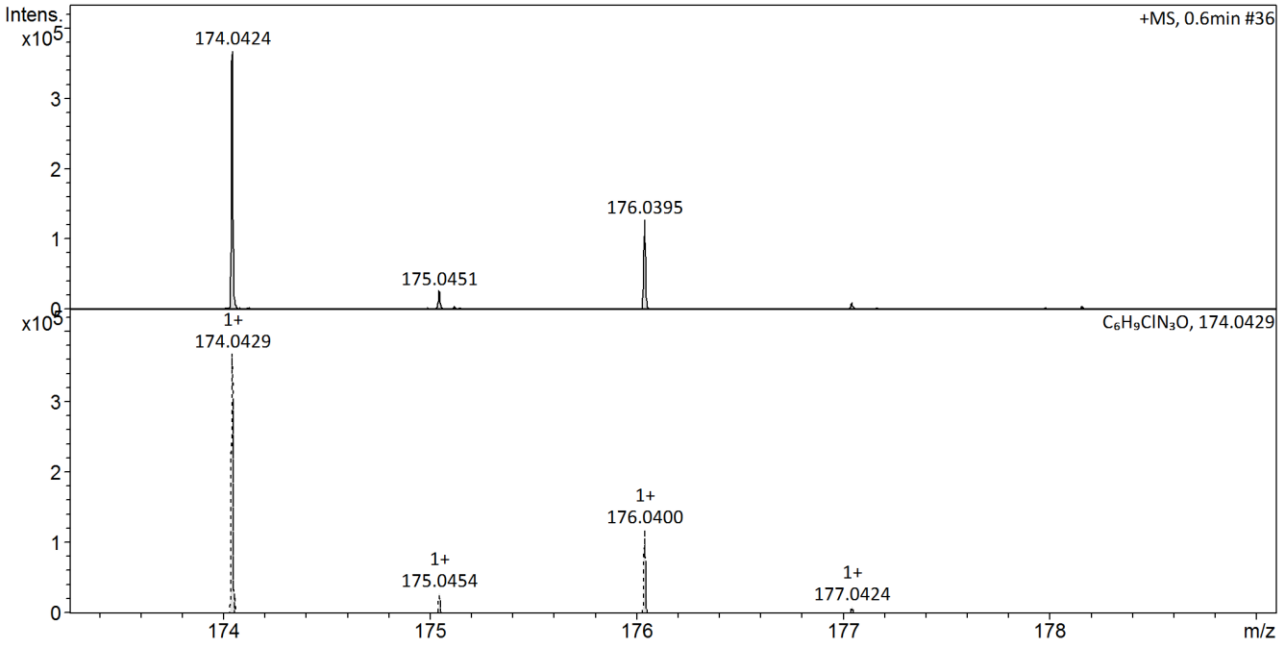
Analysis Info

Acquisition Date	11/27/2022 3:37:14 PM		
Analysis Name	D:\Data\nctu service\data\2022\20221127\CMC056_GB3_01_33255.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC056	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
174.0424	1	C6H9ClN3O	174.0429	-2.5	17.0	1	100.00	3.5	even	ok	M+H



4-Chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole **1e**

Display Report

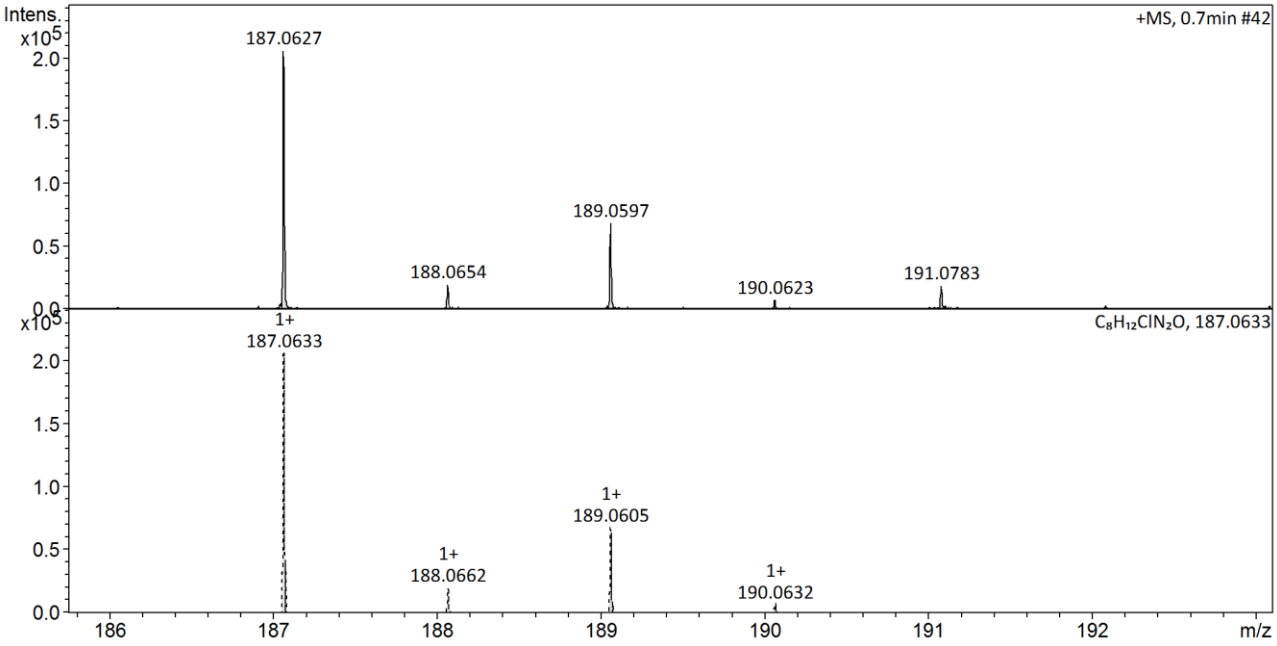
Analysis Info

Acquisition Date	11/27/2022 3:50:20 PM		
Analysis Name	D:\Data\nctu service\data\2022\20221127\CMC091_GB6_01_33258.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC091	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
187.0627	1	C8H12ClN2O	187.0633	-3.0	4.4	1	100.00	3.5	even	ok	M+H



4-Chloro-3,5-dimethyl-1-phenylpyrazole **1f**

Display Report

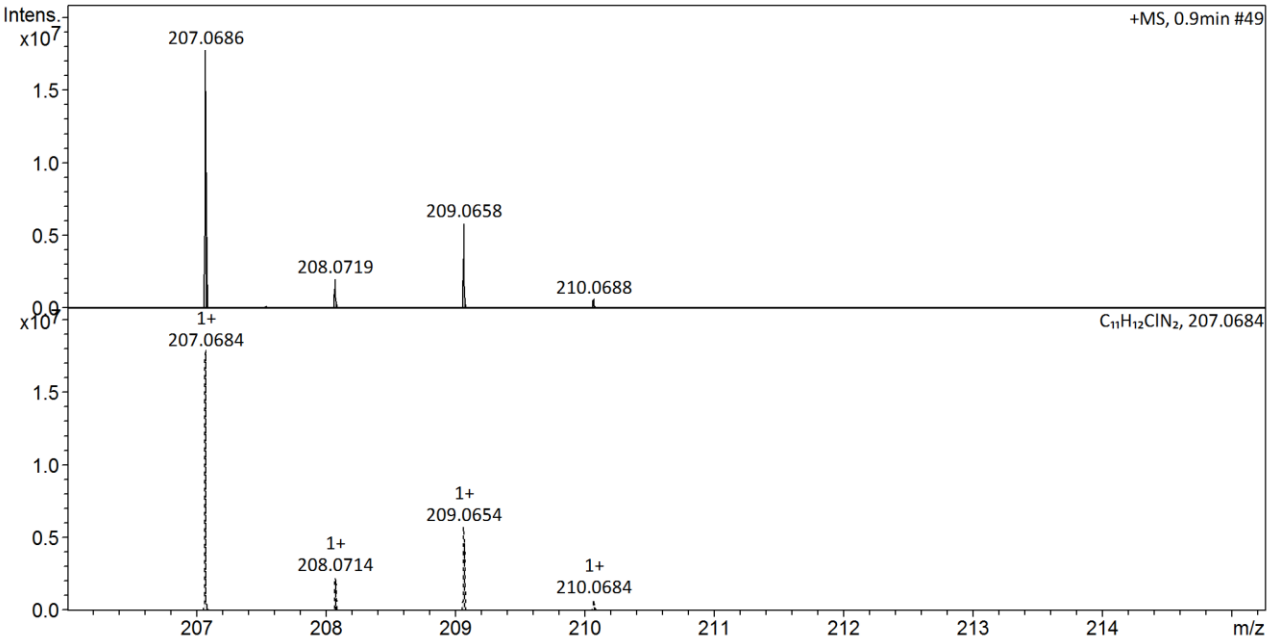
Analysis Info

Acquisition Date	3/4/2022 3:38:18 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC065_GB7_01_28944.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC065	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
207.0686	1	C11H12ClN2	207.0684	-1.3	8.8	1	100.00	6.5	even	ok	M+H



Di-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-2**

Display Report

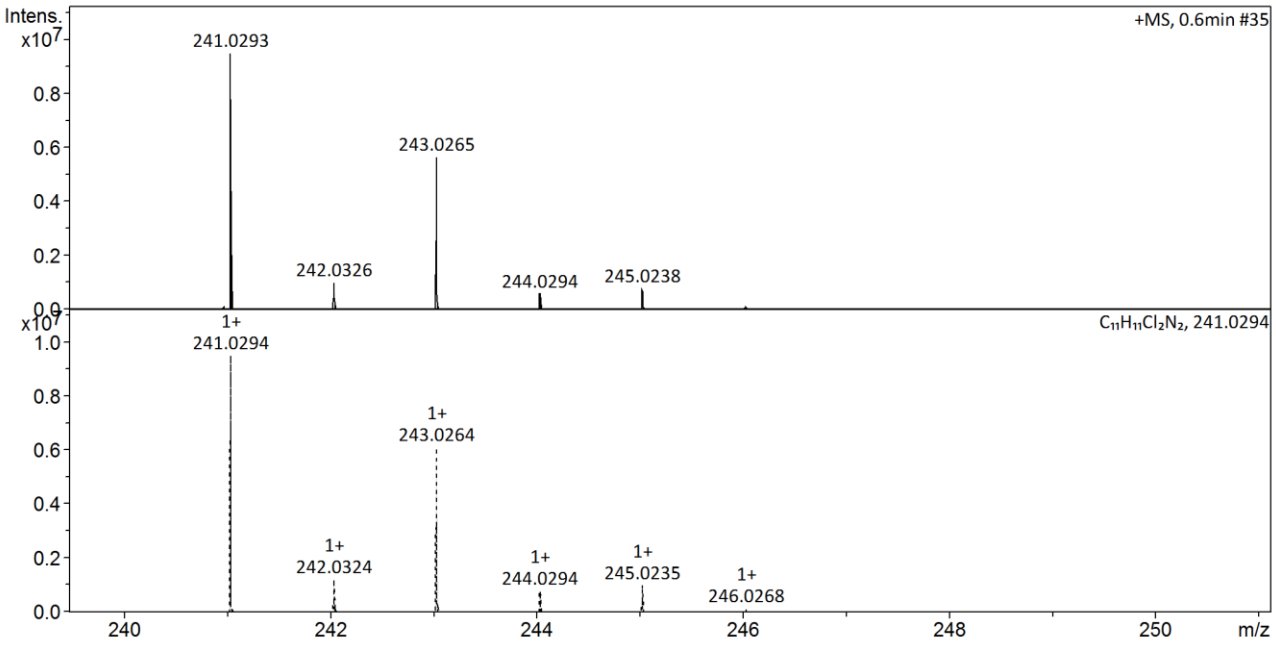
Analysis Info

Acquisition Date	3/4/2022 3:42:38 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC065 F4_GB8_01_28945.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC065 F4	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
241.0293	1	C11H11Cl2N2	241.0294	-0.3	26.6	1	100.00	6.5	even	ok	M+H



Tri-chlorinated side product of 3,5-dimethyl-1-phenylpyrazole **1f-3**

Display Report

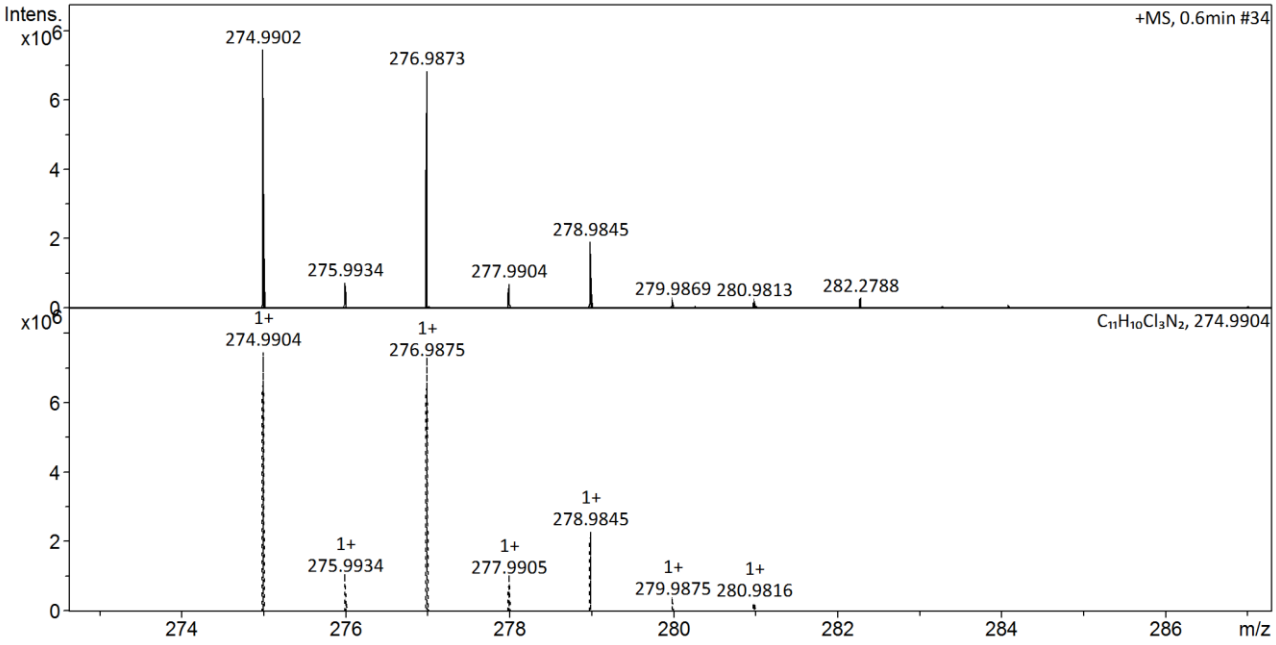
Analysis Info

Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC065 F2_GC1_01_28946.d	Acquisition Date	3/4/2022 3:46:56 PM
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC065 F2	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
274.9902	1	C11H10Cl3N2	274.9904	-0.7	30.4	1	100.00	6.5	even	ok	M+H



4-Chloro-1-phenylpyrazole **1g**

Display Report

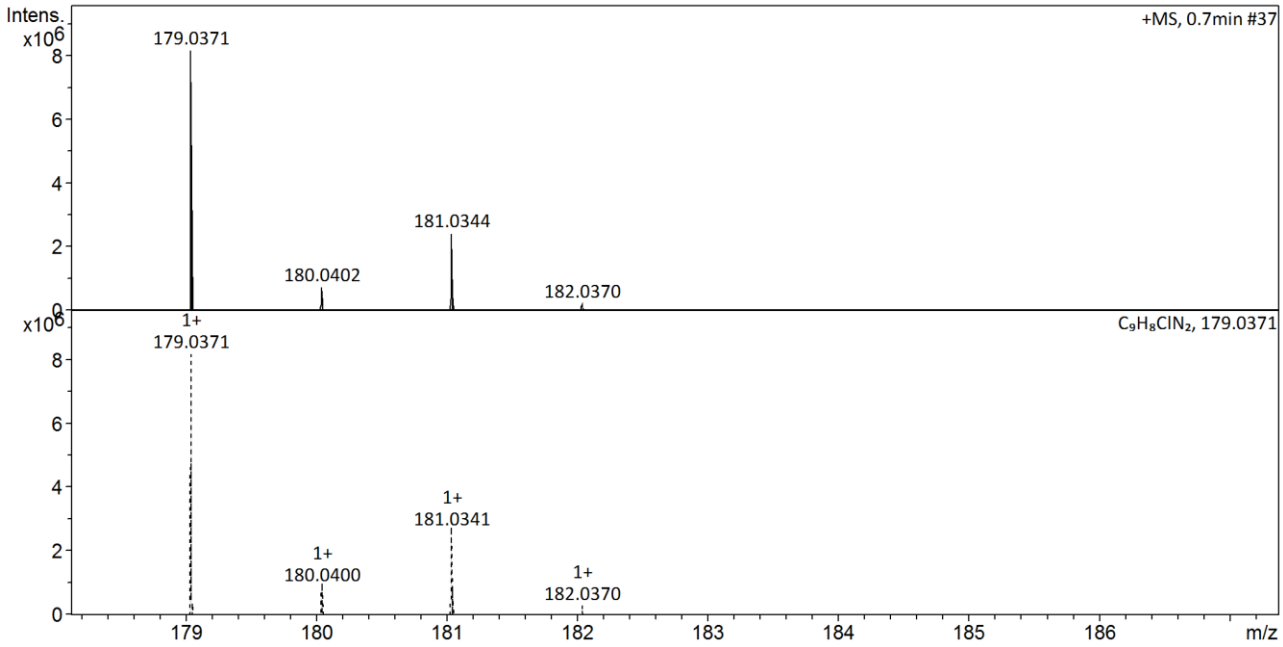
Analysis Info

Acquisition Date	3/4/2022 3:03:50 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\JXC029_GA7_01_28936.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC029	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
179.0371	1	C9H8ClN2	179.0371	-0.4	17.4	1	100.00	6.5	even	ok	M+H



4-Chloro-1-(4-methoxyphenyl)pyrazole **1h**

Display Report

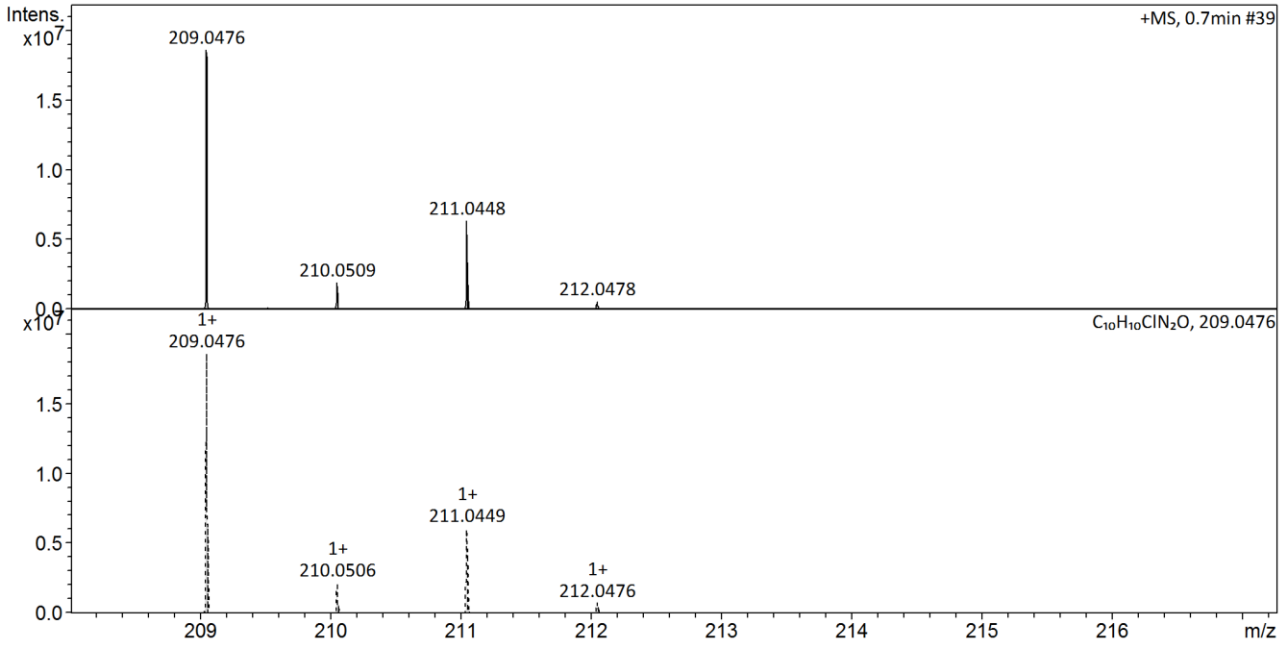
Analysis Info

Acquisition Date	3/4/2022 3:16:44 PM		
Analysis Name	D:\Data\nctu service\data\2022\20220304\CMC075_GB2_01_28939.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC075	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
209.0476	1	C10H10ClN2O	209.0476	-0.1	9.9	1	100.00	6.5	even	ok	M+H



4-Chloro-1-(4-bromophenyl)pyrazole **1i**

Display Report

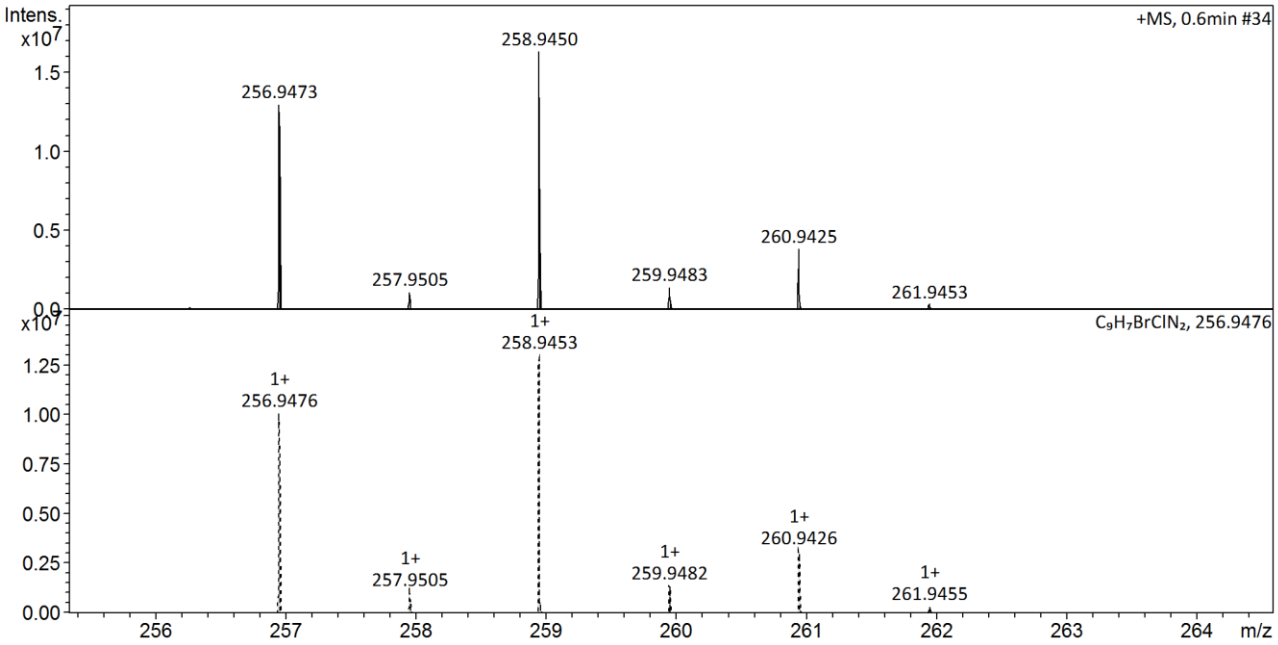
Analysis Info

Acquisition Date	11/27/2022 3:41:32 PM		
Analysis Name	D:\Data\nctu service\data\2022\20221127\JXC023_GB4_01_33256.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC023	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule	Adduct
256.9473	1	C9H7BrClN2	256.9476	1.2	14.8	1	100.00	6.5	even	ok	M+H



4-(4-chloro-1H-pyrazol-1-yl)benzaldehyde **1j**

Display Report

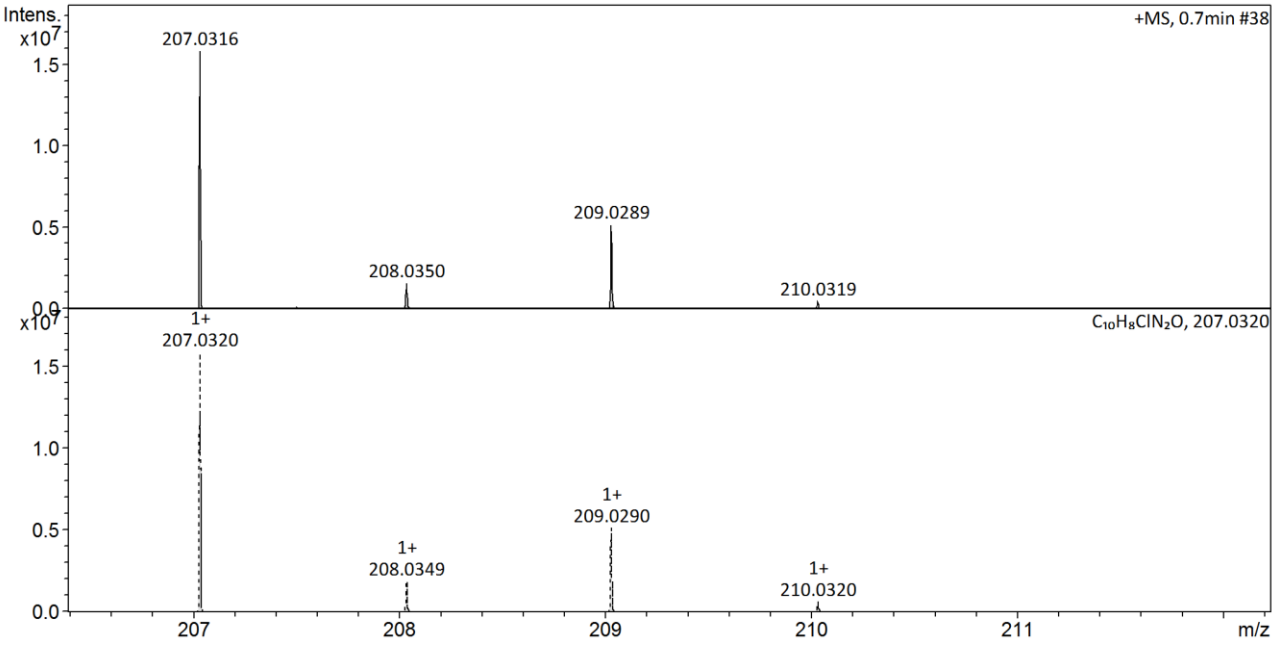
Analysis Info

Acquisition Date	11/27/2022 3:54:38 PM		
Analysis Name	D:\Data\nctu service\data\2022\20221127\CMC076_GB7_01_33259.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC076	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
207.0316	1	C10H8ClN2O	207.0320	-1.8	10.2	1	100.00	7.5	even	ok	M+H



4-(4-chloro-1H-pyrazol-1-yl)benzonitrile **1k**

Display Report

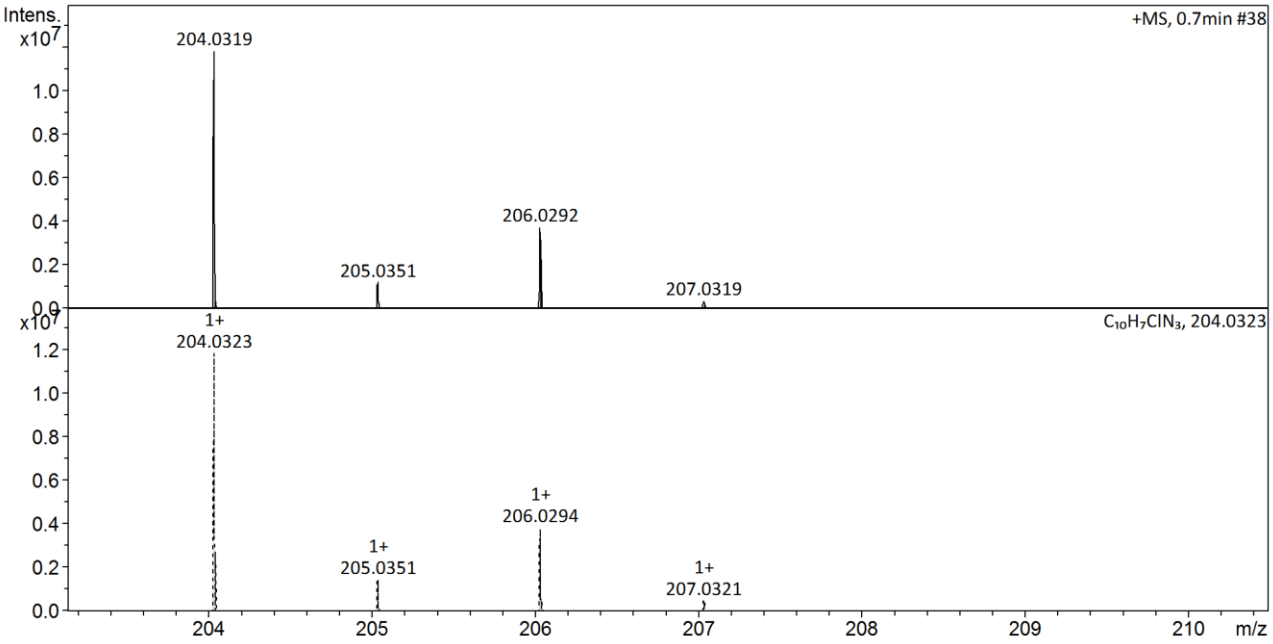
Analysis Info

Analysis Name	D:\Data\nctu service\data\2022\20221127\JXC055_GB1_01_33253.d	Acquisition Date	11/27/2022 3:28:28 PM
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC055	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
204.0319	1	C10H7ClN3	204.0323	2.1	13.0	1	100.00	8.5	even	ok	M+H



4-chloro-1-(4-nitrophenyl)-1H-pyrazole **1l**

Display Report

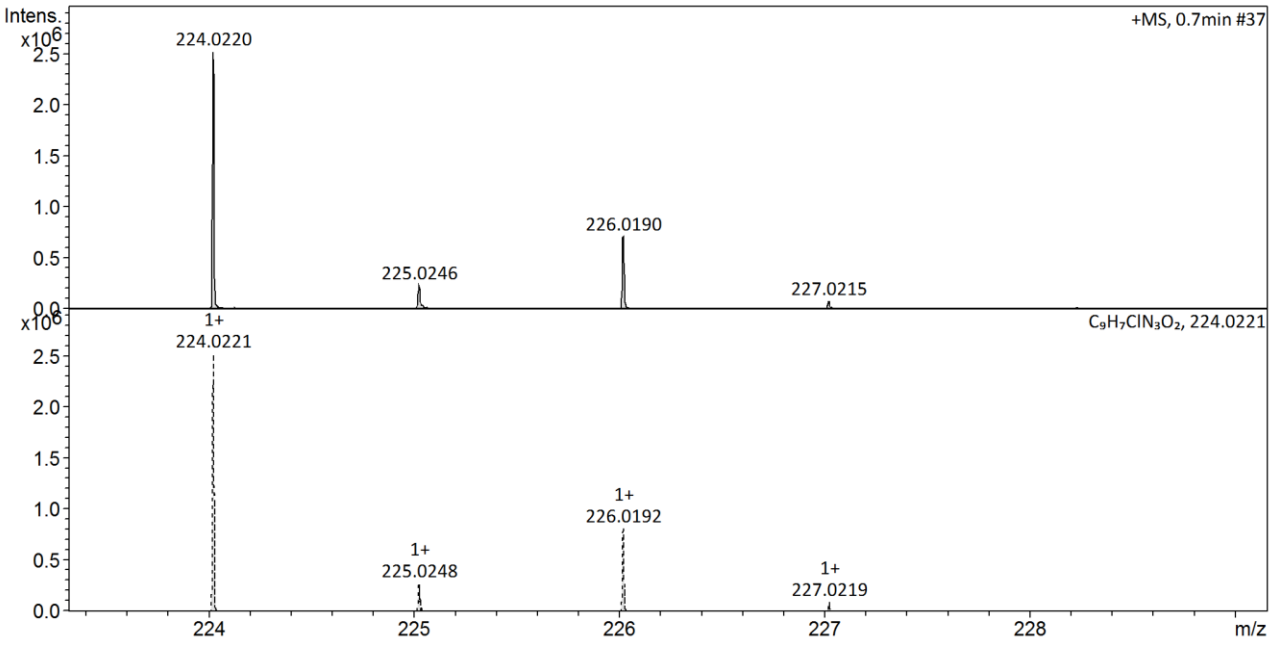
Analysis Info

Acquisition Date	11/27/2022 3:32:51 PM		
Analysis Name	D:\Data\nctu service\data\2022\20221127\JXC007_GB2_01_33254.d		
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC007	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
224.0220	1	C9H7ClN3O2	224.0221	-0.7	25.7	1	100.00	7.5	even	ok	M+H



2-(4-chloro-1H-pyrazol-1-yl)pyridine **1m**

Display Report

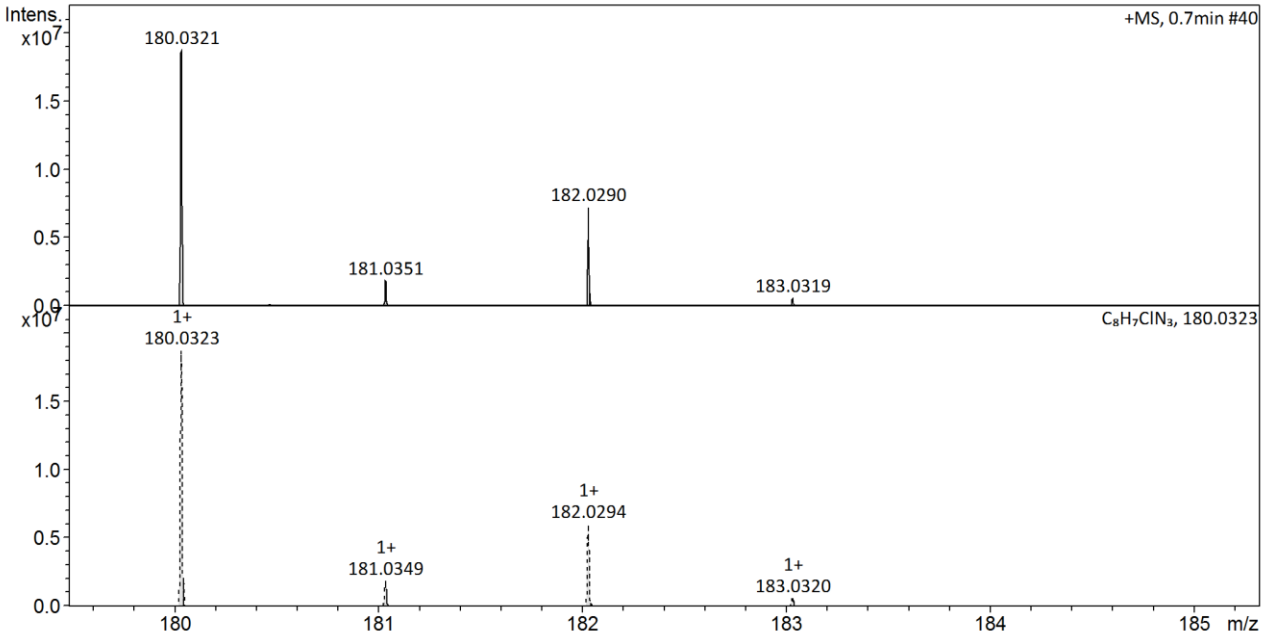
Analysis Info

Analysis Name	D:\Data\nctu service\data\2022\20221127\CMC090_GB5_01_33257.d	Acquisition Date	11/27/2022 3:45:53 PM
Method	Small molecule.m	Operator	NCTU
Sample Name	CMC090	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
180.0321	1	C8H7ClN3	180.0323	-1.3	31.7	1	100.00	6.5	even	ok	M+H



4-chloro-celecoxib **1n**

Display Report

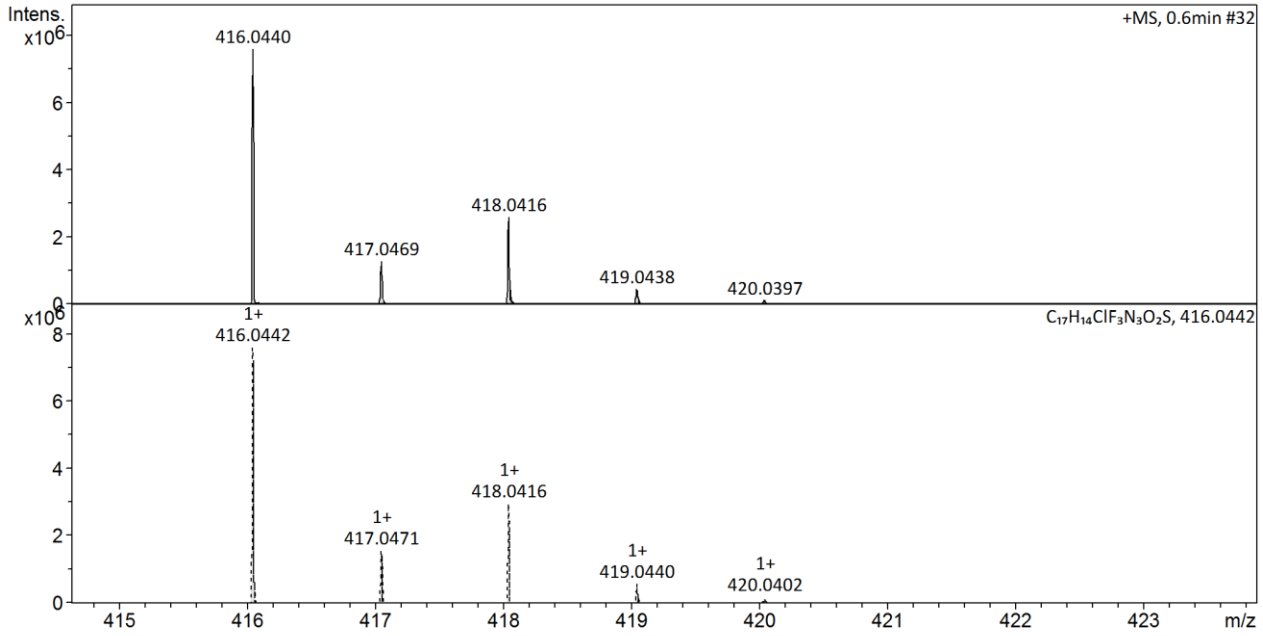
Analysis Info

Analysis Name	D:\Data\nctu service\data\2022\20220304\JXC039_GC2_01_28947.d	Acquisition Date	3/4/2022 3:51:12 PM
Method	Small molecule.m	Operator	NCTU
Sample Name	JXC039	Instrument	impact HD 1819696.00164
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule	Adduct
416.0440	1	C17H14ClF3N3O2S	416.0442	-0.5	26.4	1	100.00	10.5	even	ok	M+H



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