Decyanation–(Hetero)arylation of Malononitriles to access α-(Hetero)arylnitriles

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Supporting Information: Experimental Data, Characterization, and NMR Spectra

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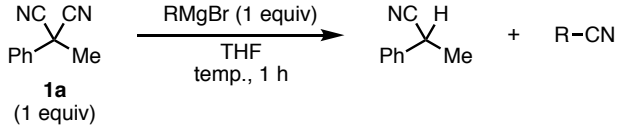
A. General Information

Unless otherwise noted, all reactions were set up on benchtop and run under Ar or N_2 using flame-dried glassware and anhydrous solvents. PhMe and THF were purchased as HPLC-grade (inhibitor-free) from Caledon or Sigma–Aldrich and were dried using a PureSolv MD 5 solvent purification system. MeMgBr and PhMgBr were purchased from Sigma–Aldrich and were titrated using I_2 before use.[1] All other commercial reagents and starting materials were used as received. Compounds were purified by flash column chromatography using SiliCycle SilicaFlash P60 silica gel. The 8- and 16-mL culture tubes used for reactions were purchased from Fisher Scientific (catalogue nos. 14-957-76A and 14-959-35A) and were sealed using size 19 rubber septa and electrical tape.

GC-MS data was obtained on a Shimadzu GCMS-QP2010 SE; yields represent peak areas calibrated against each compound's response factor relative to *n*-dodecane as internal standard. NMR spectra were recorded on Agilent DD2 500 MHz, Varian MercuryPlus 400 MHz or Bruker Avance III 400 MHz spectrometers. TLC samples were run on EMD Millipore TLC Silica gel 60 F_{254} plates and were visualized by UV or by staining with $KMnO_4$, phosphomolybdic acid (PMA), or *p*-anisaldehyde stains. Melting points were obtained on a Fisher-Johns Melting Point Apparatus. IR spectra were obtained on a Perkin-Elmer Spectrum 100 instrument equipped with a single-bounce diamond/ZnSe ATR accessory as solids or thin films. High-resolution mass spectra (HRMS) were recorded on a JEOL AccuTOF JMS-T1000LV mass spectrometer equipped with a Direct Analysis in Real Time (DART) ion source.

B. Optimization and Mechanistic Details

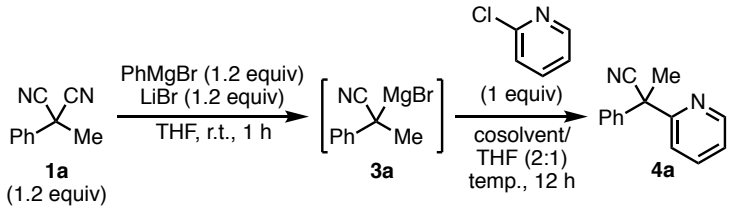
Table S1. Evaluation of Grignard reagents for transnitrilation[2]



Entry	RMgBr•LiX	temp. (ºC)	Conv. **1a** (%)[a]	Yield (%)[a]
1	PhMgBr•LiBr	23	92	73
2		70	99	96
3	MeMgBr + LiBr (1 equiv)	23	100	81
4	*n*-BuMgBr•LiBr	23	98	84
5		70	100	79
6	CyMgBr•LiBr	23	30	16
7		70	95	71
8	*i*-PrMgCl•LiCl	23	58	43
9		70	98	79

[a]Determined by GC-MS using *n*-dodecane as internal standard.

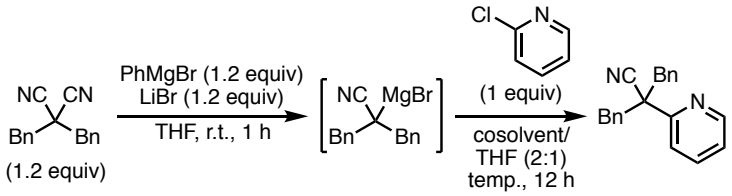
Table S2. Evaluation of decyanation–arylation conditions using 2-methyl-2-phenylmalononitrile



Entry	Cosolvent	Temp. (ºC)	Yield **4a** (%)
1	THF	23	0
2	PhMe	23	7
3	DMF	23	18
4	MeCN	23	0
5	DMSO	23	39
6	DMSO	50	82

Yields determined by GC-MS using *n*-dodecane as internal standard.

Table S3. Evaluation of decyanation–arylation conditions using 2,2-dibenzylmalononitrile



Reaction	Cosolvent	Temp. (°C)	Remaining 2-PyCl (%)	Yield (%)
1	none	23	28	9
2	PhMe	23	20	53
3	DMF	23	32	8
4	MeCN	23	34	0
5	DMSO	23	33	0
6	PhMe	50	20	80
7	PhMe	80	17	77
8	PhMe	110	11	87

Yields determined by GC-MS using *n*-dodecane as internal standard.

Table S4. Attempted decyanation–lithiation with α-arylnitrile substrates (unoptimized) (yields <20%)

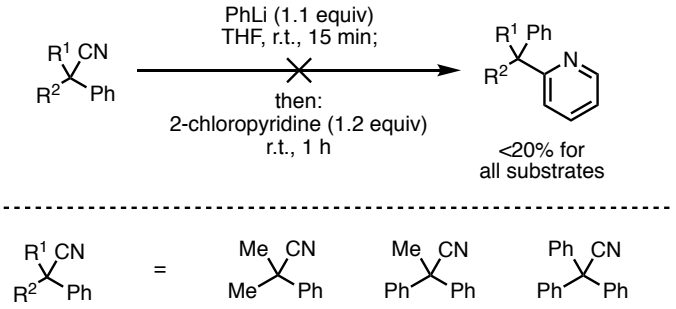
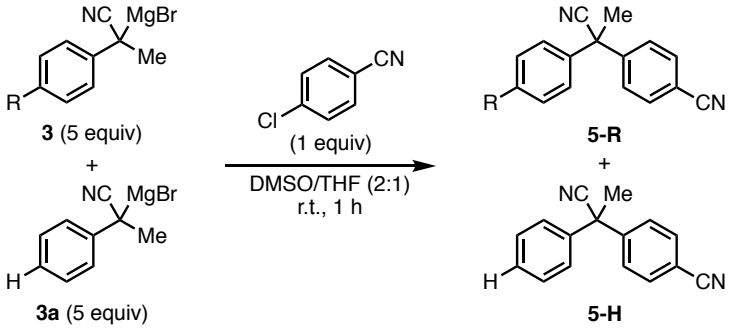


Table S5. Yields for same-pot competition experiment



Entry	R	GC-MS RAP **5-R** (%)	GC-MS RAP **5-H** (%)
1	OMe	77	23
2	*t*-Bu	69	31
3	F	51	49
4	Cl	36	64

Yields determined by GC-MS using *n*-dodecane as internal standard; RAP = relative area percent.

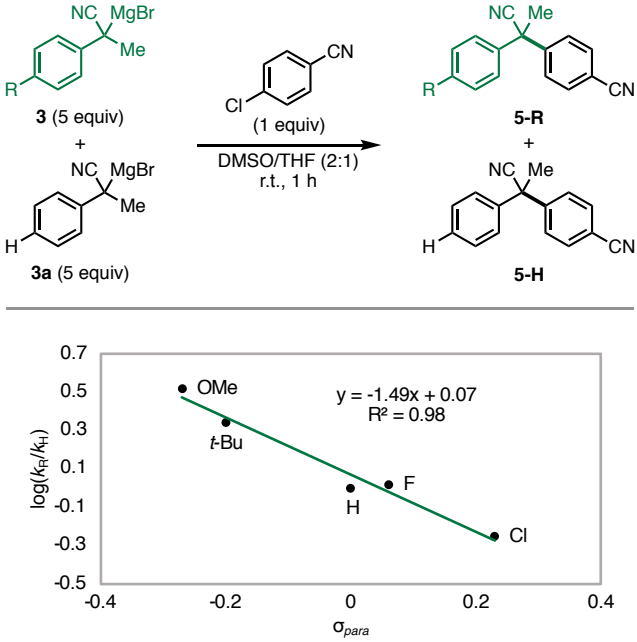
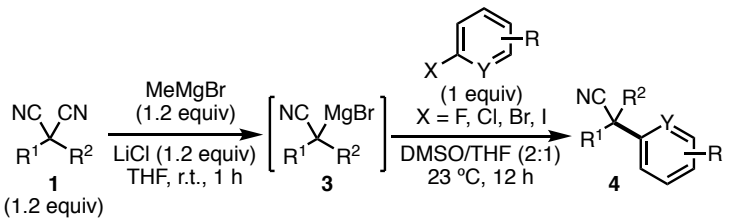


Figure S1. Hammett trend for same-pot competition experiment

C. Preparation of α-(Hetero)Arylnitrile Products

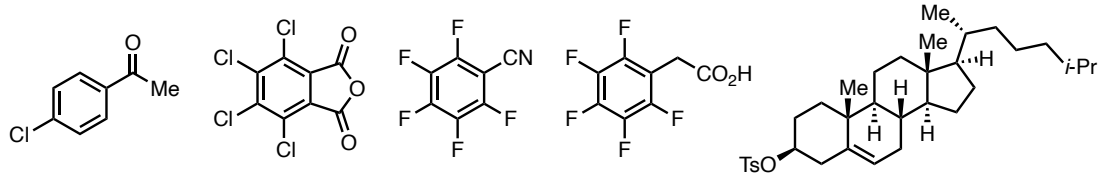


General Procedure A: Decyanation–Metalation and Arylation. An 8-mL threaded culture tube sealed with a size 19 septum was flame-dried under vacuum and cooled under N_2. To the tube was added malononitrile (**1**) (0.36 mmol, 1.2 equiv), and the tube was resealed and evacuated and backfilled with N_2 (×3). A stock solution of LiCl in THF (0.60 mL of a 0.60 M solution in THF, 0.36 mmol LiCl, 1.2 equiv) was added, followed by methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv). The reaction was stirred at r.t. for 1 h. Then, the reaction was diluted with DMSO (1.2 mL, total reaction volume = 1.8 mL of a 2:1 DMSO/THF mixture), and aryl electrophile was added (if liquid) (0.30 mmol, 1.0 equiv) (if the aryl electrophile was a solid, it was added as a stock solution in DMSO). The reaction was stirred at 23 ºC until completion, as judged by TLC. The reaction was quenched with half-saturated NH_4Cl and extracted with EtOAc (×3). The organic fractions were combined, filtered over a plug of $MgSO_4$/Celite (1:1), and the filtrate was concentrated. The crude residue was purified by flash column chromatography to yield the desired α-(hetero)arylnitrile.

LiCl Solution (0.60 M in THF). To a 25-mL round-bottom flask with a stir bar was added LiCl (0.25 g, 6.0 mmol) and the flask was flame-dried and cooled under vacuum. Once cool, THF (10 mL, 0.60 M) was added, and the solution was stirred for 15 min to yield a 0.60 M solution of LiCl in THF.

Table S6. Additional incompatible substrates (yield <10%)

Electrophiles



Malononitriles

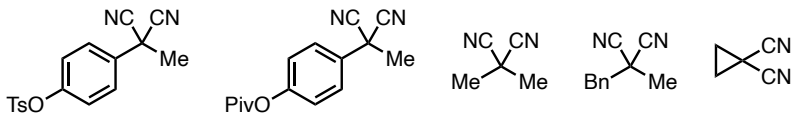
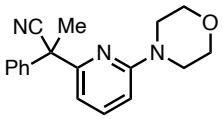
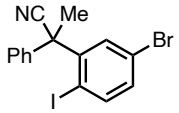


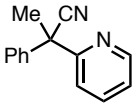
Table S7. Lower yielding substrates



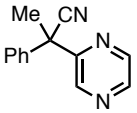
4am, 28% (X = Br)



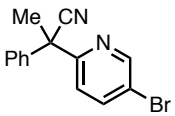
4an, 18% (X = F)



2-Phenyl-2-(pyridin-2-yl)propanenitrile (4a): Prepared according to General Procedure A on 0.30-mmol scale with the modification that the reaction was heated at 50 ºC. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyridine (28 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–40% EtOAc/hexanes) to yield the product as a colourless oil (51 mg, 0.245 mmol, 82%). Analytical data:[3] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.63 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.67 (td, *J* = 7.8, 1.9 Hz, 1H), 7.49–7.40 (m, 3H), 7.39–7.33 (m, 2H), 7.33–7.28 (m, 1H), 7.23 (dd, *J* = 7.6, 3.9 Hz, 1H), 2.18 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 159.3, 149.5, 140.5, 137.3, 129.1, 128.1, 126.5, 123.2, 122.9, 121.8, 48.9, 27.0 ppm.

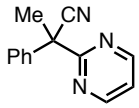


2-Phenyl-2-(pyrazin-2-yl)propanenitrile (4b): Prepared according to General Procedure A on 0.30-mmol scale using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-iodopyrazine (30 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 20–50% EtOAc/hexanes) to yield the product as a white solid (62 mg, 0.297 mmol, 99%). Analytical data:[4] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.72 (dd, *J* = 1.5, 0.4 Hz, 1H), 8.59 (dd, *J* = 2.5, 1.6 Hz, 1H), 8.54 (dd, *J* = 2.4, 0.4 Hz, 1H), 7.48–7.47 (m, 1H), 7.47–7.45 (m, 1H), 7.41–7.37 (m, 2H), 7.36–7.31 (m, 1H), 2.20 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 155.1, 144.0, 143.9, 143.5, 139.1, 129.3, 128.6, 126.4, 122.0, 47.1, 26.7 ppm.



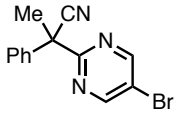
2-(5-Bromopyridin-2-yl)-2-phenylpropanenitrile (4c): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 5-bromo-2-fluoropyridine (31 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes)

to yield the product as a colourless oil (85 mg, 0.296 mmol, 99%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.67 (dd, J = 2.4, 0.8 Hz, 1H), 7.79 (dd, J = 8.4, 2.4 Hz, 1H), 7.46–7.42 (m, 2H), 7.40–7.29 (m, 4H), 2.16 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 157.8, 150.6, 139.9, 129.2, 128.3, 126.4, 123.2, 122.7, 120.3, 48.5, 26.9 ppm (one peak is overlapping); **HRMS** *m/z* (DART): calcd for $C_{14}H_{12}N_2Br$ (M+H): 287.0178; found: 287.0173; **IR** (neat): 2918, 2850, 2242, 1612, 1565, 1452, 1242, 1086, 785, 743, 697 cm^{-1}.

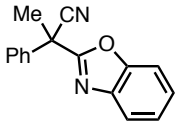


2-Phenyl-2-(pyrimidin-2-yl)propanenitrile (4d): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 20–50% EtOAc/hexanes) to yield the product as an off-white solid (55 mg, 0.263 mmol, 88%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.56–7.52 (m, 2H), 7.38–7.33 (m, 2H), 7.29 (tt, J = 6.6, 1.3 Hz, 1H), 7.23 (t, J = 4.9 Hz, 1H), 2.24 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 298 K): δ_C 168.2, 157.8, 139.5, 129.0, 128.3, 126.3, 122.4, 120.1, 51.0, 26.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{12}N_3$ (M+H): 210.1026; found: 210.1026; **IR** (neat): 2961, 2853, 2237, 1716, 1584, 1564, 1496, 1455, 1411, 1183, 800, 755, 718, 695 cm^{-1}; **m.p.:** 80–81 ºC.

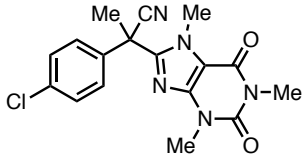
2-Phenyl-2-(pyrimidin-2-yl)propanenitrile (4d) (gram-scale): Prepared on 7.1-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (1.3 g, 8.5 mmol, 1.2 equiv), methylmagnesium bromide (2.8 mL a 3.0 M solution in Et_2O, 8.5 mmol, 1.2 equiv), LiCl solution (14 mL of a 0.60 M solution in THF, 8.5 mmol, equiv), DMSO (28 mL), and 2-chloropyrimidine (0.81 g, 7.1 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 20–50% EtOAc/hexanes) to yield the product as an off-white solid (1.1 g, 5.2 mmol, 74%). The analytical data was identical to the product prepared on 0.30-mmol scale.



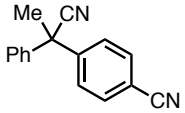
2-(5-Bromopyrimidin-2-yl)-2-phenylpropanenitrile (4e): Prepared according to General Procedure A on 0.20-mmol scale. The reaction was performed using 2-methyl-2-phenylmalononitrile (37 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL) and 5-bromo-2-chloropyrimidine (39 mg, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a white solid (54 mg, 0.188 mmol, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.79 (s, 2H), 7.56–7.48 (m, 2H), 7.40–7.24 (m, 3H), 2.22 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 298 K): δ_C 166.3, 158.5, 139.0, 129.1, 128.5, 126.2, 121.9, 119.6, 50.5, 26.4 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{11}N_3Br$ (M+H): 288.0131; found: 288.0124; **IR** (neat): 2963, 2873, 2230, 1732, 1542, 1496, 1412, 1366, 1121, 1018, 764, 737, 699 cm^{-1}; **m.p.:** 93–95 ºC.



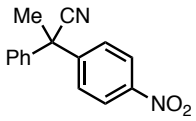
2-(Benzoxazol-2-yl)-2-phenylpropanenitrile (4f): Prepared according to General Procedure A on 0.20-mmol scale. The reaction was performed using 2-methyl-2-phenylmalononitrile (37 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL) and iodobenzoxazole (49 mg, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a colourless oil (34 mg, 0.137 mmol, 69%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.82–7.75 (m, 1H), 7.56–7.47 (m, 3H), 7.45–7.34 (m, 5H), 2.31 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 162.6, 151.4, 140.7, 137.0, 129.5, 129.1, 127.8, 125.9, 125.1, 120.8, 119.4, 111.3, 43.7, 26.8 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{13}N_2O$ (M+H): 249.1022; found: 249.1028; **IR** (neat): 2918, 2851, 2242, 1613, 1566, 1453, 1242, 1086, 785, 743, 697 cm^{-1}.



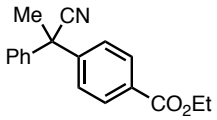
2-(4-Chlorophenyl)-2-(1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-yl)propanenitrile (4g): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(4-chlorophenyl)-2-methylmalononitrile (69 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and bromocaffeine (82 mg, 0.30 mmol, 1.0 equiv). The crude material was purified by flash column chromatography to yield the product as a white solid (58 mg, 0.162 mmol, 54%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.42–7.36 (m, 2H), 7.25–7.19 (m, 2H), 3.70 (s, 3H), 3.63 (s, 3H), 3.40 (s, 3H), 2.18 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 155.4, 151.5, 147.8, 146.8, 136.2, 135.1, 129.9, 126.6, 118.5, 109.4, 41.8, 33.1, 29.8, 29.5, 28.0 ppm; **HRMS** *m/z* (DART): calcd for $C_{17}H_{17}N_5O_2Cl$ (M+H) 358.1065; found: 318.1063.



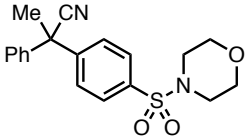
4-(1-Cyano-1-phenylethyl)benzonitrile (4h): Prepared according to General Procedure A on 0.20-mmol scale. The reaction was performed using 2-methyl-2-phenylmalononitrile (37 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL) and 4-chlorobenzonitrile (28 mg, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (40% EtOAc/hexanes) to yield the product as a colourless oil (46 mg, 0.198 mmol, 99%). Analytical data:[5] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.70–7.64 (m, 2H), 7.53–7.48 (m, 2H), 7.43–7.33 (m, 5H), 2.11 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 146.7, 139.9, 132.9, 129.4, 128.7, 127.6, 126.7, 122.5, 118.3, 112.3, 46.4, 27.9 ppm.



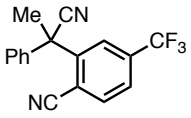
2-(4-Nitrophenyl)-2-phenylpropanenitrile (4i): Prepared according to General Procedure A on 0.20-mmol scale. The reaction was performed using 2-methyl-2-phenylmalononitrile (37 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL) and 1-chloro-4-nitrobenzene (32 mg, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (10–40% EtOAc/hexanes) to yield the product as a colourless oil (31 mg, 0.123 mmol, 62%). Analytical data:[5] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.26–8.19 (m, 2H), 7.60–7.55 (m, 2H), 7.44–7.33 (m, 5H), 2.14 (s, 3H) ppm.



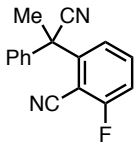
Ethyl 4-(1-cyano-1-phenylethyl)benzoate (4j): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and ethyl 4-fluorobenzoate (44 µL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a colourless oil (32 mg, 0.115 mmol, 38%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.06–8.01 (m, 2H), 7.48–7.44 (m, 2H), 7.40–7.31 (m, 5H), 4.37 (q, J = 7.1 Hz, 2H), 2.11 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 166.0, 146.1, 140.6, 130.3, 129.2, 128.4, 126.8, 126.7, 123.0, 61.3, 46.3, 28.1, 14.4 ppm (one peak is overlapping); **HRMS** *m/z* (DART): calcd for $C_{18}H_{18}NO_2$ (M+H): 280.1332; found: 280.1333; **IR** (neat): 2984, 2239, 1715, 1611, 1410, 1273, 1104, 1018, 756, 696 cm^{-1}.



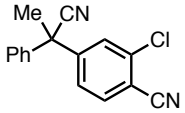
2-(4-(Morpholinosulfonyl)phenyl)-2-phenylpropanenitrile (4k): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 4-((4-fluorophenyl)sulfonyl)morpholine (74 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 30–80% EtOAc/hexanes) to yield the product as a colourless wax (63 mg, 0.177 mmol, 59%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.77–7.72 (m, 2H), 7.59–7.54 (m, 2H), 7.43–7.33 (m, 5H), 3.74 (dd, J = 4.5, 4.5 Hz, 4H), 3.04–2.97 (m, 4H), 2.12 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 146.8, 139.9, 135.1, 129.4, 128.6, 128.6, 127.6, 126.7, 122.6, 66.2, 46.3, 46.0, 28.0 ppm; **HRMS** *m/z* (DART): calcd for $C_{19}H_{21}N_2O_3S$ (M+H): 357.1267; found: 357.1261; **IR** (neat): 2918, 2851, 2241, 2210, 1613, 1566, 1452, 1242, 1086, 743, 697 cm^{-1}.



2-(1-Cyano-1-phenylethyl)-4-(trifluoromethyl)benzonitrile (4l): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-fluoro-4-(trifluoromethyl)benzonitrile (42 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a white solid (67 mg, 0.223 mmol, 74%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.11–8.08 (m, 1H), 7.86–7.82 (m, 1H), 7.79–7.74 (m, 1H), 7.45–7.36 (m, 3H), 7.35–7.30 (m, 2H), 2.28 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 144.8, 138.5, 136.6, 135.0 (q, J = 33.8 Hz), 129.4, 129.1, 127.2, 126.0 (q, J = 3.7 Hz), 124.6 (q, J = 3.8 Hz), 122.8 (q, J = 274.2 Hz), 120.8, 116.0 (q, J = 1.3 Hz), 115.4, 46.1, 27.4 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −63.3 ppm; **HRMS** *m/z* (DART): calcd for $C_{17}H_{15}N_3F_3$ (M+NH_4): 318.1213; found: 318.1206; **IR** (neat): 2960, 2247, 2229, 1739, 1487, 1326, 1179, 1140, 1074, 848, 693 cm^{-1}; **m.p.:** 123–124 ºC.

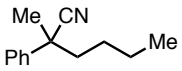


2-(1-Cyano-1-phenylethyl)-6-fluorobenzonitrile (4m): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2,6-difluorobenzonitrile (42 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as a colourless oil (26 mg, 0.104 mmol, 35%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.73–7.66 (m, 2H), 7.44–7.32 (m, 5H), 7.29–7.22 (m, 1H), 2.26 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 165.3 (d, J = 261.6 Hz), 145.4, 138.5, 134.8 (d, J = 9.3 Hz), 129.3, 128.9, 127.3, 123.4 (d, J = 3.2 Hz), 121.2, 116.6 (d, J = 20.5 Hz), 111.3 (d, J = 1.1 Hz), 101.4 (d, J = 16.9 Hz), 46.2, 27.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −102.7 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{15}N_3F$ (M+NH_4): 268.1244; found: 268.1256

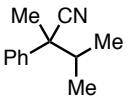


2-Chloro-4-(1-cyano-1-phenylethyl)benzonitrile (4n): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2,4-dichlorobenzonitrile (52 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as a colourless oil (36 mg, 0.135 mmol, 45%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.67 (d, J = 8.2 Hz, 1H), 7.53 (d, J = 1.8 Hz, 1H), 7.44–7.33 (m, 6H), 2.10 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 148.3, 139.1, 137.8, 134.6, 129.6, 129.0,

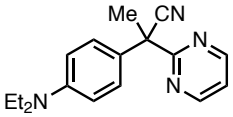
128.4, 126.7, 125.7, 122.0, 115.5, 113.3, 46.3, 27.8 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{12}N_2Cl$ (M+H): 267.0683; found: 267.0692



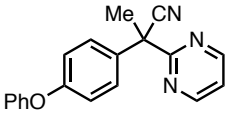
2-Methyl-2-phenylhexanenitrile (4o): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 1-iodobutane (34 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–15% EtOAc/hexanes) to yield the product as a colourless oil (32 mg, 0.171 mmol, 57%). Analytical data:[6] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.46–7.42 (m, 2H), 7.41–7.36 (m, 2H), 7.33–7.28 (m, 1H), 1.94–1.87 (m, 2H), 1.71 (s, 3H), 1.48–1.39 (m, 1H), 1.36–1.16 (m, 3H), 0.87 (t, J = 7.3 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 140.6, 129.0, 127.8, 125.6, 123.8, 42.7, 42.1, 27.9, 27.7, 22.7, 13.9 ppm.



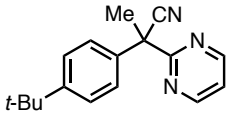
2,3-Dimethyl-2-phenylbutanenitrile (4p): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-iodopropane (20 μL, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–15% EtOAc/hexanes) to yield the product as a colourless oil (18 mg, 0.104 mmol, 35%). Analytical data:[7] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.44–7.40 (m, 2H), 7.40–7.35 (m, 2H), 7.32–7.28 (m, 1H), 2.10 (app sept, J = 6.7 Hz, 1H), 1.70 (s, 3H), 1.14 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.7 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 140.6, 128.8, 127.7, 126.0, 122.5, 48.0, 38.3, 25.1, 19.1, 18.3 ppm.



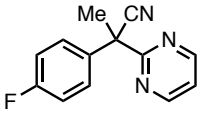
2-(4-(Diethylamino)phenyl)-2-(pyrimidin-2-yl)propanenitrile (4q): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(4-(diethylamino)phenyl)-2-methylmalononitrile (82 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as an orange solid (47 mg, 0.168 mmol, 56%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.74 (d, J = 4.9 Hz, 2H), 7.36–7.32 (m, 2H), 7.19 (t, J = 4.8 Hz, 1H), 6.63–6.57 (m, 2H), 3.31 (q, J = 7.1 Hz, 4H), 2.20 (s, 3H), 1.13 (t, J = 7.1 Hz, 6H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 169.0, 157.7, 147.5, 127.3, 125.6, 123.0, 119.7, 111.6, 50.0, 44.4, 26.2, 12.7 ppm; **HRMS** *m/z* (DART): calcd for $C_{17}H_{21}N_4$ (M+H): 281.1761; found: 281.1759; **IR** (neat): 2973, 2934, 2238, 2203, 1742, 1614, 1562, 1522, 1411, 1198, 818, 810, 792 cm^{-1}; **m.p.:** 78–79 ºC.



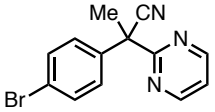
2-(4-Phenoxyphenyl)-2-(pyrimidin-2-yl)propanenitrile (4r): Prepared on 0.20-mmol scale according to General Procedure A. The reaction was performed 2-methyl-2-(4-phenoxyphenyl)malononitrile (89 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL), and 2-chloropyridine (19 μL, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as an off-white solid (45 mg, 0.149 mmol, 75%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.77 (d, J = 4.8 Hz, 2H), 7.51–7.46 (m, 2H), 7.37–7.30 (m, 2H), 7.24 (t, J = 4.9 Hz, 1H), 7.14–7.10 (m, 1H), 7.01–6.98 (m, 2H), 6.98–6.94 (m, 2H), 2.23 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.3, 157.9, 157.5, 156.6, 134.0, 130.0, 127.8, 123.9, 122.5, 120.1, 119.5, 118.8, 50.4, 26.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{19}H_{16}N_3O$ (M+H): 302.1288; found: 302.1293; **IR** (neat): 3073, 2989, 2242, 1741, 1589, 1567, 1505, 1489, 1409, 1254, 1171, 851, 821, 749 cm^{-1}; **m.p.:** 68–69 ºC.



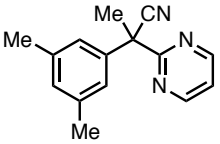
2-(4-(*tert*-Butyl)phenyl)-2-(pyrimidin-2-yl)propanenitrile (4s): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(4-(*tert*-butyl)phenyl)-2-methylmalononitrile (76 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography to yield the product as a colourless oil (52 mg, 0.196 mmol, 65% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.49–7.42 (m, 2H), 7.39–7.33 (m, 2H), 7.22 (t, J = 4.9 Hz, 1H), 2.23 (s, 3H), 1.28 (s, 9H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.2, 157.6, 151.0, 136.3, 125.8, 125.8, 122.4, 119.8, 50.4, 34.4, 31.2, 26.3 ppm; **HRMS** *m/z* (DART): calcd for $C_{17}H_{20}N_3$ (M+H): 266.1652; found: 266.1648.



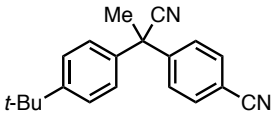
2-(4-Fluorophenyl)-2-(pyrimidin-2-yl)propanenitrile (4t): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(4-fluorophenyl)-2-methylmalononitrile (63 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography to yield the product as an off-white solid (45 mg, 0.198 mmol, 66%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.56–7.50 (m, 2H), 7.25 (t, J = 4.9 Hz, 1H), 7.08–7.01 (m, 2H), 2.23 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.1, 162.5 (d, J = 248.8 Hz), 157.9, 153.3 (d, J = 3.5 Hz), 128.2 (d, J = 8.5 Hz), 122.2, 120.2, 115.9 (d, J = 21.8 Hz), 50.4, 26.6 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{11}N_3F$ (M+H): 228.0932; found: 228.0929; **IR** (neat): 2973, 2241, 1741, 1565, 1509, 1410, 1230, 1169, 834, 816 cm^{-1}; **m.p.:** 84–85 ºC.



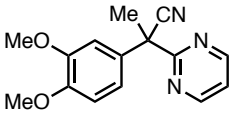
2-(4-Bromophenyl)-2-(pyrimidin-2-yl)propanenitrile (4u): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(4-bromophenyl)-2-methylmalononitrile (85 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography to yield the product as a pale yellow oil (52 mg, 0.180 mmol, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.8 Hz, 2H), 7.50–7.46 (m, 2H), 7.46–7.41 (m, 2H), 7.25 (t, J = 4.9 H, 1H), 2.22 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 167.8, 157.9, 138.6, 132.2, 128.1, 122.6, 121.9, 120.2, 50.6, 26.4 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{11}N_3Br$ (M+H): 288.0131; found: 288.0131; **IR** (neat): 2990, 2246, 1563, 1489, 1410, 1076, 1009, 818, 795 cm^{-1}.



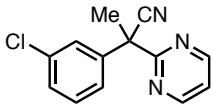
2-(3,5-Dimethylphenyl)-2-(pyrimidin-2-yl)propanenitrile (4v): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(3,5-dimethylphenyl)-2-methylmalononitrile (66 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as a colourless oil (25 mg, 0.105 mmol, 35%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.23 (t, J = 4.9 Hz, 1H), 7.14–7.11 (m, 2H), 6.93–6.90 (m, 1H), 2.29 (s, 3H), 2.29 (s, 3H), 2.21 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.4, 157.8, 139.4, 138.7, 130.0, 124.0, 122.6, 120.0, 50.8, 26.4, 21.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{15}H_{16}N_3$ (M+H): 238.1339; found: 238.1338



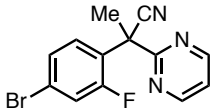
4-(1-(4-(*tert*-Butyl)phenyl)-1-cyanoethyl)benzonitrile (4w): Prepared on 0.30-mmol scale with the modification that the second step was performed at 50 ºC. The reaction was performed using 2-(4-(*tert*-butyl)phenyl)-2-methylmalononitrile (76 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 4-chlorobenzonitrile (41 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography to yield the product as a colourless oil (68 mg, 0.240 mmol, 80%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.69–7.64 (m, 2H), 7.53–7.49 (m, 2H), 7.42–7.37 (m, 2H), 7.28–7.24 (m, 2H), 2.09 (s, 3H), 1.31 (s, 9H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 151.8, 146.9, 136.7, 132.8, 127.6, 126.4, 126.3, 122.7, 118.3, 112.2, 46.1, 34.7, 31.4, 27.9 ppm; **HRMS** *m/z* (DART): calcd for $C_{20}H_{24}N_3$ (M+NH_4): 306.1965; found: 306.1961; **IR** (neat): 2964, 2906, 2231, 1607, 1505, 1407, 1016, 822 cm^{-1}.



2-(3,4-Dimethoxyphenyl)-2-(pyrimidin-2-yl)propanenitrile (4x): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(3,4-dimethoxyphenyl)-2-methylmalononitrile (78 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (70% EtOAc/hexanes) to yield the product as an orange wax (47 mg, 0.175 mmol, 58%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.23 (t, J = 4.9 Hz, 1H), 7.08 (obscured dd, J = 8.2, 2.3 Hz, 1H), 7.06 (obsc d, J = 2.2 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2.22 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.4, 157.8, 149.2, 149.0, 131.8, 122.6, 120.0, 118.5, 111.2, 109.7, 56.1, 56.0, 50.5, 26.4 ppm; **HRMS** *m/z* (DART): calcd for $C_{15}H_{16}N_3O_2$ (M+H): 270.1237; found: 270.1235; **IR** (neat): 3349, 2963, 2867, 2241, 2209, 1609, 1567, 1551, 1515, 1412, 1242, 1173, 815, 801 cm^{-1}.

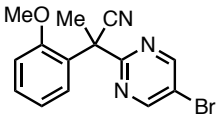


2-(3-Chlorophenyl)-2-(pyrimidin-2-yl)propanenitrile (4y): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(3-chlorophenyl)-2-methylmalononitrile (69 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as a colourless oil (59 mg, 0.242 mmol, 81%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.77 (d, J = 4.8 Hz, 2H), 7.53 (app td, J = 1.9, 0.6 Hz, 1H), 7.47 (app dt, J = 6.8, 2.0 Hz, 1H), 7.32–7.28 (m, 2H), 7.26 (obsc t, J = 4.8 Hz, 1H), 2.23 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 167.7, 158.0, 141.4, 135.0, 130.3, 128.6, 126.7, 124.7, 121.8, 120.3, 50.7, 26.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{11}N_3Cl$ (M+H): 244.0636; found: 244.0642; **IR** (neat): 2992, 2246, 1595, 1563, 1408, 811, 784, 700, 686 cm^{-1}.

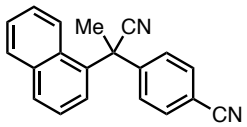


2-(4-Bromo-2-fluorophenyl)-2-(pyrimidin-2-yl)propanenitrile (4z): Prepared on 0.20-mmol scale according to General Procedure A. The reaction was performed 2-(4-bromo-2-fluorophenyl)-2-methylmalononitrile (61 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL), and 2-chloropyridine (19 µL, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as an off-white solid (38 mg, 0.124 mmol, 62%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 7.52 (t, J = 8.3 Hz, 1H), 7.40 (ddd, J = 8.4, 2.0, 0.9 Hz, 1H), 7.27 (t, J = 4.9 Hz, 1H), 7.22 (dd, J = 10.5, 2.0 Hz, 1H), 2.20 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 167.6, 160.0 (d, J = 255.4 Hz), 158.0, 129.4 (d, J = 3.8 Hz), 128.0 (d, J = 3.7 Hz), 126.2 (d, J = 12.2 Hz), 123.3 (d, J = 9.7 Hz), 120.6, 120.4, 120.3, 120.2 (the peaks between 120.6–120.2 represent two indistinguishable doublets), 47.6,

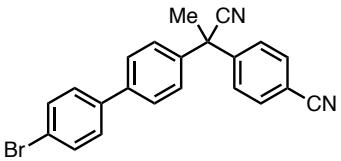
25.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −108.0 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{10}N_3FBr$ (M+H): 306.0037; found: 306.0031; **IR** (neat): 2939, 2241, 2209, 1996, 1741, 1562, 1486, 1412, 1090, 887, 817 cm^{-1}; **m.p.:** 91–92 ºC.



2-(5-Bromopyrimidin-2-yl)-2-(2-methoxyphenyl)propanenitrile (4aa): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-(2-methoxyphenyl)-2-methylmalononitrile (67 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 5-bromo-2-chloropyrimidine (58 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a colourless oil (40 mg, 0.126 mmol, 42%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.74 (s, 2H), 7.54 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.38 (ddd, *J* = 8.3, 7.5, 1.6 Hz, 1H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1H), 6.87 (dd, *J* = 8.3, 1.1 Hz, 1H), 3.58 (s, 3H), 2.13 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.1, 158.0, 156.5, 130.2, 127.1, 126.9, 121.4, 121.0, 118.4, 111.8, 55.5, 47.2, 25.3 ppm; **HRMS** *m/z* (DART): calcd for $C_{14}H_{13}BrN_3O$ (M+H): 318.0236; found: 318.0243.

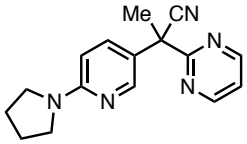


4-(1-Cyano-1-(naphthalen-1-yl)ethyl)benzonitrile (4ab): Prepared on 0.10-mmol scale with the modification that the second step was heated at 50 ºC. The reaction was performed using 2-methyl-2-(naphthalen-1-yl)malononitrile (25 mg, 0.12 mmol, 1.2 equiv), methylmagnesium bromide (0.040 mL of a 3.0 M solution in Et_2O, 0.12 mmol, 1.2 equiv), LiCl solution (0.20 mL of a 0.60 M solution in THF, 0.12 mmol, 1.2 equiv), DMSO (0.40 mL), and 4-chlorobenzonitrile (14 mg, 0.10 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 5–40% EtOAc/hexanes) to yield the product as a white solid (19 mg, 0.067 mmol, 67%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.96 (app dt, *J* = 8.2, 1.0 Hz, 1H), 7.90 (app dt, *J* = 8.1, 0.8 Hz, 1H), 7.77 (dd, *J* = 7.3, 1.1 Hz, 1H), 7.63–7.56 (m, 4H), 7.48–7.43 (m, 3H), 7.34 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H), 2.24 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 148.1, 134.9, 133.2, 132.9, 130.9, 130.0, 129.5, 126.9, 126.7, 126.2, 125.3, 125.2, 125.0, 122.2, 118.3, 112.1, 45.2, 30.6 ppm; **HRMS** *m/z* (DART): calcd for $C_{20}H_{18}N_3$ ($M+NH_4$): 300.1495; found: 300.1496; **IR** (neat): 2962, 2866, 2203, 1741, 1606, 1568, 1511, 1412, 1174, 815, 800 cm^{-1}; **m.p.:** 57–59 ºC.

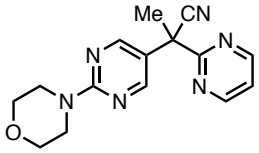


4-(1-(4'-Bromo-[1,1'-biphenyl]-4-yl)-1-cyanoethyl)benzonitrile (4ac): Prepared on 0.10-mmol scale according to General Procedure A. The reaction was performed using 2-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-methylmalononitrile (37 mg, 0.12 mmol, 1.2 equiv), methylmagnesium bromide (0.040 mL of a 3.0 M solution in Et_2O, 0.12 mmol, 1.2 equiv), LiCl solution (0.20 mL of a 0.60 M solution in THF, 0.12 mmol, 1.2 equiv), DMSO (0.40 mL), and 4-chlorobenzonitrile (14 mg, 0.10 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography

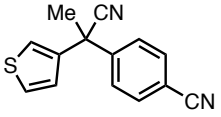
(gradient of 5–40% EtOAc/hexanes) to yield the product as a white foam (36 mg, 0.093 mmol, 93%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.71–7.66 (m, 2H), 7.60–7.52 (m, 6H), 7.45–7.40 (m, 4H), 2.14 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 146.4, 140.4, 139.2, 138.8, 132.9, 132.2, 128.8, 127.8, 127.6, 127.3, 122.3, 122.3, 118.2, 112.4, 46.2, 27.9 ppm; **HRMS** *m/z* (DART): calcd for $C_{22}H_{19}N_3Br$ ($M+NH_4$): 404.0757; found: 404.0755; **IR** (neat): 2295, 2230, 1626, 1568, 1409, 1070, 1002, 894, 811 cm^{-1}.



2-(Pyrimidin-2-yl)-2-(6-(pyrrolidin-1-yl)pyridin-3-yl)propanenitrile (4ad): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-(6-(pyrrolidin-1-yl)pyridin-3-yl)malononitrile (81 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (70% EtOAc/hexanes) to yield the product as a pale orange solid (50 mg, 0.179 mmol, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.74 (d, J = 4.9 Hz, 2H), 8.25 (dd, J = 2.6, 0.8 Hz, 1H), 7.62 (dd, J = 8.9, 2.6 Hz, 1H), 7.21 (t, J = 4.9 Hz, 1H), 6.32 (dd, J = 9.0, 0.8 Hz, 1H), 3.46–3.38 (m, 4H), 2.20 (s, 3H), 2.02–1.94 (m, 4H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 168.5, 157.8, 156.8, 146.2, 135.3, 122.3, 122.1, 119.9, 106.4, 48.6, 46.8, 26.1, 25.7 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{18}N_5$ (M+H): 280.1557; found: 280.1553; **IR** (neat): 3348, 2961, 2863, 2242, 2204, 1743, 1608, 1568, 1550, 1511, 1413, 1312, 1173, 816, 801 cm^{-1}; **m.p.:** 177–179 ºC.

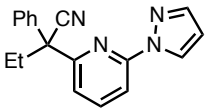


2-(2-Morpholinopyrimidin-5-yl)-2-(pyrimidin-2-yl)propanenitrile (4ae): Prepared on 0.20-mmol scale according to General Procedure A. The reaction was performed 2-methyl-2-(2-morpholinopyrimidin-5-yl)malononitrile (58 mg, 0.24 mmol, 1.2 equiv), methylmagnesium bromide (0.080 mL of a 3.0 M solution in Et_2O, 0.24 mmol, 1.2 equiv), LiCl solution (0.40 mL of a 0.60 M solution in THF, 0.24 mmol, 1.2 equiv), DMSO (0.80 mL), and 2-chloropyridine (19 µL, 0.20 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (70% EtOAc/hexanes) to yield the product as an off-white solid (41 mg, 0.138 mmol, 69%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, J = 4.9 Hz, 2H), 8.51 (s, 2H), 7.25 (obsc t, J = 4.8 Hz, 1H), 3.82–3.77 (m, 4H), 3.76–3.71 (m, 4H), 2.21 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 167.7, 161.2, 158.0, 156.2, 121.2, 121.2, 120.3, 66.9, 47.0, 44.3, 26.1 ppm; **HRMS** *m/z* (DART): calcd for $C_{15}H_{17}N_6O$ (M+H): 297.1465; found: 297.1461; **IR** (neat): 3352, 2963, 2856, 2242, 2211, 1604, 1568, 1511, 1412, 810 cm^{-1}; **m.p.:** 189–190 ºC.

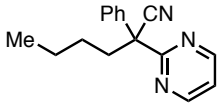


4-(1-Cyano-1-(thiophen-3-yl)ethyl)benzonitrile (4af): Prepared on 0.30-mmol scale according to General Procedure A with the modification that step 2 was heated at 50 ºC. The reaction was performed using 2-methyl-2-(thiophen-3-yl)malononitrile (58 mg, 0.36 mmol, 1.2 equiv),

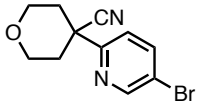
methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 4-chlorobenzonitrile (41 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 5–40% EtOAc/hexanes) to yield the product as a colourless oil (19 mg, 0.080 mmol, 27%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.70–7.65 (m, 2H), 7.54–7.49 (m, 2H), 7.38 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.30 (dd, *J* = 2.9, 1.4 Hz, 1H), 6.92 (dd, *J* = 5.1, 1.4 Hz, 1H), 2.10 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 146.1, 140.3, 132.9, 128.0, 127.2, 126.4, 122.9, 122.0, 118.2, 112.4, 43.4, 28.3 ppm.



2-(6-(1*H*-Pyrazol-1-yl)pyridin-2-yl)-2-phenylbutanenitrile (4ag): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-ethyl-2-phenylmalononitrile (61 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-bromo-6-(1*H*-pyrazol-1-yl)pyridine (67 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–50% EtOAc/hexanes) to yield the product as a colourless oil (26 mg, 0.090 mmol, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.58 (dd, *J* = 2.7, 0.8 Hz, 1H), 7.90 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.80 (t, *J* = 7.9 Hz, 1H), 7.74 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.57–7.50 (m, 2H), 7.41–7.32 (m, 3H), 6.48 (dd, *J* = 2.6, 1.7 Hz, 1H), 2.75 (dq, *J* = 14.5, 7.3 Hz, 1H), 2.51 (dq, *J* = 14.6, 7.4 Hz, 1H), 1.09 (t, *J* = 7.3 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 156.9, 150.9, 142.4, 140.0, 138.6, 128.9, 128.1, 127.1, 126.6, 121.4, 119.5, 111.2, 108.0, 55.0, 32.4, 10.1 ppm; **HRMS** *m/z* (DART): calcd for $C_{18}H_{17}N_4$ (M+H): 289.1448; found: 289.1451.

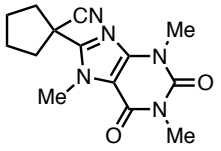


2-Phenyl-2-(pyrimidin-2-yl)hexanenitrile (4ah): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-butyl-2-phenylmalononitrile (71 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 2-chloropyrimidine (34 mg, 0.30 mmol, 1.0 equiv). The product was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as a colourless oil (24 mg, 0.095 mmol, 32%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.76 (d, *J* = 4.8 Hz, 2H), 7.61–7.57 (m, 2H), 7.37–7.32 (m, 2H), 7.30–7.26 (m, 1H), 7.22 (t, *J* = 4.8 Hz, 1H), 2.74–2.65 (m, 1H), 2.53–2.44 (m, 1H), 1.51–1.29 (m, 4H), 0.90 (app t, *J* = 7.0 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 167.7, 157.6, 138.3, 128.8, 128.0, 126.4, 121.2, 119.8, 56.7, 38.7, 27.7, 22.6, 13.8 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{18}N_3$ (M+H): 252.1495; found: 252.1496; **IR** (neat): 2953, 2931, 2873, 2229, 1567, 1411, 1002, 810, 694 cm^{-1}.

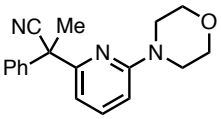


4-(5-Bromopyridin-2-yl)tetrahydro-2*H*-pyran-4-carbonitrile (4aj): Prepared on 0.30-mmol scale with the modification that step 2 was performed using PhMe as cosolvent at 50 ºC. The reaction was performed using tetrahydro-4*H*-pyran-4,4-dicarbonitrile (49 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol,

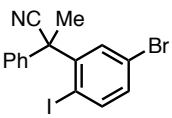
1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 5-bromo-2-fluoropyridine (31 μL, 0.30 mmol, 1.0 equiv). The product was purified by flash column chromatography to yield the product as a colourless oil (80 mg, 0.299 mmol, 99%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.66 (dd, J = 2.4, 0.8 Hz, 1H), 7.87 (dd, J = 8.4, 2.4 Hz, 1H), 7.48 (dd, J = 8.4, 0.8 Hz, 1H), 4.11–4.02 (m, 2H), 3.85 (td, J = 12.4, 1.9 Hz, 2H), 2.31 (ddd, J = 13.8, 12.3, 4.5 Hz, 2H), 2.00 (dq, J = 13.6, 2.3 Hz, 2H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 156.5, 150.9, 139.9, 121.8, 121.1, 120.3, 64.7, 43.7, 35.1 ppm; **HRMS** *m/z* (DART): calcd for $C_{11}H_{12}N_2OBr$ (M+H): 267.0128; found: 267.0127.



1-(1,3,7-Trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-yl)cyclopentane-1-carbonitrile (4ak): Prepared on 0.30-mmol scale according to General Procedure A with the modification that step 2 was performed using PhMe as cosolvent at 50 ºC. The reaction was performed using cyclopentane-1,1-dicarbonitrile (42 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and bromocaffeine (82 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography to yield the product as a white solid (42 mg, 0.146 mmol, 49%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 4.17 (s, 3H), 3.54 (s, 3H), 3.40 (s, 3H), 2.53 (ddd, J = 7.7, 5.3, 1.8 Hz, 4H), 2.06–1.86 (m, 4H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 155.4, 151.7, 149.1, 146.7, 120.8, 109.2, 41.2, 38.3, 33.3, 29.7, 28.0, 24.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{14}H_{18}N_5O_2$ (M+H): 288.1455; found: 288.1458.



2-(6-Morpholinopyridin-2-yl)-2-phenylpropanenitrile (4am): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a 3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 4-(6-bromopyridin-2-yl)morpholine (73 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 10–50% EtOAc/hexanes) to yield the product as an off-white solid (25 mg, 0.085 mmol, 28%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.50–7.47 (m, 2H), 7.45 (dd, J = 8.5, 7.5 Hz, 1H), 7.37–7.32 (m, 2H), 7.31–7.27 (m, 1H), 6.70 (dd, J = 7.4, 0.5 Hz, 1H), 6.52 (dd, J = 8.5, 0.5 Hz, 1H), 3.84–3.80 (m, 4H), 3.55–3.51 (m, 4H), 2.12 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 158.8, 157.4, 140.7, 138.7, 128.8, 127.9, 126.5, 123.4, 110.8, 105.7, 66.8, 49.0, 45.4, 26.9 ppm; **HRMS** *m/z* (DART): calcd for $C_{18}H_{20}N_3O$ (M+H): 294.1601; found: 294.1608.



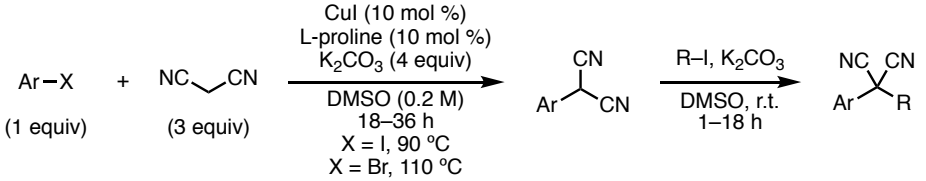
2-(5-Bromo-2-iodophenyl)-2-phenylpropanenitrile (4an): Prepared on 0.30-mmol scale according to General Procedure A. The reaction was performed using 2-methyl-2-phenylmalononitrile (56 mg, 0.36 mmol, 1.2 equiv), methylmagnesium bromide (0.12 mL of a

3.0 M solution in Et_2O, 0.36 mmol, 1.2 equiv), LiCl solution (0.60 mL of a 0.60 M solution in THF, 0.36 mmol, 1.2 equiv), DMSO (1.2 mL), and 4-bromo-2-fluoro-1-iodobenzene (90 mg, 0.30 mmol, 1.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as a colourless oil (22 mg, 0.053 mmol, 18%). **^{1}H NMR** 7.82 (d, J = 8.3 Hz, 1H), 7.78 (d, J = 2.3 Hz, 1H), 7.38–7.29 (m, 3H), 7.28–7.19 (m, 3H), 2.14 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 144.5, 142.3, 140.5, 133.3, 131.8, 129.1, 128.0, 127.0, 123.1, 121.1, 97.1, 49.3, 30.8 ppm; **HRMS** *m/z* (DART): calcd for $C_{15}H_{15}N_2BrI$ ($M+NH_4$): 428.9458; found: 428.9466.

D. Preparation of Malononitrile Starting Materials

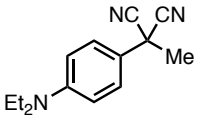
The following malononitriles were prepared as previously described by us:[2] 2-phenylmalononitrile, 2-methyl-2-phenylmalononitrile, 2-(4-fluorophenyl)-2-methylmalononitrile, 2-(4-chlorophenyl)-2-methylmalononitrile, 2-(3-chlorophenyl)-2-methylmalononitrile, and 2-(4-(*tert*-butyl)phenyl)-2-methylmalononitrile. 2,2-Dibenzylmalononitrile was prepared using a previously reported method.[8] Tetrahydro-4*H*-pyran-4,4-dicarbonitrile[9] and cyclopentane-1,1-dicarbonitrile[10] were prepared using known procedures.

General Procedure B: Preparation of malononitrile starting materials[2]



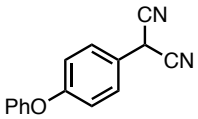
Step 1: An appropriate-sized round-bottom flask with a stir bar was flame-dried and cooled under vacuum. To the flask were added potassium carbonate (4.0 equiv), copper(I) iodide (10 mol %), L-proline (10 mol %), malononitrile (3.0 equiv), and aryl halide (if a solid) (1.0 equiv). The flask was evacuated and backfilled with N_2 (×3) and DMSO (0.20 M) was added. The flask was again evacuated and backfilled with N_2 (×3), sealed, and put under a balloon of N_2. Aryl halide (if an oil) was added (1.0 equiv). The reaction was stirred at the appropriate temperature (90 ºC for aryl iodides, 110 ºC for aryl bromides) until full conversion of aryl halide was achieved, as determined by TLC (18–36 h). The reaction was cooled to 0 ºC and opened to air, and 1.0 M HCl was added to bring the solution to pH 2–3. The solution was extracted with EtOAc (×3), and the organic fractions were combined, washed with H_2O (×3) and brine (×3), dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash column chromatography to yield the desired arylmalononitrile.

Step 2: To an appropriate-sized round-bottom flask with a stir bar were added 2-arylmalononitrile (1.0 equiv), potassium carbonate (1.2–1.5 equiv), DMSO (1.0 M), and alkyl iodide (1.1–1.5 equiv), and the reaction was stirred at r.t. until full conversion was achieved, as determined by TLC (1–18 h). The reaction was quenched with H_2O and extracted with EtOAc (×3), and the organic fractions were combined, washed with brine (×3), dried over $MgSO_4$, and concentrated. The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the disubstituted malononitrile.

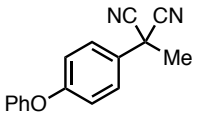


2-(4-(Diethylamino)phenyl)-2-methylmalononitrile (S1): Prepared according to General Procedure B – Step 2 using 2-(4-(diethylamino)phenyl)malononitrile (1.07 g, 5.0 mmol, 1.0 equiv), iodomethane (0.34 mL, 5.5 mmol, 1.1 equiv), potassium carbonate (0.83 g, 6.0 mmol, 1.2 equiv), and DMSO (10 mL, 0.50 M). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as a pale pink solid (1.0 g, 4.4 mmol, 88%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.38–7.32 (m, 2H), 6.73–6.65 (m, 2H), 3.37 (q, J = 7.1 Hz, 4H), 2.07 (s, 3H), 1.18 (t, J = 7.0 Hz, 6H) ppm; **^{13}C NMR** (126

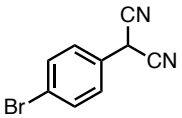
MHz, $CDCl_3$, 298 K): δ_C 148.6, 126.6, 118.4, 116.5, 111.9, 44.5, 35.7, 29.1, 12.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{14}H_{18}N_3$ (M+H): 228.1495; found: 228.1491; **IR** (neat): 3347, 2945, 2867, 2242, 2204, 1610, 1568, 1514, 1551, 1485, 1412, 1312, 1175, 1003, 815 cm^{-1}; **m.p.:** 49–50 ºC.



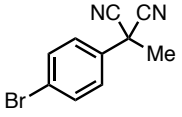
2-(4-Phenoxyphenyl)malononitrile (S2): Prepared according to General Procedure B – Step 1 using 1-bromo-4-phenoxybenzene (1.2 mL, 8.0 mmol, 1.0 equiv), malononitrile (1.6 g, 24 mmol, 3.0 equiv), copper(I) iodide (0.15 g, 0.80 mmol, 0.10 equiv), L-proline (92 mg, 0.80 mmol, 0.10 equiv), potassium carbonate (4.4 g, 32 mmol, 4.0 equiv), and DMSO (40 mL, 0.20 M), and the reaction was stirred at 110 ºC for 18 h. The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as an off-white solid (0.94 g, 4.0 mmol, 50%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.46–7.42 (m, 2H), 7.42–7.37 (m, 2H), 7.22–7.17 (m, 1H), 7.10–7.03 (m, 4H), 5.04 (s, 1H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 159.6, 155.8, 130.2, 129.0, 124.7, 120.1, 120.0, 119.4, 112.0, 27.6 ppm.



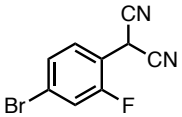
2-Methyl-2-(4-phenoxyphenyl)malononitrile (S3): Prepared according to General Procedure B – Step 2 using 2-(4-phenoxyphenyl)malononitrile (**S2**) (0.70 g, 3.0 mmol, 1.0 equiv), iodomethane (0.22 mL, 3.3 mmol, 1.1 equiv), potassium carbonate (0.50 g, 3.6 mmol, 1.2 equiv), and DMSO (5.0 mL, 0.60 M). The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as an off-white solid (0.54 g, 2.1 mmol, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.56–7.50 (m, 2H), 7.43–7.36 (m, 2H), 7.22–7.16 (m, 1H), 7.11–7.02 (m, 4H), 2.12 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$, 298 K): δ_C 159.2, 155.9, 130.2, 127.2, 127.1, 124.6, 119.9, 119.2, 115.9, 36.0, 29.4 ppm; **HRMS** *m/z* (DART): calcd for $C_{16}H_{16}N_3O$ (M+NH_4): 266.1288; found: 266.1284; **IR** (neat): 3000, 2230, 1588, 1506, 1488, 1240, 1201, 1174, 833, 753, 692 cm^{-1}; **m.p.:** 78–79 ºC.



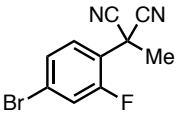
2-(4-Bromophenyl)malononitrile (S4): Prepared according to General Procedure B – Step 1 using 1-bromo-4-iodobenzene (2.3 g, 8.0 mmol, 1.0 equiv), malononitrile (1.6 g, 24 mmol, 3.0 equiv), copper(I) iodide (0.15 g, 0.80 mmol, 0.10 equiv), L-proline (92 mg, 0.80 mmol, 0.10 equiv), potassium carbonate (4.4 g, 32 mmol, 4.0 equiv), and DMSO (40 mL, 0.20 M), and the reaction was stirred at 90 ºC for 18 h. The crude residue was purified by flash column chromatography (gradient of 10–30% EtOAc/hexanes) to yield the product as an off-white solid (0.43 g, 1.95 mmol, 24%). The analytical data was consistent with literature:[11] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.67–7.61 (m, 2H), 7.42–7.35 (m, 2H), 5.05 (s, 1H) ppm.



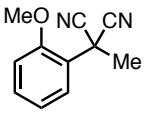
2-(4-Bromophenyl)-2-methylmalononitrile (S5): Prepared according to General Procedure B – Step 2 using 2-(4-bromophenyl)malononitrile (**S4**) (0.41 g, 1.9 mmol, 1.0 equiv), iodomethane (0.22 mL, 3.3 mmol, 1.7 equiv), potassium carbonate (0.50 g, 3.6 mmol, 1.9 equiv), and DMSO (5.0 mL, 0.38 M). The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as an off-white solid (0.37 g, 1.6 mmol, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.68–7.60 (m, 2H), 7.51–7.43 (m, 2H), 2.10 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$, 298 K): δ_C 139.1, 133.2, 127.1, 124.6, 115.3, 36.2, 29.4 ppm; **HRMS** *m/z* (DART): calcd for $C_{10}H_{11}N_3Br$ (M+NH_4): 252.0131; found: 252.0131; **IR** (neat): 3352, 2962, 2867, 2242, 2209, 1611, 1568, 1551, 1513, 1485, 1412, 1312, 1175, 815, 801 cm^{-1}; **m.p.:** 66–67 ºC.



2-(4-Bromo-2-fluorophenyl)malononitrile (S6): Prepared according to General Procedure B – Step 1 using 4-bromo-2-fluoro-1-iodobenzene (2.4 g, 8.0 mmol, 1.0 equiv), malononitrile (1.6 g, 24 mmol, 3.0 equiv), copper(I) iodide (0.15 g, 0.80 mmol, 0.10 equiv), L-proline (92 mg, 0.80 mmol, 0.10 equiv), potassium carbonate (4.4 g, 32 mmol, 4.0 equiv), and DMSO (40 mL, 0.20 M), and the reaction was stirred at 90 ºC for 18 h. The crude residue was purified by flash column chromatography (gradient of 10–30% EtOAc/hexanes) to yield the product as an off-white solid (0.56 g, 2.3 mmol, 29%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.53–7.46 (m, 2H), 7.46–7.40 (m, 1H), 5.18 (s, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$, 298 K): δ_C 159.3 (d, J = 257.2 Hz), 130.1, 129.3 (d, J = 3.8 Hz), 126.1 (d, J = 9.2 Hz), 120.6 (d, J = 23.1 Hz), 113.6 (d, J = 14.2 Hz), 110.4, 22.4 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −112.7 ppm.

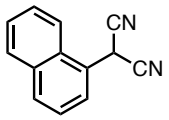


2-(4-Bromo-2-fluorophenyl)-2-methylmalononitrile (S7): Prepared according to General Procedure B – Step 2 using 2-(4-bromo-2-fluorophenyl)malononitrile (0.48 g, 2.0 mmol, 1.0 equiv), potassium carbonate (0.33 g, 2.4 mmol, 1.2 equiv), iodomethane (0.15 mL, 2.4 mmol, 1.2 equiv), and DMSO (5.0 mL, 0.40 M). The crude residue was purified by flash column chromatography (5–30% EtOAc/hexanes) to yield the product as a white solid (0.40 g, 1.6 mmol, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.54–7.39 (m, 3H), 2.17 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$, 298 K): δ_C 159.5 (d, J = 257.8 Hz), 128.8 (d, J = 3.7 Hz), 128.6 (d, J = 2.5 Hz), 125.6 (d, J = 9.6 Hz), 121.2 (d, J = 23.9 Hz), 119.4 (d, J = 11.1 Hz), 114.1, 33.0, 26.4 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −108.7 ppm; **HRMS** *m/z* (DART): calcd for $C_{10}H_{10}N_3FBr$ (M+NH_4): 270.0037; found: 270.0045; **IR** (neat): 3338, 2961, 2867, 2241, 2209, 1607, 1568, 1513, 1484, 1412, 1312, 815, 801 cm^{-1}.

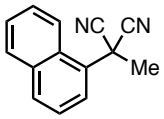


2-(2-Methoxyphenyl)-2-methylmalononitrile (S8): Prepared according to General Procedure B – Step 2 using 2-(2-methoxyphenyl)malononitrile (0.86 g, 5.0 mmol, 1.0 equiv), iodomethane (0.34 mL, 5.5 mmol, 1.1 equiv), potassium carbonate (0.83 g, 6.0 mmol, 1.2 equiv), and DMSO (10 mL, 0.50 M). The crude residue was purified by flash column chromatography (gradient of 0–30% EtOAc/hexanes) to yield the product as an off-white solid (0.88 g, 4.7 mmol, 94%). **^{1}H**

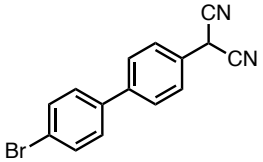
NMR (500 MHz, $CDCl_3$, 298 K): δ_H 7.51 (dd, J = 7.8, 1.5 Hz, 1H), 7.45 (ddd, J = 9.1, 7.5, 1.6 Hz, 1H), 7.06 (dd, J = 7.6, 1.1 Hz, 1H), 7.03 (dd, J = 8.5, 1.1 Hz, 1H), 3.99 (s, 3H), 2.17 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 156.7, 131.9, 126.7, 121.4, 120.2, 115.8, 112.5, 56.1, 33.5, 25.4 ppm.



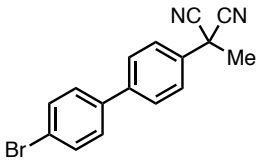
2-(Naphthalen-1-yl)malononitrile (S9): Prepared from 1-bromonaphthalene (1.7 mL, 12 mmol, 1.0 equiv), malononitrile (2.4 g, 36 mmol, 3.0 equiv), copper(I) iodide (0.23 g, 1.2 mmol, 0.10 equiv), L-proline (0.14 g, 1.2 mmol, 0.10 equiv), potassium carbonate (6.6 g, 48 mmol, 4.0 equiv), and DMSO (50 mL, 0.20 M), and the reaction was stirred at 110 ºC for 24 h. The crude residue was purified by flash column chromatography (gradient of 10–40% EtOAc/hexanes) to yield the product as an off-white solid (0.33 g, 1.7 mmol, 21%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.03–7.97 (m, 2H), 7.95–7.91 (m, 1H), 7.82–7.79 (m, 1H), 7.72 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.65 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 7.56 (dd, J = 8.2, 7.1 Hz, 1H), 5.57 (s, 1H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 134.2, 131.8, 129.7, 129.4, 128.4, 127.3, 127.1, 125.6, 121.8, 121.7, 111.8, 26.5 ppm.



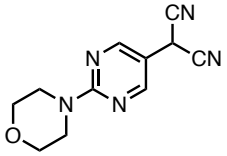
2-Methyl-2-(naphthalen-1-yl)malononitrile (S10): Prepared from 2-(naphthalen-1-yl)malononitrile (**S9**) (0.33 g, 1.7 mmol, 1.0 equiv), iodomethane (0.12 mL, 2.0 mmol, 1.2 equiv), potassium carbonate (0.36 g, 2.6 mmol, 1.5 equiv), and DMSO (5.0 mL, 0.34 M). The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as a pale pink solid (0.24 g, 1.2 mmol, 71%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.37 (app dq, J = 8.6, 0.9 Hz, 1H), 8.01–7.97 (m, 2H), 7.79 (dd, J = 7.4, 1.1 Hz, 1H), 7.72 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.63 (ddd, J = 8.1, 6.8, 1.0 Hz, 1H), 7.53 (dd, J = 8.2, 7.3 Hz, 1H), 2.43 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 134.8, 131.9, 130.0, 128.9, 127.9, 126.9, 126.8, 125.1, 124.8, 123.1, 116.0, 34.8, 26.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{14}H_{10}N_2$ (M): 206.0839; found: 206.0833; **IR** (neat): 3340, 2965, 2866, 2203, 1740, 1604, 1568, 1511, 1486, 1412, 1168, 800, 775 cm^{-1}; **m.p.:** 123–124 ºC.



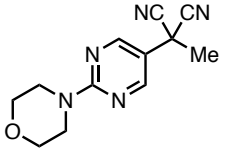
2-(4'-Bromo-[1,1'-biphenyl]-4-yl)malononitrile (S11): Prepared according to General Procedure B – Step 1 using 4,4'-dibromobiphenyl (3.7 g, 12 mmol, 1.0 equiv), malononitrile (2.4 g, 36 mmol, 3.0 equiv), copper(I) iodide (0.23 g, 1.2 mmol, 0.10 equiv), L-proline (0.14 g, 1.2 mmol, 0.10 equiv), potassium carbonate (6.6 g, 48 mmol, 4.0 equiv), and DMSO (40 mL, 0.20 M), and the reaction was stirred at 110 ºC for 18 h. The crude residue was purified by flash column chromatography (gradient of 5–40% EtOAc/hexanes) to yield the product as an off-white solid (1.3 g, 4.4 mmol, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.70–7.64 (m, 2H), 7.63–7.54 (m, 4H), 7.47–7.41 (m, 2H), 5.12 (s, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$, 298 K): δ_C 142.4, 138.4, 132.3, 128.9, 128.6, 127.9, 125.5, 122.8, 111.8, 28.0 ppm.



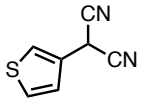
2-(4'-Bromo-[1,1'-biphenyl]-4-yl)-2-methylmalononitrile (S12): Prepared according to General Procedure B – Step 2 using 2-(4'-bromo-[1,1'-biphenyl]-4-yl)malononitrile (1.2 g, 4.0 mmol, 1.0 equiv), iodomethane (0.30 mL, 4.8 mmol, 1.2 equiv), potassium carbonate (0.83 g, 6.0 mmol, 1.5 equiv), and DMSO (10 mL, 0.40 M). The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as a white solid (0.27 g, 0.87 mmol, 22%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.69–7.64 (m, 4H), 7.62–7.58 (m, 2H), 7.47–7.42 (m, 2H), 2.15 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 142.1, 138.4, 132.5, 132.3, 128.9, 128.4, 126.1, 122.8, 115.7, 36.3, 29.5 ppm; **IR** (neat): 2965, 2867, 2210, 1741, 1607, 1568, 1511, 1483, 1412, 1177, 1095, 1003, 814 cm^{-1} **m.p.:** 113–114 ºC; **HRMS** *m/z* (DART): calcd for $C_{16}H_{11}N_2Br$ (M+): 310.0100; found: 310.0097.



2-(2-Morpholinopyrimidin-5-yl)malononitrile (S13): Prepared according to General Procedure B – Step 1 using 4-(5-bromopyrimidin-2-yl)morpholine (2.9 g, 12 mmol, 1.0 equiv), malononitrile (2.4 g, 36 mmol, 3.0 equiv), copper(I) iodide (0.23 g, 1.2 mmol, 0.10 equiv), L-proline (0.14 g, 1.2 mmol, 0.10 equiv), potassium carbonate (6.6 g, 48 mmol, 4.0 equiv), and DMSO (40 mL, 0.30 M), and the reaction was stirred at 110 ºC for 18 h. The organic extracts were concentrated and washed with Et_2O to yield an off-white solid (1.5 g, ca. 6.5 mmol, 54% crude yield) that corresponded to the desired compound as determined by ^{1}H NMR, which material was used without further purification.

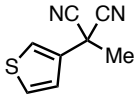


2-Methyl-2-(2-morpholinopyrimidin-5-yl)malononitrile (S14): Prepared according to General Procedure B – Step 2 using 2-(2-morpholinopyrimidin-5-yl)malononitrile (0.69 g, 3.0 mmol, 1.0 equiv), iodomethane (0.20 mL, 3.3 mmol, 1.1 equiv), potassium carbonate (0.62 g, 4.5 mmol, 1.5 equiv), and DMSO (10 mL, 0.30 M). The crude residue was purified by flash column chromatography (gradient of 25–70% EtOAc/hexanes) to yield the product as an off-white solid (0.42 g, 1.7 mmol, 57%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.49 (s, 2H), 3.89–3.84 (m, 4H), 3.79–3.74 (m, 4H), 2.10 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 161.8, 155.3, 115.0, 114.9, 66.8, 44.4, 32.3, 28.6 ppm; **HRMS** *m/z* (DART): calcd for $C_{12}H_{14}N_5O$ (M+H): 244.1193; found: 244.1198; **IR** (neat): 3348, 2964, 2866, 2210, 1741, 1608, 1568, 1551, 1513, 1483, 1412, 1176, 815 cm^{-1}; **m.p.:** 157–158 ºC.

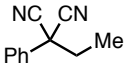


2-(Thiophen-3-yl)malononitrile (S15): Prepared according to General Procedure B – Step 1 using malononitrile (3.0 g, 45 mmol, 3.0 equiv), potassium carbonate (8.3 g, 60 mmol, 4.0

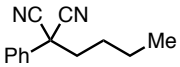
equiv), copper(I) iodide (0.44 g, 2.3 mmol, 15 mol %), L-proline (0.26 g, 2.3 mmol, 15 mol %), DMSO (75 mL, 0.20 M), and 3-bromothiophene (1.4 mL, 15 mmol, 1.0 equiv), and the reaction was stirred at 110 ºC for 16 h. The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as an off-white solid (0.74 g, 5.0 mmol, 33%). Analytical data: **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.58–7.53 (m, 1H), 7.53–7.48 (m, 1H), 7.22–7.17 (m, 1H), 5.12 (s, 1H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ_C 129.3, 125.7, 125.6, 125.3, 111.5, 23.9 ppm; **R_f** (7:3 hexanes/EtOAc; UV/$KMnO_4$): 0.47.



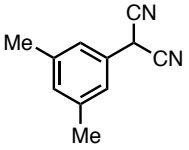
2-Methyl-2-(thiophen-3-yl)malononitrile (S16): Prepared according to General Procedure B – Step 2 using 2-(thiophen-3-yl)malononitrile (0.74 g, 5.0 mmol, 1.0 equiv), DMSO (20 mL, 0.5 M), iodomethane (0.34 mL, 5.5 mmol, 1.1 equiv), and potassium carbonate (0.83 g, 6.0 mmol, 1.2 equiv). The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as a colourless oil (0.72 g, 4.4 mmol, 88%). Analytical data: **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.57–7.51 (m, 1H), 7.51–7.46 (m, 1H), 7.24–7.18 (m, 1H), 2.13 (s, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ_C 133.1, 129.2, 124.7, 123.9, 115.6, 32.5, 28.3 ppm; **R_f** (8:2 hexanes/EtOAc; UV/$KMnO_4$): 0.47.



2-Ethyl-2-phenylmalononitrile (S17): Prepared according to General Procedure B – Step 2 using 2-phenylmalononitrile (0.71 g, 5.0 mmol, 1.0 equiv), iodoethane (0.44 mL, 5.5 mmol, 1.1 equiv), potassium carbonate (0.83 g, 6.0 mmol, 1.2 equiv), and DMSO (10 mL, 0.50 M). The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as a colourless oil (0.80 g, 4.7 mmol, 94%). Analytical data:[12] **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.59–7.54 (m, 2H), 7.52–7.44 (m, 3H), 2.29 (q, J = 7.3 Hz, 2H), 1.24 (t, J = 7.4 Hz, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 132.1, 130.0, 129.8, 125.9, 115.1, 43.3, 36.7, 10.1 ppm.

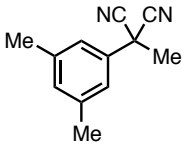


2-Butyl-2-phenylmalononitrile (S18): Prepared according to General Procedure B – Step 2 using 2-phenylmalononitrile (4.3 g, 30 mmol, 1.0 equiv), potassium carbonate (8.3 g, 60 mmol, 2.0 equiv), DMSO (75 mL, 0.40 M), and 1-iodobutane (6.8 mL, 60 mmol, 2.0 equiv). The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as a colourless oil (5.5 g, 28 mmol, 93%). Analytical data:[12] **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.64–7.45 (m, 5H), 2.30–2.20 (m, 2H), 1.71–1.58 (m, 2H), 1.43 (h, J = 7.3 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ_C 132.3, 129.8, 129.7, 125.7, 115.1, 42.5, 42.4, 27.6, 21.9, 13.6 ppm; **R_f** (9:1 hexanes/EtOAc; UV): 0.61.

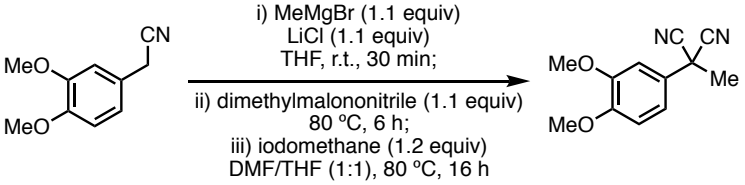


2-(3,5-Dimethylphenyl)malononitrile (S19): Prepared according to General Procedure B – Step 1 using 1-bromo-3,5-dimethylbenzene (1.1 mL, 8.0 mmol, 1.0 equiv) malononitrile (1.6 g, 24 mmol, 3.0 equiv), copper(I) iodide (0.30 g, 1.6 mmol, 0.20 equiv), L-proline (0.18 g, 1.6 mmol,

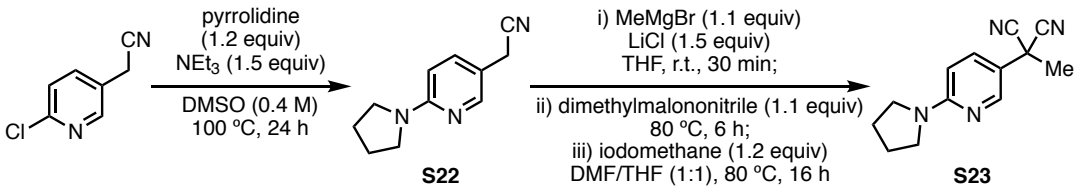
0.20 equiv), potassium carbonate (4.4 g, 32 mmol, 4.0 equiv), and DMSO (40 mL, 0.20 M), and the reaction was stirred at 110 ºC for 36 h. The crude residue was purified by flash column chromatography (gradient of 5–30% EtOAc/hexanes) to yield the product as a white solid (0.65 g, 3.8 mmol, 48%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.09 (app s, 3H), 4.97 (s, 1H), 2.37 (overlapping s, 3H), 2.37 (overlapping s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 140.2, 132.1, 126.0, 125.0, 112.1, 28.1, 21.4 ppm.



2-(3,5-Dimethylphenyl)-2-methylmalononitrile (S20): Prepared according to General Procedure B – Step 2 using 2-(3,5-dimethylphenyl)malononitrile (0.51 g, 3.0 mmol, 1.0 equiv), iodomethane (0.28 mL, 4.5 mmol, 1.5 equiv), potassium carbonate (0.50 g, 3.6 mmol, 1.2 equiv), and DMSO (10 mL, 0.30 M). The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield the product as a colourless oil (0.50 g, 2.7 mmol, 90%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 7.19–7.16 (m, 2H), 7.09–7.06 (m, 1H), 2.37 (s, 6H), 2.09 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 139.9, 133.0, 131.7, 123.1, 116.0, 36.4, 29.6, 29.6, 21.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{12}H_{13}N_2$ (M+H): 185.1073; found: 185.1073.



2-(3,4-Dimethoxyphenyl)-2-methylmalononitrile (S21):[8] To a 16-mL threaded culture tube with a stir bar was added lithium chloride (0.18 g, 4.4 mmol, 1.1 equiv). The tube was fitted with a size 19 septum and was flame-dried under vacuum and cooled under N_2. To the tube was added 2-(3,4-dimethoxyphenyl)acetonitrile (0.71 g, 4.0 mmol, 1.0 equiv), and the tube was sealed and evacuated and backfilled with N_2 (×3) and fitted with a balloon of N_2. THF (4.0 mL, 1.0 M) was added, followed by MeMgBr (1.5 mL of a 4.0 M solution in Et_2O, 4.4 mmol, 1.1 equiv), and the reaction was stirred at r.t. for 30 min. The reaction was briefly opened to air and dimethylmalononitrile (0.41 g, 4.4 mmol, 1.1 equiv) was added at once, and the reaction was stirred at 80 ºC for 6 h. The reaction was cooled to r.t., and DMF (4.0 mL) was added, followed by iodomethane (0.30 mL, 4.8 mmol, 1.2 equiv), and the reaction was stirred at 80 ºC for 16 h. The reaction was cooled to r.t., quenched with sat. aq. NH_4Cl, and extracted with EtOAc (×3). The organic extracts were combined, washed with brine (×1), dried over $MgSO_4$, and concentrated. The crude residue was purified by flash column chromatography (gradient of 20–60% EtOAc/hexanes) to yield the product as a white semisolid (0.54 g, 2.5 mmol, 63%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K); δ_H 7.13 (dd, J = 8.4, 2.4 Hz, 1H), 7.00 (d, J = 2.4 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 2.11 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 150.4, 150.0, 125.2, 118.0, 116.0, 111.7, 108.4, 56.3, 56.2, 36.2, 29.5 ppm; **HRMS** *m/z* (DART): calcd for $C_{12}H_{16}N_3O_2$ (M+NH_4): 234.1237; found: 234.1237; **IR** (neat): 3001, 2965, 2940, 2836, 2229, 1598, 1519, 1462, 1417, 1261, 1243, 1149, 1022, 856, 806 cm^{-1}.

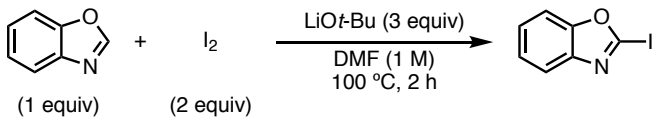


2-(6-(Pyrrolidin-1-yl)pyridin-3-yl)acetonitrile (S22): To a 100-mL flask with a stir bar were sequentially added 2-(6-chloropyridin-3-yl)acetonitrile (1.2 g, 8.0 mmol, 1.0 equiv), DMSO (20 mL, 0.40 M), pyrrolidine (0.80 mL, 9.6 mmol, 1.2 equiv), and triethylamine (1.7 mL, 12 mmol, 1.5 equiv), and the reaction was stirred at 100 ºC for 24 h. The reaction was cooled to r.t., quenched with H_2O, and extracted with EtOAc (×3), and the organic fractions were combined, washed with brine (×1), dried over $MgSO_4$, and concentrated. The crude residue was purified by flash column chromatography (gradient of 40–70% EtOAc/hexanes) to yield the desired product as an off-white solid (0.59 g, 3.2 mmol, 40%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.06–8.01 (m, 1H), 7.41–7.38 (m, 1H), 6.36 (dd, J = 8.8, 0.8 Hz, 1H), 3.58 (s, 2H), 3.48–3.40 (m, 4H), 2.05–1.98 (m, 4H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 157.1, 147.5, 136.7, 118.3, 112.3, 106.9, 46.9, 25.6, 20.5 ppm.

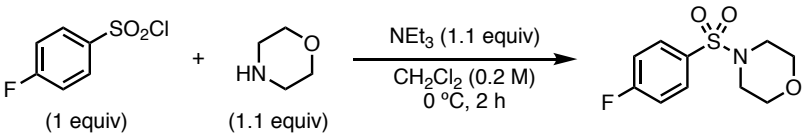
2-Methyl-2-(6-(pyrrolidin-1-yl)pyridin-3-yl)malononitrile (S23):[8] To a 16-mL threaded culture tube with a stir bar was added lithium chloride (0.18 g, 4.4 mmol, 1.5 equiv). The tube was fitted with a size 19 septum and was flame-dried under vacuum and cooled under N_2. To the tube was added 2-(6-(pyrrolidin-1-yl)pyridin-3-yl)acetonitrile (0.56 g, 3.0 mmol, 1.0 equiv), and the tube was sealed and evacuated and backfilled with N_2 (×3) and fitted with a balloon of N_2. THF (4.0 mL, 0.75 M) was added, followed by MeMgBr (1.1 mL of a 4.0 M solution in Et_2O, 3.3 mmol, 1.1 equiv), and the reaction was stirred at r.t. for 30 min. The reaction was briefly opened to air and dimethylmalononitrile (0.31 g, 3.3 mmol, 1.1 equiv) was added at once, and the reaction was stirred at 80 ºC for 6 h. The reaction was cooled to r.t., and DMF (4.0 mL) was added, followed by iodomethane (0.22 mL, 3.6 mmol, 1.2 equiv), and the reaction was stirred at 80 ºC for 16 h. The reaction was cooled to r.t., quenched with sat. aq. NH_4Cl, and extracted with EtOAc (×3). The organic extracts were combined, washed with brine (×1), dried over $MgSO_4$, and concentrated. The crude residue was purified by flash column chromatography (gradient of 20–60% EtOAc/hexanes) to yield the product as an off-white solid (0.44 g, 1.9 mmol, 63%). **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ_H 8.35–8.31 (m, 1H), 7.55 (dd, J = 8.9, 2.8 Hz, 1H), 6.41 (dd, J = 9.0, 0.7 Hz, 1H), 3.54–3.40 (m, 4H), 2.08 (s, 3H), 2.05–2.01 (m, 4H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$, 298 K): δ_C 157.6, 145.5, 134.1, 115.8, 115.3, 107.0, 47.0, 34.0, 28.7, 25.6 ppm; **HRMS** *m/z* (DART): calcd for $C_{13}H_{15}N_4$ (M+H): 227.1291; found: 227.1290; **IR** (neat): 3349, 2965, 2866, 2242, 2209, 1741, 1608, 1568, 1550, 1514, 1484, 1413, 1311, 1174, 815 cm^{-1}; **m.p.:** 56–57 ºC.

E. Preparation of (Hetero)Aryl Electrophile Starting Materials

8-Bromocaffeine was prepared from caffeine and NBS according to a literature procedure.[13]

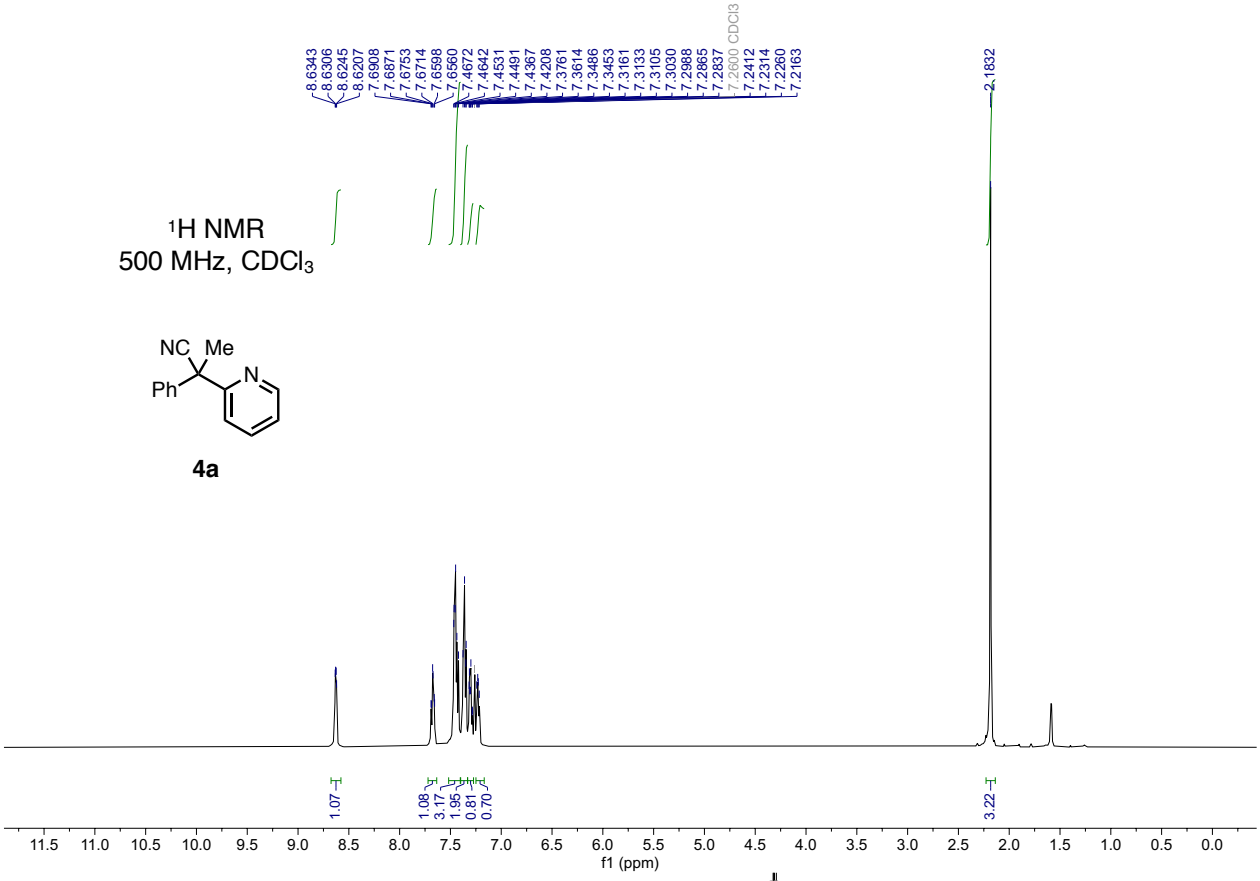


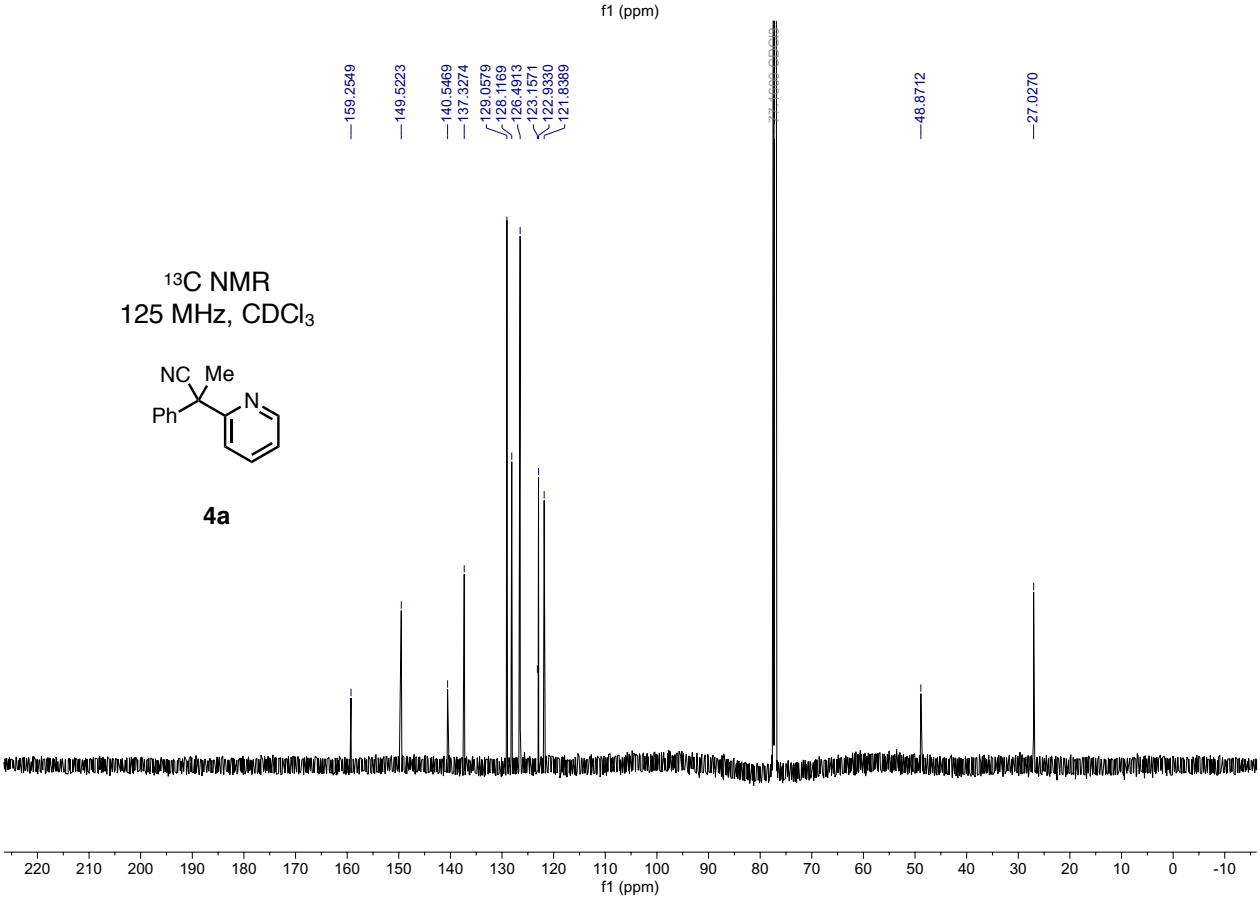
2-Iodobenzoxazole (S24):[14] To a flame-dried 25-mL flask with stir bar was added benzoxazole (0.48 g, 4.0 mmol, 1.0 equiv). The flask was evacuated and backfilled with N_2 (×3) and DMF (4.0 mL, 1.0 M) was added. The flask was briefly opened to air and iodine (2.0 g, 8.0 mmol, 2.0 equiv) was added. The reaction flask was briefly opened to air and anhydrous lithium *tert*-butoxide (0.96 g, 12 mmol, 3.0 equiv) was added at once. Under a balloon of N_2, the reaction was heated to 100 ºC for 2 h. The reaction was cooled to r.t., quenched with sat. aq. NH_4Cl, and extracted with EtOAc (×3). The organic fractions were combined, washed with sat. aq. $Na_2S_2O_3$ (×1), H_2O (×1), and brine (×1), dried over $MgSO_4$, and concentrated. The crude residue was purified by flash column chromatography (gradient of 0–20% EtOAc/hexanes) to yield 2-iodobenzoxazole as a white solid (0.25 g, 1.0 mmol, 25%). The analytical data was consistent with literature:[15] **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.75–7.67 (m, 1H), 7.58–7.50 (m, 1H), 7.36–7.27 (m, 2H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ_C 154.3, 142.9, 125.5, 124.9, 119.5, 110.3, 108.1 ppm; **R_f** (8:2 hexanes/EtOAc; UV): 0.62.

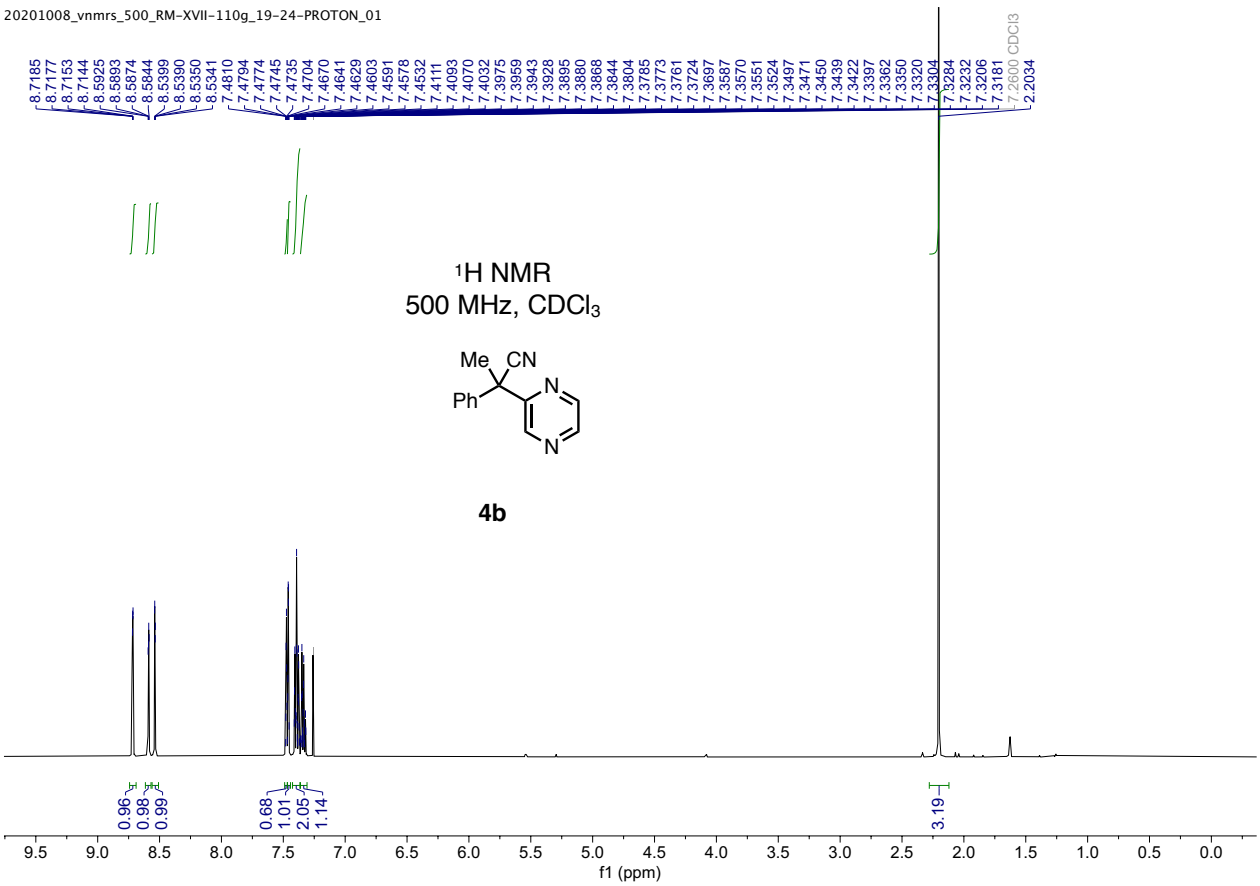


4-((4-Fluorophenyl)sulfonyl)morpholine (S25): To a 50-mL flask with a stir bar were added 4-fluorobenzenesulfonyl chloride (0.58 g, 3.0 mmol, 1.0 equiv) and dichloromethane (15 mL, 0.20 M), and the solution was cooled to 0 ºC. To the flask were sequentially added morpholine (0.29 mL, 3.3 mmol, 1.1 equiv) and triethylamine (0.46 mL, 3.3 mmol, 1.1 equiv), and the reaction was stirred at 0 ºC for 2 h. The reaction was concentrated and the concentrate was purified by flash column chromatography (gradient of 10–30% EtOAc/hexanes) to yield the product as a white solid (0.70 g, 2.9 mmol, 97%). The analytical data was consistent with literature:[16] **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ_H 7.84–7.74 (m, 2H), 7.28–7.20 (m, 2H), 3.78–3.72 (m, 4H), 3.03–2.97 (m, 4H) ppm; **^{19}F NMR** (376 MHz, $CDCl_3$, 298 K): δ_F −104.5 ppm.

F. NMR Spectra



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8.5341
7.4810
7.4794
7.4774
7.4745
7.4735
7.4704
7.4670
7.4641
7.4629
7.4603
7.4591
7.4578
7.4532
7.4111
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7.4070
7.4032
7.3975
7.3959
7.3943
7.3928
7.3895
7.3880
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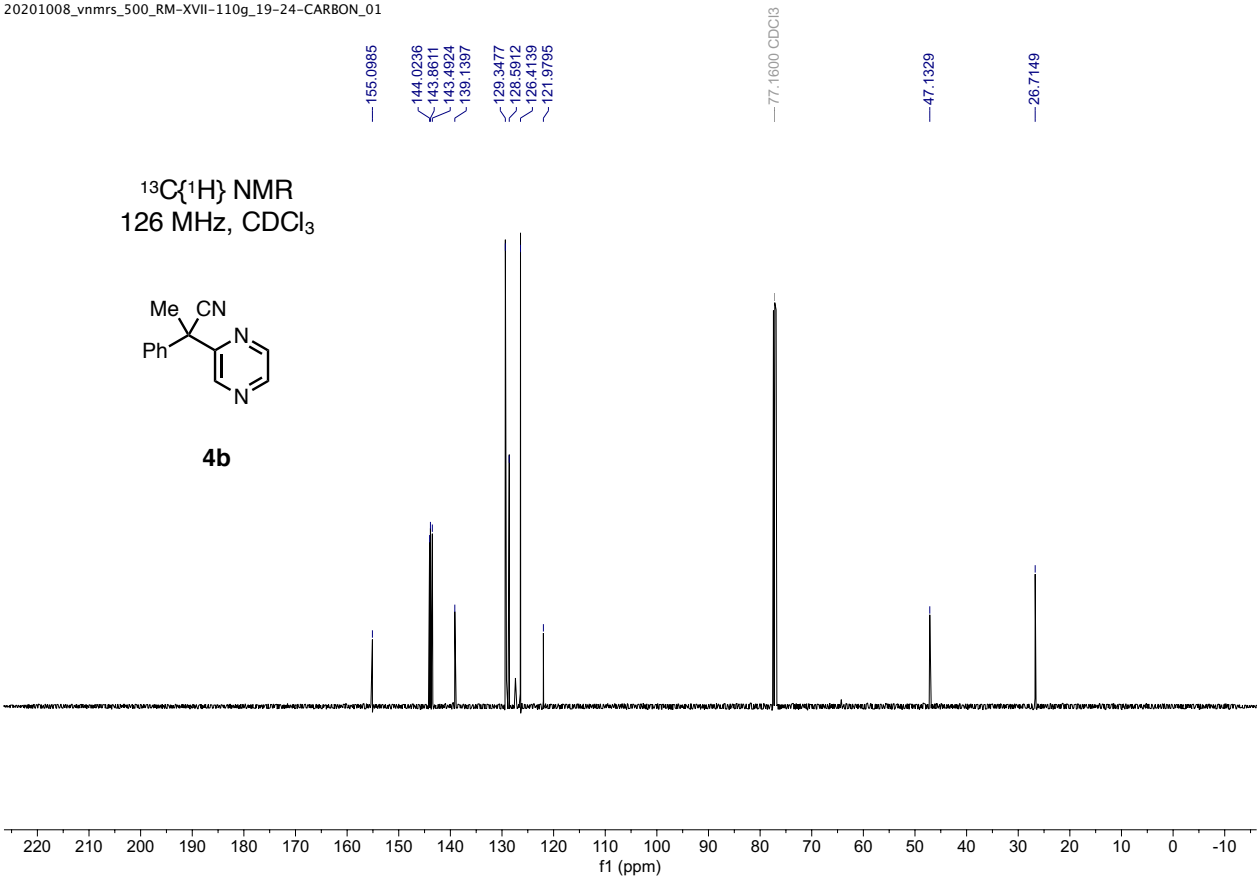
7.3844
7.3804
7.3785
7.3773
7.3761
7.3724
7.3697
7.3587
7.3570
7.3551
7.3524
7.3497
7.3471
7.3450
7.3439
7.3422
7.3397
7.3362
7.3350
7.3320
7.3304
7.3284
7.3232
7.3206
7.3181
7.2600 CDCl3
2.2034
1H NMR
500 MHz, CDCl3
Me
CN
Ph
N
N
4b
0.96
0.98
0.99
0.68
1.01
2.05
1.14
3.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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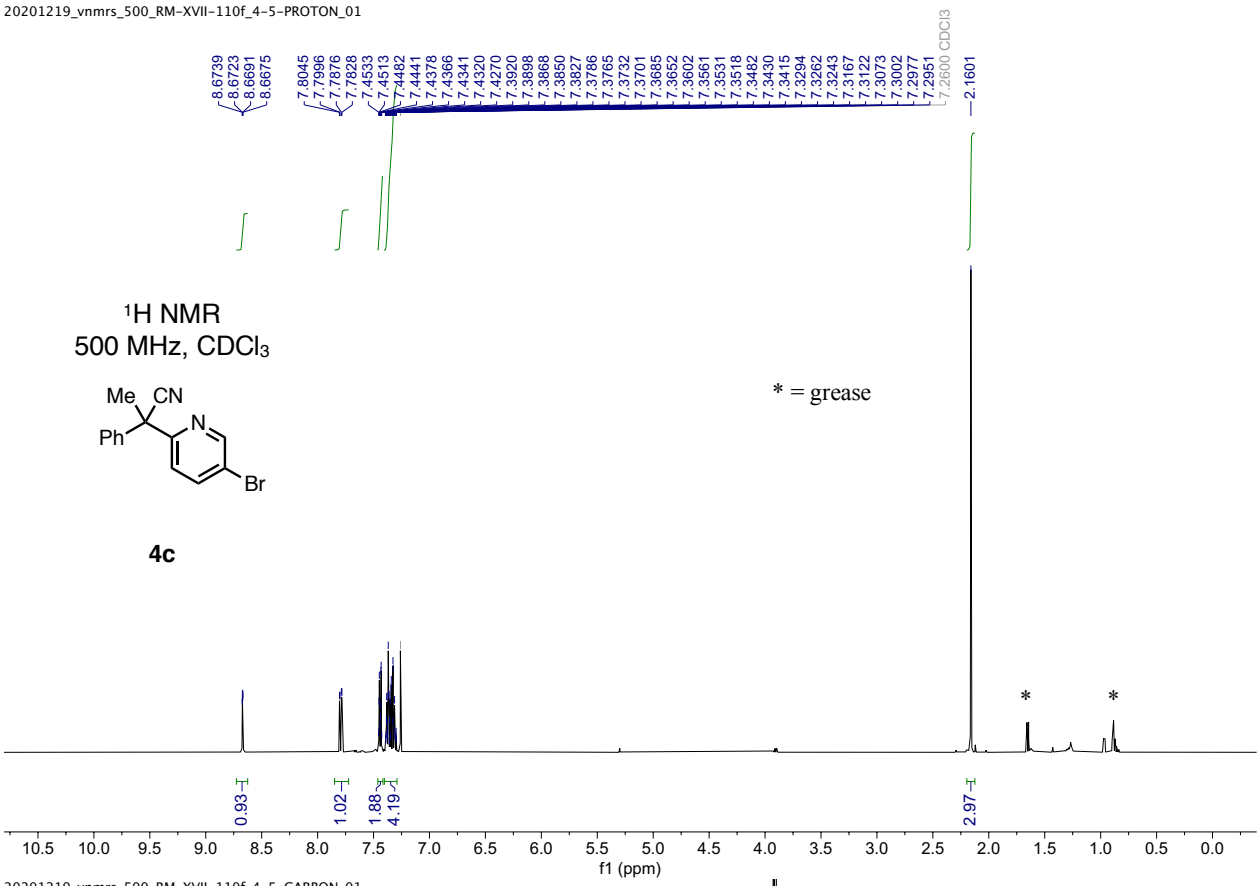
129.3477
128.5912
126.4139
121.9795
77.1600 CDCl3
47.1329
26.7149
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Ph
N
N
4b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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500 MHz, $CDCl_3$
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Ph
N
Br
4c
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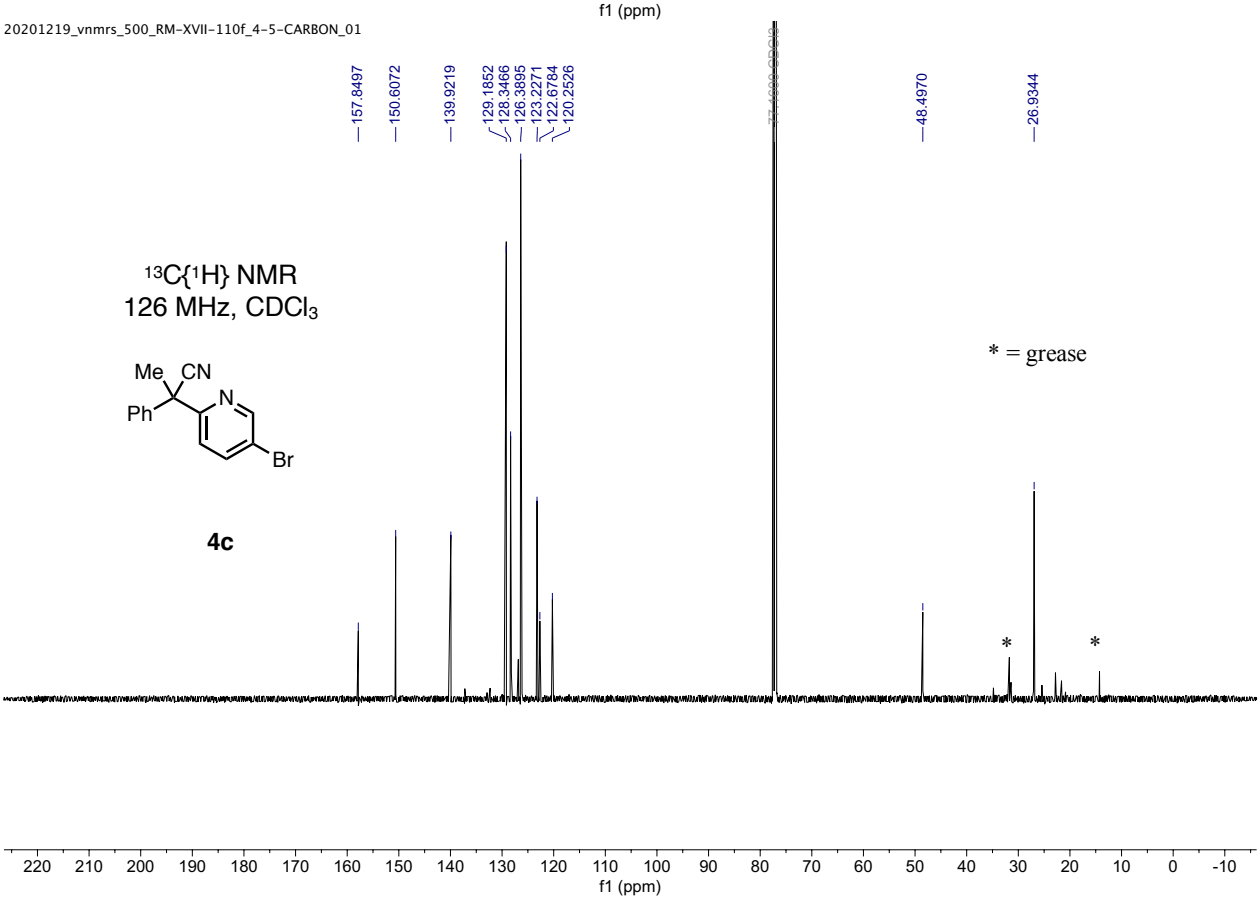
4.19
2.97
f1 (ppm)


20201219_vnmrs_500_RM-XVII-110f_4-5-CARBON_01
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126.3895
123.2271
122.6784
120.2526
48.4970
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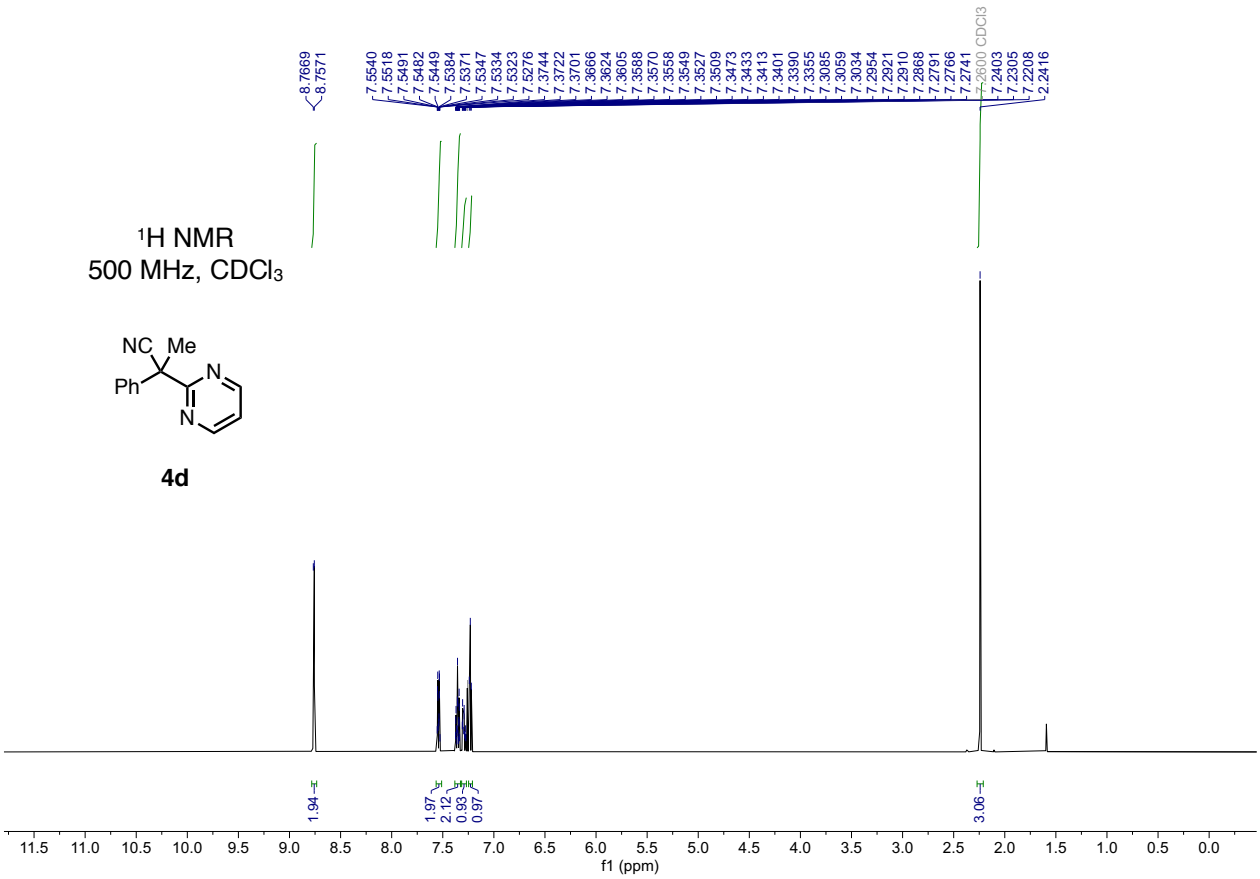
^{13}C{^{1}H} NMR
126 MHz, $CDCl_3$
Me CN
Ph
N
Br
4c
* = grease
f1 (ppm)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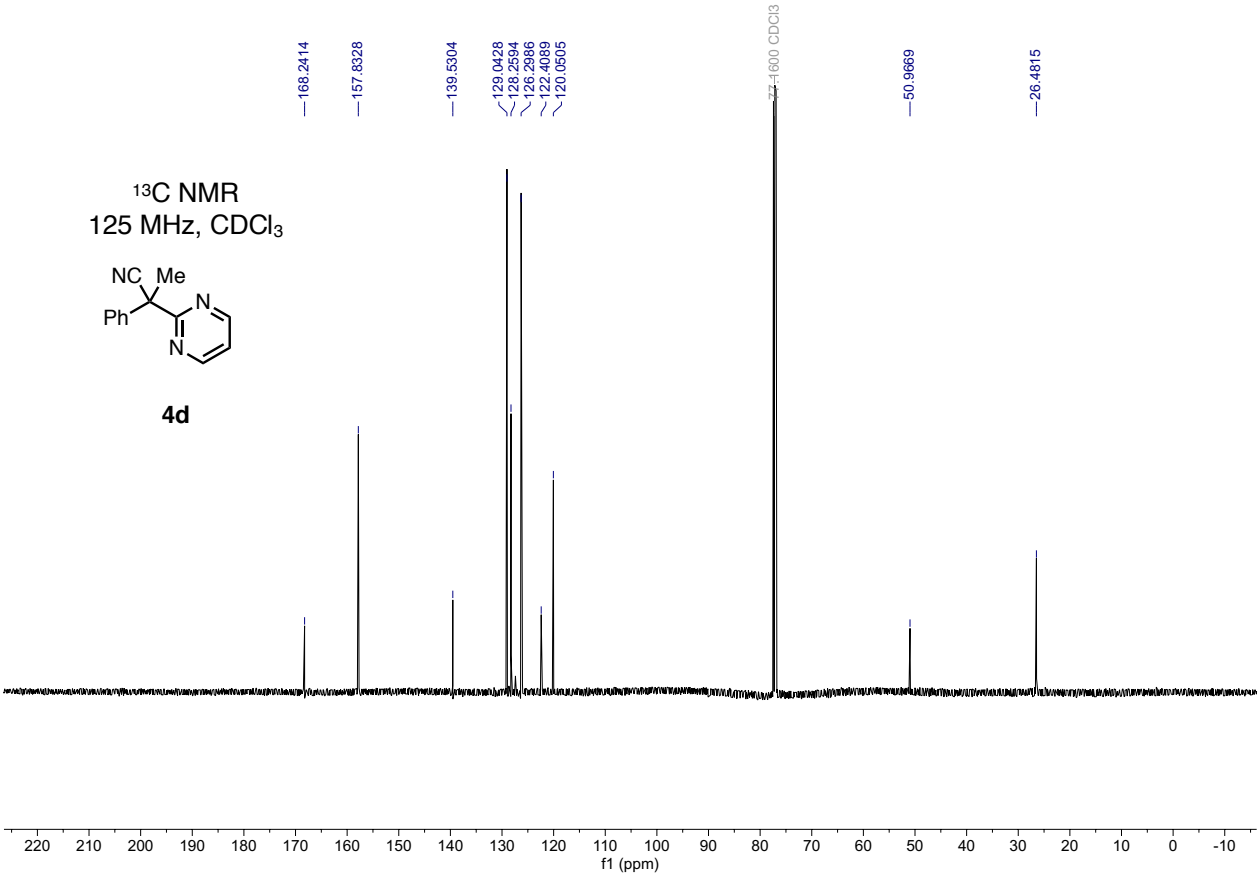
7.5371
7.5347
7.5334
7.5323
7.5276
7.3744
7.3722
7.3701
7.3666
7.3624
7.3605
7.3588
7.3570
7.3558
7.3549
7.3527
7.3509
7.3473
7.3433
7.3413
7.3401
7.3390
7.3355
7.3085
7.3059
7.3034
7.2954
7.2921
7.2910
7.2868
7.2791
7.2766
7.2741
7.2600 CDCl3
7.2403
7.2305
7.2208
2.2416
1H NMR
500 MHz, CDCl3
NC
Me
Ph
N
N
4d
1.94
1.97
2.12
0.93
0.97
3.06
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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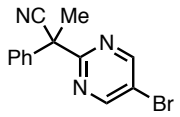
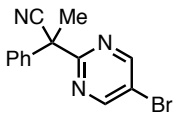
50.9669
26.4815
13C NMR
125 MHz, CDCl3
NC
Me
Ph
N
N
4d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

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

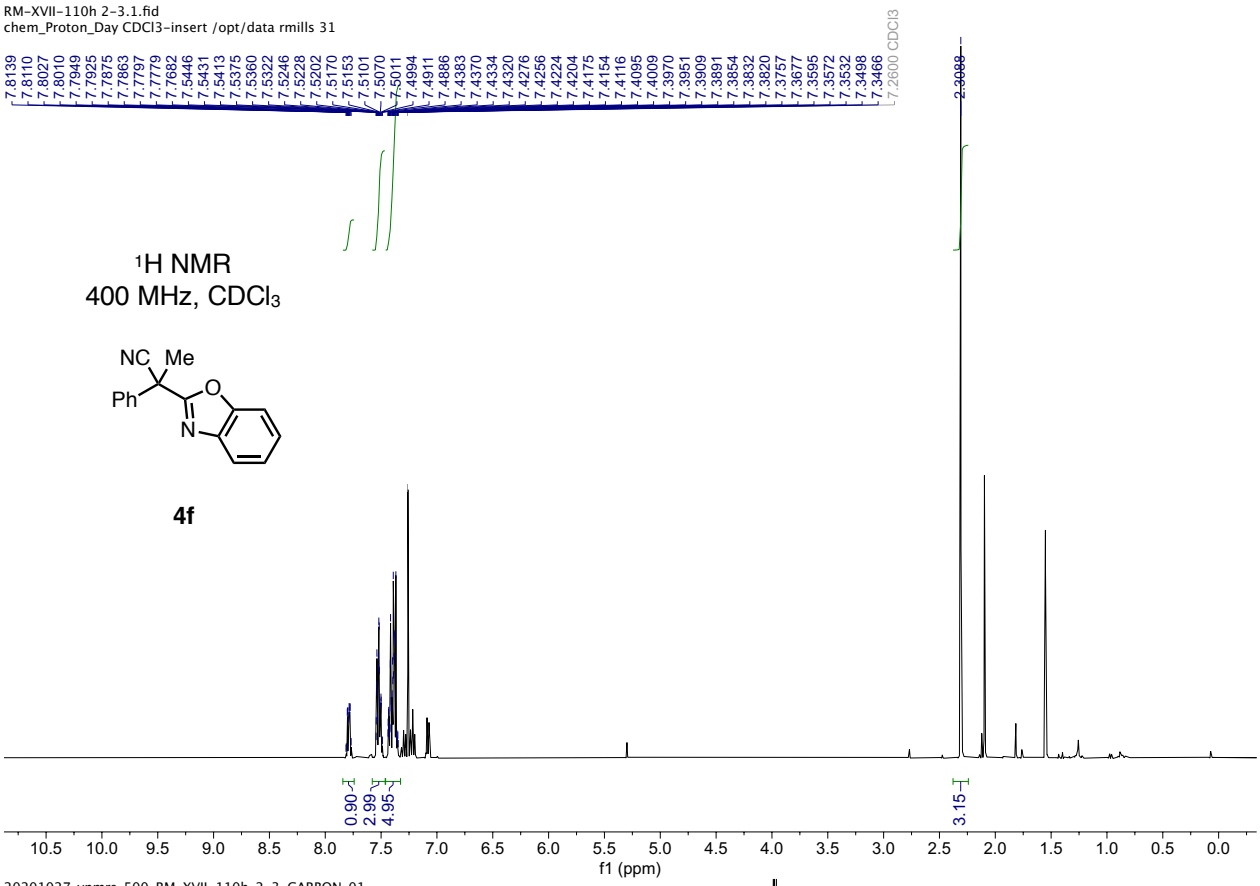


4e

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



4e


RM-XVII-110h 2-3.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 31
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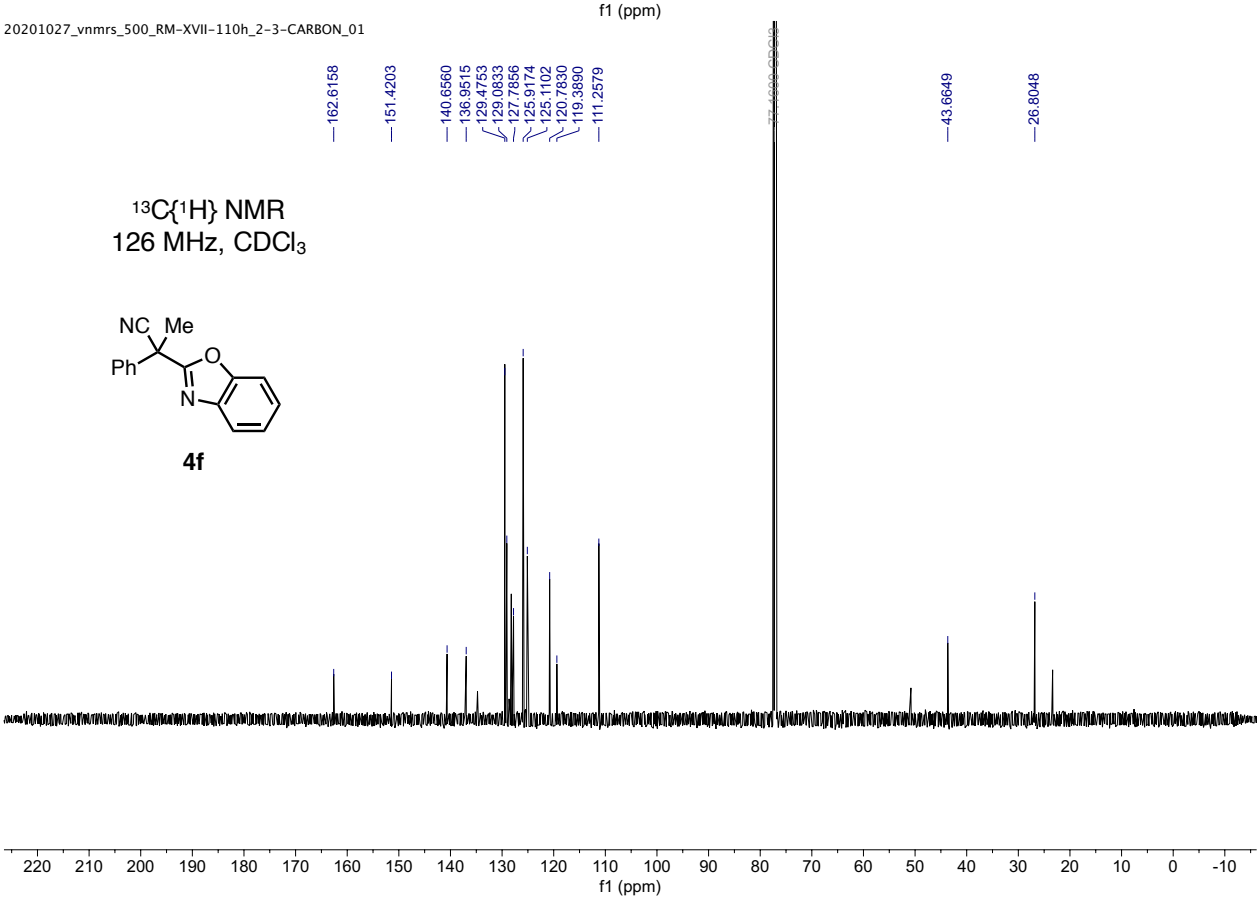
NC Me
Ph
O
N
4f
0.90
2.99
4.95
3.15
f1 (ppm)


20201027_vnmrs_500_RM-XVII-110h_2-3-CARBON_01
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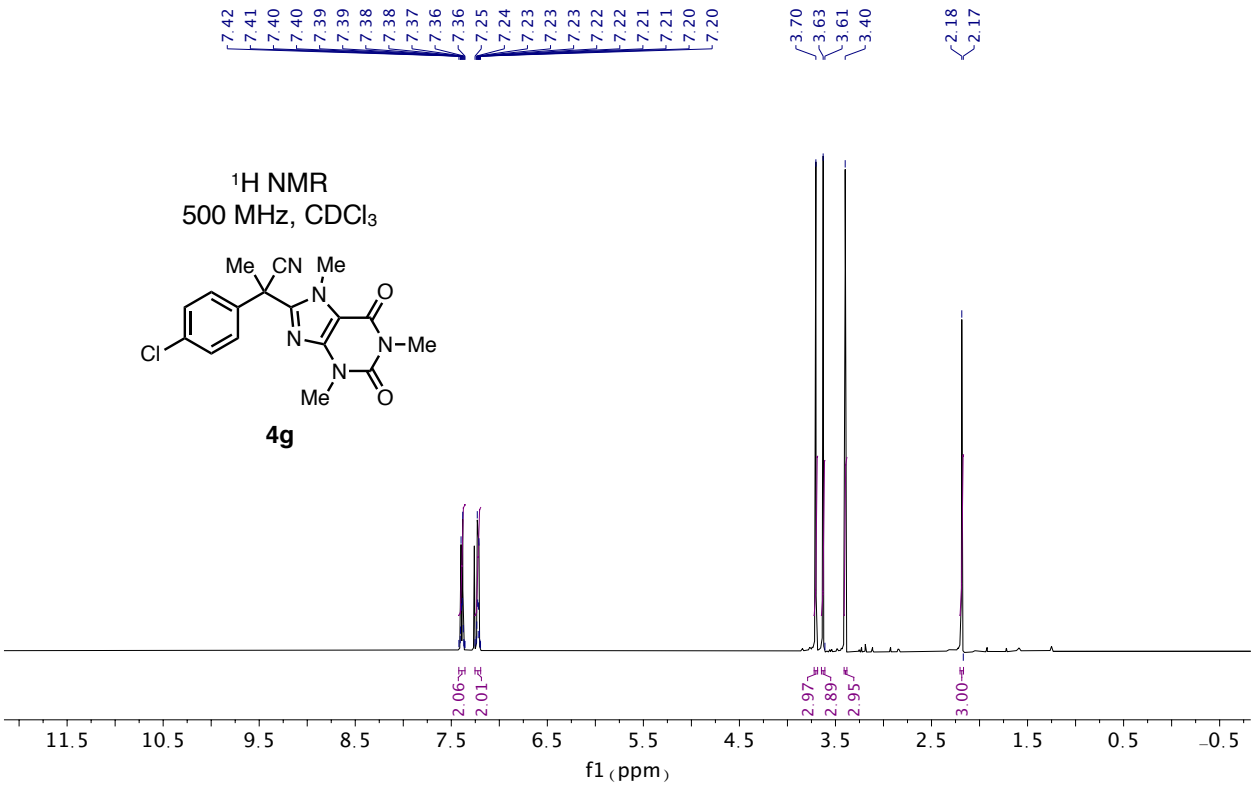
129.0833
127.7856
125.9174
125.1102
120.7830
119.3890
111.2579
43.6649
26.8048
^{13}C{^{1}H} NMR
126 MHz, $CDCl_3$
NC Me
Ph
O
N
4f
f1 (ppm)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7.24
7.23
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.20
3.70
3.63
3.61
3.40
2.18
2.17
1H NMR
500 MHz, CDCl3
Me
CN
Me
Cl
N
N
O
N–Me
N
Me
O
4g
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2.01
2.97
2.89
2.95
3.00
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
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2.5
1.5
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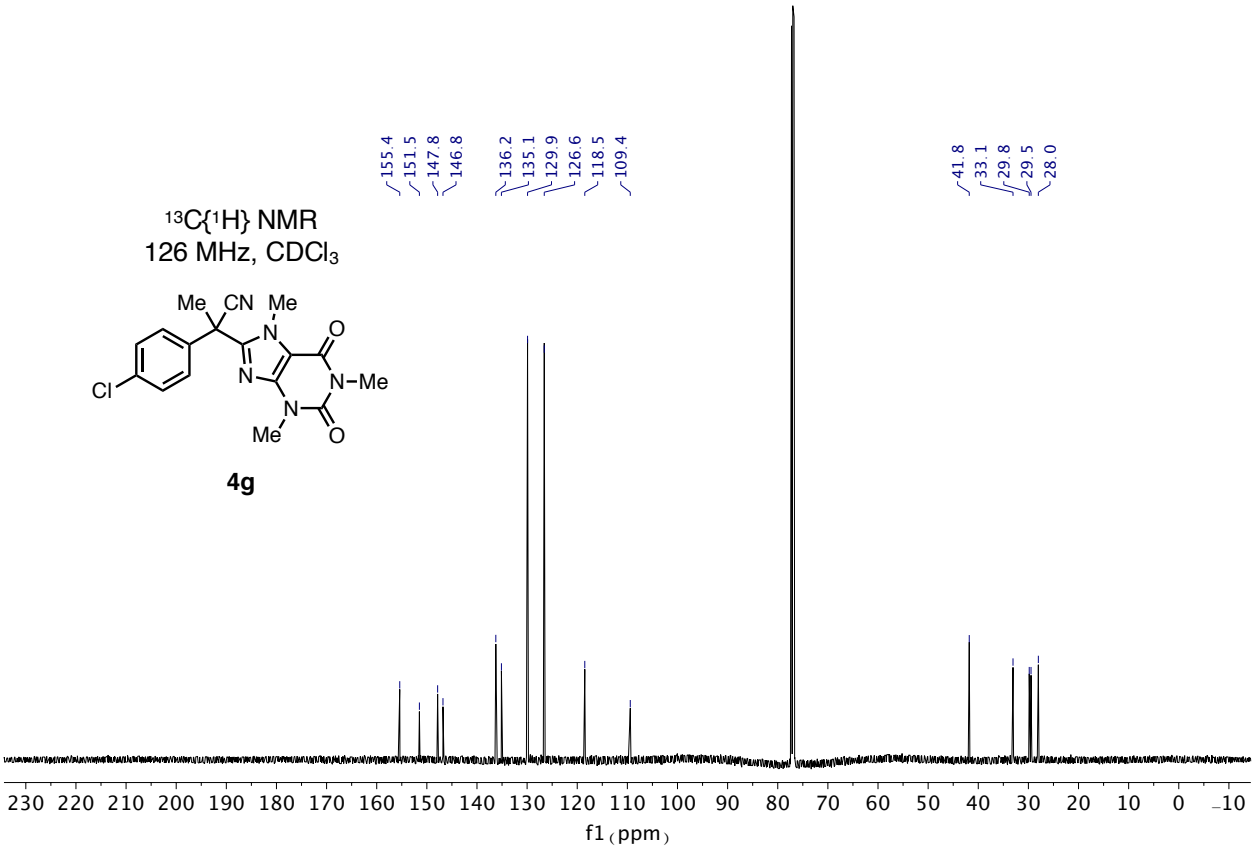
f1 (ppm)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146.8
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135.1
129.9
126.6
118.5
109.4
41.8
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29.8
29.5
28.0
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Me
Cl
N
N
O
N–Me
N
Me
O
4g
230
220
210
200
190
180
170
160
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100
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40
30
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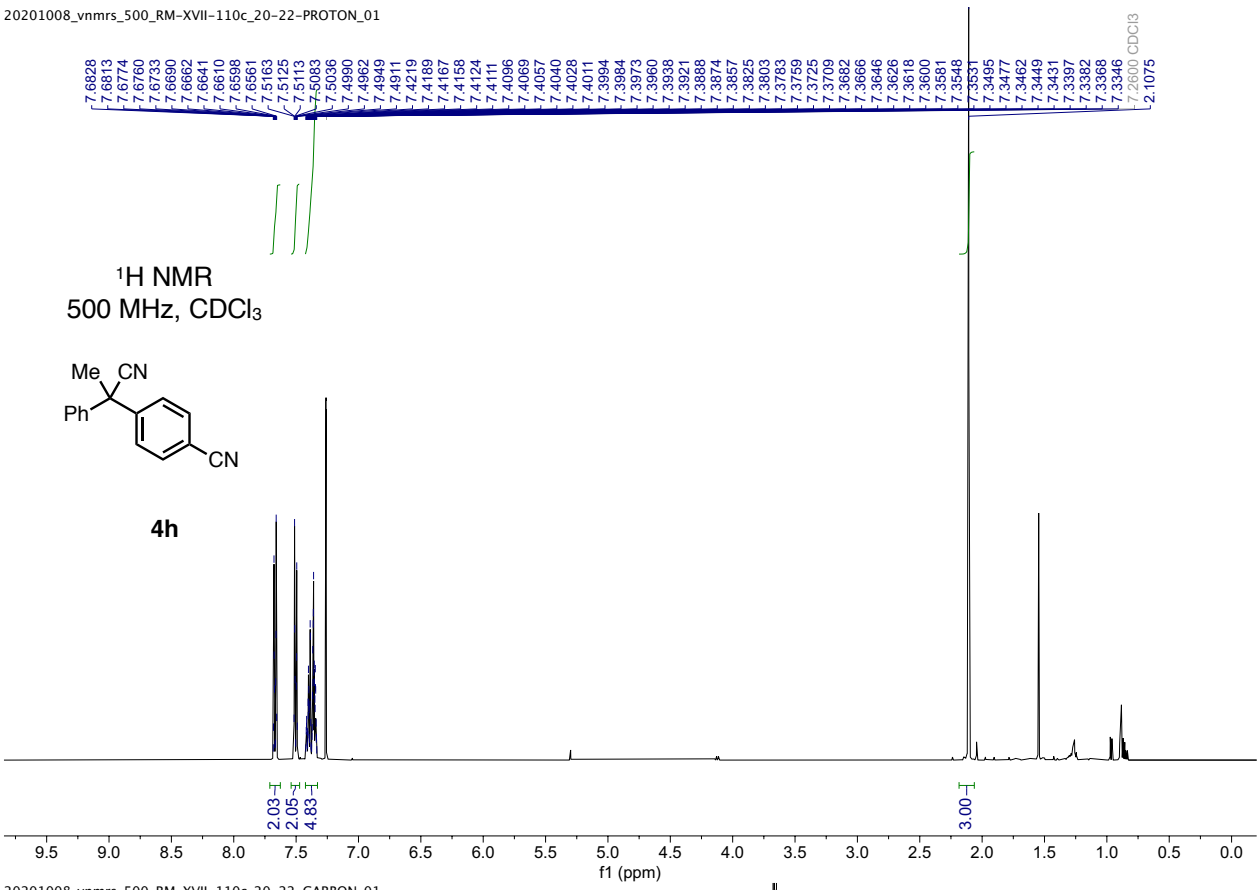
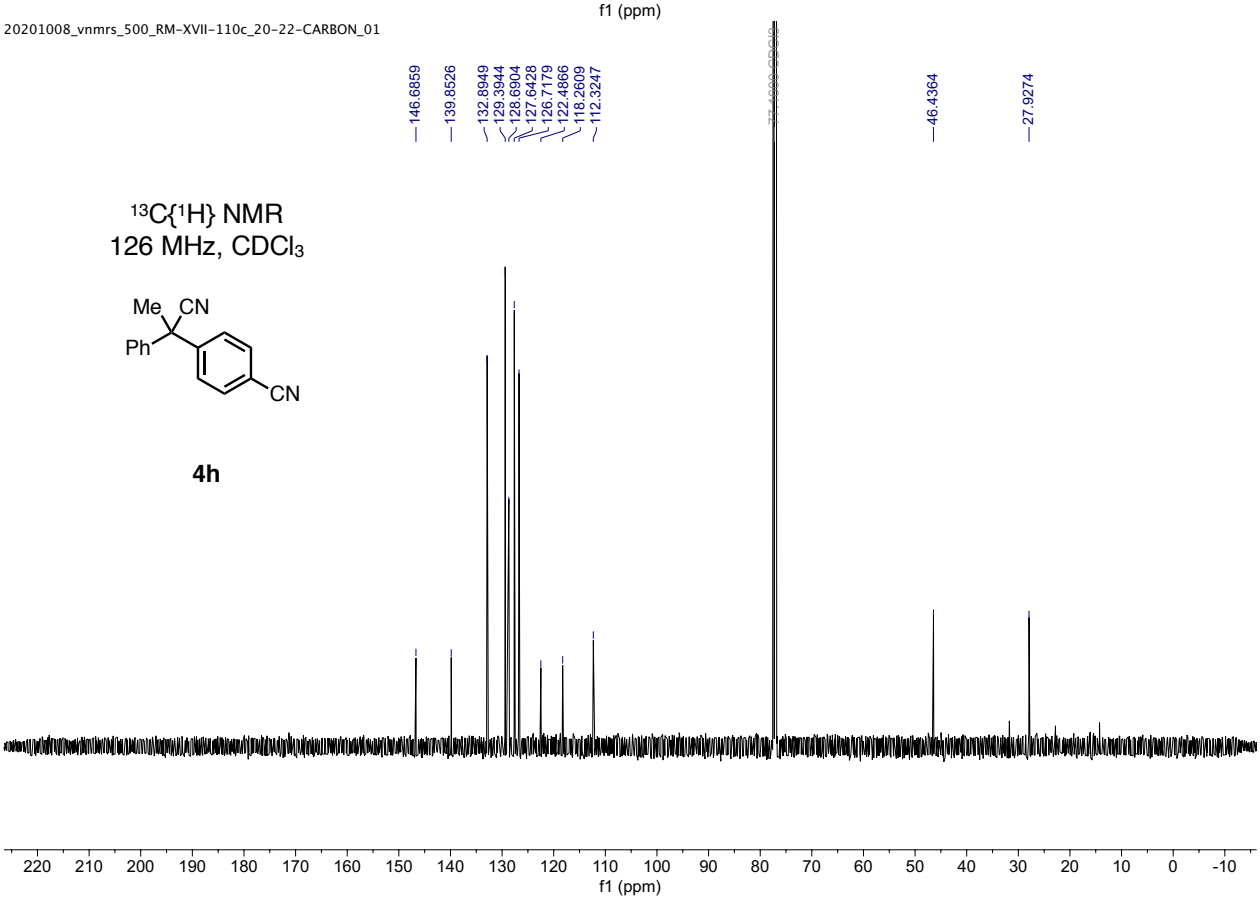
–10
f1 (ppm)


20201008_vnmrs_500_RM-XVII-110c_20-22-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Me CN
Ph
CN
4h
2.03
2.05
4.83
3.00
f1 (ppm)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122.4866
118.2609
112.3247
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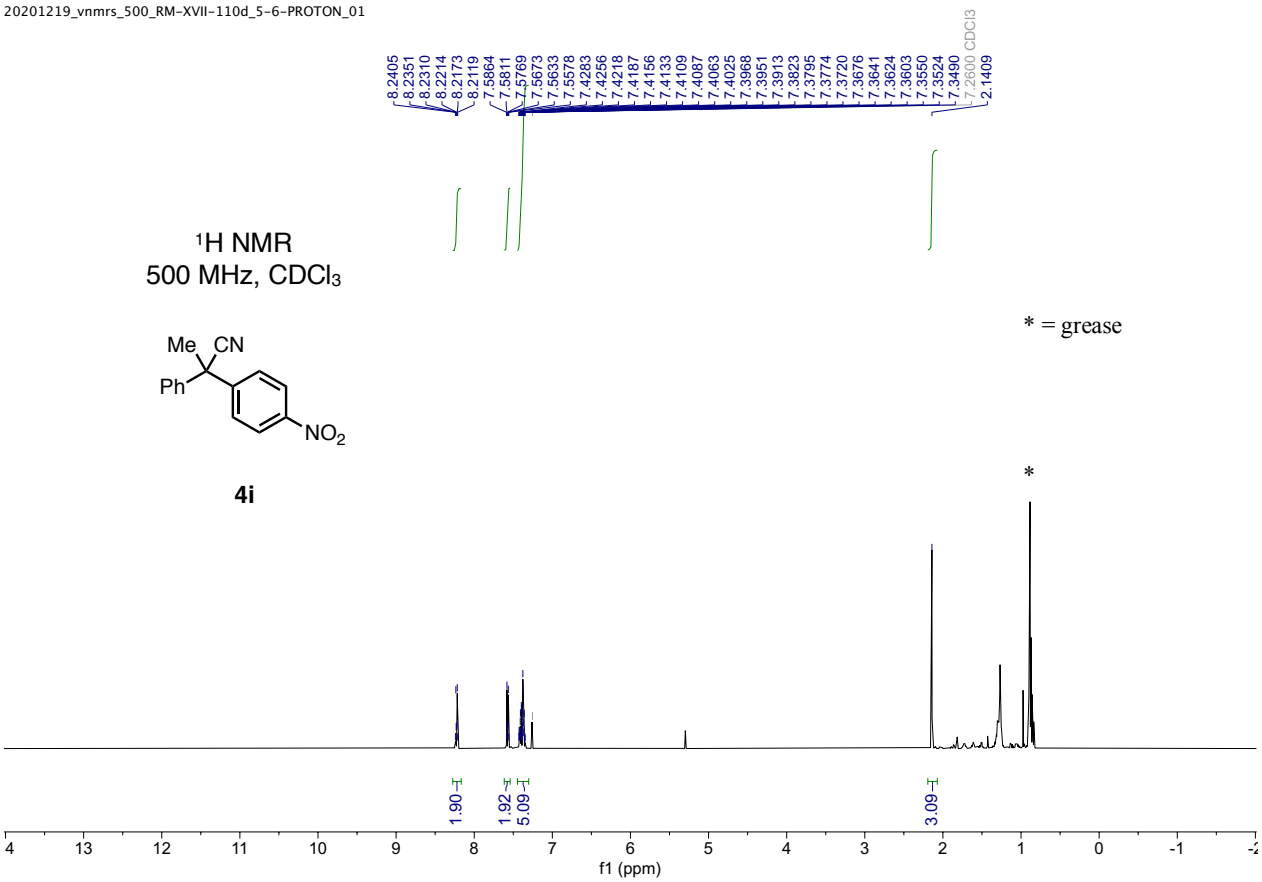
27.9274
^{13}C{^{1}H} NMR
126 MHz, $CDCl_3$
Me CN
Ph
CN
4h
f1 (ppm)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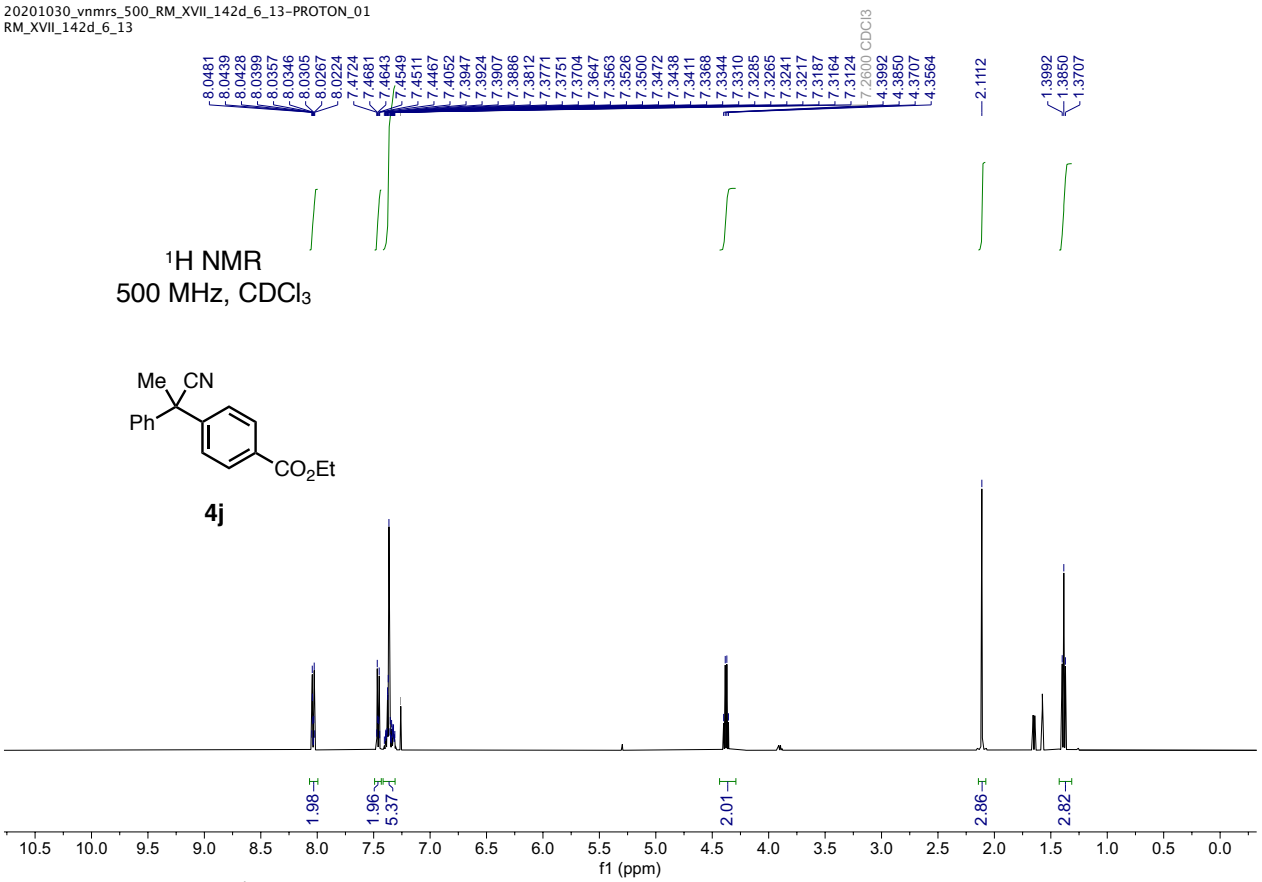
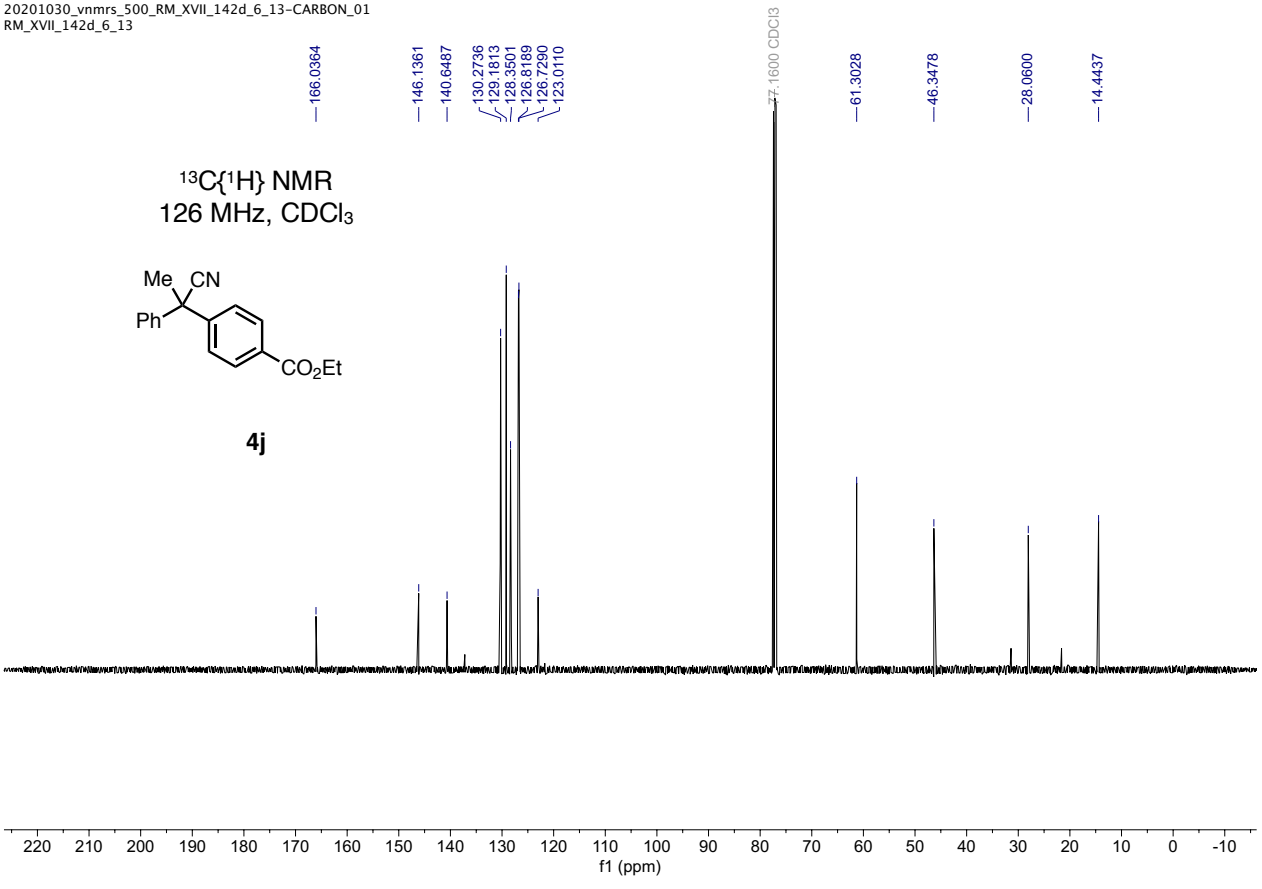
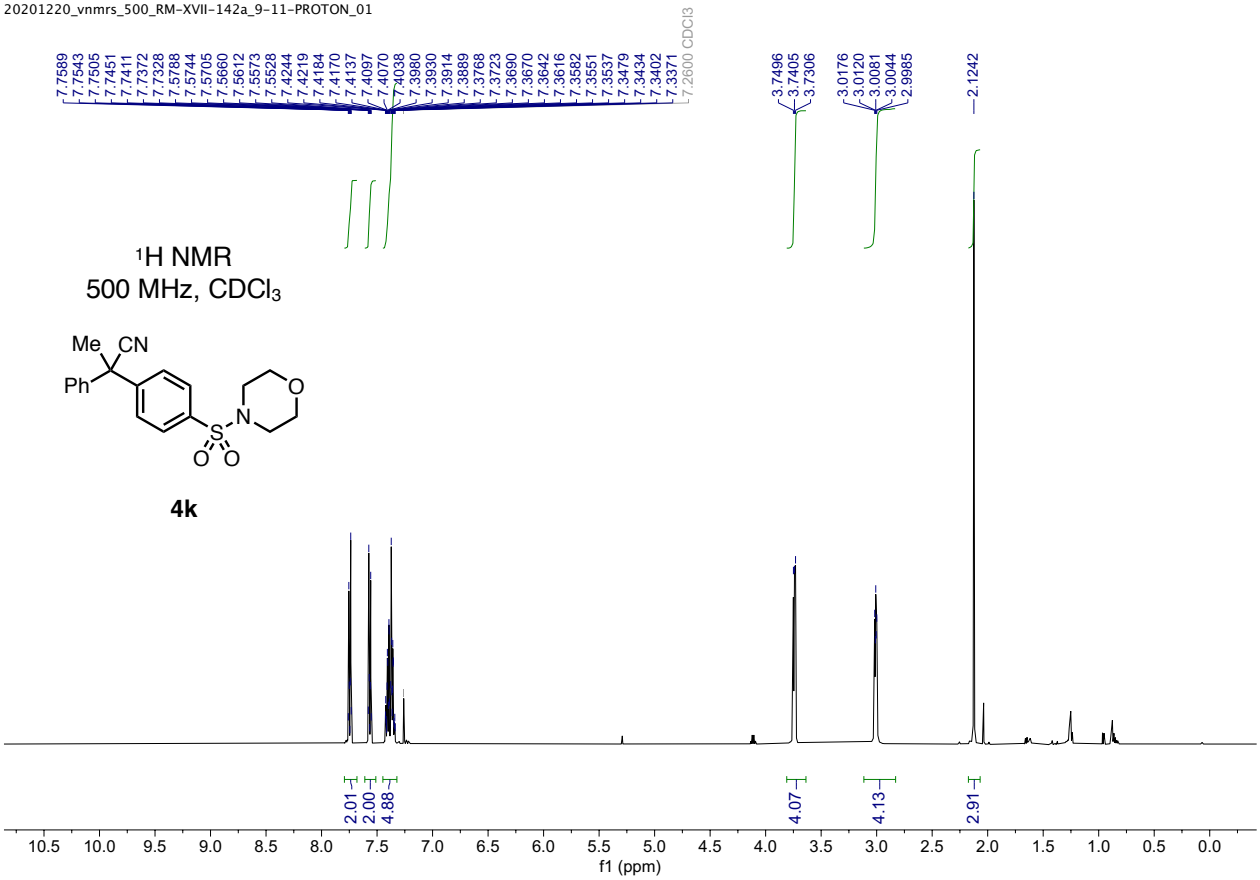
2.1409
1H NMR
500 MHz, CDCl3
* = grease
Me
CN
Ph
NO2
4i
*
1.90
1.92
5.09
3.09
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


20201030_vnmrs_500_RM_XVII_142d_6_13-PROTON_01
RM_XVII_142d_6_13
^{1}H NMR
500 MHz, $CDCl_3$
Me CN
Ph
CO_2Et
4j
f1 (ppm)


20201030_vnmrs_500_RM_XVII_142d_6_13-CARBON_01
RM_XVII_142d_6_13
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
Me CN
Ph
CO_2Et
4j
f1 (ppm)

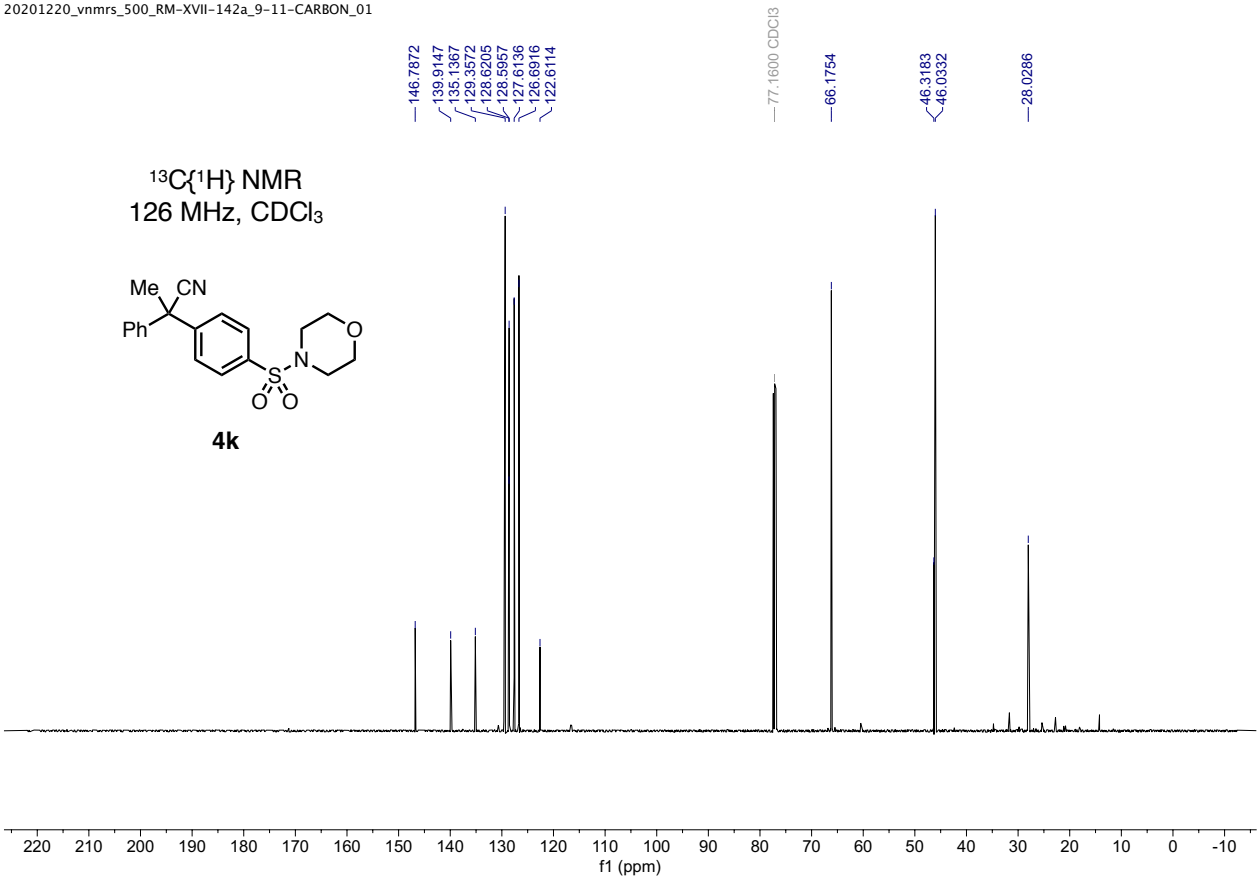
20201220_vnmrs_500_RM-XVII-142a_9-11-PROTON_01



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

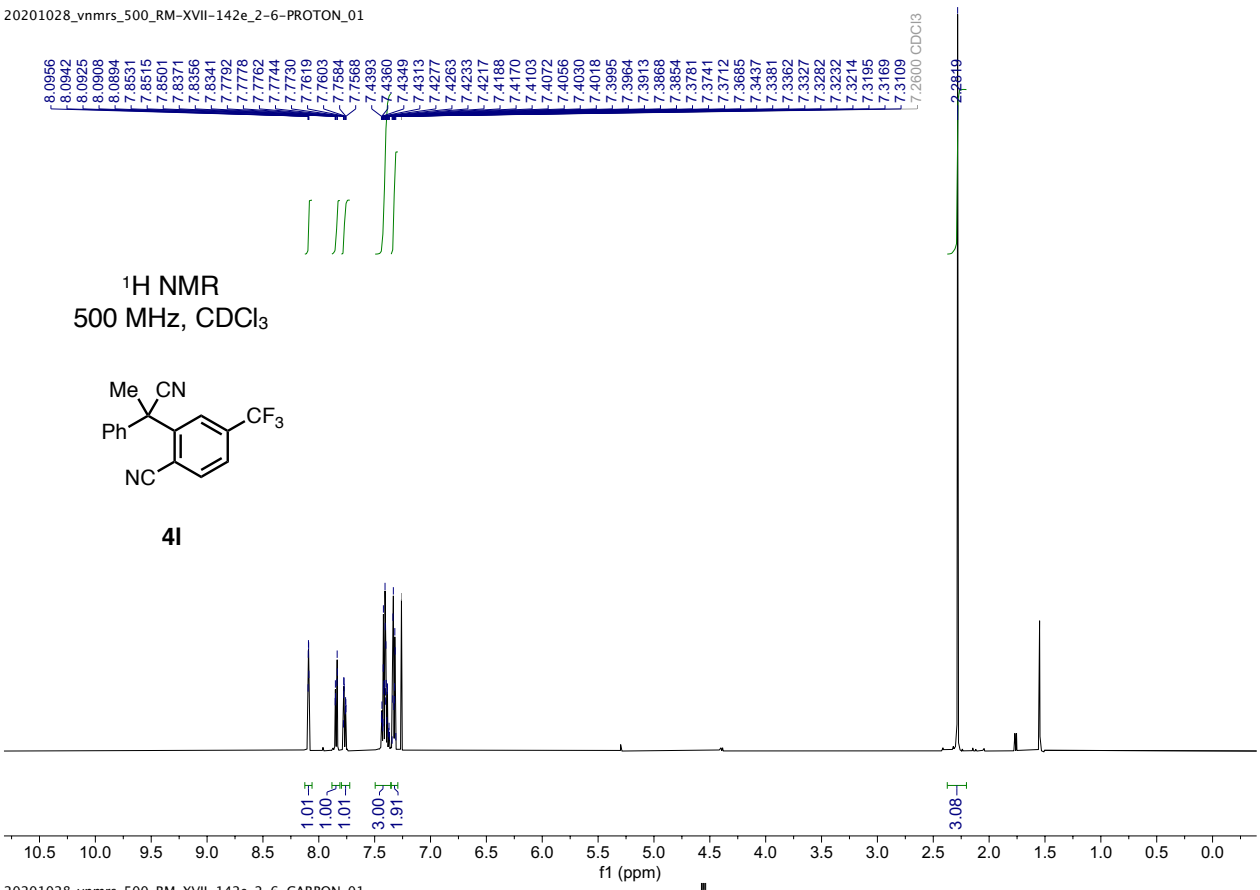
4k

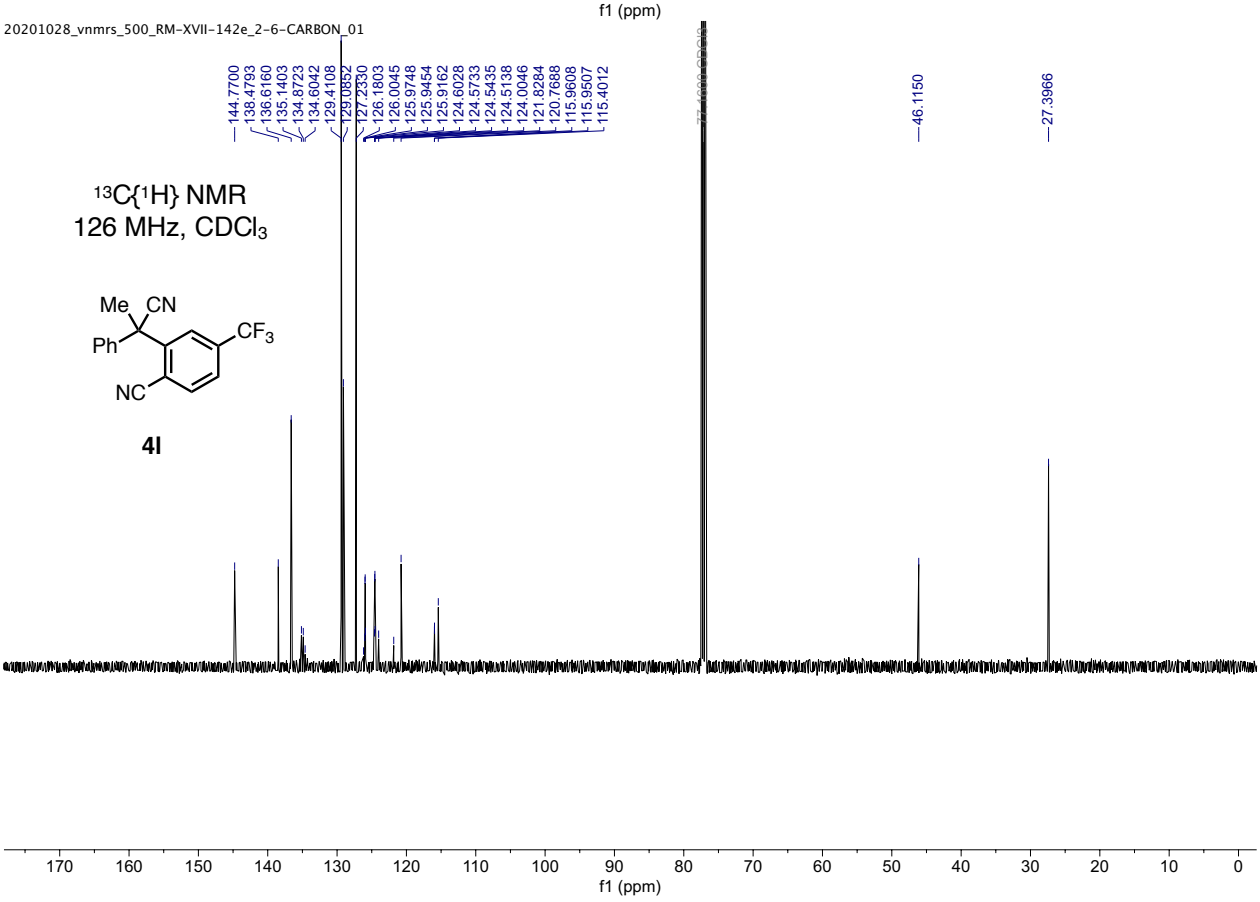
20201220_vnmrs_500_RM-XVII-142a_9-11-CARBON_01



$^{13}C\{^{1}H\}$ NMR
126 MHz, $CDCl_3$

4k

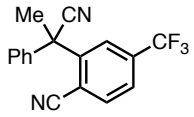

20201028_vnmrs_500_RM-XVII-142e_2-6-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Me CN
Ph
CF_3
NC
4l
1.01
1.00
1.01
3.00
1.91
3.08
f1 (ppm)


20201028_vnmrs_500_RM-XVII-142e_2-6-CARBON_01
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
Me CN
Ph
CF_3
NC
4l
46.1150
27.3966
f1 (ppm)

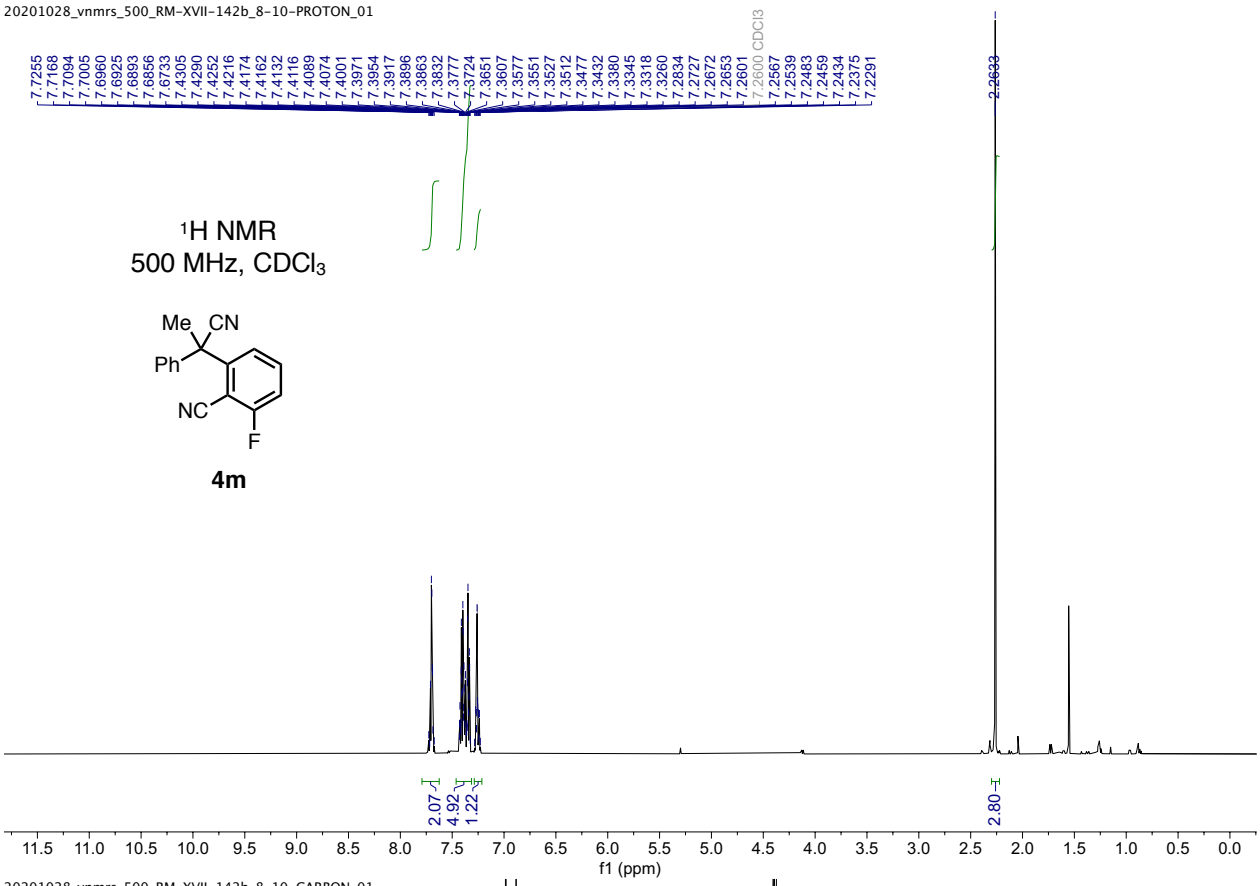
RM-XVII-142e 2-6.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 3

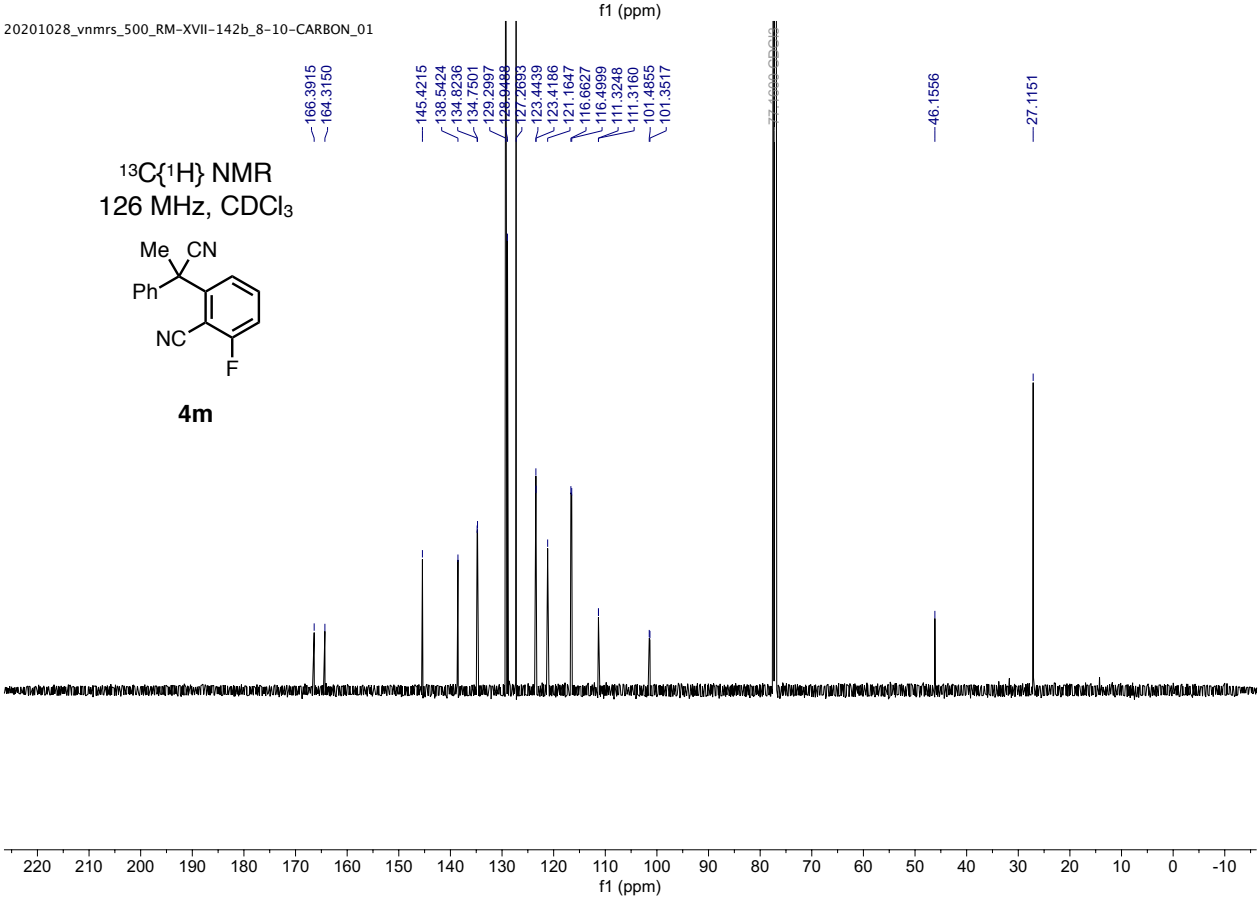
-63.3069

^{19}F NMR
376 MHz, $CDCl_3$



4l

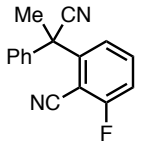

20201028_vnmrs_500_RM-XVII-142b_8-10-PROTON_01
7.7255
7.7168
7.7094
7.7005
7.6960
7.6925
7.6893
7.6856
7.6733
7.4305
7.4290
7.4252
7.4216
7.4174
7.4162
7.4132
7.4116
7.4089
7.4074
7.4001
7.3971
7.3954
7.3917
7.3896
7.3863
7.3832
7.3777
7.3724
7.3651
7.3607
7.3577
7.3551
7.3527
7.3512
7.3477
7.3432
7.3380
7.3345
7.3318
7.3260
7.2834
7.2727
7.2672
7.2653
7.2601
7.2600 CDCl3
7.2567
7.2539
7.2483
7.2459
7.2434
7.2375
7.2291
2.2833
1H NMR
500 MHz, CDCl3
Me
CN
Ph
NC
F
4m
2.07
4.92
1.22
2.80
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


20201028_vnmrs_500_RM-XVII-142b_8-10-CARBON_01
166.3915
164.3150
145.4215
138.5424
134.8236
134.7501
129.2997
128.9488
127.2693
123.4439
123.4186
121.1647
116.6627
116.4999
111.3248
111.3160
101.4855
101.3517
77.4088
77.0969
76.7849
46.1556
27.1151
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Ph
NC
F
4m
220
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)

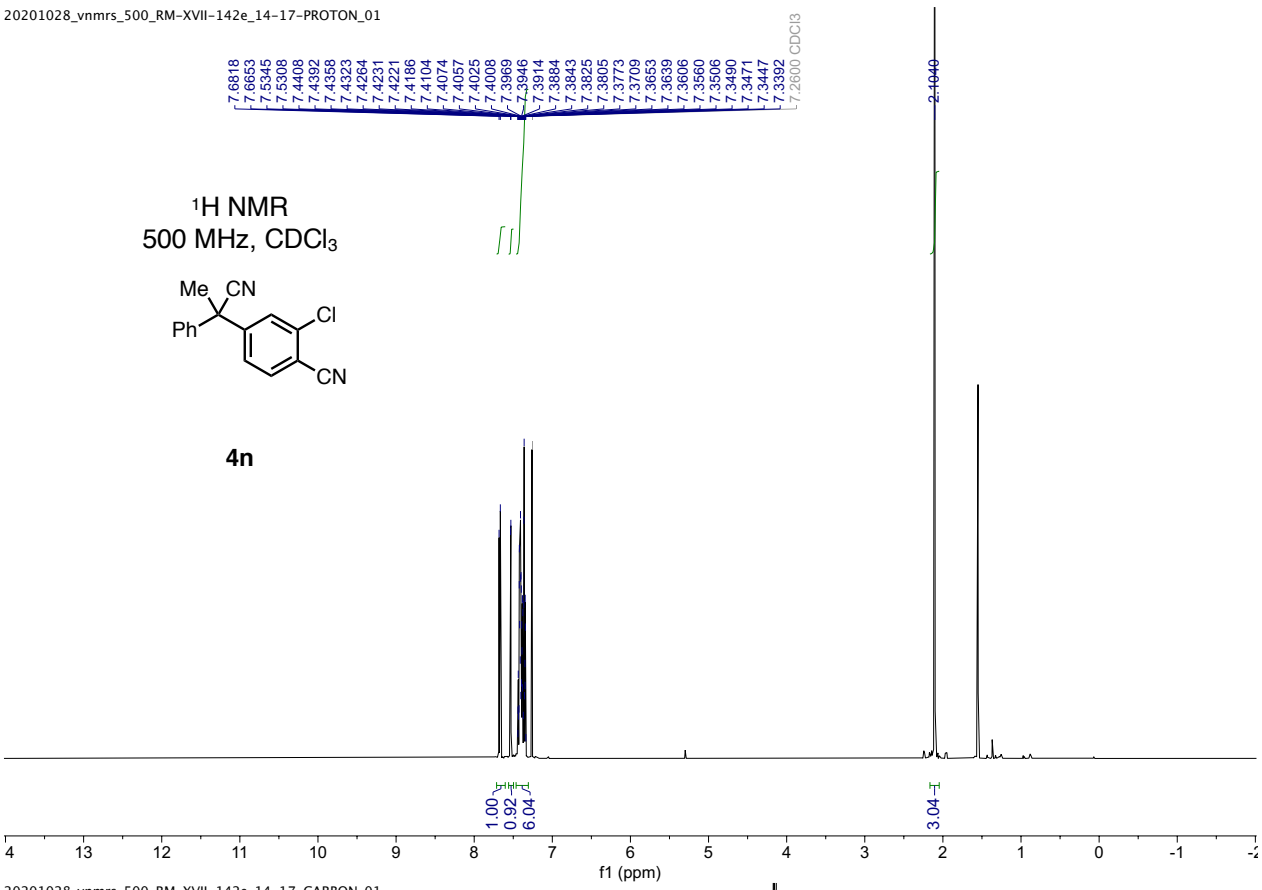
RM-XVII-142b 8-10.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 2

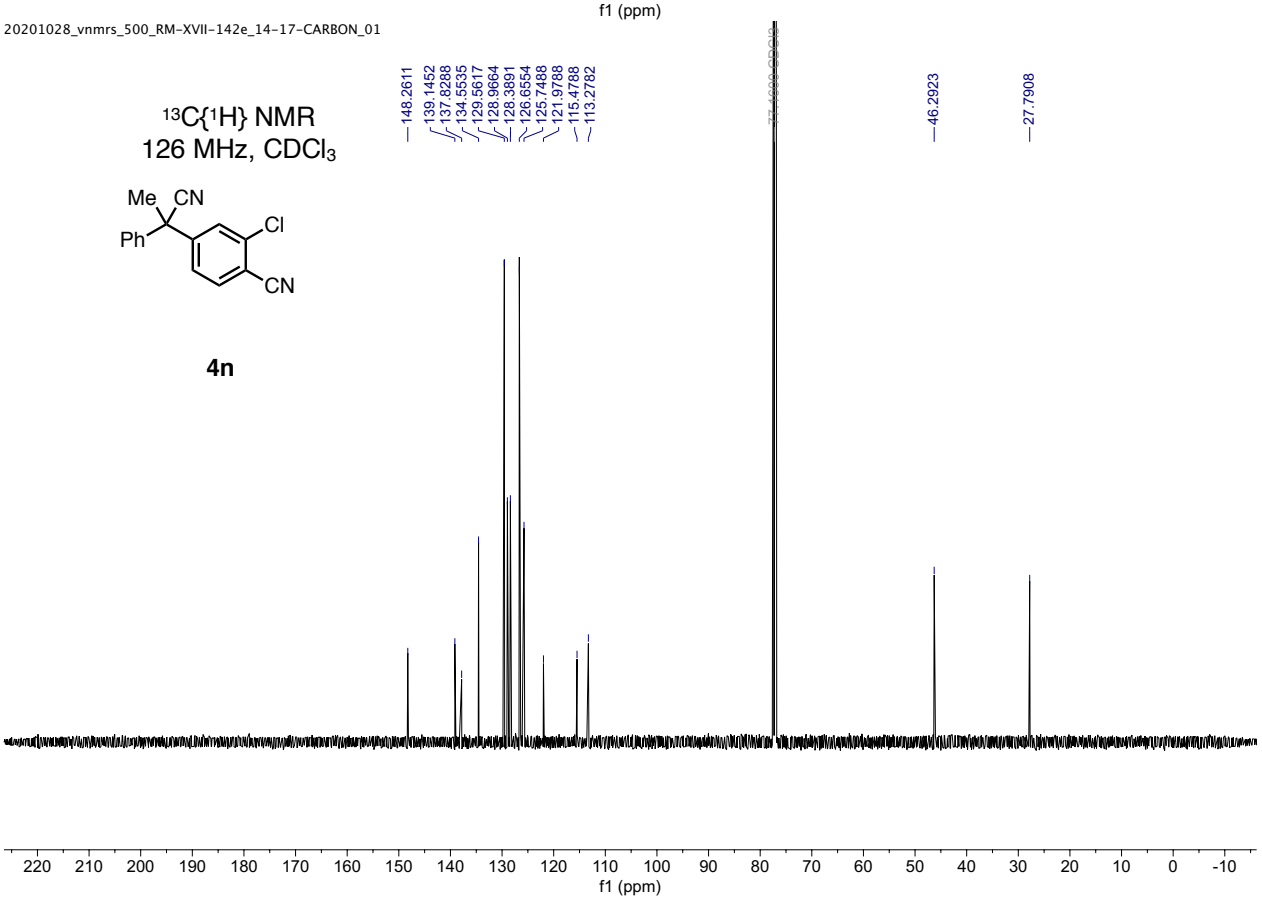
-102.6642
-102.6760
-102.6883
-102.6973

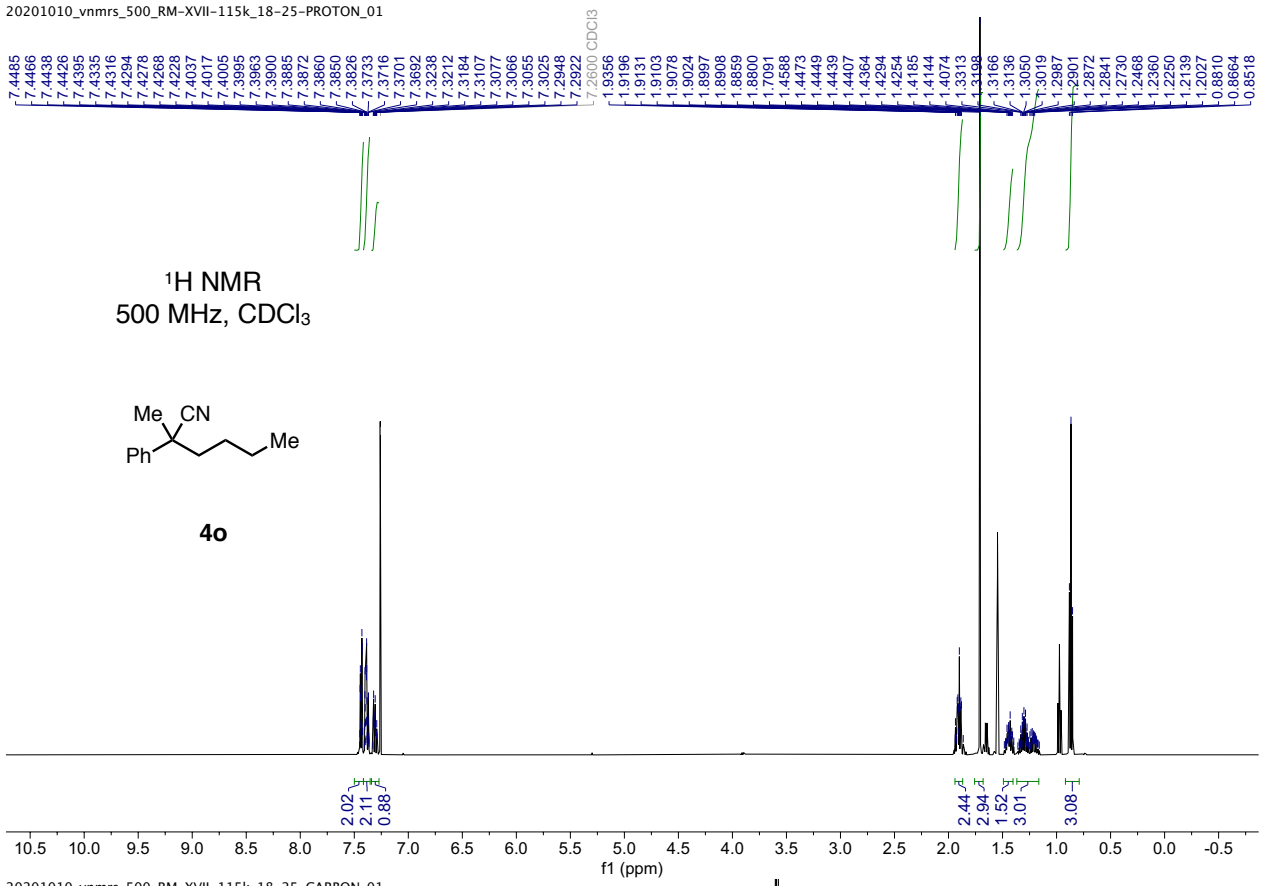
^{19}F NMR
376 MHz, $CDCl_3$

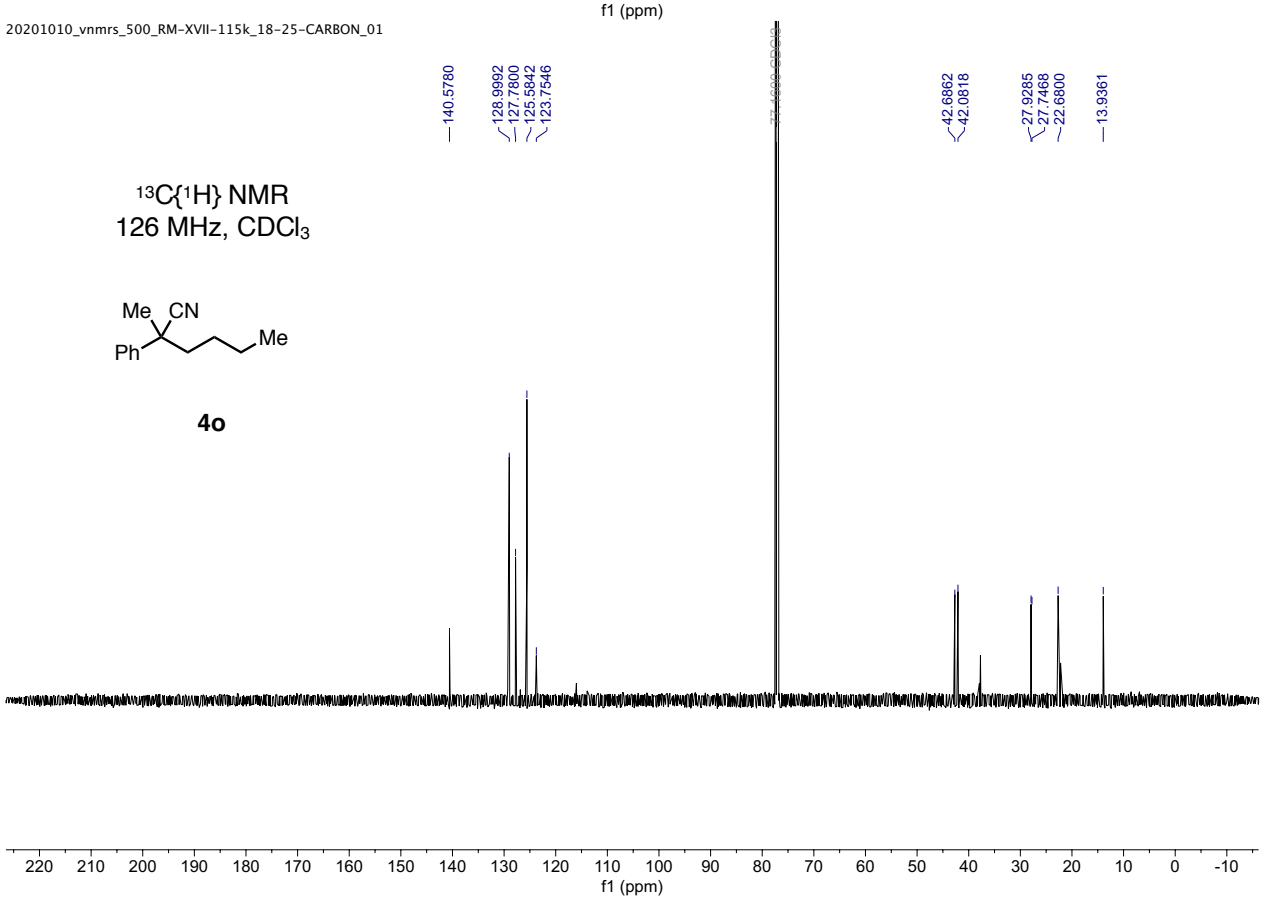


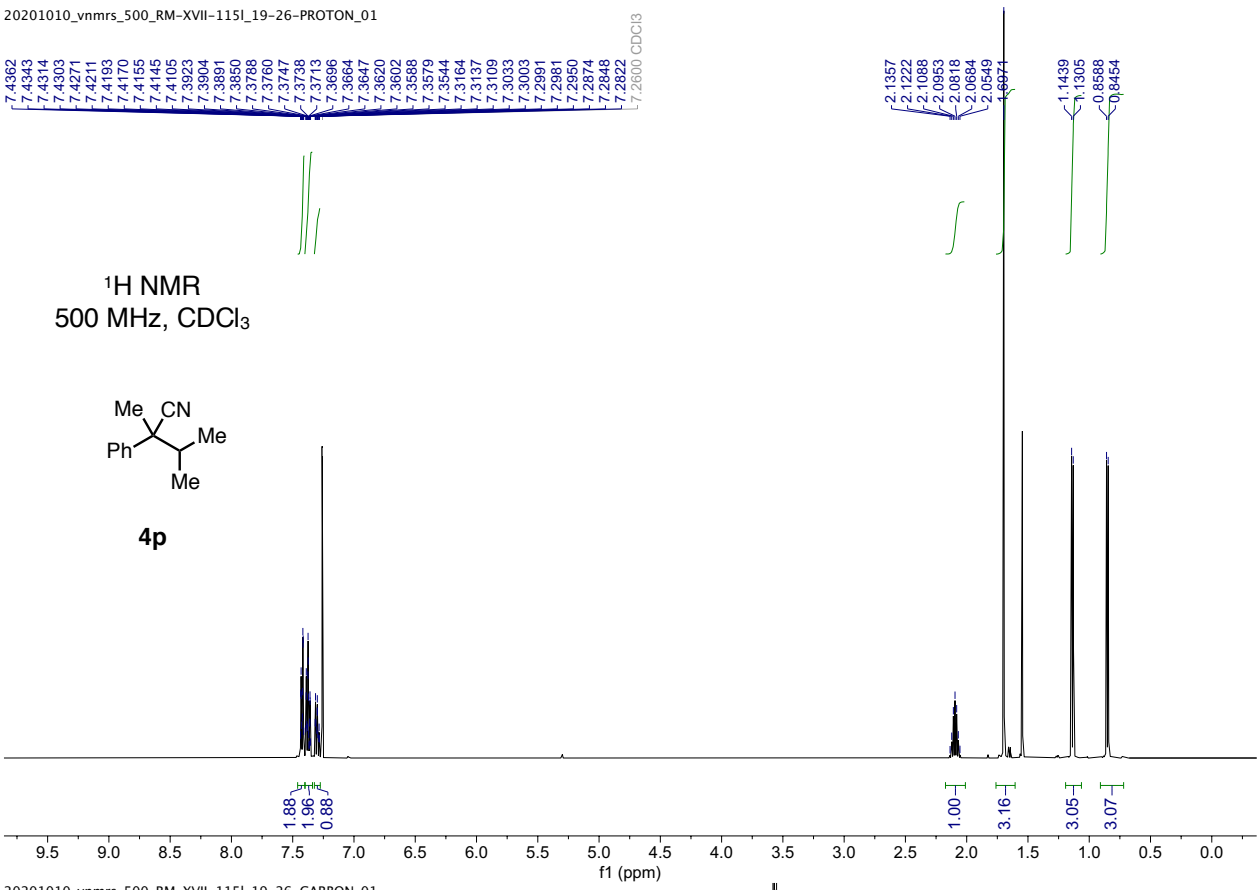
4m

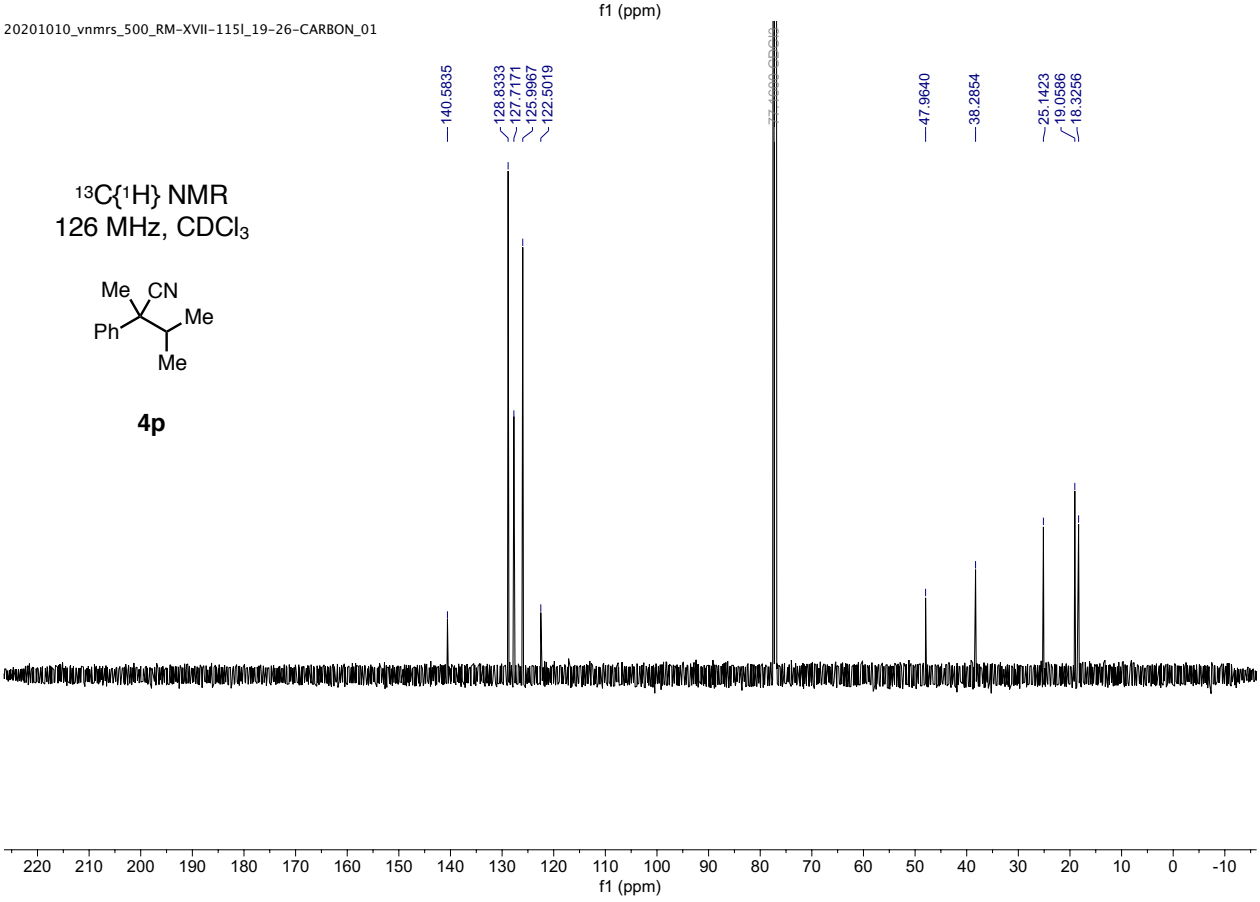

20201028_vnmrs_500_RM-XVII-142e_14-17-PROTON_01
7.6818
7.6653
7.5345
7.5308
7.4408
7.4392
7.4358
7.4323
7.4264
7.4231
7.4221
7.4186
7.4104
7.4074
7.4057
7.4025
7.4008
7.3969
7.3946
7.3914
7.3884
7.3843
7.3825
7.3805
7.3773
7.3709
7.3653
7.3639
7.3606
7.3560
7.3506
7.3490
7.3471
7.3447
7.3392
7.2600 CDCl3
2.1040
1H NMR
500 MHz, CDCl3
Me
CN
Ph
Cl
CN
4n
1.00
0.92
6.04
3.04
f1 (ppm)

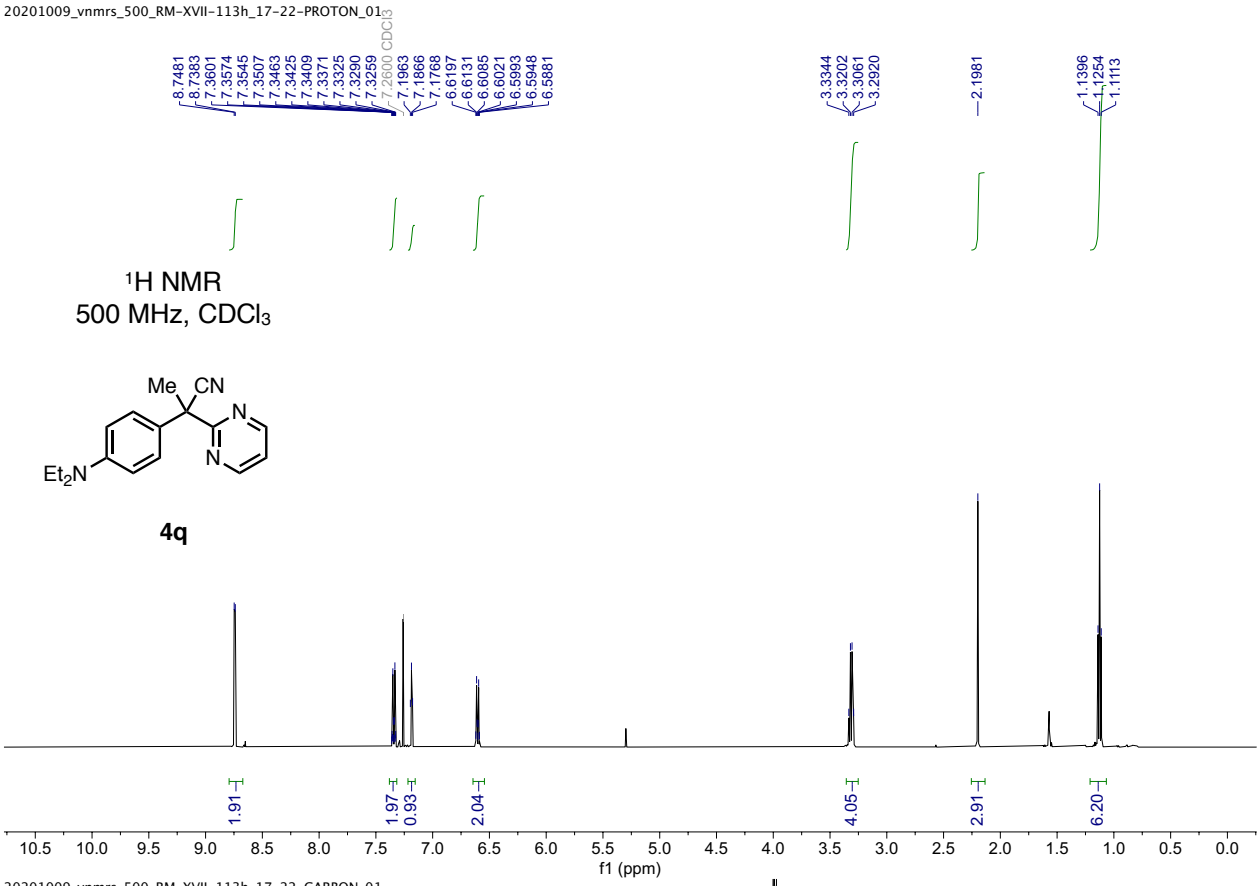

20201028_vnmrs_500_RM-XVII-142e_14-17-CARBON_01
148.2611
139.1452
137.8288
134.5535
129.5617
128.9664
128.3891
126.6554
125.7488
121.9788
115.4788
113.2782
77.4000 CDCl3
46.2923
27.7908
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Ph
Cl
CN
4n
f1 (ppm)

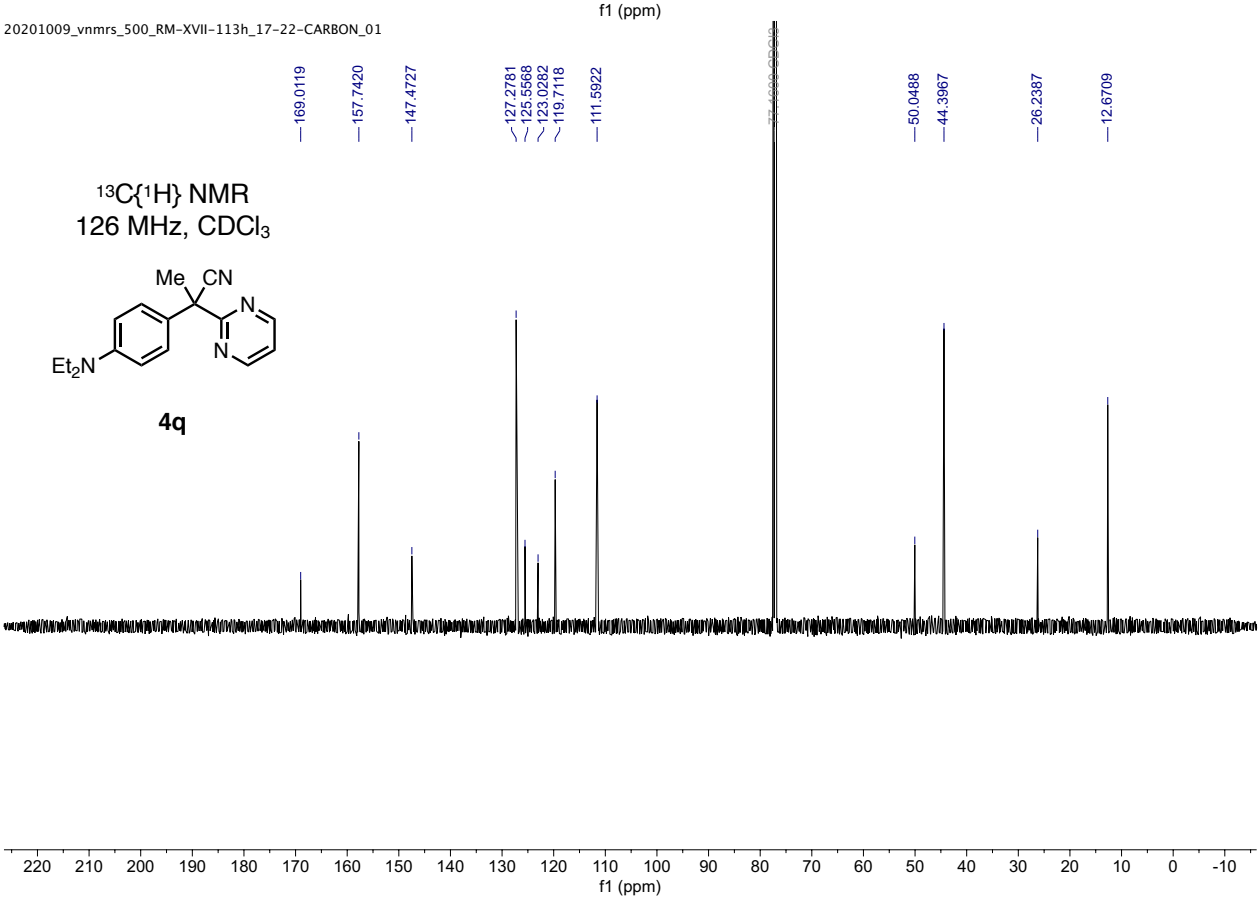

20201010_vnmrs_500_RM-XVII-115k_18-25-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Me CN
Ph
Me
4o
2.02
2.11
0.88
2.44
2.94
1.52
3.01
3.08
f1 (ppm)


20201010_vnmrs_500_RM-XVII-115k_18-25-CARBON_01
140.5780
128.9992
127.7800
125.5842
123.7546
42.6862
42.0818
27.9285
27.7468
22.6800
13.9361
^{13}C{^{1}H} NMR
126 MHz, $CDCl_3$
Me CN
Ph
Me
4o
f1 (ppm)


20201010_vnmrs_500_RM-XVII-115I_19-26-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Me CN
Ph
Me
Me
4p
1.88
1.96
0.88
1.00
3.16
3.05
3.07
f1 (ppm)

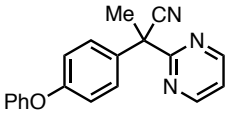

20201010_vnmrs_500_RM-XVII-115I_19-26-CARBON_01
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
Me CN
Ph
Me
Me
4p
140.5835
128.8333
127.7171
125.9967
122.5019
47.9640
38.2854
25.1423
19.0586
18.3296
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113h_17-22-PROTON_01
8.7481
8.7383
7.3601
7.3574
7.3545
7.3507
7.3463
7.3425
7.3409
7.3371
7.3325
7.3290
7.3259
7.2600 CDCl3
7.1963
7.1866
7.1768
6.6197
6.6131
6.6085
6.6021
6.5993
6.5948
6.5881
3.3344
3.3202
3.3061
3.2920
2.1981
1.1396
1.1254
1.1113
1H NMR
500 MHz, CDCl3
Me
CN
N
N
Et2N
4q
1.91
1.97
0.93
2.04
4.05
2.91
6.20
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

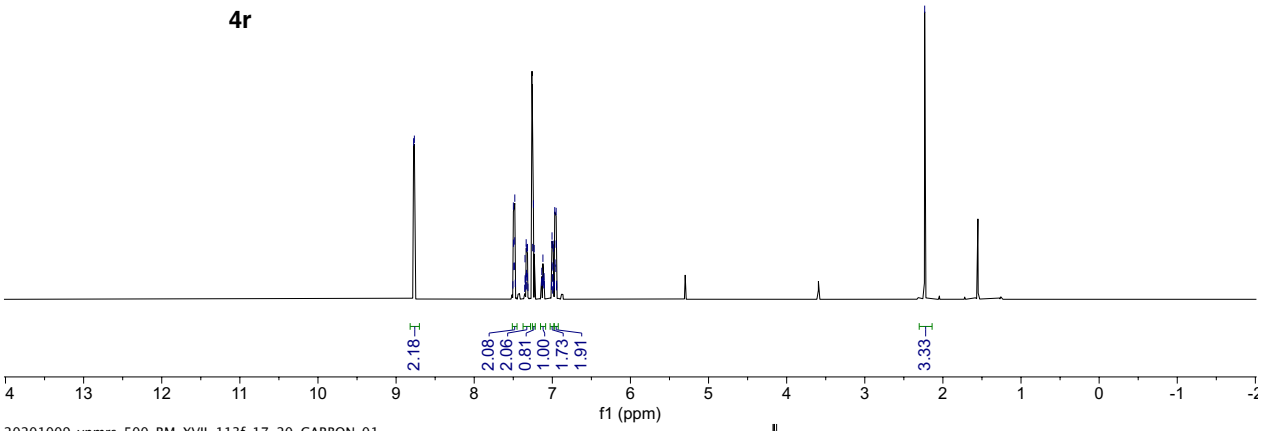

20201009_vnmrs_500_RM-XVII-113h_17-22-CARBON_01
169.0119
157.7420
147.4727
127.2781
125.5568
123.0282
119.7118
111.5922
77.4088 CDCl3
50.0488
44.3967
26.2387
12.6709
13C{1H} NMR
126 MHz, CDCl3
Me
CN
N
N
Et2N
4q
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

20201009_vnmrs_500_RM-XVII-113f_17-20-PROTON_01

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

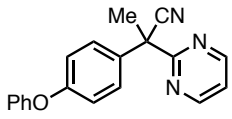


4r

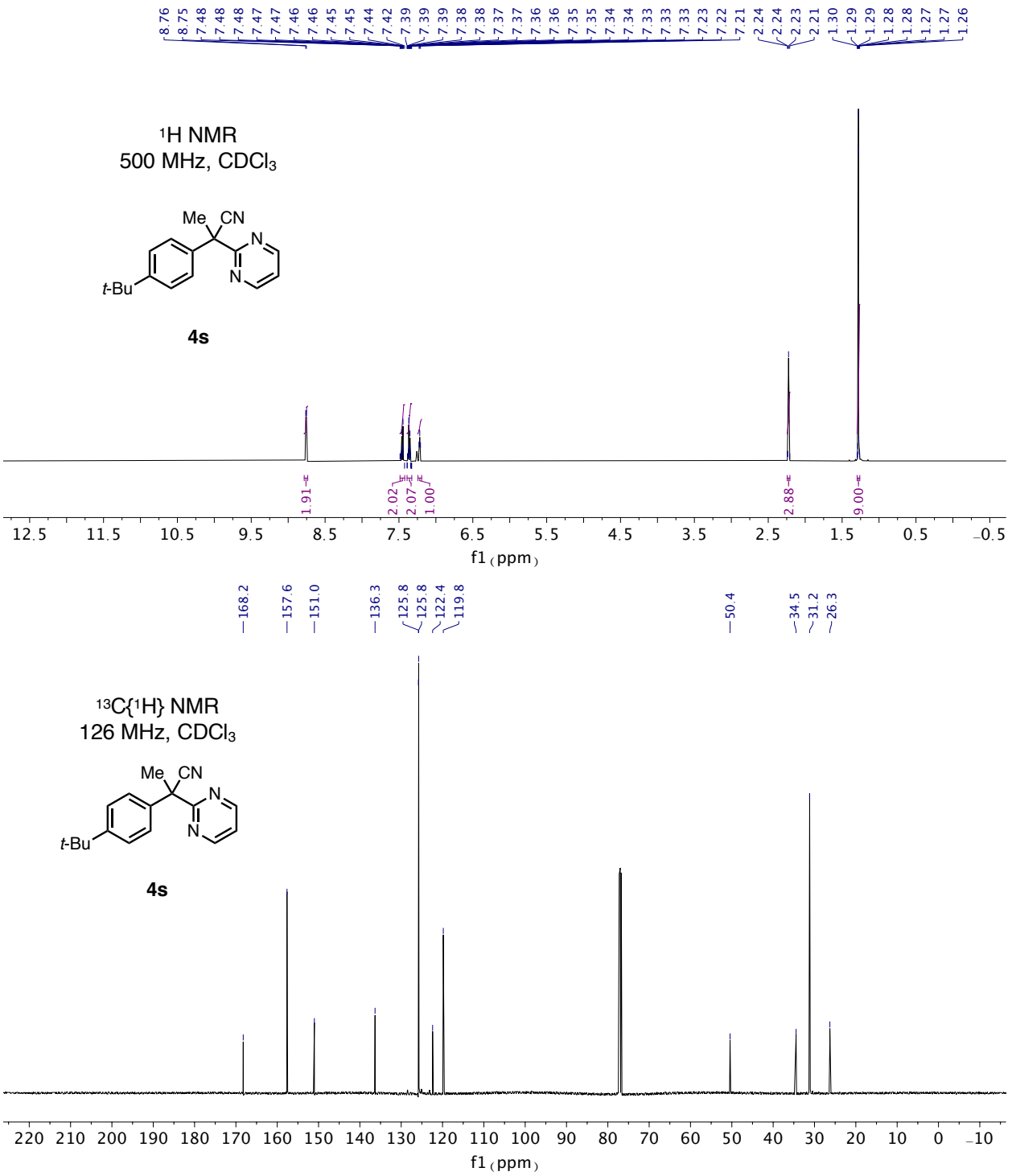


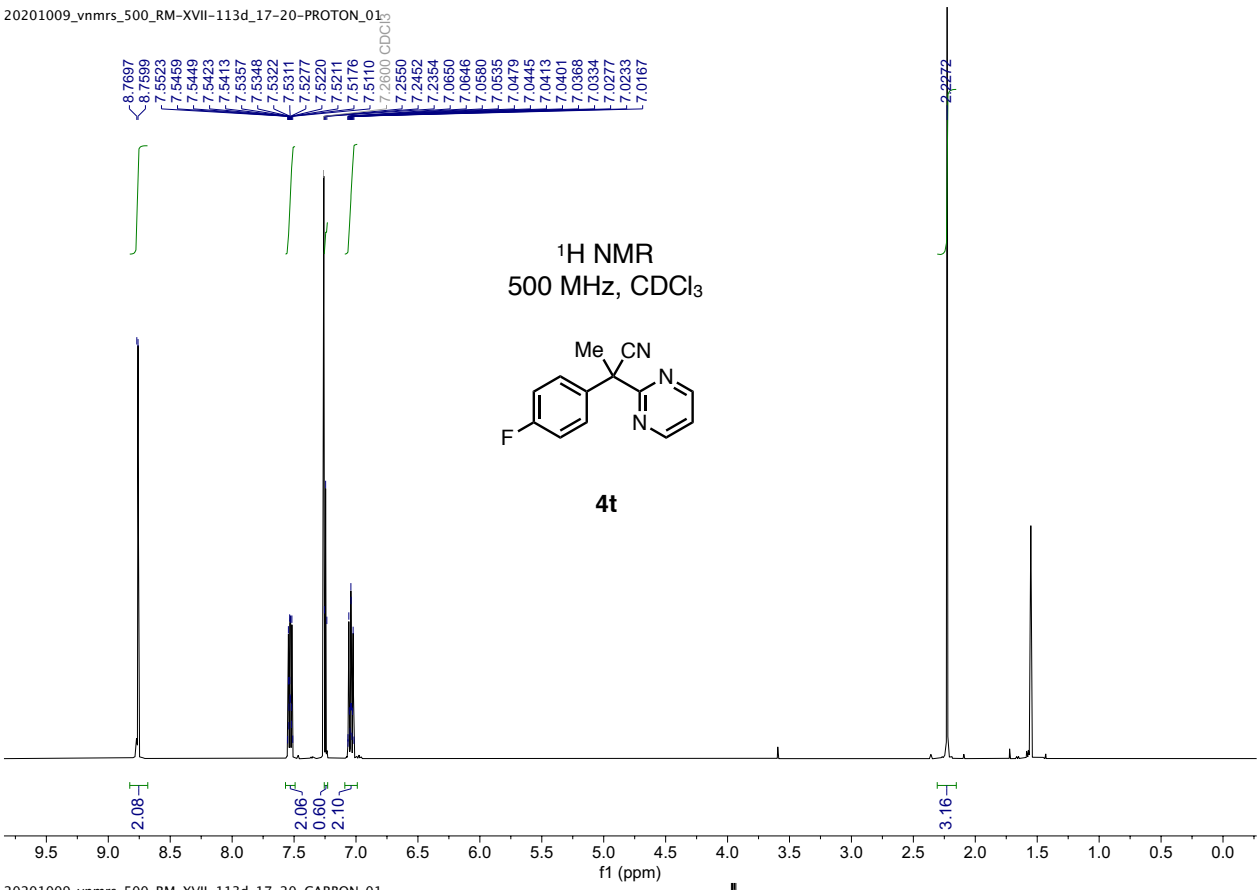
20201009_vnmrs_500_RM-XVII-113f_17-20-CARBON_01

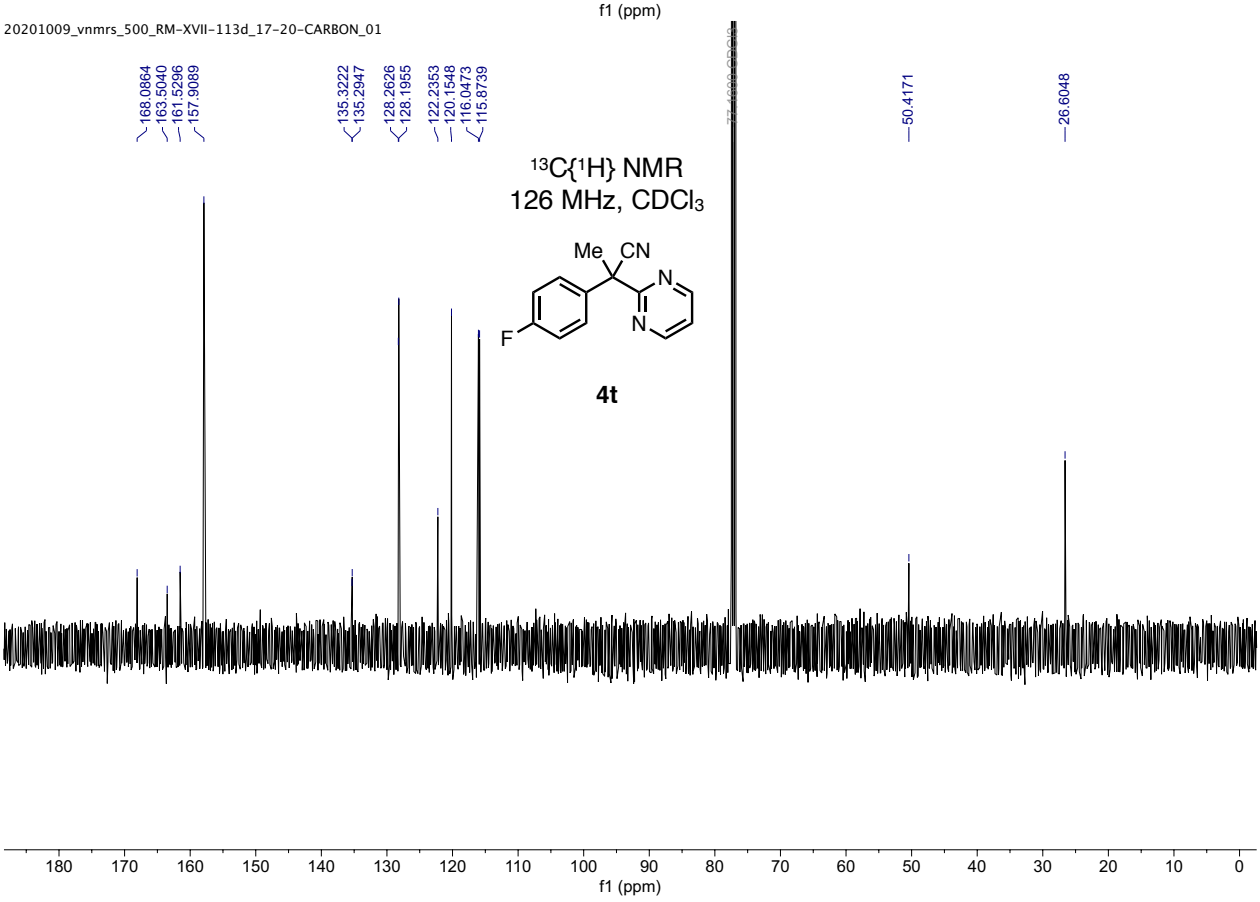
$^{13}C\{^{1}H\}$ NMR
126 MHz, $CDCl_3$

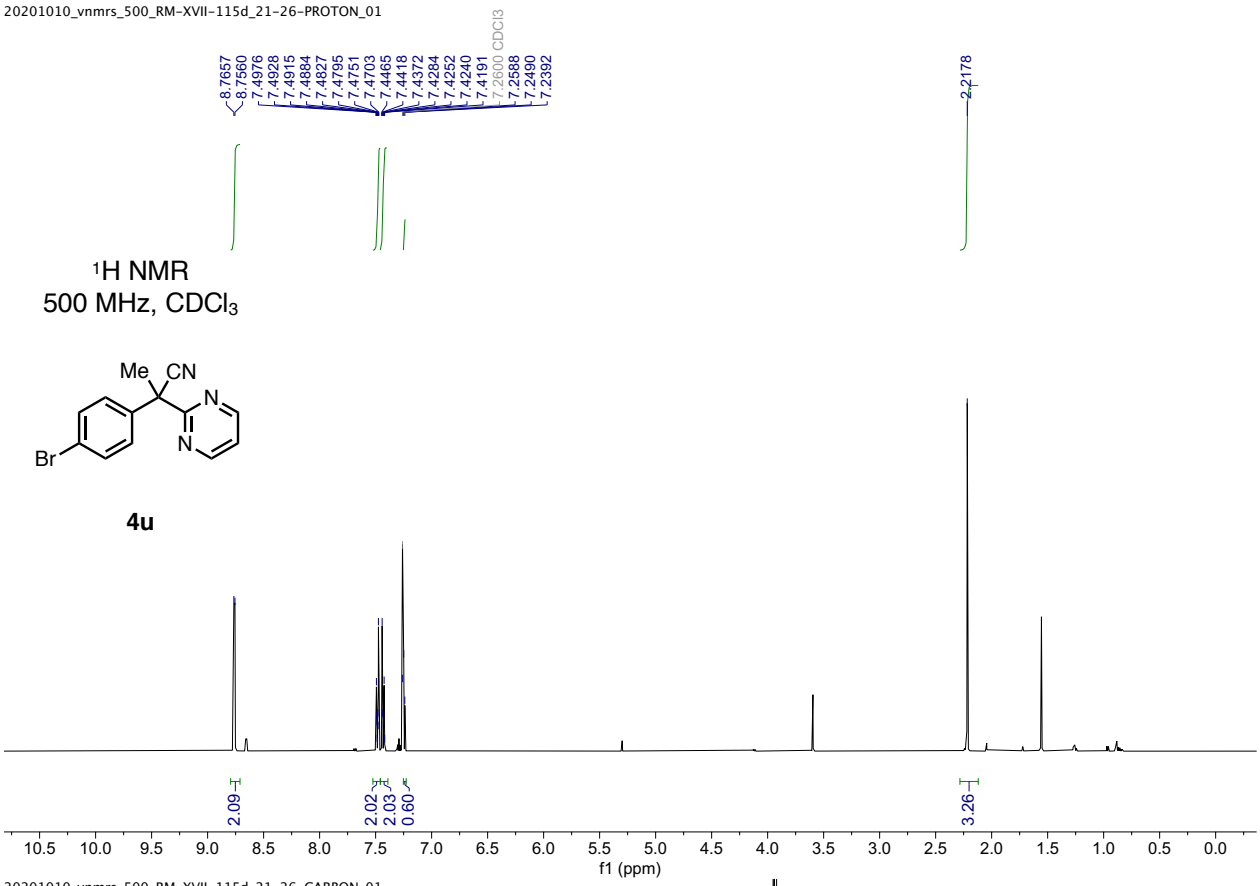


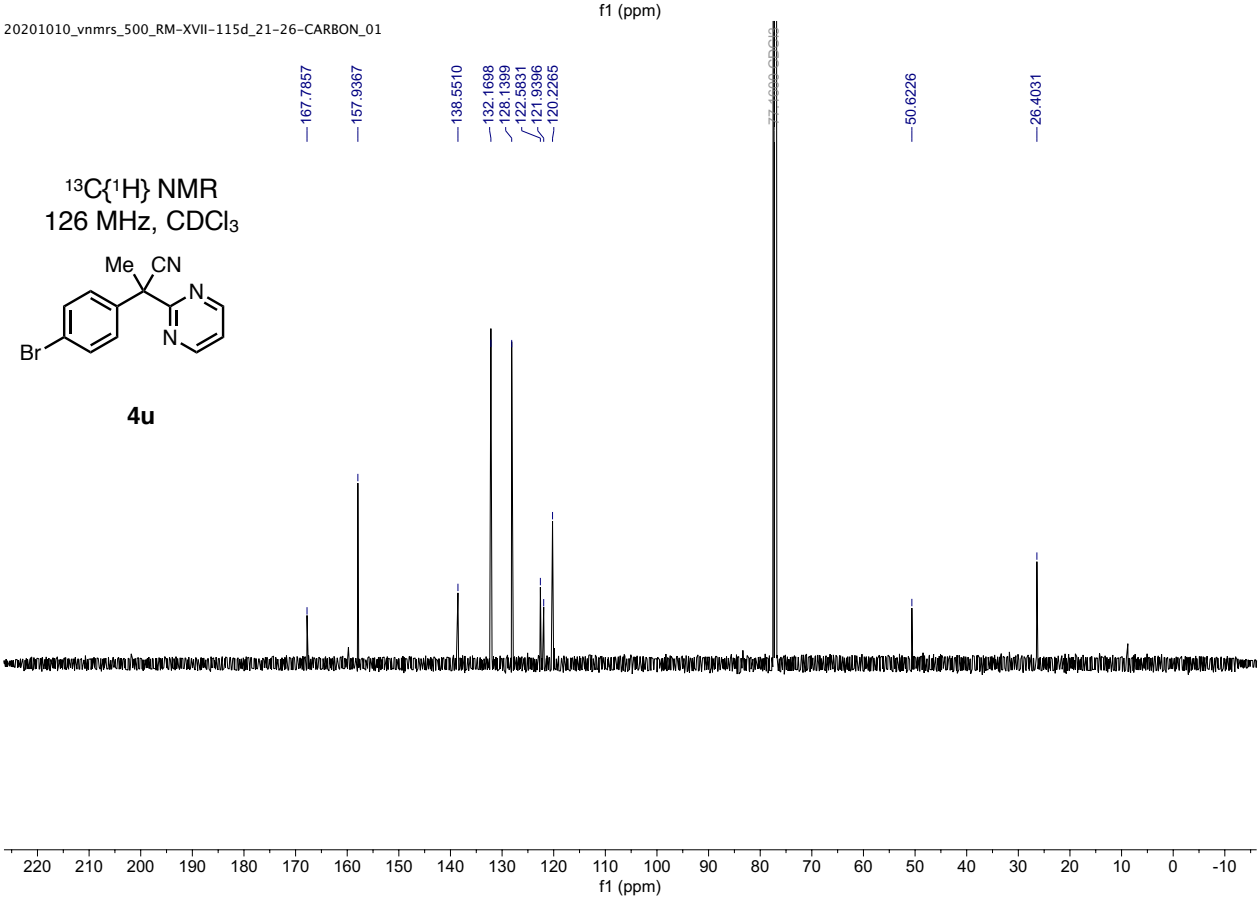
4r

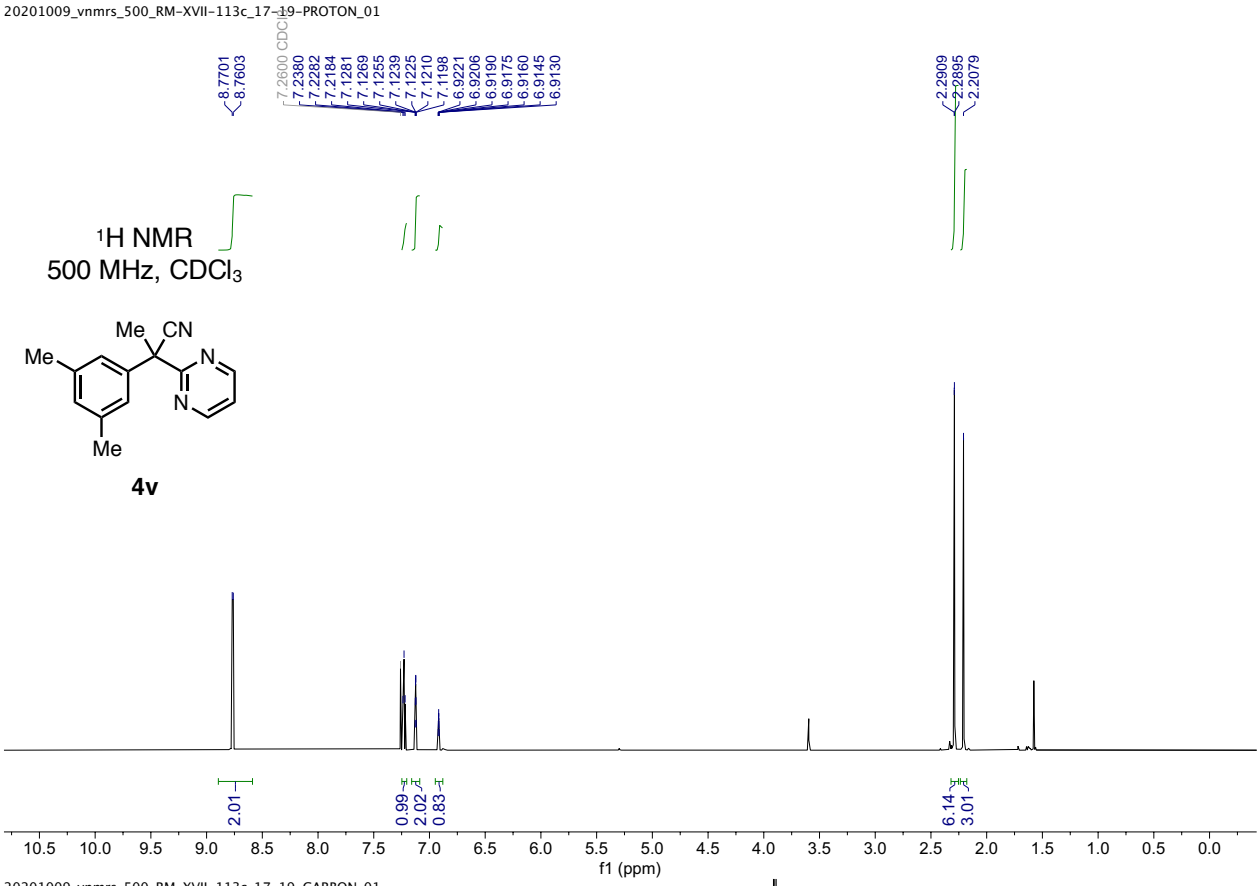

8.76 8.75 7.48 7.48 7.48 7.47 7.47 7.46 7.46 7.45 7.45 7.44 7.42 7.39 7.39 7.39 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.23 7.22 7.21 2.24 2.24 2.23 2.21 1.30 1.29 1.29 1.28 1.28 1.27 1.27 1.26
1H NMR
500 MHz, CDCl3
Me CN
N
N
t-Bu
4s
1.91 2.02 2.07 1.00 2.88 9.00
12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)
168.2 157.6 151.0 136.3 125.8 125.8 122.4 119.8 50.4 34.5 31.2 26.3
13C{1H} NMR
126 MHz, CDCl3
Me CN
N
N
t-Bu
4s
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

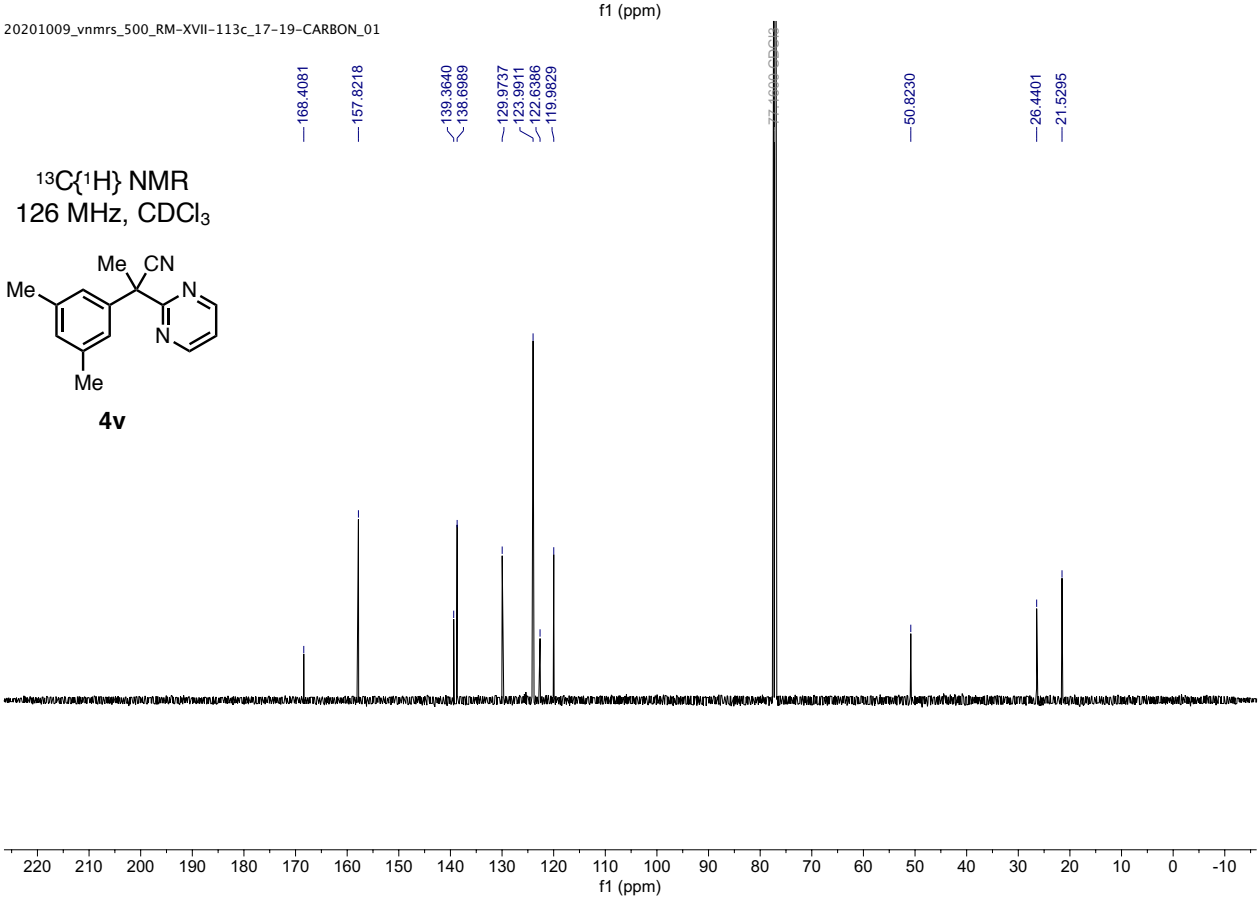

20201009_vnmrs_500_RM-XVII-113d_17-20-PROTON_01
8.7697
8.7599
7.5523
7.5459
7.5449
7.5423
7.5413
7.5357
7.5348
7.5322
7.5311
7.5277
7.5220
7.5211
7.5176
7.5110
7.2600 CDCl3
7.2550
7.2452
7.2354
7.0650
7.0646
7.0580
7.0535
7.0479
7.0445
7.0413
7.0401
7.0368
7.0334
7.0277
7.0233
7.0167
2.3272
1H NMR
500 MHz, CDCl3
Me
CN
N
N
F
4t
2.08
2.06
0.60
2.10
3.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

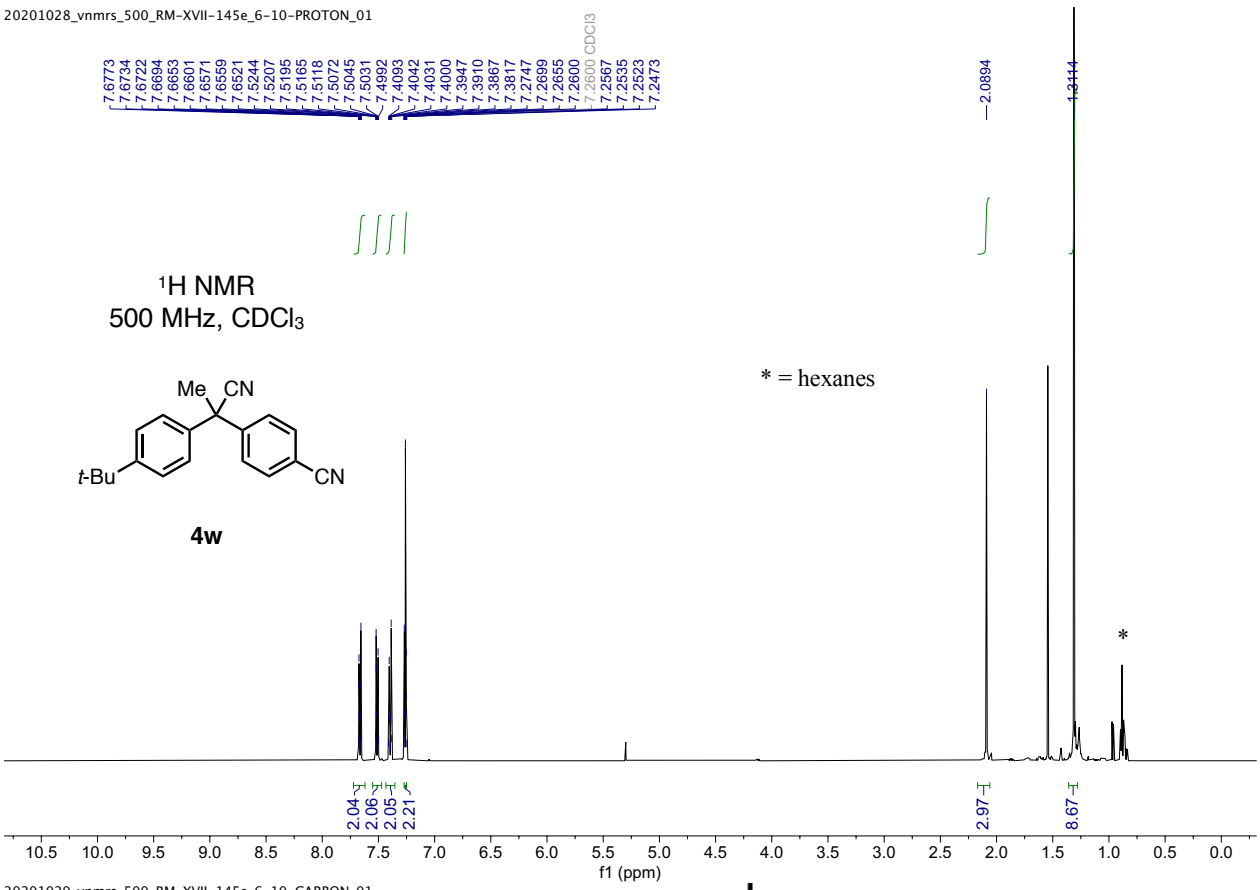

20201009_vnmrs_500_RM-XVII-113d_17-20-CARBON_01
168.0864
163.5040
161.5296
157.9089
135.3222
135.2947
128.2626
128.1955
122.2353
120.1548
116.0473
115.8739
77.4000 CDCl3
50.4171
26.6048
13C{1H} NMR
126 MHz, CDCl3
Me
CN
N
N
F
4t
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

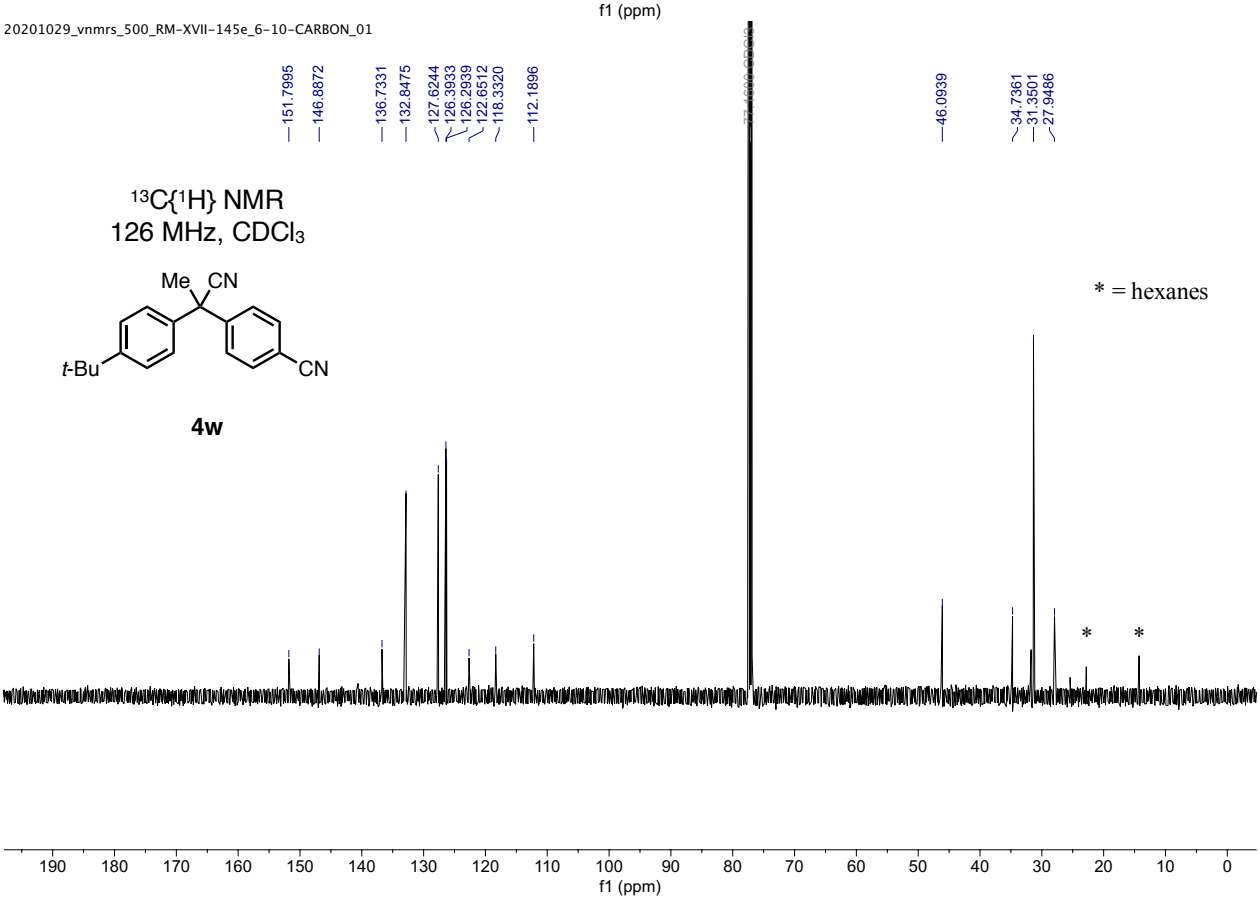

20201010_vnmrs_500_RM-XVII-115d_21-26-PROTON_01
8.7657
8.7560
7.4976
7.4928
7.4915
7.4884
7.4827
7.4795
7.4751
7.4703
7.4465
7.4418
7.4372
7.4284
7.4252
7.4240
7.4191
7.2600 CDCl3
7.2588
7.2490
7.2392
2.2178
1H NMR
500 MHz, CDCl3
Me
CN
N
N
Br
4u
2.09
2.02
2.03
0.60
3.26
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

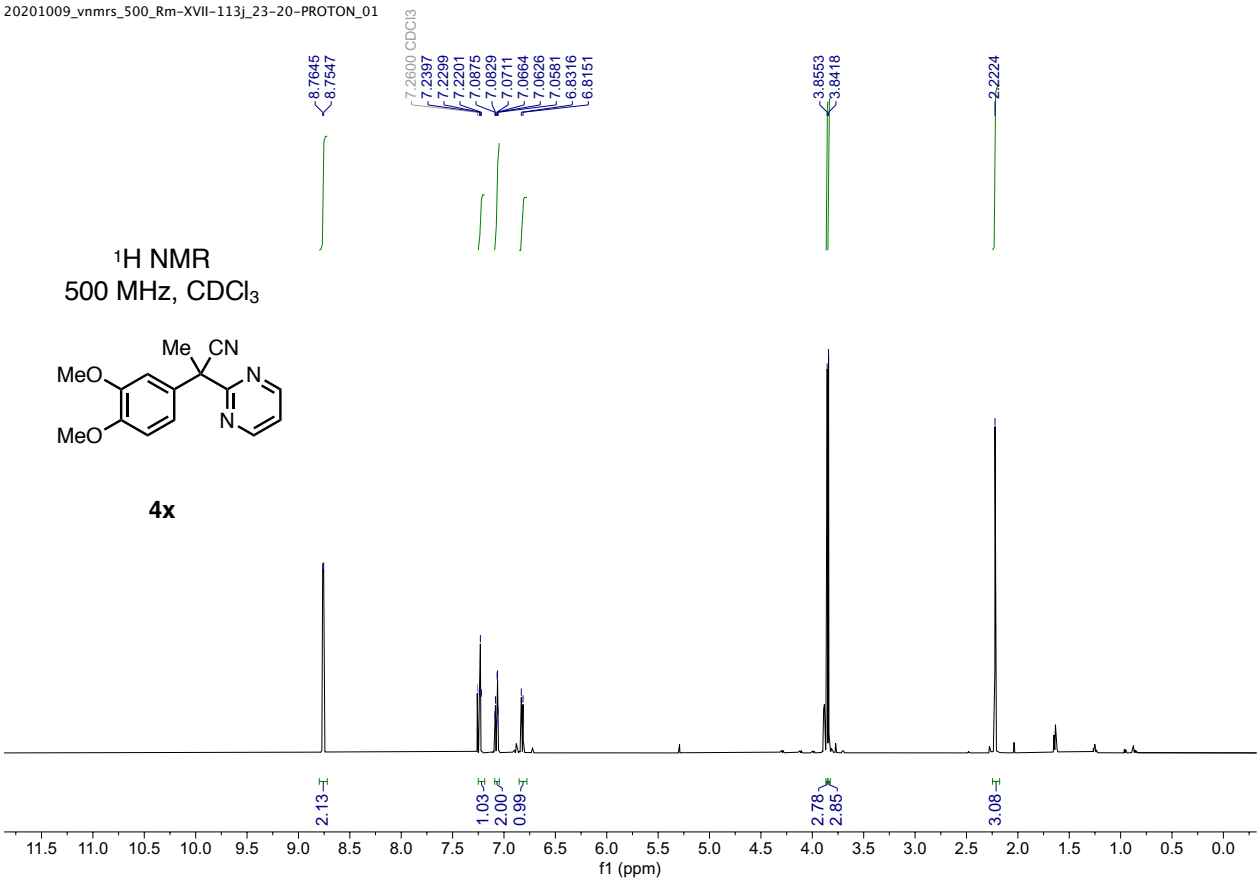

20201010_vnmrs_500_RM-XVII-115d_21-26-CARBON_01
167.7857
157.9367
138.5510
132.1698
128.1399
122.5831
121.9396
120.2265
77.4088
77.0969
76.7849
50.6226
26.4031
13C{1H} NMR
126 MHz, CDCl3
Me
CN
N
N
Br
4u
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

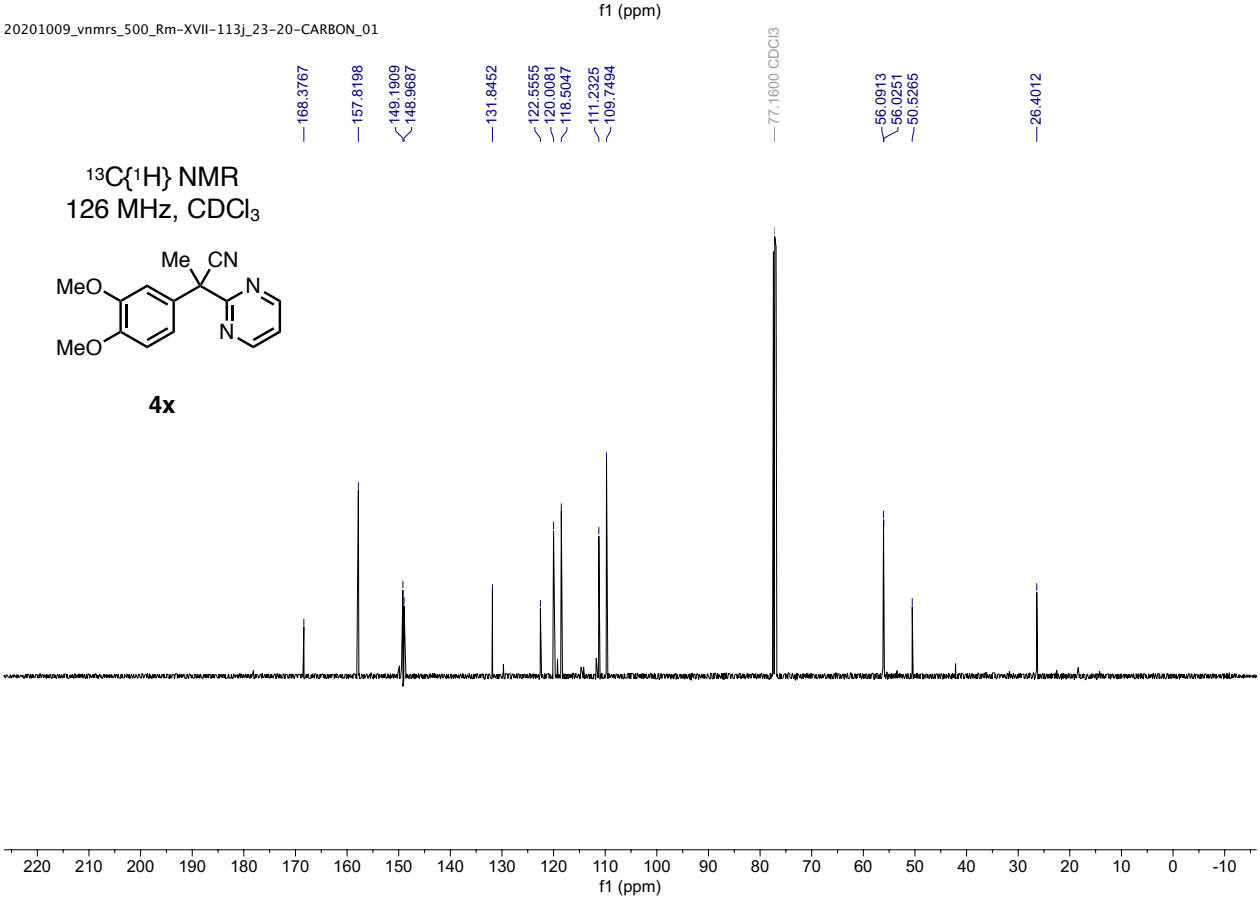

20201009_vnmrs_500_RM-XVII-113c_17-19-PROTON_01
8.7701
8.7603
7.2600 CDCl3
7.2380
7.2282
7.2184
7.1281
7.1269
7.1255
7.1239
7.1225
7.1210
7.1198
6.9221
6.9206
6.9190
6.9175
6.9160
6.9145
6.9130
2.2909
2.2895
2.2079
1H NMR
500 MHz, CDCl3
Me
CN
Me
N
N
Me
4v
2.01
0.99
2.02
0.83
6.14
3.01
f1 (ppm)

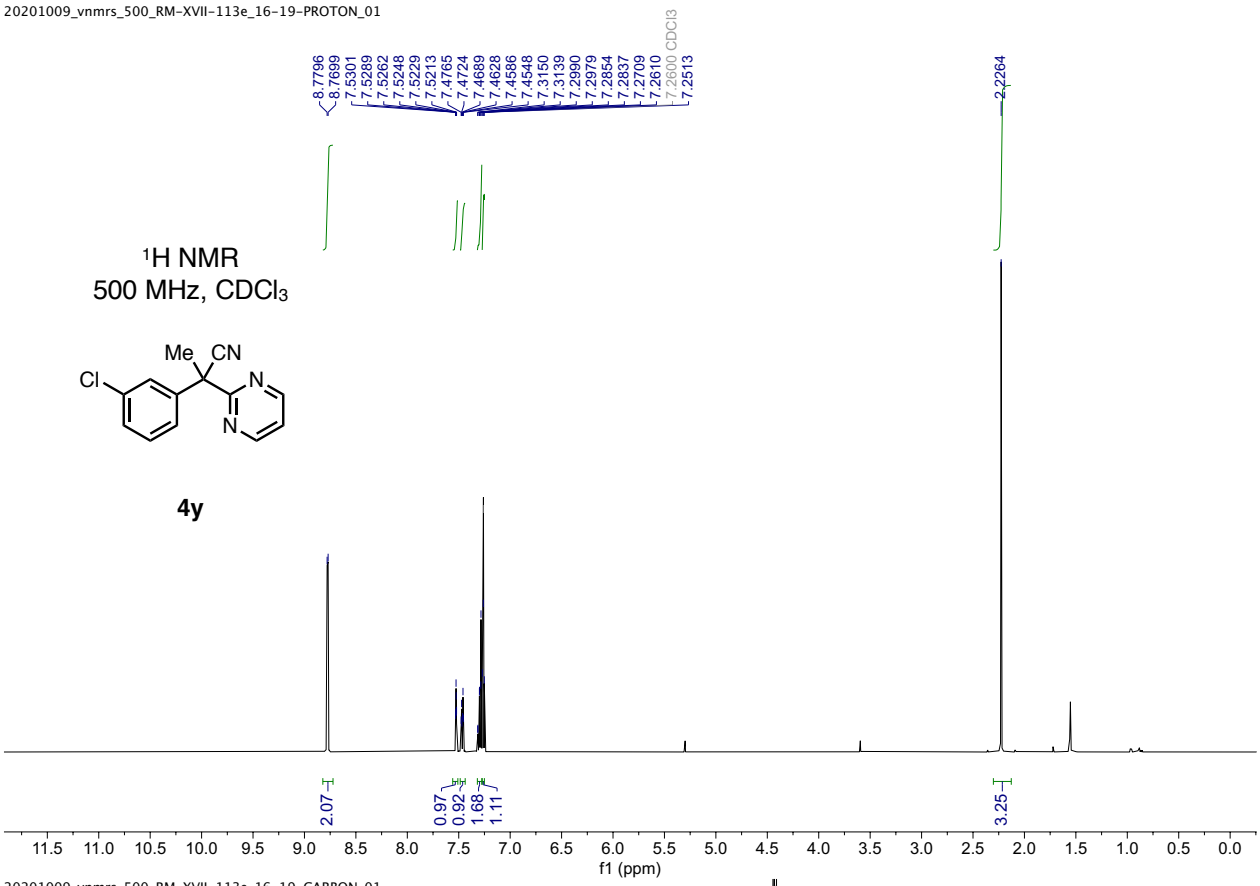

20201009_vnmrs_500_RM-XVII-113c_17-19-CARBON_01
168.4081
157.8218
139.3640
138.6989
129.9737
123.9911
122.6386
119.9829
77.4000 CDCl3
50.8230
26.4401
21.5295
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Me
N
N
Me
4v
f1 (ppm)

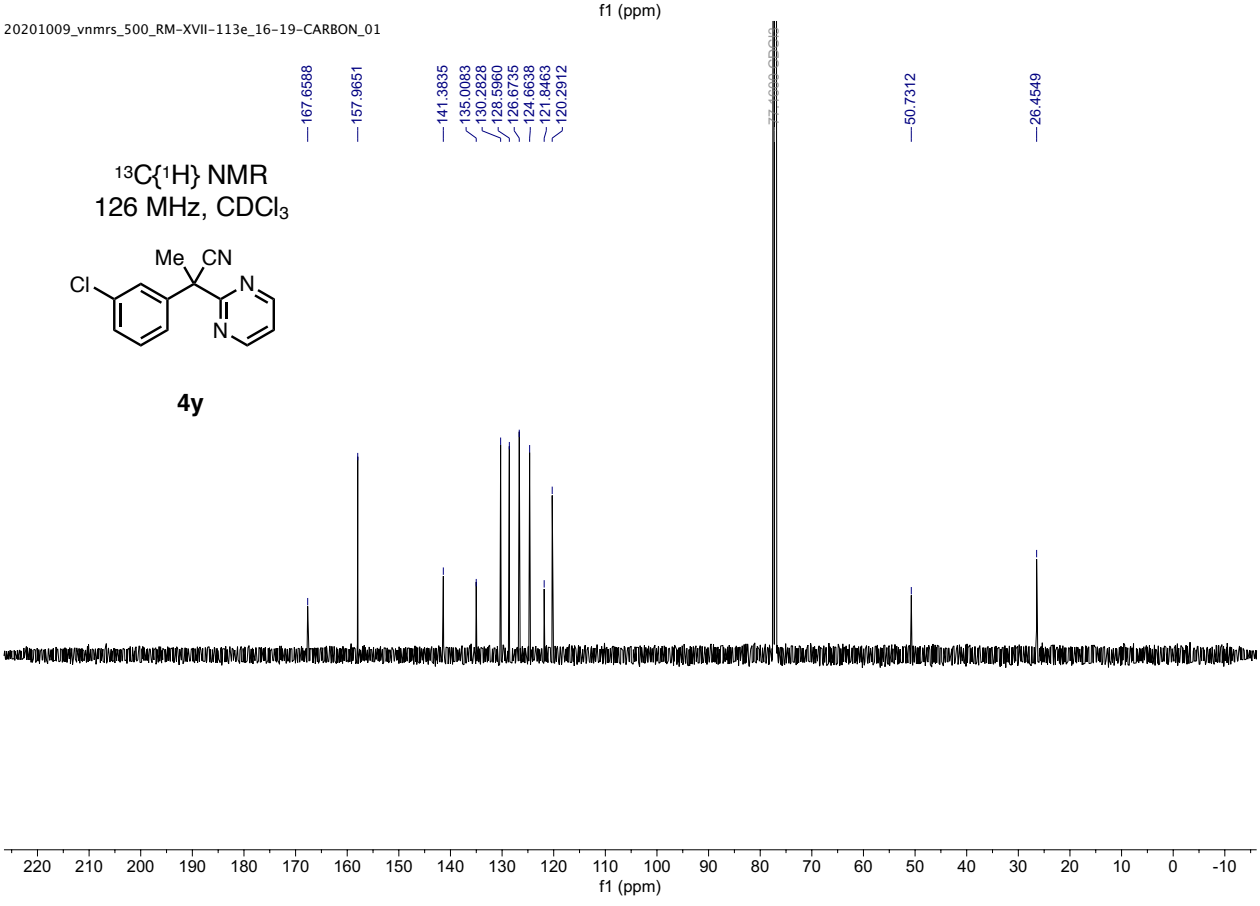

20201028_vnmrs_500_RM-XVII-145e_6-10-PROTON_01
7.6773
7.6734
7.6722
7.6694
7.6653
7.6601
7.6571
7.6559
7.6521
7.5244
7.5207
7.5195
7.5165
7.5118
7.5072
7.5045
7.5031
7.4992
7.4093
7.4042
7.4031
7.4000
7.3947
7.3910
7.3867
7.3817
7.2747
7.2699
7.2655
7.2600
7.2600 CDCl3
7.2567
7.2535
7.2523
7.2473
2.0894
1.3114
1H NMR
500 MHz, CDCl3
Me
CN
t-Bu
CN
4w
* = hexanes
*
2.04
2.06
2.05
2.21
2.97
8.67
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

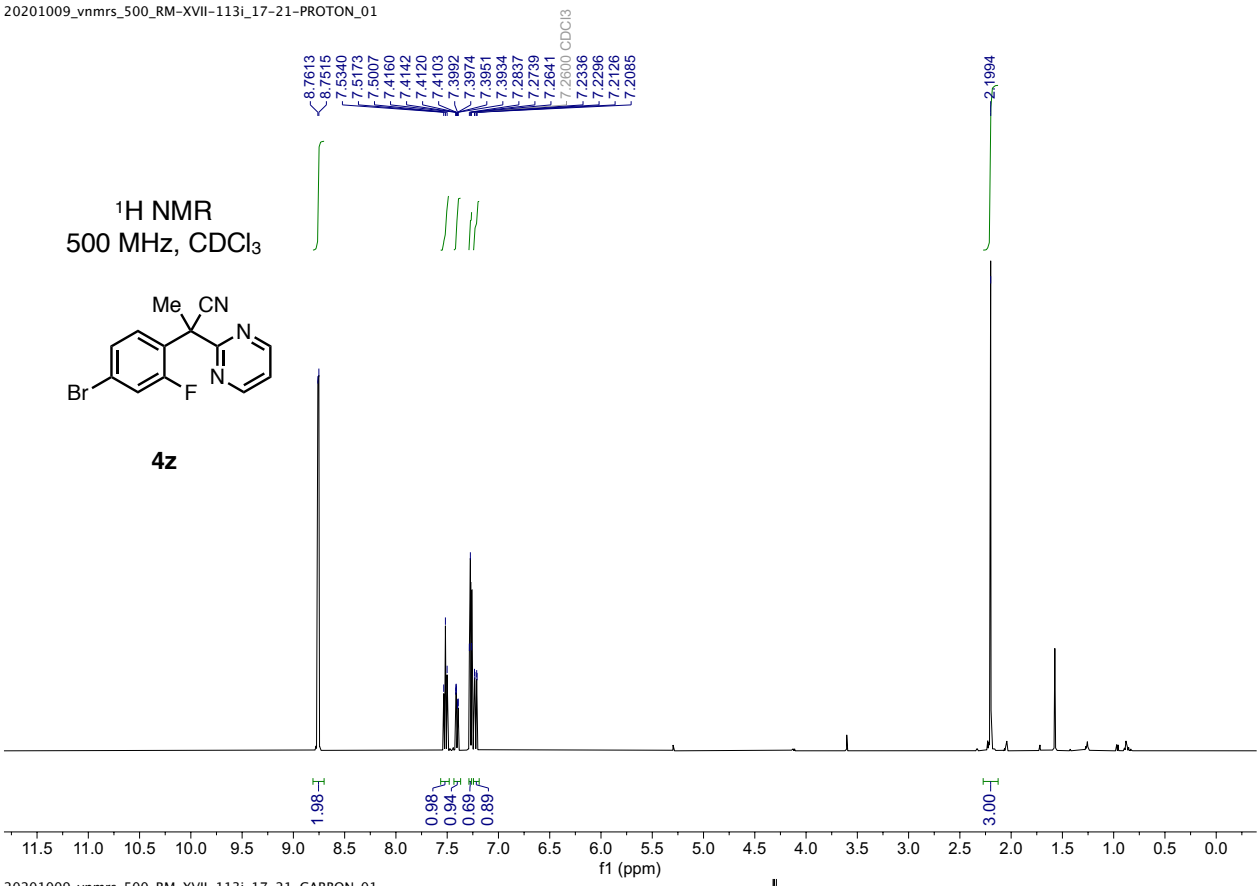

20201029_vnmrs_500_RM-XVII-145e_6-10-CARBON_01
151.7995
146.8872
136.7331
132.8475
127.6244
126.3933
126.2939
122.6512
118.3320
112.1896
77.4000
77.0000
76.5999
46.0939
34.7361
31.3501
27.9486
13C{1H} NMR
126 MHz, CDCl3
Me
CN
t-Bu
CN
4w
* = hexanes
*
*
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

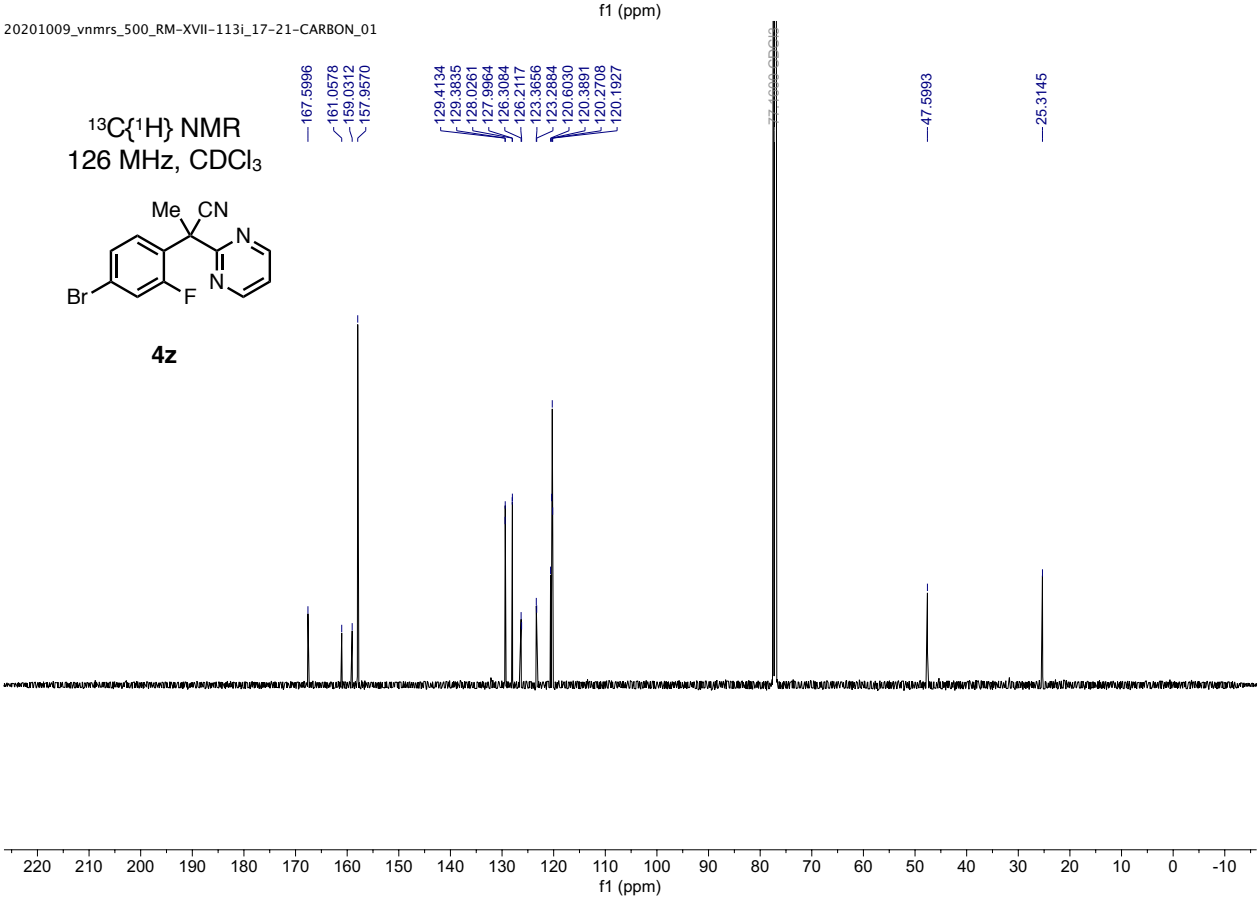

20201009_vnmrs_500_Rm-XVII-113j_23-20-PROTON_01
8.7645
8.7547
7.2600 CDCl3
7.2397
7.2299
7.2201
7.0875
7.0829
7.0711
7.0664
7.0626
7.0581
6.8316
6.8151
3.8553
3.8418
2.2224
1H NMR
500 MHz, CDCl3
Me
CN
MeO
MeO
N
N
4x
2.13
1.03
2.00
0.99
2.78
2.85
3.08
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201009_vnmrs_500_Rm-XVII-113j_23-20-CARBON_01
168.3767
157.8198
149.1909
148.9687
131.8452
122.5555
120.0081
118.5047
111.2325
109.7494
77.1600 CDCl3
56.0913
56.0251
50.5265
26.4012
13C{1H} NMR
126 MHz, CDCl3
Me
CN
MeO
MeO
N
N
4x
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113e_16-19-PROTON_01
8.7796
8.7699
7.5301
7.5289
7.5262
7.5248
7.5229
7.5213
7.4765
7.4724
7.4689
7.4628
7.4586
7.4548
7.3150
7.3139
7.2990
7.2979
7.2854
7.2837
7.2709
7.2610
7.2600 CDCl3
7.2513
2.2264
1H NMR
500 MHz, CDCl3
Me
CN
Cl
N
N
4y
2.07
0.97
0.92
1.68
1.11
3.25
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113e_16-19-CARBON_01
167.6588
157.9651
141.3835
135.0083
130.2828
128.5960
126.6735
124.6638
121.8463
120.2912
77.4088 CDCl3
50.7312
26.4549
13C{1H} NMR
126 MHz, CDCl3
Me
CN
Cl
N
N
4y
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

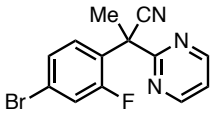

20201009_vnmrs_500_RM-XVII-113i_17-21-PROTON_01
8.7613
8.7515
7.5340
7.5173
7.5007
7.4160
7.4142
7.4120
7.4103
7.3992
7.3974
7.3951
7.3934
7.2837
7.2739
7.2641
7.2600 CDCl3
7.2336
7.2296
7.2126
7.2085
2.1994
1H NMR
500 MHz, CDCl3
Me
CN
N
N
Br
F
4z
1.98
0.98
0.94
0.69
0.89
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113i_17-21-CARBON_01
167.5996
161.0578
159.0312
157.9570
129.4134
129.3835
128.0261
127.9964
126.3084
126.2117
123.3656
123.2884
120.6030
120.3891
120.2708
120.1927
77.4088 CDCl3
47.5993
25.3145
13C{1H} NMR
126 MHz, CDCl3
Me
CN
N
N
Br
F
4z
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

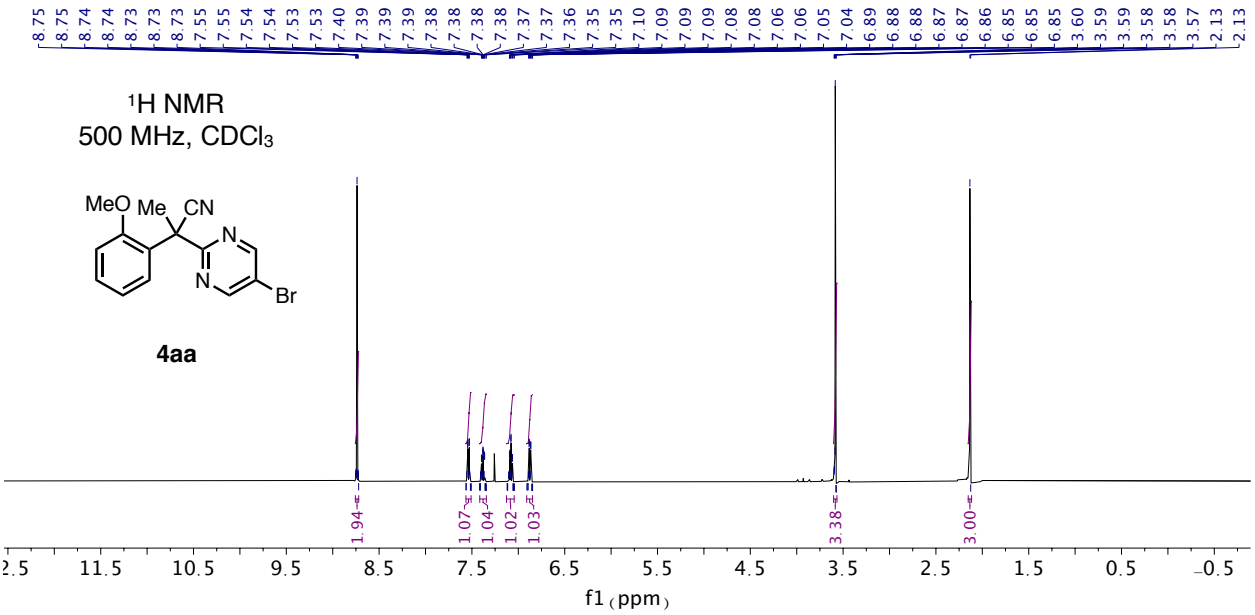
RM-XVII-113i 17-21.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 18

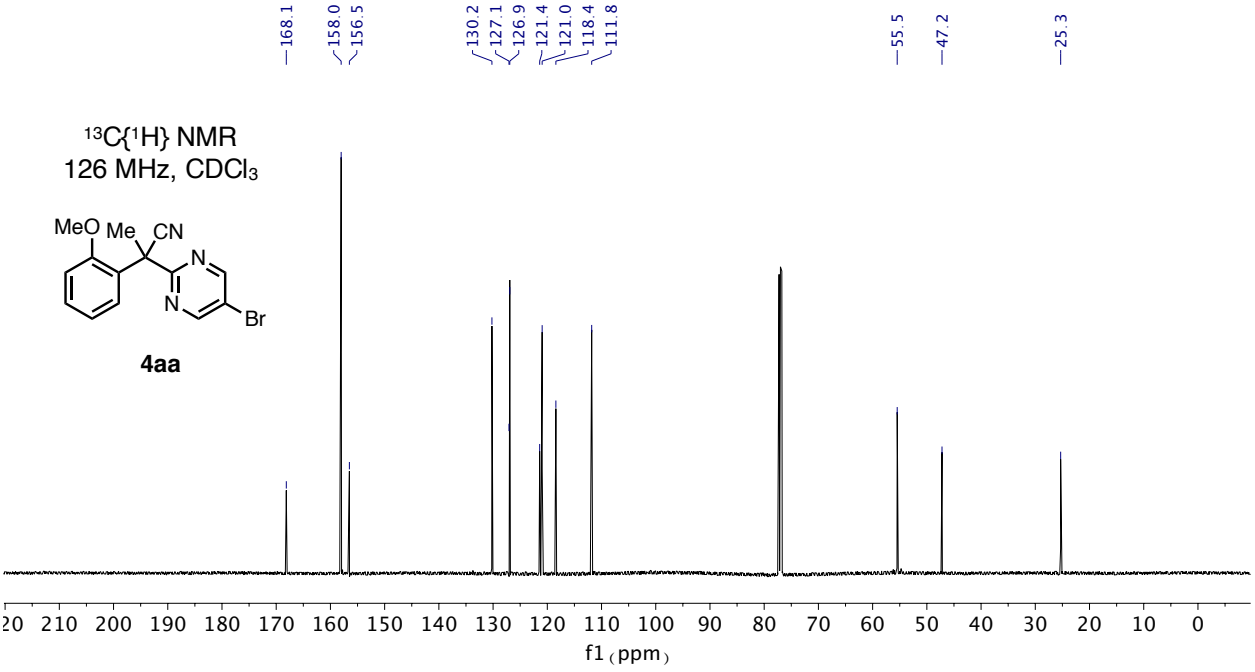
-108.0036
-108.0281
-108.0527

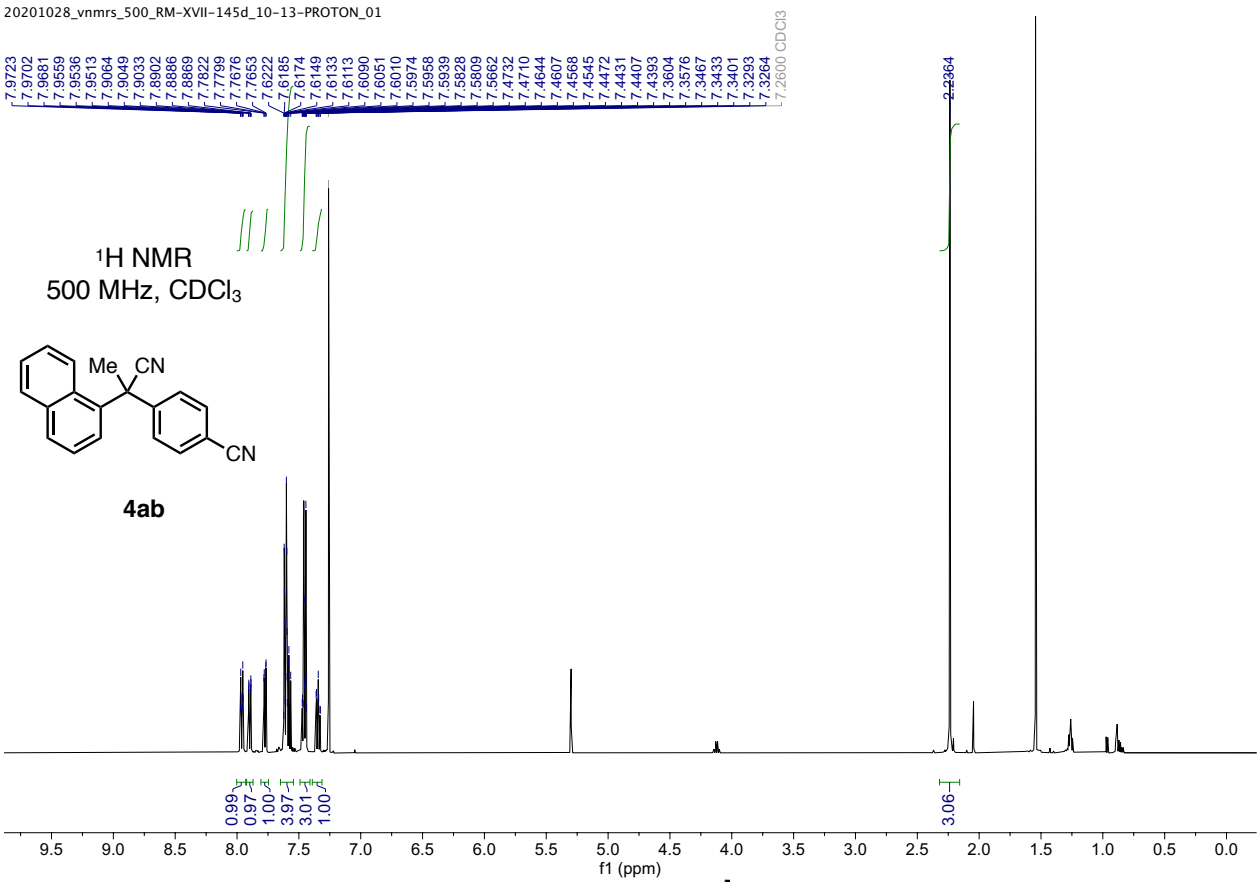
^{19}F NMR
376 MHz, $CDCl_3$

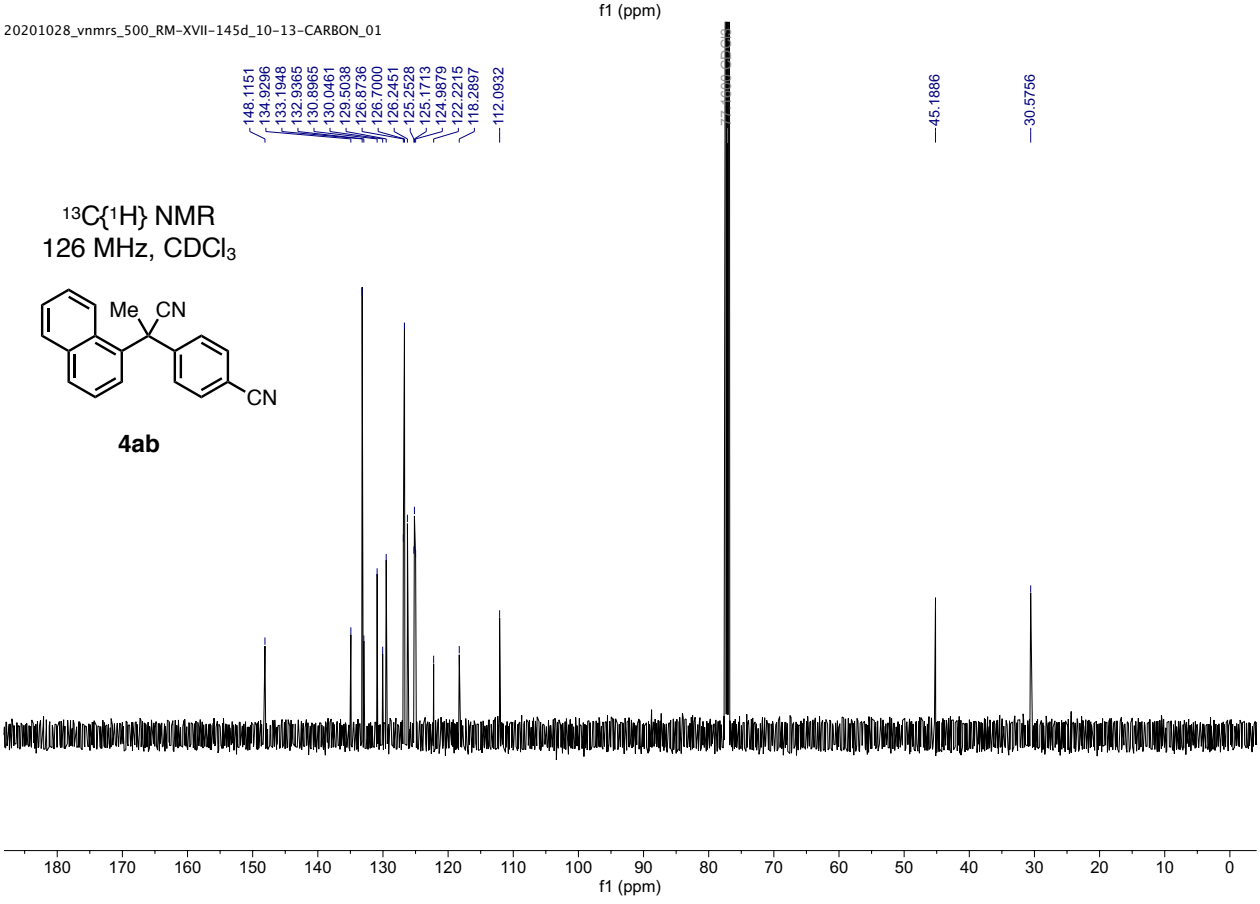


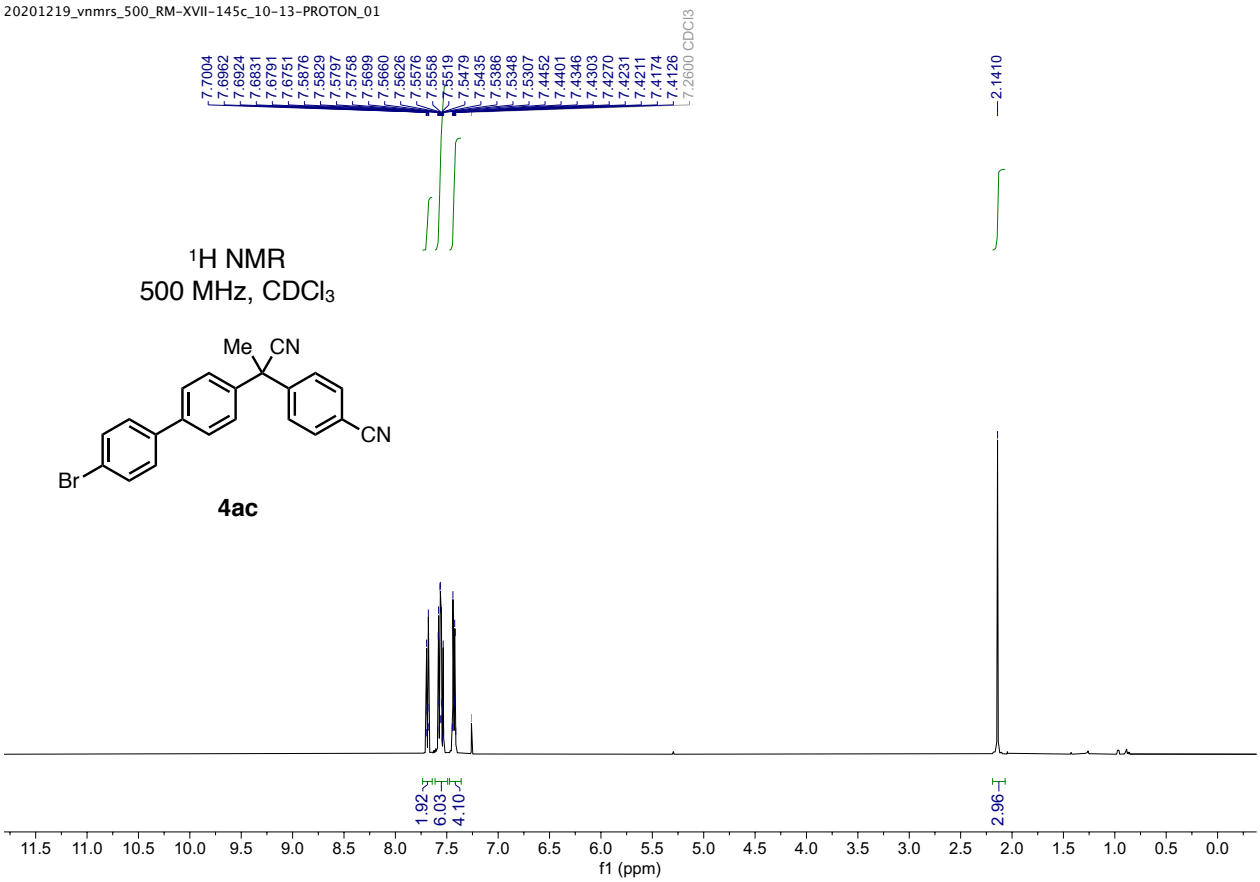
4z

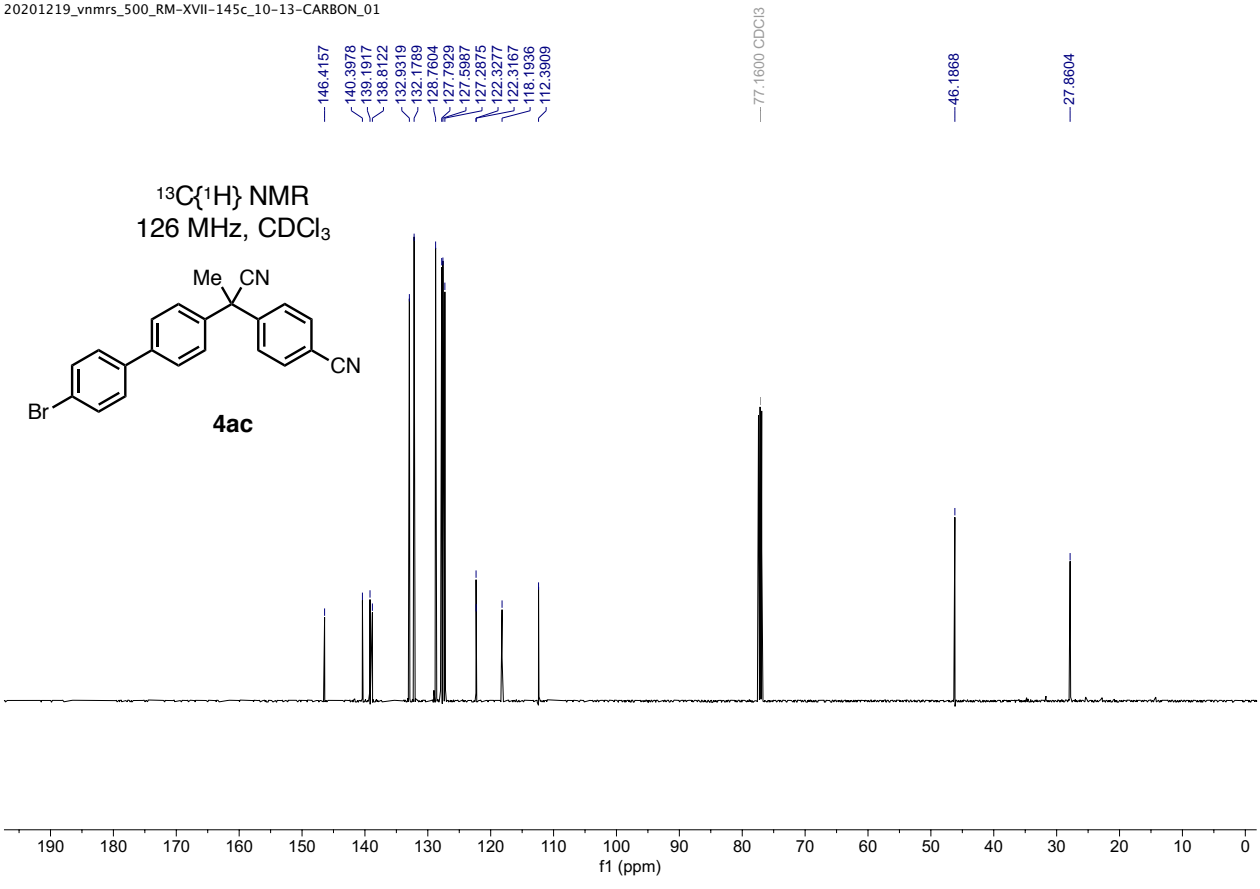

8.75 8.75 8.74 8.74 8.73 8.73 8.73 7.55 7.55 7.54 7.54 7.53 7.53 7.40 7.39 7.39 7.39 7.38 7.38 7.38 7.38 7.37 7.37 7.36 7.35 7.35 7.10 7.09 7.09 7.09 7.08 7.08 7.06 7.06 7.05 7.04 6.89 6.88 6.88 6.87 6.87 6.86 6.85 6.85 6.85 3.60 3.59 3.59 3.58 3.58 3.57 2.13 2.13
1H NMR
500 MHz, CDCl3
MeO Me CN
N
N
Br
4aa
1.94 1.07 1.04 1.02 1.03 3.38 3.00
2.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)

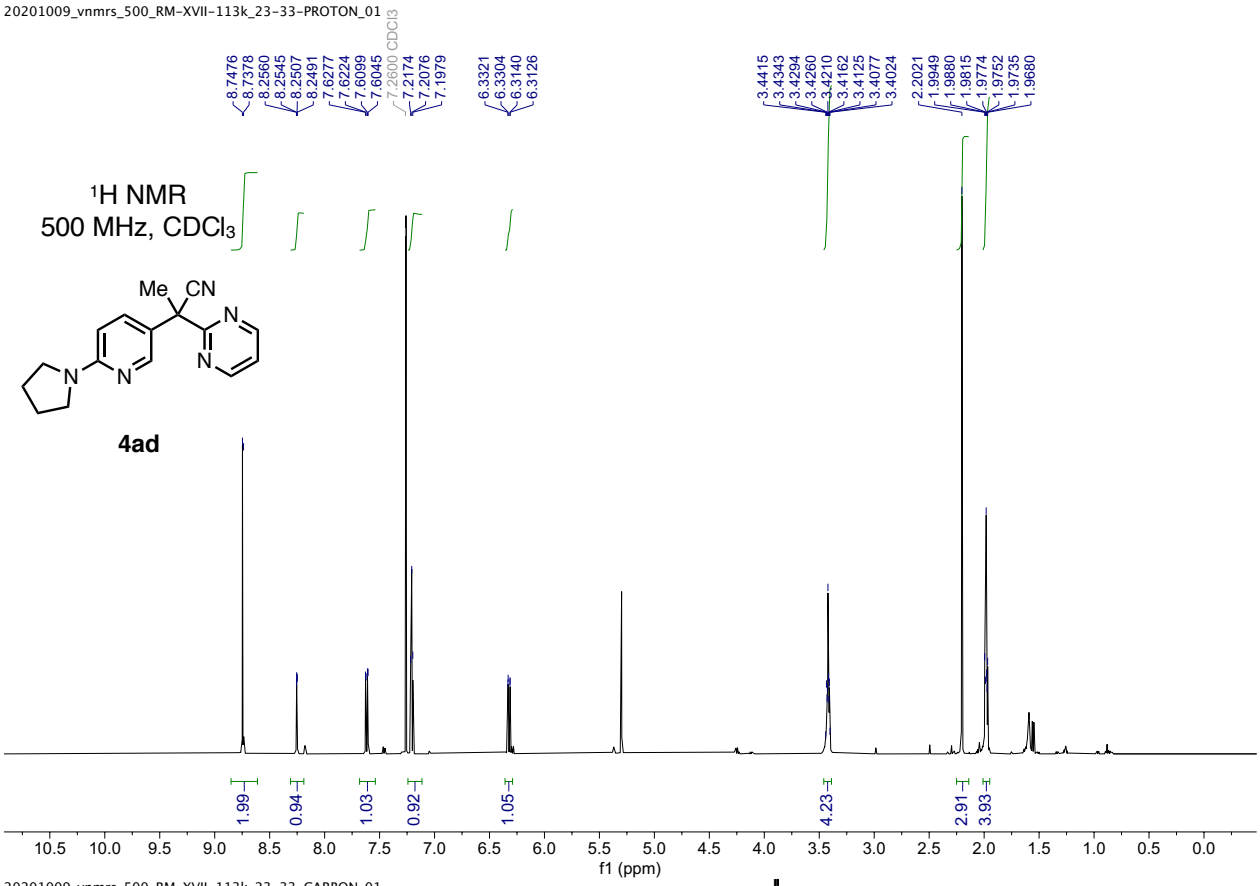

168.1 158.0 156.5 130.2 127.1 126.9 121.4 121.0 118.4 111.8 55.5 47.2 25.3
13C{1H} NMR
126 MHz, CDCl3
MeO Me CN
N
N
Br
4aa
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20201028_vnmrs_500_RM-XVII-145d_10-13-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Me
CN
CN
4ab
f1 (ppm)


20201028_vnmrs_500_RM-XVII-145d_10-13-CARBON_01
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
Me
CN
CN
4ab
f1 (ppm)


20201219_vnmrs_500_RM-XVII-145c_10-13-PROTON_01
7.7004
7.6962
7.6924
7.6831
7.6791
7.6751
7.5876
7.5829
7.5797
7.5758
7.5699
7.5660
7.5626
7.5576
7.5558
7.5519
7.5479
7.5435
7.5386
7.5348
7.5307
7.4452
7.4401
7.4346
7.4303
7.4270
7.4231
7.4211
7.4174
7.4126
7.2600 CDCl3
2.1410
1H NMR
500 MHz, CDCl3
Me
CN
CN
Br
4ac
1.92
6.03
4.10
2.96
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201219_vnmrs_500_RM-XVII-145c_10-13-CARBON_01
146.4157
140.3978
139.1917
138.8122
132.9319
132.1789
128.7604
127.7929
127.5987
127.2875
122.3277
122.3167
118.1936
112.3909
77.1600 CDCl3
46.1868
27.8604
13C{1H} NMR
126 MHz, CDCl3
Me
CN
CN
Br
4ac
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113k_23-33-PROTON_01
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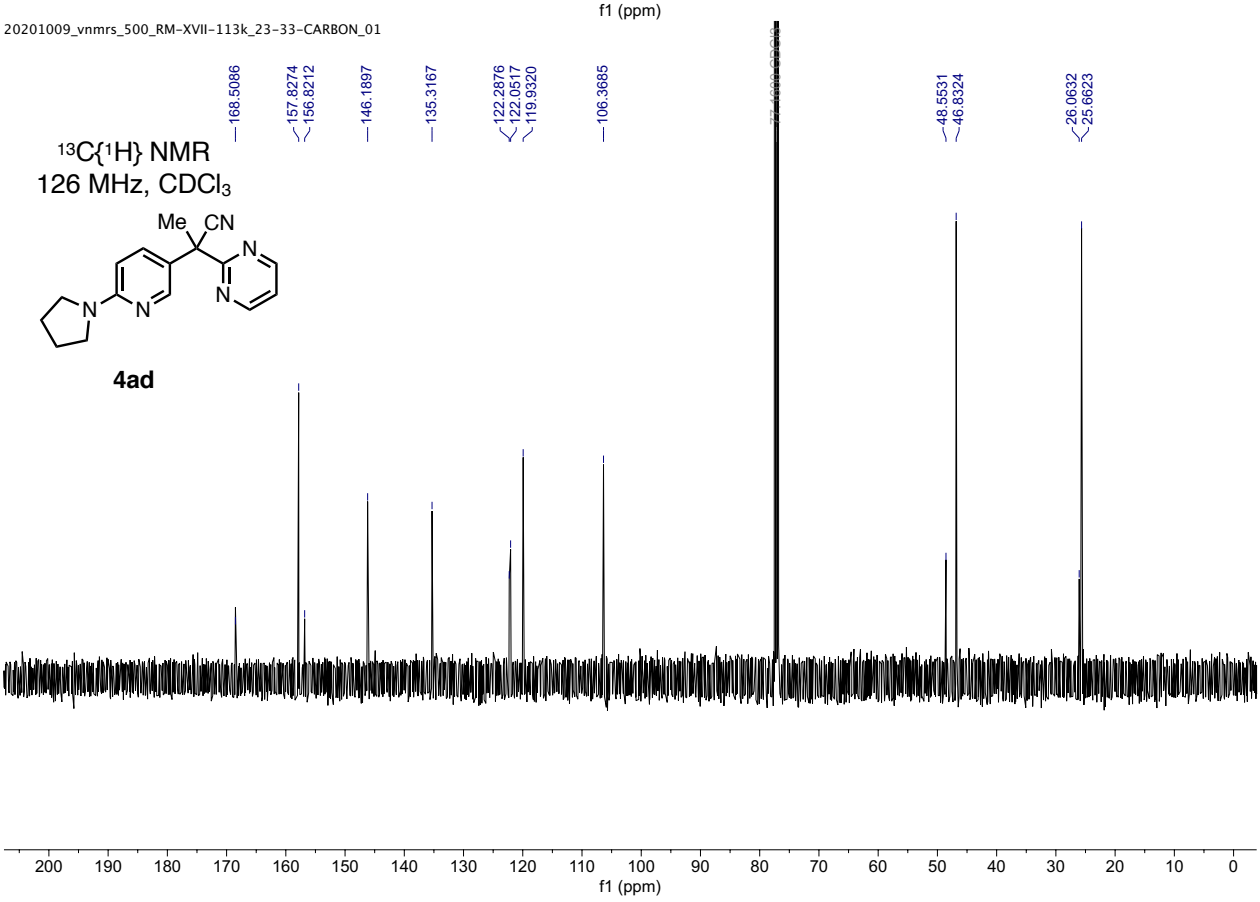
8.2545
8.2507
8.2491
7.6277
7.6224
7.6099
7.6045
7.2600 CDCl3
7.2174
7.2076
7.1979
6.3321
6.3304
6.3140
6.3126
3.4415
3.4343
3.4294
3.4260
3.4210
3.4162
3.4125
3.4077
3.4024
2.2021
1.9949
1.9880
1.9815
1.9774
1.9752
1.9735
1.9680
1H NMR
500 MHz, CDCl3
Me
CN
N
N
N
N
4ad
1.99
0.94
1.03
0.92
1.05
4.23
2.91
3.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113k_23-33-CARBON_01
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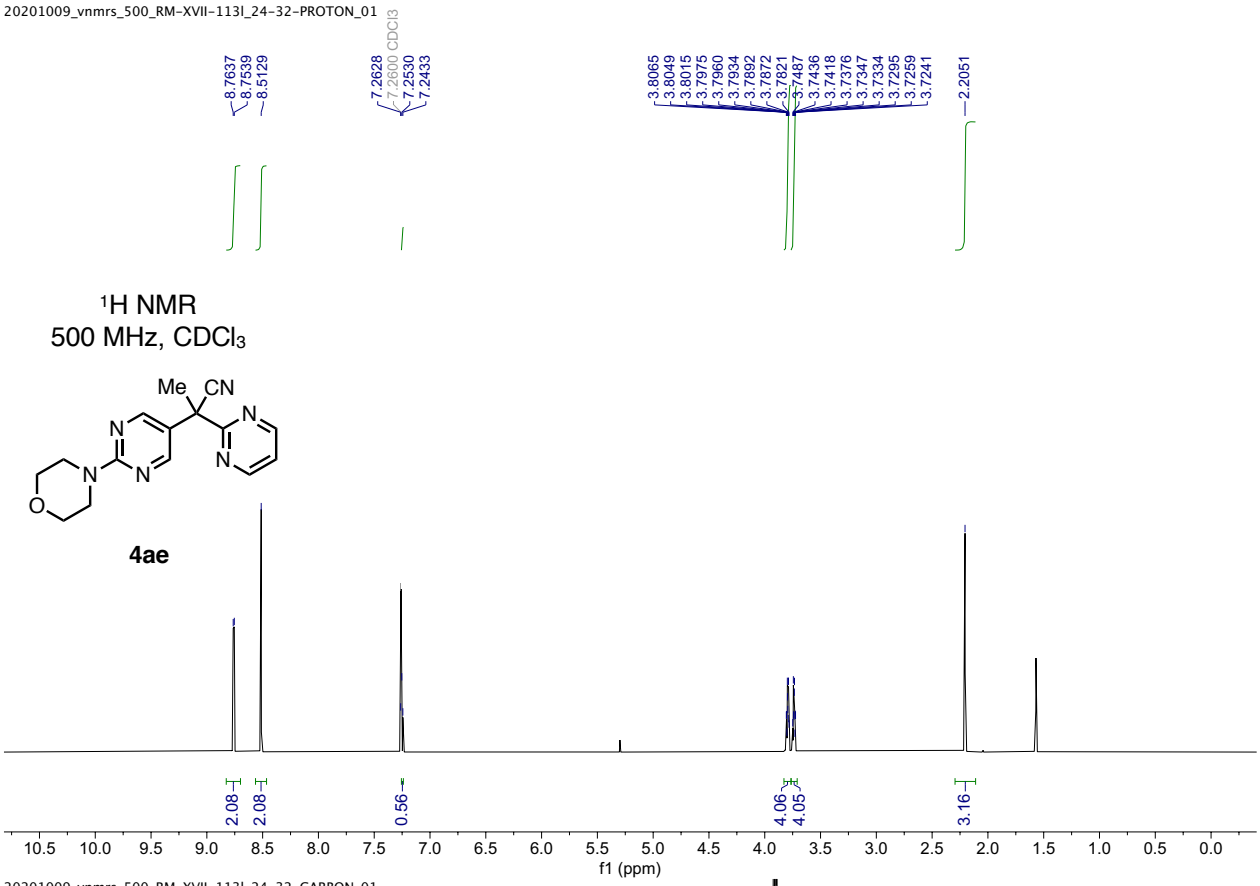
157.8274
156.8212
146.1897
135.3167
122.2876
122.0517
119.9320
106.3685
77.4000 CDCl3
48.5531
46.8324
26.0632
25.6623
13C{1H} NMR
126 MHz, CDCl3
Me
CN
N
N
N
N
4ad
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113I_24-32-PROTON_01
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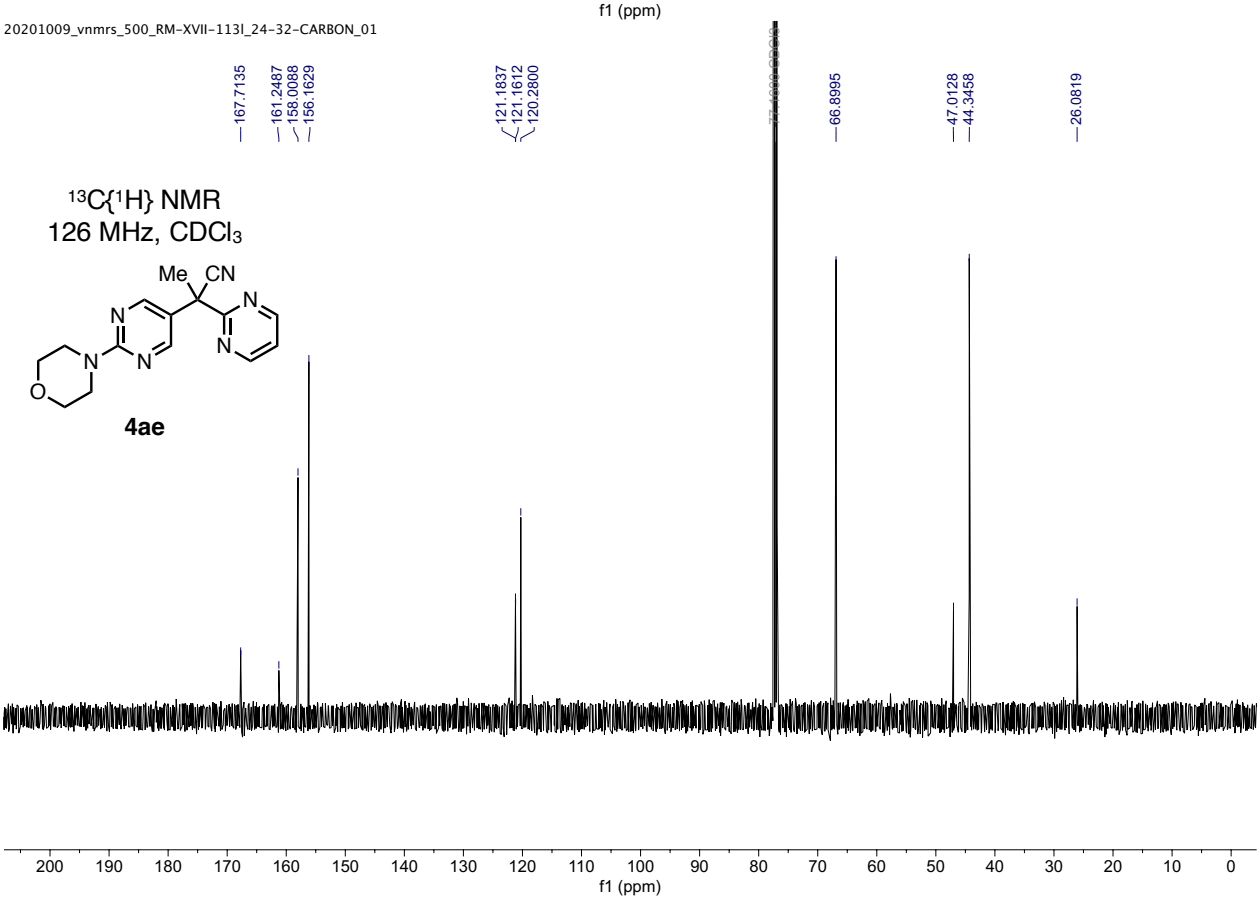
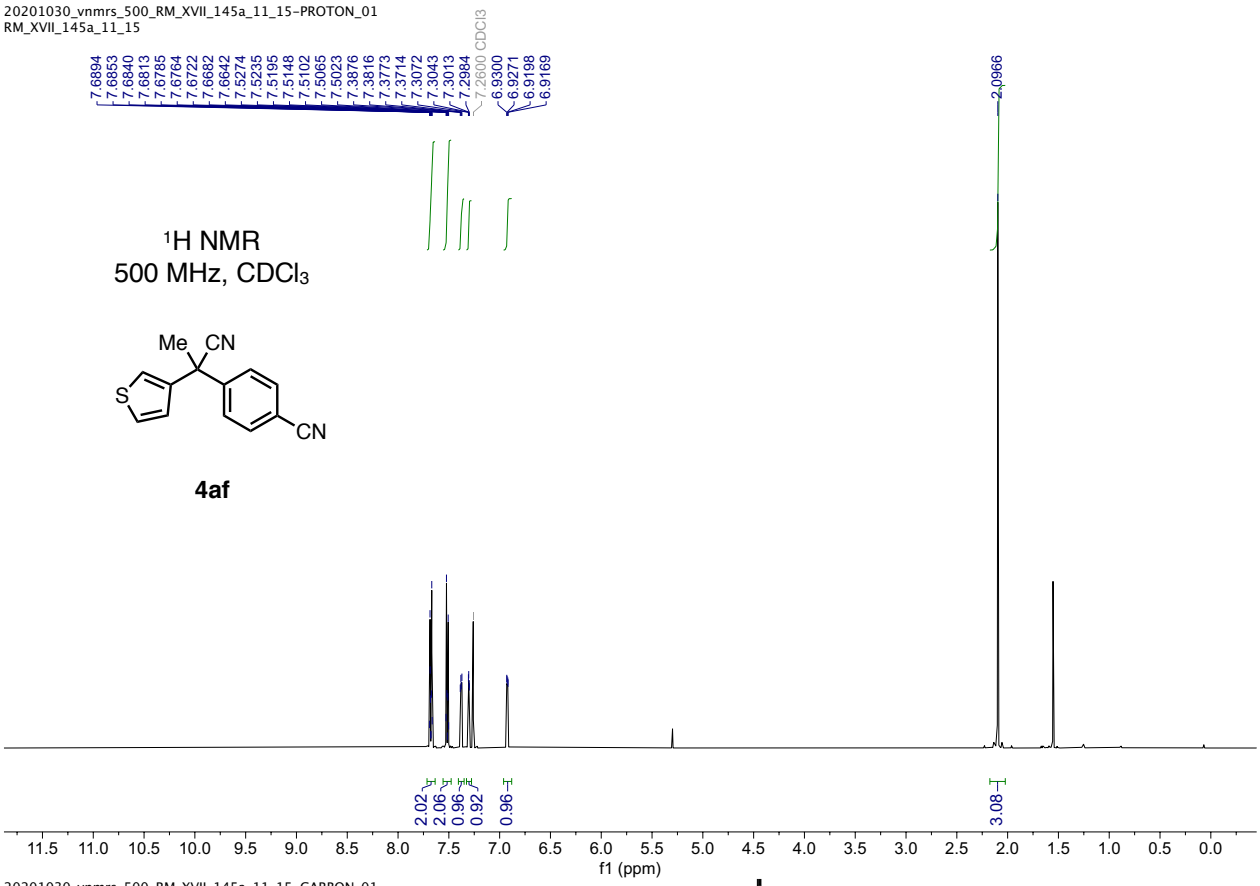
8.7539
8.5129
7.2628
7.2600 CDCl3
7.2530
7.2433
3.8065
3.8049
3.8015
3.7975
3.7960
3.7934
3.7892
3.7872
3.7821
3.7487
3.7436
3.7418
3.7376
3.7347
3.7334
3.7295
3.7259
3.7241
2.2051
1H NMR
500 MHz, CDCl3
Me
CN
4ae
2.08
2.08
0.56
4.06
4.05
3.16
f1 (ppm)


20201009_vnmrs_500_RM-XVII-113I_24-32-CARBON_01
167.7135
161.2487
158.0088
156.1629
121.1837
121.1612
120.2800
77.4000 CDCl3
66.8995
47.0128
44.3458
26.0819
13C{1H} NMR
126 MHz, CDCl3
Me
CN
4ae
f1 (ppm)


20201030_vnmrs_500_RM_XVII_145a_11_15-PROTON_01
RM_XVII_145a_11_15
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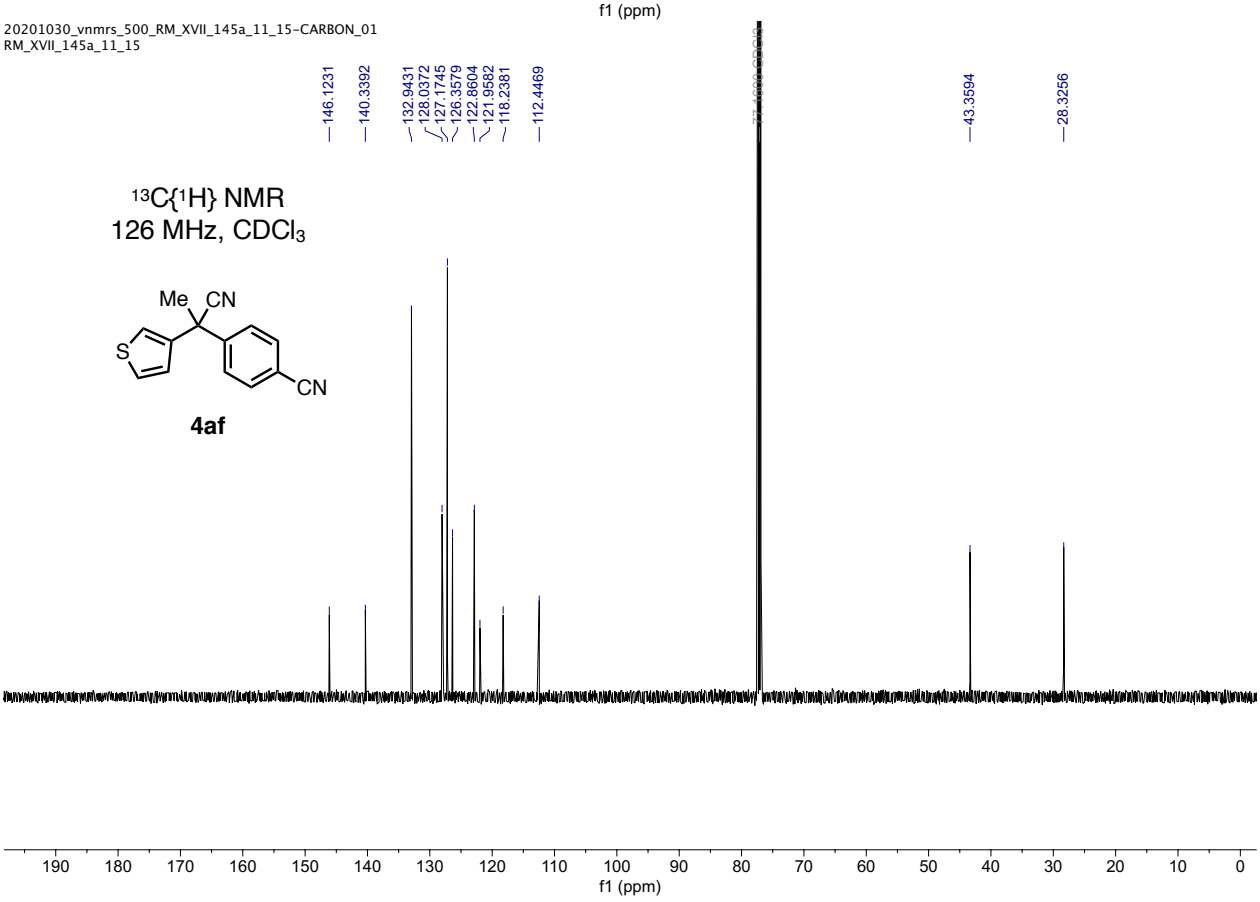
7.6853
7.6840
7.6813
7.6785
7.6764
7.6722
7.6682
7.6642
7.5274
7.5235
7.5195
7.5148
7.5102
7.5065
7.5023
7.3876
7.3816
7.3773
7.3714
7.3072
7.3043
7.3013
7.2984
7.2600 CDCl3
6.9300
6.9271
6.9198
6.9169
2.0966
1H NMR
500 MHz, CDCl3
Me
CN
S
CN
4af
2.02
2.06
0.96
0.92
0.96
3.08
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20201030_vnmrs_500_RM_XVII_145a_11_15-CARBON_01
RM_XVII_145a_11_15
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140.3392
132.9431
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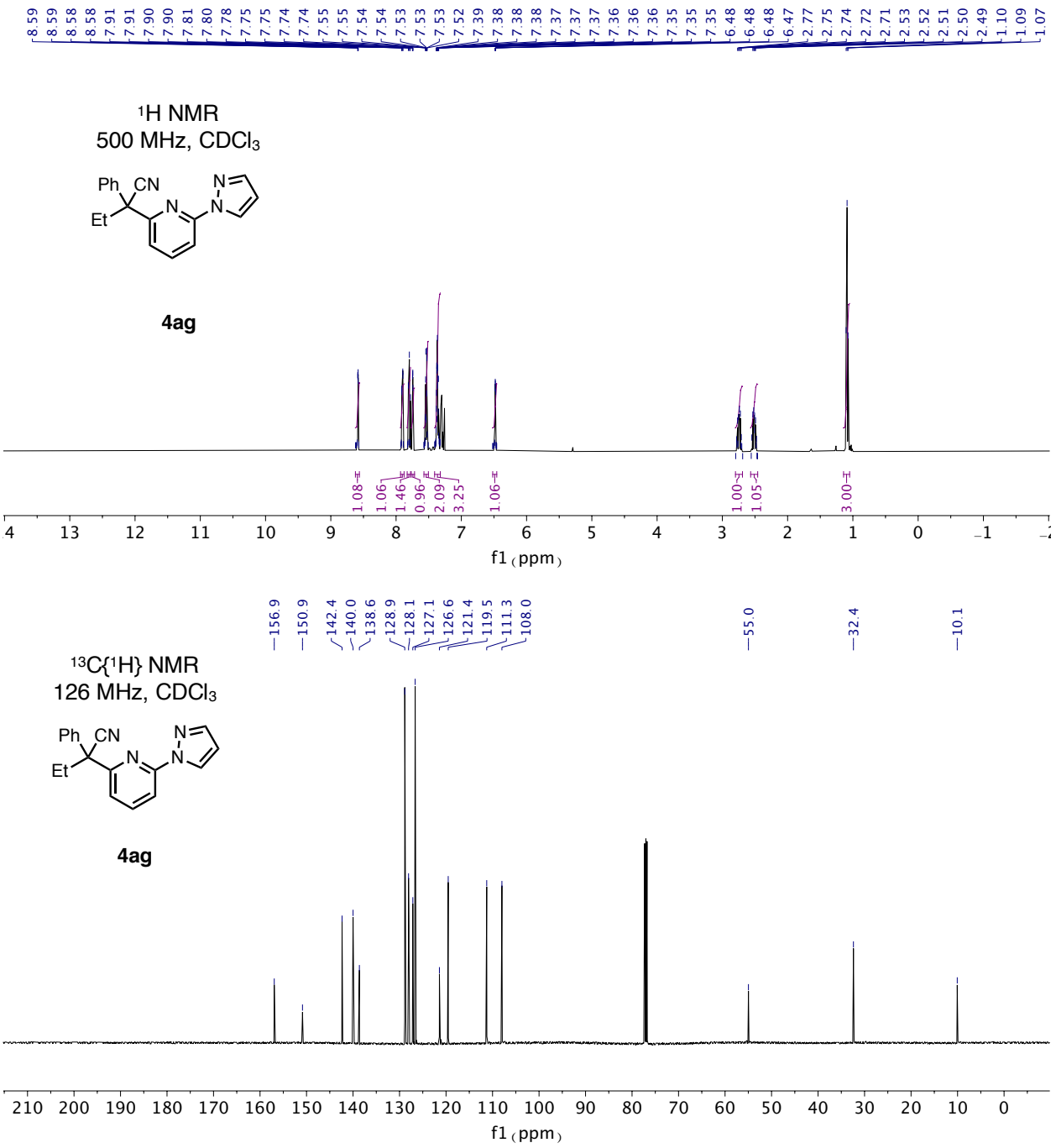
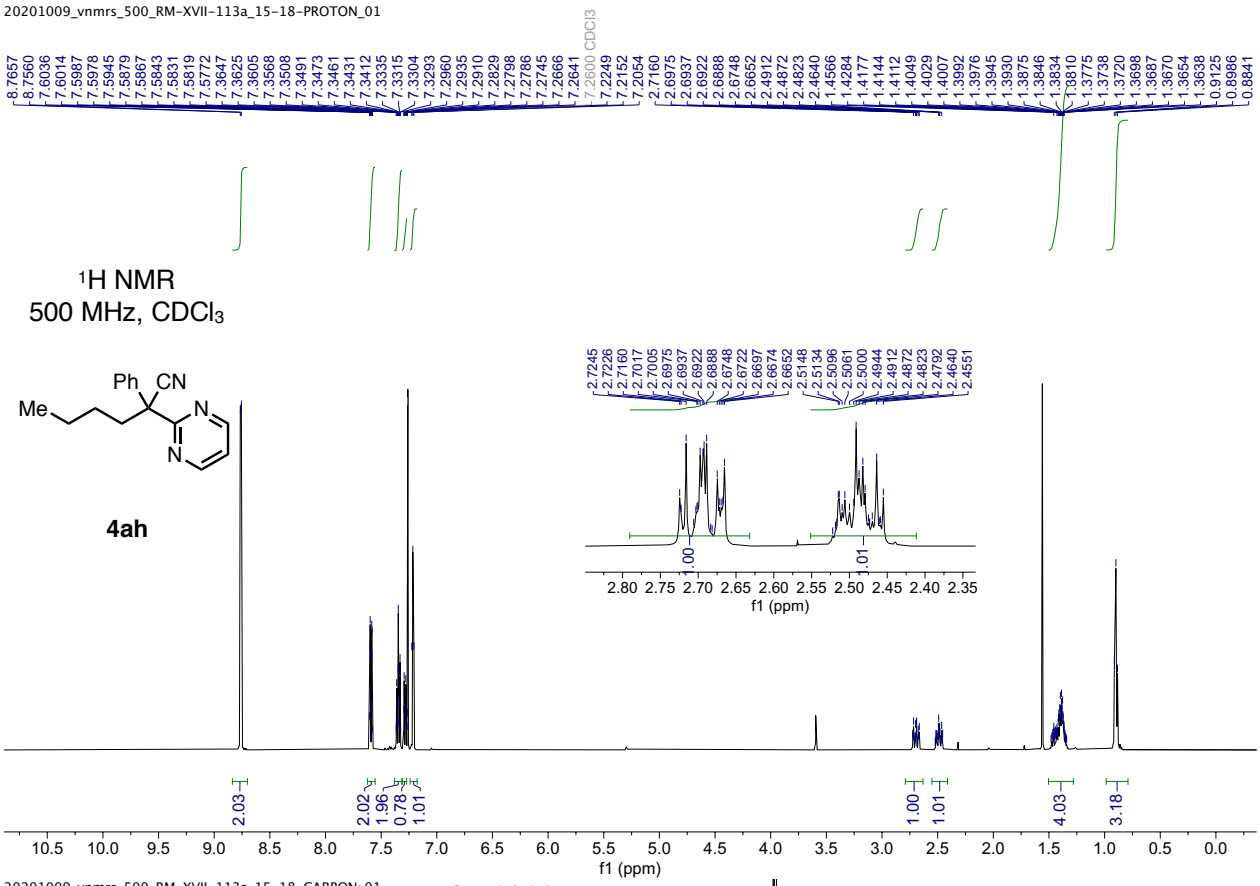
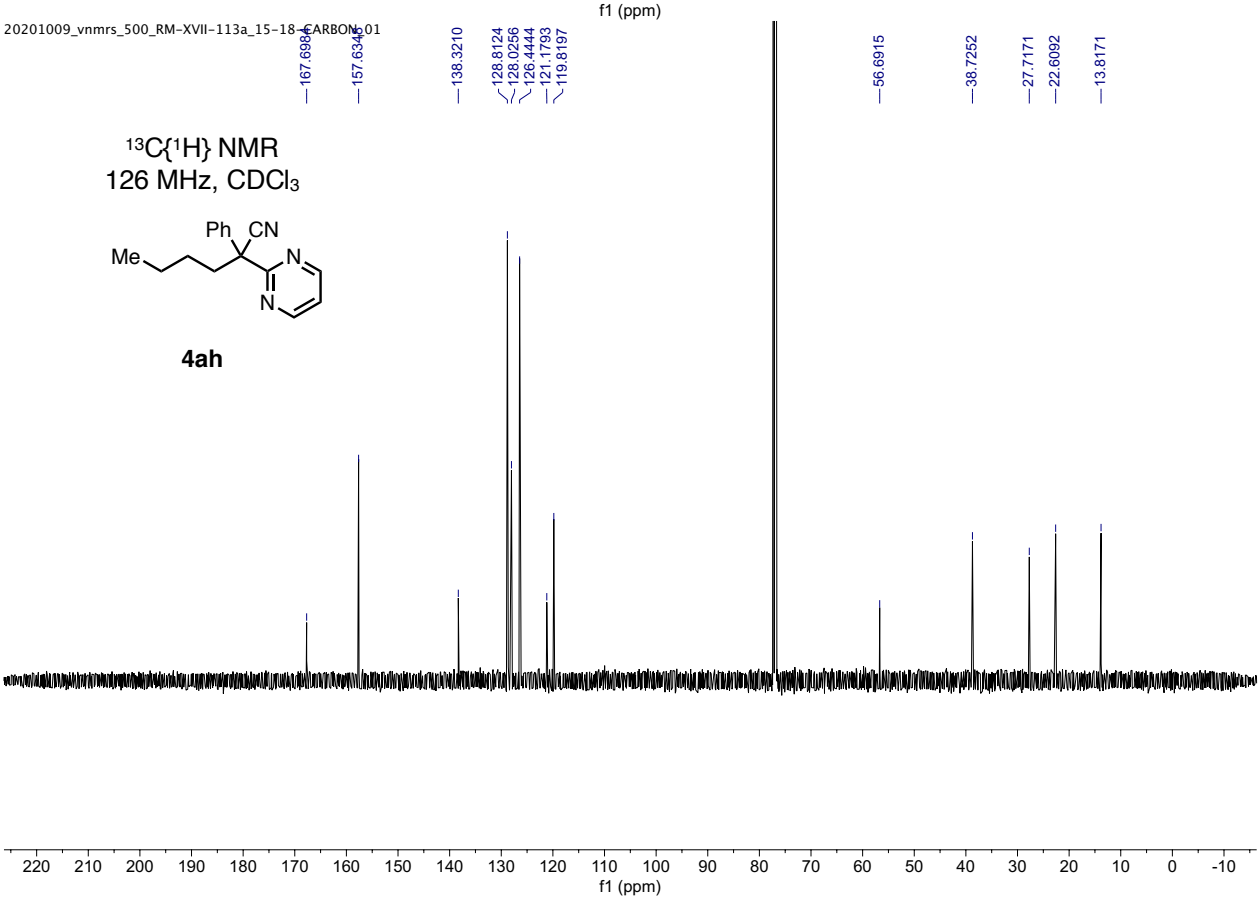
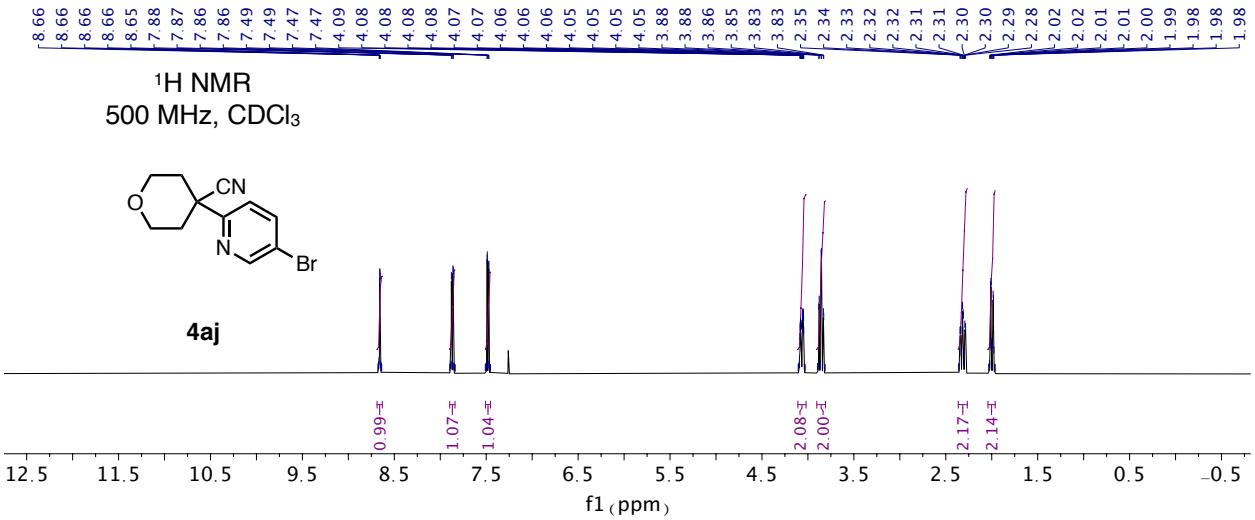
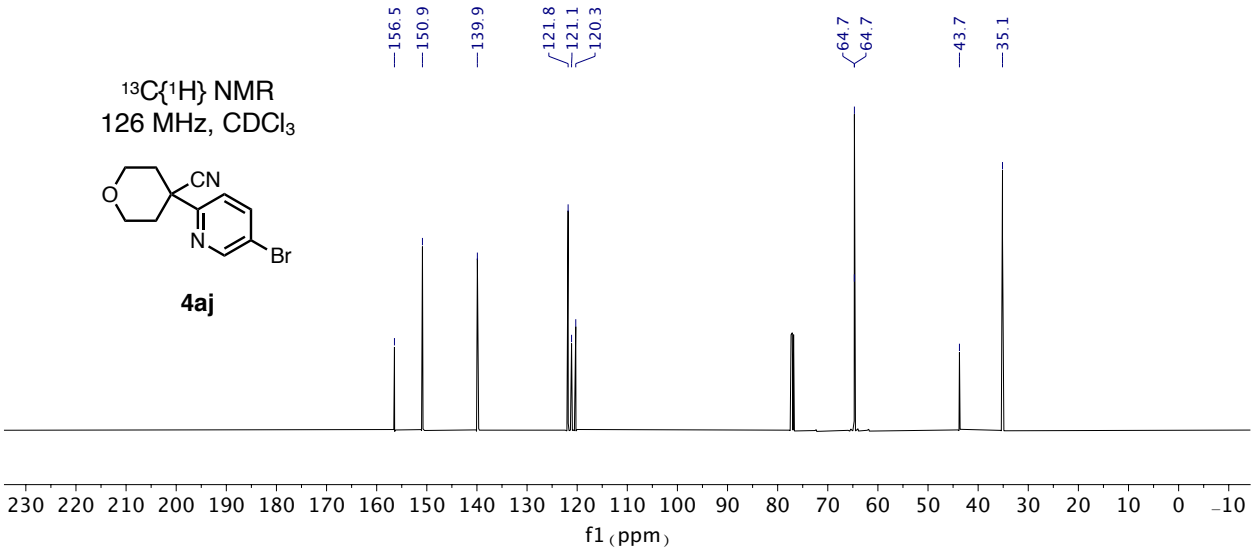
127.1745
126.3579
122.8604
121.9582
118.2381
112.4469
43.3594
28.3256
13C{1H} NMR
126 MHz, CDCl3
Me
CN
S
CN
4af
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

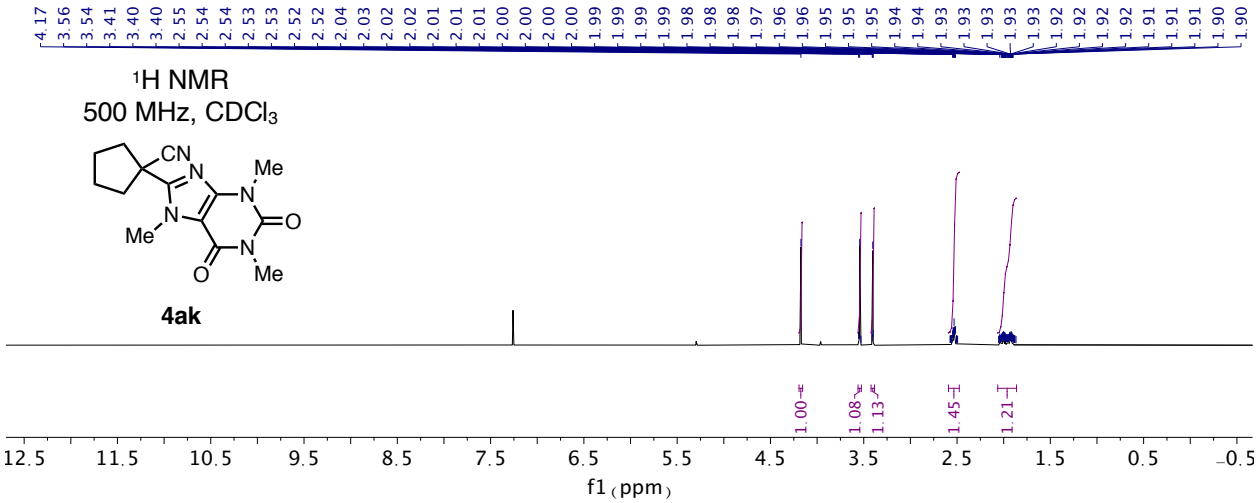

8.59 8.59 8.58 8.58 7.91 7.91 7.90 7.90 7.81 7.80 7.78 7.75 7.75 7.74 7.74 7.55 7.55 7.54 7.54 7.53 7.53 7.53 7.52 7.39 7.38 7.38 7.38 7.37 7.37 7.37 7.36 7.36 7.36 7.35 7.35 7.35 6.48 6.48 6.48 6.47 2.77 2.75 2.74 2.72 2.71 2.53 2.52 2.51 2.50 2.49 1.10 1.09 1.07
1H NMR
500 MHz, CDCl3
Ph CN
Et
N
N
N
4ag
1.08 1.06 1.46 0.96 2.09 3.25 1.06 1.00 1.05 3.00
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)
156.9 150.9 142.4 140.0 138.6 128.9 128.1 127.1 126.6 121.4 119.5 111.3 108.0 55.0 32.4 10.1
13C{1H} NMR
126 MHz, CDCl3
Ph CN
Et
N
N
N
4ag
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

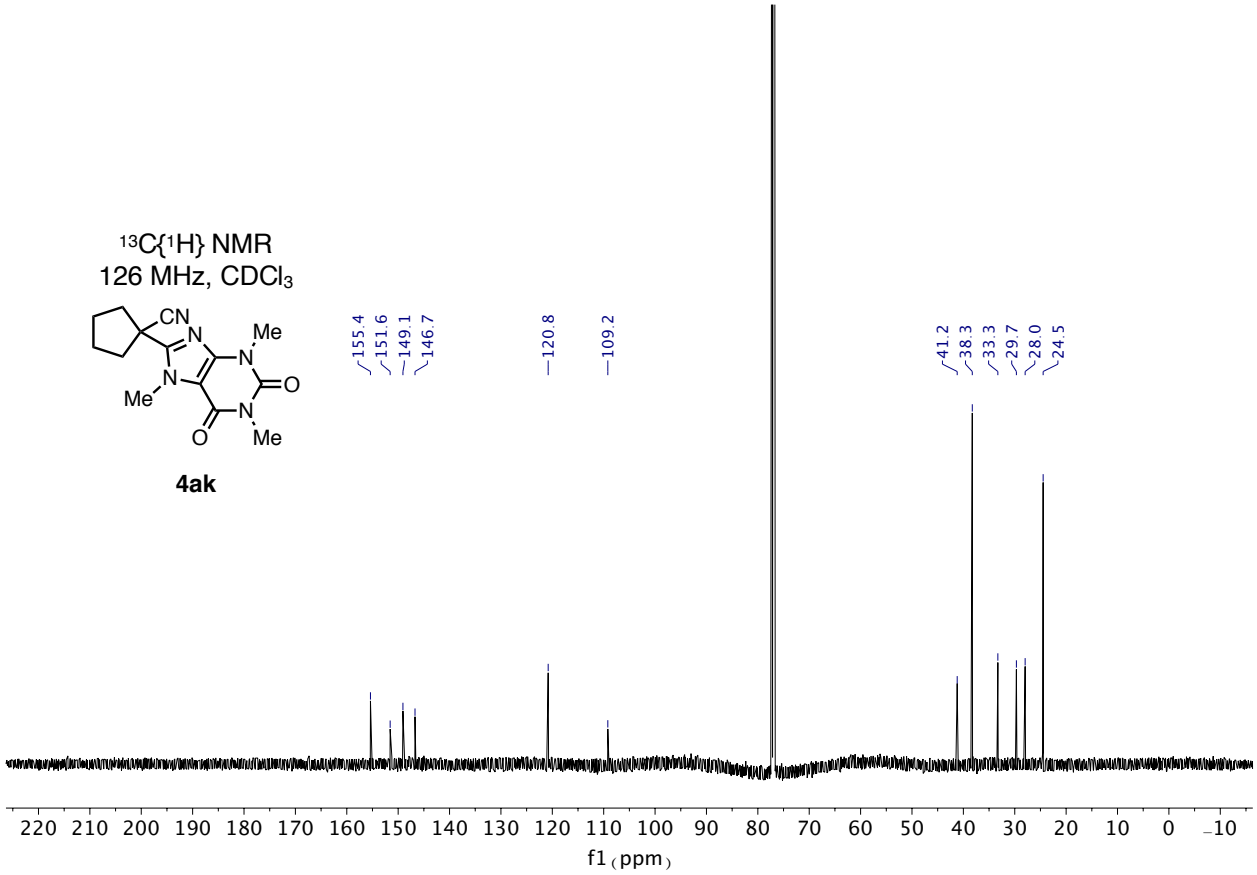

20201009_vnmrs_500_RM-XVII-113a_15-18-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
Ph CN
Me
N
N
4ah
2.03
2.02
1.96
0.78
1.01
1.00
1.01
4.03
3.18
f1 (ppm)

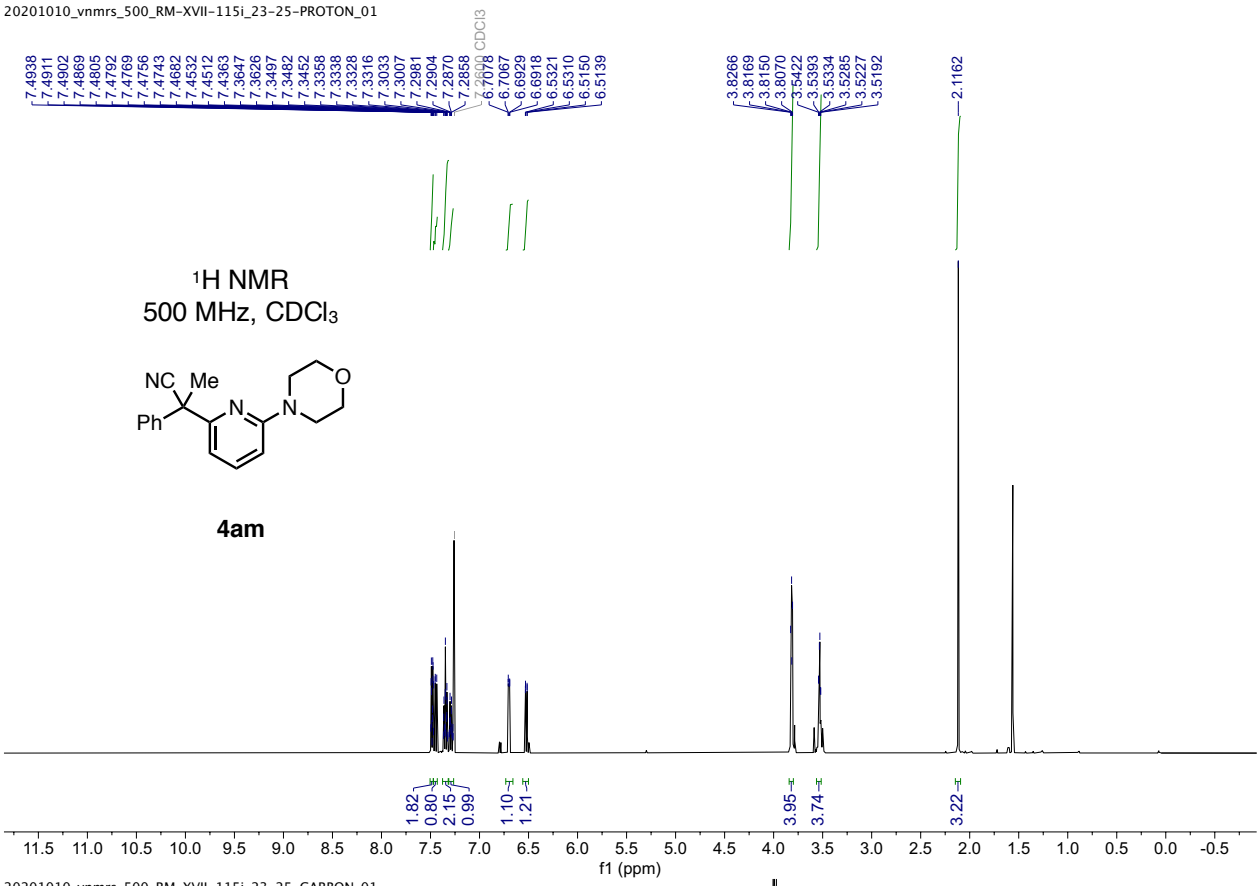

20201009_vnmrs_500_RM-XVII-113a_15-18_CARBON_01
167.6984
157.6345
138.3210
128.8124
128.0256
126.4444
121.1793
119.8197
56.6915
38.7252
27.7171
22.6092
13.8171
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
Ph CN
Me
N
N
4ah
f1 (ppm)

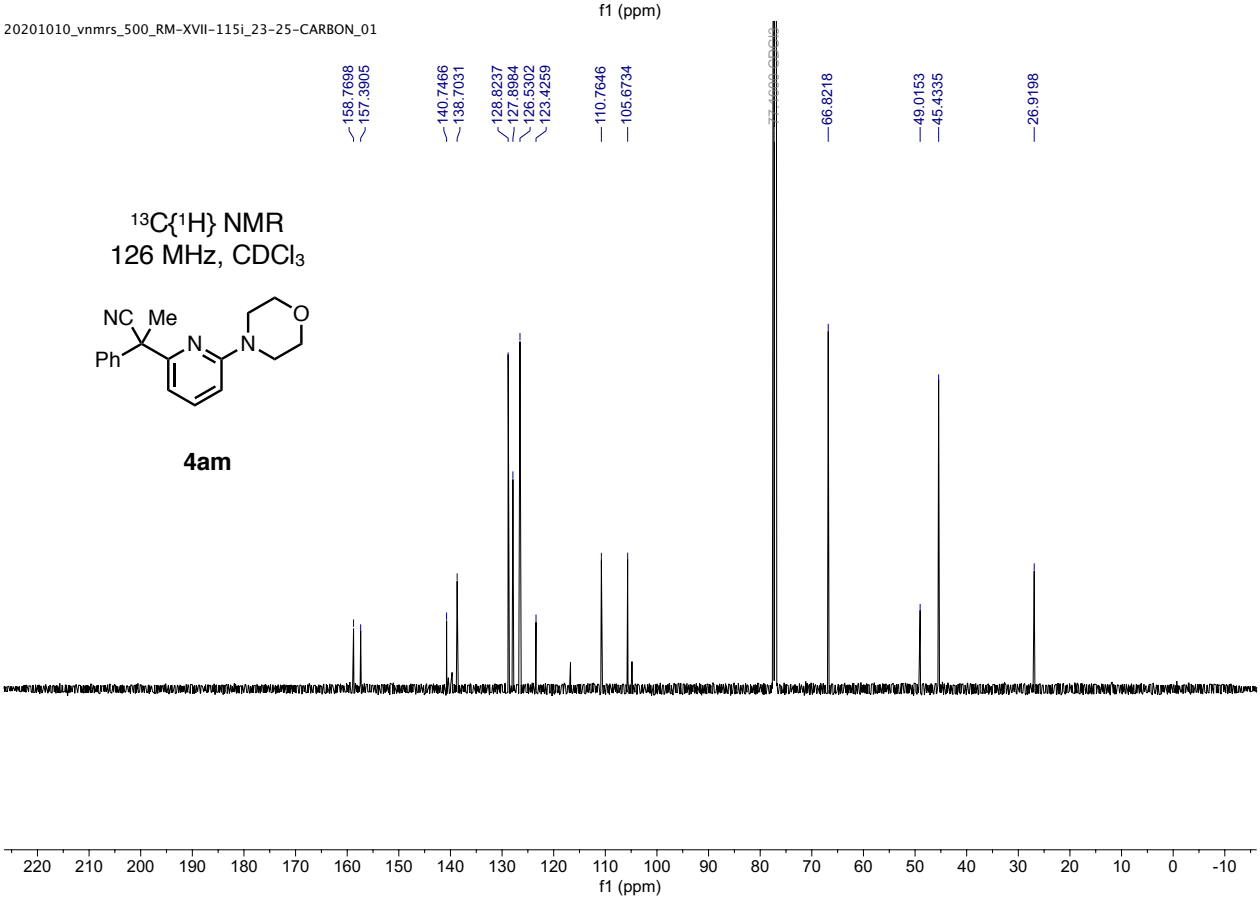

8.66 8.66 8.66 8.66 8.65 7.88 7.87 7.86 7.86 7.49 7.49 7.47 7.47 4.09 4.08 4.08 4.08 4.08 4.07 4.07 4.06 4.06 4.06 4.05 4.05 4.05 4.05 3.88 3.88 3.86 3.85 3.83 3.83 2.35 2.34 2.33 2.32 2.32 2.31 2.31 2.30 2.30 2.29 2.28 2.02 2.02 2.01 2.01 2.00 1.99 1.98 1.98 1.98
¹H NMR
500 MHz, CDCl₃
CN
O
N
Br
4aj
0.99 1.07 1.04 2.08 2.00 2.17 2.14
12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)


156.5 150.9 139.9 121.8 121.1 120.3 64.7 64.7 43.7 35.1
¹³C{¹H} NMR
126 MHz, CDCl₃
CN
O
N
Br
4aj
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


4.17 3.56 3.54 3.41 3.40 3.40 2.55 2.54 2.54 2.53 2.53 2.52 2.52 2.04 2.03 2.02 2.02 2.01 2.01 2.01 2.00 2.00 2.00 2.00 1.99 1.99 1.99 1.99 1.98 1.98 1.98 1.97 1.96 1.96 1.95 1.95 1.95 1.94 1.94 1.93 1.93 1.93 1.93 1.92 1.92 1.92 1.92 1.91 1.91 1.90 1.90
1H NMR
500 MHz, CDCl3
CN
N
Me
N
N
O
Me
N
O
Me
4ak
1.00
1.08
1.13
1.45
1.21
12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)

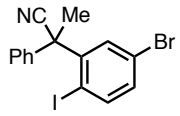

13C{1H} NMR
126 MHz, CDCl3
CN
N
Me
N
N
O
Me
N
O
Me
4ak
155.4
151.6
149.1
146.7
120.8
109.2
41.2
38.3
33.3
29.7
28.0
24.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


20201010_vnmrs_500_RM-XVII-115i_23-25-PROTON_01
7.4938
7.4911
7.4902
7.4869
7.4805
7.4792
7.4769
7.4756
7.4743
7.4682
7.4532
7.4512
7.4363
7.3647
7.3626
7.3497
7.3482
7.3452
7.3358
7.3338
7.3328
7.3316
7.3033
7.3007
7.2981
7.2904
7.2870
7.2858
7.2600 CDCl3
6.7078
6.7067
6.6929
6.6918
6.5321
6.5310
6.5150
6.5139
3.8266
3.8169
3.8150
3.8070
3.5422
3.5393
3.5334
3.5285
3.5227
3.5192
2.1162
1H NMR
500 MHz, CDCl3
NC
Me
Ph
N
N
O
4am
1.82
0.80
2.15
0.99
1.10
1.21
3.95
3.74
3.22
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


20201010_vnmrs_500_RM-XVII-115i_23-25-CARBON_01
158.7698
157.3905
140.7466
138.7031
128.8237
127.8984
126.5302
123.4259
110.7646
105.6734
77.4088 CDCl3
66.8218
49.0153
45.4335
26.9198
13C{1H} NMR
126 MHz, CDCl3
NC
Me
Ph
N
N
O
4am
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

20201010_vnmrs_500_RM-XVII-115h_25-27-PROTON_01

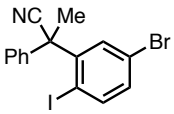
^{1}H NMR
500 MHz, $CDCl_3$



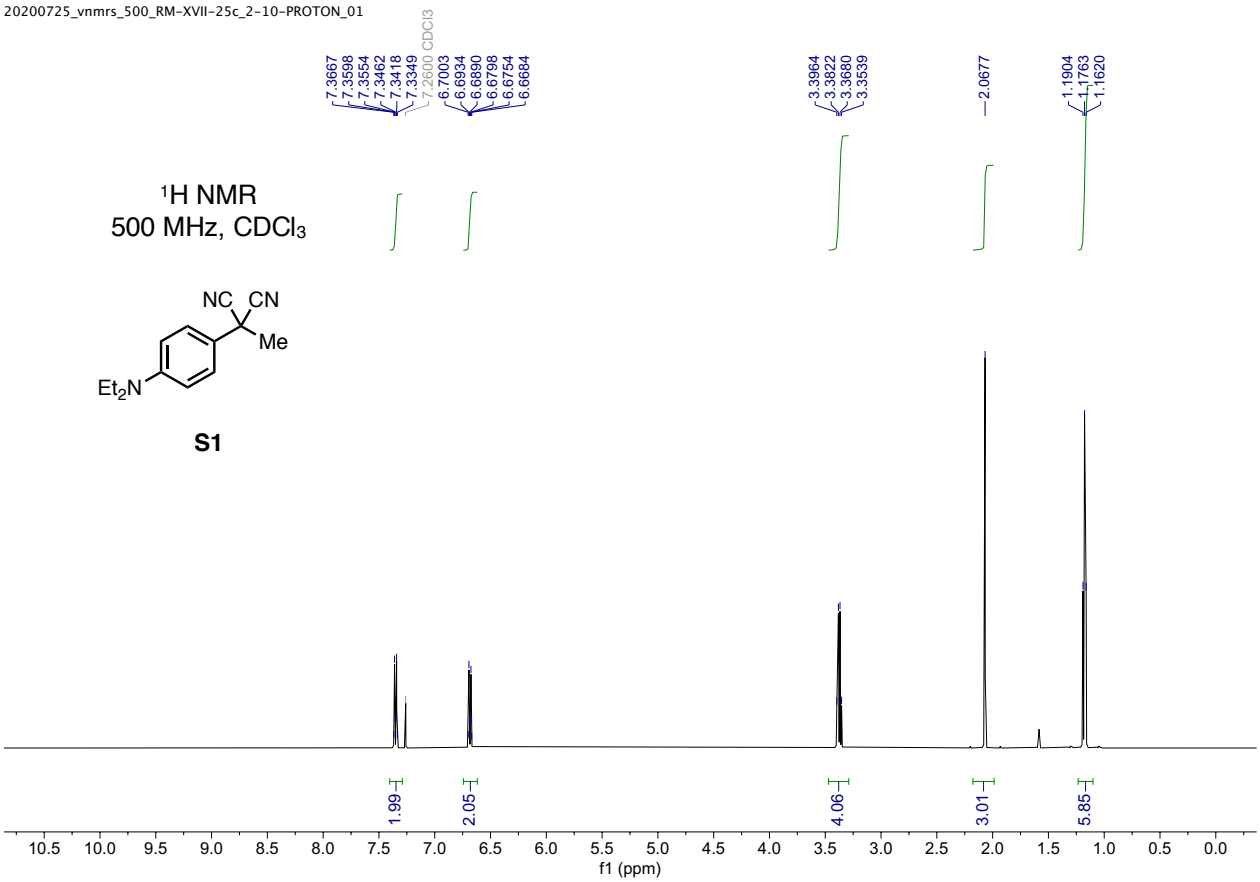
4an

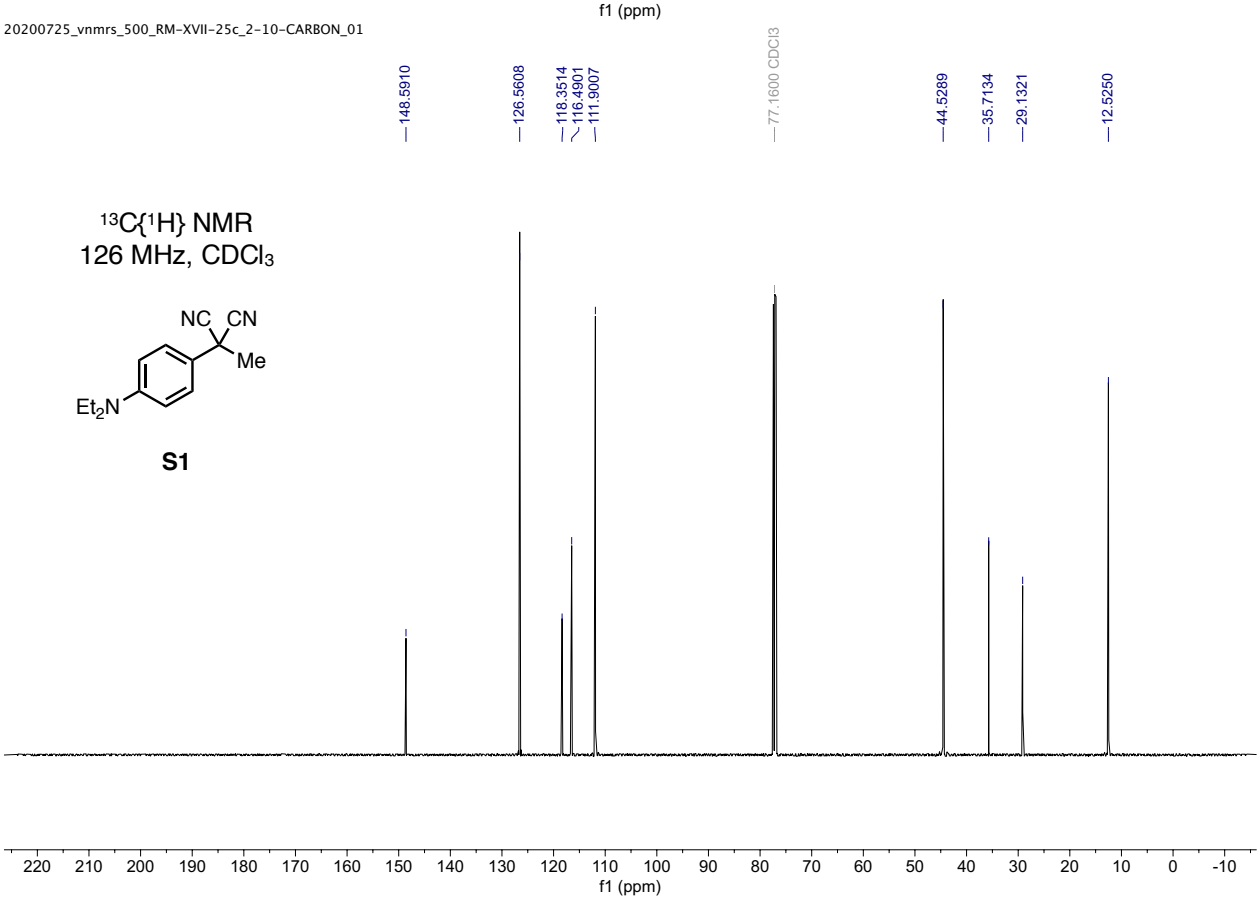
20201010_vnmrs_500_RM-XVII-115h_25-27-CARBON_01

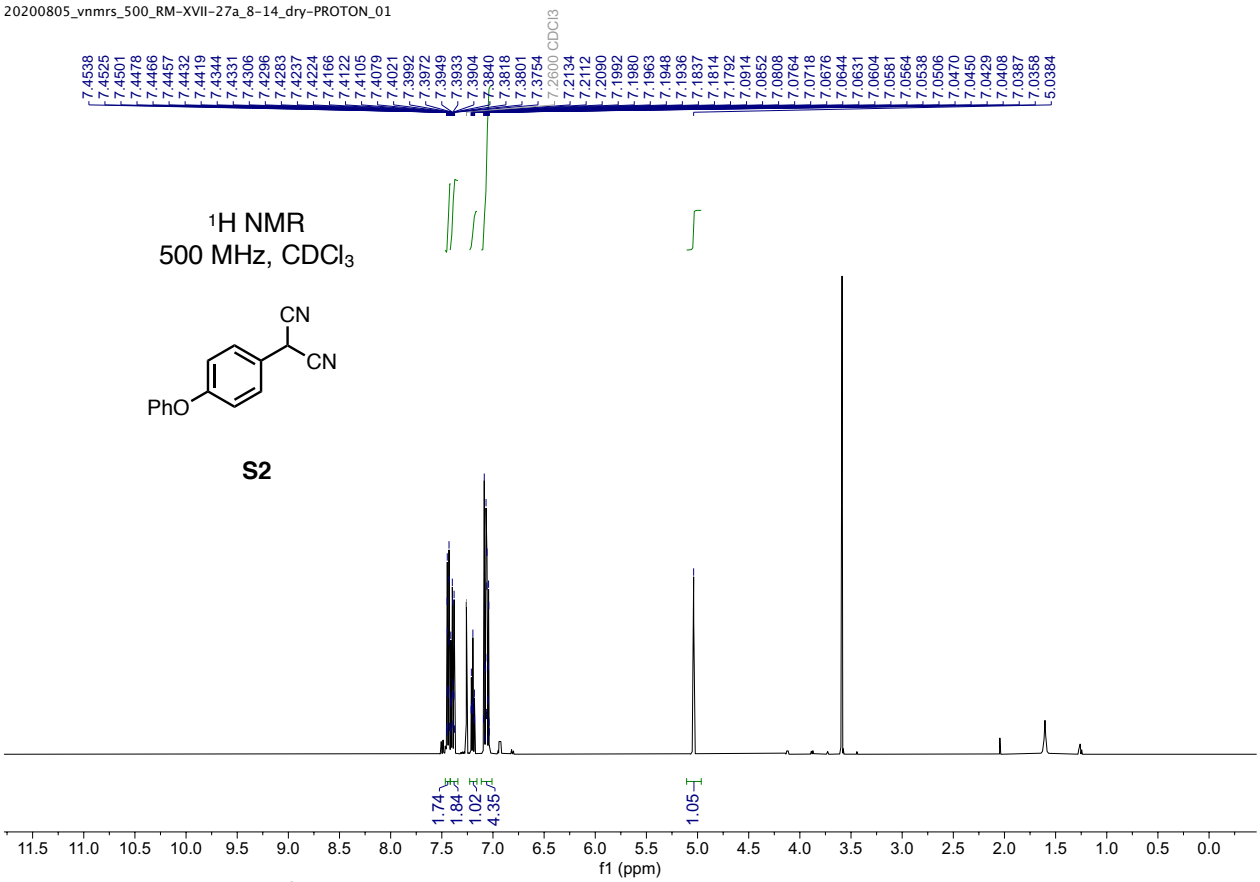
$^{13}C\{^{1}H\}$ NMR
126 MHz, $CDCl_3$

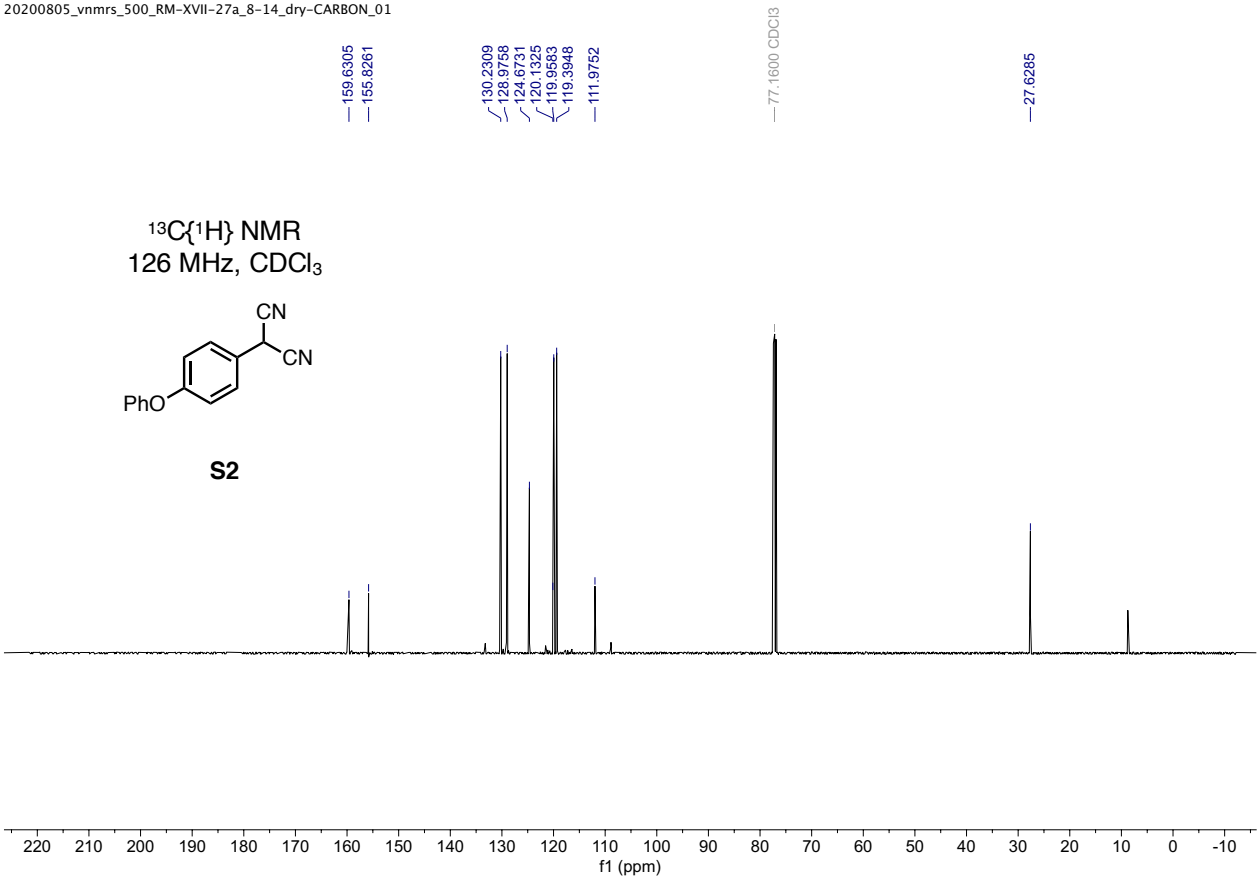


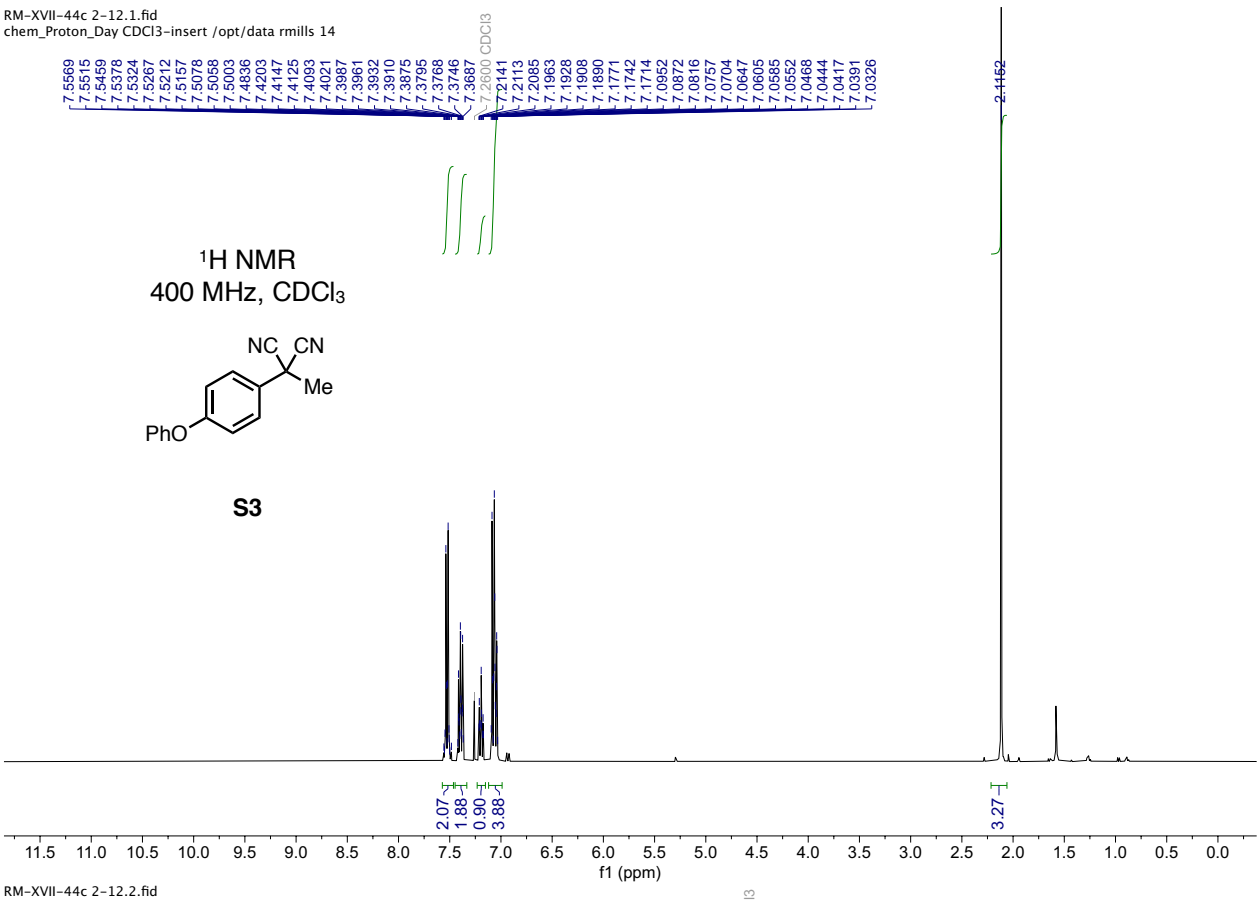
4an

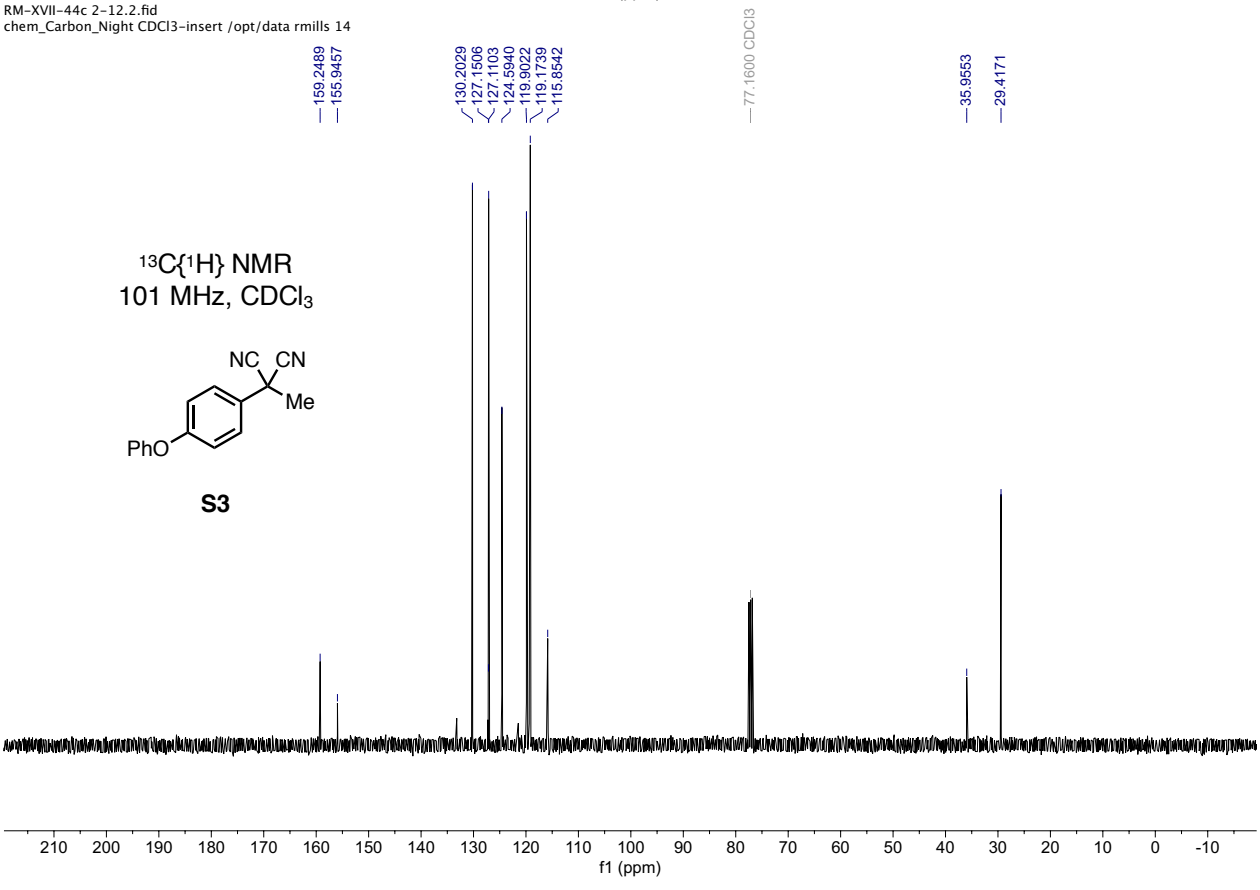

20200725_vnmrs_500_RM-XVII-25c_2-10-PROTON_01
7.3667
7.3598
7.3554
7.3462
7.3418
7.3349
7.2600 CDCl3
6.7003
6.6934
6.6890
6.6798
6.6754
6.6684
3.3964
3.3822
3.3680
3.3539
2.0677
1.1904
1.1763
1.1620
1H NMR
500 MHz, CDCl3
NC CN
Me
Et2N
S1
1.99
2.05
4.06
3.01
5.85
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

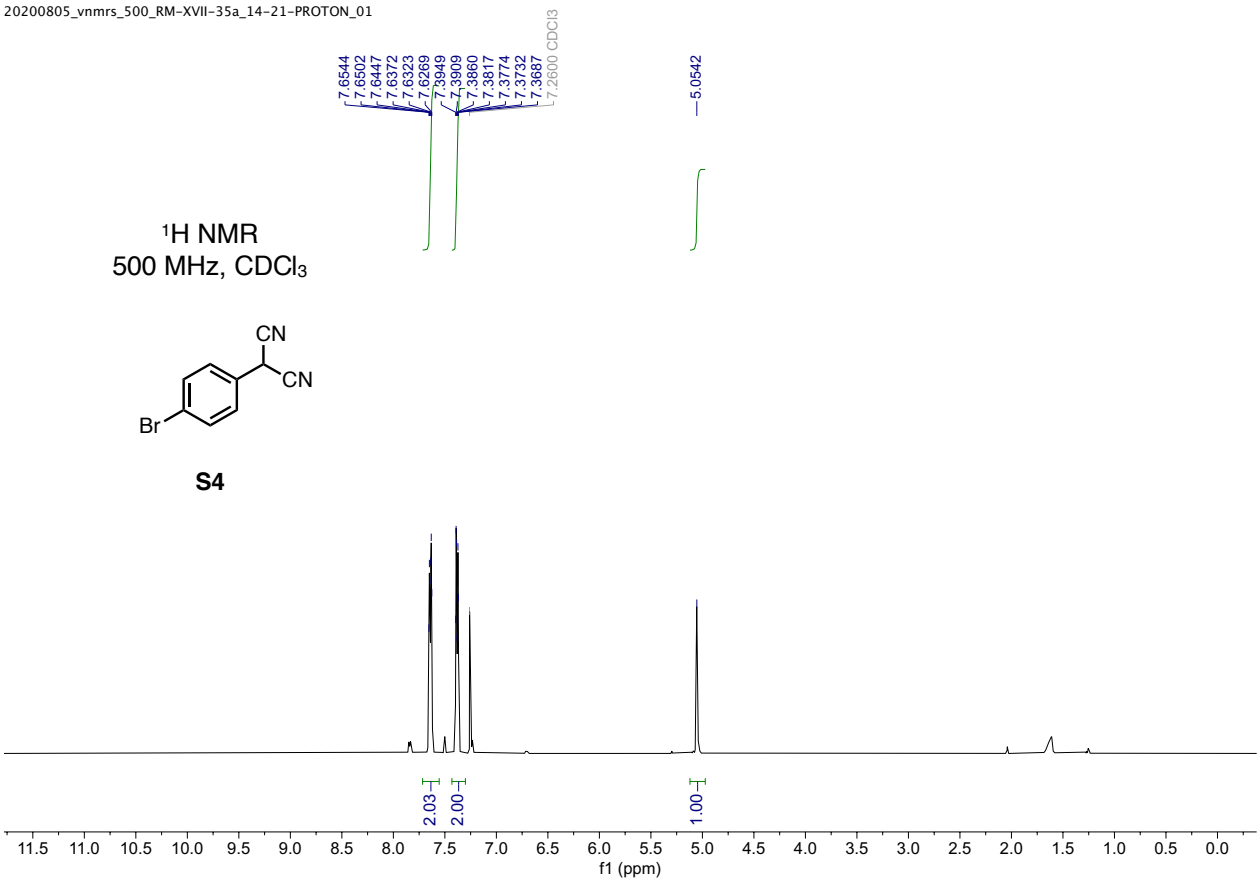

20200725_vnmrs_500_RM-XVII-25c_2-10-CARBON_01
148.5910
126.5608
118.3514
116.4901
111.9007
77.1600 CDCl3
44.5289
35.7134
29.1321
12.5250
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
Et2N
S1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


20200805_vnmrs_500_RM-XVII-27a_8-14_dry-PROTON_01
7.4538
7.4525
7.4501
7.4478
7.4466
7.4457
7.4432
7.4419
7.4344
7.4331
7.4306
7.4296
7.4283
7.4237
7.4224
7.4166
7.4122
7.4105
7.4079
7.4021
7.3992
7.3972
7.3949
7.3933
7.3904
7.3840
7.3818
7.3801
7.3754
7.2600 CDCl3
7.2134
7.2112
7.2090
7.1992
7.1980
7.1963
7.1948
7.1936
7.1837
7.1814
7.1792
7.0914
7.0852
7.0808
7.0764
7.0718
7.0676
7.0644
7.0631
7.0604
7.0581
7.0564
7.0538
7.0506
7.0470
7.0450
7.0429
7.0408
7.0387
7.0358
5.0384
1H NMR
500 MHz, CDCl3
CN
CN
PhO
S2
1.74
1.84
1.02
4.35
1.05
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

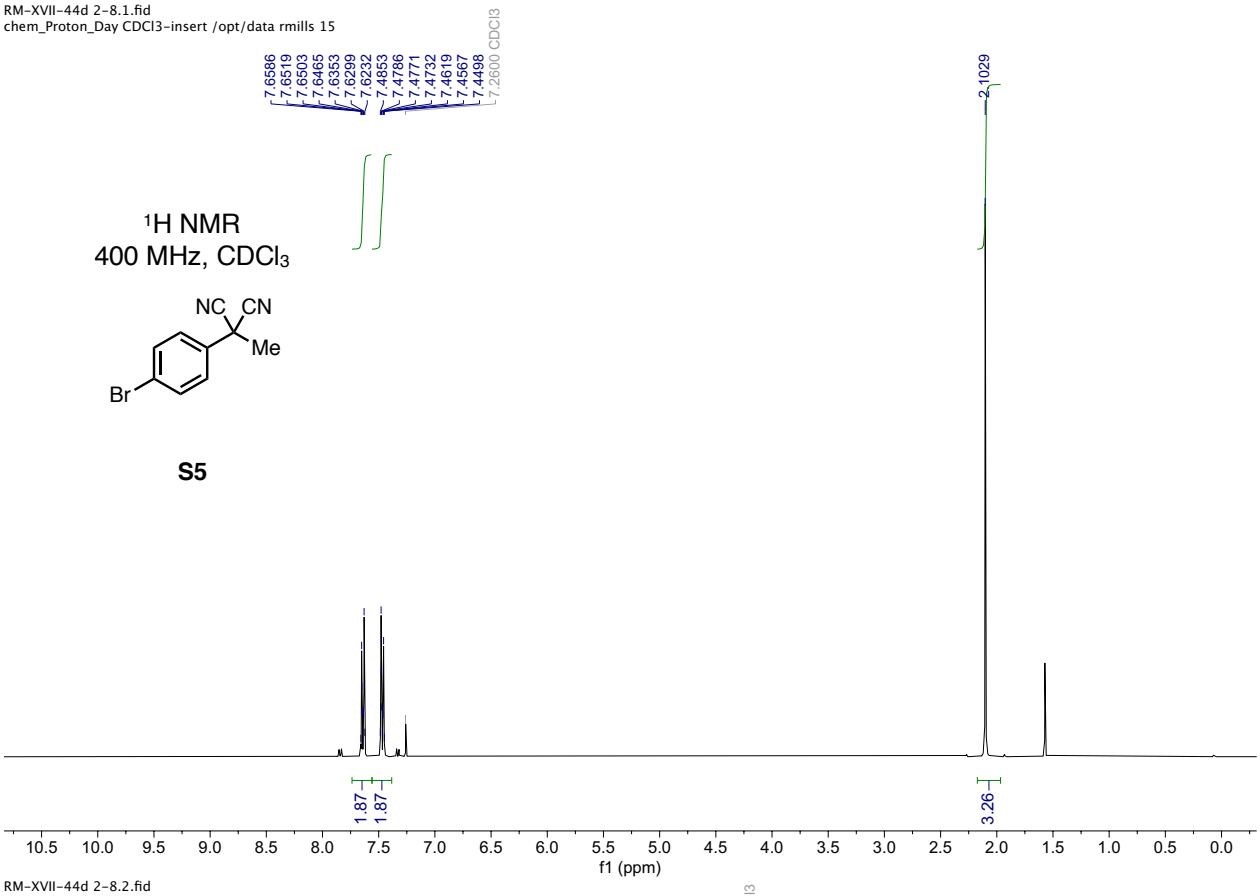

20200805_vnmrs_500_RM-XVII-27a_8-14_dry-CARBON_01
159.6305
155.8261
130.2309
128.9758
124.6731
120.1325
119.9583
119.3948
111.9752
77.1600 CDCl3
27.6285
13C{1H} NMR
126 MHz, CDCl3
CN
CN
PhO
S2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


RM-XVII-44c 2-12.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 14
7.5569
7.5515
7.5459
7.5378
7.5324
7.5267
7.5212
7.5157
7.5078
7.5058
7.5003
7.4836
7.4203
7.4147
7.4125
7.4093
7.4021
7.3987
7.3961
7.3932
7.3910
7.3875
7.3795
7.3768
7.3746
7.3687
7.2600 CDCl3
7.2141
7.2113
7.2085
7.1963
7.1928
7.1908
7.1890
7.1771
7.1742
7.1714
7.0952
7.0872
7.0816
7.0757
7.0704
7.0647
7.0605
7.0585
7.0552
7.0468
7.0444
7.0417
7.0391
7.0326
2.1152
1H NMR
400 MHz, CDCl3
NC CN
Me
PhO
S3
2.07
1.88
0.90
3.88
3.27
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


RM-XVII-44c 2-12.2.fid
chem_Carbon_Night CDCl3-insert /opt/data rmills 14
159.2489
155.9457
130.2029
127.1506
127.1103
124.5940
119.9022
119.1739
115.8542
77.1600 CDCl3
35.9553
29.4171
13C{1H} NMR
101 MHz, CDCl3
NC CN
Me
PhO
S3
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)


20200805_vnmrs_500_RM-XVII-35a_14-21-PROTON_01
7.6544
7.6502
7.6447
7.6372
7.6323
7.6269
7.3949
7.3909
7.3860
7.3817
7.3774
7.3732
7.3687
7.2600 CDCl3
5.0542
1H NMR
500 MHz, CDCl3
CN
CN
Br
S4
2.03
2.00
1.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

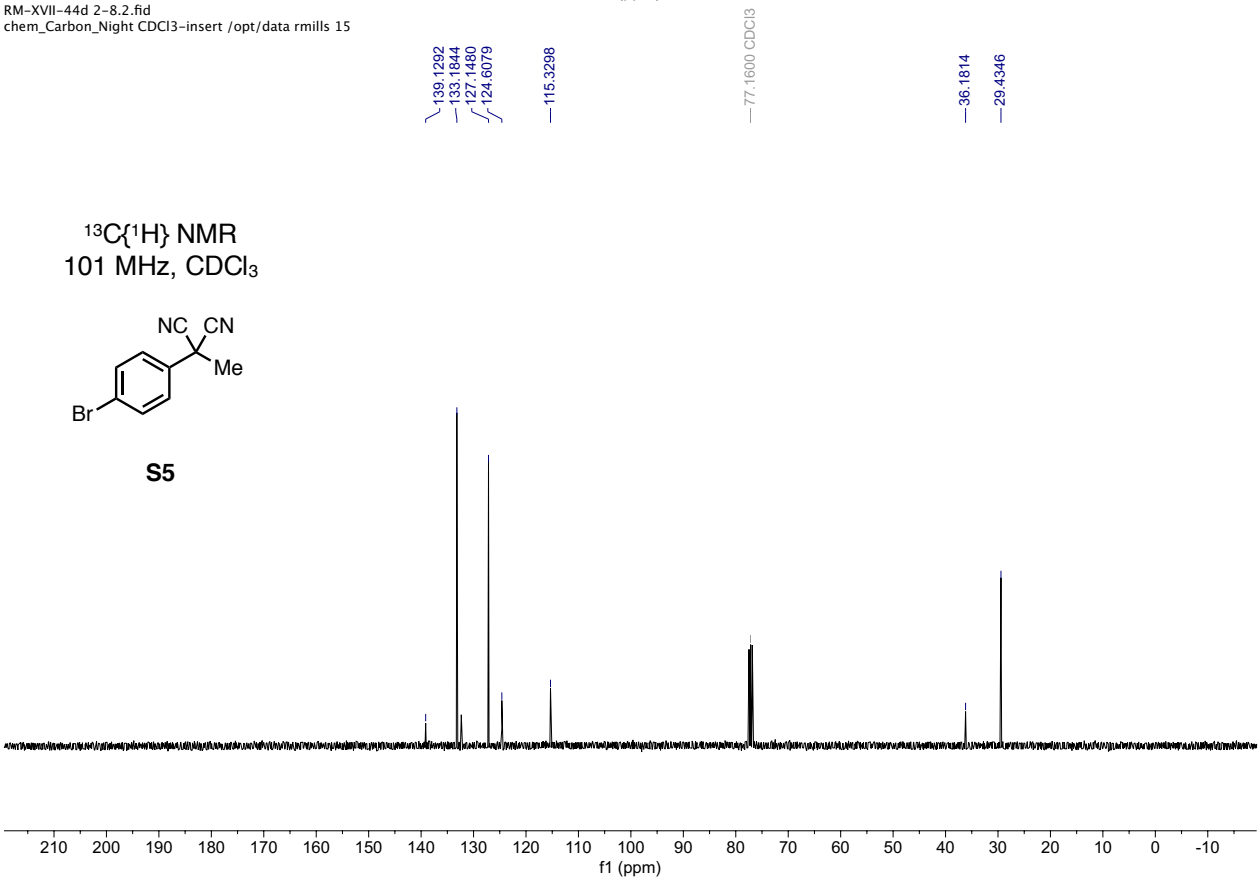
RM-XVII-44d 2-8.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 15



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

S5

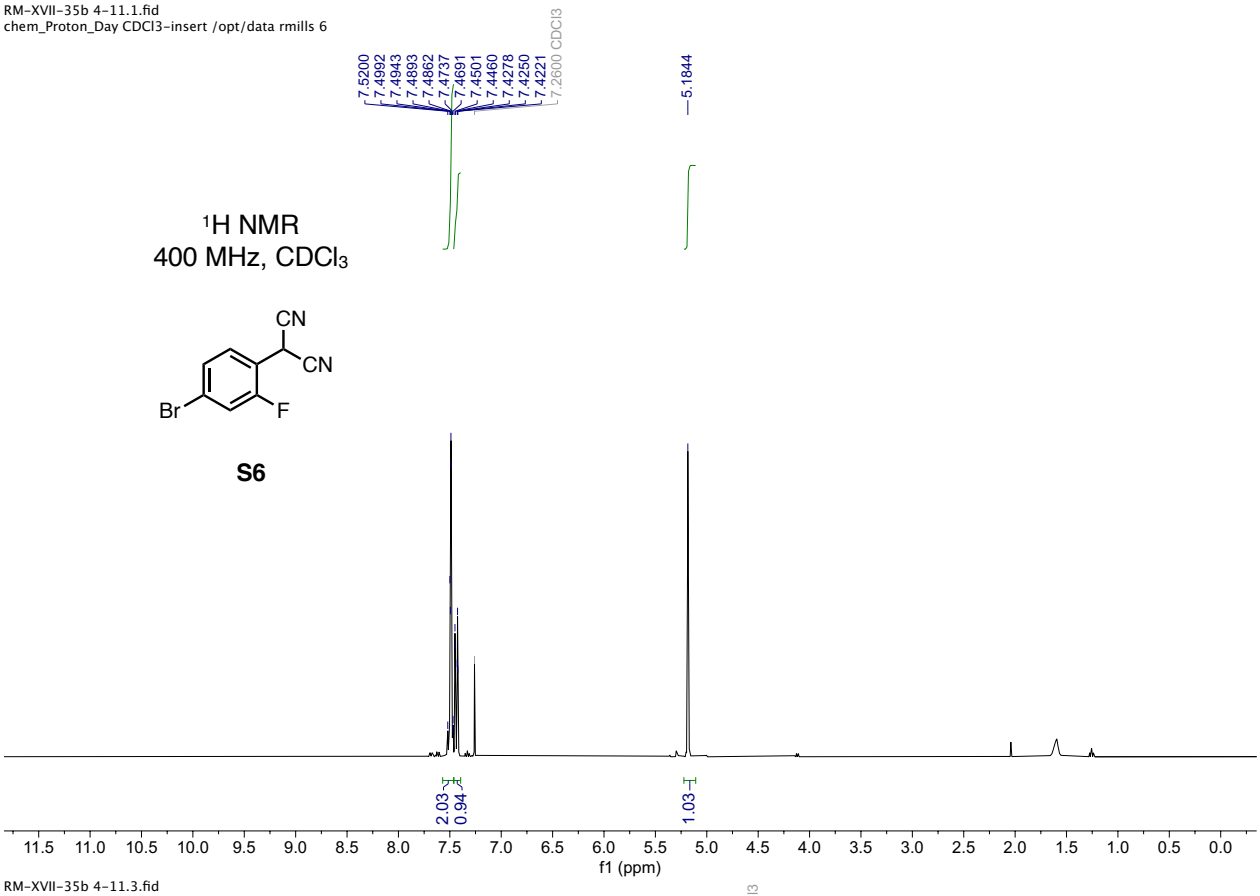
RM-XVII-44d 2-8.2.fid
chem_Carbon_Night CDCl3-insert /opt/data rmills 15



^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

S5

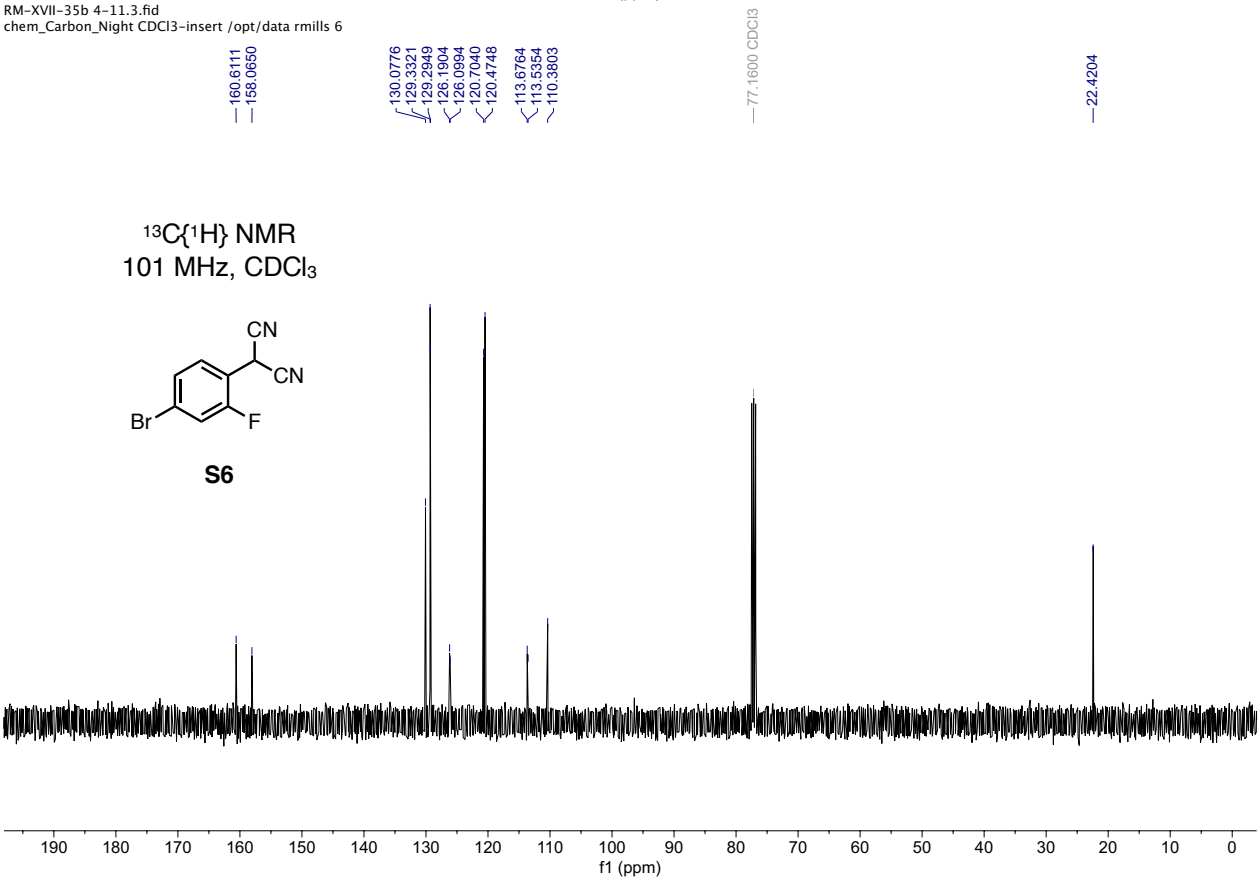
RM-XVII-35b 4-11.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 6



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

S6

RM-XVII-35b 4-11.3.fid
chem_Carbon_Night CDCl3-insert /opt/data rmills 6



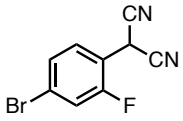
^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

S6

RM-XVII-35b 4-11.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 6

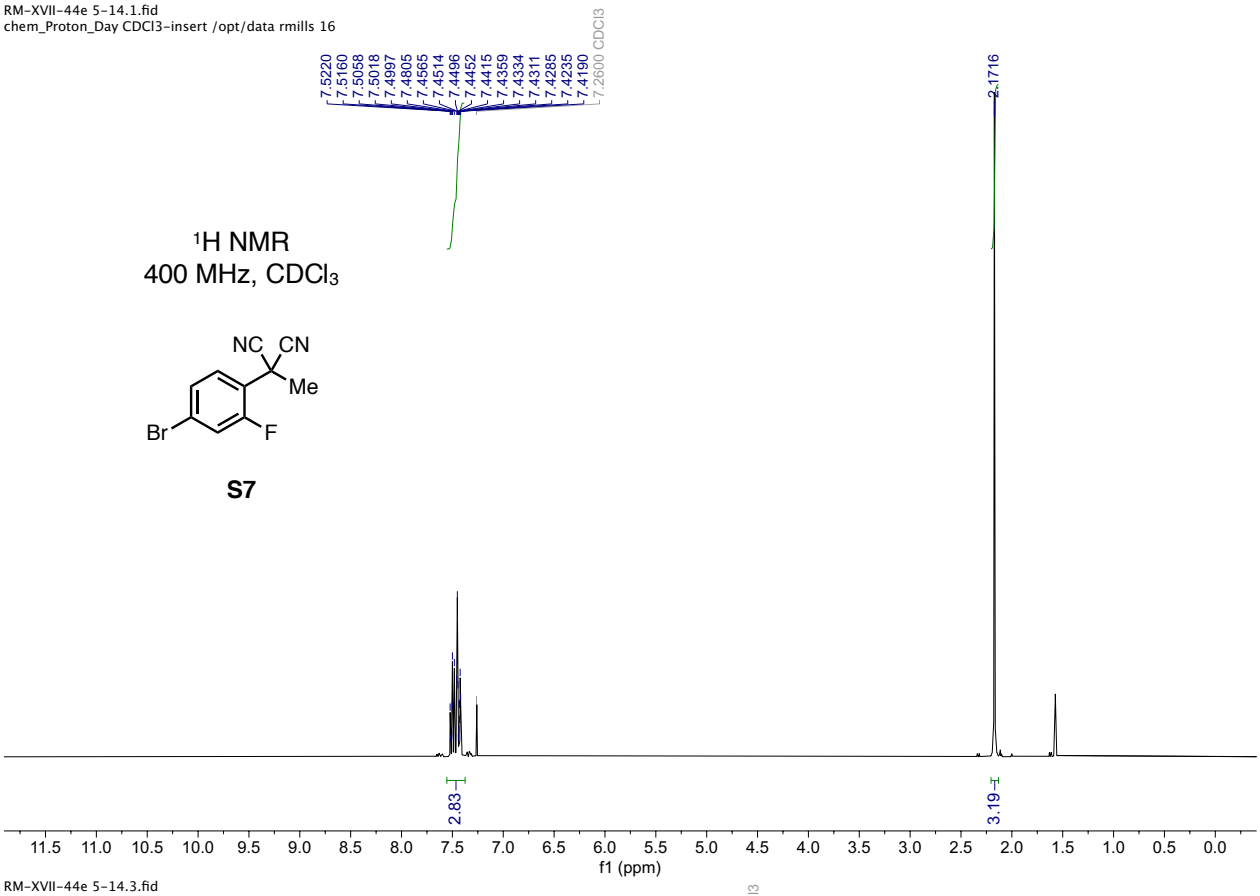
-112.7021
-112.7195
-112.7404

^{19}F NMR
376 MHz, $CDCl_3$



S6

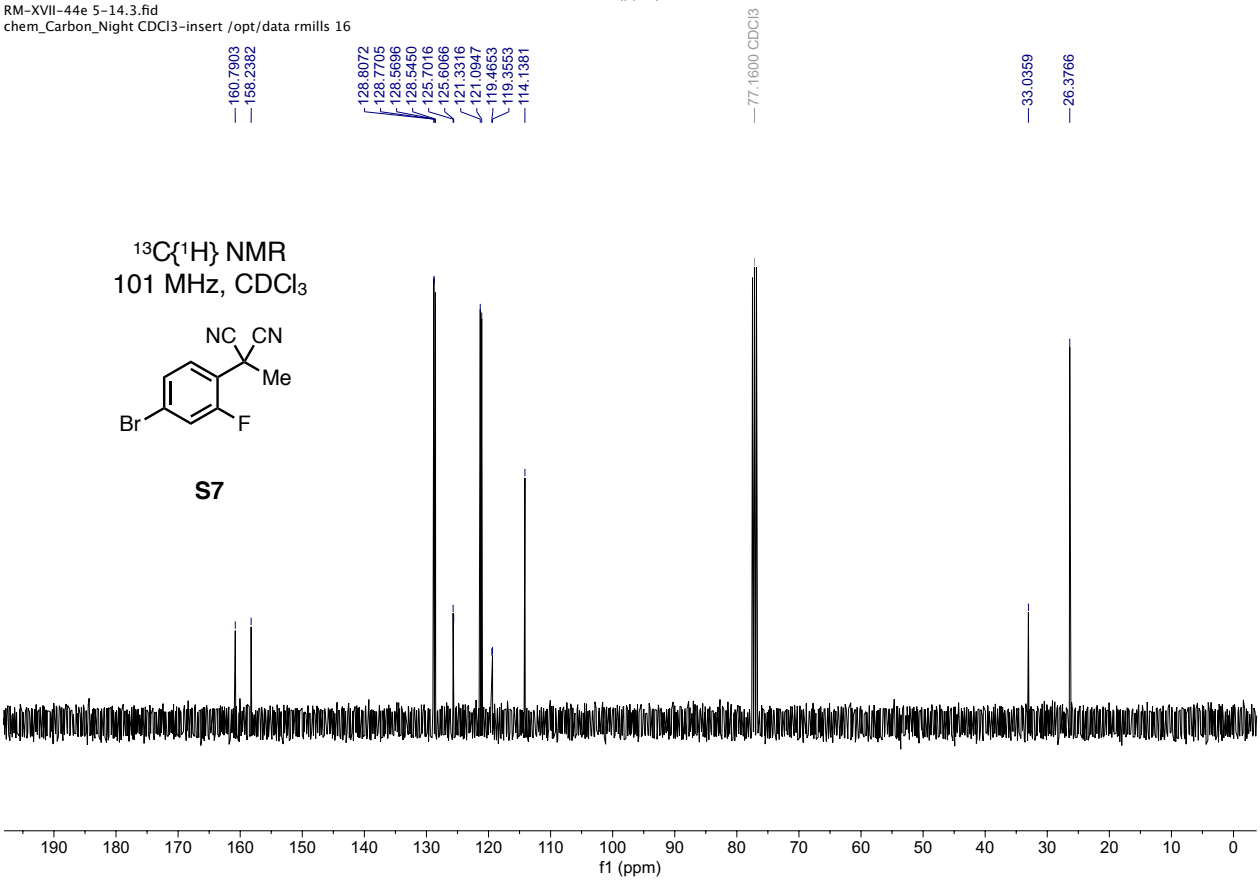
RM-XVII-44e 5-14.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 16



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

S7

RM-XVII-44e 5-14.3.fid
chem_Carbon_Night CDCl3-insert /opt/data rmills 16



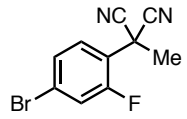
^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

S7

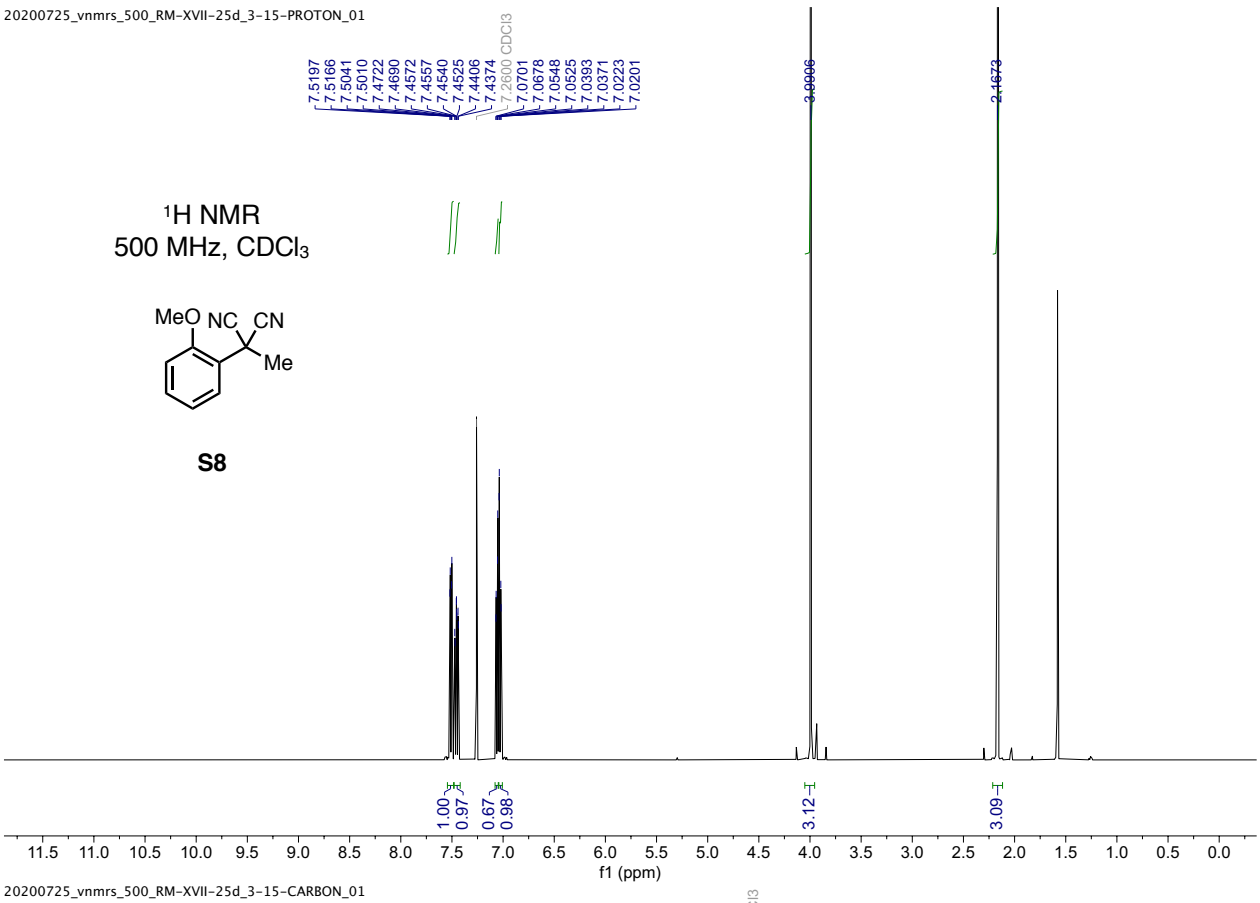
RM-XVII-44e 5-14.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 16

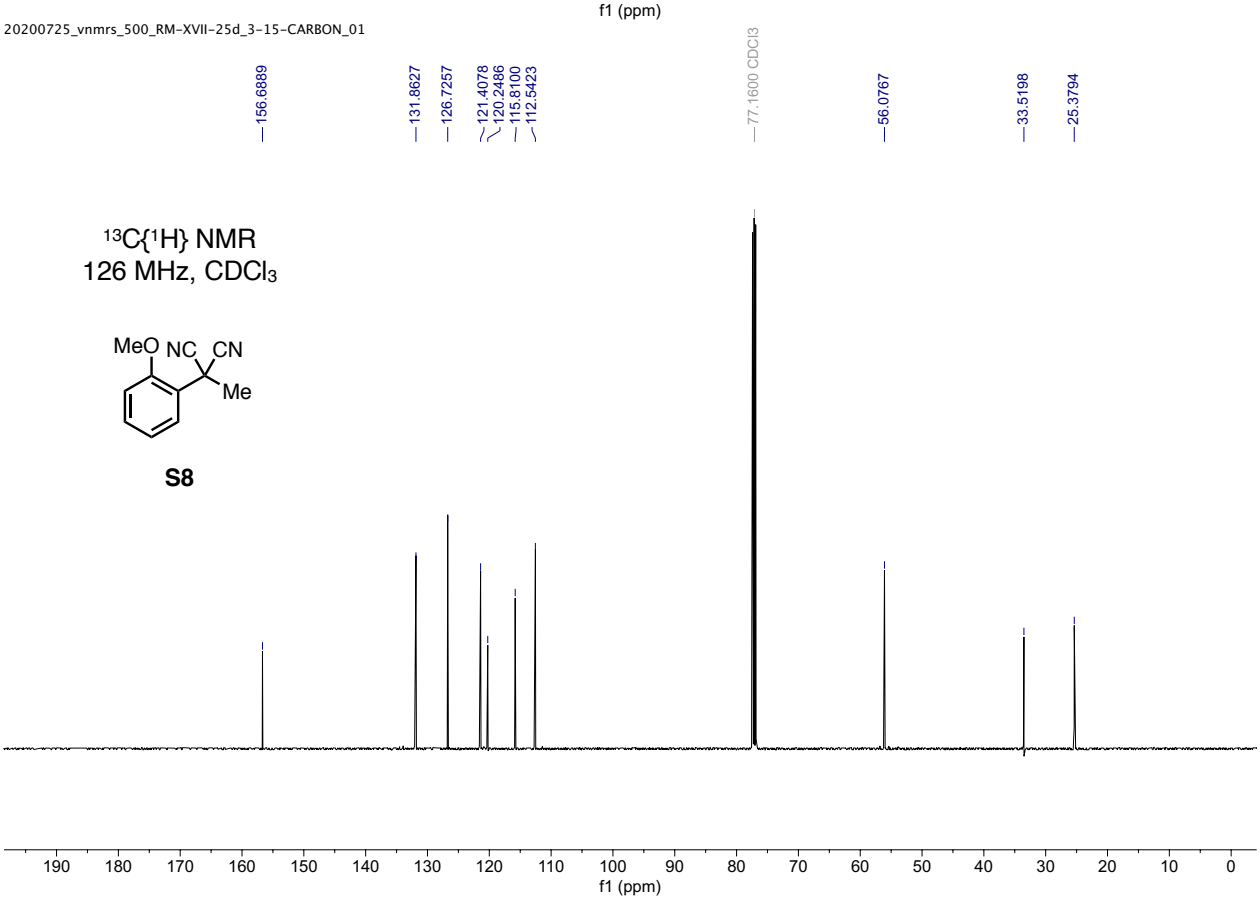
-108.6962
-108.7153
-108.7229
-108.7450

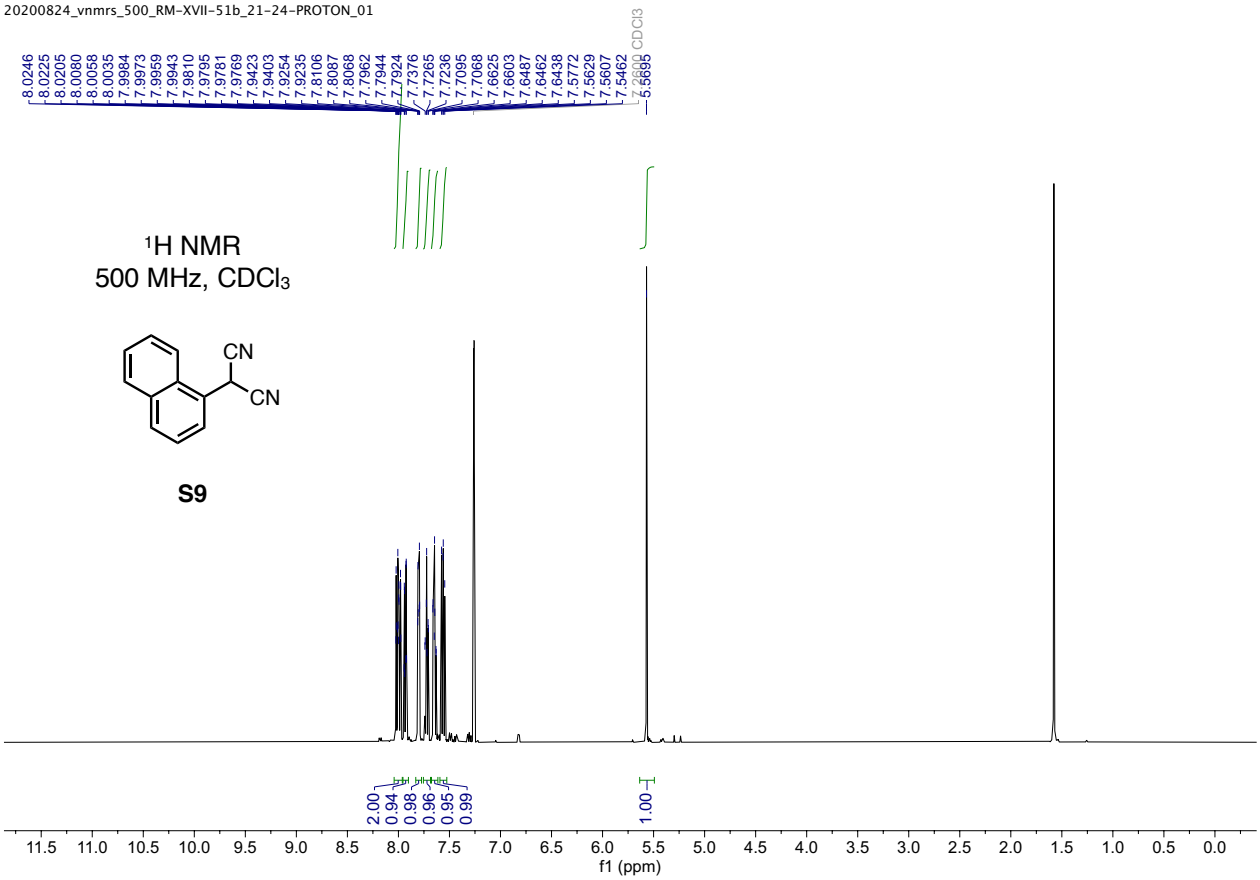
^{19}F NMR
376 MHz, $CDCl_3$

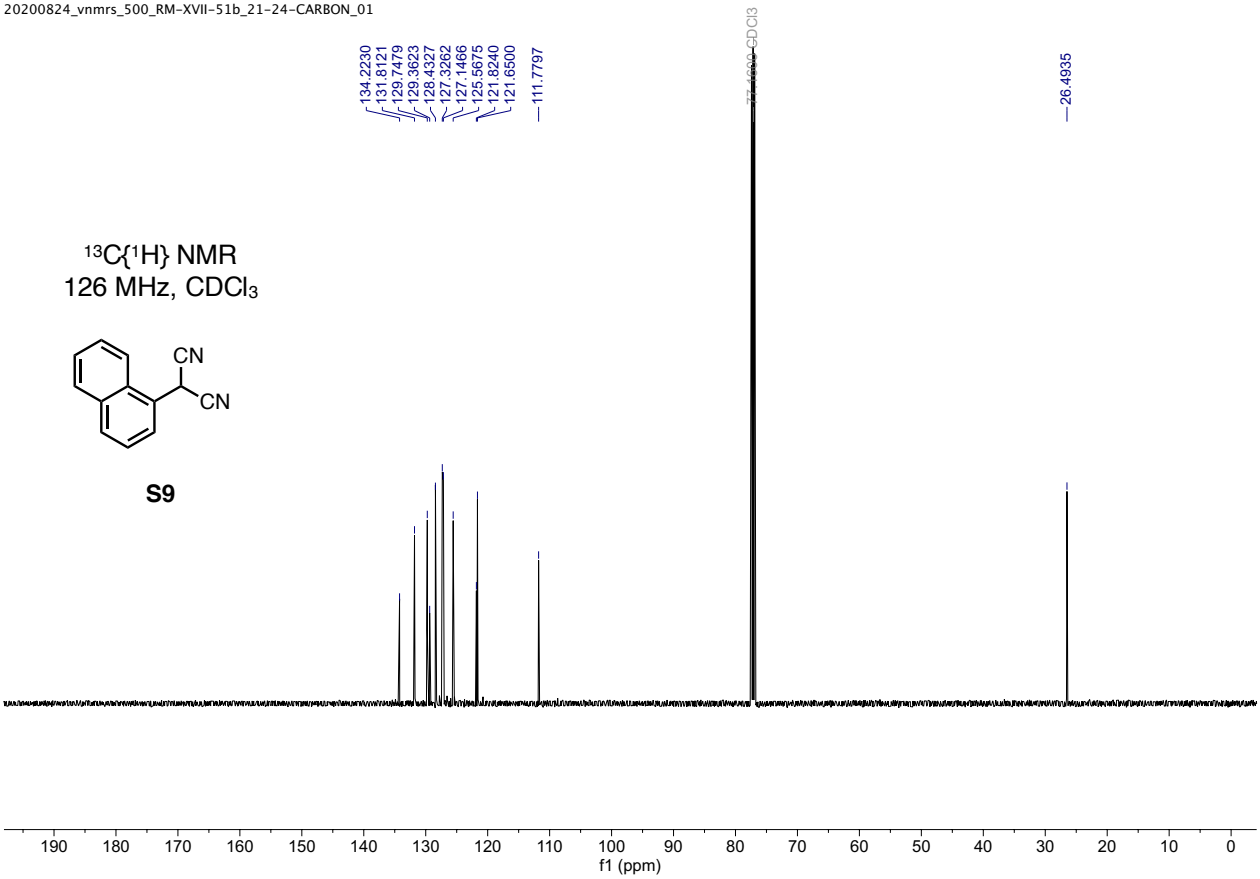


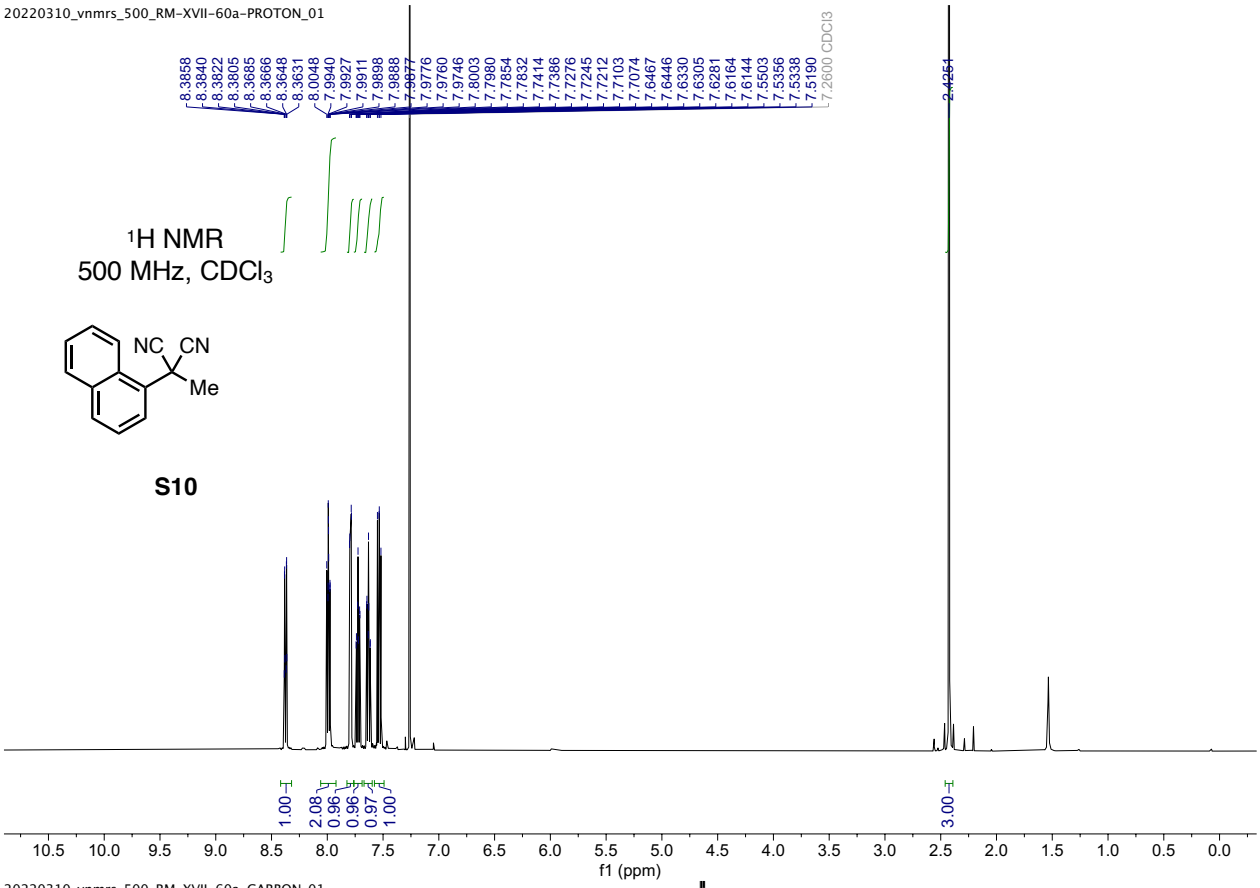
S7

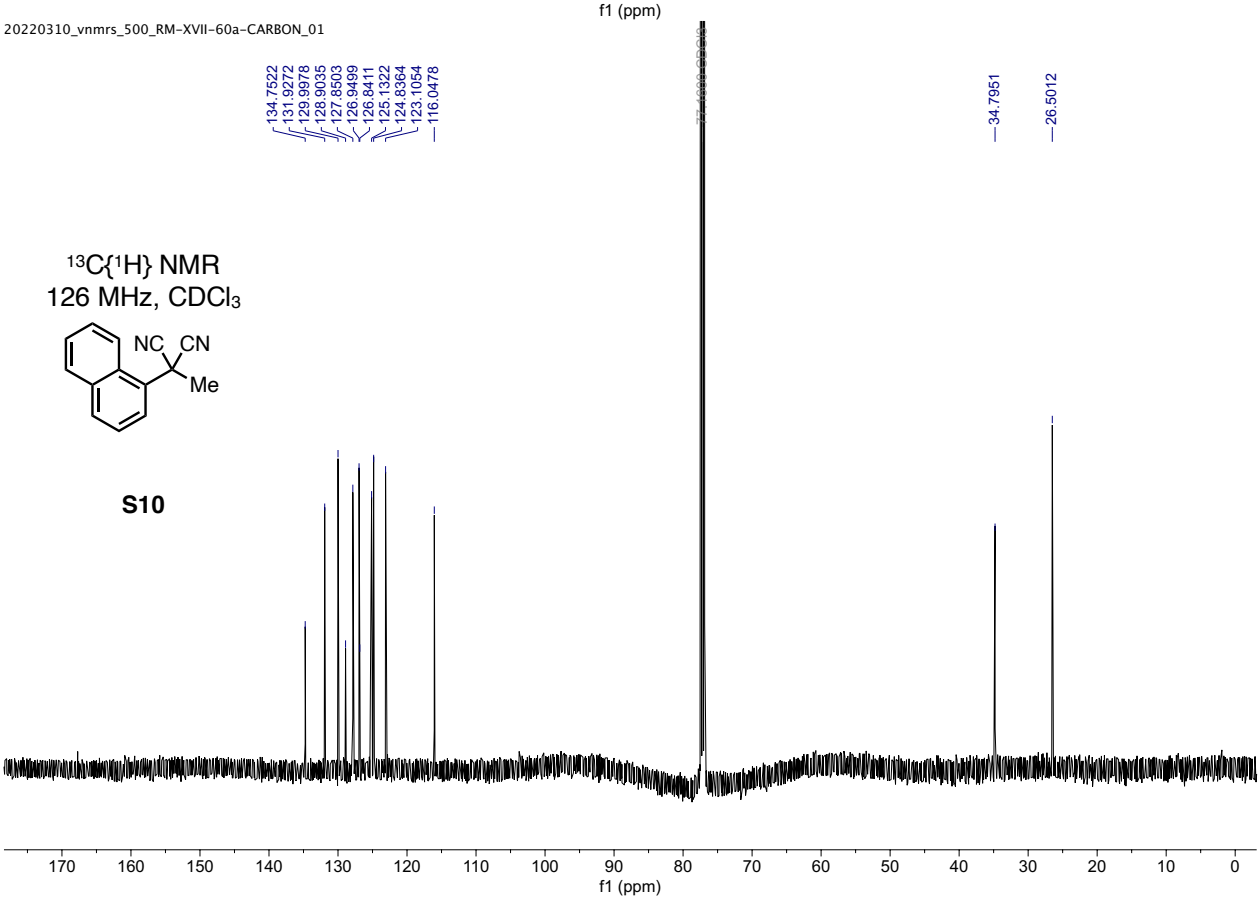

20200725_vnmrs_500_RM-XVII-25d_3-15-PROTON_01
7.5197
7.5166
7.5041
7.5010
7.4722
7.4690
7.4572
7.4557
7.4540
7.4525
7.4406
7.4374
7.2600 CDCl3
7.0701
7.0678
7.0548
7.0525
7.0393
7.0371
7.0223
7.0201
3.9906
2.1673
1H NMR
500 MHz, CDCl3
MeO
NC
CN
Me
S8
1.00
0.97
0.67
0.98
3.12
3.09
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200725_vnmrs_500_RM-XVII-25d_3-15-CARBON_01
156.6889
131.8627
126.7257
121.4078
120.2486
115.8100
112.5423
77.1600 CDCl3
56.0767
33.5198
25.3794
13C{1H} NMR
126 MHz, CDCl3
MeO
NC
CN
Me
S8
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

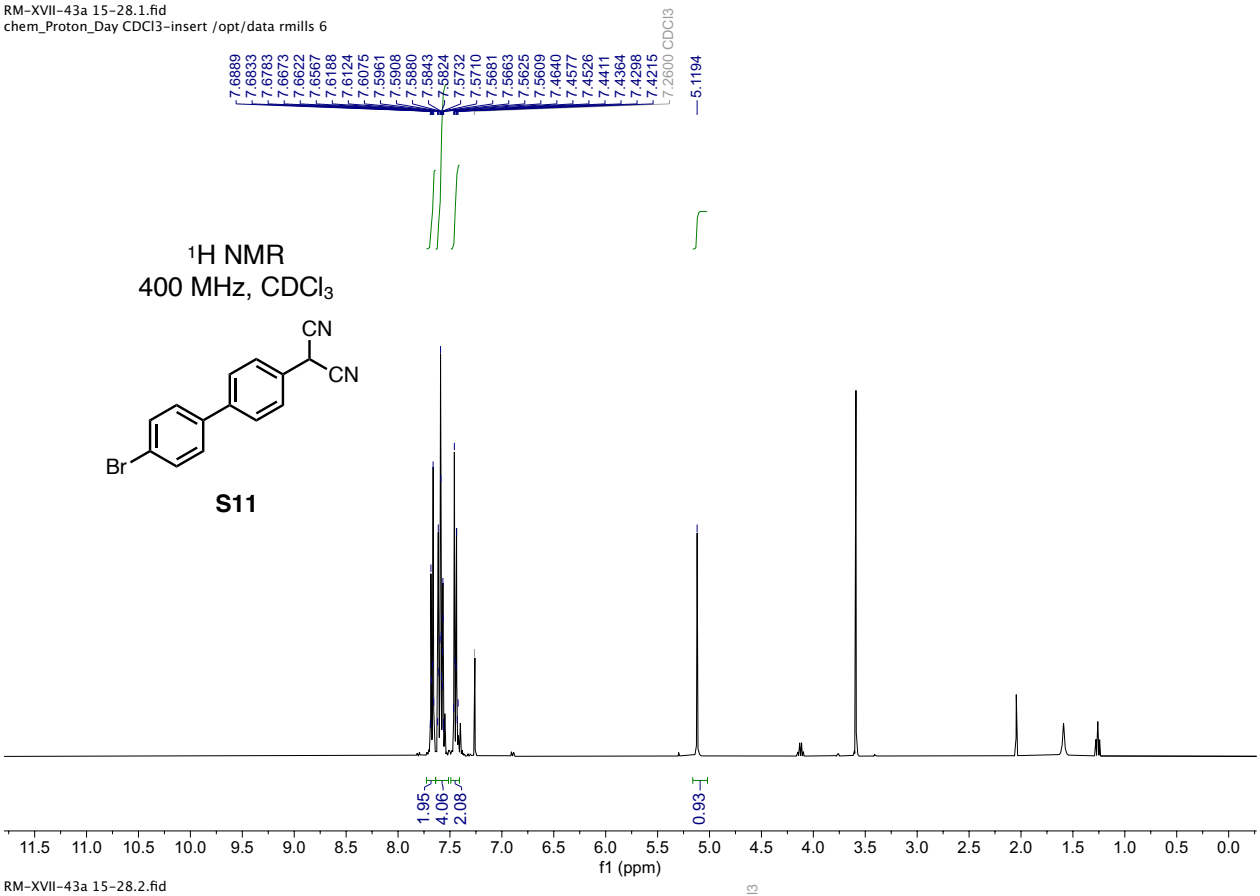

20200824_vnmrs_500_RM-XVII-51b_21-24-PROTON_01
^{1}H NMR
500 MHz, $CDCl_3$
CN
CN
S9
f1 (ppm)


20200824_vnmrs_500_RM-XVII-51b_21-24-CARBON_01
$^{13}C\{^1H\}$ NMR
126 MHz, $CDCl_3$
CN
CN
S9
f1 (ppm)

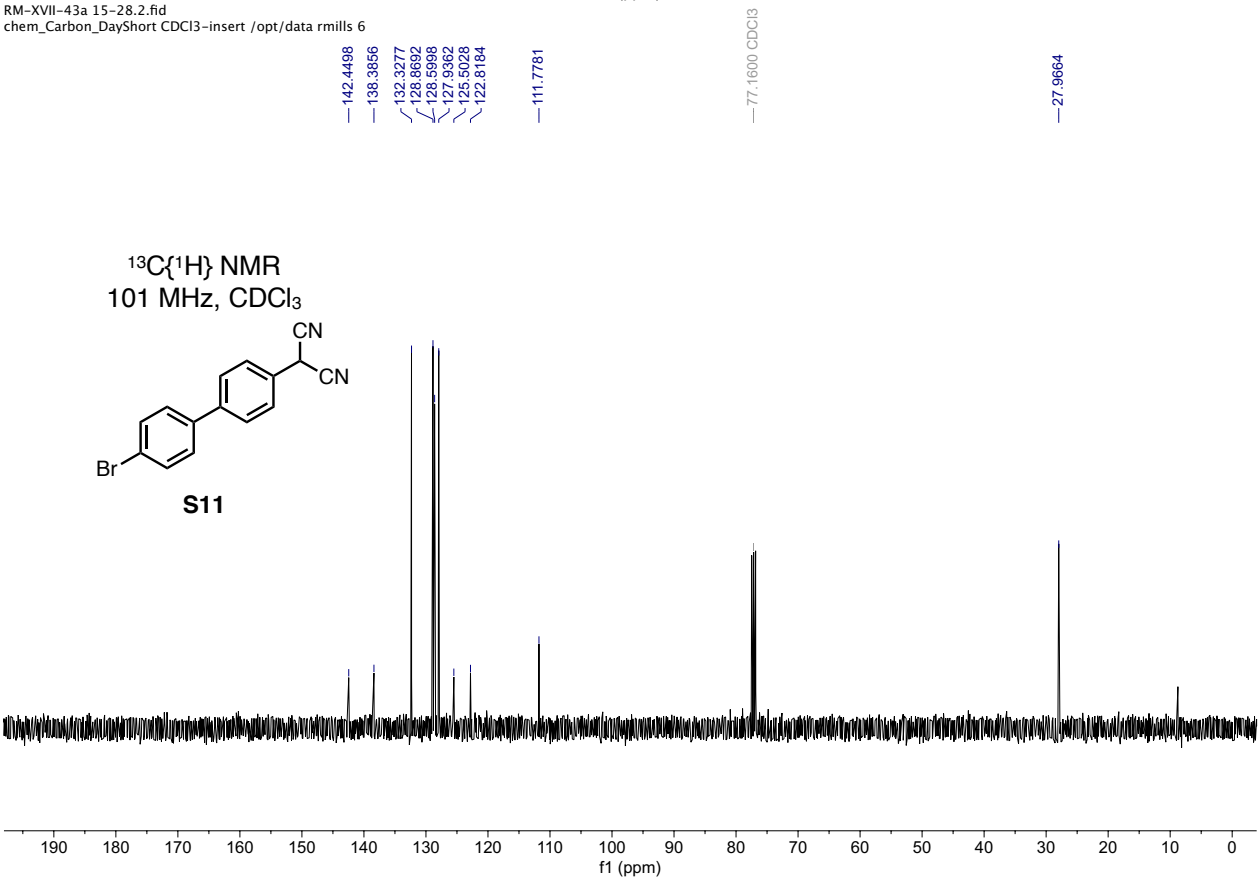

20220310_vnmrs_500_RM-XVII-60a-PROTON_01
8.3858
8.3840
8.3822
8.3805
8.3685
8.3666
8.3648
8.3631
8.0048
7.9940
7.9927
7.9911
7.9898
7.9888
7.9877
7.9776
7.9760
7.9746
7.8003
7.7980
7.7854
7.7832
7.7414
7.7386
7.7276
7.7245
7.7212
7.7103
7.7074
7.6467
7.6446
7.6330
7.6305
7.6281
7.6164
7.6144
7.5503
7.5356
7.5338
7.5190
7.2600 CDCl3
2.4251
1H NMR
500 MHz, CDCl3
NC CN
Me
S10
1.00
2.08
0.96
0.96
0.97
1.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

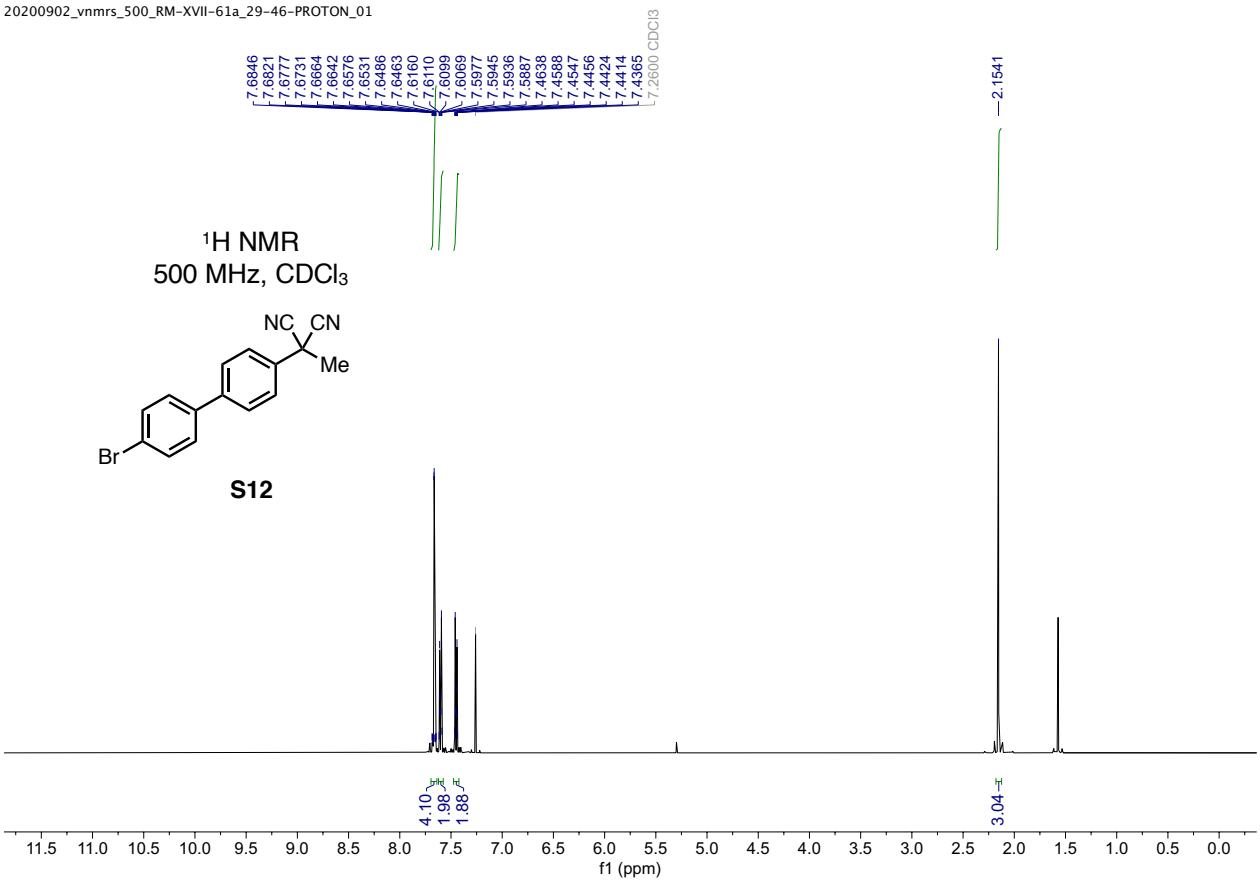

20220310_vnmrs_500_RM-XVII-60a-CARBON_01
134.7522
131.9272
129.9978
128.9035
127.8503
126.9499
126.8411
125.1322
124.8364
123.1054
116.0478
34.7951
26.5012
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
S10
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

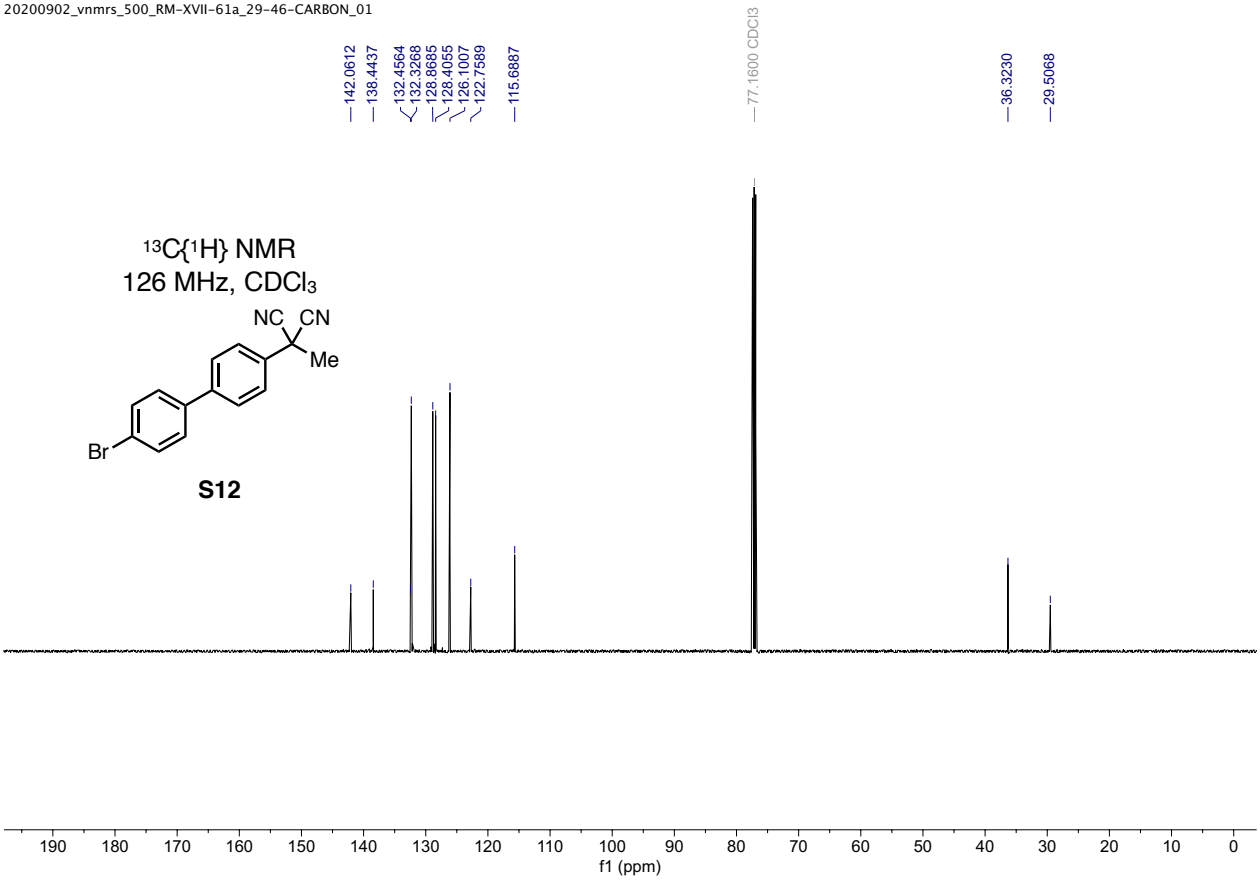
RM-XVII-43a 15-28.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 6

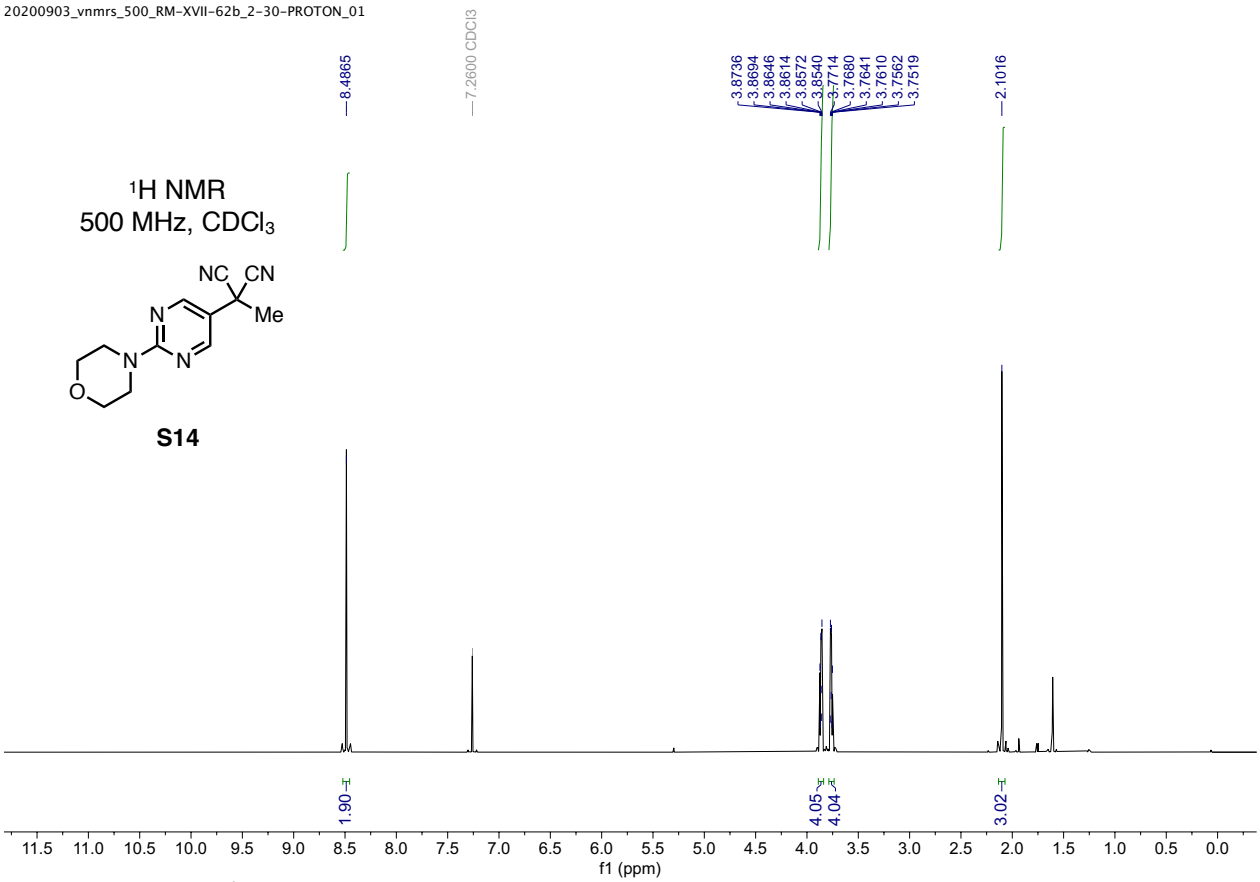


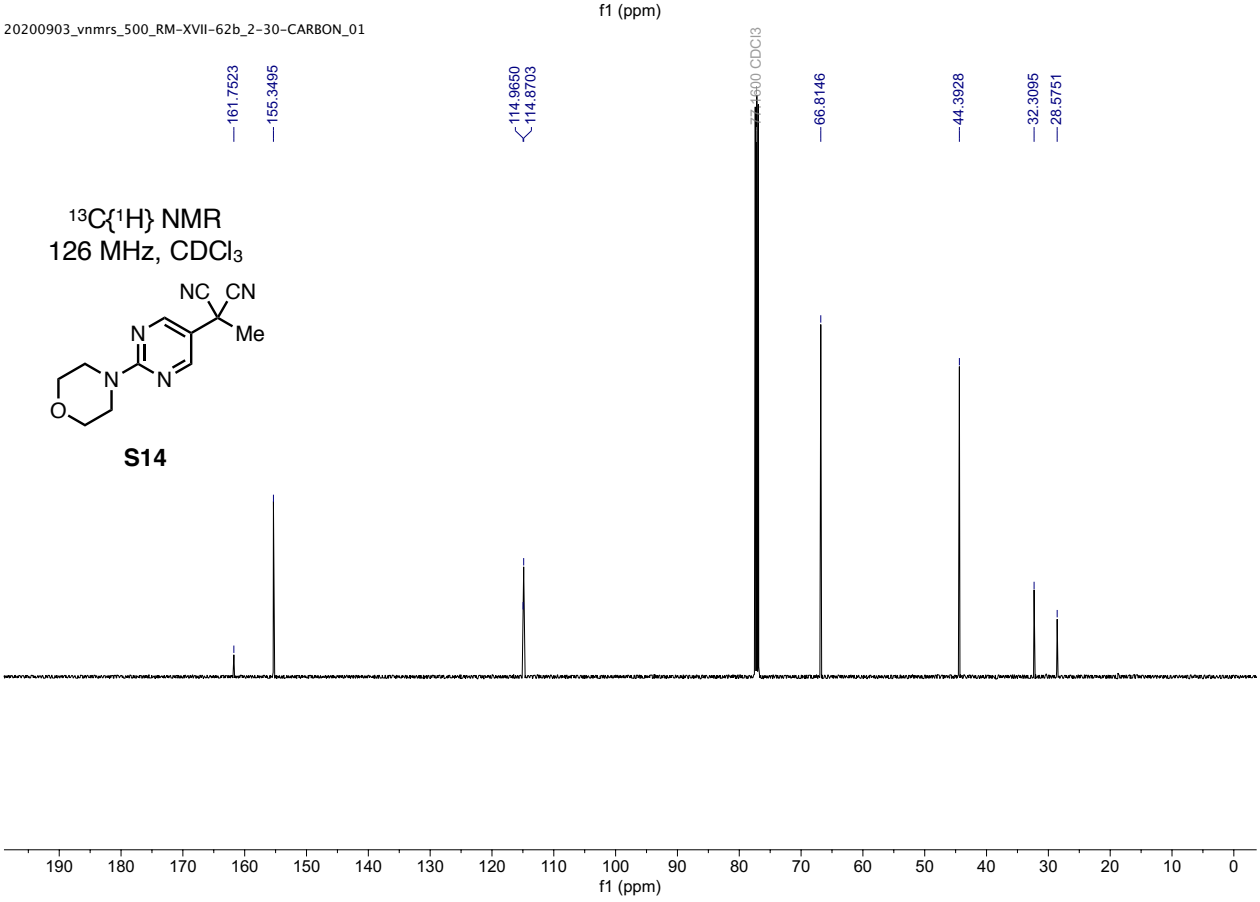
RM-XVII-43a 15-28.2.fid
chem_Carbon_DayShort CDCl3-insert /opt/data rmills 6

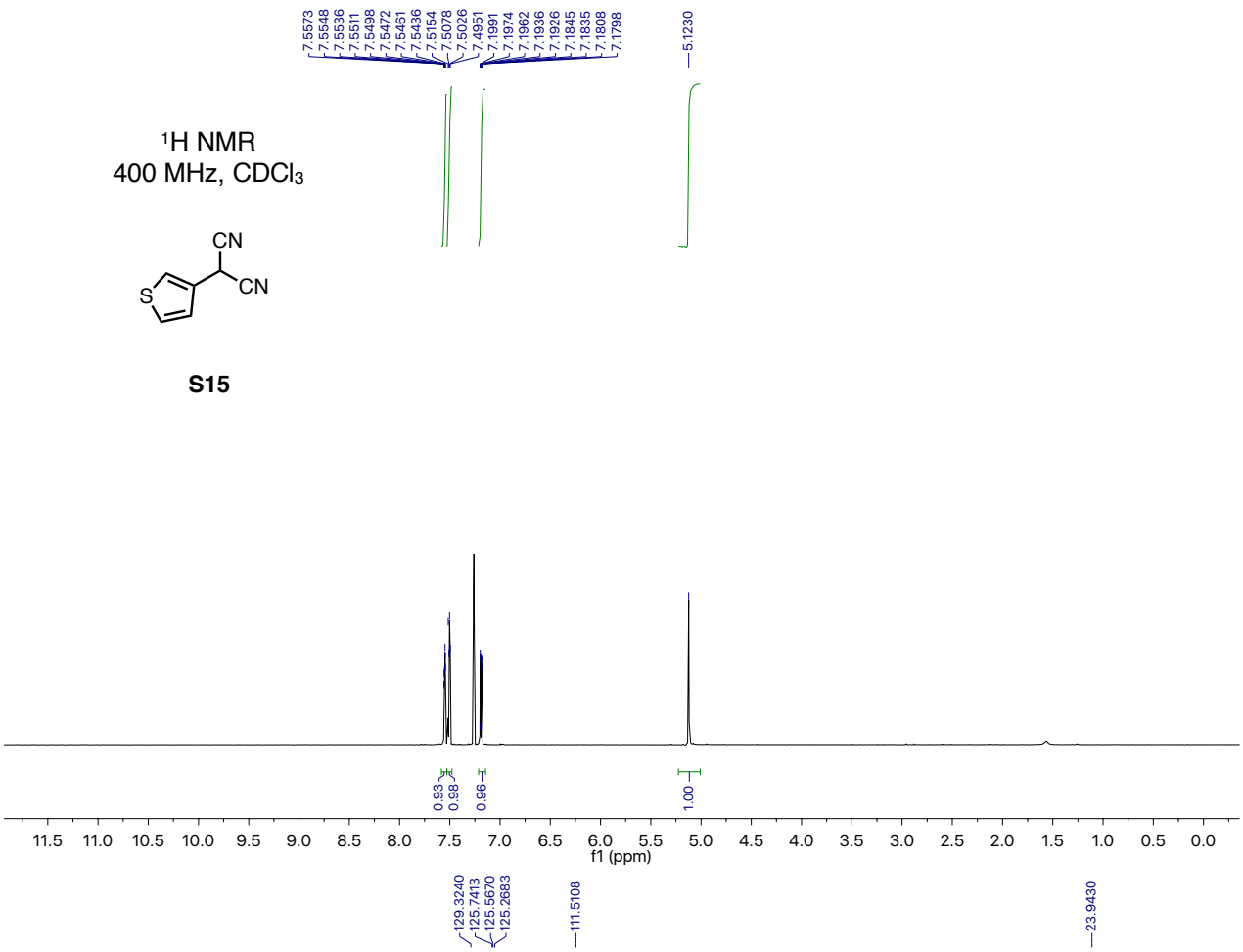



20200902_vnmrs_500_RM-XVII-61a_29-46-PROTON_01
7.6846
7.6821
7.6777
7.6731
7.6664
7.6642
7.6576
7.6531
7.6486
7.6463
7.6160
7.6110
7.6099
7.6069
7.5977
7.5945
7.5936
7.5887
7.4638
7.4588
7.4547
7.4456
7.4424
7.4414
7.4365
7.2600 CDCl3
2.1541
1H NMR
500 MHz, CDCl3
NC CN
Me
Br
S12
4.10
1.98
1.88
3.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200902_vnmrs_500_RM-XVII-61a_29-46-CARBON_01
142.0612
138.4437
132.4564
132.3268
128.8685
128.4055
126.1007
122.7589
115.6887
77.1600 CDCl3
36.3230
29.5068
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
Br
S12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

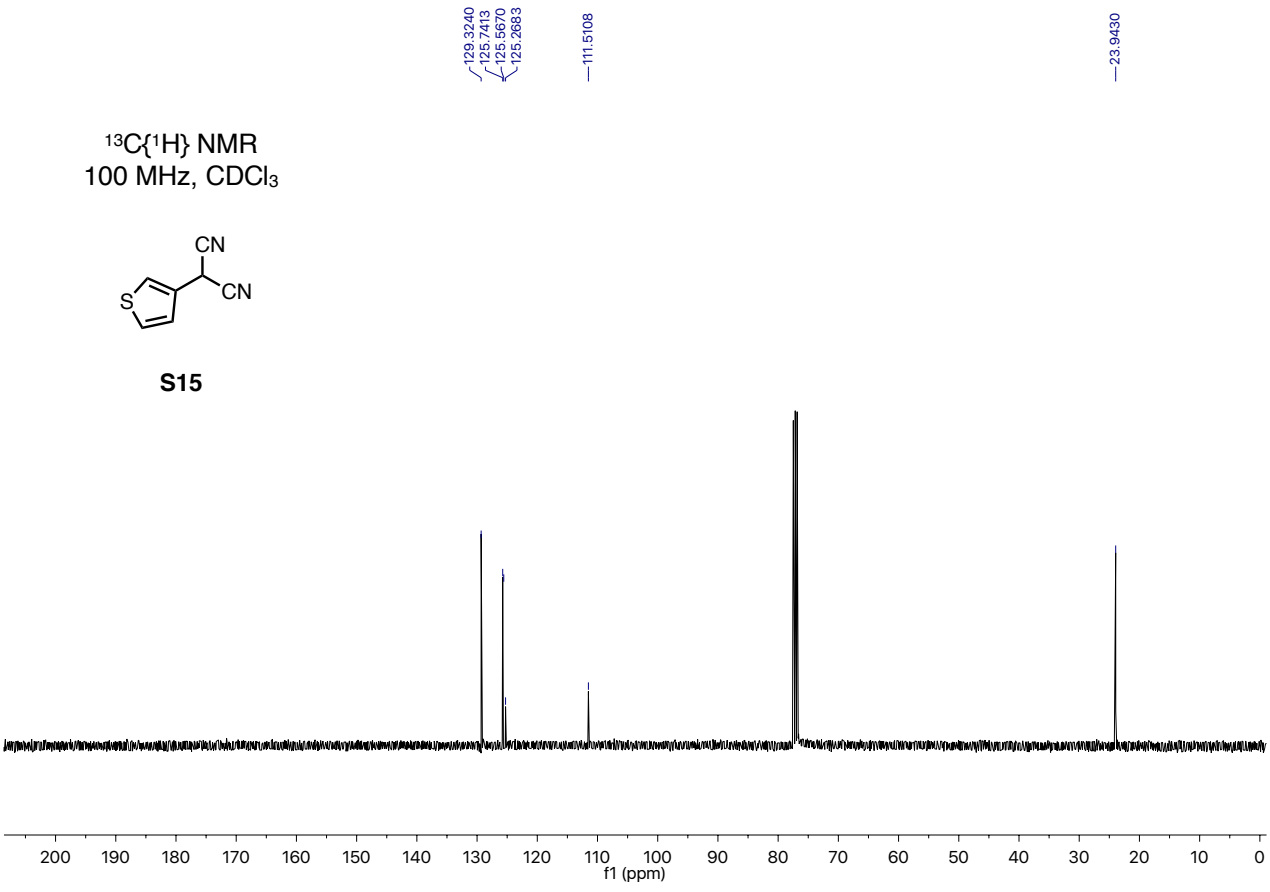

20200903_vnmrs_500_RM-XVII-62b_2-30-PROTON_01
8.4865
7.2600 CDCl3
3.8736
3.8694
3.8646
3.8614
3.8572
3.8540
3.7714
3.7680
3.7641
3.7610
3.7562
3.7519
2.1016
1H NMR
500 MHz, CDCl3
NC CN
Me
N
N
N
O
S14
1.90
4.05
4.04
3.02
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200903_vnmrs_500_RM-XVII-62b_2-30-CARBON_01
161.7523
155.3495
114.9650
114.8703
77.1600 CDCl3
66.8146
44.3928
32.3095
28.5751
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
N
N
N
O
S14
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



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

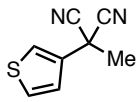
S15



^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$

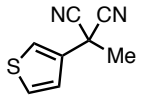
S15

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

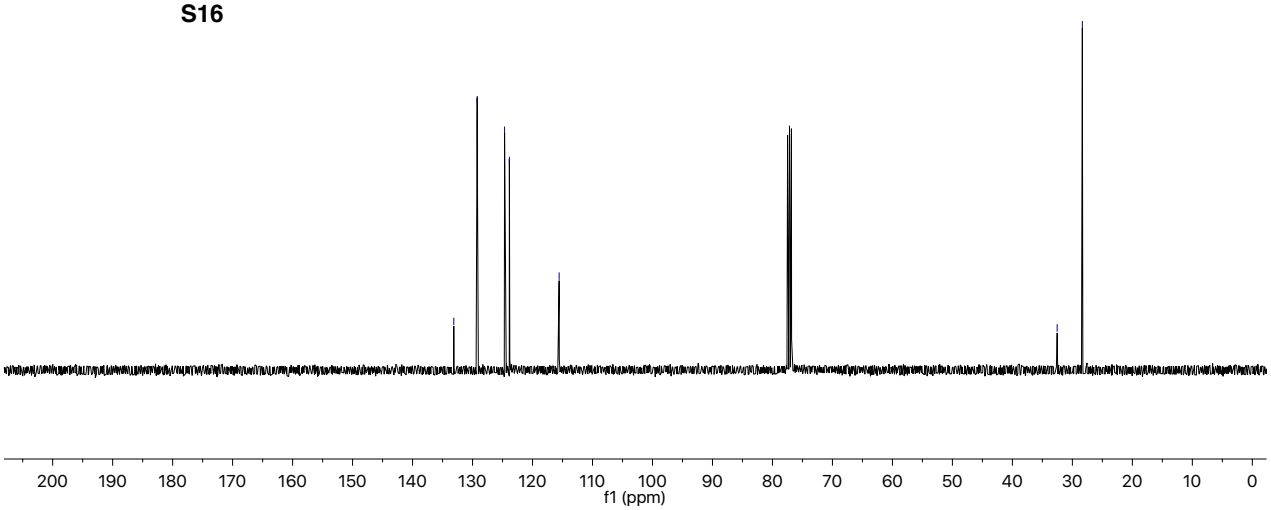


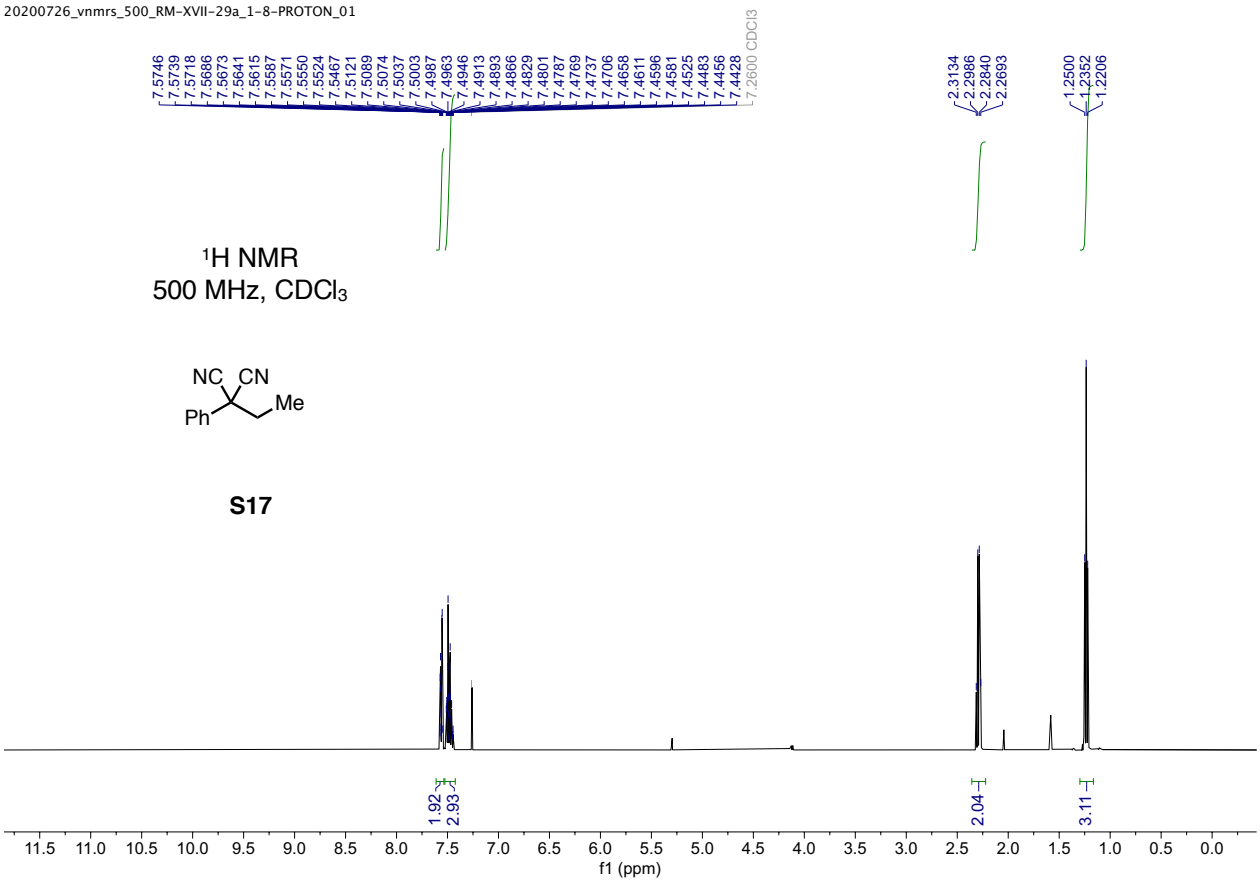
S16

^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



S16




20200726_vnmrs_500_RM-XVII-29a_1-8-PROTON_01
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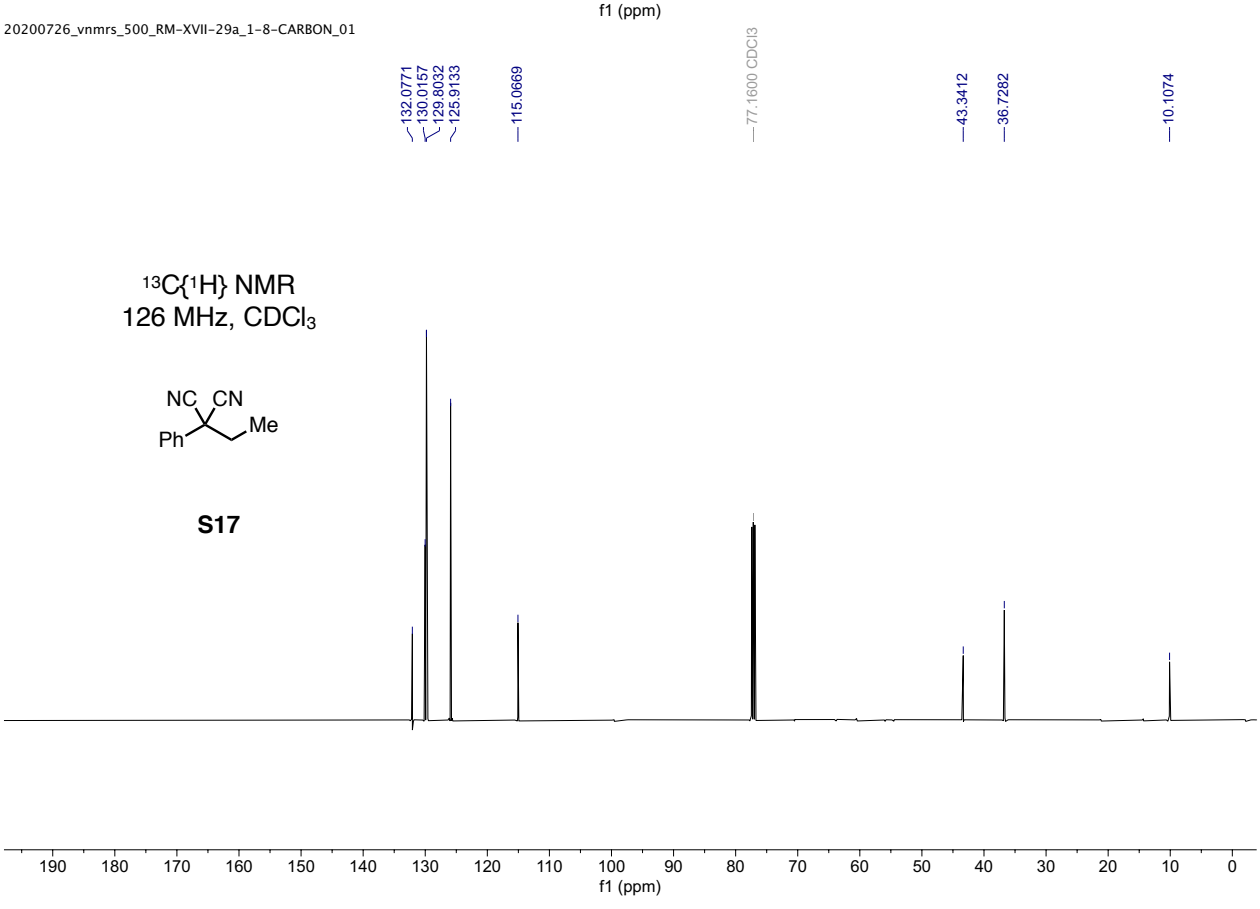
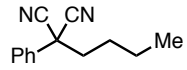
7.5739
7.5718
7.5686
7.5673
7.5641
7.5615
7.5587
7.5571
7.5550
7.5524
7.5467
7.5121
7.5089
7.5074
7.5037
7.5003
7.4987
7.4963
7.4946
7.4913
7.4893
7.4866
7.4829
7.4801
7.4787
7.4769
7.4737
7.4706
7.4658
7.4611
7.4596
7.4581
7.4525
7.4483
7.4456
7.4428
7.2600 CDCl3
2.3134
2.2986
2.2840
2.2693
1.2500
1.2352
1.2206
1H NMR
500 MHz, CDCl3
NC CN
Ph
Me
S17
1.92
2.93
2.04
3.11
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

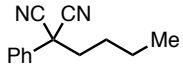

20200726_vnmrs_500_RM-XVII-29a_1-8-CARBON_01
132.0771
130.0157
129.8032
125.9133
115.0669
77.1600 CDCl3
43.3412
36.7282
10.1074
13C{1H} NMR
126 MHz, CDCl3
NC CN
Ph
Me
S17
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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

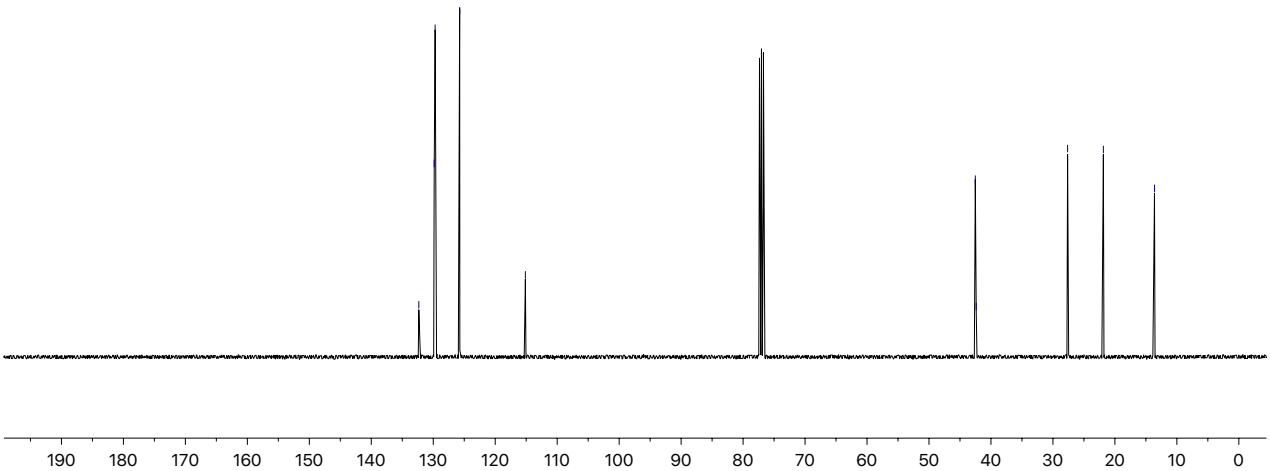


S18

^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

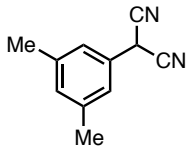


S18



20200908_vnmrs_500_RM_XVII_68b_5_12-PROTON_01
RM_XVII_68b_5_12

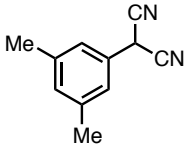
^{1}H NMR
400 MHz, $CDCl_3$



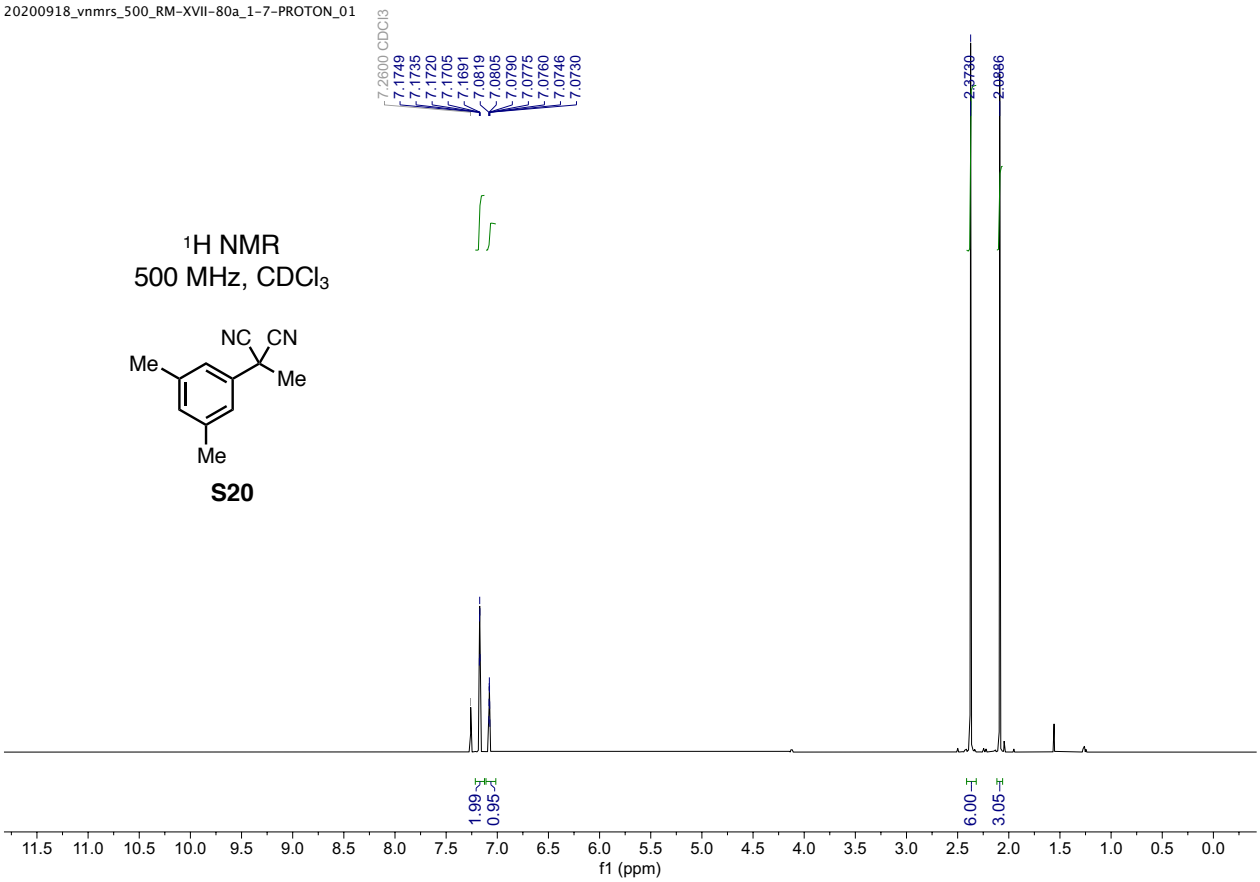
S19

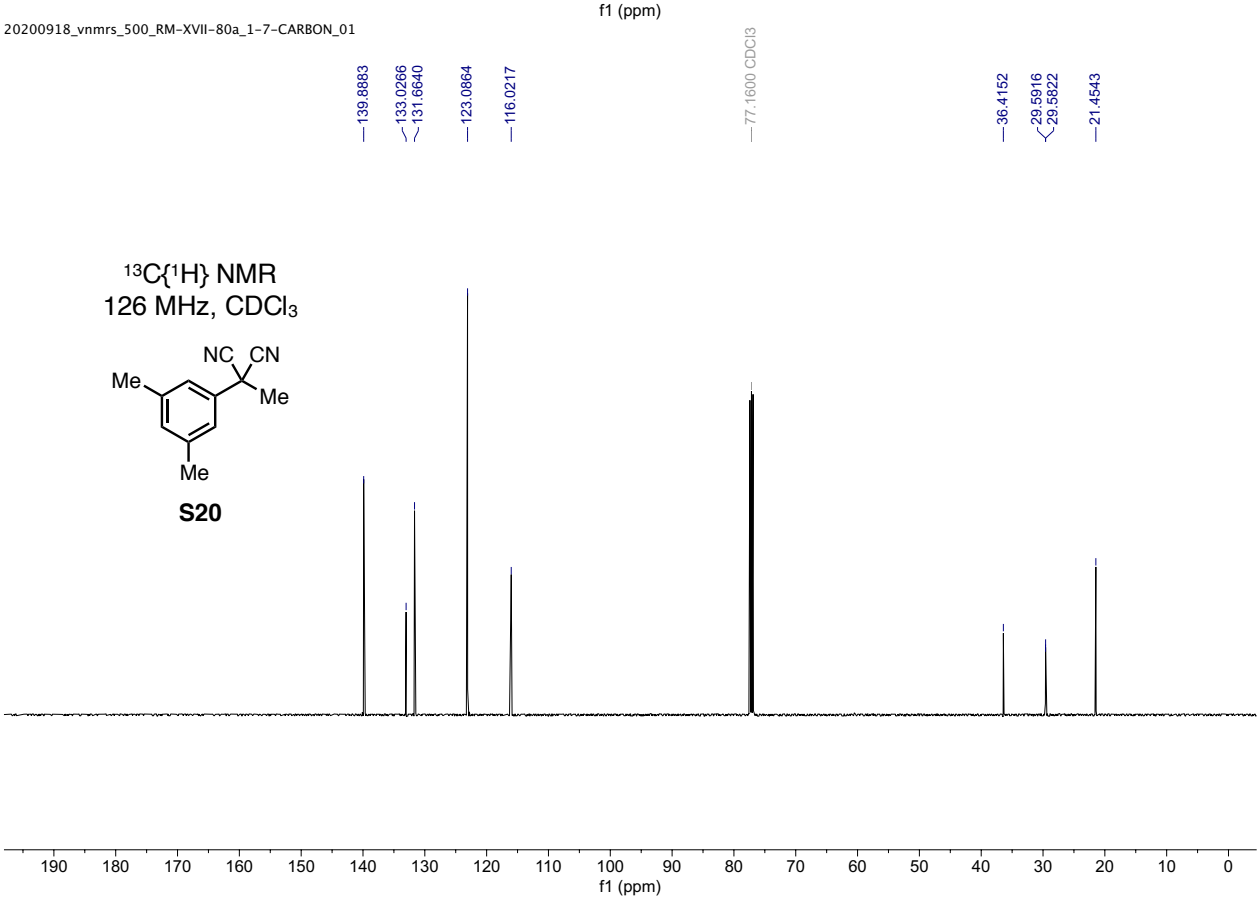
20200908_vnmrs_500_RM_XVII_68b_5_12-CARBON_01
RM_XVII_68b_5_12

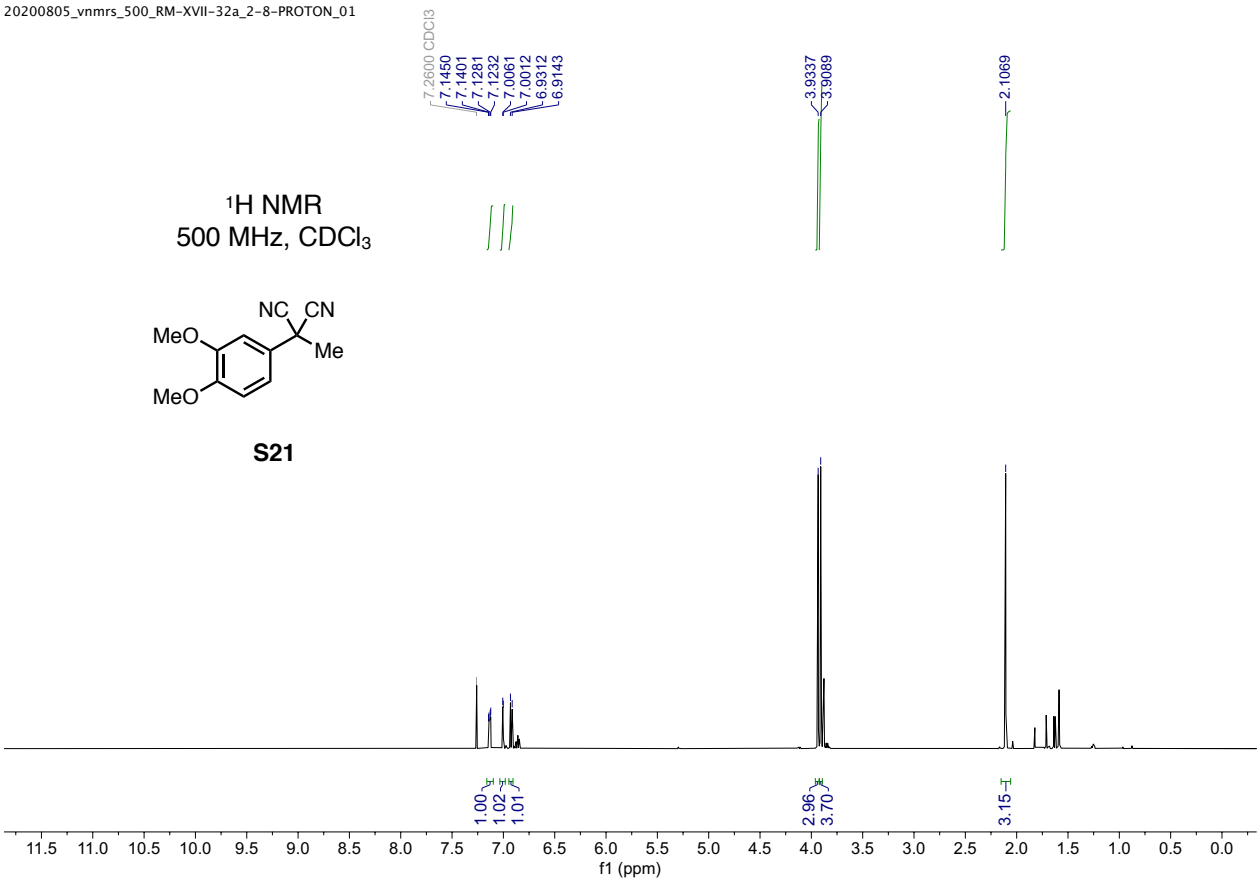
^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

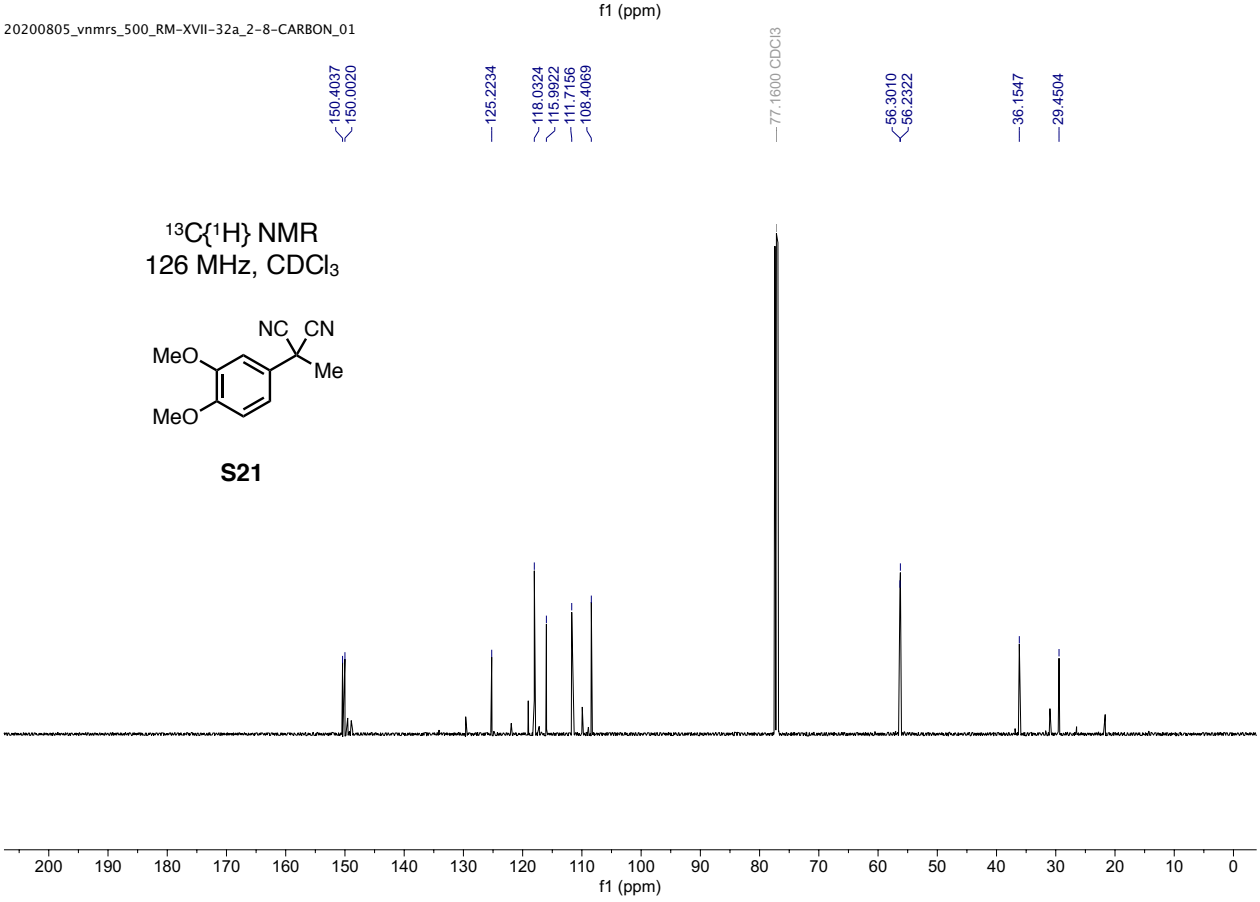


S19


20200918_vnmrs_500_RM-XVII-80a_1-7-PROTON_01
7.2600 CDCl3
7.1749
7.1735
7.1720
7.1705
7.1691
7.0819
7.0805
7.0790
7.0775
7.0760
7.0746
7.0730
2.3730
2.0886
1H NMR
500 MHz, CDCl3
NC CN
Me
Me
Me
S20
1.99
0.95
6.00
3.05
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200918_vnmrs_500_RM-XVII-80a_1-7-CARBON_01
139.8883
133.0266
131.6640
123.0864
116.0217
77.1600 CDCl3
36.4152
29.5916
29.5822
21.4543
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
Me
Me
S20
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20200805_vnmrs_500_RM-XVII-32a_2-8-PROTON_01
7.2600 CDCl3
7.1450
7.1401
7.1281
7.1232
7.0061
7.0012
6.9312
6.9143
3.9337
3.9089
2.1069
1H NMR
500 MHz, CDCl3
NC CN
MeO
Me
MeO
S21
1.00
1.02
1.01
2.96
3.70
3.15
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200805_vnmrs_500_RM-XVII-32a_2-8-CARBON_01
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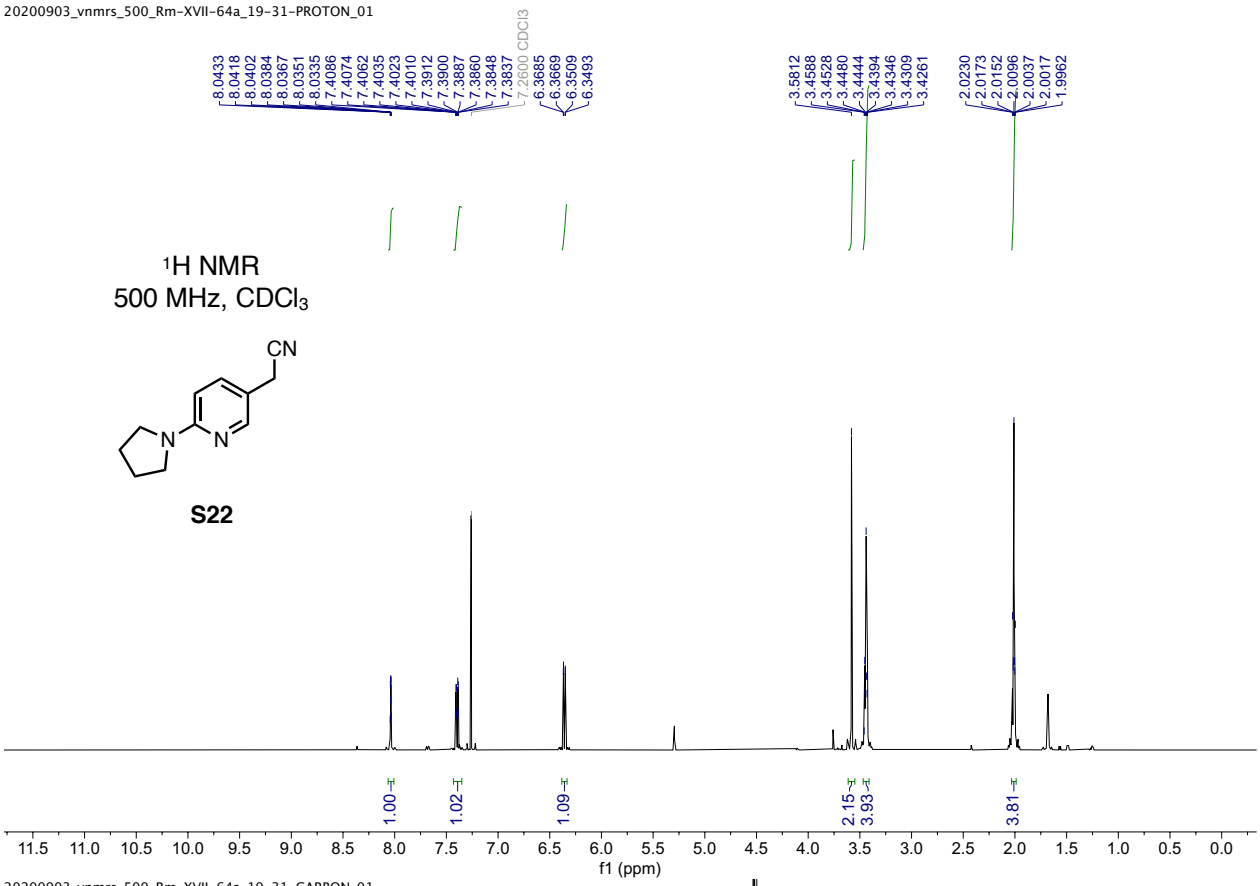
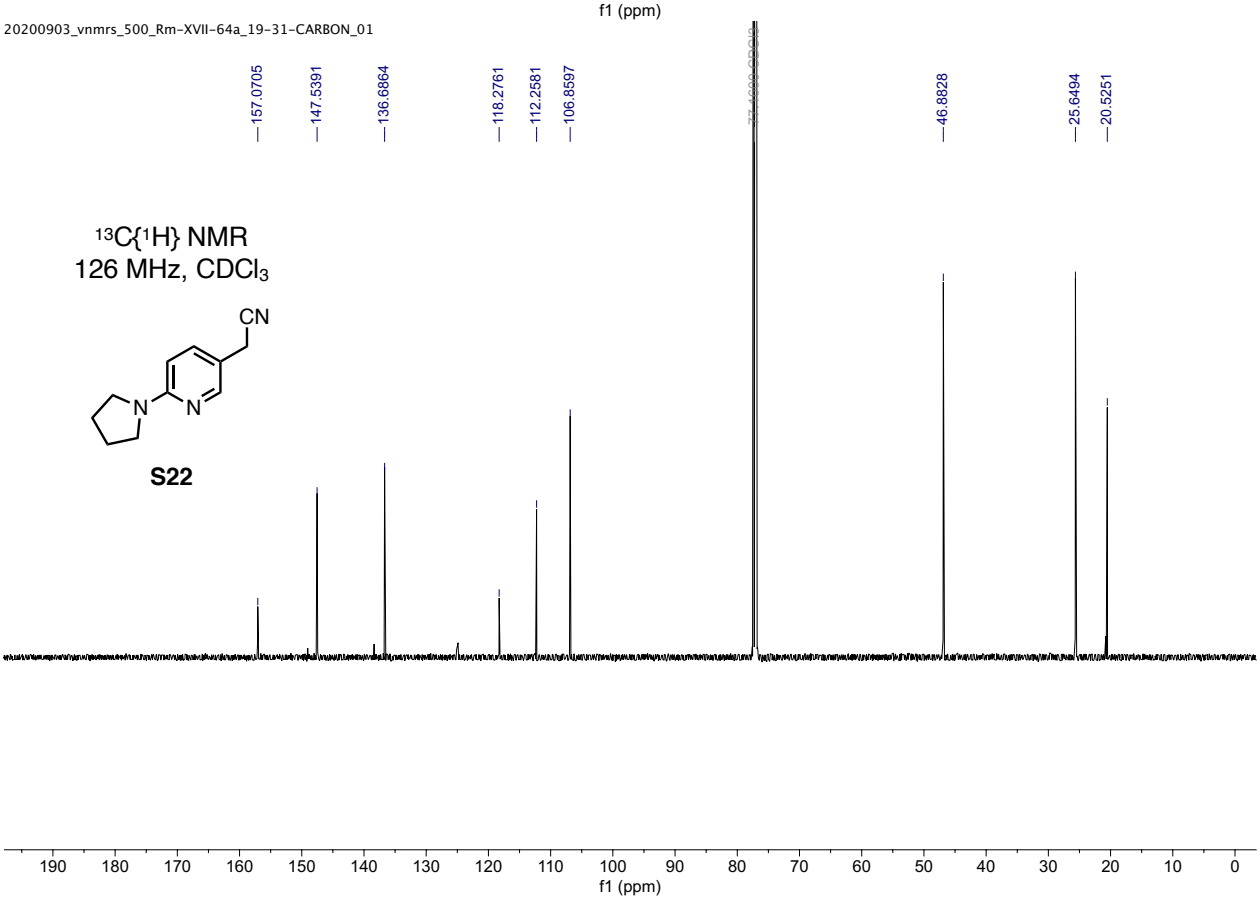
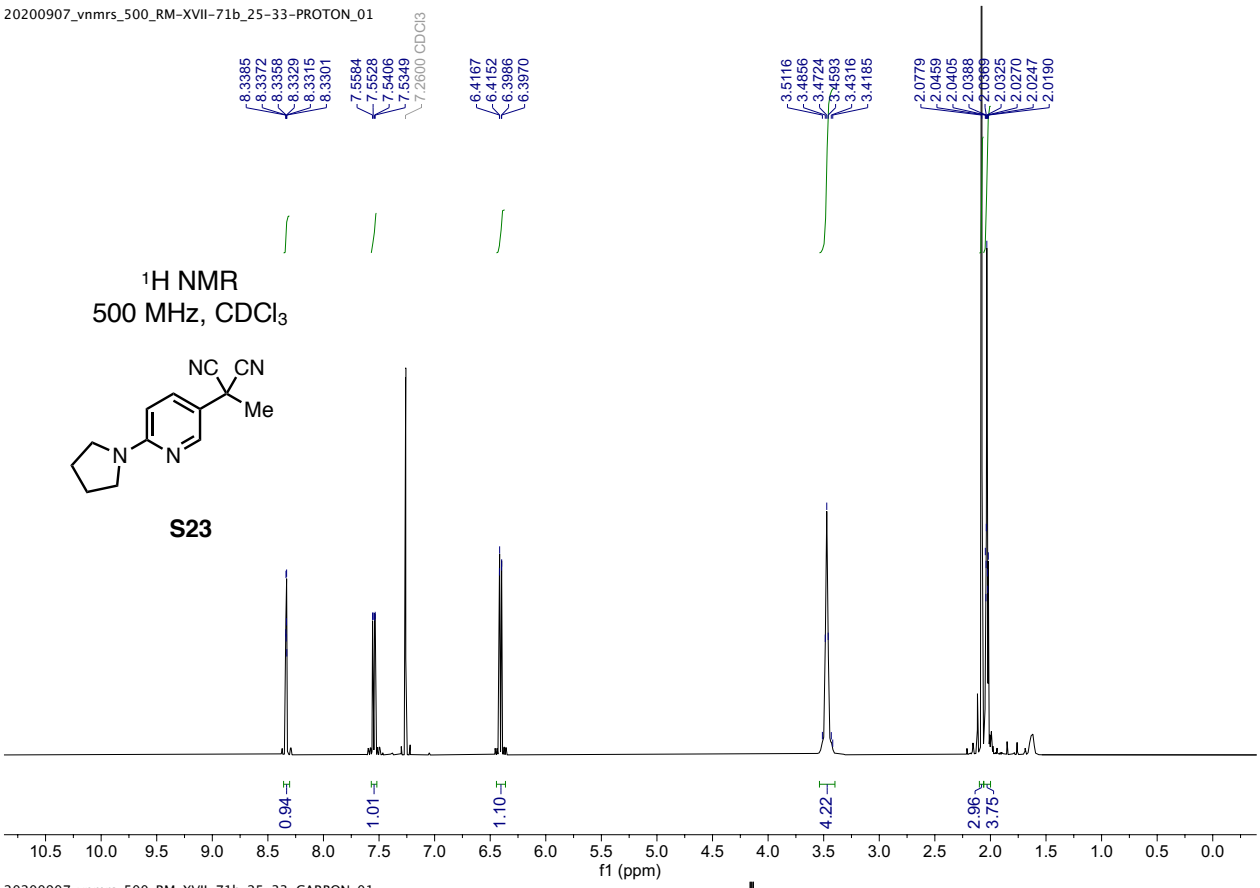
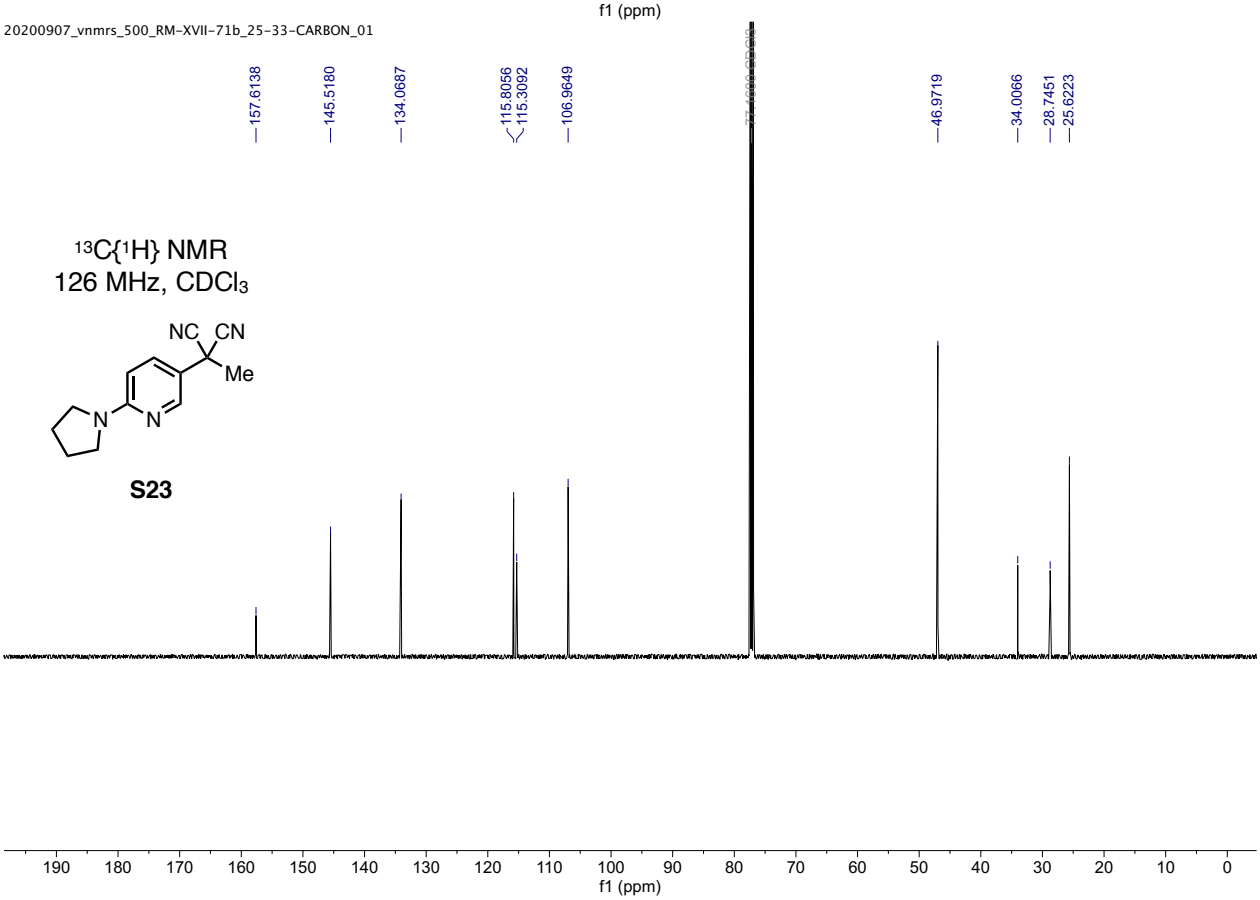
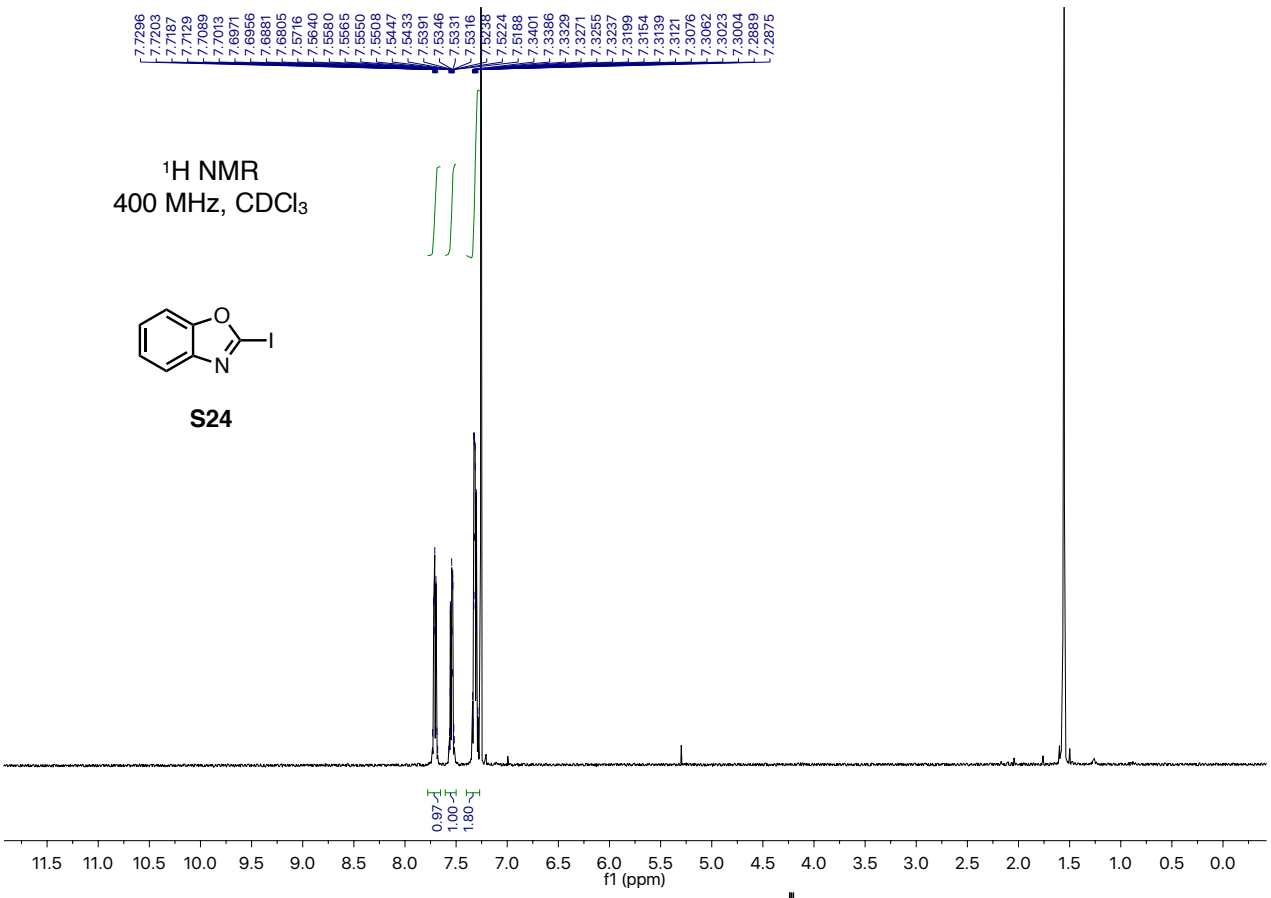
150.0020
125.2234
118.0324
115.9922
111.7156
108.4069
77.1600 CDCl3
56.3010
56.2322
36.1547
29.4504
13C{1H} NMR
126 MHz, CDCl3
NC CN
MeO
Me
MeO
S21
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20200903_vnmrs_500_Rm-XVII-64a_19-31-PROTON_01
8.0433
8.0418
8.0402
8.0384
8.0367
8.0351
8.0335
7.4086
7.4074
7.4062
7.4035
7.4023
7.4010
7.3912
7.3900
7.3887
7.3860
7.3848
7.3837
7.2600 CDCl3
6.3685
6.3669
6.3509
6.3493
3.5812
3.4588
3.4528
3.4480
3.4444
3.4394
3.4346
3.4309
3.4261
2.0230
2.0173
2.0152
2.0096
2.0037
2.0017
1.9962
1H NMR
500 MHz, CDCl3
CN
N
N
S22
1.00
1.02
1.09
2.15
3.93
3.81
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200903_vnmrs_500_Rm-XVII-64a_19-31-CARBON_01
157.0705
147.5391
136.6864
118.2761
112.2581
106.8597
77.4600 CDCl3
46.8828
25.6494
20.5251
13C{1H} NMR
126 MHz, CDCl3
CN
N
N
S22
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

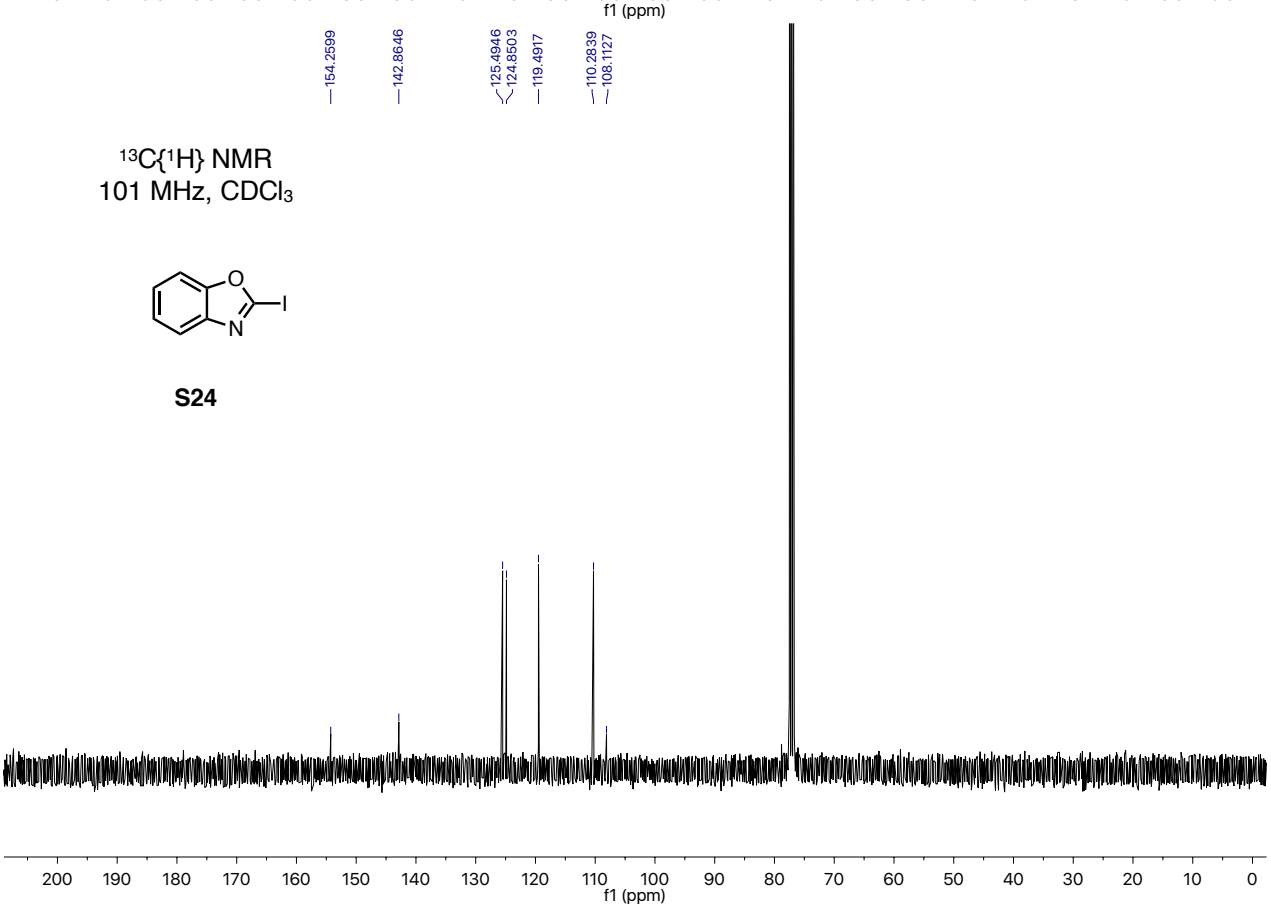

20200907_vnmrs_500_RM-XVII-71b_25-33-PROTON_01
8.3385
8.3372
8.3358
8.3329
8.3315
8.3301
7.5584
7.5528
7.5406
7.5349
7.2600 CDCl3
6.4167
6.4152
6.3986
6.3970
3.5116
3.4856
3.4724
3.4583
3.4316
3.4185
2.0779
2.0459
2.0405
2.0388
2.0369
2.0325
2.0270
2.0247
2.0190
1H NMR
500 MHz, CDCl3
NC CN
Me
N
N
S23
0.94
1.01
1.10
4.22
2.96
3.75
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


20200907_vnmrs_500_RM-XVII-71b_25-33-CARBON_01
157.6138
145.5180
134.0687
115.8056
115.3092
106.9649
77.4000 CDCl3
46.9719
34.0066
28.7451
25.6223
13C{1H} NMR
126 MHz, CDCl3
NC CN
Me
N
N
S23
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



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

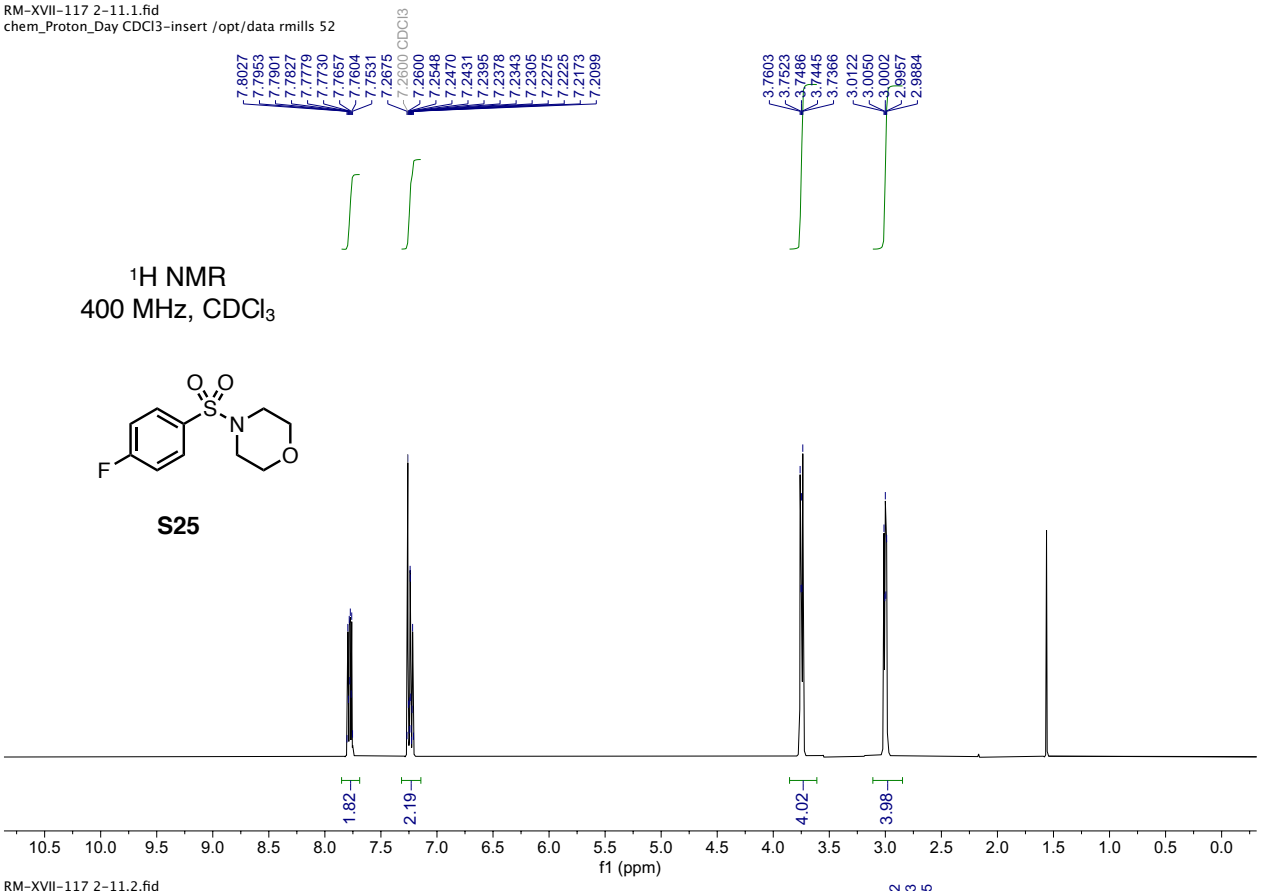
S24



^{13}C{^{1}H} NMR
101 MHz, $CDCl_3$

S24

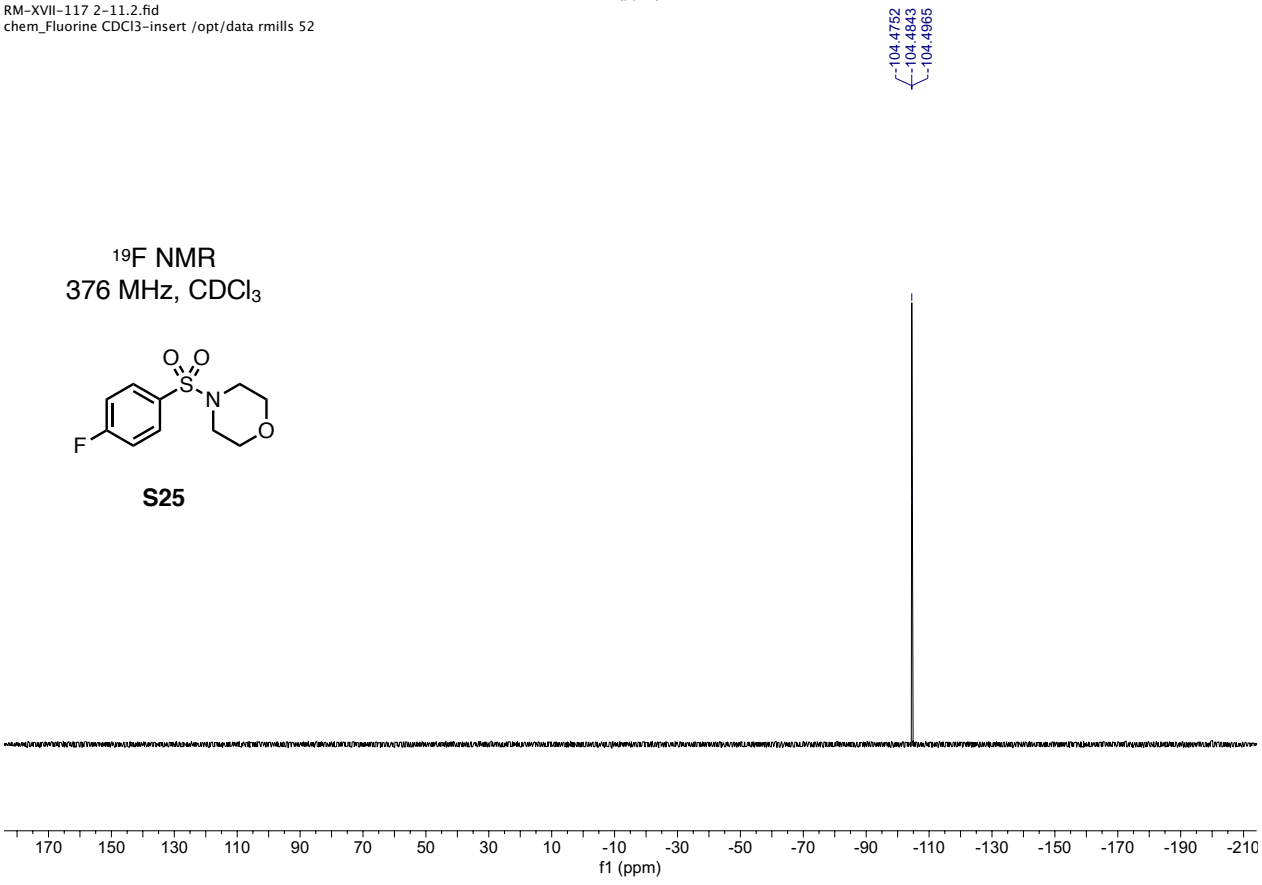
RM-XVII-117 2-11.1.fid
chem_Proton_Day CDCl3-insert /opt/data rmills 52



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

S25

RM-XVII-117 2-11.2.fid
chem_Fluorine CDCl3-insert /opt/data rmills 52



^{19}F NMR
376 MHz, $CDCl_3$

S25

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